AN ABSTRACT OF THE DISSERTATION OF

Subrata Shaw for the degree of Doctor of Philosophy in Chemistry presented on January 15, 2014.

Title: *Cis*-2,5-diaminobicyclo[2.2.2]octane: A Novel C_2-Symmetric Scaffold for Asymmetric Catalysis

Abstract approved: _____

James D. White

This thesis describes the development of a new enantioselective synthetic method employing chiral c*is*-2,5-diaminobicyclo[2.2.2]octane-based organometallic catalysts. The significance of this new method to organic synthesis is illustrated with preparation of enantioenriched products that are transformed to important pharmaceutical agents.

Chapter 1 provides a brief historical overview of asymmetric catalysis, especially the development of salen-ligands and salen-metal complexes. Focus is placed on salen frameworks derived from chiral 1,2-diamines and their application in asymmetric synthesis.

Chapter 2 introduces the concept of increasing nitrogen-nitrogen separation in a salen framework and the associated enlargement of chiral space. This leads to our proposition that the 1,4-diamine motif present in a c*is*-2,5-diaminobicyclo[2.2.2]octane scaffold would provide a superior chiral framework for the salen ligand in asymmetric

induction via a metal-salen catalyst. This chapter describes the synthesis and characterization of the new salen ligand and its complexes with various transition and p-block metals.

Chapter 3 describes the enantioselective hetero-Diels-Alder (HDA) reaction of Danishefsky diene with a large number of aldehydes catalyzed by our new chromium(III)-salen complex. The reaction provides 5,6-dihydro-4-pyranones in high yield and with enantiomeric excess up to 96%. These results compare favorably with those obtained with other chiral catalyst systems. The HDA adducts are rich in functionality and stand ready for conversion into useful chiral building blocks.

Chapter 4 further illustrates an application of our chromium(III)-salen complex in catalysis of the enantioselective Nozaki-Hiyama-Kishi (NHK) reaction of allyl halides with aromatic aldehydes. The reaction affords homoallylic alcohols in high yield and enantiomeric excess. Extension of this reaction to vinylic halides using the same catalyst is probed but further studies are needed to find optimal conditions for the synthesis of enantioenriched allylic alcohols by this method.

In chaper 5, a tetrahydrosalen derivative generated by reduction of our salen ligand in combination with copper(I) triflate was found to be an efficient catalyst for the enantioselective Henry reaction of aldehydes with nitromethane, affording β-nitro alcohols in high enantiomeric excess. The enantioenriched Henry adducts were transformed to important organic materials including beta-adrenergic receptor blocking agents. The catalyst system when used with nitropropane was shown to give a *syn*-nitro alcohol in high diastereomeric and enantiomeric excess.

Chapter 6 describes an iron(III) complex derived from our salen ligand and shows that it is an efficient catalyst for enantioselective sulfa-Michael addition (SMA) of thiols to acyclic α,β-unsaturated ketones. β-Thiaketones are produced by this method in high enantiomeric excess. This protocol was used to synthesize (*R*)-Montelukast, an anti asthma agent, from commercially available starting materials in four steps. With α-substituted acyclic enones as SMA substrates, the method was shown to give *syn* product in high diastereomeric and enantiomeric excess.

Chapter 7 shows that a novel iron(III)-salen catalyst bearing our bicyclo[2.2.2]octane scaffold leads to enantioselective intramolecular Conia-ene cyclization of a β-keto ester bearing an unactivated terminal alkyne. The product, a chiral polyfunctionalized cyclopentane derivative, constitutes a useful platform for further structural elaboration.

In chapter 8, it was demonstrated that a cobalt(II)-salen catalyst induces a high degree of diastereo- and enantioselectivity in the cyclopropanation of a 1,1'-disubstituted alkene with ethyl diazoacetate as co-reactant. A formal synthesis of the dual serotonin and norepinephrine reuptake inhibitor Synosutine was accomplished using this protocol.

Cis-2,5-diaminobicyclo[2.2.2]octane: A Novel C_2-Symmetric Scaffold for Asymmetric Catalysis

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APPROVED:

Major Professor, representing Chemistry

Chair of the Department of Chemistry

Dean of the Graduate School

I understand that my dissertation will become part of the permanent collection of Oregon State University libraries. My signature below authorizes release of my dissertation to any reader upon request.

Subrata Shaw, Author

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TABLE OF CONTENTS

TABLE OF CONTENTS (Continued)

Page

TABLE OF CONTENTS (Continued)

Page

TABLE OF CONTENTS (Continued)

LIST OF FIGURES

Figure Page

LIST OF FIGURES (Continued)

LIST OF FIGURES (Continued)

Figure Page

LIST OF FIGURES (Continued)

Figure Page

LIST OF TABLES

LIST OF TABLES (Continued)

LIST OF TABLES (Continued)

DEDICATION

This dissertation is dedicated to my parents (Baba and Maa) and Dilip for everything they have done for me. I am what I am today because of your love, support and encouragement.

CHAPTER 1

Introduction

The chemical substances that make up living organisms are predominantly chiral and often exist as single enantiomers. For example, mammalian proteins are composed exclusively of L-amino acids and carbohydrates are constituted of D-sugars. Mammals are unable to metabolize the L-enantiomer of sugars which has made those sugars prospects for reduced-calorie substitutes.[1] For the same reason, L-glucose has laxative effects that make it potentially useful as a colon-cleansing agent.[2] During the early years of pharmaceutical development, the importance of this selective biological phenomenon was not appreciated, and due to the lack of methods for generating pure stereocenters pharmaceuticals were produced and tested only in racemic form. However, racemic drug formulations contain a 50-50 mixture of two enantiomeric compounds that often act very differently within the body, the tragic consequences of thalidomide (**1**, Figure 1.1) being the most infamous example. Racemic thalidomide was prescribed to pregnant mothers between 1957 and 1961 as an antiemetic for morning sickness and caused well over 10,000 cases of birth defects.[3] It was later discovered that only the (*S*)-enantiomer of the drug is teratogenic. Since that time, numerous racemic drug formulations have been marketed worldwide. Due to rigorous safety testing required by FDA, drugs with toxic enantiomers like thalidomide no longer reach the consumer. On the other hand, many racemic formulations have been marketed in which one enantiomer is inactive, in essence doubling the minimum effective dose. History has shown that all

pharmaceuticals have some degree of undesirable side effects, a risk that could be significantly reduced by removal of the unwanted enantiomer to provide a generally safer drug. For this reason, many drugs which were earlier sold as racemic mixtures were later marketed in enantiopure form (Figure 1.1). Representative examples include Xopenex (**2**), Laxapro (**3**), Nexium (**4**) and Lunesta (**5**). Although only the (*S*)-enantiomer of Ibuprofen (**6**) is responsible for its anti-inflammatory activity, it is sold as a racemate because α-methylacyl-CoA racemase, an enzyme present in vivo, converts the (*R*)-enantiomer of **6** to the active (*S*)-enantiomer.[4]

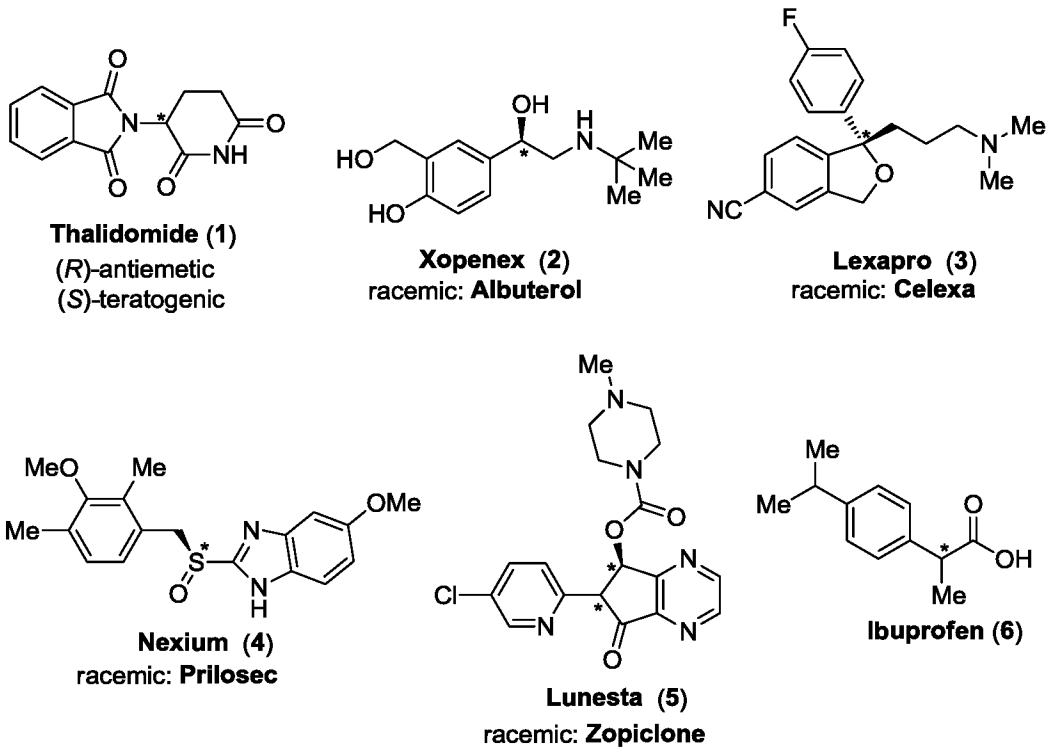


Figure 1.1 Pharmaceuticals marketed initially as racemic mixtures but later marketed in enantiopure form.

Enantiomerically pure compounds can be obtained by derivatization of substances from the *chiral pool* of naturally occurring compounds.[5] This approach has the limitation that only one enantiomer is accessible in many cases. Alternatively, pure enantiomers can be obtained through the separation of a racemic mixture[6] by crystallization, chromatography, or kinetic resolution. Although this strategy is frequently used in industry, it leads to a maximum yield of 50% if the undesired enantiomer can not be racemized and recycled. Enantioenriched compounds are also available by enantioselective synthesis. This method uses chiral reaction media,[7,8] chiral auxiliaries[9] or chiral catalysts,[10] although only the latter two strategies have been developed to the level of useful and widely applicable synthetic tools.

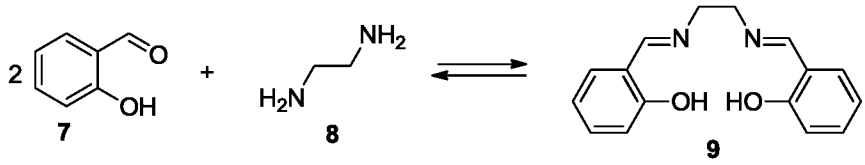
Of the methods for generating enantiomerically pure stereocenters from achiral starting materials, *asymmetric catalysis* can be an extremely efficient approach. The chiral target is produced by this technique in large quantity employing small amounts of a non-racemic chemical mediator. Additionally, catalysts are often reusable, resulting in a significant reduction in the amount of waste produced during the process compared to a stoichiometric reaction. This is especially important in industrial process chemistry. In order for an asymmetric catalyst to successfully induce chirality in the desired product, the reaction rate of the uncatalyzed process must be significantly slower than the catalyzed reaction. To achieve this, a catalyst must activate one or more of the chemical reagents, attaining essentially new reactivity. Over the years, a plethora of asymmetric catalytic reactions have been discovered, yet most employ only a few chemical activation modes. These comprise mainly metal-insertion, atom transfer, and Lewis acid

catalysis.[10,11] The importance of the discovery of these activation modes on the field of chemical synthesis was recognized by the 2001 Nobel Prize in Chemistry awarded to William S. Knowles, Ryoji Noyori, and K. Barry Sharpless for their "work on chirally catalyzed hydrogenation reactions" and "chirally catalyzed oxidation reactions."[12]

Transition metal complexes have played an especially prominent role among the numerous classes of enantioselective catalysts. These organometallic catalysts induce chirality via their enantiopure ligands and are typically highly efficient, so that only extremely small quantities of the catalyst are required for the synthesis of large amounts of enantioenriched material. Transition metal catalysts are able to catalyze a wide variety of chemical transformations and their reactivities and selectivities can be effectively tailored using variations in the ligand. Consequently, ligand development goes hand-in-hand with catalyst development and represents a particularly challenging area in catalysis research. Despite more than three decades of ligand development for asymmetric synthesis, the rational design of chiral ligands is still in its infancy and it is not yet possible to predict a ligand structure which can provide high enantioselectivity for a specific transformation. For this reason, ligand design follows an empirical approach and generally focuses on a search for *lead structures* and their subsequent variations.

Schiff bases and their metal complexes play an important role among chiral catalysts employed to generate stereogenic centers in organic molecules.[13] In 1864, Hugo Schiff discovered that azomethines, now known as Schiff bases, were formed from the reversible reaction of an active carbonyl compound with a primary amine.[14] In this

reaction, a carbinolamine intermediate is produced initially that is dehydrated to give a stable imine.[15] The term "salen" was first used to describe the bis-Schiff base *N*,*N*'-bis(salicylidene)ethylenediamine (**9**) derived from the condensation of salicylaldehyde (**7**) with 1,2-ethylenediamine (**8**, Scheme 1.1).



Scheme 1.1 Synthesis of *N*,*N*'-bis(salicylidene)ethylenediamine ("salen")

More generally, all bis-imines formed from condensation of diamines with salicylaldehydes and possessing a structure analogous to **9** are now commonly named "salen". Salen-type ligands are particularly attractive for catalysis because their structure can be easily modified. For example, different groups R^1, R^2 and R^3 have been introduced into the salen skeleton to produce a variety of active ligands (**10**, Figure 1.2).

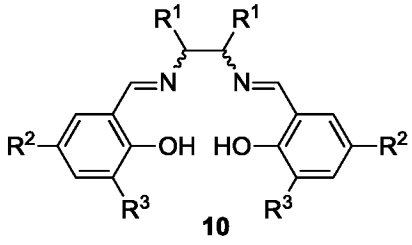
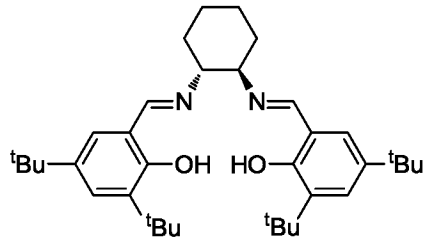


Figure 1.2 General structure of salen-type ligands

Salens are good ligands for metal catalysis due primarily to the lone pair of electrons on the nitrogen atoms. Other functional groups in the molecule such as

hydroxyl[16] and sulfide[17] can also contribute a pair of electrons to the metal. These ligand structures possess binding pockets that can coordinate many metal ions in various oxidation states. Salen ligands are especially adept at complexation with transition metals. Most salen-metal complexes are easily synthesized, are characterized by high stability compared to other organometallic complexes and are efficient promoters of many reactions by virtue of their high turnover rate.[18]

Salen ligands bind metal ions securely through four atoms, and for asymmetric catalysis their structures are manipulated to create an asymmetric environment around the metal site.[19,20] Asymmetric metal complexes of salen ligands have been studied for over six decades, but their application to industrially important asymmetric reactions only began in 1991 when Jacobsen *et al.* developed chiral *trans*-1,2-diaminocyclohexane (Figure 1.3) as the core scaffold.[21] The manganese-salen complex derived from **11** was found to be an excellent catalyst for asymmetric epoxidation of unfunctionalized olefins.



11

Figure 1.3 Jacobsen's salen ligand

During the 1990s, a large number of transition metal complexes of ligand **11** were explored for catalysis of asymmetric transformations.[18] Subsequent effort was invested in varying the steric and electronic properties of the ligand scaffold resulting in generally good levels of asymmetric induction (Figure 1.4). For example, North *et. al.* developed salen ligands **12-16** derived from salicyldehyde for the enantioselective alkylation of imino esters **19**. Copper(II) complexes of these ligands produced alkylated ester **20** containing a quaternary center in acceptable yield although with marginal enantioselectivity (Scheme 1.2).[22]

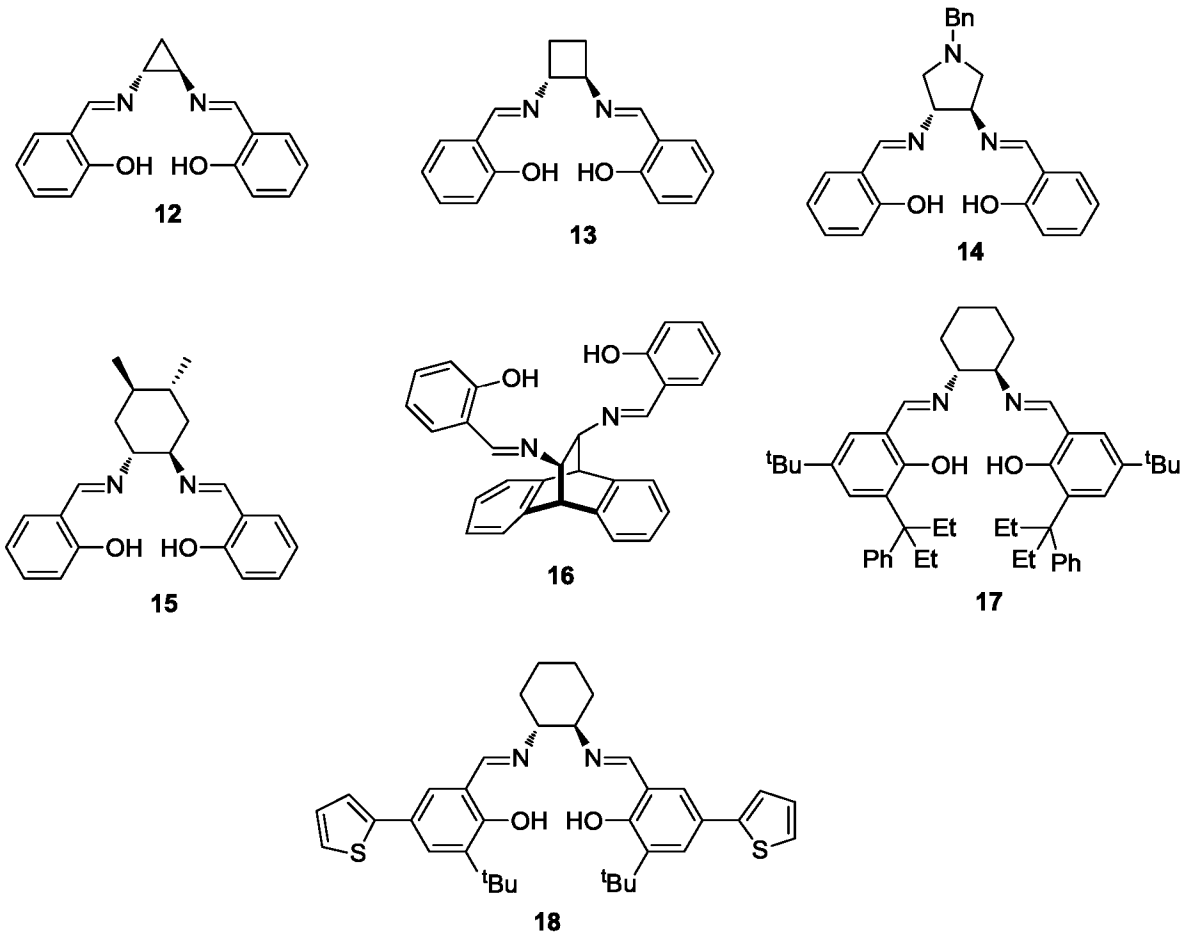
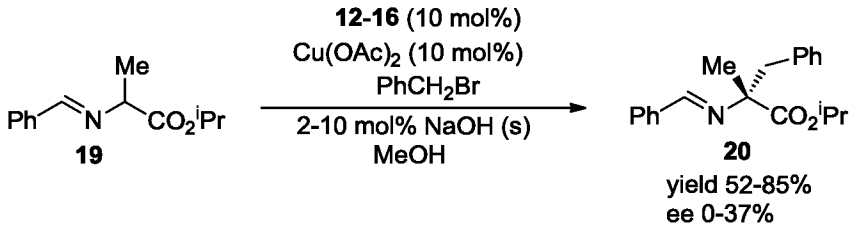
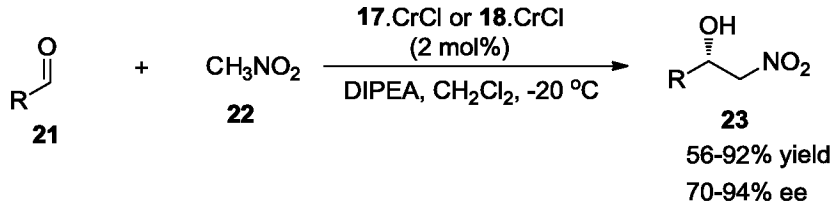


Figure 1.4 Salen ligands used in asymmetric catalysis



Scheme 1.2 Enantioselective benzylation of imino ester **19** catalyzed by $Cu(OAc)_2$-salen ligands

More recently, Jurczak[23] and Schulz[24] introduced alkyl and aryl groups into C_3 and C_5 positions of the salicyldehyde framework. Salen ligands **17** and **18** enabled a high degree of asymmetric induction in β-nitro alcohol products **23** from enantioselective Henry reactions of aldehydes **21** with nitromethane (**22**, Scheme 1.3).



Scheme 1.3 Enantioselective Henry reaction of aldehydes with nitromethane catalyzed by Cr(III)-salen complexes derived from **17** and **18**

Salen ligands used in asymmetric catalysis are almost entirely based on commercially available chiral 1,2-diamines and salicylic aldehyde components. Little attention has been paid to modification of the diamine backbone, for example, by attenuating the separation of the two nitrogen atoms. Berkessel's ligand **27** derived from

cis-2,5-diaminobicyclo[2.2.1]heptane ("DIANANE," **26**, Figure 1.5) is the sole example of this modification. [25,26] Ligand **27** containing a chiral 1,4-diamine possesses a N-N separation of 3.59 Å compared to the Jacobsen ligand **25** (2.91Å) according to X-ray crystallography.[26,27] In comparative studies of the enantioselectivity obtained in the Nozaki-Hiyama-Kishi and hetero-Diels-Alder reactions of benzaldehyde catalyzed by chromium(III) complexes derived from **25** and **27**, the latter was found to give superior asymmetric induction (Scheme 1.4). [25,28] This was attributed by Berkessel to the increased N-N separation in **27**.

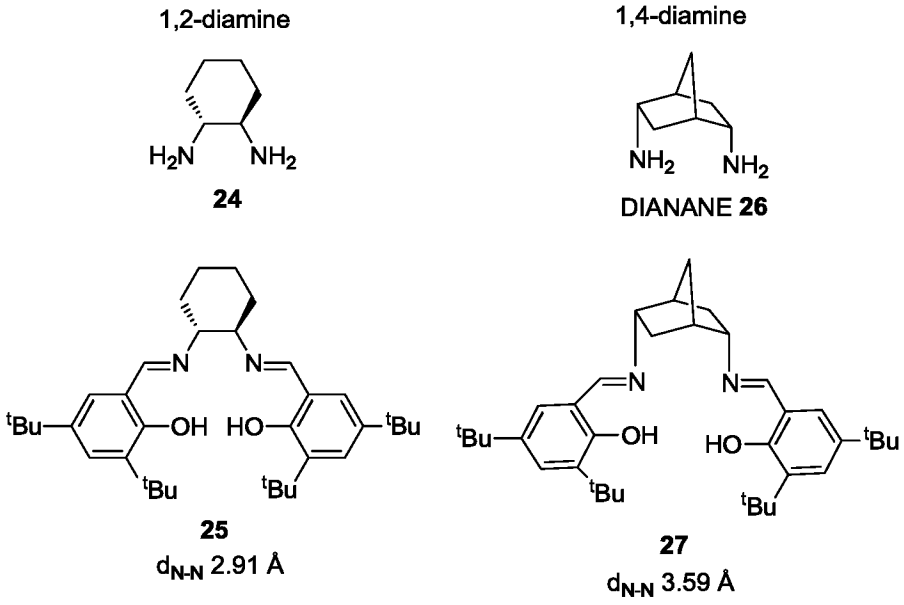
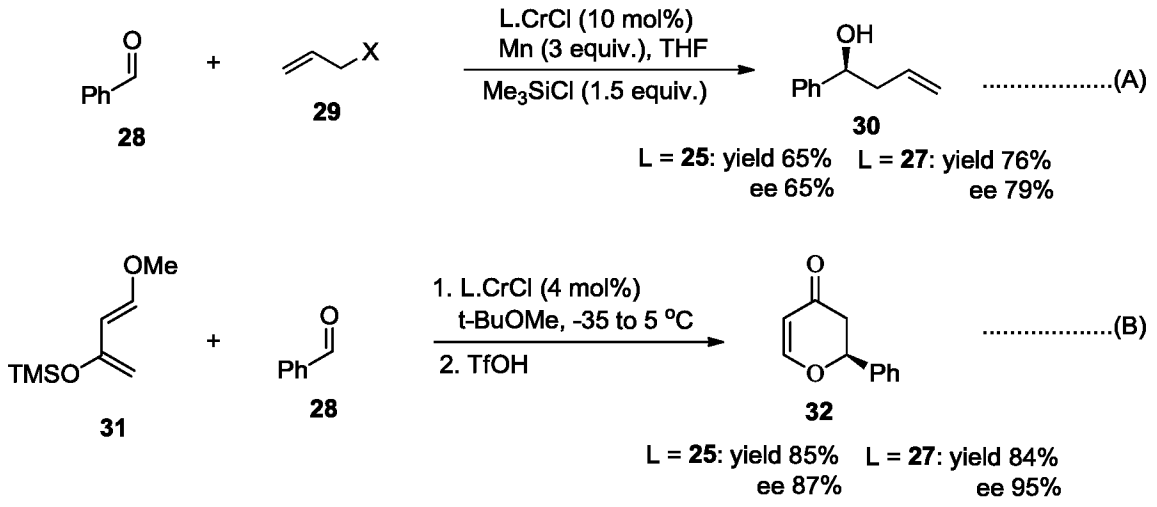


Figure 1.5 C_2-symmetric diamines *trans*-1,2-diaminocyclohexane (**24**), *endo, endo*-2,5-diaminonorbornane (DIANANE, **26**), and their salen derivatives **25** and **27**



Scheme 1.4 Comparative studies of enantioselective Nozaki-Hiyama-Kishi (A) and hetero-Diels-Alder (B) reactions of benzaldehyde catalyzed by the chromium(III)-complex derived from salen ligands **25** and **27**.

The synthesis of enantiopure diamine **26**, the parent scaffold of salen ligand **27**, required tedious HPLC separation of enantiomers and only milligram quantities of **27** were prepared by Bekessel. Probably for this reason, only the chromium(III) complex of **27** was studied as an asymmetric catalyst and no subsequent research on this promising ligand was published. This left open the door to another C_2-symmetric 1,4-diamine, one based on *cis*-2,5-diaminobicyclo[2.2.2]octane, that in principle could be easier to obtain in enantiopure form than **26**. This scaffold would have an even larger N-N separation than that in **26** yet its salen derivative should still be capable of binding metal cations. Confirmation of this hypothesis is described in the chapter that follows.

References

1. Livesey, G.; Brown, J. C. *J. Nutr.* **1995**, *125*, 3020.
2. Raymer, G. S.; Hartman, D. E.; Rowe, W. A.; Werkman, R. F.; Koch, K. L. *Gastrointest. Endosc.* **2003**, *58*, 30.
3. Bren, L. Frances Oldham Kelsey: FDA Medical Reviewer Leaves Her Mark on History. *FDA Consumer–U.S. Food and Drug Admin.* **2001**, *35*, *No. 2*.
4. Chen, C. S.; Shieh, W. R.; Lu, P. H.; Harriman, S.; Che, C. Y. *Biochimica et Biophysica Acta*, **1991**, *1078*, 411.
5. Blaser, H. U. *Chem. Rev.* **1992**, *92*, 935.
6. (a) De Vries, J. G. *Encyclopedia of Catalysis*, Vol 3. (Ed.: I. T. Horváth), Wiley, New York, **2003**, p. 295. (b) Liu, W. Resolutions at large scale: case studies. *Handbook of Chiral Chemicals (2nd Edition)* **2006**, 75.
7. Reichardt, C. Solvents and Solvent Effects in Organic Chemistry, Wiley-VCH, Weinheim, **2003**.
8. (a) Pégot, B.; Vo-Thanh, G.; Loupy, A. *Tetrahedron Lett.* **2004**, *45*, 6425. (b) Gausepohl, R.; Buskens, P.; Kleinen, J.; Bruckmann, A.; Lehmann, C. W.; Klankermayer, J.; Leitner, W. *Angew.Chem. Int. Ed.* **2006**, *45,* 3689. (c) Schulz, P.S.; Müller, N.; Bösmann, A.; Wasserscheid, P. *Angew. Chem. Int. Ed.* **2007**, *46,* 1293. (d) Branco, L. C.; Gois, P. M. P.; Lourenço, N. M. T.; Kurteva, V. B.; Afonso, C. A. M. *Chem. Commun.* **2006**, 2371. (e) Schmitkamp; M.; Chen, D.; Leitner,W.; Klankermayer, J.; Franciò, G. *Chem. Commun.* **2007**, 4012.

9. (a) Roos, G. H. *Compendium of Chiral Auxiliary Applications*, Academic Press, San Diego, **2001**. (b) Gnas, Y.; Glorius, F. *Synthesis* **2006**,1899.

10. Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H. *Comprehensive Asymmetric Catalysis*, Springer-Verlag, Berlin Heidelberg, **1999**.

11. (a) *Asymmetric Catalysis in Organic Synthesis*; Noyori, R., Ed.; Wiley: New York, **1994**. (b) *Catalytic Asymmetric Synthesis*, 2nd ed.; Ojima, I., Ed.; Wiley-VCH: New York, **2000**.

12. (a) Knowles, W. S. *Angew. Chem. Int. Ed.* **2002**, *41*, 1998. (b) Noyori, R. *Angew. Chem. Int. Ed.* **2002**, *41*, 2008. (c) Sharpless, K. B. *Angew. Chem. Int. Ed.* **2002**, *41*, 2024.

13. Larrow, J. F.; Jacobsen, E. N. *Topics Organomet. Chem.* **2004**, *6*, 123.

14. (a) Schiff, H. *Justus Liebigs Ann. Chem.* **1864**, *131*, 118. (b) Schiff, H. *Ann. Chem. Suppl.* **1864**, *3*, 343. (c) Schiff, H. *Ann. Chem.* **1869**, *150*, 193. (d) Schiff, H. *Ann. Chem.* **1869**, *151*, 186.

15. Fatibello-Filho, O.; Dockal, E. R.; Marcolino-Junior, L.H.; Teixeira M. F. S. *Analyt. Lett.* **2007**, *40*, 1825.

16. (a) Pfeiffer, P.; Breith, E.; Lübbe, E.; Tsumaki, T. *Justus Liebigs Ann. Chem.* **1933**, *503*, 84. (b) Diehl, H.; Hach, C. C. *Inorg. Synth.* **1950**, *3*, 196.

17. Ershad, S.; Sagathforoush, L. A.; Karim-nezhad, G.; Kangari, S.; *Int. J. Electrochem. Sci.* **2009**, *4*, 846.

18. Cozzi, P. G. *Chem. Soc. Rev.*, **2004**, *33*, 410.

19. Jacobsen, E.N., *Acc. Chem. Res. 2000*, *33*, 421.

20. (a) Larrow, J .F., J acobsen, E.N., Gao, Y., Hong, Y., Nie, X., Zepp, C.M., *J. Org. Chem.* **1994**, *59*, 1939. (b) Larrow, J.F., Jacobsen, E.N., *Org. Syn.***1997**, *75*, 1.

21. Jacobsen, E.N., Zhang, W., Muci, A.R., Ecker, J .R., Deng, L., *J. Am. Chem. Soc.* **1991**, *120*, 7063.

22. Belokon, Y. N.; Fuentes, J.; North, M.; Steed, J. W. *Tetrahedron*, **2004**, *60*, 3191.

23. Kowalczyk, R.; Kwiatkowski, P.; Skarzewski, J.; Jurczak, J. *J. Org. Chem.* **2009**, *74*, 753.

24. Zulauf, A.; Mellah, M.; Schulz, E. *J. Org. Chem.* **2009**, *74*, 2242.

25. Berkessel, A.; Menche, D.; Sklorz, C. A.; Schroder, M.; Paterson, I. *Angew. Chem. Int. Ed.* **2003**, *42*, 1032.

26. Berkessel, A.; Schroder, M.; Sklorz, C. A.; Tabanella, S.; Vogl,N.; Lex, J.; Neudorfl, J. M. *J. Org. Chem.* **2004**, *69*, 3050.

27. (a) Yoon, J. W.; Yoon, T.-S.; Shin, W. *Acta Crystallogr. Sect. C: Cryst. Struct. Commun.* **1997**, *53*, 1685. (b) Darensbourg, D. J.; Yarbrough, J. C. *J. Am. Chem. Soc.* **2002**, *124*, 6335.

28. Berkessel, A.; Vogl, N. *Eur. J. Org. Chem.* **2006**, 5029.

CHAPTER 2

Synthesis of the Diamine and Its Salen-Metal Complexes

2.1 *Cis*-2,5-diaminobicyclo[2.2.2]octane: hypothesis and rationale

In our quest for a chiral template that would have broad utility as a catalyst in asymmetric synthesis, we chose *cis*-2,5-diaminobicyclo[2.2.2]octane (**34**) as a scaffold. Our hypothesis was that *cis*-2,5-diaminobicyclo[2.2.2]octane (**34**) would have a larger separation between nitrogen atoms than in DIANANE (**26**), and to support our assumption a computational study was undertaken on **26** and **34** by professor Peter Freeman at Oregon State University. Using B3LYP Density Functional Theory with a 6-31G(d) basis set, the optimized structures generated are shown in Figure 2.1. The N-N separations in **26** and **34** were found to be 4.00 Å and 4.27 Å, respectively. This implies that the larger separation of nitrogen atoms in diamine **34** compared to **26** would give the salen ligand **35**, derived from diamine **34**, a broader "wingspan" that would enclose a larger volume of chiral space than the salen derivative of **26** while preserving a rigid chiral environment (Figure 2.2).

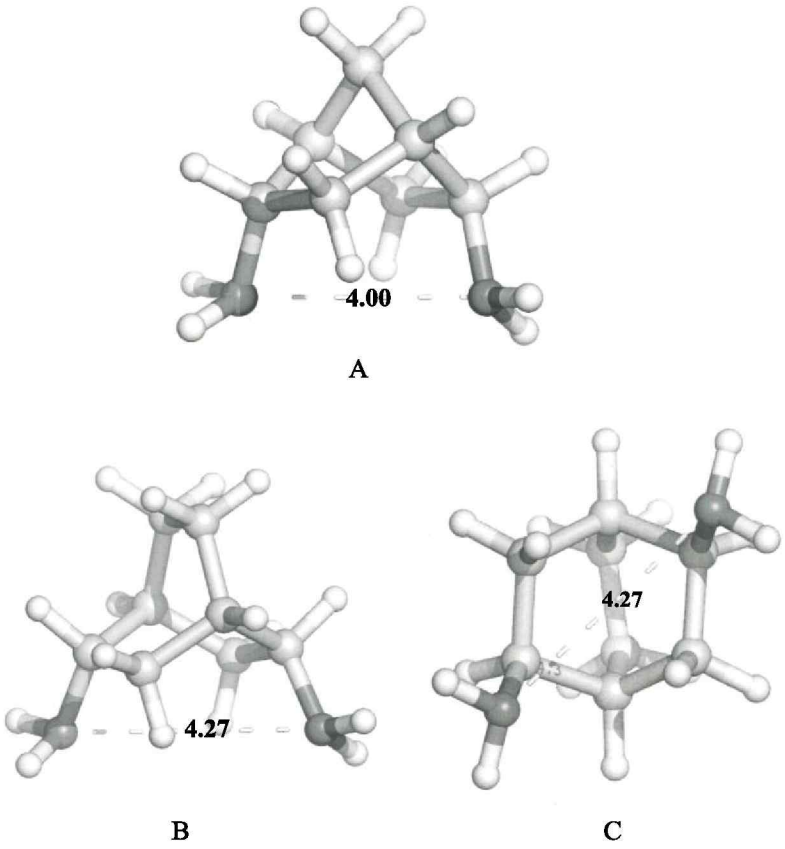


Figure 2.1 Calculated structures for DIANANE (**26**; A (side view)) and c*is*-2,5-diaminobicyclo[2.2.2]octane (**34**; B (side view) and C (bottom view)) using B3LYP/6-31G(d)

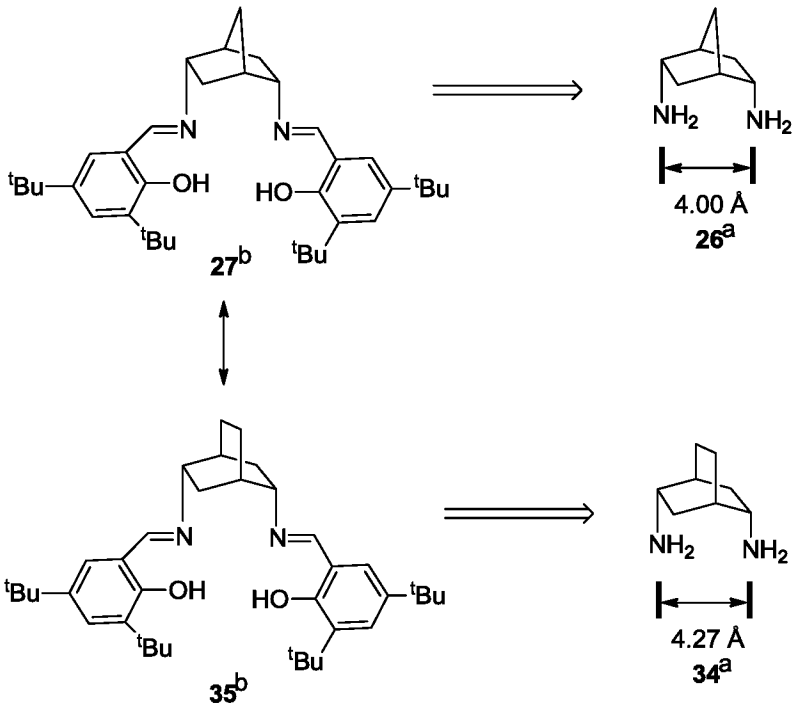


Figure 2.2 a) N-N separations in the C_2-symmetric diamines DIANANE (**26**) and *cis*-2,5-diaminobicyclo[2.2.2]octane (**34**). b) Salen ligands **27** and **35** derived from the diamines **26** and **34**.

The three dimensional structure or conformation of organic molecules can be described in terms of rotation about *dihedral (torsional) angles*. A dihedral angle is defined by four consecutively bonded atoms. Given four contiguous atoms, A_{i-2}, A_{i-1}, A_i, and A_{i+1}, the dihedral angle is defined as the smallest angle between the planes π_1 and π_2, as shown in figure 2.3. Increase of the dihedral angle is a consequence of rotation of the two outer bonds about the central bond.

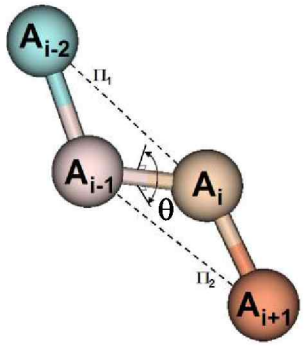


Figure 2.3 Graphical illustration of a dihedral angle

From our computational study, it was found that c*is*-2,5-diaminobicyclo[2.2.2]octane (**34**) possesses a dihedral angle of 22° between the C_a-H_a and the C_b-H_b bonds. This is the angle between planes consisting of $\Delta C_aC_bH_a$ and $\Delta C_aC_bH_b$ as shown in Figure 2.4. In c*is*-2,5-diaminobicyclo[2.2.1]heptane (**26**) the corresponding dihedral angle is 14°. The larger dihedral angle in diamine **34** gives the structure a larger degree of "twist" around its C_2 axis compared to **26**. This feature could augment the chiral properties of **34** and together with its larger N-N separation improve its efficacy for asymmetric induction.

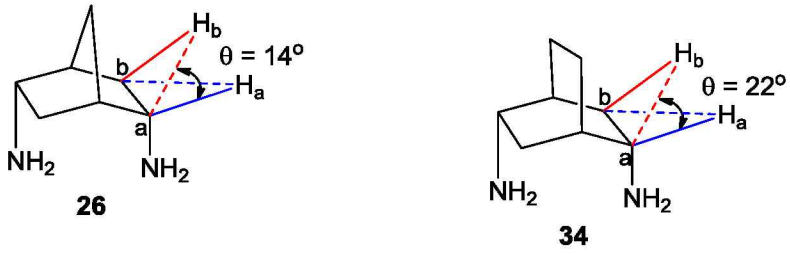


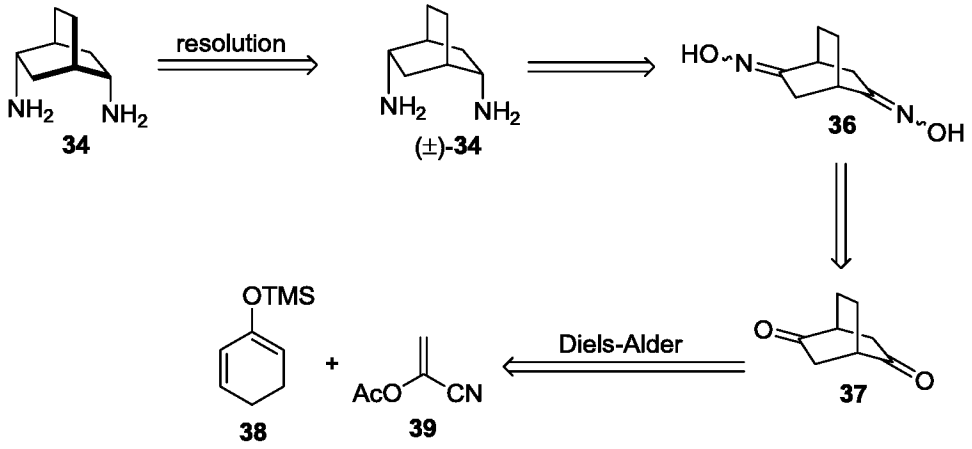
Figure 2.4 Calculated dihedral angles between the C_a-H_a and the C_b-H_b bonds of DIANANE (**26**) and c*is*-2,5-diaminobicyclo[2.2.2]octane (**34**) using B3LYP/6-31G(d)

Based on this proposition, it was decided to undertake synthesis of diamine **34** in enantiopure form.

2.2 Synthesis of c*is*-2,5-diaminobicyclo[2.2.2]octane (34)

2.2.1 First generation approach towards diamine 34

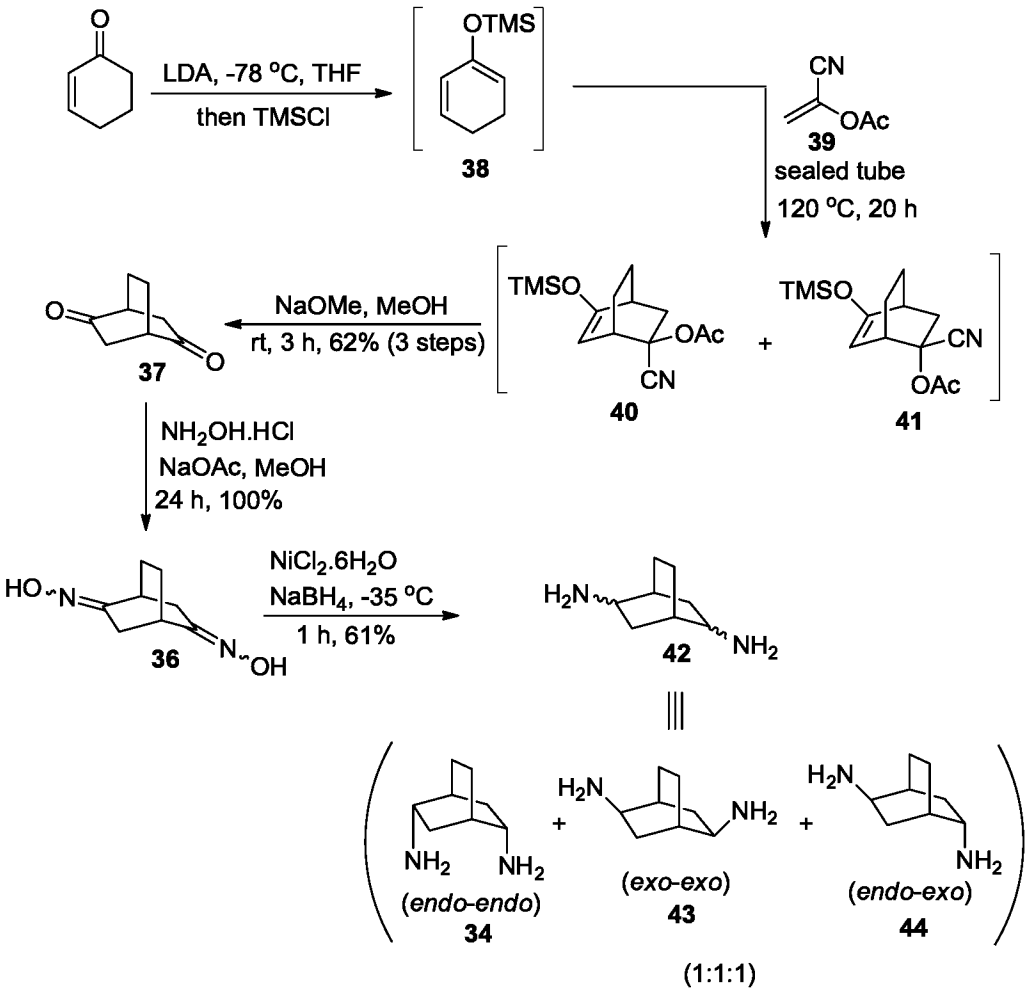
Our initial approach envisioned an enantiomer of diamine **34** originating from its racemate through resolution following Jacobsen's protocol.[1] Racemic bis-*endo* diamine ((±)-**34**) would be derived from stereoselective reduction of bis-oxime **36** which can be acquired from known diketone **37**.[2] This bicyclic diketone is available via Diels-Alder addition of silyl enol ether **38** with 1-cyanovinyl acetate (**39**, Scheme 2.1).[3]



Scheme 2.1 Retrosynthetic analysis of enantiopure diamine **34**

In the forward direction, 2-cyclohexenone was deprotonated under kinetic conditions using lithium diisopropylamide and the enolate thus formed was trapped with trimethylsilyl chloride to yield 2-trimethylsiloxy-1,3-cyclohexadiene (**38**).[4] Heating diene **38** with neat 1-cyanovinyl acetate (**39**) in a sealed tube followed by base catalyzed hydrolysis of the mixture of *exo* and *endo* products, **40** and **41**, furnished

bicyclo[2.2.2]octane-2,4-dione (**37**).[3] Condensation of this diketone with hydroxylamine yielded the corresponding dioxime **36**.[2] In order to convert dioxime **36** to diamine (±)-**34**, an *endo*-selective reduction is required. Berkessel and coworkers[5] reported an analogous transformation of bicyclo[2.2.1]heptane-2,4-dione dioxime using sodium borohydride in the presence of a catalytic amount of nickel dichloride.[6] However, this method when applied to **36** produced a diastereomeric mixture of diamines **42** containing en*do-endo, exo-exo* and *endo-exo* diamines **34**, **43** and **44** in almost 1:1:1 ratio (Scheme 2.2).



Scheme 2.2 Synthesis of *cis* and *trans* 1,4-diamines **34, 43** and **44**

We attempted to separate bis-*endo* diamine (±)-**34** from its *exo-exo* and *exo-endo* isomers via salt formation with enantiopure carboxylic acids. If successful, this protocol would also accomplish resolution via separation of diastereomers and would lead to enantiopure **34**. However, all attempts at fractional crystallization of salts formed from **42** with D-tartaric acid (**45**), L-tartaric acid (**46**), (*S*)-mandelic acid (**47**) and D-quinic acid (**48**) were unsuccessful (Figure 2.5).

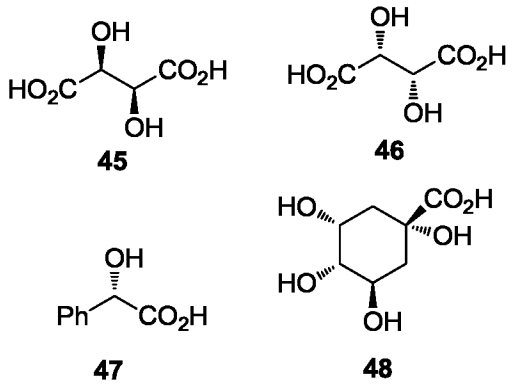
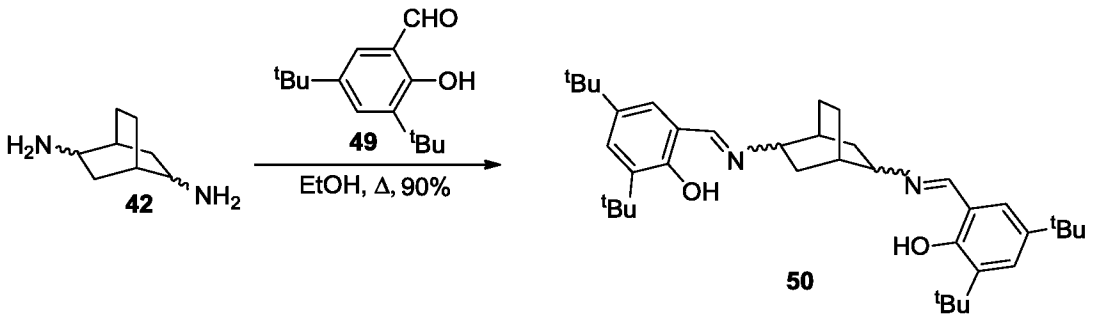


Figure 2.5 Enantiopure acids used for attempted separation of bis-endo diamine **34** from its diastereomers via salt formation

Treatment of the mixture consisting of diastereomeric diamines **42** with 3,5-di-*tert*-butylsalicylic aldehyde (**49**) yielded a mixture of diastereomeric salen-ligands **50** (Scheme 2.4).



Scheme 2.4 Synthesis of a mixture of diastereomeric salen ligands **50**

These diastereomers were observed to have variations in crystallinity under the microscope. Slow evaporation of solvent from a solution of **48** in methylene dichloride and methanol yielded crystals with distinct shapes and, inspired by the pioneering work of Louis Pasteur,[7] a set of crystals with a needle-like shape was manually separated.

A crystal obtained in this way was amenable to X-ray crystallographic analysis (Figure 2.5) and from the crystal structure it was apparent that the compound we had isolated was fortuitously the bis-*endo* salen-ligand **35**. The C=N bond distances in compound **35** at 1.273 (3) and 1.272 (3) Å are consistent with C=N imine bond lengths and are in agreement with the infrared spectrum of **35** where ν(CN) appears at 1627 cm^{-1}. An intramolecular six-membered hydrogen-bond was present between the hydroxyl hydrogen and the nitrogen of the imine function of **35** which was also evidenced by the presence of a broad infrared absorption band around 3400 cm^{-1}.

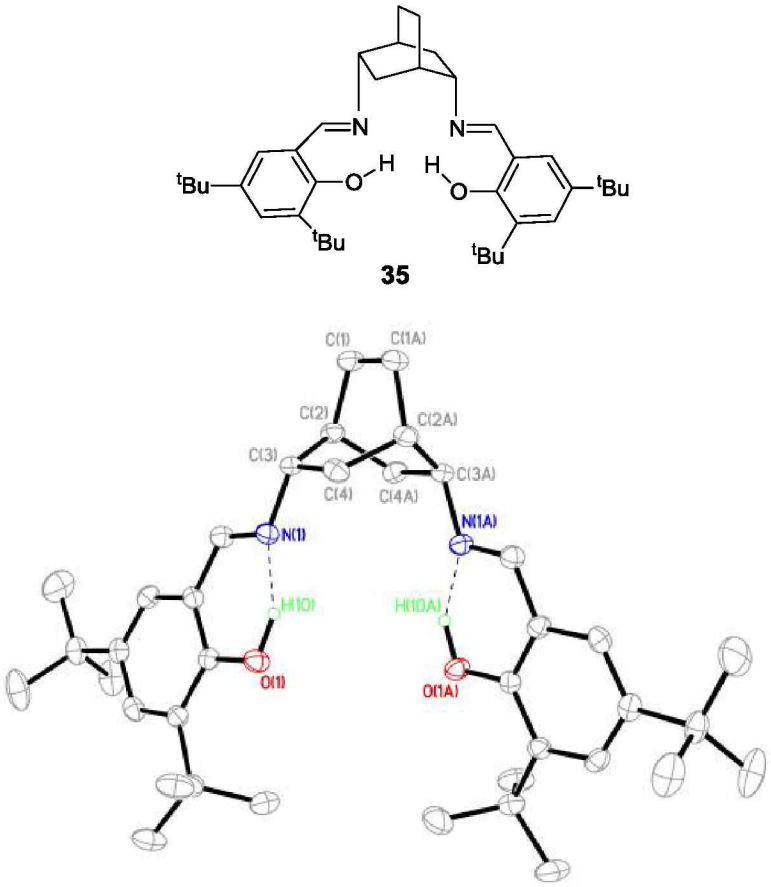
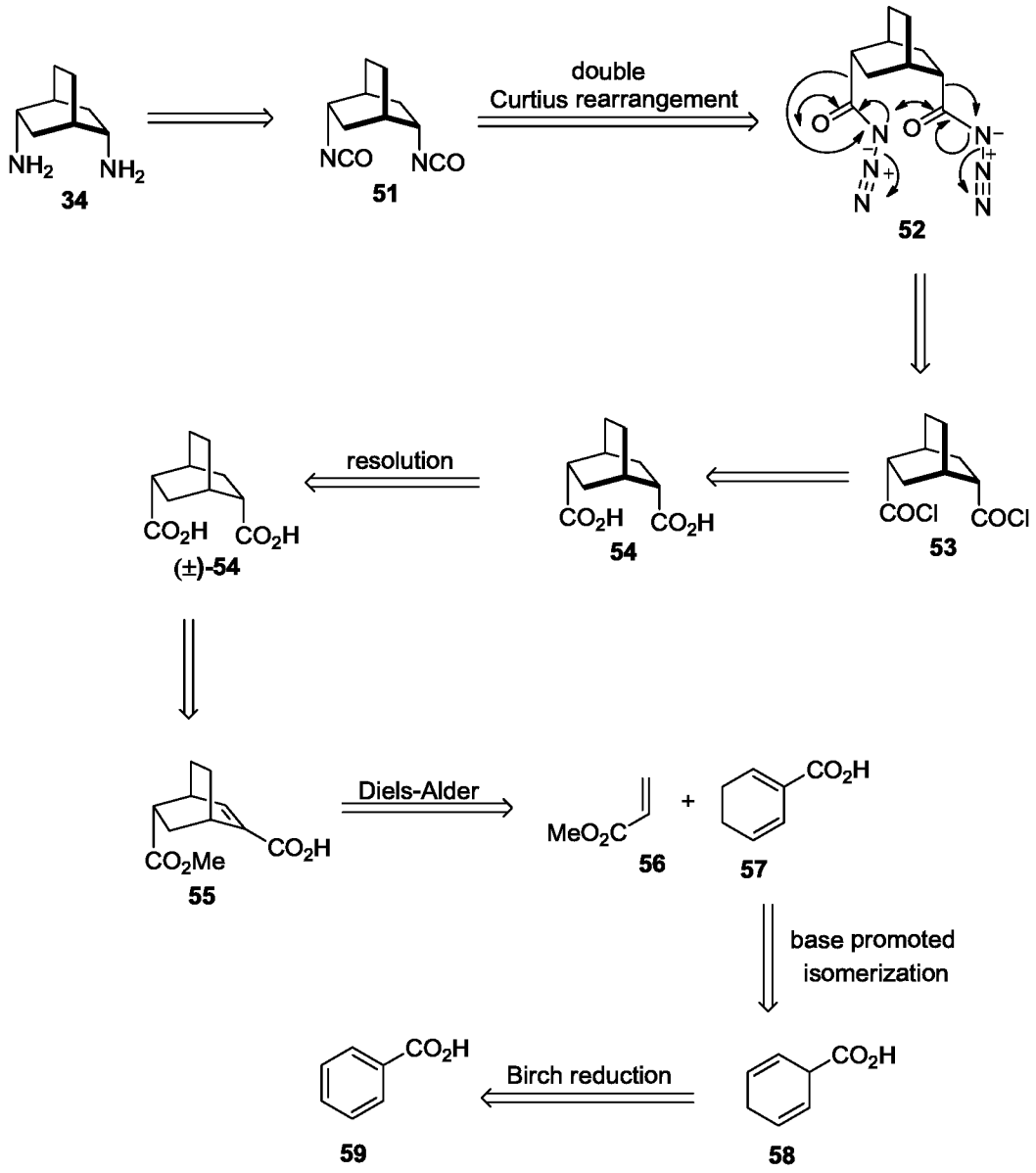


Figure 2.6 Molecular and X-ray crystal structure of racemic salen ligand **35**. Dotted lines denote hydrogen bonds.

Although we had succeeded in obtaining the racemic version of our target ligand (±)-**35** by this method, we were forced to concede the fact that this was not a practical solution in terms of scale up. A viable route to *endo-endo* diamine **34** therefore required a revised strategy.

2.2.2 Second generation approach towards diamine 34

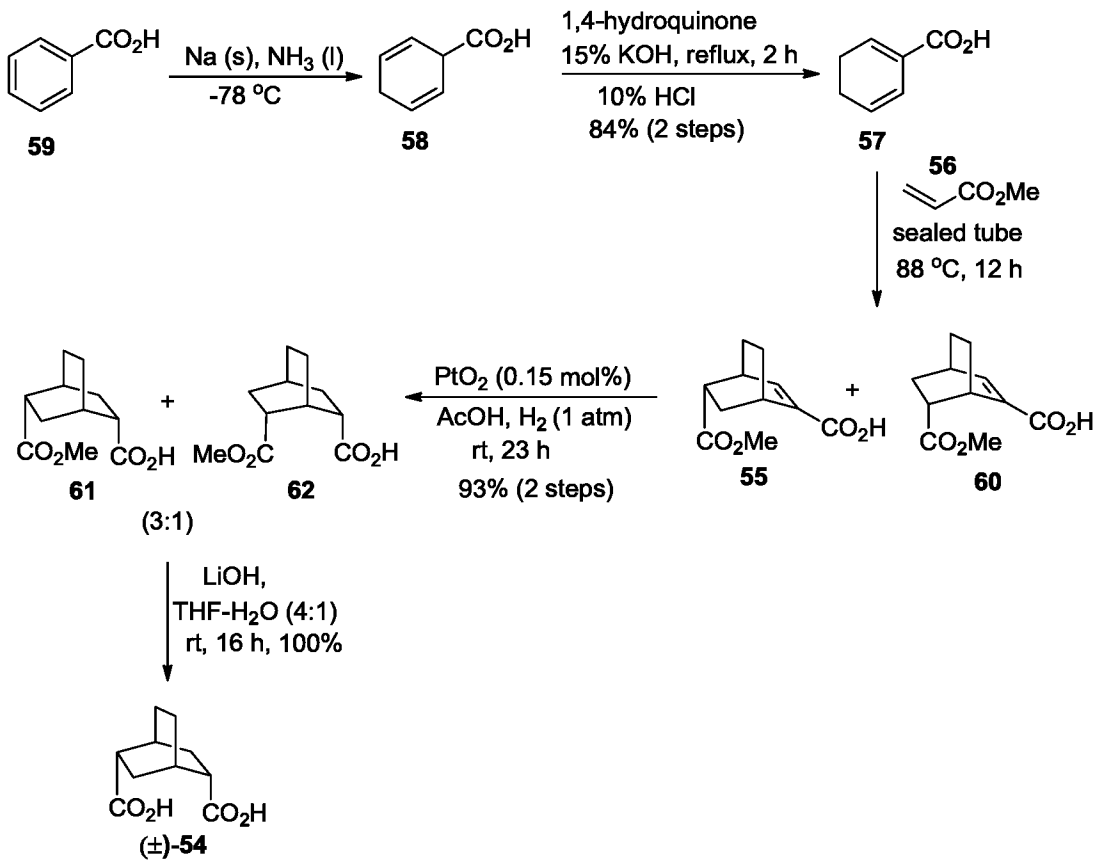
A new synthetic plan for **34** was devised in which the route would rely on resolution of racemic dicarboxylic acid (±)-**54** for obtaining the enantiopure diamine. We envisioned that diamine **34** would be obtained from bis-isocyanate **51**, generated from double Curtius rearrangement of diacyl azide **52**. The diacyl azide would be derived from the corresponding diacyl chloride **53** which in turn could be acquired from known dicarboxylic acid **54**.[8] The bicyclic framework of **54** originates from Diels-Alder cycloaddition of diene **57** and methyl acrylate (**56**)[9] followed by *endo*-selective hydrogenation of the Diels-Alder adduct **55**, and 1,3-diene **57** is prepared from benzoic acid (**59**) via Birch reduction followed by base promoted isomerization of 1,4-diene **58** (Scheme 3.5).[10]



Scheme 2.5 Second generation retrosynthetic plan for diamine **34**

In the forward direction, benzoic acid (**59**) was reduced under Birch conditions to obtain 1,4-cyclohexadiene-3-carboxylic acid (**58**) which was isomerized by potassium hydroxide to produce 1,3-cyclohexadiene-2-carboxylic acid (**57**).[10] 1,4-Hydroquinone was used to counter the aerial oxidation of **57** to benzoic acid (**59**). Conjugated diene **57**

was reacted with methyl acrylate (**56**)[9] under solvent free conditions to give regioisomeric *endo* half esters **55** and **60**. Stereoselective hydrogenation of this mixture was effected using Adams' catalyst[9] and furnished a mixture of *endo* esters **61** and **62** in 3:1 ratio. Chromatographic separation of the half ester **61** followed by saponification gave racemic dicarboxylic acid (±)-**54** (Scheme 2.6).

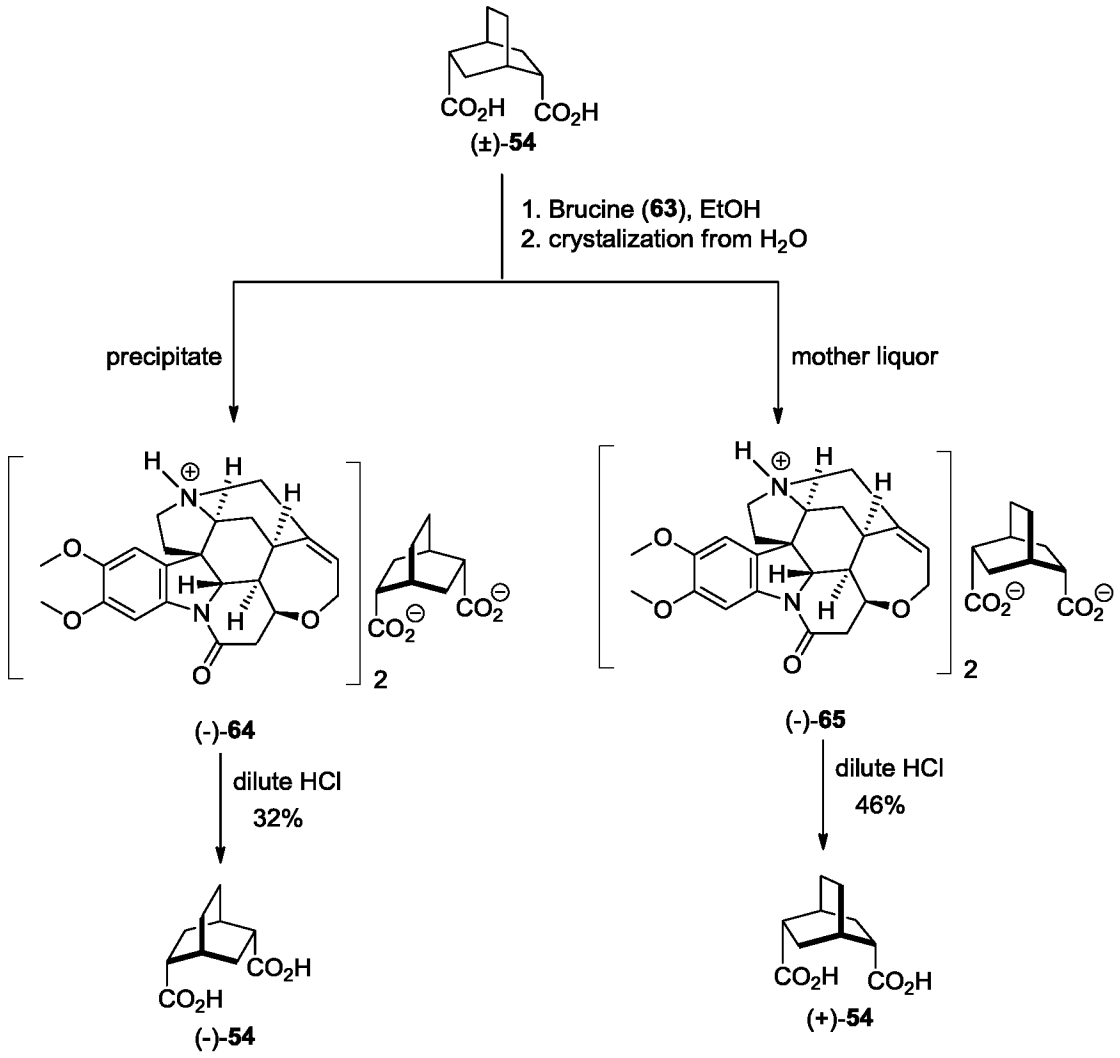


Scheme 2.6 Synthesis of racemic bicyclo[2.2.2]octane-2,5-dicarboxylic acid ((±)-**52**).

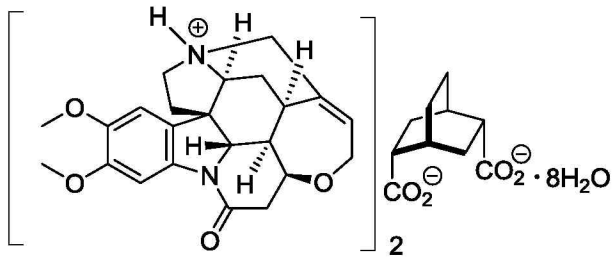
Resolution of racemic carboxylic acids can be effected with enantiopure basic amines, among which natural alkaloids such as (-)-brucine (**63**)[11] are frequently used as resolving agent. Diastereomeric salts formed between brucine and a racemic acid are

often separable by crystallization with the enantioenriched acid being recovered from the salt simply by acidification. Racemic dicarboxylic acid (±)-**54** was therefore treated with (-)-brucine (**63**) and the brucine salts were fractionally crystallized from water.[8] Pure crystalline salt (-)-**64** was obtained from this procedure and was amenable to X-ray analysis (Figure 2.6). The crystal structure of (-)-**64** revealed the absolute stereochemistry of the bicyclic framework as (1*R*,2*R*,4*R*,5*R*). Acidic hydrolysis of (-)-**64** afforded dicarboxylic acid (-)-**54** as a white amorphous solid. The optical rotation of the dicarboxylic acid (-)-**54** compared well with that of the enantiopure (-)-**54** reported in the literature.[8]

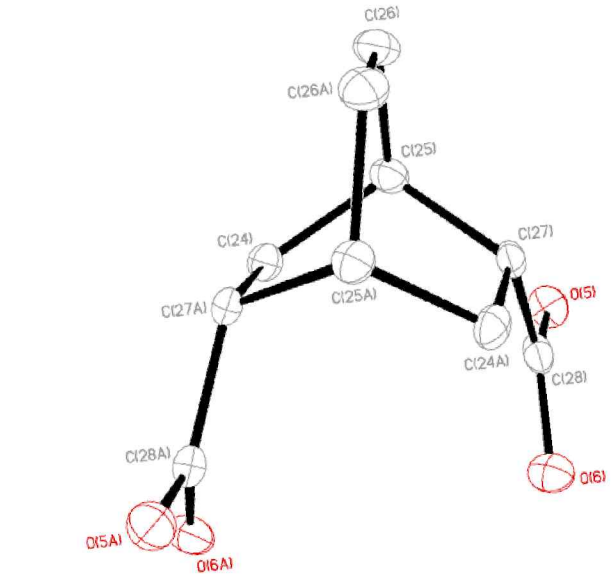
A second more soluble brucine salt (-)-**65** was obtained by evaporating the mother liquor of the fractional crystallization to dryness. Acidification of this brucine salt produced (1*S*,2*S*,4*S*,5*S*)-bicyclo[2.2.2]octane-2,5-dicarboxylic acid ((+)-**54**, Scheme 2.7).



Scheme 2.7 Resolution of racemic bicyclo[2.2.2]octane-2,5-dicarboxylic acid ((±)-**54**) via diastereomeric brucine salts



(-)-**64**



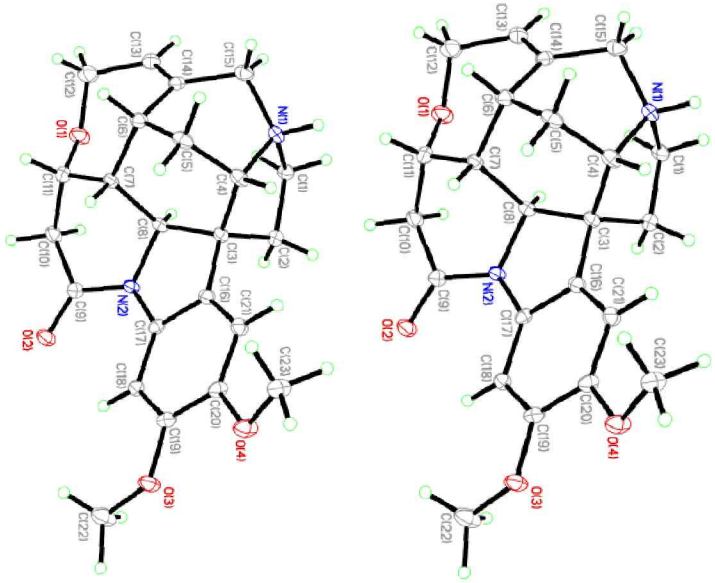
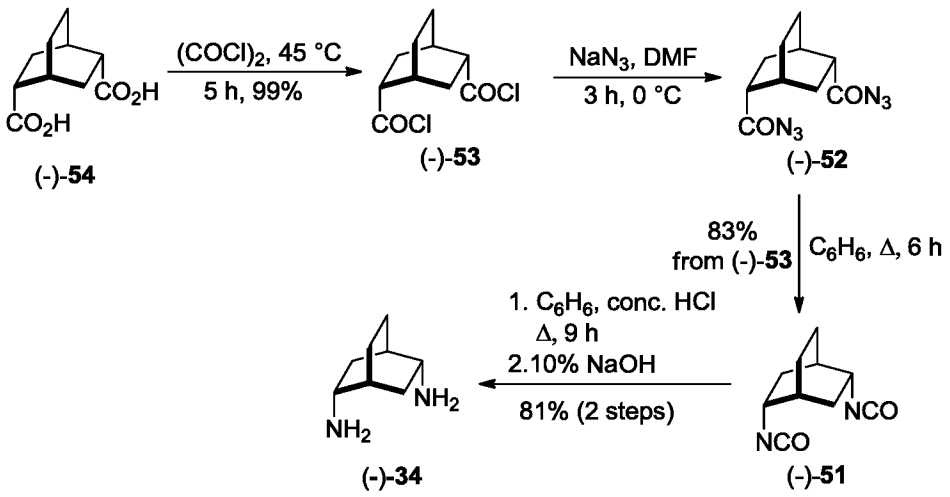


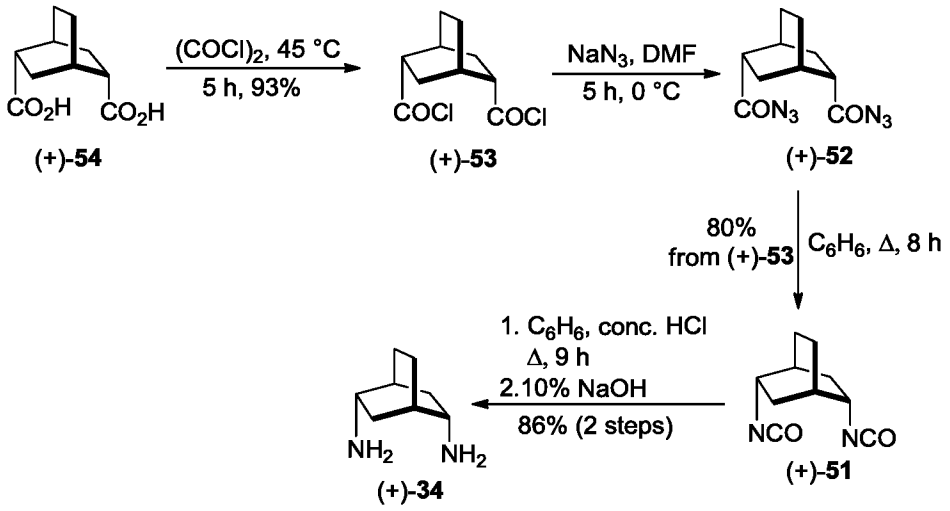
Figure 2.7 Molecular and X-ray crystal structure of brucine salt (-)-**64**

Dicarboxylic acid (-)-**54** was converted to the corresponding diacyl chloride **(-)-53** by heating with neat oxalyl chloride and **(-)-53** was advanced to diacyl azide (-)-**52** by reaction with sodium azide at low tempertature.[12] Upon heating in benzene, (-)-**52** underwent intramolecular double Curtius rearrangement to give bis isocyanate (-)-**51**.[12] Hydrolysis of (-)-**51** in hydrochloric acid and *in situ* decarboxylation of the inrermediate biscarbamic acid furnished diamine (-)-**34**[12] in an overall yield of 67% from (-)-**54** (Scheme 2.8).



Scheme 2.8 Synthesis of (1*R*, 2*R*, 4*R*, 5*R*)-2,5-diaminobicyclo[2.2.2]octane ((-)-**34**)

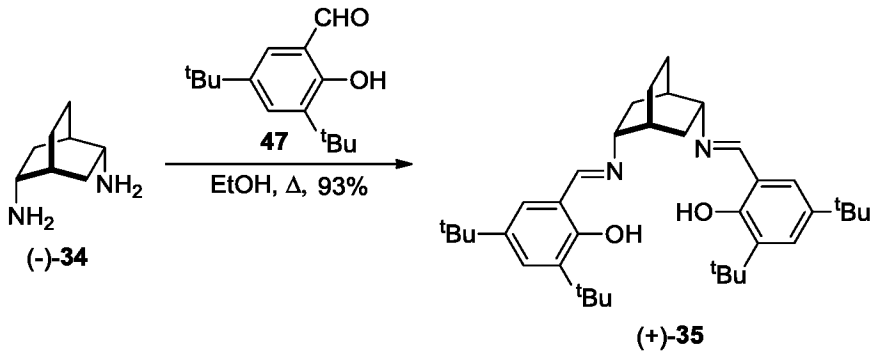
In a parallel sequence of reactions, dicarboxylic acid (+)-**54** was transformed to diamine (+)-**34** via intermediates (+)-**53**, (+)-**52**, and (+)-**51** (Scheme 2.9).[12]



Scheme 2.9 Synthesis of (1*S*, 2*S*, 4*S*, 5*S*)-2,5-diaminobicyclo[2.2.2]octane ((+)-**34**)

2.3 Synthesis of salen ligand (+)-35 and metal complexes

Condensation of diamine (-)-**34** with 3,5-di-*tert*-butylsalicylic aldehyde (**47**) in hot ethanol furnished the salen ligand (+)-**35** in good yield (Scheme 2.10).



Scheme 2.10 Synthesis of salen ligand (+)-**35** from diamine (-)-**34**

Crystallization of (+)-**35** from a methylene chloride-methanol solvent mixture yielded crystals amenable to X-ray crystallography (Figure 2.7). The crystal structure was

similar to that of its racemate ((±)-**35**, Figure 2.5) and the structural parameters were comparable.

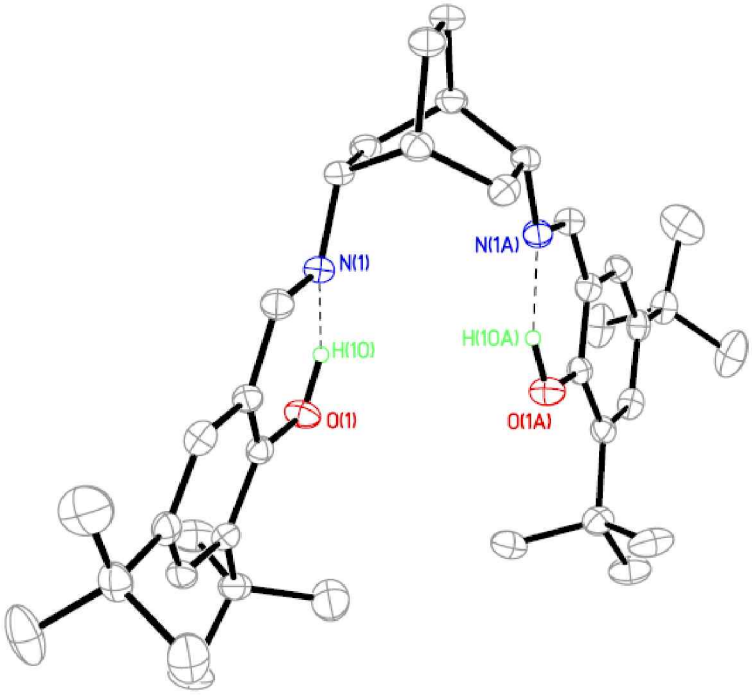
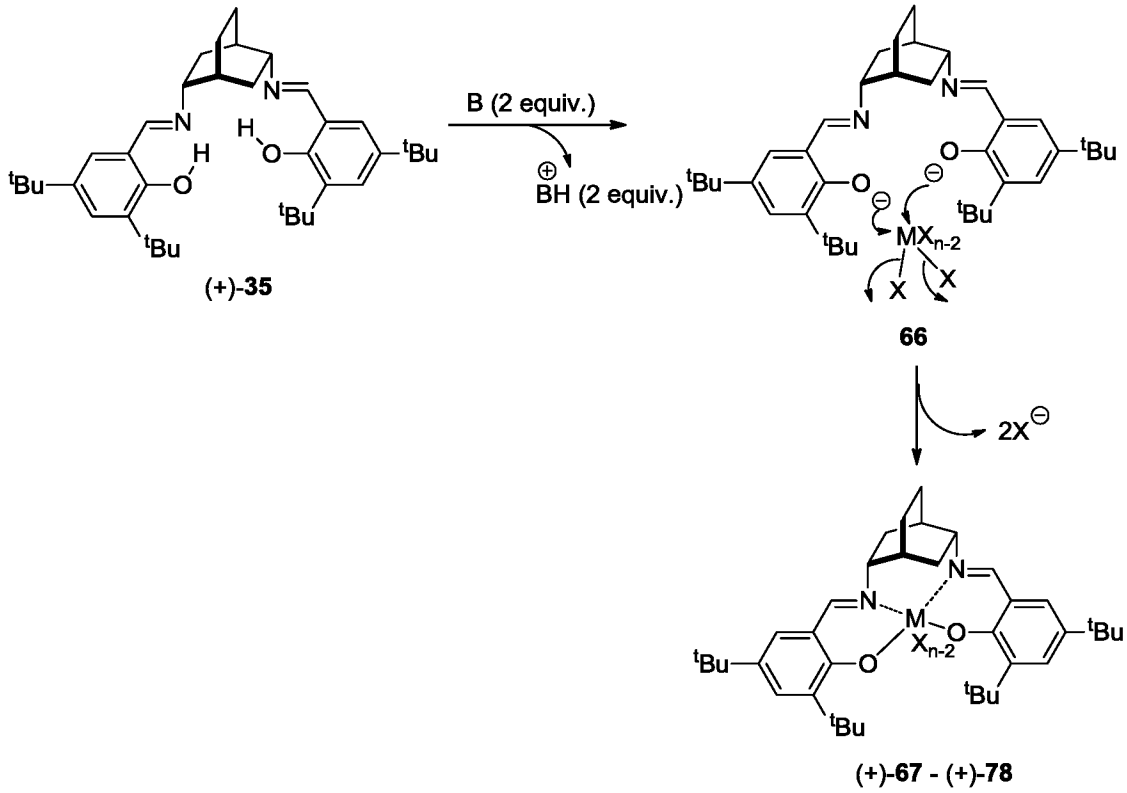


Figure 2.8 Crystal Structure of enantiopure salen ligand (+)-**35**

Salen derivative (+)-**35** with two nitrogen and two oxygen donor atoms suitably positioned below the bicyclooctane scaffold can potentially act as a tetradentate ligand for metal ions where ion size is commensurate with the chiral pocket in this ligand. With this as an hypothesis, (+)-**35** was reacted with metal salts whose cations were considered likely to form stable metal complexes with the salen ligand. It was necessary to make the salen ligand a stronger nucleophile for metal complexation in many cases and for this deprotonation of the phenolic hydroxyl group was employed. This was effected using a

stoichiometric amount of base (triethylamine or sodium hydride) in a non-protic solvent such as methylene chloride or tetrahydrofuran. The resulting phenoxide ion acts as a nucleophile to attack the metal salt, forming the salen-metal complex via a displacement mechanism (Scheme 2.11).



Scheme 2.11 Synthesis of salen-metal complexes

It was found that with acetate and acetylacetonate as the metal counterion (Table 2.1, entries 3, 5, 7, 9-11) the use of a base could be avoided by refluxing the reaction components in a protic solvent such as methanol. Metal-salen complexes (+)-**67-78** were synthesized with ligand (+)-**35** and all of the metals in the first transition metal series as well as with palladium(II) in the second transition metal series and with aluminum(III)

(p-block). Attempts to prepare metal complexes of (+)-**35** with zinc acetate and rhodium acetate were unsuccessful. The salen-metal complexes obtained with (+)-**35** were stable high-melting solids of varying color and crystallinity. Reaction conditions used to synthesize the twelve metal complexes from (+)-**35** are shown in Table 2.1.

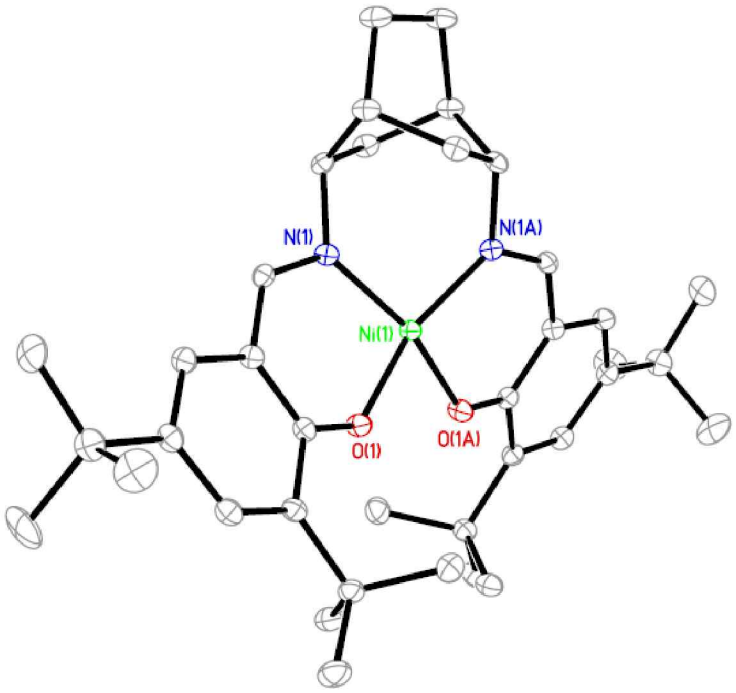
Table 2.1 Salen-metal complexes derived from (+)-**35** with metal salts.

Entry	Reagent	Solvent	Temperature	Product	Color
1	$TiCl(O^iPr)_3$, Et_3N	CH_2Cl_2	ambient	(+)-**67**, M = Ti(Cl)(O^iPr)	yellow
2	$VOCl_3$, Et_3N	CH_2Cl_2	ambient	(+)-**68**, M = V(O)(Cl)	green
3	$VO(acac)_2$	MeOH	reflux	(+)-**69**, M = V(O)(acac)	green
4	$CrCl_2$, Et_3N, O_2[a]	THF	ambient	(+)-**70**, M = Cr(Cl)	brown
5	$Mn(OAc)_2.4H_2O$ O_2, NaCl[a,b]	MeOH	reflux	(+)-**71**, M = Mn(Cl)	brown
6	$FeCl_3$, NaH	THF	reflux	(+)-**72**, M = Fe(Cl)	brown
7	$Fe(acac)_3$	MeOH	reflux	(+)-**73**, M = Fe(acac)	violet
8	$CoBr_2$, NaH	THF	reflux	(+)-**74**, M = Co	orange
9	$Ni(OAc)_2.4H_2O$	THF	reflux	(+)-**75**, M = Ni	red-orange
10	$Cu(OAc)_2.H_2O$	MeOH	reflux	(+)-**76**, M = Cu	black
11	$Pd(OAc)_2$	MeOH	reflux	(+)-**77**, M = Pd	red
12	$AlCl_3$, NaH	THF	reflux	(+)-**78**, M = Al(Cl)	pale yellow

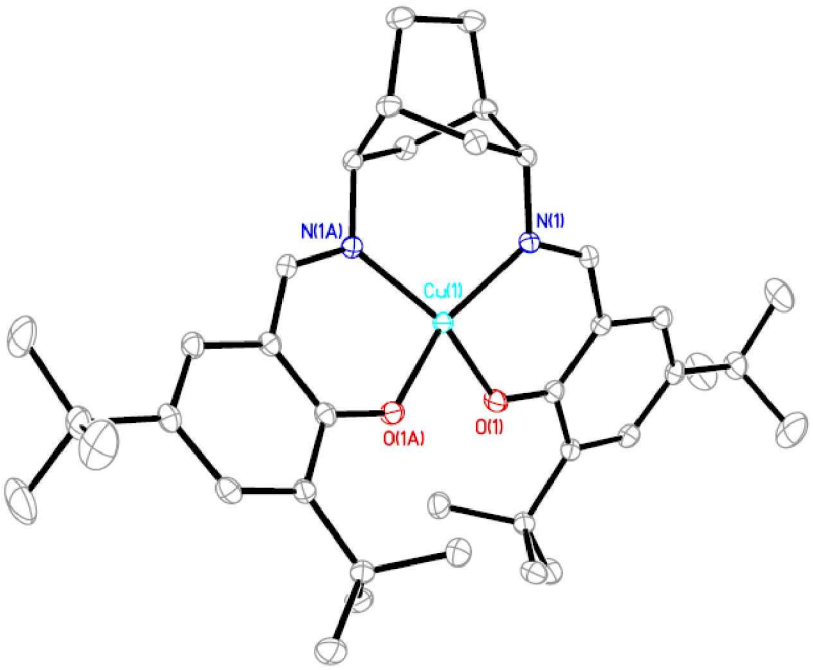
[a]The flask was opened to air after the initial reaction. [b]The reaction mixture was washed with brine during work up.

For the chromium and manganese complexes (+)-**70** and (+)-**71**, respectively (entries 4 and 5), the divalent metal salts were used and the initially formed product was oxidized to the corresponding trivalent metal complex. Of these twelve metal salen complexes, three (**75**, **76**, **77**) formed X-ray quality crystals upon crystallization from hot

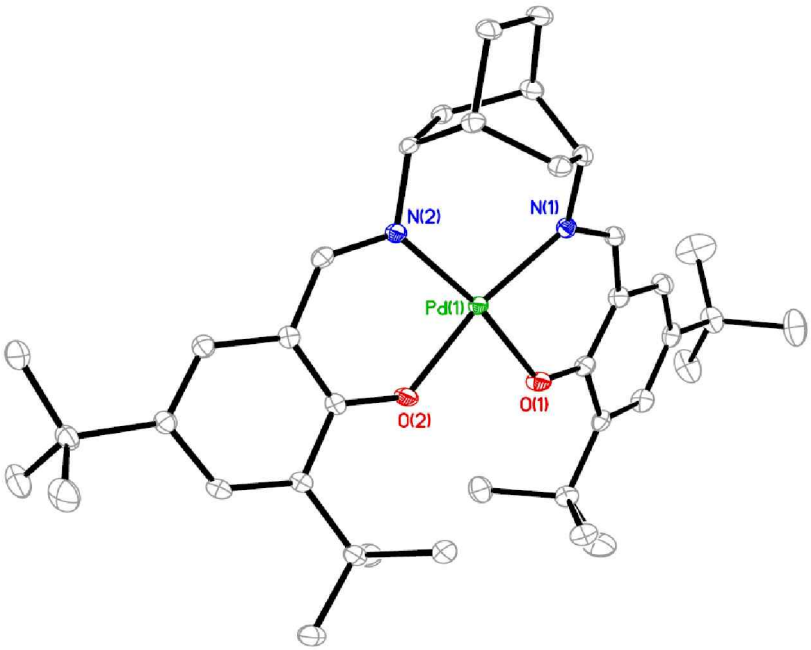
acetone. The crystal structures of the three metal-salen complexes are shown in Figure 2.8.



(+)-75



(+)-76



(+)-77

Figure 2.9 Crystal Structures of nickel(II), copper(II) and palladium(II) complexes of salen ligand (+)-**35**

The crystal structures of **75**, **76** and **77** revealed that the N^1-M-N^2 angle and the N-N distance in these metal complexes was proportional to the ionic radius of the metal ion. The largest N-N separation was observed in the case of palladium(II) complex (+)-**77** which also possessed the largest metal-nitrogen and metal-oxygen bond distances (Table 2.2). These data suggest that the binding pocket in **35** is somewhat flexible in size with adjustable dimensions that could accommodate more metal ions than those in Table 2.1.

Table 2.2 Correlation between ionic radii of metal ions, N^1-M-N^2 angle and N-N separation in metal complexes (+)-**75-77**.

entry	metal complex	ionic radii of metal ion (II) (Å)	angle N^1-M-N^2 (degree)	metal-nitrogen bond distance (Å)	metal-oxygen bond distance (Å)	N-N separation (Å)
1	(+)-**75**	0.692	96.78	1.893	1.862	2.830
2	(+)-**76**	0.737	98.38	1.963	1.903	2.972
3	(+)-**77**	0.865	97.70	2.026	2.002	3.051

The infrared spectra of all salen-metal complexes showed a significant shift of the ν(CN) vibration to lower frequency compared to the uncomplexed ligand (+)-**35**. The decrease in the ν(CN) vibration frequency upon metal complexation correlates with an increase in the C=N bond length in the crystal structures of **75-77** (Table 2.3), suggesting that the π electrons of the C=N bond are partially delocalized into the d-orbitals of the metal.

Table 2.3 Correlation between ν(C=N) and C=N bond distance of salen ligand (+)-**35** and metal complexes (+)-**75-77**.

entry	compound	ν(C=N) (cm^{-1})	C=N bond distance (Å)
1	(+)-**35**	1627	1.273
2	(+)-**76**	1616	1.292
3	(+)-**75**	1610	1.297
4	(+)-**77**	1606	1.303

With enantiopure metal-salen complexes **67-78** available in quantity, the opportunity to explore their properties as catalysts in reactions where asymmetric induction is important became attractive. Applications of several of the salen-metal complexes listed in Table 2.1 to six reactions where asymmetric induction is of importance are presented in the chapters that follow.

2.4 References

1. Larrow, J. F.; Jacobsen, E. N. *Org. Synth.* **2004**, *10*, 96.

2. Marchand, A. P.; Sharma, R.; Zope, U. P. *J. Org. Chem.* **1993**, *58*, 759.

3. Werstiuk, N. H.; Yeroushalmi, S.; Guan-Lin, H. *Can. J. Chem.* **1992**, *70*, 974.

4. Rubottom, G. M.; Gruber, J. M. *J. Org. Chem.* **1977**, *42*, 1051.

5. Berkessel, A.; Menche, D.; Sklorz, C. A.; Schroder, M.; Paterson, I. *Angew. Chem. Int. Ed.* **2003**, 42, 1032.

6. Osby, J. O.; Ganem, B. *Tetrahedron Lett.* **1985**, *26*, 6413.

7. Pasteur, L. *Annal. de Chim. et de Phys.* **1848**, *24*, 442.

8. Tichy, M.; Sicher, J. *Coll. Czech. Chem. Commun.* **1972**, *37*, 3106.

9. Hora, J.; *Recueil, J. Roy. Neth. Chem. Soc.* **1976**, *95*, 45.

10. Boger, D. L.; Patel, M.; Takusagawa, F. *J. Org. Chem.* **1985**, *50*, 1911.

11. Liu, W. Resolution at large scale: case studies. Handbook of Chiral Chemicals (2^{nd} *Edition*) **2006**, 75.

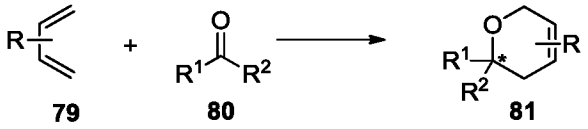
12. Aksani, R.; Eichenauer, H.; Kohler, J. *Chem. Ber.* **1982**, *115*, 748.

CHAPTER 3

The Asymmetric Hetero-Diels-Alder Reaction

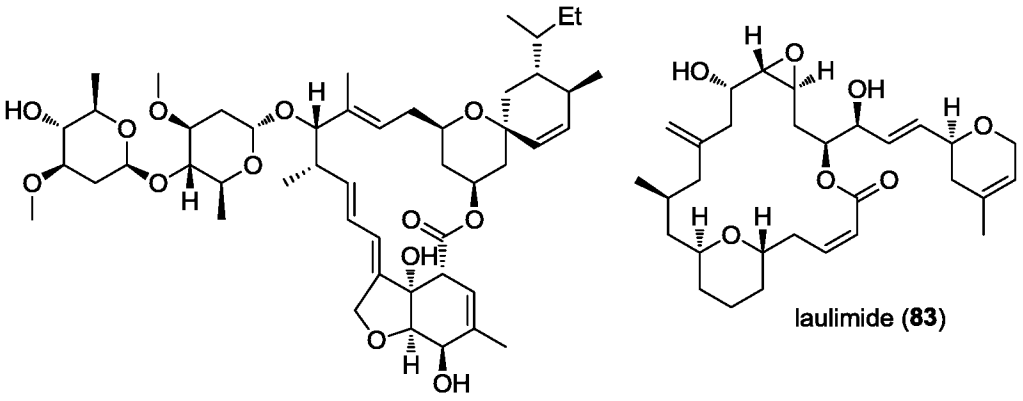
3.1 Introduction

The hetero Diels-Alder (HDA) reaction is among the most powerful methodologies available for the construction of six-membered heterocycles.[1] The reaction can be represented generally as a [4+2] cycloaddition of diene **79** with carbonyl compound **80** as the heterodienophile. The HDA reaction results in the formation of a dihydropyran **81** which can be elaborated in a variety of ways such as functionalization of the double bond (Scheme 3.1).



Scheme 3.1 The hetero-Diels-Alder reaction

The heterocycle **81** prepared by this method will contain a stereocenter adjacent to the oxygen atom in the molecule when $R_1 \neq R_2$. Chiral influence on the components of the HDA reaction can, in principle, result in preferential formation of one stereoisomer over the other, thus providing a means for preparing six-membered oxygen-containing heterocycles in enantioenriched form.[2,3] This structrural motif is frequently found in biologically active natural products such as avermectin B_{1a} (**82**), laulimide (**83**) and phorboxazole A (**84**, Figure 3.1).[4]



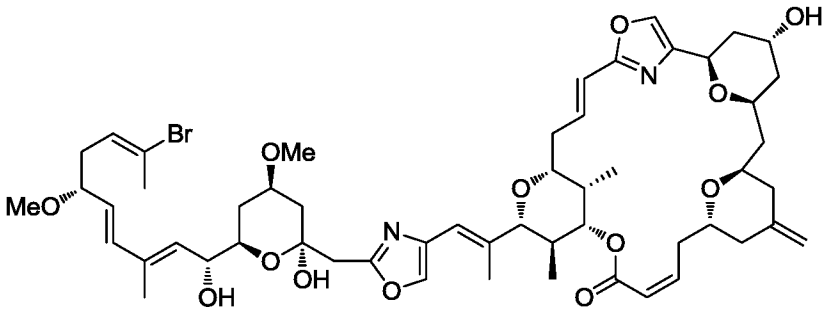


Figure 3.1 Natural products containing chiral six-membered oxygen heterocycles

3.2 Role of catalyst in hetero-Diels-Alder reaction: A FMO rationale

There are two main classes of HDA reactions. The cycloaddition of an electron rich diene and an aldehyde or other electron poor heterodienophile is known as a "normal electron demand" HDA, whereas cycloaddition of an electron poor diene with an electron rich dienophile is termed an "inverse electron demand" HDA. Frontier Molecular Orbital (FMO) analysis of the normal electron demand HDA reveals that the HOMO of the diene and LUMO of the dienophile are the controlling orbitals. The polarity of the hetero-dienophile strongly desymmetrizes the orbital coefficients of the LUMO leading to a bias

in the head-to-tail orientation of the dienophile relative to the diene. The HDA reaction is known to be accelerated in the presence of a Lewis acid. Theoretical studies of the HDA reaction catalyzed by Lewis acids have shown that binding of the Lewis acid lowers the LUMO of the dienophile, accounting for the rate enhancement, while also providing a steric effect that can influence *exo*/*endo* selectivity.[5] In this scenario, a chiral ligand environment around the Lewis acid would create a preference for reaction at one of the enantiotopic faces of the heterodienophile.

In the inverse electron demand HDA reaction, by contrast, the HOMO of the dienophile and the LUMO of the diene are the controlling orbitals. As in the normal electron demand HDA, Lewis acid coordination, in this case to the diene, can lead to a rate enhancement by decreasing the HOMO-LUMO gap for the reaction; it can also bias the stereoselectivity of the reaction. A summary of these FMO analyses is presented in Figure 3.2

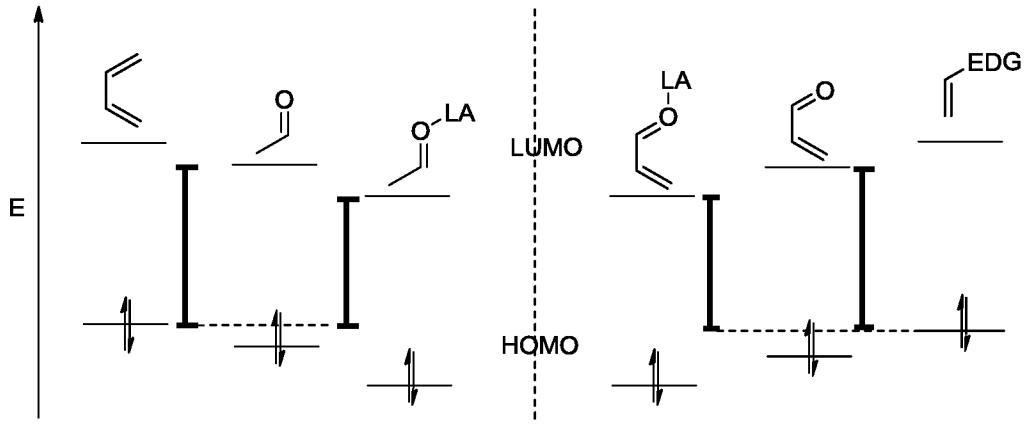
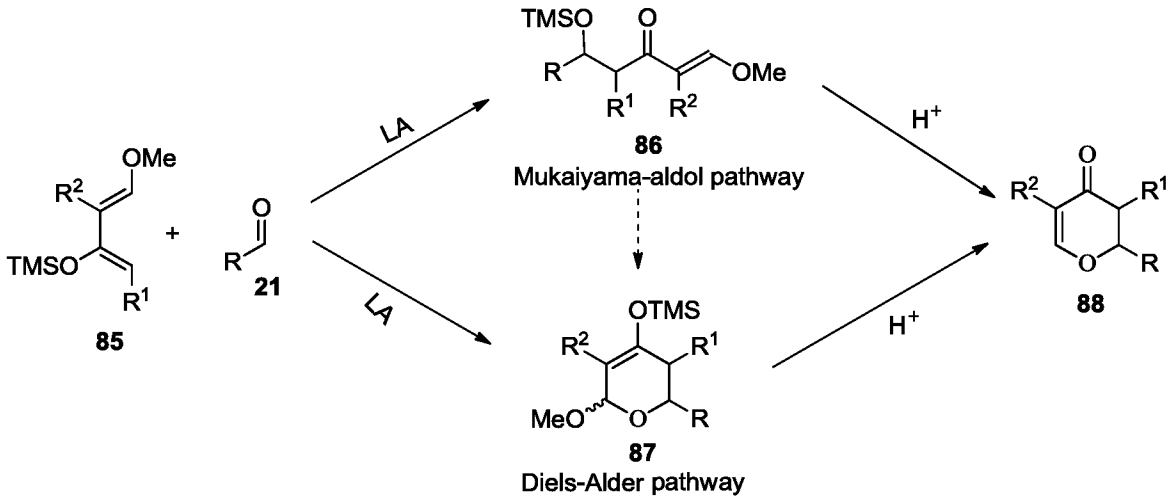


Figure 3.2 FMO diagram of the uncatalyzed and Lewis acid catalyzed normal electron demand HDA (left) and inverse electron demand HDA (right).

3.3 Mechanism of the Lewis acid-catalyzed hetero-Diels-Alder reaction

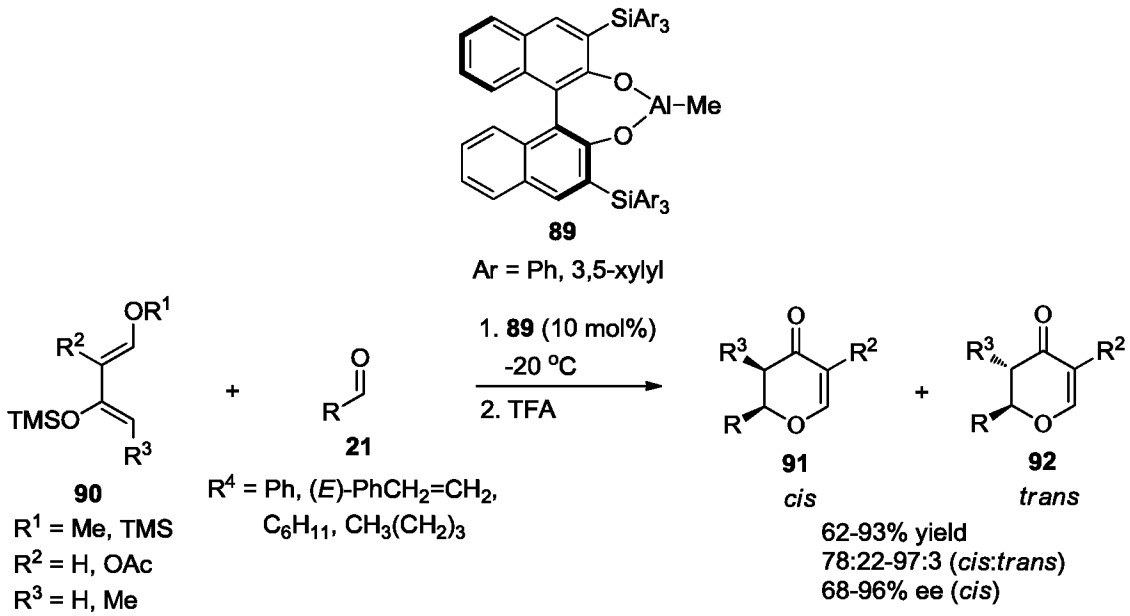
Two reaction pathways have been proposed for Lewis acid catalyzed HDA of aldehydes **21** with activated dienes e.g. **85**.[6] In one, a two-step pathway, the reaction first proceeds through a Mukaiyama-type aldol addition and leads to acyclic addition product **86** which subsequently cyclizes to give the HDA product **88**. With non-activated dienes, Lewis acid catalyzed HDA reactions take place through a concerted and synchronous [4+2] cycloaddition pathway analogous to a "normal" Diels-Alder reaction. Cyclic product **87** is usually converted to dihydropyranone **88** after acidic hydrolysis and β-elimination (Scheme 3.2). Molecular modeling suggests that the concerted cycloaddition pathway is more favorable energetically than the Mukaiyama-aldol pathway.



Scheme 3.2 Mukaiyama-aldol vs. Diels-Alder pathway for the reaction of aldehyde **21** with activated diene **85**.

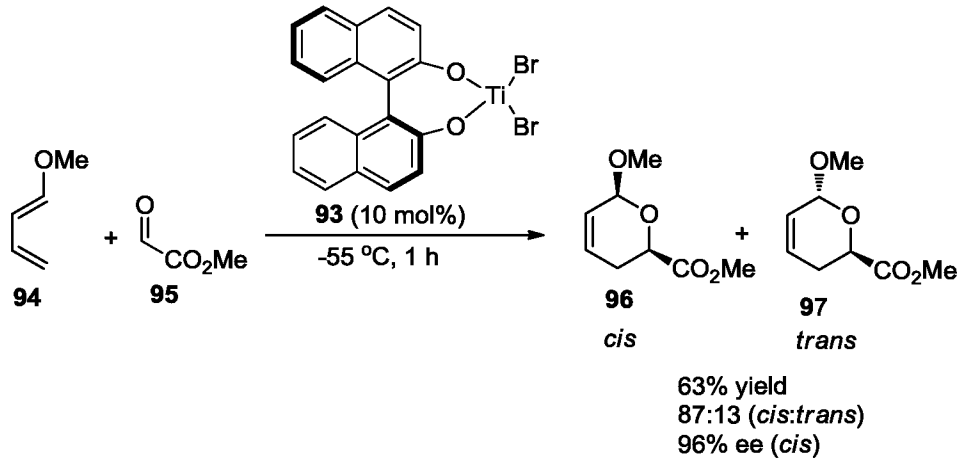
3.4 Early work on the catalytic enantioselective hetero-Diels-Alder reaction

Yamamoto and co-workers published the first example of a catalytic, enantioselective variant of this transformation using a chiral aluminum complex **89**.[7] This catalyst gave good yields and stereoselectivities of HDA products **91** for a range of aldehydes **21** and dienes **90** (Scheme 3.3).



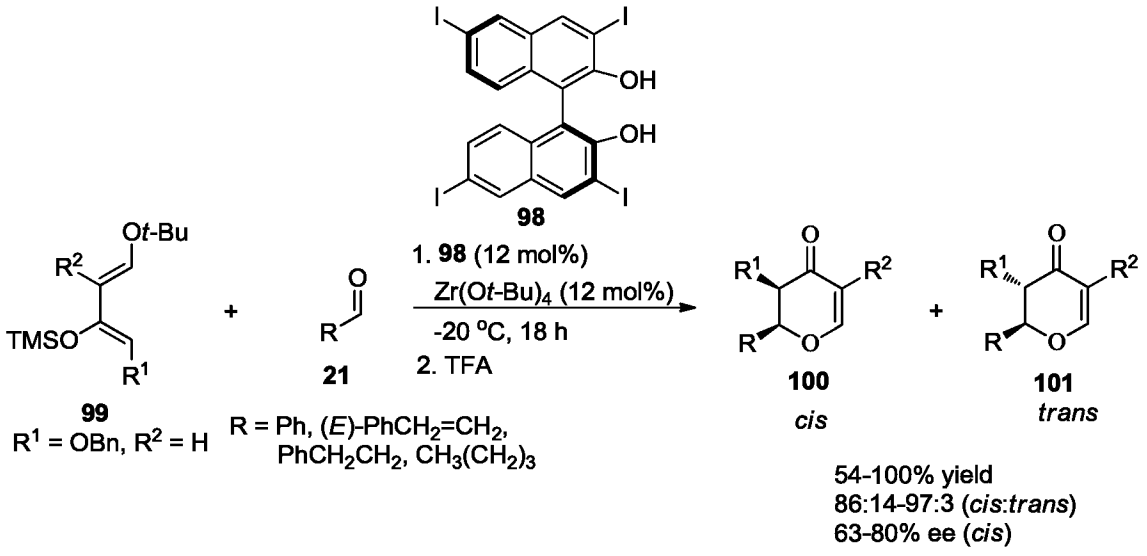
Scheme 3.3 Yamamoto's enantioselective HDA reaction catalyzed by aluminum complex **89**

Terada and coworkers reported that a chiral titanium complex **93** gave good enantioselectivity in the HDA reaction of diene **94** with methyl glyoxylate (**95**). The *cis* adduct **96** was obtained as the major diastereomer from this reaction (Scheme 3.4).[8]



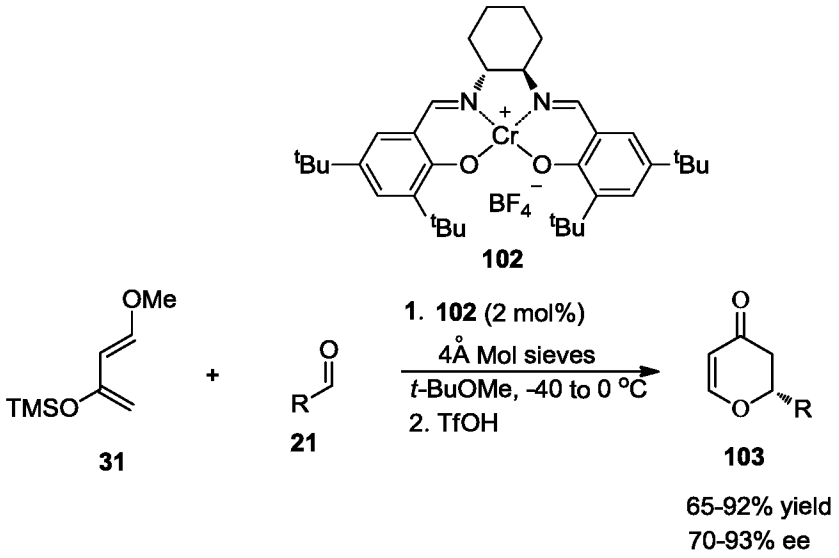
Scheme 3.4 Terada's titanium complex **93** as catalyst in an enantioselective HDA reaction

Subsequently, Kobayashi and co-workers found that zirconium tetra-*tert*-butoxide in combination with (*S*)-3,3',6,6'-tetraiodo-[1,1'-binaphthalene]-2,2'-diol (**98**) displays high reactivity in the HDA reaction of a wide range of activated dienes **99** with aldehydes **21**, affording *cis* dihydropyrone **100** as the major product and *trans* isomer **101** as a minor product (Scheme 3.5).[9]



Scheme 3.5 Kobayashi's enantioselective HDA reaction catalyzed by zirconium tetra-*tert*-butoxide and 1,1'-bi-2-naphthol **98**

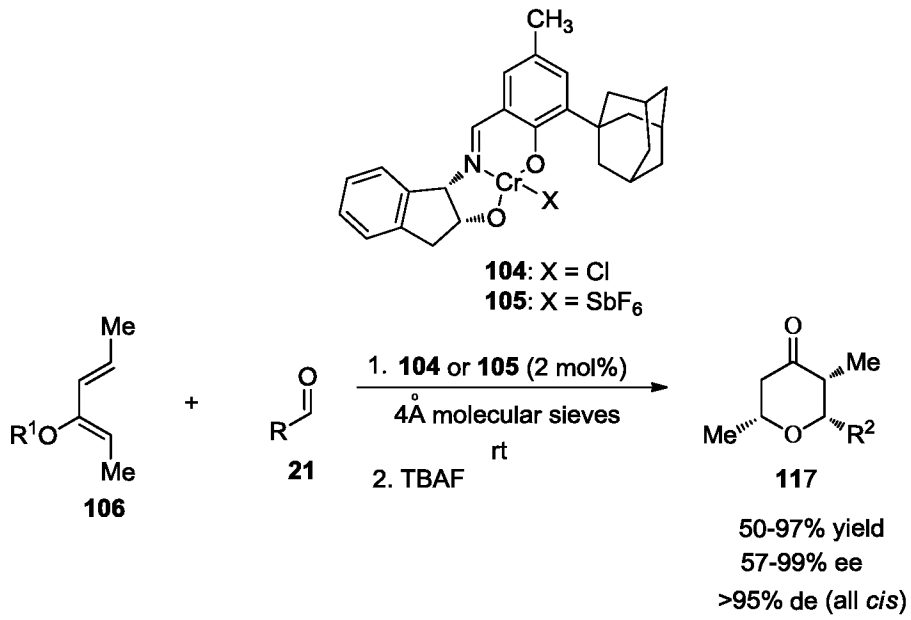
Jacobsen and co-workers prepared the first chiral chromium(III)-salen complex **102** and showed that it catalyzed the HDA reaction of Danishefsky diene (**31**) with aldehyde **21** to afford dihydropyrone **103** in good yield and enantiomeric excess (Scheme 3.6).[10]



Scheme 3.6 Enantioselective HDA reaction catalyzed by Jacobsen's first generation chromium(III)-salen catalyst **102**

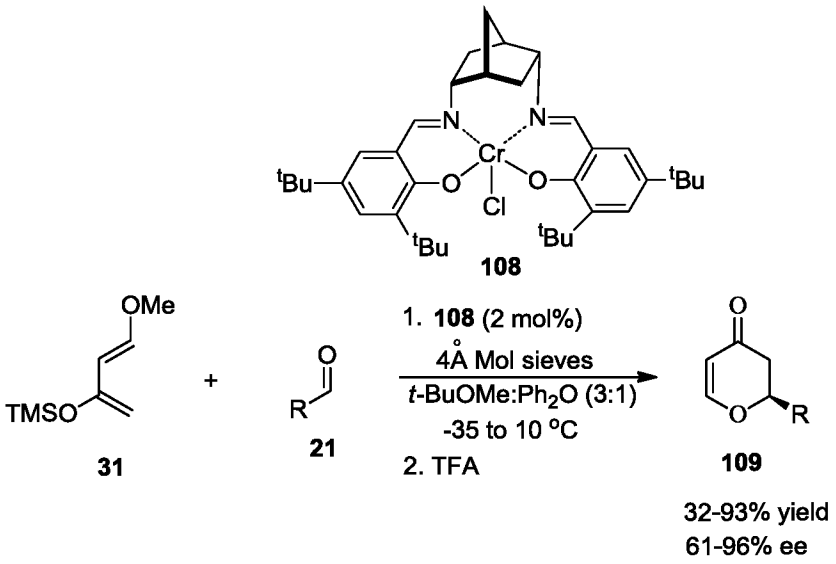
Although chromium(III)-salen complex **102** is an efficient catalyst for the HDA reaction of electron-rich dienes, it was ineffective for less reactive dienes, eg **106**, bearing fewer than two oxygen substituents. This shortcoming led to exploration of other chromium(III)-Schiff base complexes and it was found that complexes **104** and **105** showed high enantioselectivity in the HDA reaction of aliphatic and aromatic aldehydes

with less reactive dienes such as **106**. The all-*cis* HDA adduct **107** was formed exclusively in these cycloadditions (Scheme 3.7).[11]



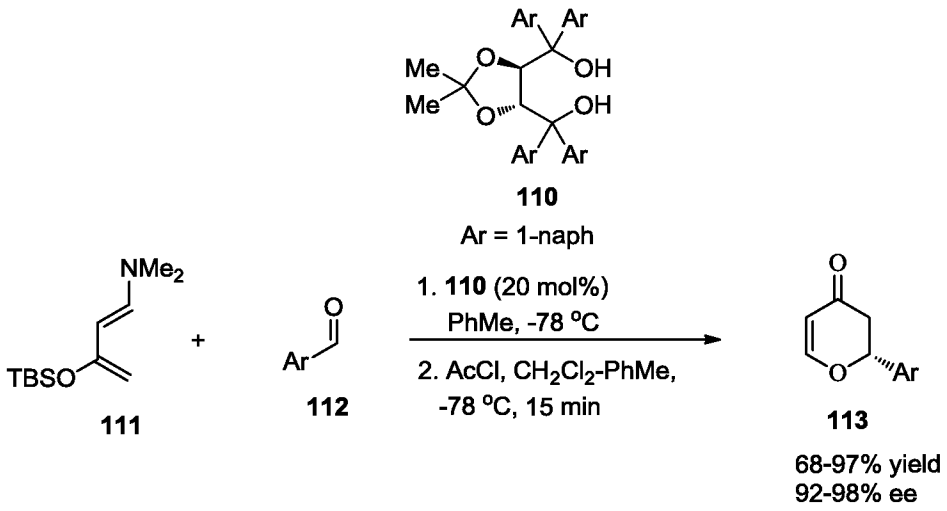
Scheme 3.7 Enantioselective HDA reaction catalyzed by Jacobsen's second generation chromium(III)-catalysts **104** and **105**

More recently, Berkessel synthesized chromium-salen complex **108** based on *cis*-2,5-diaminobicyclo[2.2.1]heptane as the chiral scaffold. The HDA reaction between Danishefsky diene (**31**) and aldehyde **21** catalyzed by **108** produced dihydropyranone **109** in variable yield and promising enantioselectivity but no other dienes were examined and the Berkessel complex appears to have been abandoned as a catalyst for the HDA reaction (Scheme 3.8).[12]



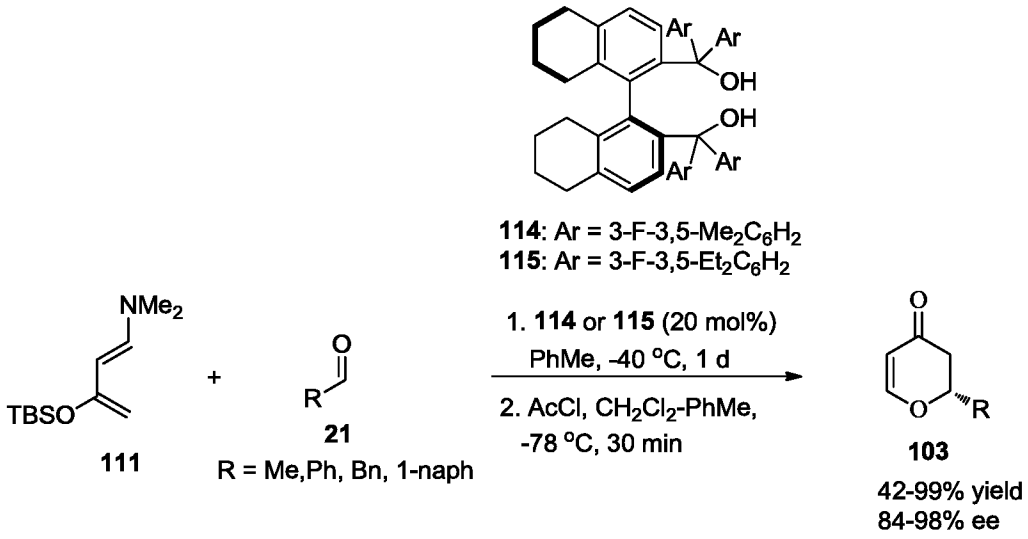
Scheme 3.8 Enantioselective HDA reaction catalyzed by Berkessel's chromium(III)-catalyst **108**

Rawal and co-workers used α, α, α′, α′-tetra-(1-naphthyl)-1,3-dioxolan-4,5-dimethanol (TADDOL, **110**) as a catalyst for the enantioselective HDA reaction of diene **111** (currently known as Rawal's diene) with aromatic aldehydes **112**. Dihydropyranones **113** were formed in good yield and enantioselectivity from this reaction (Scheme 3.9).[13,14] Rawal proposed that the TADDOL ligand induces enantioselectivity via an intermolecular hydrogen bond between one of the hydroxyl groups of the ligand and the aldehyde carbonyl.[15]



Scheme 3.9 Rawal's enantioselective HDA reaction catalyzed by α, α′, α′-tetra-(1-naphthyl)-1,3-dioxolan-4,5-dimethanol (**110**)

Further investigations by Rawal and co-workers led to the development of 1,1′-biaryl-2,2′-dimethanol (BAMOL) derivatives **114** and **115** as chiral catalysts.[16] The tetrahydronapthalene groups of BAMOL result in a significantly enhanced chiral environment around the reaction site compared to the isopropylidene ketal of TADDOL (**110**) and this leads to good enantioselectivity in the HDA reaction of diene **111** with a wide variety of aliphatic, vinylic, alkynylic, and aromatic aldehydes **21** (Scheme 3.10). The X-ray crystal structure of a benzaldehyde complex with **114** reveals that a hydrogen bond between a BAMOL hydroxyl group and the aldehyde carbonyl accounts for the origin of stereoselectivity in this HDA reaction.[17,18]

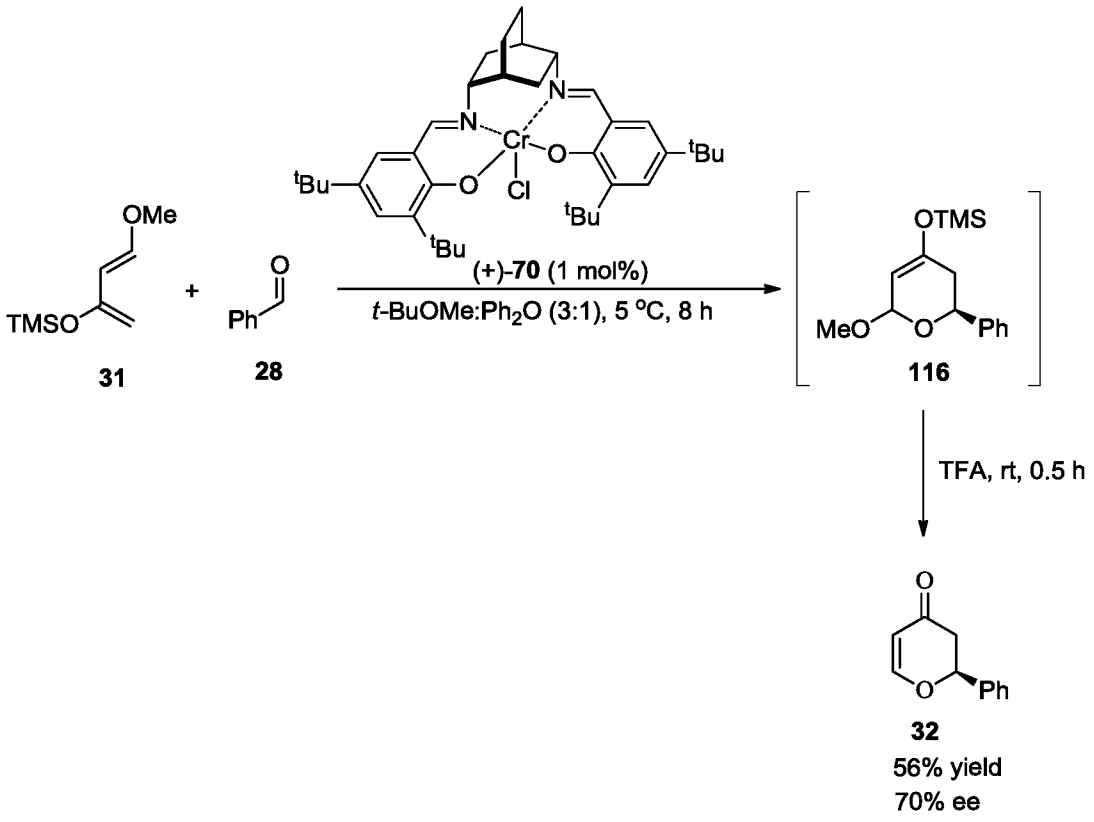


Scheme 3.10 Rawal's enantioselective HDA reaction catalyzed by chiral BAMOL derivatives **114** and **115**

3.5 *Cis*-2,5-diaminobicyclo[2.2.2]octane based chromium-salen catalyst for the enantioselective HDA reaction

We synthesized the C_2-symmetric chromium(III)-salen complex (+)-**70** (chapter 2, Scheme 2.10, entry 4) on the ground that the chiral space associated with a quadrant under the bicyclooctane scaffold would lead to high levels of asymmetric induction in a process such as the enantioselective HDA reaction. To test our hypothesis, we first compared the catalytic efficiency of (+)-**70** with that of Berkessel's chromium complex **108** in the HDA reaction of Danishefsky's diene (**31**) with benzaldehyde (**28**). Following Berkessel's protocol, a 3:1 mixture of methyl *tert*-butyl ether and diphenyl ether was used as solvent for the reaction.[12] Our first run with 1 mol% of (+)-**70** at 5 °C gave 5,6-dihydro-4-pyranone **32** in 55% yield and 70% enantioselectivity after acid-promoted

hydrolysis of the intermediate cycloadduct **116**. Comparison of the optical rotation of **32** from this experiment with the literature value established that **32** possessed (*S*) configuration (Scheme 3.11).[11]

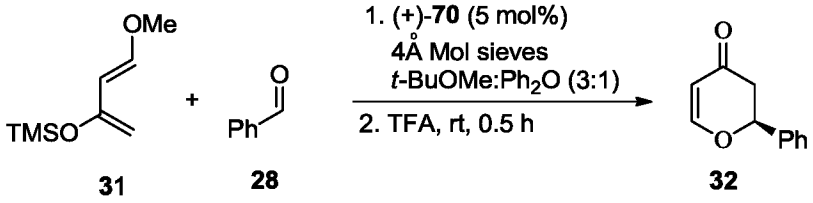


Scheme 3.11 Enantioselective HDA reaction of Danishefsky diene (**31**) with benzaldehyde (**28**) catalyzed by chromium(III)-salen complex (+)-**70**

Encouraged by this preliminary result, we increased the catalyst loading to 5 mol%. We also investigated the influence of temperature and moisture content on the course of the reaction (Table 3.1). It was found that increased catalyst loading and the addition of oven-dried powdered 3Å molecular sieves to the reaction mixture dramatically increased the yield and enantioselectivity of the cycloaddition (entry 1).

Lowering the reaction temperature had a small but beneficial effect on the enantiomeric excess of **32** (entries 2 and 3). Optimized conditions were found at a reaction temperature of -22 °C, where a quantitative yield of **32** was obtained after 30 hours (entry 3) and the *S*-(+) enantiomer of **32** was formed with an enantiomeric excess of 97%.

Table 3.1 Effect of temperature on the HDA reaction of Danishefsky diene (**31**) with benzaldehye (**28**) catalyzed by (+)-**70**[a]



31 **28** **32**

85% yield, 87% ee (Jacobsen)[10]
84% yield, 95% ee (Berkessel)[12]

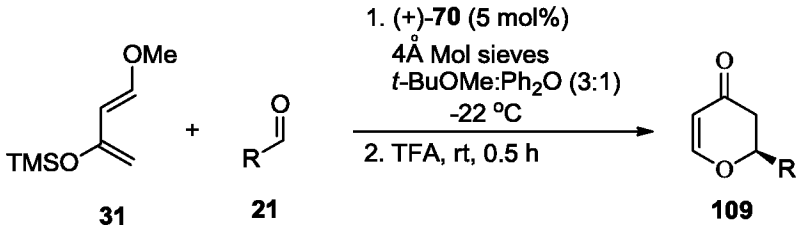
			product **32**	
entry	T [°C]	t [h]	yield [%][b]	ee [%][c]
1	5	5	99	95
2	-15	24	94	96
3	-22	30	99	97

[a]Reactions were carried out on a 0.25 mmol scale inwith 1.2 equiv of **31**. [b] Yield of isolated product. [c]Determined by HPLC using a Daicel Chialcel OD column.

These initial results prompted us to apply the optimized reaction conditions of Table 3.1 (entry 3) to the asymmetric HDA reaction of **31** with a series of aryl aldehydes and one aliphatic aldehyde (**21**, Table 3.2).

Table 3.2 Asymmetric Hetero Diels-Alder Reaction of Danisheksky diene (**31**) with

aldehydes **21** catalyzed by chromium(III)-salen complex (+)-**70**[a]



31 **21** **109**

entry	R	T (°C)	t (h)	Product **109**	
				Yield [%][b]	ee [%][c]
1	2-$CH_3C_6H_4$	-22	24	98	92
2	3-$CH_3C_6H_4$	-22	24	99	92
3	3-$CH_3OC_6H_4$	-22	36	99	96
4	4-ClC_6H_4	-22	24	98	94
5	4-$O_2NC_6H_4$	-22	24	99	94
6	3,5-$(CH_3O)_2C_6H_3$	-22	48	99	87[d]
7	3,5-$(CH_3O)_2C_6H_3$	-30	48	97	94
8	1-naphthyl	-22	35	97	84
9	1-naphthyl	-30	40	96	94
10	2-furyl	-22	18	99	67
11	2-furyl	-30	48	93	88
12	3-furyl	-22	30	99	82[d]
13	3-furyl	-30	42	96	94
14	c-C_6H_{11}	-22	36	91	68

[a]Reactions were carried out on 0.25 mmol scale at 0.625M with 1.2 equivalents of **31**. [b]Yields of isolated product. [c]Determined by HPLC using a Daicel Chiralcel OD column. [d]The absolute configuration of **109** was not determined.

Dihydropyranones **109** were obtained after acidic hydrolysis of the intermediate cycloadduct in good yield and, in most cases, high enantiomeric excess. Both, electron-rich aldehydes (entries 1-2) as well as electron-deficient aldehydes (entries 3-6) afforded

dihydropyranones **109** with high enantiomeric excess (entries 1-6). Lower enantioselectivity was observed with heteroaromatic aldehydes (67% and 82% enantiomeric excess, respectively; entries 10, 12) and with cyclohexanecarboxaldehyde (68% enantiomeric excess, entry 14). In an investigation of the temperature limit for our catalytic asymmetric HDA reaction, a decrease in the reaction temperature to -30 ^{o}C was found to lead to a slower reaction rate but to higher enantiomeric excess in HDA adduct **109** from 3,5-dimethoxybenzaldehyde, 1-napththaldehyde and heteroaromatic aldehydes (enties 7, 9, 11, 13). Cyclohexanecarboxaldehyde failed to react at the lower temperature. The absolute configuration of the dihydropyranone product was established in all cases, except for entries 6 and 12, by comparison of the measured specific rotation with the literature value.

In contrast to the foregoing results, pyridine-3-carboxaldehyde, 4-methoxybenzaldehyde, and 4-(dimethylamino)benzaldehyde, which were also tested during these studies, did not react with diene **31**. For pyridine-3-carboxaldehyde, this observation may be explained by coordination of the pyridine nitrogen atom with chromium in (+)-**70** resulting in deactivation of the catalyst. In the case of 4-methoxybenzaldehyde and 4-(dimethylamino)benzaldehyde, low electrophilicity of the aldehyde carbonyl probably accounts for their lack of reactivity.

A proposed mechanism to rationalize our chromium(III)-salen catalyzed HDA reaction is shown in Figure 3.3. This model positions the aldehyde in the open lower right hand quadrant below the bicyclo[2.2.2]octane scaffold with the metal-coordinated carbonyl oriented as shown in **117** to avoid a steric clash of the aldehyde hydrogen with a

proximal *tert*-butyl substituent. In this orientation, the *re*-face of the carbonyl group is blocked by an opposing aryl ring of the salen residue leaving the *si*-face accessible to an incoming nucleophile. Addition of diene **31** to the *si*-face of aldehyde **21** leads to (*S*) configuration of HDA adduct **109**. It is possible that a π-stacking interaction between an aryl aldehyde and a benzenoid moiety of the salen ligand contributes to stabilization of the coordination complex with aryl aldehydes, a factor that could explain the lower enantioselectivity observed with cyclohexanecarboxaldehyde (Table 3.2, entry 10).

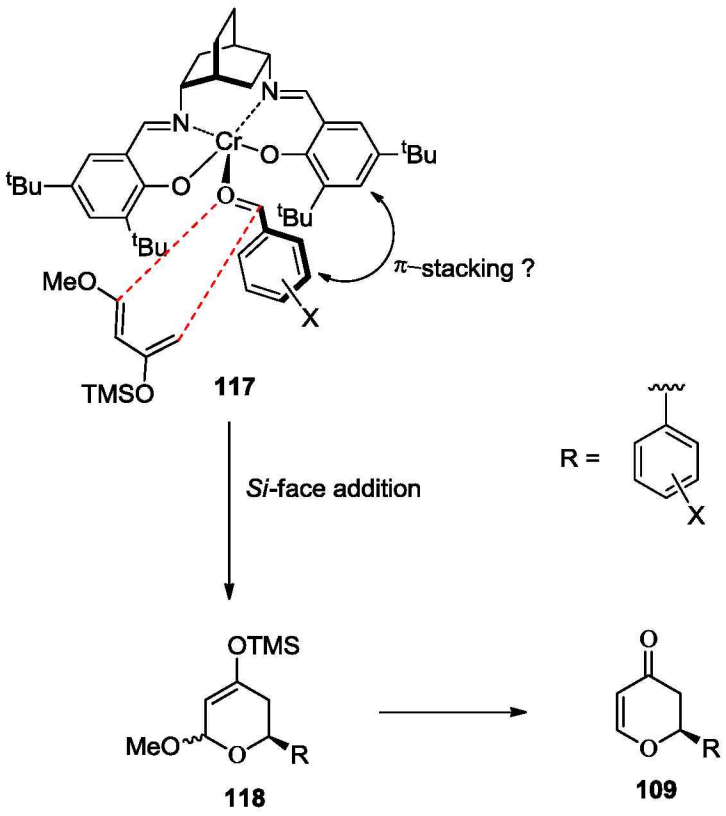


Figure 3.3 Proposed transition state for the origin of stereoselectivity in the HDA reaction of **31** with aromatic aldehydes catalyzed by (+)-**70**.

In this chapter, we showed that chromium(III)-salen complex (+)-**70** was able to catalyze the enantioselective HDA reaction of Danishefsky diene **31** with a large number of aldehydes to give cycloadducts in high enantiomeric excess. Our results compare favorably with those obtained with other chiral catalyst systems. This finding raised confidence in our selection of *cis*-2,5-diaminobicyclo[2.2.2]octane as a chiral scaffold for metal-salen catalysts that could be used for asymmetric synthesis in other contexts.

3.6 References

1. (a) Corey, E. J. *Angew. Chem., Int. Ed.* **2002**, *41*, 1650. (b) Nicolaou, K. C.; Snyder, S. A.; Montagnon, T.; Vassilikogiannakis, G. E. *Angew. Chem., Int. Ed.* **2002**, *41*, 1668. (c) Tietze, L. F.; Kettschau, G. *Top. Curr. Chem.* **1997**, *189*, 1. (d) Boger, D. L.; Weinreb, S. M. *Hetero-Diels–Alder Methodology in Organic Synthesis*; Wasserman, H. H., Ed.; Academic: San Diego, CA, **1987**.

2. Tietze, L. F.; Kettschau, G. *Stereoselective Heterocyclic Synthesis 1*; Metz, P., Ed.; Springer: Berlin, **1997**; Vol. *189*, p 1.

3. (a) Waldmann, H. *Synthesis* **1994**, 535. (b) Jorgensen, K. A.; Johannsen, M.; Yao, S.; Audrain, H.; Thorhauge, J. *Acc. Chem. Res.* **1999**, *32*, 605.

4. (a) Dansihefsky, S. J.; Armistead, D. M.; Selnick, H. G.; Wincott, F. E.; Hungate, *R. J. Am. Chem. Soc.* **1987**, *109*, 119. (b) White, J. D.; Bolton, G. L; Dantanarayana, A. P; Fox, C. M. J; Hiner, R. N; Jackson, R. W.; Sakuma, K.; Warrier, U. S. *J. Am. Chem. Soc.* **1995**, *117*, 1908. (c) Ghosh, A. K.; Mathicanan, P.; Cappiello, J.; Krishnan, K. *Tetrahedron Lett.* **1997**, *38*, 2427. (d) White, J. D.; Kuntiyong, P.; Lee, T. H. *Org. Lett.* **2006**, *8*, 6039. (e) White, J. D.; Lee, T. H.; Kuntiyong, P. *Org. Lett.* **2006**, *8*, 6043. (f) Kuntiyong, P.; Lee, T. H.; Kranemann, C. L. *Org. Biomol. Chem.* **2012**,*10*, 7884.

5. McCarrick, M. A.; Wu, Y.; and Houk, K. N. *J. Am. Chem. Soc.* **1992**, *114*, 1499.

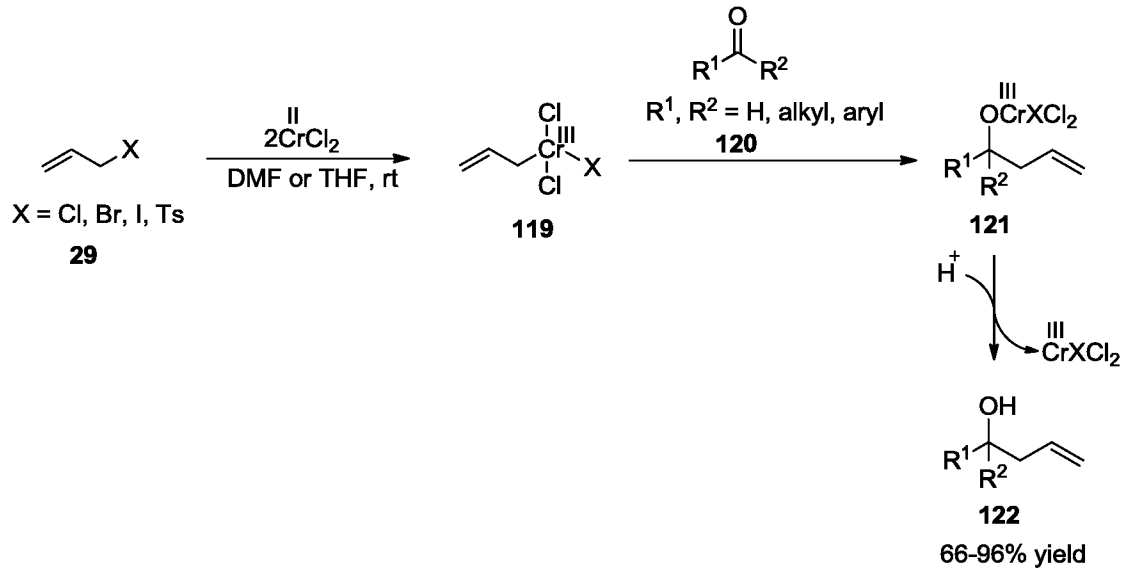
6. Roberson, M.; Jepsen, A.S.; and Jørgenson, K. A. *Tetrahedron* **2001**, *57*, 907.
7. Maruoka, K.; Itoh, T.; Shirasaka, T.; and Yamamoto, H. *J. Am. Chem. Soc.* **1988**, *110*, 310.
8. Terada, M.; Mikami, K.; and Nakai, T. *Tetrahedron Lett.* **1991**, *32*, 935.
9. Yamashita, Y.; Saito, S.; Ishitani, H.; and Kobayashi, S. *J. Am. Chem. Soc.* **2003**, *125*, 3793.
10. Schaus, S.; Branalt, J.; and Jacobsen, E. N. *J. Org. Chem.* **1998**, *63*, 403.
11. Dossetter, A. G.; Jamison, T. F.; and Jacobsen, E. N. *Angew.Chem., Int. Ed.* **1999**, *38*, 2398.
12. Berkessel, A.; Vogl, N. *Eur. J. Org. Chem.* **2006**, 5029.
13. Huang, Y. and Rawal, V. H. *Org. Lett.* **2000**, *2*, 3321.
14. Huang, Y. and Rawal, V. H. *J. Am. Chem. Soc.* **2002**, *124*, 9662.
15. Thadani, A.; Stankovik, A. R.; Rawal, V. H. *Proc. Nat. Acad. Sci.* **2004**, *101*, 5846.
16. Huang, Y.; Unni, A. K.; Thadani, A. N.; and Rawal, V. H. *Nature* **2003**, *424*, 146.
17. Du, H.; Zhao, D.; and Ding, K. *Chem. Eur. J.* **2004**, *10*, 5964
18. Unni, A. K.; Takenaka, N.; Yamamoto, H.; and Rawal, V. H. *J. Am. Chem. Soc.* **2005**, *127*, 1336.

CHAPTER 4

The Asymmetric Nozaki-Hiyama-Kishi Reaction

4.1 Introduction

An important and widely used class of carbon-carbon bond forming reactions involves nucleophilic addition of vinyl or allyl organometallic reagents to aldehydes. The product is an allylic or homoallylic alcohol and a number of strong nucleophiles, such as lithium, magnesium, and copper organometallics, as well as weaker nucleophiles, such as silicon and boron-based organometallics, have been used to achieve this transformation.[1] The poor chemoselectivity and stereochemical predictability associated with many of these allyl and vinyl organometallic species restrict their use in complex synthesis, where their role is often confined to structural environments in which functionality is limited. The need for a predictable and highly chemoselective method for the formation of allyic and homoallylic alcohols that could be used in a synthetic sequence where multiple functionality is present was recognized by Nozaki and Hiyama who attempted to solve this problem by addition of organochromium reagents to aldehydes and ketones.[2] They showed in 1977 that allyl halides **29** react with aldehydes and ketones **120** in the presence of stoichiometric amounts of chromium(II) chloride to produce homoallylic alcohols **122** in good yield. It was proposed that oxidative insertion of chromium(II) into the allylic carbon-halogen bond of **29** produces an allylchromium(III) species **119** which reacts with the carbonyl compound to form chromium alkoxide **121**. Hydrolysis of **121** produces the observed product **122** (Scheme 4.1).



Scheme 4.1 Nozaki-Hiyama-Kishi addition of an allylchromium reagent to aldehydes and ketones

In contrast to organocopper and organomagnesium (Grignard) reagents, organochromium species **119** is unreactive with functional groups such as esters, amides and nitriles.[3] The scope of this reaction was extended by Nozaki to include alkynyl halides which produced propargyl alcohols.[4]

In reactions using vinyl halides it was noted that there was a strong dependence on the source of chromium(II), different batches giving either good conversion or no conversion at all. Kishi[5] and Nozaki[6] independently determined that this batch dependence was a result of trace amounts of nickel(II) present in commercially available chromium(II) chloride. Chromium(II) is known to reduce nickel(II) to an active nickel(0) species which is believed to undergo oxidative addition to vinyl halide **123** to form vinylnickel(II) species **124**. Subsequent transmetalation of **124** with a chromium(III) salt

leads to vinylchromium(III) species **125** which adds to the carbonyl group of an aldehyde to give chromium(III) alkoxide **126** and, after hydrolysis, an allylic alcohol (Figure 4.1).

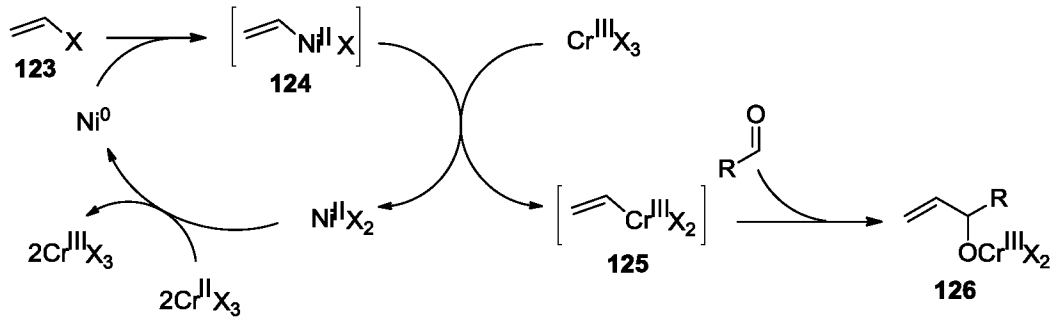
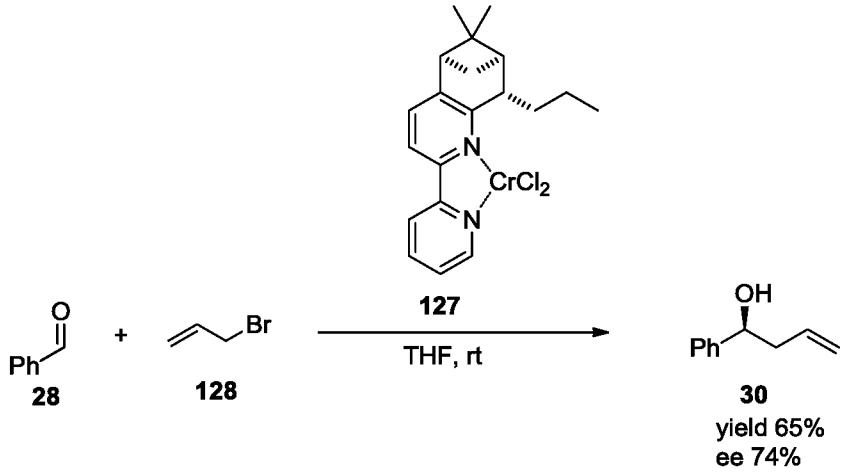


Figure 4.1 Role of nickel in the proposed catalytic cycle for the Nozaki-Hiyama-Kishi reaction

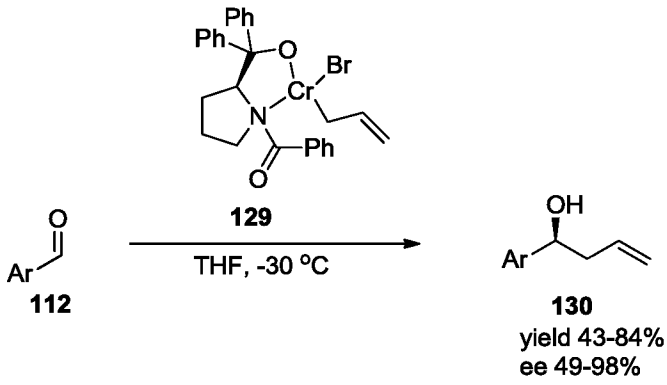
The synthetic utility of the Nozaki-Hiyama-Kishi (NHK) reaction was expanded by Furstner[7] who developed a catalytic redox process in which chromium(II) is generated from chromium(III). This protocol significantly reduces the quantity of toxic chromium salts produced and therefore makes the reaction more environmentally benign. Cheap non-toxic manganese is employed as the reducing agent for chromium(III) in the Furstner modification. Chromium(III) chloride is preferred for the NHK reaction because, in contrast to chromium(II) chloride, it is inexpensive, relatively insensitive to oxygen and moisture, and is much easier to manipulate. These advances triggered extensive efforts to find a catalytic and enantioselective version of the NHK reaction.

The first chromium catalyzed enantioselective allylation of aldehydes was published by Kishi in 1995 using chiral bipyridine ligand **127**. This reaction gave homoallylic alcohol **30** in 74% enantiomeric excess from the reaction of benzaldehyde (**28**) with allyl bromide (**128**, Scheme 4.2).[8]



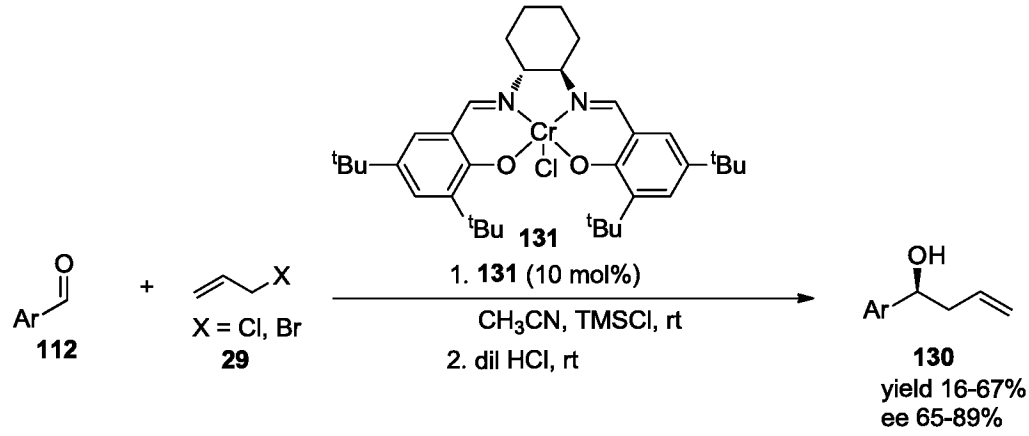
Scheme 4.2 Kishi's enantioselective NHK reaction promoted by bipyridine-chromium complex **127**

Subsequently, Kibayashi and coworkers reported proline based chiral organochromium reagent **129** for enantioselective allylation of aryl aldehydes **112**. This reaction led to homoallylic alcohol **130** in moderate to good yield and enantiomeric excess (Scheme 4.3).[9]



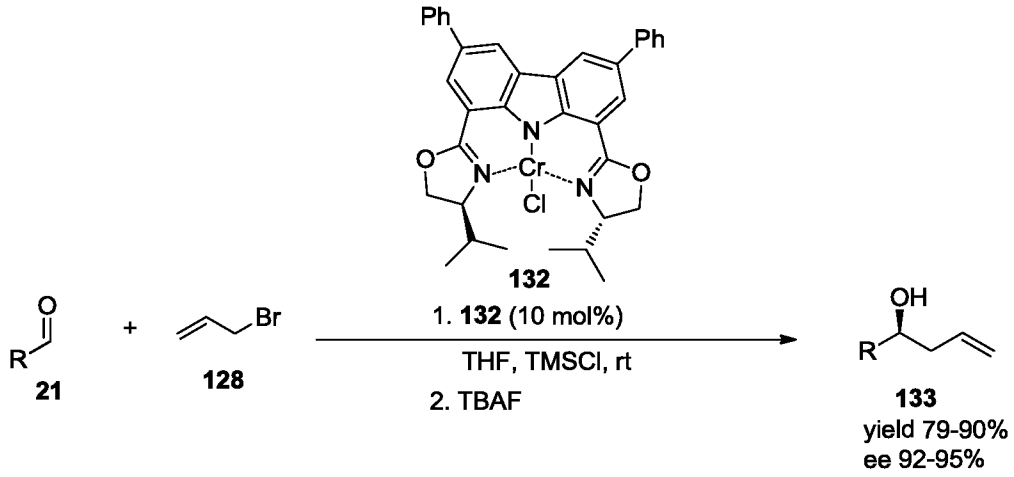
Scheme 4.3 Enantioselective NHK allylation of aryl aldehydes with Kibayashi's allyl chromium(III) reageant **129**

Cozzi and coworkers reported the first example of a *catalytic* enantioselective Nozaki-Hiyama-Kishi reaction. The reaction was performed with a catalytic amount of chiral chromium complex **131** using allyl halides **29** and aromatic aldehydes **112** as reactants. Homoallylic alcohols **130** were produced in moderate enantiomeric excess although the yield of product was poor in most cases (Schme 4.4). [10]



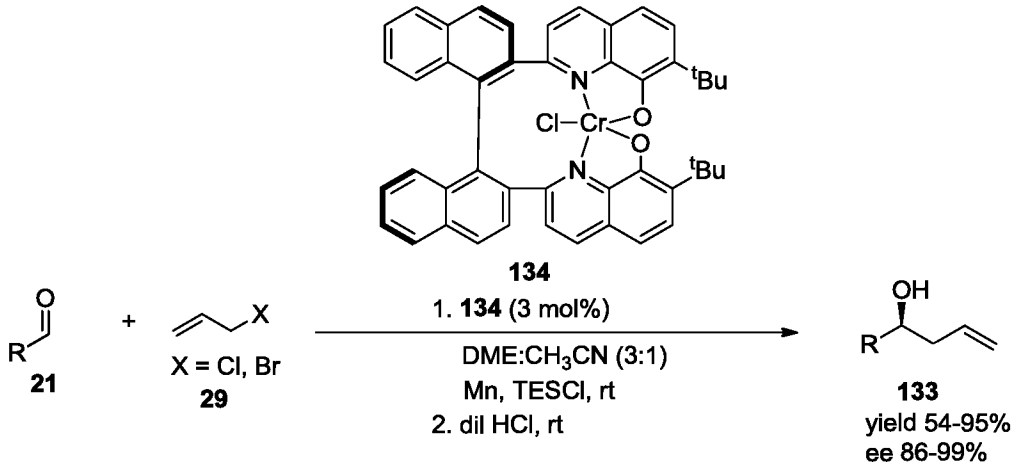
Scheme 4.4 Cozzi's enantioselective NHK reaction catalyzed by chromium(III) complex **131**

A more efficient chiral chromium(II) catalyst **132** based on a bis(oxazolinyl)carbazole as scaffold was developed by Nakada for the NHK reaction of allyl bromide (**128**) with aldehydes **21**. Catalyst **155** furnished homoallylic alcohols **133** in good yield and excellent enantiomeric excess (Scheme 4.5).[11]



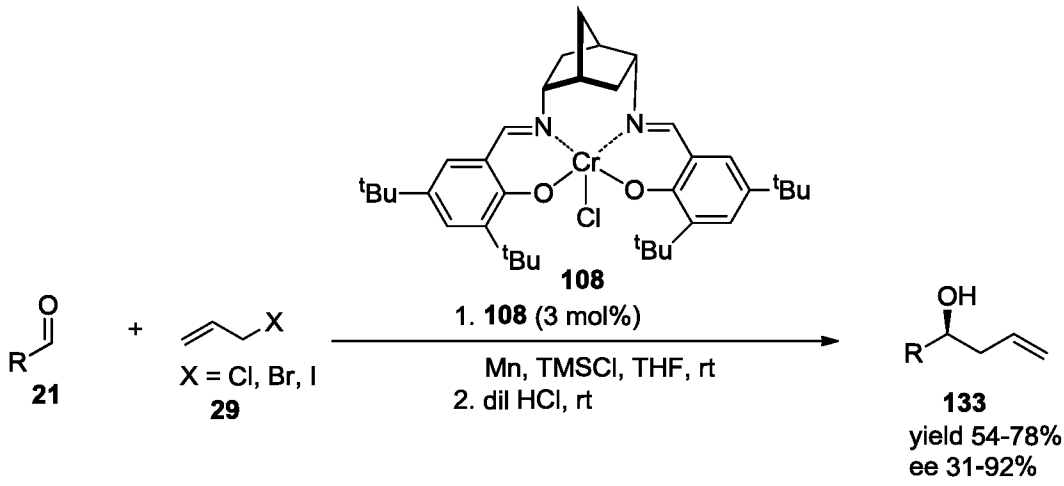
Scheme 4.5 Nakada's enantioselective NHK reaction catalyzed by chromium(II) catalyst **132**

A chiral bis-(8-quinolinolato)chromium(III) complex (TBOx, **134**) which catalyzes the NHK allylation of aldehydes at room temperature in good yield and high enantioselectivity has been reported by Yamamoto (Scheme 4.6).[12] The high turnover rate of this catalyst enables it to be used at a concentration no higher than 3 mol%.



Scheme 4.6 Yamamoto's enantioselective NHK allylation catalyzed by TBOx catalyst **134**

The chromium-salen complex **108** based on *cis*-2,5-diaminobicyclo[2.2.1] -heptane (DIANANE) that had been synthesized by Berkessel and shown to be an effective catalyst for the enantioselective hetero-Diels-Alder reaction (chapter 3) was also applied to the NHK reaction of allyl halides (**29**) with aldehydes **21**. However, **108** gave mixed results, producing homoallylic alcohols **133** in only moderate yield and in highly variable enantiomeric excess (Scheme 4.7).[13]

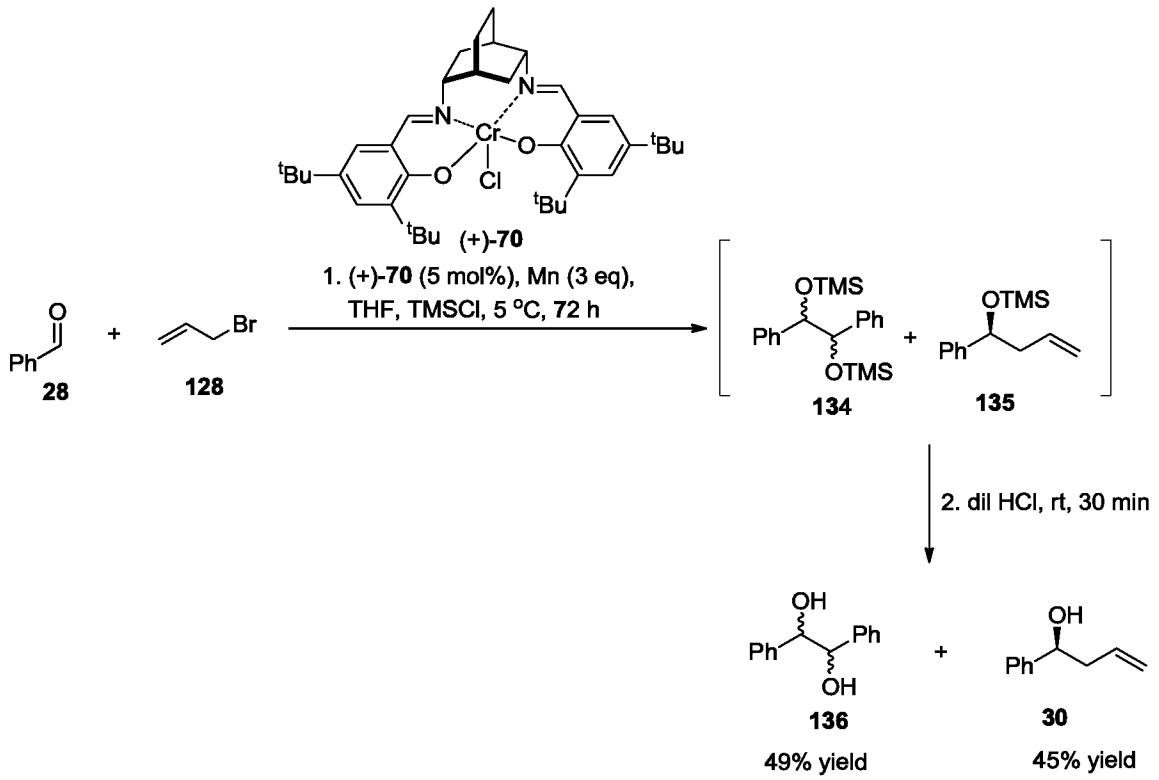


Scheme 4.7 Enantioselective NHK reaction catalyzed by Berkessel's chromium(III)-salen catalyst **108**

4.2 *Cis*-2,5-diaminobicyclo[2.2.2]octane based chromium-salen catalyst for the enantioselective Nozaki-Hiyama-Kishi reaction

The favorable results obtained with chromium(III) complex (+)-**70** (Chapter 2, Table 2.1, entry 4) as a catalyst for the enantioselective hetero-Diels-Alder reaction of an activated diene with aldehydes suggested that (+)-**70** could be a promising candidate for

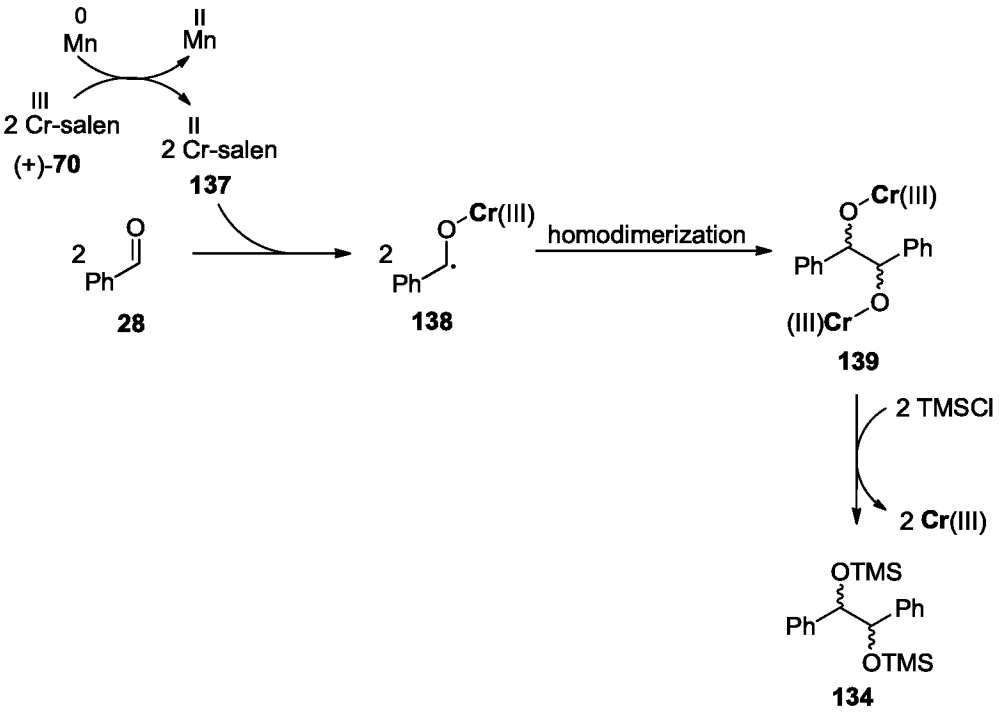
catalyzing the Nozaki-Hiyama-Kishi reaction. This proposition was tested with benzaldehyde (**28**) and allyl bromide (**128**) following a protocol analogous to that used by Berkessel with his catalyst **108**. In our first attempt using 5 mol% of (+)-**70** and 3 equivalents of manganese at 5 °C, the reaction gave a mixture of pinacol **136** (49%) and the desired homoallylic alcohol **30** (45%) after hydrolysis of the intermediate silyl ethers **134** and **135** (Scheme 4.8).



Scheme 4.8 Reaction of benzaldehyde (**28**) with allyl bromide (**128**) catalyzed by chromium(III)-salen complex (+)-**70**

Formation of pinacol product **136** can be explained by electron transfer to the carbonyl of benzaldehyde by an intermediate divalent chromium complex **137** which generates carbon centered radical **138**. Homodimerization of **138** leads to bimetalic

pinacol derivative **139** which undergoes transmetalation with trimethylsilyl chloride to give the bis-silyl ether **134** (Scheme 4.9).

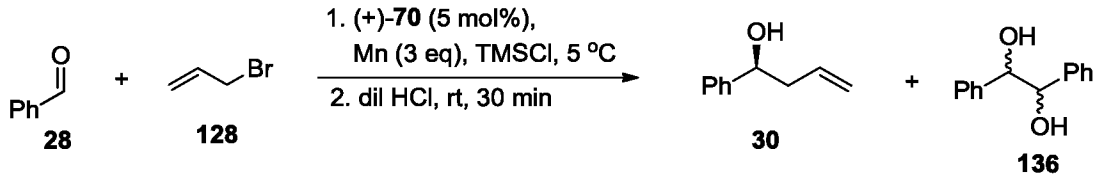


Scheme 4.9 Proposed mechanism for formation of pinacol derivative **134**

In order to increase the proportion of homoallylic alcohol **30** relative to pinacol product **136**, a comprehensive survey of reaction conditions was undertaken. Several parameters were found to influence the **136**:**30** ratio as well as the rate and enantioselectivity of the reaction. First, the influence of solvent on the reaction was studied which revealed that the proportion of alcohol **30** was related to the polarity of the solvent. For example, the polar solvent tetrahydrofuran gave an approximately 1:1 ratio of **136**:**30** whereas the non-polar solvent methylene chloride gave a much higher proportion of **136** (Table 4.1). This observation is consistent with a longer half life of

radical intermediate **138** in a non-polar solvent which would favor homodimerization leading to **136**. Alcohol **30** obtained from this study showed a disappointingly low enantiomeric excess.

Table 4.1 Effect of solvent on the reaction of allyl bromide (**128**) with benzaldehyde (**28**) catalyzed by (+)-**70**[a]



28 **128** **30** **136**

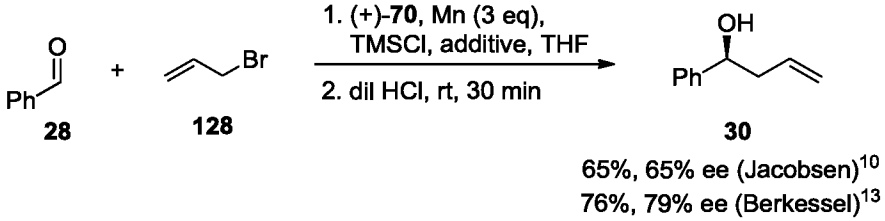
entry	solvent	t (h)	Product **30**		**136**[%]
			Yield [%][b]	ee [%][c]	
1	THF	72	45	59	49
2	CH_3CN	56	33	22	56
3	DME	82	29	27	55
4	CH_2Cl_2	68	15	16	73

[a]Reactions were carried out on 0.25 mmol scale at 0.625M with 1.5 equivalents of **128**. [b]Yields of isolated product. [c]Determined by HPLC using a Daicel Chiralcel OD column.

An increase in reaction temperature had a beneficial effect on the yield of **30** but little impact on its enantiomeric excess (Table 4.2, entry 1). However, when catalyst loading was increased from 5 mol% to 10 mol% **30** was formed in 78% yield and 72% enantiomeric excess at a reaction temperature of 10 °C (Table 4.2, entry 2). An increase in reaction temperature to 20 °C afforded **30** in higher yield but had a negative impact on its enantiomeric excess (97% yield and 69% ee, Table 4.2, entry 3). Finally, it was found that addition of oven-dried powdered 3Å molecular sieves to the reaction mixture

dramatically increased the enantiomeric excess of **30** (84% ee, Table 4.2, entry 4). These results gave confidence that we were moving towards optimized conditions for an asymmetric NHK reaction catalyzed by (+)-**70**.

Table 4.2 Effect of catalyst loading, temperature and additives on the NHK reaction of allyl bromide (**128**) with benzaldehye (**28**)[a]

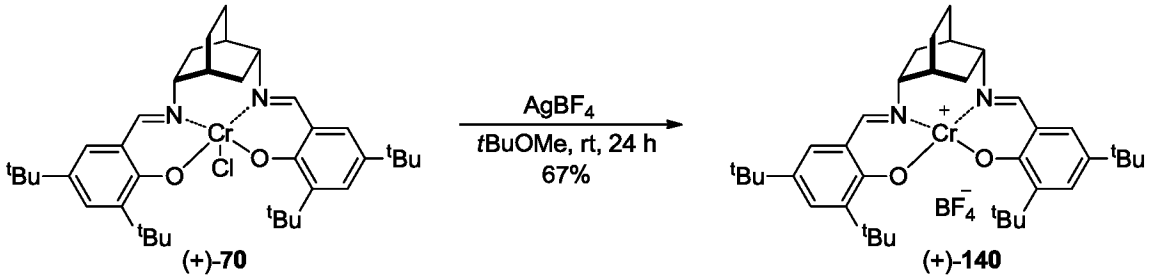


entry	catalyst loading (mol %)	additive	T [°C]	*t* [h]	product **30** yield [%][b]	product **30** ee [%][c]
1	5	-	10	68	57	56
2	10	-	10	18	78	72
3	10	-	20	15	97	69
4	10	3Å MS	10	8	92	84

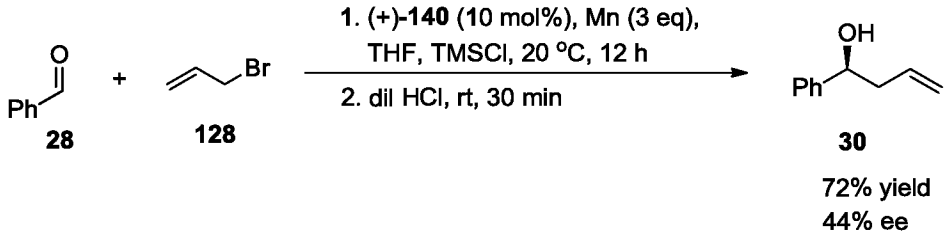
[a]Reactions were carried out on 0.125 mmol scale at 0.625M with 1.5 equivalents of **128**. [b]Yield of isolated product. [c]Determined by HPLC using a Daicel Chiralcel OD column.

One further variant in our enantioselective NHK reaction was explored, specifically exchange of chloride counter anion in chromium(III) complex (+)-**70** for tetrafluoroborate. Tetrafluoroborate complex (+)-**140** was prepared by reacting (+)-**70** with silver tetrafluoroborate in *tert*-butyl methyl ether at room temperature (Scheme 4.10) but it was found that this exchange of counter ion from chloride to non-coordinating tetrafluoroborate had an unfavorable effect on both yield and enantioselectivity of the reaction (72% yield and 44% enantiomeric excess, Scheme 4.11). This result persuaded

us to remain with (+)-**70** as the catalyst of choice for an asymmetric NHK reaction.



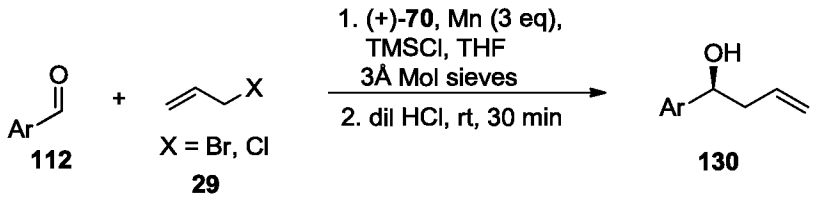
Scheme 4.10 Synthesis of tetrafluoroborate chromium(III) complex (+)-**140**



Scheme 4.11 Enantioselective NHK reaction catalyzed by chromium(III) tetrafloroborate complex (+)-**140**

Guided by the foregoing results, a broad portfolio of aromatic aldehydes **112** was studied in the NHK reaction with allyl halides **29** catalyzed by chromium(III)-salen complex (+)-**70** (Table 4.3, entries 1-9).

Table 4.3 Asymmetric NHK reaction of allyl halides **29** with aromatic aldehydes **112** catalyzed by chromium(III)-salen complex (+)-**70**: structrural effects on yield and enantioselectivity[a]

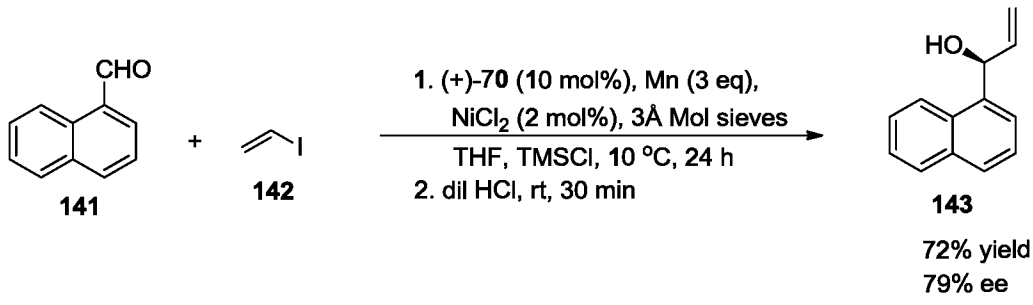


entry	Ar	T (°C)	t (h)	product **130**	
				Yield [%][b]	ee [%][c]
1[d]	C_6H_5	10	15	92	89
2	2-$CH_3C_6H_4$	10	6.5	92	92
3	4-$CH_3C_6H_4$	10	6.5	97	95
4	3-$CH_3OC_6H_4$	10	6	96	89
5	4-ClC_6H_4	20	5	96	96
6	3,5-$(CH_3O)_2C_6H_3$	10	8	95	93[e]
7	2,6-$Cl_2C_6H_3$	20	7	92	84
8	1-napthyl	20	4	97	97
9[f]	3-furyl	10	3	93	85

[a]Reactions were carried out on 0.125 mmol scale at 0.625M with 1.5 equivalents of allyl bromide. [b]Yields of isolated product. [c]Determined by HPLC using a Daicel Chiralcel OD column. [d]Reaction performed with 20 mol% of (+)-**70**. [e]The absolute configuration of **130** was not determined. [f]Allyl chloride was used instead of allyl bromide.

Homoallylic alcohols **130** were obtained in good yield and high enantiomeric excess after acidic hydrolysis of the intermediate silyl ether. Both electron-rich aldehydes (entries 2, 3) as well as electron-deficient aldehydes (entries 4-6) afforded alcohols **130** in high enantiomeric excess. Increased steric bulk around the aldehyde carbonyl led to diminished enantiomeric excess in **130** (84% enantiomeric excess; entry 7) and slightly lower enantioselectivity was also observed with an heteroaromatic aldehyde (85% enantiomeric excess, entry 9). The absolute configuration of **130** was established in all cases as (*S*), except for entry 6, by comparison of the measured specific rotation with the literature value.

The encouraging results with allylic halides noted above prompted us to examine the efficacy of our catalytic asymmetric NHK process with a vinyl halide. Vinyl iodide was chosen for this experiment due to its lower volatility compared to the corresponding chloride or bromide. A catalytic amount (2 mol%) of nickel(II) chloride was added to the reaction medium in this case.[5,6] Under the conditions specified in Table 4.2, entry 4, vinyl iodide (**142**) reacted with 1-naphthaldehyde (**141**) in the presence of (+)-**70** to afford allylic alcohol **143** in 72% yield and 79% enantiomeric excess (Scheme 4.12). The absolute configuration of **143** was found to be (*S*) by comparison of its specific rotation with the literature value.[14] Although the yield and enantiomeric excess of **143** falls short of values obtained with products from allyl halides (cf Table 4.3, entry 8), our result with vinyl iodide (**142**) compares well with previous efforts using vinyl halides in the asymmetric NHK reaction. Further studies to optimize NHK reaction conditions for the specific case of vinyl halides can be expected to improve product yield and enantioselectivity with (+)-**70**.



Scheme 4.12 Enantioselective NHK reaction of 1-naphthaldehyde (**141**) with vinyl iodide (**142**) catalyzed by chromium(III)-salen complex (+)-**70**

A catalytic cycle explaining the function of (+)-**70** as well as the role of manganese and trimethylsilyl chloride in our asymmetric NHK reaction is shown in

Figure 4.2. Chromium(III)-salen complex (+)-**70** is first reduced by manganese to chromium(II) complex **147** which then undergoes oxidative insertion into the allylic carbon-halogen bond of **29** forming allylchromium(III) species **144**. This nucleophilic organochromium species reacts with aldehyde **112** producing chromium(III) alkoxide **145** from which release of chromium(III) is facilitated by trimethylsilyl chloride. Since silicon is more oxyphilic than chromium, this exchange leads to homoallylic silyl enol ether **146**. A transition state analogous to **117** (Chapter 3, Figure 3.3) explains the preference for *si* face attack at the aldehyde carbonyl by the organochromium reagent which leads to (*S*) configuration of the homoallylic alcohol.

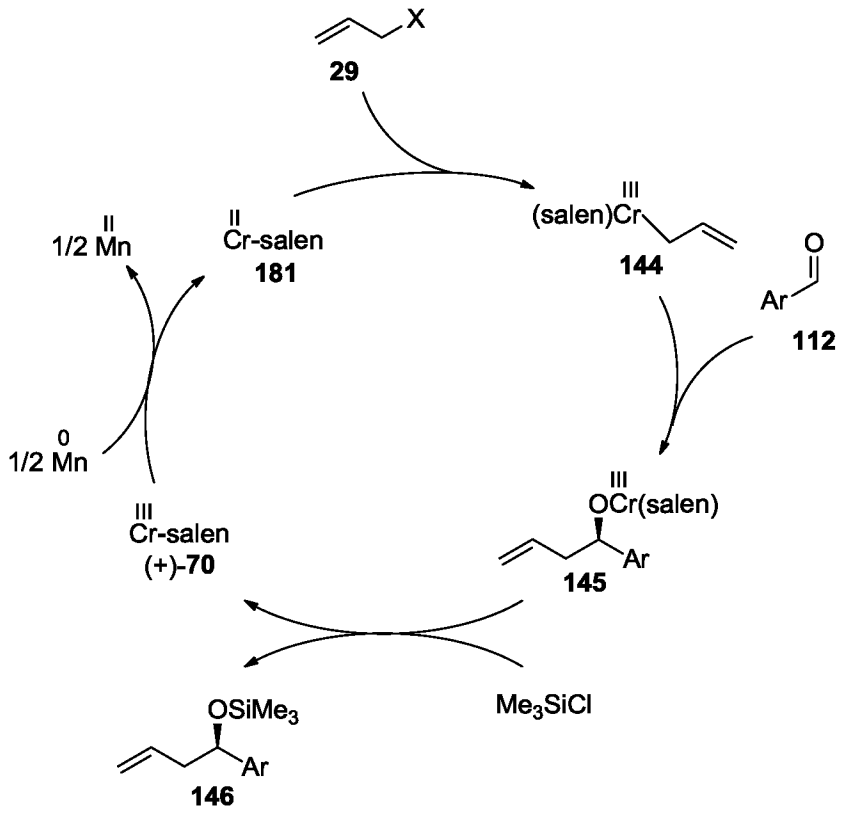


Figure 4.2 Proposed catalytic cycle for NHK allylation catalyzed by chromium(III)-salen complex (+)-**70**

In this chapter, we have shown that chromium(III)-salen complex (+)-**70** is an efficient catalyst for the asymmetric NHK reaction of an allylic halide with aldehydes, affording homoallylic alcohols in high enantiomeric excess. Extension of the asymmetric NHK reaction to a vinylic halide using (+)-**70** as catalyst appears promising but further studies are needed to find optimal conditions for the synthesis of enantioenriched allylic alcohols by this method.

4.3 References

1. Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, 93, 2207.
2. Okude, Y.; Hirano, S.; Hiyama, T.; Nozaki, H. *J. Am. Chem. Soc.*, **1977**, *99*, 3179.
3. Takai, K.; Kimura, K.; Kuroda, T.; Hiyama, T.; Nozaki, H. *Tetrahedron Lett.* **1983**, *24*, 5281.
4. Takai, K.; Kuroda, T.; Nakatasukasa, S.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1985**, *26*, 5585.
5. Jin, H.; Uenishi, J.; Christ, W.; Kishi, Y. *J. Am. Chem. Soc.* **1986**, *108*, 5644.
6. Takai, K.; Tagashira, M.; Kuroda, T.; Oshima, K.; Utimoto, K.; Nozaki, H. *J. Am. Chem. Soc.* **1986**, *108*, 6048.
7. Fürstner, A.; Shi, N. *J. Am. Chem. Soc.* **1996**, *118*, 12349.
8. Chen, C.; Tagami, K.; Kishi, Y. *J. Org. Chem.* **1995**, 60, 5386.
9. Sugimoto, K.; Aoyagi, S.; Kibayashi, C. *J. Org. Chem.* **1997**, *62*, 2322.
10. Bandini, M.; Cozzi, P.; Melchiorre, P.; Umani-Ronchi, A. *Angew. Chem. Int. Ed.*, **1999**, *38*, 3357.
11. Inoue, M.; Suzuki, T.; Nakada, M. *J. Am. Chem. Soc.* **2003**, *125*, 1140.
12. Xia, G.; Yamamoto, H. *J. Am. Chem. Soc.* **2006**, *128*, 2554.
13. Berkessel, A.; Menche, D.; Sklorz, C. A.;Schroder, M.; Paterson, I. *Angew. Chem., Int. Ed.* **2003**, *42*, 1032.

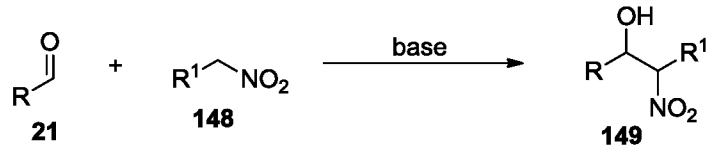
14. Da, C. S.; Wang, J. R.; Yin, X. G.; Fan, X. Y.; Liu, Y.; Yu, S. L. *Org*. *Lett*. 2**009**, *11*, 5578.

CHAPTER 5

The Asymmetric Henry Reaction

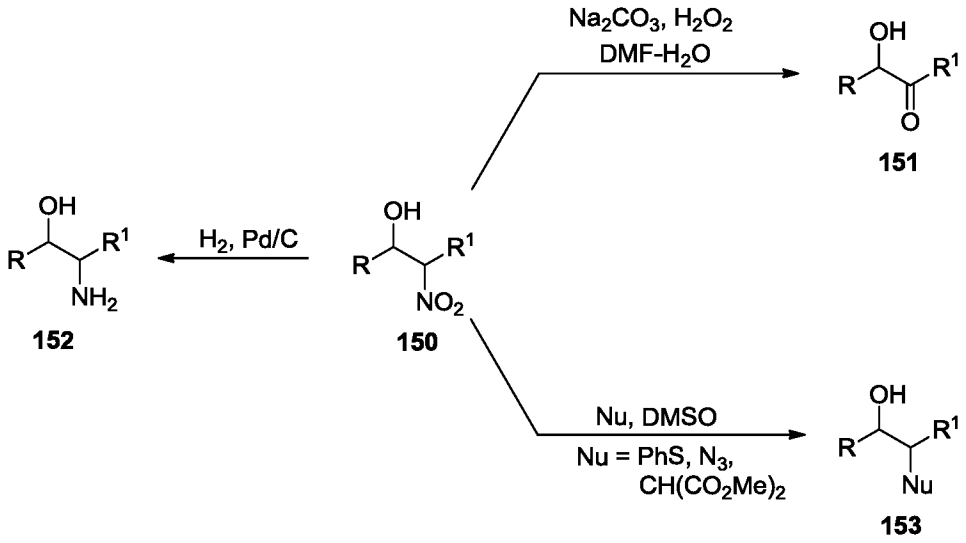
5.1 Introduction

The reaction of a nitro alkane with an aldehyde or ketone, sometimes called the nitroaldol condensation but more generally known as the Henry reaction, was first reported in 1895 when it was shown by L. Henry that base promoted addition of a nitro alkane **148** to an aldehyde **21** furnished a 1,2-functionalized nitro alcohol **149** (Scheme 5.1).[1]



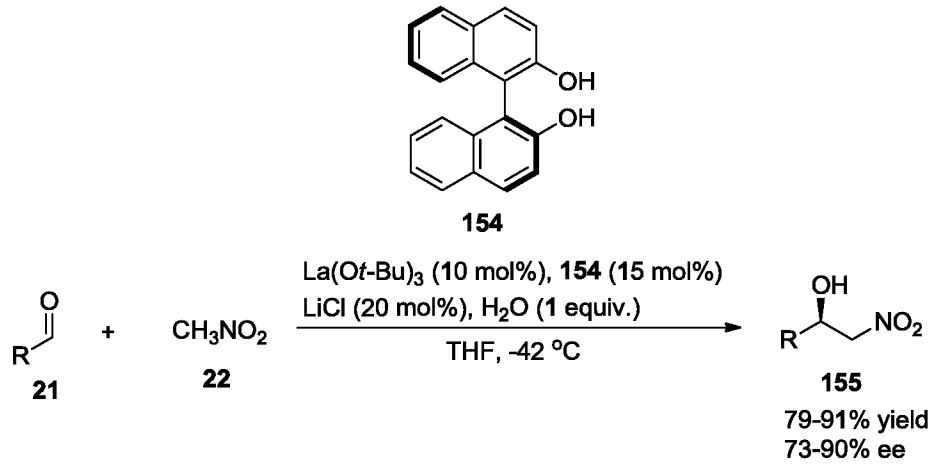
Scheme 5.1 Base promoted addition of nitroalkane **148** to aldehyde **21**

The nitroaldol or Henry reaction is one of the most widely used C-C bond forming processes since it affords versatile products which are frequently used as intermediates in organic synthesis.[2] The β-nitro alcohol product **150** from a Henry reaction can be converted into a α-hydroxy ketone **151** (Nef reaction), a 1,2-amino alcohol **152** (by hydrogenation), a vicinally substituted alcohol **153** by nucleophilic displacement of the nitro group and many other derivatives (Scheme 5.2).[3]



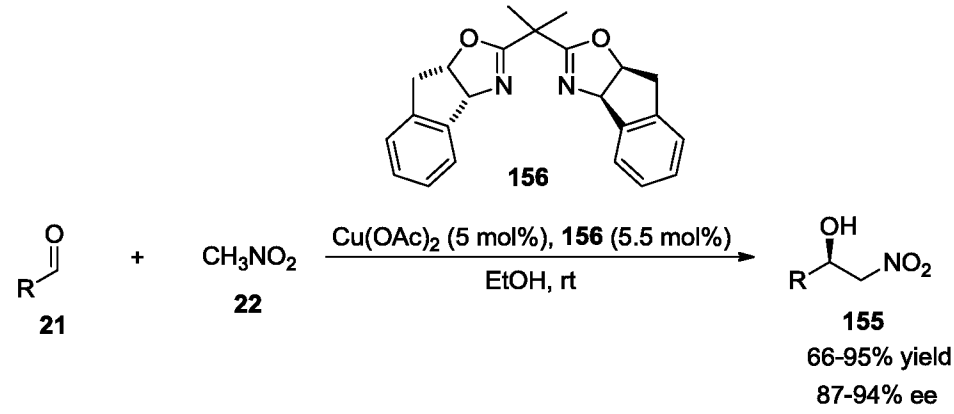
Scheme 5.2 Transformations of β-nitroalcohol **150** into α-hydroxy ketone **151**, 1,2-amino alcohol **152** and functionalized alcohol **153**

It took a century after the discovery of the Henry reaction to develop an enantioselective version of this condensation. The main obstacles were lack of stereoselectivity in the reaction due to its reversibility and facile epimerization at the nitro-substituted carbon atom. The first breakthrough in the search for an enantioselective version of the Henry reaction was due to Shibasaki and co-workers in 1992 when they synthesized nitro alcohols **155** in good enantiomeric excess using a combination of (*S*)-BINOL (**154**) and lanthanum(III) *tert*-butoxide (Scheme 5.3) as catalyst.[4] It was proposed that the lanthanum metal acts as a Lewis acid while the lithium binaphthoxide moiety functions as a Brønsted base to induce asymmetry in the nitroaldol product **155**.[5-7]



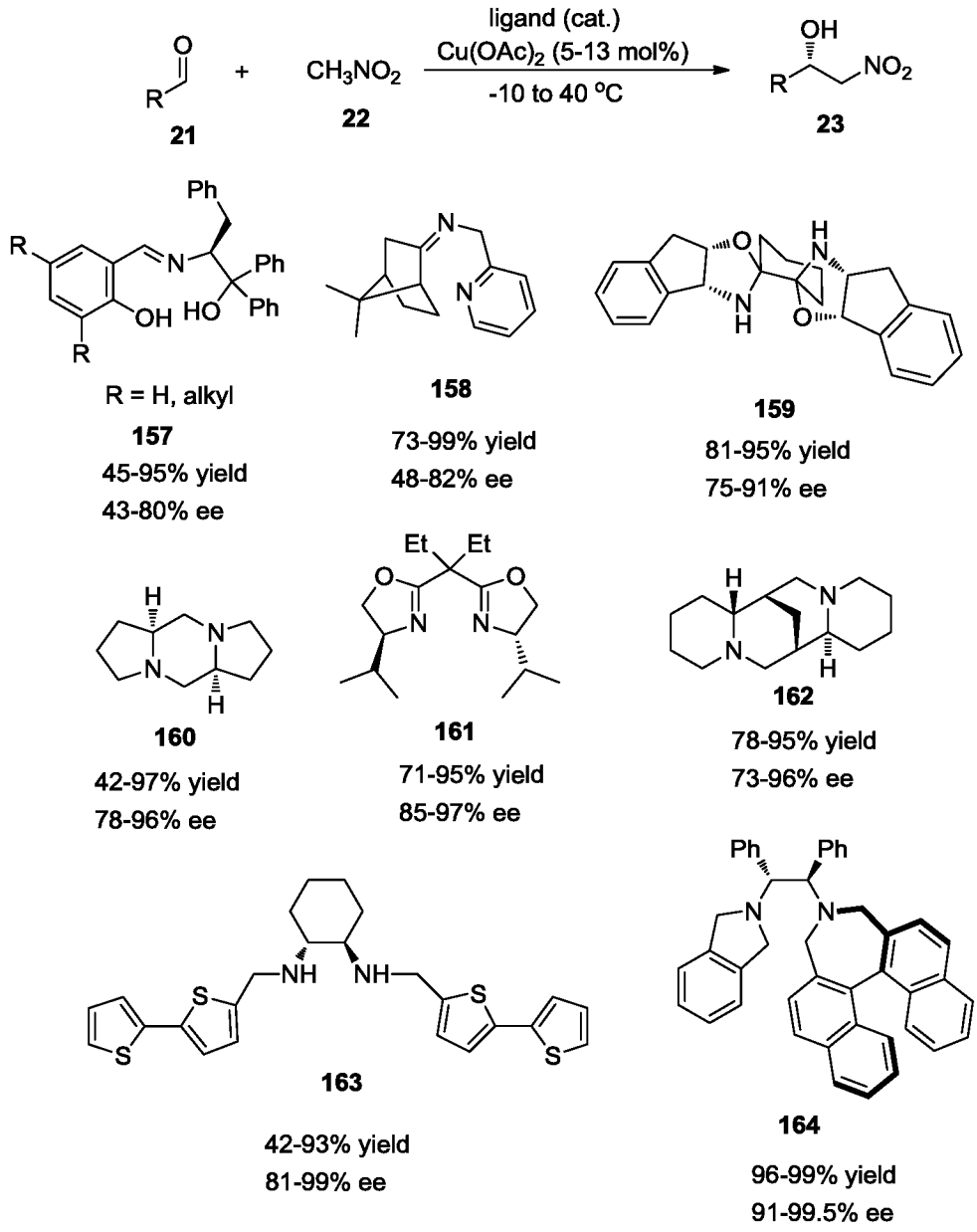
Scheme 5.3 Shibasaki's (*S*)-BINOL (**154**) and lanthanum(III) *tert*-butoxide catalyzed Henry reaction

Following Shibasaki's discovery, several transition metal catalyzed enantioselective Henry reactions were reported in which copper played a prominent role. The first copper catalyzed enantioselective Henry reaction was reported by Evans and coworkers[8] who showed that the reaction between nitromethane (**22**) and aldehyde **21** in the presence of a catalytic amount of copper acetate and bis(oxazoline) ligand **156** afforded nitro alcohols **155** in good yield and enantiomeric excess (Scheme 5.4).



Scheme 5.4 Evans' enantioselective Henry reaction catalyzed by copper acetate and bis(oxazoline) ligand **156**

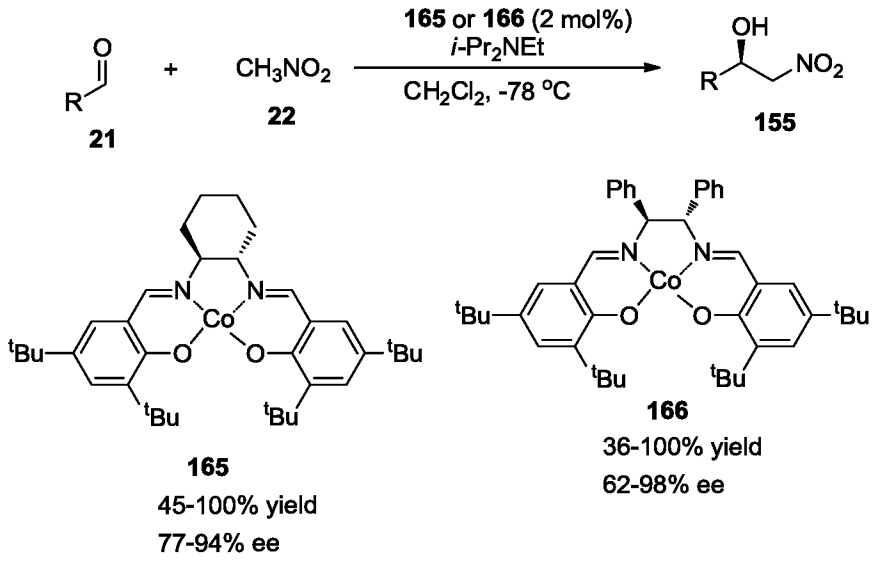
Inspired by the pioneering work of Evans, many bidentate chiral ligands (**157-164**) bearing nitrogen and oxygen as the donor atoms were synthesized. These ligands were studied in combination with copper(II) acetate as catalysts for the Henry reaction and led to moderate to good asymmetric induction in the reaction of nitromethane (**22**) with aldehydes **21** that gave β-nitro alcohols **23** (Scheme 5.5).[9-16]



Scheme 5.5 Chiral ligands used for copper(II) catalyzed enantioselective Henry reaction

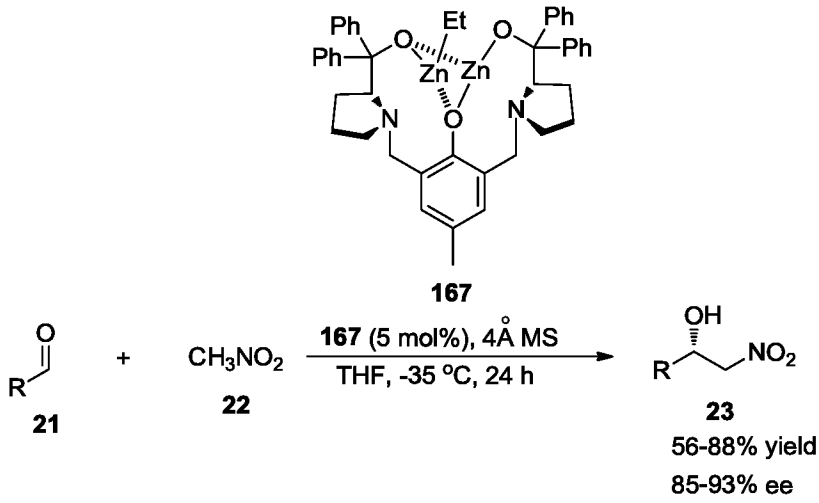
Yamada and coworkers employed cobalt(II)-salen complexes **165** and **166** derived from chiral 1,2-diamines in their study of the asymmetric Henry reaction between

nitromethane (**22**) and aromatic aldehydes **21**. These catalysts resulted in an enantiomeric excess up to 98 % in the nitroaldol product **155** (Scheme 5.6).[17]



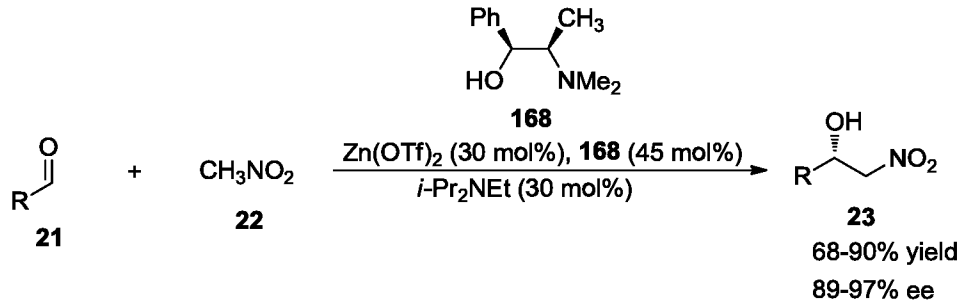
Scheme 5.6 Yamada's enantioselective Henry reaction catalyzed by cobalt(II)-salen complexes **165** and **166**

In 2002, Trost and co-workers reported that the dinuclear zinc complex **167** was a catalyst for the asymmetric nitroaldol reaction of nitromethane (**22**) with aldehydes **21**. β-Nitro alcohols **23** were produced in varying yield and enantiomeric excess from this reaction (Scheme 5.7).[18]



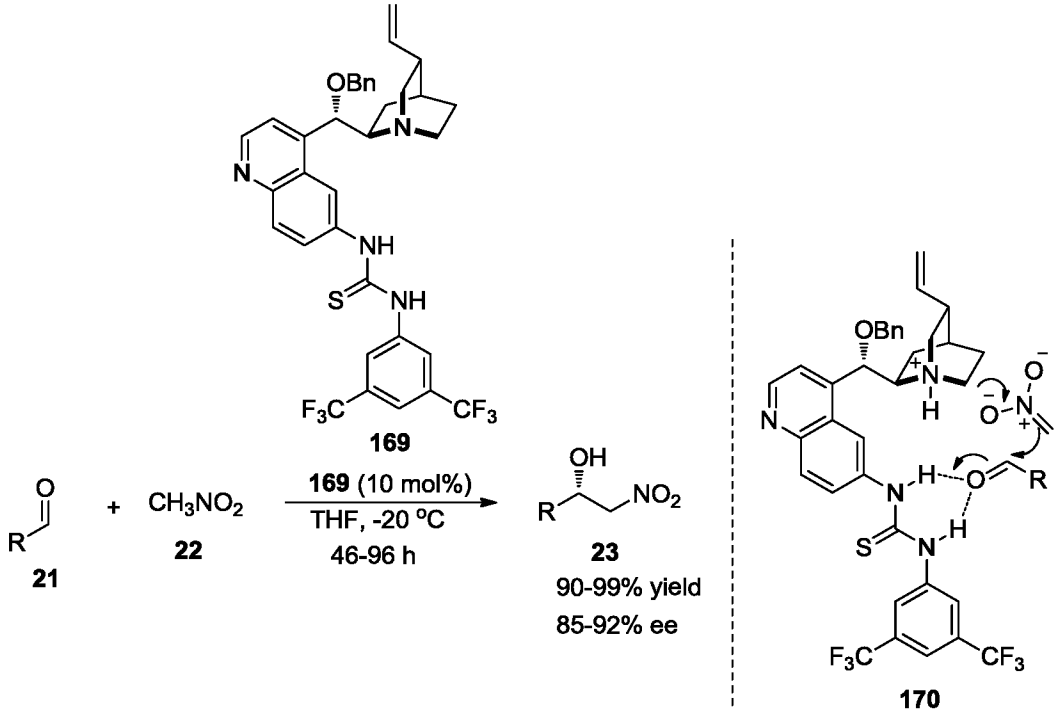
Scheme 5.7 Trost's enantioselective Henry reaction catalyzed by chiral zinc complex **167**

More recently, Palomo reported an enantioselective nitroaldol condensation using zinc (II) triflate, diisopropylethylamine and (+)-*N*-methylephedrine **168**.[19] In contrast to the dinuclear zinc complex of Trost,[18] the acidic and basic centers of Palomo's catalytic system are not integrated into the same molecular entity and therefore allow for easier screening of different combinations of catalyst components. The amino alcohol **168** plays the dual role of chiral inductor and base, affording nitro alcohol **23** in good yield and enantiomeric excess (Scheme 5.8).



Scheme 5.8 Palomo's enantioselective Henry reaction catalyzed by zinc triflate and *N*-methylephedrine **168**

Although the use of metal-free chiral catalysts in the asymmetric Henry reaction had been explored as early as 1994, they failed to induce enantiomeric excess in the nitro alcohol product higher than 54%.[20] This changed in 2006 when the Cinchona alkaloid derivative **169**, synthesized by Hiemstra and coworkers, was found to give excellent enantioselectivity in an organocatalytic nitroaldol condensation of nitromethane (**22**) with aryl aldehydes **21**.[21] A transition state **170** was proposed for this reaction in which the thiourea moiety of **169** activates the aldehyde through double hydrogen bonding with the carbonyl oxygen while nitromethane is converted to its reactive nitronate form by the basic quinuclidine moiety of the catalyst (Scheme 5.9).

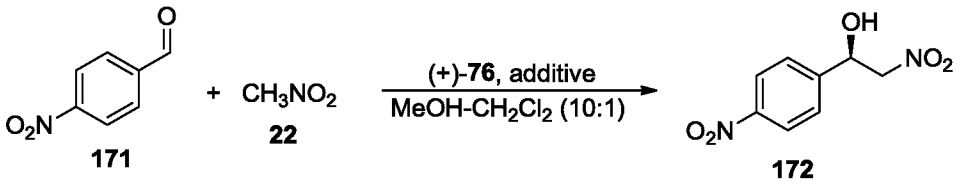


Scheme 5.9 Hiemstra's enantioselective Henry reaction and proposed transition state **170** catalyzed by Cinchona based thiourea derivative **169**

5.2 A *Cis*-2,5-diaminobicyclo[2.2.2]octane based copper catalyst for the enantioselective Henry reaction

The favorable results obtained with chromium(III) complex (+)-**70** as a catalyst for the enantioselective hetero-Diels-Alder reaction (chapter 3, Table 3.2) and for the Nozaki-Hiyama-Kishi reaction (chapter 4, Table 4.3) of aldehydes suggested that the chiral scaffold, *cis*-2,5-diaminobicyclo[2.2.2]octane, responsible for asymmetric induction in these reactions could be equally effective in other venues. The prospect of using metal complexes other than those containing chromium but especially those based on transition metals was also appealing. Transition metal complexes already prepared from salen ligand (+)-**35** include a stable copper(II) complex (+)-**76** (chapter 2, Scheme 2.10), and since it was known from the work of Evans,[8] Pedro,[10] Singh[12,13] and Arai[16] that the Henry reaction can be catalyzed by copper(II) salts, (+)-**76** was investigated as a catalyst for the Henry reaction of *p*-nitrobenzaldehyde (**171**) with nitromethane (**22**). A 10:1 mixture of methanol and methylene chloride was used as solvent for the reaction. An initial experiment at 5 mol% catalyst loading and a reaction temperature of 20 °C gave nitroaldol product **172** in low yield and poor enantiomeric excess, but addition of 4Å molecular sieves and a higher reaction temperature of 45 °C was found to give an improved yield of **172**. However, the level of asymmetric induction remained poor (Table 5.1, entry 3).

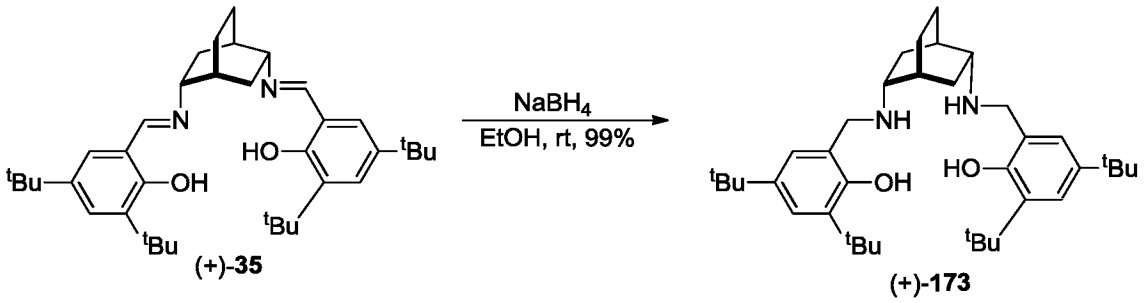
Table 5.1 Asymmetric Henry reaction catalyzed by copper(II)-salen complex (+)-**76**[a]



entry	(+)-**76** (mol%)	additive	temp (° C)	t (h)	product **172** yield [%][b]	product **172** ee [%][c]
1	5	-	20	24	22	28
2	20	4 Å MS	20	24	25	30
3	20	4 Å MS	45	8	76	10

[a]Reactions were carried out on 0.2 mmol scale with 1 mL of nitromethane.[b]Yieldof isolated product. [c]Determined by HPLC using a Daicel Chiralcel OD column.

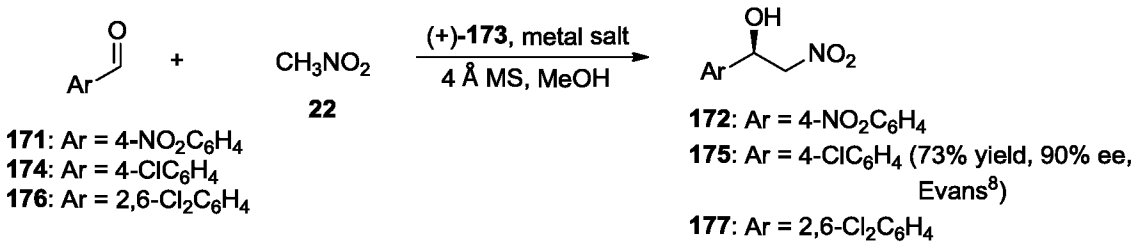
Chiral ligands known to form complexes with copper(II) salts include several based on 1,2-secondary diamines, eg **159** and **163** (Scheme 5.5), and these complexes have been shown to give products from the Henry reaction in high enantiomeric excess. Recognizing that this structural option was available to us in the form of diamine **173**, (+)-**35** was reduced with sodium borohydride in ethanol. Tetrahydrosalen ligand (+)-**173** was obtained in near quantitative yield from this reduction (Scheme 5.10).



Scheme 5.10 Synthesis of tetrahydrosalen ligand (+)-**173** from (+)-**35**

Tetrahydrosalen ligand (+)-**173** in combination with copper(I) and copper(II) salts was tested as a catalyst in the Henry reaction of nitromethane (**22**) with aryl aldehydes (Table 5.2). First results with **171** and nitromethane using (+)-**173** at 20 mol% and copper(II) triflate at 5 mol% as the metal source indicated that, while the chemical yield of **172** was acceptable, the background reaction leading to racemic **172** overwhelmed asymmetric induction from (+)-**173** (Table 5.2, entry 1). However, when the toluene complex of copper(I) triflate[22] was used at 1 mol% with (+)-**173** at 10 mol% in dry methanol (entry 5), a marked increase in the enantiomeric excess of **172** was observed (entry 5). The optimum reaction temperature was found to be 40 °C. When these conditions were applied to the Henry reaction of *p*-chlorobenzaldehyde (**174**) with nitromethane (**22**) an improved yield and enantiomeric excess of nitro alcohol **175** was observed (entry 6), while 2,6-dichlorobenzaldehyde (**176**) as substrate raised these figures further (89% yield, 94% enantiomeric excess, entry 7). The absolute configuration of **172** and **175** was established as (*R*) by comparison of their specific rotation with the literature value.[8]

Table 5.2 Asymmetric Henry reaction of aromatic aldehydes with nitromethane. Effect of varying metal ion source, copper/(+)-**173** ratio, catalyst loading and reaction temperature[a]



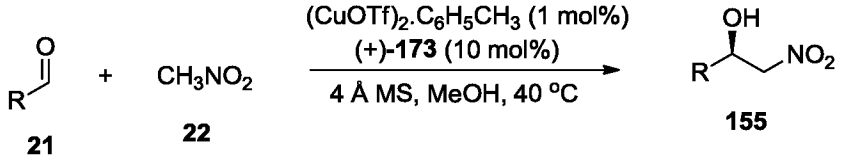
entry	Ar	ligand loading (mol%)	metal salt (mol%)	temp (° C)	t (h)	product **172**, **175** or **177** yield [%][b]	ee [%][c]
1	4-$NO_2C_6H_4$ (**171**)	20	$Cu(OTf)_2$ (5)	20	30	68	7
2	4-$NO_2C_6H_4$ (**171**	10	$Cu(OTf)_2$ (2.5)	20	30	55	28
3[d]	4-$NO_2C_6H_4$ (**171**)	10	$(CuOTf)_2.C_6H_5CH_3$ (5)	20	24	49	26
4	4-$NO_2C_6H_4$ (**171**)	10	$(CuOTf)_2.C_6H_5CH_3$ (2.5)	40	15	85	43
5	4-$NO_2C_6H_4$ (**171**)	10	$(CuOTf)_2.C_6H_5CH_3$ (1)	40	20	64	79
6	4-ClC_6H_4 (**174**)	10	$(CuOTf)_2.C_6H_5CH_3$ (1)	40	16	76	83
7	2,6-$Cl_2C_6H_3$ (**176**)	10	$(CuOTf)_2.C_6H_5CH_3$ (1)	40	20	89	94

[a]Reactions were carried out on 0.2 mmol scale with 0.6 mL of nitromethane. [b]Yield of isolatedproduct.[c]DeterminedbyHPLCusing a Daicel Chiralcel AD, OD column. [d]No molecular sieves added.

Guided by the favorable results (entries 5-7) in Table 5.2, we next examined a broad portfolio of aromatic aldehydes (Table 5.3, entries 1-11) in their reaction with nitromethane catalyzed by the copper(I) complex of (+)-**173**. It was found that with either electron donating (entries 2, 3, 6, 10) or electron withdrawing groups (entries 4, 5, 7-9) in the aromatic ring of the aldehyde, nitro alcohol **155** was formed in high yield and enantiomeric excess. Reaction times varied widely; for example 2,4-dinitrobenzaldehyde (entry 8) reacted with nitromethane (**22**) much more rapidly than did 2-methoxy-benzaldehyde (entry 2), presumably because of the high electrophilicity of the aldehyde carbonyl in the former. Heteroaromatic aldehydes (entries 12 and 13), aliphatic aldehydes

(entries 14 and 15) as well as α,β-unsaturated aldehydes (entries 16 and 17) also gave a high yield and enantiomeric excess of Henry adduct **155**. The absolute configuration of **155** was established in all cases as (*R*), except for entries 8-10 and 17, by comparison of the measured specific rotation with the literature value.

Table 5.3 Asymmetric synthesis of β-nitro alcohols with catalyst (+)-**173** and copper(I) triflate under optimized conditions. Structural effects on yield and enantioselectivity[a]



21 **22** **155**

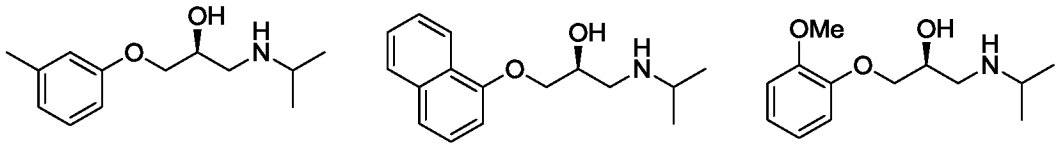
entry	R	t (h)	product **155** yield [%][b]	ee [%][c]
1	Ph	20	90	92
2	3-$CH_3C_6H_4$	24	95	96
3	2-$MeOC_6H_4$	60	81	91
4	3-$MeOC_6H_4$	18	94	96
5	4-$CF_3C_6H_4$	24	96	96
6	2-$(OH)C_6H_4$	24	97	92
7	3,5-$(OMe)_2C_6H_3$	22	93	96
8	2,4-$(NO_2)_2C_6H_3$	12	96	95[d]
9	3-(4-$MeOC_7H_6O$)-4-$(NO_2)C_6H_3$	24	99	95[d]
10	2-(OH)-3-(Br)-5-$(Me_3C)C_6H_2$	24	87	98[d]
11	1-naphthyl	18	98	93
12	2-furyl	24	87	94
13	3-furyl	20	98	95
14	cyclohexyl	42	90	94
15	Me_3C	51	89	95
16	$CH_3CH=C(CH_3)$ (*E*)	18	83	93
17	$PhCH=C(CH_3)$ (*E*)	48	95	97[d]

[a]Reactions were carried out on 0.2 mmol scale with 0.6 mL of nitromethane. [b]Yield of isolated product. [c]Determined by HPLC using a Daicel Chiralcel AD, OD, OJ, OD-H columns. [d]The absolute configuration of **155** was not determined.

Although the copper(I) complex of tetrahydrosalen ligand (+)-**173** was found to be much superior to copper(II)-salen complex (+)-**76** as a catalyst for the asymmetric Henry reaction, the complex itself is unstable and we were unable to obtain a sample suitable for characterization by X-ray crystallographic analysis. Nevertheless, the demonstration that a copper(I)-tetrahydrosalen complex prepared in situ is a powerful catalyst for the enantioselective synthesis of β-nitro alcohols provided opportunity to

showcase this catalytic system in a practical synthesis of a commercially important material. The vehicle selected for this exercise was a class of drugs known as beta-blockers.

Beta-blockers are drugs that target the beta-receptor present in cells of the heart muscle, smooth muscle, airways, arteries, kidneys, and other tissues that are part of the sympathetic nervous system. Beta-receptors are associated with stress responses, especially when they are activated by epinephrine (adrenaline). Beta-blockers interfere with binding of the beta-receptor with epinephrine and thereby diminish the effects of stress hormones. For this reason, beta-blockers are used medically for the management of hypertension[23] and cardiac arrhythmias;[24] they are especially effective in protecting the heart from a second heart attack after an initial one. The most commonly used blocking agents of the beta-adrenergic receptor are Toliprolol (**178**),[25] Moprolol (**179**)[26] and Propanolol (**180**, Figure 5.1).[27]

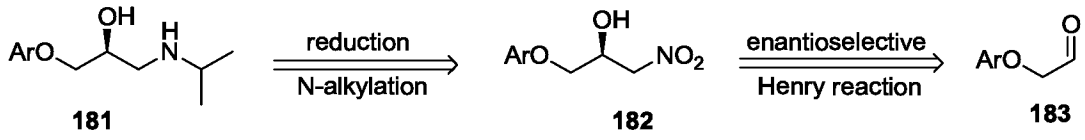


178, (*S*)-Toliprolol **179**, (*S*)-Propanolol **180**, (*S*)-Moprolol

Figure 5.1 Beta-adrenergic receptor blocking agents

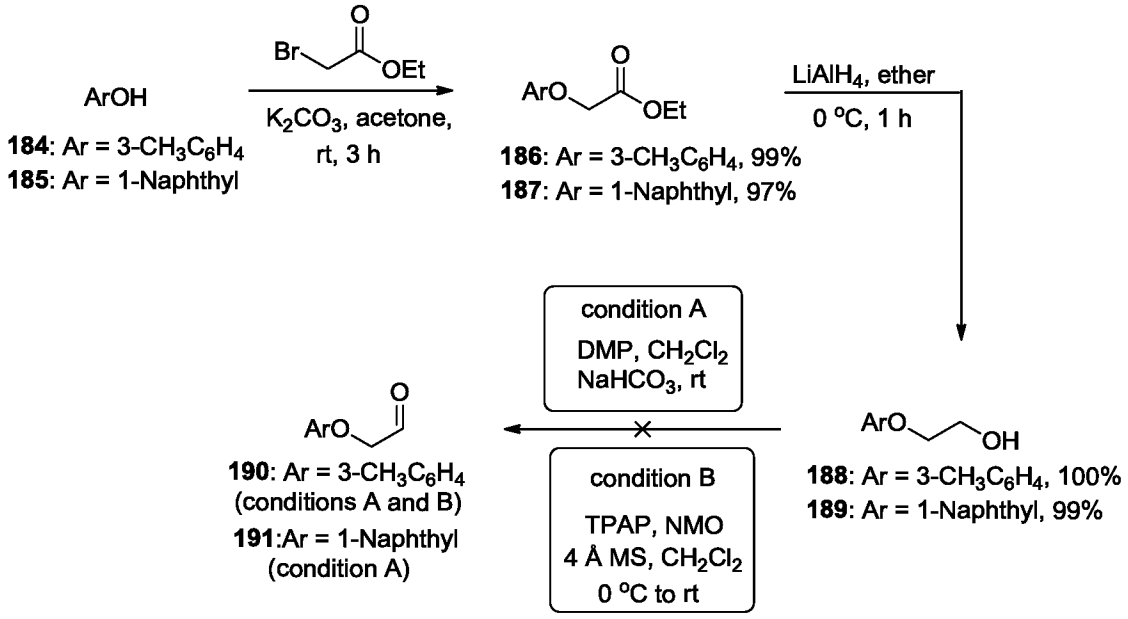
Each of these drugs features a 1-aryloxy-3-isopropylamino-2-propanol template (**181**, Scheme 5.11) with the active enantiomer having (*S*) configuration. Synthetically, they can be envisaged as reduction and *N*-alkylation products derived from β-nitro alchol **182** which in turn would be accessible from α-aryloxy aldehyde **183** via an

enantioselective Henry reaction. The step from **183** to **182** would thus afford a test of the efficacy of our copper(I)-tetrahydrosalen catalyst system based on ligand (+)-**173**.



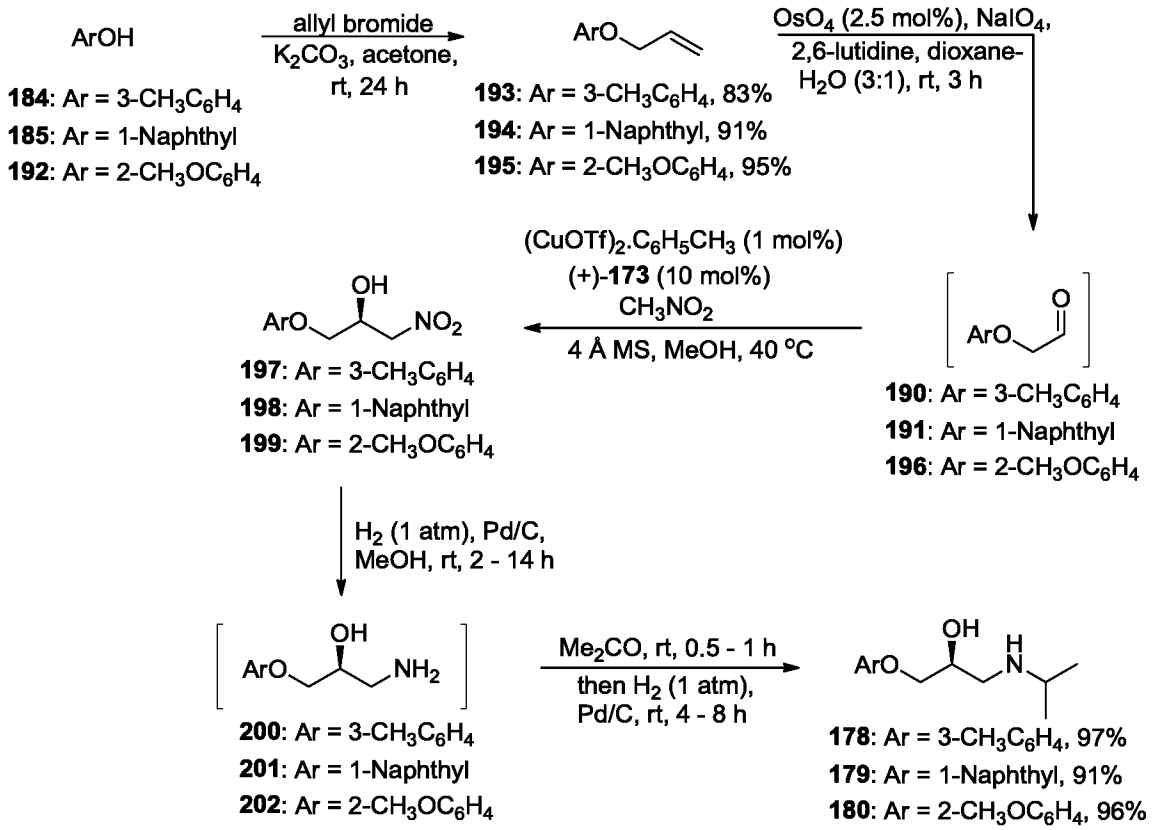
Scheme 5.11 Retrosynthetic analysis of 1-aryloxy-3-isopropylamino-2-propanol **181**

In the forward direction, *m*-cresol (**184**) and 1-naphthol (**185**) were alkylated with ethyl bromoacetate under basic conditions to give α-aryloxy esters **186** and **187** which were reduced quantitatively to 2-aryloxyethanols **188** and **189** using lithium aluminum hydride. However, attempts to oxidize **188** and **189** and isolate the corresponding aldehydes **190** and **191** using conventional oxidants were unsuccessful due to the instability associated with the desired α-aryloxy aldehydes (Scheme 5.12).



Scheme 5.12 Attempted synthesis of α-aryloxy aldehydes **190** and **191**

Our failure to isolate α-aryloxy aldehydes **190** and **191** from oxidation of the corresponding primary alcohols prompted us to devise an alternative sequence to these unstable compounds in which substituted phenols **184**, **185**, and **192** were first allylated to provide allyl aryl ethers **193-195**. Oxidative cleavage of the allyl residue in **193-195** with a catalytic amount of osmium tetroxide and sodium periodate furnished aldehydes **190**, **191** and **196** which were not isolated but were reacted in situ with nitromethane under the conditions specified in Table 5.3. The results of the asymmetric Henry reaction of **190**, **191** and **196** with nitromethane are shown in Table 5.4 and confirm that ligand (+)**-173** is an efficient catalyst for conversion of these aldehydes to highly enantioenriched nitro alcohols **197-199**. Catalytic hydrogenation of **197-199** led to the corresponding amino alcohols **200-202** which upon condensation in situ with acetone followed by a second catalytic hydrogenation furnished the target compounds **178-180** (Scheme 5.13). This sequence produced (*S*)-Toliprolol (**178**), (*S*)-Propanolol (**179**) and (*S*)-Moprolol (**180**) in 80%, 75% and 85% overall yield, respectively, starting from commercially available phenols **184**, **185** and **192**. Taking the example of Propanolol (**179**), a comparison of our synthesis with that of Sudalai and coworkers (Table 5.5)[28] shows that our synthetic sequence is shorter and much more efficient than that reported in the literature.



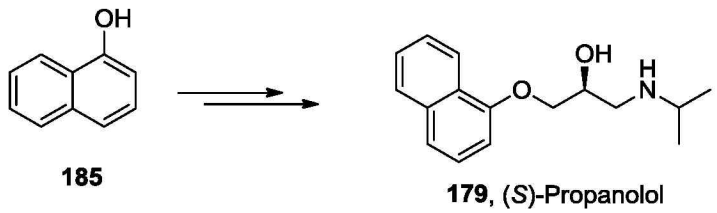
Scheme 5.13 Syntheses of beta-blockers (*S*)-Toliprolol (**178**), (*S*)-Propanolol (**179**) and (*S*)-Moprolol (**180**)

Table 5.4 Asymmetric Henry reaction of aldehydes **190**, **191** and **196** with nitromethane catalyzed by (+)-**173**[a]

entry	aldehyde (Ar)	product	Yield [%][b]	ee [%][c]
1	**190** (3-$CH_3C_6H_4$)	**197**	90	96
2	**191** (1-Naphthyl)	**198**	90	97
3	**196** (2-$CH_3OC_6H_4$)	**199**	93	94

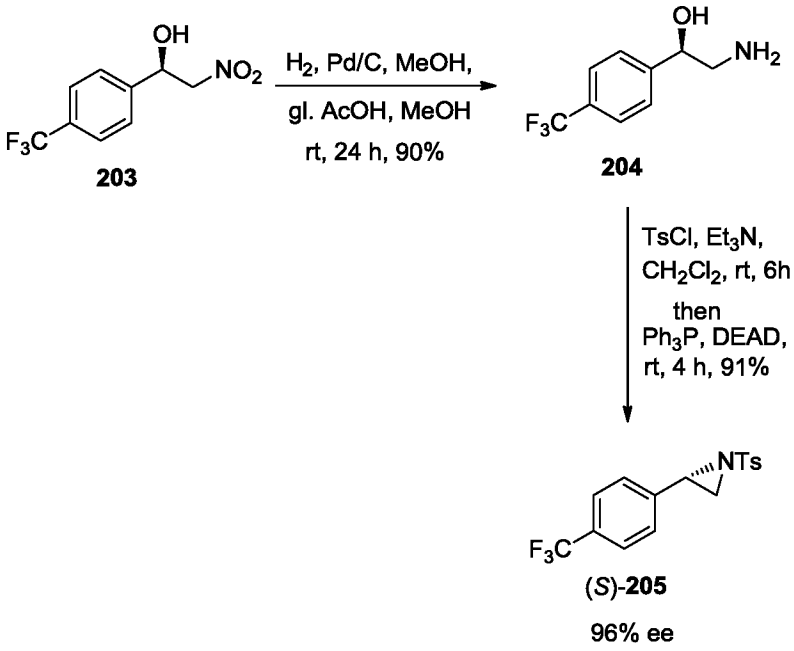
[a]Reactions were carried out on 0.2 mmol scale with 0.6 mL of nitromethane. [b]Yields based on allyl ethers **193-195**. [c]Determined by HPLC using a Daicel chiralcel OD column.

Table 5.5 Comparison of this synthesis of Propanolol (**179**) with that reported in the literature



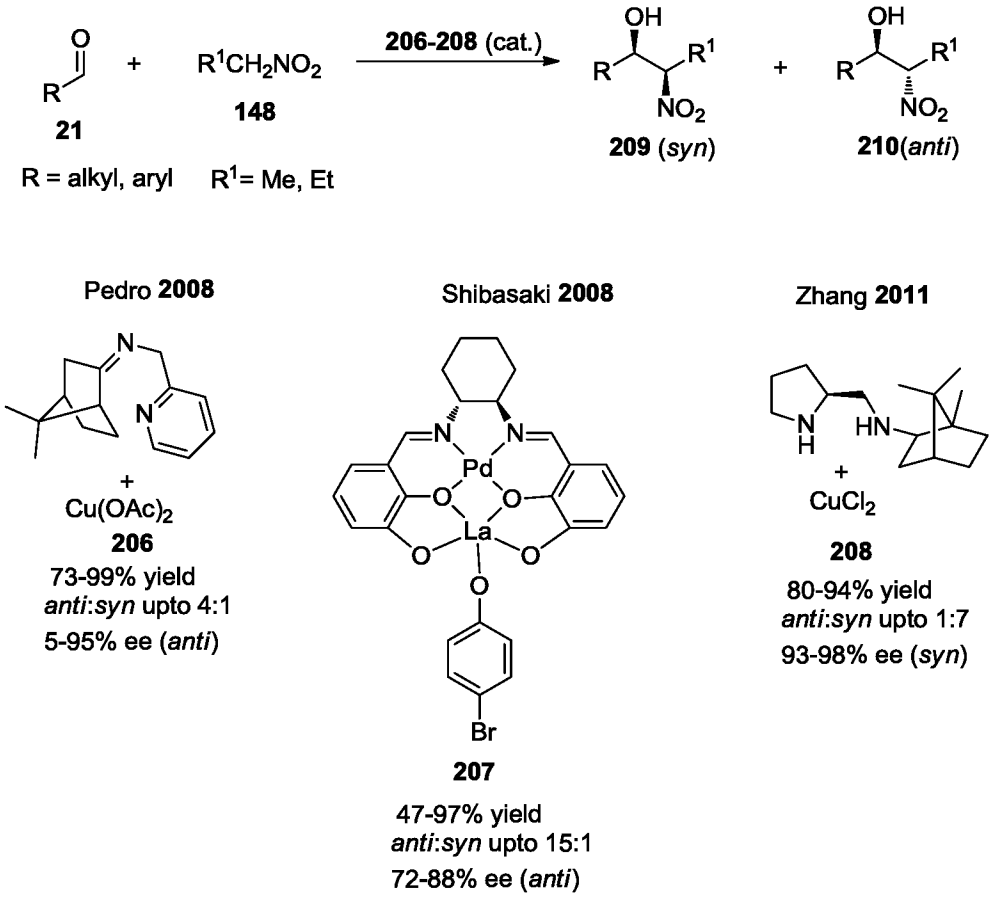
	Literature Method Sudalai *et. al. Tetrahedron* **2005**, *61*, 2831	This work
No of steps	8	**5**
Overall yield	10.4%	**74.5%**

Chiral β-nitro alcohols provide an entry to enantioenriched aziridines via reduction of the nitro group to an amine followed by intramolecular displacement of the vicinal oxygen function. To exemplify this application of our asymmetric Henry reaction, nitroaldol product **203** was converted to amino alcohol **204** by catalytic hydrogenation using 10% palladium on carbon as catalyst (Scheme 5.13). Sulfonylation of the amine moiety of **204** with *p*-toluenesulfonyl chloride followed by a Mitsunobu reaction[29] with diethyl azodicarboxylate and triphenylphosphine furnished aziridine (*S*)-**205** in good yield and 96% enantiomeric excess (Scheme 5.13). This enantioselective route from an aldehyde to an aziridine provides a pathway to a variety of nitrogen containing structures by ring opening of the aziridine.



Scheme 5.14 Transformation of β-nitro alcohol **203** to aziridine (*S*)-**205**

The high stereoselectivity obtained in addition of nitromethane to aldehydes (Tables 5.3 and 5.4) using a copper(I) complex of tetrahydrosalen ligand (+)-**173**, induced us to undertake a study of diastereoselectivity associated with higher order nitroalkanes **148** in the asymmetric Henry reaction of aldehydes. Only a very small number of catalytic systems have been investigated in the Henry reaction with nitroalkanes other than nitromethane, three examples in this category being catalytic systems **206-208** devised by Pedro,[30] Shibasaki[31] and Zhang.[32] In most cases, the *anti* nitroaldol product **210** is formed predominantly. The maximum *anti*/*syn* ratio of 15:1 was obtained with **207**; *syn* isomer **209** is formed at best with a *syn*/*anti* ratio of 7:1 with ligand **208** and copper(II) chloride (Scheme 5.15).

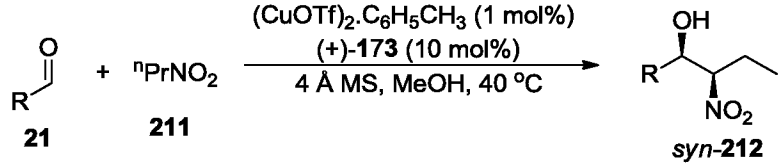


Scheme 5.15 Enantioselective Henry reaction of aldehydes **21** with higher order nitroalkanes **148** catalyzed by **206-208**

In our case, the reactions of benzaldehyde and 1-naphthaldehyde with nitropropane (**211**) in the presence of (+)-**173** and copper(I) triflate toluene complex under conditions specified in Table 5.3 gave a *syn*/*anti* ratio of nitroaldol products strongly favoring *syn* isomer **212**. Nitro alcohols **212** were formed in very high enantiomeric excess in both reactions (Table 5.5). Since **212** (R = phenyl and R = 1-naphthyl) are known compounds, their relative configuration was established by comparison of their NMR spectral properties with those from the literature while their

absolute configuration was confirmed as (*R*,*R*) by comparison of their specific rotations with the literature value.[32]

Table 5.5 Asymmetric addition of 1-nitropropane to benzaldehyde and 1-naphthaldehyde catalyzed by (+)-**173**/copper(I) triflate toluene complex[a]



21 **211** ***syn*-212**

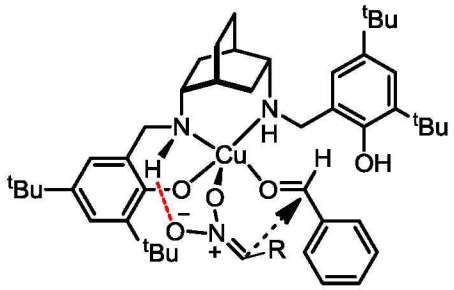
For R = Ph *syn*/*anti* 29:71 (Pedro)[30]

entry	R	t (h)	product **212** dr *syn*/*anti*[b]	yield [%][c]	ee [%][d]
1	Ph	24	>20:1	96	97
2	1-naphthyl	28	>50:1	93	98

[a]Reactions were carried out on 0.2 mmol scale with 0.6 mL of nitropropane. [b]Determined by ^{1}H NMR analysis. [c]Combined yields of *syn* and *anti* isomers. [d]Determined by HPLC using a Daicel Chiralcel OD-H, AS-H column.

It is clear from the results in tables 5.3 and 5.4 that there is a strong preference for (1*R*,2*R*,4*R*,5*R*) ligand (+)-**173** to give nitroaldol products **155** of (*R*) configuration in the reaction of aldehydes with nitromethane. This result stipulates that attack by nitromethane occurs predominantly at the *si* face of the aldehyde carbonyl group; a transition state **213** rationalizing this outcome is proposed in Figure 5.3. As with the transition state model presented in chapter 3, reactants are coordinated to copper(I) complex **213** in the right front quadrant below the bicyclic scaffold with C-C bond

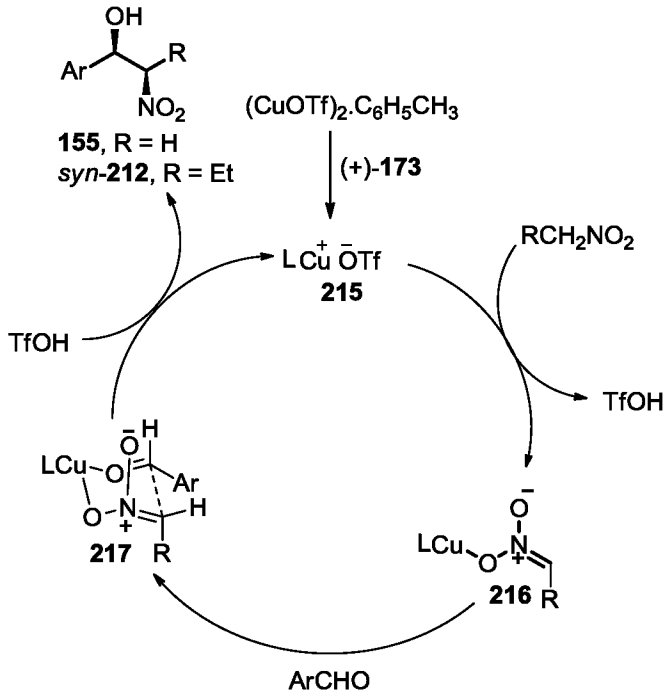
formation taking place from the less sterically encumbered direction.[33] It is likely that organization of transition state **213** is assisted by a N-H hydrogen bond with the nitronate oxygen atom since complex (+)-**76** in which this hydrogen is absent leads to lower enantioselectivity (Table 5.1). Results from Table 5.5 imply that the copper complexed nitronate of nitropropane in transition state **214** has (*Z*) configuration with attack again occurring at the *si* face of the aldehyde carbonyl through a six-membered transition state.



213, R = H
214, R = Et

Figure 5.2 Proposed transition state for the asymmetric Henry reaction of aldehydes with nitromethane and 1-nitropropane catalyzed by a (+)-**173**/copper(I) triflate toluene complex

A catalytic cycle that would incorporate transition states **213** and **214** is proposed in Scheme 5.16. Initial ligand exchange of tetrahydrosalen (+)-**173** for toluene gives copper triflate complex **215**. Progression via copper(I) complexes **216** and **217** would complete the catalytic cycle, giving **155** or **212** while regenerating the active catalyst **215**.



Scheme 5.16 Proposed catalytic cycle for the formation of **155** and **212**

In this chaper, tetrahydrosalen ligand (+)-**173** in combination with copper(I) triflate was found to be an efficient catalyst for the enantioselective Henry reaction of aldehydes with nitromethane, affording β-nitro alcohols in high enantiomeric excess. The enantioenriched Henry adducts were transformed to important organic materials including beta-adrenergic receptor blocking agents. The catalyst system when used with nitropropane was shown to give a *syn*-nitro alcohol in high diastereomeric and enantiomeric excess.

5.3 References

1. Henry, L. *Hebd. CR Seances Acad. Sci.* **1895**, *120*, 1265.
2. Seebach, D.; Beck, A. K.; Mukhopadhyay, T.; Thomas, E. *Helv. Chim. Acta* **1982**, *65*, 1101.
3. Palomo, C.; Oiarbide, M.; Laso, A. *Eur. J. Org. Chem.* **2007**, 2561.
4. Sasai, H.; Suzuki, T.; Arai, S.; Arai, T.; Shibasaki, M. *J. Am. Chem. Soc.* **1992**, *114*, 4418.
5. Sasai, H.; Tokunaga, T.; Watanabe, S.; Suzuki, T.; Itoh, N.; Shibasaki, M. *J. Org. Chem.* **1995**, *60*, 7388.
6. Arai, T.; Yamada, Y. M. A.; Yamamoto, N.; Sasai, H.; Shibasaki, M. *Chem. Eur. J.* **1996**, *2*, 1368.
7. Saá, J. M.; Tur, F.; González, J.; Vega, M. *Tetrahedron: Asymmetry* **2006**, 17, 99.
8. Evans, D. A.; Seidel, D.; Rueping, M.; Wai Lam, H.; Shaw, J. T.; Downey, C. W. *J. Am. Chem. Soc.* **2003**, *125*, 12692.
9. Gan, C.; Lai, G.; Zhang, Z.; Wang, Z.; Zhou, M.-M. *Tetrahedron: Asymmetry* **2006**, *17*, 725.
10. (a) Blay, G.; Climent, E.; Fernández, I.; Hernández-Olmos, V.; Pedro, J. R. *Tetrahedron: Asymmetry* **2006**, *17*, 2046. (b) Blay, G.; Climent, E.; Fernández, I.; Hernández-Olmos, V.; Pedro, J. R. *Tetrahedron: Asymmetry* **2007**, *18*, 1603.
11. Xu, H.; Wolf, C. *Chem. Commun.* **2010**, *46*, 8026.
12. Selvakumar, S.; Sivasankaran, D.; Singh, V. K. *Org. Biomol. Chem.*, **2009**, *7*, 3156.
13. Ginotra, S. K.; Singh, V. K. *Org. Biomol. Chem.*, **2007**, *5*, 3932.

14. Maheswaran, H.; Prasanth, K. L.; Krishna, G. G.; Ravikumar, K.; Sridhar, B.; Kantam, M. L. *Chem. Commun.* **2006**, 4066.

15. Bandini, M.; Piccinelli, F.; Tommasi, S.; Umani-Ronchi, A.; Ventrici, C. *Chem. Commun.* **2007**, 616.

16. (a) Arai, T.; Watanabe, M.; Fujiwara, A.; Yokoyama, N.. Yanagisawa, A. *Angew. Chem. Int. Ed.* **2006**, *45*, 5978. (b) Arai, T.; Watanabe, M.; Yanagisawa, A. *Org. Lett.* **2007**, *9*, 3595.

17. (a) Kogami, Y.; Nakajima, T.; Ashizawa, T.; Kezuka, S.; Ikeno, T.; Yamada, T. *Chem. Lett.* **2004**, *33,* 614. (b) Kogami, Y.; Nakajima, T.; Ikeno, T.; Yamada, T. *Synthesis* **2004**, 1947.

18. (a) Trost, B. M.; Yeh, V. S. C. *Angew. Chem. Int. Ed.* **2002**, *41*, 861. (b) Trost, B. M.; Yeh, V. S. C.; Ito, H.; Bremeyer, N. *Org. Lett.* **2002**, *4*, 2621.

19. Palomo, C.; Oiarbide, M.; Laso, A. *Angew. Chem. Int. Ed.* **2005**, *44*, 3881.

20. (a) Misumi, Y.; Bulman, R. A.; Matsumoto, K. *Heterocycles* **2002**, *56*, 599. (b) Chinchilla, R.; Najera, C.; Sanchez-Agullo, P. *Tetrahedron:Asymmetry* **1994**, *5*, 1393. (c) Allingham, M. T.; Howard-Jones, A.; Murphy, P. J.; Thomas, D. A.; Caulkett, P. W. R. *Tetrahedron Lett.* **2003**, *44*, 8677.

21. Marcelli, T.; van der Haas, R. N. S.; van Maarseveen J. H.; Hiemstra, H. *Angew. Chem. Int. Ed.* **2006**, *45*, 929.

22. Dines, M.B.; Bird, P.H. *J. Chem. Soc. Chem. Commun.* **1973**, 12.

23. Cruickshank, J. M. *Lancet*, **2010**, *376*, 415.

24. Freemantle, N.; Cleland, J.; Young, P.; Mason, J.; Harrison, J. *Brit. Med. J.* **1999**, *318*,

1730.

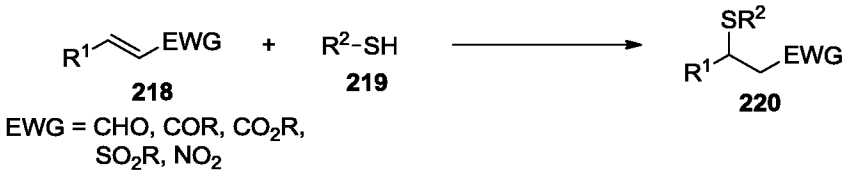
25. Howe, R.; Rao, B. S. *J. Med. Chem.* **1968**, *11*, 1118.
26. Lunsford, C. D.; Mays, R. P.; Richman, J. A.; Murphey, R. S. *J. Am. Chem. Soc.* **1960**, *82*, 1166.
27. Dukes, M.; Smith, L. H. *J. Med. Chem.* **1971**, *14*, 326.
28. Sayyed, I. A.; Thakur, V. V.; Nikalje, M. D.; Dewkar, G. K.; Kotkar, S. P.; Sudalai, A. *Tetrahedron* **2005**, *61*, 2831.
29. Mitsunobu, O.; Yamada, M. *Bull. Chem. Soc. Jpn.* **1967**, *40*, 2380.
30. Blay, G.; Domingo, L. R.; Olmos, V. H.; Pedro, J. R. *Chem. Eur. J.* **2008**, *14*, 4725.
31. Handa, S.; Nagawa, K.; Sohtome, Y.; Matsunaga, S.; Shibasaki, M. *Angew. Chem. Int. Ed.* **2008**, *47*, 3230.
32. Zhou, Y.; Dong, J.; Zhang, F.; Gong, Y. *J. Org. Chem.* **2011**, *76*, 588.
33. A 180° rotation of the aldehyde in **271** and **272** (which would lead to *re* face attack by nitromethane) is disfavored by a steric clash of the aldehyde hydrogen with a *tert*-butyl substituent on the opposing benzenoid ring of the salen ligand.

CHAPTER 6

The Asymmetric Sulfa-Michael Reaction

6.1 Introduction

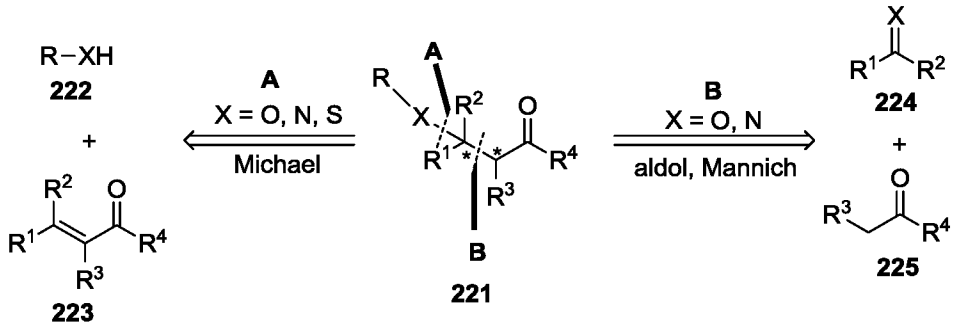
Sulfur-containing compounds are found in many living systems and they play an important role in certain biochemical processes.[1] Synthetically, sulfur-carbon bonds can be introduced into organic structures by a variety of methods,[2] one of which is the sulfa-Michael reaction.[3] This reaction, generally abbreviated as SMA, involves addition of a thiol **219** to an alkene **218** activated by an electron-withdrawing group. The addition produces a functionalized sulfide **220** that can be modified through synthesis in numerous ways (Scheme 6.1).



Scheme 6.1 Sulfa-Michael addition of thiol **219** to activated alkene **218**

In general, there are two synthetic methods for preparing a ketone **221** which contains a β-hetero atom. The first involves the hetero-atom Michael addition of nucleophile **222** to an α,β-unsaturated ketone **223** (Scheme 6.2, path A). The second entails addition of an enolate from ketone **225** to another ketone (aldol coupling) or to an imine **224** (Mannich reaction). Either pathway would generate a β-functionalized ketone

221 (Scheme 6.2, path B). However, path B with X=sulfur is of limited utility due to the fact that thiocarbonyl compounds are generally unstable under aldol reaction conditions and they are often difficult to synthesize. This makes conjugate addition of thiols to α,β-unsaturated carbonyl compounds especially valuable for preparing organosulfur compounds. Once installed, sulfur functionality can be readily removed by oxidative or reductive means, or it can be converted into other functional groups such as a sulfoxide (which may be chiral) or a disulfide. In common with all Michael additions, SMA has the potential to create either one or two stereogenic centers in a single step when an appropriately substituted unsaturated carbonyl compound (Michael acceptor) is employed. This fact places particular importance on an asymmetric version of SMA. Ideally, the reaction should be catalyzed by a chiral entity whose chirality is transferred with high efficiency to the carbon center bearing the imported sulfur atom.

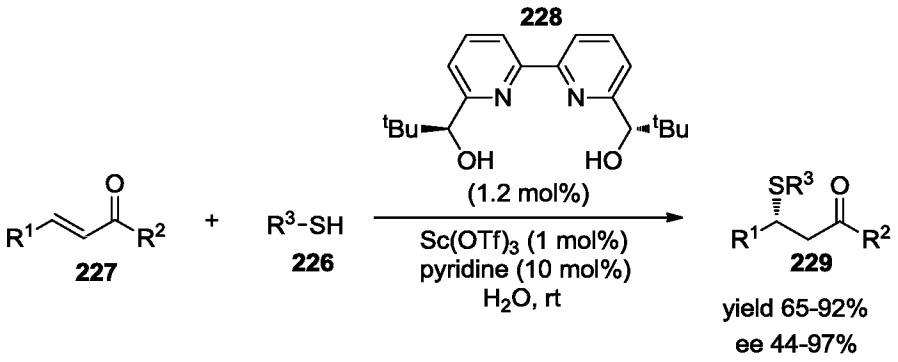


Scheme 6.2 Synthetic routes leading to carbonyl compounds containing β-heteroatoms

Although considerable effort has been directed to the catalytic asymmetric sulfa-Michael addition of thiols to electron-deficient olefins,[4] the Michael acceptors used in these reactions have been limited to nitroolefins,[5] α,β-unsaturated aldehydes,[6] carboxylic acid derivatives[7] and cyclic enones.[8] Acyclic α,β-unsaturated ketones as Michael

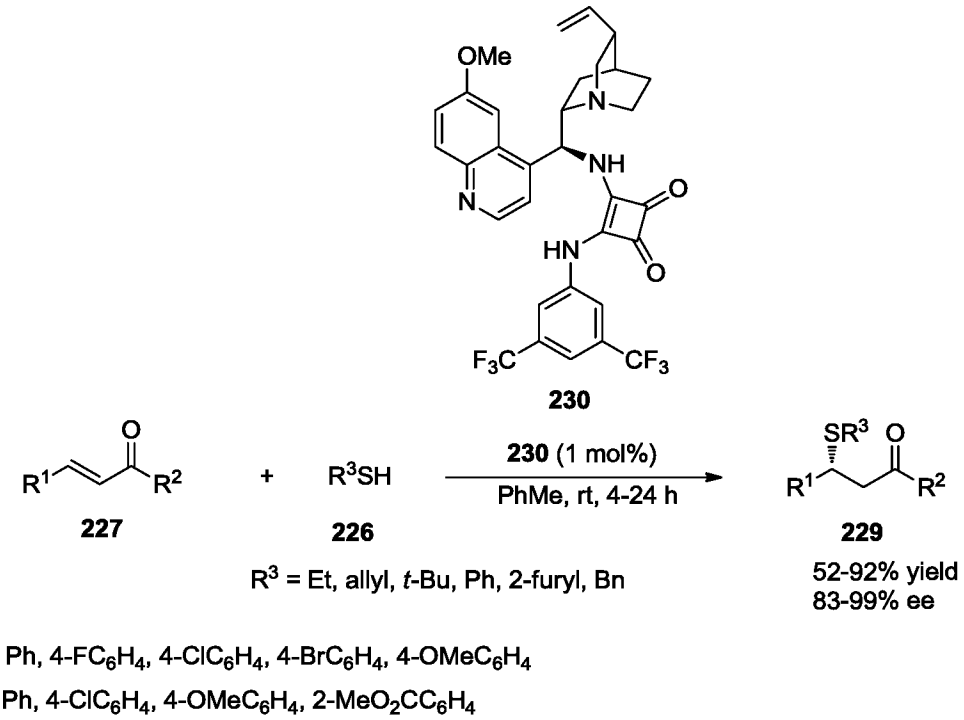
acceptors in catalytic asymmetric SMA have received very limited attention[9] and *syn*/*anti* diastereoselectivity associated with thiol addition to α-branched conjugated enones remains an unsolved problem.[10]

Among recent developments in this area, Kobayashi and co-workers in 2011 showed that a chiral bipyridine **228** in combination with scandium triflate catalyzed asymmetric sulfa-Michael addition of thiols **226** to acyclic enones **227** in an aqueous medium. SMA products **229** were formed in high yield but with variable enantiomeric excess by this method (Scheme 6.3).[9c,d]



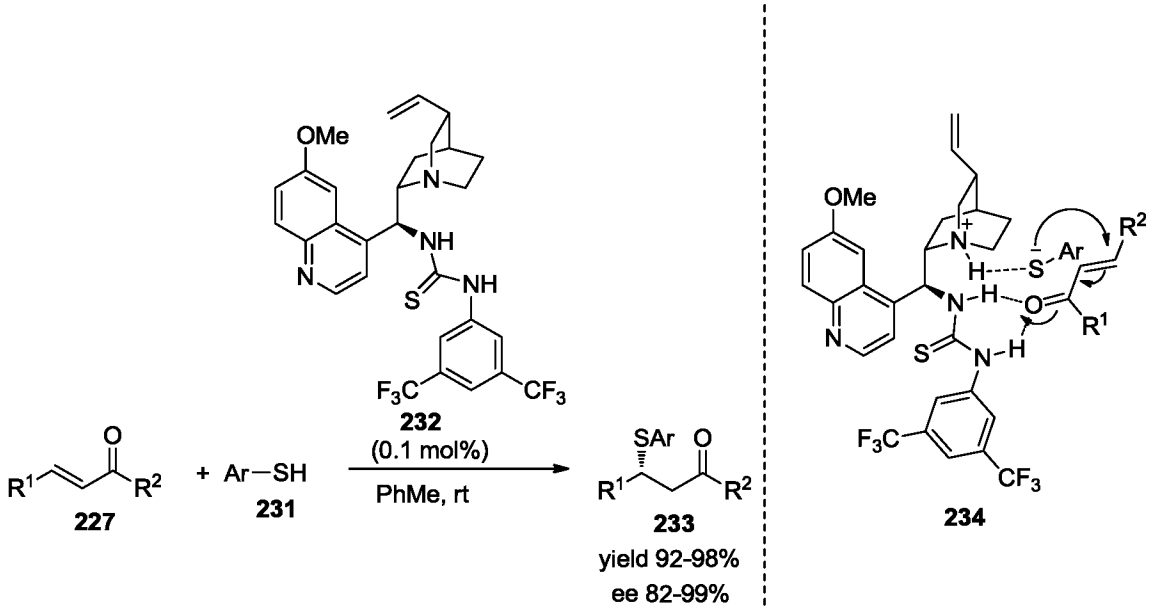
Scheme 6.3 Kobayashi's enantioselective SMA of thiols **226** to acyclic enones **227** catalyzed by scandium triflate and bipyridine **228**

In 2010, Chen and co-workers reported a chiral squaramide based Cinchona alkaloid derivative **230** as a catalyst for SMA of thiols **226** to *trans*-enones (**227**).[9e] The reaction gave moderate to good yields and high enantiomeric excess (up to 99%) of β-thiaketones **229** under mild conditions (Scheme 6.4).



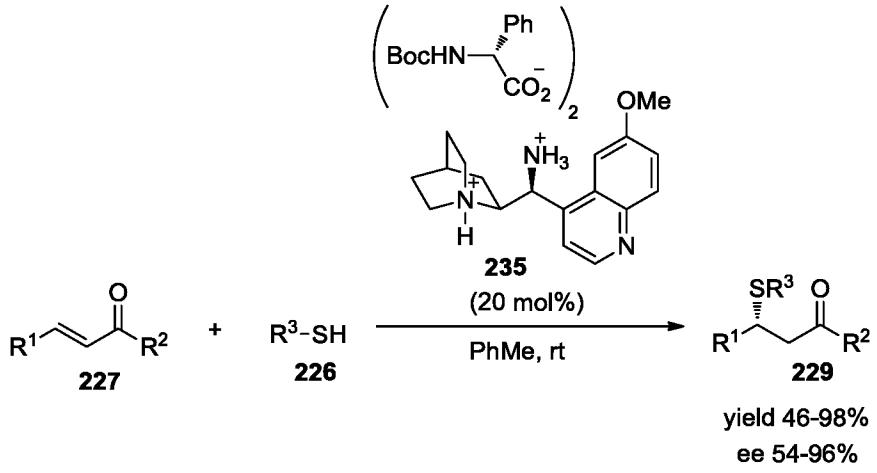
Scheme 6.4 Chen's enantioselective SMA of thiols **226** to acyclic enones **227** catalyzed by squaramide **230**

Singh *et. al.* found that SMA of aromatic thiols **231** to α,β-unsaturated ketones **227** could be catalyzed by a Cinchona alkaloid based bifunctional organocatalyst **232**.[9f] Under optimal conditions, thiourea **232** afforded β-thiaketones **233** in high yield and enantiomeric excess. Singh proposed transition state **234** for this reaction in which the thiourea moiety of **232** activates the enone through double hydrogen bonding while the thiol is deprotonated by the basic quinuclidine moiety of the catalyst (Scheme 6.5). The geometry of this transition state dictates that the thiol adds to the *si* face of the enone.



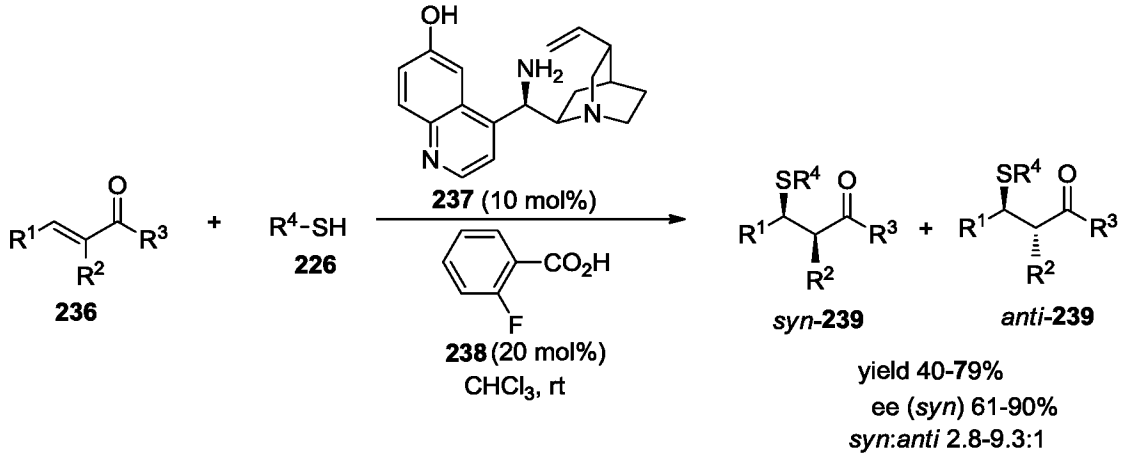
Scheme 6.5 Singh's enantioselective SMA of thiols to acyclic enones catalyzed by bifunctional thiourea **232** (left) and the proposed transition state **234** (right)

Melchiorre and co-workers discovered in 2007 that chiral primary amine salt **235**, made by combining 9-amino-(9-deoxy)-epi-hydroquinine[11] with *N*-Boc-phenylglycine, can function as an efficient catalyst for asymmetric conjugate addition of thiols **226** to α,β-unsaturated ketones **227** (Scheme 6.6).[9g]



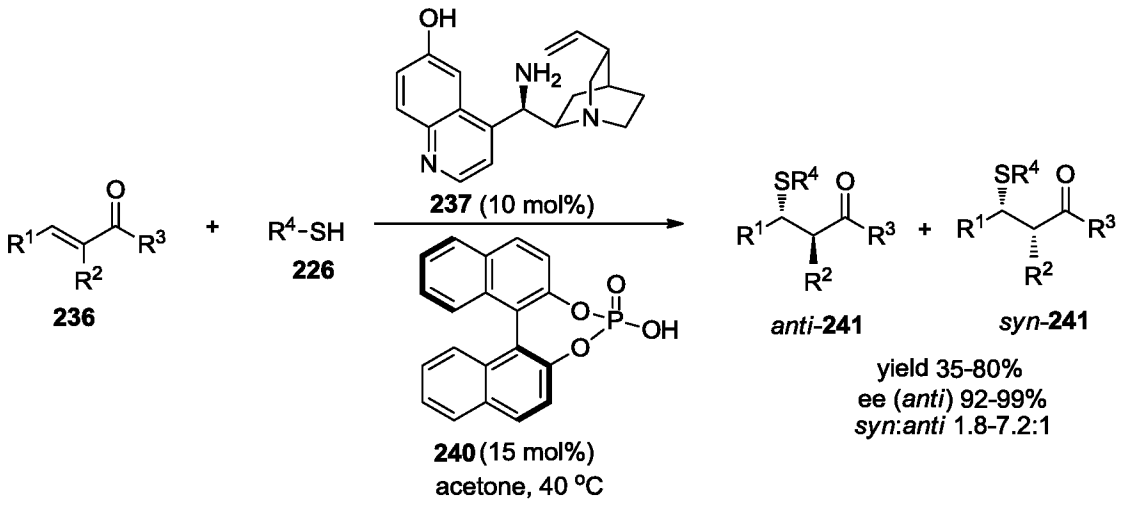
Scheme 6.6 Melchiorre's enantioselective SMA of thiols to acyclic enones catalyzed by primary ammonium salt **235**

In a subsequent paper, Melchiorre reported that the Cinchona based primary amine **237** in combination with 2-fluorobenzoic acid (**238**) was an effective catalyst system for diastereoslective SMA of thiols **226** to α-substituted acyclic enones **236**. The reaction gave a *syn*-β-thiaketone as the major product (*syn*-**239**, Scheme 6.7).[10]



Scheme 6.7 Melchiorre's *syn*-selective SMA of thiols to α-branched enones catalyzed by primary amine **237** and carboxylic acid **238**

Interestingly, when **237** was used in combination with chiral phosphoric acid **240** *anti*-SMA product (*anti*-**241**) was the major outcome. The *anti*-diastereomer was formed in high enantiomeric excess (Scheme 6.8). No explanation was offered by Melchiorre for the divergent behavior of **237** when combined with **238** versus **240**.



Scheme 6.8 Melchiorre's a*nti*-selective SMA of thiols to α-branched enones catalyzed by primary amine **237** and phosphoric acid **240**

6.2 A *cis*-2,5-diaminobicyclo[2.2.2]octane based catalyst for the enantioselective sulfa-Michael reaction

Our success with salen-complex (+)-**70** in catalyzing the asymmetric hetero-Diels-Alder reaction, the asymmetric Nozaki-Hiyama-Kishi reaction, and the asymmetric Henry reaction, and in obtaining products in high enantiomeric excess from these processes, suggested that similar advantage could be taken of this ligand in catalysis of sulfa-Michael addition. Our first approach to this question was influenced by the work of Seidel[12] who showed that chiral bis-thiourea ligands can be used to catalyze a diverse range of asymmetric organic reactions. The key structural feature that endows the reaction with the characteristically high level of asymmetric induction is hydrogen bonding by NH groups of the thiourea with one of the reactants. In fact, Singh[9f] had

already demonstrated that sulfa-Michael addition of thiols to enones can be catalyzed by a thiourea bound to an asymmetric scaffold (**232**, Scheme 6.5). C_2-symmetric bis-thioureas **246-248** based on our *cis*-2,5-diaminobicyclo[2.2.2]octane scaffold were therefore considered possible candidates for asymmetric catalysis of SMA since activation of the enone Michael acceptor through a hydrogen-bonding motif (**242**, Figure 6.1) would parallel these literature examples. To test our hypothesis, bis-thioureas **246-248** were prepared by reacting diamine (-)-**34** with isothiocyanates **243-245** (Scheme 6.9).

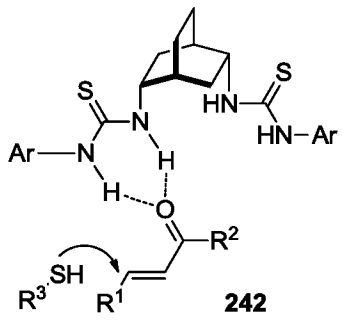
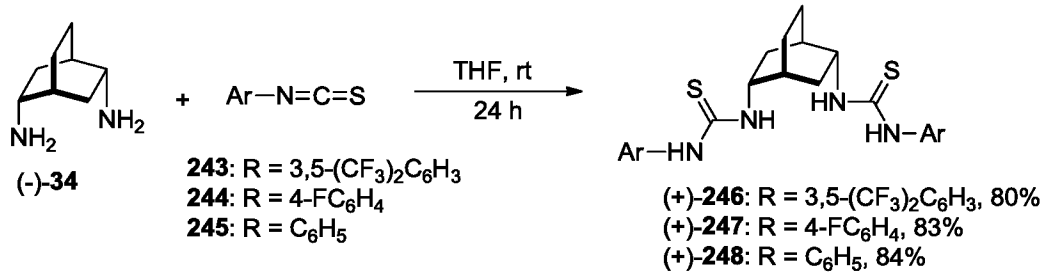


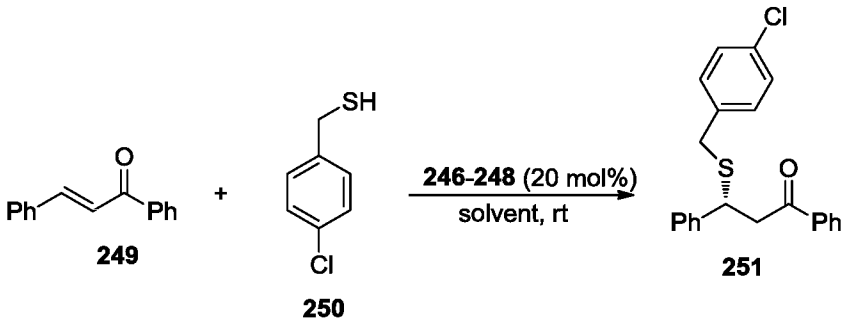
Figure 6.1 Enone activation by bis-thiourea ligand



Scheme 6.9 Synthesis of bis-thioureas **246-248** based on a *cis*-2,5-diaminobicyclo[2.2.2]-octane scaffold

The catalytic activity of bis-thiourea catalysts (+)-**246-248** was studied in the reaction of *p*-chlorobenzyl thiol (**250**) with *trans*-chalcone (**249**, Table 6.1). Results were not encouraging, however. Enantiomeric excess in the SMA product varied from 0-28% and although high yields could be obtained in polar solvents (entries 9, 10, 12) asymmetric induction in polar media was negligible.

Table 6.1 Asymmetric SMA of *p*-chlorobenzyl thiol (**250**) to *trans*-chalcone (**249**) catalyzed by thioureas (+)-**246-248**[a]



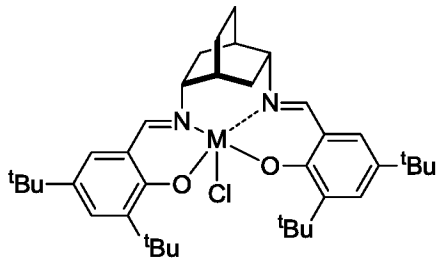
Entry	Catalyst	Solvent	t [h]	product **251**	
				yield [%][b]	ee [%][c]
1	(+)-**246**	PhMe	16	71	22
2	(+)-**247**	PhMe	30	79	28
3	(+)-**248**	PhMe	36	46	7
4	(+)-**246**	$CHCl_3$	28	57	6
5	(+)-**247**	$CHCl_3$	26	76	17
6	(+)-**247**	CH_2Cl_2	18	87	14
7	(+)-**247**	Et_2O	12	95	10
8	(+)-**247**	THF	10	93	4
9	(+)-**247**	MeCN	2	98	0
10	(+)-**247**	MeOH	2	99	0
11	(+)-**247**	DCE	20	74	7
12	(+)-**247**	Dioxane	8	98	0

[a] The reaction between *trans*-chalcone (0.1 mmol) and 4-chlorobenzyl thiol (0.12 mmol) was carried out in 1 mL solvent in the presence of 20 mol% catalyst. [b] Yield of isolated product. [c] Determined by HPLC analysis using a Chiralcel OJ-H column.

The disappointing results with thioureas (+)-**246-248** in inducing a high degree of asymmetry in the SMA of **249** to **250** implied that our hypothetical activation model represented as **242** was flawed. A different mode of enone activation was therefore sought and for this we returned to our metal-salen complexes described in chapter 2.

We previously demonstrated that the chromium(III) complex (+)-**70** is an efficient catalyst for the asymmetric hetero-Diels-Alder reaction of aldehydes with Danishefsky diene (chapter 3, Table 3.2) and for the asymmetric Nozaki-Hiyama-Kishi reaction (chapter 4, Table 4.3) of allyl bromide with aromatic aldehydes. This complex acts as a chiral Lewis acid by metal coordination with enantiotopic lone pairs on the oxygen atom of the aldehyde carbonyl. We therefore selected a subset of our metal-salen complexes,

67, **68**, **70-72**, **78** in which the embedded metal ion would be capable in principle of forming a strong coordinate bond with the carbonyl oxygen of the enone acceptor in a sulfa-Michael reaction.



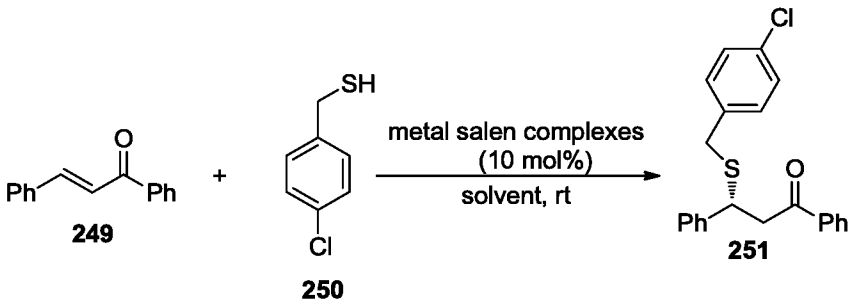
(+)-67: M = Ti(O*i*Pr) **(+)-71**: M = Mn
(+)-68: M = V(O) **(+)-72**: M = Fe
(+)-70: M = Cr **(+)-78** : M = Al

Figure 6.2 Metal-salen complexes as candidates for asymmetric SMA

Our prototype reaction for this study was again the SMA of *p*-chlorobenzyl thiol (**250**) to *trans*-chalcone (**249**). With 10 mol% of the catalyst in toluene (Table 6.2, entries 1-6), screening of the selected complexes revealed that iron(III)-salen complex (+)-**72** was a promising candidate in terms of enantiomeric excess of sulfa-Micael product **251** (entry 5). Although titanium(IV) complex (+)-**67** and aluminum(III) complex (+)-**78** gave **251** in good yield (84% and 87%, respectively), the degree of asymmetric induction with these catalysts was low (36% and 49% enantiomeric excess, entries 1 and 6). It was found that non-polar solvents gave best results in terms of enantiomeric excess of the SMA product **25** (entries 5, 7-9). Polar and coordinating solvents such as tetrahydrofuran and methanol resulted in a significant drop in yield and enantiomeric excess of **251**, probably due to competition by these solvents for the electrophilic metal center of the

catalyst (entries 10-13). Comparison of the optical rotation of **251** from this experiment with the literature value[9e] proved that **251** possessed (*R*) configuration.

Table 6.2 Asymmetric conjugate addition of *p*-chlorobenzyl thiol (**250**) to chalcone (**249**) catalyzed by salen-metal complexes[a]

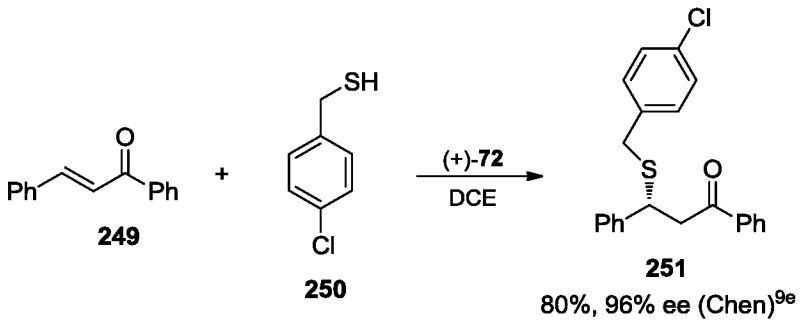


Entry	Catalyst	Solvent	t [h]	product **251**	
				yield [%][b]	ee [%][c]
1	(+)-**67**	PhMe	30	84	36
2	(+)-**68**	PhMe	36	46	37
3	(+)-**70**	PhMe	52	35	43
4	(+)-**71**	PhMe	18	63	46
5	(+)-**72**	PhMe	12	52	71
6	(+)-**78**	PhMe	6	87	49
7	(+)-**72**	$CHCl_3$	24	63	75
8	(+)-**72**	CH_2Cl_2	36	68	84
9	(+)-**72**	DCE	24	90	87
10	(+)-**72**	THF	71	33	7
11	(+)-**72**	$MeNO_2$	74	22	31
12	(+)-**72**	MeCN	59	46	36
13	(+)-**72**	MeOH	96	16	13

[a] The reaction between *trans*-chalcone (0.1 mmol) and 4-chlorobenzyl thiol (0.12 mmol) was carried out in 1 mL solvent in the presence of 10 mol% catalyst. [b] Yield of isolated product. [c] Determined by HPLC analysis using a Chiralcel OJ-H column.

Having identified (+)-**72** as the catalyst of choice for the SMA of **250** to **249**, the effects of catalyst loading and reaction temperature were investigated. Higher catalyst loading enabled the reaction to be run at lower temperature which had a beneficial effect on the enantioselectivity of the reaction (Table 6.3, entries 1-5). Optimized conditions for the reaction were found at a temperature of -5 °C in 1,2-dichloethane as solvent and with 20 mol% of catalyst (entry 5). Lowering the reaction temperature to -15 °C led to an inconveniently slow reaction rate with negligible change in enantioselectivity of the reaction (entry 6).

Table 6.3 Asymmetric SMA of thiol **250** to *trans*-chalcone (**249**) catalyzed by (+)-**72**. Effect of catalyst loading and temperature[a]

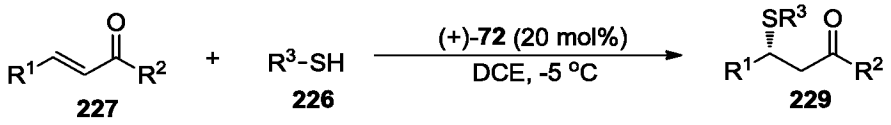


Entry	Catalyst loading (mol%)	Temp	t [h]	product **251** yield [%][b]	ee [%][c]
1	10	12	32	84	91
2	10	0	47	79	95
3	10	-5	58	76	96
4	4	-5	63	82	86
5	15	-5	49	87	97
6	20	-5	36	94	98
7	20	-15	74	59	97

[a] The reaction between *trans*-chalcone (0.1 mmol) and 4-chlorobenzyl thiol (0.12 mmol) was carried out in 1 mL solvent. [b] Yield of isolated product. [c] Determined by HPLC using a Chiralcel OD-H column.

With optimized reaction conditions established for asymmetric SMA of **250** to **249**, a broad portfolio of thiols **226** was examined in reaction with a variety of α,β-unsaturated ketones **227** using iron(III)-salen complex (+)-**72** as catalyst (Table 6.4). In every case, β-thiaketone **229**, which had the absolute configuration shown, was obtained in >90% enantiomeric excess and in high yield. Thiophenol (entry 18) as well as aliphatic thiols and a hydroxyl substituted thiol (entry 10) gave good results, and the reaction was found to tolerate a wide range of aromatic and alipatic substituents in the unsaturated ketone.

Table 6.4 Enantioselective synthesis of β-thiaketones **229** from thiols **226** and α,β-unsaturated ketones **227** catalyzed by iron-salen complex (+)-**72**[a]

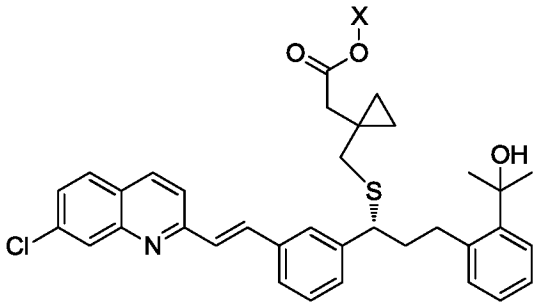


Entry	R^1	R^2	R^3	t [h]	product **229** yield [%][b]	product **229** ee [%][c]
1	Ph	Ph	^{i}Pr	41	96	94
2	Ph	Ph	$C_6H_5CH_2$	36	92	97
3	Ph	Me	^{i}Pr	38	89	96
4	Ph	Me	$C_6H_5CH_2$	31	97	96
5	Ph	Me	4-Cl-$C_6H_4CH_2$	31	93	97
6	3-$OMeC_6H_4$	Me	^{i}Pr	36	98	95
7	4-$OMeC_6H_4$	Me	^{i}Pr	36	89	92
8	4-$CF_3C_6H_4$	Me	cyclohexyl	36	97	98
9	4-ClC_6H_4	Ph	^{n}Bu	39	98	93
10	4-ClC_6H_4	Ph	CH_2CH_2OH	20	91	96
11	2,6-di-ClC_6H_3	Ph	^{n}Bu	49	98	96
12	2,4-di-$NO_2C_6H_3$	Me	^{n}Bu	26	98	95
13	4-(OH)-3-(OMe)-C_6H_3	Me	^{i}Pr	38	95	96
14	1-Naphthyl	2-furyl	^{i}Pr	49	94	97
15	1-Naphthyl	2-thiophenyl	^{i}Pr	47	96	94
16	Me	Me	$C_6H_5CH_2$	32	97	95
17	Me	Me	4-Cl-$C_6H_4CH_2$	31	95	93
18	Me	Me	Ph	34	89	98
19	C_6H_{13}	Me	$C_6H_5CH_2$	48	96	98

[a] The reaction between *trans*-enone (0.1 mmol) and 4-chlorobenzyl thiol (0.12 mmol) was carried out in 1 mL solvent in the presence of 20 mol% catalyst. [b] Yield of isolated product.[c] Determined by HPLC using a Chiralcel OD, AD, OJ, OD-H or AS-H column.

The discovery that iron-salen complex (+)-**72** could create a carbon-sulfur bond with a high level of asymmetric induction via SMA opened the possibility that this complex could have practical application in synthetic processes where introduction of a sulfur substituent plays a prominent role. One such application would be enantioselective synthesis of the leukotriene receptor antagonist (*R*)-Montelukast (**252**, Figure 6.3).[13] Singulair® (**253**, MK-0476), the sodium salt of **252** (also known as Montelukast sodium),

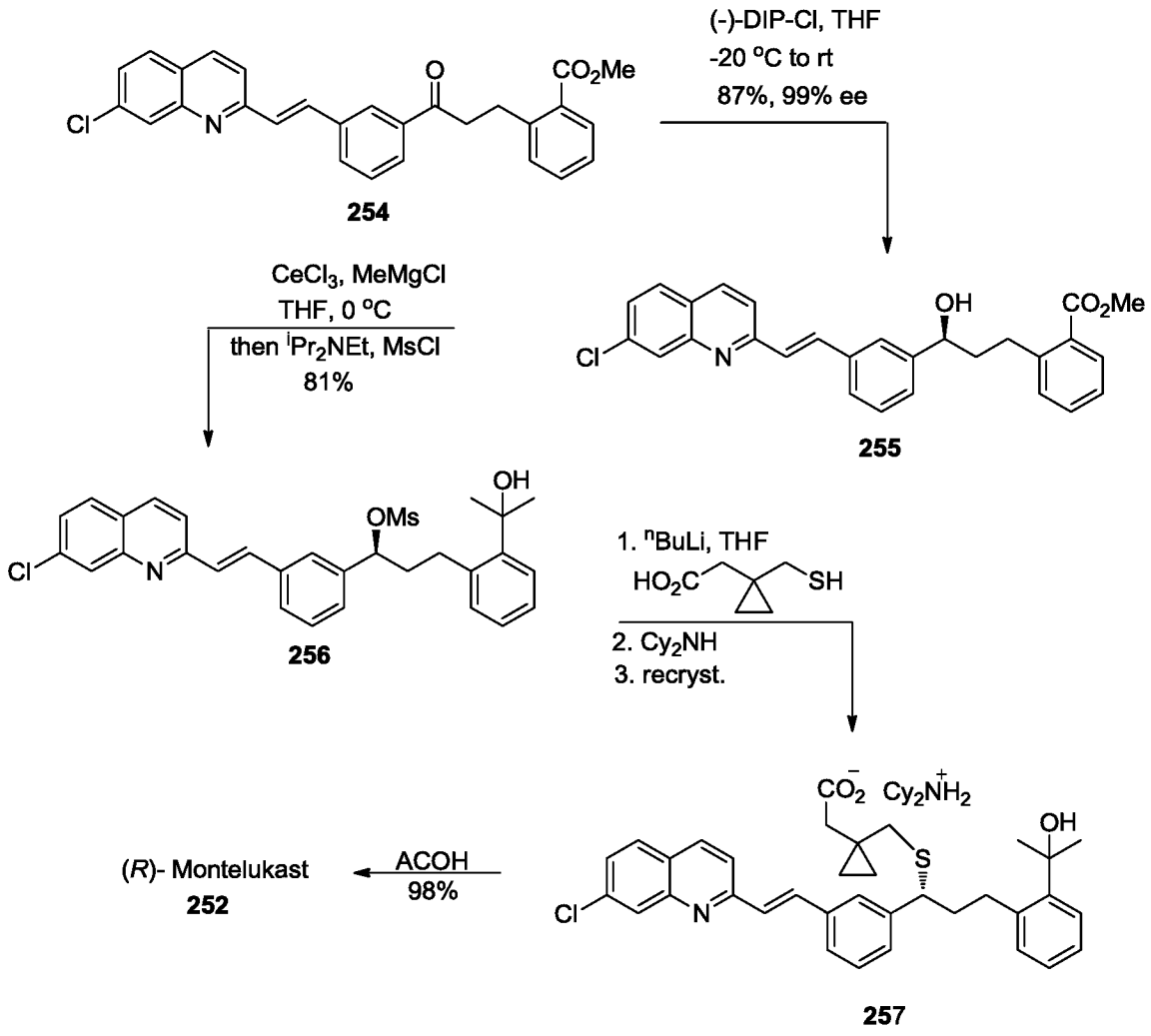
is an orally active and widely prescribed drug for treatment of asthma and other respiratory conditions.[14] Leukotrienes constitute a group of locally acting hormones produced in living systems from arachidonic acid. The major leukotrienes (LT) are designated LTB_4, LTC_4, LTD_4, and LTE_4. Biosynthesis of these leukotrienes begins with the action of the enzyme 5-lipoxygenase on arachidonic acid to produce an epoxide known as Leukotriene A_4 (LTA_4), which is converted to other leukotrienes in subsequent enzymatic steps. Singulair® is known to be a selective antagonist for the leukotriene D_4 receptor.



252: X = H: Montelukast
253: X = Na: Singulair®

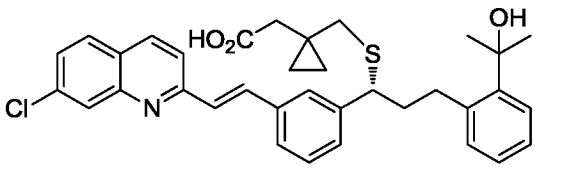
Figure 6.3 Selective leukotriene D_4 receptor antagonist Montelukast (**252**) and its sodium salt Singulair® (**253**)

Montelukast is currently synthesized from 7-chloroquinaldine (**259**) in a ten-step process developed by Merck that introduces the (*R*) sulfur substituent indirectly by displacememt of mesylate **256** (Scheme 6.10).[13] Alcohol **255** which is the precursor to mesylate **256** is generated via enantioselective reduction of ketone **254** with (−)-B-chlorodiisopinocampheylborane.[15]

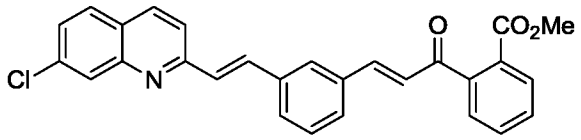


Scheme 6.10 Merck's synthesis of (*R*)-Montelukast (**252**) via ketone **254**

We envisioned that the sulfur side chain of Montelukast could be inserted directly into the skeleton of **252** with high enantioselectivity using conjugated ketone **258** as the Michael acceptor in an asymmetric SMA with (+)-**72** as catalyst (Scheme 6.11).



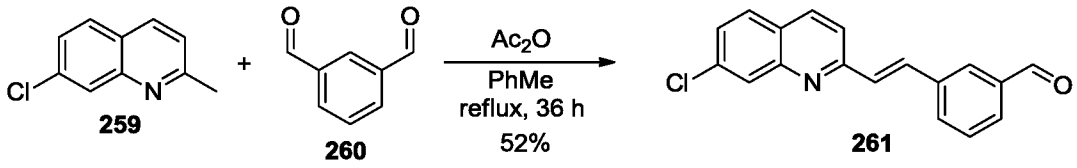
252



258

Scheme 6.11 Proposed asymmetric SMA route to the anti-asthma drug (*R*)-Montelukast (**252**)

Our initial effort toward synthesis of α,β-unsaturated ketone **258** began with the synthesis of known aldehyde **261**.[16] A mixture of 7-chloroquinaldine (**259**) and 1,3-benzene dicarboxaldehyde (**260**) underwent aldol condensationin in the presence of acetic anhydride in toluene to afford aldehyde **261** in 52% yield (Scheme 6.12).

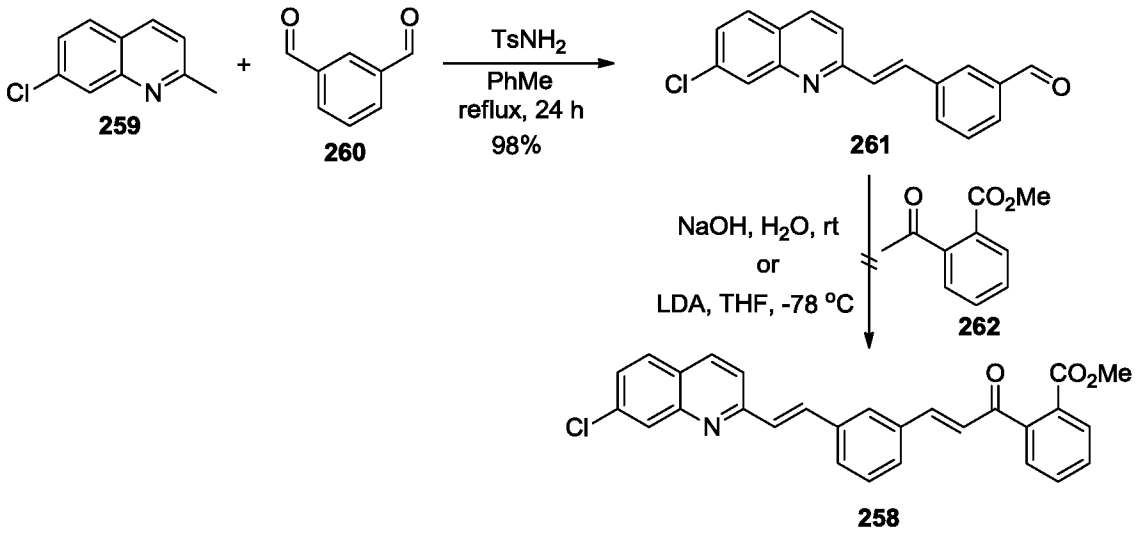


259 **260** **261**

Scheme 6.12 Synthesis of aldehyde **261** from 7-chloroquinaldine (**259**) and 1,3-benzene dicarboxaldehyde (**260**)

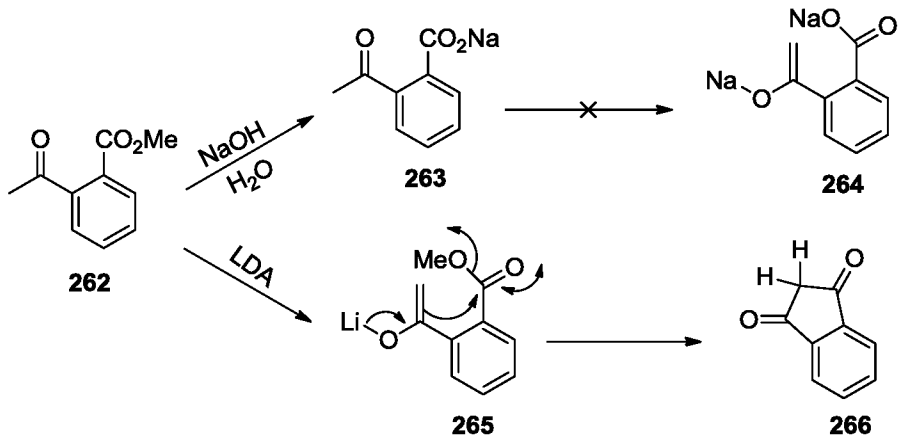
Subsequently, it was found that an improved yield of aldehyde **261** (98%) could be obtained when an equimolar mixture of **259** and **260** was refluxed in the presence of a stoichiometric amount of *p*-toluenesulfonamide (Scheme 6.13).[17] However, attempts to

advance this route towards **258** by base promoted aldol condensation of aldehyde **261** with keto ester **262** were unsuccessful.



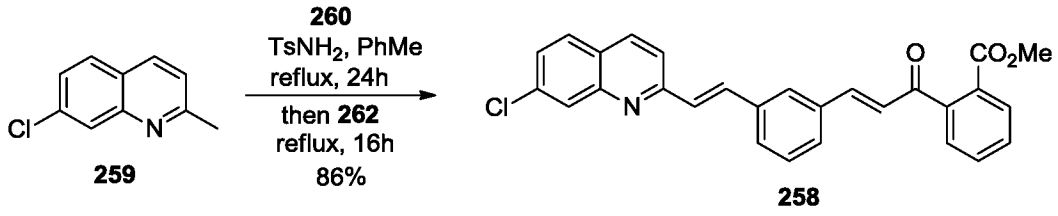
Scheme 6.13 Improved synthesis of aldehyde **261** and an unsuccessful attempt to obtain α,β-unsaturated ketone **258**

We surmised that aldol condensation of aldehyde **261** with keto ester **262** failed in aqueous sodium hydroxide because hydrolysis of the ester to give sodium salt **263** prevented formation of ketone enolate **264**. On the other hand, a strong base such as lithium diisopropylamide or lithium bis(trimethylsilyl)amide in a non-aqueous medium probably generated the desired enolate **265** but this undergoes intramolecular cyclization to diketone **266** (Scheme 6.14).



Scheme 6.14 Possible fate of intermediates generated from ketoester **262** under basic conditions

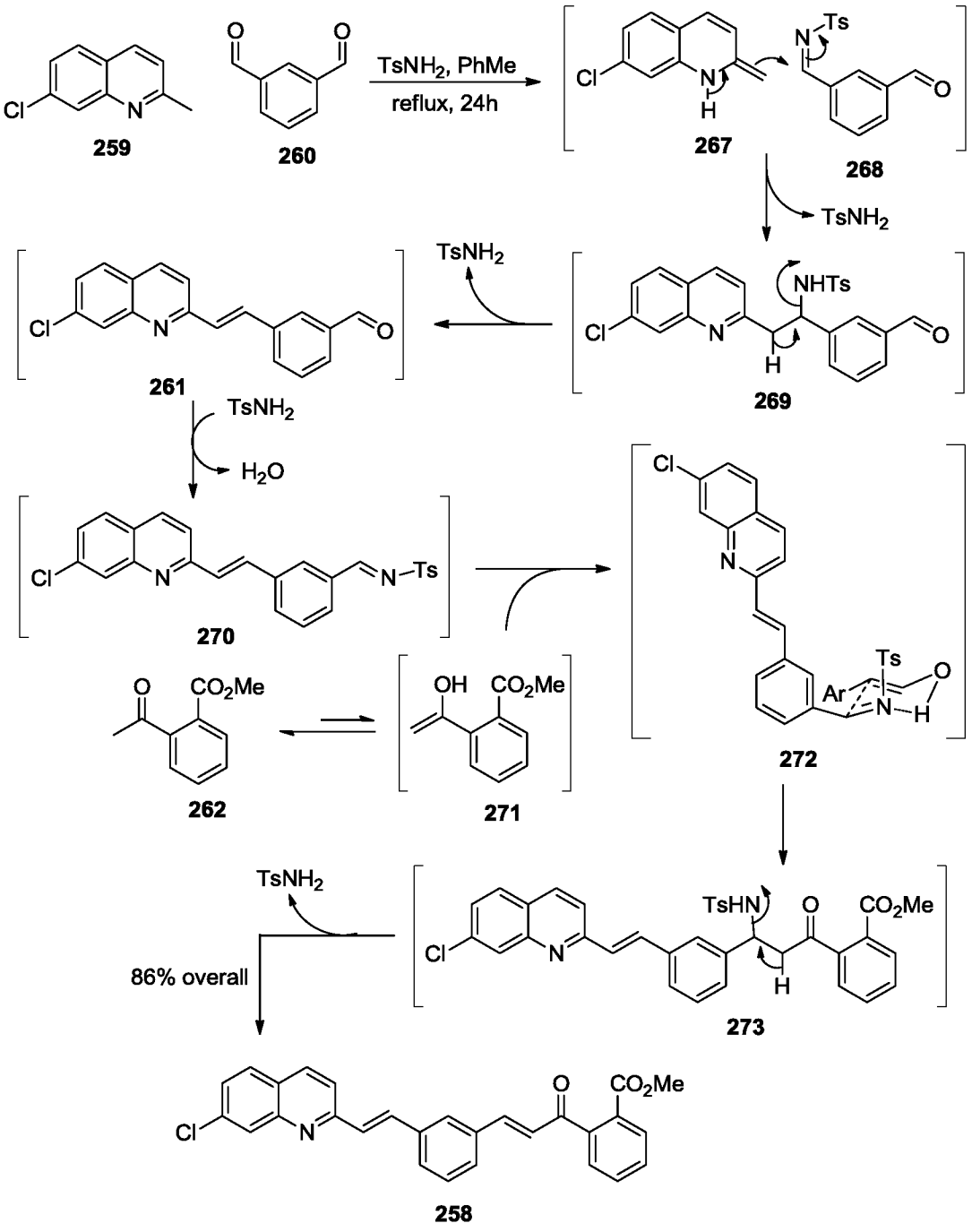
Fortunately, it was found that when an equimolar mixture of 7-chloroquinaldine (**259**), dialdehyde **260** and *p*-toluenesulfonamide is refluxed in toluene for 24 hours and this is followed by addition of a stoichiometric amount of keto ester **262** with subsequent refluxing for a further 16 hours the desired α,β-unsaturated ketone **258** is formed in excellent yield (Scheme 6.15).



Scheme 6.15 *p*-Toluenesulfonamide catalyzed tandem Mannich-Aldol synthesis of dienone **258**

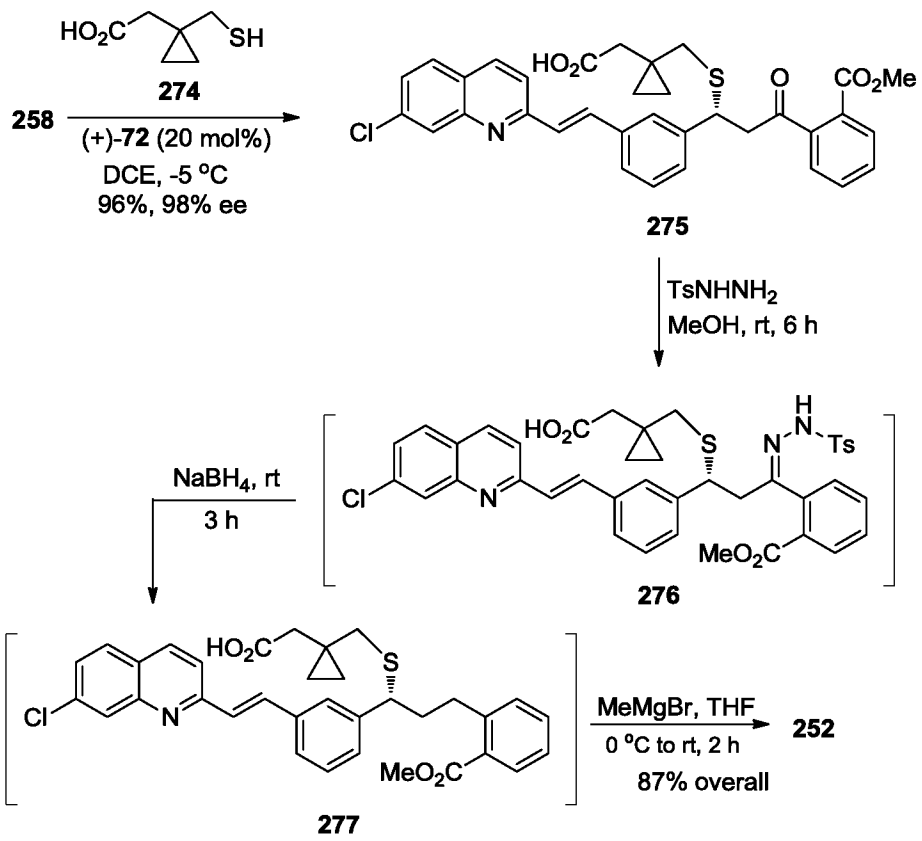
This remarkable four-component one-pot reaction sequence is believed to proceed via an initial Mannich reaction of enamine tautomer **267** with aldimine **268** which is

followed by elimination of *p*-toluenesulfonamide from **269** to generate aldehyde **261**. The latter then condenses with the liberated sulfonamide, forming a second aldimine **270** which reacts with enol **271** to produce **273**, probably via six-membered transition state **272**. Final elimination from **273** delivers α,β-unsaturated ketone **258** and regenerates *p*-toluenesulfonamide (Scheme 6.16). Although this mechanism suggests that only a catalytic amount of *p*-toluenesulfonamide is required for the transformation of **259** to **258**, in practice the reaction becomes very sluggish with a substoichiometric amount of *p*-toluenesulfonamide due to its low turnover rate.



Scheme 6.16 Proposed mechanism for formation of **258** via *p*-toluenesulfonamide catalyzed one-pot tandem Mannich-aldol sequence involving **259**, **260** and **262**

With dienone **258** in hand, its SMA with commercially available 1-(mercaptomethyl)cyclopropyl]acetic acid (**274**) was examined in the presence of catalytic (+)-**72** under the optimized conditions developed previously (Table 6.4). It was found that β-thiaketone **275** was produced in high yield and enantiomeric excess in this reaction. Ketone **275** was converted to its tosylhydrazone **276** which was reduced in situ under Caglioti's conditions with sodium borohydride in methanol at room temperature[18] to yield sulfide **277**. Finally, **277** was reacted with methylmagnesium bromide to furnish (*R*)-Montelukast (**252**) whose proton and carbon-13 NMR spectra and optical rotation were in excellent agreement with the literature.[19] The final three steps to **252** proceeded in 87% yield based on **275** (Scheme 6.17). Our synthesis of (*R*)-Montelukast (**252**), which requires only four steps from 7-chloroquinaldine (**259**) and proceeds in 72% overall yield, shortens the Merck synthesis by six steps and illustrates the advantage of SMA in generating chiral sulfur substitution from an achiral precursor.

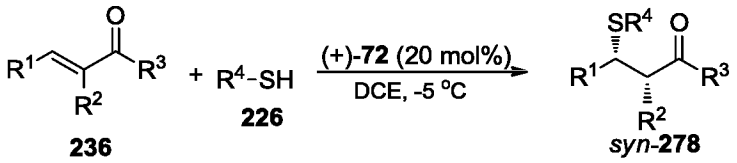


Scheme 6.17 Synthesis of (*R*)-Montelukast (**252**) from dienone **258**

An important question in all Michael reactions including heteroatom additions is whether the process can create vicinal stereocenters in the Michael acceptor simultaneously and in a stereocontrolled manner.[20] To test our asymmetric SMA methodology against this concept we employed α-substituted α,β-unsaturated ketones as Michael acceptors and found that thiols **226** underwent SMA to conjugated enones **236** in the presence of (+)-**72** as catalyst to give products in high yield with a *syn*/*anti* ratio strongly favoring *syn* isomer **278**. Increasing the size of the α- or β-substituent in the enone increased the *syn* selectivitiy of the reaction (Table 6.5, etries 1-3). The *syn* product (*syn*-**278**) was produced in high enantiomeric excess from these reactions with

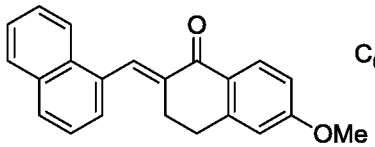
absolute configuration of the products confirmed by comparison of the optical rotation with known values.[10] The *syn* selectivity obtained with catalyst (+)-**72** compares favorably with Melchiorre's results obtained with a Cinchona alkaloid based chiral catalyst (see Scheme 6.7).

Table 6.5 Diastereoselectivity in asymmetric sulfa-Michael addition of thiols to α-branched enones catalyzed by (+)-**72**[a]



236 *syn*-**278**

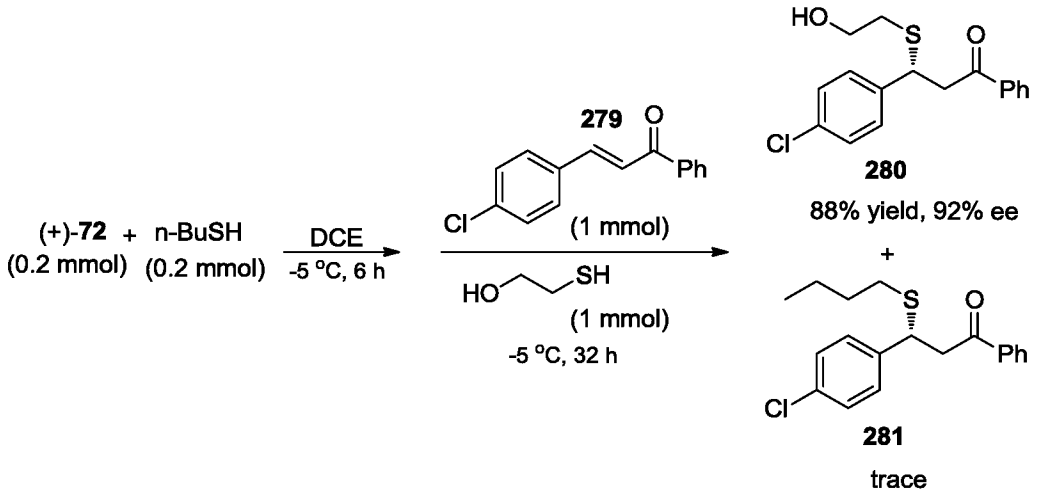
For R^1 = Ph, R^2, R^3 = Me and R^4 = Bn
syn/*anti* 3.5:1 (Melchiorre)[10]

Entry	R^1	R^2	R^3	R^4	t (h)	product **278** dr *syn*/*anti*[b]	yield [%][c]	ee [%][d]
1	Ph	Me	Me	$C_6H_5CH_2$	34	>23:1	92	98
2	4-ClC_6H_4	Me	Me	$C_6H_5CH_2$	28	>31:1	95	96
3	$(CH_3)_2CH$	n-Bu	Ph	Et	46	>50:1	92	97
4	c-C_6H_{11}	n-Bu	Ph	$(CH_3)_2CH$	40	>50:1	95	96
5	n-C_6H_{13}	n-Bu	Ph	$(CH_3)_3C$	46	>50:1	90	95
6				$C_6H_5CH_2$	18	>50:1	95	98

[a] The reaction between enone (0.1 mmol) and thiol (0.12 mmol) was carried out in 1 mL solvent in the presence of 20 mol% catalyst. [b] Determined by 1H NMR analysis. [c] Combined yields of *syn* and *anti* isomers. [d] Determined by HPLC using a Daicel Chiralcel OD, AD, OD-H or AS-H column.

An attempt to give structural definition to the role of iron-salen catalyst **(+)-72** in asymmetric SMA led to a competition experiment in which 1-butanethiol was first

incubated with the catalyst before 2-mercaptoethanol and Michael acceptor **279** were introduced. Formation of an initial iron-thiol complex is supported by the presence of a IR band centered at ca. 468 cm^{-1} consistent with a Fe-S stretching mode.[21] The preformed complex when treated with an equimolar mixture of **279** and mercaptoethanol yielded SMA product **280** almost exclusively with only a trace amount of butanethiol adduct **281** (Scheme 6.18). This result implies that the precoordinated thiol is not the Michael addend but may play a role in orienting or activating the enone acceptor within the iron-salen complex through the known *trans* directing effect of sulfur ligands in metal complexes.[22]



Scheme 6.18 Competition experiment in SMA to enone 350 with (+)-**72** as catalyst using two thiols

The knowledge that bicyclooctane complex (+)-**72** with (2*R*,3*R*,5*R*,6*R*) absolute configuration leads to sulfa-Michael adducts **229** of uniform stereochemistry [(*R*) when the β-substituent is aryl and (*S*) when the β-substituent is alkyl] stipulates that thiol attack

at the β-carbon of the enone occurs from the *si* face. A transition state **282** accomodating this finding is proposed in Figure 6.4. This model places the iron-coordinated enone acceptor in the right front quadrant below the bicyclic scaffold and *trans* to the precomplexed thiol. Five coordinated atoms surround the central iron atom and form a square pyramidal configuration with O^1, O^2, N^2 and S in the basal plane and N^1 in the apical orientation. Intermolecular approach by a thiol to an enone complexed in this fashion should occur from the more open front face leading to *si* attack since the *re* face is blocked by the decomplexed phenolic group.[23] Subsequent protonation from the *re* face, perhaps assisted by intramolecular delivery from the free phenol, results in *syn* adduct **278** (where $R^2 \neq H$) after detachment of the product from catalyst. A catalytic cycle that conforms to this proposed mechanism is shown in Scheme 6.19 although it does not specify how a proton from the sulfhydryl group of **226** is transferred stereospecifically to iron enolate **283** to give *syn* adduct **278**.

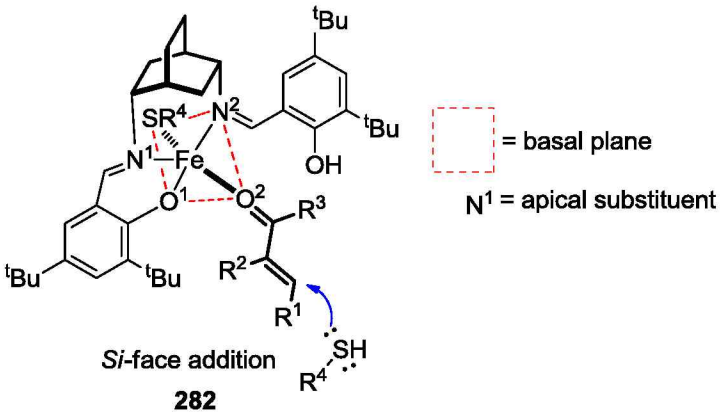
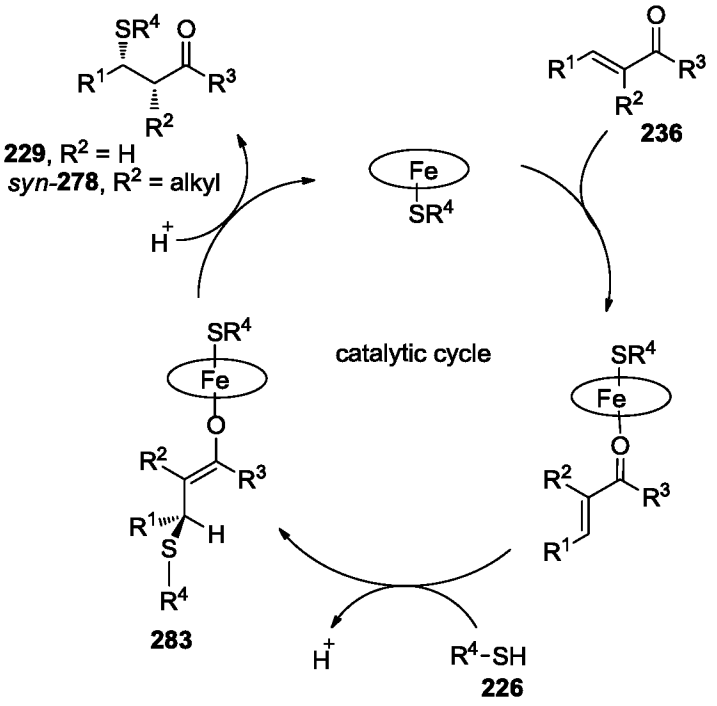


Figure 6.4 Proposed transition state for the asymmetric sulfa-Michael addition of thiols to α,β-unsaturated ketones catalyzed by iron(III)-salen complex (+)-**72**



Scheme 6.19 Catalytic cycle for the formation of **229** and **278** via asymmetric SMA in the presence of (+)-**72**

In this chapter it was shown that iron(III)-salen complex (+)-**72** is an efficient catalyst for enantioselective sulfa-Michael addition (SMA) of thiols to acyclic α,β-unsaturated ketones, producing β-thiaketones in high enantiomeric excess. This protocol was used to synthesize (*R*)-Montelukast, an anti asthma agent, from commercially available starting materials[24] in four steps and in 72% overall yield. With α-substituted acyclic enones as SMA substrates, the method was shown to give the *syn* product in high diastereomeric and enantiomeric excess.

6.3 References

1. Frausto da Silva, J. R.; Williams, R. J. P. *The Biological Chemistry of Elements*; Oxford University Press: New York, **2001**.
2. Clayden, J.; MacLellan, P. *Beilstein J. Org. Chem.* **2011,** *7,* 582.
3. Enders, D.; Luttgen, K.; Narine, A. A. *Synthesis*, **2007**, 0959.
4. (a) Sibi, M. P.; Manyem, S. *Tetrahedron* **2000**, *56*, 8033. (b) Krause, N.; Hoffmann-Roder, A. *Synthesis* **2001**, 171.
5. (a) Palacino, C.; Connon, S. J. *Chem. Commun.* **2012**, *48*, 2849. (b) Yang, W.; Du, D. *Org. Biomol. Chem.,* **2012**, *10*, 6876. (c) Kimmel, K. L.; Robak, M. T.; Thomas, S.; Lee, M.; Ellman, J. A. *Tetrahedron*, **2012**, *68*, 2704. (d) Uraguchi, D.; Kinoshita, N.; Nakashima, D.; Ooi, T. *Chem. Sci.,* **2012**, *3*, 3161.
6. (a) Saito, M.; Nakajima, M.; Hashimoto, S. *Chem. Commun.* **2000**, 1851. (b) Saito, M.; Nakajima, M.; Hashimoto, S. *Tetrahedron* **2000**, *56*, 9589. (c) Marigo, M.; Schulte, T.; Franzen, J.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2005**, *127*, 15710.
7. (a) Nishimura, K.; Ono, M.; Nagaoka, Y.; Tomioka, K. *J. Am. Chem. Soc.* **1997**, *119*, 12974. (b) Liu, Y.; Sun, B.; Wang, B.; Wakem, M.; Deng, L. *J. Am. Chem. Soc.* **2009**, *131*, 418. (c) Li, B. J.; Jiang, L.; Liu, M.; Chen, Y. C.; Ding, L. S.; Wu, Y. *Synlett* **2005**, 603. (d) Rana, N. K.; Singh, V. K. *Org. Lett.* **2011**, *13*, 6520. (e) Dong, X.; Fang, X.; Tao, H.; Zhou, X.; Wang, C. *Adv. Synth. Catal.* **2012**, *354*, 1141. (f) Fang, X.; Li, J.; Wang, C. *Org. Lett.* **2013**, *15*, 3448.

8. (a) Emori, E.; Arai, T.; Sasai, H.; Shibasaki, M. *J. Am. Chem. Soc.* **1998**, *120*, 4043. (b) Sundararajan, G.; Prabagaran, N. *Org. Lett.* **2001**, *3*, 389. (c) McDaid, P.; Chen, Y.; Deng, L.; *Angew. Chem. Int. Ed.* **2002**, *41*, 338. (d) Shirakawa, S.; Kimura, T.; S. Murata, Shimizu, S. *J. Org. Chem.* **2009**, *74*, 1288. (d) Yoshida, M.; Ohno, Y.; Hara, S. *Tetrahedron Lett.* **2010**, *51*, 5134.

9. (a) Skarzewski, J.; Zielinska-Błajet, M.; Turowska-Tyrk, I. *Tetrahedron: Asymmetry,* **2001**, *12*, 1923. (b) Suresh, P.; Pitchumani, K. *Tetrahedron: Asymmetry* **2008**, *19*, 2037. (c) Ueno, M.; Kitanosono, T.; Sakai, M.; Kobayashi, S. *Org. Biomol. Chem.* **2011**, *9*, 3619. (d) Kitanosono, T.; Sakai, M.; Ueno, M.; Kobayashi, S. *Org. Biomol. Chem.* **2012**, *12*, 7134. (e) Dai, L.; Wang, S. X.; Chen, F. E. *Adv. Syth. Catal.* **2010**, *352*, 2137. (f) Rana, N. K.; Selvakumar, S.; Singh, V. K. *J. Org. Chem.* **2010**, *75*, 2089. (g) Ricci, P.; Carone, A.; Bartoli, G.; Bosco, M.; Sambri, L.; Melchiorre, P. *Adv. Synth. Catal.* **2008**, *350*, 49.

10. Tian, X.; Cassani, C.; Liu, Y.; Moran, A.; Urakawa, A.; Galzerano, P.; Arceo, E.; Melchiorre, P. *J. Am. Chem. Soc.* **2011**, *133*, 17934.

11. Bartoli, G.; Bosco, M.; Carlone, A.; Pesciaioli, F.; Sambri, L.; Melchiorre, P. *Org. Lett.* **2007**, *9*, 1403.

12. (a) De, C. K.; Klauber, E. G.; Seidel, D. *J. Am. Chem. Soc.* **2009**, *131*, 17060. (b) Klauber, E. G.; De, C. K.; Shah, T. K.; Seidel, D. *J. Am. Chem. Soc.* **2010**, *132*, 13624.

13. Labelle, M.; Belley, M.; Gareau, Y.; Gauthier, J. Y.; Guay, D.; Gordon, R.; Grossman, S. G.; Jones, T. R.; Leblanc, Y.; McAuliffe, M.; McFarlane, C.; Masson, P.; Metters, K. M.; Ouimet, N.; Patrick, D. H.; Piechuta, H.; Rochette, C.; Sawyer, N.; Xiang, Y. B.; Ford-

Hutchinson, A. W.; Zamboni, R. J.; Young, R. N. *Bioorg. Med. Chem. Lett.* **1995,** *5*, 283.

14. (a) Jones, T. R.; Labelle, M.; Belley, M.; Champion, E.; Charette, L.; Evans, J.; Ford-Hutchinson, A. W.; Gauthier, J. -Y.; Lord, A.; Masson, P.; McAuliffe, M.; McFarlene, C. S.; Metters, K. M.; Pickett, C.; Piochuta, H.; Rochette, C.; Rodger, I. W.; Sawyer, N.; Young, R. N.; Zamboni, R.; Abraham, W. M. *Can. J. Pharmacol.* **1995**, *73*, 191. (b) Noonan, M. J.; Chervinsky, P.; Brandon, M.; Zhang, J.; Kundu, S.; McBurney, J.; Reiss, T. F. *Eur. Respir. J.* **1998**, *11*, 1232. (c) Markham, A.; Faulds, D. *Drugs* **1998**, *56*, 251.
15. King, A. O.; Corley, E. G.; Anderson, R. K.; Larsen, R. D.; Verhoeven, T. R.; Reider, P. J.; Xiang,Y. B.; Belley, M.; Leblanc, Y.; Labelle, M.; Prasit, P.; Zamboni, R. J. *J. Org. Chem.* **1993**, *58*, 3731.
16. McNamara, J. M.; Leazer, J. L.; Bhupathy, M.; Amato, J. S.; Reamer, R. A.; Reider, P. J.; Grabowski, E. J. J. *J. Org. Chem.* **1989**, *54*, 3718.
17. Yan, Y.; Xu, K.; Fang, Y.; Wang, Z. *J. Org. Chem.* **2011**, *76*, 6849.
18. Caglioti, L. *Tetrahedron* **1966**, *22*, 487.
19. B. Satyanarayana, P. P. Reddy, *Synth. Commun.* **2007**, *37*, 545.
20. Sibi, M. P.; Manyem, S. *Tetrahedron* **2000**, *56*, 8033.
21. Coucouvanis, D.; Lippard, S. J.; Zubieta, J. A. *J. Am. Chem. Soc.* **1970**, *92*, 3342-3347.
22. For a review see: Coe, B. J.; Glenwright, S. J. *Coord. Chem. Rev.* **2000**, *203*, 5.
23. A 180° rotation around the Fe-O^2 bond creates a steric clash of R^3 with the proximal *tert*-butyl group of the salen ligand.

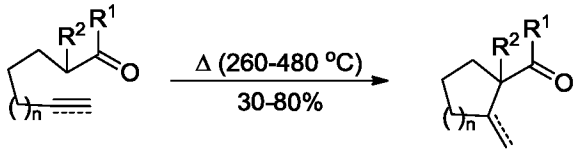
24. Compounds **301** (CAS 4965-33-7), **302** (CAS 626-19-7), and **316** (CAS 162515-68-6) were purchased from Oakwood Chemical Co., West Columbia, SC, 29172.

CHAPTER 7

The Asymmetric Intramolecular Conia-ene Reaction

7.1 Introduction

The addition of enols and enolates to unactivated alkenes or alkynes represents a valuable and atom-economic method for the formation of carbon-carbon bonds.[1] By extension, the intramolecular version of this reaction using an unsaturated carbonyl compound provides a method for the formation of carbocycles (carbocyclization) from their isomeric acyclic counterparts. In 1975, Conia reported that carbocyclization of unsaturated ketones **284** could be effected under thermal conditions,[2] with cyclized products **285** being formed in moderate yield from the reaction (Scheme 7.1).



284 **285**

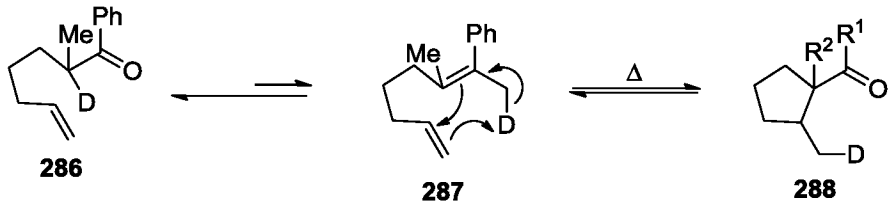
n = 1-4

R^1 = alkyl, aryl

R^1 = H, alkyl, COR, CO_2R

Scheme 7.1 Conia's carbocyclization of alkenyl and alkynyl ketones ("Conia-ene" reaction)

The mechanism of this reaction was elucidated using deuterium labeling experiments. It was found that deuterated ketone **286** first tautomerizes to its enol form **287** which undergoes a concerted 1,5-deuterium shift to afford cyclized product **288** (Scheme 7.2).

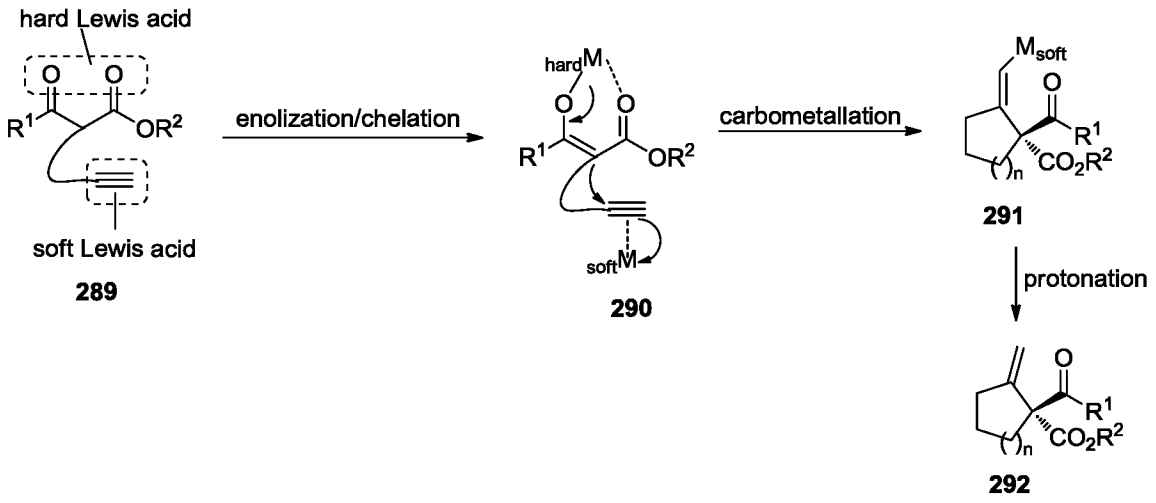


Scheme 7.2 Mechanism of carbocyclization of ketones under thermal conditions

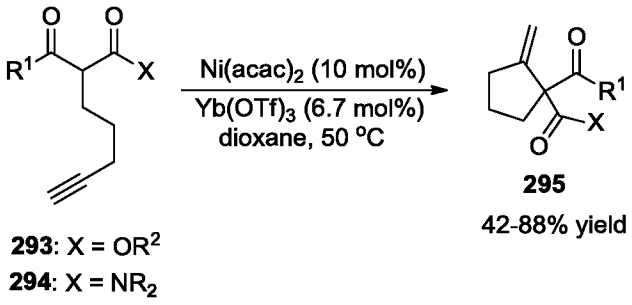
With a ketone as starting material, the reaction generally requires a temperature above 350 °C to afford a cyclopentane or cyclohexane derivative, while carbocyclization leading to a medium sized ring requires even higher temperature (above 390 °C). The need for harsh conditions, including high temperature[2] and strong acids,[3] has severely limited the synthetic utility of the Conia-ene reaction, and consequently has prompted a search for a catalytic version which would proceed at ambient temperature under mild conditions.

Recent advances in transition metal catalysis has led to the discovery of several new catalytic systems for the Conia-ene reaction.[4] In practice, these reactions employ a combination of hard and soft Lewis acids as catalysts. A general mechanism for this type of Conia-ene reaction with an alkynyl β-keto ester **289** is shown in Scheme 7.3. The hard Lewis acid assists enolization of the β-keto ester **289** and leads to chelated enol **290** while the soft Lewis acid, usually a transition metal salt, complexes with the π-electrons of the acetylenic bond. Internal carbometalation of the activated alkyne gives metalated cycloproduct **291** which after protonation produces cycloalkane **292**. Yang and coworkers were among the first to demonstrate[4h] a transition metal-catalyzed Conia-ene carbocyclization with their nickel(II)-catalyzed intramolecular addition of β-keto ester

293 and keto amide **294** to an unactivated alkyne. The reaction gave cyclopentane **295** in fair-to-good yield (Scheme 7.4). In this reaction, ytterbium(III) triflate acts as a hard Lewis acid while nickel(II) acetylacetonate plays the role of a soft Lewis acid.



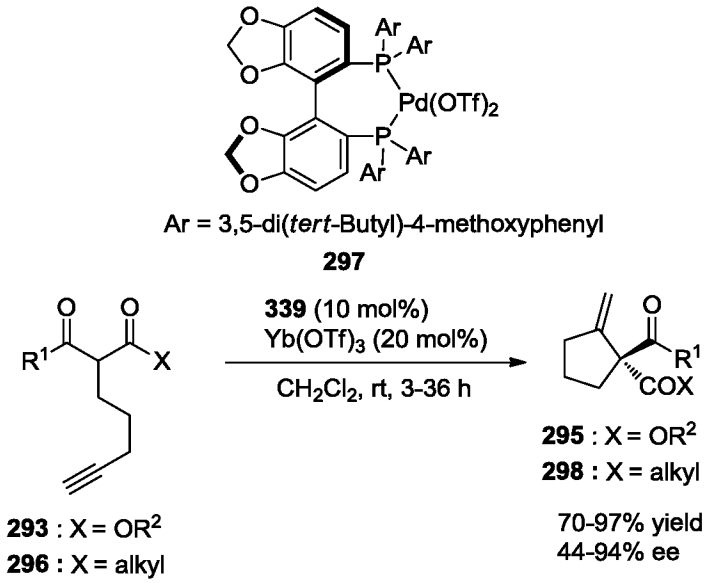
Scheme 7.3 General mechanism of carbocyclization of alkynyl β-keto esters catalyzed by a combination of hard and soft Lewis acids



Scheme 7.4 Yang's Conia-ene reaction catalyzed by nickel(II) acetylacetonate and ytterbium(III) triflate

It took three decades after the initial discovery by Conia to develop an enantioselective version of his reaction. The main obstacles to stereoselectivity in the

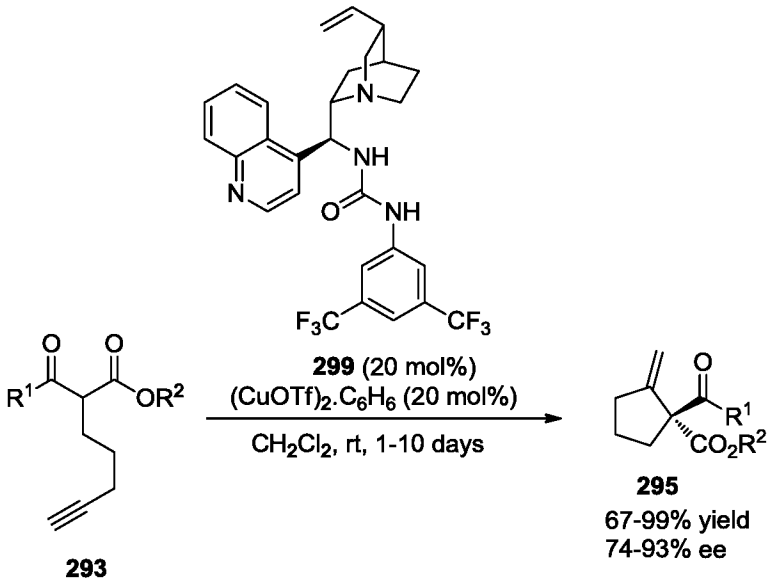
reaction were its reversibility and isomerization of the exocyclic double bond under the reaction conditions to give a more stable endocyclic alkene. The first enantioselective intramolecular Conia-ene reaction was reported in 2005 by Toste and coworkers using a α-pentynyl β-dicarbonyl substrate and a palladium(II)/ytterbium(III) catalyst system.[5a] The chiral palladium complex **297**[6] in combination with a catalytic amount of ytterbium(III) triflate transformed β-keto ester **293** and β-diketone **296** into their cyclic isomers **295** and **298**, respectively, in moderate to good enantiomeric excess (Scheme 7.5).



Scheme 7.5 Toste's enantioselective Conia-ene reaction of β-keto ester **293** and β-diketone **296** catalyzed by palladium complex **297** and ytterbium(III) triflate

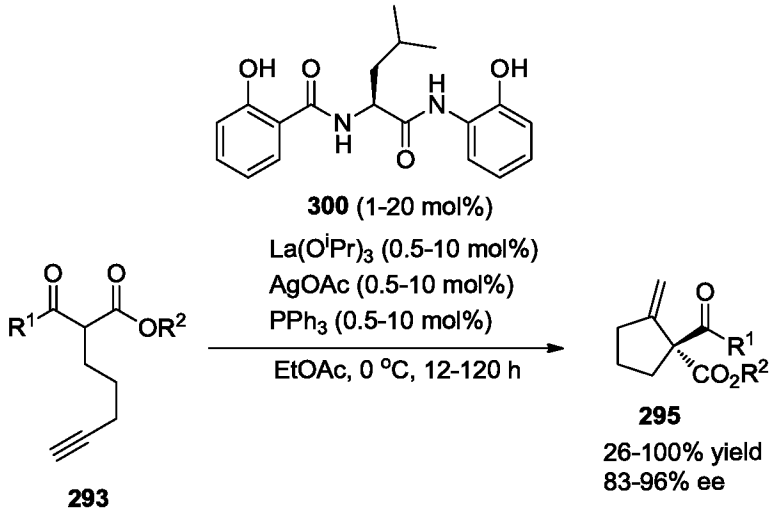
Subsequently, Dixon and coworkers reported an enantioselective Conia-ene cyclization of β-keto ester **293** catalyzed by the Cinchona alkaloid based bifunctional urea derivative **299** and copper(I) triflate-benzene complex.[5b] The reaction proceeded

very slowly (up to 10 days) at room temperature but afforded cyclopentane derivative **295** in good enantiomeric excess (Scheme 7.6)



Scheme 7.6 Dixon's enantioselective Conia-ene reaction of β-keto ester **293** catalyzed by Cinchona alkaloid derivative **299** and copper(I) triflate-benzene complex

Very recently, Shibasaki published an asymmetric Conia-ene reaction of β-keto ester **293** catalyzed by leucine-based bis-amide **300** in combination with lanthanum triflate, silver acetate and triphenylphosphine.[5c] This catalyst system afforded cyclopentane derivative **295** in good enantiomeric excess and represents the most effective catalyst developed thus far for an asymmetric Conia-ene cyclization (Scheme 7.7).



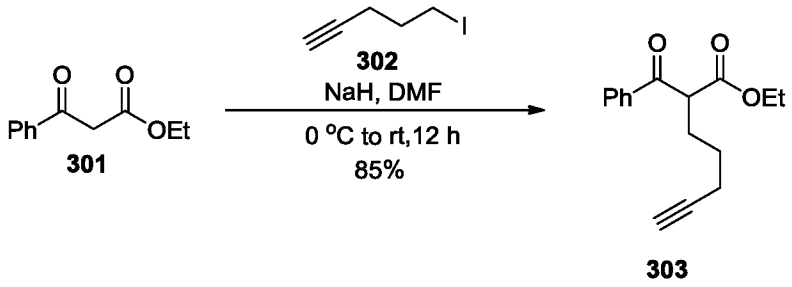
Scheme 7.7 Shibasaki's chiral bis-amide **300** catalyzed enantioselective Conia-ene cyclization of β-keto ester **293**

7.2 *Cis*-2,5-diaminobicyclo[2.2.2]octane based metal complexes for the intramolecular enantioselective Conia-ene reaction

Our initial approach to finding a suitable catalyst for asymmetric Conia-ene cyclization was influenced by the work of Yang[4h] who showed that an achiral tetracoordinate nickel(II) complex in association with ytterbium(III) triflate can catalyze carbocyclization of alkynyl substituted β-keto esters and β-keto amides (Scheme 7.3). We speculated that a chiral nickel(II)-salen complex in place of Yang's nickel acetylacetonate could induce enantioselectivity in Conia-ene carbocyclization and our nickel complex (+)-**75** (chapter 2, Table 2.1, entry 9) was therefore selected as a candidate for catalysis of an asymmetric variation of the reaction.

Our hypothesis was tested on β-keto ester **303** which was synthesized by

alkylation of the sodium enolate of commercially available ethyl 3-oxo-3-phenylpropionate (**301**) with 5-iodo-1-pentyne (**302**, Scheme 7.8).[4e]

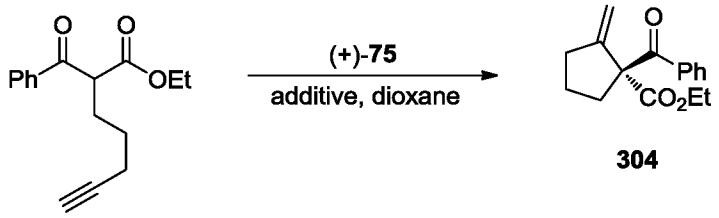


Scheme 7.8 Synthesis of Conia-ene precursor **303**

Preliminary studies with **303** to assess its reactivity were performed in dioxane as solvent in the presence of nickel-salen complex (+)-**75** with ytterbium(III) triflate as a co-catalyst. In contrast to Yang's result, when **303** was treated with 10 mol% of (+)-**75** and 6.7 mol% of ytterbium(III) triflate at 50 °C no reaction took place (Table 7.1, entry 1). Increasing the reaction temperature to 80 °C also resulted in no reaction (entry 2). However, increasing the proportion of ytterbium(III) triflate to 20 mol% gave cyclized product **304** in 89% yield although with low enantiomeric excess (entry 3). The absolute configuration of the major enantiomer of **304** was found to be (*R*) by comparison of its optical rotation with the literature value.[5a] Increased catalyst loading of (+)-**75** to 20 mol% led to decreased yield as well as lower enantiomeric excess of cyclic product (51% yield and 12% enantiomeric excess, entry 4) while a stoichiometric amount of ytterbium(III) triflate also resulted in poor enantiomeric excess of **304** (entry 5). Recognizing that other rare earth metal triflates such as scandium(III) and lanthanum(III) triflates could be used to promote enolization of **303**, those co-catalysts were also

examined (Table 7.1, entries 6, 7) but they resulted in very poor asymmetric induction (11% and 6% enantiomeric excess, respectively). The Lewis acid boron trifluoride diethyl etherate produced only racemic cycloproduct in low yield (36%, entry 8) whereas acetic acid led to decomposition of our nickel(II) complex (+)-**75** (entry 9).

Table 7.1 Asymmetric Conia-ene cyclization of β-keto ester **303** catalyzed by nickel(II)-salen complex (+)-**75**[a] and co-catalysts[a]



303 **304**

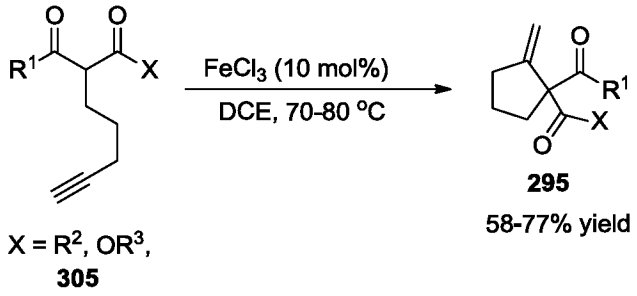
Product **304**

entry	additive (mol%)	(+)-**75** (mol%)	T (°C)	yield (%)[b]	ee (%)[c]
1	$Yb(OTf)_3$ (6.7)	10	50	nr	-
2	$Yb(OTf)_3$ (6.7)	10	80	nr	-
3	$Yb(OTf)_3$ (20)	10	60	89	35
4	$Yb(OTf)_3$ (20)	20	60	51	12
5	$Yb(OTf)_3$ (100)	10	60	63	21
6	$Sc(OTf)_3$ (20)	10	60	42	11
7	$La(OTf)_3$ (20)	10	60	23	6
8	$BF_3.OEt_2$ (20)	10	25	36	0
9	AcOH (20)	10	25	decomp.	-

[a]The reactions were carried out on a 0.25 mmol scale in a 0.0625M

solution of dioxane. [b]Yield of isolated product. [c]Determined by HPLC using a Chiralcel OD column. nr = no reaction

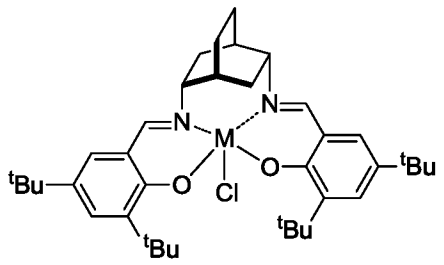
The disappointing results obtained with (+)-**75** and various co-catalysts in the Conia-ene carbocylization of **303** led us to conjecture that activation of the alkyne and enolization of the β-dicarbonyl moiety with a single catalytic species rather than a combination of hard and soft Lewis acids as shown in Scheme 7.3 could result in improved enantioselectivity of the reaction. This idea was supported by a recent finding of Kim and coworkers who showed that iron(III) chloride alone can promote Conia-ene cyclization of ε-acetylenic 1,3-dicarbonyl compound **305**.[7] The reaction proceeds at elevated temperature (70-80 °C) and produces cyclopentane derivative **295** in moderate yield (Scheme 7.9).



Scheme 7.9 Kim's Conia-ene cyclization catalyzed by iron(III) chloride

Chiral metal complexes (+)-**67**-(+)-**78** prepared from salen ligand (+)-**35** based on a *cis*-2,5-diaminobicyclo[2.2.2]octane scaffold (chapter 2, Scheme 2.10) have been shown to be efficient catalysts for a variety of asymmetric transformations. For example, we demonstrated that chromium(III) complex (+)-**70** catalyzes the asymmetric hetero-Diels-Alder reaction of aldehydes with Danishefsky diene (chapter 3, table 3.2) and the

asymmetric Nozaki-Hiyama-Kishi reaction (chapter 4, Table 4.3) of allyl bromide with aromatic aldehydes, while iron(III) complex (+)-**72** induced a high degree of asymmetry in the sulfa-Michael addition of thiols to acyclic enones (chapter 6, Tables 6.4 and 6.5). In these cases, as with the copper(I) complex of tetrahydrosalen (+)-**173** that catalyzes the Henry reaction of nitro alkanes with aldehydes, the complexes induce asymmetry by virtue of their Lewis acidic properties. We therefore selected a subset of our metal-salen complexes, **67**, **68**, **70-72**, **78** (Figure 7.1) in which the embedded metal ion could in principle form a strong coordinate bond with a carbonyl oxygen of β-keto ester **303**.



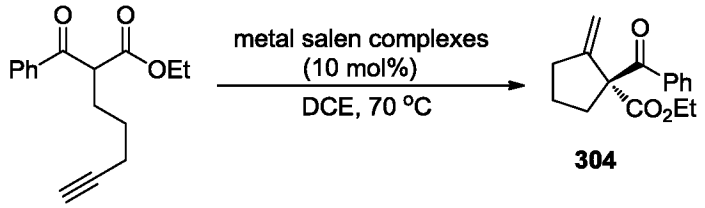
(+)-**67**: M = Ti(O*i*Pr) (+)-**71**: M = Mn
(+)-**68**: M = V(O) (+)-**72**: M = Fe
(+)-**70**: M = Cr (+)-**78** : M = Al

Figure 7.1 Metal-salen complexes as candidates for enantioselective Conia-ene reaction

The efficacy of these metal-salen complexes as asymmetric catalysts of the Conia-ene reaction of **303** was examined (Table 7.2) following Kim's protocol with iron(III) chloride in which a 10 mol% loading of the catalyst was used in 1,2-dichloroethane as solvent at 70 °C. Neither titanium complex (+)-**67** nor vanadium complex (+)-**68** reacted with **303** (entries 1, 2), and of the remaining metal-salen catalytic systems iron(III)-salen complex (+)-**72** appeared to be the most promising (entry 5). This finding led to a study of the effect of counter anions on the catalytic properties of (+)-**72**

which was conducted by premixing an equimolar amount of a silver salt with (+)-**72** (entries 7-10). Counter anions trifluoroacetate, tetrafluoroborate and triflate all had beneficial effects on Conia-ene cyclization of **303** (entries 7-10), with trifluroacetate being the most effective in terms of enantioselectivity of the reaction (53% enantiomeric excess, entry 8) and triflate anion best in terms of yield of **304** (94%, entry 10).

Table 7.2 Asymmetric Conia-ene cyclization of β-keto ester **303** catalyzed by metal-salen complexes[a]



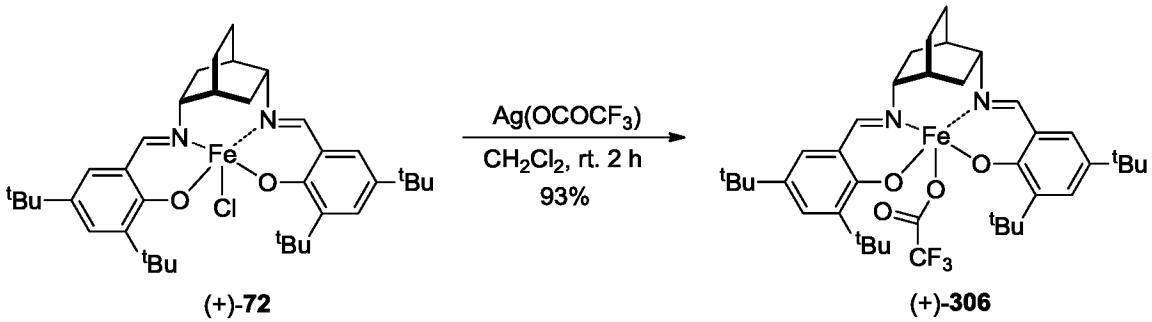
303 **304**

				Product **304**	
entry	catalyst	additive	t (h)	yield (%)[b]	ee (%)[c]
1	(+)-**67**	-	48	nr	-
2	(+)-**68**	-	48	nr	-
3	(+)-**70**	-	30	42	12
4	(+)-**71**	-	30	67	29
5	(+)-**72**	-	14	69	38
6	(+)-**78**	-	52	29	7
7	(+)-**72**	AgOAc	21	65	42
8	(+)-**72**	$Ag(OCOCF_3)$	12	91	53
9	(+)-**72**	$AgBF_4$	15	82	34

10	(+)-**72**	AgOTf	12	94	39

[a]The reactions were carried out on a 0.25 mmol scale in a 0.0625M solution of DCE using 10 mol% of metal-salen complex and additive. [b]Yield of isolated product. [c]Determined by HPLC using a Chiralcel OD column.

The encouraging results shown in Table 7.2, especially entry 8, prompted us to attempt isolation of the active catalyst formed from (+)-**72** and silver trifluoroacetate. To achieve this, (+)-**72** was reacted with an equimolar amount of silver trifluoroacetate in dichloromethane at room temperatute. After removal of the insoluble silver chloride, iron-salen complex (+)-**306** bearing trifluoroacetate as the counter anion was obtained as a brown solid in 93% yield (Scheme 7.10) and was characterized by high resolution mass spectrometry.

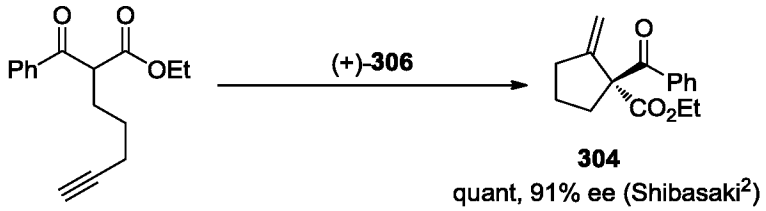


Scheme 7.10 Synthesis of iron(III) trifluoroacetate complex (+)-**306** from (+)-**72**

With isolated iron-salen complex (+)-**306** in hand, we found that the preformed catalyst gave only a marginally higher enantiomeric excess of cycloproduct **304** than the catalyst prepared in situ (Table 7.3, entry 1 *cf.* Table 7.2, entry 8). However, we noted that there was a significant effect of solvent polarity on the rate of the reaction (entries 1-6). It was observed that the reaction of **303** proceeded at a much faster rate in the non-

polar solvents 1,2-dichloroethane, toluene and chloroform (entries 1-3) and afforded **304** in higher yield and enantiomeric excess than in the polar solvents dioxane, tetrahydrofuran and acetonitrile (entries 4-6). 1,2-Dichloroethane was found to be the best choice of solvent for the reaction in terms of enantioselectivity (57% enantiomeric excess, entry 1) while increased catalyst loading from 10 mol% to 20 mol% gave only marginal improvement in yield and asymmetric induction (entry 7).

Table 7.3 Asymmetric Conia-ene cyclization of β-keto ester **303** catalyzed by iron(III)-salen complex (+)-**306**[a]



303

304
quant, 91% ee (Shibasaki[2])

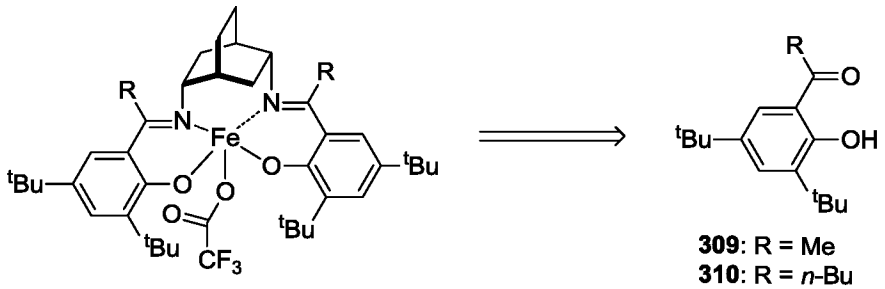
					Product **304**	
entry	(+)-**306** (mol%)	solvent	T (°C)	t (h)	yield (%)[b]	ee (%)[c]
1	10	DCE	70	12	91	57
2	10	PhMe	70	20	82	45
3	10	$CHCl_3$	60	16	91	49
4	10	dioxane	70	48	46	16
5	10	THF	66	48	51	12
6	10	MeCN	70	56	39	10
7	20	DCE	70	9	95	59

[a]The reactions were carried out on a 0.25 mmol scale in a 0.0625M solution of the solvent. [b]Yield of isolated product. [c]Determined by HPLC using a Chiralcel

OD column.

The data in Table 7.2 (entry 8) and Table 7.3 (entries 1, 7) informed us that conditions for optimized enantioselective carbocyclization of **303** required iron-salen complex (+)-**306** in 1,2-dichloroethane as solvent at a reaction temperature of 70 ^{o} C and under these conditions the yield of **304** is high. However, the enantiomeric excess of **304** at 53% falls well short of values obtained with other catalyst systems[5] and leaves this study of Conia-ene cyclization with catalyst (+)-**306** at an unsatisfactory stage. In light of this shortcoming, it was decided to modify the structure of our salen ligand.

Salen ligands derived from condensation of salicylic ketones with diamines are known to react with transition metal salts including iron(III),[8] manganese(III),[9] cobalt(II),[10,11] and nickel(II) salts.[11] Metal complexes obtained with these ligands show catalytic activity for many organic transformations.[10] Our rationale for this structural modification was that increased steric bulk around the imine nitrogen atoms ligated to the central iron atom of our catalyst would steer reaction of the metal complexed alkyne more selectively towards one face of the planar enolate without disrupting the reaction pathway expressed generically in Scheme 7.3. Methyl and *n*-butyl salicylic ketones **309** and **310** were chosen as precursors to second generation iron-salen complexes **307** and **308** because they were known compounds (Figure 7.2).[12]

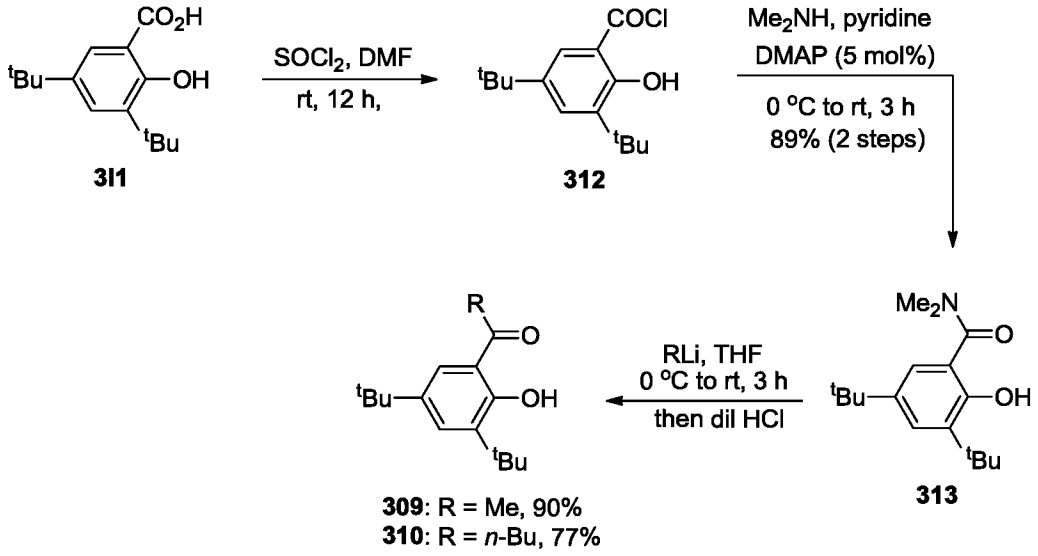


307: R = Me
308: R = *n*-Bu

309: R = Me
310: R = *n*-Bu

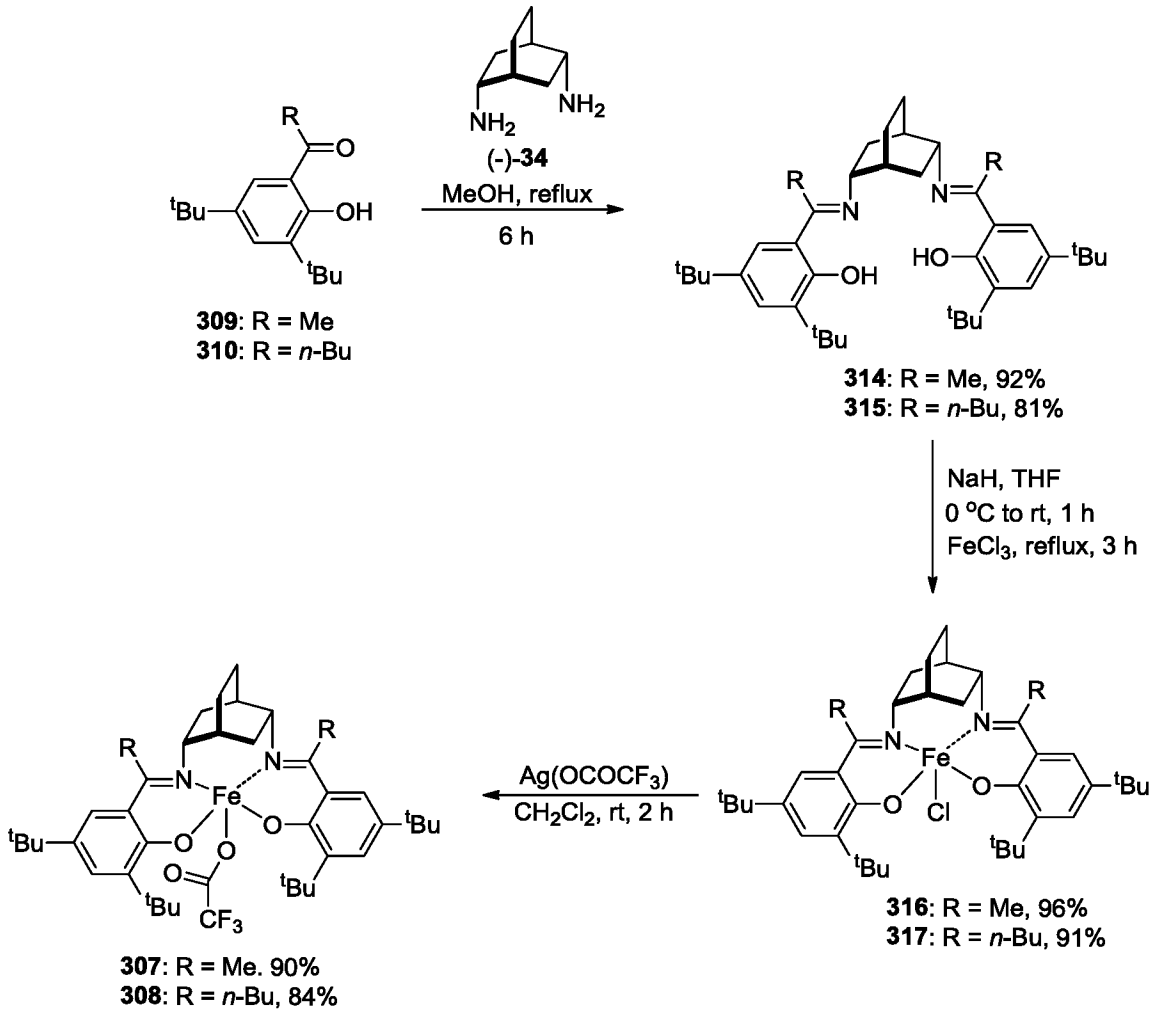
Figure 7.2 Second generation iron(III)-salen complexes **307** and **308** for catalysis of the enantioselective Conia-ene reaction

2,4-Di-*tert*-butyl-6-acylphenols **309** and **310** were synthesized from commercially available 3,5-di-*tert*-butylsalicylic acid (**311**) following Belmar's protocol (Scheme 7.11).[12] Salicylic acid **311** was reacted with thionyl chloride in the presence of a catalytic amount of dimethylformamide at room temperature to yield acid chloride **312**. Treatment of the crude acid chloride with dimethylamine in pyridine furnished *N*,*N*-dimethyl-3,5-di-*tert*-butylsalicylamide (**313**) in good yield and the amide was reacted with methyllithium or *n*-butyllithium at low temperature to afford salicylic ketones **309** and **310**, respectively.



Scheme 7.11 Synthesis of 2,4-di-*tert*-butyl-6-acylphenols **309** and **310**

Condensation of a methanolic solution of 2,4-di-*tert*-butyl-6-acylphenols **309** and **310** with diamine (-)-**34** in a 2:1 molar ratio under reflux afforded Schiff bases **314** and **315**, respectively, as yellow solids. Iron-salen complexes **316** and **317** were obtained in good yield from the sodium alkoxides of **314** and **315** by reaction with iron(III) chloride, and treatment of chloro complexes **316** and **317** with a stoichiometric amount of silver trifluoroacetate furnished iron complexes **307** and **308** (Scheme 7.12).

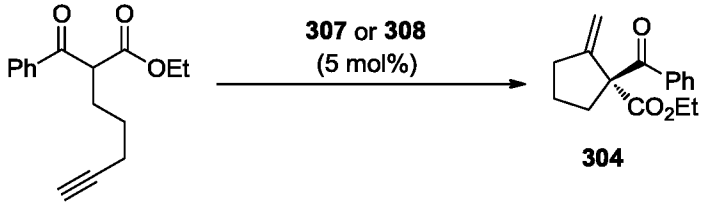


Scheme 7.12 Synthesis of the second generation iron-salen complexes **307** and **308**

It was immediately clear upon testing our second generation iron-salen complexes **307** and **308** in the Conia-ene reaction of keto ester **303** that enantioselectivity was improved over the reaction with catalyst **306** (Table 7.4). With 5 mol% of catalyst **307** in 1,2-dichloroethane at 70 °C, **303** gave Conia-ene product **304** in 71% enantiomeric excess. This increased to 84% enantiomeric excess when iron complex **308** with bulkier *n*-butyl groups in the salen framework was used (entries 1, 2). Changing the solvent to

toluene had an unfavorable effect on both yield and enantioselectivity of the reaction (entry 3) but with chloroform as the solvent cyclopentane **304** was obtained in 93% yield and 87% enantiomeric excess (entry 4). This last result represents the best outcome obtained thus far in our study of the asymmetric intramolecular Conia-ene reaction. It confirms our hypothesis that alkyl substitution at the imine function of the salen ligand improves enantioselectivity of the reaction and points to a direction for future research on this useful ring forming reaction.

Table 7.4 Asymmetric Conia-ene cyclization of β-keto ester **303** catalyzed by second generation iron(III)-salen complexes **307** and **308**



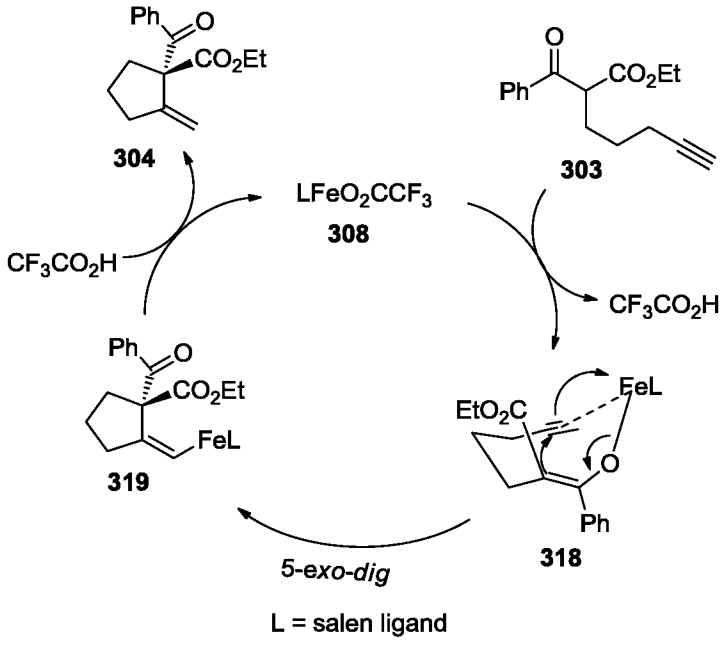
303 **304**

Product **304**

entry	catalyst	solvent	T (°C)	t (h)	Yield (%)[b]	ee (%)[c]
1	**307**	DCE	70	18	78	71
2	**308**	DCE	70	21	72	84
3	**308**	PhMe	70	24	69	76
4	**308**	$CHCl_3$	60	24	93	87

[a]The reactions were carried out on a 0.25 mmol scale in a 0.0625M solution of the solvent. [b]Yield of isolated product. [c]Determined by HPLC using a Chiralcel OD column.

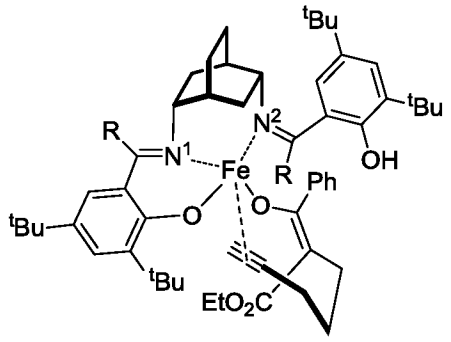
Formation of **304** from **303** in the presence of catalyst **308** can be explained by the catalytic cycle shown in Scheme 7.13. Initial loss of trifluoroacetate ion from the catalyst is followed by formation of iron(III)-enolate **318** in which the metal center coordinates with the acetylenic bond present in the molecule. Iron-enolate **318** undergoes intramolecular 5-*exo*-dig cyclization[13] leading to metalated *exo*-methylene cyclopentane **319**. Upon protonation, **319** gives Conia-ene product **304** while regenerating the catalyst.



Scheme 7.13 Proposed catalytic cycle for the formation of **304** from **303** in the presence of (+)-**308**

It is evident from the results in table 7.4 that there is a strong preference for iron-complex **308** with (1*R*,2*R*,4*R*,5*R*) configuration to give cyclization product **304** of (*R*) configuration from β-keto ester **303**. A transition state **320** explaining this stereochemical outcome is proposed in figure 7.3. This model places the enolate formed from **303** in the

right front quadrant below the bicyclic scaffold. The alkyl substituent (R) on the imino carbon effectively blocks the *si*-face of the enolate leading to *re*-face attack of enolate at the acetylenic bond (5-*exo*-dig). This transition state model explains why catalysts **306** and **307** with hydrogen and methyl groups as iminyl substituents, respectively, are not as effective as **308** with R=*n*-butyl in blocking the *si*-face of the enolate and therefore result in diminished asymmetric induction.



R = *n*-Bu

320

5-exo-dig cyclization at *re*-face of enolate

Figure 7.3 Proposed transition state for the asymmetric Conia-ene reaction of β-keto ester **303** catalyzed by iron(III)-salen complex **308**

In this chapter, we showed that a novel iron(III)-salen catalyst leads to enantioselective Conia-ene cyclization of a β-keto ester bearing an unactivated terminal alkyne. The reaction uses a single metal source that is easy to prepare and is environmentally benign. The product is a chiral cyclopentane with three substituents that can be easily differentiated and manipulated by chemical means. A cyclopentane (or cyclohexane) prepared in this manner from an acyclic precursor affords a useful platform for further structural elaboration. Additional studies on this variant of the asymmetric

Conia-ene reaction using other 1,3-dicarbonyl compounds as substrates and with further structural modifications to the salen ligand along lines explored with catalyst **308** should extend the scope of the process.

7.3 References

1. Denes, F. D.; Perez-Luna, A.; Chemla, F. *Chem. Rev.* **2010**, *110*, 2366.

2. Conia, J. M.; P. Le Perchec, P. L. *Synthesis* **1975**, 1.

3. (a) Kitagawa, O.; Suzuki, T.; Inoue, T.; Watanabe, T.;Taguchi, T. *J. Org. Chem.* **1998**, *63*, 9470. (b) Kitagawa, O.; Fujiwara, H.; Suzuki, T.; Taguchi, Shiro, T. M. *J. Org. Chem.* **2000**, *65*, 6819.

4. (a) Kennedy-Smith, J. J.; Staben, S. T.; Toste, F. D. *J. Am. Chem. Soc.* **2004**, *126*, 4526. (b) Ito, H.; Makida, Y.; Ochida, A.; Ohmiya, H.; Sawamura, M. *Org. Lett.* **2008**, *10*, 5051. (c) Balme, G.; Bouyssi, D.; Faure, R.; Gore, J.; Hemelryck,B. V. *Tetrahedron* **1992**, *48*, 3891. (d) Lomberget, T.; Bouyssi, D.; Balme, G. *Synthesis* **2005**, 311. (e) Cruciani, P.; Stammler, R.; Aubert, C.; Malacria, M. *J. Org. Chem.* **1996**, *61*, 2699. (f) Bouyssi, D.; Monteiro, N.; Balme, G. *Tetrahedron Lett.* **1999**, *40*, 1297. (g) Deng, C. L.; Zou, T.; Wang, Z. Q.; Song, R. J.; Li, J. H. *J. Org. Chem.* **2009**, *74*, 412. (h) Gao, Q.; Zheng, B. F.; Li, J. H.; Yang, D. *Org. Lett.* **2005**, *7*, 2185. (i) Kuninobu, Y.; Kawata, A.; Takai, K. *Org. Lett.* **2005**, *7*, 4823. (j) Deng, C. L.; Song, R. J.; Liu, Y. L.; Li, J. H. *Adv. Synth. Catal.* **2009**, *351*, 3096. (k) Kitagawa, O.; Fujiwara, H.; Suzuki, T.; Taguchi, T.; Shiro, M. *J. Org. Chem.* **2000**, *65*, 6819. (l) Itoh, Y.; Tsuji, H.; Yamagata, K. I.; Endo, K.; Tanaka, I.; Nakamura, M.; Nakamura, E. *J. Am. Chem. Soc.* **2008**, *130*, 17161. (m) Takahashi, K.; Midori, M.; Kawano, K.; Ishihara, J.; Hatakeyama, S. *Angew. Chem. Int. Ed.* **2008**, *47*, 6244.

5. (a) Corkey, B. K.; F. D. Toste, *J. Am Chem. Soc.* **2005**, *125*, 17168. (b) Yang, T.; Ferrali, A.; Sladojevich, F.; Campbell, L.; Dixon, D. J. *J. Am. Chem. Soc.* **2009**, *131*, 9140. (c) Matsuzawa, A.; Mashiko, T.; Kumagai, N.; Shibasaki, M. *Angew. Chem. Int. Ed.* **2011**, *50*, 7616.

6. (a) Hamashima, Y.; Yagi, K.; Takano, H.; Tamas.; Sodeoka, M. *J. Am. Chem. Soc.* **2002**, *124*, 14530. (b) Hamashima, Y.; Suzuki, T.; Shimura, T.; Umebayashi, N.; Tamura, T.; Sasamoto, N.; Sodeoka, M. *Tetrahedron: Asymmetry* **2005**, *46*, 1447.

7. Chan, L. Y.; Kim, S.; Park, Y.; Lee, P. H. *J. Org. Chem.* **2012**, *77*, 5239.

8. Shongwe, M. S.; Al-Zaabi, U. A.; Al-Mjeni, F.; Eribal, C. S.; Sinn, E.; Al-Omari, I. A.; Hamdeh, H. H.; Matoga, D.; Adams, H.; Morris, M. J.; Rheingold, A. L.; Bill, E.; Sellmyer, D. J. *Inorg. Chem.* **2012**, *51*, 8241.

9. Chakraborty, J.; Samanta, B.; Pilet, G.; Mitra, S. *Struct. Chem.* **2006**, *17*, 585.

10. Pui, A.; Berdan, I.; Morgenstern-Badarau, I.; Gref , A.; Perree-Fauvet, M. *Inorg. Chim. Acta* **2001**, *320*, 167.

11. Sibous, L.; Bentouhami, E.; Khan, M. A. *J. Inor. Chem.* **2013**, 1.

12. Jimenez, C. A.; Belmar, J. B. *Synth. Comm.* **2007**, *37*, 2391.

13. Baldwin, J. E. *J. Chem. Soc. Chem. Commun.* **1976**, 734.

CHAPTER 8

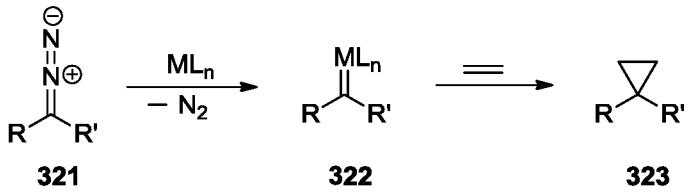
Asymmetric Cyclopropanation

8.1 Introduction

Cyclopropanes, the smallest of the cycloalkanes, are of interest due to their unique combination of reactivity and structural properties. The cyclopropane unit is found within a wide range of naturally occurring substances, including terpenes, pheromones, fatty acid metabolites as well as other compounds such as non-natural amino acids.[1] The large degree of ring strain in cyclopropanes and the ability to orchestrate fragmentation of the three-membered ring in a selective fashion make cyclopropanes extremely valuable synthetic precursors for preparation of other cyclic and acyclic compounds.[2,3] When they are available in enantiopure form, chiral cyclopropanes serve as versatile platforms for synthesizing other chiral compounds.

The most widely used method for synthesizing a cyclopropane is via addition of a carbene (or carbenoid) to an alkene. A diazo compound is frequently the source of the carbene. Decomposition of diazo compounds upon heating, irradiation, or by treatment with certain transition metal complexes usually gives rise to highly reactive carbenes which may undergo addition to a π-bond (cyclopropanation or cyclopropenation), but can also participate in C-H insertion (C-C bond formation) and ylide formation. Furthermore, decomposition of diazo compounds by heating or irradiation generates free carbenes under conditions where control of stereochemistry in addition to an alkene is difficult. On

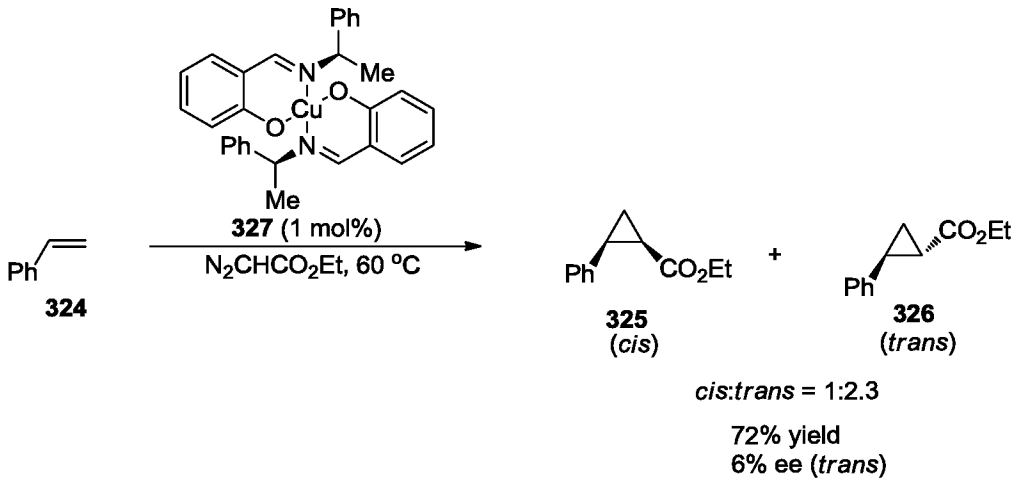
the other hand, decomposition of a diazo compound in the presence of a transition metal can lead to a carbene-transition metal complex (a carbenoid) where the stereochemistry of the reaction can be controlled by a chiral ligand (L) coordinated to the transition metal (Scheme 8.1).



Scheme 8.1 Transition metal mediated reaction of a diazo compound **321** with ethylene

Cyclopropanation of olefins via carbene transfer catalyzed by transition metal complexes represents one of the most attractive approaches to the stereoselective preparation of chiral cyclopropanes.[4] Catalysts containing copper,[5] rhodium,[6] and, more recently, ruthenium[7] and cobalt[8-12] metal ions have been employed and can achieve a high level of stereocontrol in construction of cyclopropanes. Catalysts based on late transition metals such as gold,[13] iron,[14] iridium[15] and osmium[16] have also been reported, albeit less commonly.

The first example of catalytic asymmetric cyclopropanation was reported in 1966 by Noyori and coworkers who used copper complex **327** as the catalyst.[5a] It is worth noting that this also represents the first example of an enantioselective reaction in a homogenous phase catalyzed by a transition metal. Disappointingly, the reaction afforded cyclopropane derivatives **325** and **326** with poor diastereoselectivity and even lower enantioselectivity (Scheme 8.2).



Scheme 8.2 Noyori's diastereoselctive and enantioselective cyclopropanation catalyzed by copper-salen complex **327**

For the next three decades, copper continued to be the metal of primary interest for catalytic cyclopropanation. Of the chiral ligands developed for copper-catalyzed cyclopropanation, bidentate bisoxazoline structures (**328-335**), commonly known as "Box", have been the most widely studied.[5b-h] Chiral bisoxazolines were synthesized with a large structural variation in the functionality bridging the pair of oxazolines resulting in a wide variation in electronic properties of the system. These chiral ligands when used in combination with a copper salt for catalytic enantioselective cyclopropanation of styrene with a diazo ester were found to give cyclopropanes in good yield, diastereomeric ratio and enantiomeric excess in many cases (Figure 8.1).

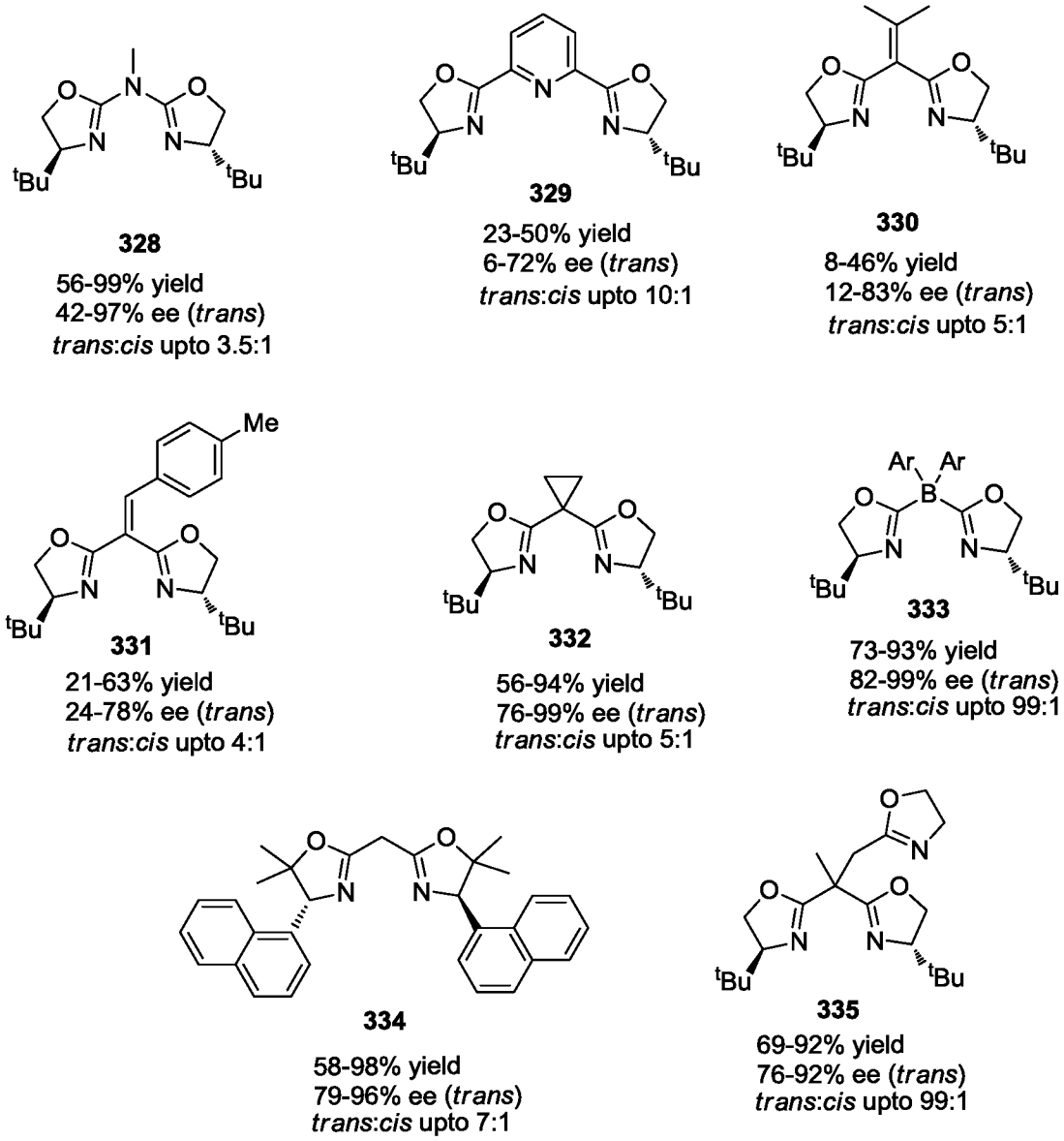
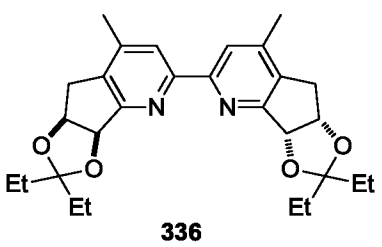


Figure 8.1 Chiral bisoxazoline ligands for copper catalyzed enantioselective cyclopropanation of alkenes

Chiral ligands other than bisoxazolines have also been investigated for asymmetric cyclopropanation.[5i-m] For example, the C_2-symmetric bipyridine-derived ligand **336** (Figure 8.2) was studied by Wilson and coworkers on the supposition that the

2,2′-bipyridine unit offers the potential for a broad range of structural modifications, including incorporation of stereogenic centers and elements of planar and axial chirality.[5i] In practice, very high diastereo- and enantioselectivity were observed (>95:5 diastereomeric ratio and up to 99% enantiomeric excess) when ligand **336** was employed in the asymmetric cyclopropanation of a series of alkenes with diazo esters. The same series of reactions was examined by Sacchetti and coworkers using the C_1-symmetric ligand **337** (Figure 8.2); up to 98% enantiomeric excess was obtained for the *trans*-cyclopropane in this case.[5j] Other ligands such as chiral binaphthyldiimine **338**[5k] and amino alcohol **339** (Figure 8.2)[5l] have also been investigated but only moderate stereoselectivity was seen with these ligands.



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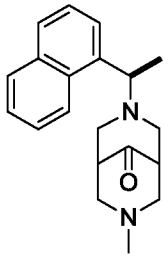

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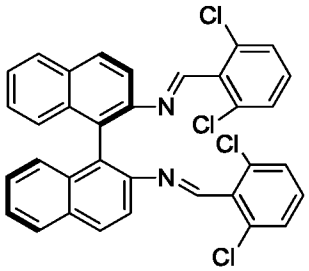

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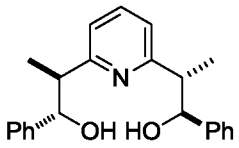
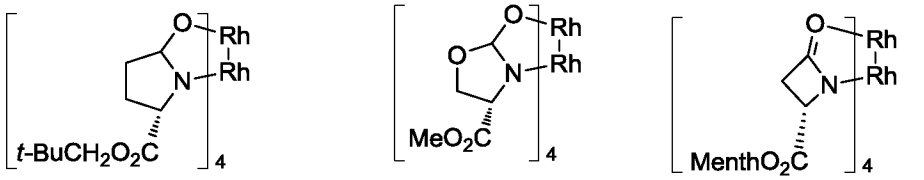


339

Figure 8.2 Other chiral ligands used for copper catalyzed enantioselective cyclopropanation of alkenes

Rhodium complexes are also a well-known family of catalysts for enantioselective cyclopropanation. The discovery of dirhodium(II) carboxamidate and

carboxylate catalysts has resulted in highly stereoselective cyclopropanation with α-diazocarbonyl compounds *via* both inter- and intramolecular reaction pathways. Thus, Rh_2(5S-MEPY)$_4$ (**340,** Figure 8.3), first reported by Doyle and coworkers in 1991, is an especially effective catalyst for enantioselective intramolecular cyclopropanation with allylic diazoacetates (up to 98% enantiomeric excess)[6a,b] and homoallylic diazoacetates (up to 90% enantiomeric excess).[6b] By tuning electronic and steric properties of the carboxamide ligand, Rh_2(4S-MEOX)$_4$ (**341,** Figure 8.3) was shown to be an efficient catalyst for enantioselective intramolecular cyclopropanation of allylic diazoacetamides (up to 98% enantiomeric excess).[6b] For intermolecular cyclopropanation, the dirhodium complex of the azetidinone-based ligand Rh_2[(*S*,*R*)-MenthAZ]$_4$ (**342,** Figure 8.3) was found to be effective in catalyzing cyclopropanation of terminal olefins using diazoacetates.[6c]



340 Rh_2(5*S*-MEPY)$_4$ **341** Rh_2(4*S*-MEOX)$_4$ **342** Rh_2[(*S*,*R*)-MenthAZ]$_4$

Figure 8.3 Chiral dirhodium(II) carboxamidates for enantioselective cyclopropanation of alkenes

Ligands derived from *N*-arylsulfonylproline were first reported by McKervey and coworkers for cyclopropanation of α-diazoketones.[6d] Later, one of its derivatives, Rh_2(*S*-DOSP) (**343**, Figure 8.4), was used by Davies and coworkers for cyclopropanation of olefins with vinyl diazomethanes.[6e] The Davies group also demonstrated that catalyst **343**

was well suited to cyclopropanation with donor/acceptor substituted diazo esters. High enantioselectivity was achieved with a wide range of diazo reagents containing aryl or vinyl functionality as the electron-donating group.[6f,g] For other donor/acceptor-substituted diazo compounds such as diazophosphonates[6h] and trifluorodiazoethanes,[6i] the adamantyl catalyst Rh_2(*S*-PTAD)$_4$ (**344**, Figure 8.4) was shown to give better results than **343**. Muller and coworkers found that Rh_2(Snttl)$_4$ (**346,** Figure 8.4), an analog of Hashimoto's phthalimido catalyst Rh_2(S-pttl)$_4$ (**345,** Figure 8.4),[6j] catalyzed cyclopropanation of styrene derivatives with (silanyloxyvinyl)diazoacetates, affording vinyl-substituted cyclopropanes with exceptional diastereo- and enantioselectivity.[6k,l] In addition to these two major families of dirhodium catalysts, a class of dirhodium(II) complexes with *ortho*-metalated arylphosphine (PC) ligands, **347** and **348** (Figure 8.4), were reported by Lahuerta and coworkers to catalyze cyclopropanation.[6m,n] These complexes, with the general formula $Rh_2(OOCR)_2$-$(PC)_2$, contain two *ortho*-metalated phosphines in a *head-to-tail* configuration, along with two polarizable aromatic ligands that offer tunable electronic characteristics. These catalysts were capable of providing high yields and a good level of enantiocontrol in the cyclopropanation of alkenes with diazo ketones.

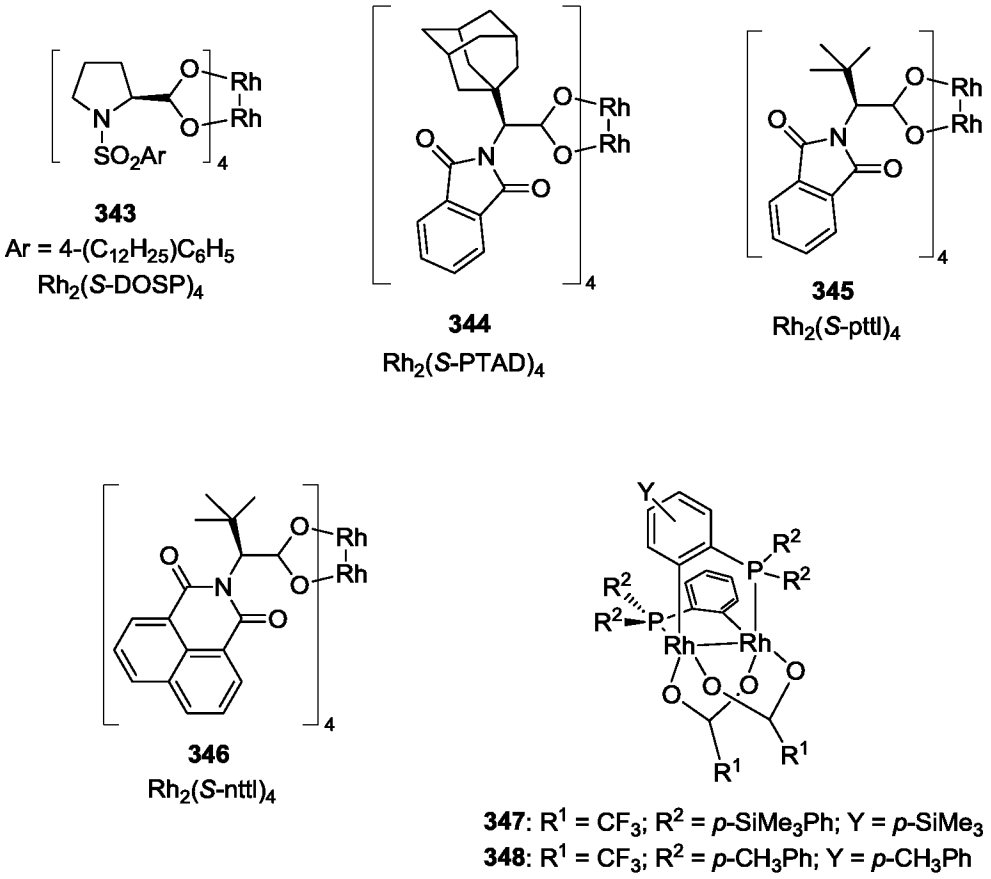
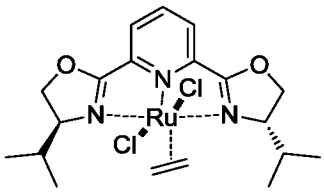


Figure 8.4 Chiral dirhodium(II) carboxylates for enantioselective cyclopropanation of alkenes

In contrast to rhodium, ruthenium is still a relatively new metal in the field of catalytic cyclopropanation, most applications having been discovered in the last decade. The attention given to ruthenium complexes arises from two sources. One is that the price of ruthenium is just one tenth the price of rhodium. The other is that ruthenium complexes have access to a larger number of oxidation states and hence a richer coordination chemistry than is available to rhodium complexes.

The chiral Ru(pybox) catalyst **349** (Figure 8.5), first developed by Nishiyama and coworkers,[7a] has become one of the most widely used catalysts for asymmetric cyclopropanation of alkenes with diazoacetates, affording cyclopropanes in high diastereomeric ratio and excellent enantiomeric excess (up to 99%). The same catalyst was applied to cyclopropanation with α-diazomethylphosphonates to generate optically-enriched cyclopropyl phosphonate derivatives.[7c] Modification to the pybox ligand includes the water soluble catalyst **350** (Figure 8.5) which has been employed for cyclopropanation in protic or biphasic media.[7d] Ruthenium-thiobox catalysts such as **351** (Figure 8.5) bearing a thiophene linker have been synthesized and perform well in cyclopropanation of substituted alkenes with ethyl diazoacetate (85% yield, 99% enantiomeric excess).[7e]



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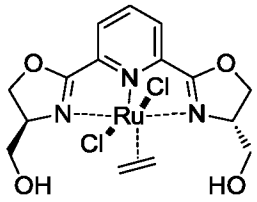

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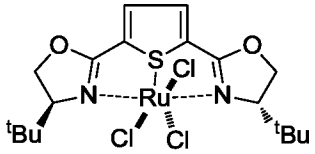
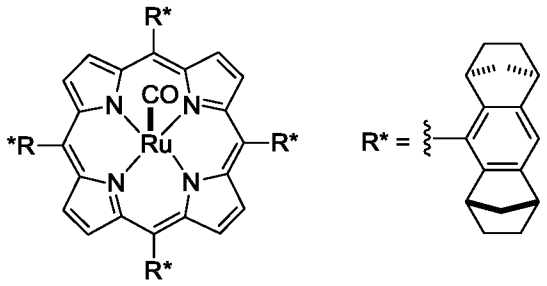


351

Figure 8.5 Chiral ruthenium bis(oxazoliny)pyridine complexes for enantioselective cyclopropanation of alkenes

Ruthenium porphyrin complex **352** (Figure 8.6), reported by both Berkessel's group and Che's group, has been used for enantioselective cyclopropanation of alkenes.[7f-i] The ruthenium porphyrin catalyst is noteworthy for its unprecedentedly high turnover rate (up to 1.1×10^4) and for the high stereoselectivity observed in cyclopropanation of styrene derivatives with ethyl diazoacetate. The same ruthenium porphyrin complex was

utilized by Simonneaux and coworkers for group and atom-transfer reactions in their synthesis of trifluoromethylphenyl cyclopropanes[7j] and cyclopropylphosphonates.[7k]



352

Figure 8.6 Chiral ruthenium porphyrin complex for enantioselective cyclopropanation of alkenes

Katsuki and coworkers reported high *enantio*- and *cis*-selective cyclopropanation of alkenes catalyzed by ruthenium-salen complex **353** (Figure 8.7)[7l,m] although product yields were generally low. Later, Nguyen and coworkers prepared ruthenium-salen complexes containing *trans*-oriented pyridine ligands such as **354** (Figure 8.7). These complexes are very efficient catalysts for asymmetric cyclopropanation of terminal olefins with ethyl diazoacetate, affording predominantly *trans*-cyclopropanes in exceptionally high enantiomeric excess and in high yield.[7n] A practical application of this chemistry is synthesis of *trans*-cyclopropyl α-amino acids.[7o] Ruthenium complex **355** containing a biaryldiimine ligand (Figure 8.7) was shown by Scott and coworkers to afford excellent diastereoselectivity and enantioselectivity in cyclopropanation of terminal alkenes with diazoacetates.[7v]

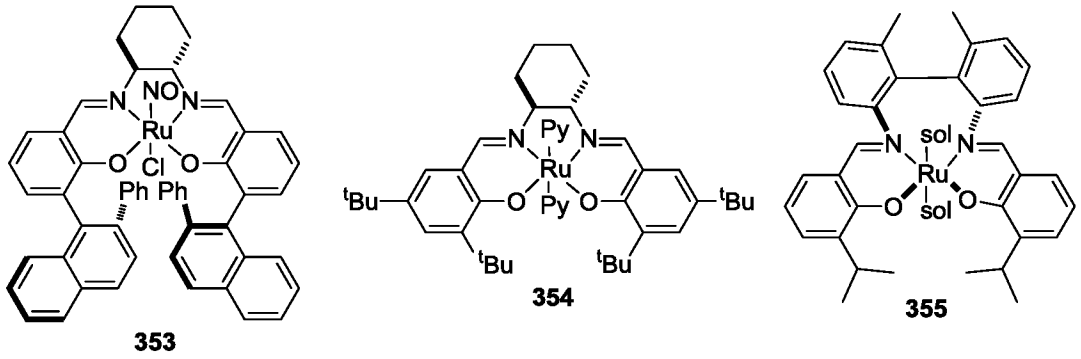
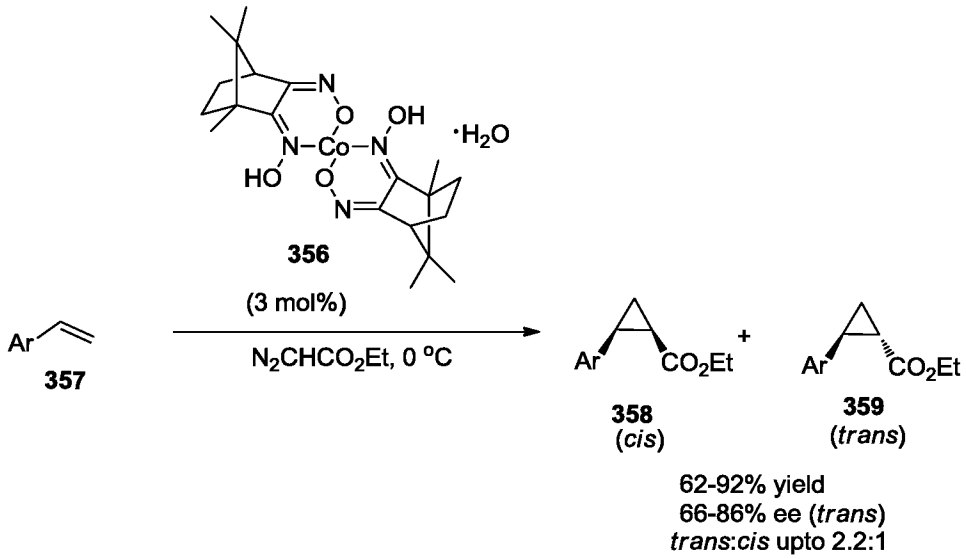


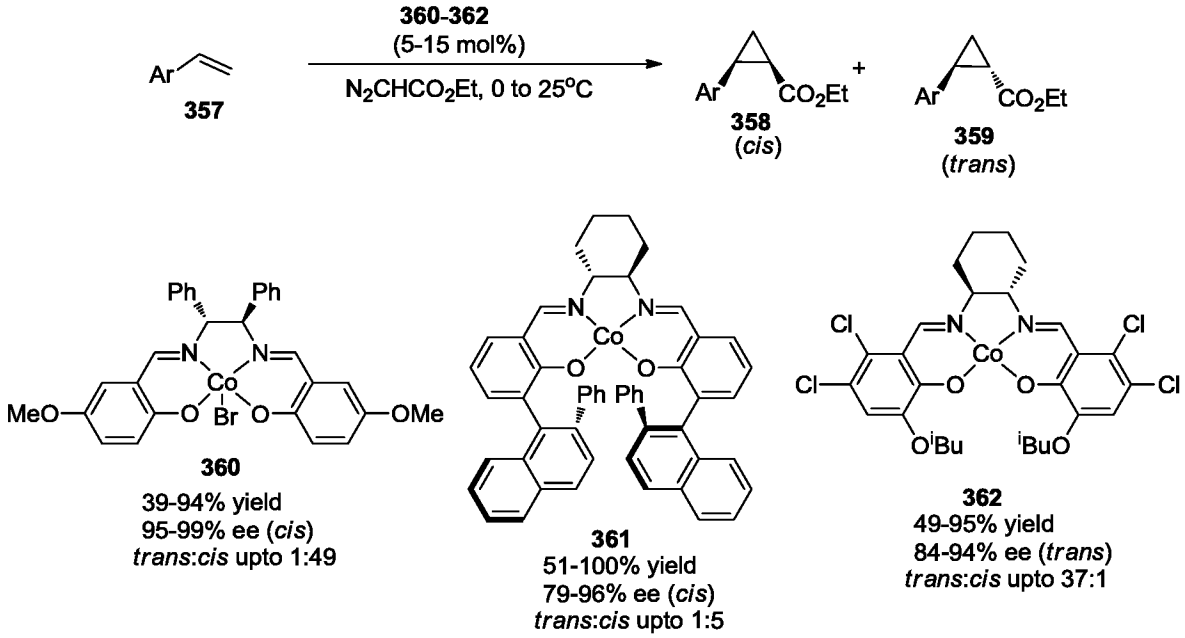
Figure 8.7 Chiral ruthenium-salen complexes for enantioselective cyclopropanation of alkenes

Cobalt compounds are among the most appealing metal complexes for catalysis due not only to the cheap source of cobalt but also to the unique reactivity of these systems. The first cobalt catalyzed enantioselective cyclopropanation was disclosed by Nakamura and coworkers who showed that chiral (dioxmato)cobalt(II) catalyst **356** derived from camphor gives moderate to high enantioselectivity in cyclopropanation of styrenes **357** with ethyl diazoacetate (Scheme 8.3).[8]



Scheme 8.3 Nakamura's enantioselective cyclopropanation catalyzed by cobalt(II) complex **356**

Inspired by the pioneering work of Nakamura,[8] much research on cobalt-salen catalysts (eg **360-362**) for enantioselective cyclopropanation has appeared in the literature.[9-12] These catalysts lead to good levels of asymmetric induction in the enantioselective cyclopropanation of styrenes **357** with ethyl diazoacetate (Scheme 8.4).

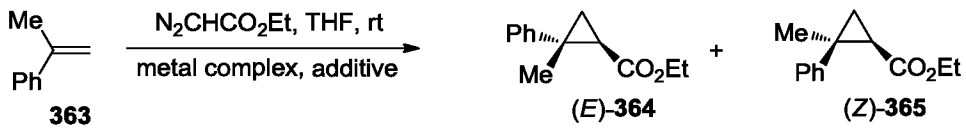


Scheme 8.4 Chiral cobalt-salen complexes for enantioselective cyclopropanation of alkenes

8.2 *Cis*-2,5-diaminobicyclo[2.2.2]octane based cobalt catalyst for enantioselective cyclopropanation

The work of Nakamura,[8] Yamada,[9] Katsuki,[10] Zhang[11] and Carreria[12] provides convincing evidence that asymmetric cyclopropanation of alkenes with α-diazo esters can be catalyzed by both cobalt and copper complexes. In this context, stable cobalt(II)-salen complex (+)-**74** and copper(II)-salen complex (+)-**76** (chapter 2, Scheme 2.10), prepared by treatment of salen ligand (+)-**35** with cobalt(II) bromide and copper(II) acetate, respectively, were considered as possible candidates for catalysis of enantioselective cyclopropanation. α-Methylstyrene and ethyl diazoacetate were the reactants chosen to test this hypothesis. Initial experiments using 5 mol% (+)-**74** and (+)-**76** yielded no product (Table 8.1, entries 1,2) and when catalyst loading of (+)-**76** was increased to 20 mol% there was still no evidence for a cyclopropanated product (entry 3). However, an experiment with 20 mol% (+)-**74** gave the first promising sign of a reaction when trace amounts of **364** and **365** were detected after 2 days although with essentially no diastereoselectivity (entry 4). The observation by Katsuki and coworkers that addition of nucleophilic promoters can increase the diastereoselectivity of cyclopropanation[10] prompted us to use *N*-methylimidazole and 4-dimethylaminopyridine as additives for the reaction of **363** with ethyl diazoacetate. In practice, these additives did increase the yield of **364** and **365** but they only marginally improved diastereoselectivity (entries 5, 6).

Table 8.1 Enantioselective cyclopropanation of α-methylstyrene (**363**) catalyzed by metal-salen complexes (+)-**74** and (+)-**76**[a]

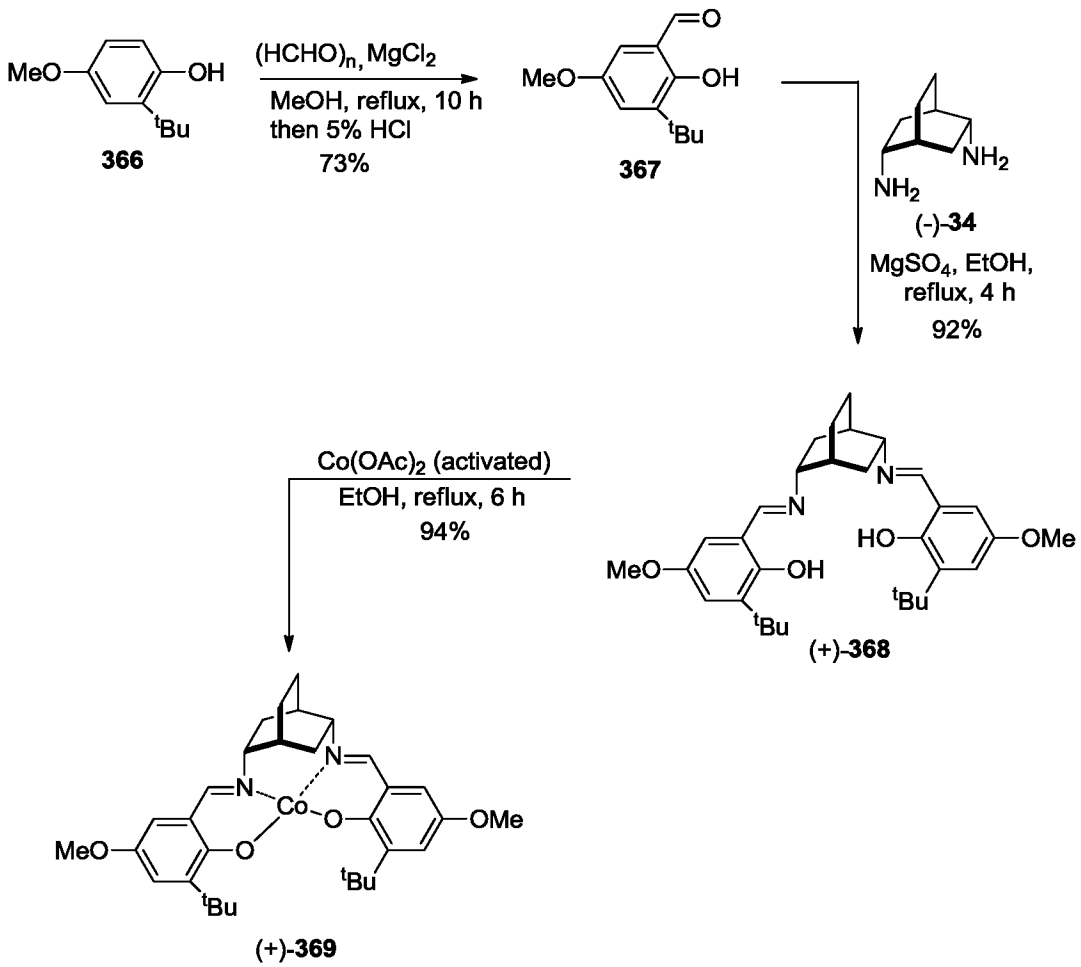


				Product **364** and **365**		
entry	metal complex (mol%)	additive	t (h)	yield (%)[c] (**364**+**365**)	dr (%)[d] (**364**:**365**)	ee (%) (**364**)
1	(+)-**74** (5)	-	36	nr	-	-
2	(+)-**76** (5)	-	36	nr	-	-
3	(+)-**76** (20)	-	48	nr	-	-
4	(+)-**74** (20)	-	48	trace	1:1	nd
5[b]	(+)-**74** (20)	NMI	18	52	1.2:1	nd
6[b]	(+)-**74** (20)	DMAP	16	64	1.7:1	nd

[a]The reactions were carried out on a 0.3 mmol scale in a 0.2M solution with 1.5 equivalents of **363**. [b]The catalyst was stirred with the additive (20 mol%) for 1 h prior to the addition of styrene. [c]Combined yields of **364** and **365**. [d]Determined by ^{1}HNMR. [e]Determined by HPLC using a Chiralcel OD-H column. nd = not determined.

Katsuki and coworkers also found[10a,b] that the presence of an electron-donating substituent at C_5 and $C_{5\square}$ positions in the salen framework of their cobalt complex increased diastereo- and enantioselectivity of cyclopropanation. This observation redirected our effort toward synthesis of cobalt-salen complex **369** bearing methoxy groups at C_5 and $C_{5\square}$ positions of the benzenoid rings. Synthesis of the modified salen ligand **368** began with formylation of commercially available 2-(*tert*-butyl)-4-methoxyphenol (**366**). Following Scott's protocol,[17] **366** was refluxed with a superstoichiometric amount of paraformaldehyde and triethylamine in the presence of magnesium chloride to afford 3-(*tert*-butyl)-2-hydroxy-5-methoxybenzaldehyde (**367**). Condensation of **367** with diamine (-)-**34** in ethanol with magnesium sulfate as catalyst

furnished salen ligand (+)-**368** in good yield. Finally, a solution of the salen ligand and cobalt(II) acetate (dried at 120 °C under high vaccum overnight) in ethanol was heated at reflux to give cobalt(II)-salen complex (+)-**369** as an amorphous brown solid (Scheme 8.5).

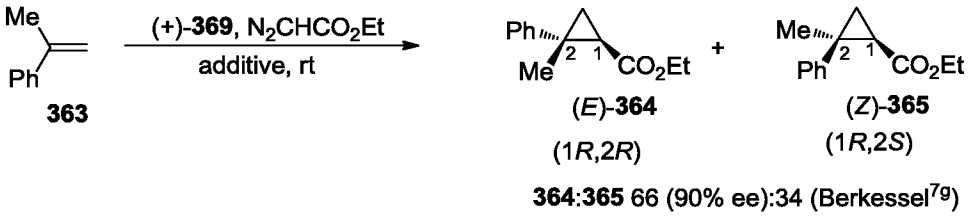


Scheme 8.5 Synthesis of the second generation cobalt(II) complex (+)-**369**

The catalytic properties of our second generation cobalt-salen complex (+)-**369** were again examined in the enantioselective cyclopropanation of α-methylstyrene with ethyl diazoacetate (Table 8.2). A 5 mol% loading of (+)-**369** in tetrahydrofuran afforded

(*E*) and (*Z*) cyclopropanes **364** and **365** in moderate yield and 2:1 diastereomeric ratio with (*E*)-**364** as the major diastereomer (Table 8.2, entry 1). Addition of nucleophilic promoters such as *N*-methylimidazole, 4-dimethylaminopyridine, 2,6-lutidine and triphenylphosphine led to cyclopropanes **364** and **365** in somewhat improved yield and diastereomeric ratio (Table 2, entries 2-7), but addition of dimethyl formamide or dimethyl sulfoxide significantly increased the diastereomeric ratio (9:1 and 12:1, respectively) of those cyclopropanes as well as raising the enantiomeric excess of **364** (72% and 68% enantiomeric excess, respectively, entries 8,9). Further improvement was obtained using 5 mol% of potassium thioacetate as additive which furnished cyclopropane **364** in 97% yield, 21:1 diastereomeric ratio and 73% enantiomeric excess (entry 11). By contrast, addition of hexamethylphosphoramide, *N*,*N*'-dimethylpropylene urea and bromine to the reaction of **363** with ethyl diazoacetate in the presence of (+)-**369** led to diminished diastereoselectivity (entries 12-14). In a study of solvent effect on this cyclopropanation, it was found that chlorinated solvents gave cyclopropane **364** in a higher diastereomeric ratio over **365** than nonchlorinated solvents (entries 15-18). Decreased catalyst loading below 5 mol% led to a slower reaction rate with diminished yield although diastereo- and enantioselectivity remained at acceptable levels (entries 19, 20). The absolute configuration of cyclopropane (*E*)-**364** was determined to be (1*R*,2*R*) by comparison of its optical rotation with that of the literature value.[7g,u]

Table 8.2 Enantioselective cyclopropanation of α-methylstyrene (**363**) catalyzed by cobalt-salen complex (+)-**369**[a,b]



364:**365** 66 (90% ee):34 (Berkessel[7g])

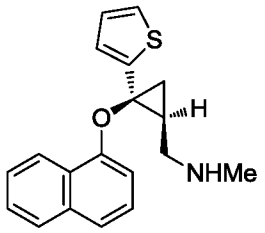
Products **364** and **365**

entry	(+)-**363** (mol%)	additive (mol%)	solvent	t (h)	yield (%)[c] (**364**+**365**)	dr (%)[d] (**364**:**365**)	ee (%)[e] (**364**)
1	5	-	THF	48	63	2:1	nd
2	5	NMI (5)	THF	30	82	3.2:1	nd
3	5	DMAP (5)	THF	36	91	2.7:1	nd
4	5	Pyridine (5)	THF	48	46	2:1	nd
5	5	2,6-lutidine (5)	THF	50	51	4.3:1	nd
6	5	Ph_3P (5)	THF	39	39	3.8:1	nd
7	5	Ph_3As (5)	THF	39	95	2.5:1	nd
8	5	DMF (5)	THF	40	89	9:1	72
9	5	DMSO (5)	THF	40	68	12:1	68
10	5	NaOAc (5)	THF	36	49	2.6:1	nd
11	5	KSAc (5)	THF	36	97	21:1	73
12	5	HMPA(5)	THF	27	56	6.3:1	54
13	5	DMPU (5)	THF	27	53	5.8:1	59
14	5	Br_2 (2.5)	THF	20	87	8.9:1	67
15	5	KSAc (5)	DCE	29	95	27.7:1	84
16	5	KSAc (5)	CH_2Cl_2	29	93	31:1	93
17	5	KSAc (5)	$CHCl_3$	28	90	30:1	91
18	5	KSAc (5)	PhMe	48	77	17.3:1	86

19	2.5	KSAc (2.5)	CH_2Cl_2	60	67	22:1	88
20	1	KSAc (1)	CH_2Cl_2	60	58	16.5:1	85

[a]The reactions were carried out on a 0.3 mmol scale in a 0.2M solution with 1.5 equivalents of **363**. [b]The catalyst was stirred with the additive for 1 h prior to the addition of styrene. [c]Combined yields of **364** and **365**. [d]Determined by ^{1}HNMR. [e]Determined by HPLC using a Chiralcel OD-H column. nd = not determined.

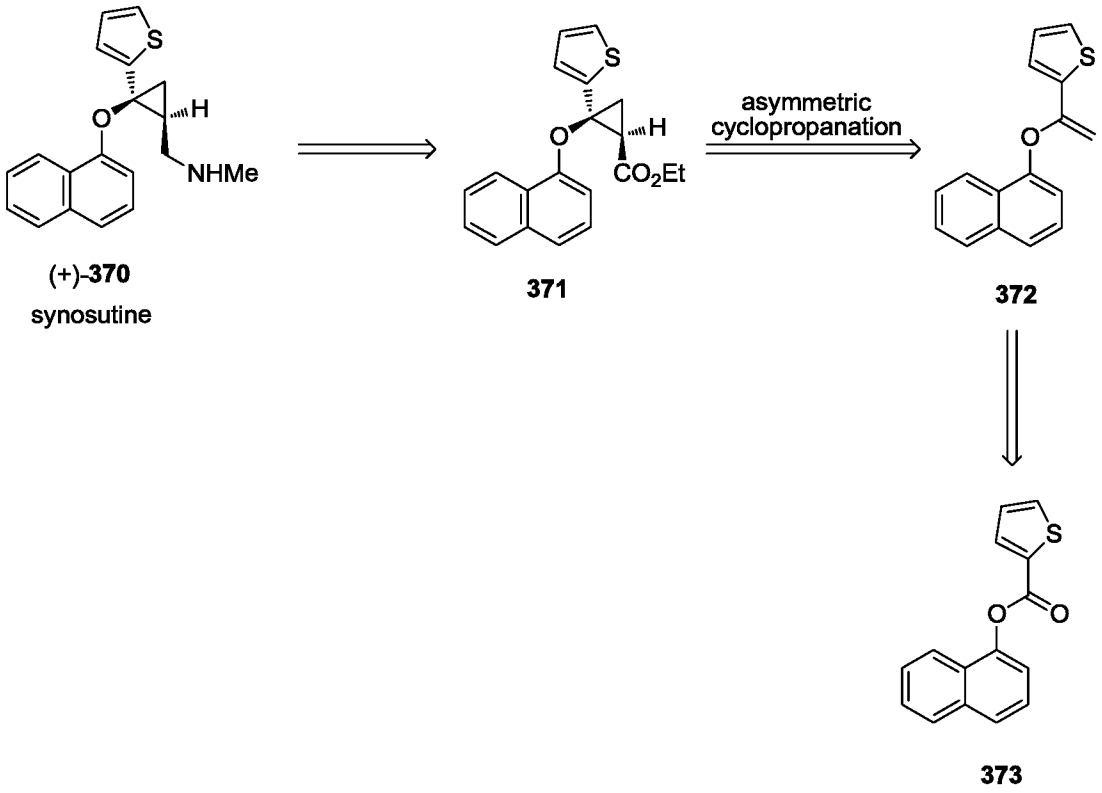
Data in Table 8.2, particularly those in entries 16 and 17, indicate that cobalt-salen complex (+)-**369** has practical utility as a catalyst for asymmetric cyclopropanation. An application of particular interest in this laboratory was a cyclopropanation step used in an asymmetric synthesis of the bioactive compound Synosutine [**(+)-370**, Figure 8.8]. Synosutine is a highly active dual inhibitor of serotonin and norepinephrin transporter[18] that was synthesized by White and coworkers and found to have IC_{50} and K_i values in the 1-2 nM range. At this level of activity, **(+)-370** compares favorably with Eli Lilly's duloxetine (Cymbalta®) as a dual reuptake inhibitor of serotonin and norepinephrine. Duloxetine is currently administered as a front line treatment for clinical depression. The White synthesis of (+)-**370** installs the cyclopropane core via Charette asymmetric cyclopropanation[19] of an allylic alcohol using a chiral boronate catalyst derived from tartrate. The reaction is scale-limited due to the cost of the catalyst[20] which is not recoverable.



(+)-370

Figure 8.8 Synosutine, a dual inhibitor of serotonin and norepinephrine transporter

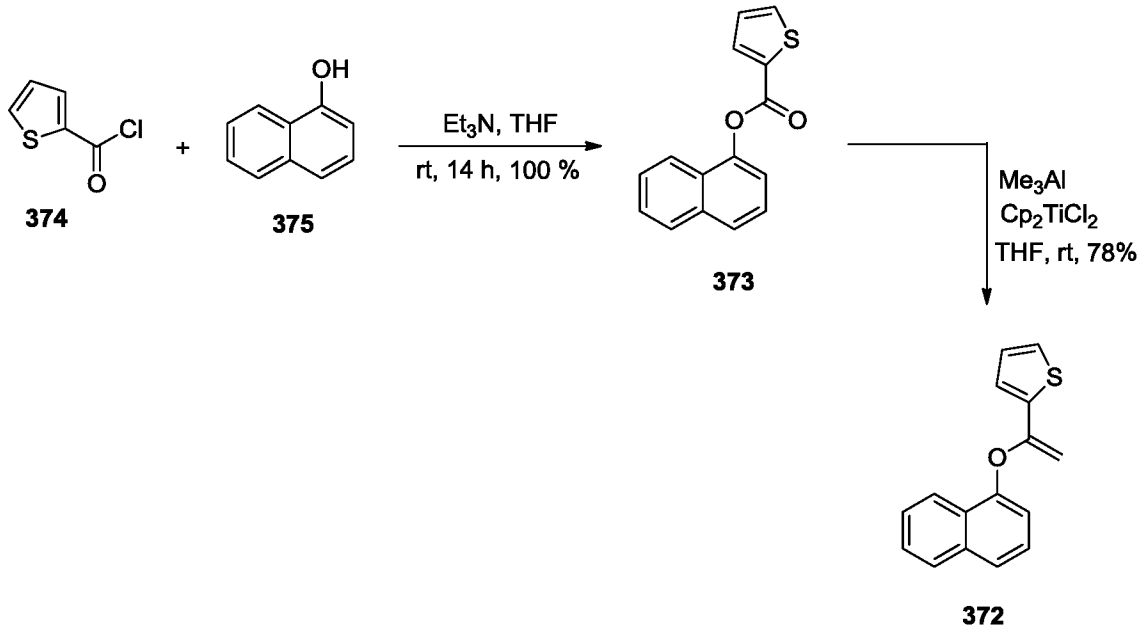
It was our belief that the key to an alternative and superior enantioselective route to Synosutine would be asymmetric cyclopropanation of alkene **372** with ethyl diazoacetate to give **371**, a known precursor of (+)-**370**.[18] Alkene **372** has been synthesized previously in the White laboratory by methylenation of the naphthyl ester **373** of thiophene-2-carboxylic acid (Scheme 8.6).



Scheme 8.6 Retrosynthetic analysis of Synosutine employing enantioselective cyclopropanation of **372**

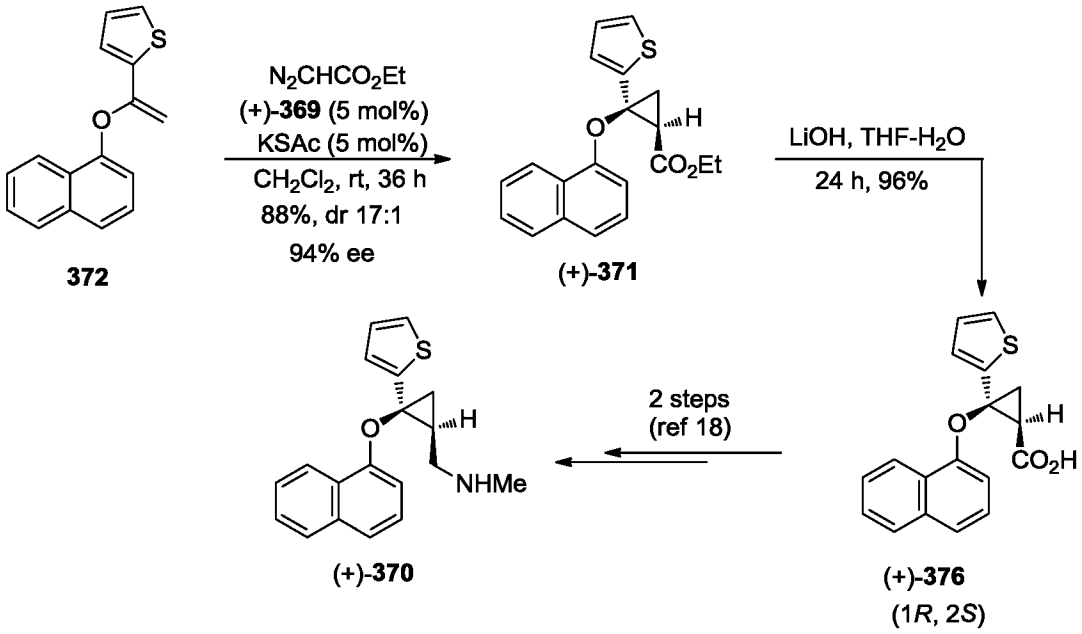
In the forward direction, thiophen-2-carbonyl chloride (**374**) was esterified with 1-naphthol (**375**) in the presence of triethylamine to give **373** which underwent Tebbe

methylenation[21] at room temperature to furnish enol ether **372** as our cyclopropanation substrate (Scheme 8.7).



Scheme 8.7 Synthesis of enol ether **372**

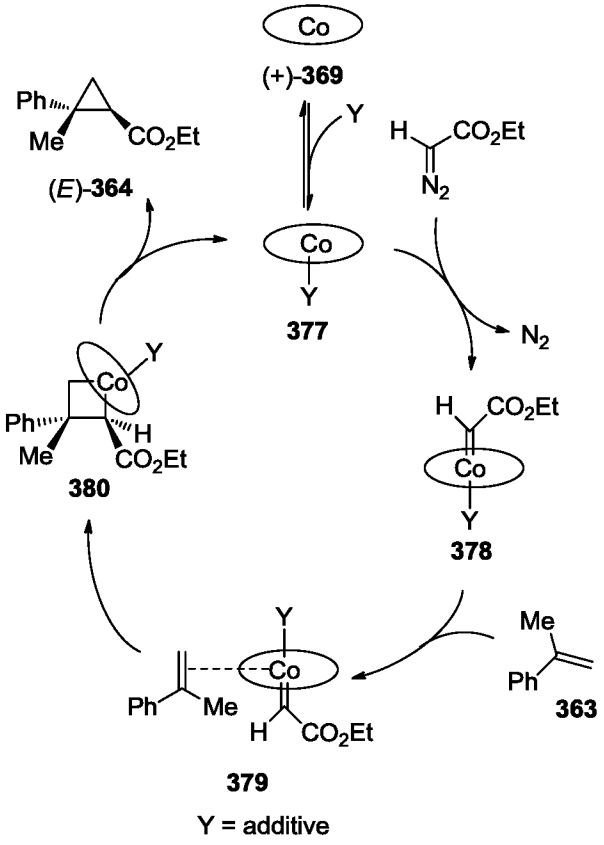
Under the optimized conditions of Table 8.2, entry 16, enol ether **372** underwent smooth enantioselective cyclopropanation with ethyl diazoacetate in the presence of (+)-**369** as catalyst and potassium thioacetate as co-catalyst to give cyclopropane (+)-**371** in 88% yield and with a diastereomeric ratio of 17:1 in favor of the (*Z*) isomer. The enantiomeric excess of (+)-**371** was found to be 94%. Chromatographic purification of (+)-**371** from its (*E*) diastereomer followed by saponification yielded carboxylic acid (+)-**376** and comparison of the optical rotation of the acid from this experiment with the literature value[18] confirmed that (+)-**376** possessed (1*R*,2*S*) configuration. At carboxylic acid (+)-**376**, this new route to Synosutine converges upon the previously published synthesis[18] which advanced (+)-**376** to (+)-**370** in two straightforward steps (Scheme 8.8).



Scheme 8.8 Enantioselective formal synthesis of Synosutine [(+)-**370**]

A mechanism for cyclopropanation of α-methylstyrene (**363**) with ethyl diazoacetate in the presence of (+)-**369** and a promoter Y is proposed in Scheme 8.9. First, the nucleophilic promoter (Y) reacts with cobalt-salen complex (+)-**369** to produce active catalyst **377** which then reacts with ethyl diazoacetate, extruding nitrogen and forming cobalt-carbenoid **378**. Next, the C=C bond of the alkene **363** π-coordinates to the cobalt center (shown as **379**) and then forms 4-membered cobaltocycle **380**. The existence of cobaltocyclobutanes derived from cobalt-salen complexes in cyclometalation reactions has been documented by Klein and coworkers and is supported by X-ray crystallography.[22] Reductive elimination of the active catalyst **377** from the metalacyclobutane **380** affords cyclopropopane (*E*)-**364**. The presence of methoxy groups at 5 and 5' positions of the salen ligand in (+)-**369**, as well as the coordinated promoter (Y), increase electron density on the metal center, thereby making the cobalt carbenoid

less reactive and more selective. The superiority of thioacetate ion in this context could be the result of the *trans* effect[23] associated with sulfur-metal coordination, a property of sulfur previously noted in a mechanistic discussion of the sulfa-Michael reaction (chapter 6).



Scheme 8.9 Catalytic cycle for the formation of (*E*)-**364** via enantioselective cyclopropanation of α-methyl styrene (**363**) in the presence of (+)-**369** and an additive Y

The relative and absolute configuration of (*E*)-**364** and (*Z*)-**365** is rationalized by the transition state model depicted in Figure 8.9 and 8.10. As shown in Figure 8.9, the carbenoid formed from (+)-**369** and ethyl diazoacetate is positioned in the right front

quadrant below the bicyclic scaffold with the carbenoid ester substituent protruding from this quadrant in a direction that avoids a steric collision with a *tert*-butyl group on the opposing benzenoid ring ("b" ring) of the salen ligand (**381** vs **382**, Figure 8.9). This leaves the *re*-face of the carbenoid exposed to attack by the incoming alkene while the *si*-face is blocked by the benzenoid ring "a" of the cobalt-salen complex. The alkene approaches the carbenoid along the O^b-Co axis with the phenyl group of **363** *trans* to the ester substituent to avoid the steric clash noted in Figure 8.10 (**383** vs **385**). Addition of the *re*-face of the carbenoid to the *si*-face of the alkene in this manner leads to cyclopropane (*E*)-**364** with (1*R*,2*R*) configuration as the predominant product. The lower diastereomeric excess of cyclopropane (+)-**371** from enol ether **372** (dr 17:1, Scheme 8.8) compared to that of (*E*)-**364** from **363** is attributed to the more similar steric size of substituents attached to the alkene of **372**.

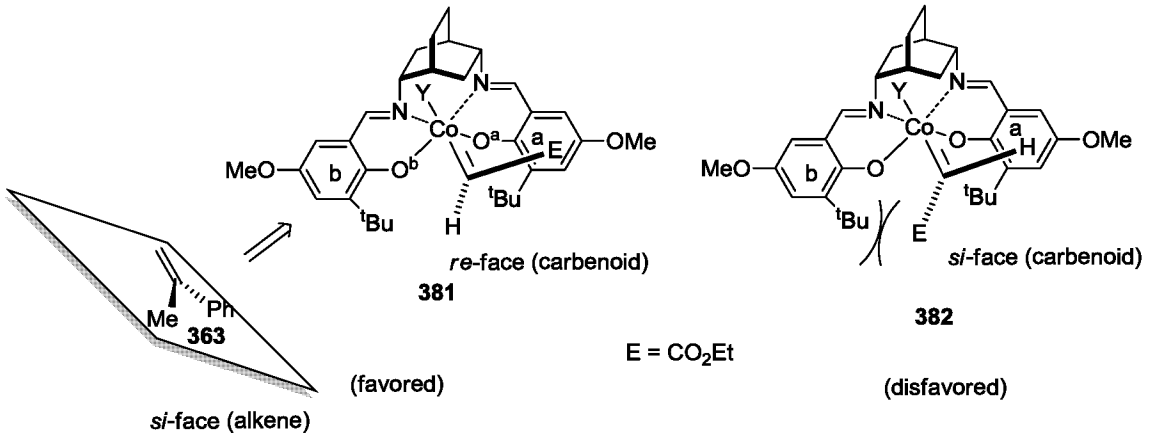


Figure 8.9 Proposed transition state for the enantioselective cyclopropanation of α-methyl styrene with ethyl diazoacetate catalyzed by cobalt(II)-salen complex (+)-**369**

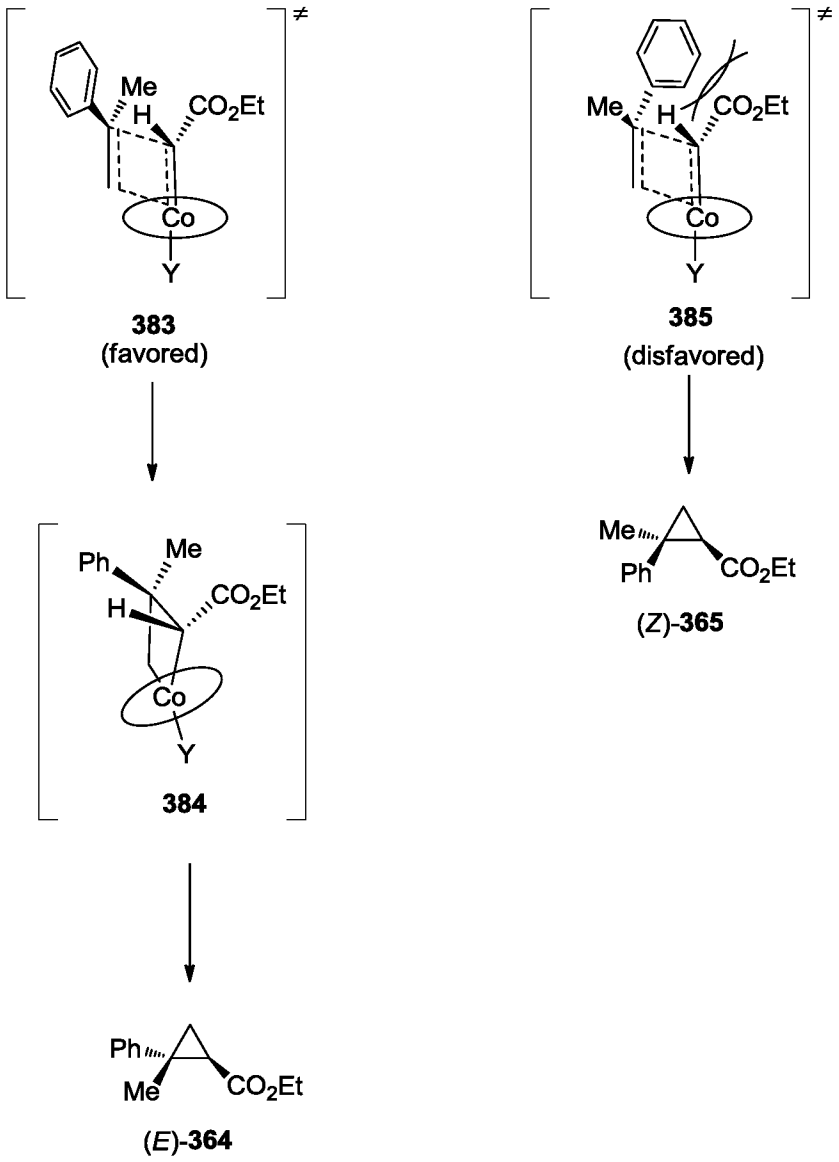


Figure 8.10 Proposed rationale for the observed diastereoselectivity in cyclopropanation of α-methyl styrene (**363**) with ethyl diazoacetate catalyzed by (+)-**369**

In this chapter, we showed that two cobalt(II)-salen catalysts promote cyclopropanation of a 1,1'-disubstituted alkene with high diastereo- and enantioselectivity. With ethyl diazoacetate as co-reactant, this reaction installs two

contiguous stereocenters in a single step with a high degree of stereochemical predictability. A formal synthesis of the cyclopropane-containing dual serotonin and norepinephrine reuptake inhibitor Synosutine was achieved using this protocol. Further studies with substituted alkenes and cobalt carbenoids derived from **74** and **369** should expand the scope of this process.

8.3 References

1. (a) Gnad, F.; Reiser, O. *Chem. Rev.* **2003,** *103*, 1603; (b) Faust, R. *Angew. Chem. Int. Ed.* **2001,** *40*, 2251.
2. (a) Mass, G. *Chem. Soc. Rev.* **2004**, *33*, 183. (b) Muller, P. *Acc. Chem. Res.* **2004**, *37*, 243. (c) Jacobsen, E. N.; Pfalz, A.; Yamamoto, H. *Comprehensive Asymmetric Catalysis*; Springer: Berlin, **1999**, Vol. 2, 513. (d) Lebel, H.; Marcoux, J.-F.; Molinaro, C.; Charette, A. B. *Chem. Rev.* **2003**, *103*, 977. (e) Davies, H. M. L.; Antoulinakis, E. *Org. React.* **2001**, *57*, 1. (f) Doyle, M. P.; Forbes, D. C. *Chem. Rev.* **1998**, *98*, 911. (g) Padwa, A.; Krumpe, K. E. *Tetrahedron* **1992**, *48*, 5385.
3. (a) Pietruszka, J. *Chem. Rev.* **2003**, *103*, 1051. (b) Wessjohann, L. A.; Brandt, W.; Thiemann, T. *Chem. Rev.* **2003**, *103*, 1625. (c) Donaldson, W. A. *Tetrahedron* **2001**, *57*, 8589. (d) Salaun, J. *Chem. Rev.* **1989**, *89*, 1247.
4. (a) Lebel, H.; Marcoux, J. F.; Molinaro, C.; Charette, A. B. *Chem. Rev.* **2003,** *103*, 977; (b) Pellissier, H. *Tetrahedron* **2008,** *64*, 7041.
5. For cyclopropanation reactions catalyzed by copper complexes, see: (a) Nozaki, H.; Moriuti, S.; Takaya, H.; Noyori, R. *Tetrahedron Lett.* **1965**, *6*, 2563. (b) Nozaki, H.; Moriuti, S.; Takaya, H.; Noyori, R. *Tetrahedron Lett.* **1966**, *7*, 5239. (c) Nozaki, H.; Moriuti, S.; Takaya, H.; Noyori, R. *Tetrahedron* **1968**, *24*, 3655. (d) Fritschi, H.; Leutenegger, U.; Pfaltz, A. *Angew. Chem., Int. Ed.* **1986**, *25*, 1005. (e) Evans, D. A.; Woerpel, K. A.; Hinman, M. M.; Faul, M. F. *J. Am. Chem. Soc.* **1991**, *113*, 726. (f) Lo, M. M. C.; Fu, G. C. *J. Am. Chem. Soc.* **1998**, *120*, 10270. (g) Lowenthal, R. E.; Abiko, A.; Masamune, S. *Tetrahedron Lett.* **1990**, *31*, 6005. (h) Evans, D. A.; Woerpel, K. A.;

Scott, M. J. *Angew. Chem., Int. Ed.* **1992**, *31*, 430. (i) Lyle, M. P. A.; Wilson, P. D. *Org. Lett.* **2004,** *6*, 855. (j) Lesma, G.; Cattenati, C.; Pilati, T.; Sacchetti, A.; Silvani, A. *Tetrahedron-Asymmetry* **2007,** *18*, 659. (k) Suga, H.; Kakehi, A.; Ito, S.; Ibata, T.; Fudo, T.; Watanabe, Y.; Kinoshita, Y. *Bull. Chem. Soc. Jpn.* **2003,** *76*, 189. (l) Gao, J. A.; Zhong, S. H. *J. Mol. Catal. A-Chem.* **2003,** *191*, 23. (m) Itagaki, M.; Hagiya, K.; Kamitamari, M.; Masumoto, K.; Suenobu, K.; Yamamoto, Y. *Tetrahedron* **2004,** *60*, 7835.

6. For cyclopropanation reactions catalyzed by rhodium complexes, see: (a) Doyle, M. P.; Pieters, R. J.; Martin, S. F.; Austin, R. E.; Oalmann, C. J.; Muller, P. *J. Am. Chem. Soc.* **1991**, *113*, 1423; (b) Doyle, M. P.; Austin, R. E.; Bailey, A. S.; Dwyer, M. P.; Dyatkin, A. B.; Kalinin, A. V.; Kwan, M. M. Y.; Liras, S.; Oalmann, C. J.; Pieters, R. J.; Protopopova, M. N.; Raab, C. E.; Roos, G. H. P.; Zhou, Q. L.; Martin, S. F. *J. Am. Chem. Soc.* **1995**, *117*, 5763. (c) Bykowski, D.; Wu, K. H.; Doyle, M. P. *J. Am. Chem. Soc.* **2006**, *128*, 16038. (d) Kennedy, M.; Mckervey, M. A.; Maguire, A. R.; Roos, G. H. P. *J. Chem. Soc. Chem. Commun.* **1990**, 361. (e) Davies, H. M. L.; Bruzinski, P. R.; Lake, D. H.; Kong, N.; Fall, M. J. *J. Am.Chem. Soc.* **1996**, *118*, 6897. (f) Hedley, S. J.; Ventura, D. L.; Dominiak, P. M.; Nygren, C. L.; Davies, H. M. L. *J. Org. Chem.* **2006**, *71*, 5349. (g) Davies, H. M. L. *Eur. J. Org. Chem.* **1999**, 2459. (h) Reddy, R. P.; Lee, G. H.; Davies, H. M. L. *Org. Lett.* **2006**, *8*, 3437. (i) Denton, J. R.; Sukumaran, D.; Davies, H. M. L. *Org. Lett.* **2007**, *9*, 2625. (j) Watanabe, N.; Ogawa, T.; Ohtake, Y.; Ikegami, S.; Hashimoto, S. *Synlett.* **1996,** 1, 85. (k) Muller, P.; Bernardinelli, G.; Allenbach, Y. F.; Ferri, M.; Flack, H. D. *Org. Lett.* **2004**, *6*, 1725. (l) Muller, P.; Bernardinelli, G.; Allenbach, Y. F.; Ferri,

M.; Grass, S. *Synlett*. **2005**, 9, 1397. (m) Estevan, F.; Lahuerta, P.; Lloret, J.; Sanau, M.; Ubeda, M. A.; Vila, J. *Chem. Commun*. **2004**, 21, 2408. (n) Barberis, M.; Perez-Prieto, J.; Herbst, K.; Lahuerta, P. *Organometallics* **2002**, *21*, 1667. (o) Krumper, J. R.; Gerisch, M.; Suh, J. M.; Bergman, R. G.; Tilley, T. D. *J. Org. Chem*. **2003**, *68*, 9705. (p) Shibata, Y.; Noguchi, K.; Tanaka, K. *J. Am. Chem. Soc*. **2010**, *132*, 7896.

7. For cyclopropanation reactions catalyzed by ruthenium complexes, see: (a) Nishiyama, H.; Itoh, Y.; Matsumoto, H.; Park, S. B.; Itoh, K. *J. Am. Chem. Soc*. **1994**, *116*, 2223. (b) Marcin, L. R.; Denhart, D. J.; Mattson, R. J. *Org. Lett*. **2005**, *7*, 2651. (c) Charette, A. B.; Bouchard, J. E. *Can. J. Chem*. **2005**, *83*, 533. (d) Iwasa, S.; Tsushima, S.; Nishiyama, K.; Tsuchiya, Y.; Takezawa, F.; Nishiyama, H. *Tetrahedron-Asymmetry* **2003**, *14*, 855. (e) Gao, M. Z.; Kong, D. Y.; Clearfield, A.; Zingaro, R. A. *Tetrahedron Lett*. **2004**, *45*, 5649. (f) Lo, W. C.; Che, C. M.; Cheng, K. F.; Mak, T. C. W. *Chem. Commun*. **1997**, 13, 1205. (g) Berkessel, A.; Kaiser, P.; Lex, J. *Chem-Eur. J*. **2003**, *9*, 4746. (h) Frauenkron, M.; Berkessel, A. *Tetrahedron Lett*. **1997**, *38*, 7175. (i) Che, C. M.; Huang, J. S.; Lee, F. W.; Li, Y.; Lai, T. S.; Kwong, H. L.; Teng, P. F.; Lee, W. S.; Lo, W. C.; Peng, S. M.; Zhou, Z. Y. *J. Am. Chem. Soc*. **2001**, *123*, 4119. (j) Le Maux, P.; Juillard, S.; Simonneaux, G. *Synthesis* **2006**, 10, 1701. (k) Ferrand, Y.; Le Maux, P.; Simonneaux, G. *Org. Lett*. **2004,** *6*, 3211. (l) Uchida, T.; Irie, R.; Katsuki, T. *Tetrahedron* **2000**, *56*, 3501. (m) Uchida, T.; Katsuki, T. *Synthesis* **2006,** 10, 1715. (n) Miller, J. A.; Jin, W. C.; Nguyen, S. T. *Angew. Chem., Int. Ed*. **2002**, *41*, 2953. (o) Miller, J. A.; Hennessy, E. J.; Marshall, W. J.; Scialdone, M. A.; Nguyen, S. T. *J. Org. Chem*. **2003**, *68*, 7884. (p) Miller, J. A.; Gross, B. A.; Zhuravel, M. A.; Jin, W. C.; Nguyen, S. T. *Angew. Chem., Int. Ed*. **2005**, *44*, 3885.

(q) Bachmann, S.; Furler, M.; Mezzetti, A. *Organometallics* **2001**, *20*, 2102. (s) Bachmann, S.; Mezzetti, A. *Helv. Chim. Acta* **2001**, *84*, 3063. (t) Bonaccorsi, C.; Bachmann, S.; Mezzetti, A. *Tetrahedron-Asymmetry* **2003**, *14*, 845. (u) Bonaccorsi, C.; Mezzetti, A. *Organometallics* **2005**, *24*, 4953. (v) Munslow, I. J.; Gillespie, K. M.; Deeth, R. J.; Scott, P. *Chem. Commun.* **2001**, 17, 1638.

8. Nakamura, A.; Konishi, A.; Tsujitani, R.; Kudo, M. A.; Otsuka, S. *J. Am. Chem. Soc.* **1978**, *100*, 3449.
9. (a) Yamada, T.; Ikeno, T.; Sekino, H.; Sato, M. *Chem. Lett.* **1999**, 719. (b) Ikeno, T.; Sato, M.; Yamada, T. *Chem. Lett.* **1999**, 1345.
10. (a) Niimi, T.; Uchida, T.; Irie, R.; Katsuki, T. *Tetrahedron Lett.* **2000**, *41*, 3647. (b) Niimi, T.; Uchida, T.; Irie, R.; Katsuki, T. *Adv. Synth. Catal.* **2001**, *343*, 79. (c) Uchida, T.; Katsuki, T. *Synthesis* **2006**, 1715. (d) Uchida, T.; Saha, B.; Katsuki, T. *Tetrahedron Lett.* **2001**, *42*, 2521.
11. (a) Huang, L.; Chen, Y.; Gao, G.-Y.; Zhang, X. P. *J. Org. Chem.* **2003**, *68*, 8179. (b) Chen, Y.; Fields, K. B.; Zhang, X. P. *J. Am. Chem. Soc.* **2004**, *126*, 14718. (c) Chen, Y.; Zhang, X. P. *Synthesis* **2006**, 1697. (d) Chen, Y.; Zhang, X. P. *J. Org. Chem.* **2007**, *72*, 5931. (e) Chen, Y.; Ruppel, J. V.; Zhang, X. P. *J. Am. Chem. Soc.* **2007**, *129*, 12074. (f) Zhu, S.; Perman, J. A.; Zhang, X. P. *Angew. Chem., Int. Ed.* **2008,** *47*, 8460. (g) Zhu, S. F.; Xu, X.; Perman, J. A.; Zhang, X. P. *J. Am. Chem. Soc.* **2010,** *132*, 12796. (h) Dzik, W. I.; Xu, X.; Zhang, X. P.; Reek, J. N. H.; de Bruin, B. *J. Am. Chem. Soc.* **2010,** *132*, 10891.
12. Morandi, B.; Mariampillai, B.; Carreira, E. M. *Angew. Chem. Int. Ed.* **2011**, *50*, 1101.

13. For cyclopropanation reactions catalyzed by gold complexes, see (a) Johansson, M. J.; Gorin, D. J.; Staben, S. T.; Toste, F. D. *J. Am. Chem. Soc.* **2005,** *127*, 18002. (b) Watson, I. D. G.; Ritter, S.; Toste, F. D. *J. Am. Chem. Soc.* **2009,** *131*, 2056.

14. For cyclopropanation reactions catalyzed by iron complexes, see: (a) Morandi, B.; Cheang, J.; Carreira, E. M. *Org. Lett.* **2011**, *13*, 3080. (b) Morandi, B.; Dolva, A.; Carreira, E. M. *Org. Lett.* **2012**, *14*, 2162. (c) Morandi, B.; Carreira, E. M. *Science* **2012**, 335, 1471. (d) Kaschel, J.; Schneider, T. F.; Weirz, D. B. *Angew. Chem. Int. Ed.* **2012**, *51*, 7085.

15. For cyclopropanation reactions catalyzed by iridium complexes, see: (a) Anding, B. J.; Ellern, A.; Woo, L. K. *Organometallics* **2012**, *31*, 3628. (b) Kanchiku S, Suematsu H, Matsumoto K, Uchida T, Katsuki T. *Angew. Chem. Int. Ed.* **2007**, *46*, 3889. (c) Ichinose, M.; Suematsu, H.; Katsuki, T. *Angew. Chem. Int. Ed.* **2009**, *48*, 3121.

16. Zhang, J.; Liang, J. L.; Sun, X. R.; Zhou, H. B.; Zhu, N. Y.; Zhou, Z. Y.; Chan, P. W. H.; Che, C. M. *Inorg. Chem.* **2005,** *44*, 3942.

17. Theaker, G. W.; Morton, C.; Scott, P. *Dalton Trans.* **2008**, *48*, 6883.

18. White, J. D.; Juniku, R.; Huang, K.; Yang., J.; Wong, D. T. *J. Med. Chem.* **2009**, *52*, 5872.

19. Charette, A. B.; Juteau, H. *J. Am. Chem. Soc.* **1994**, *116*, 2651.

20. The Charette chiral boronate catalyst (CAS 161344-84-9) costs $67.90 for a 1 gram quantity from Sigma-Adrich.

21. Tebbe, F. N.; Parshall, G. W.; Reddy, G. S. *J. Am. Chem. Soc.* **1978**, *100*, 3611.

22. (a) Klein, H. F.; Beck, R.; Florke, U.; Haupt, H. J. *Eur. J. Inorg. Chem.* **2002**, 3305. (b) Klein, H. F.; Beck, R.; Florke, U.; Haupt, H. J. *Eur. J. Inorg. Chem.* **2003**, 1380.

23. For a review see: Coe, B. J.; Glenwright, S. J. *Coord. Chem. Rev.* **2000**, *203*, 5.

CHAPTER 9

Conclusion

Over the past two decades, chiral salen-metal complexes have emerged as versatile catalysts for a broad range of carbon-carbon bond forming reactions. A new salen ligand based on a chiral diaminobicyclo[2.2.2]octane scaffold shows strong affinity for complexation with transition metals as well as certain other metals with which it forms stable, well-characterized complexes. The chromium(III) complex derived from this ligand possesses excellent catalytic activity in the asymmetric hetero-Diels-Alder reaction of aldehydes with Danishefsky diene (chapter 3, Table 3.2) and for the asymmetric Nozaki-Hiyama-Kishi reaction (chapter 4, Table 4.3) of allyl halides with aromatic aldehydes, giving products in high enantiomeric excess. A tetrahydrosalen prepared by reduction of the salen ligand, in combination with copper(I) triflate, was found to be an efficient catalyst for the enantioselective Henry reaction (chapter 5, Table 5.3) of aldehydes with nitromethane, affording β-nitro alcohols in high enantiomeric excess. The reaction was employed in a synthesis of these beta-adrenergic receptor blocking agents including the commercial drug (*S*)-Propanolol. An iron(III)-salen complex was shown to catalyze the asymmetric sulfa-Michael addition (chapter 6, Table 6.4) of thiols to acyclic conjugated enones, giving β-thiaketones with excellent stereoselectivity. The efficacy of this sulfa-Michael reaction was demonstrated in a concise synthesis of (*R*)-Montelukast, an anti-asthma drug sold as Singulair®. Iron and cobalt complexes derived from structurally modified salen ligands also proved to be good

chiral catalysts for the enantioselective intramolecular Conia-ene reaction (chapter 7, Table 7.4, entry 4) of an acetylenic β-keto ester and for asymmetric cyclopropanation (chapter 8, Table 8.2, entry 16) of α-methylstyrene with ethyl diazoacetate. The latter reaction was used for cyclopropanation of an enol ether in a formal synthesis of Synosutine, a dual inhibitor of serotonin and norepinephrine reuptake. The metal-salen complexes whose reactivity was studied were efficient catalysts for these asymmetric transformations and gave a level of asymmetric induction comparable to or better than that obtained with Jacobsen's and Berkessel's catalysts. Titanium(IV), vanadium(V), palladium(II), nickel(II) and aluminum(III) complexes were also synthesized from our bicyclooctane-salen ligand; their properties as asymmetric catalysts remain to be explored. Although C_2-symmetric bis-thioureas based on our bicyclo[2.2.2]octane scaffold failed to induce a high level of asymmetric induction as organocatalysts in the sulfa-Michael reaction, further modification to these bifunctional ligands may enhance catalytic activity and stereoselectivity. Metals such as ruthenium, rhodium and platinum are potential candidates for insertion into our chiral salen ligand, perhaps creating a different mode of asymmetric catalysis for reactions requiring a soft metal center.

Experimental section

General

Starting materials and reagents were obtained from commercial sources and were used without further purification. Solvents were dried by distillation from the appropriate drying reagents immediately prior to use. Tetrahydrofuran and ether were distilled from sodium and benzophenone under an argon atmosphere. Toluene, triethylamine and dichloromethane were distilled from calcium hydride under argon. All solvents used for routine isolation of products and chromatography were reagent grade. Moisture- and air-sensitive reactions were carried out under an atmosphere of argon. Reaction flasks were flame dried under a stream of argon gas, and glass syringes were oven dried at 120 °C prior to use.

Unless otherwise stated, concentration under reduced pressure refers to a rotary evaporator at water aspirator pressure. Residual solvent was removed by vacuum pump at a pressure less than 0.25 mm of mercury.

Analytical thin-layer chromatography (TLC) was conducted using precoated TLC plates (0.2 mm layer thickness of silica gel 60 F-254). Compounds were visualized by ultraviolet light and/or by heating the plate after dipping in a 3-5% solution of phosphomolybdic acid in ethanol, 10% ammonium molybdate in water, a 1% solution of vanillin in 0.1 M sulfuric acid in methanol or 2.5% *p*-anisaldehyde in 88% ethanol, 5% water, 3.5% concentrated sulfuric acid and 1% acetic acid. Flash chromatography was performed with the indicated eluents on 230 - 400 mesh silica gel.

Optical rotations were measured with a polarimeter at ambient temperature using a 0.9998 dm cell with 1 mL capacity. Infrared (IR) spectra were recorded on a FT-IR

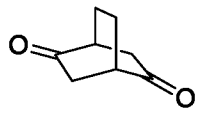
spectrometer. Proton and carbon nuclear magnetic resonance (NMR) spectra were obtained using either a 300, 400, 500 or 700 MHz spectrometer. All chemical shifts were reported in parts per million (ppm) downfield from tetramethylsilane using the δ scale. ^{1}H NMR spectral data are reported in the order: chemical shift, multiplicity (s = singlet, d = doublet, m = multiplet, and b = broad), coupling constant (*J*, in Hertz), and number of protons.

Low (MS) and high (HRMS) resolution mass spectra are reported with ion mass/charge (*m*/*z*) ratios as values in atomic mass units.

CHAPTER 2

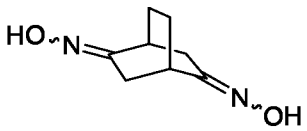
Synthesis of the Diamine and Its Salen-Metal Complexes

(±)-Bicyclo[2.2.2]octane-2,5-dione (37)[1]



2-Trimethylsiloxy-1,3-cyclohexadiene (1.18 g, 8.54 mmol)[2] and 1-cyanovinyl acetate (932 μL, 8.54 mmol) were combined in a sealed tube and the mixture was heated at 120 ^{o}C for 20 h. The viscous product was dissolved in 1M sodium methoxide/MeOH (30 mL), the solution was stirred at room temperature for 3 h and was poured into 100 mL ice-water. The aqueous solution was extracted with methylene chloride and the combined extracts were dried (Na_2SO_4) and concentrated. The residue was purified by chromatography (SiO_2, hexanes) to give **37** (734 mg, 62%) as a colorless solid: mp 203 - 204 °C, [lit.[1] 203 - 205 °C]; IR (neat) 3052, 2921, 1673, 1069 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.92 - 1.95 (m, 1H), 2.08 - 2.14 (m, 1H), 2.49 - 2.54 (m, 2H), 2.66 - 2.72 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.6, 40.4, 44.1, 211.2.

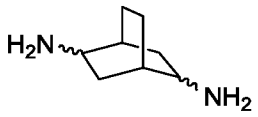
(±)-Bicyclo[2.2.2]octane-2,5-dione Dioxime (36)[3]



To a solution of **37** (720 mg, 5.22 mmol) and anhydrous sodium acetate (941 mg, 11.48 mmol) in anhydrous MeOH (65 mL) was added portionwise with stirring solid hydroxylamine hydrochloride (798 mg, 11.48 mmol), and the resulting mixture was

stirred at room temperature for 24 h. The reaction mixture was filtered and the filtrate was concentrated in vacuo to give **36** (0.886 g, 100%) as a colorless solid: mp 217 - 218 °C, [lit.[3] 219 °C]; IR (neat) 3329, 2869, 2257, 2121, 1664, 1454, 1247, 1024, 820 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.52 - 1.85 (m, 4H), 2.34 - 2.43 (m, 2H), 3.29 - 2.58 (m, 4H), 10.26 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.5, 31.1, 33.0, 160.0.

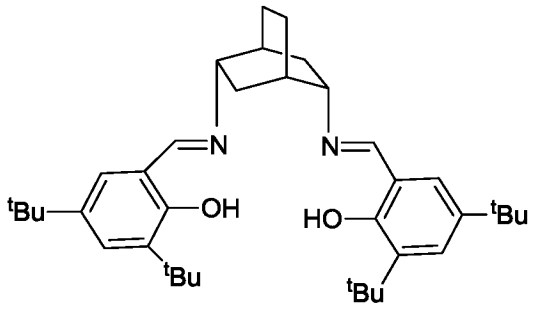
(±)-Bicyclo[2.2.2]octane-2,5-diamine (42)



To a solution of **36** (400 mg, 2.38 mmol), in dry MeOH (4 mL) was added to a suspension of anhydrous nickel(II) chloride (617 mg, 4.76 mmol) in dry MeOH (6 mL) with stirring. The mixture was cooled to -35 °C and sodium borohydride (1.80 g, 47.6 mmol) was added over a period of 1 h in small portions to maintain a temperature between -20 and -35 °C. After completion of the addition, the mixture was allowed to warm to room temperature and was concentrated in vacuo. The dark brown residue was extracted with 4M aqueous sodium hydroxide and methylene dichloride mixture in a liquid/liquid extractor. The combined extracts were dried (Na_2SO_4) and concentrated to give **42** (0.204 g, 61%) as a colorless semisolid: IR (neat) 3373, 2922, 2844, 1085, 1023, 797 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.83 - 1.19 (m, 2H), 1.20 - 1.49 (m, 11H), 1.52 - 1.68 (m, 1H), 1.71 - 1.92 (m, 2H), 1.96 - 2.12 (m, 1H), 2.23 - 2.37 (m, 1H), 2.92 - 3.11 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.3, 18.7, 24.1, 25.0, 29.6, 30.2, 31.1, 33.3,

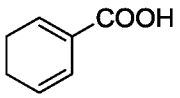
33.5, 34.0, 36.4, 37.3, 47.9, 48.5, 48.6; HRMS (EI) calcd for $C_8H_{16}N_2$ *m/z* 140.1314, found 140.1315.

(±)-2,2'-Bicyclo[2.2.2]octane-2,5-diylbis(nitrilomethylidine)]bis-4,6-di-*tert* butylphenol (35)



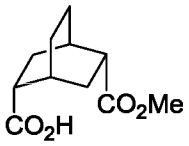
To a solution of **42** (153 mg, 1.09 mmol) in EtOH (5 mL) was added a solution of 3,5 di-*tert*-butylsalicylaldehyde (**49**, 512 mg 2.18 mmol) in EtOH (10 mL). The mixture was stirred at room temperature for 30 min, at which time a yellow precipitate had formed. The mixture was refluxed for 2 h then was stirred at room temperature overnight. The precipitate was filtered off to obtain a mixture of diastereomeric salen ligands **50** (563 mg, 90%) as a yellow solid. Crystallization of **50** from a mixture of CH_2Cl_2 and MeOH (10:1) provided a set of crystals from which a needle-like crystal (**35**) was separated manually: mp 250 - 251 °C; IR (neat) 3295, 2949, 2863, 1627, 1466, 1438, 1275, 1169, 876 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.34 (s, 9H), 1.44 (s, 9H), 1.78 (s, 3H), 1.88 - 2.01 (m, 1H), 2.10 - 2.22 (m, 1H) , 3.45 - 3.57 (m, 1H), 7.09 (d, *J* = 2.5 Hz, 1H), 7.36 (d, *J* = 2.5 Hz, 1H), 8.40 (s, 1H), 13.78 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.1, 29.5, 29.8, 31.6, 32.2, 34.1, 35.1, 66.8 , 118.0, 125.7, 126.6, 136.8, 139.8, 158.1, 163.8; HRMS (EI) calcd for $C_{38}H_{56}N_2O_2$ *m/z* 572.4342, found 572.4319.

1, 3-Cyclohexadiene 2-carboxylic Acid (57)[4]



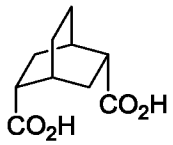
Anhydrous ammonia was condensed into a stirred solution of benzoic acid (10.0 g, 81.89 mmol) in 65 mL of dry MeOH at -78 °C and sodium (5.64 g, 245 mmol) was added in small portions at -78 °C. After the blue color had disappeared, ammonium chloride (13.11 g, 245 mmol) was added cautiously and the mixture was stirred at -78 °C for 1 h before being allowed to warm to 25 °C with the evaporation of ammonia. The solution was poured into ice water and acidified with 2M HCl to pH 4, extracted with ether (4 x 150 mL) and evaporated in vacuo to give crude 1,4-cyclohexane-3-carboxylic acid (**58**) as a white solid. A solution of crude 1,4-cyclohexane-3-carboxylic acid (**58**) in 335 mL of 15% KOH and hydroquinone (200 mg , 1.81 mmol) was added and the solution was warmed at reflux for 2 h under argon. The cold reaction mixture was acidified with 10% HCl to pH 4, after which ether extraction and concentration in vaccuo afforded crude **57**. Purification by silica gel chromatography (7:3 pentane/ether) gave **57** (8.55 g, 84%) as a pale yellow oil: IR (neat) 3397 (b), 2957, 1729, 1674, 1615, 1431, 1186, 1086, 1030, 899, 752 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.06 - 2.19 (m, 2H), 2.24 - 2.37 (m, 2H), 1.52 - 1.68 (m, 1H), 1.71 - 1.92 (m, 2H), 1.96 - 2.12 (m, 1H), 2.23 - 2.37 (m, 1H), 2.92 - 3.11 (m, 2H), 5.86 (dt, J = 10.1 & 4.3 Hz, 1H), 6.14 (dd, J = 10.1 & 1.6 Hz, 1H), 7.00 (dt, J = 4.3 & 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.8, 22.8, 121.5, 127.2, 139.0, 170.0.

(±)-Bis-endo-5-(methoxycarbonyl)bicyclo[2.2.2]octane-2-carboxylic Acid (61)[5]



To **57** (3.16 g, 25.45 mmol) was added methyl acrylate (6.5 mL, 72.18 mmol) and the solution was refluxed for 12 h. Excess methylate acrylate was distilled off at 110 °C and a solution of the residue in acetic acid (40 mL) was stirred under hydrogen at 1 atm over Adams catalyst (87 mg, 0.38 mmol) for 23 h. The mixture was filtered through Celite and the filtrate was evaporated. The residue was extracted with dichloromethane and the extract was washed with water (2 x 50 mL), dried (Na_2SO_4) and concentrated to give a crude mixture of **61** and **62** (5.029 g, 93%). The residue was purified by chromatography (SiO_2, 10% EtOAc in hexanes) to give **61** (3.781 g, 70%) as a colorless solid: mp 87 - 88 °C; IR (neat) 2945, 1739, 1696, 1451, 1427, 1240 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.49 - 1.71 (m, 6H), 1.96 - 2.19 (m, 4H), 2.46 - 2.68 (m, 2H), 3.71 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.4, 24.7, 25.2, 26.9, 27.0, 28.8, 41.0, 51.7, 175.8, 181.2.

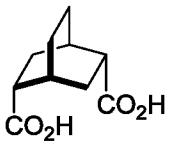
(±)-Bis-endo-bicyclo[2.2.2]octane-2,5-dicarboxylic Acid [(±)-54)



To a solution of **61** (1.13 g, 5.31 mmol) in THF (14 mL) was added $LiOH.H_2O$ (0.56 g, 13.27 mmol) followed by H_2O (3.5 mL). The mixture was stirred at room temperature for 16 h then was acidified with 1M HCl to pH 2. A white precipitate formed which was filtered off and dried to give **54** (763 mg, 72%) as a colorless solid. The filtrate was

extracted with ether (2 x 50 mL), dried (Na_2SO_4) and evaporated to give an additional amount (280 mg, 27%) of **54**: mp 198 - 199 °C; IR (neat) 3404, 2264, 2120, 1660, 1049, 999 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 1.41 - 1.64 (m, 6H), 1.71 - 1.89 (m, 2H), 1.93 (bs, 2H), 2.40 (dd, *J* = 7.9, 10.6 Hz, 3H), 11.99 (bs, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 24.8, 25.2, 27.1, 40.7, 176.6.

(-)-(1*R*,2*R*,4*R*,5*R*)-Bicyclo[2.2.2]octane-2,5-dicarboxylic Acid [(-)-54]

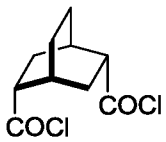


To a saturated solution of (±)-**54** (150 mg, 0.76 mmol) in EtOH (5 mL) at 50 °C was added a solution of brucine (850 mg, 1.89 mmol) in EtOH (15 mL) and the mixture was stirred at room temperature for 2 h. A white precipitate formed which was filtered off, washed with cold ethanol and dried. The collected solid was crystallized from water (3 x) to give a brucine salt (270 mg, 36%) as colorless needles whose structure was determined by X-ray crystallography: mp > 260 °C; $[\alpha]^{25}_D$ - 117.2 (*c* 0.5, DMF), [lit.[6] $[\alpha]^{25}_D$ - 118.3 (*c* 0.5, DMF)]; IR (neat) 2937, 2832,1715, 1664, 1497, 1454, 1392, 1283, 1112, 843, 734, 618, 548 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 1.38 - 141 (m, 1H),), 1.59 - 1.75 (m, 7H), 1.98 - 2.03 (m, 3H), 2.12 - 2.19 (m, 3H), 2.48 - 2.52 (m, 1H), 2.66 - 2.74 (m, 3H), 3.04 - 3.10 (m, 1H), 3.11 - 3.20 (m, 2H), 3.32 (s, 1H), 3.69 (dd, *J* = 7.9 & 3.7 Hz, 1H), 3.91 - 3.97 (m, 7H), 4.03 (d, *J* = 14.1 Hz, 1H), 4.11 (dd, *J* = 8.0 & 5.9 Hz, 1H), 4.24 (dd, *J* = 6.9 & 6.2 Hz, 1H), 4.36 (dt, *J* = 8.6 & 3.3 Hz, 1H), 4.43 (s, 1H), 6.26 (s, 1H), 6.84 (s, 1H), 7.81 (s, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 25.4, 25.7, 26.0, 27.5, 30.9, 41.1, 42.2, 44.1,

47.5, 49.8, 51.8, 52.2, 56.3, 56.6, 59.6, 59.7, 64.2, 77.6, 100.9, 105.0, 120.0, 133.6, 135.6, 146.8, 149.9, 168.6, 181.3.

To a suspension of the brucine salt obtained above (0.23 g, 0.23 mmol) in water (10 mL) was added 2M HCl (5 mL) and the mixture was extracted with ether (3 x 20 mL). The ethereal layer was washed with water (4 x 5 mL), dried (Na_2SO_4) and concentrated under reduced pressure to give (-)-**54** (41 mg, 88%) as a colorless solid: mp 200 - 202 °C; $[\alpha]^{25}_D$ - 92.7 (*c* 0.4, EtOH), [lit.[6] $[\alpha]^{25}_D$ - 125.0 (*c* 0.5, MeOH)]; IR (neat) 3445, 3440, 2951, 2871, 1733, 1713, 1625, 1436, 1380, 1325, 1260, 1225, 1087, 1058, 748 cm^{-1}; ^1H NMR (300 MHz, DMSO-d^6) δ 1.43 - 1.61 (m, 6H), 1.76 - 1.84 (m, 2H), 1.91 - 1.97 (m, 2H), 2.37 - 2.44 (m, 2H), 11.98 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d^6) δ 24.9, 25.4, 27.2, 41.3, 177.1.

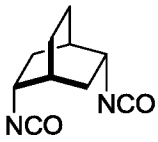
(-)-(1*R*,2*R*,4*R*,5*R*)-Bicyclo[2.2.2]octane-2,5-dicarbonyl Dichloride [(-)-53]



To (-)-**54** (86 mg, 0.43 mmol) was added oxalyl chloride (0.19 mL, 2.21 mmol) and the mixture was stirred at 40 - 45 °C for 5 h. The mixture was concentrated under reduced pressure to remove excess oxalyl chloride and the residue was dried under vacuum to give (-)-**53** (101 mg, 99%) as a brown oil: $[\alpha]^{25}_D$ -121.5 (*c* 0.4, *n*-pentane), [lit.[7] $[\alpha]^{22}_D$ - 122.9 (*c* 1.7, *n*-pentane)]; IR (neat) 2949, 2871, 1789, 1454, 1326, 1302, 1228, 1034, 925, 843, 784, 746, 703 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.61 - 1.69 (m, 2H), 1.70 - 1.78

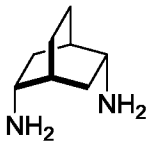
(m, 2H), 1.85 - 1.95 (m, 2H), 2.00 - 2.08 (m, 2H), 2.37 - 2.42 (m, 2H), 2.97 - 3.05 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.7 (CH_2), 25.1 (CH_2), 27.6 (CH), 53.2 (CH), 175.8.

(-)-(1*R*,2*R*,4*R*,5*R*)-2,5-Diisocyanatobicyclo[2.2.2]octane [(-)-51]



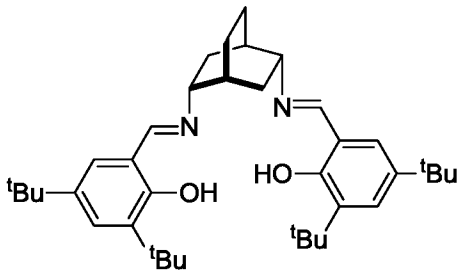
To a solution of (-)-**53** (100 mg, 0.43 mmol) in DMF (4 mL) at 0 °C was added NaN_3 (0.18 g 2.77 mmol) and the mixture was stirred at 0 °C for 3 h. The mixture was extracted with benzene (3 x 50 mL), washed with water (3 x 5 mL) and brine (5 mL), then dried (Na_2SO_4) and concentrated to give crude (-)-**52** as a pale yellow oil. This material was diluted with benzene (6 mL) and the mixture was refluxed for 6 h. The solution was concentrated under reduced pressure to give (-)-**51** (69 mg, 83% from (-)-**53**) as a yellow oil: $[\alpha]^{25}_D$ - 78.2 (*c* 0.4, *n*-pentane), [lit.[7] $[\alpha]^{22}_D$ - 77.4 (*c* 1.8, *n*-pentane)]; IR (neat) 2941, 2863, 2268 (NCO), 1715, 1649, 1365, 1217, 1092 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.46 - 1.55 (m, 4H), 1.73 - 1.81 (s, 2H), 1.82 - 1.92 (m, 2H), 1.97 - 2.09 (m, 2H), 3.71 - 3.80 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.4 (CH_2), 30.5 (CH_2), 31.6 (CH), 51.8 (CH).

(-)-(1*R*,2*R*,4*R*,5*R*)-2,5-Diaminobicyclo[2.2.2]octane [(-)-34]



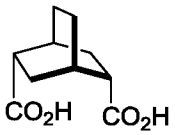
To a solution of (-)-**51** (0.10 g, 0.52 mmol) in benzene (3 mL) was added concd HCl (4 mL) and the mixture was heated at reflux for 9 h. The mixture was concentrated under reduced pressure to remove benzene and the residual solution was refluxed for 5 h. After removal of HCl under reduced pressure, the mixture was treated with 10% aqueous NaOH (12 mL) and was extracted with CH_2Cl_2 (3 x 50 mL). The extract was dried (Na_2SO_4) and concentrated under reduced pressure. The residue was dissolved in EtOH (2 mL) and was added to a solution of HCl in Et_2O (1 mL). A white precipitate was formed which was filtered off and dried to obtain the HCl salt of (-)-**34** as a colorless solid: mp > 260 °C; $[\alpha]^{25}_D$ - 95.6 (*c* 1.0, D_2O), [lit.[7] $[\alpha]^{22}_D$ - 94.2 (*c* 1.2, D_2O)]; IR (neat) 3373, 2921, 2844, 1084, 1022, 796 cm^{-1}; ^1H NMR (75 MHz, D_2O) δ 0.83 - 1.48 (m, 6H), 1.51 - 2.06 (m, 4H), 2.97 - 3.55 (m, 2H), 4.58 (bs, 6H); ^{13}C NMR (100 MHz, MeOD-d^4) δ 22.6 (CH_2), 24.5 (CH_2), 28.1 (CH), 65.5 (CH). The solid was treated with 10% aqueous NaOH (12 mL) and the solution was extracted with CH_2Cl_2 (3 x 50 mL). The extract was dried (Na_2SO_4) and concentrated under vacuum to give (-)-**34** (60 mg, 81%) as a colorless semisolid: $[\alpha]^{25}_D$ - 70.2 (*c* 0.7, CH_2Cl_2); IR (neat) 3321, 2927, 1647, 1587, 1490, 1190, 1159, 1093, 956 cm^{-1}; ^1H NMR (75 MHz, $CDCl_3$) δ 1.46 - 1.68 (m, 6H), 1.92 (s, 2H), 2.03 - 2.14 (m, 2H), 3.42 (t, *J* = 8.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.4 (CH_2), 24.3 (CH_2), 27.6 (CH), 48.2 (CH).

(+)-2,2'-[(1*R*,2*R*,4*R*,5*R*)-Bicyclo[2.2.2]octane-2,5-diylbis(nitrilomethylidine)]bis-4,6-di-*tert*-butylphenol [(+)-35]



To a solution of (-)-**34** (32 mg, 0.23 mmol) in EtOH (1 mL) was added a solution of 3,5 di-*tert*-butylsalicylaldehyde (**47**, 130 mg 0.56 mmol) in EtOH (2 mL). The mixture was stirred at room temperature for 30 min, at which time a yellow precipitate had formed. The mixture was refluxed for 2 h then was stirred at room temperature overnight. The precipitate was filtered off and was crystallized from CH_2Cl_2/MeOH (10:1) to obtain (+)-**35** (122 mg, 93%) as yellow needles: mp 252 - 254 °C; $[\alpha]^{25}_D$ + 205.6 (*c* 1.00 , CH_2Cl_2); IR (neat) 2935, 2860, 1624, 1470, 1437, 1357, 1270, 1247, 1170, 1036, 878, 774, 705 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.33 (s, 18H), 1.45 (s, 18H), 1.72 (s, 6H), 1.87 - 2.01 (m, 2H), 2.11 - 2.24 (m, 2H) , 3.46 - 3.57 (m, 2H), 7.10 (d, *J* = 2.4 Hz, 2H), 7.37 (d, *J* = 2.6 Hz, 2H), 8.41 (s, 2H), 13.75 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.1 (CH_2), 29.4 (CH_3), 29.8 (CH_2), 31.6 (CH_3), 32.2 (CH), 34.1 (Cq), 35.1 (Cq), 66.7 (CH), 117.9 (Cq), 125.7 (CH), 126.5 (CH), 136.8 (Cq), 139.8 (Cq), 158.1 (Cq), 163.8 (CH); HRMS (EI) calcd for $C_{38}H_{56}N_2O_2$ *m/z* 572.4342, found 572.4320.

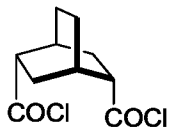
(+)-(1*S*,2*S*,4*S*,5*S*)-Bicyclo[2.2.2]octane-2,5-dicarboxylic Acid [(+)-54]



The mother liquor obtained after the fractional crystallization of (-)-**64** was evaporated in vacuo and the residue thus obtained was crystallized from hot water (3 x) to remove additional (-)-**64** while the optical rotation of the residue obtained by evaporation of the mother liquor reached a constant value. This produced a brucine salt (-)-**65** (363 mg, 48%) as a colorless amorphous solid: mp > 260 °C; $[\alpha]^{25}_{D}$ - 46.7 (*c* 1.0, DMF); IR (neat) 2963, 2868, 1660, 1459, 1378, 1364, 1281, 1264, 1218, 1161, 1120, 737, 696 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 1.31 - 140 (m, 1H),), 1.59 - 1.75 (m, 4H), 1.92 - 2.09 (m, 3H), 2.14 - 2.22 (m, 1H), 2.42 - 2.58 (m, 1H), 2.62 - 2.66 (m, 1H), 2.67 - 2.75 (m, 2H), 2.89 - 3.08 (m, 3H), 3.12 - 3.17 (m, 1H), 3.22 - 3.27 (m, 2H), 3.40 -3.49 (m, 1H), 3.87 - 3.97 (m, 9H), 4.09 - 4.28 (m, 3H), 4.33 - 4.38 (m, 1H), 6.09 - 6.14 (m, 1H), 6.79 (s, 1H), 7.84 (s, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 18.4, 19.2, 22.0, 26.8, 29.7, 29.8, 36.9, 37.7, 39.1, 48.3, 50.7, 50.8, 54.6, 57.7, 59.6, 96.2, 100.8, 116.7, 117.7, 118.4, 141.5, 144.9, 152.3, 158.8, 177.9.

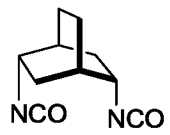
To a suspension of the brucine salt obtained above (0.36 g, 0.37 mmol) in water (10 mL) was added 2M HCl (5 mL) and the mixture was extracted with ether (3 x 20 mL). The ethereal layer was washed with water (4 x 5 mL), dried (Na_2SO_4) and concentrated under reduced pressure to give (+)-**54** (70 mg, 95%) as a colorless solid: mp 200 - 201 °C; $[\alpha]^{25}_{D}$ + 122.3 (*c* 0.5, EtOH); IR (neat) 2875, 1684, 1412, 1093 cm^{-1}; ^{1}H NMR (300 MHz, MeOD-d^4) δ 1.51 - 1.74 (m, 6H), 1.98 - 2.21 (m, 4H), 2.48 - 2.61 (m, 2H); ^{13}C NMR (100 MHz, MeOD-d^4) δ 24.4, 24.9, 27.2, 40.9, 177.9.

(+)-(1*S*,2*S*,4*S*,5*S*)-Bicyclo[2.2.2]octane-2,5-dicarbonyl Dichloride [(+)-53]



To (-)-**54** (67 mg, 0.34 mmol) was added oxalyl chloride (0.19 mL, 2.21 mmol) and the mixture was stirred at 40 - 45 °C for 5 h. The mixture was concentrated under reduced pressure to remove excess oxalyl chloride and the residue was dried under vacuum to give (+)-**53** (74 mg, 99%) as a brown oil: $[\alpha]^{25}_{D}$ +120.5 (*c* 0.5, *n*-pentane); IR (neat) 2949, 2864, 1793, 1653, 1635, 1456, 1322, 1075, 1037, 927, 845, 785, 748, 709 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.36 - 1.61 (m, 6H), 1.75 - 1.85 (m, 2H), 1.85 - 1.96 (m, 2H), 2.29 - 2.38 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.8, 25.0, 27.0, 53.9, 176.3.

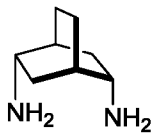
(+)-(1*S*,2*S*,4*S*,5*S*)-2,5-Diisocyanatobicyclo[2.2.2]octane [(+)-51]



To a solution of (+)-**53** (70 mg, 0.30 mmol) in DMF (4 mL) at 0 °C was added NaN_3 (0.18 g 2.77 mmol) and the mixture was stirred at 0 °C for 5 h. The mixture was extracted with benzene (3 x 50 mL), washed with water (3 x 5 mL) and brine (5 mL), then dried (Na_2SO_4) and concentrated to give crude (+)-**52** as a pale yellow oil. This material was diluted with benzene (6 mL) and the mixture was refluxed for 8 h. The solution was concentrated under reduced pressure to give (+)-**51** (46 mg, 80% from (+)-**53**) as a yellow oil: $[\alpha]^{25}_{D}$ + 78.8 (*c* 0.4, *n*-pentane); IR (neat) 2940, 2867, 2263 (NCO), 1699, 1652,

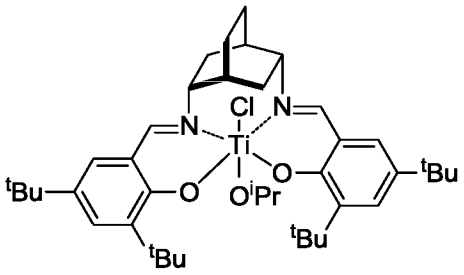
1539, 1360, 1325, 1019 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.42 - 1.67 (m, 6H), 1.84 - 1.91 (s, 2H), 2.03 - 2.12 (m, 2H), 3.42 - 3.48 (m, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 24.5, 30.2, 31.6, 51.9.

(+)-(1*S*,2*S*,4*S*,5*S*)-2,5-Diaminobicyclo[2.2.2]octane [(+)-34]



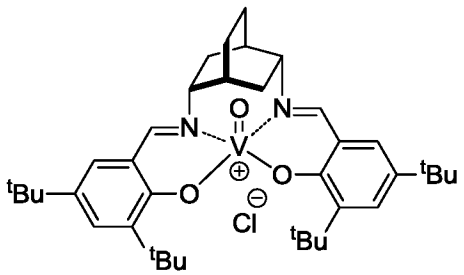
To a solution of (-)-**51** (44 mg, 0.23 mmol) in benzene (3 mL) was added concd HCl (4 mL) and the mixture was heated at reflux for 9 h. The mixture was concentrated under reduced pressure to remove benzene and the residual solution was refluxed for 5 h. After removal of HCl under reduced pressure, the mixture was treated with 10% aqueous NaOH (10 mL) and was extracted with CH_2Cl_2 (3 x 50 mL). The extract was dried (Na_2SO_4) and concentrated under reduced pressure to give (+)-**34** (28 mg, 86%) as a colorless semisolid: $[\alpha]^{25}_D$ + 73.0 (*c* 0.1, CH_2Cl_2); IR (neat) 3388, 2922, 2851, 1644, 1556, 1454, 1396, 1291, 1099 cm^{-1}; ^1H NMR (75 MHz, DMSO-d^6) δ 1.44 - 1.57 (m, 6H), 1.85 - 1.91 (m, 4H), 2.38 - 2.42 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d^6) δ 22.7, 25.5, 29.3, 49.1.

(+)-(1*R*,2*R*,4*R*,5*R*)-*N*,*N*'-Bis-(3,5-di-*tert*-butylsalicylidene)-2,5-diaminobicyclo[2.2.2]octane Isopropoxy Titanium(IV) Chloride [(+)-67]



To a solution of (+)-**35** (10 mg, 17.45 μmol) in CH_2Cl_2 (5 mL) was added Et_3N (0.01 mL, 0.07 mmol) followed by $Ti(O^iPr)_3Cl$ (2.61 mL, 0.03 mmol, 0.01M in hexanes) and the mixture was stirred at room temperature for 12 h during which the solution turned yellow. The mixture was concentrated under reduced pressure, and the residue was dissolved in CH_2Cl_2 and filtered. The filtrate was concentrated under vacuum to give (+)-**67** (11.2 mg, 90%) as a yellow solid: mp > 260 °C; $[\alpha]^{25}_D$ + 91.3 (*c* 0.06 $CHCl_3$); IR (neat) 2950, 1608, 1588, 1537, 1479, 1362, 1255, 1176, 1108, 1036, 839, 808 cm^{-1}; HRMS (FAB) calcd for $C_{41}H_{61}TiN_2O_3$ *m/z* 677.3701, found 677.3704.

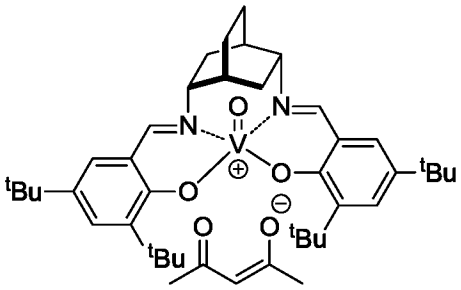
(+)-(1*R*,2*R*,4*R*,5*R*)-*N*,*N*'-Bis-(3,5-di-*tert*-butylsalicylidene)-2,5-diaminobicyclo[2.2.2]octane Oxovanadium(V) Chloride [(+)-68]



To a solution of (+)-**35** (10 mg, 17.45 μmol) in CH_2Cl_2 (5 mL) was added dropwise a solution of $VOCl_3$ (10 μL, 0.11 mmol) in CH_2Cl_2 (2 mL) and the mixture was stirred at

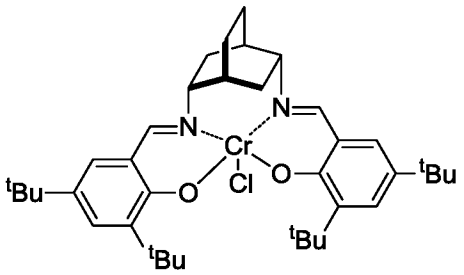
room temperature for 3 h, at which time the solution had turned green. The mixture was concentrated under reduced pressure and the residue was dried under high vacuum to give (+)-**68** (11 mg, 92%) as a green solid: mp > 260 °C; $[\alpha]^{25}_{D}$ + 153.8 (*c* 0.1 $CHCl_3$); IR (neat) 2961, 1653, 1478, 1451, 1365, 1268, 1229, 1151, 995 cm^{-1}; HRMS (ESI) calcd for $C_{38}H_{55}VN_2O_3$ *m/z* 638.3652, found 638.3705.

(+)-(1*R*,2*R*,4*R*,5*R*)-*N*,*N*'-Bis-(3,5-di-*tert*-butylsalicylidene)-2,5-diaminobicyclo[2.2.2]octane Oxovanadium(V) Acetylacetonate [(+)-69]



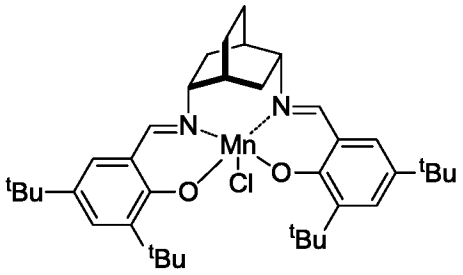
To a solution of (+)-**35** (10 mg, 17.45 μmol) in MeOH (6 mL) was added $VO(acac)_2$ (7 mg, 0.03 mmol) and the mixture was heated at reflux for 5 h, during which a green precipitate was formed. The mixture was cooled and concentrated under reduced pressure, and the green residue was dissolved in CH_2Cl_2. The mixture was filtered and the filtrate was concentrated under vacuum to give (+)-**69** (12 mg, 94%) as a green solid: mp > 260 °C; $[\alpha]^{25}_{D}$ + 161.0 (*c* 0.1 $CHCl_3$); IR (neat) 2953, 2863, 1610, 1594, 1555, 1536, 1462, 1411, 1361, 1256, 1178, 1108, 983 cm^{-1}; HRMS (EI) calcd for $C_{38}H_{54}VN_2O_3$ *m/z* 637.3574, found 637. 3586.

(+)-(1*R*,2*R*,4*R*,5*R*)-*N*,*N*'-Bis-(3,5-di-*tert*-butylsalicylidene)-2,5 diaminobicyclo[2.2.2]octane Chromium(III) Chloride [(+)-70]



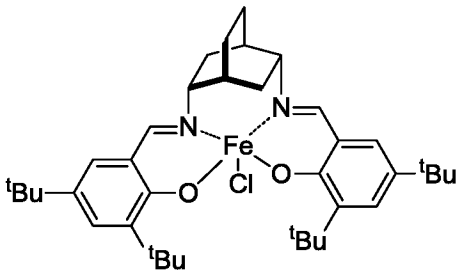
In a flame dried round bottomed flask was placed powdered Mn (2.49 g, 45.27 mmol), anhydrous $CrCl_3$ (0.24 g, 1.52 mmol) and freshly distilled THF (10 mL). The mixture was stirred at room temperature for 4 h, at which time a greenish white precipitate had formed. To this mixture was added a solution of (+)-**35** (300 mg, 0.52 mmol) in dry THF (5 mL) followed by dry Et_3N (160 μL, 1.14 mmol), and the resulting mixture was stirred at room temperature for 12 h during which time a dark brown solid had formed. The flask was opened to air and stirring was continued for an additional 24 h. The mixture was diluted with methyl *tert*-butyl ether (100 mL) and the solution was washed with saturated NH_4Cl solution (3 x 10 mL) and brine (3 x 10 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The residue was dried under vacuum overnight to give (+)-**70** (301 mg, 87%) as a dark brown solid: mp > 260 °C; $[\alpha]^{25}_D$ + 190.4 (*c* 0.35, $CHCl_3$); IR (neat) 2953, 2921, 2859, 1610, 1536, 1458, 1411, 1357, 1314, 1252, 1174, 1104, 1011, 839, 785, 746 cm^{-1}; HRMS (EI) calcd for $C_{38}H_{54}CrN_2O_2$ *m/z* 622.3536, found 622.3539.

(+)-(1*R*,2*R*,4*R*,5*R*)-*N*,*N*'-Bis-(3,5-di-*tert*-butylsalicylidene)-2,5-diaminobicyclo[2.2.2]octane Manganese(III) Chloride [(+)-71]



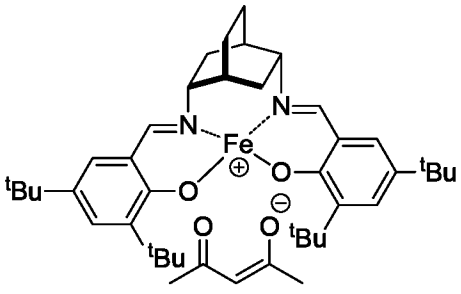
To a solution of $Mn(OAc)_2.4H_2O$ (6.1 mg, 0.03 mmol) in MeOH (3 mL) was added dropwise a solution of (+)-**35** (3.0 mg, 0.03 mmol) in toluene (2 mL) and the mixture was refluxed for 5 h. The flask was opened to air and the mixture was stirred at room temperature for an additional 3 h. Brine (5 mL) was added and the resulting mixture was stirred at room temperature overnight. The mixture was diluted with toluene (5 mL), and the solution was washed with water (5 x 2 mL) and brine (3 x 2 mL), dried ($MgSO_4$) and concentrated under reduced pressure. The crude residue was washed with *n*-heptane (3 x 2 mL) and was dried under high vacuum to give (+)-**71** (2.2 mg, 58%) as a brown solid: mp > 260 °C; $[\alpha]^{25}_D$ + 122.3 (*c* 0.1 $CHCl_3$); IR (neat) 2954, 2921, 2861, 1610, 1593, 1537, 1461, 1412, 1357, 1255, 1197, 1178, 1108, 1084, 1011, 917, 874, 841, 748 cm^{-1}; HRMS (ESI) calcd for $C_{38}H_{54}MnN_2O_2$ *m/z* 625.3566, found 625.3580.

(+)-(1*R*,2*R*,4*R*,5*R*)-*N*,*N*'-Bis-(3,5-di-*tert*-butylsalicylidene)-2,5-diaminobicyclo[2.2.2]octane Iron(III) Chloride [(+)-72]



To a solution of NaH (1.5 mg, 0.04 mmol, 60% suspension in mineral oil) in THF (2 mL) at 0 °C was added dropwise a solution of (+)-**35** (10 mg, 17.45 μmol) in THF (3 mL). The mixture was heated at reflux for 2 h, then was cooled to room temperature. Anhydrous $FeCl_3$ (4.2 mg, 0.03 mmol) was added and the mixture was refluxed for an additional 12 h. The mixture was concentrated under reduced pressure and the residue was dissolved in CH_2Cl_2 (10 mL). The solution was washed with water (3 x 2 mL), dried (Na_2SO_4) and concentrated under reduced pressure, and the residue was dried under high vacuum to give (+)-**72** (10.8 mg, 96%) as a brown solid: mp 222 - 223 °C; $[\alpha]^{25}_D$ + 174.0 (*c* 0.1 $CHCl_3$); IR (neat) 2957, 2926, 2852, 1727, 1606, 1587, 1536, 1462, 1361, 1272, 1252, 1174, 1108, 1065 cm^{-1}; HRMS (EI) calcd for $C_{38}H_{54}FeClN_2O_2$ *m/z* 661.3223, found 661.3548.

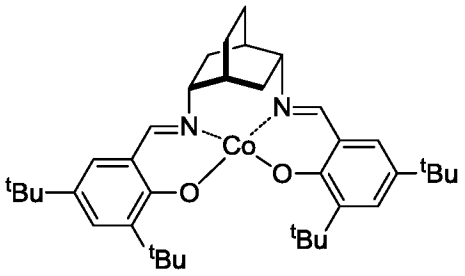
(+)-(1*R*,2*R*,4*R*,5*R*)-*N*,*N*'-Bis-(3,5-di-*tert*-butylsalicylidene)-2,5-diaminobicyclo[2.2.2]octane Iron(III) Acetylacetonate [(+)-73]



To a solution of (+)-**35** (10 g, 17.45 μmol) in MeOH (5 mL) was added $Fe(acac)_3$ (10 mg, 0.04 mmol) and the mixture was heated at reflux for 8 h during which a violet precipitate was formed. The mixture was cooled and concentrated under reduced pressure, and the residue was dissolved in CH_2Cl_2 and filtered. The filtrate was concentrated under vacuum

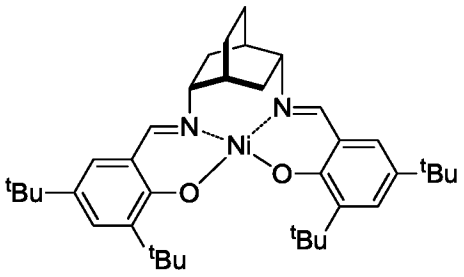
to give (+)-**73** (11.8 mg, 96%) as a violet solid: mp > 260 °C; $[\alpha]^{25}_{D}$ + 168.1 (*c* 0.12 $CHCl_3$); IR (neat) 2953, 2863, 1575, 1521, 1412, 1365, 1272, 1174, 1019, 925, 836 cm^{-1}; HRMS (EI) calcd for $C_{38}H_{54}FeN_2O_2$ *m/z* 626.3535, found 626.3554.

(+)-(1*R*,2*R*,4*R*,5*R*)-*N*,*N*'-Bis-(3,5-di-*tert*-butylsalicylidene)-2,5-diaminobicyclo[2.2.2]octane Cobalt(II) [(+)-74]



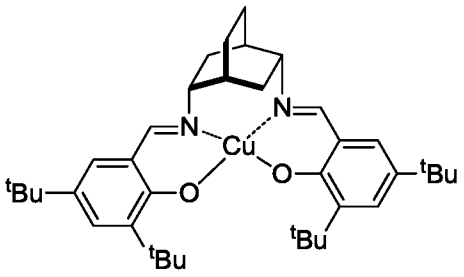
To a solution of NaH (2.1 mg, 0.04 mmol, 60% suspension in mineral oil) in THF (2 mL) at 0 °C was added dropwise a solution of (+)-**35** (10 mg, 17.45 μmol) in THF (3 mL). The mixture was stirred at room temperature for 2 h, anhydrous $CoBr_2$ (10 mg, 0.07 mmol) was added and the resulting mixture was refluxed for 10 h. The mixture was cooled, and concentrated under reduced pressure, and the residue was dissolved in CH_2Cl_2 and filtered. The filtrate was concentrated under vacuum to give (+)-**74** (9.6 mg, 88%) as an orange solid: mp > 260 °C; $[\alpha]^{25}_{D}$ + 146.3 (*c* 0.15 $CHCl_3$); IR (neat) 2950, 2867, 1614, 1531, 1470, 1360, 1325, 1257, 1203, 1173, 1108, 1018, 981, 918 cm^{-1}; HRMS (FAB) calcd for $C_{38}H_{54}CoN_2O_2$ *m/z* 629.3517, found 629.3524.

(+)-(1*R*,2*R*,4*R*,5*R*)-*N*,*N*'-Bis-(3,5-di-*tert*-butylsalicylidene)-2,5diaminobicyclo[2.2.2]octane Nickel(II) [(+)-75]



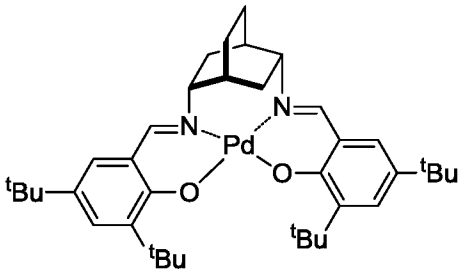
To a solution of (+)-**35** (10 mg, 17.45 μmol) in MeOH (5 mL) was added a solution of $Ni(OAc)_2.4H_2O$ (40 mg, 0.17 mmol) in MeOH (2 mL) and the mixture was heated at reflux for 4 h, at which time an orange-red precipitate had formed. The mixture was cooled and concentrated under reduced pressure, and the residue was dissolved in CH_2Cl_2 and filtered. Concentration of the filtrate under vacuum provided (+)-**75** (11 mg, 100%) as red-orrange needles: mp > 260 °C; $[\alpha]^{25}_D$ + 178.2 (*c* 0.1 $CHCl_3$); IR (neat) 2949, 2855, 1610, 1548, 1462, 1435, 1311, 1357, 1318, 1256, 1201, 1182, 1108, 1081 cm^{-1}; HRMS (ESI) calcd for $C_{38}H_{54}NiN_2O_2$ *m/z* 628.3539, found 634.3546.

(+)-(1*R*,2*R*,4*R*,5*R*)-*N*,*N*'-Bis-(3,5-di-*tert*-butylsalicylidene)-2,5-diaminobicyclo[2.2.2]octane Copper(II) [(+)-76]



To a solution of (+)-**35** (2 mg, 3.5 μmol) in MeOH (1 mL) was added a solution of $Cu(OAc)_2.H_2O$ (1.1 mg, 0.05 mmol) in MeOH (2 mL) and the mixture was heated to reflux for 12 h, at which time a brown precipitate had formed. The mixture was cooled and concentrated under reduced pressure, and the residue was dissolved in CH_2Cl_2 and filtered. Concentration of the filtrate under vacuum provided copper complex (+)-**76** (2 mg, 90%) as black needles: mp > 260 °C; $[\alpha]^{25}_D$ + 132.0 (*c* 0.1 $CHCl_3$); IR (neat) 2951, 2924, 2862, 1616, 1597, 1530, 1467, 1415, 1363, 1328, 1259, 1200, 1174,1107, 1026, 975, 920, 876, 834, 790, 755 cm^{-1}; HRMS (ESI) calcd for $C_{38}H_{54}CuN_2O_2$ *m/z* 634.3560, found 634.3549.

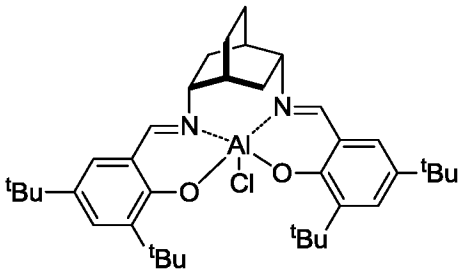
(+)-(1*R*,2*R*,4*R*,5*R*)-*N*,*N*'-Bis-(3,5-di-*tert*-butylsalicylidene)-2,5-diaminobicyclo[2.2.2]octane Palladium(II) [(+)-77]



To a solution of (+)-**35** (10 mg, 17.45 μmol) in MeOH (6 mL) was added $Pd(OAc)_2$ (20 mg, 0.07 mmol) and the mixture was heated at reflux for 5 h during which a red precipitate was formed. The mixture was cooled and concentrated under reduced pressure, and the residue was dissolved in CH_2Cl_2 and filtered. The filtrate was

concentrated under vacuum to give (+)-**77** (11 mg, 96%) as red needles: mp > 260 °C; $[\alpha]^{25}_{D}$ + 151.0 (*c* 0.11 $CHCl_3$); IR (neat) 2949, 2860, 1606, 1595, 1548, 1529, 1459, 1412, 1361, 1315, 1252, 1178, 1108, 1085, 960, 840 cm^{-1}; HRMS (FAB) calcd for $C_{38}H_{55}PdN_2O_2$ *m/z* 677.3298, found 677.3300;

(+)-(1*R*,2*R*,4*R*,5*R*)-*N*,*N*'-Bis-(3,5-di-*tert*-butylsalicylidene)-2,5-diaminobicyclo[2.2.2]octane Aluminum(III) Chloride [(+)-78]



To a solution of NaH (2 mg, 0.04 mmol, 60% suspension in mineral oil) in THF (2 mL) at 0 °C was added a solution of (+)-**35** (10 mg, 17.45 μmol) in THF (3 mL) and the mixture was stirred at room temperature for 2 h. Anhydrous $AlCl_3$ (10 mg, 0.07 mmol) was added and the mixture was refluxed for 10 h. The mixture was cooled and concentrated under reduced pressure, and the residue was dissolved in CH_2Cl_2 and filtered. The filtrate was concentrated under vacuum to give (+)-**78** (10.5 mg, 95%) as a pale yellow solid: mp > 260 °C; $[\alpha]^{25}_{D}$ + 103.1 (*c* 0.05 $CHCl_3$); IR (neat) 2960, 2856, 1625, 1587, 1462, 1380, 1353, 1271, 1250, 1206, 1162, 879 cm^{-1}; HRMS (FAB) calcd for $C_{38}H_{54}AlN_2O_2$ *m/z* 597.4001, found 597.3990.

References:

1. Werstiuk, N. H.; Yeroushalmi, S.; Guan-Lin, H. *Can. J. Chem.* **1992**, *70*, 974.

2. Rubottom, G. M.; Gruber, J. M. *J. Org. Chem.* **1977**, *42*, 1051.

3. Marchand, A. P.; Sharma, R.; Zope, U. P. *J. Org. Chem.* **1993**, *58*, 759.

4. Boger, D. L.; Patel, M.; Takusagawa, F. *J. Org. Chem.* **1985**, *50*, 1911.

5. Hora, J. *Recueil, J. Roy. Neth. Chem. Soc.* **1976**, *95*, 45.

6. Tichy, M.; Sicher, J. *Coll. Czech. Chem. Commun.* **1972**, *37*, 3106.

7. Aksani, R.; Eichenauer, H.; Kohler, J. *Chem. Ber.* **1982**, *115*, 748.

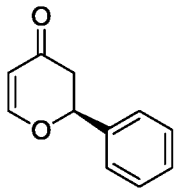
CHAPTER 3

The Asymmetric Hetero-Diels-Alder Reaction

Representative Procedure for the HDA Reaction of Danishefsky diene (31) with Aldehydes 21 Catalyzed by (+)-70:

A solution of aldehyde **21** (0.25 mmol) and diphenyl ether (0.1 mL, ACS grade) in absolute methyl *tert*-butyl ether (0.3 mL) was cooled to the temperature specified in Table 2. Molecular sieves (3 Å) and a catalytic amount of chromium complex (+)-**70** (8.3 mg, 12.6 μmol, 5 mol%) were added followed by diene **31** (0.3 mmol). The reaction was quenched by adding 5 drops of triflic acid and the mixture was stirred for 30 min. The suspension was extracted with methyl *tert*-butyl ether (2 x 20 mL), and the extract was washed with water (3 x 10 mL) and brine (10 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (30% hexane/ether) to give the product. The enantiomeric excess of the pure product was determined by HPLC on a Daicel Chiralcel OD column.

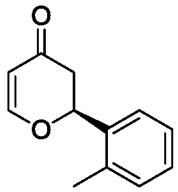
(*S*)-2-Phenyl-2,3-dihydro-4*H*-pyran-4-one (32)



Colorless oil: 97% ee [Chiralcel OD, hexane:*i*-propanol 90:10, 1.0 mL/min, t_R (major) 14.4 min, t_R (minor) 17.2 min]; $[\alpha]_D^{23}$ + 103.2 (*c* 0.5, $CHCl_3$), [lit.[1] for *(R)* enantiomer $[\alpha]^{26}_D$ - 97.1 (*c* 0.69, $CHCl_3$, 97% ee)]; IR (neat) 2921, 1678, 1595, 1401, 1264, 1228, 1205, 1034, 929, 758, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.70 (m, 1H), 2.92 (m, 1H), 5.46 (dd, *J* = 14.5, 3.9 Hz, 1H), 5.56 (dd, *J* = 6.0, 1.1 Hz, 1H), 7.44 (m, 5H), 7.51 (d,

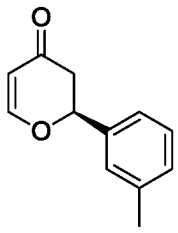
J = 6.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.4, 81.1, 107.4, 126.1, 128.1, 128.9, 137.8, 163.2, 192.2.

(*S*)-(2-Methylphenyl)-2,3-dihydro-4*H*-pyran-4-one (109a)



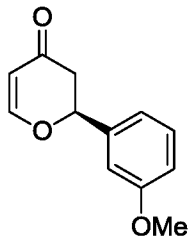
Colorless oil: 92% ee [Chiralcel OD, hexane:*i*-propanol 90:10, 1.0 mL/min, t_R (major) 13.4 min, t_R (minor) 19.6 min]; $[\alpha]_D^{16}$ + 40.6 (*c* 0.5, $CHCl_3$), [lit.[2] $[\alpha]^{25}_D$ + 46.3 (*c* 0.38, $CHCl_3$, 98% ee)]; IR (neat) 3066, 2961, 2918, 2844, 2622, 1680, 1591, 1498, 1459, 1400, 1272, 1217, 1034, 992, 929, 867, 793, 758 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.39 (s, 3H), 2.61 - 2.67 (m, 1H), 2.90 - 2.97 (m, 1H), 5.57 (d, J = 6.1 Hz, 1H), 5.67 (dd, J = 14.6, 3.3 Hz, 1H), 7.23 - 7.26 (m, 1H), 7.27 - 7.30 (m, 2H), 7.46 - 7.49 (m, 1H), 7.53 (d, J = 6.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.9, 42.4, 78.5, 107.3, 125.7, 126.5, 128.8, 130.9, 135.0, 135.9, 163.5, 192.4.

(*S*)-(3-Methylphenyl)-2,3-dihydro-4*H*-pyran-4-one (109b)



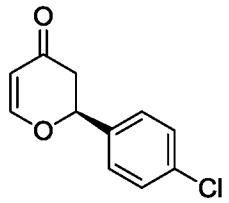
Colorless oil: 92% ee [Chiralcel OD, hexane:*i*-propanol 90:10, 1.0 mL/min, t_R (major) 12.6 min, t_R (minor) 15.7 min]; $[\alpha]_D^{16}$ + 89.8 (*c* 0.45, $CHCl_3$), [lit.[3] $[\alpha]^{20}_D$ + 67.8 (*c* 1.08, $CHCl_3$, 97% ee)]; IR (neat) 3058, 2918, 2848, 2626, 1677, 1583, 1490, 1462, 1396, 1268, 1217, 1038, 988, 941, 898, 840, 778 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.42 (s, 3H), 2.65 - 2.71 (m, 1H), 2.91 - 2.98 (m, 1H), 5.42 (d, *J* = 14.5 Hz, 1H), 5.55 (d, *J* = 5.9 Hz, 1H), 7.21 - 7.24 (m, 2H), 7.25 - 7.36 (m, 2H), 7.51 (d, *J* = 6.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 43.4, 81.2, 107.4, 123.2, 126.8, 128.7, 129.7, 137.8, 138.6, 163.1, 192.1.

(*S*)-(3,5-Dimethoxyphenyl)-2,3-dihydro-4*H*-pyran-4-one (109c)



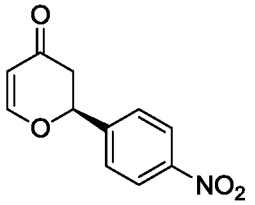
Colorless oil: 96% ee [Chiralcel OD, hexane:*i*-propanol 90:10, 1.0 mL/min, t_R (major) 21.0 min, t_R (minor) 29.7 min]; $[\alpha]_D^{16}$ + 98.4 (*c* 0.5, $CHCl_3$), [lit.[4] for *(R)* enantiomer $[\alpha]^{28}_D$ - 97.7 (*c* 1.0, $CHCl_3$, 98% ee)]; IR (neat) 3062, 2918, 2844, 2626, 1680, 1591, 1490, 1455, 1400, 1365, 1264, 121, 1151, 1042, 988, 964, 902, 781 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.67 - 2.73 (m, 1H), 2.93 (dd, *J* = 16.9, 14.5 Hz, 1H), 3.86 (s, 3H), 5.44 (dd, *J* = 14.5, 3.5 Hz, 1H), 5.56 (d, *J* = 6.1 Hz, 1H), 6.94 - 7.01 (3H, m), 7.33 (t, *J* = 7.7 Hz, 1H), 7.51 (d, *J* = 6.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.4, 55.3, 80.9, 107.4, 111.8, 114.3, 118.2, 129.9, 139.4, 160.0, 163.0, 192.0.

(*S*)-(4-Chlorophenyl)-2,3-dihydro-4*H*-pyran-4-one (109d)



Colorless solid: mp 71 - 72 °C, [lit.[5] for *(S)* enantiomer 71 - 72 °C]; 94% ee [Chiralcel OD, hexane:*i*-propanol 90:10, 5.0 mL/min, t_R (major) 15.6 min, t_R (minor) 19.4 min]; $[\alpha]_D^{23}$ + 105.0 (*c* 0.5, $CHCl_3$), [lit.[1] for *(R)* enantiomer $[\alpha]^{19}{}_D$ - 62.4 (*c* 0.56, $CHCl_3$, 84% ee)]; IR (neat) 3062, 2921, 1906, 1684, 1595, 1494, 1396, 1268, 1229, 1206, 1038, 933, 828 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.64 (dd, *J* = 16.8, 3.6 Hz, 1H), 2.88 (dd, *J* = 16.8, 14.3 Hz, 1H), 5.43 (dd, *J* = 14.4, 3.5 Hz, 1H), 5.56 (d, *J* = 6.1 Hz, 1H), 7.36 (d, *J* = 8.7 Hz, 2H), 7.43 (d, *J* = 8.7 Hz, 2H), 7.49 (d, *J* = 6.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.3, 80.3, 107.5, 127.5, 129.1, 131.7, 132.1, 163.0, 191.6.

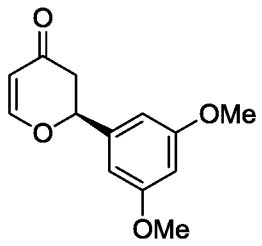
(*S*)-(4-Nitrophenyl)-2,3-dihydro-4*H*-pyran-4-one (109e)



Colorless solid: mp 100 - 101 °C, [lit.[5] for *(S)* enantiomer 100 - 102 °C]; 94% ee [Chiralcel OD, hexane:*i*-propanol 90:10, 5.0 mL/min, t_R (major) 13.4 min, t_R (minor) 17.4 min]; $[\alpha]_D^{23}$ + 58.3 (*c* 1.0, $CHCl_3$), [lit.[5] $[\alpha]^{25}{}_D$ + 59.8 (*c* 1.01, CH_2Cl_2, 94% ee)]; IR (neat) 2921, 2848, 1719, 1599, 1520, 1459, 1346, 1287, 1210, 1151, 1116, 1038, 980,

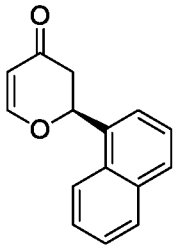
949 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.73 (m, 1H), 2.85 (dd, *J* = 16.7, 14.1 Hz, 1H), 5.56 (dd, *J* = 14.1, 3.8 Hz, 1H), 5.59 (dd, *J* = 6.0, 1.1 Hz, 1H), 7.52 (d, *J* = 6.0, 1H), 7.60 (d, *J* = 6.0, 2H), 8.29 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 46.3, 48.8, 55.2, 69.3, 99.9, 124.0, 126.5, 147.5, 202.5.

(*S*)-(3,5-Dimethoxyphenyl)-2,3-dihydro-4*H*-pyran-4-one (109f)



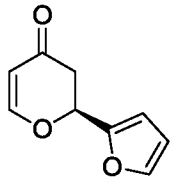
Colorless oil: 94% ee [Chiralcel OD, hexane:*i*-propanol 90:10, 1.0 mL/min, t_R (major) 19.5 min, t_R (minor) 26.4 min]; $[\alpha]_D^{16}$ + 78.3 (*c* 1.2, $CHCl_3$), [lit.[6] $[\alpha]^{21}_D$ + 75.9 (*c* 1.11, $CHCl_3$, 90% ee)]; IR (neat) 3070, 2918, 2844, 2626, 1684, 1595, 1466, 1427, 1396, 1365, 1272, 1221, 1202, 1159, 1069, 1038, 999, 910, 832, 797 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.65 - 2.71 (m, 1H), 2.91 (dd, *J* = 17.0, 14.6 Hz, 1H), 3.84 (s, 3H), 5.38 (dd, *J* = 14.3, 3.3 Hz, 1H), 5.55 (d, *J* = 6.2 Hz, 1H), 6.49 (t, *J* = 2.2Hz, 1H), 6.57 (d, *J* = 2.3 Hz, 1H), 7.51 (d, *J* = 6.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 29.7, 43.5, 55.4, 81.0, 100.5, 104.1, 107.4, 140.2, 161.2, 163.0, 192.0; HRMS (EI) calcd for $C_{13}H_{14}O_4$ 234.0892 found 234.0884.

(*S*)-(1-Naphthyl)-2,3-dihydro-4*H*-pyran-4-one (109g)



Pale yellow oil: 94% ee [Chiralcel OD, hexane:*i*-propanol 90:10, 1.0 mL/min, t_R (minor) 28.1 min, t_R (major) 33.2 min]; $[\alpha]_D^{10}$ - 35.9 (*c* 1.35, $CHCl_3$), [lit.[4] for *(R)* enantiomer $[\alpha]^{28}_D$ + 52.2 (*c* 1.0, $CHCl_3$, 97% ee)]; IR (neat) 3050, 2922, 2852, 2618, 1680, 1595, 1509, 1404, 1338, 1271, 1221, 1038, 984, 933, 801, 774 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.87 - 2.93 (m, 1H), 3.12 (dd, *J* = 17.0 , 14.3 Hz, 1H), 5.65 (dd, *J* = 6.0, 1.2 Hz, 1H), 6.22 (dd, *J* = 14.2, 3.4 Hz, 1H), 7.54 - 7.62 (m, 2H), 7.91 - 7.96 (m, 2H), 8.01 (d, *J* = 8.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 42.7, 78.4, 107.5, 122.5, 123.8, 125.3, 126.0, 126.8, 129.1, 129.6, 130.1, 133.3, 133.8, 163.4, 192.3.

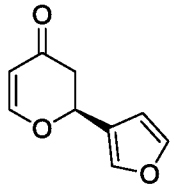
(*S*)-2-(2-Furyl)-2,3-dihydro-4*H*-pyran-4-one (109h)



Pale yellow solid: mp 68 - 69 °C, [lit.[5] for *(S)* enantiomer 66 - 67 °C]; 67% ee [Chiralcel OD, hexane:*i*-propanol 90:10, 5.0 mL/min, t_R (minor) 14.4 min, t_R (major) 15.8 min]; $[\alpha]_D^{23}$ + 255.4 (*c* 0.5, $CHCl_3$), [lit.[4] for *(R)* enantiomer $[\alpha]^{29}_D$ - 310.1 (*c* 1.0, $CHCl_3$, >99% ee)]; IR (neat) 2922, 1680, 1595, 1400, 1268, 1226, 1206, 1038, 1011, 968, 906, 797, 746 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.74 - 2.80 (m, 1H), 3.12 (dd, *J* = 17.0, 12.7 Hz,

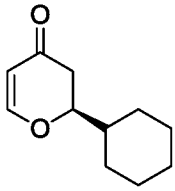
1H), 5.48 - 5.55 (m, 2H), 6.44 (dd, J = 3.3, 1.8, 1H), 6.48 (d, J = 3.5 Hz, 1H), 7.40 (d, J = 6.0 Hz, 1H), 7.51 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 39.6, 73.6, 107.4, 109.6, 110.5, 143.6, 149.4, 162.3, 191.2.

(*S*)-(3-Furyl)-2,3-dihydro-4*H*-pyran-4-one (109i)



Pale yellow solid: mp 66 - 67 °C; 94% ee [Chiralcel OD, hexane:*i*-propanol 90:10, 1.0 mL/min, t_R (major) 13.7 min, t_R (minor) 18.5 min]; $[\alpha]_D^{10}$ + 109.6 (*c* 0.5, $CHCl_3$); IR (neat) 3140, 2922, 2848, 2626, 1719, 1672, 1595, 1505, 1400, 1272, 1213, 1023, 918, 871, 797 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.71 - 2.77 (m, 1H), 2.91 (dd, J = 17.0, 13.0 Hz, 1H), 5.48 (dd, J = 12.9, 3.8 Hz, 1H), 5.53 (dd, J = 6.1, 1.0 Hz, 1H), 6.49 - 6.51 (m, 1H), 7.43 (d, J = 6.1 Hz, 1H), 7.49 (t, J = 1.8 Hz, 1H), 7.53 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 29.7, 73.9, 107.4, 108.5, 123.2, 140.3, 143.9, 162.8, 191.7; HRMS (EI) calcd for $C_9H_8O_3$ *m/z* 164.0473, found 164.0473.

(*S*)-2-Cyclohexyl-2,3-dihydro-4*H*-pyran-4-one (109j)



Colorless oil: 68% ee [Chiralcel OD, hexane:*i*-propanol 90:10, 1.0 mL/min, t_R (major) 9.8 min, t_R (minor) 10.9 min]; $[\alpha]_D^{16}$ + 112.0 (*c* 0.1, $CHCl_3$), [lit.[7] for *(R)* enantiomer $[\alpha]^{26}_D$ - 157.0 (*c* 1.03, CH_2Cl_2, 93% ee)]; IR (neat) 2926, 2852, 1731, 1595, 1459, 1381, 1276, 1256, 1174, 1038, 960, 890, 801 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.77 - 1.88 (m, 6H), 1.89 - 2.03 (m, 5H), 2.45 (m, 1 H), 2.59 (dd, *J* = 16.7, 14.4 Hz, 1H), 4.20 (ddd, *J* = 14.3, 5.6, 3.3 Hz, 1H), 5.42 (d, *J* = 5.9 Hz, 1H), 7.40 (d, *J* = 5.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.1, 28.8, 29.7, 39.1, 41.4, 83.6, 106.8, 163.6, 193.3.

References:

1. Yamashita, Y.; Saito, S.; ishitani, H.; Kobayashi, S. *J. Am. Chem. Soc.* **2003**, *125*, 3793.

2. Baldoli, C.; Maiorana, S.; Licandro, E.; Zinzalla, G.; Lanfranchi, M.; Tiripicchio, A. *Tetrahedron: Asymmetry* **2001**, *12*, 2159.

3. Du, H.; Zhang, X.; Wang, Z.; Bao, H.; You, T.; Ding, K. *Eur. J. Org. Chem.* **2008**, 2248.

4. Unni, A. K.; Takenaka, N.; Yamamoto, H.; Rawal, V. H. *J. Am. Chem. Soc.* **2005**, *127*, 1336.

5. Anada, M.; Washio, T.; Shimada, N.; Kitagaki, S.; Nakajima, M.; Shiro, M.; Hashimoto, S. *Angew. Chem. Int. Ed.* **2004**, *43*, 2665.

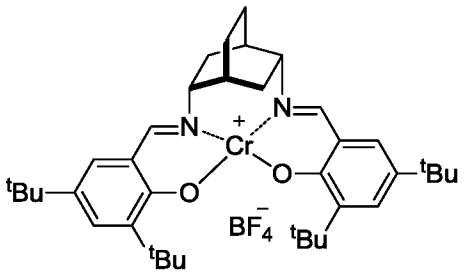
6. Watanabe, Y.; Washio, T.; Shimada, N.; Anada, M.; Hashimoto, S. *Chem. Commun.*, **2009**, 7294.

7. Schaus, S. E.; Branalt, J.; Jacobsen, E. N. *J. Org. Chem.* **1998**, *63*, 403.

CHAPTER 4

The Asymmetric Nozaki-Hiyama-Kishi Reaction

(+)-(1*R*,2*R*,4*R*,5*R*)-*N*,*N*'-Bis-(3,5-di-*tert*-butylsalicylidene)-2,5 diaminobicyclo[2.2.2]octane Chromium(III) Tetrafluoroborate [(+)-140]



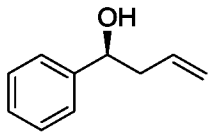
In a flame dried round bottomed flask was placed (+)-**70** (1.20 g, 1.82 mmol) and anhydrous methyl *tert*-butyl ether (5 mL). To this reaction mixture was added silver tetrafluoroborate (497 mg, 2.55 mmol) and the mixture was stirred at room temperature for 24 h. The mixture was evaporated, redisolved in CH_2Cl_2 and filtered and the filtrate was concentrated under reduced pressure to give (+)-**140** (874 mg, 67%) as a dark brown solid: mp > 260 °C; $[\alpha]^{25}_D$ + 121.2 (*c* 1.0, $CHCl_3$); IR (neat) 2949, 2925, 2852, 1651, 1611, 1537, 1463, 1418, 1315, 1257, 1175, 1107, 1015 cm^{-1}; HRMS (EI) calcd for $C_{38}H_{54}CrN_2O_2$ *m/z* 622.3591, found 622.3594.

Representative Procedure for the NHK Reaction of Allyl Halides with Aldehydes 112 Catalyzed by (+)-70:

To an oven dried vial were added molecular sieves (3 Å), Mn powder (325 mesh, 21 mg, 0.38 mmol) and a catalytic amount of chromium complex (+)-**70** (8.3 mg, 12.61 μmol, 10 mol%) and the vial was flushed with argon for 15 min. To the mixture was added anhydrous THF (1 mL) and the resulting brown suspension was stirred at room

temperature for 2 h. The suspension was treated with allyl bromide or chloride (0.19 mmol) and the mixture was stirred for 1 h. To this mixture was added neat aldehyde **112** (0.12 mmol) and TMSCl (24 μL, 0.19 mmol) at the temperature specified in Table 3 and the mixture was stirred at that temperature for the specified length of time. The reaction was quenched with saturated $NaHCO_3$ solution (1 mL), volatiles were removed in vacuo, and the residue was extracted with ether (2 x 10 mL). The extract was washed with brine (20 mL), dried (Na_2SO_4) and concentrated under reduced pressure, and the resulting crude silyl ether was treated with aqueous HCl (1M, 2 mL, 2 mmol) in THF (2 mL) at room temperature until desilylation was complete by TLC. The mixture was diluted with Et_2O (20 mL), and the solution was washed with brine (20 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (30% hexane/ether). The enantiomeric excess of the pure product was determined by HPLC on a Daicel Chiralcel OD column.

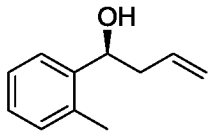
(*S*)-1-Phenylbut-3-en-1-ol (130a)



Colorless oil: 89% ee [Chiralcel OD, hexane:*i*-propanol 99:1, 0.5 mL/min, t_R (minor) 36.2 min, t_R (major) 43.2 min]; $[\alpha]_D^{20}$ - 52.4 (*c* 0.1, CH_2Cl_2), [lit.[1] for *(R)* enantiomer $[\alpha]_D^{22}$ + 56.5° (*c* 1.0, benzene, 95% ee)]; IR (neat) 3356, 3069, 3027, 2922, 2848, 1637, 1603, 1459, 1377, 1357, 1280, 1112, 1046, 910, 758, 700 cm^{-1}; ^1H NMR (700 MHz,

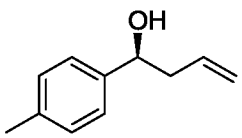
$CDCl_3$) δ 2.07 (d, *J* = 2.8 Hz, 1H), 2.50 - 2.59 (m, 2H), 4.77 (dt, *J* = 6.4, 2.4 Hz, 1H), 5.16 - 5.72 (m, 2H), 5.84 (ddt, *J* = 17.2, 10.0, 7.2 Hz, 1H), 7.31 (m, 1H), 7.37 - 7.40 (m, 4H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 43.9, 73.3, 118.5, 125.8, 127.6, 128.4, 134.5, 143.9.

(*S*)-1-*o*-Tolylbut-3-en-1-ol (130b)



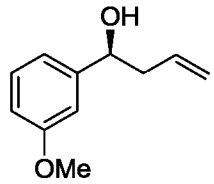
Colorless oil: 92% ee [Chiralcel OD, hexane:*i*-propanol 99:1, 1.0 mL/min, t_R (minor) 20.6 min, t_R (major) 22.4 min]; $[\alpha]_D^{20}$ - 70.0 (*c* 0.1, CH_2Cl_2), [lit.[1] for *(R)* enantiomer $[\alpha]_D^{24}$ + 75.5 (*c* 1.0, benzene, 97% ee)]; IR (neat) 3363, 3120, 3074, 2926, 2848, 1638, 1482, 1427, 1354, 1280, 1182, 1139, 1042, 995, 914, 758 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.48 (s, 3H), 2.49 - 2.51 (m, 2H), 4.96 - 5.05 (m, 1H), 5.17 - 5.24 (m, 1H), 5.87 - 5.91 (m, 1H), 7.18 -7.21 (m, 1H), 7.24 - 7.26 (m, 2H), 7.26 - 7.28 (m, 1H), 7.52 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 19.1, 42.7, 69.7, 118.2, 125.2, 126.3, 127.3, 130.4, 134.4, 134.8, 142.0.

(*S*)-1-*p*-Tolylbut-3-en-1-ol (130c)



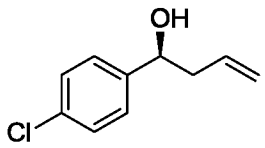
Pale yellow oil: 95% ee [Chiralcel OD, hexane:*i*-propanol 98.5:1.5, 0.5 mL/min, t_R (minor) 21.7 min, t_R (major) 28.6 min]; $[\alpha]_D^{20}$ - 66.5 (*c* 0.1, CH_2Cl_2), [lit.[2] for (*R*) enantiomer $[\alpha]_D^{25}$ + 53.0 (*c* 1.0, $CHCl_3$, 78% ee)]; IR (neat) 3332, 3074, 2922, 2860, 1638, 1606, 1513, 1435, 1295, 1260, 1245, 1182, 1112, 1046, 999, 914, 871, 813, 754, 711 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.38 (s, 3H), 2.52 (m, 2H), 4.71 (m, 1H), 5.18 (m, 2H), 6.82 (m, 1H), 7.17 (d, *J* = 7.4 Hz, 1H), 7.28 (d, *J* = 7.4 Hz, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 21.3, 43.8, 73.2, 118.6, 125.8, 129.1, 134.3, 137.3, 140.8.

(*S*)-1-(3-Methoxyphenyl)but-3-en-1-ol (130d)



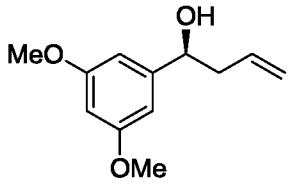
Pale yellow oil: 89% ee [Chiralcel OD, hexane:*i*-propanol 97:3, 0.5 mL/min, t_R (major) 25.2 min, t_R (minor) 29.2 min]; $[\alpha]_D^{20}$ - 51.2 (*c* 0.1, CH_2Cl_2), [lit.[3] for *(R)* enantiomer $[\alpha]_D^{25}$ + 41.0 (*c* 2.2, benzene, 73% ee)]; IR (neat) 3370, 3078, 2926, 2844, 1638, 1599, 1579, 1490, 1462, 1427, 1318, 1260, 1151, 1042, 995, 918, 871, 789, 750, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.49 - 2.57 (m, 2H), 3.85 (s, 3H), 4.75 (t, *J* = 6.0 Hz, 1H), 5.16 - 5.22 (m, 2H), 5.81 - 5.88 (m, 1H), 6.83 - 6.85 (m, 1H), 6.97 (d, *J* = 5.5 Hz, 2H), 7.28 - 7.30 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 43.8, 55.2, 73.2, 111.3, 113.0, 118.1, 118.5, 129.5, 134.4, 145.6, 159.8.

(*S*)-1-(4-Chlorophenyl)but-3-en-1-ol (130e)



Pale yellow oil: 96% ee [Chiralcel OD, hexane:*i*-propanol 99:1, 0.5 mL/min, t_R (minor) 33.6 min, t_R (major) 35.6 min]; $[\alpha]_D^{20}$ - 62.6 (*c* 0.1, CH_2Cl_2), [lit.[4] for *(R)* enantiomer $[\alpha]_D^{20}$ + 61.4 (*c* 1.2, $CHCl_3$, 94% ee)]; IR (neat) 3306, 3074, 2918, 2844, 1642, 1591, 1498, 1459, 1431, 1136, 1093, 995, 914, 832, 762 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.03 (d, *J* = 2.8 Hz, 1H), 2.41 - 2.55 (m, 2H), 4.73 (ddd, *J* = 8.0, 4.8, 3.2 Hz, 1H), 5.16 - 5.17 (m, 2H), 5.79 (dddd, *J* = 17.6, 9.6, 8.0, 6.4 Hz, 1H), 7.28 - 7.34 (m, 4H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 47.8, 72.5, 118.6, 127.2, 128.5, 129.5, 134.2, 143.6.

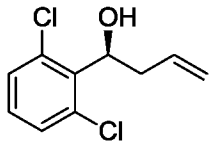
(*S*)-1-(3,5-Dimethoxyphenyl)but-3-en-1-ol (130f)



Pale yellow oil: 93% ee [Chiralcel OD, hexane:*i*-propanol 99.8:0.2, 0.5 mL/min, t_R (minor) 65.3 min, t_R (minor) 85.6 min]; $[\alpha]_D^{20}$ - 42.0 (*c* 0.1, CH_2Cl_2), [lit.[5] for *(R)* enantiomer $[\alpha]_D^{20}$ - 42.3 (*c* 1.0, $CHCl_3$, 94% ee)]; IR (neat) 3310, 3074, 3000, 2934, 2832, 1638, 1603, 1459, 1427, 1350, 1311, 1198, 1155, 1054, 995, 836, 754, 696 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 2.47 - 2.56 (m, 2H), 3.82 (s, 6H), 4.68 - 4.71 (m, 1H), 5.16

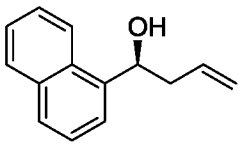
- 5.22 (m, 2H), 5.81 - 5.87 (m, 1H), 6.40 (d, J = 2.3 Hz, 1H), 6.56 (d, J = 2.3 Hz, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 43.7, 55.4, 73.3, 99.4, 103.7, 118.4, 134.4, 146.5, 160.9.

(*S*)-1-(2,6-Dichlorophenyl)but-3-en-1-ol (130g)



Colorless oil: 84% ee [Chiralcel OD, hexane:*i*-propanol 90:10, 1.0 mL/min, t_R (minor) 10.1 min, t_R (major) 12.8 min]; $[\alpha]_D^{20}$ - 59.4 (*c* 0.5, CH_2Cl_2); IR (neat) 3332, 3074, 2922, 2848, 1642, 1560, 1435, 1315, 1256, 1182, 1081, 1046, 914, 824, 778, 723 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$)[6] δ 2.69 - 2.73 (m, 1H), 2.86 - 2.92 (m, 2H), 5.11 - 5.16 (m, 2H), 5.50 - 5.55 (m, 1H), 5.83 - 5.90 (m, 1H), 7.16 (t, J = 7.7 Hz, 1H), 7.32 (d, J = 7.9 Hz, 2H); ^{13}C NMR (175 MHz, $CDCl_3$)[17] δ 40.0, 71.5, 118.1, 128.9, 129.4, 133.8, 134.3, 137.2.

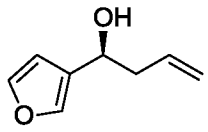
(*S*)-1-Naphthalen-1-ylbut-3-en-1-ol (130h)



Pale yellow oil: 97% ee [Chiralcel OD, hexane:*i*-propanol 99.8:0.2, 1.0 mL/min, t_R (major) 65.9 min, t_R (minor) 76.8 min]; $[\alpha]_D^{20}$ - 93.4 (*c* 0.1, CH_2Cl_2), [lit.[1] for *(R)* enantiomer $[\alpha]_D^{23}$ + 97.3 (*c* 1.0, benzene, 97% ee)]; IR (neat) 3313, 3066, 2922, 2852, 1638, 1603, 1513, 1435, 1392, 1357, 1260, 1167, 1120, 1054, 1015, 914, 879, 801, 778,

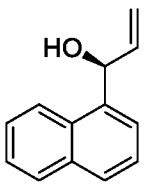
731, 696 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 2.62 - 2.67 (m, 1H), 2.78 - 2.82 (m, 1H), 5.21 - 5.28 (m, 2H), 5.57 (dd, *J* = 8.0, 4.0 Hz, 1H), 5.94 - 6.00 (m, 1H), 7.50 - 7.57 (m, 3H), 7.71 (d, *J* = 7.1 Hz, 1H), 7.82 (d, *J* = 8.4 Hz, 1H), 7.91 (d, *J* = 7.8 Hz, 1H), 8.11 (d, *J* = 8.7 Hz, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 42.9, 70.0, 118.4, 122.9, 123.0, 125.5, 125.6, 126.1, 128.0, 130.0, 130.3, 133.8, 134.8, 139.4.

(*S*)-1-(3-Furyl)but-3-en-1-ol (130i)



Pale yellow oil: 85% ee [Chiralcel OD, hexane:*i*-propanol 97:3, 0.5 mL/min, t_R (major) 18.5 min, t_R (minor) 21.4 min]; $[\alpha]_D^{20}$ - 25.4 (*c* 0.1, CH_2Cl_2), [lit.[7] $[\alpha]_D^{25}$ - 30.7 (*c* 1.72, CH_2Cl_2, 95% ee)]; IR (neat) 3365, 3074, 2922, 2848, 1638, 1486, 1435, 1295, 1252, 1217, 1178, 1046, 999, 918, 762, 711, 692 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 2.18 (s, 1H), 2.68 - 2.72 (m, 1H), 2.85 -2.89 (m, 1H), 5.06 - 5.11 (m, 2H), 5.27 (s, 1H), 5.72 (ddt, *J* = 16.8, 10.4, 6.8 Hz, 1H), 7.18 - 7.21 (m, 1H), 7.26 - 7.28 (m, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 47.9, 78.1, 108.9, 118.7, 126.1, 129.5, 134.3, 143.6.

(*S*)-1-(Naphthalen-1-yl)propan-2-en-1-ol (143)



Pale yellow oil: 79% ee [Chiralcel OD-H, hexane:*i*-propanol 95:5, 1.0 mL/min, t_R (major) 27.3 min, t_R (minor) 37.5 min]; $[\alpha]_D^{25}$ - 10.2 (*c* 0.05, $CHCl_3$), [lit.[8] for *(S)* enantiomer $[\alpha]_D^{23}$ - 11.0 (*c* 1.0, $CHCl_3$)]; IR (neat) 3381, 3425, 2924, 1641, 1581, 1562, 1437, 1182, 1085, 1046, 993, 918, 778, 769, 731, 624 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 5.31 (dt, *J* = 10.4, 1.4 Hz, 1H), 5.49 (dt, *J* = 17.2, 1.5 Hz, 1H), 5.96 (d, *J* = 5.3 Hz, 1H), 6.28 (ddd, *J* = 17.2, 10.4, 5.4 Hz, 1H), 7.50 - 7.59 (m, 3H), 7.68 (d, *J* = 6.5 Hz, 1H), 7.86 (d, *J* = 7.1 Hz, 1H), 7.92 (d, *J* = 7.1 Hz, 1H), 8.22 (d, *J* = 6.5 Hz, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 72.3, 115.7, 123.8, 124.0, 125.5, 125.7, 126.2, 128.9, 130.8, 134.0, 138.1, 139.7.

References:

1. Wadamoto, M.; Ozasa, N.; Yanagisawa, A; Yamamoto, H. *J. Org. Chem.* **2003**, *68*, 5593.

2. Bandini, M.; Giorgio, P.; Umani-Ronchi, A. *Tetrahedron* **2001**, *57*, 835.

3. Zheng, Y.; Zhou, J.; Loh. T. *Org. Lett.* **1999**, *11*, 1855.

4. Wu. T. R.; Shen, L.; Chong, M. *Org. Lett.* **2004**, *6*, 2701.

5. Brimble, M. A.; Bryant, C. *Org. Biomol. Chem.* **2007**, *5*, 2858.

6. Chretien, J. M.; Zammattio, F.; Gauthier, D.; Grongnce, E. L.; Paris, M.; Quintard, J. P. *Chem. Eur. J.* **2006**, *12*, 6816.

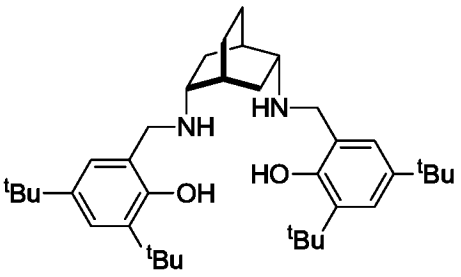
7. Bierstedt, A.; Stoltting, J.; Metz, P. *Tetrahedron: Asymmetry* **2001**, *12*, 3399.

8. Da, C. S.; Wang, J. R.; Yin, X. G.; Fan, X. Y.; Liu, Y.; Yu, S. L. *Org*. *Lett*. 2**009**, *11*, 5578.

CHAPTER 5

The Asymmetric Henry Reaction

(+)-6,6'-(((1*R*,2*R*,4*R*,5*R*)-bicyclo[2.2.2]octane-2,5-diylbis(azanediyl))bis(methylene))bis(2,4-di-tert-butylphenol) [(+)-173]

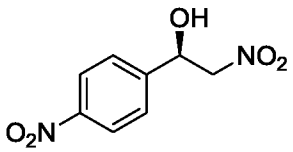


To a solution of (+)-**35** (2.0 g, 3.49 mmol) in EtOH (50 mL) at 0 °C was added $NaBH_4$ (117 mg, 3.49 mmol). After addition was complete, the cooling bath was removed and the mixture was stirred at room temperature for 24 h. Solvent was evaporated and the resulting sticky solid was taken up into H_2O (50 mL) which was extracted with CH_2Cl_2 (2x100 mL). The organic extract was dried over anhyd. Na_2SO_4 and was evaporated to obtain (+)-**173** (1.99 g , 99%) as an amorphous white solid: mp 161 - 162 °C; $[\alpha]^{18}_D$ + 22.3 (*c* 1.0 , CH_2Cl_2); IR (neat) 3483, 3292, 2953, 2905, 2866, 1480, 1455, 1435, 1361, 1234, 990, 875, 760, 700 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 1.23 - 1.25 (m, 2H), 1.27 (s, 18H), 1.29 - 1.33 (m, 2H), 1.36 - 1.44 (m, 2H), 1.47 (s, 18H), 1.50 - 1.54 (m, 2H), 2.16 (bs, 2H), 2.41 (s, 2H), 3.65 - 3.68 (m, 2H), 3.80 - 3.85 (m, 2H), 4.10 (s, 2H), 7.26 (d, *J* = 2.2 Hz, 2H), 7.29 (d, *J* = 2.2 Hz, 2H), 10.41 (bs, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 29.4, 29.7, 31.4, 31.6, 34.1, 35.0, 35.8, 51.2, 66.6, 121.7, 123.1, 123.5, 136.1, 140.6, 154.3; HRMS (ESI) calcd for $C_{38}H_{61}N_2O_2$ (M+H) *m/z* 577.4733, found 577.4716.

Representative Procedure for the Asymmetric Henry Reaction of Aldehydes with Nitroalkanes Catalyzed by Tetrahydrosalen (+)-173 and $(CuOTf)_2.C_6H_5CH_3$:

To an oven-dried vial were added molecular sieves (3 Å), tetrahydrosalen ligand (+)-**173** (12 mg, 0.02 mmol, 10 mol%) and $(CuOTf)_2.C_6H_5CH_3$ (1 mg, 0.002 mmol, 1 mol%). To this mixture was added anhydrous MeOH (0.8 mL) followed by the nitroalkane (0.6 mL) and the resulting green suspension was stirred at room temperature for 10 min. To the suspension at 40 °C was added the aldehyde (0.2 mmol) and the mixture was stirred at that temperature for the length of time specified in Tables 5.3 - 5.5. The reaction mixture was concentrated under reduced pressure and the resulting crude residue was treated with aqueous HCl (1M, 2 mL, 2 mmol) in CH_2Cl_2 (1 mL) and was stirred at room temperature until the green color had disappeared. The mixture was extracted with CH_2Cl_2 (3 x 20 mL) and the organic extracts were combined, washed with brine (20 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (15% hexane/ether) to give the product. The enantiomeric excess of the pure product was determined by HPLC on a Daicel Chiralcel OD, AD, OJ, OD-H or AS-H column.

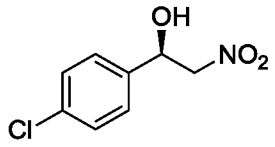
(*R*)-1-(4-Nitrophenyl)-2-nitroethanol (172)



Off-white solid: mp 83 - 84 °C, [lit[1] for (*R*) enantiomer 83 - 85 °C]; 79% ee [Chiralcel OD, hexane:*i*-propanol 75:25, 0.8 mL/min, 215 nm, t_R (major) 9.3 min, t_R (minor) 10.9 min]; $[\alpha]_D^{15}$ - 30.4 (*c* 0.5, CH_2Cl_2), [lit.[1] for *(R)* enantiomer $[\alpha]_D^{21}$ - 31.6 (*c* 1.05, CH_2Cl_2,

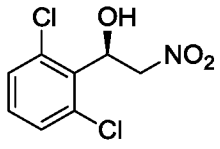
78% ee)]; IR (neat) 3533, 3077, 2929, 1607, 1555, 1519, 1381, 1350, 1194, 1084, 1014, 857, 756, 732, 697, 666 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.42 (bs, 1H), 4.61 - 4.72 (m, 2H), 5.70 - 5.75 (m, 1H), 7.71 (d, J = 7.4 Hz, 1H), 8.35 (d, J = 7.4 Hz, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 69.8, 80.6, 125.5, 127.4, 145.1, 148.0

(*R*)-1-(4-Chlorophenyl)-2-nitroethanol (175)



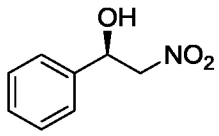
Colorless oil: 83% ee [Chiralcel OD, hexane:*i*-propanol 85:15, 0.8 mL/min, 215 nm, t_R (major) 13.0 min, t_R (minor) 15.1 min]; $[\alpha]_D^{17}$ - 34.5 (*c* 0.6, CH_2Cl_2), [lit.[1] for *(R)* enantiomer $[\alpha]_D^{23}$ - 37.6 (*c* 2.03, CH_2Cl_2, 90% ee)]; IR (neat) 3540, 2923, 2583, 1633, 1595, 1556, 1493, 1413, 1378, 1341, 1295, 1208, 1090, 1014, 970, 896, 827, 740 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.35 (bs, 1H), 4.35 - 4.53 (m, 1H), 4.54 - 4.64 (m, 1H), 5.32 - 5.51 (m, 1H), 7.31 - 7.47 (m, 4H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 70.3, 81.0, 127.4, 129.2, 134.8, 136.6.

(*R*)-1-(2,6-Dichlorophenyl)-2-nitroethanol (177)



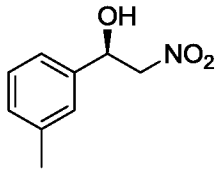
Colorless oil: 94% ee [Chiralcel AD, hexane:*i*-propanol 80:20, 1.0 mL/min, 215 nm, t_R (major) 8.6 min, t_R (minor) 9.9 min]; $[\alpha]_D^{21}$ - 26.4 (*c* 0.5, CH_2Cl_2); IR (neat) 3572, 3557, 3078, 2965, 2923, 1643, 1582, 1552, 1436, 1370, 1287, 1184, 1094, 1064, 1033, 920, 898, 853, 788, 739 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.34 (d, J = 4.1 Hz, 1H), 4.53 - 4.61 (m, 1H), 5.00 - 5.06 (m, 1H), 5.15 - 5.22 (m, 1H), 7.25 - 7.30 (m, 1H), 7.35 - 7.46 (m, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 68.6, 78.1, 130.0, 130.8, 132.8, 134.9; HRMS (EI) calcd for $C_8H_8O_3NCl_2$ *m/z* 235.9881, found 235.9879.

(*R*)-1-Phenyl-2-nitroethanol (155a)



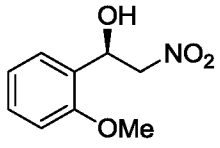
Colorless oil: 92% ee [Chiralcel OD, hexane:*i*-propanol 85:15, 0.8 mL/min, 215 nm, t_R (major) 13.1 min, t_R (minor) 16.2 min]; $[\alpha]_D^{25}$ - 39.5 (*c* 0.2, CH_2Cl_2), [lit.[1] for *(R)* enantiomer $[\alpha]_D^{23}$ - 41.6 (*c* 1.03, CH_2Cl_2, 94% ee)]; IR (neat) 3573, 3556, 3065, 3033, 2921, 1640, 1564, 1552, 1494, 153, 1379, 1193, 1092, 1067, 978, 918, 896, 847, 767, 699 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 2.91 (bs, 1H), 4.50 - 4.53 (m, 1H), 4.62 - 4.67 (m, 1H), 5.53 - 5.59 (m, 1H), 7.35 - 7.42 (m, 1H), 7.42 - 7.48 (m, 4H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 71.2, 81.1, 126.2, 128.1, 129.4, 138.3.

(*R*)-1-(3-Methylphenyl)-2-nitroethanol (155b)



Pale yellow oil: 96% ee [Chiralcel OD-H, hexane:*i*-propanol 85:15, 0.8 mL/min, 215 nm, t_R (major) 10.3 min, t_R (minor) 11.9 min]; $[\alpha]_D^{25}$ - 33.0 (*c* 0.3, CH_2Cl_2), [lit.[2] for *(R)* enantiomer $[\alpha]_D^{25}$ - 32.2 (*c* 0.27, CH_2Cl_2, 93% ee)]; IR (neat) 3540, 3027, 2921, 1608, 1552, 1419, 1377, 1287, 1158, 1073, 1036, 886, 791, 710 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 2.39 (s, 3H), 3.08 (bs, 1H), 4.55 (dd, *J* = 13.2, 3.0 Hz, 1H), 4.61 (dd, *J* = 13.2, 9.3 Hz, 1H), 5.45 (dd, J = 9.3, 3.0 Hz, 1H), 7.13 - 7.19 (m, 2H), 7.20 - 7.25 (m, 1H), 7.30 - 7.38 (m, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 21.2, 71.0, 81.5, 122.9, 126.5, 128.9, 129.8, 138.0, 138.9.

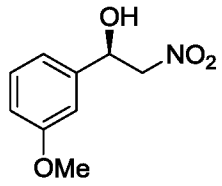
(*R*)-1-(2-Methoxyphenyl)-2-nitroethanol (155c)



Yellow oil: 91% ee [Chiralcel OD-H, hexane:*i*-propanol 90:10, 0.8 mL/min, 215 nm, t_R (major) 13.3 min, t_R (minor) 15.0 min]; $[\alpha]_D^{25}$ - 41.7 (*c* 0.71, CH_2Cl_2), [lit.[1] for *(R)* enantiomer $[\alpha]_D^{21}$ - 44.5 (*c* 1.0, CH_2Cl_2, 93% ee)]; IR (neat) 3570, 3540, 3007, 2962, 2939, 1603, 1552, 1492, 1464, 1379, 1289, 1243, 1121, 1072, 1049, 1024, 891, 789, 757 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 3.33 (bs, 1H), 3.91 (s, 3H), 4.53 - 4.52 (m, 1H), 4.62 - 4.70 (m, 1H), 5.65 (s, 1H), 6.92 (d, *J* = 8.0 Hz, 1H), 7.00 - 7.08 (m, 1H), 7.33 - 7.39 (m,

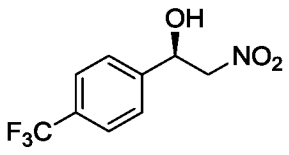
1H), 7.45 - 7.50 (m, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 55.8, 68.1, 80.1, 110.5, 120.8, 125.9, 127.3, 129.9, 156.3.

(*R*)-1-(3-Methoxyphenyl)-2-nitroethanol (155d)



Colorless oil: 96% ee [Chiralcel OD, hexane:*i*-propanol 90:10, 1 mL/min, 215 nm, t_R (major) 25.2 min, t_R (minor) 31.3 min]; $[\alpha]_D^{25}$ - 33.5 (*c* 0.2, CH_2Cl_2), [lit.[2] for *(S)* enantiomer $[\alpha]_D^{25}$ - 26.6 (*c* 0.97, CH_2Cl_2, 76% ee)]; IR (neat) 3553, 3013, 2920, 1620, 1549, 1537, 1492, 1462, 1377, 1264, 1154, 1035, 883, 786, 708, 694 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 3.08 (bs, 1H), 3.84 (s, 3H), 4.48 - 4.52 (m, 1H), 4.55 - 4.64 (m, 1H), 5.45 (s, 1H), 6.89 (dd, *J* = 8.0, 2.2 Hz, 1H), 6.96 (s, 2H), 7.32 (t, *J* = 8.0 Hz, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 55.3, 70.7, 81.1, 111.4, 114.3, 118.2, 130.1, 139.7, 160.2.

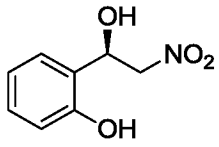
(*R*)-1-(4-Trifluoromethylphenyl)-2-nitroethanol (155e)



Yellow oil: 96% ee [Chiralcel OD-H, hexane:*i*-propanol 80:20, 1 mL/min, 215 nm, t_R (major) 9.6 min, t_R (minor) 10.4 min]; $[\alpha]_D^{25}$ - 35.6 (*c* 0.5, CH_2Cl_2), [lit.[4] for *(R)*

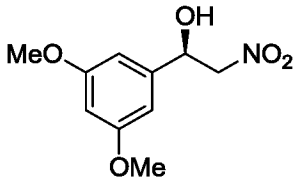
enantiomer $[\alpha]_D^{25}$ - 33.9 (*c* 1.0, $CHCl_3$, 82% ee)]; IR (neat) 3533, 3032, 2925, 1622, 1552, 1424, 1324, 1067, 1017, 894, 841, 747, 714, 644 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 3.30 (bs, 1H), 4.51 - 4.58 (m, 1H), 4.60 - 4.65 (m, 1H), 5.51 - 5.59 (m, 1H), 7.55 (d, *J* = 8.2 Hz, 2H), 7.72 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 70.4, 80.8, 121.4, 126.0, 126.4, 131.3 (q, *J* = 34.2 Hz), 142.0.

(*R*)-1-(2-Hydroxyphenyl)-2-nitroethanol (155f)



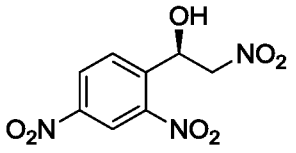
Pale yellow oil: 92% ee [Chiralcel OJ, hexane:*i*-propanol 92:8, 0.5 mL/min, 215 nm, t_R (major) 23.8 min, t_R (minor) 30.2 min]; $[\alpha]_D^{25}$ - 5.0 (*c* 0.36, CH_2Cl_2), [lit.[3] for *(S)* enantiomer $[\alpha]_D^{25}$ + 4.8 (*c* 0.21, CH_2Cl_2, 84% ee)]; IR (neat) 3500, 3014, 2960, 2918, 1605, 1552, 1503, 1459, 1380, 1336, 1250, 1192, 1107, 1066, 1029, 971, 896, 867, 758 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 3.66 (bs, 1H), 4.58 - 4.65 (m, 1H), 4.79 - 4.86 (m, 1H), 5.61 - 5.68 (m, 1H), 6.85 - 6.91 (m, 1H), 6.93 - 7.01(m, 2H), 7.18 - 7.22 (m, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 70.8, 79.5, 117.1, 121.2, 122.6, 127.5, 130.3, 154.5.

(*R*)-1-(3,5-Dimethoxyphenyl)-2-nitroethanol (155g)



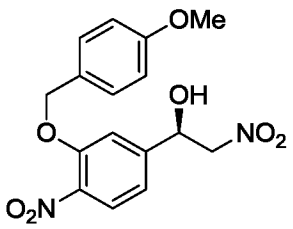
Colorless oil: 96% ee [Chiralcel AD, hexane:*i*-propanol 90:10, 0.8 mL/min, 215 nm, t_R (major) 14.6 min, t_R (minor) 17.2 min]; $[\alpha]_D^{21}$ - 22.0 (*c* 0.5, CH_2Cl_2), [lit.[6] for *(S)* enantiomer $[\alpha]_D^{25}$ + 21.8 (*c* 1.0, $CHCl_3$, 87% ee)]; IR (neat) 3515, 2940, 2842, 1599, 1552, 1468, 1432, 1381, 1351, 1296, 1205, 1157, 1063, 923, 890, 841, 698, 660 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 3.82 (s, 6H), 4.50 - 4.55 (m, 1H), 4.59 - 4.67 (m, 1H), 5.38 - 5.43 (m, 1H), 6.46 (s, 1H), 6.58 (s, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 55.7, 71.2, 81.6, 100.9, 103.9, 140.9, 161.6.

(*R*)-1-(2,4-Dinitrophenyl)-2-nitroethanol (155h)



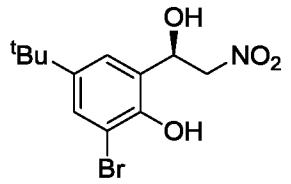
Pale yellow solid: mp 124 - 125 °C, [lit[7] for racemic 123 - 124 °C]; 95% ee [Chiralcel OD-H, hexane:*i*-propanol 85:15, 0.5 mL/min, 215 nm, t_R (major) 20.7 min, t_R (minor) 27.3 min]; $[\alpha]_D^{25}$ - 30.4 (*c* 0.5, CH_2Cl_2); IR (neat) 3415, 2924, 1582, 1564, 1537, 1521, 1498, 1474, 1347, 868, 837, 817, 792, 777, 762 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 3.51 (s, 1H), 4.54 - 4.61 (m, 1H), 4.88 - 4.94 (m, 1H), 6.19 - 6.24 (m, 1H), 8.31 (d, J = 8.2 Hz, 1H), 8.62 (d, J = 8.2 Hz, 1H), 8.97 (s, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 66.2, 79.2, 120.3, 128.1, 128.3, 129.5, 131.2, 140.5.

(*R*)-1-(3-((4-Methoxybenzyl)oxy)-4-nitrophenyl)-2-nitroethanol (155i)



Pale yellow solid: mp 112 - 113 °C; 95% ee [Chiralcel OD-H, hexane:*i*-propanol 92:8, 0.8 mL/min, 215 nm, t_R (major) 21.8 min, t_R (minor) 28.4 min]; $[\alpha]_D^{25}$ - 36.0 (*c* 0.2, CH_2Cl_2); IR (neat) 3479, 3079, 2947, 1611, 1562, 1554, 1514, 1422, 1380, 1352, 1249, 1176, 1086, 1029, 826, 758, 711 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 3.15 (s, 1H), 3.81 (s, 3H), 4.51 - 4.60 (m, 2H), 5.21 (s, 2H), 5.52 - 5.58 (m, 2H), 6.95 (d, *J* = 8.7 Hz, 1H), 7.05 (dd, *J* = 8.3 & 1.4 Hz, 1H), 7.45 (d, *J* = 8.7 Hz, 1H), 7.85 (d, *J* = 8.3 Hz, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 54.2, 69.1, 70.5, 80.8, 112.9, 113.2, 118.0, 125.1, 128.1, 129.4, 140.0, 147.1, 151.8, 159.9. HRMS (EI) calcd for $C_{16}H_{16}O_7N_2$ *m/z* 348.0958, found 348.0970.

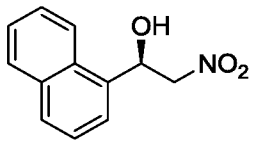
(*R*)-2-Bromo-(4-tert-butyl)-6-(1-hydroxy-2-nitroethyl)phenol (155j)



Pale yellow solid: mp 62 - 63 °C; 98% ee [Chiralcel OD-H, hexane:*i*-propanol 80:20, 1.0 mL/min, 215 nm, t_R (major) 6.1 min, t_R (minor) 9.1 min]; $[\alpha]_D^{25}$ - 9.5 (*c* 0.41, CH_2Cl_2); IR (neat) 3499, 2963, 1555, 1482, 1371, 1274, 1208, 1152, 1110, 1073, 877, 822, 750,

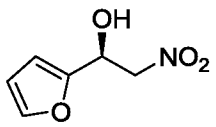
717 cm^{-1}; ^1H NMR (700 MHz, CDCl3) δ 1.32 (s, 9H), 3.49 (s, 1H), 4.60 - 4.72 (m, 2H), 5.64 - 5.70 (m, 1H), 6.22 (s, 1H), 7.37 (s, 1H), 7.48 (s, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 30.1, 34.8, 68.2, 79.1, 111.3, 124.2, 124.7, 129.2, 145.6, 147.1. HRMS (EI) calcd for $C_{12}H_{16}O_4BrN$ *m/z* 317.0262, found 317.0251.

(*R*)-1-(1-Naphthyl)-2-nitroethanol (155k)



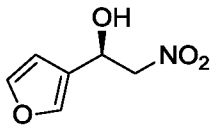
Pale yellow solid: mp 61 - 62 °C, [lit[1] for (*R*) enantiomer 59 - 61 °C]; 93% ee [Chiralcel OD-H, hexane:*i*-propanol 85:15, 0.8 mL/min, 215 nm, t_R (major) 14.4 min, t_R (minor) 17.0 min]; $[\alpha]_D^{21}$ - 25.0 (*c* 0.5, CH_2Cl_2), [lit.[1] for *(R)* enantiomer $[\alpha]_D^{23}$ - 24.9 (*c* 1.08, CH_2Cl_2, 87% ee)]; IR (neat) 3582, 3058, 2961, 2917, 1954, 1597, 1546, 1506, 1166, 1105, 1004, 970, 906, 866, 809 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 3.33 (bs, 1H), 4.62 - 4.71 (m, 2H), 6.19 - 6.30 (m, 1H), 7.48 - 7.62 (m, 3H), 7.72 - 7.75 (m, 1H), 7.82 - 7.96 (m, 2H), 8.01 - 8.07 (m, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 68.3, 80.9, 121.9, 123.9, 125.5, 126.1, 127.1, 129.3, 129.4, 129.6, 133.7, 133.7 (x2).

(*R*)-1-(2-Furyl)-2-nitroethanol (155l)



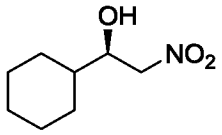
Pale yellow oil: 94% ee [Chiralcel OD, hexane:*i*-propanol 90:10, 1 mL/min, 215 nm, t_R (major) 40.7 min, t_R (minor) 45.9 min]; $[\alpha]_D^{25}$ - 40.9 (*c* 0.22, CH_2Cl_2), [lit.[8] for *(R)* enantiomer $[\alpha]_D^{16}$ - 33.2 (*c* 1.0, CH_2Cl_2, 95% ee)]; IR (neat) 3528, 3154, 2954, 2924, 1642, 1554, 1502, 1380, 1351, 1159, 1090, 1020, 966, 875, 805, 739, 691 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 2.84 (s, 1H), 4.68 - 4.73 (m, 1H), 4.82 - 4.89 (m, 1H), 5.48 - 5.56 (m, 1H), 6.41 - 6.47 (m, 2H), 7.45 (s, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 64.7, 79.2, 109.1, 110.2, 142.8, 151.1.

(*R*)-1-(3-Furyl)-2-nitroethanol (155m)



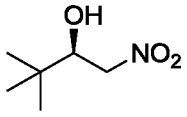
Pale yellow oil: 95% ee [Chiralcel OD-H, hexane:*i*-propanol 90:10, 1 mL/min, 215 nm, t_R (major) 15.0 min, t_R (minor) 18.9 min]; $[\alpha]_D^{25}$ - 18.2 (*c* 0.56, CH_2Cl_2), [lit.[9] for *(S)* enantiomer $[\alpha]_D^{20}$ + 17.5 (*c* 1.3, CH_2Cl_2, 89% ee)]; IR (neat) 3540, 3144, 2924, 1564, 1552, 1503, 1423, 1375, 1205, 1161, 1021, 875, 796, 738, 691, 598 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 2.76 (s, 1H), 4.53 - 4.59 (m, 1H), 4.63 - 4.69 (m, 1H), 5.48 (d, J = 8.4 Hz, 1H), 6.43 (s, 1H), 7.48 (s, 1H), 7.53 (s, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 64.2, 80.6, 108.1, 123.9, 140.5, 144.1.

(*R*)-1-Cyclohexyl-2-nitroethanol (155n)



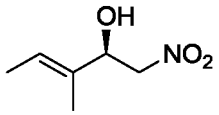
Colorless oil: 94% ee [Chiralcel AD, hexane:*i*-propanol 97:3, 0.8 mL/min, 215 nm, t_R (major) 18.9 min, t_R (minor) 23.7 min]; $[\alpha]_D^{22}$ - 22.0 (*c* 0.5, CH_2Cl_2), [lit.[1] for *(R)* enantiomer $[\alpha]_D^{21}$ -21.6 (*c* 1.3, $CHCl_3$, 93% ee)]; IR (neat) 3477, 2926, 2855, 1708, 1553, 1452, 1377, 1198, 1099, 1040, 964, 894, 652 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 1.07 - 1.23 (m, 3H), 1.23 - 1.39 (m, 2H), 1.48 - 1.52 (m, 1H), 1.68 - 1.76 (m, 2H), 1.79 - 1.91 (m, 3H), 2.46 (s, 1H), 4.13 (s, 1H), 4.42 - 4.50 (m, 1H), 4.51 - 4.59 (m, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 25.2, 25.6, 26.0, 27.9, 28.9, 41.6, 72.8, 79.5.

(*R*)-3,3-Dimethyl-1-nitrobutan-2-ol (155o)



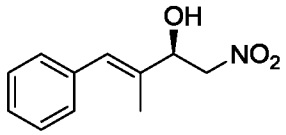
Colorless oil: 95% ee [Chiralcel OD-H, hexane:*i*-propanol 97:3, 0.8 mL/min, 215 nm, t_R (major) 19.5 min, t_R (minor) 24.0 min]; $[\alpha]_D^{25}$ - 26.9 (*c* 0.1, $CHCl_3$), [lit.[10] for *(S)* enantiomer $[\alpha]_D^{25}$ + 29.4 (*c* 3.4, CH_2Cl_2, 93% ee)]; IR (neat) 3564, 2966, 2908, 2718, 1569, 1481, 1423, 1382, 1289, 1190, 1089, 1024, 1007, 941, 924, 908, 881, 791, 700 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 0.99 (s, 9H), 2.64 (bs, 1H), 4.00 - 4.04 (m, 1H), 4.33 - 4.37 (m, 1H), 4.48 - 4.53 (m, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 25.5, 34.9, 76.2, 78.6.

(*R*,*E*)-3-Methyl-1-nitropent-3-en-2-ol (155p)



Colorless oil: 93% ee [Chiralcel OD, hexane:*i*-propanol 90:10, 0.8 mL/min, 215 nm, t_R (major) 14.4 min, t_R (minor) 17.1 min]; $[\alpha]_D^{21}$ - 15.3 (*c* 0.3, $CHCl_3$); IR (neat) 3534, 2977, 2922, 1722, 1633, 1564, 1549, 1448, 1376, 1060, 1021, 890, 838, 713 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 1.62 (s, 3H), 1.64 (s, 3H), 2.5 (bs, 1H), 4.42 - 4.47 (m, 1H), 4.49 - 4.52 (m, 1H), 4.77 - 4.80 (m, 1H), 5.72 - 5.76 (m, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 12.1, 13.5, 74.3, 79.7, 124.4, 132.6. HRMS (EI) calcd for $C_6H_{10}O_3N$ *m/z* 144.0661, found 144.0665.

(*R*, *E*)-3-Methyl-1-nitro-4-phenylbut-3-en-2-ol (155q)

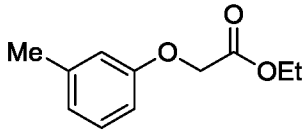


Pale yellow oil: 97% ee [Chiralcel OD, hexane:*i*-propanol 90:10, 0.5 mL/min, 215 nm, t_R (minor) 19.3 min, t_R (major) 22.5 min]; $[\alpha]_D^{25}$ - 9.6 (*c* 0.25, CH_2Cl_2), [lit.[11] for *(R)* enantiomer $[\alpha]_D^{27}$ - 9.9 (*c* 0.7, CH_2Cl_2, 98% ee)]; IR (neat) 3374, 3201, 1714, 1692, 1665, 1639, 1562, 1552, 1378, 1334, 1075 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 1.95 (s, 3H), 2.73 (s, 1H), 4.54 - 4.61 (m, 2H), 4.91 (m, 1H), 6.72 (s, 1H), 7.28 - 7.36 (m, 3H), 7.38 - 7.44 (m, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 13.9, 74.6, 79.8, 127.2, 128.1, 128.4, 129.3, 134.0, 136.8.

Representative Procedure for Synthesizing α-Aryloxy Esters 186 and 187 Starting from Phenols 184 and 185:[12]

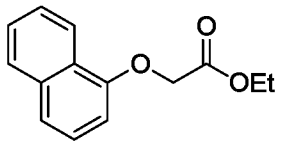
To 15 mmol of the phenol (**184** and **185**) in 40 mL of acetone at room temperature was added potassium carboate (5.92 g, 45 mmol). After stirring the mixture for 30 minutes, 17.25 mmol of ethyl bromoacetate was added and the mixture was stirred at room temperature for 3 h. The reaction mixture was filtered and the filtrate was diluted with ether (80 mL), washed with 10% aqueous NaOH solution (3 x 10 mL), dried (Na_2SO_4) and evaporated to give the product **186** and **187**.

Ethyl 2-(*m*-tolyloxy)acetate (186)



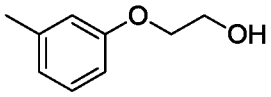
Colorless oil: IR (neat) 3042, 2985, 2918, 2864, 1761, 1737, 1605, 1582, 1491, 1440, 1383, 1299, 1208, 1150, 1096, 1032, 911, 860, 776, 725, 695 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 1.32 (t, J = 6.4 Hz, 3H), 2.39 (s, 3H), 4.33 (q, J = 6.4 Hz, 2H), 4.67 (s, 2H), 6.69 - 6.72 (m, 1H), 6.79 (s, 1H), 6.83 - 6.89 (m, 1H), 7.18 - 7.25 (m, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 14.2, 21.0, 60.9, 65.3, 111.5, 117.0, 122.8, 129.1, 140.0, 159.8, 170.1.

Ethyl 2-(naphthalen-1-yloxy)acetate (187)



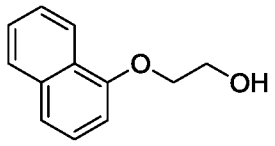
Colorless oil: IR (neat) 3281, 2924, 2853, 1698, 1683, 1603, 1583, 1509, 1465, 1396, 1261, 1220, 1152, 970, 909, 827, 800 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 1.33 (t, J = 6.8 Hz, 3H), 4.36 (q, J = 6.8 Hz, 2H), 4.89 (s, 2H), 6.74 - 6.82 (m, 1H), 7.32 - 7.39 (m, 1H), 7.51 - 7.64 (m, 3H), 7.88 - 7.93 (m, 1H), 8.46 - 8.51 (m, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 13.9, 62.3, 64.8, 106.7, 121.1, 122.5, 127.5, 128.6, 128.9, 135.2, 154.8, 169.4.

2-(*m*-Tolyloxy)ethanol (188)



Colorless oil: IR (neat) 3406 (b), 2923, 2870, 1603, 1585, 1491, 1455, 1291, 1264, 1173, 1159, 1081, 1053, 950, 900, 856, 775, 690 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 2.38 (s, 3H), 2.85 (bs, 1H), 3.94 - 4.01 (m, 2H), 4.10 - 4.15 (m, 2H), 6.77 - 6.84 (m, 2H), 6.88 - 6.91 (m, 1H), 7.21 - 7.26 (m, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 21.0, 60.8, 69.8, 110.4, 114.9, 123.2, 129.9, 140.1, 159.8.

2-(Naphthalen-1-yloxy)ethanol (189)

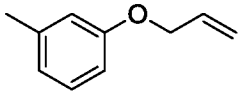


Colorless oil: IR (neat) 3424 (b), 2982, 1522, 1357, 1080, 980, 967, 847, 751, 698 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 2.19 (bs, 1H), 4.15 - 4.21 (m, 2H), 4.32 - 4.39 (m, 2H), 6.88 - 6.94 (m, 1H), 7.40 - 7.48 (m, 1H), 7.48 - 7.57 (m, 3H), 7.82 - 7.89 (m, 1H), 8.29 - 8.37 (m, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 61.7, 69.5, 105.8, 120.9, 121.3, 126.7, 126.8, 126.9, 127.5, 128.6, 136.5, 155.2.

Representative Procedure for Synthesizing Aryl Allyl Ethers 193-195 Starting from Phenols 184, 185 and 192:[12]

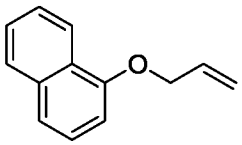
To 32.36 mmol of the phenol (**184**, **185** and **192**) in 50 mL of acetone at room temperature was added potassium carboate (6.71 g, 48.55 mmol). After stirring the mixture for 30 minutes, 35.60 mmol of ethyl bromoacetate (for **186** and **187**) or allyl bromide (for **193-195**) was added and the mixture was stirred at room temperature for 24 h. The reaction mixture was filtered and the filtrate was diluted with ether (150 mL), washed with 10% aqueous NaOH solution (3 x 10 mL), dried (Na_2SO_4) and evaporated to give the product **193 - 195**.

1-Allyloxy-3-methylbenzene (193)



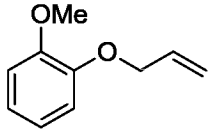
Colorless oil: IR (neat) 3078, 3019, 2979, 2919, 2857, 1602, 1585, 1489, 1454, 1423, 1290, 1259, 1159, 1033, 993, 925, 770, 690 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 2.39 (s, 3H), 4.53 - 4.60 (m, 2H), 5.30 - 5.38 (m, 1H), 5.43 - 5.51 (m, 1H), 6.08 - 6.17 (m, 1H), 6.73 - 6.81 (m, 3H), 7.19 -7.25 (m, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 21.5, 68.9, 112.0, 115.3, 117.3, 121.6, 129.4, 133.8, 139.2, 158.4.

1-Allyloxynaphthalene (194)



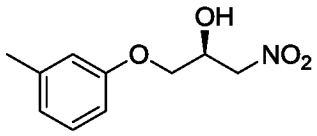
Colorless oil: IR (neat) 3054, 2923, 2858, 1726, 1648, 1628, 1595, 1580, 1509, 1463, 1423, 1401, 1358, 1347, 1271, 1231, 1178, 1157, 1097, 1068, 1019, 982, 922, 872, 791, 770, 742, 713 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 4.76 - 4.82 (m, 2H), 5.38 (d, J = 10.6 Hz, 1H), 5.60 (d, J = 17.3 Hz, 1H), 6.21 - 6.28 (m, 1H), 6.88 (d, J = 7.6 Hz, 1H), 7.39 - 7.61 (m, 4H), 7.82 - 7.90 (m, 1H), 8.38 - 8.41 (m, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 69.1, 114.5, 117.2, 118.1, 120.4, 122.0, 125.1, 125.9, 126.4, 127.5, 133.6, 134.1, 154.5.

1-Allyloxy-2-methoxybenzene (195)



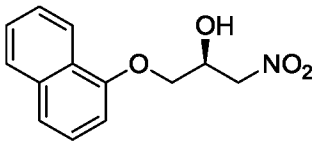
Colorless oil: IR (neat) 3065, 2959, 2925, 2854, 1729, 1647, 1593, 1505, 1455, 1439, 1424, 1254, 1226, 1124, 1027, 998, 922, 742 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 3.92 (s, 3H), 4.64 - 4.69 (m, 2H), 5.32 (dq, *J* = 10.5 & 1.4 Hz, 1H), 5.43 (dq, *J* = 17.2 & 1.4 Hz, 1H), 6.07 - 6.15 (m, 1H), 6.87 - 6.91 (m, 3H), 6.92 - 6.96 (m, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 56.0, 69.7, 111.9, 113.8, 118.1, 120.9, 121.4, 133.3, 148.2, 149.6.

(*S*)-1-Nitro-3-(*m*-tolyloxy)propan-2-ol (197)



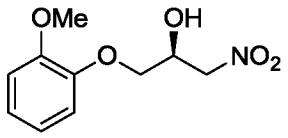
Colorless oil: 96% ee [Chiralcel OD, hexane:*i*-propanol 90:10, 0.8 mL/min, 215 nm, t_R (major) 21.6 min, t_R (minor) 25.5 min]; $[\alpha]_D^{23}$ + 21.3 (*c* 0.5, CH_2Cl_2); IR (neat) 3558, 3038, 2923, 2862, 2741, 1705, 1613, 1557, 1489, 1377, 1252, 1157, 1049, 940, 912, 877, 782, 733, 690, 635 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 2.38 (s, 3H), 3.30 (bs, 1H), 4.03 - 4.12 (m, 2H), 4.60 - 4.69 (m, 2H), 4.70 - 4.75 (m, 1H), 6.65 - 6.70 (m, 1H), 6.71 - 6.78 (m, 1H), 6.86 - 6.90 (m, 1H), 7.17 - 7.22 (m, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 20.3, 67.8, 68.2, 79.1, 111.2, 115.0, 121.9, 129.1, 139.9, 159.2. HRMS (EI) calcd for $C_{10}H_{13}O_4N$ *m/z* 211.0845, found 211.0845.

(*S*)-1-(Naphthalen-1-yloxy)-3-nitropropan-2-ol (198)



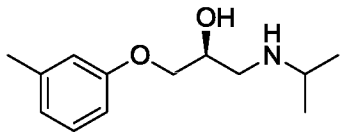
Colorless oil: 97% ee [Chiralcel OD, hexane:*i*-propanol 80:20, 1 mL/min, 215 nm, t_R (major) 7.9 min, t_R (minor) 9.2 min]; $[\alpha]_D^{28}$ + 12.2 (*c* 0.5, CH_2Cl_2); IR (neat) 3539, 3052, 2921, 1596, 1580, 1555, 1509, 1460, 1398, 1269, 1242, 1105, 1070, 1021, 962, 893, 794, 773, 727 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 4.18 - 4.22 (m, 1H), 4.24 - 4.32 (m, 1H), 4.69 - 4.82 (m, 2H), 4.86 - 4.94 (m, 1H), 6.96 - 7.04 (m, 1H), 7.36 - 7.43 (m, 1H), 7.48 - 7.59 (m, 3H), 7.79 - 7.87 (m, 1H), 8.18 - 8.22 (m, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 67.2, 68.9, 78.3, 120.9, 121.2, 125.0, 125.6, 126.4, 127.8, 134.4, 137.8, 153.9, 157.4. HRMS (EI) calcd for $C_{13}H_{13}O4N$ *m/z* 247.0845, found 247.0834.

(*S*)-1-(2-Methoxyphenoxy)-3-nitropropan-2-ol (199)



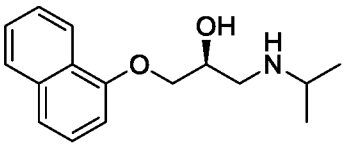
Colorless oil: 94% ee [Chiralcel OD, hexane:*i*-propanol 99:1, 0.8 mL/min, 215 nm, t_R (major) 34.3 min, t_R (minor) 41.5 min]; $[\alpha]_D^{28}$ + 12.2 (*c* 0.5, CH_2Cl_2); IR (neat) 3469, 3058, 2961, 2921, 2850, 1724, 1662, 1595, 1555, 1504, 1456, 1381, 1254, 1097, 1021, 883, 809, 743 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 3.88 (s, 3H), 4.10 - 4.21 (m, 2H), 4.67 - 4.74 (m, 3H), 6.91 - 7.01 (m, 3H), 7.03 - 7.08 (m, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 56.0, 67.5, 71.4, 77.9, 111.9, 116.5, 121.2, 123.6, 147.8, 149.9. HRMS (EI) calcd for $C_{10}H_{13}O_5N$ *m/z* 227.0794, found 227.0783.

(*S*)-Toliprolol (178)



White solid: mp 50 - 51 °C, [lit[13] for (*S*)-isomer 52 - 54 °C]; $[\alpha]_D^{26}$ - 7.6 (*c* 0.5, EtOH), [lit[14] for (*S*)-isomer $[\alpha]_D^{25}$ - 9.9 (*c* 0.83, EtOH)]; IR (neat) 3406, 3035, 2964, 2924, 2869, 1602, 1585, 1491, 1461, 1453, 1382, 1291, 1259, 1172, 1159, 1084, 1044, 935, 873, 776, 690 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 1.09 (d, *J* = 6.2 Hz, 6H), 2.35 (s, 3H), 2.67 - 2.93 (m, 4H), 3.85 - 4.12 (m, 3H), 6.67 - 6.84 (m, 3H), 7.14 - 7.22 (m, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 21.5, 22.8, 23.2, 49.1, 49.5, 68.1, 69.9, 111.2, 115.4, 121.9, 129.8, 139.4, 158.3.

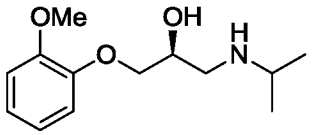
(*S*)-Propanolol (179)



Colorless solid: mp 74 - 75 °C, [lit[15] for (*S*)-isomer 73 - 74 °C]; $[\alpha]_D^{29}$ - 9.6 (*c* 0.5, $CHCl_3$), [lit[15] for (*S*)-isomer $[\alpha]_D^{25}$ - 9.0 (*c* 0.5, EtOH)]; IR (neat) 3359, 3046, 2964, 2928, 1595, 1580, 1509, 1461, 1401, 1270, 1241, 1178, 1157, 1103, 1068, 1020, 792, 771, 735, 673 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 1.21 (d, *J* = 6.0 Hz, 6H), 2.90 - 3.06 (m, 1H), 3.08 - 3.12 (m, 1H), 3.36 (bs, 3H), 4.08 - 4.29 (m, 2H), 4.32 (s, 1H), 6.78 - 6.87 (m, 1H), 7.36 - 7.43 (m, 1H), 7.45 - 7.55 (m, 3H), 7.88 - 7.89 (m, 1H), 8.22 - 8.35 (m,

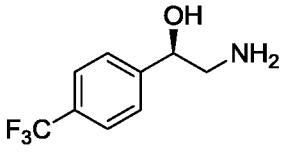
1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 22.7, 49.3, 50.1, 68.1, 70.8, 105.6, 120.7, 121.1, 125.0, 125.4, 126.3, 127.4, 128.2, 129.0, 155.1.

(*S*)-Moprolol (180)



White solid: mp 82 - 83 °C, [lit[15] for (*S*)-isomer 84 - 85 °C]; $[\alpha]_D^{27}$ - 5.6 (*c* 0.5, $CHCl_3$), [lit[15] for (*S*)-isomer $[\alpha]_D^{25}$ - 3.90 (*c* 4.50, EtOH)]; IR (neat) 3417, 3063, 2962, 2832, 1593, 1507, 1467, 1383, 1331, 1252, 1225, 1179, 1132, 1024, 934, 839, 741 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 1.10 (d, *J* = 6.1 Hz, 6H), 2.76 - 2.82 (m, 1H), 2.85 - 2.94 (m, 2H), 3.89 (s, 3H), 3.99 - 4.13 (m, 3H), 6.87 - 6.93 (m, 2H), 6.93 - 7.01 (m, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 21.9, 48.8, 49.3, 56.2, 68.9, 74.5, 111.9, 115.2, 120.9, 121.6, 148.8, 150.2.

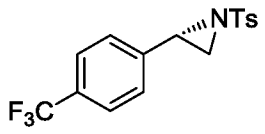
(*R*)-2-Amino-1-(4-(trifluoromethyl)phenyl)ethanol (204)



A solution of (*R*)-2-nitro-1-(4-(trifluoromethyl)phenyl)ethanol (**203**, 30 mg, 0.127 mmol) in MeOH (4 mL) and AcOH (0.2 mL) was hydrogenated (H_2, 1 atm) in the presence of 10% Pd/C (14 mg) for 24 h. The solution was filtered over Celite, and the solvent was

removed under reduced pressure. The crude material was purified via silica gel chromatography (Et_3N and EtOAc) to give **204** (27 mg, 90%) as a white solid: mp 49 - 50 °C; $[\alpha]_D^{26}$ + 46.3 (*c* 0.1, MeOH); IR (neat) 3310, 2923, 2846, 1625, 1552, 1413, 1326, 1163, 1116, 1067, 1017, 839 cm^{-1}; ^1H NMR (700 MHz, MeOD-d^4) δ 3.01 - 3.10 (m, 1H), 3.21 - 3.25 (m, 1H), 3.26 - 3.31 (m, 1H), 3.34-3.42 (m, 1H), 7.61 - 7.66 (m, 2H), 7.67 - 7.73 (m, 2H); ^{13}C NMR (175 MHz, MeOD-d^4) δ 47.6, 69.7, 123.8, 125.3, 127.2, 131.4 (q, J = 36.1 Hz), 146.9.

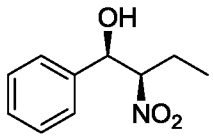
(*S*)-1-Tosyl-2-(4-(trifluoromethyl)phenyl)aziridine (205)



p-Toluene sulfonyl chloride (11 mg, 0.055 mmol) was added in portions to a solution of **204** (13 mg, 0.055 mmol) and triethylamine (16 μL, 0.11 mmol) in CH_2Cl_2 (2 mL) at 0 ◦C. After 30 min, the ice bath was removed, and the solution was allowed to warm to room temperature and was stirred for an additional 6 h. The reaction mixture was evaporated to dryness and the residue was taken up into 2 mL of THF. Triphenylphosphine (16 mg, 0.06 mmol) was added to the reaction mixture in one portion which was cooled to 0 °C and treated slowly with diethyl azodicarboxylate (10 μL, 0.06 mmol). The ice bath was removed and the yellow solution was stirred at room temperature for 6 h. The solvent was evaporated and the residue was purified by column chromatography to yield **205** (17 mg, 91%) as a white solid: mp 61 - 62 °C; 96% ee [Chiralcel OD-H, hexane:*i*-propanol 95:5, 0.8 mL/min, 215 nm, t_R (major) 34.7 min, t_R (minor) 42.3 min]; $[\alpha]_D^{21}$ - 85.3 (*c* 0.08, CH_2Cl_2); IR (neat) 3483, 2924, 851, 1730, 1622,

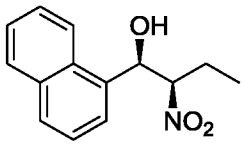
1597, 1454, 1423, 1382, 1326, 1187, 1166, 1120, 1094, 1067, 1018, 983, 912, 841, 817, 752, 715, 697 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 2.31 - 2.36 (m, 1H), 2.43 - 2.49 (m, 3H), 3.06 - 3.10 (m, 1H), 3.84 - 3.89 (m, 1H), 7.35 - 7.41 (m, 4H), 7.53-7.59 (m, 2H), 7.89 -7.93 (m, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 21.8, 36.3, 40.8, 126.6, 128.0, 128.9, 129.9, 131.5 (q, J = 42.2 Hz), 135.2, 139.7, 144.8.

(1*R*,2*R*)-2-Nitro-1-phenylbutan-1-ol (212a)



Colorless oil: *syn*:*anti* ratio >20:1; 97% ee [Chiralcel OD-H, hexane:*i*-propanol 97:3, 0.5 mL/min, 215 nm, t_R (*anti*, minor) 22.3 min, t_R (*anti*, major) 26.4 min, t_R (*syn*, minor) 34.6 min, t_R (*syn*, major) 39.8 min]; $[\alpha]_D^{22}$ - 37.8 (*c* 0.23, CH_2Cl_2), [lit[16] for (1*S*, 2*S*)-isomer $[\alpha]_D^{25}$ + 36.8 (*c* 0.54, CH_2Cl_2 for 92% ee)]; IR (neat) 3533, 3065, 3034, 2976, 2937, 2877, 2851, 1950, 1889, 1814, 1552, 1495, 1456, 1440, 1375, 1345, 1259, 1201, 1123, 1061, 1044, 996, 926, 890, 806, 767, 702, 608 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 0.89 (t, J = 7.4 Hz, 3H), 1.40 - 1.43 (m, 1H), 1.82 - 1.91 (m, 1H), 2.58 (d, J = 4.2 Hz, 1H), 4.62 - 4.68 (m, 1H), 5.05 (d, J = 9.1 Hz, 1H), 7.35 - 7.46 (m, 5H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 10.1, 23.9, 75.6, 95.2, 127.0, 129.1, 129.2, 138.7.

(1*R*,2*R*)-2-Nitro-1-(1-naphthyl)-butan-1-ol (212b)



Colorless oil: *syn*:*anti* ratio >77:1; 98% ee [Chiralcel AS-H, hexane:*i*-propanol 98:2, 0.5 mL/min, 215 nm, t_R (*syn*, minor) 47.4 min, t_R (*syn*, major) 53.5 min]; $[\alpha]_D^{22}$ - 39.6 (*c* 0.47, CH_2Cl_2); IR (neat) 3533, 3052, 2975, 2923, 1602, 1552, 1511, 1461, 1372, 1347, 1304, 1260, 1169, 1050, 926, 862, 804, 781, 751, 736, 679 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 0.84 (t, *J* = 7.4 Hz, 3H), 1.16 - 1.33 (m, 1H), 1.87 - 1.89 (m, 1H), 2.60 - 2.71 (m, 1H), 4.95 - 5.03 (m, 1H), 5.83 (d, *J* = 9.4 & 3.3 Hz, 1H), 7.50 - 7.55 (m, 1H), 7.56 - 7.59 (m, 1H), 7.60 - 7.65 (m, 2H), 7.91 (d, *J* = 8.2 Hz, 1H), 7.94 (d, *J* = 8.2 Hz, 1H), 8.31 (d, *J* = 8.6 Hz, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 10.3, 24.3, 73.2, 95.4, 123.2, 125.4, 125.6, 126.2, 127.0, 129.2, 129.8, 130.8, 134.0, 134.3.

References:

1. Evans, D. A.; Seidel, D.; Rueping, M.; Lam, H. W.; Shaw, J. T.; Downey, C. W. *J. Am. Chem. Soc.* **2003**, *125*, 12692.
2. Qin, B.; Xiao, X.; Liu, X.; Huang, J.; Wen, Y.; Feng. X. *J. Org. Chem.* **2007**, *72*, 9323.
3. Blay, G.; Climent, E.; Fernandez, I.; Hernandez-Olmos, V.; Pedro, J. R. *Tetrahedron: Asym*metry **2007**, *18*, 1603.
4. Didier, D.; Bouvier, C. M.; Schulz, E. *Adv. Synth. Catal.* **2011**, *353*, 1087.
5. Lai, G.; Guo, F.; Zheng, Y.; Fang, Y.; Song, H.; Xu, K.; Wang, S.; Zha, Z.; Wang, Z. *Chem. Eur. J.* **2011**, *17*, 1114.

6. Selvakumar, S.; Sivasankaran, D.; Singh, V. K. *Org. Biomol. Chem.* **2009**, *7*, 3156.

7. Fieser, L. F.; Daudt, W. H. *J. Am. Chem. Soc.* **1946**, *68*, 2248.

8. Cheng, H. G.; Lu, L. Q.; Wang, T.; Chen, J. R.; Xiao, W. J. *Chem. Commun.* **2012**, *48*, 5596.

9. Khadjawi, M. G.; Purkarthofer, T.; Skranc, W.; Griengl, H. . *Synth. Catal.* **2007**, *349*, 1445.

10. Trost, B.; Yeh, V. S. C. *Angew. Chem. Int. Ed.* **2002**, *41*, 861.

11. Mayani, V. J.; Abdi, S. H. R.; Kureshy, R. I.; Khan, N. H.; Das, A.; Bajaj, H. C. *J. Org. Chem.* **2010**, *75*, 6191.

12. Romeiro, L. A. S.; Ferreira, M. D. S.; Silva, L. L. D.; Castro, H. C.; Miranda, A. L. P.; Silva, C. L. M.; Noel, F.; Nascimento, J. B.; Araujo, C. V.; Tibirica, E.; Barreiro, E. J.; Fraga, C. A. M. *Eur. J. Med. Chem.* **2011**, *46*, 3000.

13. Duthion, B.; Metro, T. X.; Pardo, D. G.; Cossy, J. *Tetrahedron* **2009**, *65*, 6696.

14. Hou, X. L.; Li, B. F.; Dai, L. X. *Tetrahedron: Asymmetry* **1999**, *10*, 2319.

15. Sayyed, I. A.; Thakur, V. V.; Nikalje, M. D.; Dewkar, G. K.; Kotkar, S. P.; Sudalai, A. *Tetrahedron* **2005**, *61*, 2831.

16. Blay, G.; Domingo, L. R.; Olmos, V. H.; Pedro, J. R. *Chem. Eur. J.* **2008**, *14*, 4725.

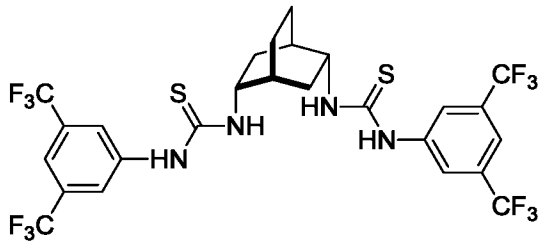
CHAPTER 6

The Asymmetric Sulfa-Michael Reaction

Representative Procedure for the Synthesis of Bis-thioureas (+)-246-(+)-248 from Diamine (-)-34:

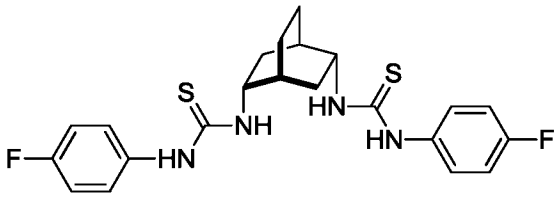
To a THF (5 mL) solution of diamine (-)-**34** (140 mg, 1 mmol) at 0 ^{o}C was added isocyanates **243-245** (2 mmol) dropwise. After stirring the reaction mixture at 0 ^{o}C for 10 min, the ice bath was removed and the mixture was allowed to warm to room temperature. Stirring was continued for an additional 24 h. After completion of the reaction, the mixture was evaporated and the crude product was purified by column chromatography (SiO_2, 20% EtOAc/hexanes) to obtain pure bis-thioureas **(+)-246-(+)-248**.

(+)-1,1'-((1*R*,2*R*,4*R*,5*R*)-Bicyclo[2.2.2]octane-2,5-diyl)bis(3-(3,5-bis(trifluoromethyl)phenyl)thiourea) [(+)-246]



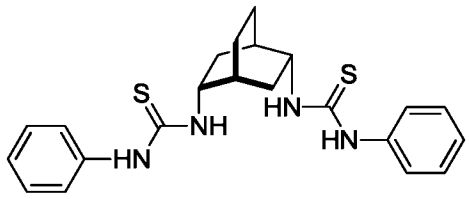
Amorphous white solid: mp 98 - 99 °C; $[\alpha]^{25}_{D}$ + 47.9 (*c* 1.0 , $CHCl_3$); IR (neat) 3225, 3023, 1534, 1372, 1272, 1188, 1139, 946, 884 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 0.86 - 0.94 (m, 3H), 1.32 - 1.41 (m, 2H), 1.58 - 1.70 (m, 2H), 2.20 - 2.31 (m, 2H), 2.61- 2.77 (m, 4H), 3.97 (s, 2H), 7.06 - 7.19 (m, 2H), 7.19 - 7.28 (m, 8H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 20.9, 25.2, 29.7, 51.3, 129.2, 129.9, 130.3, 139.6, 181.0; HRMS (ESI) calcd for $C_{26}H_{23}N_4S_2F_{12}$ *m/z* 683.1173, found 683.1188.

(+)-1,1'-((1*R*,2*R*,4*R*,5*R*)-Bicyclo[2.2.2]octane-2,5-diyl)bis(3-(4-fluorophenyl)thiourea) [(+)-247]



Amorphous white solid: mp 92 - 93 °C; $[\alpha]^{25}_{D}$ + 36.5 (*c* 1.0 , $CHCl_3$); IR (neat) 3241, 1535, 1470, 1381, 1344, 1279, 1179, 1135, 956, 889, 700, 682 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 1.43 - 1.59 (m, 4H), 1.71 - 1.87 (m, 3H), 1.94 - 2.08 (m, 2H), 2.09- 2.20 (m, 3H), 3.94 (s, 2H), 6.99 - 7.12 (m, 4H), 7.33 - 7.40 (m, 4H), 7.48 - 7.58 (m, 4H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 27.3, 29.4, 31.6, 55.9, 114.8, 129.7, 134.2, 168.0, 181.1; HRMS (ESI) calcd for $C_{22}H_{25}N_4S_2F_2$ *m/z* 447. 1489, found 447.1470.

(+)-1,1'-((1*R*,2*R*,4*R*,5*R*)-Bicyclo[2.2.2]octane-2,5-diyl)bis(3-phenylthiourea) [(+)-248]



Amorphous white solid: mp 89 - 90 °C; $[\alpha]^{25}_{D}$ + 29.2 (*c* 0.4 , $CHCl_3$); IR (neat) 3203, 1536, 1376, 1273, 1176, 1129, 953, 890 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 1.75 - 1.82 (m, 2H), 1.84 - 1.91 (m, 1H), 2.01 - 2.09 (m, 2H), 2.10- 2.22 (m, 3H), 2.36 - 2.48 (m, 4H), 4.04 (s, 2H), 7.02 - 7.20 (m, 4H), 7.53 - 7.71 (m, 4H); ^{13}C NMR (175 MHz, $CDCl_3$)

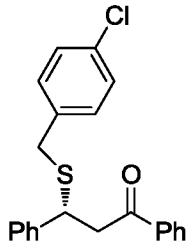
δ 24.3, 26.4, 30.3, 51.5, 122.0, 126.4, 126.7, 129.9, 131.0, 180.7; HRMS (ESI) calcd for $C_{22}H_{27}N_4S_2$ *m/z* 411.1677, found 411. 1674.

Representative Procedure for the Asymmetric Sulfa-Michael Addition of Thiols to Acyclic α,β-Unsaturated Ketones Catalyzed by Fe-salen Complex (+)-**72:**

To an oven-dried vial were added Fe-salen complex (+)-**72** (13.2 mg, 0.02 mmol, 20 mol%) and enone (0.1 mmol) followed by anhydrous DCE (1 mL) and the resulting brown suspension was stirred at room temperature for 10 min. To the suspension at -5 °C was added the thiol (0.12 mmol) and the mixture was stirred at that temperature for the length of time specified in Tables 6.4-6.5. The reaction mixture was concentrated under reduced pressure and the resulting crude residue was purified by flash chromatography on silica gel (15% hexane/ether) to give the product. The enantiomeric excess of the pure product was determined by HPLC on a Daicel Chiralcel OD, AD, OJ, OD-H or AS-H column.

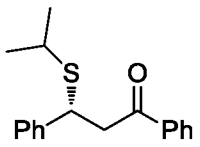
A procedure at 5 mmol scale was carried out with (*E*)-pent-3-en-2-one (421 mg, 5 mmol) and *p*-chlorobenzyl thiol (792 μL, 6 mmol) using (+)-**72** (662.2 mg, 1.0 mmol, 1 mol%) in anhydrous DCE (50 mL). The SMA adduct was obtained in 96% yield and 94% ee.

(*R*)-3-(4-Chlorobenzylthio)-1,3-diphenylpropan-1-one (251)



Colorless oil: $[\alpha]_D^{27}$ + 211.0 (*c* 0.1, $CHCl_3$), [lit.[1] for *(R)* enantiomer $[\alpha]_D^{25}$ + 209 (*c* 1.0, $CHCl_3$, 96% ee)]; 98% ee [Chiralcel OD-H, hexane:*i*-propanol 80:20, 0.8 mL/min, 215 nm, t_R (major) 19.5 min, t_R (minor) 24.0 min]; IR (neat) 2922, 1716, 1460, 1422, 1366, 1311, 1259, 1163, 1142, 1047, 748 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 3.47-3.61 (m, 4H), 4.42 (s, 1H), 7.15 (*J* = 7.3 Hz, 2H), 7.22-7.29 (m, 3H), 7.32-7.39 (m, 2H), 7.39-7.42 (m, 2H), 7.45-7.50 (m, 2H), 7.53-7.59 (m, 1H), 7.78-7.92 (m, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 34.1, 44.1, 45.6, 127.2, 128.0, 128.9, 130.2, 133.2, 134.0, 136.4, 136.7, 141.8, 196.8.

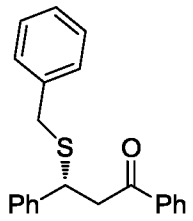
(*R*)-3-(Isopropylthio)-1,3-diphenylpropan-1-one (229a)



Colorless oil: $[\alpha]_D^{27}$ + 127.6 (*c* 0.1, $CHCl_3$), [lit.[1] for *(R)* enantiomer $[\alpha]_D^{25}$ + 107 (*c* 1.0, $CHCl_3$, 80% ee)]; 94% ee [Chiralcel OD, hexane:*i*-propanol 90:10, 0.8 mL/min, 215 nm, t_R (major) 21.6 min, t_R (minor) 25.5 min]; IR (neat) 3060, 2923, 1686, 1597, 1580, 1492, 1450, 1334, 1179, 979, 749, 697, 649 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 1.15 (d, *J* = 6.8 Hz, 3H), 1.30 (d, *J* = 6.8 Hz, 3H), 2.63-2.69 (m, 1H), 3.44-3.50 (m, 1H), 4.66-4.74

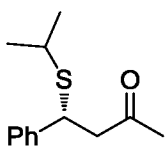
(m, 1H), 7.21-7.27 (m, 1H), 7.30-7.36 (m, 2H), 7.48-7.52 (m, 4H), 7.59-7.63 (m, 1H), 7.92-8.00 (m, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 22.4, 22.7, 34.7, 43.5, 45.7, 127.1, 127.8, 128.1, 128.6, 133.2, 136.9, 142.7, 197.4.

(*R*)-3-(Benzylthio)-1,3-diphenylpropan-1-one (229b)



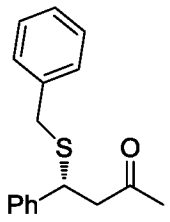
Colorless oil: $[\alpha]_D^{25}$ + 139.2 (*c* 0.14, $CHCl_3$), [lit.[1] for *(R)* enantiomer $[\alpha]_D^{25}$ + 139.7 (*c* 1.0, $CHCl_3$, 96% ee)]; 97% ee [Chiralcel OD, hexane:*i*-propanol 70:30, 0.8 mL/min, 215 nm, t_R (major) 40.7 min, t_R (minor) 45.9 min]; IR (neat) 3059, 1685, 1493, 1408, 1255, 1073, 1027, 980, 750, 696 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 3.53-3.57 (m, 1H), 3.59-3.62 (m, 1H), 3.63- 3.70 (m, 2H), 4.54 (t, *J* = 7.2 Hz, 1H), 7.29-7.32 (m, 3H), 7.35-7.38 (m, 2H), 7.39-7.42 (m, 3H), 7.45-7.51 (m, 4H), 7.58-7.61 (m, 1H), 7.92 (d, *J* = 7.4 Hz, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 35.9, 44.2, 45.3, 127.0, 127.3, 128.1, 128.4, 128.5, 128.6, 133.2, 136.8, 137.9, 141.8, 196.8.

(*R*)-4-(Isopropylthio)-4-phenylbutan-2-one (229c)



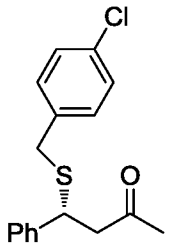
Colorless oil: $[\alpha]_D^{25}$ + 107.6 (*c* 0.1, $CHCl_3$); 97% ee [Chiralcel OD, hexane:*i*-propanol 70:30, 1.0 mL/min, 215 nm, t_R (major) 9.7 min, t_R (minor) 10.4 min]; IR (neat) 3028, 2924, 1717, 1492, 1361, 1152, 1021, 699, 534 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 1.11 (d, *J* = 6.5 Hz, 3H), 1.28 (d, *J* = 6.5 Hz, 3H), 2.08 (s, 3H), 2.59-2.64 (m, 1H), 2.91-2.98 (m, 2H), 4.50-4.54 (m, 1 H), 7.21-7.26 (m, 1H), 7.29-7.35 (m, 2H), 7.39-7.45 (m, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 22.4, 22.7, 30.7, 34.2, 43.9, 50.8, 128.7, 129.1, 129.6, 143.1, 205.7; HRMS (EI) calcd for $C_{13}H_{18}OS$ *m/z* 222.1078, found 222.1074.

(*R*)-4-(Benzylthio)-4-phenylbutan-2-one (229d)



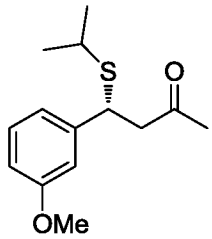
Colorless oil: $[\alpha]_D^{25}$ + 183.9 (*c* 0.1, $CHCl_3$), [lit.[2] for *(S)* enantiomer $[\alpha]_D^{25}$ - 162.5 (*c* 1.0, $CHCl_3$, 85% ee)]; 96% ee [Chiralcel OD, hexane:*i*-propanol 70:30, 1.0 mL/min, 215 nm, t_R (major) 13.0 min, t_R (minor) 16.2 min]; IR (neat) 3060, 2917, 1716, 1493, 1359, 1154, 1024, 762, 698, 531 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 2.06 (s, 3H), 2.95-3.03 (m, 2H), 3.50 (AB system, *J* = 13.3 Hz, 2H), 4.26 (t, *J* = 7.2 Hz, 1H), 7.23-7.29 (m, 3H), 7.32-7.41 (m, 7H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 30.3, 35.6, 44.2, 50.9, 127.4, 127.7, 127.9, 128.4, 128.5, 128.9, 138.6, 141.5, 207.4.

(*R*)-4-((4-Chlorobenzyl)thio)-4-phenylbutan-2-one (229e)



Colorless oil: $[\alpha]_D^{25}$ + 199.3 (*c* 0.1, $CHCl_3$); 97% ee [Chiralcel AD, hexane:*i*-propanol 85:15, 0.8 mL/min, 215 nm, t_R (major) 18.9 min, t_R (minor) 23.7 min]; IR (neat) 3028, 2919, 1716, 1598, 1490, 1452, 1092, 1015, 833, 699 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 2.06 (s, 3H), 2.90-3.00 (m, 2H), 3.50 (AB system, *J* = 13.2 Hz, 2H), 4.23 (t, *J* = 7.3 Hz, 1H), 7.16-7.20 (m, 2H), 7.27-7.33 (m, 3H), 7.37-7.42 (m, 4H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 30.2, 35.2, 43.4, 50.3, 128.9, 129.2, 129.4, 129.7, 130.4, 132.3, 138.8, 142.7, 207.3; HRMS (EI) calcd for $C_{17}H_{17}ClOS$ *m/z* 304.0689, found 304.0687.

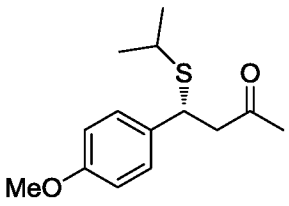
(*R*)-4-(Isopropylthio)-4-(3-methoxyphenyl)butan-2-one (229f)



Colorless oil: $[\alpha]_D^{25}$ + 117.7 (*c* 0.12, $CHCl_3$); 95% ee [Chiralcel OD, hexane:*i*-propanol 85:15, 0.8 mL/min, 215 nm, t_R (major) 15.0 min, t_R (minor) 18.9 min]; IR (neat) 2959, 2921, 1716, 1599, 1261, 1153, 1046, 873, 697 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 1.13 (d, *J* = 6.6 Hz, 3H), 1.27 (d, *J* = 6.6 Hz, 3H), 2.11 (s, 3H), 2.59-2.65 (m, 1H), 2.90-2.99

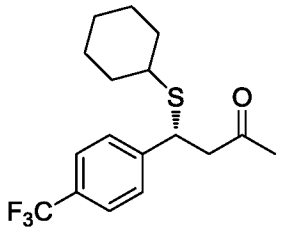
(m, 2H), 3.84 (s, 3 H), 4.37 (t, J = 7.3 Hz, 1H), 6.75-6.83 (m, 1H), 6.90-7.0 (m, 2H), 7.21-7.29 (m, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 22.5, 22.7, 30.7, 34.9, 43.9, 50.9, 55.3, 113.2, 113.7, 120.6, 130.1, 143.1, 160.2, 207.4; HRMS (EI) calcd for $C_{14}H_{20}O_2S$ *m/z* 252.1184, found 252.1186.

(*R*)-4-(Isopropylthio)-4-(4-methoxyphenyl)butan-2-one (229g)



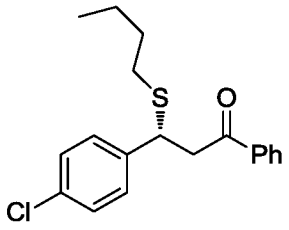
Colorless oil: $[\alpha]_D^{25}$ + 119.0 (*c* 0.14, $CHCl_3$); 92% ee [Chiralcel AD, hexane:*i*-propanol 80:20, 0.8 mL/min, 215 nm, t_R (major) 13.2 min, t_R (minor) 15.0 min]; IR (neat) 2958, 2926, 1716, 1610, 1461, 1175, 1035, 831, 805 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 1.10 (d, *J* = 6.5 Hz, 3H), 1.29 (d, *J* = 6.5 Hz, 3H), 2.06 (s, 3H), 2.50-2.61 (m, 1H), 2.89-2.98 (m, 2H), 3.82 (s, 3 H), 4.38 (t, *J* = 6.9 Hz, 1H), 6.85 (d, *J* = 8.0 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 22.3, 22.5, 30.6, 34.5, 43.3, 50.2, 55.3, 114.1, 129.6, 134.8, 159.3, 207.9; HRMS (EI) calcd for $C_{14}H_{20}O_2S$ *m/z* 252.1184, found 252.1194.

(*R*)-4-(Cyclohexylthio)-4-(4-(trifluoromethyl)phenyl)butan-2-one (229h)



Colorless oil: $[\alpha]_D^{25}$ + 157.7 (*c* 0.27, $CHCl_3$); 98% ee [Chiralcel OD-H, hexane:*i*-propanol 70:30, 1.0 mL/min, 215 nm, t_R (major) 7.9 min, t_R (minor) 9.2 min]; IR (neat) 2930, 1718, 1418, 1163, 1016, 837, 604 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 1.08-1.79 (m, 10H), 1.88-2.00 (m, 1H), 2.08 (s, 3H), 2.33-2.41 (m, 1H), 2.89-3.02 (m, 2H), 4.47 (t, *J* = 7.2 Hz, 1H), 7.48 (d, *J* = 7.8 Hz, 2H), 7.53 (d, *J* = 7.8 Hz, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 25.4, 25.5, 30.8, 31.9, 32.0, 40.8, 41.3, 50.7, 123.1, 126.2, 129.1, 129.6 (q, *J* = 35.2 Hz), 139.3, 206.8; HRMS (EI) calcd for $C_{17}H_{21}OSF_3$ *m/z* 330.1265, found 330.1263.

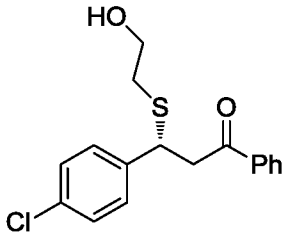
(*R*)-3-(Butylthio)-3-(4-chlorophenyl)-1-phenylpropan-1-one (229i)



Colorless oil: $[\alpha]_D^{25}$ + 204.7 (*c* 0.1, $CHCl_3$); 93% ee [Chiralcel OJ, hexane:*i*-propanol 70:30, 1.0 mL/min, 215 nm, t_R (major) 14.6 min, t_R (minor) 17.2 min]; IR (neat) 2957, 2871, 1686, 1448, 1351, 1226, 1091, 981, 821, 754, 689, 544 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.83 (t, *J* = 7.3 Hz, 3H), 1.20-1.40 (m, 2H), 1.40-1.55 (m, 2H), 2.31-2.41 (m, 2H), 3.52 (d, *J* = 7.2 Hz, 2H), 4.31 (t, *J* = 7.2 Hz, 1H), 7.30 (d, *J* = 7.9 Hz, 5H), 7.39 (d, *J*

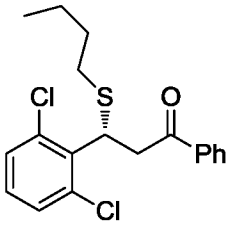
= 7.9 Hz, 2H), 7.41-7.49 (m, 2H), 7.51-7.62 (m, 1H), 7.92 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 13.3, 21.9, 30.8, 43.2, 45.8, 128.3, 128.9, 129.2, 134.6, 135.1, 137.3, 140.9, 198.2; HRMS (EI) calcd for $C_{19}H_{21}OSCl$ *m/z* 332.1002, found 332.1010.

(*R*)-3-(4-Chlorophenyl)-3-((2-hydroxyethyl)thio)-1-phenylpropan-1-one (229j)



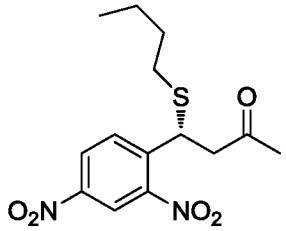
Colorless oil: $[\alpha]_D^{25}$ + 173.8 (*c* 0.1, $CHCl_3$); 96% ee [Chiralcel OD, hexane:*i*-propanol 80:20, 1.0 mL/min, 215 nm, t_R (major) 25.2 min, t_R (minor) 31.3 min]; IR (neat) 3370 (broad), 2970, 1700, 1456, 1242, 1079, 906, 755 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.59 (s, 2H), 3.48-3.51 (m, 1H), 3.58-3.61 (m, 1H), 3.66-3.71 (m, 1H), 3.88-3.93 (m, 2H), 4.51 (t, *J* = 7.2 Hz, 1H), 7.30-7.36 (m, 2H), 7.39-7.42 (m, 2H), 7.46-7.50 (m, 2H), 7.58-7.61 (m, 1H), 7.92-7.96 (m, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 34.5, 43.6, 45.3, 60.3, 128.7, 129.1, 129.6, 129.9, 133.2, 133.6, 137.1, 140.9, 198.1; HRMS (EI) calcd for $C_{17}H_{18}O_2SCl$ *m/z* 321.0716, found 321.0729.

(*R*)-3-(Butylthio)-3-(2,6-dichlorophenyl)-1-phenylpropan-1-one (229k)



Colorless oil: $[\alpha]_D^{25}$ + 197.1 (*c* 0.1, $CHCl_3$); 96% ee [Chiralcel OJ, hexane:*i*-propanol 90:10, 1.0 mL/min, 215 nm, t_R (major) 34.3 min, t_R (minor) 41.5 min]; IR (neat) 2956, 2870, 1687, 1433, 1358, 1218, 1085, 983, 772, 689 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7.2 Hz, 3H), 1.29-1.43 (m, 2H), 1.55-1.68 (m, 2H), 2.60-2.79 (m, 2H), 3.80-3.88 (m, 1H), 3.97-4.09 (m, 1H), 5.52 (t, *J* = 7.2 Hz, 1H), 7.09-7.13 (m, 1H), 7.26-7.32 (m, 1H), 7.33-7.37 (m, 1H), 7.47-7.52 (m, 2H), 7.56-7.62 (m, 1H), 7.96 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 13.0, 21.9, 31.2, 32.0, 40.8, 42.3, 128.3, 128.9, 129.8, 133.8, 135.6, 135.8, 137.3, 138.9, 198.3; HRMS (EI) calcd for $C_{19}H_{20}OSClNa$ (M+H) *m/z* 389.0510, found 389.0505.

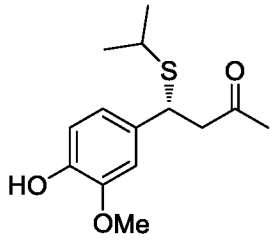
(*R*)-4-(Butylthio)-4-(2,4-dinitrophenyl)butan-2-one (229l)



Colorless oil: $[\alpha]_D^{25}$ + 153.9 (*c* 0.1, $CHCl_3$); 95% ee [Chiralcel OD-H, hexane:*i*-propanol 80:10, 1.0 mL/min, 215 nm, t_R (major) 21.8 min, t_R (minor) 28.4 min]; IR (neat) 2958, 2930, 1708, 1348, 1276, 1158, 1065, 910, 835, 740 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ

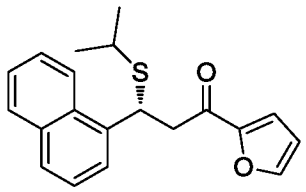
0.91 (t, *J* = 7.3 Hz, 3H), 1.34-1.42 (m, 2H), 1.49-1.56 (m, 2H), 2.36 (s, 3H), 2.38-2.44 (m, 1H), 2.50-2.58 (m, 1H), 3.37-3.44 (m, 1H), 3.59-3.65 (m, 1H), 3.69-3.74 (m, 1H), 7.71 (d, *J* = 8.2 Hz, 1H), 8.40 (d, *J* = 8.2 Hz, 1H), 8.83 (s, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 13.7, 21.9, 28.0, 29.9, 30.8, 32.4, 52.1, 120.6, 128.1, 136.5, 141.2, 147.0, 149.8, 204.1; HRMS (EI) calcd for $C_{14}H_{18}N_2O_5S$ *m/z* 326.0936, found 326.0937.

(*R*)-4-(4-Hydroxy-3-methoxyphenyl)-4-(isopropylthio)butan-2-one (229m)



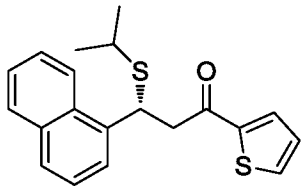
Colorless oil: $[\alpha]_D^{25}$ + 162.0 (*c* 0.1, $CHCl_3$); 96% ee [Chiralcel AD, hexane:*i*-propanol 85:15, 0.8 mL/min, 215 nm, t_R (major) 23.8 min, t_R (minor) 30.2 min]; IR (neat) 3432 (broad), 2960, 2926, 1711, 1600, 1462, 1363, 1269, 1153, 1122, 1033, 818, 792 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.12 (d, *J* = 6.8 Hz, 3H), 1.27 (d, *J* = 6.8 Hz, 3H), 2.09 (s, 3H), 2.58-2.69 (m, 1H), 2.87-2.98 (m, 2H), 3.89 (s, 3 H), 4.36 (t, *J* = 6.9 Hz, 1H), 6.80-6.89 (m, 2H), 6.92 (s, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 22.7, 22.9, 30.5, 34.5, 43.3, 50.3, 56.8, 110.4, 114.9, 120.6, 135.3, 146.1, 148.0, 208.1; HRMS (EI) calcd for $C_{14}H_{20}O_3S$ *m/z* 268.1133, found 268.1134.

(*R*)-1-(Furan-2-yl)-3-(isopropylthio)-3-(naphthalen-1-yl)propan-1-one (229n)



Colorless oil: $[\alpha]_D^{25}$ + 206.3 (*c* 0.1, $CHCl_3$); 97% ee [Chiralcel AD, hexane:*i*-propanol 70:30, 1.0 mL/min, 215 nm, t_R (major) 8.6 min, t_R (minor) 9.9 min]; IR (neat) 3442, 2958, 2923, 1672, 1467, 1394, 1159, 1050, 981, 883, 776 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.17 (d, *J* = 6.9 Hz, 3H), 1.22 (d, *J* = 6.9 Hz, 3H), 2.78-2.88 (m, 1H), 3.03-3.16 (m, 2H), 3.49-3.68 (m, 1H), 6.48-6.55 (m, 1H), 7.13-7.19 (m, 1H), 7.46-7.57 (m, 2H), 7.59-7.63 (m, 2H), 7.76-7.84 (m, 1H), 7.86-7.99 (m, 2H), 8.37 (s, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 21.9, 22.0, 32.5, 41.9, 44.2, 111.9, 117.3, 120.8, 123.9, 125.8, 125.9, 126.3, 127.2, 128.7, 130.8, 134.1, 138.3, 147.1, 152.2, 201.3; HRMS (EI) calcd for $C_{20}H_{20}O_2S$ *m/z* 324.1184, found 324.1193.

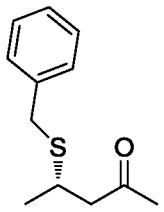
(*R*)-3-(Isopropylthio)-3-(naphthalen-1-yl)-1-(thiophen-2-yl)propan-1-one (229o)



Colorless oil: $[\alpha]_D^{25}$ + 218.7 (*c* 0.1, $CHCl_3$); 94% ee [Chiralcel AD, hexane:*i*-propanol 80:20, 0.8 mL/min, 215 nm, t_R (major) 13.0 min, t_R (minor) 15.1 min]; IR (neat) 2959, 2922, 1660, 1453, 1414, 1355, 1237, 1060, 931, 858, 795, 776, 725 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.18 (d, *J* = 6.9 Hz, 3H), 1.22 (d, *J* = 6.9 Hz, 3H), 2.81-2.91 (m, 1H), 3.09-3.18 (m, 2H), 3.54-3.70 (m, 1H), 7.09-7.14 (m, 1H), 7.45-7.59 (2H), 7.60-7.67 (m,

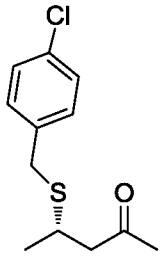
2H), 7.69-7.74 (m, 1H), 7.77-7.83 (m, 1H), 7.88-7.95 (m, 2H), 8.49 (s, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 21.7, 21.9, 32.7, 40.7, 42.9, 120.4, 126.7, 126.8, 127.2, 128.1, 128.2, 129.6, 130.9, 132.3, 134.7, 135.9, 139.0, 142.2, 145.9, 200.9; HRMS (EI) calcd for $C_{20}H_{20}OS_2$ *m/z* 340.0956, found 340.0949.

(*S*)-4-(Benzylthio)pentan-2-one (229p)



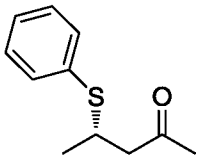
Colorless oil: $[\alpha]_D^{25}$ + 7.9 (*c* 0.1, $CHCl_3$); 96% ee [Chiralcel OD, hexane:*i*-propanol 92:8, 0.8 mL/min, 215 nm, t_R (major) 14.4 min, t_R (minor) 16.9 min]; IR (neat) 2962, 2922, 1714, 1494, 1359, 1158, 1070, 1028, 769 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.29 (d, *J* = 6.8 Hz, 3H), 2.10 (s, 3H), 2.52-2.58 (m, 1H), 2.67-2.75 (m, 1H), 3.13-3.22 (m, 1H), 3.74-3.80 (m, 2H), 7.20-7.26 (m, 1H), 7.32-7.39 (m, 4H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 21.3, 30.9, 35.3, 35.8, 51.0, 127.7, 129.3, 129.4, 139.2, 208.8; HRMS (EI) calcd for $C_{12}H_{16}OS$ *m/z* 208.0922, found 208.0919.

(*S*)-4-((4-Chlorobenzyl)thio)pentan-2-one (229q)



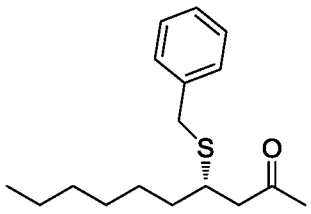
Colorless oil: $[\alpha]_D^{25}$ + 10.5 (*c* 0.1, $CHCl_3$); 93% ee [Chiralcel OD, hexane:*i*-propanol 92:8, 0.8 mL/min, 215 nm, t_R (major) 19.3 min, t_R (minor) 22.5 min]; IR (neat) 2963, 2924, 1714, 1490, 1359, 1280, 1159, 1092, 1014, 962, 832, 747 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 1.28 (d, *J* = 6.8 Hz, 3H), 2.12 (s, 3H), 2.52-2.59 (m, 1H), 2.67-2.73 (m, 1H), 3.11-3.20 (m, 1H), 3.71-3.79 (m, 2H), 7.28-7.33 (m, 4H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 22.0, 30.6, 35.3, 35.9, 51.1, 128.9, 130.0, 134.1, 139.0, 208.7; HRMS (EI) calcd for $C_{12}H_{15}OClS$ *m/z* 242.0532, found 242.0530.

(S)-4-(Phenylthio)pentan-2-one (229r)



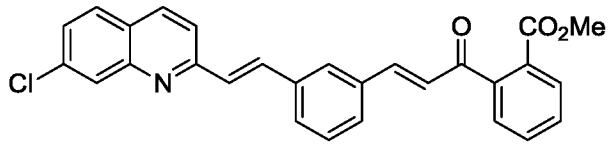
Colorless oil: $[\alpha]_D^{25}$ + 14.6 (*c* 0.1, $CHCl_3$); 98% ee [Chiralcel OD, hexane:*i*-propanol 98:2, 0.8 mL/min, 215 nm, t_R (major) 14.5 min, t_R (minor) 17.1 min]; IR (neat) 2968, 2925, 1715, 1583, 1476, 1360, 1157, 1091, 1024, 748, 693 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 1.30 (d, *J* = 6.7 Hz, 3H), 2.14 (s, 3H), 2.52-2.62 (m, 1H), 2.72-281 (m, 1H), 3.67-3.80 (m, 1H), 7.21-7.32 (m, 3H), 7.42-7.49 (m, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 20.9, 30.8, 38.9, 50.6, 128.5, 129.6, 143.0, 144.8, 208.9.

(*S*)-4-(Benzylthio)decan-2-one (229s)



Colorless oil: $[\alpha]_D^{25}$ + 19.3 (*c* 0.1, $CHCl_3$); 98% ee [Chiralcel OD, hexane:*i*-propanol 90:10, 1.0 mL/min, 215 nm, t_R (major) 6.1 min, t_R (minor) 9.1 min]; IR (neat) 3028, 2927, 2856, 1716, 1494, 1454, 1359, 1154, 1070, 960, 766, 701 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 0.91 (t, *J* = 7.3 Hz, 3H), 1.22-1.48 (m, 10H), 2.09 (s, 3H), 2.59-2.63 (m, 1H), 2.65-2.72 (m, 1H), 3.04-3.09 (m, 1H), 3.70-3.79 (m, 2H), 7.21-7.26 (m, 1H), 7.30-7.39 (m, 4H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 14.1, 22.7, 26.4, 27.8, 30.0, 31.6, 34.9, 35.2, 40.8, 50.5, 128.4, 129.5, 129.8, 139.2, 208.7; HRMS (EI) calcd for $C_{17}H_{26}OS$ *m/z* 278.1704, found 278.1695.

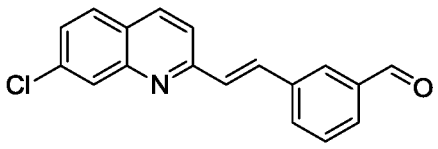
Methyl 2-((*E*)-3-(3-((*E*)-2-(7-chloroquinolin-2-yl)vinyl)phenyl)acryloyl)benzoate (258)



To a mixture of 7-chloroquinaldine (17.7 mg, 0.1 mmol) and 1,3-benzene dicarboxaldehyde (13.4 mg, 0.1 mmol) in dry toluene (2 mL) was added *p*-toluenesulfonamide (17.1 mg, 0.1 mmol) and the mixture was heated at reflux for 24 h.

To the mixture was added a solution of methyl 2-acetylbenzoate (19.6 mg, 1.1 mmol) in toluene (0.5 mL) and reflux was continued for an additional 16 h. The reaction mixture was concentrated under reduced pressure and the resulting crude residue was purified by flash chromatography on silica gel (5% EtOAc/hexanes) to give the product (39 mg, 86% yield) as a yellow solid: mp 119-120 °C; IR (neat) 3049, 2958, 2923, 2853, 1716, 1597, 1461, 1361, 1261, 797, 777, 736 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 3.91 (s, 3H), 7.42-7.51 (m, 4H), 7.59 - 7.64 (m, 2H), 7.67-7.74 (m, 2H), 7.76-7.81 (m, 2H), 7.83-7.86 (m, 2H), 7.88-7.91 (m, 1H), 7.93-7.98 (m, 1H), 8.11-8.15 (m, 1H), 8.16-8.21 (m, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 50.9, 123.4, 125.3, 125.4, 127.6, 128.2, 128.4, 128.5, 128.6, 128.8, 129.0(x2), 129.2, 129.3, 129.6(x2), 133.1, 133.5, 134.5, 137.1, 138.6, 140.9, 142.8, 142.9, 144.9, 158.0, 161.6, 189.8; HRMS (EI) calcd for $C_{28}H_{21}O_3NCl$ *m/z* 454.1210, found 454.1202.

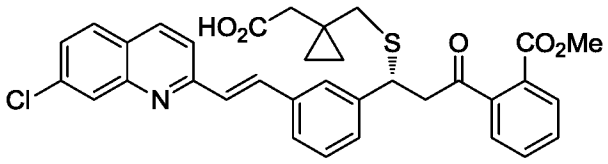
(*E*)-3-(2-(7-Chloroquinolin-2-yl)vinyl)benzaldehyde (261)



Yellow solid: mp 157 - 158 °C, [lit[3] 156 - 157 °C]; IR (neat) 3281, 2924, 2853, 1698, 1603, 1583, 1509, 1465, 1396, 1331, 1307, 1261, 1220, 1152, 970, 909, 827, 800 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.44 - 7.52 (m, 2H), 7.61 (t, *J* = 7.8 Hz, 1H), 7.66 (d, *J* = 8.3 Hz, 1H), 7.77 (d, *J* = 8.3 Hz, 1H), 7.82 (d, *J* = 16.2 Hz, 1H), 7.88 (dt, *J* = 7.8, 2.0 Hz, 1H), 7.92 (dt, *J* = 7.8, 2.0 Hz, 1H), 8.13 (d, *J* = 2.0 Hz, 1H), 8.15 - 8.19 (m, 2H), 10.11 (s,

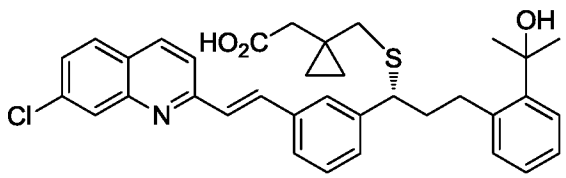
1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 119.9, 126.1, 126.5, 127.5, 128.3, 129.0, 129.2, 129.4, 129.7, 130.3, 130.5, 133.1, 133.8, 134.6, 135.1, 137.8, 157.4, 192.5.

(*R*,*E*)-2-(1-(((1-(3-(2-(7-Chloroquinolin-2-yl)vinyl)phenyl)-3-(2-(methoxycarbonyl)phenyl)-3-oxopropyl)thio)methyl)cyclopropyl)acetic Acid (275)



Pale yellow solid: mp 129 - 130 °C; $[\alpha]_D^{25}$ +93.3 (*c* 0.1, MeOH); 98% ee [Chiralcel AS-H, hexane:*i*-propanol 82:18, 0.8 mL/min, 215 nm, t_R (major) 20.7 min, t_R (minor) 27.3 min]; IR (neat) 3000 (broad), 1770, 1722, 1701, 1434, 1390, 1283, 1198, 1133, 1066, 982, 829, 764, 709 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 0.99-1.12 (m, 4H), 2.33-2.42 (m, 2H), 2.51-2.60 (m, 2H), 3.35-3.42 (m, 2H), 3.88-3.92 (m, 1H), 4.03 (s, 3H), 7.39-7.48 (m, 3H), 7.58-7.61 (m, 1H), 7.62-7.65 (m, 1H), 7.68-7.73 (m, 1H), 7.75-7.80 (m, 1H), 7.80-7.84 (m, 1H), 7.85-7.90 (m, 1H), 8.01-8.06 (m, 2H), 8.06-8.12 (m, 4H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 12.3, 17.6, 38.7, 40.9, 46.6, 49.7, 119.9, 126.1, 126.4, 127.7, 128.2, 129.0, 129.1, 129.3, 129.8, 130.4, 130.5, 131.0, 133.2, 134.8, 134.9, 135.2, 135.3, 137.8, 138.2, 138.4, 138.7, 139.1, 139.3, 149.3, 157.7, 169.1, 179.3, 199.9; HRMS (EI) calcd for $C_{34}H_{31}O_5NSCl$ *m/z* 600.1611, found 600.1614.

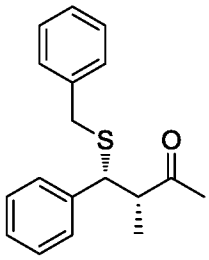
(*R*,*E*)-2-(1-(((1-(3-(2-(7-Chloroquinolin-2-yl)vinyl)phenyl)-3-(2-(2-hydroxypropan-2-yl)phenyl)propyl)thio)methyl)cyclopropyl)acetic Acid [(*R*)-Montelukast, 252)



To a solution of **21** (38 mg, 0.06 mmol) in MeOH (1.5 mL) at 25 °C was added tosylhydrazine (14.2 mg, 0.08 mmol) and the mixture was stirred for 6 h. To the reaction mixture at room temperature was added sodium borohydride (5 mg, 0.13 mmol) and the mixture was stirred for an additional 3 h. Saturated NH_4Cl was added to the reaction mixture which was extracted with EtOAc (2 x 50 mL). The organic layer was dried (Na_2SO_4) and evaporated to achieve crude **23** (45 mg). To a solution of crude **23** (45 mg) in anhydrous THF (3 mL) at 0 °C was added methylmagnesium bromide (126 μL, 0.38 mmol, 3M in Et_2O) dropwise. After the addition was complete, the mixture was allowed to warm to room temperature and was stirred for an additional 2 h. Saturated NH_4Cl was added to the reaction mixture which was extracted with EtOAc (3 x 50 mL). The crude residue was purified by flash chromatography on silica gel (15% ether/hexane) to give the product (32 mg, 87% yield) as a yellow solid: mp 147 - 148 °C, [lit.[3] 145 - 148 °C]; $[\alpha]_D^{26}$ + 101.4 (*c* 0.5, MeOH), [lit.[4] for *(S)* enantiomer $[\alpha]_D^{25}$ + 102 (*c* 1.0, $CHCl_3$)]; IR (neat) 3440 (broad), 1762, 1708, 1436, 1309, 1259, 1190, 1118, 1070, 1026, 997, 750, 721, 695 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 0.41-0.52 (m, 4H), 1.37 (s, 6H), 2.02-2.16 (m, 2H), 2.29-2.42 (m, 2H), 2.62-2.71 (m, 2H), 3.01-3.10 (m, 1H), 3.24-3.32 (m, 1H), 3.79-3.88 (m, 1H), 7.20-7.29 (m, 2H), 7.32-7.38 (m, 1H), 7.40-7.45 (m, 1H), 7.51-7.55 (m, 1H), 7.57-7.63 (m, 5H), 7.67-7.73 (m, 1H), 7.73-7.77 (m, 1H), 7.79-7.85 (m, 1H), 7.90-7.96 (m, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 12.3, 17.3, 31.6, 31.7, 39.7, 40.9, 44.4, 45.2, 74.3, 119.9, 126.8, 127.7, 128.4, 128.6, 129.0, 129.4, 129.7, 129.8, 132.0, 132.9,

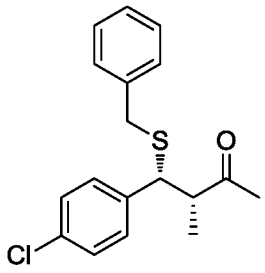
134.5, 135.6, 138.1, 138.4, 139.1, 140.3, 141.0, 141.7, 142.3, 144.2, 146.9, 159.1, 157.3, 179.8.

(3*S*,4*R*)-4-(Benzylthio)-3-methyl-4-phenylbutan-2-one (278a)



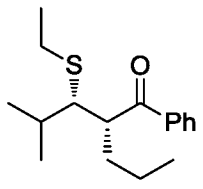
Colorless oil: *syn*:*anti* ratio > 23:1; 98% ee [Chiralcel OD-H, hexane:*i*-propanol 95:5, 0.8 mL/min, 215 nm, t_R (*syn*, major) 15.4 min, t_R (*syn*, minor) 18.3 min]; $[\alpha]_D^{25}$ + 160.2 (*c* 0.1, $CHCl_3$) [lit.[5] for *(3R,4S)* enantiomer $[\alpha]_D^{25}$ - 140.7 (*c* 0.55, $CHCl_3$, 85% ee)]; IR (neat) 3060, 3027, 2970, 2928, 1714, 1665, 1492, 1452, 1357, 1244, 1215, 1157, 1073, 698 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 0.82 (d, *J* = 5.6 Hz, 3H, minor), 1.24 (d, *J* = 6.0 Hz, 3H, major), 1.82 (s, 3H, major), 2.08 (s, 3H, minor), 2.98-3.07 (m, 1H), 3.34 (d, *J* = 13.1 Hz, 1H), 3.48 (d, *J* = 13.1 Hz, 1H), 3.97 (d, *J* = 10.2 Hz, 1H), 7.16-7.28 (m, 8H), 7.42-7.50 (m, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 16.3, 29.6, 35.9, 52.4, 52.8, 127.1, 127.5, 128.5, 128.7, 129.0, 129.1, 137.7, 140.9, 210.1; HRMS (EI) calcd for $C_{18}H_{20}OS$ *m/z* 284.1235, found 284.1232.

(3*S*,4*R*)-4-(Benzylthio)-4-(4-chlorophenyl)-3-methylbutan-2-one (278b)



Colorless oil: *syn*:*anti* ratio > 31:1; 96% ee [Chiralcel AS-H, hexane:*i*-propanol 95:5, 0.8 mL/min, 215 nm, t_R (*syn*, major) 19.5 min, t_R (*syn*, minor) 22.6 min]; $[\alpha]_D^{25}$ + 148.2 (*c* 0.1, $CHCl_3$); IR (neat) 3061, 3028, 2969, 2928, 1714, 1600, 1491, 1453, 1409, 1355, 1233, 1157, 1090, 1070, 1013, 822, 764, 699 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 0.84 (d, *J* = 6.4 Hz, 3H, minor), 1.23 (d, *J* = 7.4 Hz, 3H, major), 1.86 (s, 3H, major), 2.17 (s, 3H, minor), 2.91-3.00 (m, 1H), 3.36 (d, *J* = 12.9 Hz, 1H), 3.45 (d, *J* = 12.9 Hz, 1H), 3.93 (d, *J* = 10.1 Hz, 1H), 7.18-7.22 (m, 2H), 7.25-7.40 (m, 7H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 14.3, 29.8, 35.1, 50.7, 52.3, 127.9, 128.3, 128.9, 129.2, 130.0, 130.4, 138.8, 140.9, 200.1; HRMS (EI) calcd for $C_{18}H_{19}OSCl$ *m/z* 318.0845, found 318.0850.

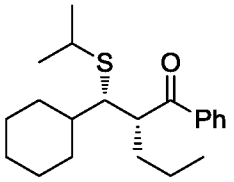
(2*S*,3*S*)-3-(Ethylthio)-4-methyl-1-phenyl-2-propylpentan-1-one (278c)



Colorless oil: *syn*:*anti* ratio > 50:1; 97% ee [Chiralcel OD-H, hexane:*i*-propanol 97:3, 0.8 mL/min, 215 nm, t_R (*anti*, minor) 22.3 min, t_R (*syn*, minor) 26.4 min, t_R (*anti*, major) 34.6 min, t_R (*syn*, major) 39.8 min]; $[\alpha]_D^{25}$ + 37.5 (*c* 0.1, $CHCl_3$); IR (neat) 2926, 2851, 1699, 1648, 14.86, 1437, 1388, 1247, 1021, 757 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 0.61 (d, *J*

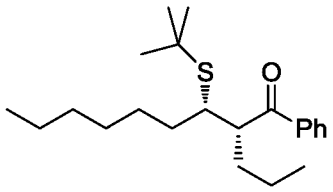
= 6.3 Hz, 3H), 0.72 (d, *J* = 6.3 Hz, 3H), 0.83-1.07 (m, 4H), 1.22 (t, *J* = 7.1 Hz, 3H), 1.41-1.49 (m, 2H), 1.72-1.82 (m, 2H), 2.96-3.05 (m, 2H), 3.50 (d, *J* = 12.2 Hz, 1H), 3.83 (d, *J* = 12.2 Hz, 1H), 7.42-7.51 (m, 2H), 7.57-7.61 (m, 1H), 7.98-8.04 (m, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 12.9, 13.2 (x2), 19.8, 20.2, 27.3, 31.6, 38.6, 49.6, 119.2, 119.8, 124.7, 138.3, 201.5; HRMS (EI) calcd for $C_{17}H_{27}OS$ *m/z* 279.1783, found 279.1789.

(*S*)-2-((*S*)-Cyclohexyl(isopropylthio)methyl)-1-phenylpentan-1-one (278d)



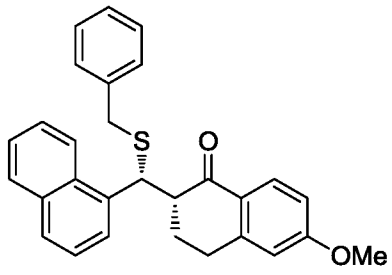
Colorless oil: *syn*:*anti* ratio > 50:1; 96% ee [Chiralcel OD-H, hexane:*i*-propanol 92:8, 0.8 mL/min, 215 nm, t_R (*syn*, major) 16.1 min, t_R (*syn*, minor) 19.2 min]; $[\alpha]_D^{25}$ + 29.3 (*c* 0.1, $CHCl_3$); IR (neat) 3056, 2957, 2919, 1685, 1597, 1448, 1346, 1217, 1179, 1007, 977, 778, 689 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 0.81-1.12 (m, 19H), 1.39-1.47 (m, 2H), 1.72-1.80 (m, 2H), 2.13-2.22 (m, 2H), 3.18 (d, *J* = 12.5 Hz, 1H), 3.96 (d, *J* = 12.5 Hz, 1H), 7.43-7.49 (m, 2H), 7.54-7.58 (m, 1H), 7.94-7.98 (m, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 13.9, 22.7, 26.2 (x2), 26.6, 27.3, 30.9, 46.9, 47.3, 39.0, 50.2, 128.8, 129.0, 134.0, 138.1, 200.8; HRMS (EI) calcd for $C_{21}H_{33}OS$ *m/z* 333.2252, found 333.2245.

(2*S*,3*S*)-3-(*tert*-Butylthio)-1-phenyl-2-propylnonan-1-one (278e)



Colorless oil: *syn*:*anti* ratio > 50:1; 95% ee [Chiralcel OD, hexane:*i*-propanol 97:3, 0.8 mL/min, 215 nm, t_R (*syn*, major) 21.3 min, t_R (*syn*, minor) 25.0 min]; $[\alpha]_D^{25}$ + 17.0 (*c* 0.1, $CHCl_3$); IR (neat) 3058, 2923, 1685, 1597, 1448, 1346, 1019, 978, 778, 760, 690 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 0.52-0.68 (m, 9H), 0.87-1.02 (m, 6H), 1.09-1.31 (m, 6H), 1.42-1.49 (m, 4H), 1.74-1.83 (m, 4H), 2.98 (d, *J* = 11.8 Hz, 1H), 3.40 (d, *J* = 11.8 Hz, 1H), 7.46-7.52 (m, 2H), 7.56-7.61 (m, 1H), 7.98-8.03 (m, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 14.2, 22.3, 24.1, 25.4, 25.9, 27.7, 28.9, 29.6 (x2), 30.4, 32.4, 46.0, 53.4, 119.7, 120.4, 134.8, 139.5, 200.9; HRMS (EI) calcd for $C_{22}H_{36}OS$ *m/z* 348.5932, found 348.5943.

(*S*)-2-((*R*)-(Benzylthio)(naphthalen-1-yl)methyl)-6-methoxy-3,4-dihydronaphthalen-1(2H)-one (278f)



White solid: mp 105 - 106 °C; *syn*:*anti* ratio > 50:1; 98% ee [Chiralcel OD, hexane:*i*-propanol 99:1, 0.8 mL/min, 215 nm, t_R (*syn*, minor) 47.4 min, t_R (*syn*, major) 53.5 min];

$[\alpha]_D^{25}$ + 103.1 (*c* 0.1, $CHCl_3$); IR (neat) 3440, 2922, 1669, 1599, 1493, 1250, 1123, 1023, 920, 778, 699 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 2.02-2.09 (m, 1H), 2.17-2.25 (m, 1H), 2.67-2.73 (m, 1H), 2.84-2.93 (m, 2H), 3.60-3.71 (m, 2H), 3.89 (s, 3H), 4.78 (d, *J* = 12.0 Hz, 1H), 6.57 (s, 1H), 6.86-6.92 (m, 1H), 7.13-7.22 (m, 5H), 7.51-7.59 (m, 3H), 7.82 (d, *J* = 8.2 Hz, 1H), 7.91 (d, *J* = 8.2 Hz, 1H), 8.09-8.20 (m, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 22.5, 28.9, 37.3, 39.6, 53.0, 55.1, 113.2, 113.7, 124.5, 126.1, 127.0, 127.2, 127.9 (x2), 128.1 (x2), 129.1, 129.3, 130.6, 130.9, 131.3, 135.5, 138.1, 138.9, 148.1, 165.3, 197.1; HRMS (EI) calcd for $C_{29}H_{26}O_2S$ *m/z* 438.1653, found 438.1643.

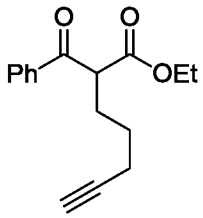
References:

1. Dai, L.; Wang, S. -X.; Chen, F. -E. *Adv. Syth. Catal.* **2010**, *352*, 2137.
2. Ricci, P.; Carone, A.; Bartoli, G.; Bosco, M.; Sambri, L.; Melchiorre, P. *Adv. Synth. Catal.* **2008**, *350*, 49.
3. McNamara, J. M.; Leazer, J. L.; Bhupathy, M.; Amato, J. S.; Reamer, R. A.; Reider, P. J.; Grabowski, E. J. J. *J. Org. Chem.* **1989**, *54*, 3718.
4. Satyanarayana, B.; Reddy, P. P. *Synth. Commun.* **2007**, *37*, 545.
5. Tian, X.; Cassani, C.; Liu, Y.; Moran, A.; Urakawa, A.; Galzerano, P.; Arceo, E.; Melchiorre, P. *J. Am. Chem. Soc.* **2011**, *133*, 17934.

CHAPTER 7

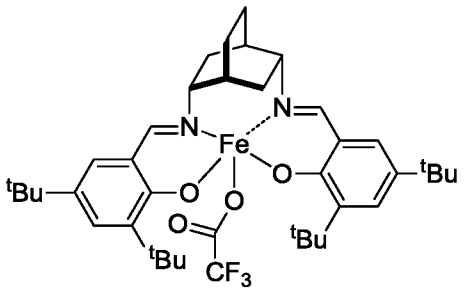
The Asymmetric Intramolecular Conia-ene Reaction

Ethyl 2-Benzoylhept-6-ynoate (303)



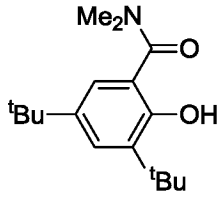
To a suspension of NaH (164 mg, 4.10 mmol, 60% in mineral oil) in DMF (6 mL) at 0 °C was added ethyl 3-oxo-3-phenylpropanoate (**301**, 750 mg, 3.9 mmol) dropwise. After being stirred at 0 °C for 10 min and at room temperature for 2 h, a solution of 5-iodo-1-pentyne (**302**, 573 mg, 3.9 mmol) in DMF (2 mL) was added dropwise over 5 min. After the addition was complete, the mixture was warmed to room temperature and stirring was continued for an additional 12 h. The reaction mixture was diluted with ether (50 mL) and was washed successively with a saturated solution of NH_4Cl (2 x 50 mL) and brine (3 x 20 mL). The organic layer was dried (Na_2SO_4) and evaporated in vacuo, and the crude residue was purified by flash chromatography (SiO_2-hexanes) to obtain **303** (856 mg, 85%) as a yellow oil: IR (neat) 3296, 2981, 2934, 1738, 1699, 1650, 1581, 1464, 1428, 1408, 1367, 1245, 1195, 1151, 1115, 1084, 1023, 990, 941, 808, 761, 737 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 0.79 - 0.99 (m, 3H), 1.12 - 120 (m, 2H), 1.42 - 1.47 (m, 1H), 1.67 - 2.71 (m, 1H), 1.96 (t, J = 2.5 Hz, 1H), 2.11 - 2.15 (m, 1H) , 2.26 (td, J = 7.0, 2.4 Hz, 2H), 4.15 - 4.21 (m, 2H), 4.33 (t, J = 7.0 Hz, 1H), 7.48 - 7.52 (m, 2H), 7.58 - 7.62 (m, 1H), 7.97 - 8.02 (m, 1H), 8.04 - 8.09 (m, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 13.9, 18.3, 26.3, 17.9, 53.8, 61.4, 68.9, 83.6, 128.6, 128.7, 133.5, 136.2, 169.8, 195.4.

(+)-(1*R*,2*R*,4*R*,5*R*)-*N*,*N*'-Bis-(3,5-di-*tert*-butylsalicylidene)-2,5-diaminobicyclo[2.2.2]octane Iron(III) Trifluoroacetate [(+)-306]



To a solution of (+)-**72** (1.99 g, 3 mmol) in CH_2Cl_2 (40 mL) at room temperature was added silver trifluoroacetate (663 mg, 3 mmol) and the mixture was stirred for 2 h, at which time a white precipitate had formed. The precipitate was removed by filtration and the filtrate was concentrated under reduced pressure to obtain (+)-**306** (2.07 g, 93%) as a brown solid: mp 212 - 213 °C; $[\alpha]^{25}_{D}$ + 103.0 (*c* 0.5 $CHCl_3$); IR (neat) 3412, 2953, 2868, 1609, 1592, 1538, 1554, 1464, 1415, 1361, 1253, 838, 749 cm^{-1}; HRMS (EI) calcd for $C_{40}H_{54}F_3FeN_2O_4$ *m*/*z* 739.7102, found 739.7106.

3,5-Di-*tert*-butyl-2-hydroxy-*N*,*N*-dimethylbenzamide (313)



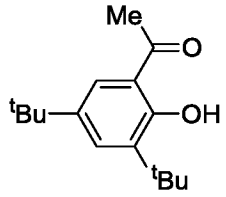
To a solution of 3,5-di-*tert*-butylsalicylic acid (**311**, 2.50 g, 10 mmol) in thionyl chloride (4.3 mL, 60 mmol) at room temperature was added a catalytic amount (5 drops) of DMF and the mixture was stirred for 12 h. Excess thionyl chloride was removed under reduced

pressure on a rotary evaporator and the residue was taken up into 25 mL of pyridine. To this mixture at 0°C were added DMAP (61 mg, 0.5 mmol) and Me_2NH (1.6 mL, 24 mmol) and the reaction mixture was warmed to room temperature. Stirring was continued for an additional 3 h. The solution was poured into 300 mL of an ice cold water containing 2N aqueous HCl (20 mL), at which time a white precipitate formed. The precipitate was filtered off and was crystallized from 100 mL of EtOH to obtain **313** (2.47 g, 89%) as a yellowish solid: mp 123 - 124 °C, [lit[1] 122 - 124 °C]; IR (neat) 3292, 2980, 2934, 2116, 1739, 1680, 1447, 1365, 1338, 1291, 1229, 1151, 1019, 988 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 1.27 (s, 9H), 1.53 (s, 9H), 3.18 (s, 6H), 7.49 (s, 1H), 7.58 (s, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 29.5, 32.4, 32.9, 33.2, 34.0, 35.6, 52.4, 117.2, 122.9, 127.8, 137.9, 139.2, 156.9, 172.5.

General Method for Synthesizing 2,4-Di-*tert*-butyl-6-acylphenols 309 and 310 from 313:

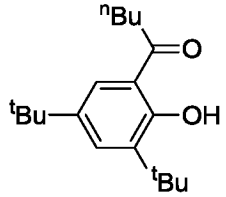
To a solution of the organolithium compound (5.07 mmol) at 0°C was added a solution of *N*,*N*-dimethyl-3,5-di-*tert*-butylsalicylamide (**313**, 670 mg, 2.42 mmol) in THF (20 mL) dropwise. After addition was complete, the reaction mixture was warmed to room temperature and was stirred for 3 h. The mixture was added to 10% aqueous HCl (100 mL) and was extracted with EtOAc (2 x 25 mL). The organic layer was washed with brine (3 x 20 mL), dried (Na_2SO_4), and evaporated in vacuo, and the crude residue was purified by flash chromatography (SiO_2-hexanes) to obtain **309** or **310**.

2,4-Di-*tert*-butyl-6-acetylphenol (309)



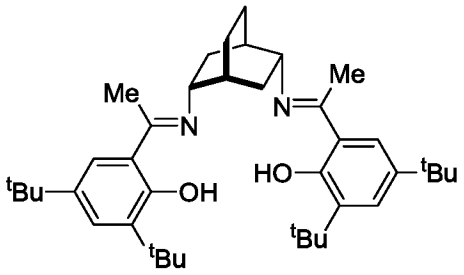
White solid: mp 48 - 49 °C, [lit[1] 47 - 49 °C]; IR (neat) 2949, 2864, 2891, 1715, 1462, 1373, 1252, 1147, 1116, 1046, 1046, 1003, 879, 836, 778, 679 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 1.55 (s, 9H), 1.72 (s, 9H), 2.61 (s, 3H), 7.59 (s, 1H), 7.63 (s, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 26.9, 29.4, 30.3, 34.4, 35.1, 119.2, 122.8, 132.2, 137.7, 139.7, 159.5, 204.6.

2,4-Di-*tert*-butyl-6-pentanoylphenol (310)



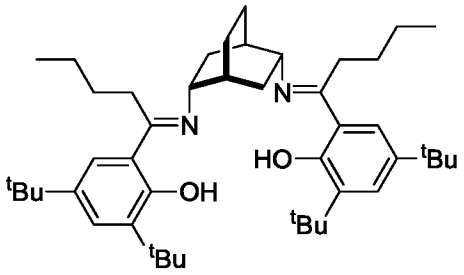
White solid: mp 60 - 61 °C, [lit[1] 61 - 63 °C]; IR (neat) 3385, 2953, 2929, 1682, 1634, 1586, 1462, 1372, 1252, 1147, 1116, 1042, 972, 832, 773 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 0.98 - 1.03 (m, 3H), 1.29 (s, 9H), 1.62 (s, 9H), 1.91 - 1.98 (m, 2H), 2.00 - 2.09 (m, 2H), 2.99 - 3.08 (m, 2H), 7.46 (s, 1H), 7.53 (s, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 14.2, 21.9, 27.3, 29.9, 30.8, 36.1, 37.2, 39.5, 119.8, 120.9, 132.4, 139.5, 142.6, 160.7, 207.4.

(+)-2,2'-[(1*R*,2*R*,4*R*,5*R*)-Bicyclo[2.2.2]octane-2,5-diylbis(nitrilomethylidine)]bis-4,6-di-*tert*-butyl-7-methylphenol [(+)-314]



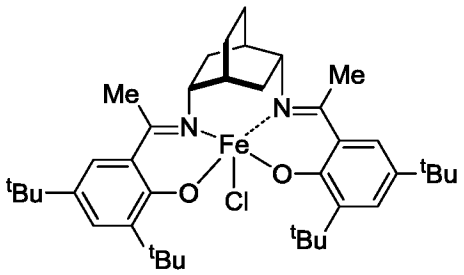
In a manner analogous to the condensation of (-)-**34** with **47** to give (+)-**35**, (-)-**34** (106 mg, 0.76 mmol) was reacted with **309** (375 mg, 1.52 mmol) to afford (+)-**314** (421 mg, 92%) as a yellow solid: mp 252 - 253 °C; $[\alpha]^{25}_{D}$ + 172.2 (*c* 1.2 , $CHCl_3$); IR (neat) 2953, 2929, 2855, 2883, 1731, 1645, 1474, 1408, 1361, 1287, 1256, 1158, 1112, 1084, 937, 835, 812, 781 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 1.31 (s, 18H), 1.43 (s, 18H), 1.69 (s, 6H), 1.89 - 1.96 (m, 2H), 2.15 - 2.24 (m, 2H) , 2.73 - 2.85 (m, 6H), 3.44 - 3.54 (m, 2H), 7.11 (d, *J* = 2.2 Hz, 2H), 7.38 (d, *J* = 2.2 Hz, 2H), 13.81 (s, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 24.2, 29.5, 29.8, 31.9, 32.6, 34.4, 35.1, 66.7, 118.9, 125.8, 126.9, 136.7, 139.9, 158.3, 163.7; HRMS (EI) calcd for $C_{40}H_{61}N_2O_2$ (M+H) *m/z* 601.4733, found 601.4712.

(+)-2,2'-[(1*R*,2*R*,4*R*,5*R*)-Bicyclo[2.2.2]octane-2,5-diylbis(nitrilomethylidine)]bis-4,6-di-*tert*-butyl-7-butylphenol [(+)-315]



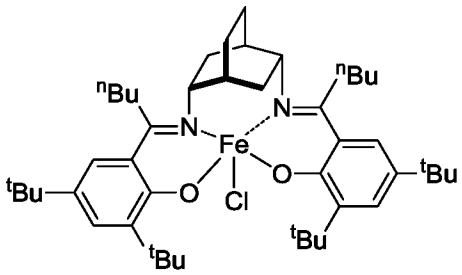
In a manner analogous to the condensation of (-)-**34** with **47** to give (+)-**35**, (-)-**34** (168 mg, 1.20 mmol) was reacted with **310** (697 mg, 2.40 mmol) to afford (+)-**315** (667 mg, 81%) as a yellow solid: mp 253 - 254 °C; $[\alpha]^{25}_{D}$ + 166.8 (*c* 0.6 , $CHCl_3$); IR (neat) 3494, 2957, 2930, 2855, 2882, 1730, 1477, 1461, 1390, 1284, 1252, 1153, 1102, 1055, 1003, 838, 778 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 1.23 - 1.25 (m, 6H), 1.27 (s, 18H), 1.29 - 1.33 (m, 2H), 1.36 - 1.44 (m, 6H), 1.47 (s, 18H), 1.50 - 1.54 (m, 4H), 2.41 (s, 2H), 2.65 – 2.74 (m, 4H), 2.91 - 2.98 (m, 2H), 3.08 - 3.12 (m, 2H), 3.35 - 3.40 (m, 2H), 7.26 (d, *J* = 2.2 Hz, 2H), 7.29 (d, *J* = 2.2 Hz, 2H), 10.42 (bs, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 11.2, 21.2, 24.3, 29.4, 29.7, 30.1, 31.4, 34.1, 35.0, 35.8, 66.6, 122.7, 125.4, 125.8, 136.1, 141.6, 156.3; HRMS (ESI) calcd for $C_{46}H_{72}N_2O_2$ *m/z* 685.5672, found 685.5680.

(+)-(1*R*,2*R*,4*R*,5*R*)-*N*,*N*'-Bis-(3,5-di-*tert*-butyl-7-methylsalicylidene)-2,5-diaminobicyclo[2.2.2]octane Iron(III) Chloride [(+)-316]



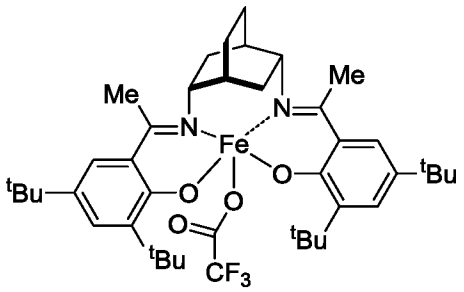
In a manner analogous to the reaction of (+)-**35** with $FeCl_3$ to give (+)-**72**, (+)-**314** (410 mg, 0.68 mmol) was treated with $FeCl_3$ (191 mg, 1.18 mmol) to afford (+)-**316** (451 mg, 96%) as a dark brown solid: mp 203 - 204 °C; $[\alpha]^{25}_D$ + 103.5 (*c* 0.3, $CHCl_3$); IR (neat) 2953, 2867, 1612, 1595, 1537, 1467, 1416, 1361, 1255, 1273, 1202, 1179, 1108, 982, 908, 837, 733 cm^{-1}; HRMS (ESI) calcd for $C_{40}H_{58}ClFeN_2O_2$ *m/z* 690.2091, found 690.2087.

(+)-(1*R*,2*R*,4*R*,5*R*)-*N*,*N*'-Bis-(3,5-di-*tert*-butyl-7-butylsalicylidene)-2,5-diaminobicyclo[2.2.2]octane Iron(III) Chloride [(+)-317]



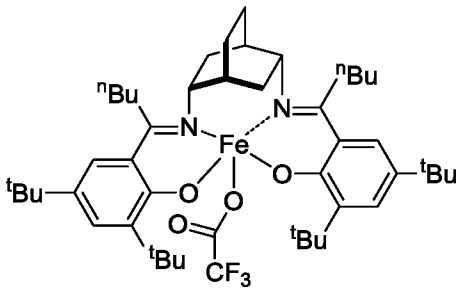
In a manner analogous to the reaction of (+)-**35** with $FeCl_3$ to give (+)-**72**, (+)-**315** (690 mg, 1.01 mmol) was treated with $FeCl_3$ (282 mg, 1.74 mmol) to afford (+)-**317** (713 mg, 91%) as a dark brown solid: mp 207 - 208 °C; $[\alpha]^{25}_D$ + 136.0 (*c* 1.0, $CHCl_3$); IR (neat) 2954, 2868, 1653, 1608, 1592, 1538, 1463, 1414, 1361, 1253, 1179, 1108, 837, 748 cm^{-1}; HRMS (ESI) calcd for $C_{46}H_{70}ClFeN_2O_2$ *m/z* 774.3599, found 774.3602.

(+)-(1*R*,2*R*,4*R*,5*R*)-*N*,*N*'-Bis-(3,5-di-*tert*-butyl-7-methylsalicylidene)-2,5-diaminobicyclo[2.2.2]octane Iron(III) Trifluoroacetate [(+)-307]



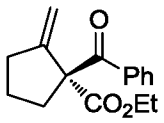
In a manner analogous to the reaction of (+)-**72** with CF_3CO_2Ag to give (+)-**306**, (+)-**316** (440 mg, 0.64 mmol) was treated with CF_3CO_2Ag (141 mg, 0.64 mmol) to afford (+)-**307** (457 mg, 90%) as a dark brown solid: mp 222 - 223 °C; $[\alpha]^{25}_{D}$ + 95.3 (*c* 0.5, $CHCl_3$); IR (neat) 2951, 2865, 1610, 1599, 1531, 1466, 1415, 1361, 1326, 1257, 1175, 1108, 1026, 836, 788 cm^{-1}; HRMS (ESI) calcd for $C_{42}H_{58}F_3FeN_2O_4$ *m*/*z* 767.7603, found 767. 7592.

(+)-(1*R*,2*R*,4*R*,5*R*)-*N*,*N*'-Bis-(3,5-di-*tert*-butyl-7-butylsalicylidene)-2,5-diaminobicyclo[2.2.2]octane Iron(III) Trifluoroacetate [(+)-308]



In a manner analogous to the reaction of (+)-**72** with CF_3CO_2Ag to give (+)-**306**, (+)-**317** (700 mg, 0.90 mmol) was treaed with CF_3CO_2Ag (199 mg, 0.90 mmol) to afford (+)-**308** (645 mg, 84%) as a dark brown solid: mp 236 - 238 °C; $[\alpha]^{25}_D$ + 83.2 (*c* 0.3, $CHCl_3$); IR (neat) 2945, 2862, 1609, 1599, 1545, 1532, 1461, 1436, 1415, 1359, 1317, 1256, 1273, 1243, 1203, 1180, 1109, 873, 837, 783, 744 cm^{-1}; HRMS (ESI) calcd for $C_{48}H_{70}F_3FeN_2O_4$ *m/z* 851.9221, found 851.9217.

(*R*)-Ethyl 1-Benzoyl-2-methylenecyclopentanecarboxylate (304)



To a solution of **303** (64.5 mg, 0.25 mmol) in $CHCl_3$ (4 mL) was added (+)-**308** and the reaction mixture was heated at 60 °C for 24 h. The solvent was evaporated and the crude residue was purified by flash chromatography (SiO_2, hexanes) to obtain **304** (60.0 mg, 93%) as a yellow oil: 87% ee [Chiralcel OD, hexane:*i*-propanol 98:2, 1.0 mL/min, t_R (minor) 11.4 min, t_R (major) 21.4 min]; $[\alpha]_D^{25}$ + 154.3 (*c* 0.2, CH_2Cl_2), [lit.[2] $[\alpha]_D^{22}$ + 152.8 (*c* 0.72, $CHCl_3$, 86% ee)]; IR (neat) 2960, 2921, 1734, 1684, 1443, 1267, 1240, 1209, 1155, 1077 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 1.10 (t, *J* = 6.7 Hz, 3H), 1.62 - 1.72 (m, 1H), 1.82 - 1.94 (m, 1H), 2.17 - 2.24 (m, 1H), 2.50 - 2.29 (m, 2H), 2.87 - 2.93 (m, 1H), 4.19 (q, *J* = 6.7 Hz, 2H), 5.26 (d, *J* = 1.7 Hz, 1H), 5.39 (d, *J* = 1.7 Hz, 1H), 7.41 - 7.49 (m, 2H). 7.41 - 7.49 (m, 2H).7.52 - 7.58 (m, 1H), 7.79 (d, *J* = 7.8 Hz, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 13.3, 24.0, 36.7, 38.8, 60.9, 67.9, 113.4, 129.6, 129.9, 131.8, 135.7, 150.2, 172.7, 196.2.

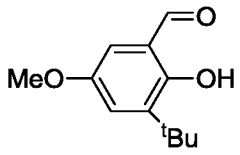
References:

1. Jimenez, C. A.; Belmar, J. B. *Synth. Comm.* **2007**, *37*, 2391.
2. Matsuzawa, A.; Mashiko, T.; Kumagai, N.; Shibasaki, M. *Angew. Chem. Int. Ed.* **2011**, *50*, 7616.

CHAPTER 8

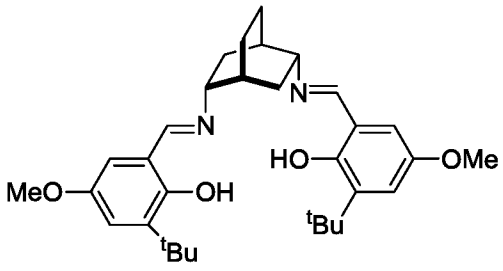
Asymmetric Cyclopropanation

3-(*tert*-Butyl)-2-hydroxy-5-methoxybenzaldehyde (367)



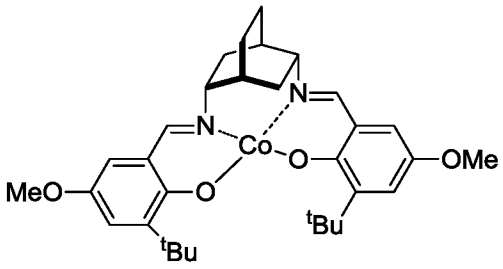
To a solution of 2-(*tert*-butyl)-4-methoxyphenol (**366**, 721 mg, 4 mmol) in CH_3CN (20 mL) at room temperature were added Et_3N (2.8 mL, 20 mmol) and $MgCl_2$ (456 mg, 4.8 mmol) and the mixture was stirred for 15 min. Paraformaldehyde (600 mg, 20 mmol) was added and the solution was refluxed for 10 h. The solution was cooled to room temperature, poured into 1M aqueous HCl (100 mL) and stirred for 30 min at room temperature. The reaction mixture was extracted with ether (4 x 100 mL) and the organic layer was washed with brine (20 mL), dried (Na_2SO_4) and concentrated under reduced pressure. The crude residue was purified by flash chromatography on silica gel (5% ether/hexanes) to obtain **367** (609 mg, 73%) as a yellow oil: IR (neat) 3534, 3301, 3062, 2925, 2854, 1622, 1598, 1508, 1472, 1422, 1378, 1206, 1149, 1967, 1030, 854, 836, 814, 749, 693 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 1.42 (s, 9H), 3.04 (s, 3H), 7.40 (s, 1H), 7.62 (s, 1H), 9.91 (s, 1H), 11.68 (s, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 29.7, 32.9, 54.7, 113.4, 119.3, 129.8, 140.3, 150.5, 152.1, 207.4.

(+)-2,2'-[(1*R*,2*R*,4*R*,5*R*)-Bicyclo[2.2.2]octane-2,5-diylbis(nitrilomethylidine)]bis-2-*tert*-butyl-4-methoxylphenol [(+)-368]



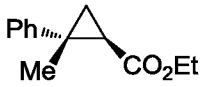
To a solution of (-)-**34** (86 mg, 0.61 mmol) in EtOH (15 mL) was added anhydrous $MgSO_4$ (367 mg, 3.05 mmol) followed by a solution of **367** (256 mg 1.23 mmol) in EtOH (5 mL). The suspension was refluxed for 4 h at which time a yellow precipitate had formed. The mixture was cooled to room temperature and the precipitate was filtered off. The crude solid was purified by flash chromatography on silica gel (5% EtOAc/hexanes) to give (+)-**368** (293 mg, 92%) as an amorphous yellow solid: mp 162 - 163 °C; $[\alpha]^{25}_{D}$ + 96.6 (*c* 0.5 , CH_2Cl_2); IR (neat) 3358 (b), 1744, 1467, 1375, 1286, 1169, 1137, 1030, 891 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 1.38 (s, 9H), 1.73 (s, 3H), 1.91 - 2.01 (m, 1H), 2.12 - 2.24 (m, 1H) , 3.53 - 3.57 (m, 1H), 3.92 (s, 3H), 7.12 (d, *J* = 2.4 Hz, 1H), 7.38 (d, *J* = 2.4 Hz, 1H), 8.43 (s, 1H), 13.86 (s, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 23.9, 31.3, 31.6, 33.9, 34.2, 57, 7, 67.5, 118.4, 128.6, 128.8, 137.1, 139.7, 159.0, 165.6; HRMS (EI) calcd for $C_{32}H_{44}N_2O_4$ *m/z* 520.7131, found 520.7128.

(+)-(1*R*,2*R*,4*R*,5*R*)-*N*,*N*'-Bis-(3-*tert*-butyl-5-methoxylsalicylidene)-2,5-diaminobicyclo[2.2.2]octane Cobalt(II) [(+)-369]



To a solution of (+)-**368** (290 mg, 0.56 mmol) in EtOH (15 mL) was added a solution of $Co(OAc)_2$ (99 mg, 0.56 mmol) in EtOH (2 mL) and the mixture was heated at reflux for 6 h, at which time an orange precipitate had formed. The mixture was cooled to room temperature and concentrated under reduced pressure. The crude residue was dissolved in CH_2Cl_2 and filtered. Concentration of the filtrate under vacuum provided (+)-**369** (324 mg, 94%) as an orange solid: mp > 260 °C; $[\alpha]^{25}_D$ + 86.0 (*c* 0.26 $CHCl_3$); IR (neat) 2949, 2859, 1606, 1594, 1548, 1528, 1458, 1411, 1361, 1314, 1252, 1178, 1108, 1084, 1011, 960, 867, 839 cm^{-1}; HRMS (EI) calcd for $C_{32}H_{42}CoN_2O_4$ *m/z* 577.4733, found 577.4716.

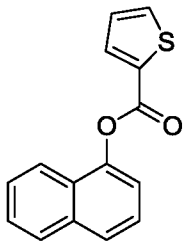
(1*R*,2*R*)-Ethyl 2-Methyl-2-phenylcyclopropanecarboxylate (364)



To a solution of (+)-**369** (9 mg, 15 μmol) in CH_2Cl_2 (1.5 mL) was added KSAc (2 mg, 15 μmol) and the mixture was stirred at room temperature for 1 h. Ethyl diazoacetate (32 μL, 0.3 mmol) and α-methylstyrene (58 μL, 0.45 mmol) were added to the reaction mixture and stirring was continued for an additional 28 h. The reaction mixture was passed through a short column of Celite which was eluted with CH_2Cl_2. The effluent was evaporated and the crude residue was purified by flash chromatography (SiO_2, hexanes) to give **304** (57 mg, 93%) as a pale yellow oil: *syn*:*anti* ratio 31:1; 93% ee [Chiralcel OD-

H, hexane:*i*-propanol 98:2, 0.5 mL/min, 215 nm, t_R [(1*S*,2*S*), minor] 22.4 min, t_R [(1*R*,2*R*), major] 38.2 min]; $[\alpha]_D^{22}$ - 291.1 (*c* 0.5, CH_2Cl_2), [lit[1] for (1*S*,2*S*) isomer $[\alpha]_D^{20}$ + 286.0 (*c* 0.3, $CHCl_3$); IR (neat) 2977, 2935, 1724, 1615, 1252, 1178, 1086, 1034, 848, 816, 790 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 1.26 (t, *J* = 7.4 Hz, 3H), 1.38 - 1.41 (m, 2H), 1.52 (s, 3H), 1.97 (dd, *J* = 8.2, 6.0 Hz, 1H), 4.10 - 4.19 (m, 2H), 7.16 - 7.24 (m, 2H), 7.27 - 7.41 (m, 3H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 15.3, 19.8, 21.3, 27.8, 30.6, 60.6, 127.3, 128.6, 128.9, 146.2, 173.1.

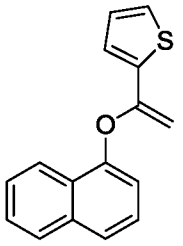
1-Naphthyl Thiophen-2-carboxylate (373)



To a solution of 2-thiophenecarbonyl chloride (**374**, 1.25 g, 8.53 mmol) in THF (30 mL) at 0°C was added a solution of 1-naphthol (**375**, 2.76 g, 19.15 mmol) in THF (20 mL) dropwise. After addition was complete, the solution was stirred at room temperature for 10 min and Et_3N (2.8 mL, 20 mmol) was added. A colorless solid was precipitated immediately and the suspension was stirred for 14 h. The reaction mixture was quenched with 5M aquoues HCl (20 mL) and was extracted with CH_2Cl_2 (4 x 120 mL). The organic layer was dried (Na_2SO_4) and evaporated in vacuo, and the crude residue was purified by flash chromatography (SiO_2-hexanes) to afford **373** (2.16 g, 100%) as an amorphous colorless solid: mp 73 - 74 °C, [lit[2] 70 - 75 °C]; IR (neat) 3295, 2980, 2934, 1738, 1698, 1650, 1580, 1560, 1463, 1428, 1408, 1367, 1244, 1195, 1151, 1084, 1022, 990, 941, 808,

760, 736 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.29 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.43 - 7.58 (m, 1H), 7.52 - 7.58 (m, 3H), 7.75 (d, *J* = 7.8 Hz, 1H), 7.80 - 7.84 (m, 1H), 7.92 (d, *J* = 8 Hz, 1H), 7.97 - 8.05 (m, 1H), 8.12 - 8.16 (m, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 118.3, 121.6, 125.2, 126.0, 126.4, 126.7, 128.0, 128.2, 132.7, 133.5, 134.7, 134.9, 146.5, 161.0.

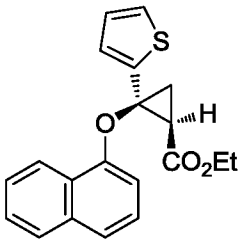
2-(1-(Naphthalen-1-yloxy)vinyl)thiophene (372)



A solution of **373** (1.27 g, 5.0 mmol) in THF (10 mL) was syringed into a flask containing Tebbe reagent,[3] prepared from titanocene dichloride (1.91 g, 7.70 mmol) and trimethylaluminum (7.70 mL of 2M solution in toluene, 112 mmol), at room temperature. The slurry was stirred for 24 h at room temperature and was diluted with ether (15 mL). The reaction mixture was extracted with ether (2 x 10 mL), washed with 1M aqueous NaOH (2 x 10 mL), dried (Na_2SO_4) and evaporated. The crude residue was passed through a short path of neutral silica, eluting with ether (120 mL) containing 5% Et_3N. The effluent was concentrated in vacuo and the crude residue was purified by flash chromatography on silica gel (95% hexanes, 5% Et_3N) to give **372** (986 mg, 78%) as a brown oil: IR (neat) 2929, 2858, 1652, 1457, 1258, 1073, 750 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 4.29 (d, *J* = 3.1 Hz, 1H), 4.99 (d, *J* =3.1 Hz, 1H), 7.05 - 7.10 (m, 1H), 7.26 - 7.29 (m, 1H), 7.30 - 7.34 (m, 1H), 7.42 -7.50 (m, 2H), 7.51 - 7.59 (m, 2H), 7.68 - 7.74

(m, 1H), 7.89 - 7.96 (m, 1H), 8.18 - 8.23 (m, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 90.7, 114.8, 116.9, 122.3, 124.7, 124.9, 125.8, 125.9, 126.3, 127.0, 127.6, 128.0, 135.3, 139.5, 151.7, 155.8.

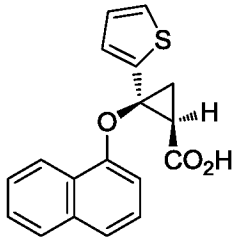
(1*R*,2*S*)-Ethyl 2-(Naphthalen-1-yloxy)-2-(thiophen-2-yl)cyclopropanecarboxylate [(+)-371]



In a manner analogous to the reaction of α-methylstyrene (**363**) with ethyl diazoacetate to give (*E*)-**364**, **372** (151 mg, 0.60 mmol) was treated with ethyl diazoacetate (42 μL, 0.40 mmol) to afford (+)-**371** (118 mg, 88%) as a yellow oil: *syn*:*anti* ratio 17:1; 94% ee [Chiralcel OJ, hexane:*i*-propanol 98:2, 0.5 mL/min, 215 nm, t_R [(1*S*,2*R*), minor] 16.3 min, t_R [(1*R*,2*S*), major] 26.7 min]; $[\alpha]_D^{22}$ + 36.3 (*c* 0.5, $CHCl_3$); IR (neat) 3473, 3029, 2931, 1735, 1496, 1454, 1380, 1260, 1174, 1037, 734, 697 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 1.21 (t, *J* = 6.9 Hz, 3H), 1.88 - 1.97 (m, 1H), 2.37 (s, 3H), 1.97 (dd, *J* = 8.2, 6.0 Hz, 1H), 2.38 (t, *J* = 6.7 Hz, 1H), 2.79 (dd, *J* = 9.9, 7.5 Hz, 1H), 4.01 (q, *J* = 6.9 Hz, 2H), 6.81 - 6.91 (m, 1H), 7.02 - 7.05 (m, 1H), 7.05 - 7.15 (m, 1H), 7.16 -7.21 (m, 1H), 7.22 - 7.27 (m, 1H), 7.28 - 7.30 (m, 1H), 7.32 - 7.40 (m, 2H), 7.41 - 7.47 (m, 1H), 7.67 - 7.72 (m, 1H), 8.12 - 8.22 (m, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 15.5, 24.2, 32.9, 61.8, 63.4,

108.4, 121.6, 122.0, 124.8, 125.2, 125.9, 126.2, 126.9, 127.7, 127.9, 128.1, 134.5, 135.6, 151.8, 169.3; HRMS (EI) calcd for $C_{20}H_{19}O_3S$ (M+H) *m/z* 339.1055, found 339.1055.

(1*R*,2*S*)-2-(Naphthalen-1-yloxy)-2-(thiophen-2-yl)cyclopropanecarboxylic Acid [(+)-376]



To a solution of (+)-**371** (113 mg, 0.33 mmol) in THF (8 mL) was added $LiOH.H_2O$ (48 mg, 2 mmol) followed by H_2O (2 mL). The mixture was stirred at room temperature for 24 h and was acidified with 1M HCl to pH 6. The reaction mixture was extracted with ether (2 x 50 mL), dried (Na_2SO_4) and evaporated to obtain (+)-**376** (99 mg, 96%) as a white solid: mp 169 - 170 °C, [lit[2] for racemate 167 - 168 °C]; $[\alpha]_D^{20}$ + 54.2 (*c* 0.4, MeOH), [lit[2] for (1*S*,2*R*) isomer $[\alpha]_D^{25}$ - 51.4 (*c* 0.07, $CHCl_3$)]; IR (neat) 3537, 2983, 2938, 1739, 1465, 1445, 1407, 1368, 1282, 1176, 1114, 1027 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 1.99 (dd, *J* = 9.1, 6.2 Hz, 1H), 2.12 (t, *J* = 7.3 Hz, 1H), 2.83 (dd, *J* = 9.1, 8.3 Hz, 1H), 6.94 (dd, *J* = 5.2, 4.7 Hz, 1H), 7.13 (d, J = 8.0 Hz, 1H), 7.20 - 7.29 (m, 3H), 7.42 (d, *J* = 8.0 Hz, 1H), 7.51 (t, *J* = 3.1 Hz, 1H), 7.62 (d, *J* = 3.1 Hz, 1H), 7.72 - 7.76 (m, 1H), 8.18 - 8.22 (m, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 20.9, 33.7, 64.2, 110.2, 120.4, 120.8, 121.3, 121.7, 122.0, 123.4, 125.6, 128.6, 129.8, 129.7, 138.7, 144.3, 158..7, 173.5.

References:

1. Berkessel, A.; Kaiser, P.; Lex, J. *Chem Eur. J.* **2003**, *9*, 4746.

2. White, J. D.; Juniku, R.; Huang, K.; Yang., J.; Wong, D. T. *J. Med. Chem.* **2009**, *52*, 5872.

3. Tebbe, F. N.; Parshall, G. W.; Reddy, G. S. *J. Am. Chem. Soc.* **1978**, *100*, 3611.

BIBLIOGRAPHY

Aksani, R.; Eichenauer, H.; Kohler, J. *Chem. Ber*. **1982**, *115*, 748.

Allingham, M. T.; Howard-Jones, A.; Murphy, P. J.; Thomas, D. A.; Caulkett, P. W. R. *Tetrahedron Lett*. **2003**, *44*, 8677.

Anada, M.; Washio, T.; Shimada, N.; Kitagaki, S.; Nakajima, M.; Shiro, M.; Hashimoto, S. *Angew. Chem. Int. Ed*. **2004**, *43*, 2665.

Anding, B. J.; Ellern, A.; Woo, L. K. *Organometallics* **2012**, *31*, 3628.

Arai, T.; Watanabe, M.; Fujiwara, A.; Yokoyama, N.. Yanagisawa, A. *Angew. Chem. Int. Ed*. **2006**, *45*, 5978.

Arai, T.; Watanabe, M.; Yanagisawa, A. *Org. Lett*. **2007**, *9*, 3595.

Arai, T.; Yamada, Y. M. A.; Yamamoto, N.; Sasai, H.; Shibasaki, M. *Chem. Eur. J*. **1996**, *2*, 1368.

B. Satyanarayana, P. P. Reddy, *Synth. Commun*. **2007**, *37*, 545.

Bachmann, S.; Furler, M.; Mezzetti, A. *Organometallics* **2001**, *20*, 2102.

Bachmann, S.; Mezzetti, A. *Helv. Chim. Acta* **2001**, *84*, 3063.

Baldoli, C.; Maiorana, S.; Licandro, E.; Zinzalla, G.; Lanfranchi, M.; Tiripicchio, A. *Tetrahedron: Asymmetry* **2001**, *12*, 2159.

Baldwin, J. E. *J. Chem. Soc. Chem. Commun*. **1976**, 734.

Balme, G.; Bouyssi, D.; Faure, R.; Gore, J.; Hemelryck,B. V. *Tetrahedron* **1992**, *48*, 3891.

Bandini, M.; Cozzi, P.; Melchiorre, P.; Umani-Ronchi, A. *Angew. Chem. Int. Ed.*, **1999**, *38*, 3357.

Bandini, M.; Giorgio, P.; Umani-Ronchi, A. *Tetrahedron* **2001**, *57*, 835.

Bandini, M.; Piccinelli, F.; Tommasi, S.; Umani-Ronchi, A.; Ventrici, C. *Chem. Commun*. **2007**, 616.

Barberis, M.; Perez-Prieto, J.; Herbst, K.; Lahuerta, P. *Organometallics* **2002**, *21*, 1667.

Bartoli, G.; Bosco, M.; Carlone, A.; Pesciaioli, F.; Sambri, L.; Melchiorre, P. *Org. Lett.* **2007**, *9*, 1403.

Belokon, Y. N.; Fuentes, J.; North, M.; Steed, J. W. *Tetrahedron*, **2004**, *60*, 3191.

Berkessel, A.; Kaiser, P.; Lex, J. *Chem-Eur. J.* **2003**, *9*, 4746.

Berkessel, A.; Menche, D.; Sklorz, C. A.; Schroder, M.; Paterson, I. *Angew. Chem. Int. Ed*. **2003**, *42*, 1032.

Berkessel, A.; Schroder, M.; Sklorz, C. A.; Tabanella, S.; Vogl,N.; Lex, J.; Neudorfl, J. M. *J. Org. Chem*. **2004**, *69*, 3050.

Berkessel, A.; Vogl, N. *Eur. J. Org. Chem*. **2006**, 5029.

Bierstedt, A.; Stoltting, J.; Metz, P. *Tetrahedron: Asymmetry* **2001**, *12*, 3399.

Blaser, H. U. *Chem. Rev*. **1992**, *92*, 935.

Blay, G.; Climent, E.; Fernández, I.; Hernández-Olmos, V.; Pedro, J. R. *Tetrahedron: Asymmetry* **2006**, *17*, 2046.

Blay, G.; Climent, E.; Fernández, I.; Hernández-Olmos, V.; Pedro, J. R. *Tetrahedron: Asymmetry* **2007**, *18*, 1603.

Blay, G.; Domingo, L. R.; Olmos, V. H.; Pedro, J. R. *Chem. Eur. J.* **2008**, *14*, 4725.

Boger, D. L.; Patel, M.; Takusagawa, F. *J. Org. Chem.* **1985**, *50*, 1911.

Boger, D. L.; Patel, M.; Takusagawa, F. *J. Org. Chem.* **1985**, *50*, 1911.

Boger, D. L.; Weinreb, S. M. *Hetero-Diels–Alder Methodology in Organic Synthesis*; Wasserman, H. H., Ed.; Academic: San Diego, CA, **1987**.

Bonaccorsi, C.; Bachmann, S.; Mezzetti, A. *Tetrahedron-Asymmetry* **2003**, *14*, 845.

Bonaccorsi, C.; Mezzetti, A. *Organometallics* **2005**, *24*, 4953.

Bouyssi, D.; Monteiro, N.; Balme, G. *Tetrahedron Lett.* **1999**, *40*, 1297.

Branco, L. C.; Gois, P. M. P.; Lourenço, N. M. T.; Kurteva, V. B.; Afonso, C. A. M. *Chem. Commun.* **2006**, 2371.

Bren, L. Frances Oldham Kelsey: FDA Medical Reviewer Leaves Her Mark on History. *FDA Consumer–U.S. Food and Drug Admin.* **2001**, *35*, *No. 2*.

Brimble, M. A.; Bryant, C. *Org. Biomol. Chem.* **2007**, *5*, 2858.

Bykowski, D.; Wu, K. H.; Doyle, M. P. *J. Am. Chem. Soc.* **2006**, *128*, 16038.

Caglioti, L. *Tetrahedron* **1966**, *22*, 487.

Chakraborty, J.; Samanta, B.; Pilet, G.; Mitra, S. *Struct. Chem.* **2006**, *17*, 585.

Chan, L. Y.; Kim, S.; Park, Y.; Lee, P. H. *J. Org. Chem.* **2012**, *77*, 5239.

Charette, A. B.; Bouchard, J. E. *Can. J. Chem.* **2005**, *83*, 533.

Charette, A. B.; Juteau, H. *J. Am. Chem. Soc.* **1994**, *116*, 2651.

Che, C. M.; Huang, J. S.; Lee, F. W.; Li, Y.; Lai, T. S.; Kwong, H. L.; Teng, P. F.; Lee, W. S.; Lo, W. C.; Peng, S. M.; Zhou, Z. Y. *J. Am. Chem. Soc.* **2001**, *123*, 4119.

Chen, C. S.; Shieh, W. R.; Lu, P. H.; Harriman, S.; Che, C. Y. *Biochimica et Biophysica Acta*, **1991**, *1078*, 411.

Chen, C.; Tagami, K.; Kishi, Y. *J. Org. Chem.* **1995**, 60, 5386.

Chen, Y.; Fields, K. B.; Zhang, X. P. *J. Am. Chem. Soc.* **2004**, *126*, 14718.

Chen, Y.; Ruppel, J. V.; Zhang, X. P. *J. Am. Chem. Soc.* **2007**, *129*, 12074.

Chen, Y.; Zhang, X. P. *J. Org. Chem.* **2007**, *72*, 5931.

Chen, Y.; Zhang, X. P. *Synthesis* **2006**, 1697.

Cheng, H. G.; Lu, L. Q.; Wang, T.; Chen, J. R.; Xiao, W. J. *Chem. Commun.* **2012**, *48*, 5596.

Chinchilla, R.; Najera, C.; Sanchez-Agullo, P. *Tetrahedron:Asymmetry* **1994**, *5*, 1393.

Chretien, J. M.; Zammattio, F.; Gauthier, D.; Grongnce, E. L.; Paris, M.; Quintard, J. P. *Chem. Eur. J.* **2006**, *12*, 6816.

Clayden, J.; MacLellan, P. *Beilstein J. Org. Chem.* **2011,** *7,* 582.

Coe, B. J.; Glenwright, S. J. *Coord. Chem. Rev.* **2000**, *203*, 5.

Conia, J. M.; P. Le Perchec, P. L. *Synthesis* **1975**, 1.

Corey, E. J. *Angew. Chem., Int. Ed.* **2002**, *41*, 1650.

Corkey, B. K.; F. D. Toste, *J. Am Chem. Soc.* **2005**, *125*, 17168.

Coucouvanis, D.; Lippard, S. J.; Zubieta, J. A. *J. Am. Chem. Soc.* **1970**, *92*, 3342-3347.

Cozzi, P. G. *Chem. Soc. Rev.*, **2004**, *33*, 410.

Cruciani, P.; Stammler, R.; Aubert, C.; Malacria, M. *J. Org. Chem.* **1996**, *61*, 2699.

Cruickshank, J. M. *Lancet*, **2010**, *376*, 415.

Da, C. S.; Wang, J. R.; Yin, X. G.; Fan, X. Y.; Liu, Y.; Yu, S. L. *Org. Lett.* 2**009**, *11*, 5578.

Dai, L.; Wang, S. -X.; Chen, F. -E. *Adv. Syth. Catal.* **2010**, *352*, 2137.

Dansihefsky, S. J.; Armistead, D. M.; Selnick, H. G.; Wincott, F. E.; Hungate, *R. J. Am. Chem. Soc.* **1987**, *109*, 119.

Darensbourg, D. J.; Yarbrough, J. C. *J. Am. Chem. Soc.* **2002**, *124*, 6335.

Davies, H. M. L. *Eur. J. Org. Chem.* **1999**, 2459.

Davies, H. M. L.; Antoulinakis, E. *Org. React.* **2001**, *57*, 1.

Davies, H. M. L.; Bruzinski, P. R.; Lake, D. H.; Kong, N.; Fall, M. J. *J. Am.Chem. Soc.* **1996**, *118*, 6897.

De Vries, J. G. *Encyclopedia of Catalysis*, Vol 3. (Ed.: I. T. Horváth), Wiley, New York, **2003**, p. 295.

De, C. K.; Klauber, E. G.; Seidel, D. *J. Am. Chem. Soc.* **2009**, *131*, 17060.

Denes, F. D.; Perez-Luna, A.; Chemla, F. *Chem. Rev.* **2010**, *110*, 2366.

Deng, C. L.; Song, R. J.; Liu, Y. L.; Li, J. H. *Adv. Synth. Catal.* **2009**, *351*, 3096.

Deng, C. L.; Zou, T.; Wang, Z. Q.; Song, R. J.; Li, J. H. *J. Org. Chem.* **2009**, *74*, 412.

Denton, J. R.; Sukumaran, D.; Davies, H. M. L. *Org. Lett.* **2007**, *9*, 2625.

Didier, D.; Bouvier, C. M.; Schulz, E. *Adv. Synth. Catal.* **2011**, *353*, 1087.

Diehl, H.; Hach, C. C. *Inorg. Synth.* **1950**, *3*, 196.

Dines, M.B.; Bird, P.H. *J. Chem. Soc. Chem. Commun.* **1973**, 12.

Donaldson, W. A. *Tetrahedron* **2001**, *57*, 8589.

Dong, X.; Fang, X.; Tao, H.; Zhou, X.; Wang, C. *Adv. Synth. Catal.* **2012**, *354*, 1141.

Dossetter, A. G.; Jamison, T. F.; and Jacobsen, E. N. *Angew.Chem., Int. Ed.* **1999**, *38*, 2398.

Doyle, M. P.; Austin, R. E.; Bailey, A. S.; Dwyer, M. P.; Dyatkin, A. B.; Kalinin, A. V.; Kwan, M. M. Y.; Liras, S.; Oalmann, C. J.; Pieters, R. J.; Protopopova, M. N.; Raab, C. E.; Roos, G. H. P.; Zhou, Q. L.; Martin, S. F. *J. Am. Chem. Soc.* **1995**, *117*, 5763.

Doyle, M. P.; Forbes, D. C. *Chem. Rev.* **1998**, *98*, 911.

Doyle, M. P.; Pieters, R. J.; Martin, S. F.; Austin, R. E.; Oalmann, C. J.; Muller, P. *J. Am. Chem. Soc.* **1991**, *113*, 1423.

Du, H.; Zhang, X.; Wang, Z.; Bao, H.; You, T.; Ding, K. *Eur. J. Org. Chem.* **2008**, 2248.

Du, H.; Zhao, D.; and Ding, K. *Chem. Eur. J.* **2004**, *10*, 5964

Dukes, M.; Smith, L. H. *J. Med. Chem.* **1971**, *14*, 326.

Duthion, B.; Metro, T. X.; Pardo, D. G.; Cossy, J. *Tetrahedron* **2009**, *65*, 6696.

Dzik, W. I.; Xu, X.; Zhang, X. P.; Reek, J. N. H.; de Bruin, B. *J. Am. Chem. Soc.* **2010,** *132*, 10891.

Emori, E.; Arai, T.; Sasai, H.; Shibasaki, M. *J. Am. Chem. Soc.* **1998**, *120*, 4043.

Enders, D.; Luttgen, K.; Narine, A. A. *Synthesis*, **2007**, 0959.

Ershad, S.; Sagathforoush, L. A.; Karim-nezhad, G.; Kangari, S.; *Int. J. Electrochem. Sci.* **2009**, *4*, 846.

Estevan, F.; Lahuerta, P.; Lloret, J.; Sanau, M.; Ubeda, M. A.; Vila, J. *Chem. Commun.* **2004**, 21, 2408.

Evans, D. A.; Seidel, D.; Rueping, M.; Lam, H. W.; Shaw, J. T.; Downey, C. W. *J. Am. Chem. Soc.* **2003**, *125*, 12692.

Evans, D. A.; Woerpel, K. A.; Hinman, M. M.; Faul, M. F. *J. Am. Chem. Soc.* **1991**, *113*, 726.

Evans, D. A.; Woerpel, K. A.; Scott, M. J. *Angew. Chem., Int. Ed.* **1992**, *31*, 430.

Fang, X.; Li, J.; Wang, C. *Org. Lett.* **2013**, *15*, 3448.

Fatibello-Filho, O.; Dockal, E. R.; Marcolino-Junior, L.H.; Teixeira M. F. S. *Analyt. Lett.* **2007**, *40*, 1825.

Ferrand, Y.; Le Maux, P.; Simonneaux, G. *Org. Lett.* **2004,** *6*, 3211.

Fieser, L. F.; Daudt, W. H. *J. Am. Chem. Soc.* **1946**, *68*, 2248.

Frauenkron, M.; Berkessel, A. *Tetrahedron Lett.* **1997**, *38*, 7175.

Frausto da Silva, J. R.; Williams, R. J. P. *The Biological Chemistry of Elements*; Oxford University Press: New York, **2001**.

Freemantle, N.; Cleland, J.; Young, P.; Mason, J.; Harrison, J. *Brit. Med. J.* **1999**, *318*, 1730.

Fritschi, H.; Leutenegger, U.; Pfaltz, A. *Angew. Chem., Int. Ed.* **1986**, *25*, 1005.

Fürstner, A.; Shi, N. *J. Am. Chem. Soc.* **1996**, *118*, 12349.

Gan, C.; Lai, G.; Zhang, Z.; Wang, Z.; Zhou, M.-M. *Tetrahedron: Asymmetry* **2006**, *17*, 725.

Gao, Q.; Zheng, B. F.; Li, J. H.; Yang, D. *Org. Lett.* **2005**, *7*, 2185.

Gao, J. A.; Zhong, S. H. *J. Mol. Catal. A-Chem.* **2003,** *191*, 23.

Gao, M. Z.; Kong, D. Y.; Clearfield, A.; Zingaro, R. A. *Tetrahedron Lett.* **2004**, *45*, 5649.

Lo, W. C.; Che, C. M.; Cheng, K. F.; Mak, T. C. W. *Chem. Commun.* **1997**, 13, 1205.

Gausepohl, R.; Buskens, P.; Kleinen, J.; Bruckmann, A.; Lehmann, C. W.; Klankermayer, J.; Leitner, W. *Angew.Chem. Int. Ed.* **2006**, *45,* 3689.

Ghosh, A. K.; Mathicanan, P.; Cappiello, J.; Krishnan, K. *Tetrahedron Lett.* **1997**, *38*, 2427.

Ginotra, S. K.; Singh, V. K. *Org. Biomol. Chem.*, **2007**, *5*, 3932.

Gnad, F.; Reiser, O. *Chem. Rev.* **2003,** *103*, 1603; (b) Faust, R. *Angew. Chem. Int. Ed.* **2001,** *40*, 2251.

Gnas, Y.; Glorius, F. *Synthesis* **2006**,1899.

Hamashima, Y.; Suzuki, T.; Shimura, T.; Umebayashi, N.; Tamura, T.; Sasamoto, N.; Sodeoka, M. *Tetrahedron: Asymmetry* **2005**, *46*, 1447.

Hamashima, Y.; Yagi, K.; Takano, H.; Tamas.; Sodeoka, M. *J. Am. Chem. Soc.* **2002**, *124*, 14530.

Handa, S.; Nagawa, K.; Sohtome, Y.; Matsunaga, S.; Shibasaki, M. *Angew. Chem. Int.*

Ed. **2008**, *47*, 3230.

Hedley, S. J.; Ventura, D. L.; Dominiak, P. M.; Nygren, C. L.; Davies, H. M. L. *J. Org. Chem*. **2006**, *71*, 5349.

Henry, L. *Hebd. CR Seances Acad. Sci*. **1895**, *120*, 1265.

Hora, J. *Recueil, J. Roy. Neth. Chem. Soc*. **1976**, *95*, 45.

Hou, X. L.; Li, B. F.; Dai, L. X. *Tetrahedron: Asymmetry* **1999**, *10*, 2319.

Howe, R.; Rao, B. S. *J. Med. Chem.* **1968**, *11*, 1118.

Huang, L.; Chen, Y.; Gao, G.-Y.; Zhang, X. P. *J. Org. Chem*. **2003**, *68*, 8179.

Huang, Y. and Rawal, V. H. *J. Am. Chem. Soc*. **2002**, *124*, 9662.

Huang, Y. and Rawal, V. H. *Org. Lett*. **2000**, *2*, 3321.

Huang, Y.; Unni, A. K.; Thadani, A. N.; and Rawal, V. H. *Nature* **2003**, *424*, 146.

Ichinose, M.; Suematsu, H.; Katsuki, T. *Angew. Chem. Int. Ed*. **2009**, *48*, 3121.

Ikeno, T.; Sato, M.; Yamada, T. *Chem. Lett*. **1999**, 1345.

Inoue, M.; Suzuki, T.; Nakada, M. *J. Am. Chem. Soc*. **2003**, *125*, 1140.

Itagaki, M.; Hagiya, K.; Kamitamari, M.; Masumoto, K.; Suenobu, K.; Yamamoto, Y. *Tetrahedron* **2004,** *60*, 7835.

Ito, H.; Makida, Y.; Ochida, A.; Ohmiya, H.; Sawamura, M. *Org. Lett*. **2008**, *10*, 5051.

Itoh, Y.; Tsuji, H.; Yamagata, K. I.; Endo, K.; Tanaka, I.; Nakamura, M.; Nakamura, E. *J. Am. Chem. Soc*. **2008**, *130*, 17161.

Iwasa, S.; Tsushima, S.; Nishiyama, K.; Tsuchiya, Y.; Takezawa, F.; Nishiyama, H. *Tetrahedron-Asymmetry* **2003**, *14*, 855.

Jacobsen, E. N.; Pfaltz, A.; Yamamoto, H. *Comprehensive Asymmetric Catalysis*, Springer-Verlag, Berlin Heidelberg, **1999**.

Jacobsen, E. N.; Pfalz, A.; Yamamoto, H. *Comprehensive Asymmetric Catalysis*; Springer: Berlin, **1999**, Vol. 2, 513.

Jacobsen, E.N., *Acc. Chem. Res. 2000*, *33*, 421.

Jacobsen, E.N., Zhang, W., Muci, A.R., Ecker, J .R., Deng, L., *J. Am. Chem. Soc.* **1991**, *120*, 7063.

Jimenez, C. A.; Belmar, J. B. *Synth. Comm.* **2007**, *37*, 2391.

Jimenez, C. A.; Belmar, J. B. *Synth. Comm.* **2007**, *37*, 2391.

Jin, H.; Uenishi, J.; Christ, W.; Kishi, Y. *J. Am. Chem. Soc.* **1986**, *108*, 5644.

Johansson, M. J.; Gorin, D. J.; Staben, S. T.; Toste, F. D. *J. Am. Chem. Soc.* **2005,** *127*, 18002.

Jones, T. R.; Labelle, M.; Belley, M.; Champion, E.; Charette, L.; Evans, J.; Ford-Hutchinson, A. W.; Gauthier, J. -Y.; Lord, A.; Masson, P.; McAuliffe, M.; McFarlene, C. S.; Metters, K. M.; Pickett, C.; Piochuta, H.; Rochette, C.; Rodger, I. W.; Sawyer, N.; Young, R. N.; Zamboni, R.; Abraham, W. M. *Can. J. Pharmacol.* **1995**, *73*, 191.

Jorgensen, K. A.; Johannsen, M.; Yao, S.; Audrain, H.; Thorhauge, J. *Acc. Chem. Res.* **1999**, *32*, 605.

Kanchiku S, Suematsu H, Matsumoto K, Uchida T, Katsuki T. *Angew. Chem. Int. Ed.* **2007**, *46*, 3889.

Kaschel, J.; Schneider, T. F.; Weirz, D. B. *Angew. Chem. Int. Ed.* **2012**, *51*, 7085.

Kennedy, M.; Mckervey, M. A.; Maguire, A. R.; Roos, G. H. P. *J. Chem. Soc. Chem. Commun*. **1990**, 361.

Kennedy-Smith, J. J.; Staben, S. T.; Toste, F. D. *J. Am. Chem. Soc*. **2004**, *126*, 4526.

Khadjawi, M. G.; Purkarthofer, T.; Skranc, W.; Griengl, H. . *Synth. Catal*. **2007**, *349*, 1445.

Kimmel, K. L.; Robak, M. T.; Thomas, S.; Lee, M.; Ellman, J. A. *Tetrahedron*, **2012**, *68*, 2704.

King, A. O.; Corley, E. G.; Anderson, R. K.; Larsen, R. D.; Verhoeven, T. R.; Reider, P. J.; Xiang,Y. B.; Belley, M.; Leblanc, Y.; Labelle, M.; Prasit, P.; Zamboni, R. J. *J. Org. Chem*. **1993**, *58*, 3731.

Kitagawa, O.; Fujiwara, H.; Suzuki, T.; Taguchi, Shiro, T. M. *J. Org. Chem*. **2000**, *65*, 6819.

Kitagawa, O.; Suzuki, T.; Inoue, T.; Watanabe, T.;Taguchi, T. *J. Org. Chem*. **1998**, *63*, 9470.

Kitanosono, T.; Sakai, M.; Ueno, M.; Kobayashi, S. *Org. Biomol. Chem*. **2012**, *12*, 7134.

Klauber, E. G.; De, C. K.; Shah, T. K.; Seidel, D. *J. Am. Chem. Soc*. **2010**, *132*, 13624.

Klein, H. F.; Beck, R.; Florke, U.; Haupt, H. J. *Eur. J. Inorg. Chem*. **2002**, 3305.

Klein, H. F.; Beck, R.; Florke, U.; Haupt, H. J. *Eur. J. Inorg. Chem*. **2003**, 1380.

Knowles, W. S. *Angew. Chem. Int. Ed*. **2002**, *41*, 1998.

Kogami, Y.; Nakajima, T.; Ashizawa, T.; Kezuka, S.; Ikeno, T.; Yamada, T. *Chem. Lett*.

2004, *33*, 614.

Kogami, Y.; Nakajima, T.; Ikeno, T.; Yamada, T. *Synthesis* **2004**, 1947.

Kowalczyk, R.; Kwiatkowski, P.; Skarzewski, J.; Jurczak, J. *J. Org. Chem.* **2009**, *74*, 753.

Krause, N.; Hoffmann-Roder, A. *Synthesis* **2001**, 171.

Krumper, J. R.; Gerisch, M.; Suh, J. M.; Bergman, R. G.; Tilley, T. D. *J. Org. Chem.* **2003**, *68*, 9705.

Kuninobu, Y.; Kawata, A.; Takai, K. *Org. Lett.* **2005**, *7*, 4823.

Kuntiyong, P.; Lee, T. H.; Kranemann, C. L. *Org. Biomol. Chem.* **2012**,*10*, 7884.

Labelle, M.; Belley, M.; Gareau, Y.; Gauthier, J. Y.; Guay, D.; Gordon, R.; Grossman, S. G.; Jones, T. R.; Leblanc, Y.; McAuliffe, M.; McFarlane, C.; Masson, P.; Metters, K. M.; Ouimet, N.; Patrick, D. H.; Piechuta, H.; Rochette, C.; Sawyer, N.; Xiang, Y. B.; Ford-Hutchinson, A. W.; Zamboni, R. J.; Young, R. N. *Bioorg. Med. Chem. Lett.* **1995,** *5*, 283.

Lai, G.; Guo, F.; Zheng, Y.; Fang, Y.; Song, H.; Xu, K.; Wang, S.; Zha, Z.; Wang, Z. *Chem. Eur. J.* **2011**, *17*, 1114.

Larrow, J .F., J acobsen, E.N., Gao, Y., Hong, Y., Nie, X., Zepp, C.M., *J. Org. Chem.* **1994**, *59*, 1939.

Larrow, J. F.; Jacobsen, E. N. *Org. Synth.* **2004**, *10*, 96.

Larrow, J. F.; Jacobsen, E. N. *Topics Organomet. Chem.* **2004**, *6*, 123.

Larrow, J.F., Jacobsen, E.N., *Org. Syn.***1997**, *75*, 1.

Le Maux, P.; Juillard, S.; Simonneaux, G. *Synthesis* **2006**, 10, 1701.

Lebel, H.; Marcoux, J. F.; Molinaro, C.; Charette, A. B. *Chem. Rev.* **2003,** *103*, 977.

Lebel, H.; Marcoux, J.-F.; Molinaro, C.; Charette, A. B. *Chem. Rev.* **2003**, *103*, 977.

Lesma, G.; Cattenati, C.; Pilati, T.; Sacchetti, A.; Silvani, A. *Tetrahedron-Asymmetry* **2007,** *18*, 659.

Li, B. J.; Jiang, L.; Liu, M.; Chen, Y. C.; Ding, L. S.; Wu, Y. *Synlett* **2005**, 603.

Liu, W. Resolution at large scale: case studies. Handbook of Chiral Chemicals (*2nd Edition*) **2006**, 75.

Liu, Y.; Sun, B.; Wang, B.; Wakem, M.; Deng, L. *J. Am. Chem. Soc.* **2009**, *131*, 418.

Livesey, G.; Brown, J. C. *J. Nutr.* **1995**, *125*, 3020.

Lo, M. M. C.; Fu, G. C. *J. Am. Chem. Soc.* **1998**, *120*, 10270.

Lomberget, T.; Bouyssi, D.; Balme, G. *Synthesis* **2005**, 311.

Lowenthal, R. E.; Abiko, A.; Masamune, S. *Tetrahedron Lett.* **1990**, *31*, 6005.

Lunsford, C. D.; Mays, R. P.; Richman, J. A.; Murphey, R. S. *J. Am. Chem. Soc.* **1960**, *82*, 1166.

Lyle, M. P. A.; Wilson, P. D. *Org. Lett.* **2004,** *6*, 855.

Maheswaran, H.; Prasanth, K. L.; Krishna, G. G.; Ravikumar, K.; Sridhar, B.; Kantam, M. L. *Chem. Commun.* **2006**, 4066.

Marcelli, T.; van der Haas, R. N. S.; van Maarseveen J. H.; Hiemstra, H. *Angew. Chem. Int. Ed.* **2006**, *45*, 929.

Marchand, A. P.; Sharma, R.; Zope, U. P. *J. Org. Chem.* **1993**, *58*, 759.

Marcin, L. R.; Denhart, D. J.; Mattson, R. J. *Org. Lett.* **2005**, *7*, 2651.

Marigo, M.; Schulte, T.; Franzen, J.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2005**, *127*, 15710.

Markham, A.; Faulds, D. *Drugs* **1998**, *56*, 251.

Maruoka, K.; Itoh, T.; Shirasaka, T.; and Yamamoto, H. *J. Am. Chem. Soc.* **1988**, *110*, 310.

Mass, G. *Chem. Soc. Rev.* **2004**, *33*, 183.

Matsuzawa, A.; Mashiko, T.; Kumagai, N.; Shibasaki, M. *Angew. Chem. Int. Ed.* **2011**, *50*, 7616.

Mayani, V. J.; Abdi, S. H. R.; Kureshy, R. I.; Khan, N. H.; Das, A.; Bajaj, H. C. *J. Org. Chem.* **2010**, *75*, 6191.

McCarrick, M. A.; Wu, Y.; and Houk, K. N. *J. Am. Chem. Soc.* **1992**, *114*, 1499.

McDaid, P.; Chen, Y.; Deng, L.; *Angew. Chem. Int. Ed.* **2002**, *41*, 338.

McNamara, J. M.; Leazer, J. L.; Bhupathy, M.; Amato, J. S.; Reamer, R. A.; Reider, P. J.; Grabowski, E. J. J. *J. Org. Chem.* **1989**, *54*, 3718.

Miller, J. A.; Gross, B. A.; Zhuravel, M. A.; Jin, W. C.; Nguyen, S. T. *Angew. Chem., Int. Ed.* **2005**, *44*, 3885.

Miller, J. A.; Hennessy, E. J.; Marshall, W. J.; Scialdone, M. A.; Nguyen, S. T. *J. Org. Chem.* **2003**, *68*, 7884.

Miller, J. A.; Jin, W. C.; Nguyen, S. T. *Angew. Chem., Int. Ed.* **2002**, *41*, 2953.

Misumi, Y.; Bulman, R. A.; Matsumoto, K. *Heterocycles* **2002**, *56*, 599.

Mitsunobu, O.; Yamada, M. *Bull. Chem. Soc. Jpn.* **1967**, *40*, 2380.

Morandi, B.; Carreira, E. M. *Science* **2012**, 335, 1471.

Morandi, B.; Cheang, J.; Carreira, E. M. *Org. Lett.* **2011**, *13*, 3080.

Morandi, B.; Dolva, A.; Carreira, E. M. *Org. Lett.* **2012**, *14*, 2162.

Morandi, B.; Mariampillai, B.; Carreira, E. M. *Angew. Chem. Int. Ed.* **2011**, *50*, 1101.

Muller, P. *Acc. Chem. Res.* **2004**, *37*, 243.

Muller, P.; Bernardinelli, G.; Allenbach, Y. F.; Ferri, M.; Flack, H. D. *Org. Lett.* **2004**, *6*, 1725.

Muller, P.; Bernardinelli, G.; Allenbach, Y. F.; Ferri, M.; Grass, S. *Synlett.* **2005**, 9, 1397.

Munslow, I. J.; Gillespie, K. M.; Deeth, R. J.; Scott, P. *Chem. Commun.* **2001**, *17*, 1638.

Nakamura, A.; Konishi, A.; Tsujitani, R.; Kudo, M. A.; Otsuka, S. *J. Am. Chem. Soc.* **1978**, *100*, 3449.

Nicolaou, K. C.; Snyder, S. A.; Montagnon, T.; Vassilikogiannakis, G. E. *Angew. Chem., Int. Ed.* **2002**, *41*, 1668.

Niimi, T.; Uchida, T.; Irie, R.; Katsuki, T. *Adv. Synth. Catal.* **2001**, *343*, 79.

Niimi, T.; Uchida, T.; Irie, R.; Katsuki, T. *Tetrahedron Lett.* **2000**, *41*, 3647.

Nishimura, K.; Ono, M.; Nagaoka, Y.; Tomioka, K. *J. Am. Chem. Soc.* **1997**, *119*, 12974.

Nishiyama, H.; Itoh, Y.; Matsumoto, H.; Park, S. B.; Itoh, K. *J. Am. Chem. Soc.* **1994**, *116*, 2223.

Noonan, M. J.; Chervinsky, P.; Brandon, M.; Zhang, J.; Kundu, S.; McBurney, J.; Reiss, T. F. *Eur. Respir. J.* **1998**, *11*, 1232.

Noyori, R. *Angew. Chem. Int. Ed.* **2002**, *41*, 2008.

Nozaki, H.; Moriuti, S.; Takaya, H.; Noyori, R. *Tetrahedron* **1968**, *24*, 3655.

Nozaki, H.; Moriuti, S.; Takaya, H.; Noyori, R. *Tetrahedron Lett.* **1965**, *6*, 2563.

Nozaki, H.; Moriuti, S.; Takaya, H.; Noyori, R. *Tetrahedron Lett.* **1966**, *7*, 5239.

Okude, Y.; Hirano, S.; Hiyama, T.; Nozaki, H. *J. Am. Chem. Soc.*, **1977**, *99*, 3179.

Osby, J. O.; Ganem, B. *Tetrahedron Lett.* **1985**, *26*, 6413.

Padwa, A.; Krumpe, K. E. *Tetrahedron* **1992**, *48*, 5385.

Palacino, C.; Connon, S. J. *Chem. Commun.* **2012**, *48*, 2849.

Palomo, C.; Oiarbide, M.; Laso, A. *Angew. Chem. Int. Ed.* **2005**, *44*, 3881.

Palomo, C.; Oiarbide, M.; Laso, A. *Eur. J. Org. Chem.* **2007**, 2561.

Pasteur, L. *Annal. de Chim. et de Phys.* **1848**, *24*, 442.

Pégot, B.; Vo-Thanh, G.; Loupy, A. *Tetrahedron Lett.* **2004**, *45*, 6425.

Pellissier, H. *Tetrahedron* **2008,** *64*, 7041.

Pfeiffer, P.; Breith, E.; Lübbe, E.; Tsumaki, T. *Justus Liebigs Ann. Chem.* **1933**, *503*, 84.

Pietruszka, J. *Chem. Rev.* **2003**, *103*, 1051.

Pui, A.; Berdan, I.; Morgenstern-Badarau, I.; Gref , A.; Perree-Fauvet, M. *Inorg. Chim. Acta* **2001**, *320*, 167.

Qin, B.; Xiao, X.; Liu, X.; Huang, J.; Wen, Y.; Feng. X. *J. Org. Chem.* **2007**, *72*, 9323.

Rana, N. K.; Selvakumar, S.; Singh, V. K. *J. Org. Chem.* **2010**, *75*, 2089.

Rana, N. K.; Singh, V. K. *Org. Lett.* **2011**, *13*, 6520.

Raymer, G. S.; Hartman, D. E.; Rowe, W. A.; Werkman, R. F.; Koch, K. L. *Gastrointest. Endosc*. **2003**, *58*, 30.

Reddy, R. P.; Lee, G. H.; Davies, H. M. L. *Org. Lett*. **2006**, *8*, 3437.

Reichardt, C. Solvents and Solvent Effects in Organic Chemistry, Wiley-VCH, Weinheim, **2003**.

Ricci, P.; Carone, A.; Bartoli, G.; Bosco, M.; Sambri, L.; Melchiorre, P. *Adv. Synth. Catal*. **2008**, *350*, 49.

Ricci, P.; Carone, A.; Bartoli, G.; Bosco, M.; Sambri, L.; Melchiorre, P. *Adv. Synth. Catal*. **2008**, *350*, 49.

Roberson, M.; Jepsen, A.S.; and Jørgenson, K. A. *Tetrahedron* **2001**, *57*, 907.

Romeiro, L. A. S.; Ferreira, M. D. S.; Silva, L. L. D.; Castro, H. C.; Miranda, A. L. P.; Silva, C. L. M.; Noel, F.; Nascimento, J. B.; Araujo, C. V.; Tibirica, E.; Barreiro, E. J.; Fraga, C. A. M. *Eur. J. Med. Chem*. **2011**, *46*, 3000.

Roos, G. H. *Compendium of Chiral Auxiliary Applications*, Academic Press, San Diego, **2001**.

Rubottom, G. M.; Gruber, J. M. *J. Org. Chem*. **1977**, *42*, 1051.

Rubottom, G. M.; Gruber, J. M. *J. Org. Chem*. **1977**, *42*, 1051.

Saá, J. M.; Tur, F.; González, J.; Vega, M. *Tetrahedron: Asymmetry* **2006**, 17, 99.

Saito, M.; Nakajima, M.; Hashimoto, S. *Tetrahedron* **2000**, *56*, 9589.

Saito, M.; Nakajima, M.; Hashimoto, S. *Chem. Commun*. **2000**, 1851.

Salaun, J. *Chem. Rev.* **1989**, *89*, 1247.

Sasai, H.; Suzuki, T.; Arai, S.; Arai, T.; Shibasaki, M. *J. Am. Chem. Soc.* **1992**, *114*, 4418.

Sasai, H.; Tokunaga, T.; Watanabe, S.; Suzuki, T.; Itoh, N.; Shibasaki, M. *J. Org. Chem.* **1995**, *60*, 7388.

Satyanarayana, B.; Reddy, P. P. *Synth. Commun.* **2007**, *37*, 545.

Sayyed, I. A.; Thakur, V. V.; Nikalje, M. D.; Dewkar, G. K.; Kotkar, S. P.; Sudalai, A. *Tetrahedron* **2005**, *61*, 2831.

Schaus, S. E.; Branalt, J.; Jacobsen, E. N. *J. Org. Chem.* **1998**, *63*, 403.

Schiff, H. *Ann. Chem. Suppl.* **1864**, *3*, 343.

Schiff, H. *Ann. Chem.* **1869**, *150*, 193.

Schiff, H. *Ann. Chem.* **1869**, *151*, 186.

Schiff, H. *Justus Liebigs Ann. Chem.* **1864**, *131*, 118.

Schmitkamp; M.; Chen, D.; Leitner,W.; Klankermayer, J.; Franciò, G. *Chem. Commun.* **2007**, 4012.

Schulz, P.S.; Müller, N.; Bösmann, A.; Wasserscheid, P. *Angew. Chem. Int. Ed.* **2007**, *46*, 1293.

Seebach, D.; Beck, A. K.; Mukhopadhyay, T.; Thomas, E. *Helv. Chim. Acta* **1982**, *65*, 1101.

Selvakumar, S.; Sivasankaran, D.; Singh, V. K. *Org. Biomol. Chem.*, **2009**, *7*, 3156.

Sharpless, K. B. *Angew. Chem. Int. Ed.* **2002**, *41*, 2024.

Shibata, Y.; Noguchi, K.; Tanaka, K. *J. Am. Chem. Soc.* **2010**, *132*, 7896.

Shirakawa, S.; Kimura, T.; S. Murata, Shimizu, S. *J. Org. Chem.* **2009**, *74*, 1288.

Shongwe, M. S.; Al-Zaabi, U. A.; Al-Mjeni, F.; Eribal, C. S.; Sinn, E.; Al-Omari, I. A.; Hamdeh, H. H.; Matoga, D.; Adams, H.; Morris, M. J.; Rheingold, A. L.; Bill, E.; Sellmyer, D. J. *Inorg. Chem.* **2012**, *51*, 8241.

Sibi, M. P.; Manyem, S. *Tetrahedron* **2000**, *56*, 8033.

Sibous, L.; Bentouhami, E.; Khan, M. A. *J. Inor. Chem.* **2013**, 1.

Skarzewski, J.; Zielinska-Błajet, M.; Turowska-Tyrk, I. *Tetrahedron: Asymmetry,* **2001**, *12*, 1923.

Suga, H.; Kakehi, A.; Ito, S.; Ibata, T.; Fudo, T.; Watanabe, Y.; Kinoshita, Y. *Bull. Chem. Soc. Jpn.* **2003,** *76*, 189.

Sugimoto, K.; Aoyagi, S.; Kibayashi, C. *J. Org. Chem.* **1997**, *62*, 2322.

Sundararajan, G.; Prabagaran, N. *Org. Lett.* **2001**, *3*, 389.

Suresh, P.; Pitchumani, K. *Tetrahedron: Asymmetry* **2008**, *19*, 2037.

Takahashi, K.; Midori, M.; Kawano, K.; Ishihara, J.; Hatakeyama, S. *Angew. Chem. Int. Ed.* **2008**, *47*, 6244.

Takai, K.; Kimura, K.; Kuroda, T.; Hiyama, T.; Nozaki, H. *Tetrahedron Lett.* **1983**, *24*, 5281.

Takai, K.; Kuroda, T.; Nakatasukasa, S.; Oshima, K.; Nozaki, H. *Tetrahedron Lett.* **1985**, *26*, 5585.

Takai, K.; Tagashira, M.; Kuroda, T.; Oshima, K.; Utimoto, K.; Nozaki, H. *J. Am. Chem. Soc.* **1986**, *108*, 6048.

Tebbe, F. N.; Parshall, G. W.; Reddy, G. S. *J. Am. Chem. Soc.* **1978**, *100*, 3611.

Terada, M.; Mikami, K.; and Nakai, T. *Tetrahedron Lett.* **1991**, *32*, 935.

Thadani, A.; Stankovik, A. R.; Rawal, V. H. *Proc. Nat. Acad. Sci.* **2004**, *101*, 5846.

Theaker, G. W.; Morton, C.; Scott, P. *Dalton Trans.* **2008**, *48*, 6883.

Tian, X.; Cassani, C.; Liu, Y.; Moran, A.; Urakawa, A.; Galzerano, P.; Arceo, E.; Melchiorre, P. *J. Am. Chem. Soc.* **2011**, *133*, 17934.

Tichy, M.; Sicher, J. *Coll. Czech. Chem. Commun.* **1972**, *37*, 3106.

Tietze, L. F.; Kettschau, G. *Stereoselective Heterocyclic Synthesis 1*; Metz, P., Ed.; Springer: Berlin, **1997**; Vol. *189*, p 1.

Tietze, L. F.; Kettschau, G. *Top. Curr. Chem.* **1997**, *189*, 1.

Trost, B. M.; Yeh, V. S. C. *Angew. Chem. Int. Ed.* **2002**, *41*, 861.

Trost, B. M.; Yeh, V. S. C.; Ito, H.; Bremeyer, N. *Org. Lett.* **2002**, *4*, 2621.

Uchida, T.; Irie, R.; Katsuki, T. *Tetrahedron* **2000**, *56*, 3501.

Uchida, T.; Katsuki, T. *Synthesis* **2006,** 10, 1715.

Uchida, T.; Saha, B.; Katsuki, T. *Tetrahedron Lett.* **2001**, *42*, 2521.

Ueno, M.; Kitanosono, T.; Sakai, M.; Kobayashi, S. *Org. Biomol. Chem.* **2011**, *9*, 3619.

Unni, A. K.; Takenaka, N.; Yamamoto, H.; and Rawal, V. H. *J. Am. Chem. Soc.* **2005**, *127*, 1336.

Uraguchi, D.; Kinoshita, N.; Nakashima, D.; Ooi, T. *Chem. Sci.,* **2012**, *3*, 3161.

Wadamoto, M.; Ozasa, N.; Yanagisawa, A; Yamamoto, H. *J. Org. Chem.* **2003**, *68*, 5593.

Waldmann, H. *Synthesis* **1994**, 535.

Watanabe, N.; Ogawa, T.; Ohtake, Y.; Ikegami, S.; Hashimoto, S. *Synlett*. **1996,** 1, 85.

Watanabe, Y.; Washio, T.; Shimada, N.; Anada, M.; Hashimoto, S. *Chem. Commun*., **2009**, 7294.

Watson, I. D. G.; Ritter, S.; Toste, F. D. *J. Am. Chem. Soc*. **2009,** *131*, 2056.

Werstiuk, N. H.; Yeroushalmi, S.; Guan-Lin, H. *Can. J. Chem*. **1992**, *70*, 974.

Wessjohann, L. A.; Brandt, W.; Thiemann, T. *Chem. Rev*. **2003**, *103*, 1625.

White, J. D.; Bolton, G. L; Dantanarayana, A. P; Fox, C. M. J; Hiner, R. N; Jackson, R. W.; Sakuma, K.; Warrier, U. S. *J. Am. Chem. Soc*. **1995**, *117*, 1908.

White, J. D.; Juniku, R.; Huang, K.; Yang., J.; Wong, D. T. *J. Med. Chem*. **2009**, *52*, 5872.

White, J. D.; Kuntiyong, P.; Lee, T. H. *Org. Lett*. **2006**, *8*, 6039.

White, J. D.; Lee, T. H.; Kuntiyong, P. *Org. Lett*. **2006**, *8*, 6043.

Wu. T. R.; Shen, L.; Chong, M. *Org. Lett*. **2004**, *6*, 2701.

Xia, G.; Yamamoto, H. *J. Am. Chem. Soc*. **2006**, *128*, 2554.

Xu, H.; Wolf, C. *Chem. Commun*. **2010**, *46*, 8026.

Yamada, T.; Ikeno, T.; Sekino, H.; Sato, M. *Chem. Lett*. **1999**, 719.

Yamamoto, Y.; Asao, N. *Chem. Rev*. **1993**, 93, 2207.

Yamashita, Y.; Saito, S.; Ishitani, H.; and Kobayashi, S. *J. Am. Chem. Soc.* **2003**, *125*, 3793.

Yan, Y.; Xu, K.; Fang, Y.; Wang, Z. *J. Org. Chem.* **2011**, *76*, 6849.

Yang, T.; Ferrali, A.; Sladojevich, F.; Campbell, L.; Dixon, D. J. *J. Am. Chem. Soc.* **2009**, *131*, 9140.

Yang, W.; Du, D. *Org. Biomol. Chem.,* **2012**, *10*, 6876.

Yoon, J. W.; Yoon, T.-S.; Shin, W. *Acta Crystallogr. Sect. C*: *Cryst. Struct. Commun.* **1997**, *53*, 1685.

Yoshida, M.; Ohno, Y.; Hara, S. *Tetrahedron Lett.* **2010**, *51*, 5134.

Zhang, J.; Liang, J. L.; Sun, X. R.; Zhou, H. B.; Zhu, N. Y.; Zhou, Z. Y.; Chan, P. W. H.; Che, C. M. *Inorg. Chem.* **2005,** *44*, 3942.

Zheng, Y.; Zhou, J.; Loh. T. *Org. Lett.* **1999**, *11*, 1855.

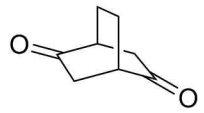
Zhou, Y.; Dong, J.; Zhang, F.; Gong, Y. *J. Org. Chem.* **2011**, *76*, 588.

Zhu, S. F.; Xu, X.; Perman, J. A.; Zhang, X. P. *J. Am. Chem. Soc.* **2010,** *132*, 12796.

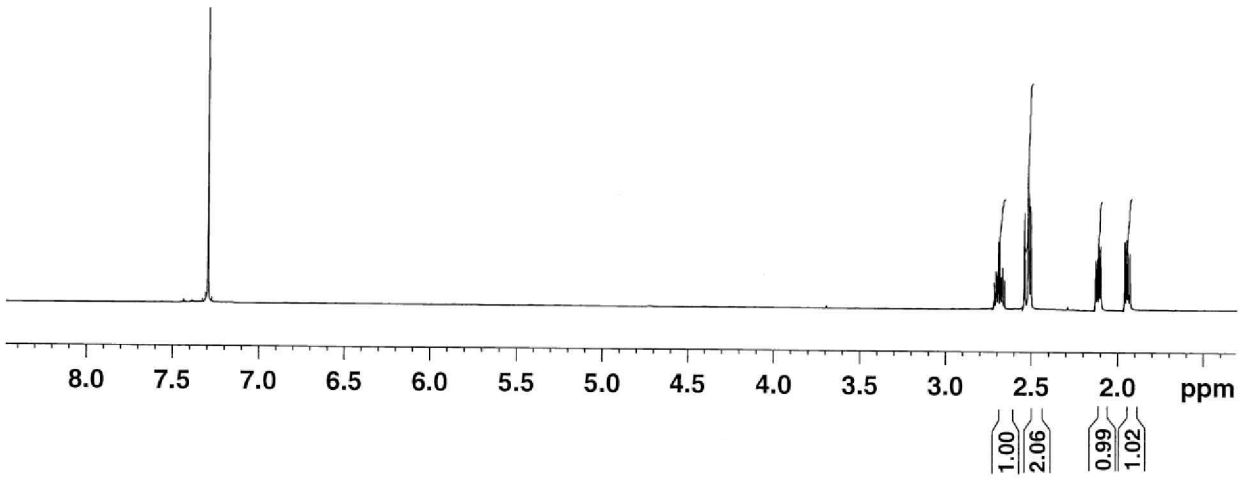
Zhu, S.; Perman, J. A.; Zhang, X. P. *Angew. Chem., Int. Ed.* **2008,** *47*, 8460.

Zulauf, A.; Mellah, M.; Schulz, E. *J. Org. Chem.* **2009**, *74*, 2242.

Appendix I



(±)–**37**

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EXPNO                   1
PROCNO                  1
DU                     /m
USER             william

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PULPROG              zg30
TD                  32768
SOLVENT             CDCl3
NS                     31
DS                      2
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AQ               3.4210291
RG                    28.5
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DE                    6.00
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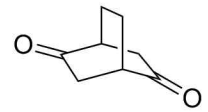
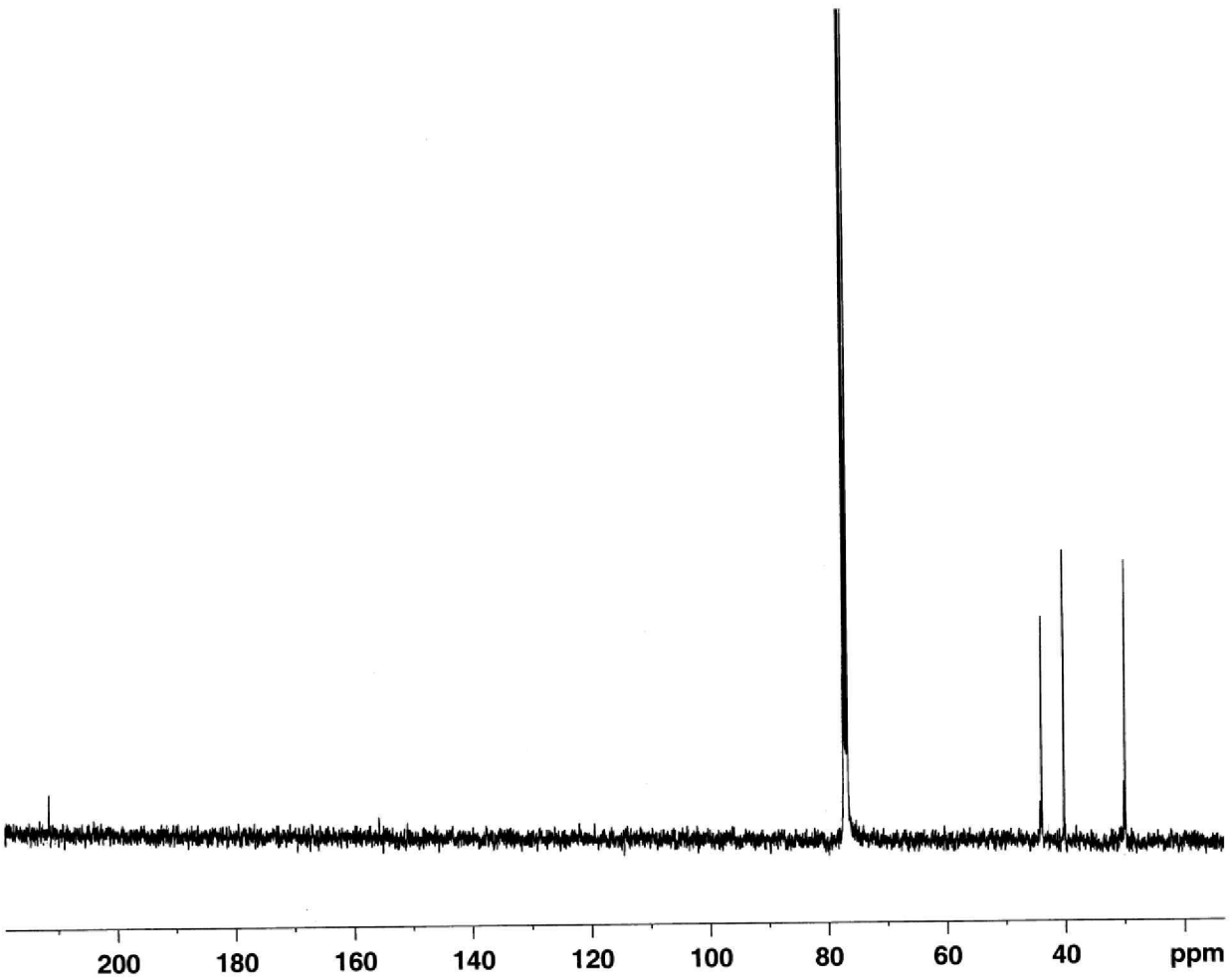
TD0                     1

======== CHANNEL f1 ===
NUC1                   1H
P1                   9.00
PL1                 -3.00
SFO1           300.1321009

F2 - Processing paramet
SI                  32768
SF             300.1300000
WDW                    EM
SSB                     0
LB                   0.30
GB                      0
PC                   1.00
```



(±)–**37**



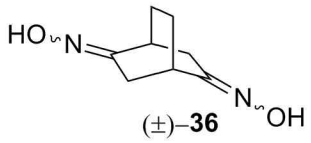

```
Current Data Parameters
NAME                  ss-1-71
EXPNO                       4
PROCNO                      1

F2 - Acquisition Parameters
Date_              20080623
Time                 20.03
INSTRUM              DPX400
PROBHD    5 mm BBO BB-1H
PULPROG              zgpg30
TD                    65536
SOLVENT
NS                     2450
DS                        4
SWH               25125.629 Hz
FIDRES             0.383387 Hz
AQ                1.3042164 sec
RG                    16384
DW                   19.900 usec
DE                    6.00 usec
TE                   298.2 K
D1             0.15000001 sec
d11            0.03000000 sec
DELTA          0.05000000 sec
TD0                       1

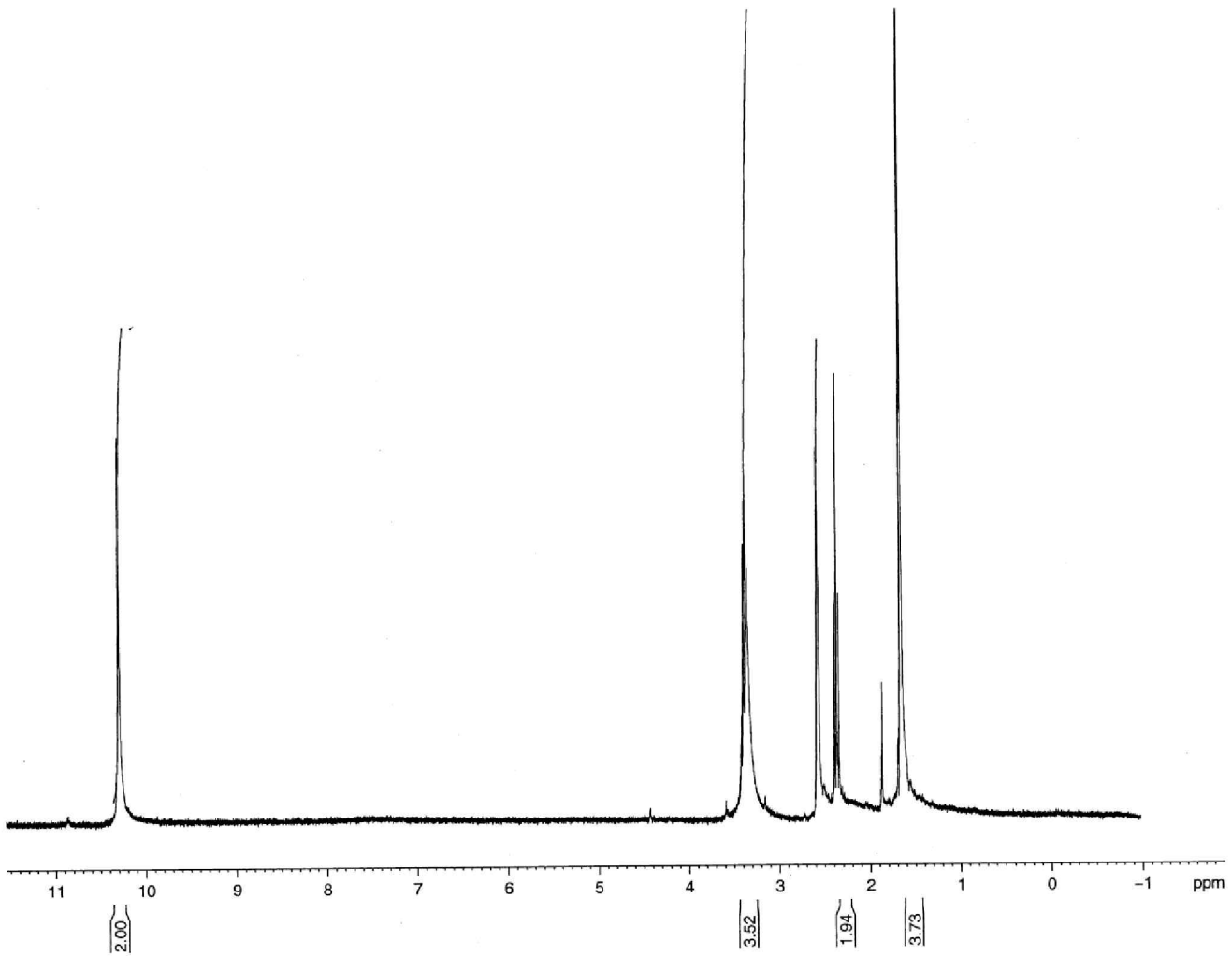
======== CHANNEL f1 ========
NUC1                    13C
P1                     7.80 usec
PL1                   -3.00 dB
SFO1          100.5785700 MHz

======== CHANNEL f2 ========
CPDPRG2            waltz16
NUC2                    1H
PCPD2                135.00 usec
PL2                   17.40 dB
PL12                  17.40 dB
PL13                  17.40 dB
SFO2          399.9516000 MHz

F2 - Processing parameters
SI                     32768
SF            100.5675080 MHz
WDW                       EM
SSB                        0
LB                     3.00 Hz
GB                         0
PC                      1.40
```



(±)–**36**

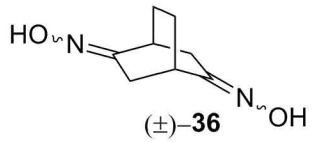



```
Current Data Parameters
NAME      ss-1-08-crude2
EXPNO                  3
PROCNO                 1
DU                    /m
USER             subrata

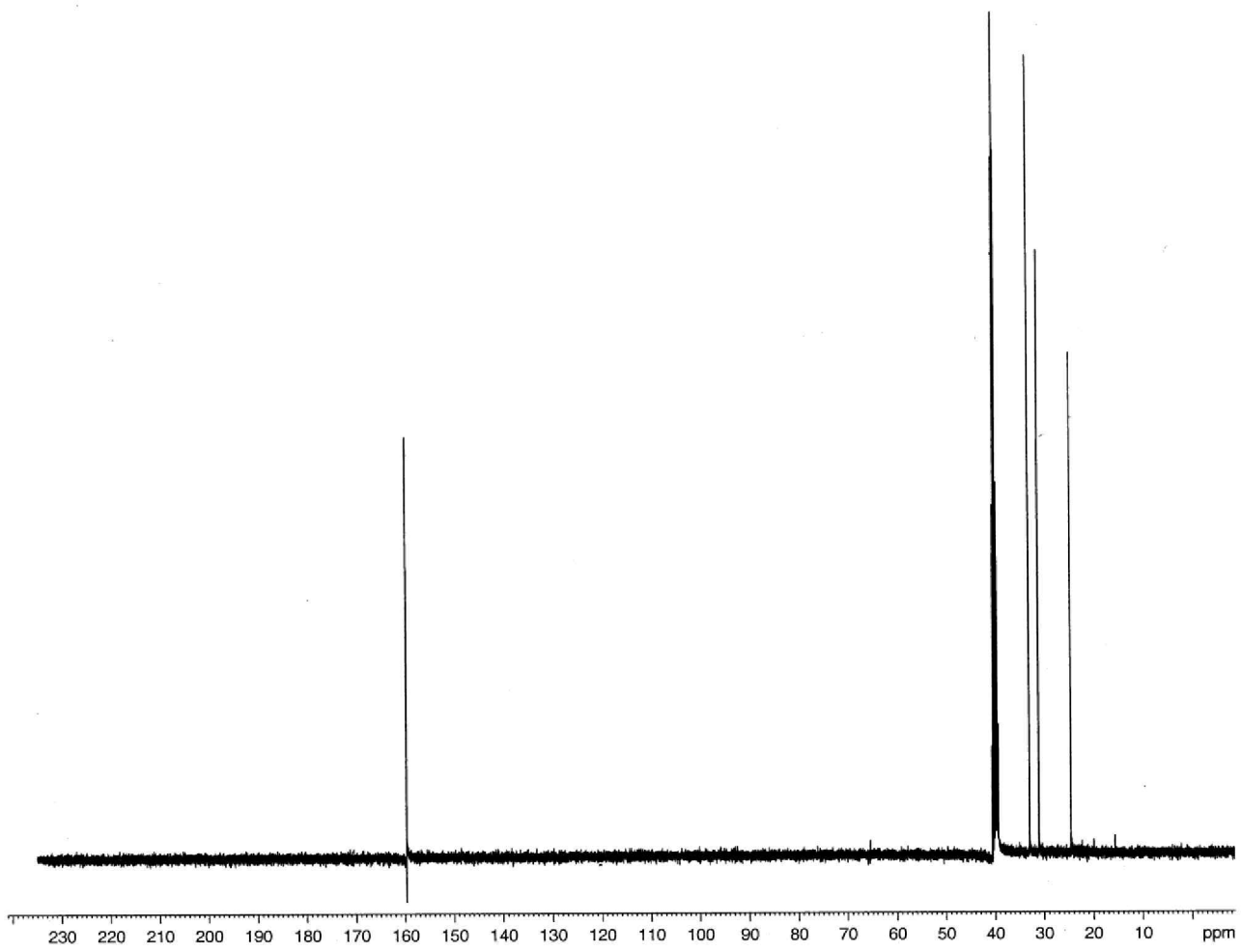
F2 - Acquisition Parameters
Date_           20070927
Time               12.00
INSTRUM          DPX300
PROBHD   5 mm QNP  1H/1
PULPROG            zg30
TD                32768
SOLVENT            DMSO
NS                   32
DS                    2
SWH           4789.272 Hz
FIDRES        0.146157 Hz
AQ            3.4210291 sec
RG                574.7
DW              104.400 usec
DE                6.00 usec
TE               298.2 K
D1           2.00000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                  1H
P1                 9.00 usec
PL1               -3.00 dB
SFO1        300.1321009 MHz

F2 - Processing parameters
SI                32768
SF          300.1300000 MHz
WDW                  no
SSB                   0
LB                 0.00 Hz
GB                    0
PC                 1.00
```



(±)–**36**



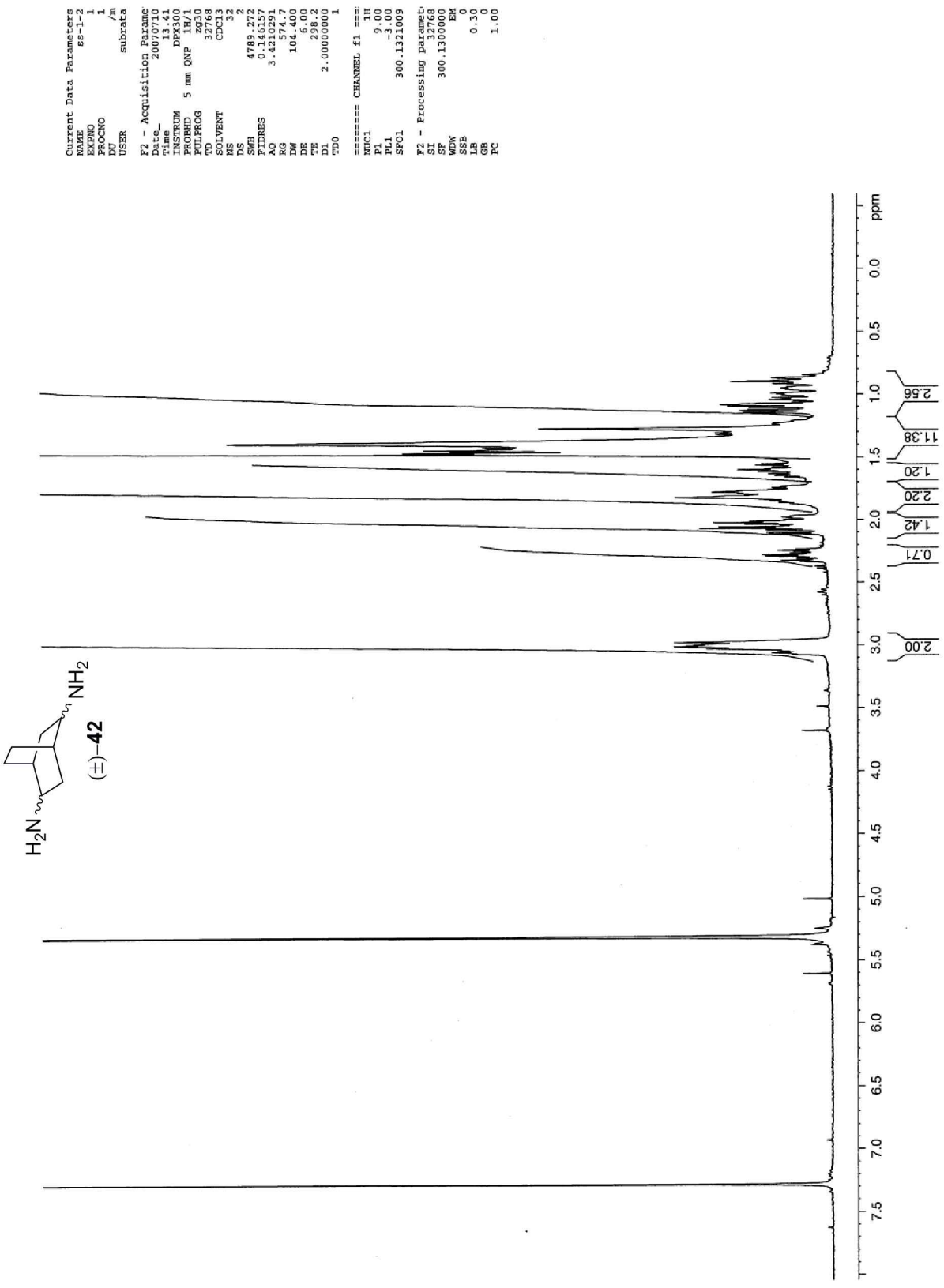

```
Current Data Parameters
NAME      ss-1-08-crude2
EXPNO                  4
PROCNO                 1
DU                    /m
USER             subrata

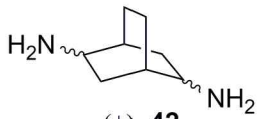
F2 - Acquisition Parameters
Date_           20070927
Time               18.00
INSTRUM          DPX400
PROBHD   5 mm BBO BB-1H
PULPROG         zgpg30
TD               65536
SOLVENT           DMSO
NS                2177
DS                   4
SWH          25125.629 Hz
FIDRES        0.383387 Hz
AQ           1.3042164 sec
RG             11585.2
DW              19.900 usec
DE               6.00 usec
TE              299.2 K
D1          0.15000001 sec
d11         0.03000000 sec
DELTA       0.05000000 sec
TD0                  1

======== CHANNEL f1 ========
NUC1                13C
P1                 7.80 usec
PL1               -3.00 dB
SFO1        100.5936591 MHz

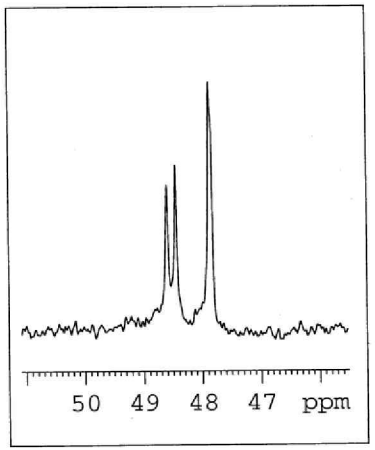
======== CHANNEL f2 ========
CPDPRG2         waltz16
NUC2                1H
PCPD2          135.00 usec
PL2             17.40 dB
PL12            17.40 dB
PL13            17.40 dB
SFO2        400.0116000 MHz

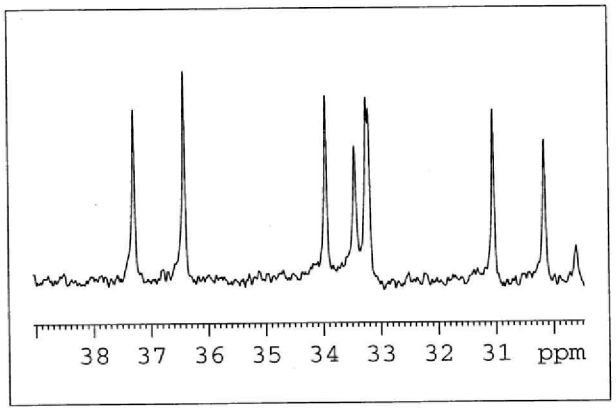
F2 - Processing parameters
SI                 32768
SF          100.5825950 MHz
WDW                   no
SSB                    0
LB                  0.00 Hz
GB                     0
PC                  1.00
```

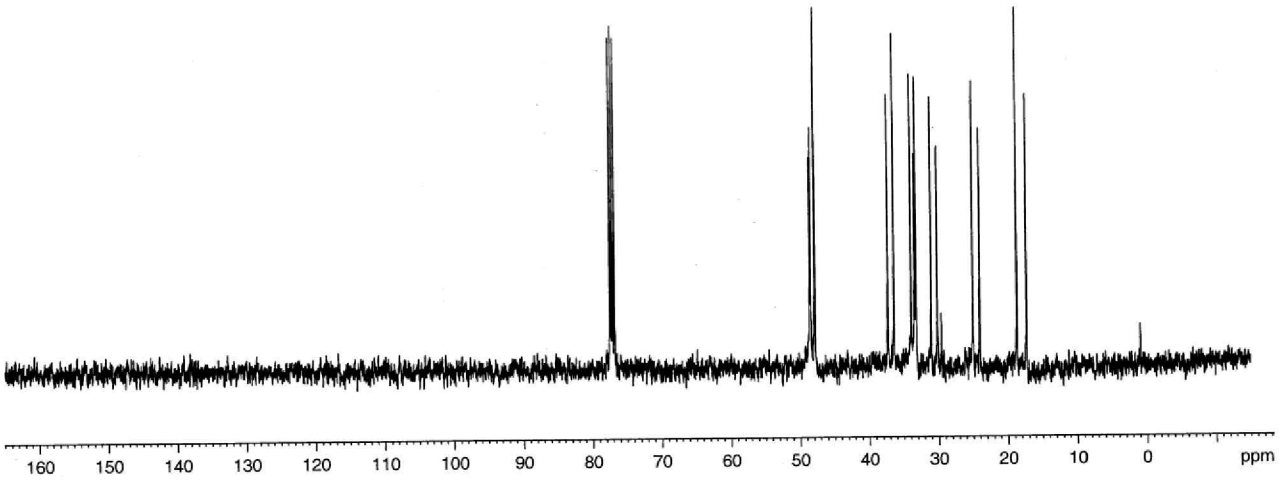

Current Data Parameters
NAME ss-1-2
EXPNO 1
PROCNO 1
F2 - Acquisition Parame
Date_ 20070710
Time 13.41
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDC13
NS 32
DS 2
SWH 4789.272
FIDRES 0.146157
AQ 3.4210291
RG 574.7
DW 104.400
DE 6.00
TE 298.2
D1 2.00000000
TD0 1
======== CHANNEL f1 ===
NUC1 1H
P1 9.00
PL1 -3.00
SFO1 300.1321009
F2 - Processing paramet
SI 32768
SF 300.1300000
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00
H2N
NH2
(±)-42
2.00
0.71
1.42
2.20
1.20
11.38
2.56
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm



(±)–**42**







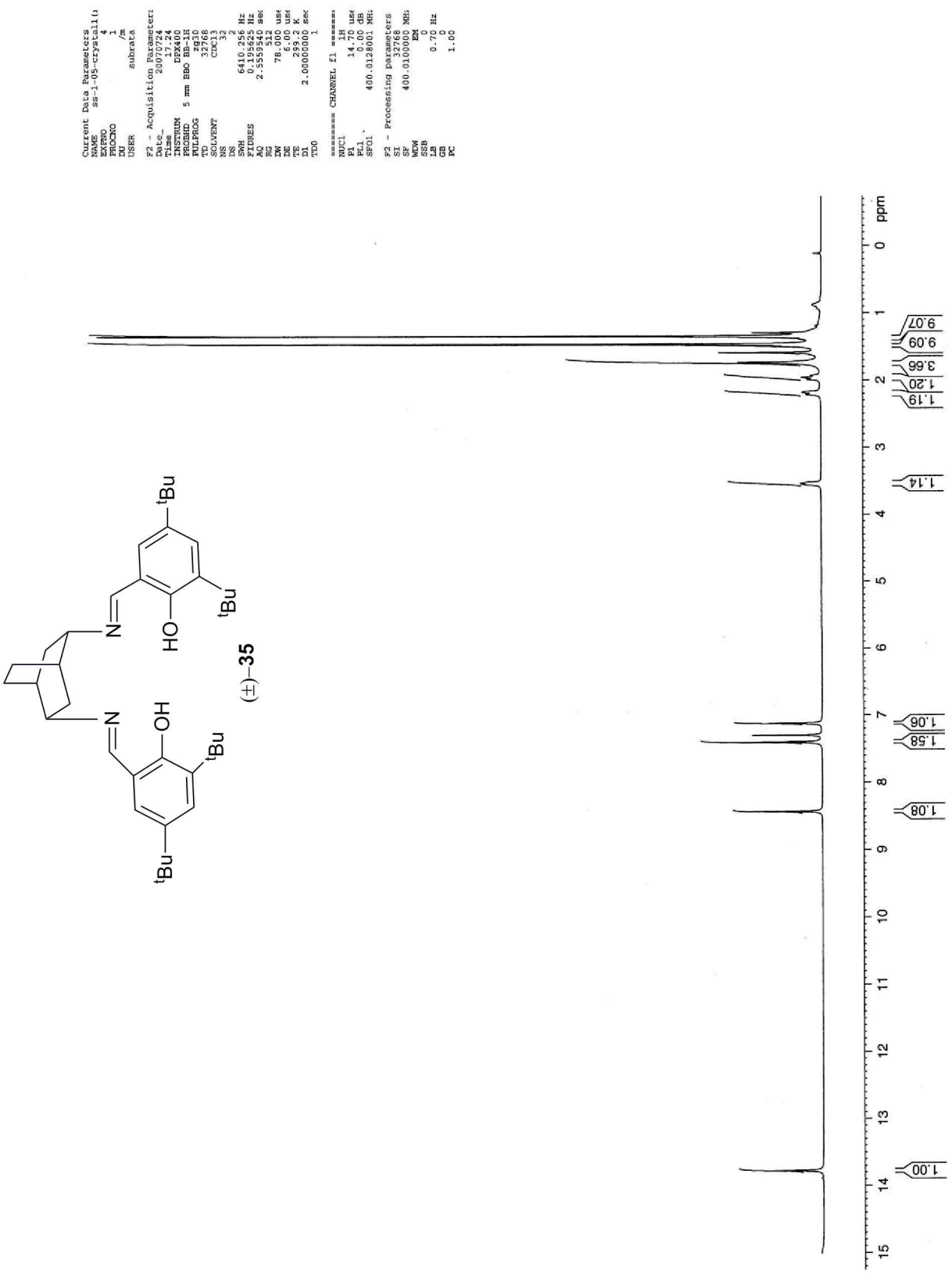

```
Current Data Parameters
NAME        ss-1-04-crude
EXPNO                   2
PROCNO                  1
DU                     /m
USER              subrata

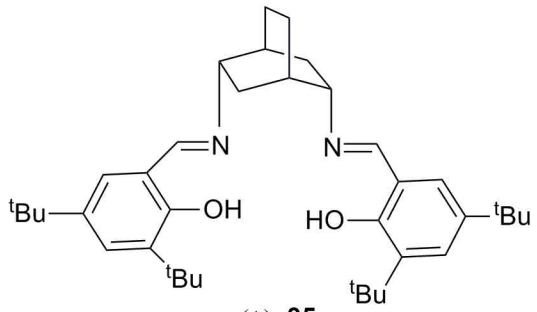
F2 - Acquisition Parameters
Date_           20070718
Time               12.17
INSTRUM          DPX400
PROBHD   5 mm BBO BB-1H
PULPROG          zgpg30
TD                65536
SOLVENT
NS                  105
DS                    4
SWH           25125.629 Hz
FIDRES        0.383387 Hz
AQ            1.3042164 sec
RG                 4096
DW               19.900 usec
DE                6.00 usec
TE               298.2 K
D1          0.15000001 sec
d11         0.03000000 sec
DELTA       0.05000000 sec
TD0                   1

======== CHANNEL f1 ========
NUC1                13C
P1                 7.80 usec
PL1               -3.00 dB
SFO1        100.5936591 MHz

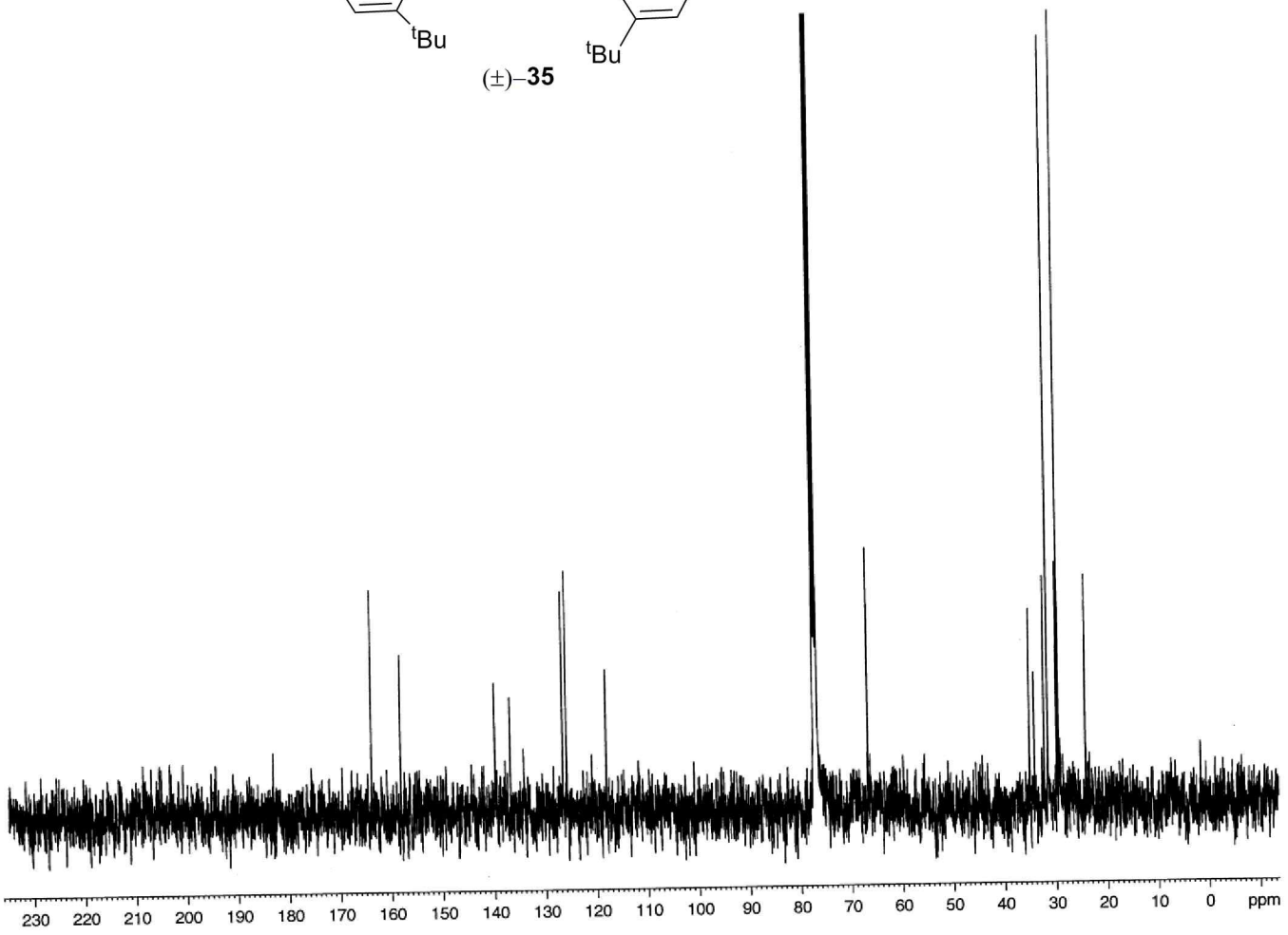
======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                1H
PCPD2             135.00 usec
PL2                17.40 dB
PL12               17.40 dB
PL13               17.40 dB
SFO2        400.0116000 MHz

F2 - Processing parameters
SI                 32768
SF          100.5825950 MHz
WDW                   EM
SSB                    0
LB                  3.00 Hz
GB                     0
PC                  1.00
```


Current Data Parameters
NAME ss-1-05-crystalli
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20070724
Time 17.24
INSTRUM spect
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 512
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 400.0128001 MHz
F2 - Processing parameters
SI 32768
SF 400.0100000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00
(±)–35
1.00
1.08
1.06
1.58
1.14
1.19
1.20
3.66
9.09
9.07
ppm



(±)–**35**



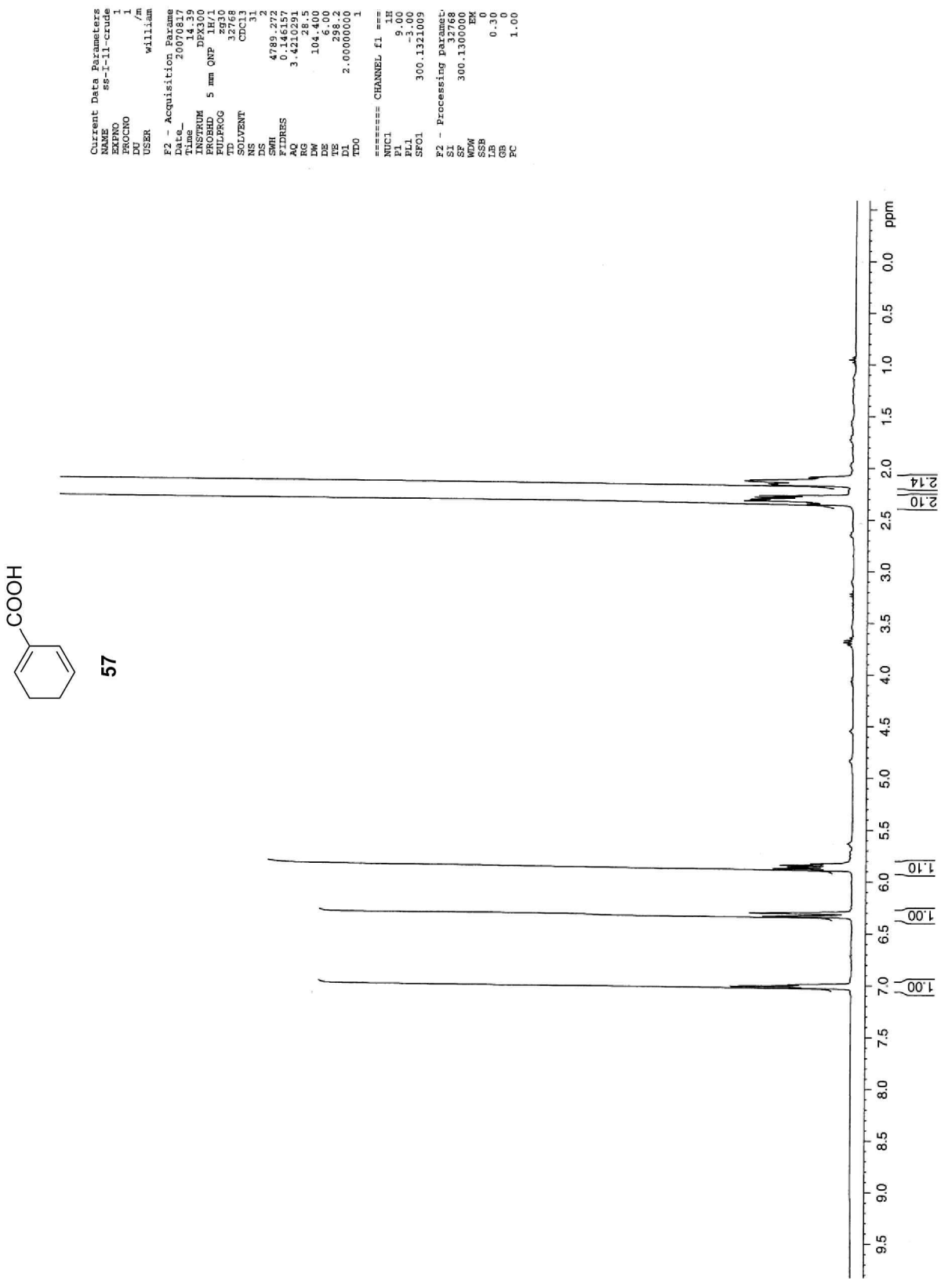

```
Current Data Parameters
NAME      ss-1-05-crystal1(re.
EXPNO                       5
PROCNO                      1
DU                         /m
USER                  subrata

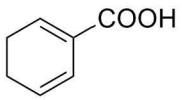
F2 - Acquisition Parameters
Date_                20070724
Time                    17.32
INSTRUM                DPX400
PROBHD    5 mm BBO BB-1H
PULPROG              zgpg30
TD                    65536
SOLVENT
NS                      562
DS                        4
SWH                25125.629 Hz
FIDRES             0.383387 Hz
AQ                 1.3042164 sec
RG                    5160.6
DW                    19.900 usec
DE                     6.00 usec
TE                    298.2 K
D1                 0.15000001 sec
d11                0.03000000 sec
DELTA              0.05000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                      13C
P1                       7.80 usec
PL1                     -3.00 dB
SFO1           100.5936591 MHz

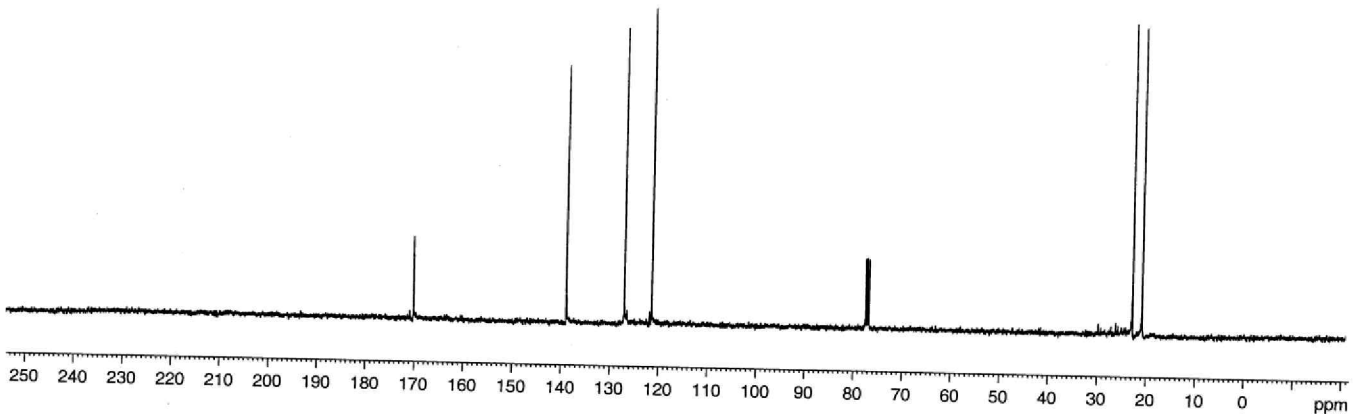
======== CHANNEL f2 ========
CPDPRG2              waltz16
NUC2                      1H
PCPD2                  135.00 usec
PL2                     17.40 dB
PL12                    17.40 dB
PL13                    17.40 dB
SFO2           400.0116000 MHz

F2 - Processing parameters
SI                        32768
SF             100.5825950 MHz
WDW                        EM
SSB                         0
LB                       3.00 Hz
GB                          0
PC                       1.40
```


COOH
57
Current Data Parameters
NAME ss-1-11-crude
EXPNO 1
PROCNO 1
F2 - Acquisition Parame
Date_ 20070817
Time 14.39
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 31
DS 2
SWH 4789.272
FIDRES 0.146157
AQ 3.4210291
RG 28.5
DW 104.400
DE 6.00
TE 298.2
D1 2.00000000
TD0 1
======== CHANNEL f1 ===
NUC1 1H
P1 9.00
PL1 -3.00
SFO1 300.1321009
F2 - Processing paramet
SI 32768
SF 300.1300000
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00
2.14
2.10
1.10
1.00
1.00
ppm



57



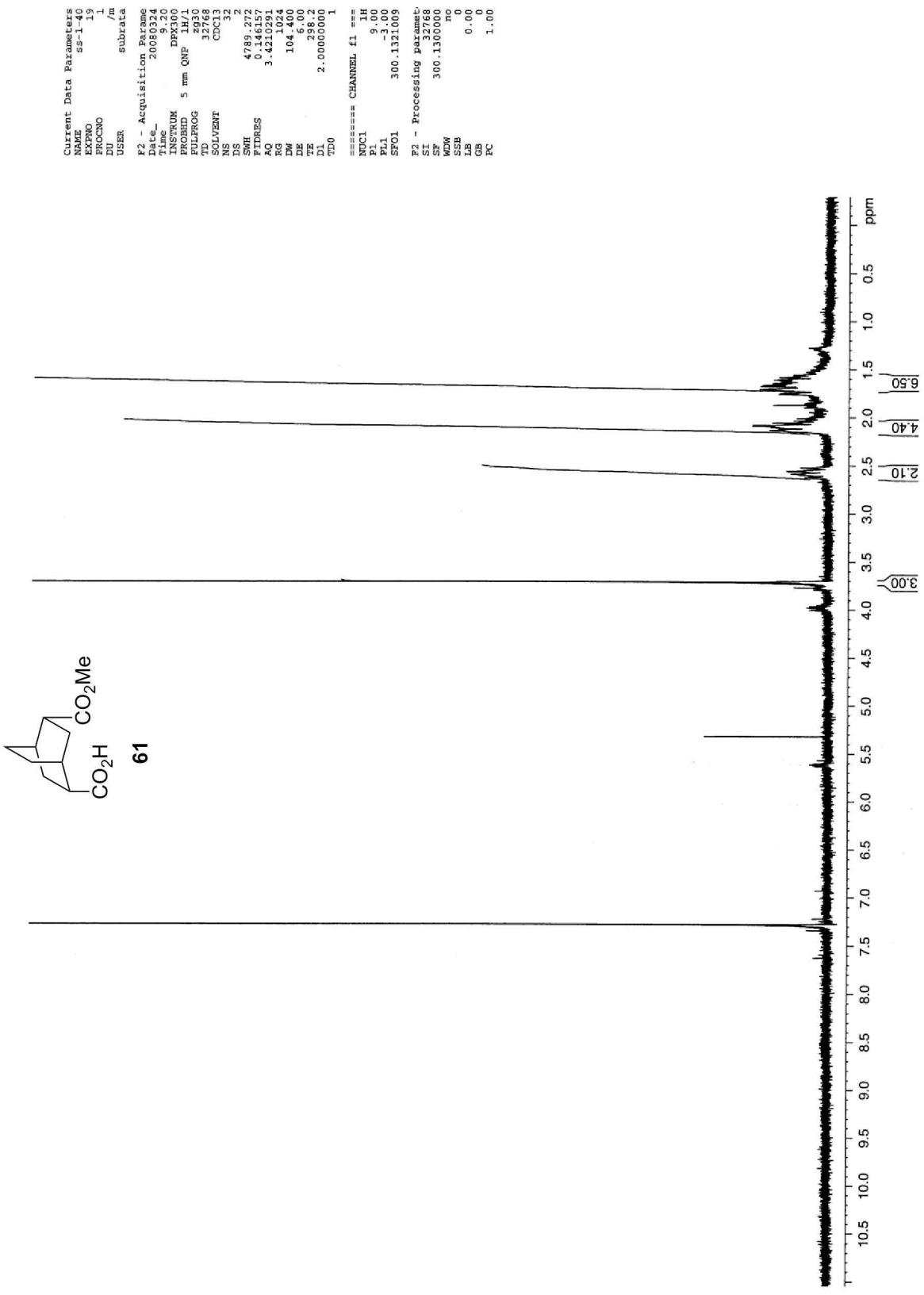

```
Current Data Parameters
NAME                 ss-1-11-crudehsqc
EXPNO                              4
PROCNO                           999
DU                               /m
USER                         subrata

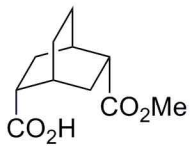
F2 - Acquisition Parameter
Date_                       20070817
Time                           16.11
INSTRUM                      DPX400
PROBHD     5 mm BBO BB-1H
PULPROG                      zgpg30
TD                            65536
SOLVENT
NS                               135
DS                                 4
SWH                      25125.629 Hz
FIDRES                     0.383387 Hz
AQ                         1.3042164 se
RG                            4597.6
DW                           19.900 us
DE                            6.00 us
TE                           299.2 K
D1                     0.15000001 se
d11                    0.03000000 se
DELTA                  0.05000000 se
TD0                              1

======== CHANNEL f1 ======
NUC1                           13C
P1                            7.80 us
PL1                          -3.00 dB
SFO1                100.5936591 MH

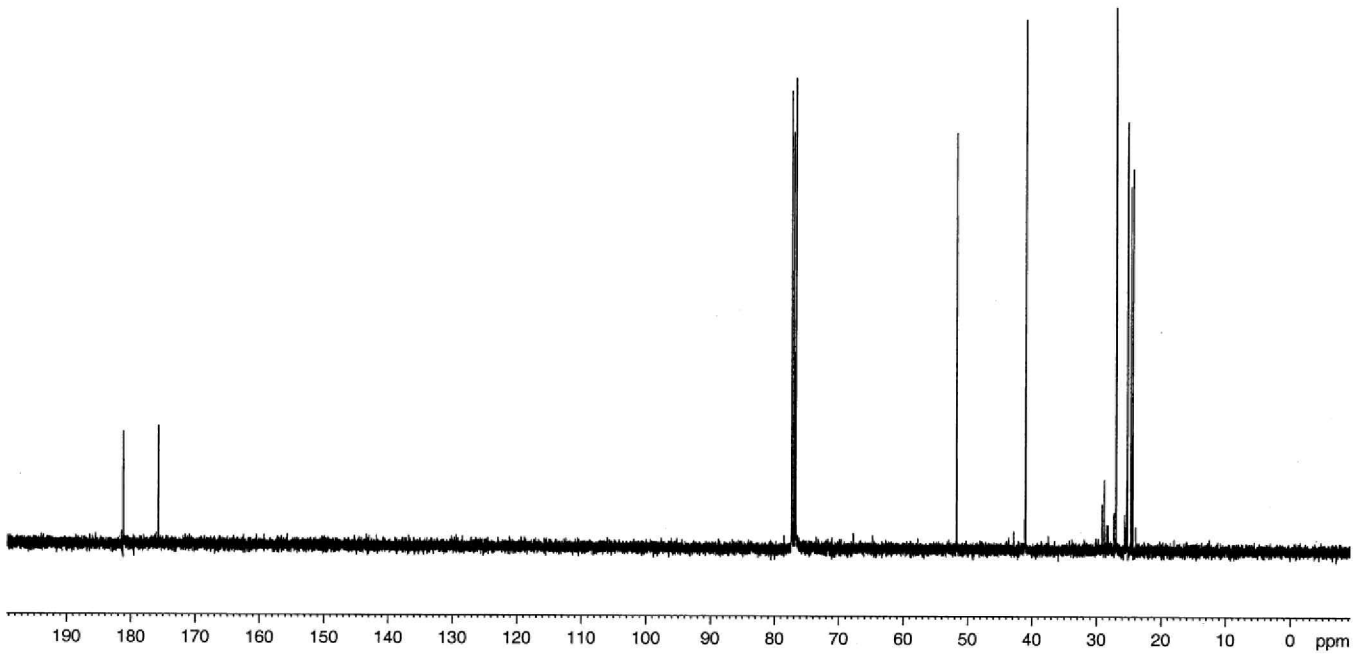
======== CHANNEL f2 ======
CPDPRG2                    waltz16
NUC2                           1H
PCPD2                       135.00 us
PL2                          17.40 dB
PL12                         17.40 dB
PL13                         17.40 dB
SFO2                400.0116000 MH

F2 - Processing parameters
SI                             32768
SF                  100.5825950 MH
WDW                               EM
SSB                                0
LB                            3.00 Hz
GB                                 0
PC                             1.40
```


Current Data Parameters
NAME ss-1-40
EXPNO 19
PROCNO 1
DU /m
USER subrata
F2 - Acquisition Parame
Date_ 20080324
Time 9.20
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4789.272
FIDRES 0.146157
AQ 3.4210291
RG 1024
DW 104.400
DE 6.00
TE 298.2
D1 2.00000000
TD0 1
======== CHANNEL f1 ===
NUC1 1H
P1 9.00
PL1 -3.00
SFO1 300.1321009
F2 - Processing paramet
SI 32768
SF 300.1300000
WDW no
SSB 0
LB 0.00
GB 0
PC 1.00
CO2Me
CO2H
61
3.00
2.10
4.40
6.50
ppm



61



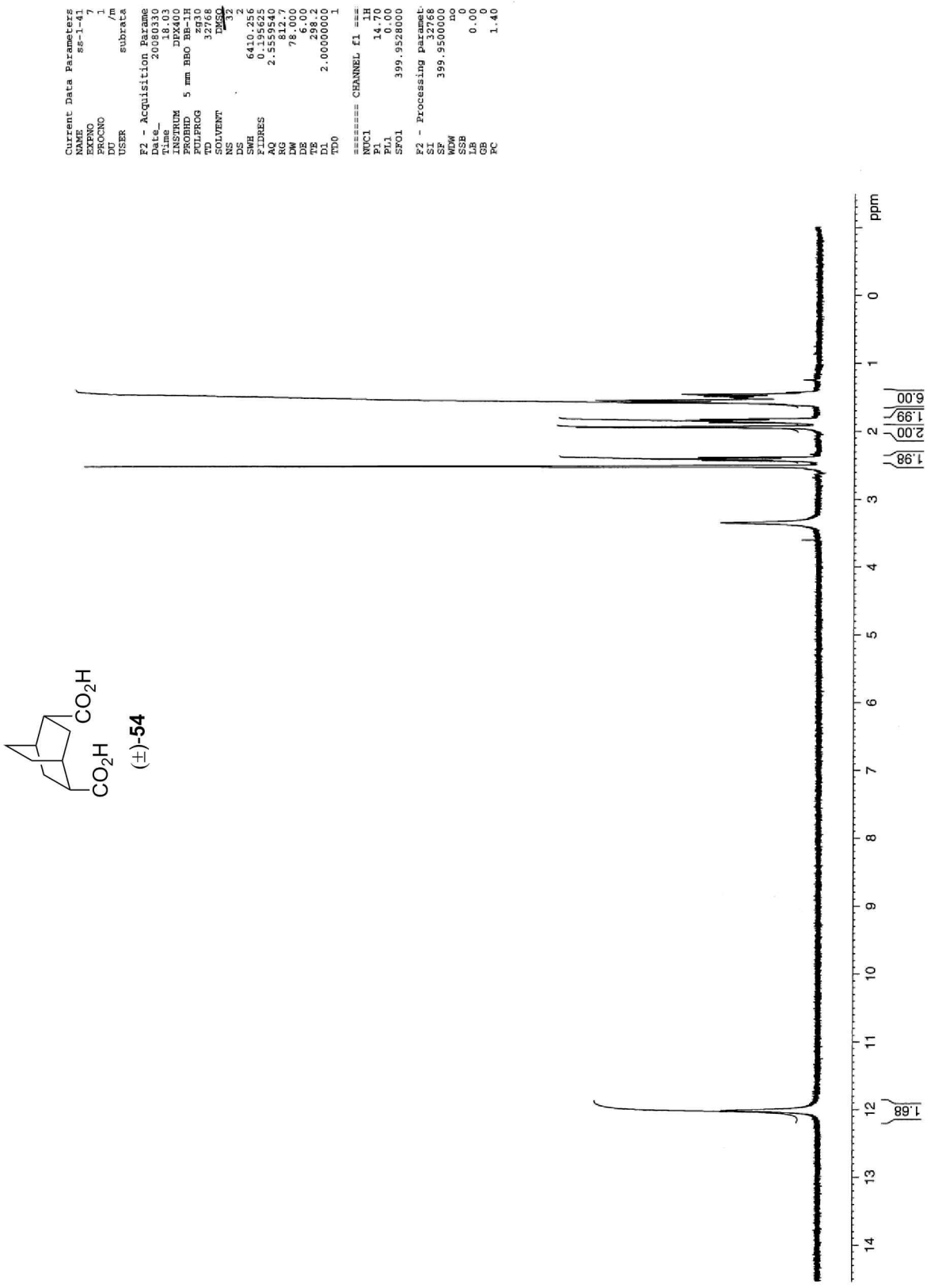

```
Current Data Parameters
NAME                  ss-1-40
EXPNO                      30
PROCNO                      1
DU                         /m
USER                  subrata

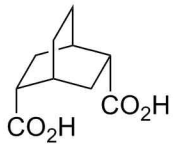
F2 - Acquisition Parameter
Date_                20080328
Time                    13.07
INSTRUM                DPX400
PROBHD   5 mm BBO BB-1H
PULPROG                zgpg30
TD                      65536
SOLVENT                 CDCl3
NS                       2450
DS                          4
SWH                25125.629 Hz
FIDRES                 0.383387 Hz
AQ                     1.3042164 se
RG                         16384
DW                        19.900 us
DE                         6.00 us
TE                       298.2 K
D1                  0.15000001 se
D11                 0.03000000 se
DELTA               0.05000000 se
TD0                         1

======== CHANNEL f1 ======
NUC1                       13C
P1                        7.80 us
PL1                      -3.00 dB
SFO1             100.5785700 MH

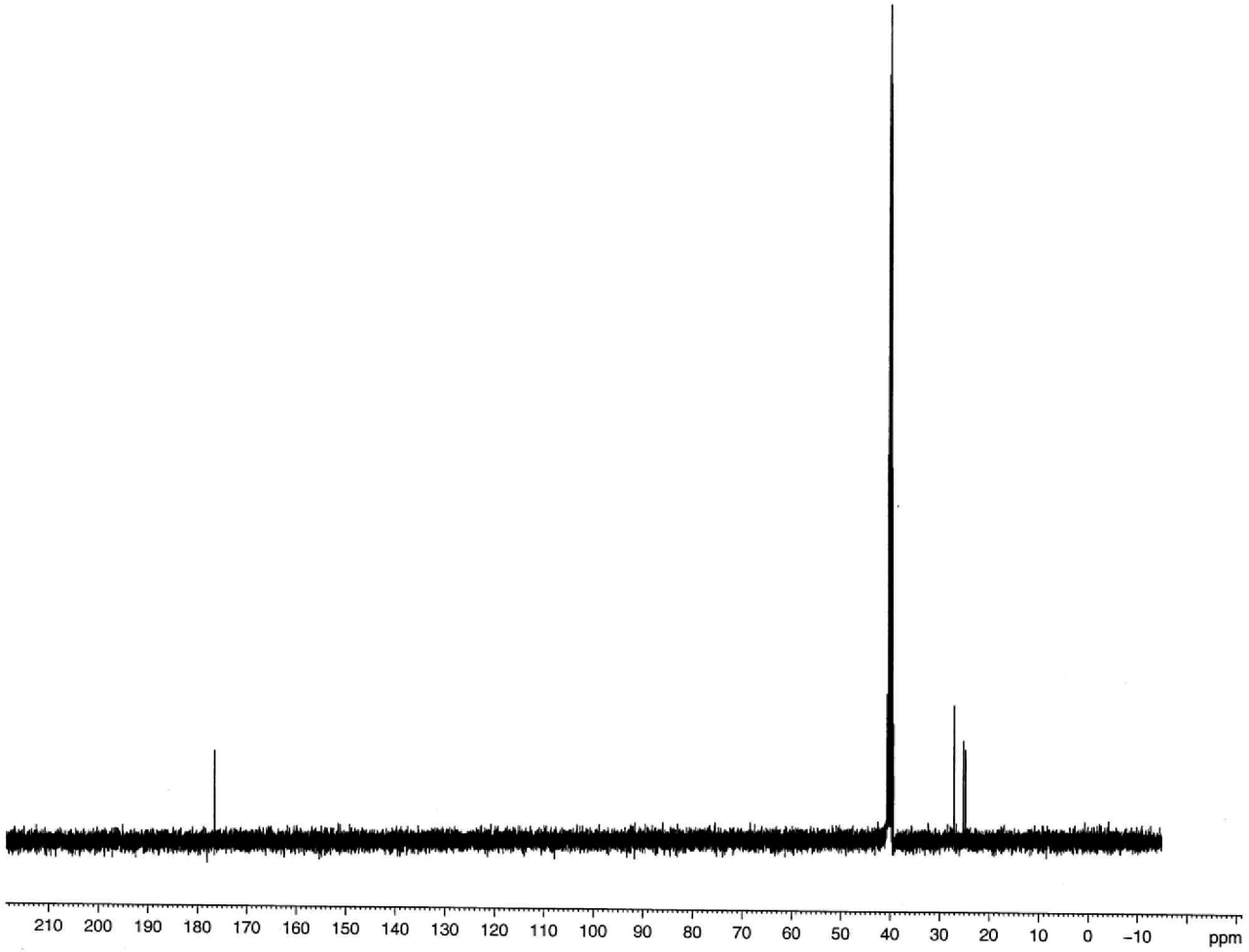
======== CHANNEL f2 ======
CPDPRG2                waltz16
NUC2                       1H
PCPD2                   135.00 us
PL2                      17.40 dB
PL12                     17.40 dB
PL13                     17.40 dB
SFO2             399.9516000 MH

F2 - Processing parameters
SI                         32768
SF               100.5675080 MH
WDW                           no
SSB                            0
LB                        0.00 Hz
GB                             0
PC                         1.40
```


Current Data Parameters
NAME ss-1-41
EXPNO 7
PROCNO 1
DU /m
USER subrata
F2 - Acquisition Parame
Date_ 20080330
Time_ 18.03
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT DMSO
NS 32
DS 2
SWH 6410.256
FIDRES 0.195625
AQ 2.5559540
RG 812.7
DW 78.000
DE 6.00
TE 298.2
D1 2.00000000
TD0 1
======== CHANNEL f1 ===
NUC1 1H
P1 14.70
PL1 0.00
SFO1 399.9528000
F2 - Processing paramet
SI 32768
SF 399.9500000
WDW no
SSB 0
LB 0.00
GB 0
PC 1.40
CO2H
CO2H
(±)-54
1.68
1.98
2.00
1.99
6.00
ppm



(±)-**54**



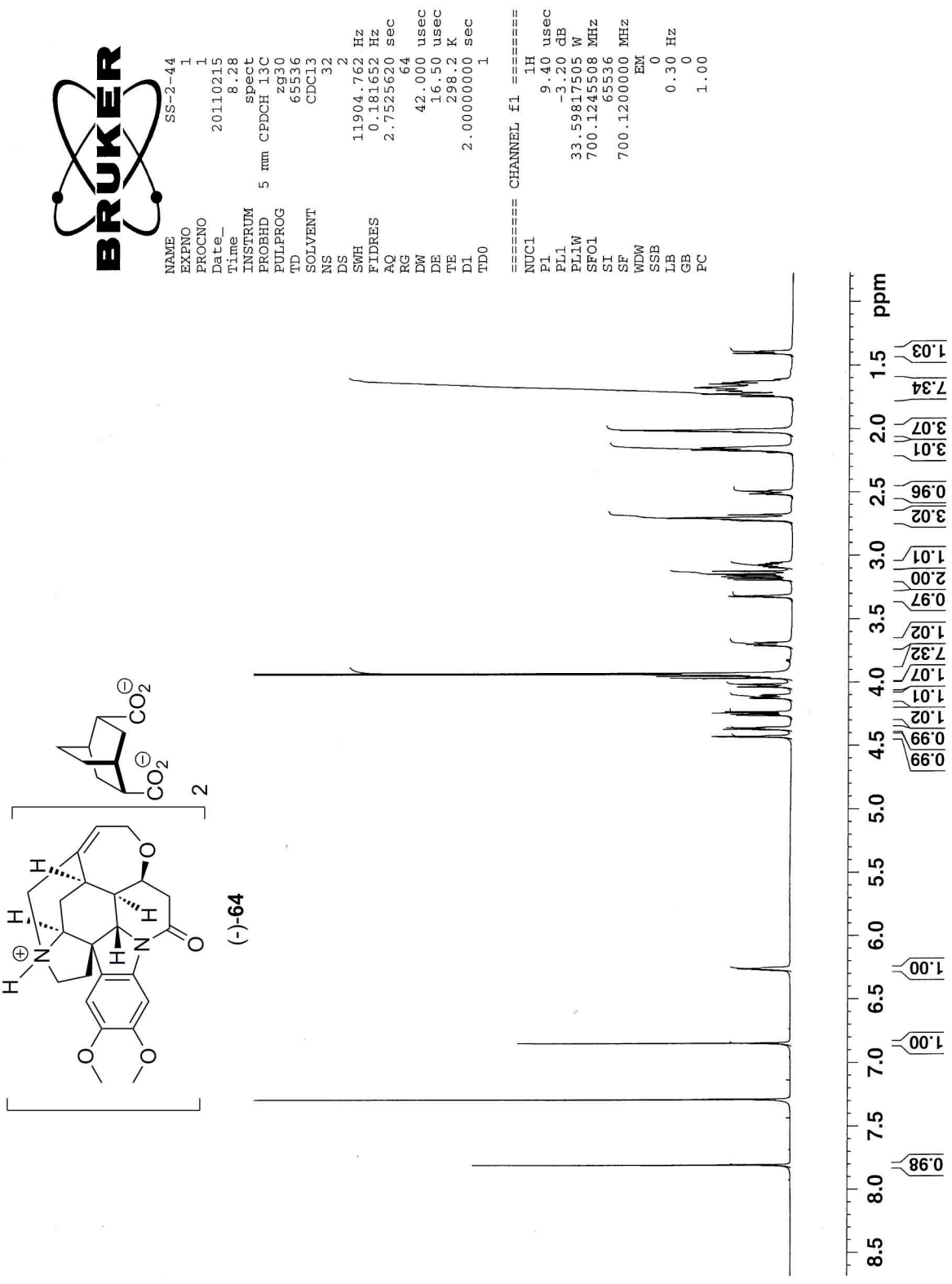

```
Current Data Parameters
NAME                  ss-1-41
EXPNO                       6
PROCNO                      1
DU                         /m
USER                  subrata

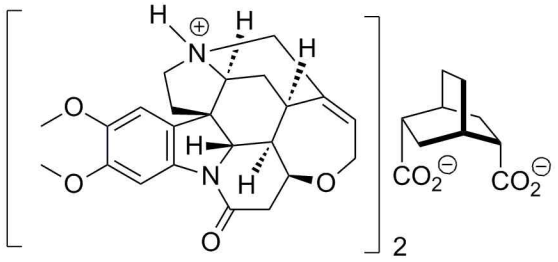
F2 - Acquisition Parameters
Date_                20080328
Time                    13.55
INSTRUM                DPX400
PROBHD   5 mm BBO BB-1H
PULPROG                zgpg30
TD                      65536
SOLVENT                  DMSO
NS                         911
DS                           4
SWH                25125.629 Hz
FIDRES                0.383387 Hz
AQ                 1.3042164 sec
RG                      2896.3
DW                     19.900 usec
DE                      6.00 usec
TE                     298.2 K
D1                 0.15000001 sec
D11                0.03000000 sec
DELTA              0.05000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                      13C
P1                       7.80 usec
PL1                     -3.00 dB
SFO1              100.5785700 MHz

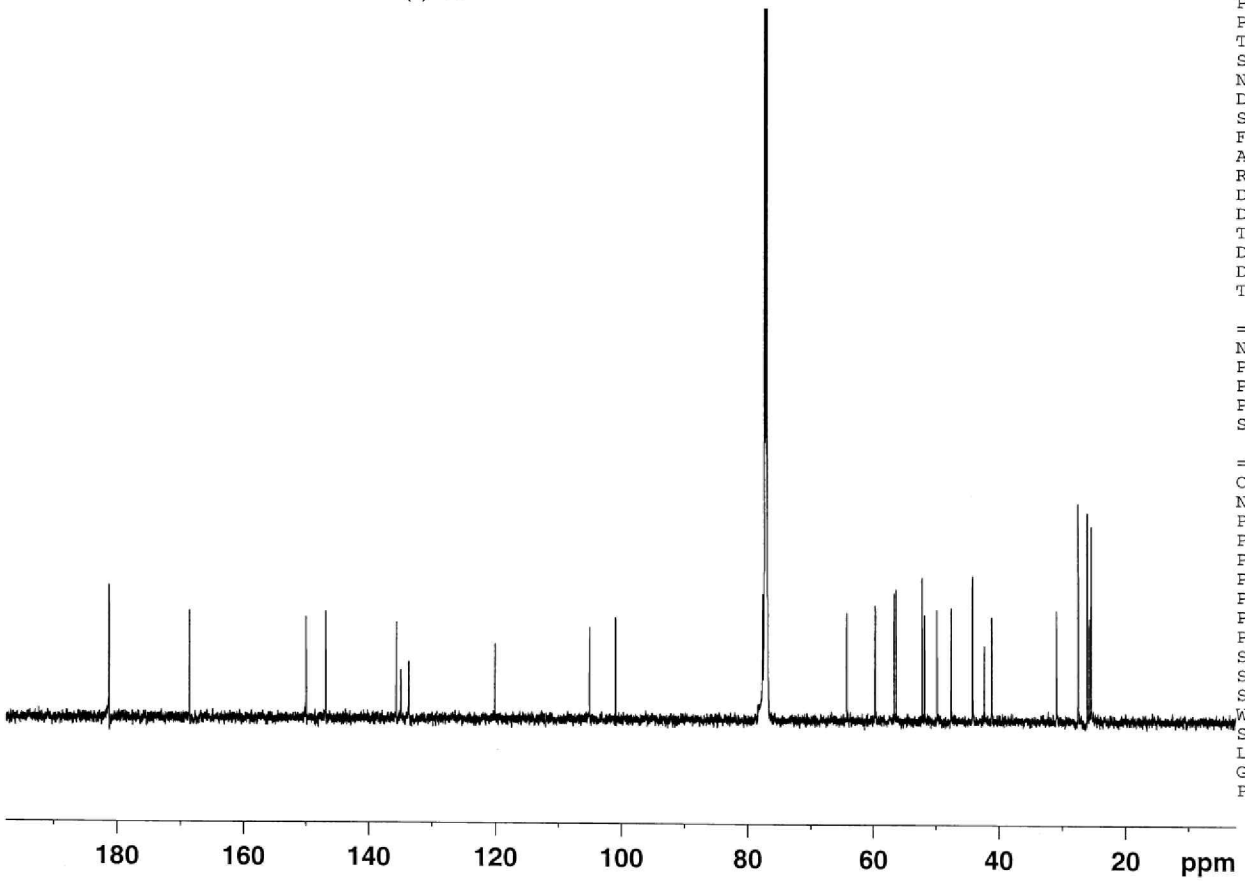
======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                  135.00 usec
PL2                     17.40 dB
PL12                    17.40 dB
PL13                    17.40 dB
SFO2              399.9516000 MHz

F2 - Processing parameters
SI                       32768
SF                100.5675080 MHz
WDW                         no
SSB                          0
LB                        0.00 Hz
GB                           0
PC                        1.00
```


BRUKER
NAME SS-2-44
EXPNO 1
PROCNO 1
Date_ 20110215
Time 8.28
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.181652 Hz
AQ 2.7525620 sec
RG 64
DW 42.000 usec
DE 16.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1245508 MHz
SI 65536
SF 700.1200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
(-)-64
2
ppm
0.98
1.00
1.00
0.99
0.99
1.02
1.01
1.07
7.32
1.02
0.97
2.00
1.01
3.02
0.96
3.01
3.07
7.34
1.03

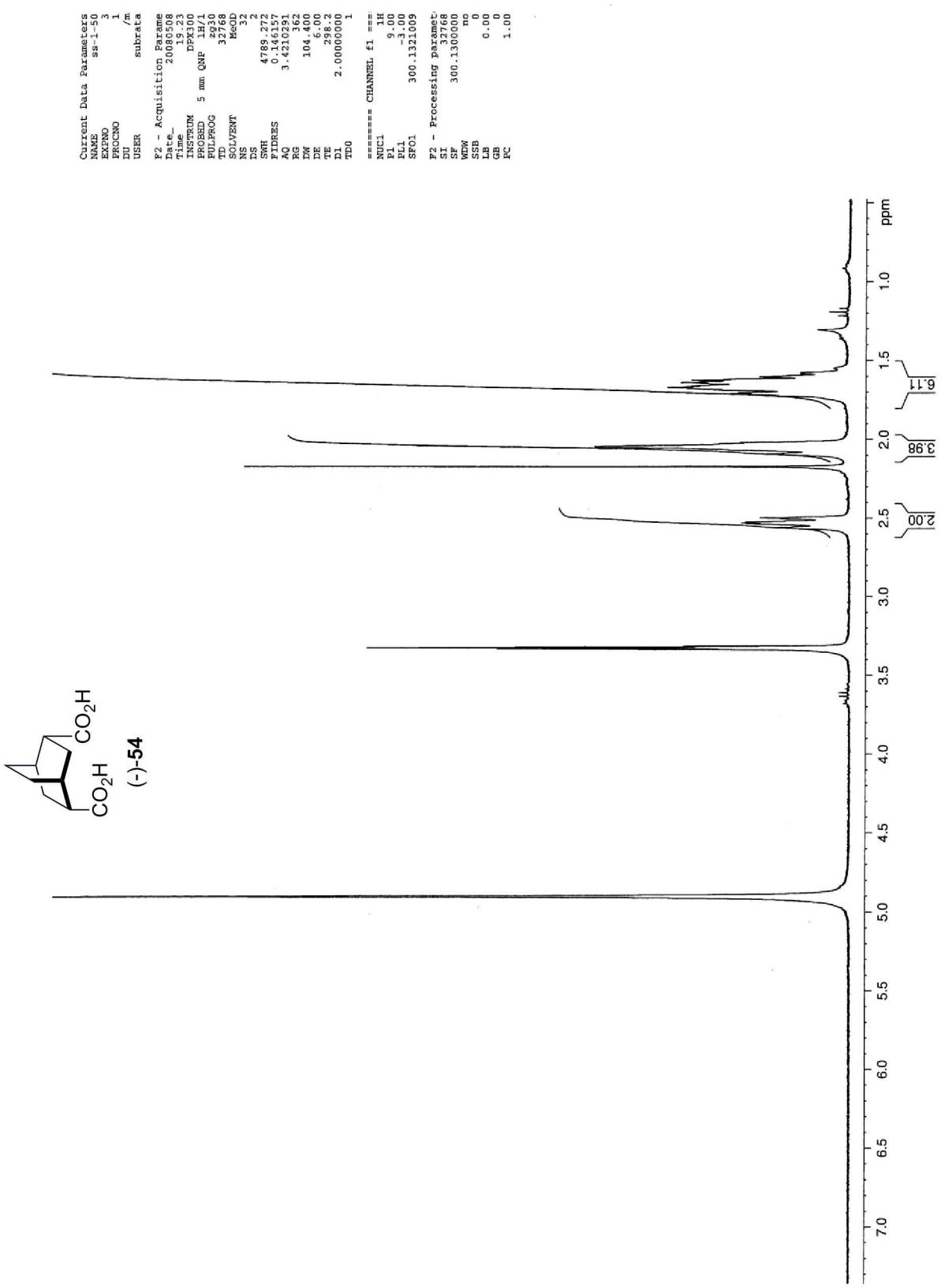


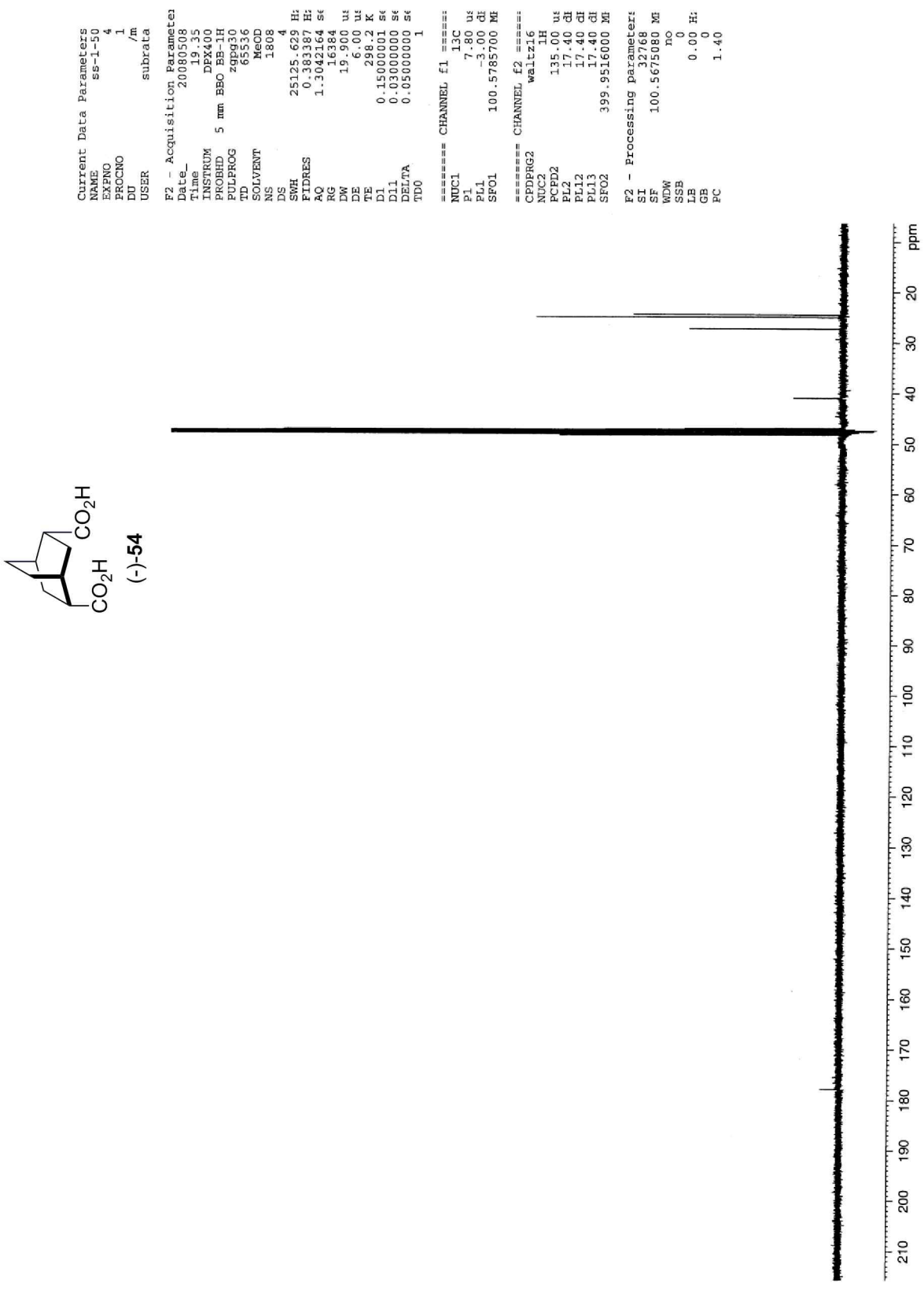
(-)-**65**

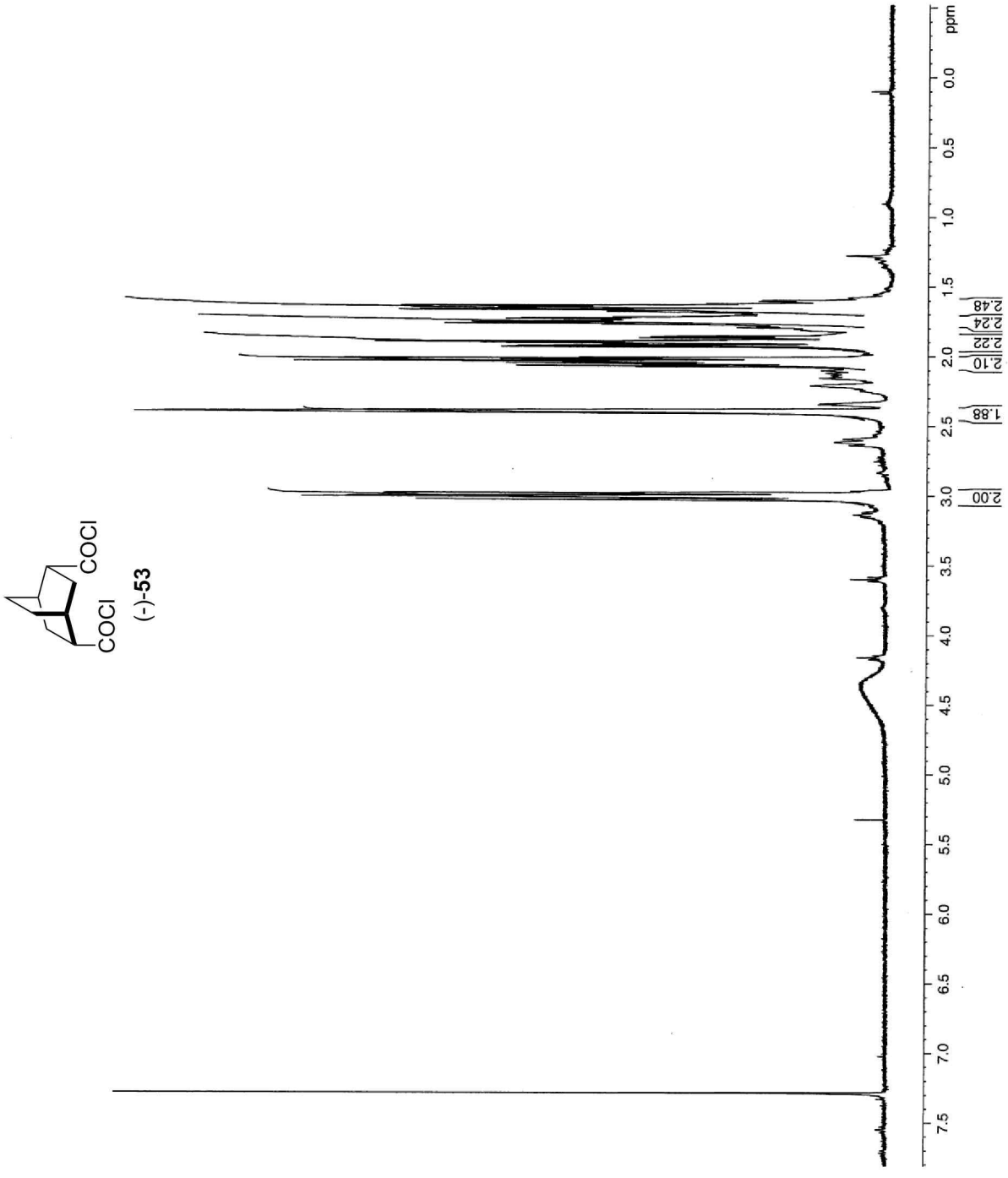


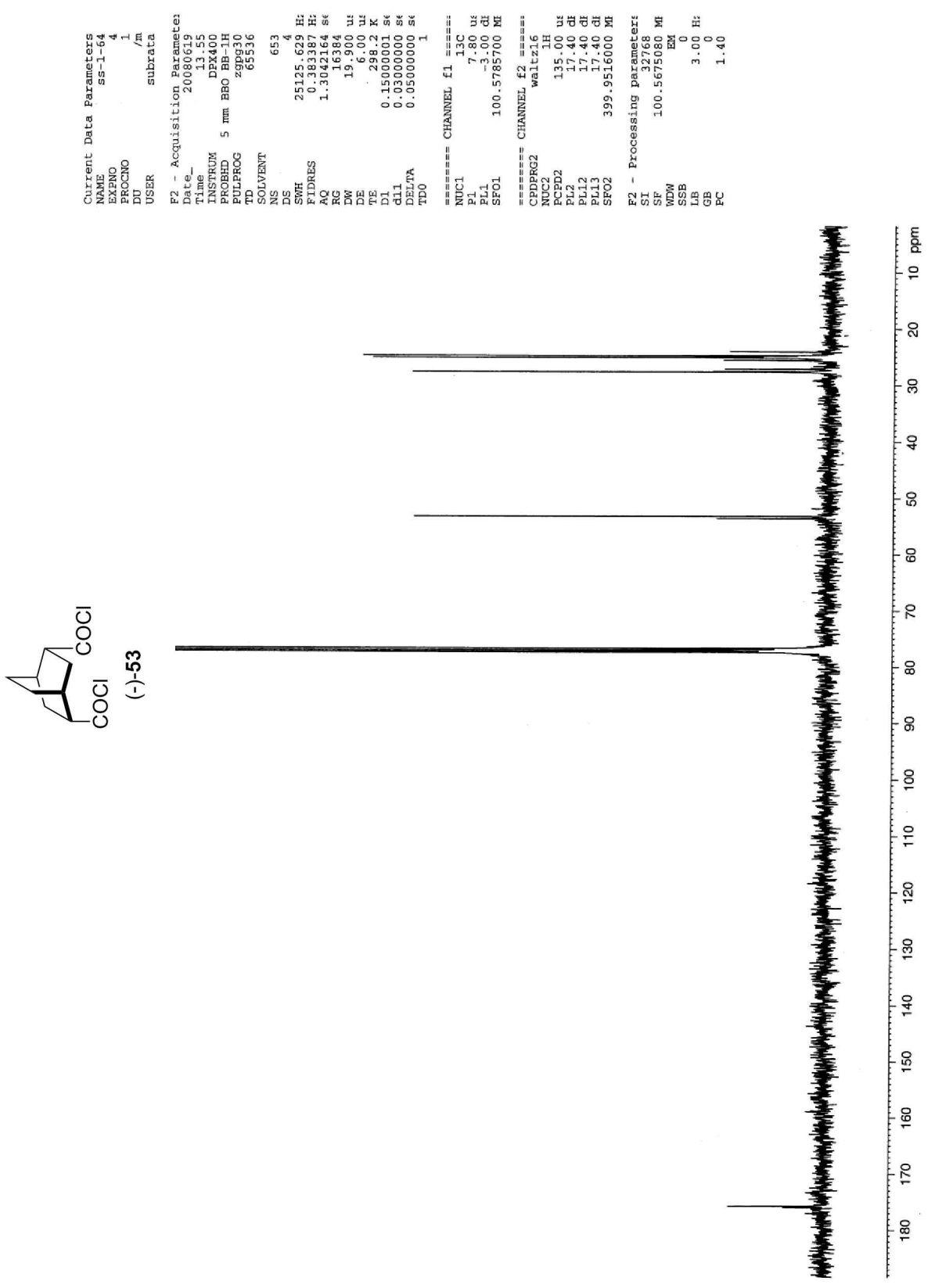
BRUKER

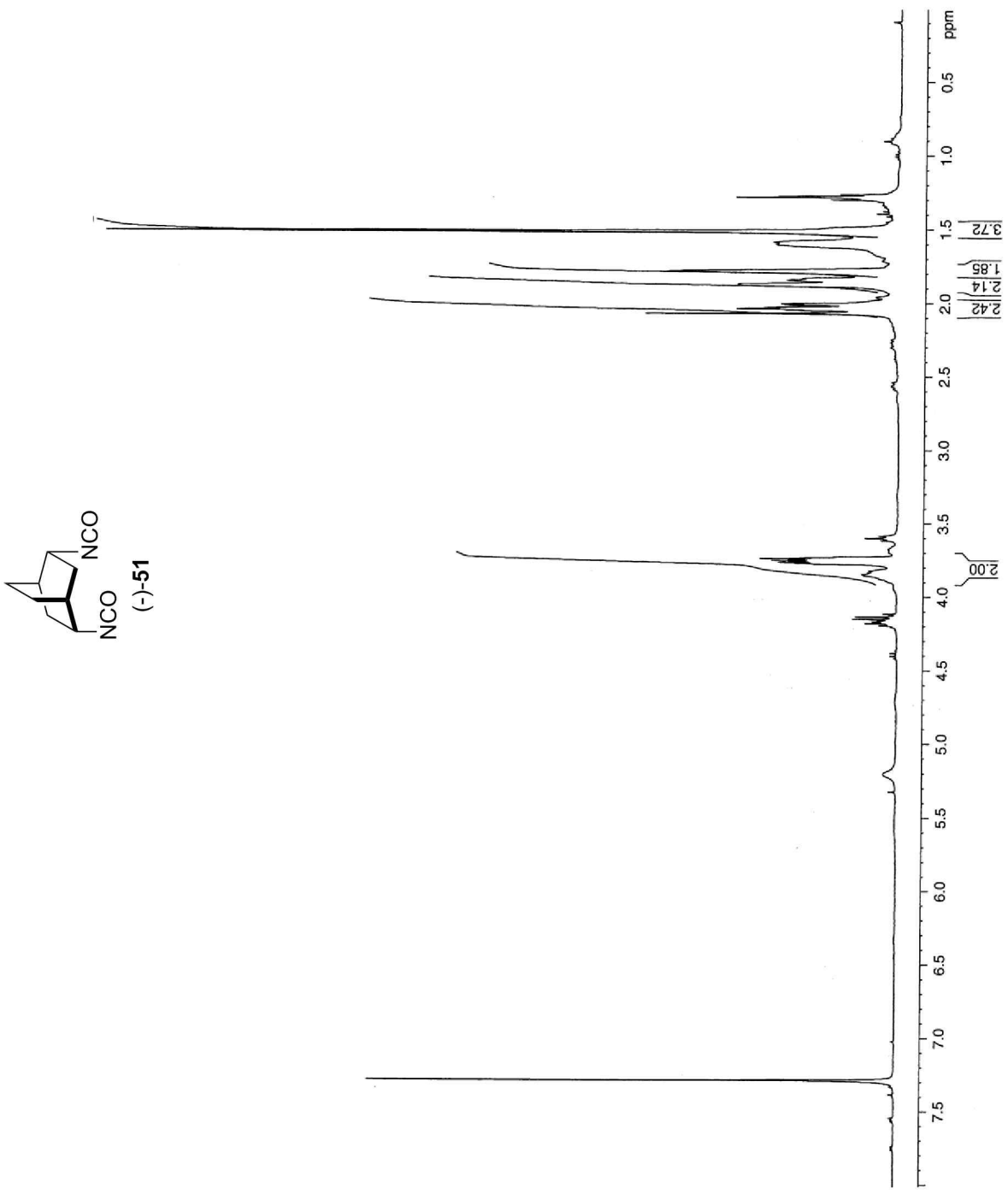
NAME	SS-2-44
EXPNO	2
PROCNO	1
Date_	20110215
Time	8.36
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	98304
SOLVENT	CDCl3
NS	142
DS	4
SWH	41666.668 Hz
FIDRES	0.423855 Hz
AQ	1.1796980 sec
RG	203
DW	12.000 usec
DE	15.00 usec
TE	298.2 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 usec
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0629186 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 usec
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1228005 MHz
SI	131072
SF	176.0453140 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40

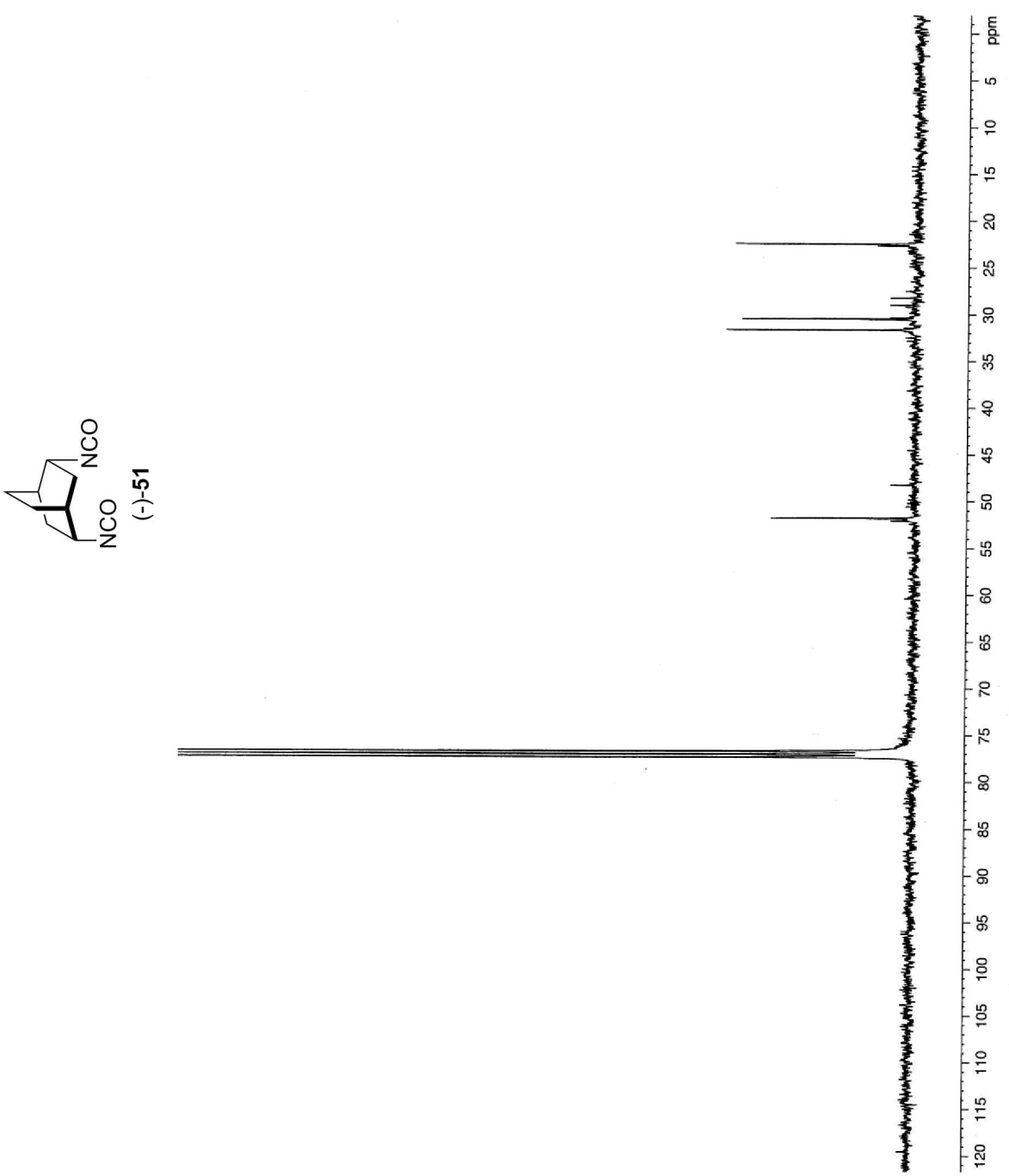

Current Data Parameters
NAME ss-1-50
EXPNO 3
PROCNO 1
DU /m
USER subrata
F2 - Acquisition Parame
Date_ 20080508
Time 19.23
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT MeOD
NS 32
DS 2
SWH 4789.272
FIDRES 0.146157
AQ 3.4210291
RG 362
DW 104.400
DE 6.00
TE 298.2
D1 2.00000000
TD0 1
======== CHANNEL f1 ===
NUC1 1H
P1 9.00
PL1 -3.00
SFO1 300.1321009
F2 - Processing paramet
SI 32768
SF 300.1300000
WDW no
SSB 0
LB 0.00
GB 0
PC 1.00
CO2H
CO2H
(-)-54
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
2.00
3.98
6.11

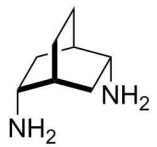

CO2H
CO2H
(-)-54
Current Data Parameters
NAME ss-1-50
EXPNO 4
PROCNO 1
DU /m
USER subrata
F2 - Acquisition Parameter
Date_ 20080508
Time 19.35
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT MeOD
NS 1808
DS 4
SWH 25125.629 H
FIDRES 0.383387 H
AQ 1.3042164 s
RG 16384
DW 19.900 u
DE 6.00 u
TE 298.2 K
D1 0.15000001 s
D11 0.03000000 s
DELTA 0.05000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 13C
P1 7.80 u
PL1 -3.00 d
SFO1 100.5785700 M
======== CHANNEL f2 ======
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 u
PL2 17.40 d
PL12 17.40 d
PL13 17.40 d
SFO2 399.9516000 M
F2 - Processing parameter
SI 32768
SF 100.5675080 M
WDW no
SSB 0
LB 0.00 H
GB 0
PC 1.40
ppm


Current Data Parameters
NAME ss-1-64
EXPNO 1
PROCNO 1
DU /m
USER subrata
F2 - Acquisition Parame
Date_ 20080619
Time 12.04
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256
FIDRES 0.195625
AQ 2.5559540
RG 256
DW 78.000
DE 6.00
TE 298.2
D1 2.00000000
TD0 1
======== CHANNEL f1 ===
NUC1 1H
P1 14.70
PL1 0.00
SFO1 399.9528000
F2 - Processing paramet
SI 32768
SF 399.9500000
WDW no
SSB 0
LB 0.00
GB 0
PC 1.00
COCl
COCl
(-)-53
2.00
1.88
2.10
2.22
2.24
2.48
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm


COCl
COCl
(-)-53
Current Data Parameters
NAME ss-1-64
EXPNO 4
PROCNO 1
DU /m
USER subrata
F2 - Acquisition Parameter
Date_ 20080619
Time_ 13.55
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 653
DS 4
SWH 25125.629 H
FIDRES 0.383387 H
AQ 1.3042164 s
RG 16384
DW 19.900 u
DE 6.00 u
TE 298.2 K
D1 0.15000001 s
d11 0.03000000 s
DELTA 0.05000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 13C
P1 7.80 u
PL1 -3.00 d
SFO1 100.5785700 M
======== CHANNEL f2 ======
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 u
PL2 17.40 d
PL12 17.40 d
PL13 17.40 d
SFO2 399.9516000 M
F2 - Processing parameter
SI 32768
SF 100.5675080 M
WDW EM
SSB 0
LB 3.00 H
GB 0
PC 1.40
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


Current Data Parameters
NAME ss-1-71
EXPNO 1
PROCNO 1
DU /m
USER subrata
F2 - Acquisition Parame
Date_ 20080623
Time 18.15
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256
FIDRES 0.195625
AQ 2.5559540
RG 512
DW 78.000
DE 6.00
TE 298.2
D1 2.00000000
TD0 1
======== CHANNEL f1 ===
NUC1 1H
P1 14.70
PL1 0.00
SFO1 399.9528000
F2 - Processing paramet
SI 32768
SF 399.9500000
WDW EM
SSB 0
LB 0.70
GB 0
PC 1.40
NCO
NCO
(-)-51
2.00
2.42
2.14
1.85
3.72
ppm


NCO
NCO
(-)-51
Current Data Parameters
NAME ss-1-71
EXPNO 4
PROCNO 1
DU /m
USER subrata
F2 - Acquisition Parameter
Date_ 20080623
Time 20.03
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 2450
DS 4
SWH 25125.629 H
FIDRES 0.383387 H
AQ 1.3042164 s
RG 16384
DW 19.900 u
DE 6.00 u
TE 298.2 K
D1 0.15000001 s
d11 0.03000000 s
DELTA 0.05000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 13C
P1 7.80 u
PL1 -3.00 d
SFO1 100.5785700 M
======== CHANNEL f2 ======
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 u
PL2 17.40 d
PL12 17.40 d
PL13 17.40 d
SFO2 399.9516000 M
F2 - Processing parameter
SI 32768
SF 100.5675080 M
WDW EM
SSB 0
LB 3.00 H
GB 0
PC 1.40
120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 ppm



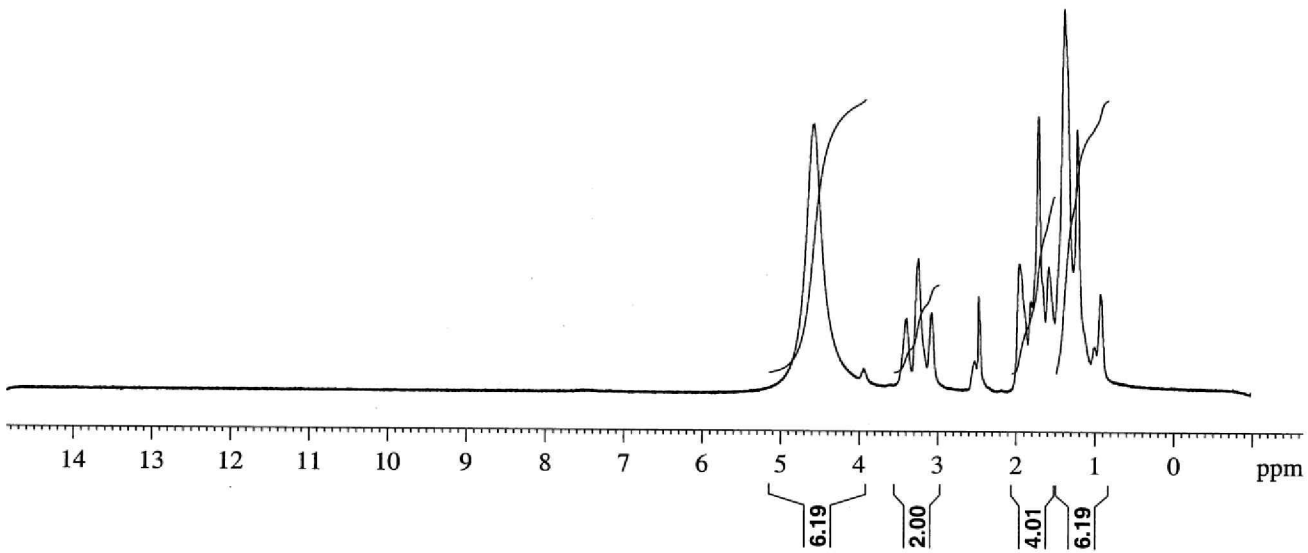
(-)-**34.HCl**

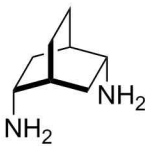
```
Current Data Parameters
NAME                  ss-1-83
EXPNO                       1
PROCNO                      1

F2 - Acquisition Parameter:
Date_              20080711
Time                  15.15
INSTRUM             DPX300
PROBHD    5 mm QNP  1H/1
PULPROG                zg30
TD                    32768
SOLVENT                 D2O
NS                         32
DS                          2
SWH                4789.272 Hz
FIDRES             0.146157 Hz
AQ                 3.4210291 se
RG                     228.1
DW                   104.400 us
DE                     6.00 us
TE                    298.2 K
D1              2.00000000 se
TD0                         1

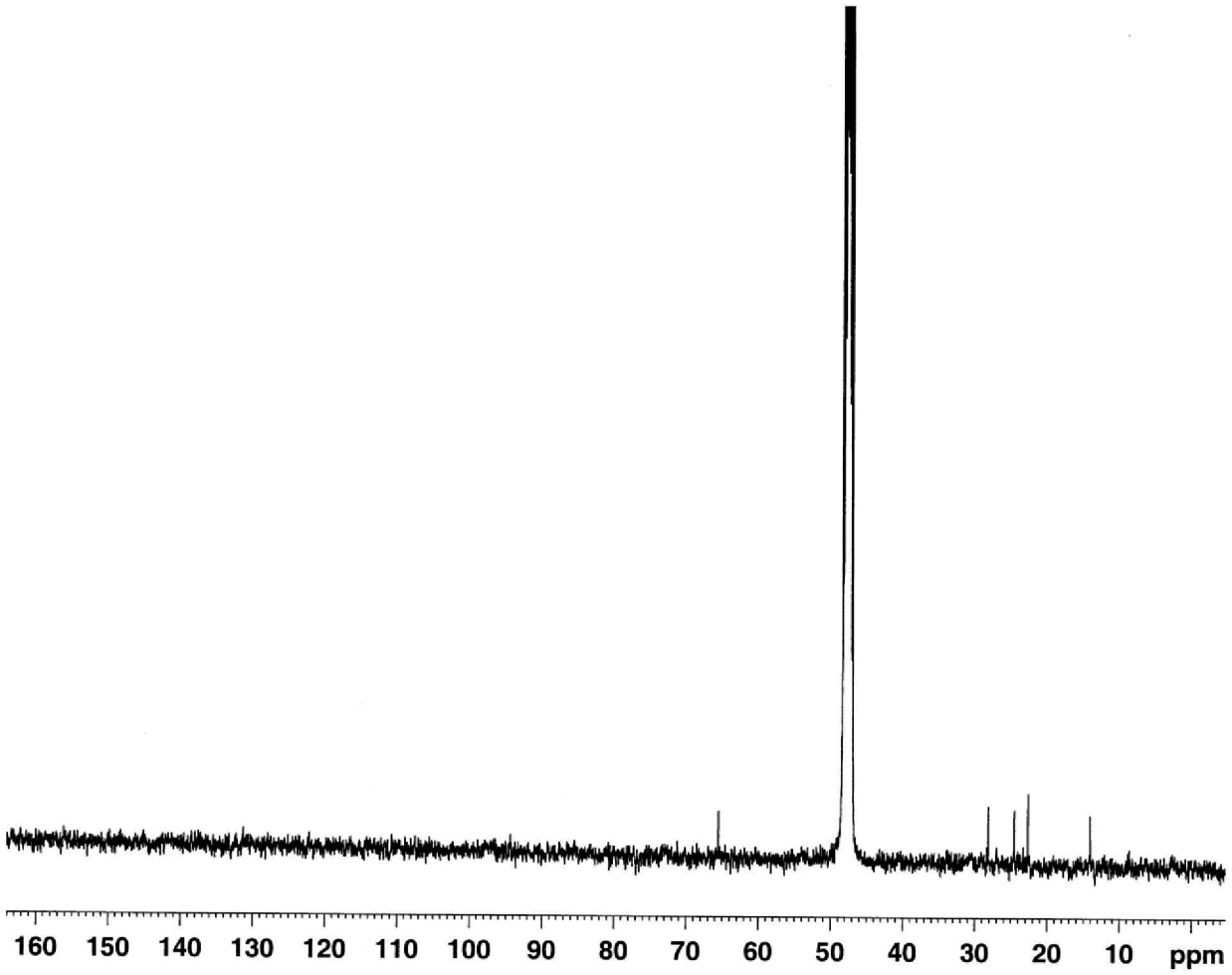
======== CHANNEL f1 =======
NUC1                       1H
P1                       9.00 us
PL1                     -3.00 dB
SFO1           300.1321009 MH:

F2 - Processing parameters
SI                        32768
SF             300.1300000 MH:
WDW                          no
SSB                           0
LB                         0.00 Hz
GB                            0
PC                         1.00
```





(-)-**34.HCl**



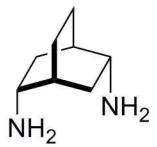

```
Current Data Parameters
NAME                  ss-1-83
EXPNO                      11
PROCNO                      1

F2 - Acquisition Parameters
Date_                20080714
Time                    16.41
INSTRUM                DPX400
PROBHD   5 mm BBO BB-1H
PULPROG                zgpg30
TD                      65536
SOLVENT
NS                       2450
DS                          4
SWH                 25125.629 Hz
FIDRES                0.383387 Hz
AQ                   1.3042164 sec
RG                       16384
DW                      19.900 usec
DE                       6.00 usec
TE                      298.2 K
D1                  0.15000001 sec
d11                 0.03000000 sec
DELTA               0.05000000 sec
TD0                         1

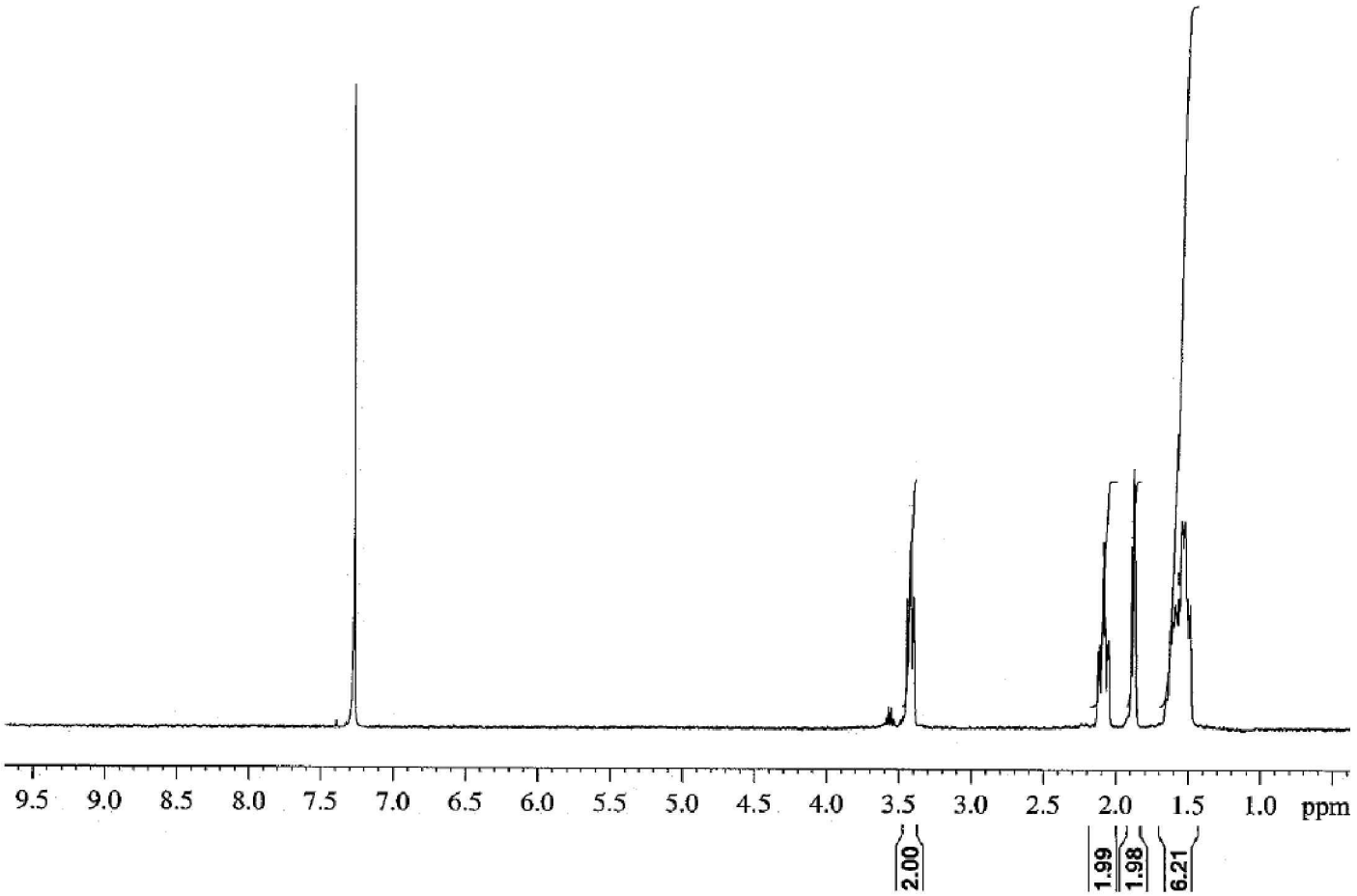
======== CHANNEL f1 ========
NUC1                       13C
P1                        7.80 usec
PL1                      -3.00 dB
SFO1               100.5785700 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                   135.00 usec
PL2                      17.40 dB
PL12                     17.40 dB
PL13                     17.40 dB
SFO2               399.9516000 MHz

F2 - Processing parameters
SI                       32768
SF                 100.5675080 MHz
WDW                         EM
SSB                          0
LB                        3.00 Hz
GB                           0
PC                        1.40
```



(-)-**34**

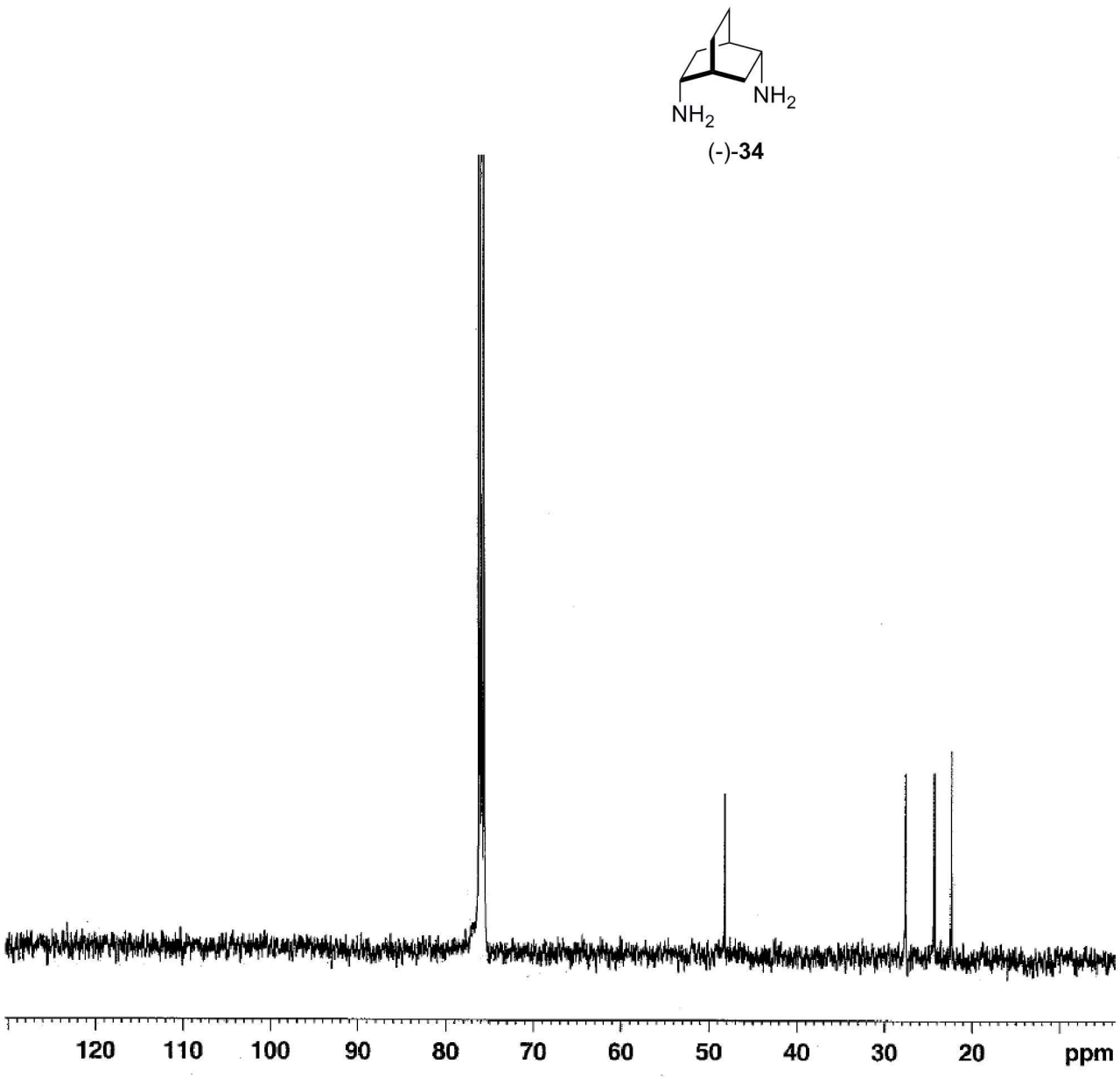



```
Current Data Parameters
NAME      ss-2-9
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameter
Date_           20080815
Time               12.10
INSTRUM          DPX400
PROBHD   5 mm BBO BB-1H
PULPROG             zg30
TD                 32768
SOLVENT
NS                    32
DS                     2
SWH             6410.256 Hz
FIDRES          0.195625 Hz
AQ              2.5559540 se
RG                1824.6
DW                78.000 us
DE                 6.00 us
TE                298.2 K
D1           2.00000000 se
TD0                    1

======== CHANNEL f1 ======
NUC1                  1H
P1                14.70 us
PL1                0.00 dB
SFO1         399.9528000 MH

F2 - Processing parameters
SI                 32768
SF          399.9500000 MH
WDW                   EM
SSB                    0
LB                  0.70 Hz
GB                     0
PC                  1.00
```



(-)-**34**

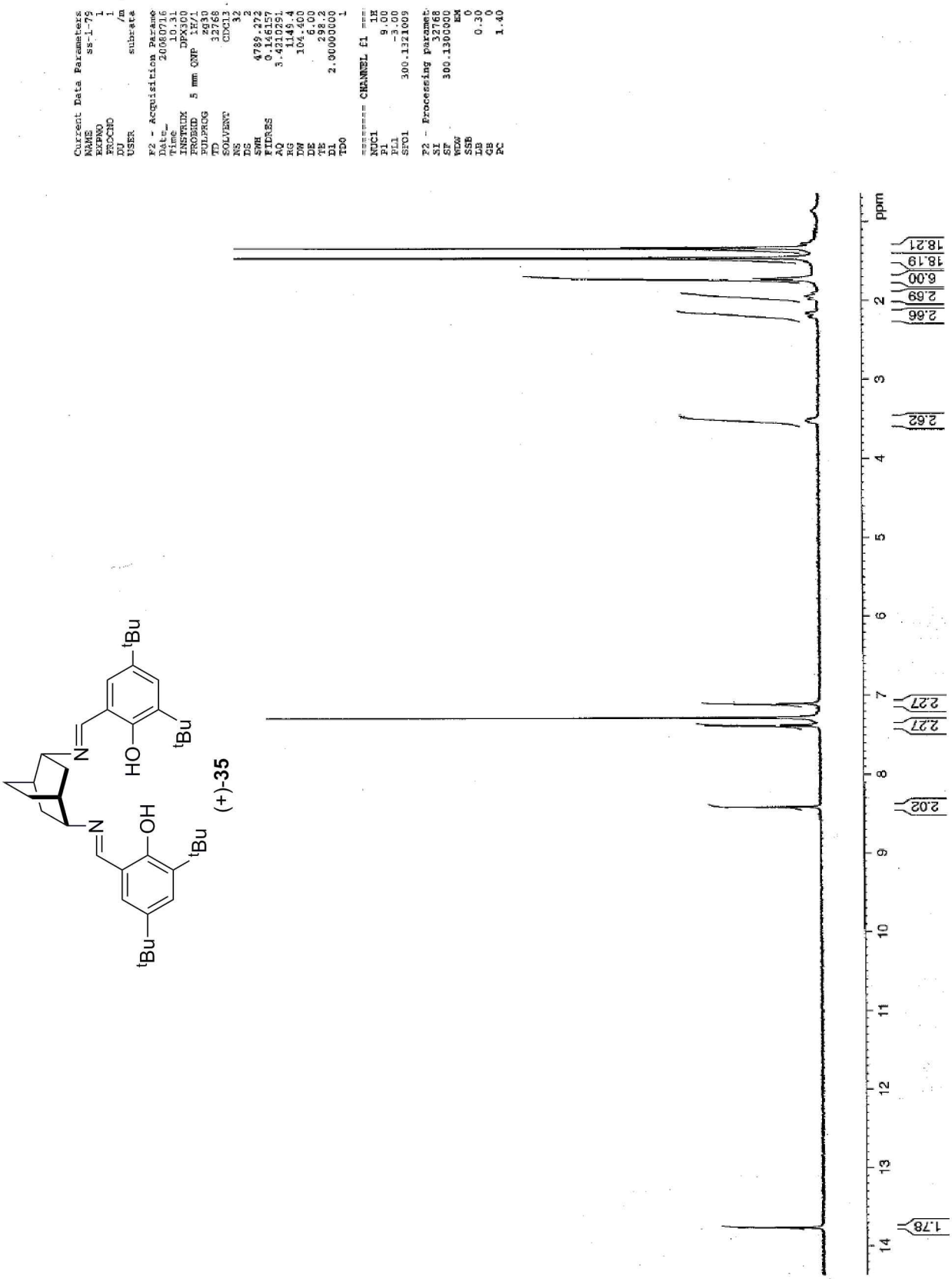
```
Current Data Parameters
NAME      ss-2-9
EXPNO                  5
PROCNO                 1

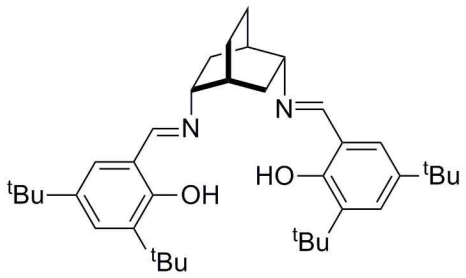
F2 - Acquisition Parameters
Date_           20080815
Time               13.45
INSTRUM           DPX400
PROBHD   5 mm BBO BB-1H
PULPROG          zgpg30
TD                65536
SOLVENT
NS                 2450
DS                    4
SWH           25125.629 Hz
FIDRES         0.383387 Hz
AQ            1.3042164 sec
RG                16384
DW               19.900 usec
DE                6.00 usec
TE                298.2 K
D1           0.15000001 sec
d11          0.03000000 sec
DELTA        0.05000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  13C
P1                   7.80 usec
PL1                 -3.00 dB
SFO1        100.5785700 MHz

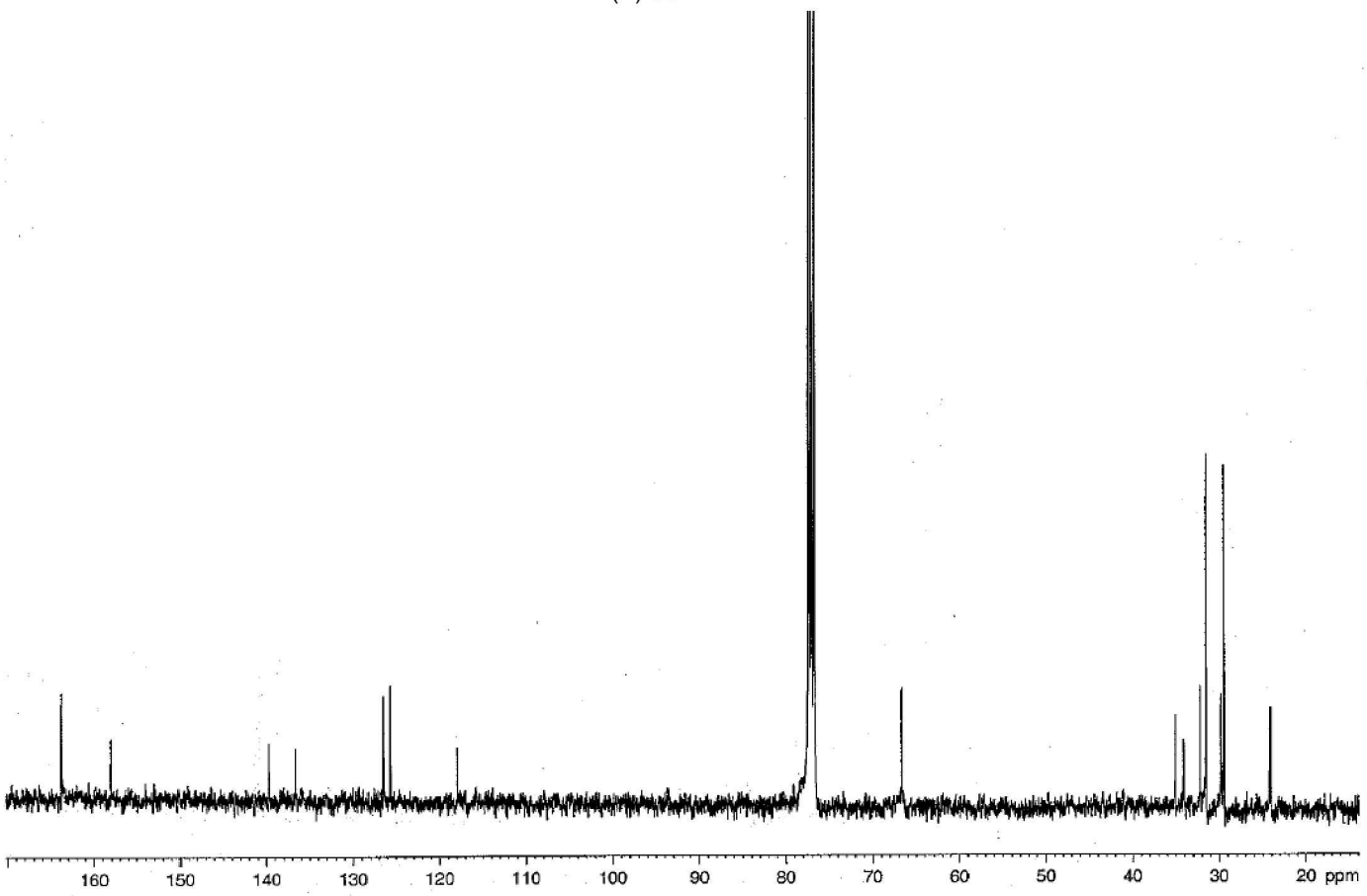
======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                  1H
PCPD2              135.00 usec
PL2                 17.40 dB
PL12                17.40 dB
PL13                17.40 dB
SFO2        399.9516000 MHz

F2 - Processing parameters
SI                 32768
SF          100.5675080 MHz
WDW                   EM
SSB                    0
LB                  3.00 Hz
GB                     0
PC                  1.40
```


Current Data Parameters
NAME ss-1-79
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4789.272
FIDRES 0.146157
AQ 3.4210251
RG 1146.4
DW 104.400
DE 6.00
TE 298.2
D1 2.00000000
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00
PL1 -3.00
SFO1 300.1321009
F2 - Processing parameters
SI 32768
SF 300.1300000
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.40
(+)-35
ppm
1.78
2.02
2.27
2.27
2.62
2.66
2.69
6.00
18.19
18.21



(+)-**35**



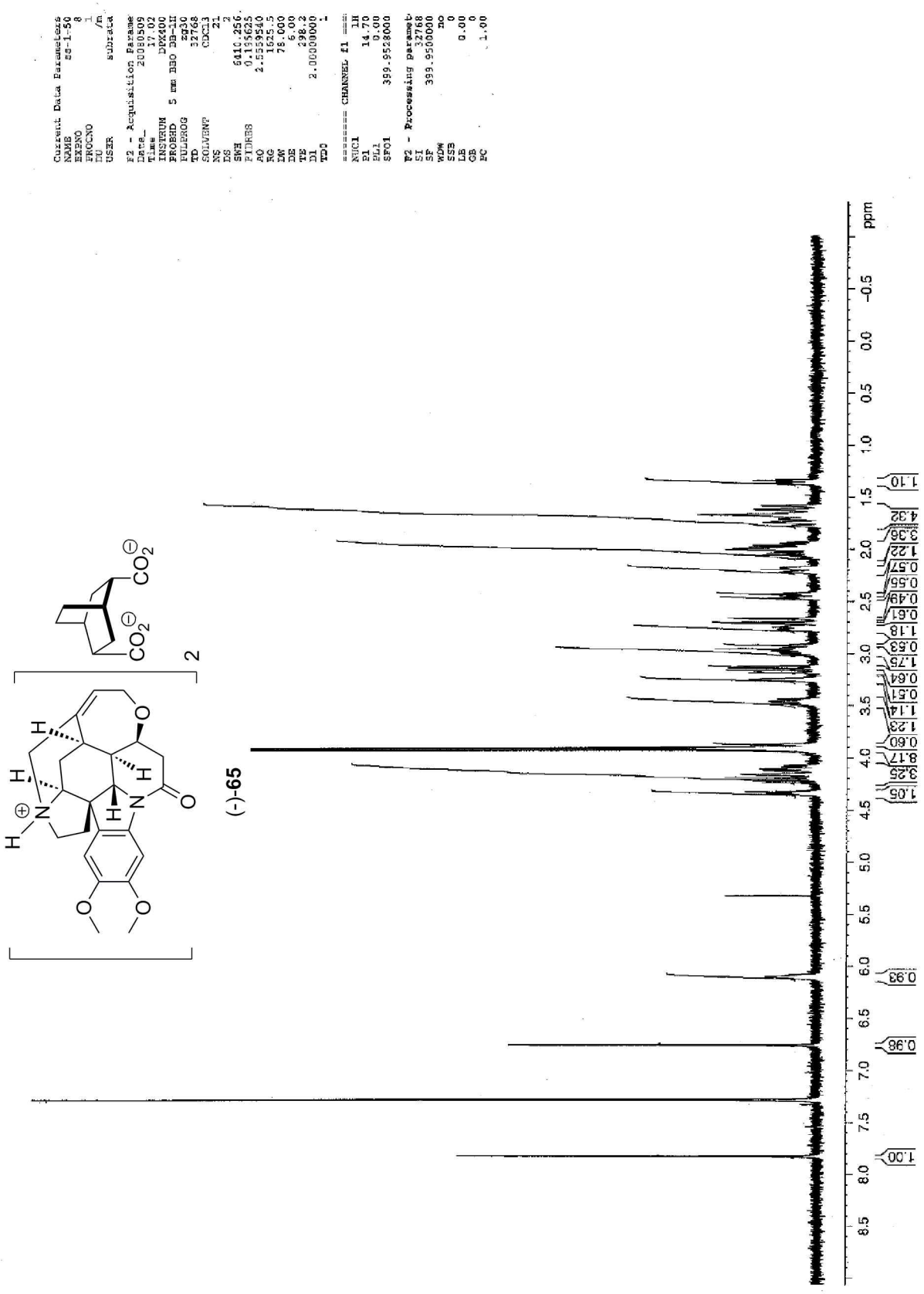

```
Current Data Parameters
NAME                  ss-1-92
EXPNO                       4
PROCNO                      1
DU                         /m
USER                  subrata

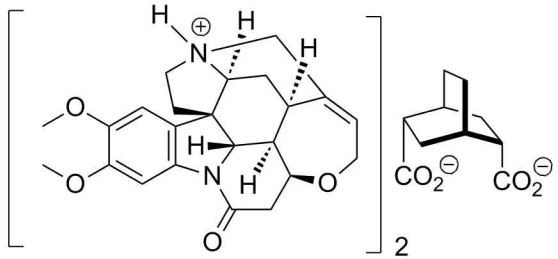
F2 - Acquisition Parameter
Date_              20080927
Time                  19.00
INSTRUM             DPX400
PROBHD    5 mm BBO BB-1H
PULPROG             zgpg30
TD                   65536
SOLVENT
NS                    2450
DS                       4
SWH              25125.629 H
FIDRES           0.383387 H
AQ               1.3042164 s
RG                   16384
DW                  19.900 u
DE                   6.00 u
TE                  298.2 K
D1               0.15000001 s
d11              0.03000000 s
DELTA            0.05000000 s
TD0                      1

======== CHANNEL f1 ======
NUC1                   13C
P1                    7.80 u
PL1                  -3.00 d
SFO1          100.5785700 M

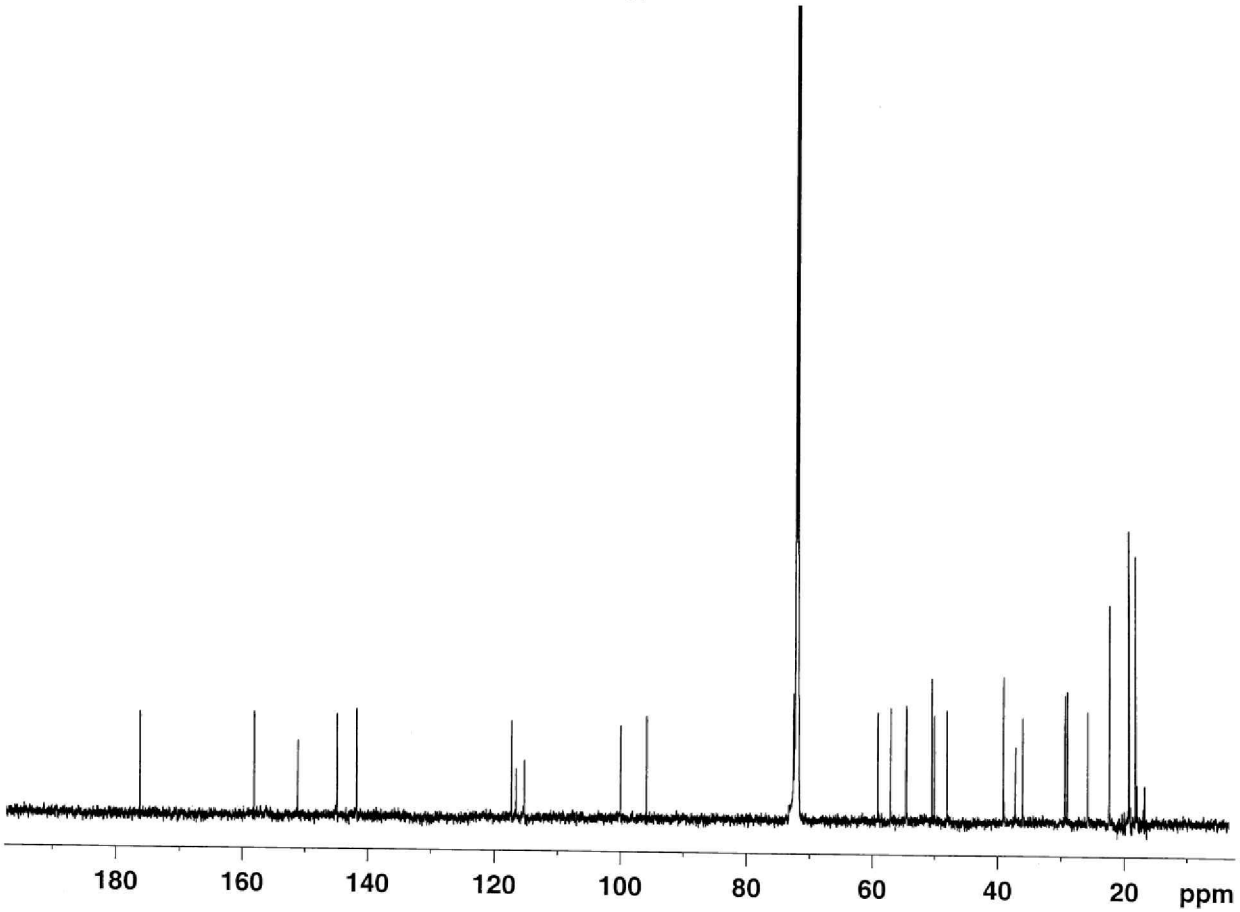
======== CHANNEL f2 ======
CPDPRG2            waltz16
NUC2                   1H
PCPD2               135.00 u
PL2                  17.40 d
PL12                 17.40 d
PL13                 17.40 d
SFO2          399.9516000 M

F2 - Processing parameter
SI                    32768
SF           100.5675080 M
WDW                     EM
SSB                      0
LB                    3.00 H
GB                       0
PC                    1.00
```


Current Data Parameters
NAME es-1-56
EXPNO 8
PROCNO 1
F2 - Acquisition Parame
Date_ 20080509
Time 17.02
INSTRUM DPX400
PROBHD 5 mm BBO BB-IF
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 21
DS 2
SWH 5410.256
FIDRES 0.165625
AQ 2.5559540
RG 1625.5
DW 78.000
DE 6.00
TE 298.2
D1 2.00000000
TD0 1
CHANNEL f1
NUC1 1H
P1 14.70
PL1 0.00
SFO1 399.9528000
F2 - Processing paramet
SI 32768
SF 399.9500000
WDW no
SSB 0
LB 0.00
GB 0
PC 1.00
(-)-65
2
ppm



(-)-**65**



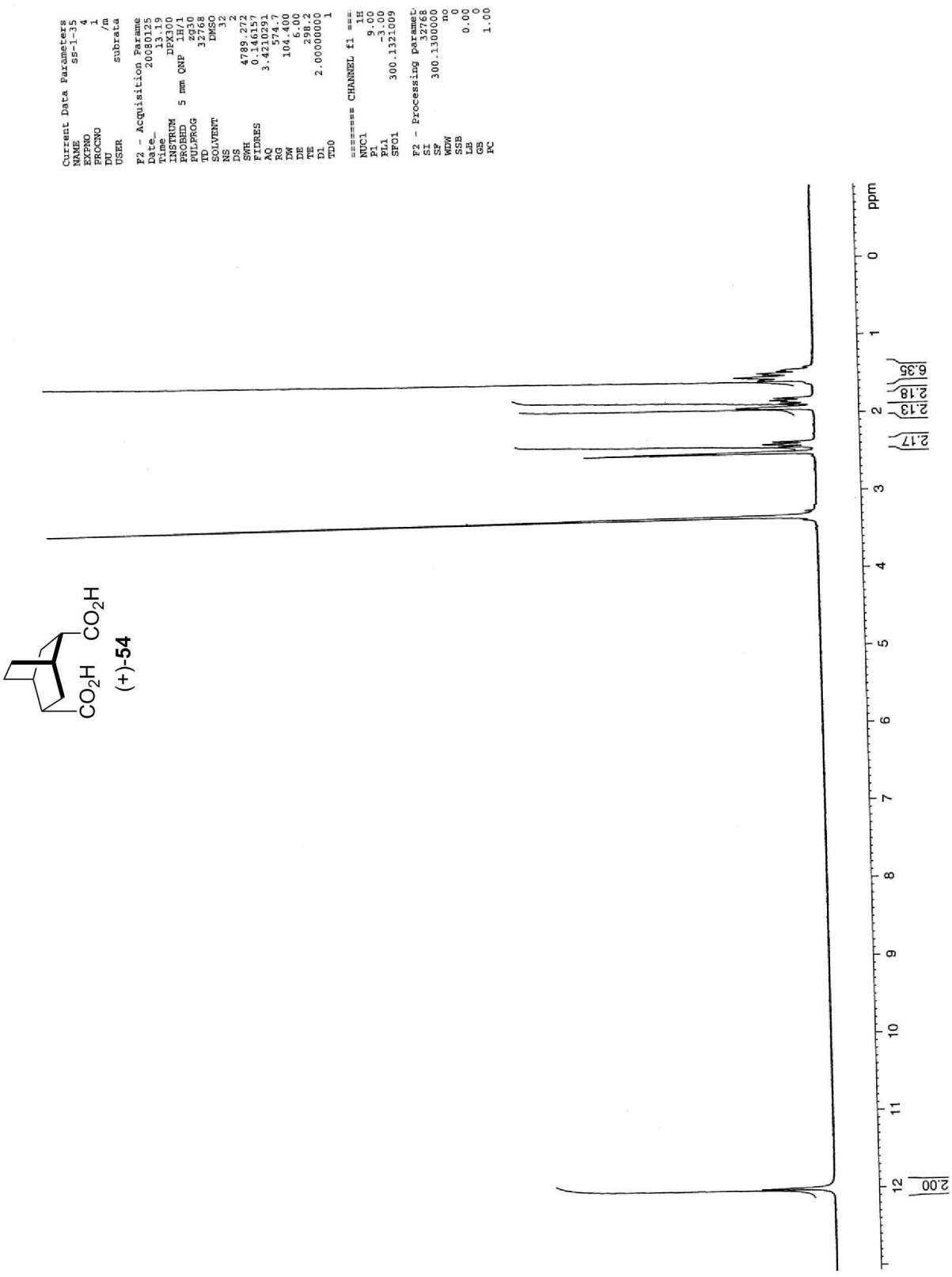

```
Current Data Parameters
NAME                  ss-1-71
EXPNO                       4
PROCNO                      1

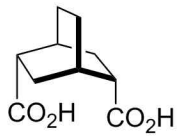
F2 - Acquisition Parameters
Date_               20080623
Time                   20.03
INSTRUM                DPX400
PROBHD   5 mm BBO BB-1H
PULPROG                zgpg30
TD                      65536
SOLVENT
NS                       2450
DS                          4
SWH                25125.629 Hz
FIDRES              0.383387 Hz
AQ                 1.3042164 sec
RG                      16384
DW                     19.900 usec
DE                      6.00 usec
TE                     298.2 K
D1                0.15000001 sec
d11               0.03000000 sec
DELTA             0.05000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                      13C
P1                       7.80 usec
PL1                     -3.00 dB
SFO1              100.5785700 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                  135.00 usec
PL2                     17.40 dB
PL12                    17.40 dB
PL13                    17.40 dB
SFO2              399.9516000 MHz

F2 - Processing parameters
SI                       32768
SF                100.5675080 MHz
WDW                         EM
SSB                          0
LB                        3.00 Hz
GB                           0
PC                        1.40
```


Current Data Parameters
NAME ss-1-35
EXPNO 4
PROCNO 1
DU /m
USER subrata
F2 - Acquisition Parame
Date_ 20080125
Time 13.19
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT DMSO
NS 32
DS 2
SWH 4789.272
FIDRES 0.146157
AQ 3.4210291
RG 574.7
DW 104.400
DE 6.00
TE 298.2
D1 2.00000000
TD0 1
======== CHANNEL f1 ===
NUC1 1H
P1 9.00
PL1 -3.00
SFO1 300.1321009
F2 - Processing paramet
SI 32768
SF 300.1300000
WDW no
SSB 0
LB 0.00
GB 0
PC 1.00
CO2H CO2H
CO2H
(+)-54
ppm
2.00
6.35
2.18
2.13
2.17



(+)-**54**

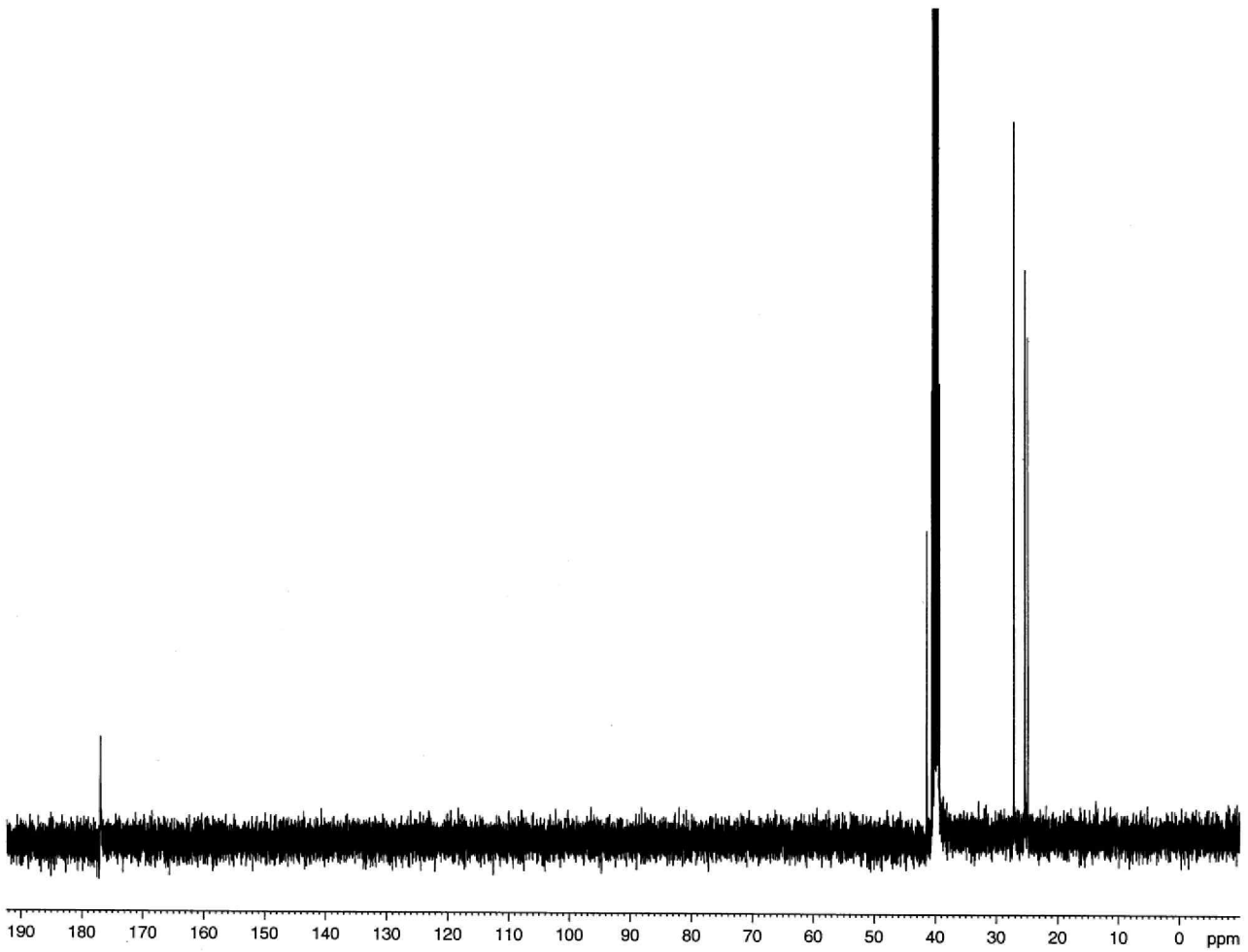
```
Current Data Parameters
NAME                  ss-1-36
EXPNO                       6
PROCNO                      1
DU                         /m
USER                  subrata

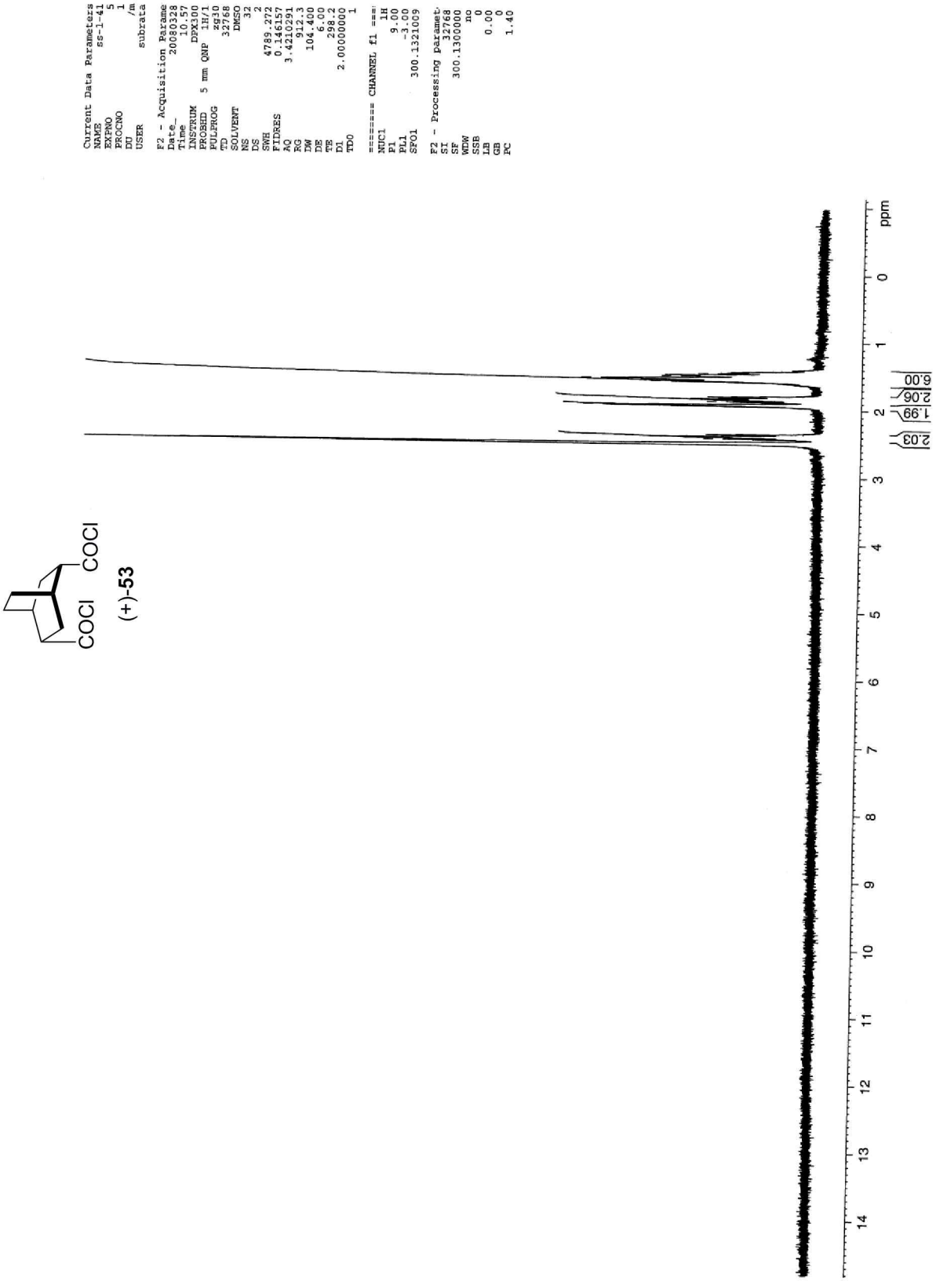
F2 - Acquisition Parameters
Date_                20080214
Time                    19.13
INSTRUM                DPX400
PROBHD    5 mm BBO BB-1H
PULPROG                zgpg30
TD                      65536
SOLVENT
NS                        2450
DS                           4
SWH                25125.629 Hz
FIDRES                 0.383387 Hz
AQ                     1.3042164 sec
RG                       11585.2
DW                        19.900 usec
DE                         6.00 usec
TE                        299.2 K
D1                  0.15000001 sec
d11                 0.03000000 sec
DELTA               0.05000000 sec
TD0                          1

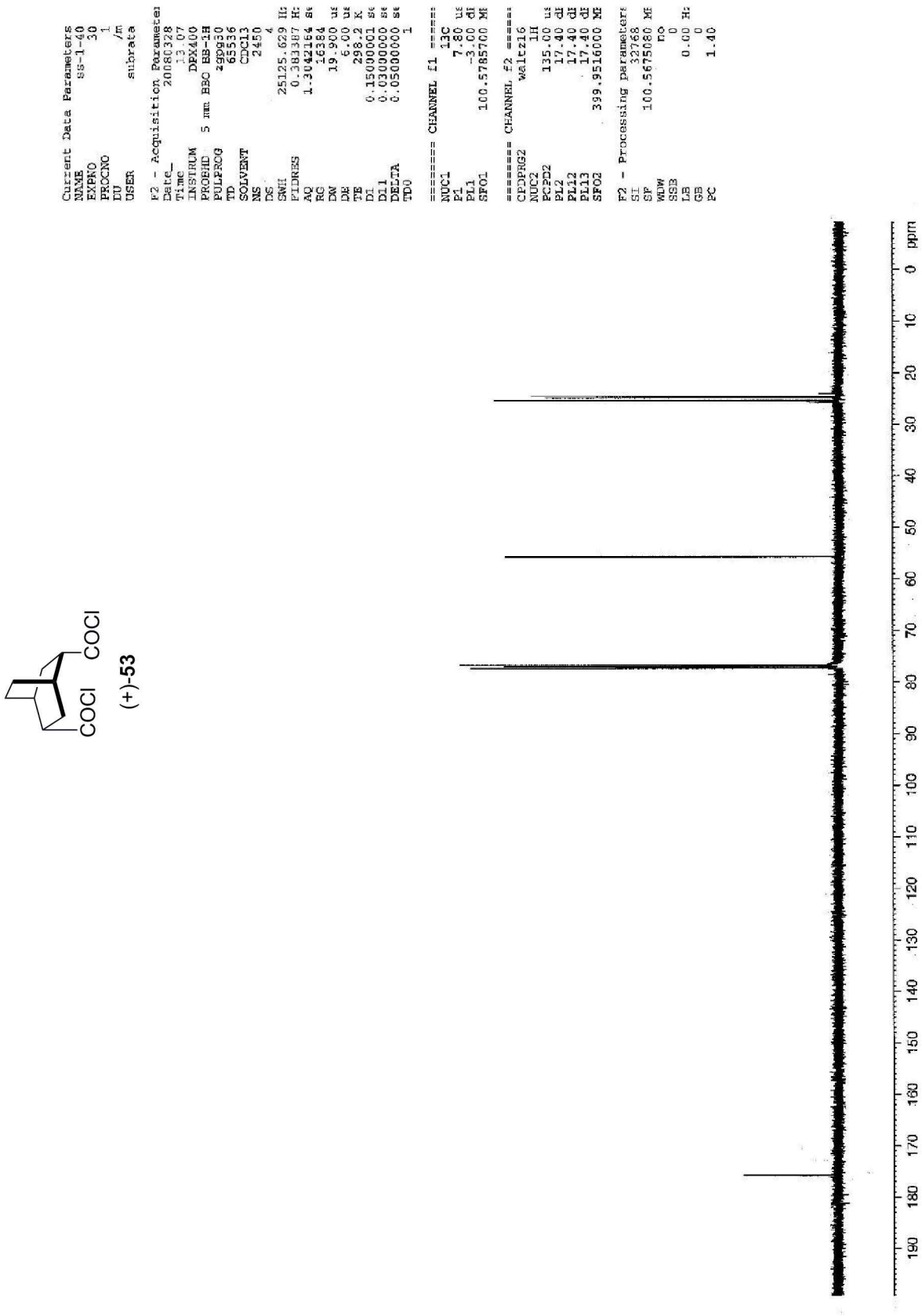
======== CHANNEL f1 ========
NUC1                        13C
P1                         7.80 usec
PL1                       -3.00 dB
SFO1               100.5936591 MHz

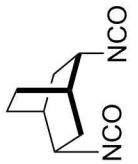
======== CHANNEL f2 ========
CPDPRG2                 waltz16
NUC2                        1H
PCPD2                    135.00 usec
PL2                       17.40 dB
PL12                      17.40 dB
PL13                      17.40 dB
SFO2               400.0116000 MHz

F2 - Processing parameters
SI                        32768
SF                 100.5825950 MHz
WDW                          no
SSB                           0
LB                         0.00 Hz
GB                            0
PC                         1.40
```

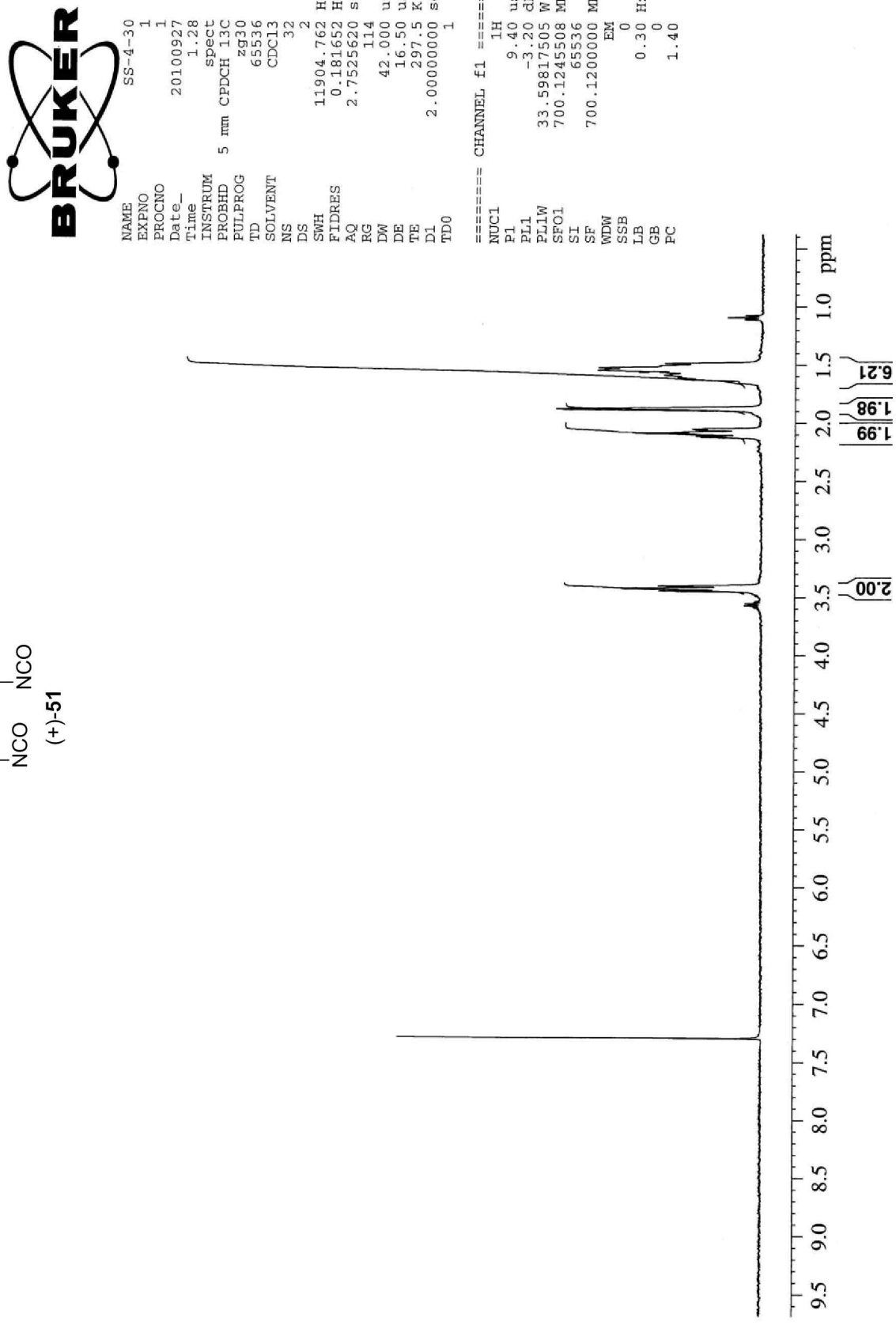


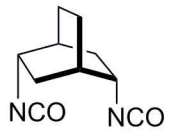

Current Data Parameters
NAME 55-1-41
EXPNO 5
PROCNO 1
DU /m
USER subrata
F2 - Acquisition Parame
Date_ 20080328
Time 10.57
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT DMSO
NS 32
DS 2
SWH 4789.272
FIDRES 0.146157
AQ 3.4210291
RG 912.3
DW 104.400
DE 6.00
TE 298.2
D1 2.00000000
TD0 1
======== CHANNEL f1 ===
NUC1 1H
P1 9.00
PL1 -3.00
SFO1 300.1321009
F2 - Processing paramet
SI 32768
SF 300.1300000
WDW no
SSB 0
LB 0.00
GB 0
PC 1.40
COCl
COCl
COCl
(+)-53
2.03
1.99
2.06
6.00
ppm


COCl
COCl
COCl
(+)-53
Current Data Parameters
NAME ss-1-40
EXPNO 30
PROCNO 1
DU /m
USER subrata
F2 - Acquisition Parameter
Date_ 20080328
Time 13.07
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 2450
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3042164 sec
RG 16384
DW 19.900 usec
DE 6.00 usec
TE 298.2 K
D1 0.15000001 sec
D11 0.03000000 sec
DELTA 0.05000000 sec
TD0 1
======== CHANNEL f1 ======
NUC1 13C
P1 7.80 usec
PL1 -3.00 dB
SFO1 100.5785700 MHz
======== CHANNEL f2 ======
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 usec
PL2 17.40 dB
PL12 17.40 dB
PL13 17.40 dB
SFO2 399.9516000 MHz
F2 - Processing parameters
SI 32768
SF 100.5675080 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.40
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

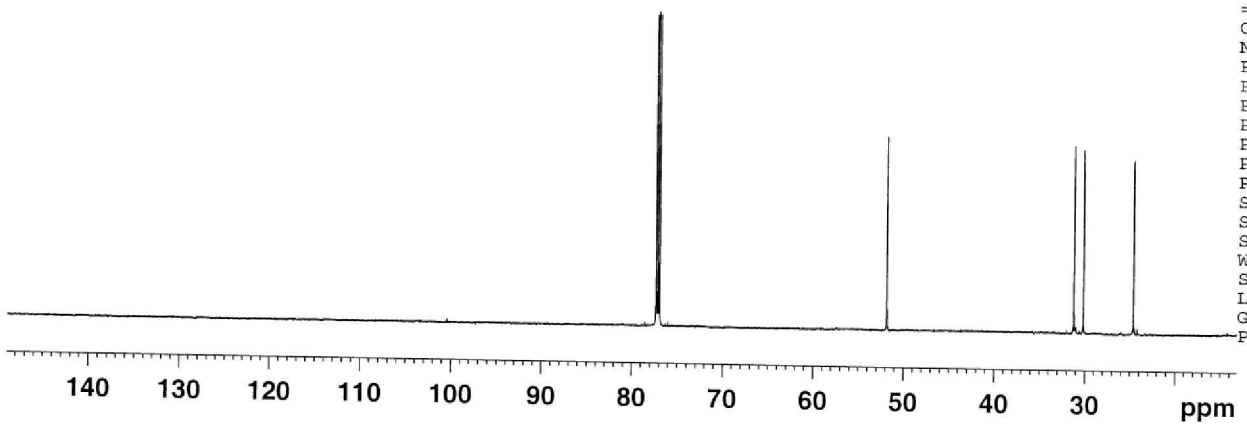

NCO
NCO
NCO

(+)-**51**


BRUKER
NAME SS-4-30
EXPNO 1
PROCNO 1
Date_ 20100927
Time 1.28
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.181652 Hz
AQ 2.7525620 sec
RG 114
DW 42.000 usec
DE 16.50 usec
TE 297.5 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1245508 MHz
SI 65536
SF 700.1200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
2.00
1.99
1.98
6.21

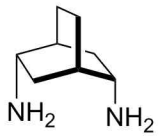


(+)-**51**

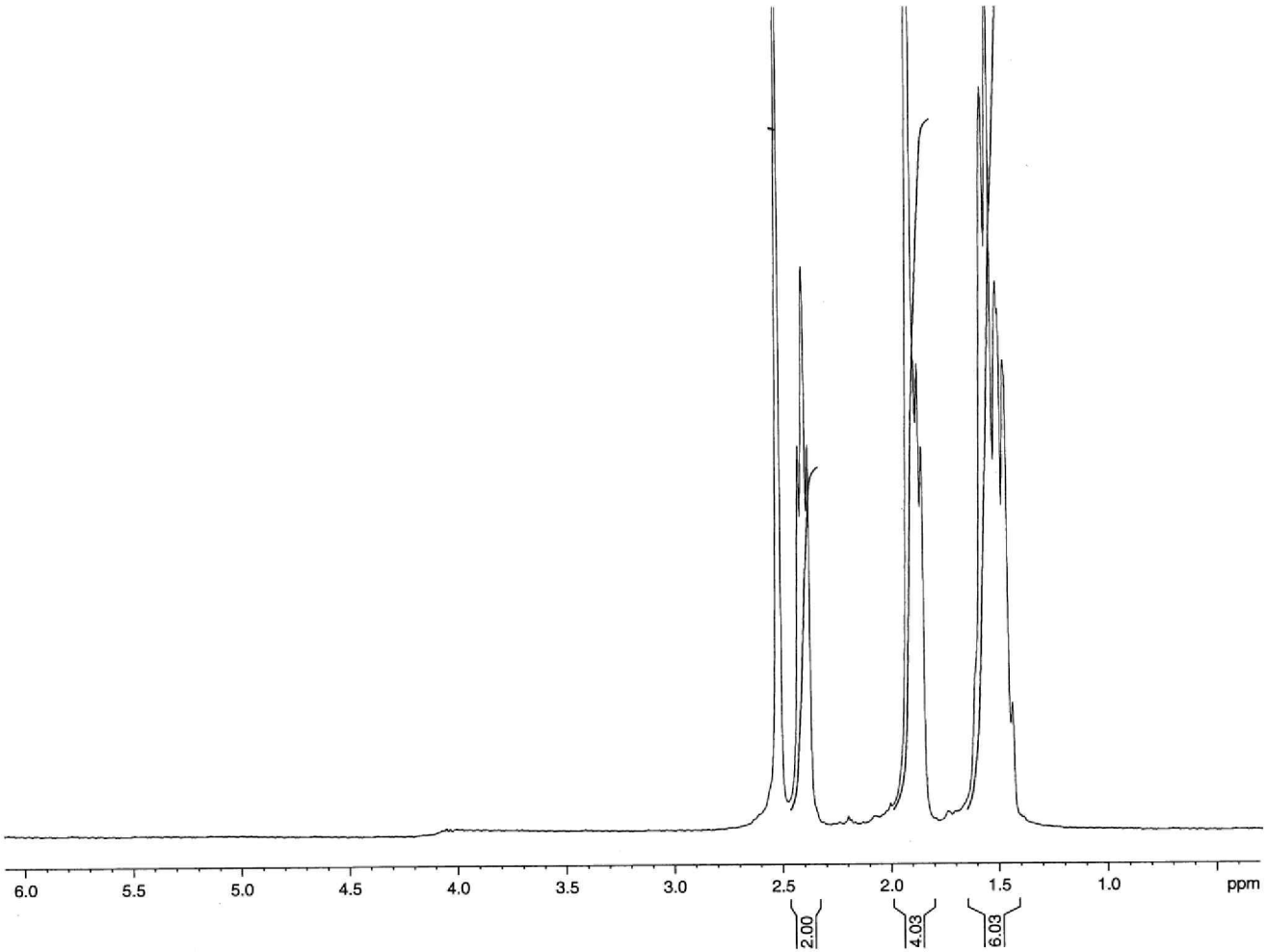


BRUKER

NAME	SS-4-22
EXPNO	5
PROCNO	1
Date_	20101112
Time	12.38
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	98304
SOLVENT	CDCl3
NS	42
DS	4
SWH	41666.668 Hz
FIDRES	0.423855 Hz
AQ	1.1796980 sec
RG	203
DW	12.000 usec
DE	15.00 usec
TE	297.5 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 usec
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0629186 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 usec
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1228005 MHz
SI	131072
SF	176.0453140 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40



(+)-**34**

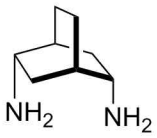



```
Current Data Parameters
NAME                  ss-1-36
EXPNO                       3
PROCNO                      1
DU                         /m
USER                  subrata

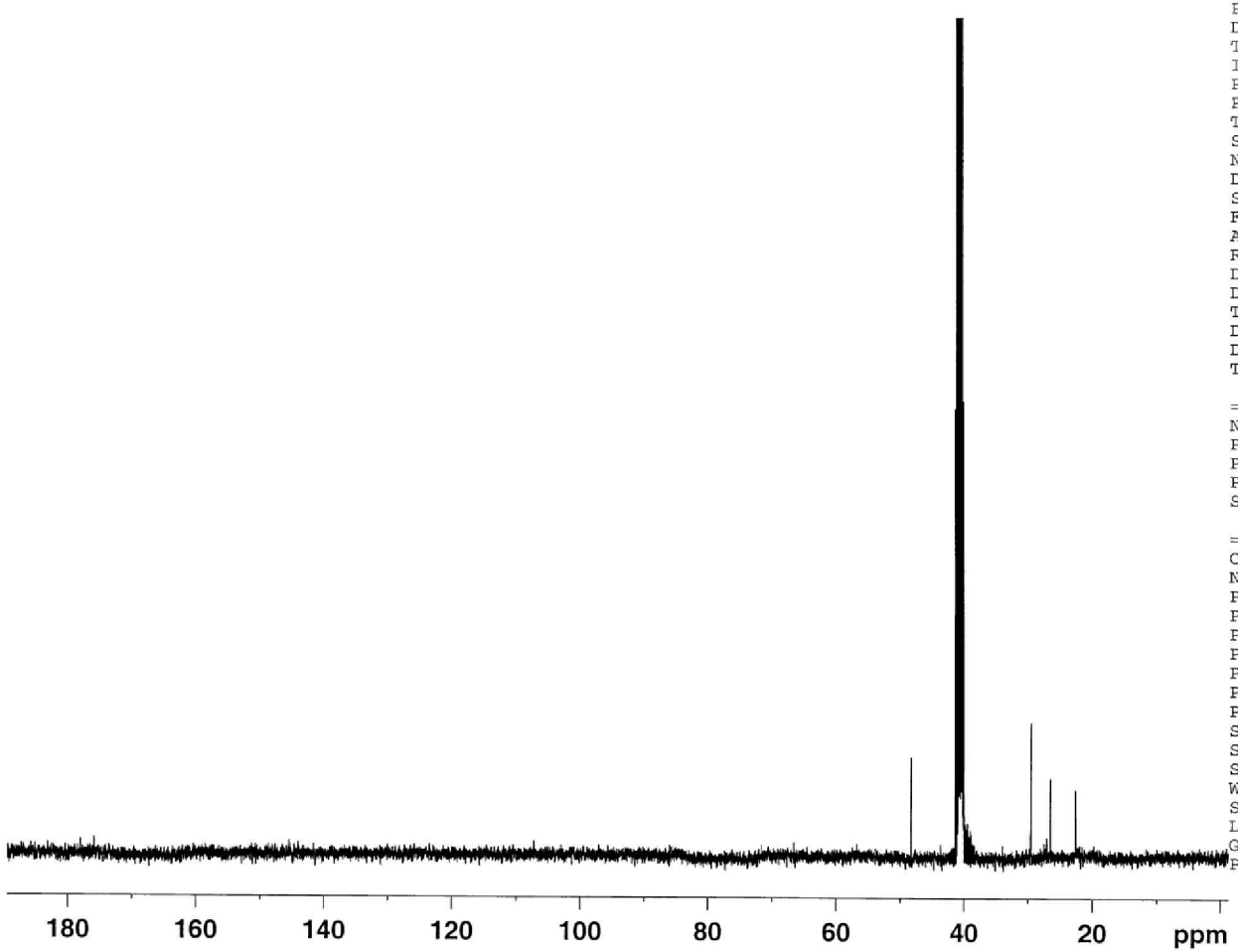
F2 - Acquisition Parameters
Date_               20080214
Time                   17.37
INSTRUM                DPX400
PROBHD   5 mm BBO BB-1H
PULPROG                 zg30
TD                     32768
SOLVENT                 DMSO
NS                         32
DS                          2
SWH                 6410.256 Hz
FIDRES              0.195625 Hz
AQ                2.5559540 sec
RG                        512
DW                   78.000 usec
DE                    6.00 usec
TE                    299.2 K
D1                2.00000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       1H
P1                    14.70 usec
PL1                    0.00 dB
SFO1             400.0128001 MHz

F2 - Processing parameters
SI                         32768
SF                400.0100000 MHz
WDW                           EM
SSB                            0
LB                     0.70 Hz
GB                             0
PC                          1.00
```

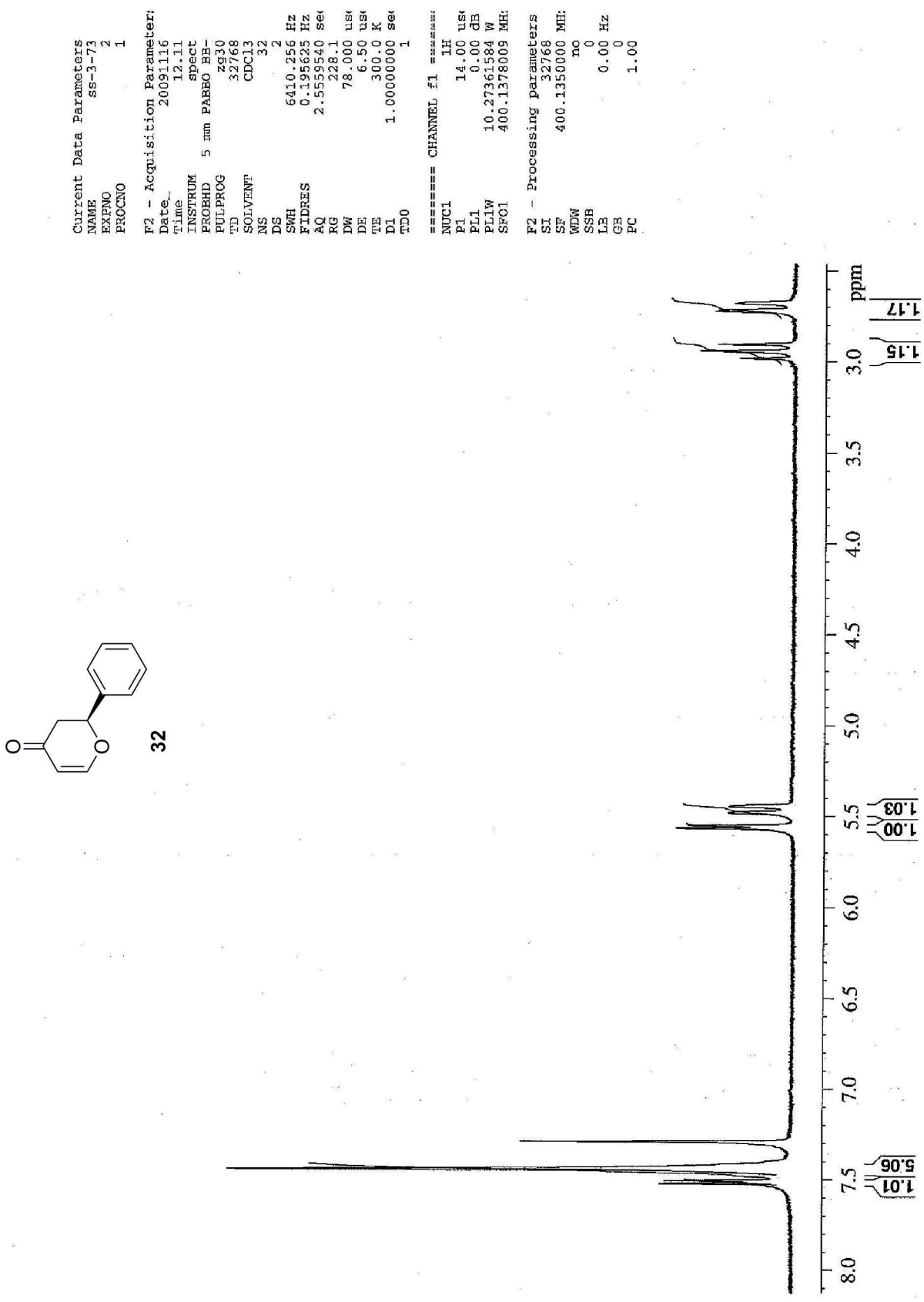


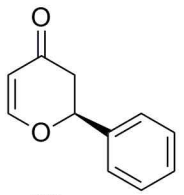
(+)-**34**



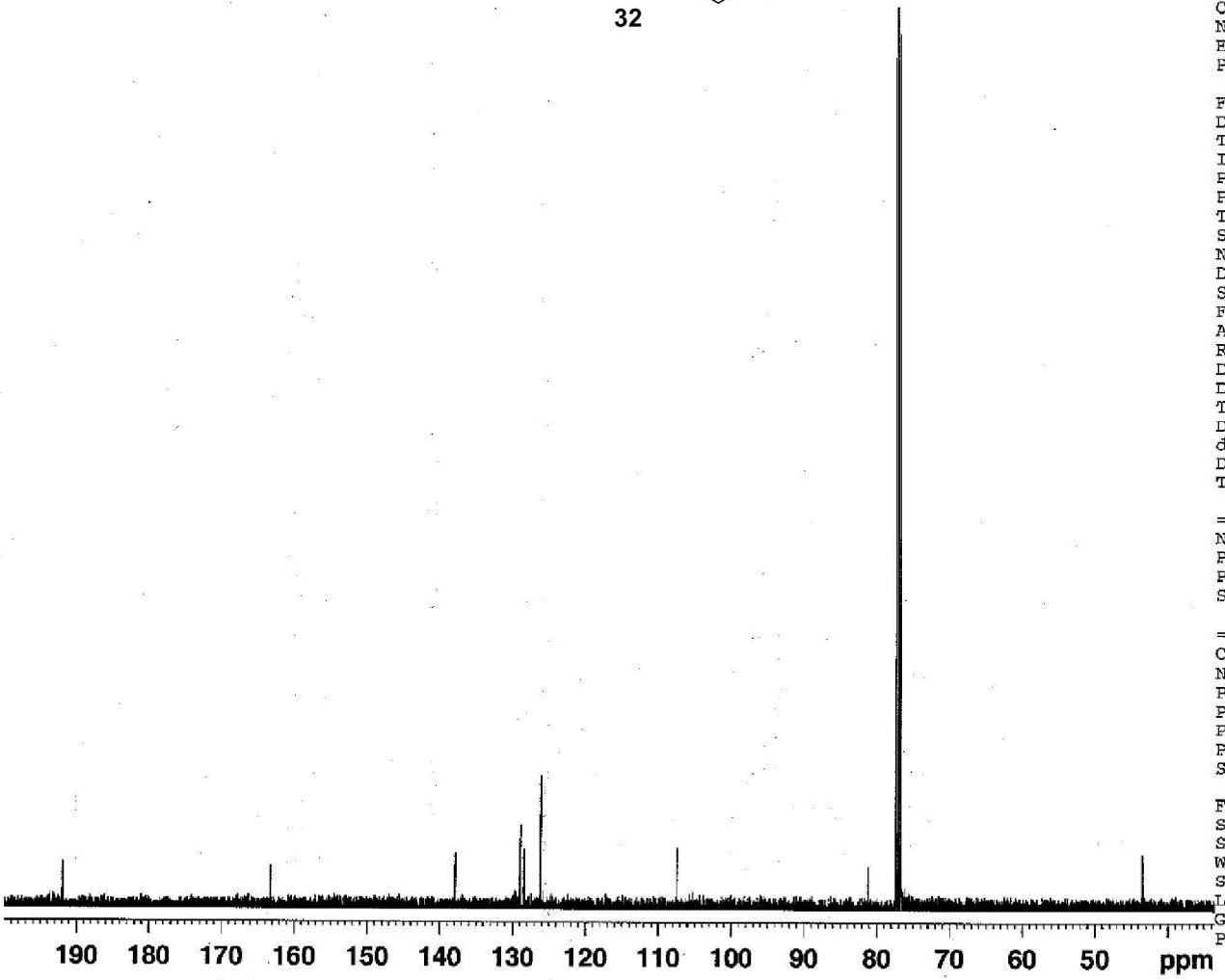
BRUKER

NAME	SS-4-35
EXPNO	2
PROCNO	1
Date_	20101013
Time	19.17
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	98304
SOLVENT	CDCl3
NS	1024
DS	4
SWH	41666.668 Hz
FIDRES	0.423855 Hz
AQ	1.1796980 sec
RG	203
DW	12.000 usec
DE	15.00 usec
TE	297.5 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 usec
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0629186 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 usec
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1228005 MHz
SI	131072
SF	176.0453140 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40


Current Data Parameters
NAME ss-3-73
EXPNO 2
PROCNO 1
F2 - Acquisition Parameter
Date_ 20091116
Time 12.11
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 se
RG 228.1
DW 78.000 us
DE 6.50 us
TE 300.0 K
D1 1.00000000 se
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 us
PL1 0.00 dB
PL1W 10.27361584 W
SFO1 400.1378009 MH
F2 - Processing parameters
SI 32768
SF 400.1350000 MH
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
32
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
ppm
1.01
5.06
1.00
1.03
1.15
1.17



32



BRUKER

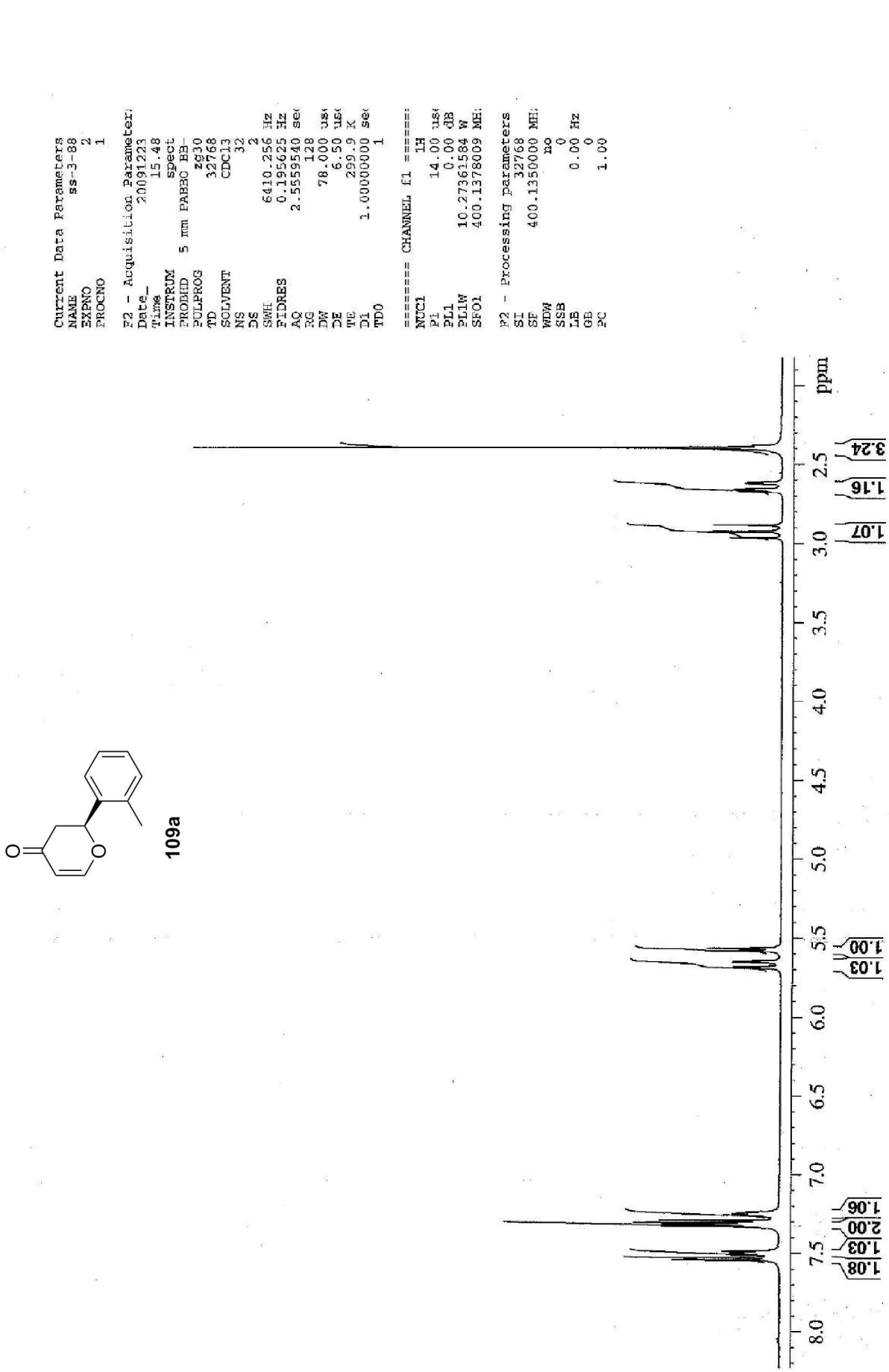
Current Data Parameters
NAME ss-3-73_m
EXPNO 2
PROCNO 1

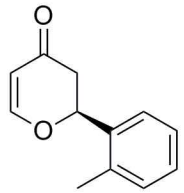
F2 - Acquisition Parameters
Date_ 20091117
Time 17.24
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1024
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 32768
DW 20.850 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1

======== CHANNEL f1 ========
NUC1 13C
P1 8.30 usec
PL1 -3.00 dB
SFO1 100.6517495 MHz

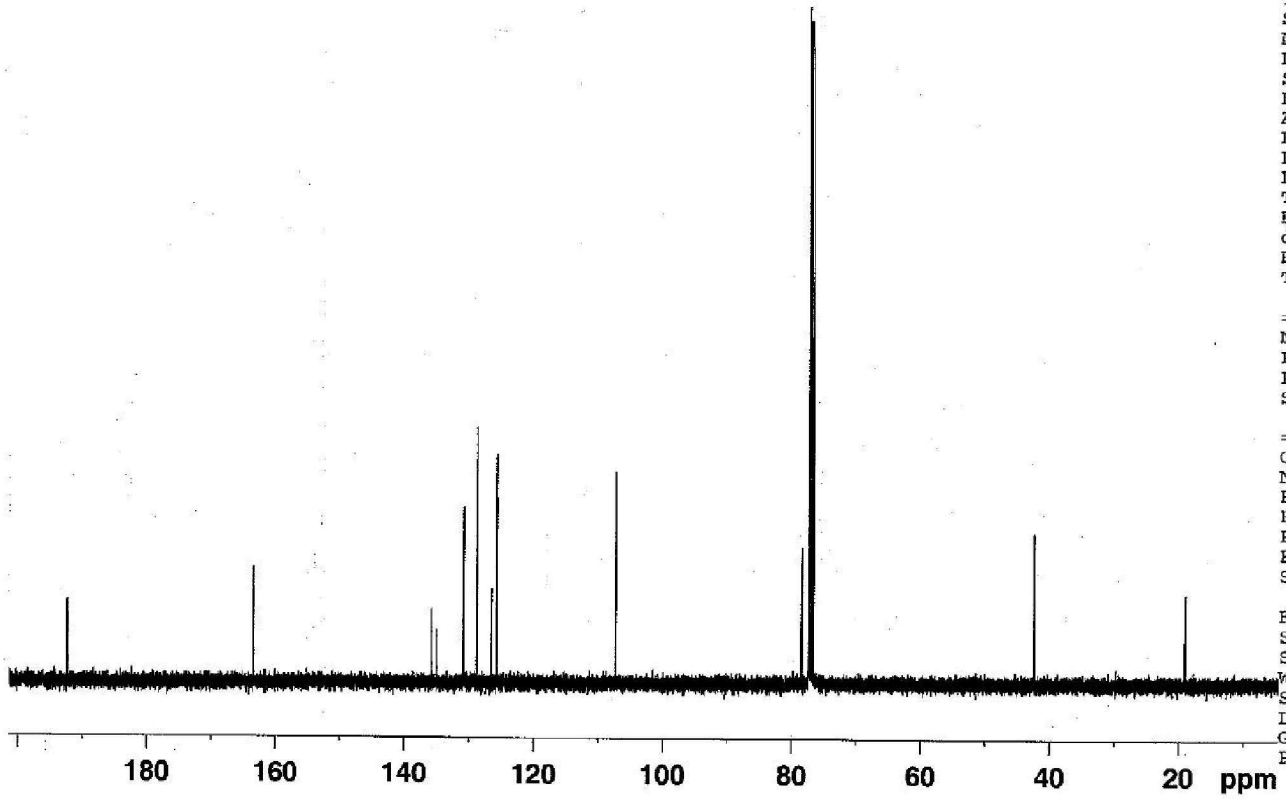
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2466010 MHz

F2 - Processing parameters
SI 32768
SF 100.6416850 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.40


Current Data Parameters
NAME ss-3-88
EXPNO 2
PROCNO 1
F2 - Acquisition Parameter
Date_ 20091223
Time 15.48
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDC13
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 se
RG 128
DW 78.000 us
DE 6.50 us
TE 299.9 K
D1 1.00000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.00 us
PL1 0.00 dB
PL1W 10.27361584 W
SFO1 400.1378009 MH
F2 - Processing parameters
SI 32768
SF 400.1350000 MH
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
109a
ppm
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
1.08
1.03
2.00
1.06
1.03
1.00
1.07
1.16
3.24



109a



BRUKER

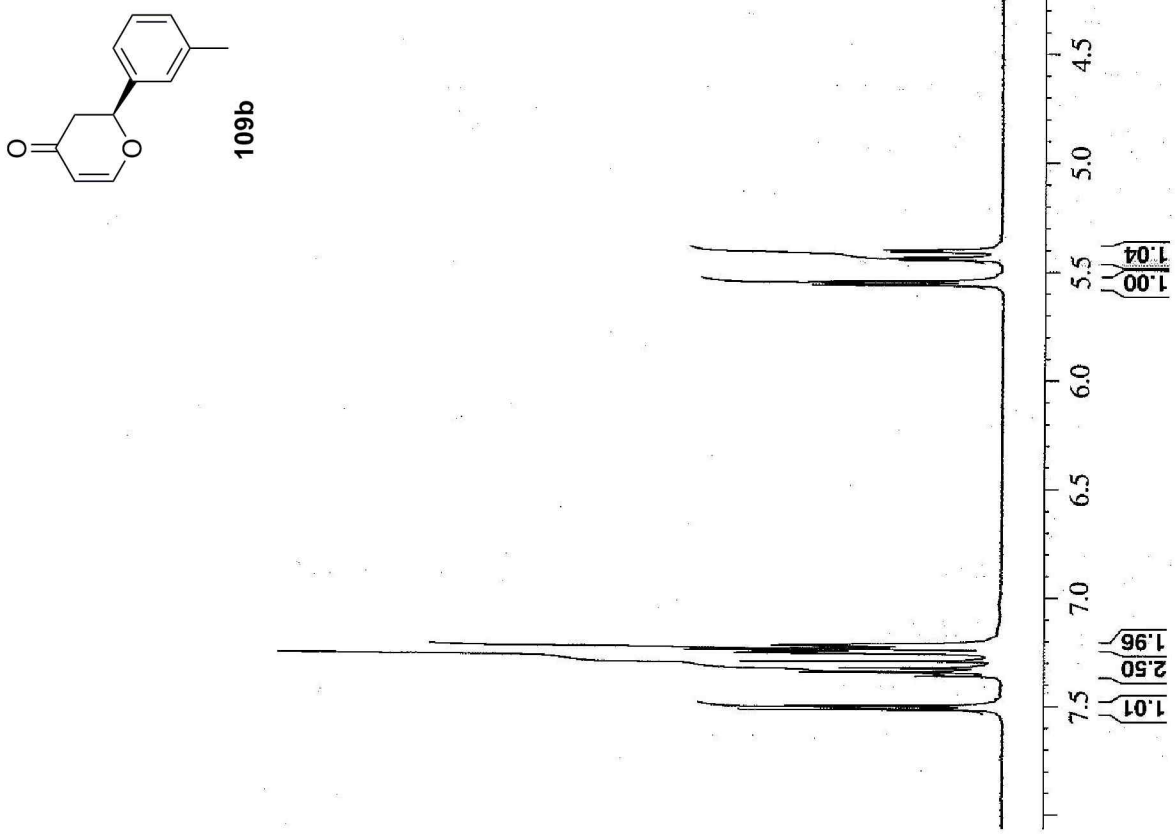
```
Current Data Parameters
NAME                 ss-3-88_m
EXPNO                        2
PROCNO                       1

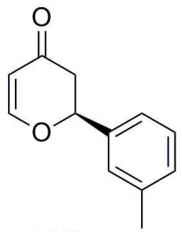
F2 - Acquisition Parameters
Date_                 20091224
Time                     17.17
INSTRUM                DPX400
PROBHD    5 mm BBO BB-1H
PULPROG                zgpg30
TD                        65536
SOLVENT                  CDCl3
NS                        1024
DS                           4
SWH                23980.814 Hz
FIDRES              0.365918 Hz
AQ                  1.3664756 sec
RG                       32768
DW                     20.850 usec
DE                      6.00 usec
TE                      297.2 K
D1                 2.00000000 sec
d11                0.03000000 sec
DELTA              1.89999998 sec
TD0                          1

======== CHANNEL f1 ========
NUC1                       13C
P1                       8.30 usec
PL1                     -3.00 dB
SFO1              100.6517495 MHz

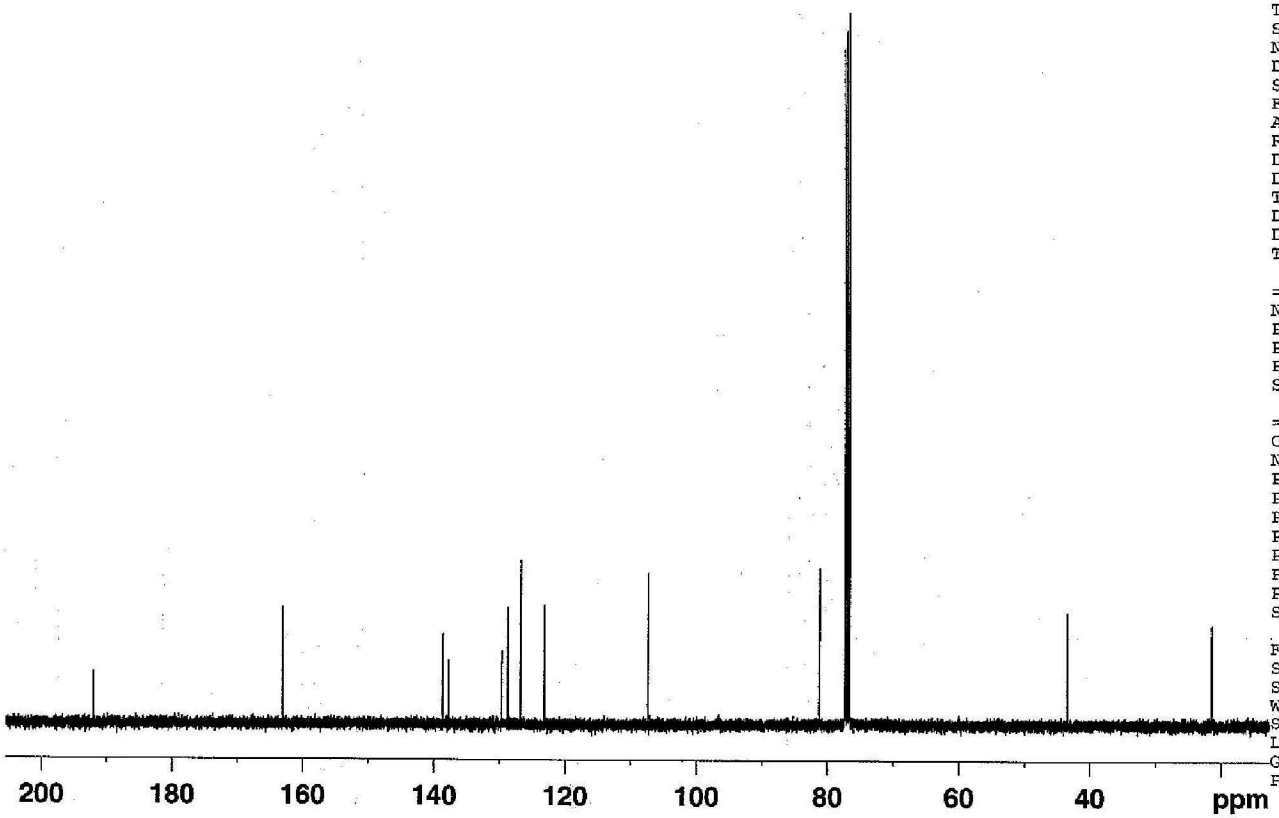
======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                   90.00 usec
PL2                     -3.00 dB
PL12                    15.00 dB
PL13                    15.00 dB
SFO2              400.2466010 MHz

F2 - Processing parameters
SI                       32768
SF                400.6416850 MHz
WDW                         no
SSB                          0
LB                      0.00 Hz
GB                           0
PC                        1.00
```


Current Data Parameters
NAME ss-3-89
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20091224
Time 21.40
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 se
RG 128
DW 78.000 us
DE 6.50 us
TE 300.8 K
D1 1.00000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.00 us
PL1 0.00 dB
PL1W 10.27361584 W
SFO1 400.1378009 MH
F2 - Processing parameters
SI 32768
SF 400.1350000 MH
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
109b
O
O
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
ppm
1.01
2.50
1.96
1.00
1.04
1.03
1.04
3.26



109b



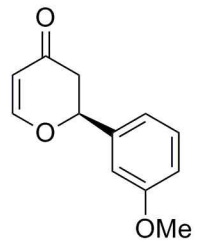
Current Data Parameters
NAME ss-3-89
EXPNO 3
PROCNO 1

F2 - Acquisition Parameters
Date_ 20091224
Time 21.46
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1024
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 32768
DW 20.850 usec
DE 6.50 usec
TE 300.9 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

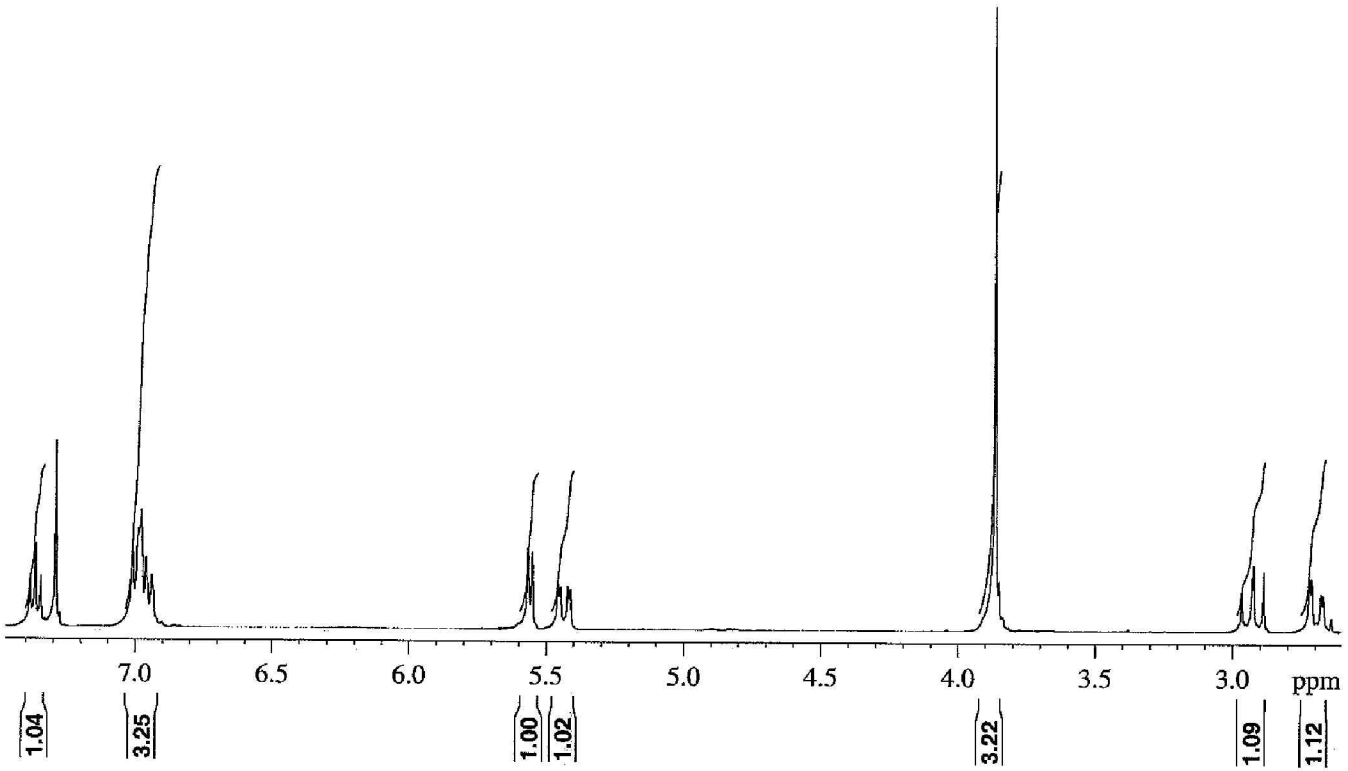
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 -2.00 dB
PL1W 46.89702606 W
SFO1 100.6240872 MHz

======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 0.00 dB
PL12 16.16 dB
PL13 17.00 dB
PL2W 10.27361584 W
PL12W 0.24872722 W
PL13W 0.20498557 W
SFO2 400.1366005 MHz

F2 - Processing parameters
SI 32768
SF 100.6140260 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00



109c

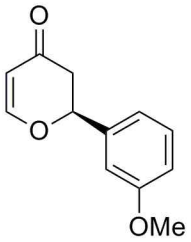



```
Current Data Parameters
NAME                  ss-3-91
EXPNO                       2
PROCNO                      1

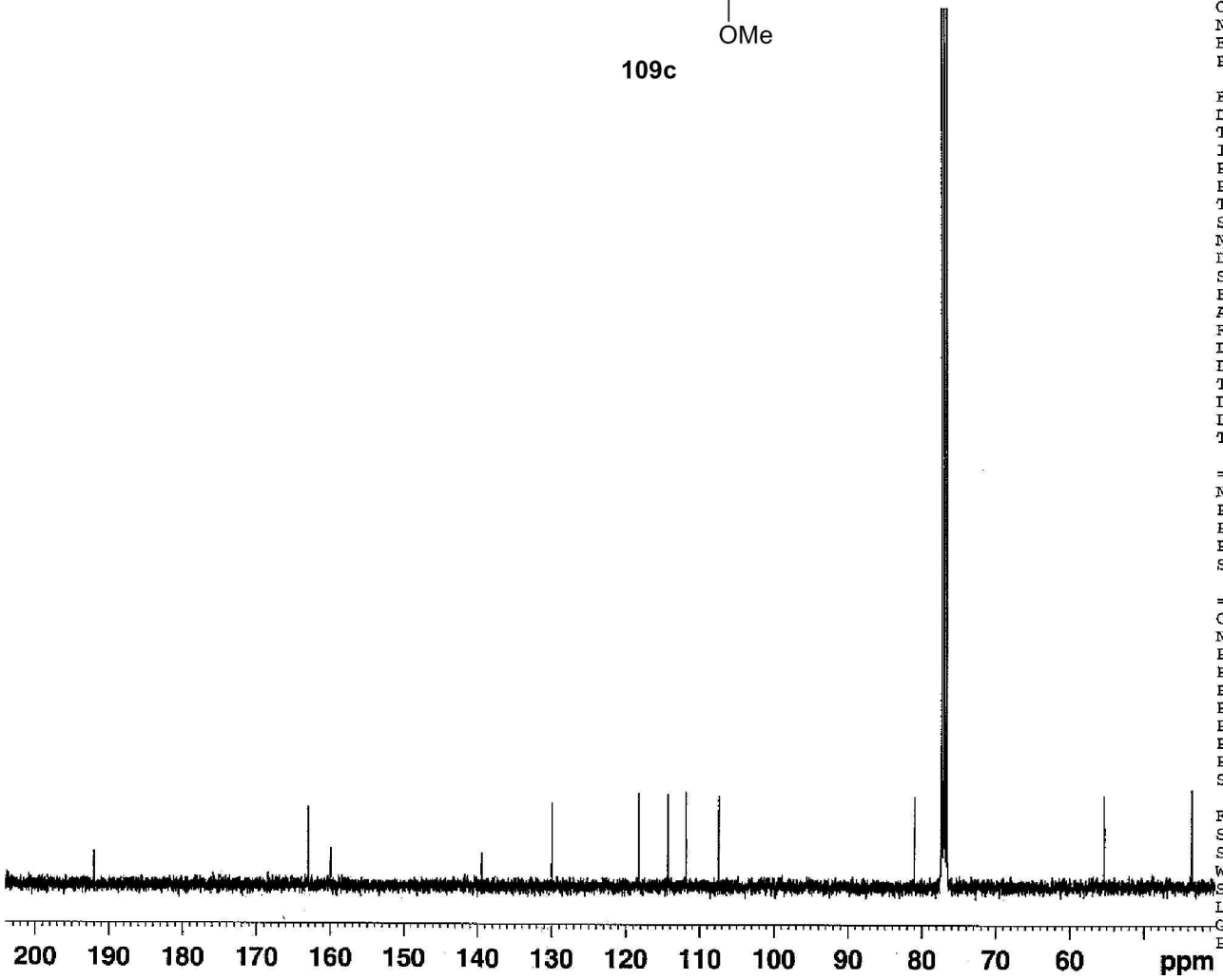
F2 - Acquisition Parameter:
Date_              20091224
Time                  17.01
INSTRUM               spect
PROBHD    5 mm PABBO BB-
PULPROG                zg30
TD                    32768
SOLVENT               CDCl3
NS                       32
DS                        2
SWH                6410.256 Hz
FIDRES             0.195625 Hz
AQ                 2.5559540 se
RG                      128
DW                   78.000 us
DE                    6.50 us
TE                   300.4 K
D1              1.00000000 se
TD0                       1

======== CHANNEL f1 =======:
NUC1                    1H
P1                   14.00 us
PL1                   0.00 dB
PL1W          10.27361584 W
SFO1          400.1378009 MH:

F2 - Processing parameters
SI                    32768
SF            400.1350000 MH:
WDW                     no
SSB                      0
LB                    0.00 Hz
GB                       0
PC                    1.00
```



109c



BRUKER

Current Data Parameters

NAME	ss-3-91
EXPNO	3
PROCNO	1

F2 - Acquisition Parameters

Date_	20091224	
Time	17.17	
INSTRUM	spect	
PROBHD	5 mm PABBO BB-	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	1024	
DS	4	
SWH	23980.814	Hz
FIDRES	0.365918	Hz
AQ	1.3664756	sec
RG	32768	
DW	20.850	usec
DE	6.50	usec
TE	301.7	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	

======== CHANNEL f1 ========

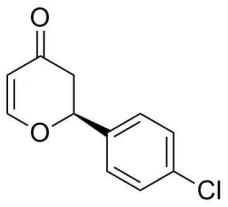
NUC1	13C	
P1	9.00	usec
PL1	-2.00	dB
PL1W	46.89702606	W
SFO1	100.6240872	MHz

======== CHANNEL f2 ========

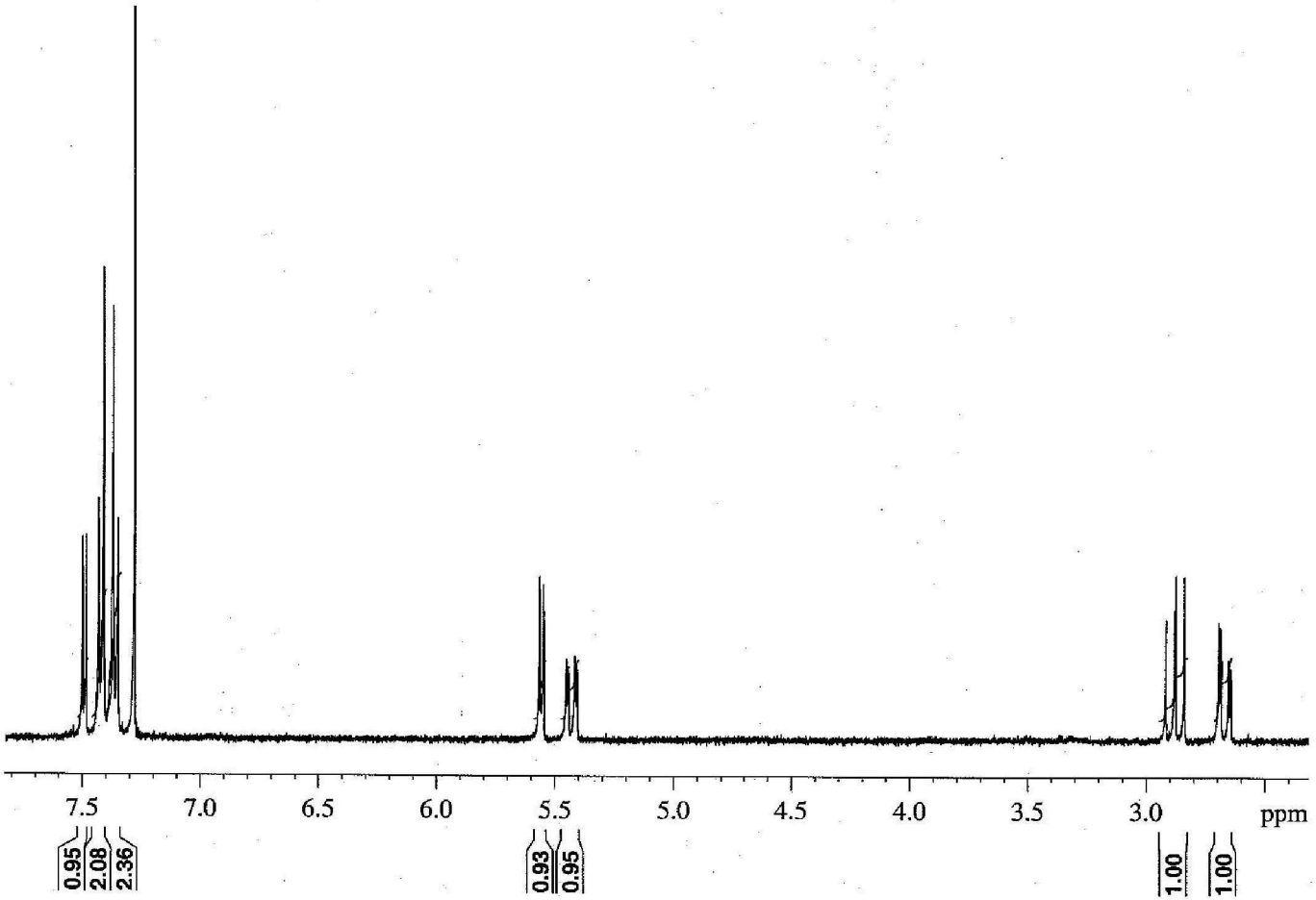
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	90.00	usec
PL2	0.00	dB
PL12	16.16	dB
PL13	17.00	dB
PL2W	10.27361584	W
PL12W	0.24872722	W
PL13W	0.20498557	W
SFO2	400.1366005	MHz

F2 - Processing parameters

SI	32768	
SF	100.6140260	MHz
WDW	EM	
SSB	0	
LB	1.00	Hz
GB	0	
PC	1.40	



109d

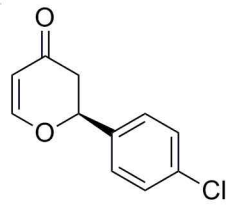



```
Current Data Parameters
NAME                  ss-3-79_m
EXPNO                         3
PROCNO                        1

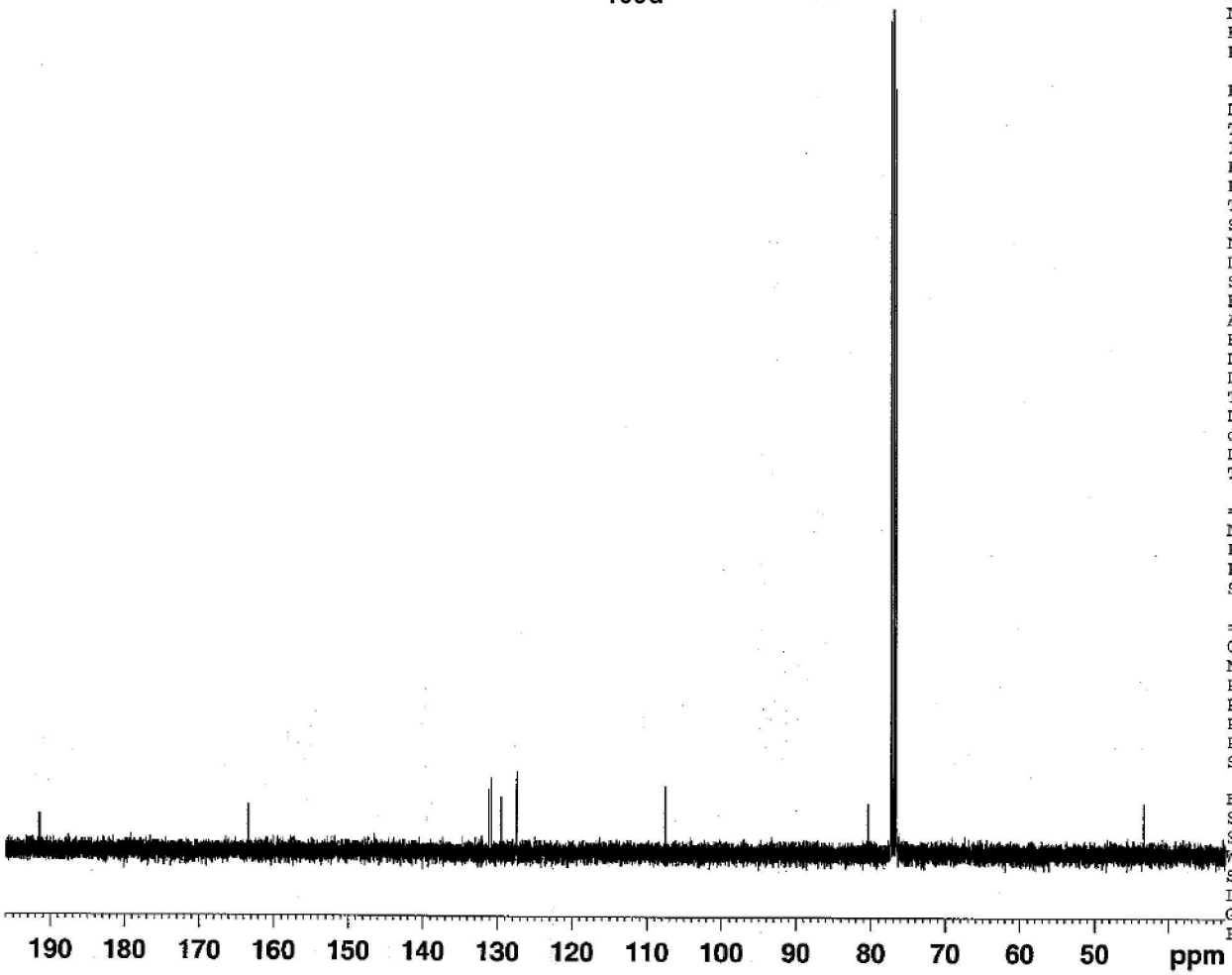
F2 - Acquisition Parameter:
Date_                  20091201
Time                      14.06
INSTRUM                DPX400
PROBHD    5 mm BBO BB-1H
PULPROG                   zg30
TD                       32768
SOLVENT                  CDCl3
NS                          32
DS                           2
SWH                   6410.256 Hz
FIDRES                0.195625 Hz
AQ                    2.5559540 se
RG                        812.7
DW                       78.000 us
DE                        6.00 us
TE                       297.2 K
D1                  1.00000000 se
TD0                           1

======== CHANNEL f1 =======
NUC1                         1H
P1                        13.50 us
PL1                       -3.00 dB
SFO1                400.2478017 MH:

F2 - Processing parameters
SI                       32768
SF                  400.2450000 MH:
WDW                         no
SSB                          0
LB                        0.00 Hz
GB                           0
PC                        1.00
```



109d



BRUKER

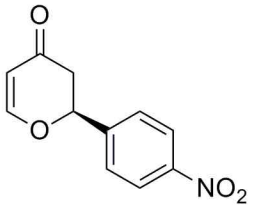
Current Data Parameters
NAME ss-3-79_m
EXPNO 4
PROCNO 1

F2 - Acquisition Parameters
Date_ 20091201
Time 15.11
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1024
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 32768
DW 20.850 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1

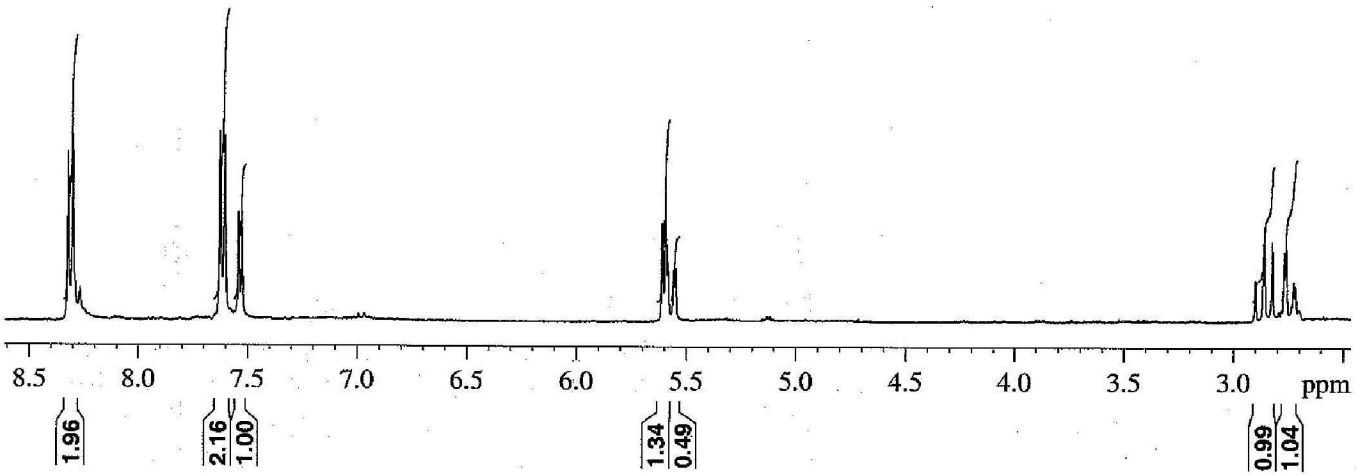
======== CHANNEL f1 ========
NUC1 13C
P1 8.30 usec
PL1 -3.00 dB
SFO1 100.6517495 MHz

======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2466010 MHz

F2 - Processing parameters
SI 32768
SF 100.6416850 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.40



109e

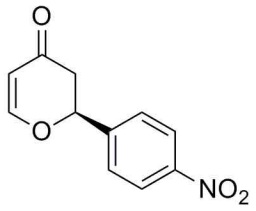



```
Current Data Parameters
NAME                  ss-3-80_m
EXPNO                         1
PROCNO                        1

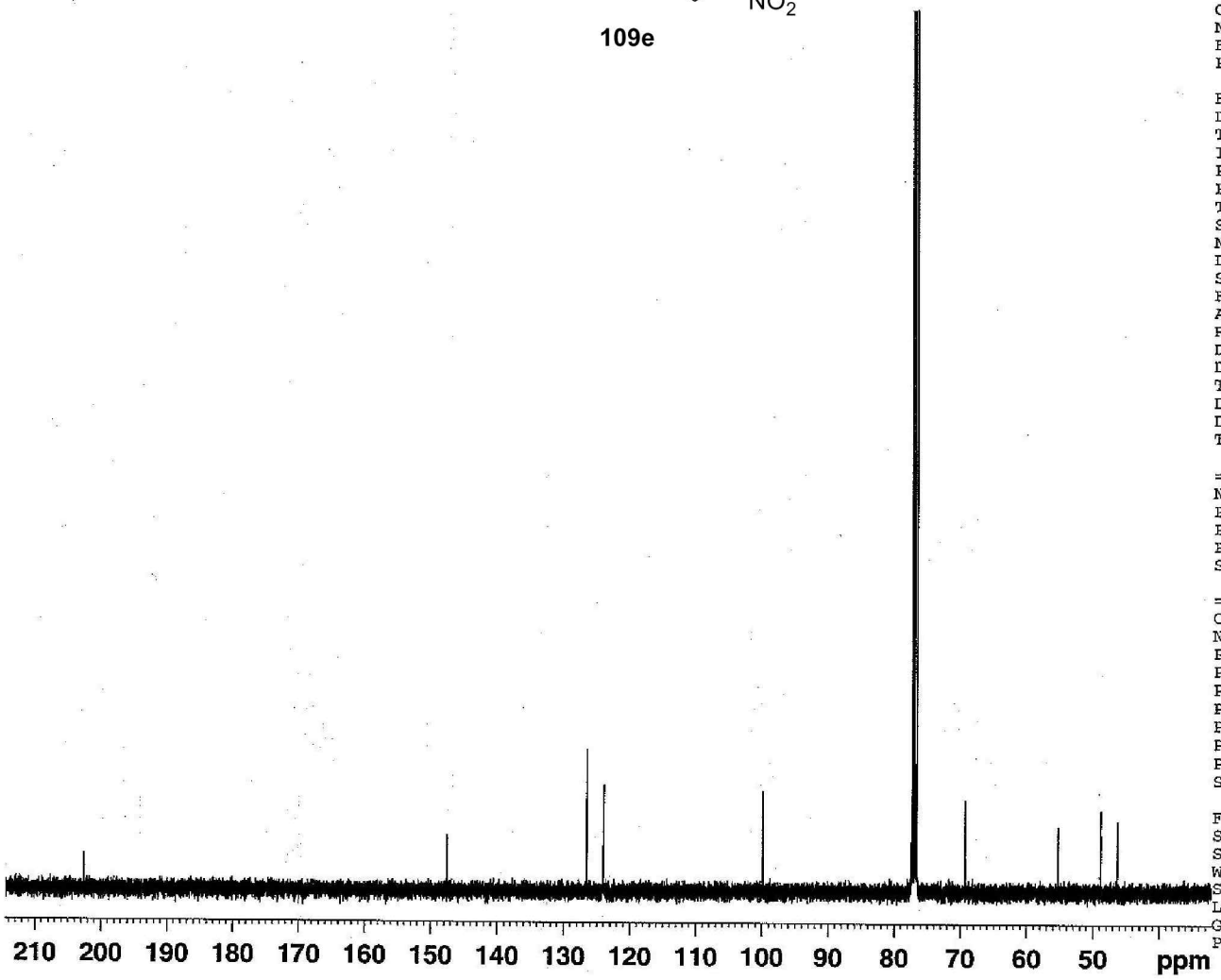
F2 - Acquisition Parameter
Date_                  20091130
Time                      17.14
INSTRUM                  DPX400
PROBHD    5 mm BBO BB-1H
PULPROG                   zg30
TD                       32768
SOLVENT                  CDCl3
NS                           32
DS                            2
SWH                    6410.256 Hz
FIDRES                 0.195625 Hz
AQ                     2.5559540 se
RG                          128
DW                       78.000 us
DE                        6.00 us
TE                       297.2 K
D1                  1.00000000 se
TD0                           1

======== CHANNEL f1 =======
NUC1                         1H
P1                        13.50 us
PL1                       -3.00 dB
SFO1                400.2478017 MH

F2 - Processing parameters
SI                           32768
SF                  400.2450000 MH
WDW                          no
SSB                           0
LB                         0.00 Hz
GB                            0
PC                         1.00
```



109e



BRUKER

Current Data Parameters

NAME	ss-3-80
EXPNO	6
PROCNO	1

F2 - Acquisition Parameters

Date_	20091226
Time	9.32
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	13000
DS	4
SWH	23980.814 Hz
FIDRES	0.365918 Hz
AQ	1.3664756 sec
RG	32768
DW	20.850 usec
DE	6.50 usec
TE	301.8 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1

======== CHANNEL f1 ========

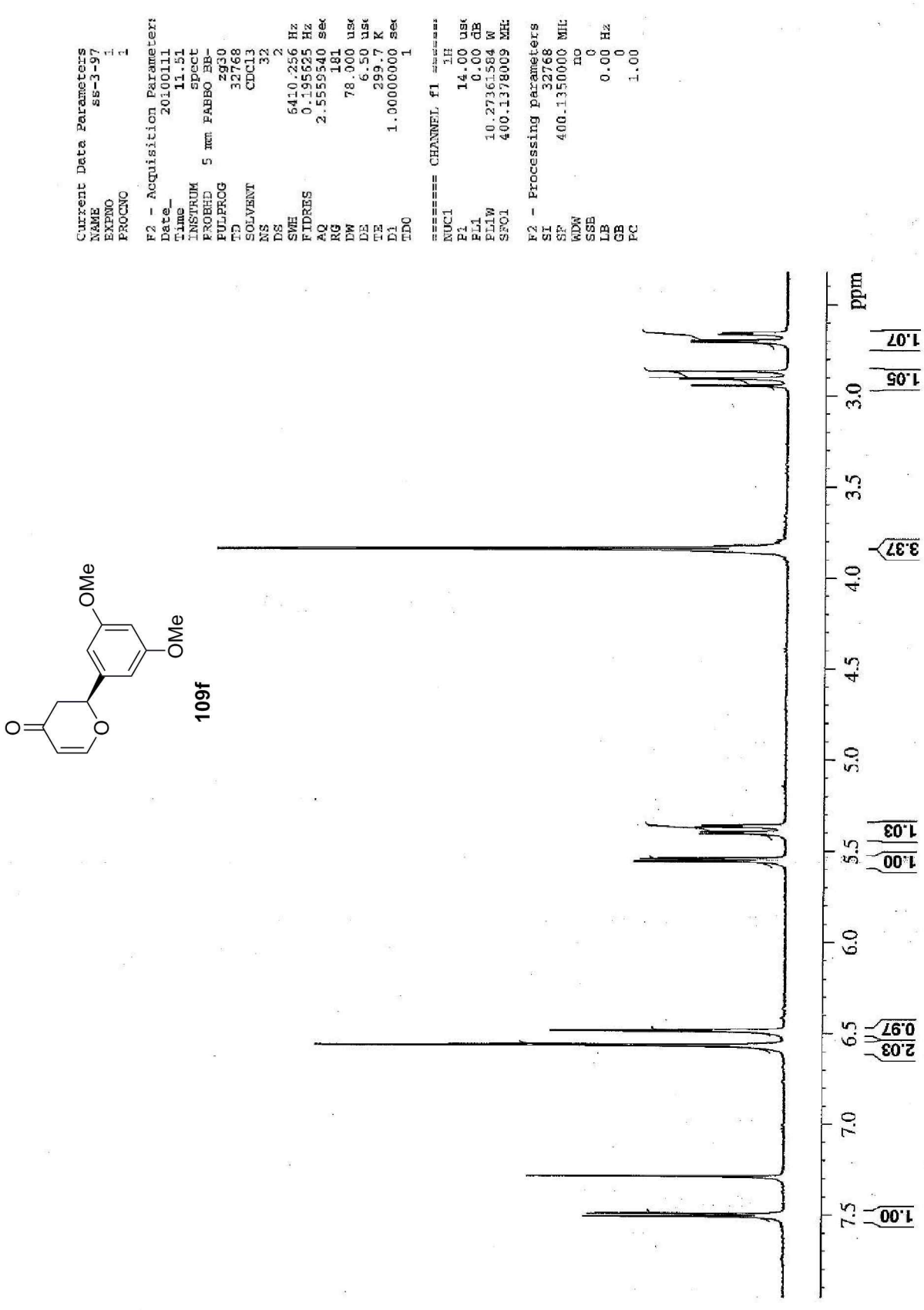
NUC1	13C
P1	9.00 usec
PL1	-2.00 dB
PL1W	46.89702606 W
SFO1	100.6240872 MHz

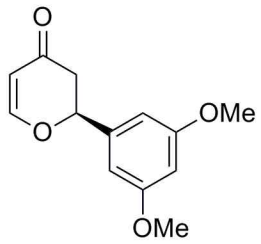
======== CHANNEL f2 ========

CPDPRG2	waltz16
NUC2	1H
PCPD2	90.00 usec
PL2	0.00 dB
PL12	16.16 dB
PL13	17.00 dB
PL2W	10.27361584 W
PL12W	0.24872722 W
PL13W	0.20498557 W
SFO2	400.1366005 MHz

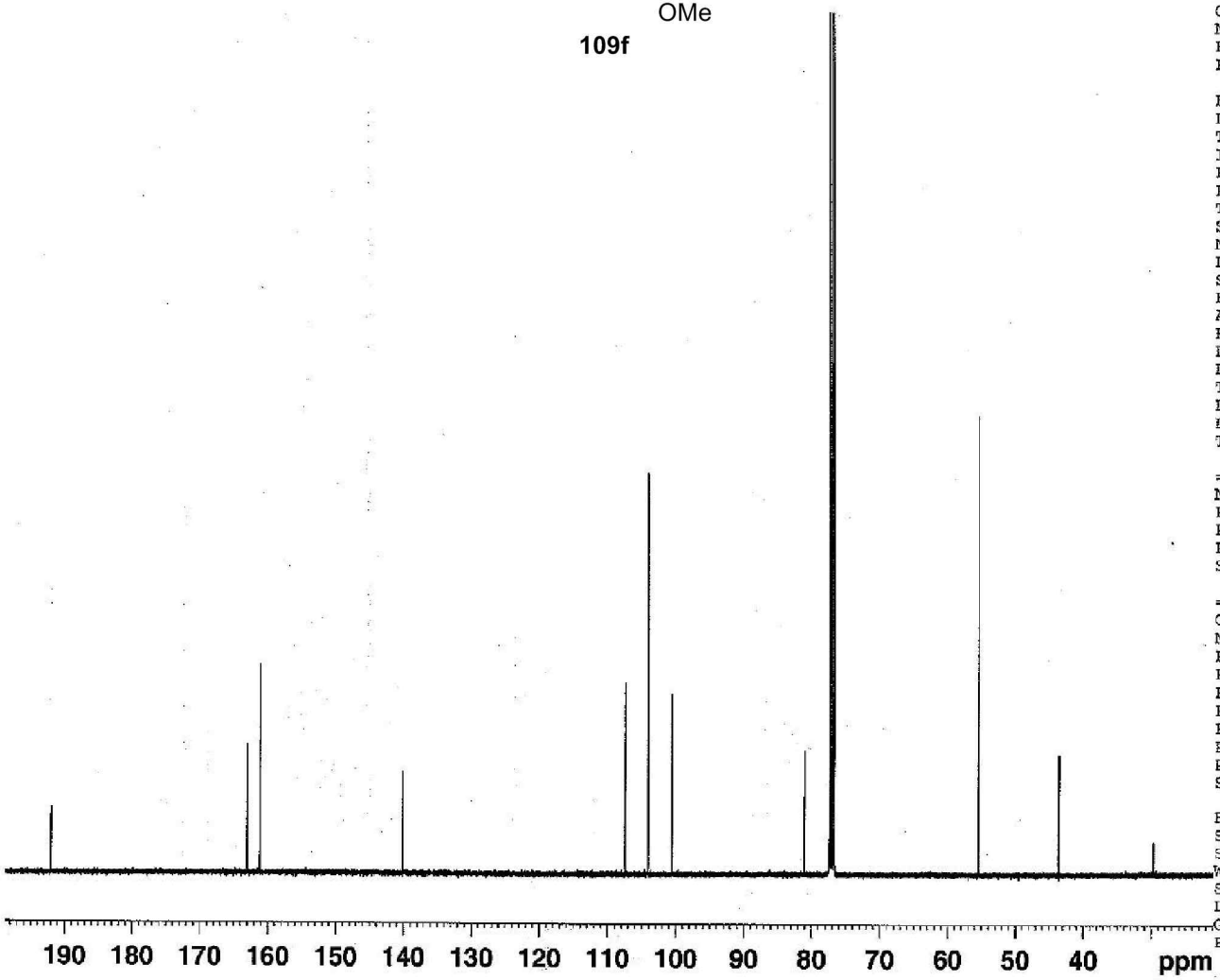
F2 - Processing parameters

SI	32768
SF	100.6140260 MHz
WDW	no
SSB	0
LB	0.00 Hz
GB	0
PC	1.40


OMe
OMe
O
O
109f
Current Data Parameters
NAME ss-3-97
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20100111
Time 11.51
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 181
DW 78.000 use
DE 6.50 use
TE 299.7 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 use
PL1 0.00 dB
PL1W 10.27361584 W
SFO1 400.1378009 MH
F2 - Processing parameters
SI 32768
SF 400.1350000 MH
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
ppm
1.00
2.03
0.97
1.00
1.03
3.37
1.05
1.07



109f



BRUKER

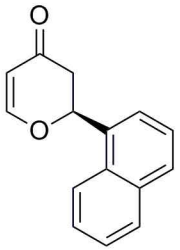
```
Current Data Parameters
NAME                  ss-3-97
EXPNO                       3
PROCNO                      1

F2 - Acquisition Parameters
Date_              20100121
Time                    8.20
INSTRUM                spect
PROBHD    5 mm PABBO BB-
PULPROG              zgpg30
TD                    65536
SOLVENT               CDCl3
NS                    11752
DS                        4
SWH               23980.814 Hz
FIDRES            0.365918 Hz
AQ                1.3664756 sec
RG                    32768
DW                   20.850 usec
DE                    6.50 usec
TE                   300.6 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                       1

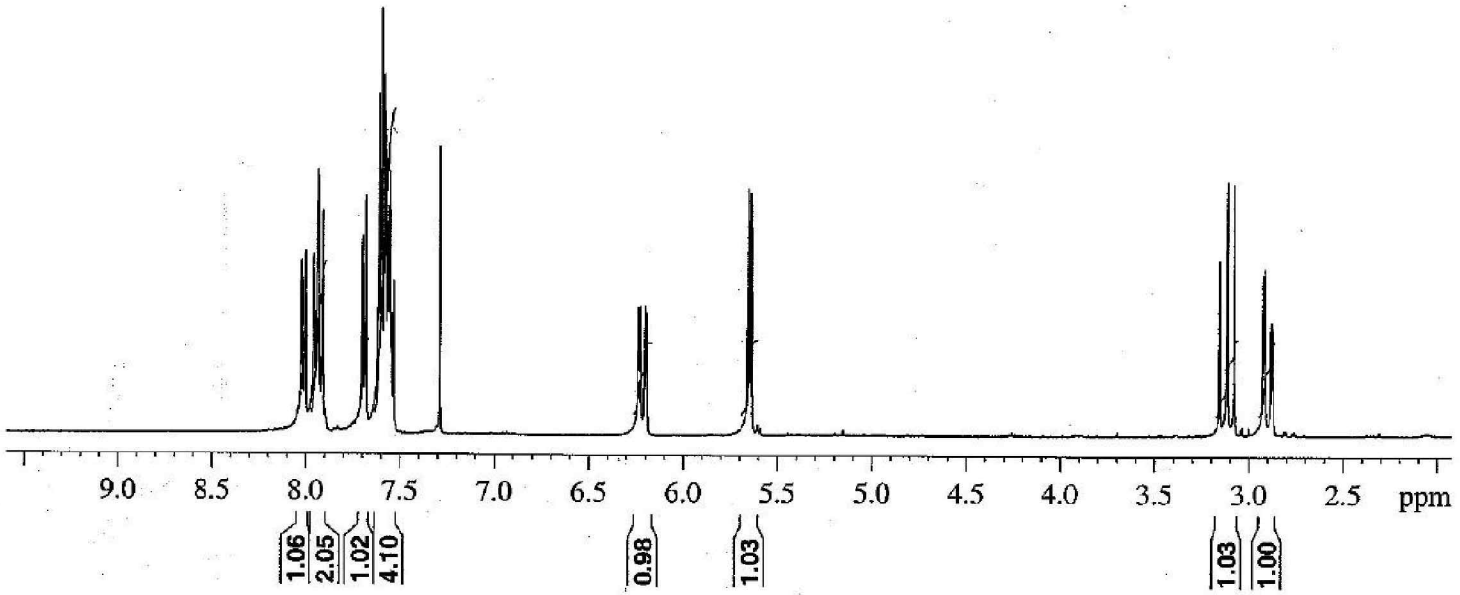
======== CHANNEL f1 ========
NUC1                    13C
P1                    9.00 usec
PL1                  -2.00 dB
PL1W           46.89702606 W
SFO1          100.6240872 MHz

======== CHANNEL f2 ========
CPDPRG2            waltz16
NUC2                    1H
PCPD2                90.00 usec
PL2                   0.00 dB
PL12                 16.16 dB
PL13                 17.00 dB
PL2W           10.27361584 W
PL12W           0.24872722 W
PL13W           0.20498557 W
SFO2          400.1366005 MHz

F2 - Processing parameters
SI                    32768
SF            100.6140260 MHz
WDW                      no
SSB                       0
LB                    0.00 Hz
GB                        0
PC                    1.40
```



109g

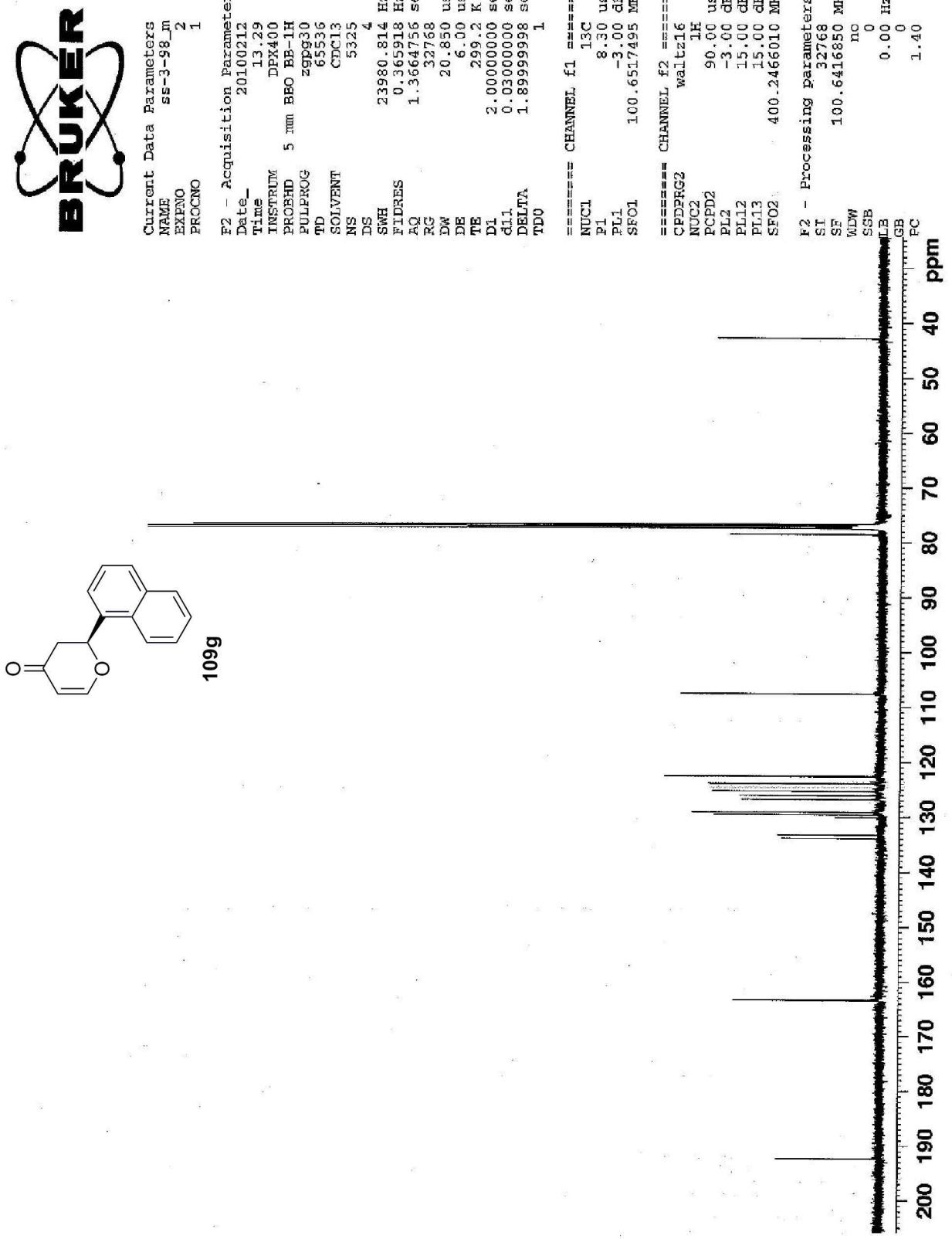



```
Current Data Parameters
NAME                  ss-3-98
EXPNO                       1
PROCNO                      1

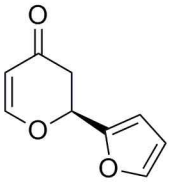
F2 - Acquisition Parameters
Date_              20100112
Time                  10.18
INSTRUM               spect
PROBHD   5 mm PABBO BB-
PULPROG                zg30
TD                    32768
SOLVENT               CDCl3
NS                       32
DS                        2
SWH                6410.256 Hz
FIDRES            0.195625 Hz
AQ                2.5559540 sec
RG                      128
DW                 78.000 use
DE                  6.50 use
TE                 300.4 K
D1              1.00000000 sec
TD0                       1

======== CHANNEL f1 =======
NUC1                      1H
P1                 14.00 use
PL1                 0.00 dB
PL1W          10.27361584 W
SFO1          400.1378009 MH

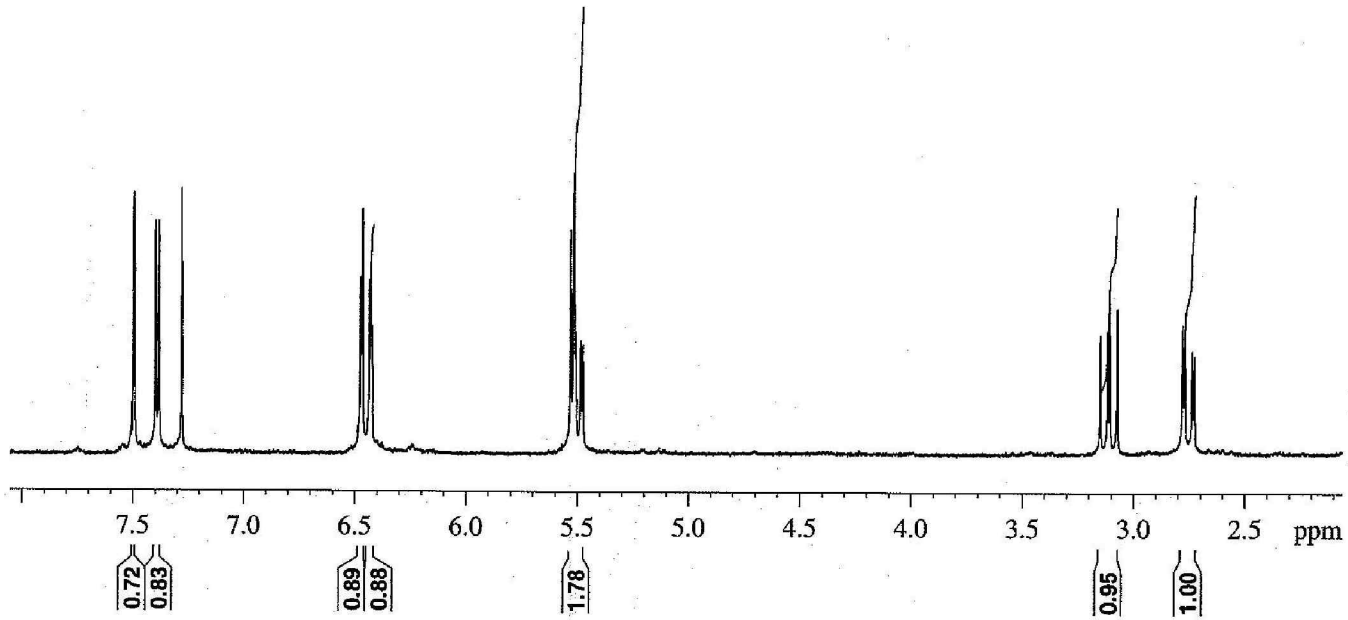
F2 - Processing parameters
SI                    32768
SF            400.1350000 MH
WDW                      no
SSB                       0
LB                 0.00 Hz
GB                        0
PC                     1.00
```


BRUKER
Current Data Parameters
NAME ss-3-98_m
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20100212
Time 13.29
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 5325
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 32768
DW 20.850 usec
DE 6.00 usec
TE 299.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.30 usec
PL1 -3.00 dB
SFO1 100.6517495 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2466010 MHz
F2 - Processing parameters
SI 32768
SF 100.6416850 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.40
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 ppm

109g



109h

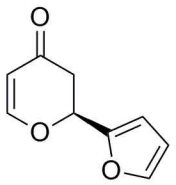



```
Current Data Parameters
NAME                  ss-3-78_m
EXPNO                         2
PROCNO                        1

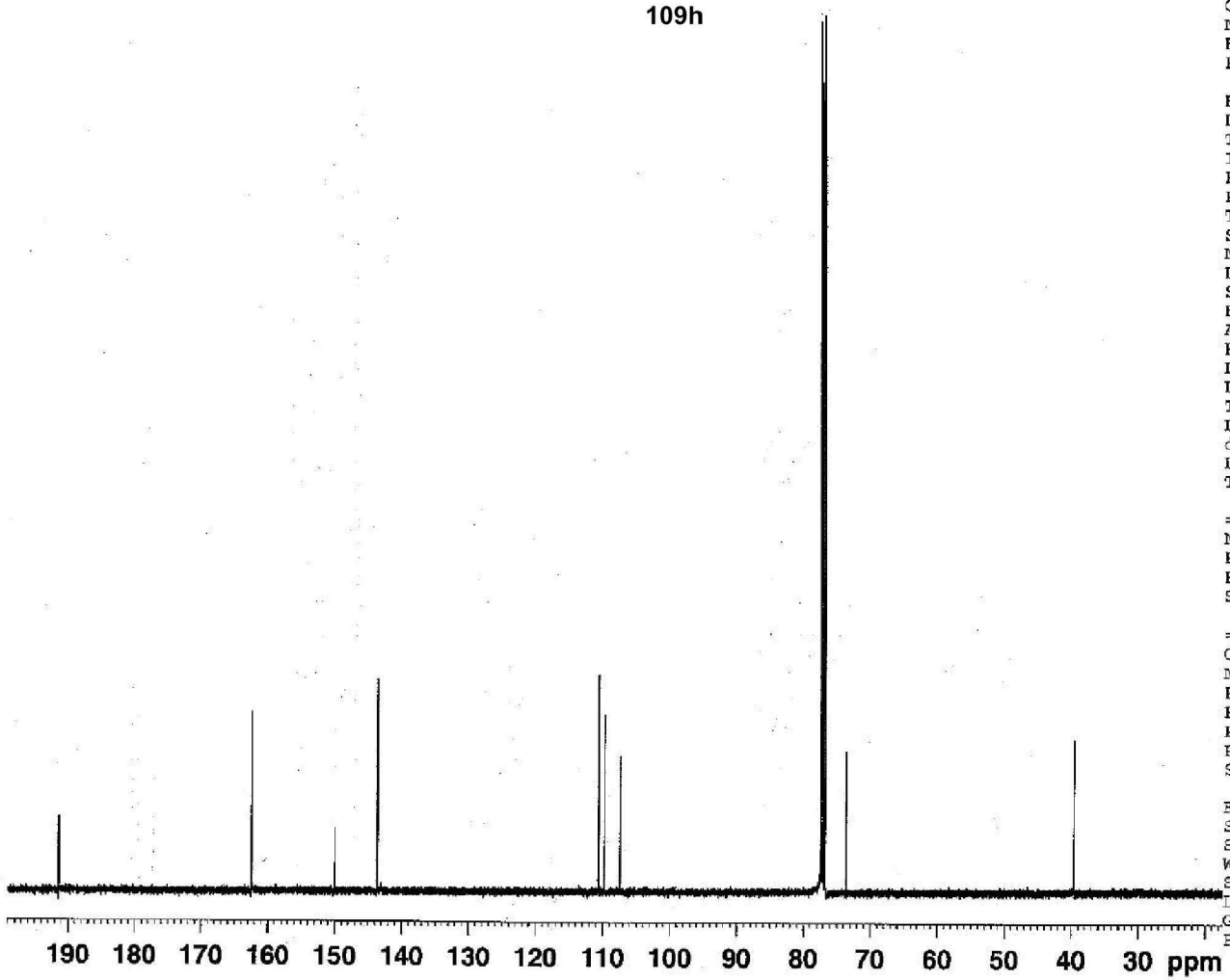
F2 - Acquisition Parameter:
Date_                  20091226
Time                      22.40
INSTRUM                  DPX400
PROBHD    5 mm BBO BB-1H
PULPROG                    zg30
TD                        32768
SOLVENT                   CDCl3
NS                           32
DS                            2
SWH                    6410.256 Hz
FIDRES                 0.195625 Hz
AQ                     2.5559540 se
RG                          362
DW                       78.000 us
DE                        6.00 us
TE                       297.2 K
D1                  1.00000000 se
TD0                           1

======== CHANNEL f1 =======
NUC1                         1H
P1                       13.50 us
PL1                      -3.00 dB
SFO1                400.2478017 MH:

F2 - Processing parameters
SI                        32768
SF                  400.2450000 MH:
WDW                          no
SSB                           0
LB                       0.00 Hz
GB                            0
PC                         1.00
```



109h



BRUKER

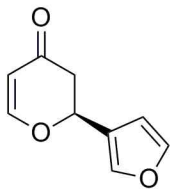
```
Current Data Parameters
NAME                  ss-3-78_m
EXPNO                         3
PROCNO                        1

F2 - Acquisition Parameters
Date_                  20091226
Time                      22.47
INSTRUM                  DPX400
PROBHD    5 mm BBO BB-1H
PULPROG                 zgpg30
TD                       65536
SOLVENT                  CDCl3
NS                       10500
DS                           4
SWH                  23980.814 Hz
FIDRES                0.365918 Hz
AQ                    1.3664756 sec
RG                        32768
DW                       20.850 usec
DE                        6.00 usec
TE                       297.2 K
D1                  2.00000000 sec
d11                 0.03000000 sec
DELTA               1.89999998 sec
TD0                           1

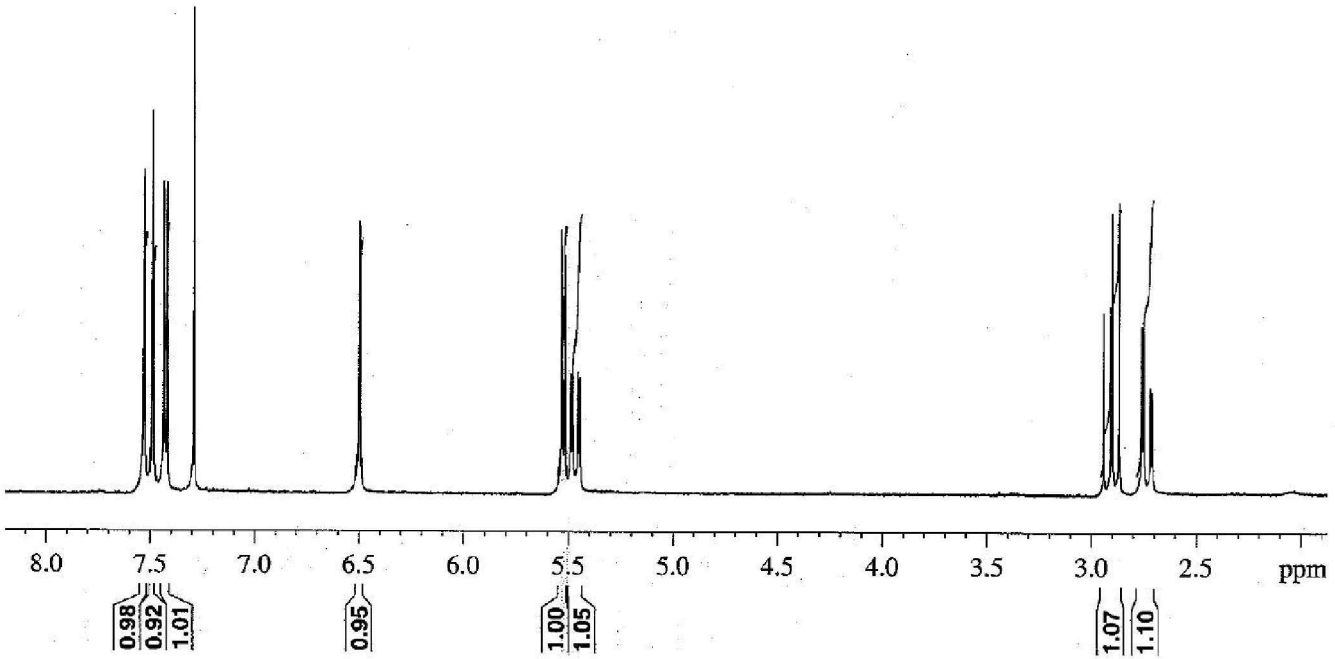
======== CHANNEL f1 ========
NUC1                        13C
P1                         8.30 usec
PL1                       -3.00 dB
SFO1                100.6517495 MHz

======== CHANNEL f2 ========
CPDPRG2                 waltz16
NUC2                         1H
PCPD2                     90.00 usec
PL2                       -3.00 dB
PL12                      15.00 dB
PL13                      15.00 dB
SFO2                400.2466010 MHz

F2 - Processing parameters
SI                        32768
SF                  100.6416850 MHz
WDW                          no
SSB                           0
LB                         0.00 Hz
GB                            0
PC                         1.40
```



109i

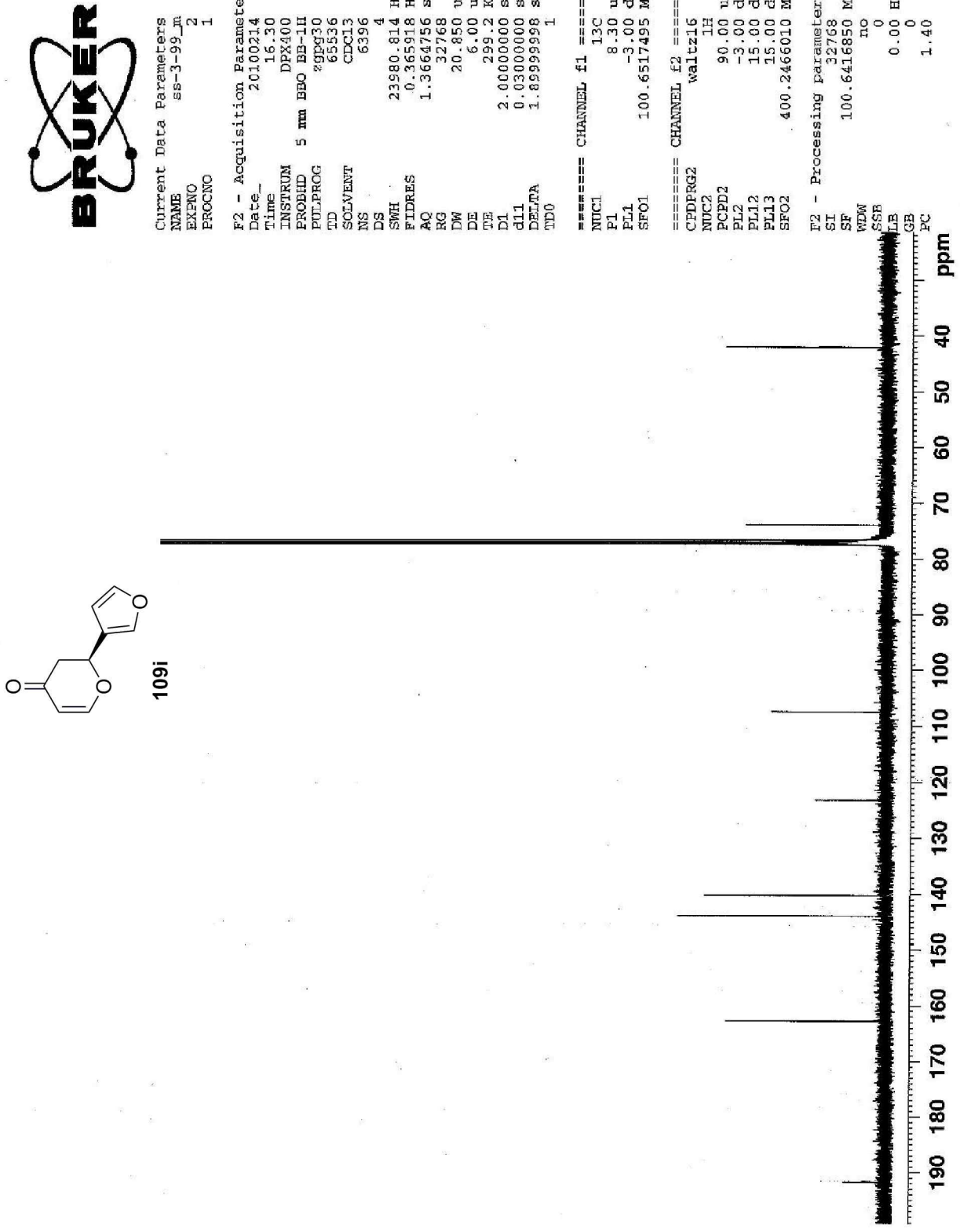


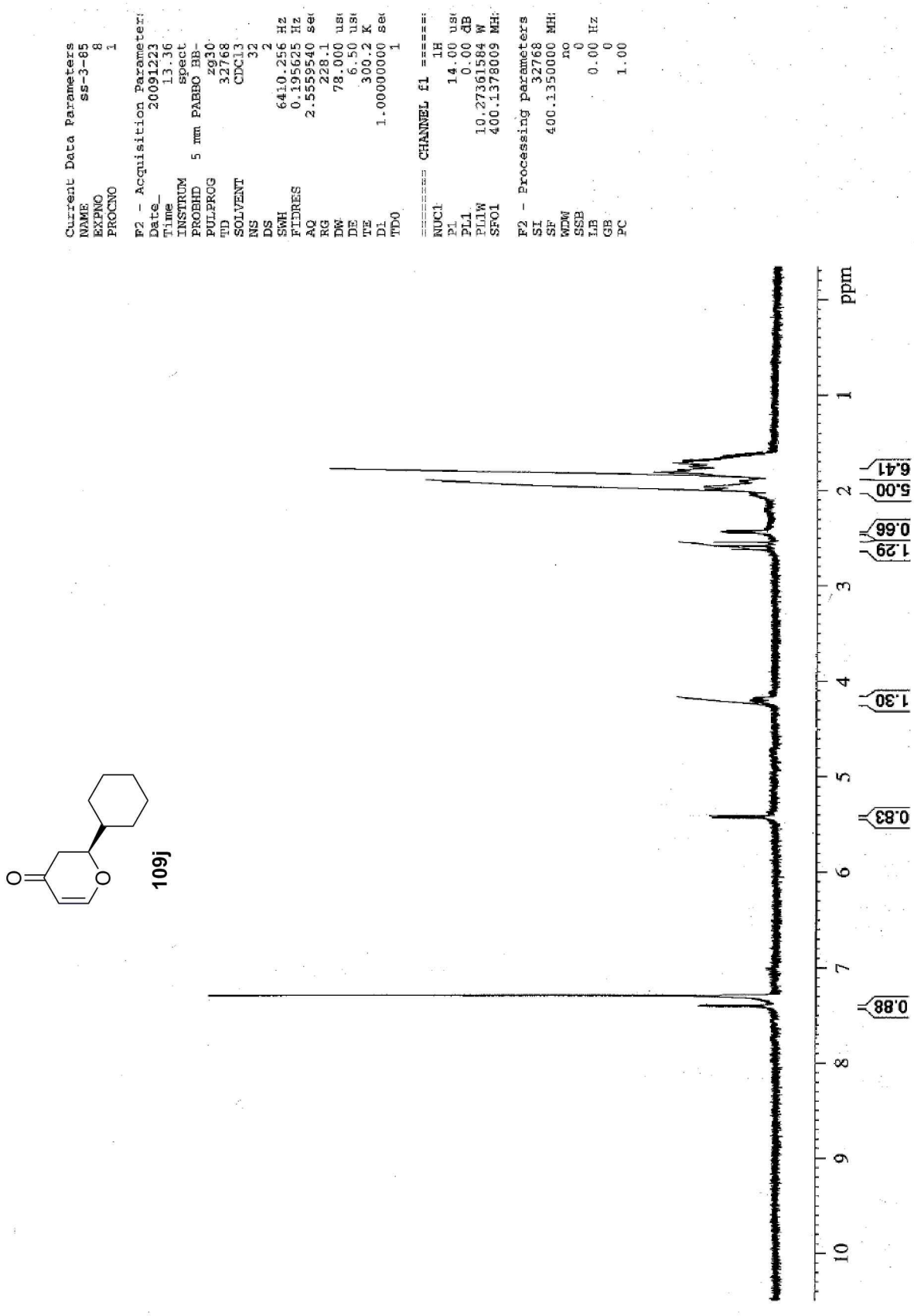

```
Current Data Parameters
NAME                  ss-3-99
EXPNO                       1
PROCNO                      1

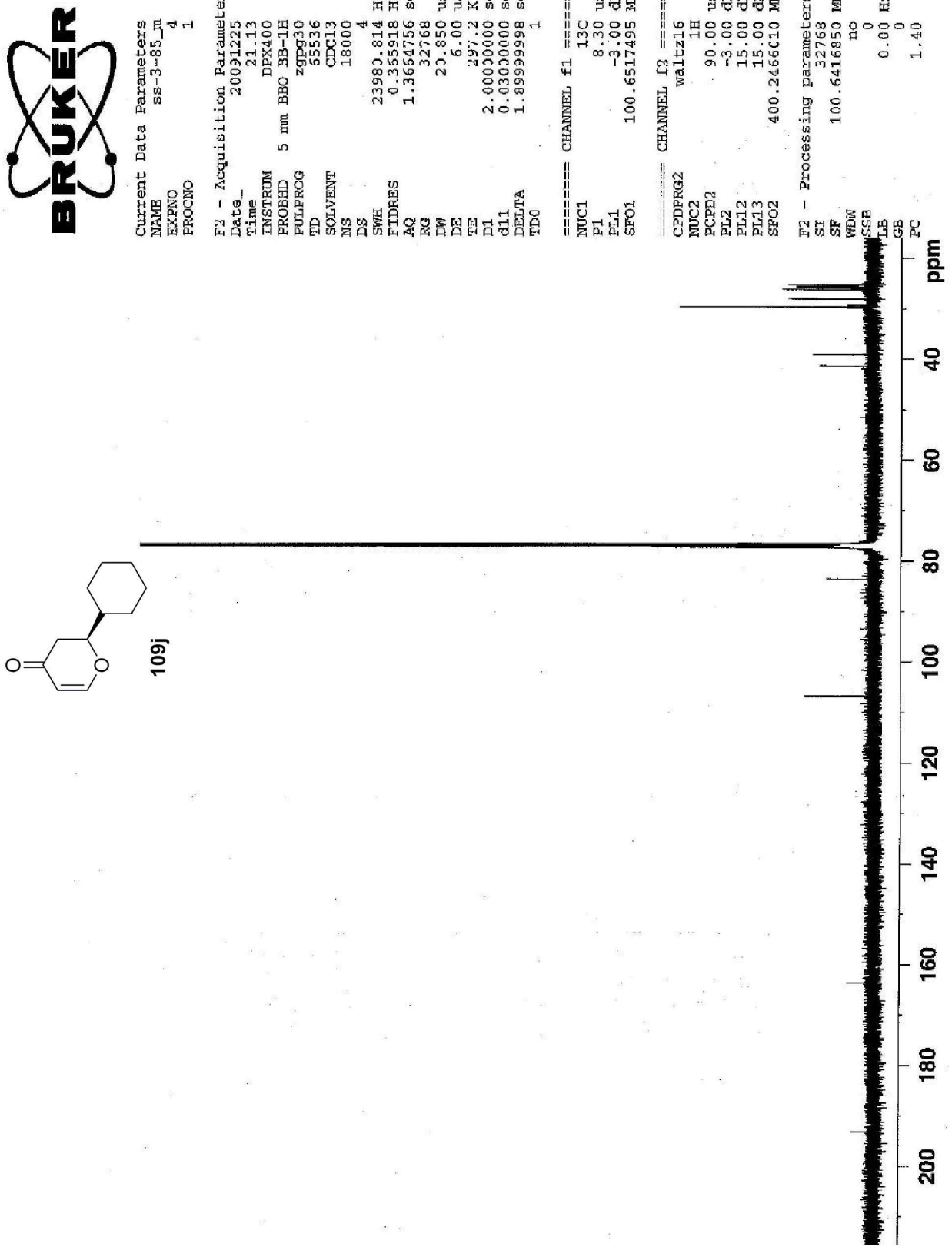
F2 - Acquisition Parameters
Date_              20100112
Time                  10.23
INSTRUM               spect
PROBHD    5 mm PABBO BB-
PULPROG                zg30
TD                    32768
SOLVENT               CDCl3
NS                       32
DS                        2
SWH                6410.256 Hz
FIDRES            0.195625 Hz
AQ                2.5559540 sec
RG                      256
DW                   78.000 use
DE                    6.50 use
TE                   300.2 K
D1                1.00000000 sec
TD0                       1

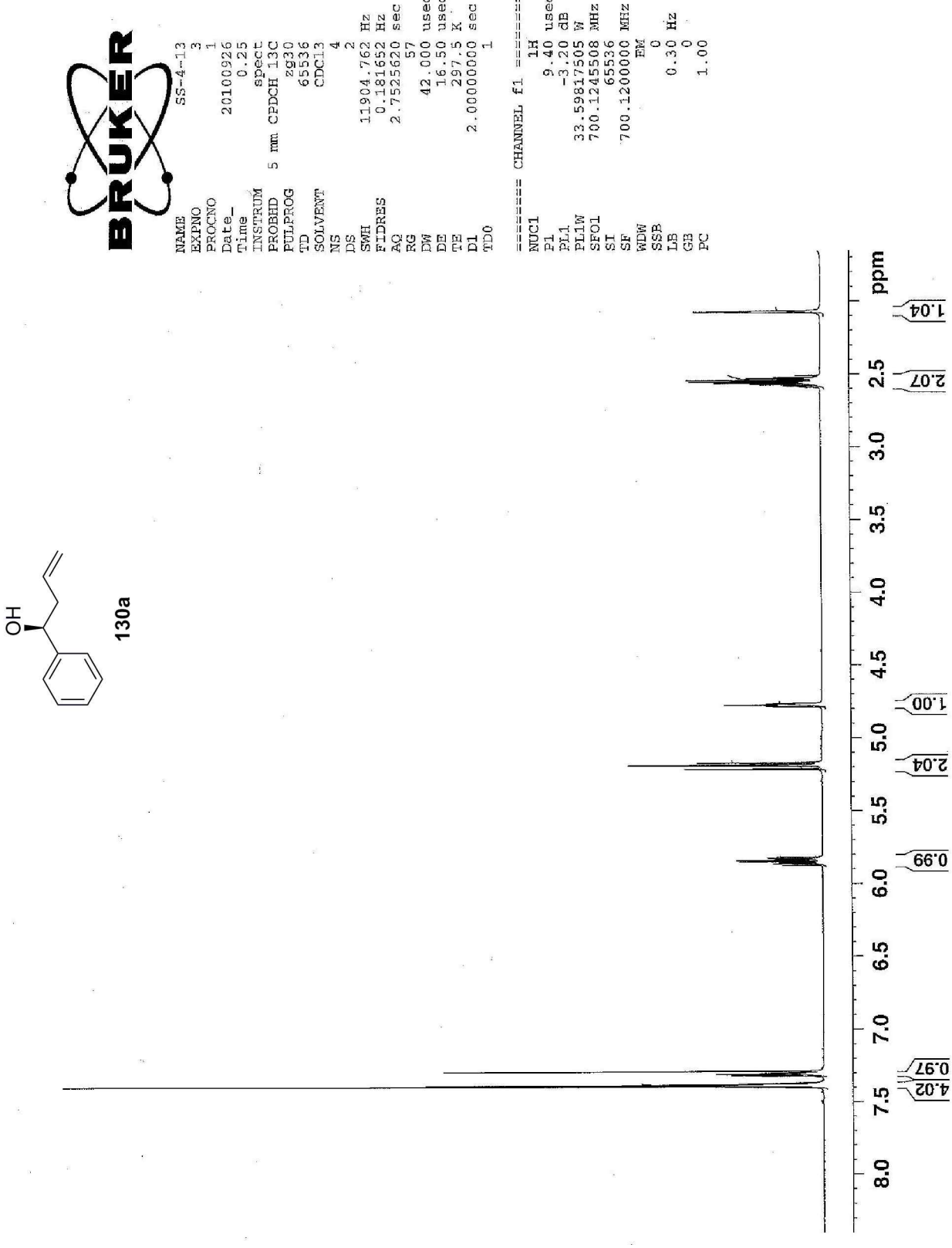
======== CHANNEL f1 =======
NUC1                      1H
P1                    14.00 use
PL1                    0.00 dB
PL1W          10.27361584 W
SFO1          400.1378009 MH:

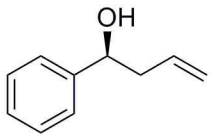
F2 - Processing parameters
SI                    32768
SF            400.1350000 MH:
WDW                     no
SSB                      0
LB                    0.00 Hz
GB                       0
PC                    1.00
```


109i
Current Data Parameters
NAME ss-3-99_m
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20100214
Time 16.30
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG %gpg30
TD 65536
SOLVENT CDCl3
NS 6396
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 32768
DW 20.850 usec
DE 6.00 usec
TE 299.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.30 usec
PL1 -3.00 dB
SFO1 100.6517495 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2466010 MHz
F2 - Processing parameters
SI 32768
SF 100.6416850 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.40
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 ppm

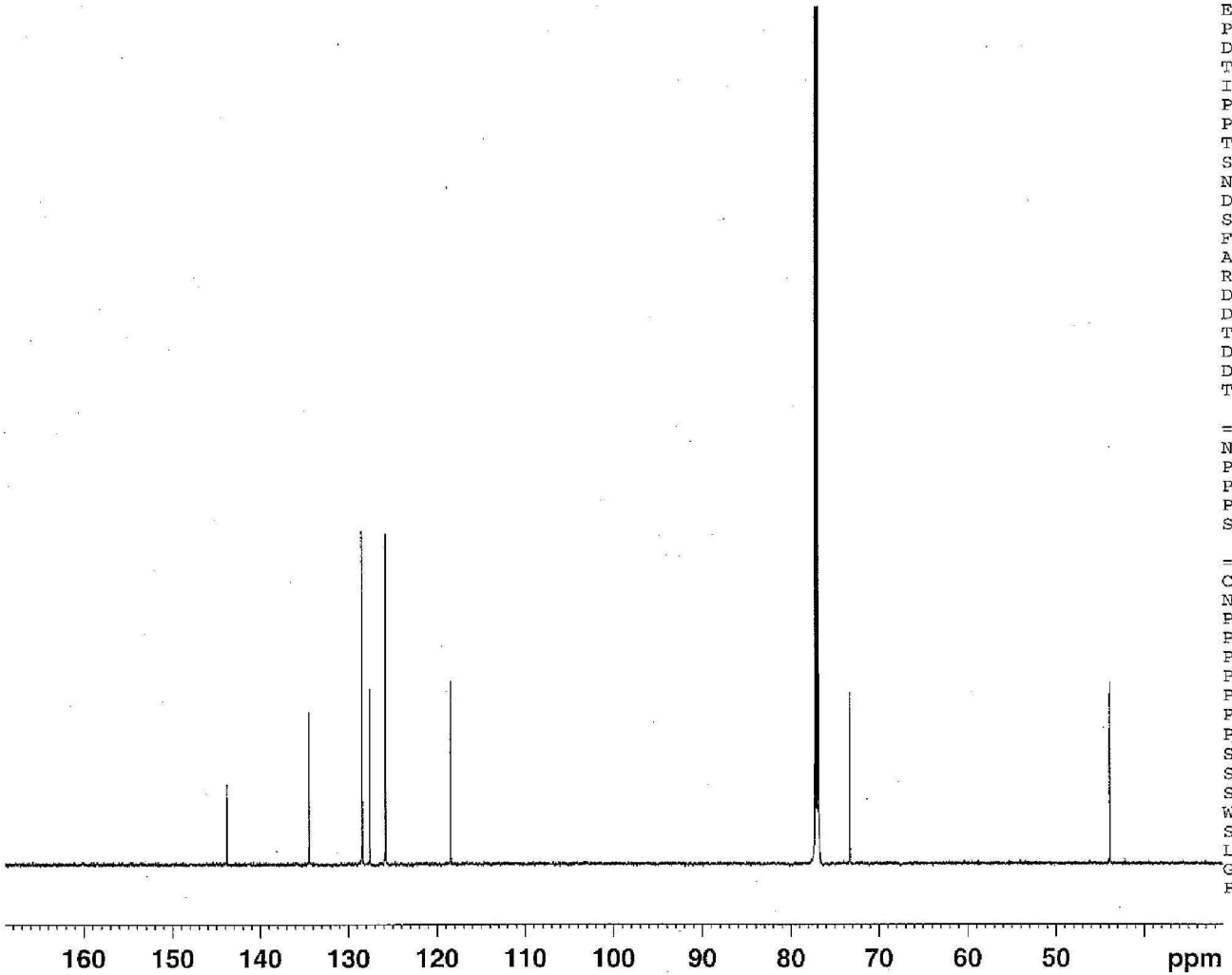

Current Data Parameters
NAME ss-3-65
EXPNO 8
PROCNO 1
F2 - Acquisition Parameter
Date_ 20091223
Time 13.36
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 se
RG 228.1
DW 78.000 us
DE 6.50 us
TE 300.2 K
D1 1.00000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.00 us
PL1 0.00 dB
PL1W 10.27361584 W
SFO1 400.1378009 MH
F2 - Processing parameters
SI 32768
SF 400.1350000 MH
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
0.88
0.83
1.30
1.29
0.66
5.00
6.41
ppm
109j


109j
Current Data Parameters
NAME ss-3-85_m
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20091225
Time 21.13
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 18000
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 32768
DW 20.850 usec
DE 6.00 usec
TE 297.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.30 usec
PL1 -3.00 dB
SFO1 100.6517495 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2466010 MHz
F2 - Processing parameters
SI 32768
SF 100.6416850 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.40
200
180
160
140
120
100
80
60
40
ppm

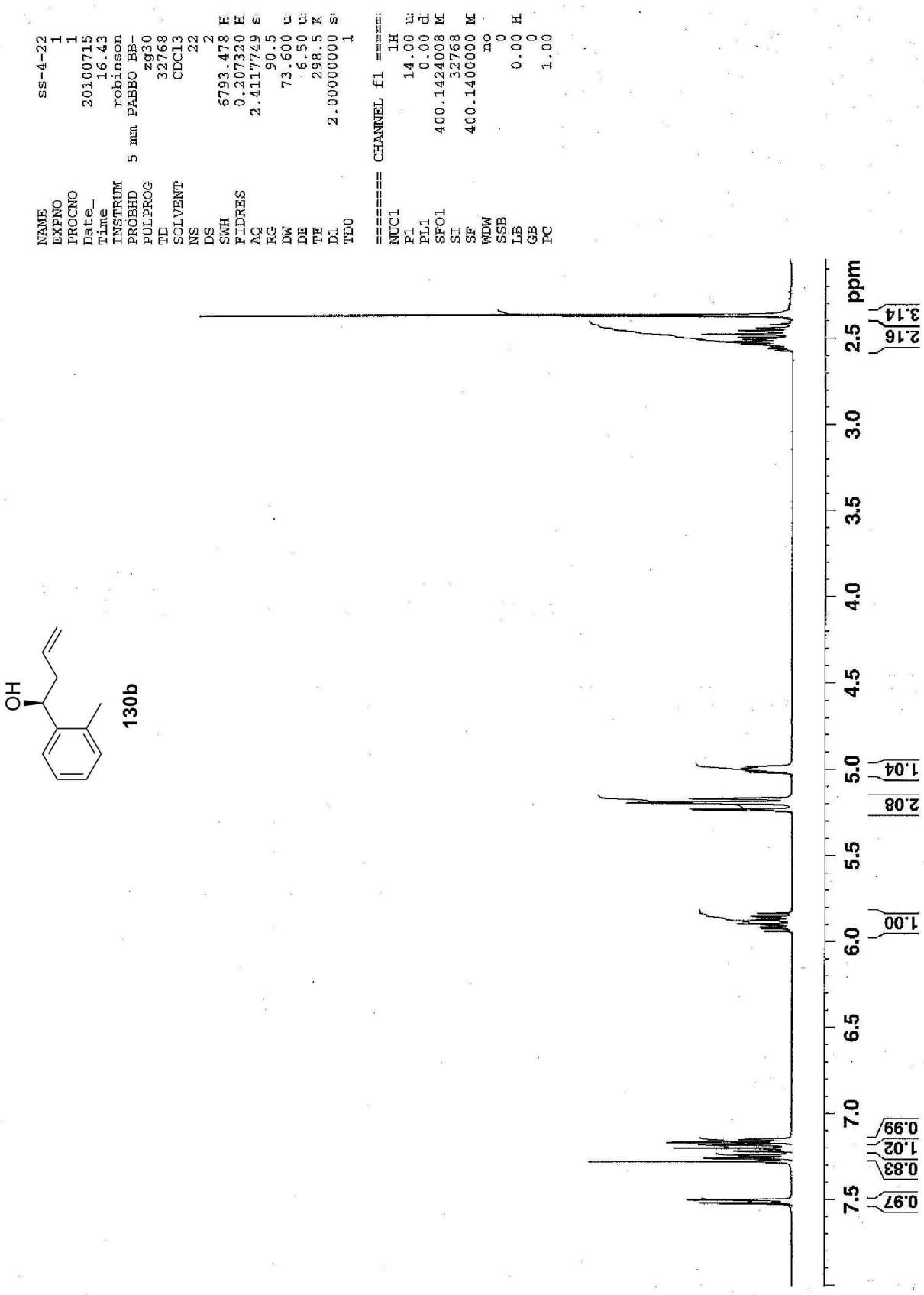

130a
OH
BRUKER
NAME SS-4-13
EXPNO 3
PROCNO 1
Date_ 20100926
Time 0.25
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 4
DS 2
SWH 11904.762 Hz
FIDRES 0.181652 Hz
AQ 2.7525620 sec
RG 57
DW 42.000 usec
DE 16.50 usec
TE 297.5 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1245508 MHz
SI 65536
SF 700.1200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
ppm
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
4.02
0.97
0.99
2.04
1.00
2.07
1.04

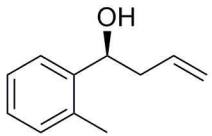


130a

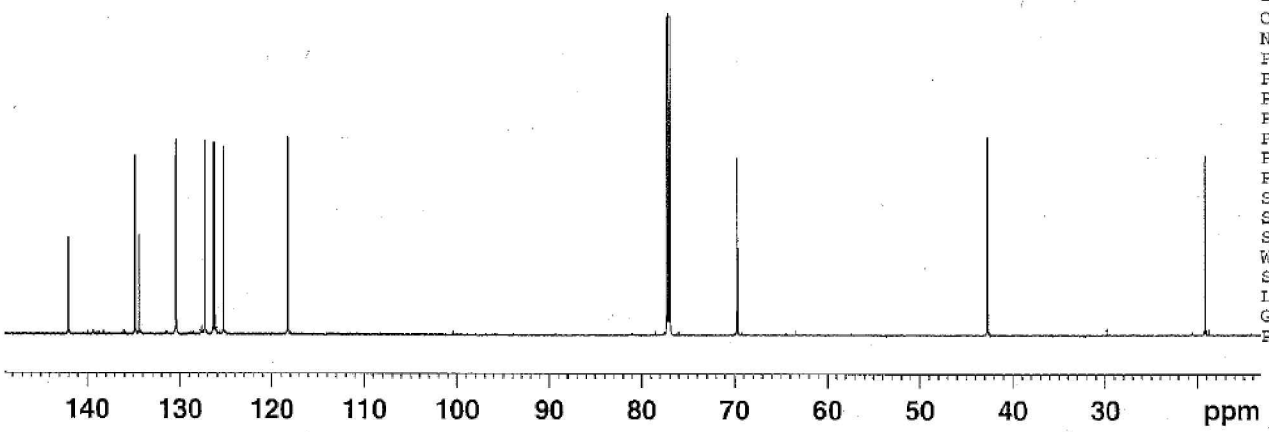


NAME	SS-4-13
EXPNO	4
PROCNO	1
Date_	20100926
Time	0.32
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	98304
SOLVENT	CDCl3
NS	53
DS	4
SWH	41666.668 Hz
FIDRES	0.423855 Hz
AQ	1.1796980 sec
RG	203
DW	12.000 usec
DE	15.00 usec
TE	297.5 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 usec
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0629186 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 usec
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1228005 MHz
SI	131072
SF	176.0453140 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40

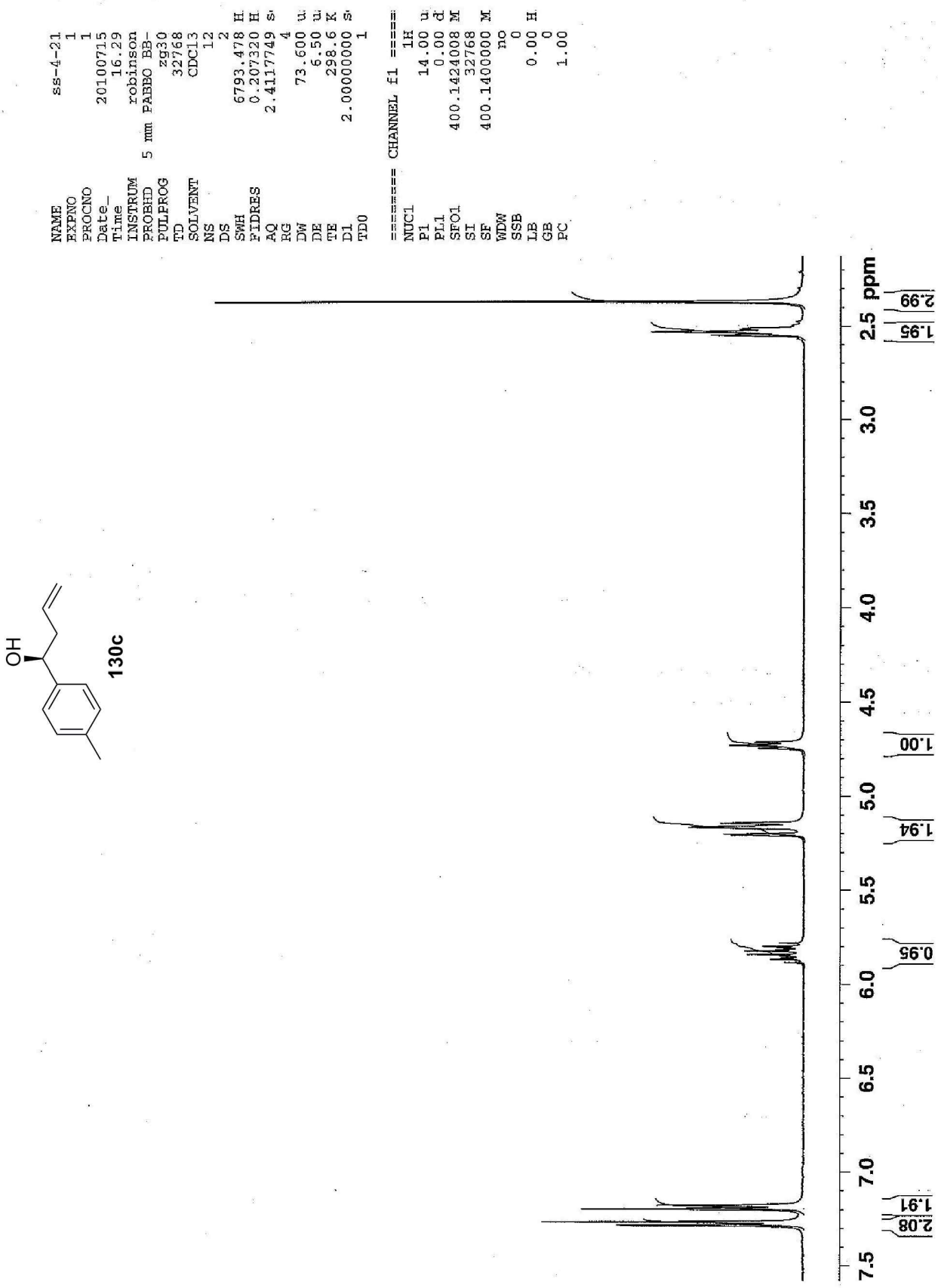

NAME ss-4-22
EXPNO 1
PROCNO 1
Date_ 20100715
Time 16.43
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 22
DS 2
SWH 6793.478 H
FIDRES 0.207320 H
AQ 2.4117749 s
RG 90.5
DW 73.600 u
DE 6.50 u
TE 298.5 K
D1 2.00000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.00 u
PL1 0.00 d
SFO1 400.1424008 M
SI 32768
SF 400.1400000 M
WDW no
SSB 0
LB 0.00 H
GB 0
PC 1.00
OH
130b
ppm
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
0.97
0.83
1.02
0.99
1.00
2.08
1.04
2.16
3.14

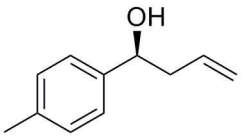


130b

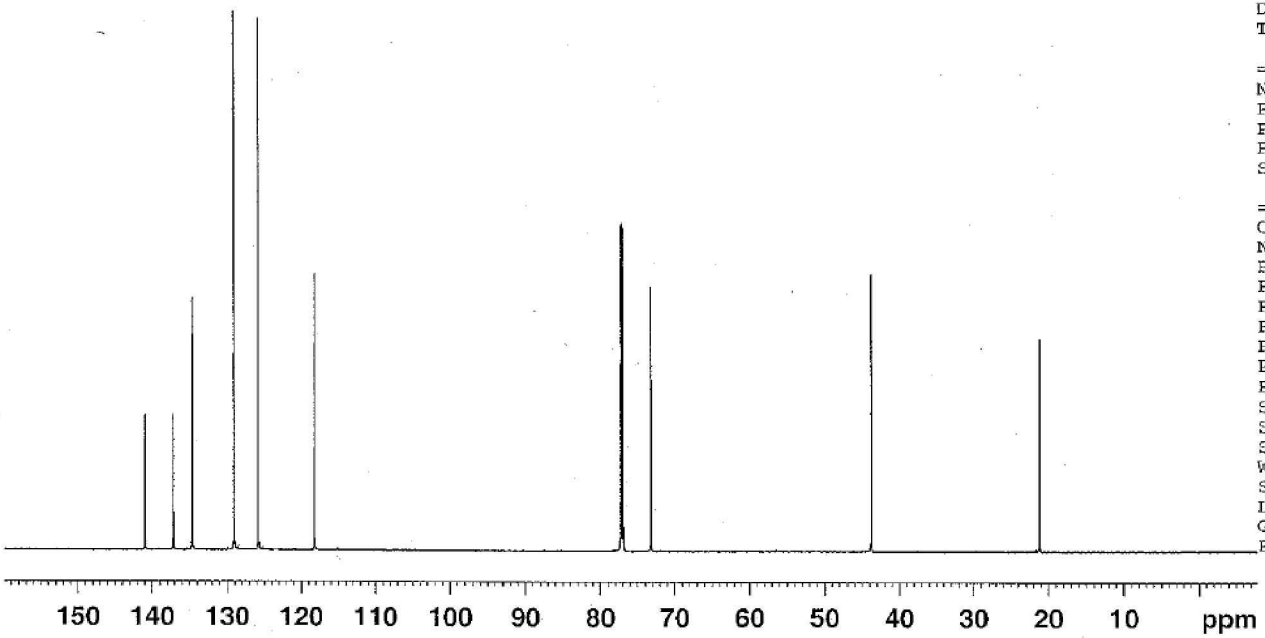


NAME	SS-4-22
EXPNO	5
PROCNO	1
Date_	20101112
Time	12.38
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	98304
SOLVENT	CDCl3
NS	42
DS	4
SWH	41666.668 Hz
FIDRES	0.423855 Hz
AQ	1.1796980 sec
RG	203
DW	12.000 usec
DE	15.00 usec
TE	297.5 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 usec
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0629186 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 usec
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1228005 MHz
SI	131072
SF	176.0453140 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40

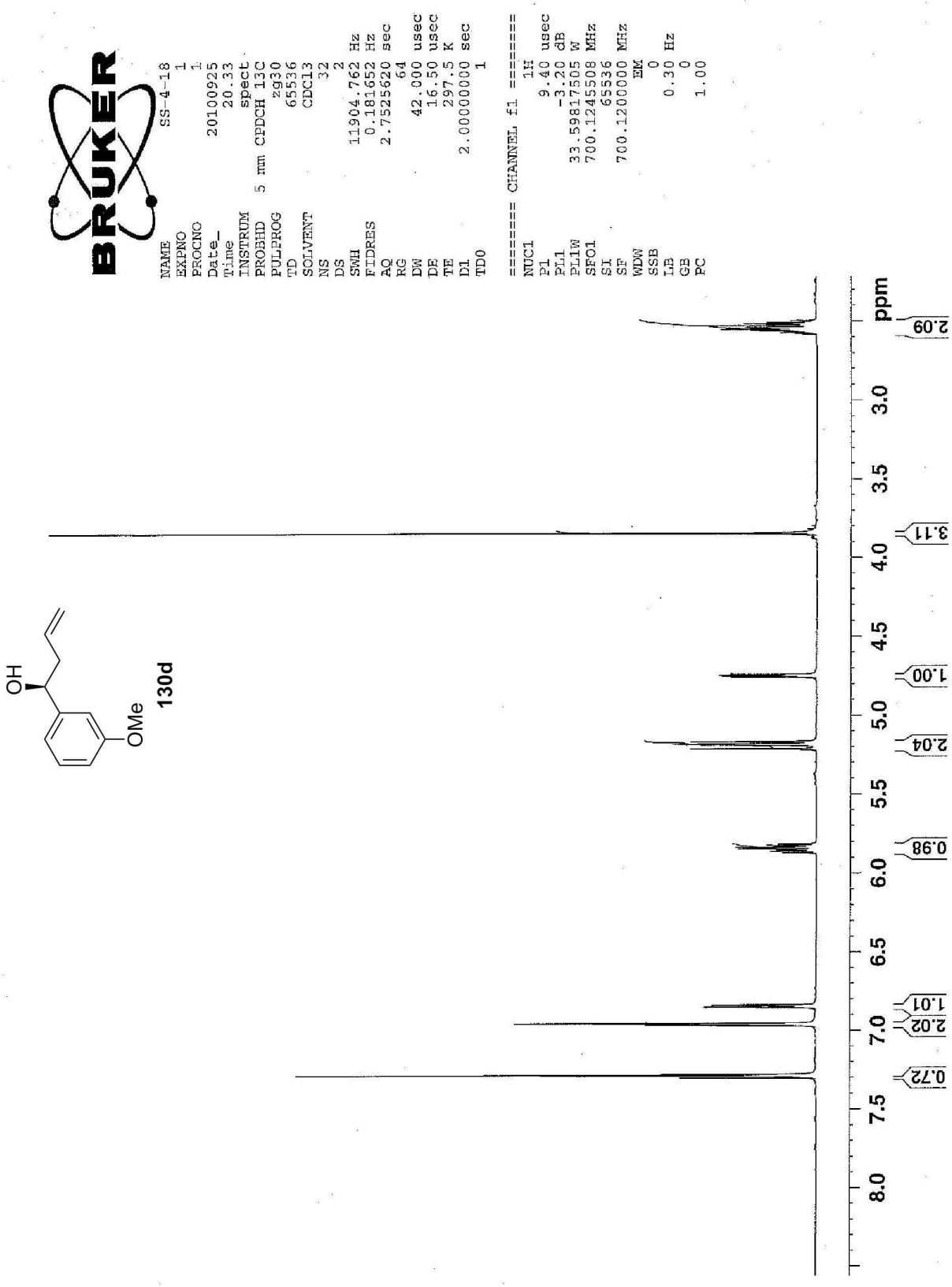

OH
130c
NAME ss-4-21
EXPNO 1
PROCNO 1
Date_ 20100715
Time 16.29
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 12
DS 2
SWH 6793.478 H
FIDRES 0.207320 H
AQ 2.4117749 s
RG 4
DW 73.600 u
DE 6.50 u
TE 298.6 K
D1 2.00000000 s
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.00 u
PL1 0.00 d
SFO1 400.1424008 M
SI 32768
SF 400.1400000 M
WDW no
SSB 0
LB 0.00 H
GB 0
PC 1.00
ppm
2.99
1.95
1.00
1.94
0.95
2.08
1.91

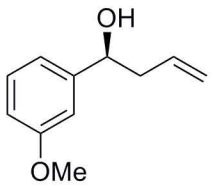


130c

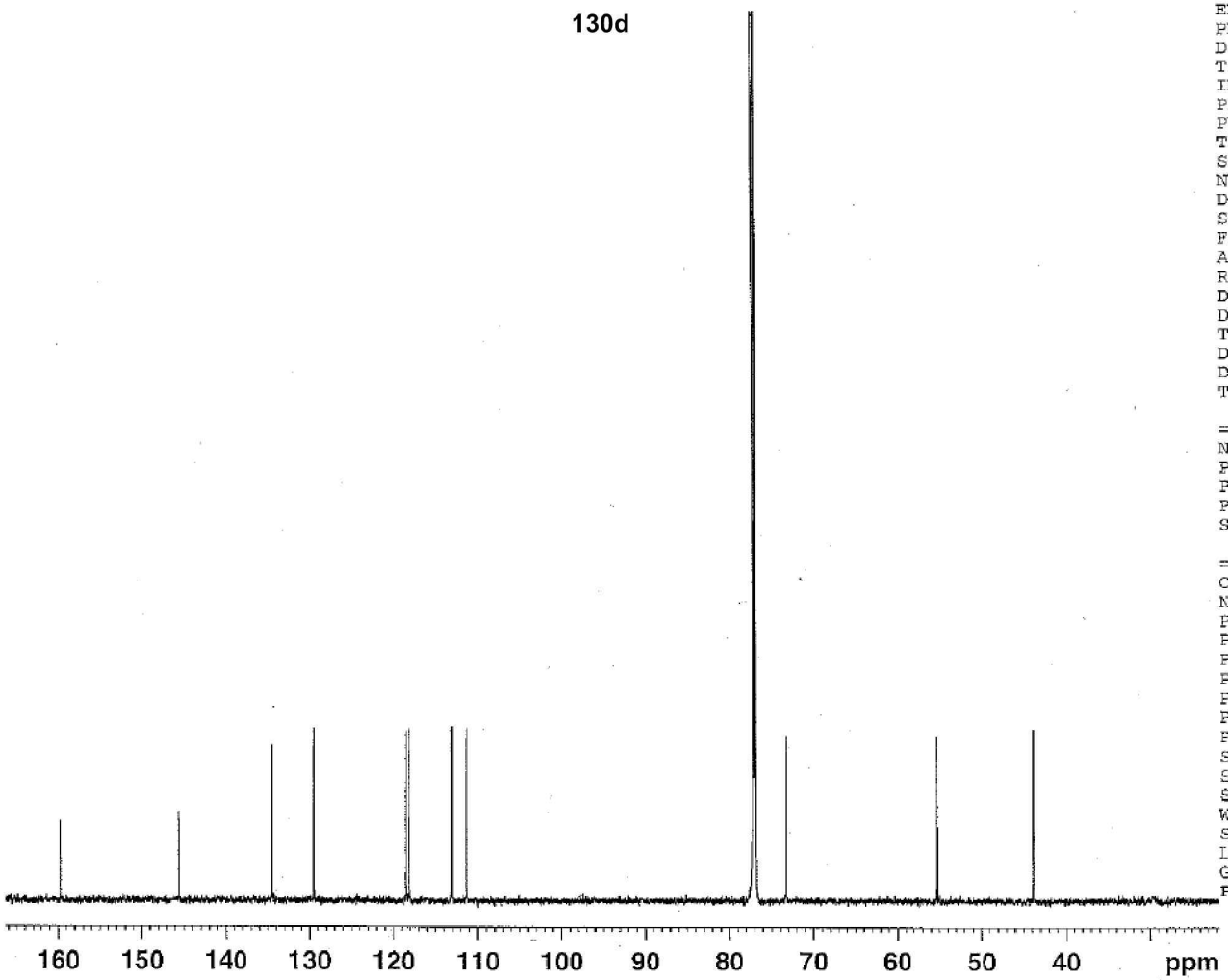


NAME	SS-4-21
EXPNO	6
PROCNO	1
Date_	20101112
Time	12.24
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	98304
SOLVENT	CDCl3
NS	67
DS	4
SWH	41666.668 Hz
FIDRES	0.423855 Hz
AQ	1.1796980 sec
RG	203
DW	12.000 usec
DE	15.00 usec
TE	297.5 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 usec
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0629186 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 usec
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1228005 MHz
SI	131072
SF	176.0453140 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40


OH
OMe
130d
BRUKER
NAME SS-4-18
EXPNO 1
PROCNO 1
Date_ 20100925
Time 20.33
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.181652 Hz
AQ 2.7525620 sec
RG 64
DW 42.000 usec
DE 16.50 usec
TE 297.5 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1245508 MHz
SI 65536
SF 700.1200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
ppm
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
0.72
2.02
1.01
0.98
2.04
1.00
3.11
2.09

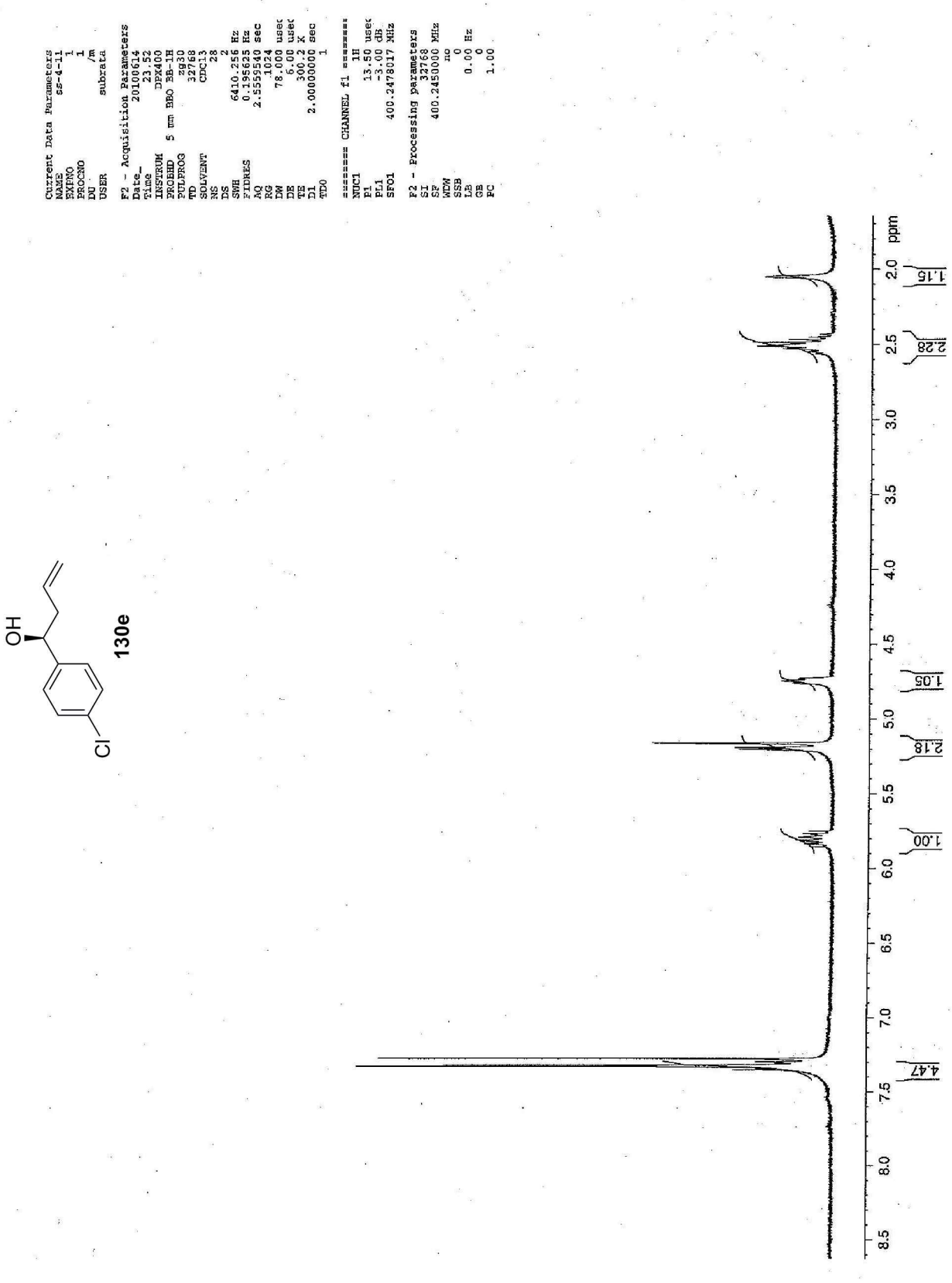


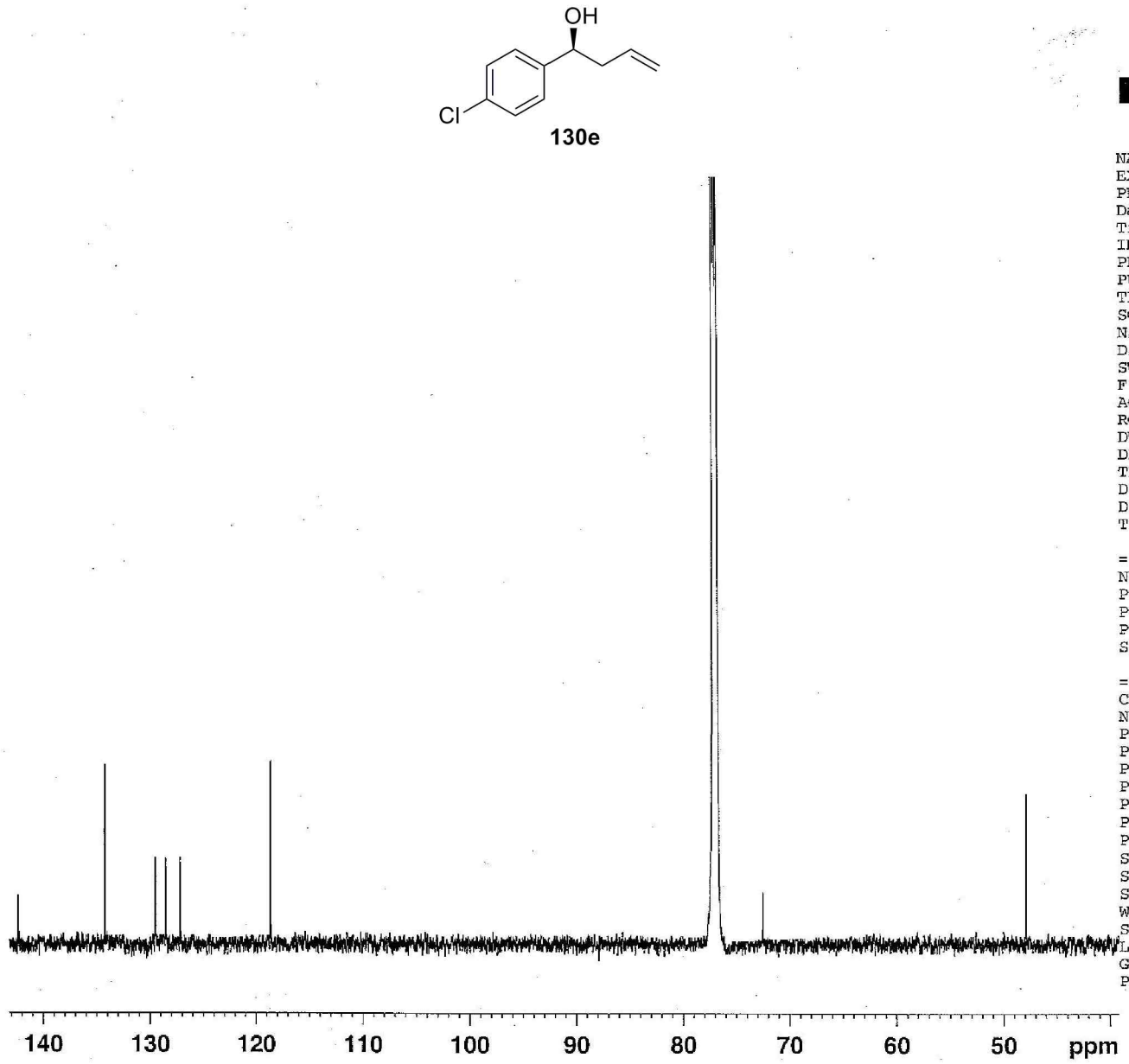
130d



BRUKER

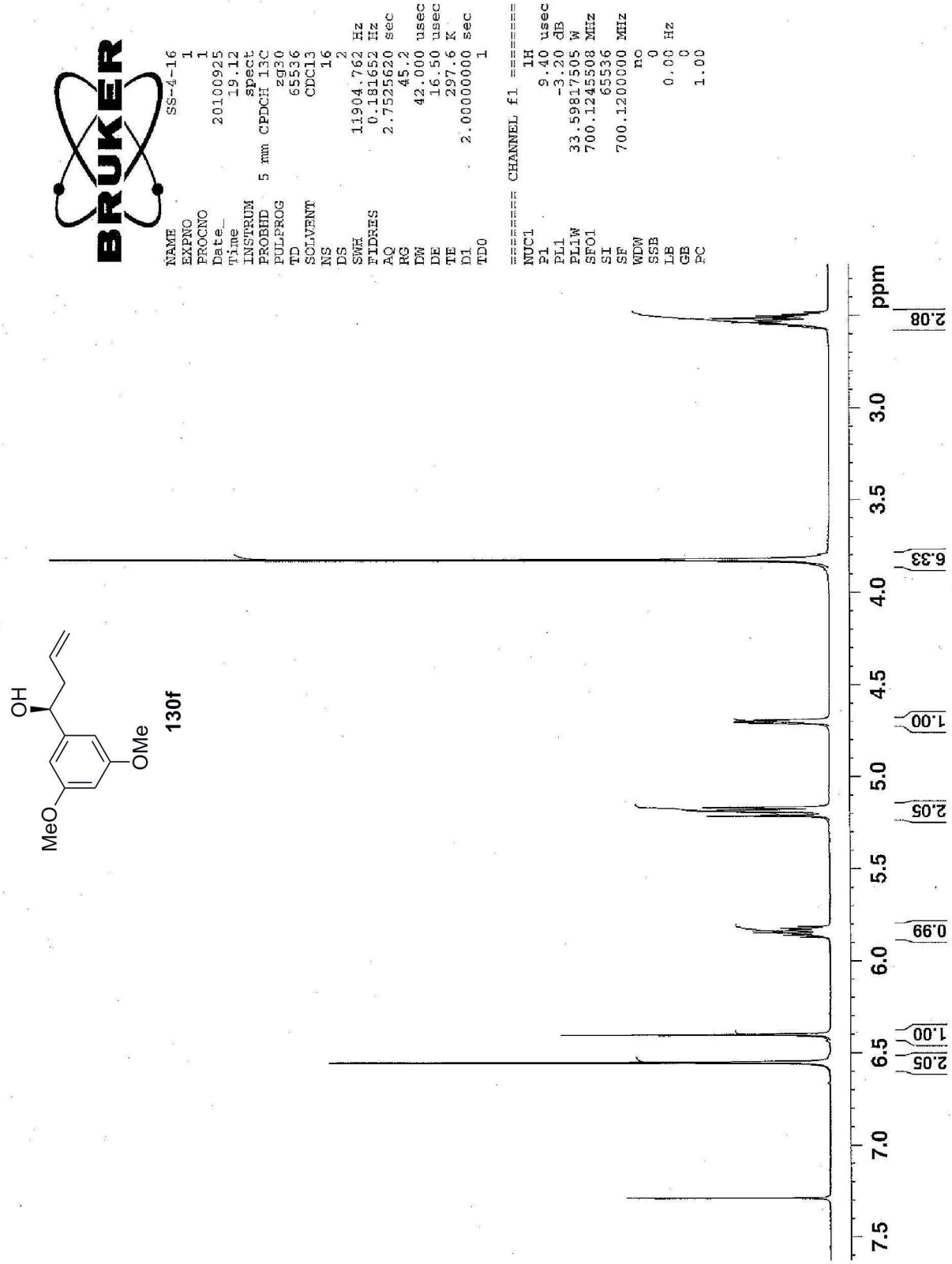
NAME	SS-4-18
EXPNO	2
PROCNO	1
Date_	20100925
Time	20.43
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	98304
SOLVENT	CDCl3
NS	84
DS	4
SWH	41666.668 Hz
FIDRES	0.423855 Hz
AQ	1.1796980 sec
RG	203
DW	12.000 usec
DE	15.00 usec
TE	297.5 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 usec
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0629186 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 usec
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1228005 MHz
SI	131072
SF	176.0453140 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40

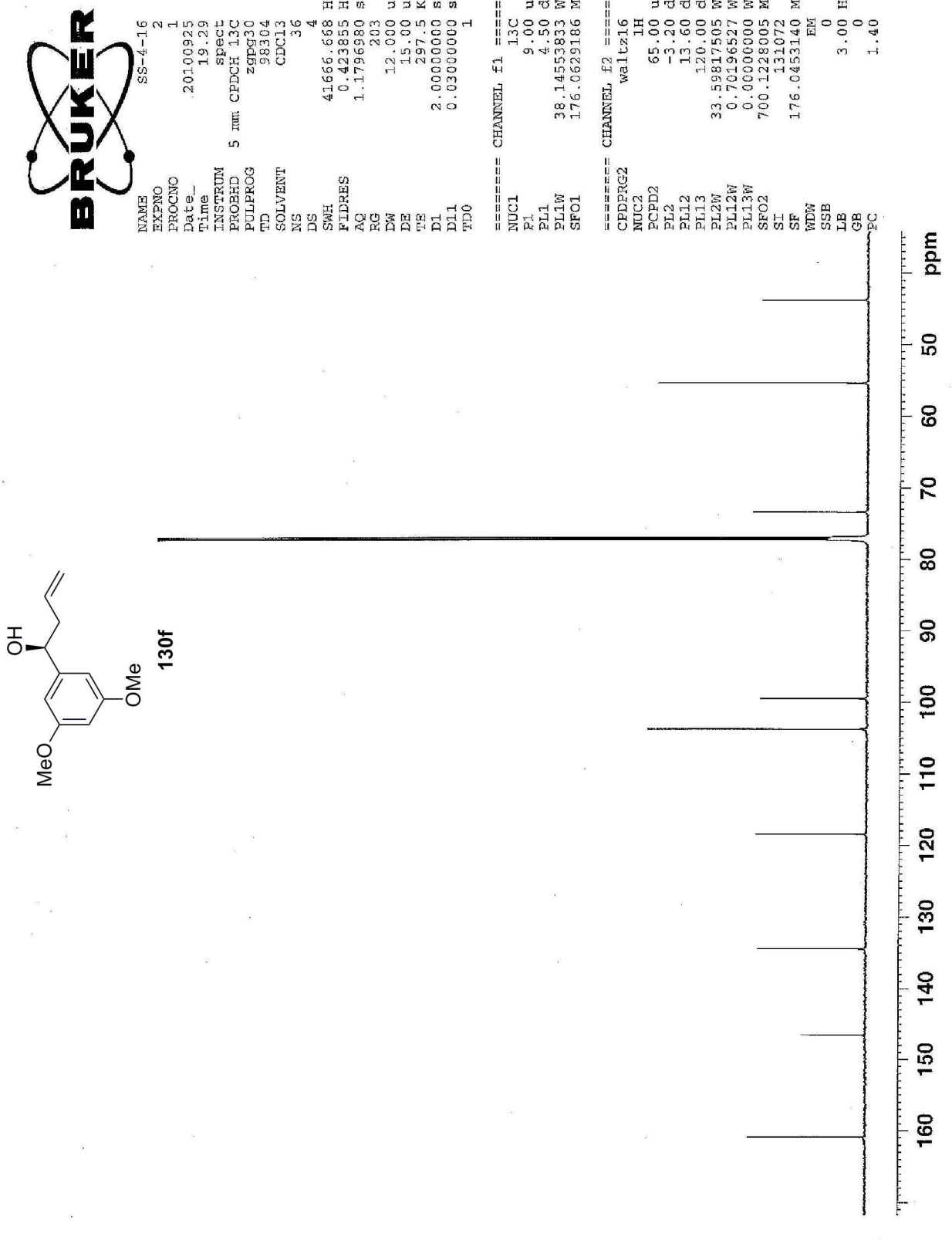

OH
Cl
130e
Current Data Parameters
NAME ss-4-11
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20100614
Time 23.52
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 28
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5555540 sec
RG 1024
DW 78.000 usec
DE 6.00 usec
TE 300.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.50 usec
PL1 -3.00 dB
SFO1 400.2478017 MHz
F2 - Processing parameters
SI 32768
SF 400.2450000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
4.47
1.00
2.18
1.05
2.28
1.15
ppm

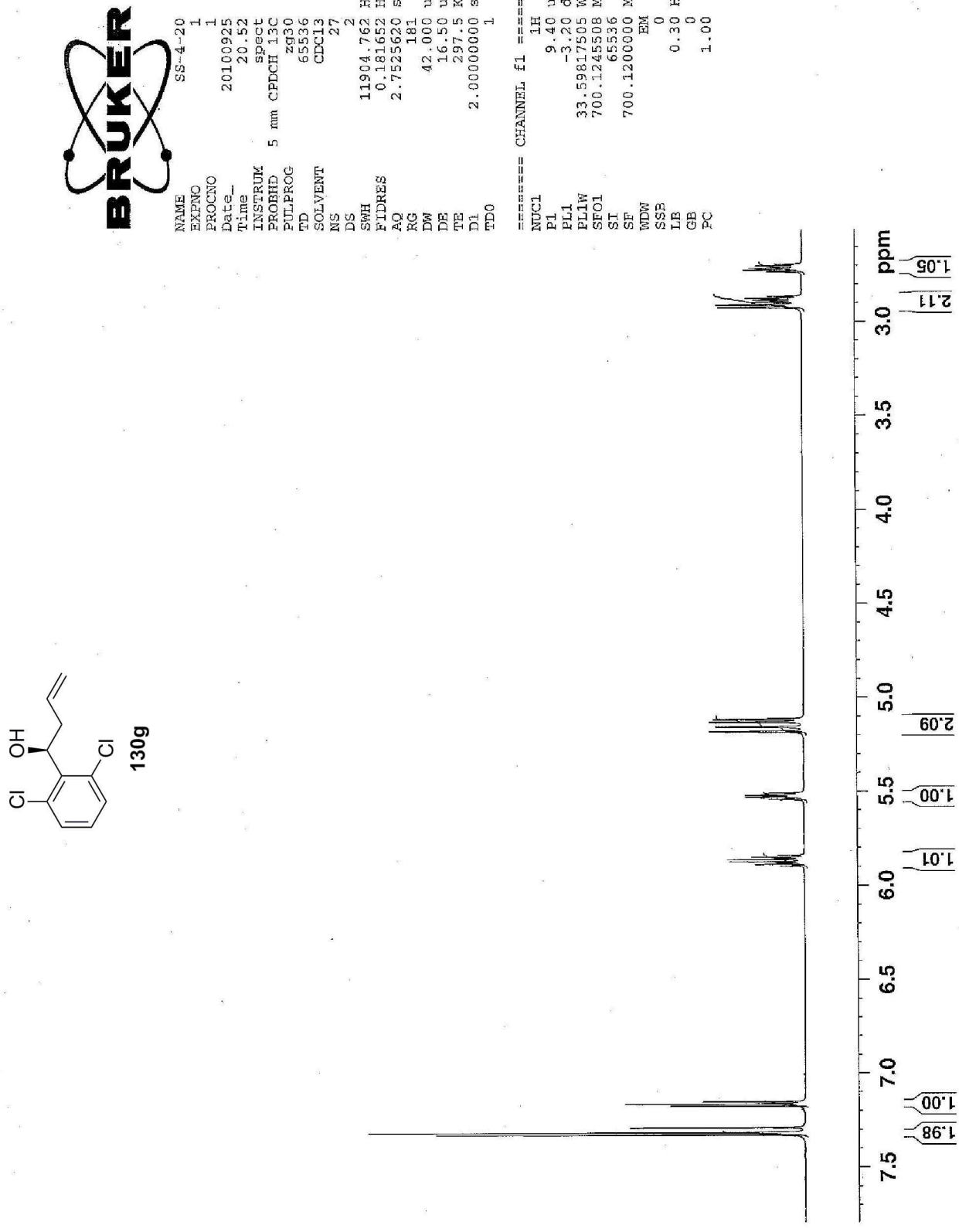


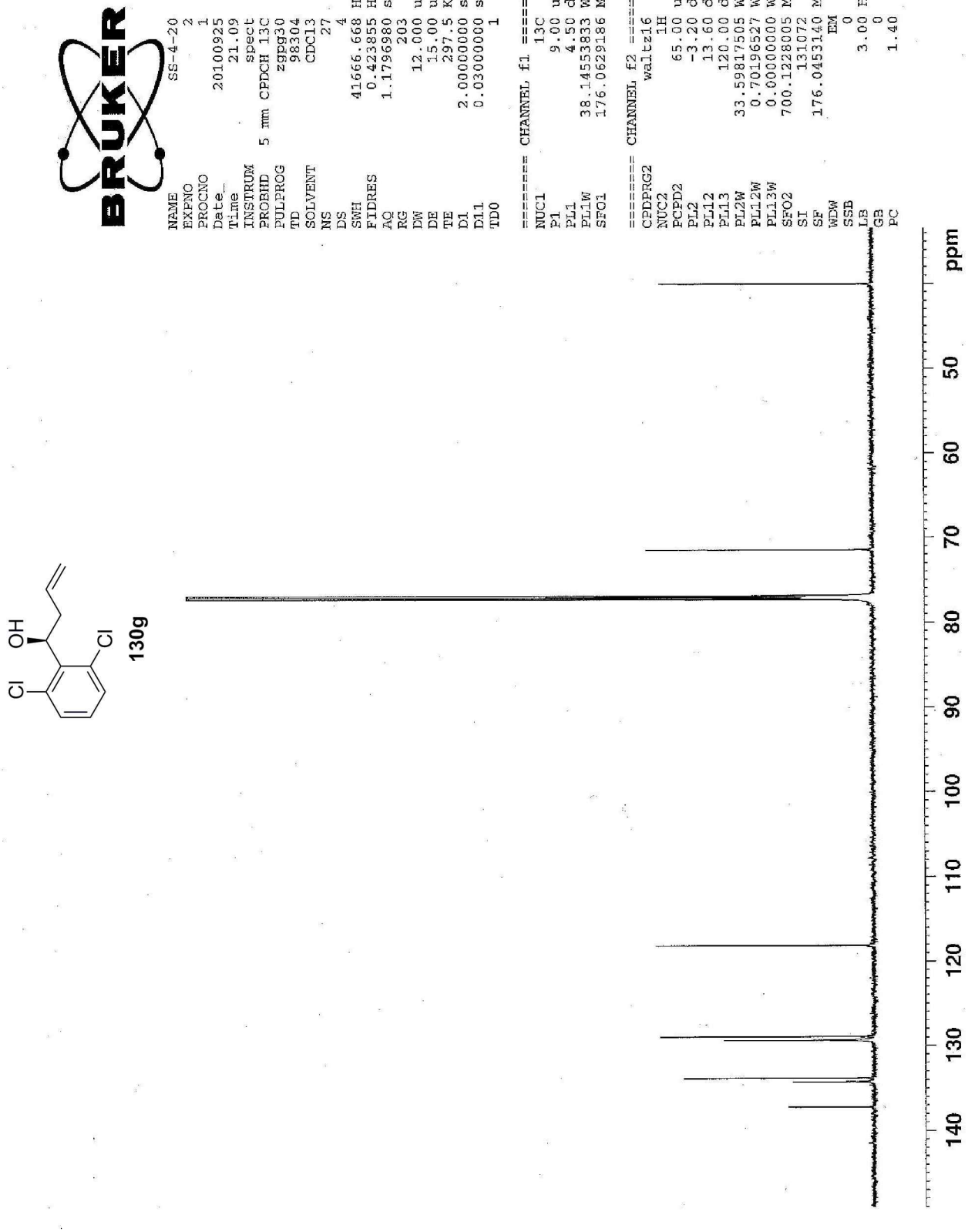
BRUKER

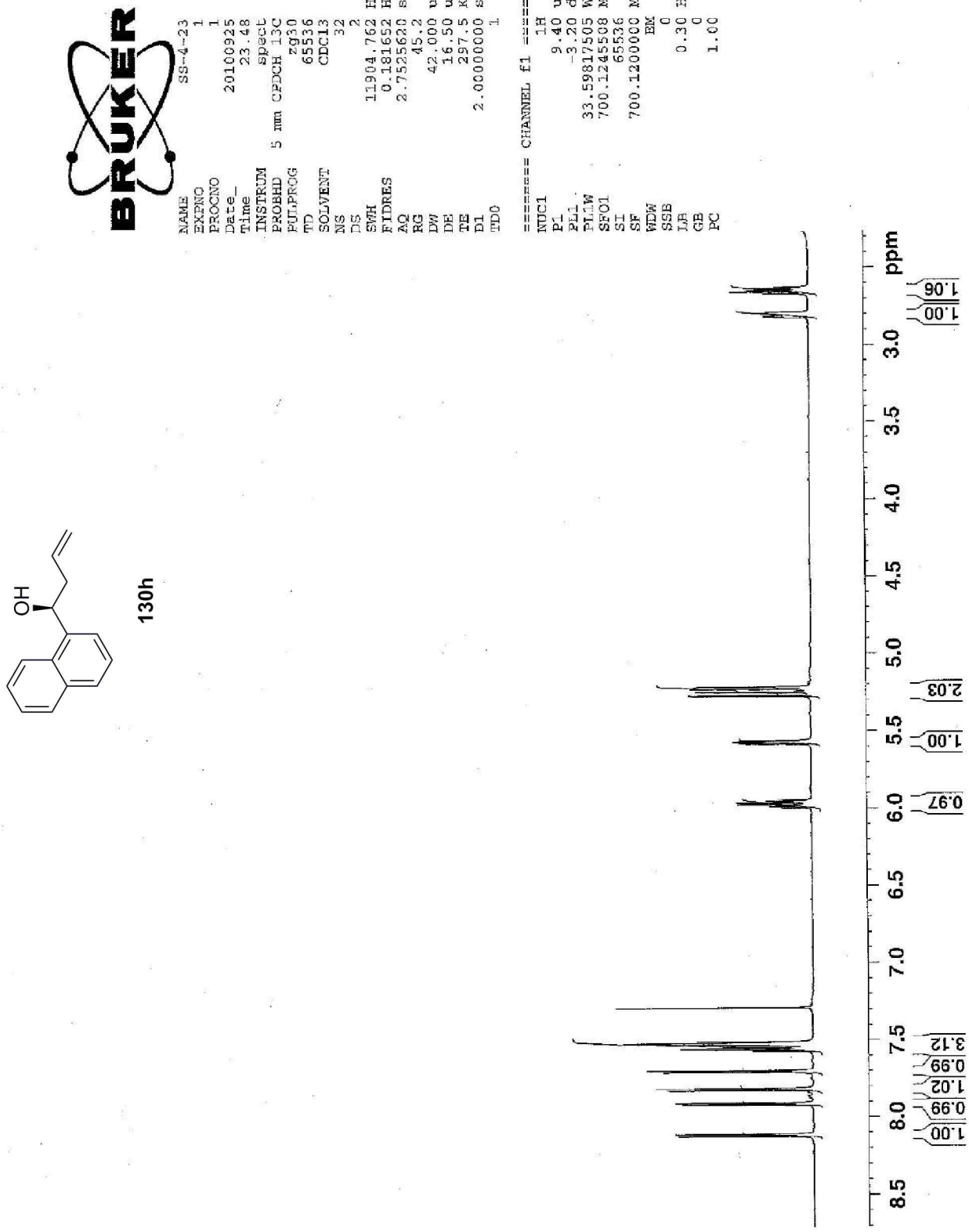
NAME	SS-4-11
EXPNO	3
PROCNO	1
Date_	20100926
Time	23.32
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	98304
SOLVENT	CDCl3
NS	1024
DS	4
SWH	41666.668 Hz
FIDRES	0.423855 Hz
AQ	1.1796980 sec
RG	203
DW	12.000 usec
DE	15.00 usec
TE	297.5 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 usec
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0629186 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 usec
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1228005 MHz
SI	131072
SF	176.0453140 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40

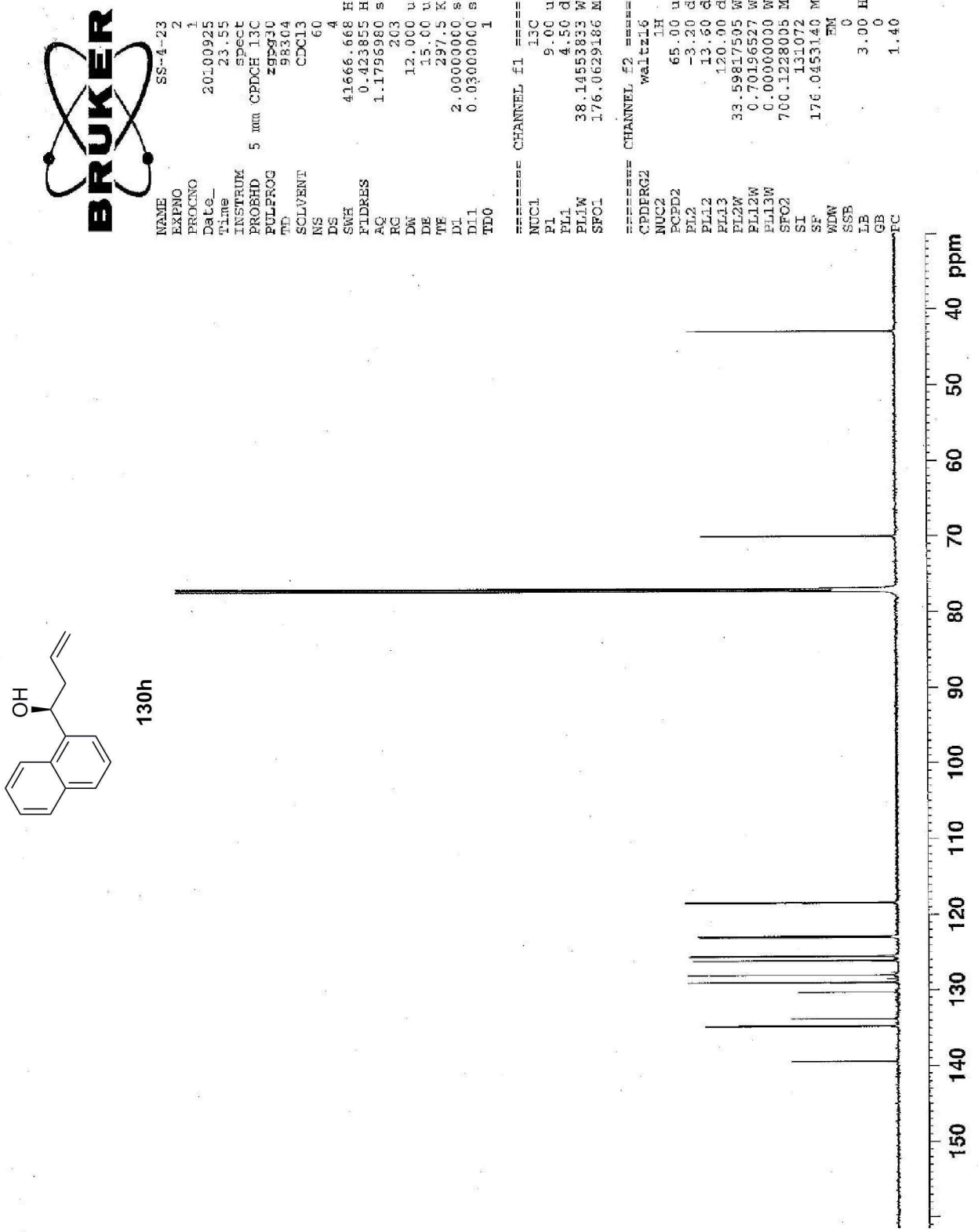

BRUKER
NAME SS-4-16
EXPNO 1
PROCNO 1
Date_ 20100925
Time 19.12
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 11904.762 Hz
FIDRES 0.181652 Hz
AQ 2.7525620 sec
RG 45.2
DW 42.000 usec
DE 16.50 usec
TE 297.6 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1245508 MHz
SI 65536
SF 700.1200000 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
OH
OMe
MeO
130f
ppm
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.08
6.33
1.00
2.05
0.99
1.00
2.05

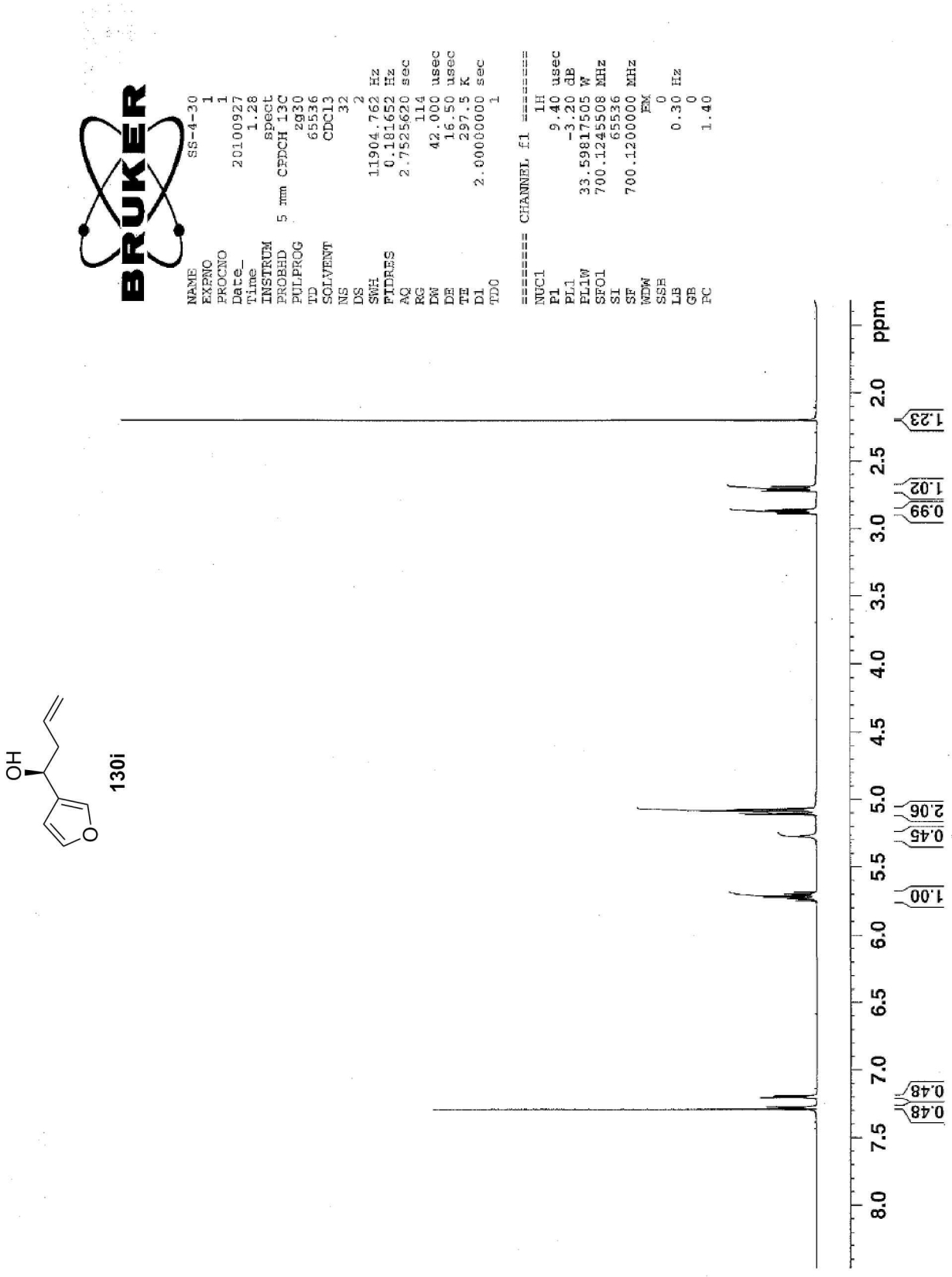

130f
OH
OMe
MeO
BRUKER
NAME SS-4-16
EXPNO 2
PROCNO 1
Date_ 20100925
Time 19.29
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDCl3
NS 36
DS 4
SWH 41666.668 Hz
FIDRES 0.423855 Hz
AQ 1.1796980 sec
RG 203
DW 12.000 usec
DE 15.00 usec
TE 297.5 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0629186 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 usec
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1228005 MHz
SI 131072
SF 176.0453140 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
160 150 140 130 120 110 100 90 80 70 60 50 ppm

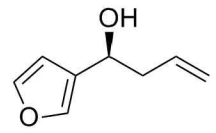

BRUKER
NAME SS-4-20
EXPNO 1
PROCNO 1
Date_ 20100925
Time 20.52
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 27
DS 2
SWH 11904.762 Hz
FIDRES 0.181652 Hz
AQ 2.7525620 sec
RG 181
DW 42.000 usec
DE 16.50 usec
TE 297.5 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1245508 MHz
SI 65536
SF 700.1200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
OH
Cl
Cl
130g
ppm
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
1.98
1.00
1.01
1.00
2.09
1.00
2.11
1.05


BRUKER
NAME SS-4-20
EXPNO 2
PROCNO 1
Date_ 20100925
Time 21.09
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDCl3
NS 27
DS 4
SWH 41666.668 Hz
FIDRES 0.423855 Hz
AQ 1.1796980 sec
RG 203
DW 12.000 usec
DE 15.00 usec
TE 297.5 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0629186 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 usec
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1228005 MHz
SI 131072
SF 176.0453140 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
OH
Cl
Cl
130g
140 130 120 110 100 90 80 70 60 50 ppm

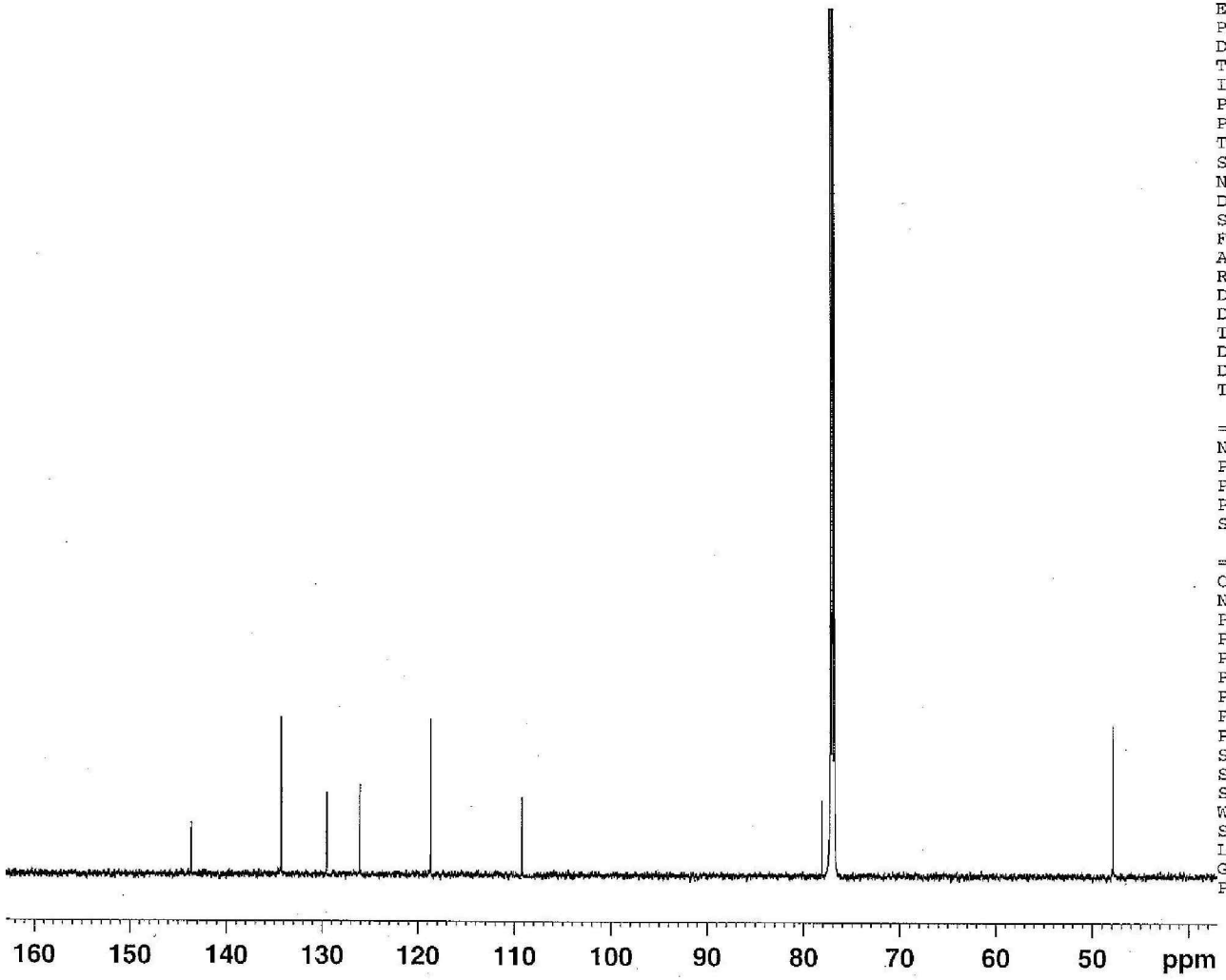

130h
OH
BRUKER
NAME ss-4-23
EXPNO 1
PROCNO 1
Date_ 20100925
Time_ 23.48
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.181652 Hz
AQ 2.7525620 sec
RG 45.2
DW 42.000 usec
DE 16.50 usec
TE 297.5 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1245508 MHz
SI 65536
SF 700.1200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
ppm
1.00
0.99
1.02
0.99
3.12
0.97
1.00
2.03
1.00
1.06


130h
OH
BRUKER
NAME SS-4-23
EXPNO 2
PROCNO 1
Date_ 20100925
Time 23.55
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDCl3
NS 60
DS 4
SWH 41666.668 Hz
FIDRES 0.423855 Hz
AQ 1.1796980 sec
RG 203
DW 12.000 usec
DE 15.00 usec
TE 297.5 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0629186 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 usec
PL2 -3.30 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1228095 MHz
SI 131072
SF 176.0453140 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
150 140 130 120 110 100 90 80 70 60 50 40 ppm

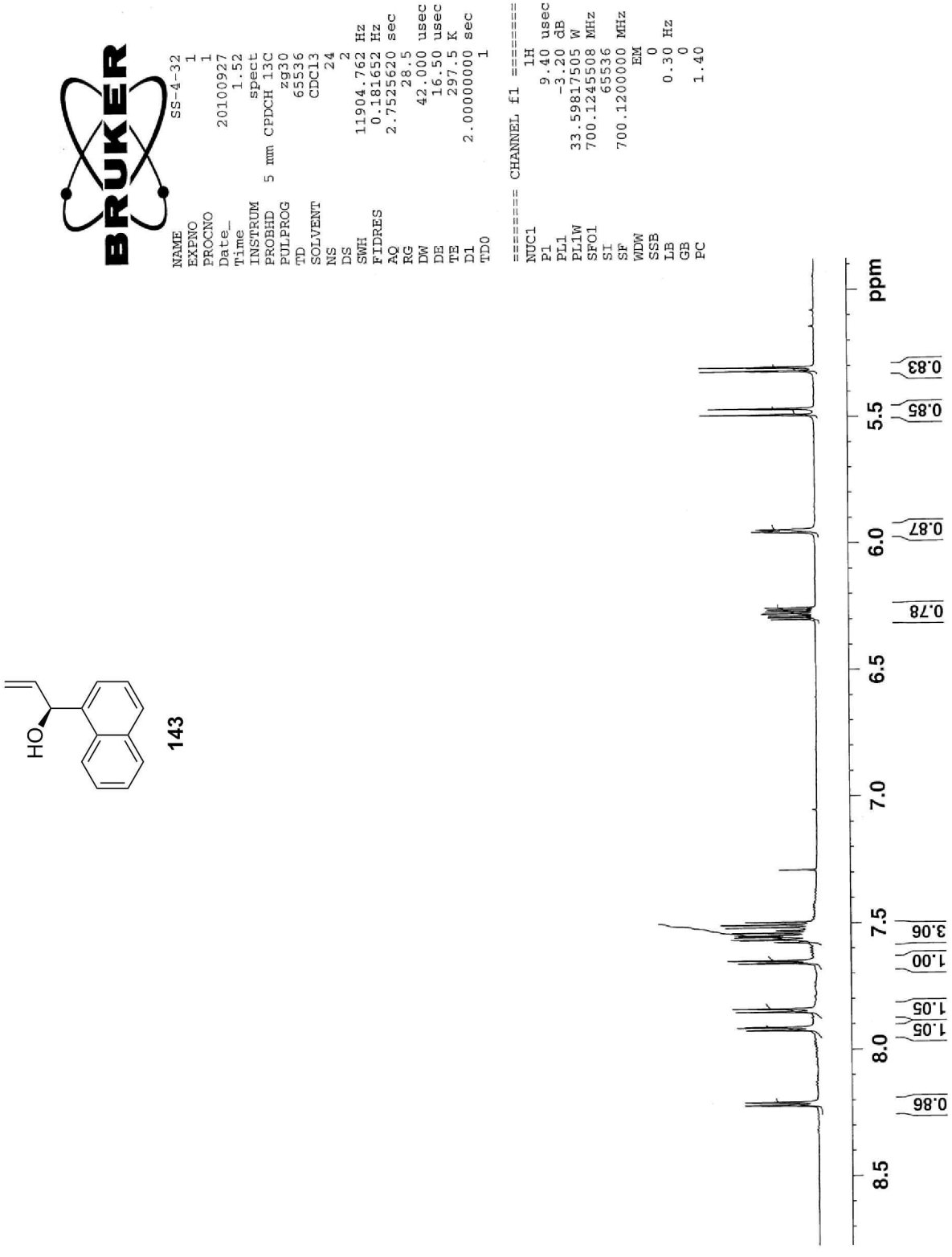

OH
O
130i
BRUKER
NAME SS-4-30
EXPNO 1
PROCNO 1
Date_ 20100927
Time 1.28
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.181652 Hz
AQ 2.7525620 sec
RG 114
DW 42.000 usec
DE 16.50 usec
TE 297.5 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1245508 MHz
SI 65536
SF 700.1200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
ppm
0.48
0.48
1.00
0.45
2.06
0.99
1.02
1.23

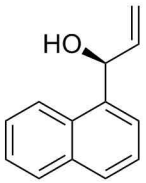


130i

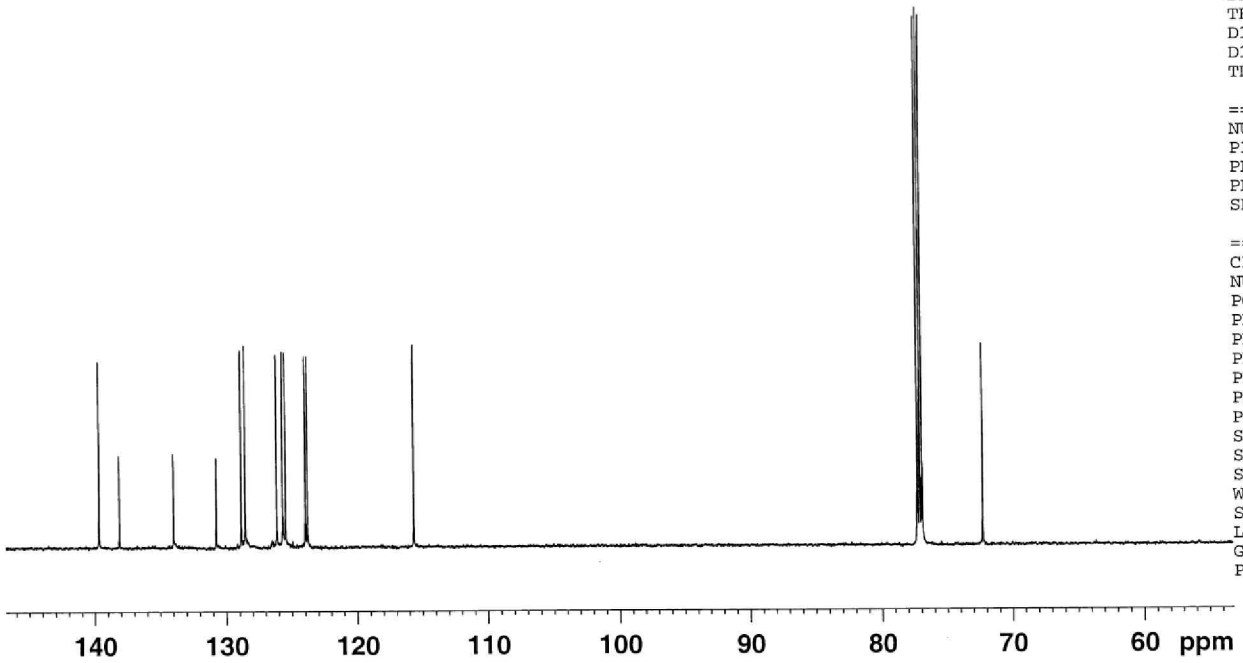


NAME	SS-4-30
EXPNO	2
PROCNO	1
Date_	20100927
Time	1.38
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	98304
SOLVENT	CDCl3
NS	136
DS	4
SWH	41666.668 Hz
FIDRES	0.423855 Hz
AQ	1.1796980 sec
RG	203
DW	12.000 usec
DE	15.00 usec
TE	297.5 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 usec
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0629186 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 usec
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1228005 MHz
SI	131072
SF	176.0453140 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40


BRUKER
NAME SS-4-32
EXPNO 1
PROCNO 1
Date_ 20100927
Time_ 1.52
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 65536
SOLVENT CDC13
NS 24
DS 2
SWH 11904.762 Hz
FIDRES 0.181652 Hz
AQ 2.7525620 sec
RG 28.5
DW 42.000 usec
DE 16.50 usec
TE 297.5 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1245508 MHz
SI 65536
SF 700.1200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40
HO
143
ppm
8.5
8.0
7.5
7.0
6.5
6.0
5.5
0.86
1.05
1.05
1.00
3.06
0.78
0.87
0.85
0.83

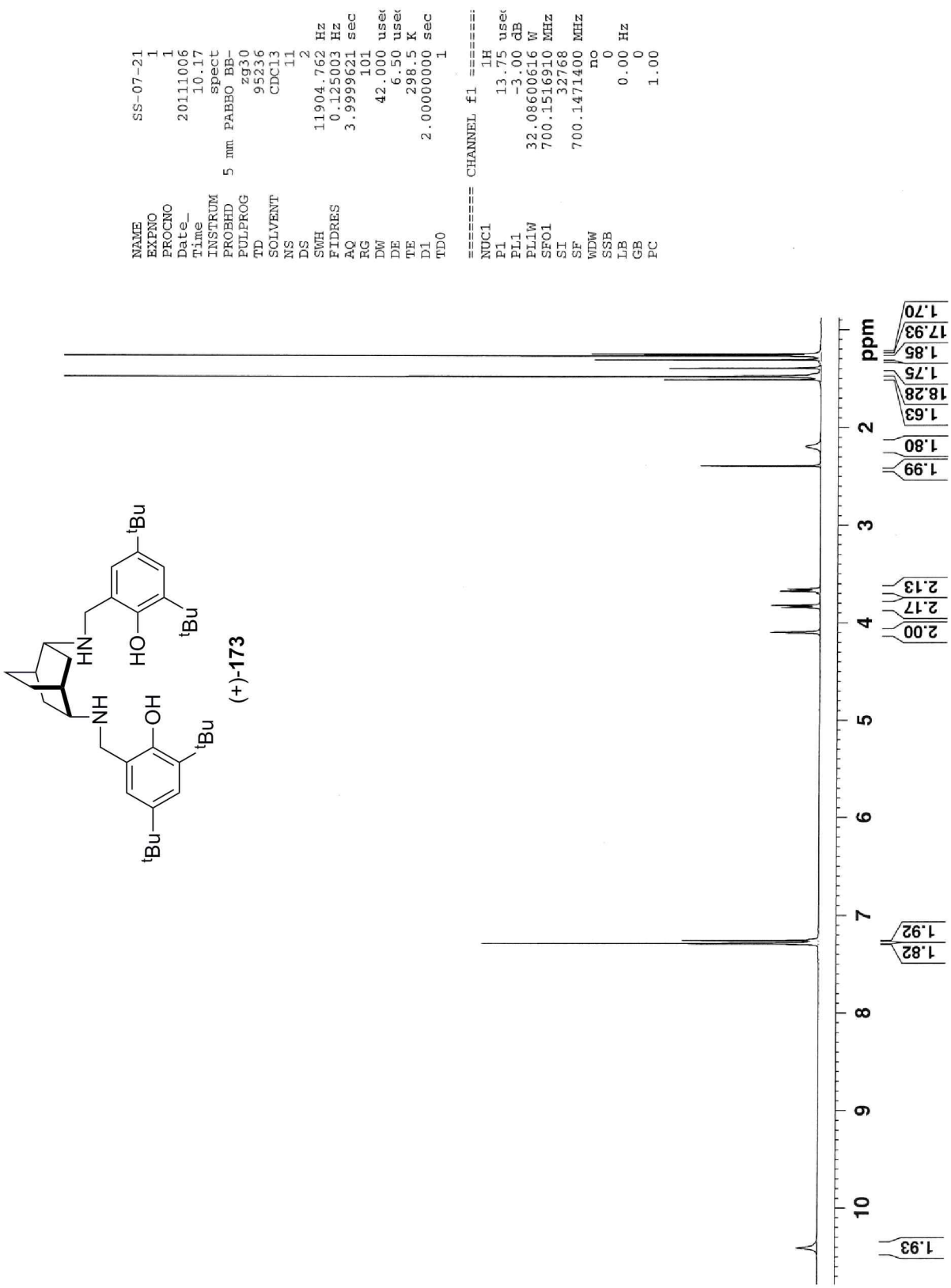


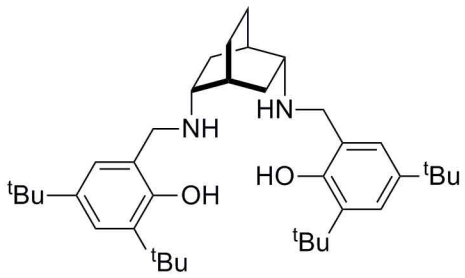
143



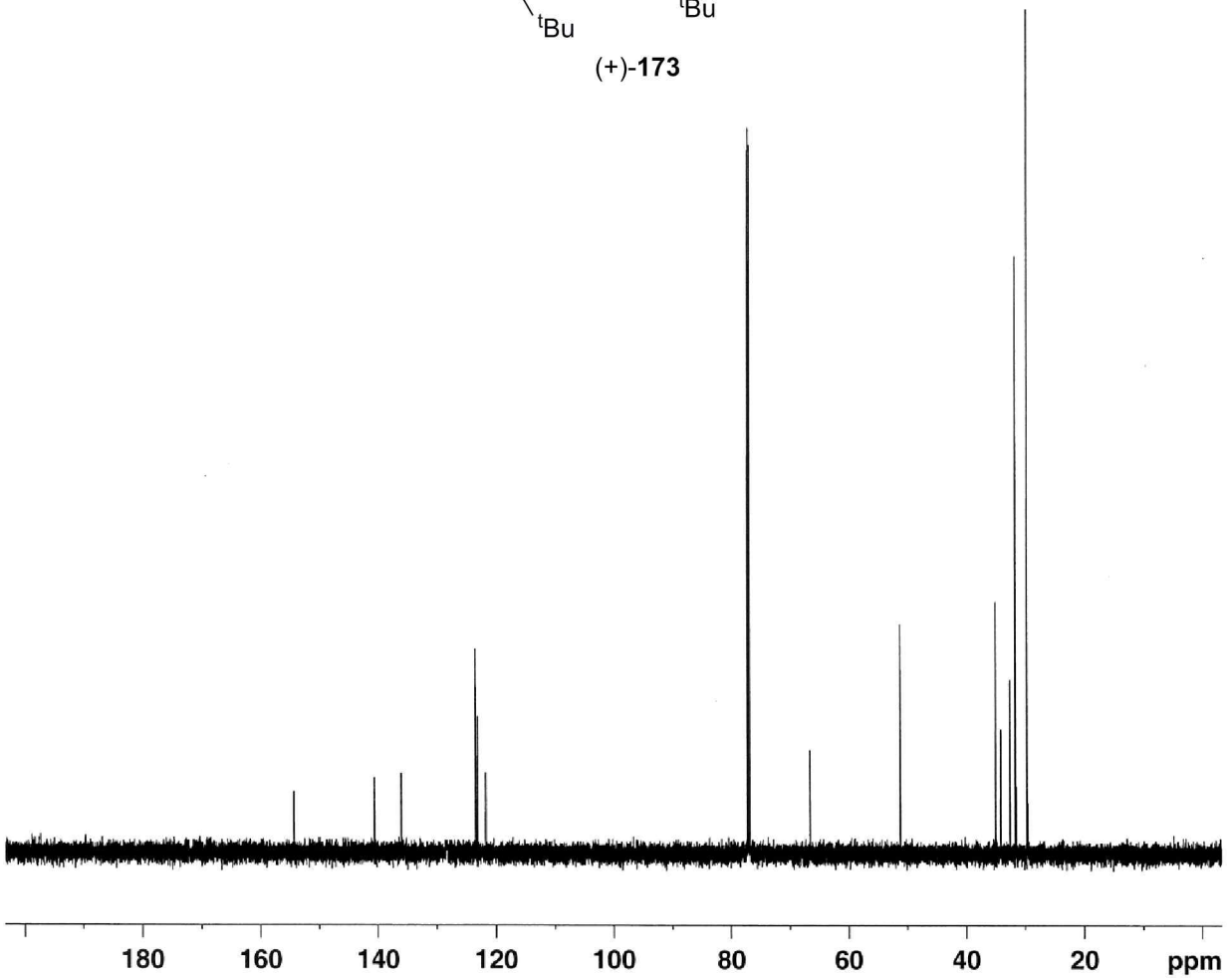
BRUKER

NAME	SS-4-32
EXPNO	2
PROCNO	1
Date_	20100927
Time	2.01
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	98304
SOLVENT	CDCl3
NS	24
DS	4
SWH	41666.668 Hz
FIDRES	0.423855 Hz
AQ	1.1796980 sec
RG	203
DW	12.000 usec
DE	15.00 usec
TE	297.5 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 usec
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0629186 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 usec
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1228005 MHz
SI	131072
SF	176.0453140 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40

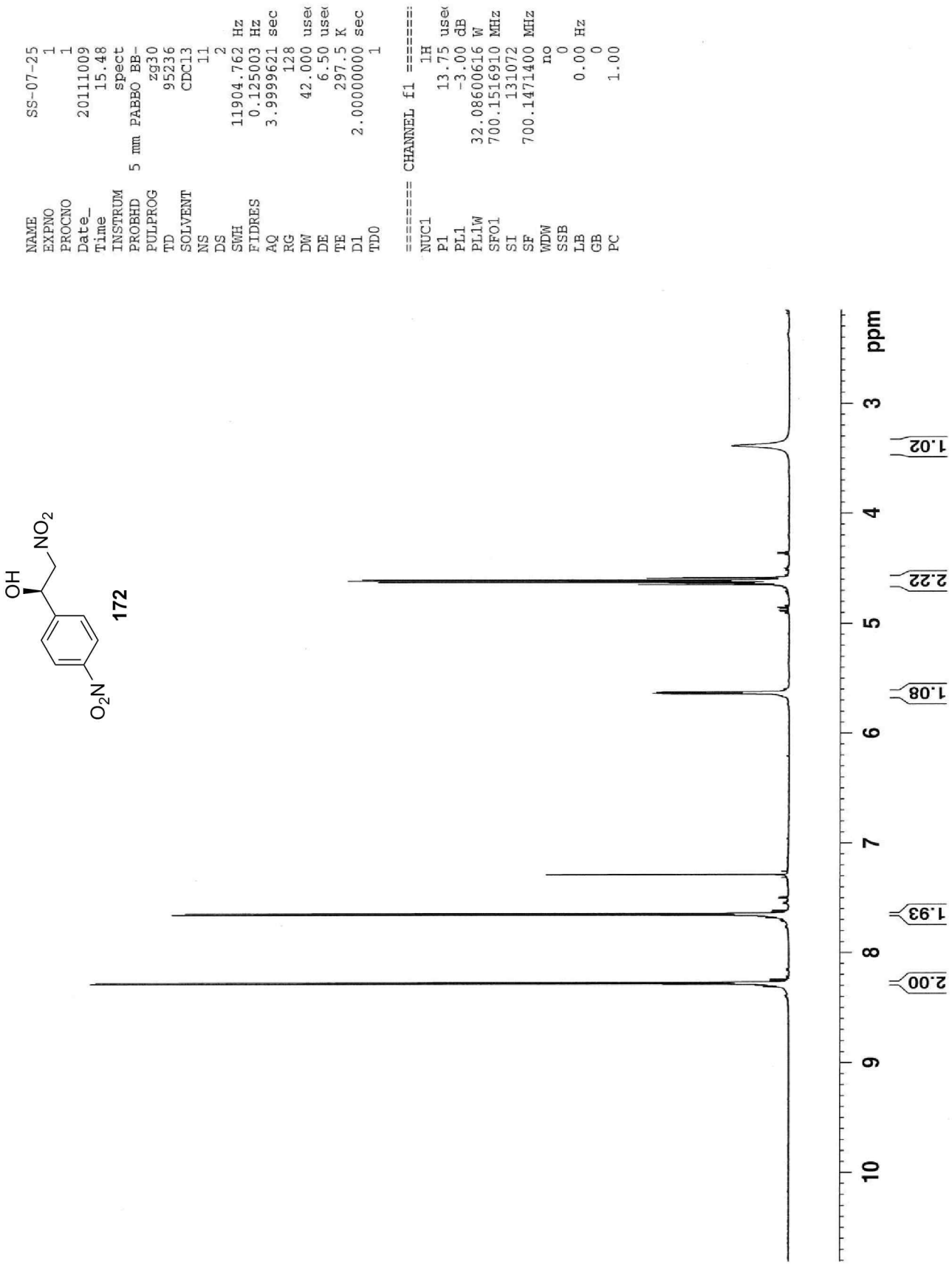

NAME SS-07-21
EXPNO 1
PROCNO 1
Date_ 20111006
Time 10.17
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 11
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 101
DW 42.000 use
DE 6.50 use
TE 298.5 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.75 use
PL1 -3.00 dB
PL1W 32.08600616 W
SFO1 700.1516910 MHz
SI 32768
SF 700.1471400 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
(+)-173
ppm
1.93
1.82
1.92
2.00
2.17
2.13
1.99
1.80
1.63
18.28
1.75
1.85
17.93
1.70

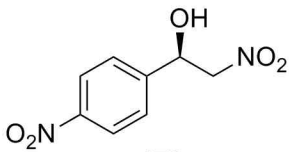


(+)-**173**

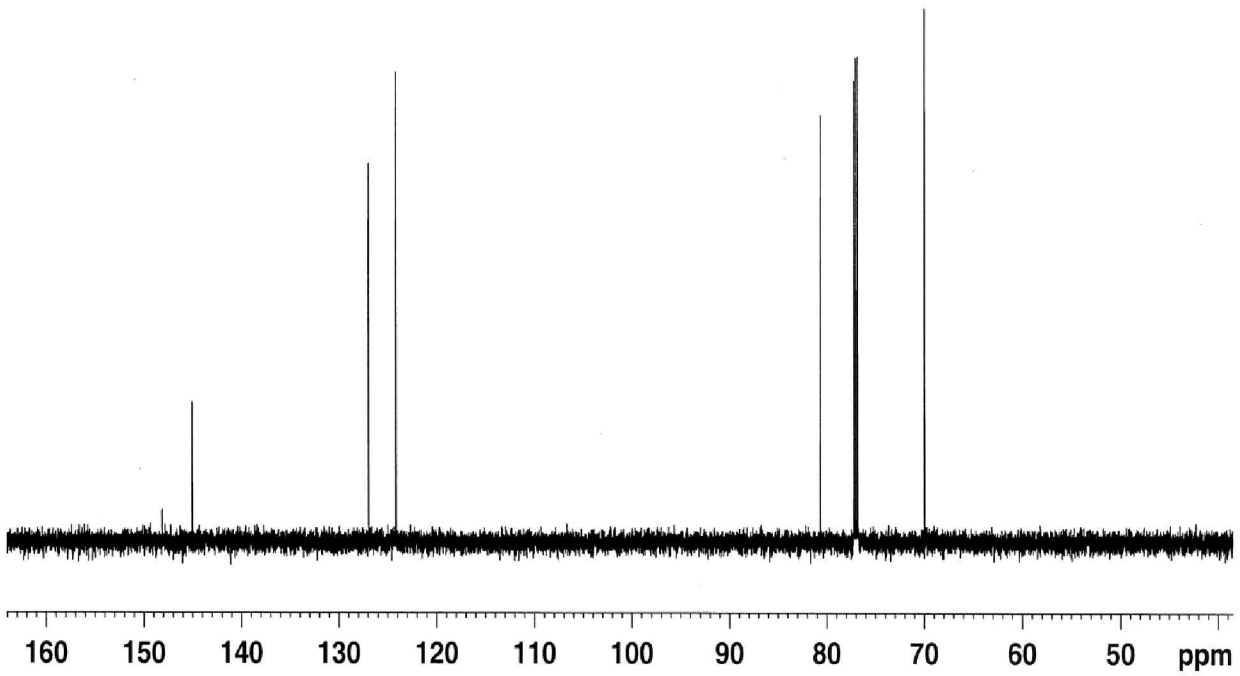


NAME	SS-07-21	
EXPNO	2	
PROCNO	1	
Date_	20111006	
Time	10.19	
INSTRUM	spect	
PROBHD	5 mm PABBO BB-	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	160	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	usec
DE	6.50	usec
TE	299.3	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	9.30	usec
PL1	2.00	dB
PL1W	67.83342743	W
SFO1	176.0697436	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	80.00	usec
PL2	-3.00	dB
PL12	12.30	dB
PL13	12.30	dB
PL2W	32.08600616	W
PL12W	0.94692516	W
PL13W	0.94692516	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	no	
SSB	0	
LB	0.00	Hz
GB	0	
PC	1.40	

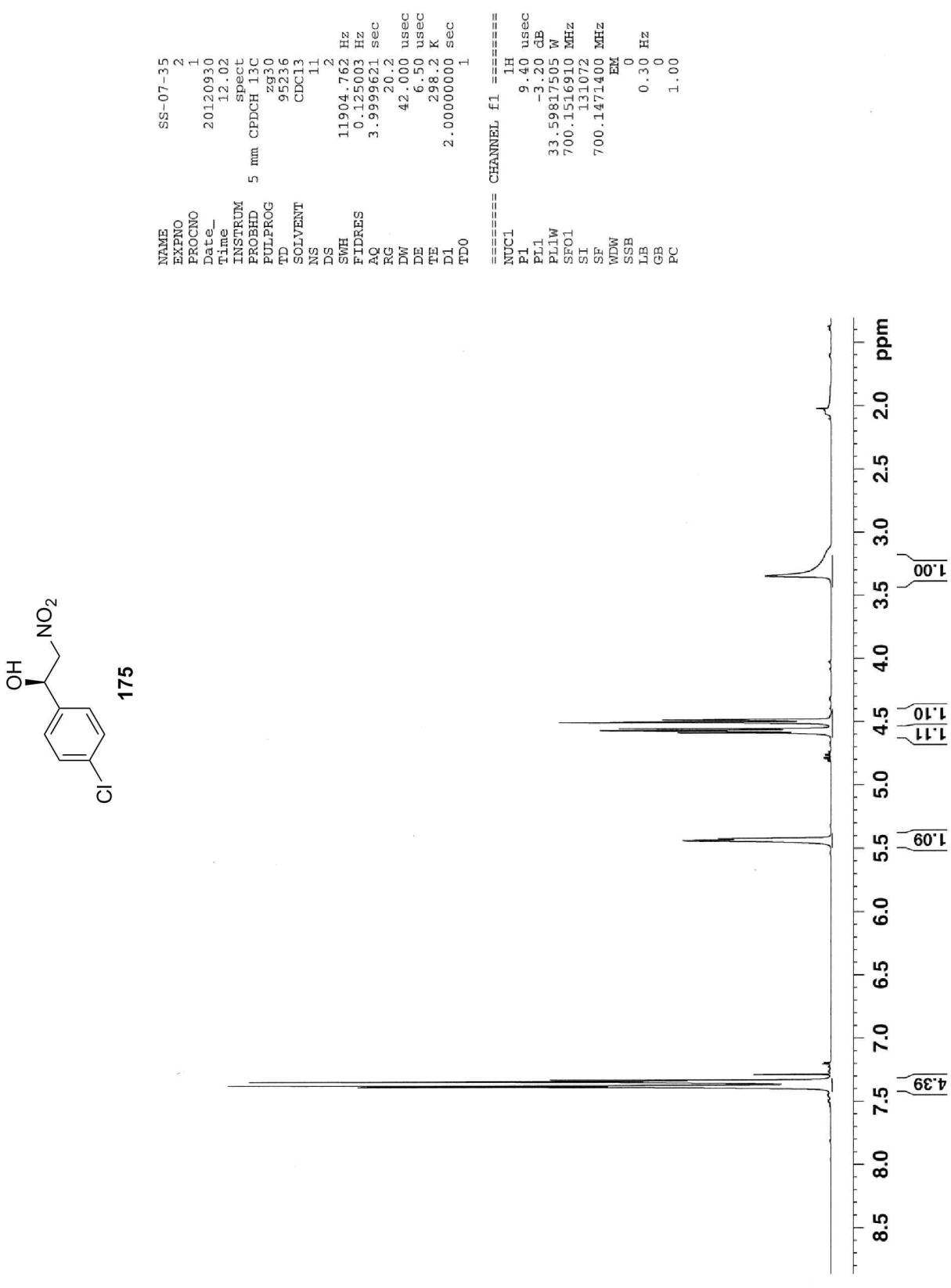

NAME SS-07-25
EXPNO 1
PROCNO 1
Date_ 20111009
Time 15.48
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 95236
SOLVENT CDC13
NS 11
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 128
DW 42.000 use
DE 6.50 use
TE 297.5 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.75 use
PL1 -3.00 dB
PL1W 32.08600616 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
OH
NO2
O2N
172
10
9
8
7
6
5
4
3
ppm
2.00
1.93
1.08
2.22
1.02

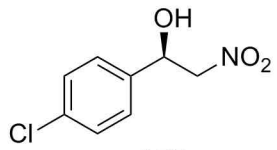


172

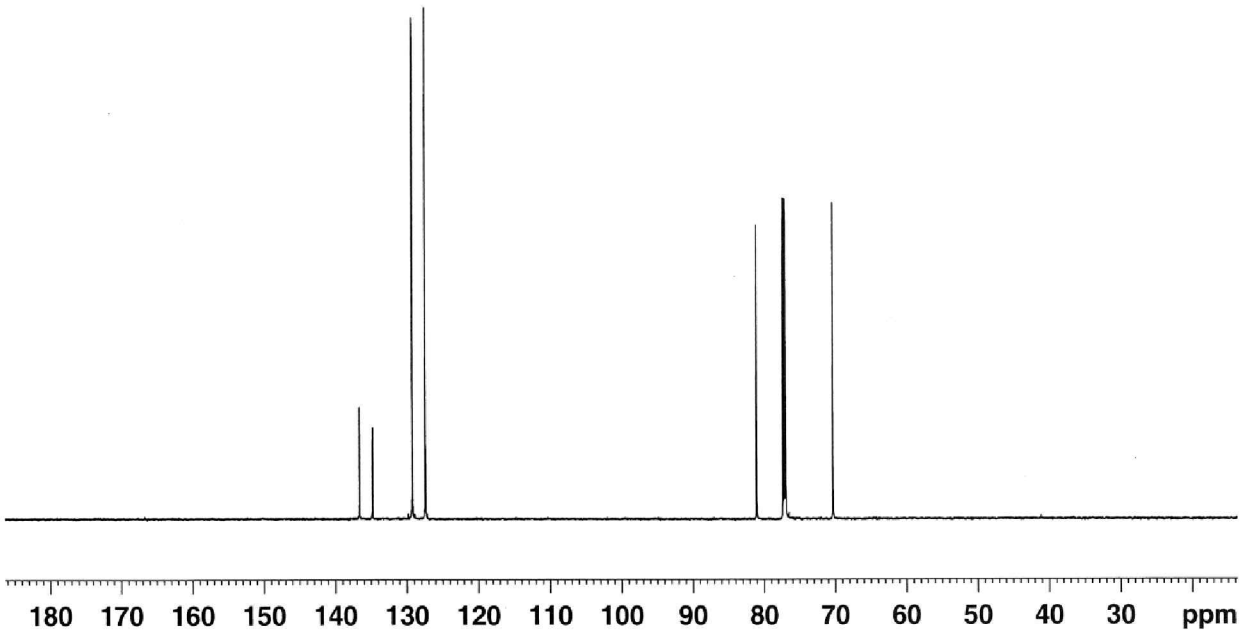


NAME	SS-07-25	
EXPNO	2	
PROCNO	1	
Date_	20111009	
Time	15.54	
INSTRUM	spect	
PROBHD	5 mm PABBO BB-	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	64	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	usec
DE	6.50	usec
TE	300.3	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	9.30	usec
PL1	2.00	dB
PL1W	67.83342743	W
SFO1	176.0697436	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	80.00	usec
PL2	-3.00	dB
PL12	12.30	dB
PL13	12.30	dB
PL2W	32.08600616	W
PL12W	0.94692516	W
PL13W	0.94692516	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	no	
SSB	0	
LB	0.00	Hz
GB	0	
PC	1.40	

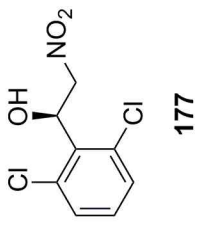

NAME SS-07-35
EXPNO 2
PROCNO 1
Date_ 20120930
Time_ 12.02
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 11
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 20.2
DW 42.000 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
OH
NO2
Cl
175
4.39
1.09
1.10
1.11
1.00
ppm



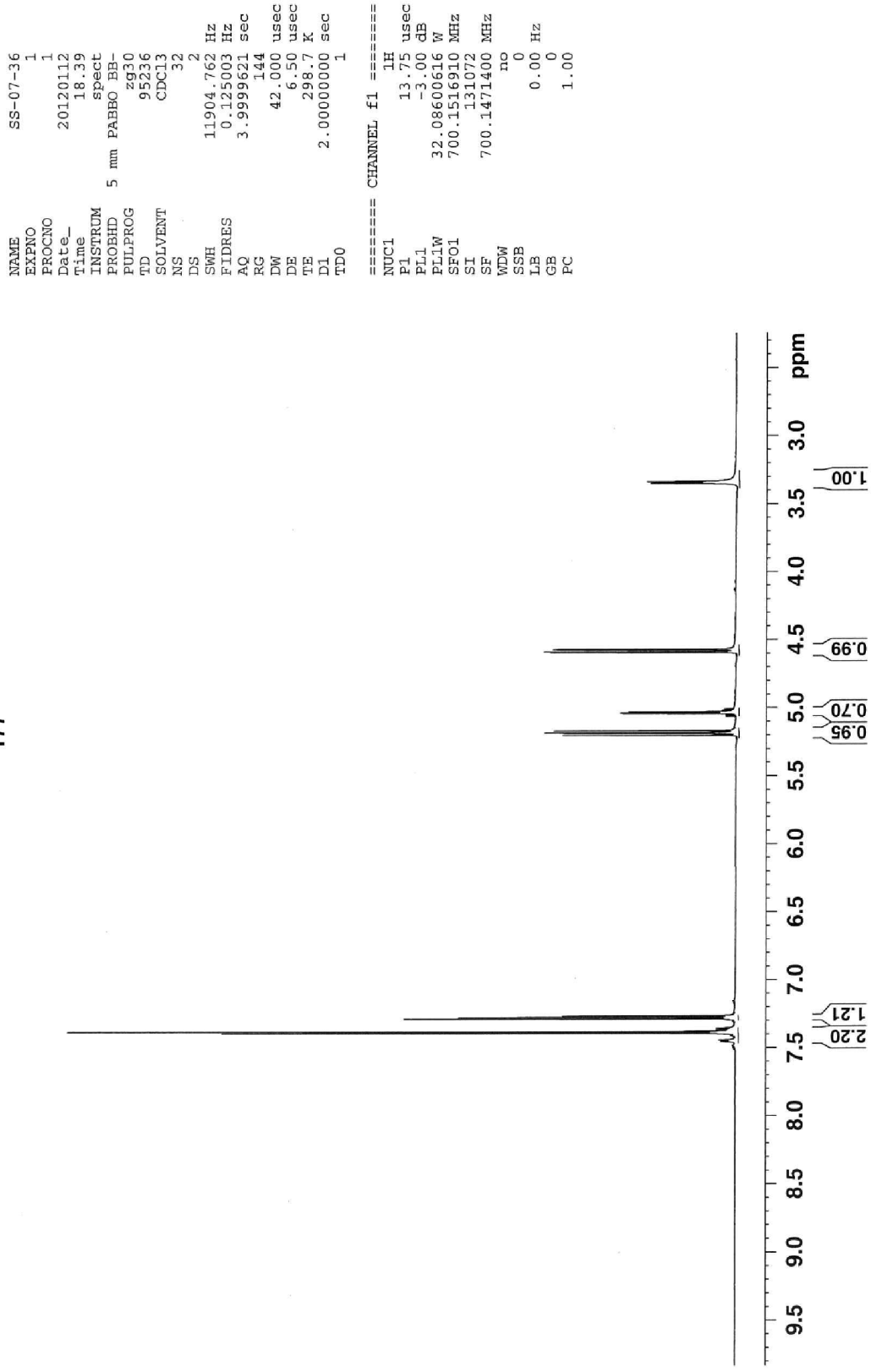
175

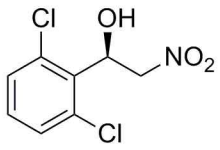


NAME	SS-07-35
EXPNO	3
PROCNO	1
Date_	20120930
Time	12.07
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	21
DS	4
SWH	41666.668 Hz
FIDRES	0.635783 Hz
AQ	0.7864820 sec
RG	203
DW	12.000 usec
DE	16.50 usec
TE	298.2 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 usec
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0697436 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 usec
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1499406 MHz
SI	32768
SF	176.0521380 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.00

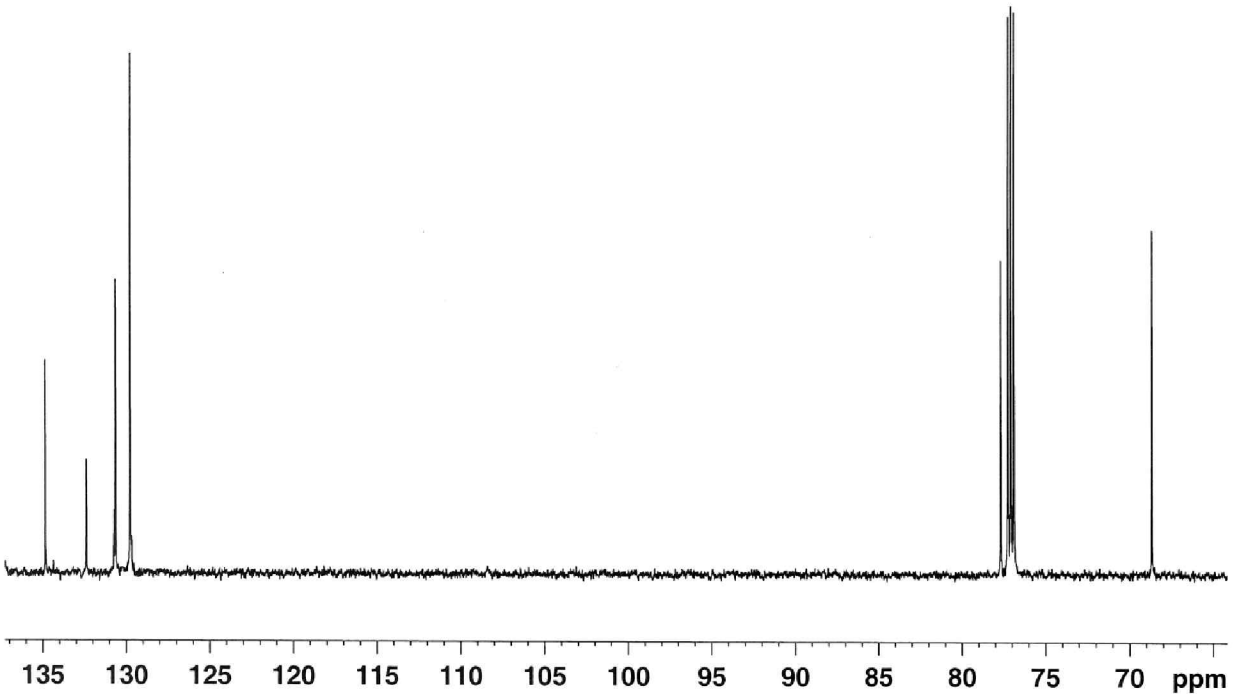


177

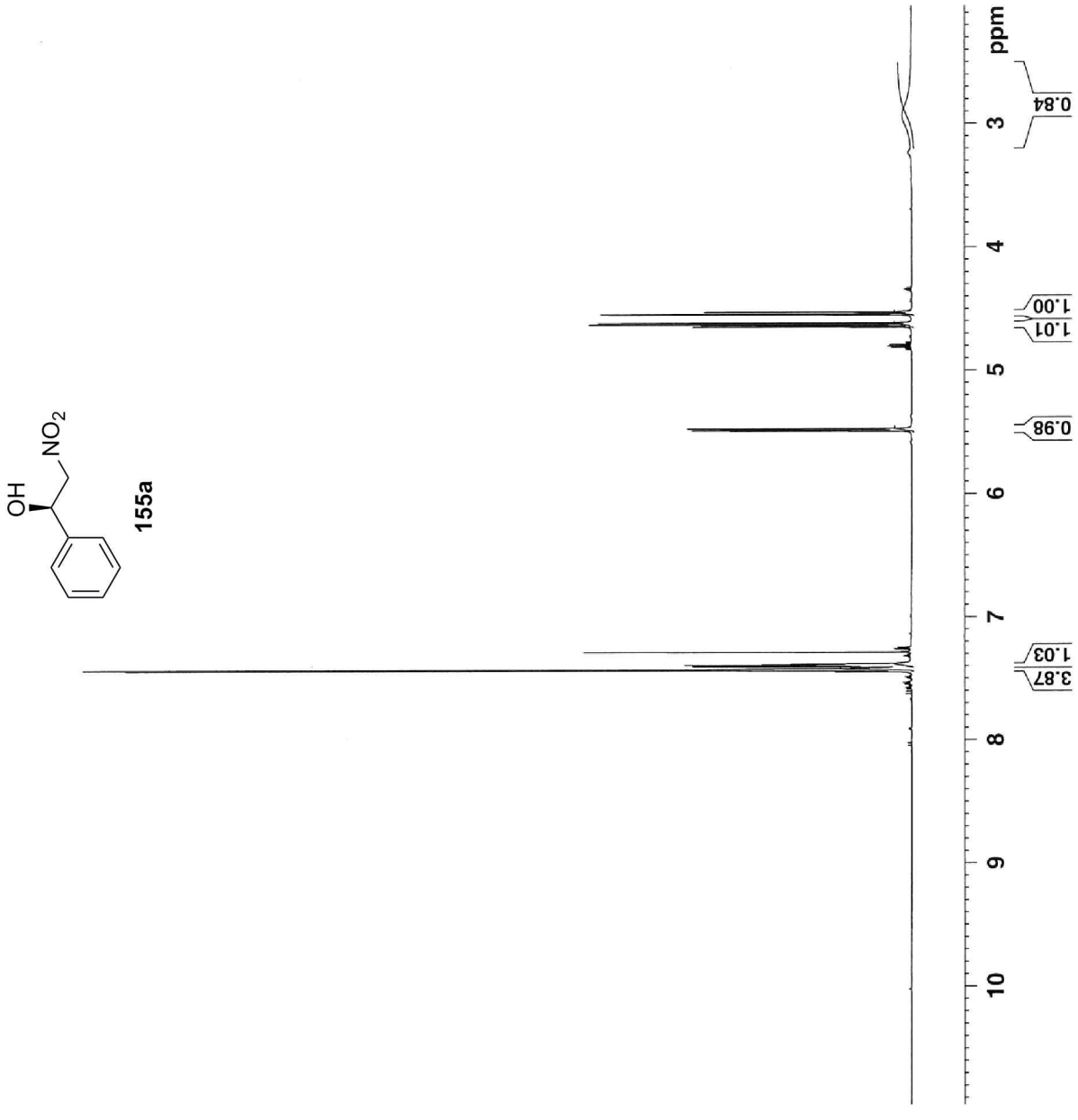

NAME SS-07-36
EXPNO 1
PROCNO 1
Date_ 20120112
Time 18.39
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 144
DW 42.000 usec
DE 6.50 usec
TE 298.7 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.75 usec
PL1 -3.00 dB
PL1W 32.08600616 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 ppm
2.20
1.21
0.95
0.70
0.99
1.00

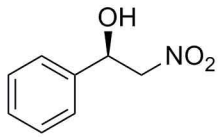


177

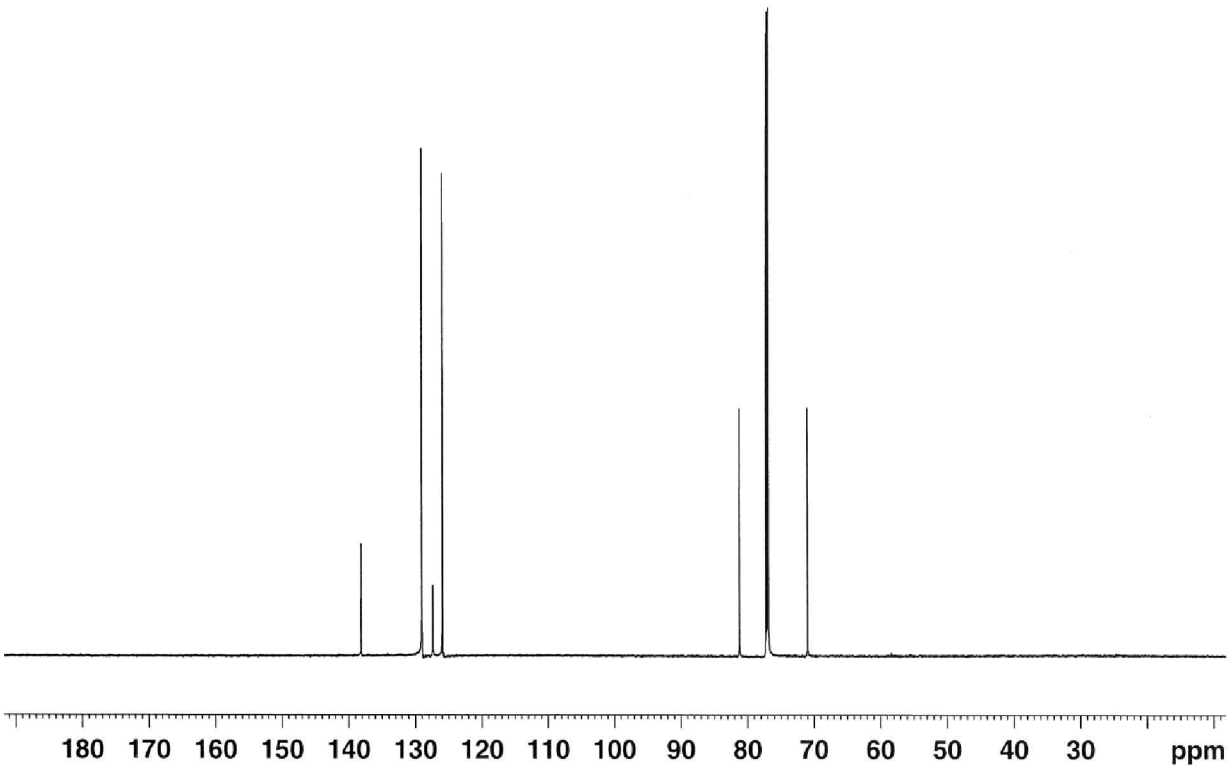


NAME	SS-07-36
EXPNO	2
PROCNO	1
Date_	20120112
Time	18.50
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	84
DS	4
SWH	41666.668 Hz
FIDRES	0.635783 Hz
AQ	0.7864820 se
RG	203
DW	12.000 us
DE	6.50 us
TE	298.8 K
D1	2.00000000 se
D11	0.03000000 se
TD0	1
========	CHANNEL f1 ======
NUC1	13C
P1	9.30 us
PL1	2.00 dB
PL1W	67.83342743 W
SFO1	176.0697436 MH
========	CHANNEL f2 ======
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 us
PL2	-3.00 dB
PL12	12.30 dB
PL13	12.30 dB
PL2W	32.08600616 W
PL12W	0.94692516 W
PL13W	0.94692516 W
SFO2	700.1499406 MH
SI	32768
SF	176.0521380 MH
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.00

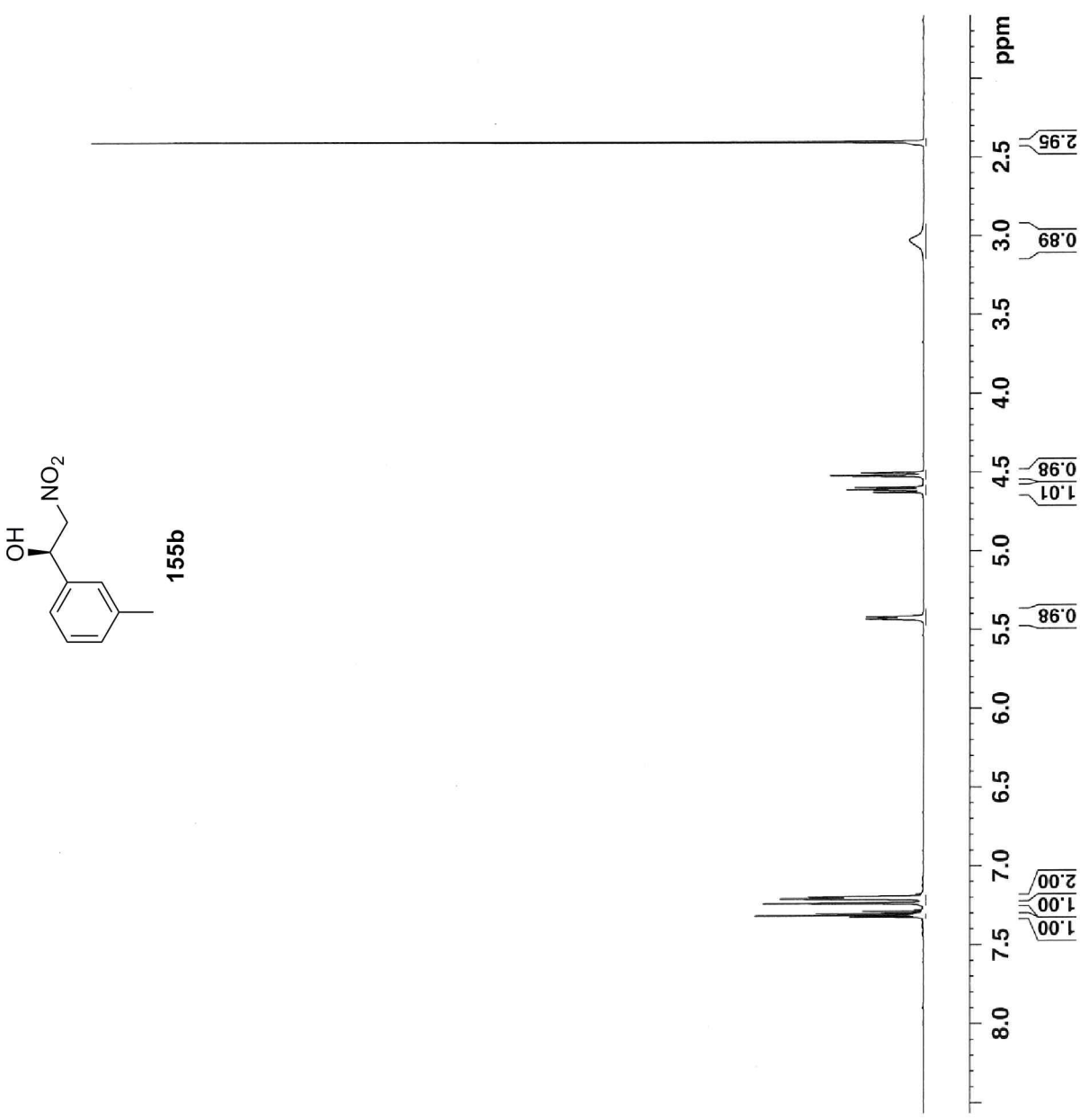

NAME SS-07-56
EXPNO 1
PROCNO 1
Date_ 20120404
Time 9.34
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDC13
NS 16
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 28.5
DW 42.000 usec
DE 6.50 usec
TE 303.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
OH
NO2
155a
ppm
0.84
1.01
1.00
0.98
3.87
1.03

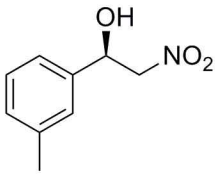


155a

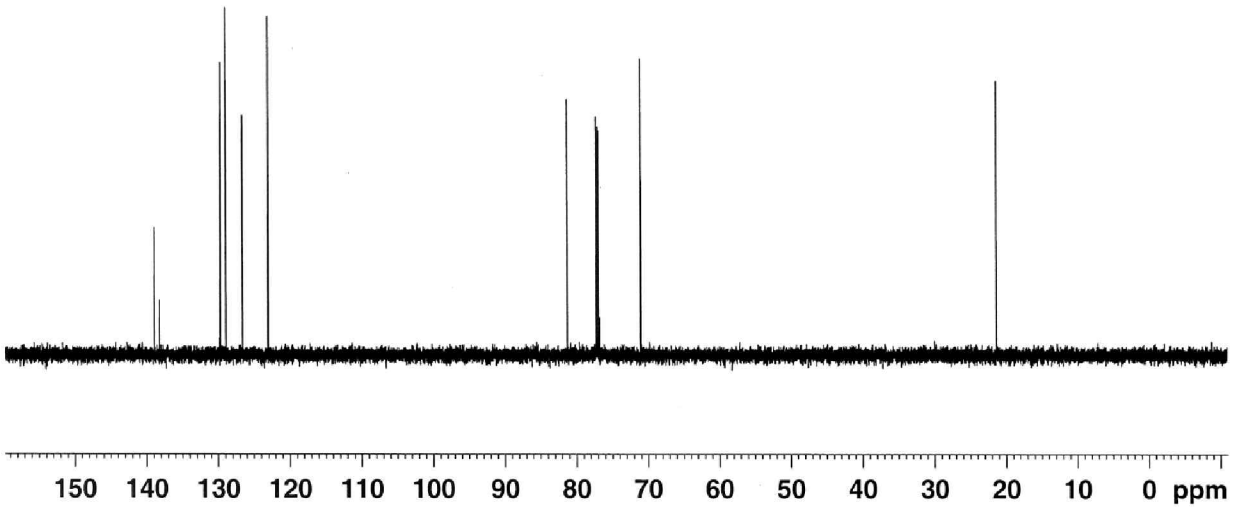


NAME	SS-07-56	
EXPNO	2	
PROCNO	1	
Date_	20120404	
Time	9.41	
INSTRUM	spect	
PROBHD	5 mm CPDCH 13C	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	52	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	usec
DE	16.50	usec
TE	303.2	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	9.00	usec
PL1	4.50	dB
PL1W	38.14553833	W
SFO1	176.0697436	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	65.00	usec
PL2	-3.20	dB
PL12	13.60	dB
PL13	120.00	dB
PL2W	33.59817505	W
PL12W	0.70196527	W
PL13W	0.00000000	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.00	

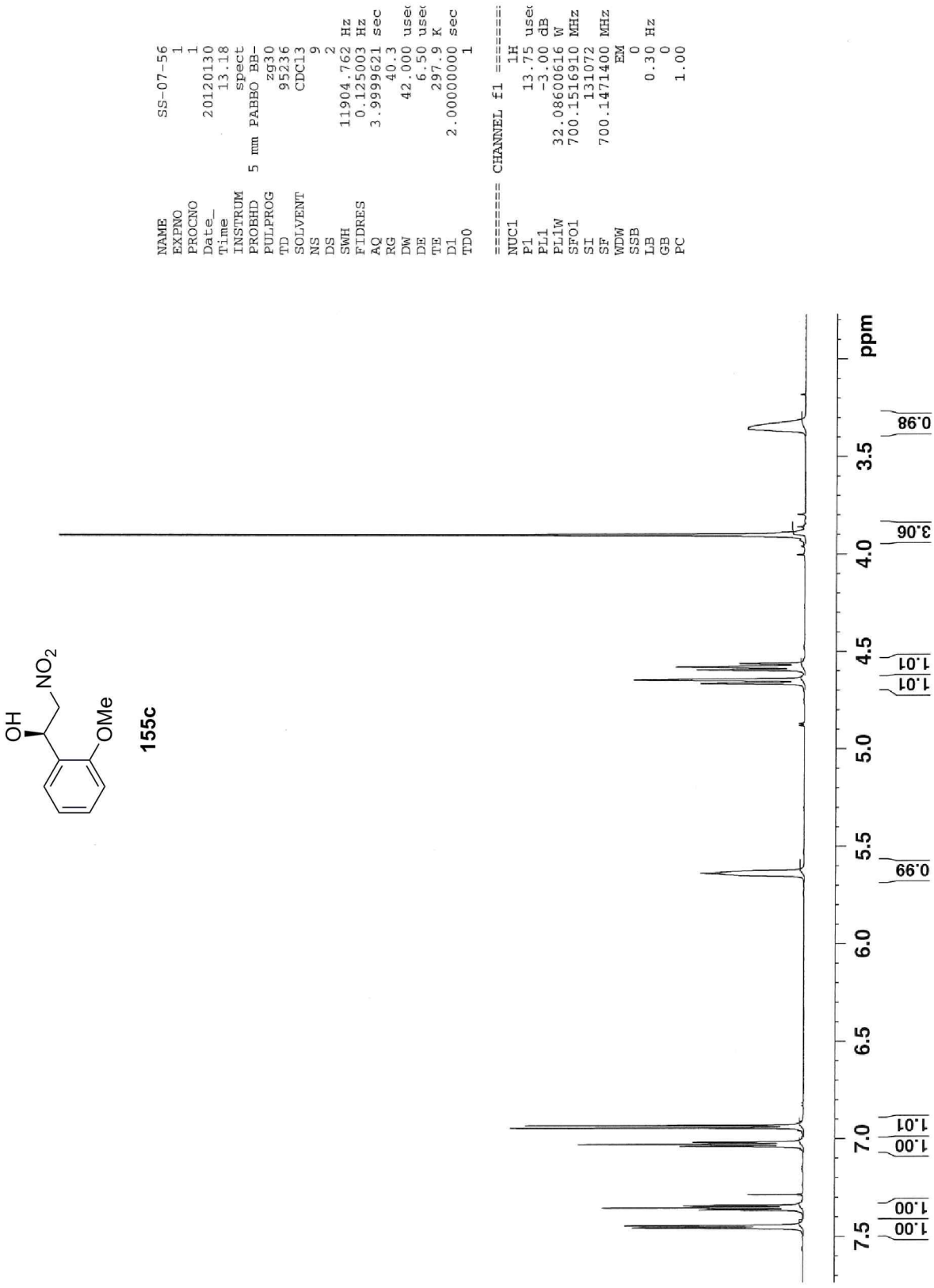

OH
NO2
155b
NAME SS-07-38
EXPNO 1
PROCNO 1
Date_ 20120112
Time 19.45
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 95236
SOLVENT CDC13
NS 24
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 45.2
DW 42.000 use
DE 6.50 use
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.75 use
PL1 -3.00 dB
PL1W 32.08600616 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
ppm
1.00
1.00
2.00
0.98
1.01
0.98
0.89
2.95

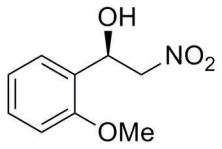


155b

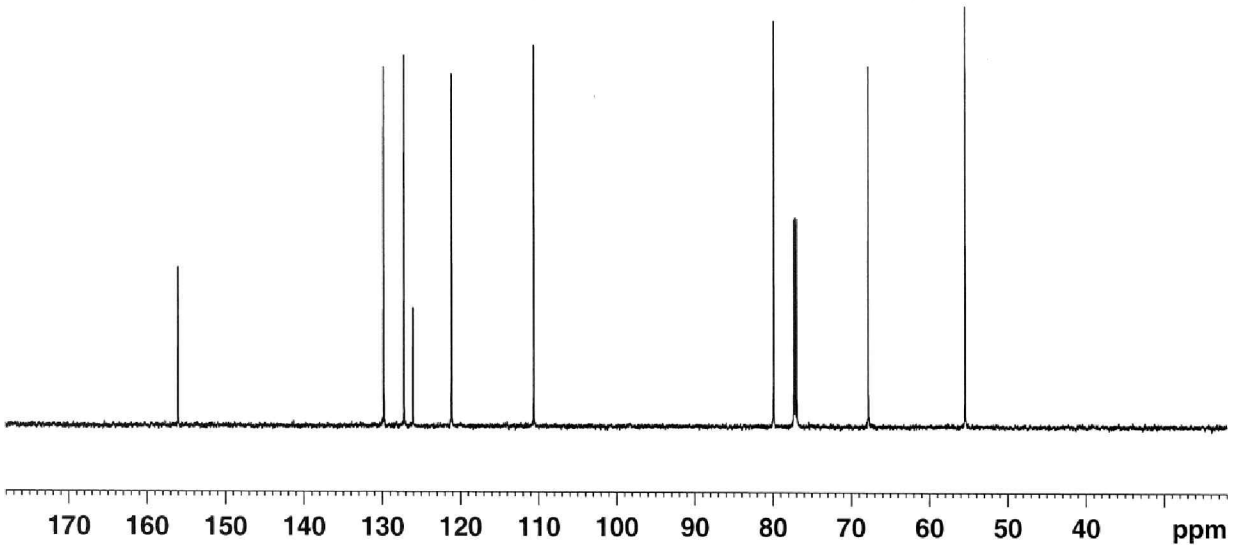


NAME	SS-07-38	
EXPNO	2	
PROCNO	1	
Date_	20120112	
Time	19.49	
INSTRUM	spect	
PROBHD	5 mm PABBO BB-	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	50	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	se
RG	203	
DW	12.000	us
DE	6.50	us
TE	299.2	K
D1	2.00000000	se
D11	0.03000000	se
TD0	1	
======== CHANNEL f1 =======		
NUC1	13C	
P1	9.30	us
PL1	2.00	dB
PL1W	67.83342743	W
SFO1	176.0697436	MH
======== CHANNEL f2 =======		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	80.00	us
PL2	-3.00	dB
PL12	12.30	dB
PL13	12.30	dB
PL2W	32.08600616	W
PL12W	0.94692516	W
PL13W	0.94692516	W
SFO2	700.1499406	MH
SI	32768	
SF	176.0521380	MH
WDW	no	
SSB	0	
LB	0.00	Hz
GB	0	
PC	1.00	

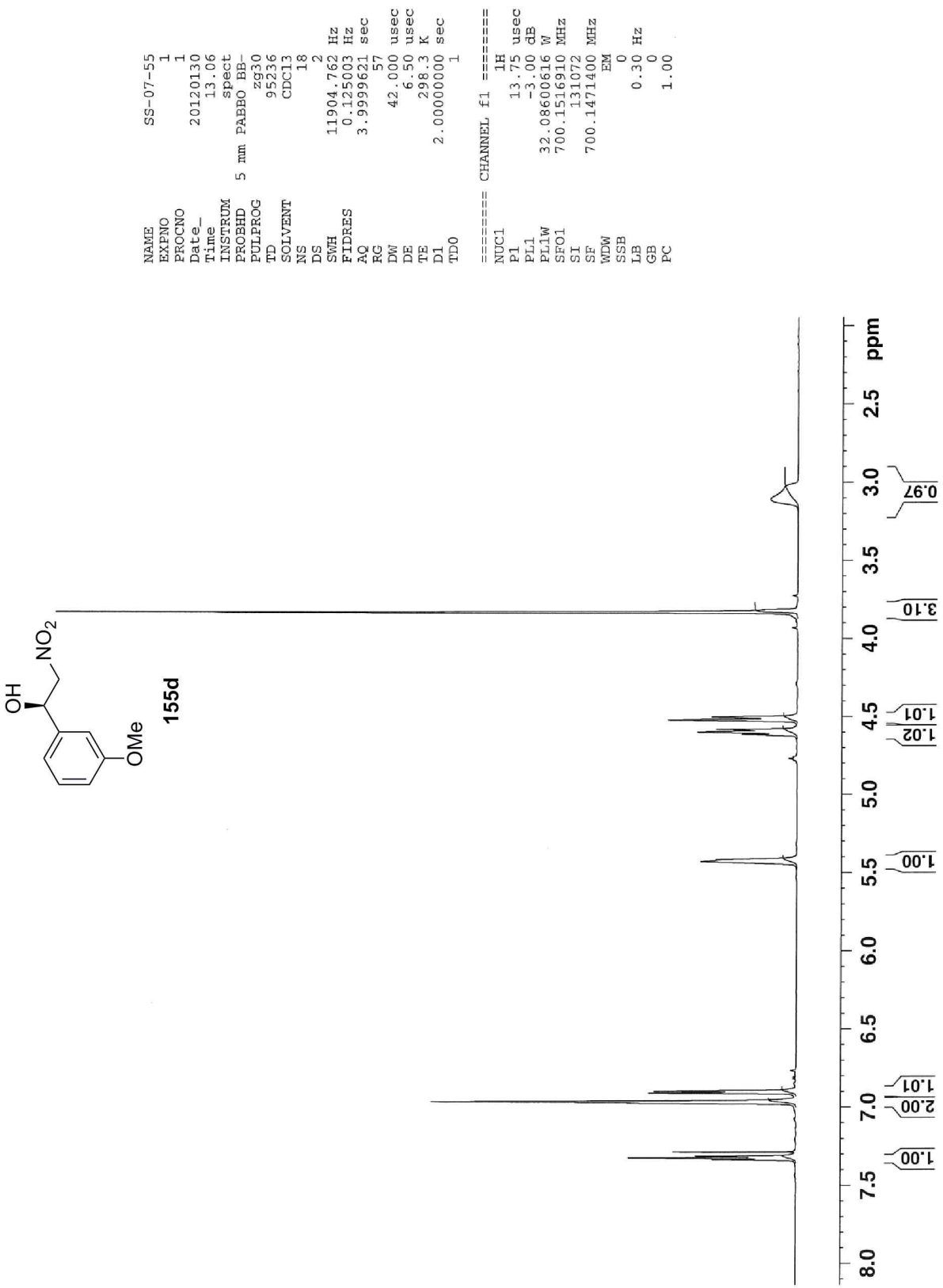

OH
NO2
OMe
155c
NAME SS-07-56
EXPNO 1
PROCNO 1
Date_ 20120130
Time 13.18
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 9
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 40.3
DW 42.000 use
DE 6.50 use
TE 297.9 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.75 use
PL1 -3.00 dB
PL1W 32.08600616 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
ppm
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
1.00
1.00
1.01
1.00
1.01
3.06
0.98
0.99

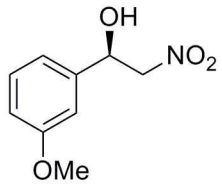


155c

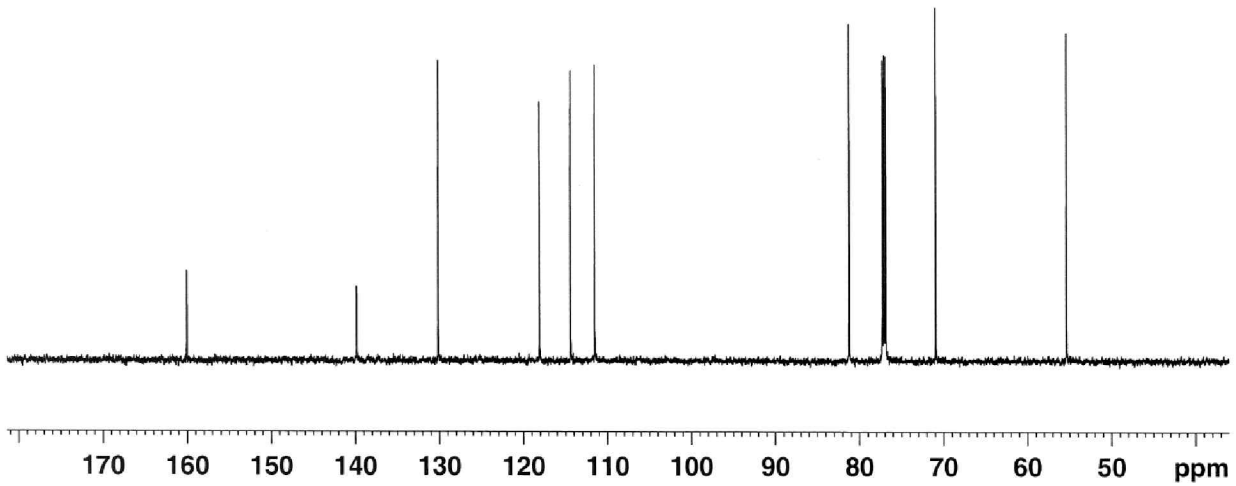


NAME	SS-07-56
EXPNO	2
PROCNO	1
Date_	20120130
Time	13.24
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	53
DS	4
SWH	41666.668 Hz
FIDRES	0.635783 Hz
AQ	0.7864820 sec
RG	203
DW	12.000 use
DE	6.50 use
TE	298.9 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.30 use
PL1	2.00 dB
PL1W	67.83342743 W
SFO1	176.0697436 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 use
PL2	-3.00 dB
PL12	12.30 dB
PL13	12.30 dB
PL2W	32.08600616 W
PL12W	0.94692516 W
PL13W	0.94692516 W
SFO2	700.1499406 MHz
SI	32768
SF	176.0521380 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.00

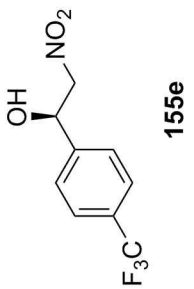

NAME SS-07-55
EXPNO 1
PROCNO 1
Date_ 20120130
Time 13.06
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 95236
SOLVENT CDC13
NS 18
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 57
DW 42.000 usec
DE 6.50 usec
TE 298.3 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.75 usec
PL1 -3.00 dB
PL1W 32.08600616 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
OH
NO2
OMe
155d
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
ppm
1.00
2.00
1.01
1.00
1.01
1.02
3.10
0.97



155d



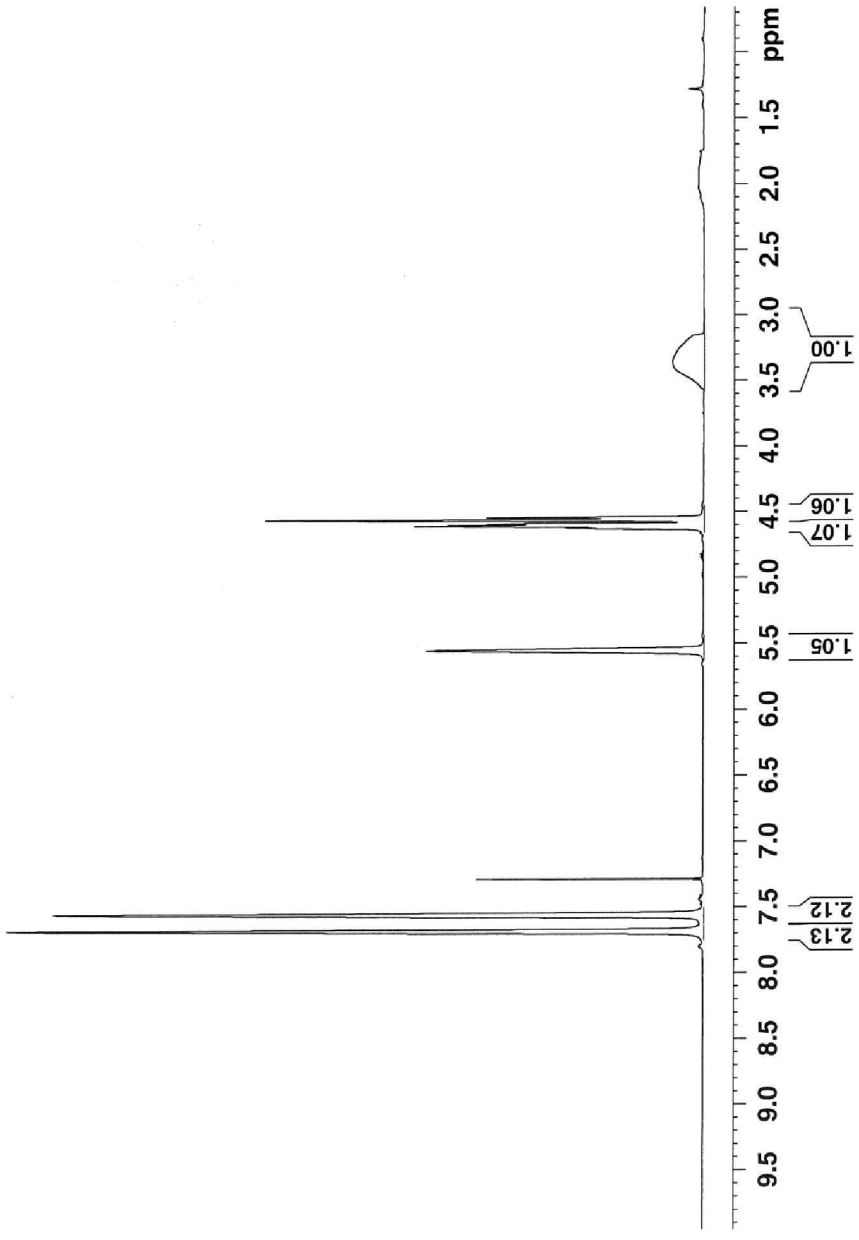
NAME	SS-07-55
EXPNO	2
PROCNO	1
Date_	20120130
Time	13.10
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	95
DS	4
SWH	41666.668 Hz
FIDRES	0.635783 Hz
AQ	0.7864820 sec
RG	203
DW	12.000 use
DE	6.50 use
TE	298.4 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.30 use
PL1	2.00 dB
PL1W	67.83342743 W
SFO1	176.0697436 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 use
PL2	-3.00 dB
PL12	12.30 dB
PL13	12.30 dB
PL2W	32.08600616 W
PL12W	0.94692516 W
PL13W	0.94692516 W
SFO2	700.1499406 MHz
SI	32768
SF	176.0521380 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.00

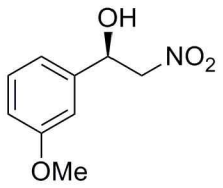


155e

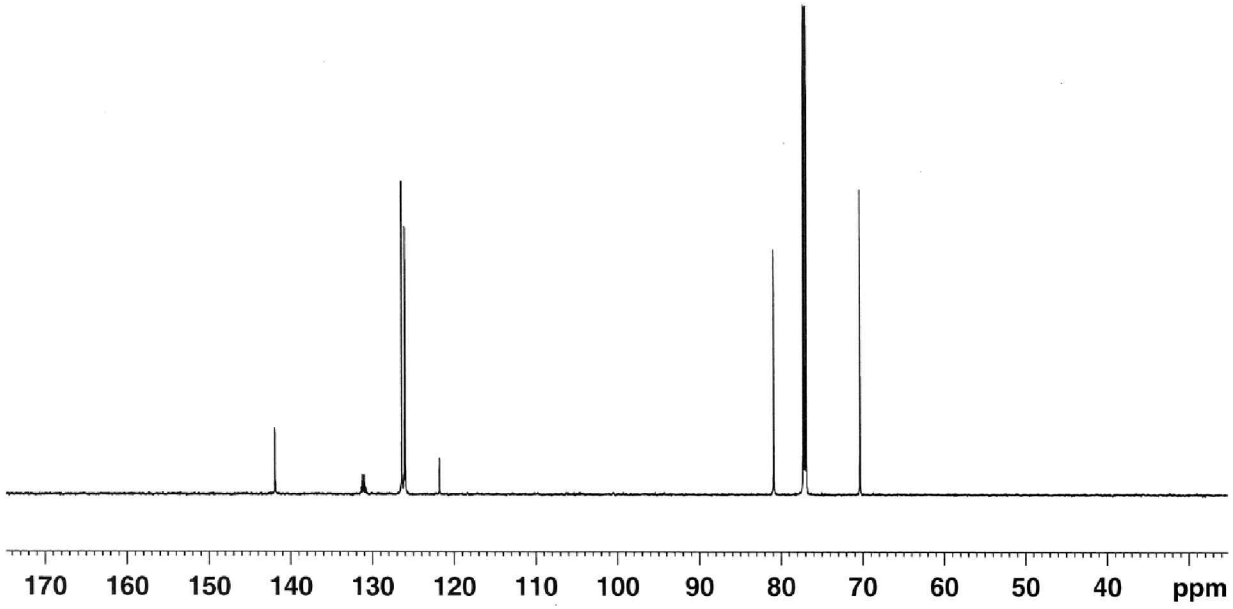
```
NAME                SS-07-51
EXPNO                      1
PROCNO                     1
Date_               20120930
Time                   12.53
INSTRUM                spect
PROBHD   5 mm CPDCH 13C
PULPROG                 zg30
TD                     95236
SOLVENT                CDC13
NS                        22
DS                         2
SWH                11904.762 Hz
FIDRES             0.125003 Hz
AQ                 3.9999621 sec
RG                      20.2
DW                    42.000 usec
DE                     6.50 usec
TE                    298.3 K
D1                 2.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     9.40 usec
PL1                    -3.20 dB
PL1W              33.59817505 W
SFO1              700.1516910 MHz
SI                     131072
SF                700.1471400 MHz
WDW                        EM
SSB                         0
LB                     0.30 Hz
GB                          0
PC                     1.00
```

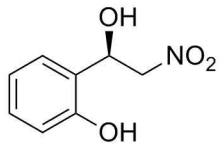




155d

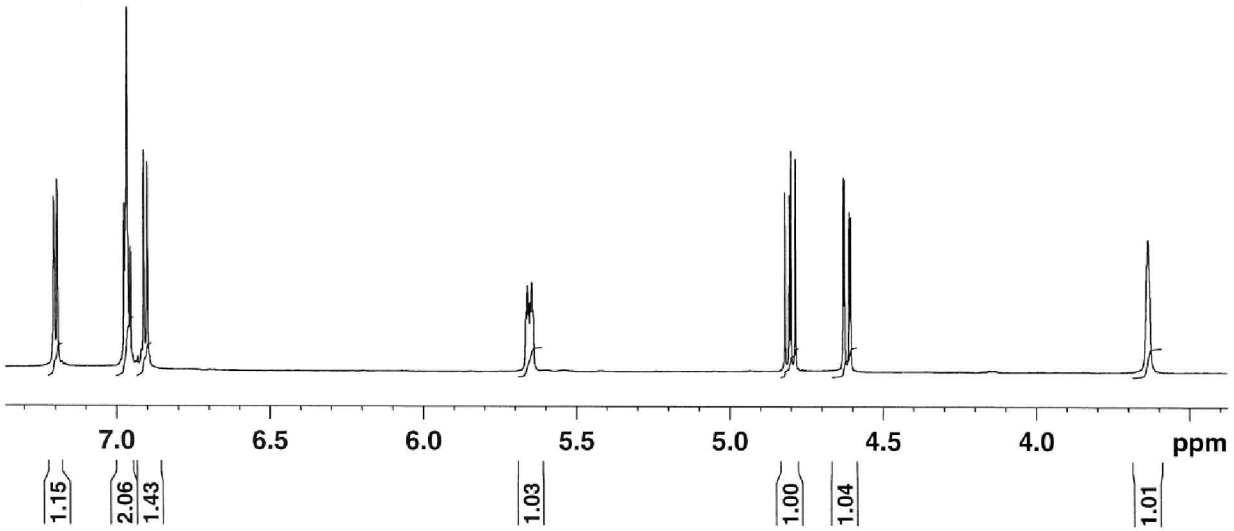


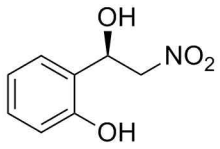
NAME	SS-07-51	
EXPNO	2	
PROCNO	1	
Date_	20120930	
Time	12.58	
INSTRUM	spect	
PROBHD	5 mm CPDCH 13C	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	15	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	usec
DE	16.50	usec
TE	298.2	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	9.00	usec
PL1	4.50	dB
PL1W	38.14553833	W
SFO1	176.0697436	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	65.00	usec
PL2	-3.20	dB
PL12	13.60	dB
PL13	120.00	dB
PL2W	33.59817505	W
PL12W	0.70196527	W
PL13W	0.00000000	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.00	



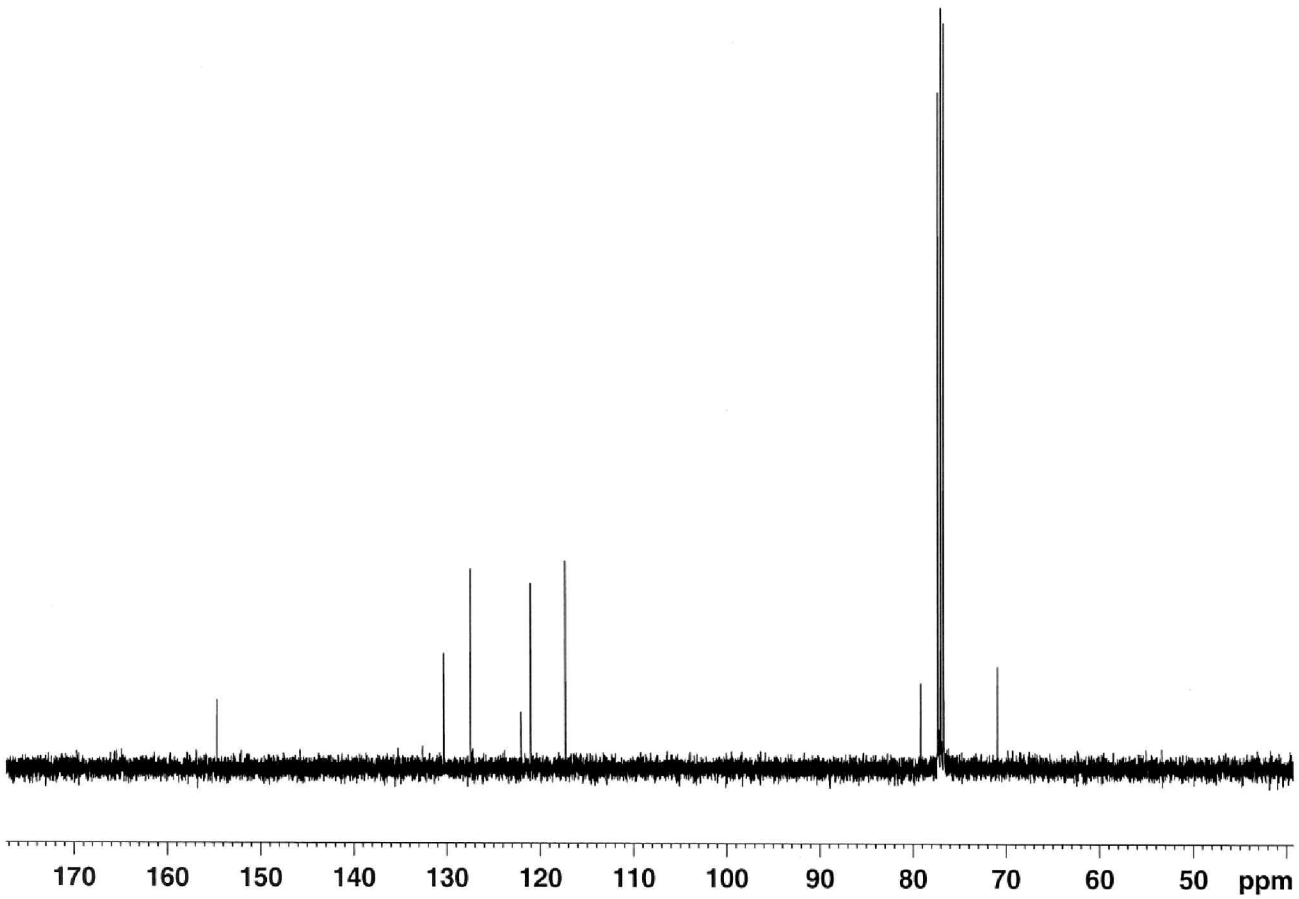
155f

NAME	SS-07-44
EXPNO	7
PROCNO	1
Date_	20120204
Time	19.40
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zg30
TD	95236
SOLVENT	CDCl3
NS	16
DS	2
SWH	11904.762 Hz
FIDRES	0.125003 Hz
AQ	3.9999621 sec
RG	28.5
DW	42.000 usec
DE	6.50 usec
TE	298.1 K
D1	2.00000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	1H
P1	9.40 usec
PL1	-3.20 dB
PL1W	33.59817505 W
SFO1	700.1516910 MHz
SI	131072
SF	700.1471400 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00





155f



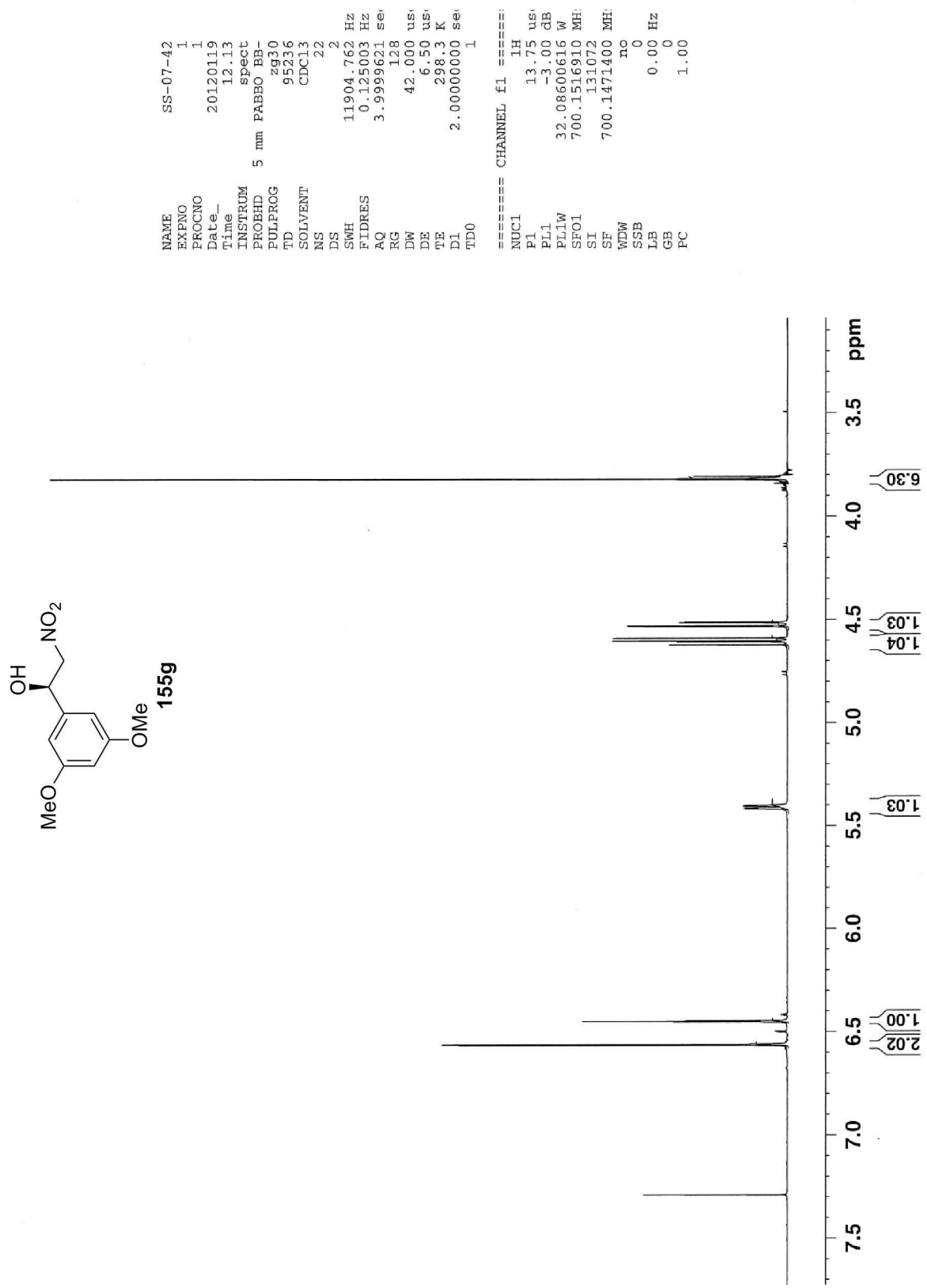

```
Current Data Parameters
NAME                  SS-07-44
EXPNO                        2
PROCNO                       1

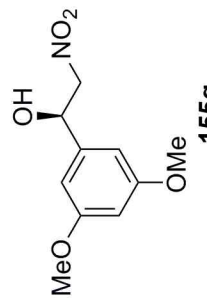
F2 - Acquisition Parameters
Date_                 20120206
Time                     21.26
INSTRUM                DPX400
PROBHD    5 mm Multinucl
PULPROG                zgpg30
TD                        65536
SOLVENT                   CDCl3
NS                         2048
DS                            4
SWH                  23980.814 Hz
FIDRES                0.365918 Hz
AQ                    1.3664756 sec
RG                        32768
DW                       20.850 use
DE                        6.00 use
TE                       299.2 K
D1                  0.20000000 sec
d11                 0.03000000 sec
DELTA               0.10000000 sec
TD0                          1

======== CHANNEL f1 =======
NUC1                        13C
P1                        8.30 use
PL1                      -3.00 dB
SFO1               100.6555216 MHz

======== CHANNEL f2 =======
CPDPRG2                waltz16
NUC2                        1H
PCPD2                    90.00 use
PL2                      -3.00 dB
PL12                     15.00 dB
PL13                     15.00 dB
SFO2               400.2620013 MHz

F2 - Processing parameters
SI                        32768
SF                 100.6454570 MHz
WDW                          no
SSB                           0
LB                        0.00 Hz
GB                            0
PC                        1.40
```


OH
NO2
MeO
OMe
155g
NAME SS-07-42
EXPNO 1
PROCNO 1
Date_ 20120119
Time 12.13
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 95236
SOLVENT CDC13
NS 22
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 se
RG 128
DW 42.000 us
DE 6.50 us
TE 298.3 K
D1 2.00000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 13.75 us
PL1 -3.00 dB
PL1W 32.08600616 W
SFO1 700.1516910 MH
SI 131072
SF 700.1471400 MH
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
ppm
2.02
1.00
1.03
1.03
1.04
1.03
6.30

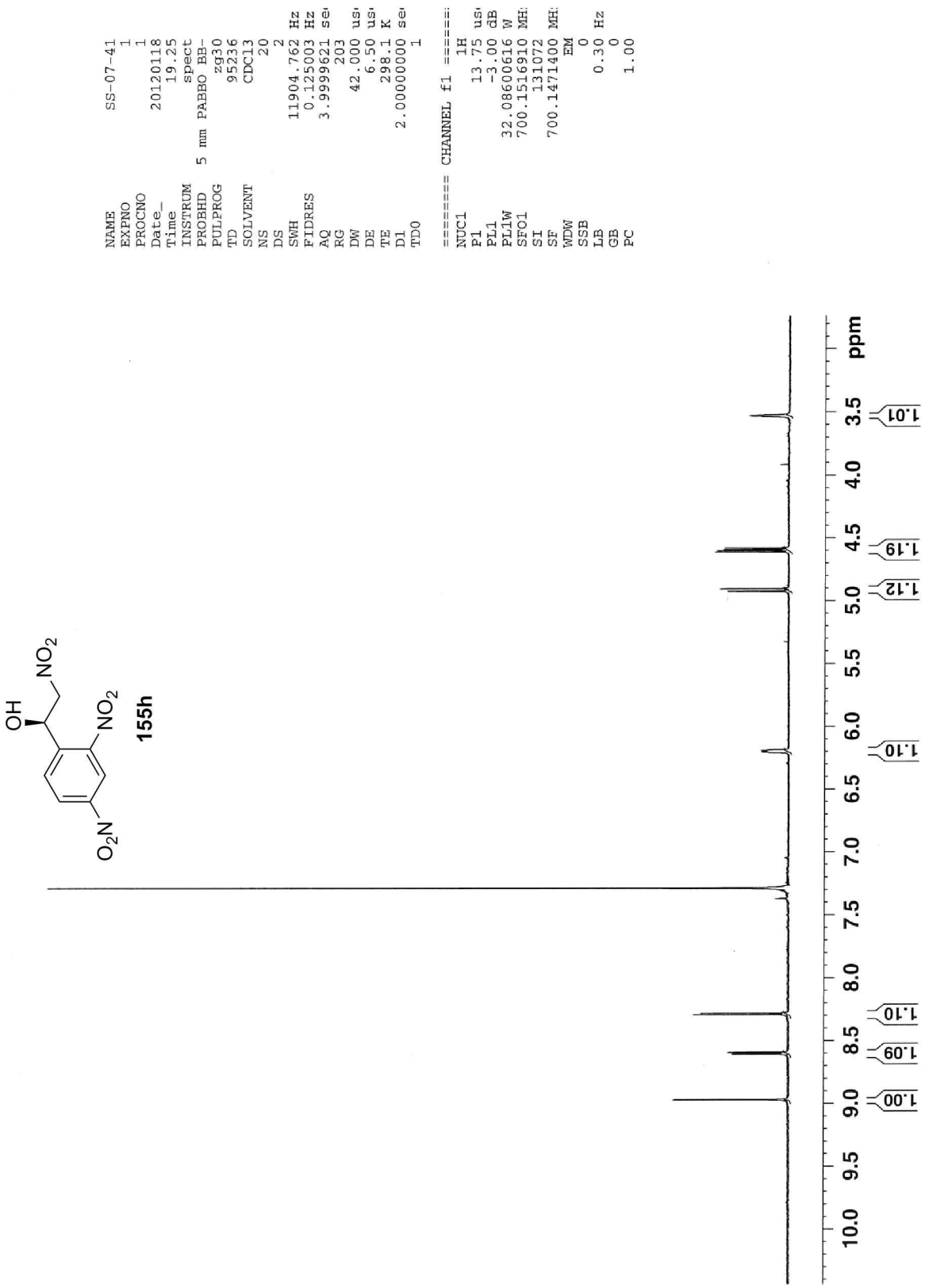


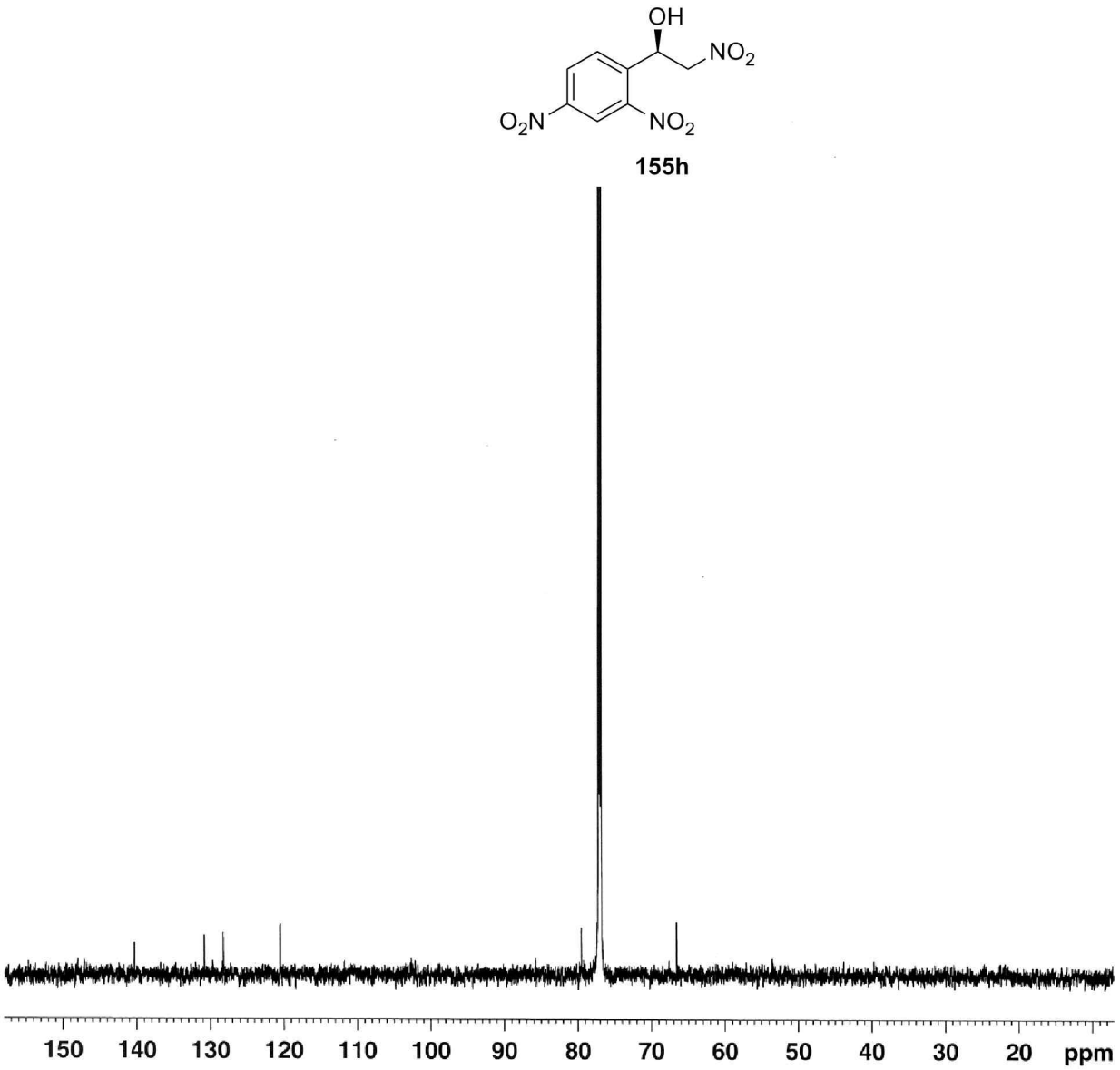
155g

```
NAME                SS-07-42
EXPNO                      2
PROCNO                     1
Date_               20120119
Time                   12.21
INSTRUM                spect
PROBHD  5 mm PABBO BB-
PULPROG                zgpg30
TD                      65536
SOLVENT                CDCl3
NS                       133
DS                         4
SWH                41666.668 Hz
FIDRES                 0.635783 Hz
AQ                     0.7864820 sec
RG                       203
DW                      12.000 use
DE                       6.50 use
TE                     298.7 K
D1                     2.00000000 sec
D11                    0.03000000 sec
TD0                        1

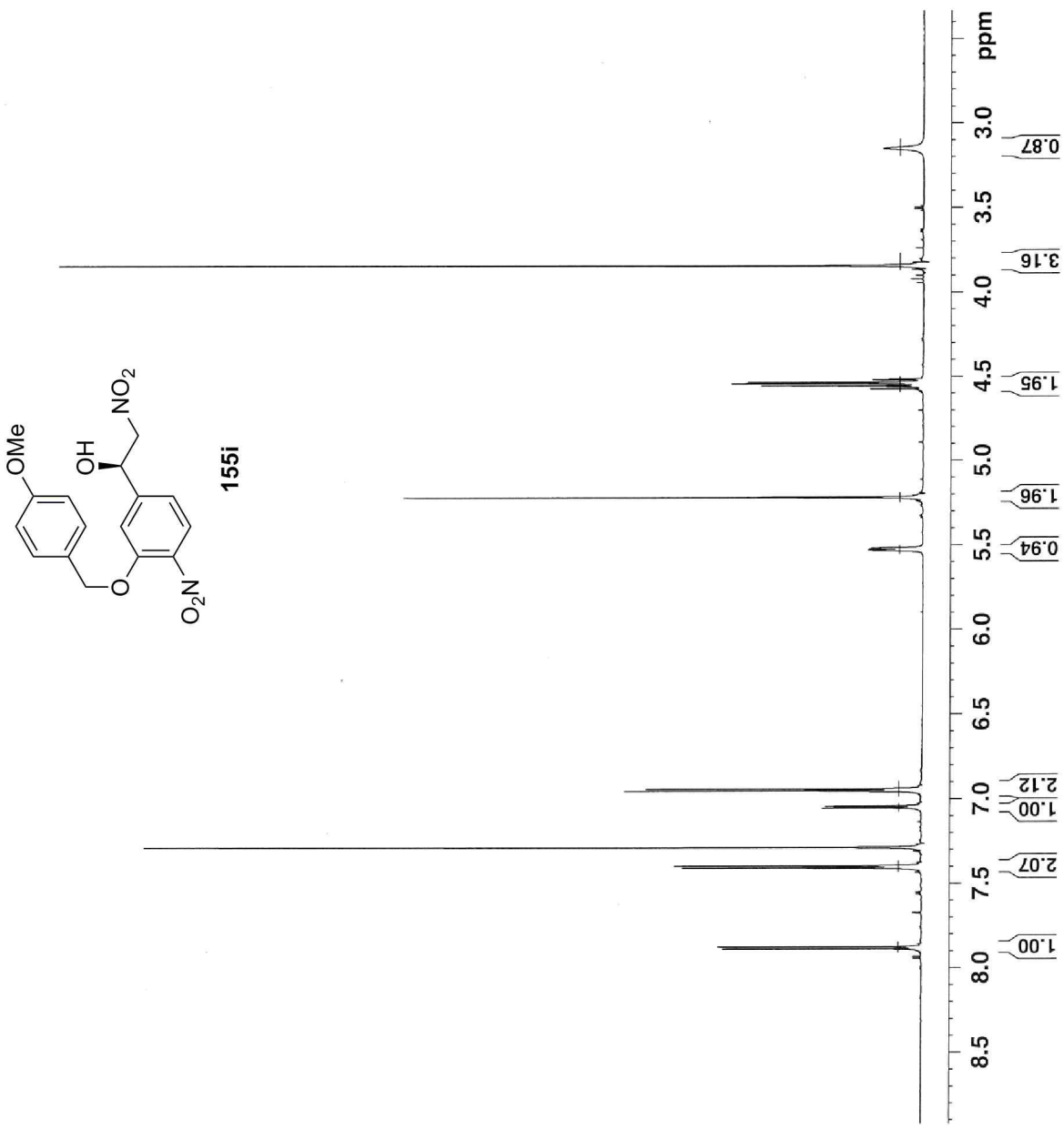
======== CHANNEL f1 ========
NUC1                      13C
P1                       9.30 use
PL1                      2.00 dB
PL1W                67.83342743 W
SFO1               176.0697436 MHz

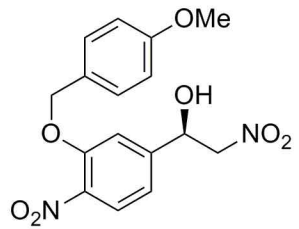
======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                   80.00 use
PL2                     -3.00 dB
PL12                    12.30 dB
PL13                    12.30 dB
PL2W               32.08600616 W
PL12W               0.94692516 W
PL13W               0.94692516 W
SFO2               700.1499406 MHz
SI                      32768
SF                 176.0521380 MHz
WDW                        EM
SSB                         0
LB                       3.00 Hz
GB                          0
PC                       1.00
```


NAME SS-07-41
EXPNO 1
PROCNO 1
Date_ 20120118
Time 19.25
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 95236
SOLVENT CDC13
NS 20
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 se
RG 203
DW 42.000 us
DE 6.50 us
TE 298.1 K
D1 2.00000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 13.75 us
PL1 -3.00 dB
PL1W 32.08600616 W
SFO1 700.1516910 MH
SI 131072
SF 700.1471400 MH
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
OH
NO2
NO2
O2N
155h
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
ppm
1.00
1.09
1.10
1.10
1.12
1.19
1.01



NAME	SS-07-41	
EXPNO	3	
PROCNO	1	
Date_	20120118	
Time	19.43	
INSTRUM	spect	
PROBHD	5 mm PABBO BB-	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	977	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	use
DE	6.50	use
TE	298.6	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 =======		
NUC1	13C	
P1	9.30	use
PL1	2.00	dB
PL1W	67.83342743	W
SFO1	176.0697436	MHz
======== CHANNEL f2 =======		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	80.00	use
PL2	-3.00	dB
PL12	12.30	dB
PL13	12.30	dB
PL2W	32.08600616	W
PL12W	0.94692516	W
PL13W	0.94692516	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.00	


OMe
OH
NO2
O
O2N
155i
NAME SS-07-59
EXPNO 1
PROCNO 1
Date_ 20120605
Time 13.27
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDC13
NS 5
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 32
DW 42.000 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
ppm
1.00
2.07
1.00
2.12
0.94
1.96
1.95
3.16
0.87



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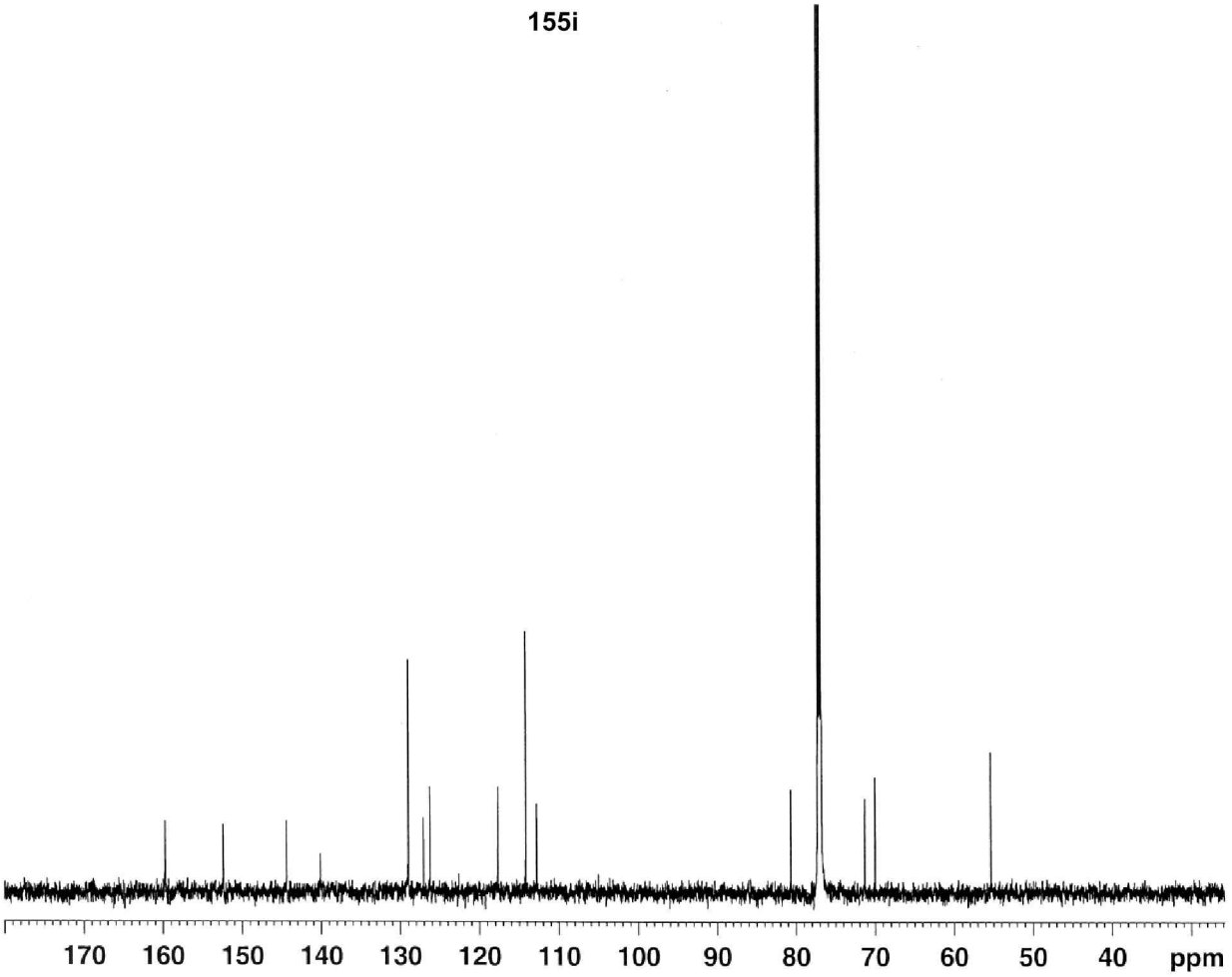
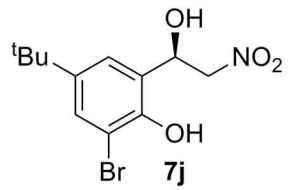
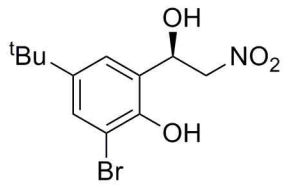


NAME	SS-07-59	
EXPNO	21	
PROCNO	1	
Date_	20120605	
Time	13.32	
INSTRUM	spect	
PROBHD	5 mm CPDCH 13C	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	45	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	usec
DE	16.50	usec
TE	298.2	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	9.00	usec
PL1	4.50	dB
PL1W	38.14553833	W
SFO1	176.0697436	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	65.00	usec
PL2	-3.20	dB
PL12	13.60	dB
PL13	120.00	dB
PL2W	33.59817505	W
PL12W	0.70196527	W
PL13W	0.00000000	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.00	

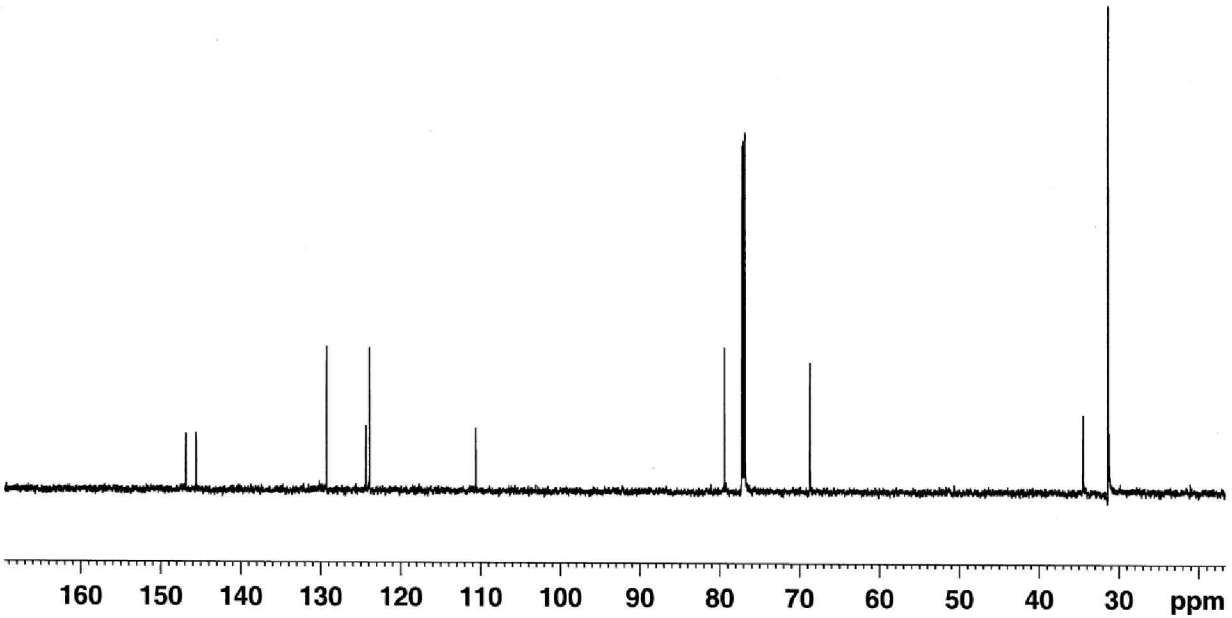


7j

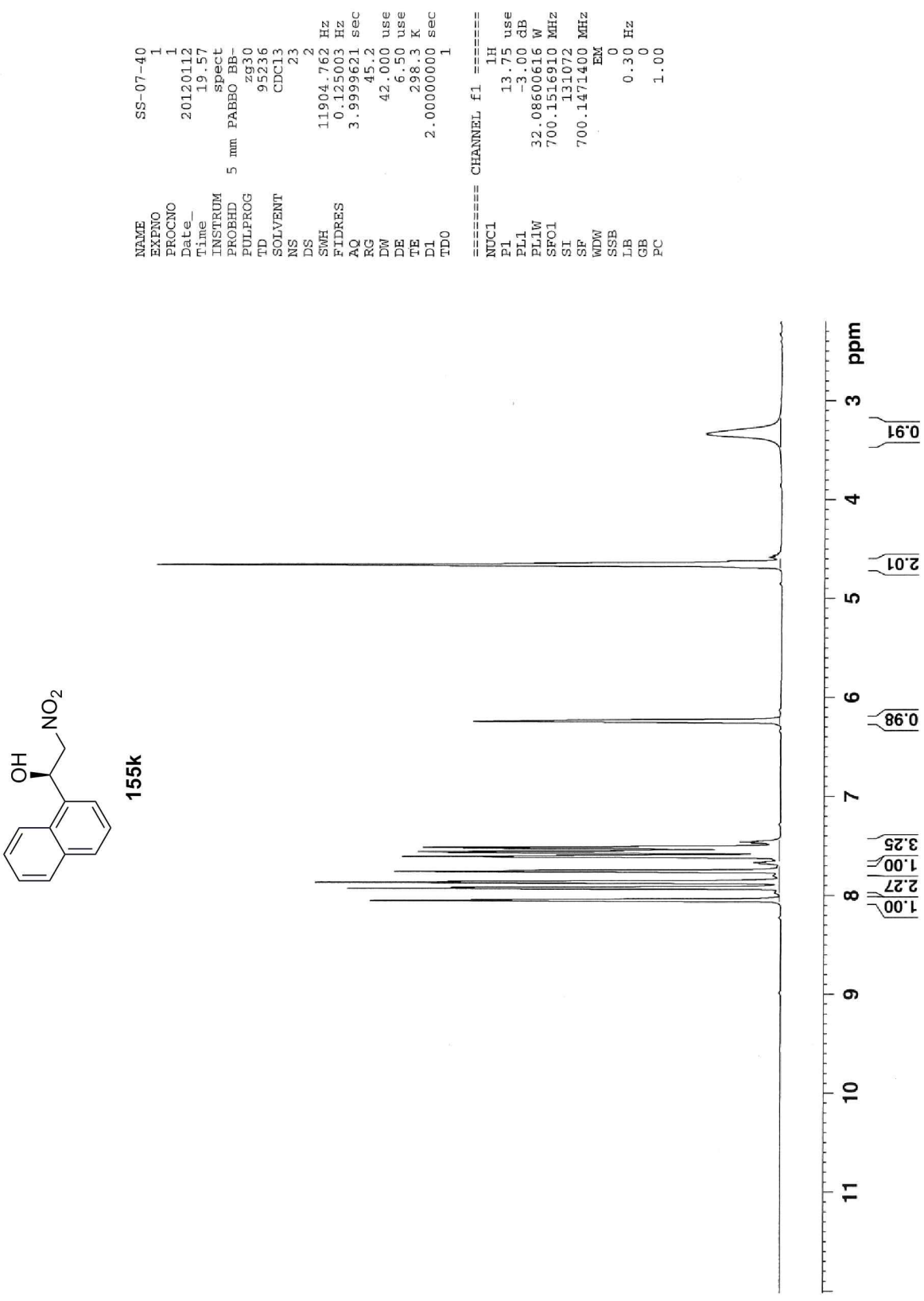
NAME	SS-07-43	
EXPNO	1	
PROCNO	1	
Date_	20120119	
Time	12.29	
INSTRUM	spect	
PROBHD	5 mm PABBO BB-	
PULPROG	zg30	
TD	95236	
SOLVENT	CDCl3	
NS	32	
DS	2	
SWH	11904.762	Hz
FIDRES	0.125003	Hz
AQ	3.9999621	sec
RG	101	
DW	42.000	usec
DE	6.50	usec
TE	297.9	K
D1	2.00000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	1H	
P1	13.75	usec
PL1	-3.00	dB
PL1W	32.08600616	W
SFO1	700.1516910	MHz
SI	131072	
SF	700.1471400	MHz
WDW	EM	
SSB	0	
LB	0.30	Hz
GB	0	
PC	1.00	

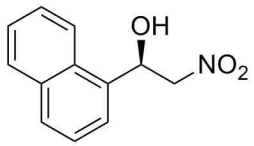


155j

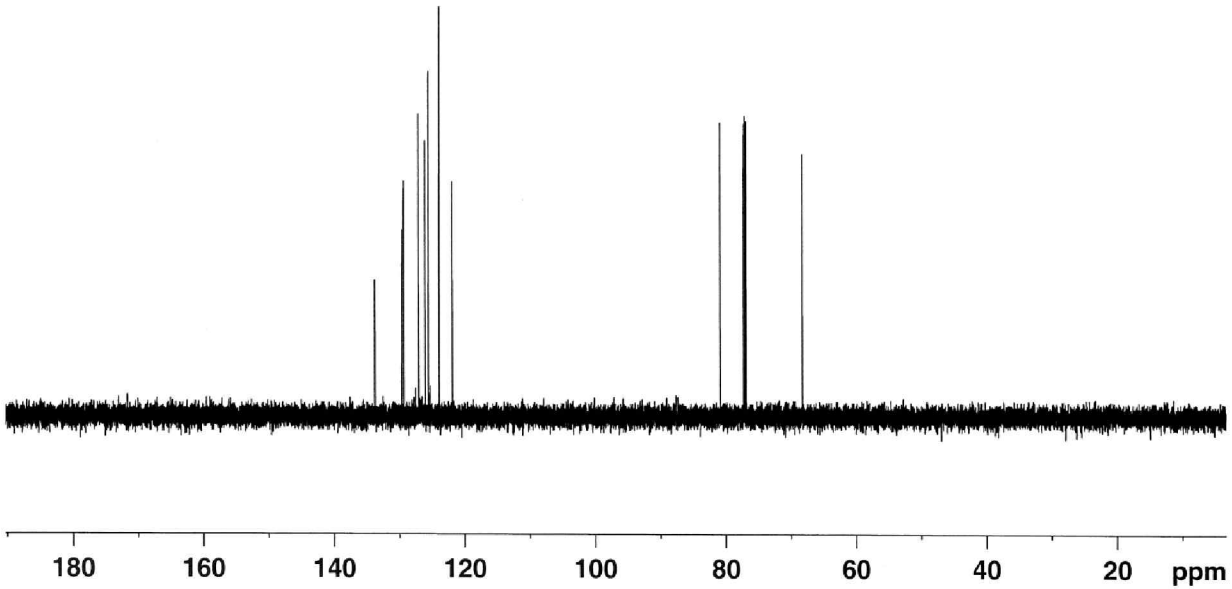


NAME	SS-07-43	
EXPNO	2	
PROCNO	1	
Date_	20120119	
Time	12.38	
INSTRUM	spect	
PROBHD	5 mm PABBO BB-	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	65	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	se
RG	203	
DW	12.000	us
DE	6.50	us
TE	299.0	K
D1	2.00000000	se
D11	0.03000000	se
TD0	1	
========	CHANNEL f1	======
NUC1	13C	
P1	9.30	us
PL1	2.00	dB
PL1W	67.83342743	W
SFO1	176.0697436	MH
========	CHANNEL f2	======
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	80.00	us
PL2	-3.00	dB
PL12	12.30	dB
PL13	12.30	dB
PL2W	32.08600616	W
PL12W	0.94692516	W
PL13W	0.94692516	W
SFO2	700.1499406	MH
SI	32768	
SF	176.0521380	MH
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.00	

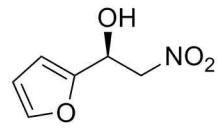

OH
NO2
155k
NAME SS-07-40
EXPNO 1
PROCNO 1
Date_ 20120112
Time 19.57
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 23
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 45.2
DW 42.000 use
DE 6.50 use
TE 298.3 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.75 use
PL1 -3.00 dB
PL1W 32.08600616 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
11 10 9 8 7 6 5 4 3 ppm
0.91
2.01
0.98
3.25
1.00
2.27
1.00



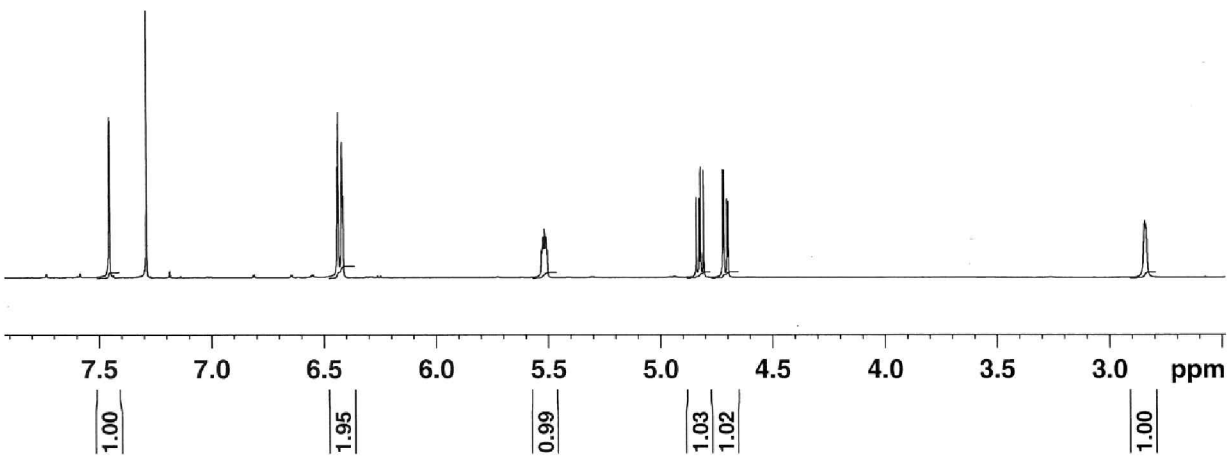
155k



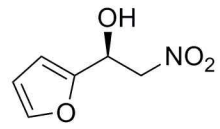
NAME	SS-07-40	
EXPNO	2	
PROCNO	1	
Date_	20120112	
Time	20.01	
INSTRUM	spect	
PROBHD	5 mm PABBO BB-	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	23	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	usec
DE	6.50	usec
TE	299.2	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	9.30	usec
PL1	2.00	dB
PL1W	67.83342743	W
SFO1	176.0697436	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	80.00	usec
PL2	-3.00	dB
PL12	12.30	dB
PL13	12.30	dB
PL2W	32.08600616	W
PL12W	0.94692516	W
PL13W	0.94692516	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	no	
SSB	0	
LB	0.00	Hz
GB	0	
PC	1.00	



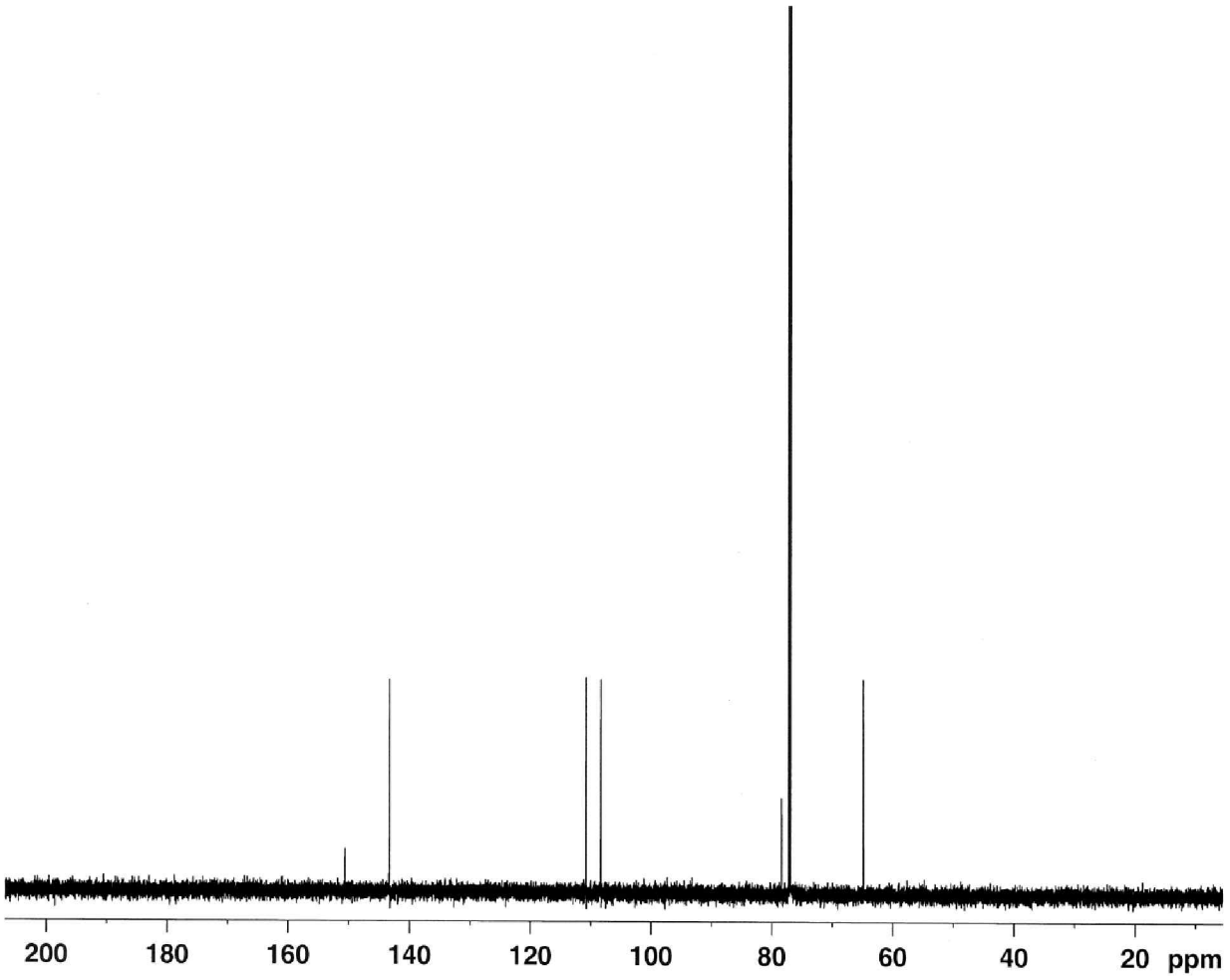
155l



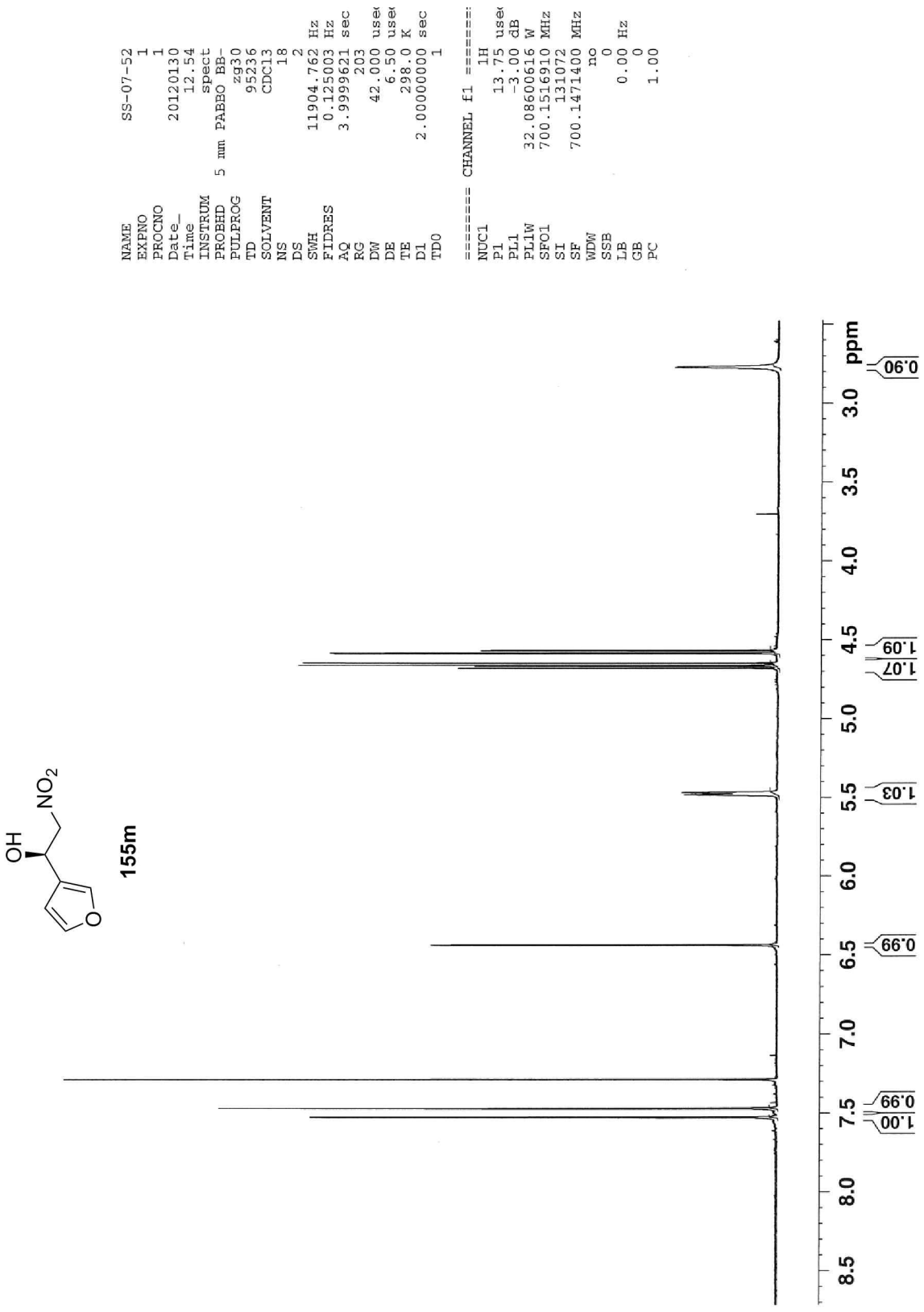
NAME	SS-07-49	
EXPNO	2	
PROCNO	1	
Date_	20120204	
Time	22.06	
INSTRUM	spect	
PROBHD	5 mm CPDCH 13C	
PULPROG	zg30	
TD	95236	
SOLVENT	CDCl3	
NS	16	
DS	2	
SWH	11904.762	Hz
FIDRES	0.125003	Hz
AQ	3.9999621	sec
RG	32	
DW	42.000	usec
DE	6.50	usec
TE	298.2	K
D1	2.00000000	sec
TD0	1	
========	CHANNEL f1	========
NUC1	1H	
P1	9.40	usec
PL1	-3.20	dB
PL1W	33.59817505	W
SFO1	700.1516910	MHz
SI	131072	
SF	700.1471400	MHz
WDW	EM	
SSB	0	
LB	0.30	Hz
GB	0	
PC	1.00	

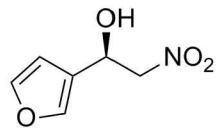


155l



NAME	SS-07-49	
EXPNO	5	
PROCNO	1	
Date_	20120206	
Time	22.06	
INSTRUM	spect	
PROBHD	5 mm CPDCH 13C	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	62	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	2.56	
DW	12.000	usec
DE	6.50	usec
TE	298.2	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	9.00	usec
PL1	4.50	dB
PL1W	38.14553833	W
SFO1	176.0697436	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	65.00	usec
PL2	-3.20	dB
PL12	13.60	dB
PL13	120.00	dB
PL2W	33.59817505	W
PL12W	0.70196527	W
PL13W	0.00000000	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	no	
SSB	0	
LB	0.00	Hz
GB	0	
PC	1.00	


OH
NO2
O
155m
NAME SS-07-52
EXPNO 1
PROCNO 1
Date_ 20120130
Time 12.54
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 18
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 203
DW 42.000 use
DE 6.50 use
TE 298.0 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.75 use
PL1 -3.00 dB
PL1W 32.08600616 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
ppm
0.90
1.09
1.07
1.03
0.99
1.00
0.99



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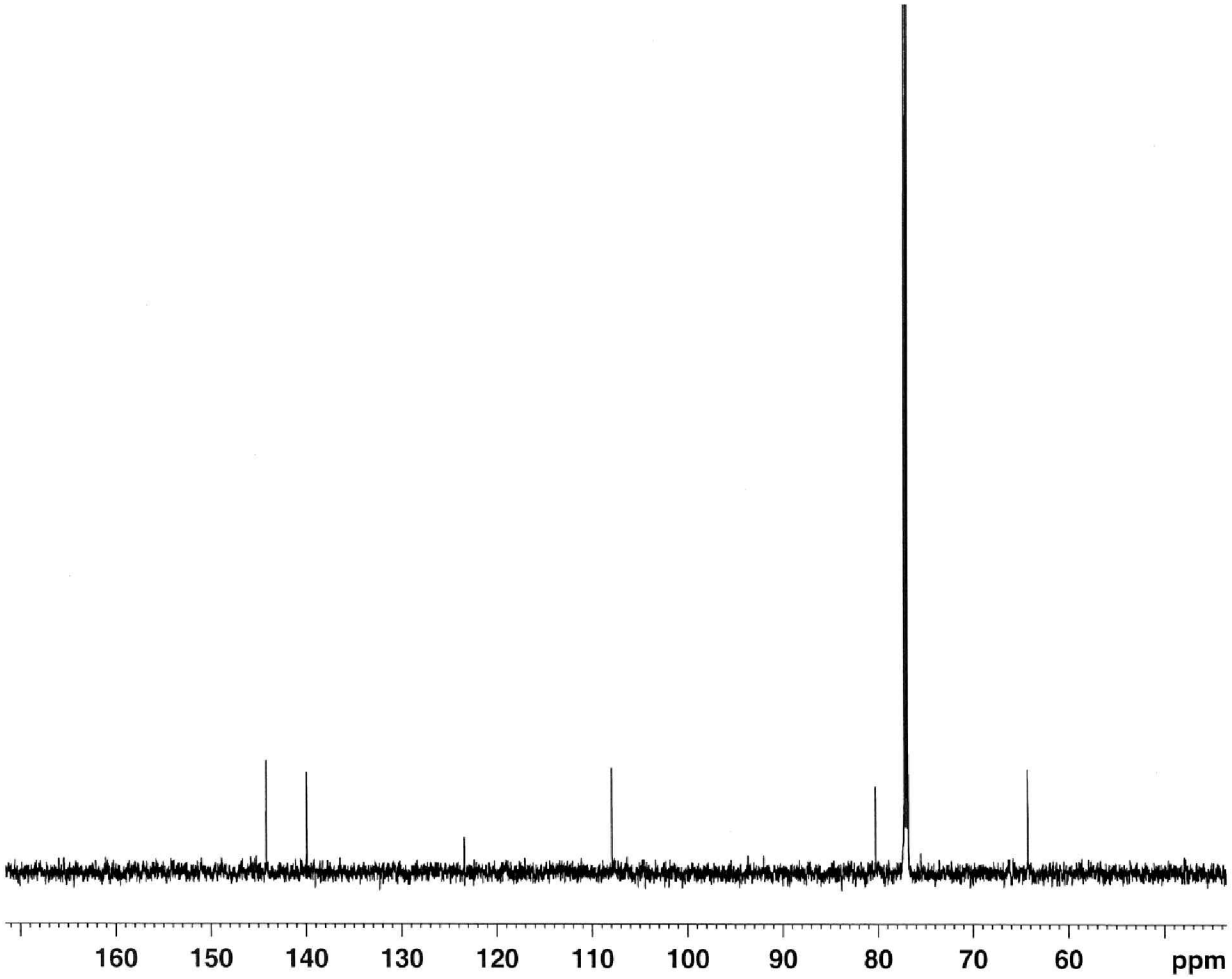
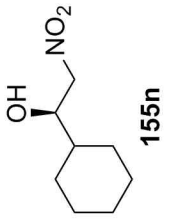


NAME	SS-07-52	
EXPNO	2	
PROCNO	1	
Date_	20120130	
Time	12.58	
INSTRUM	spect	
PROBHD	5 mm PABBO BB-	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	53	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	usec
DE	6.50	usec
TE	298.7	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	9.30	usec
PL1	2.00	dB
PL1W	67.83342743	W
SFO1	176.0697436	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	80.00	usec
PL2	-3.00	dB
PL12	12.30	dB
PL13	12.30	dB
PL2W	32.08600616	W
PL12W	0.94692516	W
PL13W	0.94692516	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.00	


```
NAME                SS-07-68
EXPNO                      1
PROCNO                     1
Date_               20120506
Time                   20.15
INSTRUM                spect
PROBHD     5 mm CPDCH 13C
PULPROG                 zg30
TD                     95236
SOLVENT                CDC13
NS                         9
DS                         2
SWH                11904.762 Hz
FIDRES             0.125003 Hz
AQ                 3.9999621 sec
RG                        32
DW                    42.000 usec
DE                     6.50 usec
TE                    298.2 K
D1                 2.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     9.40 usec
PL1                   -3.20 dB
PL1W               33.59817505 W
SFO1               700.1516910 MHz
SI                      131072
SF                 700.1471400 MHz
WDW                        EM
SSB                         0
LB                   0.30 Hz
GB                          0
PC                       1.00
```

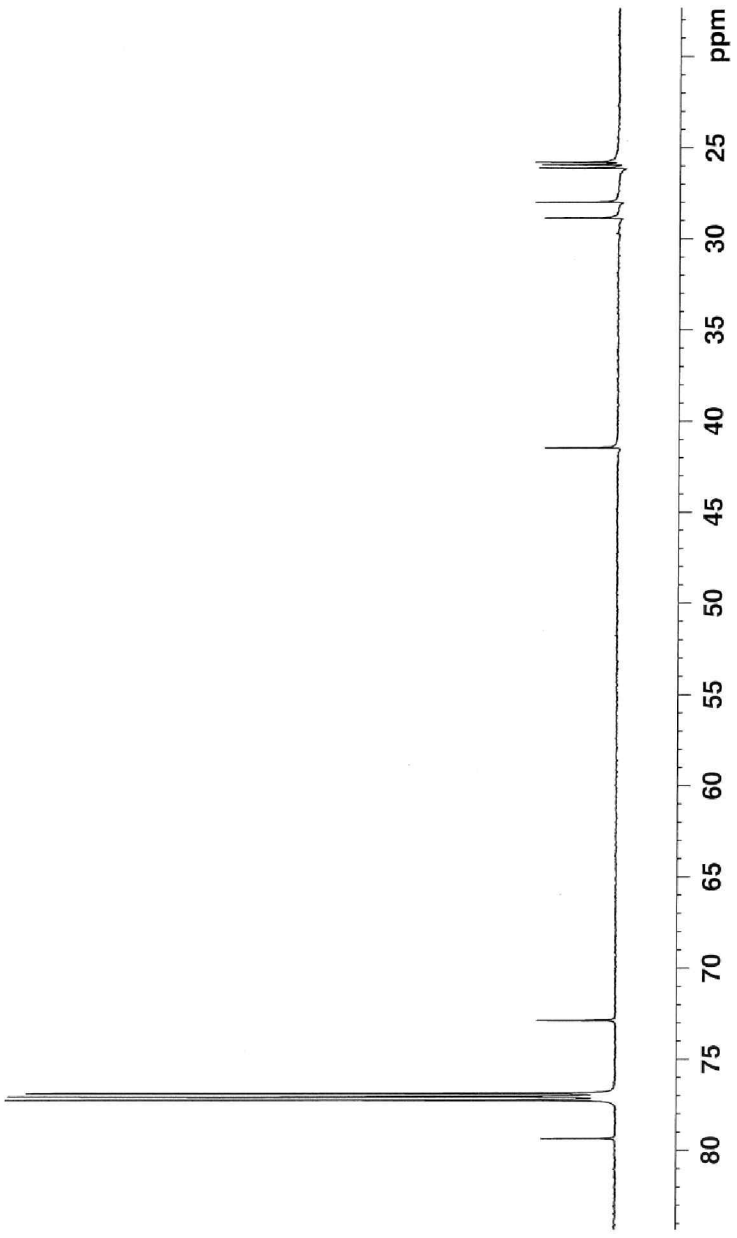


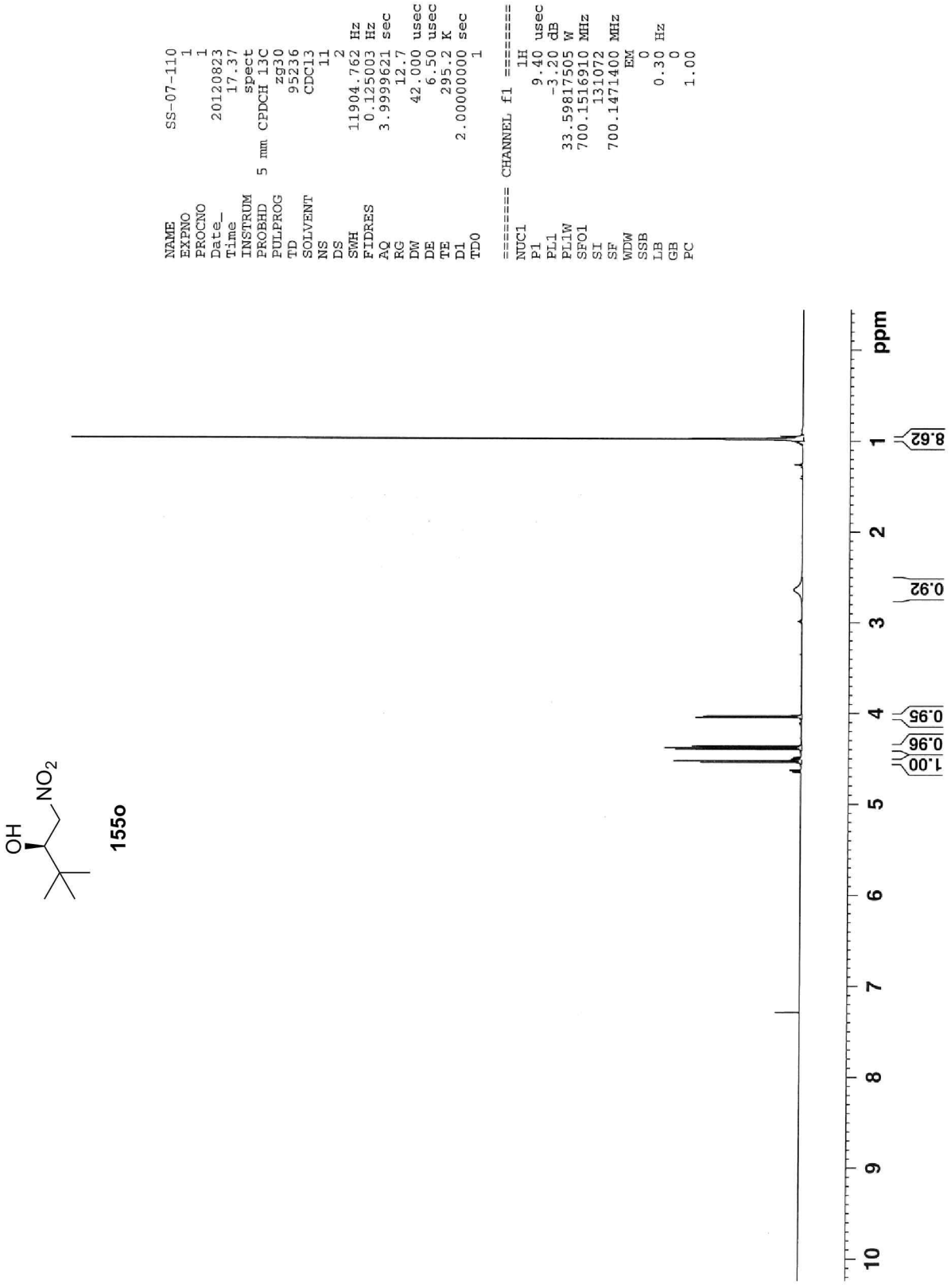
155n

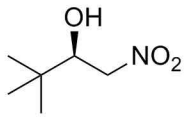
```
NAME                SS-07-68
EXPNO                      2
PROCNO                     1
Date_               20120506
Time                   20.22
INSTRUM                spect
PROBHD  5 mm CPDCH 13C
PULPROG                zgpg30
TD                      65536
SOLVENT                CDCl3
NS                         34
DS                          4
SWH                 41666.668 Hz
FIDRES                 0.635783 Hz
AQ                     0.7864820 sec
RG                        203
DW                     12.000 usec
DE                     16.50 usec
TE                     298.2 K
D1                     2.00000000 sec
D11                    0.03000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      13C
P1                     9.00 usec
PL1                    4.50 dB
PL1W                38.14553833 W
SFO1                176.0697436 MHz

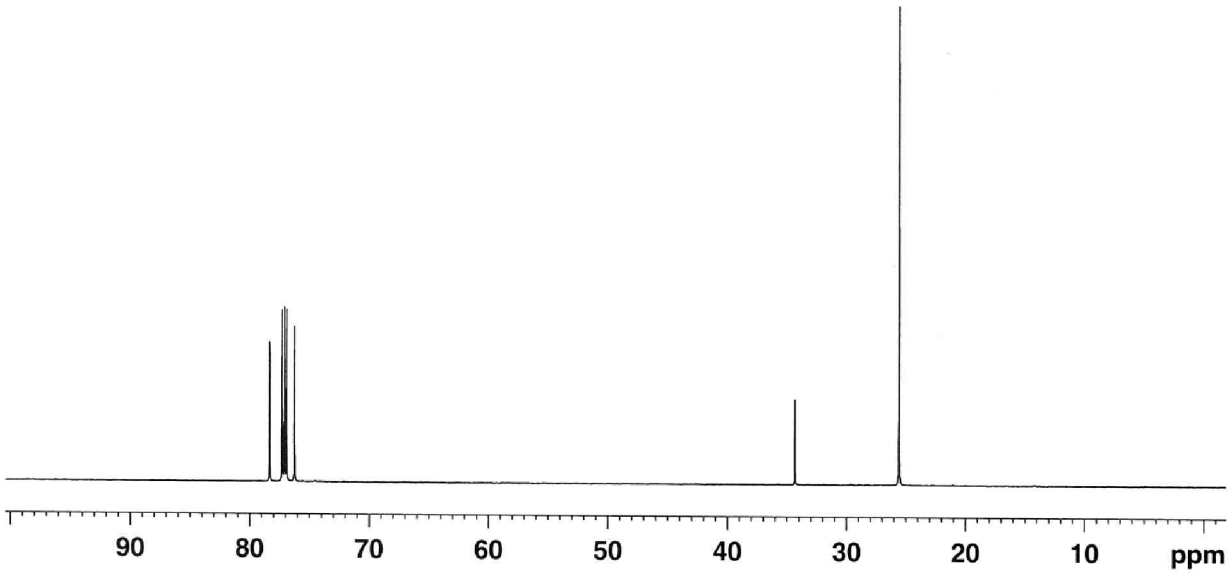
======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                  65.00 usec
PL2                    -3.20 dB
PL12                   13.60 dB
PL13                  120.00 dB
PL2W                33.59817505 W
PL12W                0.70196527 W
PL13W                0.00000000 W
SFO2                700.1499406 MHz
SI                         32768
SF                  176.0521380 MHz
WDW                        EM
SSB                         0
LB                     3.00 Hz
GB                          0
PC                     1.00
```



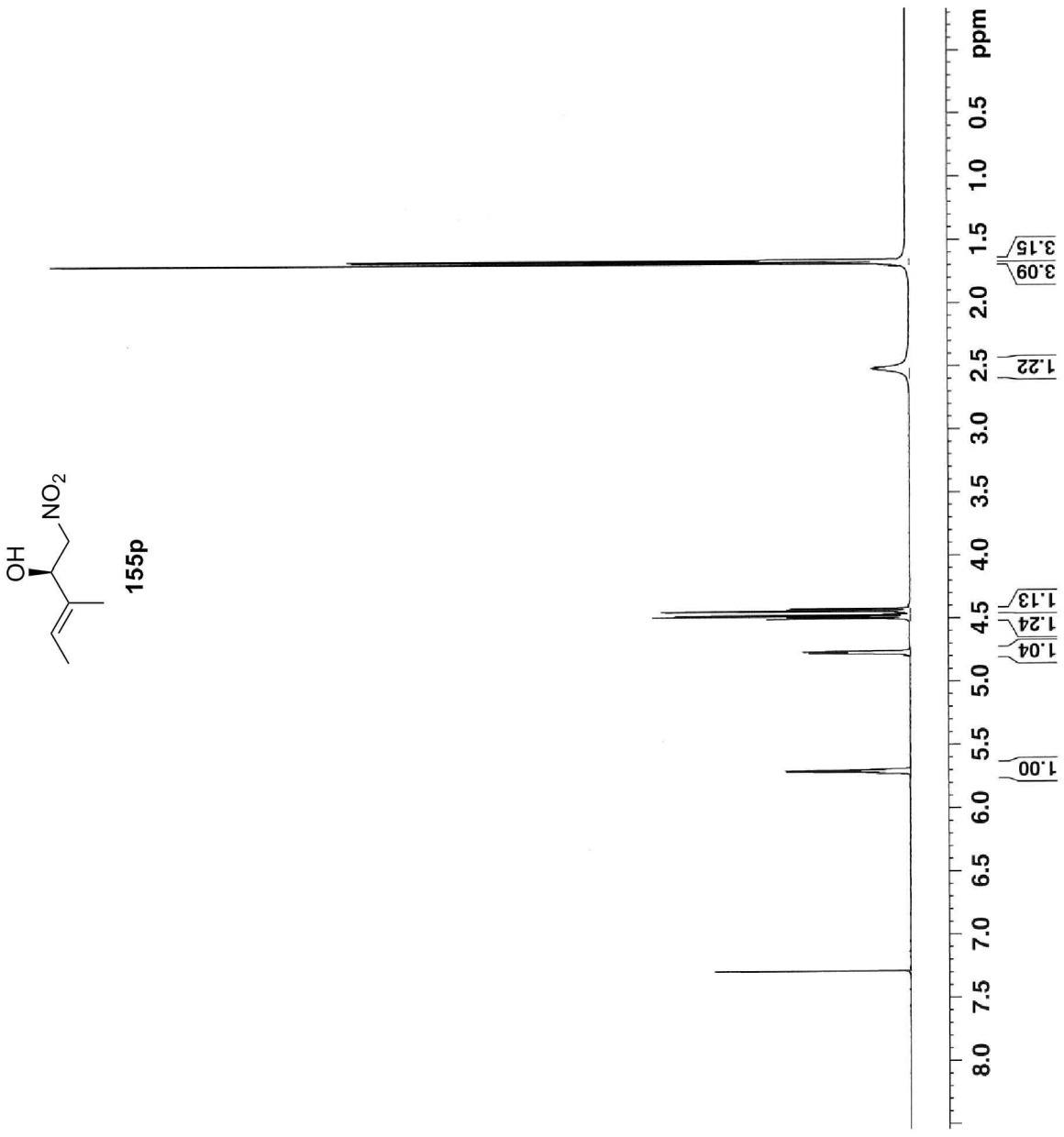

OH
NO2
155o
NAME SS-07-110
EXPNO 1
PROCNO 1
Date_ 20120823
Time 17.37
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 11
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 12.7
DW 42.000 usec
DE 6.50 usec
TE 295.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
8.62
0.92
0.95
0.96
1.00
ppm

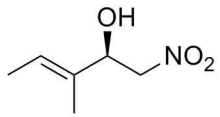


155o

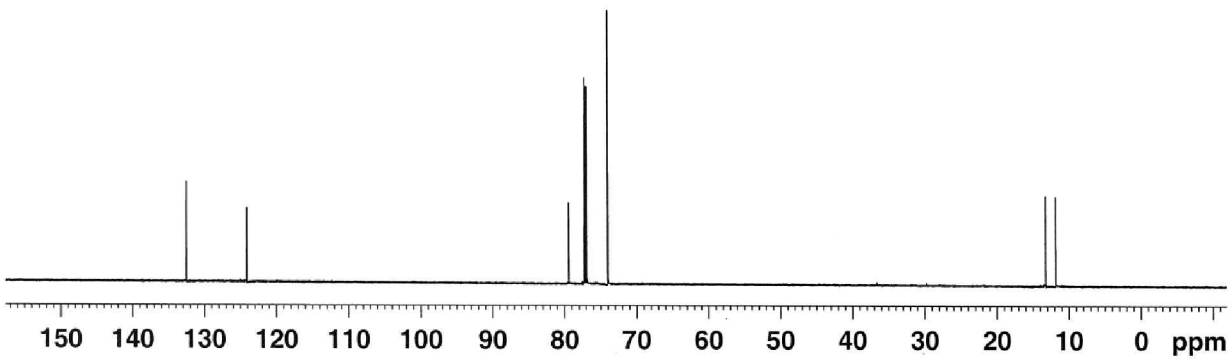


NAME	SS-07-110
EXPNO	2
PROCNO	1
Date_	20120823
Time	17.39
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	17
DS	4
SWH	41666.668 Hz
FIDRES	0.635783 Hz
AQ	0.7864820 sec
RG	203
DW	12.000 usec
DE	16.50 usec
TE	295.2 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 usec
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0697436 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 usec
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1499406 MHz
SI	32768
SF	176.0521380 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.00

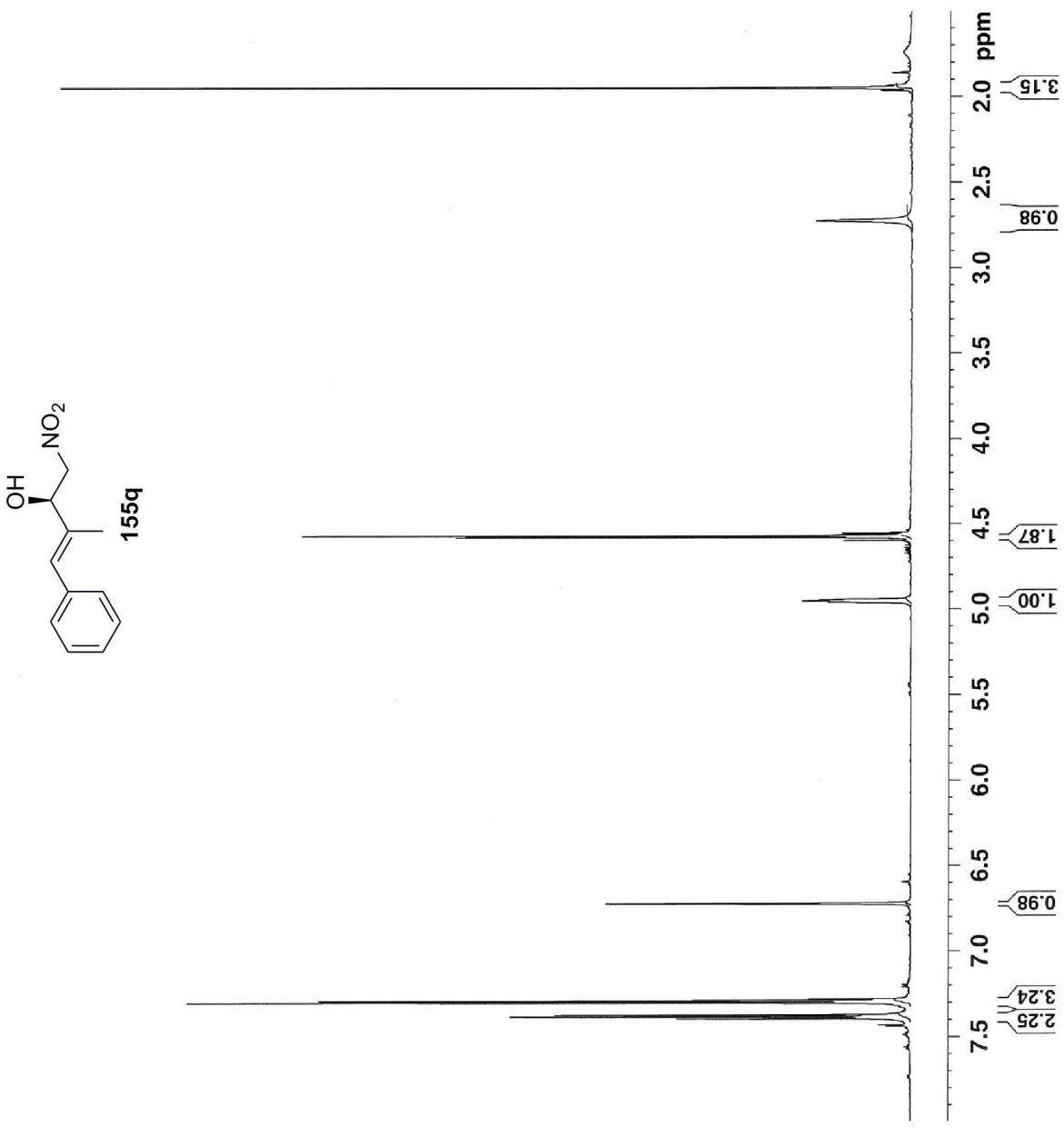

OH
NO2
155p
NAME SS-07-62
EXPNO 3
PROCNO 1
Date_ 20120205
Time 12.17
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 15
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 25.4
DW 42.000 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.00
1.04
1.24
1.13
1.22
3.09
3.15

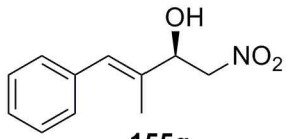


155p



NAME	SS-07-62
EXPNO	2
PROCNO	1
Date_	20120205
Time	12.04
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	37
DS	4
SWH	41666.668 Hz
FIDRES	0.635783 Hz
AQ	0.7864820 sec
RG	203
DW	12.000 use
DE	6.50 use
TE	298.2 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 use
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0697436 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 use
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1499406 MHz
SI	32768
SF	176.0521380 MHz
WDW	no
SSB	0
LB	0.00 Hz
GB	0
PC	1.00


OH
NO2
155q
NAME SS-07-47
EXPNO 1
PROCNO 1
Date_ 20120130
Time 12.29
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 95236
SOLVENT CDC13
NS 23
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 se
RG 90.5
DW 42.000 us
DE 6.50 us
TE 298.1 K
D1 2.00000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 13.75 us
PL1 -3.00 dB
PL1W 32.08600616 W
SFO1 700.1516910 MH
SI 131072
SF 700.1471400 MH
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
ppm
2.25
3.24
0.98
1.00
1.87
0.98
3.15



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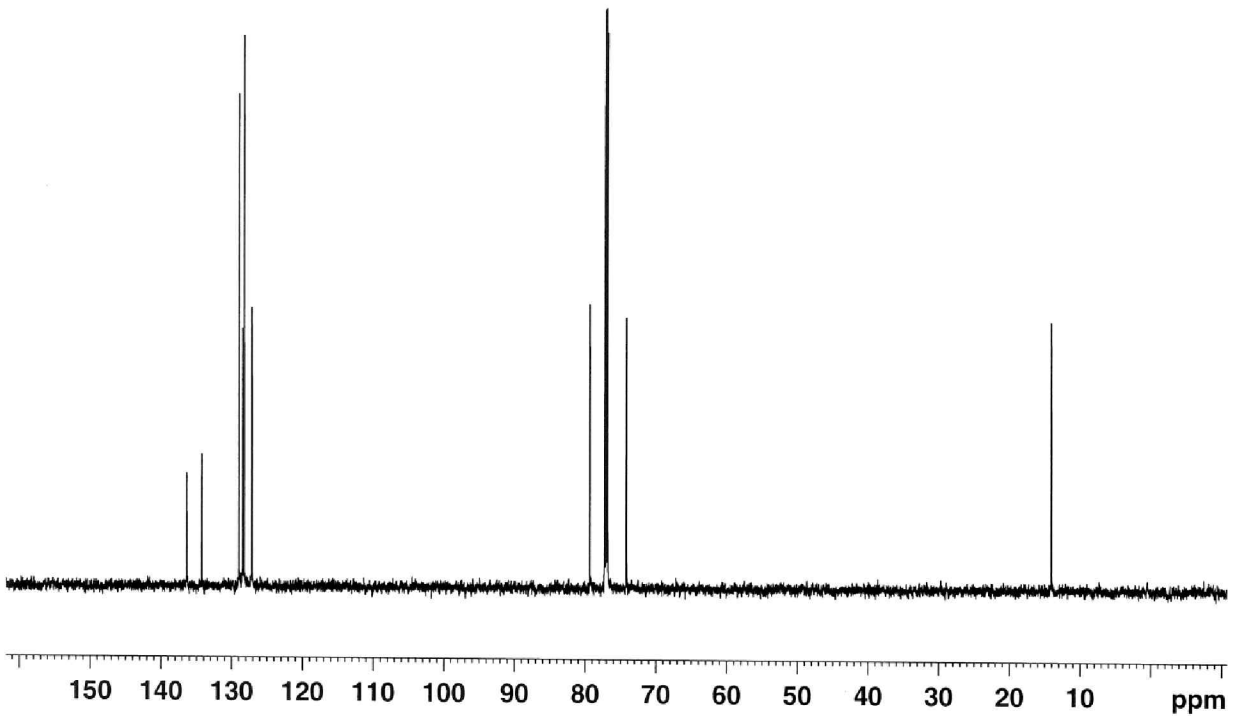
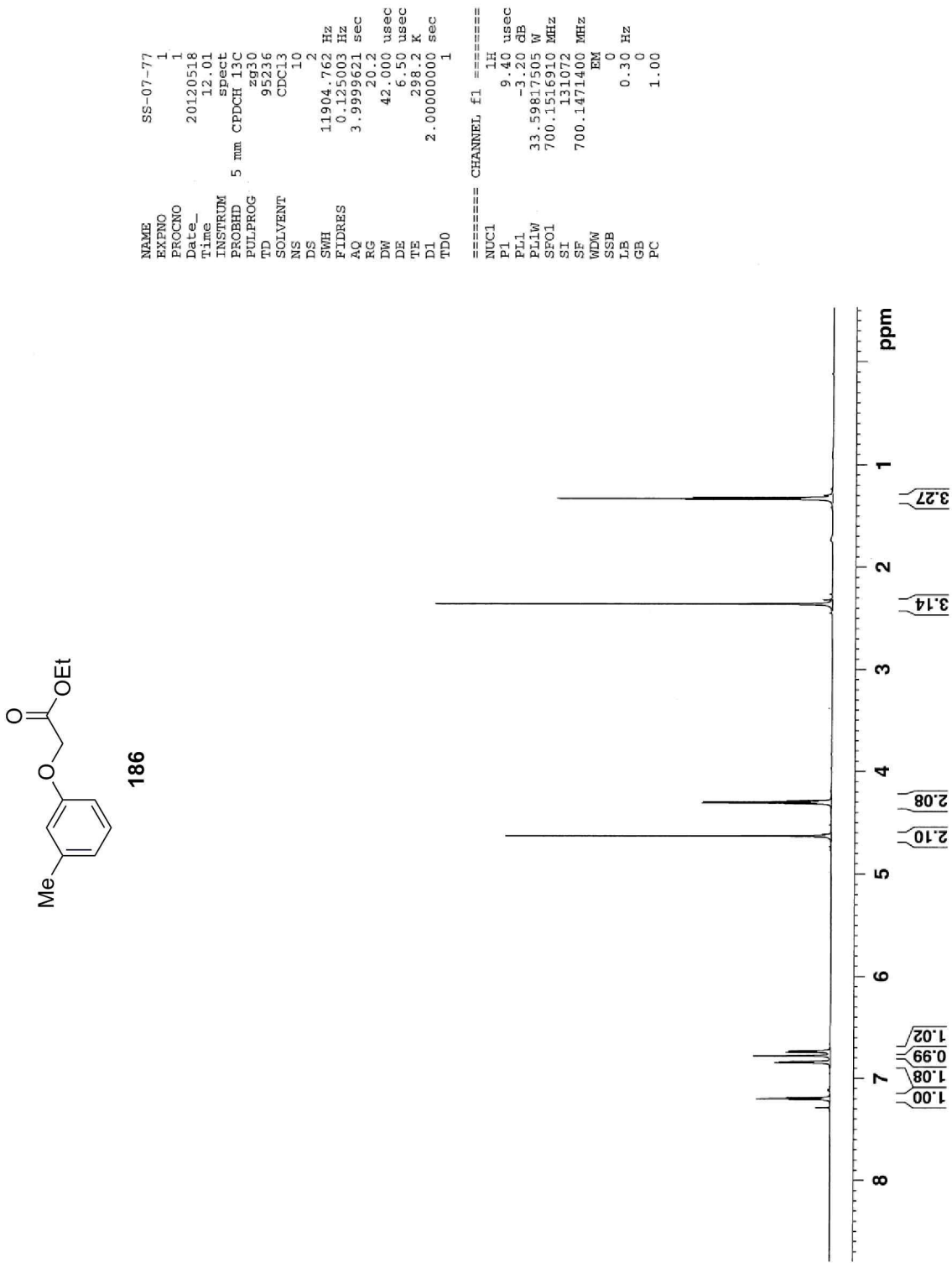
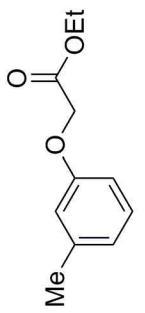


NAME	SS-07-47	
EXPNO	2	
PROCNO	1	
Date_	20120130	
Time	12.33	
INSTRUM	spect	
PROBHD	5 mm PABBO BB-	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	75	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	usec
DE	6.50	usec
TE	298.6	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
========	CHANNEL f1	========
NUC1	13C	
P1	9.30	usec
PL1	2.00	dB
PL1W	67.83342743	W
SFO1	176.0697436	MHz
========	CHANNEL f2	========
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	80.00	usec
PL2	-3.00	dB
PL12	12.30	dB
PL13	12.30	dB
PL2W	32.08600616	W
PL12W	0.94692516	W
PL13W	0.94692516	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.00	


O
OEt
O
Me
186
NAME SS-07-77
EXPNO 1
PROCNO 1
Date_ 20120518
Time 12.01
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 10
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 20.2
DW 42.000 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
3.27
3.14
2.08
2.10
1.00
1.08
0.99
1.02
ppm
8
7
6
5
4
3
2
1



186

```
NAME                SS-07-77
EXPNO                      2
PROCNO                     1
Date_               20120518
Time                   12.05
INSTRUM                spect
PROBHD  5 mm CPDCH 13C
PULPROG                zgpg30
TD                      65536
SOLVENT                CDC13
NS                         31
DS                          4
SWH                 41666.668 Hz
FIDRES              0.635783 Hz
AQ                  0.7864820 sec
RG                        203
DW                     12.000 usec
DE                     16.50 usec
TE                     298.2 K
D1                  2.00000000 sec
D11                 0.03000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                      13C
P1                     9.00 usec
PL1                    4.50 dB
PL1W            38.14553833 W
SFO1            176.0697436 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                  65.00 usec
PL2                    -3.20 dB
PL12                   13.60 dB
PL13                  120.00 dB
PL2W            33.59817505 W
PL12W            0.70196527 W
PL13W            0.00000000 W
SFO2            700.1499406 MHz
SI                      32768
SF              176.0521380 MHz
WDW                        EM
SSB                         0
LB                     3.00 Hz
GB                          0
PC                      1.00
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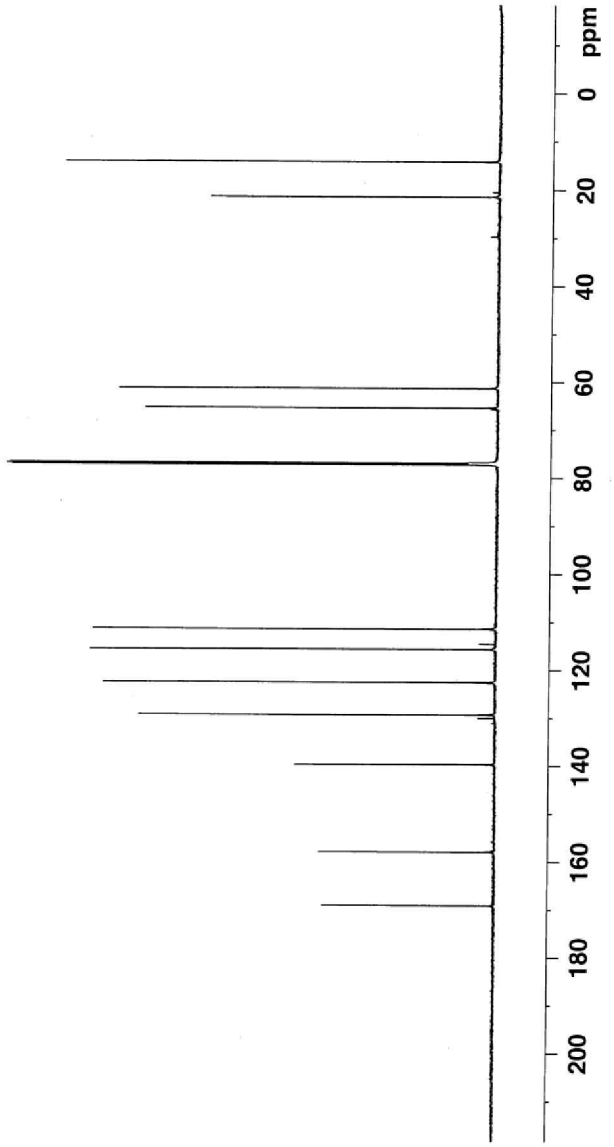
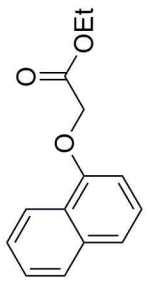
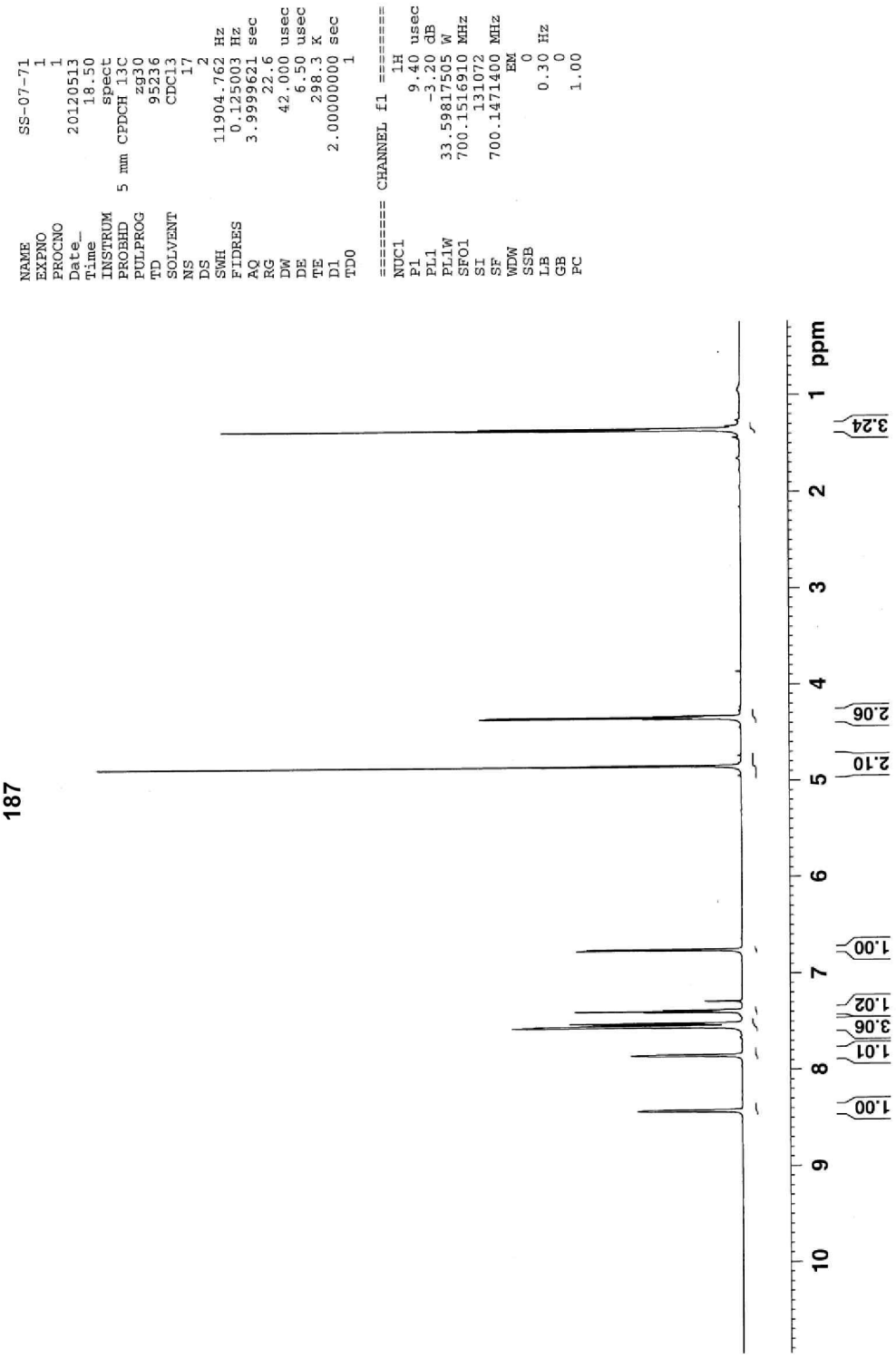
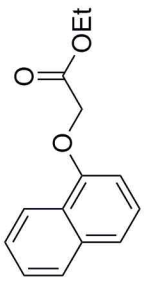


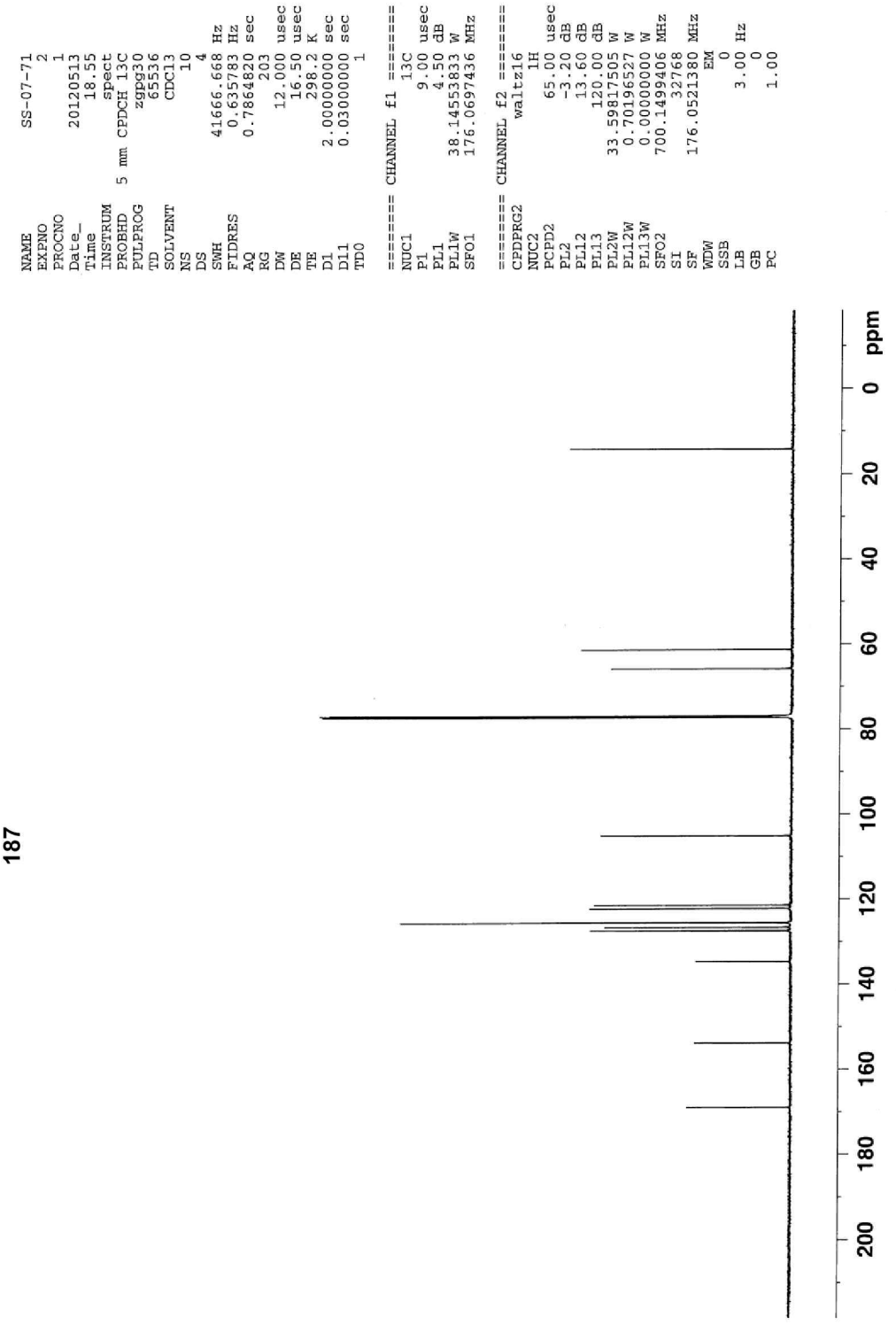


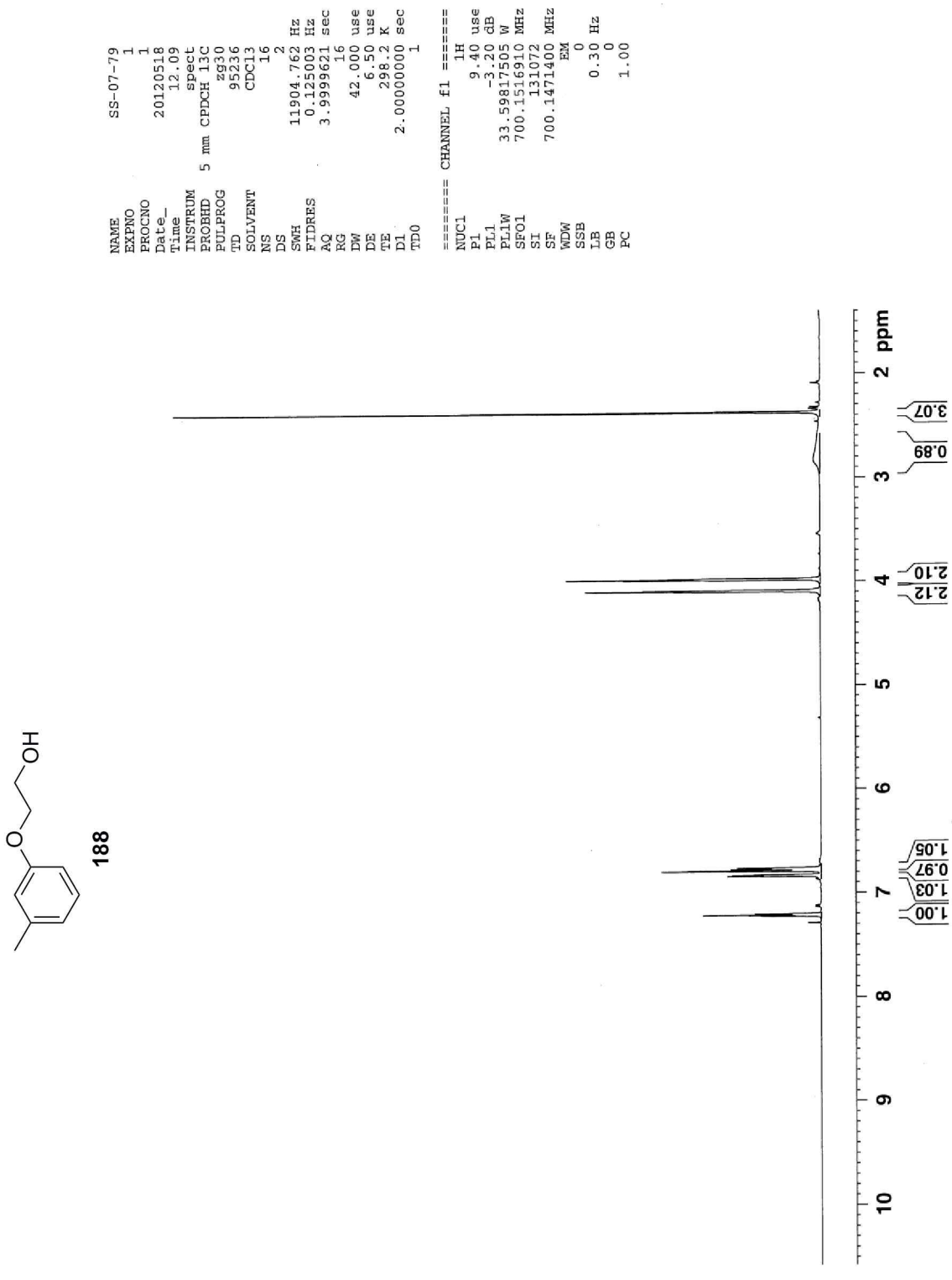
187

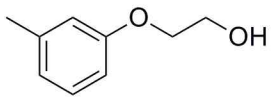

NAME SS-07-71
EXPNO 1
PROCNO 1
Date_ 20120513
Time_ 18.50
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 17
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 22.6
DW 42.000 usec
DE 6.50 usec
TE 298.3 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
10
9
8
7
6
5
4
3
2
1 ppm
1.00
1.01
3.06
1.02
1.00
2.10
2.06
3.24



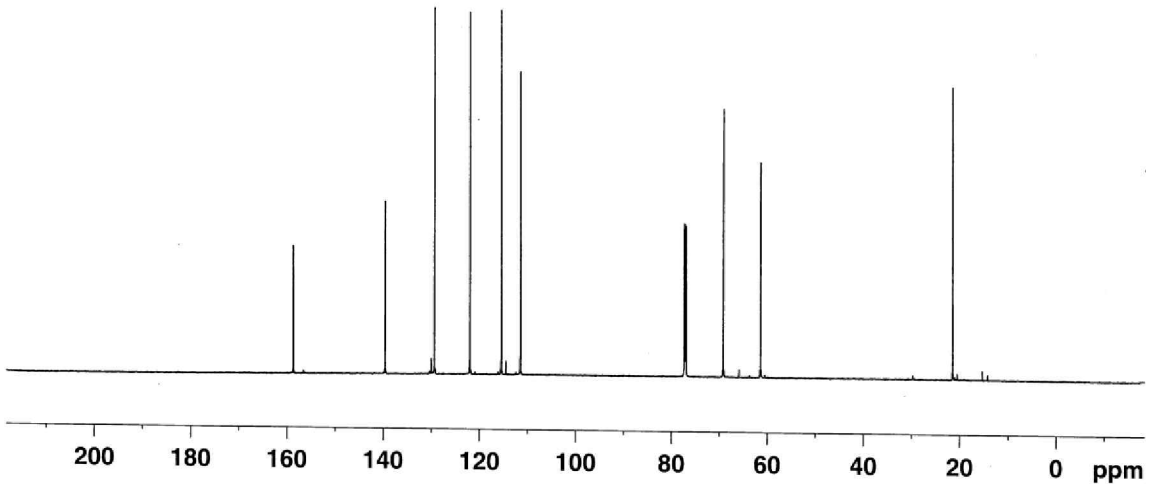
187


NAME SS-07-71
EXPNO 2
PROCNO 1
Date_ 20120513
Time 18.55
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 10
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864820 sec
RG 203
DW 12.000 usec
DE 16.50 usec
TE 298.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0697436 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 usec
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1499406 MHz
SI 32768
SF 176.0521380 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.00
200
180
160
140
120
100
80
60
40
20
0
ppm

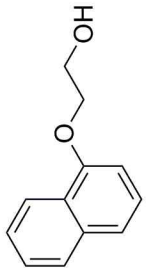

188
NAME SS-07-79
EXPNO 1
PROCNO 1
Date_ 20120518
Time 12.09
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 16
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 16
DW 42.000 use
DE 6.50 use
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 use
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
10
9
8
7
6
5
4
3
2 ppm
1.00
1.03
0.97
1.05
2.12
2.10
0.89
3.07



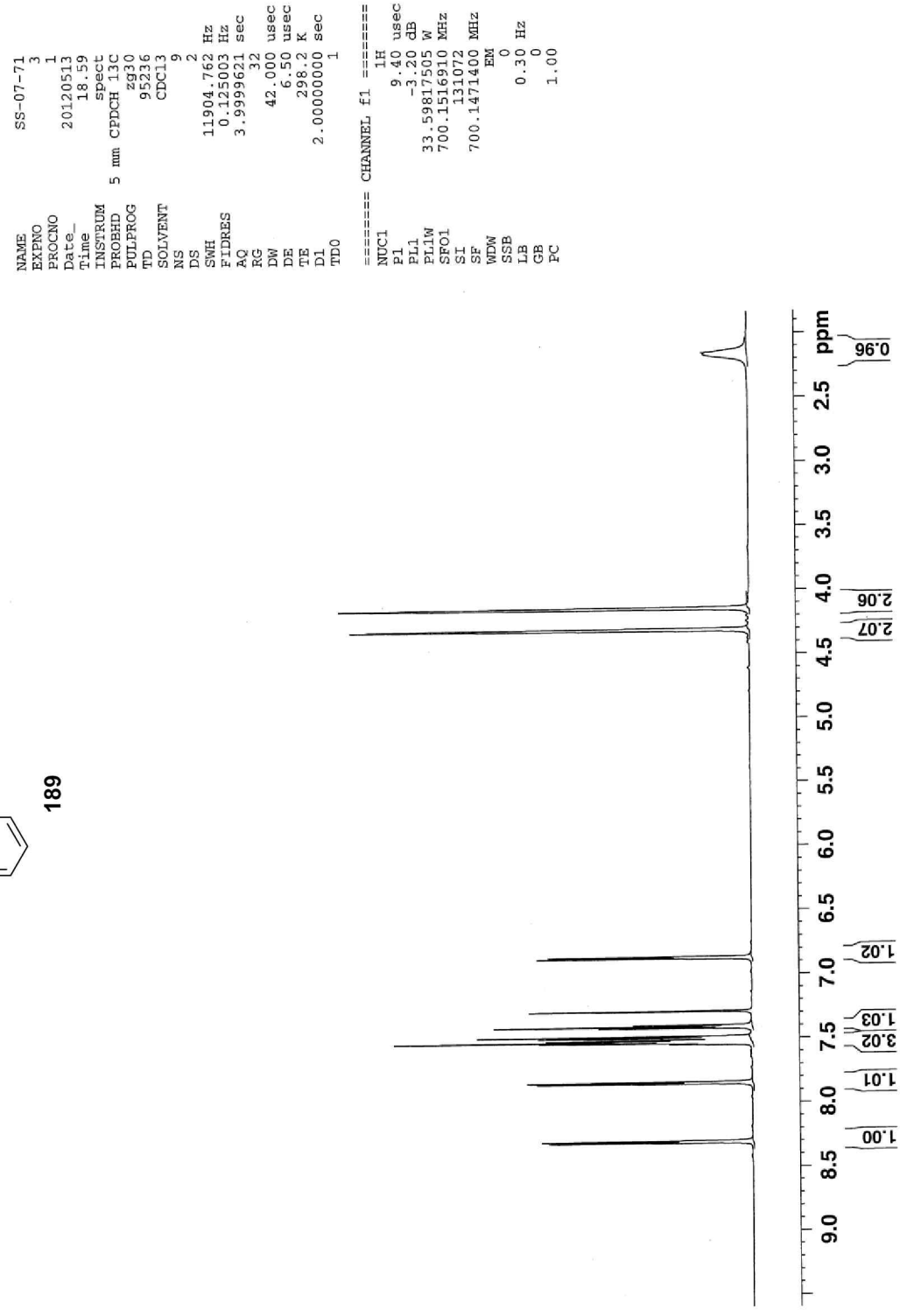
188

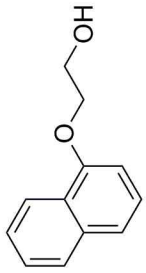


NAME	SS-07-79	
EXPNO	2	
PROCNO	1	
Date_	20120518	
Time	12.14	
INSTRUM	spect	
PROBHD	5 mm CPDCH 13C	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	34	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	usec
DE	16.50	usec
TE	298.2	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	9.00	usec
PL1	4.50	dB
PL1W	38.14553833	W
SFO1	176.0697436	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	65.00	usec
PL2	-3.20	dB
PL12	13.60	dB
PL13	120.00	dB
PL2W	33.59817505	W
PL12W	0.70196527	W
PL13W	0.00000000	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.00	

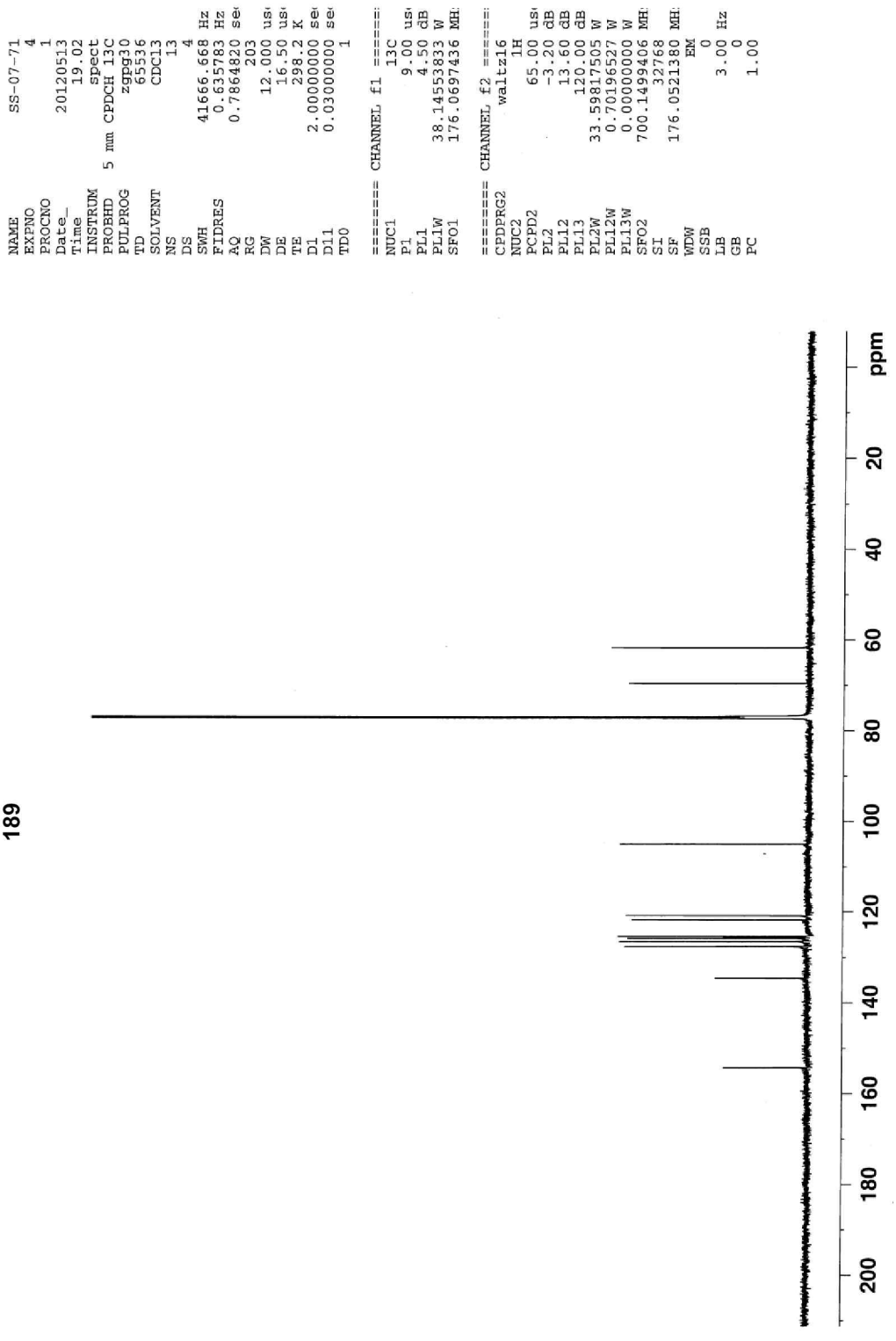


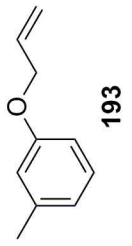
189


NAME SS-07-71
EXPNO 3
PROCNO 1
Date_ 20120513
Time 18.59
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 9
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 32
DW 42.000 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
ppm
1.00
1.01
3.02
1.03
1.02
2.07
2.06
0.96



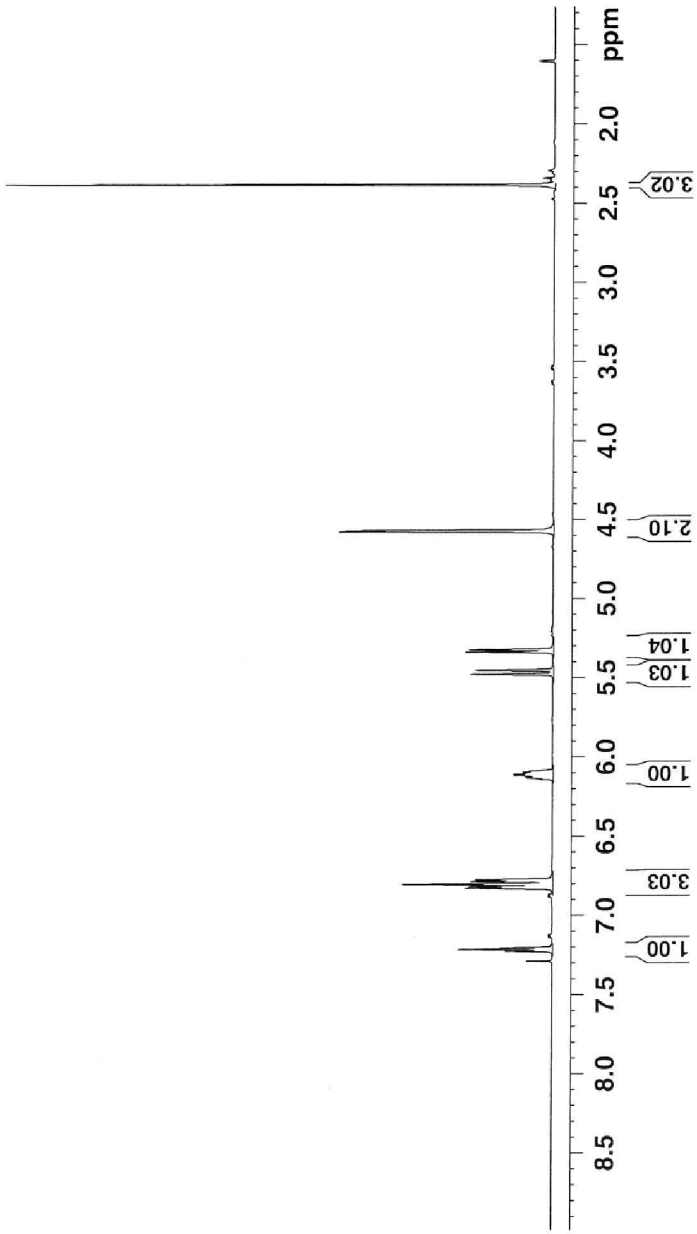
189

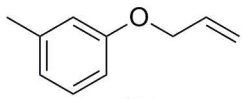

NAME SS-07-71
EXPNO 4
PROCNO 1
Date_ 20120513
Time 19.02
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDC13
NS 13
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864820 se
RG 203
DW 12.000 us
DE 16.50 us
TE 298.2 K
D1 2.00000000 se
D11 0.03000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 13C
P1 9.00 us
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0697436 MH
======== CHANNEL f2 ======
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 us
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1499406 MH
SI 32768
SF 176.0521380 MH
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.00
200
180
160
140
120
100
80
60
40
20
ppm



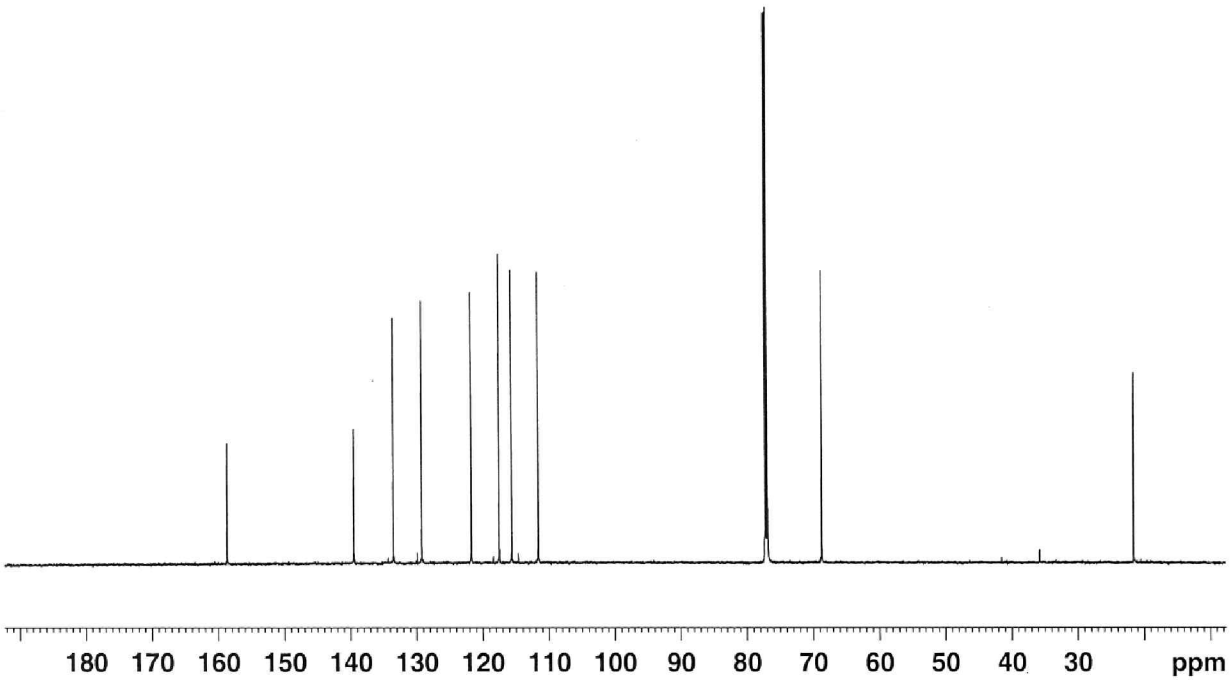
193

```
NAME          SS-07-88
EXPNO                1
PROCNO               1
Date_         20120614
Time             11.56
INSTRUM           spect
PROBHD   5 mm CPDCH 13C
PULPROG            zg30
TD                95236
SOLVENT           CDCl3
NS                    8
DS                    2
SWH           11904.762 Hz
FIDRES            0.125003 Hz
AQ                3.9999621 sec
RG                   20.2
DW                42.000 usec
DE                 6.50 usec
TE                298.2 K
D1                2.00000000 sec
TD0                   1

======== CHANNEL f1 ======
NUC1                 1H
P1                9.40 usec
PL1               -3.20 dB
PL1W        33.59817505 W
SFO1        700.1516910 MHz
SI               131072
SF          700.1471400 MHz
WDW                 EM
SSB                  0
LB                0.30 Hz
GB                   0
PC                1.40
```

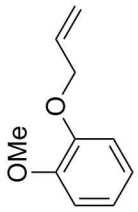




193

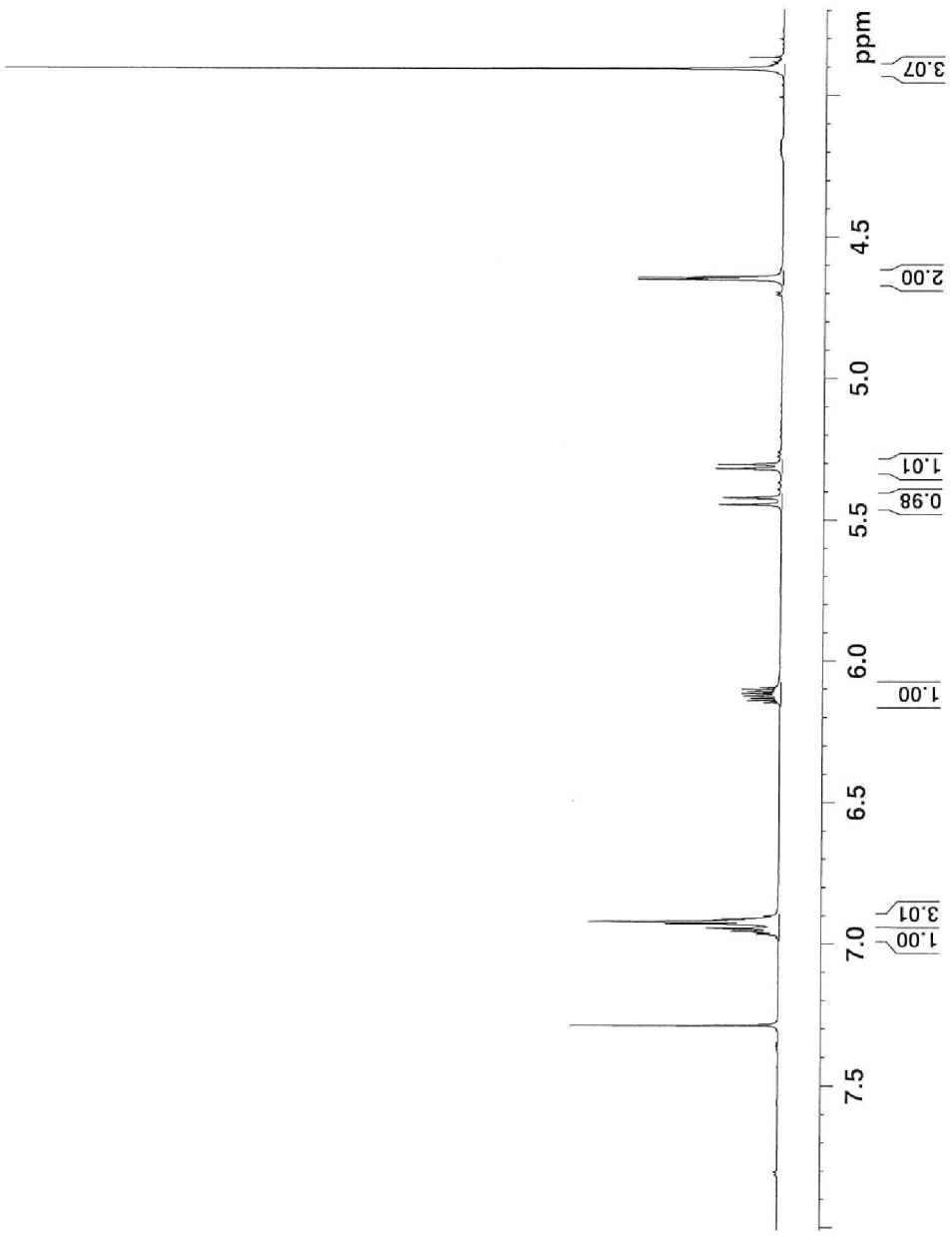


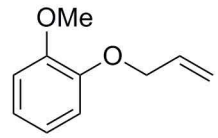
NAME	SS-07-88
EXPNO	2
PROCNO	1
Date_	20120614
Time	12.00
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	11
DS	4
SWH	41666.668 Hz
FIDRES	0.635783 Hz
AQ	0.7864820 sec
RG	203
DW	12.000 use
DE	16.50 use
TE	298.2 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 =======	
NUC1	13C
P1	9.00 use
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0697436 MHz
======== CHANNEL f2 =======	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 use
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1499406 MHz
SI	32768
SF	176.0521380 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40



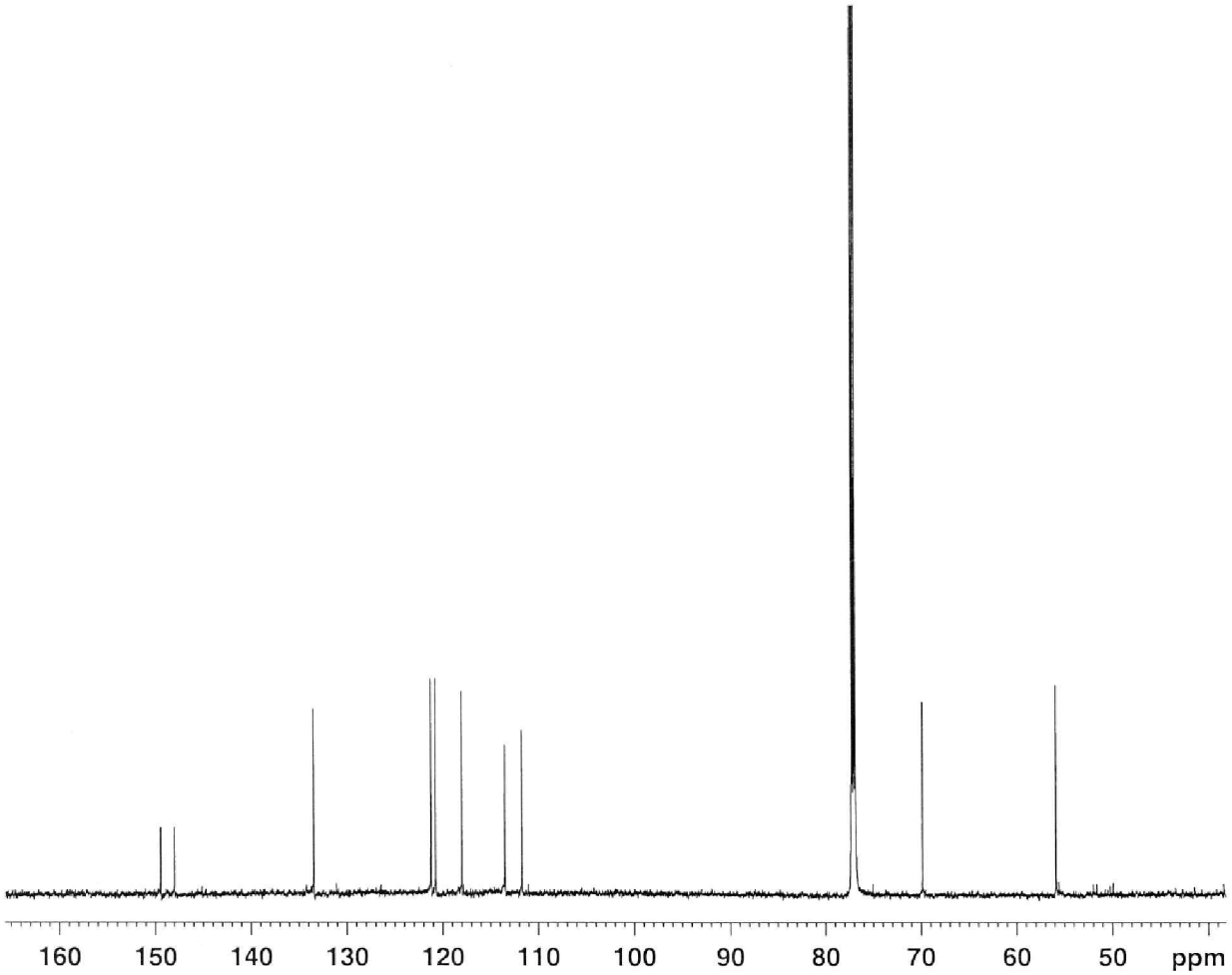
195

```
NAME                SS-07-97
EXPNO                     19
PROCNO                     1
Date_               20120806
Time                   14.52
INSTRUM                spect
PROBHD     5 mm CPDCH 13C
PULPROG                 zg30
TD                     95236
SOLVENT                CDCl3
NS                        21
DS                         2
SWH                11904.762 Hz
FIDRES             0.125003 Hz
AQ                 3.9999621 sec
RG                      22.6
DW                     42.000 usec
DE                      6.50 usec
TE                     295.2 K
D1                 2.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                      9.40 usec
PL1                    -3.20 dB
PL1W               33.59817505 W
SFO1               700.1516910 MHz
SI                     131072
SF                 700.1471400 MHz
WDW                        EM
SSB                         0
LB                       0.30 Hz
GB                          0
PC                       1.00
```

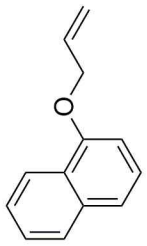




195

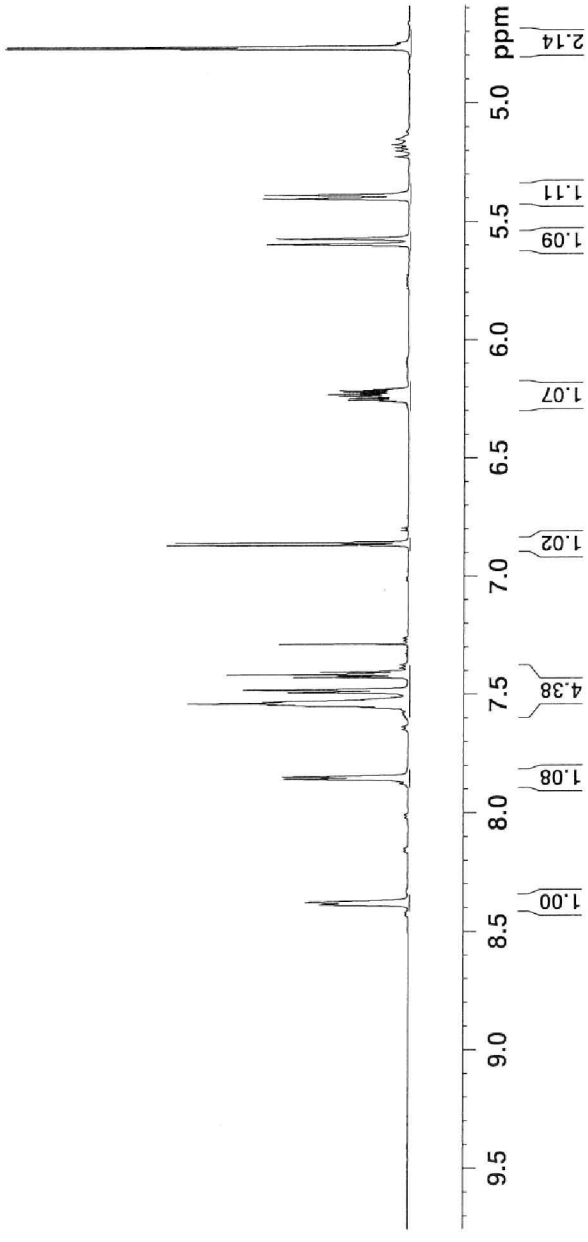


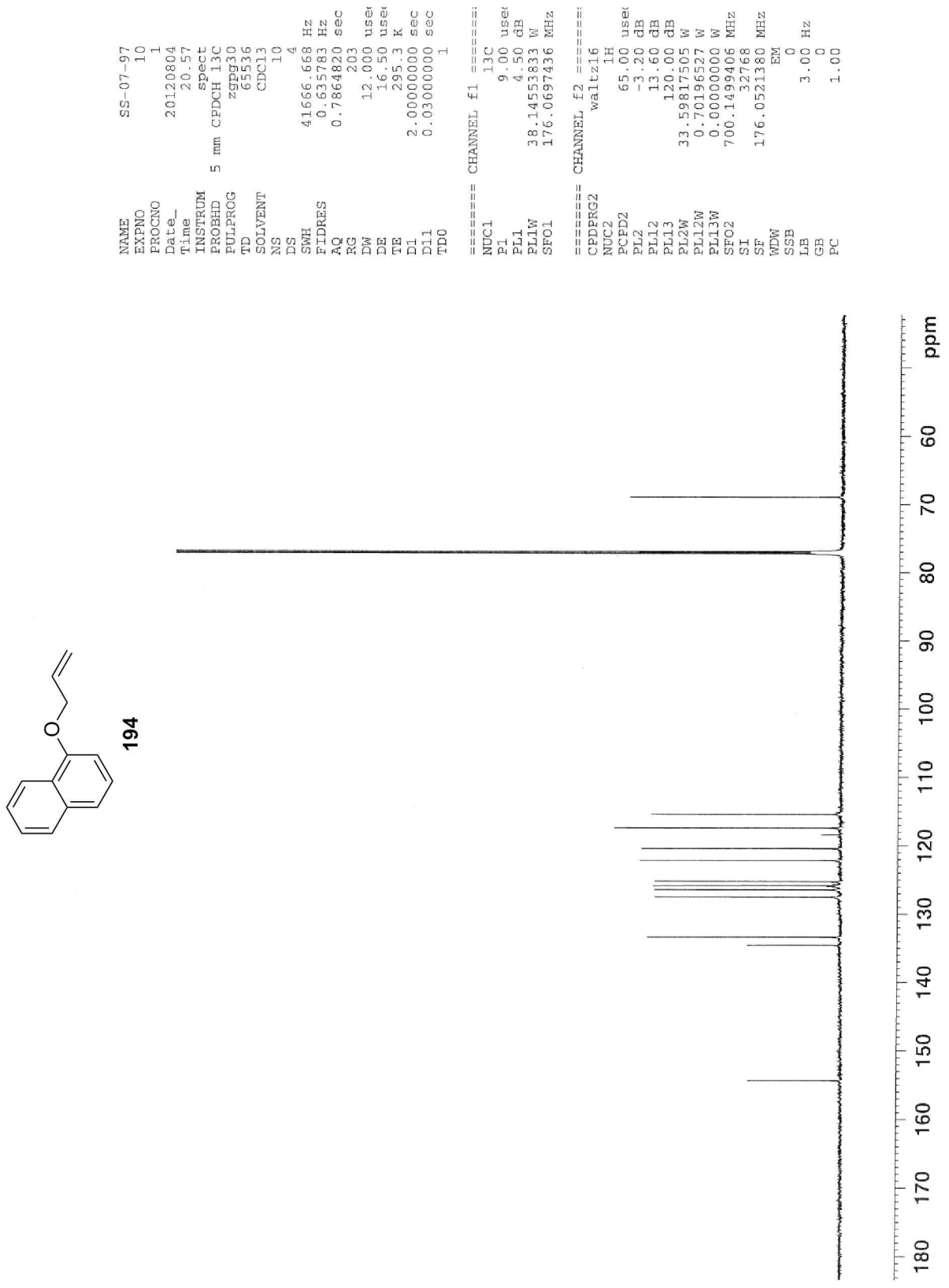
NAME	SS-07-97
EXPNO	20
PROCNO	1
Date_	20120806
Time	14.57
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	61
DS	4
SWH	41666.668 Hz
FIDRES	0.635783 Hz
AQ	0.7864820 sec
RG	203
DW	12.000 usec
DE	16.50 usec
TE	295.2 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 usec
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0697436 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 usec
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1499406 MHz
SI	32768
SF	176.0521380 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.00

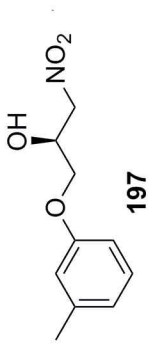


194

```
NAME                SS-07-97
EXPNO                      9
PROCNO                     1
Date_               20120804
Time                   20.52
INSTRUM                spect
PROBHD     5 mm CPDCH 13C
PULPROG                 zg30
TD                     95236
SOLVENT                CDCl3
NS                        10
DS                         2
SWH                11904.762 Hz
FIDRES             0.125003 Hz
AQ                 3.9999621 sec
RG                      22.6
DW                     42.000 use
DE                      6.50 use
TE                     295.2 K
D1                 2.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                      9.40 use
PL1                    -3.20 dB
PL1W               33.59817505 W
SFO1               700.1516910 MHz
SI                      131072
SF                 700.1471400 MHz
WDW                        EM
SSB                         0
LB                       0.30 Hz
GB                          0
PC                       1.00
```

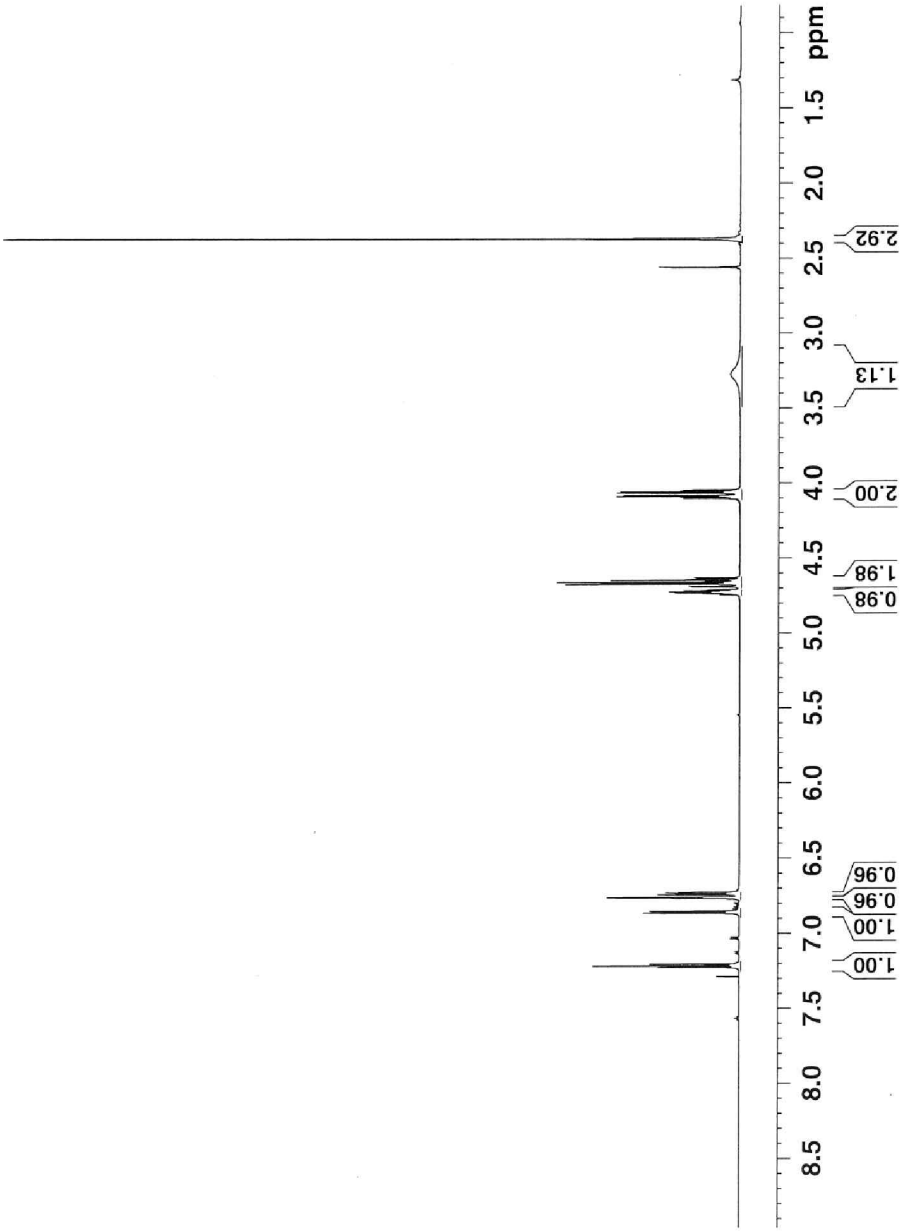


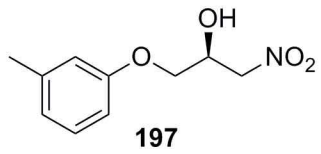

194
NAME SS-07-97
EXPNO 10
PROCNO 1
Date_ 20120804
Time 20.57
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 10
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864820 sec
RG 203
DW 12.000 use
DE 16.50 use
TE 295.3 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 use
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0697436 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 use
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1499406 MHz
SI 32768
SF 176.0521380 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.00
180 170 160 150 140 130 120 110 100 90 80 70 60 ppm



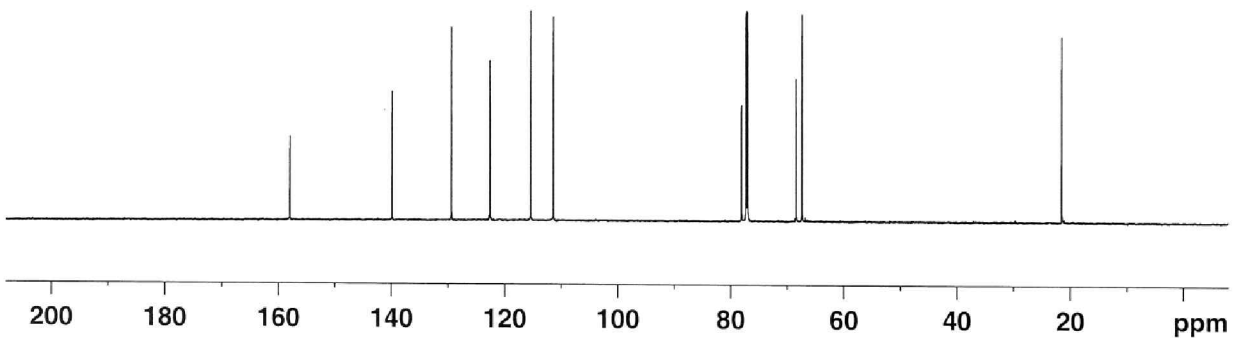
197

```
NAME                SS-07-93
EXPNO                      1
PROCNO                     1
Date_               20120615
Time                    9.29
INSTRUM                 spect
PROBHD     5 mm CPDCH 13C
PULPROG                 zg30
TD                     95236
SOLVENT                CDCl3
NS                         7
DS                         2
SWH                11904.762 Hz
FIDRES             0.125003 Hz
AQ                 3.9999621 sec
RG                        16
DW                    42.000 usec
DE                     6.50 usec
TE                    298.2 K
D1                 2.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     9.40 usec
PL1                    -3.20 dB
PL1W               33.59817505 W
SFO1               700.1516910 MHz
SI                       131072
SF                 700.1471400 MHz
WDW                        EM
SSB                         0
LB                      0.30 Hz
GB                          0
PC                       1.40
```

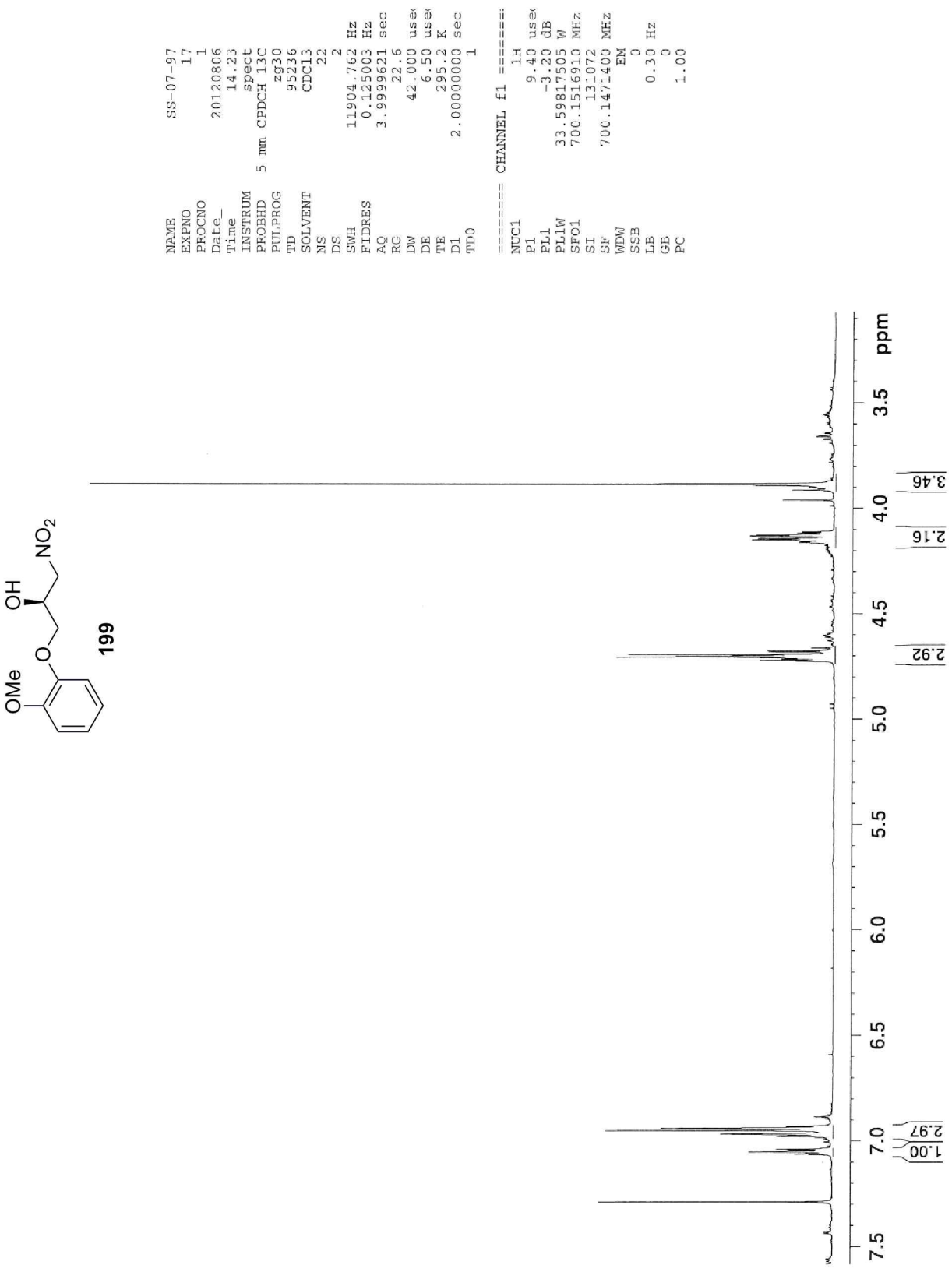


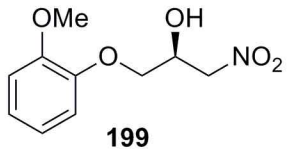


197

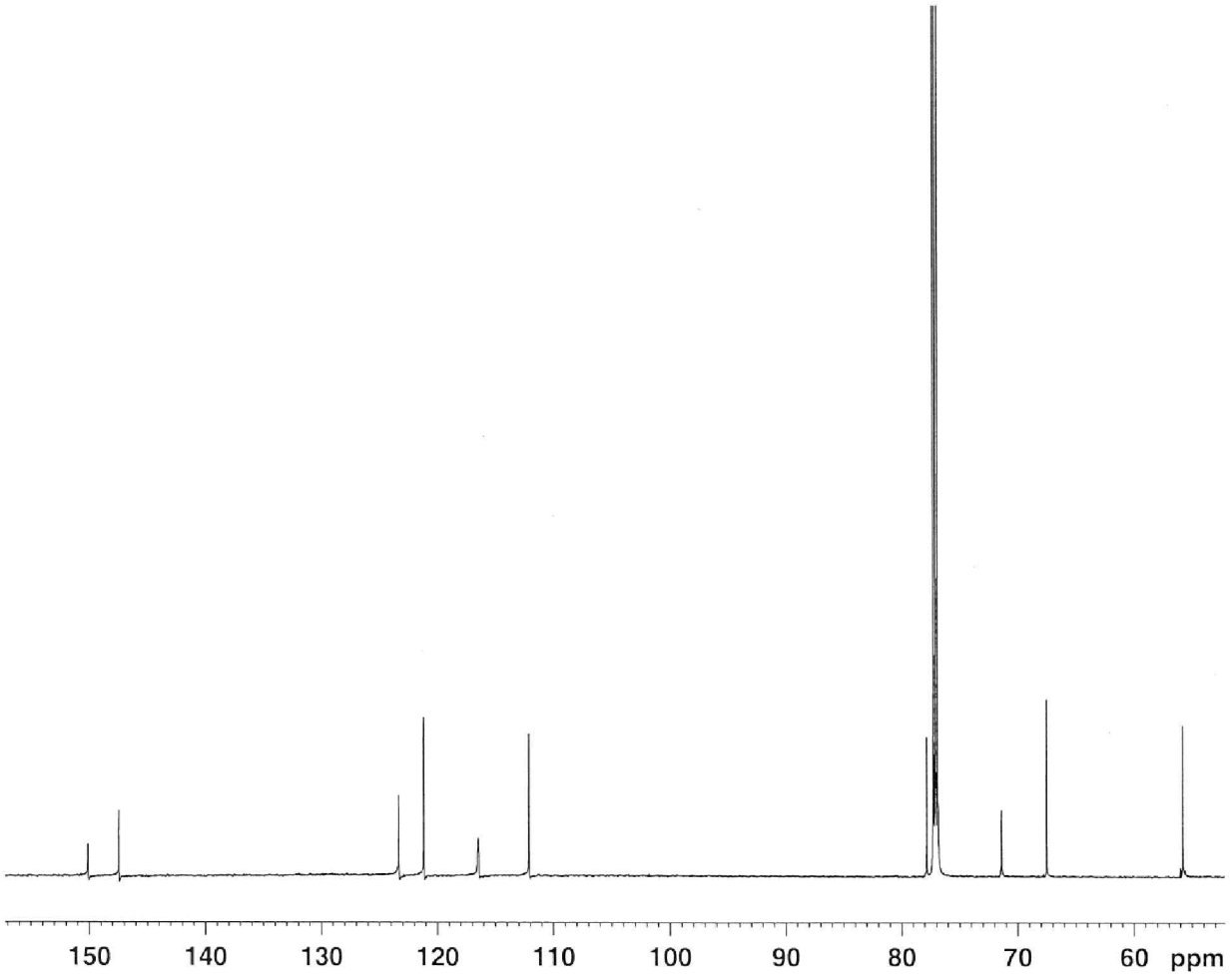


NAME	SS-07-91	
EXPNO	5	
PROCNO	1	
Date_	20120614	
Time	12.12	
INSTRUM	spect	
PROBHD	5 mm CPDCH 13C	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	12	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	usec
DE	16.50	usec
TE	298.2	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	9.00	usec
PL1	4.50	dB
PL1W	38.14553833	W
SFO1	176.0697436	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	65.00	usec
PL2	-3.20	dB
PL12	13.60	dB
PL13	120.00	dB
PL2W	33.59817505	W
PL12W	0.70196527	W
PL13W	0.00000000	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.40	

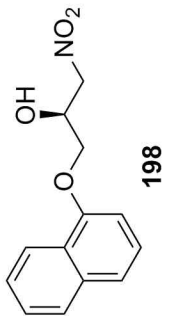

199
OMe
OH
NO2
NAME SS-07-97
EXPNO 17
PROCNO 1
Date_ 20120806
Time 14.23
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDC13
NS 22
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 22.6
DW 42.000 use
DE 6.50 use
TE 295.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 use
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
ppm
1.00
2.97
2.92
2.16
3.46



199

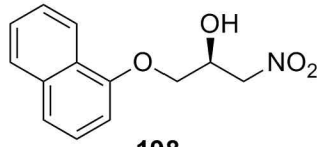


NAME	SS-07-97	
EXPNO	18	
PROCNO	1	
Date_	20120806	
Time	14.26	
INSTRUM	spect	
PROBHD	5 mm CPDCH 13C	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDC13	
NS	210	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	usec
DE	16.50	usec
TE	295.2	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	9.00	usec
PL1	4.50	dB
PL1W	38.14553833	W
SFO1	176.0697436	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	65.00	usec
PL2	-3.20	dB
PL12	13.60	dB
PL13	120.00	dB
PL2W	33.59817505	W
PL12W	0.70196527	W
PL13W	0.00000000	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.00	

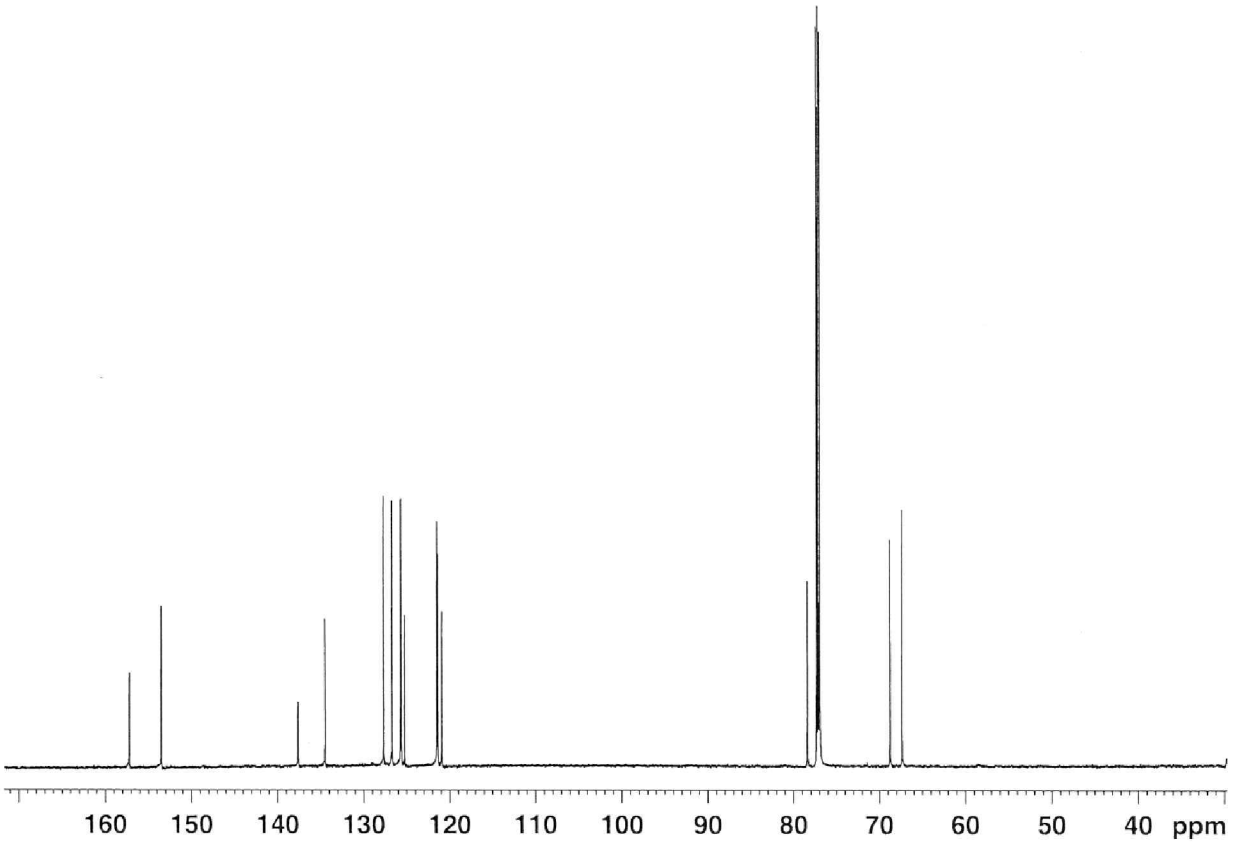


198

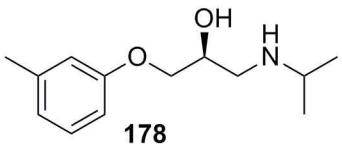
```
NAME                SS-07-97
EXPNO                     15
PROCNO                     1
Date_               20120806
Time                   14.08
INSTRUM                 spect
PROBHD   5 mm CPDCH 13C
PULPROG                 zg30
TD                     95236
SOLVENT                CDCl3
NS                        32
DS                         2
SWH                11904.762 Hz
FIDRES             0.125003 Hz
AQ                 3.9999621 se
RG                      25.4
DW                    42.000 us
DE                     6.50 us
TE                    295.3 K
D1                 2.00000000 se
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     9.40 us
PL1                   -3.20 dB
PL1W               33.59817505 W
SFO1               700.1516910 MH
SI                      131072
SF                 700.1471400 MH
WDW                       EM
SSB                        0
LB                      0.30 Hz
GB                         0
PC                      1.00
```



198



NAME	SS-07-97	
EXPNO	16	
PROCNO	1	
Date_	20120806	
Time	14.15	
INSTRUM	spect	
PROBHD	5 mm CPDCH 13C	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	40	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	use
DE	16.50	use
TE	295.2	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	9.00	use
PL1	4.50	dB
PL1W	38.14553833	W
SFO1	176.0697436	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	65.00	use
PL2	-3.20	dB
PL12	13.60	dB
PL13	120.00	dB
PL2W	33.59817505	W
PL12W	0.70196527	W
PL13W	0.00000000	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.00	



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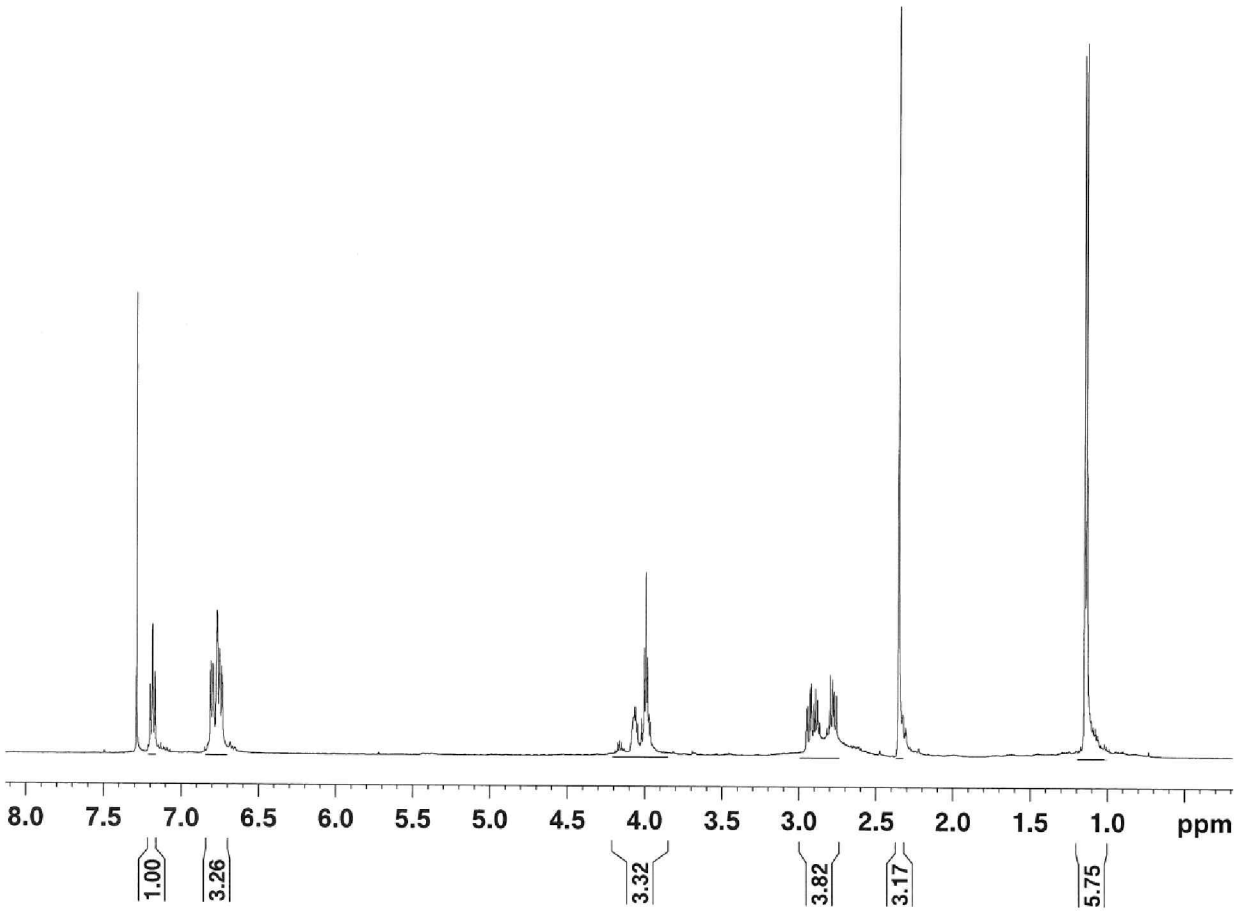
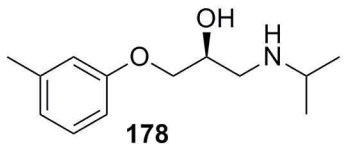


BRUKER

	ameters
NAME	SS-05-05
EXPNO	5
PROCNO	1
F2 - Acquisition Parameters	
Date_	20120723
Time	16.40
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	16
DS	2
SWH	8012.820 Hz
FIDRES	0.122266 Hz
AQ	4.0894465 sec
RG	131.79
DW	62.400 usec
DE	6.50 usec
TE	298.0 K
D1	1.00000000 sec
TD0	1
======== CHANNEL f1 ========	
SFO1	500.1330008 MHz
NUC1	1H
P1	11.50 usec
PLW1	15.00000000 W
F2 - Processing parameters	
SI	65536
SF	500.1300000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00



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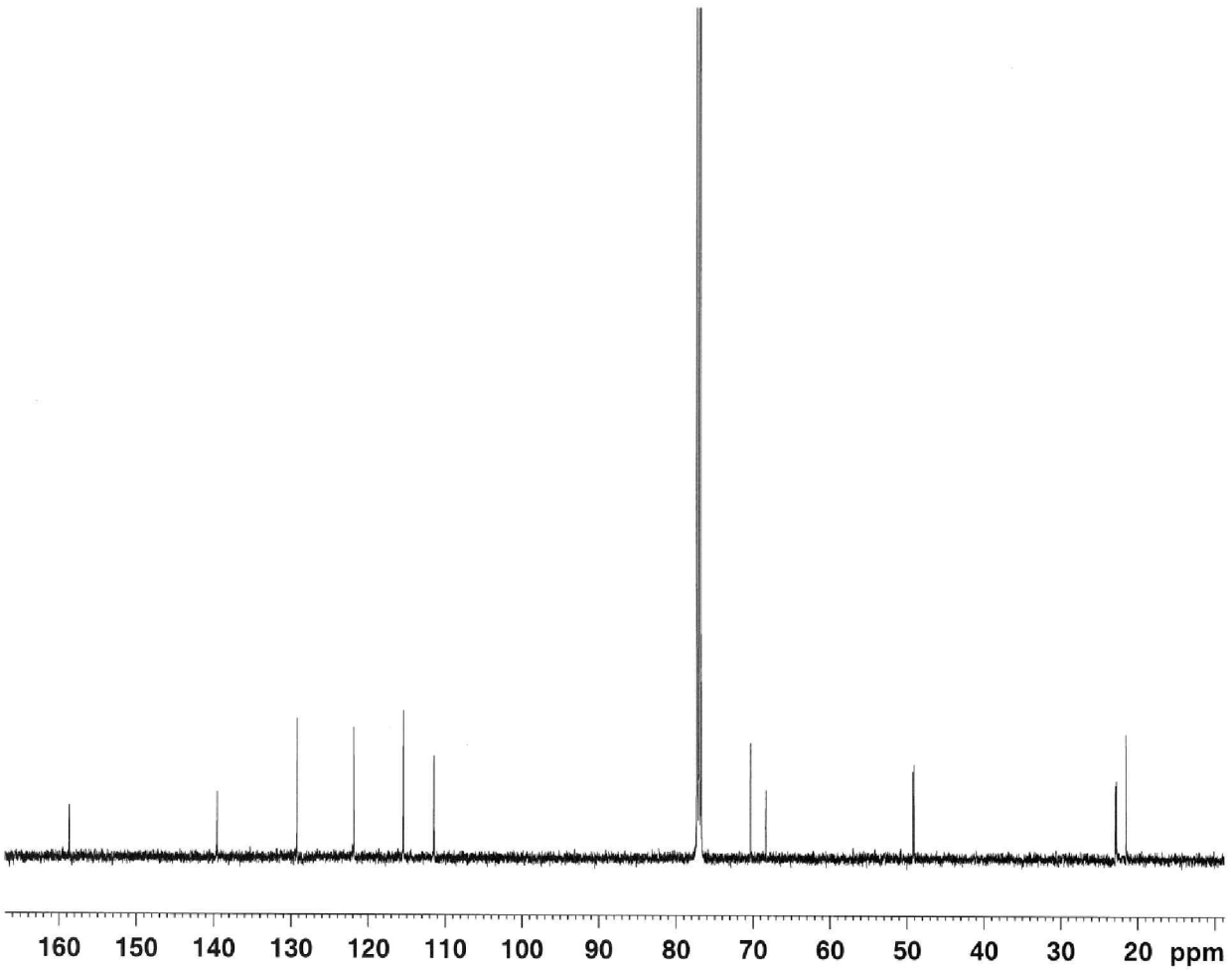
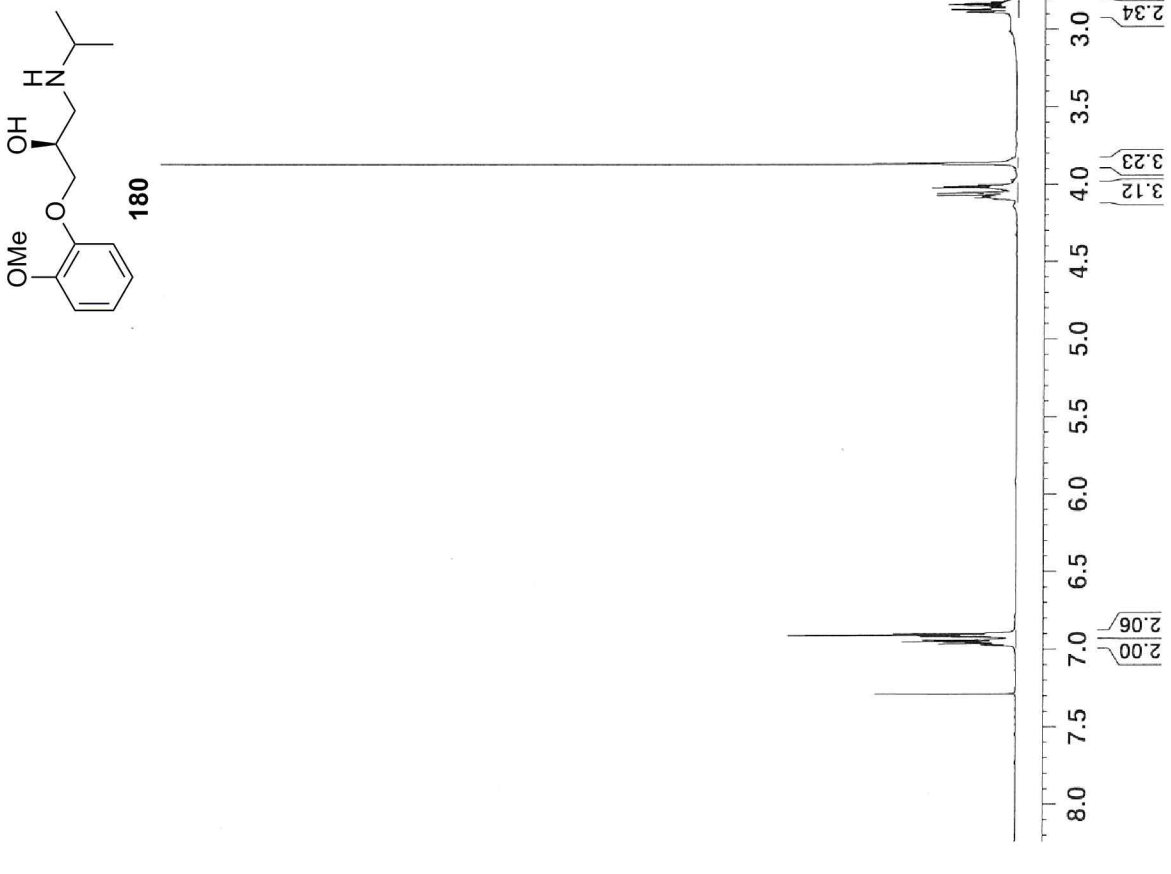
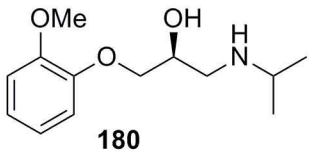


BRUKER

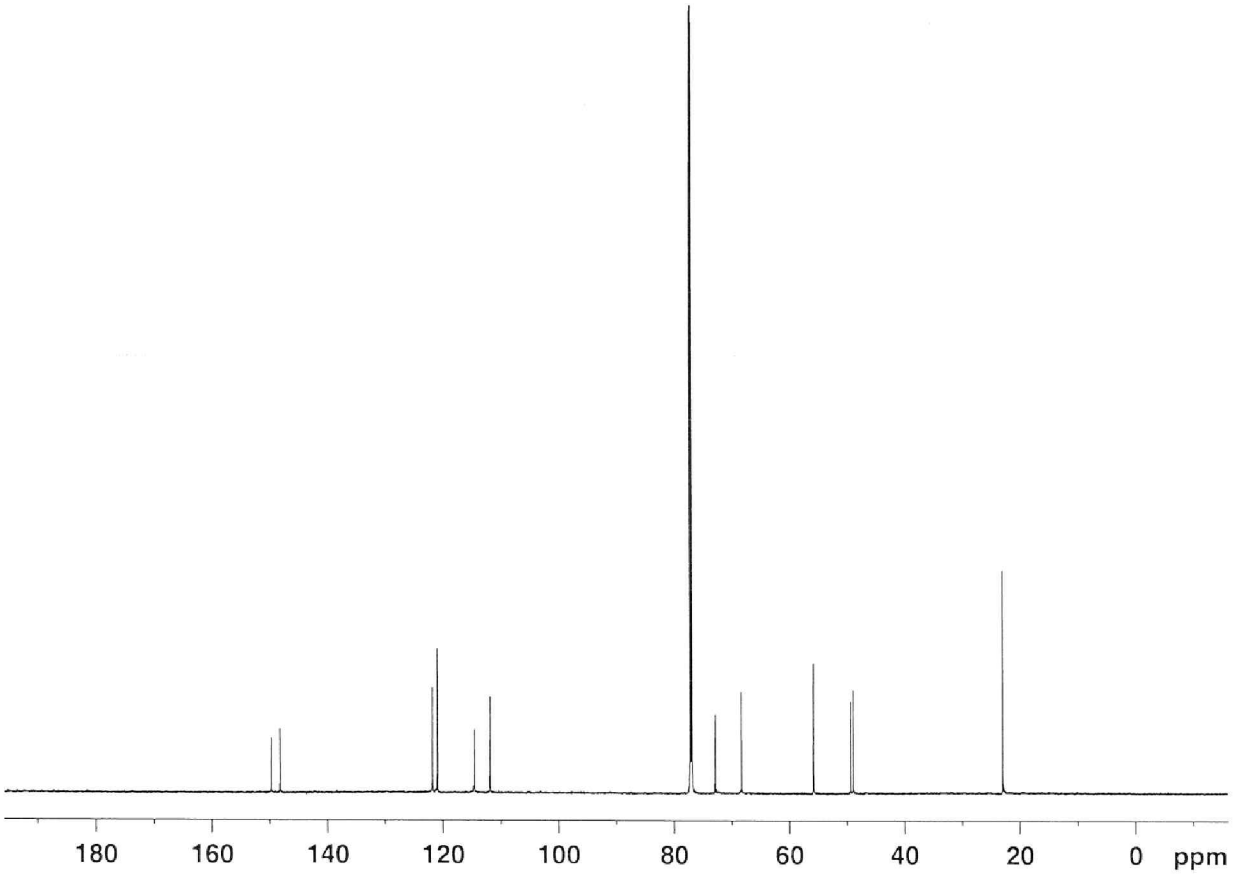
```
Current Data Parameters
NAME                  SS-05-05
EXPNO                        6
PROCNO                       1

F2 - Acquisition Parameters
Date_                 20120723
Time                     16.48
INSTRUM                  spect
PROBHD    5 mm PABBO BB/
PULPROG                zgpg30
TD                      65536
SOLVENT                 CDCl3
NS                       1036
DS                          2
SWH                 35714.285 Hz
FIDRES                0.544957 Hz
AQ                    0.9175040 sec
RG                       190.98
DW                       14.000 usec
DE                        6.50 usec
TE                       298.0 K
D1                  2.00000000 sec
D11                 0.03000000 sec
TD0                          1

======== CHANNEL f1 ========
SFO1               125.7753951 MHz
NUC1                       13C
P1                       10.00 usec
PLW1                84.00000000 W

======== CHANNEL f2 ========
SFO2               500.1320005 MHz
NUC2                       1H
CPDPRG[2                waltz16
PCPD2                    80.00 usec
PLW2                15.00000000 W
PLW12                0.30996001 W
PLW13                0.19836999 W

F2 - Processing parameters
SI                       32768
SF                 125.7577890 MHz
WDW                         EM
SSB          0
LB                        1.00 Hz
GB           0
PC                        1.40
```



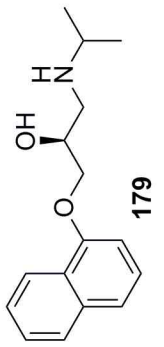

```
NAME                SS-07-97
EXPNO                     37
PROCNO                     1
Date_               20120818
Time                   20.11
INSTRUM                spect
PROBHD   5 mm CPDCH 13C
PULPROG                 zg30
TD                     95236
SOLVENT                CDCl3
NS                        32
DS                         2
SWH                11904.762 Hz
FIDRES             0.125003 Hz
AQ                 3.9999621 sec
RG                      20.2
DW                     42.000 use
DE                      6.50 use
TE                     295.3 K
D1                 2.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                      9.40 use
PL1                    -3.20 dB
PL1W               33.59817505 W
SFO1               700.1516910 MHz
SI                     131072
SF                 700.1471400 MHz
WDW                        EM
SSB                         0
LB                     0.30 Hz
GB                          0
PC                      1.00
```



180



NAME	SS-07-97	
EXPNO	38	
PROCNO	1	
Date_	20120818	
Time	20.18	
INSTRUM	spect	
PROBHD	5 mm CPDCH 13C	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	46	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	use
DE	16.50	use
TE	295.2	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	9.00	use
PL1	4.50	dB
PL1W	38.14553833	W
SFO1	176.0697436	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	65.00	use
PL2	-3.20	dB
PL12	13.60	dB
PL13	120.00	dB
PL2W	33.59817505	W
PL12W	0.70196527	W
PL13W	0.00000000	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.00	



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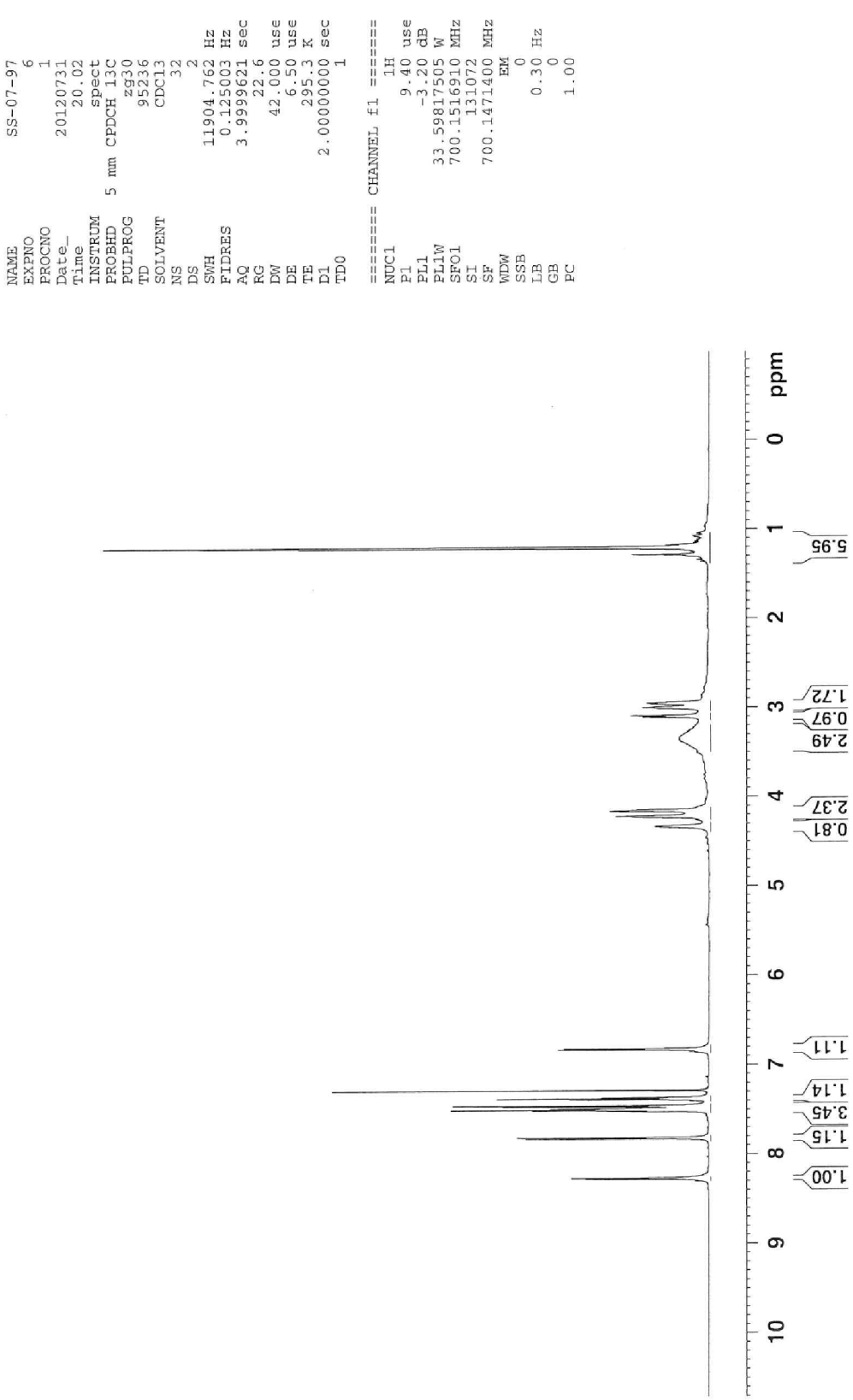
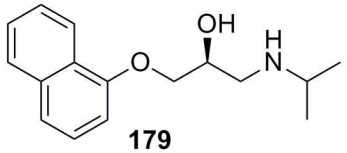

NAME SS-07-97
EXPNO 6
PROCNO 1
Date_ 20120731
Time 20.02
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 22.6
DW 42.000 use
DE 6.50 use
TE 295.3 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 =======
NUC1 1H
P1 9.40 use
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
1.15
3.45
1.14
1.11
0.81
2.37
2.49
0.97
1.72
5.95



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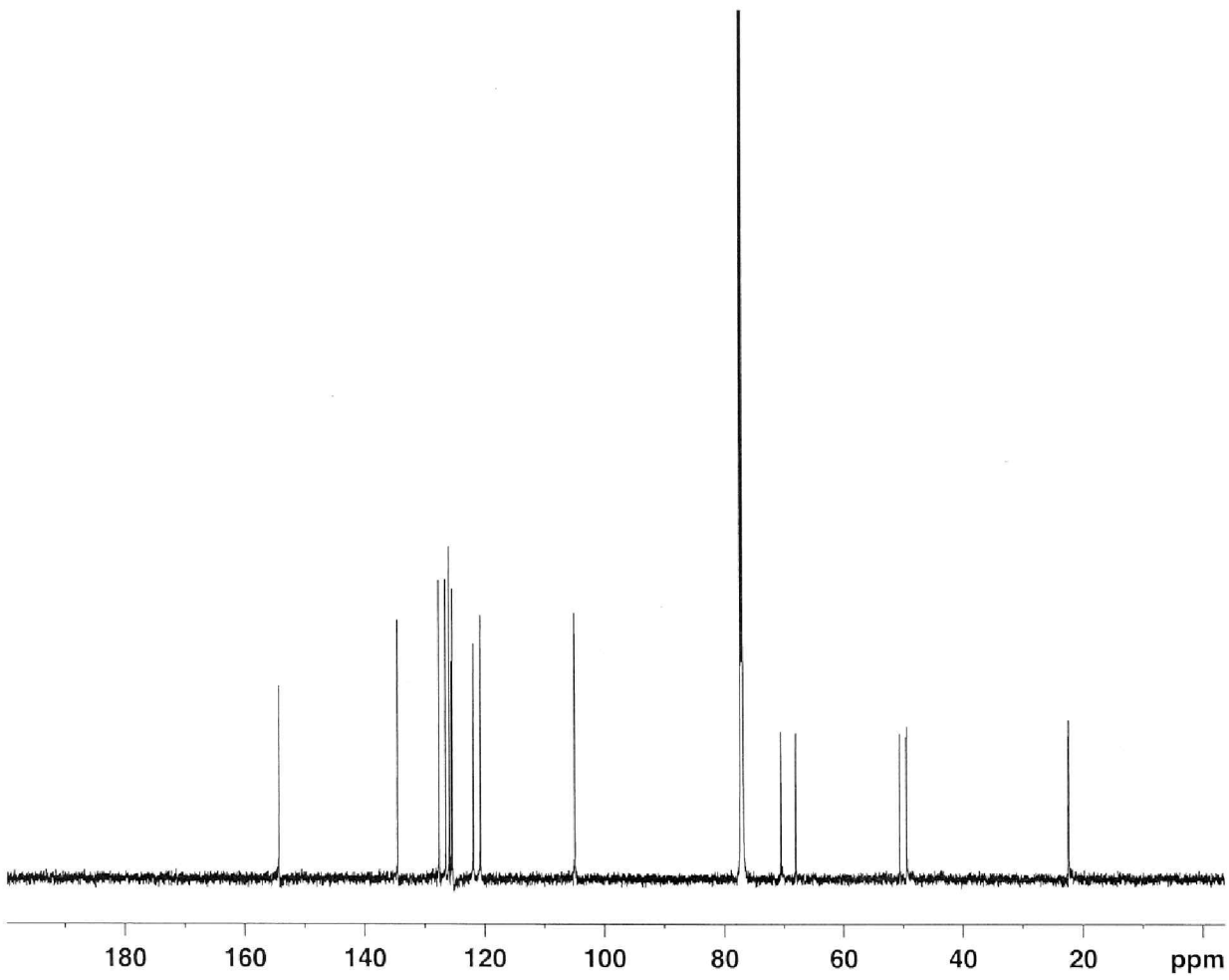
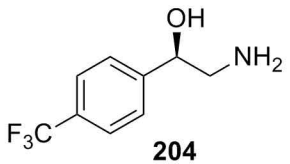
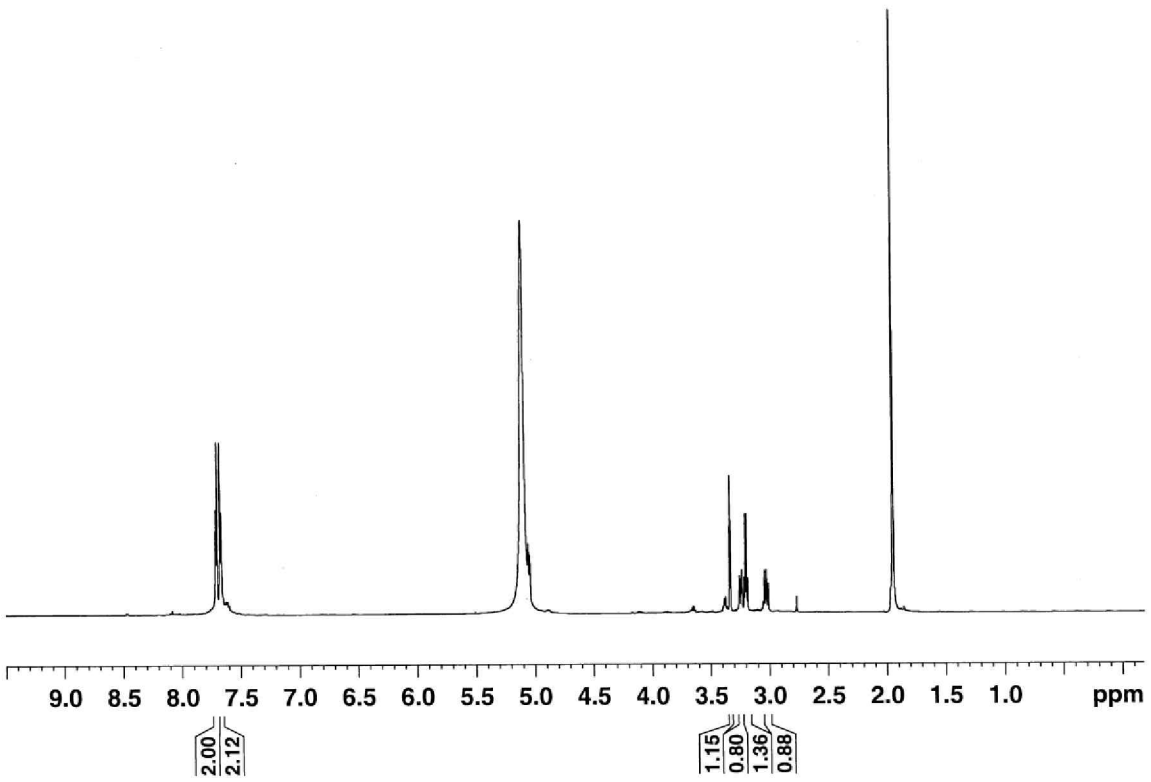


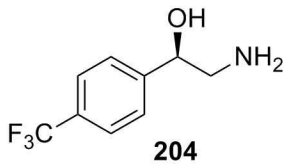
NAME	SS-07-97	
EXPNO	7	
PROCNO	1	
Date_	20120731	
Time	20.12	
INSTRUM	spect	
PROBHD	5 mm CPDCH 13C	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	65	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	usec
DE	16.50	usec
TE	295.2	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	9.00	usec
PL1	4.50	dB
PL1W	38.14553833	W
SFO1	176.0697436	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	65.00	usec
PL2	-3.20	dB
PL12	13.60	dB
PL13	120.00	dB
PL2W	33.59817505	W
PL12W	0.70196527	W
PL13W	0.00000000	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.00	



204



NAME	SS-07-67
EXPNO	9
PROCNO	1
Date_	20120513
Time	19.32
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zg30
TD	95236
SOLVENT	MeOD
NS	8
DS	2
SWH	11904.762 Hz
FIDRES	0.125003 Hz
AQ	3.9999621 sec
RG	18
DW	42.000 usec
DE	6.50 usec
TE	298.2 K
D1	2.00000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	1H
P1	9.40 usec
PL1	-3.20 dB
PL1W	33.59817505 W
SFO1	700.1516910 MHz
SI	131072
SF	700.1471400 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00



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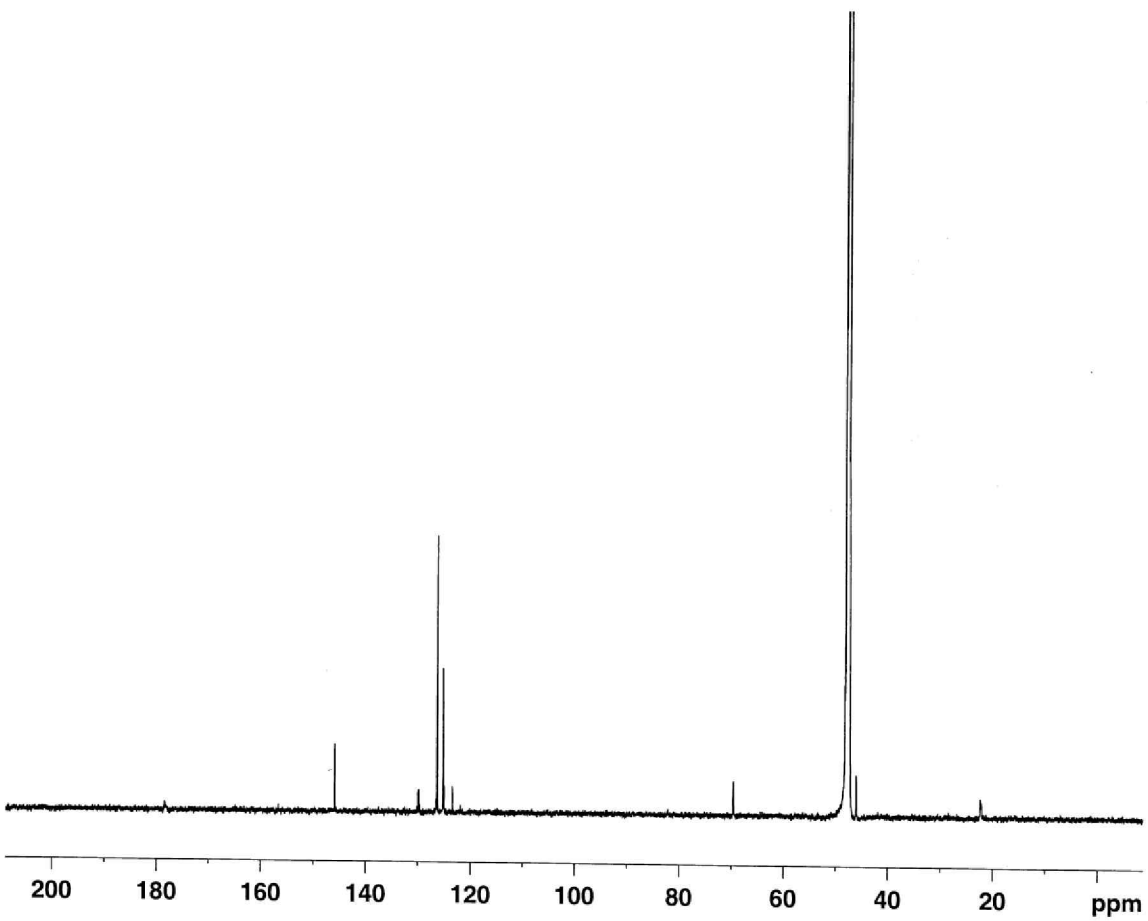
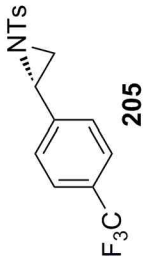
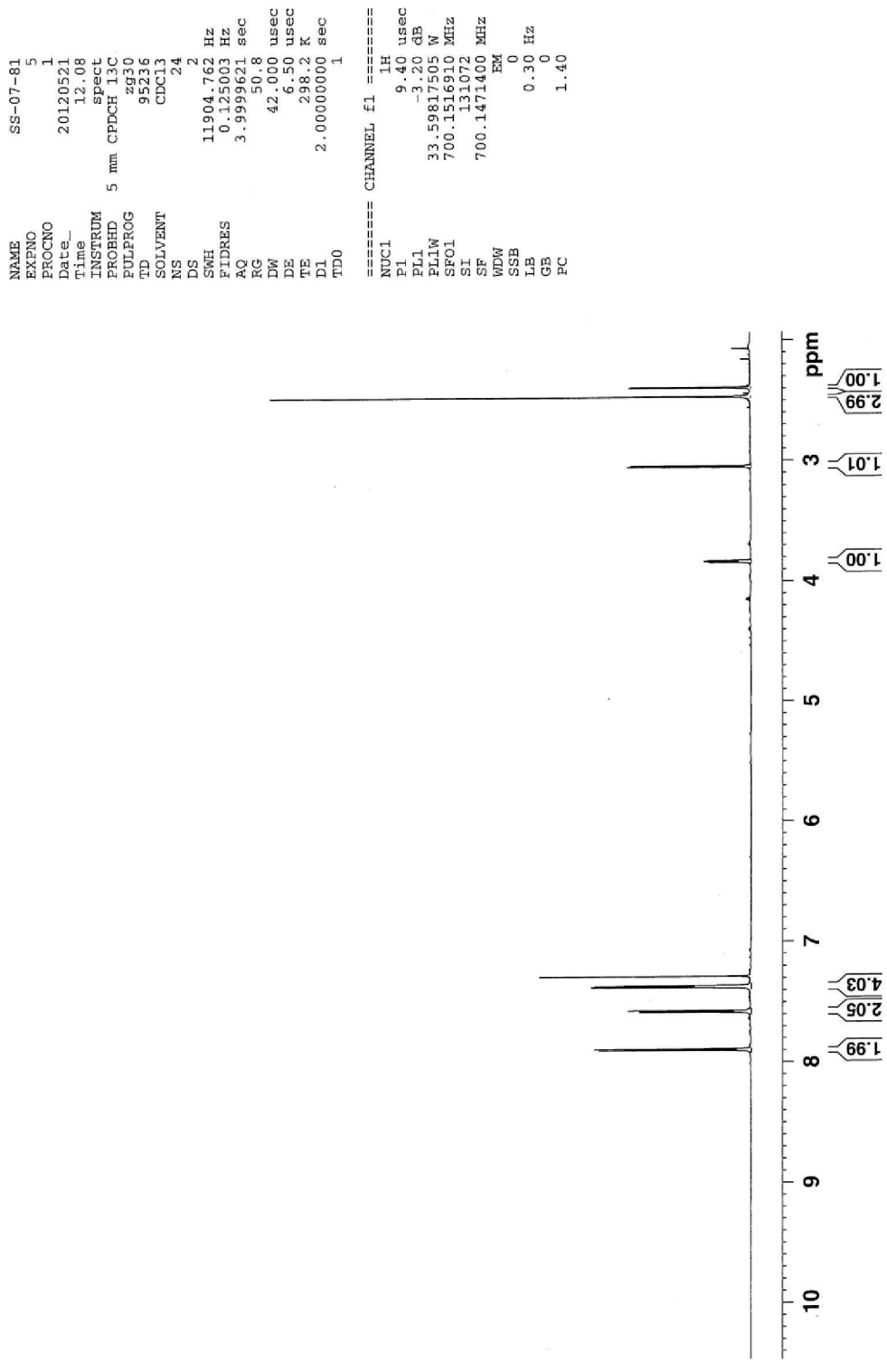
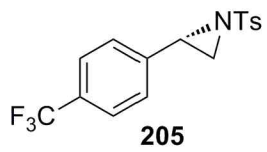


NAME	SS-07-67	
EXPNO	13	
PROCNO	1	
Date_	20120515	
Time	11.29	
INSTRUM	spect	
PROBHD	5 mm CPDCH 13C	
PULPROG	zgpg30	
TD	65536	
SOLVENT	MeOD	
NS	1024	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	usec
DE	16.50	usec
TE	298.2	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	9.00	usec
PL1	4.50	dB
PL1W	38.14553833	W
SFO1	176.0697436	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	65.00	usec
PL2	-3.20	dB
PL12	13.60	dB
PL13	120.00	dB
PL2W	33.59817505	W
PL12W	0.70196527	W
PL13W	0.00000000	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.00	

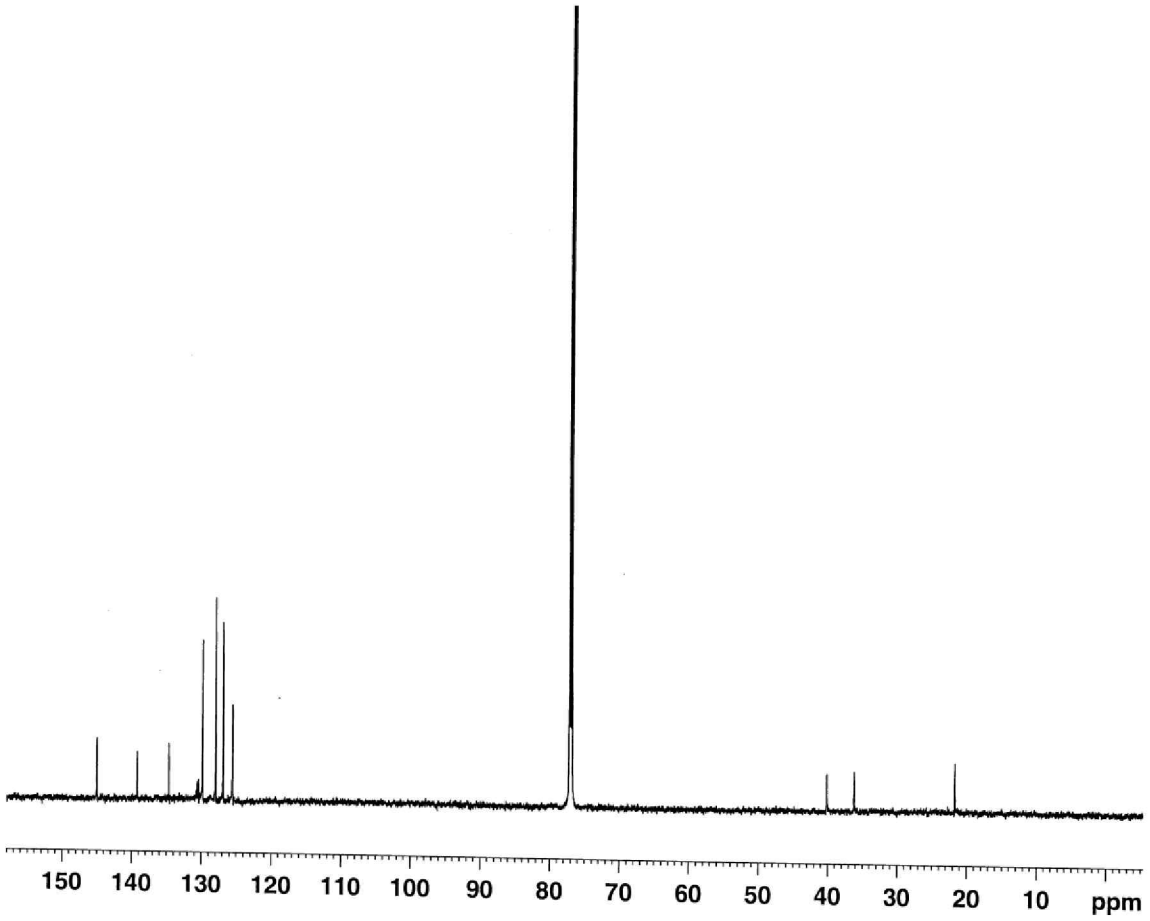

NTs
F3C

205

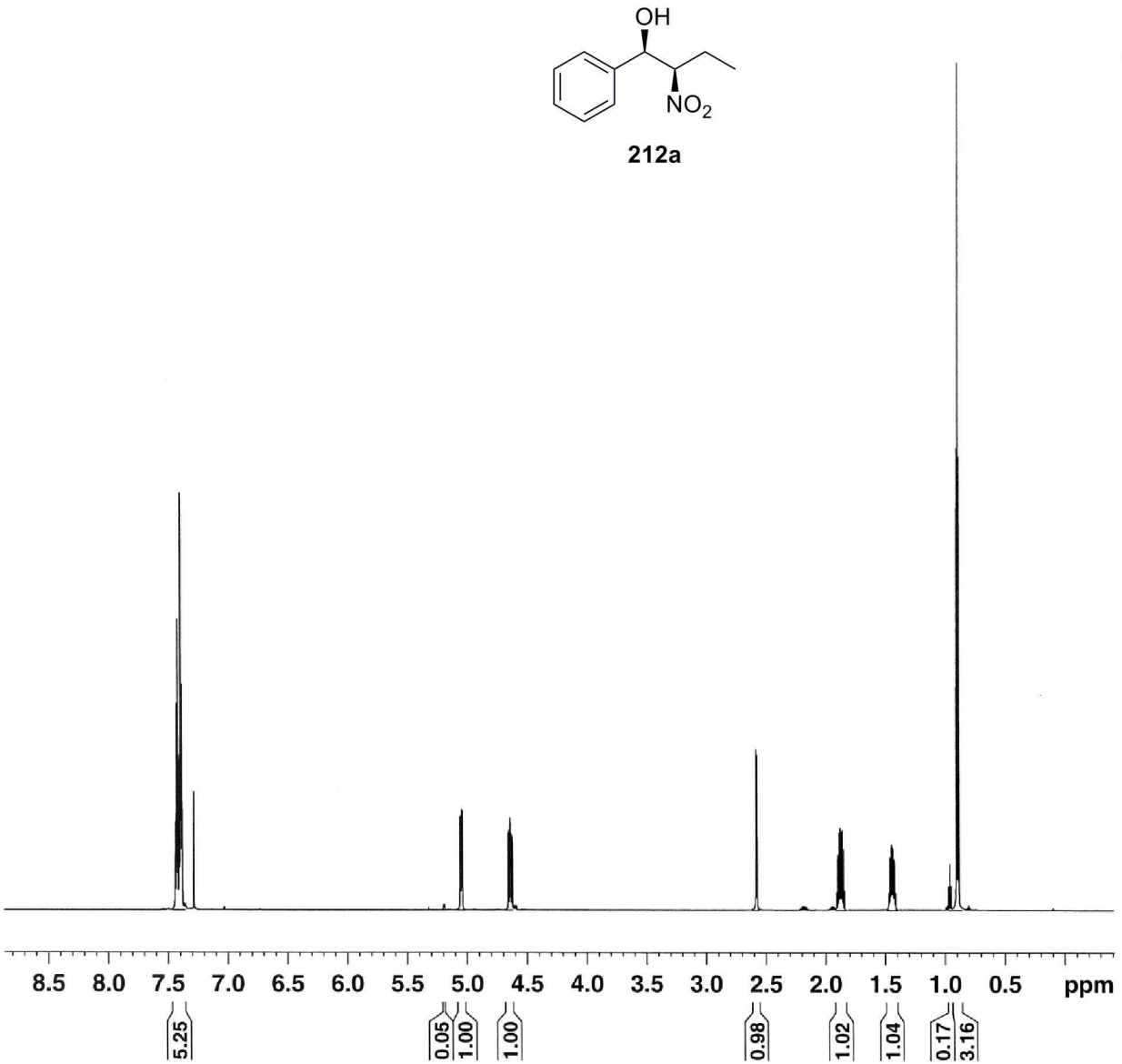

NAME SS-07-81
EXPNO 5
PROCNO 1
Date_ 20120521
Time_ 12.08
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 24
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.99999621 sec
RG 50.8
DW 42.000 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40
ppm
1.99
2.05
4.03
1.00
1.01
1.00
2.99
1.00



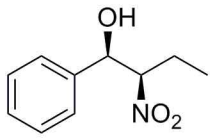
205



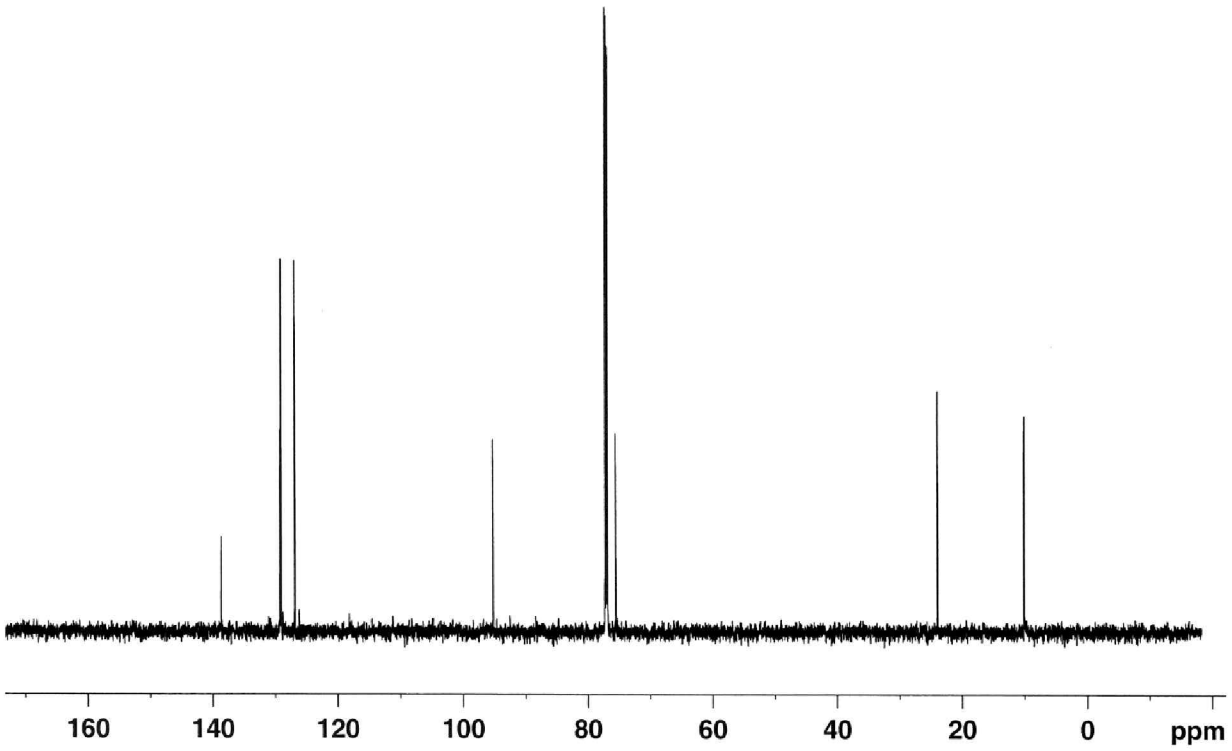
NAME	SS-07-81	
EXPNO	6	
PROCNO	1	
Date_	20120521	
Time	12.12	
INSTRUM	spect	
PROBHD	5 mm CPDCH 13C	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	42	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	usec
DE	16.50	usec
TE	298.2	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	9.00	usec
PL1	4.50	dB
PL1W	38.14553833	W
SFO1	176.0697436	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	65.00	usec
PL2	-3.20	dB
PL12	13.60	dB
PL13	120.00	dB
PL2W	33.59817505	W
PL12W	0.70196527	W
PL13W	0.00000000	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.40	



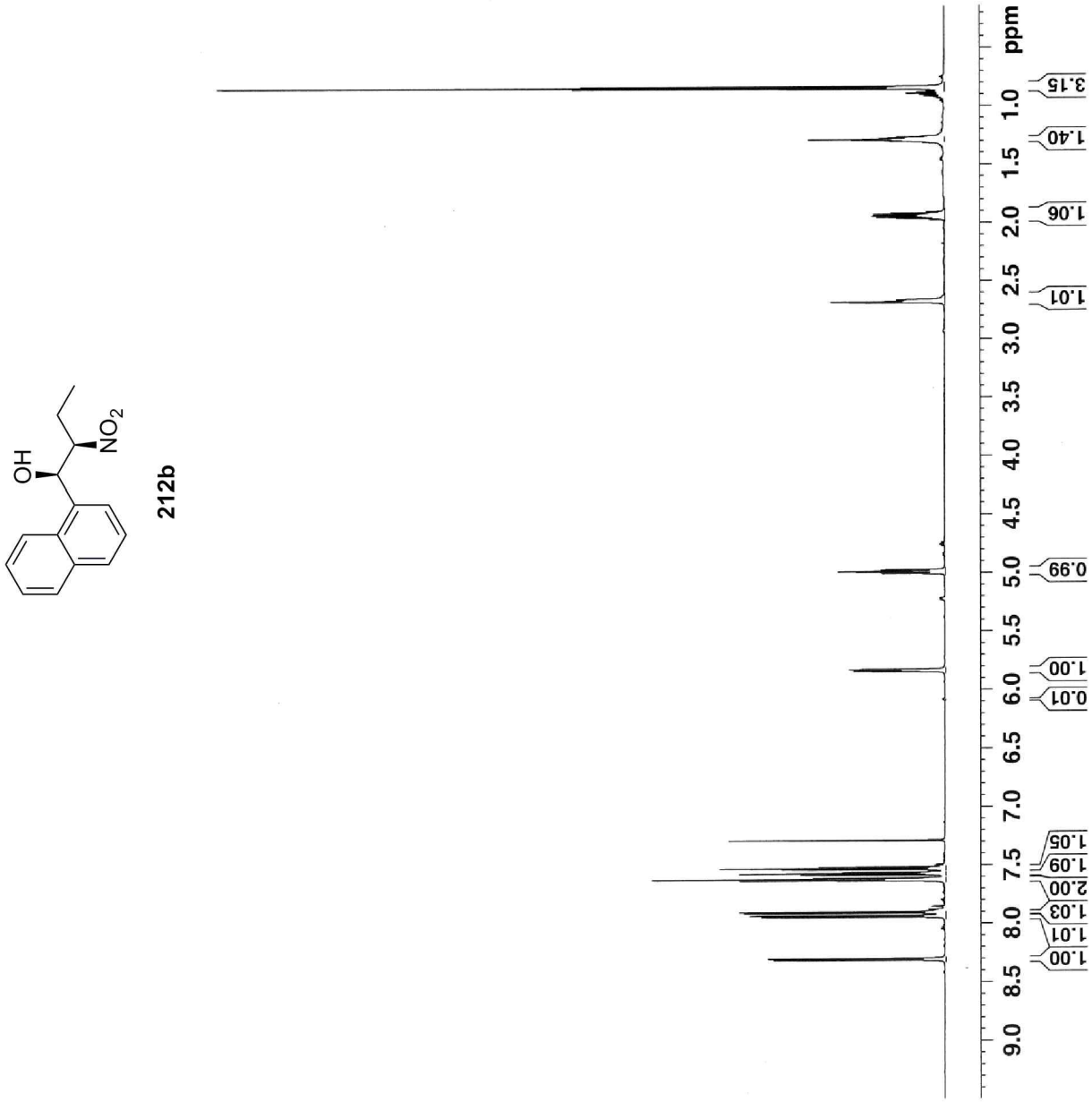
NAME	SS-07-112
EXPNO	1
PROCNO	1
Date_	20120912
Time	17.12
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	95236
SOLVENT	CDCl3
NS	9
DS	2
SWH	11904.762 Hz
FIDRES	0.125003 Hz
AQ	3.9999621 sec
RG	128
DW	42.000 usec
DE	6.50 usec
TE	298.2 K
D1	2.00000000 sec
TD0	1
========	CHANNEL f1 ========
NUC1	1H
P1	13.75 usec
PL1	-3.00 dB
PL1W	32.08600616 W
SFO1	700.1516910 MHz
SI	131072
SF	700.1471400 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

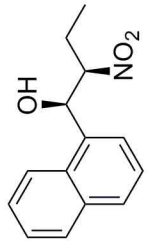


212a

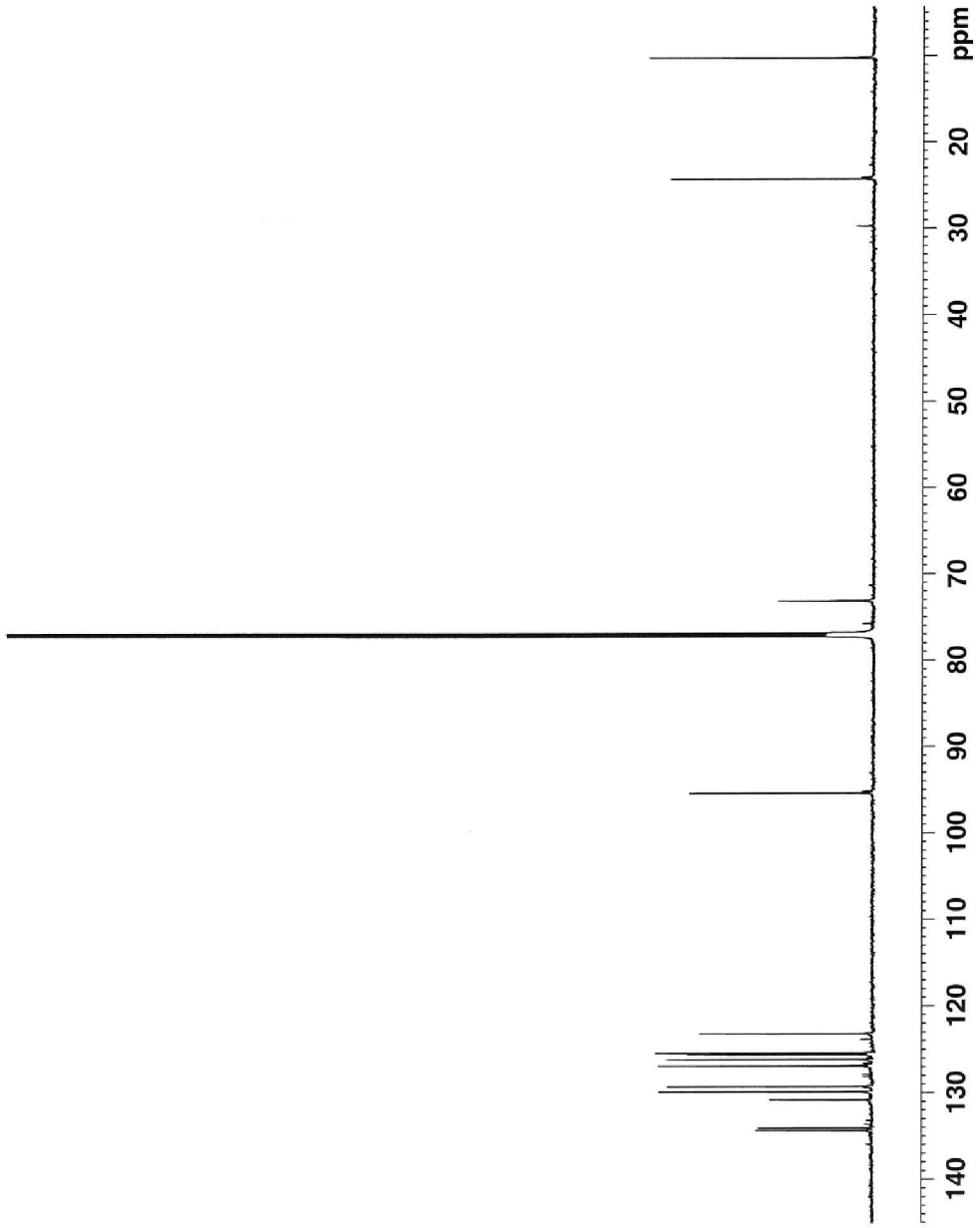


NAME	SS-07-112	
EXPNO	2	
PROCNO	1	
Date_	20120912	
Time	17.15	
INSTRUM	spect	
PROBHD	5 mm PABBO BB-	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	22	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	usec
DE	16.50	usec
TE	298.7	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	9.30	usec
PL1	2.00	dB
PL1W	67.83342743	W
SFO1	176.0697436	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	80.00	usec
PL2	-3.00	dB
PL12	12.30	dB
PL13	12.30	dB
PL2W	32.08600616	W
PL12W	0.94692516	W
PL13W	0.94692516	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.00	

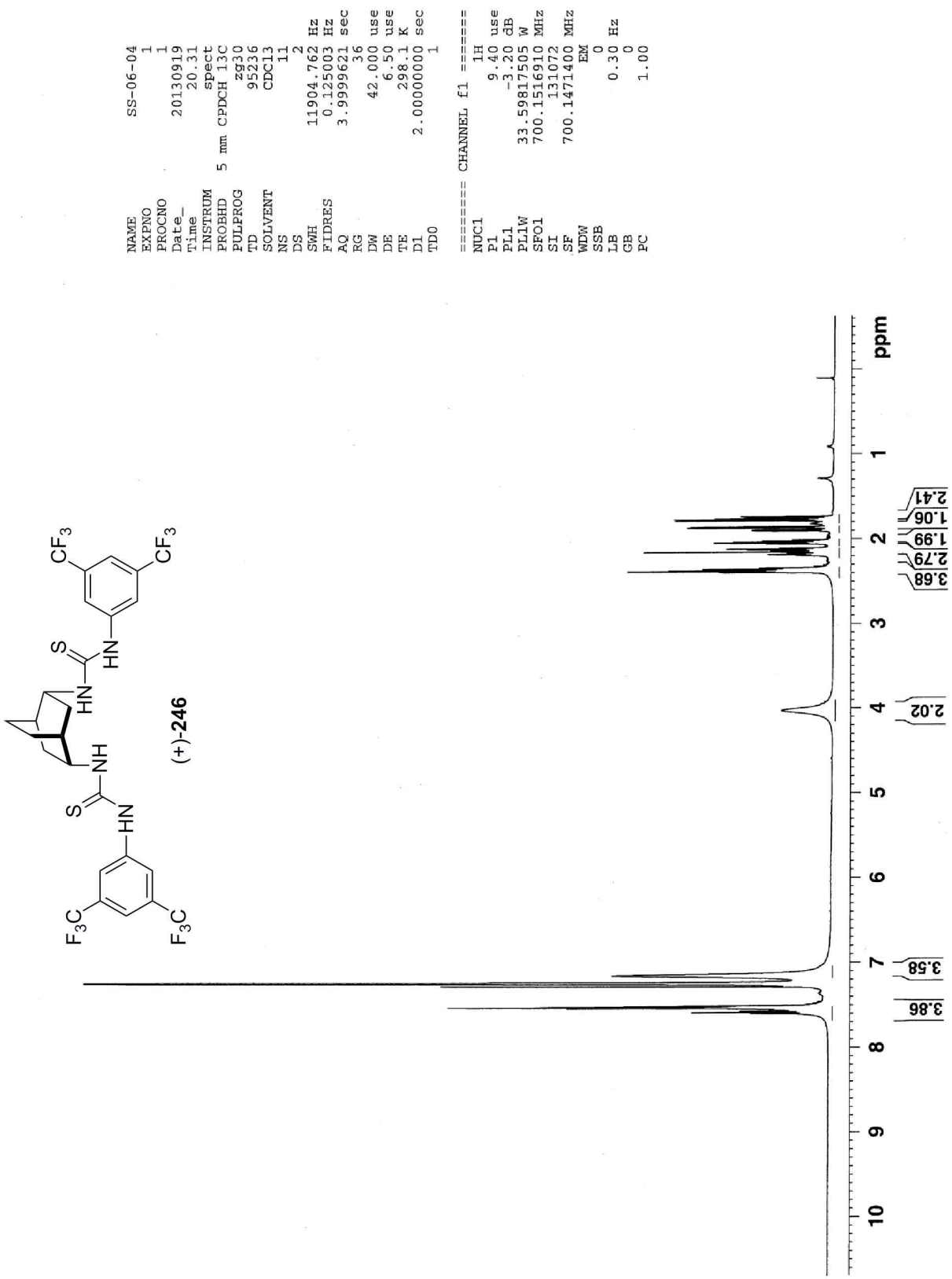

OH
NO2
212b
NAME SS-07-113
EXPNO 7
PROCNO 1
Date_ 20120904
Time 17.39
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 22.6
DW 42.000 usec
DE 6.50 usec
TE 296.3 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
1.00
1.01
1.03
2.00
1.09
1.05
0.01
1.00
0.99
1.01
1.06
1.40
3.15

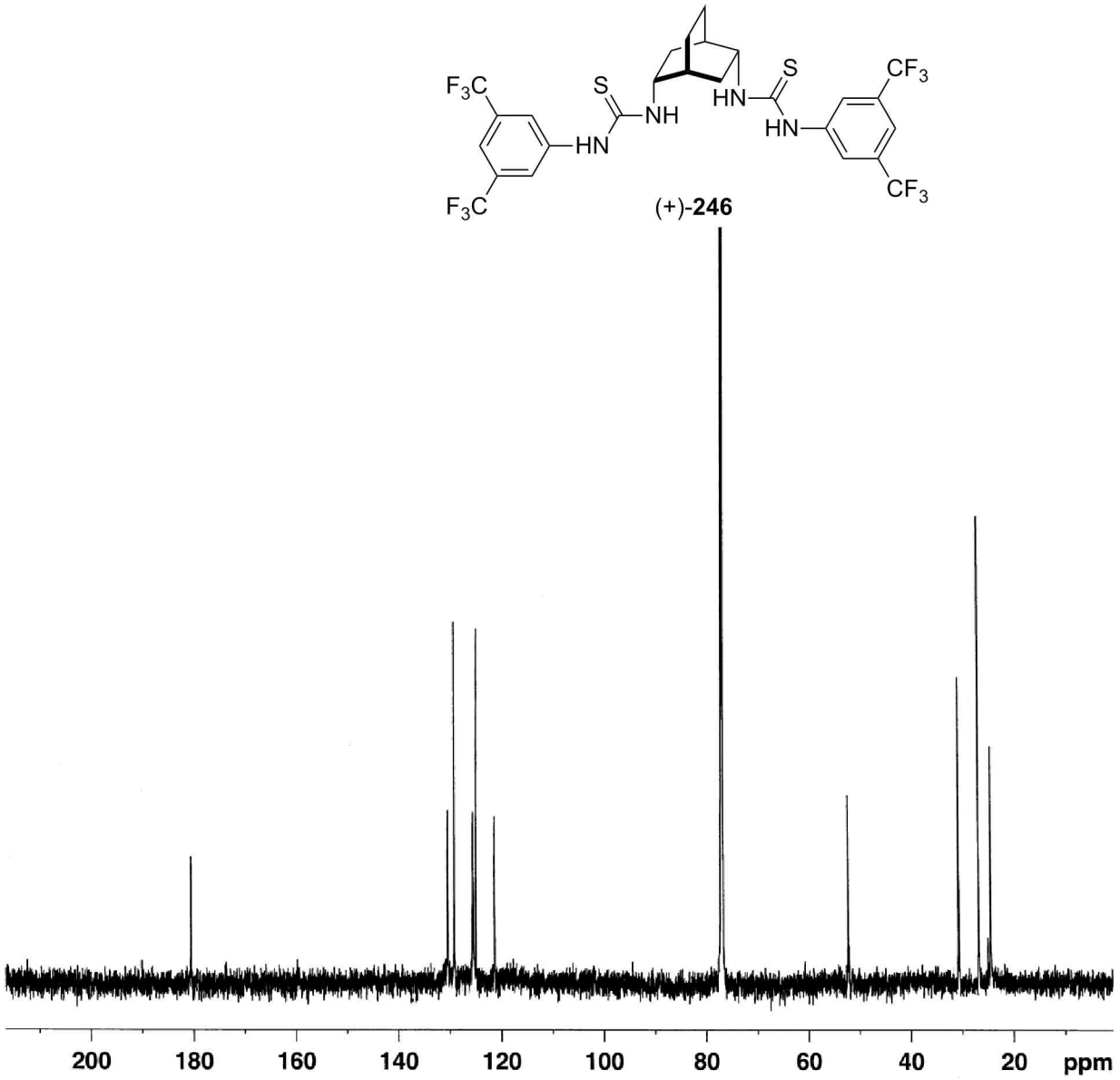


212b

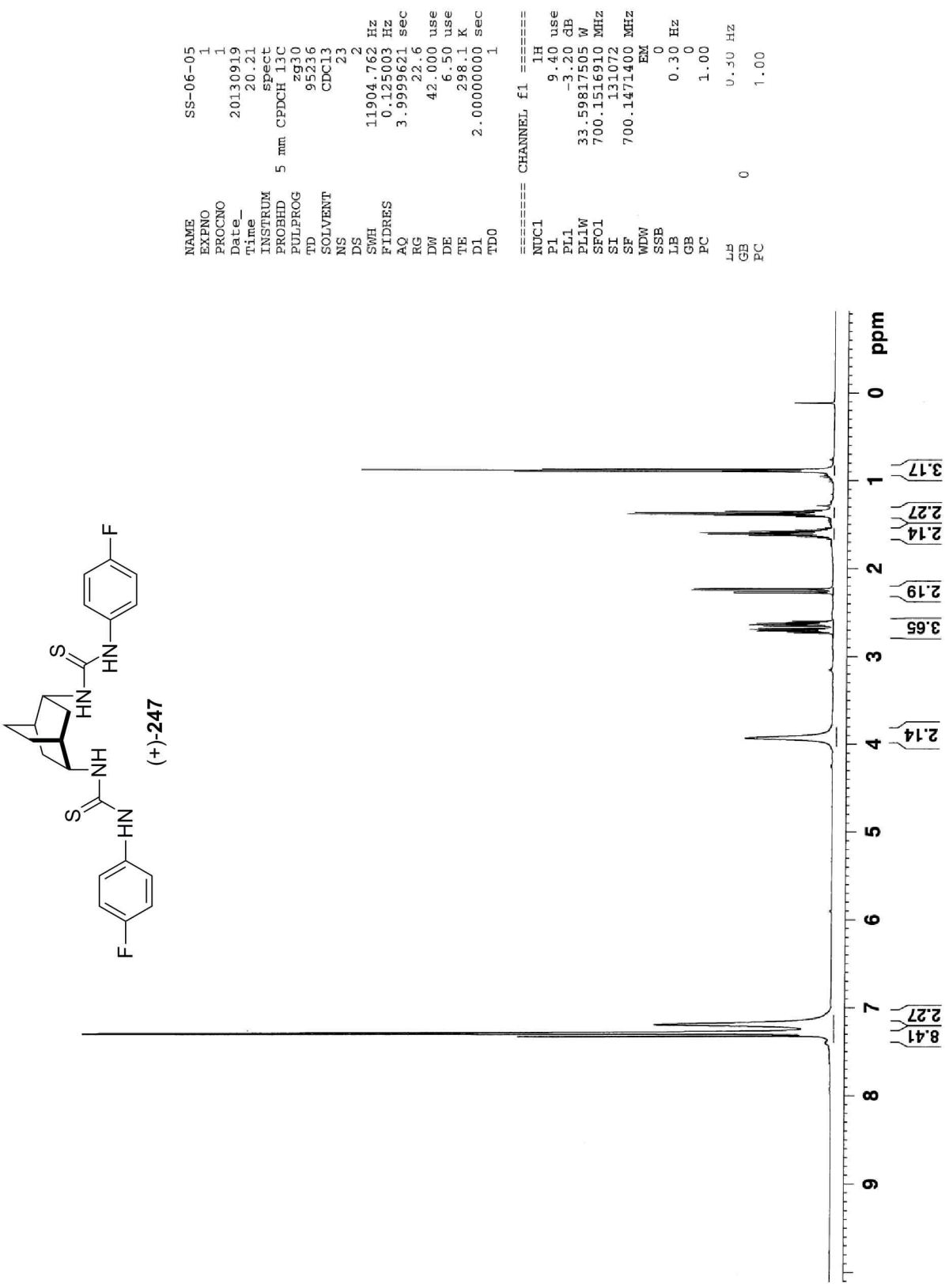


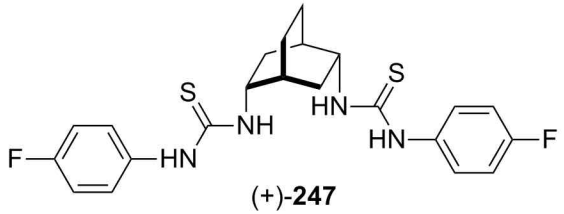

```
NAME            SS-07-113
EXPNO                   8
PROCNO                  1
Date_            20120904
Time                17.53
INSTRUM              spect
PROBHD  5 mm CPDCH 13C
PULPROG             zgpg30
TD                   65536
SOLVENT              CDCl3
NS                      49
DS                       4
SWH              41666.668 Hz
FIDRES               0.635783 Hz
AQ                0.7864820 sec
RG                      203
DW                   12.000 usec
DE                   16.50 usec
TE                   296.2 K
D1                2.00000000 sec
D11               0.03000000 sec
TD0                      1

========  CHANNEL f1 ========
NUC1                   13C
P1                    9.00 usec
PL1                   4.50 dB
PL1W            38.14553833 W
SFO1            176.0697436 MHz

========  CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                   1H
PCPD2                65.00 usec
PL2                  -3.20 dB
PL12                 13.60 dB
PL13                120.00 dB
PL2W            33.59817505 W
PL12W            0.70196527 W
PL13W            0.00000000 W
SFO2            700.1499406 MHz
SI                    32768
SF              176.0521380 MHz
WDW                     EM
SSB                      0
LB                    3.00 Hz
GB                       0
PC                    1.00
```


NAME SS-06-04
EXPNO 1
PROCNO 1
Date_ 20130919
Time 20.31
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 11
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 36
DW 42.000 use
DE 6.50 use
TE 298.1 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 use
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
(+)-246
ppm
3.86
3.58
2.02
3.68
2.79
1.99
1.06
2.41

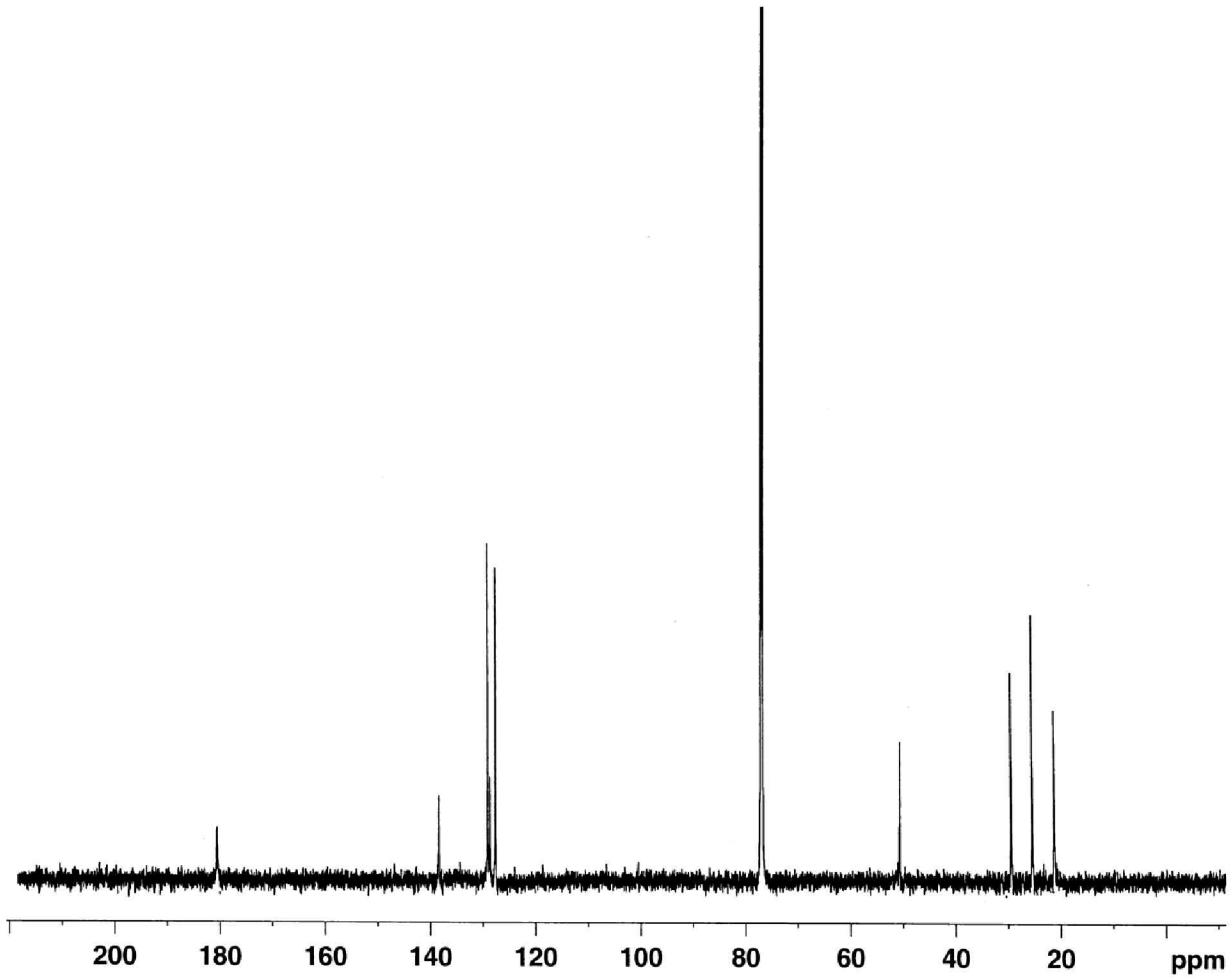


NAME	SS-06-04	
EXPNO	2	
PROCNO	1	
Date_	20130919	
Time	20.33	
INSTRUM	spect	
PROBHD	5 mm CPDCH 13C	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	44	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	use
DE	16.50	use
TE	298.1	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	9.00	use
PL1	4.50	dB
PL1W	38.14553833	W
SFO1	176.0697436	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	65.00	use
PL2	-3.20	dB
PL12	13.60	dB
PL13	120.00	dB
PL2W	33.59817505	W
PL12W	0.70196527	W
PL13W	0.00000000	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.40	

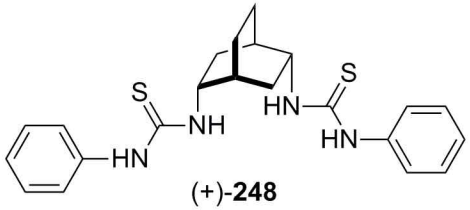

NAME SS-06-05
EXPNO 1
PROCNO 1
Date_ 20130919
Time_ 20.21
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDC13
NS 23
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 22.6
DW 42.000 use
DE 6.50 use
TE 298.1 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 use
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
LB 0.30 Hz
GB 0
PC 1.00
(+)-247
3.17
2.27
2.14
2.19
3.65
2.14
8.41
2.27
ppm



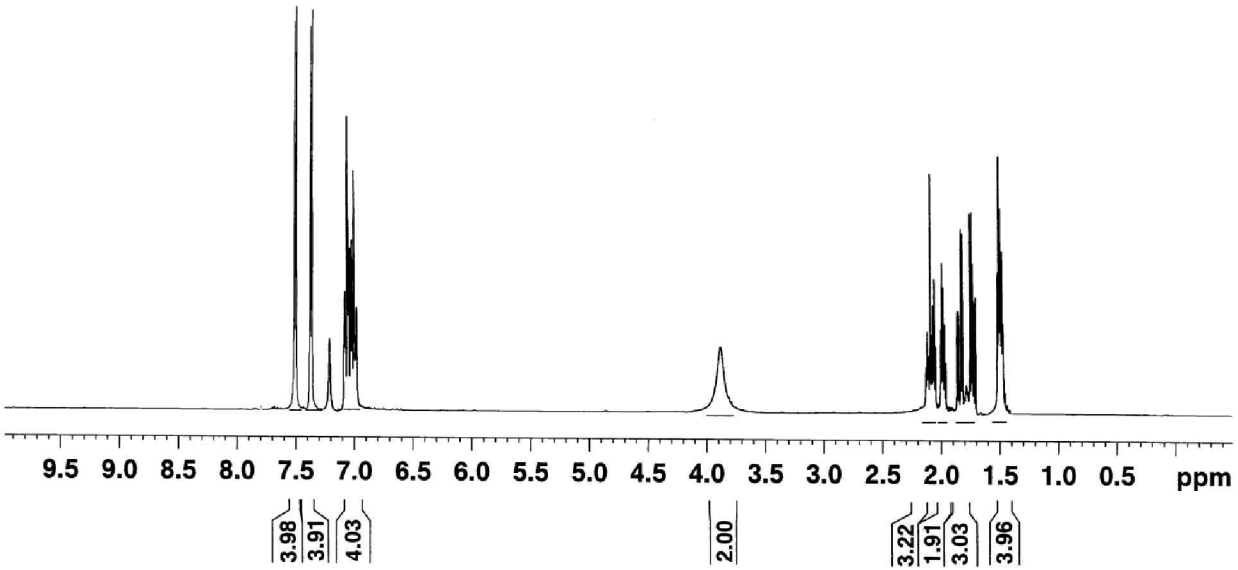
(+)-**247**



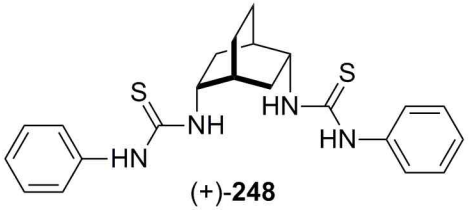
NAME	SS-06-05	
EXPNO	2	
PROCNO	1	
Date_	20130919	
Time	20.26	
INSTRUM	spect	
PROBHD	5 mm CPDCH 13C	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	38	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	usec
DE	16.50	usec
TE	298.2	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	9.00	usec
PL1	4.50	dB
PL1W	38.14553833	W
SFO1	176.0697436	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	65.00	usec
PL2	-3.20	dB
PL12	13.60	dB
PL13	120.00	dB
PL2W	33.59817505	W
PL12W	0.70196527	W
PL13W	0.00000000	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.40	



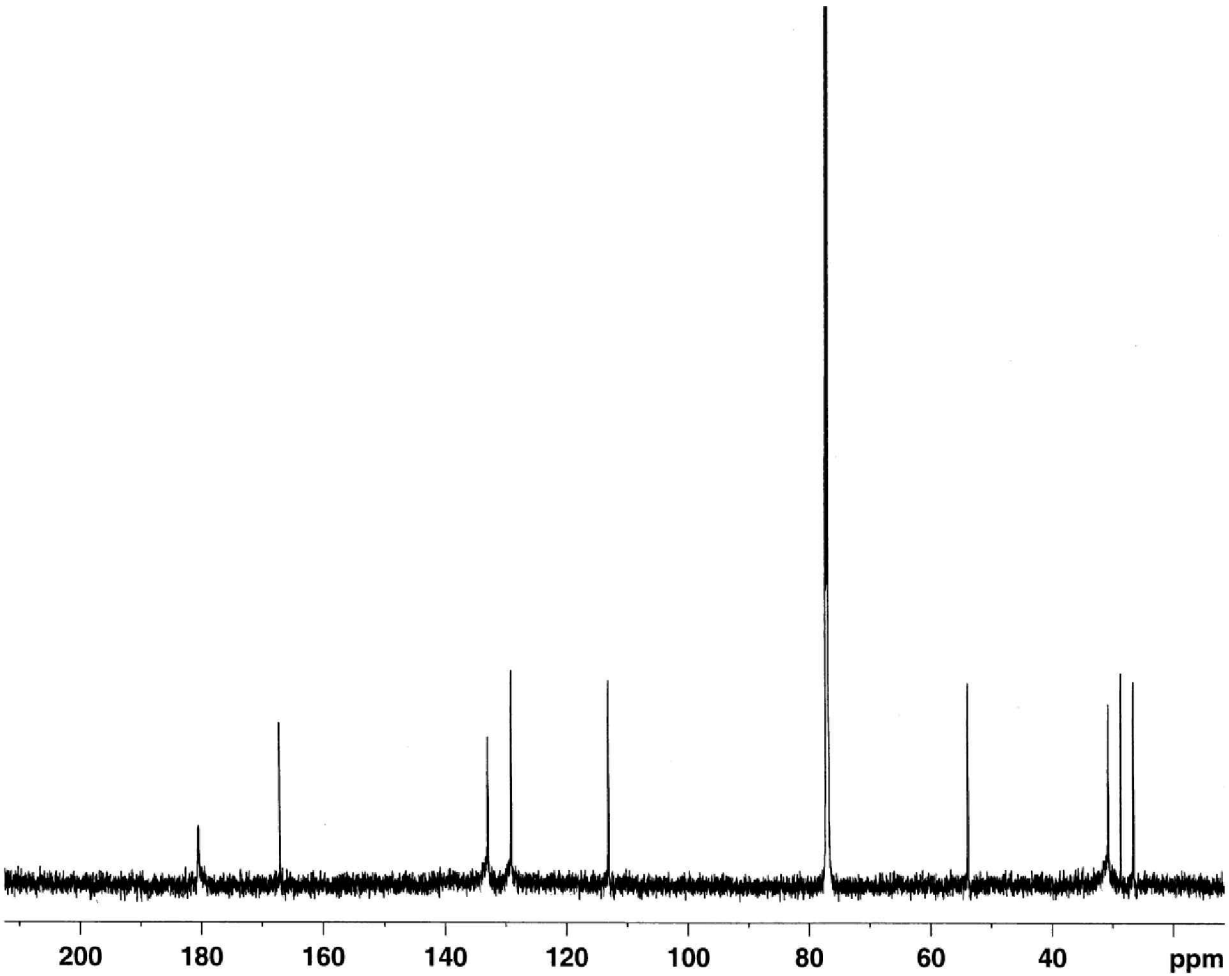
(+)-**248**



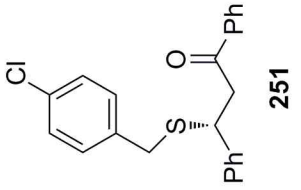
NAME	SS-05-26
EXPNO	1
PROCNO	1
Date_	20130919
Time	20.39
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zg30
TD	95236
SOLVENT	CDCl3
NS	26
DS	2
SWH	11904.762 Hz
FIDRES	0.125003 Hz
AQ	3.9999621 sec
RG	36
DW	42.000 usec
DE	6.50 usec
TE	298.1 K
D1	2.00000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	1H
P1	9.40 usec
PL1	-3.20 dB
PL1W	33.59817505 W
SFO1	700.1516910 MHz
SI	131072
SF	700.1471400 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00



(+)-**248**

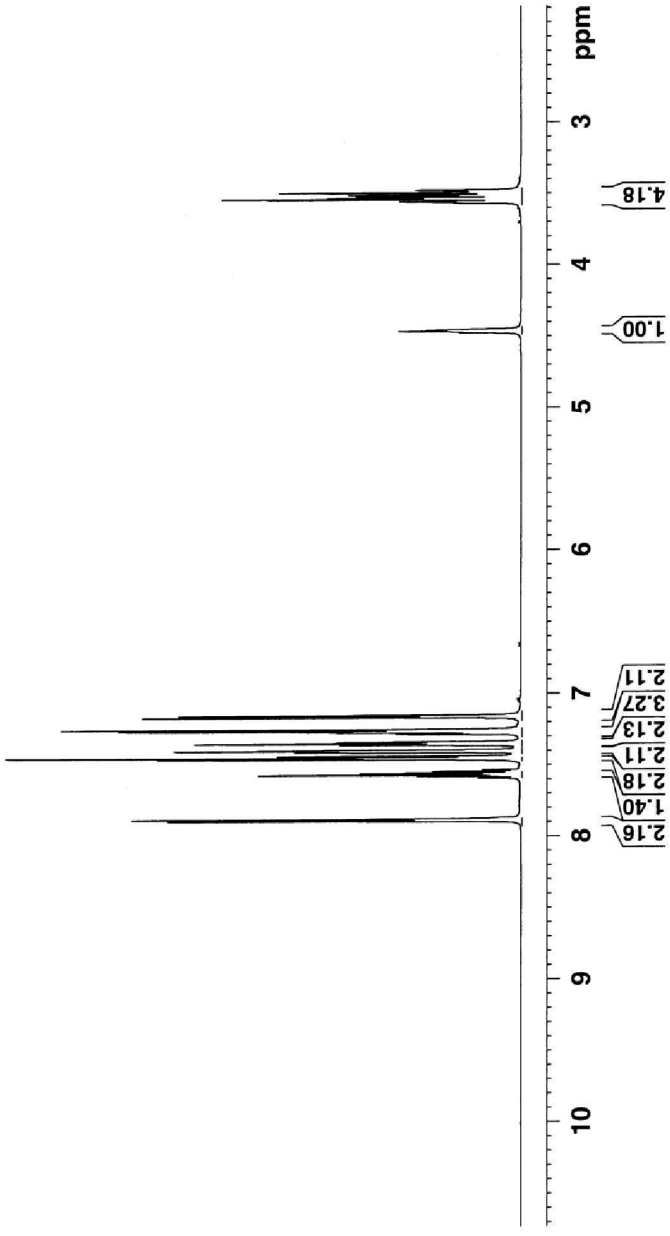


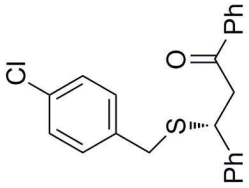
NAME	SS-05-26	
EXPNO	2	
PROCNO	1	
Date_	20130919	
Time	20.43	
INSTRUM	spect	
PROBHD	5 mm CPDCH 13C	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	52	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	use
DE	16.50	use
TE	298.1	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	9.00	use
PL1	4.50	dB
PL1W	38.14553833	W
SFO1	176.0697436	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	65.00	use
PL2	-3.20	dB
PL12	13.60	dB
PL13	120.00	dB
PL2W	33.59817505	W
PL12W	0.70196527	W
PL13W	0.00000000	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.40	



251

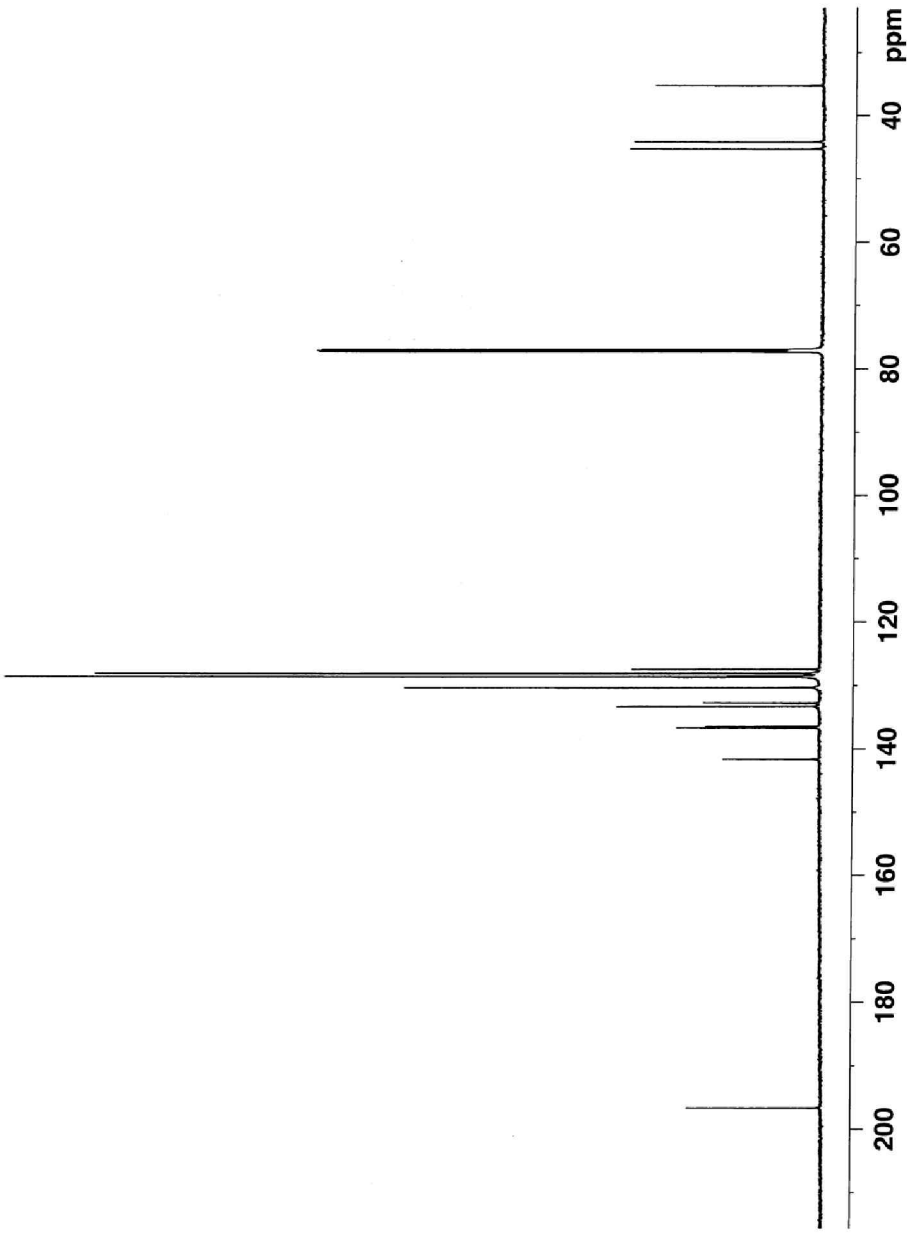
```
NAME                SS-06-26
EXPNO                      1
PROCNO                     1
Date_               20121213
Time_                 15.08
INSTRUM                spect
PROBHD   5 mm CPDCH 13C
PULPROG                zg30
TD                    95236
SOLVENT               CDCl3
NS                       28
DS                        2
SWH                11904.762 Hz
FIDRES                0.125003 Hz
AQ                    3.9999621 sec
RG                       20.2
DW                      42.000 usec
DE                       6.50 usec
TE                      303.2 K
D1                    2.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                      9.40 usec
PL1                     -3.20 dB
PL1W               33.59817505 W
SFO1               700.1516910 MHz
SI                       131072
SF                 700.1471400 MHz
WDW                        EM
SSB                         0
LB                       0.30 Hz
GB                          0
PC                       1.00
```

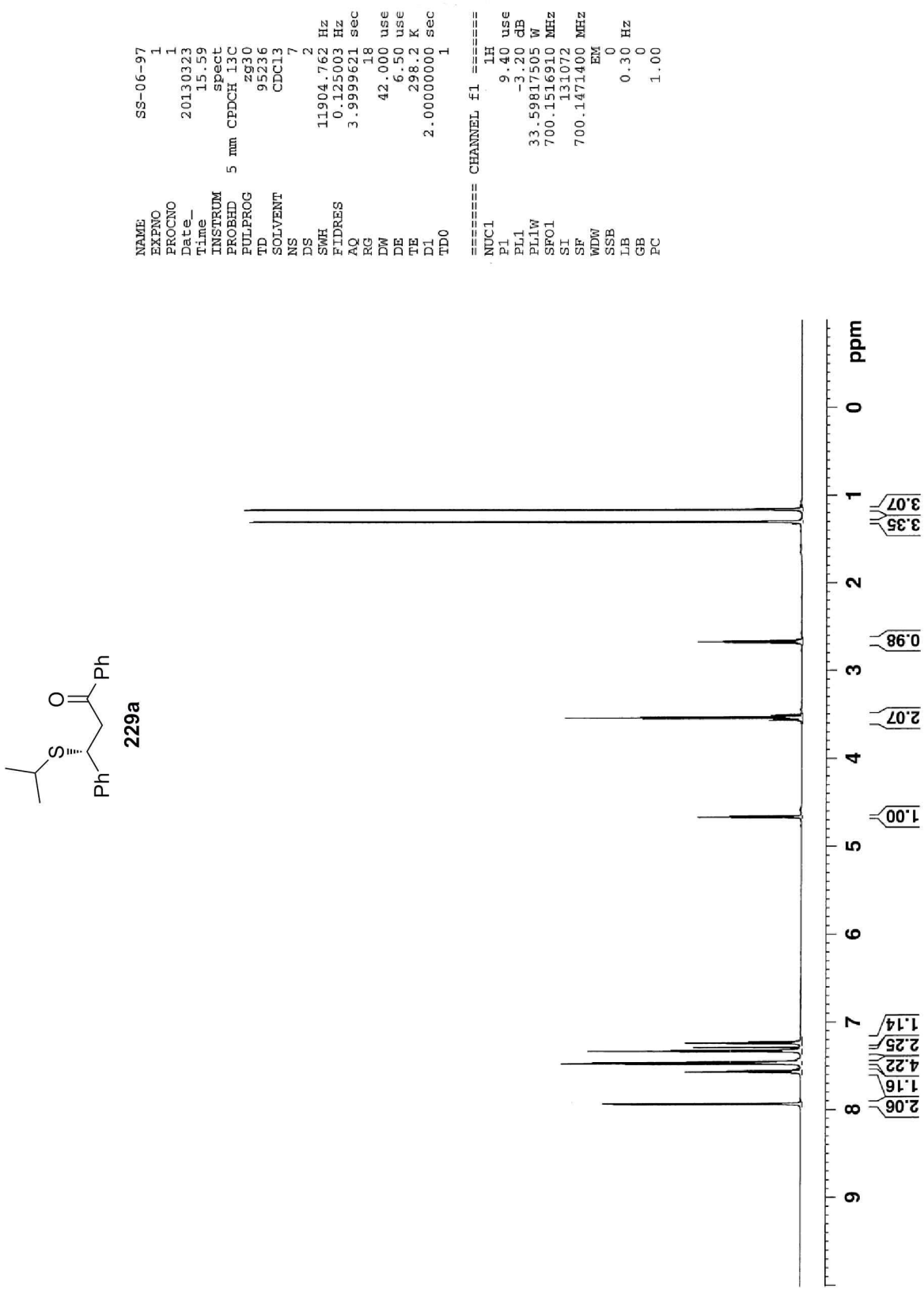


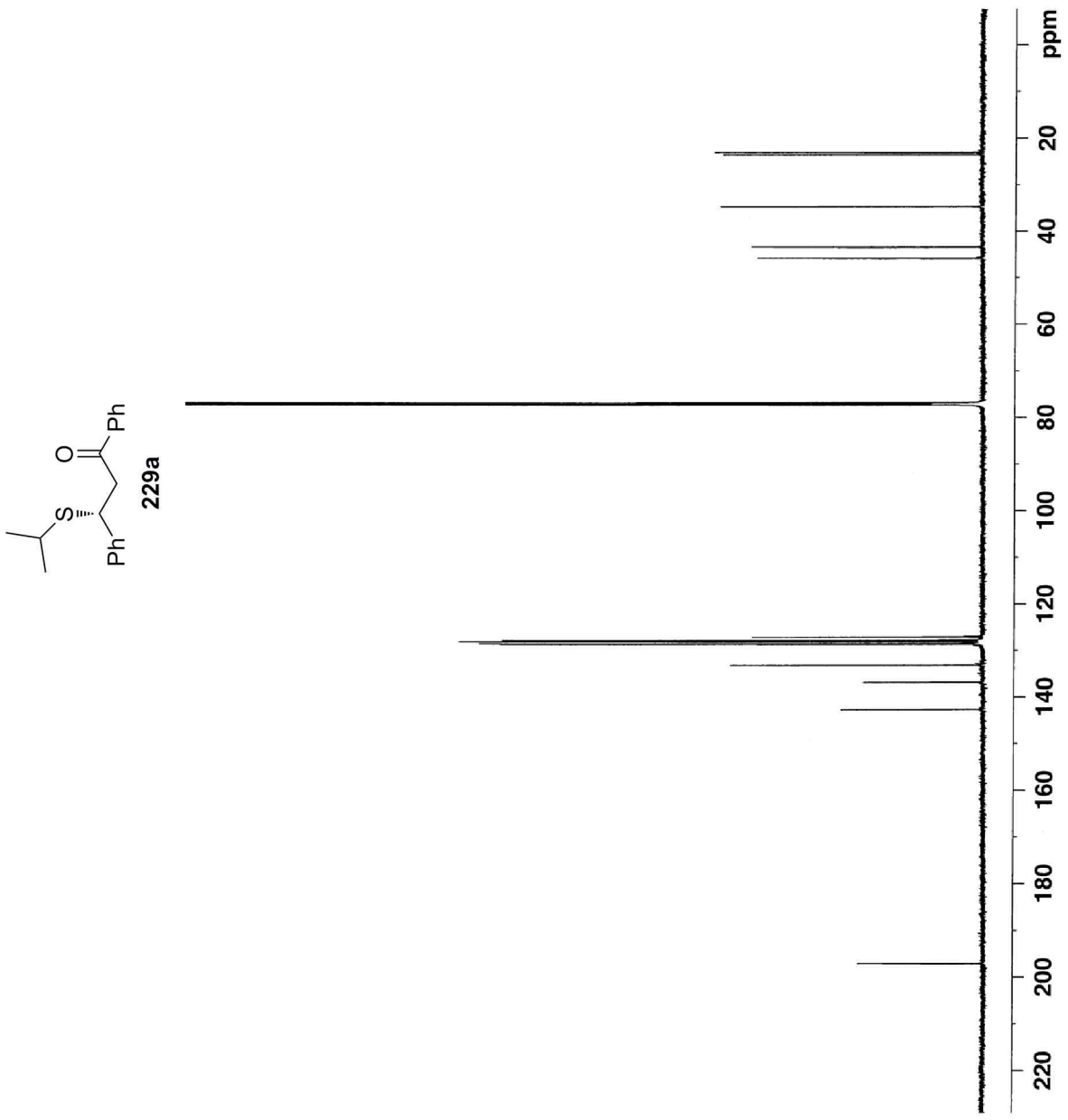


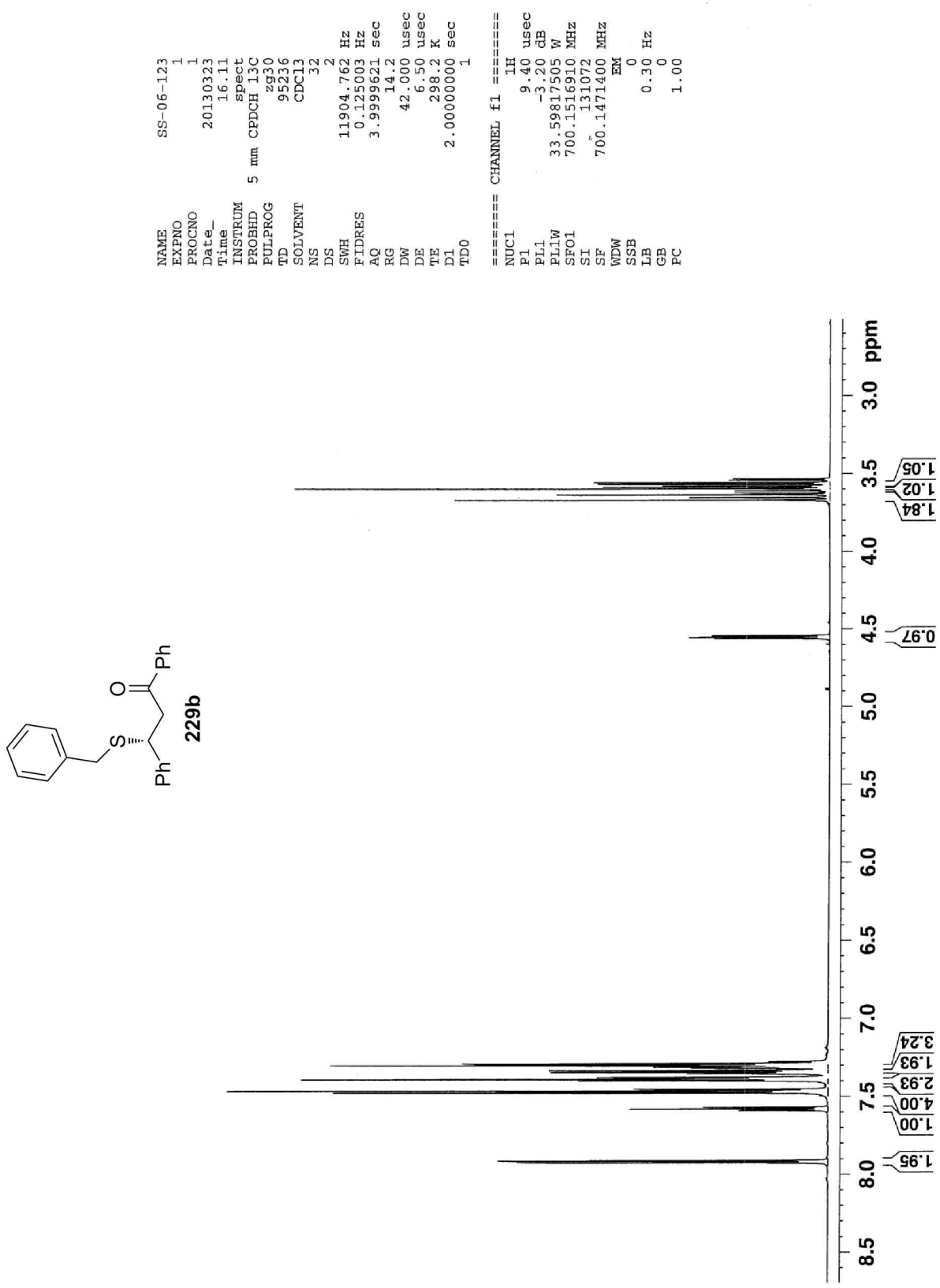
251

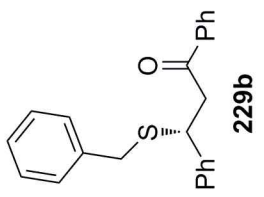
```
NAME                SS-06-26
EXPNO                      2
PROCNO                     1
Date_               20121213
Time                   15.14
INSTRUM                spect
PROBHD   5 mm CPDCH 13C
PULPROG                zgpg30
TD                      65536
SOLVENT                CDCl3
NS                         38
DS                          4
SWH                 41666.668 Hz
FIDRES                0.635783 Hz
AQ                    0.7864820 sec
RG                        203
DW                     12.000 use
DE                     16.50 use
TE                     303.2 K
D1                  2.00000000 sec
D11                 0.03000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                      13C
P1                     9.00 use
PL1                    4.50 dB
PL1W               38.14553833 W
SFO1               176.0697436 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                        1H
PCPD2                  65.00 use
PL2                    -3.20 dB
PL12                   13.60 dB
PL13                  120.00 dB
PL2W               33.59817505 W
PL12W               0.70196527 W
PL13W               0.00000000 W
SFO2               700.1499406 MHz
SI                       32768
SF                 176.0521380 MHz
WDW                        EM
SSB                         0
LB                     3.00 Hz
GB                          0
PC                     1.00
```



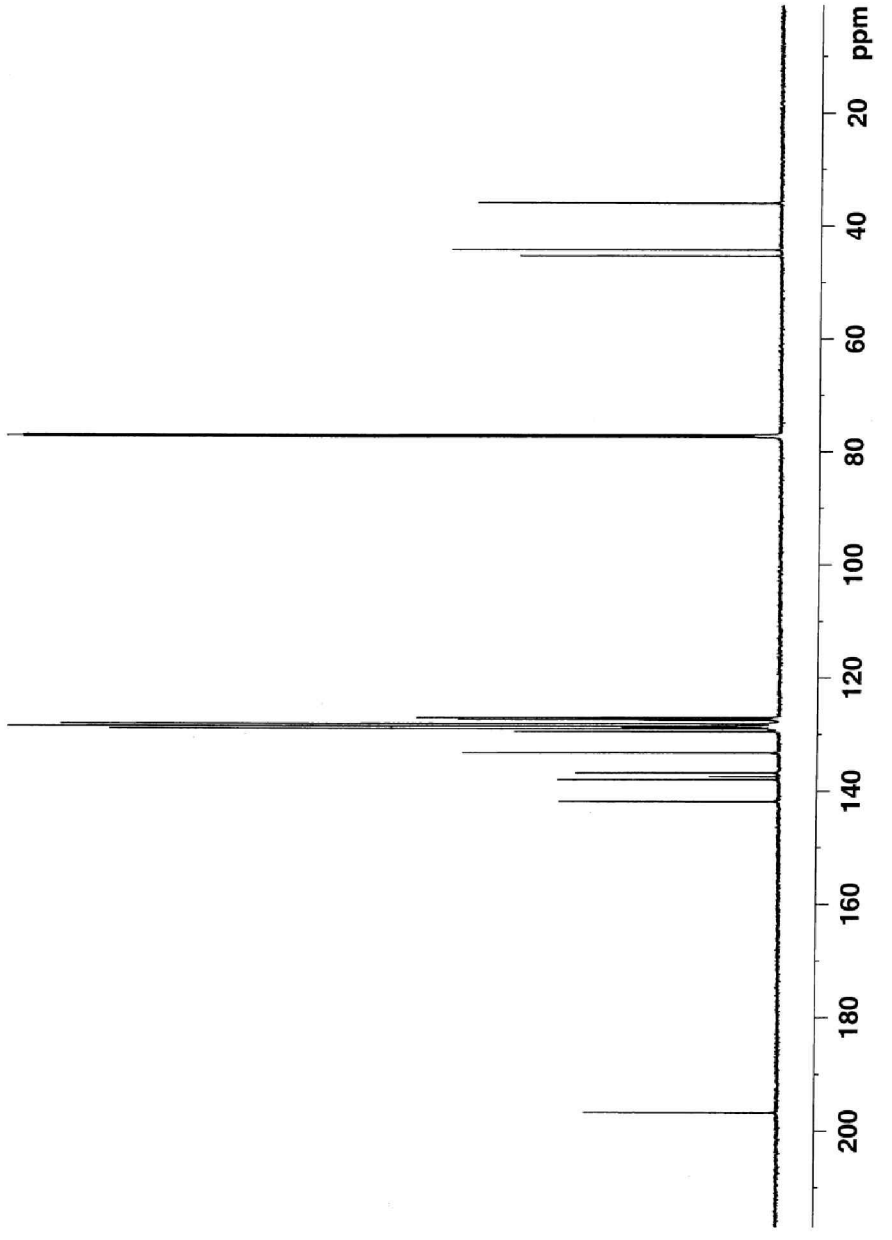

NAME SS-06-97
EXPNO 1
PROCNO 1
Date_ 20130323
Time 15.59
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 7
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 18
DW 42.000 use
DE 6.50 use
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 =======
NUC1 1H
P1 9.40 use
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
Ph
O
S
Ph
229a
ppm
0
1
2
3
4
5
6
7
8
9
3.07
3.35
0.98
2.07
1.00
2.06
1.16
4.22
2.25
1.14


229a
Ph
O
S
Ph
NAME SS-06-97
EXPNO 2
PROCNO 1
Date_ 20130323
Time 16.05
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 24
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864820 sec
RG 203
DW 12.000 usec
DE 16.50 usec
TE 298.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0697436 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 usec
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1499406 MHz
SI 32768
SF 176.0521380 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.00
220
200
180
160
140
120
100
80
60
40
20
ppm

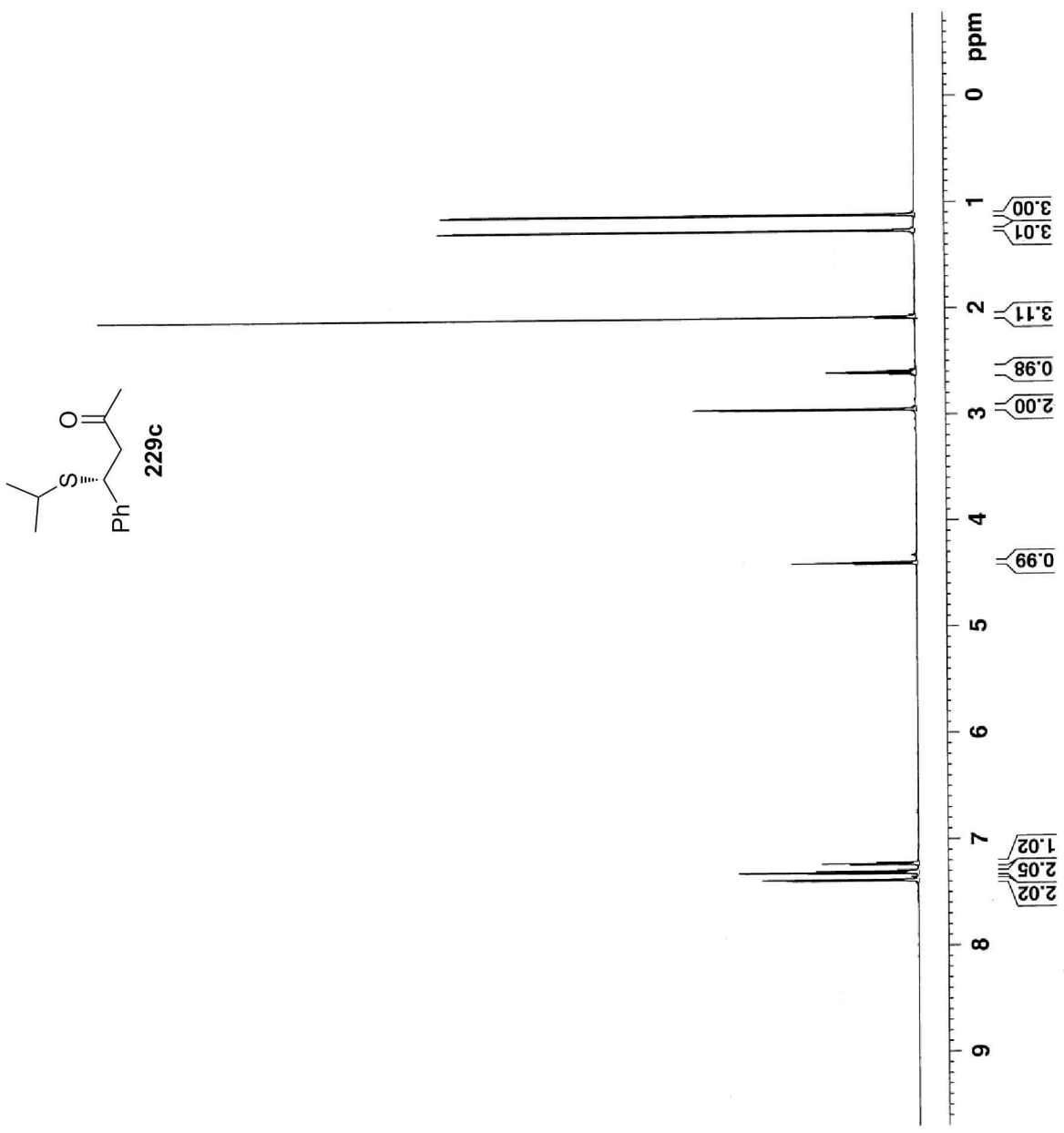

229b
Ph
O
S
Ph
NAME SS-06-123
EXPNO 1
PROCNO 1
Date_ 20130323
Time 16.11
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 14.2
DW 42.000 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
ppm
1.95
1.00
4.00
2.93
1.93
3.24
0.97
1.84
1.02
1.05

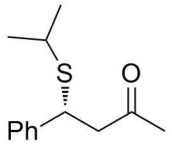


229b

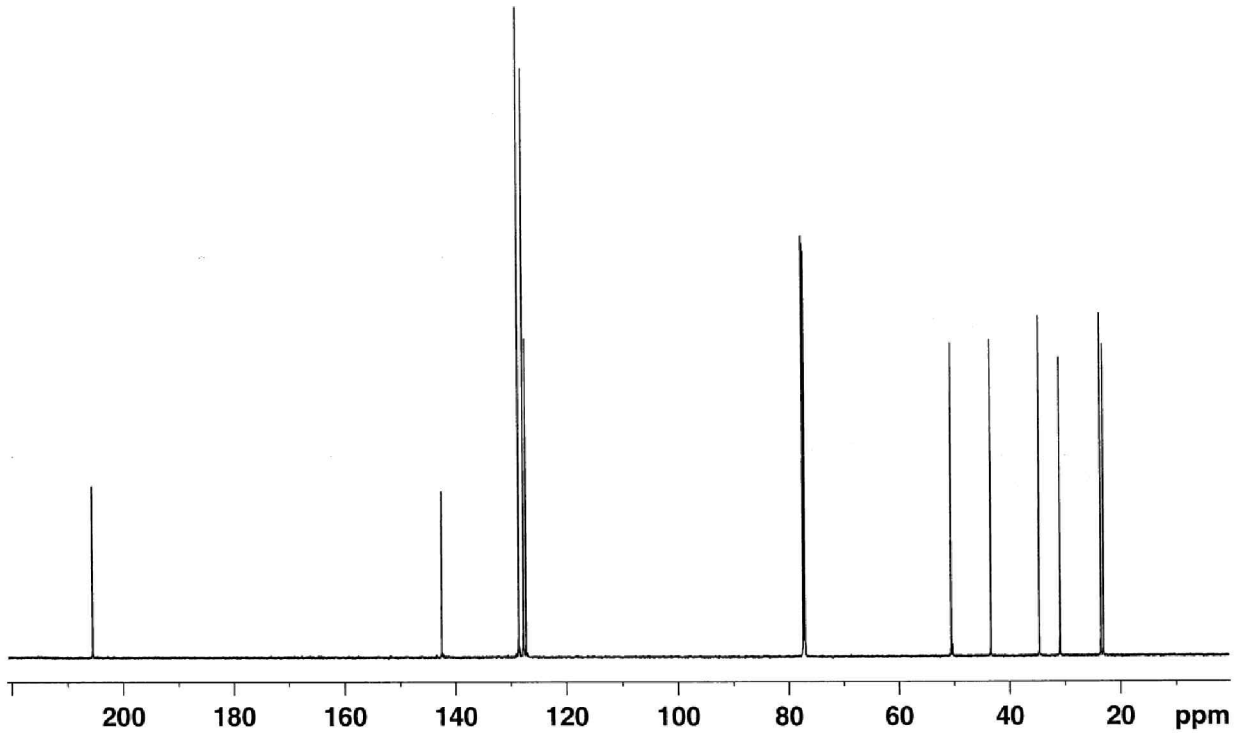



```
NAME                SS-06-123
EXPNO                       2
PROCNO                      1
Date_                20130323
Time                    16.21
INSTRUM                  spect
PROBHD     5 mm CPDCH 13C
PULPROG                 zgpg30
TD                       65536
SOLVENT                 CDCl3
NS                         13
DS                          4
SWH                 41666.668 Hz
FIDRES              0.635783 Hz
AQ                  0.7864820 sec
RG                        203
DW                     12.000 use
DE                      16.50 use
TE                     298.1 K
D1                  2.00000000 sec
D11                 0.03000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                      13C
P1                     9.00 use
PL1                    4.50 dB
PL1W               38.14553833 W
SFO1               176.0697436 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                  65.00 use
PL2                    -3.20 dB
PL12                   13.60 dB
PL13                  120.00 dB
PL2W               33.59817505 W
PL12W               0.70196527 W
PL13W               0.00000000 W
SFO2               700.1499406 MHz
SI                       32768
SF                 176.0521380 MHz
WDW                        EM
SSB                         0
LB                     3.00 Hz
GB                          0
PC                     1.00
```

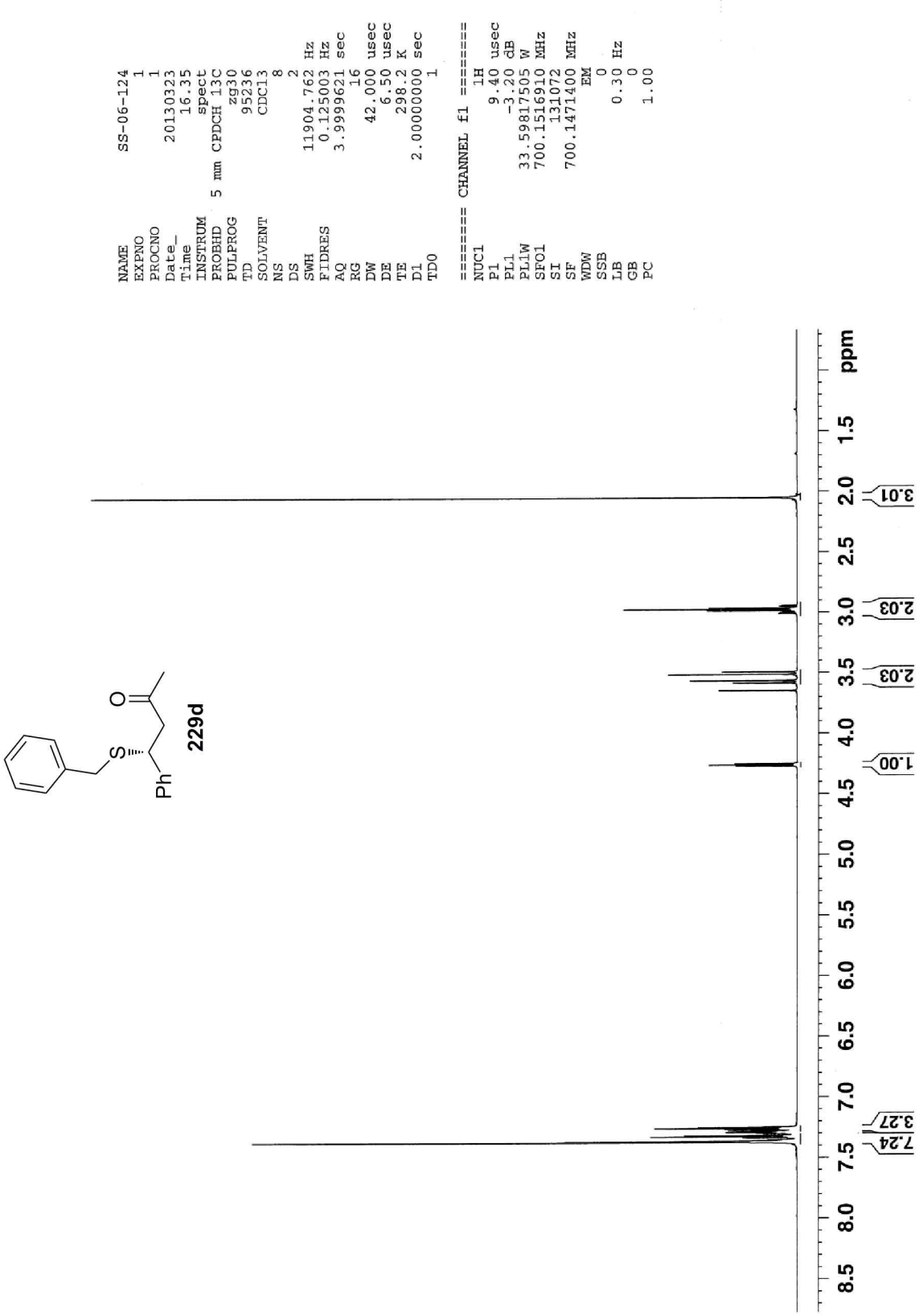

229c
Ph
S
O
NAME SS-06-106
EXPNO 1
PROCNO 1
Date_ 20130323
Time 16.27
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDC13
NS 11
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 12.7
DW 42.000 use
DE 6.50 use
TE 298.3 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 use
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
3.00
3.01
3.11
0.98
2.00
0.99
2.02
2.05
1.02
9
8
7
6
5
4
3
2
1
0 ppm

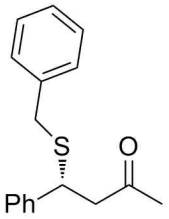


229c

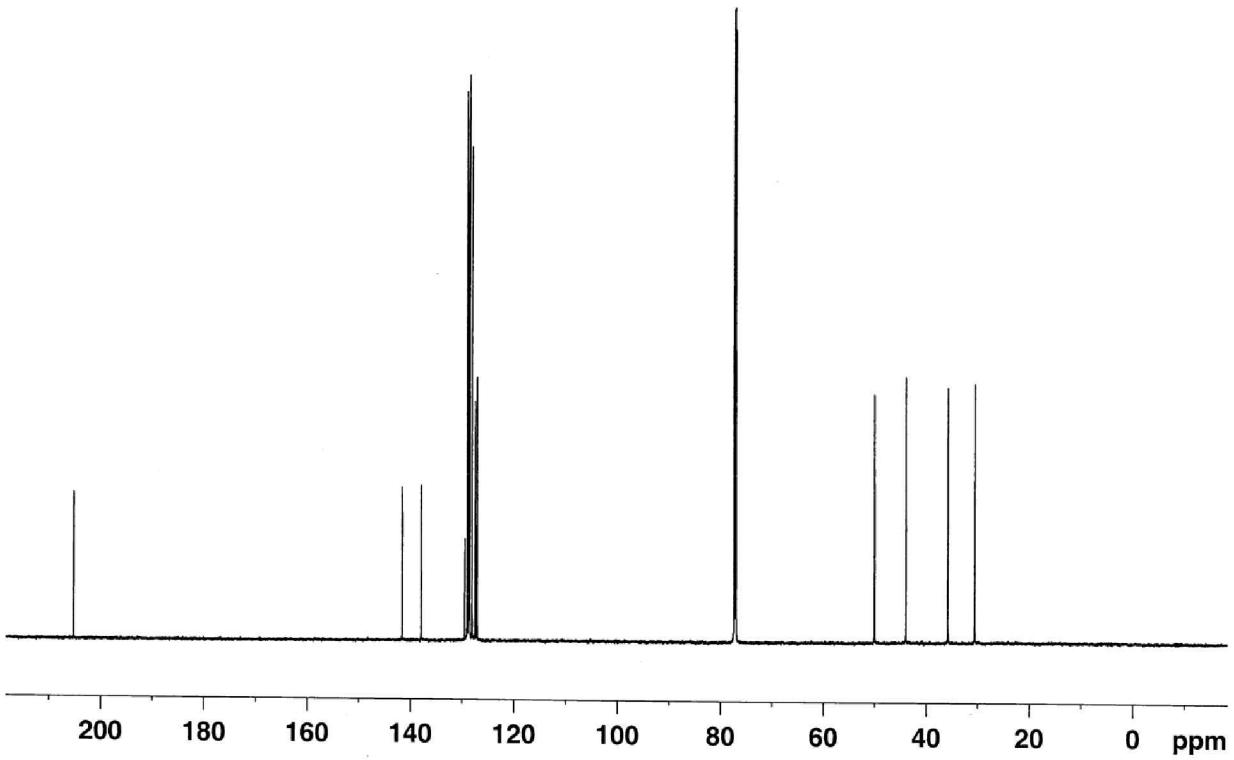


NAME	SS-06-106	
EXPNO	2	
PROCNO	1	
Date_	20130323	
Time	16.30	
INSTRUM	spect	
PROBHD	5 mm CPDCH 13C	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	17	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	usec
DE	16.50	usec
TE	298.2	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
========	CHANNEL f1	========
NUC1	13C	
P1	9.00	usec
PL1	4.50	dB
PL1W	38.14553833	W
SFO1	176.0697436	MHz
========	CHANNEL f2	========
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	65.00	usec
PL2	-3.20	dB
PL12	13.60	dB
PL13	120.00	dB
PL2W	33.59817505	W
PL12W	0.70196527	W
PL13W	0.00000000	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.00	

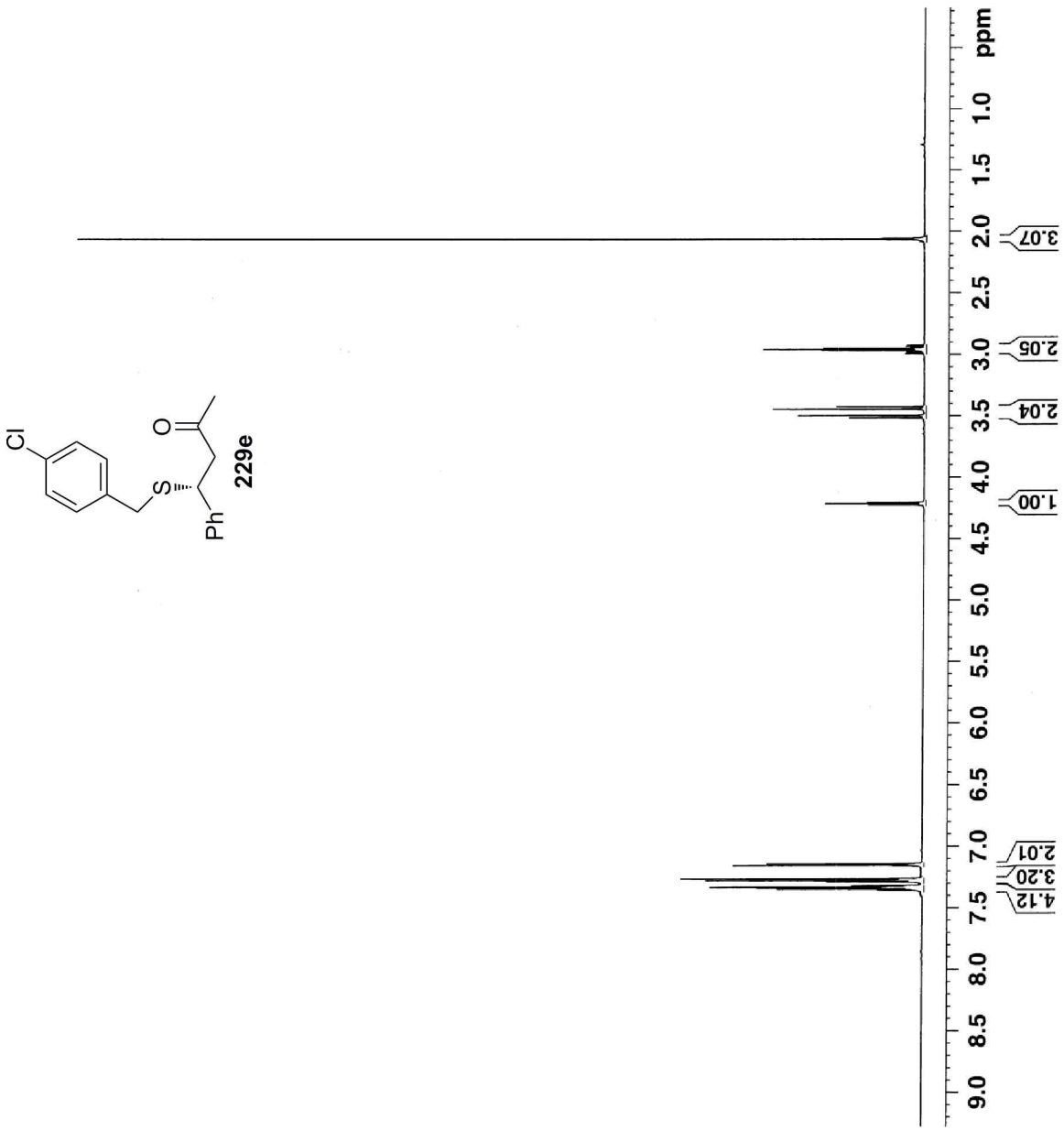

229d
NAME SS-06-124
EXPNO 1
PROCNO 1
Date_ 20130323
Time 16.35
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 8
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 16
DW 42.000 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
3.01
2.03
2.03
1.00
7.24
3.27
ppm

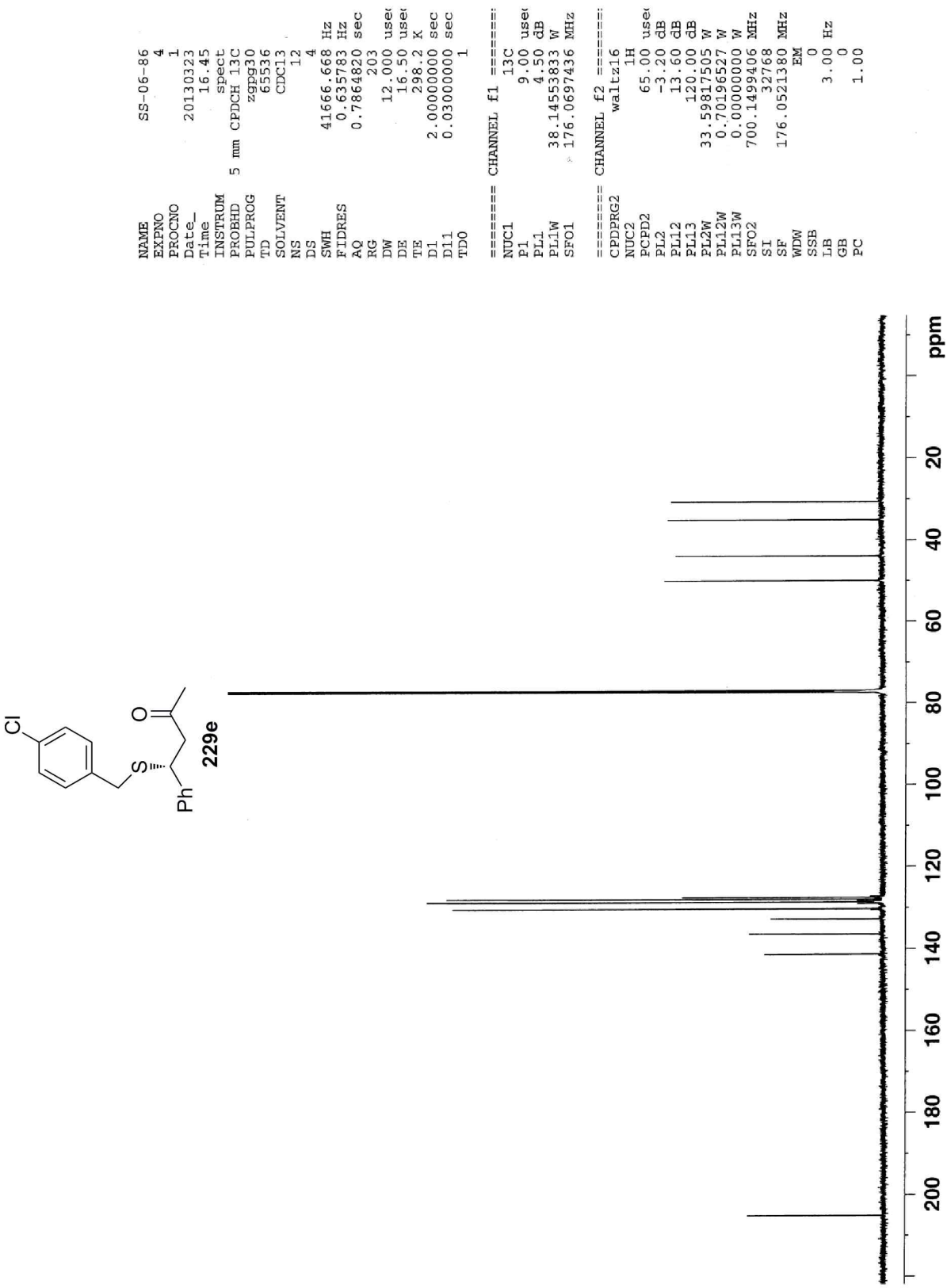


229d

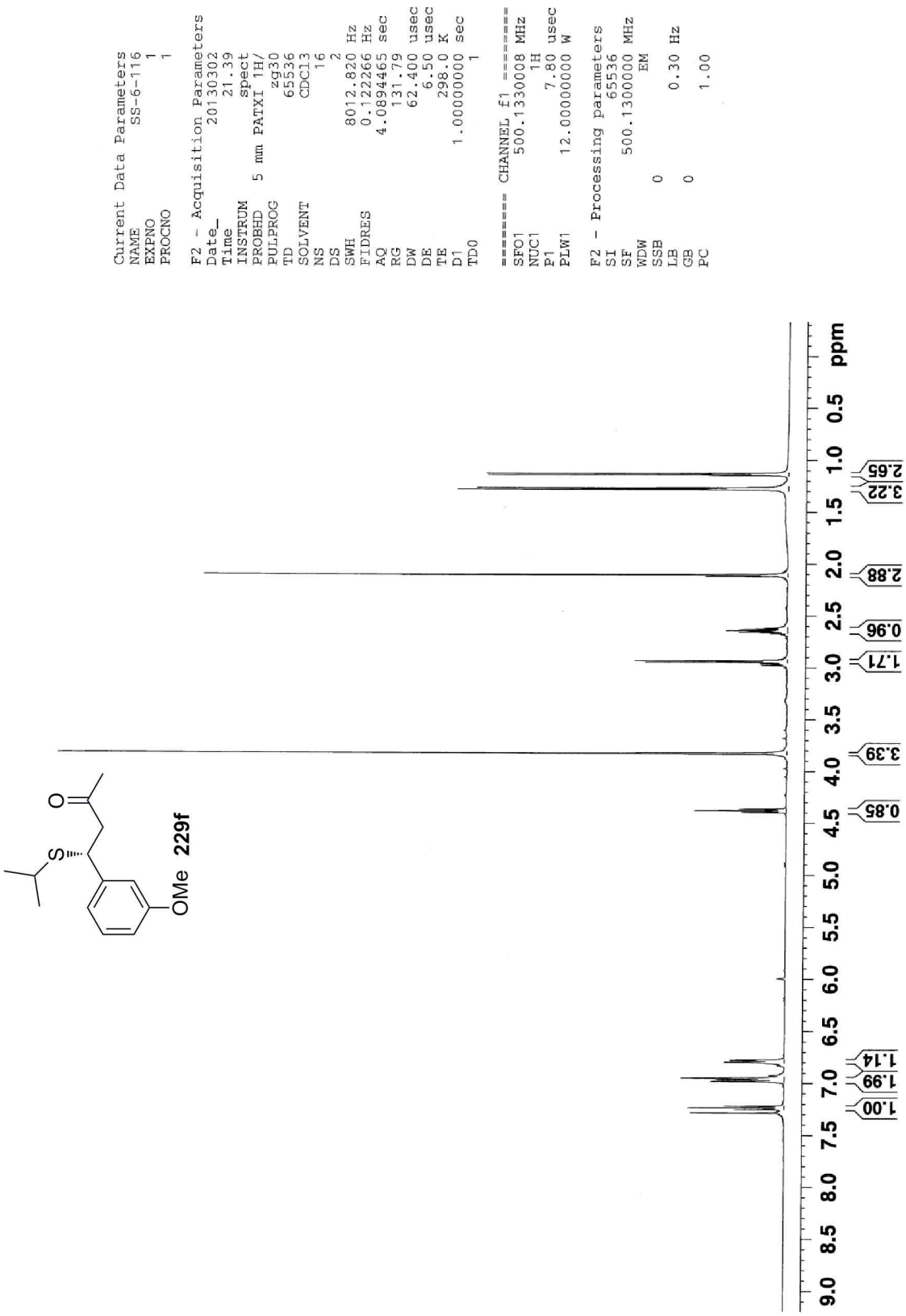


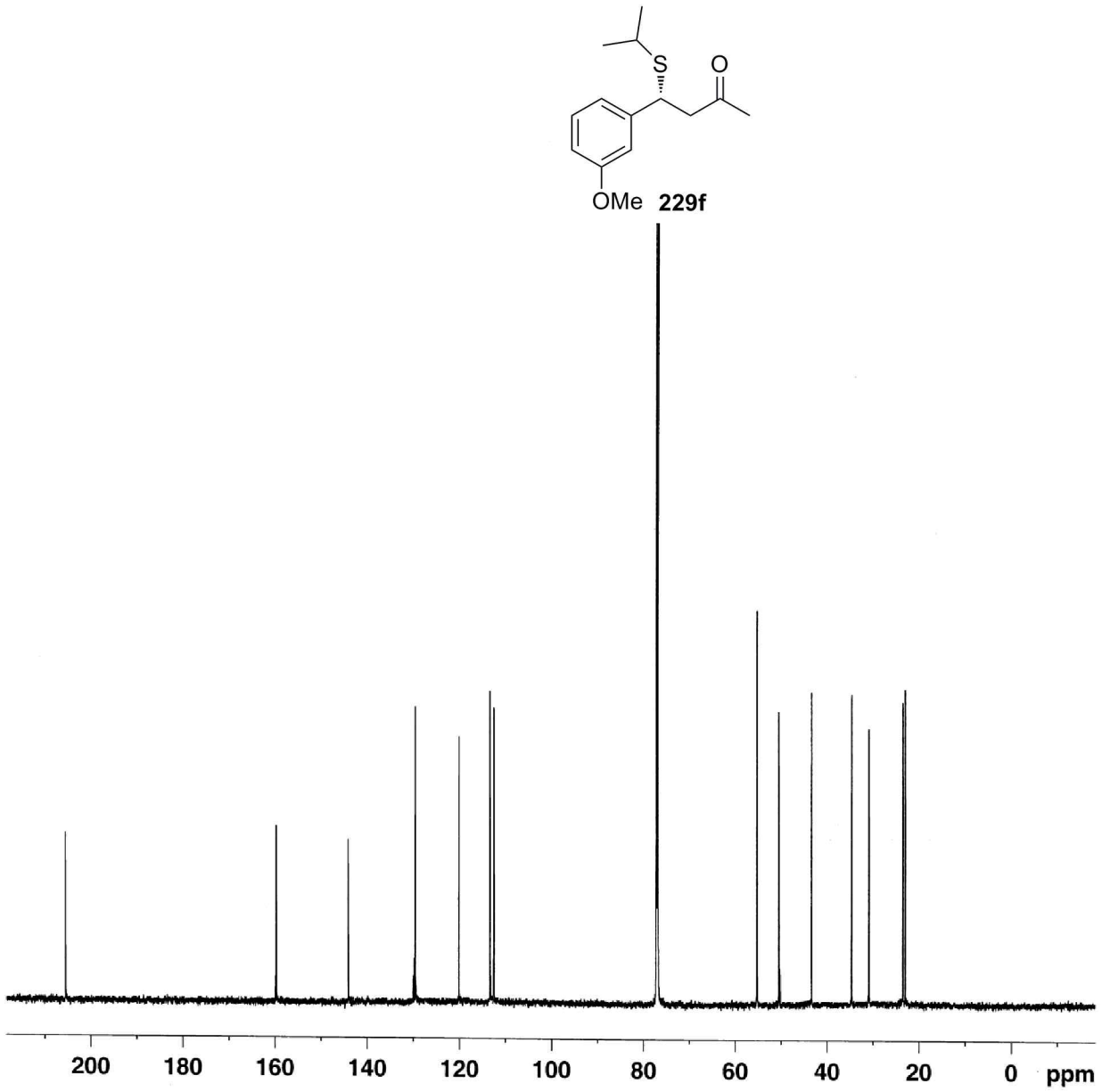
NAME	SS-06-124	
EXPNO	2	
PROCNO	1	
Date_	20130323	
Time	16.38	
INSTRUM	spect	
PROBHD	5 mm CPDCH 13C	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	12	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	usec
DE	16.50	usec
TE	298.1	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	9.00	usec
PL1	4.50	dB
PL1W	38.14553833	W
SFO1	176.0697436	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	65.00	usec
PL2	-3.20	dB
PL12	13.60	dB
PL13	120.00	dB
PL2W	33.59817505	W
PL12W	0.70196527	W
PL13W	0.00000000	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.00	


NAME SS-06-86
EXPNO 3
PROCNO 1
Date_ 20130323
Time 16.42
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDC13
NS 10
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 25.4
DW 42.000 use
DE 6.50 use
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 use
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
Cl
O
S
Ph
229e
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
2.01
3.20
4.12
1.00
2.04
2.05
3.07

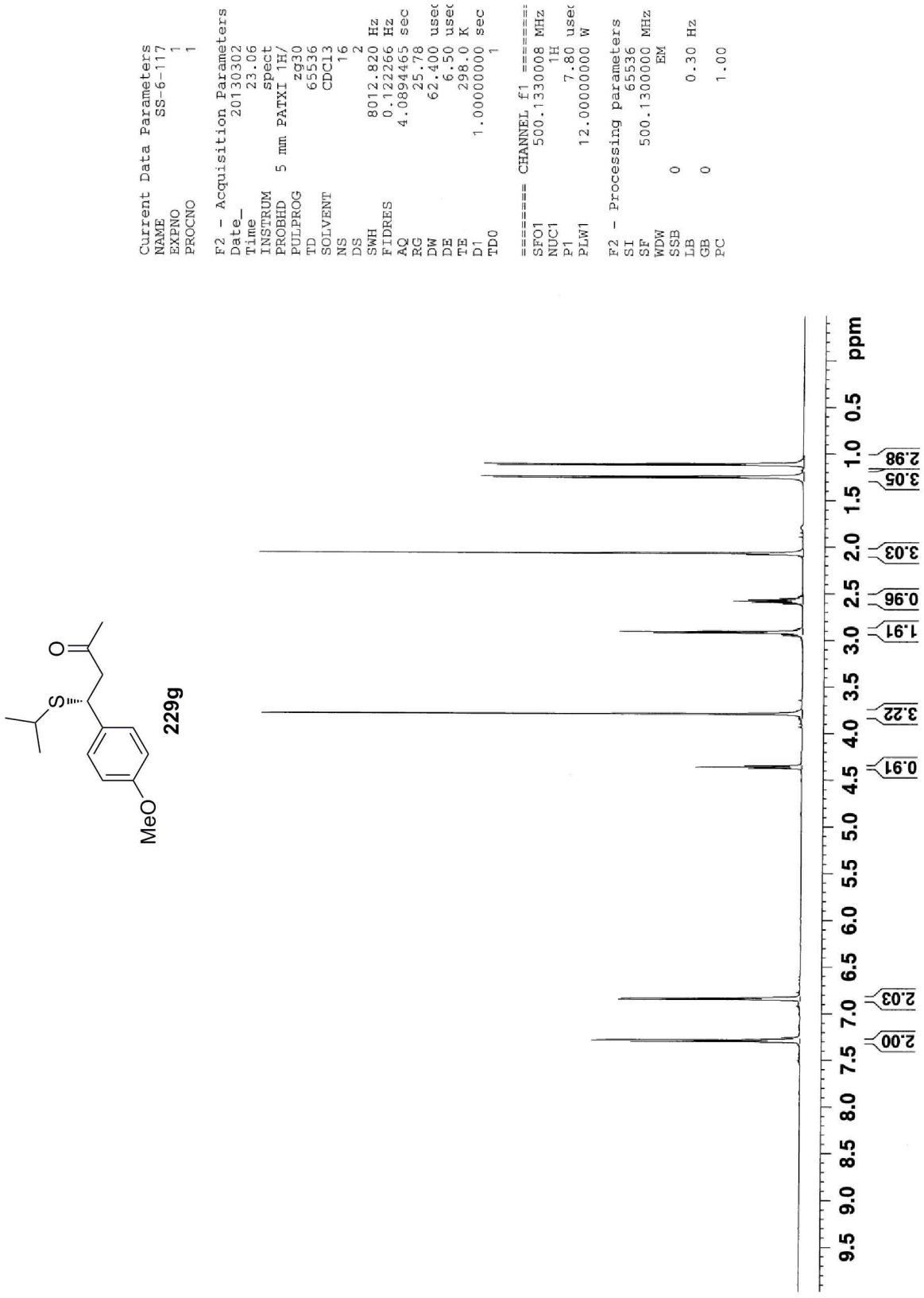


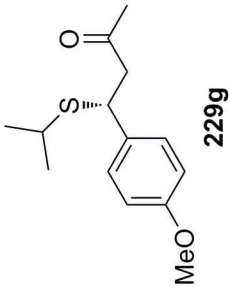

```
NAME                 SS-06-86
EXPNO                       4
PROCNO                      1
Date_                20130323
Time                    16.45
INSTRUM                  spect
PROBHD     5 mm CPDCH 13C
PULPROG                 zgpg30
TD                       65536
SOLVENT                  CDCl3
NS                          12
DS                           4
SWH                  41666.668 Hz
FIDRES                0.635783 Hz
AQ                    0.7864820 sec
RG                         203
DW                      12.000 use
DE                      16.50 use
TE                      298.2 K
D1                    2.00000000 sec
D11                   0.03000000 sec
TD0                          1

======== CHANNEL f1 ========
NUC1                       13C
P1                        9.00 use
PL1                       4.50 dB
PL1W                38.14553833 W
SFO1               176.0697436 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                        1H
PCPD2                   65.00 use
PL2                      -3.20 dB
PL12                     13.60 dB
PL13                    120.00 dB
PL2W                33.59817505 W
PL12W                0.70196527 W
PL13W                0.00000000 W
SFO2               700.1499406 MHz
SI                       32768
SF                 176.0521380 MHz
WDW                         EM
SSB                          0
LB                        3.00 Hz
GB                           0
PC                        1.00
```


Current Data Parameters
NAME SS-6-116
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130302
Time 21.39
INSTRUM spect
PROBHD 5 mm PATXI 1H/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 131.79
DW 62.400 usec
DE 6.50 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 500.1330008 MHz
NUC1 1H
P1 7.80 usec
PLW1 12.00000000 W
F2 - Processing parameters
SI 65536
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
OMe 229f
1.00
1.99
1.14
0.85
3.39
1.71
0.96
2.88
3.22
2.65
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm



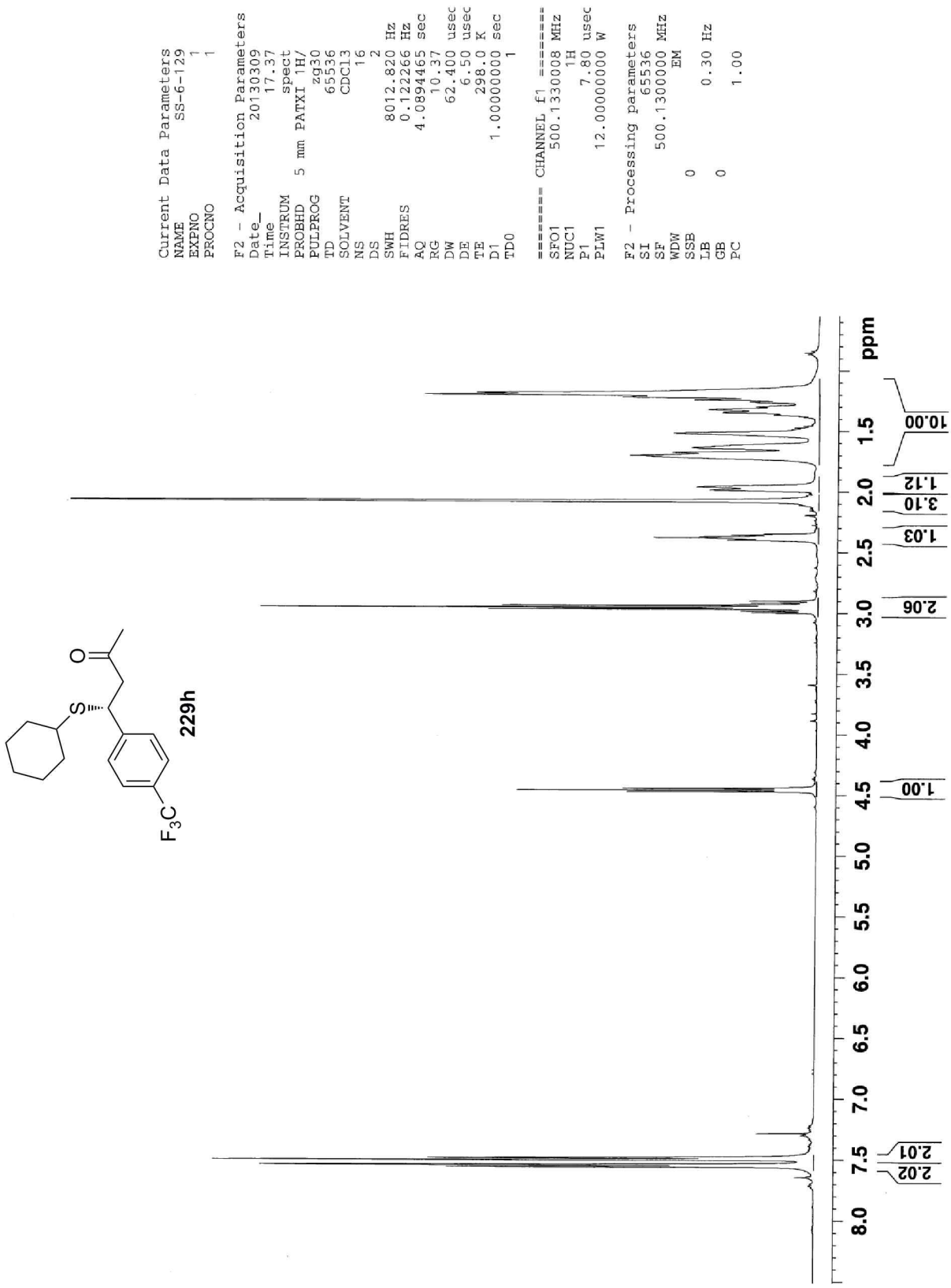
NAME	SS-06-116
EXPNO	2
PROCNO	1
Date_	20130323
Time	18.18
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	56
DS	4
SWH	41666.668 Hz
FIDRES	0.635783 Hz
AQ	0.7864820 sec
RG	203
DW	12.000 use
DE	16.50 use
TE	298.1 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
========	CHANNEL f1 ========
NUC1	13C
P1	9.00 use
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0697436 MHz
========	CHANNEL f2 ========
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 use
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1499406 MHz
SI	32768
SF	176.0521380 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.00


Current Data Parameters
NAME SS-6-117
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130302
Time 23.06
INSTRUM spect
PROBHD 5 mm PATXI 1H/
PULPROG zg30
TD 65536
SOLVENT CDC13
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 25.78
DW 62.400 usec
DE 6.50 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 500.1330008 MHz
NUC1 1H
P1 7.80 usec
PLW1 12.00000000 W
F2 - Processing parameters
SI 65536
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
O
S
MeO
229g
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
2.00
2.03
0.91
3.22
1.91
0.96
3.03
3.05
2.98

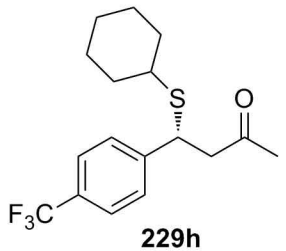


229g

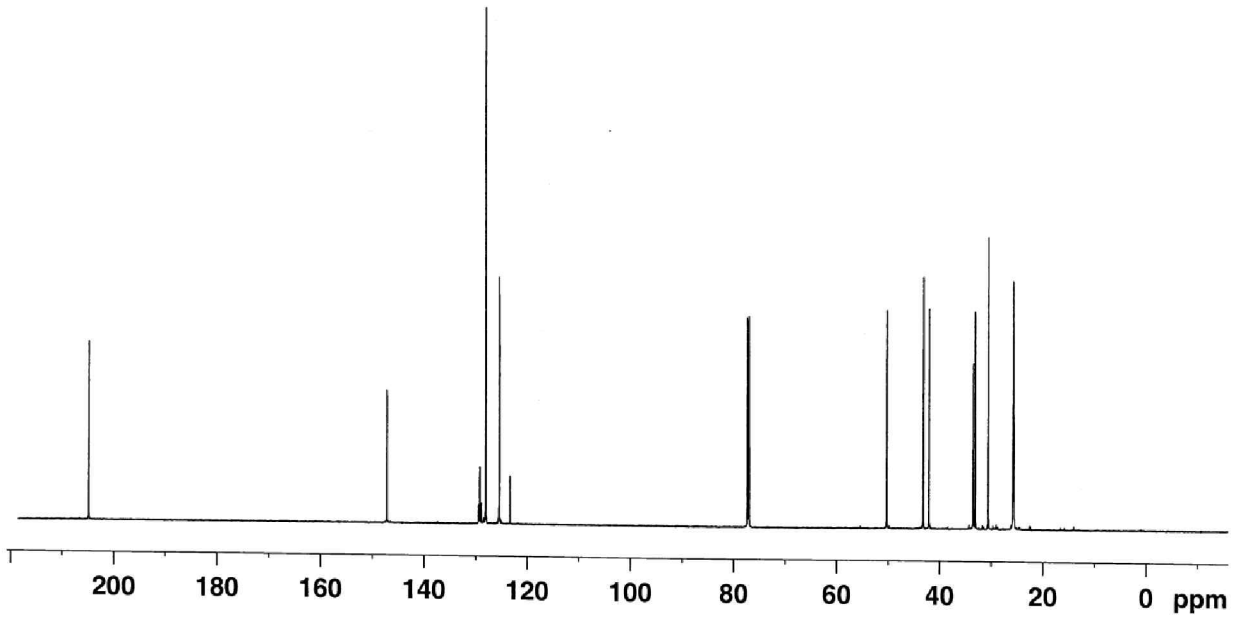
```
NAME                SS-06-117
EXPNO                       2
PROCNO                      1
Date_                20130323
Time                    18.29
INSTRUM                  spect
PROBHD     5 mm CPDCH 13C
PULPROG                 zgpg30
TD                       65536
SOLVENT                  CDCl3
NS                          35
DS                           4
SWH                  41666.668 Hz
FIDRES               0.635783 Hz
AQ                   0.7864820 sec
RG                         203
DW                      12.000 usec
DE                      16.50 usec
TE                      298.1 K
D1                   2.00000000 sec
D11                  0.03000000 sec
TD0                          1

======== CHANNEL f1 ========
NUC1                       13C
P1                        9.00 usec
PL1                       4.50 dB
PL1W                38.14553833 W
SFO1               176.0697436 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                        1H
PCPD2                     65.00 usec
PL2                       -3.20 dB
PL12                      13.60 dB
PL13                     120.00 dB
PL2W                33.59817505 W
PL12W                0.70196527 W
PL13W                0.00000000 W
SFO2               700.1499406 MHz
SI                       32768
SF                 176.0521380 MHz
WDW                         EM
SSB                          0
LB                        3.00 Hz
GB                           0
PC                        1.00
```



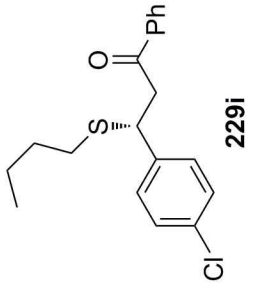

```
Current Data Parameters
NAME          SS-6-129
EXPNO                1
PROCNO               1

F2 - Acquisition Parameters
Date_         20130309
Time              17.37
INSTRUM           spect
PROBHD   5 mm PATXI 1H/
PULPROG           zg30
TD               65536
SOLVENT          CDCl3
NS                  16
DS                   2
SWH           8012.820 Hz
FIDRES           0.122266 Hz
AQ            4.0894465 sec
RG                10.37
DW               62.400 usec
DE                6.50 usec
TE              298.0 K
D1              1.00000000 sec
TD0                  1

======== CHANNEL f1 ========
SFO1        500.1330008 MHz
NUC1                   1H
P1                 7.80 usec
PLW1        12.00000000 W

F2 - Processing parameters
SI                  65536
SF          500.1300000 MHz
WDW                    EM
SSB                 0
LB                  0.30 Hz
GB                  0
PC                  1.00
```



229h

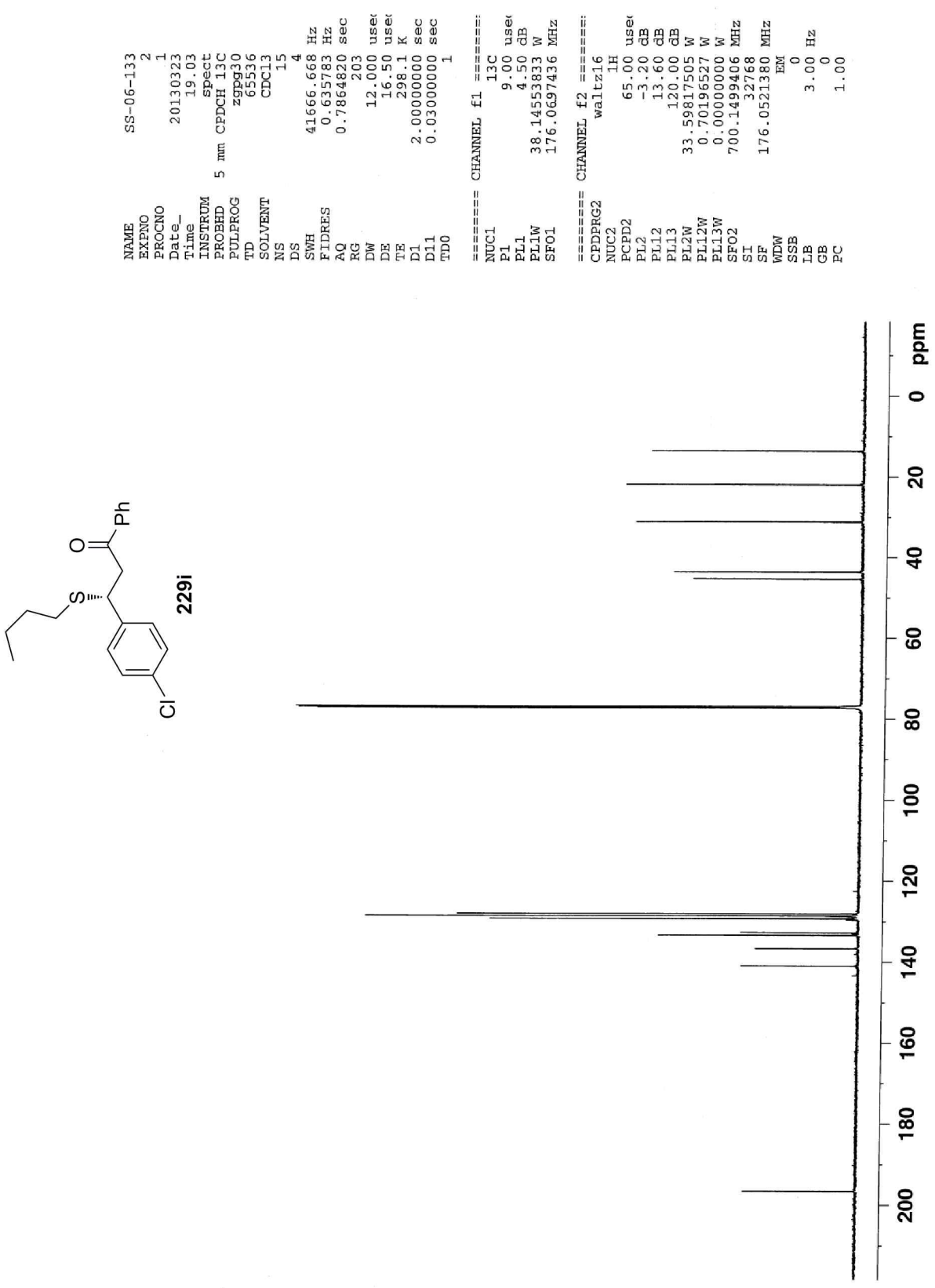


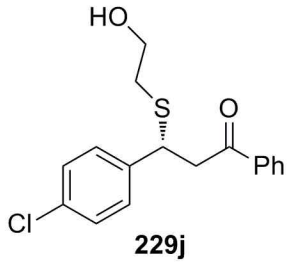
NAME	SS-06-129	
EXPNO	2	
PROCNO	1	
Date_	20130323	
Time	18.50	
INSTRUM	spect	
PROBHD	5 mm CPDCH 13C	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	25	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	usec
DE	16.50	usec
TE	298.1	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
========	CHANNEL f1 ========	
NUC1	13C	
P1	9.00	usec
PL1	4.50	dB
PL1W	38.14553833	W
SFO1	176.0697436	MHz
========	CHANNEL f2 ========	
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	65.00	usec
PL2	-3.20	dB
PL12	13.60	dB
PL13	120.00	dB
PL2W	33.59817505	W
PL12W	0.70196527	W
PL13W	0.00000000	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.00	



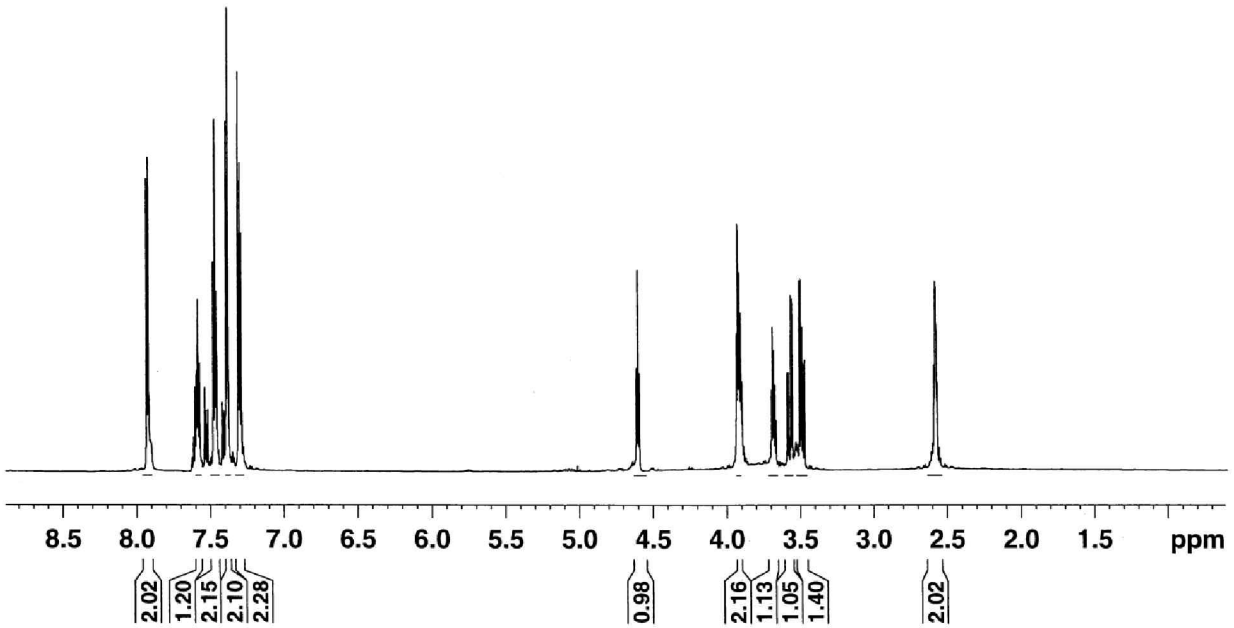
229i

```
Current Data Parameters
NAME          SS-6-133
EXPNO                1
PROCNO               1

F2 - Acquisition Parameters
Date_         20130309
Time              20.42
INSTRUM            spect
PROBHD   5 mm PATXI 1H/
PULPROG            zg30
TD                65536
SOLVENT           CDCl3
NS                   16
DS                    2
SWH           8012.820 Hz
FIDRES           0.122266 Hz
AQ            4.0894465 sec
RG                25.78
DW               62.400 usec
DE                6.50 usec
TE              298.0 K
D1              1.00000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1        500.1330008 MHz
NUC1               1H
P1                7.80 usec
PLW1       12.00000000 W

F2 - Processing parameters
SI                65536
SF          500.1300000 MHz
WDW                EM
SSB                0
LB                 0.30 Hz
GB                 0
PC                 1.00
```

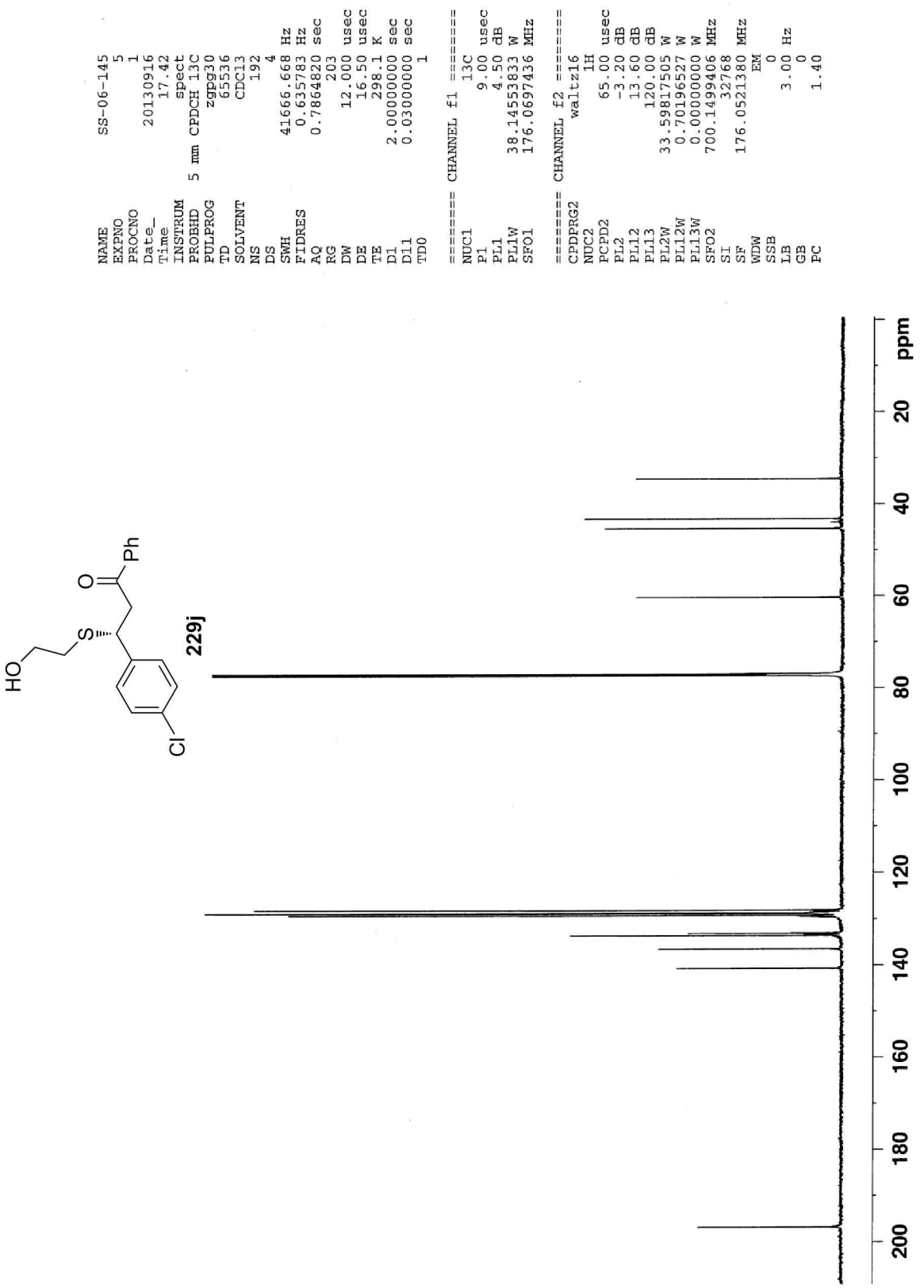

229i
Ph
O
S
Cl
NAME SS-06-133
EXPNO 2
PROCNO 1
Date_ 20130323
Time 19.03
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 15
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864820 sec
RG 203
DW 12.000 use
DE 16.50 use
TE 298.1 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 use
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0697436 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 use
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1499406 MHz
SI 32768
SF 176.0521380 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.00
200
180
160
140
120
100
80
60
40
20
0
ppm



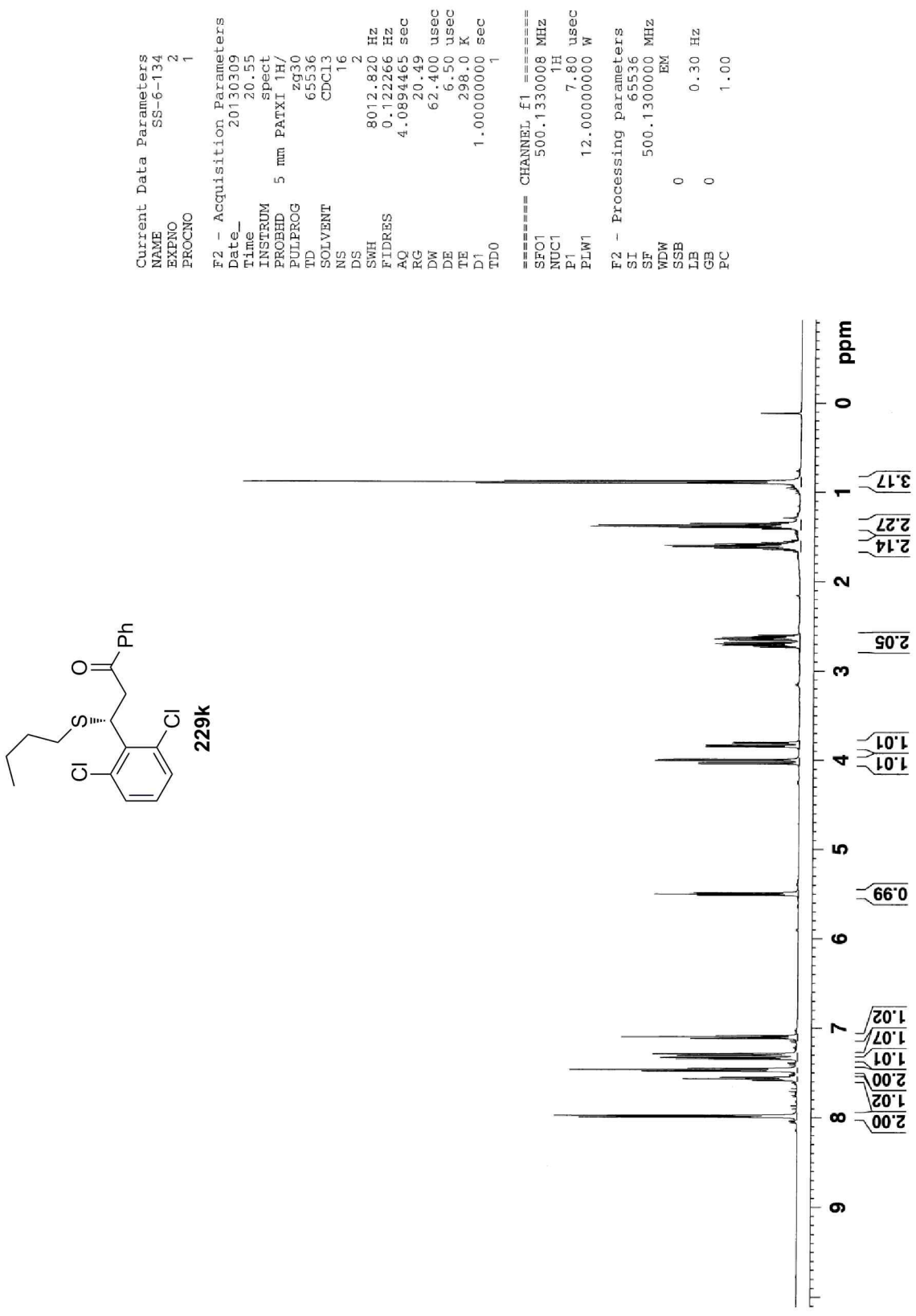
229j

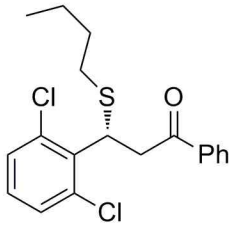


NAME	SS-06-145
EXPNO	4
PROCNO	1
Date_	20130916
Time	17.30
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zg30
TD	95236
SOLVENT	CDCl3
NS	16
DS	2
SWH	11904.762 Hz
FIDRES	0.125003 Hz
AQ	3.9999621 sec
RG	22.6
DW	42.000 use
DE	6.50 use
TE	298.2 K
D1	2.00000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	1H
P1	9.40 use
PL1	-3.20 dB
PL1W	33.59817505 W
SFO1	700.1516910 MHz
SI	131072
SF	700.1471400 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

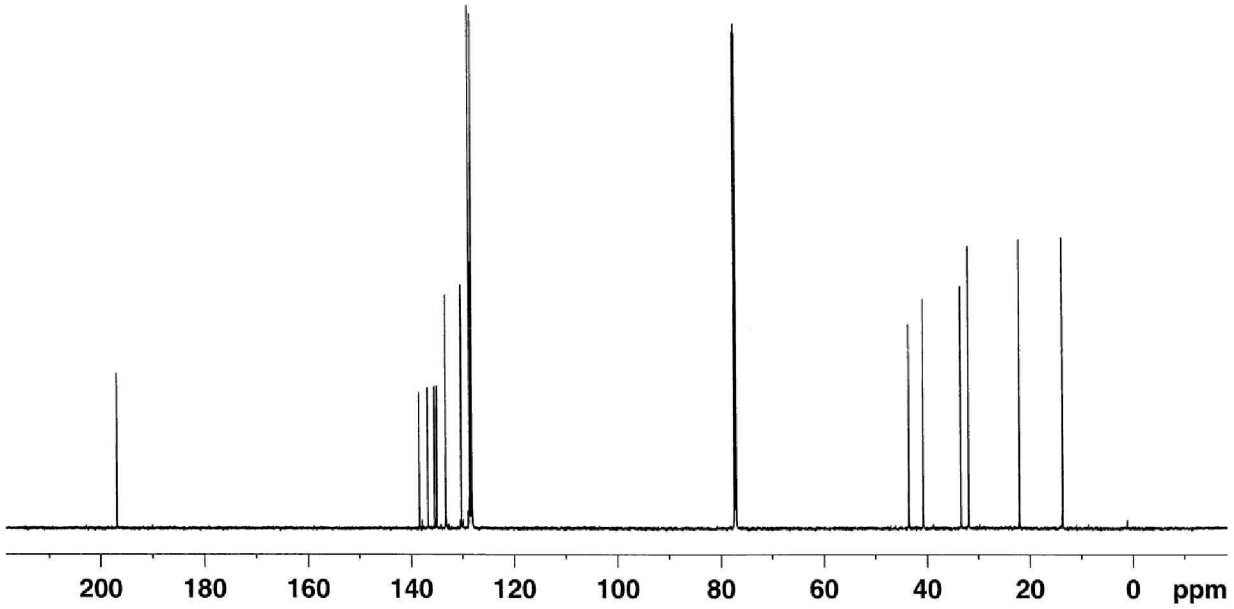



```
NAME                SS-06-145
EXPNO                       5
PROCNO                      1
Date_            20130916
Time_                 17.42
INSTRUM                spect
PROBHD     5 mm CPDCH 13C
PULPROG                zgpg30
TD                      65536
SOLVENT                 CDCl3
NS                        192
DS                          4
SWH                 41666.668 Hz
FIDRES              0.635783 Hz
AQ                  0.7864820 sec
RG                        203
DW                     12.000 usec
DE                     16.50 usec
TE                     298.1 K
D1                  2.00000000 sec
D11                 0.03000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                      13C
P1                     9.00 usec
PL1                    4.50 dB
PL1W            38.14553833 W
SFO1            176.0697436 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                  65.00 usec
PL2                    -3.20 dB
PL12                   13.60 dB
PL13                   120.00 dB
PL2W            33.59817505 W
PL12W            0.70196527 W
PL13W            0.00000000 W
SFO2            700.1499406 MHz
SI                      32768
SF              176.0521380 MHz
WDW                        EM
SSB                         0
LB                   3.00 Hz
GB                          0
PC                     1.40
```

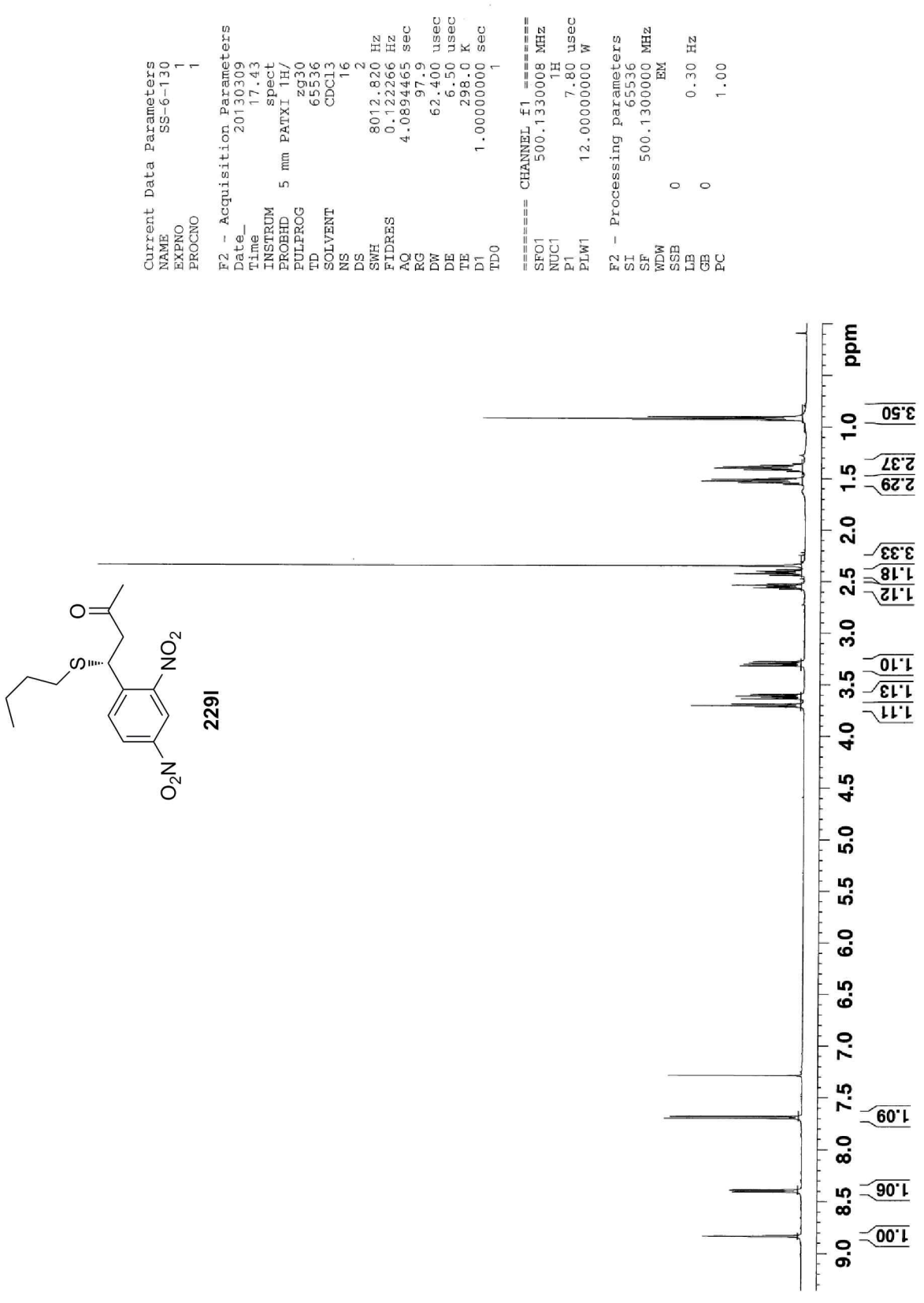

Current Data Parameters
NAME SS-6-134
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130309
Time 20.55
INSTRUM spect
PROBHD 5 mm PATXI 1H/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 20.49
DW 62.400 usec
DE 6.50 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 500.1330008 MHz
NUC1 1H
P1 7.80 usec
PLW1 12.00000000 W
F2 - Processing parameters
SI 65536
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
Ph
O
S
Cl
Cl
229k
ppm
3.17
2.27
2.14
2.05
1.01
1.01
0.99
2.00
1.02
2.00
1.01
1.07
1.02

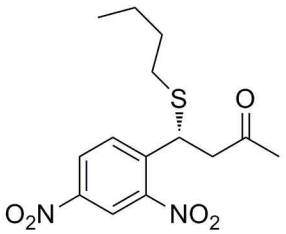


229k

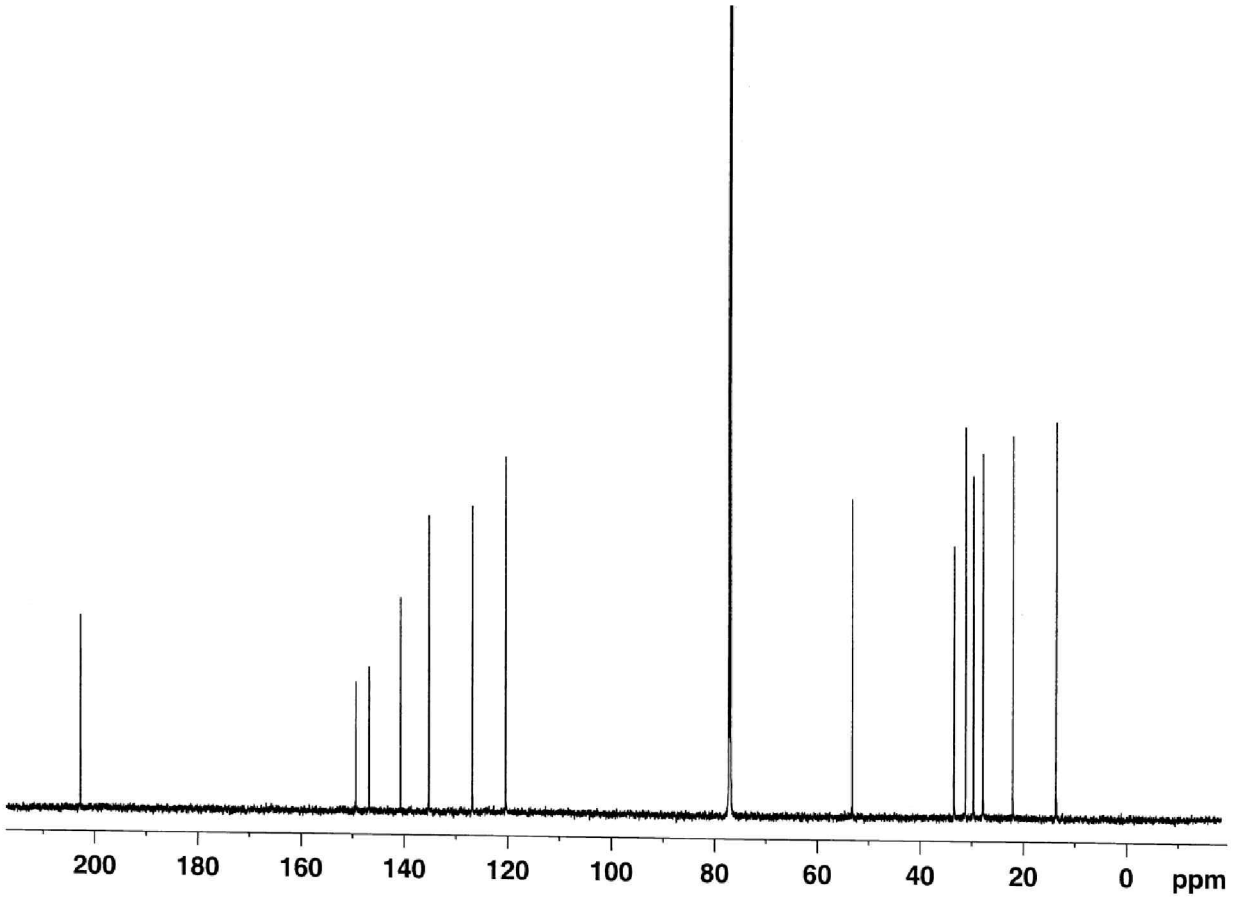


NAME	SS-06-134	
EXPNO	2	
PROCNO	1	
Date_	20130323	
Time	19.10	
INSTRUM	spect	
PROBHD	5 mm CPDCH 13C	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	10	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	use
DE	16.50	use
TE	298.2	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	9.00	use
PL1	4.50	dB
PL1W	38.14553833	W
SFO1	176.0697436	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	65.00	use
PL2	-3.20	dB
PL12	13.60	dB
PL13	120.00	dB
PL2W	33.59817505	W
PL12W	0.70196527	W
PL13W	0.00000000	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.00	

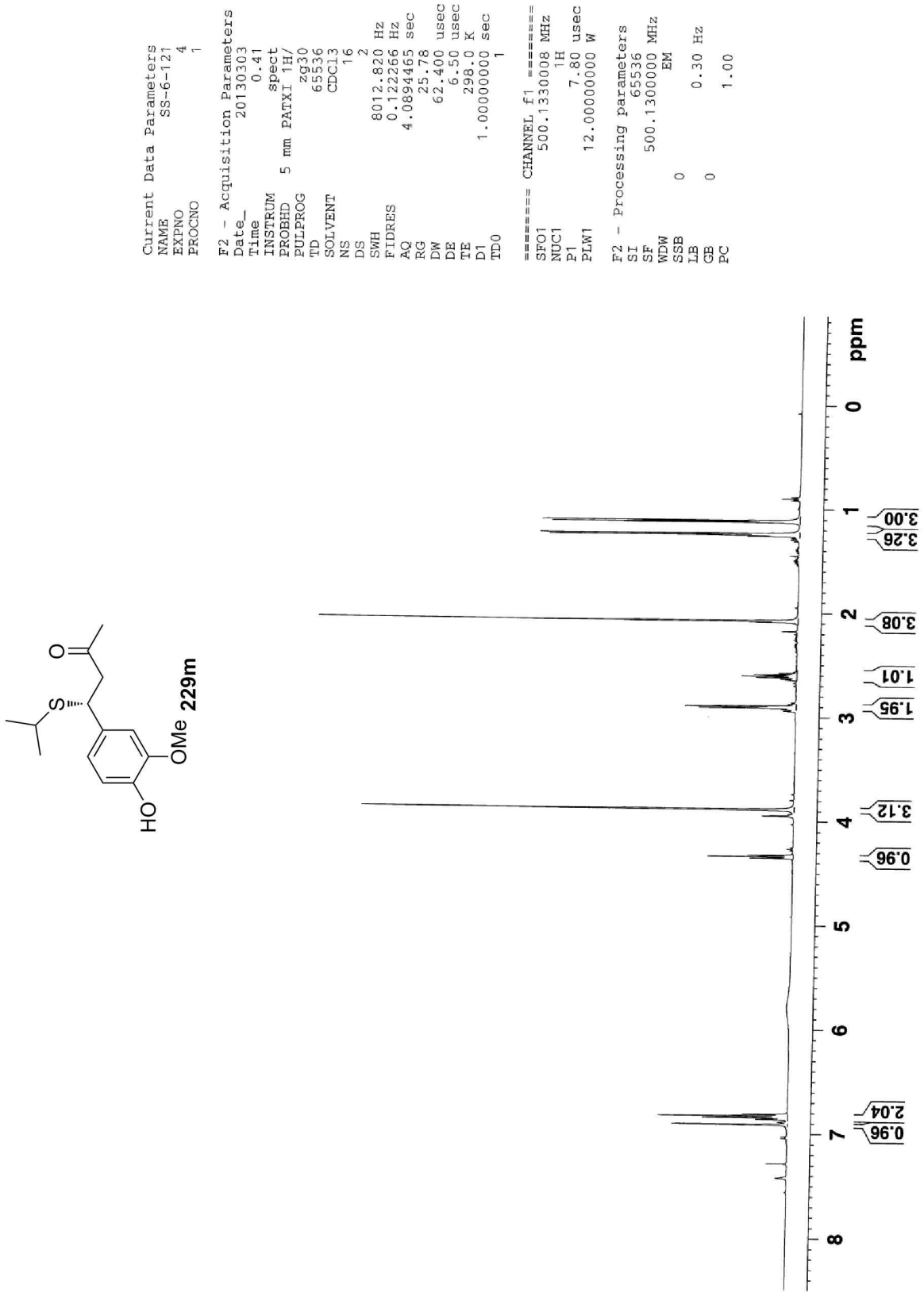

Current Data Parameters
NAME SS-6-130
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130309
Time 17.43
INSTRUM spect
PROBHD 5 mm PATXI 1H/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 97.9
DW 62.400 usec
DE 6.50 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 500.1330008 MHz
NUC1 1H
P1 7.80 usec
PLW1 12.00000000 W
F2 - Processing parameters
SI 65536
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
O
S
NO2
O2N
229l
ppm
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
1.00
1.06
1.09
1.11
1.13
1.10
1.12
1.18
3.33
2.29
2.37
3.50

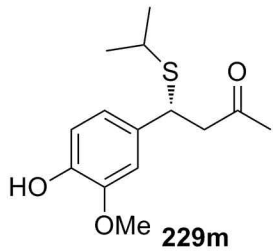


229I

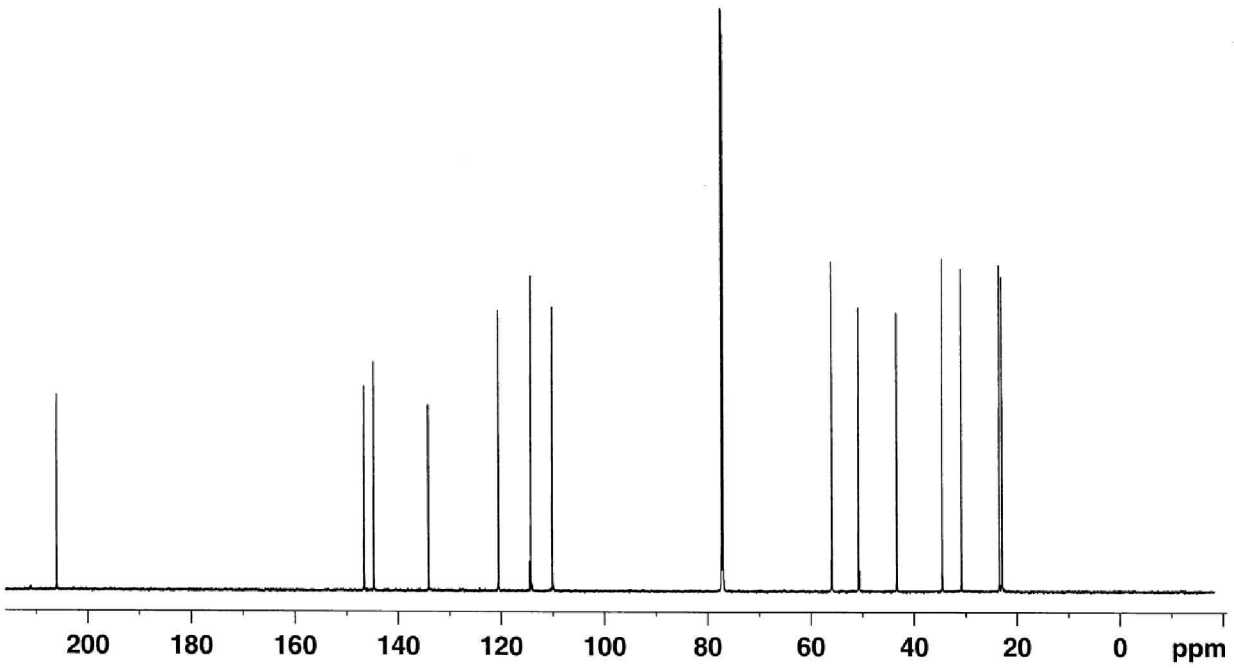


NAME	SS-06-130	
EXPNO	2	
PROCNO	1	
Date_	20130323	
Time	18.57	
INSTRUM	spect	
PROBHD	5 mm CPDCH 13C	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	20	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	use
DE	16.50	use
TE	298.1	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
========	CHANNEL f1	=======
NUC1	13C	
P1	9.00	use
PL1	4.50	dB
PL1W	38.14553833	W
SFO1	176.0697436	MHz
========	CHANNEL f2	=======
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	65.00	use
PL2	-3.20	dB
PL12	13.60	dB
PL13	120.00	dB
PL2W	33.59817505	W
PL12W	0.70196527	W
PL13W	0.00000000	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.00	

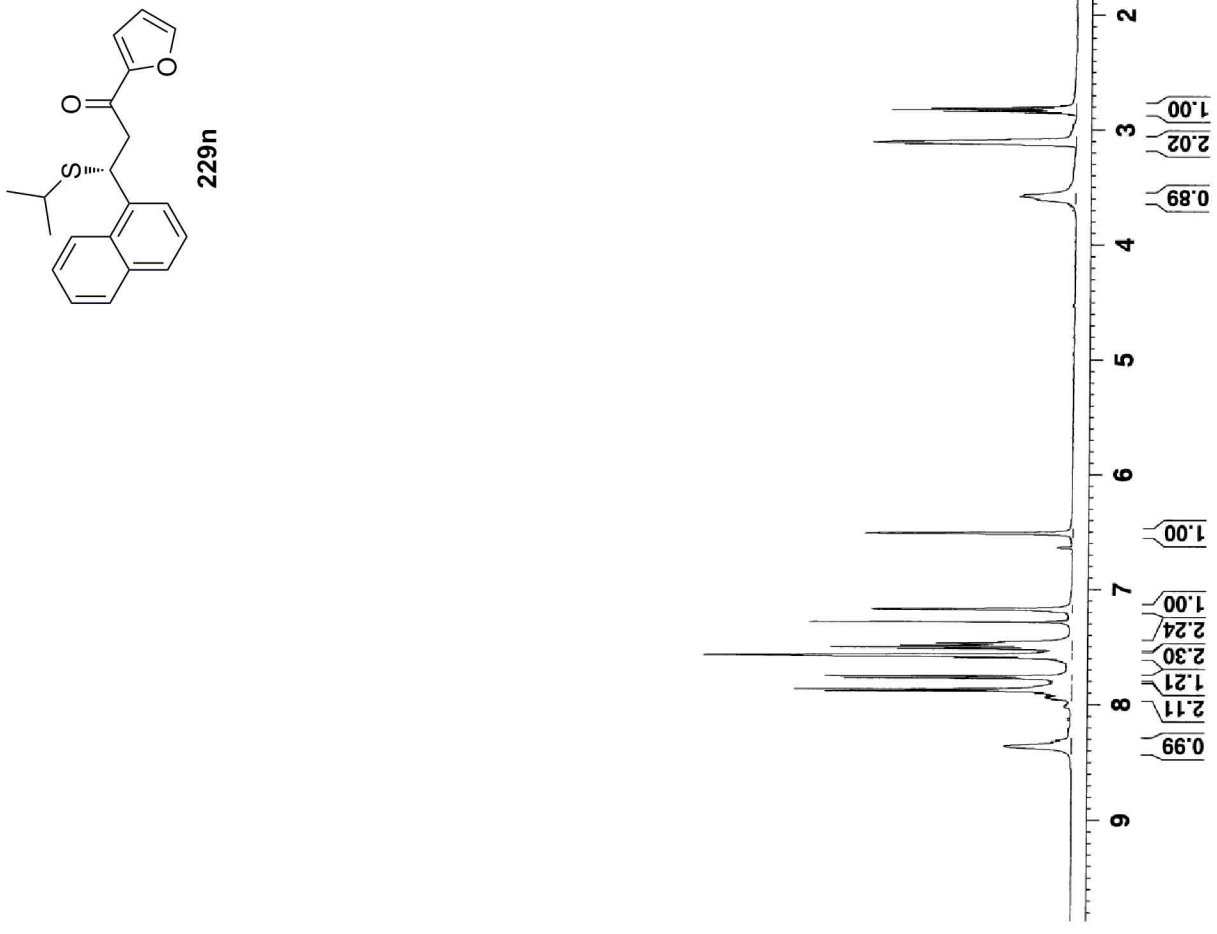

229m
OMe
HO
O
S
Current Data Parameters
NAME SS-6-121
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130303
Time 0.41
INSTRUM spect
PROBHD 5 mm PATXI 1H/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 25.78
DW 62.400 usec
DE 6.50 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 500.1330008 MHz
NUC1 1H
P1 7.80 usec
PLW1 12.00000000 W
F2 - Processing parameters
SI 65536
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
3.26
3.00
3.08
1.01
1.95
3.12
0.96
0.96
2.04
ppm

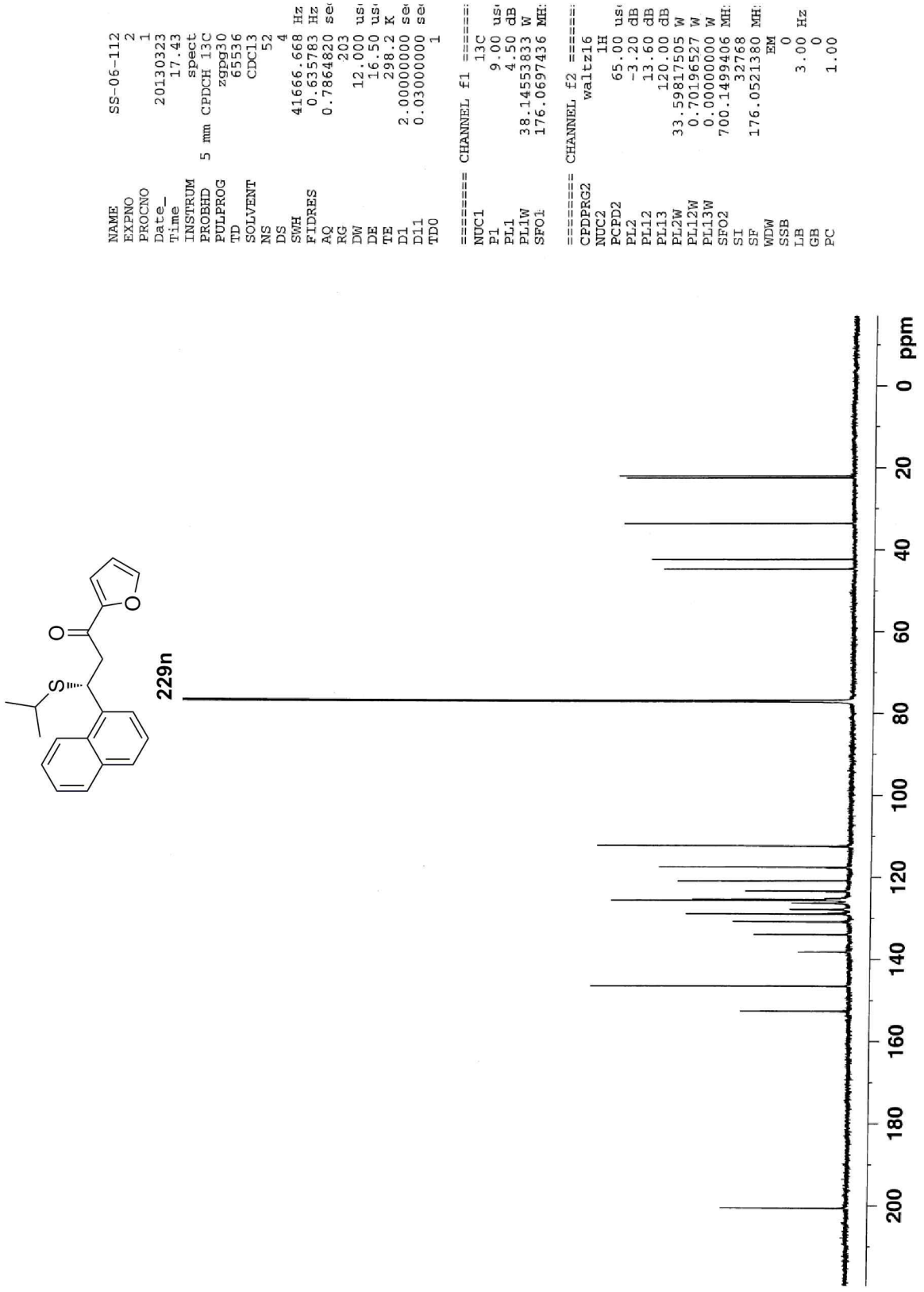


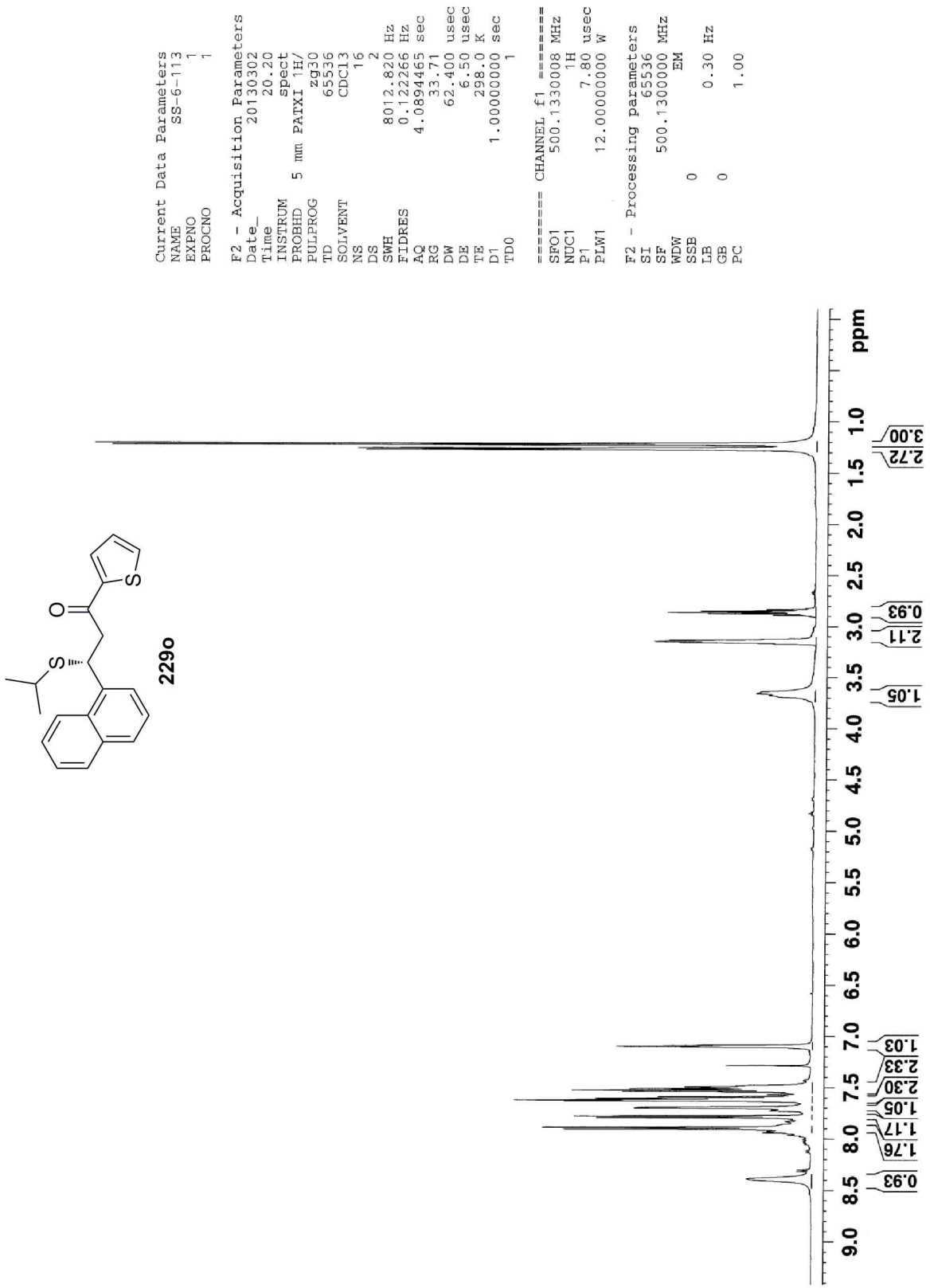
229m

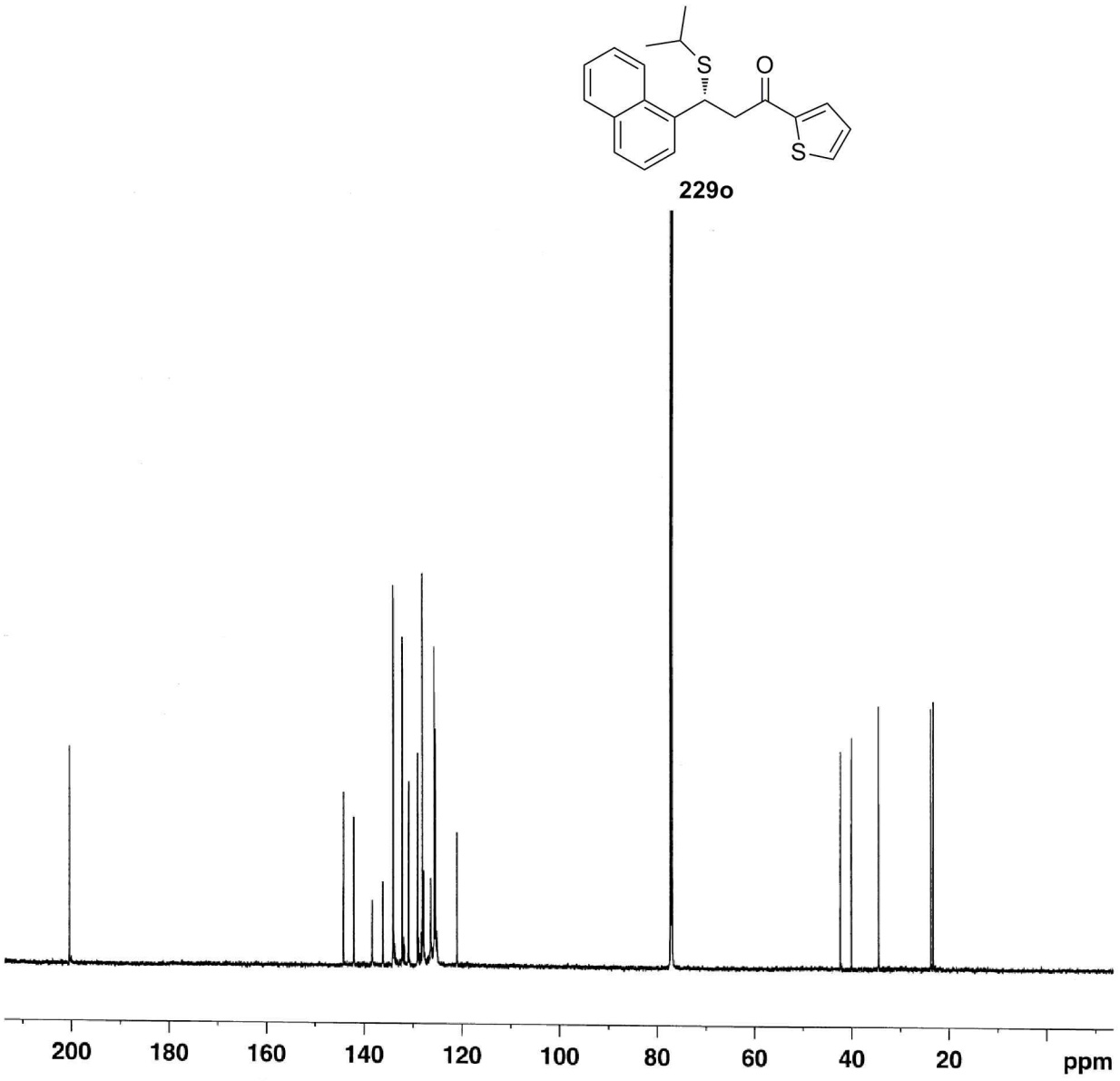


NAME	SS-06-121	
EXPNO	2	
PROCNO	1	
Date_	20130323	
Time	18.36	
INSTRUM	spect	
PROBHD	5 mm CPDCH 13C	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	22	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	usec
DE	16.50	usec
TE	298.2	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	9.00	usec
PL1	4.50	dB
PL1W	38.14553833	W
SFO1	176.0697436	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	65.00	usec
PL2	-3.20	dB
PL12	13.60	dB
PL13	120.00	dB
PL2W	33.59817505	W
PL12W	0.70196527	W
PL13W	0.00000000	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.00	

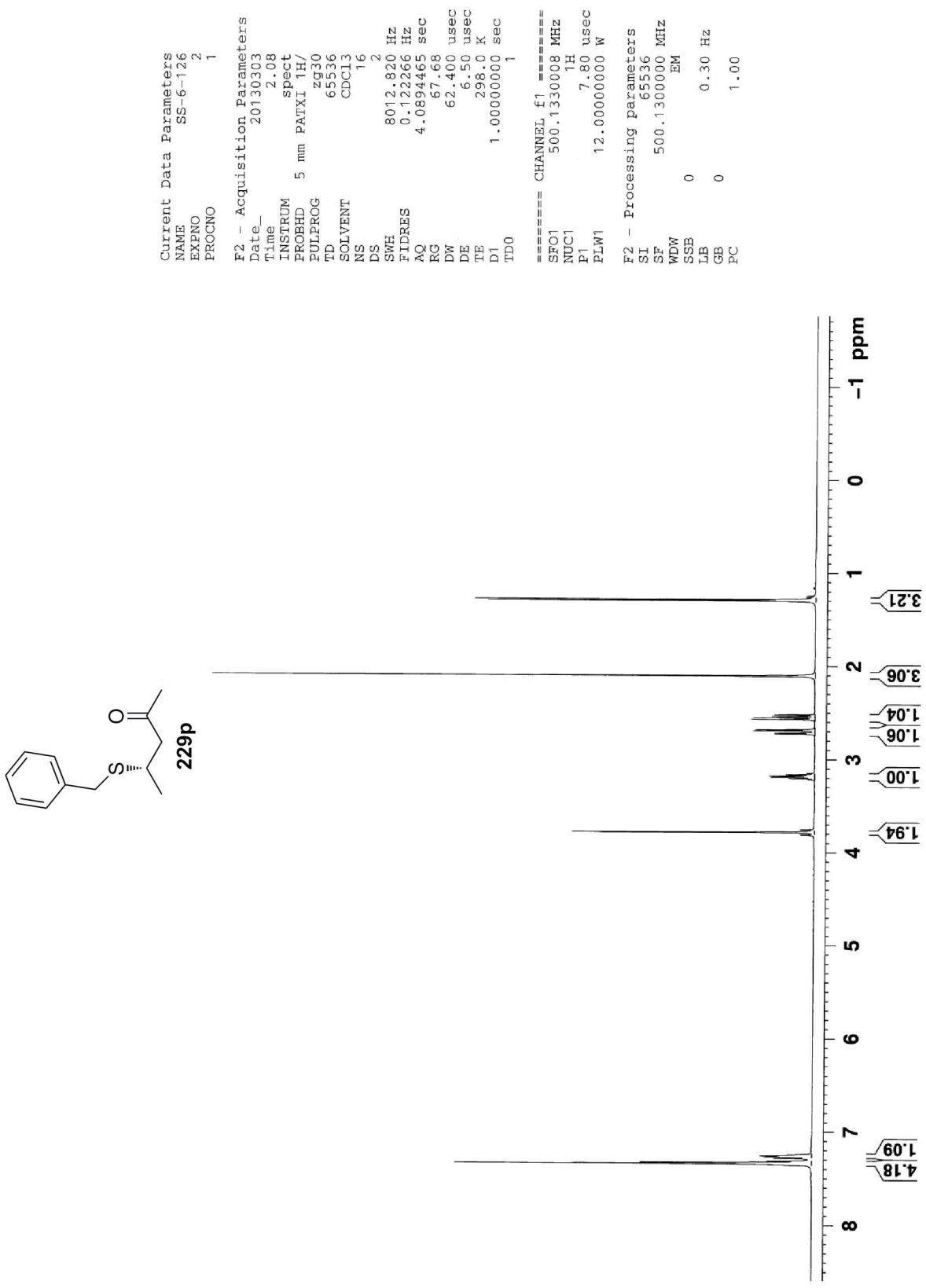

229n
Current Data Parameters
NAME SS-6-112
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130302
Time 20.00
INSTRUM spect
PROBHD 5 mm PATXI 1H/
PULPROG zg30
TD 65536
SOLVENT CDC13
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 97.9
DW 62.400 usec
DE 6.50 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 500.1330008 MHz
NUC1 1H
P1 7.80 usec
PLW1 12.00000000 W
F2 - Processing parameters
SI 65536
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
3.20
3.07
1.00
2.02
0.89
1.00
1.00
2.24
2.30
1.21
2.11
0.99
ppm

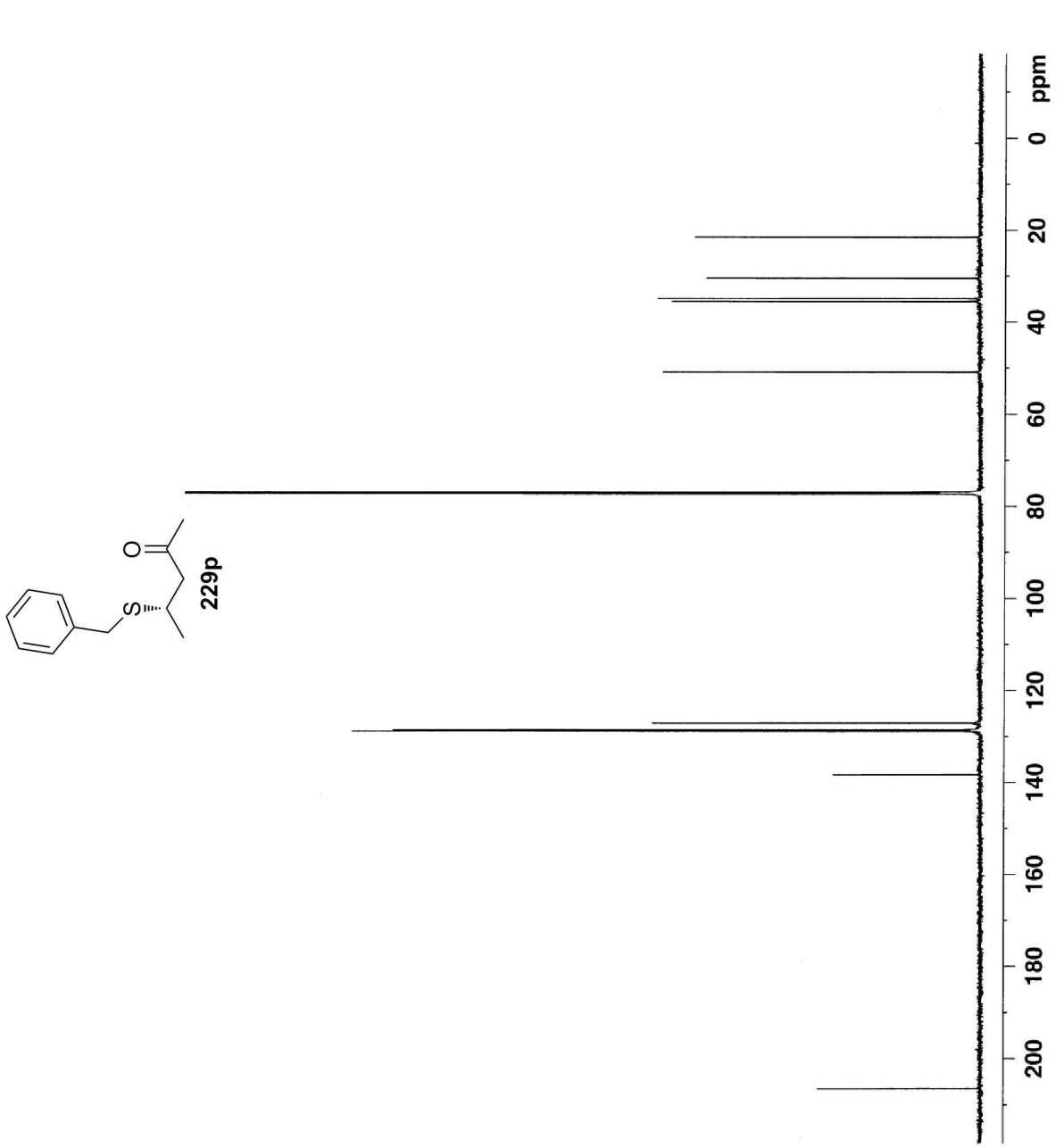

229n
NAME SS-06-112
EXPNO 2
PROCNO 1
Date_ 20130323
Time 17.43
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 52
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864820 se
RG 203
DW 12.000 us
DE 16.50 us
TE 298.2 K
D1 2.00000000 se
D11 0.03000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 13C
P1 9.00 us
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0697436 MH
======== CHANNEL f2 ======
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 us
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1499406 MH
SI 32768
SF 176.0521380 MH
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.00
200
180
160
140
120
100
80
60
40
20
0
ppm


Current Data Parameters
NAME SS-6-113
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130302
Time 20.20
INSTRUM spect
PROBHD 5 mm PATXI 1H/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 33.71
DW 62.400 usec
DE 6.50 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 500.1330008 MHz
NUC1 1H
P1 7.80 usec
PLW1 12.00000000 W
F2 - Processing parameters
SI 65536
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
229o
ppm
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.93
1.76
1.17
1.05
2.30
2.33
1.03
1.05
2.11
0.93
3.00
2.72

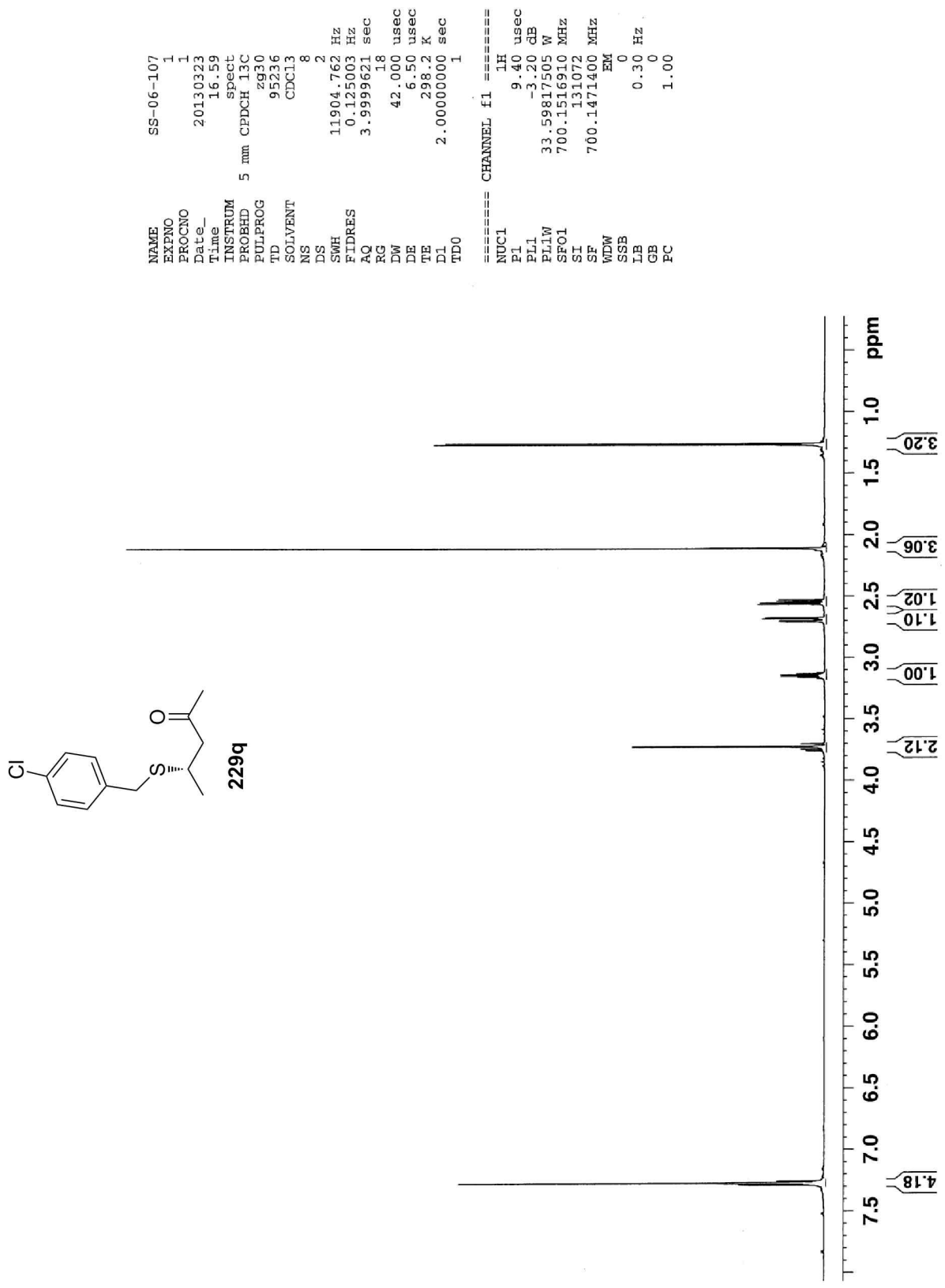


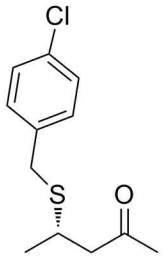
NAME	SS-06-113	
EXPNO	2	
PROCNO	1	
Date_	20130323	
Time	17.51	
INSTRUM	spect	
PROBHD	5 mm CPDCH 13C	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	36	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	use
DE	16.50	use
TE	298.1	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	9.00	use
PL1	4.50	dB
PL1W	38.14553833	W
SFO1	176.0697436	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	65.00	use
PL2	-3.20	dB
PL12	13.60	dB
PL13	120.00	dB
PL2W	33.59817505	W
PL12W	0.70196527	W
PL13W	0.00000000	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.00	


229p
Current Data Parameters
NAME SS-6-126
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130303
Time 2.08
INSTRUM spect
PROBHD 5 mm PATXI 1H/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 67.68
DW 62.400 usec
DE 6.50 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 500.1330008 MHz
NUC1 1H
P1 7.80 usec
PLW1 12.00000000 W
F2 - Processing parameters
SI 65536
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
4.18
1.09
1.94
1.00
1.06
1.04
3.06
3.21
8
7
6
5
4
3
2
1
0
−1 ppm

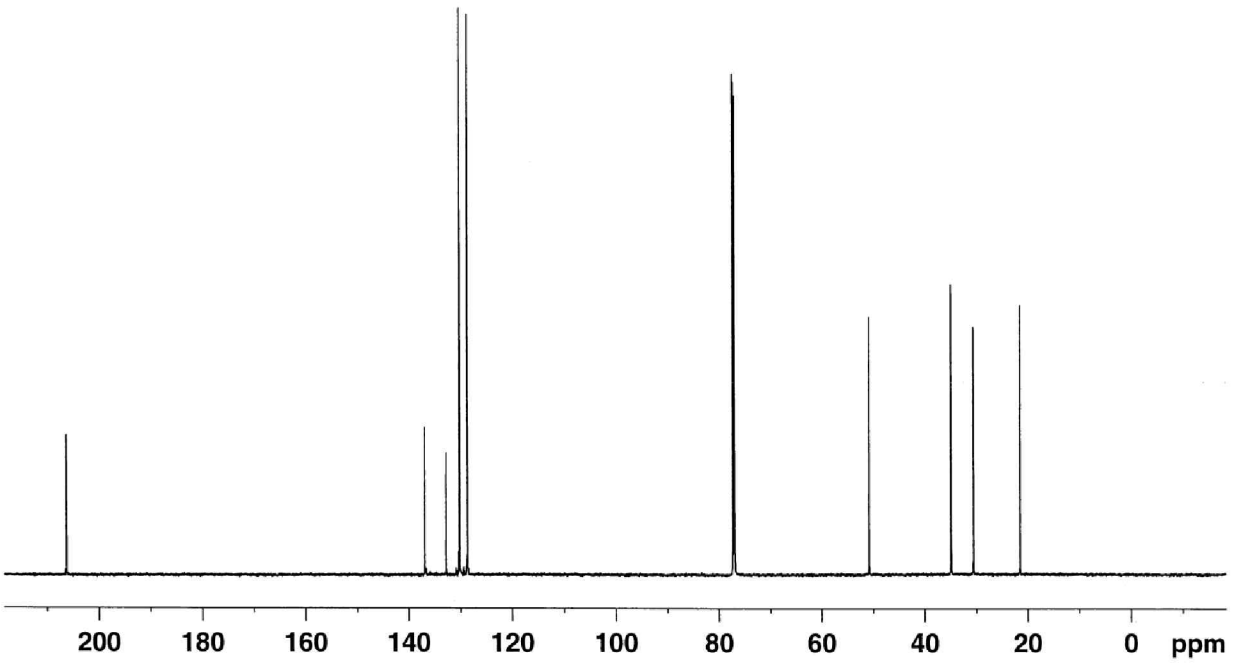



```
NAME                SS-06-126
EXPNO                       2
PROCNO                      1
Date_                20130323
Time_                   16.54
INSTRUM                  spect
PROBHD     5 mm CPDCH 13C
PULPROG                 zgpg30
TD                       65536
SOLVENT                  CDCl3
NS                          15
DS                           4
SWH                  41666.668 Hz
FIDRES               0.635783 Hz
AQ                   0.7864820 sec
RG                         203
DW                      12.000 use
DE                       16.50 use
TE                      298.2 K
D1                   2.00000000 sec
D11                  0.03000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       13C
P1                        9.00 use
PL1                       4.50 dB
PL1W                38.14553833 W
SFO1                176.0697436 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                    65.00 use
PL2                      -3.20 dB
PL12                     13.60 dB
PL13                    120.00 dB
PL2W                33.59817505 W
PL12W                0.70196527 W
PL13W                0.00000000 W
SFO2                700.1499406 MHz
SI                        32768
SF                  176.0521380 MHz
WDW                         EM
SSB                          0
LB                        3.00 Hz
GB                           0
PC                        1.00
```

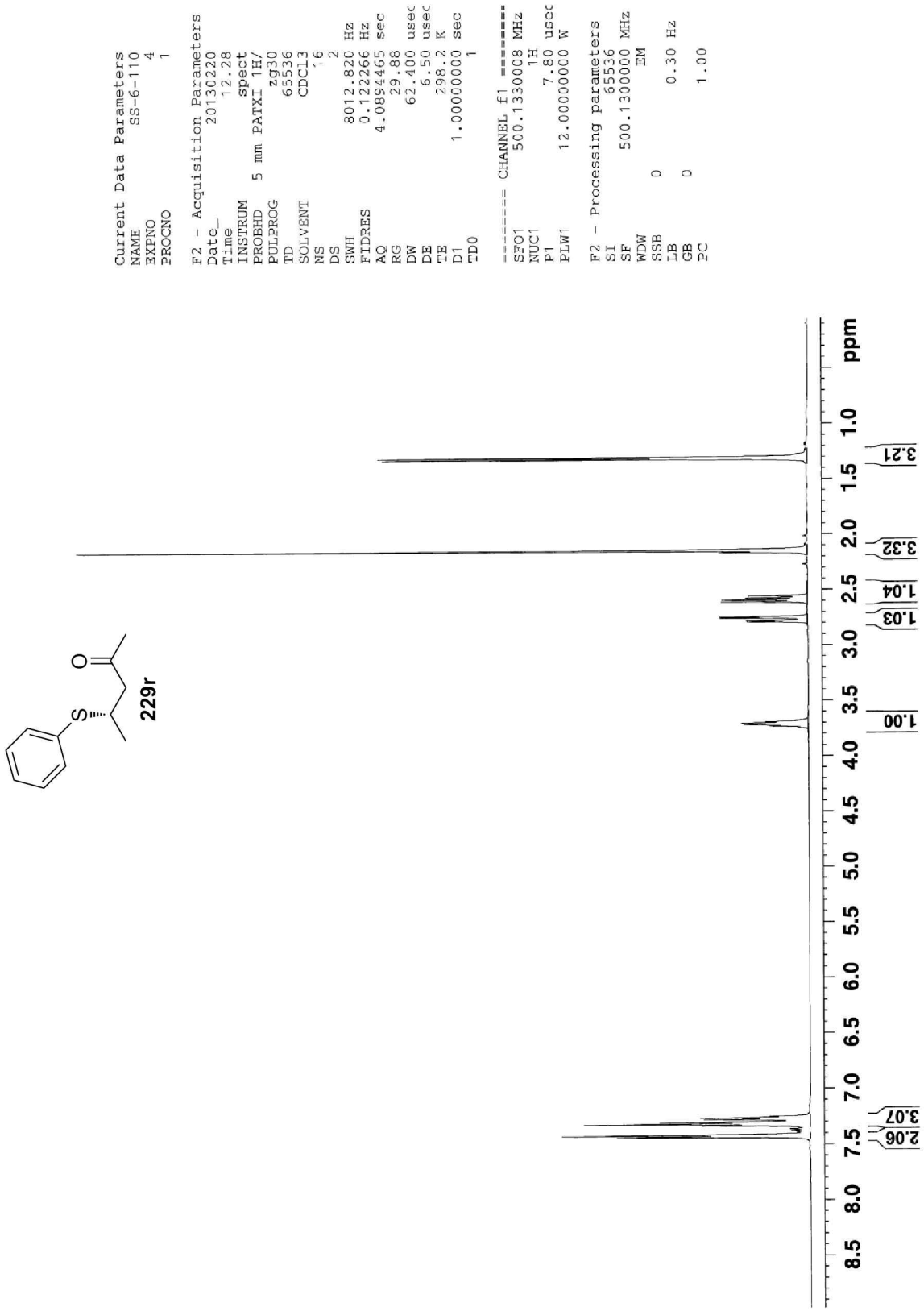

NAME SS-06-107
EXPNO 1
PROCNO 1
Date_ 20130323
Time 16.59
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 8
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 18
DW 42.000 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
Cl
S
O
229q
ppm
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
4.18
2.12
1.00
1.10
1.02
3.06
3.20

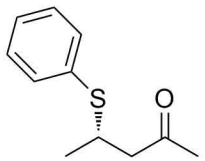


229q

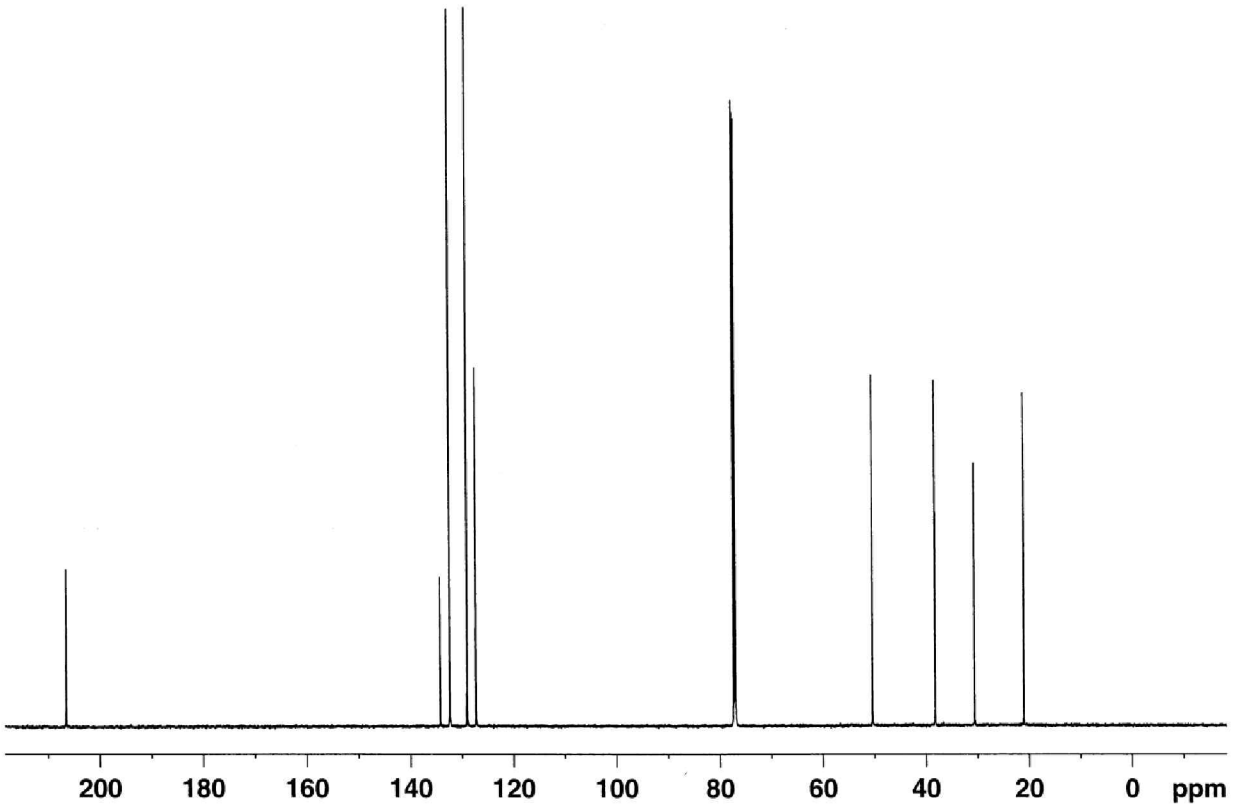


NAME	SS-06-107
EXPNO	2
PROCNO	1
Date_	20130323
Time	17.02
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	13
DS	4
SWH	41666.668 Hz
FIDRES	0.635783 Hz
AQ	0.7864820 sec
RG	203
DW	12.000 use
DE	16.50 use
TE	298.2 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 use
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0697436 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 use
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1499406 MHz
SI	32768
SF	176.0521380 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.00

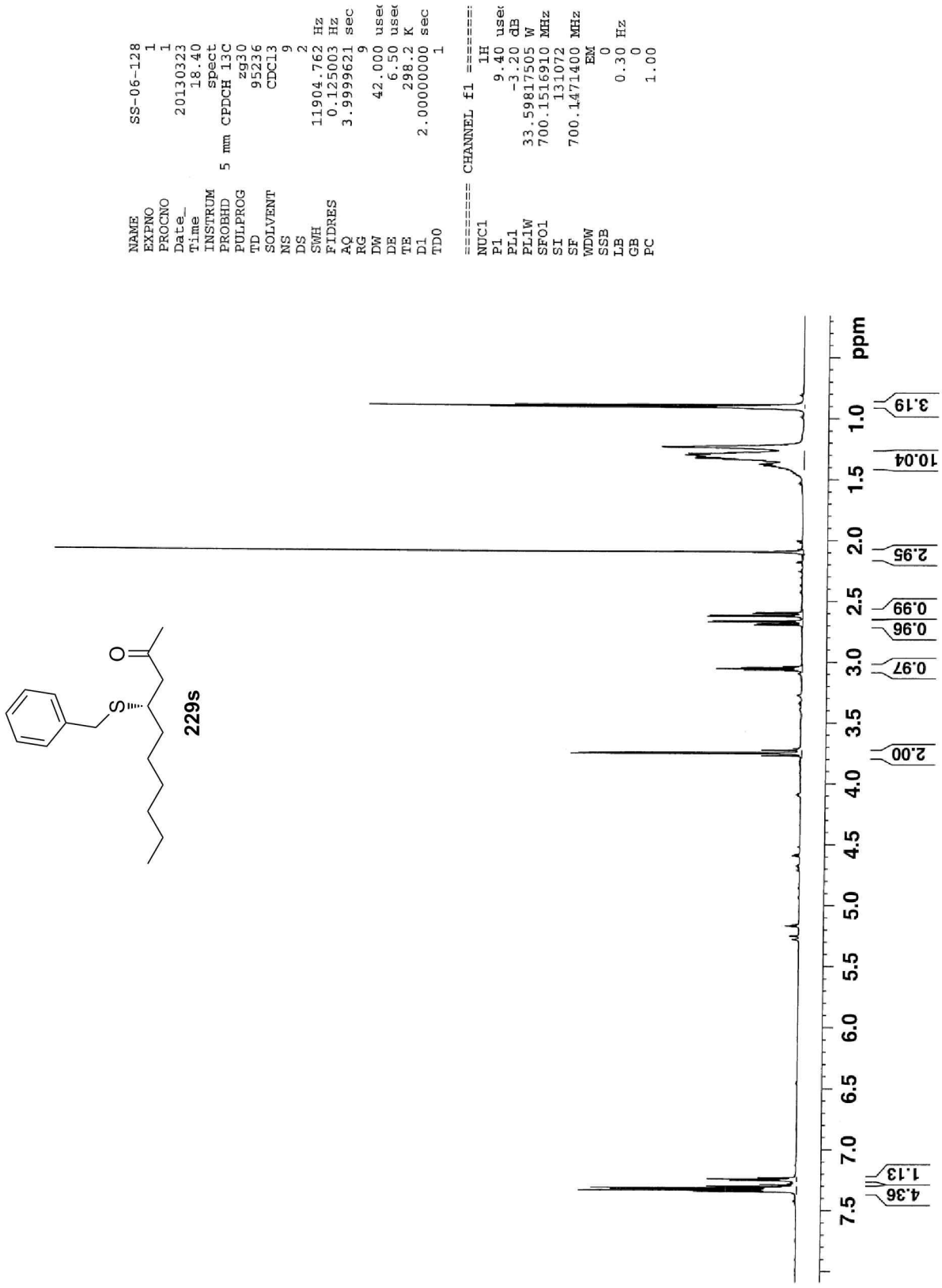

229r
Current Data Parameters
NAME SS-6-110
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130220
Time 12.28
INSTRUM spect
PROBHD 5 mm PATXI 1H/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 29.88
DW 62.400 usec
DE 6.50 usec
TE 298.2 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 500.1330008 MHz
NUC1 1H
P1 7.80 usec
PLW1 12.00000000 W
F2 - Processing parameters
SI 65536
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
3.21
3.32
1.04
1.03
1.00
3.07
2.06
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm

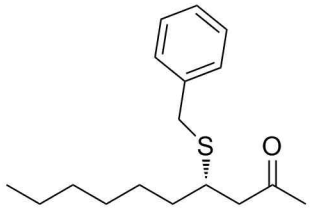


229r

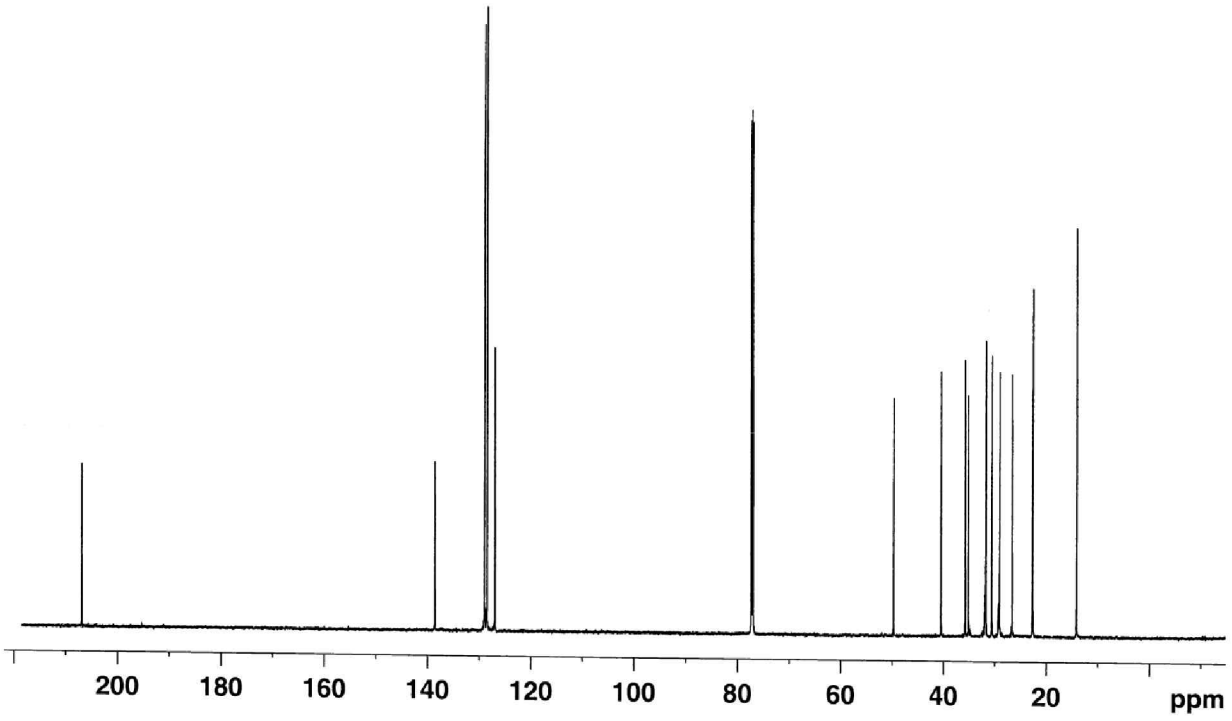


NAME	SS-06-110	
EXPNO	2	
PROCNO	1	
Date_	20130323	
Time	17.08	
INSTRUM	spect	
PROBHD	5 mm CPDCH 13C	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	14	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	usec
DE	16.50	usec
TE	298.2	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	9.00	usec
PL1	4.50	dB
PL1W	38.14553833	W
SFO1	176.0697436	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	65.00	usec
PL2	-3.20	dB
PL12	13.60	dB
PL13	120.00	dB
PL2W	33.59817505	W
PL12W	0.70196527	W
PL13W	0.00000000	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.00	

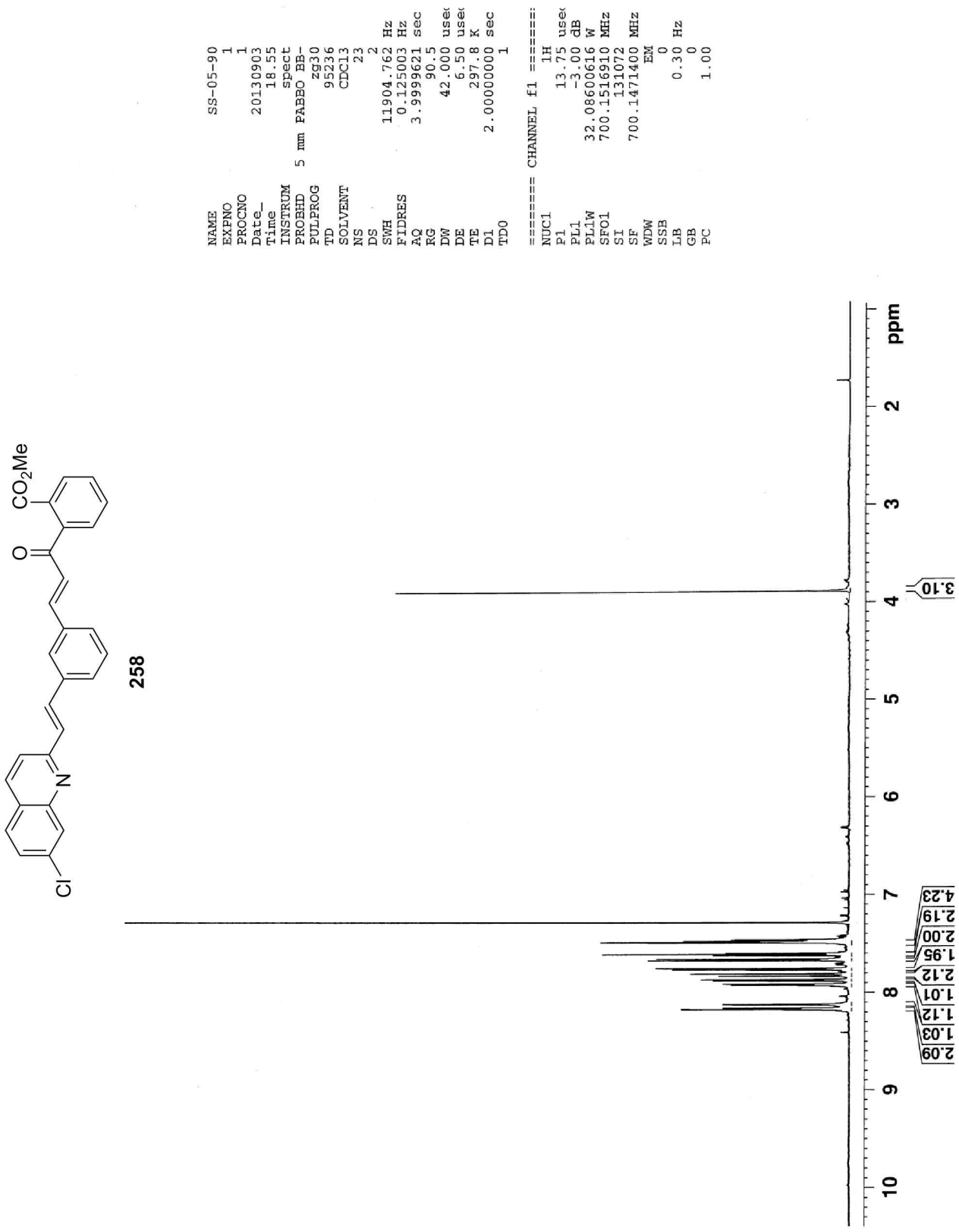

229s
NAME SS-06-128
EXPNO 1
PROCNO 1
Date_ 20130323
Time 18.40
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 9
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 9
DW 42.000 use
DE 6.50 use
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 use
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
ppm
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
4.36
1.13
2.00
0.97
0.96
0.99
2.95
10.04
3.19

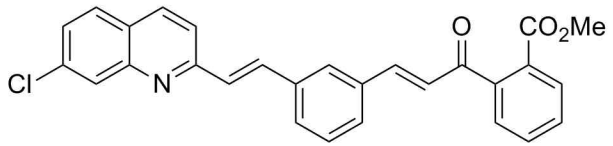


229s

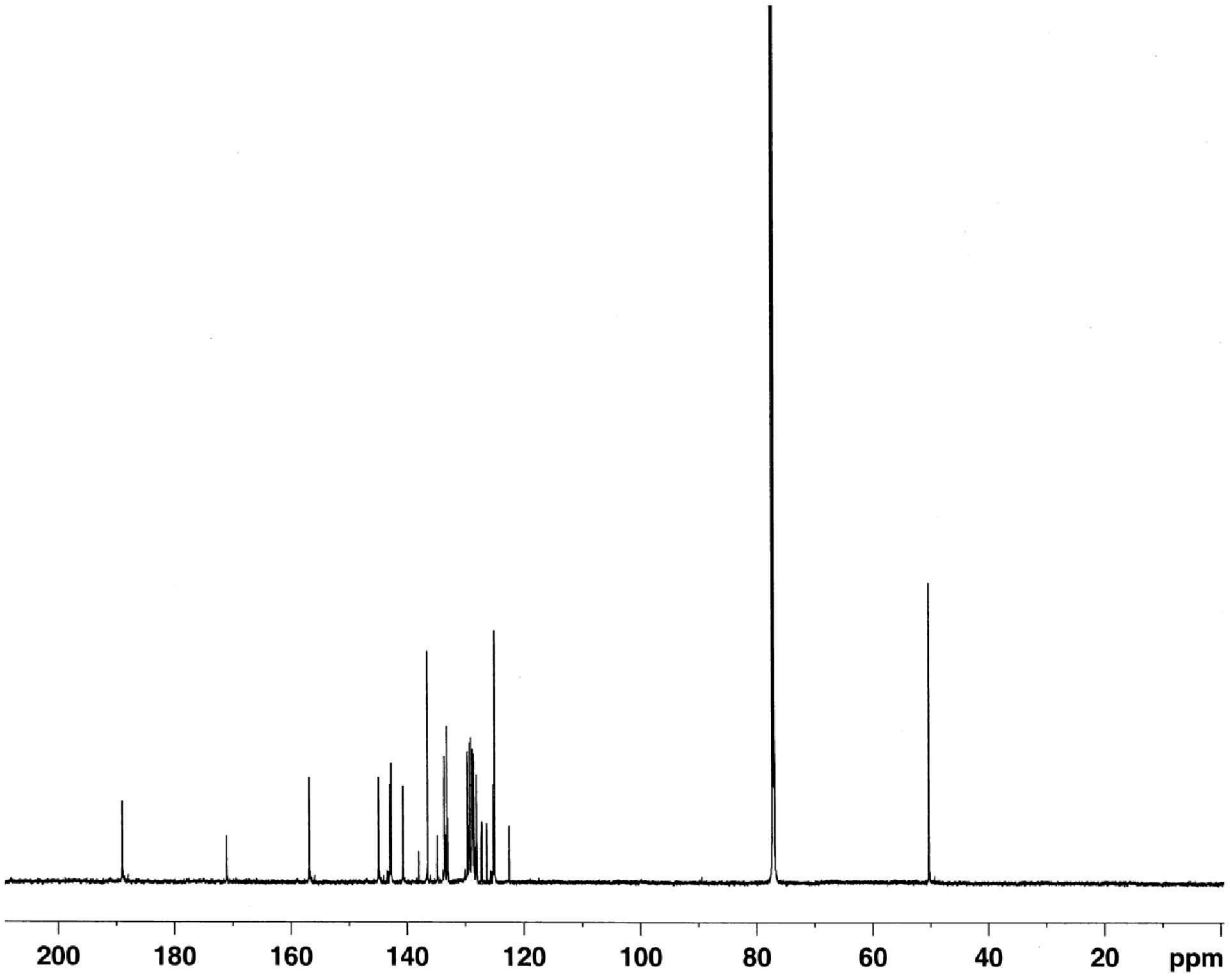


NAME	SS-06-128	
EXPNO	2	
PROCNO	1	
Date_	20130323	
Time	18.43	
INSTRUM	spect	
PROBHD	5 mm CPDCH 13C	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	12	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	usec
DE	16.50	usec
TE	298.1	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
========	CHANNEL f1 ========	
NUC1	13C	
P1	9.00	usec
PL1	4.50	dB
PL1W	38.14553833	W
SFO1	176.0697436	MHz
========	CHANNEL f2 ========	
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	65.00	usec
PL2	-3.20	dB
PL12	13.60	dB
PL13	120.00	dB
PL2W	33.59817505	W
PL12W	0.70196527	W
PL13W	0.00000000	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.00	

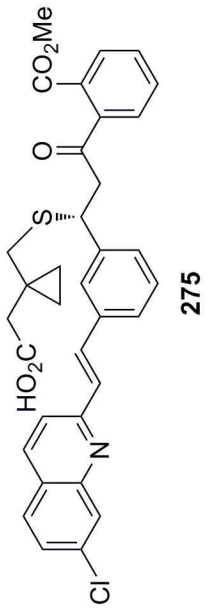

CO2Me
O
N
Cl
258
NAME SS-05-90
EXPNO 1
PROCNO 1
Date_ 20130903
Time 18.55
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 95236
SOLVENT CDC13
NS 23
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 90.5
DW 42.000 use
DE 6.50 use
TE 297.8 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.75 use
PL1 -3.00 dB
PL1W 32.08600616 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
ppm
10
9
8
7
6
5
4
3
2
3.10
2.09
1.03
1.12
1.01
2.12
1.95
2.00
2.19
4.23



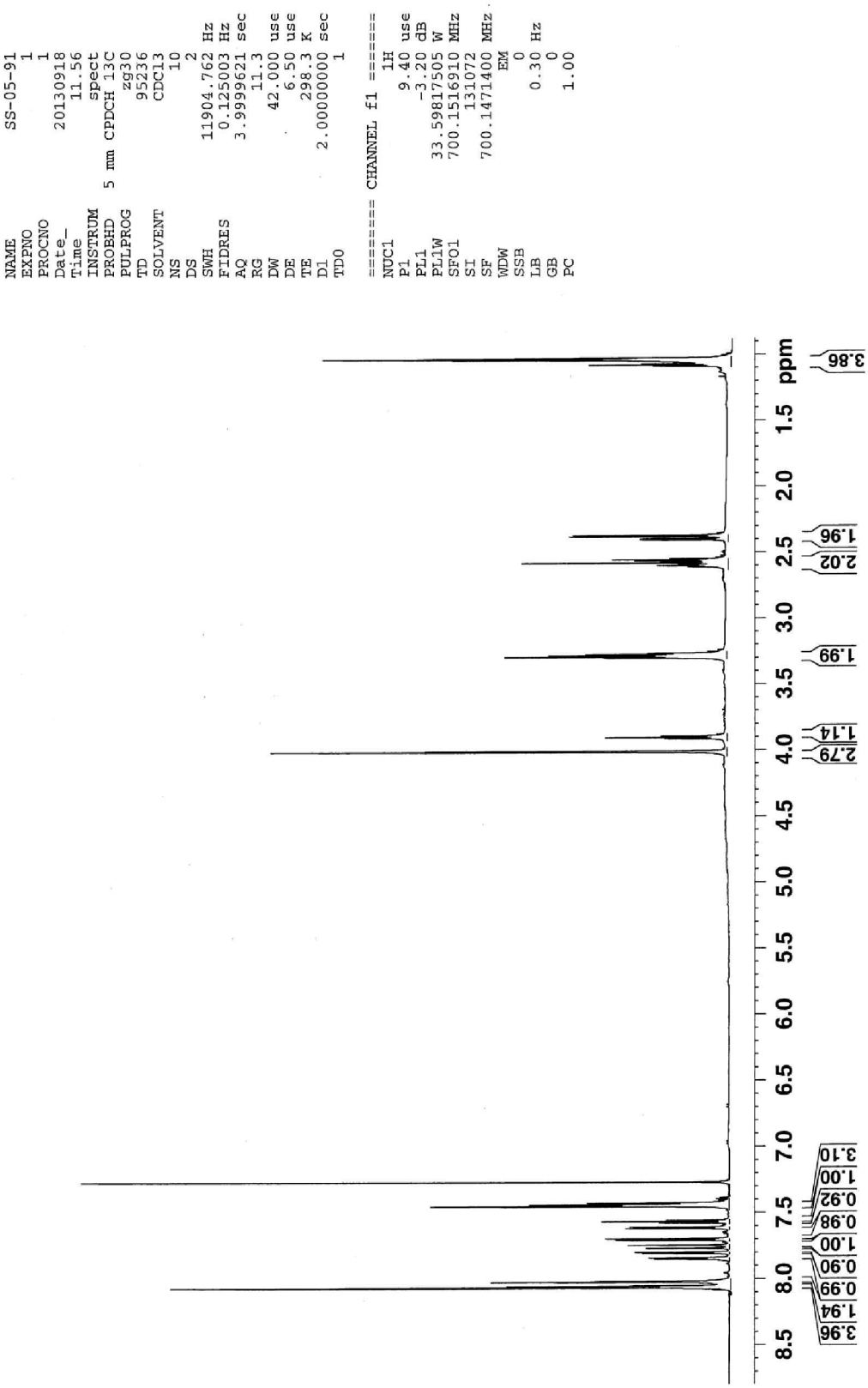
258

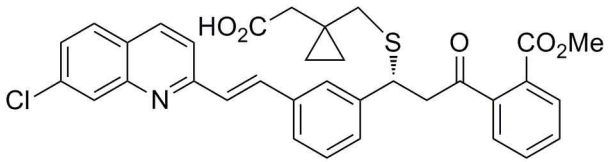


NAME	SS-06-145
EXPNO	5
PROCNO	1
Date_	20130916
Time	17.42
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	192
DS	4
SWH	41666.668 Hz
FIDRES	0.635783 Hz
AQ	0.7864820 sec
RG	203
DW	12.000 usec
DE	16.50 usec
TE	298.1 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 usec
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0697436 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 usec
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1499406 MHz
SI	32768
SF	176.0521380 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40

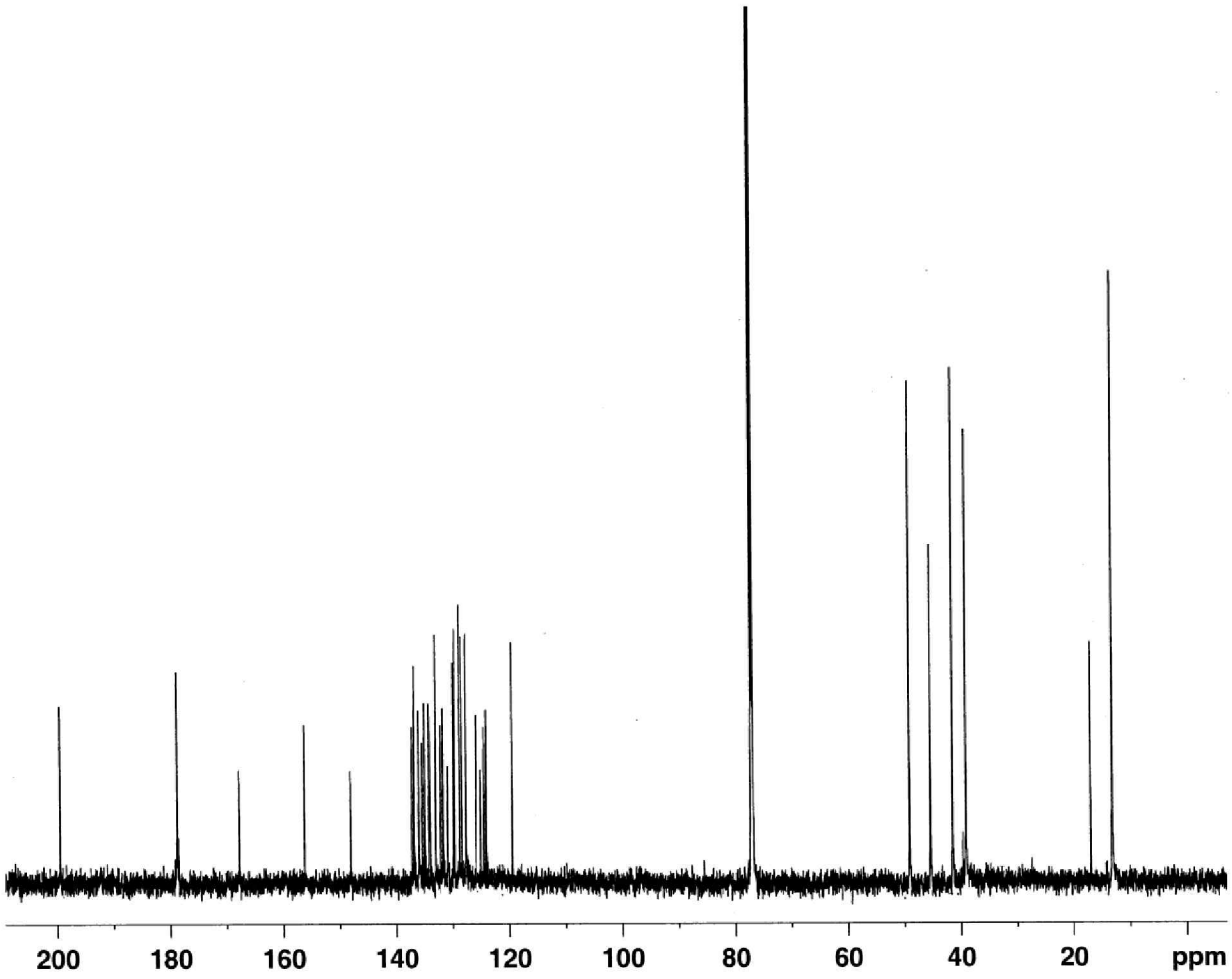

CO2Me
O
S
HO2C
N
Cl

275

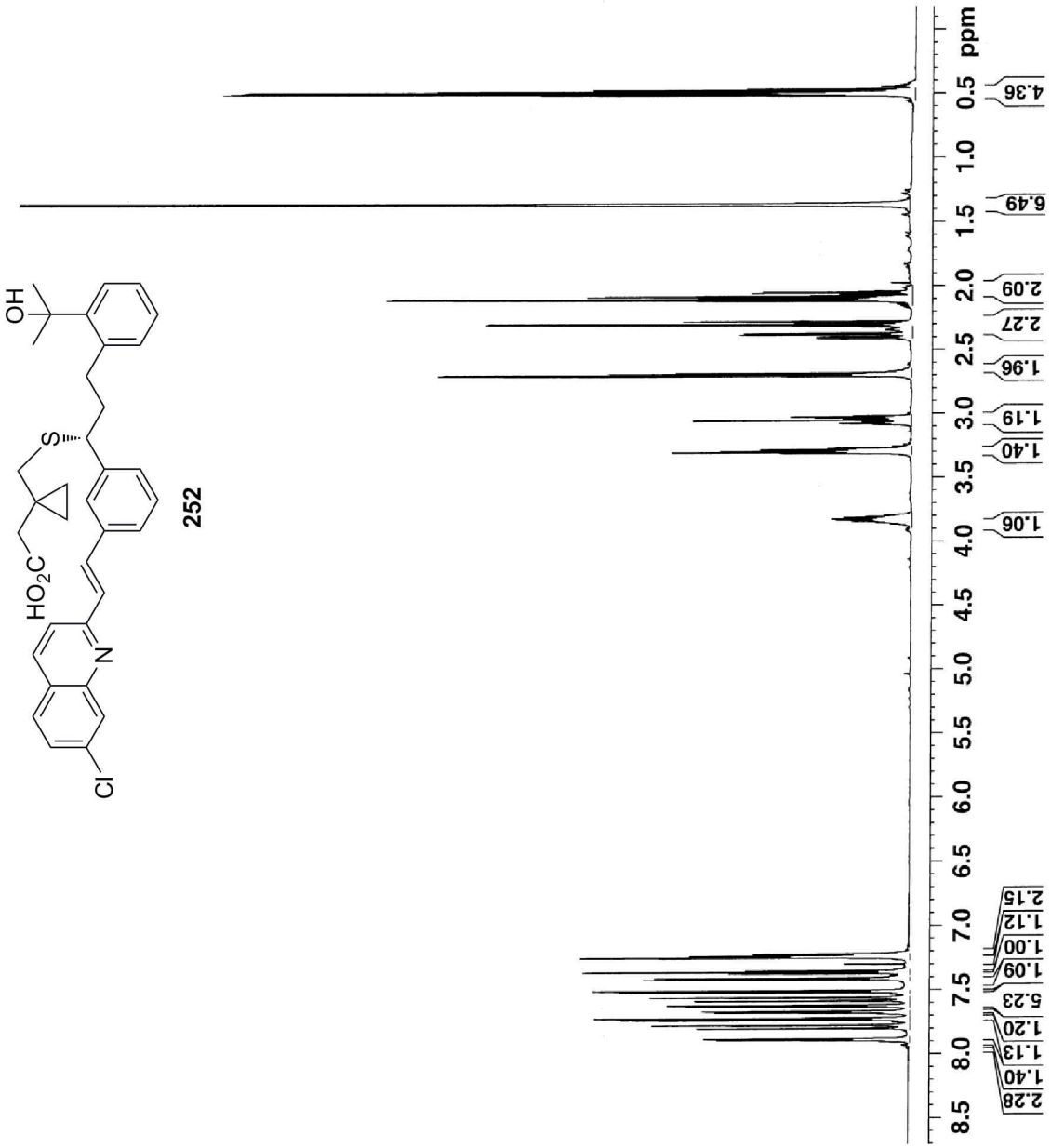

NAME SS-05-91
EXPNO 1
PROCNO 1
Date_ 20130918
Time 11.56
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 10
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 11.3
DW 42.000 use
DE 6.50 use
TE 298.3 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 use
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 ppm
3.96
1.94
0.99
0.90
1.00
0.98
0.92
1.00
3.10
3.86
1.96
2.02
1.99
2.79
1.14

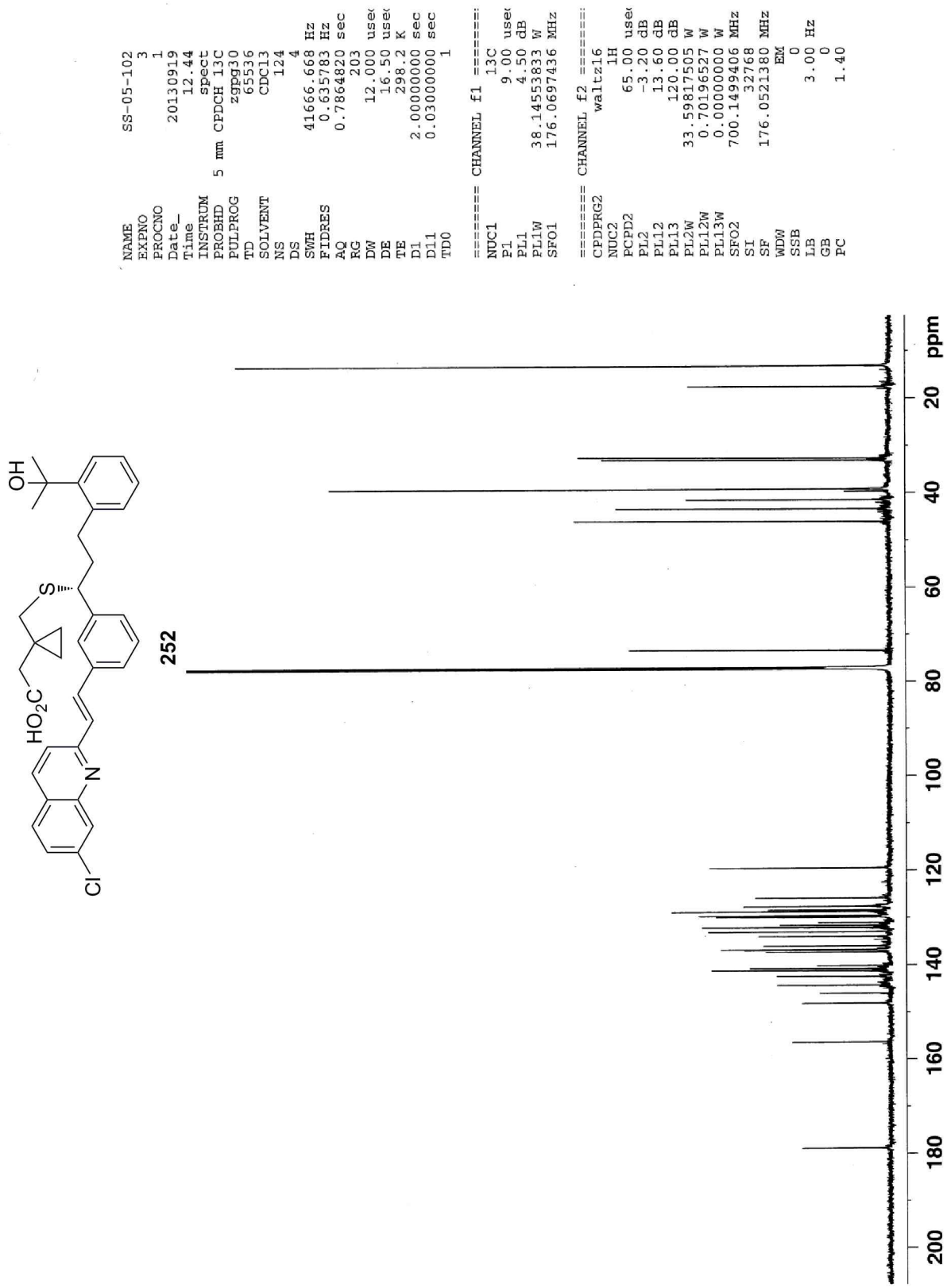


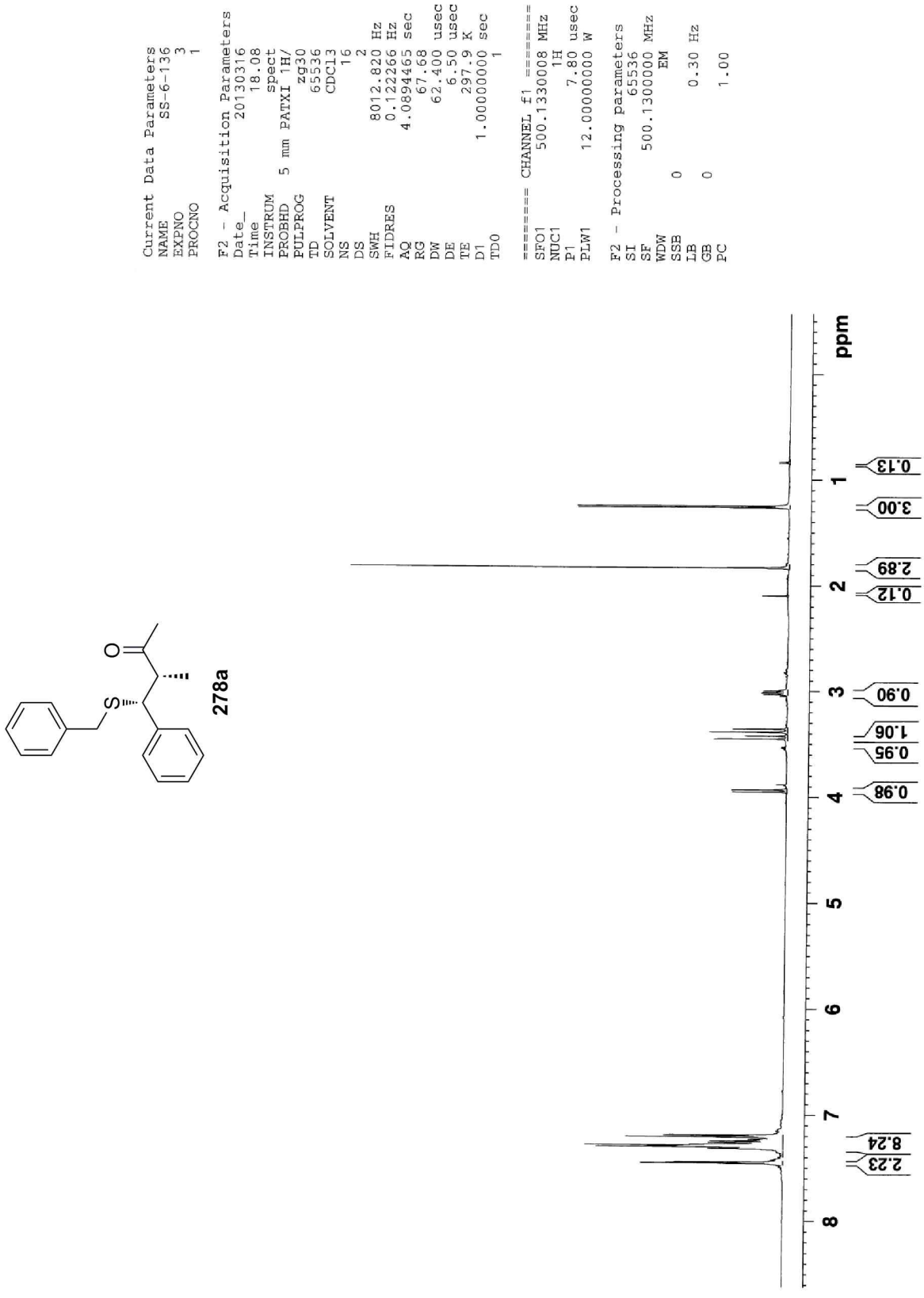
275

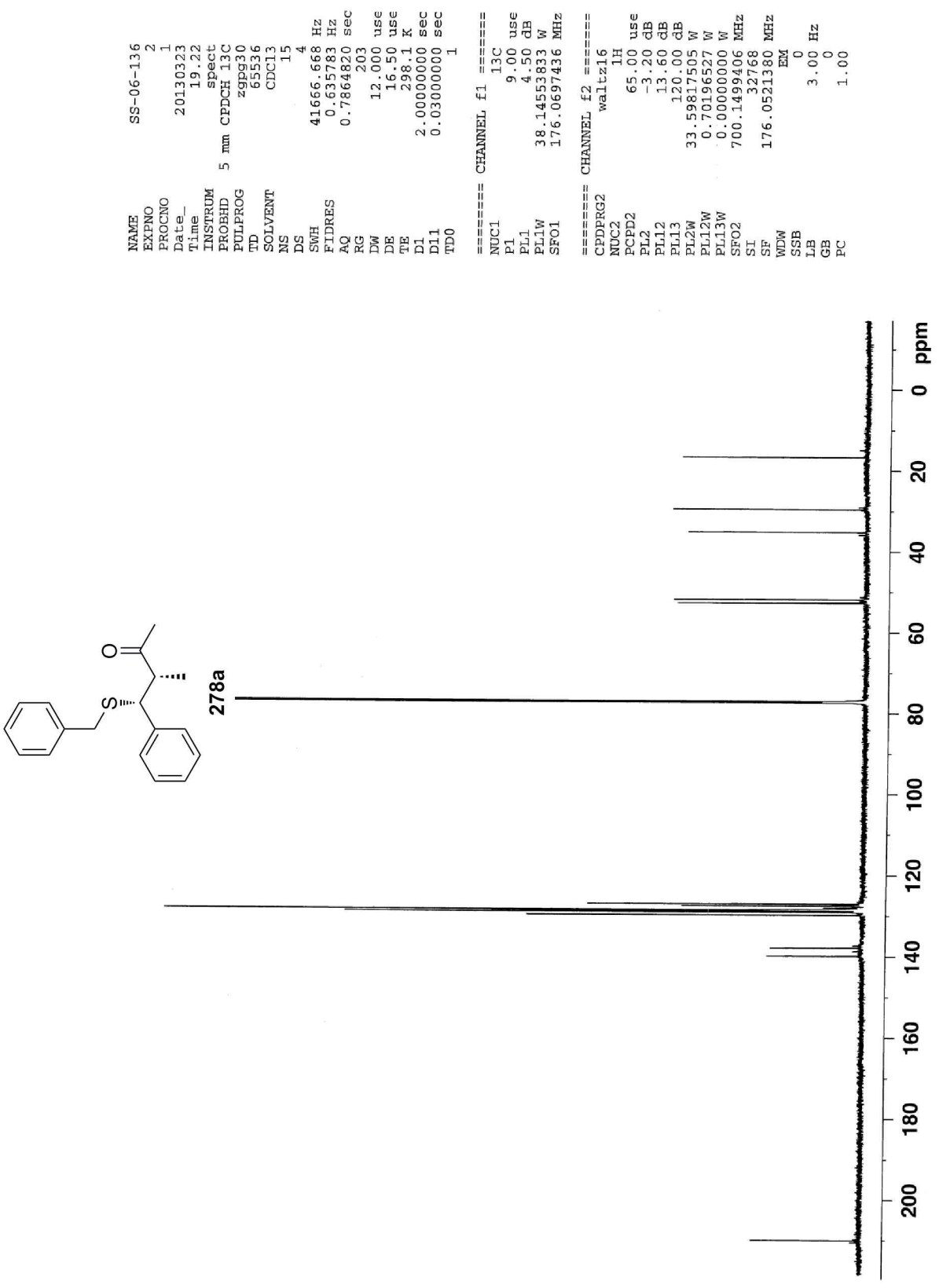


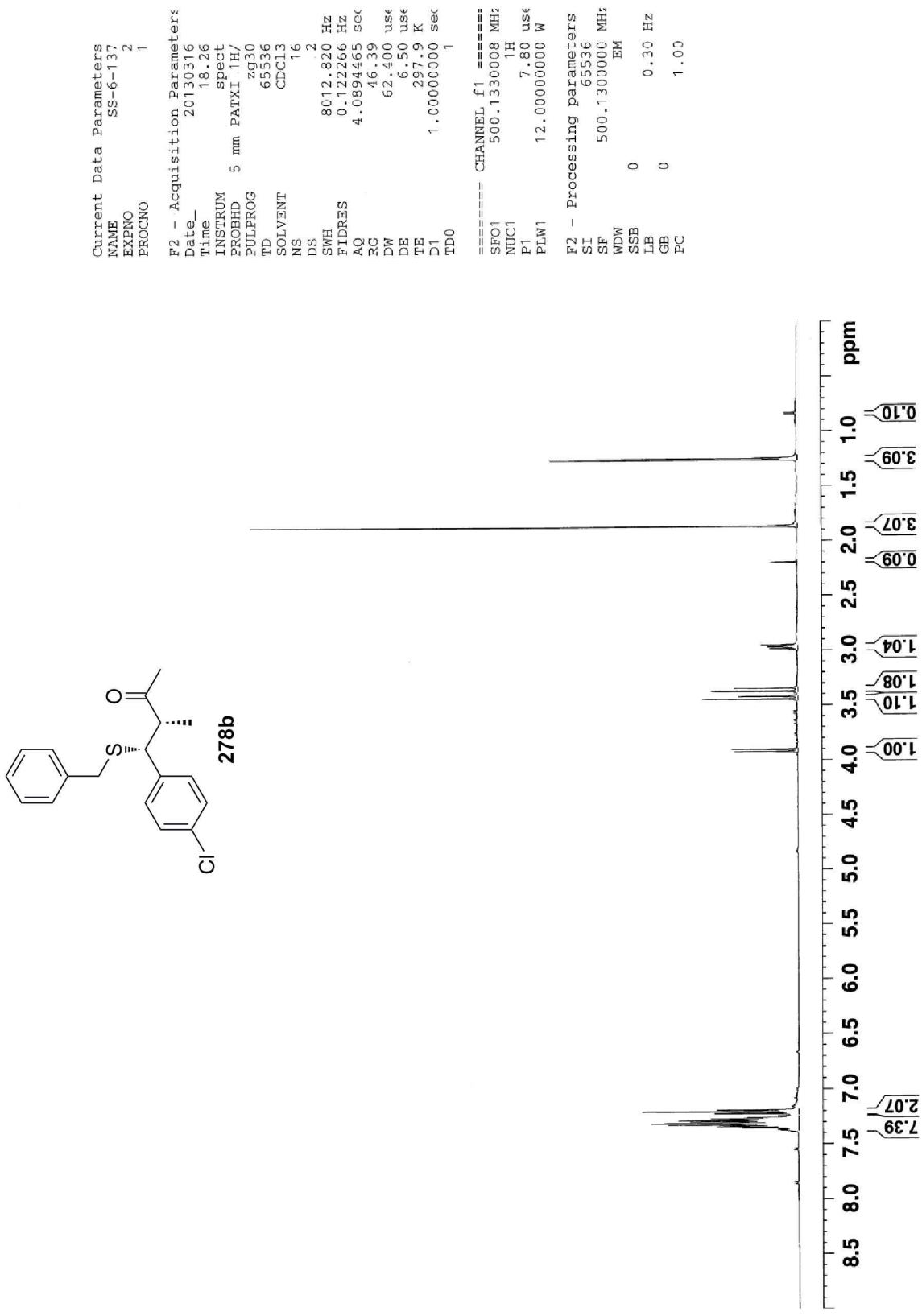
NAME	SS-05-91
EXPNO	4
PROCNO	1
Date_	20130919
Time	12.35
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	51
DS	4
SWH	41666.668 Hz
FIDRES	0.635783 Hz
AQ	0.7864820 sec
RG	203
DW	12.000 use
DE	16.50 use
TE	298.3 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 use
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0697436 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 use
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1499406 MHz
SI	32768
SF	176.0521380 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40

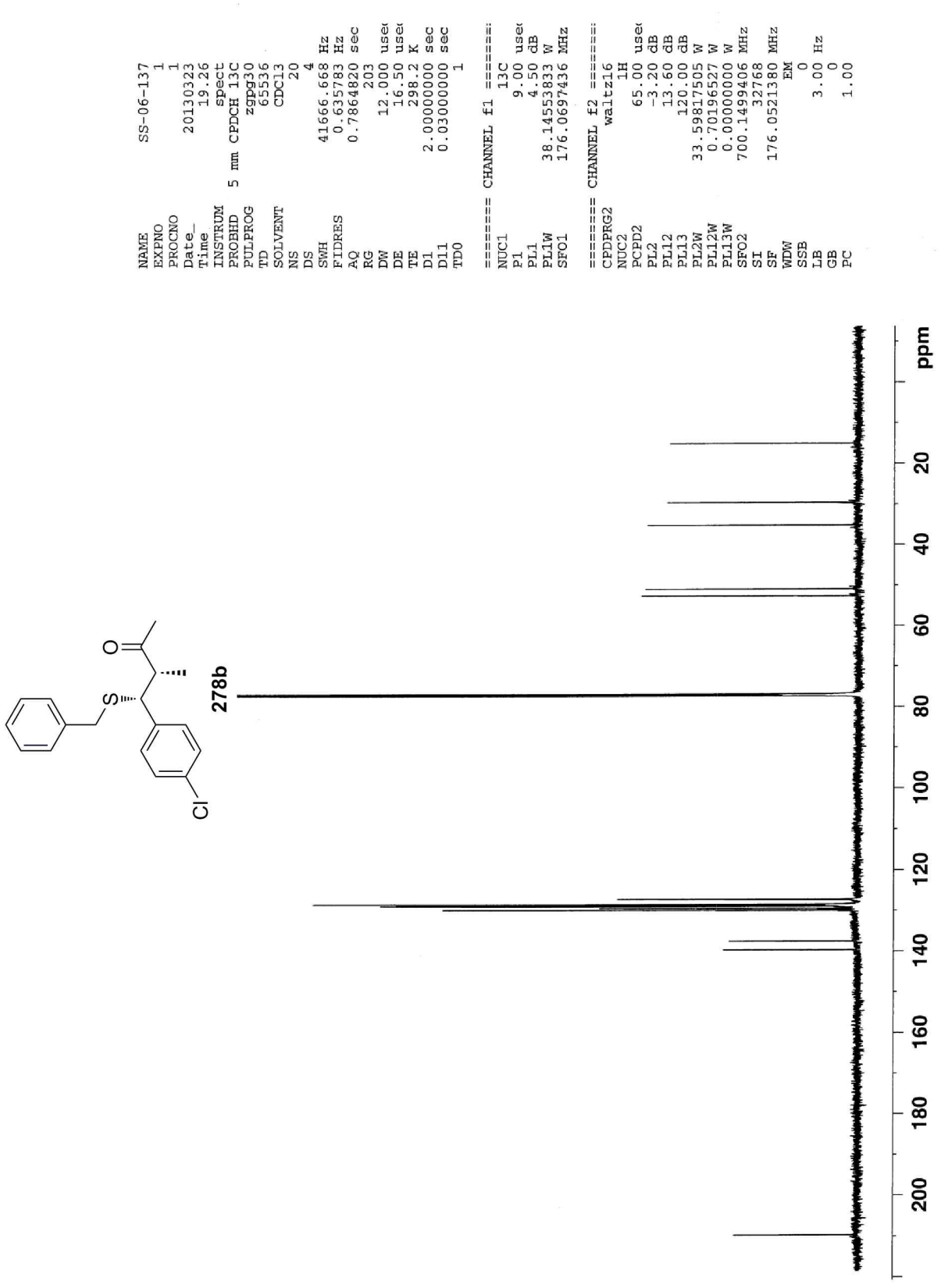

252
OH
S
HO2C
N
Cl
NAME SS-05-102
EXPNO 1
PROCNO 1
Date_ 20130918
Time 12.20
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 12
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 12.7
DW 42.000 use
DE 6.50 use
TE 298.1 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 use
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
2.28
1.40
1.13
1.20
5.23
1.09
1.00
1.12
2.15
1.06
1.40
1.19
1.96
2.27
2.09
6.49
4.36


OH
S
HO2C
N
Cl
252
NAME SS-05-102
EXPNO 3
PROCNO 1
Date_ 20130919
Time 12.44
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 124
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864820 sec
RG 203
DW 12.000 use
DE 16.50 use
TE 298.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 use
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0697436 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 use
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1499406 MHz
SI 32768
SF 176.0521380 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
200
180
160
140
120
100
80
60
40
20
ppm

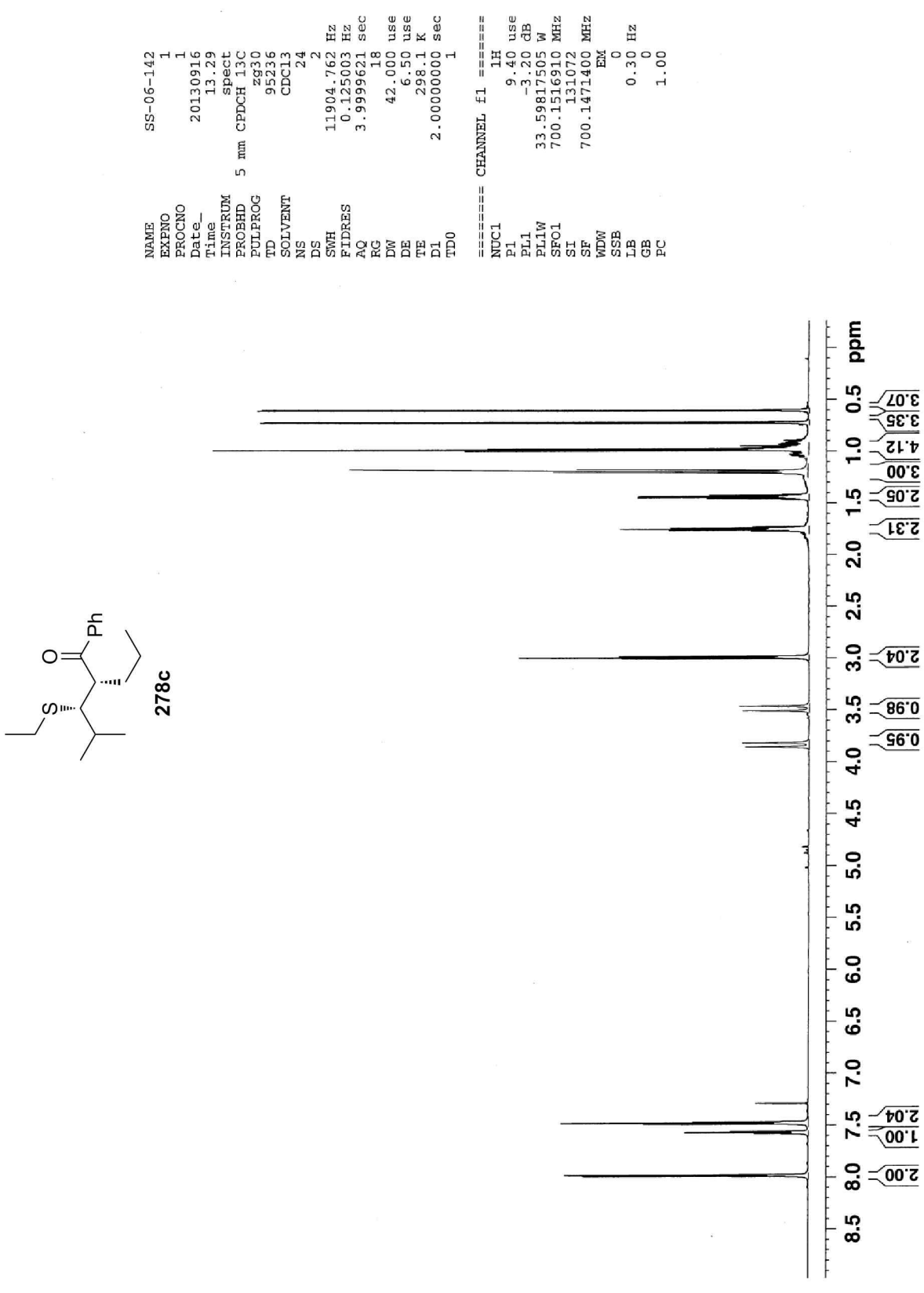

Current Data Parameters
NAME SS-6-136
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130316
Time 18.08
INSTRUM spect
PROBHD 5 mm PATXI 1H/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 67.68
DW 62.400 usec
DE 6.50 usec
TE 297.9 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 500.1330008 MHz
NUC1 1H
P1 7.80 usec
PLW1 12.00000000 W
F2 - Processing parameters
SI 65536
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
278a
O
S
ppm
1
2
3
4
5
6
7
8
0.13
3.00
2.89
0.12
0.90
1.06
0.95
0.98
2.23
8.24

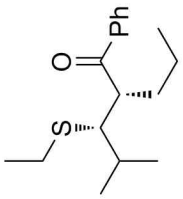

278a
O
S
NAME SS-06-136
EXPNO 2
PROCNO 1
Date_ 20130323
Time 19.22
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 15
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864820 sec
RG 203
DW 12.000 use
DE 16.50 use
TE 298.1 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 =======
NUC1 13C
P1 9.00 use
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0697436 MHz
======== CHANNEL f2 =======
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 use
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1499406 MHz
SI 32768
SF 176.0521380 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.00
200
180
160
140
120
100
80
60
40
20
0
ppm


Current Data Parameters
NAME SS-6-137
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130316
Time 18.26
INSTRUM spect
PROBHD 5 mm PATXI 1H/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 46.39
DW 62.400 use
DE 6.50 use
TE 297.9 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 500.1330008 MHz
NUC1 1H
P1 7.80 use
PLW1 12.00000000 W
F2 - Processing parameters
SI 65536
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
278b
O
S
Cl
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
ppm
0.10
3.09
3.07
0.09
1.04
1.08
1.10
1.00
7.39
2.07

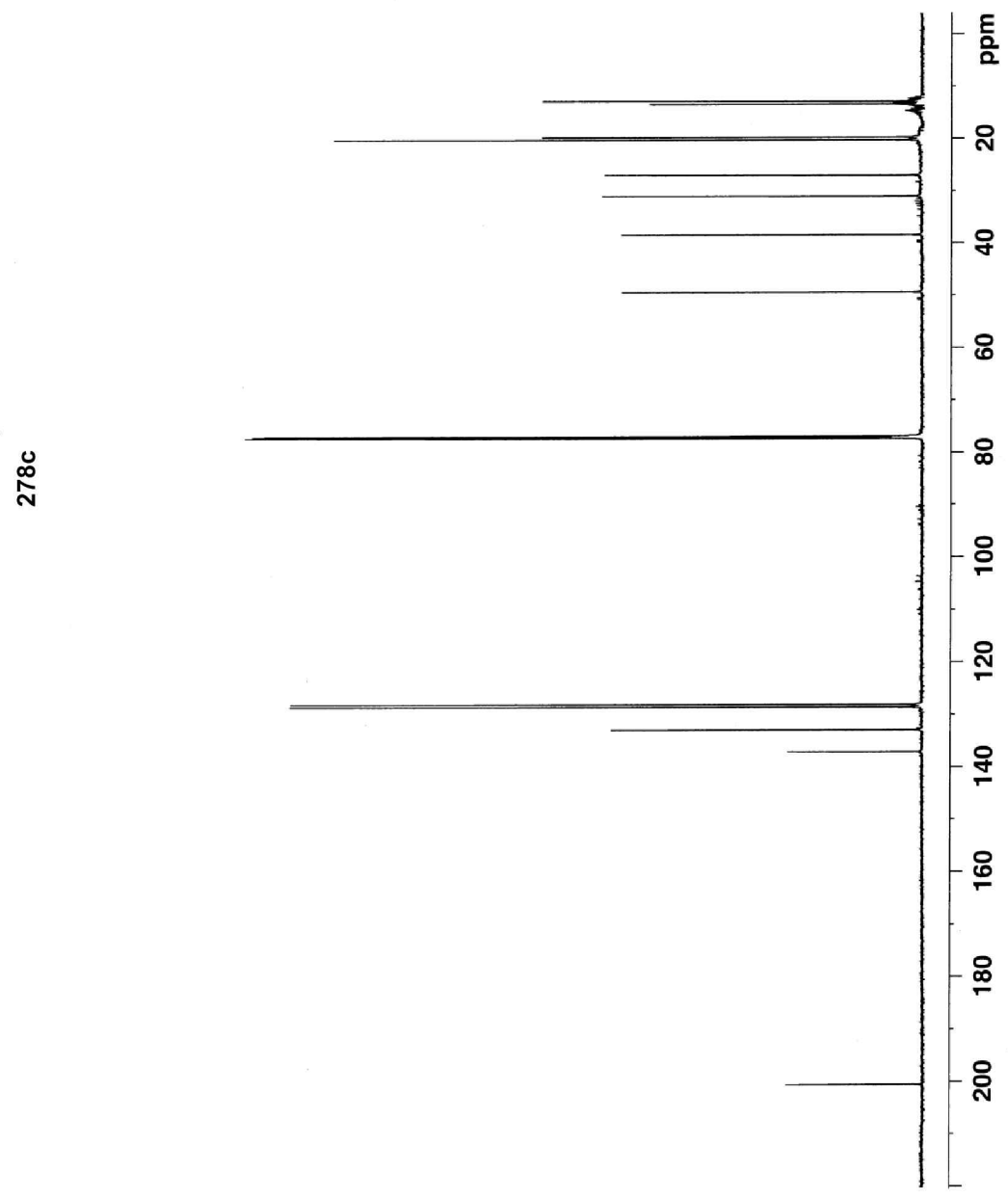



```
NAME                SS-06-137
EXPNO                       1
PROCNO                      1
Date_                20130323
Time                    19.26
INSTRUM                  spect
PROBHD     5 mm CPDCH 13C
PULPROG                 zgpg30
TD                       65536
SOLVENT                  CDCl3
NS                          20
DS                           4
SWH                  41666.668 Hz
FIDRES                0.635783 Hz
AQ                    0.7864820 sec
RG                         203
DW                      12.000 use
DE                      16.50 use
TE                      298.2 K
D1                   2.00000000 sec
D11                  0.03000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                       13C
P1                       9.00 use
PL1                      4.50 dB
PL1W                38.14553833 W
SFO1               176.0697436 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                        1H
PCPD2                   65.00 use
PL2                     -3.20 dB
PL12                    13.60 dB
PL13                   120.00 dB
PL2W                33.59817505 W
PL12W                0.70196527 W
PL13W                0.00000000 W
SFO2               700.1499406 MHz
SI                       32768
SF                 176.0521380 MHz
WDW                         EM
SSB                          0
LB                        3.00 Hz
GB                           0
PC                        1.00
```

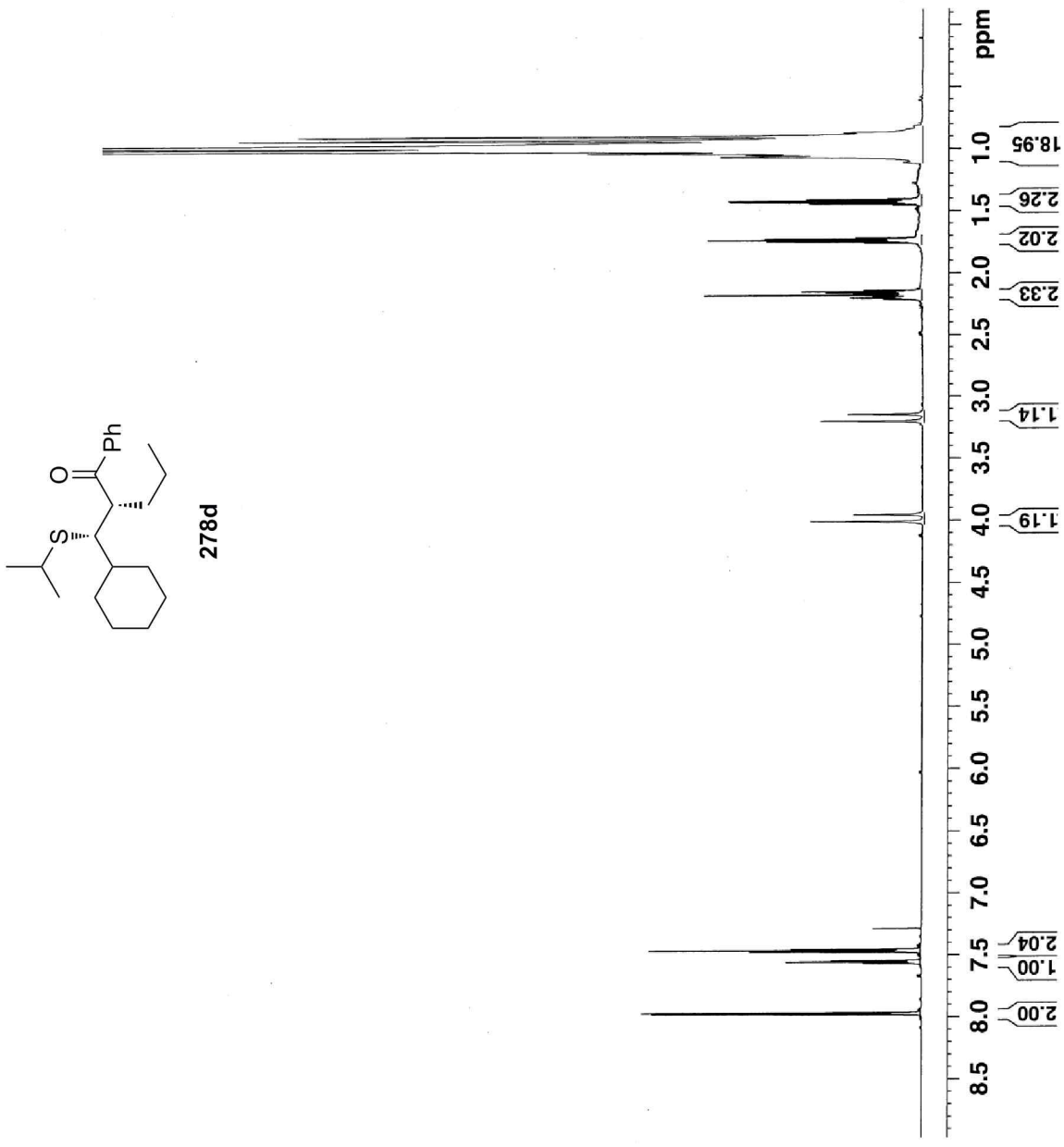

278c
NAME SS-06-142
EXPNO 1
PROCNO 1
Date_ 20130916
Time 13.29
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDC13
NS 24
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 18
DW 42.000 use
DE 6.50 use
TE 298.1 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 use
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
ppm
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
2.00
1.00
2.04
0.95
0.98
2.04
2.31
2.05
3.00
4.12
3.35
3.07



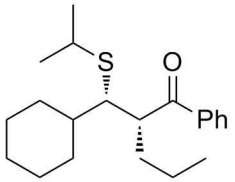
278c



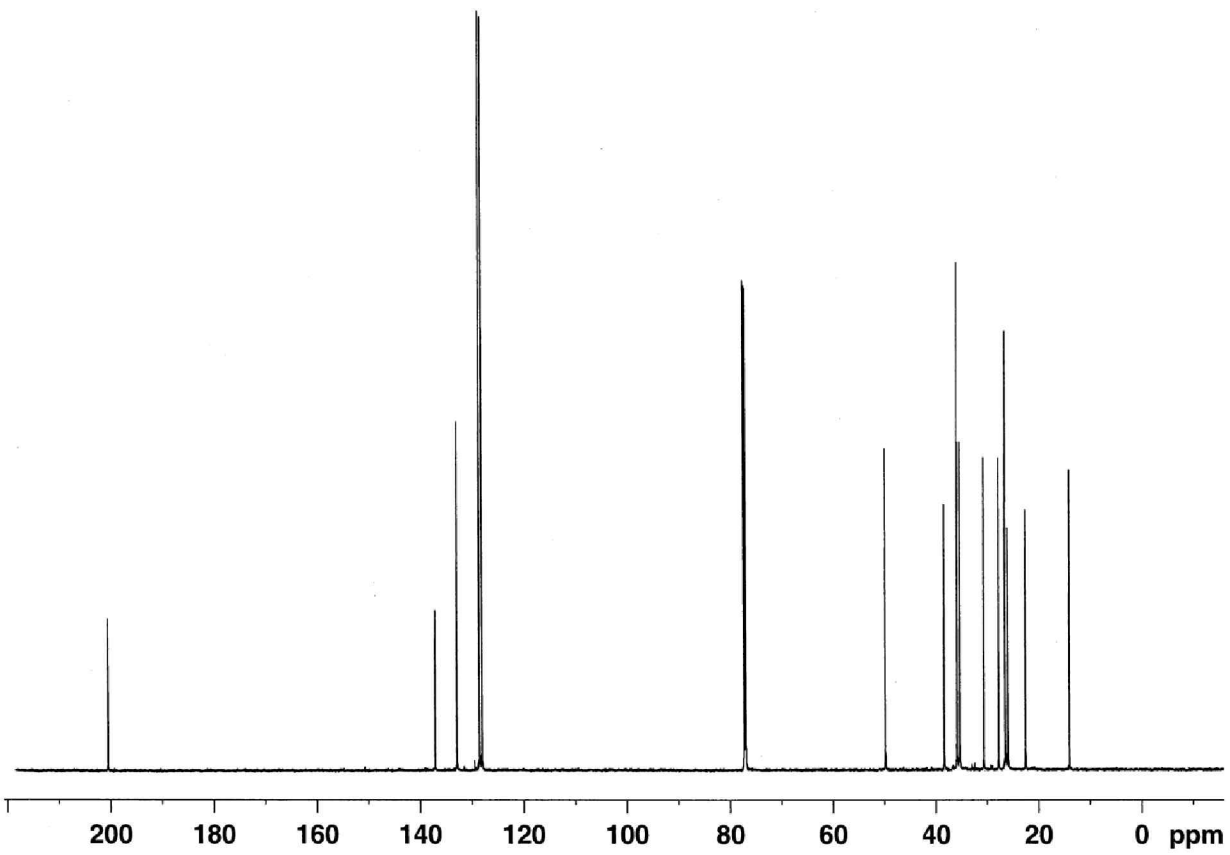

```
NAME            SS-06-142
EXPNO                   2
PROCNO                  1
Date_            20130916
Time                13.33
INSTRUM             spect
PROBHD   5 mm CPDCH 13C
PULPROG             zgpg30
TD                   65536
SOLVENT              CDCl3
NS                      29
DS                       4
SWH              41666.668 Hz
FIDRES           0.635783 Hz
AQ               0.7864820 sec
RG                     203
DW                  12.000 usec
DE                  16.50 usec
TE                 298.1 K
D1               2.00000000 sec
D11              0.03000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                  13C
P1                 9.00 usec
PL1                4.50 dB
PL1W         38.14553833 W
SFO1         176.0697436 MHz

======== CHANNEL f2 ========
CPDPRG2           waltz16
NUC2                   1H
PCPD2              65.00 usec
PL2                -3.20 dB
PL12               13.60 dB
PL13              120.00 dB
PL2W         33.59817505 W
PL12W         0.70196527 W
PL13W         0.00000000 W
SFO2         700.1499406 MHz
SI                  32768
SF           176.0521380 MHz
WDW                    EM
SSB                     0
LB                 3.00 Hz
GB                      0
PC                 1.40
```



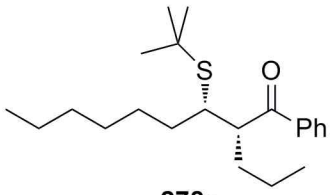

```
NAME            SS-06-143
EXPNO                   1
PROCNO                  1
Date_            20130916
Time                13.44
INSTRUM             spect
PROBHD   5 mm CPDCH 13C
PULPROG               zg30
TD                   95236
SOLVENT              CDCl3
NS                      14
DS                       2
SWH             11904.762 Hz
FIDRES              0.125003 Hz
AQ                3.9999621 sec
RG                     14.2
DW                   42.000 usec
DE                    6.50 usec
TE                   298.2 K
D1                2.00000000 sec
TD0                     1

======== CHANNEL f1 ========
NUC1                   1H
P1                   9.40 usec
PL1                  -3.20 dB
PL1W           33.59817505 W
SFO1           700.1516910 MHz
SI                  131072
SF             700.1471400 MHz
WDW                    EM
SSB                     0
LB                   0.30 Hz
GB                      0
PC                   1.00
```



278d

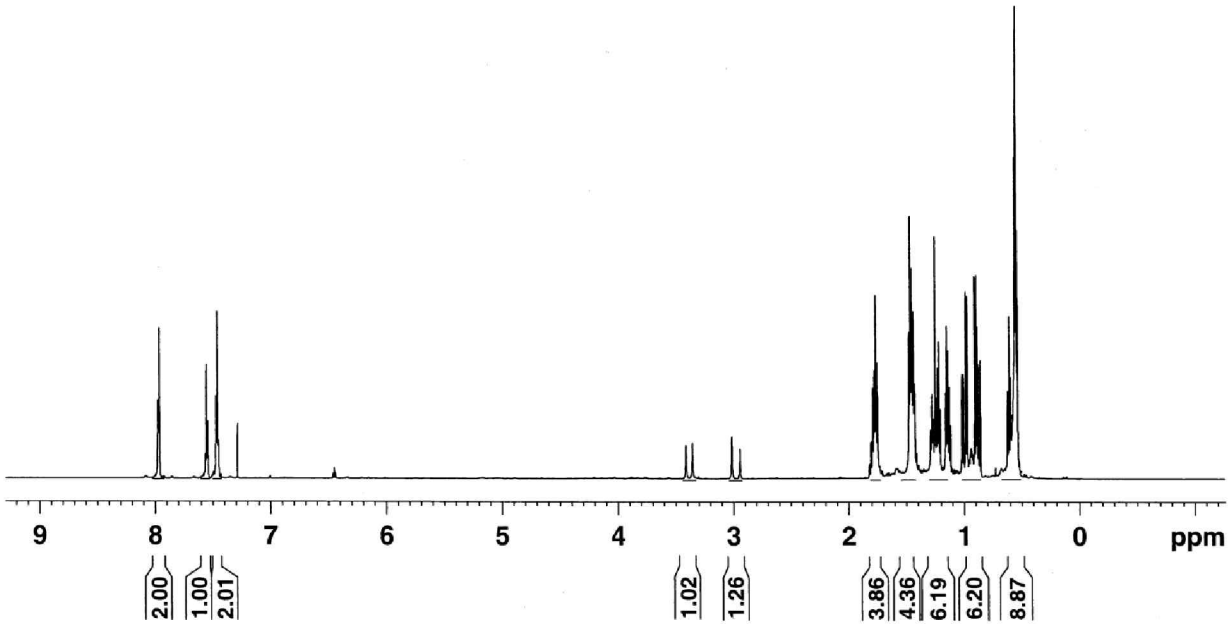


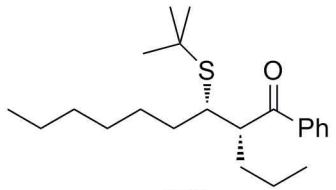
NAME	SS-06-143
EXPNO	2
PROCNO	1
Date_	20130916
Time	13.48
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	13
DS	4
SWH	41666.668 Hz
FIDRES	0.635783 Hz
AQ	0.7864820 sec
RG	203
DW	12.000 usec
DE	16.50 usec
TE	298.2 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 usec
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0697436 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 usec
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1499406 MHz
SI	32768
SF	176.0521380 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40



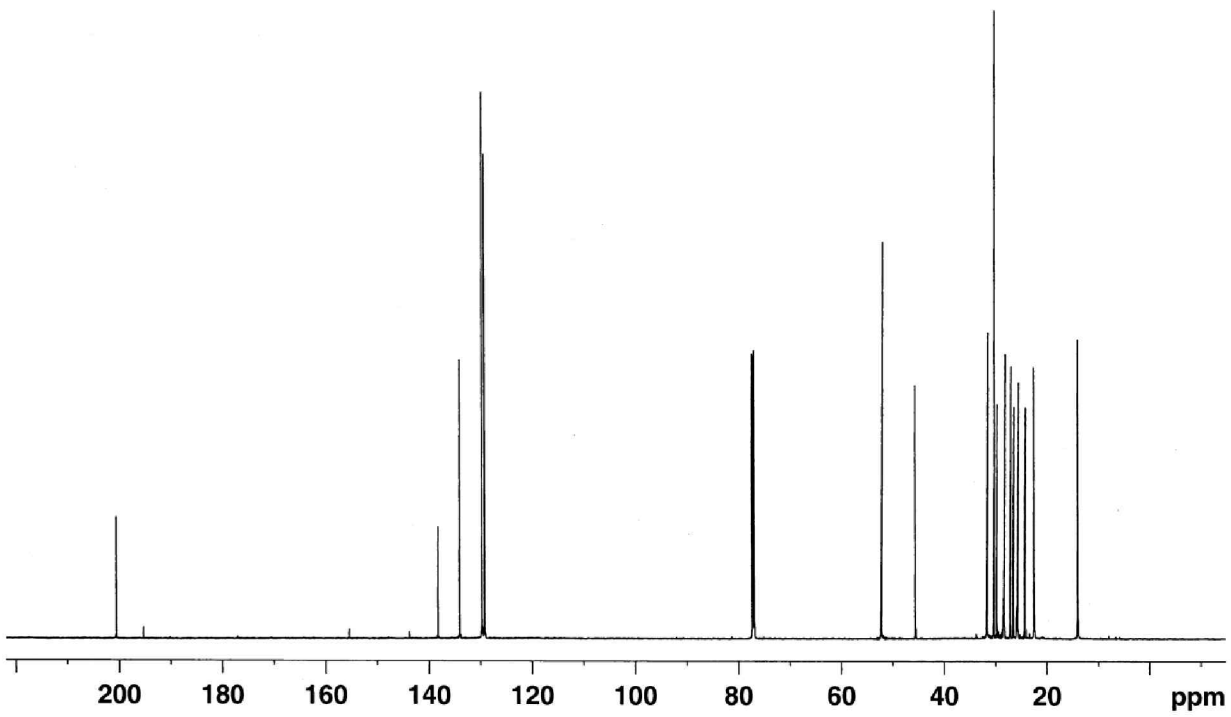
278e

NAME	SS-06-144
EXPNO	1
PROCNO	1
Date_	20130916
Time	13.56
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zg30
TD	95236
SOLVENT	CDCl3
NS	15
DS	2
SWH	11904.762 Hz
FIDRES	0.125003 Hz
AQ	3.9999621 sec
RG	14.2
DW	42.000 use
DE	6.50 use
TE	298.2 K
D1	2.00000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	1H
P1	9.40 use
PL1	-3.20 dB
PL1W	33.59817505 W
SFO1	700.1516910 MHz
SI	131072
SF	700.1471400 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

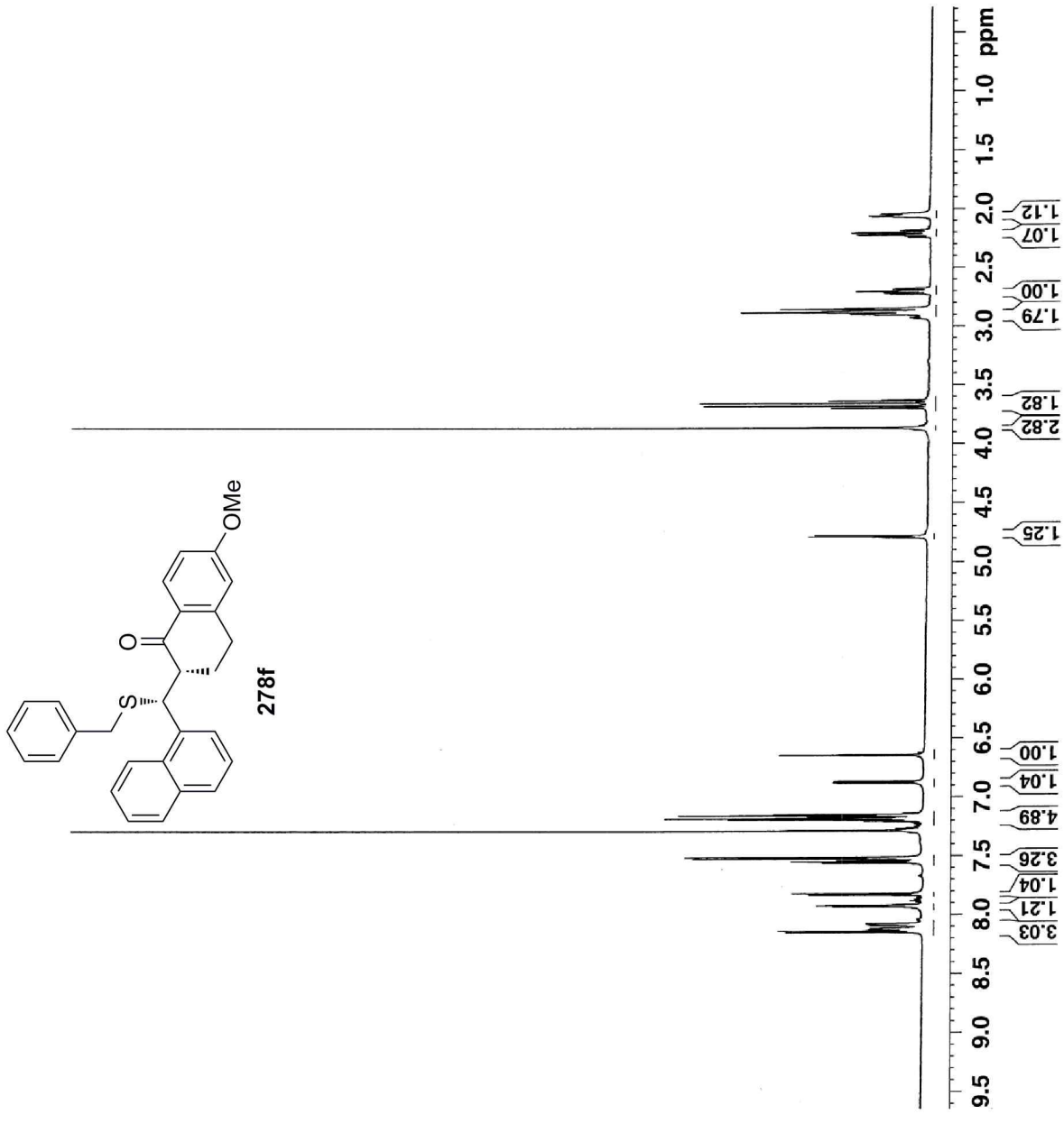


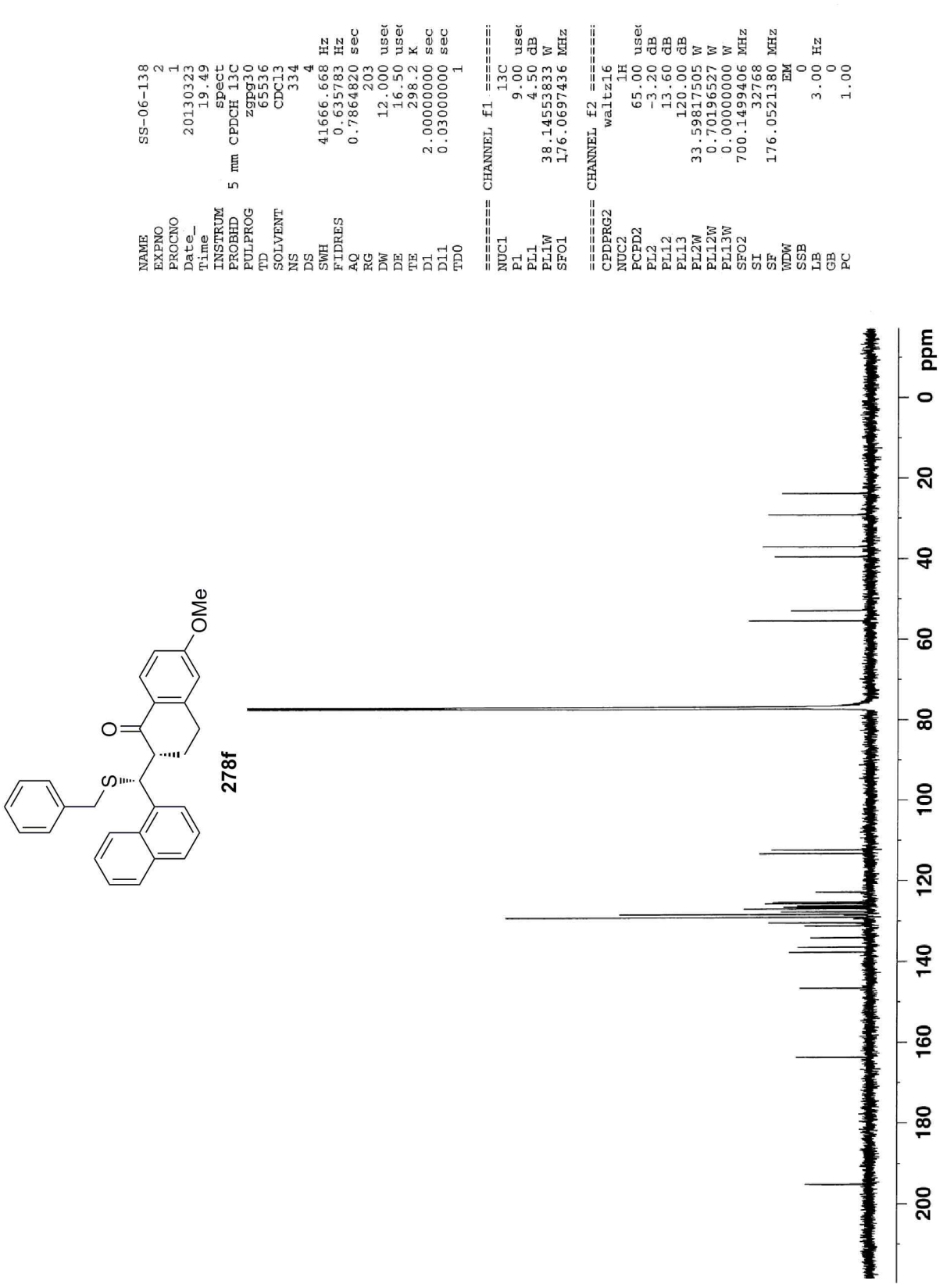


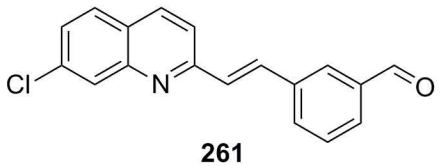
278e



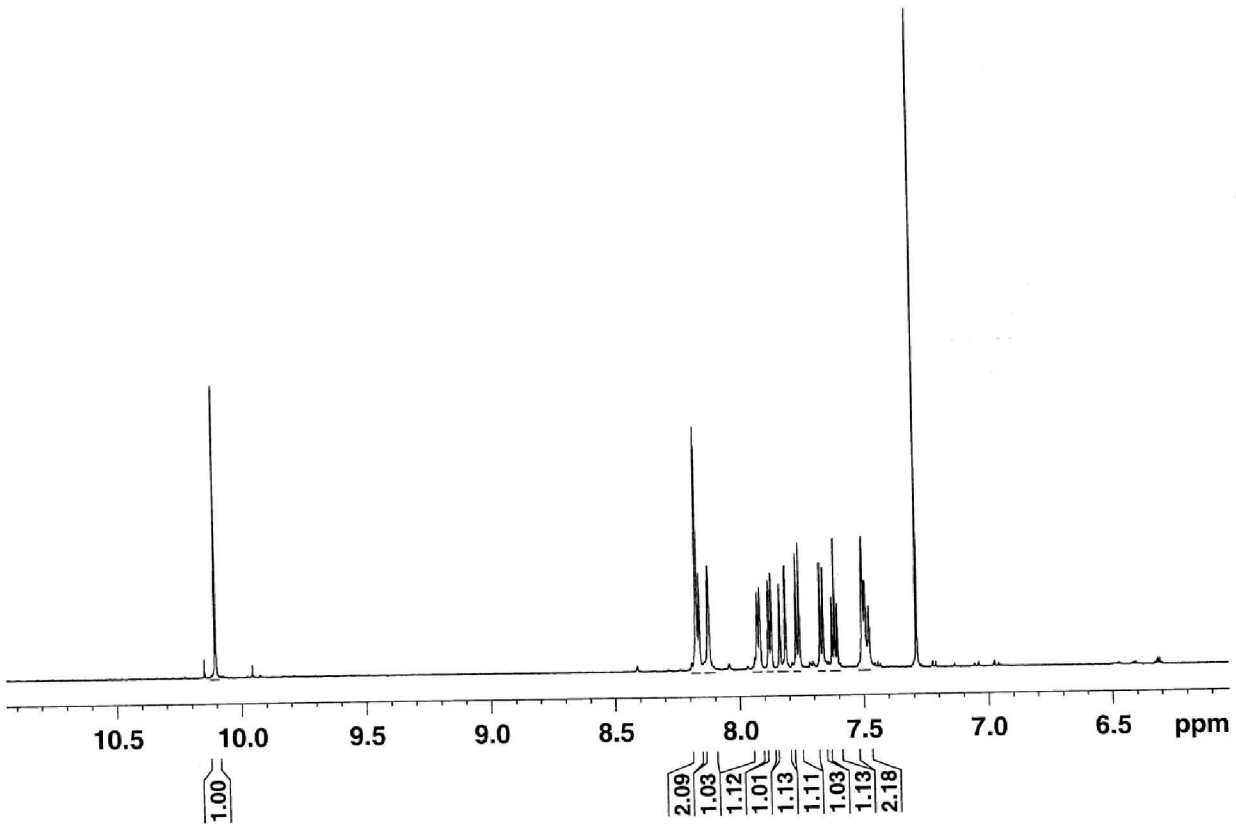
NAME	SS-06-144
EXPNO	2
PROCNO	1
Date_	20130916
Time	14.01
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	65536
SOLVENT	CDC13
NS	45
DS	4
SWH	41666.668 Hz
FIDRES	0.635783 Hz
AQ	0.7864820 sec
RG	203
DW	12.000 use
DE	16.50 use
TE	298.2 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 use
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0697436 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 use
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1499406 MHz
SI	32768
SF	176.0521380 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40


NAME SS-06-138
EXPNO 1
PROCNO 1
Date_ 20130323
Time 19.47
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 13
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.99999621 sec
RG 20.2
DW 42.000 use
DE 6.50 use
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 =======
NUC1 1H
P1 9.40 use
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
278f
OMe
O
S
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
3.03
1.21
1.04
3.26
4.89
1.04
1.00
1.25
2.82
1.82
1.79
1.00
1.07
1.12

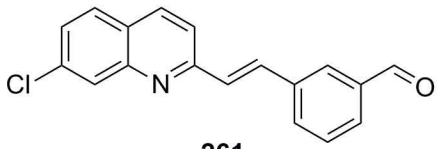

OMe
O
S
278f
NAME SS-06-138
EXPNO 2
PROCNO 1
Date_ 20130323
Time 19.49
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 334
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864820 sec
RG 203
DW 12.000 use
DE 16.50 use
TE 298.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 use
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0697436 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 use
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1499406 MHz
SI 32768
SF 176.0521380 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.00
200
180
160
140
120
100
80
60
40
20
0
ppm



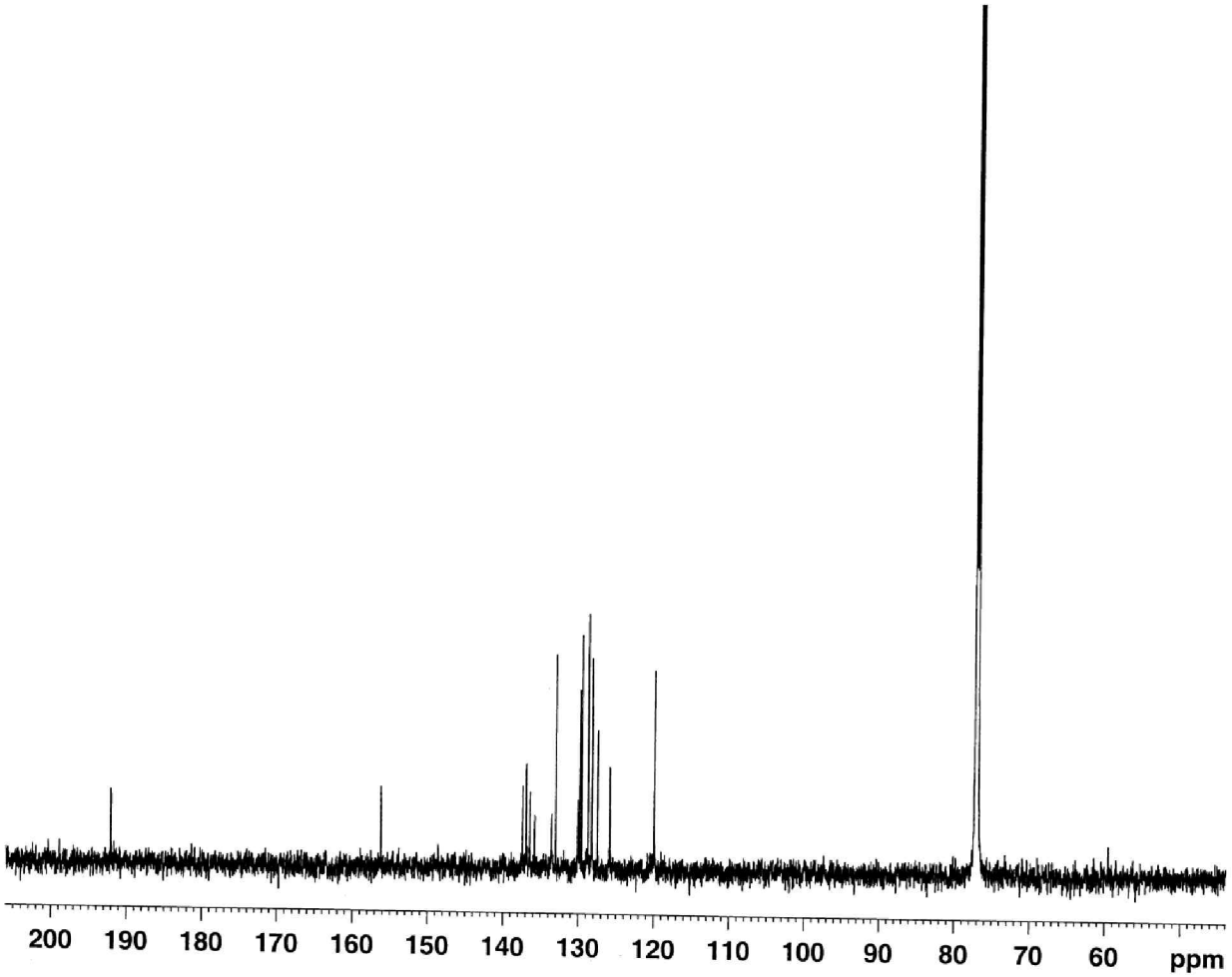
261



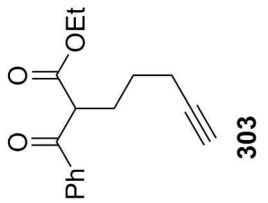
NAME	SS-04-190
EXPNO	1
PROCNO	1
Date_	20130710
Time	19.53
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	95236
SOLVENT	CDCl3
NS	32
DS	2
SWH	11904.762 Hz
FIDRES	0.125003 Hz
AQ	3.9999621 sec
RG	203
DW	42.000 use
DE	6.50 use
TE	298.2 K
D1	2.00000000 sec
TD0	1
======== CHANNEL f1 =======	
NUC1	1H
P1	13.75 use
PL1	-3.00 dB
PL1W	32.08600616 W
SFO1	700.1516910 MHz
SI	131072
SF	700.1471400 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00



261

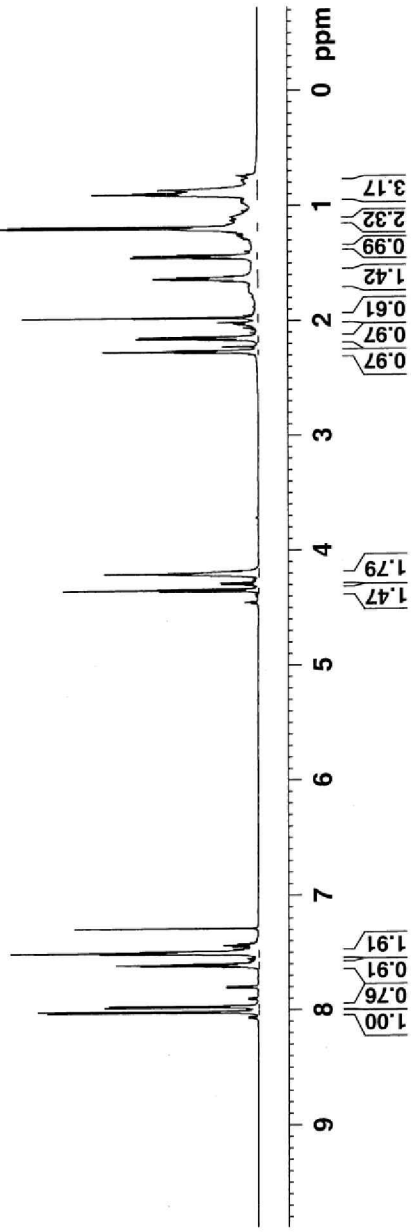


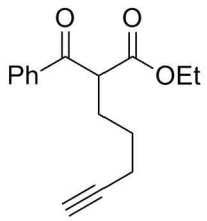
NAME	SS-04-190
EXPNO	2
PROCNO	1
Date_	20130710
Time	19.59
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	1024
DS	4
SWH	41666.668 Hz
FIDRES	0.635783 Hz
AQ	0.7864820 sec
RG	203
DW	12.000 use
DE	16.50 use
TE	299.3 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
========	CHANNEL f1 ========
NUC1	13C
P1	9.30 use
PL1	2.00 dB
PL1W	67.83342743 W
SFO1	176.0697436 MHz
========	CHANNEL f2 ========
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 use
PL2	-3.00 dB
PL12	12.30 dB
PL13	12.30 dB
PL2W	32.08600616 W
PL12W	0.94692516 W
PL13W	0.94692516 W
SFO2	700.1499406 MHz
SI	32768
SF	176.0521380 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40



303

```
NAME          SS-04-118
EXPNO                 1
PROCNO                1
Date_          20130327
Time              20.22
INSTRUM            spect
PROBHD  5 mm CPDCH 13C
PULPROG             zg30
TD                 95236
SOLVENT            CDCl3
NS                    21
DS                     2
SWH           11904.762 Hz
FIDRES            0.125003 Hz
AQ                3.9999621 sec
RG                    16
DW                42.000 use
DE                 6.50 use
TE                298.2 K
D1                2.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 9.40 use
PL1                -3.20 dB
PL1W          33.59817505 W
SFO1          700.1516910 MHz
SI                131072
SF            700.1471400 MHz
WDW                   EM
SSB                    0
LB                 0.30 Hz
GB                     0
PC                  1.00
```





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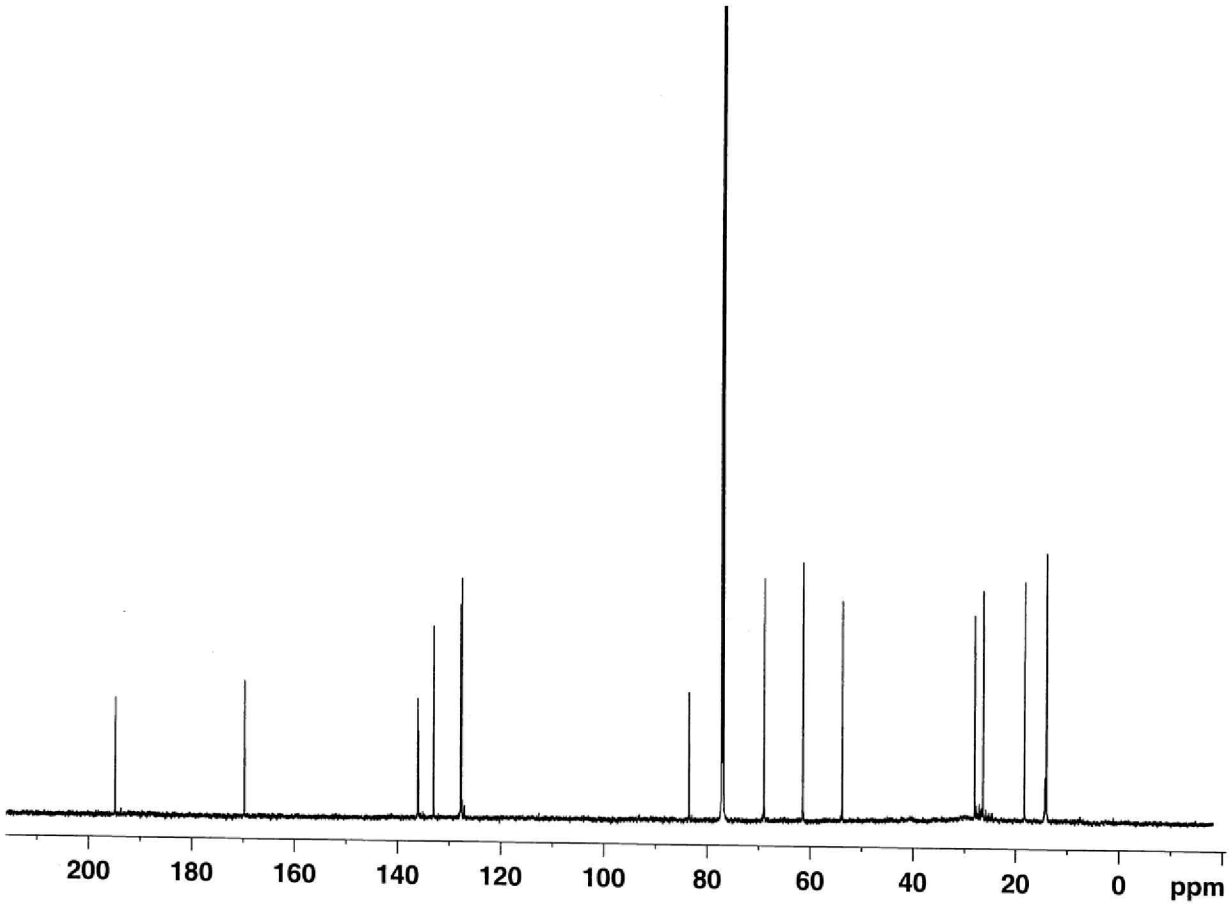
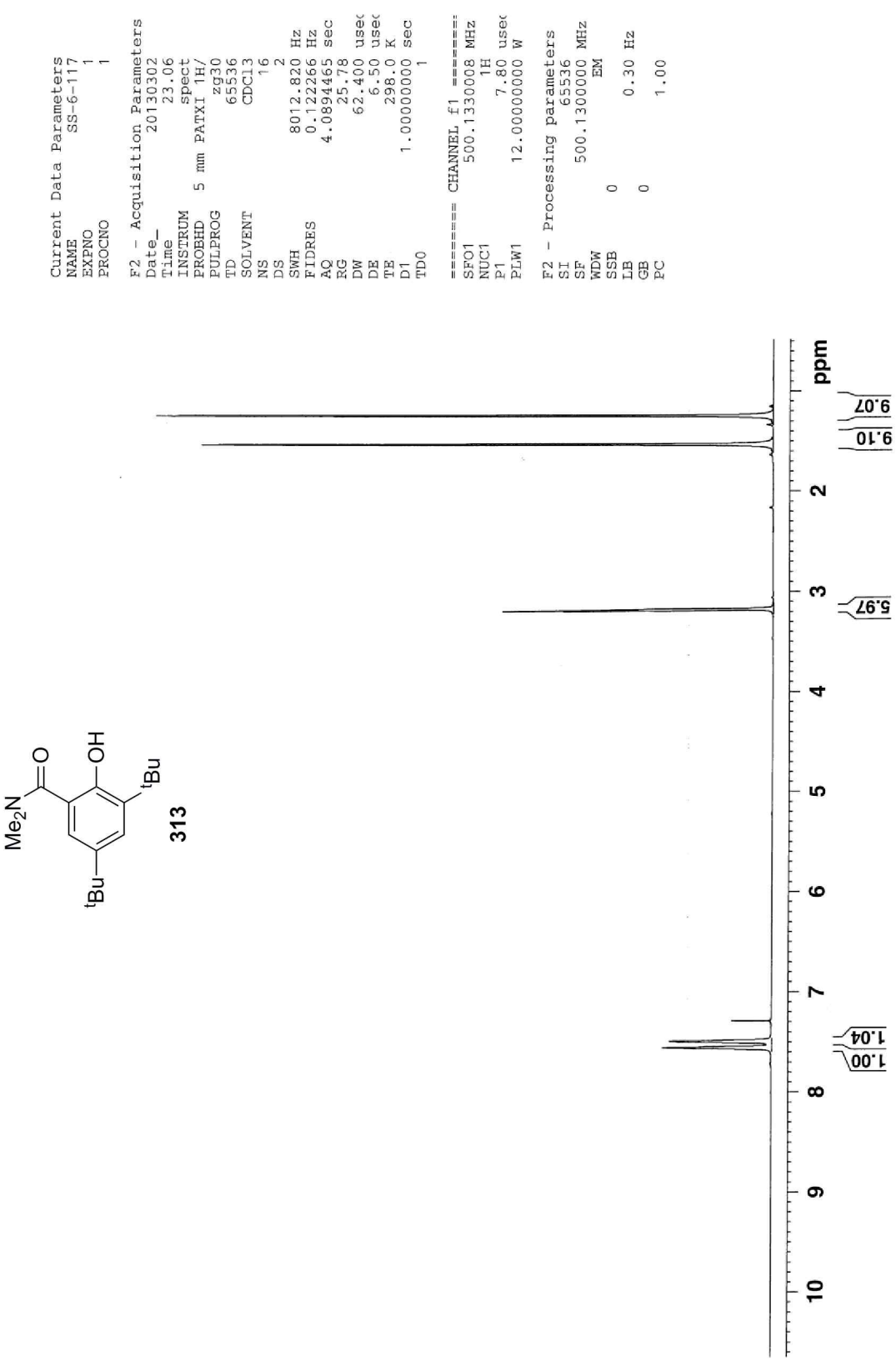
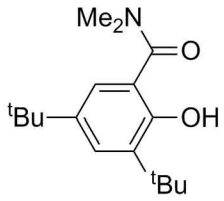
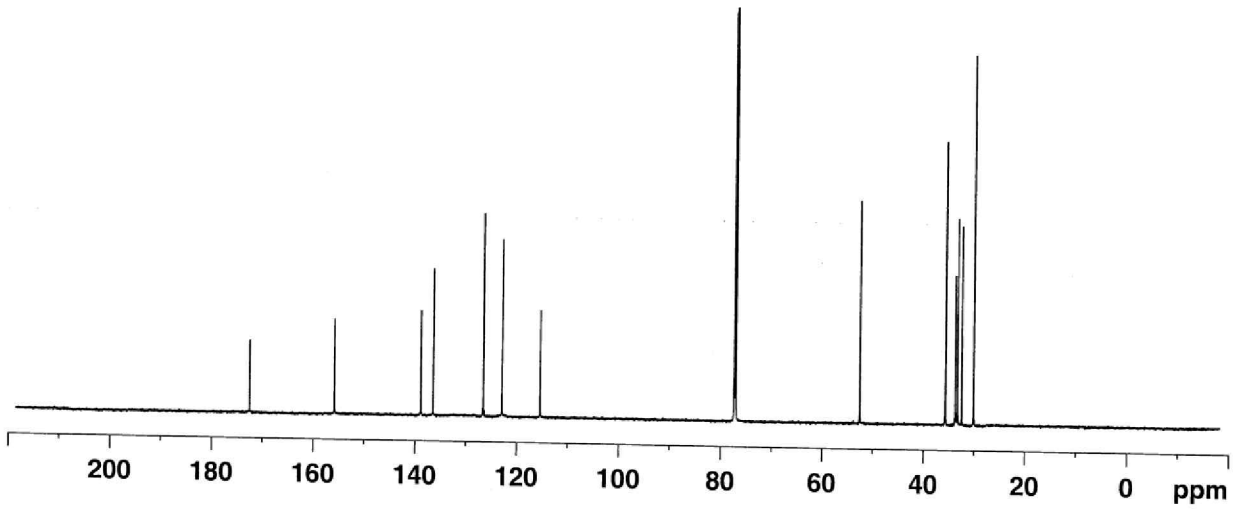


NAME	SS-04-118
EXPNO	2
PROCNO	1
Date_	20130327
Time	20.27
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	48
DS	4
SWH	41666.668 Hz
FIDRES	0.635783 Hz
AQ	0.7864820 sec
RG	203
DW	12.000 use
DE	16.50 use
TE	298.2 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
========	CHANNEL f1 =======
NUC1	13C
P1	9.00 use
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0697436 MHz
========	CHANNEL f2 =======
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 use
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1499406 MHz
SI	32768
SF	176.0521380 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.00

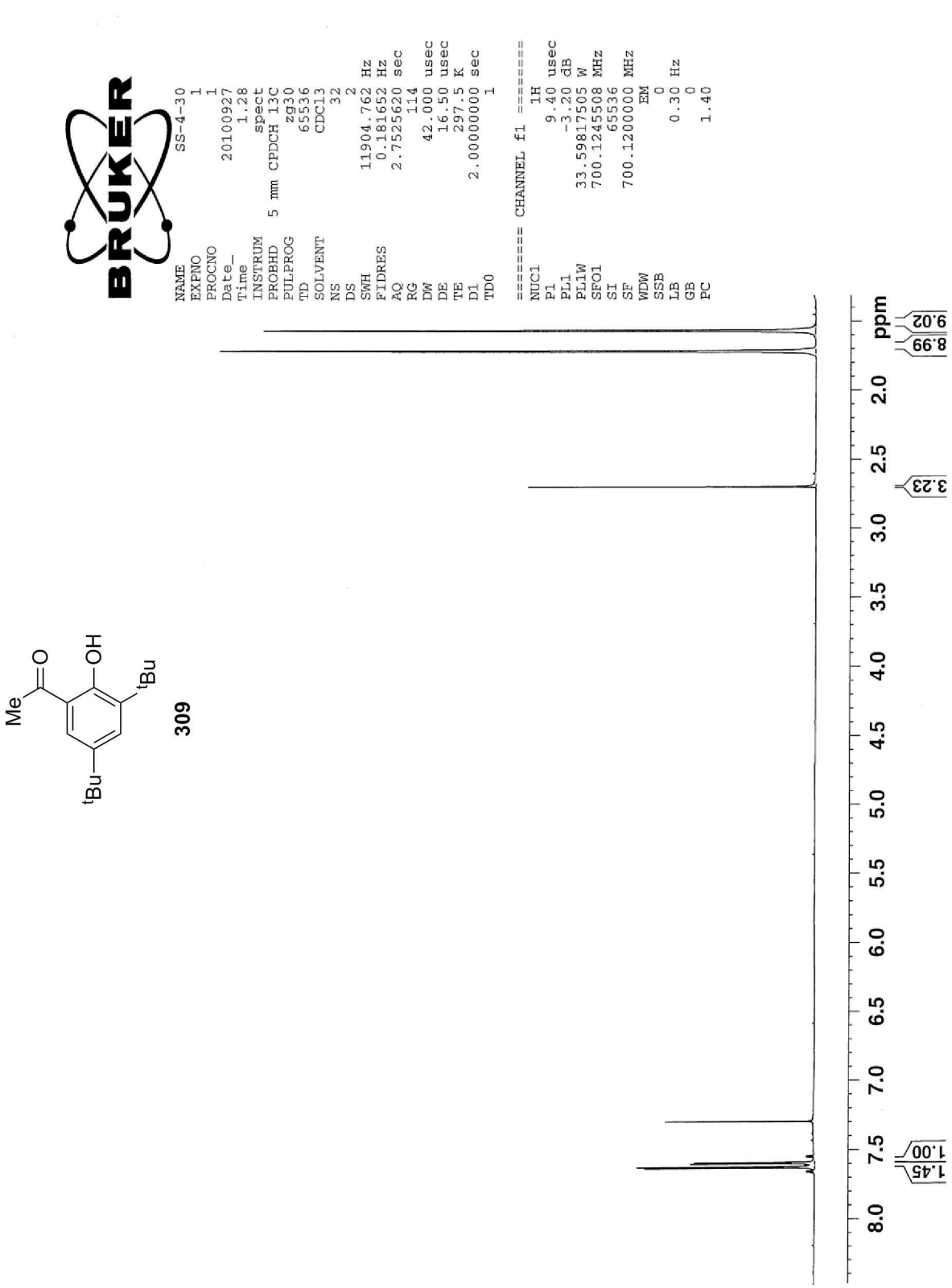

Current Data Parameters
NAME SS-6-117
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130302
Time 23.06
INSTRUM spect
PROBHD 5 mm PATXI 1H/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 25.78
DW 62.400 use
DE 6.50 use
TE 298.0 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 500.1330008 MHz
NUC1 1H
P1 7.80 use
PLW1 12.00000000 W
F2 - Processing parameters
SI 65536
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
Me2N
O
OH
tBu
tBu
313
ppm
1
2
3
4
5
6
7
8
9
10
9.07
9.10
5.97
1.00
1.04



313



NAME	SS-06-117
EXPNO	2
PROCNO	1
Date_	20130323
Time	18.29
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	35
DS	4
SWH	41666.668 Hz
FIDRES	0.635783 Hz
AQ	0.7864820 sec
RG	203
DW	12.000 usec
DE	16.50 usec
TE	298.1 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 usec
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0697436 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 usec
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1499406 MHz
SI	32768
SF	176.0521380 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.00


Me
O
OH
tBu
tBu
309
BRUKER
NAME SS-4-30
EXPNO 1
PROCNO 1
Date_ 20100927
Time 1.28
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.181652 Hz
AQ 2.7525620 sec
RG 114
DW 42.000 usec
DE 16.50 usec
TE 297.5 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1245508 MHz
SI 65536
SF 700.1200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40
ppm
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
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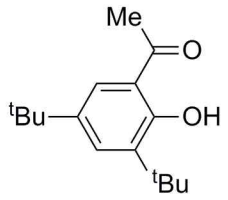
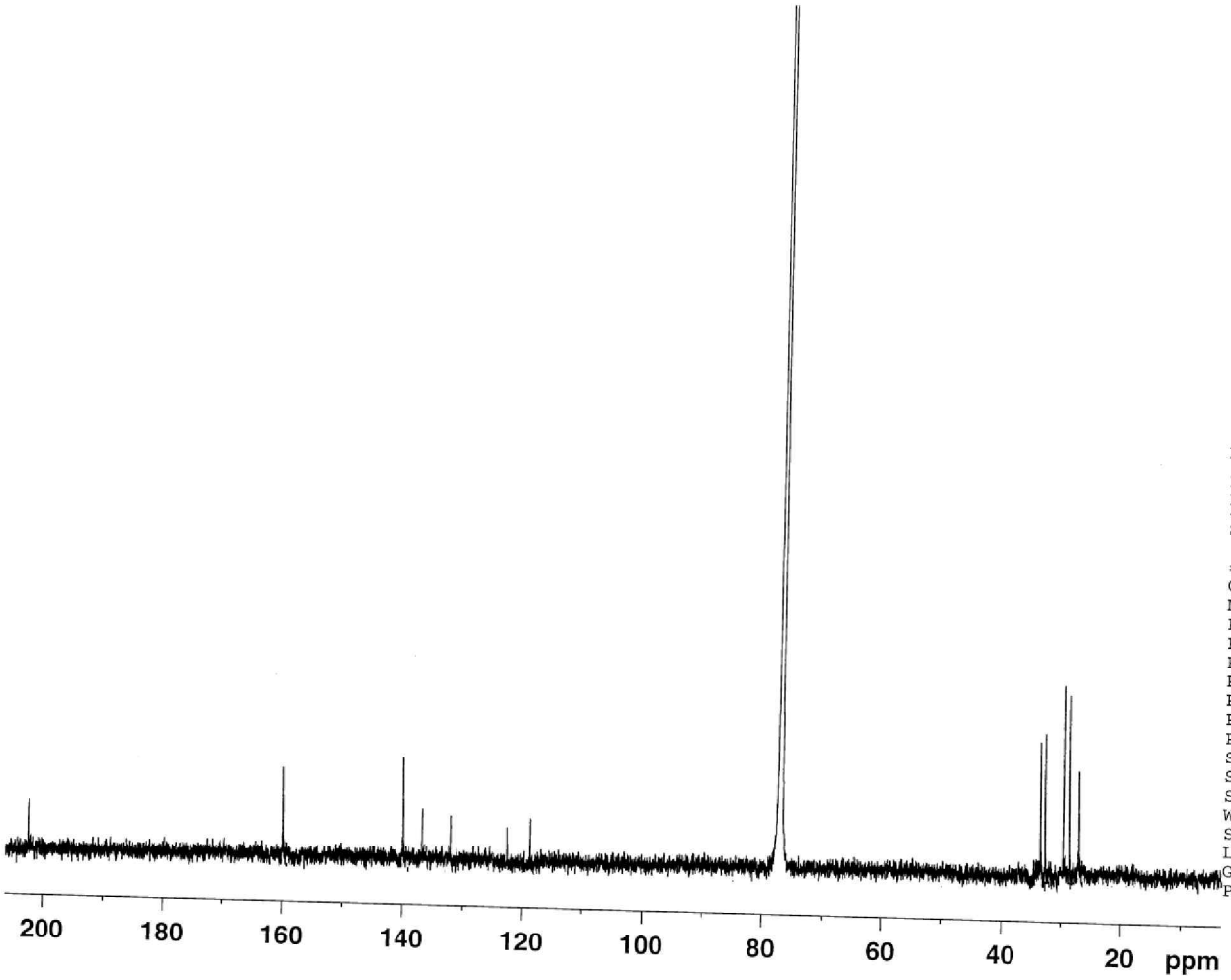
2.5
2.0
1.45
1.00
3.23
8.99
9.02

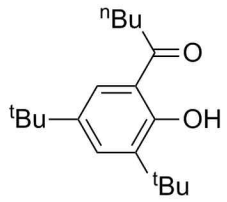


309

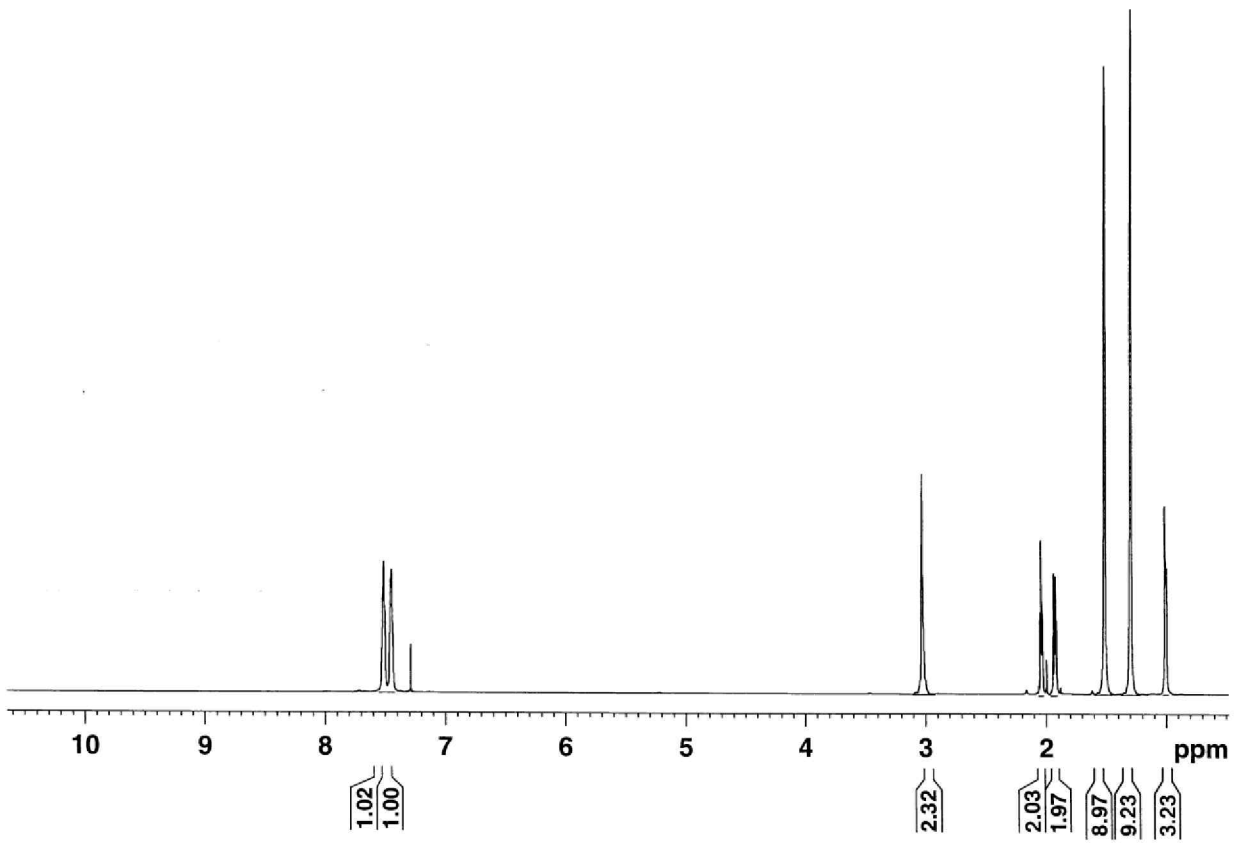


BRUKER

NAME	SS-4-24
EXPNO	5
PROCNO	1
Date_	20101013
Time	18.48
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	98304
SOLVENT	CDCl3
NS	237
DS	4
SWH	41666.668 Hz
FIDRES	0.423855 Hz
AQ	1.1796980 sec
RG	203
DW	12.000 usec
DE	15.00 usec
TE	297.5 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 usec
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0629186 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 usec
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1228005 MHz
SI	131072
SF	176.0453140 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40



310

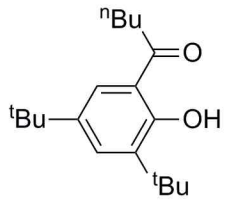



```
Current Data Parameters
NAME                  SS-6-133
EXPNO                        1
PROCNO                       1

F2 - Acquisition Parameters
Date_                 20130309
Time                     20.42
INSTRUM                  spect
PROBHD    5 mm PATXI 1H/
PULPROG                  zg30
TD                      65536
SOLVENT                 CDCl3
NS                         16
DS                          2
SWH                  8012.820 Hz
FIDRES               0.122266 Hz
AQ                   4.0894465 sec
RG                       25.78
DW                      62.400 usec
DE                       6.50 usec
TE                      298.0 K
D1                   1.00000000 sec
TD0                          1

======== CHANNEL f1 ========
SFO1            500.1330008 MHz
NUC1                       1H
P1                       7.80 usec
PLW1            12.00000000 W

F2 - Processing parameters
SI                      65536
SF              500.1300000 MHz
WDW                        EM
SSB          0
LB                       0.30 Hz
GB           0
PC                       1.00
```



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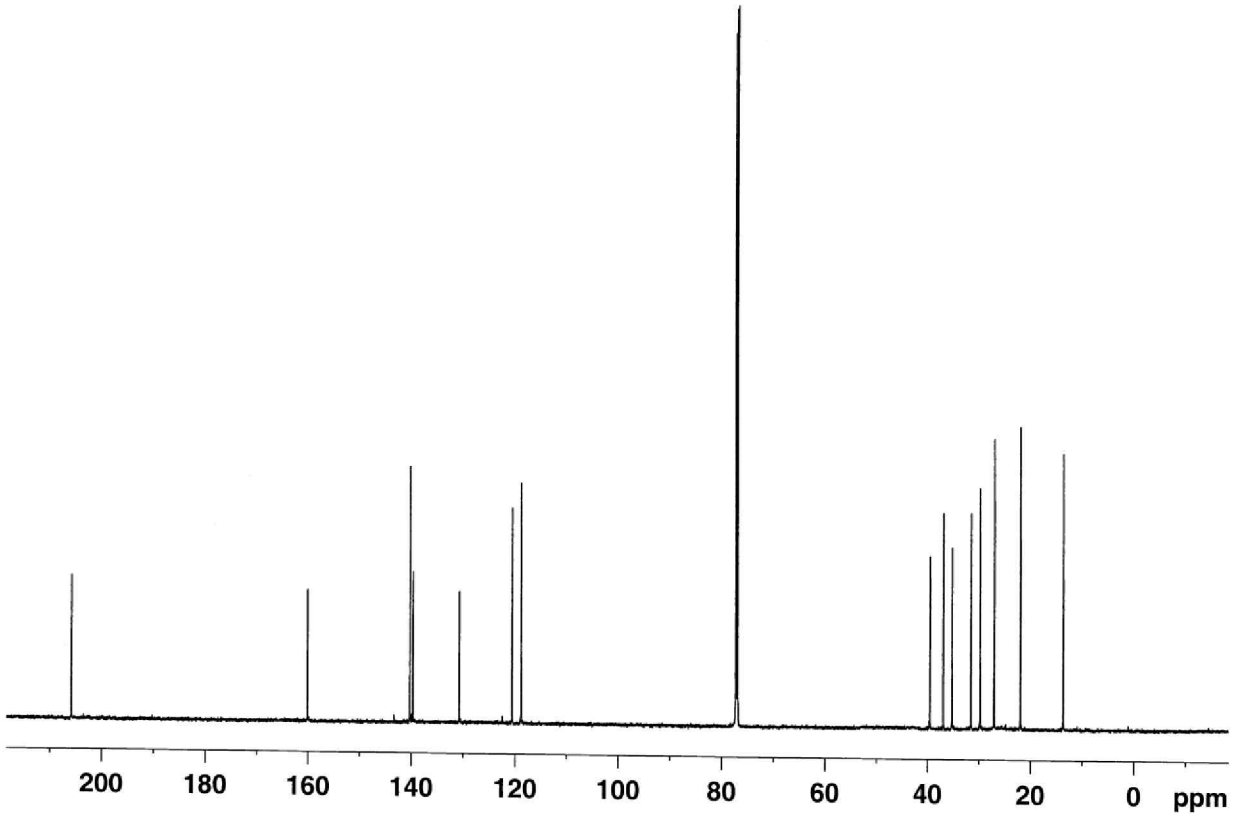
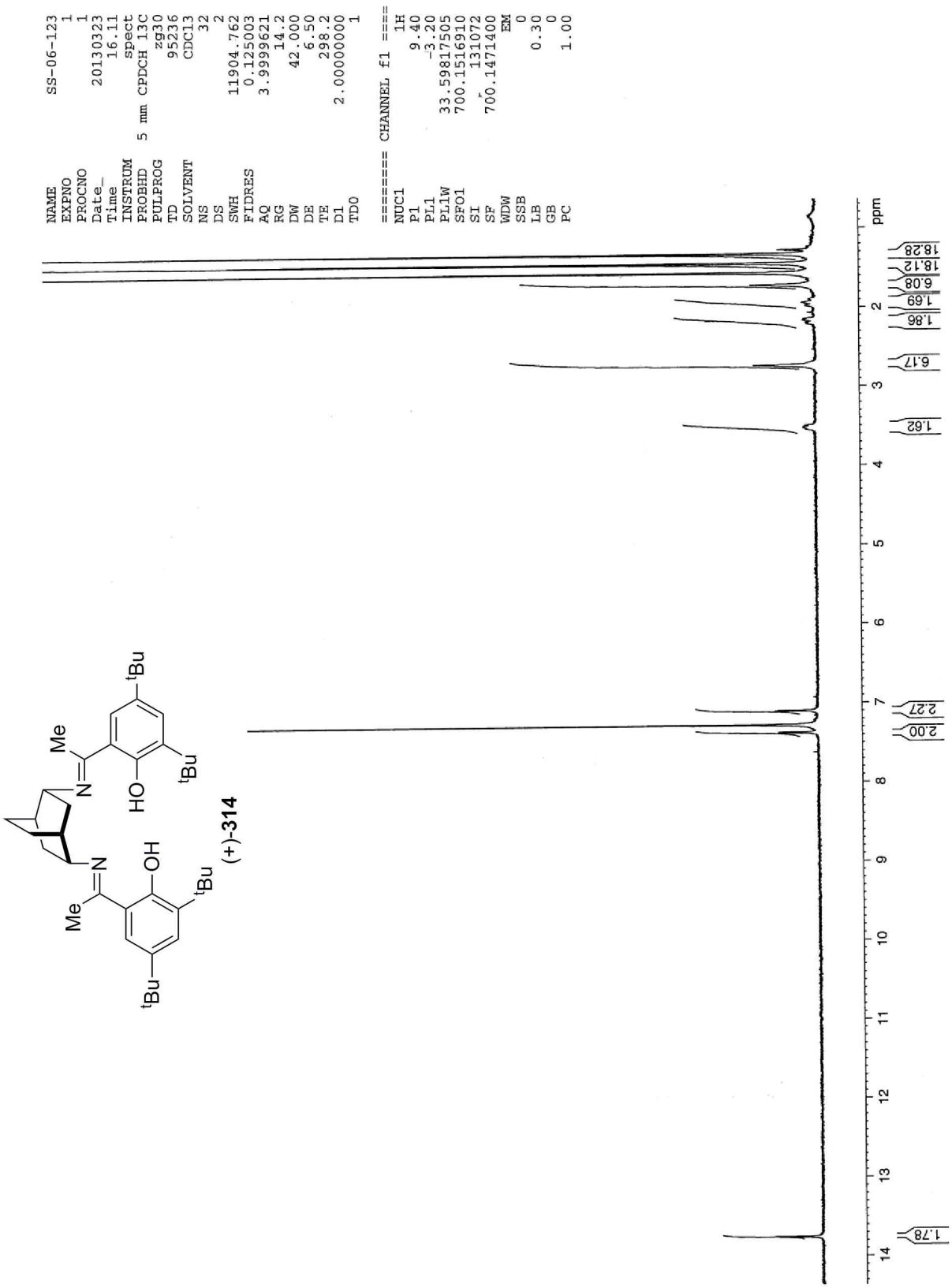


NAME	SS-06-133	
EXPNO	2	
PROCNO	1	
Date_	20130323	
Time	19.03	
INSTRUM	spect	
PROBHD	5 mm CPDCH 13C	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	15	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	use
DE	16.50	use
TE	298.1	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
========	CHANNEL f1	========
NUC1	13C	
P1	9.00	use
PL1	4.50	dB
PL1W	38.14553833	W
SFO1	176.0697436	MHz
========	CHANNEL f2	========
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	65.00	use
PL2	-3.20	dB
PL12	13.60	dB
PL13	120.00	dB
PL2W	33.59817505	W
PL12W	0.70196527	W
PL13W	0.00000000	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.00	


NAME SS-06-123
EXPNO 1
PROCNO 1
Date_ 20130323
Time 16.11
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDC13
NS 32
DS 2
SWH 11904.762
FIDRES 0.125003
AQ 3.9999621
RG 14.2
DW 42.000
DE 6.50
TE 298.2
D1 2.00000000
TD0 1
======== CHANNEL f1 ====
NUC1 1H
P1 9.40
PL1 -3.20
PL1W 33.59817505
SFO1 700.1516910
SI 131072
SF 700.1471400
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00
Me
N
HO
tBu
tBu
Me
N
OH
tBu
tBu
(+)-314
ppm
1.78
2.00
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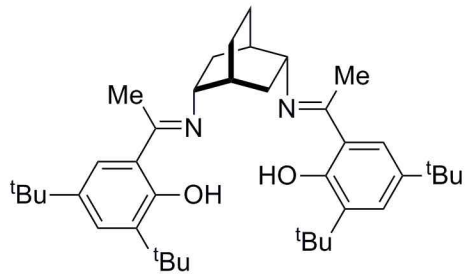
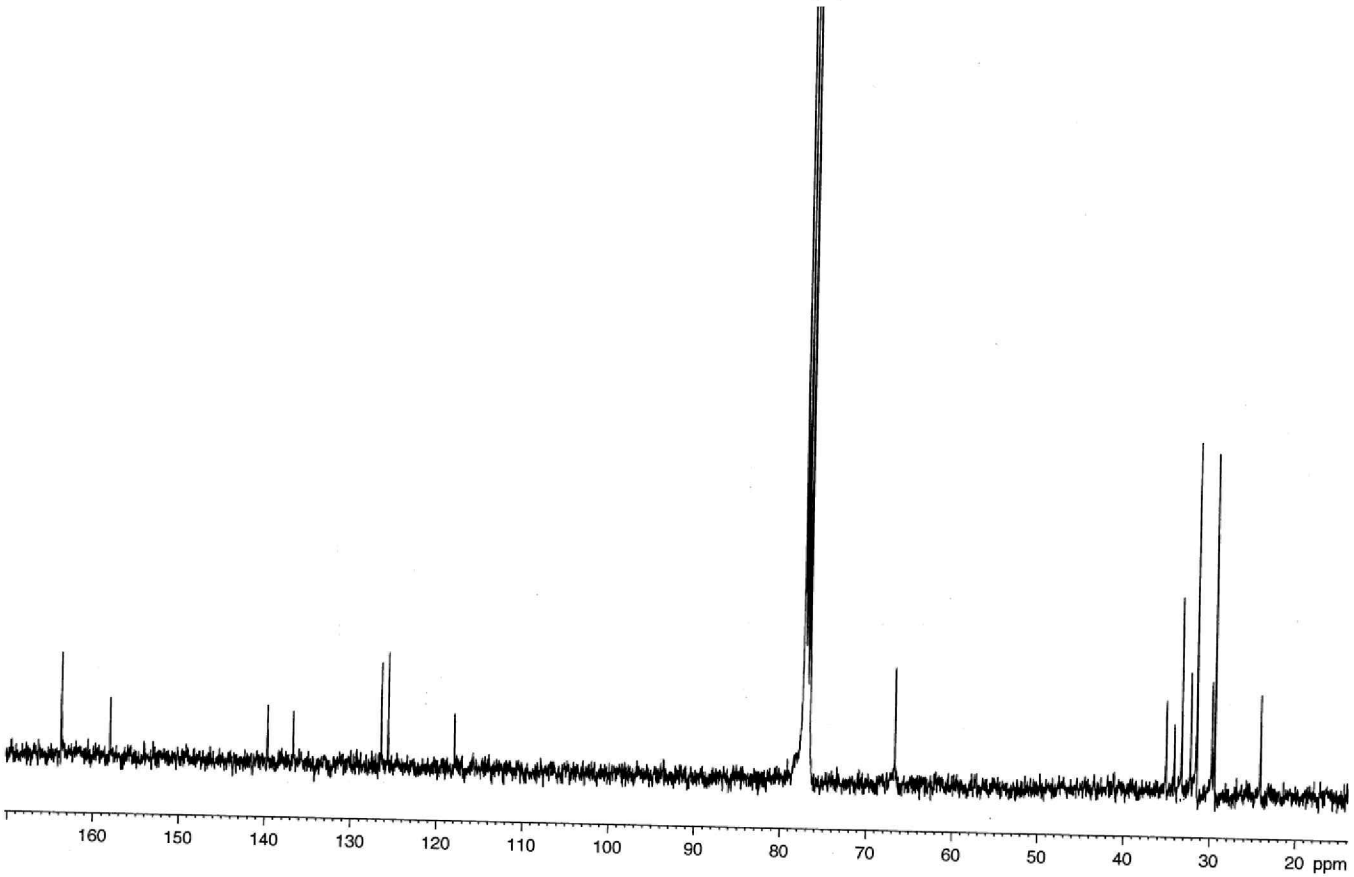
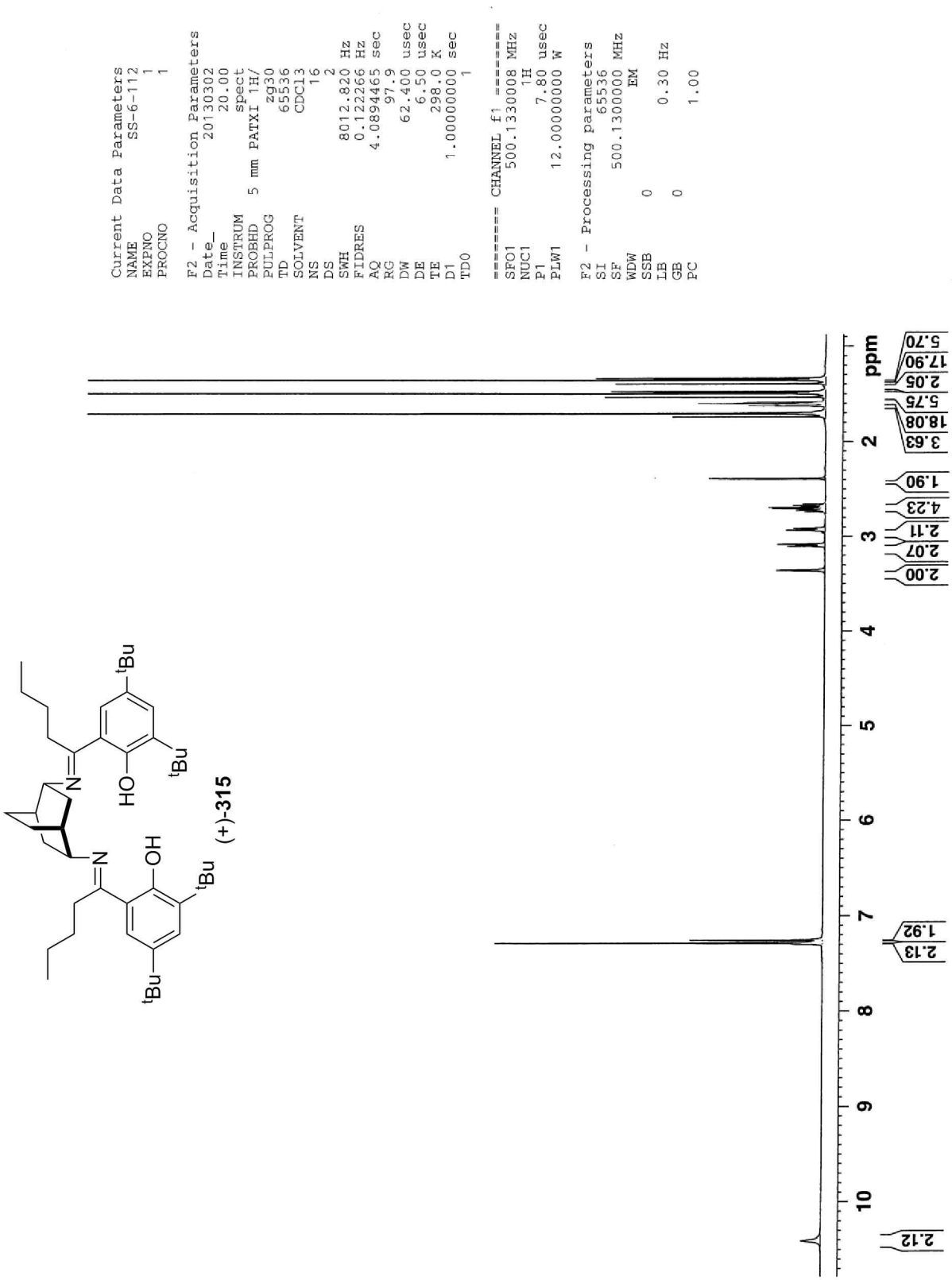
1.62
6.17
1.86
1.69
6.08
18.12
18.28

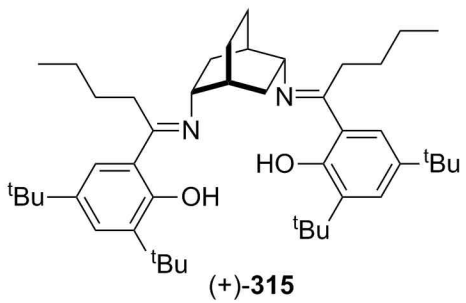


(+)-**314**

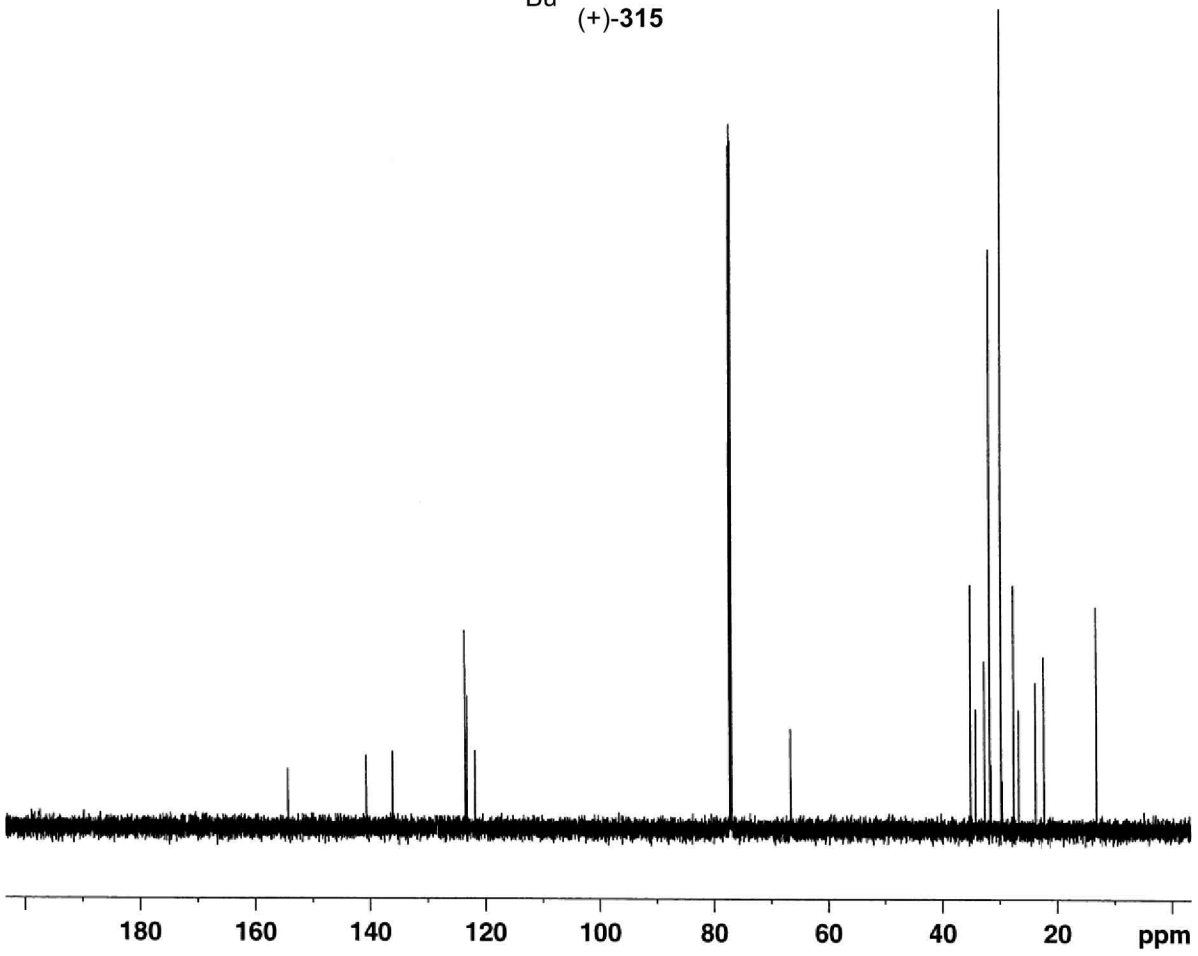


NAME	SS-06-126	
EXPNO	2	
PROCNO	1	
Date_	20130323	
Time	16.54	
INSTRUM	spect	
PROBHD	5 mm CPDCH 13C	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDC13	
NS	15	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	use
DE	16.50	use
TE	298.2	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
========	CHANNEL f1 =======	
NUC1	13C	
P1	9.00	use
PL1	4.50	dB
PL1W	38.14553833	W
SFO1	176.0697436	MHz
========	CHANNEL f2 =======	
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	65.00	use
PL2	-3.20	dB
PL12	13.60	dB
PL13	120.00	dB
PL2W	33.59817505	W
PL12W	0.70196527	W
PL13W	0.00000000	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.00	

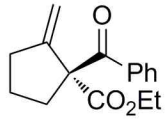

Current Data Parameters
NAME SS-6-112
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130302
Time 20.00
INSTRUM spect
PROBHD 5 mm PATXI 1H/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 97.9
DW 62.400 usec
DE 6.50 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 500.1330008 MHz
NUC1 1H
P1 7.80 usec
PLW1 12.00000000 W
F2 - Processing parameters
SI 65536
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
HO
OH
tBu
tBu
tBu
tBu
(+)-315
ppm
2.12
2.13
1.92
2.00
2.07
2.11
4.23
1.90
3.63
18.08
5.75
2.05
17.90
5.70



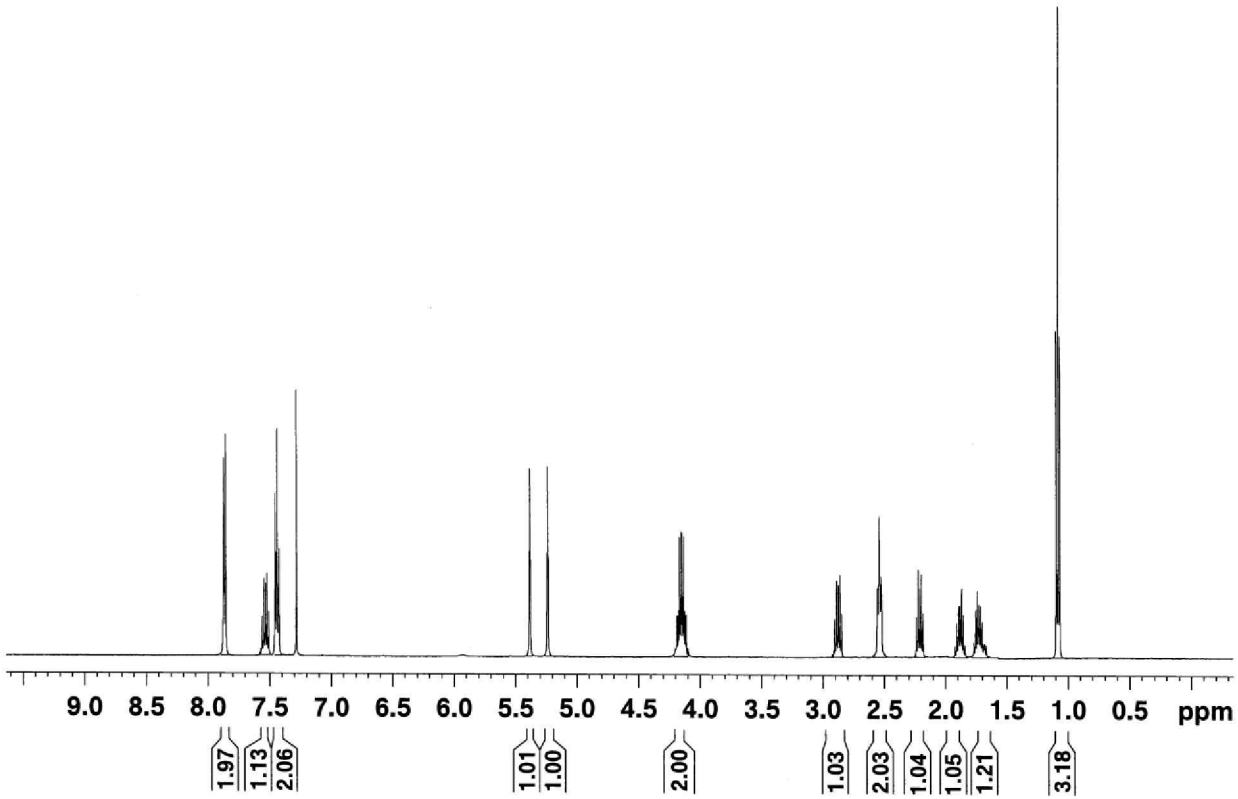
(+)-**315**



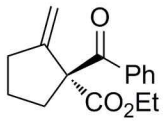
NAME	SS-06-112
EXPNO	2
PROCNO	1
Date_	20130323
Time	17.43
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	52
DS	4
SWH	41666.668 Hz
FIDRES	0.635783 Hz
AQ	0.7864820 se
RG	203
DW	12.000 us
DE	16.50 us
TE	298.2 K
D1	2.00000000 se
D11	0.03000000 se
TD0	1
======== CHANNEL f1 ======	
NUC1	13C
P1	9.00 us
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0697436 MH
======== CHANNEL f2 ======	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 us
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1499406 MH
SI	32768
SF	176.0521380 MH
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.00



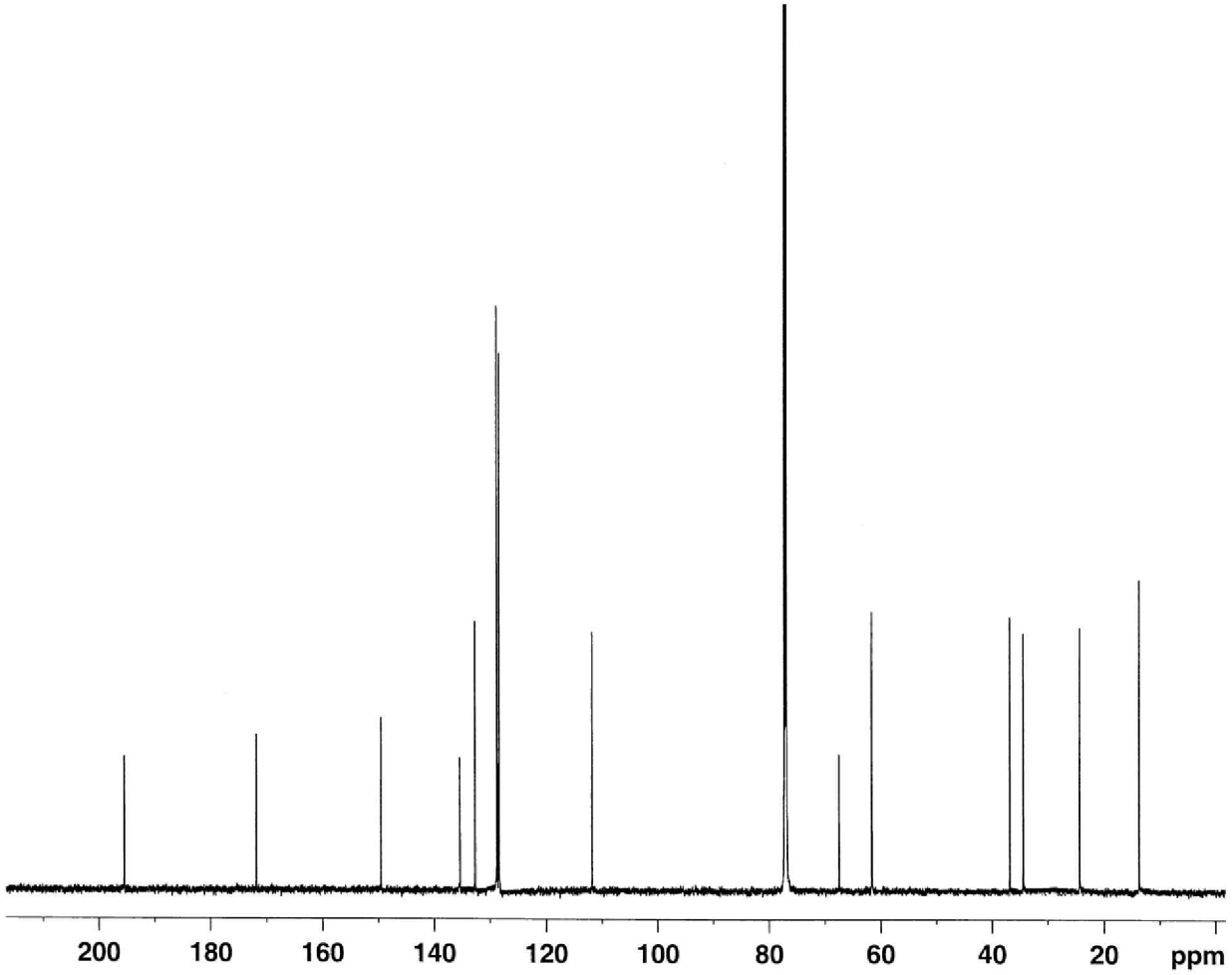
304



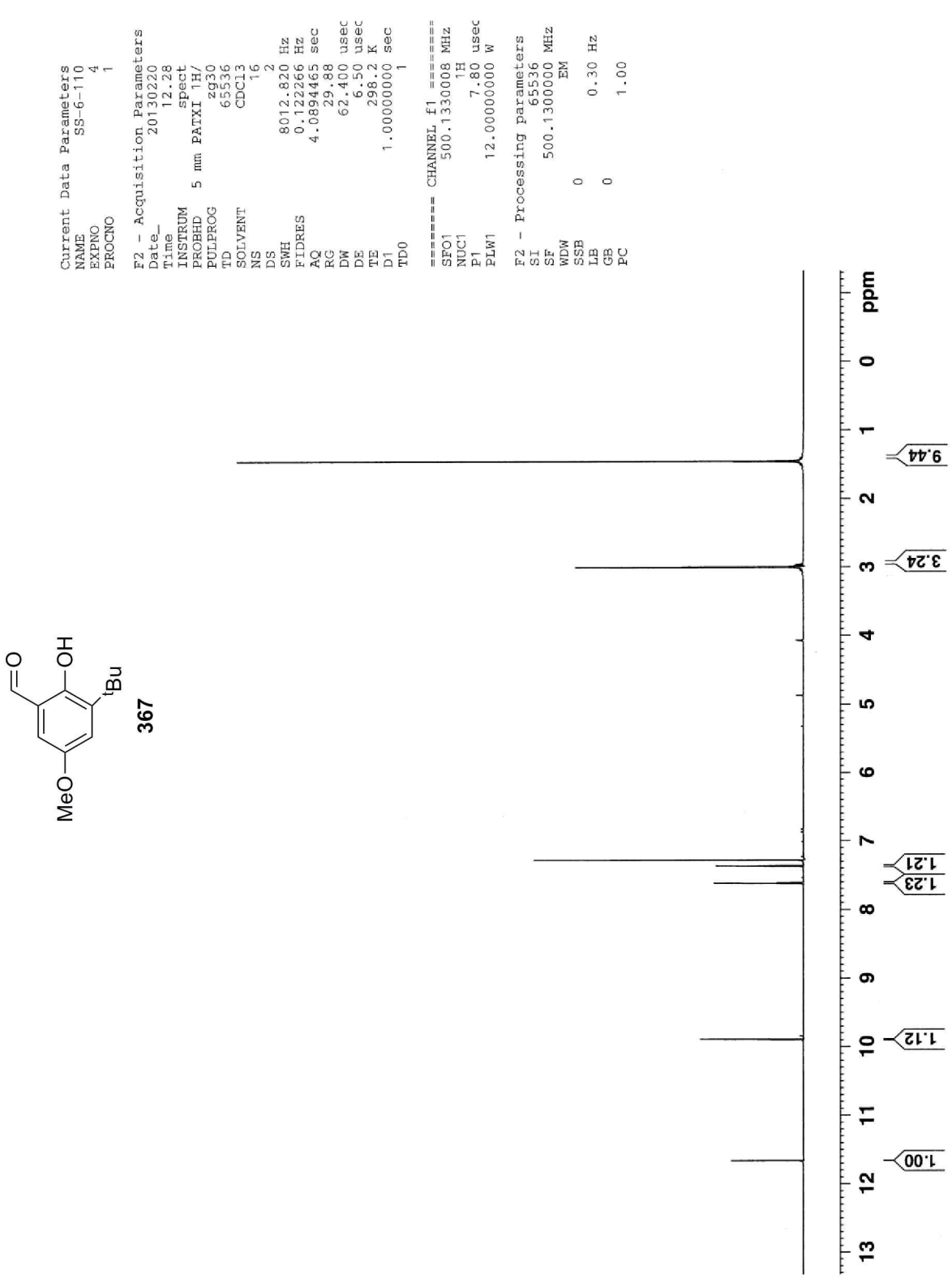

```
Current Data Parameters
NAME            SS-4-149
EXPNO                  4
PROCNO                 1

F2 - Acquisition Parameters
Date_           20130404
Time               11.58
INSTRUM            spect
PROBHD   5 mm PATXI 1H/
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.122266 Hz
AQ              4.0894465 sec
RG                190.98
DW                62.400 usec
DE                 6.50 usec
TE                296.7 K
D1           1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
SFO1         500.1330008 MHz
NUC1                   1H
P1                 7.80 usec
PLW1        12.00000000 W

F2 - Processing parameters
SI                 65536
SF          500.1300000 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

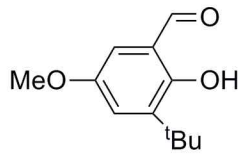


304

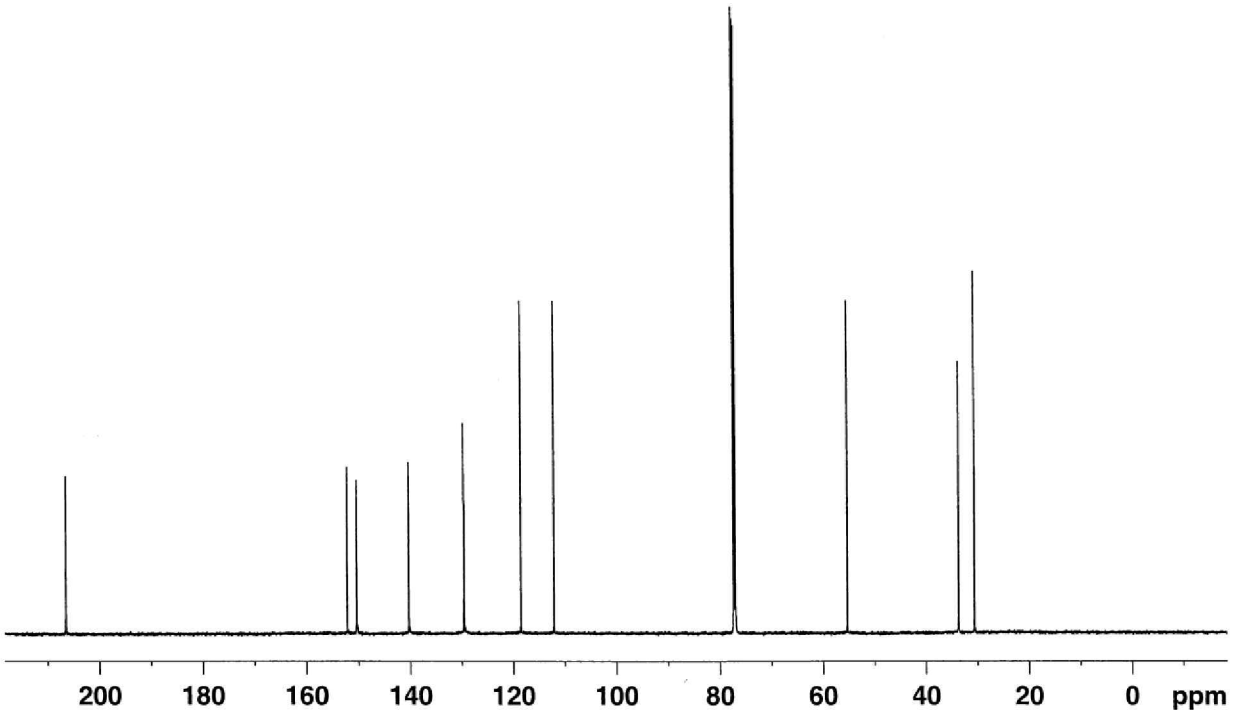


NAME	SS-07-149	
EXPNO	2	
PROCNO	1	
Date_	20130602	
Time	15.35	
INSTRUM	spect	
PROBHD	5 mm CPDCH 13C	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	71	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	use
DE	16.50	use
TE	298.1	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
========	CHANNEL f1 ========	
NUC1	13C	
P1	9.00	use
PL1	4.50	dB
PL1W	38.14553833	W
SFO1	176.0697436	MHz
========	CHANNEL f2 ========	
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	65.00	use
PL2	-3.20	dB
PL12	13.60	dB
PL13	120.00	dB
PL2W	33.59817505	W
PL12W	0.70196527	W
PL13W	0.00000000	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.40	

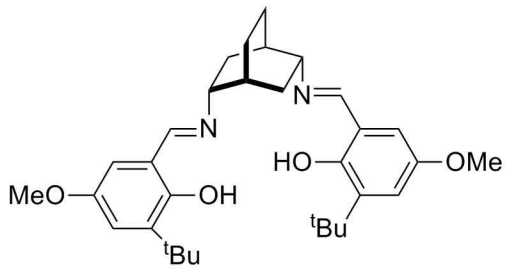

Current Data Parameters
NAME SS-6-110
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130220
Time 12.28
INSTRUM spect
PROBHD 5 mm PATXI 1H/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8012.820 Hz
FIDRES 0.122266 Hz
AQ 4.0894465 sec
RG 29.88
DW 62.400 usec
DE 6.50 usec
TE 298.2 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
SFO1 500.1330008 MHz
NUC1 1H
P1 7.80 usec
PLW1 12.00000000 W
F2 - Processing parameters
SI 65536
SF 500.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
O
OH
tBu
MeO
367
9.44
3.24
1.21
1.23
1.12
1.00
ppm



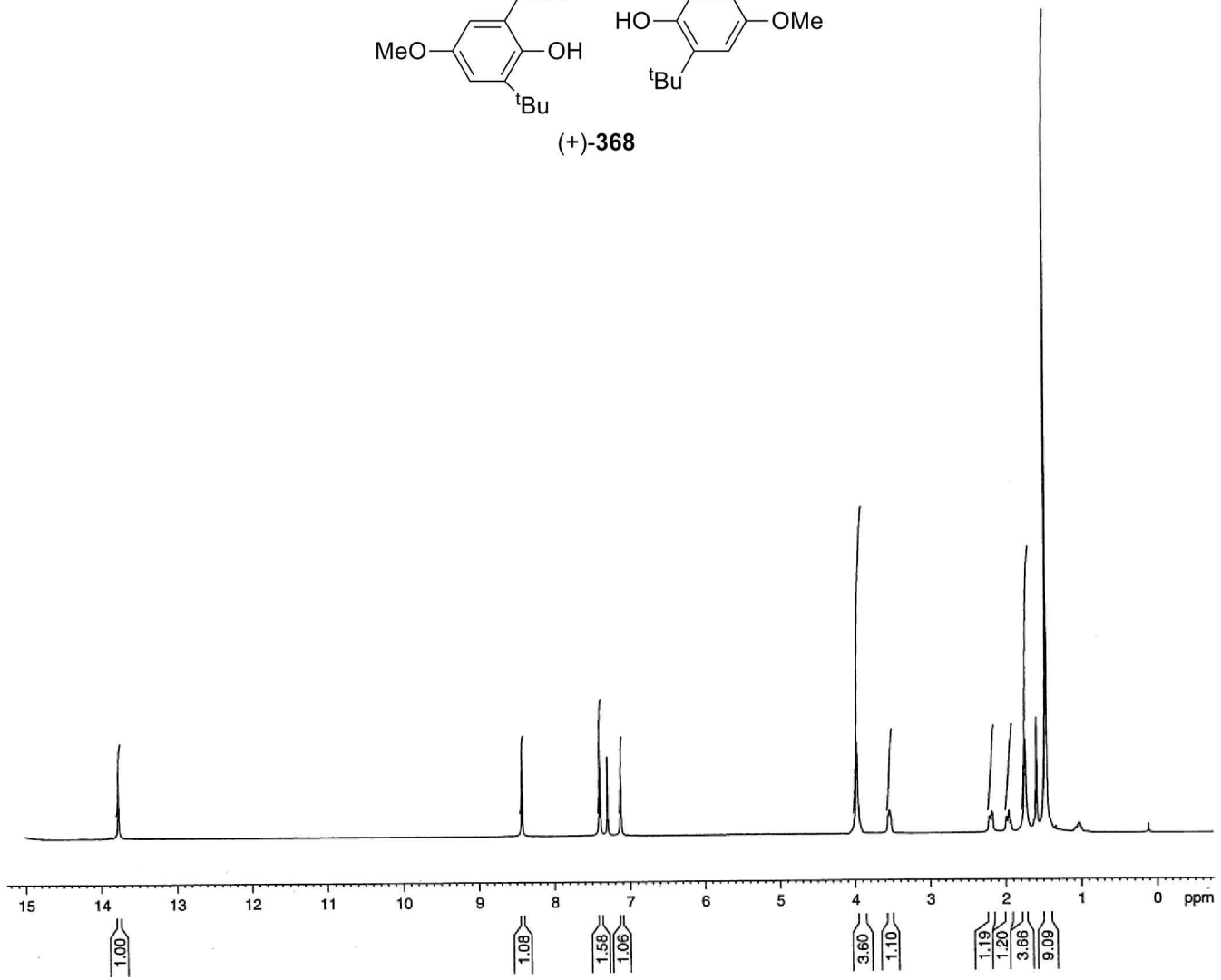
367



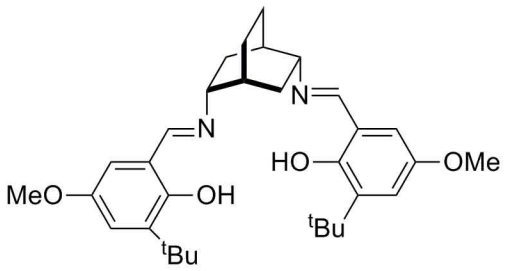
NAME	SS-06-110	
EXPNO	2	
PROCNO	1	
Date_	20130323	
Time	17.08	
INSTRUM	spect	
PROBHD	5 mm CPDCH 13C	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	14	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	usec
DE	16.50	usec
TE	298.2	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	9.00	usec
PL1	4.50	dB
PL1W	38.14553833	W
SFO1	176.0697436	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	65.00	usec
PL2	-3.20	dB
PL12	13.60	dB
PL13	120.00	dB
PL2W	33.59817505	W
PL12W	0.70196527	W
PL13W	0.00000000	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.00	



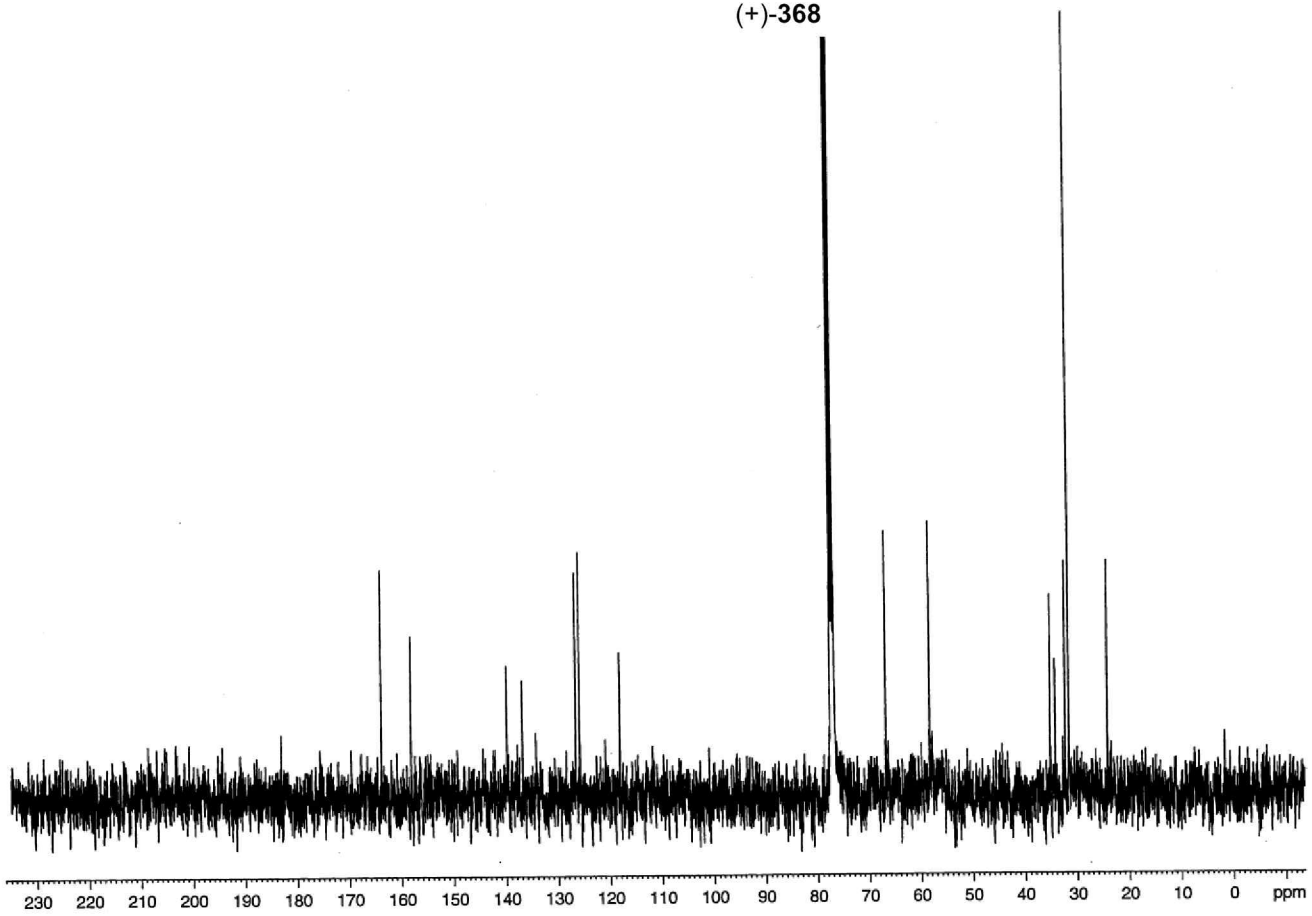
(+)-**368**



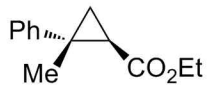

```
Current Data Parameters
NAME                  SS-6-130
EXPNO                        1
PROCNO                       1

F2 - Acquisition Parameters
Date_                 20130309
Time                     17.43
INSTRUM                  spect
PROBHD    5 mm PATXI 1H/
PULPROG                  zg30
TD                      65536
SOLVENT                 CDCl3
NS                         16
DS                          2
SWH                  8012.820 Hz
FIDRES               0.122266 Hz
AQ                   4.0894465 sec
RG                        97.9
DW                     62.400 usec
DE                      6.50 usec
TE                     298.0 K
D1                1.00000000 sec
TD0                         1

======== CHANNEL f1 ========
SFO1           500.1330008 MHz
NUC1                     1H
P1                     7.80 usec
PLW1             12.00000000 W

F2 - Processing parameters
SI                      65536
SF             500.1300000 MHz
WDW                        EM
SSB          0
LB                     0.30 Hz
GB           0
PC                     1.00
```



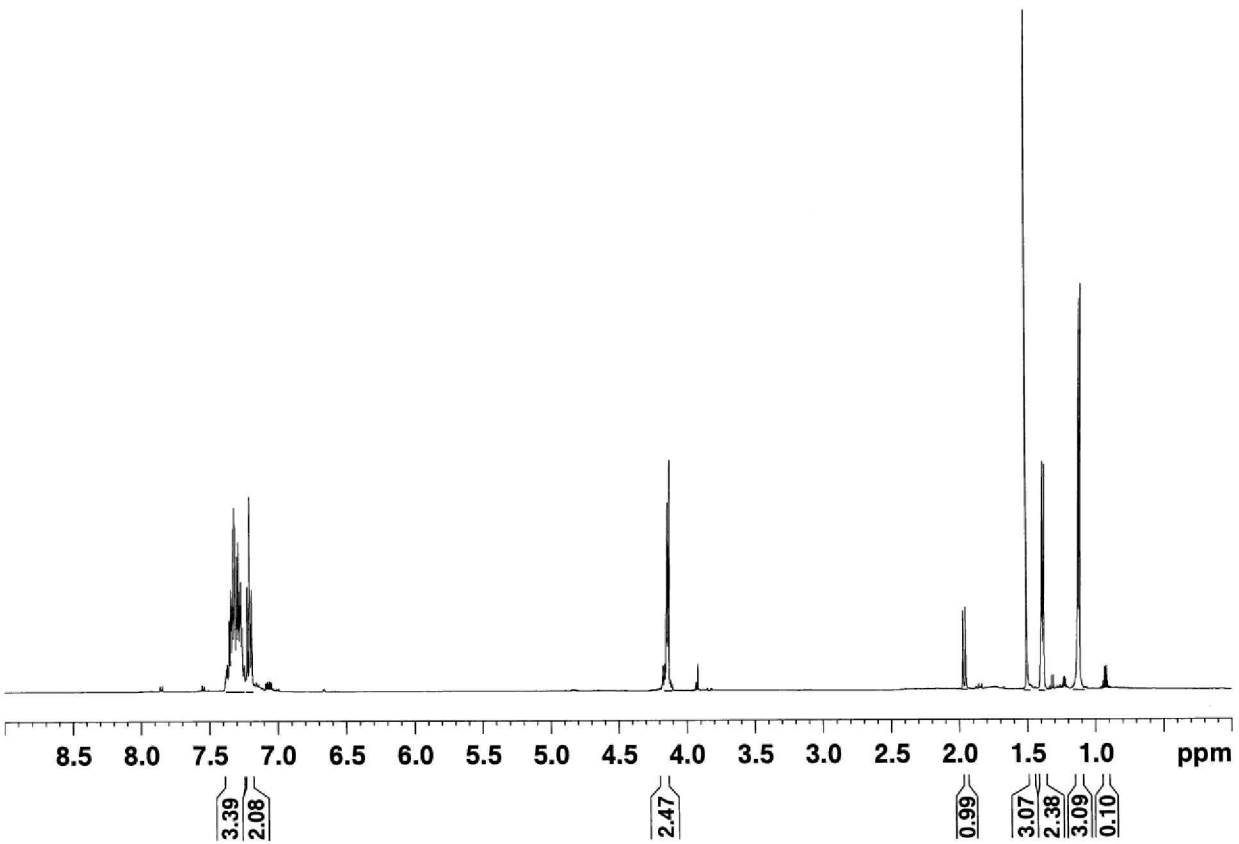
(+)-**368**



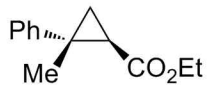
NAME	SS-06-130	
EXPNO	2	
PROCNO	1	
Date_	20130323	
Time	18.57	
INSTRUM	spect	
PROBHD	5 mm CPDCH 13C	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	20	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	use
DE	16.50	use
TE	298.1	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	9.00	use
PL1	4.50	dB
PL1W	38.14553833	W
SFO1	176.0697436	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	65.00	use
PL2	-3.20	dB
PL12	13.60	dB
PL13	120.00	dB
PL2W	33.59817505	W
PL12W	0.70196527	W
PL13W	0.00000000	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.00	



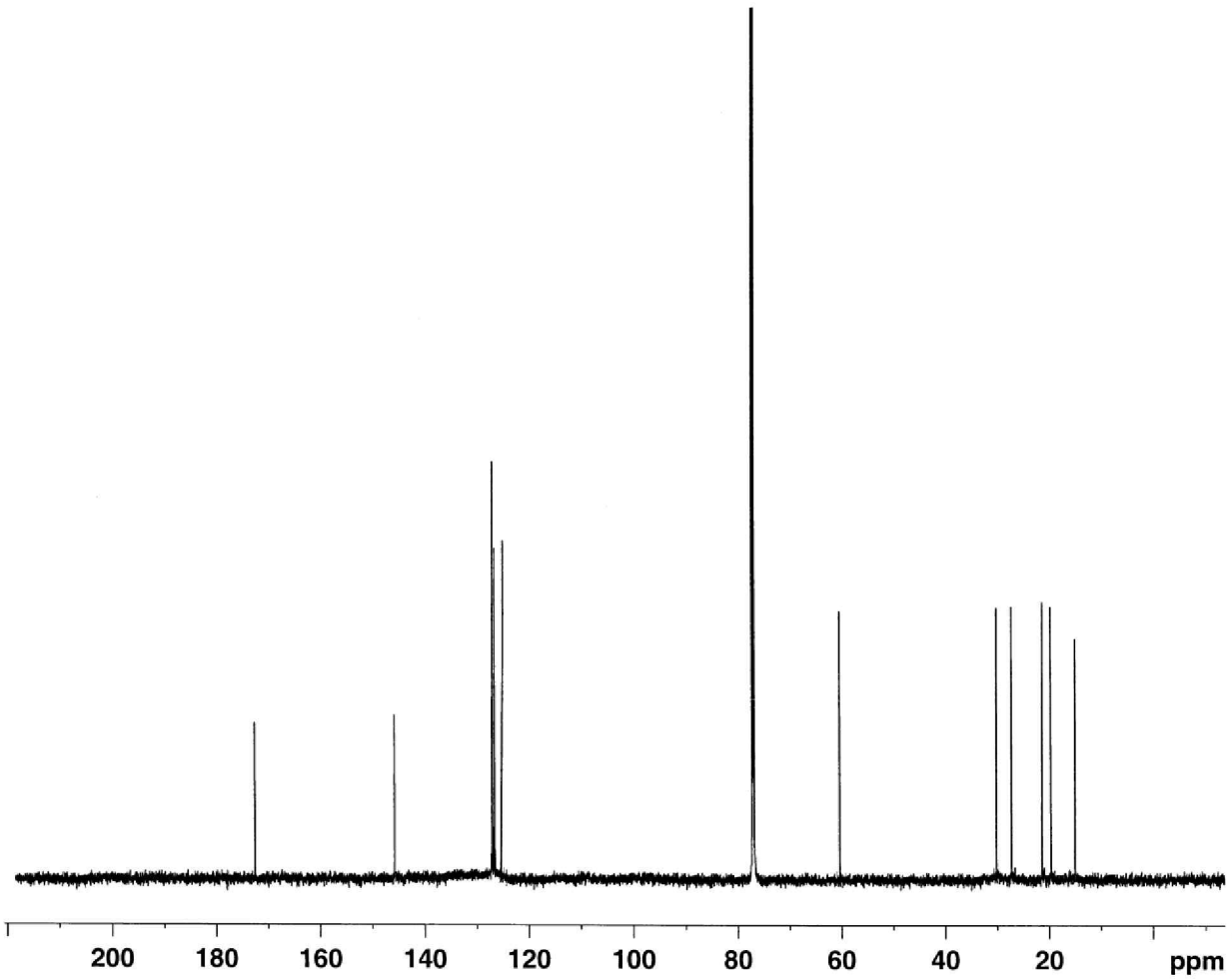
364



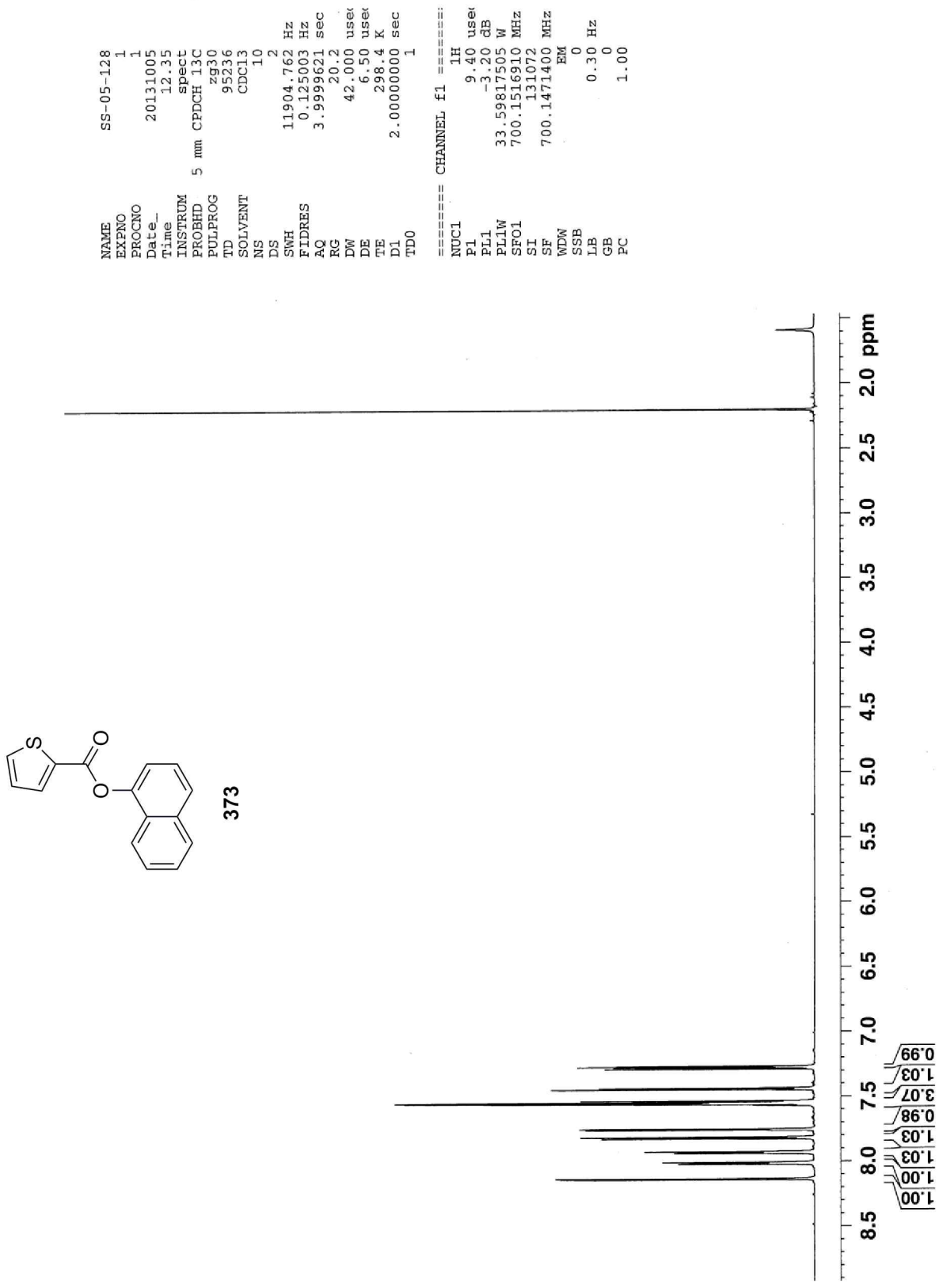

```
Current Data Parameters
NAME                  SS-6-137
EXPNO                        2
PROCNO                       1

F2 - Acquisition Parameters
Date_                 20130316
Time                     18.26
INSTRUM                  spect
PROBHD    5 mm PATXI 1H/
PULPROG                  zg30
TD                      65536
SOLVENT                 CDCl3
NS                         16
DS                          2
SWH                  8012.820 Hz
FIDRES               0.122266 Hz
AQ                   4.0894465 sec
RG                       46.39
DW                      62.400 use
DE                       6.50 use
TE                      297.9 K
D1                1.00000000 sec
TD0                          1

======== CHANNEL f1 =======
SFO1           500.1330008 MHz
NUC1                      1H
P1                      7.80 use
PLW1          12.00000000 W

F2 - Processing parameters
SI                      65536
SF             500.1300000 MHz
WDW                        EM
SSB       0
LB                      0.30 Hz
GB        0
PC                      1.00
```

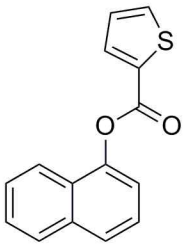


364

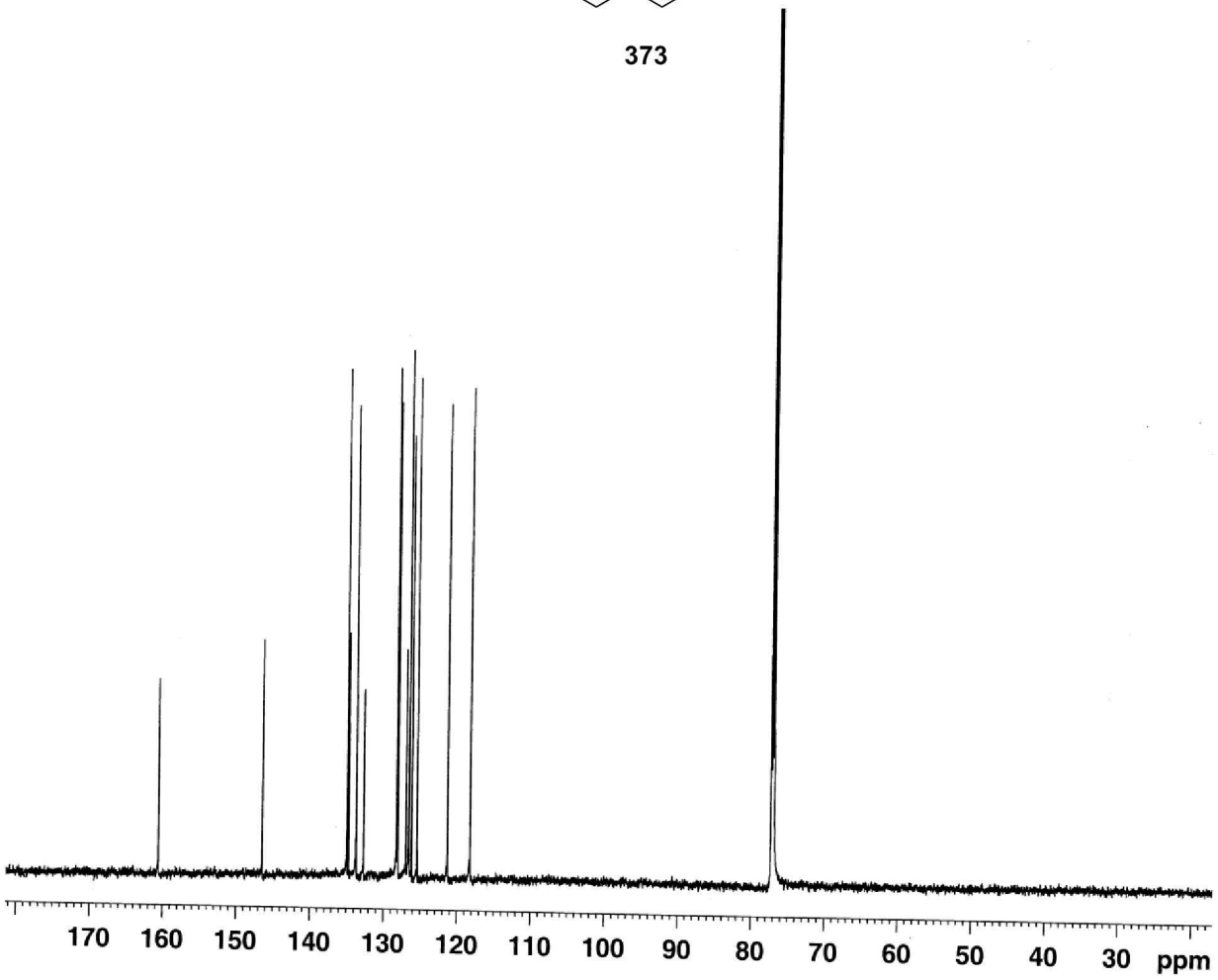


NAME	SS-06-137	
EXPNO	1	
PROCNO	1	
Date_	20130323	
Time	19.26	
INSTRUM	spect	
PROBHD	5 mm CPDCH 13C	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	20	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	use
DE	16.50	use
TE	298.2	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	9.00	use
PL1	4.50	dB
PL1W	38.14553833	W
SFO1	176.0697436	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	65.00	use
PL2	-3.20	dB
PL12	13.60	dB
PL13	120.00	dB
PL2W	33.59817505	W
PL12W	0.70196527	W
PL13W	0.00000000	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.00	

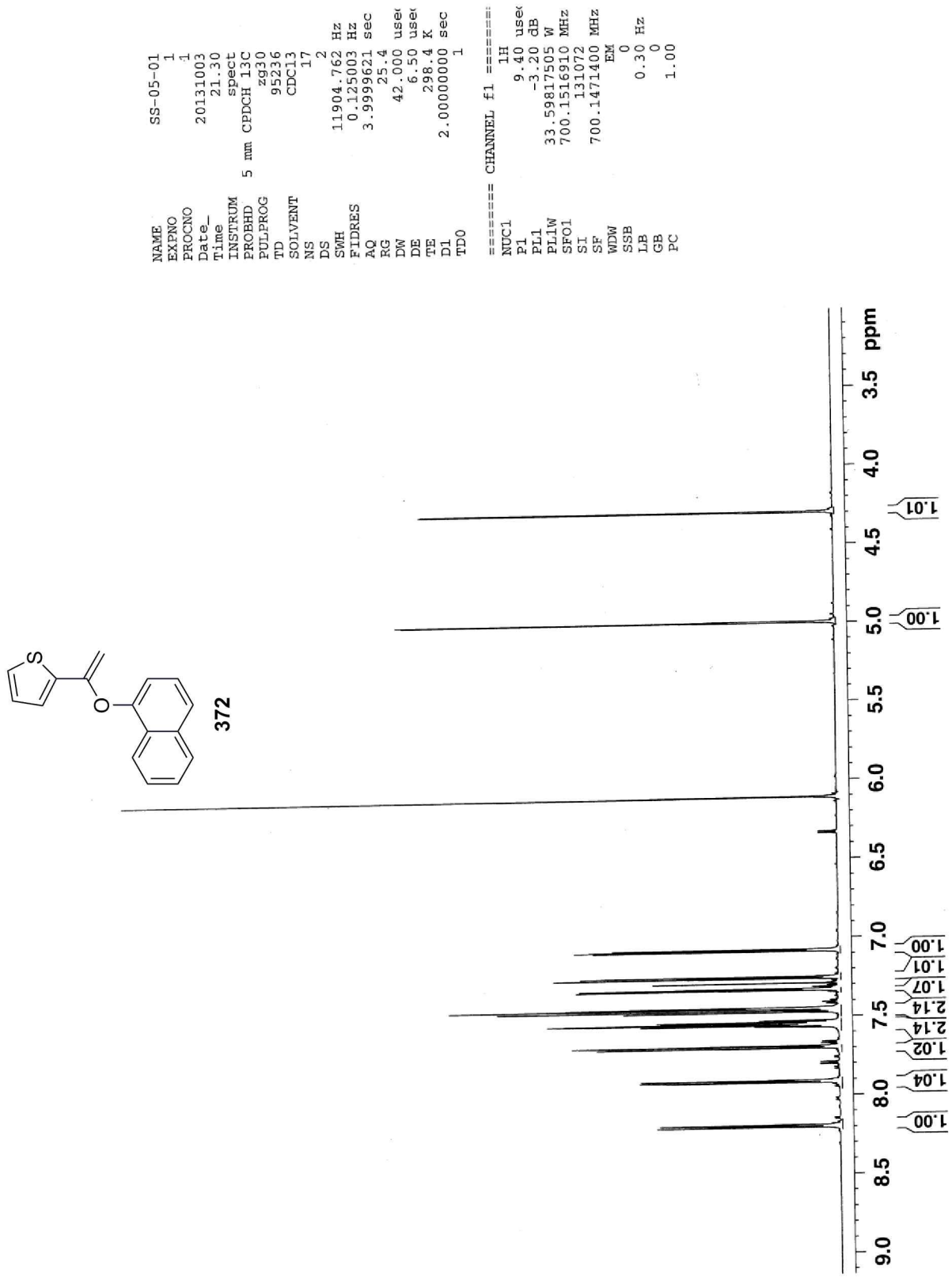

373
NAME SS-05-128
EXPNO 1
PROCNO 1
Date_ 20131005
Time 12.35
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDC13
NS 10
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 20.2
DW 42.000 use
DE 6.50 use
TE 298.4 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 use
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0 ppm
1.00
1.00
1.03
1.03
0.98
3.07
1.03
0.99

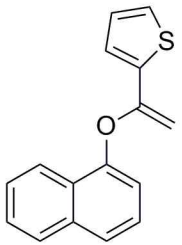


373

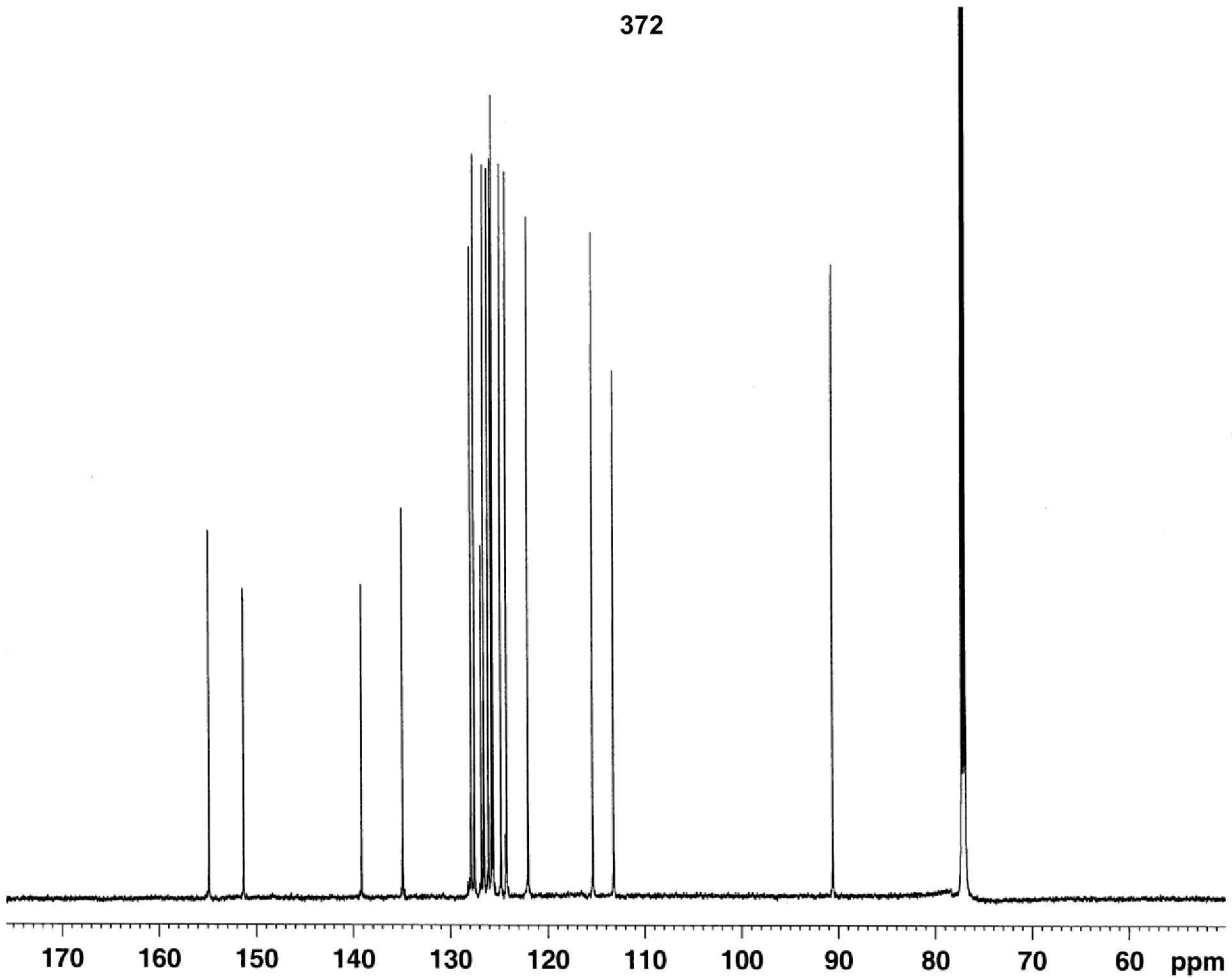


NAME	SS-05-128
EXPNO	2
PROCNO	1
Date_	20131005
Time	12.40
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	117
DS	4
SWH	41666.668 Hz
FIDRES	0.635783 Hz
AQ	0.7864820 sec
RG	203
DW	12.000 usec
DE	16.50 usec
TE	298.3 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 usec
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0697436 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 usec
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1499406 MHz
SI	32768
SF	176.0521380 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40

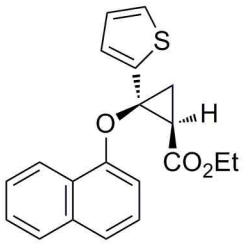

NAME SS-05-01
EXPNO 1
PROCNO 1
Date_ 20131003
Time 21.30
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 17
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 25.4
DW 42.000 use
DE 6.50 use
TE 298.4 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 use
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
372
S
O
ppm
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
1.00
1.04
1.02
2.14
2.14
1.07
1.01
1.00
1.00
1.01



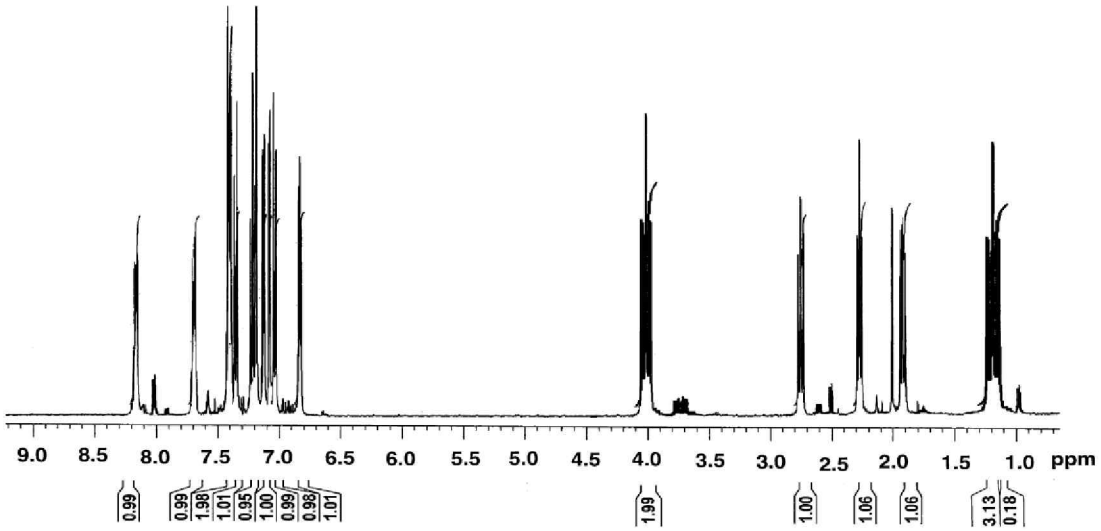
372



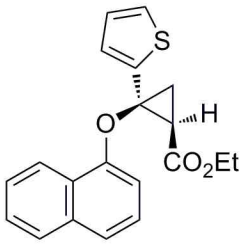
NAME	SS-05-01
EXPNO	2
PROCNO	1
Date_	20131003
Time	21.34
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	224
DS	4
SWH	41666.668 Hz
FIDRES	0.635783 Hz
AQ	0.7864820 sec
RG	203
DW	12.000 usec
DE	16.50 usec
TE	298.3 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 usec
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0697436 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 usec
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1499406 MHz
SI	32768
SF	176.0521380 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40



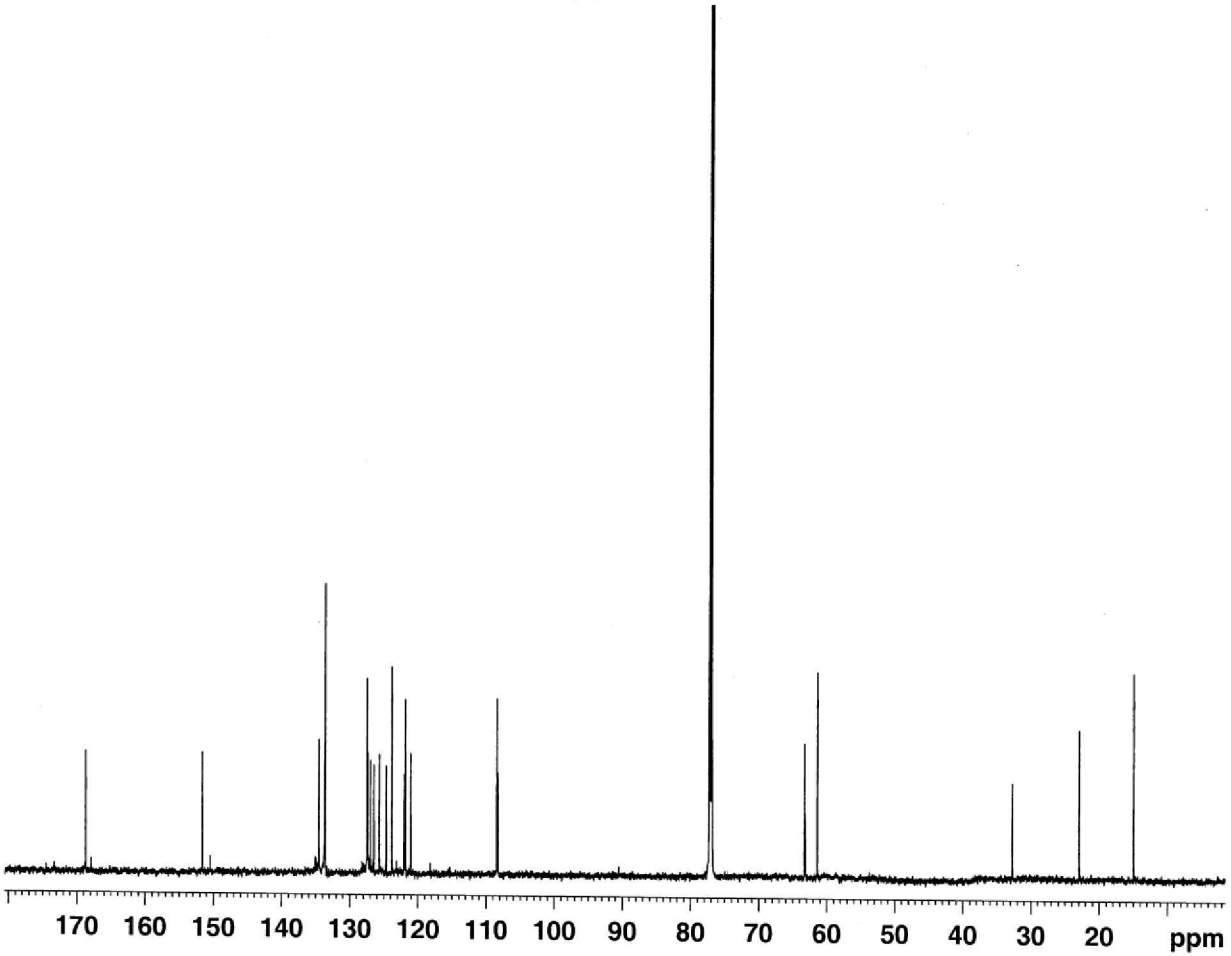
(+)-**371**



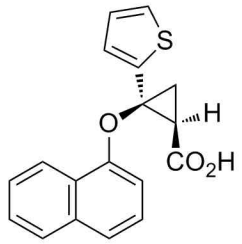
NAME	SS-05-130
EXPNO	1
PROCNO	1
Date_	20131005
Time	12.49
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zg30
TD	95236
SOLVENT	CDCl3
NS	32
DS	2
SWH	11904.762 Hz
FIDRES	0.125003 Hz
AQ	3.9999621 sec
RG	20.2
DW	42.000 use
DE	6.50 use
TE	298.2 K
D1	2.00000000 sec
TD0	1
========	CHANNEL f1 ========
NUC1	1H
P1	9.40 use
PL1	-3.20 dB
PL1W	33.59817505 W
SFO1	700.1516910 MHz
SI	131072
SF	700.1471400 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00



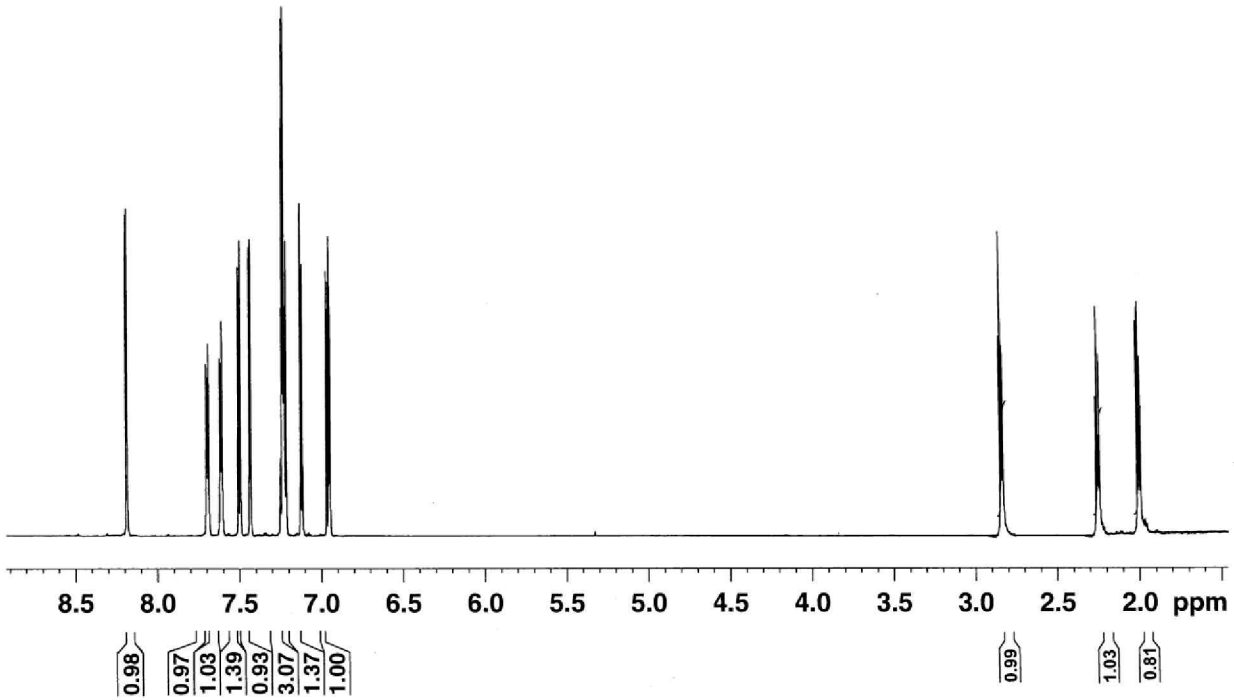
(+)-**371**



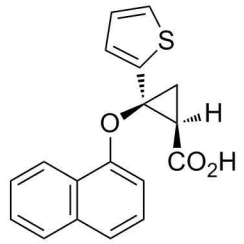
NAME	SS-05-130
EXPNO	2
PROCNO	1
Date_	20131005
Time	12.57
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	86
DS	4
SWH	41666.668 Hz
FIDRES	0.635783 Hz
AQ	0.7864820 sec
RG	203
DW	12.000 use
DE	16.50 use
TE	298.2 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 use
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0697436 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 use
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1499406 MHz
SI	32768
SF	176.0521380 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40



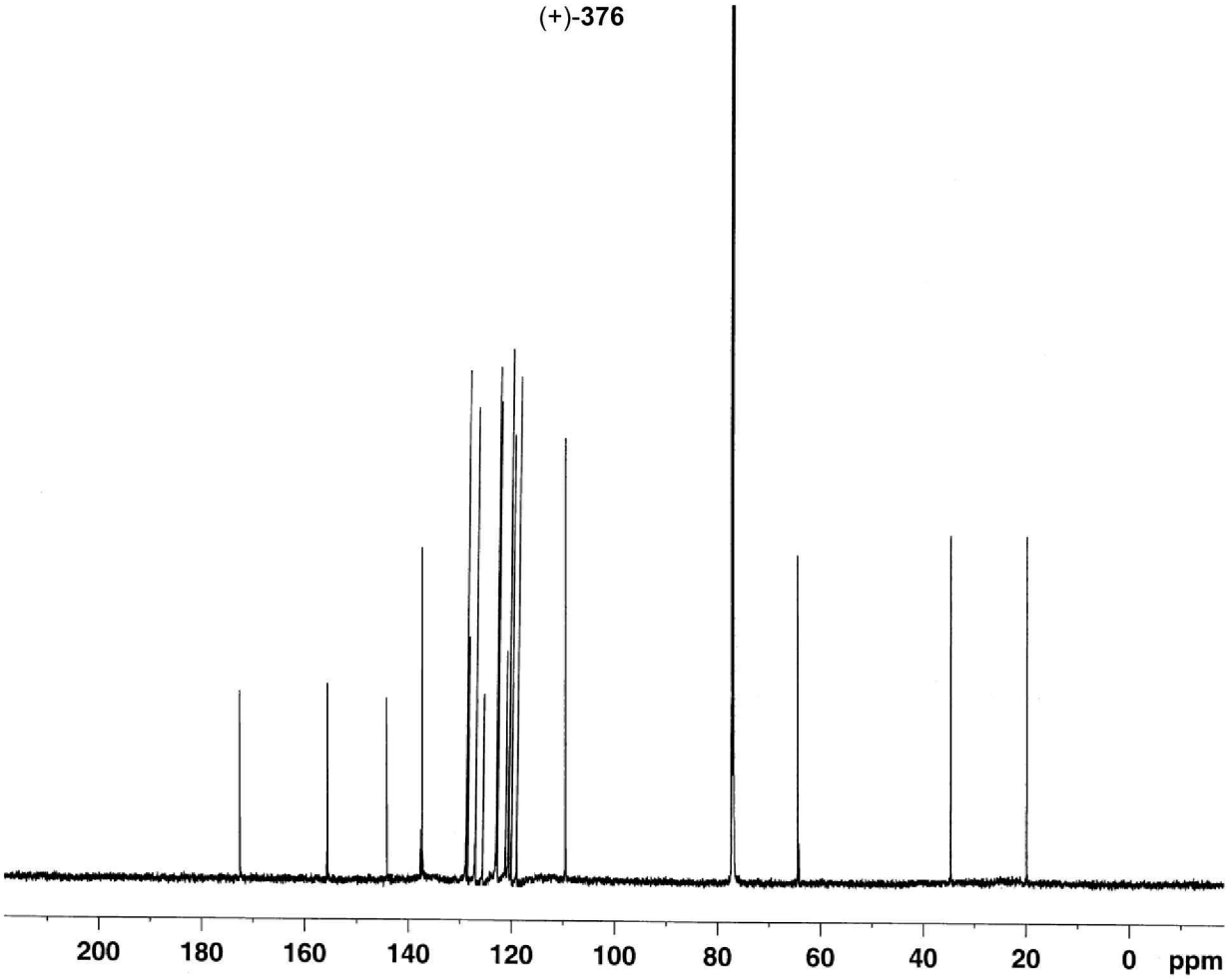
(+)-376




```
Current Data Parameters
NAME                  SS-6-116
EXPNO                        1
PROCNO                       1

F2 - Acquisition Parameters
Date_                 20130302
Time                     21.39
INSTRUM                  spect
PROBHD    5 mm PATXI 1H/
PULPROG                  zg30
TD                      65536
SOLVENT                 CDCl3
NS                         16
DS                          2
SWH                  8012.820 Hz
FIDRES               0.122266 Hz
AQ                   4.0894465 sec
RG                      131.79
DW                      62.400 usec
DE                       6.50 usec
TE                      298.0 K
D1                 1.00000000 sec
TD0                          1

======== CHANNEL f1 ========
SFO1               500.1330008 MHz
NUC1                        1H
P1                       7.80 usec
PLW1               12.00000000 W

F2 - Processing parameters
SI                          65536
SF                 500.1300000 MHz
WDW                           EM
SSB          0
LB                       0.30 Hz
GB           0
PC                       1.00
```



(+)-**376**



NAME	SS-06-116
EXPNO	2
PROCNO	1
Date_	20130323
Time	18.18
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	56
DS	4
SWH	41666.668 Hz
FIDRES	0.635783 Hz
AQ	0.7864820 sec
RG	203
DW	12.000 use
DE	16.50 use
TE	298.1 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 use
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0697436 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 use
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1499406 MHz
SI	32768
SF	176.0521380 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.00

Appendix II

X-Ray diffraction Data

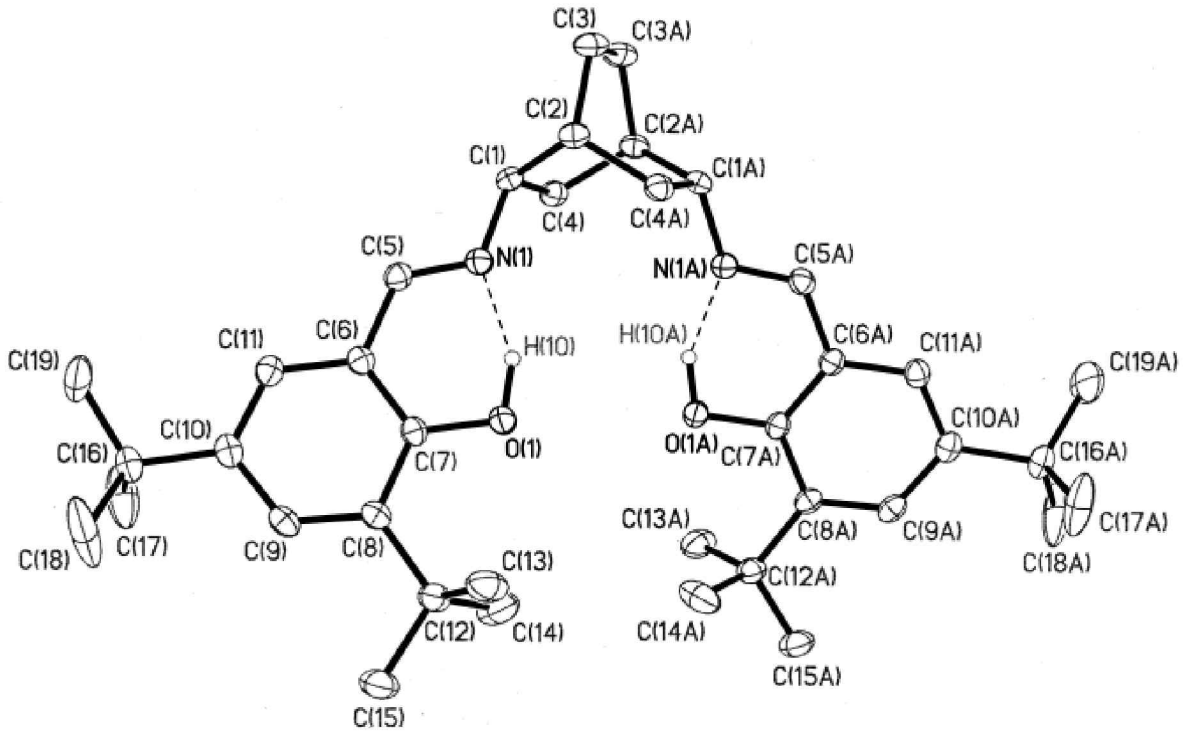


Figure 1: Crystal Structure of racemic salen ligand **(±)-35**

Table 1. Crystal data and structure refinement for **(±)-35**

Identification code	**35**	
Empirical formula	C38 H56 N2 O2	
Formula weight	572.85	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C2/c	
Unit cell dimensions	a = 29.745(4) Å	a= 90°.
	b = 12.5984(17) Å	b= 95.943(2)°.
	c = 9.5542(13) Å	g = 90°.
Volume	3561.1(8) $Å^3$	
Z	4	
Density (calculated)	1.068 Mg/m^3	
Absorption coefficient	0.065 mm^{-1}	
F(000)	1256	
Crystal size	0.38 x 0.12 x 0.07 mm^3	
Theta range for data collection	1.38 to 25.00°.	
Index ranges	-35<=h<=35, -14<=k<=14, -11<=l<=11	
Reflections collected	14624	
Independent reflections	3133 [R(int) = 0.0335]	
Completeness to theta = 25.00°	100.0 %	
Absorption correction	Semi-empirical from equivalents	

Max. and min. transmission	0.9955 and 0.9758
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3133 / 0 / 266
Goodness-of-fit on F^2	1.056
Final R indices [I>2sigma(I)]	R1 = 0.0634, wR2 = 0.1626
R indices (all data)	R1 = 0.0785, wR2 = 0.1759
Largest diff. peak and hole	0.459 and -0.345 e.$Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3)

for jw18. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	4285(1)	8583(1)	2218(2)	38(1)
N(1)	4367(1)	10514(1)	1389(2)	33(1)
C(1)	4589(1)	11552(2)	1436(2)	31(1)
C(2)	4598(1)	12053(2)	2902(2)	32(1)
C(3)	4768(1)	13193(2)	2797(3)	42(1)
C(4)	5079(1)	11429(2)	1059(2)	33(1)
C(5)	4057(1)	10320(2)	400(2)	32(1)
C(6)	3835(1)	9290(2)	222(2)	31(1)
C(7)	3963(1)	8438(2)	1124(2)	30(1)
C(8)	3760(1)	7436(2)	887(2)	31(1)
C(9)	3433(1)	7348(2)	-257(2)	34(1)
C(10)	3292(1)	8181(2)	-1170(2)	35(1)
C(11)	3501(1)	9147(2)	-909(2)	34(1)
C(12)	3899(1)	6484(2)	1845(3)	39(1)
C(13)	3800(1)	6738(2)	3353(3)	57(1)

C(14)	4401(1)	6238(3)	1798(5)	64(1)
C(15)	3632(1)	5480(2)	1416(4)	52(1)
C(16)	2937(1)	7999(2)	-2434(2)	41(1)
C(17)	3173(1)	7531(4)	-3615(3)	94(2)
C(18)	2572(1)	7255(4)	-2094(4)	115(2)
C(19)	2728(2)	9041(3)	-2976(5)	127(2)

—

Table 3. Bond lengths [Å] and angles [°] for jw18.

O(1)-C(7)	1.356(3)
O(1)-H(1O)	0.99(3)
N(1)-C(5)	1.273(3)
N(1)-C(1)	1.465(3)
C(1)-C(2)	1.534(3)
C(1)-C(4)	1.545(3)
C(1)-H(1)	0.98(2)
C(2)-C(4)#1	1.527(3)
C(2)-C(3)	1.530(3)
C(2)-H(2)	0.96(2)
C(3)-C(3)#1	1.544(5)
C(3)-H(3A)	1.02(3)
C(3)-H(3B)	0.98(3)
C(4)-C(2)#1	1.527(3)
C(4)-H(4A)	0.96(3)
C(4)-H(4B)	0.99(2)
C(5)-C(6)	1.457(3)
C(5)-H(5)	0.96(3)
C(6)-C(11)	1.403(3)
C(6)-C(7)	1.404(3)
C(7)-C(8)	1.407(3)

C(8)-C(9)	1.390(3)
C(8)-C(12)	1.539(3)
C(9)-C(10)	1.401(3)
C(9)-H(9)	0.95(2)
C(10)-C(11)	1.378(3)
C(10)-C(16)	1.535(3)
C(11)-H(11)	0.98(2)
C(12)-C(15)	1.527(3)
C(12)-C(14)	1.529(4)
C(12)-C(13)	1.534(4)
C(13)-H(13A)	1.01(5)
C(13)-H(13B)	0.97(4)
C(13)-H(13C)	0.97(4)
C(14)-H(14A)	0.98(4)
C(14)-H(14B)	1.01(4)
C(14)-H(14C)	1.01(4)
C(15)-H(15A)	0.98(3)
C(15)-H(15B)	0.99(3)
C(15)-H(15C)	0.99(3)
C(16)-C(18)	1.496(4)
C(16)-C(17)	1.508(4)
C(16)-C(19)	1.521(5)
C(17)-H(17A)	0.9800

C(17)-H(17B)	0.9800
C(17)-H(17C)	0.9800
C(18)-H(18A)	0.9800
C(18)-H(18C)	0.9800
C(18)-H(18B)	0.9800
C(19)-H(19A)	0.9800
C(19)-H(19B)	0.9800
C(19)-H(10C)	0.9800

C(7)-O(1)-H(1O)	105.1(18)
C(5)-N(1)-C(1)	118.92(19)
N(1)-C(1)-C(2)	111.15(18)
N(1)-C(1)-C(4)	109.62(18)
C(2)-C(1)-C(4)	109.06(18)
N(1)-C(1)-H(1)	108.2(14)
C(2)-C(1)-H(1)	110.1(13)
C(4)-C(1)-H(1)	108.7(13)
C(4)#1-C(2)-C(3)	109.6(2)
C(4)#1-C(2)-C(1)	109.42(18)
C(3)-C(2)-C(1)	107.51(19)
C(4)#1-C(2)-H(2)	111.5(14)
C(3)-C(2)-H(2)	109.9(14)
C(1)-C(2)-H(2)	108.8(14)

C(2)-C(3)-C(3)#1	109.78(13)
C(2)-C(3)-H(3A)	111.4(15)
C(3)#1-C(3)-H(3A)	109.1(15)
C(2)-C(3)-H(3B)	109.4(15)
C(3)#1-C(3)-H(3B)	108.6(16)
H(3A)-C(3)-H(3B)	108(2)
C(2)#1-C(4)-C(1)	110.00(18)
C(2)#1-C(4)-H(4A)	110.2(14)
C(1)-C(4)-H(4A)	110.2(14)
C(2)#1-C(4)-H(4B)	111.3(13)
C(1)-C(4)-H(4B)	107.2(13)
H(4A)-C(4)-H(4B)	107.8(19)
N(1)-C(5)-C(6)	122.8(2)
N(1)-C(5)-H(5)	122.5(14)
C(6)-C(5)-H(5)	114.7(14)
C(11)-C(6)-C(7)	119.9(2)
C(11)-C(6)-C(5)	118.7(2)
C(7)-C(6)-C(5)	121.26(19)
O(1)-C(7)-C(6)	119.63(19)
O(1)-C(7)-C(8)	120.12(19)
C(6)-C(7)-C(8)	120.2(2)
C(9)-C(8)-C(7)	116.8(2)
C(9)-C(8)-C(12)	121.9(2)

C(7)-C(8)-C(12)	121.3(2)
C(8)-C(9)-C(10)	124.8(2)
C(8)-C(9)-H(9)	114.2(14)
C(10)-C(9)-H(9)	121.0(14)
C(11)-C(10)-C(9)	116.6(2)
C(11)-C(10)-C(16)	122.3(2)
C(9)-C(10)-C(16)	121.0(2)
C(10)-C(11)-C(6)	121.6(2)
C(10)-C(11)-H(11)	122.3(14)
C(6)-C(11)-H(11)	116.1(14)
C(15)-C(12)-C(14)	107.8(2)
C(15)-C(12)-C(13)	106.2(2)
C(14)-C(12)-C(13)	110.7(3)
C(15)-C(12)-C(8)	112.6(2)
C(14)-C(12)-C(8)	110.1(2)
C(13)-C(12)-C(8)	109.3(2)
C(12)-C(13)-H(13A)	111(3)
C(12)-C(13)-H(13B)	108(2)
H(13A)-C(13)-H(13B)	112(3)
C(12)-C(13)-H(13C)	114(2)
H(13A)-C(13)-H(13C)	103(3)
H(13B)-C(13)-H(13C)	109(3)
C(12)-C(14)-H(14A)	109(2)

C(12)-C(14)-H(14B)	110(2)
H(14A)-C(14)-H(14B)	110(3)
C(12)-C(14)-H(14C)	110.0(19)
H(14A)-C(14)-H(14C)	112(3)
H(14B)-C(14)-H(14C)	105(3)
C(12)-C(15)-H(15A)	109.3(17)
C(12)-C(15)-H(15B)	109.5(17)
H(15A)-C(15)-H(15B)	108(2)
C(12)-C(15)-H(15C)	112.6(16)
H(15A)-C(15)-H(15C)	107(2)
H(15B)-C(15)-H(15C)	111(2)
C(18)-C(16)-C(17)	108.7(3)
C(18)-C(16)-C(19)	109.5(3)
C(17)-C(16)-C(19)	106.7(3)
C(18)-C(16)-C(10)	112.2(2)
C(17)-C(16)-C(10)	108.3(2)
C(19)-C(16)-C(10)	111.3(2)
C(16)-C(17)-H(17A)	109.5
C(16)-C(17)-H(17B)	109.5
H(17A)-C(17)-H(17B)	109.5
C(16)-C(17)-H(17C)	109.5
H(17A)-C(17)-H(17C)	109.5
H(17B)-C(17)-H(17C)	109.5

C(16)-C(18)-H(18A)	109.5
C(16)-C(18)-H(18C)	109.5
H(18A)-C(18)-H(18C)	109.5
C(16)-C(18)-H(18B)	109.5
H(18A)-C(18)-H(18B)	109.5
H(18C)-C(18)-H(18B)	109.5
C(16)-C(19)-H(19A)	109.5
C(16)-C(19)-H(19B)	109.5
H(19A)-C(19)-H(19B)	109.5
C(16)-C(19)-H(10C)	109.5
H(19A)-C(19)-H(10C)	109.5
H(19B)-C(19)-H(10C)	109.5

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,y,-z+1/2

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$)for jw18. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2 a^{*2} U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	46(1)	33(1)	33(1)	4(1)	-7(1)	-8(1)
N(1)	38(1)	29(1)	31(1)	1(1)	1(1)	-2(1)
C(1)	37(1)	24(1)	32(1)	6(1)	0(1)	0(1)
C(2)	34(1)	27(1)	36(1)	-1(1)	8(1)	3(1)
C(3)	52(2)	25(1)	49(2)	-4(1)	9(1)	6(1)
C(4)	44(1)	30(1)	27(1)	3(1)	6(1)	-1(1)
C(5)	37(1)	32(1)	26(1)	2(1)	4(1)	2(1)
C(6)	32(1)	33(1)	28(1)	-3(1)	5(1)	0(1)
C(7)	31(1)	35(1)	24(1)	-4(1)	4(1)	-1(1)
C(8)	33(1)	31(1)	29(1)	-6(1)	8(1)	-2(1)
C(9)	31(1)	37(1)	36(1)	-11(1)	9(1)	-5(1)
C(10)	29(1)	45(1)	31(1)	-8(1)	6(1)	1(1)
C(11)	34(1)	39(1)	30(1)	-2(1)	3(1)	5(1)
C(12)	45(1)	31(1)	40(1)	-1(1)	5(1)	-5(1)
C(13)	93(3)	39(2)	40(2)	4(1)	8(2)	-15(2)
C(14)	47(2)	45(2)	100(3)	24(2)	8(2)	6(1)
C(15)	68(2)	32(1)	56(2)	-5(1)	4(2)	-9(1)
C(16)	33(1)	53(2)	35(1)	-9(1)	-1(1)	-3(1)

C(17)	59(2)	180(4)	40(2)	-39(2)	-2(2)	1(2)
C(18)	81(3)	205(5)	54(2)	26(3)	-26(2)	-86(3)
C(19)	119(4)	86(3)	151(4)	-28(3)	-103(3)	31(3)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for jw18.

	x	y	z	U(eq)
H(17A)	3354	8080	-4016	140
H(17B)	2946	7259	-4347	140
H(17C)	3370	6949	-3251	140
H(18A)	2316	7664	-1810	173
H(18C)	2688	6785	-1323	173
H(18B)	2472	6829	-2926	173
H(19A)	2957	9603	-2871	190
H(19B)	2477	9226	-2434	190
H(10C)	2616	8965	-3972	190
H(1O)	4388(11)	9330(30)	2130(30)	72(10)
H(1)	4422(8)	12013(19)	730(20)	33(6)
H(2)	4298(8)	12055(18)	3180(20)	33(6)
H(3A)	4547(9)	13650(20)	2160(30)	50(7)
H(3B)	4805(9)	13510(20)	3740(30)	49(7)
H(4A)	5101(8)	11671(18)	120(30)	37(6)

H(4B)	5151(8)	10658(19)	1090(20)	32(6)
H(5)	3951(8)	10843(19)	-290(30)	34(6)
H(9)	3310(8)	6660(20)	-390(20)	33(6)
H(11)	3427(8)	9771(19)	-1500(20)	35(6)
H(13A)	3470(17)	6900(40)	3380(50)	126(17)
H(13B)	3901(12)	6140(30)	3940(40)	86(11)
H(13C)	3948(12)	7380(30)	3740(40)	83(11)
H(14A)	4488(11)	5660(30)	2460(40)	79(10)
H(14B)	4460(12)	6030(30)	820(40)	86(12)
H(14C)	4586(12)	6900(30)	2020(30)	79(10)
H(15A)	3690(9)	5280(20)	460(30)	55(8)
H(15B)	3737(10)	4890(20)	2060(30)	57(8)
H(15C)	3303(11)	5580(20)	1410(30)	57(8)

—

Table 6. Hydrogen bonds for jw18 [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1)-H(1O)...N(1)	0.99(3)	1.65(3)	2.577(2)	153(3)

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,y,-z+1/2

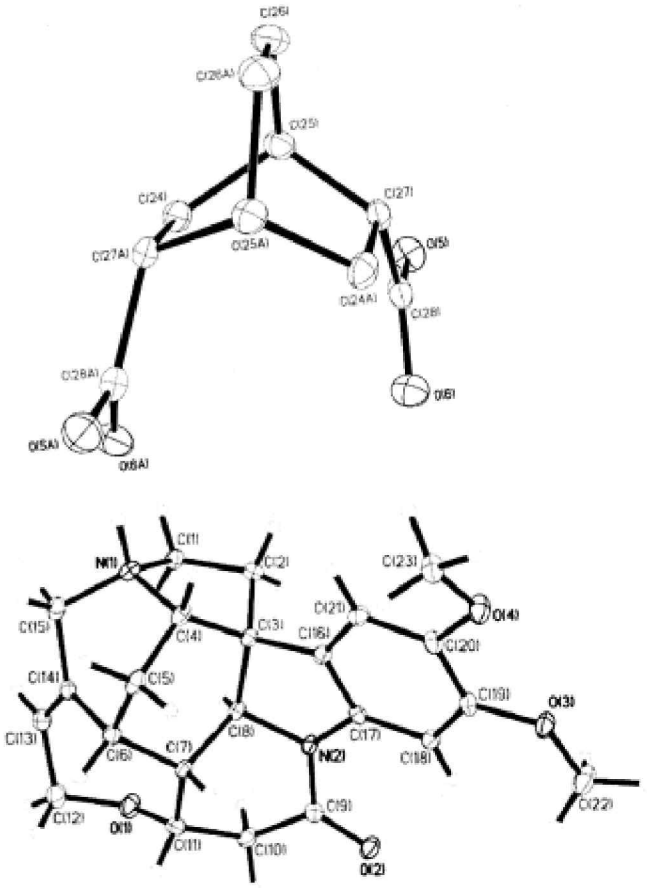


Figure 2: Crystal Structure of brucine salt of **(-)-64**

Table 1. Crystal data and structure refinement for brucine salt of **(-)-64**

Identification code	**64**	
Empirical formula	C56 H84 N4 O20	
Formula weight	1133.27	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2	
Unit cell dimensions	a = 32.487(3) Å	a= 90°.
	b = 7.6214(8) Å	b= 90°.
	c = 10.9285(11) Å	g = 90°.
Volume	2705.8(5) $Å^3$	
Z	2	
Density (calculated)	1.391 Mg/m^3	
Absorption coefficient	0.105 mm^{-1}	
F(000)	1216	
Crystal size	0.42 x 0.06 x 0.02 mm^3	
Theta range for data collection	1.25 to 26.99°.	
Index ranges	-41<=h<=41, -9<=k<=9, -13<=l<=13	
Reflections collected	30366	
Independent reflections	5893 [R(int) = 0.0868]	
Completeness to theta = 26.99°	100.0 %	
Absorption correction	Semi-empirical from equivalents	

Max. and min. transmission	0.9979 and 0.9571
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5893 / 0 / 526
Goodness-of-fit on F^2	1.078
Final R indices [I>2sigma(I)]	R1 = 0.0532, wR2 = 0.1053
R indices (all data)	R1 = 0.0849, wR2 = 0.1295
Absolute structure parameter	-0.4(13)
Largest diff. peak and hole	0.350 and -0.333 e.$Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for brucine salt of **6**. U (eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	6352(1)	10432(3)	5620(2)	33(1)
O(2)	7740(1)	9635(3)	4535(2)	29(1)
O(3)	8292(1)	8109(3)	374(2)	27(1)
O(4)	7735(1)	7568(3)	-1260(2)	29(1)
O(5)	4355(1)	1818(3)	8986(2)	33(1)
O(6)	4428(1)	4316(3)	9998(2)	33(1)
N(1)	5921(1)	7371(4)	1858(2)	21(1)
N(2)	7195(1)	8472(3)	3500(2)	18(1)
C(1)	6070(1)	5893(4)	2658(3)	23(1)
C(2)	6519(1)	5667(4)	2307(3)	24(1)
C(3)	6664(1)	7563(4)	2105(3)	19(1)
C(4)	6303(1)	8337(4)	1373(3)	23(1)
C(5)	6245(1)	10292(4)	1475(3)	24(1)
C(6)	6195(1)	10773(4)	2827(3)	24(1)
C(7)	6609(1)	10410(4)	3462(3)	20(1)
C(8)	6739(1)	8492(4)	3354(3)	18(1)
C(9)	7364(1)	9423(4)	4424(3)	22(1)

C(10)	7062(1)	10152(5)	5331(3)	26(1)
C(11)	6668(1)	10979(4)	4787(3)	25(1)
C(12)	5945(1)	11114(6)	5392(4)	40(1)
C(13)	5716(1)	9964(5)	4513(3)	30(1)
C(14)	5834(1)	9760(4)	3363(3)	24(1)
C(15)	5619(1)	8552(5)	2496(3)	25(1)
C(16)	7079(1)	7727(4)	1496(3)	19(1)
C(17)	7380(1)	8125(4)	2342(3)	19(1)
C(18)	7797(1)	8223(4)	2032(3)	20(1)
C(19)	7896(1)	7991(4)	816(3)	23(1)
C(20)	7594(1)	7677(4)	-73(3)	21(1)
C(21)	7186(1)	7502(4)	263(3)	23(1)
C(22)	8617(1)	8270(7)	1251(4)	39(1)
C(23)	7442(1)	8008(5)	-2183(3)	27(1)
C(24)	5319(1)	3710(4)	7927(3)	26(1)
C(25)	4922(1)	3335(5)	7210(3)	26(1)
C(26)	4967(1)	3988(5)	5885(3)	33(1)
C(27)	4567(1)	4326(4)	7826(3)	23(1)
C(28)	4446(1)	3433(5)	9024(3)	28(1)
O(1S)	6410(1)	5539(4)	5719(3)	46(1)
O(2S)	5000	0	10064(3)	33(1)
O(3S)	4623(1)	7224(4)	1376(3)	47(1)
O(4S)	6377(1)	8171(4)	7666(3)	50(1)

O(5S)	5000	5000	3016(4)	85(2)

Table 3. Bond lengths [Å] and angles [°] for brucine salt of **64**.

O(1)-C(11)	1.435(4)
O(1)-C(12)	1.442(4)
O(2)-C(9)	1.237(3)
O(3)-C(19)	1.376(4)
O(3)-C(22)	1.431(4)
O(4)-C(20)	1.378(4)
O(4)-C(23)	1.426(4)
O(5)-C(28)	1.266(4)
O(6)-C(28)	1.260(4)
N(1)-C(15)	1.503(4)
N(1)-C(1)	1.506(4)
N(1)-C(4)	1.537(4)
N(1)-H(1N)	0.98(4)
N(2)-C(9)	1.359(4)
N(2)-C(17)	1.426(4)
N(2)-C(8)	1.488(4)
C(1)-C(2)	1.519(4)
C(1)-H(1A)	1.03(3)
C(1)-H(1B)	0.99(4)
C(2)-C(3)	1.535(4)
C(2)-H(2B)	0.94(3)

C(2)-H(12A)	0.97(3)
C(3)-C(16)	1.509(4)
C(3)-C(4)	1.537(4)
C(3)-C(8)	1.557(4)
C(4)-C(5)	1.506(5)
C(4)-H(4)	0.99(3)
C(5)-C(6)	1.531(5)
C(5)-H(5A)	1.02(3)
C(5)-H(5B)	0.96(3)
C(6)-C(14)	1.521(4)
C(6)-C(7)	1.540(4)
C(6)-H(6)	0.95(3)
C(7)-C(11)	1.524(4)
C(7)-C(8)	1.526(4)
C(7)-H(7)	0.90(3)
C(8)-H(8)	0.98(3)
C(9)-C(10)	1.502(4)
C(10)-C(11)	1.545(5)
C(10)-H(10A)	0.93(3)
C(10)-H(10B)	1.01(4)
C(11)-H(11)	0.98(4)
C(12)-C(13)	1.499(5)
C(12)-H(12A)	1.02(4)

C(12)-H(12B)	1.06(4)
C(13)-C(14)	1.323(4)
C(13)-H(13)	0.96(3)
C(14)-C(15)	1.495(5)
C(15)-H(15A)	0.88(3)
C(15)-H(15B)	0.97(4)
C(16)-C(17)	1.379(4)
C(16)-C(21)	1.402(4)
C(17)-C(18)	1.399(4)
C(18)-C(19)	1.379(4)
C(18)-H(18)	0.97(3)
C(19)-C(20)	1.402(4)
C(20)-C(21)	1.382(4)
C(21)-H(21)	0.97(3)
C(22)-H(22A)	0.95(4)
C(22)-H(22B)	1.09(4)
C(22)-H(22C)	1.02(4)
C(23)-H(23A)	0.95(4)
C(23)-H(23B)	1.02(3)
C(23)-H(23C)	1.03(3)
C(24)-C(25)	1.535(4)
C(24)-C(27)#1	1.546(5)
C(24)-H(24A)	1.02(3)

C(24)-H(24B)	1.04(4)
C(25)-C(27)	1.535(4)
C(25)-C(26)	1.537(5)
C(25)-H(25)	1.01(3)
C(26)-C(26)#1	1.557(7)
C(26)-H(26A)	0.99(3)
C(26)-H(26B)	1.03(4)
C(27)-C(28)	1.528(5)
C(27)-C(24)#1	1.546(5)
C(27)-H(27)	0.92(3)
O(1S)-H(1SA)	1.09(5)
O(1S)-H(1SB)	0.78(5)
O(2S)-H(2SA)	0.83(3)
O(3S)-H(3SA)	1.02(5)
O(3S)-H(3SB)	0.97(7)
O(3S)-H(3SC)	1.12(7)
O(4S)-H(4SA)	1.01(6)
O(4S)-H(4SB)	0.88(5)

C(11)-O(1)-C(12)	116.2(3)
C(19)-O(3)-C(22)	117.4(3)
C(20)-O(4)-C(23)	115.5(2)
C(15)-N(1)-C(1)	112.9(2)

C(15)-N(1)-C(4)	113.6(3)
C(1)-N(1)-C(4)	107.4(2)
C(15)-N(1)-H(1N)	107(2)
C(1)-N(1)-H(1N)	111(2)
C(4)-N(1)-H(1N)	105(2)
C(9)-N(2)-C(17)	126.0(2)
C(9)-N(2)-C(8)	118.5(2)
C(17)-N(2)-C(8)	109.0(2)
N(1)-C(1)-C(2)	104.3(2)
N(1)-C(1)-H(1A)	108.1(18)
C(2)-C(1)-H(1A)	115.5(17)
N(1)-C(1)-H(1B)	104(2)
C(2)-C(1)-H(1B)	118(2)
H(1A)-C(1)-H(1B)	106(3)
C(1)-C(2)-C(3)	102.9(3)
C(1)-C(2)-H(2B)	114.5(18)
C(3)-C(2)-H(2B)	108.9(19)
C(1)-C(2)-H(12A)	110.2(17)
C(3)-C(2)-H(12A)	110.8(18)
H(2B)-C(2)-H(12A)	109(3)
C(16)-C(3)-C(2)	114.4(2)
C(16)-C(3)-C(4)	114.9(2)
C(2)-C(3)-C(4)	101.7(2)

C(16)-C(3)-C(8)	102.0(2)
C(2)-C(3)-C(8)	110.5(3)
C(4)-C(3)-C(8)	113.8(3)
C(5)-C(4)-C(3)	115.8(3)
C(5)-C(4)-N(1)	110.4(3)
C(3)-C(4)-N(1)	104.6(2)
C(5)-C(4)-H(4)	107.1(15)
C(3)-C(4)-H(4)	113.5(15)
N(1)-C(4)-H(4)	104.9(15)
C(4)-C(5)-C(6)	108.8(3)
C(4)-C(5)-H(5A)	110.9(18)
C(6)-C(5)-H(5A)	109.7(19)
C(4)-C(5)-H(5B)	108.0(17)
C(6)-C(5)-H(5B)	110.4(18)
H(5A)-C(5)-H(5B)	109(2)
C(14)-C(6)-C(5)	109.5(3)
C(14)-C(6)-C(7)	114.1(3)
C(5)-C(6)-C(7)	107.3(3)
C(14)-C(6)-H(6)	108.3(19)
C(5)-C(6)-H(6)	110.1(19)
C(7)-C(6)-H(6)	107.5(19)
C(11)-C(7)-C(8)	108.1(3)
C(11)-C(7)-C(6)	119.2(3)

C(8)-C(7)-C(6)	112.3(3)
C(11)-C(7)-H(7)	104(2)
C(8)-C(7)-H(7)	107(2)
C(6)-C(7)-H(7)	105.5(19)
N(2)-C(8)-C(7)	106.1(2)
N(2)-C(8)-C(3)	104.3(2)
C(7)-C(8)-C(3)	117.3(3)
N(2)-C(8)-H(8)	107.7(16)
C(7)-C(8)-H(8)	110.9(16)
C(3)-C(8)-H(8)	109.9(16)
O(2)-C(9)-N(2)	122.8(3)
O(2)-C(9)-C(10)	122.1(3)
N(2)-C(9)-C(10)	115.0(3)
C(9)-C(10)-C(11)	115.9(3)
C(9)-C(10)-H(10A)	104(2)
C(11)-C(10)-H(10A)	101(2)
C(9)-C(10)-H(10B)	109(2)
C(11)-C(10)-H(10B)	110(2)
H(10A)-C(10)-H(10B)	117(3)
O(1)-C(11)-C(7)	115.5(3)
O(1)-C(11)-C(10)	103.3(3)
C(7)-C(11)-C(10)	110.7(3)
O(1)-C(11)-H(11)	109(2)

C(7)-C(11)-H(11)	106(2)
C(10)-C(11)-H(11)	113(2)
O(1)-C(12)-C(13)	110.9(3)
O(1)-C(12)-H(12A)	110(2)
C(13)-C(12)-H(12A)	110(2)
O(1)-C(12)-H(12B)	106.1(19)
C(13)-C(12)-H(12B)	109.4(19)
H(12A)-C(12)-H(12B)	110(3)
C(14)-C(13)-C(12)	122.2(3)
C(14)-C(13)-H(13)	121(2)
C(12)-C(13)-H(13)	117(2)
C(13)-C(14)-C(15)	122.6(3)
C(13)-C(14)-C(6)	122.0(3)
C(15)-C(14)-C(6)	115.4(3)
C(14)-C(15)-N(1)	110.9(3)
C(14)-C(15)-H(15A)	110.9(19)
N(1)-C(15)-H(15A)	106.1(19)
C(14)-C(15)-H(15B)	111(2)
N(1)-C(15)-H(15B)	105(2)
H(15A)-C(15)-H(15B)	113(3)
C(17)-C(16)-C(21)	119.7(3)
C(17)-C(16)-C(3)	110.9(3)
C(21)-C(16)-C(3)	129.4(3)

C(16)-C(17)-C(18)	122.4(3)
C(16)-C(17)-N(2)	109.7(2)
C(18)-C(17)-N(2)	127.8(3)
C(19)-C(18)-C(17)	116.9(3)
C(19)-C(18)-H(18)	124.7(19)
C(17)-C(18)-H(18)	118.3(19)
O(3)-C(19)-C(18)	123.2(3)
O(3)-C(19)-C(20)	115.0(3)
C(18)-C(19)-C(20)	121.7(3)
O(4)-C(20)-C(21)	124.2(3)
O(4)-C(20)-C(19)	115.5(3)
C(21)-C(20)-C(19)	120.3(3)
C(20)-C(21)-C(16)	118.8(3)
C(20)-C(21)-H(21)	119.7(18)
C(16)-C(21)-H(21)	121.6(18)
O(3)-C(22)-H(22A)	107(2)
O(3)-C(22)-H(22B)	104(2)
H(22A)-C(22)-H(22B)	115(3)
O(3)-C(22)-H(22C)	111(2)
H(22A)-C(22)-H(22C)	111(3)
H(22B)-C(22)-H(22C)	110(3)
O(4)-C(23)-H(23A)	114(2)
O(4)-C(23)-H(23B)	107.2(17)

H(23A)-C(23)-H(23B)	112(3)
O(4)-C(23)-H(23C)	108.6(18)
H(23A)-C(23)-H(23C)	106(3)
H(23B)-C(23)-H(23C)	109(2)
C(25)-C(24)-C(27)#1	110.2(3)
C(25)-C(24)-H(24A)	112.1(17)
C(27)#1-C(24)-H(24A)	110.7(17)
C(25)-C(24)-H(24B)	108(2)
C(27)#1-C(24)-H(24B)	112(2)
H(24A)-C(24)-H(24B)	104(3)
C(27)-C(25)-C(24)	108.4(3)
C(27)-C(25)-C(26)	108.9(3)
C(24)-C(25)-C(26)	110.0(3)
C(27)-C(25)-H(25)	106.7(16)
C(24)-C(25)-H(25)	111.1(17)
C(26)-C(25)-H(25)	111.6(17)
C(25)-C(26)-C(26)#1	109.49(18)
C(25)-C(26)-H(26A)	108.5(19)
C(26)#1-C(26)-H(26A)	110(2)
C(25)-C(26)-H(26B)	111(2)
C(26)#1-C(26)-H(26B)	112(3)
H(26A)-C(26)-H(26B)	106(3)
C(28)-C(27)-C(25)	110.5(3)

C(28)-C(27)-C(24)#1	115.6(3)
C(25)-C(27)-C(24)#1	109.1(3)
C(28)-C(27)-H(27)	108(2)
C(25)-C(27)-H(27)	103(2)
C(24)#1-C(27)-H(27)	110(2)
O(6)-C(28)-O(5)	122.5(3)
O(6)-C(28)-C(27)	119.8(3)
O(5)-C(28)-C(27)	117.7(3)
H(1SA)-O(1S)-H(1SB)	102(5)
H(3SA)-O(3S)-H(3SB)	111(4)
H(3SA)-O(3S)-H(3SC)	109(4)
H(3SB)-O(3S)-H(3SC)	93(5)
H(4SA)-O(4S)-H(4SB)	106(4)

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,-y+1,z

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for brucine salt of **6**. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2 a^{*2} U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	21(1)	50(2)	27(1)	-8(1)	5(1)	0(1)
O(2)	18(1)	41(1)	26(1)	-6(1)	-2(1)	-2(1)
O(3)	16(1)	41(1)	23(1)	-3(1)	3(1)	-1(1)
O(4)	22(1)	47(1)	18(1)	-2(1)	1(1)	6(1)
O(5)	33(1)	28(1)	37(1)	4(1)	-2(1)	-5(1)
O(6)	39(1)	34(1)	26(1)	2(1)	4(1)	-9(1)
N(1)	18(1)	24(1)	21(1)	1(1)	-3(1)	-5(1)
N(2)	13(1)	26(1)	16(1)	-1(1)	-1(1)	1(1)
C(1)	20(2)	20(2)	28(2)	5(1)	1(1)	-3(1)
C(2)	24(2)	22(2)	25(2)	-3(2)	0(2)	0(1)
C(3)	17(1)	22(2)	18(2)	1(1)	-2(1)	-1(1)
C(4)	18(2)	33(2)	18(2)	4(2)	0(1)	-5(1)
C(5)	16(2)	28(2)	27(2)	12(2)	-2(1)	-3(1)
C(6)	19(2)	20(2)	34(2)	4(2)	-2(1)	0(1)
C(7)	14(2)	20(2)	26(2)	1(1)	1(1)	-1(1)
C(8)	14(2)	22(2)	19(2)	5(1)	0(1)	-2(1)
C(9)	23(2)	24(2)	17(2)	2(1)	0(1)	1(1)
C(10)	23(2)	32(2)	23(2)	-4(2)	-1(1)	-4(2)

C(11)	24(2)	22(2)	28(2)	-5(1)	3(1)	-1(1)
C(12)	26(2)	51(3)	43(2)	-17(2)	3(2)	5(2)
C(13)	21(2)	33(2)	36(2)	-7(2)	4(2)	0(2)
C(14)	17(2)	20(2)	35(2)	0(2)	-2(1)	3(1)
C(15)	19(2)	26(2)	30(2)	4(2)	3(2)	-1(1)
C(16)	17(2)	21(2)	20(2)	0(1)	-1(1)	2(1)
C(17)	23(2)	21(2)	14(2)	-1(1)	2(1)	3(1)
C(18)	19(2)	21(2)	22(2)	-1(1)	-2(1)	0(1)
C(19)	20(2)	24(2)	24(2)	1(1)	4(1)	4(1)
C(20)	22(2)	27(2)	14(1)	0(1)	2(1)	4(1)
C(21)	22(2)	29(2)	19(2)	-3(1)	-4(1)	-1(1)
C(22)	21(2)	63(3)	32(2)	-1(2)	-4(2)	-1(2)
C(23)	26(2)	36(2)	17(2)	2(2)	-1(1)	8(2)
C(24)	23(2)	28(2)	28(2)	-4(2)	-2(2)	9(1)
C(25)	27(2)	26(2)	24(2)	-3(2)	-2(1)	-3(2)
C(26)	35(2)	40(2)	23(2)	-5(2)	-2(2)	-5(2)
C(27)	15(2)	33(2)	22(2)	2(2)	-3(1)	1(1)
C(28)	17(2)	36(2)	30(2)	4(2)	-4(1)	-1(2)
O(1S)	32(2)	50(2)	56(2)	-1(2)	1(1)	3(1)
O(2S)	35(2)	29(2)	35(2)	0	0	7(2)
O(3S)	49(2)	37(2)	54(2)	-4(2)	18(2)	-2(2)
O(4S)	38(2)	55(2)	58(2)	9(2)	15(2)	-1(1)
O(5S)	91(4)	92(4)	71(3)	0	0	-25(3)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for brucine salt of **6**.

	x	y	z	U(eq)
H(1N)	5781(10)	6920(50)	1130(30)	38(10)
H(1A)	6017(9)	6230(40)	3550(30)	24(9)
H(1B)	5878(11)	4920(50)	2470(30)	39(10)
H(2B)	6684(9)	5150(40)	2920(30)	15(8)
H(4)	6313(8)	8050(30)	490(30)	3(7)
H(5A)	5992(10)	10690(40)	1000(30)	31(9)
H(5B)	6484(9)	10850(40)	1140(30)	14(8)
H(6)	6139(9)	12000(40)	2910(30)	23(9)
H(7)	6796(9)	11040(40)	3040(30)	19(8)
H(8)	6621(8)	7790(40)	4020(30)	10(7)
H(10A)	6954(10)	9160(50)	5720(30)	32(10)
H(10B)	7209(10)	11020(50)	5870(30)	37(10)
H(11)	6678(10)	12260(50)	4770(30)	33(9)
H(12A)	6542(9)	4990(40)	1560(30)	18(8)
H(12A)	5964(10)	12370(50)	5060(30)	38(10)
H(12B)	5792(10)	11120(50)	6250(30)	38(10)
H(13)	5489(10)	9300(40)	4840(30)	29(9)

H(15A)	5449(9)	7860(40)	2890(30)	14(8)
H(15B)	5488(11)	9210(50)	1840(30)	45(11)
H(18)	7995(9)	8460(40)	2680(30)	28(9)
H(21)	6980(9)	7240(40)	-360(30)	20(8)
H(22A)	8571(11)	9340(50)	1670(30)	41(11)
H(22B)	8897(12)	8230(50)	700(40)	60(12)
H(22C)	8613(11)	7240(50)	1840(30)	37(10)
H(23A)	7286(11)	9020(50)	-2000(30)	33(10)
H(23B)	7599(9)	8130(40)	-2980(30)	25(8)
H(23C)	7232(9)	6990(40)	-2260(30)	24(9)
H(24A)	5558(9)	2940(40)	7640(30)	25(9)
H(24B)	5272(10)	3340(50)	8830(40)	42(10)
H(25)	4849(8)	2050(40)	7240(30)	17(8)
H(26A)	5208(10)	3400(50)	5510(30)	27(9)
H(26B)	4715(13)	3630(60)	5370(40)	68(14)
H(27)	4353(10)	4190(40)	7290(30)	24(9)
H(1SA)	6358(14)	6610(70)	6360(40)	83(16)
H(1SB)	6647(16)	5380(70)	5780(50)	77(18)
H(2SA)	4823(11)	460(50)	9620(30)	46(12)
H(3SA)	4783(13)	8230(60)	990(40)	22(13)
H(3SB)	4802(18)	6470(100)	1860(60)	60(20)
H(3SC)	4570(18)	6200(80)	660(60)	56(18)
H(4SA)	6124(18)	8380(80)	8180(50)	110(20)

H(4SB)	6388(14)	9040(70)	7130(50)	69(16)

Table 6. Torsion angles [°] for brucine salt of **6**.

C(15)-N(1)-C(1)-C(2)	-143.4(3)
C(4)-N(1)-C(1)-C(2)	-17.4(3)
N(1)-C(1)-C(2)-C(3)	38.0(3)
C(1)-C(2)-C(3)-C(16)	-168.1(3)
C(1)-C(2)-C(3)-C(4)	-43.7(3)
C(1)-C(2)-C(3)-C(8)	77.4(3)
C(16)-C(3)-C(4)-C(5)	-81.5(3)
C(2)-C(3)-C(4)-C(5)	154.3(3)
C(8)-C(3)-C(4)-C(5)	35.5(4)
C(16)-C(3)-C(4)-N(1)	156.8(3)
C(2)-C(3)-C(4)-N(1)	32.6(3)
C(8)-C(3)-C(4)-N(1)	-86.2(3)
C(15)-N(1)-C(4)-C(5)	-9.5(4)
C(1)-N(1)-C(4)-C(5)	-135.0(3)
C(15)-N(1)-C(4)-C(3)	115.8(3)
C(1)-N(1)-C(4)-C(3)	-9.8(3)
C(3)-C(4)-C(5)-C(6)	-56.6(3)
N(1)-C(4)-C(5)-C(6)	62.0(3)
C(4)-C(5)-C(6)-C(14)	-57.1(3)
C(4)-C(5)-C(6)-C(7)	67.3(3)
C(14)-C(6)-C(7)-C(11)	-66.0(4)

C(5)-C(6)-C(7)-C(11)	172.5(3)
C(14)-C(6)-C(7)-C(8)	61.9(4)
C(5)-C(6)-C(7)-C(8)	-59.6(3)
C(9)-N(2)-C(8)-C(7)	45.8(3)
C(17)-N(2)-C(8)-C(7)	-107.5(3)
C(9)-N(2)-C(8)-C(3)	170.3(2)
C(17)-N(2)-C(8)-C(3)	17.0(3)
C(11)-C(7)-C(8)-N(2)	-70.1(3)
C(6)-C(7)-C(8)-N(2)	156.4(2)
C(11)-C(7)-C(8)-C(3)	173.9(3)
C(6)-C(7)-C(8)-C(3)	40.4(4)
C(16)-C(3)-C(8)-N(2)	-19.9(3)
C(2)-C(3)-C(8)-N(2)	102.2(3)
C(4)-C(3)-C(8)-N(2)	-144.1(2)
C(16)-C(3)-C(8)-C(7)	97.1(3)
C(2)-C(3)-C(8)-C(7)	-140.8(3)
C(4)-C(3)-C(8)-C(7)	-27.1(4)
C(17)-N(2)-C(9)-O(2)	-23.7(5)
C(8)-N(2)-C(9)-O(2)	-172.0(3)
C(17)-N(2)-C(9)-C(10)	158.4(3)
C(8)-N(2)-C(9)-C(10)	10.1(4)
O(2)-C(9)-C(10)-C(11)	138.3(3)
N(2)-C(9)-C(10)-C(11)	-43.8(4)

C(12)-O(1)-C(11)-C(7)	-63.0(4)
C(12)-O(1)-C(11)-C(10)	175.9(3)
C(8)-C(7)-C(11)-O(1)	-78.9(3)
C(6)-C(7)-C(11)-O(1)	50.9(4)
C(8)-C(7)-C(11)-C(10)	38.0(3)
C(6)-C(7)-C(11)-C(10)	167.8(3)
C(9)-C(10)-C(11)-O(1)	140.9(3)
C(9)-C(10)-C(11)-C(7)	16.7(4)
C(11)-O(1)-C(12)-C(13)	87.4(4)
O(1)-C(12)-C(13)-C(14)	-65.1(5)
C(12)-C(13)-C(14)-C(15)	177.1(3)
C(12)-C(13)-C(14)-C(6)	-4.1(5)
C(5)-C(6)-C(14)-C(13)	-178.3(3)
C(7)-C(6)-C(14)-C(13)	61.4(4)
C(5)-C(6)-C(14)-C(15)	0.6(4)
C(7)-C(6)-C(14)-C(15)	-119.7(3)
C(13)-C(14)-C(15)-N(1)	-130.2(3)
C(6)-C(14)-C(15)-N(1)	51.0(4)
C(1)-N(1)-C(15)-C(14)	76.8(3)
C(4)-N(1)-C(15)-C(14)	-45.8(4)
C(2)-C(3)-C(16)-C(17)	-102.2(3)
C(4)-C(3)-C(16)-C(17)	140.7(3)
C(8)-C(3)-C(16)-C(17)	17.1(3)

C(2)-C(3)-C(16)-C(21)	76.5(4)
C(4)-C(3)-C(16)-C(21)	-40.7(5)
C(8)-C(3)-C(16)-C(21)	-164.2(3)
C(21)-C(16)-C(17)-C(18)	-3.5(5)
C(3)-C(16)-C(17)-C(18)	175.3(3)
C(21)-C(16)-C(17)-N(2)	174.0(3)
C(3)-C(16)-C(17)-N(2)	-7.2(3)
C(9)-N(2)-C(17)-C(16)	-157.5(3)
C(8)-N(2)-C(17)-C(16)	-6.7(3)
C(9)-N(2)-C(17)-C(18)	19.9(5)
C(8)-N(2)-C(17)-C(18)	170.6(3)
C(16)-C(17)-C(18)-C(19)	3.2(5)
N(2)-C(17)-C(18)-C(19)	-173.8(3)
C(22)-O(3)-C(19)-C(18)	7.7(5)
C(22)-O(3)-C(19)-C(20)	-174.5(3)
C(17)-C(18)-C(19)-O(3)	177.8(3)
C(17)-C(18)-C(19)-C(20)	0.2(5)
C(23)-O(4)-C(20)-C(21)	26.0(4)
C(23)-O(4)-C(20)-C(19)	-153.9(3)
O(3)-C(19)-C(20)-O(4)	-1.3(4)
C(18)-C(19)-C(20)-O(4)	176.5(3)
O(3)-C(19)-C(20)-C(21)	178.9(3)
C(18)-C(19)-C(20)-C(21)	-3.3(5)

O(4)-C(20)-C(21)-C(16)	-176.8(3)
C(19)-C(20)-C(21)-C(16)	3.0(5)
C(17)-C(16)-C(21)-C(20)	0.3(5)
C(3)-C(16)-C(21)-C(20)	-178.2(3)
C(27)#1-C(24)-C(25)-C(27)	-65.2(3)
C(27)#1-C(24)-C(25)-C(26)	53.8(4)
C(27)-C(25)-C(26)-C(26)#1	56.6(5)
C(24)-C(25)-C(26)-C(26)#1	-62.0(5)
C(24)-C(25)-C(27)-C(28)	-73.7(3)
C(26)-C(25)-C(27)-C(28)	166.6(3)
C(24)-C(25)-C(27)-C(24)#1	54.5(3)
C(26)-C(25)-C(27)-C(24)#1	-65.2(3)
C(25)-C(27)-C(28)-O(6)	127.4(3)
C(24)#1-C(27)-C(28)-O(6)	2.8(4)
C(25)-C(27)-C(28)-O(5)	-54.5(4)
C(24)#1-C(27)-C(28)-O(5)	-179.1(3)

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,-y+1,z

Table 7. Hydrogen bonds for brucine salt of **6** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(1)-H(1N)...O(6)#2	0.98(4)	1.70(4)	2.659(3)	167(3)
N(1)-H(1N)...O(5)#2	0.98(4)	2.57(4)	3.322(4)	133(3)
O(1S)-H(1SA)...O(4S)	1.09(5)	1.86(5)	2.927(5)	165(4)
O(1S)-H(1SB)...O(2)#3	0.78(5)	2.10(5)	2.861(4)	164(5)
O(2S)-H(2SA)...O(5)	0.83(3)	1.97(3)	2.775(3)	164(4)
O(3S)-H(3SB)...O(5S)	0.97(7)	1.81(7)	2.753(5)	163(5)
O(3S)-H(3SC)...O(6)#4	1.12(7)	1.67(7)	2.753(4)	161(5)
O(3S)-H(3SA)...O(2S)#5	1.02(5)	1.83(5)	2.834(4)	169(4)
O(4S)-H(4SA)...O(5)#1	1.01(6)	1.79(6)	2.781(4)	165(5)
O(4S)-H(4SB)...O(1)	0.88(5)	1.97(5)	2.824(4)	163(4)

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,-y+1,z #2 -x+1,-y+1,z-1 #3 -x+3/2,y-1/2,-z+1

#4 x,y,z-1 #5 x,y+1,z-1

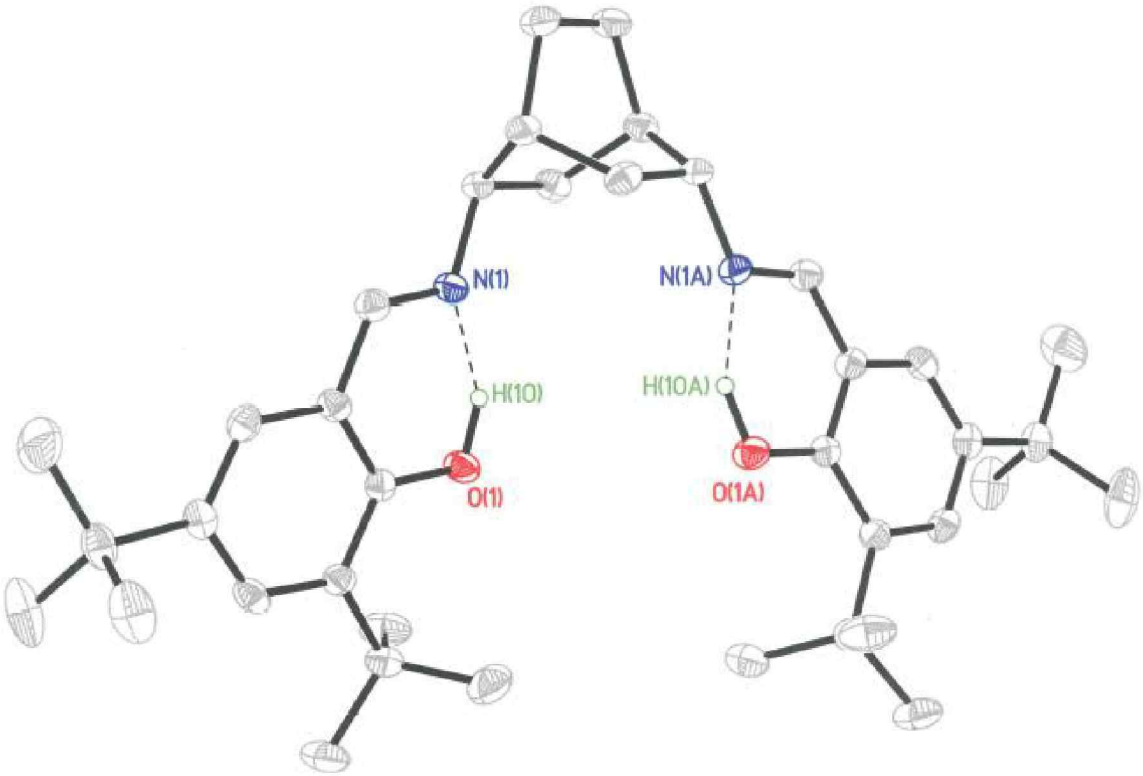


Figure 3: Crystal Structure of enantiopure salen ligand **(+)-35**

Table 1. Crystal data and structure refinement for **(+)-35**

Identification code	**35**	
Empirical formula	C38 H56 N2 O2	
Formula weight	572.85	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C2	
Unit cell dimensions	a = 30.274(3) Å	a= 90°.
	b = 12.6304(13) Å	b= 97.186(2)°.
	c = 9.3737(10) Å	g = 90°.
Volume	3556.1(6) $Å^3$	
Z	4	
Density (calculated)	1.070 Mg/m^3	
Absorption coefficient	0.065 mm^{-1}	
F(000)	1256	
Crystal size	0.42 x 0.16 x 0.10 mm^3	
Theta range for data collection	2.19 to 25.00°.	
Index ranges	-35<=h<=35, -15<=k<=12, -11<=l<=11	
Reflections collected	12342	
Independent reflections	5679 [R(int) = 0.0321]	
Completeness to theta = 25.00°	98.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9935 and 0.9733	

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5679 / 1 / 387
Goodness-of-fit on F^2	1.012
Final R indices [I>2sigma(I)]	R1 = 0.0576, wR2 = 0.1437
R indices (all data)	R1 = 0.0772, wR2 = 0.1619
Absolute structure parameter	4(2)
Largest diff. peak and hole	0.443 and -0.281 e.$Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for (+)-**11**. U (eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	5669(1)	8557(2)	5127(2)	41(1)
N(1)	5640(1)	10544(2)	5590(3)	36(1)
C(1)	5139(1)	13305(3)	5752(4)	48(1)
C(2)	5234(1)	12167(3)	6244(3)	37(1)
C(3)	5499(1)	11628(2)	5150(3)	35(1)
C(4)	5204(1)	11594(3)	3679(3)	37(1)
C(5)	5952(1)	10423(3)	6627(3)	37(1)
C(6)	6137(1)	9395(3)	7042(3)	34(1)
C(7)	5998(1)	8477(3)	6240(3)	31(1)
C(8)	6202(1)	7500(3)	6594(3)	34(1)
C(9)	6527(1)	7478(3)	7780(3)	38(1)
C(10)	6671(1)	8365(3)	8620(3)	36(1)
C(11)	6471(1)	9310(3)	8214(3)	37(1)
C(12)	6070(1)	6501(3)	5690(3)	42(1)
C(13)	6145(2)	6685(3)	4124(4)	61(1)
C(14)	6349(2)	5539(3)	6218(4)	60(1)
C(15)	5578(1)	6231(4)	5774(6)	72(1)
C(16)	7018(1)	8237(3)	9946(3)	45(1)

C(17)	7407(1)	7563(5)	9608(4)	77(2)
C(18)	6792(1)	7686(4)	11118(3)	65(1)
C(19)	7188(2)	9305(4)	10534(5)	80(2)
O(1')	5751(1)	1492(2)	10193(2)	42(1)
N(1')	5649(1)	-396(2)	11106(3)	36(1)
C(1')	5219(1)	-3048(3)	9658(4)	47(1)
C(2')	5387(1)	-1906(3)	9552(3)	36(1)
C(3')	5418(1)	-1422(2)	11063(3)	34(1)
C(4')	4946(1)	-1275(3)	11465(3)	38(1)
C(5')	5965(1)	-218(3)	12110(3)	34(1)
C(6')	6195(1)	797(3)	12264(3)	32(1)
C(7')	6075(1)	1633(3)	11316(3)	34(1)
C(8')	6283(1)	2627(3)	11542(3)	36(1)
C(9')	6610(1)	2722(3)	12708(3)	40(1)
C(10')	6751(1)	1895(3)	13657(3)	40(1)
C(11')	6533(1)	937(3)	13414(3)	39(1)
C(12')	6139(1)	3560(3)	10536(4)	43(1)
C(13')	6412(2)	4571(3)	10969(4)	60(1)
C(14')	6233(1)	3273(3)	9004(4)	57(1)
C(15')	5644(1)	3810(4)	10554(5)	69(1)
C(16')	7115(1)	2080(3)	14915(4)	48(1)
C(17')	6924(2)	2727(7)	16035(5)	125(3)
C(18')	7505(2)	2640(7)	14474(5)	129(3)

C(19')	7274(2)	1045(6)	15674(7)	139(3)

Table 3. Bond lengths [Å] and angles [°] for (+)-**11**.

O(1)-C(7)	1.353(4)
O(1)-H(1O)	0.99(5)
N(1)-C(5)	1.278(4)
N(1)-C(3)	1.477(4)
C(1)-C(2)	1.525(5)
C(1)-C(1)#1	1.550(7)
C(1)-H(1B)	0.9900
C(1)-H(1A)	0.9900
C(2)-C(4)#1	1.519(4)
C(2)-C(3)	1.539(4)
C(2)-H(2A)	1.0000
C(3)-C(4)	1.546(4)
C(3)-H(3)	1.0000
C(4)-C(2)#1	1.519(4)
C(4)-H(4B)	0.9900
C(4)-H(4A)	0.9900
C(5)-C(6)	1.448(5)
C(5)-H(5A)	0.9500
C(6)-C(11)	1.402(4)
C(6)-C(7)	1.418(4)
C(7)-C(8)	1.401(4)

C(8)-C(9)	1.390(4)
C(8)-C(12)	1.545(5)
C(9)-C(10)	1.407(5)
C(9)-H(9A)	0.9500
C(10)-C(11)	1.370(5)
C(10)-C(16)	1.533(4)
C(11)-H(11A)	0.9500
C(12)-C(14)	1.526(5)
C(12)-C(13)	1.531(5)
C(12)-C(15)	1.539(5)
C(13)-H(13A)	0.9800
C(13)-H(13B)	0.9800
C(13)-H(13C)	0.9800
C(14)-H(14A)	0.9800
C(14)-H(14B)	0.9800
C(14)-H(14C)	0.9800
C(15)-H(15A)	0.9800
C(15)-H(15B)	0.9800
C(15)-H(15C)	0.9800
C(16)-C(17)	1.517(5)
C(16)-C(19)	1.522(6)
C(16)-C(18)	1.532(5)
C(17)-H(17A)	0.9800

C(17)-H(17B)	0.9800
C(17)-H(17C)	0.9800
C(18)-H(18A)	0.9800
C(18)-H(18B)	0.9800
C(18)-H(18C)	0.9800
C(19)-H(19A)	0.9800
C(19)-H(19B)	0.9800
C(19)-H(19C)	0.9800
O(1')-C(7')	1.358(4)
O(1')-H(1O')	0.95(5)
N(1')-C(5')	1.274(4)
N(1')-C(3')	1.471(4)
C(1')-C(2')	1.537(5)
C(1')-C(1')#2	1.543(7)
C(1')-H(1'B)	0.9900
C(1')-H(1'A)	0.9900
C(2')-C(4')#2	1.523(4)
C(2')-C(3')	1.535(4)
C(2')-H(2')	1.0000
C(3')-C(4')	1.536(4)
C(3')-H(3')	1.0000
C(4')-C(2')#2	1.523(4)
C(4')-H(4'B)	0.9900

C(4')-H(4'A)	0.9900
C(5')-C(6')	1.459(4)
C(5')-H(5'A)	0.9500
C(6')-C(7')	1.399(4)
C(6')-C(11')	1.401(4)
C(7')-C(8')	1.408(5)
C(8')-C(9')	1.387(4)
C(8')-C(12')	1.538(5)
C(9')-C(10')	1.402(5)
C(9')-H(9'A)	0.9500
C(10')-C(11')	1.383(5)
C(10')-C(16')	1.528(5)
C(11')-H(11B)	0.9500
C(12')-C(15')	1.533(5)
C(12')-C(14')	1.542(5)
C(12')-C(13')	1.547(5)
C(13')-H(13D)	0.9800
C(13')-H(13E)	0.9800
C(13')-H(13F)	0.9800
C(14')-H(14D)	0.9800
C(14')-H(14E)	0.9800
C(14')-H(14F)	0.9800
C(15')-H(15D)	0.9800

C(15')-H(15E)	0.9800
C(15')-H(15F)	0.9800
C(16')-C(18')	1.479(5)
C(16')-C(17')	1.502(6)
C(16')-C(19')	1.537(7)
C(17')-H(17D)	0.9800
C(17')-H(17E)	0.9800
C(17')-H(17F)	0.9800
C(18')-H(18D)	0.9800
C(18')-H(18E)	0.9800
C(18')-H(18F)	0.9800
C(19')-H(19D)	0.9800
C(19')-H(19E)	0.9800
C(19')-H(19F)	0.9800

C(7)-O(1)-H(1O)	108(2)
C(5)-N(1)-C(3)	119.0(3)
C(2)-C(1)-C(1)#1	109.58(18)
C(2)-C(1)-H(1B)	109.8
C(1)#1-C(1)-H(1B)	109.8
C(2)-C(1)-H(1A)	109.8
C(1)#1-C(1)-H(1A)	109.8
H(1B)-C(1)-H(1A)	108.2

C(4)#1-C(2)-C(1)	109.4(3)
C(4)#1-C(2)-C(3)	110.6(3)
C(1)-C(2)-C(3)	108.0(3)
C(4)#1-C(2)-H(2A)	109.6
C(1)-C(2)-H(2A)	109.6
C(3)-C(2)-H(2A)	109.6
N(1)-C(3)-C(2)	112.4(3)
N(1)-C(3)-C(4)	109.8(3)
C(2)-C(3)-C(4)	108.4(2)
N(1)-C(3)-H(3)	108.8
C(2)-C(3)-H(3)	108.7
C(4)-C(3)-H(3)	108.8
C(2)#1-C(4)-C(3)	110.7(3)
C(2)#1-C(4)-H(4B)	109.5
C(3)-C(4)-H(4B)	109.5
C(2)#1-C(4)-H(4A)	109.5
C(3)-C(4)-H(4A)	109.5
H(4B)-C(4)-H(4A)	108.1
N(1)-C(5)-C(6)	122.4(3)
N(1)-C(5)-H(5A)	118.8
C(6)-C(5)-H(5A)	118.8
C(11)-C(6)-C(7)	119.4(3)
C(11)-C(6)-C(5)	119.8(3)

C(7)-C(6)-C(5)	120.8(3)
O(1)-C(7)-C(8)	120.6(3)
O(1)-C(7)-C(6)	119.3(3)
C(8)-C(7)-C(6)	120.1(3)
C(9)-C(8)-C(7)	117.0(3)
C(9)-C(8)-C(12)	122.1(3)
C(7)-C(8)-C(12)	120.9(3)
C(8)-C(9)-C(10)	124.8(3)
C(8)-C(9)-H(9A)	117.6
C(10)-C(9)-H(9A)	117.6
C(11)-C(10)-C(9)	116.3(3)
C(11)-C(10)-C(16)	123.4(3)
C(9)-C(10)-C(16)	120.2(3)
C(10)-C(11)-C(6)	122.3(3)
C(10)-C(11)-H(11A)	118.8
C(6)-C(11)-H(11A)	118.8
C(14)-C(12)-C(13)	106.9(3)
C(14)-C(12)-C(15)	107.8(3)
C(13)-C(12)-C(15)	110.1(3)
C(14)-C(12)-C(8)	112.2(3)
C(13)-C(12)-C(8)	110.0(3)
C(15)-C(12)-C(8)	109.7(3)
C(12)-C(13)-H(13A)	109.5

C(12)-C(13)-H(13B)	109.5
H(13A)-C(13)-H(13B)	109.5
C(12)-C(13)-H(13C)	109.5
H(13A)-C(13)-H(13C)	109.5
H(13B)-C(13)-H(13C)	109.5
C(12)-C(14)-H(14A)	109.5
C(12)-C(14)-H(14B)	109.5
H(14A)-C(14)-H(14B)	109.5
C(12)-C(14)-H(14C)	109.5
H(14A)-C(14)-H(14C)	109.5
H(14B)-C(14)-H(14C)	109.5
C(12)-C(15)-H(15A)	109.5
C(12)-C(15)-H(15B)	109.5
H(15A)-C(15)-H(15B)	109.5
C(12)-C(15)-H(15C)	109.5
H(15A)-C(15)-H(15C)	109.5
H(15B)-C(15)-H(15C)	109.5
C(17)-C(16)-C(19)	109.7(3)
C(17)-C(16)-C(18)	108.8(4)
C(19)-C(16)-C(18)	107.7(3)
C(17)-C(16)-C(10)	111.2(3)
C(19)-C(16)-C(10)	111.5(3)
C(18)-C(16)-C(10)	107.9(3)

C(16)-C(17)-H(17A)	109.5
C(16)-C(17)-H(17B)	109.5
H(17A)-C(17)-H(17B)	109.5
C(16)-C(17)-H(17C)	109.5
H(17A)-C(17)-H(17C)	109.5
H(17B)-C(17)-H(17C)	109.5
C(16)-C(18)-H(18A)	109.5
C(16)-C(18)-H(18B)	109.5
H(18A)-C(18)-H(18B)	109.5
C(16)-C(18)-H(18C)	109.5
H(18A)-C(18)-H(18C)	109.5
H(18B)-C(18)-H(18C)	109.5
C(16)-C(19)-H(19A)	109.5
C(16)-C(19)-H(19B)	109.5
H(19A)-C(19)-H(19B)	109.5
C(16)-C(19)-H(19C)	109.5
H(19A)-C(19)-H(19C)	109.5
H(19B)-C(19)-H(19C)	109.5
C(7')-O(1')-H(1O')	108(2)
C(5')-N(1')-C(3')	119.0(3)
C(2')-C(1')-C(1')#2	109.62(17)
C(2')-C(1')-H(1'B)	109.7
C(1')#2-C(1')-H(1'B)	109.7

C(2')-C(1')-H(1'A)	109.7
C(1')#2-C(1')-H(1'A)	109.7
H(1'B)-C(1')-H(1'A)	108.2
C(4')#2-C(2')-C(3')	109.2(3)
C(4')#2-C(2')-C(1')	109.4(3)
C(3')-C(2')-C(1')	107.3(3)
C(4')#2-C(2')-H(2')	110.3
C(3')-C(2')-H(2')	110.3
C(1')-C(2')-H(2')	110.3
N(1')-C(3')-C(2')	110.5(2)
N(1')-C(3')-C(4')	109.9(3)
C(2')-C(3')-C(4')	108.9(3)
N(1')-C(3')-H(3')	109.2
C(2')-C(3')-H(3')	109.2
C(4')-C(3')-H(3')	109.2
C(2')#2-C(4')-C(3')	110.3(2)
C(2')#2-C(4')-H(4'B)	109.6
C(3')-C(4')-H(4'B)	109.6
C(2')#2-C(4')-H(4'A)	109.6
C(3')-C(4')-H(4'A)	109.6
H(4'B)-C(4')-H(4'A)	108.1
N(1')-C(5')-C(6')	122.2(3)
N(1')-C(5')-H(5'A)	118.9

C(6')-C(5')-H(5'A)	118.9
C(7')-C(6')-C(11')	120.0(3)
C(7')-C(6')-C(5')	121.2(3)
C(11')-C(6')-C(5')	118.8(3)
O(1')-C(7')-C(6')	119.9(3)
O(1')-C(7')-C(8')	119.9(3)
C(6')-C(7')-C(8')	120.1(3)
C(9')-C(8')-C(7')	117.2(3)
C(9')-C(8')-C(12')	122.5(3)
C(7')-C(8')-C(12')	120.3(3)
C(8')-C(9')-C(10')	124.5(3)
C(8')-C(9')-H(9'A)	117.8
C(10')-C(9')-H(9'A)	117.8
C(11')-C(10')-C(9')	116.5(3)
C(11')-C(10')-C(16')	122.9(3)
C(9')-C(10')-C(16')	120.5(3)
C(10')-C(11')-C(6')	121.6(3)
C(10')-C(11')-H(11B)	119.2
C(6')-C(11')-H(11B)	119.2
C(15')-C(12')-C(8')	110.6(3)
C(15')-C(12')-C(14')	110.7(3)
C(8')-C(12')-C(14')	108.6(3)
C(15')-C(12')-C(13')	108.5(3)

C(8')-C(12')-C(13')	111.8(3)
C(14')-C(12')-C(13')	106.5(3)
C(12')-C(13')-H(13D)	109.5
C(12')-C(13')-H(13E)	109.5
H(13D)-C(13')-H(13E)	109.5
C(12')-C(13')-H(13F)	109.5
H(13D)-C(13')-H(13F)	109.5
H(13E)-C(13')-H(13F)	109.5
C(12')-C(14')-H(14D)	109.5
C(12')-C(14')-H(14E)	109.5
H(14D)-C(14')-H(14E)	109.5
C(12')-C(14')-H(14F)	109.5
H(14D)-C(14')-H(14F)	109.5
H(14E)-C(14')-H(14F)	109.5
C(12')-C(15')-H(15D)	109.5
C(12')-C(15')-H(15E)	109.5
H(15D)-C(15')-H(15E)	109.5
C(12')-C(15')-H(15F)	109.5
H(15D)-C(15')-H(15F)	109.5
H(15E)-C(15')-H(15F)	109.5
C(18')-C(16')-C(17')	109.0(5)
C(18')-C(16')-C(10')	112.4(3)
C(17')-C(16')-C(10')	108.7(3)

C(18')-C(16')-C(19')	108.7(5)
C(17')-C(16')-C(19')	105.4(4)
C(10')-C(16')-C(19')	112.4(4)
C(16')-C(17')-H(17D)	109.5
C(16')-C(17')-H(17E)	109.5
H(17D)-C(17')-H(17E)	109.5
C(16')-C(17')-H(17F)	109.5
H(17D)-C(17')-H(17F)	109.5
H(17E)-C(17')-H(17F)	109.5
C(16')-C(18')-H(18D)	109.5
C(16')-C(18')-H(18E)	109.5
H(18D)-C(18')-H(18E)	109.5
C(16')-C(18')-H(18F)	109.5
H(18D)-C(18')-H(18F)	109.5
H(18E)-C(18')-H(18F)	109.5
C(16')-C(19')-H(19D)	109.5
C(16')-C(19')-H(19E)	109.5
H(19D)-C(19')-H(19E)	109.5
C(16')-C(19')-H(19F)	109.5
H(19D)-C(19')-H(19F)	109.5
H(19E)-C(19')-H(19F)	109.5

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,y,-z+1 #2 -x+1,y,-z+2

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for (+)-**11**. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2 a^{*2} U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	47(1)	33(1)	38(1)	1(1)	-8(1)	5(1)
N(1)	37(2)	28(2)	43(2)	6(1)	6(1)	3(1)
C(1)	52(2)	28(2)	65(2)	-7(2)	12(2)	-2(2)
C(2)	42(2)	29(2)	40(2)	-7(1)	2(2)	-2(2)
C(3)	36(2)	23(2)	47(2)	3(1)	6(2)	-1(1)
C(4)	46(2)	34(2)	32(2)	7(1)	10(1)	5(2)
C(5)	41(2)	34(2)	37(2)	-1(1)	3(2)	0(2)
C(6)	35(2)	35(2)	32(2)	7(1)	6(1)	2(2)
C(7)	31(2)	34(2)	28(2)	3(1)	5(1)	-1(1)
C(8)	35(2)	32(2)	37(2)	5(1)	9(1)	-1(2)
C(9)	38(2)	42(2)	36(2)	14(2)	8(1)	9(2)
C(10)	33(2)	49(2)	28(2)	7(2)	7(1)	2(2)
C(11)	38(2)	42(2)	31(2)	-2(2)	4(1)	-7(2)
C(12)	49(2)	34(2)	42(2)	6(2)	7(2)	4(2)
C(13)	102(3)	40(2)	42(2)	-6(2)	9(2)	7(2)
C(14)	84(3)	31(2)	62(2)	2(2)	-1(2)	11(2)
C(15)	62(3)	42(3)	113(4)	-22(2)	17(3)	-11(2)
C(16)	38(2)	63(3)	32(2)	6(2)	0(1)	5(2)

C(17)	45(2)	137(5)	46(2)	-9(3)	-7(2)	26(3)
C(18)	56(2)	110(4)	30(2)	16(2)	6(2)	10(2)
C(19)	76(3)	86(4)	67(3)	10(3)	-30(2)	-14(3)
O(1')	45(1)	38(2)	38(1)	4(1)	-7(1)	-6(1)
N(1')	41(2)	34(2)	33(1)	3(1)	1(1)	-1(1)
C(1')	59(2)	34(2)	47(2)	-5(2)	6(2)	4(2)
C(2')	42(2)	33(2)	34(2)	0(1)	12(1)	3(2)
C(3')	44(2)	26(2)	33(2)	4(1)	2(1)	0(1)
C(4')	47(2)	39(2)	29(2)	0(1)	8(1)	0(2)
C(5')	37(2)	39(2)	28(2)	2(1)	7(1)	5(1)
C(6')	32(2)	37(2)	29(2)	-2(1)	5(1)	1(1)
C(7')	32(2)	40(2)	30(2)	-2(1)	4(1)	-1(2)
C(8')	36(2)	40(2)	33(2)	-7(2)	8(1)	-5(2)
C(9')	43(2)	42(2)	38(2)	-11(2)	13(2)	-6(2)
C(10')	34(2)	54(2)	32(2)	-11(2)	8(1)	-4(2)
C(11')	35(2)	52(2)	30(2)	2(2)	6(1)	3(2)
C(12')	47(2)	34(2)	49(2)	0(2)	6(2)	-7(2)
C(13')	79(3)	40(2)	61(2)	-5(2)	8(2)	-14(2)
C(14')	73(3)	53(3)	43(2)	8(2)	3(2)	-18(2)
C(15')	62(3)	48(3)	98(3)	10(2)	10(2)	9(2)
C(16')	37(2)	73(3)	34(2)	-6(2)	3(2)	-6(2)
C(17')	66(3)	250(9)	57(3)	-68(4)	-7(2)	11(4)
C(18')	75(3)	239(9)	64(3)	30(4)	-21(3)	-84(5)

C(19')	139(6)	116(6)	137(5)	20(4)	-86(5)	-13(4)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for (+)-**11**.

	x	y	z	U(eq)
H(1B)	5424	13684	5706	58
H(1A)	4974	13677	6449	58
H(2A)	5413	12167	7214	45
H(3)	5770	12062	5052	42
H(4B)	5364	11932	2940	44
H(4A)	5144	10849	3393	44
H(5A)	6067	11030	7145	44
H(9A)	6662	6816	8042	46
H(11A)	6563	9929	8745	45
H(13A)	6060	6049	3558	92
H(13B)	6460	6841	4080	92
H(13C)	5963	7285	3731	92
H(14A)	6309	5392	7221	90
H(14B)	6663	5684	6153	90
H(14C)	6253	4924	5622	90
H(15A)	5534	6107	6778	108
H(15B)	5497	5592	5208	108

H(15C)	5390	6823	5389	108
H(17A)	7296	6878	9227	115
H(17B)	7613	7453	10488	115
H(17C)	7562	7925	8891	115
H(18A)	6683	6990	10774	98
H(18B)	6542	8118	11349	98
H(18C)	7007	7599	11982	98
H(19A)	7409	9196	11379	120
H(19B)	6939	9722	10807	120
H(19C)	7327	9686	9794	120
H(1'B)	5446	-3477	10251	56
H(1'A)	5167	-3367	8686	56
H(2')	5686	-1902	9202	43
H(3')	5587	-1915	11767	41
H(4'B)	4936	-1516	12466	45
H(4'A)	4865	-515	11411	45
H(5'A)	6052	-766	12782	41
H(9'A)	6749	3392	12877	48
H(11B)	6615	360	14042	47
H(13D)	6361	4787	11940	90
H(13E)	6318	5141	10289	90
H(13F)	6729	4426	10955	90
H(14D)	6064	2638	8677	85

H(14E)	6552	3135	9010	85
H(14F)	6144	3862	8351	85
H(15D)	5467	3178	10271	104
H(15E)	5556	4386	9878	104
H(15F)	5594	4025	11525	104
H(17D)	6821	3410	15621	188
H(17E)	7154	2847	16853	188
H(17F)	6673	2348	16362	188
H(18D)	7407	3297	13977	193
H(18E)	7651	2187	13825	193
H(18F)	7715	2805	15327	193
H(19D)	7508	1202	16467	209
H(19E)	7393	572	14985	209
H(19F)	7023	700	16053	209
H(1O)	5569(14)	9310(40)	5060(50)	81(14)
H(1O')	5634(14)	790(40)	10260(40)	70(13)

Table 6. Torsion angles [°] for (+)-**11**.

C(1)#1-C(1)-C(2)-C(4)#1	-59.8(4)
C(1)#1-C(1)-C(2)-C(3)	60.6(4)
C(5)-N(1)-C(3)-C(2)	-72.7(3)
C(5)-N(1)-C(3)-C(4)	166.6(3)
C(4)#1-C(2)-C(3)-N(1)	-65.0(3)
C(1)-C(2)-C(3)-N(1)	175.3(3)
C(4)#1-C(2)-C(3)-C(4)	56.4(3)
C(1)-C(2)-C(3)-C(4)	-63.2(3)
N(1)-C(3)-C(4)-C(2)#1	127.2(3)
C(2)-C(3)-C(4)-C(2)#1	4.1(3)
C(3)-N(1)-C(5)-C(6)	-174.4(3)
N(1)-C(5)-C(6)-C(11)	-178.4(3)
N(1)-C(5)-C(6)-C(7)	4.4(4)
C(11)-C(6)-C(7)-O(1)	178.7(3)
C(5)-C(6)-C(7)-O(1)	-4.1(4)
C(11)-C(6)-C(7)-C(8)	-1.7(4)
C(5)-C(6)-C(7)-C(8)	175.5(3)
O(1)-C(7)-C(8)-C(9)	-178.0(2)
C(6)-C(7)-C(8)-C(9)	2.4(4)
O(1)-C(7)-C(8)-C(12)	2.5(4)
C(6)-C(7)-C(8)-C(12)	-177.1(3)

C(7)-C(8)-C(9)-C(10)	-1.5(4)
C(12)-C(8)-C(9)-C(10)	178.0(3)
C(8)-C(9)-C(10)-C(11)	-0.2(4)
C(8)-C(9)-C(10)-C(16)	177.3(3)
C(9)-C(10)-C(11)-C(6)	1.0(4)
C(16)-C(10)-C(11)-C(6)	-176.4(3)
C(7)-C(6)-C(11)-C(10)	-0.1(4)
C(5)-C(6)-C(11)-C(10)	-177.3(3)
C(9)-C(8)-C(12)-C(14)	-2.3(4)
C(7)-C(8)-C(12)-C(14)	177.2(3)
C(9)-C(8)-C(12)-C(13)	-121.2(3)
C(7)-C(8)-C(12)-C(13)	58.4(4)
C(9)-C(8)-C(12)-C(15)	117.5(4)
C(7)-C(8)-C(12)-C(15)	-63.0(4)
C(11)-C(10)-C(16)-C(17)	-135.8(4)
C(9)-C(10)-C(16)-C(17)	46.8(4)
C(11)-C(10)-C(16)-C(19)	-13.1(4)
C(9)-C(10)-C(16)-C(19)	169.6(3)
C(11)-C(10)-C(16)-C(18)	105.0(4)
C(9)-C(10)-C(16)-C(18)	-72.4(4)
C(1')#2-C(1')-C(2')-C(4')#2	-64.2(4)
C(1')#2-C(1')-C(2')-C(3')	54.1(4)
C(5')-N(1')-C(3')-C(2')	-130.9(3)

C(5')-N(1')-C(3')-C(4')	108.9(3)
C(4')#2-C(2')-C(3')-N(1')	-71.3(3)
C(1')-C(2')-C(3')-N(1')	170.2(3)
C(4')#2-C(2')-C(3')-C(4')	49.6(3)
C(1')-C(2')-C(3')-C(4')	-68.9(3)
N(1')-C(3')-C(4')-C(2')#2	136.1(3)
C(2')-C(3')-C(4')-C(2')#2	14.9(3)
C(3')-N(1')-C(5')-C(6')	-177.1(3)
N(1')-C(5')-C(6')-C(7')	0.9(4)
N(1')-C(5')-C(6')-C(11')	178.8(3)
C(11')-C(6')-C(7')-O(1')	179.2(3)
C(5')-C(6')-C(7')-O(1')	-2.9(4)
C(11')-C(6')-C(7')-C(8')	-2.1(4)
C(5')-C(6')-C(7')-C(8')	175.8(3)
O(1')-C(7')-C(8')-C(9')	179.9(3)
C(6')-C(7')-C(8')-C(9')	1.2(4)
O(1')-C(7')-C(8')-C(12')	1.0(4)
C(6')-C(7')-C(8')-C(12')	-177.7(3)
C(7')-C(8')-C(9')-C(10')	0.9(4)
C(12')-C(8')-C(9')-C(10')	179.8(3)
C(8')-C(9')-C(10')-C(11')	-2.0(4)
C(8')-C(9')-C(10')-C(16')	-179.9(3)
C(9')-C(10')-C(11')-C(6')	1.1(4)

C(16')-C(10')-C(11')-C(6')	178.9(3)
C(7')-C(6')-C(11')-C(10')	0.8(4)
C(5')-C(6')-C(11')-C(10')	-177.1(3)
C(9')-C(8')-C(12')-C(15')	-119.4(3)
C(7')-C(8')-C(12')-C(15')	59.4(4)
C(9')-C(8')-C(12')-C(14')	118.8(3)
C(7')-C(8')-C(12')-C(14')	-62.3(4)
C(9')-C(8')-C(12')-C(13')	1.6(4)
C(7')-C(8')-C(12')-C(13')	-179.6(3)
C(11')-C(10')-C(16')-C(18')	134.7(5)
C(9')-C(10')-C(16')-C(18')	-47.6(5)
C(11')-C(10')-C(16')-C(17')	-104.6(5)
C(9')-C(10')-C(16')-C(17')	73.1(5)
C(11')-C(10')-C(16')-C(19')	11.7(5)
C(9')-C(10')-C(16')-C(19')	-170.6(4)

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,y,-z+1 #2 -x+1,y,-z+2

Table 7. Hydrogen bonds for (+)-**11** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1)-H(1O)...N(1)	0.99(5)	1.65(5)	2.550(4)	149(4)
O(1')-H(1O')...N(1')	0.95(5)	1.70(5)	2.566(4)	150(4)

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,y,-z+1 #2 -x+1,y,-z+2

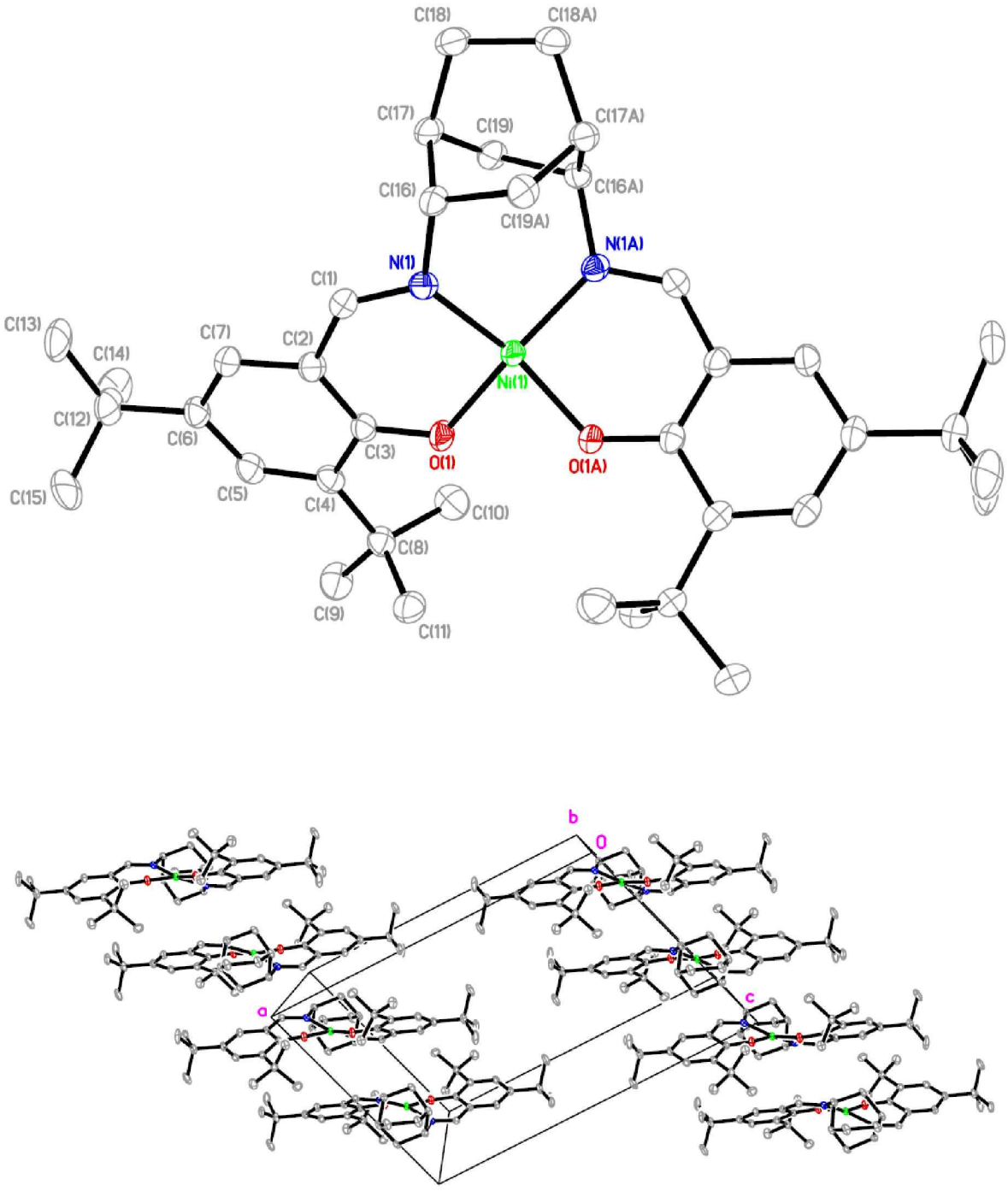


Figure 4: Crystal Structure of Nickel(II)-salen Complex (+)-**75**

Table 1. Crystal data and structure refinement for (+)-**75**

Identification code	**75**	
Empirical formula	C38 H54 N2 Ni O2	
Formula weight	629.54	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C2/c	
Unit cell dimensions	a = 16.768(3) Å	a= 90°.
	b = 20.434(3) Å	b= 107.415(3)°.
	c = 11.1052(18) Å	g = 90°.
Volume	3630.7(10) $Å^3$	
Z	4	
Density (calculated)	1.152 Mg/m^3	
Absorption coefficient	0.567 mm^{-1}	
F(000)	1360	
Crystal size	0.45 x 0.05 x 0.04 mm^3	
Theta range for data collection	1.62 to 27.00°.	
Index ranges	-21<=h<=21, -26<=k<=26, -14<=l<=14	
Reflections collected	17667	
Independent reflections	3959 [R(int) = 0.0608]	
Completeness to theta = 27.00°	100.0 %	
Absorption correction	Semi-empirical from equivalents	

Max. and min. transmission	0.9777 and 0.7845
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3959 / 6 / 222
Goodness-of-fit on F^2	1.088
Final R indices [I>2sigma(I)]	R1 = 0.0487, wR2 = 0.1085
R indices (all data)	R1 = 0.0641, wR2 = 0.1161
Largest diff. peak and hole	0.481 and -0.229 e.$Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **14**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Ni(1)	0	4939(1)	2500	18(1)
O(1)	587(1)	4251(1)	2063(2)	25(1)
N(1)	355(1)	5555(1)	1493(2)	20(1)
C(1)	904(1)	5421(1)	918(2)	22(1)
C(2)	1412(1)	4848(1)	1047(2)	22(1)
C(3)	1253(1)	4288(1)	1672(2)	21(1)
C(4)	1828(1)	3753(1)	1853(2)	23(1)
C(5)	2505(1)	3823(1)	1384(2)	26(1)
C(6)	2656(1)	4372(1)	720(2)	25(1)
C(7)	2096(1)	4878(1)	557(2)	25(1)
C(8)	1696(2)	3129(1)	2542(2)	26(1)
C(9)	2414(2)	2639(1)	2705(3)	38(1)
C(10)	1644(2)	3299(1)	3866(3)	37(1)
C(11)	887(2)	2788(1)	1787(3)	31(1)
C(12)	3399(2)	4402(1)	185(3)	34(1)
C(13)	3441(4)	5036(3)	-501(6)	39(1)
C(14)	4199(3)	4319(3)	1293(7)	49(2)
C(15)	3319(4)	3819(3)	-741(7)	56(2)

C(13A)	3891(5)	5040(3)	646(11)	78(3)
C(14A)	3062(5)	4409(6)	-1253(7)	93(3)
C(15A)	4014(4)	3849(4)	594(8)	57(2)
C(16)	64(1)	6250(1)	1286(2)	22(1)
C(17)	706(1)	6666(1)	2262(2)	24(1)
C(18)	374(2)	7368(1)	2227(3)	32(1)
C(19)	807(1)	6370(1)	3562(2)	24(1)

Table 3. Bond lengths [Å] and angles [°] for **14**.

Ni(1)-O(1)#1	1.8620(15)
Ni(1)-O(1)	1.8620(15)
Ni(1)-N(1)	1.8929(18)
Ni(1)-N(1)#1	1.8929(18)
O(1)-C(3)	1.317(3)
N(1)-C(1)	1.297(3)
N(1)-C(16)	1.498(3)
C(1)-C(2)	1.430(3)
C(1)-H(1A)	0.9500
C(2)-C(3)	1.405(3)
C(2)-C(7)	1.410(3)
C(3)-C(4)	1.431(3)
C(4)-C(5)	1.390(3)
C(4)-C(8)	1.539(3)
C(5)-C(6)	1.407(3)
C(5)-H(5A)	0.9500
C(6)-C(7)	1.370(3)
C(6)-C(12)	1.535(3)
C(7)-H(7A)	0.9500
C(8)-C(11)	1.533(3)
C(8)-C(9)	1.534(3)

C(8)-C(10)	1.538(3)
C(9)-H(9A)	0.9800
C(9)-H(9B)	0.9800
C(9)-H(9C)	0.9800
C(10)-H(10A)	0.9800
C(10)-H(10B)	0.9800
C(10)-H(10C)	0.9800
C(11)-H(11A)	0.9800
C(11)-H(11B)	0.9800
C(11)-H(11C)	0.9800
C(12)-C(13)	1.515(6)
C(12)-C(15A)	1.505(6)
C(12)-C(14A)	1.526(7)
C(12)-C(14)	1.535(6)
C(12)-C(15)	1.552(6)
C(12)-C(13A)	1.546(7)
C(13)-H(13A)	0.9800
C(13)-H(13B)	0.9800
C(13)-H(13C)	0.9800
C(14)-H(14A)	0.9800
C(14)-H(14B)	0.9800
C(14)-H(14C)	0.9800
C(15)-H(15A)	0.9800

C(15)-H(15B)	0.9800
C(15)-H(15C)	0.9800
C(13A)-H(13D)	0.9800
C(13A)-H(13E)	0.9800
C(13A)-H(13F)	0.9800
C(14A)-H(14D)	0.9800
C(14A)-H(14E)	0.9800
C(14A)-H(14F)	0.9800
C(15A)-H(15D)	0.9800
C(15A)-H(15E)	0.9800
C(15A)-H(15F)	0.9800
C(16)-C(17)	1.536(3)
C(16)-C(19)#1	1.540(3)
C(16)-H(16A)	1.0000
C(17)-C(19)	1.528(3)
C(17)-C(18)	1.534(3)
C(17)-H(17A)	1.0000
C(18)-C(18)#1	1.548(5)
C(18)-H(18A)	0.9900
C(18)-H(18B)	0.9900
C(19)-C(16)#1	1.540(3)
C(19)-H(19A)	0.9900
C(19)-H(19B)	0.9900

O(1)#1-Ni(1)-O(1)	81.90(9)
O(1)#1-Ni(1)-N(1)	160.01(8)
O(1)-Ni(1)-N(1)	93.63(7)
O(1)#1-Ni(1)-N(1)#1	93.63(7)
O(1)-Ni(1)-N(1)#1	160.01(8)
N(1)-Ni(1)-N(1)#1	96.78(11)
C(3)-O(1)-Ni(1)	127.54(14)
C(1)-N(1)-C(16)	111.73(18)
C(1)-N(1)-Ni(1)	123.15(15)
C(16)-N(1)-Ni(1)	125.10(14)
N(1)-C(1)-C(2)	127.7(2)
N(1)-C(1)-H(1A)	116.1
C(2)-C(1)-H(1A)	116.1
C(3)-C(2)-C(7)	121.4(2)
C(3)-C(2)-C(1)	121.4(2)
C(7)-C(2)-C(1)	117.1(2)
O(1)-C(3)-C(2)	121.0(2)
O(1)-C(3)-C(4)	120.8(2)
C(2)-C(3)-C(4)	118.2(2)
C(5)-C(4)-C(3)	117.4(2)
C(5)-C(4)-C(8)	121.8(2)
C(3)-C(4)-C(8)	120.79(19)

C(4)-C(5)-C(6)	125.0(2)
C(4)-C(5)-H(5A)	117.5
C(6)-C(5)-H(5A)	117.5
C(7)-C(6)-C(5)	116.5(2)
C(7)-C(6)-C(12)	121.5(2)
C(5)-C(6)-C(12)	122.0(2)
C(6)-C(7)-C(2)	121.4(2)
C(6)-C(7)-H(7A)	119.3
C(2)-C(7)-H(7A)	119.3
C(11)-C(8)-C(9)	107.7(2)
C(11)-C(8)-C(4)	109.9(2)
C(9)-C(8)-C(4)	112.00(19)
C(11)-C(8)-C(10)	109.4(2)
C(9)-C(8)-C(10)	107.6(2)
C(4)-C(8)-C(10)	110.25(19)
C(8)-C(9)-H(9A)	109.5
C(8)-C(9)-H(9B)	109.5
H(9A)-C(9)-H(9B)	109.5
C(8)-C(9)-H(9C)	109.5
H(9A)-C(9)-H(9C)	109.5
H(9B)-C(9)-H(9C)	109.5
C(8)-C(10)-H(10A)	109.5
C(8)-C(10)-H(10B)	109.5

H(10A)-C(10)-H(10B)	109.5
C(8)-C(10)-H(10C)	109.5
H(10A)-C(10)-H(10C)	109.5
H(10B)-C(10)-H(10C)	109.5
C(8)-C(11)-H(11A)	109.5
C(8)-C(11)-H(11B)	109.5
H(11A)-C(11)-H(11B)	109.5
C(8)-C(11)-H(11C)	109.5
H(11A)-C(11)-H(11C)	109.5
H(11B)-C(11)-H(11C)	109.5
C(13)-C(12)-C(15A)	131.6(4)
C(13)-C(12)-C(14A)	61.6(5)
C(15A)-C(12)-C(14A)	109.3(5)
C(13)-C(12)-C(14)	109.7(4)
C(15A)-C(12)-C(14)	47.1(4)
C(14A)-C(12)-C(14)	143.3(4)
C(13)-C(12)-C(6)	113.2(3)
C(15A)-C(12)-C(6)	114.5(3)
C(14A)-C(12)-C(6)	108.4(3)
C(14)-C(12)-C(6)	107.5(3)
C(13)-C(12)-C(15)	109.3(4)
C(15A)-C(12)-C(15)	62.6(4)
C(14A)-C(12)-C(15)	51.9(5)

C(14)-C(12)-C(15)	109.2(4)
C(6)-C(12)-C(15)	107.9(3)
C(13)-C(12)-C(13A)	49.1(4)
C(15A)-C(12)-C(13A)	106.5(5)
C(14A)-C(12)-C(13A)	109.4(6)
C(14)-C(12)-C(13A)	64.9(5)
C(6)-C(12)-C(13A)	108.6(3)
C(15)-C(12)-C(13A)	143.0(4)
C(12)-C(13)-H(13A)	109.5
C(12)-C(13)-H(13B)	109.5
H(13A)-C(13)-H(13B)	109.5
C(12)-C(13)-H(13C)	109.5
H(13A)-C(13)-H(13C)	109.5
H(13B)-C(13)-H(13C)	109.5
C(12)-C(14)-H(14A)	109.5
C(12)-C(14)-H(14B)	109.5
H(14A)-C(14)-H(14B)	109.5
C(12)-C(14)-H(14C)	109.5
H(14A)-C(14)-H(14C)	109.5
H(14B)-C(14)-H(14C)	109.5
C(12)-C(15)-H(15A)	109.5
C(12)-C(15)-H(15B)	109.5
H(15A)-C(15)-H(15B)	109.5

C(12)-C(15)-H(15C)	109.5
H(15A)-C(15)-H(15C)	109.5
H(15B)-C(15)-H(15C)	109.5
C(12)-C(13A)-H(13D)	109.5
C(12)-C(13A)-H(13E)	109.5
H(13D)-C(13A)-H(13E)	109.5
C(12)-C(13A)-H(13F)	109.5
H(13D)-C(13A)-H(13F)	109.5
H(13E)-C(13A)-H(13F)	109.5
C(12)-C(14A)-H(14D)	109.5
C(12)-C(14A)-H(14E)	109.5
H(14D)-C(14A)-H(14E)	109.5
C(12)-C(14A)-H(14F)	109.5
H(14D)-C(14A)-H(14F)	109.5
H(14E)-C(14A)-H(14F)	109.5
C(12)-C(15A)-H(15D)	109.5
C(12)-C(15A)-H(15E)	109.5
H(15D)-C(15A)-H(15E)	109.5
C(12)-C(15A)-H(15F)	109.5
H(15D)-C(15A)-H(15F)	109.5
H(15E)-C(15A)-H(15F)	109.5
N(1)-C(16)-C(17)	106.84(18)
N(1)-C(16)-C(19)#1	114.23(17)

C(17)-C(16)-C(19)#1	108.84(18)
N(1)-C(16)-H(16A)	108.9
C(17)-C(16)-H(16A)	108.9
C(19)#1-C(16)-H(16A)	108.9
C(19)-C(17)-C(16)	107.63(18)
C(19)-C(17)-C(18)	109.3(2)
C(16)-C(17)-C(18)	109.1(2)
C(19)-C(17)-H(17A)	110.3
C(16)-C(17)-H(17A)	110.3
C(18)-C(17)-H(17A)	110.3
C(17)-C(18)-C(18)#1	108.73(13)
C(17)-C(18)-H(18A)	109.9
C(18)#1-C(18)-H(18A)	109.9
C(17)-C(18)-H(18B)	109.9
C(18)#1-C(18)-H(18B)	109.9
H(18A)-C(18)-H(18B)	108.3
C(17)-C(19)-C(16)#1	109.05(19)
C(17)-C(19)-H(19A)	109.9
C(16)#1-C(19)-H(19A)	109.9
C(17)-C(19)-H(19B)	109.9
C(16)#1-C(19)-H(19B)	109.9
H(19A)-C(19)-H(19B)	108.3

Symmetry transformations used to generate equivalent atoms:

#1 -x,y,-z+1/2

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **14**. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2 a^{*2} U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Ni(1)	16(1)	17(1)	24(1)	0	8(1)	0
O(1)	22(1)	22(1)	36(1)	3(1)	17(1)	3(1)
N(1)	16(1)	20(1)	25(1)	-1(1)	5(1)	1(1)
C(1)	21(1)	23(1)	22(1)	2(1)	7(1)	-2(1)
C(2)	17(1)	24(1)	26(1)	0(1)	7(1)	1(1)
C(3)	17(1)	24(1)	24(1)	-3(1)	7(1)	-1(1)
C(4)	22(1)	23(1)	25(1)	-2(1)	7(1)	3(1)
C(5)	19(1)	28(1)	30(1)	-2(1)	7(1)	4(1)
C(6)	19(1)	30(1)	29(1)	-3(1)	11(1)	0(1)
C(7)	22(1)	26(1)	29(1)	-1(1)	12(1)	-2(1)
C(8)	25(1)	24(1)	30(1)	3(1)	11(1)	5(1)
C(9)	37(2)	33(1)	49(2)	12(1)	19(1)	13(1)
C(10)	43(2)	36(1)	31(2)	5(1)	11(1)	6(1)
C(11)	32(1)	25(1)	39(2)	4(1)	14(1)	2(1)
C(12)	23(1)	38(1)	45(2)	2(1)	19(1)	4(1)
C(13)	29(3)	50(3)	48(4)	5(3)	26(3)	1(3)
C(14)	17(3)	62(4)	70(5)	9(4)	18(3)	2(3)
C(15)	52(4)	58(4)	79(5)	-28(4)	52(4)	-10(3)

C(13A)	50(4)	62(5)	144(9)	-18(5)	62(6)	-21(4)
C(14A)	56(5)	188(11)	50(5)	34(6)	40(4)	49(6)
C(15A)	40(4)	72(5)	73(5)	18(4)	38(4)	22(3)
C(16)	20(1)	21(1)	26(1)	6(1)	8(1)	3(1)
C(17)	17(1)	21(1)	37(2)	0(1)	10(1)	-1(1)
C(18)	28(1)	19(1)	52(2)	1(1)	17(1)	-1(1)
C(19)	14(1)	25(1)	31(1)	-4(1)	5(1)	-5(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for **14**.

	x	y	z	U(eq)
H(1A)	978	5743	342	26
H(5A)	2895	3474	1524	31
H(7A)	2171	5256	104	29
H(9A)	2463	2521	1875	58
H(9B)	2301	2245	3130	58
H(9C)	2938	2839	3215	58
H(10A)	2162	3515	4352	55
H(10B)	1567	2897	4299	55
H(10C)	1170	3593	3790	55
H(11A)	919	2679	943	47
H(11B)	411	3080	1712	47
H(11C)	813	2385	2222	47
H(13A)	3091	5001	-1380	59
H(13B)	4021	5121	-479	59
H(13C)	3240	5397	-89	59
H(14A)	4277	3856	1526	73
H(14B)	4152	4574	2017	73

H(14C)	4680	4475	1045	73
H(15A)	2876	3524	-664	84
H(15B)	3850	3581	-535	84
H(15C)	3179	3985	-1607	84
H(13D)	4110	5035	1569	117
H(13E)	3518	5417	377	117
H(13F)	4356	5074	285	117
H(14D)	2755	4003	-1547	139
H(14E)	3528	4446	-1610	139
H(14F)	2686	4784	-1525	139
H(15D)	3732	3433	303	86
H(15E)	4236	3845	1517	86
H(15F)	4474	3909	230	86
H(16A)	59	6389	420	26
H(17A)	1254	6665	2075	29
H(18A)	193	7531	1347	38
H(18B)	820	7660	2734	38
H(19A)	1129	6672	4228	29
H(19B)	1117	5952	3648	29

Table 6. Torsion angles [°] for **14**.

O(1)#1-Ni(1)-O(1)-C(3)	-175.0(2)
N(1)-Ni(1)-O(1)-C(3)	24.6(2)
N(1)#1-Ni(1)-O(1)-C(3)	-96.8(3)
O(1)#1-Ni(1)-N(1)-C(1)	-82.9(3)
O(1)-Ni(1)-N(1)-C(1)	-6.67(19)
N(1)#1-Ni(1)-N(1)-C(1)	156.2(2)
O(1)#1-Ni(1)-N(1)-C(16)	98.9(2)
O(1)-Ni(1)-N(1)-C(16)	175.04(17)
N(1)#1-Ni(1)-N(1)-C(16)	-22.05(14)
C(16)-N(1)-C(1)-C(2)	169.7(2)
Ni(1)-N(1)-C(1)-C(2)	-8.8(3)
N(1)-C(1)-C(2)-C(3)	12.4(4)
N(1)-C(1)-C(2)-C(7)	-165.5(2)
Ni(1)-O(1)-C(3)-C(2)	-26.7(3)
Ni(1)-O(1)-C(3)-C(4)	154.40(17)
C(7)-C(2)-C(3)-O(1)	-176.1(2)
C(1)-C(2)-C(3)-O(1)	6.0(4)
C(7)-C(2)-C(3)-C(4)	2.8(3)
C(1)-C(2)-C(3)-C(4)	-175.0(2)
O(1)-C(3)-C(4)-C(5)	178.4(2)
C(2)-C(3)-C(4)-C(5)	-0.6(3)

O(1)-C(3)-C(4)-C(8)	-1.8(3)
C(2)-C(3)-C(4)-C(8)	179.3(2)
C(3)-C(4)-C(5)-C(6)	-1.7(4)
C(8)-C(4)-C(5)-C(6)	178.5(2)
C(4)-C(5)-C(6)-C(7)	1.6(4)
C(4)-C(5)-C(6)-C(12)	-177.5(2)
C(5)-C(6)-C(7)-C(2)	0.8(4)
C(12)-C(6)-C(7)-C(2)	179.8(2)
C(3)-C(2)-C(7)-C(6)	-3.0(4)
C(1)-C(2)-C(7)-C(6)	174.9(2)
C(5)-C(4)-C(8)-C(11)	-116.0(2)
C(3)-C(4)-C(8)-C(11)	64.1(3)
C(5)-C(4)-C(8)-C(9)	3.6(3)
C(3)-C(4)-C(8)-C(9)	-176.3(2)
C(5)-C(4)-C(8)-C(10)	123.3(2)
C(3)-C(4)-C(8)-C(10)	-56.6(3)
C(7)-C(6)-C(12)-C(13)	0.8(4)
C(5)-C(6)-C(12)-C(13)	179.7(4)
C(7)-C(6)-C(12)-C(15A)	172.2(4)
C(5)-C(6)-C(12)-C(15A)	-8.8(5)
C(7)-C(6)-C(12)-C(14A)	-65.5(6)
C(5)-C(6)-C(12)-C(14A)	113.5(5)
C(7)-C(6)-C(12)-C(14)	122.0(4)

C(5)-C(6)-C(12)-C(14)	-59.0(4)
C(7)-C(6)-C(12)-C(15)	-120.3(4)
C(5)-C(6)-C(12)-C(15)	58.6(4)
C(7)-C(6)-C(12)-C(13A)	53.3(5)
C(5)-C(6)-C(12)-C(13A)	-127.7(5)
C(1)-N(1)-C(16)-C(17)	-83.9(2)
Ni(1)-N(1)-C(16)-C(17)	94.60(19)
C(1)-N(1)-C(16)-C(19)#1	155.7(2)
Ni(1)-N(1)-C(16)-C(19)#1	-25.8(3)
N(1)-C(16)-C(17)-C(19)	-53.1(2)
C(19)#1-C(16)-C(17)-C(19)	70.7(2)
N(1)-C(16)-C(17)-C(18)	-171.59(18)
C(19)#1-C(16)-C(17)-C(18)	-47.8(2)
C(19)-C(17)-C(18)-C(18)#1	-47.6(3)
C(16)-C(17)-C(18)-C(18)#1	69.9(3)
C(16)-C(17)-C(19)-C(16)#1	-48.4(2)
C(18)-C(17)-C(19)-C(16)#1	69.9(2)

Symmetry transformations used to generate equivalent atoms:

#1 -x,y,-z+1/2

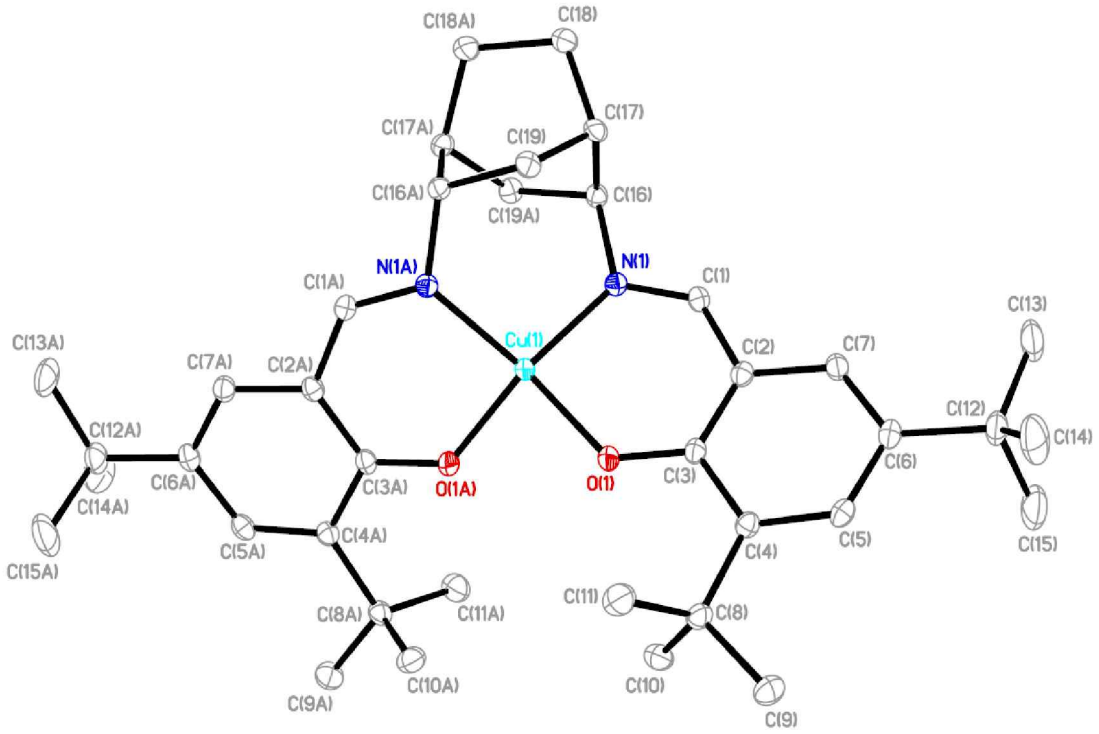


Figure 5: Crystal Structure of Copper(II)-salen complex (+)-**76**

Table 1. Crystal data and structure refinement for (+)-**76**.

Identification code	**76**	
Empirical formula	C38.50 H56 Cu N2 O2.50	
Formula weight	650.39	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C2/c	
Unit cell dimensions	a = 16.953(2) Å	a= 90°.
	b = 20.663(3) Å	b= 107.751(2)°.
	c = 11.0738(16) Å	g = 90°.
Volume	3694.5(9) $Å^3$	
Z	4	
Density (calculated)	1.169 Mg/m^3	
Absorption coefficient	0.626 mm^{-1}	
F(000)	1400	
Crystal size	0.48 x 0.06 x 0.04 mm^3	
Theta range for data collection	1.60 to 27.00°.	
Index ranges	-21<=h<=21, -26<=k<=26, -14<=l<=14	
Reflections collected	20495	
Independent reflections	4029 [R(int) = 0.0476]	
Completeness to theta = 27.00°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9754 and 0.7533	

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4029 / 6 / 205
Goodness-of-fit on F^2	1.078
Final R indices [I>2sigma(I)]	R1 = 0.0452, wR2 = 0.1152
R indices (all data)	R1 = 0.0561, wR2 = 0.1211
Largest diff. peak and hole	0.402 and -0.317 e.$Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **13**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Cu(1)	0	4944(1)	2500	20(1)
O(1)	698(1)	4272(1)	2239(2)	28(1)
N(1)	368(1)	5565(1)	1442(2)	20(1)
C(1)	942(1)	5428(1)	938(2)	23(1)
C(2)	1439(1)	4854(1)	1082(2)	22(1)
C(3)	1313(1)	4305(1)	1759(2)	22(1)
C(4)	1879(1)	3772(1)	1898(2)	23(1)
C(5)	2523(1)	3838(1)	1385(2)	26(1)
C(6)	2653(1)	4380(1)	697(2)	26(1)
C(7)	2098(1)	4878(1)	551(2)	26(1)
C(8)	1761(2)	3152(1)	2589(2)	27(1)
C(9)	2451(2)	2659(1)	2682(3)	38(1)
C(10)	934(2)	2833(1)	1868(2)	33(1)
C(11)	1766(2)	3306(1)	3952(2)	38(1)
C(12)	3371(2)	4398(1)	128(3)	35(1)
C(13)	3398(3)	5016(2)	-593(5)	52(1)
C(14)	4176(2)	4303(3)	1170(5)	59(1)
C(15)	3246(3)	3829(3)	-839(5)	68(2)

C(13A)	3991(7)	3855(6)	582(13)	52(1)
C(14A)	3037(6)	4443(7)	-1256(10)	59(1)
C(15A)	3885(9)	5047(6)	686(15)	68(2)
C(16)	94(1)	6249(1)	1276(2)	22(1)
C(17)	713(1)	6651(1)	2311(2)	24(1)
C(18)	388(2)	7344(1)	2267(3)	33(1)
C(19)	781(1)	6354(1)	3606(2)	24(1)

Table 3. Bond lengths [Å] and angles [°] for **13**.

Cu(1)-O(1)	1.9029(15)
Cu(1)-O(1)#1	1.9029(15)
Cu(1)-N(1)#1	1.9634(17)
Cu(1)-N(1)	1.9634(18)
O(1)-C(3)	1.308(3)
N(1)-C(1)	1.292(3)
N(1)-C(16)	1.483(3)
C(1)-C(2)	1.435(3)
C(1)-H(1A)	0.9500
C(2)-C(3)	1.411(3)
C(2)-C(7)	1.413(3)
C(3)-C(4)	1.438(3)
C(4)-C(5)	1.382(3)
C(4)-C(8)	1.537(3)
C(5)-C(6)	1.409(3)
C(5)-H(5A)	0.9500
C(6)-C(7)	1.370(3)
C(6)-C(12)	1.534(3)
C(7)-H(7A)	0.9500
C(8)-C(9)	1.532(3)
C(8)-C(10)	1.533(3)

C(8)-C(11)	1.540(3)
C(9)-H(9A)	0.9800
C(9)-H(9B)	0.9800
C(9)-H(9C)	0.9800
C(10)-H(10A)	0.9800
C(10)-H(10B)	0.9800
C(10)-H(10C)	0.9800
C(11)-H(11A)	0.9800
C(11)-H(11B)	0.9800
C(11)-H(11C)	0.9800
C(12)-C(14A)	1.465(11)
C(12)-C(13A)	1.514(10)
C(12)-C(14)	1.507(5)
C(12)-C(13)	1.513(4)
C(12)-C(15)	1.561(5)
C(12)-C(15A)	1.615(11)
C(13)-H(13A)	0.9800
C(13)-H(13B)	0.9800
C(13)-H(13C)	0.9800
C(14)-H(14A)	0.9800
C(14)-H(14B)	0.9800
C(14)-H(14C)	0.9800
C(15)-H(15A)	0.9800

C(15)-H(15B)	0.9800
C(15)-H(15C)	0.9800
C(13A)-H(13D)	0.9800
C(13A)-H(13E)	0.9800
C(13A)-H(13F)	0.9800
C(14A)-H(14D)	0.9800
C(14A)-H(14E)	0.9800
C(14A)-H(14F)	0.9800
C(15A)-H(15D)	0.9800
C(15A)-H(15E)	0.9800
C(15A)-H(15F)	0.9800
C(16)-C(17)	1.540(3)
C(16)-C(19)#1	1.542(3)
C(16)-H(16A)	1.0000
C(17)-C(19)	1.531(3)
C(17)-C(18)	1.529(3)
C(17)-H(17A)	1.0000
C(18)-C(18)#1	1.553(5)
C(18)-H(18A)	0.9900
C(18)-H(18B)	0.9900
C(19)-C(16)#1	1.542(3)
C(19)-H(19A)	0.9900
C(19)-H(19B)	0.9900

O(1)-Cu(1)-O(1)#1	86.28(9)
O(1)-Cu(1)-N(1)#1	153.26(8)
O(1)#1-Cu(1)-N(1)#1	93.48(7)
O(1)-Cu(1)-N(1)	93.48(7)
O(1)#1-Cu(1)-N(1)	153.26(8)
N(1)#1-Cu(1)-N(1)	98.38(10)
C(3)-O(1)-Cu(1)	129.27(14)
C(1)-N(1)-C(16)	113.81(18)
C(1)-N(1)-Cu(1)	122.23(15)
C(16)-N(1)-Cu(1)	123.56(13)
N(1)-C(1)-C(2)	128.8(2)
N(1)-C(1)-H(1A)	115.6
C(2)-C(1)-H(1A)	115.6
C(3)-C(2)-C(7)	121.1(2)
C(3)-C(2)-C(1)	123.0(2)
C(7)-C(2)-C(1)	115.8(2)
O(1)-C(3)-C(2)	121.7(2)
O(1)-C(3)-C(4)	120.34(19)
C(2)-C(3)-C(4)	117.93(19)
C(5)-C(4)-C(3)	117.8(2)
C(5)-C(4)-C(8)	121.7(2)
C(3)-C(4)-C(8)	120.50(19)

C(4)-C(5)-C(6)	124.9(2)
C(4)-C(5)-H(5A)	117.5
C(6)-C(5)-H(5A)	117.5
C(7)-C(6)-C(5)	116.5(2)
C(7)-C(6)-C(12)	122.4(2)
C(5)-C(6)-C(12)	121.0(2)
C(6)-C(7)-C(2)	121.7(2)
C(6)-C(7)-H(7A)	119.1
C(2)-C(7)-H(7A)	119.1
C(9)-C(8)-C(10)	107.9(2)
C(9)-C(8)-C(4)	112.04(19)
C(10)-C(8)-C(4)	109.67(19)
C(9)-C(8)-C(11)	107.2(2)
C(10)-C(8)-C(11)	109.3(2)
C(4)-C(8)-C(11)	110.63(19)
C(8)-C(9)-H(9A)	109.5
C(8)-C(9)-H(9B)	109.5
H(9A)-C(9)-H(9B)	109.5
C(8)-C(9)-H(9C)	109.5
H(9A)-C(9)-H(9C)	109.5
H(9B)-C(9)-H(9C)	109.5
C(8)-C(10)-H(10A)	109.5
C(8)-C(10)-H(10B)	109.5

H(10A)-C(10)-H(10B)	109.5
C(8)-C(10)-H(10C)	109.5
H(10A)-C(10)-H(10C)	109.5
H(10B)-C(10)-H(10C)	109.5
C(8)-C(11)-H(11A)	109.5
C(8)-C(11)-H(11B)	109.5
H(11A)-C(11)-H(11B)	109.5
C(8)-C(11)-H(11C)	109.5
H(11A)-C(11)-H(11C)	109.5
H(11B)-C(11)-H(11C)	109.5
C(14A)-C(12)-C(13A)	113.7(8)
C(14A)-C(12)-C(14)	141.3(5)
C(13A)-C(12)-C(14)	43.5(5)
C(14A)-C(12)-C(13)	57.3(6)
C(13A)-C(12)-C(13)	132.2(5)
C(14)-C(12)-C(13)	110.4(3)
C(14A)-C(12)-C(6)	109.2(5)
C(13A)-C(12)-C(6)	113.7(4)
C(14)-C(12)-C(6)	109.2(2)
C(13)-C(12)-C(6)	113.1(2)
C(14A)-C(12)-C(15)	53.3(6)
C(13A)-C(12)-C(15)	66.7(6)
C(14)-C(12)-C(15)	109.2(3)

C(13)-C(12)-C(15)	107.1(3)
C(6)-C(12)-C(15)	107.7(2)
C(14A)-C(12)-C(15A)	109.9(8)
C(13A)-C(12)-C(15A)	104.5(8)
C(14)-C(12)-C(15A)	63.8(6)
C(13)-C(12)-C(15A)	53.3(6)
C(6)-C(12)-C(15A)	105.4(4)
C(15)-C(12)-C(15A)	146.4(5)
C(12)-C(13)-H(13A)	109.5
C(12)-C(13)-H(13B)	109.5
H(13A)-C(13)-H(13B)	109.5
C(12)-C(13)-H(13C)	109.5
H(13A)-C(13)-H(13C)	109.5
H(13B)-C(13)-H(13C)	109.5
C(12)-C(14)-H(14A)	109.5
C(12)-C(14)-H(14B)	109.5
H(14A)-C(14)-H(14B)	109.5
C(12)-C(14)-H(14C)	109.5
H(14A)-C(14)-H(14C)	109.5
H(14B)-C(14)-H(14C)	109.5
C(12)-C(15)-H(15A)	109.5
C(12)-C(15)-H(15B)	109.5
H(15A)-C(15)-H(15B)	109.5

C(12)-C(15)-H(15C)	109.5
H(15A)-C(15)-H(15C)	109.5
H(15B)-C(15)-H(15C)	109.5
C(12)-C(13A)-H(13D)	109.5
C(12)-C(13A)-H(13E)	109.5
H(13D)-C(13A)-H(13E)	109.5
C(12)-C(13A)-H(13F)	109.5
H(13D)-C(13A)-H(13F)	109.5
H(13E)-C(13A)-H(13F)	109.5
C(12)-C(14A)-H(14D)	109.5
C(12)-C(14A)-H(14E)	109.5
H(14D)-C(14A)-H(14E)	109.5
C(12)-C(14A)-H(14F)	109.5
H(14D)-C(14A)-H(14F)	109.5
H(14E)-C(14A)-H(14F)	109.5
C(12)-C(15A)-H(15D)	109.5
C(12)-C(15A)-H(15E)	109.5
H(15D)-C(15A)-H(15E)	109.5
C(12)-C(15A)-H(15F)	109.5
H(15D)-C(15A)-H(15F)	109.5
H(15E)-C(15A)-H(15F)	109.5
N(1)-C(16)-C(17)	107.77(17)
N(1)-C(16)-C(19)#1	113.33(18)

C(17)-C(16)-C(19)#1	108.39(18)
N(1)-C(16)-H(16A)	109.1
C(17)-C(16)-H(16A)	109.1
C(19)#1-C(16)-H(16A)	109.1
C(19)-C(17)-C(18)	109.20(19)
C(19)-C(17)-C(16)	108.74(17)
C(18)-C(17)-C(16)	108.89(19)
C(19)-C(17)-H(17A)	110.0
C(18)-C(17)-H(17A)	110.0
C(16)-C(17)-H(17A)	110.0
C(17)-C(18)-C(18)#1	108.80(12)
C(17)-C(18)-H(18A)	109.9
C(18)#1-C(18)-H(18A)	109.9
C(17)-C(18)-H(18B)	109.9
C(18)#1-C(18)-H(18B)	109.9
H(18A)-C(18)-H(18B)	108.3
C(17)-C(19)-C(16)#1	109.61(18)
C(17)-C(19)-H(19A)	109.7
C(16)#1-C(19)-H(19A)	109.7
C(17)-C(19)-H(19B)	109.7
C(16)#1-C(19)-H(19B)	109.7
H(19A)-C(19)-H(19B)	108.2

Symmetry transformations used to generate equivalent atoms:

#1 -x,y,-z+1/2

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **13**. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2 a^{*2} U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Cu(1)	19(1)	20(1)	23(1)	0	10(1)	0
O(1)	28(1)	24(1)	39(1)	5(1)	21(1)	4(1)
N(1)	18(1)	22(1)	20(1)	2(1)	5(1)	2(1)
C(1)	23(1)	26(1)	20(1)	1(1)	9(1)	-1(1)
C(2)	19(1)	25(1)	22(1)	-3(1)	7(1)	0(1)
C(3)	19(1)	25(1)	24(1)	-2(1)	9(1)	0(1)
C(4)	24(1)	25(1)	21(1)	0(1)	7(1)	3(1)
C(5)	21(1)	29(1)	28(1)	-2(1)	7(1)	6(1)
C(6)	21(1)	33(1)	25(1)	-4(1)	9(1)	0(1)
C(7)	25(1)	29(1)	26(1)	-2(1)	12(1)	-3(1)
C(8)	32(1)	25(1)	27(1)	5(1)	12(1)	9(1)
C(9)	38(2)	33(1)	47(2)	10(1)	18(1)	14(1)
C(10)	35(1)	27(1)	38(1)	5(1)	13(1)	-1(1)
C(11)	52(2)	36(1)	28(1)	4(1)	16(1)	9(1)
C(12)	28(1)	43(2)	40(2)	2(1)	20(1)	5(1)
C(13)	41(2)	65(3)	65(3)	21(2)	38(2)	11(2)
C(14)	26(2)	86(3)	69(3)	19(3)	20(2)	9(2)
C(15)	66(3)	77(3)	86(3)	-33(3)	58(3)	-17(2)

C(13A)	41(2)	65(3)	65(3)	21(2)	38(2)	11(2)
C(14A)	26(2)	86(3)	69(3)	19(3)	20(2)	9(2)
C(15A)	66(3)	77(3)	86(3)	-33(3)	58(3)	-17(2)
C(16)	24(1)	23(1)	22(1)	4(1)	9(1)	3(1)
C(17)	19(1)	22(1)	33(1)	1(1)	10(1)	-3(1)
C(18)	32(1)	24(1)	48(2)	1(1)	20(1)	0(1)
C(19)	18(1)	28(1)	25(1)	-4(1)	4(1)	-5(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for **13**.

	x	y	z	U(eq)
H(1A)	1050	5752	400	27
H(5A)	2907	3491	1505	31
H(7A)	2158	5250	80	31
H(9A)	2987	2851	3144	57
H(9B)	2453	2536	1828	57
H(9C)	2356	2274	3135	57
H(10A)	930	2734	1000	49
H(10B)	479	3130	1843	49
H(10C)	867	2433	2299	49
H(11A)	2294	3508	4416	57
H(11B)	1695	2905	4379	57
H(11C)	1311	3604	3927	57
H(13A)	3045	4969	-1472	78
H(13B)	3969	5101	-581	78
H(13C)	3198	5377	-193	78
H(14A)	4264	3840	1356	88
H(14B)	4153	4532	1934	88

H(14C)	4633	4474	898	88
H(15A)	2790	3553	-773	102
H(15B)	3755	3572	-650	102
H(15C)	3113	4003	-1701	102
H(13D)	3724	3440	277	78
H(13E)	4189	3853	1511	78
H(13F)	4459	3920	252	78
H(14D)	2723	4049	-1588	88
H(14E)	3493	4489	-1619	88
H(14F)	2670	4820	-1484	88
H(15D)	3670	5235	1335	102
H(15E)	3824	5359	-1	102
H(15F)	4471	4939	1064	102
H(16A)	103	6404	424	27
H(17A)	1267	6651	2169	29
H(18A)	241	7512	1389	39
H(18B)	822	7627	2817	39
H(19A)	1101	6646	4289	29
H(19B)	1076	5935	3698	29

Table 6. Torsion angles [°] for **13**.

O(1)#1-Cu(1)-O(1)-C(3)	166.3(2)
N(1)#1-Cu(1)-O(1)-C(3)	-103.3(2)
N(1)-Cu(1)-O(1)-C(3)	13.10(19)
O(1)-Cu(1)-N(1)-C(1)	-3.68(17)
O(1)#1-Cu(1)-N(1)-C(1)	-92.3(2)
N(1)#1-Cu(1)-N(1)-C(1)	152.3(2)
O(1)-Cu(1)-N(1)-C(16)	-175.96(16)
O(1)#1-Cu(1)-N(1)-C(16)	95.4(2)
N(1)#1-Cu(1)-N(1)-C(16)	-19.99(13)
C(16)-N(1)-C(1)-C(2)	169.2(2)
Cu(1)-N(1)-C(1)-C(2)	-3.8(3)
N(1)-C(1)-C(2)-C(3)	5.5(4)
N(1)-C(1)-C(2)-C(7)	-171.6(2)
Cu(1)-O(1)-C(3)-C(2)	-14.6(3)
Cu(1)-O(1)-C(3)-C(4)	166.12(15)
C(7)-C(2)-C(3)-O(1)	-178.9(2)
C(1)-C(2)-C(3)-O(1)	4.1(3)
C(7)-C(2)-C(3)-C(4)	0.4(3)
C(1)-C(2)-C(3)-C(4)	-176.6(2)
O(1)-C(3)-C(4)-C(5)	-179.2(2)
C(2)-C(3)-C(4)-C(5)	1.5(3)

O(1)-C(3)-C(4)-C(8)	1.2(3)
C(2)-C(3)-C(4)-C(8)	-178.1(2)
C(3)-C(4)-C(5)-C(6)	-2.2(3)
C(8)-C(4)-C(5)-C(6)	177.4(2)
C(4)-C(5)-C(6)-C(7)	0.9(3)
C(4)-C(5)-C(6)-C(12)	-178.0(2)
C(5)-C(6)-C(7)-C(2)	1.1(3)
C(12)-C(6)-C(7)-C(2)	180.0(2)
C(3)-C(2)-C(7)-C(6)	-1.7(3)
C(1)-C(2)-C(7)-C(6)	175.5(2)
C(5)-C(4)-C(8)-C(9)	3.0(3)
C(3)-C(4)-C(8)-C(9)	-177.5(2)
C(5)-C(4)-C(8)-C(10)	-116.8(2)
C(3)-C(4)-C(8)-C(10)	62.7(3)
C(5)-C(4)-C(8)-C(11)	122.6(2)
C(3)-C(4)-C(8)-C(11)	-57.9(3)
C(7)-C(6)-C(12)-C(14A)	-61.5(7)
C(5)-C(6)-C(12)-C(14A)	117.3(7)
C(7)-C(6)-C(12)-C(13A)	170.3(7)
C(5)-C(6)-C(12)-C(13A)	-10.9(7)
C(7)-C(6)-C(12)-C(14)	123.6(3)
C(5)-C(6)-C(12)-C(14)	-57.6(4)
C(7)-C(6)-C(12)-C(13)	0.2(4)

C(5)-C(6)-C(12)-C(13)	179.1(3)
C(7)-C(6)-C(12)-C(15)	-117.9(3)
C(5)-C(6)-C(12)-C(15)	60.9(4)
C(7)-C(6)-C(12)-C(15A)	56.4(7)
C(5)-C(6)-C(12)-C(15A)	-124.7(7)
C(1)-N(1)-C(16)-C(17)	-82.4(2)
Cu(1)-N(1)-C(16)-C(17)	90.51(19)
C(1)-N(1)-C(16)-C(19)#1	157.71(19)
Cu(1)-N(1)-C(16)-C(19)#1	-29.4(2)
N(1)-C(16)-C(17)-C(19)	-54.2(2)
C(19)#1-C(16)-C(17)-C(19)	68.82(19)
N(1)-C(16)-C(17)-C(18)	-173.09(17)
C(19)#1-C(16)-C(17)-C(18)	-50.1(2)
C(19)-C(17)-C(18)-C(18)#1	-48.9(3)
C(16)-C(17)-C(18)-C(18)#1	69.7(3)
C(18)-C(17)-C(19)-C(16)#1	68.8(2)
C(16)-C(17)-C(19)-C(16)#1	-49.9(2)

Symmetry transformations used to generate equivalent atoms:

#1 -x,y,-z+1/2

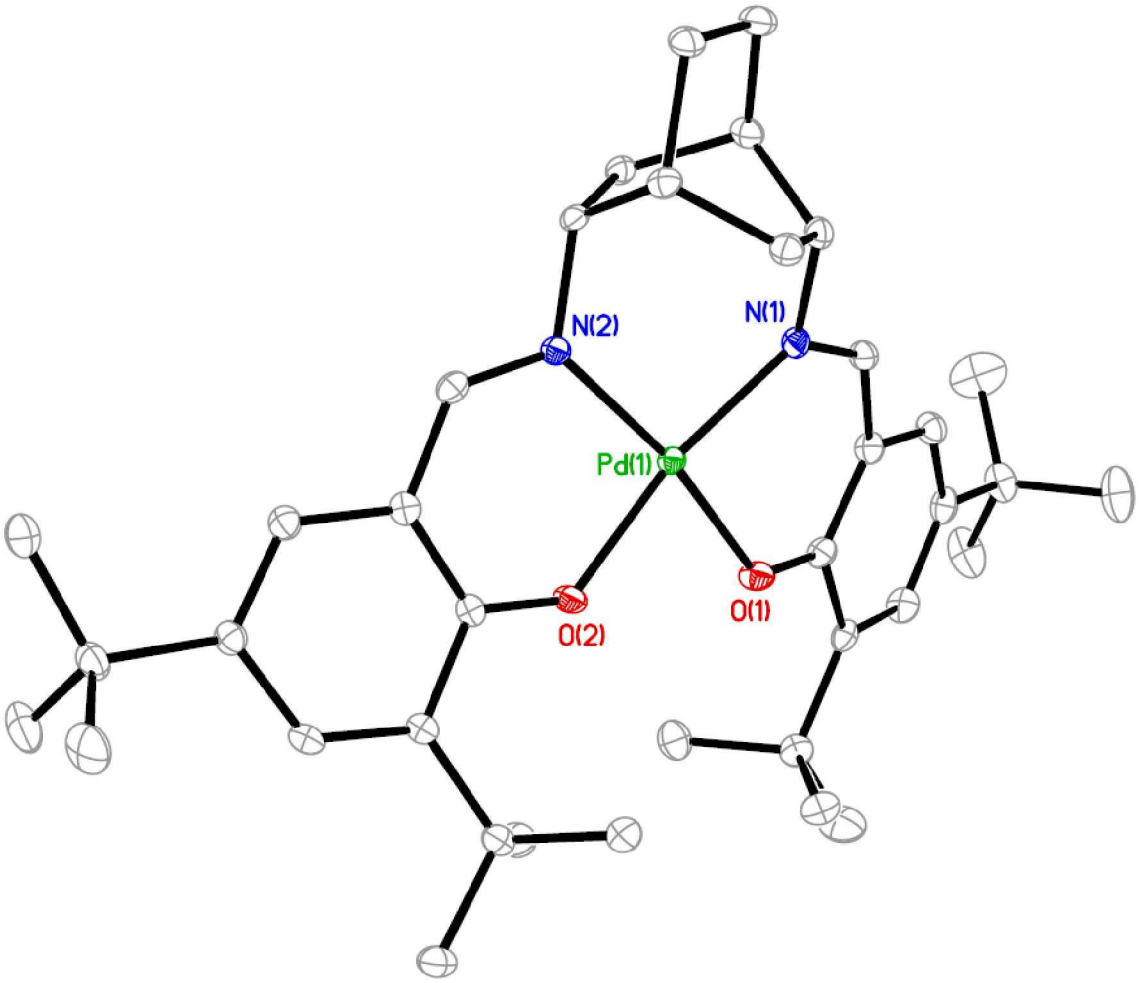


Figure 6: Crystal Structure of Palladium(II)-Salen Complex (+)-**77**

Table 1. Crystal data and structure refinement for (+)-**77**

Identification code	**77**
Empirical formula	C39.50 H57 N2 O2.50 Pd
Formula weight	706.27
Temperature	173(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	P2(1)
Unit cell dimensions	a = 14.0325(15) Å □= 90°.
	b = 10.2155(11) Å □= 102.3820(10)°.
	c = 26.161(3) Å □ = 90°.
Volume	3662.9(7) $Å^3$
Z	4
Density (calculated)	1.281 Mg/m^3
Absorption coefficient	0.543 mm^{-1}
F(000)	1496
Crystal size	0.38 x 0.27 x 0.10 mm^3
Theta range for data collection	0.80 to 27.00°.
Index ranges	-17<=h<=17, -13<=k<=13, -33<=l<=33
Reflections collected	41434
Independent reflections	15937 [R(int) = 0.0320]
Completeness to theta = 27.00°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9477 and 0.8203

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	15937 / 1 / 811
Goodness-of-fit on F^2	1.016
Final R indices [I>2sigma(I)]	R1 = 0.0306, wR2 = 0.0673
R indices (all data)	R1 = 0.0339, wR2 = 0.0696
Absolute structure parameter	0.000(13)
Largest diff. peak and hole	0.515 and -0.348 e.Å^{-3}

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (Å^{2}x 10^3) for **22**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Pd(1)	9534(1)	8800(1)	4620(1)	17(1)
O(1)	8133(1)	9252(2)	4332(1)	24(1)
O(2)	9520(1)	8539(2)	3867(1)	24(1)
N(1)	9388(2)	9329(2)	5340(1)	20(1)
N(2)	10911(1)	8090(2)	4823(1)	19(1)
C(1)	8541(2)	9408(3)	5467(1)	22(1)
C(2)	7588(2)	9230(3)	5137(1)	23(1)
C(3)	7422(2)	9216(3)	4586(1)	22(1)
C(4)	6421(2)	9173(3)	4301(1)	22(1)
C(5)	5701(2)	9054(3)	4586(1)	28(1)
C(6)	5852(2)	9004(3)	5129(1)	26(1)

C(7)	6802(2)	9137(3)	5399(1)	26(1)
C(8)	6175(2)	9149(3)	3699(1)	26(1)
C(9)	5073(2)	9282(4)	3473(1)	46(1)
C(10)	6672(2)	10277(3)	3470(1)	32(1)
C(11)	6493(2)	7818(3)	3526(1)	34(1)
C(12)	5007(2)	8842(4)	5414(1)	32(1)
C(13)	5323(2)	8012(5)	5907(2)	62(1)
C(14)	4681(3)	10183(4)	5566(2)	51(1)
C(15)	4134(2)	8148(4)	5071(1)	48(1)
C(16)	10232(2)	9704(3)	5768(1)	23(1)
C(17)	10614(2)	8504(3)	6097(1)	22(1)
C(18)	11563(2)	8890(4)	6477(1)	28(1)
C(19)	12363(2)	9119(3)	6163(1)	26(1)
C(20)	11872(2)	9299(3)	5583(1)	21(1)
C(21)	11066(2)	10314(3)	5544(1)	24(1)
C(22)	10818(2)	7424(3)	5738(1)	21(1)
C(23)	11457(2)	7972(3)	5378(1)	18(1)
C(24)	11371(2)	7638(2)	4483(1)	21(1)
C(25)	11116(2)	7654(2)	3922(1)	21(1)
C(26)	10222(2)	8173(3)	3639(1)	19(1)
C(27)	10106(2)	8313(3)	3084(1)	21(1)
C(28)	10809(2)	7796(3)	2851(1)	22(1)
C(29)	11672(2)	7172(3)	3119(1)	22(1)

C(30)	11808(2)	7135(3)	3654(1)	22(1)
C(31)	9217(2)	9048(3)	2768(1)	24(1)
C(32)	9174(2)	10429(3)	2997(1)	33(1)
C(33)	8276(2)	8310(3)	2795(1)	31(1)
C(34)	9257(2)	9198(3)	2191(1)	30(1)
C(35)	12380(2)	6583(3)	2809(1)	27(1)
C(36)	13257(2)	5948(4)	3169(1)	38(1)
C(37)	12748(2)	7667(3)	2488(1)	41(1)
C(38)	11847(2)	5529(3)	2436(1)	41(1)
Pd(1')	5958(1)	7935(1)	9818(1)	21(1)
O(1')	5295(1)	8314(2)	9078(1)	32(1)
O(2')	6955(1)	7119(2)	9477(1)	30(1)
N(1')	4878(2)	8836(3)	10084(1)	30(1)
N(2')	6741(2)	7421(3)	10523(1)	31(1)
C(1')	4031(2)	9037(3)	9782(1)	31(1)
C(2')	3713(2)	8806(3)	9231(1)	26(1)
C(3')	4367(2)	8560(3)	8899(1)	24(1)
C(4')	3986(2)	8618(3)	8342(1)	23(1)
C(5')	2999(2)	8792(3)	8166(1)	24(1)
C(6')	2324(2)	8947(3)	8493(1)	21(1)
C(7')	2704(2)	8984(3)	9021(1)	24(1)
C(8')	4676(2)	8491(3)	7957(1)	28(1)
C(9')	4126(2)	8663(4)	7388(1)	42(1)

C(10')	5464(2)	9540(3)	8070(1)	35(1)
C(11')	5134(2)	7107(3)	8008(1)	38(1)
C(12')	1236(2)	9122(3)	8248(1)	25(1)
C(13')	615(2)	9175(3)	8657(1)	31(1)
C(14')	1104(2)	10387(3)	7930(1)	38(1)
C(15')	875(2)	7988(4)	7880(1)	39(1)
C(16')	4944(2)	9263(3)	10644(1)	31(1)
C(17')	4643(2)	8134(3)	10942(1)	32(1)
C(18')	4833(2)	8514(4)	11527(1)	38(1)
C(19')	5935(2)	8514(4)	11748(1)	45(1)
C(20')	6454(2)	8621(4)	11283(1)	39(1)
C(21')	5970(2)	9702(3)	10909(1)	32(1)
C(22')	5253(2)	6915(3)	10882(1)	31(1)
C(23')	6329(2)	7318(3)	11010(1)	35(1)
C(24')	7664(2)	7177(3)	10599(1)	35(1)
C(25')	8277(2)	7055(3)	10230(1)	28(1)
C(26')	7891(2)	6948(3)	9686(1)	26(1)
C(27')	8544(2)	6573(3)	9357(1)	25(1)
C(28')	9524(2)	6461(3)	9590(1)	29(1)
C(29')	9938(2)	6669(3)	10127(1)	29(1)
C(30')	9288(2)	6944(3)	10434(1)	31(1)
C(31')	8167(2)	6351(3)	8772(1)	29(1)
C(32')	7352(2)	5317(3)	8679(1)	35(1)

C(33')	7780(2)	7647(3)	8513(1)	36(1)
C(34')	8965(2)	5854(4)	8504(1)	39(1)
C(35')	11039(2)	6550(3)	10333(1)	34(1)
C(36')	11322(3)	6708(4)	10932(1)	53(1)
C(37')	11377(3)	5187(4)	10212(2)	70(1)
C(38')	11540(3)	7617(4)	10100(2)	63(1)
O(1S)	1681(2)	2865(3)	3469(1)	71(1)
C(1S)	1951(3)	1759(4)	3551(2)	63(1)
C(2S)	1880(4)	1102(5)	4049(2)	97(2)
C(3S)	2350(4)	990(6)	3167(2)	115(2)

Table 3. Bond lengths [Å] and angles [°] for **22**.

Pd(1)-O(2)	1.9860(17)
Pd(1)-O(1)	2.0024(17)
Pd(1)-N(1)	2.011(2)
Pd(1)-N(2)	2.026(2)
O(1)-C(3)	1.313(3)
O(2)-C(26)	1.310(3)
N(1)-C(1)	1.303(3)
N(1)-C(16)	1.495(3)
N(2)-C(24)	1.291(3)
N(2)-C(23)	1.493(3)
C(1)-C(2)	1.439(4)
C(2)-C(3)	1.411(4)
C(2)-C(7)	1.421(4)
C(3)-C(4)	1.443(3)
C(4)-C(5)	1.383(4)
C(4)-C(8)	1.538(4)
C(5)-C(6)	1.393(4)
C(6)-C(7)	1.375(4)
C(6)-C(12)	1.539(4)
C(8)-C(11)	1.530(4)
C(8)-C(10)	1.534(4)

C(8)-C(9)	1.538(4)
C(12)-C(14)	1.524(5)
C(12)-C(15)	1.527(4)
C(12)-C(13)	1.529(5)
C(16)-C(17)	1.527(4)
C(16)-C(21)	1.549(4)
C(17)-C(22)	1.515(4)
C(17)-C(18)	1.532(4)
C(18)-C(19)	1.543(4)
C(19)-C(20)	1.537(3)
C(20)-C(21)	1.522(4)
C(20)-C(23)	1.527(4)
C(22)-C(23)	1.540(3)
C(24)-C(25)	1.434(4)
C(25)-C(26)	1.416(4)
C(25)-C(30)	1.418(4)
C(26)-C(27)	1.433(3)
C(27)-C(28)	1.372(4)
C(27)-C(31)	1.536(4)
C(28)-C(29)	1.414(4)
C(29)-C(30)	1.372(4)
C(29)-C(35)	1.535(4)
C(31)-C(34)	1.532(3)

C(31)-C(33)	1.535(4)
C(31)-C(32)	1.539(4)
C(35)-C(36)	1.524(4)
C(35)-C(38)	1.535(4)
C(35)-C(37)	1.543(4)
Pd(1')-O(2')	1.9956(19)
Pd(1')-O(1')	1.9966(18)
Pd(1')-N(2')	2.004(2)
Pd(1')-N(1')	2.020(2)
O(1')-C(3')	1.310(3)
O(2')-C(26')	1.321(3)
N(1')-C(1')	1.294(3)
N(1')-C(16')	1.512(4)
N(2')-C(24')	1.291(4)
N(2')-C(23')	1.513(4)
C(1')-C(2')	1.435(4)
C(2')-C(3')	1.414(4)
C(2')-C(7')	1.417(3)
C(3')-C(4')	1.441(4)
C(4')-C(5')	1.375(3)
C(4')-C(8')	1.545(4)
C(5')-C(6')	1.413(3)
C(6')-C(7')	1.369(3)

C(6')-C(12')	1.535(3)
C(8')-C(10')	1.522(4)
C(8')-C(9')	1.532(4)
C(8')-C(11')	1.546(4)
C(12')-C(13')	1.519(4)
C(12')-C(15')	1.522(4)
C(12')-C(14')	1.527(4)
C(16')-C(17')	1.503(4)
C(16')-C(21')	1.526(4)
C(17')-C(22')	1.538(4)
C(17')-C(18')	1.545(4)
C(18')-C(19')	1.529(4)
C(19')-C(20')	1.549(4)
C(20')-C(23')	1.503(5)
C(20')-C(21')	1.535(4)
C(22')-C(23')	1.531(4)
C(24')-C(25')	1.431(4)
C(25')-C(30')	1.409(4)
C(25')-C(26')	1.414(4)
C(26')-C(27')	1.437(4)
C(27')-C(28')	1.384(4)
C(27')-C(31')	1.524(4)
C(28')-C(29')	1.418(4)

C(29')-C(30')	1.367(4)
C(29')-C(35')	1.528(4)
C(31')-C(34')	1.530(4)
C(31')-C(33')	1.533(4)
C(31')-C(32')	1.538(4)
C(35')-C(38')	1.497(5)
C(35')-C(37')	1.526(5)
C(35')-C(36')	1.540(5)
O(1S)-C(1S)	1.196(5)
C(1S)-C(3S)	1.476(6)
C(1S)-C(2S)	1.487(7)

O(2)-Pd(1)-O(1)	81.79(7)
O(2)-Pd(1)-N(1)	169.91(8)
O(1)-Pd(1)-N(1)	90.13(8)
O(2)-Pd(1)-N(2)	90.99(8)
O(1)-Pd(1)-N(2)	170.25(8)
N(1)-Pd(1)-N(2)	97.70(8)
C(3)-O(1)-Pd(1)	126.44(16)
C(26)-O(2)-Pd(1)	129.92(16)
C(1)-N(1)-C(16)	114.4(2)
C(1)-N(1)-Pd(1)	122.44(18)
C(16)-N(1)-Pd(1)	123.14(16)

C(24)-N(2)-C(23)	114.3(2)
C(24)-N(2)-Pd(1)	122.53(17)
C(23)-N(2)-Pd(1)	123.07(15)
N(1)-C(1)-C(2)	128.4(2)
C(3)-C(2)-C(7)	121.2(2)
C(3)-C(2)-C(1)	122.8(2)
C(7)-C(2)-C(1)	115.9(2)
O(1)-C(3)-C(2)	122.7(2)
O(1)-C(3)-C(4)	120.0(2)
C(2)-C(3)-C(4)	117.2(2)
C(5)-C(4)-C(3)	117.8(2)
C(5)-C(4)-C(8)	121.3(2)
C(3)-C(4)-C(8)	120.6(2)
C(4)-C(5)-C(6)	125.7(2)
C(7)-C(6)-C(5)	116.1(2)
C(7)-C(6)-C(12)	121.7(3)
C(5)-C(6)-C(12)	122.2(2)
C(6)-C(7)-C(2)	121.7(3)
C(11)-C(8)-C(10)	111.4(2)
C(11)-C(8)-C(4)	107.6(2)
C(10)-C(8)-C(4)	111.6(2)
C(11)-C(8)-C(9)	107.3(2)
C(10)-C(8)-C(9)	106.7(2)

C(4)-C(8)-C(9)	112.3(2)
C(14)-C(12)-C(15)	108.8(3)
C(14)-C(12)-C(13)	109.0(3)
C(15)-C(12)-C(13)	106.8(3)
C(14)-C(12)-C(6)	109.6(3)
C(15)-C(12)-C(6)	111.7(2)
C(13)-C(12)-C(6)	110.7(3)
N(1)-C(16)-C(17)	110.0(2)
N(1)-C(16)-C(21)	111.2(2)
C(17)-C(16)-C(21)	109.5(2)
C(22)-C(17)-C(16)	109.0(2)
C(22)-C(17)-C(18)	109.6(2)
C(16)-C(17)-C(18)	108.0(2)
C(17)-C(18)-C(19)	108.9(2)
C(20)-C(19)-C(18)	108.7(2)
C(21)-C(20)-C(23)	111.0(2)
C(21)-C(20)-C(19)	108.5(2)
C(23)-C(20)-C(19)	107.3(2)
C(20)-C(21)-C(16)	108.1(2)
C(17)-C(22)-C(23)	109.1(2)
N(2)-C(23)-C(20)	110.4(2)
N(2)-C(23)-C(22)	112.3(2)
C(20)-C(23)-C(22)	109.6(2)

N(2)-C(24)-C(25)	130.4(2)
C(26)-C(25)-C(30)	120.3(2)
C(26)-C(25)-C(24)	122.6(2)
C(30)-C(25)-C(24)	117.0(2)
O(2)-C(26)-C(25)	122.5(2)
O(2)-C(26)-C(27)	119.9(2)
C(25)-C(26)-C(27)	117.6(2)
C(28)-C(27)-C(26)	118.4(2)
C(28)-C(27)-C(31)	121.9(2)
C(26)-C(27)-C(31)	119.8(2)
C(27)-C(28)-C(29)	125.1(2)
C(30)-C(29)-C(28)	115.8(2)
C(30)-C(29)-C(35)	124.3(2)
C(28)-C(29)-C(35)	119.9(2)
C(29)-C(30)-C(25)	122.3(2)
C(34)-C(31)-C(33)	107.9(2)
C(34)-C(31)-C(27)	112.5(2)
C(33)-C(31)-C(27)	110.1(2)
C(34)-C(31)-C(32)	107.8(2)
C(33)-C(31)-C(32)	109.1(2)
C(27)-C(31)-C(32)	109.5(2)
C(36)-C(35)-C(38)	108.2(3)
C(36)-C(35)-C(29)	111.6(2)

C(38)-C(35)-C(29)	109.1(2)
C(36)-C(35)-C(37)	108.8(2)
C(38)-C(35)-C(37)	109.4(2)
C(29)-C(35)-C(37)	109.6(2)
O(2')-Pd(1')-O(1')	82.78(8)
O(2')-Pd(1')-N(2')	90.13(9)
O(1')-Pd(1')-N(2')	172.84(9)
O(2')-Pd(1')-N(1')	173.74(9)
O(1')-Pd(1')-N(1')	91.03(8)
N(2')-Pd(1')-N(1')	96.08(9)
C(3')-O(1')-Pd(1')	127.18(17)
C(26')-O(2')-Pd(1')	126.94(18)
C(1')-N(1')-C(16')	113.7(2)
C(1')-N(1')-Pd(1')	121.3(2)
C(16')-N(1')-Pd(1')	124.83(17)
C(24')-N(2')-C(23')	114.1(2)
C(24')-N(2')-Pd(1')	121.8(2)
C(23')-N(2')-Pd(1')	124.09(18)
N(1')-C(1')-C(2')	129.4(3)
C(3')-C(2')-C(7')	120.8(2)
C(3')-C(2')-C(1')	122.9(2)
C(7')-C(2')-C(1')	116.0(2)
O(1')-C(3')-C(2')	122.7(2)

O(1')-C(3')-C(4')	119.6(2)
C(2')-C(3')-C(4')	117.7(2)
C(5')-C(4')-C(3')	118.1(2)
C(5')-C(4')-C(8')	121.4(2)
C(3')-C(4')-C(8')	120.5(2)
C(4')-C(5')-C(6')	124.7(2)
C(7')-C(6')-C(5')	116.6(2)
C(7')-C(6')-C(12')	123.7(2)
C(5')-C(6')-C(12')	119.7(2)
C(6')-C(7')-C(2')	121.8(2)
C(10')-C(8')-C(9')	107.6(3)
C(10')-C(8')-C(4')	110.2(2)
C(9')-C(8')-C(4')	111.6(2)
C(10')-C(8')-C(11')	110.8(2)
C(9')-C(8')-C(11')	107.6(3)
C(4')-C(8')-C(11')	109.1(2)
C(13')-C(12')-C(15')	108.0(2)
C(13')-C(12')-C(14')	109.5(2)
C(15')-C(12')-C(14')	108.3(2)
C(13')-C(12')-C(6')	112.3(2)
C(15')-C(12')-C(6')	110.0(2)
C(14')-C(12')-C(6')	108.6(2)
C(17')-C(16')-N(1')	108.5(2)

C(17')-C(16')-C(21')	109.4(2)
N(1')-C(16')-C(21')	112.3(2)
C(16')-C(17')-C(22')	110.1(2)
C(16')-C(17')-C(18')	108.3(3)
C(22')-C(17')-C(18')	108.9(2)
C(19')-C(18')-C(17')	108.6(2)
C(18')-C(19')-C(20')	108.2(2)
C(23')-C(20')-C(21')	110.1(2)
C(23')-C(20')-C(19')	106.4(3)
C(21')-C(20')-C(19')	109.5(3)
C(16')-C(21')-C(20')	108.9(3)
C(23')-C(22')-C(17')	107.7(3)
C(20')-C(23')-N(2')	108.2(3)
C(20')-C(23')-C(22')	110.6(3)
N(2')-C(23')-C(22')	111.8(2)
N(2')-C(24')-C(25')	129.8(3)
C(30')-C(25')-C(26')	120.8(3)
C(30')-C(25')-C(24')	117.0(3)
C(26')-C(25')-C(24')	122.0(3)
O(2')-C(26')-C(25')	122.6(3)
O(2')-C(26')-C(27')	119.5(3)
C(25')-C(26')-C(27')	117.9(2)
C(28')-C(27')-C(26')	117.3(3)

C(28')-C(27')-C(31')	121.8(3)
C(26')-C(27')-C(31')	120.9(2)
C(27')-C(28')-C(29')	125.6(3)
C(30')-C(29')-C(28')	115.4(3)
C(30')-C(29')-C(35')	124.1(3)
C(28')-C(29')-C(35')	120.4(3)
C(29')-C(30')-C(25')	122.6(3)
C(27')-C(31')-C(34')	112.3(2)
C(27')-C(31')-C(33')	109.2(2)
C(34')-C(31')-C(33')	108.0(3)
C(27')-C(31')-C(32')	110.3(2)
C(34')-C(31')-C(32')	107.0(3)
C(33')-C(31')-C(32')	110.0(2)
C(38')-C(35')-C(37')	112.6(3)
C(38')-C(35')-C(29')	109.0(3)
C(37')-C(35')-C(29')	109.6(3)
C(38')-C(35')-C(36')	107.3(3)
C(37')-C(35')-C(36')	106.5(3)
C(29')-C(35')-C(36')	111.8(3)
O(1S)-C(1S)-C(3S)	122.1(5)
O(1S)-C(1S)-C(2S)	120.4(4)
C(3S)-C(1S)-C(2S)	117.5(5)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **22**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2} U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Pd(1)	14(1)	20(1)	17(1)	1(1)	4(1)	1(1)
O(1)	14(1)	36(1)	21(1)	3(1)	3(1)	1(1)
O(2)	18(1)	37(1)	16(1)	1(1)	4(1)	4(1)
N(1)	15(1)	23(1)	21(1)	-2(1)	4(1)	2(1)
N(2)	16(1)	22(1)	18(1)	0(1)	4(1)	0(1)
C(1)	20(1)	28(2)	20(1)	-1(1)	8(1)	3(1)
C(2)	16(1)	28(2)	26(1)	0(1)	8(1)	1(1)
C(3)	17(1)	22(1)	27(1)	1(1)	5(1)	1(1)
C(4)	17(1)	20(1)	30(1)	0(1)	4(1)	2(1)
C(5)	15(1)	31(2)	38(2)	-3(1)	4(1)	-2(1)
C(6)	19(1)	24(2)	38(2)	-2(1)	13(1)	1(1)
C(7)	24(1)	31(2)	26(1)	-4(1)	7(1)	-1(1)
C(8)	16(1)	32(2)	29(2)	-2(1)	1(1)	-1(1)
C(9)	22(2)	73(3)	38(2)	0(2)	-3(1)	-2(2)
C(10)	29(2)	33(2)	32(2)	5(1)	2(1)	1(1)
C(11)	36(2)	31(2)	38(2)	-7(2)	11(1)	-5(2)
C(12)	22(1)	37(2)	41(2)	-7(2)	18(1)	-8(2)
C(13)	34(2)	87(3)	71(3)	29(3)	25(2)	-8(2)

C(14)	38(2)	46(2)	79(3)	-20(2)	35(2)	-8(2)
C(15)	27(2)	61(3)	64(2)	-23(2)	26(2)	-17(2)
C(16)	20(1)	26(2)	23(1)	-4(1)	5(1)	3(1)
C(17)	18(1)	32(2)	19(1)	0(1)	7(1)	-1(1)
C(18)	23(1)	41(2)	20(1)	-1(1)	2(1)	4(2)
C(19)	19(1)	32(2)	22(1)	-4(1)	-1(1)	-1(1)
C(20)	16(1)	27(1)	21(1)	4(1)	4(1)	0(1)
C(21)	21(1)	24(2)	23(1)	-2(1)	1(1)	-1(1)
C(22)	23(1)	20(1)	19(1)	4(1)	5(1)	3(1)
C(23)	16(1)	22(1)	17(1)	3(1)	3(1)	6(1)
C(24)	16(1)	21(2)	25(1)	2(1)	2(1)	1(1)
C(25)	21(1)	21(2)	23(1)	-1(1)	6(1)	-1(1)
C(26)	19(1)	19(2)	20(1)	-1(1)	7(1)	-3(1)
C(27)	21(1)	23(1)	19(1)	-1(1)	4(1)	-2(1)
C(28)	23(1)	27(2)	16(1)	0(1)	4(1)	-4(1)
C(29)	20(1)	24(1)	22(1)	0(1)	7(1)	-1(1)
C(30)	18(1)	25(1)	24(1)	-2(1)	5(1)	-1(1)
C(31)	26(1)	29(2)	19(1)	-1(1)	5(1)	3(1)
C(32)	43(2)	27(2)	26(2)	1(1)	4(1)	8(1)
C(33)	23(1)	42(2)	28(2)	1(1)	4(1)	1(1)
C(34)	31(2)	37(2)	21(1)	3(1)	2(1)	4(1)
C(35)	26(2)	35(2)	23(2)	-4(1)	9(1)	1(1)
C(36)	34(2)	52(2)	32(2)	-2(2)	15(1)	12(2)

C(37)	35(2)	53(2)	41(2)	2(2)	24(1)	-3(2)
C(38)	38(2)	50(2)	39(2)	-20(2)	14(2)	-2(2)
Pd(1')	17(1)	25(1)	21(1)	4(1)	4(1)	3(1)
O(1')	20(1)	55(2)	21(1)	6(1)	5(1)	7(1)
O(2')	19(1)	43(1)	30(1)	-2(1)	6(1)	10(1)
N(1')	26(1)	40(1)	23(1)	4(1)	5(1)	7(1)
N(2')	26(1)	41(2)	26(1)	3(1)	7(1)	11(1)
C(1')	25(1)	44(2)	28(2)	6(1)	13(1)	7(1)
C(2')	22(1)	34(2)	21(1)	6(1)	5(1)	4(1)
C(3')	21(1)	26(2)	26(1)	5(1)	6(1)	5(1)
C(4')	24(1)	24(2)	22(1)	4(1)	7(1)	1(1)
C(5')	25(1)	26(1)	19(1)	2(1)	3(1)	0(1)
C(6')	19(1)	20(1)	24(1)	2(1)	2(1)	2(1)
C(7')	23(1)	26(2)	25(1)	4(1)	10(1)	4(1)
C(8')	25(1)	40(2)	20(1)	-1(1)	7(1)	3(1)
C(9')	37(2)	69(2)	22(1)	-1(2)	11(1)	11(2)
C(10')	36(2)	41(2)	31(2)	3(1)	17(1)	-1(2)
C(11')	33(2)	41(2)	40(2)	-4(2)	10(1)	6(2)
C(12')	19(1)	28(2)	26(1)	-1(1)	2(1)	0(1)
C(13')	20(1)	43(2)	30(2)	-6(1)	1(1)	0(1)
C(14')	32(2)	40(2)	39(2)	9(2)	-2(1)	11(2)
C(15')	33(2)	44(2)	41(2)	-15(2)	9(1)	-9(2)
C(16')	27(2)	36(2)	28(2)	-3(1)	4(1)	6(1)

C(17')	26(2)	41(2)	27(2)	0(1)	4(1)	9(1)
C(18')	35(2)	55(2)	23(2)	4(1)	4(1)	15(2)
C(19')	38(2)	70(3)	24(2)	0(2)	-1(1)	16(2)
C(20')	30(2)	50(2)	32(2)	-2(2)	-6(1)	6(2)
C(21')	32(2)	31(2)	29(2)	-6(1)	-1(1)	3(1)
C(22')	33(2)	37(2)	24(2)	7(1)	10(1)	3(1)
C(23')	31(2)	41(2)	32(2)	10(2)	3(1)	13(2)
C(24')	28(2)	47(2)	28(2)	4(1)	3(1)	8(2)
C(25')	21(1)	30(2)	32(2)	7(1)	4(1)	7(1)
C(26')	18(1)	24(2)	36(2)	4(1)	6(1)	2(1)
C(27')	22(1)	19(1)	37(2)	0(1)	10(1)	-1(1)
C(28')	20(1)	26(2)	45(2)	6(1)	14(1)	0(1)
C(29')	19(1)	26(2)	42(2)	7(1)	6(1)	1(1)
C(30')	24(2)	32(2)	33(2)	9(1)	0(1)	3(1)
C(31')	22(1)	30(2)	37(2)	-3(1)	12(1)	-1(1)
C(32')	27(2)	33(2)	48(2)	-6(2)	14(1)	-5(1)
C(33')	34(2)	38(2)	36(2)	3(1)	7(1)	-5(1)
C(34')	27(2)	49(2)	45(2)	-9(2)	16(1)	-1(2)
C(35')	16(1)	41(2)	45(2)	7(2)	4(1)	3(1)
C(36')	33(2)	75(3)	47(2)	11(2)	2(2)	-4(2)
C(37')	38(2)	66(3)	95(3)	-18(3)	-12(2)	20(2)
C(38')	33(2)	78(3)	69(3)	34(2)	-7(2)	-22(2)
O(1S)	86(2)	54(2)	75(2)	-7(2)	25(2)	11(2)

C(1S)	43(2)	52(3)	89(3)	-32(2)	3(2)	-11(2)
C(2S)	107(4)	46(3)	130(5)	3(3)	11(4)	-19(3)
C(3S)	78(4)	110(5)	160(6)	-84(4)	33(4)	6(3)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for **22**.

	x	y	z	U(eq)
H(1A)	8554	9611	5823	27
H(5A)	5046	9002	4394	34
H(7A)	6936	9169	5771	32
H(9A)	4951	9263	3090	69
H(9B)	4840	10114	3587	69
H(9C)	4728	8555	3597	69
H(10A)	7379	10230	3604	48
H(10B)	6426	11114	3571	48
H(10C)	6529	10207	3088	48
H(11A)	7194	7700	3664	52
H(11B)	6356	7780	3142	52
H(11C)	6133	7121	3659	52
H(13A)	4775	7920	6082	93
H(13B)	5870	8440	6144	93
H(13C)	5526	7145	5811	93
H(14A)	4142	10077	5747	76
H(14B)	4463	10713	5251	76

H(14C)	5228	10620	5799	76
H(15A)	3612	8063	5265	73
H(15B)	4333	7277	4977	73
H(15C)	3899	8660	4752	73
H(16A)	10006	10364	5998	27
H(17A)	10122	8202	6297	27
H(18A)	11767	8185	6737	34
H(18B)	11461	9698	6666	34
H(19A)	12746	9909	6295	31
H(19B)	12812	8360	6205	31
H(20A)	12364	9599	5383	25
H(21A)	10820	10568	5174	28
H(21B)	11320	11107	5745	28
H(22A)	10197	7089	5525	25
H(22B)	11159	6691	5948	25
H(23A)	12015	7357	5387	22
H(24A)	11977	7229	4628	25
H(28A)	10709	7864	2481	26
H(30A)	12387	6749	3851	27
H(32A)	8607	10898	2796	49
H(32B)	9771	10908	2978	49
H(32C)	9118	10361	3363	49
H(33A)	8299	7429	2649	47

H(33B)	7713	8785	2591	47
H(33C)	8215	8245	3160	47
H(34A)	9285	8331	2035	45
H(34B)	9839	9699	2163	45
H(34C)	8673	9661	2005	45
H(36A)	13032	5257	3374	57
H(36B)	13616	6610	3405	57
H(36C)	13686	5568	2958	57
H(37A)	13088	8341	2726	61
H(37B)	12191	8061	2246	61
H(37C)	13197	7288	2289	61
H(38A)	11614	4840	2640	62
H(38B)	12297	5149	2237	62
H(38C)	11291	5923	2194	62
H(1'A)	3551	9388	9950	37
H(5'A)	2751	8809	7799	28
H(7'A)	2278	9133	9252	29
H(9'A)	3827	9534	7344	63
H(9'B)	3616	7994	7303	63
H(9'C)	4582	8570	7155	63
H(10D)	5158	10407	8035	52
H(10E)	5891	9458	7820	52
H(10F)	5849	9430	8427	52

H(11D)	5573	7021	7764	56
H(11E)	4616	6449	7924	56
H(11F)	5504	6975	8367	56
H(13D)	-72	9287	8484	47
H(13E)	823	9914	8894	47
H(13F)	693	8359	8859	47
H(14D)	412	10511	7771	58
H(14E)	1477	10334	7654	58
H(14F)	1340	11129	8160	58
H(15D)	180	8107	7726	59
H(15E)	970	7164	8076	59
H(15F)	1243	7964	7601	59
H(16B)	4482	10007	10647	37
H(17B)	3934	7942	10810	38
H(18C)	4562	9393	11566	45
H(18D)	4512	7878	11721	45
H(19C)	6132	7696	11945	54
H(19D)	6117	9263	11989	54
H(20B)	7163	8817	11414	47
H(21C)	5938	10523	11106	38
H(21D)	6360	9871	10642	38
H(22C)	5135	6217	11123	37
H(22D)	5070	6579	10519	37

H(23B)	6709	6646	11248	42
H(24B)	7984	7061	10955	42
H(28B)	9955	6224	9371	35
H(30B)	9527	7065	10799	37
H(32D)	7605	4492	8846	52
H(32E)	7121	5177	8302	52
H(32F)	6809	5622	8830	52
H(33D)	8304	8300	8574	54
H(33E)	7238	7957	8663	54
H(33F)	7550	7512	8136	54
H(34D)	9500	6489	8555	59
H(34E)	8694	5742	8129	59
H(34F)	9211	5011	8657	59
H(36D)	12031	6625	11050	79
H(36E)	11000	6027	11098	79
H(36F)	11115	7572	11030	79
H(37D)	11211	5041	9833	106
H(37E)	11051	4528	10386	106
H(37F)	12085	5118	10338	106
H(38D)	11376	7545	9718	94
H(38E)	12248	7534	10225	94
H(38F)	11326	8469	10205	94
H(2SA)	1606	1714	4268	145

H(2SB)	2531	827	4235	145
H(2SC)	1455	334	3972	145
H(3SA)	2358	1531	2859	173
H(3SB)	1941	218	3062	173
H(3SC)	3016	712	3326	173

Table 6. Torsion angles [°] for **22**.

O(2)-Pd(1)-O(1)-C(3)	157.9(2)
N(1)-Pd(1)-O(1)-C(3)	-28.2(2)
N(2)-Pd(1)-O(1)-C(3)	115.3(5)
O(1)-Pd(1)-O(2)-C(26)	-179.6(2)
N(1)-Pd(1)-O(2)-C(26)	143.4(4)
N(2)-Pd(1)-O(2)-C(26)	-6.1(2)
O(2)-Pd(1)-N(1)-C(1)	56.2(6)
O(1)-Pd(1)-N(1)-C(1)	19.6(2)
N(2)-Pd(1)-N(1)-C(1)	-154.5(2)
O(2)-Pd(1)-N(1)-C(16)	-121.7(5)
O(1)-Pd(1)-N(1)-C(16)	-158.3(2)
N(2)-Pd(1)-N(1)-C(16)	27.5(2)
O(2)-Pd(1)-N(2)-C(24)	-3.4(2)
O(1)-Pd(1)-N(2)-C(24)	38.6(6)
N(1)-Pd(1)-N(2)-C(24)	-178.3(2)
O(2)-Pd(1)-N(2)-C(23)	-179.8(2)
O(1)-Pd(1)-N(2)-C(23)	-137.8(4)
N(1)-Pd(1)-N(2)-C(23)	5.4(2)
C(16)-N(1)-C(1)-C(2)	174.2(3)
Pd(1)-N(1)-C(1)-C(2)	-4.0(4)
N(1)-C(1)-C(2)-C(3)	-14.5(5)

N(1)-C(1)-C(2)-C(7)	168.8(3)
Pd(1)-O(1)-C(3)-C(2)	19.6(4)
Pd(1)-O(1)-C(3)-C(4)	-161.01(18)
C(7)-C(2)-C(3)-O(1)	-177.5(3)
C(1)-C(2)-C(3)-O(1)	6.1(4)
C(7)-C(2)-C(3)-C(4)	3.1(4)
C(1)-C(2)-C(3)-C(4)	-173.4(3)
O(1)-C(3)-C(4)-C(5)	176.1(2)
C(2)-C(3)-C(4)-C(5)	-4.5(4)
O(1)-C(3)-C(4)-C(8)	0.8(4)
C(2)-C(3)-C(4)-C(8)	-179.7(2)
C(3)-C(4)-C(5)-C(6)	1.7(4)
C(8)-C(4)-C(5)-C(6)	176.9(3)
C(4)-C(5)-C(6)-C(7)	2.7(4)
C(4)-C(5)-C(6)-C(12)	-178.7(3)
C(5)-C(6)-C(7)-C(2)	-4.2(4)
C(12)-C(6)-C(7)-C(2)	177.2(3)
C(3)-C(2)-C(7)-C(6)	1.4(4)
C(1)-C(2)-C(7)-C(6)	178.1(3)
C(5)-C(4)-C(8)-C(11)	-105.6(3)
C(3)-C(4)-C(8)-C(11)	69.5(3)
C(5)-C(4)-C(8)-C(10)	132.0(3)
C(3)-C(4)-C(8)-C(10)	-52.9(3)

C(5)-C(4)-C(8)-C(9)	12.3(4)
C(3)-C(4)-C(8)-C(9)	-172.6(3)
C(7)-C(6)-C(12)-C(14)	83.7(4)
C(5)-C(6)-C(12)-C(14)	-94.8(3)
C(7)-C(6)-C(12)-C(15)	-155.5(3)
C(5)-C(6)-C(12)-C(15)	26.0(4)
C(7)-C(6)-C(12)-C(13)	-36.7(4)
C(5)-C(6)-C(12)-C(13)	144.8(3)
C(1)-N(1)-C(16)-C(17)	89.6(3)
Pd(1)-N(1)-C(16)-C(17)	-92.3(2)
C(1)-N(1)-C(16)-C(21)	-148.8(2)
Pd(1)-N(1)-C(16)-C(21)	29.3(3)
N(1)-C(16)-C(17)-C(22)	52.8(3)
C(21)-C(16)-C(17)-C(22)	-69.7(3)
N(1)-C(16)-C(17)-C(18)	171.8(2)
C(21)-C(16)-C(17)-C(18)	49.3(3)
C(22)-C(17)-C(18)-C(19)	49.1(3)
C(16)-C(17)-C(18)-C(19)	-69.5(3)
C(17)-C(18)-C(19)-C(20)	17.2(3)
C(18)-C(19)-C(20)-C(21)	50.0(3)
C(18)-C(19)-C(20)-C(23)	-70.0(3)
C(23)-C(20)-C(21)-C(16)	47.6(3)
C(19)-C(20)-C(21)-C(16)	-70.1(3)

N(1)-C(16)-C(21)-C(20)	-104.5(2)
C(17)-C(16)-C(21)-C(20)	17.3(3)
C(16)-C(17)-C(22)-C(23)	50.9(3)
C(18)-C(17)-C(22)-C(23)	-67.1(3)
C(24)-N(2)-C(23)-C(20)	104.0(3)
Pd(1)-N(2)-C(23)-C(20)	-79.4(2)
C(24)-N(2)-C(23)-C(22)	-133.4(2)
Pd(1)-N(2)-C(23)-C(22)	43.2(3)
C(21)-C(20)-C(23)-N(2)	57.9(3)
C(19)-C(20)-C(23)-N(2)	176.30(19)
C(21)-C(20)-C(23)-C(22)	-66.3(3)
C(19)-C(20)-C(23)-C(22)	52.1(3)
C(17)-C(22)-C(23)-N(2)	-109.6(3)
C(17)-C(22)-C(23)-C(20)	13.4(3)
C(23)-N(2)-C(24)-C(25)	-175.6(3)
Pd(1)-N(2)-C(24)-C(25)	7.8(4)
N(2)-C(24)-C(25)-C(26)	-2.7(4)
N(2)-C(24)-C(25)-C(30)	176.6(3)
Pd(1)-O(2)-C(26)-C(25)	12.1(4)
Pd(1)-O(2)-C(26)-C(27)	-166.83(18)
C(30)-C(25)-C(26)-O(2)	172.8(2)
C(24)-C(25)-C(26)-O(2)	-7.9(4)
C(30)-C(25)-C(26)-C(27)	-8.2(4)

C(24)-C(25)-C(26)-C(27)	171.0(2)
O(2)-C(26)-C(27)-C(28)	-173.3(2)
C(25)-C(26)-C(27)-C(28)	7.8(4)
O(2)-C(26)-C(27)-C(31)	7.7(4)
C(25)-C(26)-C(27)-C(31)	-171.3(2)
C(26)-C(27)-C(28)-C(29)	-2.6(4)
C(31)-C(27)-C(28)-C(29)	176.4(3)
C(27)-C(28)-C(29)-C(30)	-2.3(4)
C(27)-C(28)-C(29)-C(35)	177.4(3)
C(28)-C(29)-C(30)-C(25)	1.9(4)
C(35)-C(29)-C(30)-C(25)	-177.8(3)
C(26)-C(25)-C(30)-C(29)	3.4(4)
C(24)-C(25)-C(30)-C(29)	-175.9(3)
C(28)-C(27)-C(31)-C(34)	-3.7(4)
C(26)-C(27)-C(31)-C(34)	175.3(2)
C(28)-C(27)-C(31)-C(33)	116.7(3)
C(26)-C(27)-C(31)-C(33)	-64.3(3)
C(28)-C(27)-C(31)-C(32)	-123.4(3)
C(26)-C(27)-C(31)-C(32)	55.6(3)
C(30)-C(29)-C(35)-C(36)	0.1(4)
C(28)-C(29)-C(35)-C(36)	-179.6(3)
C(30)-C(29)-C(35)-C(38)	119.6(3)
C(28)-C(29)-C(35)-C(38)	-60.0(3)

C(30)-C(29)-C(35)-C(37)	-120.5(3)
C(28)-C(29)-C(35)-C(37)	59.9(3)
O(2')-Pd(1')-O(1')-C(3')	158.5(2)
N(2')-Pd(1')-O(1')-C(3')	150.8(7)
N(1')-Pd(1')-O(1')-C(3')	-22.4(2)
O(1')-Pd(1')-O(2')-C(26')	154.7(2)
N(2')-Pd(1')-O(2')-C(26')	-26.3(2)
N(1')-Pd(1')-O(2')-C(26')	146.6(9)
O(2')-Pd(1')-N(1')-C(1')	27.1(12)
O(1')-Pd(1')-N(1')-C(1')	19.1(3)
N(2')-Pd(1')-N(1')-C(1')	-160.1(3)
O(2')-Pd(1')-N(1')-C(16')	-156.6(9)
O(1')-Pd(1')-N(1')-C(16')	-164.7(3)
N(2')-Pd(1')-N(1')-C(16')	16.2(3)
O(2')-Pd(1')-N(2')-C(24')	21.8(3)
O(1')-Pd(1')-N(2')-C(24')	29.4(10)
N(1')-Pd(1')-N(2')-C(24')	-157.4(3)
O(2')-Pd(1')-N(2')-C(23')	-159.8(2)
O(1')-Pd(1')-N(2')-C(23')	-152.3(7)
N(1')-Pd(1')-N(2')-C(23')	20.9(3)
C(16')-N(1')-C(1')-C(2')	177.4(3)
Pd(1')-N(1')-C(1')-C(2')	-6.0(5)
N(1')-C(1')-C(2')-C(3')	-14.0(6)

N(1')-C(1')-C(2')-C(7')	172.9(3)
Pd(1')-O(1')-C(3')-C(2')	10.8(4)
Pd(1')-O(1')-C(3')-C(4')	-170.7(2)
C(7')-C(2')-C(3')-O(1')	-175.9(3)
C(1')-C(2')-C(3')-O(1')	11.4(5)
C(7')-C(2')-C(3')-C(4')	5.6(5)
C(1')-C(2')-C(3')-C(4')	-167.2(3)
O(1')-C(3')-C(4')-C(5')	175.7(3)
C(2')-C(3')-C(4')-C(5')	-5.7(4)
O(1')-C(3')-C(4')-C(8')	-4.4(4)
C(2')-C(3')-C(4')-C(8')	174.2(3)
C(3')-C(4')-C(5')-C(6')	1.4(5)
C(8')-C(4')-C(5')-C(6')	-178.4(3)
C(4')-C(5')-C(6')-C(7')	3.1(5)
C(4')-C(5')-C(6')-C(12')	-179.5(3)
C(5')-C(6')-C(7')-C(2')	-3.3(4)
C(12')-C(6')-C(7')-C(2')	179.5(3)
C(3')-C(2')-C(7')-C(6')	-1.1(5)
C(1')-C(2')-C(7')-C(6')	172.2(3)
C(5')-C(4')-C(8')-C(10')	122.7(3)
C(3')-C(4')-C(8')-C(10')	-57.2(4)
C(5')-C(4')-C(8')-C(9')	3.3(4)
C(3')-C(4')-C(8')-C(9')	-176.5(3)

C(5')-C(4')-C(8')-C(11')	-115.4(3)
C(3')-C(4')-C(8')-C(11')	64.7(3)
C(7')-C(6')-C(12')-C(13')	-6.9(4)
C(5')-C(6')-C(12')-C(13')	175.9(3)
C(7')-C(6')-C(12')-C(15')	-127.3(3)
C(5')-C(6')-C(12')-C(15')	55.5(4)
C(7')-C(6')-C(12')-C(14')	114.3(3)
C(5')-C(6')-C(12')-C(14')	-62.9(3)
C(1')-N(1')-C(16')-C(17')	89.2(3)
Pd(1')-N(1')-C(16')-C(17')	-87.3(3)
C(1')-N(1')-C(16')-C(21')	-149.8(3)
Pd(1')-N(1')-C(16')-C(21')	33.7(4)
N(1')-C(16')-C(17')-C(22')	54.1(3)
C(21')-C(16')-C(17')-C(22')	-68.8(3)
N(1')-C(16')-C(17')-C(18')	173.0(2)
C(21')-C(16')-C(17')-C(18')	50.2(3)
C(16')-C(17')-C(18')-C(19')	-72.0(3)
C(22')-C(17')-C(18')-C(19')	47.7(4)
C(17')-C(18')-C(19')-C(20')	19.6(4)
C(18')-C(19')-C(20')-C(23')	-72.5(3)
C(18')-C(19')-C(20')-C(21')	46.4(4)
C(17')-C(16')-C(21')-C(20')	16.3(3)
N(1')-C(16')-C(21')-C(20')	-104.2(3)

C(23')-C(20')-C(21')-C(16')	48.4(3)
C(19')-C(20')-C(21')-C(16')	-68.3(3)
C(16')-C(17')-C(22')-C(23')	50.5(3)
C(18')-C(17')-C(22')-C(23')	-68.1(3)
C(21')-C(20')-C(23')-N(2')	56.0(3)
C(19')-C(20')-C(23')-N(2')	174.6(2)
C(21')-C(20')-C(23')-C(22')	-66.7(3)
C(19')-C(20')-C(23')-C(22')	51.9(3)
C(24')-N(2')-C(23')-C(20')	87.3(3)
Pd(1')-N(2')-C(23')-C(20')	-91.2(3)
C(24')-N(2')-C(23')-C(22')	-150.7(3)
Pd(1')-N(2')-C(23')-C(22')	30.9(4)
C(17')-C(22')-C(23')-C(20')	14.8(3)
C(17')-C(22')-C(23')-N(2')	-105.8(3)
C(23')-N(2')-C(24')-C(25')	173.3(3)
Pd(1')-N(2')-C(24')-C(25')	-8.3(5)
N(2')-C(24')-C(25')-C(30')	172.3(3)
N(2')-C(24')-C(25')-C(26')	-12.4(6)
Pd(1')-O(2')-C(26')-C(25')	15.1(4)
Pd(1')-O(2')-C(26')-C(27')	-168.20(19)
C(30')-C(25')-C(26')-O(2')	-176.1(3)
C(24')-C(25')-C(26')-O(2')	8.8(5)
C(30')-C(25')-C(26')-C(27')	7.1(4)

C(24')-C(25')-C(26')-C(27')	-168.0(3)
O(2')-C(26')-C(27')-C(28')	177.3(3)
C(25')-C(26')-C(27')-C(28')	-5.8(4)
O(2')-C(26')-C(27')-C(31')	-0.9(4)
C(25')-C(26')-C(27')-C(31')	175.9(3)
C(26')-C(27')-C(28')-C(29')	0.8(4)
C(31')-C(27')-C(28')-C(29')	179.0(3)
C(27')-C(28')-C(29')-C(30')	3.1(4)
C(27')-C(28')-C(29')-C(35')	-178.3(3)
C(28')-C(29')-C(30')-C(25')	-1.9(4)
C(35')-C(29')-C(30')-C(25')	179.6(3)
C(26')-C(25')-C(30')-C(29')	-3.2(5)
C(24')-C(25')-C(30')-C(29')	172.1(3)
C(28')-C(27')-C(31')-C(34')	6.5(4)
C(26')-C(27')-C(31')-C(34')	-175.4(3)
C(28')-C(27')-C(31')-C(33')	-113.3(3)
C(26')-C(27')-C(31')-C(33')	64.9(3)
C(28')-C(27')-C(31')-C(32')	125.7(3)
C(26')-C(27')-C(31')-C(32')	-56.2(3)
C(30')-C(29')-C(35')-C(38')	-115.6(4)
C(28')-C(29')-C(35')-C(38')	66.0(4)
C(30')-C(29')-C(35')-C(37')	120.7(4)
C(28')-C(29')-C(35')-C(37')	-57.7(4)

C(30')-C(29')-C(35')-C(36')	2.9(4)
C(28')-C(29')-C(35')-C(36')	-175.5(3)

Symmetry transformations used to generate equivalent atoms: