AN ABSTRACT OF THE DISSERTATION OF

Rajan Juniku for the degree of Doctor of Philosophy in Chemistry presented June 5, 2012.

Title:

Part I: Synthesis and Evaluation of Synosutine as an Inhibitor of Serotonin, Norepinephrine, and Dopamine Transporters

Part II: Asymmetric Approach to the Tetracyclic Core of Neomangicol A

Abstract approved: _____

James D. White

Part I: Racemic and asymmetric syntheses of a new substance with prospective antidepressant properties were achieved. *In vitro* assays with synthetic racemates (±)-**25** and (±)-**26** suggested that the former is a relatively selective inhibitor of serotonin transporter whereas the latter is a more balanced inhibitor of both serotonin and norepinephrine transporter. An initial approach to enantiomers of **25** and **26** via resolution of carboxylic acids **21** and **22** was unsuccessful but a *de novo* strategy which introduced asymmetry by means of Charette enantioselective cyclopropanation led to (+)-**25**, (-)-**25**, (+)-**26** and (-)-**26**. *In vitro* assays with (+)-**26**, now known as synosutine (synthesis/OSU), indicate that this substance is a highly effective dual inhibitor of serotonin and norepinephrine transporter. With IC_{50} and K_i values in the 1-2 nM range, (+)-**26** compares favorably with Eli Lilly's duloxetine (Cymbalta®) as a dual reuptake inhibitor of serotonin and norepinephrine and is thus a potential candidate for development as a drug for treatment of clinical depression. Synosutine

was also assayed *in vivo* for its binding to human monoamine transporters. These studies indicate that synosutine, with a K_i of 1.2 nM for norepinephrine and 2.1 nM for serotonin, is a more balanced inhibitor than duloxetin.

Part II: Synthetic studies towards the tetracyclic core structure of neomangicol A (**129**) led to advanced intermediate **245** which bears rings A and D of the neomangicol nucleus. This bicylic enone carries the correct stereochemical imprint for tetracycle **129** at C5, C6 and C14 and it contains all of carbon atoms needed to assemble the remaining two rings. Synthesis of bicyclic lactone **170**, the precursor for ring A, was accomplished from the monoterpene (*S*)-(+)-carvone via radical cyclization and a series of Baeyer-Villiger oxidations as the key steps. Alkylation of **170** with alkyl iodide **217**, obtained from the monoterpene (*S*)-(-)-citronellol furnished advanced intermediate **218** which was converted into diene **244**. Ring closing metathesis of **244** with Grubbs-Hoveyda second generation catalyst afforded **245**. Exploratory functionalization of **245** was carried out for the purpose of assembling rings B and C of the complete neomangicol skeleton.

Part I: Synthesis and Evaluation of Synosutine as an Inhibitor of Serotonin, Norepinephrine, and Dopamine Transporters

Part II: Asymmetric Approach to the Tetracyclic Core of Neomangicol A

by

Rajan Juniku

A DISSERTATION

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degree of

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Doctor of Philosophy dissertation of Rajan Juniku presented on June 5, 2012

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.

Rajan Juniku, Author

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Dedicated to Doruntina E. Juniku, my daughter and favorite natural product, to my wife, Alicia M. Juniku, and to my family residing both in Europe and United States.

PART I

Synthesis and evaluation of synosutine as an inhibitor of serotonin, norepinephrine, and dopamine transporters

CHAPTER 1

1.1 Neurons and their networking – the brain domain

The nervous system is a complex assembly of two kinds of cells: neurons and glia (or neuroglia).[1] Neurons are separated from the outside environment by a selectively permeable membrane, a double layered strip of phospholipids which are arranged in such manner that their polar termini are pointing outwards rendering them hydrophobic. Membranes filter traffic between the outside world and the interior of the cell through proteins which serve as transporters of specific chemicals needed for the survival and growth of the cell (Fig 1).

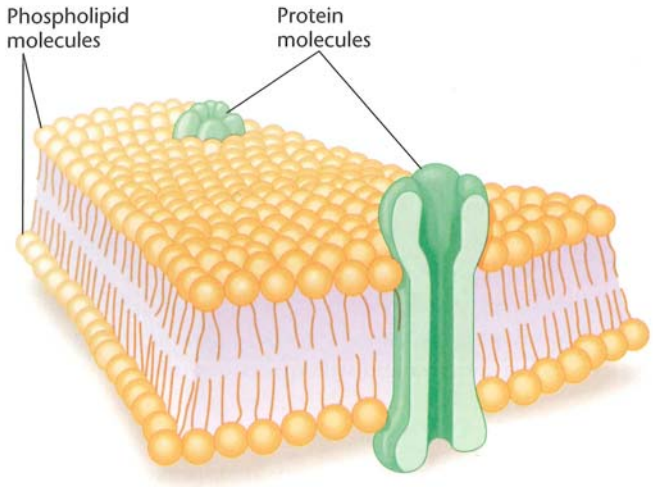


Fig 1. The structure of a cell membrane (From KALAT. *Biological Psychology*, 10E. © 2009 Wadsworth, a part of Cengage Learning, Inc. Reproduced by permission)

Neurons consist of a cell body (soma), an axon, dendrites and presynaptic terminals (Fig 2). Neurons stand out compared to other cells mainly for two reasons: their shape and their function. A unique feature of neurons is their ability to communicate with other neurons and to store chemical information which accounts for

memory storage, learning, consciousness, and many other essential functions. To perform these tasks, neurons are structurally and functionally polarized.

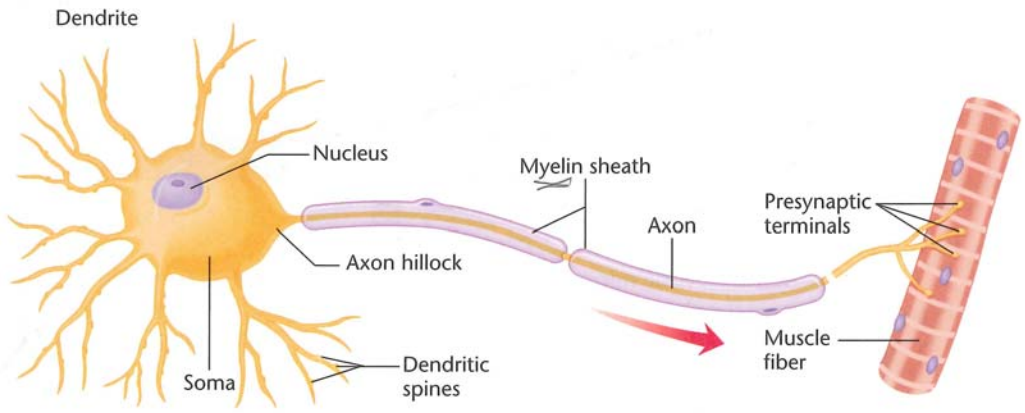


Fig 2. The structure of a neuron (From KALAT. *Biological Psychology*, 10E. © 2009 Wadsworth, a part of Cengage Learning, Inc. Reproduced by permission)

A crucial structural part of the neuron for signal transmission between neurons is the presynaptic terminal. It is in this particular location that the presynaptic neuron releases special chemicals of paramount importance to communication, known as neurotransmitters. These neurotransmitters will be received by a neighboring neuron (the postsynaptic neuron) triggering an action potential. At that moment, the postsynaptic neuron synthesizes neurotransmitters (specifically neuropeptides) in the cell membrane and transports them to the synaptic terminal. However, some neurotransmitters are synthesized in the presynaptic terminal. At the same time, action potentials will be traveling down the axon through sodium-potassium channels. At the synaptic terminal, action potentials will cause the opening of voltage dependent channels (so called L-type channels) which enables calcium ions to enter the cell. The

increase of calcium(II) concentration in the presynaptic terminal is the major process that causes the release of neurotransmitters from the terminal into the synaptic cleft, the medium between the presynaptic and postsynaptic neurons. The released neurotransmitters will diffuse across the cleft and attach to the receptors (proteins embedded in the membrane) of the postsynaptic neuron. The binding of the neurotransmitter to the receptor, depending on the neurotransmitter, may either cause the opening of a channel, known as an ionotropic effect, or it can cause a more complicated and longer effect known as a metabotropic effect. After these events, neurotransmitters will separate from their receptors and will drift back to the synaptic cleft. Alternatively, they may continue exciting or inhibiting the receptor (Fig 3).

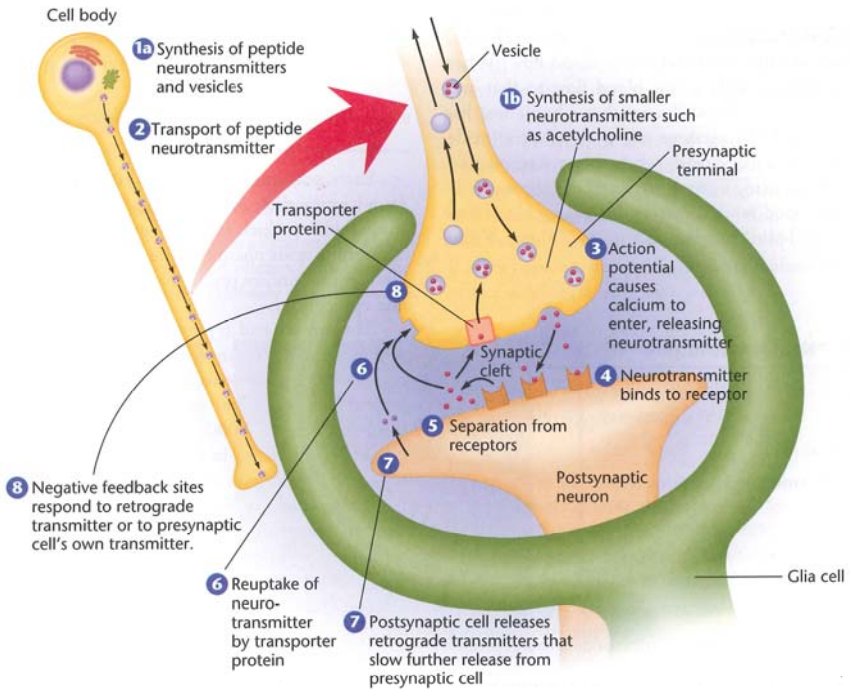


Fig 3. Events when neurotransmitters are released from the presynaptic neuron (From KALAT. *Biological Psychology*, 10E. © 2009 Wadsworth, a part of Cengage Learning, Inc. Reproduced by permission)

The released neurotransmitter, depending on its function, may be metabolized into an inactive chemical or recycled to the neuron that released it to be used again. After it activates its receptor, the neurotransmitter acetylcholine (**1**) is metabolized into choline and acetate by the enzyme acetylcholinesterase. Choline is diffused back to the presynaptic neuron, converted again into acetylcholine and then reused. There are known drugs that inhibit acetylcholinesterase which impair acetylcholine transmission and provide relief for certain symptoms associated with diseases such myasthenia gravis. On the other hand, transmitters such as serotonin (**2**) and the catecholamines (norepinephrine (**3**) epinephrine (**4**) and dopamine (**5**)) are not converted into inactive species at the postsynaptic membrane but instead break free from the receptor on the postsynaptic neuron (Fig 4).[2]

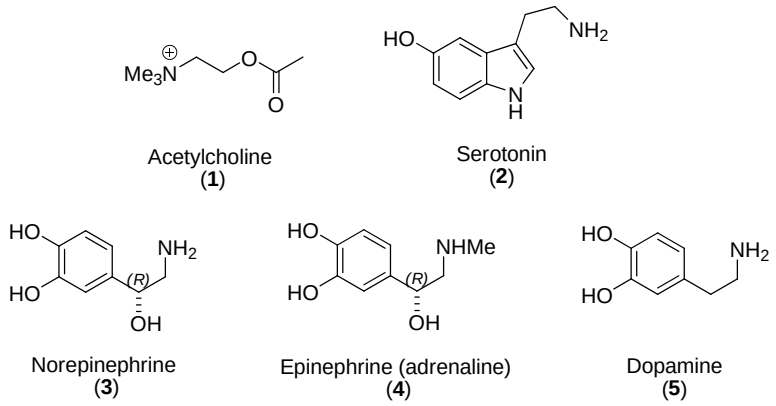


Fig 4. Some neurotransmitters

Depending on the area of the brain, presynaptic neurons collect most of the released neurotransmitters and reuse them. This process is called reuptake and it takes place at uniquely designed membrane proteins called transporters. In some brain areas, few transporters are available and reuptake is slow. If dopamine is released too rapidly

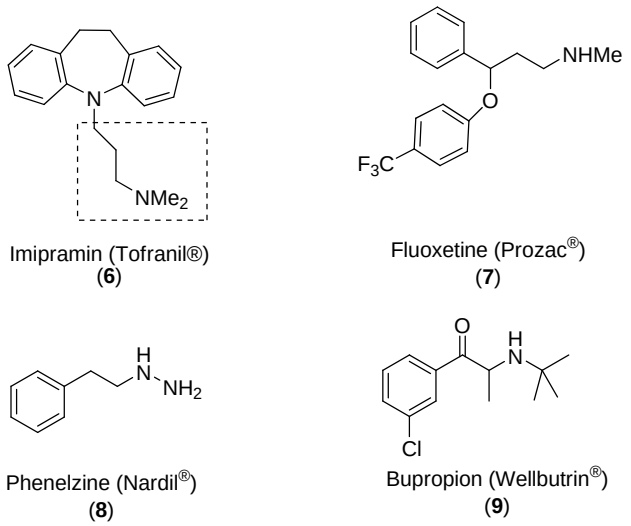
in these areas, large amounts of neurotransmitters begin to accumulate. An enzyme called catechol-O-methyltransferase (COMT) then catalyzes conversion of the excess dopamine into inactive chemicals. Neuropeptides, another class of neurotransmitters, are neither rendered inactive or reabsorbed, but are simply diffused away. Due to their large molecular mass, these neurotransmitters are biosynthesized slowly and a neuron can temporarily exhaust its supply.

1.2 Major depression disorder and antidepressant drugs

Major depression disorder is a serious health problem that is estimated to affect 17 % of the population in the USA during their lifetime.[3] Depression is currently the fourth leading cause of diseases and disability worldwide.[4] First line treatment for depression usually entails administration of an antidepressant or combination thereof. Antidepressant drugs can be categorized into four groups: (1) tricyclic antidepressants (TCA), (2) selective serotonin reuptake inhibitors (SSRI), (3) monoamine oxidase inhibitors (MAOI), and (4) atypical antidepressants (AA).[5]

TCAs, such as Imipramin (Tofranil®) (**6**), have a mode of action which consists of blocking the transport proteins that reabsorb serotonin, dopamine, and norepinephrine into the presynaptic neuron after their release. As a consequence, the presence of neurotransmitters in the synaptic cleft is prolonged and the stimulus on the postsynaptic neuron is continued. It has been shown that the amine side chain (in the dotted square) (Fig 5) is crucial for pharmacological activity. TCAs also block histamine receptors, acetylcholine receptors and certain sodium channels causing many side effects. For this reason, TCAs have been largely replaced by SSRIs.[6]

Fluoxetine (Prozac®) (**7**),[7] a SSRI which operates in a similar way to TCAs is specific to the neurotransmitter serotonin. SSRIs cause fewer side effects than TCAs, but their effectiveness is about the same. Although SSRIs are known to be safer than TCAs, they are not devoid of side effects. MAIOs, such as Phenelzine (Nardil®) (**8**), block the enzyme monoamine oxidase which is responsible for oxidizing serotonin and catecholamines to inactive chemicals. AAs comprise a miscellaneous class of compounds – *ie* any drug other than the three types mentioned above. An example is Bupropion (Wellbutrin®) (**9**), which is a dopamine and to some extent a norepinephrine but not a serotonin reuptake inhibitor.



Imipramin (Tofranil®) (**6**)

Fluoxetine (Prozac®) (**7**)

Phenelzine (Nardil®) (**8**)

Bupropion (Wellbutrin®) (**9**)

Fig 5. Examples of different types of antidepressant drugs

1.3 Designing new antidepressant drugs - dual reuptake inhibitors[8]

Current medications for the treatment of depression have limited efficacy and are often characterized by delayed onset of therapeutic action.[9] SSRIs have emerged as a class of antidepressant drugs with comparable effectiveness to the early generation of tricyclic antidepressant (TCA) drugs. The rate of response by patients to SSRIs and TCAs is similar (60-70 %) and the rate of remission is between 30-40 %. The onset of the therapeutic effects of these two classes of antidepressant drugs is comparable and takes 2-4 weeks to appear. A large body of ongoing research is attempting to address antidepressant efficacy and the onset of action.[10]

Several studies have suggested that combining SSRIs with norepinephrine transporter inhibitors in a depressed patient may provide better therapeutic response and faster onset of action. This has led to the development of dual reuptake inhibitors of serotonin and norepinephrine, which simultaneously activate both pathways and have a more rapid and robust antidepressant effect. Examples of dual reuptake inhibitors are Duloxetine (Cymbalta®) (**10**) and Milnacipran (Ixel®)[11] (**11**), the former being proven to be effective in clinical trials for treatment of severe depression. It is important to note that subtle changes in the chemical properties of the antidepressant drugs leads to a change from a SSRI, *eg* Fluoxetine (Prozac®) (**13**), to a selective norepinephrine reuptake inhibitor, *eg* Atomoxetine. Both drugs have a common 1,3-propanolamine moiety (**12**), but the former has an electron-poor benzene ring whereas the latter has a more electron-rich benzene ring. By contrast, Milnacipran (Ixel®), which is a moderate SSRI, features a cyclopropane ring. It has been shown that

modification of functional groups in Milnacipran does not improve its activity for the NMDA receptors.[12] However, designing conformationaly more restricted analogs of Milnacipran (Ixel®) improved activity.[13] By the same token, it was envisioned that incorporating a cyclopropane ring into Duloxetine (Cymbalta®) would increase binding to serotonin and norepinephrine receptors (Fig 6). This new structure, designated synosutine, would resemble that of a TCA and thus might have binding activity toward dopamine as well, thereby generating a drug that is a triple reuptake inhibitor but with fewer side effects than a SSRI.

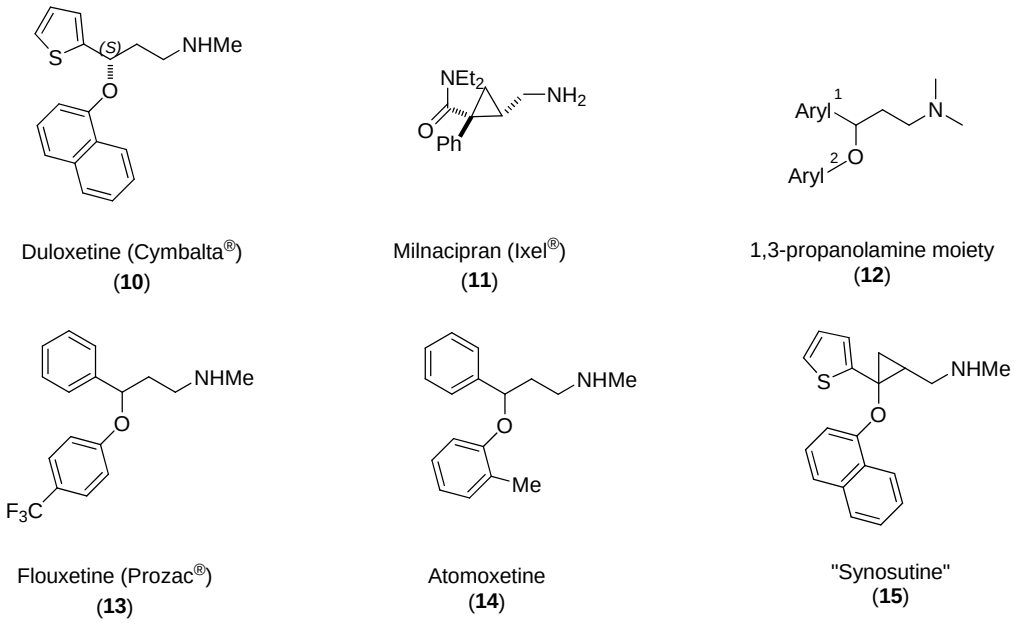


Fig 6. Designing new reuptake inhibitors

These considerations led to a plan to synthesize in racemic form (*E*) and (*Z*) trisubstituted cyclopropanes bearing a 1-naphthyloxy and a 2-thiophenyl substituent at C1 and a (*N*-methylamino)methylene group at C2. After evaluation of these candidates

as inhibitors of serotonin and norepinephrine transporters, one or both of the isomers would be synthesized in enantiomerically pure form. We anticipated that substances based on this structural design would be effective reuptake inhibitors of serotonin and norepinephrine and perhaps also dopamine.

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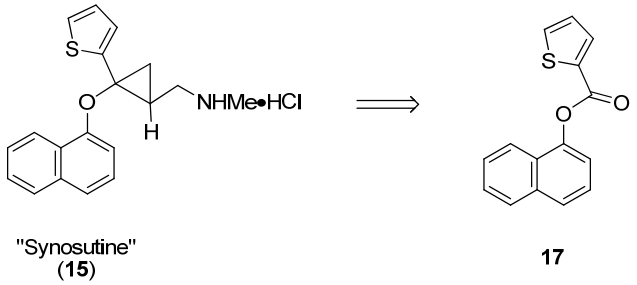
CHAPTER 2

2. Synthesis of Synosutine

The structural design of the proposed inhibitor synosutine laid out in the previous chapter led to a consideration of various strategies for its synthesis.[1] First, a racemic synthesis of synosutine was planned using cyclopropanation of the alkene generated from methylenation of known ester **17**[2] as a key step. Subsequently, a plethora of examples of asymmetric cyclopropanation techniques could pave the way to synthesis of enantiopure stereoisomers of synosutine if classical resolution of the racemic mixture should not be fruitful (Scheme 1).

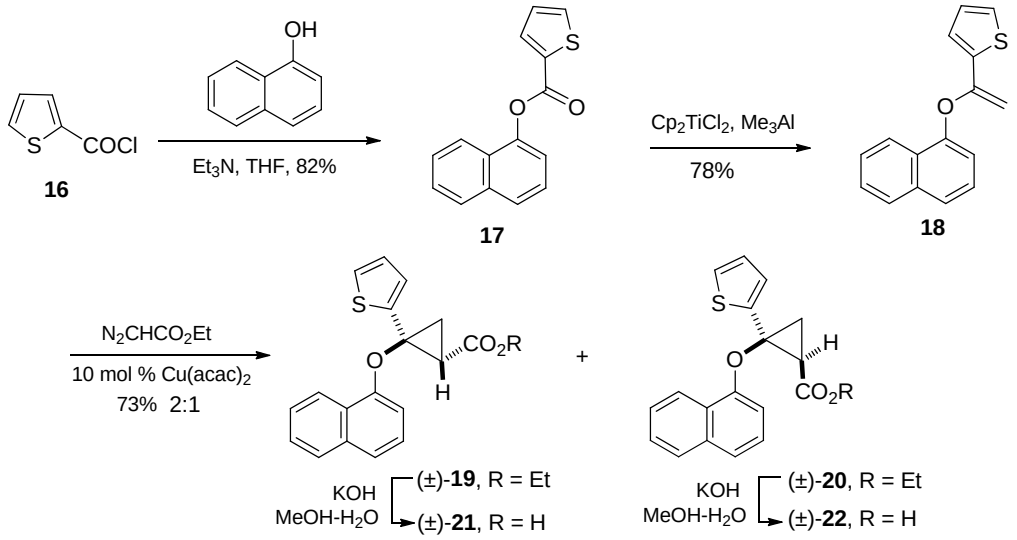


Scheme 1. Synthetic plan for synthesis of "Synosutine"

2.1 Racemic synthesis of 25 and 26

The route to racemic diastereomers of synosutine commenced with coupling of thiophen-2-carbonyl chloride (**16**) with 1-naphthol to give **17**, an esterefication that proceeded in high yield. Tebbe methylenation[3] of **17** furnished enol ether **18** which underwent cyclopropanation[4] with ethyl diazoacetate in the presence of 10 mol% of copper(II) acetylacetonate to yield a 2:1 mixture of (*E*)- and (*Z*)-cyclopropyl esters **19**

and **20**, respectively. The isomers, which were not separated, were taken forward by saponification of the mixture to provide a 2:1 mixture of (*E*)- and (*Z*)-carboxylic acids **21** and **22** (Scheme 2).



Scheme 2. Racemic synthesis of (*E*) and (*Z*) carboxylic acids **21** and **22**

The carboxylic acids were obtained in pure form by fractional crystallization and an X–ray crystallographic structure determination of **22** established that this acid possessed (Z) configuration (Fig 7).[5]

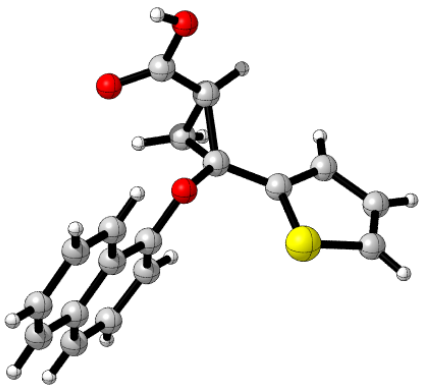
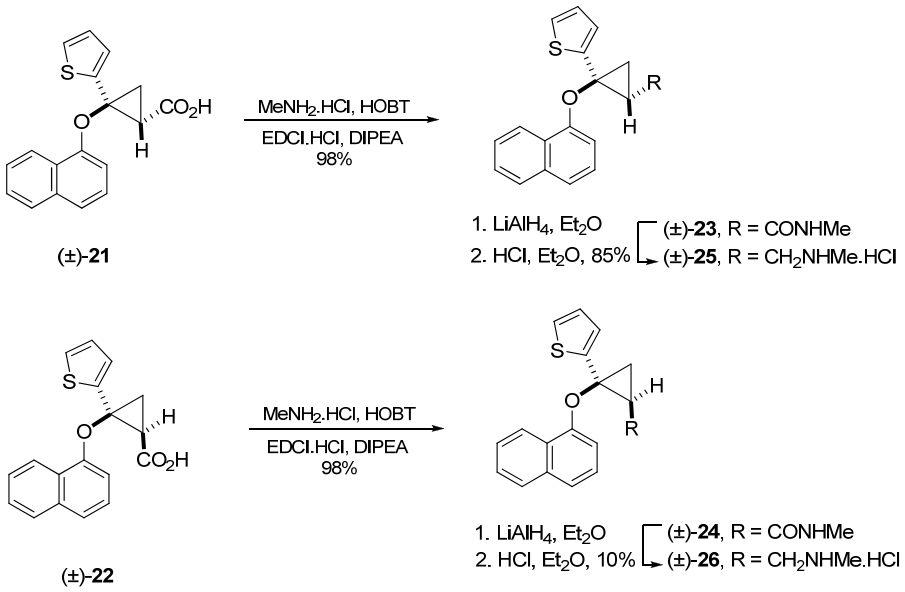


Fig 7. X-ray crystal structure of (Z)-carboxylic acid **22**

The carboxylic acids **21** and **22** were advanced separately to *N*-methyl amides **23** and **24** which were reduced to the corresponding secondary amines with lithium aluminum hydride. In each case, the amines were characterized and assayed for bioactivity as their hydrochloride salts **25** and **26** (Scheme 3).

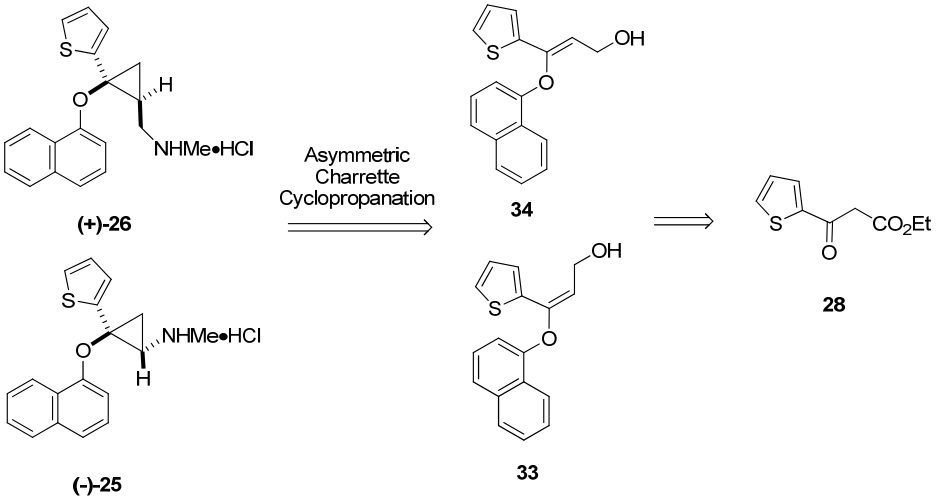


Scheme 3. Racemic synthesis of (*E*) and (*Z*) trisubstituted cyclopropanes **25** and **26**

2.2 Asymmetric synthesis of (-)-25, (+)-25, (-)-26, (+)-26

The favorable *in vitro* assays obtained with racemates **25** and **26** (Chapter 3) persuaded us to prepare these substances in enantiomerically pure form. Our initial approach via resolution of carboxylic acids **21** and **22** was unsuccessful, the diastereomeric salts of these acids obtained with several chiral bases, including (-)-brucine and α-methylbenzyl amines being inseparable by fractional crystallization. Therefore, a *de novo* approach to enantiomers of **25** and **26** was devised which

introduced asymmetry by means of Charette enantioselective cyclopropanation.[6] Retrosynthetically, Charette cyclopropanation of allyl alcohols **33** and **34** would furnish enantiopure cyclopropane **25** and **26**, respectively. The allyl alcohols could, in principle, be accessed from β-ketoester **28** (Scheme 4).



Scheme 4. Synthetic plan for asymmetric synthesis of Synosutine

The asymmetric route to synosutine began from 2-acetylthiophene (**27**) which was condensed with diethyl carbonate to give β-keto ester **28** (Scheme 5).[7] Exposure of **28** to a basic solution of triflic anhydride produced a 1:1 mixture of (*E*)- and (*Z*)-enol triflates **29** and **30**, respectively,[8] which was reacted with 1-naphthol in the presence of copper(I) chloride and cesium carbonate to afford enol ethers **31** and **32**. The latter were separated and obtained pure by careful column chromatography.[9] Reduction of esters **31** and **32** gave (*E*)- and (*Z*)-allylic alcohols **33** and **34**, respectively, each of which was taken forward as a substrate for Charette asymmetric cyclopropanation. This reaction was carried out with diiodomethane and diethylzinc in the presence of a stoichiometric quantity of the (*S*,*S*)-tartrate derived boronate **35** and

produced (*E*)- and (*Z*)-cyclopropylmethanols (-)-**36** and (+)-**37**, as single enantiomers according to the ^{13}C and ^{19}F nuclear magnetic resonance spectroscopic data of the Mosher ester of (-)-**36**. A two-step oxidation sequence first took alcohols **36** and **37** to their corresponding aldehydes under Swern conditions[10] and then to carboxylic acids **21** and **22** by Pinnick oxidation.[11] Condensation of enantiomerically pure acids **21** and **22** with methylamine in the presence of *N*-ethyl-*N*′-(3-dimethylaminopropyl)carbodiimide hydrochloride and 1-hydroxybenzotriazole hydrate afforded amides (-)-**23** and (-)-**24** which were reduced to the corresponding amines. High-performance liquid chromatographic analysis performed on a DAICEL chiral OD column (10 % isopropanol in hexanes) reconfirmed the enantiopurity of amide (-)-**24**. Each amines was acidified with hydrochloric acid to furnish hydrochlorides (-)-**25** and (+)-**26** (Scheme 5). An X-ray crystal structure of (+)-**26** confirmed its stereostructure, including its absolute configuration, as (*1S*, *2S*) (Fig 8).

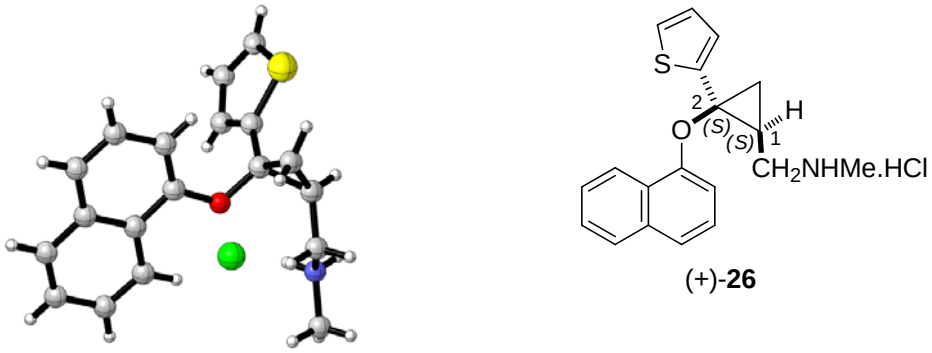
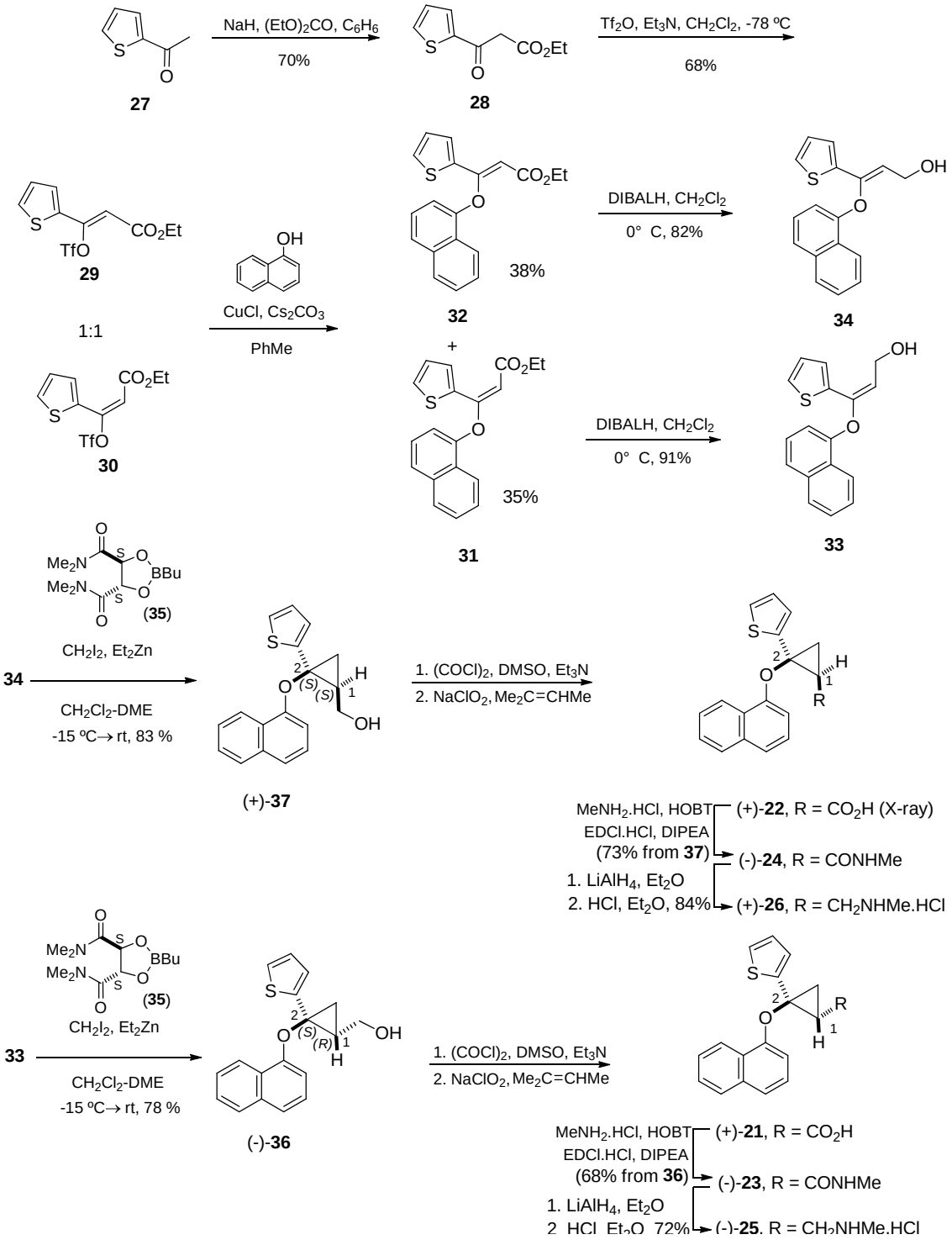


Fig 8. X-ray crystal structure of hydrochloride (+)-**26**



Scheme 5. Synthesis of ammonium salts (-)-**25** and (+)-**26**

A parallel cyclopropanation sequence to that shown in Scheme 5 with **38**, was used to synthesize diastereomeric hydrochlorides (+)-**25** and (-)-**26** for evaluation of their pharmacological properties. Thus, asymmetric cyclopropanation of **33** and **34** with boronate **38**, the enantiomers of **35** prepared from (*R*,*R*)-tartrate, led to (*E*)- and (*Z*)-cyclopropanes (+)-**39** and (-)-**40**, respectively. The alcohols were oxidized to carboxylic acids (+)-**21** and (-)-**22**, respectively, which were converted separately to amides (+)-**23** and (+)-**24**. The amides were reduced to the corresponding amines and acidified to give hydrochlorides (+)-**25** and (-)-**26**, respectively (Scheme 6). X-ray crystallographic structure determination of (+)-**25 and** (-)-**26** confirmed that these substances possessed the (*1S*, *2R*) and (*1R*, *2R*) absolute configuration shown (Fig 9).

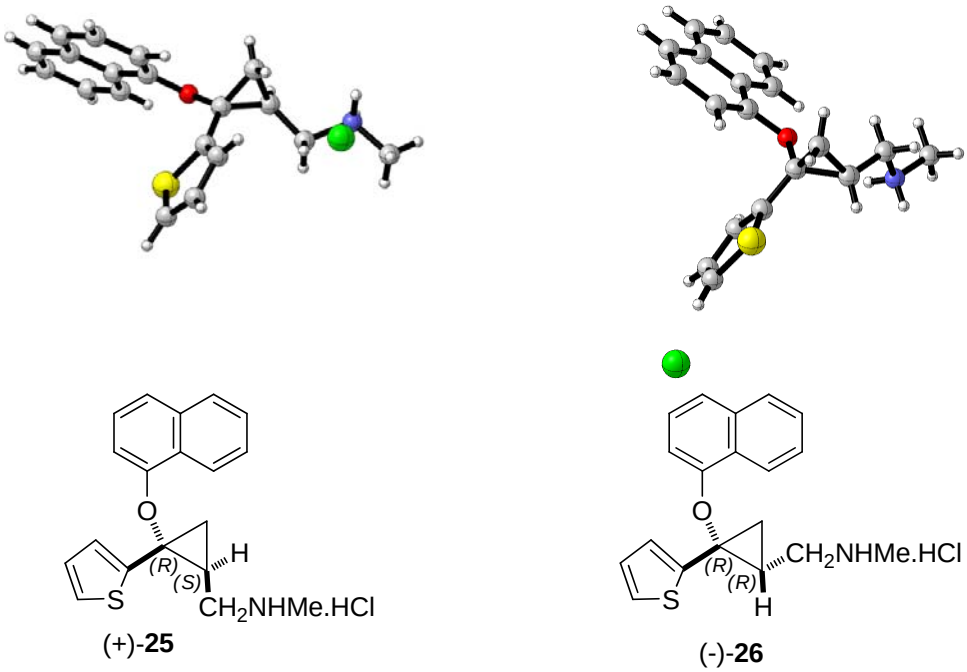
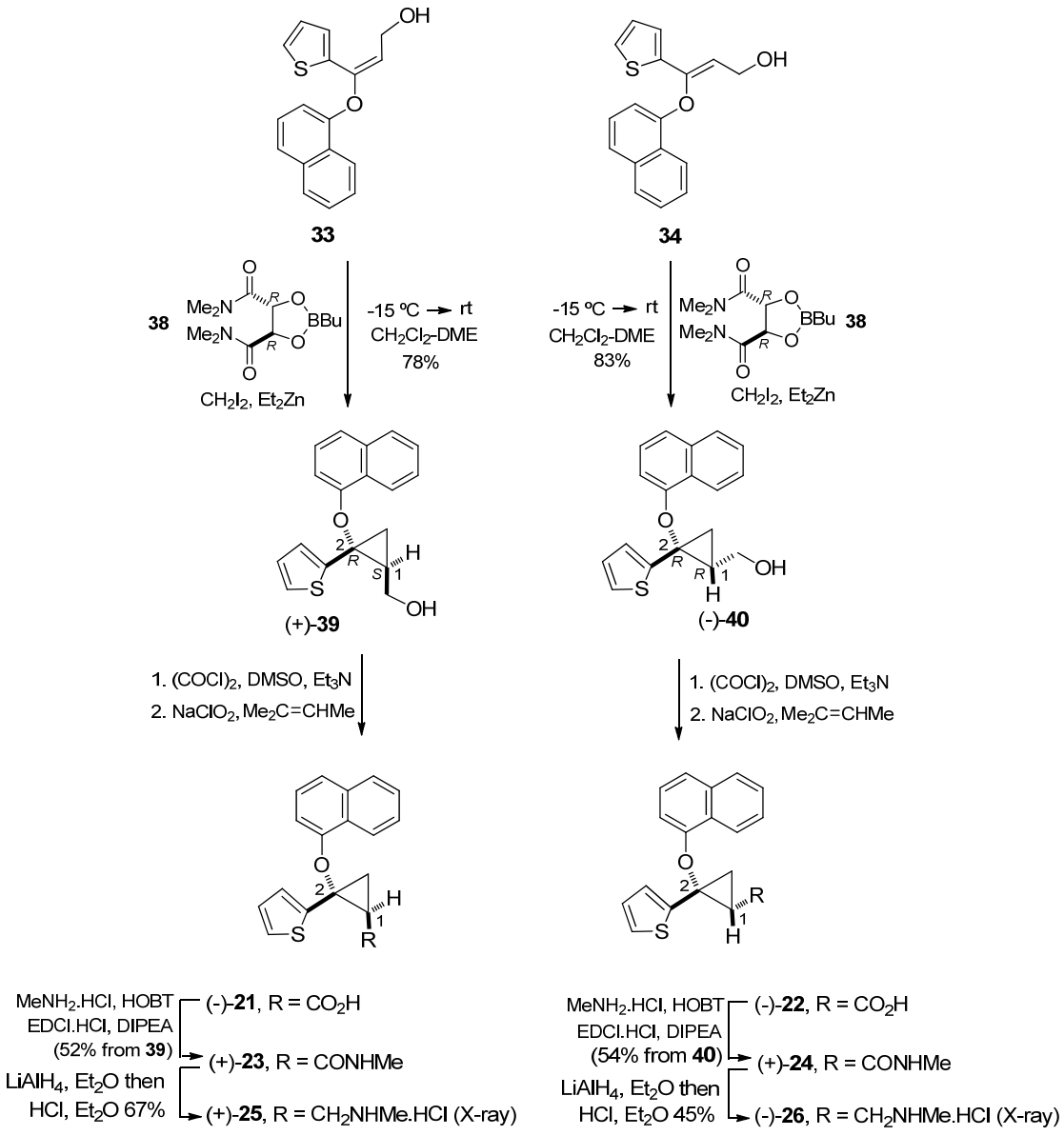


Fig 9. X-ray crystal structures of hydrochlorides (+)-**25** and (-)-**26**



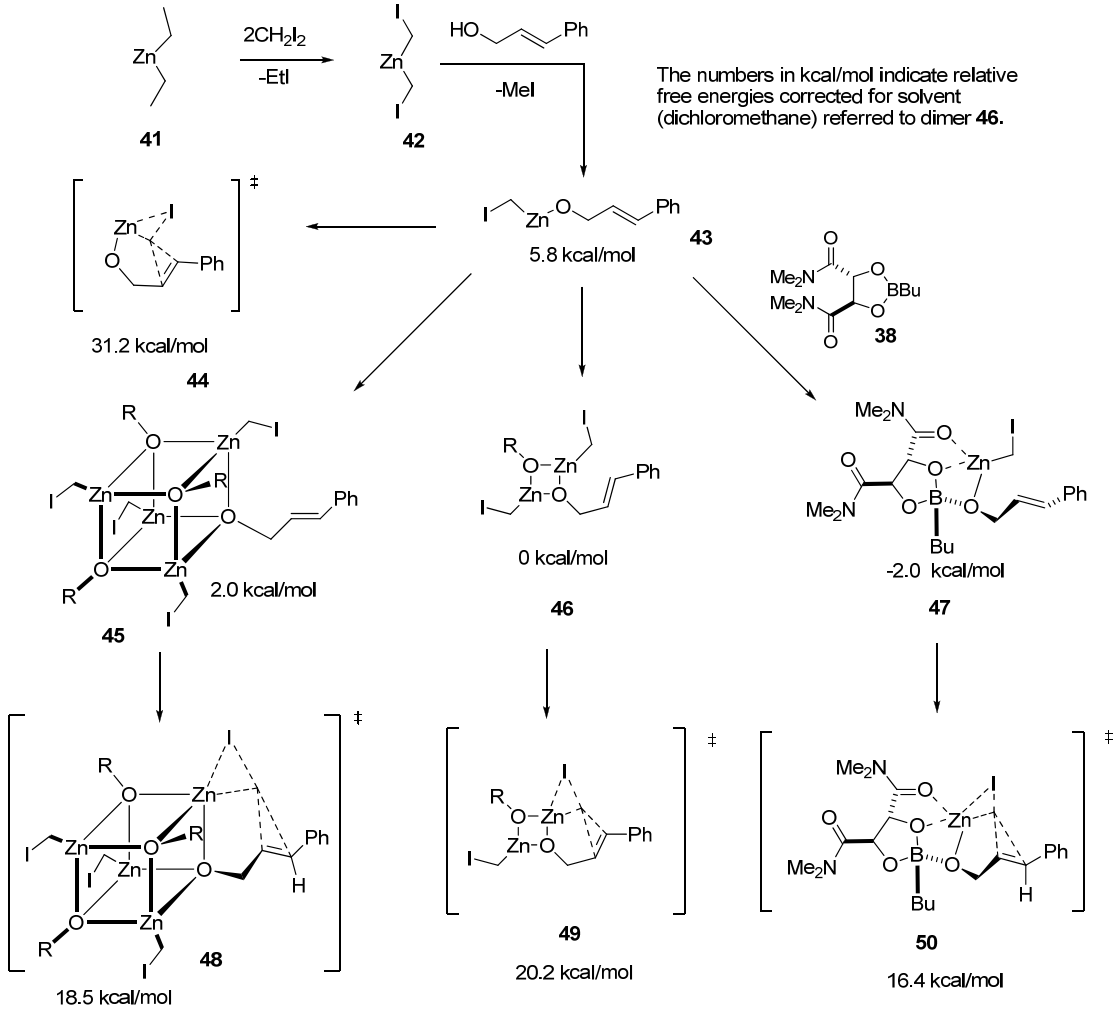
Scheme 6. Synthesis of ammonium salts (+)-**25** and (-)-**26**

2.3 Charette cyclopropanation: the origin of asymmetry

Previous studies, mainly by Nakamura and coworkers,[12] have demonstrated the involvement of zinc carbenoids in Simmons-Smith cyclopropanation of allylic alcohols. The reaction is known to proceed via a [2+1] concerted methylene transfer mechanism. In 1994, Charette published a key modification of the Simmons-Smith reaction using an asymmetric dioxaborolane ligand. Since its first appearance the Charette version of this process has emerged as a powerful strategy for installing cyclopropanes stereoselectively. A recent density functional theory study at the B3LYP level of theory by Yu and coworkers shed light on the role of the dioxaborolane ligand in the Charrette cyclopropanation (Scheme 7).[13] The following discussion is based on those results.

A Sawada-Denmark carbenoid **42** is formed first, and then zinc coordinates to the oxygen atom of the allylic alcohol to generate carbenoid **43** after expelling methyl iodide. In this model, zinc coordinative unsaturation in carbenoid **43** results in association to form dimer **46** or tetramer **45**. These species are more reactive than monomers in cyclopropanation (compare transition states **44**, **48** and **49**) and are more stable than monomeric zinc carbenoid **43**. In the presence of stoichiometric amounts of dioxaborolane ligand **38,** a favorable chelation of zinc with the ligand takes place to give complex **47.** This complex is more stable than either monomer **43**, dimer **46**, or tetramer **45** and is more reactive (compare transition states **44**, **48**, **49** to **50**) in cyclopropanation. Under these conditions, background cyclopropanation leading to racemic product is suppressed and an enantioselective pathway through transition state

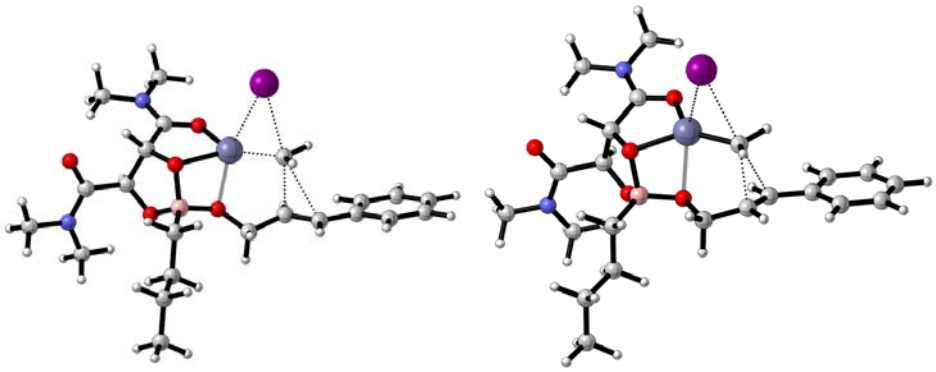
50 predominates. With less than one equivalent of the chiral dioxaborolane ligand present, erosion of enantioselectivity occurs due to the background cyclopropanation.

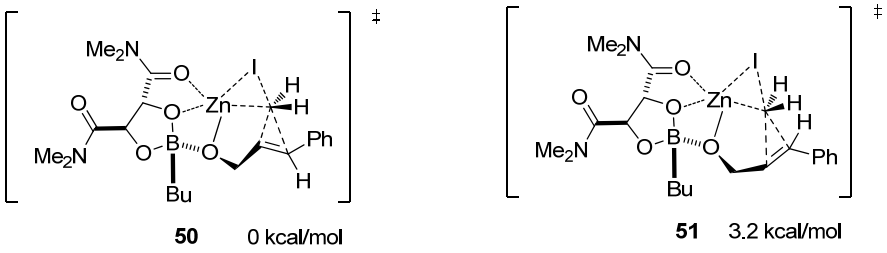


Scheme 7. The mechanism of Charette cyclopropanation

Transition state modeling revealed factors that can impact the enantioselectivity of Charette cyclopropanation (Fig 10). The modeling algorithm located two first order saddle points, **50** and **51**, each leading to a different enantiomer of product. The energy difference between **50** and **51** was calculated to be 3.2 kcal/mol, in good agreement

with the experimental evidence for an enantiomeric excess of 99%. An important contributor to this energy difference is torsional strain. Transition state **50**, which leads to the major product, has a staggered conformation with a dihedral angle of 66° between a vinyl hydrogen atom and a methylene hydrogen atom in the carbenoid moiety, while the energetically disfavored transtition state **51** is partially eclipsed with a corresponding dihedral angle of 33°.





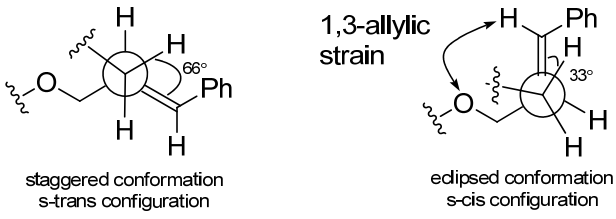


Fig 10. Diastereomeric transition states in Charette cyclopropanation
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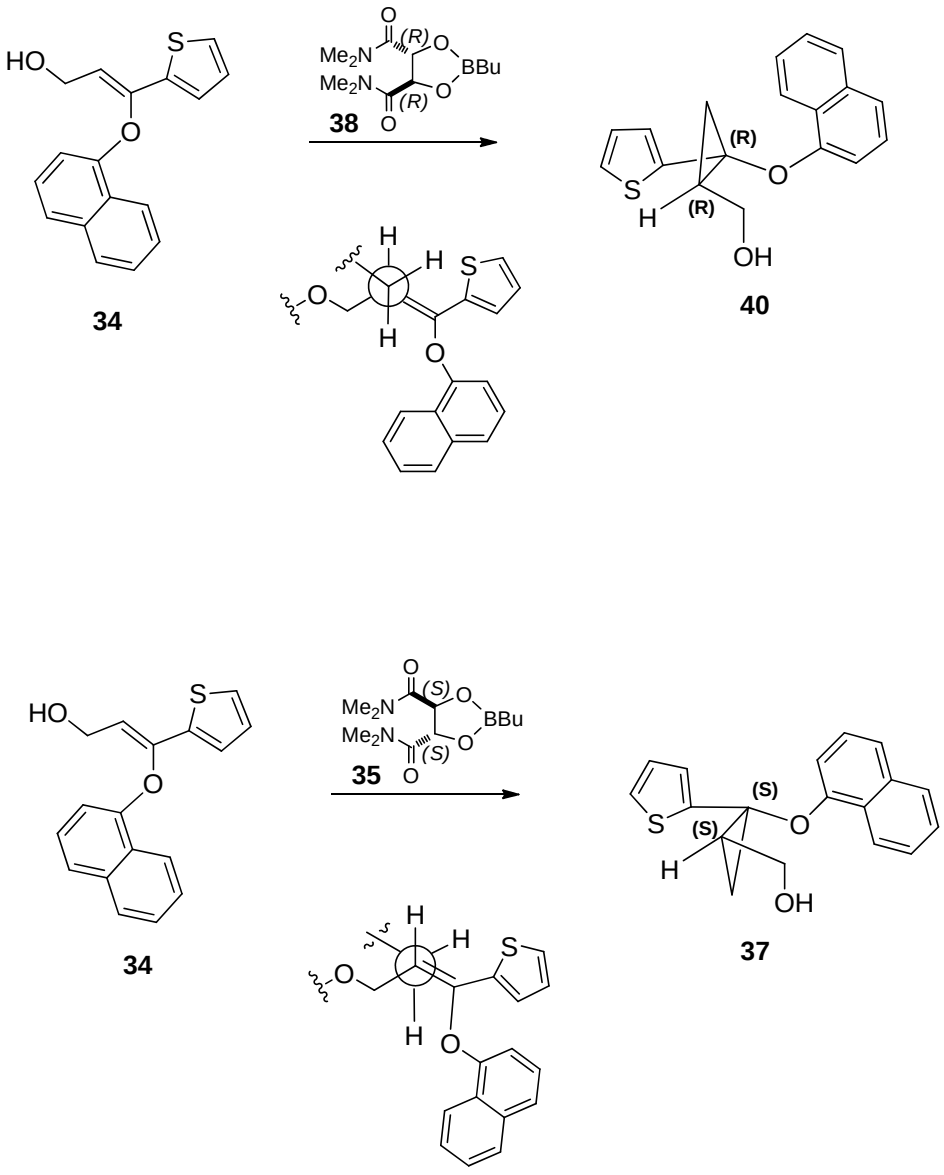
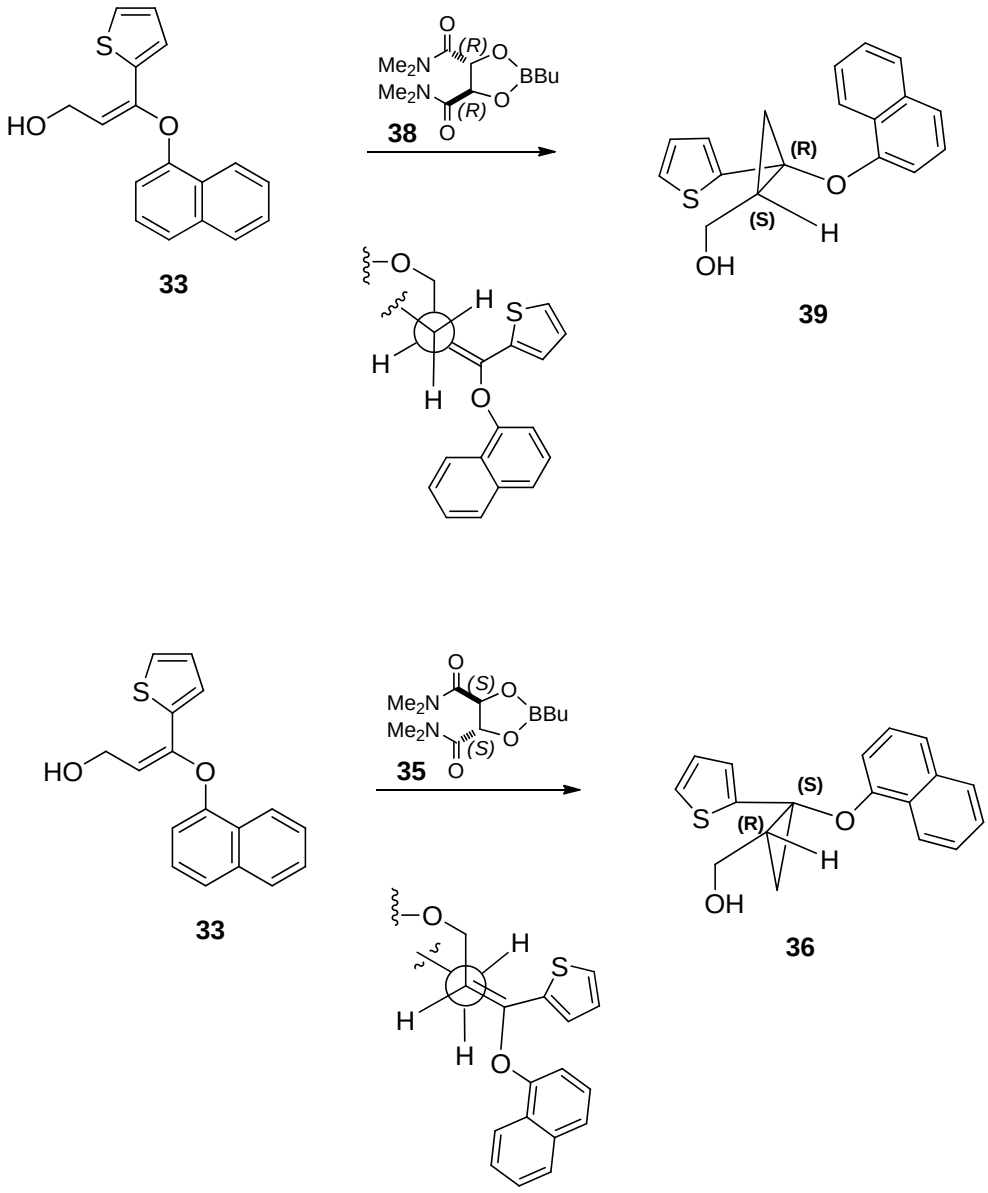
In addition, transition state **51** exhibits a second unfavorable steric interaction, namely 1,3-allylic strain between a hydrogen atom and the alkoxide branch. A third more subtle factor that impacts enantioselectivy to this cyclopropanation is strain build up in the five-membered ring when the zinc atom is included. In the case of transition state **50**, the length of the zinc-oxygen bond is 2.14 Å as compared with 2.34 Å in case of transition state **51**. This implies a higher degree of strain during cyclopropanation that leads to the minor enantiomer.

The model developed by Yu and coworkers for Charette cyclopropantion accounts for the enantionselectivity observed in the key step of our synthesis of synosutine. This model predicts that (*R*,*R*)-dioxaborolane **38** directs cyclopropanation from the top face, whereas (*S*,*S*)-dioxaborolane **35** from the bottom face. The naphthyloxy moiety of **33** and **34** will be pointing away from the dioxaborolane-zinc complex in the transition state to avoid unfavorable interactions. This explains why, in the case of (*R*,*R*)-dioxaborolane **38**, *E*-allylic alcohol **33** and *Z*-allylic alcohol **34** give rise to cyclopropylcarbinols **39** and **40**, respectively (Scheme 8). By the same token, (*S*,*S*)-dioxaborolane **35** produces cyclopropylcarbinols **36** and **37** exclusively (Scheme 9).



Scheme 8. A model for Charette cyclopropanation of **34**

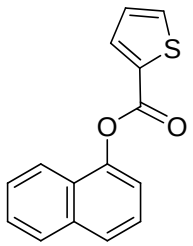


Scheme 9. A model for Charette cyclopropanation of **33**

2.4 Experimental procedures

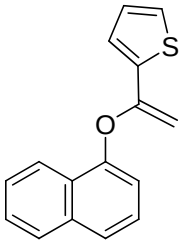
All reactions requiring anhydrous conditions were conducted in flame-dried glass apparatus under an atmosphere of argon. Tetrahydrofuran, ether, dichloromethane, ethyl acetate and hexanes were dried by passage through an activated alumina column under argon. Dimethyl sulfoxide was distilled from calcium hydride at 15 mm Hg and stored over activated 4Å molecular sieves. Methanol and 1,2-dimethoxyethane were freshly distilled from calcium hydride. Preparative chromatographic separations were performed on silica gel (35-75 μm); reactions were followed by thin layer chromatography using silica plates with a fluorescent indicator (254 nm) which were visualized with a UV lamp or phosphomolybdic acid. All commercially available reagents were purchased and used as received unless stated otherwise. Optical rotations were measured with a polarimeter using a 1 mL capacity cell with 1 dm path length. Infrared spectra were recorded using a thin film supported between KBr discs or dispersed in a KBr pellet. ^{1}H and ^{13}C NMR spectra were recorded in Fourier transform mode at the field strength specified on either a 300 or 400 MHz spectrometer. Spectra were obtained on solutions in 5 mm diameter tubes, and chemical shifts in ppm are quoted relative to the residual signals of $CHCl_3$ (δ_H 7.26 ppm, or δ_C 77.0 ppm). Multiplicities in the ^{1}H NMR spectra are described as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad; coupling constants are reported in Hz. Low (MS) and high (HRMS) resolution mass spectra are reported with ion mass/charge (*m/z*) ratios in atomic mass units. High-performance liquid chromatographic analysis was performed under the following conditions: sample (1.0 mg) was dissolved in a 0.1 mL hexanes-isopropanol (9:1) mixture and 2.5

μL of this solution was injected into a column (DAICEL chiral OD). The eluent was 10 % isopropanol in hexanes and the rate of elution was 1 mL/min.



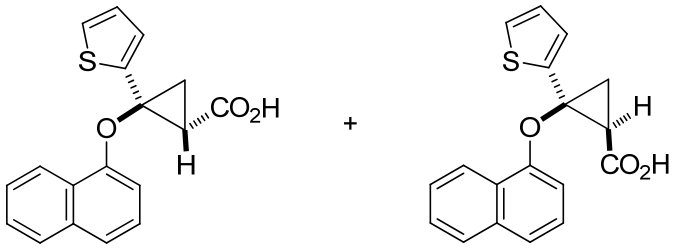
17

1-Naphthyl Thiophen-2-carboxylate (17). To a solution of 2-thiophenecarbonyl chloride (5.00 g, 34.1 mmol) in tetrahydrofuran (85 mL) at 0 °C was added a solution of 1-naphthol (9.80 g, 68.2 mmol) in tetrahydrofuran (68 mL) by syringe pump. After addition was complete, the solution was stirred at room temperature for 10 min and triethylamine (68.2 mmol, 9.5 mL) was added. A colorless solid precipitated immediately and the mixture was stirred for a further 4 h, after which the reaction was quenched with hydrochloric acid (5M). The mixture was extracted with dichloromethane and the extract was dried (Na_2SO_4). The solvent was removed under vacuum and the residue was chromatographed on silica gel (hexanes) to give **17** (9.30 g, 99 %) as a colorless solid: mp 70-75 °C; IR (KBr) 3062, 1729, 1598, 1522, 1507 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.25-7.28 (m, 1H), 7.43 (dd, *J* = 7.5, 0.8 Hz, 1H), 7.50-7.59 (m, 3H), 7.75 (dd, *J* = 5.0, 1.1 Hz, 1H), 7.81 (d, *J* = 8.5 Hz, 1H), 7.97-8.05 (m, 1H), 8.12 (dd, *J* = 3.8, 1.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 118.2, 121.3, 125.4, 126.2, 126.5, 126.9, 128.0, 128.2, 132.7, 133.7, 134.7, 134.9, 146.5, 160.7; HRMS (EI) *m/z* 254.0395 (calcd for $C_{15}H_{10}O_2S$ 254.0402).



18

2-(1-(Naphthalen-1-yloxy)vinyl)thiophene (18). A solution of **17** (9.30 g, 36.6 mmol) in tetrahydrofuran (30 mL) was added into a flask containing Tebbe reagent, prepared from titanocene dichloride (14.0 g, 56.4 mmol) and trimethylaluminum (56.4 mL of 2M solution in toluene, 112 mmol), at room temperature. The slurry was stirred for 10 h at room temperature and was diluted with ether. The mixture was washed with aqueous sodium hydroxide (1M), dried (Na_2SO_4) and filtered through a short pad of silica gel. Removal of the solvent under vacuum gave a brown oil which was chromatographed on silica gel (95 % hexanes, 5 % triethylamine) to give **18** (5.50 g, 60 %) as an oil: IR (KBr) 3105, 3053, 1641, 1596, 1576, 1507, 1461, 1434, 1391, 1358, 1259, 1230, 1091, 1063, 1041, 944, 801, 744, 704 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.25 (d, *J* = 2.8 Hz, 1H), 4.95 (d, *J* = 2.9 Hz, 1H), 7.02-7.07 (m, 1H), 7.18-7.24 (m, 1H), 7.25-7.33 (m, 1H), 7.40-7.45 (m, 2H), 7.49-7.54 (m, 2H), 7.63-7.86 (m, 1H), 7.84-7.90 (m, 1H), 8.12-8.19 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 90.7, 115.5, 122.2, 124.4, 124.9, 125.8, 125.9, 126.3, 126.7, 127.0, 127.7, 128.1, 135.1, 139.3, 151.5, 155.5; HRMS (EI) *m/z* 252.0613 (calcd for $C_{16}H_{12}OS$: 252.0609).



(±)-**21** (±)-**22**

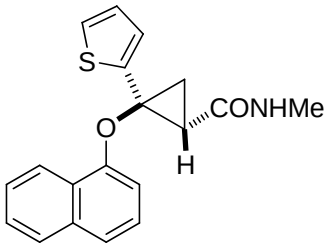
Ethyl 2-(Naphthalen-1-yloxy)-2-(thiophen-2-yl)cyclopropanecarboxylates ((±)-19 and (±)-20). To a solution of **18** (336 mg, 1.32 mmol) in dichloromethane (20 mL) was added copper(II) acetylacetonate (34.5 mg, 132 mmol). To this mixture was added a solution of ethyl diazoacetate (1.0 mL, 6.60 mmol) in dichloromethane (10 mL) over 3 h and the mixture was stirred for a further 5 h at room temperature. The solvent was removed under vacuum and the residue was chromatographed on silica gel (0-10 % ethyl acetate in hexanes) to afford a mixture of (±)-**19** and (±)-**20** (375 mg, *E*:*Z* 2:1):

(*E*)- and (*Z*)-2-(Naphthalen-1-yloxy)-2-(thiophen-2-yl)cyclopropanecarboxylic Acids ((±)-21 and (±)-22). To a solution of potassium hydroxide (436 mg, 7.77 mmol) in methanol (6 mL) was added a solution containing the mixture of **19** and **20** prepared above (263 mg, 0.777 mmol) in methanol (6 mL). The solution was heated at reflux for 10 h, cooled to room temperature, poured into ice-water (60 mL) and extracted with dichloromethane (2 x 30 mL). The aqueous phase was adjusted to pH 1 with hydrochloric acid (2N) and was extracted with dichloromethane (3 x 30 mL). The combined extracts were dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give a mixture of (±)-**21** and (±)-**22** (226 mg, 78 % from **18**, *E*:*Z* 2:1). The carboxylic acids were separated by fractional crystallization from ethyl acetate-

pentane at -20 °C to give pure (±)-**21** and (±)-**22**.

(±)-**21**: colorless solid; mp 167-168 °C; IR (neat) 3054, 1700, 1439, 1392, 1353, 1261, 1230, 1177, 898, 789, 768, 714 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.96 (dd, *J* = 9.8, 6.3 Hz, 1H), 2.31 (t, *J* = 6.8 Hz, 1H), 2.8 (dd, *J* = 9.6, 7.5 Hz, 1H), 6.90 (dd, *J* = 5.3, 3.9 Hz, 1H), 7.11 (d, *J* = 7.8 Hz, 1H), 7.15 (d, *J* = 3.4 Hz, 1H), 7.20 (d, *J* = 5.2, 1H), 7.29 (t, *J* = 7.9 Hz, 1H), 7.42 (d, *J* = 8.2 Hz, 1H), 7.47 (d, *J* = 3.4 Hz, 1H), 7.49 (d, *J* = 3.3 Hz, 1H), 7.76-7.78 (m, 1H), 8.23-8.25 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 21.3, 31.1, 64.2, 108.7, 121.6, 122.0, 125.6, 125.7, 126.0, 126.6, 126.7, 127.7, 134.8, 138.5, 151.7, 173.2; HRMS (EI) *m/z* 310.0674 (calcd for $C_{18}H_{14}O_3S$: 310.0664).

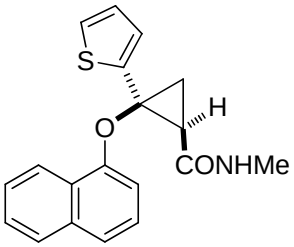
(±)-**22**: colorless solid; mp 144-147 °C; IR (neat) 3054, 1703, 1435, 1394, 1256, 1234, 1216, 1089, 792, 770, 701 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.03 (dd, *J* = 8.5, 6.4 Hz, 1H), 2.28 (t, *J* = 7.1 Hz, 1H), 2.51 (dd, *J* = 9.5, 7.6 Hz, 1H), 6.93 (dd, *J* = 5.1, 3.4 Hz, 1H), 6.97 (d, *J* = 7.9 Hz, 1H), 7.01 (dd, *J* = 3.6, 1.1 Hz, 1H), 7.20 (dd, *J* = 5.0, 1.0 Hz, 1H), 7.25 (t, *J* = 7.8 Hz, 1H), 7.38-7.47 (m, 3H), 7.75 (d, *J* = 8.1 Hz, 1H), 8.22 (d, *J* = 8.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.9, 32.9, 64.0, 108.6, 121.6, 122.3, 123.3, 125.2, 125.5, 125.7, 125.9, 126.6, 127.3, 127.6, 134.8, 143.8, 152,3, 173.0; HRMS (EI) *m/z* 310.0674 (calcd for $C_{18}H_{14}O_3S$: 310.0664).



(±)-**23**

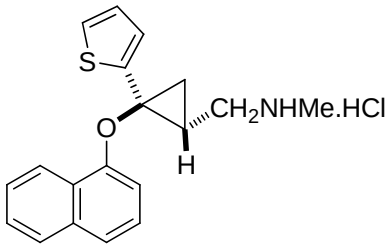
(*E*)-*N*-Methyl-2-(naphthalen-1-yloxy)-2-(thiophen-2-yl)cyclopropane Carboxamide ((±)-23). To a solution of (±)-**21** (14.0 mg, 45.1 μmol), methylamine hydrochloride (3.40 mg, 49.6 μmol), 1-hydroxybenzotriazole hydrate (6.70 mg, 46.6 μmol), and *N*-(3-dimethylaminopropyl)-*N*'-ethylcarbodiimide hydrochloride (9.50 mg, 49.6 μmol) in dichloromethane (10 mL) was added diisopropylethylamine (11.7 μL, 67 μmol). The solution was stirred for 14 h at room temperature and then was diluted with dichloromethane (10 mL). The solution was washed with sodium bicarbonate (2 x 10 mL) and water (10 mL), dried ($MgSO_4$), filtered and concentrated under reduced pressure. The residue was chromatographed on silica gel (petroleum ether: ethyl acetate 1:2) to yield (±)-**23** (14.3 mg, 98 %) as a colorless solid: mp 156-157 °C; IR (neat) 3301, 1651, 1574, 1559, 1394, 1263, 1231, 1182, 1166, 793, 772, 756, 702 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.83 (dd, *J* = 9.6, 6.3 Hz, 1H), 2.35 (t, *J* = 7.3 Hz, 1H), 2.57 (dd, *J* = 10.0, 7.2 Hz, 1H), 2.74 (d, *J* = 5.0 Hz, 3H), 5.75 (d, *J* = 3.3 Hz, 1H), 6.90 (dd, *J* = 5.0, 3.6 Hz, 1H), 7.07-7.13 (m, 2H), 7.16 (dd, *J* = 5.0, 1.1 Hz, 1H), 7.28 (t, *J* = 7.7 Hz, 1H), 7.41 (d, *J* = 8.5 Hz, 1H), 7.47 (d, *J* = 3.1 Hz, 1H), 7.49 (d, *J* = 3.3 Hz, 1H), 7.76-7.79 (m, 1H), 8.23 (dd, *J* = 6.4, 3.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.9, 26.9, 33.4, 63.3, 108.7, 121.3, 121.9, 125.5, 125.8, 125.9, 126.5, 126.7, 127.8, 124.8, 139.6, 152.0, 167.8; HRMS (EI) *m/z* 323.0986 (calcd for

$C_{19}H_{17}O_2NS$ 323.0980).



(±)-**24**

(*Z*)-*N*-Methyl-2-(naphthalene-1-yloxy)-2-(thiophen-2-yl)cyclopropane Carboxamide ((±)-24). In a manner analogous to that used to prepare (±)-**23** from (±)-**21**, (±)-**22** (14.0 mg, 45.1 mmol) yielded (±)-**24** (14.3 mg, 98 %) as a colorless solid: mp 144-145 °C; IR (neat) 3292, 1650, 1576, 1394, 1253, 1234, 1216, 792, 771, 756, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.01 (dd, *J* = 9.5, 6.6 Hz, 1H), 2.01 (t, *J* = 7.5 Hz, 1H), 2.33 (dd, *J* = 10.4, 7.7 Hz, 1H), 2.82 (d, *J* = 4.6 Hz, 1H), 5.88 (br. s, 1H), 6.90 (dd, *J* = 5.1, 3.7 Hz, 1H), 6.95 (dd, *J* = 3.6, 1.1 Hz, 1H), 7.00 (d, *J* = 7.6 Hz, 1H), 7.16 (dd, *J* = 5.0, 1.1 Hz, 1H), 7.26 (t, *J* = 7.1 Hz, 1H), 7.43 (d, *J* = 8.1 Hz, 1H), 7.48 (d, *J* = 3.5 Hz, 1H), 7.50 (d, *J* = 3.5 Hz, 1H), 7.77-7.80 (m, 1H), 8.18-8.20 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.9, 26.9, 35.1, 62.5, 108.9, 121.7, 121.8, 123.9, 124.9, 125.6, 125.9, 126.6, 127.8, 134.8, 144.3, 152.0, 168.0; HRMS (EI) *m/z* 323.0981 (calcd for $C_{19}H_{17}O_2NS$ 323.0980).

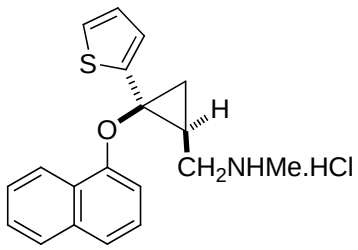


(±)-**25**

(*E*)-*N*-Methyl-2-(naphthalen-1-yloxy)-2-(thiophen-2-yl)cyclopropyl)methanamine Hydrochloride ((±)-25). To a suspension of lithium aluminum hydride (281 mg, 7.42 mmol) in ether (26 mL) was added a solution of (±)-**23** (835 mg, 2.60 mmol) and the stirred slurry was heated at reflux for 2 h. The reaction was quenched with moistened sodium sulfate and the mixture was filtered. The filter cake was washed thoroughly with ether and the filtrate was concentrated under reduced pressure to give crude amine (678 mg, 85 %) which was converted immediately to its hydrochloride salt.

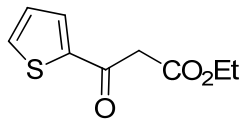
To a solution of the amine prepared above (137 mg, 0.440 mmol) in ether (10 mL) was added hydrochloric acid (1M) in ether (528 μL, 0.528 mmol). The resulting solid was filtered off, washed with ether (2 x 5 mL) and was crystallized from methanol-ether at -20 °C to give (±)-**25** (95.0 mg, 82 %) as a colorless solid: mp 224-225 °C (decomp); IR (neat) 2958, 2716, 2419, 1596, 1579, 1462, 1394, 1263, 1233, 1204, 1185, 793, 772, 755 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.76 (dd, *J* = 10.1, 7.3 Hz, 1H), 2.07 (t, *J* = 7.3 Hz, 1H), 2.32-2.41 (m, 1H), 2.59 (dd, *J* = 12.8, 9.5 Hz, 1H), 2.66 (s, 3H), 3.21 (dd, *J* = 13.8, 5.5 Hz, 1H), 6.89 (dd, *J* = 5.0, 3.7 Hz, 1H), 6.98 (d, *J* = 7.5 Hz, 1H), 7.10-7.13 (m, 1H), 7.20 (t, *J* = 7.7 Hz, 1H), 7.37 (d, *J* = 8.2 Hz, 1H), 7.46 (dd, *J* = 6.3, 3.4 Hz, 1H), 7.74 (dd, *J* = 6.0, 3.2 Hz, 1H), 8.21 (dd, *J* = 6.3, 3.3, 1H), 9.76 (s, 2H); ^{13}C NMR (100 MHz $CDCl_3$) δ 19.7, 23.3, 32.4, 48.0, 62.2, 121.4,

122.0, 125.6, 125.9, 126.6, 126.8, 126.9, 127.2, 127.7, 134.7, 140.3, 151.9; HRMS (EI) *m/z* 309.1194 (calcd for $C_{19}H_{19}NOS$ (M-[HCl]) 309.1187).



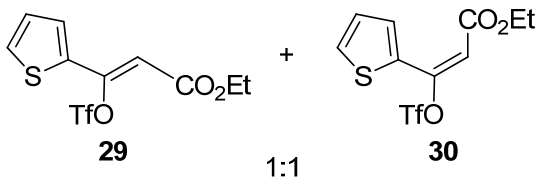
(±)-**26**

(*Z*)-*N*-Methyl-2-(naphthalen-1-yloxy)-2-(thiophen-2-yl)cyclopropyl)methanamine Hydrochloride ((±)-26). In a manner analogous to the preparation of (±)-**25** from (±)-**23**, (±)-**24** (242 mg, 0.700 mmol) gave (±)-**26** (8.30 mg, 44 %) as a colorless solid which was crystallized from methanol-ether at -20 °C: mp 223-224 ºC; IR (neat) 3053, 2932, 2843, 2787, 1578, 1506, 1461, 1394, 1251, 1233, 1089, 792, 771, 698 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.51 (t, *J* = 6.1 Hz, 1H), 1.95-2.06 (m, 2H), 2.83 (s, 3H), 3.37 (d, *J* = 4.8 Hz, 2H), 6.87 (dd, *J* = 5.2, 3.3 Hz, 1H), 6.95 (dd, *J* = 3.3, 0.7 Hz, 1H), 6.99 (d, *J* = 7.5 Hz, 1H), 7.12 (dd, *J* = 5.0, 0.7 Hz, 1H), 7.25 (t, *J* = 8.0 Hz, 1H), 7.43 (d, *J* = 8.3 Hz, 1H), 7.47-7.54 (m, 2H), 7.77-7.81 (m, 1H), 8.18-8.22 (m, 1H), 9.84 (br. s, 1H), 9.94 (br. s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 25.9, 32.4, 47.5, 61.3, 108.8, 121.5, 121.8, 124.0, 125.0, 125.7, 126.1, 126.8, 127.3, 128.0, 134.8, 142.7, 151.9; HRMS (EI) *m/z* 309.1180 (calcd for $C_{19}H_{19}NOS$ (M-[HCl]) 309.1187).

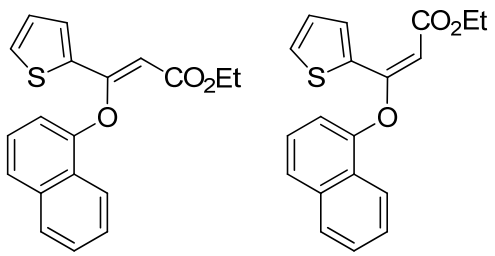


28

Ethyl 3-Oxo-3-(thiophen-2-yl)propanoate (**28**). To a suspension of sodium hydride (7.13 g, 178 mmol, 60 % in mineral oil) in benzene (100 mL) was added diethyl carbonate (14.0 g, 118 mmol). The mixture was heated to reflux and a solution of 2-acetylthiophene (7.48 g, 59.4 mmol) in benzene (20 mL) was added dropwise over 1 h. When addition was complete, the mixture was refluxed for a further 3 h, after which hydrogen evolution had ceased. The reaction was quenched with acetic acid (15 mL) and then with ice-cold water (45 mL). The organic phase was separated, the aqueous layer was extracted with benzene and the combined extracts were washed with cold water, dried (Na_2SO_4) and concentrated under reduced pressure. The residue was distilled under high vacuum to give **28** (8.15 g, 69 %) as a colorless oil: bp 130 °C (0.3 torr): IR (neat) 2925, 2848, 1742, 1669, 1459, 1373, 1030, 851, 723 cm^{-1}; ^1H NMR (400 MHz, $CHCl_3$) δ 1.28 (t, *J* = 7.7 Hz, 3H), 3.93 (s, 2H), 4.25 (q, *J* = 6.8 Hz, 2H), 7.14-7.18 (m, 1H), 7.72 (dd, *J* = 5.0, 1.1 Hz, 1H), 7.76 (dd, *J* = 3.8, 1.1 Hz, 1H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 14.1, 46.5, 61.6, 128.3, 133.2, 134.9, 142.4, 167.0, 185.2: HRMS (EI) *m/z* 198.0349 (calcd for $C_9H_{10}O_3S$ 198.0351).



(*E*)- and (*Z*)-Ethyl 3-(Thiophen-2-yl)-3-(trifluoromethylsulfonyloxy)acrylates (29 and 30). To a solution of **28** (1.98 g, 10.0 mmol) and triethylamine (1.8 mL, 13.0 mmol) in dichloromethane (80 mL) at -78 °C was added trifluoromethanesulfonic anhydride (1.85 mL, 11.0 mmol) dropwise. The resulting solution was allowed to warm to -10 °C and was stirred at this temperature for 0.5 h. The reaction was quenched with aqueous sodium bicarbonate and the aqueous phase was extracted with dichloromethane. The combined extracts were washed with brine, dried (Na_2SO_4) and concentrated under reduced pressure. The residue was dried overnight under high vacuum to give a 1:1 mixture of **29** and **30** as a pale yellow solid (2.20 g, 68 %): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.37 (t, *J* = 7 Hz, 3H), 1.42 (t, *J* = 7 Hz, 3H), 3.16-3.24 (m, 2H), 4.33 (q, *J* = 7 Hz, 2H), 6.23 (s, 1H), 7.13 (t, *J* = 4.2 Hz, 1H), 7.46 (d, *J* = 3.3 Hz, 1H), 7.52 (d, *J* = 4.8 Hz, 1H); The mixture was used immediately in the next reaction.



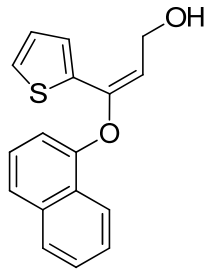
32 **31**

(*E*)- and (Z)-Ethyl 3-(Naphthalene-1-yloxy)-3-thiophen-2-ylacrylates (31 and 32). A solution containing a mixture of **29** and **30** (50.0 g, 15.0 mmol), α-naphthol (3.24 g, 22.5 mmol), copper(I) chloride (368 mg, 3.72 mmol) and cesium carbonate (9.78, 30.0 mmol) in toluene (75 mL) was refluxed for 4 h. The cooled mixture was filtered through a short pad of Celite and the filtrate was washed with aqueous ammonium hydroxide, dried (K_2CO_3) and concentrated under reduced pressure. The residue was purified by chromatography on silica gel (hexane:ethyl acetate 40:1) to give less polar **31** (1.69 g, 35 %) and more polar **32** (1.84 g, 38%), each as a pale yellow solid.

31: mp 90-92 °C; IR (KBr) 3060, 2980, 2923, 2854, 1712, 1602, 1571, 1427, 1393, 1386, 1335, 1242, 1232, 1205, 1139, 1088, 1046, 858, 807 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.19 (t, *J* = 7.1 Hz, 3H), 4.08 (q, *J* = 7.1 Hz, 2H), 5.16 (s, 1H), 7.19 (t, *J* = 4.5 Hz, 1H), 7.25 (d, *J* = 7.3 Hz, 1H), 7.49-7.61 (m, 4H), 7.77 (d, *J* = 8.1 Hz, 1H), 7.95 (d, *J* = 8.1 Hz, 1H), 8.02 (d, *J* = 7.4 Hz, 1H), 8.30 (d, *J* = 3.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 60.0, 97.4, 117, 121.7, 125.7, 125.8, 126.69, 126.7, 126.8, 127.2, 128.1, 129.8, 132.5, 134.9, 135.0, 149.7, 162.3, 166.3; HRMS (EI) *m/z* 324.0851 (calcd for $C_{19}H_{16}O_3S$ 324.0820).

32: mp 85-86 °C; IR (KBr) 3052, 2956, 2920, 2845, 1714, 1692, 1618, 1507, 1457,

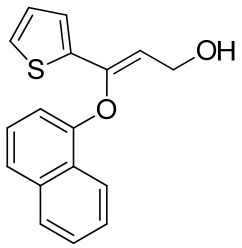
1393, 1368, 1325, 1258, 1225, 1150, 1090, 1039, 790, 769, 708 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.97 (t, *J* = 7.7 Hz, 3H), 4.01 (q, *J* = 6.8 Hz, 2H), 6.26 (s, 1H), 6.86 (d, *J* = 7.7 Hz, 1H), 6.97 (t, *J* = 4.1 Hz, 1H), 7.28 (t, *J* = 7.5 Hz, 1H), 7.36 (d, *J* =4.3 Hz, 2H), 7.50-7.62 (m, 3H), 7.86 (d, *J* = 7.5 Hz, 1H), 8.48 (d, *J* = 7.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 60.2, 105.3, 107.8, 122.0, 122.2, 125.2, 125.6, 125.9, 126.6, 127.6, 128.2, 128.7, 128.9, 134.7, 138.1, 153.3, 156.4, 164.2; HRMS (EI) *m/z* 324.0827 (calcd for $C_{19}H_{16}O_3S$ 324.0820).



33

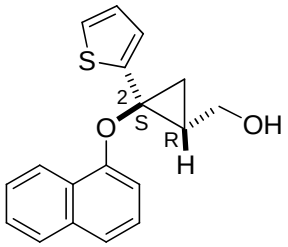
(*E*)-3-(Naphthalen-1-yloxy)-3-thiophen-2-ylprop-2-en-1-ol (33). To a solution of **31** (1.69 g, 5.22 mmol) in dichloromethane (50 mL) at 0 °C was added diisobutylaluminum hydride (1.0M solution in dichloromethane, 10.5 mL, 10.4 mmol). The mixture was stirred for 30 min at 0 °C, then was diluted with dichloromethane (50 mL) and the reaction was quenched carefully with saturated aqueous sodium potassium tartrate (70 mL). The mixture was stirred for 1 h at room temperature and the aqueous phase was separated and extracted with dichloromethane. The combined extracts were dried (Na_2SO_4), the solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (hexane-ethyl acetate, 5:1) to give **33** (1.21 g, 82 %) as a pale yellow oil: IR (neat)

3336, 3101, 3050, 2924, 1641, 1597, 1573, 1505, 1457, 1420, 1389, 1362, 1259, 1226, 1174, 1157, 090, 1018, 991, 793, 770, 705 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.44 (t, *J* = 5.0 Hz, 1H), 4.45 (t, *J* = 6.0 Hz, 2H), 5.36 (t, *J* = 7.8 Hz, 1H), 7.09 (t, *J* = 4.5 Hz, 1H), 7.12 (d, *J* = 7.3 Hz, 1H), 7.34-7.42 (m, 3H), 7.54 (dd, *J* = 5.9, 3.4 Hz, 2H), 7.60 (d, *J* = 8.2 Hz, 1H), 7.86-7.90 (m, 1H), 8.21-8.23 (m, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 58.9, 110.3, 113.9, 121.9, 123.7, 125.8, 126.0, 126.6, 127.0, 127.2, 127.8, 128.2, 134.9, 150.5, 151.6; HRMS (EI) *m/z* 282.0711 (calcd for $C_{17}H_{14}O_2S$ 282.0715).



34

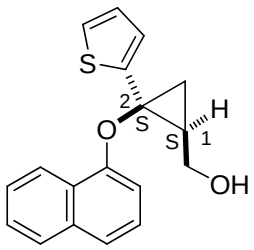
(*Z*)-3-(Naphthalen-1-yloxy)-3-thiophen-2-ylprop-2-en-1-ol (34). In a manner analogous to the conversion of **31** to **33**, **32** (763 mg, 2.36 mmol) was reduced with diisobutylaluminum hydride to give **34** (608 mg, 91 %) as a colorless oil: IR (neat) 3323, 3054, 2926, 2871, 1653, 1598, 1575, 1509, 1459, 1427, 1392, 1256, 1229, 1085, 1054, 1015, 796, 769, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.48 (t, *J* = 6.0 Hz, 1H), 4.34 (t, *J* = 6.6 Hz, 2H), 6.13 (t, *J* = 6.7 Hz, 1H), 6.88-6.92 (m, 2H), 7.10 (d, *J* = 3.2 Hz, 1H), 7.20 (dd, *J* = 5.2, 0.75 Hz, 1H), 7.29 (t, *J* = 8.4 Hz, 1H), 7.51 (d, *J* = 8.4 Hz, 1H), 7.56-7.61 (m, 2H), 7.84-7.90 (m, 1H), 8.42-8.47 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 57.5, 107.5, 115.3, 121.7, 122.0, 125.4, 125.8 (x2), 126.0, 126.7, 127.6, 127.7, 134.8, 138.4, 146.4, 152.9.



(-)-**36**

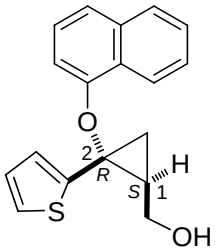
(-)-(1*R*,2*S*)-[2-(Naphthalen-1-yloxy)-2-thiophen-2-ylcyclopropyl]methanol (36). To a mixture of dichloromethane (20 mL) and 1,2-dimethoxyethane (0.5 mL) was added diethylzinc (530 μmL, 5.00 mmol). To this stirred solution was added diiodomethane (800 μmL, 10.0 mmol) over 15-20 min and the resulting clear solution was stirred for 10 min at -15 °C. To this mixture was added a solution of **35** (470 μL, 1.90 mmol) in dichloromethane (8 mL) followed by a solution of **33** (486 mg, 1.72 mmol) in dichloromethane (8 mL). The cooling bath was removed and the mixture was allowed to warm to room temperature and was stirred for 14 h. Saturated aqueous ammonium chloride (30 mL) was added to quench the reaction, the aqueous phase was extracted with dichloromethane and the combined extracts were dried ($NaSO_4$). The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (pentane:ethyl acetate 9:1) to give **36** (372 mg, 78 %) as a colorless oil: $[\alpha]_D^{25}$ -126 (c 0.53 $CHCl_3$); IR (neat) 3050, 2954, 2922, 2849, 1596, 1577, 1503, 1462, 1392, 1363, 1315, 1264, 1235, 1181, 1095, 1050, 1015, 792, 773, 703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.55 (t, *J* = 6.5 Hz, 1H), 1.62 (dd, *J* = 9.3, 6.1 Hz, 1H), 2.21-2.31 (m, 1H), 3.44 (t, *J* = 11.2 Hz, 1H), 3.75-3.82 (m, 1H), 6.98 (dd, *J* = 5.0, 3.5 Hz, 1H), 7.15 (dd, *J* = 3.7, 1.1 Hz, 1H), 7.18 (d, *J* = 7.5 Hz, 1H), 7.25 (dd,

J = 5.1, 1.1 Hz, 1H), 7.30 (t, *J* = 8.0 Hz, 1H), 7.42 (d, *J* = 7.8 Hz, 1H), 7.49-7.53 (m, 2H), 7.77-7.81 (m, 1H), 8.30-8.34 (m, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 18.1, 29.7, 61.6, 62.2, 108.2, 120.6, 122.0, 125.2, 125.4, 125.9 (x2), 126.2, 126.3, 126.8, 127.4, 134.5, 141.4, 152.1; HRMS (EI) *m/z* 296.0861 (calcd for $C_{18}H_{16}O_2S$ 296.0871).



(+)-**37**

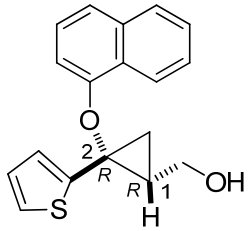
(+)-(1*S*,2*S*)-[2-(Naphthalen-1-yloxy)-2-thiophen-2-ylcyclopropyl]methanol (37). In a manner analogous to the cyclopropanation of **33** to give (-)-**36**, **34** (390 mg, 1.38 mmol) was reacted with **35** (407 mg, 1.52 mmol) to afford (+)-**37** (340 mg, 83 %): $[\alpha]_D$ +7.6 (c 0.97, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.43 (t, *J* = 6.6 Hz, 1H), 1.76 (dd, *J* = 8.8, 6.4 Hz, 1H), 1.95-2.05 (m, 1H), 3.87 (dd, *J* = 11.7, 8.6 Hz, 1H), 4.03-4.11 (m, 1H), 6.93-6.98 (m, 2H), 7.10 (d, *J* = 7.4 H 1H), 7.17 (dd, *J* = 4.7, 1.2 Hz, 1H), 7.31 (t, *J* = 7.9 Hz, 1H), 7.47 (d, *J* = 8.2 Hz, 1H), 7.54 (dd, *J* = 6.6, 3.2 Hz, 2H), 7.84 (dd, *J* = 6.0, 3.5 Hs, 1H), 8.27 (dd, *J* = 6.6, 3.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.9, 32.6, 62.1, 62.3, 108.6, 121.2, 121.4, 123.0, 124.1, 125.4, 125.5, 125.6, 126.5, 126.9, 127.7, 134.6, 145.6, 152.4; HRMS (EI) *m/z* 296.0876 (calcd for $C_{18}H_{16}O_2S$ 296.0871).



(+)-**39**

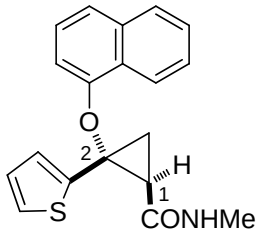
(+)-(1*S*,2*R*)-[2-(Naphthalen-1-yloxy)-2-thiophen-2-ylcyclopropyl]methanol (39). To a mixture of dichloromethane (20 mL) and 1,2-dimethoxyethane (0.5 mL) at -15 °C was added diethylzinc (530 μL, 5.00 mmol). To this stirred solution was added diiodomethane (800 μL, 10.0 mmol) over 15-20 min and the resulting clear solution was stirred for 10 min at -15 °C. To this mixture was added a solution of **38** (520 μL, 2.12 mmol) in dichloromethane (4 mL) followed by a solution of **33** (500 mg, 1.77 mmol) in dichloromethane (8 mL). The cooling bath was removed and the mixture was allowed to warm to room temperature and was stirred for 14 h. Saturated aqueous ammonium chloride (30 mL) was added to quench the reaction, the aqueous phase was extracted with dichloromethane and the combined extracts were dried (Na_2SO_4). The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (pentane-ethyl acetate 9:1) to give (+)-**39** (490 mg, 93 %) as a colorless oil: $[\alpha]_D^{20}$ +138.0 (c 0.19, $CHCl_3$); IR (neat) 3050, 2957, 2922, 2852, 1579, 1505, 1459, 1392, 1365, 1315, 1291, 1264, 1232, 1182, 1093, 1011, 793, 773, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.53 (t, *J* = 6.7 Hz, 1H), 1.65 (dd, *J* = 10.2, 6.3 Hz, 1H), 2.21-2.31 (m, 1H), 3.44 (dd, *J* = 11.4, 9.0 Hz, 1H), 3.77 (dd, *J* = 12.0, 5.7 Hz, 1H), 6.96 (t, *J* = 4.4 Hz, 1H), 7.14 (d, *J* = 3.2 Hz, 1H), 7.20 (d, *J* = 7.6 Hz, 1H), 7.24 (d, *J* = 5.1 Hz, 1H), 7.29 (d, *J* = 2.4 Hz, 1H), 7.32 (d, *J* = 7.4 Hz, 1H), 7.44

(d, *J* = 8.5 Hz, 1H) 7.52-7.54 (m, 1H), 7.78-7.82 (m, 1H), 8.31-8.36 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.1, 29.7, 61.6, 62.2, 108.2, 120.8, 122.0, 125.2, 125.5, 125.9, 126.2, 126.3, 126.8, 127.5, 134.5, 141.4, 152.1; HRMS (EI) *m/z* 296.0867 (calcd for $C_{18}H_{16}O_2S$ 296.0871).



(-)-**40**

(-)-(1*R*,2*R*)-[2-Naphthalen-1-yloxy)-2-thiophen-2-ylcyclopropyl]methanol (40). In a manner analogous to the cyclopropanation of **33** to give (+)-**39**, alcohol **34** (410 mg, 1.45 mmol) was reacted with **38** (429 mg, 1.60 mmol) to yield (-)-**40** (381 mg, 89 %): $[\alpha]_D^{25}$ -35.0 (c 0.75 $CHCl_3$); IR (neat) 3389, 3049, 2954, 2920, 1596, 1576, 1505, 1461, 1390, 1370, 1313, 1249, 1232, 1212, 1087, 1057, 1019, 905, 790, 774, 733, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.41 (t, *J* = 7.2 Hz, 1H), 1.77 (dd, *J* = 9.5, 6.1 Hz, 1H) 1.92-2.06 (m, 1H), 3.88 (dd, *J* = 11.9, 8.2 Hz, 1H), 4.06 (dd, *J* = 12.1, 5.8 Hz, 1H), 6.89-6.97(m, 2H), 7.09 (d, *J* = 7.3 Hz, 1H), 7.17 (d, *J* = 5.0 Hz, 1H), 7.20 (t, *J* = 8.4 Hz, 1H) 7.47 (d, *J* = 8.4 Hz, 1H), 7.53 (dd, *J* = 6.3, 3.2 Hz, 2H), 7.83 (dd, *J* = 6.1, 3.1 Hz, 1H), 8.28 (dd, *J* = 6.4, 3.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.9, 32.6, 62.1, 62.3, 108.6, 121.2, 121.4, 123.0, 124.1, 125.4, 125.5, 125.6, 126.5, 126.9, 127.7, 134.6, 145.6, 152.4; HRMS (CI) *m/z* 297.0936 (calcd for $C_{18}H_{17}O_2S$ 297.0949).



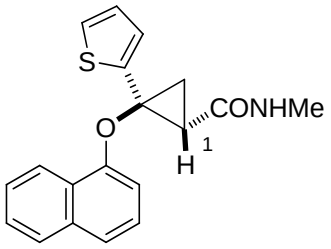
(+)-**23**

(+)-(1*R*,2*R*)-23. To a mixture of dimethyl sulfoxide (180 μL, 2.58 mmol) and dichloromethane (10 mL) at -78 °C was added oxallyl chloride (110 μL, 1.30 mmol) and the mixture was stirred at this temperature for 30 min. A solution of (+)-**39** (296 mg, 0.860 mmol) in dichloromethane (4 mL) was added dropwise and the resulting mixture was stirred for 30 min at -78 °C. Triethylamine (0.360 mL, 2.58 mmol) was added, the mixture was allowed to warm to room temperature and the reaction was quenched with ice-cold water. The mixture was extracted with dichloromethane and the combined extracts were dried (Na_2SO_4) and concentrated under reduced pressure at 35 °C. The crude aldehyde obtained was used directly in the next step.

To a solution of the crude aldehyde in *tert*-butanol (23 mL) and tetrahydrofuran (7 mL) was added 2-methyl-2-butene (1.80 mL, 17.2 mmol). A solution of sodium dihydrogen phosphate (1.80 g, 12.5 mol) and sodium chloride (1.20 g, 13.0 mmol) in water (40 mL) was added and the biphasic mixture was stirred overnight at room temperature. Brine was added and the mixture was extracted with dichloromethane. The combined extracts were dried (Na_2SO_4) and concentrated under reduced pressure to leave crude (-)-**21** which was used directly in the next step.

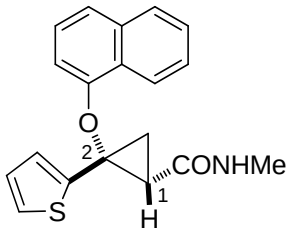
To a solution of the crude carboxylic acid in dichloromethane was added methylamine hyrochloride (100 mg, 1.50 mmol), N-(3-dimethylaminopropyl-N'-

ethylcarbodiimide hydrochloride (135 mg, 1.00 mmol), 1-hydroxybenzotriazole hydrate (155 mg, 1.00 mmol) and diisopropylethylamine (0.260 mL, 1.90 mmol). The mixture was stirred overnight at room temperature and the reaction was quenched with saturated aqueous sodium bicarbonate. The mixture was extracted with dichloromethane, the combined extracts were dried (Na_2SO_4), and the residue after evaporation of the solvent was chromatographed on silica gel (pentane:ethyl acetate 9:1) to give (+)-**23** (145 mg, 52%) as a colorless oil: $[\alpha]_D^{25}$ +138.0 (c 0.19, $CHCl_3$); IR (neat) 3300, 3048, 2921, 2848, 1650, 1577, 1556, 1503, 1457, 1391, 1261, 1230, 1184, 1163, 1093, 1047, 1016, 904, 794, 770, 732, 707 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.85 (d, *J* = 7.4 Hz, 1H), 2.38 (d, *J* = 7.4 Hz, 1H), 2.57 (d, *J* = 8.7 Hz, 1H), 2.77 (d, *J* = 4.7 Hz, 3H), 5.73 (s, 1H), 6.92 (s, 1H), 7.11-7.15 (m, 2H), 7.19 (d, *J* = 4.5 Hz, 1H), 7.29-7.33 (m, 1H), 7.45 (d, *J* = 7.8 Hz, 1H), 7.48-7.52 (m, 2H), 7.79 (br. s, 1H), 8.26 (br. s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.7, 26.7, 33.2, 63.1, 108.5, 121.2, 121.5, 121.7, 125.3, 125.6, 125.7, 126.3, 126.5, 126.53, 127.6, 134.6, 139.4, 151.8, 167.5; HRMS (EI) *m/z* 323.0981 (calcd for $C_{19}H_{17}NO_2S$ 323.0980).



(-)-**23**

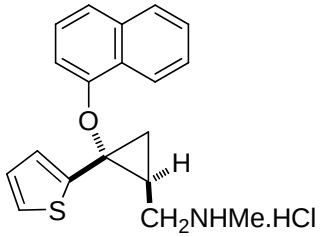
(-)-(1*S*,2*S*)-23. In a manner analogous to the conversion of **39** to (+)-**23**, alcohol (-)-**36** (350 mg, 1.18 mmol) was oxidized to carboxylic acid (+)-**21** which was reacted with methylamine hydrochloride to afford (-)-**23** (140 mg, 37 %): $[\alpha]_D^{25}$ –187.0 (0.36 $CHCl_3$).



(+)-**24**

(+)-(1*S*,2*R*)-24. In a manner analogous to the conversion of (+)-**39** to (+)-**23**, alcohol (-)-**40** (70.0 mg, 0.240 mmol) was oxidized to carboxylic acid (-)-**22** which was reacted with methylamine hydrochloride to give (+)-**24** (40.0 mg, 54 %): $[\alpha]_D^{25}$ +59.4 (c 0.36, $CHCl_3$); IR (neat) 3295, 2919, 2845, 1651, 1576, 1556, 1394, 1255, 1231, 1096, 1052, 1015, 788, 771, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.01 (dd, *J* = 10.1, 7.0 Hz, 1H), 2.12 (t, *J* = 7.3 Hz, 1H), 2.34 (dd, *J* = 10.9, 7.8 Hz, 1H), 2.83 (d, *J* = 4.2 Hz, 3H), 5.94 (br. s, 1H), 6.91 (dd, *J* = 5.0, 3.8 Hz, 1H), 6.95-6.98 (m, 1H), 7.02

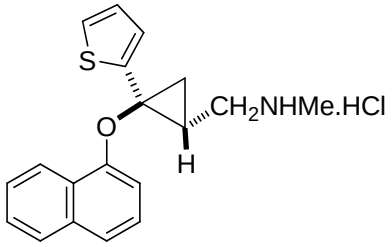
(d, *J* = 7.5 Hz, 1H), 7.12 (d, *J* = 5.0 Hz, 1H), 7.27 (t, *J* = 7.0 Hz, 1H), 7.42-7.54 (m, 3H), 7.80 (dd, *J* = 6.1, 3.2 Hz, 1H), 8.21 (dd, *J* = 6.4, 3.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 26.2, 34.8, 62.5, 108.7, 121.4, 121.6, 123.7, 124.6, 125.4, 125.6, 125.7, 126.4, 127.0, 127.6, 134.6, 144.4, 151.9, 167.9; HRMS (EI) *m/z* 323.0983 (calcd for $C_{19}H_{17}NO_2S$, 23.0980).



(+)-**25**

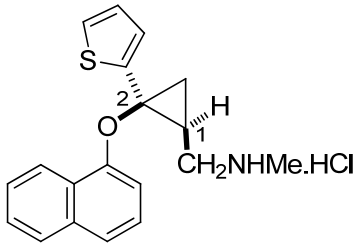
(+)-(1*S*,2*R*)-25. A slurry containing (+)-**23** (145 mg, 0.445 mmol) and lithium aluminum hydride (304 mg, 8.00 mmol) in ether (22 mL) was heated at reflux for 5 h. The mixture was cooled to 0 °C and the reaction was quenched with damp sodium sulfate. The mixture was filtered, the collected solid was washed with ether (30 mL) and the filtrate was evaporated under reduced pressure. The resulting oil was taken up into ether (20 mL) and hydrochloric acid (1M solution in ether, 1 mL) was added. The colorless solid that precipitated was filtered, washed with ether (3 x 20 mL) and was crystallized from ether (5 mL) containing methanol (0.4 mL) to afford (+)-**25** (103 mg, 67 %): $[\alpha]_D^{20}$ +207.0 (c 0.26, $CHCl_3$); IR (neat) 3369, 2957, 2922, 2848, 1599, 1579, 1505, 1459, 1392, 1260, 1233, 1186, 1089, 793, 774, 705 cm^{-1};^{1}H NMR (400 MHz, $CDCl_3$) δ 1.82 (dd, *J* = 10.1, 6.8 Hz, 1H), 2.08 (t, *J* = 7.1 Hz. 1H), 2.34-2.44 (m, 1H), 2.63 (t, *J* = 11.6 Hz, 1H), 2.69 (s, 3H), 3.19-3.27 (m, 1H), 6.92 (dd, *J* = 5.3, 3.6 Hz, 1H), 7.00 (d, *J* = 7.7 Hz, 1H), 7.14-7.24 (m, 3H), 7.39 (d, *J* = 7.9 Hz, 1H), 7.48 (dd, *J*

= 6.3, 3.2 Hz, 2H), 7.76 (dd, *J* = 6.0, 3.2 Hz, 1H), 8.24 (dd, *J* = 6.0, 3.7 Hz, 1H), 9.78 (br, s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.5, 23.2, 32.2, 47.9, 62.0, 108.2, 121.2, 121.8, 125.3, 125.4, 125.7, 126.4, 126.6, 126.7, 127.0, 127.5, 134.5, 140.1, 151.6; HRMS (EI) *m/z* 309.1181 (calcd for $C_{19}H_{19}NOS$ 309.1187).



(-)-**25**

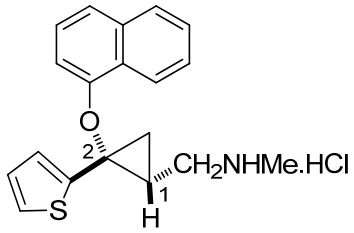
(-)-(1*R*,2*S*)-25. In a manner analogous to the conversion of (+)-**23** to (+)-**25**, amide (-)-**23** (140 mg, 0.433 mmol) was reduced to an amine which was acidified with hydrochloric acid to give (-)-**25** (108 mg, 72 %): $[\alpha]_D^{20}$ -189.0 (c 0.43, $CHCl_3$); HRMS (EI) *m/z* 309.1171 (calcd for $C_{19}H_{19}NOS$ 309.1187).



(+)-**26**

(+)-(1*S*,2*S*)-26. In a manner analogous to the conversion of (+)-**23** to (+)-**25**, amide (-)-**24** (140 mg, 0.430 mmol) was reduced with lithium aluminum hydride and the resulting amine was acidified with hydrochloric acid to give (+)-**26** (120 mg, 84%) as

a colorless solid: mp 252 °C (decomp); $[\alpha]_D^{20}$ +51.4 (c 0.07, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 1.56 (br. s, 1H), 2.03 (br. s, 2H), 2.88 (br. s, 3H), 3.42 (br. s, 2H), 6.90 (br. s, 1H), 6.95-7.05 (m, 2H), 7.15 (d, *J* = 5.0 Hz, 1H), 7.25-7.32 (m, 2H), 7.45 (d, *J* = 9.2 Hz, 1H), 7.50-7.57 (m, 2H) 7.81 (d, *J* = 8.0 Hz, 1H), 8.22 (br. s, 1H), 9.86 (br. s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.0, 26.4, 48.3, 61.4, 83.5, 108.7, 121.6, 121.8, 124.3, 125.0, 125.48, 125.52, 126.1, 126.6, 127.3, 127.8, 134.6, 143.6, 151.7.



(-)-**26**

(-)-(1*R*,2*R*)-26. In a manner analogous to the conversion of (+)-**23** to (+)-**25**, amide (+)-**24** (52.0 mg, 0.170 mmol) was reduced with lithium aluminum hydride and the resulting amine was acidified with hydrochloric acid to give (-)-**26** (25.0 mg, 45 %) as a colorless solid: mp 240 °C (decomp); $[\alpha]_D^{25}$ -65.6 (c 0.32, $CHCl_3$).

2.5 References

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CHAPTER 3

3.1 Evaluation (*in vivo* and *in vitro*) of Synosutine as an inhibitor of serotonin, norepinephrine, and dopamine transporters

Initial *in vitro* assays to determine the efficacy of cyclopropanes **25** and **26** as reuptake inhibitors of serotonin, norepinephrine, and dopamine were conducted on the racemates as well as the pure enantiomers by NovaScreen Inc. (Fig 11). Assays were conducted with reference compounds imipramine (**52**), desipramine (**53**) and GBR12909 (**54**) for comparison with synosutine stereoisomers. The *in vitro* data suggested that (±)-**25** is a relatively selective inhibitor of serotonin transporter whereas (±)-**26** is a more balanced inhibitor of both serotonin and norepinephrine transporter (Table 1). When enantiomers of **25** and **26** were synthesized and tested it became apparent that one enantiomer in particular, (+)-**26**, now known as synosutine, was a highly effective dual inhibitor of serotonin and norepinephrine transporter. With IC_{50} and K_i values in the 1-2 nM range, (+)-**26** compares favorably with Eli Lilly's duloxetine (Cymbalta®) as a dual reuptake inhibitor of serotonin and norepinephrine. Duloxetine is currently a front line drug for treatment of clinical depression.

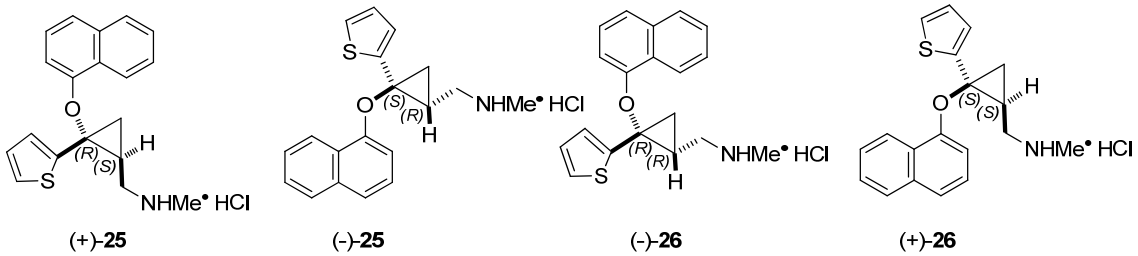
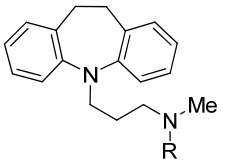


Fig 11. Stereoisomers of synosutine screened for bioactivity

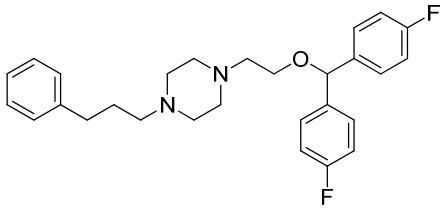
Table 1.
Inhibition of monamine transporters serotonin (5-HT), norepinephrine (NE) and dopamine (DA) by racemic **25** and **26**, their enantiomers and reference compounds.[a]

	Serotonin K_i (nM)	**Norepinephri** K_i (nM)	**Dopamine** K_i (nM)
(±)-**25**	7.47±0.45	75.7±17.2	586±120
(+)-**25**	33.2	153	913
(–)-**25**	17.6	330	790
(±)-**26**	2.01±0.16	4.16±1.27	283±5.3
(+)-**26**	2.10±0.60	1.19±0.08	223±20.5
(–)-**26**	30.4±0.78	27.8±0.32	1910±205
52	7.57±0.72		
53		5.11±0.70	
54			5.07±0.56

[a]Values in parentheses are those for reference compounds: imipramine (**52**) for serotonin transport, desipramine (**53**) for norepinephrine transport, and GBR12909 (**54**). IC_{50} is concentration of the drug required to reduce cell viability by 50 %.



52, R = Me (Imipramine)
53, R = H (Desipramine)

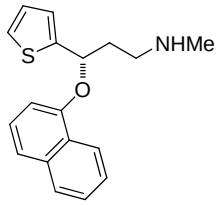


54 (GBR12909)

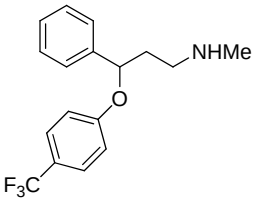
Synosutine was also assayed *in vivo* for its binding to human monoamine transporters and to various receptor sites *in vitro* using radioligand binding assays. These studies indicate that synosutine is a six fold more efficient reuptake inhibitor of norepinephrine and a threefold weaker reuptake inhibitor of serotonin compared to duloxetine. Overall, synosutine with a K_i of 1.2 nM for norepinephrine and 2.1 nM for serotonin is a more balanced inhibitor than duloxetine (Table 2).

Table 2.
Inhibition of transporters of norepinephrine, serotonin and dopamine by synosutine and reference inhibitors expressed as K_i (nM)

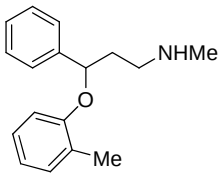
Inhibitor	Norepinephrine	Serotonin	Dopamine
Synosutine	1.2±0.1	2.1±0.6	223±0.1
Duloxetine	7.5±0.3	0.8±0.01	240±23
Fluoxetine	1022	7	4752
Atomoxetine	5	77	1451
52	98	19	>10000
53	3.8	179	>10000



Duloxetine (Cymbalta®)
10



Flouxetine (Prozac®)
13



Atomoxetine
14

Synosutine was tested at 1000 nM in duplicate samples using radioligand binding to their respective neuronal receptors. The study revealed that synosutine has high binding affinity towards serotonin receptors, especially 5-HT7, and moderate binding affinity towards serotonin 5-HT6, h and histamine H1, h neuronal receptors.

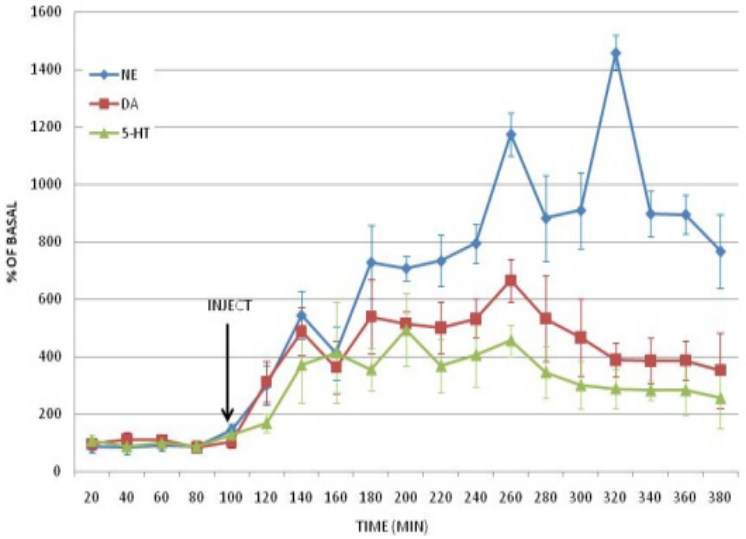
The binding affinity of synosutine towards adrenergic (alpha1, alpha2 and beta), muscarinic acetylcholine, M1 receptor, non-selective QNB, dopamine (D1, h and D2s, h), GABA (A and B), glutamate (NMDA agonist, and MK801 sites and serotonin (5-HT-1A, h; 1B; 1D, h; 2A, h; 2C; 3, h; 4; and 5A, h) neuronal receptors were found to be weaker (inhibition less than 50 % is considered to be inactive) (Table 3).

Table 3. Binding affinity of synosutine towards various neuronal receptors

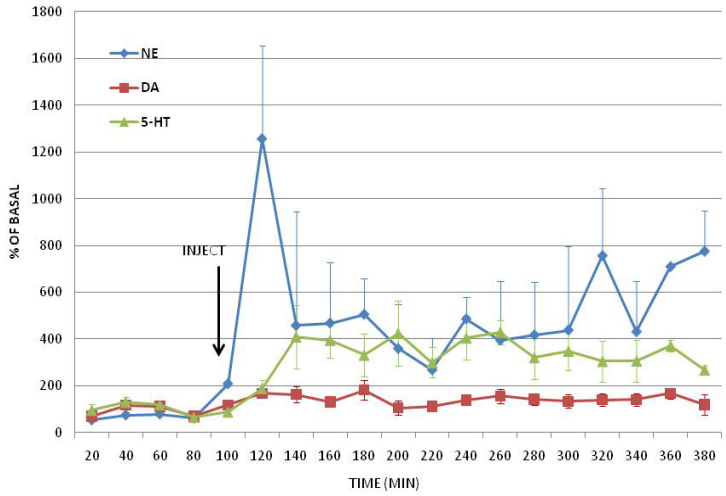
Receptors	**Inhibition (%)**
Histamine (H1, h)	65
Serotonin (5-HT6, h)	62
Serotonin (5-HT7)	88
Adrenergic (alpha1, alpha2, beta)	< 50
Muscarinic acetylcholine	< 50
M1 receptor	< 50
Non-selective QNB	< 50
Dopamine (D1, h and D2s, h)	< 50
GABA (A and B)	< 50
Glutamate (NMDA agonist, and MK801 sites)	< 50
Serotonin (5-HT-1A, h; 1B; 1D, h; 2A, h; 2C; 3, h; 4; and 5A, h)	< 50

A variety of analytical techniques have been employed to determine the level of monoamine neurotransmitters *in vivo*. Among them, *in vivo* microdialysis is able to

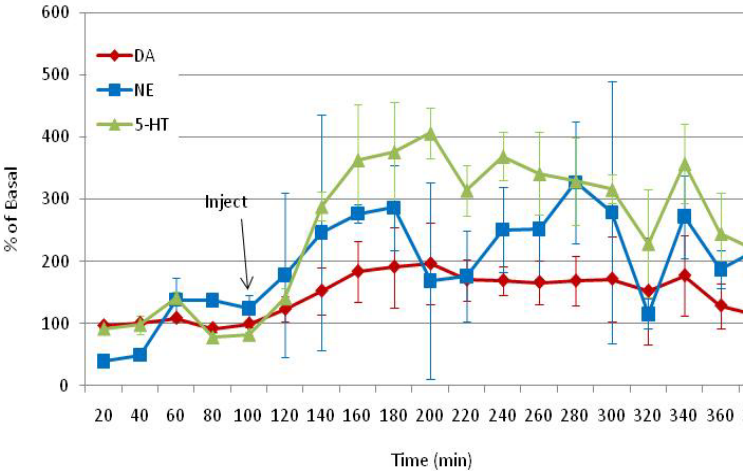
detect these neurotransmitters at low concentration (0.5 -1 nM). The technique entails installation of small probes with semipermeable membranes into different brain regions of interest. The effect of systemic administration of 10 mg/kg of synosutine on extracellular levels of serotonin, norepinephrine and dopamine in the prefrontal cortex, the nucleus accumbens, and the striatum of male Wistar rats was studied using *in vivo* microdialysis. These different areas of the rat brain were chosen due to their importance in normal brain functioning. In particular, chemistry occurring in the prefrontal cortex is directly related to depression in humans. The study showed that synosutine increases the levels of serotonin, norepinephrine, and dopamine in the prefrontal cortex (Fig 12 a), whereas it is more selective towards reuptake inhibition of serotonin and norepinephrine in the nucleus accumbens and the striatum. This is reflected in the elevated levels of these neurotransmitters shown in Fig 12 b-c. The increased level of dopamine in the prefrontal cortex but not in the nucleus accumbens is indicative of inhibition of norepinephrine transport in the prefrontal cortex as a result of selective clearance of dopamine by norepinephrine neurons in the prefrontal cortex. These findings suggest that the pharmacological profile of synosutine is similar to that of duloxetine. In conclusion, it appears that synosutine would be at least as successful as duloxetine (Cymbalta®) for treatment of clinical depression in humans.



a) Levels of NE, DA and 5-HT in the prefrontal cortex



b) Levels of NE, DA and 5-HT in the nucleus accumbens



c) Levels of NE, DA and 5-HT in the striatum

Fig 12. Synosutine elevations of norepinephrine (NE), serotonin (5-HT) and dopamine (DA) level in different brain regions

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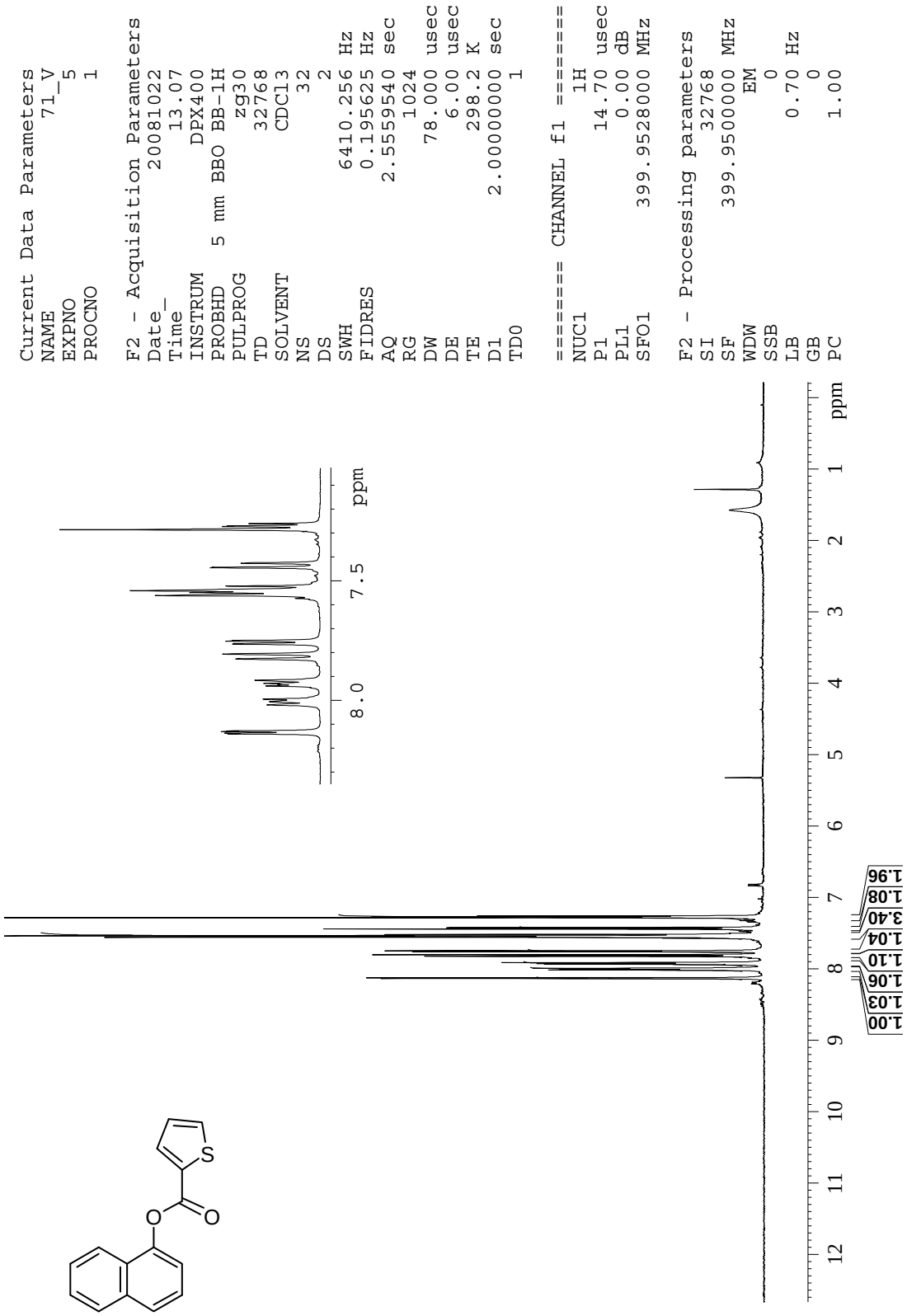
APPENDIX

APPENDIX I
NMR Spectra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FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 1024
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
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NUC1 1H
P1 14.70 usec
PL1 0.00 dB
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WDW EM
SSB 0
LB 0.70 Hz
GB 0
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8.0
7.5
ppm
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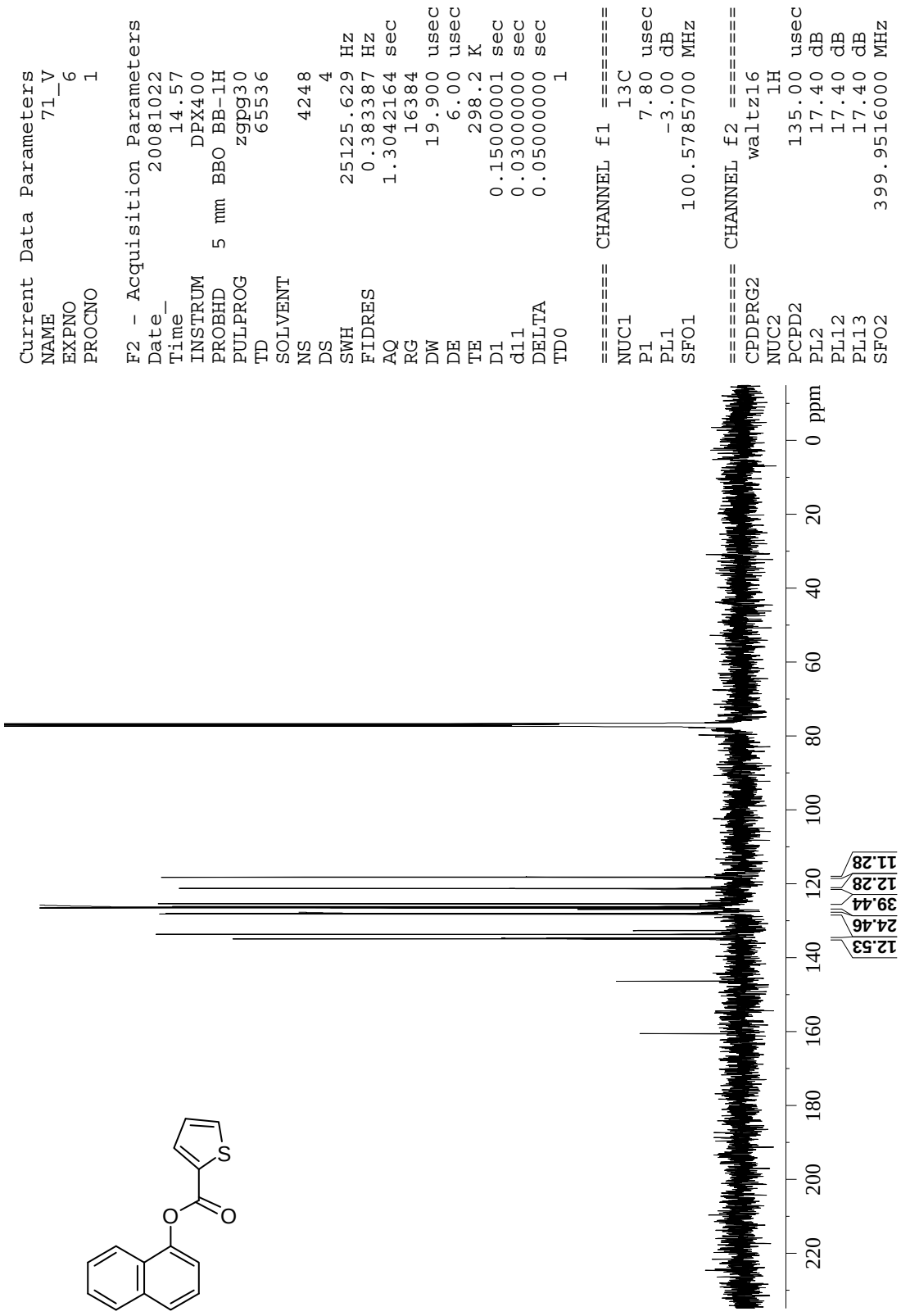
3.40
1.08
1.96
ppm
S
O
O

17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FIDRES 0.383387 Hz
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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
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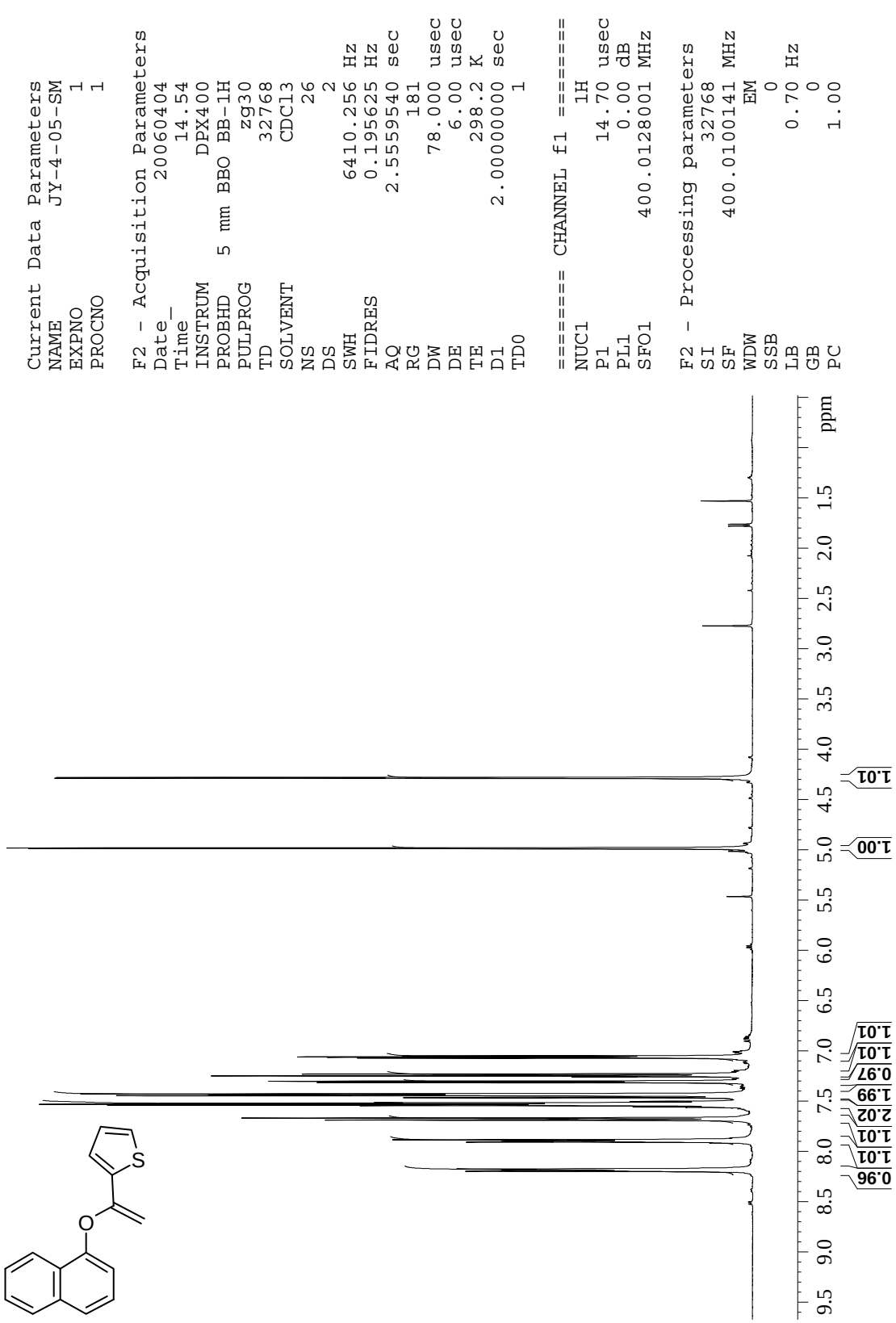
12.28
39.44
24.46
12.53
S
O
O

17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FIDRES 0.195625 Hz
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RG 181
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DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
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P1 14.70 usec
PL1 0.00 dB
SFO1 400.0128001 MHz
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SI 32768
SF 400.0100141 MHz
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SSB 0
LB 0.70 Hz
GB 0
PC 1.00
0.96
1.01
1.01
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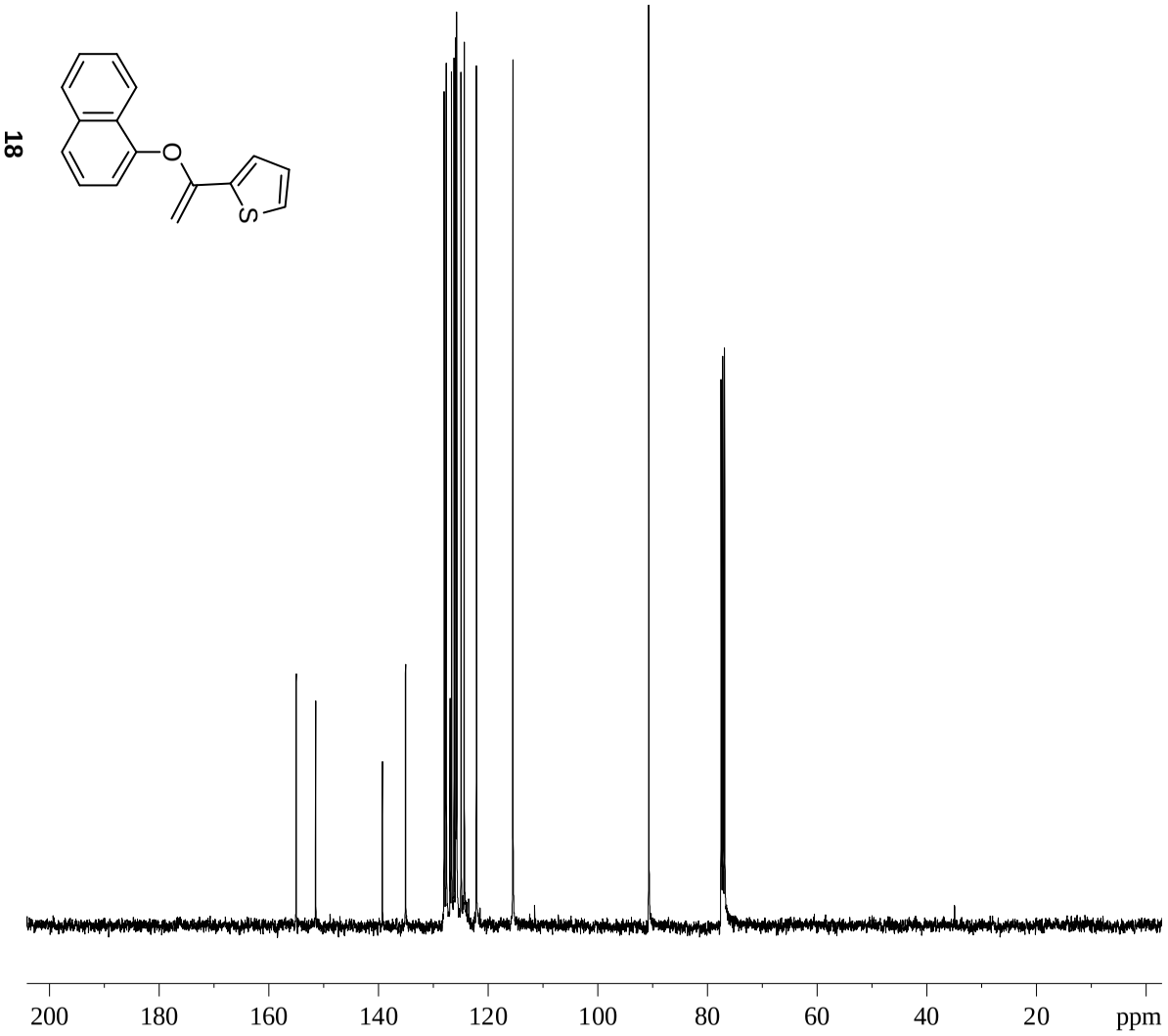
1.01
1.00
1.01
ppm
S
O

18

18

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SOLVENT
NS                 1799
DS                    4
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FIDRES         0.383387 Hz
AQ            1.3042164 sec
RG               4597.6
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 ========
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PL12               17.40 dB
PL13               17.40 dB
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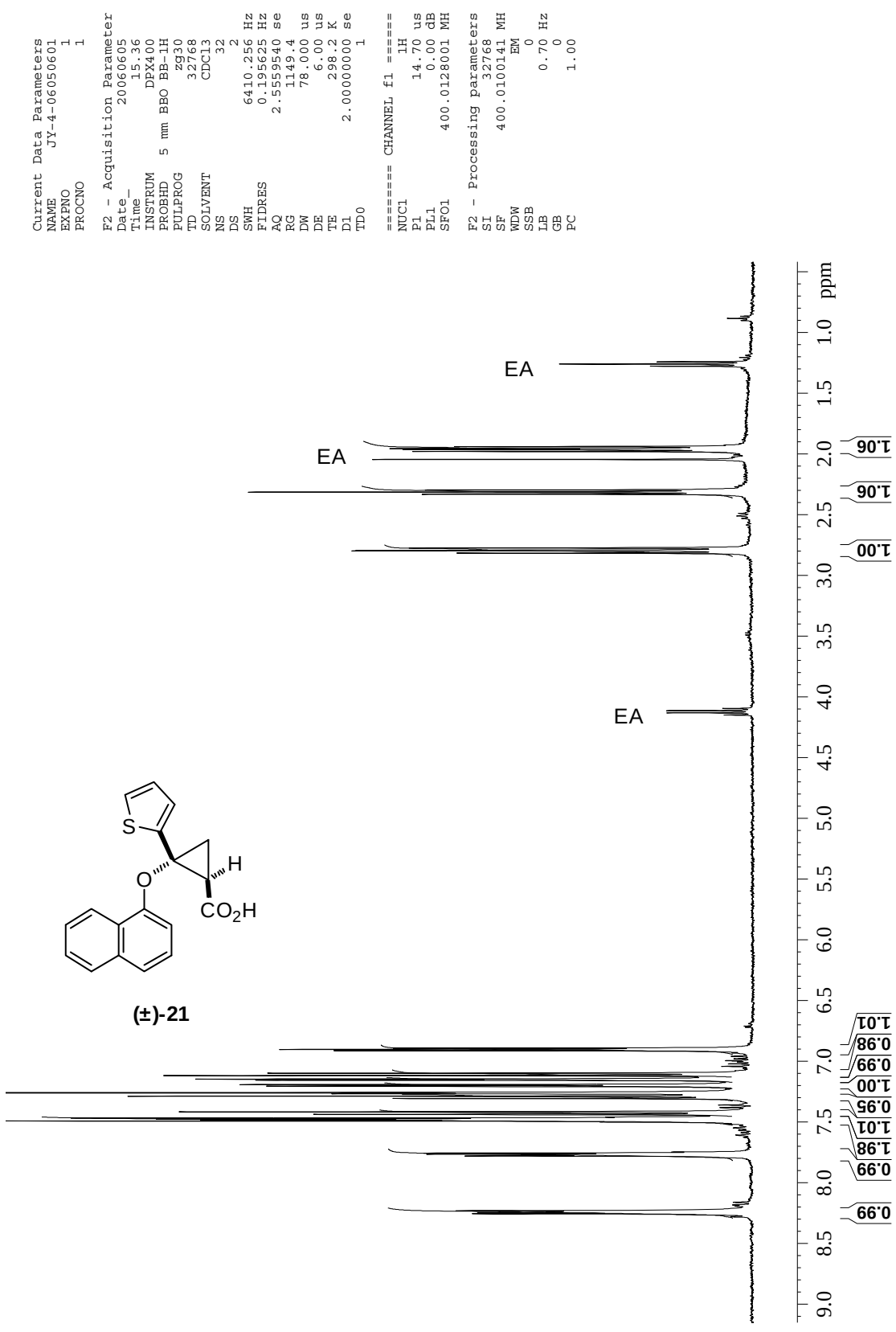
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FIDRES 0.195625 Hz
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RG 1149.4
DW 78.000 us
DE 6.00 us
TE 298.2 K
D1 2.00000000 se
TD0 1
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PL1 0.00 dB
SFO1 400.0128001 MH
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SI 32768
SF 400.0100141 MH
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LB 0.70 Hz
GB 0
PC 1.00
EA
EA
EA
S
O
H
CO2H
(±)-21
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1.98
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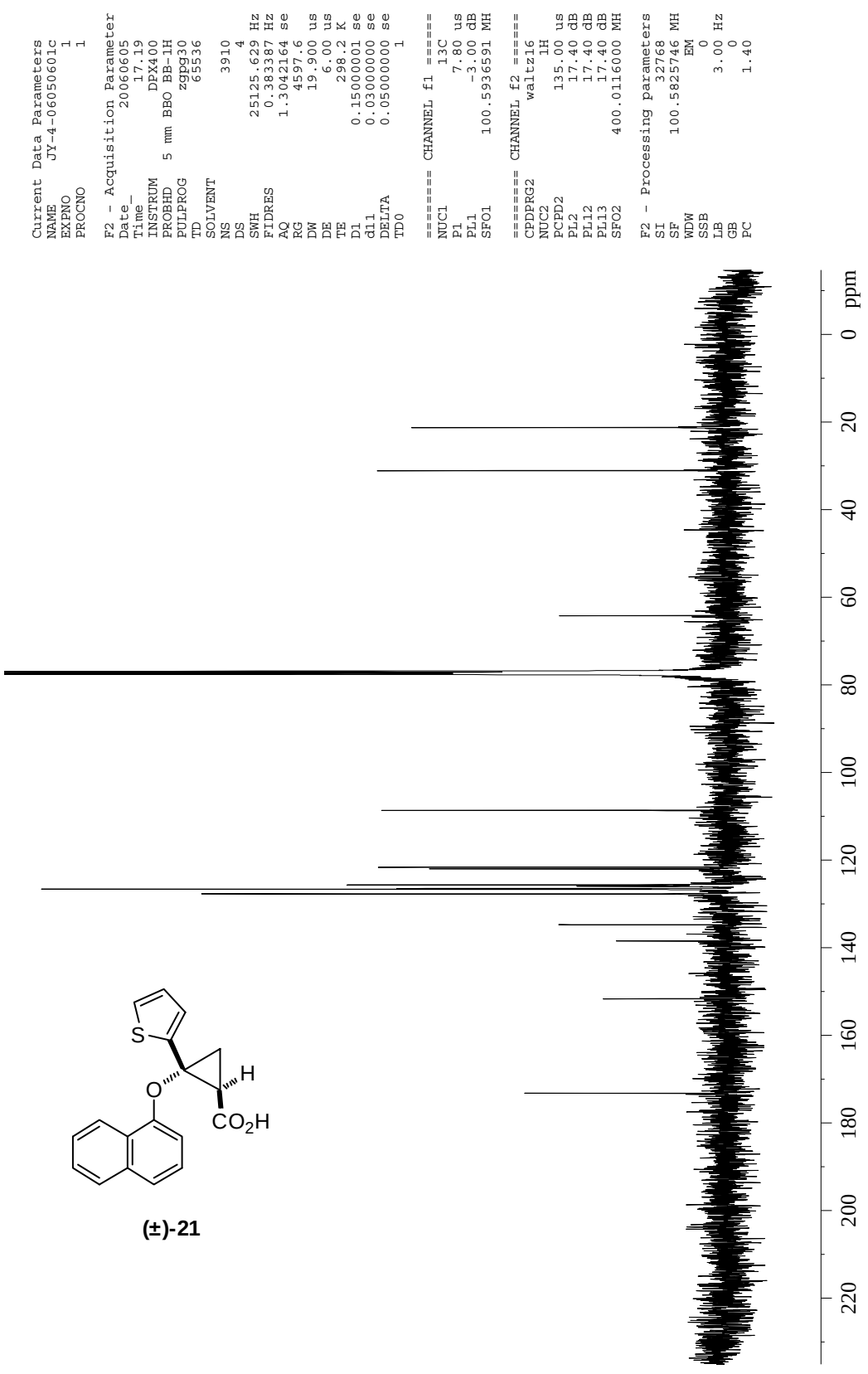
0.99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FIDRES 0.383387 Hz
AQ 1.3042164 se
RG 4597.6
DW 19.900 us
DE 6.00 us
TE 298.2 K
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d11 0.03000000 se
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NUC1 13C
P1 7.80 us
PL1 -3.00 dB
SFO1 100.5936591 MH
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NUC2 1H
PCPD2 135.00 us
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PL13 17.40 dB
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F2 - Processing parameters
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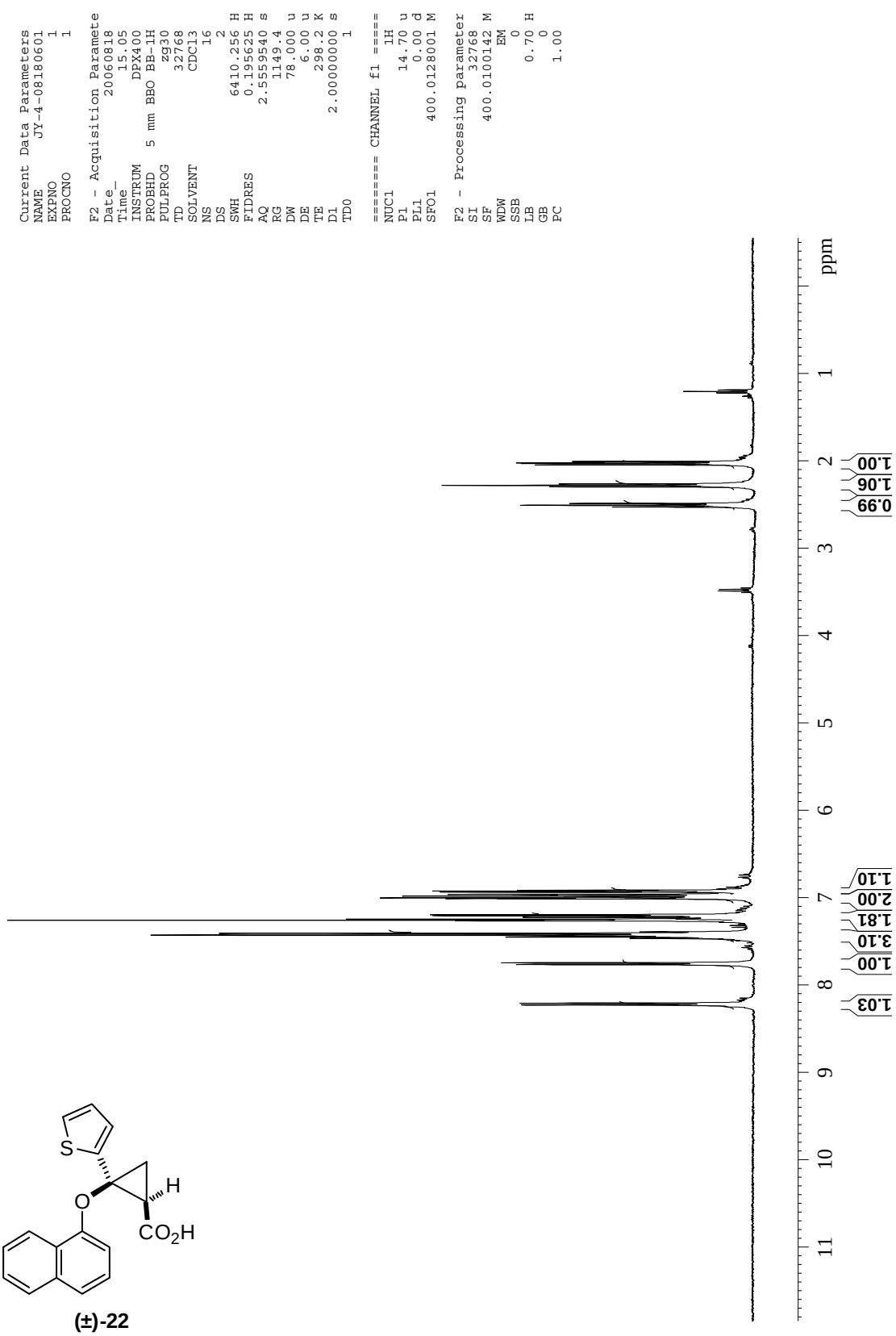
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RG 1149.4
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SSB 0
LB 0.70 Hz
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PC 1.00
1.03
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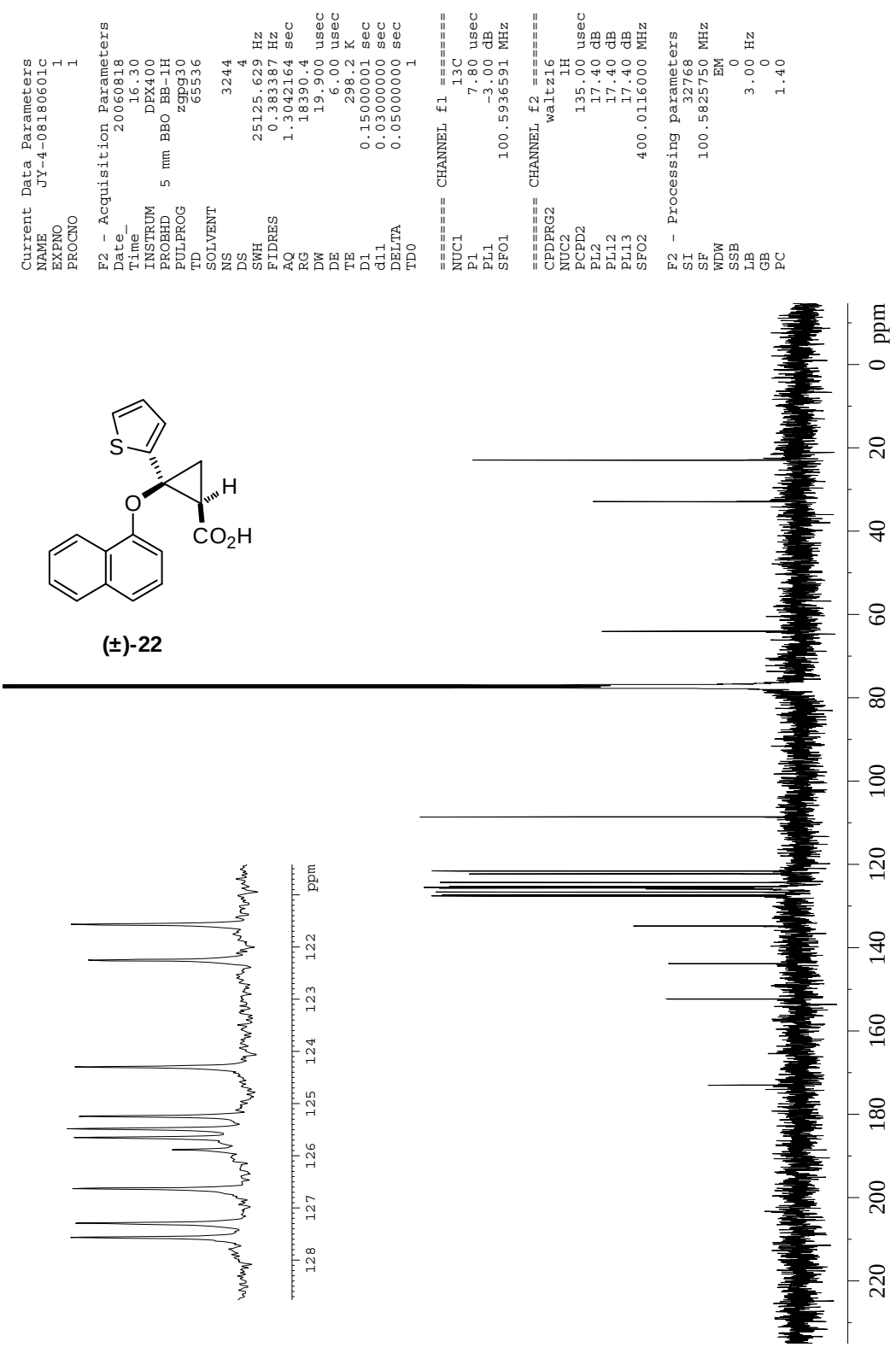
ppm
S
O
H
CO2H

(±)-22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d11 0.03000000 sec
DELTA 0.05000000 sec
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P1 7.80 usec
PL1 -3.00 dB
SFO1 100.5936591 MHz
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NUC2 1H
PCPD2 135.00 usec
PL2 17.40 dB
PL12 17.40 dB
PL13 17.40 dB
SFO2 400.0116000 MHz
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SF 100.5825750 MHz
WDW EM
SSB 0
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H
CO2H
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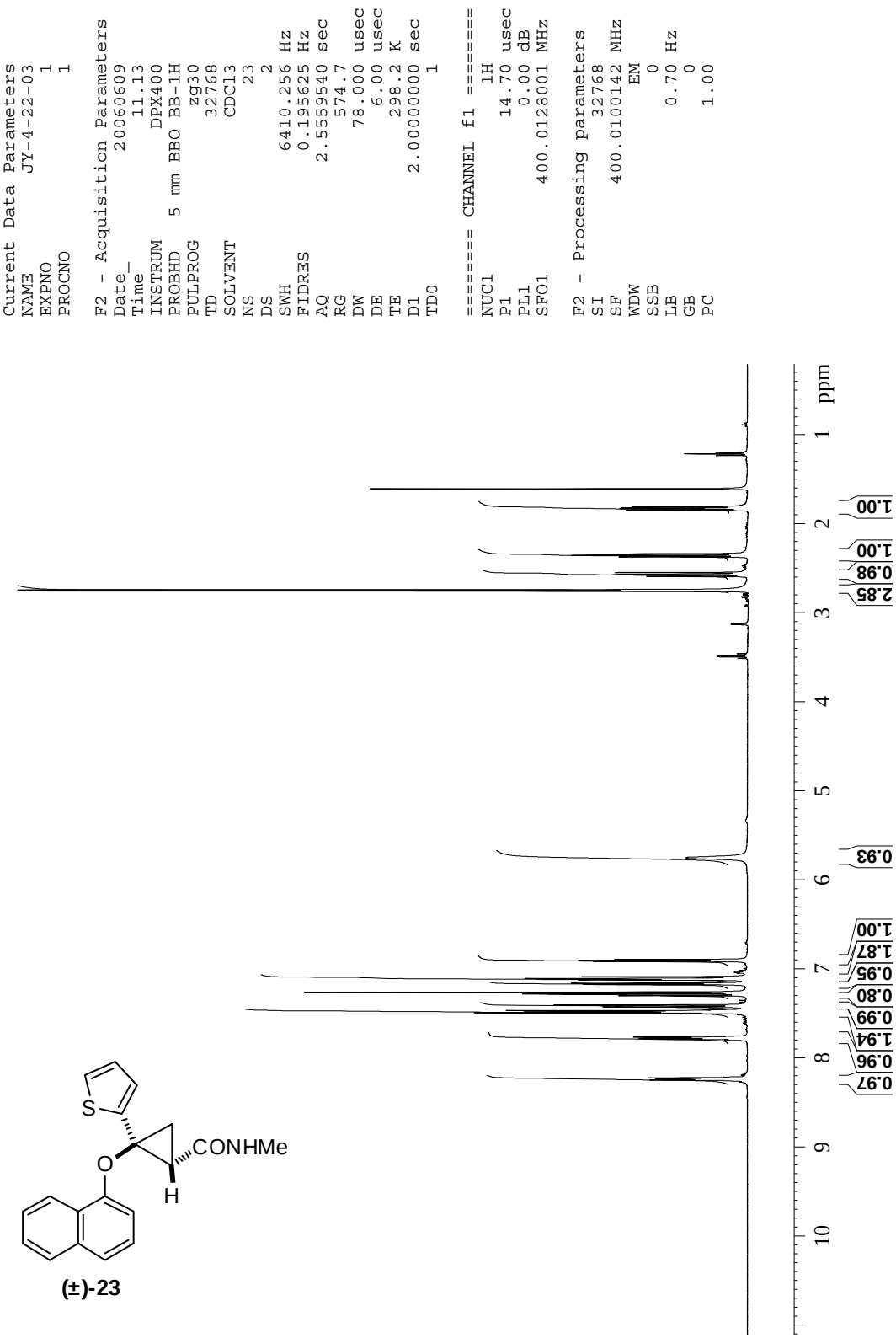
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S
O
H
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(±)-23
ppm
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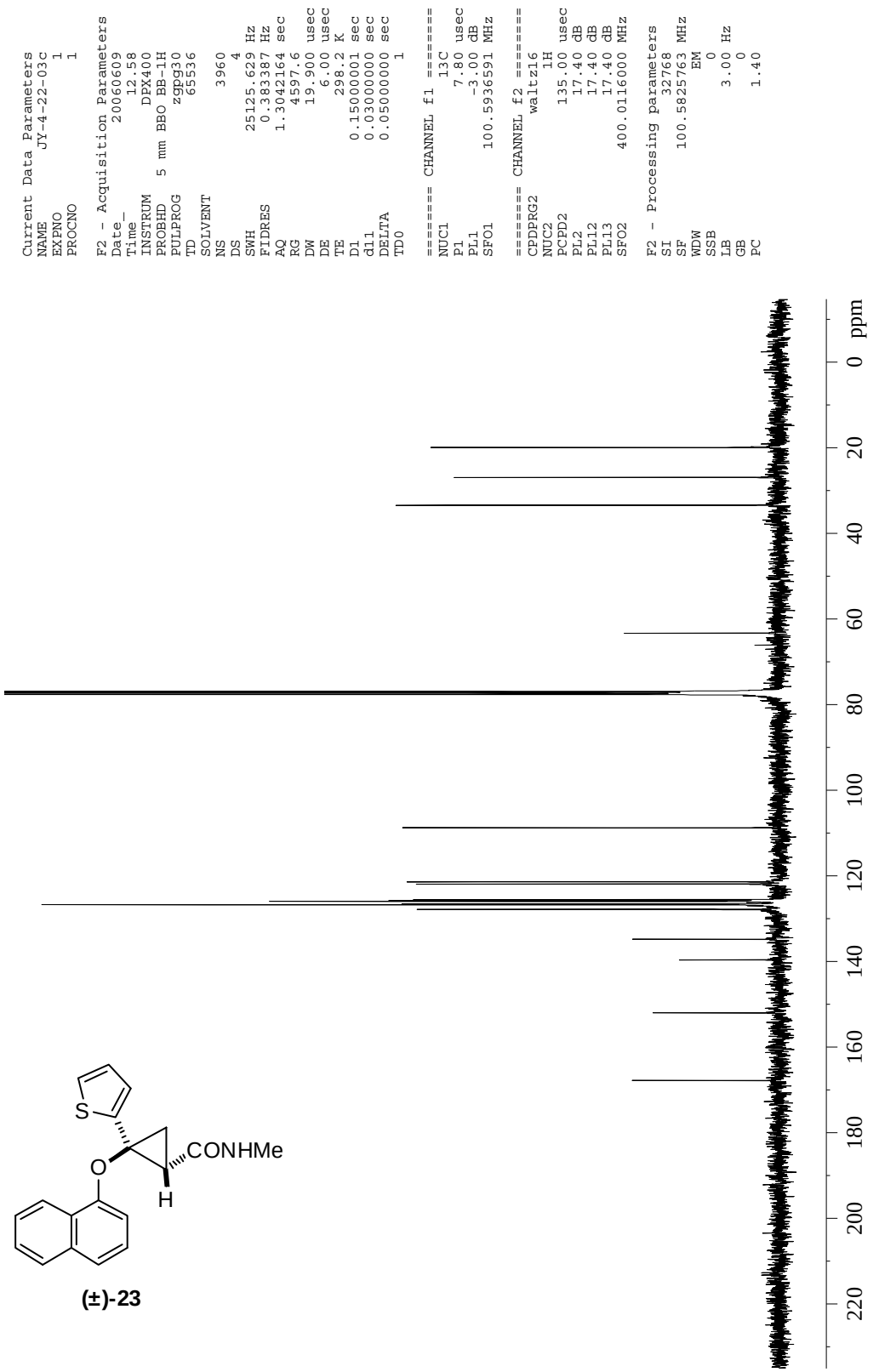
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DE 6.00 usec
TE 298.2 K
D1 0.15000001 sec
d11 0.03000000 sec
DELTA 0.05000000 sec
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P1 7.80 usec
PL1 -3.00 dB
SFO1 100.5936591 MHz
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NUC2 1H
PCPD2 135.00 usec
PL2 17.40 dB
PL12 17.40 dB
PL13 17.40 dB
SFO2 400.0116000 MHz
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WDW EM
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GB 0
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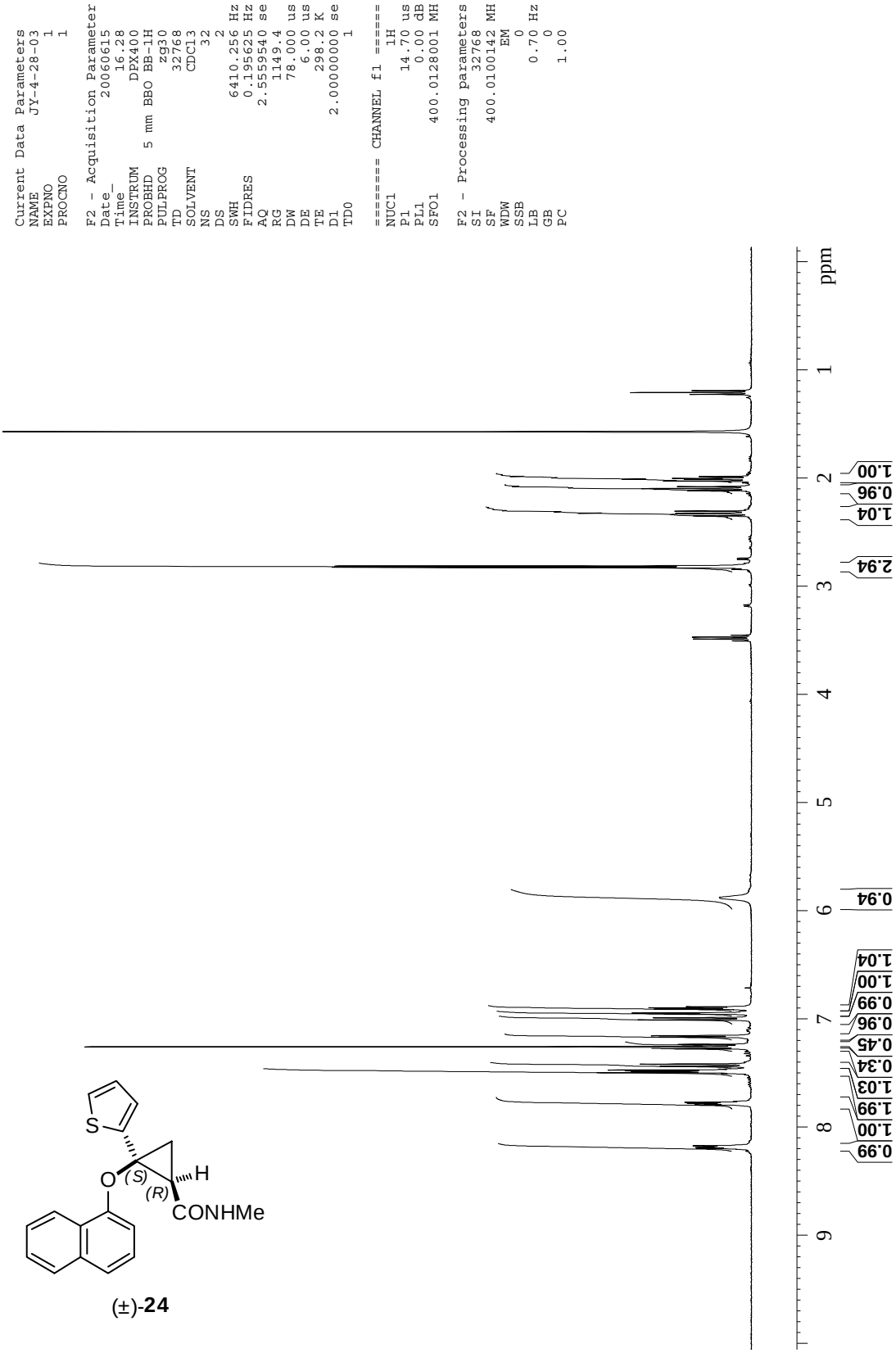
180
200
220

(±)-23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FIDRES 0.195625 Hz
AQ 2.5559540 se
RG 1149.4
DW 78.000 us
DE 6.00 us
TE 298.2 K
D1 2.00000000 se
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ppm
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2.94
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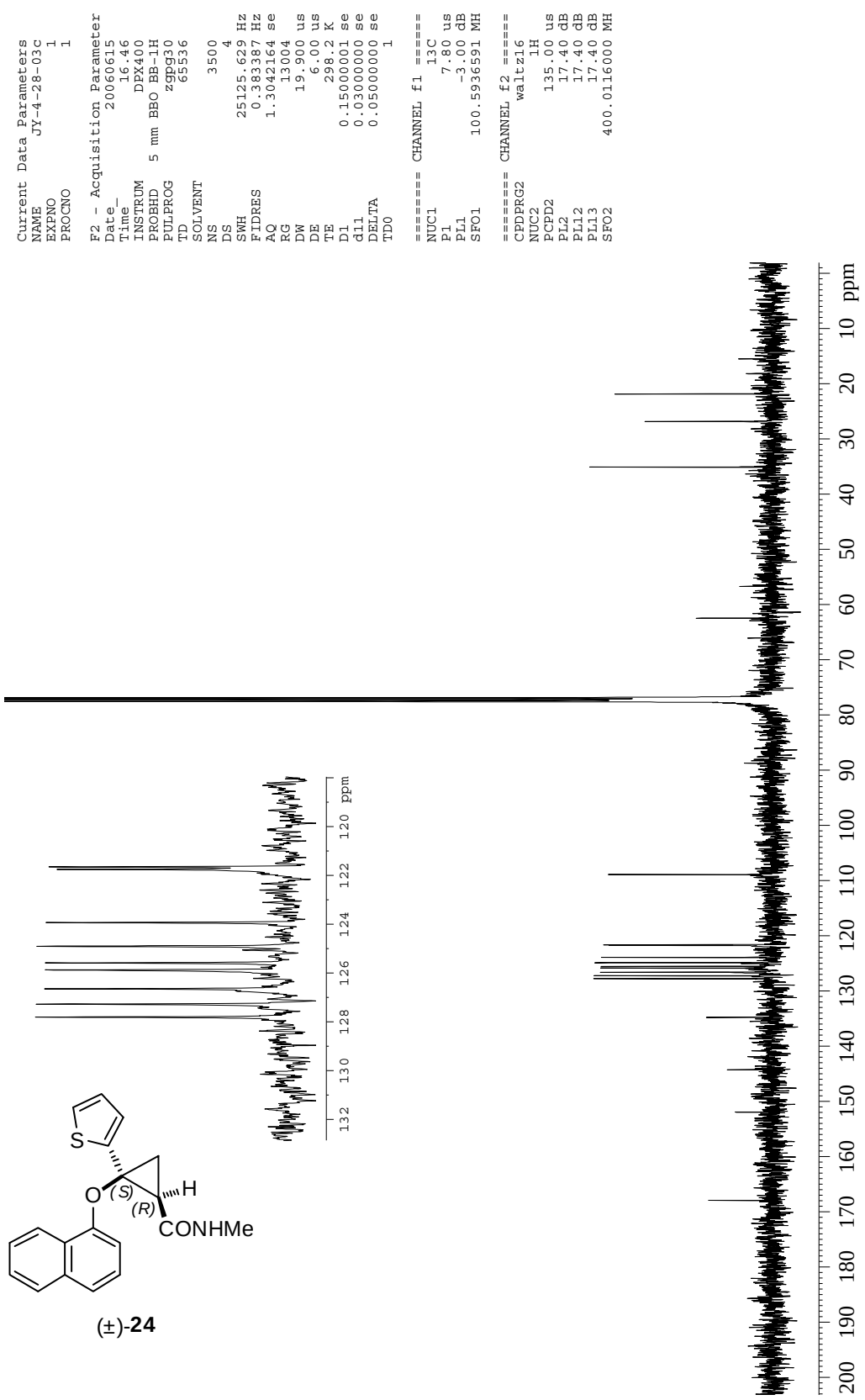
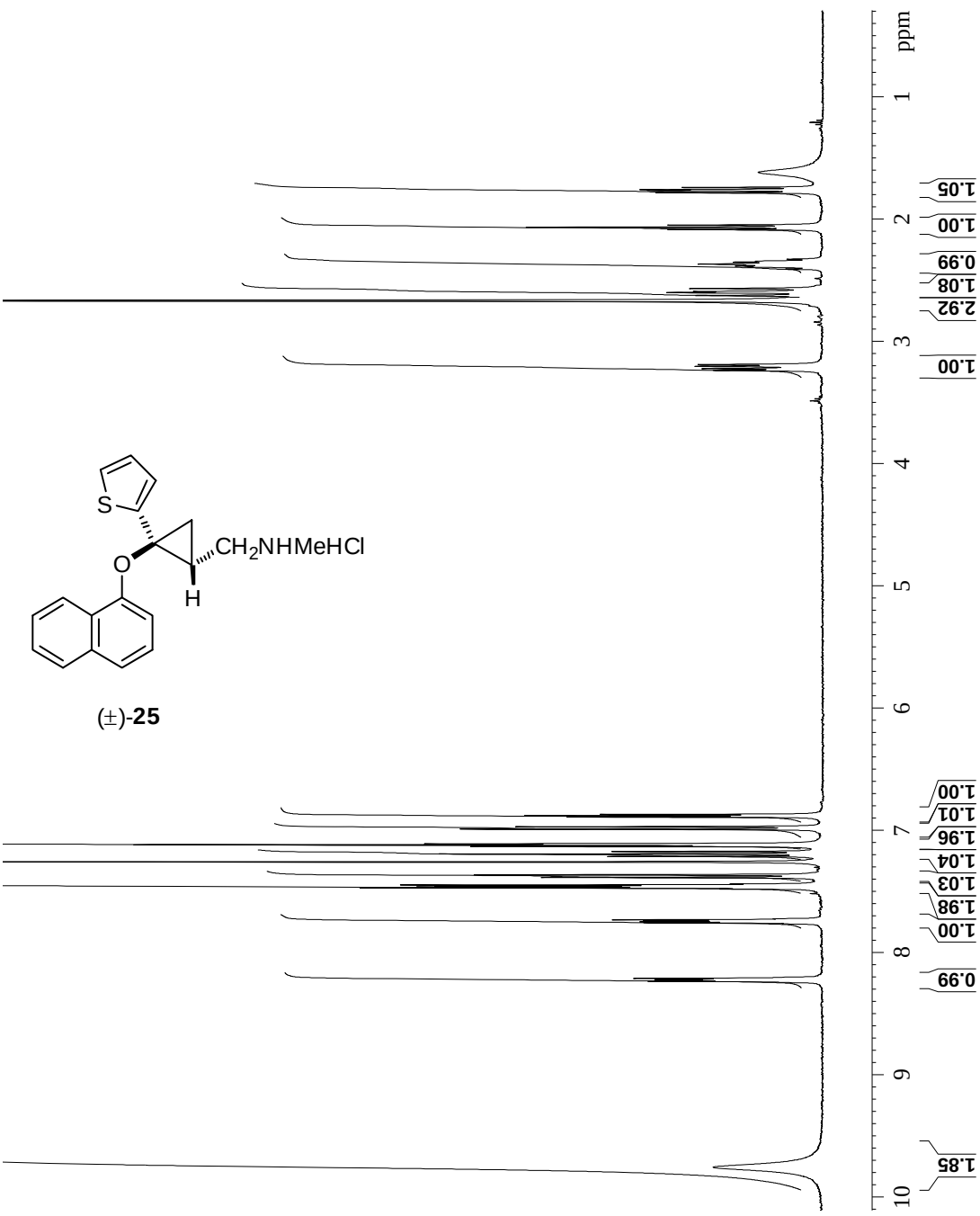
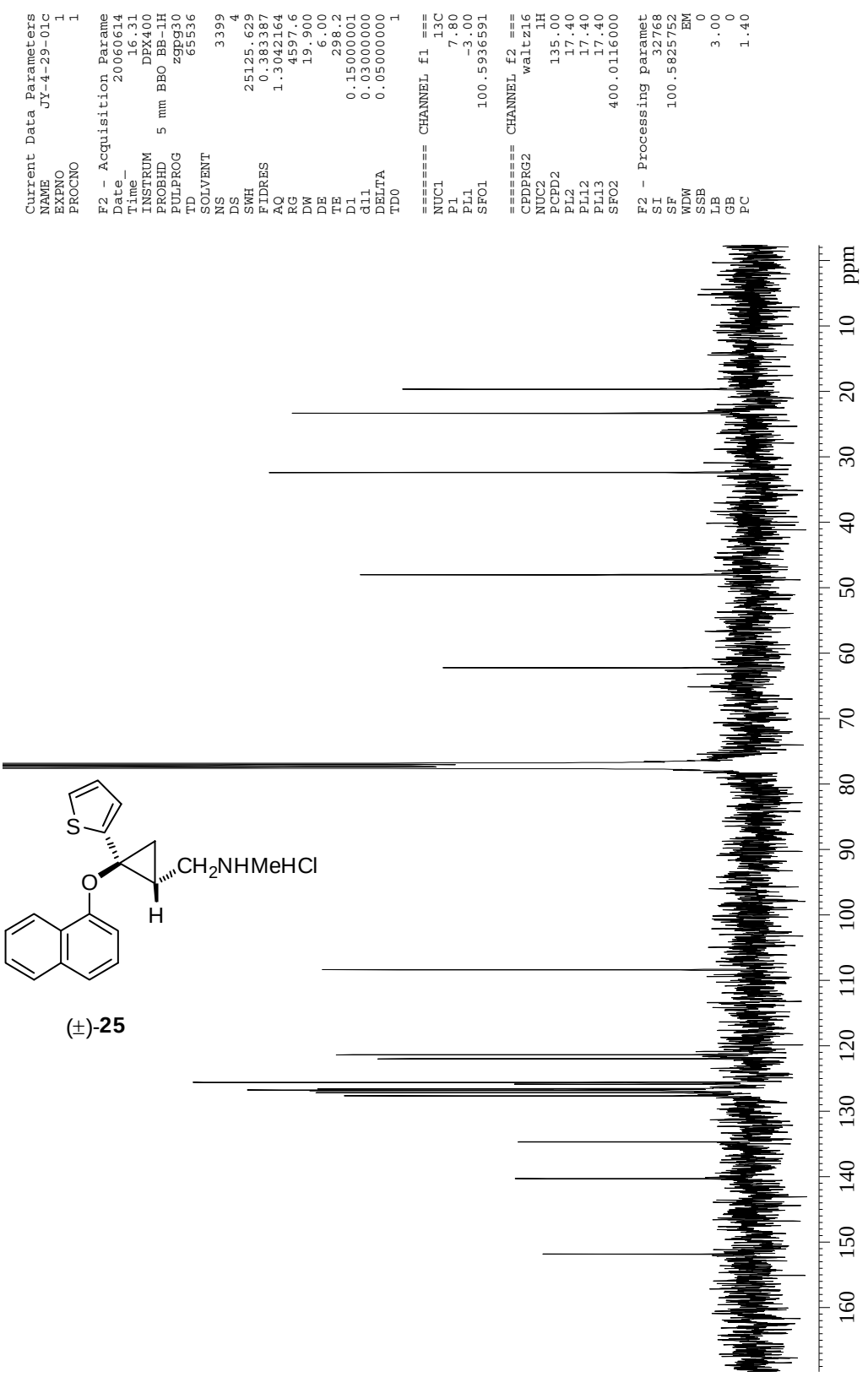
1.00
0.99
0.96
0.45
0.34
1.03
1.99
1.00
0.99
S
O
(S)
(R)
H
CONHMe

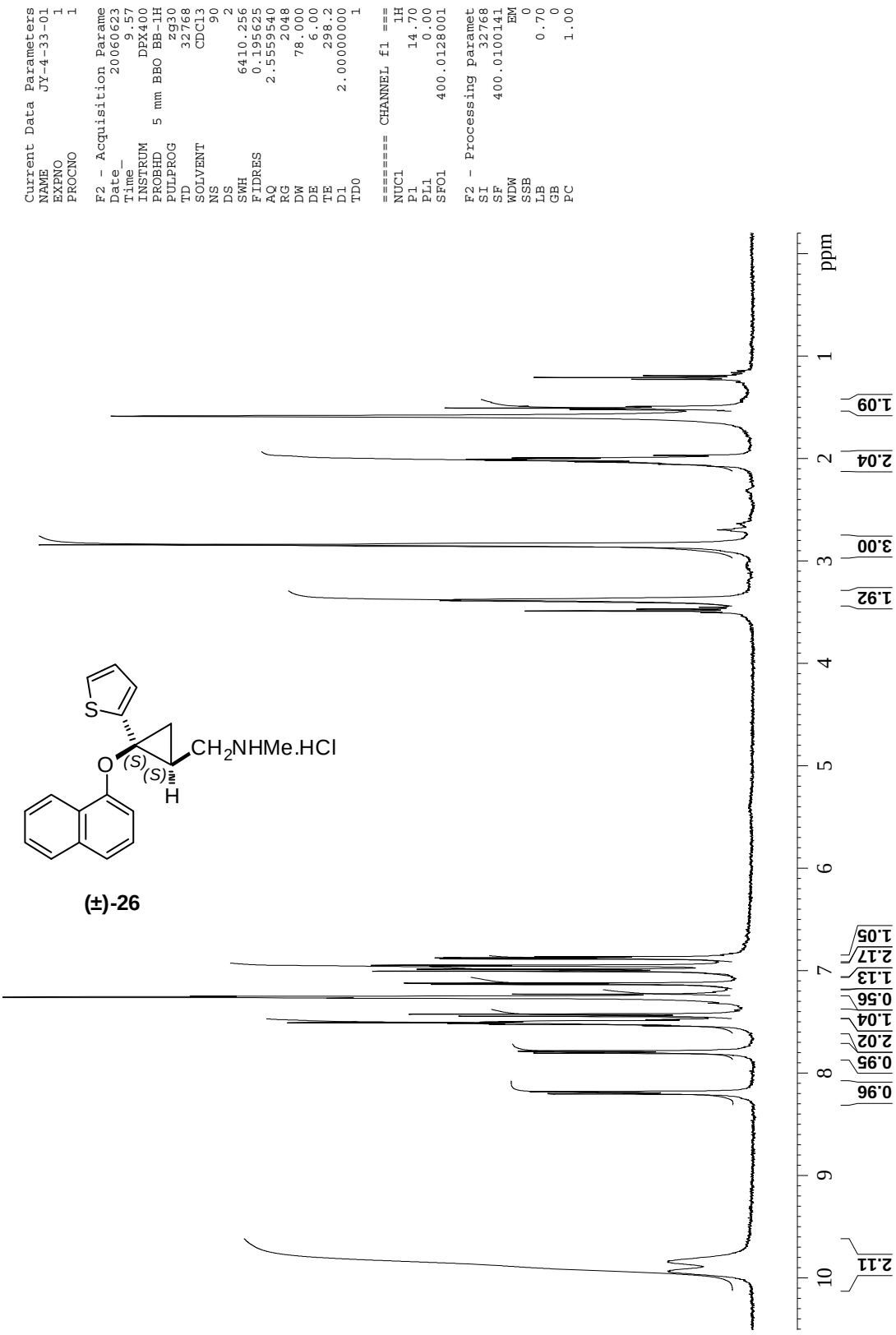
(±)-**24**

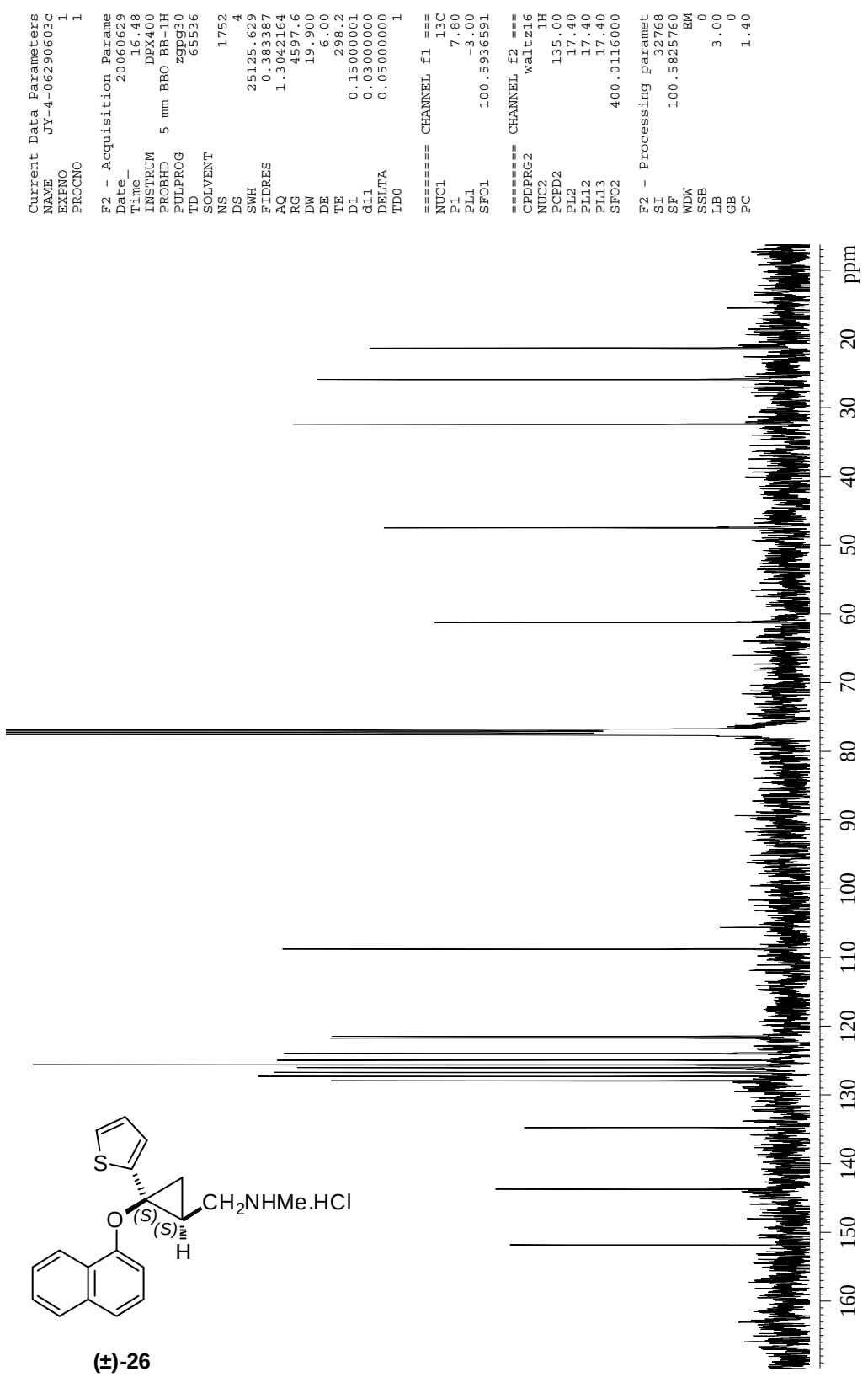

Current Data Parameters
NAME JY-4-28-03c
EXPNO 1
PROCNO 1
F2 - Acquisition Parameter
Date_ 20060615
Time_ 16.46
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 3500
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3042164 se
RG 13004
DW 19.900 us
DE 6.00 us
TE 298.2 K
D1 0.15000001 se
d11 0.03000000 se
DELTA 0.05000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 13C
P1 7.80 us
PL1 -3.00 dB
SFO1 100.5936591 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
S
O
(S)
(R)
H
CONHMe
ppm
ppm

(±)-**24**

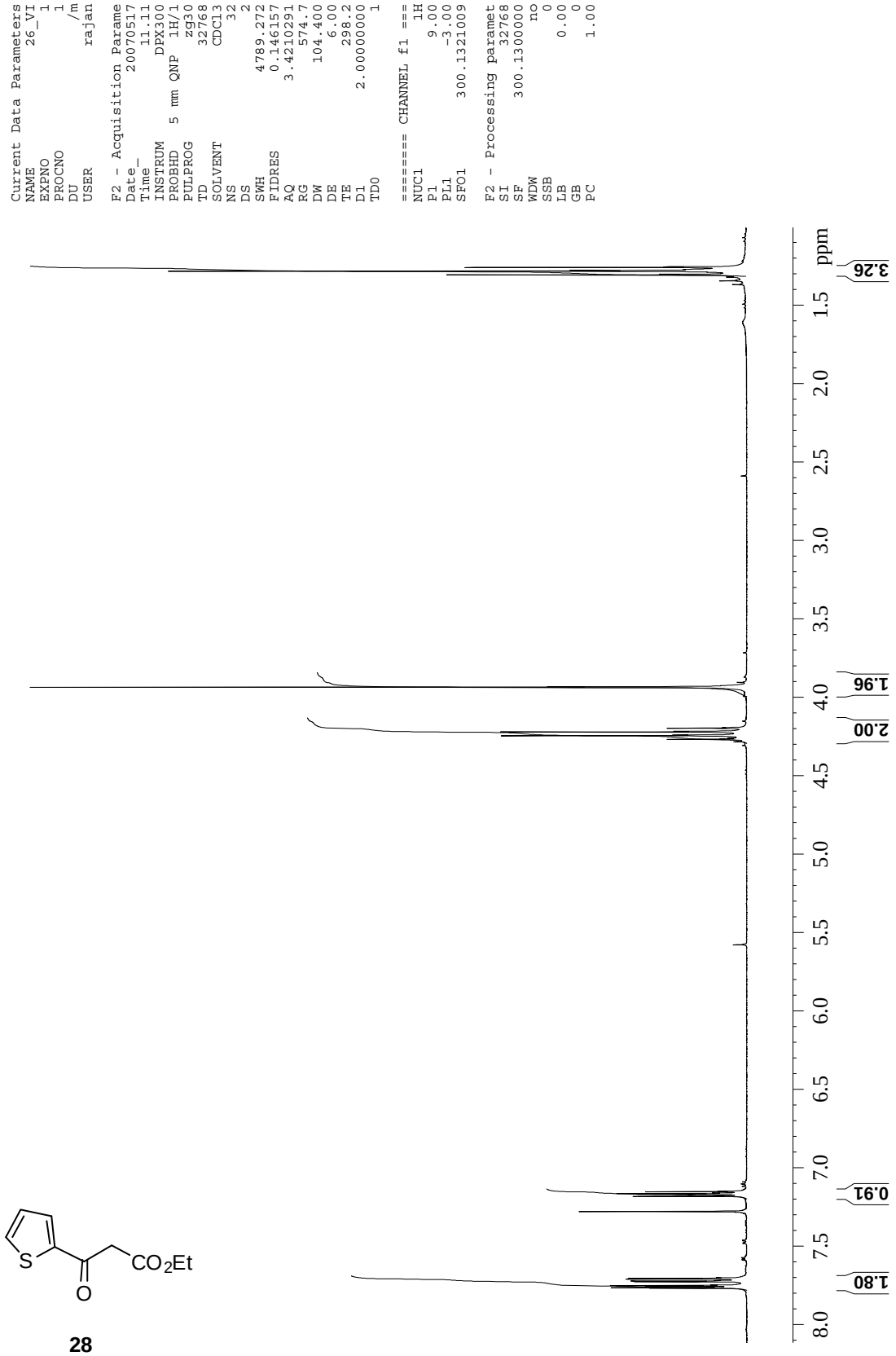

Current Data Parameters
NAME JY-4-29-01
EXPNO 1
PROCNO 1
F2 - Acquisition Parame
Date_ 20060614
Time_ 15.00
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256
FIDRES 0.195625
AQ 2.5559540
RG 1149.4
DW 78.000
DE 6.00
TE 298.2
D1 2.00000000
TD0 1
======== CHANNEL f1 ===
NUC1 1H
P1 14.70
PL1 0.00
SFO1 400.0128001
F2 - Processing paramet
SI 32768
SF 400.0100142
WDW EM
SSB 0
LB 0.70
GB 0
PC 1.00
S
O
H
CH2NHMeHCl
(±)-25
ppm
1.85
0.99
1.00
1.98
1.03
1.04
1.96
1.01
1.00
1.00
2.92
1.08
0.99
1.00
1.05


Current Data Parameters
NAME JY-4-29-01c
EXPNO 1
PROCNO 1
F2 - Acquisition Parame
Date_ 20060614
Time_ 16.31
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 3399
DS 4
SWH 25125.629
FIDRES 0.383387
AQ 1.3042164
RG 4597.6
DW 19.900
DE 6.00
TE 298.2
D1 0.15000001
d11 0.03000000
DELTA 0.05000000
TD0 1
======== CHANNEL f1 ===
NUC1 13C
P1 7.80
PL1 -3.00
SFO1 100.5936591
======== CHANNEL f2 ===
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00
PL2 17.40
PL12 17.40
PL13 17.40
SFO2 400.0116000
F2 - Processing paramet
SI 32768
SF 100.5825752
WDW EM
SSB 0
LB 3.00
GB 0
PC 1.40
S
O
H
CH2NHMeHCl
(±)-25
ppm

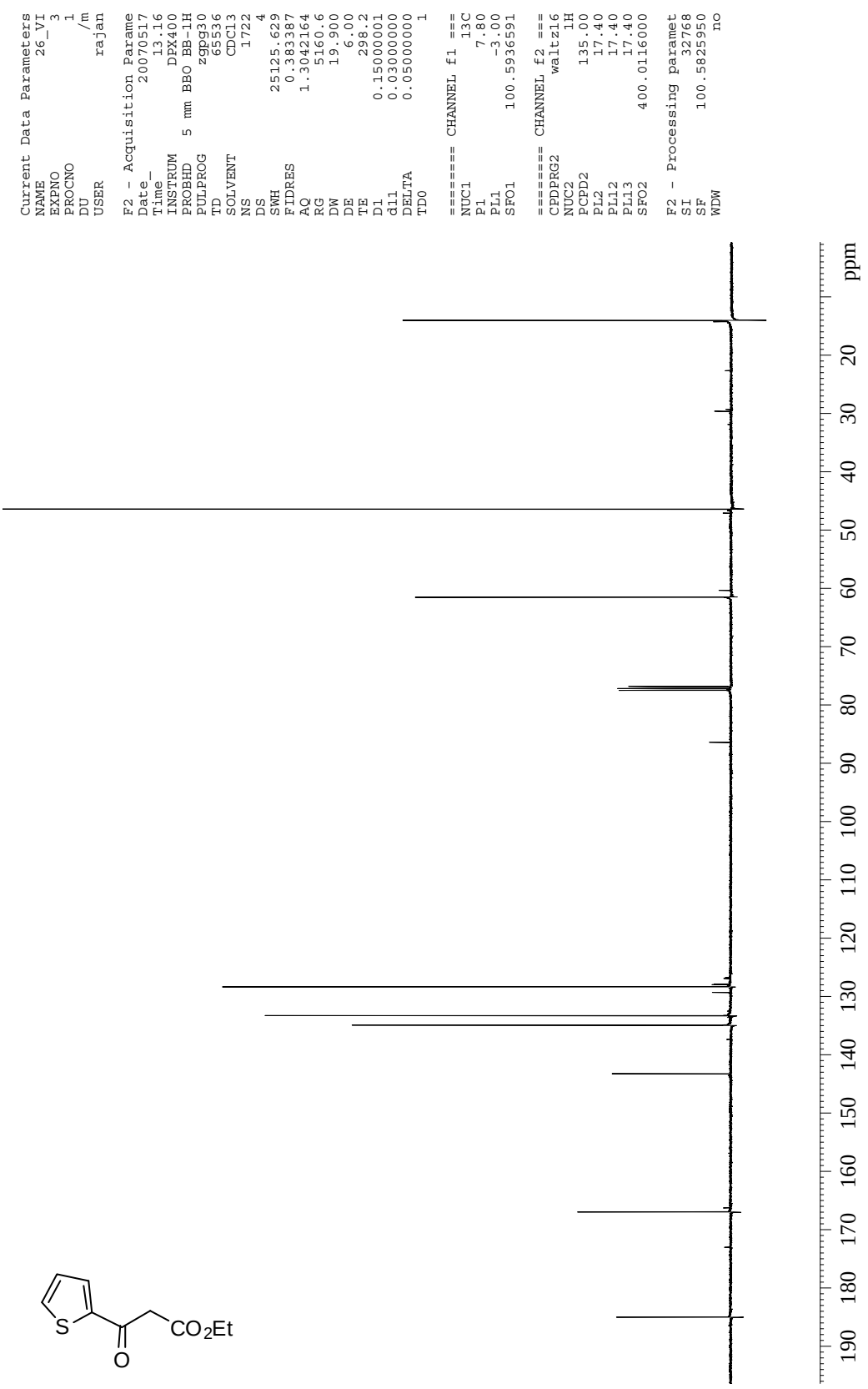

Current Data Parameters
NAME JY-4-33-01
EXPNO 1
PROCNO 1
F2 - Acquisition Parame
Date_ 20060623
Time_ 9.57
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 90
DS 2
SWH 6410.256
FIDRES 0.195625
AQ 2.5559540
RG 2048
DW 78.000
DE 6.00
TE 298.2
D1 2.00000000
TD0 1
======== CHANNEL f1 ===
NUC1 1H
P1 14.70
PL1 0.00
SFO1 400.0128001
F2 - Processing paramet
SI 32768
SF 400.0100141
WDW EM
SSB 0
LB 0.70
GB 0
PC 1.00
S
O
(S)
(S)
H
CH2NHMe.HCl
(±)-26
ppm
1
2
3
4
5
6
7
8
9
10
1.09
2.04
3.00
1.92
0.96
0.95
2.02
1.04
0.56
1.13
2.17
1.05
2.11


Current Data Parameters
NAME JY-4-062906 03c
EXPNO 1
PROCNO 1
F2 - Acquisition Parame
Date_ 20060629
Time_ 16.48
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 1752
DS 4
SWH 25125.629
FIDRES 0.383387
AQ 1.3042164
RG 4597.6
DW 19.900
DE 6.00
TE 298.2
D1 0.15000001
d11 0.03000000
DELTA 0.05000000
TD0 1
======== CHANNEL f1 ===
NUC1 13C
P1 7.80
PL1 -3.00
SFO1 100.5936591
======== CHANNEL f2 ===
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00
PL2 17.40
PL12 17.40
PL13 17.40
SFO2 400.0116000
F2 - Processing paramet
SI 32768
SF 100.5825760
WDW EM
SSB 0
LB 3.00
GB 0
PC 1.40
ppm
S
O
(S)
(S)
H
CH2NHMe.HCl

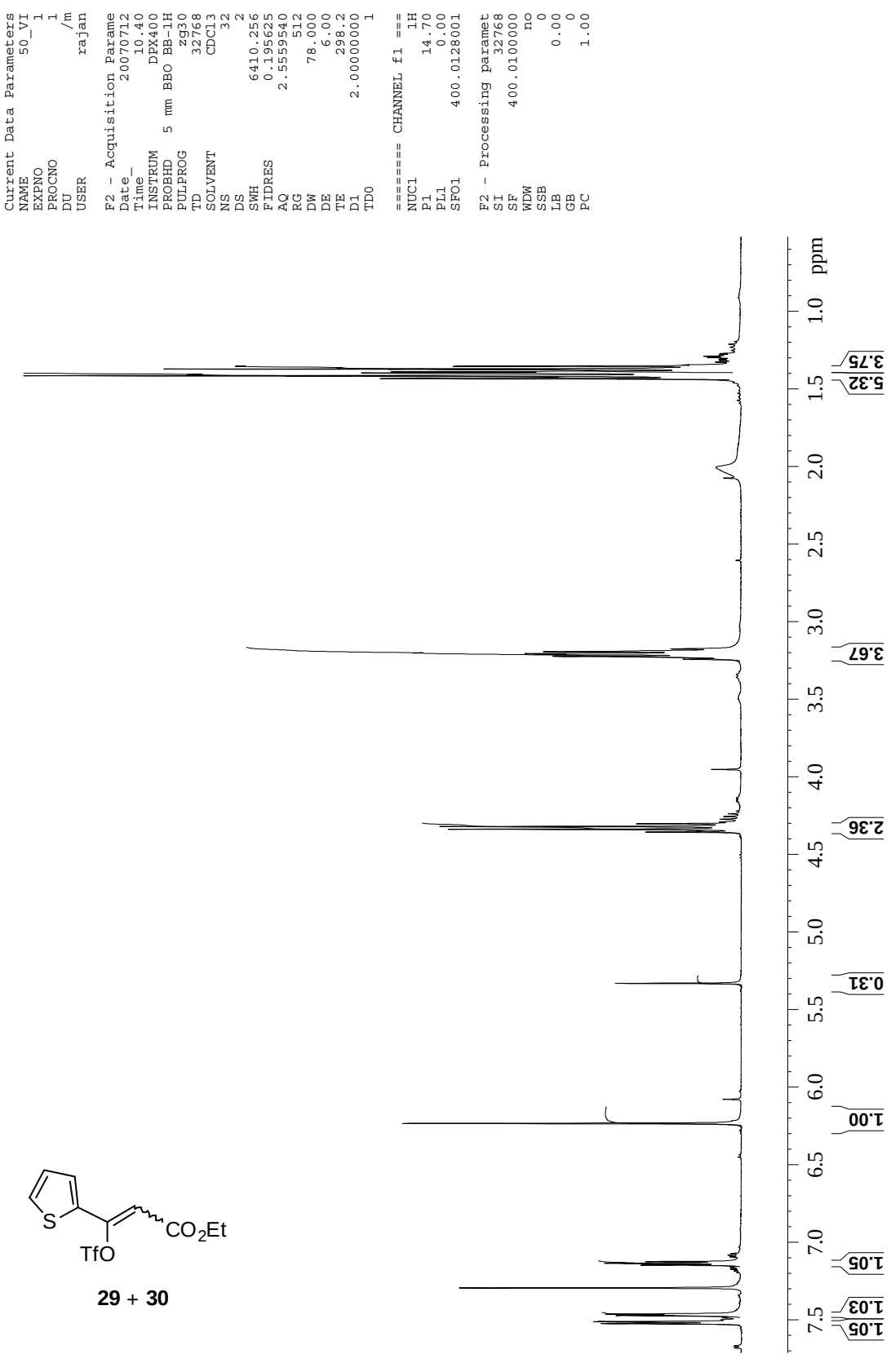
(±)-26


Current Data Parameters
NAME 26_VI
EXPNO 1
PROCNO 1
DU /m
USER rajan
F2 - Acquisition Parame
Date_ 20070517
Time_ 11.11
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 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
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
2.0
1.5
1.80
0.91
2.00
1.96
3.26
S
O
CO2Et

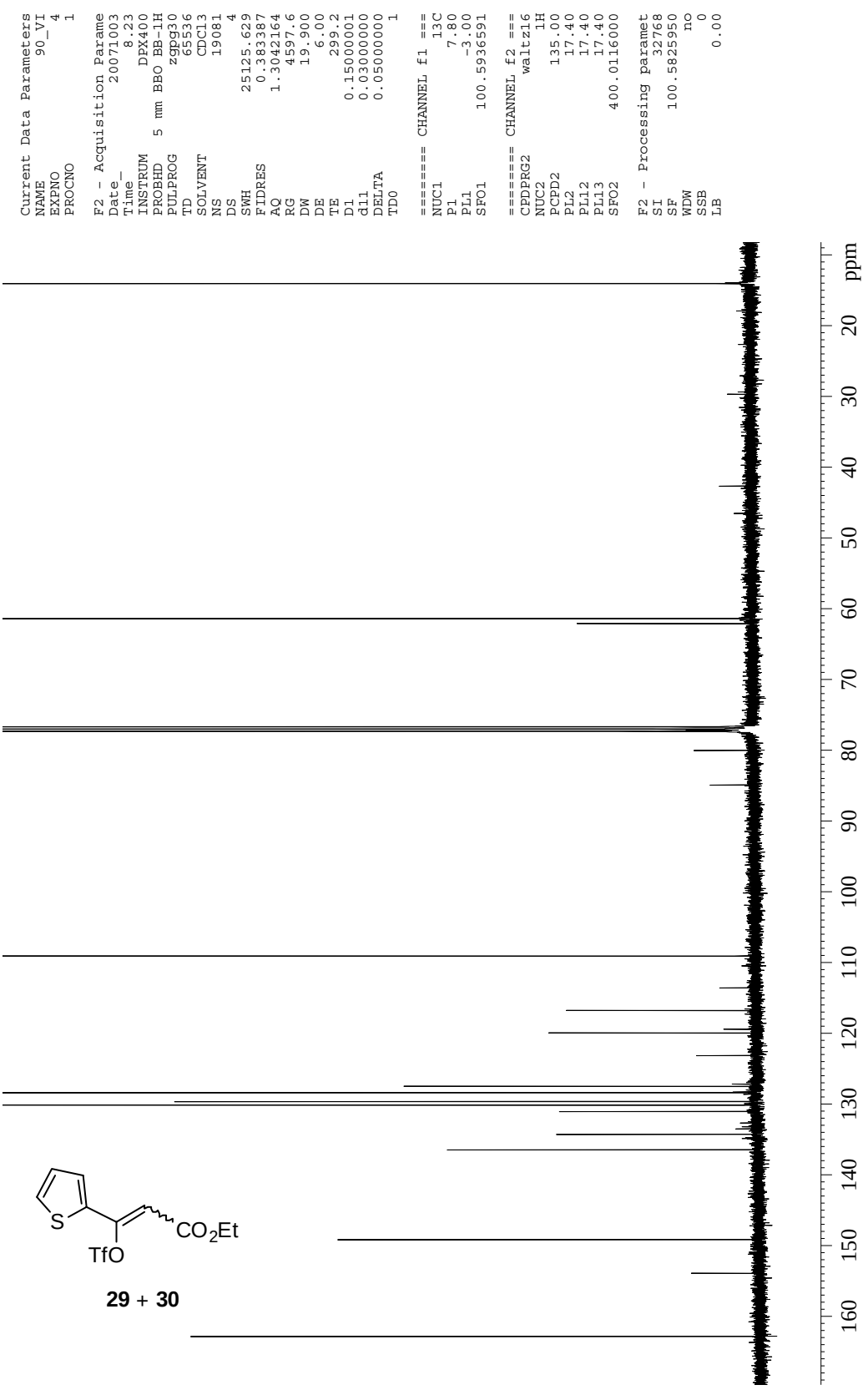
28


Current Data Parameters
NAME 26_VI
EXPNO 3
PROCNO 1
DU /m
USER rajan
F2 - Acquisition Parame
Date_ 20070517
Time_ 13.16
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1722
DS 4
SWH 25125.629
FIDRES 0.383387
AQ 1.3042164
RG 5160.6
DW 19.900
DE 6.00
TE 298.2
D1 0.15000001
d11 0.03000000
DELTA 0.05000000
TD0 1
======== CHANNEL f1 ===
NUC1 13C
P1 7.80
PL1 -3.00
SFO1 100.5936591
======== CHANNEL f2 ===
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00
PL2 17.40
PL12 17.40
PL13 17.40
SFO2 400.0116000
F2 - Processing paramet
SI 32768
SF 100.5825950
WDW no
S
O
CO2Et
ppm
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20

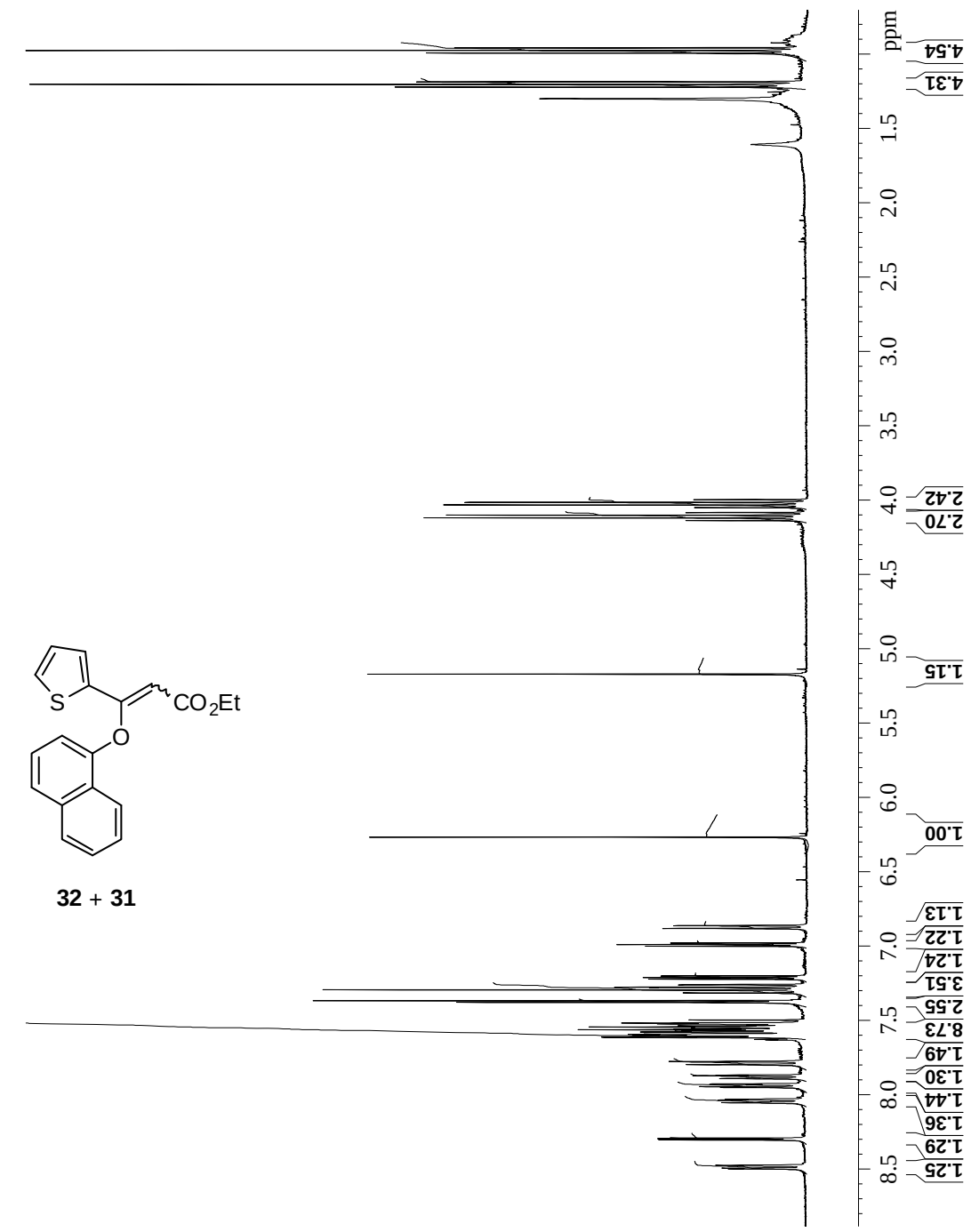
28

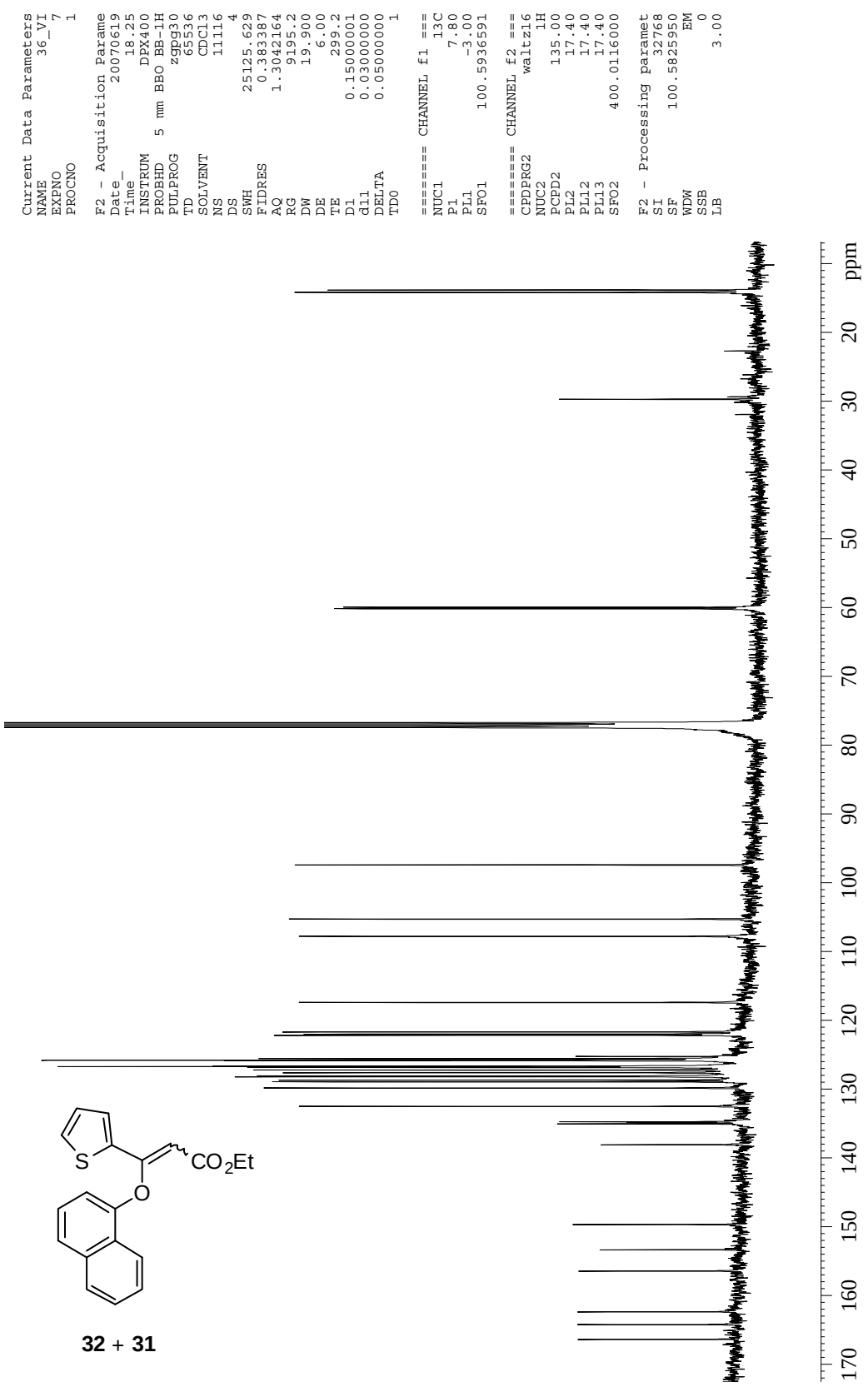

Current Data Parameters
NAME 50_VI
EXPNO 1
PROCNO 1
DU /m
USER rajan
F2 - Acquisition Parame
Date_ 20070712
Time_ 10.40
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256
FIDRES 0.195625
AQ 2.5559540
RG 512
DW 78.000
DE 6.00
TE 298.2
D1 2.00000000
TD0 1
======== CHANNEL f1 ===
NUC1 1H
P1 14.70
PL1 0.00
SFO1 400.0128001
F2 - Processing paramet
SI 32768
SF 400.0100000
WDW no
SSB 0
LB 0.00
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
1.05
1.03
1.05
1.05
1.00
0.31
2.36
3.67
5.32
3.75
S
TfO
CO2Et

29 + **30**

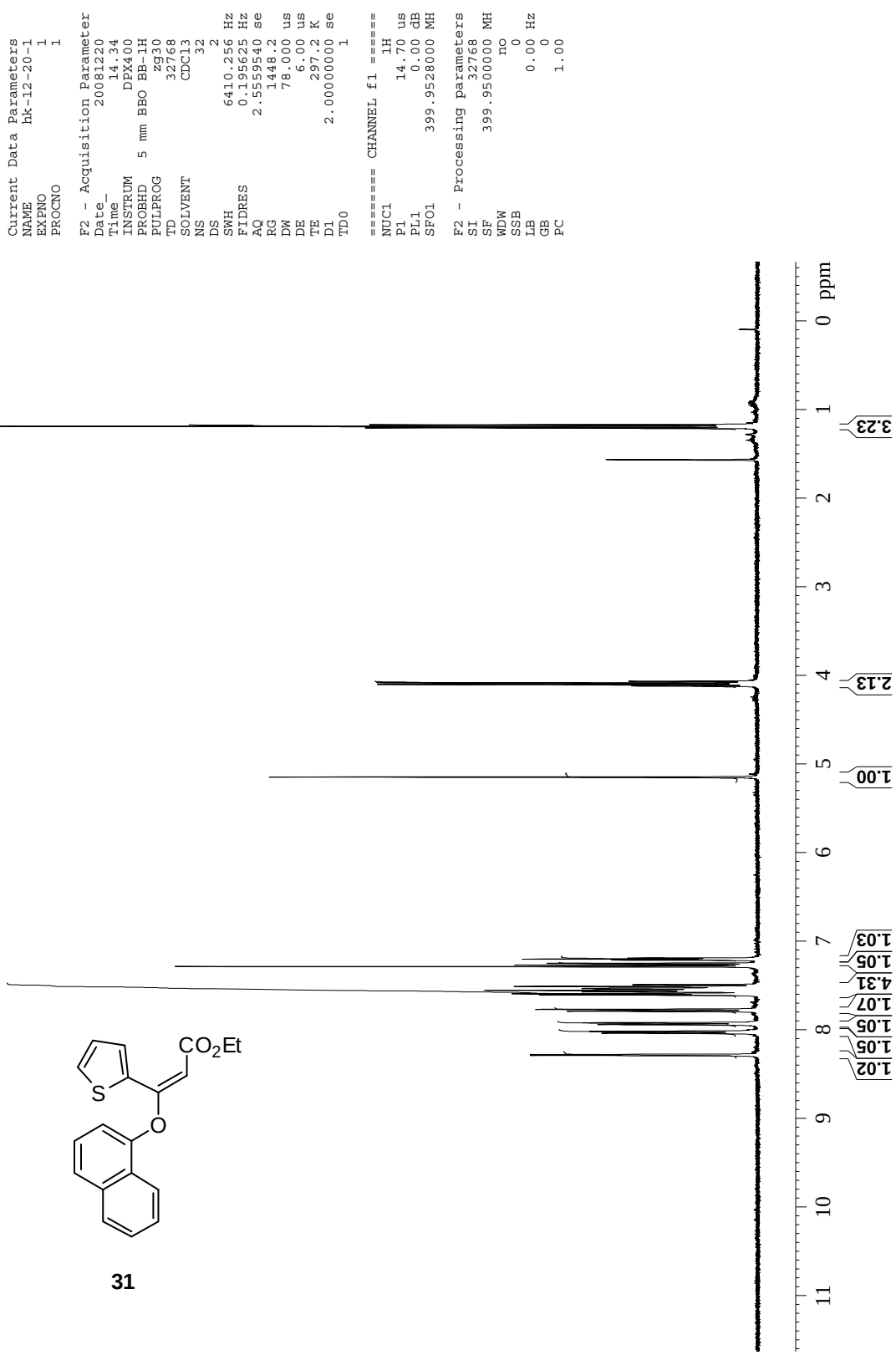

Current Data Parameters
NAME 90_VI
EXPNO 4
PROCNO 1
F2 - Acquisition Parame
Date_ 20071003
Time 8.23
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1908l
DS 4
SWH 25125.629
FIDRES 0.383387
AQ 1.3042164
RG 4597.6
DW 19.900
DE 6.00
TE 299.2
D1 0.15000001
d11 0.03000000
DELTA 0.05000000
TD0 1
======== CHANNEL f1 ===
NUC1 13C
P1 7.80
PL1 -3.00
SFO1 100.5936591
======== CHANNEL f2 ===
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00
PL2 17.40
PL12 17.40
PL13 17.40
SFO2 400.0116000
F2 - Processing paramet
SI 32768
SF 100.5825950
WDW no
SSB 0
LB 0.00
ppm
S
CO2Et
TfO

29 + **30**

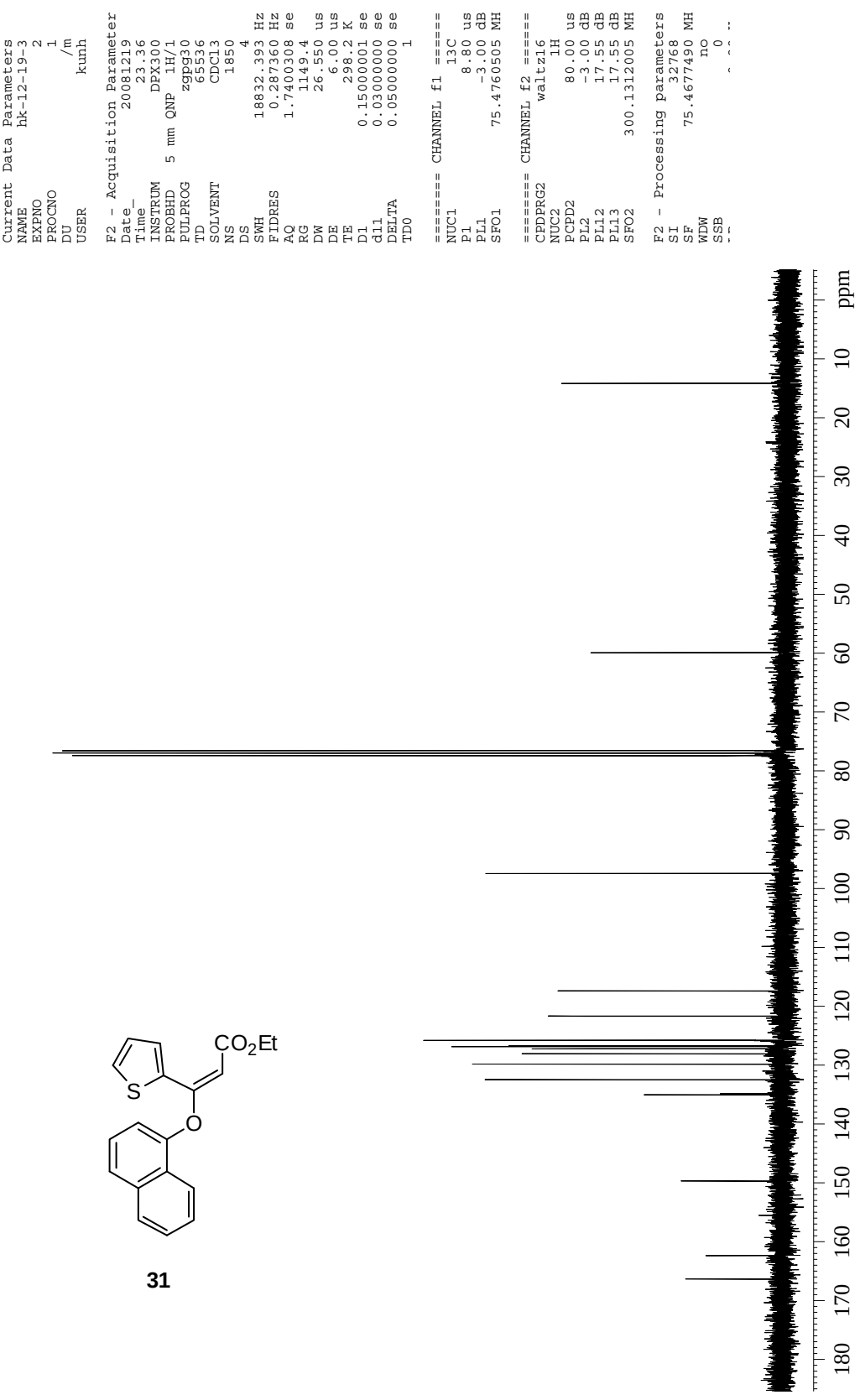

Current Data Parameters
NAME 36_VI
EXPNO 5
PROCNO 1
DU /m
USER rajan
F2 - Acquisition Parame
Date_ 20070619
Time_ 16.19
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 17
DS 2
SWH 6410.256
FIDRES 0.195625
AQ 2.5559540
RG 228.1
DW 78.000
DE 6.00
TE 299.2
D1 2.00000000
TD0 1
======== CHANNEL f1 ===
NUC1 1H
P1 14.70
PL1 0.00
SFO1 400.0128001
F2 - Processing paramet
SI 32768
SF 400.0100000
WDW no
SSB 0
LB 0.00
GB 0
PC 1.00
S
O
CO2Et
32 + 31
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
1.25
1.29
1.36
1.44
1.30
1.49
8.73
2.55
3.51
1.24
1.22
1.13
1.00
1.15
2.70
2.42
4.31
4.54


Current Data Parameters
NAME 36_VI
EXPNO 7
PROCNO 1
F2 - Acquisition Parame
Date_ 20070619
Time 18.25
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 11116
DS 4
SWH 25125.629
FIDRES 0.383387
AQ 1.3042164
RG 9195.2
DW 19.900
DE 6.00
TE 299.2
D1 0.15000001
d11 0.03000000
DELTA 0.05000000
TD0 1
======== CHANNEL f1 ===
NUC1 13C
P1 7.80
PL1 -3.00
SFO1 100.5936591
======== CHANNEL f2 ===
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00
PL2 17.40
PL12 17.40
PL13 17.40
SFO2 400.0116000
F2 - Processing paramet
SI 32768
SF 100.5825950
WDW EM
SSB 0
LB 3.00
S
CO2Et
O
ppm

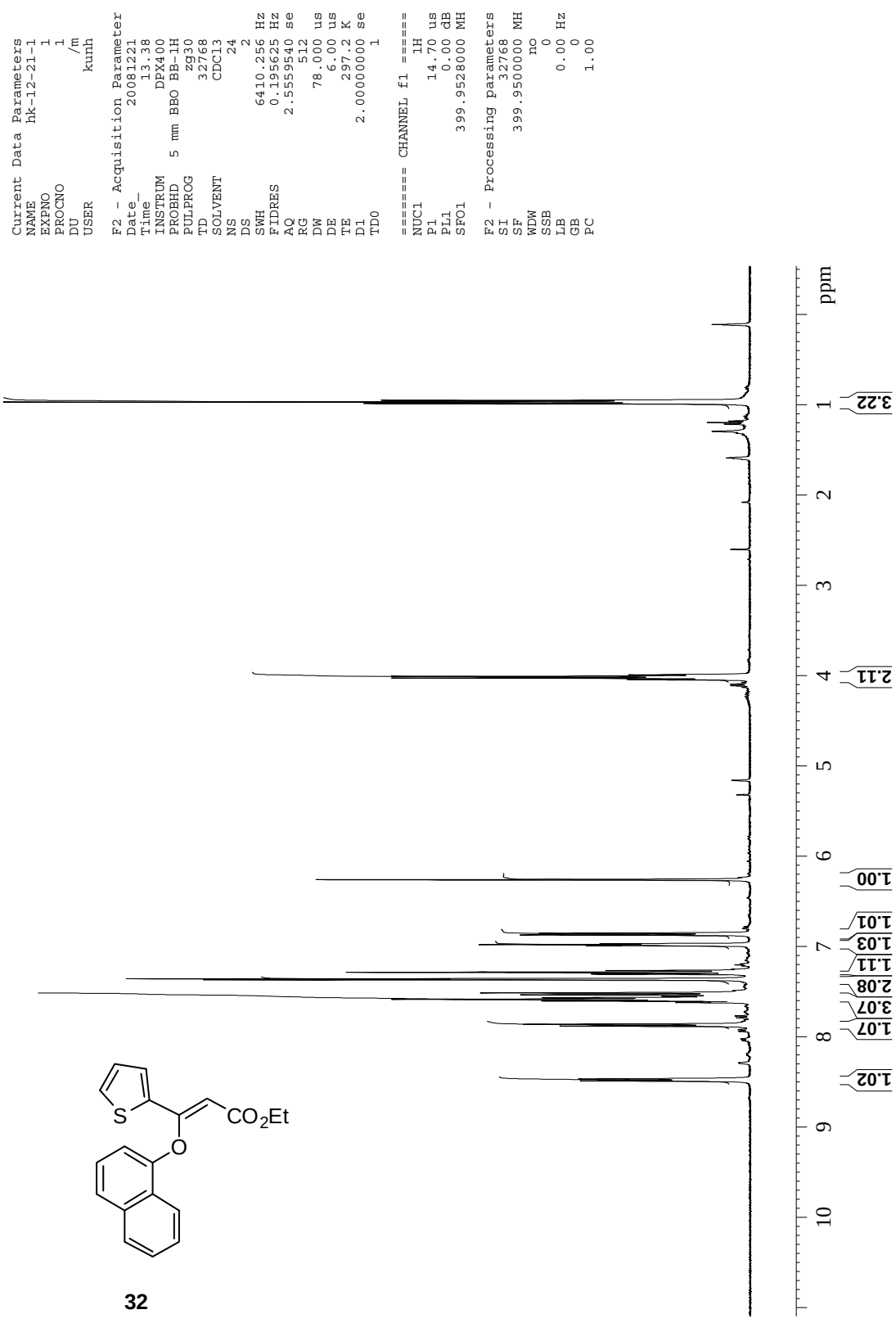
32 + **31**


Current Data Parameters
NAME hk-12-20-1
EXPNO 1
PROCNO 1
F2 - Acquisition Parameter
Date_ 20081220
Time_ 14.34
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDC13
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 se
RG 1448.2
DW 78.000 us
DE 6.00 us
TE 297.2 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 no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
3.23
2.13
1.00
1.02
1.05
1.05
1.07
4.31
1.05
1.03
ppm
CO2Et
S
O

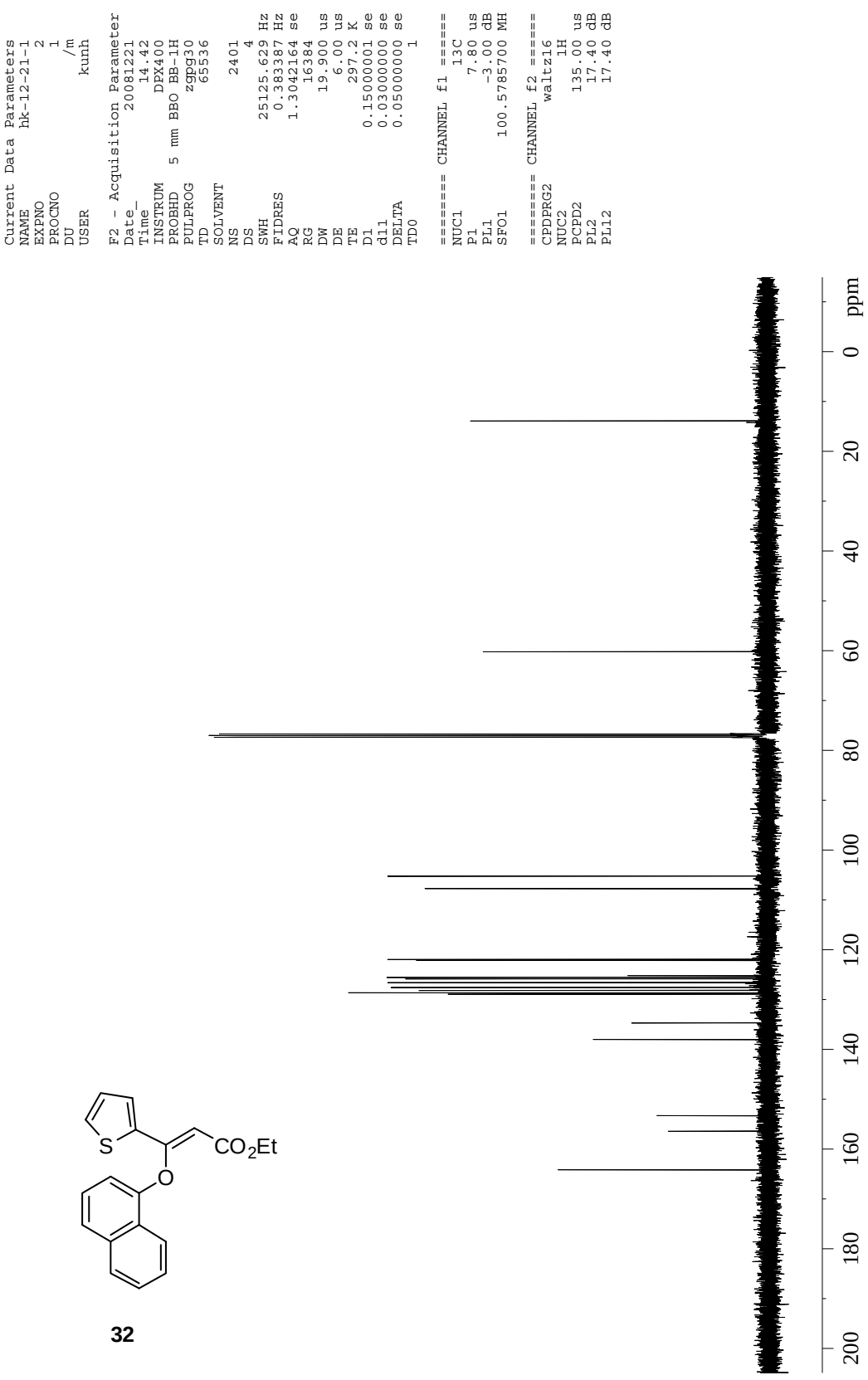
31


Current Data Parameters
NAME hk-12-19-3
EXPNO 2
PROCNO 1
DU /m
USER kunh
F2 - Acquisition Parameter
Date_ 20081219
Time_ 23.36
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1850
DS 4
SWH 18832.393 Hz
FIDRES 0.287360 Hz
AQ 1.7400308 se
RG 1149.4
DW 26.550 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 8.80 us
PL1 -3.00 dB
SFO1 75.4760505 MH
======== CHANNEL f2 ======
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 us
PL2 -3.00 dB
PL12 17.55 dB
PL13 17.55 dB
SFO2 300.1312005 MH
F2 - Processing parameters
SI 32768
SF 75.4677490 MH
WDW no
SSB 0
ppm
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
CO2Et
S
O

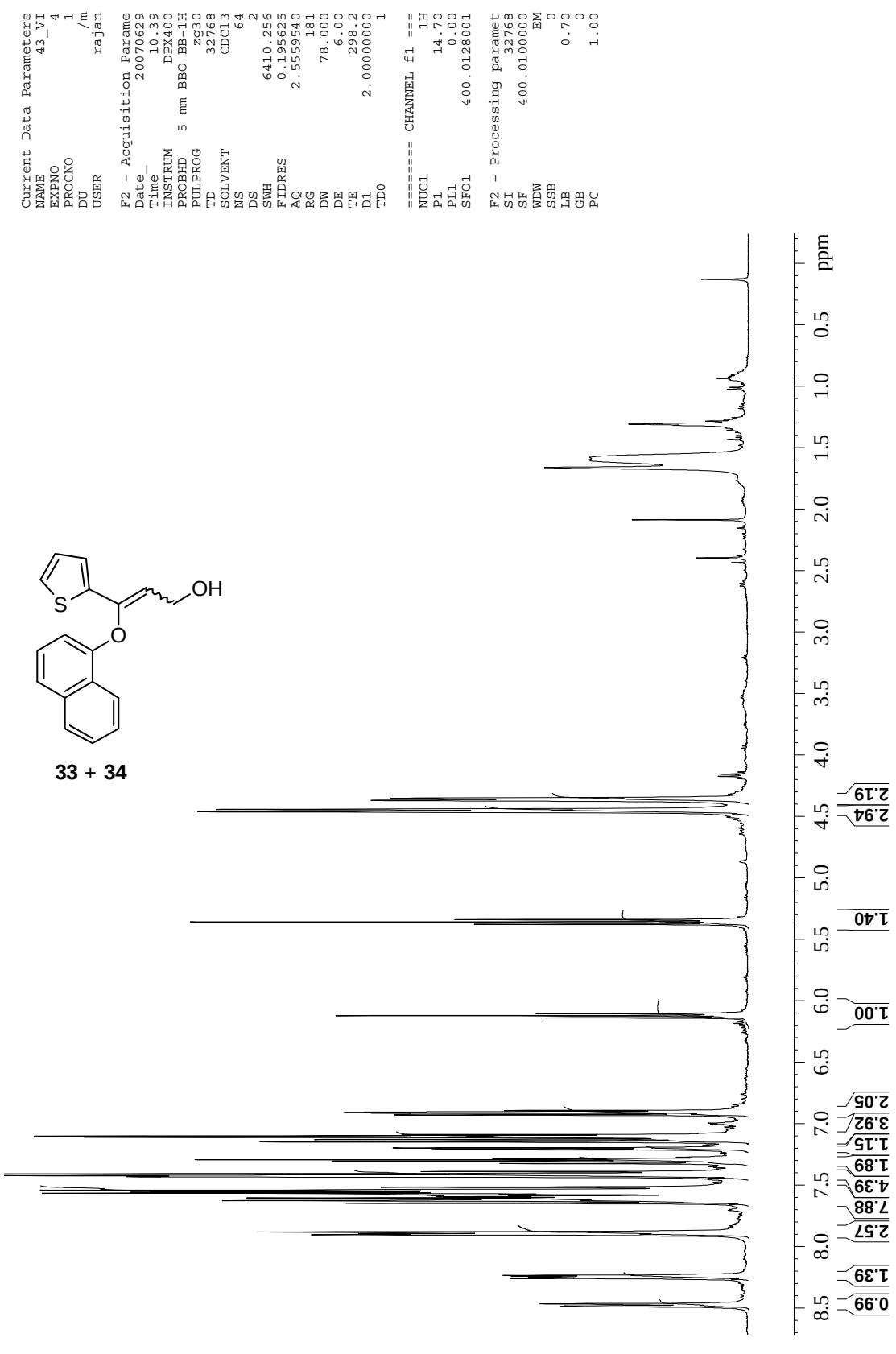
31

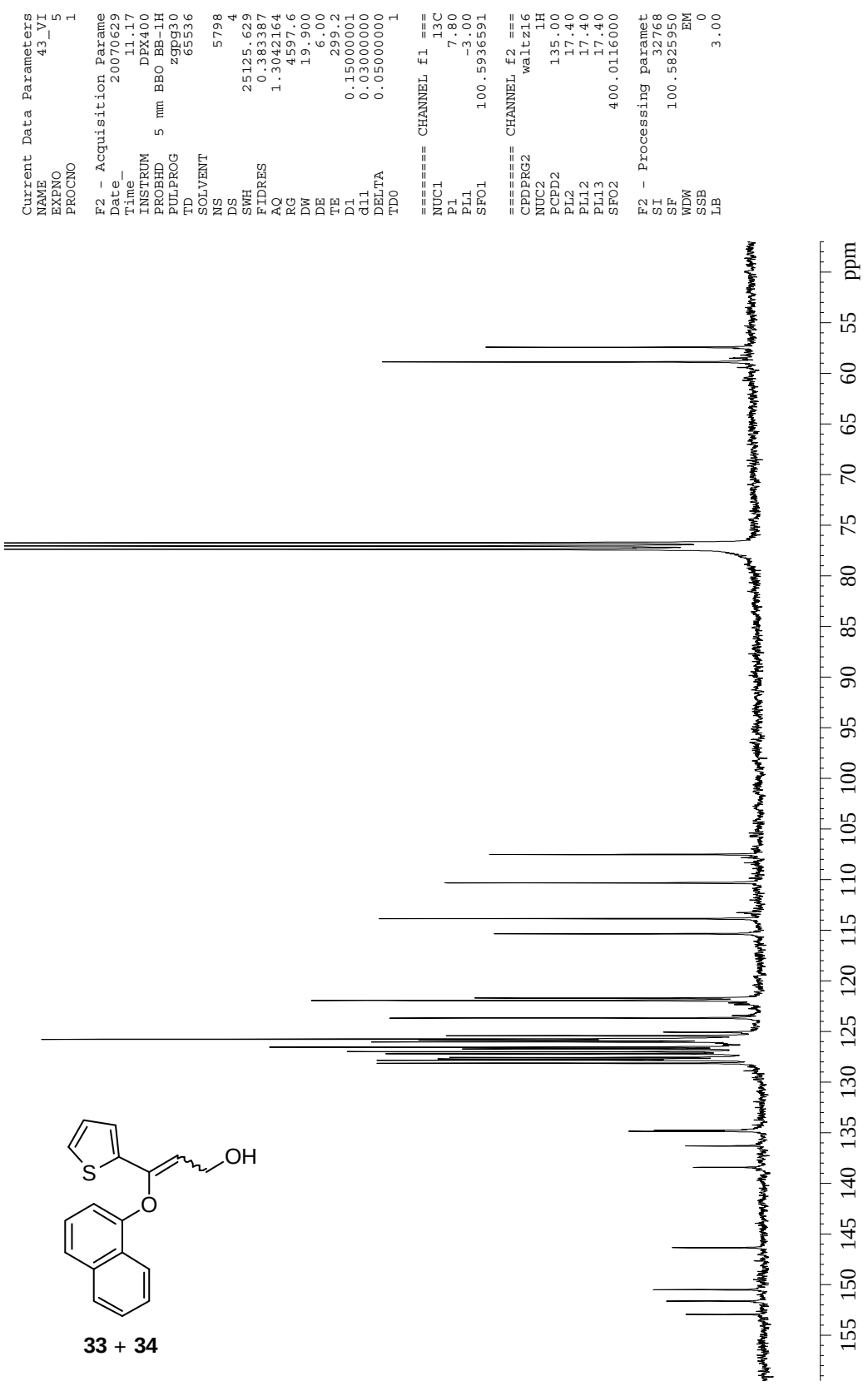

Current Data Parameters
NAME hk-12-21-1
EXPNO 1
PROCNO 1
DU /m
USER kunh
F2 - Acquisition Parameter
Date_ 20081221
Time_ 13.38
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDC13
NS 24
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 se
RG 512
DW 78.000 us
DE 6.00 us
TE 297.2 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 no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
3.22
2.11
1.00
1.01
1.03
1.11
2.08
3.07
1.07
1.02
ppm
1
2
3
4
5
6
7
8
9
10
S
O
CO2Et

32

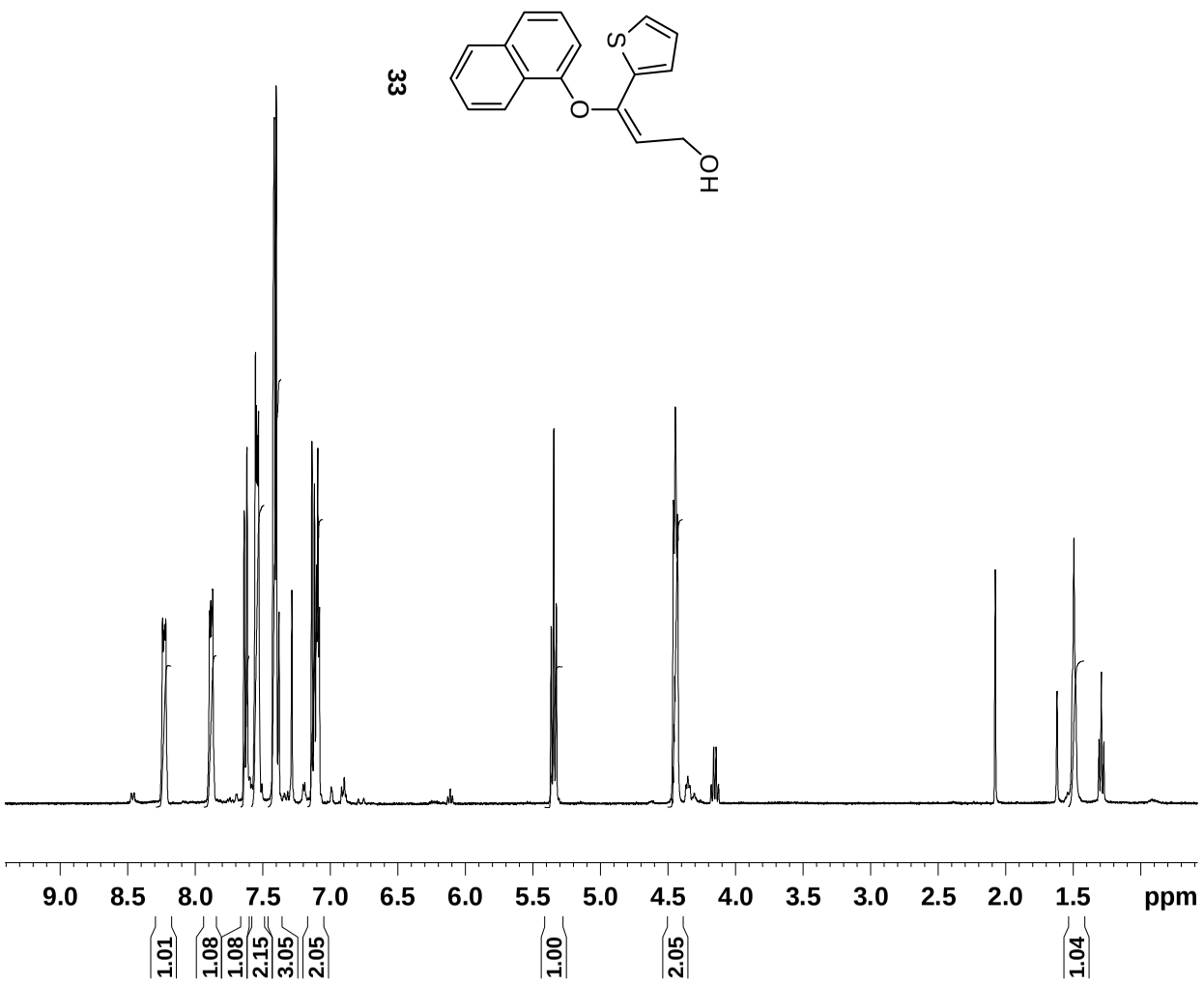

Current Data Parameters
NAME hk-12-21-1
EXPNO 2
PROCNO 1
DU /m
USER kunh
F2 - Acquisition Parameter
Date_ 20081221
Time_ 14.42
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 2401
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3042164 se
RG 16384
DW 19.900 us
DE 6.00 us
TE 297.2 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
200
180
160
140
120
100
80
60
40
20
0
ppm
S
O
CO2Et

32


Current Data Parameters
NAME 43_VI
EXPNO 4
PROCNO 1
DU /m
USER rajan
F2 - Acquisition Parame
Date_ 20070629
Time_ 10.39
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 64
DS 2
SWH 6410.256
FIDRES 0.195625
AQ 2.5559540
RG 181
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 400.0128001
F2 - Processing paramet
SI 32768
SF 400.0100000
WDW EM
SSB 0
LB 0.70
GB 0
PC 1.00
S
O
OH
33 + 34
0.99
1.39
2.57
7.88
4.39
1.89
1.15
3.92
2.05
1.00
1.40
2.94
2.19
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

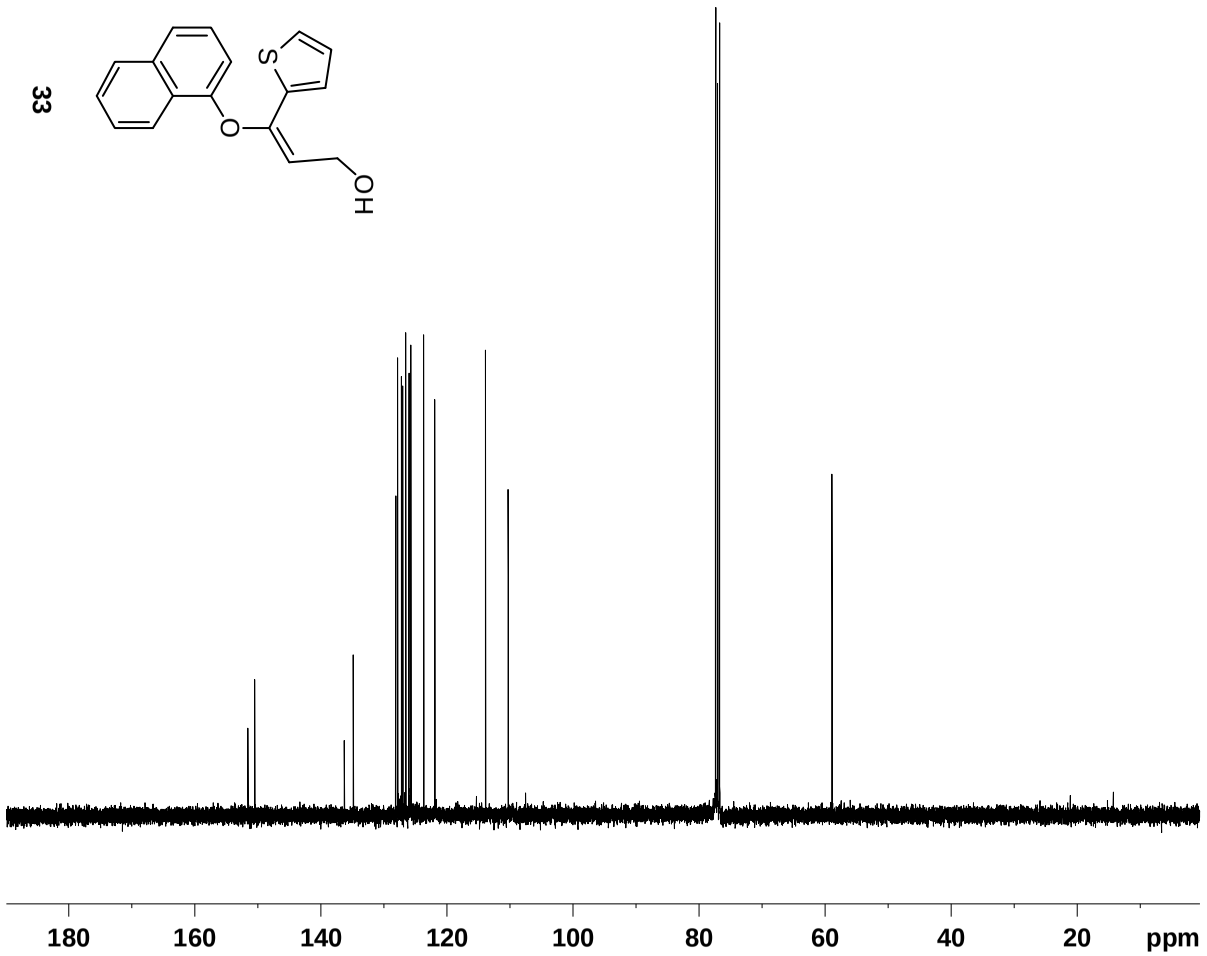

Current Data Parameters
NAME 43_VI
EXPNO 5
PROCNO 1
F2 - Acquisition Parame
Date_ 20070629
Time 11.17
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 5798
DS 4
SWH 25125.629
FIDRES 0.383387
AQ 1.3042164
RG 4597.6
DW 19.900
DE 6.00
TE 299.2
D1 0.15000001
d11 0.03000000
DELTA 0.05000000
TD0 1
======== CHANNEL f1 ===
NUC1 13C
P1 7.80
PL1 -3.00
SFO1 100.5936591
======== CHANNEL f2 ===
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00
PL2 17.40
PL12 17.40
PL13 17.40
SFO2 400.0116000
F2 - Processing paramet
SI 32768
SF 100.5825950
WDW EM
SSB 0
LB 3.00
S
O
OH
155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 ppm

33 + **34**



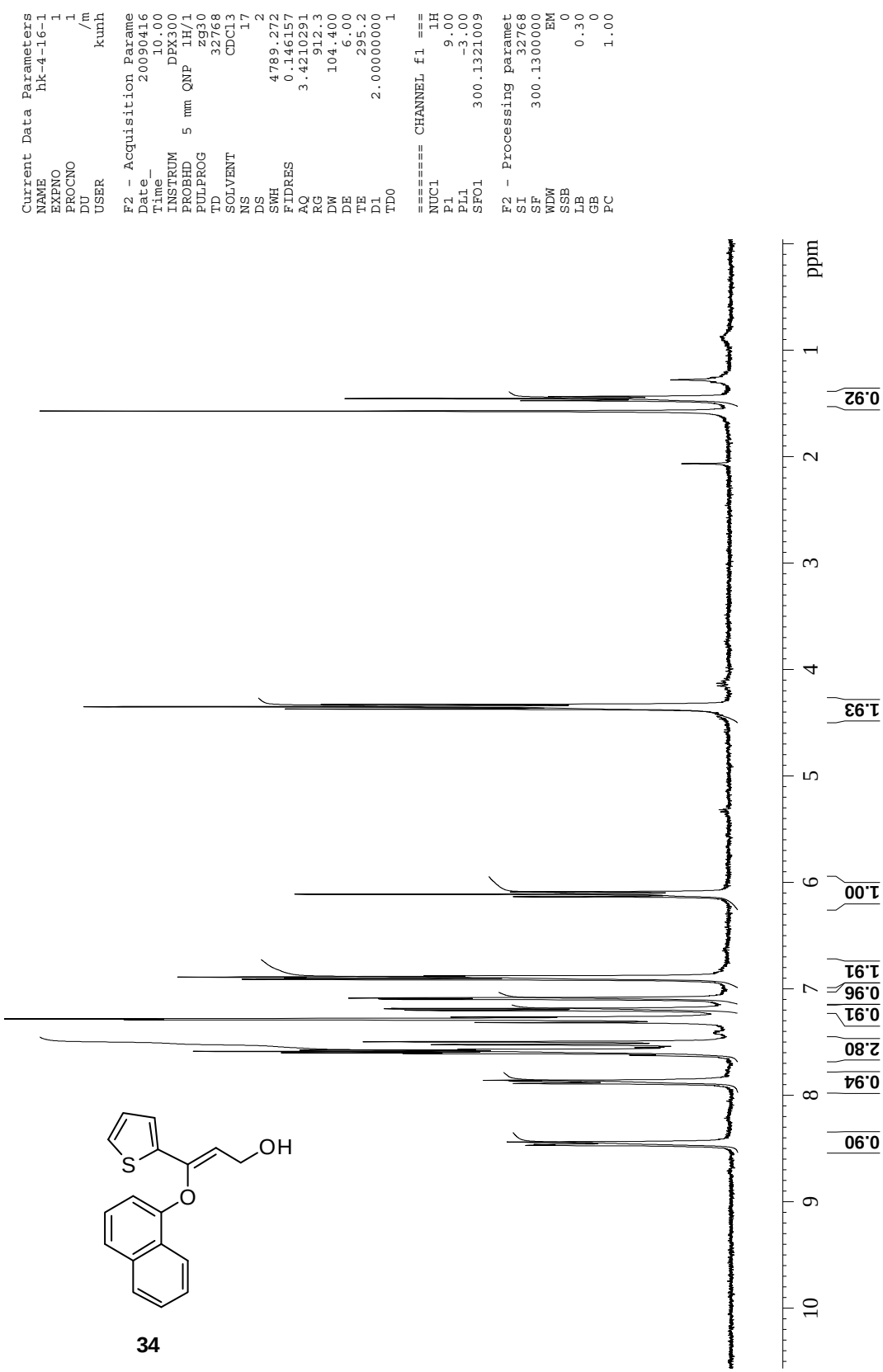
BRUKER

```
Current Data Parameters
NAME          hk-12-21-2
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20081221
Time               14.49
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              2.5559039 sec
RG                   512
DW                78.000 usec
DE                 6.00 usec
TE                297.2 K
D1             2.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                14.70 usec
PL1       0 dB
SFO1         399.9528000 MHz

F2 - Processing parameters
SI                 32768
SF           399.9500000 MHz
WDW                   no
SSB       0
LB        0 Hz
GB        0
PC                  1.00
```



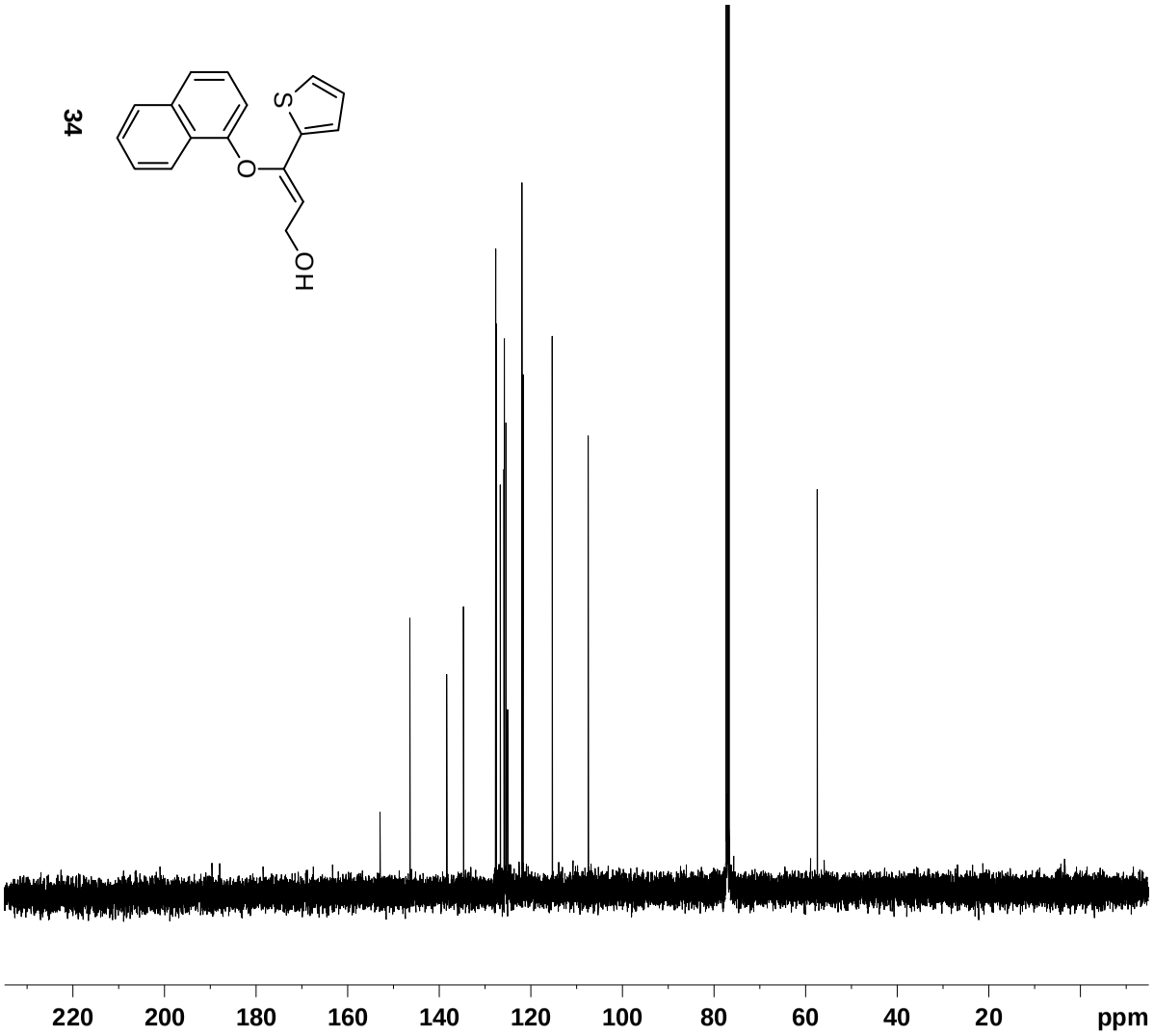
BRUKER

```
Current Data Parameters
NAME          hk-12-21-2
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20081221
Time               15.54
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             1.3041664 sec
RG                16384
DW               19.900 usec
DE                6.00 usec
TE                297.2 K
D1           0.15000001 sec
d11          0.03000000 sec
DELTA        0.05000000 sec
TD0                   1
SFO1        100.5785700 MHz
NUC1               13C
P1                7.80 usec
PLW1        -1.00000000 W
SFO2        399.9516000 MHz
NUC2               1H
CPDPRG[2         waltz16
PCPD2            135.00 usec
PLW2        -1.00000000 W
PLW12       -1.00000000 W
PLW13       -1.00000000 W

F2 - Processing parameters
SI                32768
SF          100.5675080 MHz
WDW                 no
SSB       0
LB        0 Hz
GB        0
PC                1.40
```

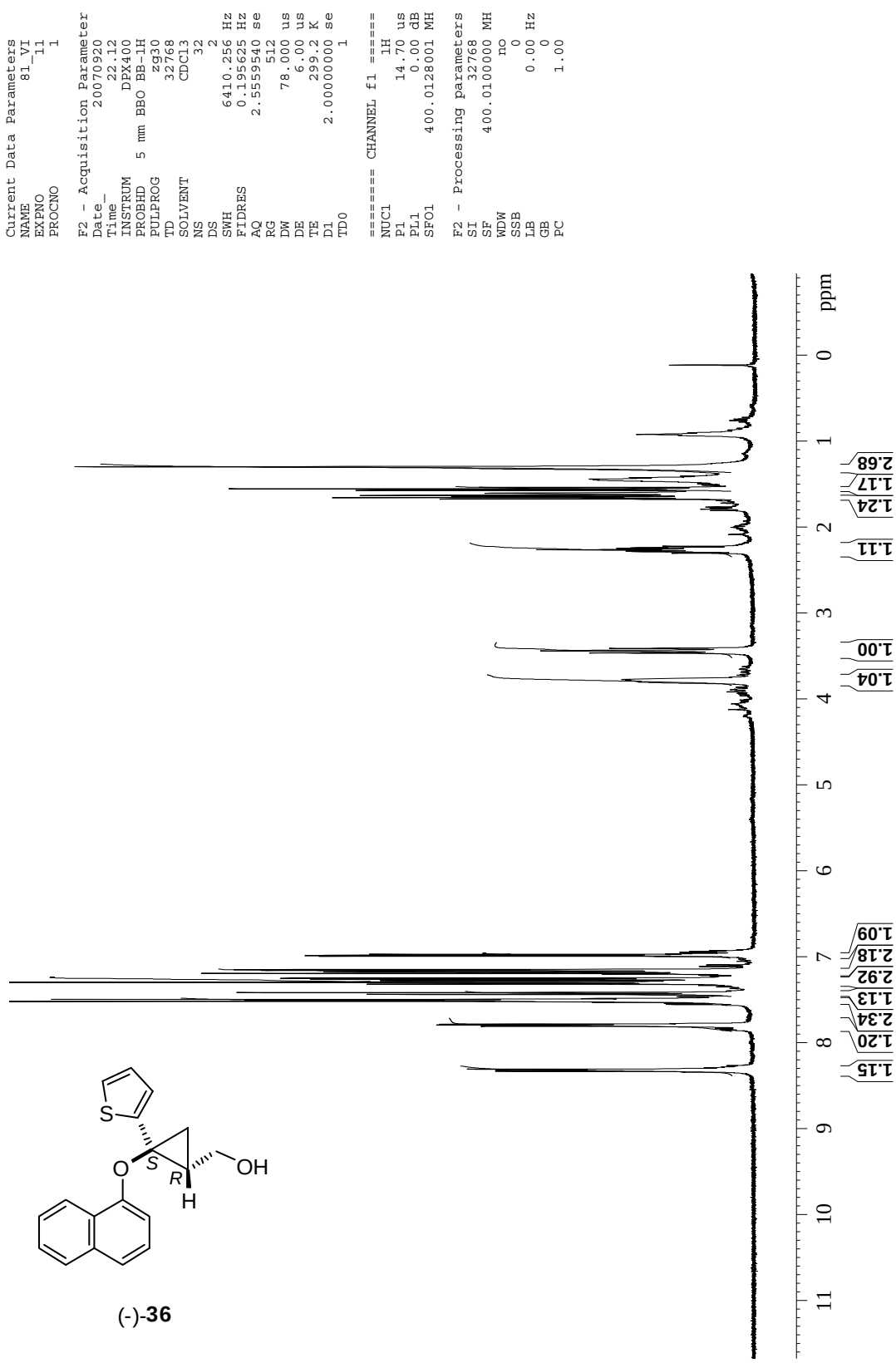

Current Data Parameters
NAME hk-4-16-1
EXPNO 1
PROCNO 1
DU /m
USER kunh
F2 - Acquisition Parame
Date_ 20090416
Time_ 10.00
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 17
DS 2
SWH 4789.272
FIDRES 0.146157
AQ 3.4210291
RG 912.3
DW 104.400
DE 6.00
TE 295.2
D1 2.00000000
TD0 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
ppm
0.92
1.93
1.00
1.91
0.96
0.91
2.80
0.94
0.90
S
O
OH

34

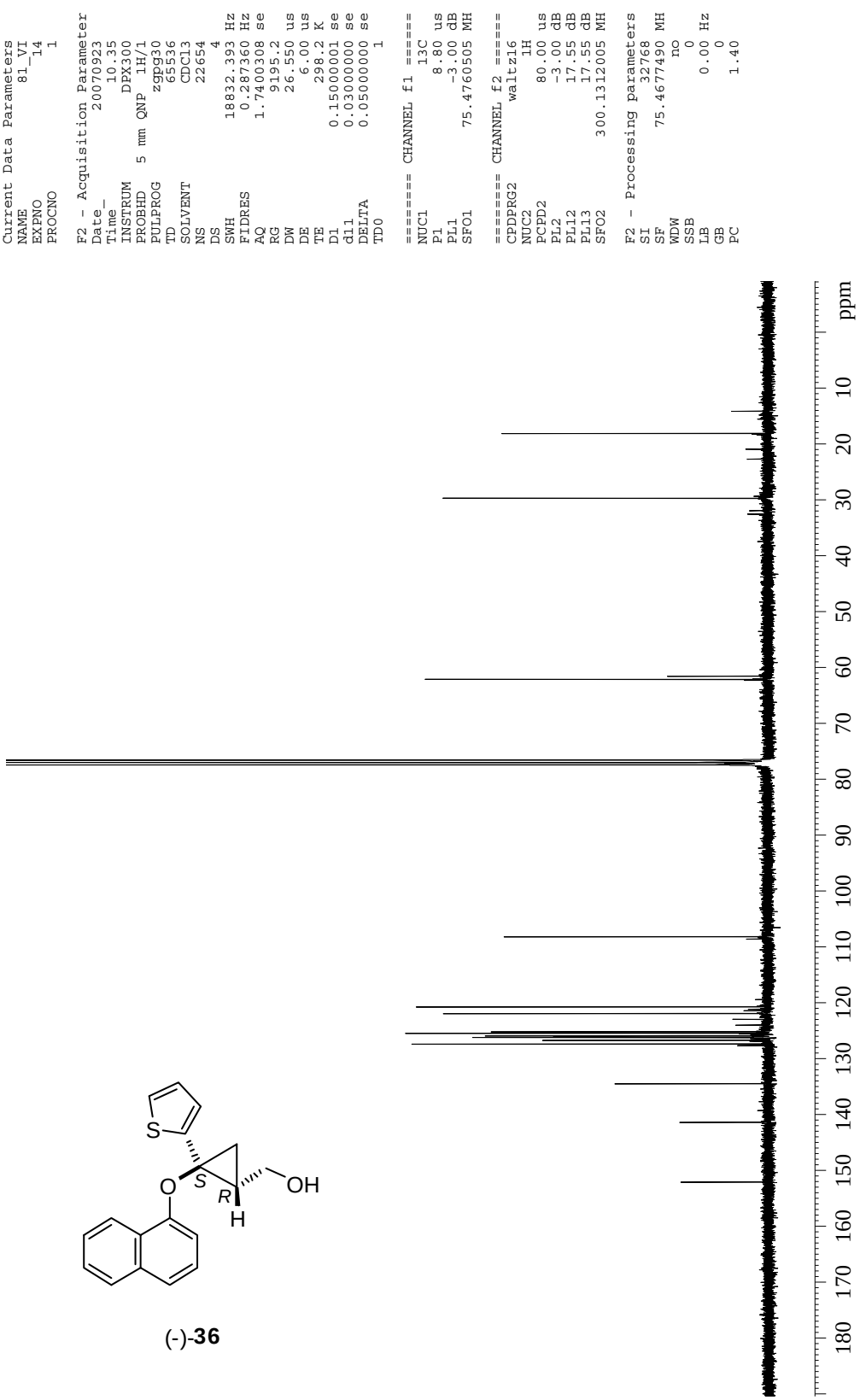
34



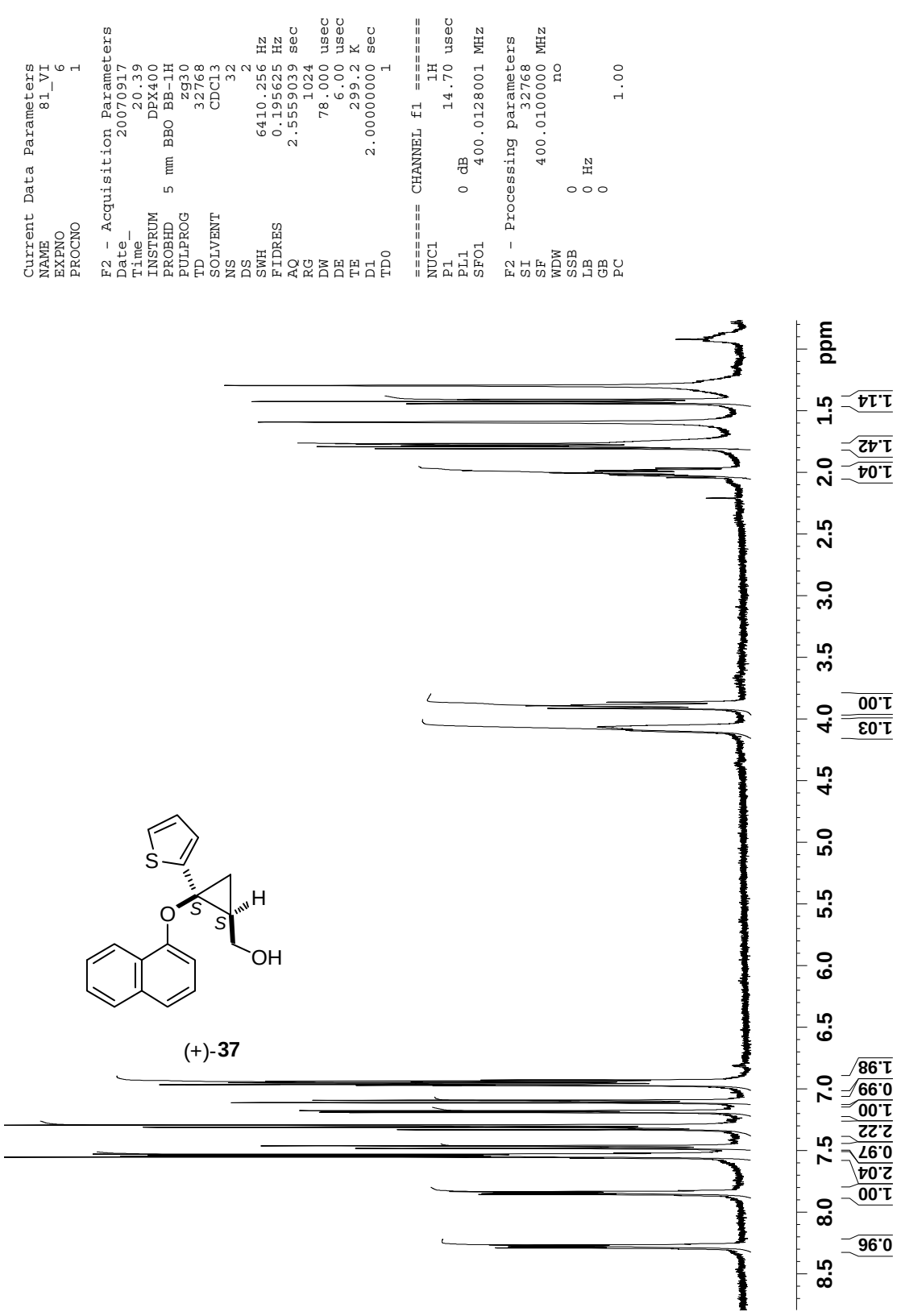

```
Current Data Parameters
NAME          hk-12-26-1
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20081226
Time              13.35
INSTRUM           DPX400
PROBHD   5 mm BBO BB-1H
PULPROG           zgpg30
TD                65536
SOLVENT
NS                 6350
DS                    4
SWH           25125.629 Hz
FIDRES         0.383387 Hz
AQ             1.3041664 sec
RG                16384
DW               19.900 usec
DE                6.00 usec
TE               297.2 K
D1            0.15000001 sec
d11           0.03000000 sec
DELTA         0.05000000 sec
TD0                   1
SFO1         100.5785700 MHz
NUC1                 13C
P1                 7.80 usec
PLW1         -1.00000000 W
SFO2         399.9516000 MHz
NUC2                 1H
CPDPRG[2          waltz16
PCPD2             135.00 usec
PLW2         -1.00000000 W
PLW12        -1.00000000 W
PLW13        -1.00000000 W

F2 - Processing parameters
SI                32768
SF           100.5675080 MHz
WDW                  no
SSB       0
LB        0 Hz
GB        0
PC                 1.40
```

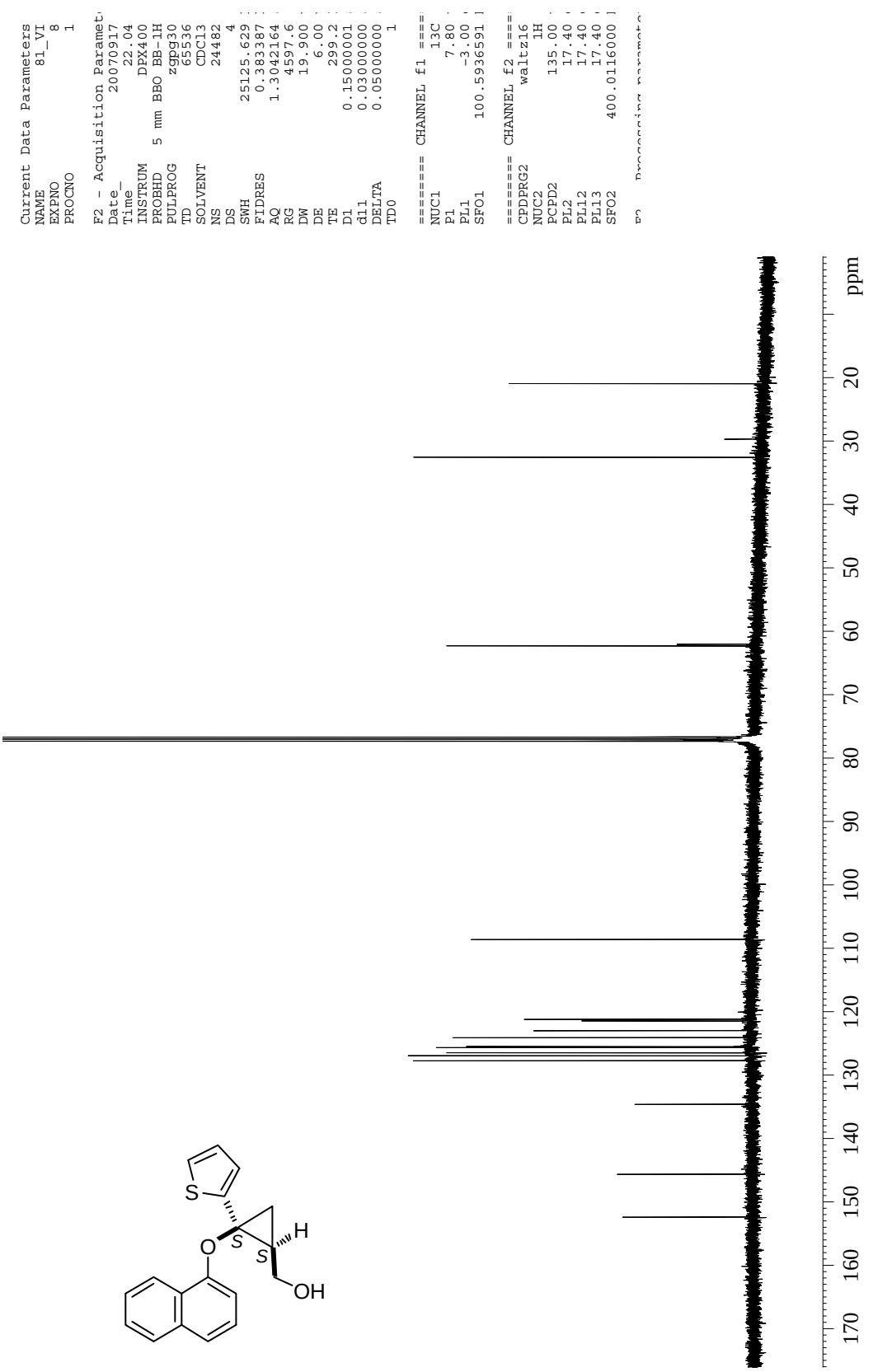

Current Data Parameters
NAME 81_VI
EXPNO 11
PROCNO 1
F2 - Acquisition Parameter
Date_ 20070920
Time_ 22.12
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 se
RG 512
DW 78.000 us
DE 6.00 us
TE 299.2 K
D1 2.00000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.70 us
PL1 0.00 dB
SFO1 400.0128001 MH
F2 - Processing parameters
SI 32768
SF 400.0100000 MH
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
1.15
1.20
2.34
1.13
2.92
2.18
1.09
1.04
1.00
1.11
1.24
1.17
2.68
ppm
S
O
S
R
H
OH

(-)-**36**

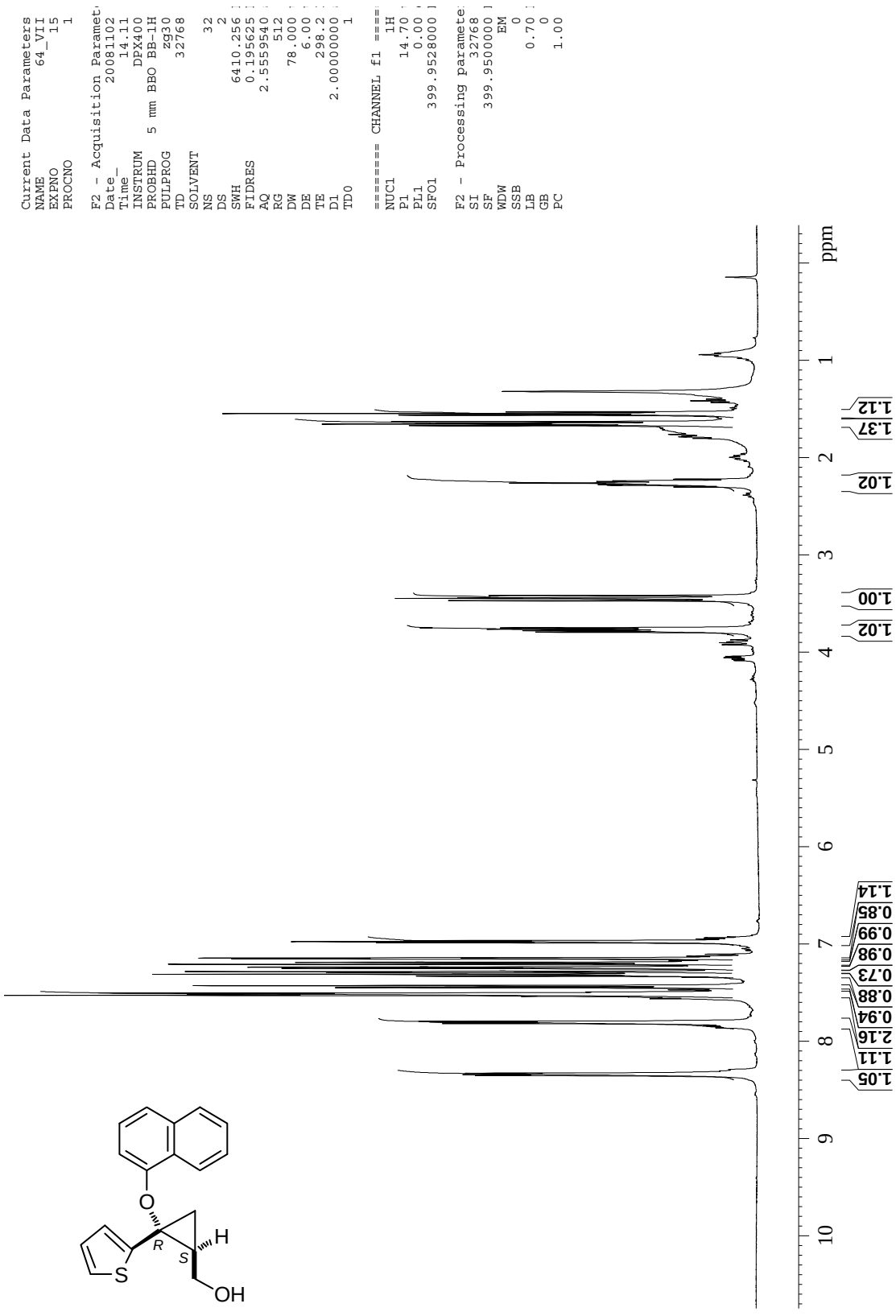

Current Data Parameters
NAME 81_VI
EXPNO 14
PROCNO 1
F2 - Acquisition Parameter
Date_ 20070923
Time_ 10.35
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 22654
DS 4
SWH 18832.393 Hz
FIDRES 0.287360 Hz
AQ 1.7400308 se
RG 9195.2
DW 26.550 us
DE 6.00 us
TE 298.2 K
D1 0.15000001 se
d11 0.03000000 se
DELTA 0.05000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 13C
P1 8.80 us
PL1 -3.00 dB
SFO1 75.4760505 MH
======== CHANNEL f2 ======
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 us
PL2 -3.00 dB
PL12 17.55 dB
PL13 17.55 dB
SFO2 300.1312005 MH
F2 - Processing parameters
SI 32768
SF 75.4677490 MH
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.40
S
O
S
R
H
OH
ppm
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10

(-)-**36**

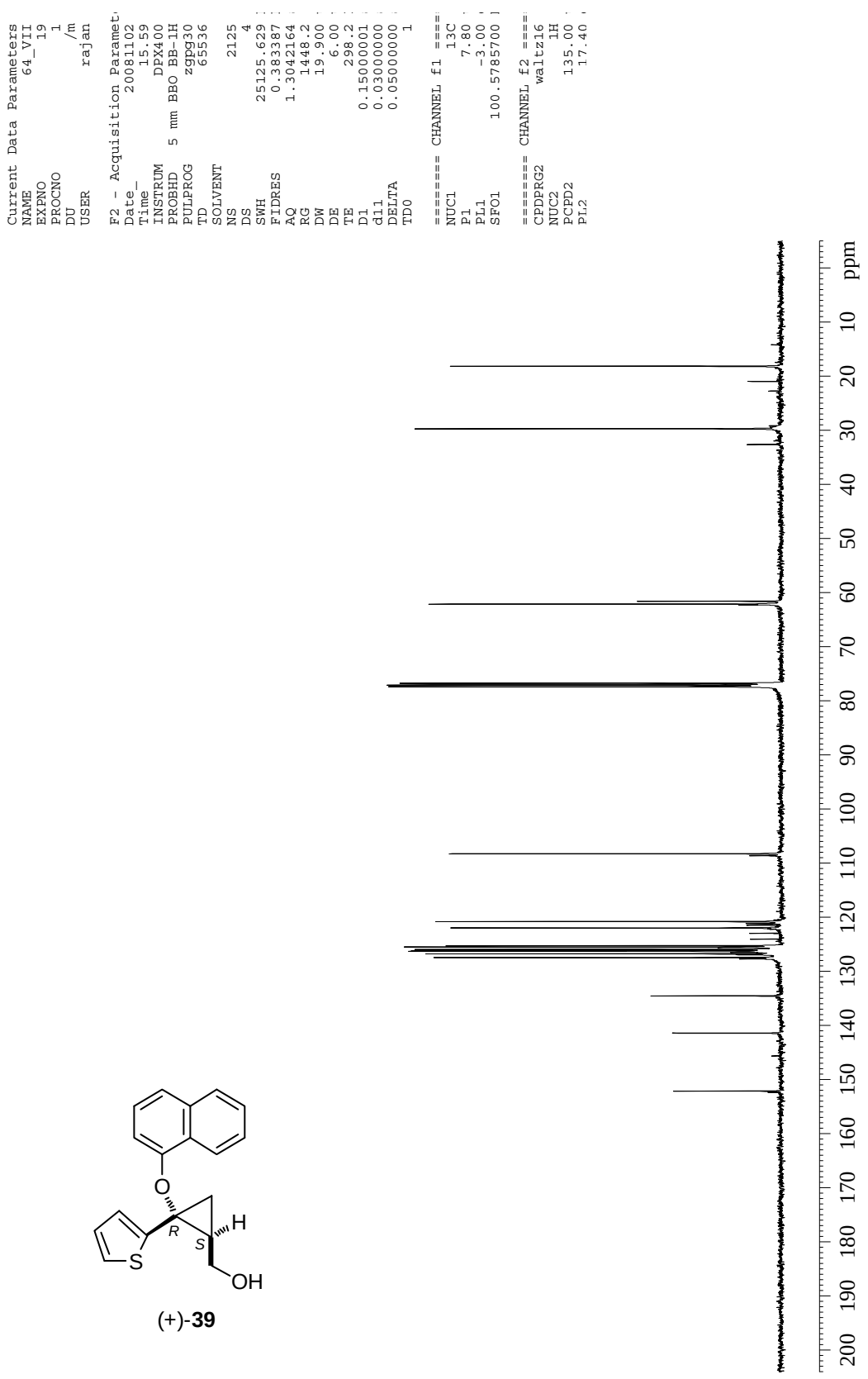

Current Data Parameters
NAME 81_VI
EXPNO 6
PROCNO 1
F2 - Acquisition Parameters
Date_ 20070917
Time 20.39
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559039 sec
RG 1024
DW 78.000 usec
DE 6.00 usec
TE 299.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0 dB
SFO1 400.0128001 MHz
F2 - Processing parameters
SI 32768
SF 400.0100000 MHz
WDW no
SSB 0
LB 0 Hz
GB 0
PC 1.00
S
O
S
S
H
OH
(+)-37
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
0.96
1.00
2.04
0.97
2.22
1.00
0.99
1.98
1.03
1.00
1.04
1.42
1.14


Current Data Parameters
NAME 81_VI
EXPNO 8
PROCNO 1
F2 - Acquisition Paramet
Date_ 20070917
Time 22.04
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 24482
DS 4
SWH 25125.629
FIDRES 0.383387
AQ 1.3042164
RG 4597.6
DW 19.900
DE 6.00
TE 299.2
D1 0.15000001
d11 0.03000000
DELTA 0.05000000
TD0 1
======== CHANNEL f1 ====
NUC1 13C
P1 7.80
PL1 -3.00
SFO1 100.5936591
======== CHANNEL f2 ====
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00
PL2 17.40
PL12 17.40
PL13 17.40
SFO2 400.0116000
F2 - Processing paramete
ppm
S
O
S
S
H
OH

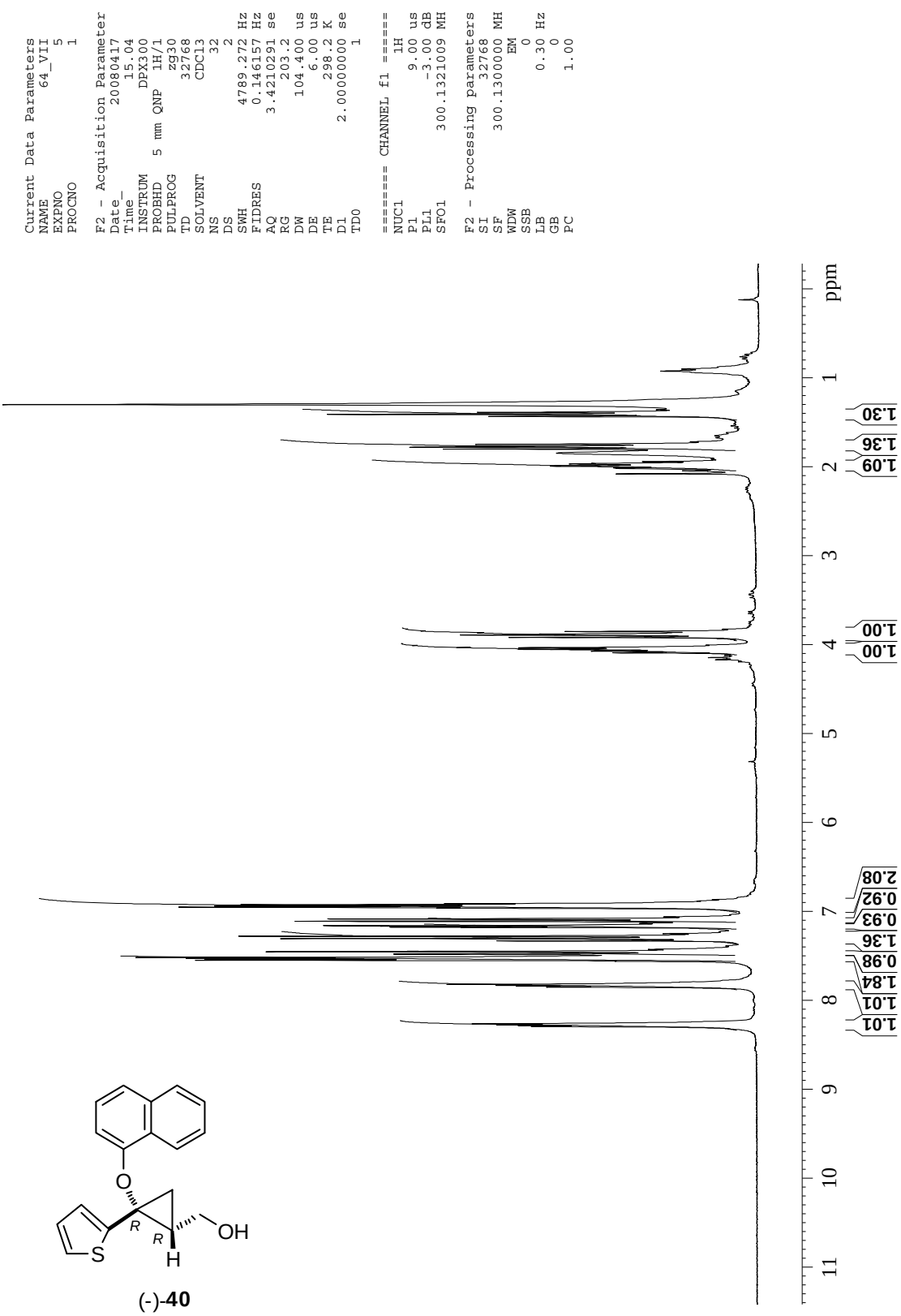
(+)-**37**


Current Data Parameters
NAME 64_VII
EXPNO 15
PROCNO 1
F2 - Acquisition Parameters
Date_ 20081102
Time 14.11
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT
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 parameters
SI 32768
SF 399.9500000
WDW EM
SSB 0
LB 0.70
GB 0
PC 1.00
ppm
1.05
1.11
2.16
0.94
0.88
0.73
0.98
0.99
0.85
1.14
1.00
1.02
1.00
1.02
1.37
1.12
O
R
S
H
S
OH

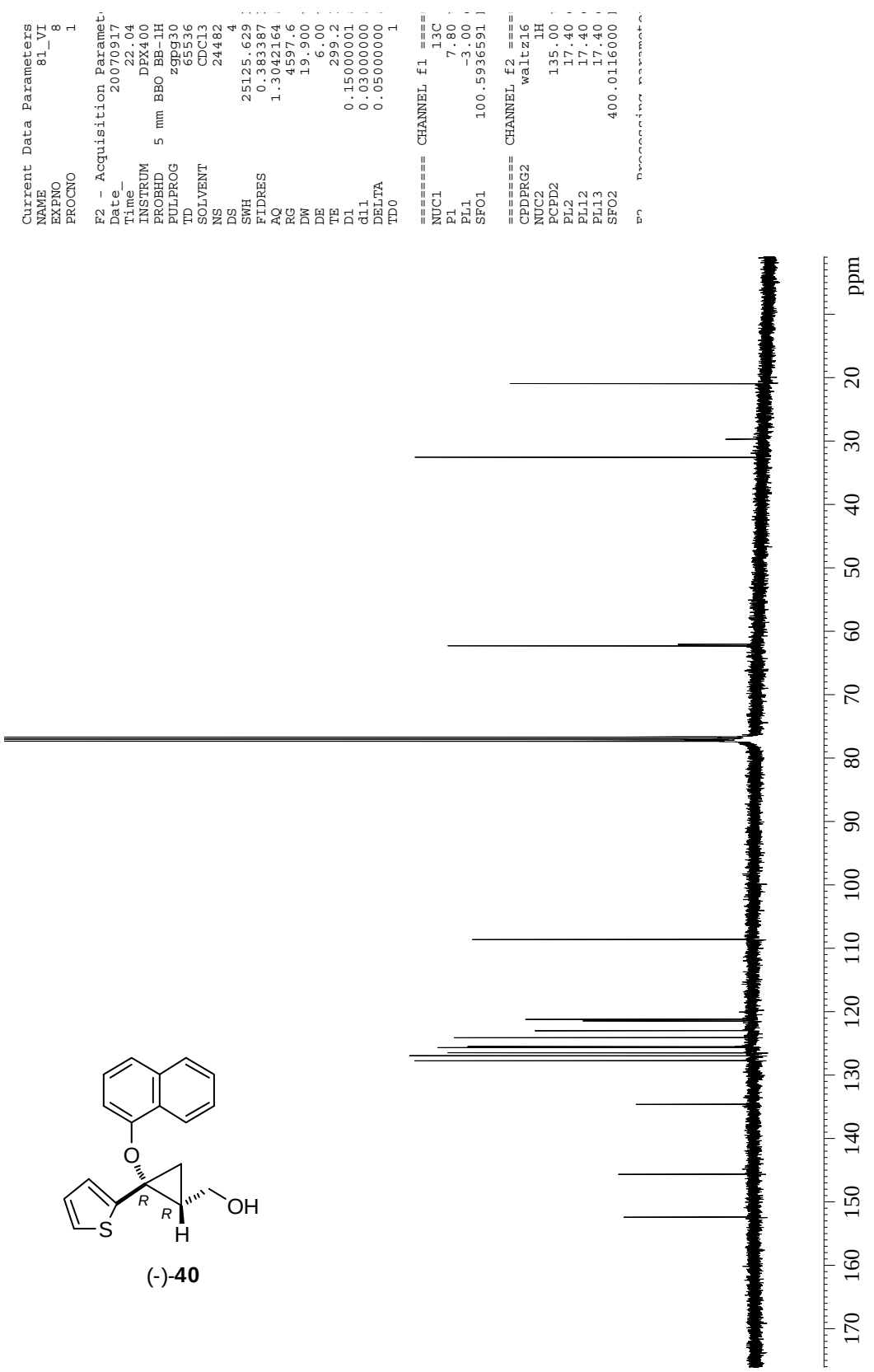
(+)-**39**

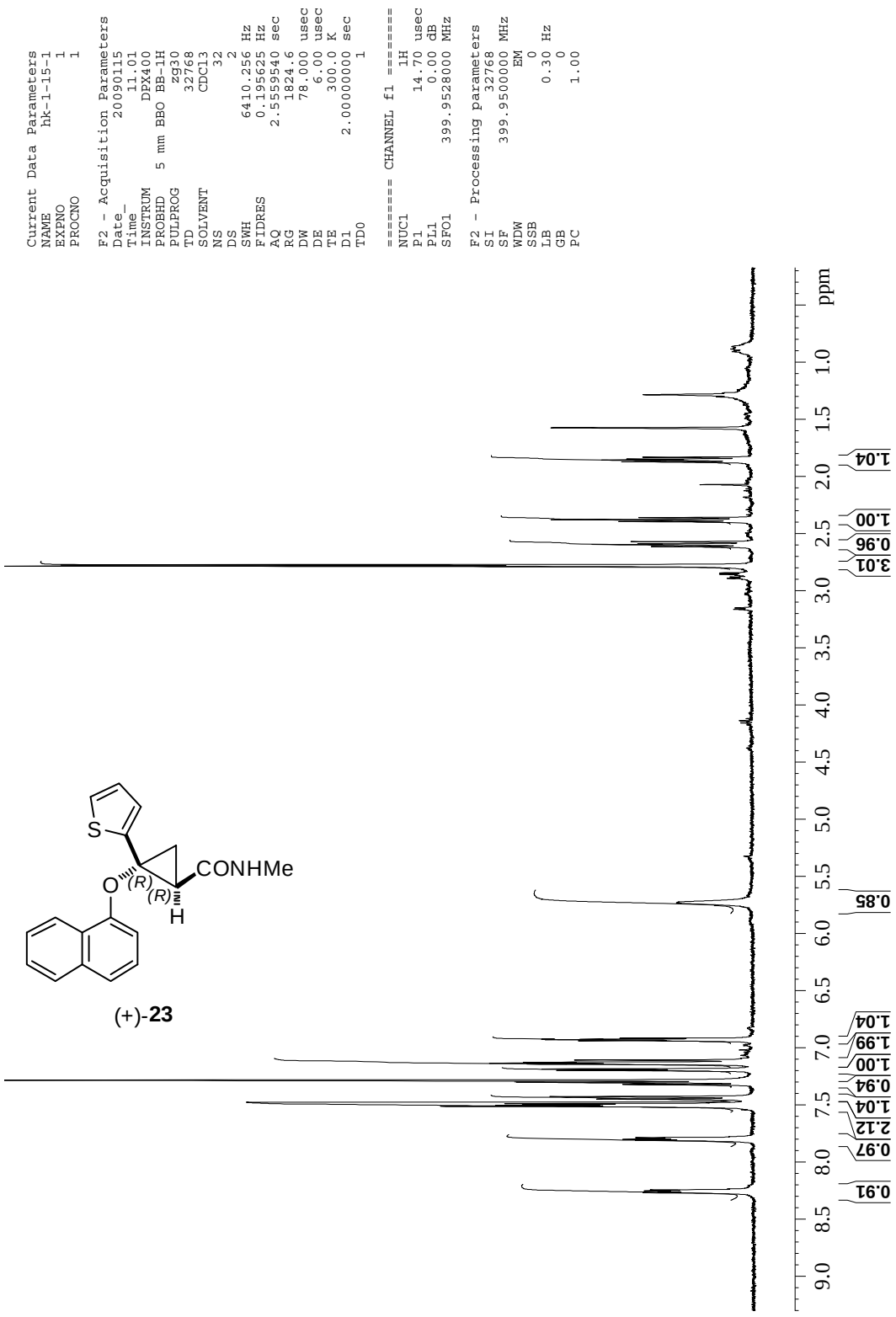

Current Data Parameters
NAME 64_VII
EXPNO 19
PROCNO 1
DU /m
USER rajan
F2 - Acquisition Paramet
Date_ 20081102
Time_ 15.59
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 2125
DS 4
SWH 25125.629
FIDRES 0.383387
AQ 1.3042164
RG 1448.2
DW 19.900
DE 6.00
TE 298.2
D1 0.15000001
d11 0.03000000
DELTA 0.05000000
TD0 1
======== CHANNEL f1 ====
NUC1 13C
P1 7.80
PL1 -3.00
SFO1 100.5785700
======== CHANNEL f2 ====
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00
PL2 17.40
ppm
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
O
R
S
H
S
OH

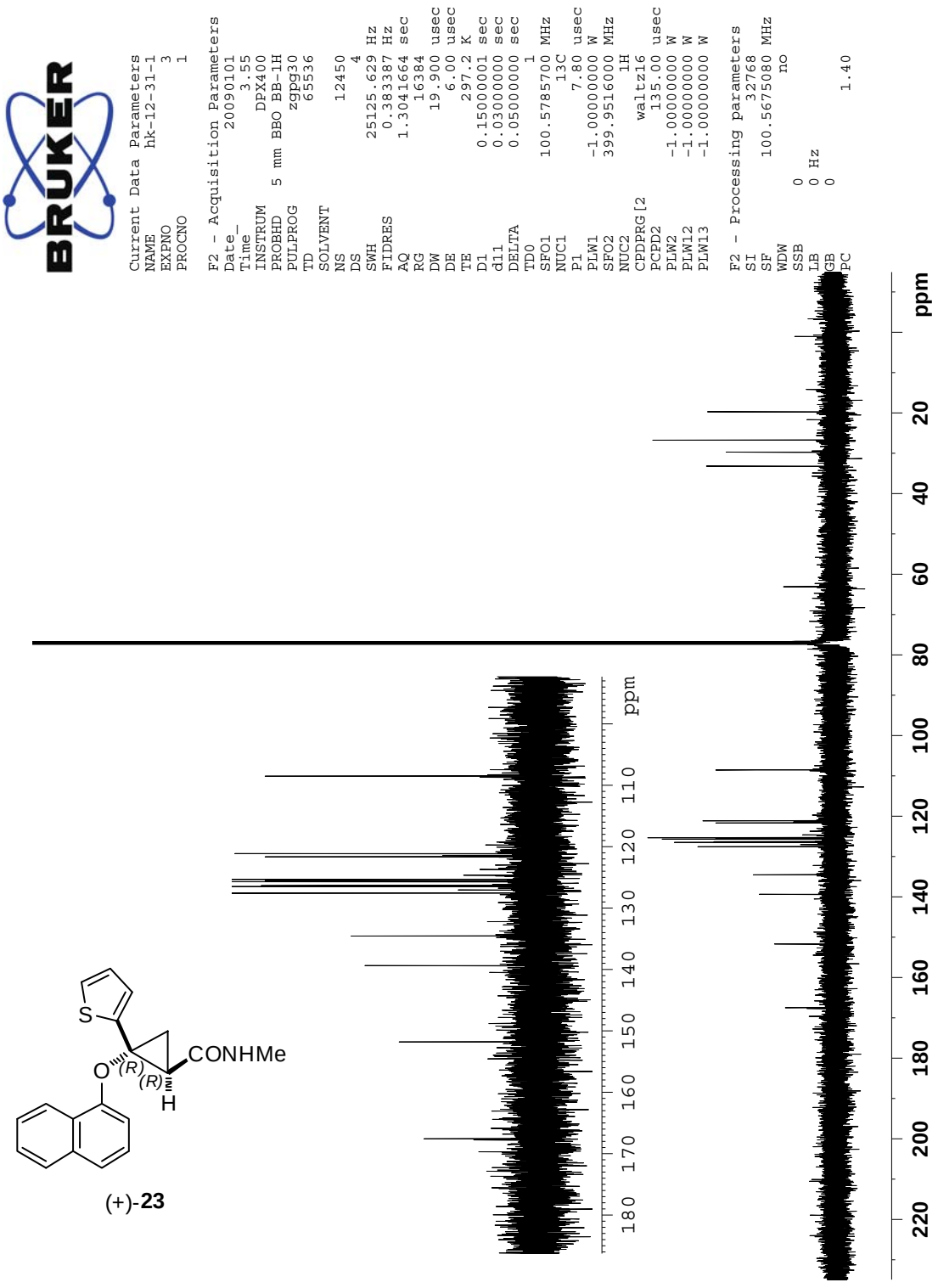
(+)-**39**


Current Data Parameters
NAME 64_VII
EXPNO 5
PROCNO 1
F2 - Acquisition Parameter
Date_ 20080417
Time_ 15.04
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4210291 se
RG 203.2
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 EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
ppm
1.30
1.36
1.09
1.00
1.00
1.01
1.01
1.84
0.98
1.36
0.93
0.92
2.08
O
R
R
OH
S
H

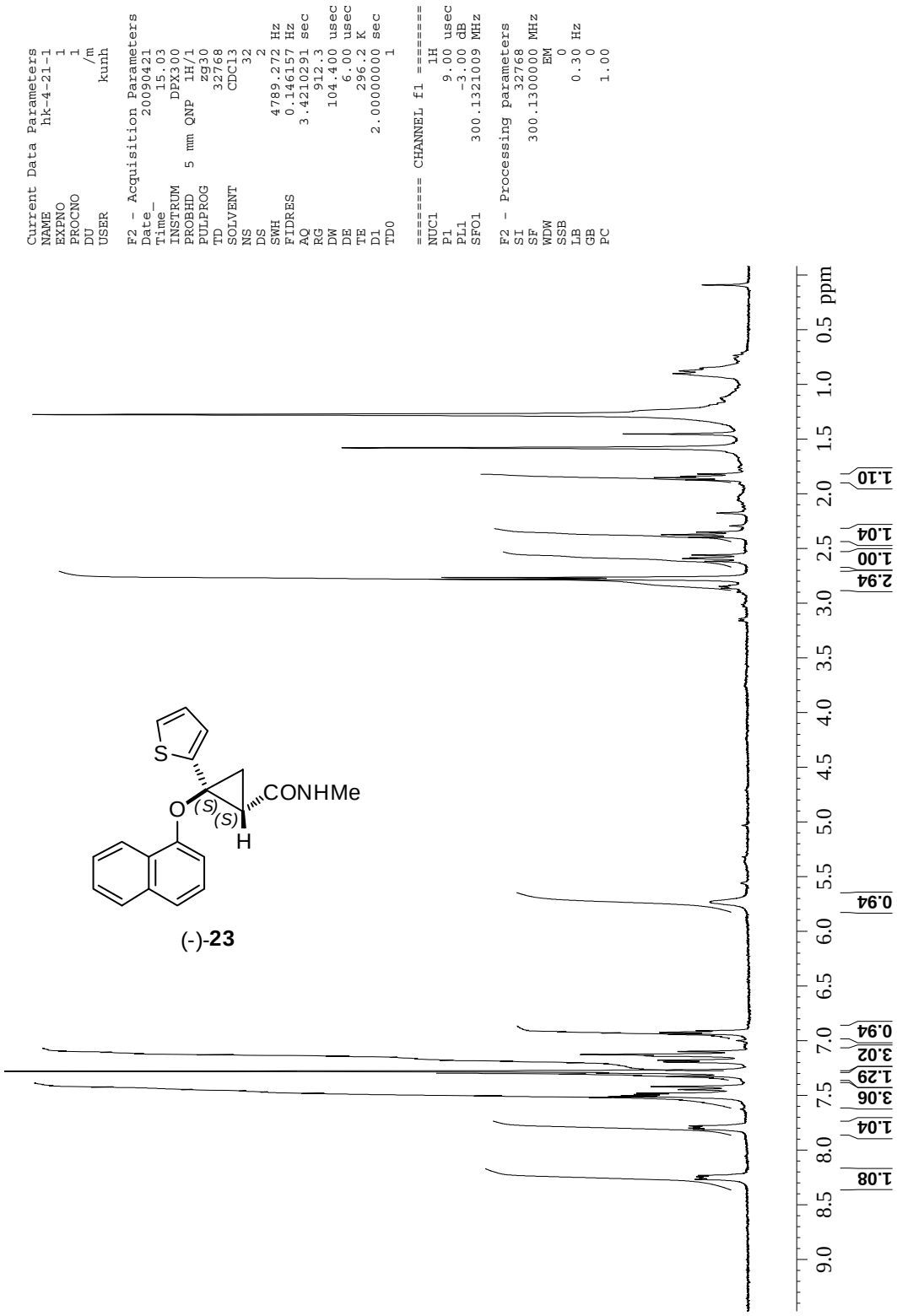
(-)-**40**

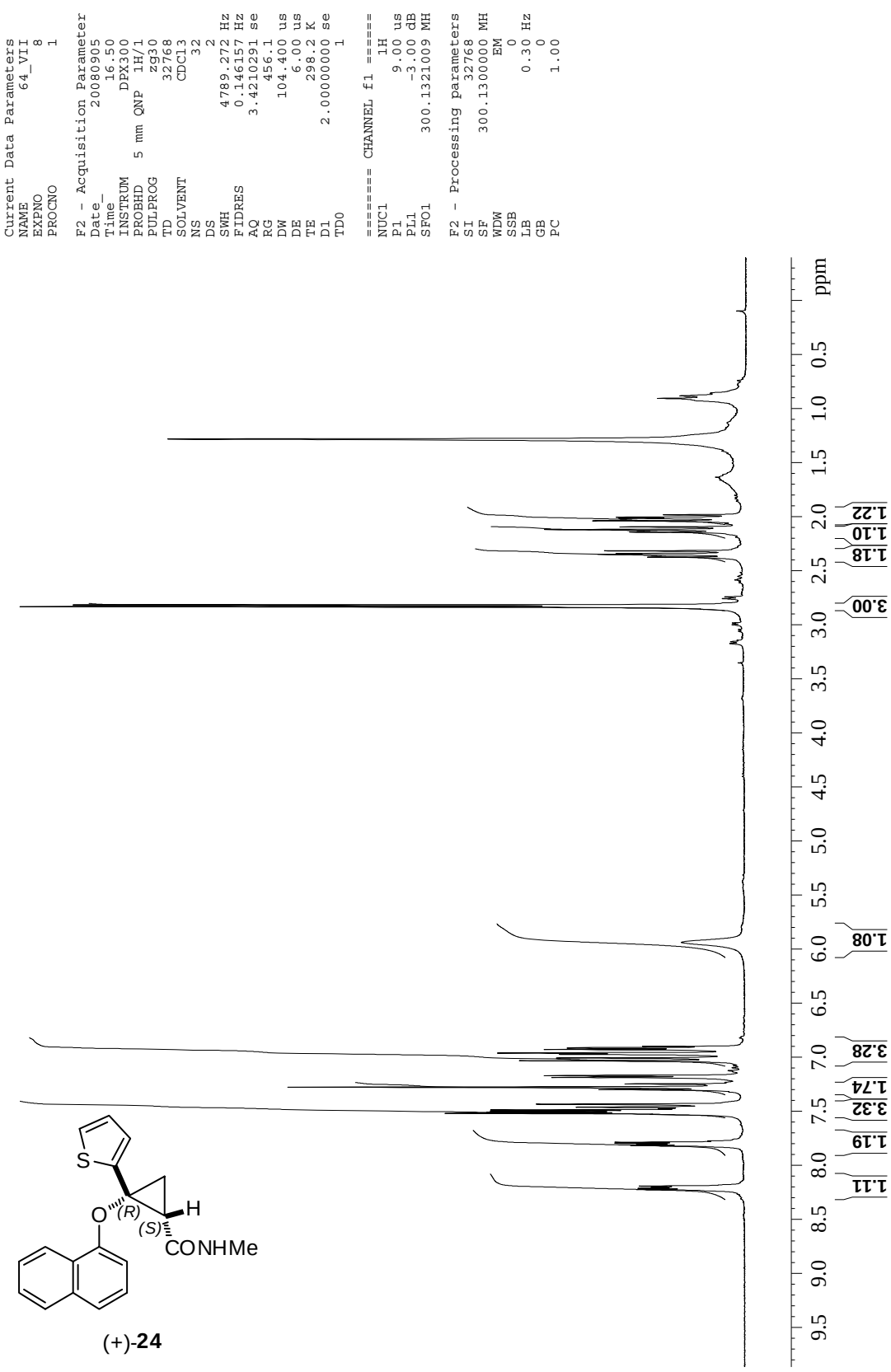

Current Data Parameters
NAME 81_VI
EXPNO 8
PROCNO 1
F2 - Acquisition Paramet
Date_ 20070917
Time 22.04
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 24482
DS 4
SWH 25125.629
FIDRES 0.383387
AQ 1.3042164
RG 4597.6
DW 19.900
DE 6.00
TE 299.2
D1 0.15000001
d11 0.03000000
DELTA 0.05000000
TD0 1
======== CHANNEL f1 ====
NUC1 13C
P1 7.80
PL1 -3.00
SFO1 100.5936591
======== CHANNEL f2 ====
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00
PL2 17.40
PL12 17.40
PL13 17.40
SFO2 400.0116000
F2 - Processing paramete
O
R
R
OH
S
H
(-)-40
ppm
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20

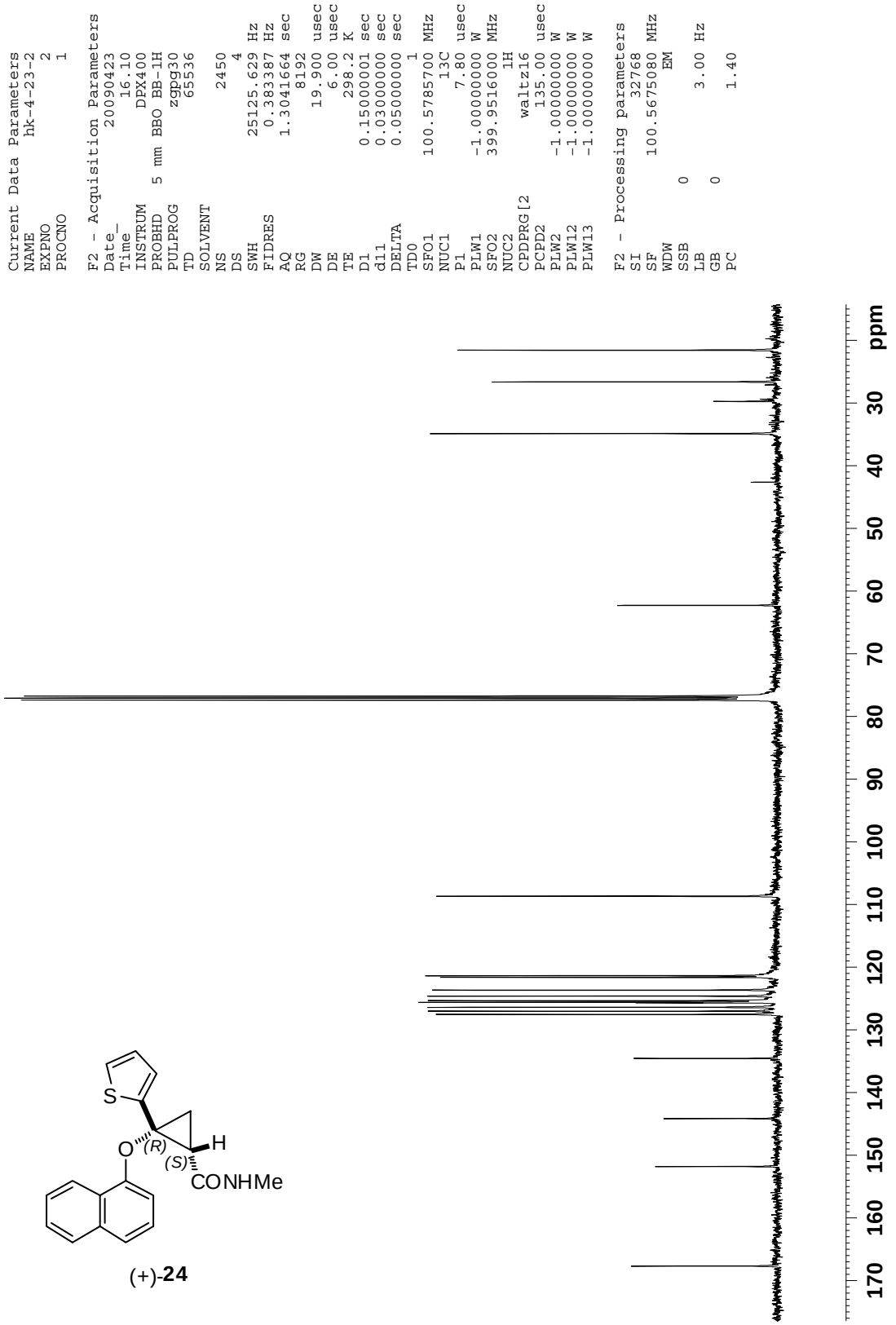

Current Data Parameters
NAME hk-1-15-1
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20090115
Time_ 11.01
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 1824.6
DW 78.000 usec
DE 6.00 usec
TE 300.0 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 399.9528000 MHz
F2 - Processing parameters
SI 32768
SF 399.9500000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
S
O
(R)
(R)
H
CONHMe
(+)-23
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
0.91
0.97
2.12
1.04
0.94
1.00
1.99
1.04
0.85
3.01
0.96
1.00
1.04


Current Data Parameters
NAME hk-12-31-1
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20090101
Time_ 3.55
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 12450
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3041664 sec
RG 16384
DW 19.900 usec
DE 6.00 usec
TE 297.2 K
D1 0.15000001 sec
d11 0.03000000 sec
DELTA 0.05000000 sec
TD0 1
SFO1 100.5785700 MHz
NUC1 13C
P1 7.80 usec
PLW1 -1.00000000 W
SFO2 399.9516000 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 135.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 32768
SF 100.5675080 MHz
WDW no
SSB 0
LB 0 Hz
GB 0
PC 1.40
ppm
S
O
(R)
(R)
H
CONHMe

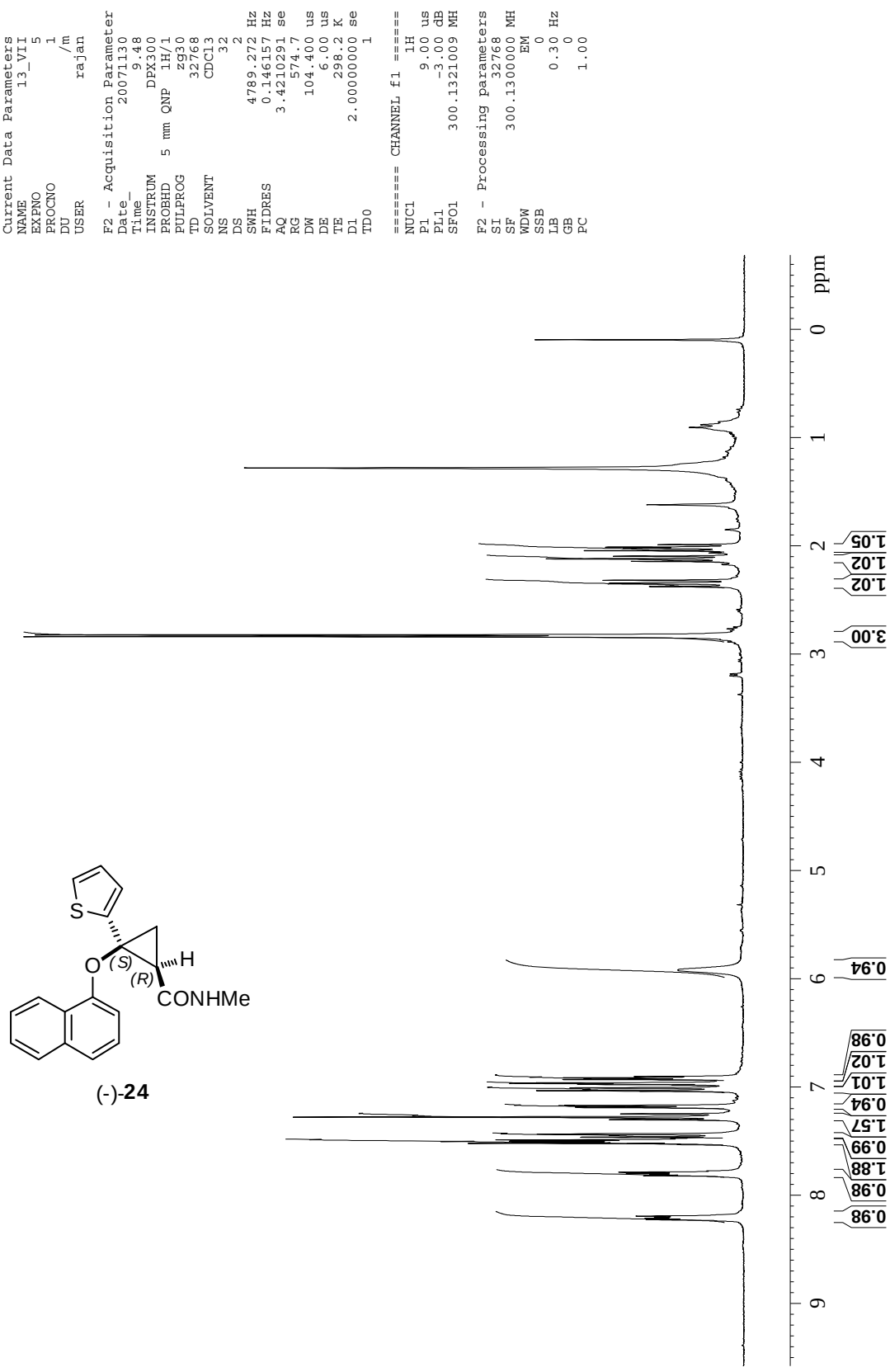
(+)-**23**

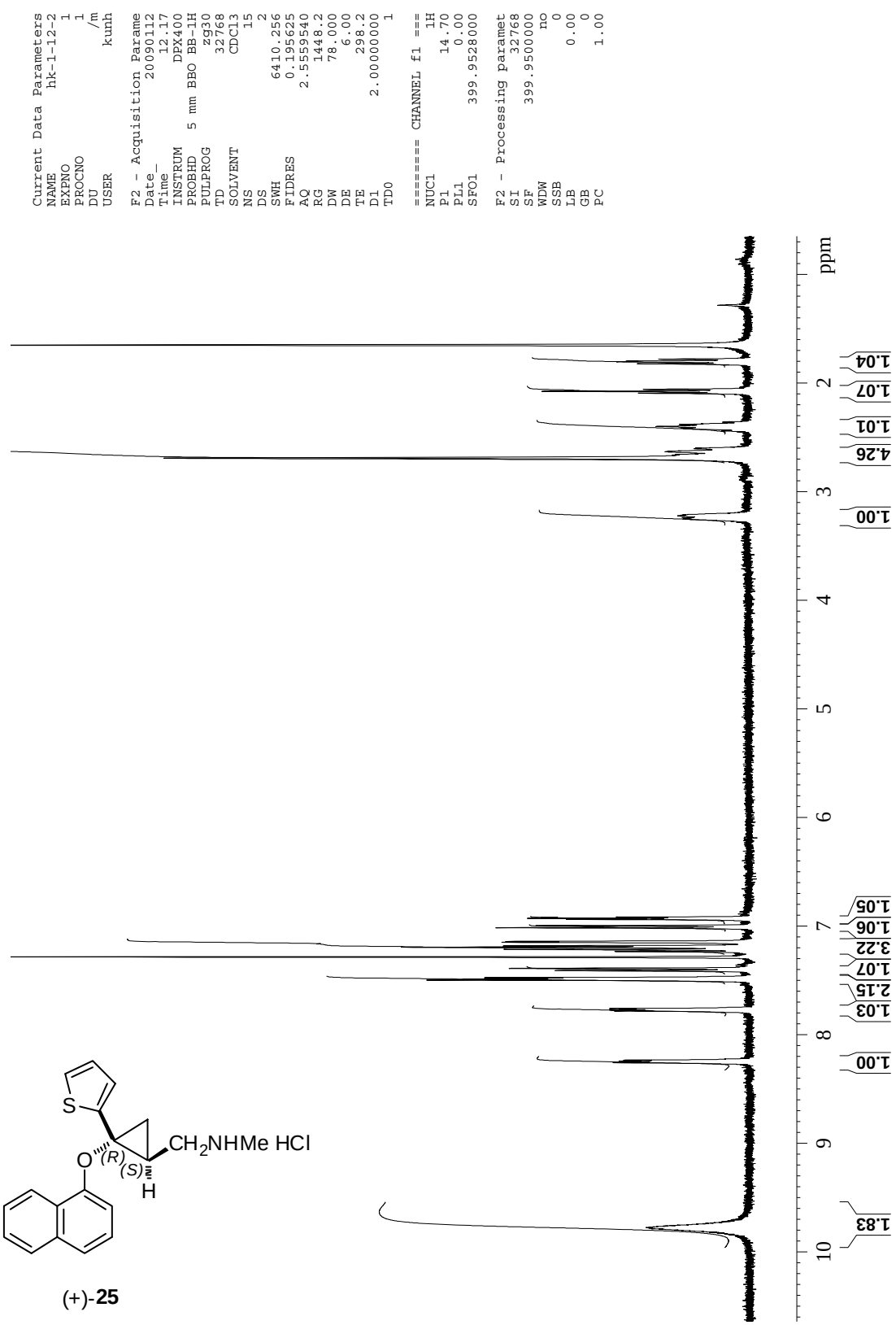

Current Data Parameters
NAME hk-4-21-1
EXPNO 1
PROCNO 1
DU /m
USER kunh
F2 - Acquisition Parameters
Date_ 20090421
Time 15.03
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4210291 sec
RG 912.3
DW 104.400 usec
DE 6.00 usec
TE 296.2 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 EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
S
O
(S)
(S)
CONHMe
H
(-)-23
1.08
1.04
3.06
1.29
3.02
0.94
0.94
2.94
1.00
1.04
1.10
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


Current Data Parameters
NAME 64_VII
EXPNO 8
PROCNO 1
F2 - Acquisition Parameter
Date_ 20080905
Time_ 16.50
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4210291 sec
RG 456.1
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 EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1.11
1.19
3.32
1.74
3.28
1.08
3.00
1.18
1.10
1.22
ppm
S
O
(R)
(S)
H
CONHMe
(+)-24

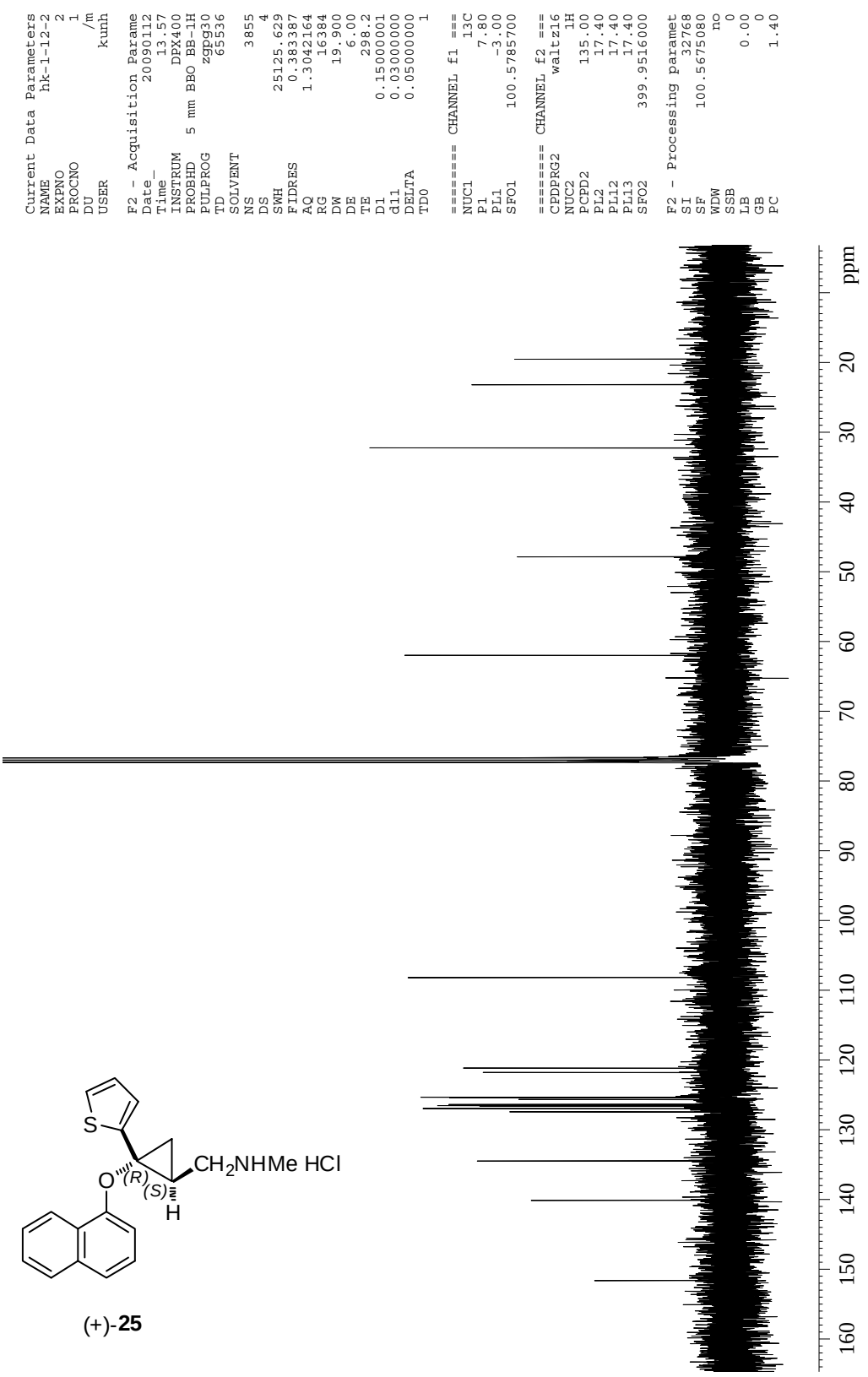

Current Data Parameters
NAME hk-4-23-2
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20090423
Time_ 16.10
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 2450
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3041664 sec
RG 8192
DW 19.900 usec
DE 6.00 usec
TE 298.2 K
D1 0.15000001 sec
d11 0.03000000 sec
DELTA 0.05000000 sec
TD0 1
SFO1 100.5785700 MHz
NUC1 13C
P1 7.80 usec
PLW1 -1.00000000 W
SFO2 399.9516000 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 135.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 32768
SF 100.5675080 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
ppm
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30
S
O
(R)
(S)
H
CONHMe

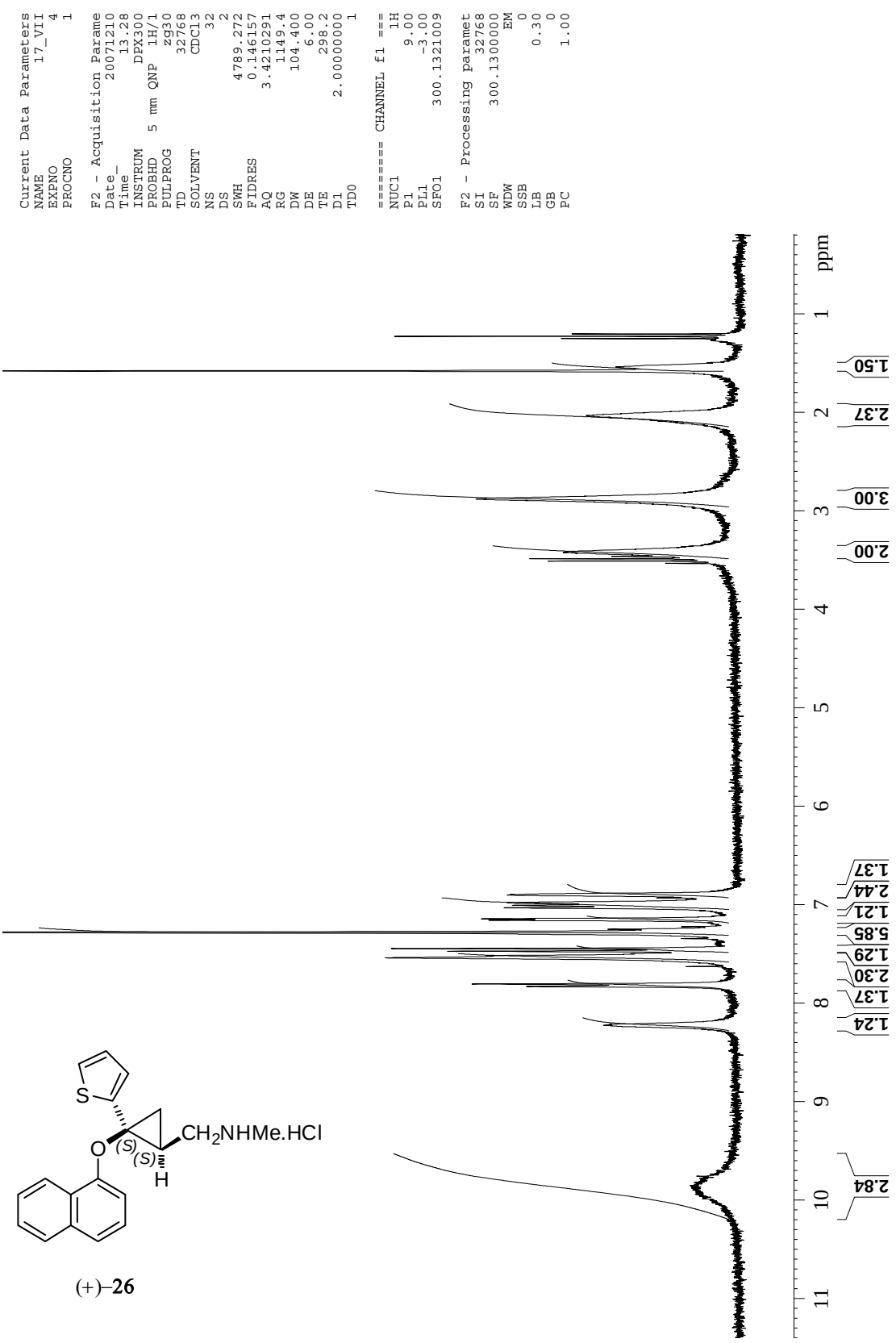
(+)-**24**


Current Data Parameters
NAME 13_VII
EXPNO 5
PROCNO 1
DU /m
USER rajan
F2 - Acquisition Parameter
Date_ 20071130
Time_ 9.48
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.42210291 se
RG 574.7
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 EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
S
O
(S)
(R)
H
CONHMe
(-)-24
ppm
0
1
2
3
4
5
6
7
8
9
0.98
0.98
1.88
0.99
1.57
0.94
1.01
1.02
0.98
0.94
3.00
1.02
1.02
1.05

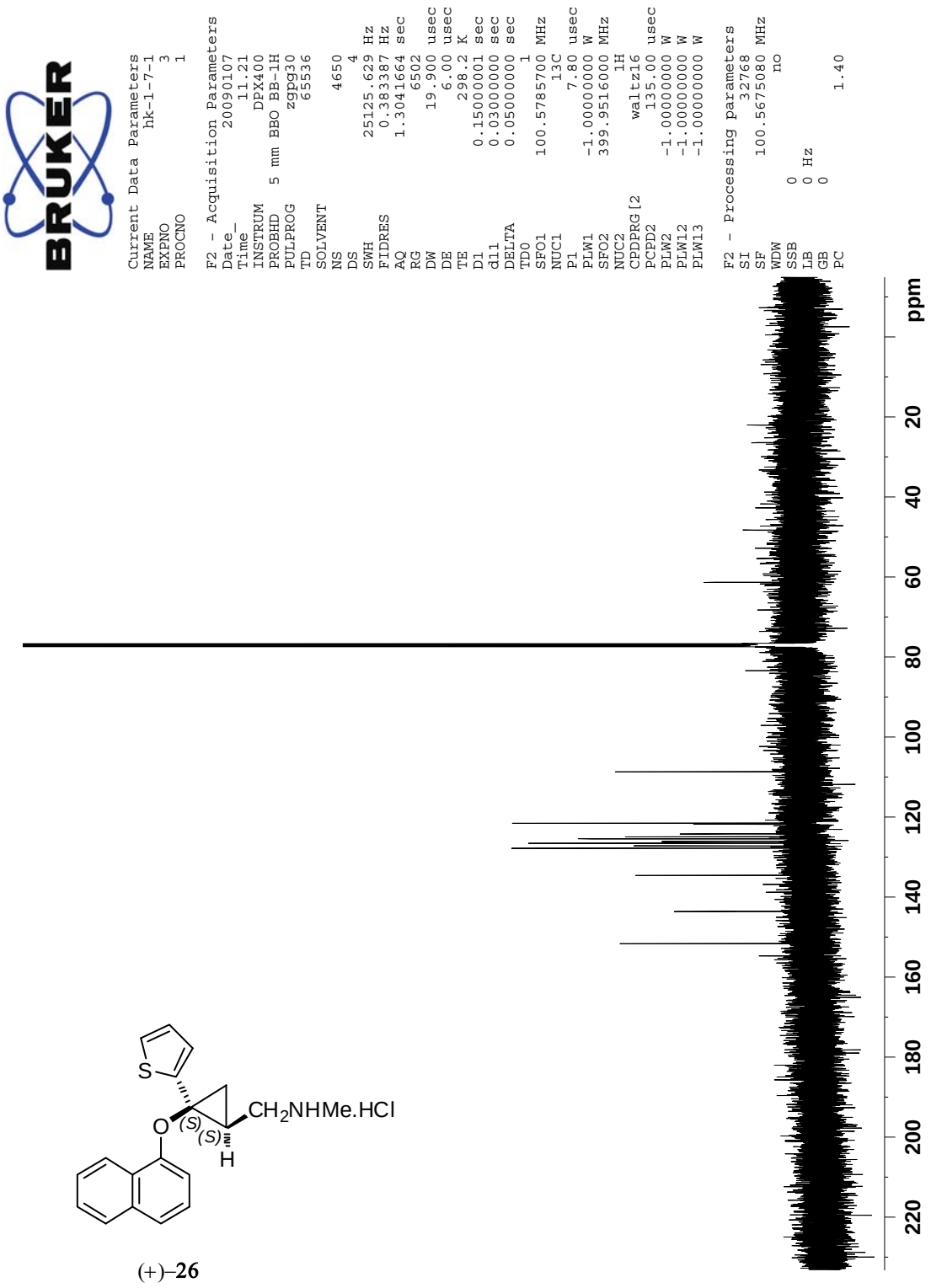

Current Data Parameters
NAME hk-1-12-2
EXPNO 1
PROCNO 1
DU /m
USER kunh
F2 - Acquisition Parame
Date_ 20090112
Time 12.17
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 15
DS 2
SWH 6410.256
FIDRES 0.195625
AQ 2.5559540
RG 1448.2
DW 78.000
DE 6.00
TE 298.2
D1 2.00000000
TD0 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
ppm
1.04
1.07
1.01
4.26
1.00
1.05
1.06
3.22
1.07
2.15
1.03
1.00
1.83
S
O
(R)
(S)
H
CH2NHMe HCl

(+)-**25**

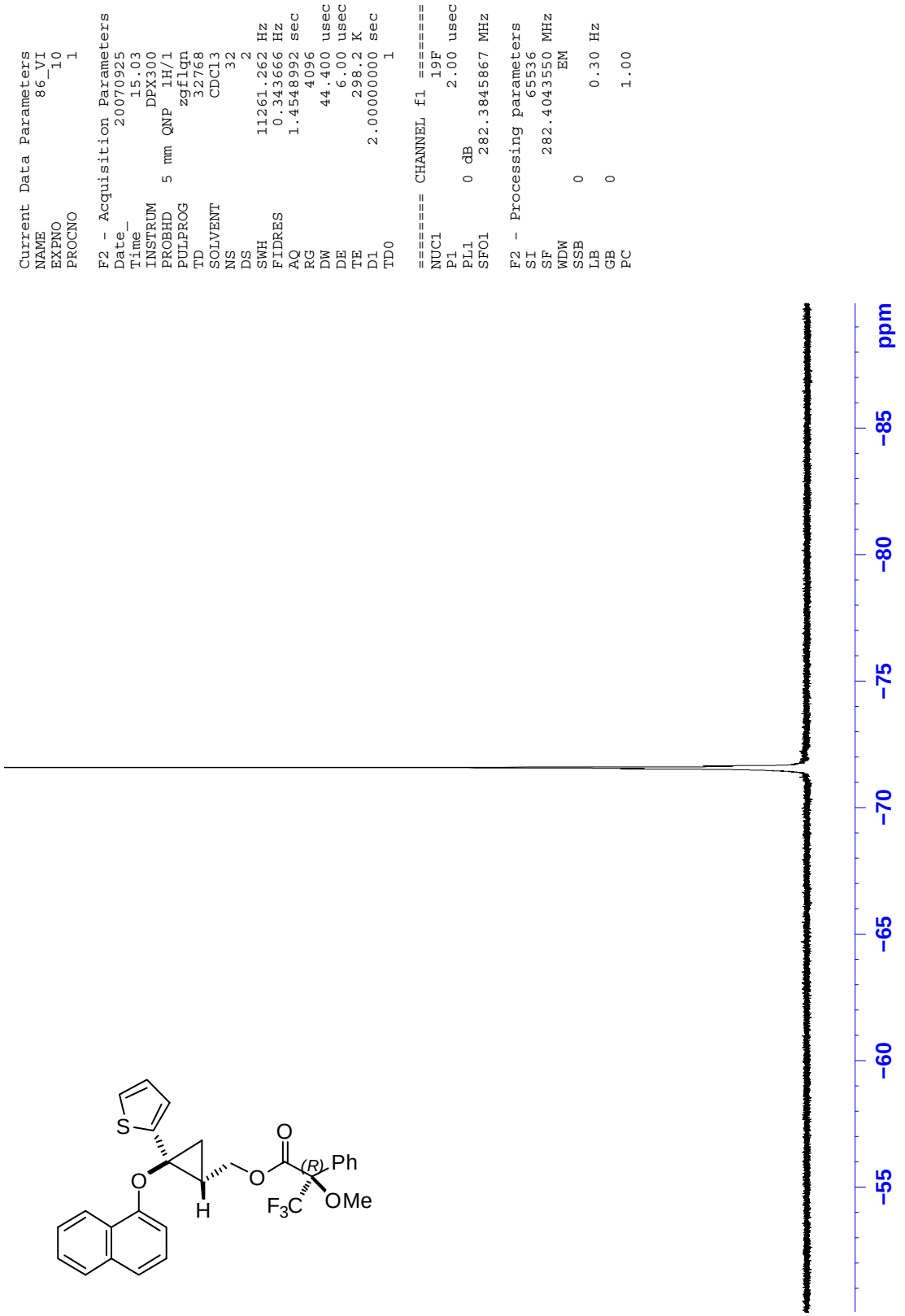

Current Data Parameters
NAME hk-1-12-2
EXPNO 2
PROCNO 1
DU /m
USER kunh
F2 - Acquisition Parame
Date_ 20090112
Time 13.57
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 3855
DS 4
SWH 25125.629
FIDRES 0.383387
AQ 1.3042164
RG 16384
DW 19.900
DE 6.00
TE 298.2
D1 0.15000001
d11 0.03000000
DELTA 0.05000000
TD0 1
======== CHANNEL f1 ===
NUC1 13C
P1 7.80
PL1 -3.00
SFO1 100.5785700
======== CHANNEL f2 ===
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00
PL2 17.40
PL12 17.40
PL13 17.40
SFO2 399.9516000
F2 - Processing paramet
SI 32768
SF 100.5675080
WDW no
SSB 0
LB 0.00
GB 0
PC 1.40
S
O
(R)
(S)
H
CH2NHMe HCl
(+)-25
ppm

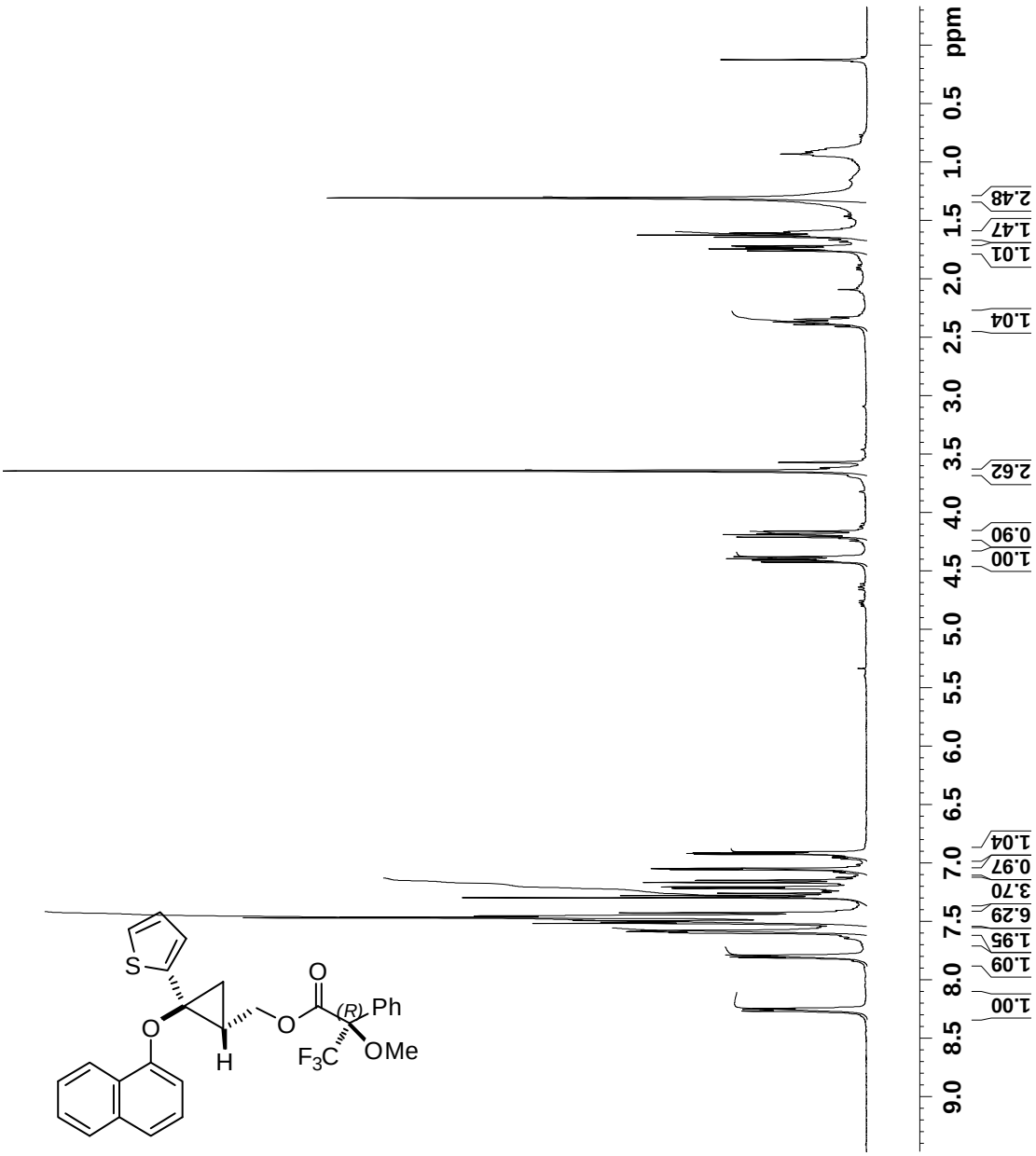

Current Data Parameters
NAME 17_VII
EXPNO 4
PROCNO 1
F2 - Acquisition Parame
Date_ 20071210
Time 13.28
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4789.272
FIDRES 0.146157
AQ 3.4210291
RG 1149.4
DW 104.400
DE 6.00
TE 298.2
D1 2.00000000
TDO 1
======== CHANNEL 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
ppm
1.50
2.37
3.00
2.00
1.37
2.44
1.21
5.85
1.29
2.30
1.37
1.24
2.84
S
O
(S)
(S)
H
CH2NHMe.HCl

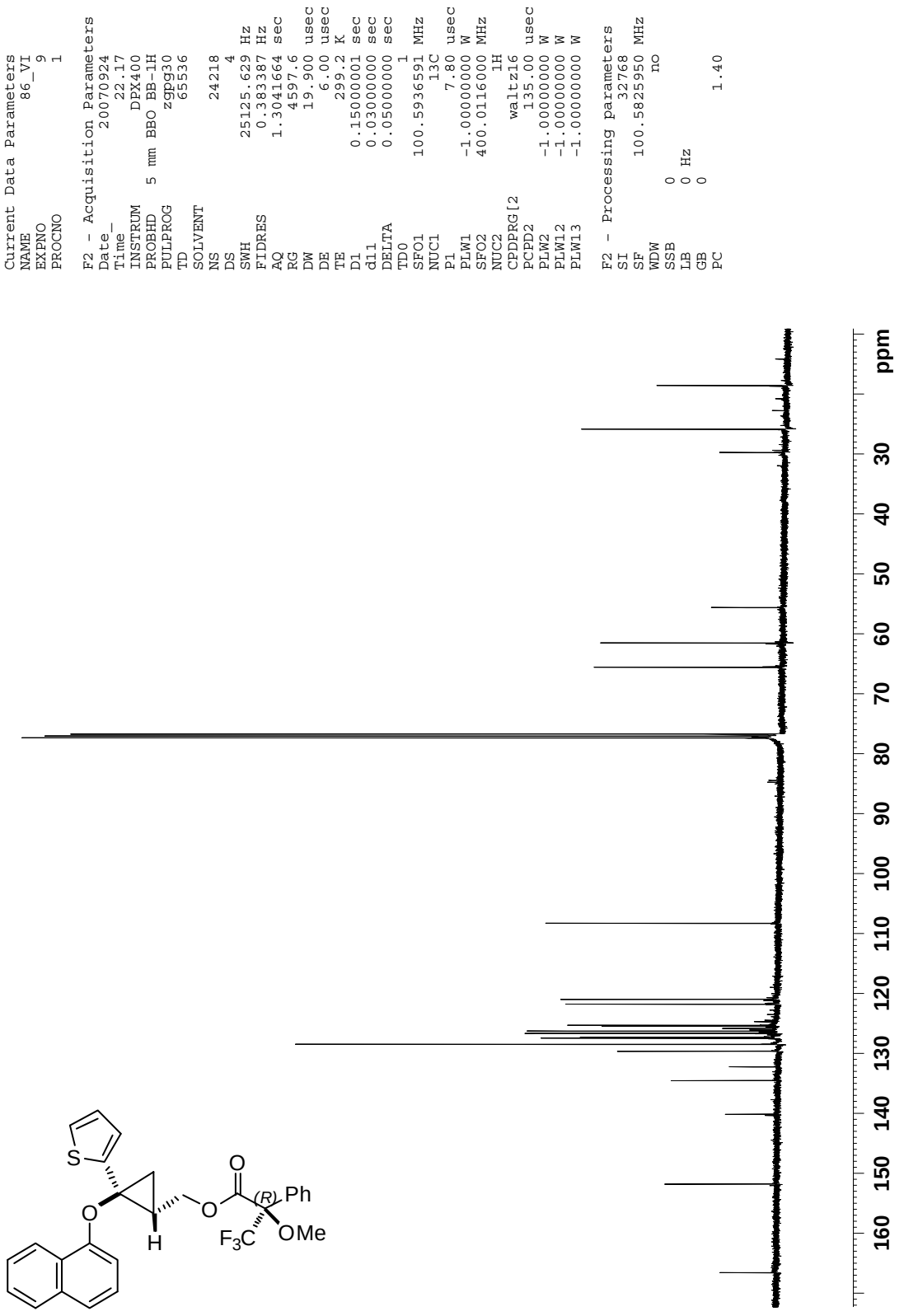
(+)–**26**


Current Data Parameters
NAME hk-1-7-1
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20090107
Time_ 11.21
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 4650
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3041664 sec
RG 6502
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
SFO1 100.5785700 MHz
NUC1 13C
P1 7.80 usec
PLW1 -1.00000000 W
SFO2 399.9516000 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 135.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 32768
SF 100.5675080 MHz
WDW no
SSB 0
LB 0 Hz
GB 0
PC 1.40
ppm
220
200
180
160
140
120
100
80
60
40
20
S
O
(S)
(S)
H
CH2NHMe.HCl

(+)–**26**

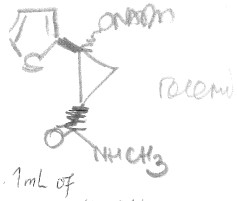

Current Data Parameters
NAME 86_VI
EXPNO 10
PROCNO 1
F2 - Acquisition Parameters
Date_ 20070925
Time_ 15.03
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zgflqn
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 11261.262 Hz
FIDRES 0.343666 Hz
AQ 1.4548992 sec
RG 4096
DW 44.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 19F
P1 2.00 usec
PL1 0 dB
SFO1 282.3845867 MHz
F2 - Processing parameters
SI 65536
SF 282.4043550 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
S
O
H
O
O
(R)
Ph
F3C
OMe
-55
-60
-65
-70
-75
-80
-85
ppm


Current Data Parameters
NAME 86_VI
EXPNO 7
PROCNO 1
F2 - Acquisition Parameters
Date_ 20070924
Time_ 22.00
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 2.5559039 sec
RG 322.5
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 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
S
O
O
O
(R)
Ph
H
F3C
OMe
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
0.5
1.00
1.09
1.95
6.29
3.70
0.97
1.04
1.00
0.90
2.62
1.04
1.01
1.47
2.48


Current Data Parameters
NAME 86_VI
EXPNO 9
PROCNO 1
F2 - Acquisition Parameters
Date_ 20070924
Time 22.17
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 24218
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3041664 sec
RG 4597.6
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
SFO1 100.5936591 MHz
NUC1 13C
P1 7.80 usec
PLW1 -1.00000000 W
SFO2 400.0116000 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 135.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 32768
SF 100.5825950 MHz
WDW no
SSB 0
LB 0 Hz
GB 0
PC 1.40
S
O
O
O
H
(R)
Ph
F3C
OMe
160 150 140 130 120 110 100 90 80 70 60 50 40 30
ppm

APPENDIX II
Chiral HPLC Data

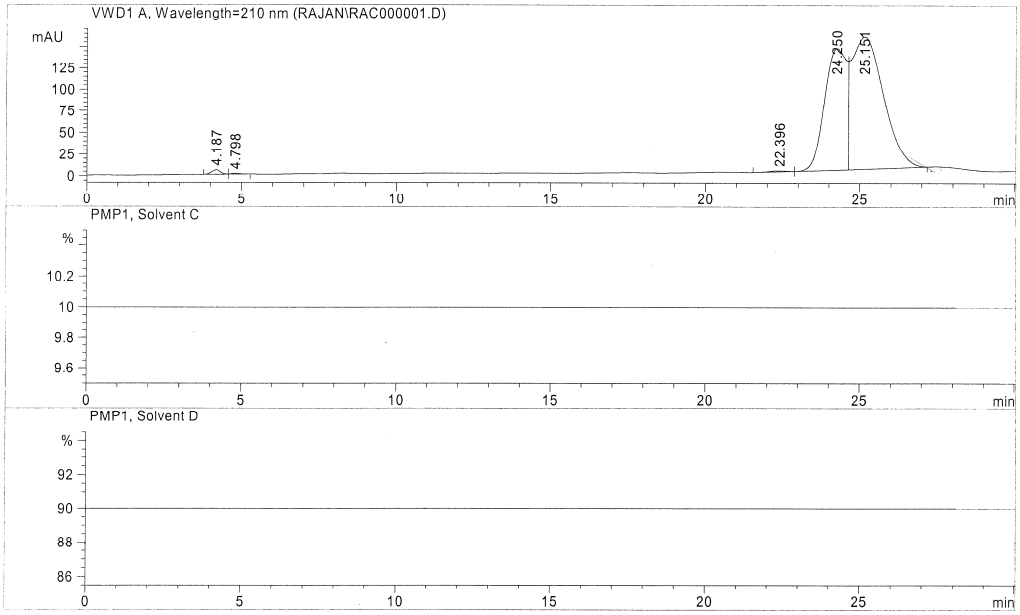
Data File D:\CHEM32\1\DATA\RAJAN\rac000001.D
Sample Name: racemic



Acq. Operator	: Rajan	Seq. Line	: 1
Acq. Instrument	: Instrument 1	Location	: Vial 81
Injection Date	: 4/10/2007 10:06:39 AM	Inj	: 1
		Inj Volume	: 2.5 µl
Sequence File	: C:\CHEM32\1\SEQUENCE\RAJAN0410.S		
Method	: C:\CHEM32\1\METHODS\RAJAN0410.M		
Last changed	: 4/10/2007 10:03:15 AM by Erik		
Method Info	:		

1mg in 0.1mL of 9:1 hex/iPrOH

90:10 hex : iPrOH, 1mL/min



Fraction Information

Fraction collection off

No Fractions found.

Area Percent Report

Sorted By : Signal
Multiplier : 1.0000
Dilution : 1.0000
Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=210 nm

Data File D:\CHEM32\1\DATA\RAJAN\rac000001.D
Sample Name: racemic

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	4.187	BV	0.2850	102.19122	5.25723	0.5661
2	4.798	VB	0.3062	21.60043	1.04077	0.1197
3	22.396	BV	0.4929	47.02597	1.18670	0.2605
4	24.250	VV	0.7561	6981.42041	141.51900	38.6739
5	25.151	VB	1.0558	1.08998e4	153.45508	60.3798
Totals :				1.80520e4	302.45878	

Summed Peaks Report

Signal 1: VWD1 A, Wavelength=210 nm

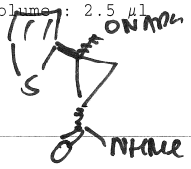
Final Summed Peaks Report

Signal 1: VWD1 A, Wavelength=210 nm

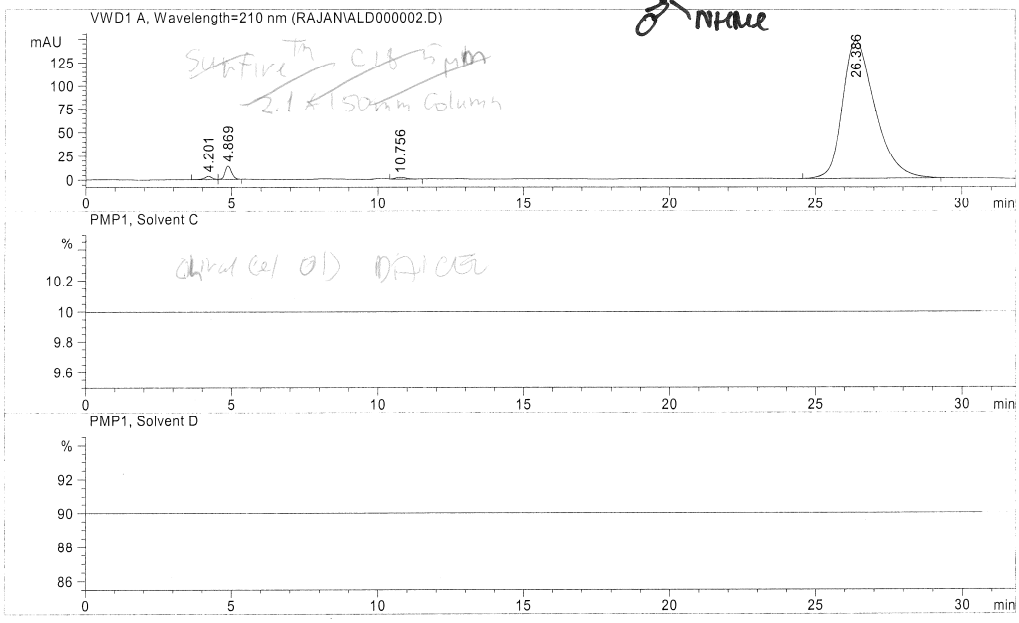
*** End of Report ***

Data File C:\Chem32\1\DATA\RAJAN\ald000002.D
Sample Name: racemic

Acq. Operator	: sephton	Seq. Line	: 1
Acq. Instrument	: Instrument 1	Location	: Vial 81
Injection Date	: 11/30/2007 11:07:39 AM	Inj	: 1
		Inj Volume	: 2.5 µl
Sequence File	: C:\CHEM32\1\SEQUENCE\RAJAN0410.S		
Method	: C:\CHEM32\1\METHODS\RAJAN0410.M		
Last changed	: 4/10/2007 10:03:15 AM by Erik		
Method Info	:		



13-VII
R CONFIG



Fraction Information

Fraction collection off

No Fractions found.

Area Percent Report

Sorted By	:	Signal
Multiplier	:	1.0000
Dilution	:	1.0000

Use Multiplier & Dilution Factor with ISTDs

Signal 1: VWD1 A, Wavelength=210 nm

Data File C:\Chem32\1\DATA\RAJAN\ald000002.D
Sample Name: racemic

Peak #	RetTime [min]	Type	Width [min]	Area mAU *s	Height [mAU]	Area %
1	4.201	BV	0.2668	63.43945	3.45305	0.5471
2	4.869	VB	0.2444	217.61060	13.85332	1.8766
3	10.756	VB	0.3938	46.77321	1.82417	0.4034
4	26.386	BB	1.1582	1.12681e4	147.18127	97.1730
Totals :				1.15960e4	166.31181	

Summed Peaks Report

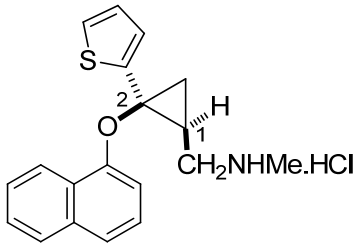
Signal 1: VWD1 A, Wavelength=210 nm

Final Summed Peaks Report

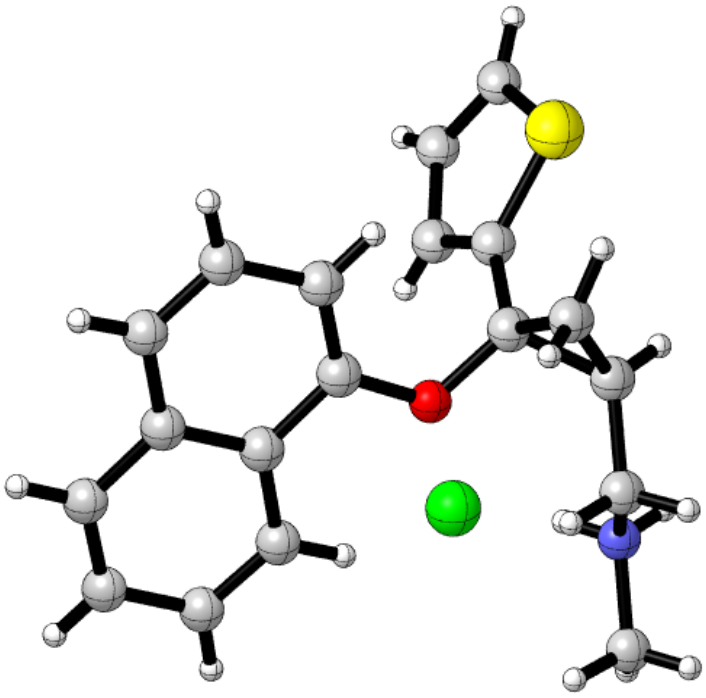
Signal 1: VWD1 A, Wavelength=210 nm
*** End of Report ***

APPENDIX III

X-ray Crystallographic Data



(+)-**26**



(+)-**26**

Table 4. Crystal data and structure refinement for (+)-**26**

Identification code	jw20	
Empirical formula	C19 H20 Cl N O S	
Formula weight	345.87	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 9.2407(6) Å	a= 90°.
b = 6.7846(4) Å	b= 104.3170(10)°.	
	c = 14.9432(10) Å	g = 90°.
Volume	907.76(10) $Å^3$	
Z	2	
Density (calculated)	1.265 Mg/m^3	
Absorption coefficient	0.329 mm^{-1}	
F(000)	364	
Crystal size	0.25 x 0.16 x 0.12 mm^3	
Theta range for data collection	1.41 to 26.99°.	
Index ranges	-11<=h<=11, -8<=k<=8, -19<=l<=18	
Reflections collected	10237	
Independent reflections	3942 [R(int) = 0.0174]	
Completeness to theta = 26.99°	99.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9616 and 0.9223	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3942 / 1 / 288	
Goodness-of-fit on F^2	1.025	
Final R indices [I>2sigma(I)]	R1 = 0.0300, wR2 = 0.0735	
R indices (all data)	R1 = 0.0317, wR2 = 0.0751	
Absolute structure parameter	0.04(5)	
Largest diff. peak and hole	0.218 and -0.152 $e.Å^{-3}$	

Table 5. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for (+)-**26**

U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Cl(1)	4042(1)	5633(1)	5554(1)	38(1)
S(1)	10398(1)	4110(1)	6708(1)	59(1)
O(1)	6701(1)	4485(2)	7641(1)	31(1)
N(1)	4674(2)	1315(3)	6157(1)	36(1)
C(1)	10525(2)	6179(4)	6081(2)	53(1)
C(2)	9323(3)	7301(4)	5980(2)	50(1)
C(3)	8222(2)	6496(3)	6392(1)	41(1)
C(4)	8656(2)	4753(3)	6824(1)	32(1)
C(5)	7816(2)	3478(3)	7321(1)	32(1)
C(6)	8495(2)	1685(3)	7865(1)	44(1)
C(7)	7331(2)	1435(3)	6963(1)	35(1)
C(8)	5822(2)	675(3)	6981(1)	37(1)
C(9)	3163(2)	592(4)	6151(2)	48(1)
C(10)	7139(2)	5777(3)	8367(1)	30(1)
C(11)	8587(2)	6071(3)	8848(1)	35(1)
C(12)	8913(2)	7457(3)	9582(1)	40(1)
C(13)	7806(2)	8488(3)	9816(1)	39(1)
C(14)	6289(2)	8230(3)	9321(1)	33(1)
C(15)	5941(2)	6833(2)	8586(1)	29(1)
C(16)	4427(2)	6566(3)	8101(1)	34(1)
C(17)	3328(2)	7643(3)	8329(1)	40(1)
C(18)	3671(2)	9031(3)	9054(1)	46(1)
C(19)	5105(2)	9304(3)	9532(1)	42(1)

Table 6. Bond lengths [Å] and angles [°] for (+)-**26**

S(1)-C(1)	1.708(3)
S(1)-C(4)	1.7174(17)
O(1)-C(10)	1.3759(19)
O(1)-C(5)	1.415(2)
N(1)-C(8)	1.478(2)
N(1)-C(9)	1.478(3)
N(1)-H(1N)	0.87(3)
N(1)-H(2N)	0.83(2)
C(1)-C(2)	1.324(3)
C(1)-H(1)	0.93(2)
C(2)-C(3)	1.422(3)
C(2)-H(2)	0.84(3)
C(3)-C(4)	1.360(3)
C(3)-H(3)	0.79(2)
C(4)-C(5)	1.479(2)
C(5)-C(6)	1.510(2)
C(5)-C(7)	1.513(2)
C(6)-C(7)	1.511(3)
C(6)-H(6A)	1.01(2)
C(6)-H(6B)	0.91(2)
C(7)-C(8)	1.493(3)
C(7)-H(7)	0.91(2)
C(8)-H(8A)	0.95(2)
C(8)-H(8B)	0.99(2)
C(9)-H(9A)	0.97(3)
C(9)-H(9B)	0.91(3)
C(9)-H(9C)	0.97(2)
C(10)-C(11)	1.367(2)
C(10)-C(15)	1.423(2)
C(11)-C(12)	1.420(3)
C(11)-H(11)	0.94(2)
C(12)-C(13)	1.354(3)
C(12)-H(12)	0.91(2)
C(13)-C(14)	1.425(3)

C(13)-H(13)	0.94(2)
C(14)-C(19)	1.414(3)
C(14)-C(15)	1.426(2)
C(15)-C(16)	1.419(2)
C(16)-C(17)	1.361(3)
C(16)-H(16)	0.95(2)
C(17)-C(18)	1.410(3)
C(17)-H(17)	0.93(2)
C(18)-C(19)	1.354(3)
C(18)-H(18)	0.91(2)
C(19)-H(19)	0.96(2)

C(1)-S(1)-C(4)	92.28(10)
C(10)-O(1)-C(5)	118.53(12)
C(8)-N(1)-C(9)	112.97(16)
C(8)-N(1)-H(1N)	108.6(15)
C(9)-N(1)-H(1N)	109.9(15)
C(8)-N(1)-H(2N)	105.0(14)
C(9)-N(1)-H(2N)	114.2(15)
H(1N)-N(1)-H(2N)	106(2)
C(2)-C(1)-S(1)	111.46(16)
C(2)-C(1)-H(1)	128.3(16)
S(1)-C(1)-H(1)	120.3(15)
C(1)-C(2)-C(3)	113.5(2)
C(1)-C(2)-H(2)	125.8(17)
C(3)-C(2)-H(2)	120.6(17)
C(4)-C(3)-C(2)	112.44(19)
C(4)-C(3)-H(3)	121.8(18)
C(2)-C(3)-H(3)	125.5(18)
C(3)-C(4)-C(5)	128.13(16)
C(3)-C(4)-S(1)	110.27(14)
C(5)-C(4)-S(1)	121.59(13)
O(1)-C(5)-C(4)	113.81(14)
O(1)-C(5)-C(6)	116.59(15)
C(4)-C(5)-C(6)	122.75(16)

O(1)-C(5)-C(7)	112.66(15)
C(4)-C(5)-C(7)	120.33(14)
C(6)-C(5)-C(7)	59.99(12)
C(5)-C(6)-C(7)	60.08(11)
C(5)-C(6)-H(6A)	117.6(14)
C(7)-C(6)-H(6A)	118.1(13)
C(5)-C(6)-H(6B)	117.9(15)
C(7)-C(6)-H(6B)	118.3(15)
H(6A)-C(6)-H(6B)	114(2)
C(8)-C(7)-C(6)	119.01(16)
C(8)-C(7)-C(5)	120.42(16)
C(6)-C(7)-C(5)	59.94(12)
C(8)-C(7)-H(7)	116.5(13)
C(6)-C(7)-H(7)	116.1(13)
C(5)-C(7)-H(7)	112.8(14)
N(1)-C(8)-C(7)	111.39(15)
N(1)-C(8)-H(8A)	108.7(12)
C(7)-C(8)-H(8A)	112.7(12)
N(1)-C(8)-H(8B)	108.7(11)
C(7)-C(8)-H(8B)	108.7(11)
H(8A)-C(8)-H(8B)	106.5(17)
N(1)-C(9)-H(9A)	109.9(15)
N(1)-C(9)-H(9B)	109.8(16)
H(9A)-C(9)-H(9B)	112(2)
N(1)-C(9)-H(9C)	105.9(13)
H(9A)-C(9)-H(9C)	114(2)
H(9B)-C(9)-H(9C)	106(2)
C(11)-C(10)-O(1)	124.48(15)
C(11)-C(10)-C(15)	121.43(15)
O(1)-C(10)-C(15)	114.09(14)
C(10)-C(11)-C(12)	119.70(17)
C(10)-C(11)-H(11)	120.0(12)
C(12)-C(11)-H(11)	120.3(12)
C(13)-C(12)-C(11)	120.80(17)
C(13)-C(12)-H(12)	118.3(16)

C(11)-C(12)-H(12)	120.8(15)
C(12)-C(13)-C(14)	120.75(16)
C(12)-C(13)-H(13)	121.3(12)
C(14)-C(13)-H(13)	118.0(12)
C(19)-C(14)-C(13)	122.50(16)
C(19)-C(14)-C(15)	118.36(17)
C(13)-C(14)-C(15)	119.15(16)
C(16)-C(15)-C(10)	122.86(15)
C(16)-C(15)-C(14)	118.98(16)
C(10)-C(15)-C(14)	118.15(15)
C(17)-C(16)-C(15)	120.37(17)
C(17)-C(16)-H(16)	121.6(11)
C(15)-C(16)-H(16)	118.1(11)
C(16)-C(17)-C(18)	120.74(18)
C(16)-C(17)-H(17)	121.1(13)
C(18)-C(17)-H(17)	118.2(13)
C(19)-C(18)-C(17)	120.07(18)
C(19)-C(18)-H(18)	122.6(13)
C(17)-C(18)-H(18)	117.2(13)
C(18)-C(19)-C(14)	121.49(17)
C(18)-C(19)-H(19)	119.5(12)
C(14)-C(19)-H(19)	119.0(12)

Symmetry transformations used to generate equivalent atoms:

Table 7. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for (+)-**26**

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}
Cl(1)	40(1)	43(1)	35(1)	8(1)	17(1)	10(1)
S(1)	34(1)	59(1)	88(1)	-5(1)	23(1)	10(1)
O(1)	33(1)	34(1)	26(1)	-6(1)	8(1)	2(1)
N(1)	45(1)	34(1)	33(1)	1(1)	19(1)	4(1)
C(1)	38(1)	67(2)	61(1)	-22(1)	25(1)	-19(1)
C(2)	56(1)	46(1)	54(1)	2(1)	26(1)	-9(1)
C(3)	38(1)	43(1)	50(1)	4(1)	23(1)	6(1)
C(4)	27(1)	36(1)	32(1)	-9(1)	8(1)	3(1)
C(5)	33(1)	33(1)	29(1)	-2(1)	6(1)	6(1)
C(6)	49(1)	39(1)	41(1)	5(1)	3(1)	10(1)
C(7)	45(1)	28(1)	33(1)	0(1)	12(1)	6(1)
C(8)	54(1)	28(1)	32(1)	2(1)	15(1)	-2(1)
C(9)	46(1)	43(1)	58(1)	-1(1)	19(1)	1(1)
C(10)	41(1)	28(1)	21(1)	1(1)	9(1)	1(1)
C(11)	36(1)	39(1)	29(1)	0(1)	5(1)	4(1)
C(12)	41(1)	42(1)	32(1)	-1(1)	0(1)	-5(1)
C(13)	53(1)	34(1)	28(1)	-6(1)	5(1)	-7(1)
C(14)	49(1)	27(1)	26(1)	1(1)	13(1)	-1(1)
C(15)	39(1)	27(1)	23(1)	4(1)	10(1)	0(1)
C(16)	41(1)	35(1)	26(1)	1(1)	11(1)	0(1)
C(17)	39(1)	48(1)	33(1)	2(1)	10(1)	3(1)
C(18)	54(1)	44(1)	45(1)	-3(1)	21(1)	13(1)
C(19)	59(1)	35(1)	35(1)	-6(1)	17(1)	1(1)

Table 8. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for (+)-**26**

	x	y	z	U(eq)
H(1N)	4670(20)	2600(40)	6134(15)	48(6)
H(2N)	4990(20)	940(30)	5710(15)	39(5)
H(1)	11370(30)	6410(40)	5869(16)	58(7)
H(2)	9190(30)	8400(40)	5709(18)	62(8)
H(3)	7410(30)	6930(40)	6344(16)	54(7)
H(6A)	9570(30)	1360(40)	7878(15)	50(6)
H(6B)	8230(30)	1420(40)	8402(17)	53(6)
H(7)	7680(20)	1100(30)	6465(14)	40(5)
H(8A)	5520(20)	1070(30)	7515(14)	40(5)
H(8B)	5850(20)	-790(40)	6992(12)	36(5)
H(9A)	2880(30)	1050(40)	6703(17)	61(7)
H(9B)	3140(30)	-740(50)	6105(17)	61(7)
H(9C)	2510(30)	1070(40)	5578(16)	50(6)
H(11)	9360(20)	5380(30)	8684(12)	34(5)
H(12)	9870(30)	7640(40)	9924(17)	49(6)
H(13)	8010(20)	9370(30)	10319(14)	44(5)
H(16)	4210(20)	5620(30)	7614(13)	32(4)
H(17)	2330(20)	7510(30)	8000(14)	41(5)
H(18)	2900(20)	9770(30)	9155(14)	44(6)
H(19)	5330(20)	10280(30)	10012(15)	41(5)

Table 9. Torsion angles [°] for (+)-**26**

C(4)-S(1)-C(1)-C(2)	0.87(18)
S(1)-C(1)-C(2)-C(3)	-1.4(3)
C(1)-C(2)-C(3)-C(4)	1.4(3)
C(2)-C(3)-C(4)-C(5)	-179.49(18)
C(2)-C(3)-C(4)-S(1)	-0.7(2)
C(1)-S(1)-C(4)-C(3)	-0.06(15)
C(1)-S(1)-C(4)-C(5)	178.81(14)
C(10)-O(1)-C(5)-C(4)	-71.25(18)
C(10)-O(1)-C(5)-C(6)	80.65(19)
C(10)-O(1)-C(5)-C(7)	147.25(14)
C(3)-C(4)-C(5)-O(1)	-22.9(2)
S(1)-C(4)-C(5)-O(1)	158.40(11)
C(3)-C(4)-C(5)-C(6)	-172.90(18)
S(1)-C(4)-C(5)-C(6)	8.4(2)
C(3)-C(4)-C(5)-C(7)	115.3(2)
S(1)-C(4)-C(5)-C(7)	-63.3(2)
O(1)-C(5)-C(6)-C(7)	102.03(17)
C(4)-C(5)-C(6)-C(7)	-108.78(18)
C(5)-C(6)-C(7)-C(8)	-110.37(19)
O(1)-C(5)-C(7)-C(8)	-0.6(2)
C(4)-C(5)-C(7)-C(8)	-139.26(17)
C(6)-C(5)-C(7)-C(8)	108.05(19)
O(1)-C(5)-C(7)-C(6)	-108.61(17)
C(4)-C(5)-C(7)-C(6)	112.69(18)
C(9)-N(1)-C(8)-C(7)	-179.92(17)
C(6)-C(7)-C(8)-N(1)	155.16(17)
C(5)-C(7)-C(8)-N(1)	85.0(2)
C(5)-O(1)-C(10)-C(11)	-4.4(2)
C(5)-O(1)-C(10)-C(15)	175.10(13)
O(1)-C(10)-C(11)-C(12)	179.45(16)
C(15)-C(10)-C(11)-C(12)	-0.1(3)
C(10)-C(11)-C(12)-C(13)	0.3(3)
C(11)-C(12)-C(13)-C(14)	-1.1(3)

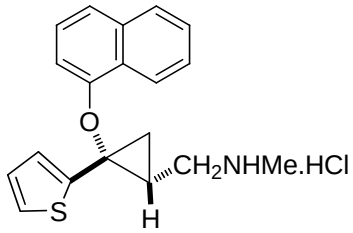
C(12)-C(13)-C(14)-C(19)	-178.78(18)
C(12)-C(13)-C(14)-C(15)	1.5(3)
C(11)-C(10)-C(15)-C(16)	179.91(16)
O(1)-C(10)-C(15)-C(16)	0.4(2)
C(11)-C(10)-C(15)-C(14)	0.5(2)
O(1)-C(10)-C(15)-C(14)	-179.04(13)
C(19)-C(14)-C(15)-C(16)	-0.3(2)
C(13)-C(14)-C(15)-C(16)	179.37(16)
C(19)-C(14)-C(15)-C(10)	179.07(16)
C(13)-C(14)-C(15)-C(10)	-1.2(2)
C(10)-C(15)-C(16)-C(17)	-178.80(16)
C(14)-C(15)-C(16)-C(17)	0.6(2)
C(15)-C(16)-C(17)-C(18)	-0.3(3)
C(16)-C(17)-C(18)-C(19)	-0.1(3)
C(17)-C(18)-C(19)-C(14)	0.4(3)
C(13)-C(14)-C(19)-C(18)	-179.85(19)
C(15)-C(14)-C(19)-C(18)	-0.1(3)

Symmetry transformations used to generate equivalent atoms:

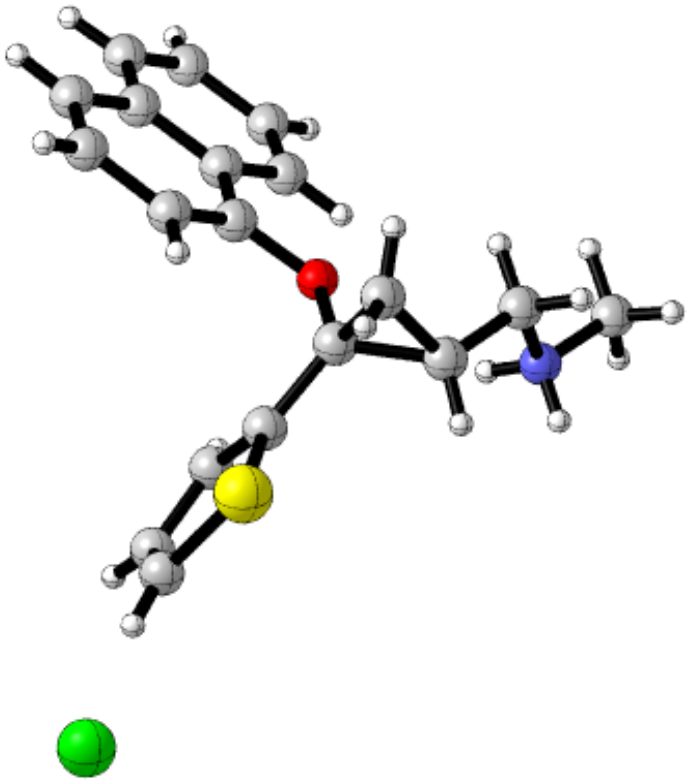
Table 10. Hydrogen bonds for (+)-**26** [Å and °].

D-H.A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(1)-H(2N)...Cl(1)#1	0.83(2)	2.29(2)	3.1079(16)	167(2)
N(1)-H(1N)...Cl(1)	0.87(3)	2.26(3)	3.0782(18)	158(2)

Symmetry transformations used to generate equivalent atoms:
#1 -x+1,y-1/2,-z+1



(-)-**26**



(-)-**26**

Table 11. Crystal data and structure refinement for (-)-**26**

Identification code	jw25	
Empirical formula	C19 H20 Cl N O S	
Formula weight	345.87	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 9.2343(11) Å	a= 90°.
	b = 6.7831(8) Å	b= 104.353(2)°.
	c = 14.9383(18) Å	g = 90°.
Volume	906.49(19) $Å^3$	
Z	2	
Density (calculated)	1.267 Mg/m^3	
Absorption coefficient	0.329 mm^{-1}	
F(000)	364	
Crystal size	0.36 x 0.12 x 0.08 mm^3	
Theta range for data collection	1.41 to 27.00°.	
Index ranges	-11<=h<=11, -8<=k<=8, -19<=l<=19	
Reflections collected	10218	
Independent reflections	3938 [R(int) = 0.0298]	
Completeness to theta = 27.00°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9741 and 0.8906	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3938 / 1 / 288	
Goodness-of-fit on F^2	1.064	
Final R indices [I>2sigma(I)]	R1 = 0.0379, wR2 = 0.0780	
R indices (all data)	R1 = 0.0452, wR2 = 0.0830	
Absolute structure parameter	0.04(5)	
Largest diff. peak and hole	0.267 and -0.155 $e.Å^{-3}$	

Table 12. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for (-)-**26**
U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
S(1)	4602(1)	298(1)	8293(1)	60(1)
Cl(1)	959(1)	-1222(1)	9446(1)	39(1)
O(1)	8297(2)	-79(2)	7359(1)	31(1)
N(1)	10325(2)	3102(3)	8842(1)	36(1)
C(1)	4480(3)	-1769(4)	8919(2)	55(1)
C(2)	5677(3)	-2890(5)	9021(2)	49(1)
C(3)	6772(3)	-2087(4)	8608(2)	41(1)
C(4)	6341(2)	-344(3)	8177(1)	31(1)
C(5)	7185(2)	933(3)	7681(1)	32(1)
C(6)	6505(3)	2718(4)	7134(2)	44(1)
C(7)	7664(3)	2972(3)	8038(2)	36(1)
C(8)	9174(3)	3731(4)	8019(2)	38(1)
C(9)	11836(3)	3827(5)	8847(2)	48(1)
C(10)	7858(2)	-1366(3)	6633(1)	29(1)
C(11)	6415(2)	-1664(3)	6151(1)	36(1)
C(12)	6096(3)	-3048(4)	5421(2)	40(1)
C(13)	7196(3)	-4074(3)	5186(2)	40(1)
C(14)	8713(3)	-3814(3)	5680(1)	34(1)
C(15)	9058(2)	-2422(3)	6412(1)	29(1)
C(16)	10572(2)	-2159(3)	6900(2)	33(1)
C(17)	11670(3)	-3234(4)	6672(2)	40(1)
C(18)	11334(3)	-4617(4)	5948(2)	47(1)
C(19)		9897(3)		-4892(4) 5469(2)

Table 13. Bond lengths [Å] and angles [°] for (-)-**26**

S(1)-C(1)	1.703(3)
S(1)-C(4)	1.713(2)
O(1)-C(10)	1.373(2)
O(1)-C(5)	1.414(2)
N(1)-C(8)	1.475(3)
N(1)-C(9)	1.477(3)
N(1)-H(1N)	0.86(3)
N(1)-H(2N)	0.86(3)
C(1)-C(2)	1.319(4)
C(1)-H(1)	0.91(3)
C(2)-C(3)	1.417(3)
C(2)-H(2)	0.90(3)
C(3)-C(4)	1.358(3)
C(3)-H(3)	0.78(3)
C(4)-C(5)	1.481(3)
C(5)-C(6)	1.508(3)
C(5)-C(7)	1.509(3)
C(6)-C(7)	1.510(3)
C(6)-H(6A)	1.00(2)
C(6)-H(6B)	0.93(3)
C(7)-C(8)	1.493(3)
C(7)-H(7)	0.93(2)
C(8)-H(8A)	0.95(2)
C(8)-H(8B)	0.93(2)
C(9)-H(9A)	1.00(3)
C(9)-H(9B)	0.93(4)
C(9)-H(9C)	0.95(3)
C(10)-C(11)	1.363(3)
C(10)-C(15)	1.426(3)
C(11)-C(12)	1.413(3)
C(11)-H(11)	0.95(2)
C(12)-C(13)	1.348(3)
C(12)-H(12)	0.87(3)

C(13)-C(14)	1.424(3)
C(13)-H(13)	0.93(2)
C(14)-C(19)	1.414(3)
C(14)-C(15)	1.419(3)
C(15)-C(16)	1.419(3)
C(16)-C(17)	1.359(3)
C(16)-H(16)	0.96(2)
C(17)-C(18)	1.406(4)
C(17)-H(17)	0.93(2)
C(18)-C(19)	1.355(3)
C(18)-H(18)	0.92(3)
C(19)-H(19)	0.93(3)

C(1)-S(1)-C(4)	92.17(13)
C(10)-O(1)-C(5)	118.68(15)
C(8)-N(1)-C(9)	113.1(2)
C(8)-N(1)-H(1N)	109.4(15)
C(9)-N(1)-H(1N)	109.3(15)
C(8)-N(1)-H(2N)	106.2(17)
C(9)-N(1)-H(2N)	112.0(18)
H(1N)-N(1)-H(2N)	106(3)
C(2)-C(1)-S(1)	111.7(2)
C(2)-C(1)-H(1)	128.1(18)
S(1)-C(1)-H(1)	120.1(18)
C(1)-C(2)-C(3)	113.3(3)
C(1)-C(2)-H(2)	129.5(17)
C(3)-C(2)-H(2)	117.2(17)
C(4)-C(3)-C(2)	112.6(2)
C(4)-C(3)-H(3)	122(2)
C(2)-C(3)-H(3)	125(2)
C(3)-C(4)-C(5)	128.1(2)
C(3)-C(4)-S(1)	110.19(18)
C(5)-C(4)-S(1)	121.68(16)
O(1)-C(5)-C(4)	113.76(17)
O(1)-C(5)-C(6)	116.45(19)

C(4)-C(5)-C(6)	122.68(19)
O(1)-C(5)-C(7)	113.03(18)
C(4)-C(5)-C(7)	120.28(18)
C(6)-C(5)-C(7)	60.08(15)
C(5)-C(6)-C(7)	59.98(14)
C(5)-C(6)-H(6A)	117.1(14)
C(7)-C(6)-H(6A)	118.7(13)
C(5)-C(6)-H(6B)	117.2(17)
C(7)-C(6)-H(6B)	116.4(17)
H(6A)-C(6)-H(6B)	116(2)
C(8)-C(7)-C(6)	118.7(2)
C(8)-C(7)-C(5)	120.1(2)
C(6)-C(7)-C(5)	59.94(15)
C(8)-C(7)-H(7)	116.4(16)
C(6)-C(7)-H(7)	116.4(15)
C(5)-C(7)-H(7)	113.3(16)
N(1)-C(8)-C(7)	111.59(19)
N(1)-C(8)-H(8A)	108.8(12)
C(7)-C(8)-H(8A)	110.0(12)
N(1)-C(8)-H(8B)	107.0(13)
C(7)-C(8)-H(8B)	112.2(12)
H(8A)-C(8)-H(8B)	107.0(18)
N(1)-C(9)-H(9A)	110.4(16)
N(1)-C(9)-H(9B)	108.5(17)
H(9A)-C(9)-H(9B)	110(3)
N(1)-C(9)-H(9C)	105.1(15)
H(9A)-C(9)-H(9C)	114(2)
H(9B)-C(9)-H(9C)	109(3)
C(11)-C(10)-O(1)	124.80(19)
C(11)-C(10)-C(15)	121.09(19)
O(1)-C(10)-C(15)	114.11(17)
C(10)-C(11)-C(12)	119.8(2)
C(10)-C(11)-H(11)	119.9(13)
C(12)-C(11)-H(11)	120.2(13)
C(13)-C(12)-C(11)	121.1(2)

C(13)-C(12)-H(12)	119.7(18)
C(11)-C(12)-H(12)	119.1(18)
C(12)-C(13)-C(14)	120.6(2)
C(12)-C(13)-H(13)	120.5(14)
C(14)-C(13)-H(13)	118.9(14)
C(19)-C(14)-C(13)	122.4(2)
C(19)-C(14)-C(15)	118.5(2)
C(13)-C(14)-C(15)	119.1(2)
C(16)-C(15)-C(14)	118.94(19)
C(16)-C(15)-C(10)	122.75(19)
C(14)-C(15)-C(10)	118.30(19)
C(17)-C(16)-C(15)	120.3(2)
C(17)-C(16)-H(16)	122.2(12)
C(15)-C(16)-H(16)	117.5(12)
C(16)-C(17)-C(18)	121.0(2)
C(16)-C(17)-H(17)	121.1(15)
C(18)-C(17)-H(17)	117.9(15)
C(19)-C(18)-C(17)	119.9(2)
C(19)-C(18)-H(18)	121.0(16)
C(17)-C(18)-H(18)	119.0(15)
C(18)-C(19)-C(14)	121.4(2)
C(18)-C(19)-H(19)	120.5(14)
C(14)-C(19)-H(19)	118.1(14)

Symmetry transformations used to generate equivalent atoms:

Table 14. Anisotropic displacement parameters ($Å^2 x\ 10^3$)for (-)-**26**
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}
S(1)	34(1)	60(1)	89(1)	-5(1)	23(1)	9(1)
Cl(1)	41(1)	44(1)	35(1)	8(1)	17(1)	10(1)
O(1)	32(1)	34(1)	25(1)	-5(1)	6(1)	3(1)
N(1)	46(1)	32(1)	34(1)	0(1)	20(1)	4(1)
C(1)	39(1)	69(2)	62(2)	-24(1)	25(1)	-20(1)
C(2)	55(2)	45(2)	54(2)	0(1)	26(1)	-6(1)
C(3)	37(1)	43(1)	48(1)	5(1)	21(1)	7(1)
C(4)	28(1)	35(1)	31(1)	-8(1)	7(1)	4(1)
C(5)	33(1)	35(1)	28(1)	-3(1)	7(1)	7(1)
C(6)	46(2)	40(1)	43(1)	5(1)	4(1)	8(1)
C(7)	44(1)	29(1)	35(1)	0(1)	12(1)	4(1)
C(8)	55(1)	28(1)	32(1)	2(1)	15(1)	1(1)
C(9)	47(1)	44(2)	57(2)	0(2)	18(1)	-1(1)
C(10)	40(1)	27(1)	21(1)	0(1)	8(1)	-1(1)
C(11)	38(1)	39(1)	28(1)	1(1)	4(1)	4(1)
C(12)	40(1)	45(1)	31(1)	-2(1)	0(1)	-6(1)
C(13)	54(2)	34(1)	29(1)	-6(1)	6(1)	-6(1)
C(14)	49(1)	29(1)	26(1)	2(1)	13(1)	-2(1)
C(15)	37(1)	27(1)	23(1)	4(1)	9(1)	0(1)
C(16)	41(1)	34(1)	26(1)	0(1)	10(1)	0(1)
C(17)	37(1)	48(2)	35(1)	1(1)	11(1)	3(1)
C(18)	54(2)	44(2)	47(1)	-2(1)	23(1)	12(1)
C(19)	59(2)	35(1)	34(1)	-6(1)	16(1)	1(1)

Table 15. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for (-)-**26**.

	x	y	z	U(eq)
H(1N)	10340(20)	1840(40)	8873(14)	29(6)
H(2N)	10030(30)	3510(50)	9310(18)	51(7)
H(1)	3670(30)	-1970(40)	9148(18)	59(8)
H(2)	5870(30)	-4070(50)	9295(19)	59(9)
H(3)	7570(30)	-2520(40)	8655(18)	50(8)
H(6A)	5430(30)	3020(40)	7113(16)	41(6)
H(6B)	6810(30)	3000(40)	6600(20)	57(8)
H(7)	7310(30)	3330(40)	8548(17)	45(7)
H(8A)	9160(20)	5130(40)	7992(13)	24(5)
H(8B)	9480(20)	3280(30)	7503(14)	27(5)
H(9A)	12140(30)	3360(50)	8281(19)	62(8)
H(9B)	11830(30)	5200(50)	8865(19)	60(8)
H(9C)	12470(30)	3350(40)	9410(18)	48(7)
H(11)	5630(20)	-1010(40)	6332(13)	31(6)
H(12)	5170(30)	-3210(40)	5111(19)	47(7)
H(13)	6970(20)	-4970(40)	4698(16)	43(7)
H(16)	10780(20)	-1200(40)	7387(15)	31(5)
H(17)	12670(30)	-3080(40)	6991(15)	36(6)
H(18)	12090(30)	-5400(40)	5842(16)	49(7)
H(19)	9660(20)	-5830(40)	5003(16)	

Table 16. Torsion angles [°] for (-)-**26**

C(4)-S(1)-C(1)-C(2)	-0.8(2)
S(1)-C(1)-C(2)-C(3)	1.3(3)
C(1)-C(2)-C(3)-C(4)	-1.3(3)
C(2)-C(3)-C(4)-C(5)	179.3(2)
C(2)-C(3)-C(4)-S(1)	0.6(3)
C(1)-S(1)-C(4)-C(3)	0.11(19)
C(1)-S(1)-C(4)-C(5)	-178.69(18)
C(10)-O(1)-C(5)-C(4)	71.2(2)
C(10)-O(1)-C(5)-C(6)	-80.2(2)
C(10)-O(1)-C(5)-C(7)	-147.04(17)
C(3)-C(4)-C(5)-O(1)	23.2(3)
S(1)-C(4)-C(5)-O(1)	-158.28(14)
C(3)-C(4)-C(5)-C(6)	172.6(2)
S(1)-C(4)-C(5)-C(6)	-8.9(3)
C(3)-C(4)-C(5)-C(7)	-115.6(3)
S(1)-C(4)-C(5)-C(7)	63.0(2)
O(1)-C(5)-C(6)-C(7)	-102.6(2)
C(4)-C(5)-C(6)-C(7)	108.8(2)
C(5)-C(6)-C(7)-C(8)	110.2(2)
O(1)-C(5)-C(7)-C(8)	0.5(3)
C(4)-C(5)-C(7)-C(8)	139.5(2)
C(6)-C(5)-C(7)-C(8)	-107.8(2)
O(1)-C(5)-C(7)-C(6)	108.3(2)
C(4)-C(5)-C(7)-C(6)	-112.7(2)
C(9)-N(1)-C(8)-C(7)	-180.0(2)
C(6)-C(7)-C(8)-N(1)	-155.1(2)
C(5)-C(7)-C(8)-N(1)	-85.1(3)
C(5)-O(1)-C(10)-C(11)	4.4(3)
C(5)-O(1)-C(10)-C(15)	-175.25(17)
O(1)-C(10)-C(11)-C(12)	-179.3(2)
C(15)-C(10)-C(11)-C(12)	0.3(3)
C(10)-C(11)-C(12)-C(13)	-0.5(3)
C(11)-C(12)-C(13)-C(14)	1.1(4)

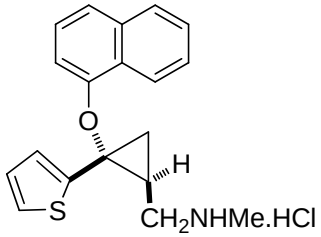
C(12)-C(13)-C(14)-C(19)	178.5(2)
C(12)-C(13)-C(14)-C(15)	-1.4(3)
C(19)-C(14)-C(15)-C(16)	0.3(3)
C(13)-C(14)-C(15)-C(16)	-179.7(2)
C(19)-C(14)-C(15)-C(10)	-178.8(2)
C(13)-C(14)-C(15)-C(10)	1.1(3)
C(11)-C(10)-C(15)-C(16)	-179.74(19)
O(1)-C(10)-C(15)-C(16)	-0.1(3)
C(11)-C(10)-C(15)-C(14)	-0.6(3)
O(1)-C(10)-C(15)-C(14)	178.98(17)
C(14)-C(15)-C(16)-C(17)	-0.4(3)
C(10)-C(15)-C(16)-C(17)	178.7(2)
C(15)-C(16)-C(17)-C(18)	0.3(4)
C(16)-C(17)-C(18)-C(19)	-0.2(4)
C(17)-C(18)-C(19)-C(14)	0.1(4)
C(13)-C(14)-C(19)-C(18)	179.9(2)
C(15)-C(14)-C(19)-C(18)	-0.2(3)

Symmetry transformations used to generate equivalent atoms:

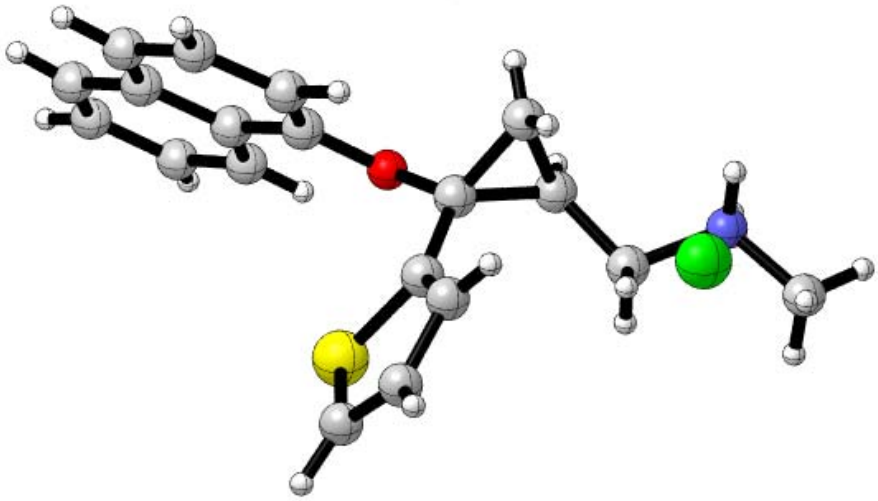
Table 17. Hydrogen bonds for (-)-**26** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(1)-H(1N)...Cl(1)#1	0.86(3)	2.27(3)	3.082(2)	159.3(19)
N(1)-H(2N)...Cl(1)#2	0.86(3)	2.27(3)	3.109(2)	165(3)

Symmetry transformations used to generate equivalent atoms:
#1 x+1,y,z #2 -x+1,y+1/2,-z+2



(+)-**25**



(+)-**25**

Table 18. Crystal data and structure refinement for (+)-**25**

Identification code	jw26	
Empirical formula	C20 H18 Cl N O S	
Formula weight	355.86	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 6.9481(4) Å	a= 90°.
	b = 8.9988(5) Å	b= 90°.
	c = 31.8427(17) Å	g = 90°.
Volume	1990.95(19) $Å^3$	
Z	4	
Density (calculated)	1.187 Mg/m^3	
Absorption coefficient	0.302 mm^{-1}	
F(000)	744	
Crystal size	0.26 x 0.12 x 0.08 mm^3	
Theta range for data collection	2.35 to 27.00°.	
Index ranges	-8<=h<=8, -11<=k<=11, -40<=l<=40	
Reflections collected	22350	
Independent reflections	4343 [R(int) = 0.0267]	
Completeness to theta = 27.00°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.9762 and 0.9256	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4343 / 0 / 322	
Goodness-of-fit on F^2	1.084	
Final R indices [I>2sigma(I)]	R1 = 0.0376, wR2 = 0.0931	
R indices (all data)	R1 = 0.0411, wR2 = 0.0965	
Absolute structure parameter	0.03(6)	
Largest diff. peak and hole	0.509 and -0.187 $e.Å^{-3}$	

Table 19. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3)for (+)-**25**.
U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Cl(1)	2330(1)	8404(1)	405(1)	42(1)
S(1)	5496(1)	5547(1)	1957(1)	51(1)
O(1)	7894(2)	3973(2)	1318(1)	39(1)
N(1)	7901(2)	8358(2)	438(1)	33(1)
C(1)	3273(5)	6274(3)	2053(1)	60(1)
C(2)	2278(4)	6503(3)	1702(1)	52(1)
C(3)	3313(3)	6085(2)	1338(1)	37(1)
C(4)	5115(3)	5554(2)	1423(1)	31(1)
C(5)	6656(3)	5034(2)	1137(1)	31(1)
C(6)	6355(3)	4958(2)	668(1)	36(1)
C(7)	7755(3)	6074(2)	852(1)	34(1)
C(8)	7299(3)	7692(2)	846(1)	32(1)
C(9)	7328(4)	9928(3)	388(1)	47(1)
C(10)	7133(3)	2603(2)	1421(1)	32(1)
C(11)	5386(3)	2079(2)	1281(1)	38(1)
C(12)	4751(3)	665(2)	1411(1)	41(1)
C(13)	5825(4)	-188(2)	1671(1)	42(1)
C(14)	7642(3)	311(2)	1815(1)	35(1)
C(15)	8833(4)	-552(3)	2081(1)	44(1)
C(16)	10543(4)	-32(3)	2221(1)	47(1)
C(17)	11191(4)	1385(3)	2104(1)	44(1)
C(18)	10108(3)	2259(2)	1844(1)	36(1)
C(19)	8311(3)	1746(2)	1692(1)	32(1)
O(1S)	2751(3)	2031(3)	323(1)	64(1)
C(1S)	1264(4)	2698(3)	550(1)	56(1)

Table 20. Bond lengths [Å] and angles [°] for (+)-**25**.

S(1)-C(1)	1.705(3)
S(1)-C(4)	1.7201(18)
O(1)-C(10)	1.381(2)
O(1)-C(5)	1.408(2)
N(1)-C(9)	1.476(3)
N(1)-C(8)	1.490(2)
N(1)-H(1NA)	0.90(3)
N(1)-H(1NB)	0.94(3)
C(1)-C(2)	1.329(4)
C(1)-H(1)	0.98(3)
C(2)-C(3)	1.416(3)
C(2)-H(2)	0.84(3)
C(3)-C(4)	1.367(3)
C(3)-H(3)	0.84(3)
C(4)-C(5)	1.481(3)
C(5)-C(6)	1.511(3)
C(5)-C(7)	1.513(3)
C(6)-C(7)	1.516(3)
C(6)-H(6A)	0.88(2)
C(6)-H(6B)	0.91(2)
C(7)-C(8)	1.490(3)
C(7)-H(7)	0.94(3)
C(8)-H(8A)	1.00(3)
C(8)-H(8B)	0.97(2)
C(9)-H(9A)	0.93(3)
C(9)-H(9B)	0.93(3)
C(9)-H(9C)	0.94(3)
C(10)-C(11)	1.377(3)
C(10)-C(19)	1.417(3)
C(11)-C(12)	1.409(3)
C(11)-H(11)	0.96(2)
C(12)-C(13)	1.354(3)
C(12)-H(12)	0.87(2)
C(13)-C(14)	1.416(3)

C(13)-H(13)	0.97(3)
C(14)-C(15)	1.416(3)
C(14)-C(19)	1.427(3)
C(15)-C(16)	1.352(4)
C(15)-H(15)	0.90(3)
C(16)-C(17)	1.402(4)
C(16)-H(16)	0.92(3)
C(17)-C(18)	1.367(3)
C(17)-H(17)	0.94(3)
C(18)-C(19)	1.417(3)
C(18)-H(18)	0.92(3)
O(1S)-C(1S)	1.397(3)
O(1S)-H(1S)	0.84(4)
C(1S)-H(1SA)	1.03(4)
C(1S)-H(1SB)	1.01(3)
C(1S)-H(1SC)	1.07(3)
C(1)-S(1)-C(4)	92.10(12)
C(10)-O(1)-C(5)	117.99(15)
C(9)-N(1)-C(8)	113.79(17)
C(9)-N(1)-H(1NA)	108.7(18)
C(8)-N(1)-H(1NA)	110.7(18)
C(9)-N(1)-H(1NB)	110.9(16)
C(8)-N(1)-H(1NB)	106.9(15)
H(1NA)-N(1)-H(1NB)	106(2)
C(2)-C(1)-S(1)	112.34(18)
C(2)-C(1)-H(1)	125.9(18)
S(1)-C(1)-H(1)	121.7(18)
C(1)-C(2)-C(3)	112.5(2)
C(1)-C(2)-H(2)	129(2)
C(3)-C(2)-H(2)	119(2)
C(4)-C(3)-C(2)	113.3(2)
C(4)-C(3)-H(3)	120.5(18)
C(2)-C(3)-H(3)	126.1(18)
C(3)-C(4)-C(5)	130.59(17)
C(3)-C(4)-S(1)	109.76(15)

C(5)-C(4)-S(1)	119.65(15)
O(1)-C(5)-C(4)	113.92(15)
O(1)-C(5)-C(6)	117.21(17)
C(4)-C(5)-C(6)	121.46(17)
O(1)-C(5)-C(7)	110.92(16)
C(4)-C(5)-C(7)	122.64(17)
C(6)-C(5)-C(7)	60.19(13)
C(5)-C(6)-C(7)	59.97(13)
C(5)-C(6)-H(6A)	116.1(14)
C(7)-C(6)-H(6A)	113.4(15)
C(5)-C(6)-H(6B)	116.0(13)
C(7)-C(6)-H(6B)	118.6(13)
H(6A)-C(6)-H(6B)	119(2)
C(8)-C(7)-C(5)	120.32(17)
C(8)-C(7)-C(6)	120.41(18)
C(5)-C(7)-C(6)	59.85(13)
C(8)-C(7)-H(7)	118.4(15)
C(5)-C(7)-H(7)	112.4(15)
C(6)-C(7)-H(7)	112.0(15)
N(1)-C(8)-C(7)	110.14(16)
N(1)-C(8)-H(8A)	104.2(14)
C(7)-C(8)-H(8A)	113.7(15)
N(1)-C(8)-H(8B)	104.4(12)
C(7)-C(8)-H(8B)	112.7(13)
H(8A)-C(8)-H(8B)	110.9(19)
N(1)-C(9)-H(9A)	110.0(19)
N(1)-C(9)-H(9B)	109.1(18)
H(9A)-C(9)-H(9B)	112(3)
N(1)-C(9)-H(9C)	107.4(17)
H(9A)-C(9)-H(9C)	109(2)
H(9B)-C(9)-H(9C)	109(2)
C(11)-C(10)-O(1)	124.46(18)
C(11)-C(10)-C(19)	121.32(18)
O(1)-C(10)-C(19)	114.22(17)
C(10)-C(11)-C(12)	119.4(2)

C(10)-C(11)-H(11)	118.4(14)
C(12)-C(11)-H(11)	122.1(14)
C(13)-C(12)-C(11)	121.2(2)
C(13)-C(12)-H(12)	118.4(16)
C(11)-C(12)-H(12)	120.3(16)
C(12)-C(13)-C(14)	120.64(19)
C(12)-C(13)-H(13)	119.9(15)
C(14)-C(13)-H(13)	119.3(15)
C(13)-C(14)-C(15)	122.7(2)
C(13)-C(14)-C(19)	119.29(18)
C(15)-C(14)-C(19)	118.0(2)
C(16)-C(15)-C(14)	121.4(2)
C(16)-C(15)-H(15)	117.4(15)
C(14)-C(15)-H(15)	121.0(15)
C(15)-C(16)-C(17)	120.6(2)
C(15)-C(16)-H(16)	120.4(16)
C(17)-C(16)-H(16)	118.9(16)
C(18)-C(17)-C(16)	120.5(2)
C(18)-C(17)-H(17)	120.1(16)
C(16)-C(17)-H(17)	119.4(16)
C(17)-C(18)-C(19)	120.3(2)
C(17)-C(18)-H(18)	120.4(15)
C(19)-C(18)-H(18)	119.2(15)
C(18)-C(19)-C(10)	122.66(18)
C(18)-C(19)-C(14)	119.24(18)
C(10)-C(19)-C(14)	118.10(19)
C(1S)-O(1S)-H(1S)	104(2)
O(1S)-C(1S)-H(1SA)	112(2)
O(1S)-C(1S)-H(1SB)	107.2(18)
H(1SA)-C(1S)-H(1SB)	113(3)
O(1S)-C(1S)-H(1SC)	99.8(17)
H(1SA)-C(1S)-H(1SC)	114(3)
H(1SB)-C(1S)-H(1SC)	110(3)

Symmetry transformations used to generate equivalent atoms:

Table 21. Anisotropic displacement parameters ($Å^2 x\ 10^3$)for (+)-**25**
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}
Cl(1)	33(1)	57(1)	35(1)	-1(1)	-2(1)	0(1)
S(1)	85(1)	40(1)	29(1)	4(1)	-5(1)	1(1)
O(1)	31(1)	33(1)	51(1)	11(1)	-8(1)	0(1)
N(1)	32(1)	34(1)	31(1)	2(1)	3(1)	-3(1)
C(1)	98(2)	38(1)	45(1)	-2(1)	37(1)	-12(1)
C(2)	48(1)	43(1)	64(2)	-5(1)	24(1)	-2(1)
C(3)	34(1)	41(1)	38(1)	-2(1)	2(1)	0(1)
C(4)	40(1)	27(1)	26(1)	2(1)	1(1)	-5(1)
C(5)	30(1)	30(1)	33(1)	5(1)	-2(1)	0(1)
C(6)	39(1)	37(1)	31(1)	-2(1)	4(1)	5(1)
C(7)	30(1)	37(1)	35(1)	4(1)	4(1)	3(1)
C(8)	31(1)	34(1)	31(1)	4(1)	1(1)	0(1)
C(9)	45(1)	36(1)	59(1)	14(1)	7(1)	-1(1)
C(10)	34(1)	28(1)	34(1)	1(1)	2(1)	2(1)
C(11)	38(1)	35(1)	43(1)	-2(1)	-3(1)	4(1)
C(12)	38(1)	35(1)	49(1)	-8(1)	4(1)	-3(1)
C(13)	53(1)	28(1)	44(1)	-6(1)	14(1)	-2(1)
C(14)	47(1)	27(1)	29(1)	-4(1)	7(1)	9(1)
C(15)	67(2)	30(1)	36(1)	3(1)	6(1)	11(1)
C(16)	65(2)	43(1)	33(1)	2(1)	-3(1)	22(1)
C(17)	47(1)	47(1)	37(1)	-6(1)	-4(1)	14(1)
C(18)	42(1)	34(1)	33(1)	-2(1)	0(1)	6(1)
C(19)	38(1)	30(1)	27(1)	-4(1)	4(1)	9(1)
O(1S)	62(1)	59(1)	71(1)	5(1)	13(1)	2(1)
C(1S)	47(1)	56(2)	65(2)	-7(1)	-1(1)	-3(1)

Table 22. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for (+)-**25**

	x	y	z	U(eq)
H(1NA)	7420(40)	7830(30)	221(9)	58(8)
H(1NB)	9240(40)	8260(30)	420(7)	43(6)
H(1)	2830(40)	6490(30)	2340(10)	71(8)
H(2)	1170(50)	6860(40)	1675(9)	67(9)
H(3)	2940(40)	6180(30)	1087(9)	48(7)
H(6A)	6920(30)	4220(30)	538(7)	32(5)
H(6B)	5200(30)	5290(20)	573(6)	23(5)
H(7)	9050(40)	5780(30)	814(7)	46(7)
H(8A)	8010(40)	8280(30)	1060(8)	49(7)
H(8B)	5930(30)	7890(20)	861(6)	27(5)
H(9A)	6000(50)	9990(30)	352(9)	62(8)
H(9B)	7750(40)	10470(30)	620(9)	58(8)
H(9C)	7940(40)	10290(30)	146(8)	53(7)
H(11)	4660(30)	2680(30)	1089(7)	38(6)
H(12)	3640(40)	330(30)	1330(7)	39(6)
H(13)	5400(40)	-1180(30)	1744(8)	47(6)
H(15)	8520(30)	-1490(30)	2146(7)	39(6)
H(16)	11270(40)	-580(30)	2404(7)	45(6)
H(17)	12400(40)	1710(30)	2196(8)	46(7)
H(18)	10520(30)	3200(30)	1772(7)	41(6)
H(1S)	2560(50)	1120(40)	353(11)	76(10)
H(1SA)	850(60)	2060(40)	800(12)	102(12)
H(1SB)	1730(50)	3720(40)	635(10)	74(9)
H(1SC)	210(50)	2800(40)	308(10)	79(10)

Table 23. Torsion angles [°] for (+)-**25**.

C(4)-S(1)-C(1)-C(2)	0.4(2)
S(1)-C(1)-C(2)-C(3)	0.1(3)
C(1)-C(2)-C(3)-C(4)	-0.7(3)
C(2)-C(3)-C(4)-C(5)	-178.6(2)
C(2)-C(3)-C(4)-S(1)	1.0(2)
C(1)-S(1)-C(4)-C(3)	-0.83(17)
C(1)-S(1)-C(4)-C(5)	178.84(16)
C(10)-O(1)-C(5)-C(4)	65.7(2)
C(10)-O(1)-C(5)-C(6)	-84.7(2)
C(10)-O(1)-C(5)-C(7)	-151.03(16)
C(3)-C(4)-C(5)-O(1)	-152.2(2)
S(1)-C(4)-C(5)-O(1)	28.3(2)
C(3)-C(4)-C(5)-C(6)	-3.1(3)
S(1)-C(4)-C(5)-C(6)	177.32(15)
C(3)-C(4)-C(5)-C(7)	69.4(3)
S(1)-C(4)-C(5)-C(7)	-110.16(18)
O(1)-C(5)-C(6)-C(7)	-99.67(18)
C(4)-C(5)-C(6)-C(7)	112.2(2)
O(1)-C(5)-C(7)-C(8)	-140.03(18)
C(4)-C(5)-C(7)-C(8)	-0.5(3)
C(6)-C(5)-C(7)-C(8)	109.8(2)
O(1)-C(5)-C(7)-C(6)	110.20(18)
C(4)-C(5)-C(7)-C(6)	-110.3(2)
C(5)-C(6)-C(7)-C(8)	-109.6(2)
C(9)-N(1)-C(8)-C(7)	174.22(19)
C(5)-C(7)-C(8)-N(1)	-156.15(17)
C(6)-C(7)-C(8)-N(1)	-85.5(2)
C(5)-O(1)-C(10)-C(11)	14.8(3)
C(5)-O(1)-C(10)-C(19)	-164.97(16)
O(1)-C(10)-C(11)-C(12)	-179.51(18)
C(19)-C(10)-C(11)-C(12)	0.2(3)
C(10)-C(11)-C(12)-C(13)	0.2(3)
C(11)-C(12)-C(13)-C(14)	-1.3(3)

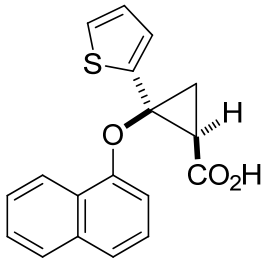
C(12)-C(13)-C(14)-C(15)	-178.75(19)
C(12)-C(13)-C(14)-C(19)	1.9(3)
C(13)-C(14)-C(15)-C(16)	-178.4(2)
C(19)-C(14)-C(15)-C(16)	0.9(3)
C(14)-C(15)-C(16)-C(17)	-0.2(3)
C(15)-C(16)-C(17)-C(18)	-0.5(3)
C(16)-C(17)-C(18)-C(19)	0.4(3)
C(17)-C(18)-C(19)-C(10)	-179.83(19)
C(17)-C(18)-C(19)-C(14)	0.3(3)
C(11)-C(10)-C(19)-C(18)	-179.46(18)
O(1)-C(10)-C(19)-C(18)	0.3(3)
C(11)-C(10)-C(19)-C(14)	0.4(3)
O(1)-C(10)-C(19)-C(14)	-179.81(16)
C(13)-C(14)-C(19)-C(18)	178.44(18)
C(15)-C(14)-C(19)-C(18)	-1.0(3)
C(13)-C(14)-C(19)-C(10)	-1.5(3)
C(15)-C(14)-C(19)-C(10)	179.15(17)

Symmetry transformations used to generate equivalent atoms:

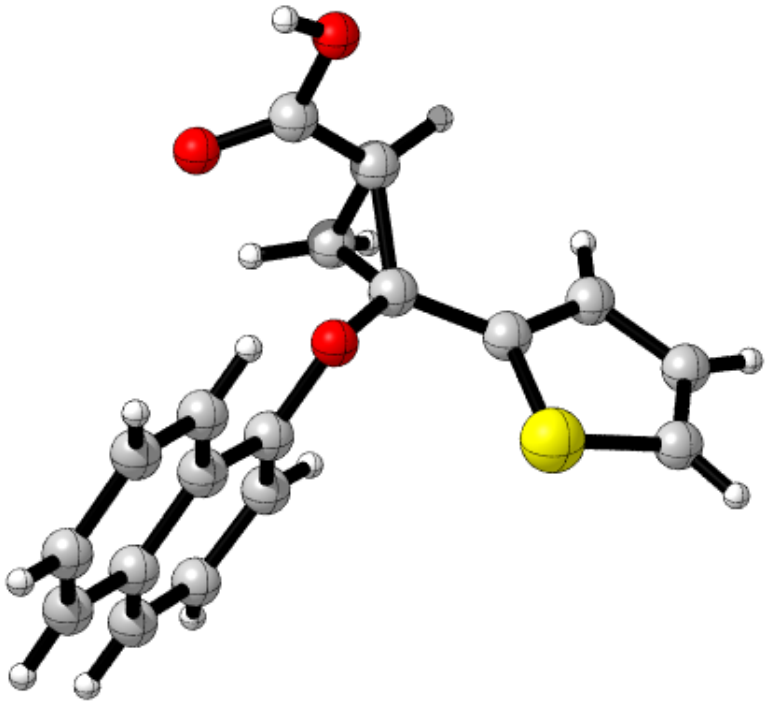
Table 24. Hydrogen bonds for (+)-**25** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(1)-H(1NA)...Cl(1)#1	0.90(3)	2.28(3)	3.1425(18)	159(3)
N(1)-H(1NB)...Cl(1)#2	0.94(3)	2.15(3)	3.0793(17)	171(2)
O(1S)-H(1S)...Cl(1)#3	0.84(4)	2.46(4)	3.288(2)	174(3)

Symmetry transformations used to generate equivalent atoms:
#1 x+1/2,-y+3/2,-z #2 x+1,y,z #3 x,y-1,z



(±)-**20**



(±)-**22**.

Table 25. Crystal data and structure refinement for (±)-**22**

Identification code	jwb10	
Empirical formula	C18 H14 O3 S	
Formula weight	310.35	
Temperature	153(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/c	
Unit cell dimensions	a = 10.9015(18) Å	a= 90°.
	b = 11.2121(19) Å	b= 111.688(3)°.
	c = 13.644(2) Å	g = 90°.
Volume	1549.7(5) $Å^3$	
Z	4	
Density (calculated)	1.330 Mg/m^3	
Absorption coefficient	0.218 mm^{-1}	
F(000)	648	
Crystal size	0.17 x 0.14 x 0.07 mm^3	
Theta range for data collection	2.01 to 24.99°.	
Index ranges	-12<=h<=12, -13<=k<=13, -16<=l<=15	
Reflections collected	9625	
Independent reflections	2721 [R(int) = 0.0293]	
Completeness to theta = 24.99°	99.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.000 and 0.822	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2721 / 0 / 203	
Goodness-of-fit on F^2	1.090	
Final R indices [I>2sigma(I)]	R1 = 0.0533, wR2 = 0.1363	
R indices (all data)	R1 = 0.0693, wR2 = 0.1483	
Largest diff. peak and hole	0.417 and -0.509 $e.Å^{-3}$	

Table 26. 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)
S(1)	8186(1)	5736(1)	2182(1)	47(1)
O(1)	10606(2)	8439(2)	56(2)	37(1)
O(2)	8627(2)	9315(2)	-394(2)	37(1)
O(3)	7912(2)	7899(2)	1016(1)	29(1)
C(1)	9313(3)	8416(2)	-231(2)	31(1)
C(2)	8773(3)	7195(2)	-312(2)	33(1)
C(3)	7944(3)	6938(2)	364(2)	30(1)
C(4)	7292(3)	7053(3)	-800(2)	38(1)
C(5)	8095(3)	5768(2)	903(2)	30(1)
C(6)	8238(3)	4605(2)	511(2)	36(1)
C(7)	8354(3)	3760(3)	1332(2)	45(1)
C(8)	8339(3)	4229(3)	2244(2)	40(1)
C(9)	6708(3)	8303(2)	1012(2)	28(1)
C(10)	5520(3)	7758(3)	502(2)	38(1)
C(11)	4373(3)	8267(3)	564(2)	44(1)
C(12)	4425(3)	9265(3)	1142(3)	44(1)
C(13)	5647(3)	9837(3)	1690(2)	34(1)
C(14)	5759(3)	10878(3)	2309(2)	43(1)
C(15)	6942(3)	11428(3)	2798(2)	43(1)
C(16)	8094(3)	10962(3)	2708(2)	38(1)
C(17)	8032(3)	9948(2)	2131(2)	30(1)
C(18)	6816(2)	9362(2)	1611(2)	26(1)

Table 27. Bond lengths [Å] and angles [°] for (±)-**22**.

S(1)-C(8)	1.697(3)
S(1)-C(5)	1.713(3)
O(1)-C(1)	1.317(3)
O(1)-H(1)	0.79(4)
O(2)-C(1)	1.225(3)
O(3)-C(9)	1.386(3)
O(3)-C(3)	1.406(3)
C(1)-C(2)	1.478(4)
C(2)-C(4)	1.511(4)
C(2)-C(3)	1.538(4)
C(2)-H(2A)	1.0000
C(3)-C(5)	1.483(4)
C(3)-C(4)	1.487(4)
C(4)-H(4A)	0.9900
C(4)-H(4B)	0.9900
C(5)-C(6)	1.440(4)
C(6)-C(7)	1.436(4)
C(6)-H(6A)	0.9500
C(7)-C(8)	1.357(4)
C(7)-H(7A)	0.9500
C(8)-H(8A)	0.9500
C(9)-C(10)	1.367(4)
C(9)-C(18)	1.421(4)
C(10)-C(11)	1.406(4)
C(10)-H(10A)	0.9500
C(11)-C(12)	1.357(5)
C(11)-H(11A)	0.9500
C(12)-C(13)	1.417(4)
C(12)-H(12A)	0.9500
C(13)-C(14)	1.420(4)
C(13)-C(18)	1.421(4)
C(14)-C(15)	1.361(5)
C(14)-H(14A)	0.9500
C(15)-C(16)	1.407(4)

C(15)-H(15A)	0.9500
C(16)-C(17)	1.370(4)
C(16)-H(16A)	0.9500
C(17)-C(18)	1.414(4)
C(17)-H(17A)	0.9500
C(8)-S(1)-C(5)	92.24(14)
C(1)-O(1)-H(1)	103(3)
C(9)-O(3)-C(3)	119.5(2)
O(2)-C(1)-O(1)	123.5(3)
O(2)-C(1)-C(2)	123.3(3)
O(1)-C(1)-C(2)	113.2(2)
C(1)-C(2)-C(4)	117.5(2)
C(1)-C(2)-C(3)	115.7(2)
C(4)-C(2)-C(3)	58.36(18)
C(1)-C(2)-H(2A)	117.4
C(4)-C(2)-H(2A)	117.4
C(3)-C(2)-H(2A)	117.4
O(3)-C(3)-C(5)	112.8(2)
O(3)-C(3)-C(4)	119.7(2)
C(5)-C(3)-C(4)	121.9(2)
O(3)-C(3)-C(2)	113.2(2)
C(5)-C(3)-C(2)	118.7(2)
C(4)-C(3)-C(2)	59.88(18)
C(3)-C(4)-C(2)	61.75(18)
C(3)-C(4)-H(4A)	117.6
C(2)-C(4)-H(4A)	117.6
C(3)-C(4)-H(4B)	117.6
C(2)-C(4)-H(4B)	117.6
H(4A)-C(4)-H(4B)	114.7
C(6)-C(5)-C(3)	128.7(2)
C(6)-C(5)-S(1)	112.7(2)
C(3)-C(5)-S(1)	118.55(19)
C(7)-C(6)-C(5)	107.4(3)
C(7)-C(6)-H(6A)	126.3
C(5)-C(6)-H(6A)	126.3

C(8)-C(7)-C(6)	115.6(3)
C(8)-C(7)-H(7A)	122.2
C(6)-C(7)-H(7A)	122.2
C(7)-C(8)-S(1)	112.0(2)
C(7)-C(8)-H(8A)	124.0
S(1)-C(8)-H(8A)	124.0
C(10)-C(9)-O(3)	125.0(3)
C(10)-C(9)-C(18)	121.8(2)
O(3)-C(9)-C(18)	113.2(2)
C(9)-C(10)-C(11)	119.0(3)
C(9)-C(10)-H(10A)	120.5
C(11)-C(10)-H(10A)	120.5
C(12)-C(11)-C(10)	121.5(3)
C(12)-C(11)-H(11A)	119.2
C(10)-C(11)-H(11A)	119.2
C(11)-C(12)-C(13)	120.6(3)
C(11)-C(12)-H(12A)	119.7
C(13)-C(12)-H(12A)	119.7
C(12)-C(13)-C(14)	122.9(3)
C(12)-C(13)-C(18)	119.0(3)
C(14)-C(13)-C(18)	118.1(3)
C(15)-C(14)-C(13)	121.4(3)
C(15)-C(14)-H(14A)	119.3
C(13)-C(14)-H(14A)	119.3
C(14)-C(15)-C(16)	120.3(3)
C(14)-C(15)-H(15A)	119.9
C(16)-C(15)-H(15A)	119.9
C(17)-C(16)-C(15)	120.2(3)
C(17)-C(16)-H(16A)	119.9
C(15)-C(16)-H(16A)	119.9
C(16)-C(17)-C(18)	120.8(3)
C(16)-C(17)-H(17A)	119.6
C(18)-C(17)-H(17A)	119.6
C(17)-C(18)-C(9)	122.6(2)
C(17)-C(18)-C(13)	119.3(2)

C(9)-C(18)-C(13) 118.1(2)

Symmetry transformations used to generate equivalent atoms:

Table 28. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for (±)-**22**
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}
S(1)	66(1)	40(1)	39(1)	3(1)	24(1)	6(1)
O(1)	37(1)	30(1)	45(1)	1(1)	17(1)	4(1)
O(2)	39(1)	29(1)	43(1)	6(1)	17(1)	4(1)
O(3)	28(1)	28(1)	33(1)	-7(1)	12(1)	0(1)
C(1)	39(2)	33(2)	24(1)	2(1)	15(1)	2(1)
C(2)	44(2)	30(2)	29(2)	-2(1)	18(1)	1(1)
C(3)	35(2)	27(1)	29(2)	-5(1)	13(1)	-2(1)
C(4)	48(2)	35(2)	27(2)	0(1)	10(1)	-4(1)
C(5)	31(2)	30(2)	28(1)	-4(1)	10(1)	-4(1)
C(6)	48(2)	27(2)	29(2)	7(1)	8(1)	-9(1)
C(7)	54(2)	29(2)	48(2)	-5(1)	14(2)	-4(1)
C(8)	50(2)	32(2)	38(2)	6(1)	17(1)	-3(1)
C(9)	29(1)	29(1)	29(1)	6(1)	14(1)	3(1)
C(10)	38(2)	37(2)	38(2)	3(1)	15(1)	-6(1)
C(11)	28(2)	57(2)	44(2)	8(2)	11(1)	-9(1)
C(12)	31(2)	59(2)	46(2)	15(2)	19(1)	9(1)
C(13)	37(2)	37(2)	32(2)	14(1)	18(1)	12(1)
C(14)	54(2)	42(2)	43(2)	13(2)	28(2)	25(2)
C(15)	63(2)	29(2)	41(2)	2(1)	26(2)	12(2)
C(16)	49(2)	29(2)	35(2)	-1(1)	17(1)	1(1)
C(17)	35(2)	27(2)	31(2)	5(1)	16(1)	6(1)
C(18)	31(1)	26(1)	25(1)	9(1)	14(1)	5(1)

Table 29. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for (±)-**22**.

	x	y	z	U(eq)
H(2A)	9325	6529	-413	40
H(4A)	6759	7778	-1079	45
H(4B)	6942	6318	-1210	45
H(6A)	8252	4428	-166	44
H(7A)	8437	2927	1242	54
H(8A)	8407	3768	2846	48
H(10A)	5471	7046	111	45
H(11A)	3542	7905	193	53
H(12A)	3636	9583	1179	53
H(14A)	4992	11198	2384	52
H(15A)	6990	12129	3201	51
H(16A)	8917	11351	3048	45
H(17A)	8816	9635	2079	36
H(1)	10770(40)	9130(40)	110(30)	73(14)

Table 30. Hydrogen bonds for (±)-**22** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1)-H(1)...O(2)#1	0.79(4)	1.86(4)	2.640(3)	172(4)

Symmetry transformations used to generate equivalent atoms:
#1 -x+2,-y+2,-z

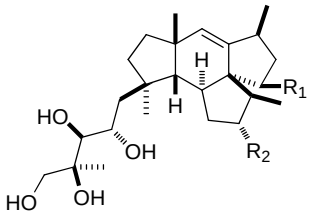
PART II

Asymmetric approach to the tetracyclic core of neomangicol A

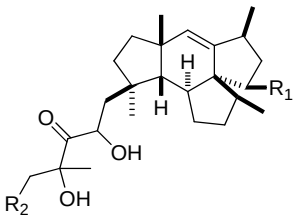
CHAPTER 1

1.1 Isolation, structure elucidation and biological activity

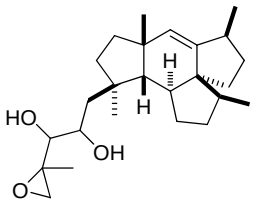
Marine microorganisms, especially marine fungi, have emerged as significant resource for novel bioactive natural products.[1] For example, two reports published by the Fenical group in 1998 and 2000[2] described the isolation, structural elucidation, bioactivity and biosynthesis of a new class of cytotoxic sesterterpenoids, named mangicols and neomangicols.[3] These compounds are generated by a marine fungus believed to be *Fusarium heterosporum*, which was collected from driftwood discovered in a mangrove habitat of Sweetings Cay in the Bahamas in 1995. Hence, the general name associated with this subset of fungal metabolites (Fig 1).[4]



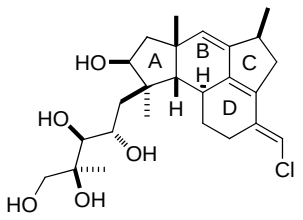
1, R_1 = OH, R_2 = H, Mangicol A
2, R_1 = H, R_2 = OH, Mangicol B
3, R_1 = H, R_2 = H, Mangicol C



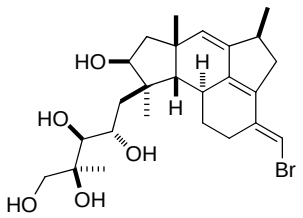
4, R_1 = OH, R_2 = H, Mangicol D
5, R_1 = H, R_2 = OH, Mangicol E
6, R_1 = H, R_2 = H, Mangicol F



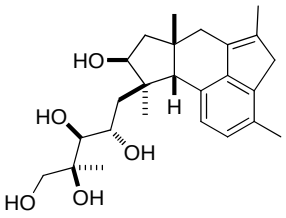
7, Mangicol G



8, Neomangicol A



9, Neomangicol B



10, Neomangicol C

Fig 1. Mangicols and neomangicols, a new class of rearranged sesterterpenes

Isoprenoids containing 25 carbon atoms are the rarest of the terpenoid classes of natural products. Several have been isolated from terrestrial fungi, such as fusaproleferin,[5] variecolin[6] and retigeranic acid[7] among others, although none have been found in marine fungi.[8] The mangicols and neomangicols possess an unprecedented and rearranged isoprenoid C_{25} tetracyclic carbon skeleton. The structures of the members of this class were elucidated mainly by 1D and extensive 2D NMR techniques, and by high resolution mass spectral analysis of the natural products and derivatives thereof. While halogenated terpenoids are ubiquitous in marine natural products,[9] neomangicols A and B appear to be the first examples of halogenated sesterterpenes.[10]

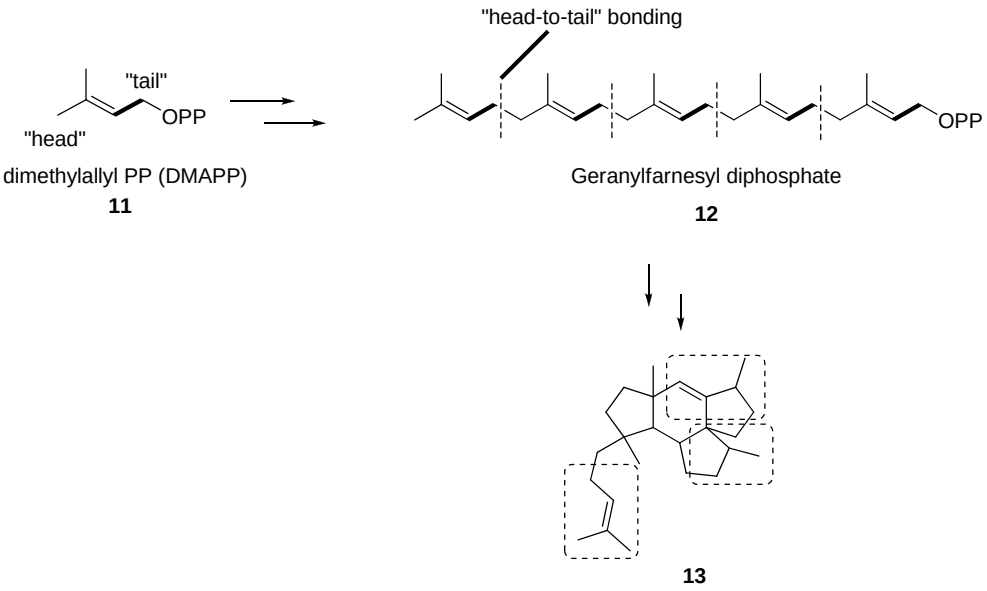
Fenical and coworkers demonstrated that several mangicols display bioactivity.[11] Although mangicols showed only modest cytotoxicities toward cancer cells *in vitro,* mangicols A-G possesed IC_{50} values (GI_{50}) ranging from 18 to 36 μM in the National Cancer Institutes 60 cell line panel (mangicol A, 24.5 μM; mangicol B, 20.4 μM; mangicol C, 17 μM; mangicol D, 24.5 μM; mangicol E, 17.8 μM; mangicol F, 36.3 μM; mangicol G, 25.1 μM). The selectivity of mangicols against specific cancer cell lines in these assays was not sufficient to be of any value in chemotherapy. However, mangicols A and C showed inhibition of phorbol myristate acetate-induced edema (inflammation) in the mouse ear edema assay (81 and 57% reduction in edema, respectively) at the standard testing dose of 50 μg per ear. These values are comparable to the potencies of existing antiinflammatory agents in this assay (indomethacin shows 71% reduction), a sign that the mangicols may be considered in

drug development. Neomangicol A was significantly selective against MCF-7 (human breast carcinoma) and CACO-2 (human colon carcinoma) cell lines (IC_{50} values of 4.9 and 5.7 μM, respectively). Neomangicol B was less selective with a mean IC_{50} value of 27 μM across the entire cell line panel (versus 10 μM for neomangicol A). However, neomangicol B displayed comparable antibacterial activity to that of known antibiotic gentamycin against the Gram-positive bacterium *Bacillus subtilus*. Neomangicol C was shown biologically inactive in all assays. The observation that neomancigol A can be converted into neomangicol C and that the latter was not found in the crude extracts when mild methods were carried out, hints to fact that neomangicol C is an isolation artifact arising from neomangicol A or B.

1.2 Biosynthesis of the mangicols and the neomangicols

Ružička's biogenetic "Isoprene Rule" is a widely accepted hypothesis used to explain the formation of terpenoids *in vivo*.[12] According to this rule, terpenes are natural products assembled biogenetically by a linear ("head-to-tail") combination of isoprene units.[13]

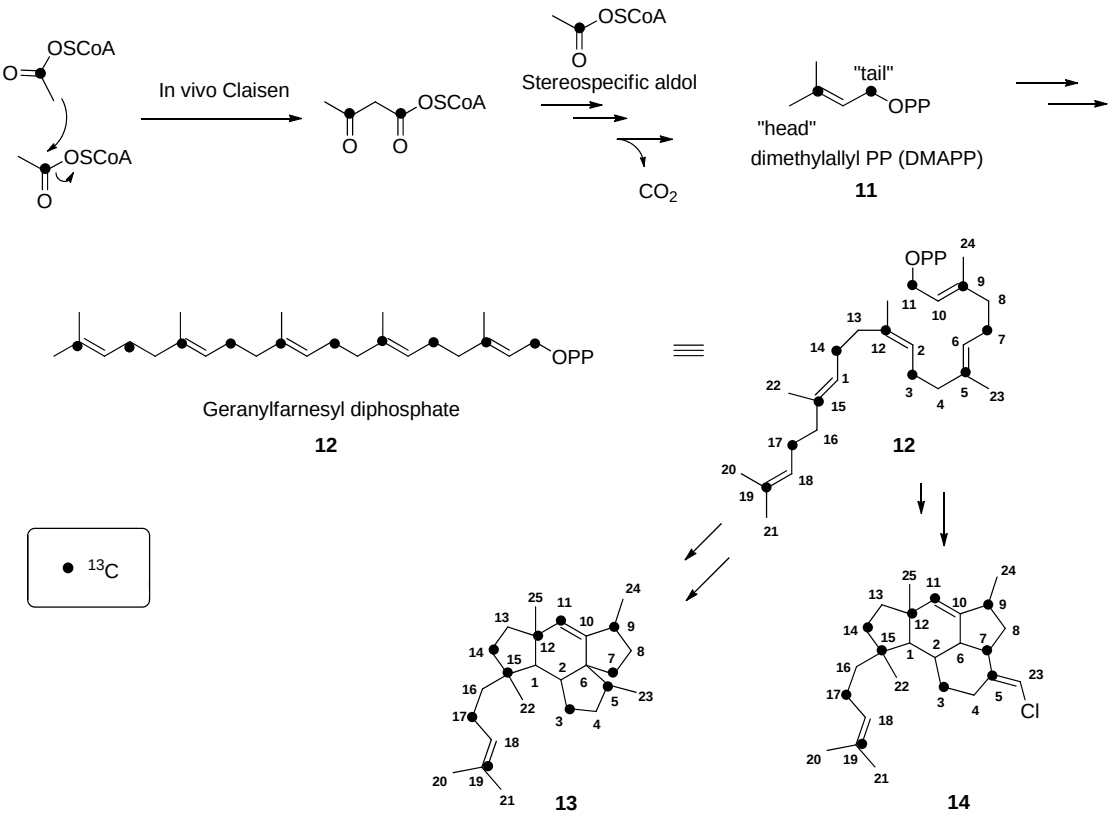
A closer inspection of the mangicol and neomangicol carbon framework reveals five individual isoprene precursors (**11**) which implies biosynthesis from the C_{25} precursor geranylfarnesyl diphosphate (**12**). In the case of the mangicols, only three isoprenoid fragments (shown in dotted squares) are engaged in "head-to-tail" bonding. The remaining isoprenoid units appear to have inserted with rearrangement to give the mangicol tetracyclic core (Scheme 1).



Scheme 1. Isoprenoid biogenesis of mangicols and neomangicols

Fenical and coworkers performed feeding studies with fungal strain CNC-477 (*Fusarium* cf. *heterosporum*) using sodium [1-^{13}C]acetate and sodium [1,2-^{13}C]acetate. Mangicol A (**1**) and neomangicol A (**8**) were extracted from the mycelium and analyzed using ^{13}C NMR spectroscopy. The feeding experiment using sodium [1,2-^{13}C]acetate showed specific incorporation of ~0.81 % at each carbon of mangicol A and neomangicol A which is in concordance with an isoprenoid genesis of these metabolites. The labeling pattern using sodium [1-^{13}C]acetate demonstrated that none of the methyl groups of mangicol A or neomangicol A migrated during the biosynthesis. Furthermore, the feeding experiments revealed that three isoprene units, C-17 through C-21 (the tail), C-4 through C-7 plus C-23 and C-8 through C-11 plus C-24 (the head) were incorporated intact in the carbon framework of mangicol A. The

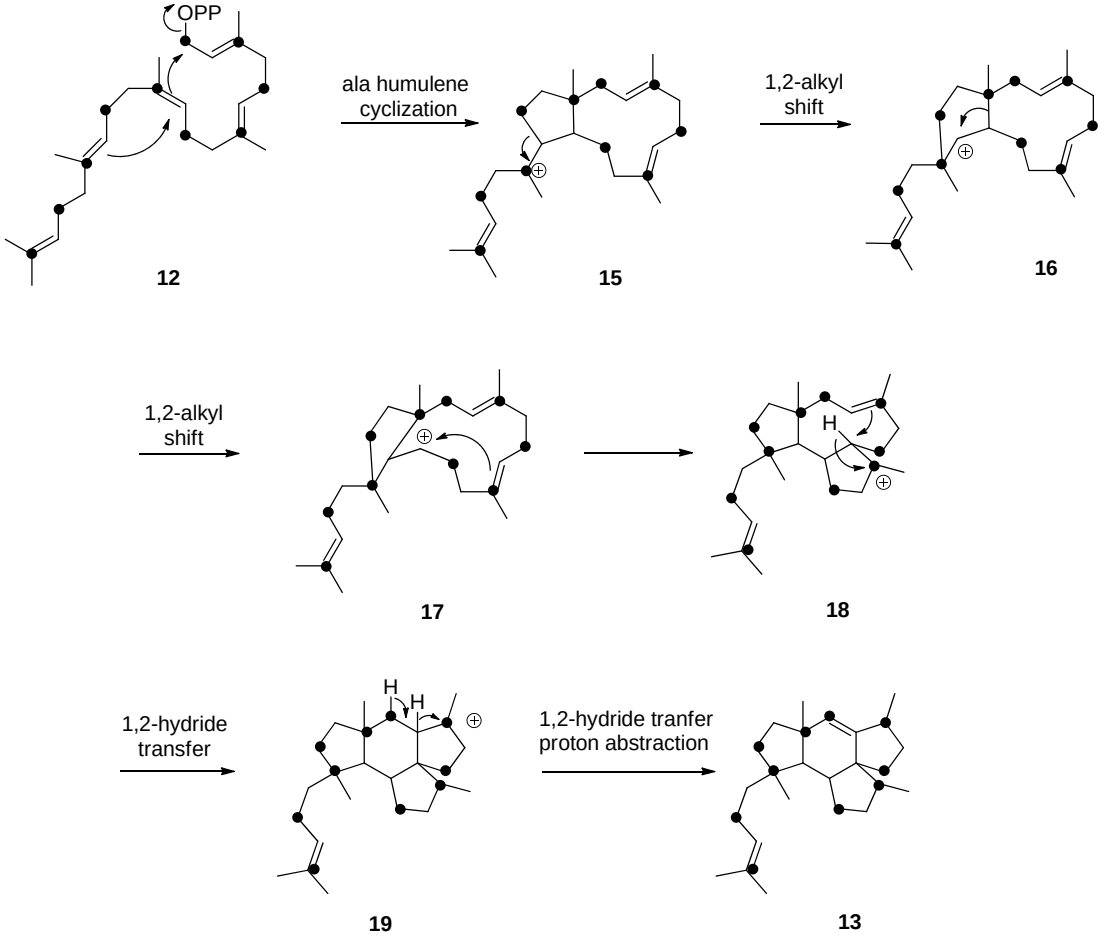
two remaining isoprene units had undergone several 1,2-alkyl shifts resulting in C-1 insertion into the isoprene unit of C-13, C-12, C-25, C-2 and C-3. Assuming the same process occurs in the case of neomangicol A, the isoprenoid unit C-4 through C-7 is also to be rearranged (Scheme 2).



Scheme 2. Feeding experiment using sodium [1-^{13}C]acetate

Based on these studies, Fenical and coworkers proposed a complete biosynthetic origin of the neomangicols and the mangicols. Cyclization of geranylfarnesyl diphosphate (**12**) would give rise to [9.3.0]tetradecadiene **15**. Ring expansion of diene **15** followed by ring contraction via two consecutive 1,2-alkyl

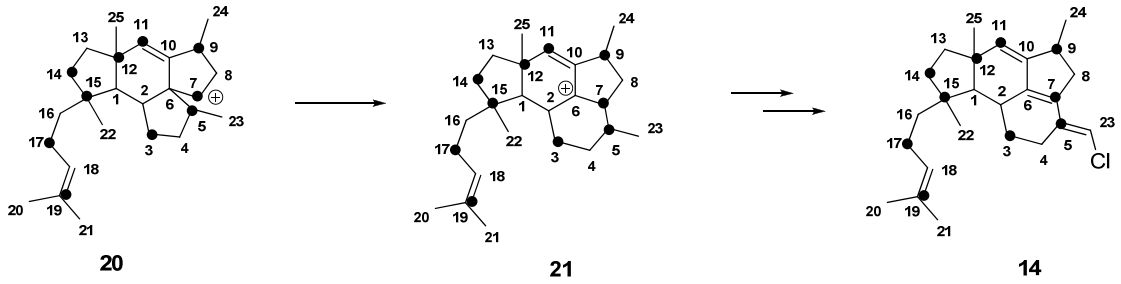
shifts would produce secondary carbenium ion **17**. A cationic-driven ring closure of the latter followed by a 1,2-hydride shift and cyclization leads to tetracyclic carbenium intermediate **19**. Final deprotonation and two hydride shifts yield the mangicol carbon skeleton **13** (Scheme 3).



Scheme 3. Biosynthesis of the mangicols and the neomangicols

The ^{13}C incorporation patterns in mangicol A and neomangicol A are similar, implying a close biosynthetic relationship between these two sesterterpenes. However, the labeling pattern for neomangicol reveals that C-5 is connected to C-7 and not to C-

6 as in mangicol A. A feasible explanation would be ring expansion of the putative intermediate **20** driven by formation of a tertiary carbenium at C-6 to forge the neomangicol A skeleton **14** after deprotonation and halogenation (Scheme 4).



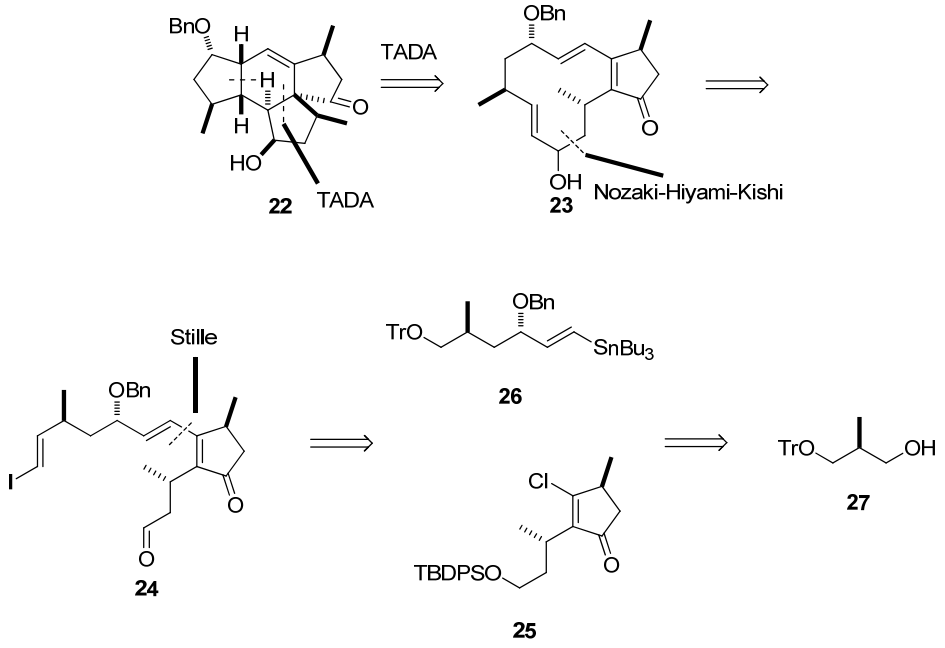
Scheme 4. Biosynthetic relationship between mangicol A and neomangicol A

1.3 Previous synthetic efforts on the mangicols and neomangicols

The mangicols and neomangicols are challenging targets from the synthetic point of view. They possess unique fused [5,6,5,5] and [5,6,5,6] tetracyclic carbon frameworks, respectively, and they house numerous chiral centers (6 in neomangicol C, 9 in neomangicol A and B and 11 in mangicol A and B), several of which are quaternary. Although it has been more than a decade since their isolation and structural elucidation, no total synthesis has been reported to date on any members of this class of rearranged sesterterpenes. Two communications have appeared on synthetic studies towards mangicol A by Uemura in 2004[14] and Paquette in 2006.[15] One report towards the synthesis of the core of neomangicol C by Sarpong appeared in 2009.[16]

1.3.1 Synthetic studies on mangicol by the Uemura group

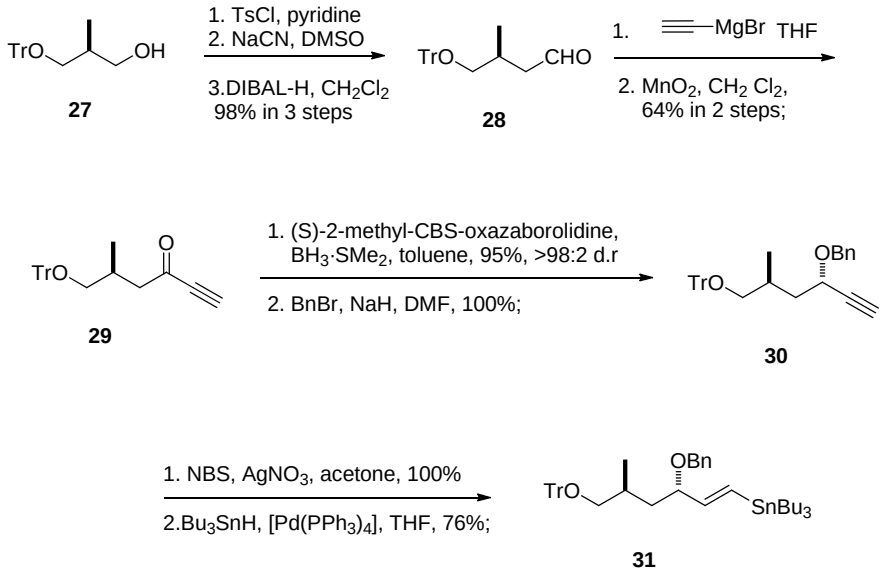
At the heart of Uemura's stereoselective approach to constructing the spirotretracyclic of mangicol core is a transannular Diels-Alder (TADA)[17] reaction of triene **23**. The TADA precursor was assembled using intramolecular Nozaki-Hiyami-Kishi[18] and Stille[19] couplings as key steps (Scheme 5).



Scheme 5. Uemura's approach to assembling the mangicol core

Stannane **26** and vinyl chloride **25** were prepared from the known trityl protected alcohol **27**.[20] The alcohol was converted to a nitrile by tosylation followed by nucleophilic displacement of the tosylate with sodium cyanide. The nitrile afforded aldehyde **28** after reduction with diisobutylaluminum hydride. Ethynylmagnesium

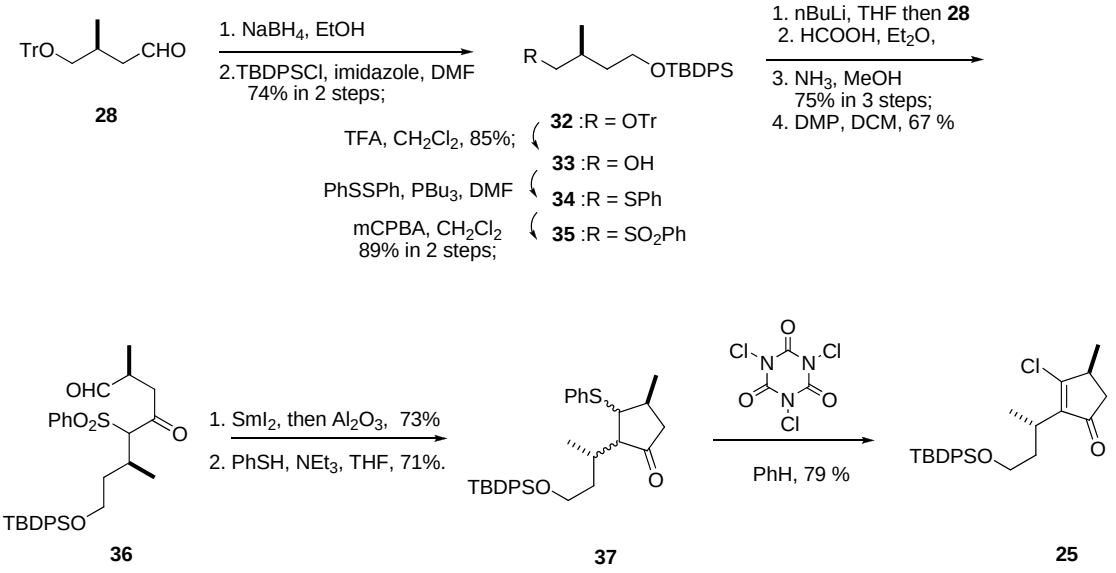
bromide addition to aldehyde **28** gave rise to a 1:1 diastereomeric mixture of alcohols which was submitted to manganese dioxide oxidation to give ketone **29**. After diastereoselective reduction of this ketone using Corey-Bakshi-Shibata methodology,[21] the alcohol was protected as benzyl ether **30**. Terminal halogenation of the alkyne moiety with NBS[22] followed by hydrostannylation[23] yielded regio and stereoselectively pure vinyl stannane **31** (Scheme 6).



Scheme 6. Uemura's synthesis of stannane **31**

Synthesis of cyclopentenone **25** also commenced from common intermediate aldehyde **28**. Reduction of **28** followed by protection gave *tert*-butyldimethylsilyl ether **32**. The trityl group was removed under acidic conditions and the revealed alcohol was transformed into sulfone **35** using Grieco's method**.** Julia coupling[24] of sulfone **35** with aldehyde **28** gave a diastereomeric mixture of hydroxy sulfones. After

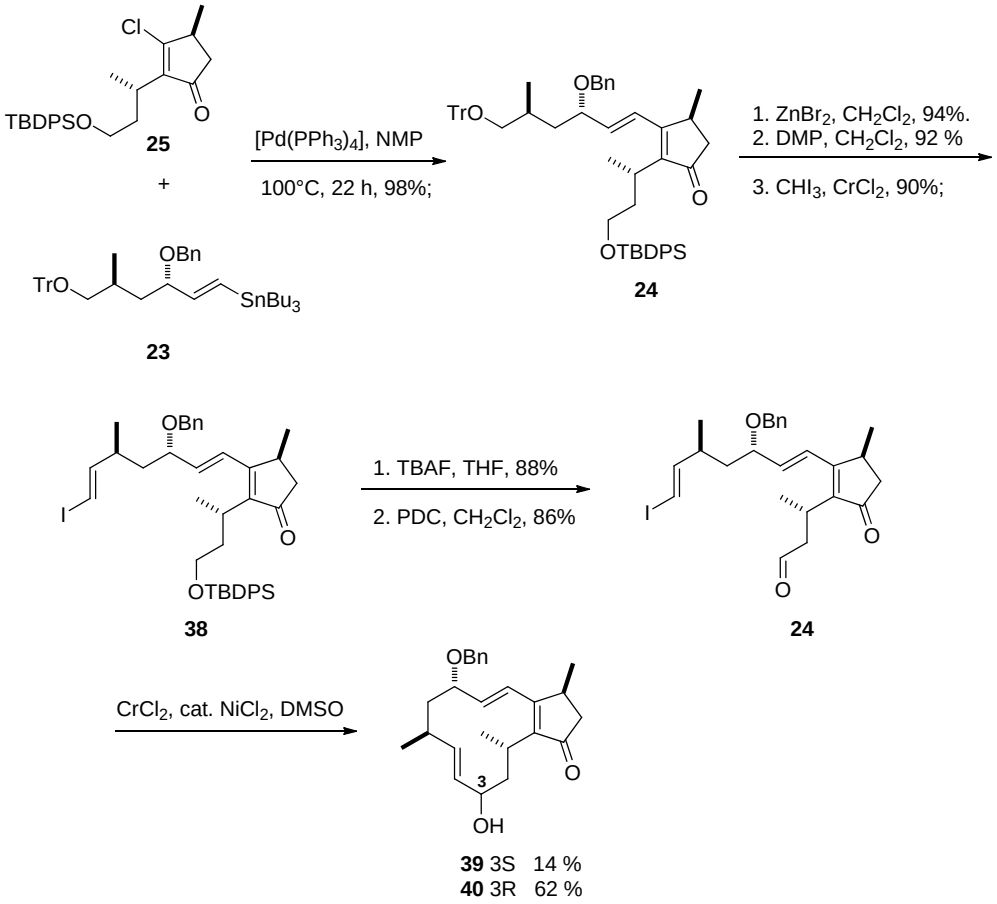
trityl removal, global oxidation with Dess-Martin periodinane afforded the precursor for intramolecular aldol condensation of **36**. A reductive aldol sequence in the presence of samarium(II) iodite effected cyclization which was followed by dehydration to give a cyclopentenone. Micheal addition of thiophenol to the cyclopentenone then produced a diastereomeric mixture of β-thiophenylcyclopentanones **37**. Oxidation of **37** with trichloroisocyanuric acid generated β-chlorocyclopentenone **25** (Scheme 7).



Scheme 7. Uemura's synthesis of cyclopentenone **25**

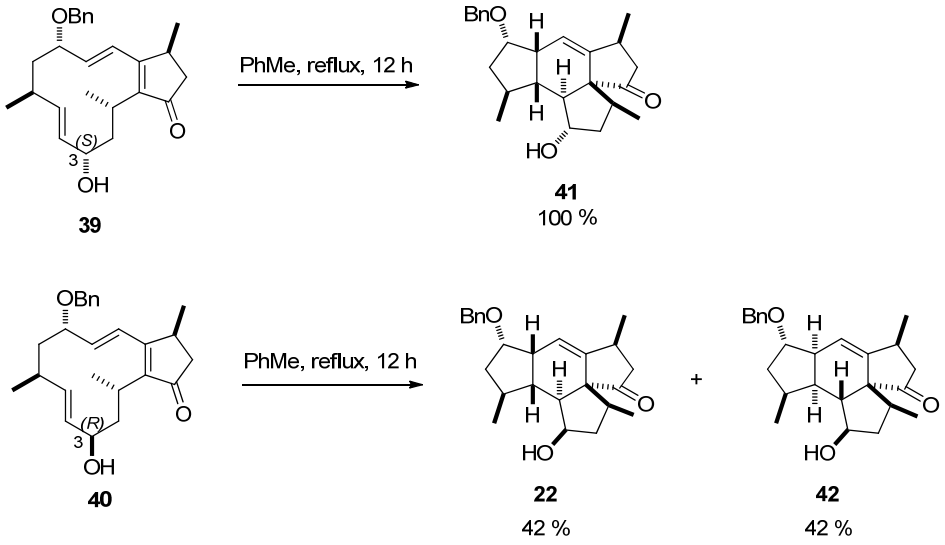
Stille coupling of vinyl chloride **25** with stannane **23** using catalytic palladium(0) gave rise to dienone **24** in excellent yield. Trityl removal under Lewis acidic conditions[25] followed by Dess-Martin oxidation set the stage for a Takai olefination to give iodoalkene **38**.[26] *Tert*-butyldimethylsilyl deprotection revealed a primary alcohol, which was oxidized to aldehyde **24**. Intramolecular Nozaki-Hiyama-

Kishi coupling of **24** then gave a separable mixture of two diastereomeric trienones **39** and **40** (Scheme 8).



Scheme 8. Uemura's synthesis of TADA precursors **39** and **40**

Trienone (3S)-**39** underwent TADA in refluxing toluene to give the tetracyclic core **41** of mangicol A in quantitative yield. Exo diastereoselectivity observed with TADA of **39** is believed to be due to the configuration of the C-3 alcohol in the triene precursor.[27] In the case of **40** where C3 configuration is reversed, a 1:1 diastereomeric mixture of tetracyclic ketones **22** and **42** were produced (Scheme 9).

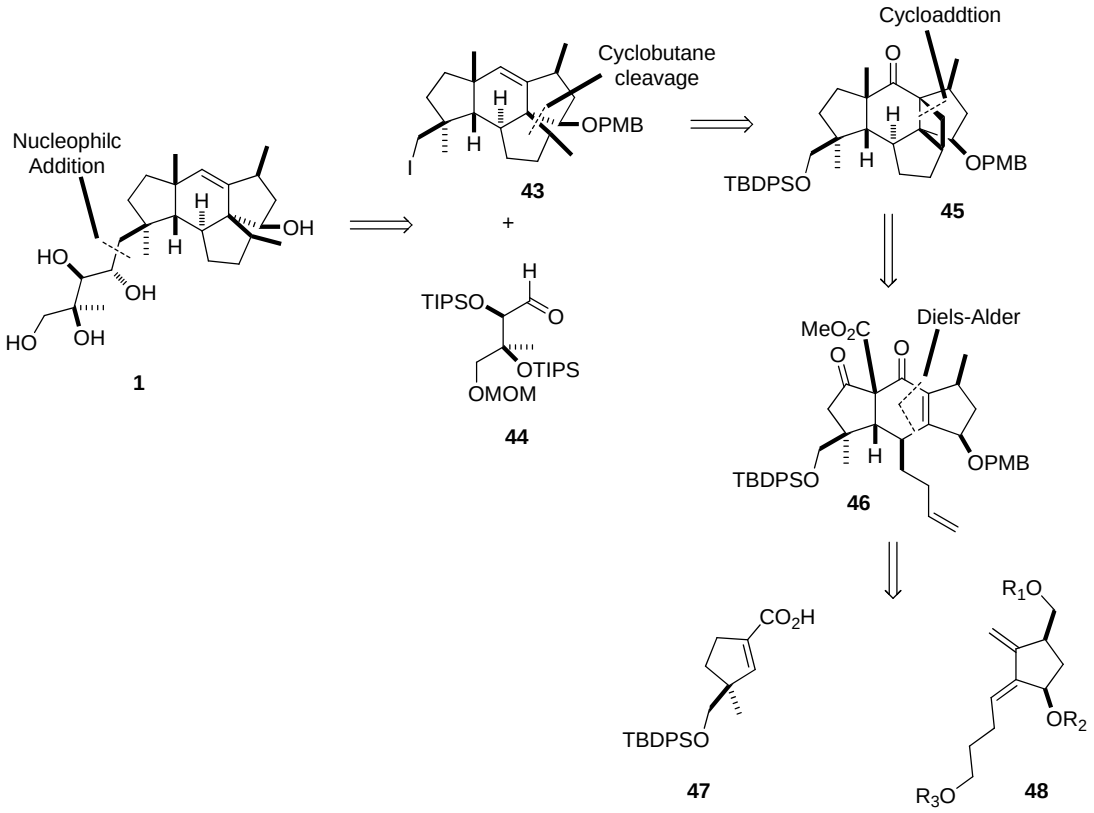


Scheme 9. Uemura's assembly of the core of mangicol A

1.3.2 Synthetic studies on mangicol by the Paquette group

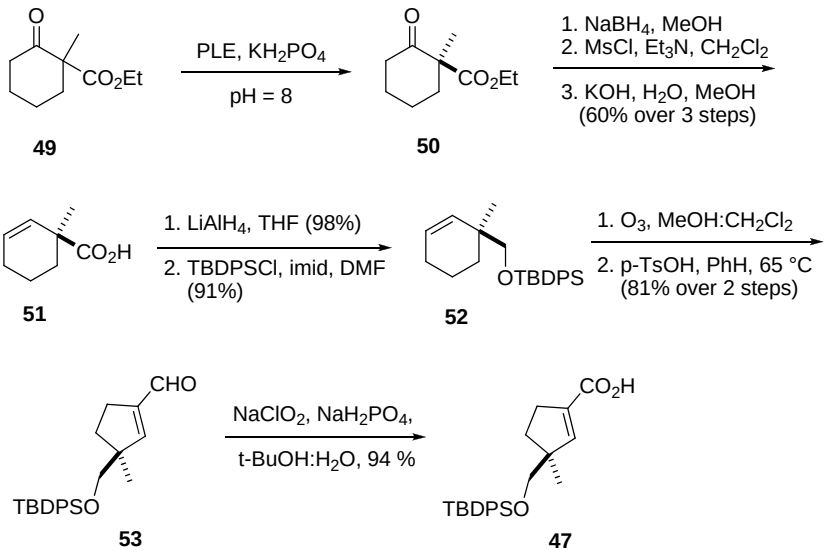
1.3.2.1 The Diels-Alder approach[28]

The Paquette approach to synthesis of mangicol A (**1**) hinges on an intramolecular [2+2] cycloaddition of cyclohexenone **46,** which would forge pentacyclic ketone **45**. Samarium(II) iodide promoted cyclobutane fragmentation of the ketone would produce the core of mangicol A. Cyclohexenone **46** was programmed from Diels-Alder addition of cyclopentene **47** to diene **48**. The tetraol appendage was envisioned from a diastereoselective addition of an organometallic intermediate generated from iodide **43** to aldehyde **44** (Scheme 10).



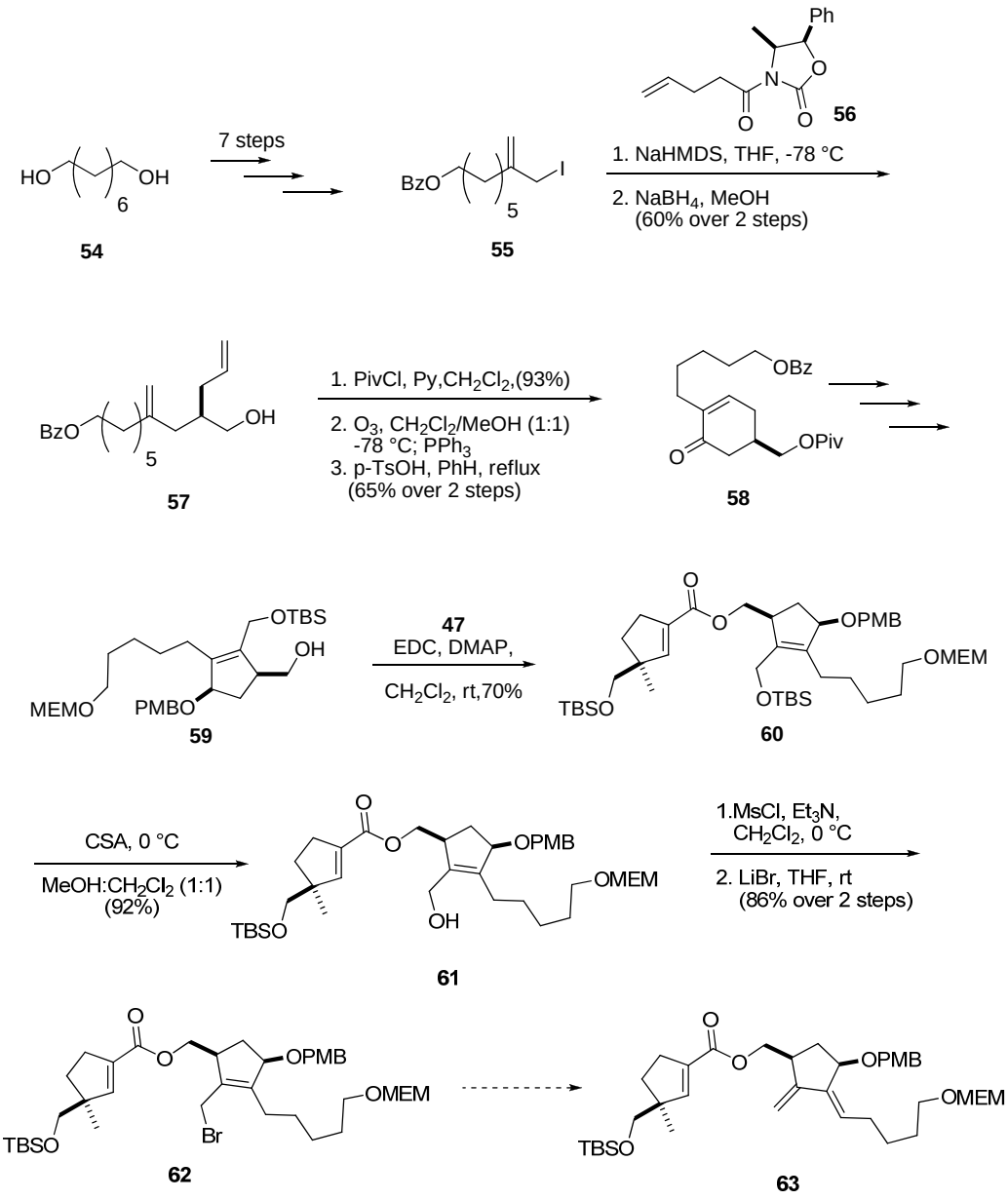
Scheme 10. Paquette's strategy for assembling mangicol A

Cyclopentenecarboxylic acid **47** originated from a pig liver esterase-mediated kinetic resolution of racemic ketoester **49**. Reduction of the ketone functionality of **49** followed by a mesylation-elimination-saponification sequence produced cyclohexenecarboxylic acid **51**. Lithium aluminum hydride reduction of the carboxylic gave rise to an alcohol which was converted to its *tert*-butyldimethylsilyl ether **52**. Ozonolysis of **52** afforded a keto aldehyde which underwent acid-catalyzed intramolecular aldol ring closure to give cyclopentenecarbaldehyde **53**. This aldehyde was converted to cyclopentenecarboxylic **47** using Pinnick oxidation (Scheme 11).



Scheme 11. The synthesis of dienophile **47**

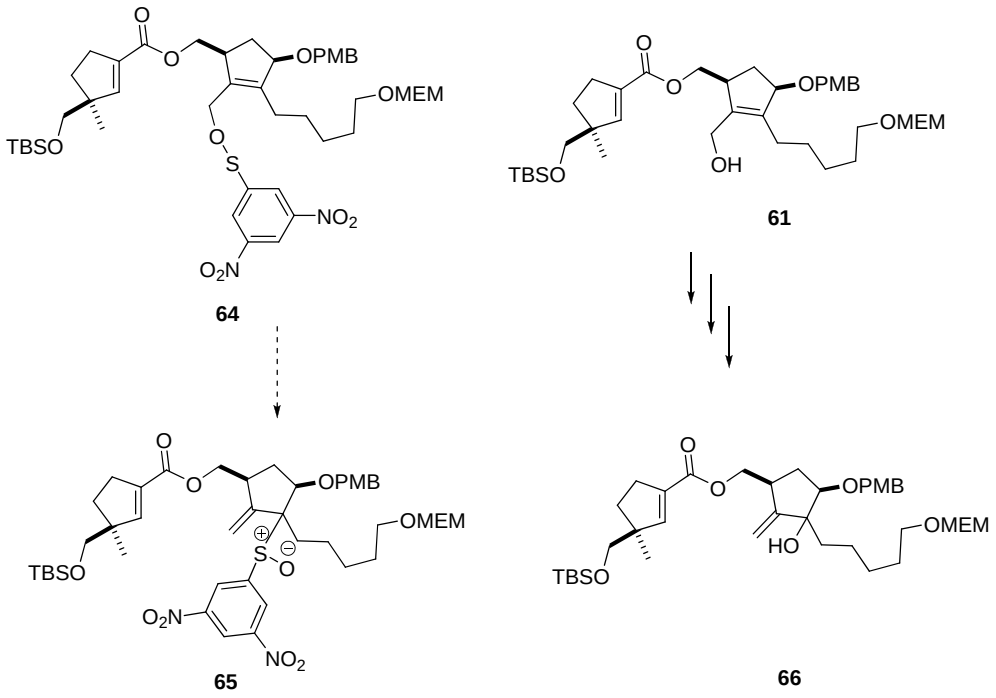
Synthesis of the indented Diels-Alder precursor **63** began from diol **54,** which was converted to allylic iodide **55** in seven steps. Enantioselective alkylation of the sodium enolate derived from oxazolidinone **56** with iodide **55** proceeded smoothly and with high enantioselectivity. Reductive cleavage of the auxiliary then gave alcohol **57** in good yield. After protection of the primary alcohol and ozonolysis of the two alkenes, acid-mediated aldol condensation generated cyclohexenone **58**. Further functional group manipulation provided tetrasubstituted cyclopentene **59** which was coupled with carboxylic acid **47** using N-(3-dimethylaminopropyl)-N′-ethylcarbodiimide hydrochloride and 4-(dimethylamino)pyridine to produce ester **60**. Acid-promoted deprotection of the allylic *tert*-butyldimethylsilyl ether **60** revealed primary alcohol **61** which was activated as its mesytylate, and reacted with lithium bromide to yield allyllic bromide **62** (Scheme 12).



Scheme 12. Paquette's attempted synthesis of cycloaddition precursor **63**

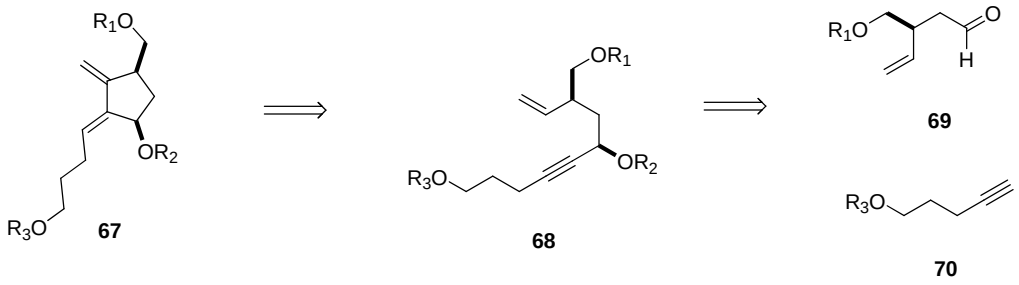
Paquette found that attempts to effect elimination of allyllic bromide **62** either gave no reaction or resulted in decomposition and in an attempt to overcome this hurdle, alcohol **61** was converted to its sulfenate **64**. When **64** was heated at elevated

temperature in the hope it would undergo a [1,3]-sigmatropic rearrangement, sulfoxide **65** was not detected. In a different route from **61**, the latter was converted to allylic alcohol **66** via a three step sequence involving epoxidation, iodination and elimination. The plan was to transform **66** to a xanthate and then execute syn elimination but this tertiary allylic alcohol failed to form a xanthate (Scheme 13).



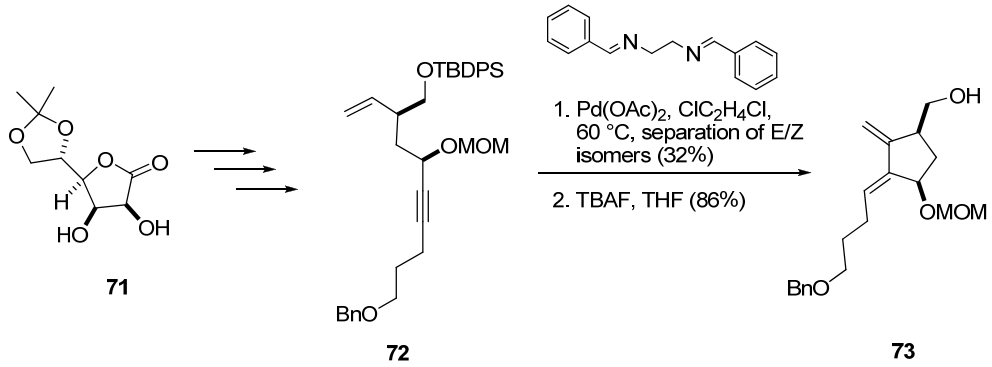
Scheme 13. Two attempts to access diene **63**

After failures with the above approaches, a new route employing palladium-mediated diene cycloisomerization to prepare diene **67** was investigated (Scheme 14).



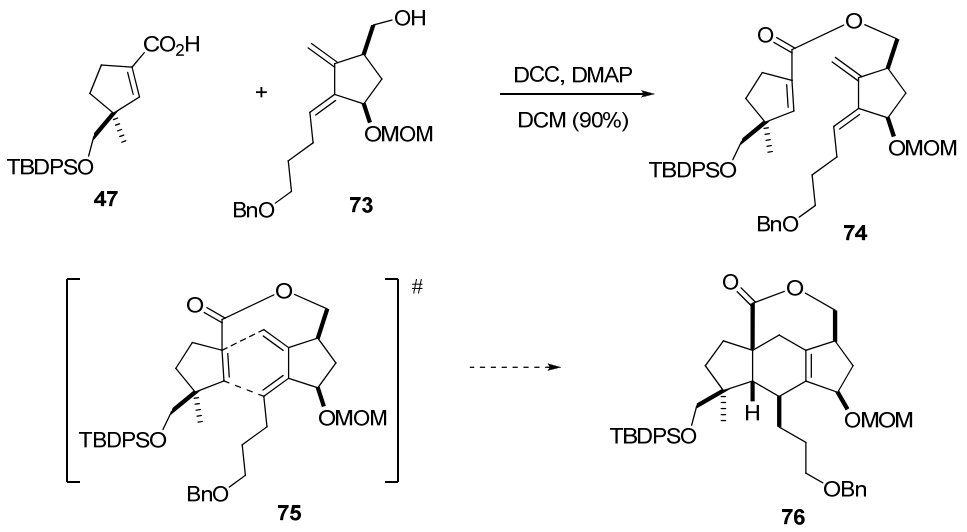
Scheme 14. A new strategy towards diene **67**

Lactone **71**, prepared in two steps from ascorbic acid,[29] was converted to cyclization precursor **72** in several steps. Under optimized conditions, cycloisomeration took pace to give a cyclopentane. Subsequent desilylation with tetrabutylammonium fluoride gave rise to alcohol **73** (Scheme 15).



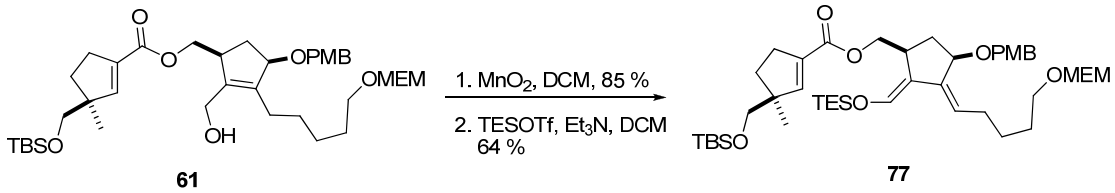
Scheme 15. Exploiting cycloisomerization in the synthesis of diene **73**

After alcohol **73** was esterified with carboxylic acid **47,** intramolecular Diels-Alder cycloaddition of **74** was attempted under both thermal and Lewis-acid mediated conditions but the desired transformation was never observed (Scheme 16).



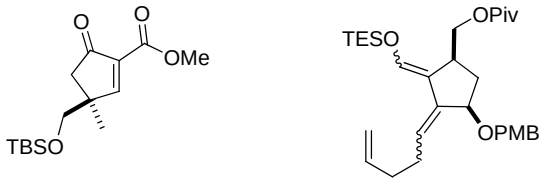
Scheme 16. Attempted intramolecular Diels-Alder cycloaddition of **74**

A possible remedy to this dilemma was explored by incorporating an activated diene or dienophile. To this end, diene **77** was prepared from alcohol **61** by manganese(IV) oxide oxidation and O-silylation (Scheme 17).



Scheme 17. Synthesis of activated diene **77**

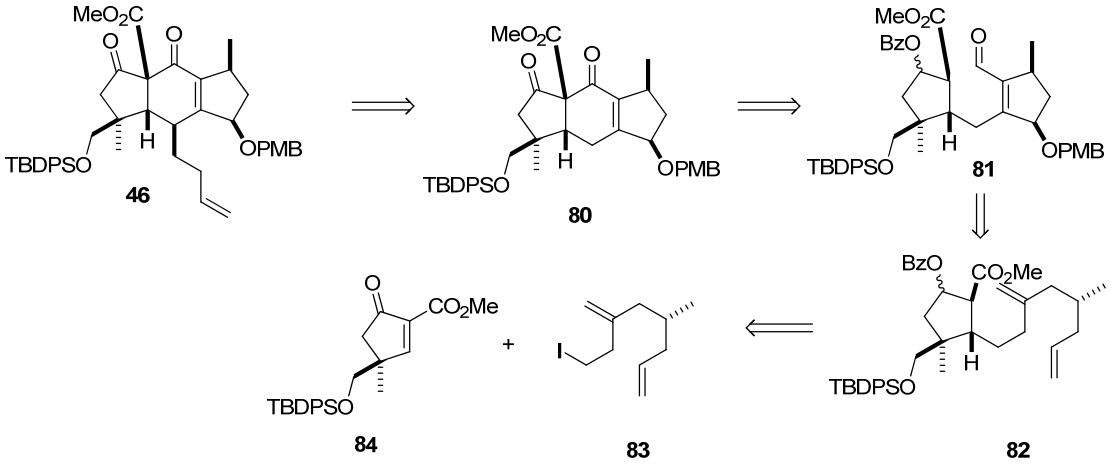
Diene **77** was resistant to cycloaddition under a variety of conditions, while attempts to engage activated dienophile **78** in cycloaddition with diene **79** were also fruitless.



78 **79**

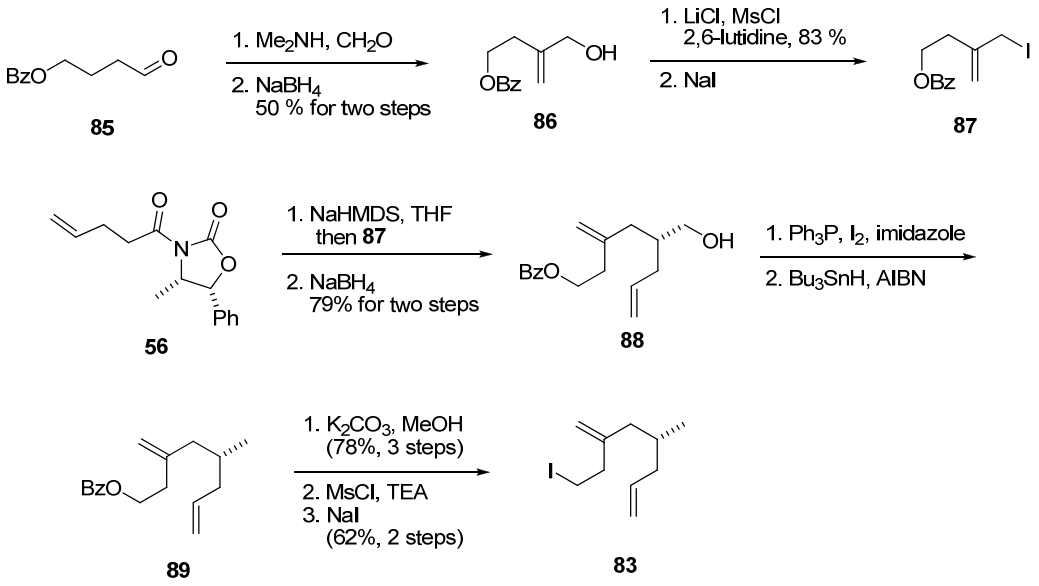
1.3.2.2 The Michael addition approach[30]

In light of the foregoing results, Paquette began an alternative route to assemble the pivotal enedione **46**. Michael addition of the cuprate generated from iodide **83** to cyclopentenonecarboxylate **84**[31] was anticipated to take place predominantly under kinetic control and in *anti* fashion. Aldol condensation was planned as the key step in taking methyl ester **82** to enedione **80** and γ-alkylation of the latter would then yield enedione **46** (Scheme 18).



Scheme 18. Paquette's Michael addition strategy towards enedione **46**

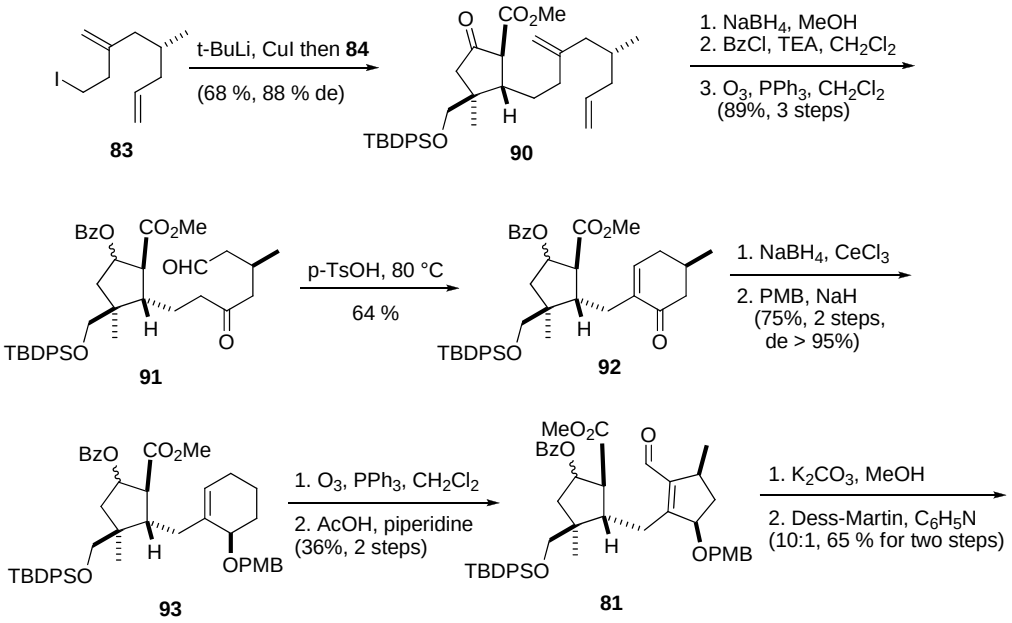
Iodide **87** was prepared from known benzoate **85**[32] in four steps. Mannich methylenation followed by hydride reduction furnished allyl alcohol **86**. *In situ* formed alkyl chloride was reacted with sodium iodide to provide **87**. Iodide **87** was used to alkylate the enolate of oxazolidinone **56**. Reductive removal of the chiral auxiliary produced alcohol **88,** which was deoxygenated in two steps to yield diene **89**. After saponification of benzoate **89**, the alcohol was activated as a mesylate and reacted with sodium iodide to afford homoallylic iodide **83** (Scheme 19).



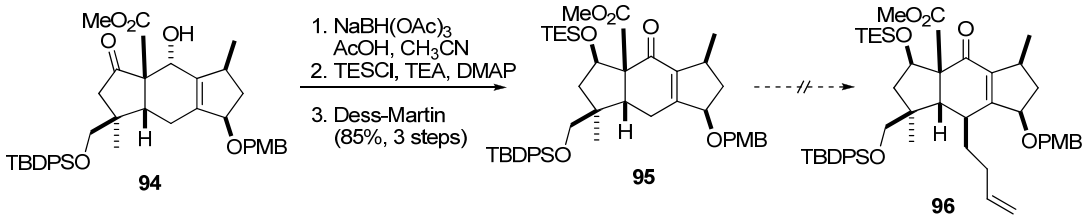
Scheme 19. Synthesis of homoallylic iodide **83**

Iodide **83** was converted *in situ* to a cuprate and added to cyclopentenonecarboxylate **84** to give a 16:1 mixture of diastereomers in favor of the desired isomer **90**. Chemoselective sodium borohydride reduction of the ketone functionality of **90** gave rise to a 2:1 mixture of diastereomeric alcohols, which were protected as their benzoates. Subsequent reductive ozonolysis furnished keto aldehyde

91, which underwent aldol condensation under acidic catalysis to afford cyclohexenone **92**. Luche reduction of **92** followed by protection of derived alcohol produced *p*-methoxybenzyl ether **93**. Ozonolytic ring opening and then piperidine-mediated aldol condensation converted **93** to aldehyde **81**. Basic hydrolysis of the benzoate mixture **81** revealed β-hydroxy esters which, when exposed to Dess-Martin periodinane in pyridine, underwent concomitant oxidation and cyclization to yield tricyclic β-keto ester **94.** Hydroxyl-directed delivery of hydride ion stereoselectively reduced the ketone of **94** to afford an alcohol which was protected as it's silyl ether and then subjected to Dess-Martin oxidation to yield cyclohexenone **95.** This set the stage for γ-alkylation of the enone moiety but all efforts to install the butenyl group in the γ position of **95** were unsuccessful (Scheme 20).

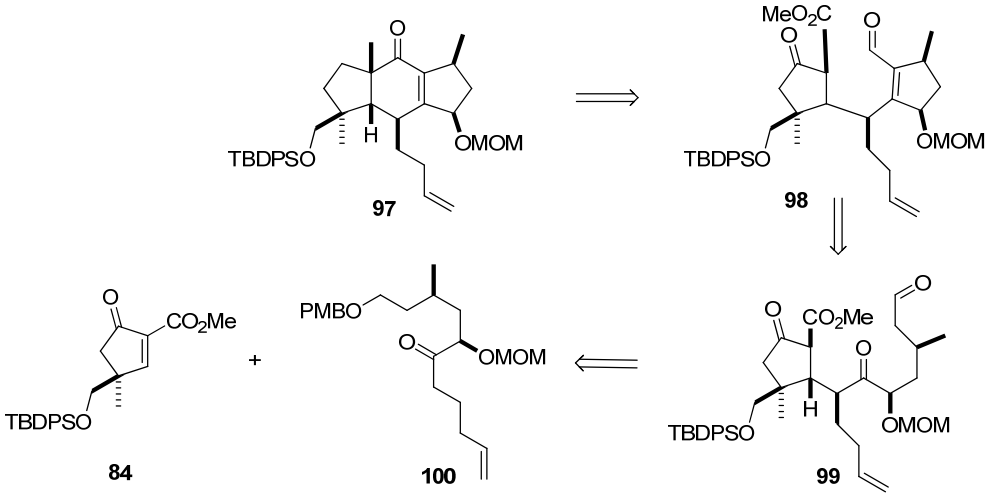


Scheme 20. Attempted synthesis of enone **96**



Scheme 20. Attempted synthesis of enone **96** (continued)

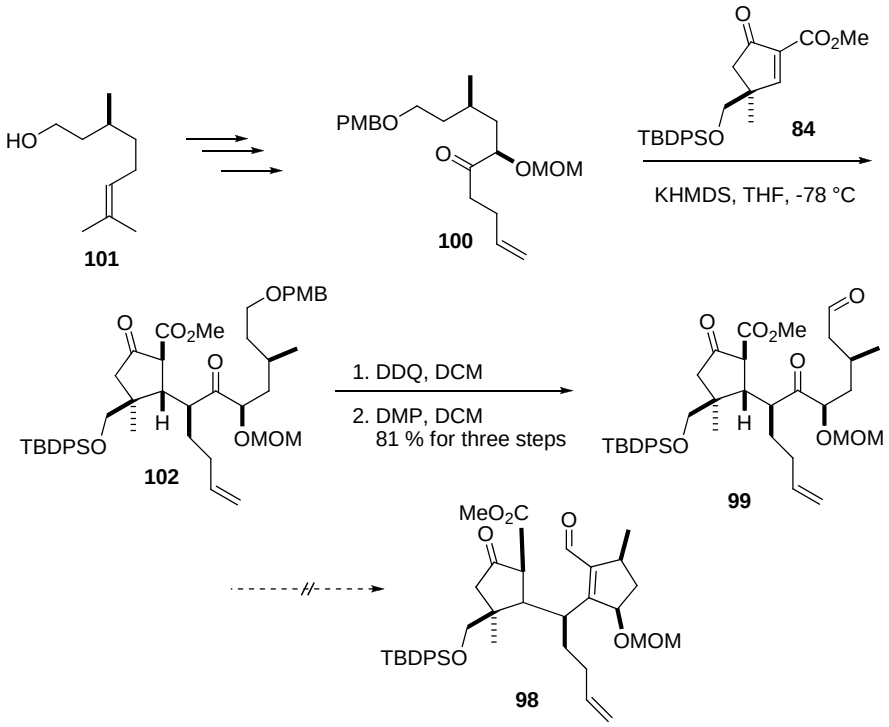
To circumvent the problematic installation of the butenyl substituent, Paquette turned his attention to ketone **100** in place of iodide **83.** In this approach enone **97** would be accessed via a tandem intramolecular aldol condensation of aldehyde **99** (Scheme 21).



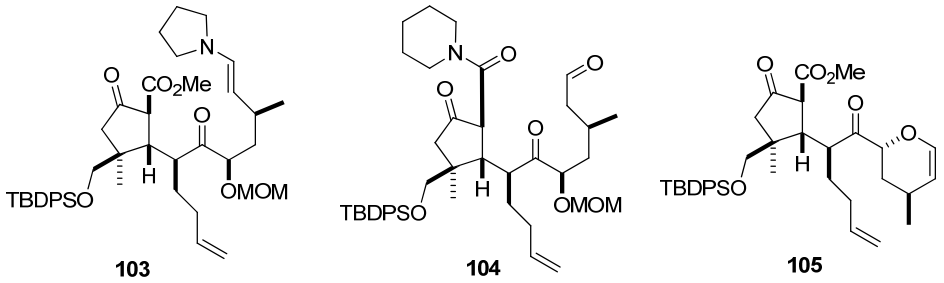
Scheme 21. Paquette's new strategy with preset butenyl appendage

Ketone **100** was prepared in ten steps from *(S)*-(-)-citronellol (**101**). After deprotonation of **100** with potassium hexamethyldisilazane, Michael addition to **84** took place to give diastereomerically pure cyclopentanone **102**. Chemoselective deprotection of *p*-methoxybenzyl ether was accomplished with 2,3-dichloro-5,6-

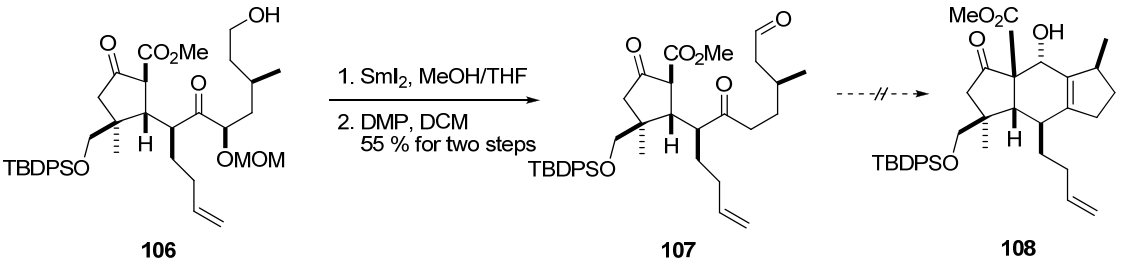
dicyanobenzoquinone and periodinane oxidation of the resulted alcohol produced diketo aldehyde **99**. Aldol condensation of **99** was attempted under a variety of conditions without success but when the diketo aldehyde was exposed to piperidine in refluxing ether, enamine **103** was detected. A similar outcome was observed when pyrrolidine was used. Switching to benzene and toluene as solvent, formation of amide **104** was observed. When camphorsulphonic acid in refluxing benzene was used with **99**, deprotection of the methoxymethyl group took place which was followed by facile hemiacetal formation and dehydration to afford cyclic vinyl ether **105** (Scheme 22).



Scheme 22. Attempted synthesis of cyclopentecarboxaldehyde **98**



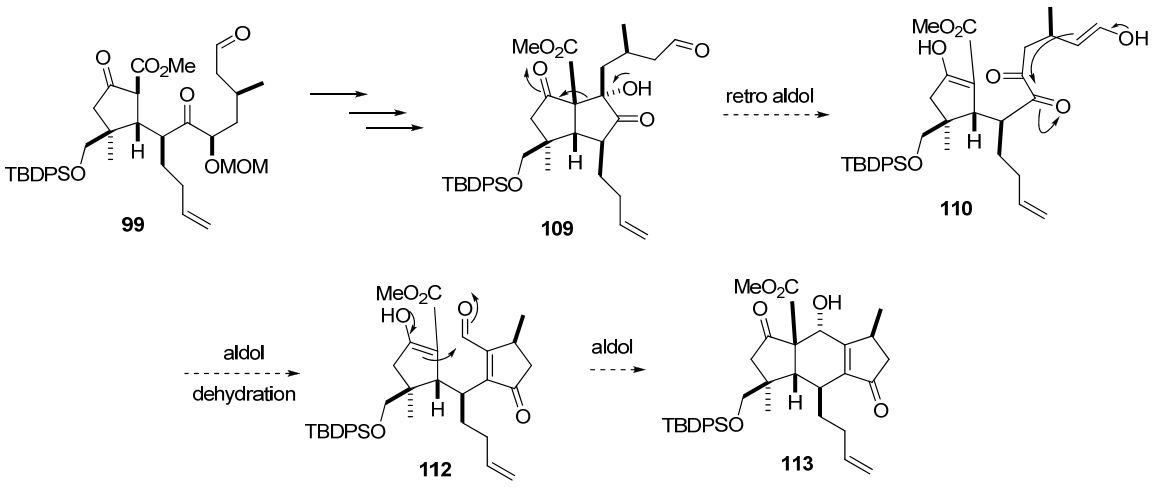
The failure to close the ring C of mangicol A was ascribed to steric hindrance surrounding the ketone moiety in **99**. It was conjectured that removal of the methoxymethyl group would relieve this strain and perhaps decrease the activation energy for aldol condensation. To this end, aldehyde **107** was prepared in two steps from alcohol **106**. However, the aldehyde proved resistant to a variety of bases typically used for aldol condensations and no evidence for formation of **106** was found (Scheme 23).



Scheme 23. Attempted condensation on substrate **107** lacking methoxymethyl group

Another route to mangicol A that Paquette's group explored was based on harnessing the reversibility of the aldol condensation. The requisite precursor for this approach, cis-bicyclic α-hydroxy ketone **109,** was prepared in six steps from cyclopentanone **99**. It was envisioned that treatment of this ketone would initiate a

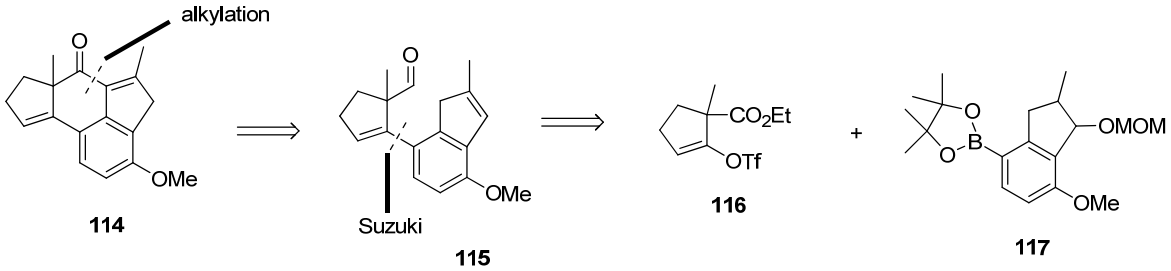
retroaldol reaction which would be followed by a tandem aldol condensation-dehydration sequence (Scheme 24). In the event, there was no reaction of **109** when a variety of bases was used.



Scheme 24. Paquette's retroaldol-aldol strategy to access β-keto ester **113**

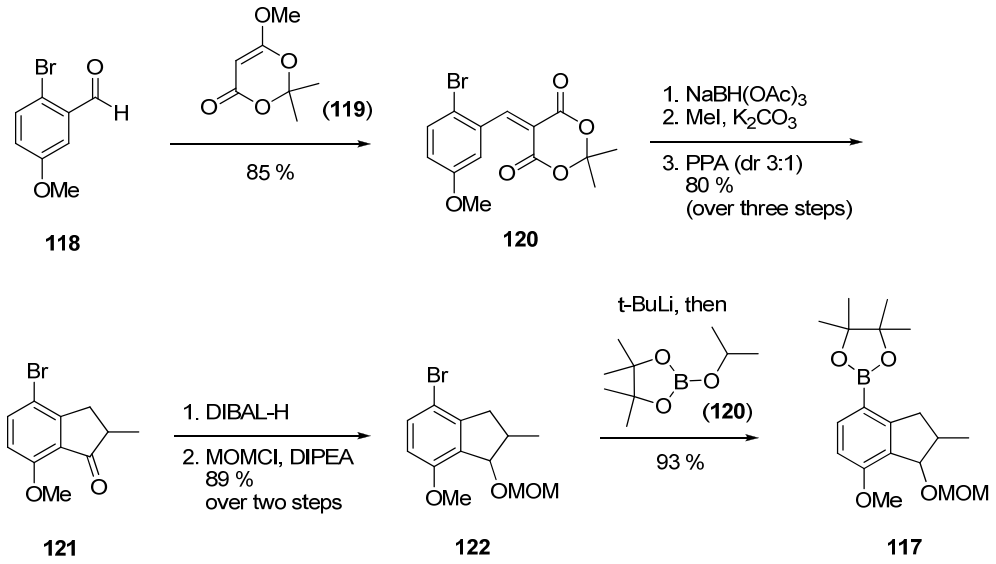
1.3.3 Synthetic studies on neomangicol C by the Sarpong group

Sarpong's approach to constructing the core of neomangicol C relies on late stage intramolecular alkylation of indene **115**, which would be generated from coupling of vinyl triflate **116** with boronic ester **117** (Scheme 25).



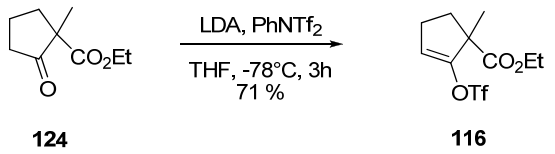
Scheme 25. Sarpong's strategy for racemic synthesis of the neomangicol C core

The synthesis of boronic ester **117** started with Knoevenagel condensation of benzaldehyde **118**[33] with Meldrum's acid (**119**).[34] Reduction of alkylidene **120** followed by methylation and formal Friedel-Crafts acylation, was accompanied by loss of acetone and decarboxylation, to produce indanone **121**. Diisobutylaluminum hydride reduction of **121** and methoxymethyl protection of the resulting alcohol yielded ether **122**. Lithiation aryl bromide **122** with *tert*-butyllithium and quenching with dioxaborolane **123**, gave boronic ester **117** (Scheme 26).



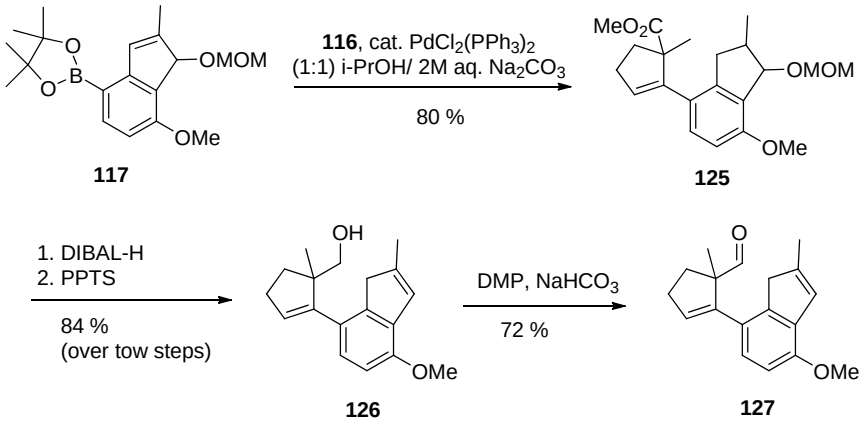
Scheme 26. Sarpong's synthesis of boronic ester **117**

Vinyl triflate **116** was obtained from known β-ketoester **124**[35] (Scheme 27) which can be prepared in enantiopure form thus opening the door for the enantioselective synthesis of neomangicol C.[36]



Scheme 27. The synthesis of vinyl triflate **116**

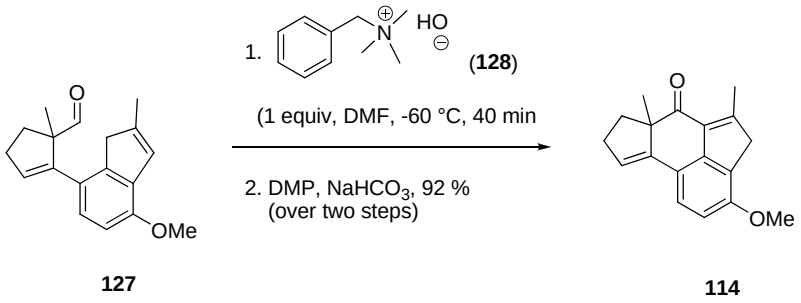
Suzuki coupling of boronate **117** with vinyl triflate **116** afforded methyl ester **125** in high yield. Diisobutylaluminium hydride reduction of **125** followed by deprotection of the methoxymethyl ether and dehydration produced indene **126** which upon exposure to Dess-Martin periodinane yielded aldehyde **127** (Scheme 28).



Scheme 28. Sarpong's synthesis of aldehyde **127**

Deprotonation of indenes and subsequent trapping of the anion is a well studied process.[37] In the case of **127**, however, commonly used bases to effect deprotonation of indenes (*tert*-butyllithium, potassium *tert*-butoxide, lithium tetramethylpiperidide) gave no desired product. Fortunately, trimethylbenzylammonium hydroxide (**128**)[38] proved to be an effective base for

cyclization of **127**. Oxidation of the resultant alcohol generated ketone **114**. The tetracycle **114** resembles the core of mangicol C but no further progress towards **10** has been recorded (Scheme 29).



127 **114**

Scheme 29. Sarpong's synthesis of the tetracyclic core of neomangicol C

1.4 References

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[3] The name mangicols is derived from the term "mangicolous," which is used to describe microorganisms that grow in mangrove environments. The neomangicols were named so because the mangicol skeleton is thought to be related biosynthetically to the neomangicols skeleton.

[4] This fungus was identified as a strain of *Fusarium heterosporum*, by David Porter (U. Georgia) based on morphological characteristics as *Fusarium* sp. by FAME analysis (Microbial I.D., Inc., Newark, DE) with similarity index of 0.965.

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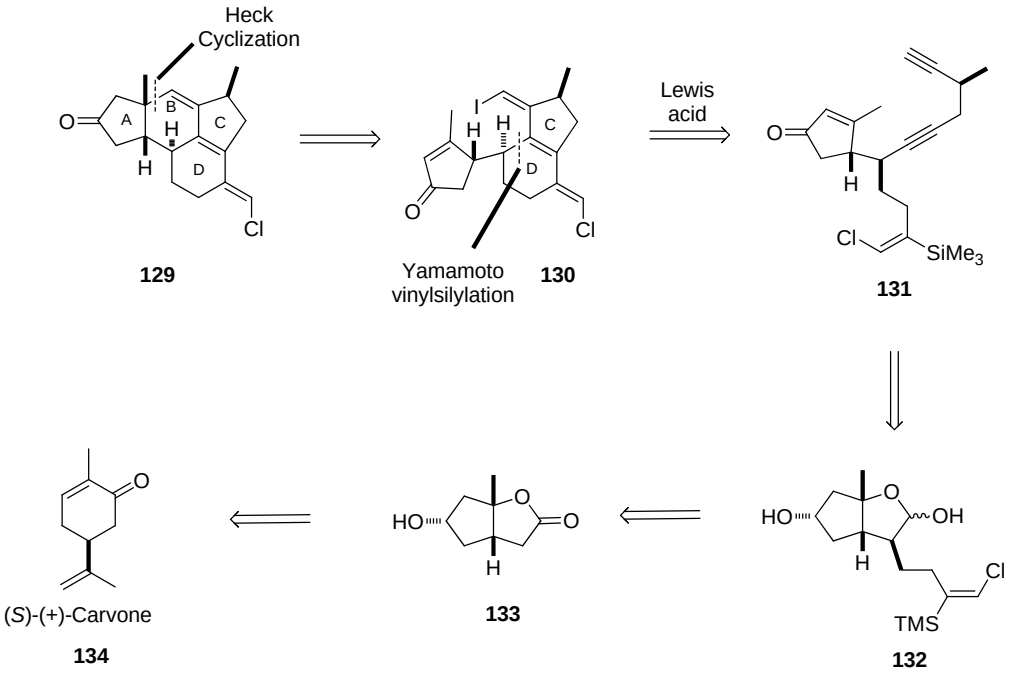
CHAPTER 2

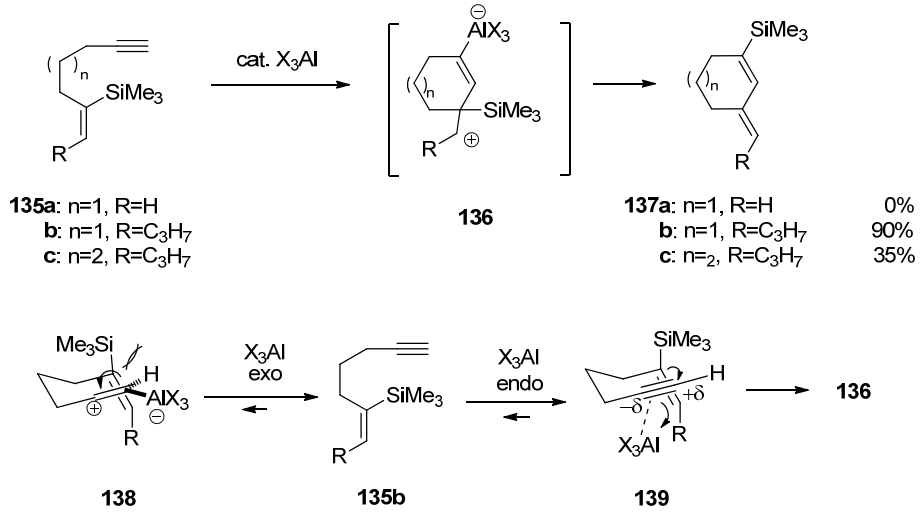
2.1 First generation approach to the core of neomangicol A

Our first approach to assembling tetracyclic core of neomancigol A **129** was designed around reductive Heck cyclization of tricyclic vinyl iodide **130** as the final move to install ring B. The synthesis of Heck precursor **130** would hinge on a cascade intramolecular vinylsilylation of diyne **131** which would simultaneously create rings C and D of **130** and install the hydrindane core embedded in the natural product. Diyne **131** would originate from lactol **132**, prepared by alkylation of known lactone **133**. (*S*)-(+)-carvone (**134**) is the source of asymmetry in **133** (Scheme 30).



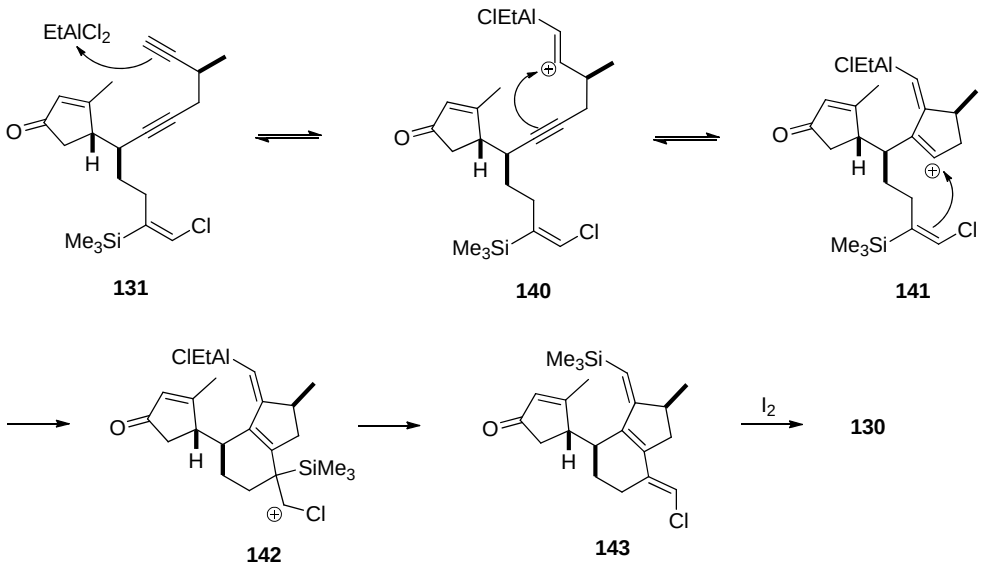
Scheme 30. First generation retrosynthetic analysis of the core of neomangicol A

A key step in the retrosynthetic plan shown in Scheme 30 is the transformation of **131** to **130**. Yamamoto has shown that vinylsilanes **135** undergo intramolecular stereoselective (*trans* addition) and regioselective (*endo* cyclization) carbometalation of unactivated alkynes in the presence of a catalytic amount of a Lewis acid to give carbocycles **137**. Zwitterion **136** is proposed as an intermediate, which then undergoes trimethylsilyl migration followed by regeneration of the catalyst (Scheme 31).[1] The R group of **135** plays a crucial role in the cyclization process by stabilizing the cationic center in **136**. To account for *endo* selectivity in this cyclization, Yamamoto considered intermediates **138** and **139** that lead to *exo* and *endo* cyclization products, respectively. Due to steric repulsion between the vinyl hydrogen and the trimethylsilyl moiety in **138**, π-complex **139** is believed to be the major component in the equilibrium and cyclization proceeds through this complex towards **136**. Retention of alkene geometry in this process, as in other cases of electrophilic substitution of vinylsilanes, is well documented in the literature.[2]



Scheme 31. *Endo* carbometalation of unactivated alkynes

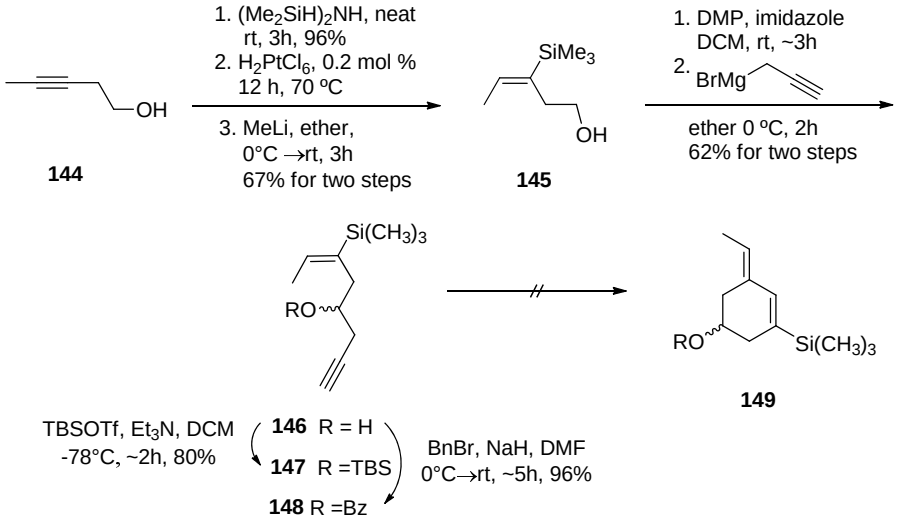
As outlined in our retrosynthetic analysis (Scheme 30), the plan was to expose diyne **131** to a Lewis acid in order to forge hydrindane **130** via a cascade cyclization initiated by vinyl carbenium ion **140**. The latter would hypothetically produce vinyl carbenium ion **141** via a first endo cyclization; subsequent cyclization of **141** would be driven by formation of carbenium ion **142** in which stabilization by a β-silicon atom plays the dominant role. After silyl transfer to give vinylsilane **143**, exchange with iodine would afford vinyl iodide **130**. Extended π electron conjugation in **143** adds driving force to the overall sequence (Scheme 32).



Scheme 32. An approach to **130** via cascade Lewis acid-catalyzed vinylsilylation of **131**

Before we set out to prepare **131**, we decided to test our plan in a model system that would mimic ring D formation in **130**. Vinylsilanol **145** was prepared in three steps from homoallylic alcohol **144**, as described by Marshall.[3] After alcohol **145** was exposed to Dess-Martin reagent, the resultant aldehyde was reacted with

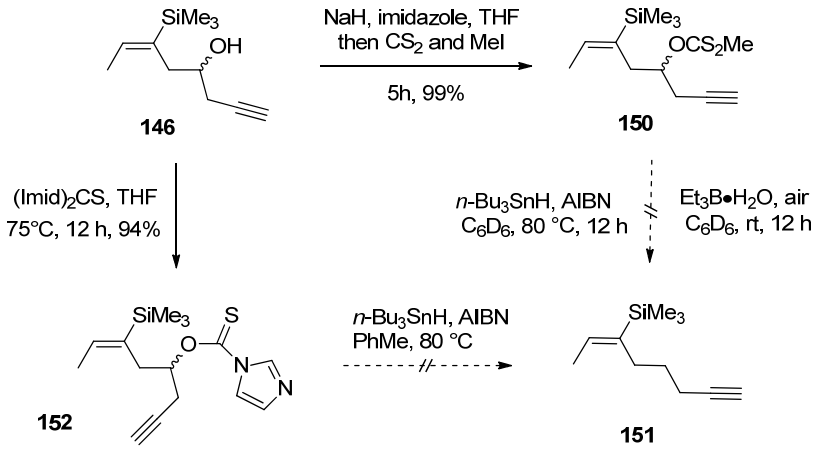
propargylmagnesium bromide[4] to yield alcohol **146**. However, initial attempts to cyclize alcohol **146** using stoichiometric dichloroethylaluminum(III) chloride as a Lewis acid in dichloromethane led to decomposition of the starting material. As an alternative to alcohol **146**, *tert*-butyldimethylsilyl and benzyl ethers of **146** were tested as cyclization precursors. Exposure of **147** to either a catalytic amount or an equivalent of dichloroethylaluminum(III) chloride led to recovery of starting material but when excess of the Lewis acid was used we observed an identifiable mixture. Exposure of **148** to either catalytic or stoichiometric dichloroethylaluminum(III) chloride led to complex mixtures whereas use of stoichiometric aluminum(III) bromide caused decomposition of **148** (Scheme 33).



Scheme 33. Attempts to effect cyclization of vinylsilanes **146**, **147** and **148**

A possible explanation for the failure of our substrates **146**-**148** to undergo intramolecular Yamamoto vinylsilylation is competing coordination of the catalyst

with the homopropargylic oxygen function. A solution to this problem could be a substrate in which the oxygen substituent is removed, and to this end Barton-McCombie deoxygenation was investigated for excising the hydroxyl group from **146**. Deprotonation of **146** with sodium hydride and interception of the resultant alkoxide with carbon disulfide yielded a sodium xanthate which was reacted with methyl iodide to furnish methyl xanthate **150**. When **150** was exposed to an equivalent of tri-*n*-butyltin hydride in the presence of a catalytic amount of 2,2′-azobis(2-methylpropionitrile) in benzene no reaction occurred.[5] Deoxygenation of **150** to **151** was also attempted under tin-free conditions with triethylborane-water complex in the presence of air[6] but again no change took place (Scheme 34).

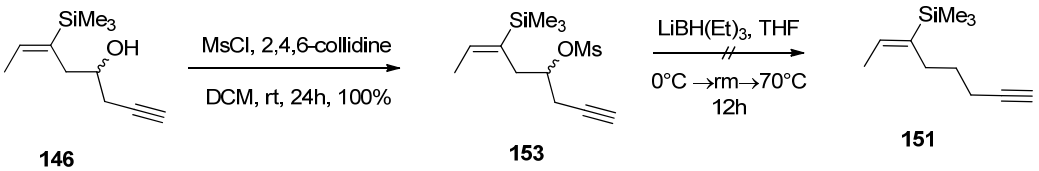


Scheme 34. Deoxygenation of alcohol **146** via a Barton-McCombie reaction

Another commonly used reagent to accomplish Barton-McCombie deoxygenation of alcohols is 1,1'-thiocarbonyldiimidazole,[7] and when **146** was exposed to this reagent in tetrahydrofuran it furnished in high yield thioester **152**.

Unfortunately, all efforts to deoxygenate **152** with tri-*n*-butyltin hydride resulted in decomposition of the starting material (Scheme 34).

An alternative method to remove a hydroxyl group consists of a two step sequence in which the alcohol is first converted to a sulfonate ester and the sulfonate is then cleaved reductively. To this end, alcohol **146** was reacted with methanesulfonyl chloride in the presence of 2,4,6-collidine to provide mesylate **153**. However, attempts to reduce **153** with lithium triethylborohydride (Super Hydride®)[8] either led to recovery or to decomposition of the starting material depending on the equivalence of the reducing agent used (Scheme 35).

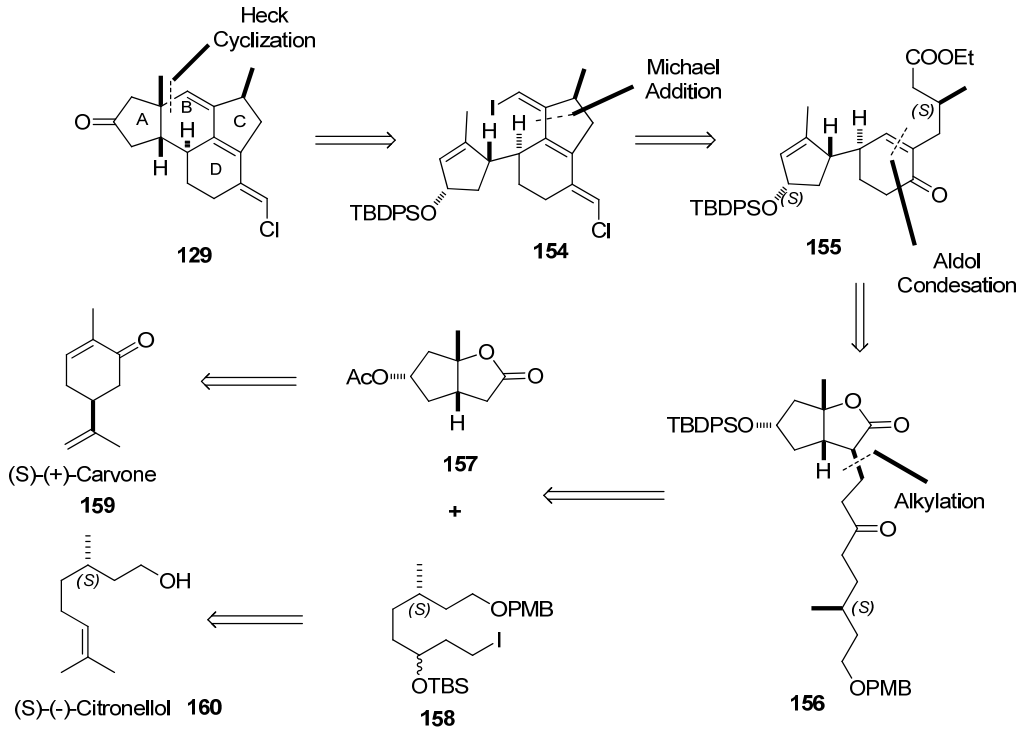


Scheme 35. Attempted deoxygenation of **146** via mesylate reduction

The failure to demonstrate intramolecular vinylsilylation with model substrates **146-148** convinced us that the strategy outlined in Scheme 30 for elaboration of rings C and D of neomangicol A from diyne **131** is unworkable. Consequently, this approach was abandoned and a new route was designed for building the hydrindane sector of the neomangicol framework.

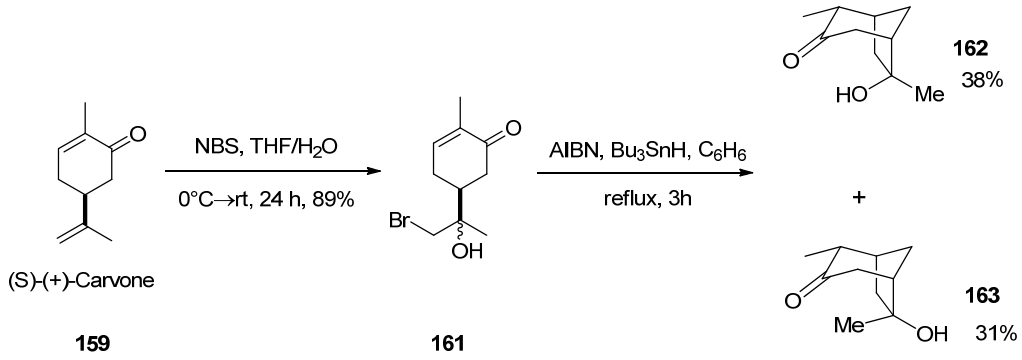
2.2 Second generation approach to the core of neomangicol A

As with our first generation approach to ketone **129** which bears the tetracyclic core of neomangicol A, the key move towards installation of ring B in this new route is an intramolecular reductive Heck[9] reaction of vinyl iodide **154**. The novel aspect of the new plan is construction of ring C via intramolecular Michael addition to cyclohexenone **155** and construction of ring D via an intramolecular aldol condensation of keto lactone **156**. Alkylation of known lactone **157**[10] with alkyl iodide **158** would pave the way to **156**, and monoterpenes (*S*)-(+)-carvone (**159**) and (*S*)-(-)-citronellol (**160**) would be the chiral precursor of **157** and **158**, respectively (Scheme 36).



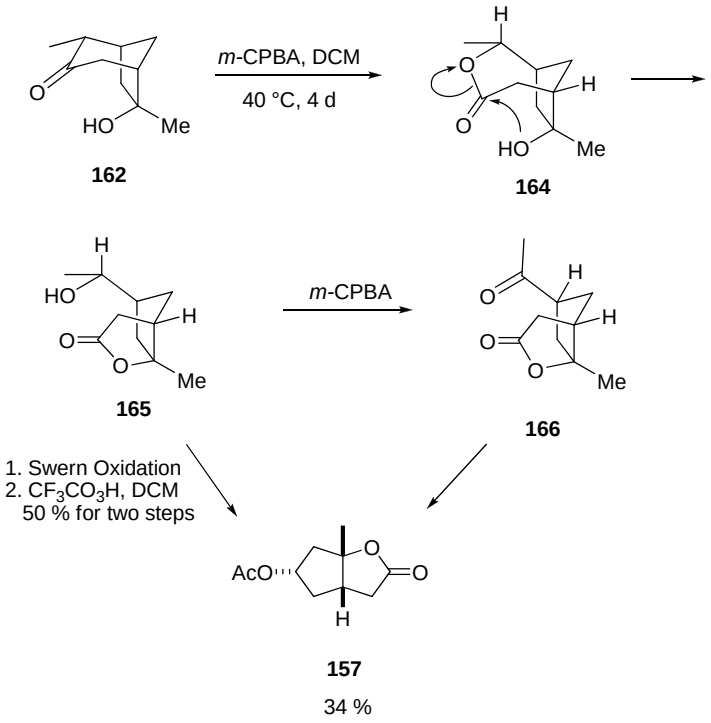
Scheme 36. Second generation retrosynthetic analysis of the core of neomangicol A

Synthesis of lactone **157** commenced with treatment of (*S*)-(+)-carvone (**159**) with *N*-bromosuccinimide in aqueous tetrahydrofuran to furnish bromohydrin **161** as a 1:1 mixture of diastereoisomers.[11] When this mixture was reacted with *n*-tributyltin hydride in the presence of a catalytic amount of 2,2′-azobis(2-methylpropionitrile), cyclization took place to yield a mixture of separable bicyclic hydroxy ketones **162** and **163** (Scheme 37).[12]



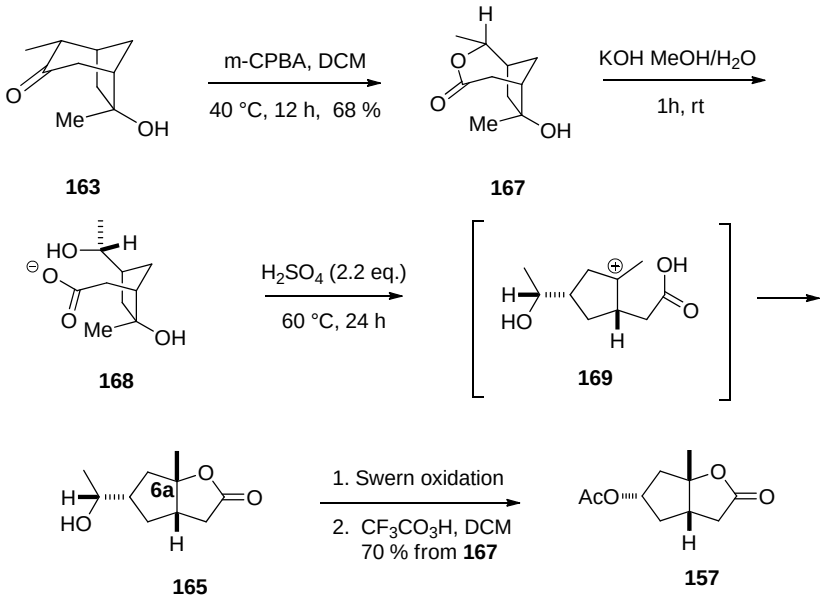
Scheme 37. Synthesis of bicyclic hydroxy ketones **162** and **163**

Oxidation of **162** with *m*-chloroperoxybenzoic acid effected three sequential oxidative processes in one pot. The cascade began with Baeyer-Villiger oxidation of **162** to give lactone **164** which underwent intramolecular translactonization to yield hydroxy lactone **165**. This alcohol was partially oxidized with *m*-chloroperoxybenzoic to keto lactone **166** which underwent a second Baeyer-Villiger oxidation to give desired lactone **157**. The remaining unreacted **165** was subjected to Swern oxidation to provide keto lactone **166** which served as a substrate for Baeyer-Villiger oxidation with trifluoroperacetic acid to give a further quantity of **157**. In this manner, **162** was transformed to lactone **157** in an overall yield of 34 % (Scheme 38).[13]



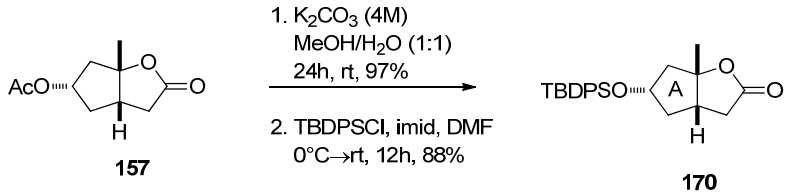
Scheme 38. Synthesis of *cis* fused bicyclic lactone **157** from **162**

The diastereomeric bicyclic ketone **163** from **161** was also subjected to Baeyer-Villiger oxidation and gave seven-membered lactone **167** in good yield. Basic hydrolysis of **167** formed carboxylate **168** which was relactonized under acidic conditions, most likely through carbenium ion **169** to furnish alcohol **165** in a process that was accompanied by inversion at C6a. A two-step oxidation sequence first took alcohol **165** to its corresponding methyl ketone under Swern conditions and then to acetate **157** by Baeyer-Villiger oxidation (Scheme 39).[14]



Scheme 39. Synthesis of *cis* fused bicyclic lactone **157** from **163**

Thus, both stereoisomeric ketones **162** and **163** obtained from bromohydrin **161** were ultimately converted to our desired lactone **157**. The total yield of **157** from bromohydrin **161** via this sequence was 11 %. Saponification of lactone **157** under basic conditions revealed a secondary alcohol which was promptly protected as its *t*-butyldiphenylsilyl ether **170** in preparation for appending the side chain of **156** (Scheme 40).



Scheme 40. Synthesis of *cis* fused bicyclic lactone **170** from **157**

Our first approach toward alkylation of γ-lactone **170** was based on Michael addition of the enolized lactone to methyl vinyl ketone (**172**) but this resulted only in recovery of the starting material, probably due to facile reversibility of this 1,4-addition. However, when methyl iodide or pentyl iodide were reacted with **170** in the presence of lithium diisopropylamide, the alkylated lactones were obtained in almost quantitative yield as single diastereomers according to nuclear magnetic resonance analysis. The folded conformation of lactone **170**, as well as literature precedent,[15] suggests that alkylation of this bicycle took place exclusively from the *exo* face to produce **173** and **174** (Scheme 41).

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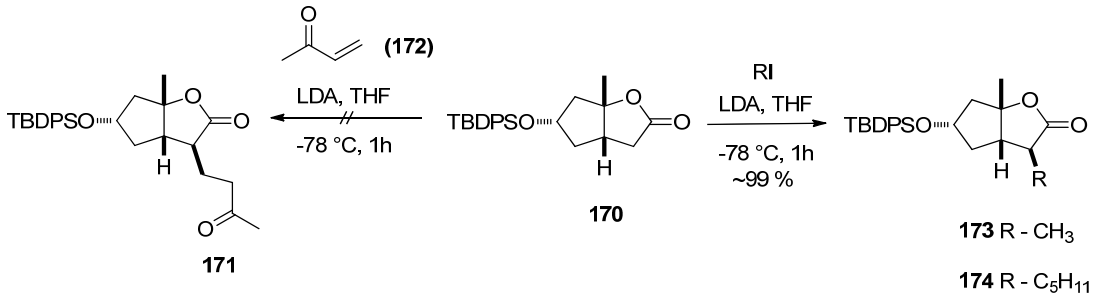


Scheme 41. Model studies on alkylation of lactone **170**

Support for the stereochemistry of **173** was provided by nuclear Overhauser (nOe) experiments. When each of the methyl groups on the lactone was irradiated, nOe interactions were observed between the methyl substituent at C6a and the hydrogen at C3a, as expected for a cis fused bicyclic[3.3.0]octane framework, and between the methyl group at C3 and the hydrogen at C3a. This strongly implies that

the methyl substituent at C3 is exo and that this carbon therefore has (*S*) configuration (Fig 2).

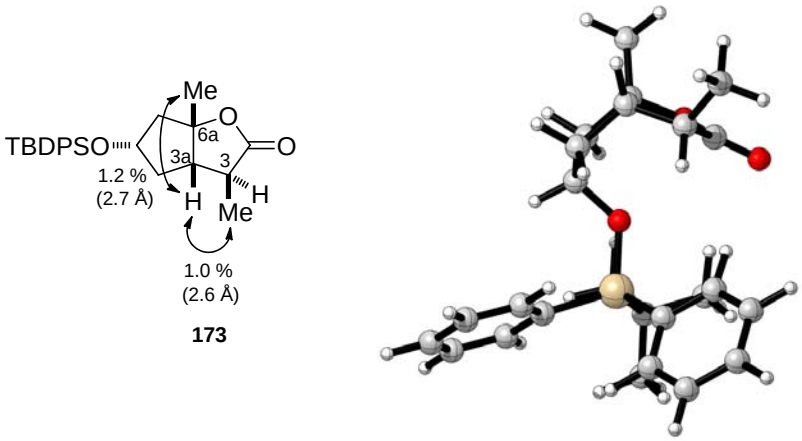
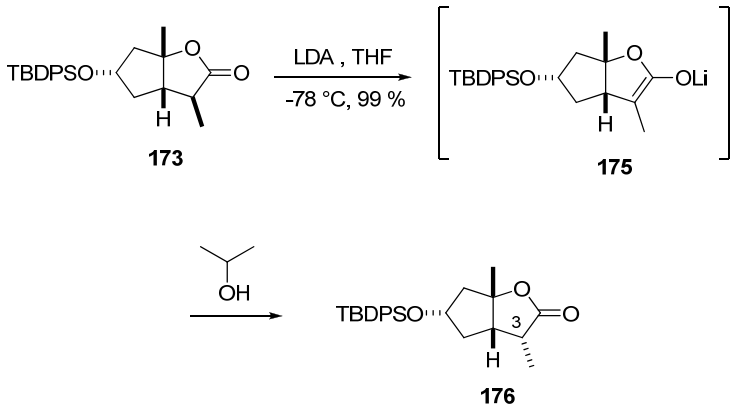


Fig 2. nOe interactions of *exo* lactone **173**[16]

Additional evidence for the configuration of **173** came from its exposure to lithium diisopropylamide. This generated lithium enolate **175** which was kinetically protonated with isopropyl alcohol from the exo face to give C3 epimeric lactone **176** in almost quantitative yield (Scheme 42).[17]



Scheme 42. Kinetic protonation of lithium enolate **175** to give **176**

When hydrogen atoms at carbons C3 and C3a in **176** were irradiated, reciprocal nOe interactions were observed confirming that the C3 methyl substituent in this stereoisomer is in the *endo* orientation (Fig 3).

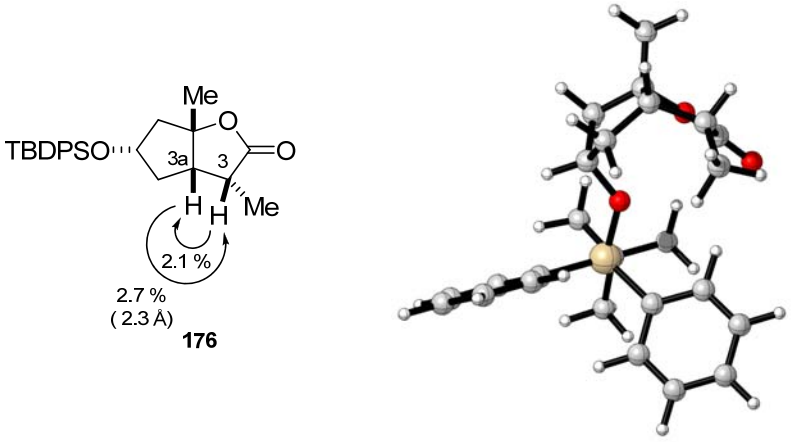
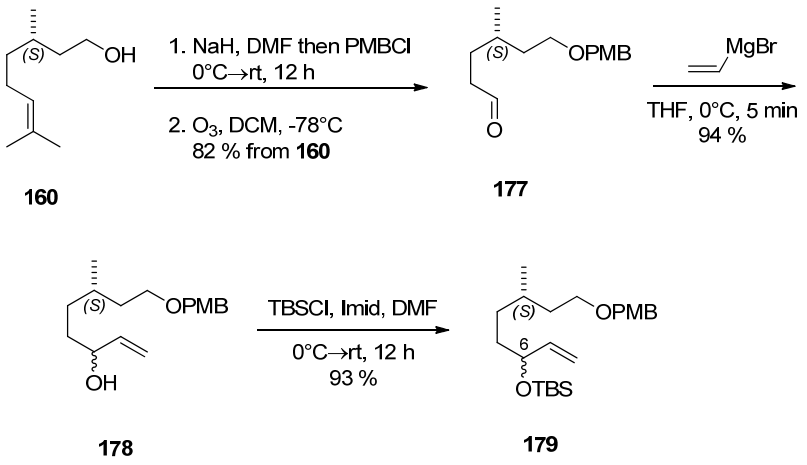


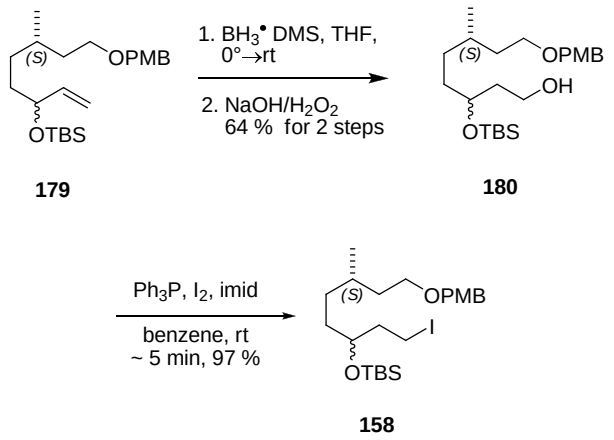
Fig 3. nOe interactions of *endo* lactone **176**

Having established that bicyclic latone **170** can be alkylated cleanly to give the *exo* product, attention turned towards synthesis of the fully functionalized chain needed for neomangicol A. Synthesis of alkyl iodide **158** commenced from commercially available (*S*)-(-)-citronellol (**160**), the primary alcohol of which was first protected as its *p*-methoxybenzyl ether. The ether was immediately submitted to ozonolytic fission of the carbon-carbon double bond to produce aldehyde **177** which was reacted with vinylmagnesium bromide to give a 1:1 diastereomeric mixture of allylic alcohols **178**. The alcohols, which were inseparable, were protected as their *t*-butyldimethylsilyl ethers **179**. Since the oxygen at C6 of **179** was destined to become a ketone at a later stage, no attempt was made to separate epimers at this point (Scheme 43).



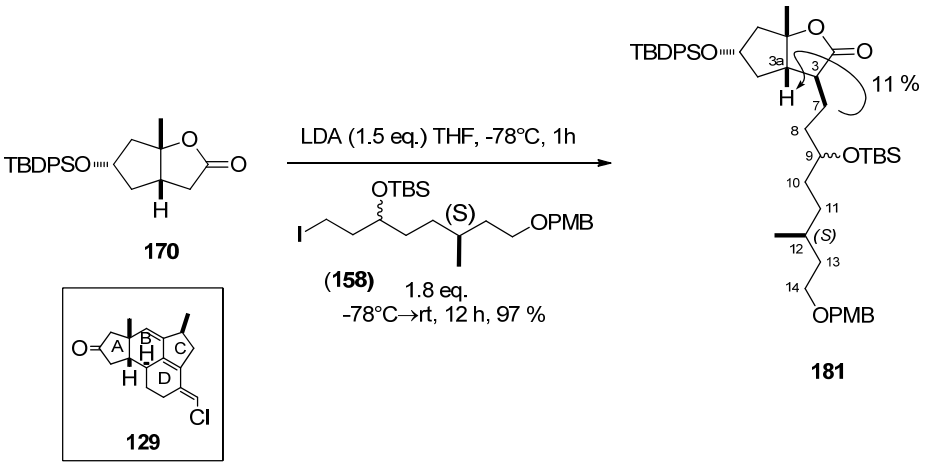
Scheme 43. Synthesis of ethers **179** from **160**

The mixture of ethers **179** was taken forward through a hydroboration-oxidation sequence to furnish a stereoisomeric mixture of alcohols **180** which was exposed to iodine in the presence of triphenylphosphine and imidazole to give alkyl iodide **158** in high yield (Scheme 44).



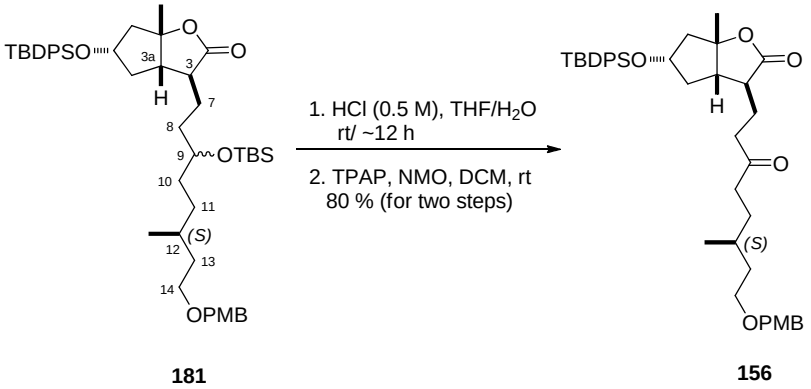
Scheme 44. Synthesis of alkyl iodide **158** from **179**

The conditions used to alkylate lactone **170** with methyl iodide were used for alkylation of **170** with alkyl iodide **158**. Thus, reaction of **170** with 1.5 equivalents of lithium diisopropylamide to effect deprotonation of the lactone followed by exposure of the resultant enolate to 1.8 equivalents of iodide **158** at -78 ºC and then warming of the mixture to room temperature yielded a 1:1 diastereomeric mixture of alkylated lactone **181** in almost quantitative yield. The diastereomers were inseparable because of the presence of (*R*) and (*S*) *t*-butyldimethylsilyl ethers but this was inconsequential as the carbon bearing *t*-butyldimethylsilyloxy group (C9) was destined to become a ketone at the next step. The configuration at C3 of **181** was again confirmed by a nOe experiment. Thus, when the hydrogen at C3a was irradiated, a nOe interaction was observed between this hydrogen and a methylene hydrogen at C7 of the side chain. This indicated, as expected, that alkylation of **170** by **158** had taken place at the *exo* face of the bicyclic lactone. It is noteworthy that **181** contains not only all fourteen of the carbon atoms needed to assemble the core of neomangicol A but also carries the correct stereochemical signature for tetracycle **129** at C3, C3a and C12 (Scheme 45).[18]



Scheme 45. Alkylation of lactone **170** by iodide **158**

Having secured a route to **181**, we set out to prepare keto lactone **156**, the prospective candidate for an intramolecular aldol condensation. Triether **181** was taken forward by performing selective deprotection of the *t*-butyldimethylsilyl ether under acidic conditions to reveal a secondary alcohol at C9 which was oxidized with tetrapropylammonium perruthenate to give diastereomerically pure ketone **156** (Scheme 46).

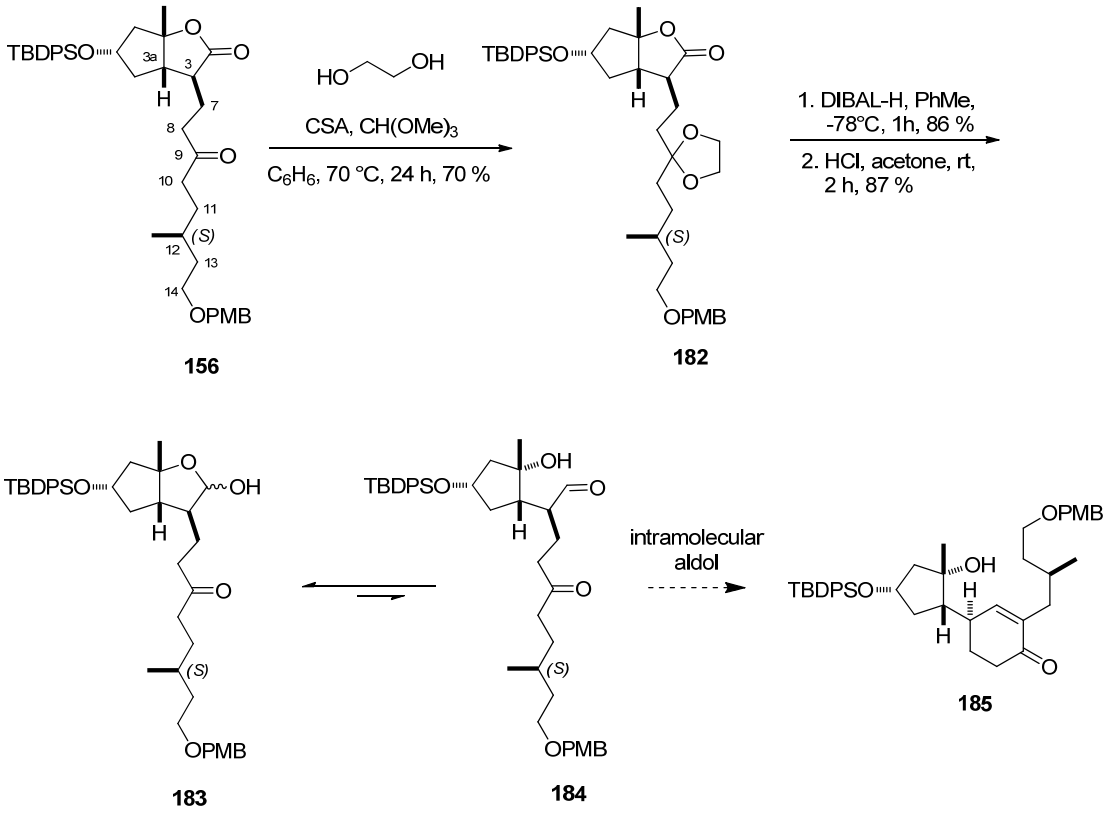


181 **156**

Scheme 46. Synthesis of diastereomerically pure ketone **156** from **181**

In order to reduce the γ-lactone of **156** selectively, it was first necessary to mask the keto group at C9. Conversion of **156** to a ketal with ethylene glycol in the presence of a catalytic amount of camphorsulfonic acid furnished **182** which was submitted to reduction with diisobutylaluminum hydride. This afforded a 1:1 diastereomeric mixture of lactols, deketalization of which under acidic catalysis proceeded uneventfully to furnish keto lactol **183**. It was assumed that **183** would be in equilibrium with hydroxy aldehyde **184**, and although **184** was undetectable by

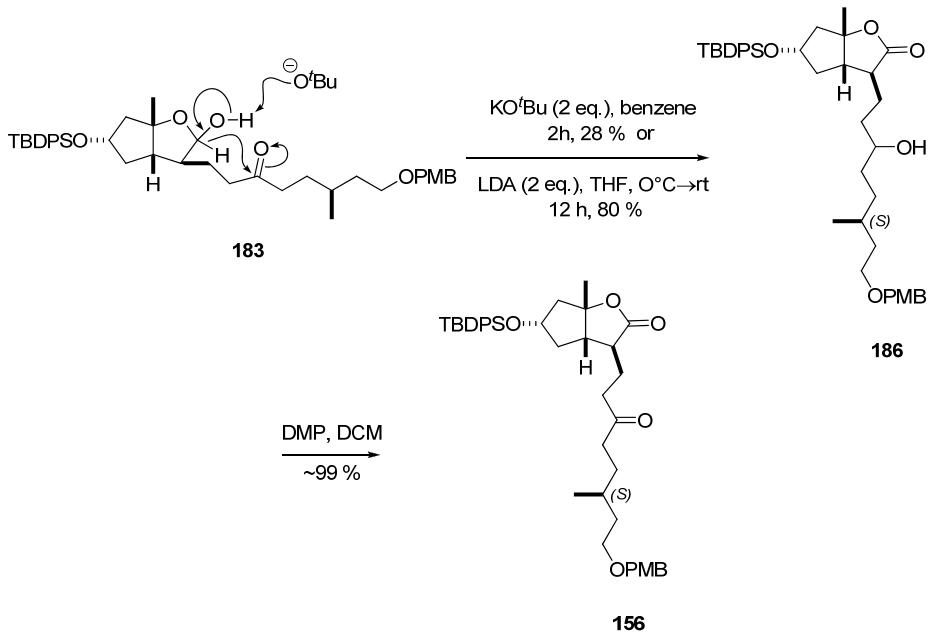
spectroscopic means chemical evidence (*vide infra*) suggested the presence of **184** in equilibrium with **183** (Scheme 47).



Scheme 47. Synthesis of intramolecular aldol precursor **183** from **156**

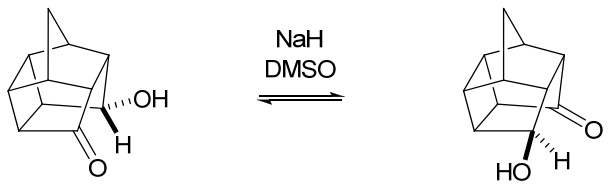
Initial attempts at promoting intramolecular condensation of the **183**/**184** mixture were executed under acidic conditions.[19] A variety of Brønsted and Lewis acids were screened but none of the desired product **185** could be detected; only decomposition or recovery of the starting material was encountered. We then turned our attention to aldol condensation of **183**/**184** under basic conditions. It was found

that when lactol **183** was exposed to potassium *t*-butoxide it consistently gave a new compound and that when lithium diisopropylamide was used as a base the same transformation transpired in higher yield. Careful analysis of spectroscopic properties of the product from **183** revealed that the ketone had been reduced to an alcohol and that the γ-lactone had been regenerated. Thus, an internal redox process had taken place characteristic of an intramolecular Cannizzaro reaction to give **186** as a single diastereomer (according to ^{13}C nuclear magnetic resonance data). Additional evidence for the identity of this unexpected product came from oxidation of **186** with Dess-Martin periodinane to yield keto lactone **156** (Scheme 48). A mechanism delineating the putative 1,5-hydride transfer required to produce **186** from **183** is shown in Scheme 48.



Scheme 48. Intramolecular Cannizaro reaction of lactol **183** to give **186**

The intramolecular Cannizaro reaction[20] of **183** leading to **186** was a surprise and in order to better understand this hydride transfer process a density functional theory (DFT) calculation at Becke, three-parameter, Lee-Yang-Parr (B3LYP) level of theory with 6-31G* basic sets was undertaken. Single point energy calculations at DFT (B3LYP/6-31G**) level were conducted on the optimized structures to estimate solvation energy using the Poisson-Boltzmann-solver. Free energies (G) are expressed in kcal/mol for gas phase and solvent phase reactions and are zero point energy (ZPE) corrected.[21] Initial reference calculations were performed on a degenerate transposition of hydroxy ketone **187** into its enantiomer **188** in dimethyl sulfoxide. Hydride transfer in this polycyclic hydroxy ketone and similar caged carbocyclic systems has been extensively studied using dynamic nuclear magnetic resonance, mainly by Henry *et al* (Scheme 49).[22]

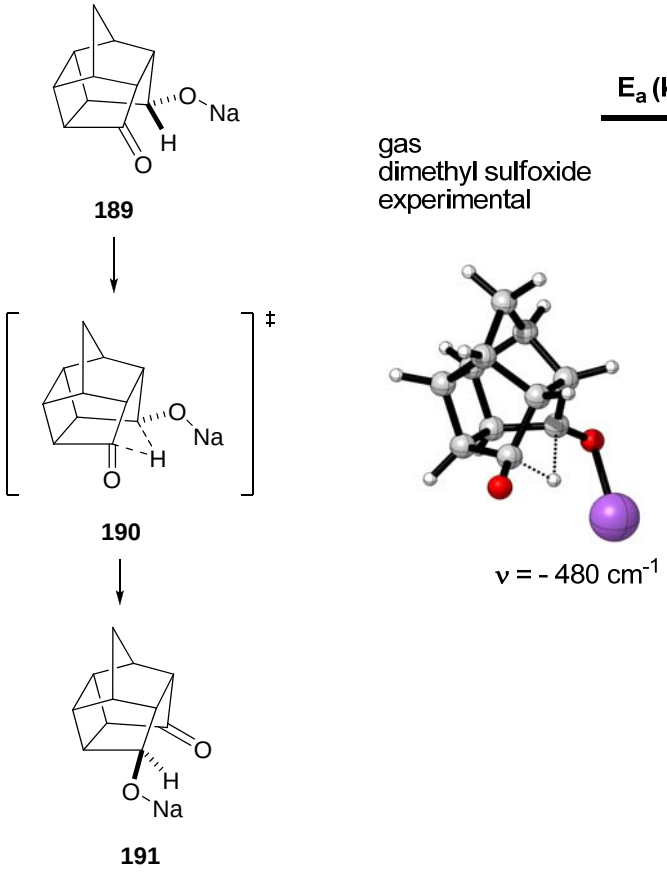


187 **188**

Scheme 49. Degenerate interconversion of **187** and **188**

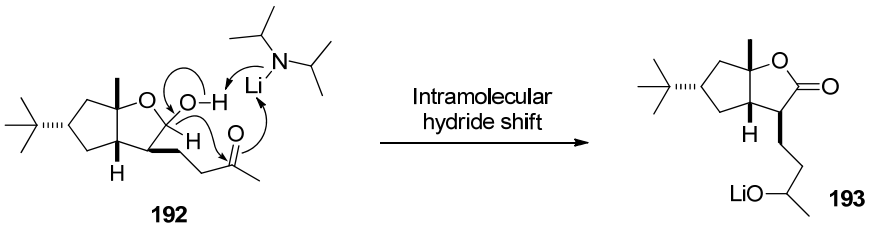
A DFT transition state search for this system converged on one first order saddle point **190** which possessed a single imaginary vibration mode (-480 cm^{-1}) that corresponds to the stretching vibration of the C-H bond geminal to the alkoxide oxygen atom. The activation energy calculated for the hydride shift between **189** and

191 was 28.0 kcal/mol for the gas phase reaction and 27.0 kcal/mol for the solvent phase process in dimethyl sulfoxide. These values are in reasonably good agreement with the reported activation energy for this process (21.7 kcal/mol) (Scheme 50).[23]



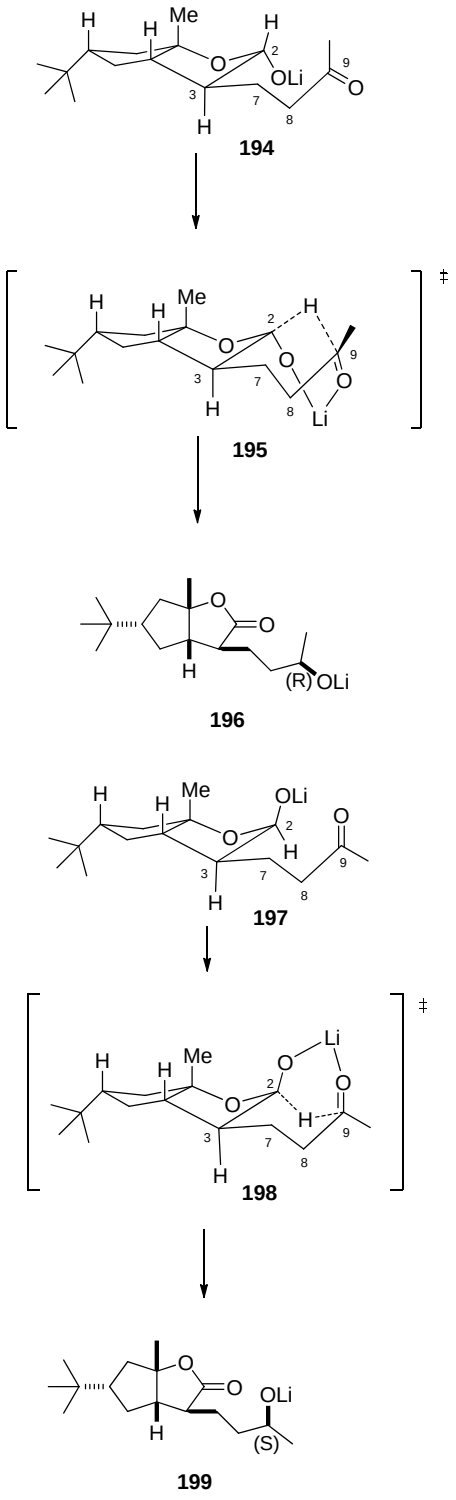
Scheme 50. Transition state, imaginary vibration and activation energies for the intramolecular hydride shift which interconverts sodium alkoxides **189** and **191**

Having established the reliability of this computational methodology in a model system, we carried out a transition state search on a close analogue of **183**. In order to render calculations less time consuming, modeling was done on the conversion of **192** to **193**. For the same reason, lithium diisopropylamide rather than potassium *t*-butoxide was chosen as the base (Scheme 51).

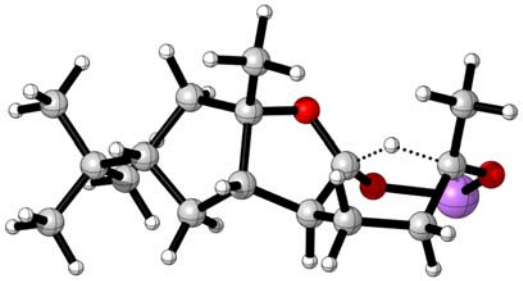


Scheme 51.Transition state modeling for the conversion of **192** to **193**

A transition state searching algorithm for the transformation of **194** to **196** and **197** to **199** located two out four possible transition states (**195** and **198**) respectively showing only one imaginary frequency in each case. This result indicates that the lithium ion is chelated to both the alkoxide and the ketone oxygen atoms during intramolecular transfer of hydride ion. Transition state **198** is higher in energy than **195** by 12.5 kcal/mol in the gas phase and 11.6 kcal/mol in the solvent phase, respectively, due to a (1,3) steric interaction between the methyl group at the ring fusion and the alkoxide oxygen. Calculation revealed that solvation has a decelerating effect on hydride ion transfer which could be attributed to interaction of the lithium ion with the electrostatic field of the solvent. Coordination of the lithium ion with the ketone oxygen atoms brings the hydrogen atom at C2 closer to the ketone carbon at C9, thus facilitating the hydride shift. In this way, if solvent disrupted the coordination of the lithium ion with the ketone oxygen at C9, it would slow the rate of hydride shift. Another consequence of the solvent effect is the increase in ionic character of the lithium-oxygen bond. This concurs with the finding that the dipole moments of transition states **195** and **198** are larger in the solvent phase compared to the gas phase (Scheme 52).

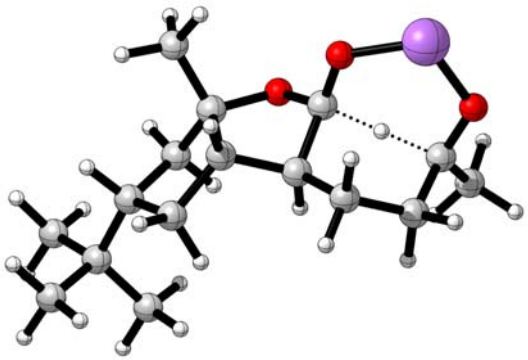


	gas	THF
E_a (kcal/mol)	8.6	12.2
μ (debye)	1.7	2.6



$\nu = -550\ cm^{-1}$

	gas	THF
E_a (kcal/mol)	21.1	23.8
μ (debye)	2.2	3.0



$\nu = -774\ cm^{-1}$

Scheme 52. Transition state, imaginary vibration and activation energies for intramolecular hydride transfer in **194** and **197**

Assuming that the calculations performed on **194** and **197** are applicable to **183**, we propose the following order of events in the conversion to **183** to **186**. Lithium alkoxide species **200** and **201** equilibrate through alkoxy aldehyde **202** in the presence of a base. Endo alkoxide **201** undergoes a relatively rapid intramolecular hydride shift to produce hydroxy lactone **203** as a single (9*R*) diastereomer whereas hydride transfer from **200** leading to (9*S*) hydroxy lactone **204** is slower (Figure 4).

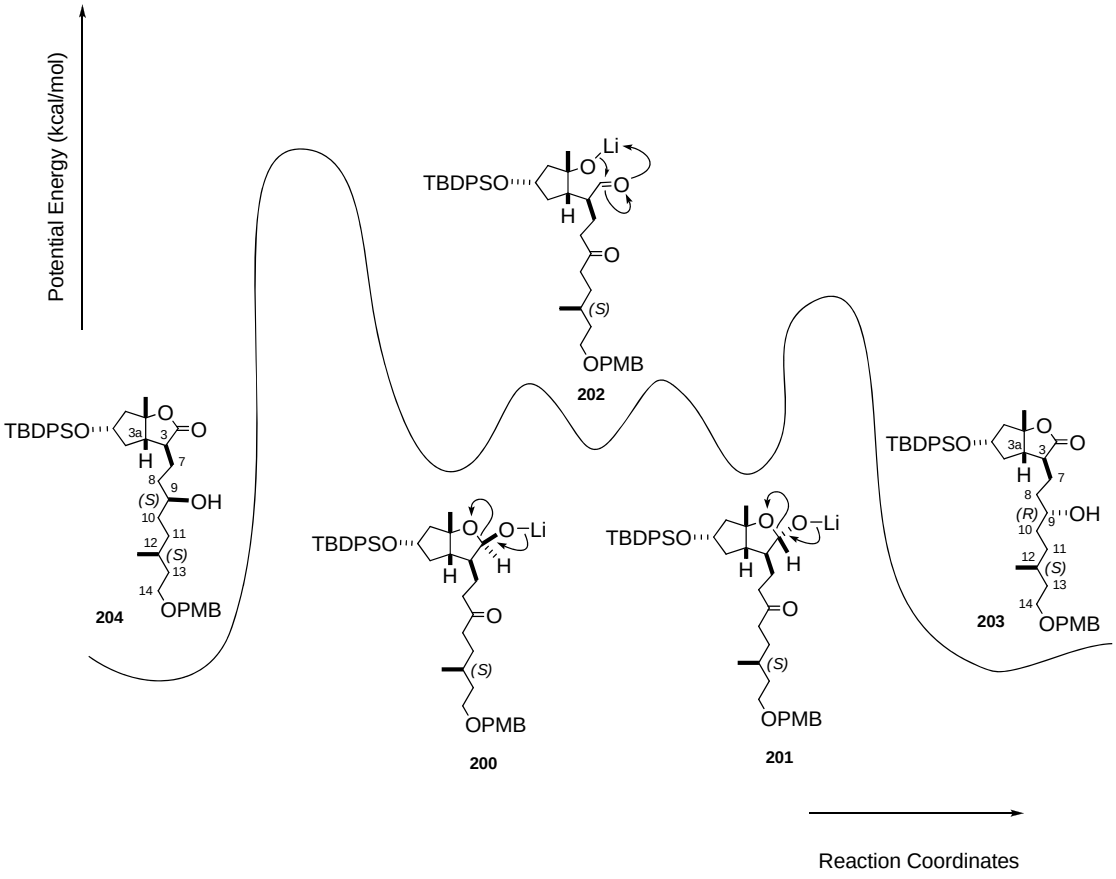
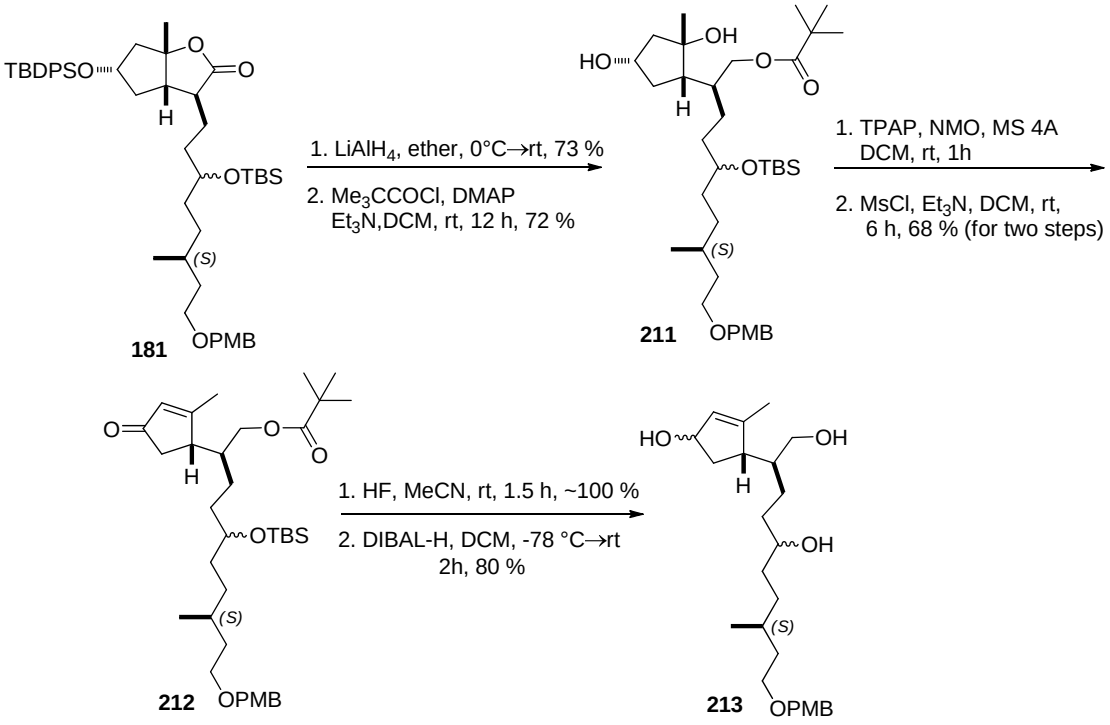


Fig 4. Proposed mechanism for conversion of **183** to **186**

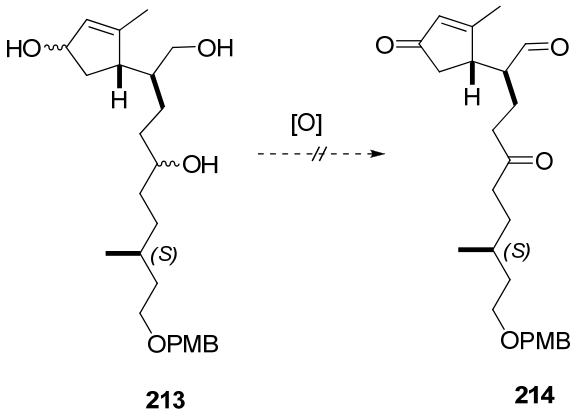
It is possible that steric bulk associated with the *endo t*-butyldiphenylsilyloxy group in **183** at C5 impedes intramolecular aldol condensation and to test this

hypothesis we decided to attempt aldol cyclization on a substrate devoid of the *t*-butyldiphenylsilyl protecting group present in **181**. Synthesis of this aldol precursor commenced with lithium aluminum hydride reduction of lactone **181** to give cleanly a triol that was monoprotected as its pivaloate **211**. Selective oxidation of the secondary alcohol with tetrapropylammonium perruthenate followed by *in situ* elimination of the tertiary methanesulfonate ester yielded enone **212.** The *t*-butyldimethylsilyl protecting group of **212** was removed efficiently with hydrofluoric acid but all attempts to hydrolyze the pivaloate ester proved fruitless. Thus, it was necessary to reduce the pivaloate ester with diisobutylaluminum hydride which also caused reduction of the enone moiety to give triol **213** as a mixture of four diastereomers (Scheme 53).



Scheme 53. Synthesis of triol **213** from **181**

A variety of oxidants were screened to effect global oxidation of **213** to a diketo aldehyde but to no avail. A complex mixture of unidentified compounds was the only outcome (Scheme 54). At this point, the prospect of an intramolecular aldol route to ring D of neomangicol A seemed remote and a decision was therefore made to explore a new approach to this substructure of the neomangicol nucleus (Scheme 54).

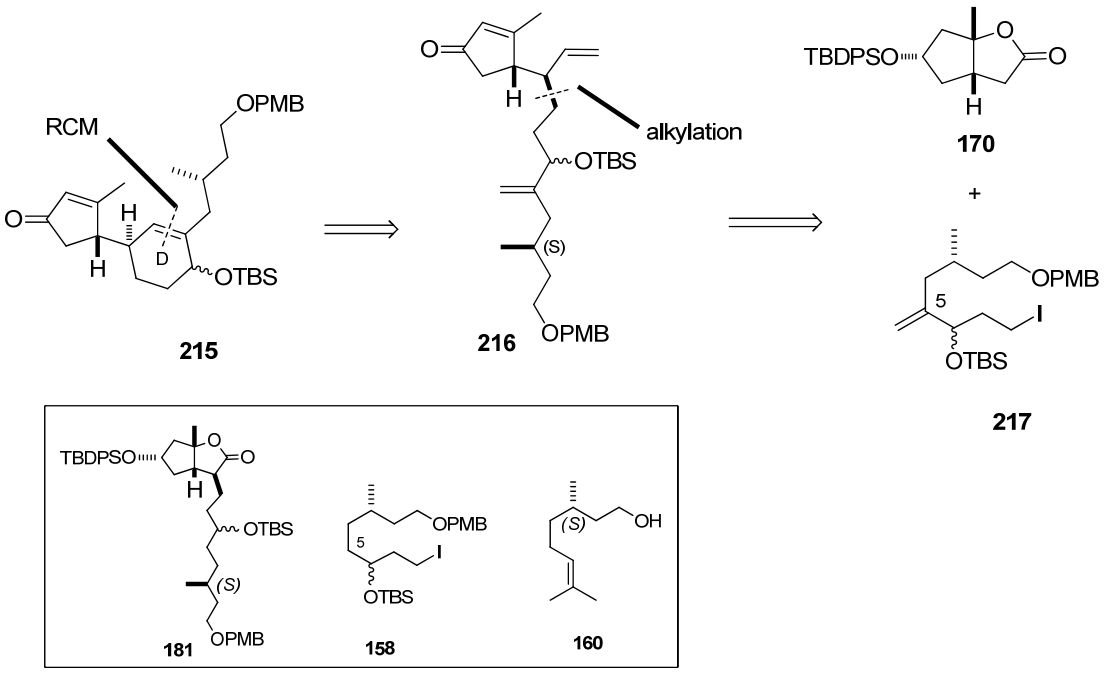


213 **214**

Scheme 54. Attempted synthesis of aldol condensation precursor **214** from triol **213**

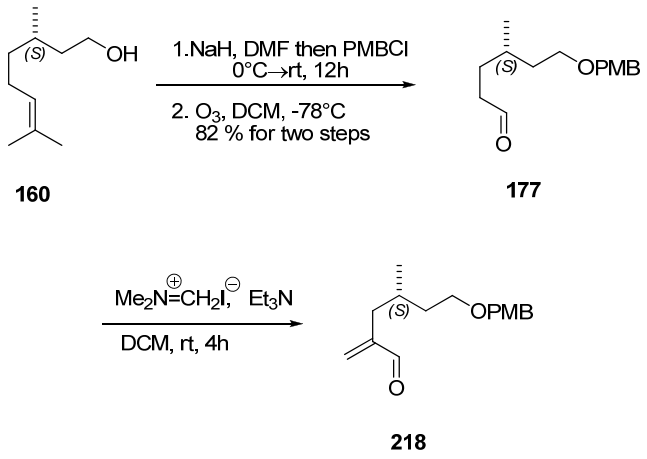
2.3 A revised approach to installation of ring D in neomangicol A

In view of the difficulty associated with preparing a precursor such as **214** for an intramolecular aldol route to ring D, we decided to pursue an alternative approach based on harnessing ring-closing metathesis of diene **216**. The metathesis precursor would be prepared, in principle, via the same technology we employed to prepare lactone **181** in our previous approach (Scheme 45), but using modified alkyl iodide **217** as an alkylating agent with lactone **170**. Synthetically, **217** would originate from the monoterpene (*S*)-(-)-citronellol (**160**) along lines similar to the preparation of **158** but with an additional step that installs an *exo* methylene function at C5 (Scheme 55).



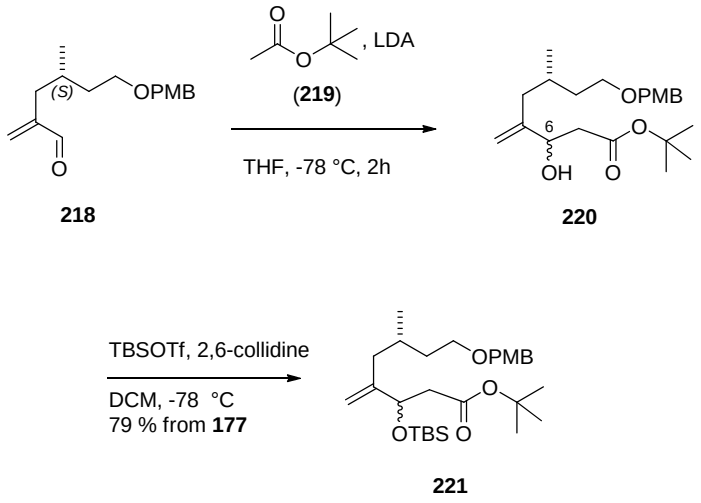
Scheme 55. Revised approach to installation of ring D in neomangicol A

Synthesis of alkyl iodide **217** commenced from commercially available (*S*)-(-)-citronellol (**160**), the primary alcohol of which was first protected as its *p*-methoxybenzyl ether. The ether was immediately submitted to ozonolytic fission of the carbon-carbon double bond to produce aldehyde **177** which was reacted with dimethylmethylideneammonium iodide and triethylamine to effect α-methylenation[24] and furnished **218** (Scheme 56).



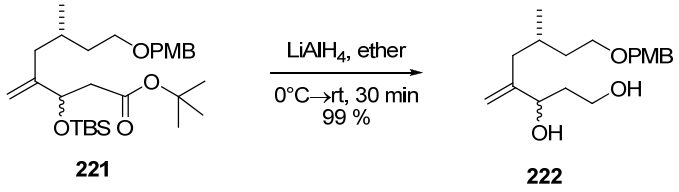
Scheme 56. Synthesis of aldehyde **218** via Eschenmoser methylenation

In order to append a two-carbon unit to enone **218**, the lithium enolate of *t*-butyl acetate was prepared *in situ* from **219** and lithium diisopropylamide and was reacted with **218** to yield an inseparable 1:1 mixture of diastereomeric allyllic alcohols **220**. This mixture of alcohols was not separated since carbon 6 was to be oxidized to a ketone and was converted to a stereoisomeric mixture of *t*-butyldimethylsilyl ethers **221** (Scheme 57).[25]



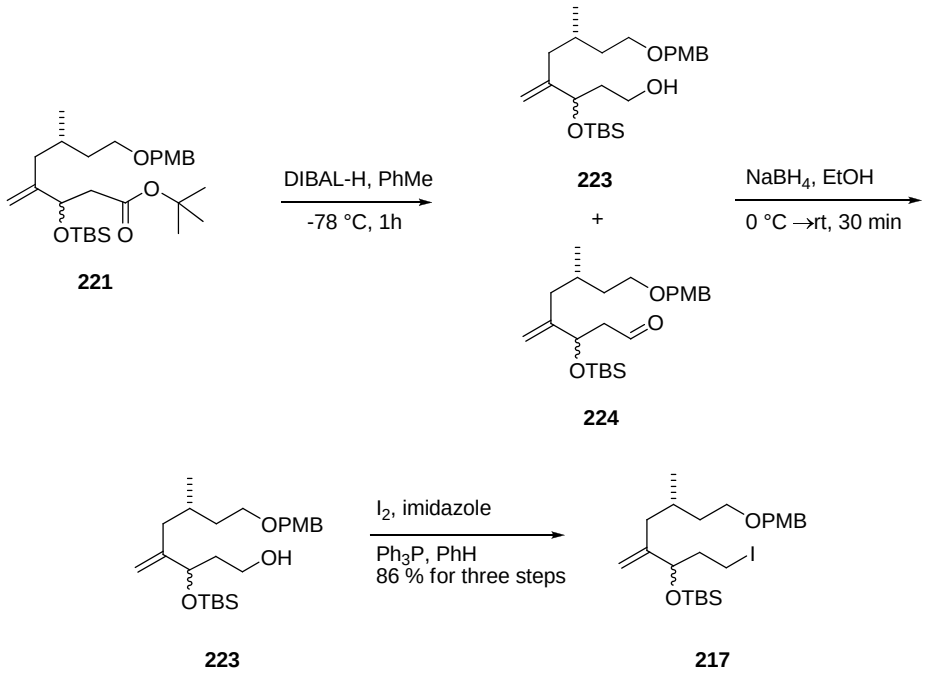
Scheme 57. Synthesis of *t*-butyl ester **221** from **218**

Our first attempt to reduce the ester moiety of **221** with lithium aluminum hydride resulted in both reduction of the ester and reductive deprotection of the *t*-butyldimethylsilyl ether to afford diol **222**. Although reductive cleavage of silyl ethers is rare, it has been encountered in cases where a *t*-butyldimethylsilyl ether is in a 1,3-relationship with an alcohol.[26] Hence, it is likely that the ester group of **221** is reduced first and then a hydride ion is delivered in intramolecular fashion to the silicon atom resulting in silicon-carbon bond cleavage (Scheme 58).



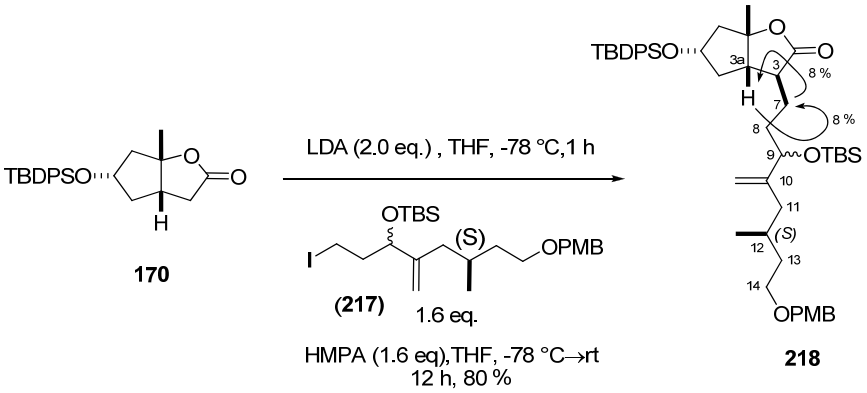
Scheme 58. Reduction of **221** with lithium aluminum hydride

Recourse to diisobutylaluminum hydride as reductant solved the problem of *t*-butyldimethylsilyl ether cleavage but it did not completely reduce the ester moiety and gave a 7:3 mixture of aldehyde **224** and alcohol **223**. Separation of the components of this mixture was not attempted but instead the mixture was subjected to treatment with sodium borohydride to effect complete reduction of **224** to **223**. Exposure of alcohol **223** to iodine in the presence of triphenylphosphine and imidazole yielded iodide **217** in an overall yield of 86 % for the three steps from **221** (Scheme 59).



Scheme 59. Synthesis of iodide **217** from ester **221**

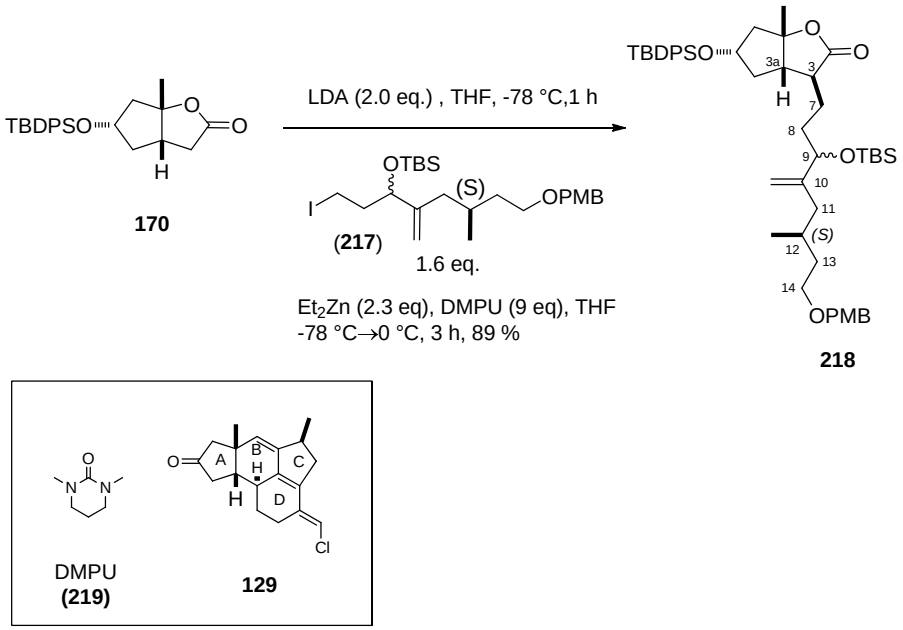
After securing a route to alkyl iodide **217,** we engaged in its alkylation of γ-lactone **170**. Surprisingly, conditions used to alkylate **170** with alkyl iodide **158** proved to be ineffective for alkylation of this lactone with **217** and resulted only in recovery of **170**. Therefore, we had to resort to more drastic conditions for this coupling and to that end, **217** was treated with the *in situ* prepared lithium enolate of **170** in the presence of hexamethylphosphoramide (HMPA). This furnished our desired product **218** in high yield. The configuration at C3 of **218** was confirmed by a series of nOe experiments in which irradiation of hydrogen atoms at C7 and C3a caused reciprocal nOe interactions. This proved that alkylation of **170** by **217** had taken place at the *exo* face of the bicyclic lactone (Scheme 60).



Scheme 60. Alkylation of lactone **170** with **217** in the presence of HMPA

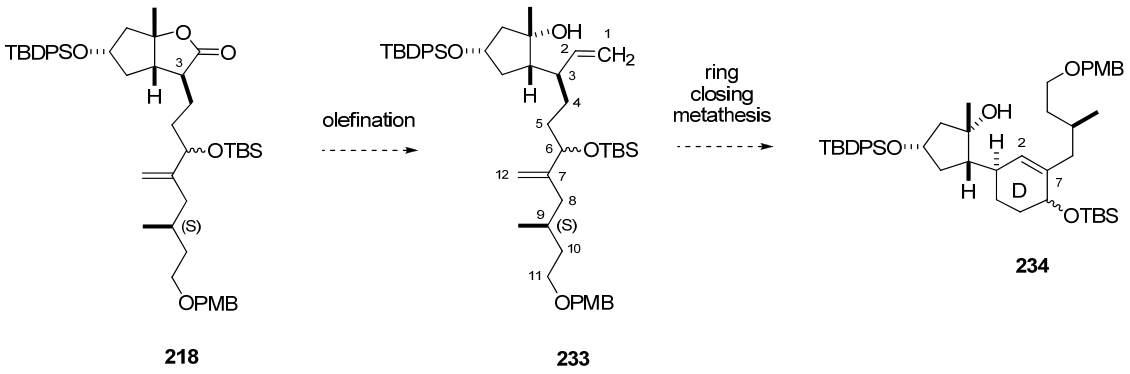
Upon further study of the alkylation of **170** with **217**, we discovered that treatment of the lithium enolate of **170** with diethylzinc in the presence of *N*,*N*'-dimethyl-*N*,*N*'-trimethyleneurea (DMPU, **219**) and then reaction with alkyl iodide **217** improved the yield of **218**.[27] As compared to alkylation of **170** in the presence of

hexamethylphosphoramide, which required 12 hours to reach completion (Scheme 61), these modified conditions required only 3 hours for complete reaction. It is noteworthy that **218** not only contains the requisite methylene moiety at C10 to be used for ring-closing metathesis to forge ring D of neomangicol A but that **218** also bears the correct stereochemical imprint for tetracycle **129** at C3, C3a and C12 (Scheme 61).



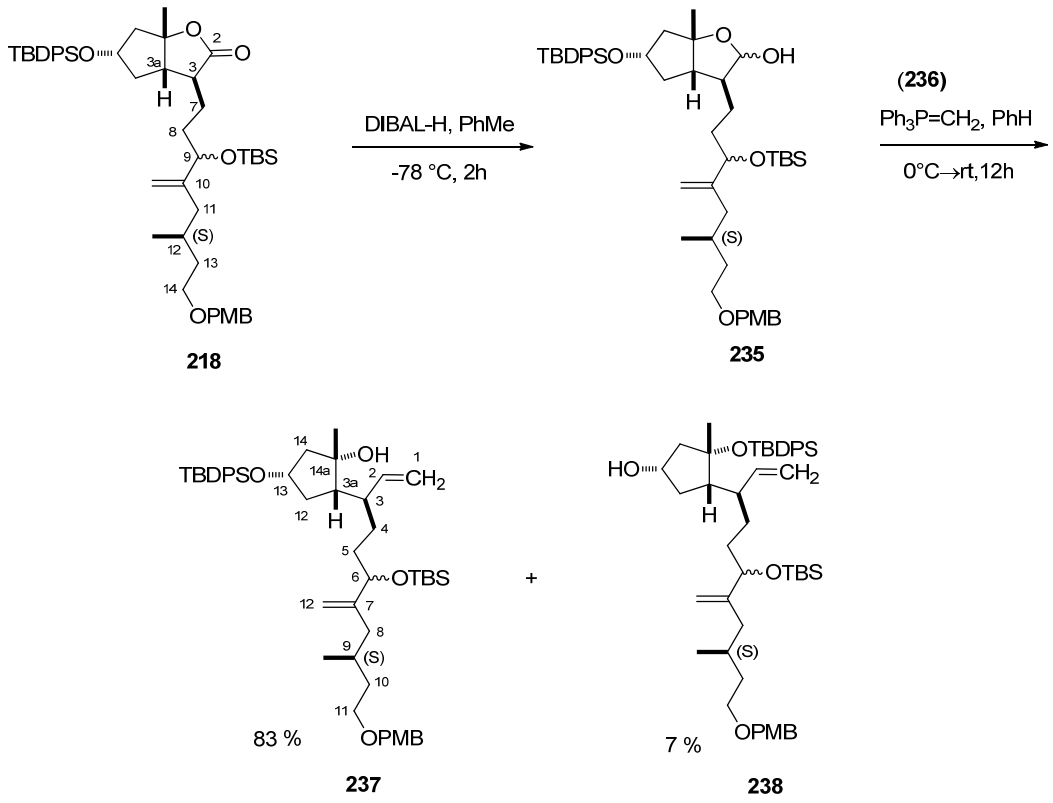
Scheme 61. Alkylation of lactone **170** with **217** in the presence of DMPU

After successfully appending the side chain to γ-lactone **170**, the task at hand became installation of a methylene moiety at C2 of **218**. This would produce diene **233** bearing methylene moieties at C2 and C7 that would be used in the ring closing metathesis step to fabricate ring D of neomangicol A (Scheme 62).



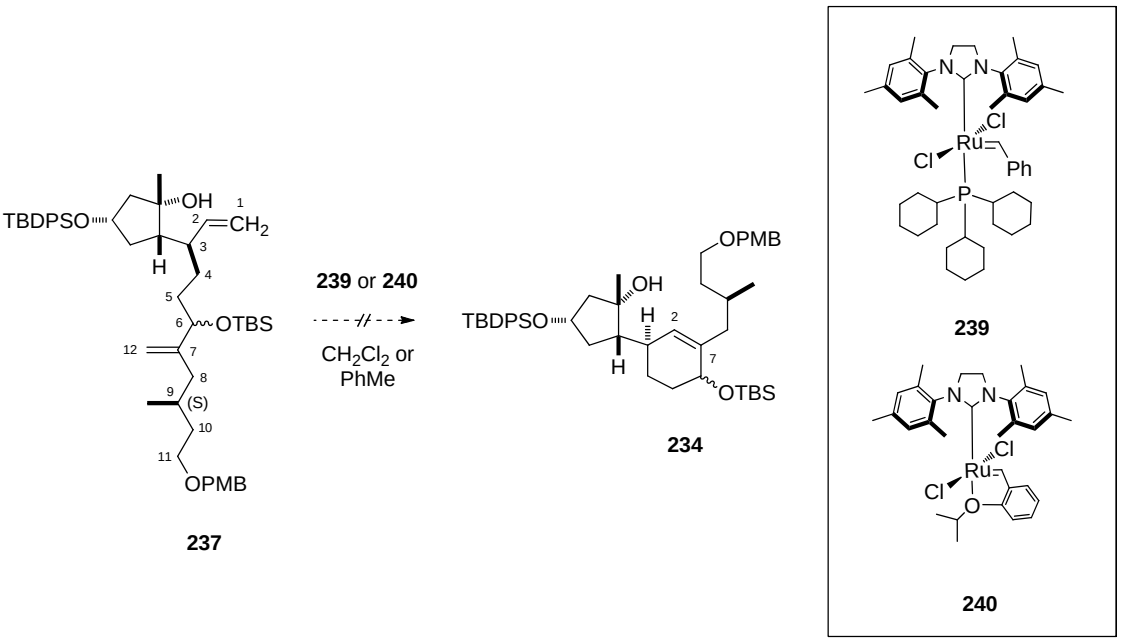
Scheme 62. Olefination-ring closing metathesis approach towards **234**

When **218** was exposed to diisobutylaluminum hydride it underwent reduction from both faces of the carbonyl group to give a 1:1 diastereomeric mixture of lactols **235** in high yield. Wittig olefination of **235** with triphenylphosphonium ylide **236**, prepared beforehand from triphenylphosphonium bromide and *n*-butyllithium, gave diene **237** in 40 % yield as a 1:1 mixture of diastereomers at C3 according to its nuclear magnetic resonance spectrum. However, when **236** was prepared from triphenylphosphonium bromide and potassium *t*-butoxide in refluxing benzene and then reacted with **235**, the yield of **237** improved to 83 % and C3 was epimerized to only a small extent (d.r. 10:1). Diene **237** was accompanied by **238** as a minor product (7 %) of the olefination reaction, which was separable from **227** by chromatography. Diene **238** is the result of a precedent *t*-butyldiphenylsilyl group migration from the oxygen atom at C13 to the *syn* oriented oxygen atom at C14a (Scheme 63).[28]



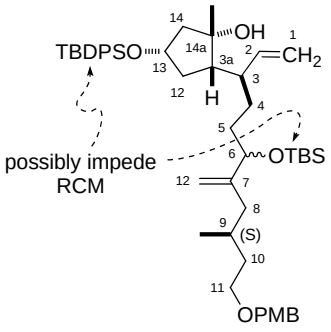
Scheme 63. Reduction-olefination sequence converting **218** to **227**

Having secured a route to diene **237**, we next explored ring-closing metathesis for the elaboration of neomangicols's ring D.[29] Reaction of **237** with catalytic amounts of Grubbs second generation catalyst (**239**) and Grubbs-Hoveyda second generation catalyst (**240**) was carried out under a variety of conditions in the expectation that **234** would result. To investigate the role of the concentration of **237** on the reaction, diene **237** was refluxed with **239** or **240** in dichloromethane and toluene using catalyst loading from 5 to 30 %. However, only starting material was recovered in each case (Scheme 64).



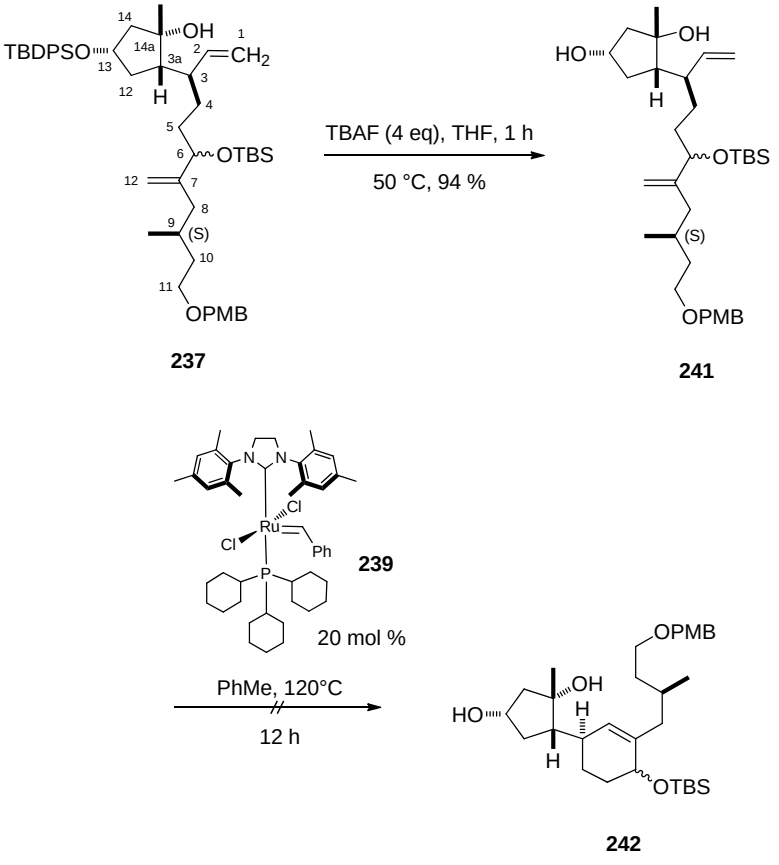
Scheme 64. Attempted ring-closing metathesis of **237**

It was thought that a possible reason for this failure to prepare **234** by ring-closing metathesis could be due to the steric bulk imposed on the reaction by the *t*-butyldiphenylsilyloxy group at C13 and *t*-butyldimethylsilyloxy group at C6 (see below). To test this hypothesis, we attempted to cleave both silyl ethers at C13 and C6 of **237** then take that triol as a substrate for ring-closing metathesis.



237

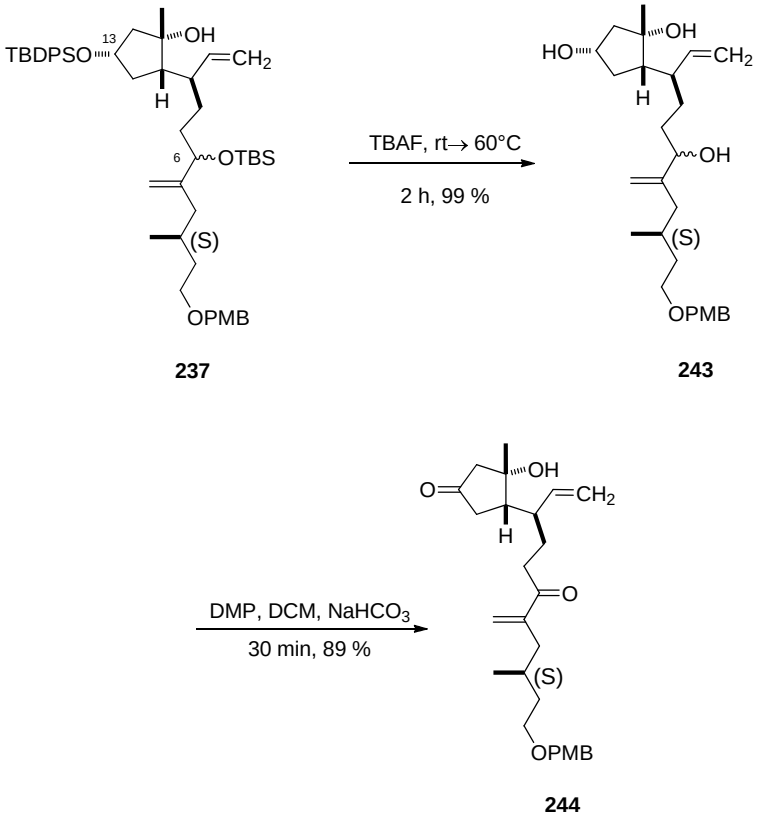
In the event, reaction of **237** with tetra-*n*-butylammonium fluoride deprotected only the hydroxyl group at C13 to give diol **241**. When **241** was treated with a catalytic amount of **239** in refluxing toluene only unreacted **241** was recovered (Scheme 65).



237 **241** **239** **242**

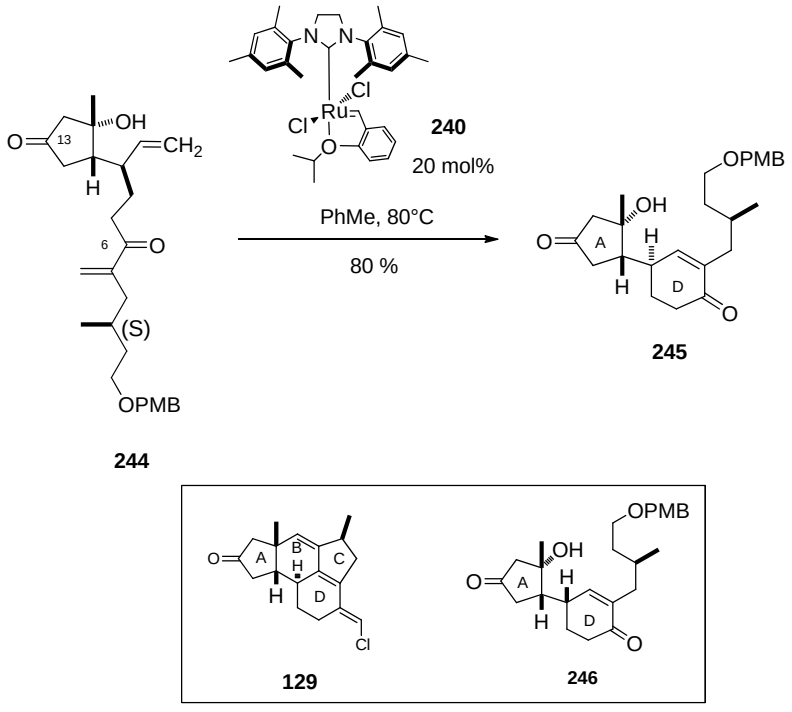
Scheme 65. Attempted ring-closing metathesis of **241**

The observation that **241** did not undergo ring-closing metathesis suggested that either the steric effect exerted by the *t*-butyldimethylsilyloxy group at C6 or perhaps the free alcohol at C13 (by coordinating to the ruthenium atom in the catalyst) was preventing ring formation. This suggested that a substrate bearing a keto function at C13 and lacking the *t*-butyldimethylsilyloxy group at C6 could be a candidate for ring-closing metathesis. To this end, **237** was reacted with tetra-*n*-butylammonium fluoride to give triol **243** which was then exposed to Dess-Martin periodinane to afford diketone **244** (Scheme 66).



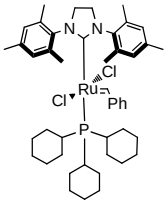
Scheme 66. Synthesis of diketone **244** from **237**

To our delight, exposure of **244** in hot toluene to a catalytic amount of **240** gave cyclohexenone **245** in high yield (Scheme 67). At this stage, **245** was separable from minor diastereomers **246** which was a result of epimerization during the methylenation reaction (Scheme 63). Screening of various reaction conditions showed that this cyclization is quite facile and is relatively insensitive to catalyst loading, temperature and solvent, with yields of **245** being in the range of 50-89 % (Table 1). With the acquisition of **245**, a substance containing rings A and D of the neomangicol nucleus now became accessible and set the stage for progress towards our goal of tetracycle **129**.

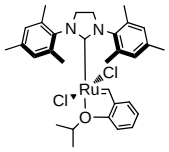


Scheme 67. Synthesis of cyclohexenone **245** from diene **244**

Table 1. Conditions for ring-closing metathesis for **244**



239



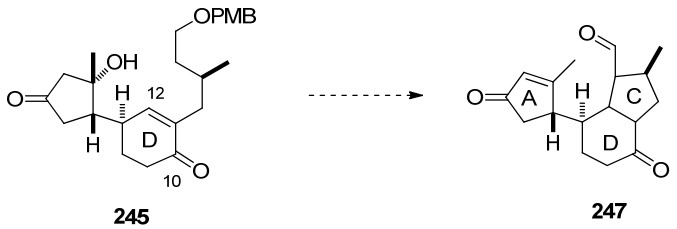
240

Entry	Catalyst	Loading (mol %)	Time (h)	Solvent	Temp (°C)	Yield (%)
1	**240**	20	6	PhMe	80	80
2	**240**	20	12	PhMe	80	52
3	**240**	10	15	PhMe	80	89
4	**240**	5	15	PhMe	80	71
5	**239**	5	5	DCM	rt	50
6	**239**	5	12	DCM	45	50
7	**239**	10	5	PhMe	rt	50
8	**239**	10	5	PhMe	80	64
9	**240**	10	12	PhMe	80	71
10	**239**	10	12	PhMe	80	83

2.4 Attempted installation of ring C in neomagicol A

2.4.1 A conjugate addition approach

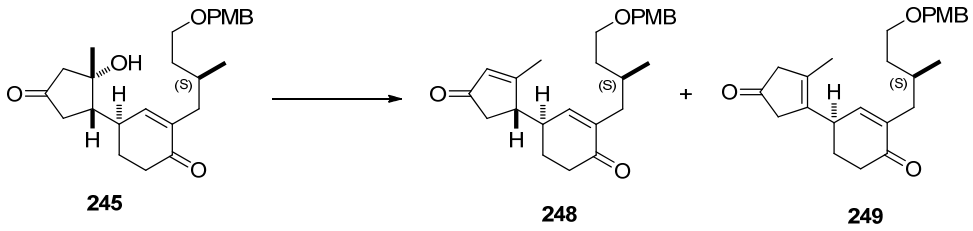
After successful installation of ring D of the neomangicol A nucleus, the next objective was assembling ring C. We anticipated that aldehyde **247**, which would be prepared from **245**, would be a productive substrate for intramolecular 1,4-conjugate addition to the cyclohexenone of ring D via a Michael reaction.[30] If this approach were successful, it would forge ring C in neomangicol A and leave functionality in place for fabricating ring B, thus completing the entire tetracyclic core (Scheme 68).



Scheme 68. Synthetic plan for installation of ring C in the neomangicol A nucleus

Synthesis of **247** commenced with dehydration of **245** to cyclopentenone **248**. Reaction of tertiary alcohol **245** with methanesulfonyl chloride afforded a mesylate which, in the presence of triethylamine, underwent elimination to give a mixture of separable cyclopentenones **248** and **249**. In an attempt to avoid formation of the undesired β,γ- cyclopentenone **249**, **245** was reacted with thionyl chloride in pyridine but this also gave a mixture of **248** and **249**. By contrast, when **245** was exposed to

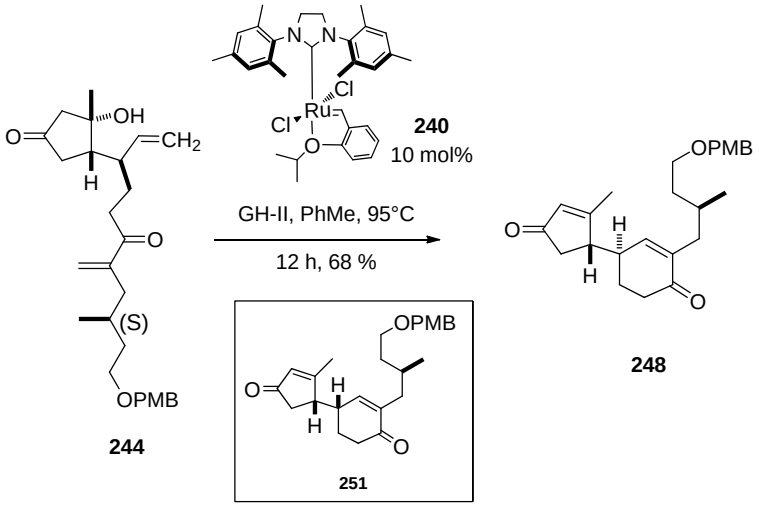
Martin's sulfurane (**250**), cyclopentenone **248** was formed as the sole product in 63 % yield (Scheme 69).



Conditions	248	249
MsCl, Et_3N,DCM, 0 °→rt, 9 h	20 %	33 %
$SOCl_2$, pyridine 0°, 30 min	30 %	42 %
$Ph(F_3C)_2CO$-S-$OC(CF_3)_2Ph$ Ph Ph (**250**) DCM, 0°→ 4°C, 5 h	63 %	0%

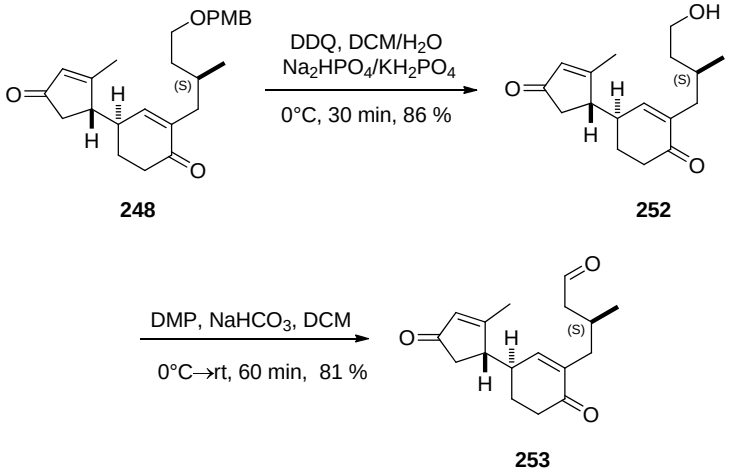
Scheme 69. Synthesis of cyclopentenones **248** and **249** from alcohol **245**

A further advance toward **248** occurred when **244** was heated in toluene at 95°C in the presence of Grubbs-Hoveyda second generation catalyst (**240**). This caused dehydration to take place concomitant with ring-closing metathesis and afforded **248** in 68% yield for the two steps from diene **244** (Scheme 74). At this stage, **248** was separable from minor diastereomers **251** which was a result of epimerization during the methylenation reaction (Scheme 70).



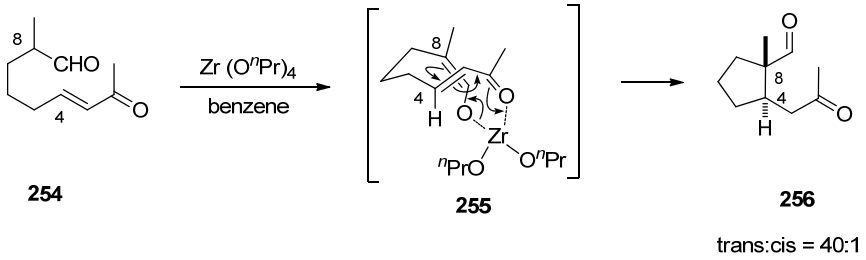
Scheme 70. Synthesis of **248** from **244**

After securing a pathway to cyclopentenone **248**, we advanced this *p*-methoxybenzyl ether to the corresponding aldehyde. Treatment of **248** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in a pH-buffered medium cleaved the *p*-methoxybenzyl ether without incident to reveal a primary alcohol which was immediately oxidized with Dess-Martin periodinane to give **253** in high overall yield (Scheme 71).



Scheme 71. Synthesis of aldehyde **253** from **248**

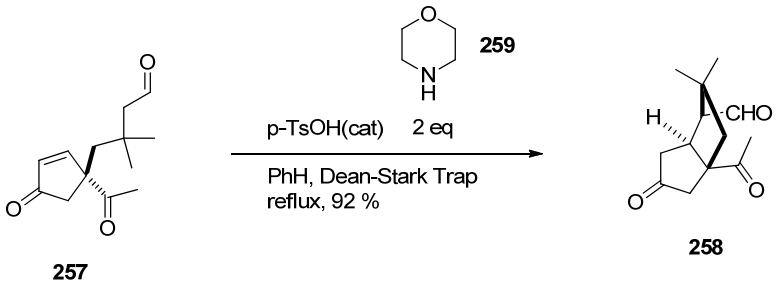
As precedent for our proposed cyclization of **253** to **247**, we noted that Stork demonstrated that keto aldehyde **254** undergoes intramolecular conjugate addition of the aldehyde enolate to the enone in the presence of metal alkoxides to give keto aldehyde **256**.[31] Although a variety of metal alkoxides effected cyclization of **254** to **256**, the highest *trans:cis* selectivity was achieved with oxyphilic metal alkoxides such as zirconium tetra *n*-propylalkoxide (40:1). The authors proposed the transition state depicted in **255** to explain the role of the metal alkoxy species in the cyclization (Scheme 72). Inspired by Stork's work, we attempted a similar cyclization of **253**. A variety of metal alkoxides were screened but unfortunately, the result was either recovered **253** or its decomposition.



Scheme 72. Synthesis of ketoaldehyde **256** from enone **254**

In light of our failure to effect cyclization of **253** via a Michael reaction, our focus turned to an enamine promoted intramolecular conjugate addition.[32] Initial results were not encouraging since treatment of **253** with a catalytic amount of pyrrolidine led to decomposition whereas exposure to L-proline even after 24 h caused no detectable change. Nevertheless, despite these portents, we found a remarkable

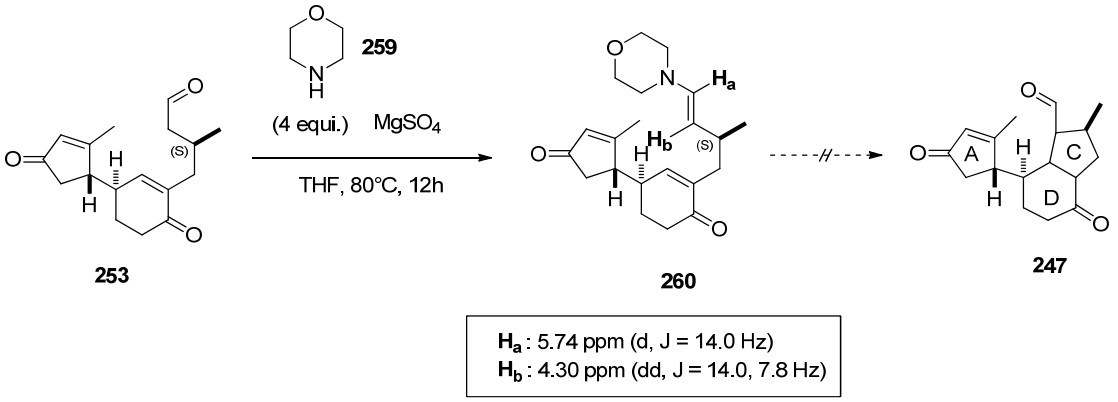
example which demonstrates the power of enamine promoted conjugate addition in building a complex natural product scaffold in the work of Burke *et al*. In Burke's total synthesis of quadrone,[33] **257** was reacted with morpholine (**259**) and *p*-toluenesulfonic acid to give diketo aldehyde **258** in high yield, presumably via intramolecular conjugate addition of the aldehyde enamine and subsequent hydrolysis (Scheme 73).



Scheme 73. Burke's synthesis of **258** from **257** via enamine promoted Michael addition

Following the precedent set by Burke (Scheme 77), aldehyde **253** was reacted with an excess of morpholine (**259**) in the presence of a catalytic amount of *p*-toluenesulfonic acid and anhydrous magnesium sulfate but under these conditions the expected enamine **260** was not observed. However, when the reaction was run in the absence of *p*-toluenesulfonic acid, an unstable product was seen transiently whose ^{1}H nuclear magnetic resonance spectrum was consistent with **260**. In particular, vinyl protons at δ 4.30 and 5.74 ppm with a coupling constant of 14.0 Hz were indicative of (*E*) geometry of this putative enamine. However, if **260** was indeed formed, it failed to

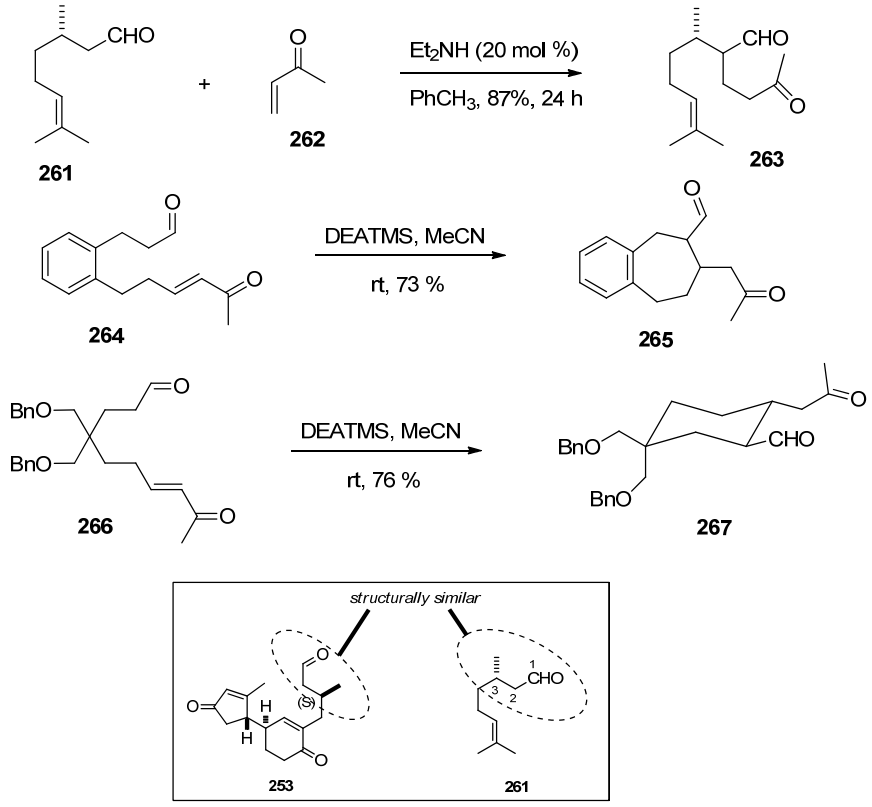
undergo intramolecular conjugate addition and hydrolysis to give **247**. A possible explanation for this failure is the susceptibility of **260** itself towards hydrolysis and/or decomposition in the presence of *p*-toluenesulfonic acid, a property that would make this enamine an impractical vehicle for acquiring **247**. Nevertheless, hints that **260** had been formed encouraged us to explore other secondary amines for this purpose (Scheme 74).



Scheme 74. Reaction of **253** with morpholine in the presence of magnesium sulfate

Hagiwara and coworkers found that catalytic diethylamine can promote intermolecular 1,4-addtion of aldehydes to vinyl ketones,[34] as in the reaction of (*S*)-(-)-citronellal (**261**) with methyl vinyl ketone (**262**) to give **263**. Subsequently, this research group discovered that diethylamine(trimethyl)silane (DEATMS) is a more potent Lewis base for this purpose compared to diethylamine. The advantages of DEATMS are lower volatility, higher nucleophilicity of the nitrogen atom and higher Lewis acidity of the silicon atom. In particular, Hagiwara showed that intramolecular Michael addition of

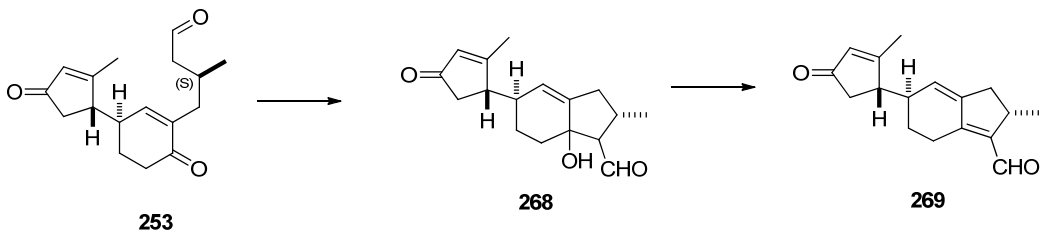
264 and **266** takes place in the presence of DEATMS to afford **265** and **267**, respectively (Scheme 75).



Scheme 75. Intermolecular and intramolecular Michael addition of **261**, **264** and **266**

Unfortunately, when aldehyde **253** was reacted with diethylamine in hot toluene it underwent intramolecular aldol condensation rather than conjugate addition and gave *β*-hydroxy aldehyde **268** which promptly dehydrated to afford dienal **269**. The same result was obtained when diethylamine(trimethyl)silane was used instead of diethylamine although **269** was produced in higher yield in this case (Scheme 76). The preference of **253** for intramolecular aldol condensation over conjugate addition prompted reconsideration of a sequence that would proceed through an enamine

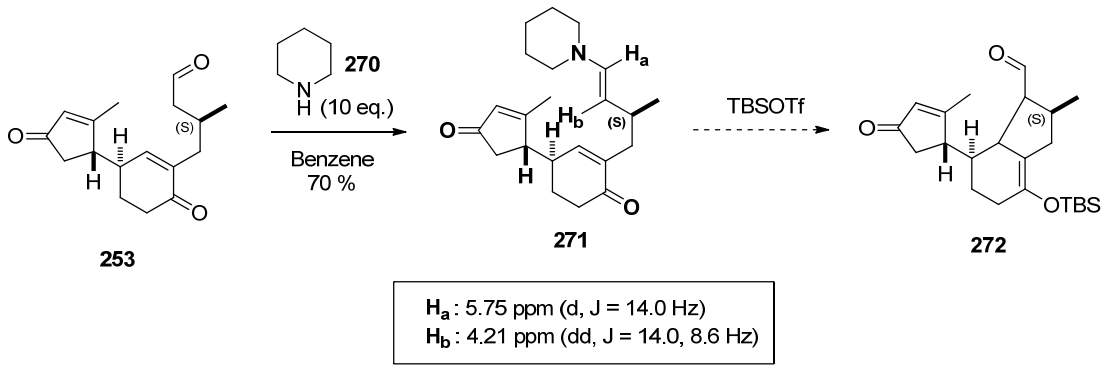
derived from this aldehyde. In that case, it was clear that an enamine more stable than **260** would be required to effect the desired mode of cyclization.



Base	Conditions	Yield of 269
$NHEt_2$ 1.2 equi.	PhH, 80°C, 12h	30 %
DEATMS 1.2 equi.	PhH, 80°C, 12h	50 %

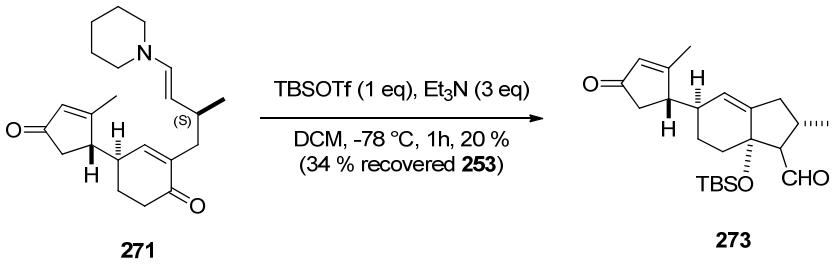
Scheme 76. Formation of **269** from **253**

Kim and coworkers have shown that *t*-butydimethylsilyl trifluoromethansulfonate (TBSOTf) can promote conjugate addition of enamines to a variety of enones under mild conditions[35] and we hoped that this reagent would instigate conjugate addition of **271** to give tricyclic product **272**. To that end, we discovered that exposing **253** to piperidine (**270**) in benzene and removing water from the reaction mixture by azeotropic distillation converted the aldehyde to a substance with the properties of enamine **271** but was difficult to purify.[36] As with **260**, a coupling constant of 14.0 Hz for vinyl protons of the putative enamine **271** suggested that it was exclusively a *trans* diastereomer (Scheme 77).



Scheme 77. Synthesis of enamine **271** from **253**

However, exposure of the impure enamine **271** to *t*-butydimethylsilyl trifluoromethansulfonate and triethylamine again resulted in intramolecular aldol condensation and after aqueous work up afforded *β*-*t*-butydimethylsiloxy aldehyde **273** as a single diastereomer (Scheme 78).

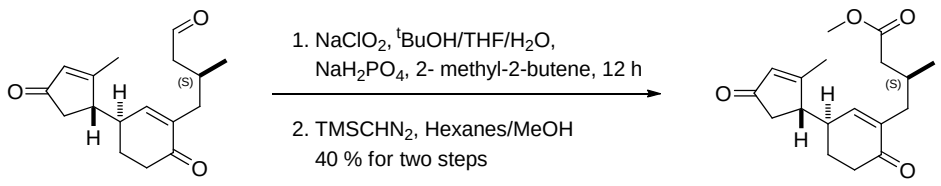


Scheme 78. Intramolecular aldol condensation of **271** to give aldehyde **273**

The foregoing results provided clear evidence that neither an intramolecular Michael reaction of **253** nor conjugate addition of the derived enamine could be used to construct ring C of the neomangicol A core. This caused us to consider silyl enol

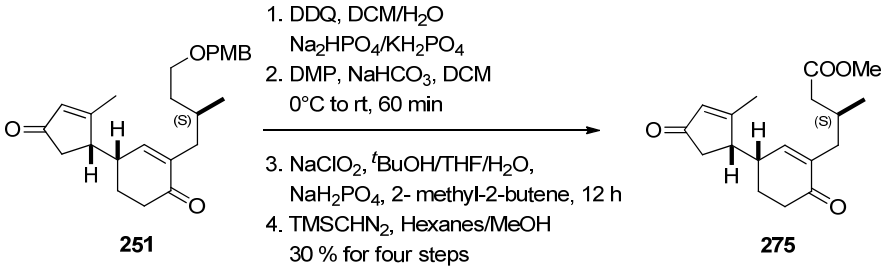
ethers of **253** for our purpose since Mukaiyama has shown that silyl enol ethers are enolate equivalents with high nucleophilicity.[37] Typically, ketones and aldehydes are converted into silyl enol ethers by treatment with alkylsilyl chlorides and triethylamine in refluxing dimethylformamide,[38] but in view of the sensitivity of aldehyde **253**, we chose milder conditions to accomplish this transformation. However, when **253** was treated with *t*-butydimethylsilyl trifluoromethansulfonate or trimethyl trifluoromethansulfonate in the presence of triethylamine only starting material was recovered, whereas excess of *t*-butydimethylsilyl trifluoromethansulfonate caused decomposition of the aldehyde.

In light of this failure, we decided on a related strategy that would convert aldehyde **253** into a silylketene acetal, since these species are well known to undergo Mukaiyama-Michael addition to Lewis acid activated enones.[39] To that end, **253** was oxidized with sodium chlorite to give a carboxylic acid which was treated with trimethylsilyldiazomethane to afford methyl ester **274** (Scheme 79).



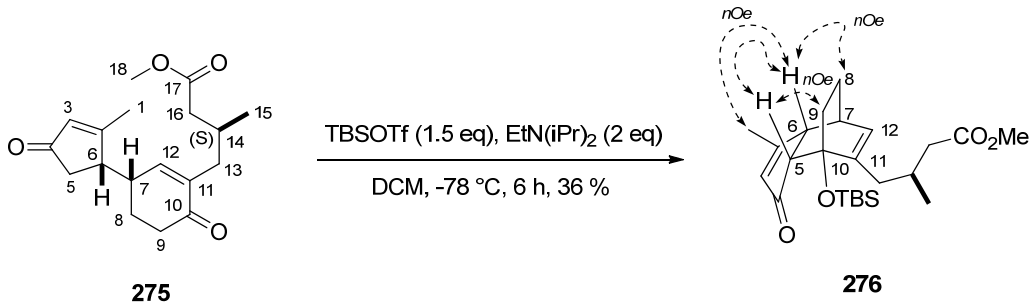
Scheme 79. Synthesis of methyl ester **274** from aldehyde **253**

The diastereomer of **274** was prepared from **251** in the same manner as **274** was prepared from **253** (Scheme 75 and 83). To that end, *p*-methoxybenzyl ether **251** was treated with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) to afford a primary alcohol which was advanced forward via Dess-Martin oxidation. Finally, the aldehyde was submitted to Pinnick oxidation to afford a carboxylic acid which was esterified with trimethylsilyldiazomethane to give ester **275** (Scheme 80).



Scheme 80. Synthesis of methyl ester **275** from **251**

However, when **275** was exposed to *t*-butydimethylsilyl trifluoromethansulfonate in the presence of *N*,*N*-diisopropylethylamine with the intent to prepare silylketene acetal of this ester, another surprise awaited us in the form of **276** (Scheme 81).



Scheme 81. Intramolecular aldol condensation of **275** to afford **276**

Evidence for the assignment of structure to **276** came from HSQC (Heteronuclear Single Quantum Coherence), COSY (COrrelation SpectroscopY), HMBC (Heteronuclear Multiple Bond Correlation) and NOESY (Nuclear Overhauser Effect Spectroscopy) nuclear magnetic resonance experiments (Table 2). Specifically, HSQC revealed the presence of three methyl (CH_3) groups, four methylene (CH_2) units, four methyne (CH) units and two vinyl (CH=) units. Carbon 13 nuclear magnetic resonance uncovered the presence of four vinyl carbons (two of which bear no hydrogen atoms) and two carbonyl carbons (a ketone and an ester carbon). The Infrared spectrum of **272** confirms the presence of an enone (C=0 at 1701 cm^{-1} and C=C at 1625 cm^{-1}) and an ester carbonyl (C=O at 1737 cm^{-1}). A combination of HMBC and COSY correlations unravels signatures for the bridgehead (I through VIII) and side chain (IX through XIII) substructures. For example, substructure I shows HMBC correlations between the protons at C9 (number 9 is circled) and C5, C8, C10 and C11 as well as a COSY correlation of the proton at C9 to the protons at C8 (Fig 5). Additional structural information pertaining to **276** came from a series of nOe experiments. Thus, when the hydrogen at C5 was irradiated, a nOe interaction was observed between this hydrogen and the hydrogen at C9. Additionally, when the hydrogen at C6 was irradiated, a nOe interaction was observed between this hydrogen and the hydrogens at C1, C5 and C8 (Scheme 81). Thus, tricyclic ketone **276** is formed from **275** by deprotonation at C5, subsequent intramolecular aldol addition to the cyclohexenone carbonyl and final entrapment of the new hydroxyl group as its

silyl ether. In retrospect, this result is not altogether surprising given the greater acidity of the proton at C5 relative to those adjacent to the ester at C16.

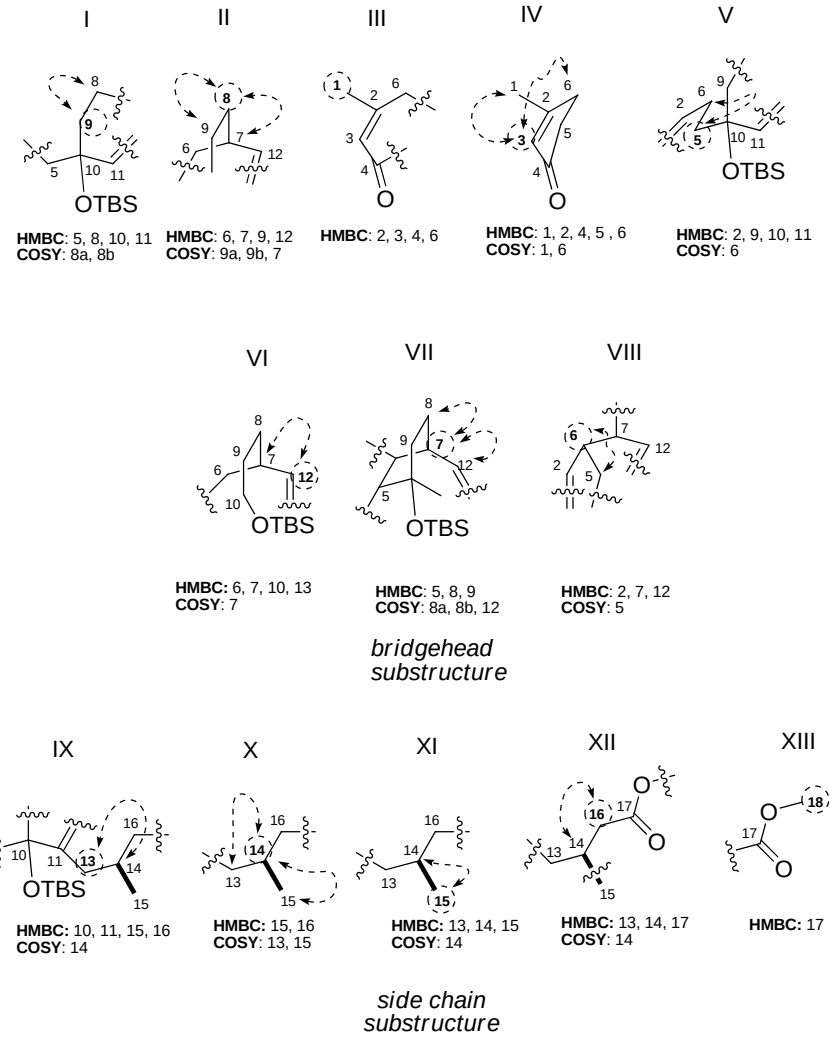
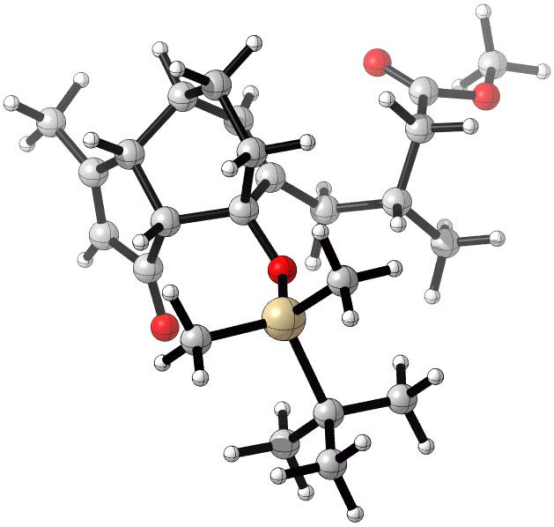
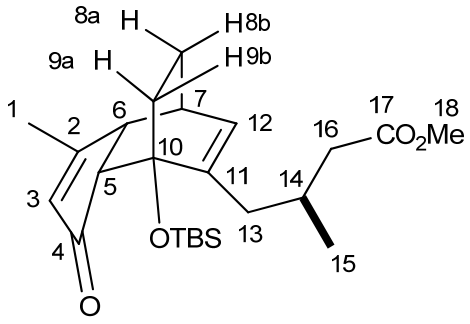


Fig 5. Bridgehead and side chain substructures of **276** from HMBC and COSY correlations

Table 2. One-dimensional and two-dimensional nuclear resonance magnetic data for **276** (in $CDCl_3$)



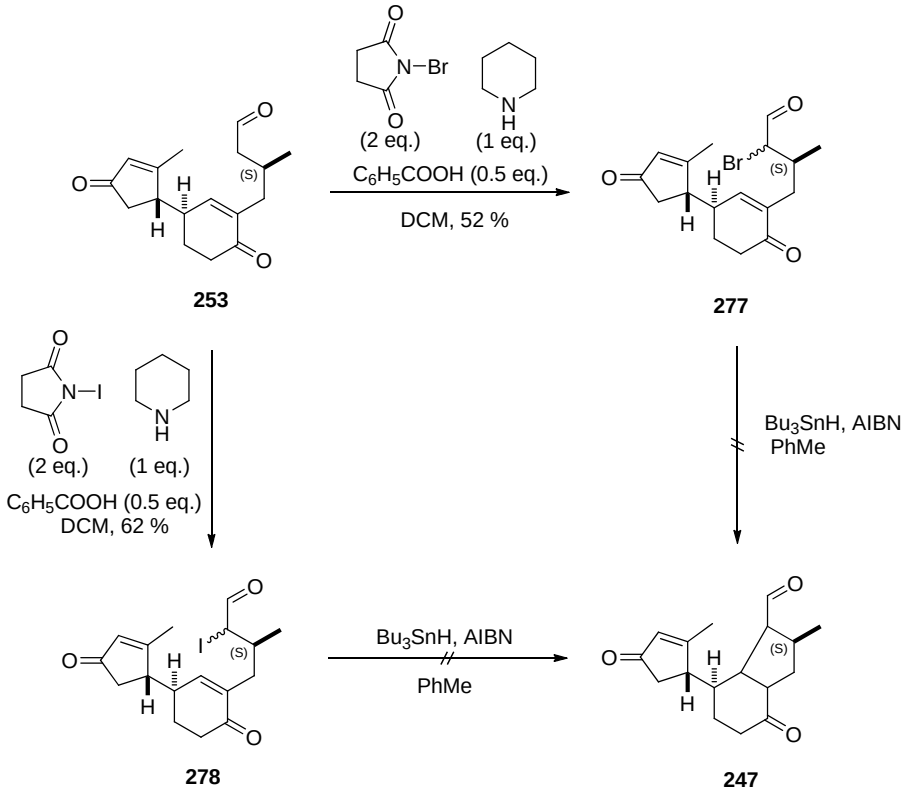


	^{1}H NMR	^{13}C NMR	COSY	HMBC	NOESY
1	2.02 (s)	17.0		2, 3, 4, 6	3
2		177			
3	5.85 (quint, *J* = 1.4 Hz)	133.7	6, 1	1, 2, 4, 5, 6	1
4		206.8			
5	2.45 (d, *J* = 5.7 Hz)	54.3	10	2, 9, 10, 11	TBS, 9a
6	2.82 (d, *J* = 5.7 Hz)	50.6	5	2, 7, 12	5, 1, 8a
7	2.73 (dt, J=6.5, 3.0 Hz)	32.5	12, 8a, 8b	5, 8, 9	1, 8a, 8b, 12
8a 8b	1.65-1.71 (m); 1.55 (tt, *J* = 12.0, 4.0 Hz)	25.89	9a, 9b, 7	6, 7, 9, 12	8b, 6, 7 8a, 7
9a 9b	1.77 (ddd, *J* = 12.0, 8.8, 4.2 Hz); 1.44 (dt, *J* = 12.6, 4.1 Hz)	34.4	8a, 8b	5, 8, 10, 11	9b, 5 9a
10		78.7			
11		145.1			
12	5.43 (d, J= 6.4 Hz)	121.5	7	6, 7, 10, 13	7, 13a, 13b
13	1.83-1.88 (m); 2.14-2.17 (m)	37.5	14	10, 11, 15, 16	
14	2.13 (m)	27.9	13, 15	15, 16	
15	0.86 (d, *J* = 6.5 Hz)	19.4	14	13, 14, 16	
16	2.36 (dd, *J* = 15.0, 3.9 Hz); 2.02 (dd, *J* = 15.0, 9.1 Hz)	41.4	14	13, 14, 17	
17		173.8			
18	3.67 (s)	51.3		17	

The final possibility we decided to investigate was the radical mediated conjugate addition. Although this version of 1,4-addition is not as popular as the enolate or enamine conjugate additions, there are plenty of precedents of radicals engaging in 1,4-addition processes with enones.[40] Our intent was to prepare the bromoaldehyde **277** and expose it to radical initiators in the hope it would cyclize to afford **247**. In the event, bromoaldehyde **277** was prepared by reaction of **253** with *N*-bromosuccinimide in the presence of piperidine and benzoic acid as a 1:1 mixture of diastereomers at the carbon bearing the bromine atom.[41] However, treatment of **277** with tributyltin hydride in the presence of a catalytic amount of 2,2'-azoisobutyronitrile (AIBN) in refluxing benzene lead to recovery of the starting material (Scheme 82). Iodides are typically more reactive then bromides in radical cyclization reactions and iodoaldehyde **277** was considered to be a better candidate for closure of ring C. Reaction of **253** with *N*-iodosuccinimide in the presence of piperidine and benzoic acid gave **278** as a 1:1 mixture of diastereomers but when **278** was exposed to tributyltin hydride in the presence of a catalytic amount of 2,2'-azoisobutyronitrile (AIBN) in refluxing benzene only reduction of the carbon-iodine bond took place to regenerate aldehyde **253** (Scheme 82).

Our failure to convert **253** into a tricyclic scaffold such as **272** via intramolecular Michael addition of enolates, conjugated addition of enamines and radical cyclization prompted a reevaluation of this aldehyde as a precursor to the core. A lesson learnt

from the facile intramolecular aldol condensation that **253** and its derivatives displayed was that ring D would need to be modified in order to reach our goal. A new plan based on this strategy is presented in the section that follows.

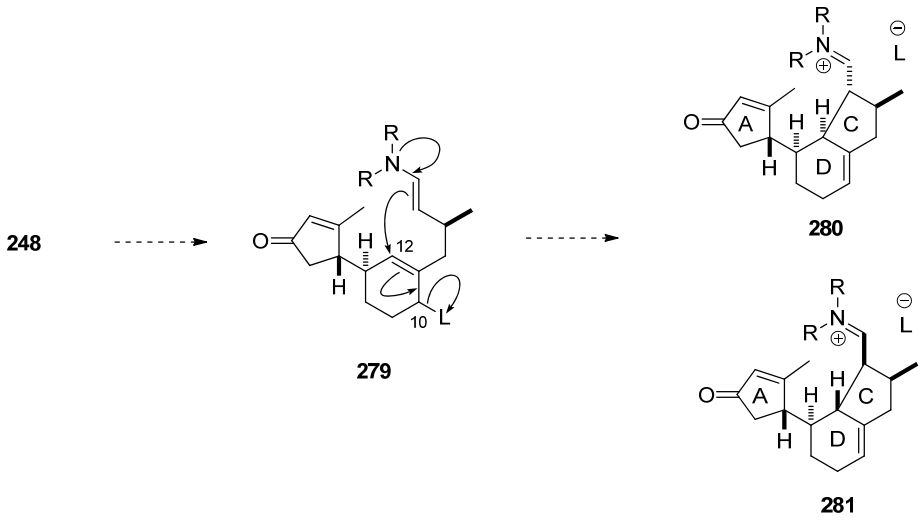


Scheme 82. Synthesis of bromoaldehyde **277** and iodoaldehyde **278**, and attempted radical cyclization

2.4.2 A S_N2' displacement approach to ring C of neomangicol A

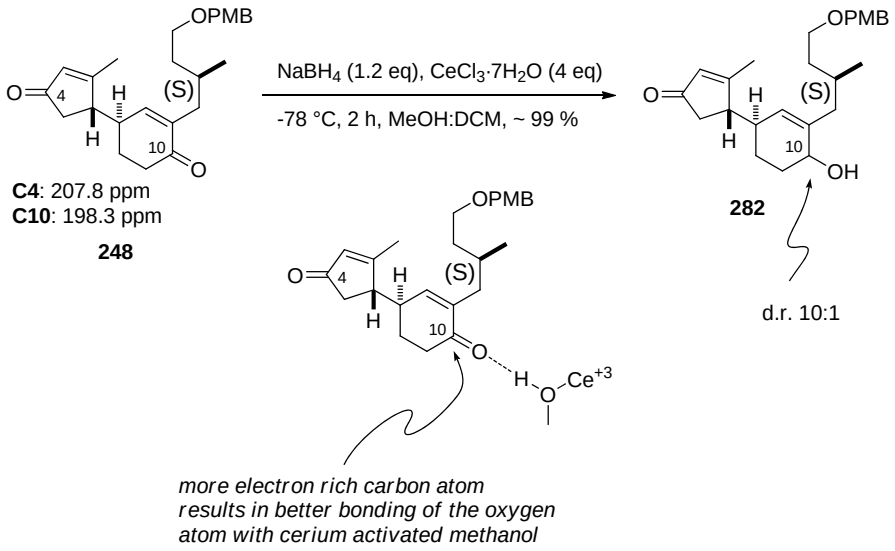
In view of the failure of the cyclohexenone moiety of **253** to undergo conjugate addition and the clear preference for intramolecular nucleophilic attack at the C10 ketone instead, it was decided to modify **253** in a way that would prevent this undesired cyclization mode. Our new strategy envisioned reduction of the C10 ketone to an alcohol which would be converted to a leaving group (L) so that intramolecular S_N2' displacement,[42] for example by enamine **279**, would lead to tricycle **280**. Our expectation that intramolecular S_N2' displacement would predominate over direct S_N2 substitution was based on the known fact that branching at the position α to the leaving group drastically inhibits direct S_N2 attack.[43] This argument presupposes that enamine **279** engages in a favorable 5-exo-trig cyclization to produce **280** but it leaves in doubt the configuration at the CD ring fusion since, even if the configuration at C10 is defined, S_N2' substitution can proceed by either *syn* or *anti* pathways.[44] The favored stereoelectronic orientation through which most S_N2' reactions proceed has the leaving group σ bond parallel to the p-orbital of the carbon-carbon double bond, thus allowing better overlap of the π system in the transition state. This overlap is optimal if the leaving group is in a quasi-axial position and the incoming nucleophile attacks axially (*syn*). Regardless of the stereochemistry at C10, nucleophilic attack at the *re* face of **279** would afford **280**; conversely if substitution occurs from the *si* face **281**, would result (Scheme 83). Despite these uncertainties, the plan outlined in Scheme 87

appeared to offer reasonable prospect for gaining access to the core structure of neomangicol A.



Scheme 83. Synthetic plan for construction of ring C based on S_N2' displacement

Synthesis of our desired substrate for this plan commenced with reduction of enone **248** with sodium borohydride in the presence of cerium(III) chloride[45] to furnish allylic alcohol **282** as one major diastereomer (d.r. 10:1). Regioselective reduction of the C10 ketone over reduction of C4 was anticipated based on carbon-13 nuclear magnetic resonance analysis of **253**. A chemical shift comparison revealed that the carbonyl carbon C4 is more electron-deficient than the cyclohexenone carbonyl carbon at C10. As a consequence, the oxygen atom bound to C10 coordinates more strongly with cerium activated methanol[46] and renders C10 more reactive toward hydride addition (Scheme 84).



Scheme 84. Synthesis of allylic alcohol **282** from **248**

On the possibility that the configuration of the leaving group at C10 may play a role in the stereochemical outcome of the S_N2' displacement shown in scheme 87, we decided to determine the configuration of this stereocenter in alcohol **282**. A technique to determine the absolute stereochemistry of secondary alcohols is Mosher ester analysis, first used by Dale and Mosher in 1973[47] and further developed by Kakisawa.[48] This empirical method measures nuclear magnetic resonance chemical shifts of protons in the neighborhood of the stereocenter to be determined by converting the secondary alcohol into esters of (*R*)-α-methoxy-α-(trifluoromethyl)phenylacetic acid (*R*-MTPA acid) and (*S*)-α-methoxy-α-(trifluoromethyl)phenylacetic acid (*S*-MTPA). After proton chemical shifts are assigned, the difference in chemical shift between protons in the (*S*) and the (*R*) Mosher esters is determined. Next, the conformation of the (S) Mosher

ester with the R_2R_1CH-O-C(=O)-C-CF_3 substructure in an eclipsed conformation and with the carbonyl of the ester function in a *cis* orientation with the secondary alcohol hydrogen atom is analyzed (Fig 6a). Protons residing on the same side of the plane as the phenyl group will experience an anisotropic shielding effect and will appear upfield in the proton NMR spectrum, whereas protons residing on the same side as the methoxy group will be deshielded due to a through-space electron-withdrawing effect of the methoxy substituent and will therefore appear downfield in the proton NMR spectrum. As a consequence, if the difference in the chemical shift for the same proton in (*S*) and (*R*) Mosher esters is positive (δ_s-δ_R>0), the proton is on the same side of the plane as the methoxy group (above plane A) in the (*S*) Mosher ester (R_1); conversely, if this difference is negative (δ_s-δ_R<0) that proton is on the same side (below plane A) as the phenyl group in the (*S*) Mosher ester (R_2) (Fig 6b). In this way, the absolute configuration of a secondary alcohol can be assigned with a high degree of confidence.

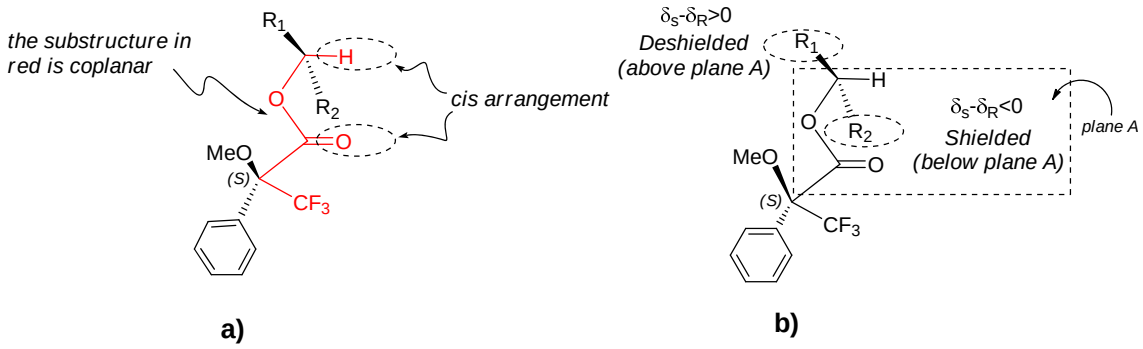
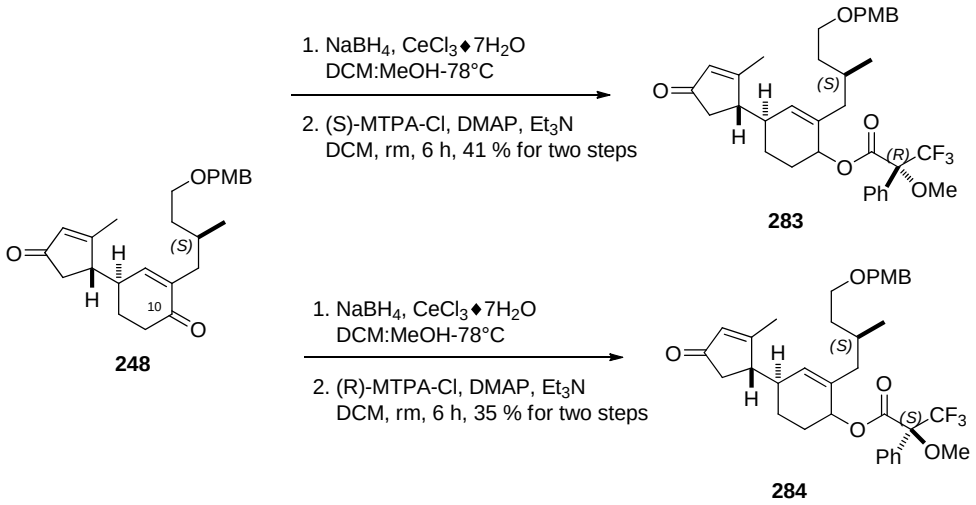


Fig 6. The general Mosher ester analysis scheme

In order to apply the above analysis to determination of the alcohol configuration at C10 of **282**, the latter was reacted with (*S*)-MTPA chloride and (*R*)-MTPA chloride to give (*R*)-MTPA ester **283** and (*S*)-MTPA ester **284**, respectively (Scheme 85). It is important to note that R/S configurational assignments reverse going from the MTPA chlorides to their esters. Table 3 displays the chemical shifts of protons in (*S*)-MTPA ester **284** and (*R*)-MTPA ester **283** and their difference expressed in ppm.



Scheme 85. Synthesis of Mosher esters **283** and **284**

Mapping the chemical shift differences between **283** and **284** reveals that the right hemisphere of each molecule has δ_s-δ_R<0 whereas the left hemisphere has δ_s-δ_R>0 (Fig 7a). Figure 8 presents all possible stereoisomers of (*R*) and (*S*) Mosher esters (**286**, **287**, **288** and **289**) in their ideal conformation. If we consider two possible configurations for the (*S*)-Mosher ester (**286** and **288**), we find that in **286** the methoxy group is in the hemisphere of the molecule with δ_s-δ_R>0. This establishes that the

structure of the (*S*)-Mosher ester is **286** and therefore the stereochemistry of alcohol **282** is (R), shown as **285** in Fig 7b. Thus, hydride addition to **248** had taken place from the *si* face of the C10 ketone.

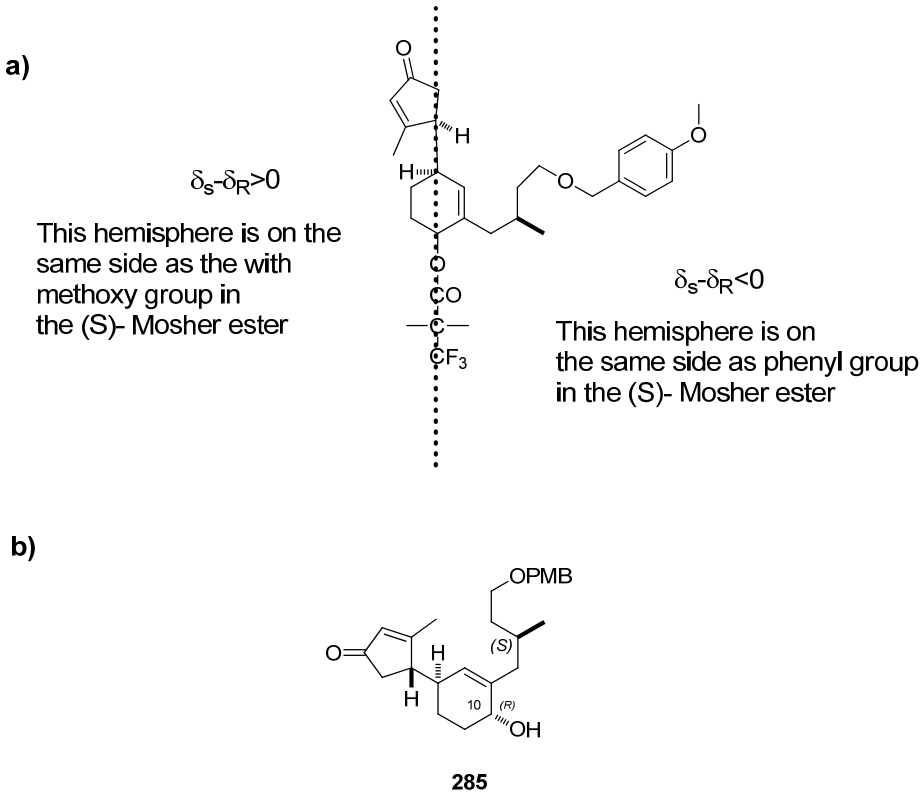
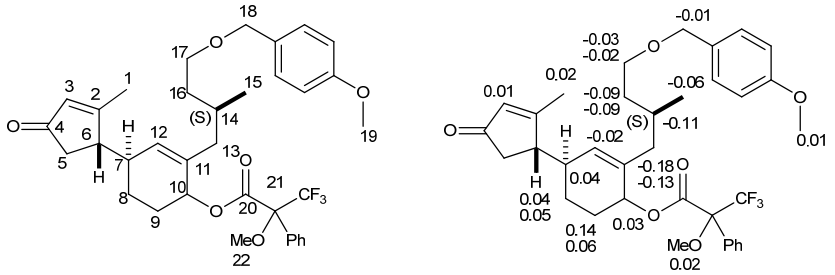


Fig 7. a) δ_S-δ_R index in two hemispheres of the molecule.
b) The predicted stereochemistry at C10 of **282** by Mosher analysis

Table 3. Chemical shifts of protons in **283** and **284** and their difference



Atom number	δ (ppm) for (*R*)- MTPA ester (283)	δ (ppm) for (*S*)- MTPA ester (284)	δ_s-δ_R (ppm)
1	2.09	2.11	0.02
3	6.00	6.01	0.01
7	2.72	2.76	0.04
8	1.38	1.43	0.05
8	1.07	1.11	0.04
9	2.29	2.35	0.06
9	1.51	1.65	0.14
10	5.49	5.52	0.03
12	5.43	5.41	-0.02
13	2.24	2.06	-0.18
13	1.62	1.49	-0.13
14	1.68	1.57	-0.11
15	0.79	0.73	-0.06
16	1.60	1.51	-0.09
16	1.35	1.26	-0.09
17	3.46	3.43	-0.03
17	3.41	3.39	-0.02
18	4.43	4.42	-0.01
19	3.83	3.84	0.01
22	3.51	3.53	0.02

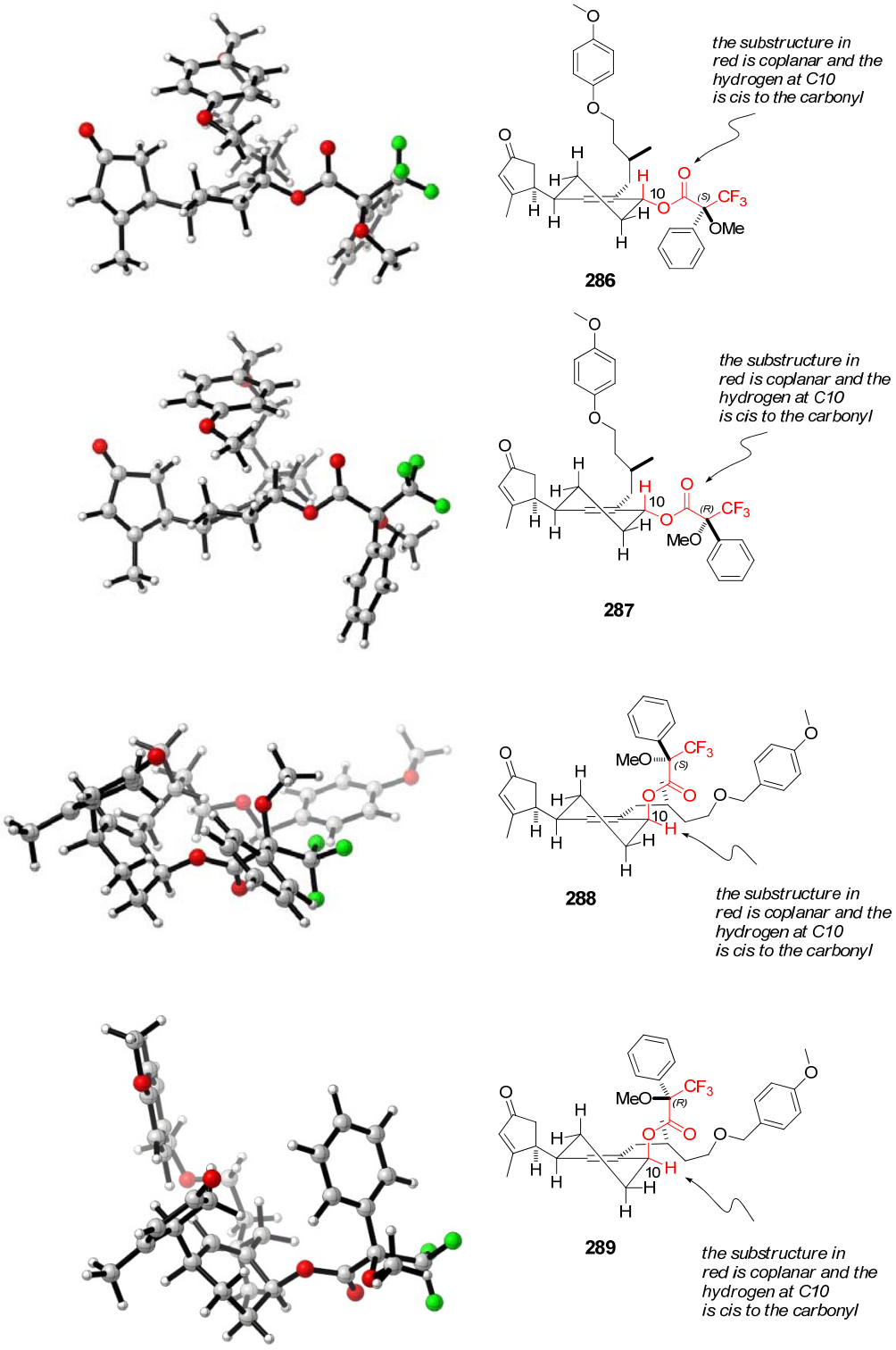
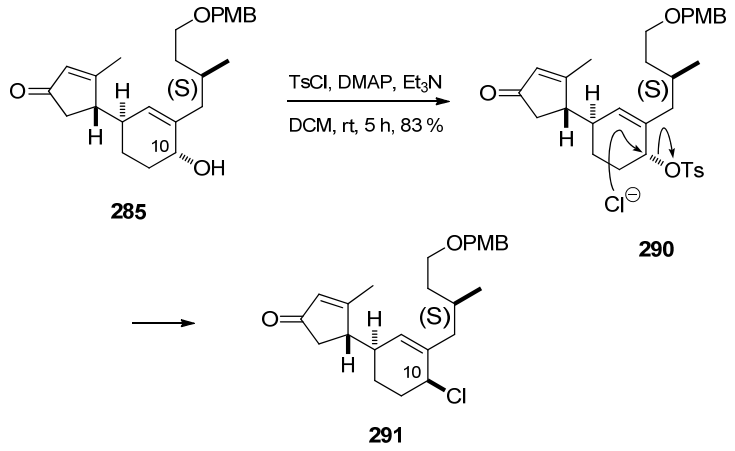


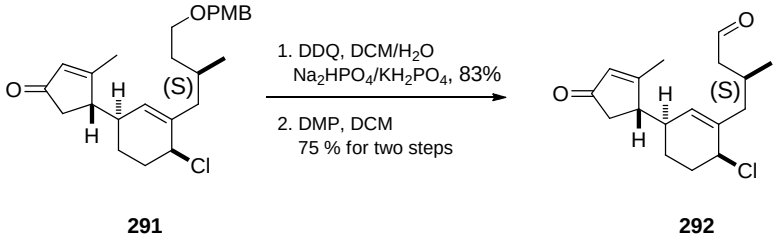
Fig 8. Four possible stereoisomers of Mosher esters of **283** and **284** in their ideal conformation

With the configuration of **285** defined, the alcohol was reacted with tosyl chloride in the presence of triethylamine. The product from this reaction was found to be chloride **291**, presumably formed from tosylate **290** as an intermediate via nucleophilic replacement with chloride ion. It is assumed that this displacement caused inversion at C10 and that chloride **291** possesses (*S*) configuration at C10 (Scheme 86).



Scheme 86. Synthesis of chloride **291** from **285**

When chloride **291** was exposed to 2,3-dichloro-5,6-dicyano-1,4-benzoquinone to excise the *p*-methoxybenzyl group, a primary alcohol was produced which was oxidized to aldehyde **292** with Dess-Martin periodinane (Scheme 87).

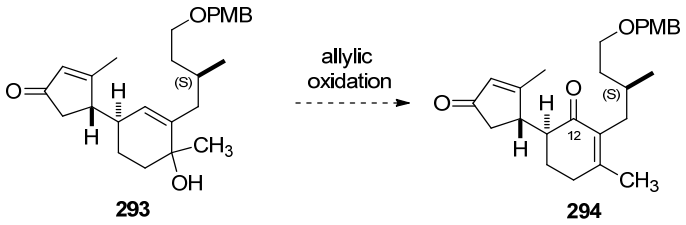


Scheme 87. Synthesis of **292** via deprotection and oxidation of **291**

Unfortunately, neither aldehyde **292** nor its enamine derivates prepared with piperidine or morpholine could be induced to undergo the desired S_N2'displacement of the allylic chloride. This approach to constitute ring C of neomangicol A was therefore abandoned in favor of one that introduced functionality at the cyclohexene double bond in the hope that direct reaction at C12 would lead to ring C formation.

2.4.3 Intramolecular aldol and epoxidation approaches to ring C of neomangicol A

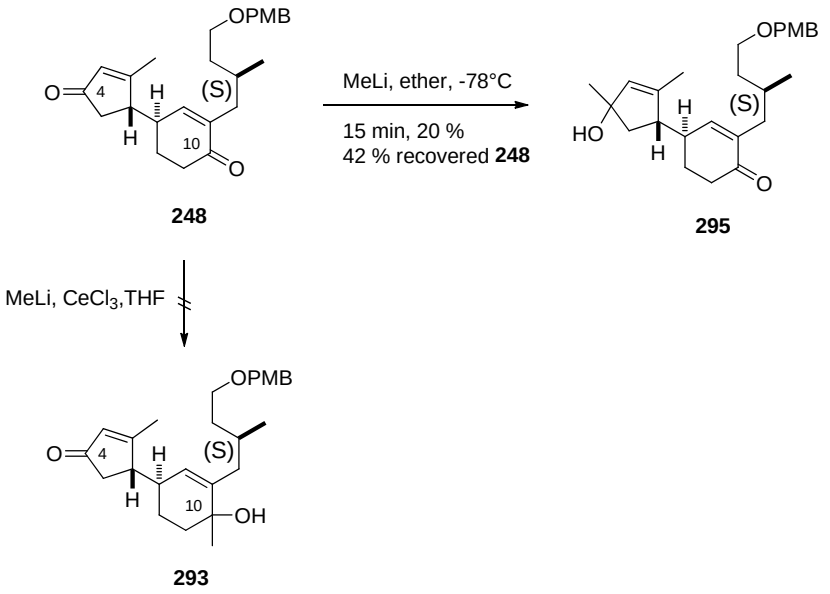
The preference by aldehyde **253** and its enamine derivatives for intramolecular aldol condensation over conjugate addition (Schemes 80 and 82) suggested an alternative mode of aldol condensation as a means to install ring C in neomangicol A. A potential candidate for this alternative aldol condensation would be **294** bearing a ketone at C12. In principle, **294** could be prepared from allylic alcohol **293** via oxidation with rearrangement (Scheme 88).



Scheme 88. A prospective route to enone **294** from **293**

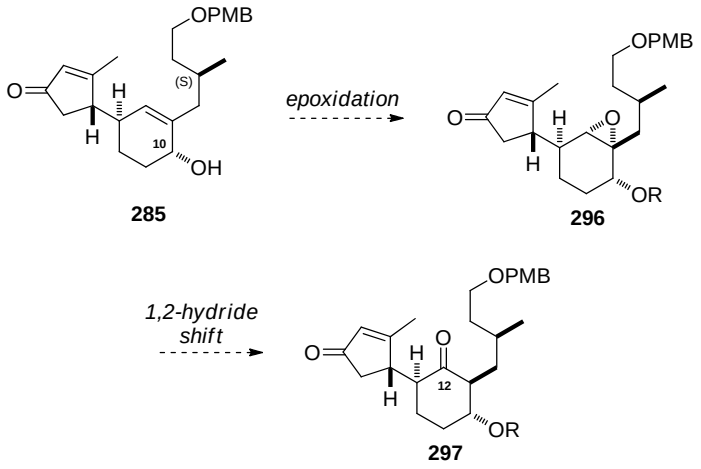
This route hinges on regioselective addition of methyllithium at C10 of **248**, for which precedent existed in the reduction of **248** with sodium borohydride in the presence of anhydrous cerium(III) chloride. In that case, we found that the C10 ketone of **248** was reduced cleanly to afford alcohol **285** while the C4 ketone would remain intact (Scheme 84). In the event, treatment of **248** with methyllithium in the presence of cerium(III) chloride heptahydrate resulted in complete recovery of **248**. However, when **248** was exposed to methyllithium alone, it was the more electron deficient

ketone at C4 that reacted to give tertiary alcohol **295** as a single diastereomer according to its carbon-13 nuclear magnetic resonance spectrum (Scheme 89).



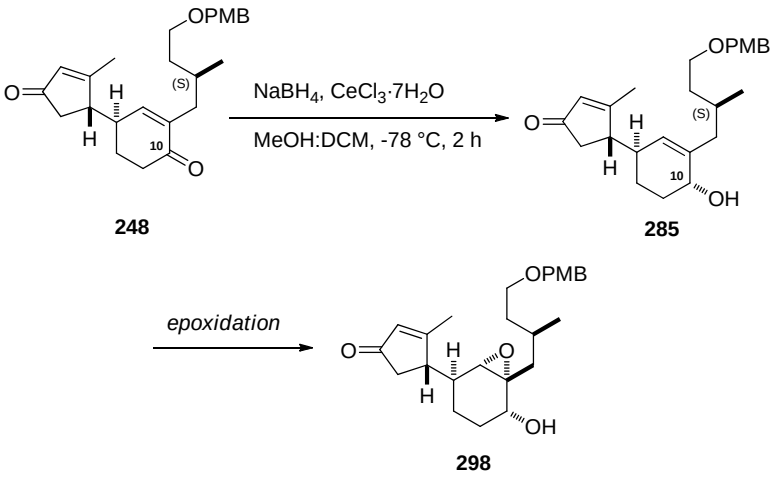
Scheme 89. Addition of methyllithium to **248** to give **295**

An alternative approach to introducing a ketone function at C12 would be via epoxidation of allylic alcohol **285**. This should give epoxide **296**, rearrangement of which could lead to **297**. After cleaving the *p*-methoxybenzyl ether from **297**, oxidation of the resultant alcohol would furnish an aldehyde which could undergo intramolecular aldol condensation to afford ring C of neomangicol A (Scheme 90).

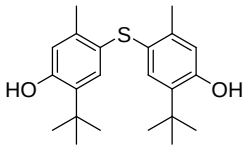


Scheme 90. Synthetic plan for synthesis of **296** and **297**

Our approach along this line commenced with epoxidation of cyclohexenol **285** which we assumed would be directed by the allylic alcohol. In the event, reaction of **285** with *m*-chloroperoxybenzoic acid in dichloromethane produced a mixture of the desired epoxide **298** (as a single diastereomer), enone **248** and unreacted **285**. The configuration of epoxide **298** is believed to be as shown and is based not only on the assumption that epoxidation is directed by the (10*R*) alcohol but also on the fact that β face of the alkene is blocked by the bulky cyclopentenone substituent.[49] In a separate experiment, treatment of **285** with vanadyl acetylacetonate and *t*-butyl hydroperoxide produced a similar mixture of products. However, when **285** was treated with *m*-chloroperoxybenzoic acid in the presence of a catalytic amount of the diaryl sulfide radical inhibitor **299**[50] in dichloroethane it afforded epoxide **298** in 77 % yield as a single diastereomer according to its carbon-13 nuclear magnetic spectrum (Scheme 91).



epoxidation of 285	yield from 248
mCPBA, DCM, rt	33 %
*m*CPBA (4 eq), DCE, reflux	77 %

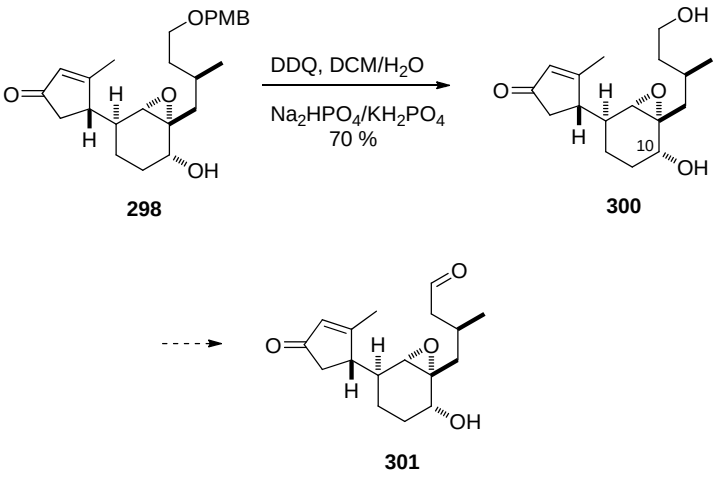


5 mol %

299

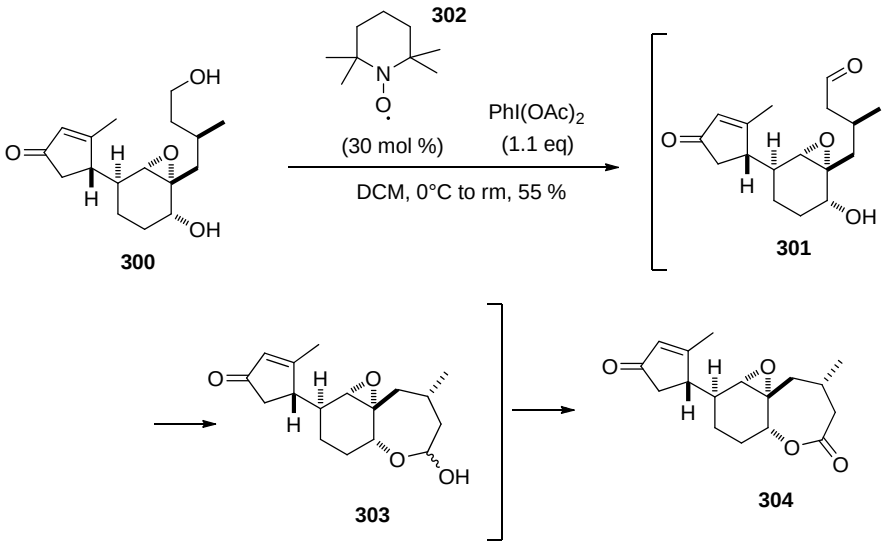
Scheme 91. Epoxidation of **285** to give **298**

After epoxidation of **285** to **298**, the latter was advanced to primary alcohol **300** by cleavage of the *p*-methoxybenzyl ether with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone. Our next goal was selective oxidation of the primary alcohol of **300** in the presence of the secondary alcohol at C10 to obtain aldehyde **301**, a process for which the reagent 2,2,6,6-tetramethylpiperidine 1-oxyl (TEMPO)[51] appeared to be well suited (Scheme 92).



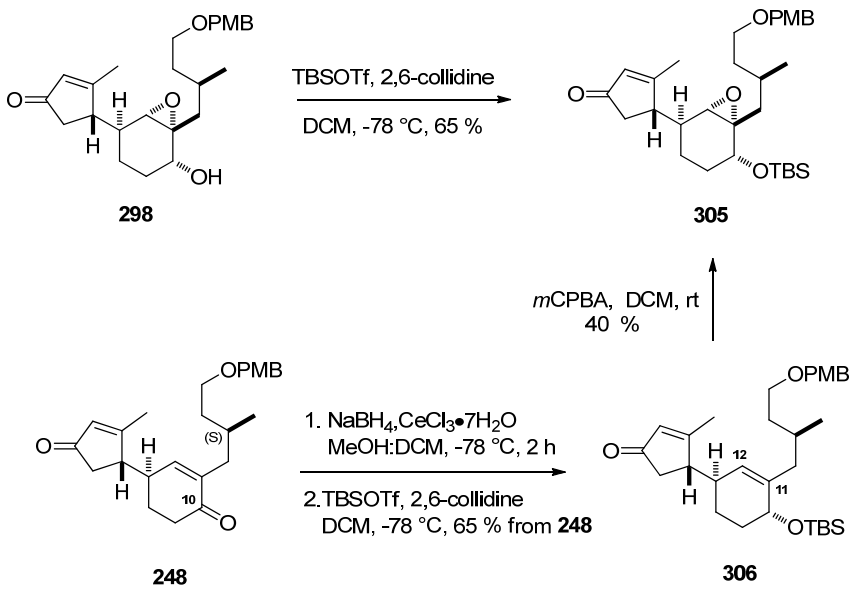
Scheme 92. Conversion of *p*-methoxybenzyl ether **298** to **300** and attempted oxidation to aldehyde **301**

However, when alcohol **300** was treated with catalytic TEMPO (**302**) in the presence of a stoichiometric amount of [bis(acetoxy)iodo]benzene we were surprised to find that the seven-membered lactone **304** was formed. It is believed that **300** was oxidized to aldehyde **301** as planned but that **301** cyclized to form hemiacetal **303**. In the presence of excess [bis(acetoxy)iodo]benzene, **303** was then oxidized to lactone **304** (Scheme 93). This unexpected result forced us to revise our plan for accessing ring C.



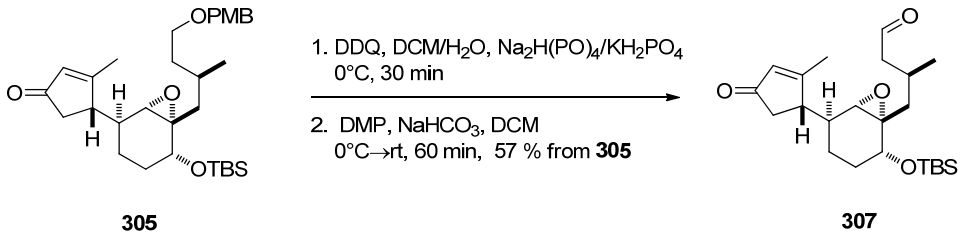
Scheme 93. Oxidation of **300** to **304**

In order to avoid formation of hemiacetal **303** and then **304** from **300**, epoxy alcohol **298** was converted into its *t*-butyldimethylsilyl ether **305**; removal of the *p*-methoxybenzyl ether moiety and oxidation of the resultant primary alcohol should then lead to aldehyde **307**. To that end, **298** was treated with *t*-butyldimethylsilyl trifluoromethanesulfonate in the presence of 2,6-collidine to give silyl ether **305**. The same epoxide, **305**, was obtained from diketone **248** by Luche reduction, subsequent silylation to give **306** and final epoxidation with *m*-chloroperoxybenzoic acid. The fact that **305** is prepared from epoxidation of **298** and **306** supports the view that epoxidation had taken place from the less hindered face of the C11, C12-alkene in both cases (Scheme 94).



Scheme 94. Synthesis of **305** from **298** and **306**

As expected, treatment of **305** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone afforded a primary alcohol which, upon exposure to Dess-Martin periodinane, yielded aldehyde **307** (Scheme 95).

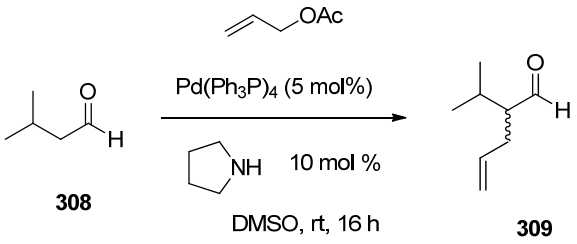


Scheme 95. Synthesis of aldehyde **307** from epoxide **305**

Although there are many examples in the literature in which epoxides undergo stereoselective opening with amines in the presence of metal-based Lewis acids,[52] there are only a few cases in which enamines have been used.[53] Nonetheless, we decided to explore this possible avenue to ring C of the neomangicol core with aldehyde **307**. To that end, **307** in dimethyl sulfoxide was allowed to react with piperidine to form an enamine, after which lithium tetrafluoroborate was introduced into the system to activate the epoxide. Unfortunately, no detectable change was noted after running the reaction at room temperature or at 60º. When, acetonitrile was used as the solvent at elevated temperatures, a complex mixture resulted that was difficult to purify.

2.5 π-Allyl approach to ring C of neomangicol A

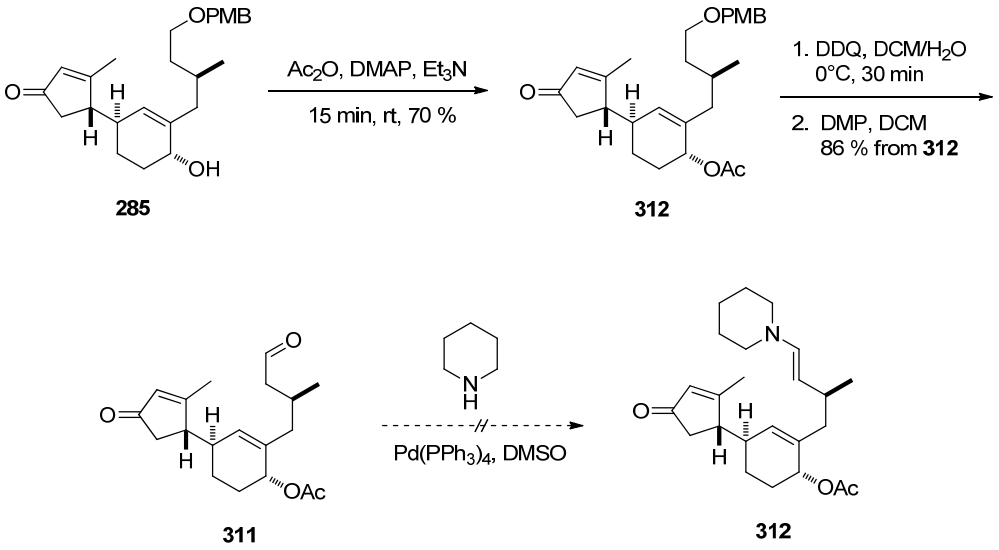
In 2006, Cordova[54] and co-workers published the first direct intermolecular α-alkylation of aldehydes with allylic acetates in the presence of a catalytic amount of secondary amine and a palladium(0) catalyst. An example from this work is alkylation of isovaleraldehyde (**308**) with allyl acetate to give alkylated aldehyde **309**. Presumably, the pyrrolidine enamine from **308** is formed initially and reacts *in situ* with the π-allylpalladium complex from allyl acetate to give **309** (Scheme 96).



Scheme 96. Palladium(0) catalyzed alkylation of **308** with allyl acetate

In our case, allylic acetate **311** would be a potential candidate for extending this method to an intramolecular setting that would install ring C of neomangicol A. Synthesis of **311** commenced with acetytion of alcohol **285** with acetic anhydride to give acetate **312**. The *p*-methoxybenzyl ether of **312** was cleaved and the resulting alcohol was oxidized to aldehyde **311**. Treatment of **311** with piperidine and tetrakis(triphenylphosphine)palladium(0) in dimethyl sulfoxide resulted in formation

of enamine **312** which unfortunately failed to react further under these conditions (Scheme 97).

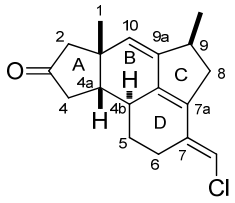


Scheme 97. Synthesis of alkylation precursor **311** from alcohol **285**

At this point, all possible approaches to assembling ring C of the neomangicol core from our existing precursors appeared to be exhausted and no further attempts were made to solve this difficult problem.

2.6 Conclusion

Our synthetic approach toward the core structure **129** of neomangicol A, was successful in forging rings A and D of the tetracycle and in appending a functionalized five-carbon chain to ring D that could serve as an entry point to ring C.

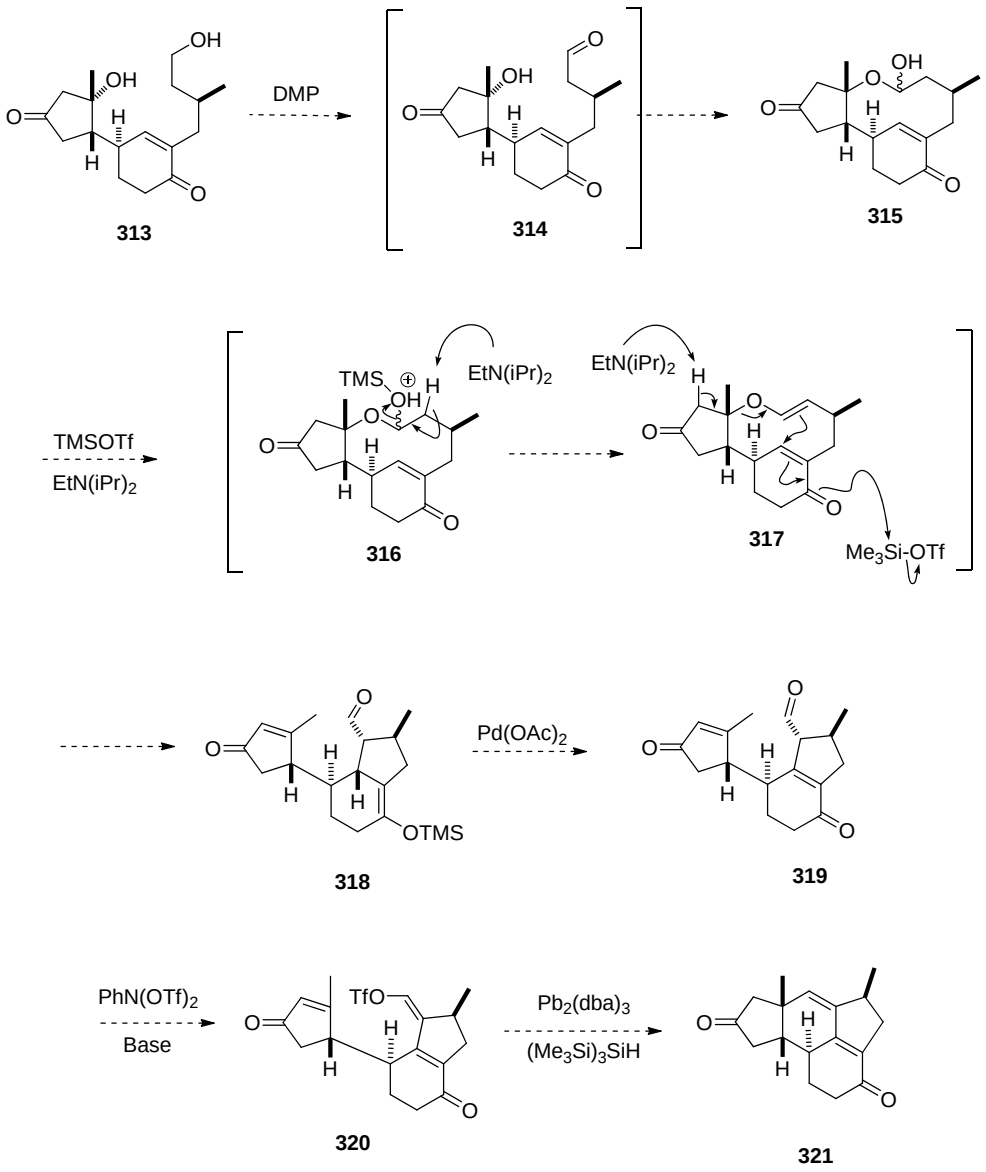


129

Ring A was constructed from (*S*)-(+)-carvone (**160**) in five steps (21 % overall yield) using a radical mediated cyclization and a series of Baeyer–Villiger oxidations as key steps. Acetate **157** was advanced to lactone **218** via stereoselective alkylation with alkyl iodide **217**, prepared from (*S*)-(-)-citronellol **160** in seven steps (56 % overall yield). Ring D of the neomangicol nucleus was assembled from **218** in five steps (50 % overall yield) using ring-closing metathesis. It is noteworthy that **218** not only contains all fourteen of the carbon atoms needed for the core of neomangicol A but also carries the correct stereochemical signature for tetracycle **129** at C4a, C4b and C9.

The challenge remaining to complete the tetracyclic core of neomangicol A will involve assembling rings C and B, for which a new strategy will probably be

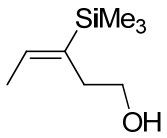
required. A prospective blueprint that would approach this challenge from a direction different from our existing route is shown in Scheme 98. An approach we suggest for setting ring C of neomangicol A is based on a transannular Mukaiyama-Michael reaction of cyclic hemiactal **315**, which could be prepared from diol **313** via Dess-Martin oxidation and subsequent cyclization. It is anticipated that exposing **315** to trimethylsilyl triflate and Hünig's base would cause dehydration of **315** via **316** to form *in situ* enol ether **317**, which would undergo Mukaiyama-Michael cyclization initiated by elimination of the β-alkoxy cyclopentanone to furnish trimethylsilyl enol ether **318**. Saegusa oxidation of **318** with palladium(II) acetate would regenerate the cyclohexenone substructure of **319**, and after reaction with Comins' reagent this aldehyde would afford vinyl triflate **320**. Completion of the tetracyclic core would entail a reductive Heck coupling of **320** in the presence of a palladium(0) catalyst and a hydride source (Scheme 98).



Scheme 98. A potential approach toward rings B and C of the neomangicol core from **313**

2.7 Experimental procedures

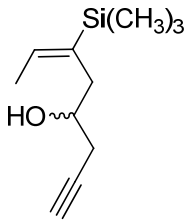
All reactions requiring anhydrous conditions were conducted in flame-dried glass apparatus under an atmosphere of argon. Tetrahydrofuran, ether, dichloromethane, ethyl acetate and hexanes were dried by passage through an activated alumina column under argon. Dimethyl sulfoxide was distilled from calcium hydride at 15 mm Hg and stored over activated 4Å molecular sieves. Methanol and 1,2-dimethoxyethane were freshly distilled from calcium hydride. Preparative chromatographic separations were performed on silica gel (35-75 μm); reactions were followed by thin layer chromatography using silica plates with a fluorescent indicator (254 nm) which were visualized with a UV lamp or phosphomolybdic acid. All commercially available reagents were purchased and used as received unless stated otherwise. Optical rotations were measured with a polarimeter using a 1 mL capacity cell with 1 dm path length. Infrared spectra were recorded using a thin film supported between KBr discs or dispersed in a KBr pellet. ^{1}H and ^{13}C NMR spectra were recorded in Fourier transform mode at the field strength specified on either a 300, 400 or 700 MHz spectrometer. Spectra were obtained on solutions in 5 mm diameter tubes, and chemical shifts in ppm are quoted relative to the residual signals of $CHCl_3$ (δ_H 7.26 ppm, or δ_C 77.0 ppm). Multiplicities in the ^{1}H NMR spectra are described as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad; coupling constants are reported in Hz. Low (MS) and high (HRMS) resolution mass spectra are reported with ion mass/charge (*m/z*) ratios in atomic mass units.



145

(*E*)-3-(Trimethylsilyl)pent-3-en-1-ol (145). A solution of (but-3-yn-1-yloxy)dimethylsilane (**144**, 1.40 g, 9.80 mmol) and hydrogen hexachloroplatinate (0.21 mL, 0.0750M in tetrahydrofuran, 0.2 mol %) in tetrahydrofuran (32 mL) was heated at 70 °C for 12 h. The cooled mixture was filtered through a short pad of Celite and eluted with ether (50 mL). The solvent was evaporated under reduced pressure to give crude (*E*)-3-ethylidene-2,2-dimethyl-1,2-oxasilolane that was used in the next step without purification.

To a stirred solution of crude (*E*)-3-ethylidene-2,2-dimethyl-1,2-oxasilolane in ether (7.5 mL) at 0 °C was added methyllithium (1.40M solution in ether, 7 mL, 20.6 mmol) and the reaction mixture was stirred at room temperature for 3 h. Saturated aqueous ammonium chloride (20 mL) was added to quench the reaction, the aqueous phase was extracted with ether (3 x 20 mL), and the combined extracts were dried with anhydrous sodium sulfate. The solution was distilled under reduced pressure (water aspirator) to give **145** (1.00 g, 67 %) as a yellow oil: bp 40 °C; IR (neat) 3322, 3010, 2954, 1933, 1863, 1615, 1438, 1371, 1247, 1195, 1136, 1018, 940, 838, 688, 619 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.07 (s, 9H) 1.73 (d, J = 6.7 Hz, 3H), 2.47 (t, J = 7.7 Hz, 2H), 3.58 (q, J = 4.6 Hz, 2H), 6.03 (q, J = 6.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ -0.9, 15.0, 33.0, 62.3, 137.7, 138.0; HRMS (EI) *m/z* 143.0891 (calcd for $C_7H_{15}OSi$ 143.0892).

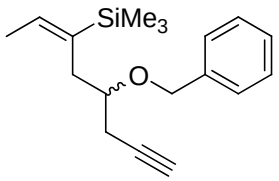


146

(*E*)-6-(Trimethylsilyl)oct-6-en-1-yn-4-ol (146). To a stirred solution of (*E*)-3-(trimethylsilyl)pent-3-en-1-ol (**145**, 1.30 g, 8.20 mmol) and imidazole (1.10 g, 16.4 mmol) in dichloromethane (80 mL) at 0 °C was added Dess-Martin reagent (7.00 g, 16.4 mmol). The slurry was stirred at room temperature for 3 h and then saturated aqueous sodium thiosulfate (20 mL) and sodium bicarbonate (20 mL) were added to quench the reaction. The aqueous phase was extracted with ether (3 x 10 mL) and the combined extracts were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure to give crude (*E*)-3-(trimethylsilyl)pent-3-enal that was used immediately.

To a stirred solution of crude (*E*)-3-(trimethylsilyl)pent-3-enal in ether (30 mL) at 0 °C was added freshly prepared propargylmagnesium bromide (50 mmol) and the mixture was stirred for 3 h. Saturated aqueous ammonium chloride (20 mL) was added to quench the reaction, the aqueous phase was extracted with ether (3 x 10), and the combined extracts were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (5 % ethyl acetate in hexanes) to give **146** (1.00 g, 62 % for two steps) as a yellow oil: IR (neat) 3440, 3311, 2953, 2120, 1612, 1432, 1354, 1284, 1132, 1055, 949, 837, 752, 689, 638 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.08 (s, 9H), 1.76 (d, *J* =

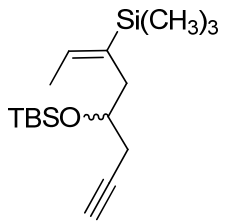
6.6 Hz, 3H), 1.94 (OH, d, *J* = 3.5 Hz, 1H), 2.07 (t, *J* = 2.6 Hz, 1H), 2.40 (ddd, *J* = 6.1, 4.7, 2.6 Hz, 1H), 2.47 (dd, *J* = 6.7, 2.1 Hz, 1H), 3.86-3.76 (m, 1H), 6.12 (q, *J* = 6.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 0.5, 15.5, 27.1, 36.5, 69.8, 71.1, 81.4, 138.3, 138.8; HRMS (CI+) *m/z* 197.1365 (calcd for $C_{11}H_{21}OSi$ 197.1362).



148

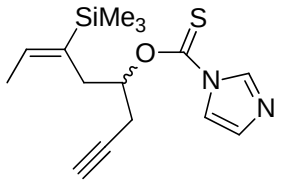
(*E*)-(5-(Benzyloxy)oct-2-en-7-yn-3-yl)trimethylsilane (148). To a stirred solution of (*E*)-6-(trimethylsilyl)oct-6-en-1-yn-4-ol (**146**, 10.0 mg, 51.0 μmol) in dimethylformamide (1.5 mL) at 0 °C was added sodium hydride (4.10 mg, 100 μmol, 60% mineral oil suspension). The suspension was stirred for 30 min and benzyl bromide (6.00 μL, 100 μmol) was added. The reaction mixture was stirred at room temperature for 5 h and the reaction was quenched with ethanol (1 mL) and water (20 mL). The aqueous phase was extracted with ether (3 x 10 mL) and the combined extracts were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (2 % ethyl acetate in hexanes) to give **148** (13.5 mg, 96 %) as a yellow oil: IR (neat) 3309, 2923, 2954, 2854, 2120, 1667, 1613, 1496, 1454, 1349, 1094, 1072, 1027, 837, 801, 748, 697, 635 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.06 (s, 9H), 1.72 (d, *J* = 6.6 Hz, 3H), 2.01 (t, *J* = 2.6 Hz, 1H), 2.41-2.39 (m, 2H), 2.55-2.50 (m, 2H), 4.59 (q, *J* = 5.6

Hz, 1H), 4.53 (d, *J* = 11.8 Hz, 1 H), 4.67 (d, *J* = 11.8 Hz, 1H), 6.01 (q, *J* = 6.6 Hz, 1H), 7.37-7.32 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$) δ -0.4, 15.6, 24.1, 34.5, 70.3, 72.1, 77.8, 82.1, 127.9, 128.2, 128.7, 128.8, 138.1, 138.4, 138.9.



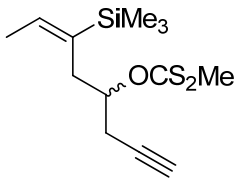
147

(*E*)-tert-Butyldimethyl((6-(trimethylsilyl)oct-6-en-1-yn-4-yl)oxy)silane (147). To a stirred solution of (*E*)-6-(trimethylsilyl)oct-6-en-1-yn-4-ol (**146**, 10.0 mg, 50.0 μmol) and triethylamine (0.1 mL) in dichloromethane at -78 °C was added *t*-butyldimethylsilyl trifluoromethanesulfonate (28.0 μL, 120 μmol). The mixture was stirred for 2 h and the reaction was quenched with saturated aqueous sodium bicarbonate (5 mL). The aqueous phase was extracted with ether (3 x 10 mL) and the combined extracts were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (100 % hexanes) to give **147** (12.0 mg, 80 %) as a colorless oil: IR (neat) 3314, 2954, 2929, 2857, 2122, 1615, 1472, 1388, 1249, 1096, 1006, 938, 836, 775, 637 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.08 (s, 15H), 0.89 (s, 9H), 1.76 (d, *J* = 6.6 Hz, 3H), 1.99 (t, *J* = 2.0 Hz, 1H), 2.49-2.38 (m, 4H), 3.86-3.76 (m, 1H), 6.12 (d, *J* = 6.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) -4.5, -4.2, -0.7, 15.3, 18.1, 25.9, 27.1, 37.0, 69.8, 71.2, 82.3, 137.6, 137.9.



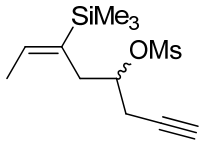
152

(*E*)-O-(6-(Trimethylsilyl)oct-6-en-1-yn-4-yl) 1H-Imidazole-1-carbothioate (152). A solution of (*E*)-6-(trimethylsilyl)oct-6-en-1-yn-4-ol (**146**, 22.0 mg, 110 μmol,) and thiocarbonyldiimidazole (39.9 mg, 220 μmol) in tetrahydrofuran (1 mL) was heated at 75 °C for 12 h. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (10% ethyl acetate in hexanes) to give **152** (32.0 mg, 94 %) as a colorless oil: IR (neat) 3307, 2953, 1615, 1464, 1388, 1366, 1352, 1284, 1246, 1229, 1101, 989, 967, 836, 749 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.08 (s, 9H), 1.80 (d, *J* = 6.7 Hz, 3H), 2.06 (t, *J* = 2.7 Hz, 1H), 2.60 (ddd, *J* = 17.0, 4.8, 2.7 Hz, 1H), 2.67-2.81 (m, 2H), 2.88 (dd, *J* = 13.8, 7.7 Hz, 1H), 5.78-5.60 (m, 1H), 6.05 (q, *J* = 6.7 Hz, 1H), 7.03 (s, 1H), 7.64 (s, 1H), 8.34 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ -0.5, 15.5, 23.1, 32.4, 71.7, 79.1, 81.0, 118.5, 130.9, 136.2, 137.3, 139.5, 183.9; HRMS (CI+) *m/z* 307.1292 (calcd for $C_{15}H_{23}ON_2SiS$ 307.1300).



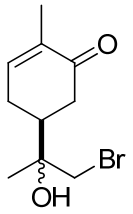
150

(*E*)-S-Methyl O-(6-(trimethylsilyl)oct-6-en-1-yn-4-yl) Carbonodithioate 150. To a stirred solution of (*E*)-6-(trimethylsilyl)oct-6-en-1-yn-4-ol (**146**, 20.0 mg, 100 μmol) and imidazole (10.0 mg, 150 μmol) in tetrahydrofuran (2 mL) at 0 °C was added sodium hydride (30.0 mg, 1.25 mmol, 60% mineral oil suspension). The slurry was stirred at room temperature for 30 min and carbon disulfide (300 μL, 4.00 mmol) was added. The reaction mixture was stirred for 2 h at 60 °C, methyl iodide (100 μL, 1.60 mmol) at 0 °C was added, and the mixture was stirred for 5 h. The solvent was evaporated under reduced pressure and after addition of water (5 ml), the aqueous phase was extracted with ether (3 x 10 ml). The combined extracts were dried with anhydrous sodium sulfate, the solvent was evaporated under reduced pressure, and the residue was purified by chromatography on silica gel (100% hexanes) to give **150** (30.0 mg, 99 %) as a light rose-colored oil: IR (neat) 3311, 2953, 2923, 2853, 2120, 1615, 1455, 1426, 1247, 1209, 1057, 837, 752, 689, 643 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.09 (s, 9H), 1.80 (d, *J* = 6.6 Hz, 3H), 2.05 (t, *J* = 2.1, 1H), 2.55 (s, 3H), 2.60 (dd, *J* = 5.4, 2.6 Hz, 2H), 2.70 (ddd, *J* = 20.0, 14.0, 7.1 Hz, 1H), 5.72-5.80 (m, 1H), 6.06 (q, *J* = 6.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ -0.5, 15.6, 19.4, 23.6, 30.2, 32.6, 71.3, 79.8, 81.3, 136.7, 139.1, 215.9.



153

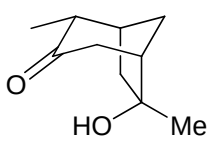
(*E*)-6-(Trimethylsilyl)oct-6-en-1-yn-4-yl Methanesulfonate (153). To a stirred solution of (*E*)-6-(trimethylsilyl)oct-6-en-1-yn-4-ol (**146**, 27.0 mg, 140 μmol) and 2,4,6-collidine (27.0 μL, 200 μmol) in dichloromethane (0.4 mL) at 0 °C was added methanesulfonyl chloride (15.8 μL, 200 μmol). The mixture was stirred at room temperature for 12 h and the reaction was quenched with saturated aqueous ammonium chloride (10 mL). The aqueous phase was extracted with ether (3 x 10 mL) and the combined extracts were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (5% ethyl acetate in hexanes) to give **153** (37.0 mg, 99 %) as a colorless oil: IR (neat) 3290, 2953, 1615, 1359, 1248, 1175, 958, 912, 839 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.08 (s, 9H) , 1.76 (d, *J* = 6.7 Hz, 3H), 2.09 (t, *J* = 2.6 Hz, 1H), 2.64-2.53 (m, 2H), 2.77-2.64 (m, 2H), 3,00 (s, 3H), 4.73 (quint, *J* = 7.4 Hz, 1H), 6.10 (q, *J* = 6.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ -0.65, 15.6, 25.1, 34.1, 38.9, 71.7, 79.6, 80.7, 136.5, 139.7; HRMS(CI+) *m/z* 275.1147 (calcd for $C_{12}H_{23}O_3SiS$ 275.1137).



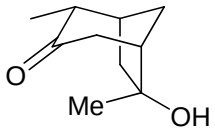
161

d.r. 1/1

(S)-5-(1-Bromo-2-hydroxypropan-2-yl)-2-methylcyclohex-2-enone (161). To a stirred solution of (*S*)-(+)-carvone (**159**, 1.00 g, 6.70 mmol) in a tetrahydrofuran-water mixture (3:2, 10 mL) at 0 °C was added *N*-bromosuccinimide (1.30 g, 7.20 mmol) in portions over 90 min. The mixture was stirred at room temperature for 24 h and sodium chloride (5.00 g) was added. The aqueous phase was extracted with ether (3 x 50 mL) and the combined extracts were washed with brine (50 mL) and dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (20 % ethyl acetate in hexanes) to give **161** (1.50 g, 89 %) as a colorless oil: IR (neat) 3445, 2974, 2923, 1660, 1450, 1432, 1371, 1305, 1256, 1182, 1107, 1078, 1011, 963, 924, 905, 822, 800, 694, 657 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.30 (s, 3H) , 1.77 (s, 3H), 2.02 (1H, s), 3.25 (s, 1H), 2.69-2.19 (m, 5H), 3.55-3.44 (m, 2H), 6.79-6.70 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 15.9, 22.8, 23.1, 26.7, 27.7, 38.9, 39.8, 42.4, 42.7, 43.4, 43.5, 135.5, 144.6, 145.8, 200.2; HRMS(CI+) *m/z* 247.0321 (calcd for $C_{10}H_{16}O_2Br$ 247.0334).



162



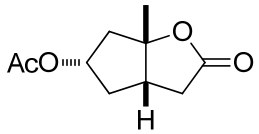
163

(1S,2R,5S,6S)-6-Hydroxy-2,6-dimethylbicyclo[3.2.1]octan-3-one (162) and (1S,2R,5S,6R)-6-Hydroxy-2,6-dimethylbicyclo[3.2.1]octan-3-one (163). A solution containing (*S*)-5-(1-bromo-2-hydroxypropan-2-yl)-2-methylcyclohex-2-enone (**161**, 1.10 g, 4.50 mmol), 2,2′-azobis(2-methylpropionitrile) (400 mg, 2.20 mmol) and *n*-tributyltin hydride (1.30 mL, 5.00 mmol) in benzene (350 mL) was refluxed for 16 h. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (20 % ethyl acetate in hexanes) to give **162** (295 mg, 38%) as a yellow oil (a mixture of ketone and hemiacetal) and **163** (230 mg, 31 %) as a yellow oil.

162: $[\alpha]_D^{25}$ -23.6 (c 0.56, $CHCl_3$); IR (neat) 3426, 2964, 2872, 1705, 1449, 1411, 1375, 1331, 1303, 1264, 1224, 1171, 1115, 1081, 1062, 984, 937, 898, 850, 817, 777, 730, 663 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.03-1.12 (m, 3H), 1.13-1.33 (m, 1H), 1.40 (s, 3H), 1.58 (s, 1H), 1.62-1.94 (m, 2H), 1.95-2.03 (m, 1H), 2.04-2.12 (m, 1H), 2.18 -2.38 (m, 2H), 2.49-2.58 (m, 1H), 2.69-2.81 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.3, 12.8, 23.5, 31.6, 38.6, 39.7, 40.8, 41.5, 41.7, 42.1, 42.6, 44.2, 44.7, 46.6, 47.3, 51.5, 79.8, 85.9, 103.9, 212.7; HRMS(CI+) *m/z* 169.1219 (calcd for $C_{10}H_{17}O_2$ 169.1228).

163: $[\alpha]_D^{25}$ -15.1 (c 0.51, $CHCl_3$); IR (neat) 3430, 2963, 2933, 2874, 1704, 1455, 1422, 1376, 1333, 1264, 1213, 1179, 1085, 1028, 999, 961, 934, 892, 803, 770, 713,

643 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.99 (d, *J* = 7.4 Hz, 3H), 1.30 (s, 3H), 1.55 (dd, *J* = 14.8, 1.3 Hz, 1H), 1.65 (d, *J* = 2.0 Hz, OH), 1.81 (dd, *J* = 15.1, 7.4 Hz, 1H), 1.89 (dd, *J* = 12.0, 1.2 Hz, 1H), 2.23 (br. s, 1H), 2.32-2.52, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.8, 25.5, 38.1, 41.6, 42.3, 45.7, 49.3, 51.8, 80.5, 212.4.



157

(3aS,5S,6aS)-6a-Methyl-2-oxohexahydro-2H-cyclopenta[b]furan-5-yl Acetate (157). **From 162**. To a stirred solution of **162** (7.00 g, 41.6 mmol) in dichloromethane (170 mL) was added *m*-chloroperoxybenzoic acid (7.90 g, 46.0 mmol) and the mixture was heated at 40 °C for 24 h. An additional amount of *m*-chloroperoxybenzoic acid (6.50 g, 37.4 mmol) was then added at room temperature and the mixture was heated at 40 °C for three days. The reaction was quenched with saturated aqueous sodium bicarbonate (200 mL) and sodium thiosulfate (200 mL), and the aqueous phase was extracted with dichloromethane (3 x 50 mL). The combined extracts were dried with anhydrous sodium sulfate, concentrated under reduced pressure and the residue was purified by chromatography on silica gel (20 % ethyl acetate in hexanes) to give alcohol **165** (3.80 g, 50 %), acetate **157** (1.10 g, 13 %) and unreacted **162** (800 mg).

To a stirred solution of dimethyl sulfoxide (6.00 mL, 82.4 mmol) in dichloromethane (55 mL) at -78 °C was added oxalyl chloride (3.50 mL, 41.2 mmol) and the mixture was stirred at this temperature for 30 min. A cold solution of alcohol **165** (3.80 g) in

dichloromethane (14 mL) was added and the mixture was stirred at -78 °C for 45 min. Diethylisopropylamine (103 mmol, 14.0 mL) was added and the mixture was allowed to warm to 0 °C. The reaction was quenched with saturated aqueous ammonium chloride (200 mL) and the aqueous phase was extracted with dichloromethane (3 x 50 mL). The combined extracts were washed with water (200 mL) and hydrochloric acid (2M, 200 mL) and dried with anhydrous sodium sulfate, after which they were concentrated under reduced pressure. The resulting crude ketone **166** was used in the next step without purification.

To a solution of crude **166** in dichloromethane (70 mL) at 0 °C was added hydrogen peroxide-urea (10.0 g, 103 mmol) followed by slow addition of trifluoroacetic anhydride (61.8 mmol, 8.60 mL). The mixture was stirred for 12 h at 4 °C and the reaction was quenched with saturated aqueous sodium bicarbonate (300 mL) and sodium thiosulfate (300 mL). The aqueous phase was extracted with dichloromethane (3 x 100 mL) and the combined extracts were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (30 % ethyl acetate in hexanes) to give acetate **157** (1.70 g overall, 34 % from **162**) as a colorless plate-like crystalline substance: $[\alpha]_D^{20}$ -42.5 (c 0.43, $CHCl_3$); mp 34 °C; IR (neat) 2973, 2935, 1766, 1735, 1425, 1376, 1286, 1316, 1241, 1162, 1101, 1022, 957 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.50 (s, 3H), 1.80-1.95 (m, 2H), 2.00 (s, 3H), 2.30 (ddd, *J* = 14.3, 9.3, 5.0 Hz, 1H), 2.40 (td, *J* = 15.3, 2.2 Hz, 1H), 2.50 (dd, *J* = 17.8, 2.4 Hz, 1H), 2.60-2.75 (m, 1H), 2.95 (dd, *J* = 17.9,

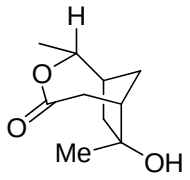
10.4 Hz, 1H), 5.25 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.6, 26.5, 37.9, 40.5, 43.3, 45.4, 94.2, 172.0, 176.0; HRMS(CI+) *m/z* 199.0980 (calcd for $C_{10}H_{15}O_4$ 199.0970).

(3aS,5S,6aS)-6a-Methyl-2-oxohexahydro-2H-cyclopenta[b]furan-5-yl Acetate (157). **From 167**. To a stirred solution of **167** (2.70 g, 15.0 mmol) in a methanol-water mixture (1:1, 25 mL) at room temperature was added potassium hydroxide (3.6M, 4.50 mL, 16.2 mmol) and the mixture was stirred for 1.5 h. Sulfuric acid (9M, 34.0 mmol, 3.70 mL) was added and the mixture was heated at 60 °C for 24 h. Saturated aqueous sodium bicarbonate (100 mL) was added to quench the reaction and the aqueous phase was extracted with dichloromethane (3 x 50 mL). The combined extracts were dried with anhydrous sodium sulfate and concentrated under reduced pressure to give crude alcohol **165** which was used in the next step without purification.

To a stirred solution of dimethyl sulfoxide (4.30 mL, 60.0 mmol) in dichloromethane (40 mL) at -78 °C was added oxalyl chloride (2.50 mL, 30.0 mmol), and the mixture was stirred at this temperature for 30 min. A solution of crude alcohol **165** in dichloromethane (10 mL) was added to the reaction mixture and the stirring was continued for 30 min. Diethylisopropylamine (12.8 mL, 75.0 mmol) was added and the mixture was allowed to warm to 0 °C. The reaction was quenched with saturated aqueous ammonium chloride (200 mL) and the aqueous phase was extracted with dichloromethane (3 x 50 mL). The combined extracts were washed with water (200 mL) and hydrochloric acid (2M, 200 mL), and dried with anhydrous sodium sulfate.

The solvent was evaporated under reduced pressure to give the crude ketone which was used in the next step without purification.

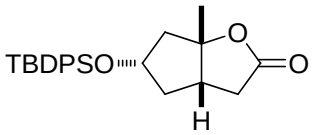
To a stirred solution of the crude ketone in dichloromethane (50 mL) at 0 °C was added hydrogen peroxide-urea (7.00 g, 75.0 mmol) and subsequently triflouroacetic anhydride (45.0 mmol, 6.20 mL). The mixture was stirred at 4 °C for 12 h and the reaction was quenched with saturated aqueous sodium bicarbonate (300 mL) and sodium thiosulfate (300 mL). The aqueous phase was extracted with dichloromethane (3 x 50 mL) and the combined extracts were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (30 % ethyl acetate in hexanes) to give acetate **157** (2.00 g, 70 %) as a colorless crystalline substance.



167

(1S,2R,6S,7R)-7-Hydroxy-2,7-dimethyl-3-oxabicyclo[4.2.1]nonan-4-one (167). To a stirred solution of **163** (3.20 g, 19.3 mmol) in dichloromethane (40 mL) at 0 ºC was added in small portions *m*-chloroperoxybenzoic acid (13.3 g, 77.4 mmol). The mixture was heated at 40 °C for 12 h and the reaction was quenched with saturated aqueous sodium bicarbonate (300 mL) and sodium thiosulfate (300 mL). The aqueous phase was extracted with dichloromethane (3 x 100 mL) and the combined extracts were

dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (20 → 50 % ethyl acetate in hexanes) to give **167** (2.40 g, 68 %) as a white solid: $[\alpha]_D^{18}$ +32.5 (c 0.37, $CHCl_3$); mp 110-115 ºC; IR (neat) 3433, 2936, 1705, 1457, 1422, 1378, 1308, 1254, 1182, 1133, 1057, 1033, 960, 931, 858, 756, 595 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.31 (d, *J* = 6.5 Hz, 3H), 1.45 (s, 3H), 1.87 (dd, *J* = 14.2, 8.4 Hz, 1H), 2.00 (d, *J* = 14.7 Hz, 1H), 2.02-2.06 (m, 1H), 2.43 (t, *J* = 8.1 Hz, 1H), 2.51 (dd, *J* = 16.5, 2.0 Hz, 1H), 2.65-2.57 (m, 1H), 2.98 (ddd, *J* = 16.7, 6.7, 2.0 Hz, 1H), 4.47 (q, *J* = 6.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.2, 24.4, 38.8, 40.6, 41.5, 43.2, 46.4, 81.3, 81.5, 174.8; HRMS(CI+) *m/z* 185.1184 (calcd for $C_{10}H_{17}O_3$ 185.1178).



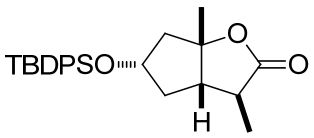
170

Lactone 170. To a stirred solution of acetate **157** (5.00 g, 25.3 mmol) in a methanol-water mixture (1:1, 126 mL) was added aqueous potassium carbonate (4M, 19.0 mL, 76.0 mmol) and the mixture was stirred at room temperature for 24 h. The reaction was quenched with hydrochloric acid (20 mL, 5M) and the aqueous phase was extracted with dichloromethane (3 x 20 mL). The combined extracts were dried with anhydrous sodium sulfate and the solvent was evaporated under reduced pressure. The residue was purified by chromatography on silica gel (50% ethyl acetate in hexanes) to give the corresponding alcohol (2.80 g, 71 %) as a white crystalline solid: $[\alpha]_D^{20}$ +4.6

(c 1.08, $CHCl_3$); mp 89-91 °C; IR (neat) 3455, 2995. 2972, 2934, 1737, 1440, 1411, 1379, 1309, 1287, 1222, 1160, 1107, 1034, 997, 959, 894, 821, cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.54 (s, 3H), 1.85 (dd, *J* = 14.0, 2.6 Hz, 1H), 1.90 (dd, *J* = 15.1, 4.4 Hz, 1H), 2.16 (ddd, *J* = 14.0, 8.8, 4.5 Hz, 1H), 2.23 (dt, *J* = 15.0, 2.2 Hz, 1H), 2.55-2.65 (m, 2H), 2.97 (dd, *J* = 18.9, 11.2 Hz, 1H), 4.48 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.5, 29.7, 37.9, 42.6, 43.2, 48.1, 73.9, 94.0, 178.0; HRMS(EI+) *m/z* 156.0792 (calcd for $C_8H_{12}O_3$ 156.0787).

To a stirred solution of the alcohol (2.80 g, 18.0 mmol) and imidazole (2.50 g, 36.0 mmol) in dimethylformamide (90 mL) at 0 °C was added *t*-butyldimethylsilyl chloride (9.40 mL, 36.0 mmol). The mixture was stirred at room temperature for 12 h and the reaction was quenched with brine (100 mL). The aqueous phase was extracted with dichloromethane (3 x 50 mL) and the combined extracts were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica (10 % ethyl acetate in hexanes) to give **170** (5.40 g, 13.7 mmol, 76 %) as a white solid: $[\alpha]_D^{18}$ -7.8 (c 1.48, $CHCl_3$); mp 96-97 °C; IR (neat) 3071, 2930, 2857, 1767, 1653, 1589, 1487, 1472, 1427, 1379, 1282, 1219, 1109, 1025, 960, 901, 822, 703, 612, 504 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.10 (s, 9H), 1.45 (s, 3H), 1.68 (dd, *J* = 14.6, 5.2 Hz, 1H), 1.79 (dd, *J* = 14.3, 2.0 Hz, 1H), 2.00 (ddd, *J* = 14.0, 8.7, 4.6 Hz, 1H), 2.28 (d, *J* = 15.1 Hz, 1H), 2.46-2.55 (m, 1H), 2.68 (dd, *J* = 18.5, 3.7 Hz, 1H), 2.95 (dd, *J* = 18.5, 10.7 Hz, 1H), 4.40-4.45 (m, 1H), 7.30-7.50 (m, 6H), 7.65-7.80 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 26.7, 27.0, 37.6,

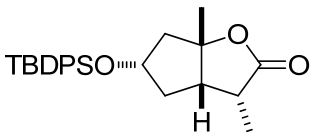
42.8, 43.3, 47.9, 75.2, 93.9, 127.6, 129.7, 135.8, 135.9, 176.8; HRMS(TIC) *m/z* 395.2066 (calcd for $C_{24}H_{31}O_3Si$ 395.2043).



173

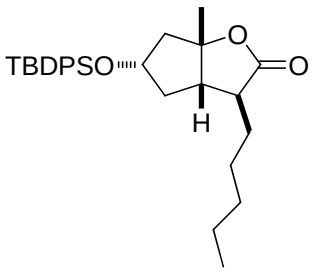
α-Methyl Lactone 173. To a stirred solution of lactone **170** (6.30 mg, 23.0 μmol) in tetrahydrofuran (0.2 mL) at -78 °C was added lithium diisopropylamide (46.0 μL, 46.0 μmol, 1M solution in tetrahydrofuran) and the mixture was stirred for 1 h at the same temperature. Methyl iodide (7.00 μL, 0.110 mmol,) was added and stirring was continued for 2 h. Saturated aqueous ammonium chloride (10 mL) was added to quench the reaction and the aqueous phase was extracted with dichloromethane (3 x 20 mL). The combined extracts were dried with anhydrous sodium sulfate and the solvent was evaporated under reduced pressure. The residue was purified by chromatography on silica gel (10 % ethyl acetate in pentane) to give **173** (6.60 mg, 99 %) as a colorless oil: $[\alpha]_D^{25}$ –15.9 (c 0.49, $CHCl_3$); IR (neat) 3071, 2964, 2931, 2857, 1766, 1589, 1472, 1427, 1378, 1287, 1192, 1111, 1037, 997, 953, 898, 822, 787, 703, 681, 612; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.06 (s, 9H), 1.38 (d, *J* = 7.6 Hz, 3H), 1.46 (s, 3H), 1.66 (dd, *J* = 14.7, 4.8 Hz, 1H), 1.85 (ddd, *J* = 13.8, 5.6, 2.3 Hz, 1H), 1.99 (ddd, *J* = 13.5, 8.4, 4.5 Hz, 1H), 2.14-2.21 (m, 1H), 2.24 (t, *J* = 2.3 Hz, 1H), 2.90 (dq, *J* = 7.5, 4.7 Hz, 1H), 4.33 (ddd, *J* = 7.3, 4.8, 2.1 Hz, 1H), 7.36-7.49 (m, 6H), 7.62-7.70 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.6, 18.9, 26.8, 28.2, 42.1, 44.9, 48.1,

52.3, 75.5, 91.9, 127.7, 129.74, 129.71, 133.5, 133.7, 135.8, 135.9, 180.0; HRMS(TOF MS ES+) *m/z* 431.2014 (calcd for $C_{25}H_{32}O_3NaSi$ 431.2018).



176

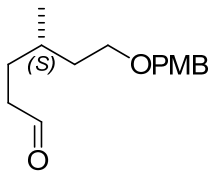
α-Methyl Lactone 176. To a stirred solution of lactone **173** (16.0 mg, 40.0 μmol) in tetrahydrofuran (0.4 mL) at -78 °C was added lithium diisopropylamide (80.0 μL, 80.0 μmol, 1M solution in tetrahydrofuran) and the mixture was stirred for 2 h at the same temperature. Isopropyl alcohol (0.5 mL) was added and the mixture was allowed to warm to room temperature. The reaction was quenched with saturated aqueous sodium bicarbonate (10 mL) and the aqueous phase was extracted with dichloromethane (3 x 20 mL). The combined extracts were dried with anhydrous sodium sulfate and the solvent was evaporated under reduced pressure to give **176** (15.5 mg, 99 %) as a colorless oil: $[\alpha]_D^{25}$ –14.9 (c 1.03, $CHCl_3$); IR (neat) 2930, 2856, 1766, 1427, 1379, 1286, 1248, 1217, 1109, 1076, 1022, 984, 943, 897, 822, 734, 702, 612; ^{1}H NMR (700 MHz, $CDCl_3$) δ 1.07 (s, 9H), 1.25 (d, *J* = 7.2 Hz, 3H), 1.37 (s, 3H), 1.77-1.88 (3H, m), 2.14 (dd, *J* = 14.4, 5.4 Hz, 1H), 2.38 (q, *J* = 8.6 Hz, 1H), 2.92 (dq, *J* = 8.3, 7.5 Hz, 1H), 4.25 (q, *J* = 6.2 Hz, 1H), 7.39-7.48 (m, 6H), 7.66-7.70 (m, 4H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 11.4, 19.1, 25.8, 26.8, 36.5, 37.8, 47.2, 47.8, 73.8, 90.3, 127.6, 129.6, 129.7, 133.8, 133.9, 135.7, 135.8, 178.6; HRMS(TOF MS ES+) *m/z* 431.2021 (calcd for $C_{25}H_{32}O_3NaSi$ 431.2018).



174

α-Pentyl Lactone 174. To a stirred solution of lactone **170** (25.0 mg, 63.0 μmol) in tetrahydrofuran (0.25 mL) at -78 °C was added lithium diisopropylamide (126 μL, 0.130 mmol, 1M solution in tetrahydrofuran) and the mixture was stirred for 1 h at the same temperature. 1-Iodopentane (50.0 μL, 0.320 mmol) was added and the mixture was allowed to warm to room temperature. After 12 h the reaction was quenched with saturated aqueous ammonium chloride (5 mL) and the aqueous phase was extracted with ether (3 x 5 mL). The combined extracts were washed brine (5 mL) and dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica (10 % ethyl acetate in hexanes) to give **174** (single diastereomer) (25.4 mg, 86 %) as a colorless oil: $[\alpha]_D^{18}$ -9.8 (c 0.61, $CHCl_3$); IR (neat) 2930, 2857, 1762, 1471, 1427, 1378, 1313, 1279, 1242, 1220, 1193, 1111, 1052, 1025, 998, 965, 900, 822, 797, 742, 702, 681, 662, 612, 505 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.92 (t, *J* = 7.2 Hz, 3H), 1.06 (s, 9H), 1.33-1.37 (br. s, 4H), 1.44 (s, 3H), 1.41-1.47 (br. s, 2H), 1.49-1.56 (m, 1H), 1.65 (dd, *J* = 14.5, 4.7 Hz, 1H), 1.81 (ddd, *J* = 13.9, 5.5, 2.0 Hz, 1H), 1.88-1.93 (m, 1H), 1.96-2.00 (m, 1H), 2.02-2.24 (m, 1H), 2.20-2.25 (m, 1H), 2.84 (td, *J* = 9.4, 4.6 Hz, 1H), 4.33 (q, 2.3 Hz, 1H), 7.36-7.47 (m, 6H), 7.64-7.70 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2,

19.0, 22.4, 26.8, 26.9, 28.2, 31.1, 33.1, 42.5, 48.3, 50.2, 50.3, 75.6, 92.0, 127.6, 129.7, 135.8, 135.9, 179.4; HRMS(TOF MS ES+) *m/z* 487.2647 (calcd for $C_{29}H_{40}O_3SiNa$ 487.2644).

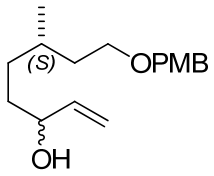


177

(S)-6-((4-Methoxybenzyl)oxy)-4-methylhexanal (177). To a stirred solution of alcohol **160** (1.00 g, 6.40 mmol) in dimethylformamide (20 mL) at 0 ˚C was added sodium hydride (5.10 mg, 12.8 mmol) and the suspension was stirred for 30 min. *p*-Methoxybenzyl bromide (1.20 mL, 8.85 mmol) was added and the mixture was allowed to warm to room temperature for 12 h. Ethanol (2 mL) and water (20 mL) were added to quench the reaction and the aqueous phase was extracted with dichloromethane (3 x 50 mL). The combined extracts were dried with anhydrous sodium sulfate and the solvent was evaporated under reduced pressure to give crude *p*-methoxybenzyl ether which was used in next step without purification.

Ozone was bubbled into a stirred solution of the crude *p*-methoxybenzyl ether and a few crystals of Sudan III in dichloromethane (40 mL) at -78 ˚C for 1 h. The reaction was quenched at -78 ˚C with triphenylphosphine (3.00 g) and was allowed to warm to room temperature. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (10 % ethyl acetate in hexanes) to give **177** (1.30 g, 82 %) as a colorless oil: $[\alpha]_D^{20}$ 0 (c 0.88, $CHCl_3$); IR(neat) 2929, 2858,

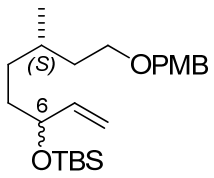
2719, 1723, 1612, 1585, 1513, 1463, 1410, 1364, 1379, 1301, 1247, 1172, 1093, 1034, 820, 756, 707, 637 cm^{-1};^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90 (d, *J* = 6.2 Hz, 3H), 1.40-1.50 (m, 2H), 1.60-1.75 (m, 3H), 2.40-2.50 (m, 2H), 3.47 (ddd, *J* = 12.9, 6.2, 2.8 Hz, 2H), 3.70 (s, 3H), 4.40 (s, 2H), 6.90 (d, *J* = 7.8 Hz, 2H), 7.35 (d, *J* = 6.7 Hz, 2H), 9.80 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.3, 28.9, 29.5, 36.5, 41.6, 55.3, 68.0, 72.6, 113.8, 123.4, 129.2, 130.6, 159.1, 202.8; HRMS(TIC) *m/z* 250.1568 (calcd for $C_{15}H_{22}O_3$ 250.1569).



178

(6S)-8-((4-Methoxybenzyl)oxy)-6-methyloct-1-en-3-ol (178). To a stirred solution of aldehyde **177** (40.2 mg, 0.160 mmol) in tetrahydrofuran (0.4 mL) at 0 ˚C was added vinylmagnesium bromide (1M solution in tetrahydrofuran, 0.160 mmol, 160 μL) and the mixture was stirred for 5 min. Aqueous hydrochloric acid (5M, 2 mL) was added to quench the reaction and the aqueous phase was extracted with ether (3 x 5 mL). The combined extracts were washed with brine (5 mL) and dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (10 % ethyl acetate in hexanes) to give **178** (41.4 mg, 94%) as a colorless oil: IR (neat) 3418, 3000, 2931, 2858, 1642, 1612, 1586, 1513, 1463, 1423, 1364, 1301, 1247, 1173, 1094, 1035, 993, 921, 821, 756 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90 (d, *J* = 6.2 Hz, 3H), 1.70-1.36 (m, 7H), 3.44-3.52 (m,

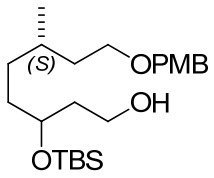
2H), 3.83 (s, 3H), 4.04-4.11 (m, 1H), 4.44 (s, 2H), 5.14 (d, *J* = 10.6 Hz, 1H), 5.26 (d, *J* = 17.8 Hz , 1H), 5.87 (dddd, *J* = 17.3, 10.2, 6.1, 1.5 Hz, 1H), 6.87-6.93 (m, 2H), 7.25 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.6, 29.8, 32.4, 34.3, 36.6, 55.3, 68.3, 72.5, 73.5, 113.7, 114.6, 129.2, 130.7, 141.3, 159.1; HRMS(EI+) *m/z* 278.1836 (calcd for $C_{17}H_{26}O_3$ 278.1882).



179

tert-Butyl(((6S)-8-((4-methoxybenzyl)oxy)-6-methyloct-1-en-3-yl)oxy)dimethylsilane (179). To a stirred solution of **178** (24.0 mg, 90.0 μmol) and imidazole (12.0 mg, 0.170 mmol) in dimethylformamide (0.4 mL) at 0 °C was added *t*-butyldimethylsilyl chloride (26.0 mg, 0.170 mmol) and the mixture was stirred at room temperature for 12 h. Water (3 mL) was added to quench the reaction and the aqueous phase was extracted with ether (3 x 5 mL). The combined extracts were washed with brine (5 mL) and dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (100% hexanes to 5 % ethyl acetate in hexanes) to give **179** (31.3 mg, 93 %) as a colorless oil: IR (neat) 2954, 2929, 2856, 1613, 1513, 1463, 1361, 1248, 172, 1097, 1038, 1005, 920, 835, 775, 679 cm $^{-1}$; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.05 (s, 6H), 0.90-1.00 (m, 12H), 1.70-1.30 (m, 7H), 3.50-3.49 (m, 2H), 3.83 (s, 3H), 4.10-4.00 (m, 1H), 4.44 (s, 2H), 5.05 (d, *J* = 10.6 Hz, 1H), 5.15 (d, *J* = 17.8 Hz , 1H), 5.87

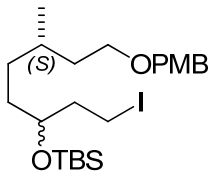
(dddd, J = 17.3, 10.2, 6.1, 1.5 Hz, 1H), 6.87-6.93 (m, 2H), 7.30-7.25 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -4.8, -4.3, 14.1, 18.3, 19.7, 22.7, 26.0, 30.0, 31.6, 32.4, 35.4, 36.8, 55.3, 68.4, 72.8, 74.1, 113.5, 129.2, 141.8, 159.1; HRMS(CI+) *m/z* 391.2664 (calcd for $C_{23}H_{39}O_3$ 391.2668).



180

(6S)-3-((tert-Butyldimethylsilyl)oxy)-8-((4-methoxybenzyl)oxy)-6-methyloctan-1-ol (180). To a stirred solution of **179** (3.60 g, 9.20 mmol) in tetrahydrofuran (30 mL) at 0 °C was added borane-dimethyl sulfide complex (2M in tetrahydrofuran, 27.5 mmol, 13.0 mL) and the reaction mixture was stirred at room temperature for 3 h. Ethanol (2 mL), sodium hydroxide (8 mL, 6M) and aqueous hydrogen peroxide (16 mL 30%) were added at 0 °C and the mixture was stirred overnight at room temperature. The aqueous phase was extracted with ether (3 x 20 mL), the combined extracts were washed with brine (15 mL) and dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (20 % ethyl acetate in hexanes) to give **180** (2.40 g, 64 %) as a colorless oil: IR (neat) 3406, 2930, 1612, 1586, 1513, 1463, 1361, 1301, 1248, 1172, 1097, 936, 835, 775, 710 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.10 (s, 6H), 0.88-0.90 (m, 12H), 1.90-1.10 (m, 9H), 2.50-2.40 (m, 1H), 3.51-3.461 (m, 2H), 3.70-

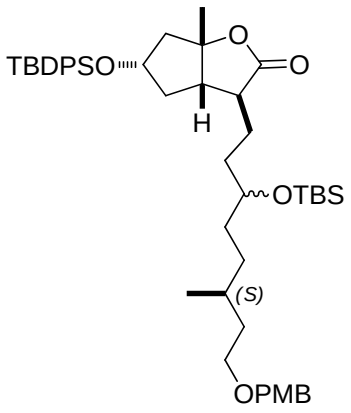
3.75 (m, 1H), 4.90-4.80 (m, 5H), 4.45 (s, 2H), 6.91-6.88 (m, 2H), 7.28-7.27 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ -4.3, -4.4, 18.0, 19.6, 19.7, 25.9, 30.1, 32.6, 34.1, 36.6, 36.8, 37.6, 37.8, 55.3, 60.3, 68.3, 72.2, 72.3, 72.6, 113.8, 129.2, 130.7, 159.1; HRMS(TOF MS ES+) *m/z* 433.2736 (calcd for $C_{23}H_{42}O_4SiNa$ 433.2750).



158

tert-Butyl(((6S)-1-iodo-8-((4-methoxybenzyl)oxy)-6-methyloctan-3-yl)oxy)dimethylsilane (158). To a stirred solution of alcohol **180** (1.00 g, 2.44 mmol), triphenylphosphine (700 mg, 2.68 mmol) and imidazole (373 mg, 5.48 mmol) in benzene (6 mL) was added a solution of iodine (762 mg, 2.92 mmol) in benzene (25 mL) and the reaction was stirred for 5 min. Saturated aqueous sodium bicarbonate (15 mL) and sodium thiosulfate (20 mL) were added to quench the reaction and the aqueous phase was extracted with ether (3 x 10 mL). The combined extracts were washed with brine (10 mL), dried with anhydrous sodium sulfate and concentrated under reduced pressure. The residue was purified by chromatography on silica gel (5 % ethyl acetate in hexanes) to give **158** (1.20 g, 97 %) as a colorless oil: IR (neat) 2953, 2928, 2855, 1612, 1513, 1462, 1361, 1301, 1248, 1171, 1097, 1038, 835, 774 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.10 (s, 6H), 0.88-0.90 (m, 12H), 1.60-1.41 (m, 7H), 1.96-1.946 (m, 2H), 3.24-3.21 (m, 2H), 3.51-3.461 (m, 2H), 3.75-3.65 (m, 1H), 3.83 (s, 3H), 4.45 (s, 2H), 6.91-6.88 (m, 2H), 7.28-7.27 (m, 2H); ^{13}C NMR (75 MHz,

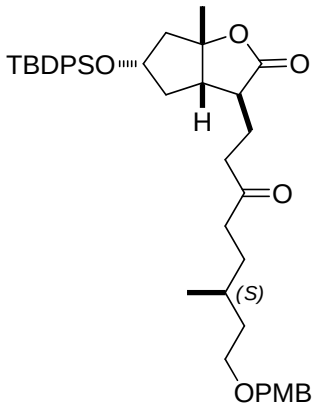
$CDCl_3$) δ -4.3, -3.4, 18.1, 19.6, 27.1, 30.8, 32.0, 32.1, 34.2, 36.1, 40.9, 55.3, 68.3, 72.4, 72.6, 113.7, 129.2, 130.7, 159.1; HRMS(TOF MS ES+) *m/z* 521.1938 (calcd for $C_{23}H_{42}O_3SiNa$ 521.1948).



181

Lactone 181. To a stirred solution of lactone **170** (523 mg, 1.33 mmol) in tetrahydrofuran (5 mL) at -78 °C was added lithium diisopropylamide (2.00 mL, 2.00 mmol, 1M solution in tetrahydrofuran) and the mixture was stirred for 1 h at the same temperature. A solution of alkyl iodide **158** (1.23 g, 2.36 mmol) in tetrahydrofuran (7 mL) was added and the mixture was allowed to warm to room temperature for 12 h. The reaction was quenched with saturated aqueous ammonium chloride (20 mL) and the aqueous phase was extracted with dichloromethane (3 x 50 mL). The combined extracts were dried with anhydrous sodium sulfate, concentrated under reduced pressure and the residue was purified by chromatography on silica (10 % ethyl acetate in hexanes) to give **181** (1.00 g, 97 %) as a colorless oil: IR (neat) 2929, 2856, 1764, 1715, 1612, 1587, 1513, 1462, 1427, 1378, 1301, 1248, 1171, 1035, 1006, 964, 900, 835, 774, 742, 682, 612 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 0.10 (s, 6H), 0.90 (s,

12H), 1.07 (s, 9H), 1.27-1.36 (m, 2H), 1.38-1.47 (m, 5H), 1.48-1.71 (m, 7H), 1.79-1.84 (m, 1H), 1.84-1.96 (m, 1H), 1.97-2.02 (m, 1H), 2.19-2.26 (m, 2H), 2.75-2.82 (m, 1H), 3.46-3.54 (m, 2H), 3.64-3.71 (m, 1H), 3.83 (s, 1H), 4.32-4.35 (m, 1H), 4.42-4.49 (m, 2H),6.90 (d, J = 8.3 Hz, 2H), 7.27-7.30 (m, 2H), 7.39-7.7.48 (m, 6H), 7.65-7.70 (m, 4H); ^{13}C NMR (175 MHz, $CDCl_3$) δ -4.39, -4.36, 4.34, 4.30, 14.4, 18.7, 18.9, 19.6, 22.7, 25.9, 26.8, 28.1, 28.5, 29.4, 30.1, 31.6, 32.5, 32.7, 34.1, 34.5, 34.7, 34.9, 36.7, 36.8, 42.6, 48.2, 50.3, 50.36, 50.4, 50.44, 55.3, 68.4, 71.9, 72.2, 72.6, 75.5. 92.08, 113.8, 127.7, 129.2, 129.7, 130.8, 133.6, 133.7, 135.8, 136.0, 159.1, 179.2; HRMS(TIC) *m/z* 786.4752 (calcd for $C_{47}H_{70}O_6Si$ 786.4711);



156

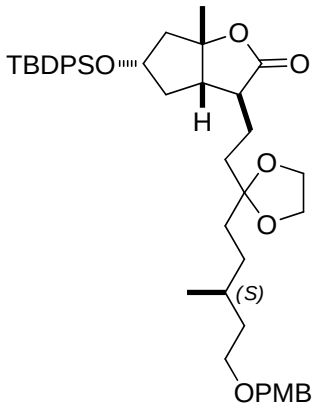
Ketone 156. **From 181**. To a stirred solution of lactone **181** (176 mg, 0.220 mmol) in tetrahydrofuran (46 mL) at room temperature was added aqueous hydrochloric acid (9 mL, 3M) and the reaction mixture was stirred for 12 h. The reaction was quenched with saturated aqueous sodium bicarbonate (50 mL) and the aqueous phase was extracted with dichloromethane (3 x 50 mL). The combined extracts were dried with

anhydrous sodium sulfate, concentrated under reduced pressure to give the crude alcohol, which was used in the next step without purification.

To a stirred solution of the crude alcohol in dichloromethane (2.2 mL) were added activated molecular sieves (4Å), *N*-methylmorpholine-*N*-oxide (64.0 mg, 0.540 mmol) and tetrapropylammonium perruthenate (8.00 mg, 10.0 mol %) and the mixture was stirred at room temperature for 1 h. The reaction mixture was loaded into a column of silica gel and purified (20 % ethyl acetate in hexanes) to give **156** (as a single diastereomer, 117 mg, 80 % for two steps) as an oil: $[\alpha]_D^{18}$ –11.7 (c 2.55, $CHCl_3$); IR (neat) 2928, 2855, 1759, 1712, 1613, 1587, 1513, 1427, 1247, 1110, 933, 703 cm^{-1} ; ^1H NMR (700 MHz, $CDCl_3$) δ 0.90 (d, *J* = 6.0 Hz, 3H), 1.06 (s, 9H), 1.42-1.48 (m, 5H), 1.57-1.68 (m, 4H), 1.82-1.87 (m, 1H), 1.95-2.01 (m, 2H), 2.02-2.25 (m, 2H), 2.39-2.52 (m, 2H), 2.70 (t, *J* = 7.1 Hz, 2H), 2.80-2.84 (m, 1H), 3.46-3.54 (m, 2H), 3.83 (s, 3H), 4.32-4.34 (m, 1H), 4.45 (d, *J* = 4.2 Hz, 1H), 6.90 (d, *J* = 8.5 Hz, 2H), 7.28 (d, *J* = 8.5 Hz, 2H), 7.39-7.48 (m, 6H), 7.67 (dd, *J* = 14.2, 6.8 Hz, 4H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 18.9, 19.4, 26.8, 27.3, 28.1, 29.6, 30.7, 36.5, 40.0, 40.6, 42.4, 48.1, 49.0, 50.9, 55.3, 68.2, 72.7, 75.6, 92.3, 113.8, 127.7, 127.7, 129.3, 129.7, 130.7, 133.5, 133.6, 135.8, 135.9, 159.2, 178.8, 210.4; HRMS(TIC) *m/z* 671.3776 (calcd for $C_{41}H_{55}O_6Si$ 671.3768).

Ketone 156. **From 186**. To a stirred solution of alcohol **186** (8.60 mg, 13.0 μmol) in dichloromethane (0.1 mL) at room temperature was added Dess-Martin reagent (8.50 mg, 20.0 μmol) and the mixture was stirred for 2 h. The reaction was quenched with

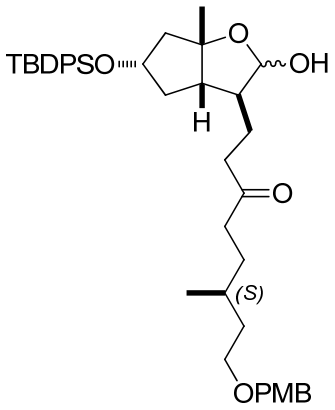
saturated aqueous sodium bicarbonate (10 mL) and sodium thiosulfate (10 mL), and the aqueous phase was extracted with ether (3 x 5 mL). The combined extracts were dried with anhydrous sodium sulfate and concentrated under reduced pressure to give **156** (9.00 mg, 99 %).



182

Ketal 182. To a stirred solution of ketone **156** (117 mg, 0.170 mmol) in benzene (1.7 mL) were added camphorsulfonic acid (4.00 mg, 17.0 μmol), 1,2-ethandiol (66.0 μL, 1.20 mmol) and trimethyl orthoformate (112 μL, 1.10 mmol) and the reaction mixture was heated at 85 °C for 24 h. The reaction was quenched with saturated aqueous sodium bicarbonate (5 mL) and the aqueous phase was extracted with dichloromethane (3 x 20 mL). The combined extracts were dried with anhydrous sodium sulfate, concentrated under reduced pressure and the residue was purified by chromatography on silica (20 % ethyl acetate in hexane) to give **182** (85.0 mg, 70 %) as a colorless oil: $[\alpha]_D^{18}$ –29.4 (c 0.17, $CHCl_3$); IR (neat) 2928, 2857, 1760, 1650, 1613, 1587, 1513, 1427, 1392, 1247, 1103, 985, 901, 821, 703, 613 cm^{-1}; ^1H NMR

(700 MHz, $CDCl_3$) δ 0.90 (d, *J* = 6.4 Hz, 3H), 1.05 (s, 9H), 1.20-1.27 (m, 1H), 1.39-1.45 (m, 2H), 1.45 (s, 3H), 1.54-1.74 (m, 7H), 1.78-1.85 (m, 2H), 1.96-2.02 (m, 2H), 2.19-2.25 (m, 2H), 2.82-2.87 (m, 1H), 3.47-3.54 (m, 2H), 3.83 (s, 3H), 3.95 (s, 4H), 4.32-4.35 (m, 1H), 4.45 (s, 2H), 6.90 (d, *J* = 8.3 Hz, 2H), 7.28 (d, *J* = 8.7 Hz, 2H), 7.39-7.48 (m, 6H), 7.65-7.70 (m, 4H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 18.9, 19.6, 26.7, 27.5, 28.1, 30.0, 30.8, 34.6, 34.7, 36.7, 42.5, 48.2, 50.1, 50.4, 55.3, 64.9, 65.0, 68.4, 72.6, 75.6, 92.1, 111.4, 113.7, 127.6, 129.3, 129.7, 130.8, 133.5, 133.7, 135.8, 135.9, 159.1, 179.0; HRMS(TIC) *m/z* 715.4005 (calcd for $C_{43}H_{59}O_7Si$ 715.4030).



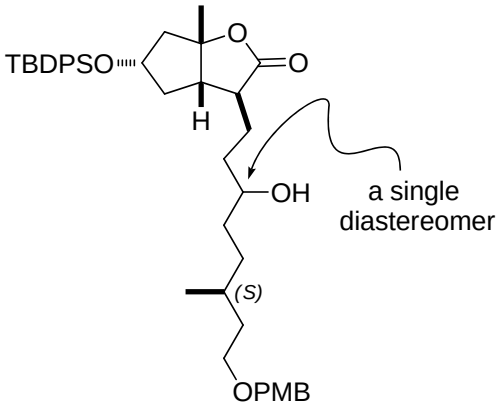
183

Lactol 183. To a stirred solution of ketal **182** (85.0 mg, 120 μmol) in toluene (3 mL) at -78 ºC was added diisobutylaluminum hydride (180 μl, 180 μmol, 1M solution in dichloromethane) and the mixture was stirred for 1 h at the same temperature. The reaction was quenched by transferring the cold mixture into aqueous 10% sodium potassium tartrate (Rochelle's salt) (20 mL). The aqueous phase was extracted with dichloromethane (3 x 20 mL) and the combined extracts were dried with anhydrous

sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica (20 % to 50 % ethyl acetate in hexanes) to give a lactol (65.0 mg, 80 %) as a colorless oil: IR (neat) 3406, 2953, 2858, 1888, 1612, 1587, 1462, 1513, 1462, 1427, 1373, 1302, 1247, 1173, 1110, 1037, 948, 892, 827, 741, 704, 612 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 0.90 (d, *J* = 6.8 Hz, 3H), 1.06 + 1.09 (two s, 9H), 1.18-1.25 (m, 1H), 1.26 +1.35 (two s, 3H), 1.40-1.47 (m, 3H), 1.52-1.78 9 (m, 10H), 1.84 (dd, *J* = 14.4, 6.2 Hz, 1H), 1.86 -1.90 (m, 1H), 1.92-1.99 (m, 2H), 2.01-2.07 (m, 4H), 2.16-2.21 + 2.49-2.55 (m, 1H), 2.38 (dd, *J* = 14.2, 3.1 Hz, 1H), 3.47 -3.54 (m, 2H), 3.83 (s, 3H), 3.94 + 3.95 (two s, 4H), 4.26-4.30 (m, 1H), 4.45 + 4.46 (two s, 2H), 4.74-4.77 (m, OH), 5.19 (dd, J= 8.8, 1.4 Hz, 0.6 H), 5.45 (dd, *J* = 4.5, 2.8 Hz, 0.4H), 6.90 (d, *J* = 8.7 Hz, 2H), 7.28 (d, *J* = 7.8 Hz, 2H), 7.38-7.48 (m, 6H), 7.65-7.73 (m, 4H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 18.9, 19.1, 19.5, 19.6, 23.4, 26.9, 28.6, 29.4, 30.0, 30.4, 30.8, 30.9, 34.2, 34.5, 35.4, 35.6, 36.7, 40.2, 42.3, 49.6, 50.5, 52.7, 53.5, 53.6, 55.3, 56.6, 64.8, 64.9, 68.3, 68.4, 72.6, 76.0, 76.7, 91.8, 92.1, 100.5, 106.1, 111.6, 111.8, 113.7, 127.5, 127.6, 127.70, 127.72, 129.2, 129.6, 129.81, 129.85, 130.8, 133.3, 133.4, 134.1, 135.7, 135.82, 135.88, 159.1; HRMS (TOF MS ES+) *m/z* 739.3975 (calcd for $C_{43}H_{60}O_7NaSi$ 739.4006).

To a stirred solution of the lactol (9.00 mg, 12.0 μmol) in acetone (0.1 mL) at room temperature was added a drop of hydrochloric acid (2.5 %) and the reaction mixture was stirred for 4 h at the same temperature. The reaction was quenched with saturated aqueous sodium bicarbonate (10 mL) and the aqueous phase was extracted with ether (3 x 10 mL). The combined extracts were dried with anhydrous sodium sulfate,

concentrated under reduced pressure and the residue was purified by chromatography on silica (40 % ethyl acetate in hexanes) to give **183** (7.00 mg, 87 %) as a an oil: IR (neat) 3402, 2956, 2929, 2957, 1713, 1612, 1587, 1513, 1462, 1427, 1373, 1302, 1248, 1173, 1036, 821, 741, 703, 612 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 0.9 (d, *J* = 6.4 Hz, 3H), 1.06 + 1.09 (two s, 9H), 1.26 + 1.35 (two s, 3H), 1.41-1.47 (m, 2H), 1.56-2.06 (m, 10H), 2.34-2.56 (m, 5H), 3.46-3.53 (m, 2H), 3.83 (s, 3H), 4.27-4.30 (m, 1H), 4.44 + 4.45 (two s, 2H), 5.18 (dd, *J* = 9.3, 1.6 Hz, 0.4H), 5.47 (dd, *J* = 4.7, 2.6 Hz, 0.6 H), 6.90 (d, *J* = 8.5 Hz, 2H, 7.28 (d, *J* = 8.5 Hz, 2H), 7.38-7.45 (m, 6H), 7.65-7.72 (m, 4H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 18.9, 19.1, 19.4, 19.5, 23.3, 26.8, 26.9, 28.3, 29.3, 29.6, 30.4, 30.7, 36.5, 40.0, 40.2, 41.0, 41.5, 42.2, 49.5, 50.4, 52.6, 53.0, 53.8, 55.3, 55.32, 56.1, 68.1, 72.6, 76.0, 91.9, 92.3, 101.2, 105.6, 113.7, 127.60, 127.64, 127.74, 127.80, 129.3, 129.6, 129.8, 129.9, 130.6, 133.1, 133.2, 134.0, 135.7, 135.8, 135.88, 135.9, 159.1, 210.7, 211.3; HRMS(EI+) *m/z* 672.3867 (calcd for $C_{41}H_{56}O_5Si$ 672.3846).

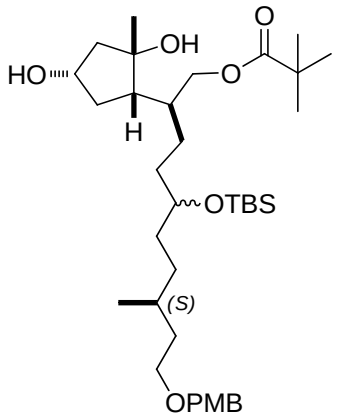


186

Alcohol 186. **Method A**. To a stirred solution of lactol **183** (27.0 mg, 40.0 μmol) in benzene (0.4 mL) at 0 °C was added potassium *t*-butoxide (80.0 μmol, 64.0 μL, 1.25M solution in *t*-butanol) and the mixture was stirred for 5.5 h at room temperature. The reaction was quenched with saturated aqueous ammonium chloride (10 mL) and the aqueous phase was extracted with dichloromethane (3 x 10 mL). The combined extracts were dried with anhydrous sodium sulfate, concentrated under reduced pressure and the residue was purified by chromatography on silica gel (30 % ethyl acetate in hexanes) to give **186** (as a single diastereomer, 8.00 mg, 28 %) as a colorless oil.

Method B: To a stirred solution of lactol **183** (10.2 mg, 15.0 μmol) in tetrahydrofuran (0.1 mL) at 0 °C was added lithium diisopropylamide (30.0 μL, 30.0 μmol, 1M solution in tetrahydrofuran) and the mixture was stirred at room temperature for 12 h. Brine (10 mL) was added to quench the reaction, the aqueous phase was extracted with ether (3 x 5 mL), and the combined extracts were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure to give **186** (8.10 mg, 80

%) as an oil: $[\alpha]_D^{18}$ –5.0 (c 0.18, $CHCl_3$); IR (neat) 3451, 2929, 2856, 1759, 1612, 1587, 1513, 1462, 1427, 1378, 1247, 1172, 1110, 1034, 901, 821, 740, 703, 682 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.92 (d, *J* = 6.8 Hz, 3H), 1.07 (s, 9H), 1.17-1.24 (m, 1H), 1.40-1.54 (m, 6H), 1.56-1.76 (m, 5H), 1.84 (dd, *J* = 13.7, 2.0 Hz, 1H), 1.95-2.08 (m, 2H), 2.21-2.23 (m, 1H), 2.24-2.28 (m, 1H), 2.87-2.94 (m, 1H), 2.47-3.54 (m, 2H), 3.58-3.64 (m, 1H), 3.84 (s, 3H), 4.32-4.37 (m, 1H), 4.46 (s, 2H), 6.91 (d, *J* = 8.5 Hz, 2H), 7.29 (d, *J* = 8.2 Hz, 2H), 7.39-7.49 (m, 6H), 7.65-7.70 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.8, 19.7, 26.8, 28.1, 29.0, 29.7, 32.9, 34.6, 34.8, 36.6, 42.5, 48.4, 50.0, 50.3, 55.3, 68.4, 71.9, 72.6, 75.6, 92.2, 113.8, 127.6, 127.7, 129.2, 129.8, 130.8, 133.7, 133.8, 135.8, 135.9, 159.2, 179.4; HRMS(TOF MS ES+) *m/z* 695.3734 (calcd for $C_{41}H_{56}O_5Si$ 695.3744).



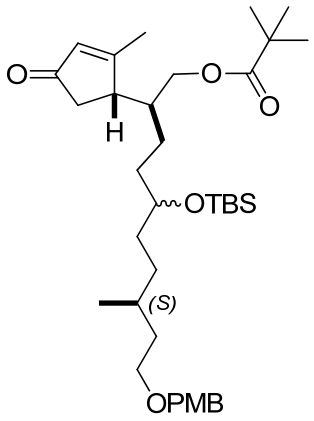
211

Pivoloate 211. To a stirred solution of lactone **181** (131 mg, 0.170 mmol) in ether (1.6 mL) at 0 °C was added lithium aluminum hydride slurry in ether (30.0 mg in 700 μL) and the mixture was stirred for 30 min at room temperature. Damp sodium sulfate was added to quench the reaction and the mixture was filtered. The solution was

concentrated under reduced pressure and the residue was purified by chromatography on silica gel (50 % ethyl acetate in hexanes) to give a triol (67.0 mg, 73 %) as a colorless oil: IR (neat) 3354, 2928, 2856, 1613, 1513, 1458, 1374, 1301, 1249, 1171, 1087, 1036, 834, 773 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.08 (s, 6H), 0.91 (s, 12H), 1.05-1.23 (m, 2H), 1.23-1.37 (m, 7H), 1.38-1.50 (m, 8H), 1.51-1.61 (m, 1H), 1.62-1.75 (m, 5H), 1.76-1.86 (m, 2H), 1.93-2.00 (d, *J* = 13.4 Hz, 1H), 2.35-2.47 (m, 1H), 3.45-3.55 (m, 2H), 3.57-3.68 (m, 2H), 3.76-3.83 (m, 1H), 3.84 (s, 3H), 4.22-4.28 (m, 1H), 4.46 (s, 2H), 6.91(d, *J* = 8.9 Hz, 2H), 7.29 (d, *J* = 8.5 Hz, 2H); ^{13} C NMR (100 MHz, $CDCl_3$) δ -4.31, 18.1, 19.7, 26.0, 26.9, 27.0, 27.1, 29.7, 29.9, 30.1, 32.4, 32.5, 34.2, 34.3, 36.6, 36.7, 36.8, 42.7, 44.3, 51.1, 52.0, 52.1, 55.4, 64.0, 64.1, 68.3, 72.2, 75.5, 72.6, 80.8, 113.7, 129.3, 130.8, 159.1; HRMS(EI+) *m/z* 552.3870 (calcd for $C_{31}H_{56}O_6Si$ 552.3846).

To a stirred solution of the triol (9.10 mg, 20.0 μmol) in dichloromethane (0.2 mL) at 0 °C were added triethylamine (20.0 μmol, 3.30 μL) and trimethylacetyl chloride (29.0 μmol, 3.00 μL). The reaction mixture was stirred for 12 h at room temperature and the reaction was quenched with saturated aqueous sodium bicarbonate (10 mL). The aqueous phase was extracted with dichloromethane (3 x 10 mL) and the combined extracts were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (30 % ethyl acetate in pentane) to furnish **211** (9.20 mg, 72%) as a colorless oil: IR (neat) 3350, 2955, 2928, 2855, 1726, 1513, 1458, 1248, 1163, 1087, 1037, 834, 773 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.07 (s, 6H), 0.90 (s, 9H), 1.23 (s, 9H), 1.29 (s, 2H), 1.35

(s, 4H), 1.39-1.50 (m, 5H), 1.51-1.59 (m, 2H), 1.60-1.73 (m, 6H), 1.73-1.85 (m, 1H), 1.85-1.96 (m, 2H), 2.30-2.41 (m, 1H), 2.50-2.60 (m, 1H), 2.76-2.86 (m, 1H), 3.45-3.56 (m, 2H), 3.57-3.68 (m, 1H), 3.84 (s, 3H), 4.11-4.23 (m, 2H), 4.24-4.32 (m, 1H), 4.46 (s, 2H), 6.91 (d, J= 8.5 Hz, 2H), 7.29 (d, J= 8.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ -4.3, 18.3, 19.7, 25.5, 26.0, 27.1, 27.3, 30.1, 30.2, 32.4, 32.6, 34.1, 34.3, 34.4, 36.7, 36.8, 38.9, 39.0, 40.2, 40.4, 49.0, 49.1, 51.2, 51.3, 55.3, 65.8, 65.9, 68.4, 68.5, 72.1, 72.2, 72.5, 72.6, 72.7, 72.8, 80.9, 81.0, 113.7, 129.2, 130.8, 159.1, 178.5; HRMS(TOF MS EI+) *m/z* 659. 4290 (calcd for $C_{36}H_{64}O_7NaSi$ 659. 4319).

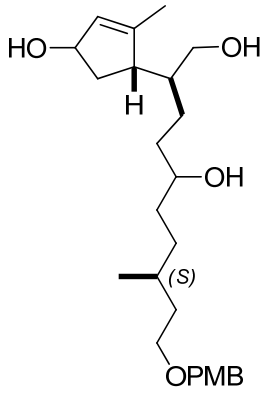


212

Enone 212. To a stirred solution of diol **211** (7.70 mg, 10.0 μmol) in dichloromethane (0.1 mL) were added activated molecular sieves (20.0 mg, 4 Å), *N*-methylmorpholine-*N*-oxide (3.00 mg, 25.0 μmol) and tetrapropylammonium perruthenate (400 μg, 1.00 μmol). The reaction mixture was stirred at room temperature for 1 h and filtered through a short pad of silica gel eluting with dichloromethane (20 mL). The solvent

was evaporated under reduced pressure to give the crude ketone which was used in the next step without purification.

To a stirred solution of the ketone in dichloromethane (0.1 mL) were added triethylamine (30.0 μmol, 4.00 μL) and methanesulfonyl chloride (25.0 μmol, 2.00 μL), and the mixture was stirred for 6 h at room temperature. The reaction was quenched with saturated aqueous sodium bicarbonate (10 mL) and the aqueous phase was extracted with dichloromethane (3 x 5 mL). The combined extracts were dried with anhydrous sodium sulfate, concentrated under reduced pressure and the residue was purified by chromatography on silica gel (10 % ethyl acetate in pentane) to afford **212** (4.30 mg, 68 % for two steps) as a colorless oil: IR (neat) 2954, 2927, 2854, 1727, 1715, 1621, 1513, 1458, 1248, 1152, 1035, 835, 773 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ -0.02-0.02 (four s, 6H), 0.87 (s, 12H), 1.24 (s, 9H), 1.25-1.32 (m, 5H), 1.34-1.46 (m, 5H,), 1.47-1.56 (m, 2H), 1.58-1.69 (m, 2H), 2.08 (s, 3H), 2.10-2.17 (m, 1H), 2.24-2.30 (m, 1H), 2.31-2.44 (m, 1H), 3.07 (br. s, 1H), 3.44-3.53 (m, 3H), 3.82 (s, 3H), 3.87-3.99 (m, 1H), 4.14-4.24 (m, 1H), 4.44 (s, 2H), 6.03 (s, 1H), 6.91 (d, J = 8.5 Hz, 2H), 7.28 (d, J = 7.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -4.6, -4.5, -4.4, -4.3, 17.4, 17.5, 18.0, 18.1, 19.5, 19.6, 20.1, 21.4, 25.8, 27.2, 29.7, 30.0, 30.1, 32.3, 32.8, 34.1, 34.7, 34.9, 35.4, 36.7, 36.8, 36.9, 37.0, 38.0, 38.1, 38.8, 45.9, 46.1, 55.3, 66.3, 66.4, 68.3, 38.4, 72.2, 72.5, 72.6, 72.6, 113.7, 129.2, 130.7, 132.5, 132.6, 159.1, 178.4, 178.5, 179.5, 179.6, 208.3, 208.5; HRMS(TOF MS EI+) *m/z* 639.4058 (calcd for $C_{36}H_{60}O_6NaSi$ 639.4057).

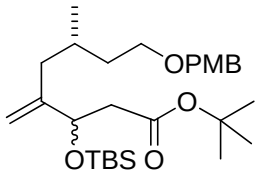


213

Triol 213. To a stirred solution of *t*-butyldimethylsilyl ether **212** (5.50 mg, 9.00 μmol) in acetonitrile (0.1 mL) was added aqueous hydrofluoric acid (30.0 μmol, 1.20 μL, 48 %) and the mixture was stirred for 1.5 h at room temperature. The reaction was quenched with saturated aqueous sodium bicarbonate (10 mL) and the aqueous phase was extracted with dichloromethane (3 x 10 mL). The combined extracts were dried with anhydrous sodium sulfate, concentrated under reduced pressure and the residue was purified by chromatography on silica gel (50 % ethyl acetate in pentane) to afford an alcohol (4.50 mg, 100 %) as a colorless oil: IR (neat) 3446, 2929, 2854, 1725, 1683, 1616, 1513, 1457, 1364, 1282, 1247, 1155, 1095, 1034, 820 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.92 (s, 3H), 1.06-1.17 (m, 1H), 1.17-1.22 (s, 2H), 1.22-.153 (m, 19H), 1.54-1.73 (m, 6H), 2.12 (s, 3H), 2.14-2.34 (m, 3H), 2.35-2.45 (m, 1H), 3.07-3.13 (m, 1H), 3.49-3.55 (m, 3H), 3.84 (s, 3H), 3.94-4.02 (m, 1H), 4.19-4.26 (m, 1H), 4.46 (s, 2H), 6.05 (s, 1H), 6.91 (d, *J* = 8.6 Hz, 2H), 7.28 (d, J= 8.3, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2, 17.5, 19.5, 20.7, 21.4, 22.7, 27.2, 29.7, 30.0, 31.9, 32.6, 32.9, 34.8, 35.1, 35.2, 35.6, 36.6, 36.7, 37.0, 37.2, 37.8, 38.0, 38.9, 46.1, 55.3, 66.1, 66.3,

68.2, 71.8, 72.3, 72.6, 114.8, 129.3, 130.7, 132.5, 132.6, 178.4, 179.5, 208.5; HRMS(CI+) *m/z* 502.3319 (calcd for $C_{30}H_{46}O_6$ 502.3294).

To a stirred solution of the alcohol (9.20 mg, 18.0 μmol) in dichloromethane (0.2 mL) at -78 °C was added diisobutylaluminum hydride (90.0 μL, 90.0 μmol, 1M solution in dichloromethane) and the mixture was allowed to warm to room temperature. The reaction was quenched with saturated aqueous potassium sodium tartrate (10 mL) and the aqueous phase was extracted with dichloromethane (3 x 5 mL). The combined extracts were dried with anhydrous sodium sulfate, concentrated under reduced pressure and the residue was purified by chromatography on silica gel (100 % ethyl acetate) to furnish **213** (8.00 mg, 80 %) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (m, 3H), 1.05-1.90 (m, 23H). 1.93-2.30 (m, 3H), 2.33-2.50 (m, 1H), 3.63-2.84 (m, 1H), 3.44-3.62 (m, 4H), 3.63-3.80 (m, 1H), 3.84 (s, 3H), 4.47 (s, 2H), 4.72-4.79 (m, 1H), 5.56-5.66 (m, 1H), 6.90 (d, *J* = 8.5 Hz, 2H), 7.23 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 1.1, 15.6, 19.7, 23.2, 23.9, 25.3, 29.7, 29.8, 29.9, 30.0, 32.7, 32.9, 34.8, 34.9, 35.6, 35.7, 35.8, 36.9, 36.2, 36.6, 36.7, 41.3, 41.4, 48.4, 49.6, 49.7, 52.2, 52.3, 55.3, 65.4, 65.8, 68.3, 70.9, 72.1, 72.2, 72.3, 72.4, 72.6, 76.1, 113.7, 129.3, 129.5, 129.6, 130.7, 131.3, 131.4, 134.9, 135.1, 146.4, 146.6, 159.1. HRMS(CI+) *m/z* 420.2849 (calcd for $C_{25}H_{40}O_5$ 420.2876).

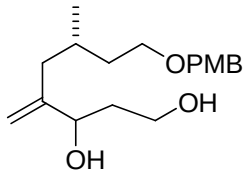


221

***t*-Butyl Ester 221**: To a stirred solution of aldehyde **177** (1.20 g, 5.00 mmol) in dichloromethane (50 mL) were added Eschenmoser's salt (1.80 g, 10.0 mmol) and triethylamine (1.40 mL, 15.0 mmol), and the mixture was stirred for 12 h at room temperature. The reaction was quenched with saturated aqueous sodium bicarbonate (50 mL) and the aqueous phase was extracted with dichloromethane (3 x 50 mL). The combined extracts were dried with anhydrous sodium sulfate and concentrated under reduced pressure to give crude aldehyde **218** which was used in the next step without purification.

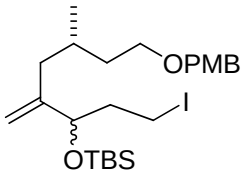
To a stirred solution of *t*-butyl acetate (1.00 g, 8.61 mmol) in tetrahydrofuran (86 mL) at -78 °C was added lithium diisopropylamide (7.40 mmol, 7.40 mL, 1M solution in tetrahydrofuran) and the mixture was stirred for 1 h. To this solution at -78 °C was added solution of crude aldehyde **218** in tetrahydrofuran (38 mL) and the mixture was stirred for 2 h at the same temperature. The reaction was quenched with saturated aqueous sodium bicarbonate (100 mL) and the aqueous phase was extracted with dichloromethane (3 x 100 mL). The combined extracts were dried with anhydrous sodium sulfate and concentrated under reduced pressure to give crude *t*-butyl ester **220** which was used in the next step without purification.

To a stirred solution of crude *t*-butyl ester **220** and collidine (7.90 mmol, 919 μL) in dichloromethane (20 mL) at -78 °C was added *t*-butyldimethylsilyl trifluoromethanesulfonate (1.70 mL, 7.60 mmol) and the mixture was stirred for 1 h at the same temperature. The reaction was quenched with saturated aqueous sodium bicarbonate (50 mL) and the aqueous phase was extracted with dichloromethane (3 x 50 mL). The combined extracts were dried with anhydrous sodium sulfate, concentrated under reduced pressure and the residue was purified by chromatography on silica gel (10 % ethyl acetate in pentane) to give **221** (1.50 g, 79 % for three steps) as an oil: IR (neat) 2955, 2929, 2856, 1732, 1647, 1613, 1513, 1463, 1391, 1301, 1249, 1152, 1096, 1039, 1005, 956, 905, 835, 777, 668 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.061 (s, 6H), 0.89 (s, d, 12H), 1.45 (s, 9H), 1.82-1.62 (m, 2H), 1.92-1.83(m, 2H), 2.13-2.02 (m, 1H), 2.40 (dd, *J* = 6.8, 3.5 Hz, 2H), 3.56-3.47 (m, 2H), 3.83 (s, 3H), 4.45 (s, 2H), 4.51 (t, *J* = 6.2 Hz, 1H), 4.83 (s, 1H), 5.14 (s, 1H), 6.89 (d, *J* = 8.2 Hz, 2H), 7.28 (d, *J* = 7.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.2, -4.5, 18.4, 19.5, 20.9, 25.9, 27.8, 28.3, 29.9, 36.6, 37.2, 38.8, 44.0, 55.2, 68.4, 72.6, 72.9, 73.5, 80.0, 111.2, 113.6, 129.1, 131.0, 148.6, 159.1, 170.4; HRMS (TOF MS ES+) *m/z* 515.3185 (calcd for $C_{28}H_{48}O_5NaSi$ 515.3169).



222

Diol 222. To a stirred slurry of lithium aluminum hydride (5.00 mg, 0.120 mmol) in ether (1.2 mL) at 0 °C was added a solution of *t*-butyl ester **221** (20.0 mg, 40.0 μmol) in ether (0.4 mL) and the mixture was stirred for 30 min at room temperature. The reaction was quenched with wet sodium sulfate and filtered. The solvent was evaporated under reduced pressure to give diol **222** (9.30 mg, 99 %) as an oil: IR (neat) 3378, 2923, 1607, 1513, 1457, 1250, 1170, 1034, 903, 820 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.90 (d, *J* = 6.7 Hz, 3H), 1.35-1.49 (m, 1H), 1.61-1.96 (m, 5H), 1.99-2.15 (m, 1H), 2.50 (br. s, 2H), 3.45-3.57 (m, 2H), 3.89 (s, 5H), 4.27-4.32 (m, 1H), 4.44 (s, 2H), 4.90 (s, 1H), 5.18 (s, 1H), 6.90 (d, *J* = 7.7 Hz, 2H), 7.28 (d, *J* = 8.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.7, 20.0, 28.2, 28.4, 29.7, 36.1, 36.7, 36.9, 40.5, 55.5, 61.6, 68.2, 72.6, 74.6, 110.8, 113.8, 129.2, 131.0, 150.3, 159.3; HRMS(TOF MS ES+) *m/z* 331.1884 (calcd for $C_{18}H_{28}O_4Na$ 331.1885).



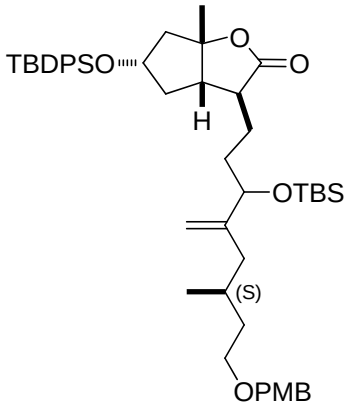
217

Iodide 217. To a stirred solution of *t*-butyl ester **221** (600 mg, 1.20 mmol) in toluene (10 mL) at -78 °C was added diisobutylaluminum hydride (12.0 mL, 2.40 mmol, 1M in dichloromethane) and the mixture was stirred for 1 h at the same temperature. The reaction was quenched by pouring the cold (-78 °C) mixture into saturated aqueous potassium sodium tartrate (50 mL). Dichloromethane (100 mL) was added to the emulsion and the mixture was vigorously stirred for 12 h. The aqueous phase was extracted with dichloromethane (3 x 50 mL) and the combined extracts were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure to give crude product (a 3:7 mixture of alcohol **223** and aldehyde **224**) which was used in the next step without purification.

To a stirred solution of the crude mixture in ethanol (12 mL) at 0 °C was added sodium borohydride (4.80 mmol, 178 mg) and the mixture was stirred for 30 min at the same temperature. The reaction was quenched with water (50 mL) and the aqueous phase was extracted with dichloromethane (3 x 50 mL). The combined extracts were dried with anhydrous sodium sulfate and concentrated under reduced pressure to give crude alcohol **223** which was used in the next step without purification.

To a stirred solution of crude alcohol **223**, triphenylphosphine (345 mg, 1.32 mmol) and imidazole (204 mg, 3.00 mmol) in benzene (3 mL) at room temperature was

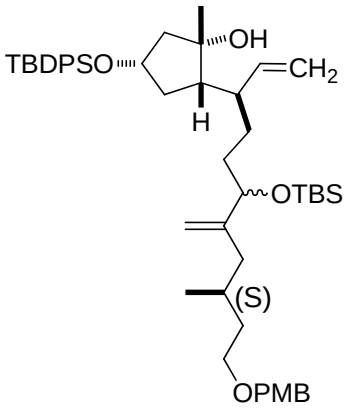
added a solution containing iodine (366 mg, 1.44 mmol) in benzene (14.0 mL) and the mixture was stirred for 5 min. Saturated aqueous sodium thiosulfate (10 ml) and sodium bicarbonate (10 mL) were added to quench the reaction and the aqueous phase was extracted with dichloromethane (3 x 50 mL). The combined extracts were dried with anhydrous sodium sulfate, concentrated under reduced pressure and the residue was purified by chromatography on silica gel (5 % ethyl acetate in pentane) to give **217** (500 mg, 86 %) as an oil: IR (neat) 2953, 2927, 2855, 1646, 1513, 1462, 1248, 1093, 1039, 938, 835, 776 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.08 (s, 6H), 0.93 (s, 12H), 1.33-1.54 (m, 1H), 1.65-1.93 (m, 3H), 1.99-2.11 (m, 3H), 3.19 (t, *J* = 6.8, 2H), 3.48-3.56 (m, 2H), 3.84 (s, 3H), 4.12 (t, *J* = 5.7 Hz, 1H), 4.47 (s, 2H), 4.87 (s, 1H), 5.10 (s, 1H), 6.90 (dd, *J* = 8.3, 1.0 Hz, 2H), 7.29 (dd, *J* = 8.8, 2.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -4.7, -4.4, 3.0, 18.2, 19.6, 20.0, 25.9, 27.9, 28.1, 36.5, 37.2, 39.3, 39.4, 40.82, 40.87, 55.4, 68.2, 68.3, 72.6, 72.7, 75.3, 76.0, 111.5, 113.8, 129.20, 129.25, 130.7, 130.8, 148.5, 148.6, 159.1; HRMS(EI+) *m/z* 555.1736 (calcd for $C_{24}H_{41}O_3NaISi$ 555.1767).



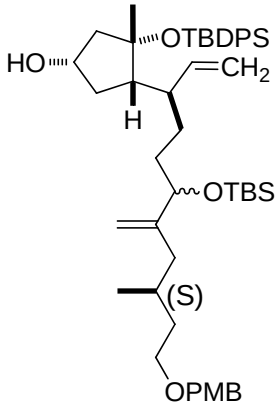
218

Lactone 218. To a stirred solution of lactone **170** (1.00 g, 2.54 mmol) in tetrahydrofuran (3.60 mL) at -78 °C was added lithium diisopropylamide (5.10 mmol, 5.00 mL, 1M solution in tetrahydrofuran) and the mixture was stirred for 1 h. To this mixture were added, in the following order, diethylzinc (5.84 mmol, 636 μL), alkyl iodide **217** (4.00 mmol, 2.10 g) in tetrahydrofuran (7.00 mL) and *N*, *N*′-dimethyl-*N*, *N*′-propylene urea (23.0 mmol, 2.80 mL) and the mixture was allowed to warm to 0 °C. The reaction was quenched with saturated aqueous ammonium chloride (50 mL) and the aqueous phase was extracted with dichloromethane (3 x 50 mL). The combined extracts were dried with anhydrous sodium sulfate, concentrated under reduced pressure and the reside was purified by chromatography on silica gel (10 % ethyl acetate in pentane) to afford **218** (1.80 g, 89 %) as a light yellow oil: IR (neat) 2955, 2929, 2856, 1762, 1733, 1717, 1700, 1652, 1646, 1635, 1615, 1587, 1576, 1558, 1540, 1513, 1488, 1471, 1463, 1427 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.04 (s, 6H), 0.92 (s, 12H), 1.05 (s, 9H), 1.18-1.50 (m, 7H), 1.51-1.68 (m, 5H), 1.71-1.92 (m, 5H),

1.94-2.12 (m, 2H), 2.15-2.26 (m, 2H), 2.71-2.80 (m, 2H), 3.44-3.58 (m, 2H), 3.82 (s, 3H), 4.05 (t, J = 5.3 Hz, 1H), 4.28-4.34 (m, 1H), 4.45 (s, 2H), 4.83 (s, 1H), 5.09 (s, 1H), 6.89 (d, J = 8.1 Hz, 2H), 7.27 (d, J = 6.2 Hz, 2H), 7.36-7.48 (m, 6H), 7.62-7.70 (m , 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -4.9, -4.6, -4.5, 18.2, 18.9, 19.5, 20.0, 25.9, 26.8, 27.9, 28.0, 28.1, 28.2, 28.4, 29.4, 29.7, 33.7, 34.5, 36.5, 37.2, 39.4, 39.6, 42.6, 48.2, 50.2, 50.4, 55.3, 68.3, 68.4, 72.6, 74.4, 75.6, 92.0, 92.1, 110.7, 111.2, 113.7, 127.7, 129.2, 129.7, 130.8, 133.6, 133.7, 135.8, 135.9, 148.7, 149.4, 159.1, 179.1; HRMS(TOF ES+) *m/z* 821.4616 (calcd for $C_{48}H_{70}O_6Si_2Na$ 821.4609).



237



238

Alcohol 237. To a solution of lactone **218** (1.00 g, 1.25 mmol) in toluene (30.0 mL) at -78 °C was added diisobutylaluminum hydride (2.50 ml, 2.50 mmol, 1M solution in dichloromethane) and the mixture was stirred for 2 h at the same temperature. The excess of diisobutylaluminum hydride was quenched by pouring the cold mixture (-78 °C) into saturated aqueous sodium potassium tartrate (50 mL). The emulsion was diluted with dichloromethane (20 mL) and the mixture was vigorously stirred

overnight. The organic phase was separated and dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure to give crude lactol **235** which was used in the next step without purification.

To a stirred solution of crude lactol **235** in benzene (4.50 mL) at 0 °C was added a solution of triphenylmethylenephosphorane (**236**) in benzene prepared as described below (15.0 mL, 4.50 mmol) and the mixture was stirred for 12 h at room temperature. The reaction was quenched with saturated aqueous ammonium chloride (50 mL) and the aqueous phase was extracted with dichloromethane (3 x 20 mL). The combined extracts were dried with anhydrous sodium sulfate, concentrated under reduced pressure and the residue was purified by chromatography on silica gel (10 % ethyl acetate in pentane) to give **237** (827 mg, 83%) and **238** (73.0 mg, 7%) as colorless oils.

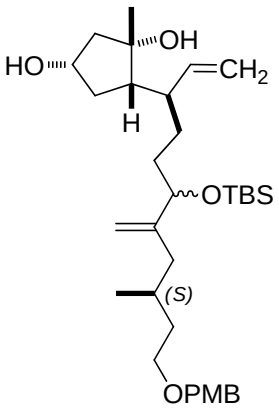
237: IR (neat) 3525, 3071, 2955, 2929, 2856, 1641, 1612, 1576, 1513, 1471, 16622, 1427, 1362, 1302, 1245, 1172, 1105, 1036, 997, 938, 903, 835, 774, 740, 702, 613 cm^{-1};^{1}H NMR (400 MHz, $CDCl_3$) δ 0.032 (s, 6H), 0.97 (s, 12H), 1.08 (s, 9H), 1.97-1.96 (m, 18H), 1.97-2.11 (m, 1H), 2.12-2.25 (m, 1H), 2.26-2.43 (m, 1H), 3.11 (s, OH), 3.51 (dd, *J* = 9.4, 3.9 Hz, 2H), 3.82 (s, 3H), 4.03 (dd, *J* = 9.5, 4.9 Hz, 1H), 4.23 (dd, *J* = 6.7, 2.9 Hz, 1H), 4.46 (s, 3H), 4.78 (s, 1H), 4.97-5.12 (m, 3H), 5.53-.5.73 (m, 1H), 6.89 (d, *J* = 8.6 Hz), 7. 24 -7.32 (m, 2 H), 7.35 - 7.49 (m, 6H), 7.64 -7.72 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -4.9, -4.6, -4.6, 18.2, 18.9, 19.4, 19.5, 20.0, 25.9, 26.6, 26.9, 27.1, 27.2, 26.6, 27.7, 27.8, 27.9, 28.0, 28.1, 28.4, 29.1, 29.5, 29.7, 29.8, 33.5, 33.7, 34.4, 34.4, 36.5, 36.7, 37.2, 39.0, 39.1, 39.2, 39.4, 39.8, 40.9, 41.0, 44.6, 45.0,

51.2, 51.3, 51.4, 51.4, 51.5, 51.9, 52.0, 55.3, 68.4, 68.5, 72.5, 72.6, 72.7, 72.8, 73.9, 74.0, 75.0, 75.7, 79.9, 80.2, 80.3, 110.1, 110.2, 110.4, 110.5, 113.7, 115.0, 115.2, 127.6, 127.7, 129.2, 129.7, 130.7, 130.8, 133.6, 134.8, 135.7, 142.2, 143.1, 143.3, 149.6, 149.7, 150.0, 159.1; HRMS (EI) *m/z* 821.5004 (calcd for $C_{49}H_{74}O_5NaSi_2$, 821.4973).

238: IR (neat) 3406, 2955, 2929, 2856, 1612, 1513, 1471, 1427, 1361, 1248, 1171, 1105, 1039, 997, 938, 906, 835, 775, 741, 703, 612 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.06 (s, 6H), 0.91 (s, 12 H), 1.09 (s, 9H), 1.28 (s, 3H), 1.34 -1.53 (m, 4H), 1.54-1.68 (m, 3H), 1.70-1.93 (m, 5H), 1.95-2.11 (m, 1H), 2.26-2.36 (m, 1H), 2.49-2.62 (m, 1H), 3.47-3.66 (m, 2H), 3.82 (s, 3H), 3.96-4.08 (m, 2H), 4.45 (s, 2H), 4.80 (s, 1H), 4.93-5.08 (m, 3H), 5.63 (dt, *J* = 17.2, 9.4 Hz, 1H), 6.89 (d, *J* = 8.3 Hz, 2H), 7.28 (d, *J* = 7.9 Hz, 2H), 7.34-7.46 (m, 6H), 7.76 (t, *J* = 6.3 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -4.8, -4.8, -4.5, 18.2, 19.5, 20.1, 26.0, 27.6, 27.9, 28.1, 28.9, 29.1, 29.7, 33.3, 33.7, 36.7, 37.2, 39.0, 39.6, 40.4, 42.6, 51.7, 54.5, 54.7, 55.3, 68.4, 68.5, 70.4, 70.45, 72.6, 74.8, 75.5, 83.9, 110.3, 110.7, 113.7, 114.5, 114.6, 127.2, 127.6, 129.2, 129.5, 129.6, 130.8, 130.9, 135.2, 135.6, 136.4, 136.7, 143.7, 143.7, 149.5, 149.8, 159.1; HRMS (EI) *m/z* 821.4981 (calcd for $C_{49}H_{74}O_5NaSi_2$, 821.4973).

Preparation of triphenylmethylenephosphorane (236). To a slurry of potassium *t*-butoxide (4.50 mmol, 505 mg) in benzene (15.0 mL) was added triphenylmethylphosphonium bromide (5.00 mmol, 1.78 g, dried under vacuum at 120 °C overnight) and the mixture was refluxed for 4 h. The resulting orange slurry was

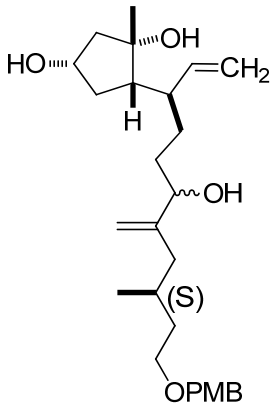
allowed to reach room temperature, and after a white solid had precipitated the solution was used immediately.



241

Diol 241. To a stirred solution of alcohol **237** (37.0 mg, 50.0 μmmol) in tetrahydrofuran (100 μL) at room temperature was added tetra-*n*-butylammonium fluoride (1M tetrahydrofuran solution, 200 μmol, 200 μL) and the mixture was stirred for 1h. The reaction was quenched with saturated aqueous sodium bicarbonate (20 mL) and the aqueous phase was extracted with dichloromethane (3 x 10 mL). The combined extracts were dried with anhydrous sodium sulfate, concentrated under reduced pressure and the residue was purified by chromatography on silica gel (20 % ethyl acetate in pentane) to afforded **241** (20.0 mg, 71 %) as a colorless oil: IR (neat) 3395, 3072, 2954, 2928, 2856, 1716, 1641, 1612, 1586, 1513, 1462, 1361, 1301, 1248, 1172, 1085, 1038, 1005, 978, 906, 835, 774, 667. cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 0.032 (s, 6H), 0.91 (s, 12H), 1.00-1.13 (m, 1H), 1.23-1.48 (m, 7H), 1.49-1.93 (m,

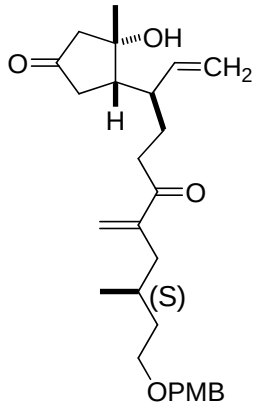
11H), 1.96-2.10 (m, 1H), 2.11-2.21 (m, 1H), 2.26-2.32 (m, 1H), 2.34-2.46 (m, 1H), 2.96 (br. s, 1H), 3.45-3.55 (m, 2H), 3.82 (s, 3H), 3.98-4.06 (m, 1H), 4.13-4.20 (m, 1H), 4.45 (s, 2H), 4.79 (s, 1H), 5.01-5.17 (m, 3H), 5.67 (ddd, J= 16.7, 12.2, 10.2 Hz, 1H), 6.89 (d, J = 8.4 Hz, 2H), 7.28 (d, J = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -4.9, -4.6, 18.2, 19.5, 20.1, 25.9, 27.9, 28.1, 28.4, 28.9, 29.3, 29.7, 29.9, 33.6, 34.1, 36.6, 37.2, 37.4, 39.2, 39.5, 39.7, 41.2, 43.6, 47.3, 47.5, 50.7, 51.1, 51.8, 52.3, 55.3, 68.5, 71.4, 71.5, 72.5, 75.2, 75.9, 81.4, 110.5, 110.7, 113.7, 115.3, 115.4, 116.5, 129.1, 130.9, 141.9, 143.6, 149.6, 159.1; HRMS (EI) *m/z* 583.3770 (calcd for $C_{33}H_{56}O_5NaSi$, 583.3795).



243

Triol 243. To a 12:1 mixture of alcohols **237** and **238** (844 mg, 1.06 mmol) was added tetra-*n*-butylammonium fluoride (1M solution in tetrahydrofuran, 7.00 mmol, 7.00 mL) and the mixture was heated at 60 °C for 2 h. The reaction was quenched with saturated aqueous sodium bicarbonate (20 mL) and the aqueous phase was extracted with dichloromethane (3 x 10 mL). The combined extracts were dried with anhydrous

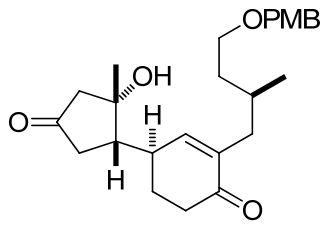
sodium sulfate, concentrated under reduced pressure and the residue was purified by chromatography on silica gel (80 % ethyl acetate in hexane) to give **243** (477 mg, 99 %) as a colorless oil: IR (neat) 3395, 3072, 2955, 2926, 2865, 1733, 1637, 1612, 1513, 1456, 1419, 1375, 1301, 1248, 1172, 1087, 1035, 907, 821 cm^{-1};^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92 (d, J= 6.0 Hz, 3H), 1.35 (s, 3H), 1.37-1.47 (m, 1H), 1.47-1.57 (m, 1H), 1.58-1.78 (m, 7H), 1.82-195 (m, 3H), 1.97-2.15 (m, 1H), 2.18-2.31 (m, 1H), 2.33-2.45 (m, 1H), 2.94-3.02 (m, 1H), 3.43-3.57 (m, 2H), 3.82 (s, 3H), 3.96-4.09 (m, 1H), 4.14-4.23 (m, 1H), 4.44 (s, 2H), 4.85 (s, 1H), 5.03-5.15 (m, 3H), 5.32 (s, 1H), 5.62-5.74 (m, 1H), 6.89 (d, *J* = 8.1 Hz, 2H), 7.27 (d, *J* = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.6, 20.1, 28.2, 28.3, 28.4, 29.1, 29.5, 32.7, 36.4, 36.8, 39.9, 40.2, 41.7, 41.9, 46.6, 47.4, 50.9, 51.0, 51.7, 55.3, 68.2, 68.3, 71.7, 72.6, 74.2, 75.4, 81.5, 110.7, 111.2, 113.8, 115.5, 115.6, 129.2, 130.6, 143.5, 150.1, 150.5, 159.1; HRMS (EI) *m/z* 447.3128 (calcd for $C_{27}H_{43}O_5$ 447.3110).



244

Diketone 244. To a stirred solution of triol **243** (600 mg, 1.36 mmol) in dichloromethane (13.6 mL) at 0 °C were added sodium bicarbonate (3.40 g, 1.00 mmol) and Dess-Martin reagent (1.70 g, 4.00 mmol) and the mixture was stirred at room temperature for 1 h. Saturated aqueous sodium bicarbonate (20 mL) and sodium thiosulfate (20 mL) were added to quench the reaction and the aqueous phase was extracted with dichloromethane (3 x 20 mL). The combined extracts were dried with anhydrous sodium sulfate, concentrated under reduced pressure and the residue was purified by chromatography on silica gel (30 % ethyl acetate in pentane) to yield **244** (530 mg, 89 %) as a colorless oil: $[\alpha]_D^{25}$ -21.0 (c 0.20, $CHCl_3$); IR (neat) 3446, 3073, 2957, 2924, 2869, 1740, 1699, 1674, 16.53, 1635, 1615, 1585, 1569, 1558, 1540, 1513, 1488, 1456, 1418, 1395, 1376, 1301, 1247, 1172, 1099, 1033, 931, 822, 746, 699 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.86 (d, *J* = 6.7 Hz, 3H), 1.24-1.45 (m, 2H), 1.46-1.56 (m, 3H), 1.57-1.81 (m, 2H), 1.98-2.17 (m, 3H), 2.23-2.36 (m, 3H), 2.37-2.49 (m, 3H), 2.66-2.83 (m, 2H), 3.44-3.54 (m, 2H), 3.82 (s, 3H), 4.43 (s, 2H), 5.02-5.13 (m , 2H), 5.63-5.70 (m, 1H), 5.76 (s, 1H), 6.03 (s, 1H), 6.89 (d, *J* = 8.0 Hz, 2H),

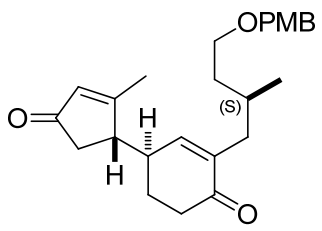
7.26 (d, *J* = 9.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.4, 25.7, 27.5, 29.3, 29.6, 34.9, 36.5, 38.6, 40.6, 43.7, 50.1, 54.8, 55.3, 68.3, 72.6, 113.7, 115.7, 125.2, 129.2, 130.8, 142.3, 147.8, 159.2, 202.4, 215.8. HRMS (EI) *m/z* 442.2717 (calcd 442.2719).



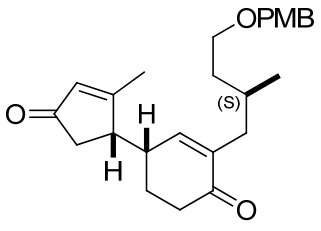
245

Enone 245. To a solution of diketone **244** (13.0 mg, 30.0 μmol) in toluene (300 μL) was added **240** as a solution in toluene (12.0 mg/ mL, 300 μL, 6.00 μmol) and the mixture was degassed three times using a pump-thaw technique. The flask containing the mixture was placed in a preheated oil bath at 80 °C. After 6 h, the solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (50 % ethyl acetate in pentane) to give **245** (10.0 mg, 80 %) as an oil: $[\alpha]_D^{25}$ -21.8 (c 0.28, $CHCl_3$); IR (neat) 3445, 2956, 2925, 2867, 1743, 1670, 1612, 1585, 1513, 1456, 1377, 1247, 1173, 1095, 1032, 933, 821, 553 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.86 (s, 3H), 1.20 (s, 1H), 1.31-1.45 (m, 2H), 1.47-1.72 (m, 6H), 1.72-1.88 (m, 2H), 1.95-2.10 (m, 1H), 2.11-2.32 (m, 3H), 2.33-2.47 (m, 5H), 2.47-2.53 (m, 1H), 2.88-2.97 (m, 1H), 3.45-3.56 (m, 2H), 3.82 (s, 3H), 4.44 (s, 2H), 6.75 (d, *J* = 2.7 Hz, 1H), 6.89 (d, *J* = 8.7 Hz, 2H), 7.27 (d, *J* = 8.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.8, 27.3, 27.9, 29.5, 35.9, 36.5, 36.9, 37.2, 41.2, 50.0, 55.4, 65.9, 68.4, 72.7, 113.8,

129.3, 130.8, 138.1, 150.0, 159.2, 198.9, 214.6; HRMS(TOF MS ES+) *m/z* 437.2293 (calcd for $C_{25}H_{34}O_5Na$ 437.2304).



248



251

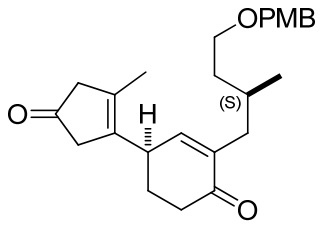
Dienones 248 and 251. **From 245.** To a stirred solution of cyclopentanone **245** (104 mg, 0.250 mmol) in dichloromethane (2.50 mL) at 0 °C was added Martin's sulfurane (253 mg, 0.370 mmol) and the mixture was stirred at 4 °C for 5 h. The reaction was quenched with saturated aqueous sodium bicarbonate (10 mL) and the aqueous phase was extracted with dichloromethane (3 x 10 mL). The combined extracts were dried with anhydrous sodium sulfate, concentrated under reduced pressure and the residue was purified by chromatography on silica gel (50 % ethyl acetate in pentane) to give **248** (62.0 mg, 63 %) as a colorless oil and **251** (4.00 mg, 4 %) as a colorless oil.

248: $[\alpha]_D^{20}$ +17.0 (c 0.30, $CHCl_3$); IR (neat) 2923, 2851, 1707, 1674, 1617, 1585, 1513, 1456, 1378, 1301, 1247, 1301, 1182, 1096, 1033, 821 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.85 (d, *J* = 6.8 Hz, 3H), 1.34-1.53 (m, 2H), 1.58-1.70 (m, 2H), 1.74-1.85 (m, 1H), 1.94-2.03 (m, 1H), 2.05-2.11 (m, 1H), 2.15 (s, 3H), 2.21-3.32 (m, 1H), 2.34-2.47 (m, 2H), 2.48-2.60 (m, 1H), 2.94-3.05 (m, 1H), 3.08-3.16 (m, 1H), 3.44-3.56 (m, 2H), 3.83 (s, 3H), 4.45 (s, 3H), 6.05 (t, J=1.2 Hz, 1H), 6.46 (br. s, 1H), 6.90 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.4, 19.7, 22.7,

29.2, 36.6, 37.2, 37.3, 37.31, 37.5, 47.7, 55.3, 68.4, 72.7, 113.4, 129.4, 130.8, 133.1, 139.8, 148.3, 159.2, 177.6, 198.2, 207.5; HRMS(EI+) *m/z* 396.2301 (calcd for $C_{25}H_{32}O_4$ 396.2300).

251: $[\alpha]_D^{20}$ +19.2 (c 0.26, $CHCl_3$); IR (neat) 2926, 2864, 1708, 1674, 1618, 1585, 1513, 1453, 1377, 1299, 1247, 1182, 1096, 1033, 934, 821, 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.80 (d, *J* = 6.9 Hz, 3H), 1.35-1.41 (m, 1H), 1.57-1.62 (m, 1H), 1.69-1.79 (m, 2H), 1.99 (dd, *J* = 13.0, 8.0 Hz, 1H), 2.06-2.11 (m, 2H), 2.15 (s, 3H), 2.22 (dd, *J* = 14.0, 6.2 Hz, 1H), 2.40-2.50 (m, 2H), 2.97 (s, 2H), 3.44-3.52 (m, 2H), 3.83 (s, 3H), 4.43 (dd, *J* = 20.0, 11.2 Hz, 2H), 6.11 (s, 1H), 6.20 (s, 1H), 6.90 (d, *J* = 9.0 Hz, 2H), 7.27 (d, *J* = 8.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.6, 19.4, 28.8, 29.4, 36.5, 36.9, 37.1, 38.0, 38.5, 48.1, 55.3, 68.2, 72.7, 113.7, 129.2, 130.8, 133.2, 141.4, 144.1, 159.3, 177.9, 198.4, 207.4; HRMS(EI+) *m/z* 396.2297 (calcd for $C_{25}H_{32}O_4$ 396.2300).

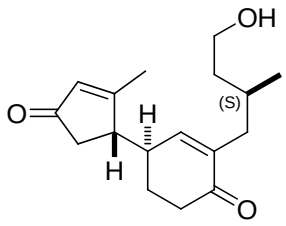
Dienone 248. **From 244**. To a solution of ketone **244** (530 mg, 1.20 mmol) in toluene (24.0 mL) was added **240** (75.0 mg, 0.120 mmmol) and the reaction mixture was degassed three times using a pump-thaw technique. The flask containing the mixture was placed in a preheated oil bath at 95 °C. After 12, h the solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (50 % ethyl acetate in pentane) to give **248** (324 mg, 68 %) and unreacted **244** (116 mg).



249

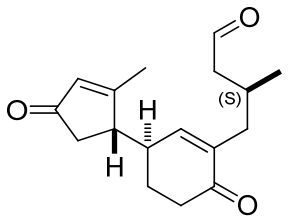
Dienone 249. To a stirred solution of cyclopentanone **245** (8.00 mg, 20.0 μmol) in pyridine (200 μL) at 0 °C was added thionyl chloride (3.00 μL, 40.0 μmol) and the mixture was stirred at the same temperature for 30 min. The reaction was quenched with saturated aqueous cupper sulfate (10 mL) and the aqueous phase was extracted with dichloromethane (3 x 10 mL). The combined extracts were dried with anhydrous sodium sulfate, concentrated under reduced pressure and the residue was purified by chromatography on silica gel (50 % ethyl acetate in pentane) to give **248** (3.30 mg, 30 %) as a colorless oil and **249** (3.30 mg, 42 %) as a colorless oil.

249: d.r. (10:1) $[\alpha]_D^{20}$ +37.8 (c 0.23, $CHCl_3$); IR (neat) 2923, 2852, 1749, 1673, 1612, 1513, 1462, 1377, 1247, 1204, 1171, 1099, 1034, 820 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.84 (d, *J* = 6.4 Hz, 3H), 1.53-1.76 (m, 1H), 1.87 (s, 3H), 1.93-2.95 (m, 4H), 2.24-2.35 (m, 1H), 2.40-2.50 (m, 1H), 2.52-2.61 (m, 1H), 2.88 (s, 2H), 2.94 (s, 2H), 3.46-3.58 (m, 2H), 3.69 (br. s, 1H), 3.83 (s, 3H), 4.49 (s, 2H), 6.45 (s, 1H), 6.90 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 14.1, 19.6, 22.7, 28.1, 29.3, 29.4, 31.9, 36.1, 36.6, 37.4, 37.8, 43.6, 48.5, 55.3, 68.5, 72.7, 113.8, 129.3, 130.8, 131.1, 134.2, 139.2, 148.2, 159.2, 198.52, 214.9; HRMS(EI+) *m/z* 396.2307 (calcd for $C_{25}H_{32}O_4$ 396.2301).



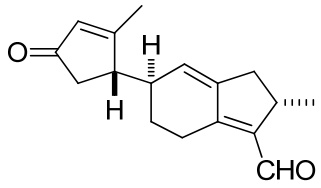
252

Alcohol 252. To a stirred solution of *p*-methoxybenzyl ether **248** (50.0 mg, 0.130 mmol) in a dichloromethane-water solution of disodium hydrogen phosphate-potassium dihydrogen phosphate mixture (1.3 mL dichloromethane and 65 μL buffer) at 0 °C was added 2,3-dichloro-5,6-dicyanobenzoquinone (35.0 mg, 0.150 mmol) and the mixture was stirred for 30 min at 0 °C. The reaction was quenched with saturated aqueous sodium bicarbonate (10 mL) and the aqueous phase was extracted with dichloromethane (3 x 10 mL). The combined extracts were dried with anhydrous sodium sulfate, concentrated under reduced pressure and the residue was purified by chromatography on silica gel (80 % ethyl acetate in pentane) to give **252** (31.0 mg, 86 %) as a colorless oil: $[\alpha]_D^{20}$ +13.6 (c 0.11, $CHCl_3$); IR (neat) 3427, 2923, 2851, 1705, 1673, 1618, 1456, 1378, 1302, 1269, 1112, 1054, 932, 845 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.85 (d, *J* = 6.3 Hz, 3H), 1.39-1.56 (m, 3H), 1.59-1.84 (m, 3H), 1.93-2.05 (m, 1H), 2.17 (s, 3H), 2.29-2.59 (m, 4H), 3.05 (br. s, 1H), 3.21 (br. s, 1H), 3.69 (ddd, *J* = 10.9, 6.8, 6.4 Hz, 1H), 3.79 (ddd, *J* = 10.7, 6.6, 6.5 Hz, 1H), 6.06 (s, 1H), 6.49 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.4, 19.8, 22.7, 28.8, 29.7, 36.9, 37.2, 37.5, 39.4, 47.5, 60.7, 133.1, 140.0, 148.9, 177.6, 198.8, 207.6; HRMS(TOS ES+) *m/z* 299.1617 (calcd for $C_{17}H_{24}O_3Na$ 299.1623).



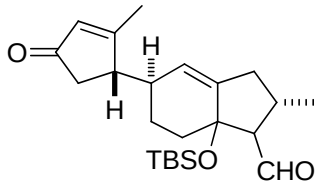
253

Aldehyde 253. To a stirred solution of alcohol **252** (31.0 mg, 0.110 mmol) in dichloromethane (1.10 mL) at 0 °C were added sodium bicarbonate (141 mg, 1.70 mmol) and Dess-Martin reagent (72.0 mg, 0.170 mmol). The mixture was stirred at room temperature for 1 h and the reaction was quenched with saturated aqueous sodium bicarbonate (10 mL) and sodium thiosulfate (10 mL). The aqueous phase was extracted with dichloromethane (3 x 10 mL) and the combined extracts were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (50 % ethyl acetate in pentane) to give **253** (25.0 mg, 81 %) as a colorless oil: $[\alpha]_D^{20}$ +26.9 (c 0.19, $CHCl_3$); IR (neat) 3369, 2924, 2853, 1718, 1674, 1619, 1458, 1379, 1301, 1268, 1185, 1114, 1024, 933, 846,720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.98 (d, *J* = 6.0 Hz, 3H), 1.47-1.55 (m, 1H), 1.59-1.72 (m, 1H), 2.05-2.15 (m, 2H), 2.16 (s, 3H), 2.21-2.59 (m, 7H), 3.02-3.07 (m, 1H), 3.19-3.23 (br. s, 1H), 6.07 (s, 1H), 6.50 (s, 1H), 9.75 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 17.4, 20.0, 22.7, 27.5, 37.19, 37.22, 37.4, 37.5, 47.6, 50.8, 113.3, 139.3, 149.4, 177.5, 198.4, 202.9, 207.5; HRMS(CI+) *m/z* 275.1657 (calcd for $C_{17}H_{22}O_3$ 275.1647).



269

Aldehyde 269. **Method A**. To a stirred solution of aldehyde **253** (7.00 mg, 25.0 μmol) in toluene (500 μL) was added diethylamine (3.20 μL, 30.0 μmol) and the mixture was heated at 80 °C in a sealed vial for 12 h. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (50 % ethyl acetate in hexanes) to give **269** (2.00 mg, 30 %) as an oil and unreacted aldehyde **253** (4.00 mg). **Method B.** To a stirred solution of aldehyde **253** (4.00 mg, 14.0 μmol) in toluene (350 μL) was added trimethylsilyldiethylamine (3.30 μL, 17.0 μmol) and the mixture was heated at 80 °C in a sealed vial for 12 h. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (50 % ethyl acetate in hexanes) to give **269** (2.00 mg, 50 %) and unreacted aldehyde **253** (2.00 mg): $[\alpha]_D^{28}$ +50.0 (c 0.10 $CHCl_3$); IR (neat) 2954, 2852, 1707, 1678, 1657, 1618, 1549, 1450, 1379, 1177, 1110, 1089, 1018, 939, 864, 803, 701, 611 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 1.15-1.17 (m, 1H), 1.18 (d, *J* = 6.1 Hz, 3H), 1.53-1.57 (m, 1H), 2.08-2.14 (m, 2H), 2.15 (s, 3H), 2.37-2.47 (m, 2H), 2.82-2.91 (m, 2H), 3.10-3.19 (m, 3H), 5.75 (br. s, 1H), 6.03 (q, *J* = 1.3 Hz, 1H), 10.04 (s, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 17.7, 20.9, 22.2, 22.7, 36.1, 36.17, 36.76, 48.1, 129.7, 132.9, 143.8, 147.3, 155.1, 178.9, 188.4, 209.2; HRMS(CI+) *m/z* 256.1453 (calcd for $C_{17}H_{20}O_2$ 256.1463).

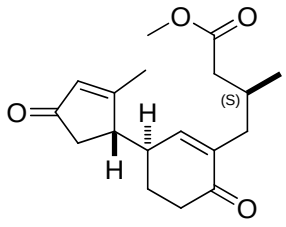


273

Aldehyde 273. Benzene was distilled under atmospheric pressure from a solution of aldehyde **253** (17.2 mg, 63.0 μmol) and piperidine (68.0 μL, 690 μmol) in benzene (1.60 mL) while gradually increasing the temperature to 90 ºC. The oily residue was placed under high vacuum to remove excess piperidine and afford crude enamine **271** which was used in the next step without purification.

To a stirred solution of crude enamine **271** in dichloromethane at -78˚C was added triethylamine (25.0 μL, 20.0 μmol) and *t*-butyldimethylsilyl trifluoromethanesulfonate (15.0 μL, 63.0 μmol,) and the mixture was stirred for 1 h at the same temperature. The reaction was quenched with saturated aqueous sodium bicarbonate (10 mL) and the aqueous phase was extracted with dichloromethane (3 x 10 mL). The combined extracts were dried with anhydrous sodium sulfate, concentrated under reduced pressure and the residue was purified by chromatography on silica gel (30 % to 50 % ethyl acetate on hexanes) to give **273** (4.50 mg, 20 %) as an oil and recovered aldehyde **253** (6.50 mg): $[\alpha]_D^{28}$ +12.5 (c 0.20 $CHCl_3$); IR (neat) 2956, 2927, 2855, 1719, 1680, 1621, 1571, 1462, 1378, 1259, 1094, 1011, 836, 800 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 0.10 (s, 3H), 0.17 (s, 3H), 0.90 (s, 9H), 1.11 (d, *J* = 6.3 Hz, 3H), 1.10-1.13 (m, 1H), 1.20-1.24 (m, 1H), 1.81-1.84 (m, 2H), 1.95 (dd, *J* = 18.9, 2.0 Hz, 1H),

2.11 (s, 3H), 2.10-2.13 (m, 1H), 2.26-2.32 (m, 1H), 2.37 (dd, *J* = 18.5, 6.7 Hz, 1H), 2.48 (dd, *J* = 14.8, 6.2 Hz, 1H), 2.66-2.69 (m, 2H), 2.97-3.00 (br. s, 1H), 5.40 (s, 1H), 6.05 (s, 1H), 9.78 (d, *J* = 3.0 Hz, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ -3.1, -2.5, 17.5, 18.3, 19.1, 25.7, 31.8, 32.6, 32.9, 38.4, 40.8, 49.3, 71.7, 79.4, 123.8, 132.6, 146.2, 179.5, 202.2, 208.7; HRMS(TOF MS ES+) *m/z* 389.2493 (calcd for $C_{23}H_{37}O_3Si$ 389.2512).

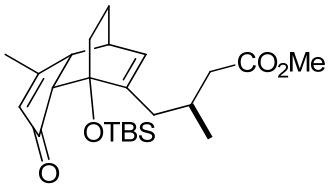


274

Ester 274. To a stirred solution of aldehyde **253** (3.00 mg, 11.0 μmol) in a *t*-butanol-tetrahydrofuran mixture (0.45 mL-0.15 mL) at room temperature were added 2-methyl-2-butene (25.0 μL, 0.240 mmol) and a solution of sodium chlorite (20.0 mg, 0.180 mmol) and sodium dihydrogen phosphate (25.0 mg, 0.180 mmol) in water (0.45 mL). The mixture was stirred for 12 h and the reaction was quenched with water (10 ml). The aqueous phase was extracted with dichloromethane (3 x 10 mL) and the combined extracts were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure to give the crude carboxylic acid which was used in the next step without purification.

To a solution of the crude carboxylic acid in a hexanes-methanol mixture (0.1 mL-0.04 mL) at room temperature was added trimethylsilyldiazomethane (16.0 μmol, 8.00

μL, 2M solution in hexanes) and the mixture was stirred for 12 h. Saturated aqueous ammonium chloride (10 mL) was added to quench the reaction and the aqueous phase was extracted with dichloromethane (3 x 10 mL). The combined extracts were dried with anhydrous sodium sulfate, concentrated under reduced pressure and the residue was purified by chromatography on silica gel (20 % to 50 % ethyl acetate in hexanes) to give **274** (1.40 mg, 40 % for two steps) as an oil: $[\alpha]_D^{25}$ +34.0 (c 0.10, $CHCl_3$); IR (neat) 2922, 2850, 1734, 1710, 1676, 1620, 1461, 1378, 1261, 1160, 1461, 1378, 1261, 1160, 1109, 801, 719 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 0.92 (d, *J* = 6.2 Hz, 3H), 1.46-1.52 (m, 1H), 1.65-1.67 (m, 1H), 2.10-2.15 (m, 1H), 2.12-2.13 (m, 1H), 2.13-2.16 (m, 1H), 2.26-2.29 (m, 1H), 2.30-2.34 (m, 1H), 2.35-2.40 (m, 1H), 2.46 (dd, *J* = 9.5, 7.1 Hz, 1H), 2.55 (ddd, *J* = 16.4, 4.2, 2.8 Hz, 1H), 3.02-3.06 (m, 1H), 3.19-3.22 (m, 1H), 3.69 (s, 3H), 6.07 (quintet, *J* = 1.3 Hz, 1H), 6.51 (s, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 17.5, 19.8, 22.7, 29.6, 36.6, 37.21, 37.24, 37.5, 41.2, 47.6, 51.5, 133.1, 139.2, 148.7, 173.3, 177.5, 198.0, 207.6; HRMS(TOF MS ES+) *m/z* 327.1588 (calcd for $C_{18}H_{24}O_4Na$ 327.1572).



276

Ester 276. To a stirred solution of *p*-methoxybenzyl ether **251** (34.5 mg, 87.0 μmol) in a dichloromethane-water solution of disodium hydrogen phosphate-potassium dihydrogen phosphate (0.8 mL dichloromethane and 0.1 mL buffer) at 0 °C was added 2,3-dichloro-5,6-dicyanobenzoquinone (23.3 mg, 0.100 mmol). The mixture was stirred for 2 h at 0 °C and the reaction was quenched with saturated aqueous sodium bicarbonate (10 mL). The aqueous phase was extracted with dichloromethane (3 x 10 mL) and the combined extracts were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure to give the crude alcohol which was used in the next step without purification.

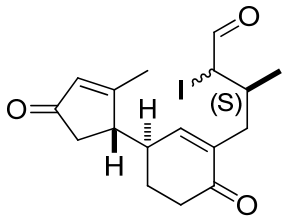
To a stirred solution of the crude alcohol in dichloromethane (0.7 mL) at 0 °C were added sodium bicarbonate (92.0 mg, 1.10 mmol) and Dess-Martin reagent (46.0 mg, 0.110 mmol). The mixture was stirred at room temperature for 1 h and the reaction was quenched with saturated aqueous sodium bicarbonate (10 mL) and sodium thiosulfate (10 mL). The aqueous phase was extracted with dichloromethane (3 x 10 mL) and the combined extracts were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure to give crude aldehyde which was used in the next step without purification.

To a stirred solution of the crude aldehyde in a *t*-butanol-tetrahydrofuran mixture (2.8 mL-0.86 mL) at room temperature were added 2-methyl-2-butene (160 μL, 1.50 mmol) followed by a solution of sodium chlorite (99.0 mg, 1.10 mmol) and sodium dihydrogen phosphate (156 mg, 1.10 mmol) in water (3.5 mL). The reaction mixture was stirred for 4.5 h and was diluted with water (10 mL). The aqueous phase was extracted with dichloromethane (3 x 10 mL) and the combined extracts were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure to give the crude carboxylic acid which was used in the next step without purification.

To a solution of the crude carboxylic acid in a hexanes-methanol mixture (0.5 mL-0.2 mL) at room temperature was added trimethylsilyldiazomethane (0.360 mmol, 180 μL, 2M solution in hexanes) and the mixture was stirred for 12 h. The reaction was quenched with saturated aqueous ammonium chloride (10 mL) and the aqueous phase was extracted with dichloromethane (3 x 10 mL). The combined extracts were dried with anhydrous sodium sulfate, concentrated under reduced pressure and the residue was purified by chromatography on silica gel (80 % ethyl acetate in hexanes) to give **275** (8.00 mg, 30 % for four steps) as a colorless oil.

To a stirred solution of methyl ester **275** (3.20 mg, 10.0 μmol) in dichloromethane (0.1 mL) at -78 °C were added diisopropylethylamine (20.0 μmol, 3.50 μL) and *t*-butyldimethylsilyl trifluoromethanesulfonate (3.50 μL, 15.0 μmol). The reaction mixture was stirred for 2 h at the same temperature and allowed to warm to 0 ºC. The reaction was quenched with aqueous disodium hydrogen phosphate-potassium dihydrogen phosphate and the aqueous phase was extracted with dichloromethane (3 x

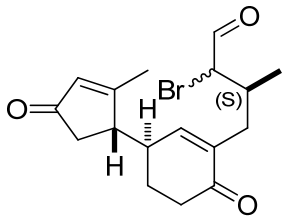
10 mL). The combined extracts were dried with anhydrous sodium sulfate, concentrated under reduced pressure and the residue was purified by chromatography on silica gel (20 % to 50 % ethyl acetate in hexanes) to give **276** (1.50 mg, 36 %) as an oil along with recovered methyl ester **275** (2.00 mg): $[\alpha]_D^{28}$ -83.0 (c 0.10 $CHCl_3$); IR (neat) 2924, 2850, 1737, 1701, 1625, 1462, 1157, 835, 664 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 0.18 (s, 3H), 0.30 (s, 3H), 0.86 (d, *J* = 6.5 Hz, 3H), 1.01 (s, 9H), 1.44 (dt, J= 12.6, 4.1 Hz, 1H), 1.55 (tt, *J* = 12.0, 4.0 Hz, 1H), 1.65 -1.71 (m, 1H), 1.77 (ddd, *J* = 12.0, 8.8, 4.2 Hz, 1H), 1.83-1.88 (m, 1H), 2.02 (dd, *J* = 15.0, 9.1 Hz, 1H), 2.0 (s, 3H), 2.10-2.18 (m, 2H), 2.36 (dd, *J* = 14.2, 3.9 Hz, 1H), 2.45 (d, *J* = 5.7 Hz, 1H), 2.73 (dt, *J* = 6.5, 3.0 Hz, 1H), 2.82 (d, *J* = 5.7 Hz, 1H), 3.67 (s, 3H), 5.43 (d, *J* = 6.8 Hz, 1H), 5.85 (quint, *J* = 1.4 Hz, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ -2.0, -1.3, 17.0, 19.4, 25.9, 26.2, 27.9, 32.5, 34.4, 37.5, 41.4, 50.6, 51.3, 54.3, 78.7, 121.5, 133.7, 145.1, 173.8, 177, 206.8; HRMS(EI+) *m/z* 418.2540 (calcd for $C_{24}H_{38}O_4Si$ 418.2539).



278

Iodoaldehyde 278. To a stirred solution of aldehyde **253** (7.00 mg, 30.0 μmol), piperidine (30.0 μmol, 3.00 μL) and benzoic acid (2.00 mg, 15.0 μmol) in ether (200 μL) at 0 ºC was added *N*-iodosuccinimide (13.0 mg. 60.0 μmol). The mixture was stirred for 1 h and the reaction was quenched with saturated aqueous sodium

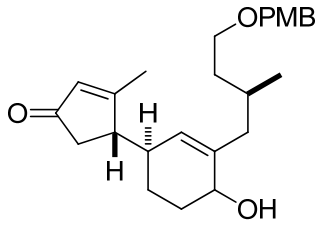
thiosulfate (10 mL). The aqueous phase was extracted with dichloromethane (3 x 10 mL) and the combined extracts were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (50 % ethyl acetate in hexanes) to give **278** (7.00 mg, 62 %, dr 10:6) as an oil: IR (neat) 2921, 2850, 1712, 1673, 1618, 1461, 1378, 1260, 1182 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 1.00 (d, *J* = 6.0 Hz, 3H), 1.48-1.53 (m, 1H), 1.64.1.67 (m, 1H), 1.84 (q, *J* = 6.5 Hz, 1H), 2.08-2.13 (m, 1H), 2.15-2.21 (m, 4H), 2.24-2.30 (m, 1H), 2.35-2.41 (m, 1H), 2.52-2.59 (m, 1H), 2.45-2.50 (m, 1H), 2.52-2.59 (m, 1H), 3.05 (br. s, 1H), 3.23 (br. s, 1H), 4.42 (dd, *J* = 5.6, 3.6 Hz, 1H) [other diastereomer 4.45 (dd, *J* = 6.8, 3.6 Hz)], 6.08 (s, 1H), 6.58 (s, 1H), [other diastereomer 6.59(s)], 9.31 (d, *J* = 3.5 Hz, 1H) [other diastereomer 9.33 (d, *J* = 3.5 Hz)]; ^{13}C NMR (175 MHz, $CDCl_3$) δ 17.4, 18.6, 19.5, 22.5, 22.6, 31.9, 32.0, 36.9, 37.08, 37.1, 37.2, 37.3, 37.4, 46.1, 47.5, 47.9, 133.19, 133.2, 138.1, 138.6, 149.96, 150.1, 176.7, 192.1, 192.2, 198.0, 198.1, 207.3, 207.4; HRMS(CI+) *m/z* 401.0615 calcd for $C_{17}H_{22}O_3I$: 401.0614.



277

Bromoaldehyde 277. To a stirred solution of aldehyde **253** (17.0 mg, 60.0 μmol), benzoic acid (4.00 mg, 30.0 μmol,) and piperidine (60.0 μmol, 6.00 μL) in dichloromethane (600 μL) at 0 ºC was added *N*-bromosuccinimide (22.0 mg, 0.120 mmol). The mixture was stirred for 1 h at 0 ºC and for an additional 30 min at room temperature. The reaction was quenched with saturated aqueous sodium thiosulfate (10 mL) and the aqueous phase was extracted with dichloromethane (3 x 10 mL). The combined extracts were dried with anhydrous sodium sulfate, concentrated under reduced pressure and the residue was purified by chromatography on silica gel (50 % ethyl acetate in hexanes) to give **277** (10.0 mg, 50 %): IR (neat) 2961, 2928, 2872, 2855, 1714, 1674, 1619, 1450, 1430, 1379, 1300, 1269, 1183, 1023, 911, 847 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 0.97 and 1.04 (d, *J* = 6.8 Hz, 3H), 1.48-1.52 (m, 1H), 1.64-1.68 (m, 1H), 2.05-2.14 (m, 2H), 2.18 (s, 3H), 2.21-2.25 (m, 1H), 2.31-2.43 (m, 3H), 2.44- 2.59 (m, 3H), 3.00-3.05 and 3.06-3.09 (m, 1H), 3.24 (br. s, 1H), 4.21-4.24 (m, 1H), 6.08 (s, 1H), 6.60 and 6.58 (s, 1H), 9.49 and 9.51 (d, *J* = 2.9 Hz, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 16.1, 17.4, 17.8, 22.7, 32.7, 34.3, 37.1, 37.2, 37.3, 37.4, 47.5, 63.17, 63.2, 133.1, 133.2, 138.0, 138.4, 150.4, 177.6, 177.7, 193.9, 193.95,

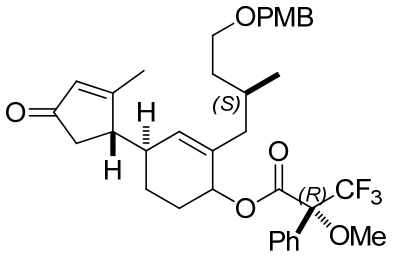
198.1, 198.2, 207.6, 207.7; HRMS(TOF MS ES+) *m/z* 353.0760 (calcd for $C_{17}H_{22}O_3Br$ 353.0752).



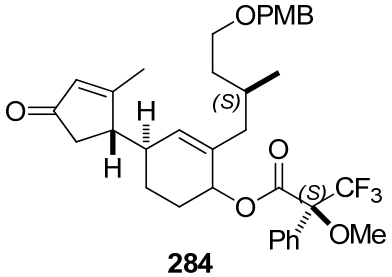
282

Allylic alcohol 282. To a stirred solution of enone **248** (50.0 mg, 0.130 mmol) in dichloromethane (1.30 mL) at -78 °C was added cerium(III) chloride heptahydrate solution in methanol (0.390 mmol, 1.00 mL, 0.4M) followed by sodium borohydride (0.140 mmol, 5.40 mg). The mixture was stirred for 2 h and poured into saturated aqueous sodium bicarbonate (10 mL). The aqueous phase was extracted with dichloromethane (3 x 10 mL) and the combined extracts were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure to afford **282** (54.0 mg, 99 %, d.r. 10:1) as a colorless oil: $[\alpha]_D^{28}$ +11.3 (c 0.31 $CHCl_3$); IR (neat) 3418, 2927, 2858, 1706, 1679, 1615, 1585, 1513, 1454, 1376, 1302, 1248, 1180, 1091, 1033, 822, 664 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 0.84 (d, *J* = 6.6 Hz, 3H), 0.98-1.03 (m, 1H), 1.35-1.39 (m, 1H), 1.47-1.52 (m, 1H), 1.54-1.61 (m, 3H), 1.81-1.86 (m, 1H), 2.07-2.14 (m, 5H), 2.34 (dd, *J* = 19.7, 6.7 Hz, 1H), 2.63 (d, *J* = 14.0, 1H), 2.73 (br. s, 1H), 2.98 (br. s, 1H), 3.49-3.53 (m, 1H), 3.56-3.59 (m, 1H), 3.84 (s, 3H), 4.17 (br. s, 1H), 4.46 (dd, *J* = 20.5, 11.6 Hz, 2H), 5.25 (s, 1H), 5.99 (t, *J* = 1.4 Hz, 1H), 6.91 (d, *J* = 8.8 Hz, 2H), 7.29 (d, *J* = 8.9 Hz, 2H); ^{13}C NMR (175 δ MHz, $CDCl_3$) δ 17.5, 19.7, 20.9, 27.4, 31.7, 36.5, 36.9, 37.7, 40.4, 48.4, 55.3, 67.7, 67.9, 72.7, 113.9,

128.2, 129.6, 130.5, 132.3, 142.3, 159.6, 179.7, 209.3; HRMS (TOF MS ES+) *m/z* 421.2378 (calculated for $C_{25}H_{34}O_4Na$ 421.2359).



283



284

Mosher Esters 283 and 284. To a stirred solution of allylic alcohol **282** (11.0 mg, 27.0 μmol) in dichloromethane (0.25 mL) at -78 °C were added cerium(III) chloride heptahydrate solution in methanol (0.4M, 200 μL) and sodium borohydride (1.10 mg, 30.0 μmol). The mixture was stirred for 2 h and the reaction was quenched with saturated aqueous sodium bicarbonate (10 mL) at -78 °C. The aqueous phase was extracted with dichloromethane (3 x 5 mL) and the combined extracts were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure to give crude alcohol **282** which was used in the next step without purification.

To a stirred solution of the crude alcohol, 4-dimethylaminopyridine (5.00 mg, 36.0 μmol) and triethylamine (8.40 μL, 60 μmmol) in dichloromethane (0.3 mL) at room temperature was added (*R*)-(−)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride. The reaction mixture was stirred for 6 h and the reaction was quenched with saturated aqueous sodium bicarbonate (10 mL). The aqueous phase was extracted with dichloromethane (3 x 5 mL) and the combined extracts were dried with anhydrous

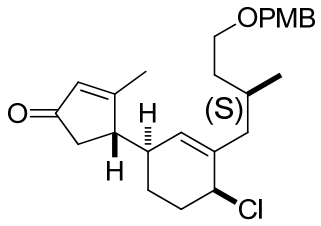
sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (30 % ethyl acetate in hexanes) to give (S)-α-methoxy-α-(trifluoromethyl)phenyl acetate **284** (6.00 mg, 35 % for two steps) as an oil.

Under the same conditions, reaction of **282** with (S)-(+)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride was run to give (*R*)-α-methoxy-α-(trifluoromethyl)phenyl acetate **283** (7.00 mg, 41 % for two steps).

283: $[\alpha]_D^{28}$ +40.0 (c 0.50 $CHCl_3$); IR (neat) 2927, 2849, 1742, 1709, 1619, 1585, 1513, 1452, 1379, 1248, 1169, 1120, 1018, 995, 908, 847, 766, 719, 698, 664 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 0.79 (d, *J* = 6.5 Hz, 3H), 1.05-1.09 (m, 1H), 1.33-1.41 (m, 2H), 1.48-1.54 (m, 1H), 1.59-1.65 (m, 2H), 1.65-1.71 (m, 1H), 2.06 (dd, *J* = 18.8, 1.6 Hz, 1H), 2.09 (s, 3H), 2.24 (d, *J* = 13.2 Hz, 1H), 2.27-2.31 (m, 1H), 2.35 (dd, *J* = 18.7, 6.7 Hz, 1H), 2.72 (s, 1H), 2.96 (s, 1H), 3.39-3.44 (m, 1H), 3.45-3.48 (m, 1H), 3.51 (s, 3H), 3.83 (s, 3H), 4.43 (dd, *J* = 27.8, 10.3 Hz, 2H), 5.43 (s, 1H), 5.49 (s, 1H), 6.00 (s, 1H), 6.90 (d, *J* = 9.8 Hz, 2H), 7.27 (d, *J* = 9.8 Hz, 2H), 7.40-7.44 (m, 3H), 7.51-7.54 (m, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 17.5, 18.7, 20.6, 27.3, 27.6, 36.0, 37.6, 41.4, 47.9, 55.3, 55.5, 68.3, 72.2, 72.3, 113.8, 127.5, 128.8, 129.3, 129.6, 130.7, 132.0, 132.6, 136.4, 159.1, 166.6, 178.9, 208.5; HRMS (TOF MS ES+): *m/z* 615.2938 (calculated for $C_{35}H_{42}O_6F_3$ 615.2933).

284: $[\alpha]_D^{28}$ -5.0 (c 0.40 $CHCl_3$); IR (neat) 2928, 2849, 1743, 1708, 1619, 1585, 1513, 1451, 1379, 1250, 1168, 1121, 1020, 994, 907, 847, 767, 718, 698, 664 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 0.73 (d, *J* = 6.5 Hz, 3H), 1.08-1.14 (m, 1H), 1.24-1.28 (m, 1H),

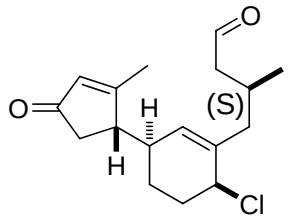
1.41-1.45 (m, 1H), 1.47-1.58 (m, 3H), 1.63-1.67 (m, 1H), 2.04-2.06 (m, 2H), 2.11 (s, 3H), 2.33-2.38 (m, 2H), 2.76 (s, 1H), 2.96 (s, 1H), 3.37-3.41 (m, 1H), 3.41-3.45 (m, 1H), 3.56 (s, 3H), 3.84 (s, 3H), 4.42 (dd, *J* = 24.2, 11.5 Hz, 2H), 5.14 (s, 1H), 5.52 (s, 1H), 6.02 (s, 1H), 6.91 (d, *J* = 9.8 Hz, 2H), 7.28 (d, *J* = 9.8 Hz, 2H), 7.39 -7.43 (m, 3H), 7.50-7.57 (m, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 17.5, 18.7, 27.4, 28.1, 36.1, 37.1, 37.6, 41.0, 48.0, 55.3, 68.2, 72.6, 73.2, 113.7, 127.11, 128.5, 129.3, 129.6, 130.7, 131.6, 132.4, 132.6, 136.7, 159.1, 178.8, 207.0, 208.5; HRMS (TOF MS ES+): *m/z* 615.2941 (calculated for $C_{35}H_{42}O_6F_3$ 615.2933).



291

Allyllic Chloride 291. To a stirred solution of allylic alcohol **285** (3.50 mg, 10.0 μmol) in dichloromethane (100 μL) at room temperature were added triethylamine (5.50 μL, 40.0 μmol,) and tosyl chloride (3.80 mg, 20.0 μmmol). The mixture was stirred for 5 h at room temperature and the reaction was quenched with saturated aqueous sodium bicarbonate (5 mL). The aqueous phase was extracted with dichloromethane (3 x 5 mL) and the combined extracts were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (30 % ethyl acetate in hexanes) to give **291** (3.50 mg, 83 %) as an oil: $[\alpha]_D^{28}$ -7.0 (c 0.10 $CHCl_3$); IR (neat) 2956, 2924, 2844,

1707, 1684, 1618, 1512, 1461, 1435, 1373, 1301, 1247, 1176, 1094, 1033 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 0.97 (d, *J* = 6.5 Hz, 3H), 1.24-1.29 (m, 2H), 1.42-1.51 (m, 1H), 1.65-1.70 (m, 1H), 1.84-1.88 (m, 1H), 1.89-1.94 (m, 1H), 1.85-1.98 (m, 1H), 2.10-2.15 (m, 5H), 2.22 (dd, *J* = 19.0, 1.9 Hz, 1H), 2.34 (dd, *J* = 19.0, 6.6 Hz, 1H), 2.72 (t, *J* = 4.5 Hz, 1H), 2.93-2.95 (br. s, 1H), 3.43-3.48 (m, 1H), 3.49-3.54 (m, 1H), 3.81 (s, 3H), 4.43-4.47 (m, 3H), 5.36 (s, 1H), 6.01 (t, *J* = 1.4 Hz, 1H), 6.90 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.8 Hz, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 16.5, 17.4, 20.2, 28.1, 31.5, 35.8, 36.4, 37.7, 42.9 47.8, 55.3, 57.4, 68.2, 72.7, 113.7, 128.4, 129.3, 130.4, 130.7, 132.6, 138.3, 159.1, 178.8, 208.9; HRMS (TOF MS ES+) *m/z* 439.2031 (calculated for $C_{25}H_{33}O_3NaCl$ 439.2016).

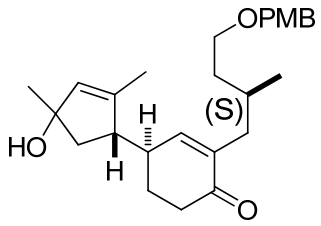


292

Aldehyde 292. To a stirred solution of allylic chloride **291** (8.00 mg, 20.0 μmol) in a mixture of dichloromethane (0.2 mL) and aqueous disodium hydrogen phosphate-potassium dihydrogen phosphate (50 μL) at 0°C was added 2,3-dichloro-5,6-dicyanobenzoquinone (5.30 mg, 23.0 μmol). The mixture was stirred for 50 min and the reaction was quenched with saturated aqueous sodium bicarbonate (5 mL). The aqueous phase was extracted with dichloromethane (3 x 10 mL) and the combined extracts were dried with anhydrous sodium sulfate. The solvent was evaporated under

reduced pressure to give crude alcohol which was used in the next step without purification.

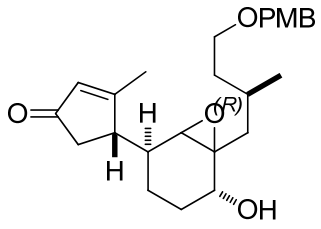
To a solution of crude alcohol in dichloromethane (0.2 mL) at 0 °C were added sodium bicarbonate (25.0 mg, 300 μmol) and Dess-Martin reagent (13.0 mg, 30.0 μmol). The reaction mixture was stirred at room temperature for 1h and the reaction was quenched with saturated aqueous sodium bicarbonate (5 mL) and sodium thiosulfate (5 mL). The aqueous phase was extracted with dichloromethane (3 x 5 mL) and the combined extracts were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (30 % ethyl acetate in hexane) to give pure **292** (4.40 mg, 75 %): $[\alpha]_D^{28}$ -5.8 (c 0.08 $CHCl_3$); IR (neat) 2960, 2924, 2863, 2851, 1718, 1709, 1684, 1619, 1462, 1437, 1378, 1313, 1259, 1181, 1112.cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 1.04 (d, *J* = 6.5 Hz, 3H), 1.26-1.30 (m, 1H), 1.46-1.50 (m, 1H), 1.89-1.98 (m, 2H), 2.11-2.14 (m, 4H), 2.20-2.29 (m, 3H), 2.33-2.45 (m, 3H), 2.72-2.75 (m, 1H), 3.01-3.04 (br s, 1H), 4.46 (s, 1H), 5.38 (s, 1H), 6.02 (s, 1H), 9.72 (d, *J* = 1.5 Hz, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 16.6, 17.5, 21.0, 26.6, 31.4, 36.5, 37.7, 42.7, 48.0, 50.5, 56.9, 131.2, 133.8, 138.1, 178.6, 202.4, 208.6; HRMS(TOF MS ES+): *m/z* 295.1465 (Calculated for $C_{17}H_{24}O_2Cl$ 295.1465).



295

Alcohol 295. To a stirred solution of enone **248** (6.00 mg, 15.0 μmol) in ether (0.2 mL) at -78 °C was added methyllithium (11.0 μL, 17.6 μmol, 1.6M solution in ether) and the mixture was stirred for 15 min. The reaction was quenched with saturated aqueous ammonium chloride (5 mL) and the aqueous phase was extracted with dichloromethane (3 x 5 mL). The combined extracts were dried with anhydrous sodium sulfate, concentrated under reduced pressure and the residue was purified by chromatography on silica gel (50 % ethyl acetate in hexanes) to give **295** as a single diastereomer (1.20 mg, 20 %) along with recovered enone **248** (2.40 mg): $[\alpha]_D^{28}$ +17.5 (c 0.08, $CHCl_3$); IR (neat) 3428, 2960, 2924, 2852, 1712, 1672, 1612, 1513, 1461, 1377, 1302, 1248, 1172, 1097, 1034, 820, 664 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 0.84 (d, *J* = 6.7 Hz, 3H), 1.36-1.44 (m, 4H), 1.64-1.69 (m, 2H), 1.72-1.77 (m, 6H), 1.93-.97 (m, 1H), 2.08-2.12 (m, 1H), 2.65 (dd, *J* = 14.0, 6.5 Hz, 1H), 2.31-2.38 (m, 1H), 2.55 (dt, *J* = 16.4, 3.3 Hz, 1H), 2.81-2.84 (m, 1H), 2.85-2.89 (m, 1H), 3.47-3.57 (m, 2H), 3.84 (s, 3H), 4.46 (dd, *J* = 20.9, 12.0 Hz, 2H), 5.45 (t, *J* = 1.6 Hz, 1H), 6.48 (s, 1H), 6.90 (d, *J* = 8.7 Hz, 2H), 7.29 (d, *J* = 8.7 Hz, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 15.1, 19.6, 23.9, 28.7, 29.2, 36.6, 37.5, 37.7, 37.8, 41.9, 50.9, 55.4,

68.6, 72.6, 81.5, 113.6, 129.3, 130.7, 134.7, 138.8, 142.3, 150.5, 159.3, 199.5; HRMS (CI+) *m/z* 412.2621 (calculated for $C_{26}H_{36}O_4$ 412.2614).

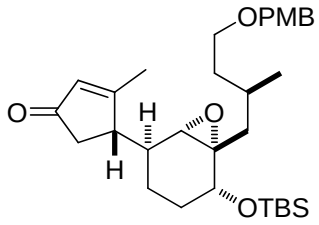


298

Epoxide 298. To a stirred solution of enone **248** (8.00 mg, 20.0 μmol) in dichloromethane (0.2 mL) at -78 °C was added a solution of cerium(III) chloride heptahydrate in methanol (0.4M, 150 μL, 60.0 μmol) and sodium borohydride (0.800 mg, 22.0 μmol). The mixture was stirred for 1 h and the reaction was quenched with saturated aqueous sodium bicarbonate (5 mL). The aqueous phase was extracted with dichloromethane (3 x 10 mL) and the combined extracts were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure to give crude alcohol **285** which was used in the next step without purification.

To a stirred solution of crude alcohol **285** in dichloroethane (1 mL) was added *m*-chloroperoxybenzoic acid solution in dichloroethane (0.5M, 40.0 μmol, 80.0 μL) and **299** (1.00 mg, 20.0 μmol). The reaction mixture was heated at 90°C for 2.5 h and then cooled to room temperature. Another portion of *m*-chloroperoxybenzoic acid solution in dichloroethane (0.5M, 40.0 μmol, 80.0 μL) was added and the reaction mixture was refluxed for 3.5 h. The reaction was quenched with saturated aqueous sodium thiosulfate (5 mL) and sodium bicarbonate (5 mL). The aqueous phase was extracted

with dichloromethane (3 x 10 mL) and the combined extracts were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (50 % ethyl acetate in hexane) to give **298** (6.00 mg, 77 % for two steps): $[\alpha]_D^{28}$ +4.8 (c 0.23, $CHCl_3$); IR (neat) 3424, 2924, 2852, 1679, 1614, 1513, 1461, 1378, 1248, 1175, 1089, 1033, 939, 820 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 0.79 (ddd, *J* = 26.5, 14.1, 2.5 Hz, 1H), 0.96 (d, *J* = 6.5 Hz, 3H), 0.98-1.04 (m, 1H), 1.14-1.20 (m, 1H), 1.39 (ddd, *J* = 25.7, 12.2, 2.5, 1H), 1.53 (dt, *J* = 20.7, 6.8 Hz, 1H), 1.59-1.63 (m, 1H), 1.75-1.78 (m, 1H), 1.82-1.87 (m, 1H), 2.09 (s, 3H), 2.12 (dd, *J* = 18.8, 1.7 Hz, 1H), 2.34-2.38 (m, 2H), 2.47 (dd, *J* = 18.2, 6.8 Hz, 1H), 3.01 (d, *J* = 1.3 Hz, 1H), 3.05-3.07 (m, 1H), 3.50-3.57 (m, 2H), 3.83 (s, 3H), 3.86-3.90 (br. s, 1H), 4.45 (s, 2H), 6.01 (t, *J* = 1.3 Hz, 1H), 6.90 (d, *J* = 8.6 Hz, 2H), 7.28 (d, *J* = 8.6 Hz, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 17.3, 20.2, 20.9, 26.2, 27.5, 35.2, 37.8, 37.8, 39.4, 46.5, 55.3, 63.0, 66.1, 67.8, 69.1, 72.8, 113.7, 129.5, 130.5, 132.6, 159.5, 179.2, 208.2; HRMS (TOF MS ES+) *m/z* 437.2315 (437.2304 calculated for $C_{25}H_{34}O_5Na$).



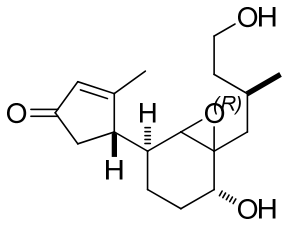
305

Epoxide 305. **From 298**. To a stirred solution of epoxide **298** (8.00 mg, 20.0 μmol) in dichloromethane (0.2 mL) at -78°C were added 2,6-lutidine (5.00 μL, 40.0 μmol) and

t-butyldimethylsilyl triflate (9.00 μL, 40.0 μmol). The mixture was stirred for 1 h and quenched with saturated aqueous sodium bicarbonate (5 mL). The aqueous phase was extracted with dichloromethane (3 x 10 mL) and the combined extracts were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (30 % ethyl acetate in hexanes) to give **305** (6.90 mg, 65 %) as a colorless oil: $[\alpha]_D^{28}$ +12.0 (c 0.15, $CHCl_3$); IR (neat) 2953, 2927, 2854, 1711, 1688, 1619, 1513, 1462, 1378, 1302, 1249, 1173, 1096, 1035, 941, 890, 837, 775, 664 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.08 (two s, 6H), 0.73-0.80 (m, 1H), 0.90-0.93 (m, 12 H), 1.05-1.15 (m, 2H), 1.38-1.46 (m, 1H), 1.14-1.57 (m, 2H), 1.62-1.75 (m, 2H), 2.07 (s, 3H), 2.08-2.21 (m, 2H), 2.30-2.37 (m, 1H), 2.44 (dd, *J* = 18.3, 6.8 Hz, 1H), 2.93 (s, 1H), 2.98 -3.04 (br s, 1H), 3.45-3.51 (m, 2H), 3.82 (s, 3H), 3.89 (dd, *J* = 10.7, 5.4 Hz, 1H), (s, 2H), 5.99 (s, 1H), 6.88 (d, *J* = 8.4 Hz, 2H), 7.26 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -4.6, -3.7, 17.2, 20.2, 20.33, 20.33, 25.9, 26.0, 27.6, 35.3, 37.9, 38.0, 39.8, 46.6, 64.6, 68.0, 70.5, 72.7, 113.7, 129.3, 130.8, 132.4, 132.5, 159.3, 179.3, 208.1; HRMS (TOF MS ES+) *m/z* 551.3162 (551.3169 calculated for $C_{31}H_{48}O_5NaSi$).

Epoxide 305. **From 306**. To a stirred solution of *t*-butyldimethylsilyl ether **306** (5.50 mg, 11.0 μmol) in dichloromethane (0.1 mL) at 0 °C were added sodium bicarbonate (14.0 mg, 200 μmol) and *m*-chloroperoxybenzoic acid (2.80 mg, 16.0 μmol). The mixture was stirred for 4 h at room temperature and the reaction was quenched with saturated aqueous sodium bicarbonate (5 mL) and sodium thiosulfate (5 mL). The

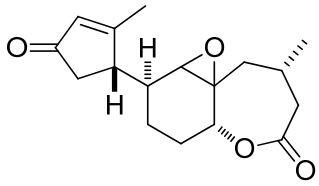
aqueous phase was extracted with dichloromethane (3 x 5 mL) and the combined extracts were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (30 % ethyl acetate, 2 % triethylamine in hexanes) to afford **305** (2.30 mg, 40 %) as a colorless oil.



300

Diol 300. **From 298**. To a stirred solution of epoxide **298** (4.10 mg, 10.0 μmol) in a mixture of dichloromethane (0.15 mL) and aqueous disodium hydrogen phosphate-potassium dihydrogen phosphate (30 μL) at 0 °C was added 2,3-dichloro-5,6-dicyanobenzoquinone (2.70 mg, 12.0 μmol). The mixture was stirred for 1 h at the same temperature and the reaction was quenched with saturated aqueous sodium bicarbonate (5 mL). The aqueous phase was extracted with dichloromethane (3 x 10 mL) and the combined extracts were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (99% ethyl acetate, 1 % triethylamine in hexanes) to afford **300** (2.00 mg, 70 %) as a colorless oil: $[\alpha]_D^{28}$ +6.0 (c 0.10, $CHCl_3$); IR (neat) 3363, 2953, 2625, 2854, 1728, 1681, 1617, 1460, 1378, 1261, 1120, 1070, 799, 664; cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 0.79 -0.85 (m, 1H), 0.97 (dd, *J* = 14.2, 10.0 Hz, 1H), 1.00 (d, J= 6.8 Hz, 3H), 1.19-1.23 (m, 1H), 1.42 (ddd, *J* = 26.0, 13.0, 2.7 Hz,

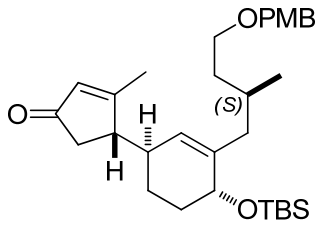
1H), 1.55-1.59 (m, 2H), 1.78-1.82 (m, 1H), 1.92-1.97 (m, 1H), 2.13 (s, 3H), 2.16 (dd, J = 18.3, 1.5 Hz, 1H), 3.95-3.98 (m, 1H), 2.43 (dd, J = 14.3, 3.6 Hz, 1H), 2.51 (dd, J = 18.2, 7.4 Hz, 1H), 3.00 (s, 1H), 3.71 (s, 1H), 3.72-3.82 (m, 2H), 3.95-3.98 (m, 1H), 6.03 (s, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 17.2, 20.3, 21.1, 25.6, 27.4, 35.2, 37.8, 39.3, 40.0, 46.7, 60.7, 63.0, 66.4, 69.0, 132.6, 179.0, 208.2; HRMS (CI+) *m/z* 295.1902 (295.1909 calculated for $C_{17}H_{27}O_4$).



304

Lactone 304. To a stirred solution of allylic epoxide **300** (3.00 mg, 10.0 μmol) in dichloromethane (0.1 mL) at 0 °C was added 2,2,6,6-tetramethylpiperidine 1-oxyl (500 μg, 3.00 μmol) and (bisacetoxyiodo)benzene (3.60 mg, 11.0 μmol). The mixture was stirred at room temperature for 1 h and the reaction was quenched with saturated aqueous sodium bicarbonate (5 mL) and sodium thiosulfate (5 mL). The aqueous phase was extracted with dichloromethane (3 x 5 mL) and the combined extracts were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (80 % ethyl acetate, 2 % triethylamine in hexanes) to give **304** (1.60 mg, 55 %) as a colorless oil: $[\alpha]_D^{28}$ +20.9 (c 0.11, $CHCl_3$); IR (neat) 2924, 2850, 1730, 1690, 1620, 1461, 1379, 1217, 1105, 1037, 893, 739, 704, 664 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 0.74-0.81

(m, 1H), 1.18-1.21 (m, 4H), 1.49-1.53 (m, 1H), 1.61-1.65 (m, 1H), 1.86-1.91 (m, 1H), 2.05 (dd, *J* = 18.5, 1.6 Hz, 1H), 2.14 (s, 3H), 2.29-2.35 (m, 4H), 2.54 (dd, *J* = 18.5, 7.2 Hz, 1H), 2.77 (d, *J* = 1.6 Hz, 1H), 2.79 (dd, *J* = 6.6, 1.5 Hz, 1H), 2.95 (dd, *J* = 14.3, 2.0 Hz, 1H), 3.17 (br. s, 1H), 4.58 (dd, *J* = 10.4, 6.0 Hz, 1H), 6.06 (t, *J* = 1.4 Hz, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 17.3, 18.2, 20.1, 25.0, 26.5, 34.0, 37.8, 40.6, 43.3, 46.6, 58.2, 64.0, 76.9, 132.8, 172.9, 178.8, 208.0; HRMS (TOF MS ES+) *m/z* 291.1582 (291.1572 calculated for $C_{15}H_{24}O_4Na$).

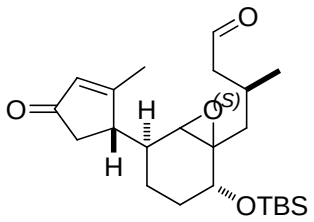


306

t-Butyldimethylsilyl Ether 306. To a stirred solution of enone **248** (12.3 mg, 30.0 μmol) in dichloromethane (0.3 mL) at -78 °C was added a solution of cerium(III) chloride heptahydrate in methanol (0.4M, 250 μL, 100 μmol) and sodium borohydride (1.30 mg, 33.0 μmol). The mixture was stirred for 2 h and the reaction was quenched with saturated aqueous sodium bicarbonate (5 mL). The aqueous phase was extracted with dichloromethane (3 x 10 mL) and the combined extracts were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure to give crude alcohol **285** which was used in the next step without purification.

To a stirred solution of crude alcohol **285** in dichloromethane (0.3 mL) at -78 °C were added 2,6-lutidine (7.5 0μL, 65.0 μmol) and *t*-butyldimethylsilyl triflate (15.0 μL, 65.0

μmol). The mixture was stirred for 30 min and the reaction was quenched with saturated aqueous sodium bicarbonate (5 mL). The aqueous phase was extracted with dichloromethane (3 x 10 mL) and the combined extracts were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (30 % ethyl acetate in hexanes) to furnish **306** (10.0 mg, 65 %) as a colorless oil: $[\alpha]_D^{28}$ +16.7 (c 0.37, $CHCl_3$); IR (neat) 2949, 2927, 2855, 1709, 1688, 1619, 1513, 1462, 1377, 1301, 1248, 1181, 1086, 1037, 920, 836, 775, 664 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.08 (s, 6H), 0.82 (d, *J* = 6.5 Hz, 3H), 0.90 (s, 9H), 0.94-1.06 (m, 1H), 1.30-1.35 (m, 1H), 1.37-1.44 (m, 1H), 1.49-1.52 (m, 1H), 1.58-1.63 (m, 1H), 1.69-1.75 (m, 2H), 1.98-2.04 (m, 1H), 2.08-2.12 (m, 4H), 2.32 (dd, *J* = 19.0, 6.3 Hz, 1H), 2.45 (d, *J* = 12.7 Hz, 1H), 2.67-2.74 (br s, 1H), 2.92-2.96 (br s, 1H), 3.44-3.55 (m, 2H), 3.82 (s, 3H), 4.11-4.15 (br s, 1H), 4.44 (d, *J* = 4.0 Hz, 2H), 5.21 (s, 1H), 5.98 (s, 1H), 6.89 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.0, -3.7, 17.3, 18.1, 18.9, 21.0, 25.9, 27.6, 32.8, 36.3, 37.5, 37.8, 41.4, 48.3, 55.4, 68.5, 68.9, 72.6, 113.6, 128.0, 129.2, 130.9, 132.3, 142.1, 159.1, 179.6, 209.1; HRMS (CI+) *m/z* 513.3403 (calculated for $C_{31}H_{49}O_4Si$ 513.3400).

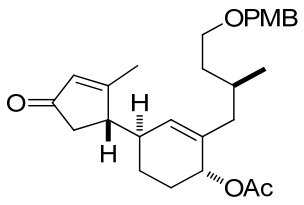


307

Aldehyde 307. To a stirred solution of epoxide **305** (5.00 mg, 9.40 μmol) in a mixture of dichloromethane (0.1 mL) and aqueous disodium hydrogen phosphate-potassium dihydrogen phosphate (30 μL) at 0°C was added 2,3-dichloro-5,6-dicyanobenzoquinone (2.60 mg, 11.0 μmol). The mixture was stirred for 4 h at 0 °C and the reaction was quenched with saturated aqueous sodium bicarbonate (5 mL). The aqueous phase was extracted with dichloromethane (3 x 5 mL) and the combined extracts were dried with anhydrous sodium sulfate and concentrated under reduced pressure to give crude alcohol which was used in the next step without purification.

To a stirred solution of the crude alcohol in dichloromethane (0.1 mL) at 0 °C were added sodium bicarbonate (12.0 mg, 140 μmol) and Dess-Martin reagent (6.00 mg, 14.0 μmol). The mixture was stirred for 1 h at room temperature and the reaction was quenched with saturated aqueous sodium thiosulfate (5 mL). The aqueous phase was extracted with dichloromethane (3 x 5 mL) and the combined extracts were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (20 % ethyl acetate, 2 % triethylamine in hexanes) to give **307** (2.20 mg, 57 % for two steps) as a colorless oil: $[\alpha]_D^{28}$ +20.0 (c 0.15 $CHCl_3$); IR (neat) 2953, 2926, 2854, 1716, 1684, 1620, 1553, 1462, 1379, 1312, 1257, 1183, 1098, 942, 916, 837, 775, 700, 664 cm^{-1}; ^1H NMR (700

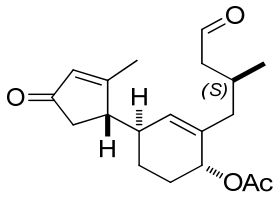
MHz, $CDCl_3$) δ 0.57-0.13 (a series of s, 6H), 0.75-0.81 (m, 1H), 0.89-0.90 (a series of s, 12H), 1.17-1.44 (m, 1H), 1.18-1.21 (m, 1H), 1.49-1.53 (m, 1H), 1.58-1.1.64 (m, 1H), 2.10 (s, 3H), 2.12-2.16 (m, 1H), 2.17-2.22 (m, 1H), 2.32-2.43 (m, 3H), 2.51 (dd, *J* = 18.2, 8.0 Hz, 1H), 2.90 (s, 1H), 3.16 (s, 1H), 3.94 (dd, *J* = 11.0, 5.3 Hz, 1H), 6.02 (s, 1H), 9.77 (t, *J* = 1.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -4.6, -3.6, 1.0, 17.2, 20.2, 20.7, 24.2, 25.8, 27.5, 35.0, 37.8, 39.3, 46.5, 51.7, 62.4, 64.7, 70.6, 132.6, 178.9, 201.6, 207.9; HRMS (CI +) *m/z* 407.2610 (407.2618 calculated for $C_{23}H_{39}O_4Si$).



312

Acetate 312: To a stirred solution of alcohol **285** (11.0 mg, 27.0 μmol), 4-dimethylaminopyridine (5.00 mg, 40.0 μmol,) and triethylamine (80.0 μmol, 12.0 μL) in dichloromethane (0.3 mL) at 0°C was added acetic anhydride (40.0 μmol, 4.00 μL) and the mixture was stirred at room temperature for 15 min. The reaction was quenched with saturated aqueous solution of sodium bicarbonate (5 mL). The aqueous phase was extracted with dichloromethane (3 x 5 mL) and the combined extracts were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (20 % ethyl acetate in hexanes) to give **312** (8.20 mg, 70 %) as an oil: $[\alpha]_D^{28}$ +17.2 (c 0.39,

$CHCl_3$); IR (neat) 2953, 2923, 2866, 1731, 1707, 1684, 1616, 1454, 1371, 1302, 1243, 1181, 1094, 1029, 822, 664 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 0.82 (d, *J* = 6.1 Hz, 3H), 1.04-1.12 (m, 1H), 1.37-1.42 (m, 1H), 1.45-1.54 (m, 2H), 1.55-1.62 (m, 2H), 1.63-1.69 (m, 1H), 2.03 (s, 3H), 2.07 (dd, *J* = 18.7, 1.9 Hz, 1H), 2.11 (s, 3H), 2.16-2.21 (m, 1H), 2.33-2.37 (m, 2H), 2.72-2.76 (m, 1H), 2.97-3.00 (br. s, 1H), 3.44-3.51 (m, 2H), 3.84 (s, 3H), 4.43 (dd, *J* = 20.5, 11.5 Hz, 2H), 5.29-5.32 (m, 1H), 5.39 (s, 1H), 6.00 (t, *J* = 1.4 Hz, 1H), 6.90 (d, *J* = 8.7 Hz, 2H), 7.28 (d, *J* = 8.7 Hz, 2H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 17.5, 19.4, 20.6, 21.8, 27.6, 28.4, 36.2, 37.4, 37.7, 40.9, 48.2, 55.4, 68.4, 70.4, 72.7, 130.6, 132.5, 138.1, 170.7, 179.1, 208.6; HRMS (TOF MS ES+): *m/z* 441.2647 calculated for $C_{27}H_{37}O_5$ 441.2641).



311

Aldehyde 311: To a stirred solution of acetate **312** (6.00 mg, 14.0 μmol) in a mixture of dichloromethane (0.14 mL) and aqueous disodium hydrogen phosphate-potassium dihydrogen phosphate (50 μL) at 0°C was added 2,3-dichloro-5,6-dicyanobenzoquinone (3.70 mg, 16.0 μmol). The reaction mixture was stirred for 40 min and the reaction was quenched with saturated aqueous sodium bicarbonate (5 mL). The aqueous phase was extracted with dichloromethane (3 x 5 mL) and the combined extracts were dried with anhydrous sodium sulfate. The solvent was

evaporated under reduced pressure to give crude alcohol which was used in the next step without purification.

To a solution of crude alcohol in dichloromethane (0.15 mL) at 0 °C was added sodium bicarbonate (0.210 mmol, 18.0 mg) and Dess-Martin reagent (21.0 μmol, 9.00 mg). The mixture was stirred at room temperature for 30 min and the reaction was quenched with saturated aqueous sodium bicarbonate (5 mL) and sodium thiosulfate (5 mL). The aqueous phase was extracted with dichloromethane (3 x 5 mL) and the combined extracts were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the residue was purified by chromatography on silica gel (30 % ethyl acetate in hexanes) to give **311** (3.80 mg, 86% for two steps) as an oi: $[\alpha]_D^{28}$ +37.5 (c 0.12, $CHCl_3$); IR (neat) 2956, 2924, 2853, 1730, 1684, 1618, 1456, 1374, 1241, 1077, 1027, 802, 664 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 0.91 (d, *J* = 6.5 Hz, 3H), 1.07-1.11 (m, 1H), 1.41-1.44 (m, 1H), 1.50-1.56 (m, 1H), 1.60-1.65 (m, 1H), 2.06 (dd, *J* = 18.9, 1.9 Hz, 1H), 2.12 (s, 3H), 2.15 (s, 3H), 2.15 -2.20 (m, 2H), 2.34-2.39 (m, 4H), 2.75-2.79 (br. s, 1H), 3.01-3.04 (br. s, 1H), 5.35-5.39 (m, 1H), 5.41 (s, 1H), 6.01 (t, *J* = 1.4 Hz, 1H), 9.75 (t, *J* = 1.8 Hz, 1H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 17.5, 19.7, 20.7, 21.3, 25.4, 28.4, 36.2, 37.6, 40.6, 48.1, 51.4, 69.9, 131.3, 132.6, 137.5, 170.9, 178.9, 202.1, 208.4; HRMS (EI+) *m/z* 318.1822 (calculated for $C_{19}H_{26}O_4$ 318.1831).

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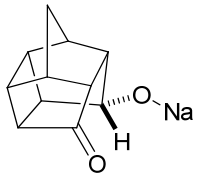
APPENDIX

APPENDIX I
Computational data

Ground state structures were optimized and transition states were verified using Jaguar, version 6.5, release 112 and Jaguar, version 7.8, release 109 available in Maestro 7.0 and 9.2 suite respectively. The solvation free energies were estimated by performing single point energy calculations on optimized gas phase structures using Poisson-Boltzmann solver available in Jaguar. The conformational search was performed on MacroModel available in Maestro at MMF4 force field level of study. Different conformers were scanned and optimized at DFT/B3LYP level of theory using 6-31G* as a basic set in Spartan 6.0 and Jaguar. The box where calculations were carried out was running Slackware (GNU/Linux). The calculations were done remotely via secure shell tunneled vnc platform.

APPENDIX Ia: Computational data for the intramolecular hydride shift which interconverts sodium alkoxides **189** and **191**

Table 4. Coordinates for **189**



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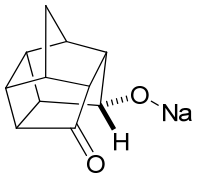
	Coordinates (angstroms)		
atom	**x**	**y**	**z**
H1	1.4976384037	1.0123929120	-1.2529654847
C2	1.3297942164	0.8897684059	-0.1785804782
C3	1.3944453615	2.6370185046	1.5421462837
C4	-0.1337223292	0.7285971507	1.7072736078
C5	0.8658219013	1.5751283987	2.5627882543
C6	-0.0549064422	1.4051378447	0.3086823365
C7	2.3485108363	1.7640955081	0.6738610195
H8	1.8701753309	3.5128786111	1.9938281218
H9	0.5252980452	1.9820210137	3.5181967343
H10	3.0660094959	2.3193772846	0.0660719650
H11	-1.1423706833	0.5746378612	2.1007888172
H12	-0.8803202220	1.1724610842	-0.3677266141
C13	0.1772859017	2.8875047628	0.6396854594
H14	0.4086407632	3.5010161244	-0.2400746910
H15	-0.6613172778	3.3510912633	1.1764755628
C16	1.8820507405	0.3865165171	2.5873701692
H17	2.2000198431	-0.0336988750	3.5427397554
C18	3.0255364892	0.8794498221	1.7170000610
C19	0.8773175645	-0.4626863540	1.7127039814
H20	0.5590311923	-1.4103622968	2.1550977921
C21	1.3366660140	-0.6085122188	0.2409626576
H22	2.3732897862	-1.0088775672	0.2084950657
O23	4.2139320847	0.6692943165	1.8532697594
O24	0.4693167935	-1.3552967970	-0.5047939213
Na25	-0.6826126719	-2.5186162161	-1.5528967409

Table 5. Thermodynamic data for **189**



189

T = 298.15 K

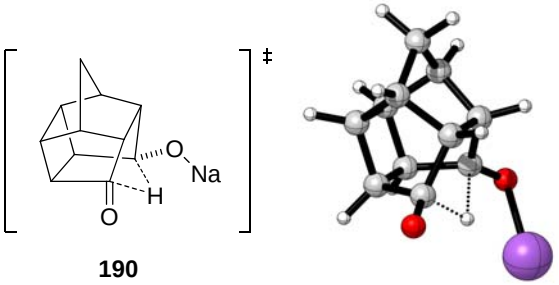
	U	**Cv**	**S**	**H**	**G**
trans.	0.889	2.981	41.755	1.481	-10.968
rot.	0.889	2.981	31.317	0.889	-8.448
vib.	4.474	35.325	27.793	4.474	-3.813
elec.	0.000	0.000	0.000	0.000	0.000
total	6.251	41.287	100.865	6.844	-23.229

Total internal energy, Utot (SCFE + ZPE + U): -738.295521 hartrees
Total enthalpy, Htot (Utot + pV): -738.294577 hartrees
Total Gibbs free energy, Gtot (Htot - T*S): -738.342501 hartrees

solvation energy

Hartrees	kcal/mol
-0.0623338	-39.1150

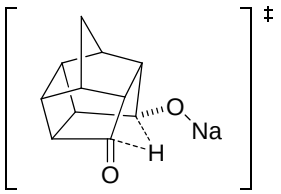
Table 6. Coordinates for **190**



190

	Coordinates (angstroms)		
atom	**x**	**y**	**z**
H1	0.5283462855	-0.0232232628	-2.5570898895
C2	0.2860989734	-0.0074681881	-1.4913519494
C3	0.9378208654	1.5885840024	0.2490452780
C4	-1.2355632531	0.4724327848	0.3117979466
C5	-0.0327153380	0.8617049581	1.2309495096
C6	-0.8122371894	1.0261039417	-1.0843464937
C7	1.4974802828	0.3876853305	-0.5629462575
H8	1.7052518588	2.2019901064	0.7269260072
H9	-0.2451231173	1.3971771253	2.1589531011
H10	2.4109507478	0.6010154814	-1.1226736155
H11	-2.2460337633	0.7343169996	0.6331885414
H12	-1.6252329674	1.1318261072	-1.8084094243
C13	-0.0167148287	2.2943448258	-0.7300933537
H14	0.4964180557	2.7385026544	-1.5916772435
H15	-0.6355485817	3.0683225427	-0.2575332461
C16	0.3869117927	-0.6434835080	1.3114301409
H17	0.4407300547	-1.1262748944	2.2885180341
C18	1.7292823894	-0.7032233126	0.5273707789
C19	-0.8108470507	-1.0390986313	0.3887101904
H20	-1.5280281711	-1.7764845164	0.7563235400
C21	-0.3035951575	-1.3333208513	-1.0146436328
H22	1.3484675484	-1.8716437884	-0.3237916661
O23	2.8280232050	-0.8347894573	1.0972140616
O24	-0.7257414677	-2.2486740118	-1.7702083280
Na25	0.9388711530	-3.5643222434	-1.4572702291

Table 7. Thermodynamic data for **190**



190

T = 298.15 K

	U	Cv	S	H	G
trans.	0.889	2.981	41.755	1.481	-10.968
rot.	0.889	2.981	30.986	0.889	-8.350
vib.	4.197	35.295	23.887	4.197	-2.925
elec.	0.000	0.000	0.000	0.000	0.000
total	5.974	41.257	96.628	6.567	-22.243

Total internal energy, Utot (SCFE + ZPE + U):-738.253107 hartrees
Total enthalpy, Htot (Utot + pV):-738.252163 hartrees
Total Gibbs free energy, Gtot (Htot - T*S):-738.298074 hartrees

solvation energy

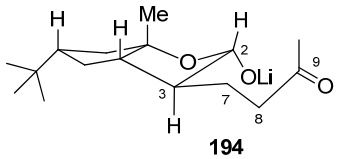
Hartrees	kcal/mol
-0.0637455	-40.0009

Table 8. Gas and solvent phase activation energies for **189→191**

	Gtot (gas) (hartrees)	**Solvation (hartrees)**	**Gtot (sol) (hartrees)**
190	-738.298074	-0.06374549	-738.3618195
189	-738.342501	-0.06233376	-738.4048348
	Gas phase	**DMSO**	
E_a (189→191) (kcal/mol)	27.98901	27.09962036	

APPENDIX Ib: Computational data for intramolecular hydride transfer in **194** and **197**

Table 9. Coordinates for **194**



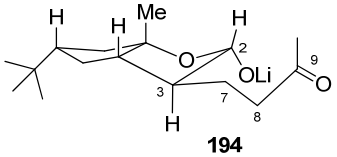
194

Coordinates (angstroms)

atom	x	y	z
C1	1.6708847573	-0.9356436300	-0.5051298390
C2	0.2653429309	-0.3843917843	-0.9538208140
C3	-0.5232001973	-1.5896316820	-1.5261336863
C4	0.5287439133	-2.7067190040	-1.7490169767
C5	1.5271776147	-2.4698066534	-0.5968537542
H6	0.3953273725	0.3860921307	-1.7261730771
H7	-1.2754775983	-1.9204003940	-0.7985065785
H8	-1.0621441533	-1.3390234535	-2.4464825861
H9	1.0535211303	-2.4695151076	-2.6884364914
H10	2.4900075844	-2.9697563864	-0.7474476244
H11	1.1167036776	-2.8200594947	0.3570499918
C12	-0.0161122233	-4.1544311278	-1.9285359453
C13	-0.9971713432	-4.1806191274	-3.1197151212
H14	-1.8892128038	-3.5748043333	-2.9244186005
H15	-1.3315359913	-5.2049217500	-3.3260137684
H16	-0.5235622741	-3.7954493093	-4.0320298227
C17	1.1605503941	-5.1001888198	-2.2493739819
H18	0.7982785557	-6.1150875241	-2.4552862566
H19	1.8683604495	-5.1638141020	-1.4157564840
H20	1.7136463874	-4.7585260007	-3.1336783014
C21	-0.7425316084	-4.6787474264	-0.6740042289
H22	-1.6035696693	-4.0558586079	-0.4061395326
H23	-0.0765086460	-4.7229407901	0.1943090874
H24	-1.1181150672	-5.6939906074	-0.8524106836
C25	2.8239955328	-0.4131287184	-1.3730352512
H26	2.8591426973	0.6820485494	-1.3528954868
H27	2.7214046405	-0.7298125336	-2.4192365663
H28	3.7792854782	-0.7895686619	-0.9905922624
O29	1.8647911399	-0.5244051981	0.8457958931
C30	-0.2828275637	0.2535297229	0.3327711486
H31	-0.7804195172	-0.5218755153	0.9326947654

C32	1.0059805506	0.6253073480	1.1174295163
C33	-1.2674360938	1.4057560276	0.0969041496
H34	-0.7294743474	2.2559916545	-0.3475233193
H35	-2.0103921438	1.1011938541	-0.6493685475
C36	-2.0454154486	1.8606143327	1.3832617931
H37	-1.9198705741	1.1128400230	2.1701406709
H38	-3.1149765433	1.9306372970	1.1455547863
C39	-1.6241258905	3.2090192140	1.9182596699
C40	-2.1134826747	4.4361693989	1.1865884661
H41	-2.0290304446	4.3090317657	0.1021454160
H42	-1.5635271613	5.3217275170	1.5102381852
H43	-3.1798122051	4.5778394323	1.4088755572
O44	-0.9305727779	3.3410746721	2.9309669847
H45	1.4757895093	1.5017580408	0.5989080842
O46	0.8606400678	0.8348713854	2.4246384803
LI47	0.2887491171	1.9987650557	3.4830027219

Table 10. Thermodynamic data for **194**



194

T = 298.15 K

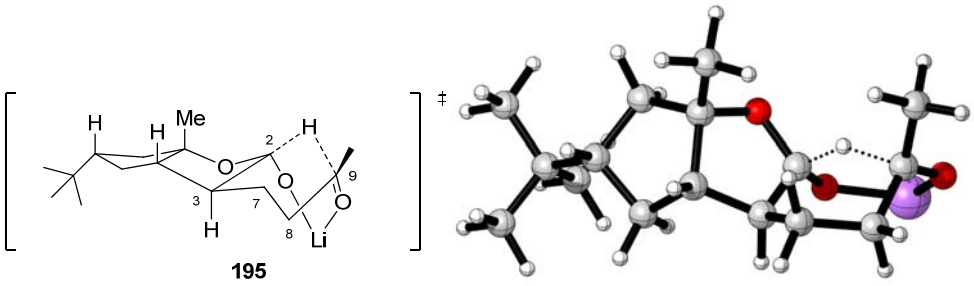
	U	**Cv**	**S**	**H**	**G**
trans.	0.889	2.981	42.725	1.481	-11.257
rot.	0.889	2.981	34.121	0.889	-9.284
vib.	11.806	77.433	76.972	11.806	-11.143
elec.	0.000	0.000	0.000	0.000	0.000
total	13.584	83.395	153.818	14.176	-31.684

Total internal energy, Utot (SCFE + ZPE + U): -858.801994 hartrees
Total enthalpy, Htot (Utot + pV): -858.801049 hartrees
Total Gibbs free energy, Gtot (Htot - T*S): -858.874133 hartrees

solvation energy

Hartrees	kcal/mol
-0.0404542	-25.3854

Table 11. Coordinates for **195**

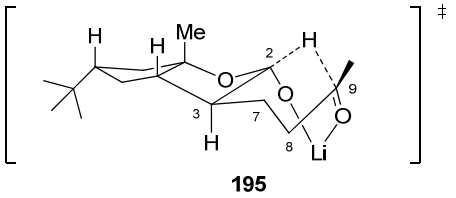


Coordinates (angstroms)

atom	x	y	z
H1	-1.0269396883	2.8167422452	1.3256369312
C2	-0.9505439180	1.7246670655	1.2999135026
C3	0.0377285567	1.2387593631	0.2043186012
C4	0.9452820931	0.1654616921	0.8900137515
C5	0.1922961585	-0.2004601606	2.1827244672
C6	-0.4363677502	1.1329296569	2.6345298111
H7	-1.9405933080	1.3317521390	1.0499952207
H8	1.9203236837	0.5994688296	1.1460903242
H9	0.8516005025	-0.6522285670	2.9315583997
H10	-0.5932155225	-0.9310084682	1.9512258957
H11	0.3915328214	1.7758105089	2.9776205219
C12	-1.4528763913	1.0822472670	3.8122614127
C13	-1.9777739116	2.5079234199	4.0844798746
H14	-1.1516375857	3.2064607729	4.2703642791
H15	-2.6278728509	2.5199299371	4.9678368164
H16	-2.5599114214	2.8942072909	3.2404799886
C17	-0.7311598850	0.5811305868	5.0809958130
H18	-1.4067410428	0.6011408739	5.9449697706
H19	0.1337217154	1.2127647434	5.3213198543
H20	-0.3735825010	-0.4482417398	4.9658304444
C21	-2.6507265445	0.1557106100	3.5236093349
H22	-3.3540258962	0.1771581718	4.3652437541
H23	-2.3388952539	-0.8853018639	3.3847836293
H24	-3.2028439014	0.4626035673	2.6284895683
C25	0.7896421807	2.3933437340	-0.4600874374
H26	1.5220984687	2.0331880552	-1.1901564001
H27	1.3209057785	2.9920974690	0.2899652533
H28	0.0850143024	3.0478989433	-0.9847445106
C29	1.0836523532	-0.9659451994	-0.1405148782
H30	0.9453357488	-1.9500311031	0.3216782100
O31	-0.7063751945	0.5103808661	-0.7983786418

C32	-0.1279836053	-0.7368348039	-1.0995202662
C33	2.4197127989	-0.9594098591	-0.9111511712
H34	3.2141839958	-1.3677821619	-0.2747282606
H35	2.7119708019	0.0753315884	-1.1343067101
C36	2.3379519129	-1.7527830536	-2.2266931011
H37	2.0636599067	-2.7953848051	-2.0261338386
H38	3.3218652302	-1.7629971630	-2.7163841820
C39	1.3028996266	-1.1799419022	-3.2155185050
C40	1.7364752107	0.0520650797	-4.0078717246
H41	0.8644734486	0.5308202292	-4.4613124713
H42	2.4053333818	-0.2723818403	-4.8166987957
H43	2.2708148686	0.7836209488	-3.3930188203
H44	0.5098317034	-0.5314031764	-2.2058115391
O45	0.5031650217	-1.9971908142	-3.8031641285
O46	-0.9620412349	-1.6875284998	-1.3485153708
Li47	-0.8871978316	-2.6120382648	-2.8539180782

Table 12. Thermodynamic data **195**



195

T = 298.15 K

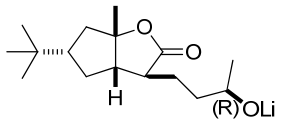
	U	Cv	S	H	G
trans.	0.889	2.981	42.725	1.481	-11.257
rot.	0.889	2.981	33.756	0.889	-9.175
vib.	10.978	75.339	67.839	10.978	-9.248
elec.	0.000	0.000	0.000	0.000	0.000
total	12.756	81.301	144.320	13.348	-29.681

Total internal energy, Utot (SCFE + ZPE + U): -858.792857 hartrees
Total enthalpy, Htot (Utot + pV): -858.791912 hartrees
Total Gibbs free energy, Gtot (Htot - T*S): -858.860483 hartrees

solvation energy

Hartrees	kcal/mol
-0.0347066	-21.7787

Table 13. Coordinates for **196**



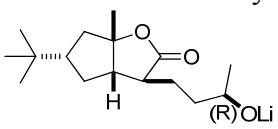
196

angstroms

atom	x	y	z
C1	0.1032729795	-2.3379472058	-1.1178002912
C2	-0.2179628794	-1.4575648440	0.1288882707
C3	1.1554304247	-0.9325857107	0.5899027473
C4	2.1248573342	-2.0904135318	0.2747875454
C5	1.6323066067	-2.5696912990	-1.1137596116
H6	-0.6638852540	-2.0707827275	0.9189766238
H7	1.4263198289	-0.0413298060	0.0080266718
H8	1.1479590917	-0.6396854949	1.6441840907
H9	1.9026619139	-2.8964628930	0.9931114860
H10	1.8824411782	-3.6153937119	-1.3167314848
H11	2.0734236603	-1.9689176105	-1.9156542937
C12	3.6489472872	-1.8045437813	0.4101806113
C13	4.4335411055	-3.0853212923	0.0543355831
H14	4.3030898191	-3.3647524333	-0.9972456756
H15	4.1098478137	-3.9336545540	0.6709627596
H16	5.5069996703	-2.9414866339	0.2259864643
C17	4.1234976577	-0.6572709968	-0.5038535169
H18	3.6356009560	0.2925576136	-0.2585074273
H19	3.9394668088	-0.8684265208	-1.5633736358
H20	5.2034784094	-0.5076249718	-0.3868125383
C21	3.9609731672	-1.4351619021	1.8757491422
H22	3.4713746663	-0.5015087906	2.1741286869
H23	5.0399362024	-1.3020696540	2.0193648432
H24	3.6296065606	-2.2239406650	2.5630837144
C25	-0.7242030569	-3.6085141893	-1.2587472196
H26	-0.4727544225	-4.3079720832	-0.4536051783
H27	-0.5179762172	-4.0976911017	-2.2164788044
H28	-1.7967761805	-3.3940868982	-1.2045983533
O29	-0.2378252618	-1.4668486573	-2.2628883342
C30	-1.2064166777	-0.3959628379	-0.3845934387
H31	-0.9710775677	0.6072109422	-0.0162863742
C32	-0.9388455965	-0.4000980326	-1.8798038702
C33	-2.7124417751	-0.6528191943	-0.0457488610
H34	-3.3267478844	-0.5514825920	-0.9493134561
H35	-2.8192187665	-1.6933443891	0.2860107926

C36	-3.2510187044	0.3141694749	1.0262631811
H37	-2.4693282280	0.4923811497	1.7808976565
H38	-4.0925159706	-0.1564166278	1.5538174272
C39	-3.7147808494	1.6675024199	0.4184409101
C40	-4.0374967814	2.6705834240	1.5380993885
H41	-4.7943584795	2.2885857170	2.2375611044
H42	-4.4100555317	3.6029295735	1.0994685472
H43	-3.1265577612	2.9065561042	2.1033207505
H44	-4.6817952086	1.4434781126	-0.0933149716
O45	-2.7954628075	2.1705919199	-0.4735961221
LI46	-2.1723499525	1.9686195399	-2.0168554452
O47	-1.2824429421	0.4454804560	-2.7044206809

Table 14. Thermodynamic data for **196**



196

T = 298.15 K

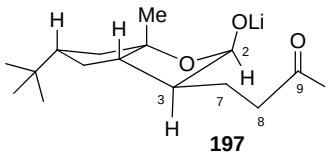
	U	**Cv**	**S**	**H**	**G**
trans.	0.889	2.981	42.725	1.481	-11.257
rot.	0.889	2.981	34.097	0.889	-9.277
vib.	11.444	76.641	72.174	11.444	-10.074
elec.	0.000	0.000	0.000	0.000	0.000
total	13.222	82.603	148.995	13.814	-30.609

Total internal energy, Utot (SCFE + ZPE + U):-858.825543 hartrees
Total enthalpy, Htot (Utot + pV): -858.824599 hartrees
Total Gibbs free energy, Gtot (Htot - T*S): -858.895391 hartrees

solvation energy

Hartrees	kcal/mol
-0.0308551	-19.3619

Table 15. Coordinates for **197**

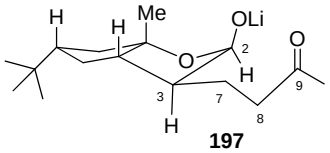


197

	angstroms		
atom	**x**	**y**	**z**
C1	0.3929265613	0.7102216410	0.3116928091
C2	0.3379771245	-0.4388184776	-0.7541246269
C3	1.6920532682	-1.1867726712	-0.6721185141
C4	2.6357134722	-0.2441877830	0.1174086130
C5	1.6764159588	0.4275699596	1.1224741585
H6	0.1943216167	-0.0134559997	-1.7548934280
H7	1.5646526264	-2.1321156866	-0.1278011396
H8	2.0915001390	-1.4425549743	-1.6598376848
H9	2.9682042912	0.5368466526	-0.5855193967
H10	2.0894498496	1.3344143430	1.5774686274
H11	1.4148161603	-0.2622106139	1.9335004344
C12	3.9382081835	-0.8752513629	0.6912342850
C13	4.7991378361	0.2369033386	1.3268607764
H14	5.7561210102	-0.1659555048	1.6813926050
H15	4.2961346260	0.6989609940	2.1833310454
H16	5.0202219557	1.0296640552	0.6007770326
C17	3.6590673131	-1.9534273312	1.7571981298
H18	3.0570018968	-2.7785677959	1.3597614599
H19	3.1336132337	-1.5413563228	2.6253827910
H20	4.6026940688	-2.3822094434	2.1169352465
C21	4.7429504779	-1.5117962224	-0.4615549175
H22	5.7109049954	-1.8827136940	-0.1021239644
H23	4.9411010023	-0.7818775468	-1.2570500885
H24	4.2100205736	-2.3581083389	-0.9094456814
C25	0.3977143776	2.1116377038	-0.3104880527
H26	0.3662435506	2.8697895919	0.4801181153
H27	-0.4875829960	2.2351229446	-0.9393488917
H28	1.2985978613	2.2820252429	-0.9156739371
O29	-0.7679937846	0.5482960657	1.1338774659
C30	-0.9181006149	-1.2401065587	-0.3546992647
H31	-0.6233045404	-1.9853982413	0.4004962255
C32	-1.7831904407	-0.1595283491	0.3743934665
C33	-1.5658079619	-1.9807114235	-1.5320365476
H34	-1.9120035631	-1.2562904838	-2.2801269706
H35	-0.7909786301	-2.5761765932	-2.0320827543

C36	-2.7116811051	-2.9429686019	-1.1678029365
H37	-2.5302439092	-3.4288933786	-0.1990249724
H38	-2.7458278244	-3.7783756143	-1.8883934018
C39	-4.1358256532	-2.4244256534	-1.1707330640
C40	-5.1665795628	-3.2846475655	-0.4776418930
H41	-5.1008215657	-3.0932165000	0.6021619702
H42	-4.9713773947	-4.3517585651	-0.6267941635
H43	-6.1718178011	-3.0278338974	-0.8172968824
O44	-4.4852940231	-1.3838063780	-1.7276960731
H45	-2.4098471401	-0.6174517829	1.1689601623
O46	-2.4918089001	0.6215721802	-0.4598612922
LI47	-3.7199531287	0.3278815382	-1.5683072989

Table 16. Thermodynamic data for **197**



197

T = 298.15 K

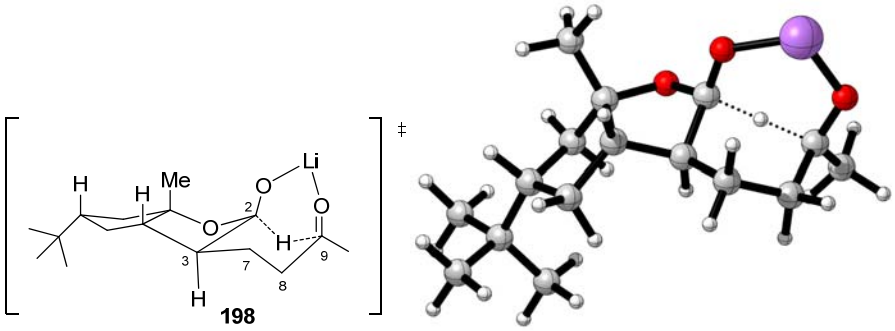
	U	**Cv**	**S**	**H**	**G**
trans.	0.889	2.981	42.725	1.481	-11.257
rot.	0.889	2.981	34.051	0.889	-9.264
vib.	11.729	77.307	76.063	11.729	-10.949
elec.	0.000	0.000	0.000	0.000	0.000
total	13.507	83.268	152.839	14.099	-31.470

Total internal energy, Utot (SCFE + ZPE + U): -858.803868 hartrees
Total enthalpy, Htot (Utot + pV): -858.802923 hartrees
Total Gibbs free energy, Gtot (Htot - T*S): -858.875542 hartrees

solvation energy

Hartrees	kcal/mol
-0.0385826	-24.2109

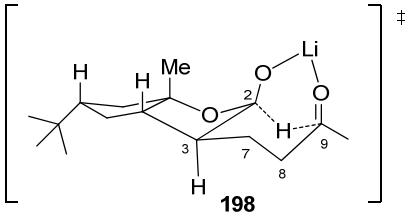
Table 17. Coordinates for **198**



	angstroms		
atom	**x**	**y**	**z**
H1	-1.8186460867	1.3977549319	1.2771152645
C2	-0.7326134772	1.4095958424	1.1378073106
C3	-0.2503594245	0.2579368630	0.2412785527
C4	1.1506728079	0.7528614024	-0.3048368917
C5	1.1943023396	2.2819259163	-0.0650815705
C6	-0.2208015106	2.6861987269	0.4350187130
H7	-0.2727600292	1.2928201457	2.1255037748
H8	1.2624270997	0.4981433000	-1.3646016975
H9	1.4783523595	2.8305091526	-0.9686403382
H10	1.9511338076	2.5177859437	0.6934284944
H11	-0.8468889914	2.8359829718	-0.4582646057
C12	-0.3131513578	4.0170755367	1.2390984241
C13	0.2435535545	5.1652372167	0.3710109962
H14	0.1151617026	6.1304736527	0.8757344172
H15	-0.2778884006	5.2228354057	-0.5931190374
H16	1.3125837329	5.0385518067	0.1666198959
C17	0.4718918164	3.9708703259	2.5648837661
H18	0.0933216059	3.1947661029	3.2389422857
H19	0.3834768478	4.9308537576	3.0878344950
H20	1.5405042818	3.7861599426	2.4053569033
C21	-1.7947383191	4.3158564421	1.5515687987
H22	-1.8986761719	5.2916191507	2.0415047660
H23	-2.2293416123	3.5628635192	2.2183549500
H24	-2.3965061919	4.3395060992	0.6341209592
C25	-1.2403919679	-0.1054593082	-0.8630993882
H26	-0.8243912084	-0.8961290423	-1.4950086652
H27	-1.4663669581	0.7634862480	-1.4936799091
H28	-2.1772334898	-0.4695724164	-0.4278354217
C29	2.0961462579	-0.0897264244	0.5617106381
H30	2.0420580963	0.3522131440	1.5678551189
O31	-0.0007770679	-0.9588099385	1.0230841577

C32	1.2836915671	-1.3835065905	0.6455307728
C33	3.5581304974	-0.4004900447	0.2910254263
H34	4.1584791589	0.5056670811	0.1472617429
H35	3.6577027771	-1.0014432233	-0.6222276109
C36	4.0974062539	-1.1734041735	1.5299821741
H37	4.2336548714	-0.4482908176	2.3427997221
H38	5.0813613550	-1.6055045460	1.3130988370
C39	3.2114138485	-2.3486095347	2.0415695175
C40	3.0835952132	-2.4378788493	3.5655680237
H41	2.3898820193	-3.2405635121	3.8299964788
H42	2.7366595906	-1.4982405113	4.0082332683
H43	4.0666857067	-2.6790837227	3.9932529581
O44	3.3371327165	-3.4764732389	1.4139726961
H45	1.9574879315	-1.8742253664	1.7429436139
O46	1.3563814769	-2.3095464296	-0.2322710648
Li47	2.5031372859	-3.6726154024	-0.1194268876

Table 18. Thermodynamic data for **198**



198

T = 298.15 K

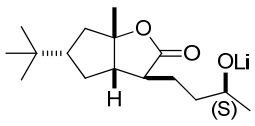
	U	Cv	S	H	G
trans.	0.889	2.981	42.725	1.481	-11.257
rot.	0.889	2.981	33.841	0.889	-9.201
vib.	10.925	75.354	66.694	10.925	-8.960
elec.	0.000	0.000	0.000	0.000	0.000
total	12.703	81.316	143.260	13.295	-29.418

Total internal energy, Utot (SCFE + ZPE + U): -858.774978 hartrees
Total enthalpy, Htot (Utot + pV): -858.774034 hartrees
Total Gibbs free energy, Gtot (Htot - T*S): -858.842101 hartrees

solvation energy

Hartrees	kcal/mol
-0.0341604	-21.4360

Table 19. Coordinates for **199**

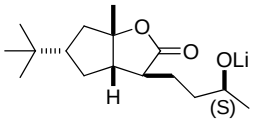


199

	angstroms		
atom	**x**	**y**	**z**
C1	1.1056735186	0.6008894882	-0.0614031502
C2	-0.2997125783	0.0650070551	-0.4837763829
C3	-0.0078535213	-0.9595442140	-1.5981825638
C4	1.2495491082	-0.4054827392	-2.3005386217
C5	2.1115966172	0.0644867912	-1.1039986915
H6	-0.9048801487	0.8847634169	-0.8849100900
H7	0.2083288063	-1.9401935095	-1.1531152432
H8	-0.8636354911	-1.0902443260	-2.2674053930
H9	0.9376293461	0.4977220562	-2.8502528063
H10	2.8536275513	0.8200202878	-1.3779561812
H11	2.6519628249	-0.7783341283	-0.6602570009
C12	1.9490008619	-1.3224198597	-3.3462784230
C13	3.1694434881	-0.5791803869	-3.9300616272
H14	2.8795944609	0.3930385430	-4.3489148842
H15	3.6285382204	-1.1635710286	-4.7364064644
H16	3.9406082947	-0.4023636761	-3.1718463137
C17	2.4198824389	-2.6614338007	-2.7444957636
H18	3.1391522552	-2.5192358217	-1.9299453732
H19	2.9174586415	-3.2634740337	-3.5141753246
H20	1.5840980773	-3.2553122035	-2.3582214563
C21	0.9617927993	-1.6128463505	-4.4967100057
H22	0.5916197456	-0.6829958733	-4.9470267966
H23	0.0950055833	-2.1891935699	-4.1548291232
H24	1.4511663031	-2.1925978317	-5.2884040911
C25	1.1838850098	2.1046509400	0.1670212104
H26	2.1601790705	2.3822608481	0.5779304599
H27	0.4075662870	2.4418036290	0.8624759322
H28	1.0465290689	2.6331335021	-0.7829793579
O29	1.3720396279	-0.0453967817	1.2387399735
C30	-0.9160594779	-0.4962570616	0.8099859784
H31	-1.3076411642	-1.5061094348	0.6537105131
C32	0.2845992136	-0.6336826332	1.7331285418
C33	-2.0418461454	0.3549514512	1.4778683597

H34	-1.8578701118	0.4095772361	2.5549810619
H35	-1.9845826566	1.3838991688	1.0984584278
C36	-3.4600825424	-0.2065582618	1.2842616201
H37	-3.7821073145	-0.1003258932	0.2372102193
H38	-4.1372851848	0.4172518709	1.8852436800
C39	-3.5923400062	-1.6970701503	1.7317490334
H40	-3.2578669360	-2.3111083403	0.8584531881
C41	-5.0755119917	-2.0498012428	1.9374575789
H42	-5.6798921345	-1.8493627667	1.0415312457
H43	-5.4842014553	-1.4665326358	2.7722520916
H44	-5.1705917674	-3.1116822424	2.1898821181
O45	-2.8343445174	-1.9685172333	2.8413271206
LI46	-1.2910156525	-1.9775256081	3.4859820565
O47	0.3220941310	-1.2026075071	2.8219342492

Table 20. Coordinates for **199**



199

T = 298.15 K

	U	**Cv**	**S**	**H**	**G**
trans.	0.889	2.981	42.725	1.481	-11.257
rot.	0.889	2.981	34.108	0.889	-9.281
vib.	11.451	76.676	72.147	11.451	-10.060
elec.	0.000	0.000	0.000	0.000	0.000
total	13.228	82.638	148.980	13.821	-30.598

Total internal energy, Utot (SCFE + ZPE + U): -858.824499 hartrees
Total enthalpy, Htot (Utot + pV): -858.823554 hartrees
Total Gibbs free energy, Gtot (Htot - T*S): -858.894340 hartrees

solvation energy

Hartrees	kcal/mol
-0.0327670	-20.5616

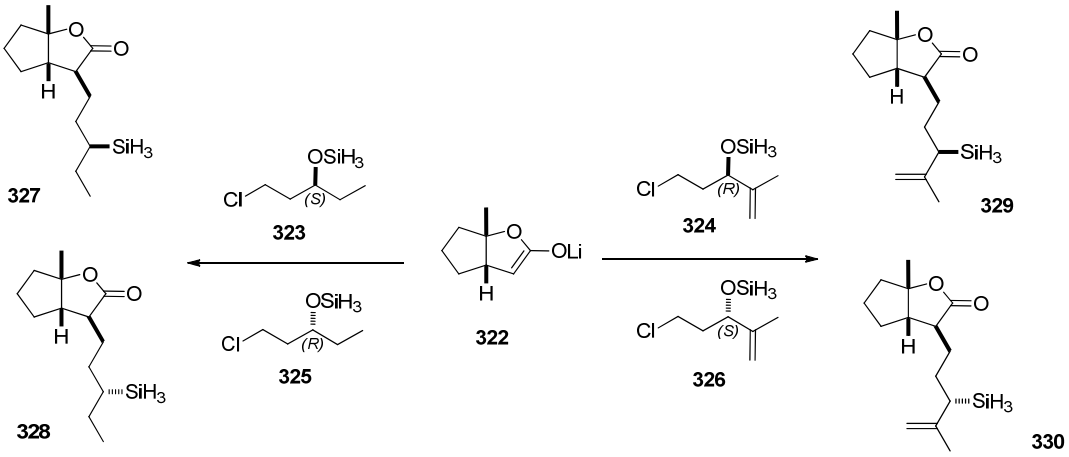
Table 21. Gas and solvent phase activation energies for **194→196** and **197→199**

	Gtot (gas) (hartrees)	**Solvation (hartrees)**	**Gtot (sol) (hartrees)**
195	-858.860483	-0.03470663	-858.8951896
194	-858.874133	-0.04045418	-858.9145872
	Gas phase	**THF**	
E_a(194→196) (kcal/mol)	8.5995	12.22045312	
	Gtot (gas) (hartrees)	**Solvation (hartrees)**	**Gtot (sol) (hartrees)**
198	-858.842101	-0.03416039	-858.9141246
197	-858.875542	-0.03858257	-858.8762614
	Gas phase	**THF**	
E_a(197→199) (kcal/mol)	21.06783	23.85380358	

APPENDIX Ic: Computational data for alkylation of **322** with alkyl chlorides **323**, **324**, **325** and **326**

In view of the contrasting results obtained in the alkylation of **170** under different conditions, we decided to study theoretically the energetics of this process using a density functional theory (DFT) calculation at 6-31-G*/B3LYP level of theory in order to better understand the reason why alkylation of **170** with **217** was unsuccessful. A correction for the solvent effect was estimated by performing a single point energy calculation (6-31-G**/B3LYP) of optimized transition state structures in

the gas phase. To make the calculation less time consuming, transition state modeling was performed on a simpler enolate **322** which was alkylated with alkyl chlorides **323**, **324**, **325** and **326**. As alkyl iodide **217** in the real system is a 1:1 mixture of diastereomers, all possible stereoisomers of alkyl chlorides (**323**, **324**, **325** and **326**) and alkylated lactones (**327**, **328**, **329** and **330**) were considered in the modeling algorithm (Scheme 99).



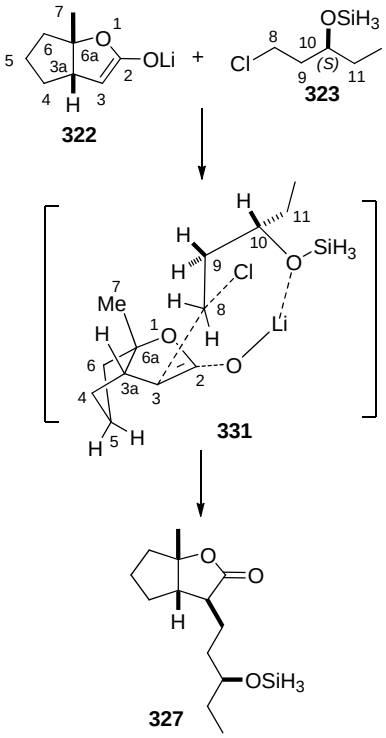
Scheme 99. Alkylation of **322** with alkyl chlorides **323**, **324**, **325** and **326**

A transition state search over the potential energy surface for alkylation located a state with one imaginary frequency in each case corresponding to the carbon-chlorine bond being broken and carbon-carbon bond being formed. A common feature of these transition states (**331**, **332**, **333**, **334**) is the coordination of the oxygen atom of the silyloxy group with the lithium ion of the enolate. Modeling revealed that the energy difference between diastereomeric transition states **331** and **332** is 1.07 kcal/mol in the gas phase and 1.05 kcal/mol in the solvent phase (Schemes 100 and 101). The effect of

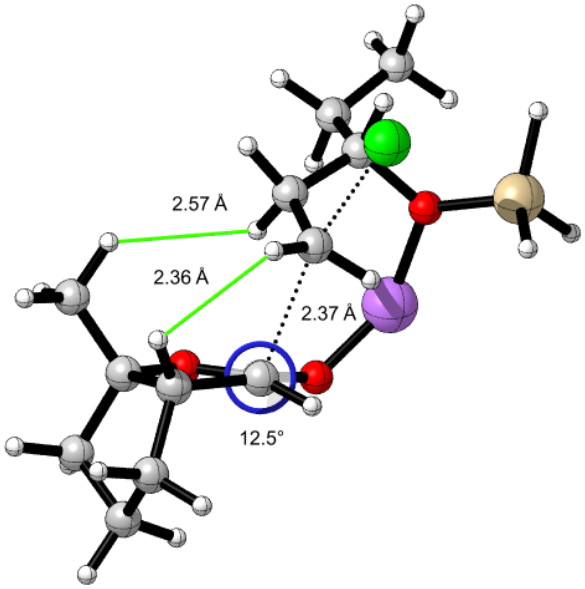
a methylene moiety at C11 in **323** on the alkylation process can be understood by comparing **331** and **333**. The energy difference between these two transition states in the gas phase is 0.48 kcal/mol whereas in the solvent phase it is 2.77 kcal/mol. Transition state **333** is higher in energy than **331** due to an eclipsed conformation of atoms around the C10-C11 (θ = 30.4º) and C9-C10 (θ = 45.8º) carbon-carbon bonds (c, d, Fig 9). On the other hand, in **331** atoms around the C10-C11 (θ = 51.9º) and C9-C10 (θ = 52.3º) carbon-carbon bonds are oriented in a staggered conformation (a, b, Fig 9). A further reason for the higher energy of **333** is a severe steric clash between the hydrogen atom at C9 and the methyl group at C6a (2.48 Å) compared to the same hydrogen atom in **331** (2.57 Å). By the same analysis, the effect of a methylene moiety at C11 in **325** can be explained by comparing **332** and **334**. The energy difference between these two transition states in the gas phase is 9.21 kcal/mol, whereas in the solvent phase it is 6.58 kcal/mol. Again, **334** is higher in energy than **332** due to an eclipsed conformation of atoms around the C10-C11 (θ = 21.4º) and C9-C10 (θ = 25.4º) carbon-carbon bonds (c, d, Fig 10) in **334**. By contrast, atoms around the C10-C11 (θ = 57.0º) and C9-C10 (θ = 56.5º) carbon-carbon bonds in **332** occupy a staggered conformation (a, b, Fig 10). An additional energy penalty in **334** stems from unfavorable steric interactions, first between the hydrogen atom at C8 and the hydrogen atom at C3a (2.18 Å), and second between the hydrogen atom at C10 and the methyl group at C6a (2.21 Å). Furthermore, transition state **334** is unique among the other three transition states due to the fact that the conformation of the cyclopentane ring causes a severe steric interaction between the hydrogen atom at C5

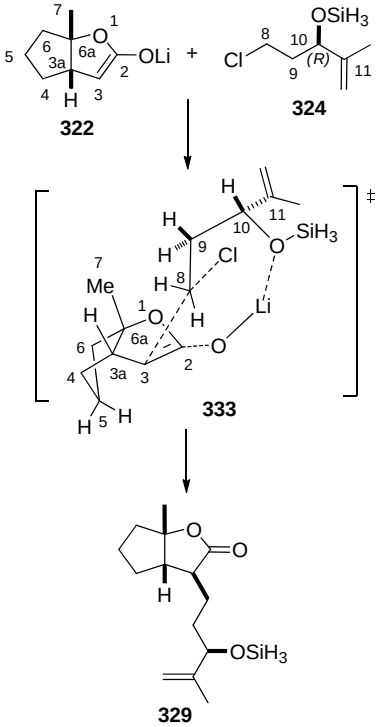
and the methyl group at C6a (2.66 Å).

This study predicts that solvation has a rather subtle effect on the kinetics of the alkylation process. In the cases of **332** and **331**, solvation does not have any appreciable effect on the activation energy of alkylation whereas in **333** and **334** solvation has decelerating and accelerating effects, respectively. This implies that in **331** and **332** coordination of the lithium ion with the oxygen atom of the silyloxy group is stronger because there are no unfavorable steric interactions to prevent this bonding. Coordination of the lithium ion with the oxygen atom of the silyloxy group facilitates the alkylation by bringing lithium enolate **322** and the electrophile closer to each other. Weakening of this interaction would retard this process. Due to the unfavorable eclipsed conformation present in **333**, coordination of the lithium ion with the oxygen atom of the silyloxy group is weaker compared to **331** and **332.** Solvation further weakens this coordination and therefore increases the activation energy. In **334** there are even more severe unfavorable steric interactions, especially one involving the steric clash between the hydrogen atom at C5 and the methyl group at C6a. Although weakening of lithium ion coordination to the oxygen atom of the silyloxy group would increase activation energy, in **334** this would probably trigger flipping of the cyclopentane ring into a more stable conformation in which C5 points away from the methyl group at C6a and thus decreases the activation energy.

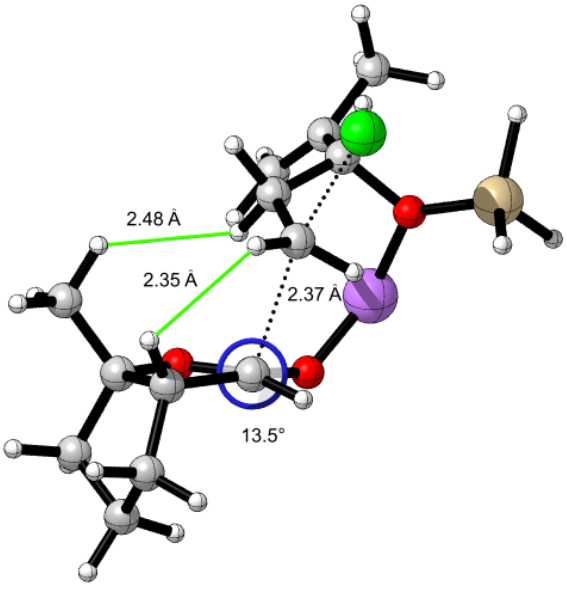


$\Delta G_{gas}^{\#}$ = 1.07 kcal/ mol ν = - 417 cm^{-1}
$\Delta G_{THF}^{\#}$ = 1.05 kcal/ mol μ = 4.8 debye
(relative to **332**)

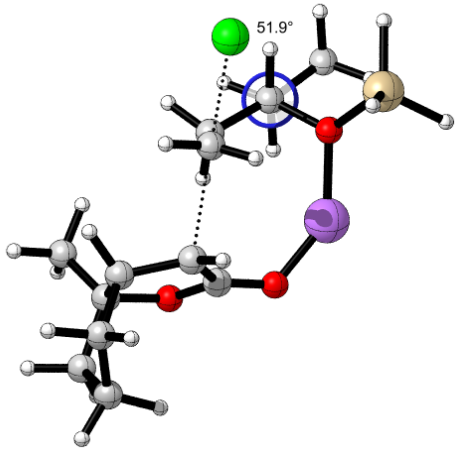




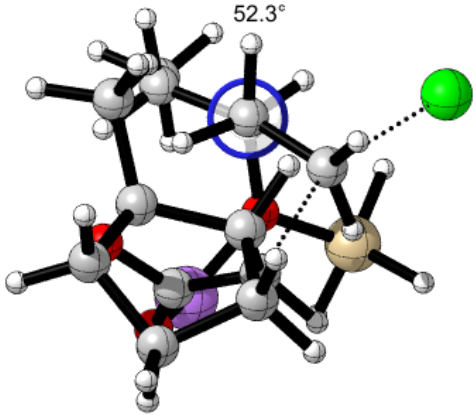
$\Delta G_{gas}^{\#}$ = 1.55 kcal/ mol ν = - 423 cm^{-1}
$\Delta G_{THF}^{\#}$ = 3.82 kcal/ mol μ = 5.5 debye
(relative to **332**)



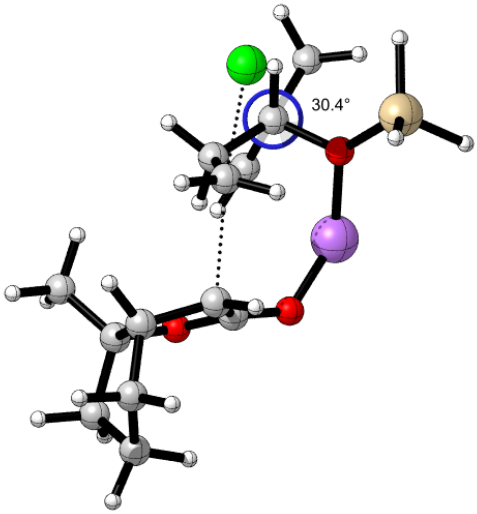
Scheme 100. Transition states, imaginary vibrations and activation energies in the gas and solvent phase for alkylation of **322** with **323** and **324**



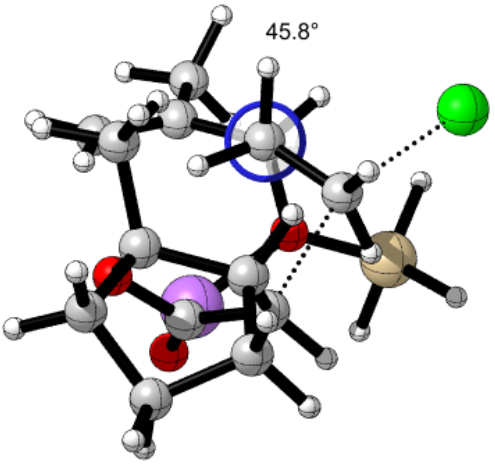
a) A view through the C10-C11 bond in **331**



b) A view through the C9-C10 bond in **331**

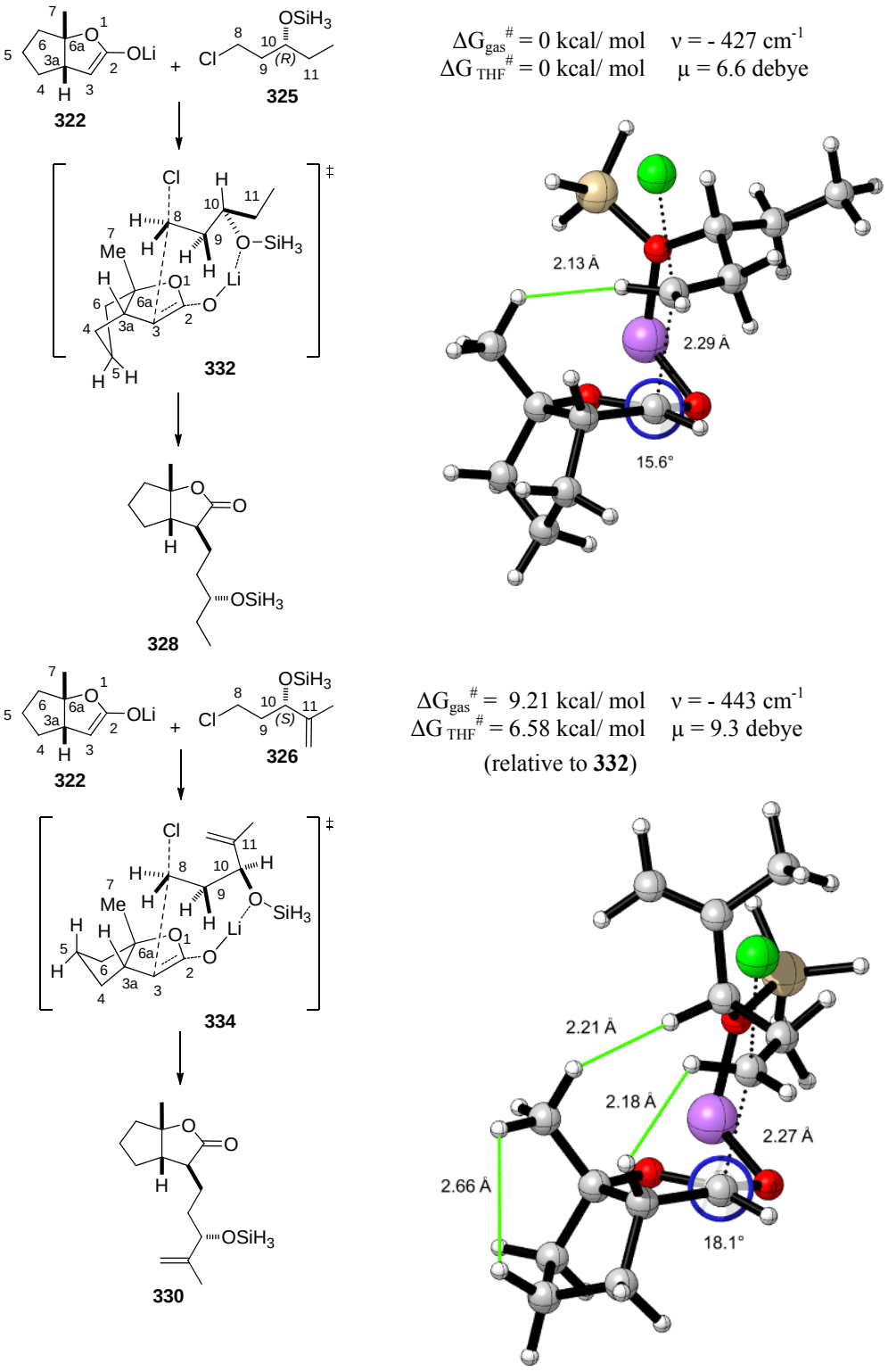


c) A view through the C10-C11 bond in **333**

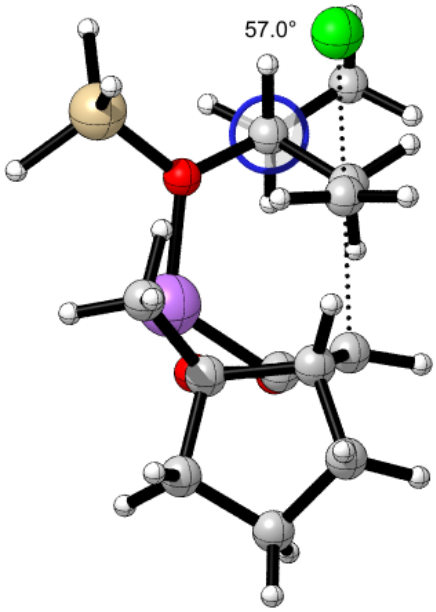


d) A view through the C9-C10 bond in **333**

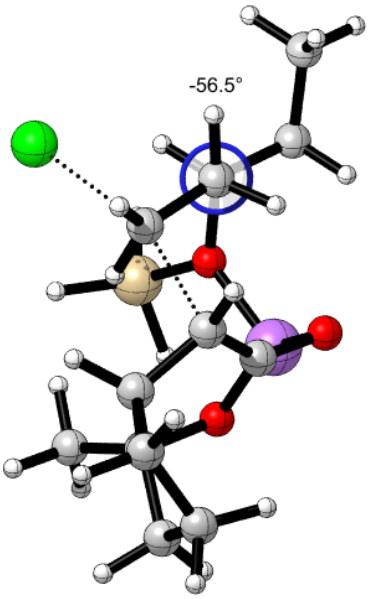
Fig 9. Conformational analysis of **331** and **333**



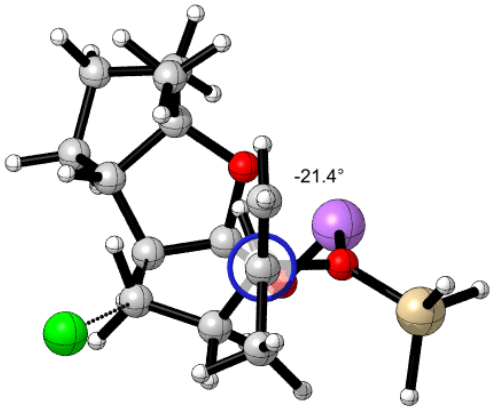
Scheme 101. Transition states, imaginary vibrations and activation energies in the gas and solvent phase for alkylation of **322** with **325** and **326**



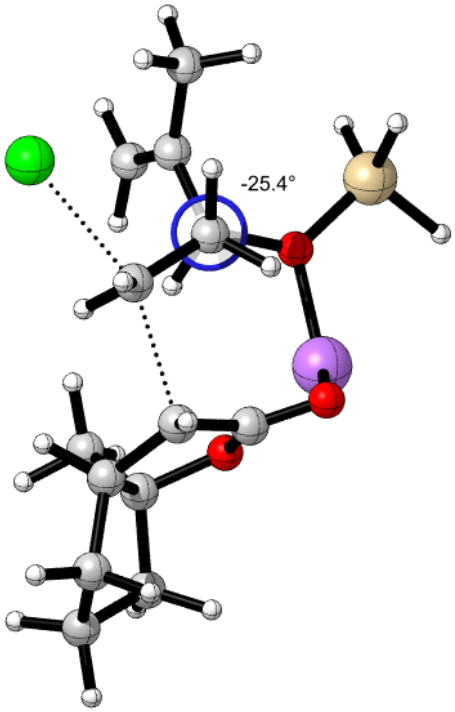
a) A view through the C10-C11 bond in **332**



b) A view through the C9-C10 bond in **332**



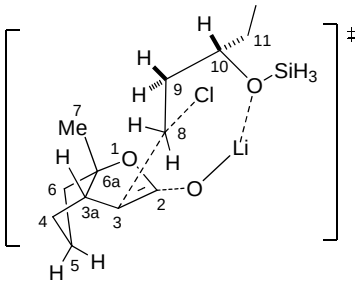
c) A view through the C10-C11 bond in **334**



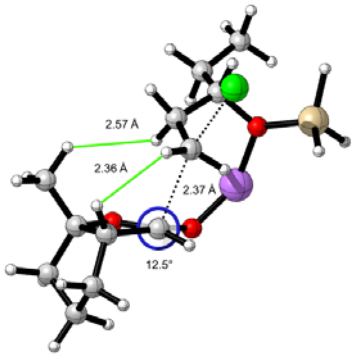
d) A view through the C9-C10 bond in **334**

Fig 10. Conformational analysis of **332** and **334**

Table 21. Coordinate for **331**



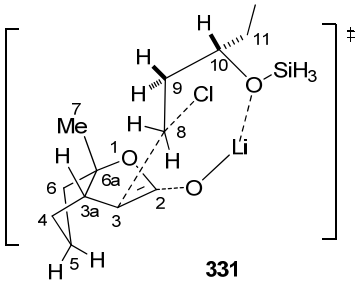
331



	angstroms		
atom	**x**	**y**	**z**
C1	0.5572584142	0.0813684674	-3.1341528595
C2	1.6021994659	0.1755963341	-1.9595501862
C3	2.3550797055	1.5156636748	-2.1844214095
C4	1.3665702985	2.3832369185	-2.9829062546
C5	0.7360909611	1.3745865812	-3.9564338983
H6	2.3094391251	-0.6657696200	-1.9861097946
H7	2.6716807521	1.9738335549	-1.2411283003
H8	3.2607291356	1.3401939433	-2.7812718652
H9	1.8467355122	3.2257103723	-3.4918323356
H10	1.4285980128	1.1769598133	-4.7855521821
H11	-0.2161304997	1.6985775387	-4.3877826490
C12	0.6084021390	-1.1949504018	-3.9621758019
H13	1.5803737061	-1.2841123284	-4.4600193199
H14	-0.1728228258	-1.1920257843	-4.7305473311
H15	0.4659268288	-2.0790589504	-3.3321451960
O16	-0.7615513902	0.1309423761	-2.4893895483
C17	-0.6179537882	0.2870908226	-1.1411984614
C18	0.7133916977	0.1490650362	-0.7386093228
O19	-1.6803636631	0.4226426645	-0.4610927031
Li20	-2.3767705356	-0.7082767635	0.6723026780
H21	1.0433837125	0.5672543408	0.2054682580
H22	0.5993791172	2.7967000303	-2.3167049456
O23	-1.9585153762	-2.3663226262	1.4546509182
Si24	-1.6536305636	-2.5339570549	3.1259605168
C25	-1.5142232978	-3.3728562731	0.4730967898
H26	-1.0561498563	-4.1892977730	1.0339700406
C27	-2.7368322764	-3.8744280874	-0.2948742115
H28	-3.2287652426	-3.0260264710	-0.7956027311
H29	-2.3723665923	-4.5276391909	-1.0989007908

C30	-3.7464208951	-4.6376131917	0.5673462876
H31	-4.1589606435	-4.0027849321	1.3592320052
H32	-3.2798440573	-5.5083524813	1.0427478734
H33	-4.5834323872	-4.9977854210	-0.0398780557
C34	-0.4505042442	-2.7630066086	-0.4539198735
H35	-0.0147485891	-3.5891292704	-1.0266596166
H36	-0.9529714540	-2.1161553977	-1.1858015477
C37	0.6649252748	-2.0140448771	0.2375483734
H38	0.4785673086	-1.4236668342	1.1154174146
H39	1.6620830937	-2.0242685755	-0.1659574570
Cl40	1.3622856802	-3.7179582545	1.7023175986
H41	-1.6563937165	-3.9622477807	3.5014266997
H42	-0.4298872658	-1.8201131442	3.5446695626
H43	-2.8296547819	-1.8370057769	3.7226317933

Table 23. Thermodynamic data for **331**



331

T = 298.15 K

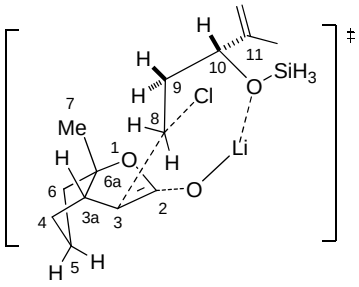
	U	Cv	S	H	G	ln(Q)
trans.	0.889	2.981	42.974	1.481	-11.332	19.12544
rot.	0.889	2.981	34.300	0.889	-9.338	15.76032
vib.	11.843	75.609	78.499	11.843	-11.562	19.51425
elec.	0.000	0.000	0.000	0.000	0.000	0.00000
total	13.620	81.571	155.773	14.212	-32.231	54.40001

Total internal energy, Utot (SCFE + ZPE + U): -1492.422010 hartrees
Total enthalpy, Htot (Utot + pV): -1492.421066 hartrees
Total Gibbs free energy, Gtot (Htot - T*S): -1492.495079 hartrees

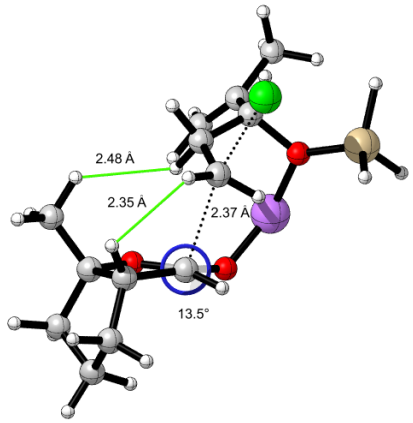
solvation energy

Hartrees	kcal/mol
-0.0378989	-23.7819

Table 24. Coordinates for **333**



333

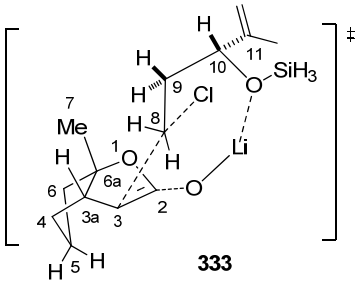


angstroms

atom	x	y	z
C1	0.4919301832	-0.3806010321	-2.8902593860
C2	1.5236179445	-0.1914612890	-1.7157037074
C3	2.1802625864	1.1945309788	-1.9640441151
C4	1.1350233944	1.9764185770	-2.7784531735
C5	0.5784467042	0.9088823269	-3.7340196662
H6	2.2895530840	-0.9800111427	-1.7270300366
H7	2.4625856556	1.6906213826	-1.0291342704
H8	3.0969048519	1.0724104912	-2.5575420941
H9	1.5563071046	2.8408452629	-3.3026108754
H10	1.2836448925	0.7475624156	-4.5603508433
H11	-0.3941292844	1.1568932228	-4.1703768167
C12	0.6418372013	-1.6611043132	-3.6997762083
H13	0.5662869254	-2.5458765325	-3.0593134404
H14	1.6192580921	-1.6827957578	-4.1943896146
H15	-0.1341435979	-1.7278600157	-4.4705327608
O16	-0.8286762382	-0.4172668877	-2.2476863594
C17	-0.7019162207	-0.2126921593	-0.8986998080
C18	0.6359443534	-0.2605397388	-0.4949659040
O19	-1.7740921922	-0.1249391158	-0.2309848983
Li20	-2.6063693639	-1.3332237985	0.7341874827
H21	0.9372484344	0.1857464227	0.4457776650
H22	0.3398006160	2.3476177836	-2.1203665988
O23	-1.8397667607	-2.7441379981	1.7303055104
Si24	-1.4427239894	-2.8540058480	3.3851875397
C25	-1.4783210742	-3.7487102701	0.7148473751
H26	-1.0677936747	-4.6070812391	1.2496919030
C27	-2.7973904116	-4.1286242382	0.0482087658
C28	-3.5835721979	-5.1921740702	0.7750247284

H29	-4.5656220212	-5.3549075945	0.3216387151
H30	-3.7303923163	-4.9266394977	1.8296848983
H31	-3.0379485126	-6.1450259459	0.7649473183
C32	-0.3870147894	-3.2081917560	-0.2248154338
H33	0.0521408571	-4.0742532182	-0.7315946882
H34	-0.8347037995	-2.5941261046	-1.0099435621
C35	0.7114334413	-2.4323727059	0.4589926165
H36	0.5204289115	-1.8526972542	1.3414475207
H37	1.7038469227	-2.4182181140	0.0421050956
Cl38	1.4216881653	-4.1538872062	1.9019931191
H39	-2.5814906286	-2.1258349072	4.0148423071
H40	-0.1910518362	-2.1491201539	3.7252250223
H41	-1.4545762261	-4.2704745246	3.8077976225
C42	-3.2654682076	-3.5349633636	-1.0608504862
H43	-4.2372575809	-3.8083726441	-1.4646847278
H44	-2.7129218423	-2.7898717376	-1.6264941500

Table 25. Thermodynamic data for **333**



333

T = 298.15 K

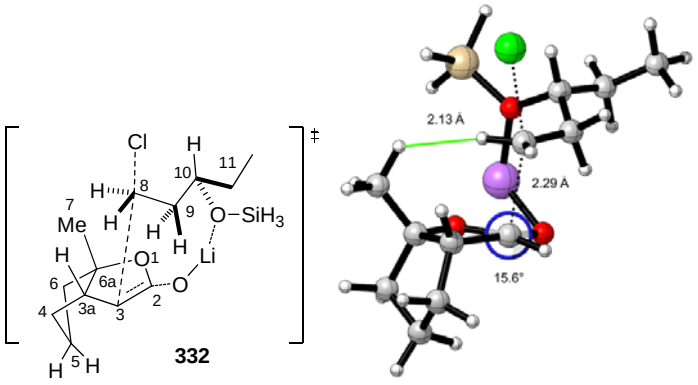
	U	Cv	S	H	G	ln(Q)
trans.	0.889	2.981	43.092	1.481	-11.367	19.18463
rot.	0.889	2.981	34.438	0.889	-9.379	15.82974
vib.	12.347	79.086	81.893	12.347	-12.069	20.37089
elec.	0.000	0.000	0.000	0.000	0.000	0.00000
total	14.124	85.048	159.423	14.717	-32.815	55.38526

Total internal energy, Utot (SCFE + ZPE + U): -1530.496987 hartrees
Total enthalpy, Htot (Utot + pV): -1530.496043 hartrees
Total Gibbs free energy, Gtot (Htot - T*S): -1530.571790 hartrees

solvation energy

Hartrees	kcal/mol
-0.0352317	-22.1082

Table 26. Coordinates for **332**



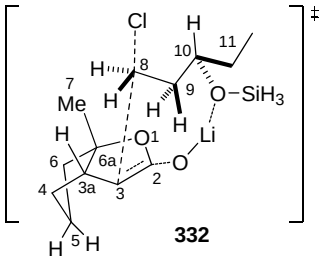
332

angstroms

atom	x	y	z
C1	-0.6956885999	0.6940987971	-1.7973689478
C2	0.8445137469	0.4736645042	-1.5266556909
C3	1.5281202823	1.7890513899	-1.9869318425
C4	0.4432593849	2.8668101371	-1.8220186492
C5	-0.8260535056	2.1476582911	-2.3049288418
H6	1.2296873937	-0.3816022775	-2.0981376866
H7	2.4406414146	1.9999683300	-1.4195458105
H8	1.8134680493	1.7086209531	-3.0447019433
H9	0.6545280243	3.7799435742	-2.3881616151
H10	-0.8488917468	2.1360024492	-3.4025363500
H11	-1.7613718639	2.6006027832	-1.9611463321
C12	-1.3699583568	-0.3231625264	-2.7067227313
H13	-0.9022371766	-0.3020380486	-3.6971927580
H14	-2.4339600330	-0.0883977311	-2.8322167669
H15	-1.2820084400	-1.3434418506	-2.3220616031
O16	-1.3264821603	0.6165201292	-0.4648207850
C17	-0.3354974328	0.5243497384	0.5339271213
C18	0.8981747422	0.2230066636	-0.0353485617
O19	-0.7839024642	0.5410966824	1.7094053421
Li20	-2.2713758993	-0.4126833956	1.0706395658
H21	1.8113745402	0.3330354012	0.5375271499
H22	0.3442532629	3.1507975422	-0.7671801649
O23	-2.1341968139	-2.3039253407	0.9700803798
Si24	-3.1305427801	-3.1741629120	-0.0921467456
Cl25	0.6721756492	-4.3616477378	-0.6636387359
C26	-1.0720501652	-3.0263183957	1.7142928445
H27	-0.9886835260	-4.0225575207	1.2709830633
C28	0.2735273933	-2.3176812011	1.5218128507
H29	1.0419054056	-2.9502600786	1.9762423851

H30	0.2499810076	-1.3747038888	2.0842384455
C31	0.6665104369	-2.0532435064	0.0926624180
H32	1.7032009032	-2.0586009181	-0.1977526975
H33	-0.0683445113	-1.9389037866	-0.6813950943
C34	-1.5192670459	-3.1204782270	3.1734537979
H35	-2.5293948158	-3.5502233074	3.1872031930
H36	-1.5991495237	-2.1076342505	3.5937010207
C37	-0.5936651941	-3.9790414428	4.0457504052
H38	-1.0176449570	-4.0978973012	5.0483089525
H39	-0.4599777622	-4.9790688146	3.6170039788
H40	0.3973321752	-3.5275745679	4.1582948897
H41	-2.4871375038	-3.4478584649	-1.3923116151
H42	-4.2859132372	-2.2521746711	-0.2790628661
H43	-3.5743770142	-4.4311138915	0.5568586134

Table 27. Thermodynamic data for **332**



332

T = 298.15 K

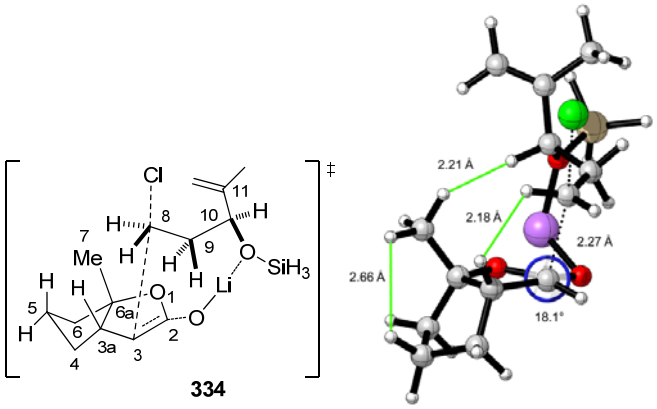
	U	**Cv**	**S**	**H**	**G**	**ln(Q)**
trans.	0.889	2.981	42.974	1.481	-11.332	19.12544
rot.	0.889	2.981	34.041	0.889	-9.261	15.63010
vib.	11.748	75.777	76.649	11.748	-11.105	18.74313
elec.	0.000	0.000	0.000	0.000	0.000	0.00000
total	13.525	81.738	153.664	14.118	-31.697	53.49867

Total internal energy, Utot (SCFE + ZPE + U): -1492.424711 hartrees
Total enthalpy, Htot (Utot + pV): -1492.423767 hartrees
Total Gibbs free energy, Gtot (Htot - T*S): -1492.496777 hartrees

solvation energy

Hartrees	kcal/mol
-0.0378727	-23.7655

Table 28. Coordinates for **334**

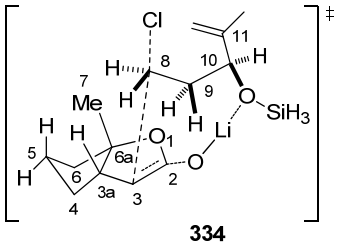


334

	angstroms		
atom	**x**	**y**	**z**
C1	-0.6009399036	0.3803531676	-1.9049660329
C2	0.9346443830	0.3823730357	-1.5451311303
C3	1.5295458673	1.6270308905	-2.2608286312
C4	0.5398035185	1.9253424884	-3.4009649828
C5	-0.8283620589	1.6507909162	-2.7552368679
H6	1.4123768925	-0.5208180701	-1.9493597984
H7	1.5589074311	2.4753874822	-1.5656652874
H8	2.5525333795	1.4555922829	-2.6111915558
H9	0.7082398912	1.2403189364	-4.2428166688
H10	-1.6435542367	1.5324545196	-3.4775547069
H11	-1.0951432395	2.4763131911	-2.0846906344
C12	-1.0920111266	-0.8839195268	-2.5979485084
H13	-0.6568599404	-0.9476772631	-3.6018224941
H14	-2.1830541399	-0.8714069703	-2.7054327437
H15	-0.8017067790	-1.7896803066	-2.0566736913
O16	-1.2937761221	0.5109218202	-0.6137001096
C17	-0.3449505646	0.7226974906	0.4120821549
C18	0.9402950322	0.4060569110	-0.0324563101
O19	-0.8491808446	0.9903825679	1.5295138901
Li20	-2.3859391125	0.0115014429	1.0859685288
H21	1.7959036989	0.7701001430	0.5240950410
H22	0.6256475200	2.9445358928	-3.7917595469
O23	-2.3993627778	-1.7928173654	1.7088944657
Si24	-3.3035928695	-2.2668474939	3.0535458209
Cl25	2.0576830472	-4.0409135126	0.5710036359
C26	-1.2545312754	-2.5306232493	1.0822118310
H27	-1.3345932367	-2.2211235233	0.0391298257

C28	0.0682537806	-1.9878187921	1.6661921825
H29	0.4712129959	-2.6576065145	2.4288792437
H30	-0.1449159075	-1.0364513747	2.1693509321
C31	1.1295064430	-1.7629313140	0.6196343159
H32	2.1300480149	-1.5172689407	0.9299760374
H33	0.9660829147	-1.9989028723	-0.4167615972
C34	-1.4869097175	-4.0288649805	1.1421871449
C35	-0.9607504434	-4.8230964016	2.3127443238
H36	-1.1846321517	-4.3607620967	3.2829937796
H37	-1.3875602559	-5.8302704088	2.3143143172
H38	0.1297419245	-4.9096924008	2.2272846972
H39	-2.4613709495	-2.4031627179	4.2664656502
H40	-4.0666790376	-3.5137197934	2.8194200004
H41	-4.2398604734	-1.1229769370	3.2142595080
C42	-2.1449855783	-4.6058811839	0.1292137239
H43	-2.4760731663	-4.0417760190	-0.7396948415
H44	-2.3546593490	-5.6720580847	0.1198954838

Table 29. Coordinates for **334**



334

T = 298.15 K

	U	Cv	S	H	G	ln(Q)
trans.	0.889	2.981	43.092	1.481	-11.367	19.18463
rot.	0.889	2.981	34.428	0.889	-9.376	15.82504
vib.	12.270	79.299	81.130	12.270	-11.919	20.11743
elec.	0.000	0.000	0.000	0.000	0.000	0.00000
total	14.047	85.261	158.650	14.640	-32.662	55.12710

Total internal energy, Utot (SCFE + ZPE + U): -1530.485202 hartrees
Total enthalpy, Htot (Utot + pV): -1530.484258 hartrees
Total Gibbs free energy, Gtot (Htot - T*S): -1530.559638 hartrees

solvation energy

Hartrees	kcal/mol
-0.0430094	-26.9888

Table 30. Thermodynamic data for **322**, **323**, **324**, **325**, **326**, **331**, **332**, **333**, **334**

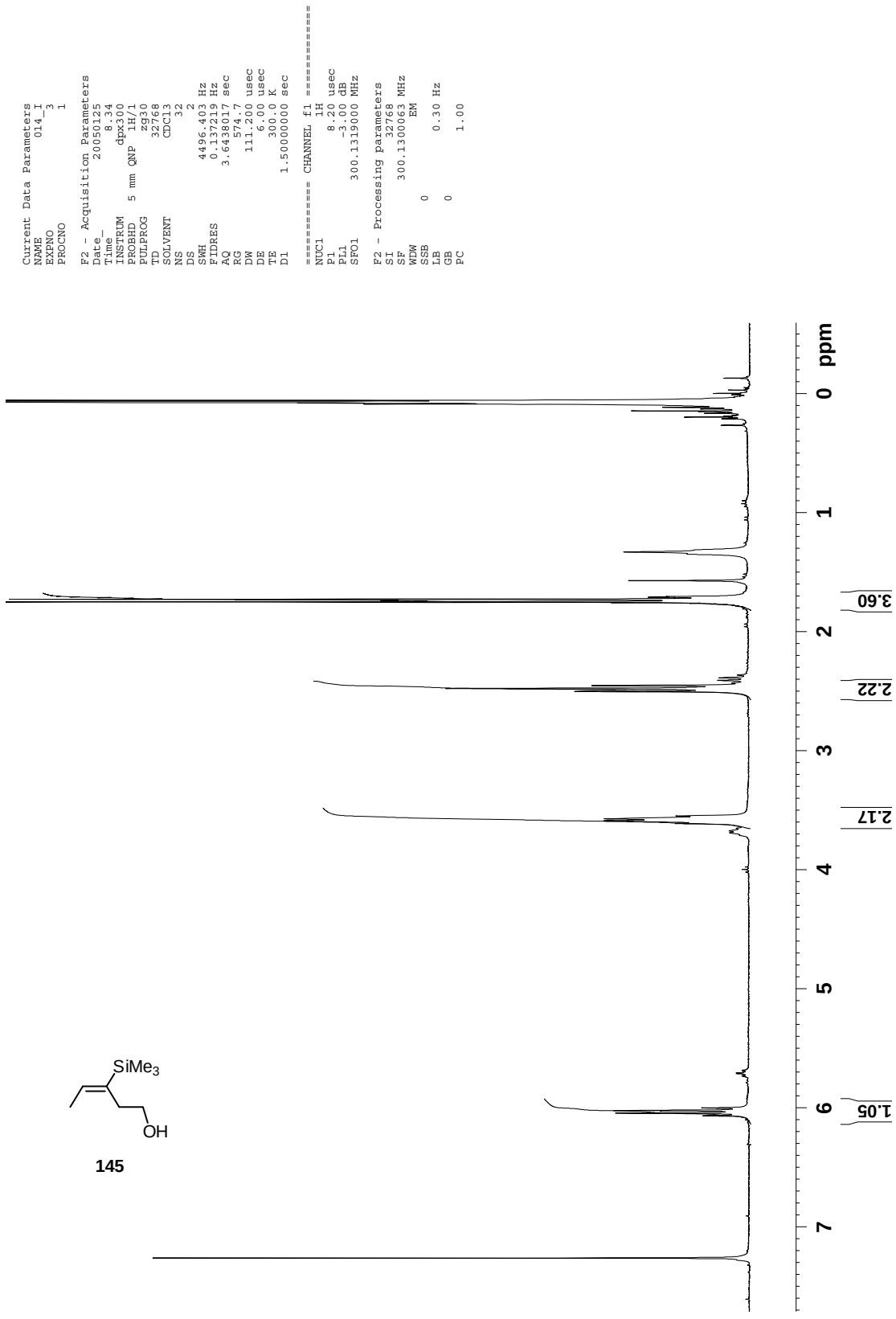
	G_{tot} (gas) (hartrees)	G_{tot} (THF) (hartrees)	
331	-1492.495079	-0.0378989	-1492.532978
322	-626.498213	-0.0447247	-626.5429377
324 or **326**	-1061.25039	-0.0059019	-1061.256292
323 or **325**	-1023.172912	-0.0049413	-1023.177853
332	-1492.496777	-0.0378727	-1492.53465
333	-1530.57179	-0.0352317	-1530.607022
334	-1530.559638	-0.0430094	-1530.602647

Table 31. Gas and solvent phase activation energies for **322→327**, **322→328**, **322→330**, **322→329**

	E_a (gas) (hartrees)	E_a (solution) (hartrees)	Rel E_a (gas) (kcal/mol)	Rel E_a (THF) (kcal/mol)
322→327	157.176046	157.1878131	1.06974	1.053234
322→328	157.174348	157.1861413	0	0
322→329	157.176813	157.1922079	1.55295	3.821958
322→330	157.188965	157.1965822	9.20871	6.577767

APPENDIX II

NMR Spectra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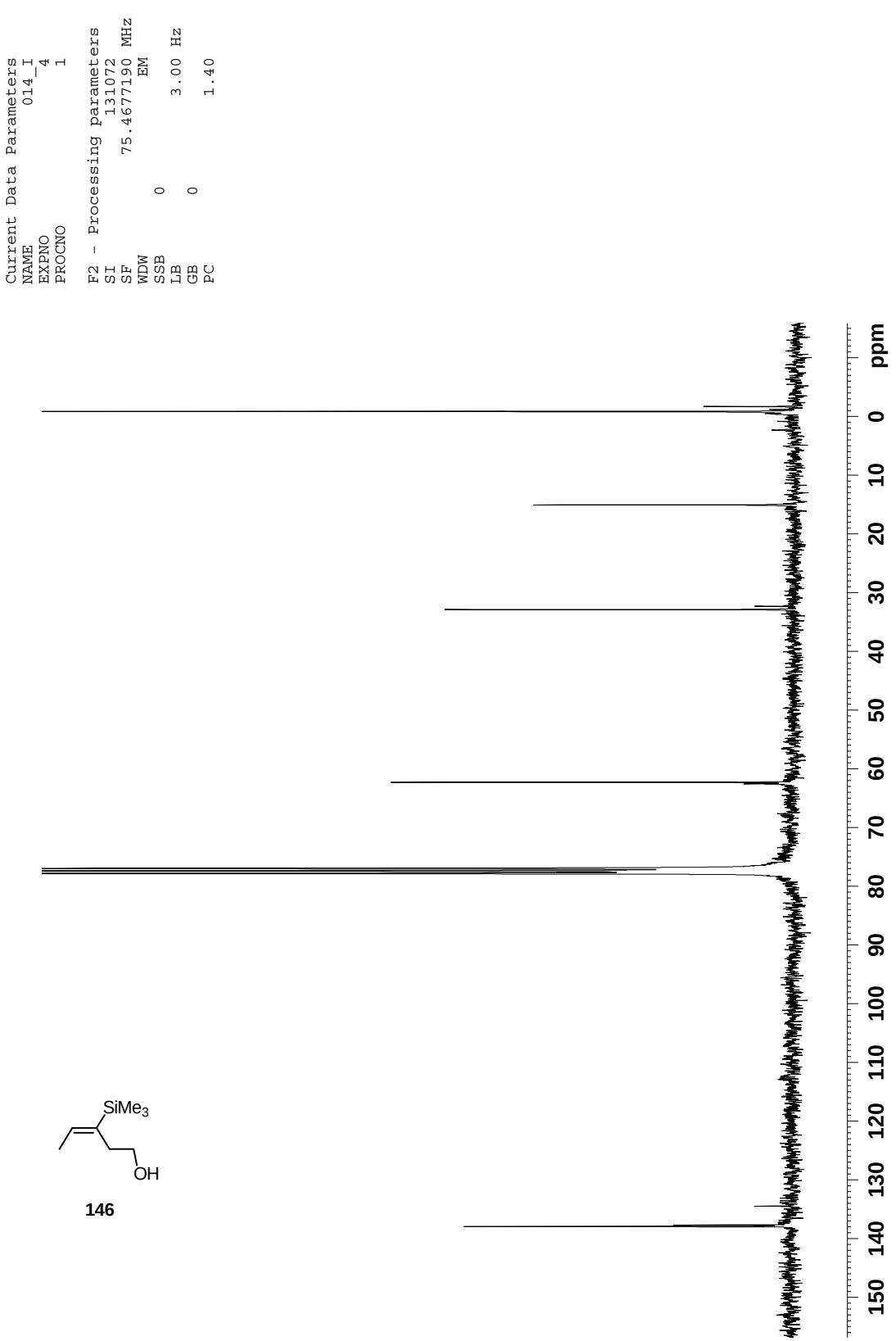
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20050125
Time_ 8.34
INSTRUM dpx300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4496.403 Hz
FIDRES 0.137219 Hz
AQ 3.6438017 sec
RG 574.7
DW 111.200 usec
DE 6.00 usec
TE 300.0 K
D1 1.50000000 sec
========== CHANNEL f1 ==========
NUC1 1H
P1 8.20 usec
PL1 -3.00 dB
SFO1 300.1319000 MHz
F2 - Processing parameters
SI 32768
SF 300.1300063 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
ppm
0
1
2
3
4
5
6
7
3.60
2.22
2.17
1.05
SiMe3
OH
145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PROCNO 1
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SF 75.4677190 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
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OH
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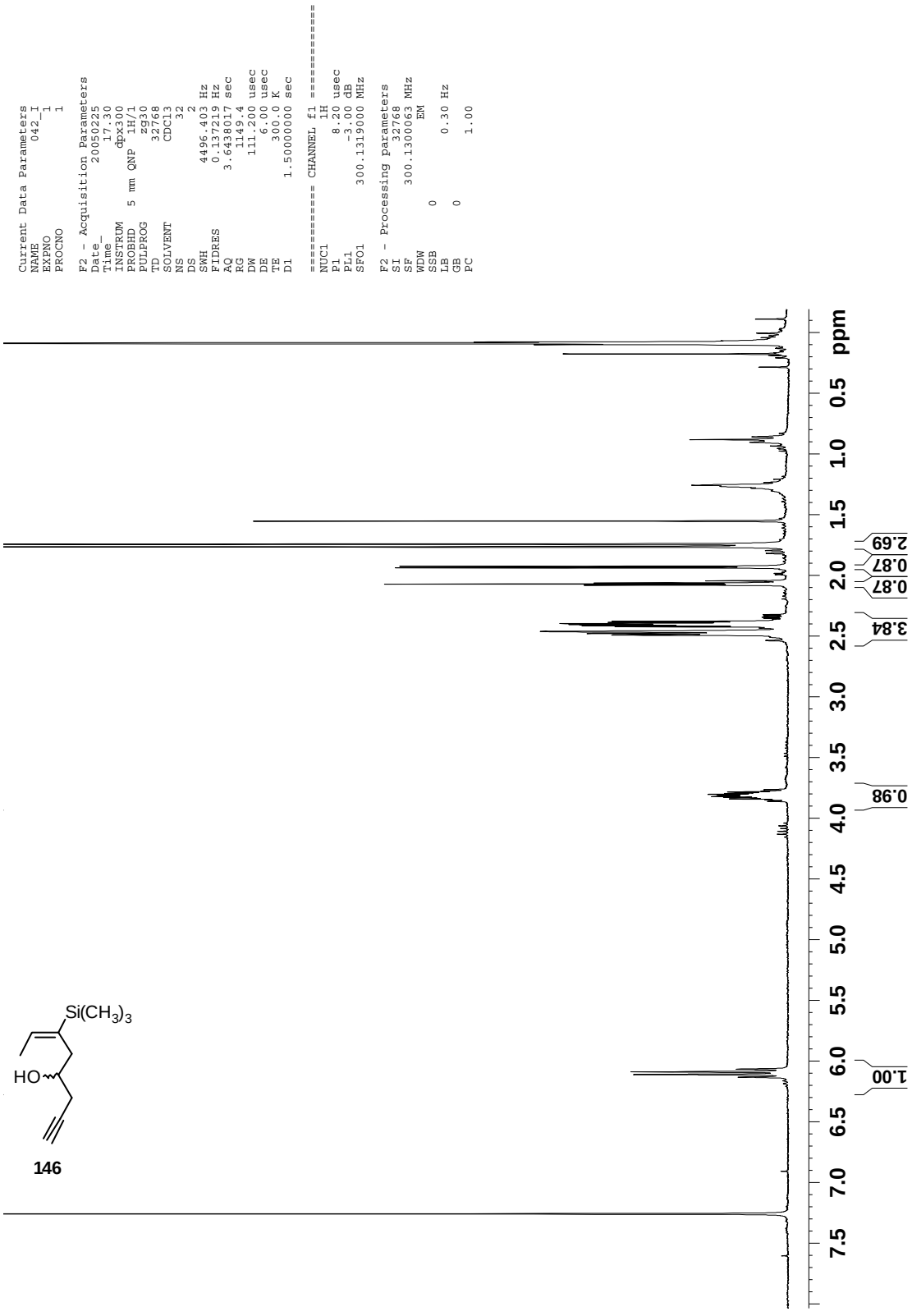
20
30
40
50
60
70
80
90
100
110
120
130
140
150

146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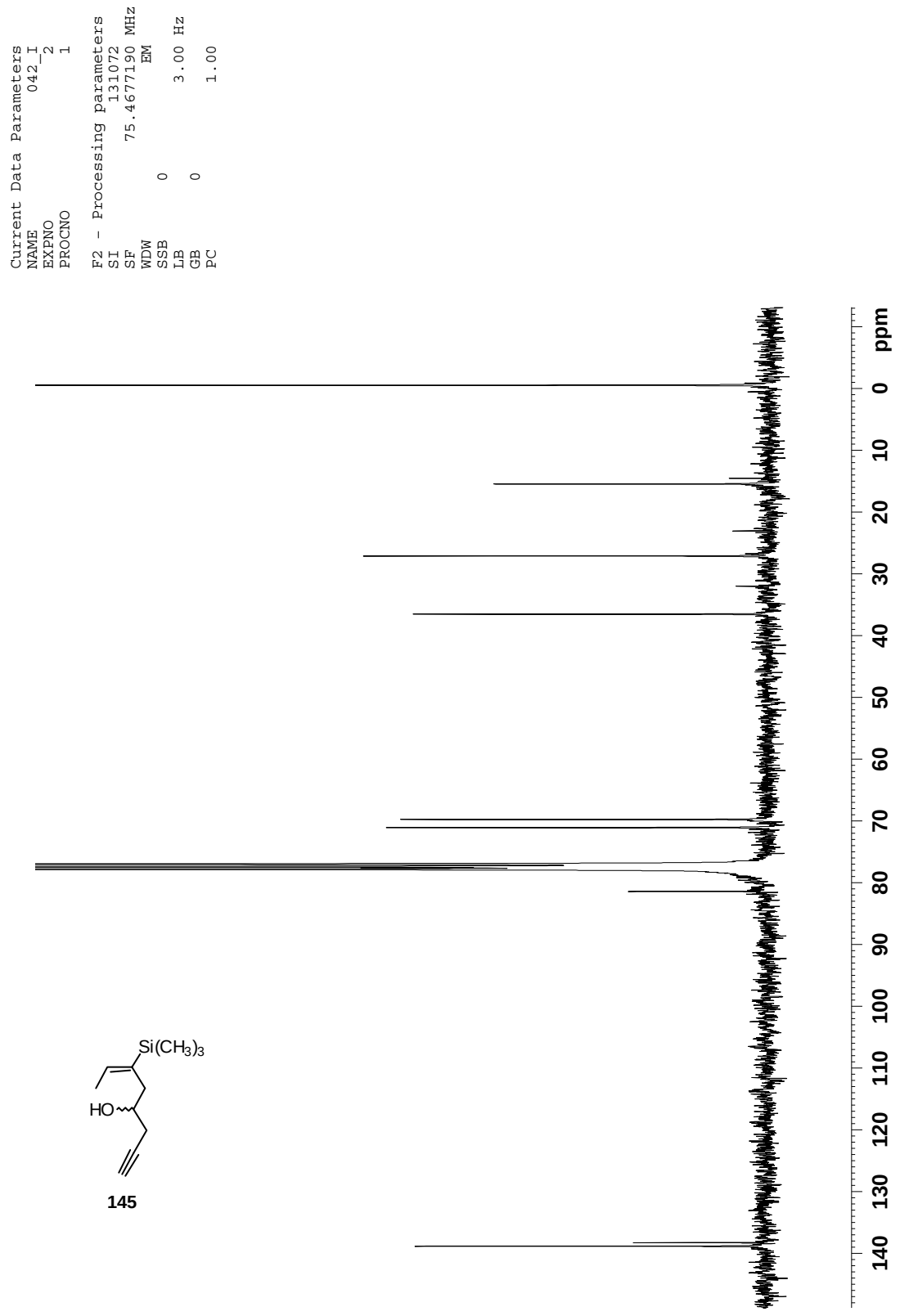
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4496.403 Hz
FIDRES 0.137219 Hz
AQ 3.6438017 sec
RG 1149.4
DW 111.200 usec
DE 6.00 usec
TE 300.0 K
D1 1.50000000 sec
========== CHANNEL f1 ==========
NUC1 1H
P1 8.20 usec
PL1 -3.00 dB
SFO1 300.1319000 MHz
F2 - Processing parameters
SI 32768
SF 300.1300063 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
Si(CH3)3
HO
146
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
0.5
1.00
0.98
3.84
0.87
0.87
2.69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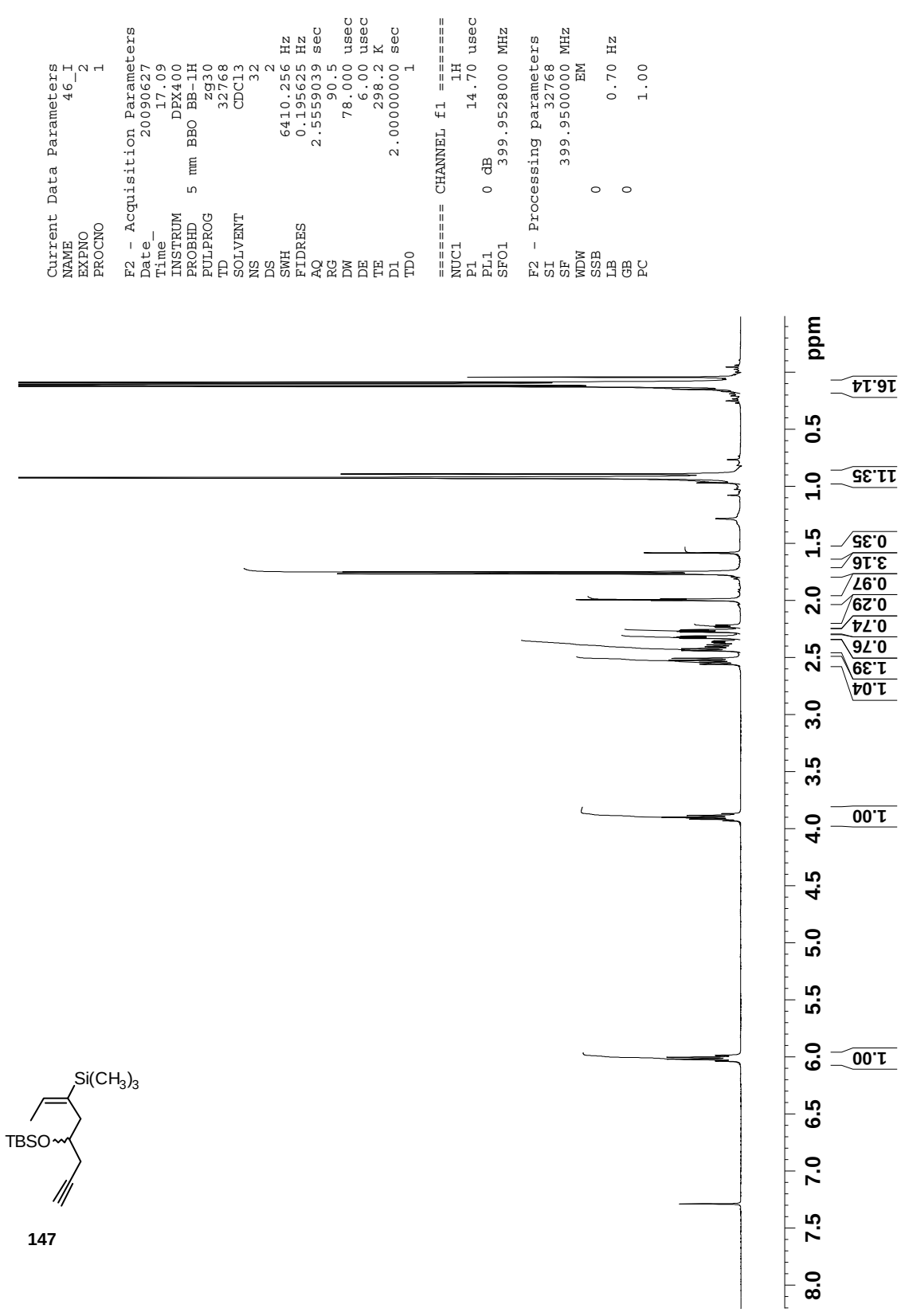
PROCNO 1
F2 - Processing parameters
SI 131072
SF 75.4677190 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.00
Si(CH3)3
HO
ppm
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140

145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PROCNO 1
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Time 17.09
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PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559039 sec
RG 90.5
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 dB
SFO1 399.9528000 MHz
F2 - Processing parameters
SI 32768
SF 399.9500000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00
ppm
16.14
11.35
0.35
3.16
0.97
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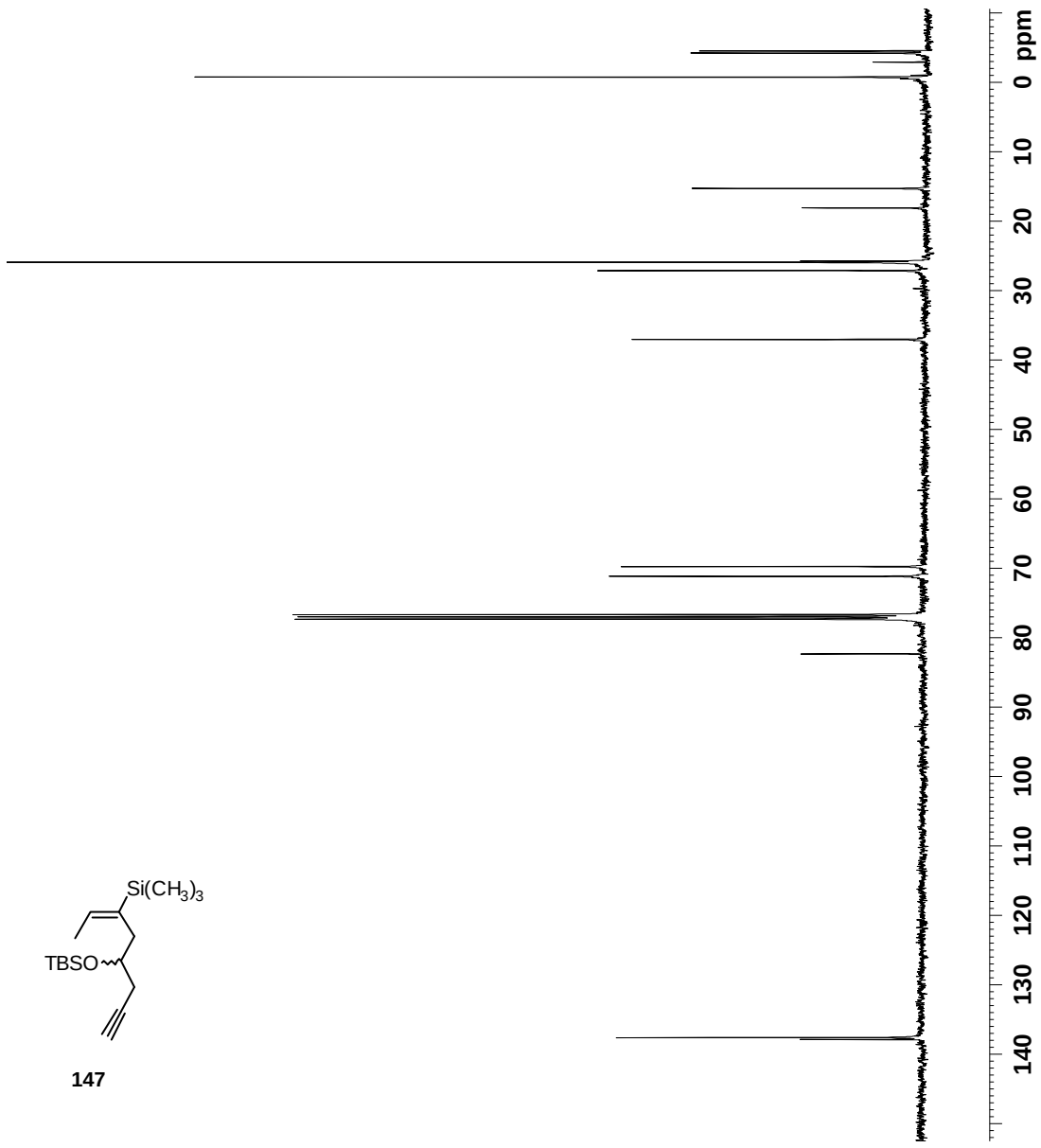
0.74
0.76
1.39
1.04
1.00
1.00
Si(CH3)3
TBSO

147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Time_ 19.05
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PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 2450
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3041664 sec
RG 16384
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
SFO1 100.5785700 MHz
NUC1 13C
P1 7.80 usec
PLW1 -1.00000000 W
SFO2 399.9516000 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 135.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 32768
SF 100.5675080 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
Si(CH3)3
TBSO
147
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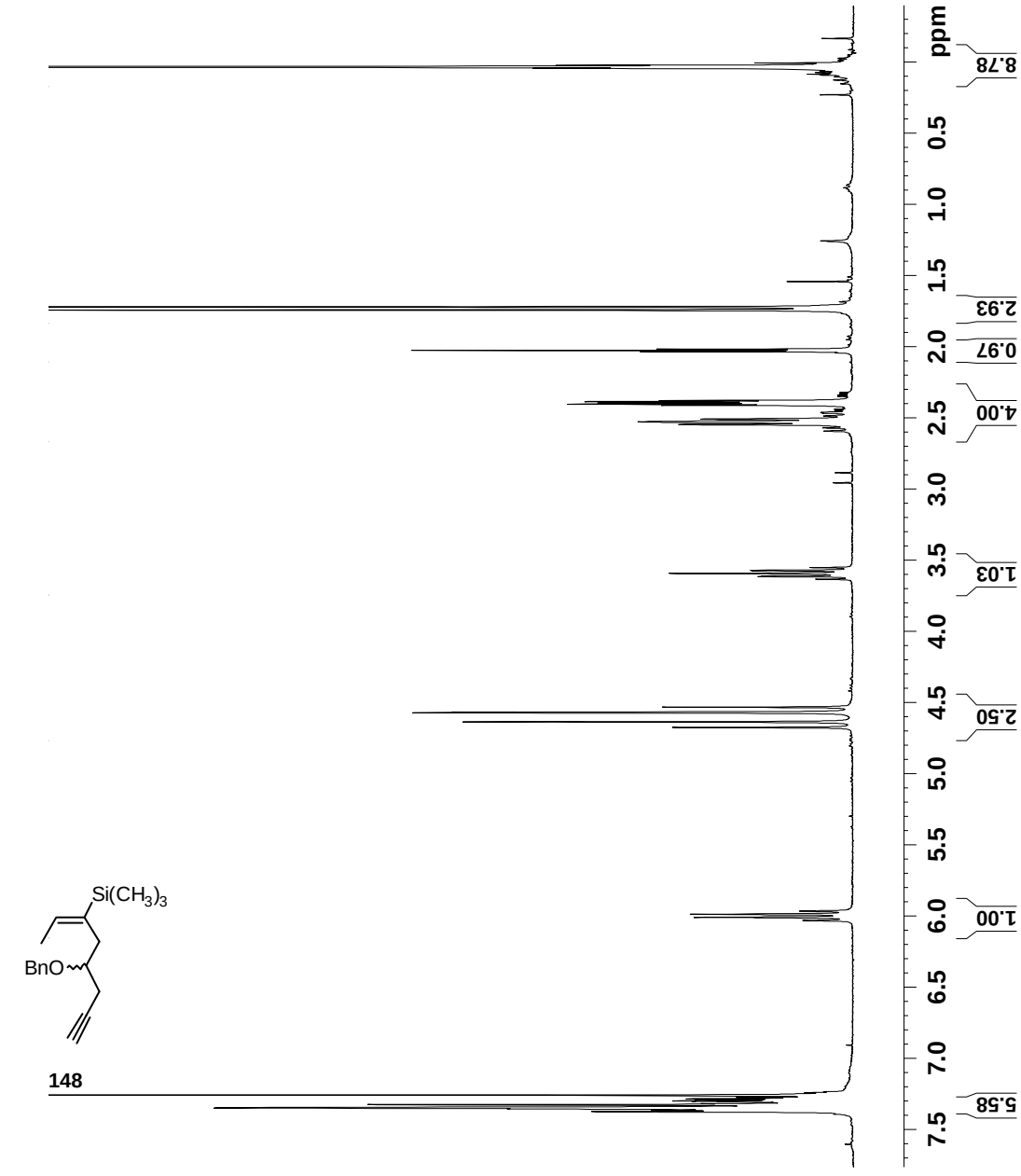
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PROCNO 1
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PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4496.403 Hz
FIDRES 0.137219 Hz
AQ 3.6438017 sec
RG 574.7
DW 111.200 usec
DE 6.00 usec
TE 300.0 K
D1 1.50000000 sec
========== CHANNEL f1 ==========
NUC1 1H
P1 8.20 usec
PL1 -3.00 dB
SFO1 300.1319000 MHz
F2 - Processing parameters
SI 32768
SF 300.1300063 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
Si(CH3)3
BnO
148
8.78
2.93
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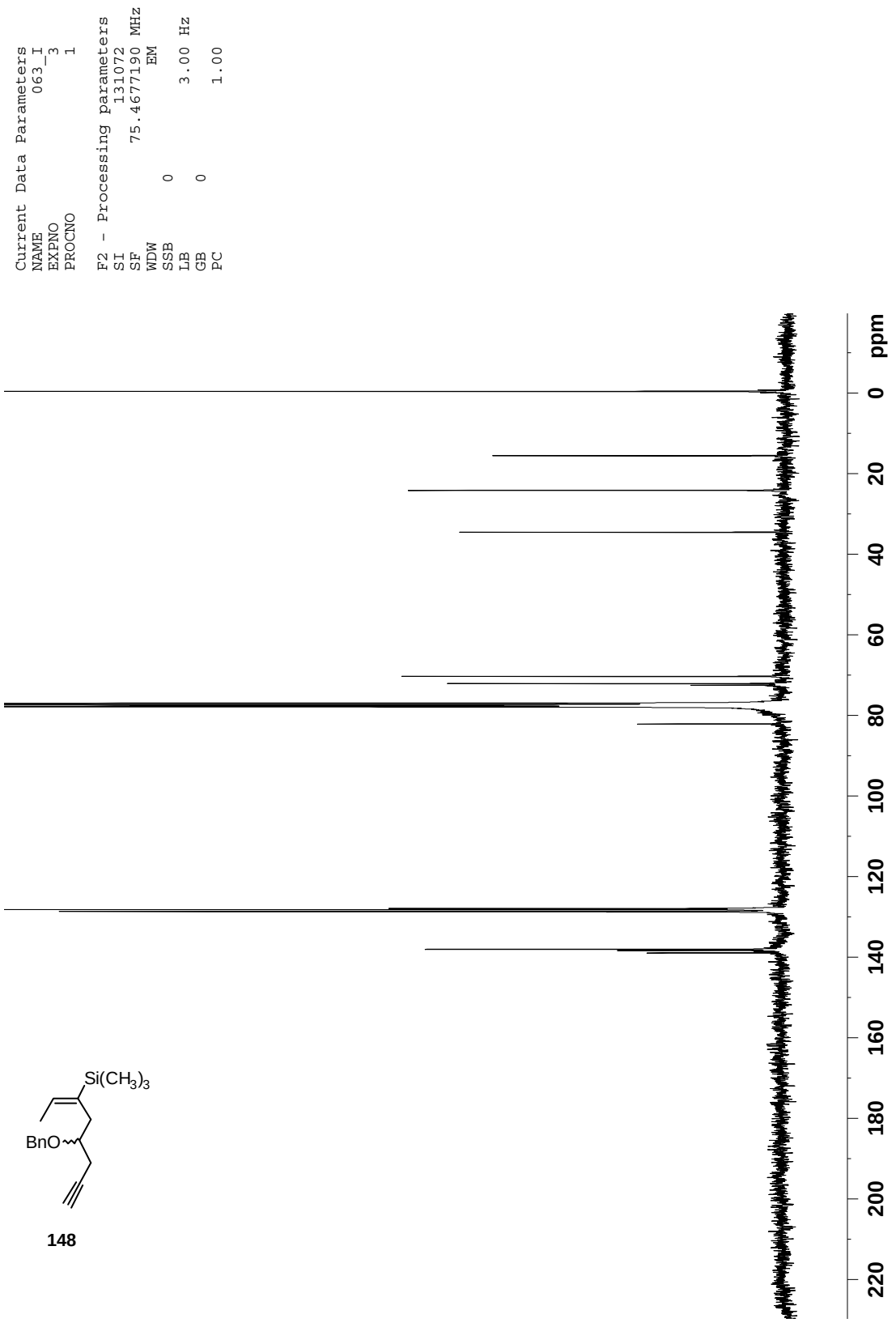
4.00
1.03
2.50
1.00
5.58
ppm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PROCNO 1
F2 - Processing parameters
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SF 75.4677190 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.00
Si(CH3)3
BnO
ppm
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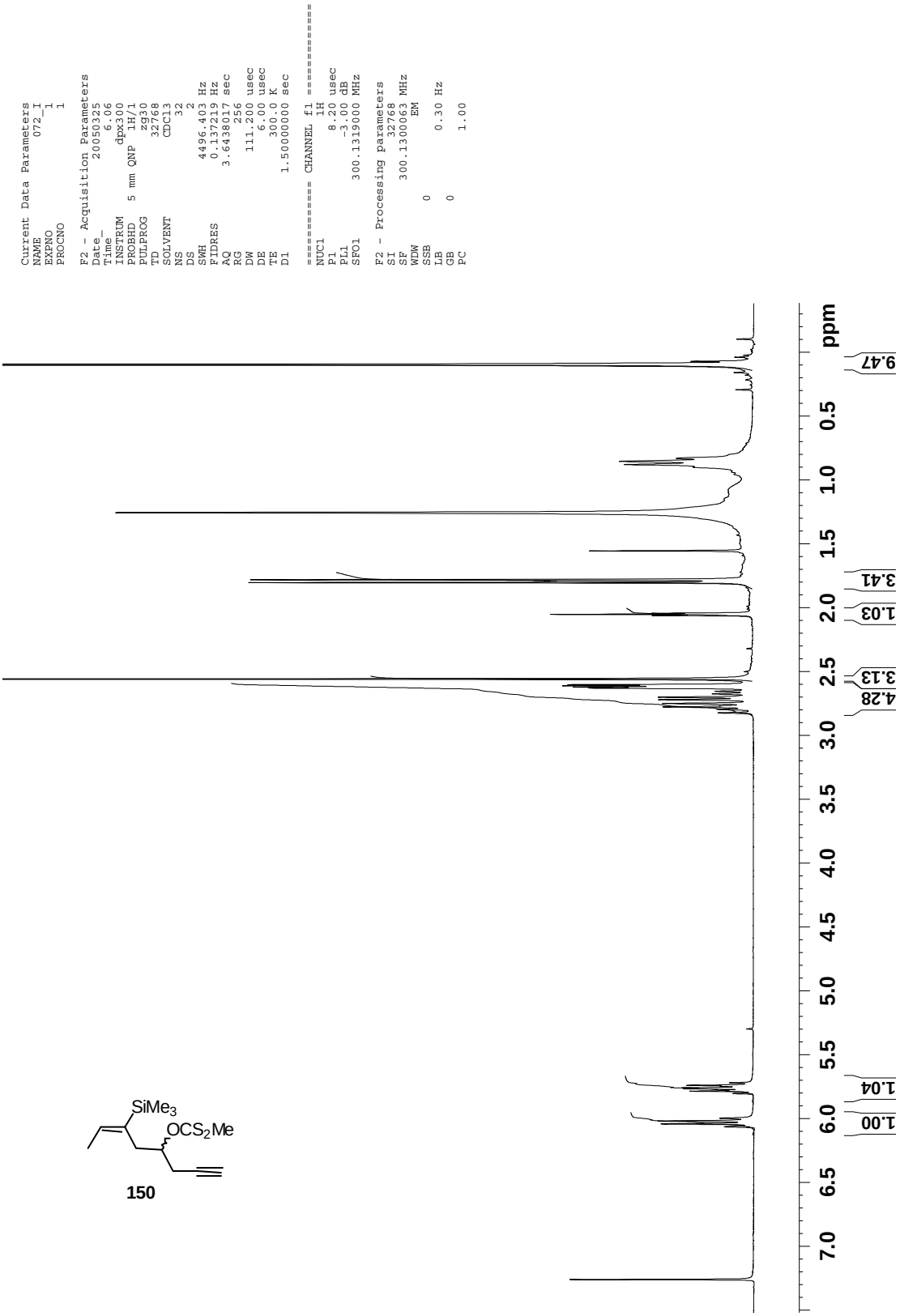
40
60
80
100
120
140
160
180
200
220

148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PROCNO 1
F2 - Acquisition Parameters
Date_ 20050325
Time_ 6.06
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PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4496.403 Hz
FIDRES 0.137219 Hz
AQ 3.6438017 sec
RG 256
DW 111.200 usec
DE 6.00 usec
TE 300.0 K
D1 1.50000000 sec
========== CHANNEL f1 ==========
NUC1 1H
P1 8.20 usec
PL1 -3.00 dB
SFO1 300.1319000 MHz
F2 - Processing parameters
SI 32768
SF 300.1300063 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
ppm
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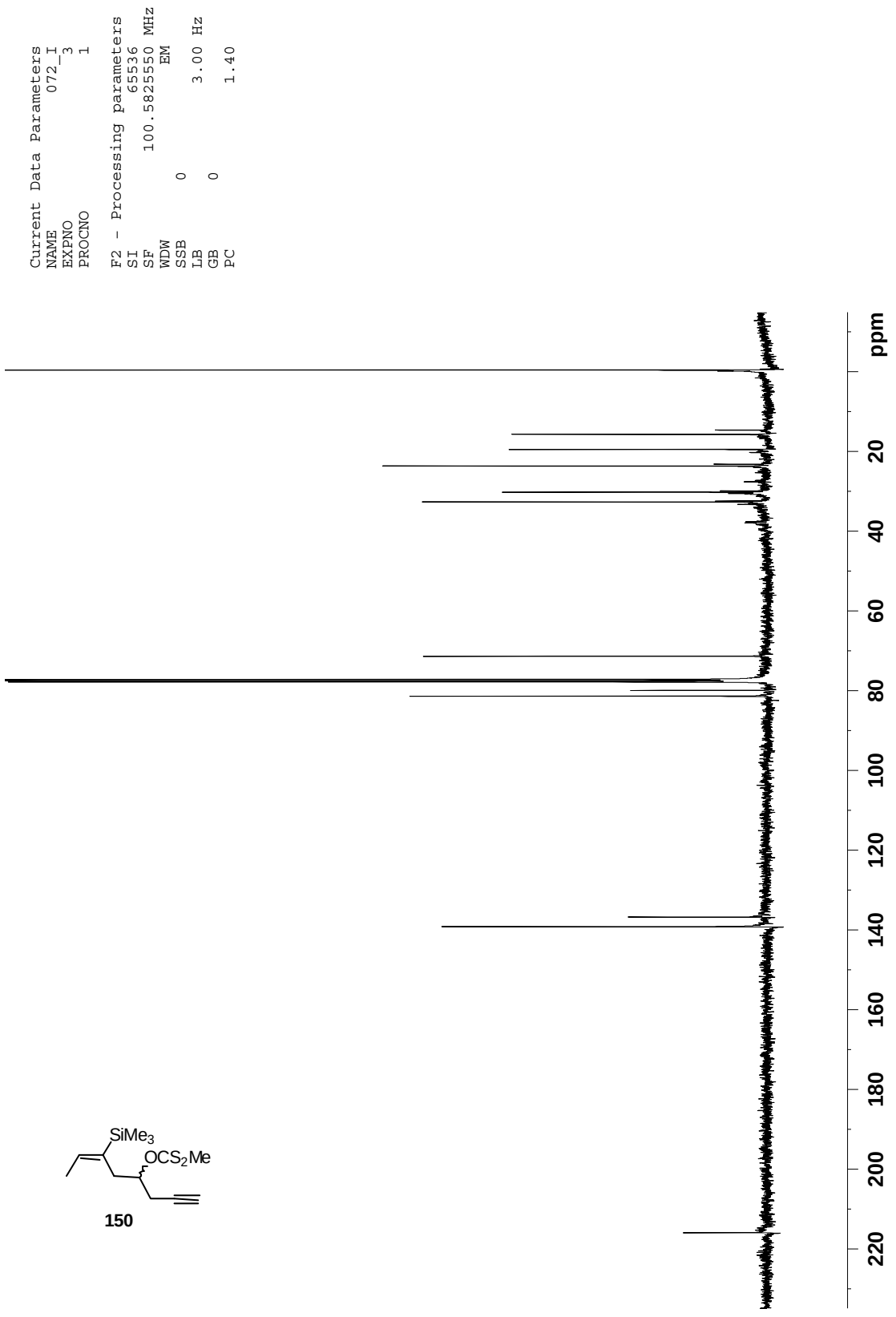
3.41
1.03
3.13
4.28
1.04
1.00
SiMe3
OCS2Me
150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EXPNO 3
PROCNO 1
F2 - Processing parameters
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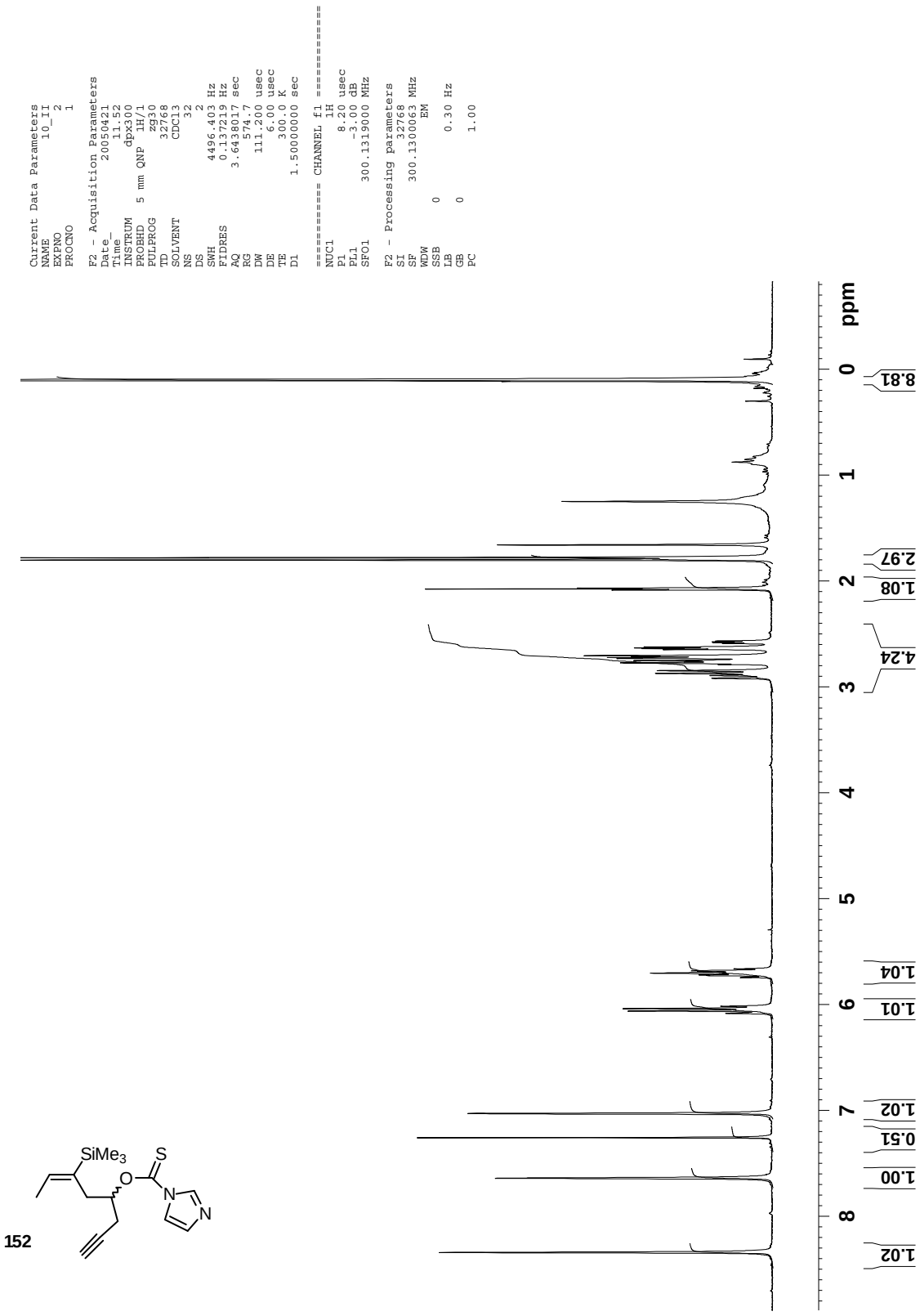
SF 100.5825550 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
ppm
220
200
180
160
140
120
100
80
60
40
20
SiMe3
OCS2Me

150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EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
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Time_ 11.52
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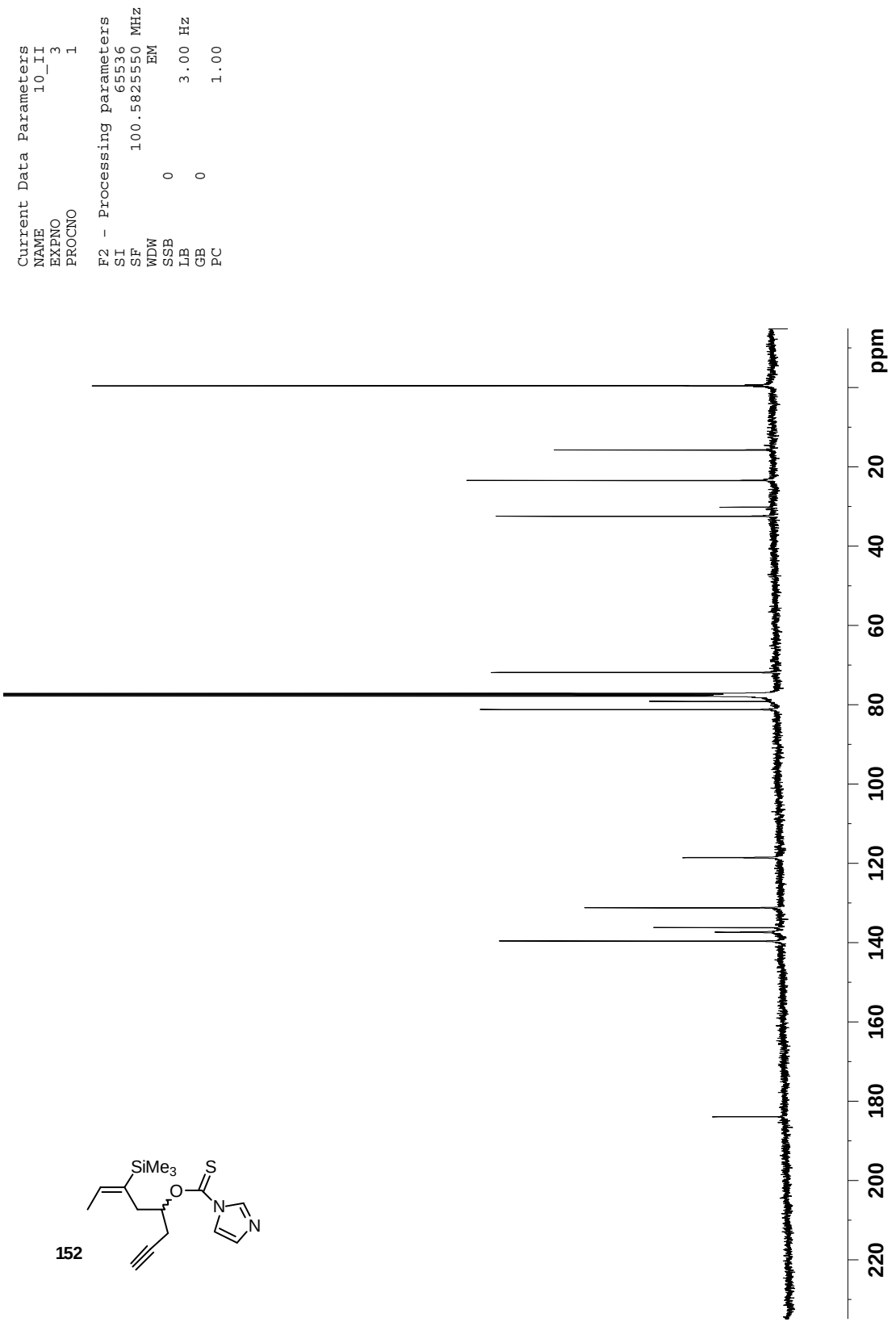
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4496.403 Hz
FIDRES 0.137219 Hz
AQ 3.6438017 sec
RG 574.7
DW 111.200 usec
DE 6.00 usec
TE 300.0 K
D1 1.50000000 sec
========== CHANNEL f1 ==========
NUC1 1H
P1 8.20 usec
PL1 -3.00 dB
SFO1 300.1319000 MHz
F2 - Processing parameters
SI 32768
SF 300.1300063 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
ppm
0
1
2
3
4
5
6
7
8
8.81
2.97
1.08
4.24
1.04
1.01
1.02
0.51
1.00
1.02
SiMe3
S
O
N
N

152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PROCNO 1
F2 - Processing parameters
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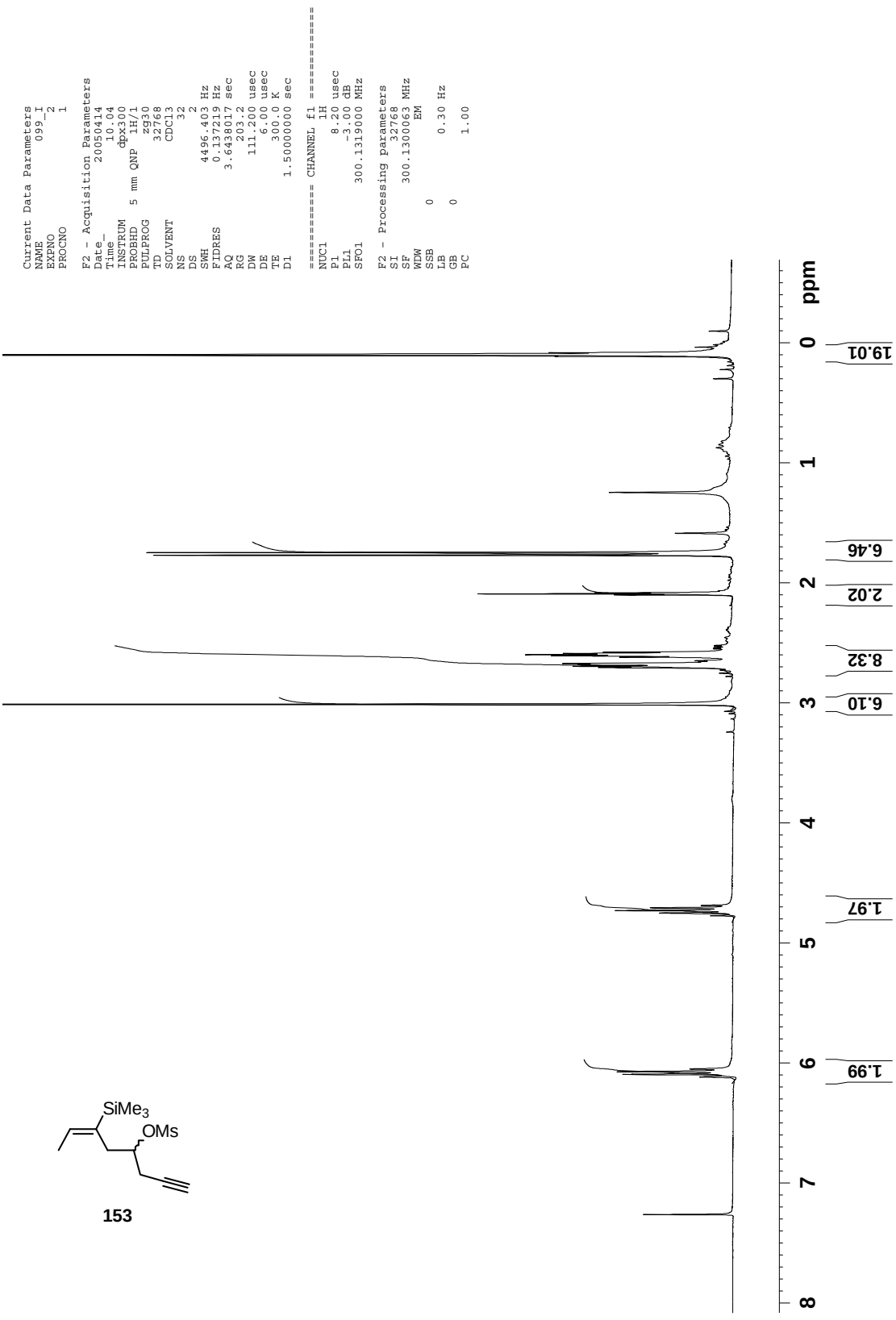
SF 100.5825550 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.00
ppm
20
40
60
80
100
120
140
160
180
200
220
SiMe3
S
O
N
N

152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EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
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Time_ 10.04
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PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4496.403 Hz
FIDRES 0.137219 Hz
AQ 3.6438017 sec
RG 203.2
DW 111.200 usec
DE 6.00 usec
TE 300.0 K
D1 1.50000000 sec
========== CHANNEL f1 ==========
NUC1 1H
P1 8.20 usec
PL1 -3.00 dB
SFO1 300.1319000 MHz
F2 - Processing parameters
SI 32768
SF 300.1300063 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
ppm
0
1
2
3
4
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6
7
8
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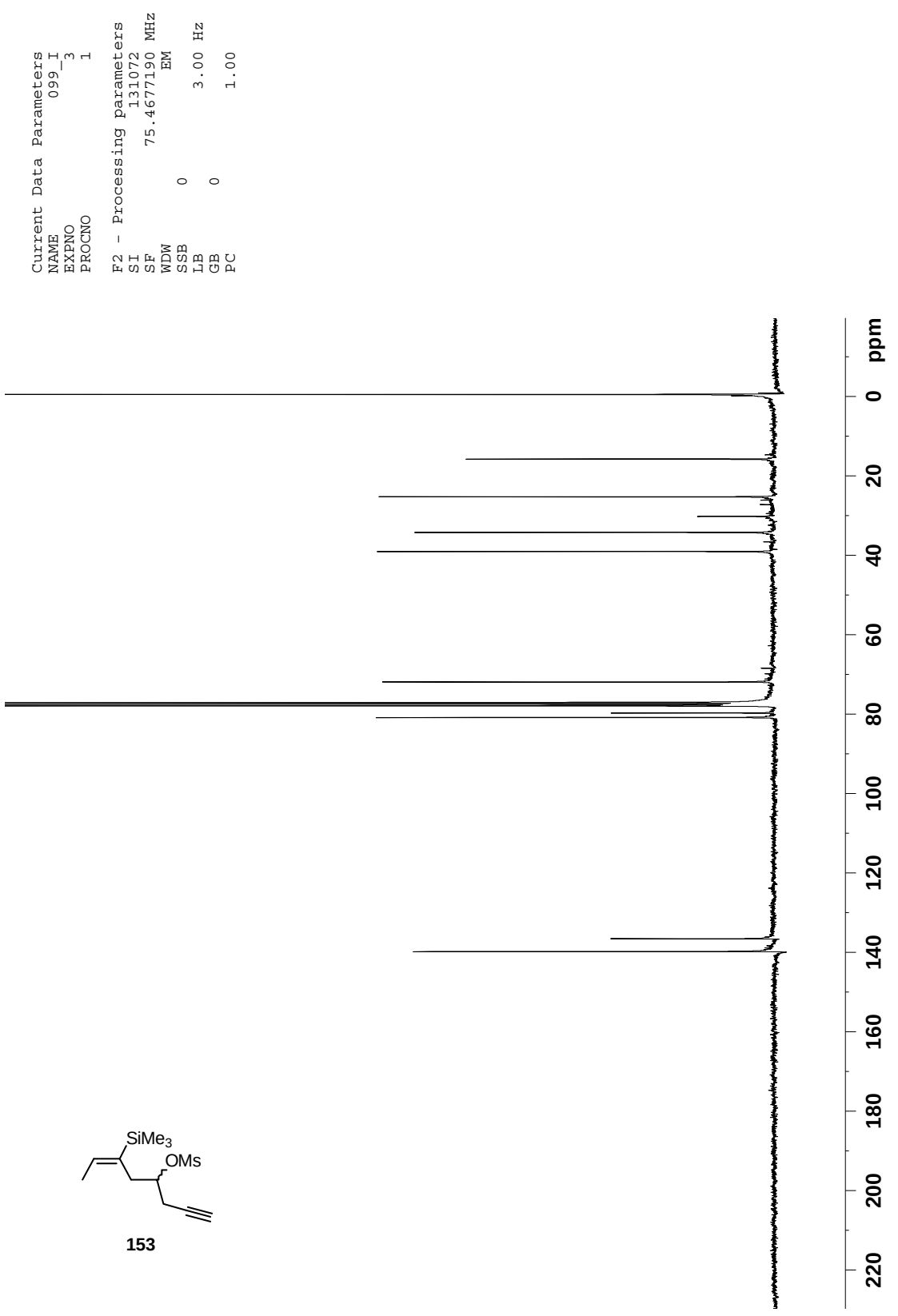
6.46
2.02
8.32
6.10
1.97
1.99
SiMe3
OMs

153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PROCNO 1
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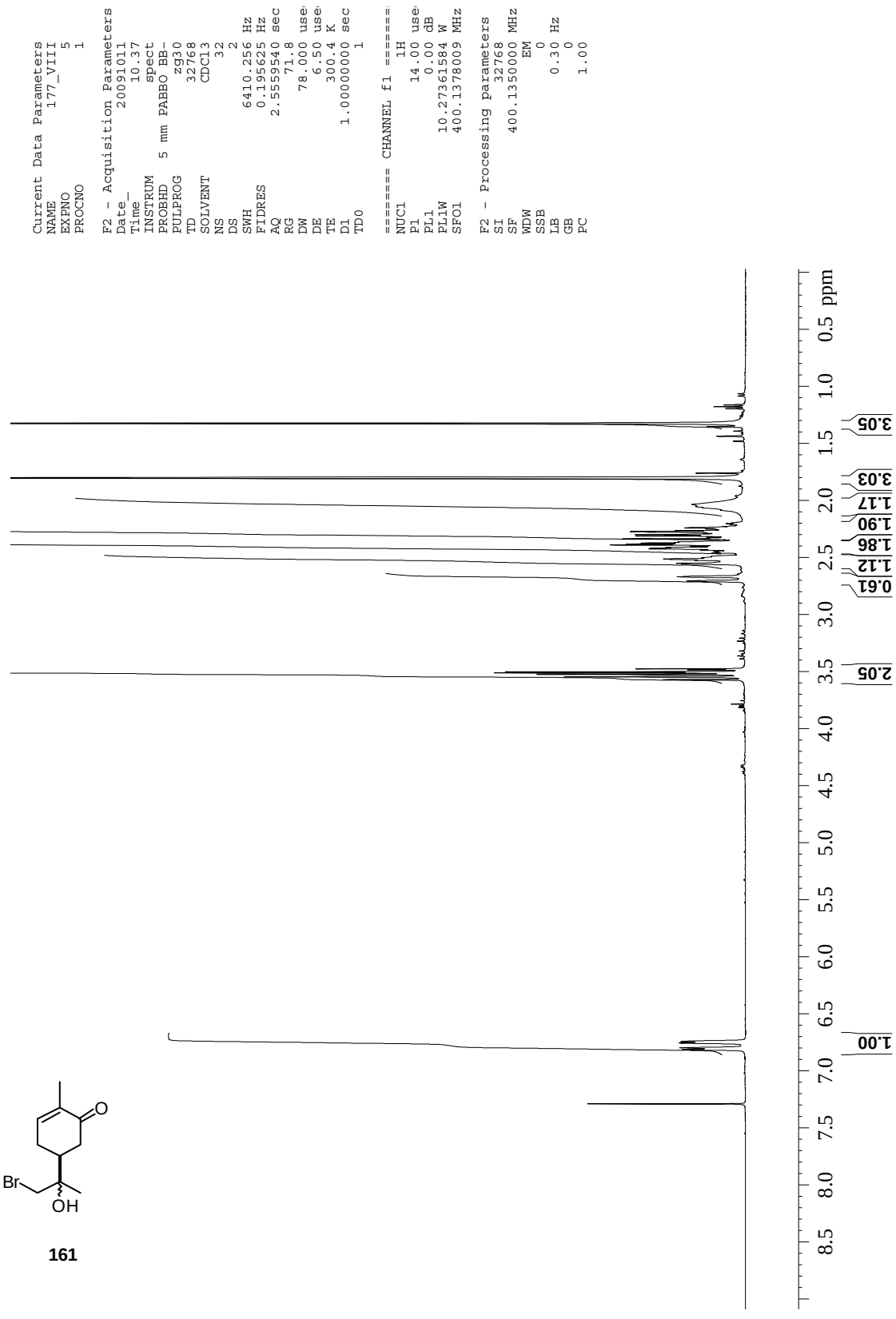
SF 75.4677190 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.00
SiMe3
OMs
ppm
0
20
40
60
80
100
120
140
160
180
200
220

153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EXPNO 5
PROCNO 1
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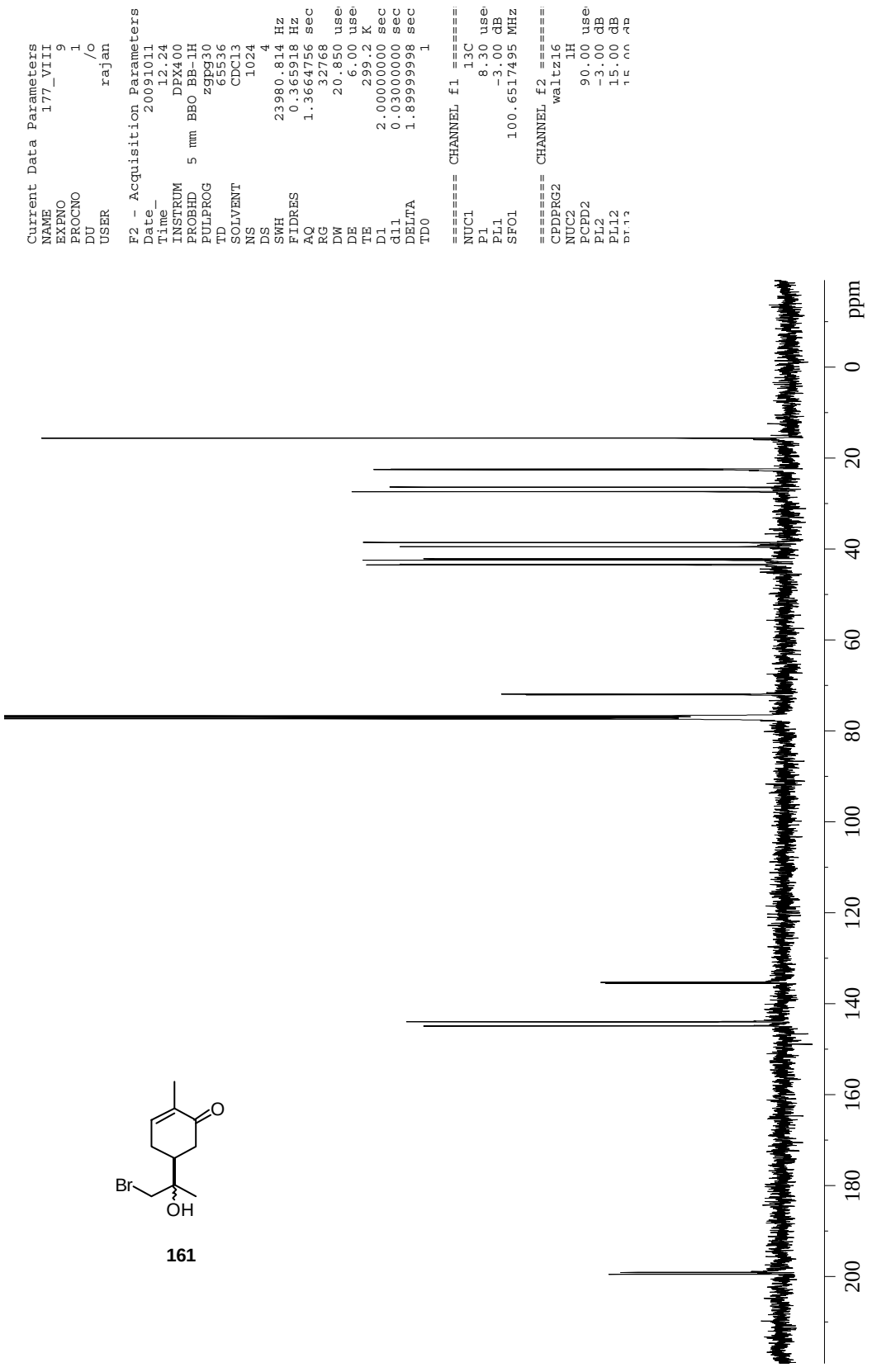
Date_ 20091011
Time_ 10.37
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 71.8
DW 78.000 use
DE 6.50 use
TE 300.4 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 use
PL1 0.00 dB
PL1W 10.27361584 W
SFO1 400.1378009 MHz
F2 - Processing parameters
SI 32768
SF 400.1350000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
3.05
3.03
1.17
1.90
1.86
1.12
0.61
2.05
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
Br
OH
O

161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NAME 177_VIII
EXPNO 9
PROCNO 1
DU /o
USER rajan
F2 - Acquisition Parameters
Date_ 20091011
Time 12.24
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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 use
DE 6.00 use
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 use
PL1 -3.00 dB
SFO1 100.6517495 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 use
PL2 -3.00 dB
PL12 15.00 dB
ppm
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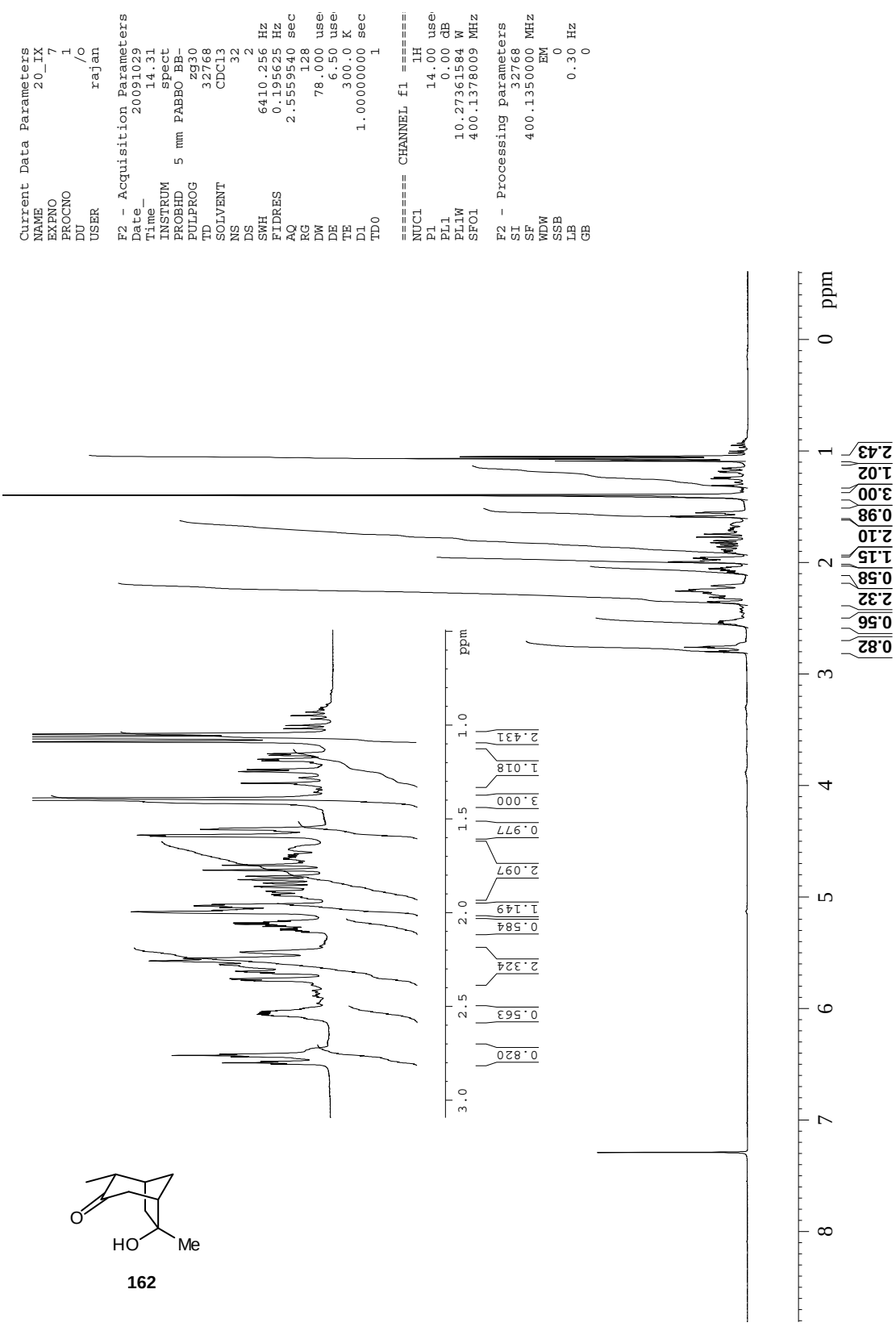
20
40
60
80
100
120
140
160
180
200
Br
OH
O

161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EXPNO 7
PROCNO 1
DU /o
USER rajan
F2 - Acquisition Parameters
Date_ 20091029
Time_ 14.31
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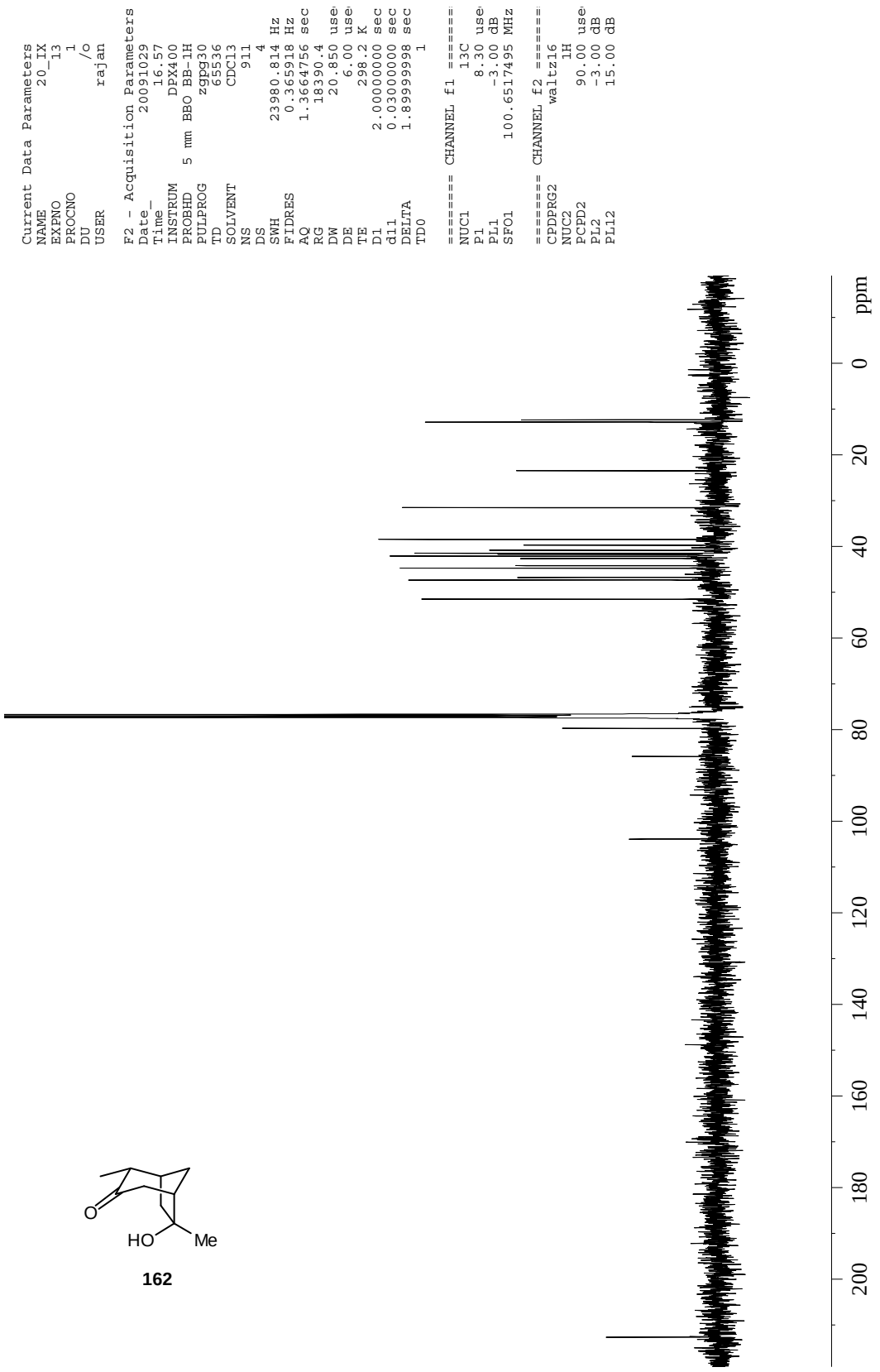
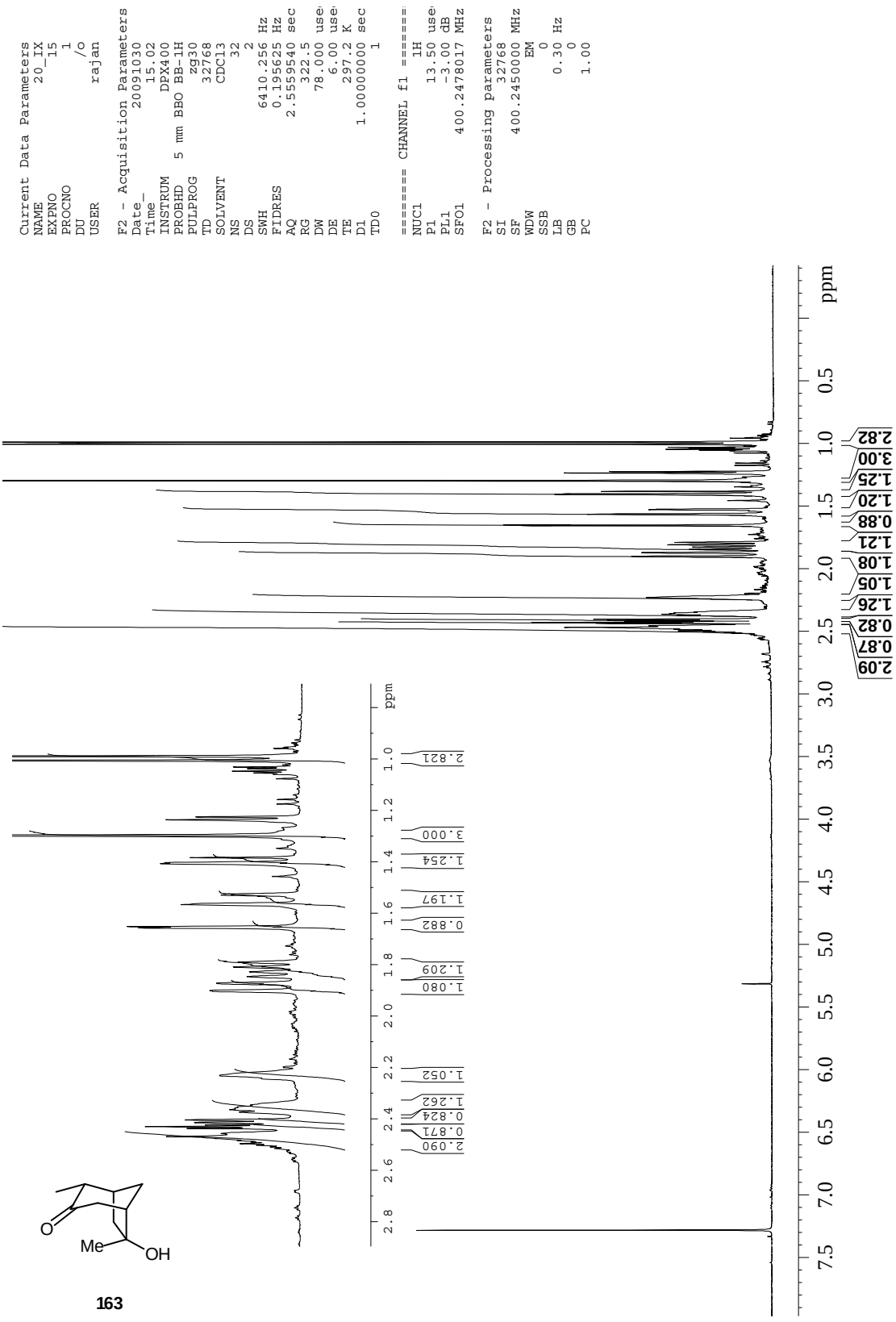
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 128
DW 78.000 use
DE 6.50 use
TE 300.0 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 use
PL1 0.00 dB
PL1W 10.27361584 W
SFO1 400.13780009 MHz
F2 - Processing parameters
SI 32768
SF 400.1350000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
0.82
0.56
2.32
0.58
1.15
2.10
0.98
3.00
1.02
2.43
0.820
0.563
2.324
0.584
1.149
2.097
0.977
3.000
1.018
2.431
ppm
O
HO
Me

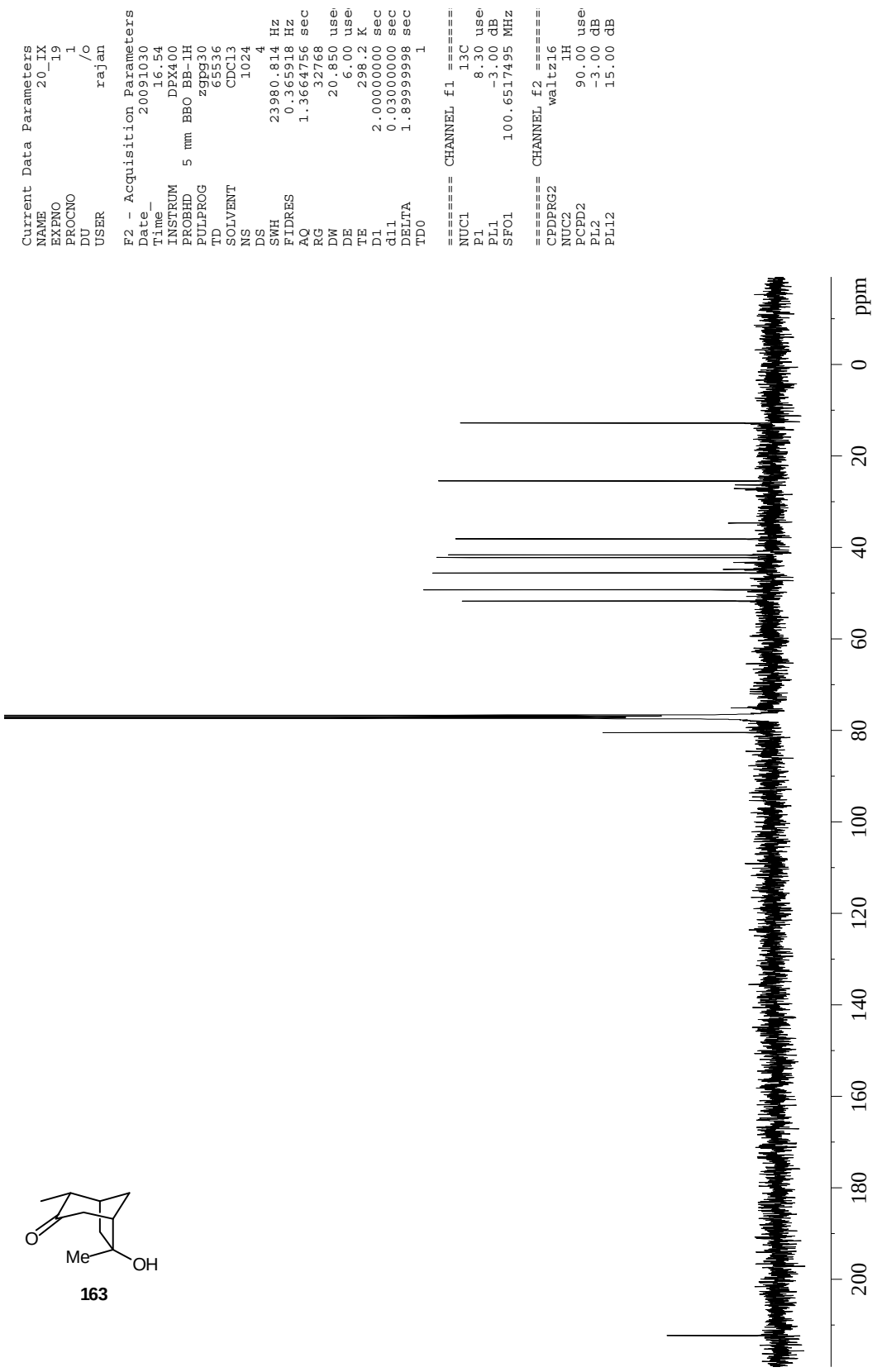
162


Current Data Parameters
NAME 20_IX
EXPNO 13
PROCNO 1
DU /o
USER rajan
F2 - Acquisition Parameters
Date_ 20091029
Time_ 16.57
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 911
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 18390.4
DW 20.850 use
DE 6.00 use
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 use
PL1 -3.00 dB
SFO1 100.6517495 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 use
PL2 -3.00 dB
PL12 15.00 dB
200
180
160
140
120
100
80
60
40
20
0
ppm
O
HO
Me

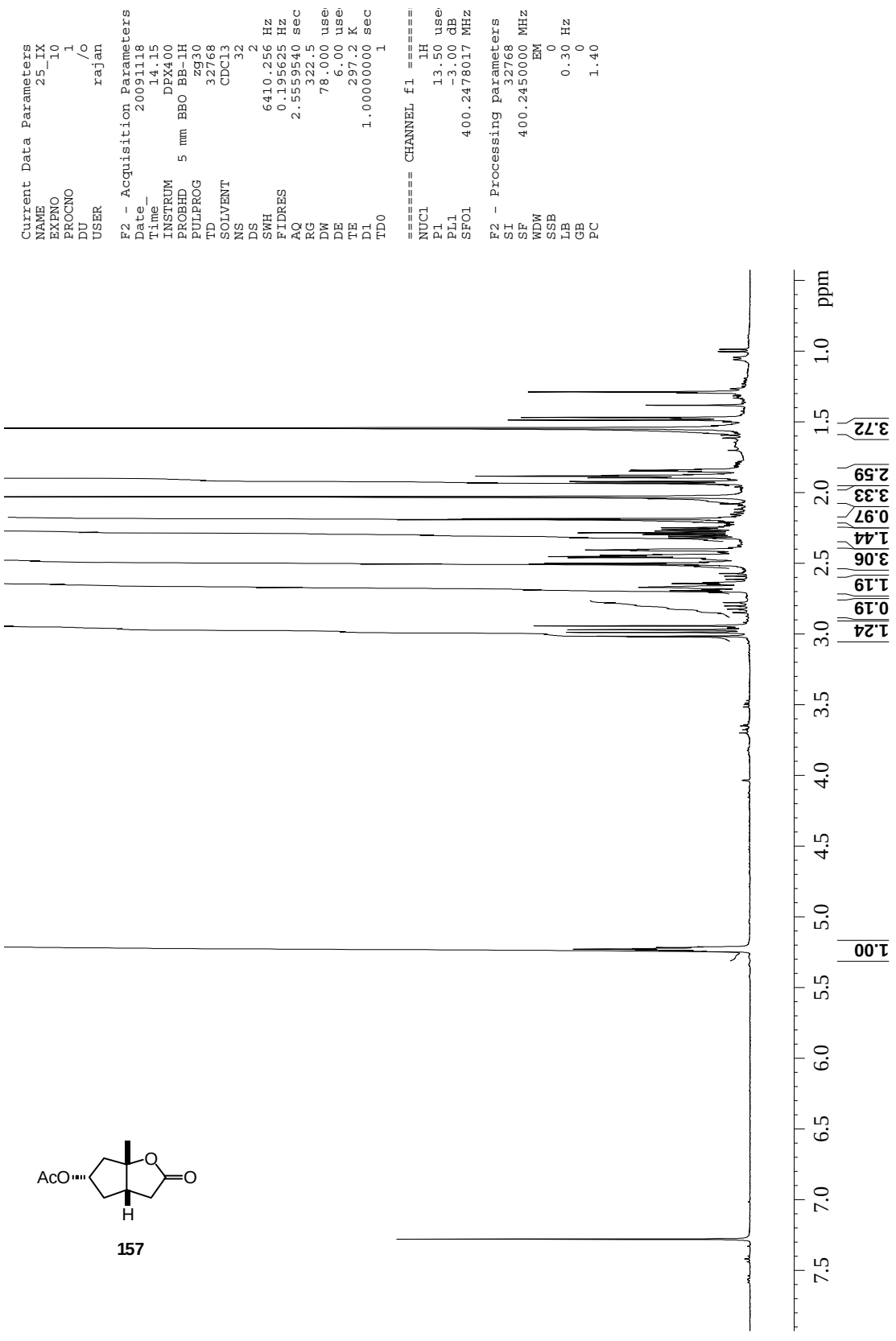
162


Current Data Parameters
NAME 20_IX
EXPNO 15
PROCNO 1
DU /o
USER rajan
F2 - Acquisition Parameters
Date_ 20091030
Time_ 15.02
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 sec
RG 322.5
DW 78.000 use
DE 6.00 use
TE 297.2 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.50 use
PL1 -3.00 dB
SFO1 400.2478017 MHz
F2 - Processing parameters
SI 32768
SF 400.2450000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
2.09
0.87
0.82
1.26
1.05
1.08
1.21
0.88
1.20
1.25
3.00
2.82
2.821
3.000
1.254
1.197
0.882
1.209
1.080
1.052
1.262
0.824
0.871
2.090
ppm
O
Me
OH

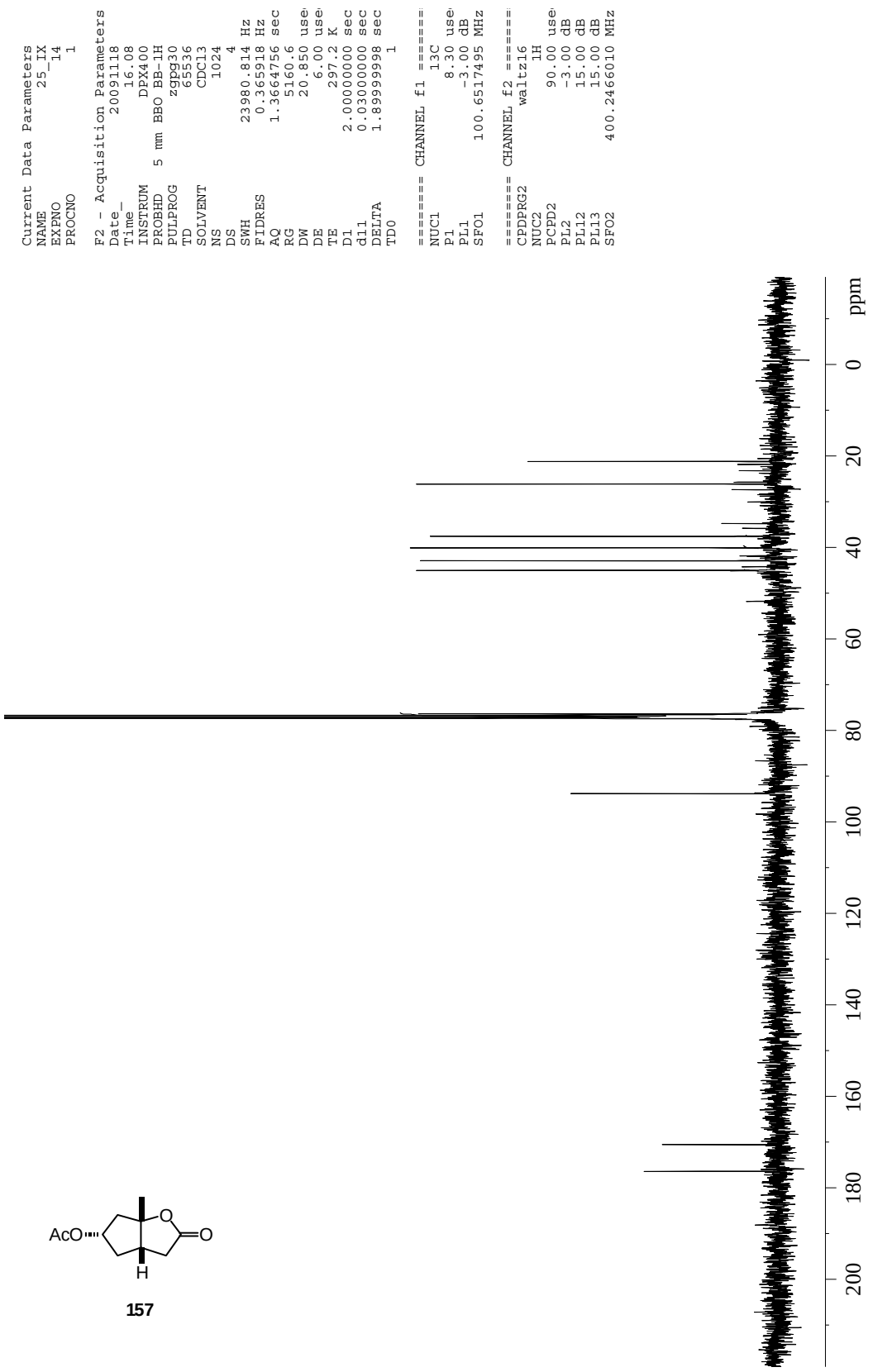
163


Current Data Parameters
NAME 20_IX
EXPNO 19
PROCNO 1
DU /o
USER rajan
F2 - Acquisition Parameters
Date_ 20091030
Time_ 16.54
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 use
DE 6.00 use
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 use
PL1 -3.00 dB
SFO1 100.6517495 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 use
PL2 -3.00 dB
PL12 15.00 dB
200
180
160
140
120
100
80
60
40
20
0
ppm
O
Me
OH

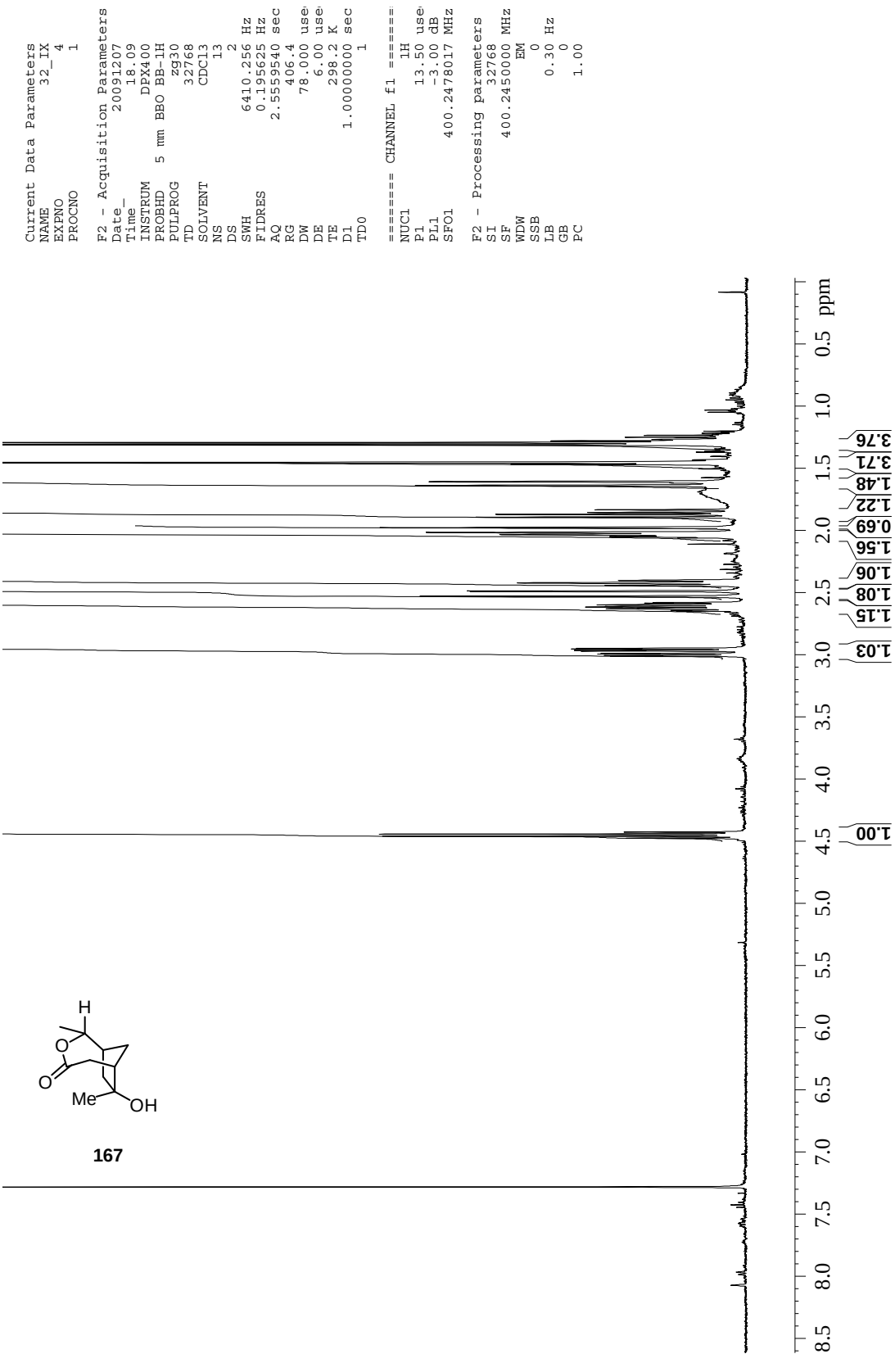
163


Current Data Parameters
NAME 25_IX
EXPNO 10
PROCNO 1
DU /o
USER rajan
F2 - Acquisition Parameters
Date_ 20091118
Time_ 14.15
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDC13
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 322.5
DW 78.000 use
DE 6.00 use
TE 297.2 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.50 use
PL1 -3.00 dB
SFO1 400.2478017 MHz
F2 - Processing parameters
SI 32768
SF 400.2450000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40
3.72
2.59
3.33
0.97
1.44
3.06
1.19
0.19
1.24
1.00
ppm
AcO
O
O
H

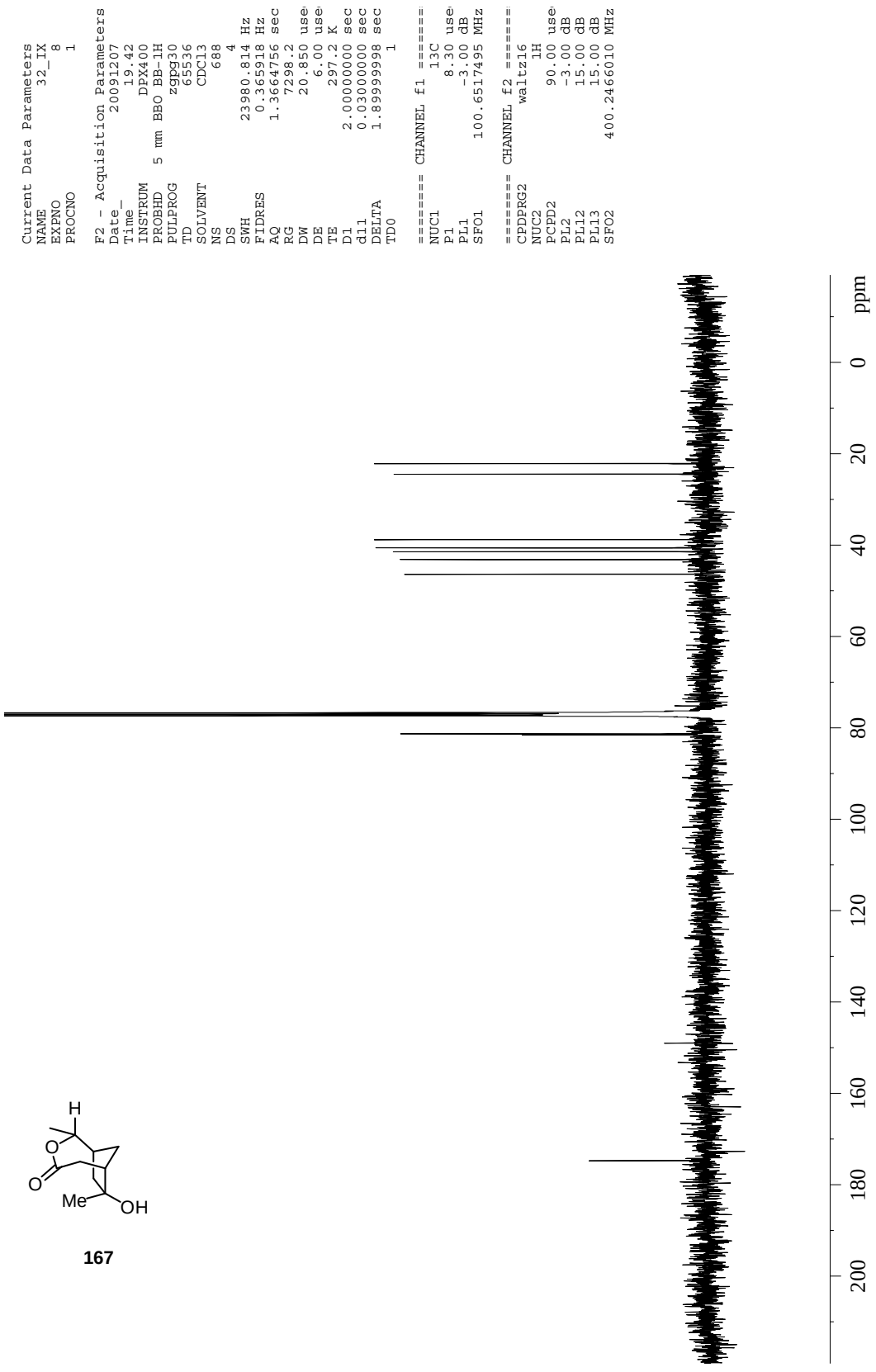
157


Current Data Parameters
NAME 25_IX
EXPNO 14
PROCNO 1
F2 - Acquisition Parameters
Date_ 20091118
Time 16.08
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 5160.6
DW 20.850 use
DE 6.00 use
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 use
PL1 -3.00 dB
SFO1 100.6517495 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 use
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2466010 MHz
ppm
0
20
40
60
80
100
120
140
160
180
200
AcO
O
O
H

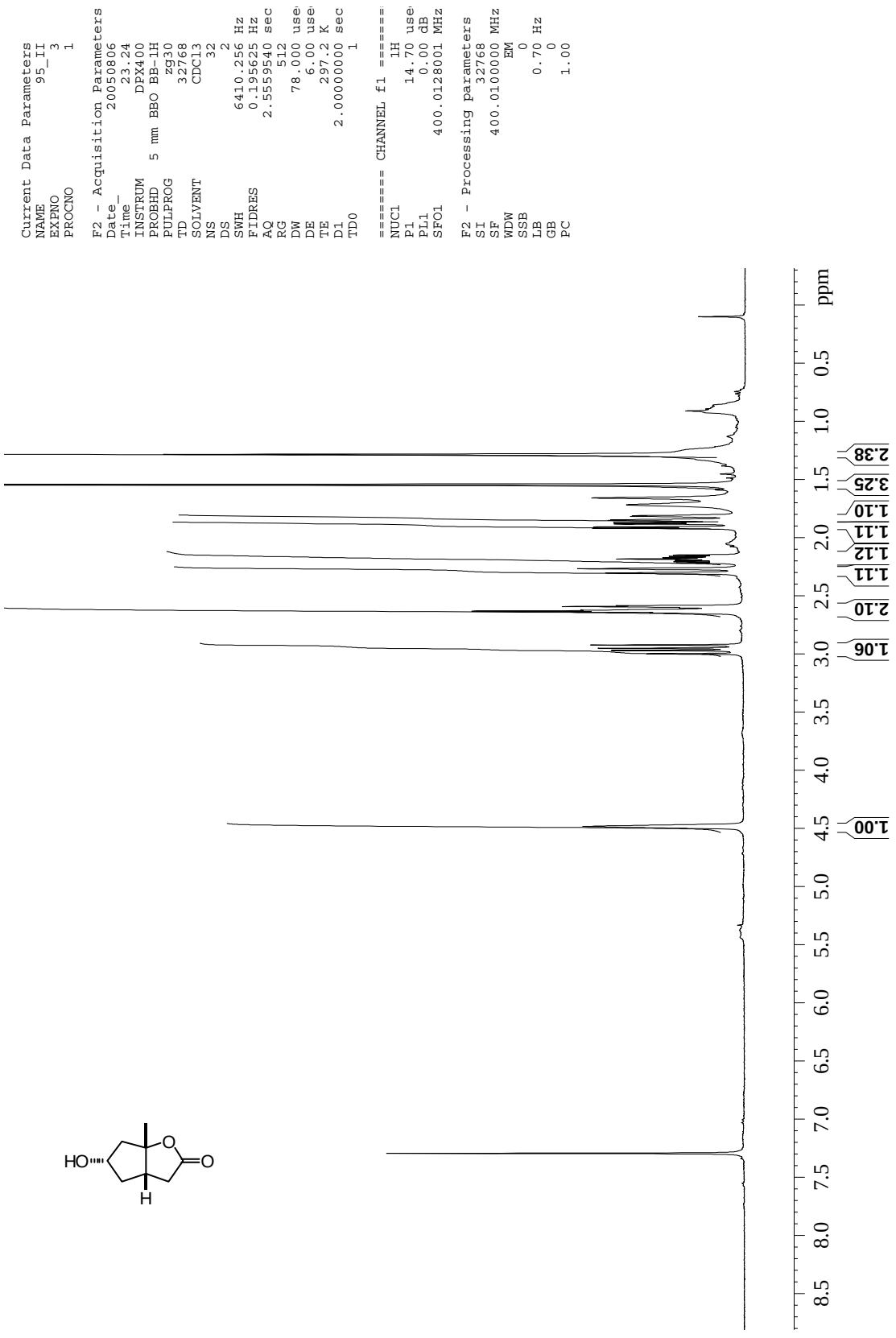
157

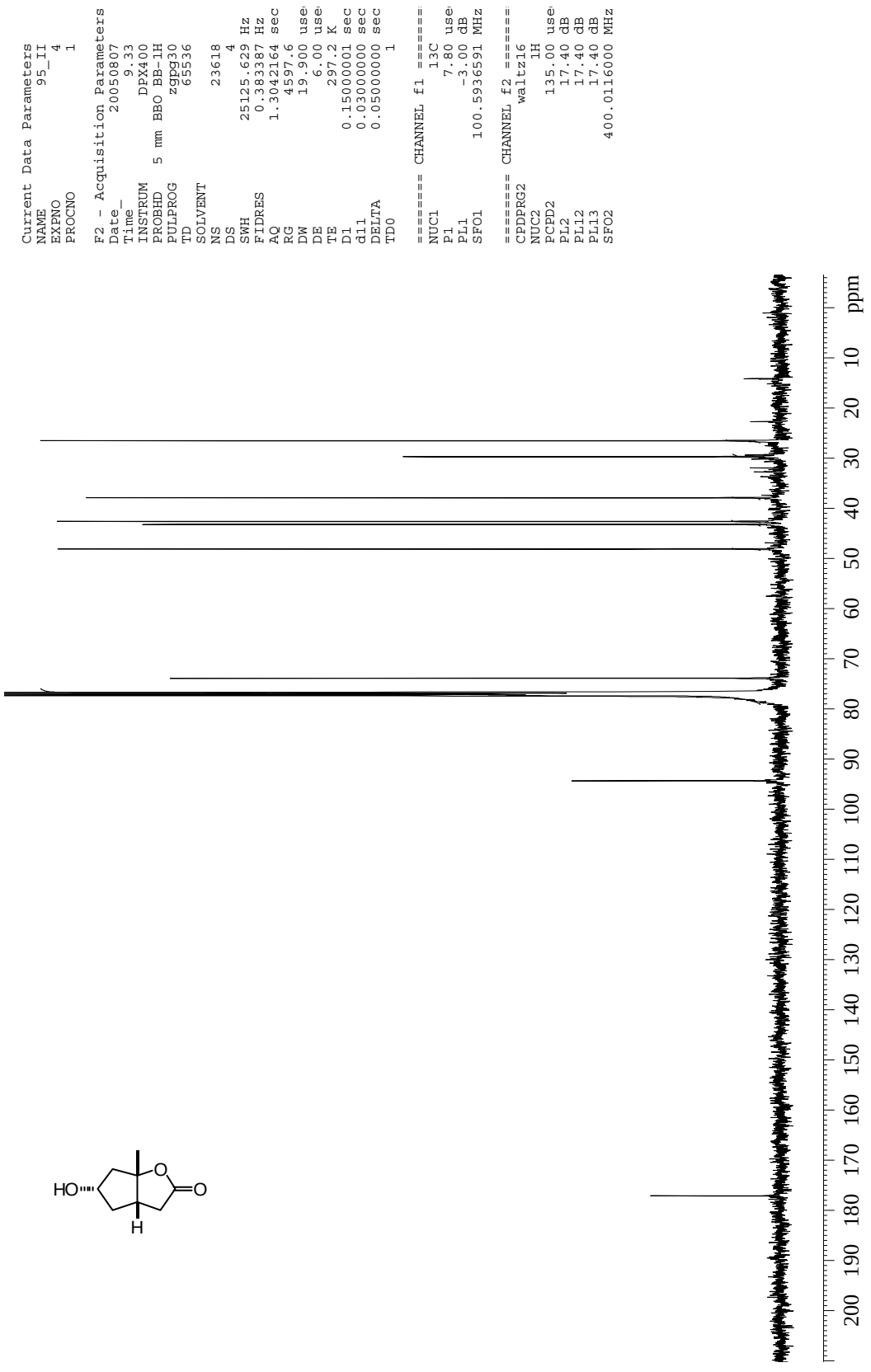

Current Data Parameters
NAME 32_IX
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20091207
Time_ 18.09
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDC13
NS 2
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 406.4
DW 78.000 use
DE 6.00 use
TE 298.2 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.50 use
PL1 -3.00 dB
SFO1 400.2478017 MHz
F2 - Processing parameters
SI 32768
SF 400.2450000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1.00
1.03
1.15
1.08
1.06
1.56
0.69
1.22
1.48
3.71
3.76
ppm
H
O
O
Me
OH

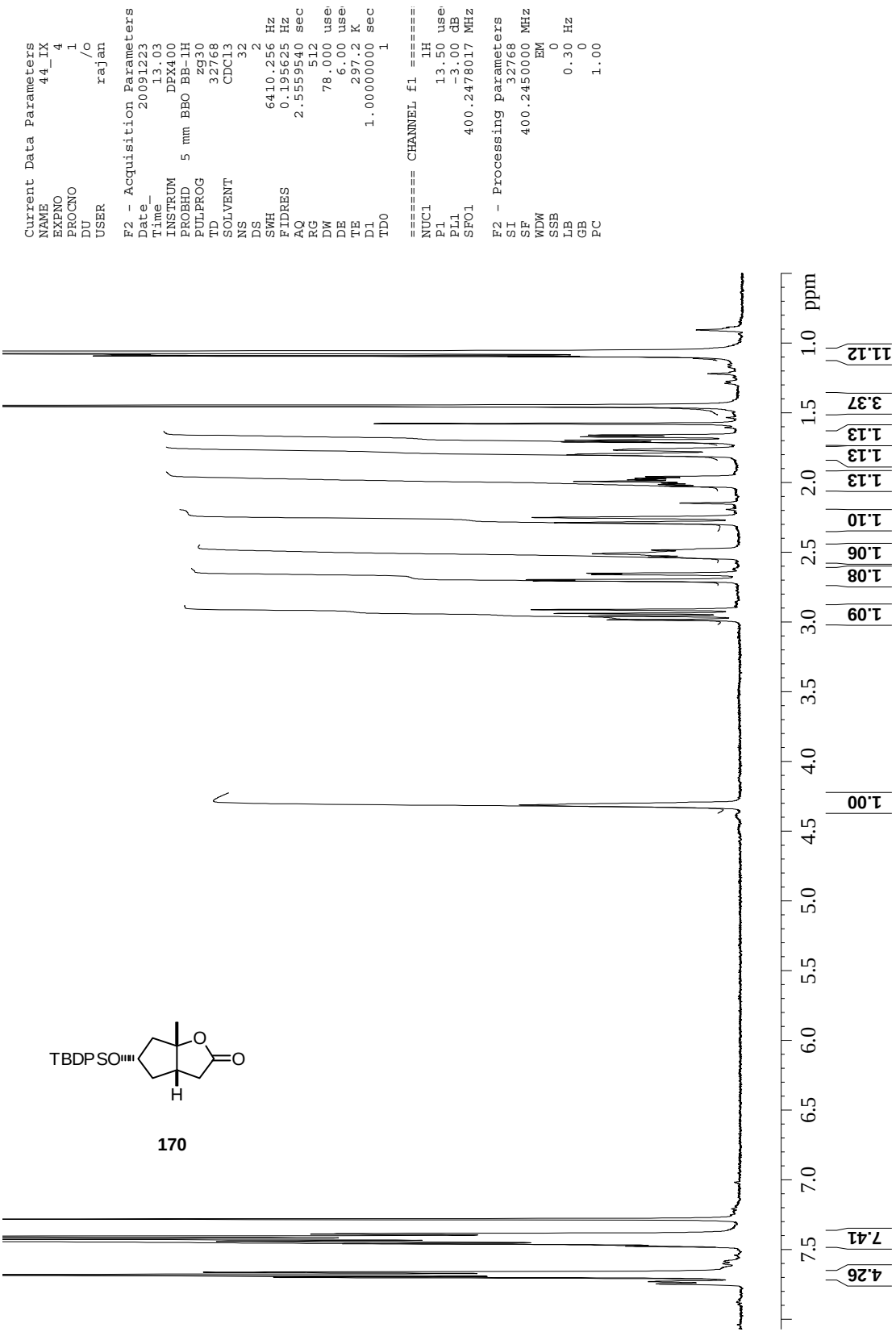
167

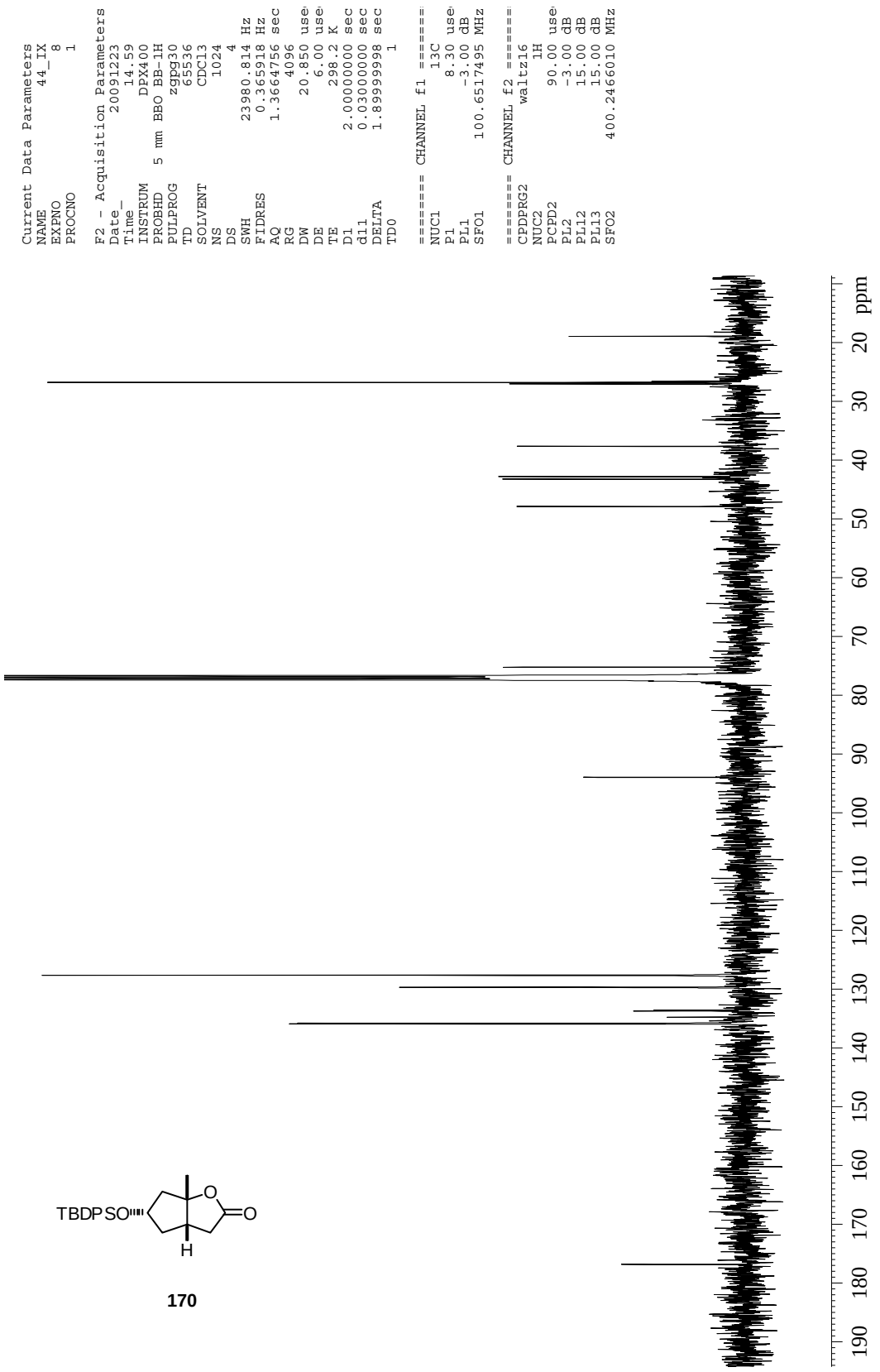

Current Data Parameters
NAME 32_IX
EXPNO 8
PROCNO 1
F2 - Acquisition Parameters
Date_ 20091207
Time 19.42
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 688
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 7298.2
DW 20.850 use
DE 6.00 use
TE 297.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.30 use
PL1 -3.00 dB
SFO1 100.6517495 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 use
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2466010 MHz
200
180
160
140
120
100
80
60
40
20
0
ppm
H
O
O
Me
OH

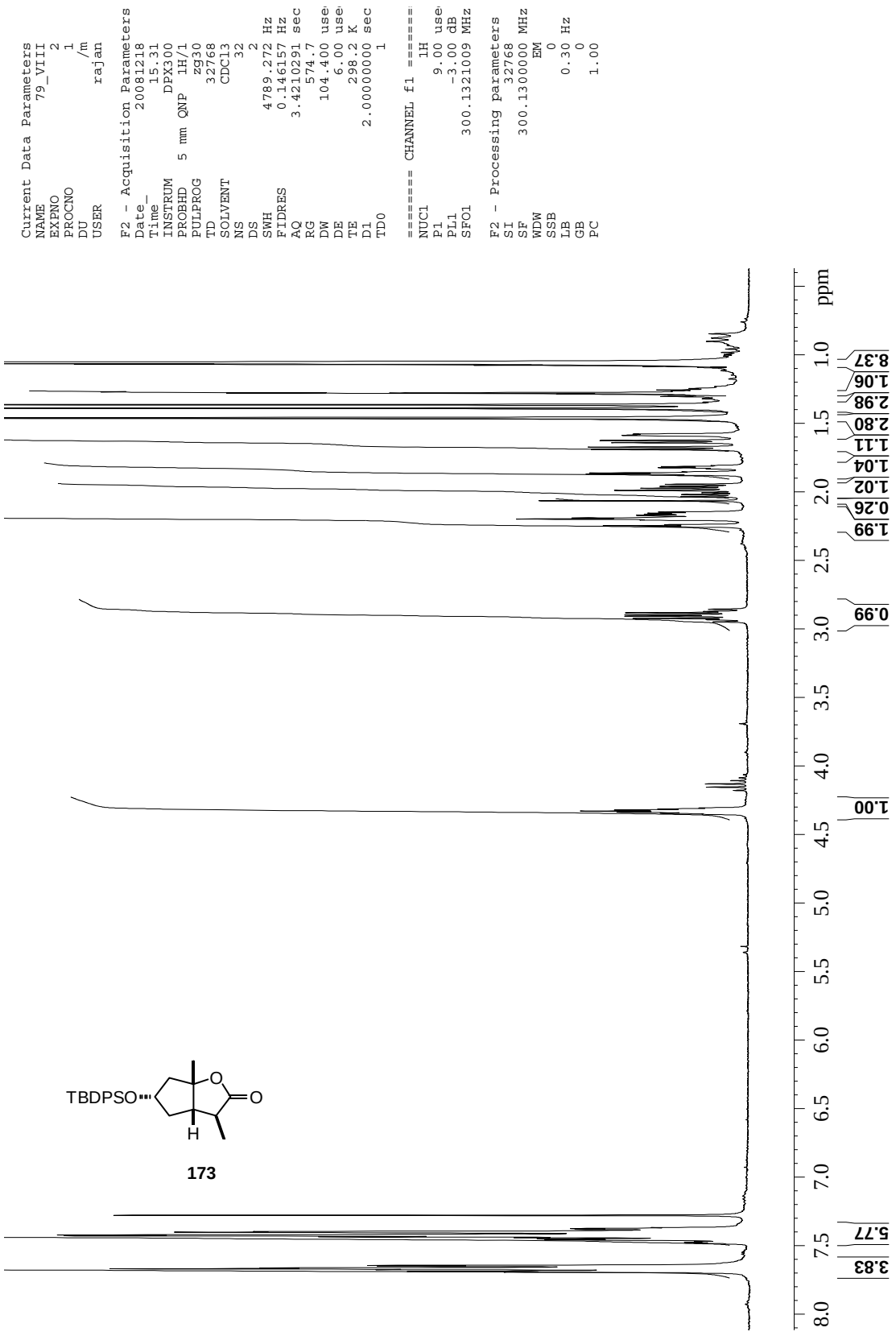
167

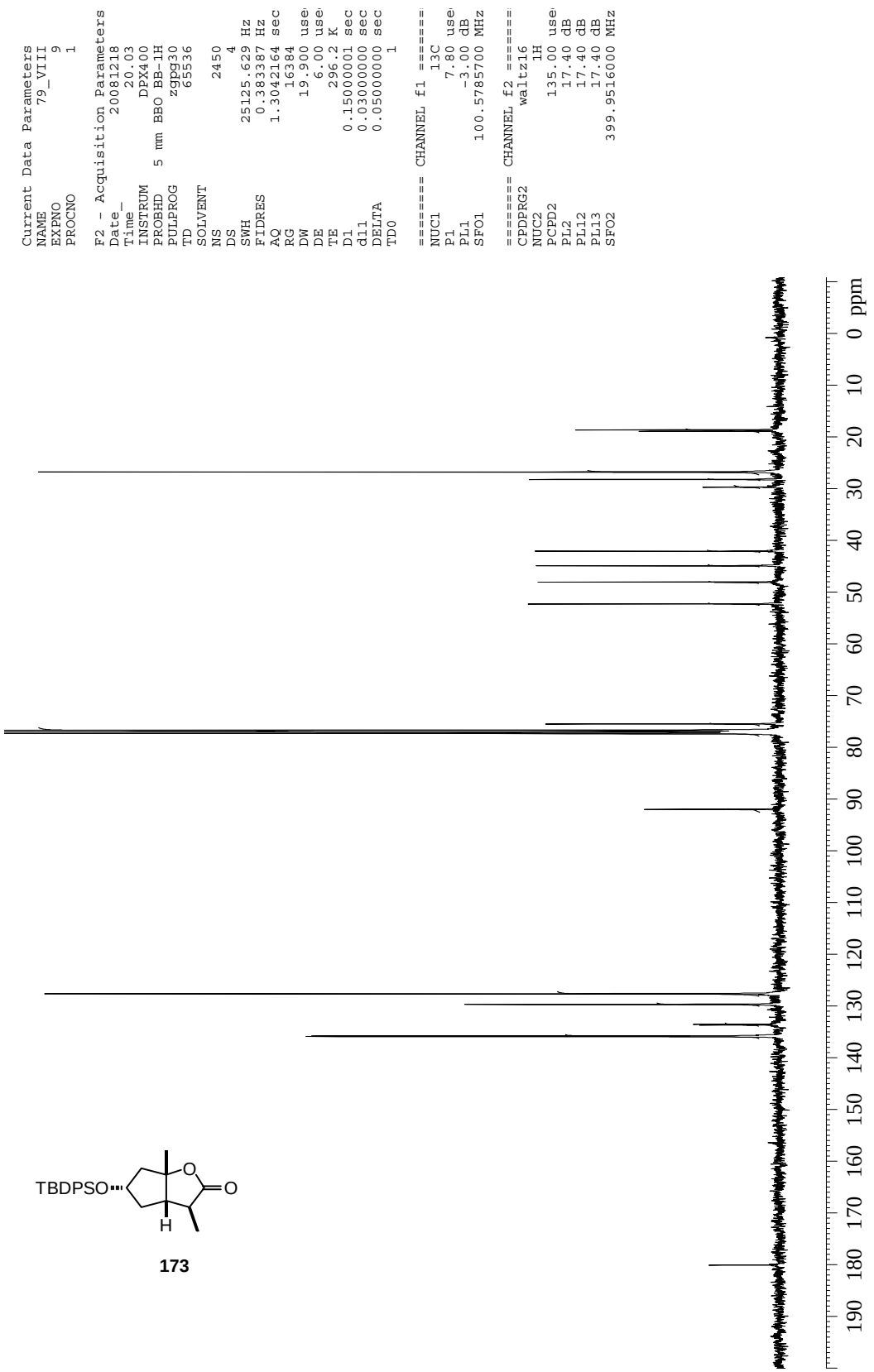

Current Data Parameters
NAME 95_II
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20050806
Time 23.24
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 512
DW 78.000 use
DE 6.00 use
TE 297.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 use
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
1.00
1.06
2.10
1.11
1.12
1.11
1.10
3.25
2.38
ppm
HO
O
O
H

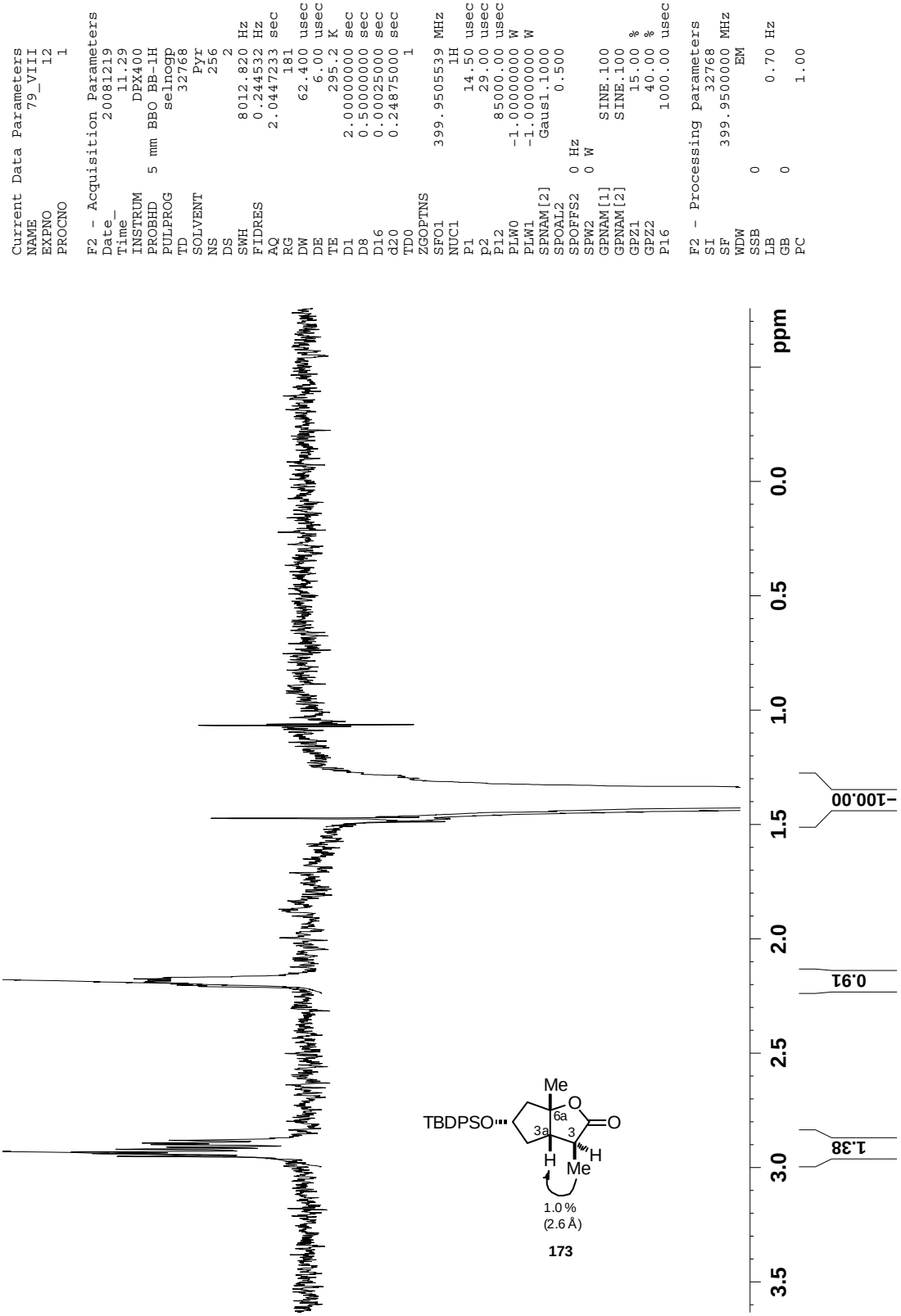

Current Data Parameters
NAME 95_II
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20050807
Time 9.33
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 23618
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3042164 sec
RG 4597.6
DW 19.900 use
DE 6.00 use
TE 297.2 K
D1 0.15000001 sec
d11 0.03000000 sec
DELTA 0.05000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 7.80 use
PL1 -3.00 dB
SFO1 100.5936591 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 use
PL2 17.40 dB
PL12 17.40 dB
PL13 17.40 dB
SFO2 400.0116000 MHz
HO
O
O
H
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


Current Data Parameters
NAME 44_IX
EXPNO 4
PROCNO 1
DU /o
USER rajan
F2 - Acquisition Parameters
Date_ 20091223
Time 13.03
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 sec
RG 512
DW 78.000 use
DE 6.00 use
TE 297.2 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.50 use
PL1 -3.00 dB
SFO1 400.2478017 MHz
F2 - Processing parameters
SI 32768
SF 400.2450000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
TBDPSO
O
O
H
170
ppm
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
11.12
3.37
1.13
1.13
1.13
1.10
1.06
1.08
1.09
1.00
7.41
4.26

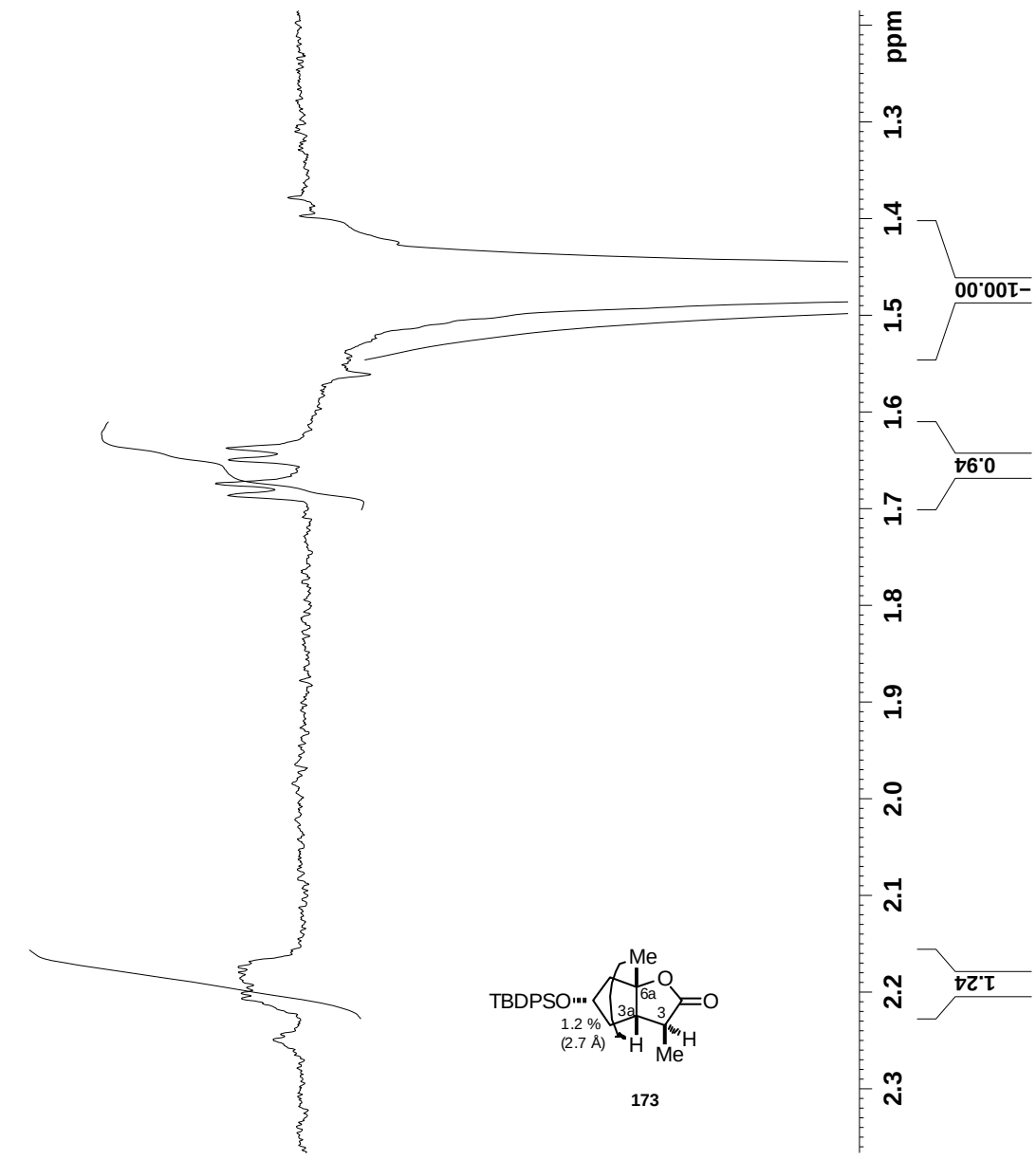

Current Data Parameters
NAME 44_IX
EXPNO 8
PROCNO 1
F2 - Acquisition Parameters
Date_ 20091223
Time 14.59
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1024
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 4096
DW 20.850 use
DE 6.00 use
TE 298.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.30 use
PL1 -3.00 dB
SFO1 100.6517495 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 use
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2466010 MHz
TBDPSO
O
O
H
170
ppm


Current Data Parameters
NAME 79_VIII
EXPNO 2
PROCNO 1
DU /m
USER rajan
F2 - Acquisition Parameters
Date_ 20081218
Time_ 15.31
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDC13
NS 32
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4210291 sec
RG 574.7
DW 104.400 use
DE 6.00 use
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 use
PL1 -3.00 dB
SFO1 300.1321009 MHz
F2 - Processing parameters
SI 32768
SF 300.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
ppm
8.37
1.06
2.98
2.80
1.11
1.04
1.02
0.26
1.99
0.99
1.00
3.83
5.77
TBDPSO
O
O
H
173

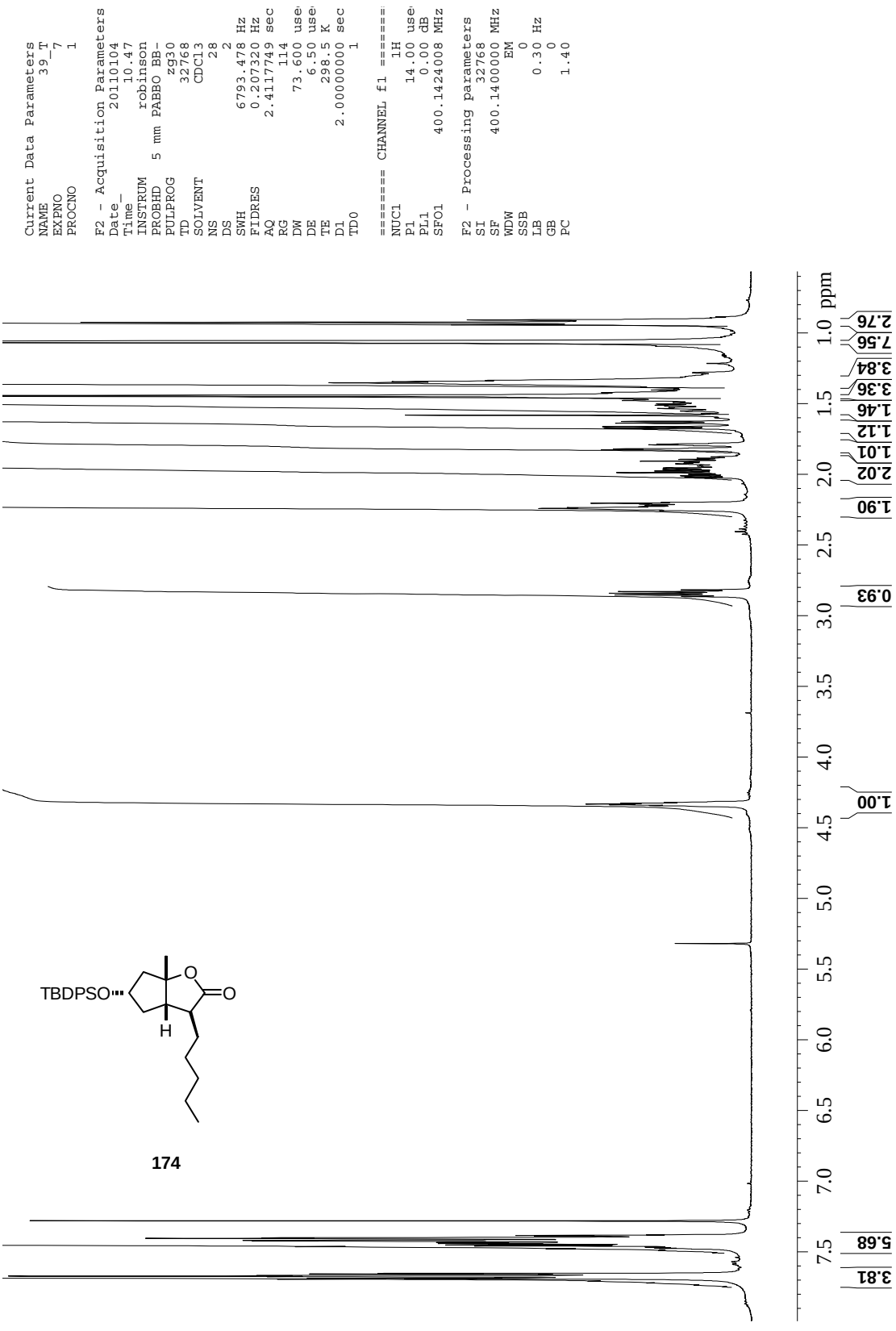

Current Data Parameters
NAME 79_VIII
EXPNO 9
PROCNO 1
F2 - Acquisition Parameters
Date_ 20081218
Time 20.03
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 2450
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3042164 sec
RG 16384
DW 19.900 use
DE 6.00 use
TE 296.2 K
D1 0.15000001 sec
d11 0.03000000 sec
DELTA 0.05000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 7.80 use
PL1 -3.00 dB
SFO1 100.5785700 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 use
PL2 17.40 dB
PL12 17.40 dB
PL13 17.40 dB
SFO2 399.9516000 MHz
TBDPSO
O
O
H
173
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

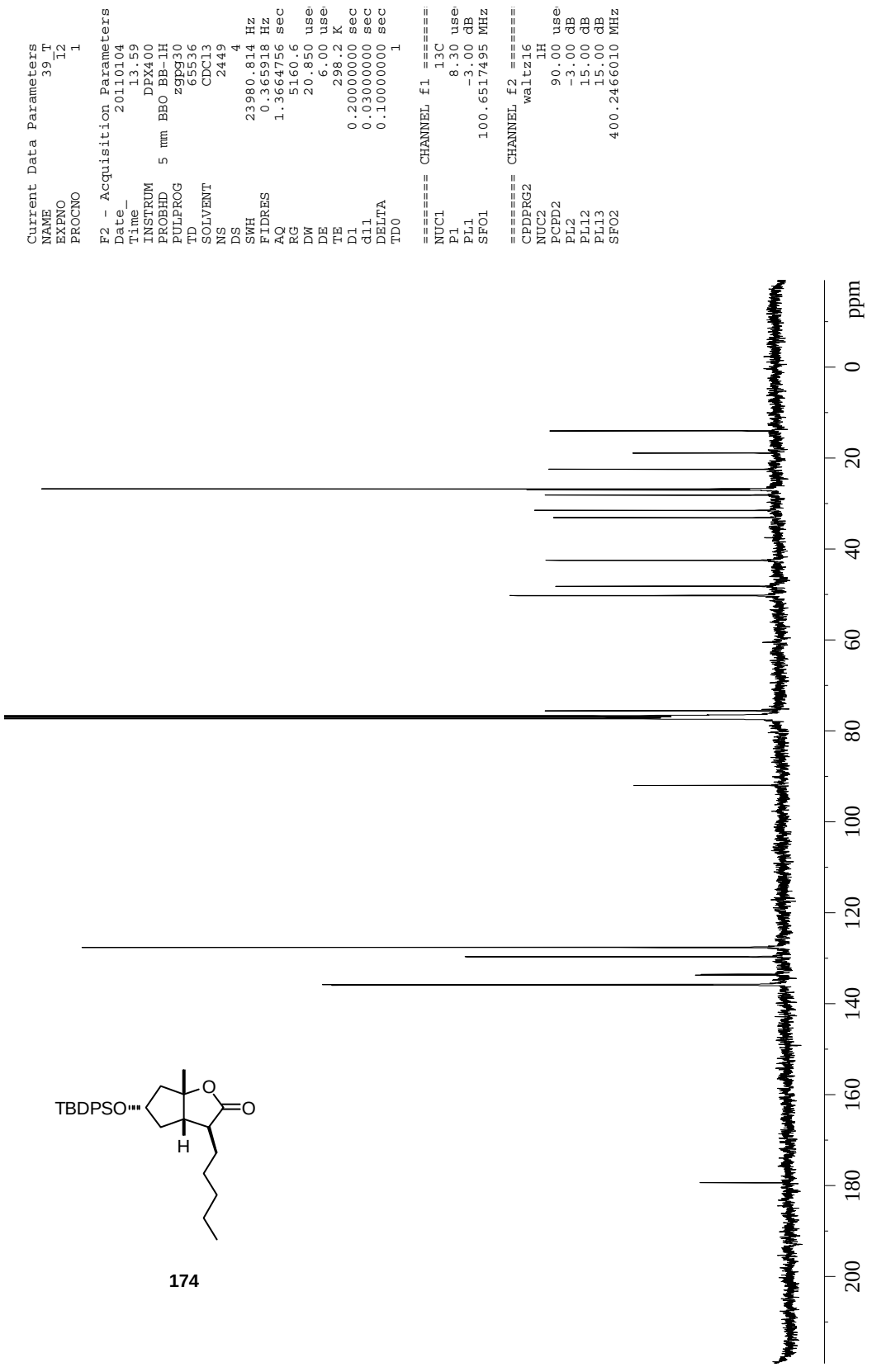

Current Data Parameters
NAME 79_VIII
EXPNO 12
PROCNO 1
F2 - Acquisition Parameters
Date_ 20081219
Time_ 11.29
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG selnogp
TD 32768
SOLVENT Pyr
NS 256
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 2.04472333 sec
RG 181
DW 62.400 usec
DE 6.00 usec
TE 295.2 K
D1 2.00000000 sec
D8 0.50000000 sec
D16 0.00025000 sec
d20 0.24875000 sec
TD0 1
ZGOPTNS
SFO1 399.9505539 MHz
NUC1 1H
P1 14.50 usec
p2 29.00 usec
P12 85000.00 usec
PLW0 -1.00000000 W
PLW1 -1.00000000 W
SPNAM[2] Gaus1.1000
SPOAL2 0.500
SPOFFS2 0 Hz
SPW2 0 W
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPZ1 15.00 %
GPZ2 40.00 %
P16 1000.00 usec
F2 - Processing parameters
SI 32768
SF 399.9500000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00
ppm
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
100.00
0.91
1.38
Me
O
6a
3a
3
O
TBDPSO
H
H
Me
1.0 %
(2.6 Å)

173

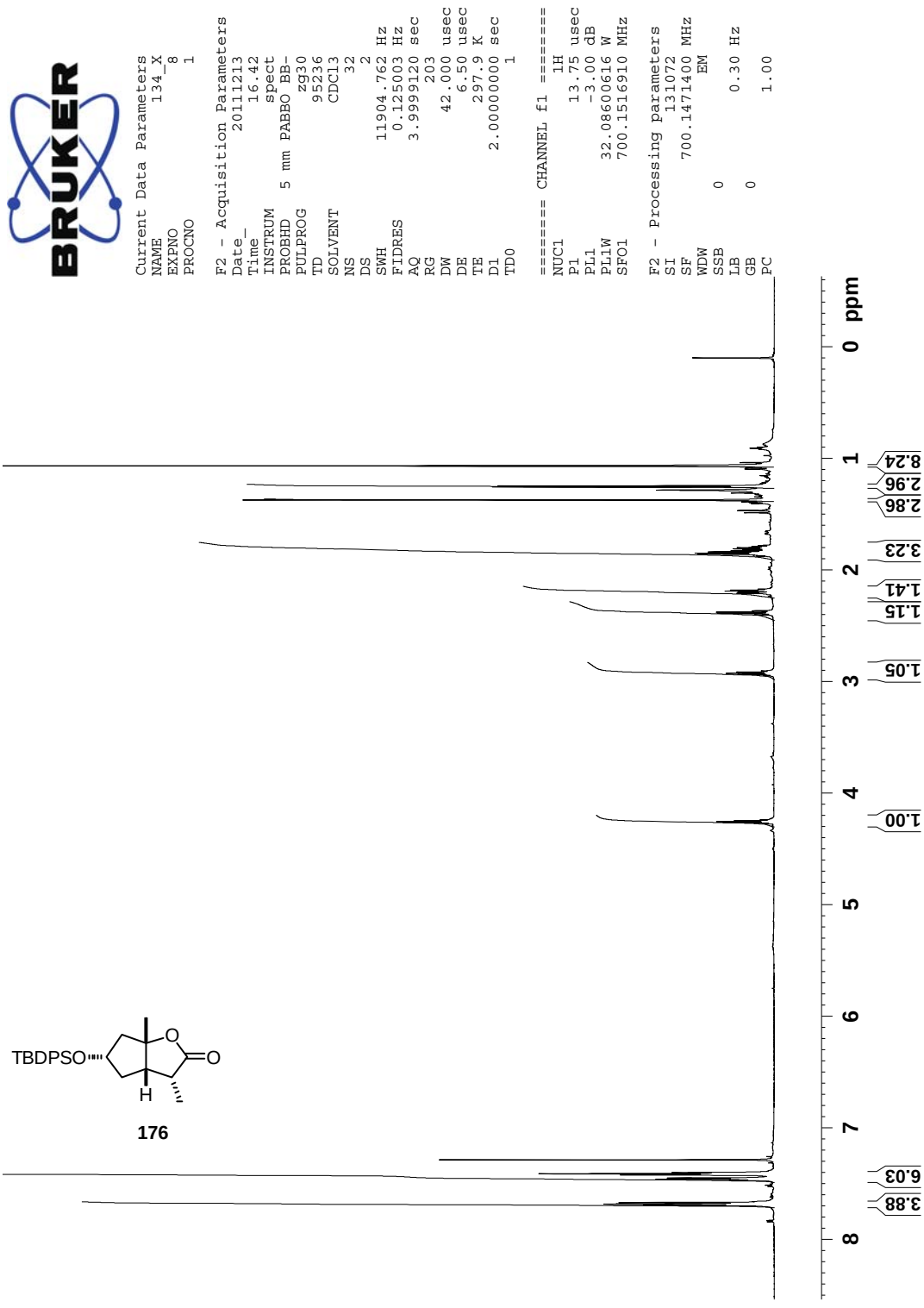

Current Data Parameters
NAME 79_VIII
EXPNO 14
PROCNO 1
F2 - Acquisition Parameters
Date_ 20081219
Time_ 12.20
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG selnogp
TD 32768
SOLVENT Pyr
NS 256
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 2.0447233 sec
RG 181
DW 62.400 usec
DE 6.00 usec
TE 296.2 K
D1 2.00000000 sec
D8 0.50000000 sec
D16 0.00025000 sec
d20 0.24875000 sec
TD0 1
ZGOPTNS
SFO1 399.9505843 MHz
NUC1 1H
P1 14.50 usec
p2 29.00 usec
P12 85000.00 usec
PLW0 -1.00000000 W
PLW1 -1.00000000 W
SPNAM[2] Gaus1.1000
SPOAL2 0.500
SPOFFS2 0 Hz
SPW2 0 W
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPZ1 15.00 %
GPZ2 40.00 %
P16 1000.00 usec
F2 - Processing parameters
SI 32768
SF 399.9500000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
ppm
1.24
0.94
100.00
TBDPSO
Me
O
6a
O
3a
3
1.2 %
(2.7 Å)
H
H
Me
H

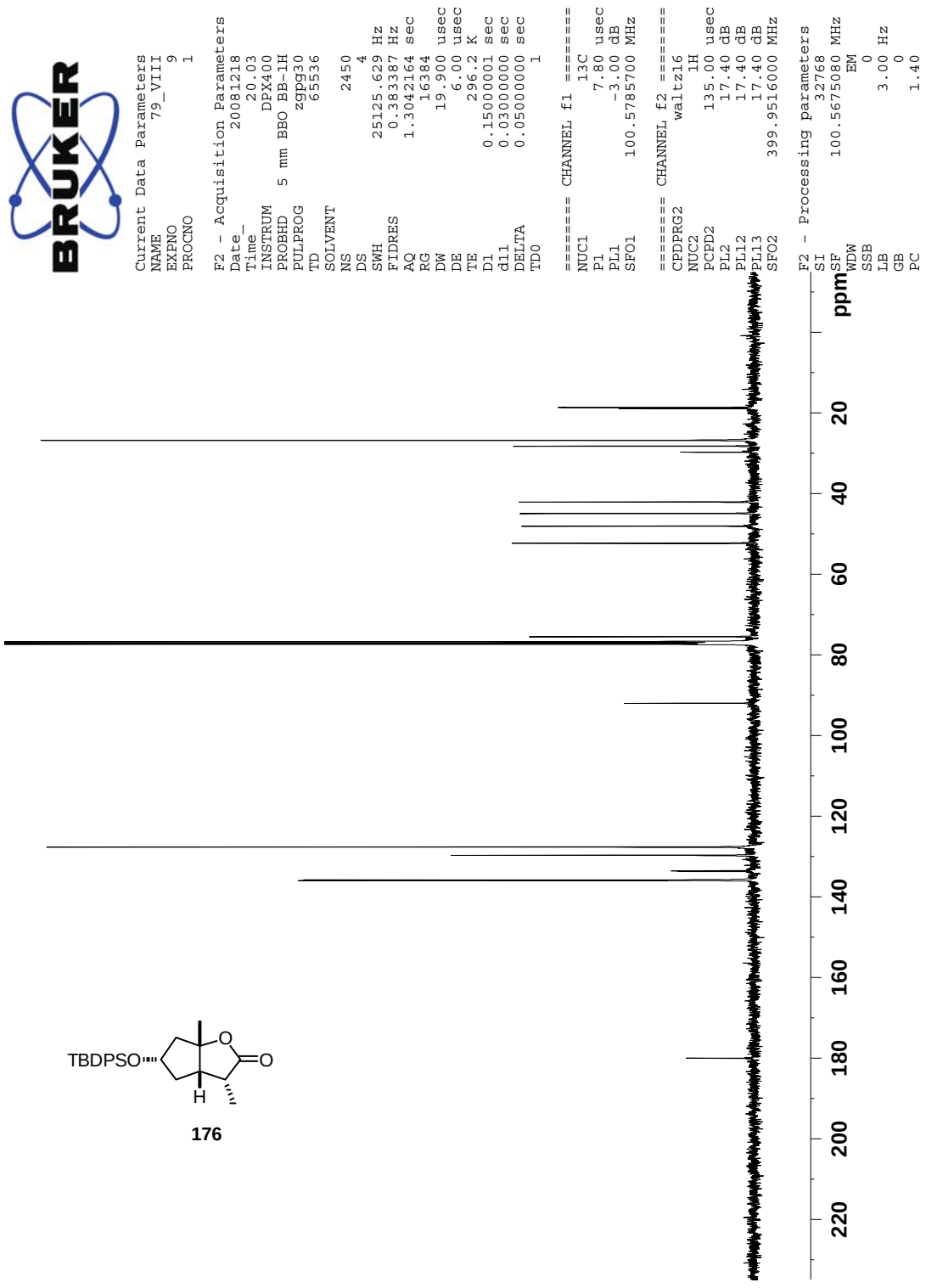
173


Current Data Parameters
NAME 39_T
EXPNO 7
PROCNO 1
F2 - Acquisition Parameters
Date_ 20110104
Time_ 10.47
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 28
DS 2
SWH 6793.478 Hz
FIDRES 0.207320 Hz
AQ 2.4117749 sec
RG 114
DW 73.600 use
DE 6.50 use
TE 298.5 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 use
PL1 0.00 dB
SFO1 400.1424008 MHz
F2 - Processing parameters
SI 32768
SF 400.1400000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40
TBDPSO
O
O
H
174
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
5.68
3.81
1.00
0.93
1.90
2.02
1.01
1.12
1.46
3.36
3.84
7.56
2.76

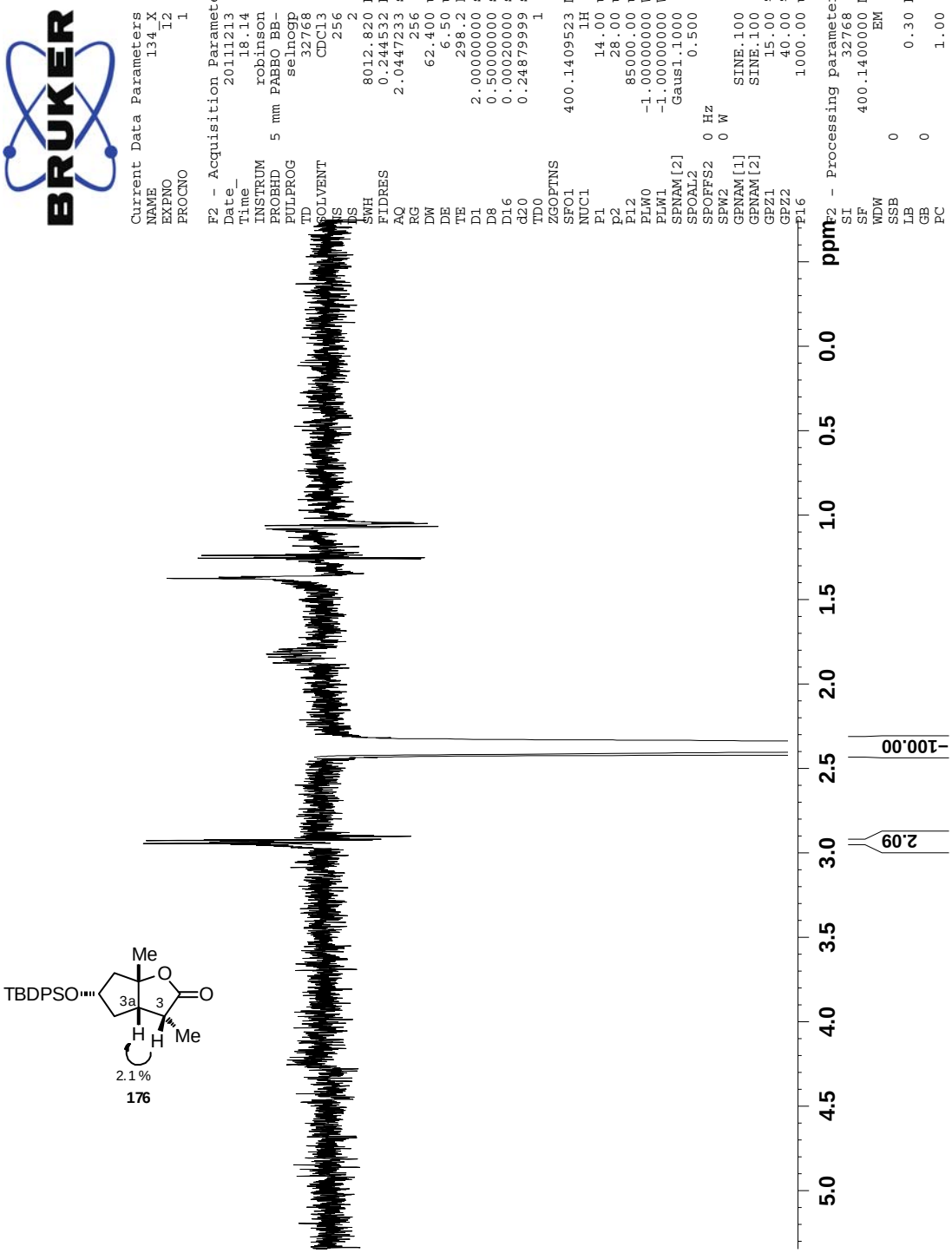

Current Data Parameters
NAME 39_T
EXPNO 12
PROCNO 1
F2 - Acquisition Parameters
Date_ 20110104
Time_ 13.59
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 2449
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 5160.6
DW 20.850 use
DE 6.00 use
TE 298.2 K
D1 0.20000000 sec
d11 0.03000000 sec
DELTA 0.10000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.30 use
PL1 -3.00 dB
SFO1 100.6517495 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 use
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2466010 MHz
TBDPSO
O
O
H
ppm
200
180
160
140
120
100
80
60
40
20
0

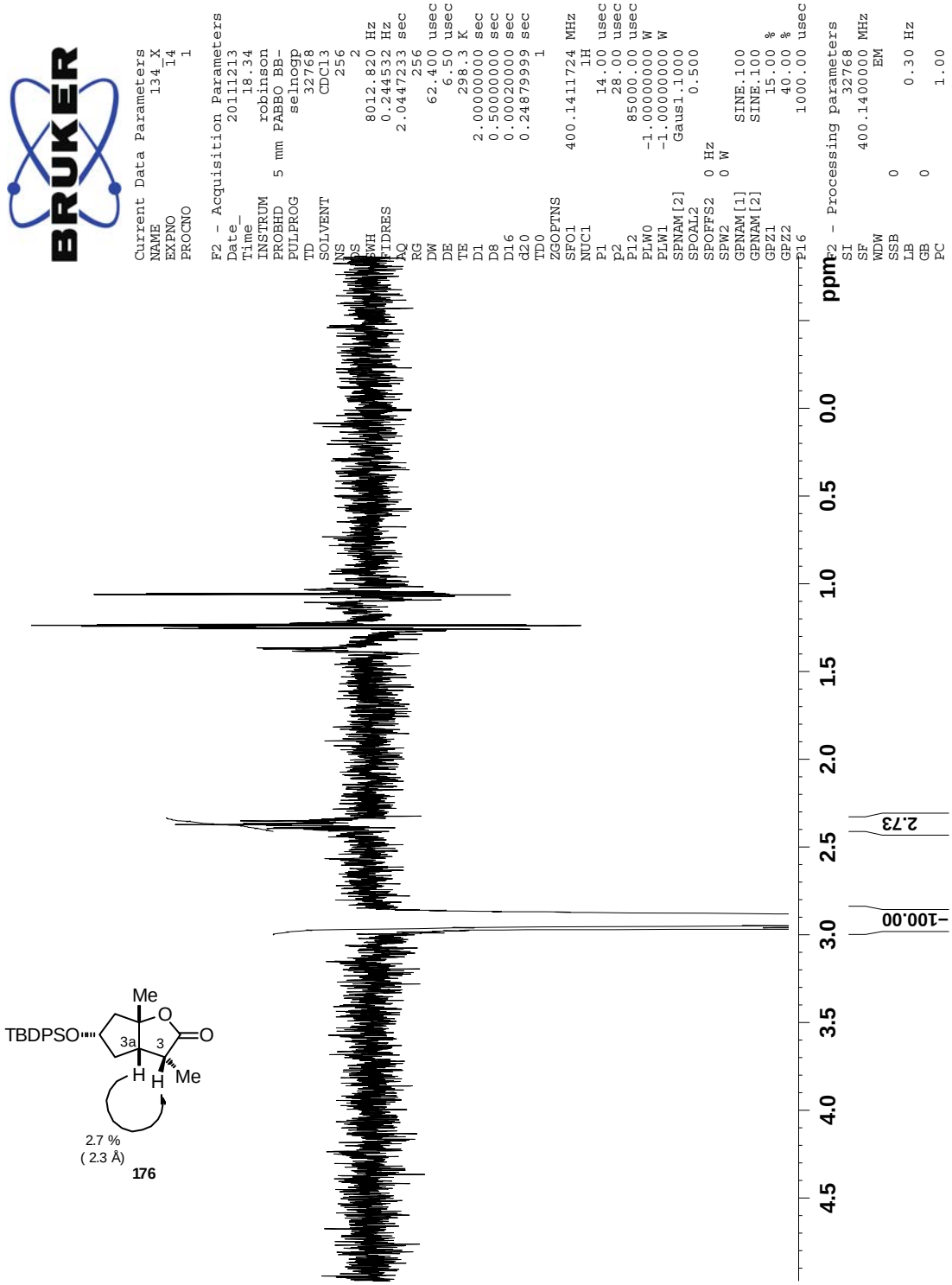
174

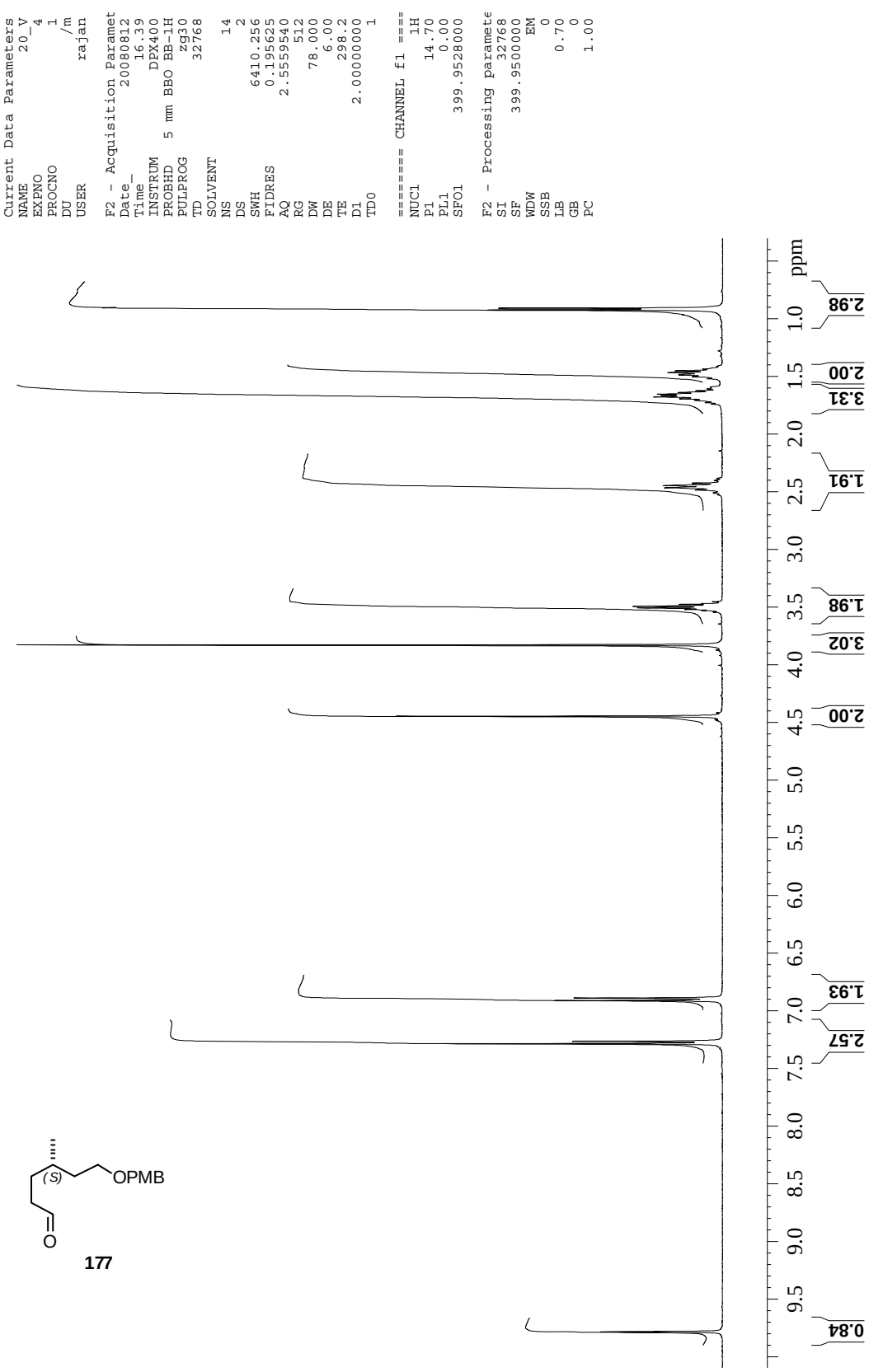

Current Data Parameters
NAME 134_X
EXPNO 8
PROCNO 1
F2 - Acquisition Parameters
Date_ 20111213
Time_ 16.42
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999120 sec
RG 203
DW 42.000 usec
DE 6.50 usec
TE 297.9 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.75 usec
PL1 -3.00 dB
PL1W 32.08600616 W
SFO1 700.1516910 MHz
F2 - Processing parameters
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
8.24
2.96
2.86
3.23
1.41
1.15
1.05
1.00
6.03
3.88
ppm
TBDPSO
O
O
H
176

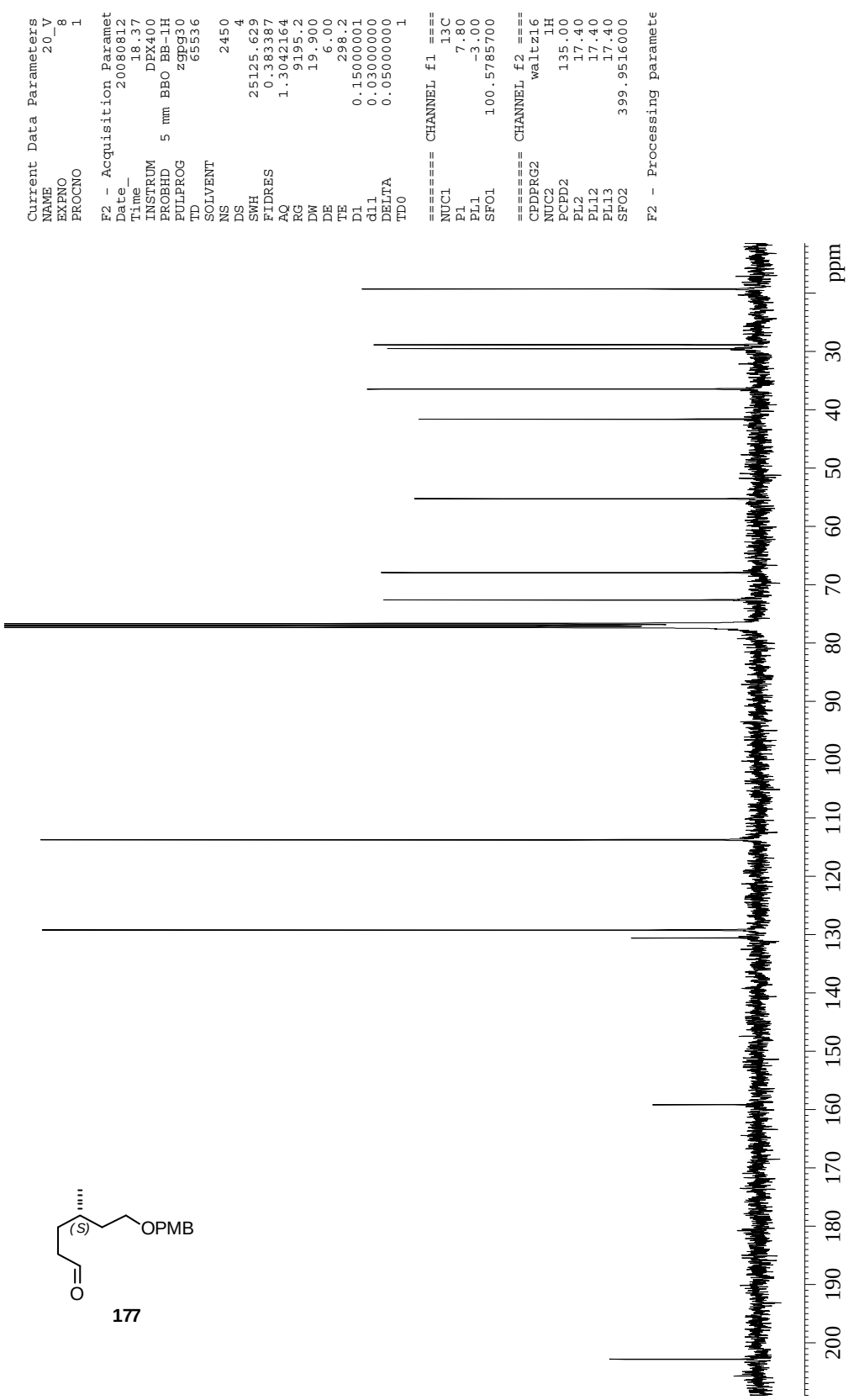

Current Data Parameters
NAME 79_VIII
EXPNO 9
PROCNO 1
F2 - Acquisition Parameters
Date_ 20081218
Time_ 20.03
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 2450
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.30042164 sec
RG 16384
DW 19.900 usec
DE 6.00 usec
TE 296.2 K
D1 0.15000001 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
ppm
220
200
180
160
140
120
100
80
60
40
20
TBDPSO
O
O
H

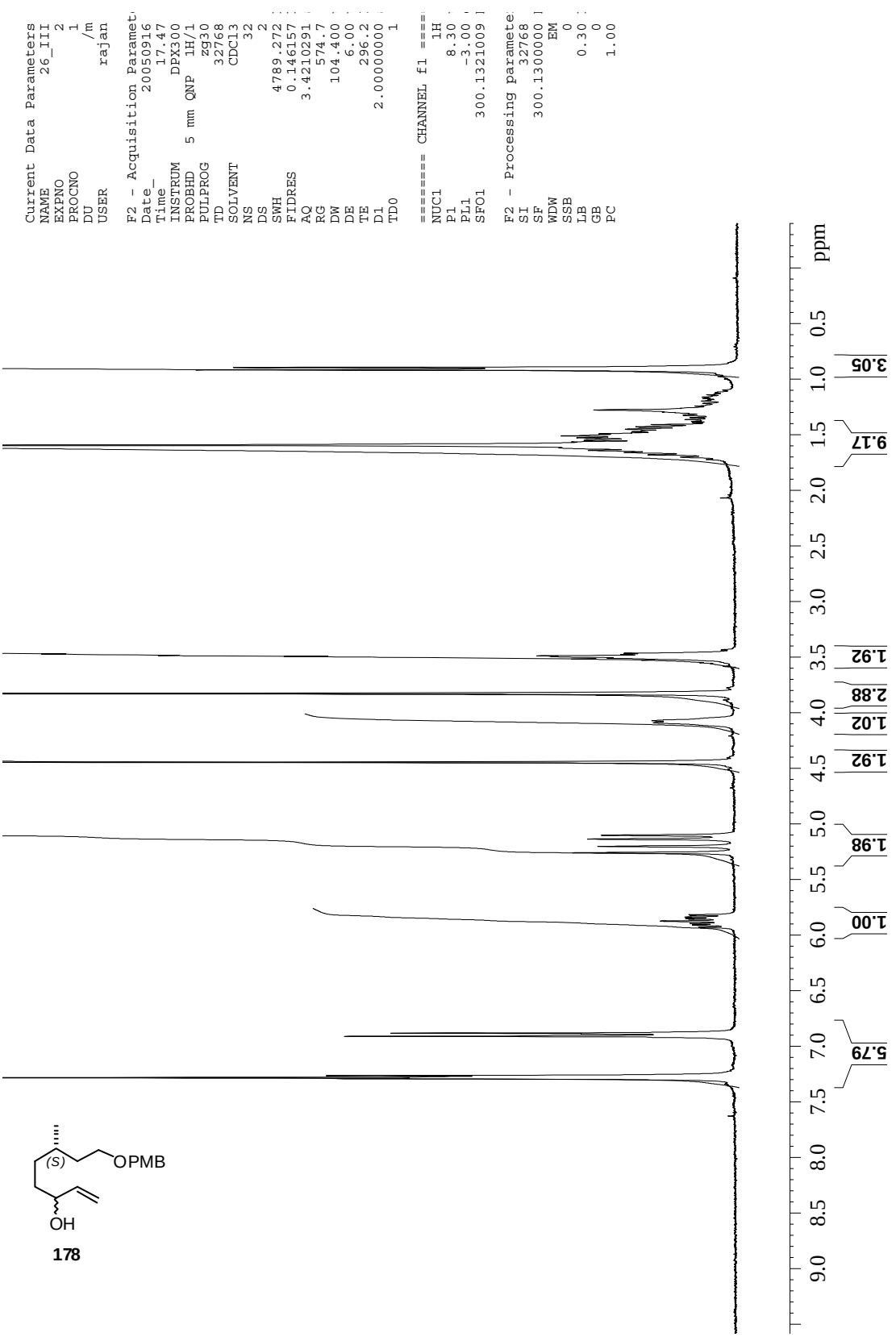
176

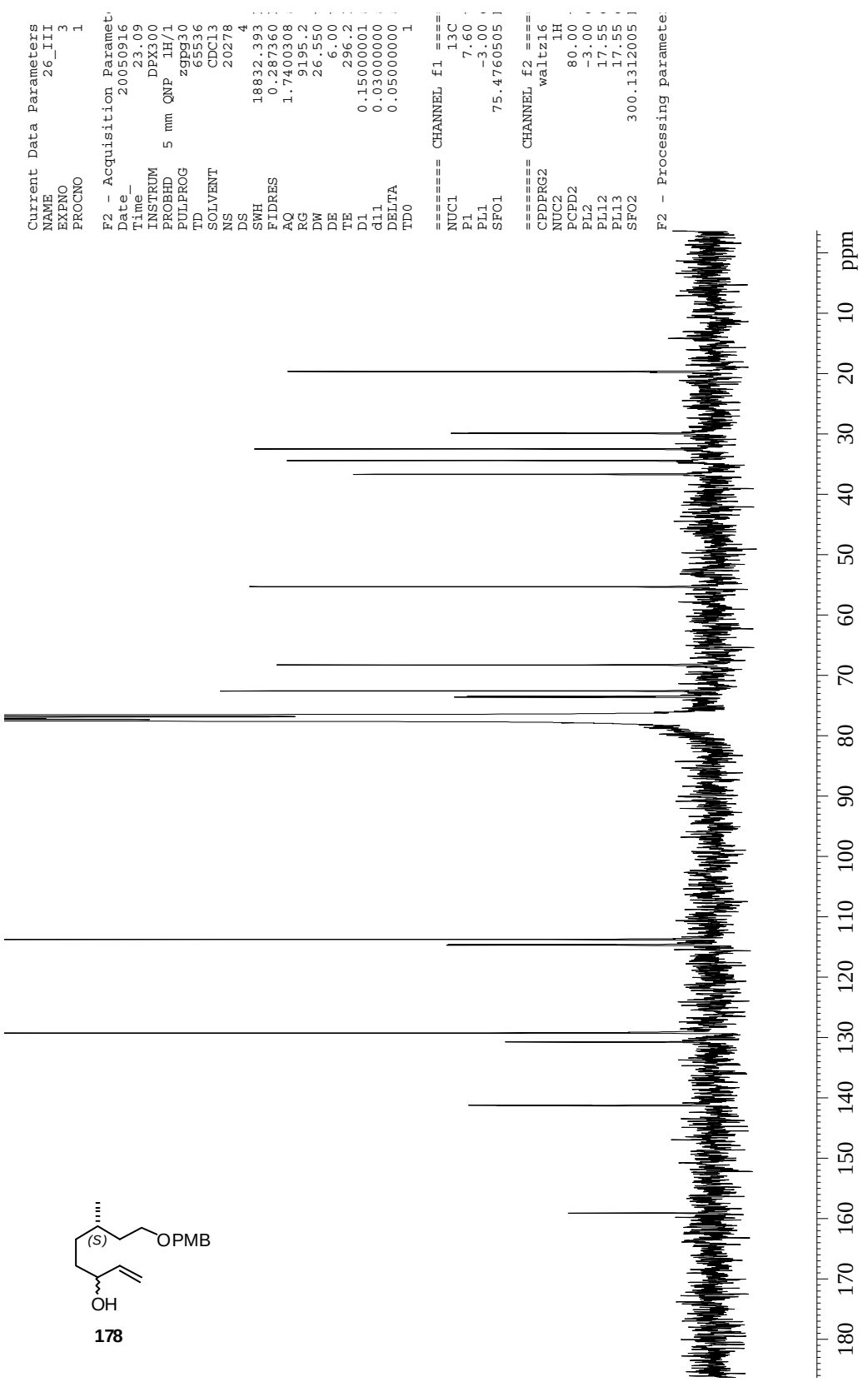

Current Data Parameters
NAME 134_X
EXPNO 12
PROCNO 1
F2 - Acquisition Parameters
Date_ 20111213
Time 18.14
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG selnogp
TD 32768
SOLVENT CDCl3
NS 256
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 2.0447233 sec
RG 256
DW 62.400 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
D8 0.50000000 sec
D16 0.00020000 sec
d20 0.24879999 sec
TD0 1
ZGOPTNS
SFO1 400.1409523 MHz
NUC1 1H
P1 14.00 usec
p2 28.00 usec
P12 85000.00 usec
PLW0 -1.00000000 W
PLW1 -1.00000000 W
SPNAM[2] Gaus1.1000
SPOAL2 0.500
SPOFFS2 0 Hz
SPW2 0 W
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPZ1 15.00 %
GPZ2 40.00 %
P16 1000.00 usec
F2 - Processing parameters
SI 32768
SF 400.1400000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
ppm
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
100.00
2.09
TBDPSO
Me
O
O
3a
3
H
H
Me
2.1%
176

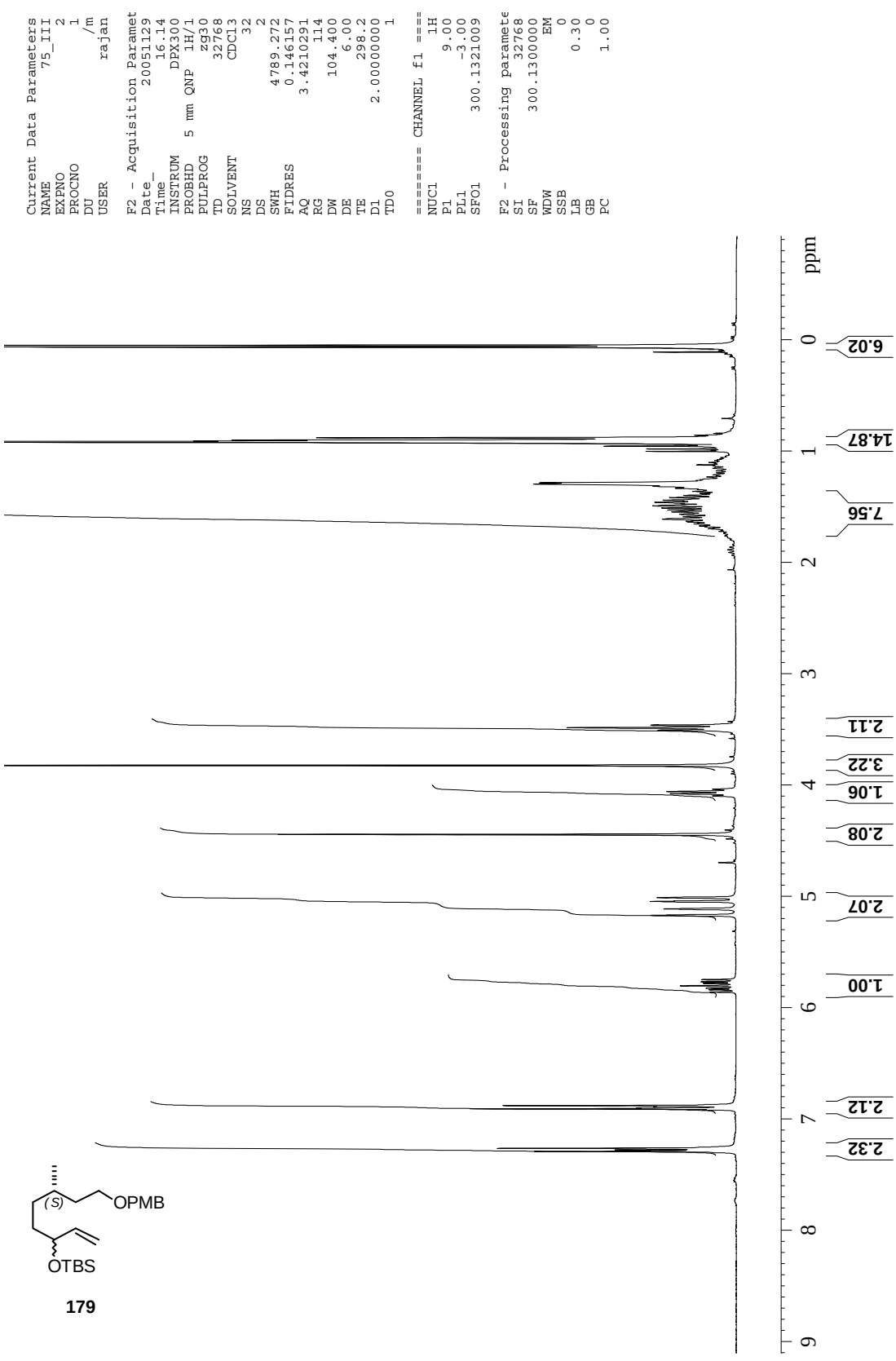

Current Data Parameters
NAME 134_X
EXPNO 14
PROCNO 1
F2 - Acquisition Parameters
Date_ 20111213
Time 18.34
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG selnogp
TD 32768
SOLVENT CDCl3
NS 256
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 2.0447233 sec
RG 256
DW 62.400 usec
DE 6.50 usec
TE 298.3 K
D1 2.00000000 sec
D8 0.50000000 sec
D16 0.00020000 sec
d20 0.24879999 sec
TD0 1
ZGOPTNS
SFO1 400.1411724 MHz
NUC1 1H
P1 14.00 usec
p2 28.00 usec
P12 85000.00 usec
PLW0 -1.00000000 W
PLW1 -1.00000000 W
SPNAM[2] Gaus1.1000
SPOAL2 0.500
SPOFFS2 0 Hz
SPW2 0 W
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPZ1 15.00 %
GPZ2 40.00 %
P16 1000.00 usec
F2 - Processing parameters
SI 32768
SF 400.1400000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
ppm
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
2.73
100.00
Me
O
O
TBDPSO
3a
3
H
H
Me
2.7 %
(2.3 Å)
176


Current Data Parameters
NAME 20_V
EXPNO 4
PROCNO 1
DU /m
USER rajan
F2 - Acquisition Paramet
Date_ 20080812
Time 16.39
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT
NS 14
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 paramete
SI 32768
SF 399.9500000
WDW EM
SSB 0
LB 0.70
GB 0
PC 1.00
(S)
OPMB
O
177
ppm
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
0.84
2.57
1.93
2.00
3.02
1.98
1.91
3.31
2.00
2.98

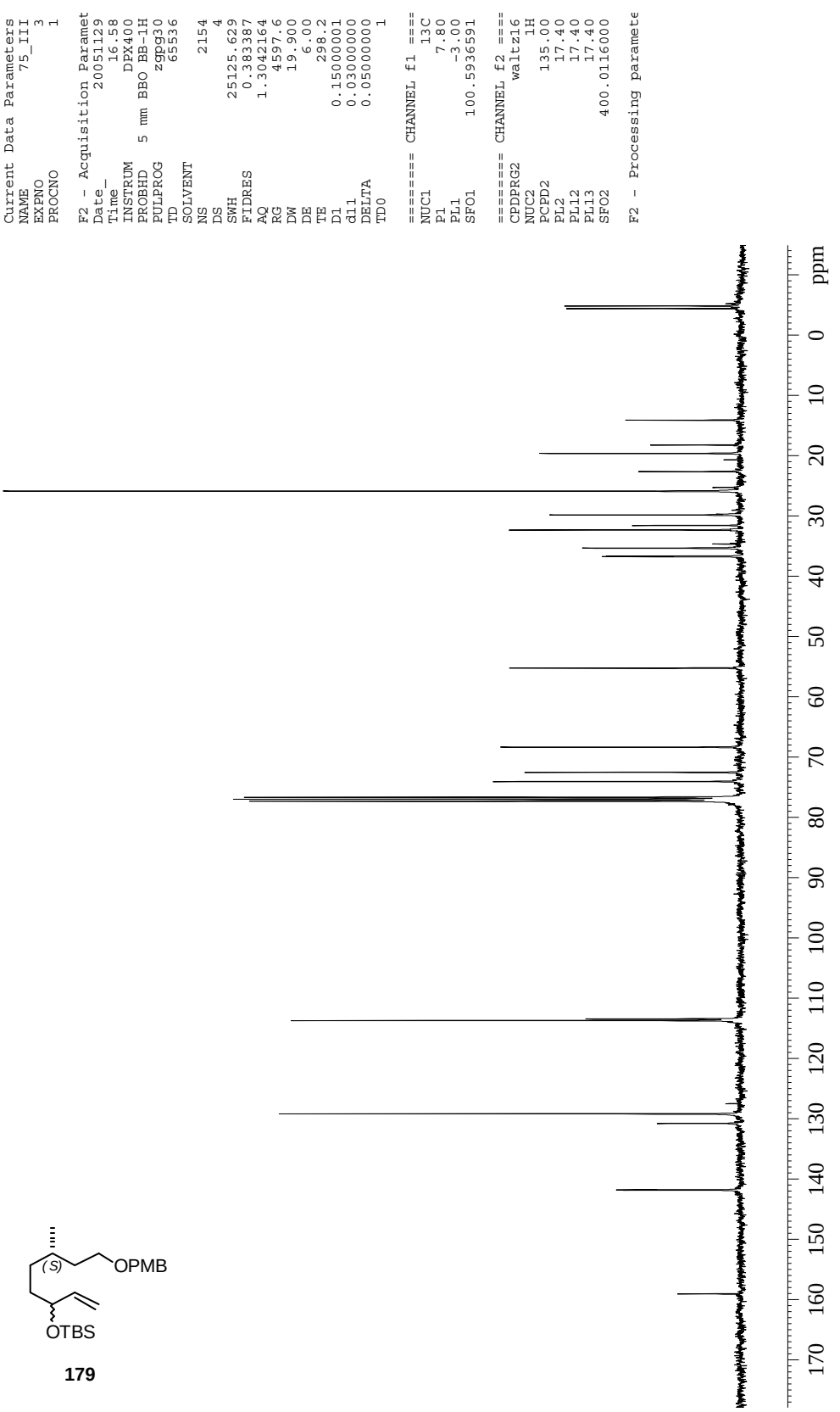

Current Data Parameters
NAME 20_V
EXPNO 8
PROCNO 1
F2 - Acquisition Paramet
Date_ 20080812
Time_ 18.37
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 2450
DS 4
SWH 25125.629
FIDRES 0.383387
AQ 1.3042164
RG 9195.2
DW 19.900
DE 6.00
TE 298.2
D1 0.15000001
d11 0.03000000
DELTA 0.05000000
TD0 1
======== CHANNEL f1 ====
NUC1 13C
P1 7.80
PL1 -3.00
SFO1 100.5785700
======== CHANNEL f2 ====
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00
PL2 17.40
PL12 17.40
PL13 17.40
SFO2 399.9516000
F2 - Processing paramete
(S)
OPMB
O
177
ppm


Current Data Parameters
NAME 26_III
EXPNO 2
PROCNO 1
DU /m
USER rajan
F2 - Acquisition Paramet
Date_ 20050916
Time_ 17.47
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 574.7
DW 104.400
DE 6.00
TE 296.2
D1 2.00000000
TD0 1
======== CHANNEL f1 ====
NUC1 1H
P1 8.30
PL1 -3.00
SFO1 300.1321009
F2 - Processing parameter
SI 32768
SF 300.1300000
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00
3.05
9.17
1.92
2.88
1.02
1.92
1.98
1.00
5.79
ppm
(S)
OPMB
OH
178

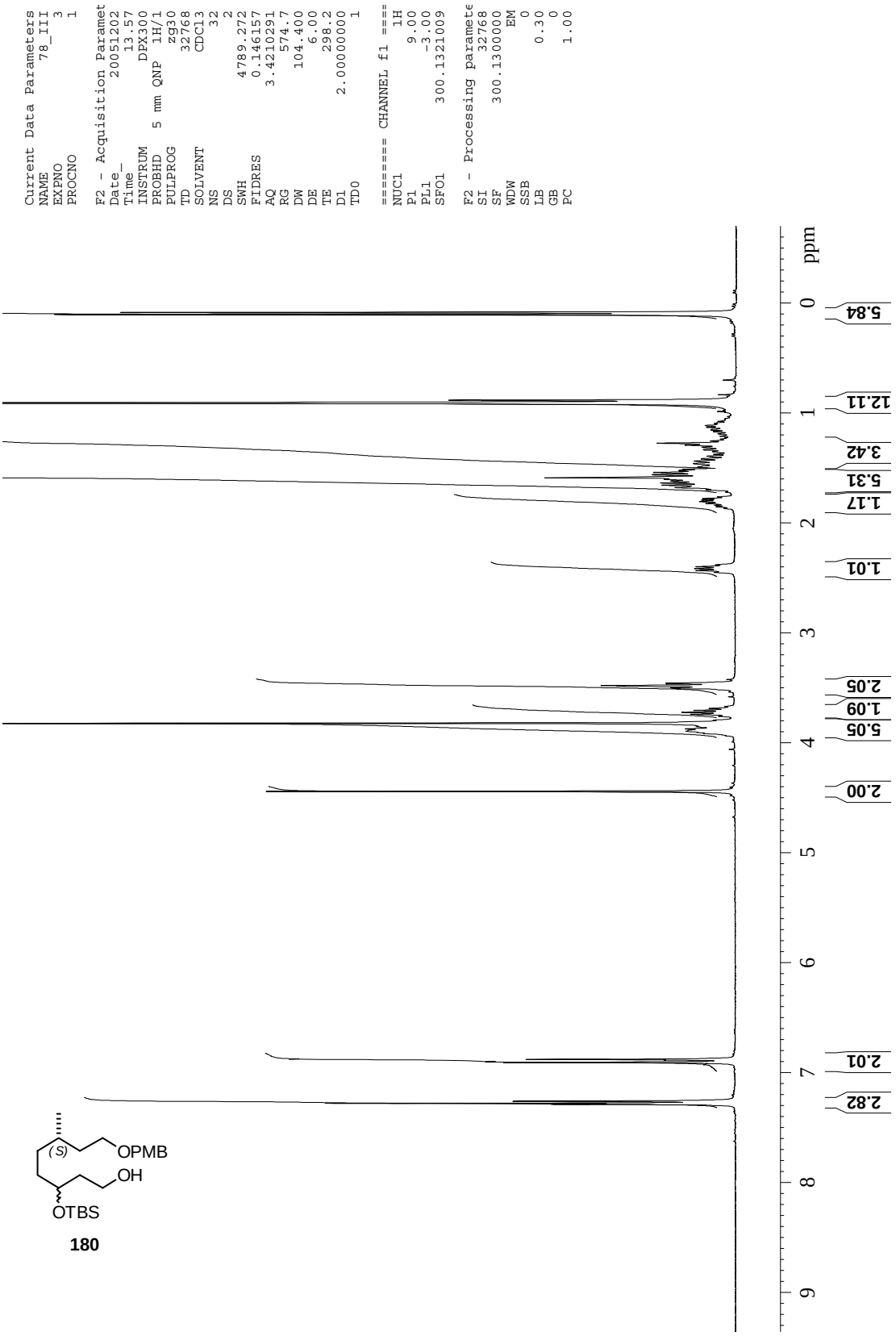

Current Data Parameters
NAME 26_III
EXPNO 3
PROCNO 1
F2 - Acquisition Paramet
Date_ 20050916
Time_ 23.09
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 20278
DS 4
SWH 18832.393
FIDRES 0.287360
AQ 1.7400308
RG 9195.2
DW 26.550
DE 6.00
TE 296.2
D1 0.15000001
d11 0.03000000
DELTA 0.05000000
TD0 1
======== CHANNEL f1 ====
NUC1 13C
P1 7.60
PL1 -3.00
SFO1 75.4760505
======== CHANNEL f2 ====
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00
PL2 -3.00
PL12 17.55
PL13 17.55
SFO2 300.1312005
F2 - Processing paramete
(S)
OPMB
OH
178
ppm


Current Data Parameters
NAME 75_III
EXPNO 2
PROCNO 1
DU /m
USER rajan
F2 - Acquisition Paramet
Date_ 20051129
Time 16.14
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 114
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 parameter
SI 32768
SF 300.1300000
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00
ppm
6.02
14.87
7.56
2.11
3.22
1.06
2.08
2.07
1.00
2.12
2.32
(S)
OPMB
OTBS

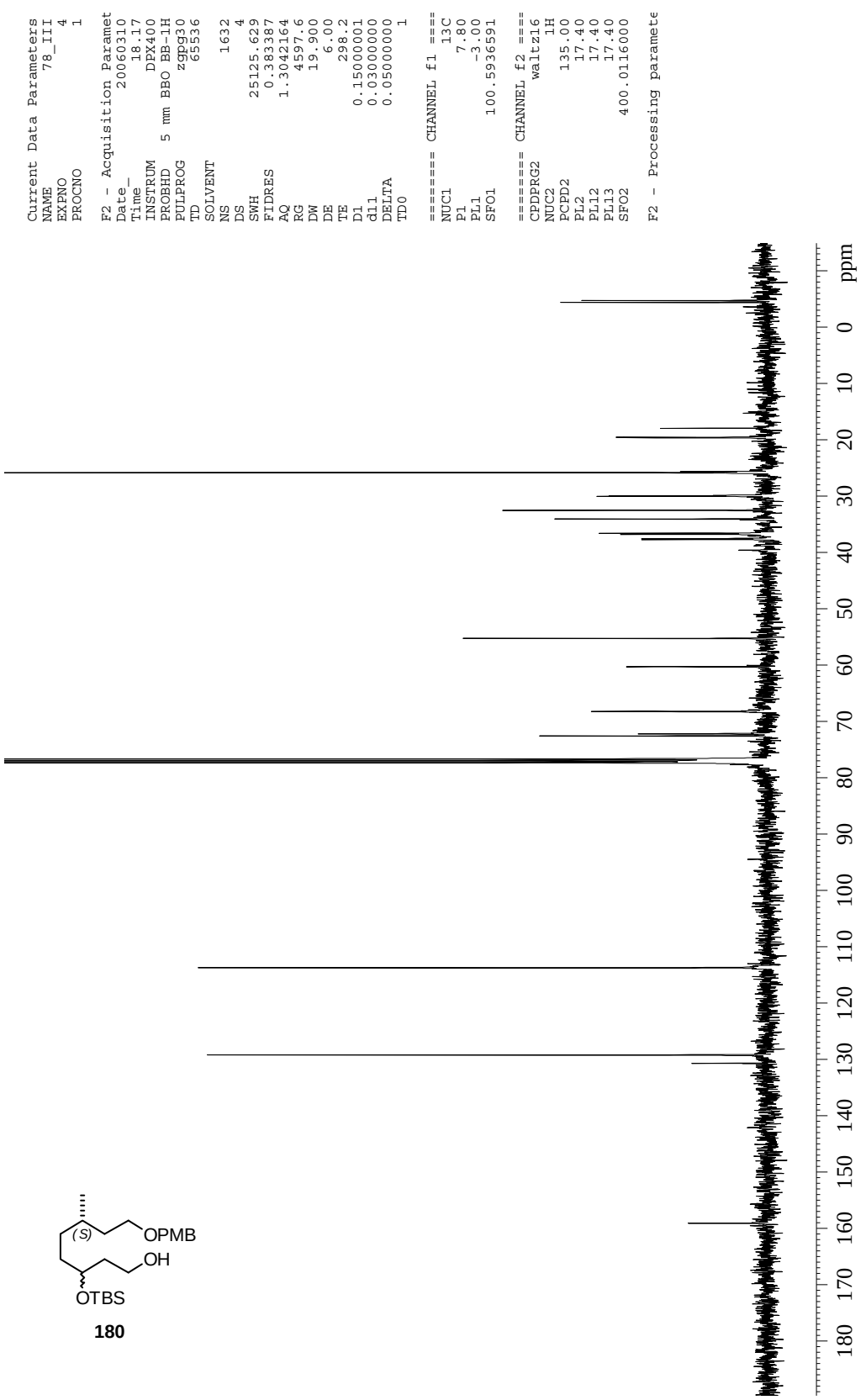
179


Current Data Parameters
NAME 75_III
EXPNO 3
PROCNO 1
F2 - Acquisition Paramet
Date_ 20051129
Time_ 16.58
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 2154
DS 4
SWH 25125.629
FIDRES 0.383387
AQ 1.3042164
RG 4597.6
DW 19.900
DE 6.00
TE 298.2
D1 0.15000001
d11 0.03000000
DELTA 0.05000000
TD0 1
======== CHANNEL f1 ====
NUC1 13C
P1 7.80
PL1 -3.00
SFO1 100.5936591
======== CHANNEL f2 ====
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00
PL2 17.40
PL12 17.40
PL13 17.40
SFO2 400.0116000
F2 - Processing paramete
ppm
(S)
OPMB
OTBS

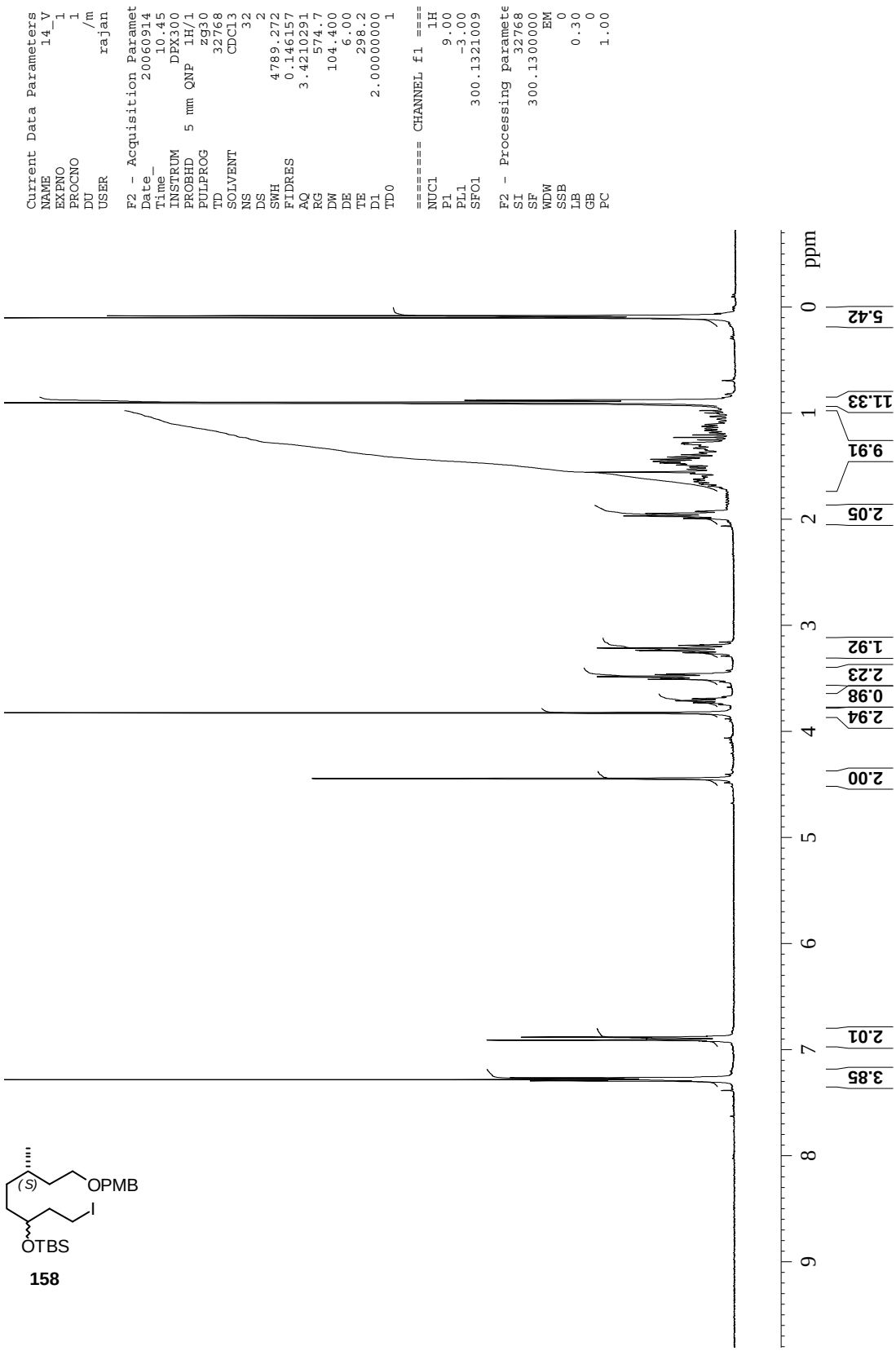
179


Current Data Parameters
NAME 78_III
EXPNO 3
PROCNO 1
F2 - Acquisition Paramet
Date_ 20051202
Time_ 13.57
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 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 parameter
SI 32768
SF 300.1300000
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00
ppm
0
1
2
3
4
5
6
7
8
9
5.84
12.11
3.42
5.31
1.17
1.01
2.05
1.09
5.05
2.00
2.01
2.82
(S)
OPMB
OH
OTBS

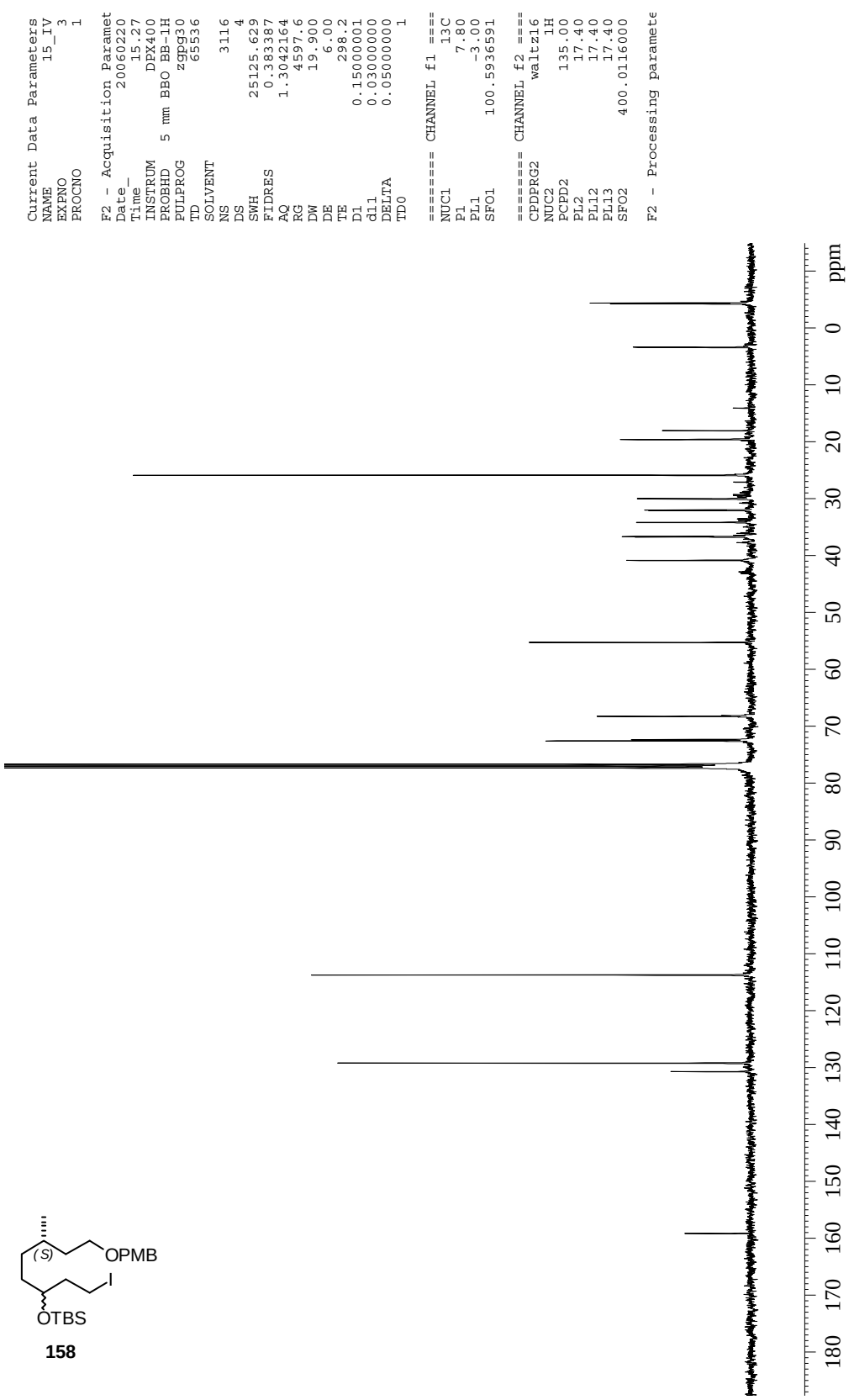
180


Current Data Parameters
NAME 78_III
EXPNO 4
PROCNO 1
F2 - Acquisition Paramet
Date_ 20060310
Time_ 18.17
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 1632
DS 4
SWH 25125.629
FIDRES 0.383387
AQ 1.3042164
RG 4597.6
DW 19.900
DE 6.00
TE 298.2
D1 0.15000001
d11 0.03000000
DELTA 0.05000000
TD0 1
======== CHANNEL f1 ====
NUC1 13C
P1 7.80
PL1 -3.00
SFO1 100.5936591
======== CHANNEL f2 ====
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00
PL2 17.40
PL12 17.40
PL13 17.40
SFO2 400.0116000
F2 - Processing paramete
ppm
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
(S)
OPMB
OH
OTBS

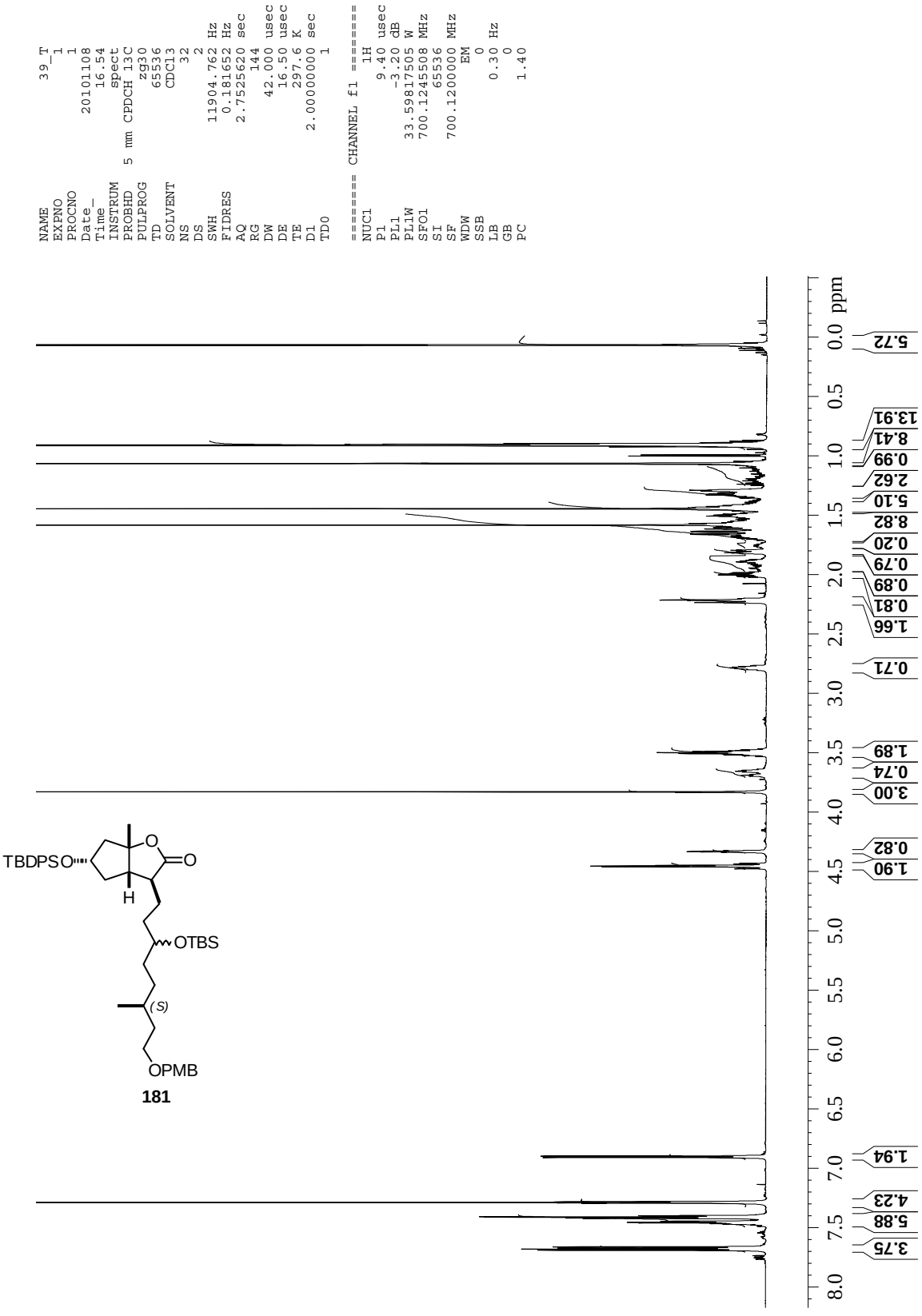
180

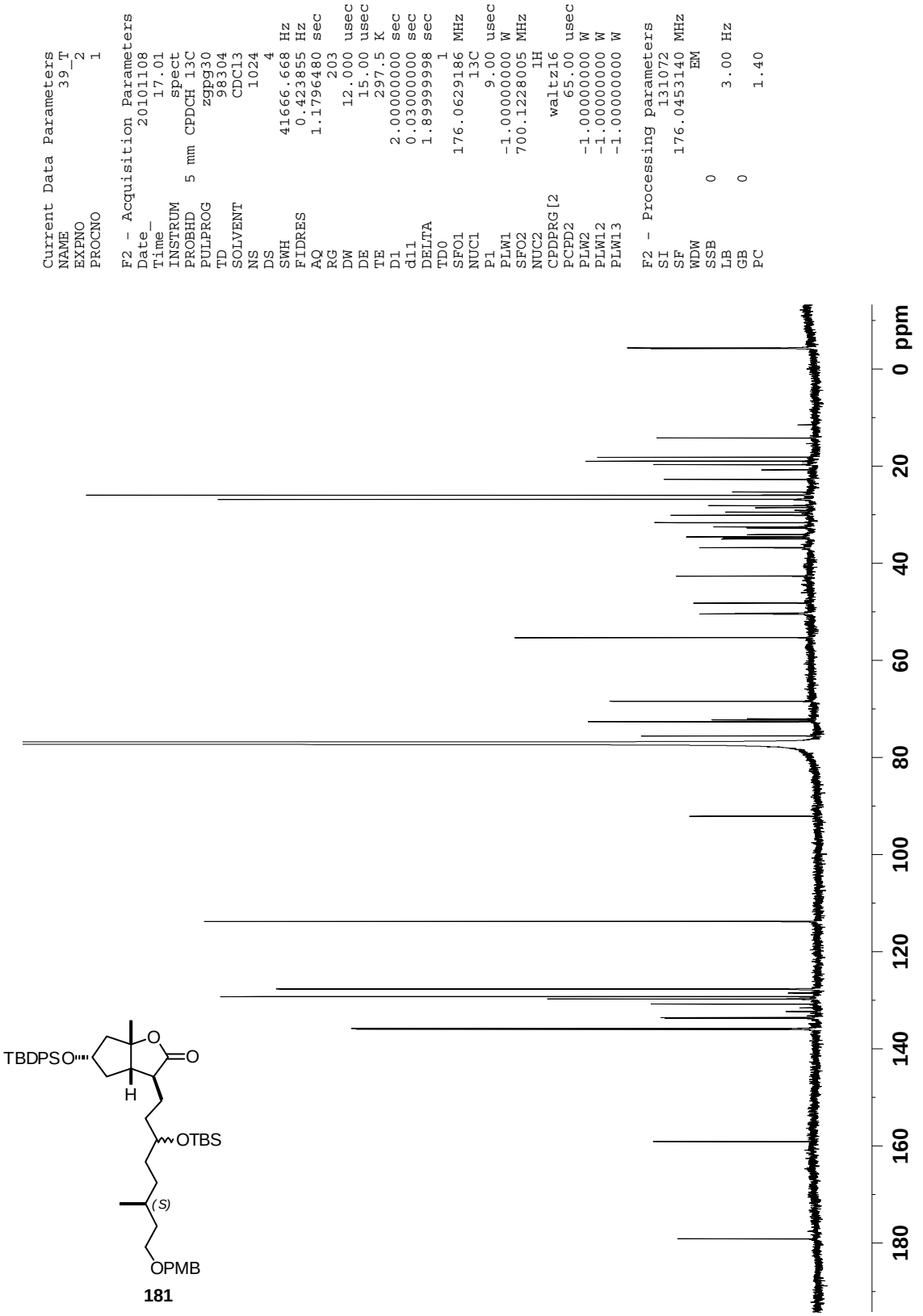

Current Data Parameters
NAME 14_V
EXPNO 1
PROCNO 1
DU /m
USER rajan
F2 - Acquisition Paramet
Date_ 20060914
Time 10.45
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4789.272
FIDRES 0.146157
AQ 3.4210291
RG 574.7
DW 104.400
DE 6.00
TE 298.2
D1 2.00000000
TD0 1
======== CHANNEL f1 ====
NUC1 1H
P1 9.00
PL1 -3.00
SFO1 300.1321009
F2 - Processing paramete
SI 32768
SF 300.1300000
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00
ppm
0
1
2
3
4
5
6
7
8
9
5.42
11.33
9.91
2.05
1.92
2.23
0.98
2.94
2.00
2.01
3.85
(S)
OPMB
I
OTBS

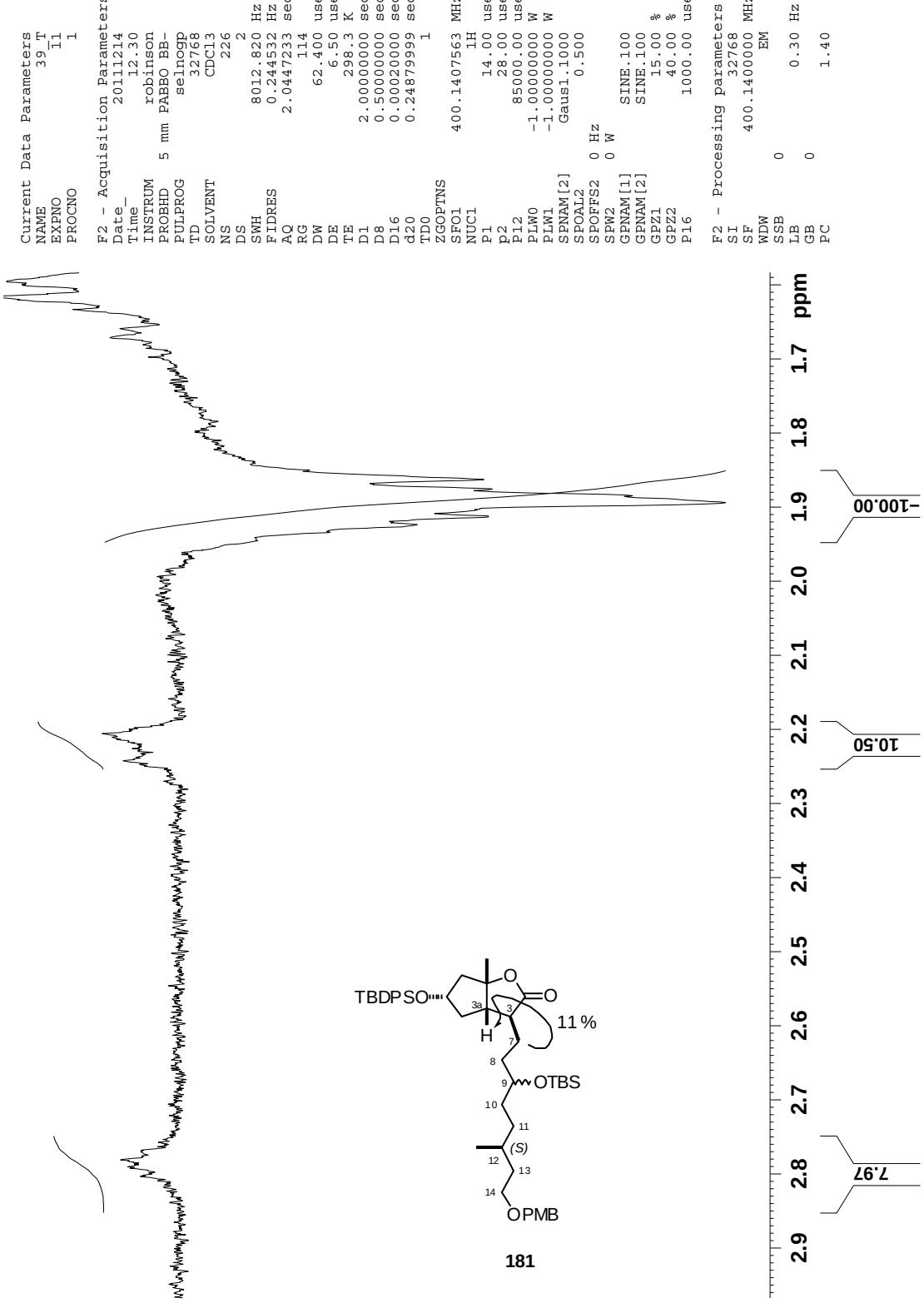
158

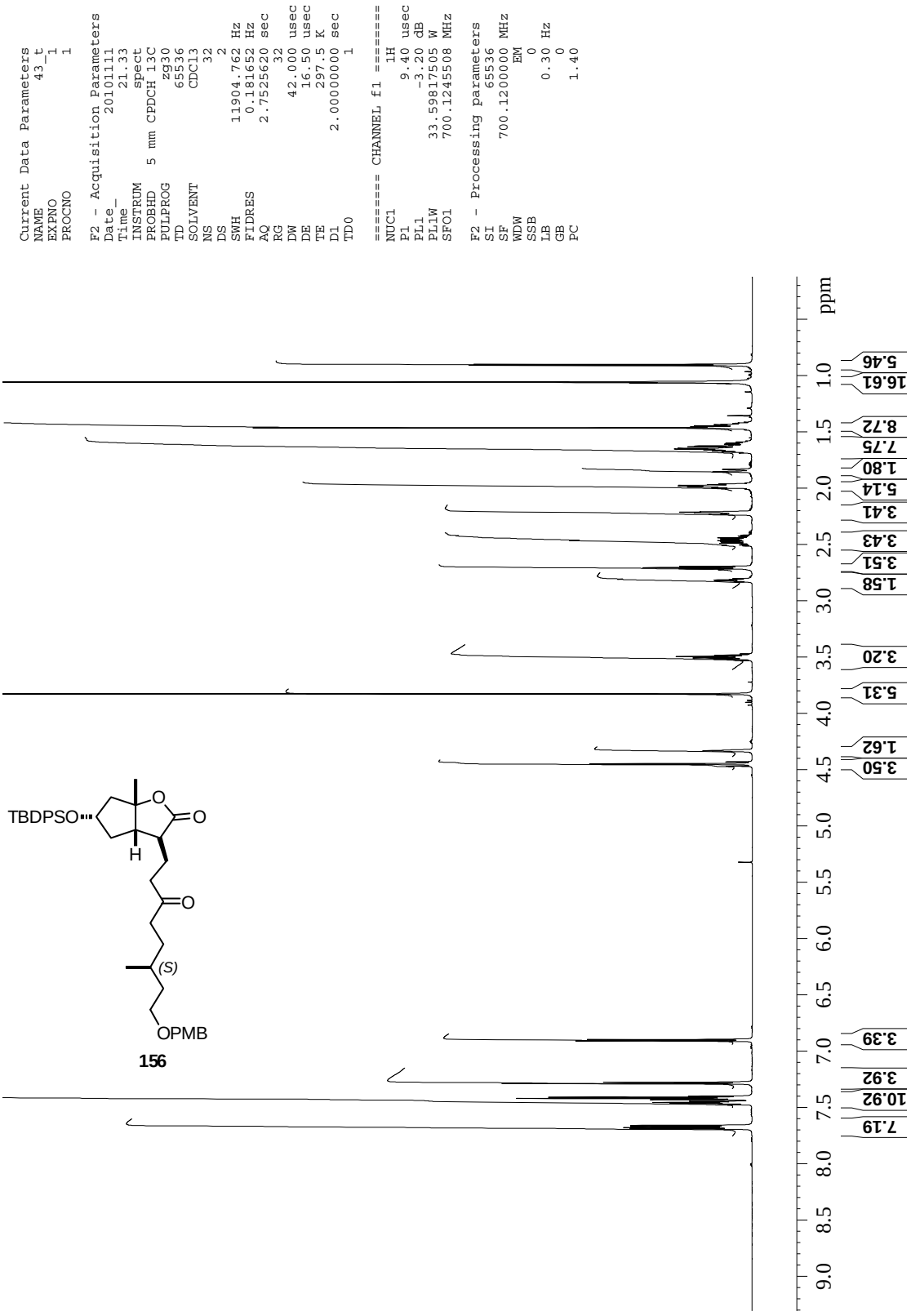

Current Data Parameters
NAME 15_IV
EXPNO 3
PROCNO 1
F2 - Acquisition Paramet
Date_ 20060220
Time_ 15.27
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 3116
DS 4
SWH 25125.629
FIDRES 0.383387
AQ 1.3042164
RG 4597.6
DW 19.900
DE 6.00
TE 298.2
D1 0.15000001
d11 0.03000000
DELTA 0.05000000
TD0 1
======== CHANNEL f1 ====
NUC1 13C
P1 7.80
PL1 -3.00
SFO1 100.5936591
======== CHANNEL f2 ====
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00
PL2 17.40
PL12 17.40
PL13 17.40
SFO2 400.0116000
F2 - Processing paramete
ppm
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
(S)
OPMB
I
OTBS

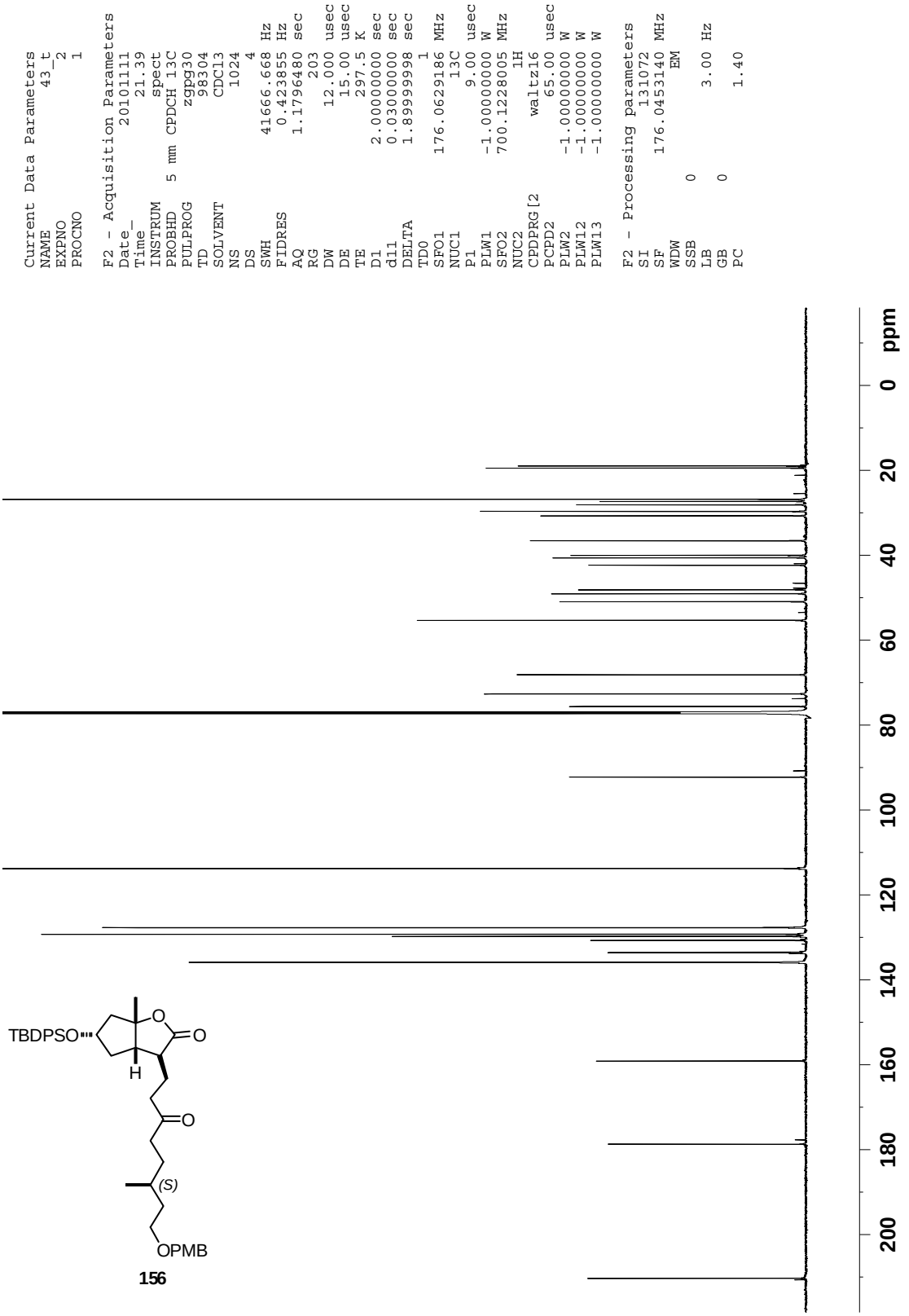
158

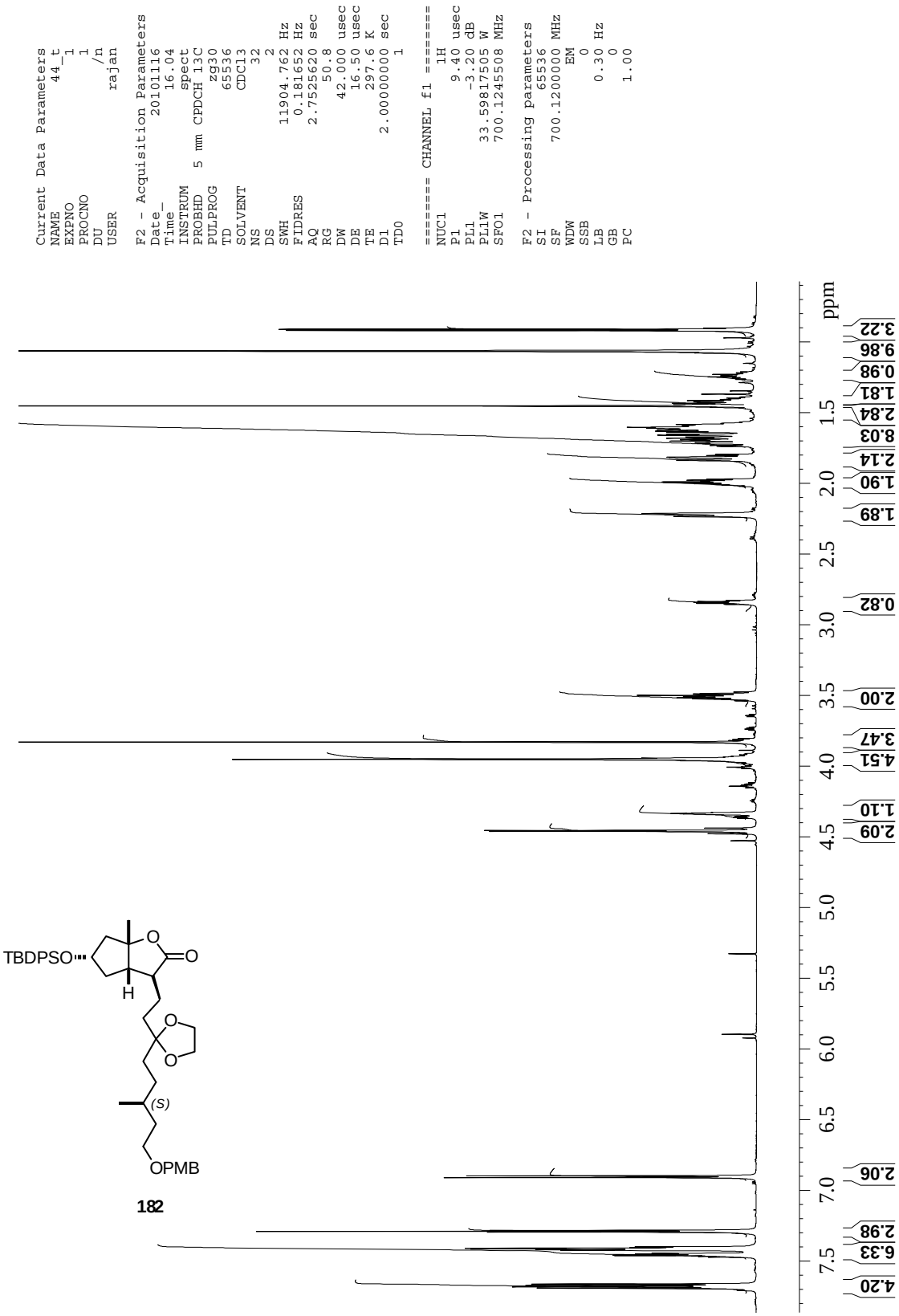

NAME 39_T
EXPNO 1
PROCNO 1
Date_ 20101108
Time 16.54
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.181652 Hz
AQ 2.7525620 sec
RG 144
DW 42.000 usec
DE 16.50 usec
TE 297.6 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1245508 MHz
SI 65536
SF 700.1200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40
ppm
5.72
13.91
8.41
0.99
2.62
5.10
8.82
0.20
0.79
0.89
0.81
1.66
0.71
1.89
0.74
3.00
0.82
1.90
1.94
4.23
5.88
3.75
TBDPSO
O
O
H
OTBS
(S)
OPMB
181


Current Data Parameters
NAME 39_T
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20101108
Time_ 17.01
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 1.1796480 sec
RG 203
DW 12.000 usec
DE 15.00 usec
TE 297.5 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
SFO1 176.0629186 MHz
NUC1 13C
P1 9.00 usec
PLW1 -1.00000000 W
SFO2 700.1228005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 65.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 131072
SF 176.0453140 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
0 ppm
20
40
60
80
100
120
140
160
180
TBDPSO
O
O
H
OTBS
(S)
OPMB
181

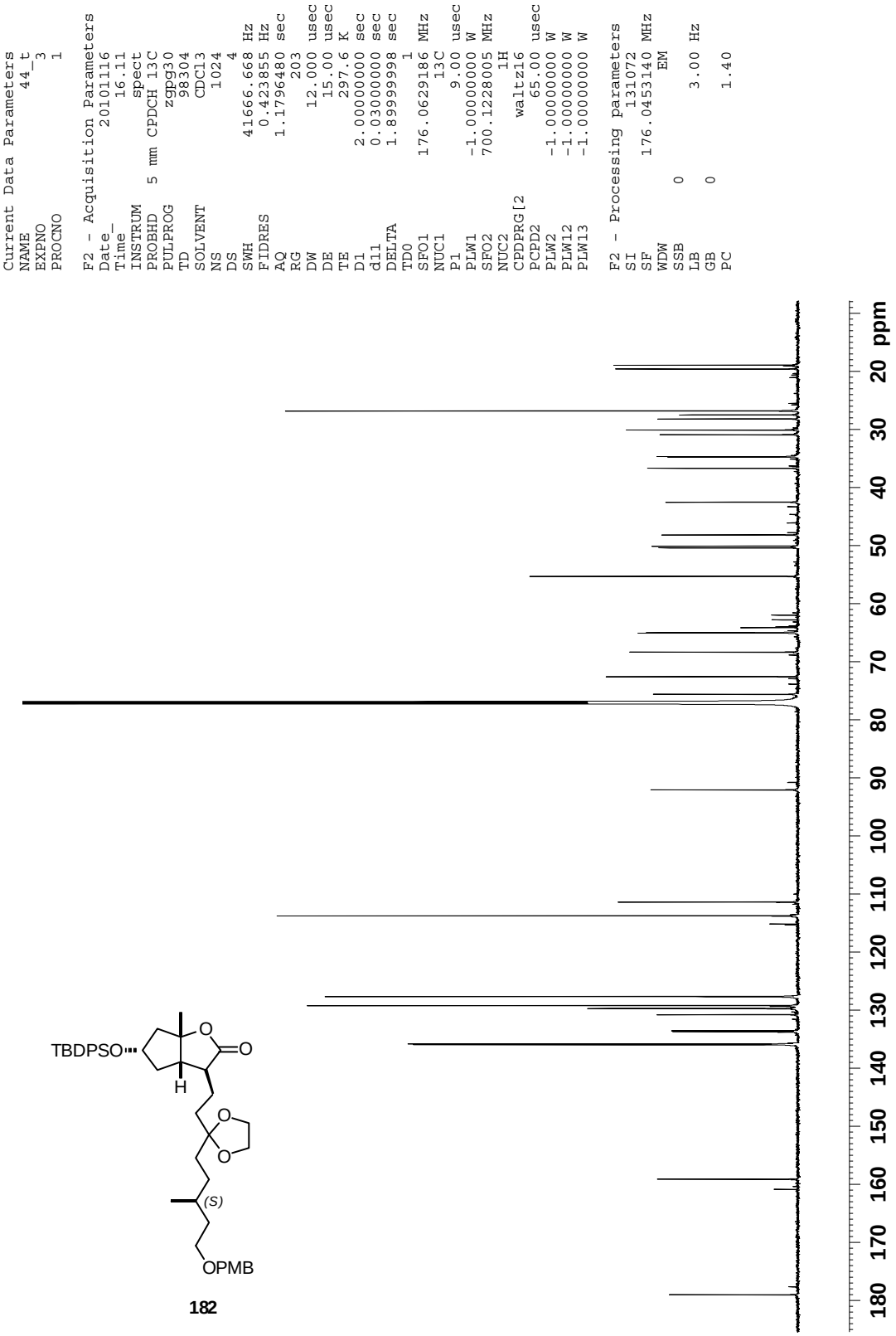

Current Data Parameters
NAME 39_T
EXPNO 11
PROCNO 1
F2 - Acquisition Parameters
Date_ 20111214
Time_ 12.30
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG selnogp
TD 32768
SOLVENT CDC13
NS 226
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 2.0447233 sec
RG 114
DW 62.400 usec
DE 6.50 usec
TE 298.3 K
D1 2.00000000 sec
D8 0.50000000 sec
D16 0.00020000 sec
d20 0.24879999 sec
TD0 1
ZGOPTNS
SFO1 400.1407563 MHz
NUC1 1H
P1 14.00 usec
p2 28.00 usec
P12 85000.00 usec
PLW0 -1.00000000 W
PLW1 -1.00000000 W
SPNAM[2] Gaus1.1000
SPOAL2 0.500
SPOFFS2 0 Hz
SPW2 0 W
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPZ1 15.00 %
GPZ2 40.00 %
P16 1000.00 usec
F2 - Processing parameters
SI 32768
SF 400.1400000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40
TBDPSO
O
O
3a
3
H
7
11 %
8
9
OTBS
10
11
(S)
12
13
14
OPMB
181
2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
ppm
7.97
10.50
100.00

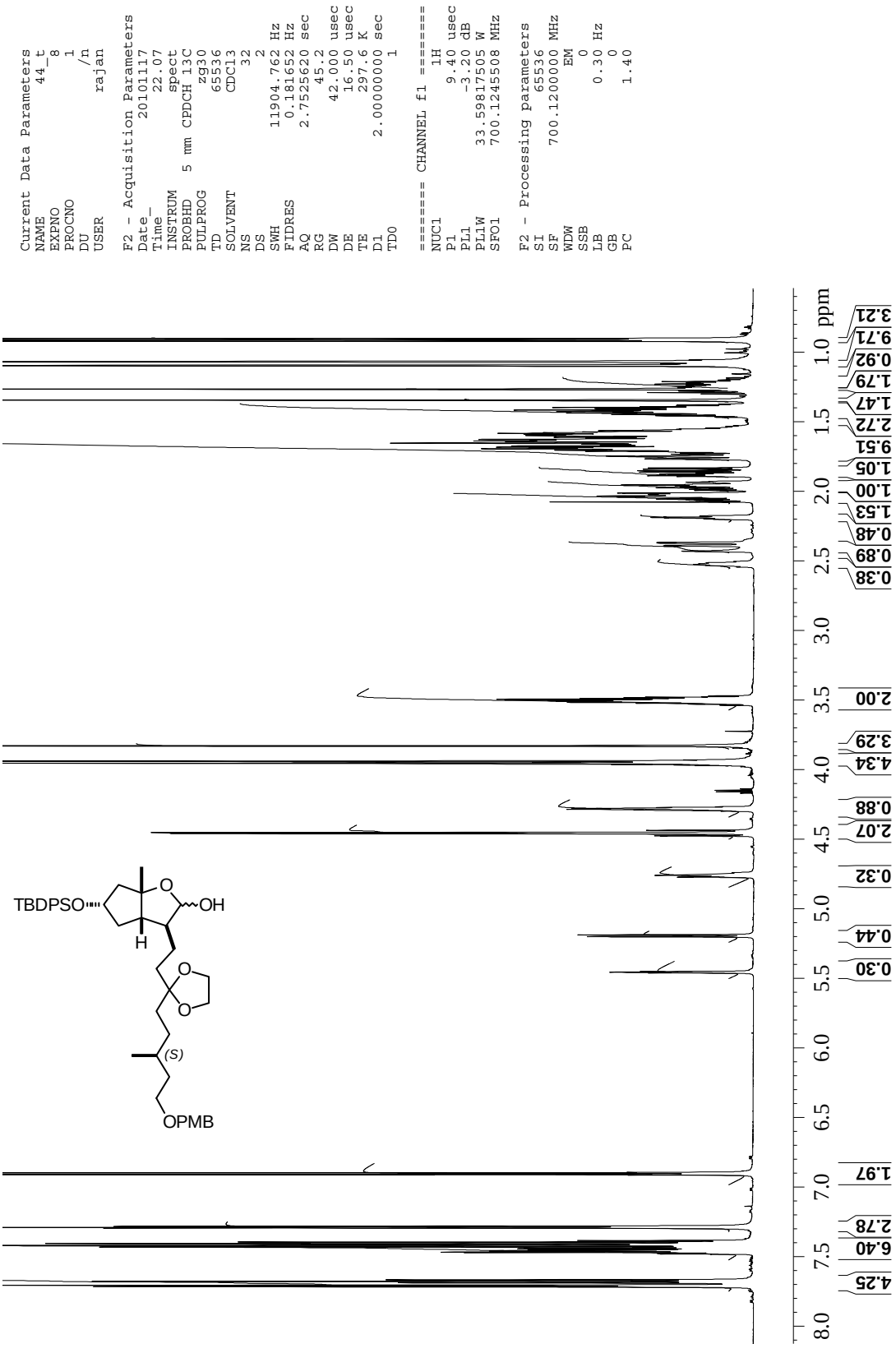

Current Data Parameters
NAME 43_t
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20101111
Time_ 21.33
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.181652 Hz
AQ 2.7525620 sec
RG 32
DW 42.000 usec
DE 16.50 usec
TE 297.5 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1245508 MHz
F2 - Processing parameters
SI 65536
SF 700.1200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40
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
5.46
16.61
8.72
7.75
1.80
5.14
3.41
3.43
3.51
1.58
3.20
5.31
1.62
3.50
3.39
3.92
10.92
7.19
TBDPSO
O
O
H
O
(S)
OPMB
156

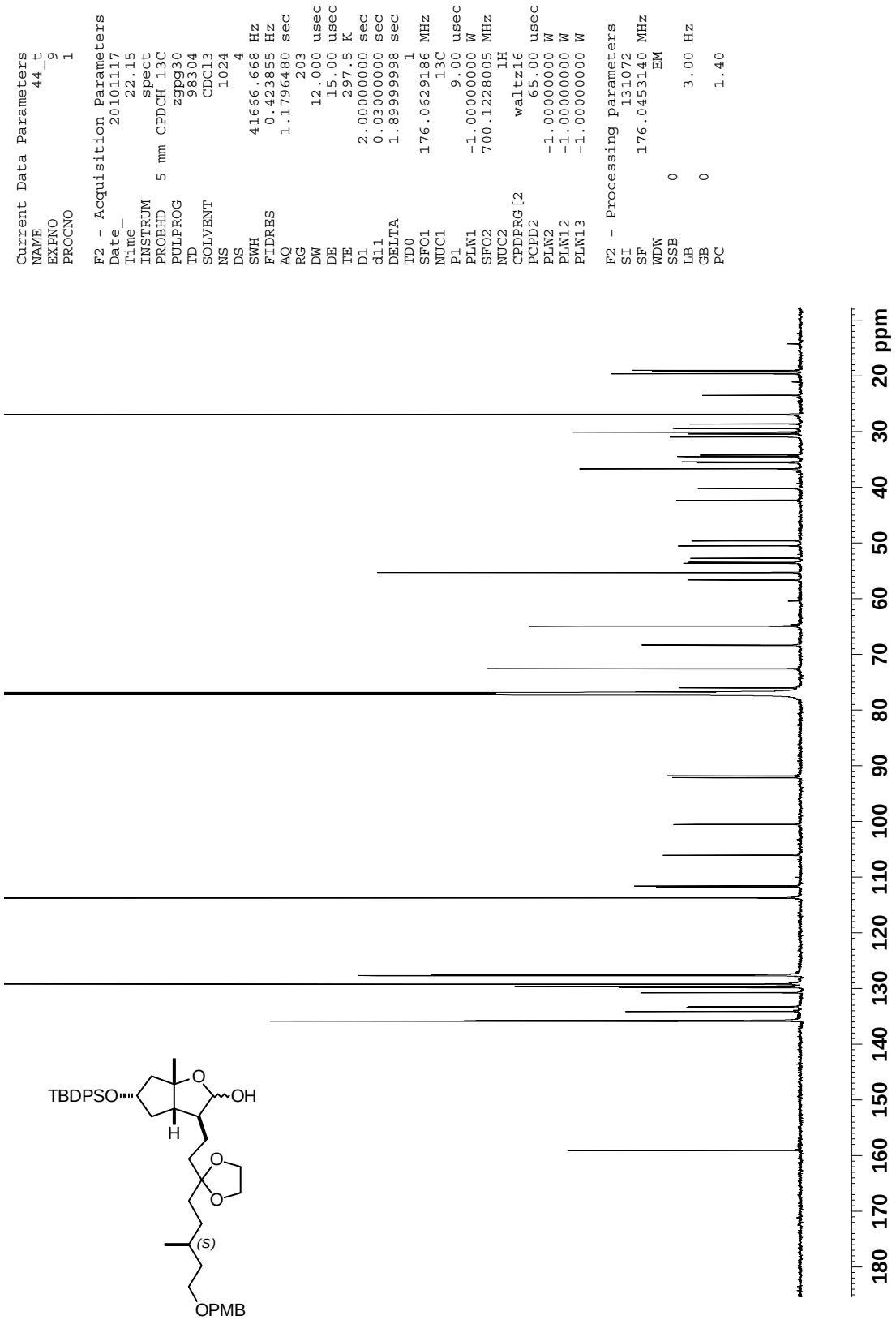

Current Data Parameters
NAME 43_t
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20101111
Time_ 21.39
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDC13
NS 1024
DS 4
SWH 41666.668 Hz
FIDRES 0.423855 Hz
AQ 1.1796480 sec
RG 203
DW 12.000 usec
DE 15.00 usec
TE 297.5 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
SFO1 176.0629186 MHz
NUC1 13C
P1 9.00 usec
PLW1 -1.00000000 W
SFO2 700.1228005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 65.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 131072
SF 176.0453140 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
TBDPSO
O
O
H
O
(S)
OPMB
156
200
180
160
140
120
100
80
60
40
20
0
ppm

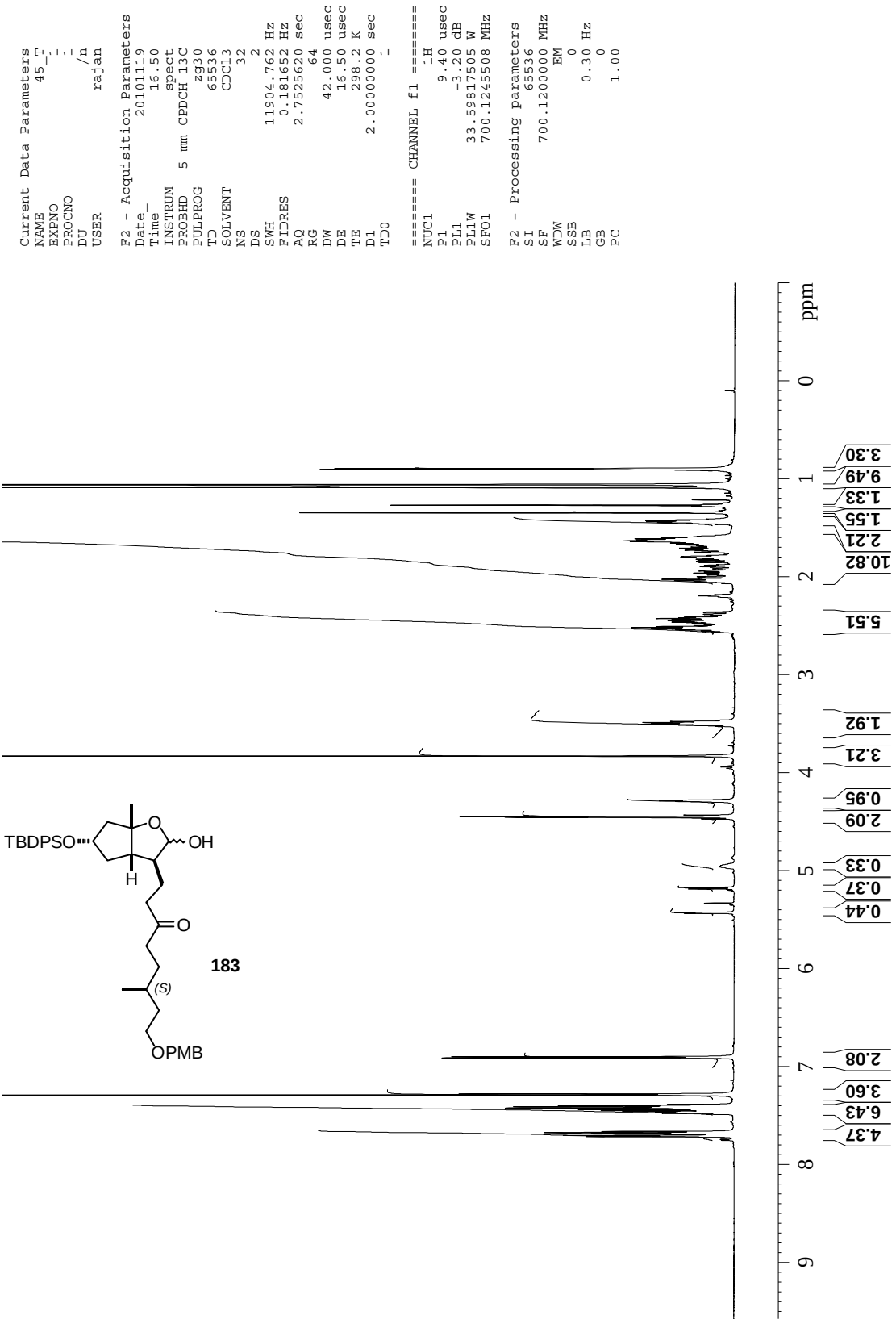

Current Data Parameters
NAME 44_t
EXPNO 1
PROCNO 1
DU /n
USER rajan
F2 - Acquisition Parameters
Date_ 20101116
Time 16.04
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.1816652 Hz
AQ 2.7525620 sec
RG 50.8
DW 42.000 usec
DE 16.50 usec
TE 297.6 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
F2 - Processing parameters
SI 65536
SF 700.1200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
TBDPSO
O
O
H
O
O
(S)
OPMB
ppm
4.20
6.33
2.98
2.06
0.98
9.86
3.22
1.81
2.84
8.03
2.14
1.90
1.89
0.82
2.00
3.47
4.51
1.10
2.09

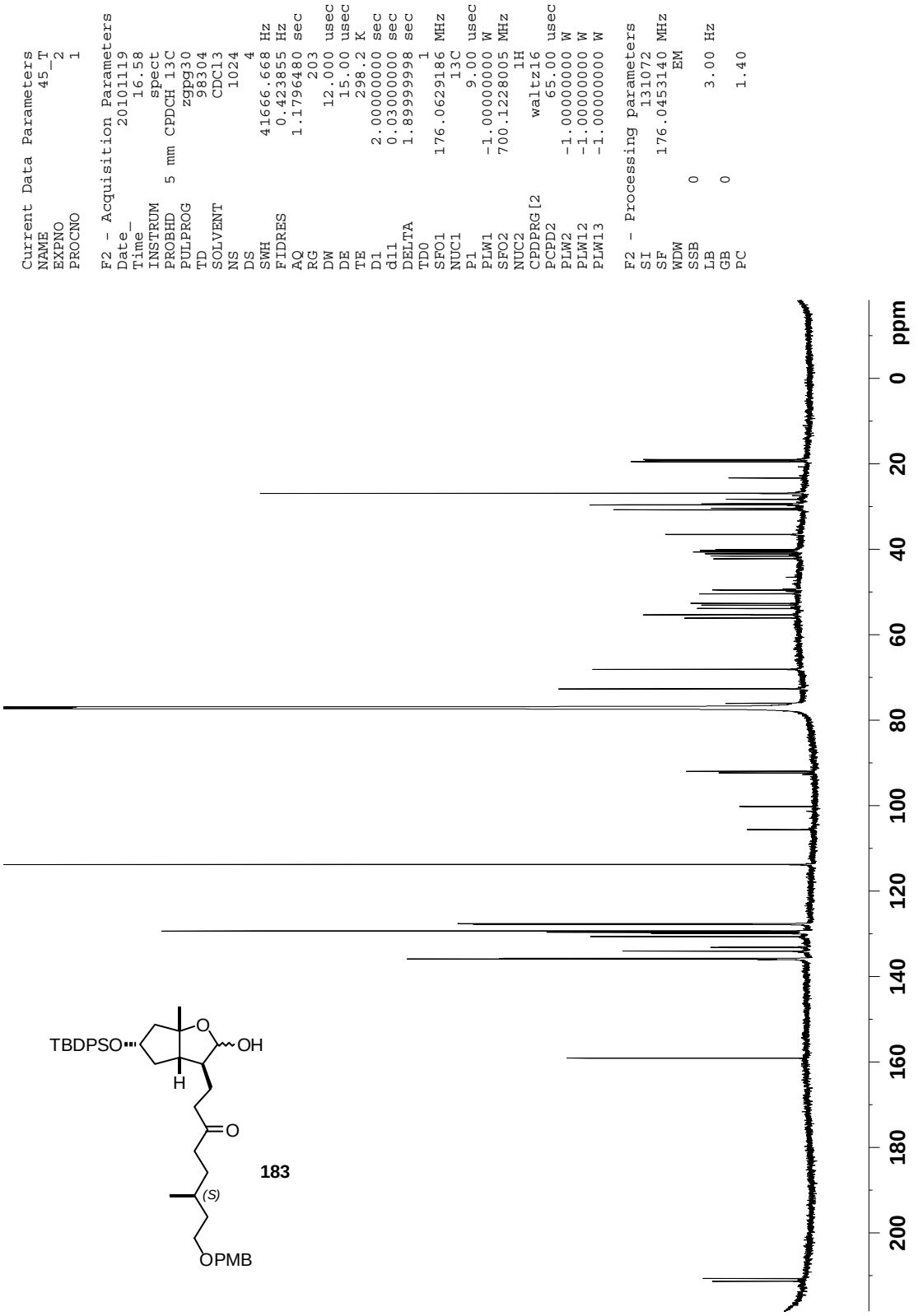
182

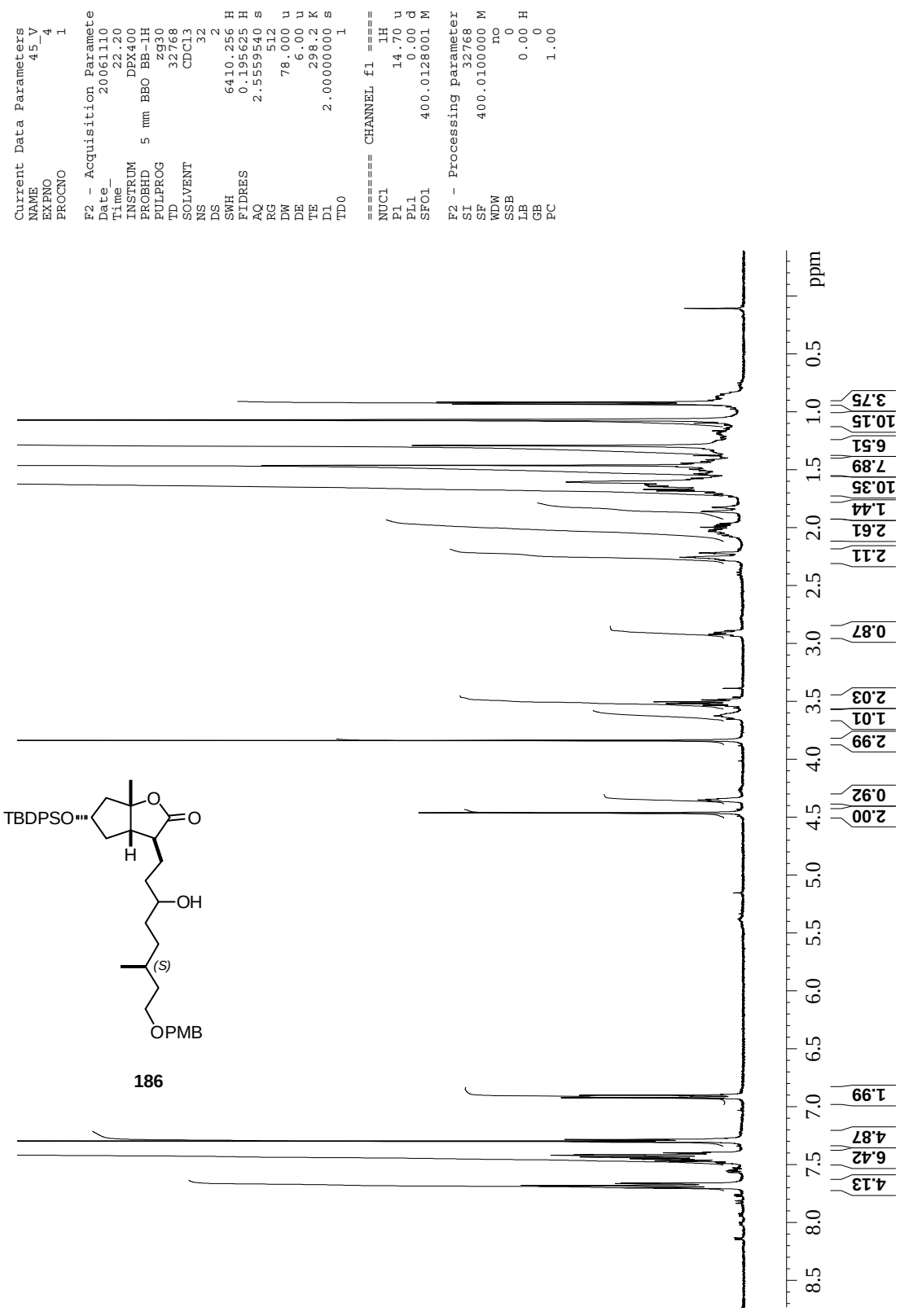

Current Data Parameters
NAME 44_t
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20101116
Time_ 16.11
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDCl3
NS 1024
DS 4
SWH 41666.668 Hz
FIDRES 0.423855 Hz
AQ 1.1796480 sec
RG 203
DW 12.000 usec
DE 15.000 usec
TE 297.6 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
SFO1 176.0629186 MHz
NUC1 13C
P1 9.00 usec
PLW1 -1.00000000 W
SFO2 700.1228005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 65.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 131072
SF 176.0453140 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
TBDPSO
O
O
H
O
O
(S)
OPMB
182
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

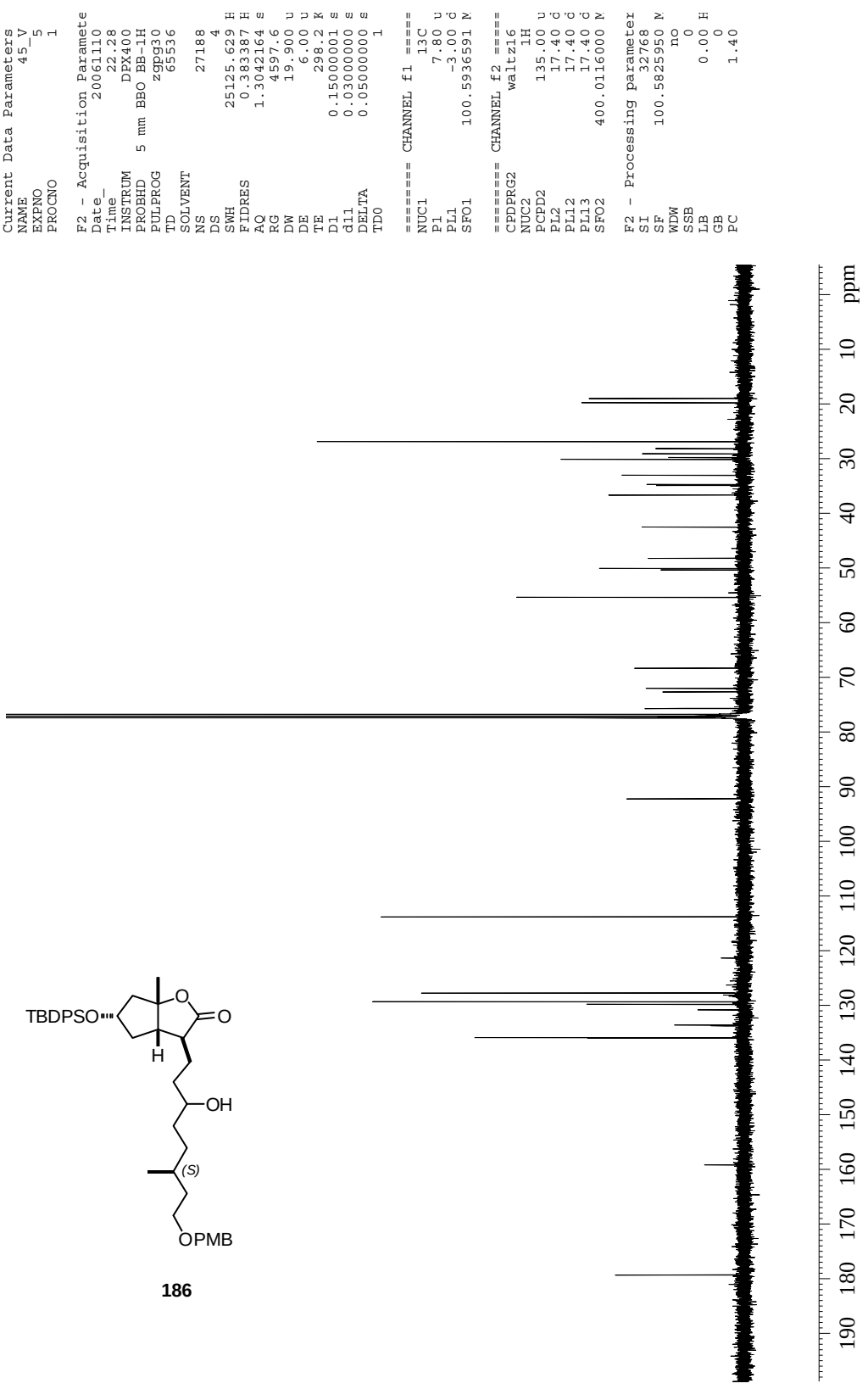

Current Data Parameters
NAME 44_t
EXPNO 8
PROCNO 1
DU /n
USER rajan
F2 - Acquisition Parameters
Date_ 20101117
Time 22.07
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.1816652 Hz
AQ 2.7525620 sec
RG 45.2
DW 42.000 usec
DE 16.50 usec
TE 297.6 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
F2 - Processing parameters
SI 65536
SF 700.1200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40
TBDPSO
O
OH
H
O
O
(S)
OPMB
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
2.0
1.5
1.0
4.25
6.40
2.78
1.97
0.30
0.44
0.32
2.07
0.88
4.34
3.29
2.00
0.38
0.89
0.48
1.53
1.00
1.05
9.51
2.72
1.47
1.79
0.92
9.71
3.21


Current Data Parameters
NAME 44_t
EXPNO 9
PROCNO 1
F2 - Acquisition Parameters
Date_ 20101117
Time 22.15
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 1.1796480 sec
RG 203
DW 12.000 usec
DE 15.00 usec
TE 297.5 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
SFO1 176.0629186 MHz
NUC1 13C
P1 9.00 usec
PLW1 -1.00000000 W
SFO2 700.1228005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 65.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 131072
SF 176.0453140 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
TBDPSO
OH
H
O
O
O
(S)
OPMB
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

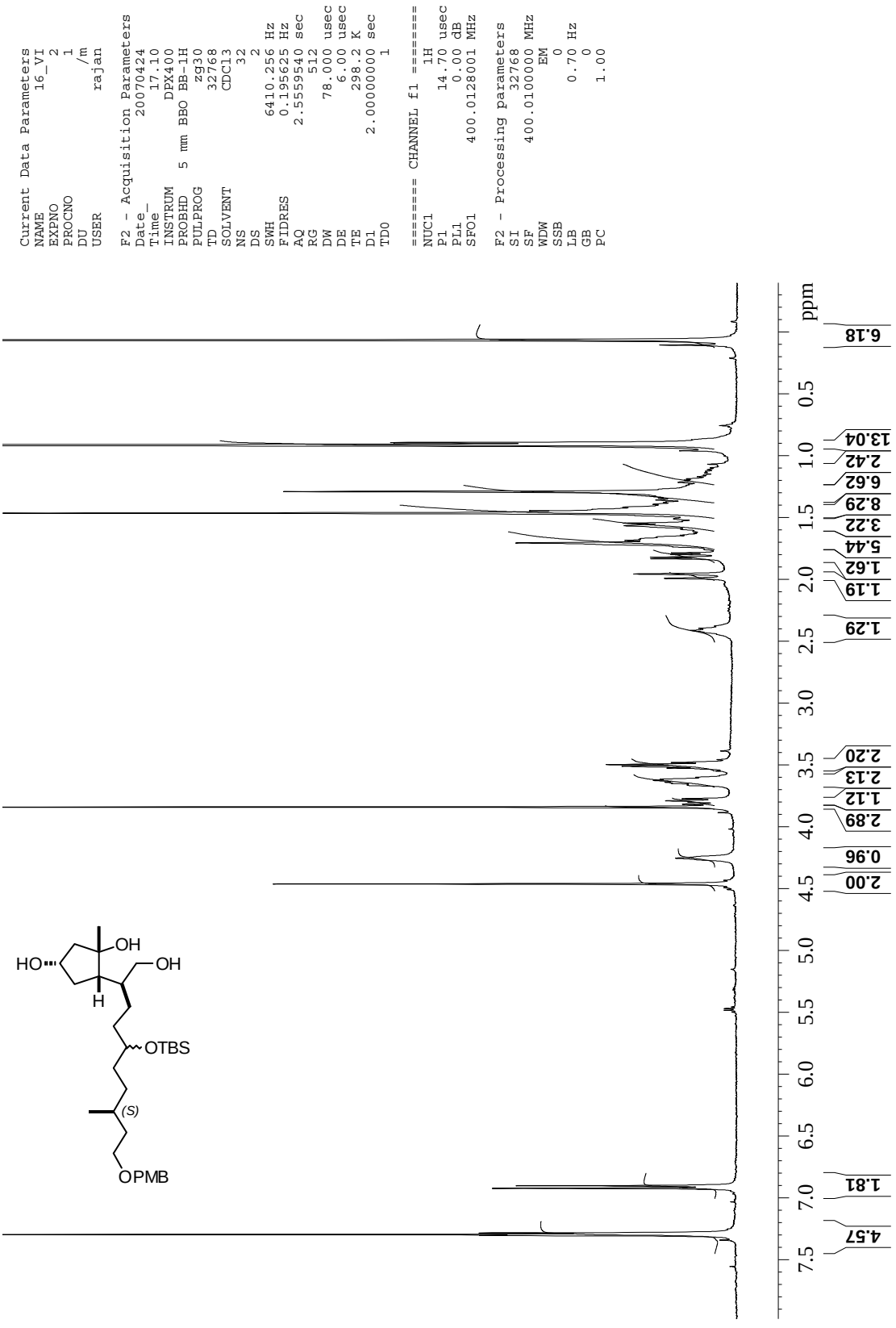

Current Data Parameters
NAME 45_T
EXPNO 1
PROCNO 1
DU /n
USER rajan
F2 - Acquisition Parameters
Date_ 20101119
Time 16.50
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.1816652 Hz
AQ 2.7525620 sec
RG 64
DW 42.000 usec
DE 16.50 usec
TE 298.2 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
F2 - Processing parameters
SI 65536
SF 700.1200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
TBDPSO
OH
O
H
O
(S)
OPMB
183
ppm
3.30
9.49
1.33
1.55
2.21
10.82
5.51
1.92
3.21
0.95
2.09
0.33
0.37
0.44
2.08
3.60
6.43
4.37

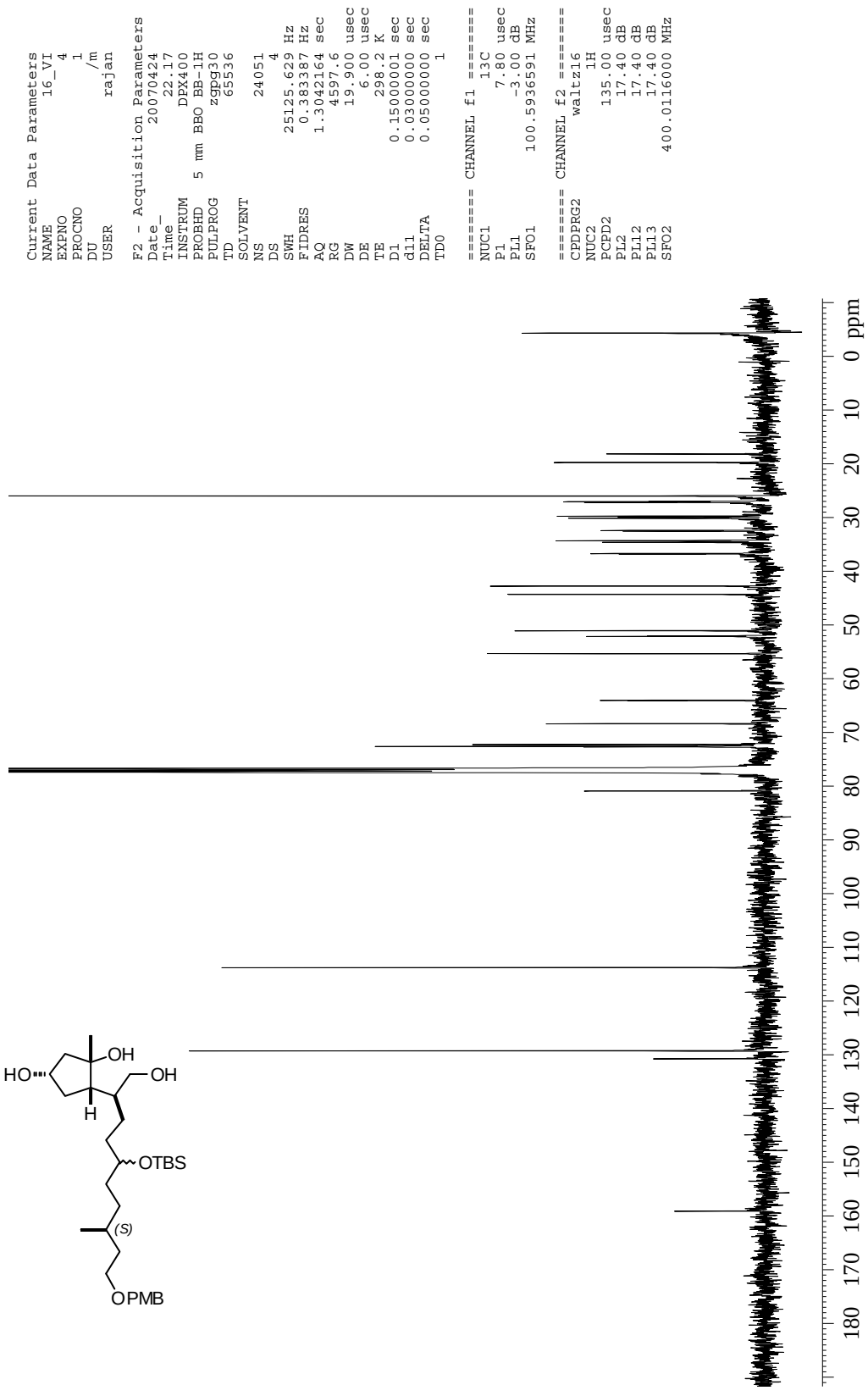

Current Data Parameters
NAME 45_T
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20101119
Time 16.58
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDCl3
NS 1024
DS 4
SWH 41666.668 Hz
FIDRES 0.423855 Hz
AQ 1.1796480 sec
RG 203
DW 12.000 usec
DE 15.00 usec
TE 298.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
SFO1 176.0629186 MHz
NUC1 13C
P1 9.00 usec
PLW1 -1.00000000 W
SFO2 700.1228005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 65.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 131072
SF 176.0453140 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
TBDPSO
OH
O
H
O
(S)
OPMB
183
200
180
160
140
120
100
80
60
40
20
0
ppm

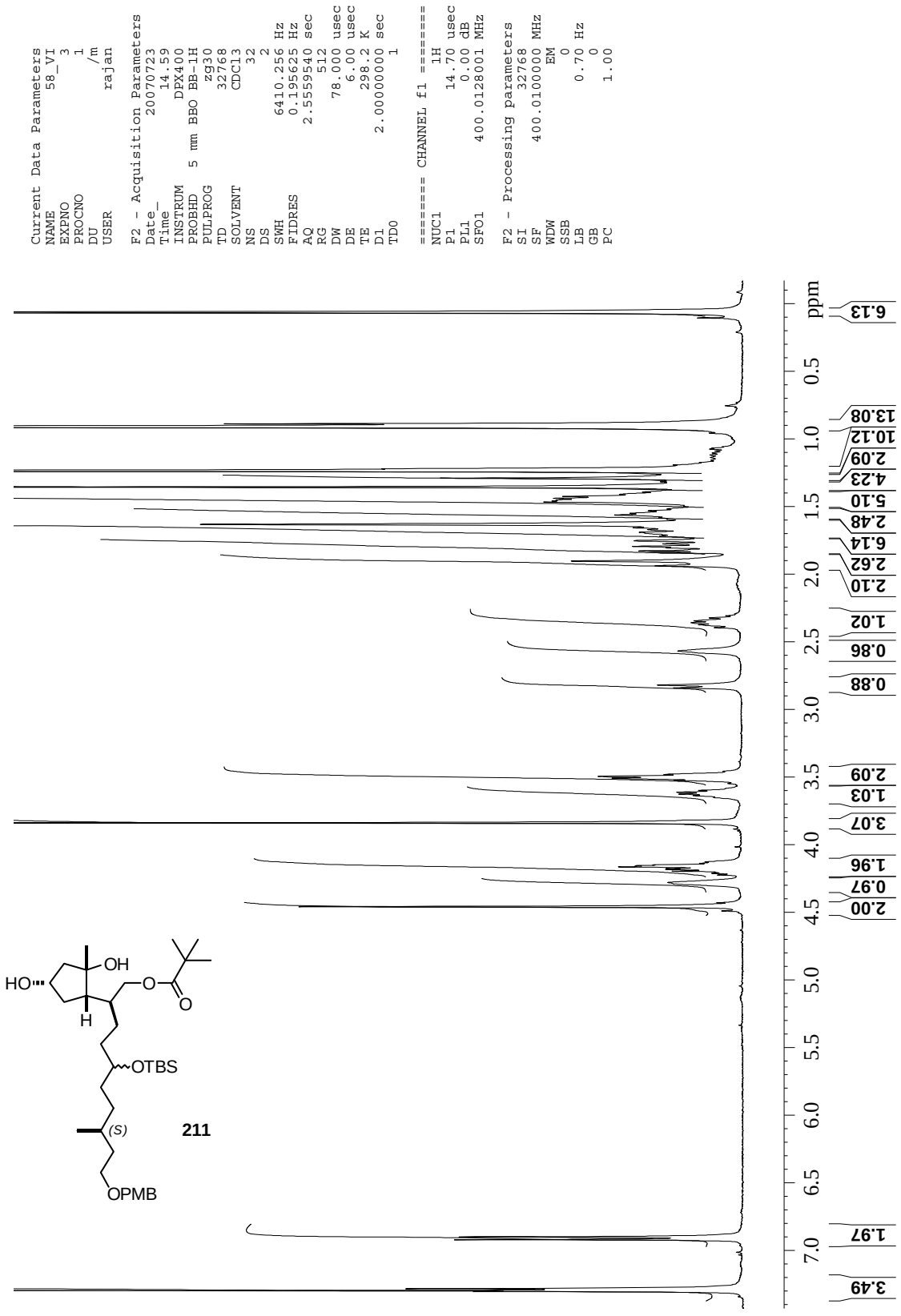

Current Data Parameters
NAME 45_V
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20061110
Time 22.20
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 512
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 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 no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
TBDPSO
O
O
H
OH
(S)
OPMB
186
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
4.13
6.42
4.87
1.99
0.92
2.00
2.99
1.01
2.03
0.87
2.11
2.61
1.44
10.35
7.89
6.51
10.15
3.75

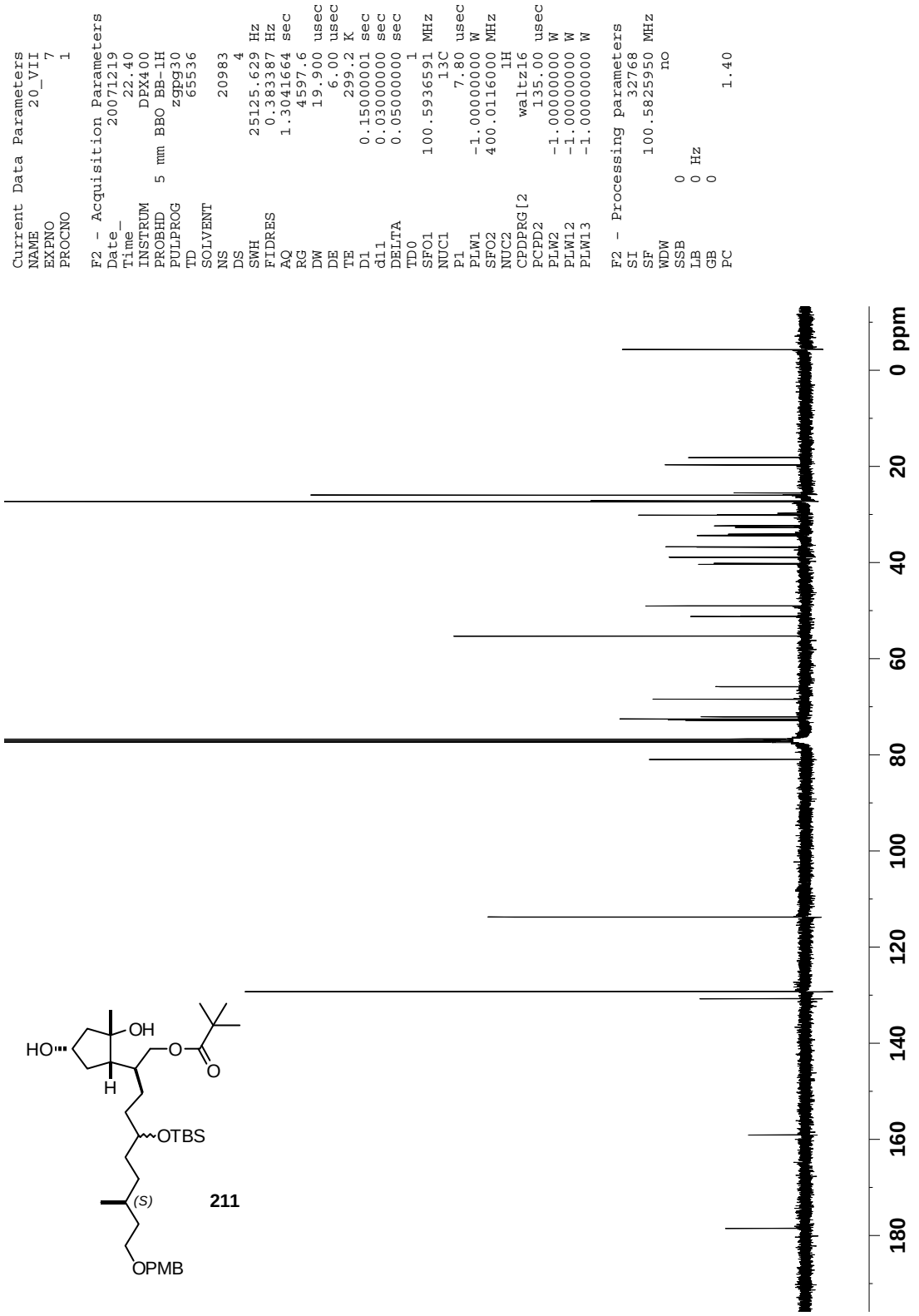

Current Data Parameters
NAME 45_V
EXPNO 5
PROCNO 1
F2 - Acquisition Parameters
Date_ 20061110
Time 22.28
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 27188
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3042164 sec
RG 4597.6
DW 19.900 usec
DE 6.00 usec
TE 298.2 K
D1 0.15000001 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 no
SSB 0
LB 0.00 Hz
GB 0
PC 1.40
TBDPSO
O
O
H
OH
(S)
OPMB
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
190

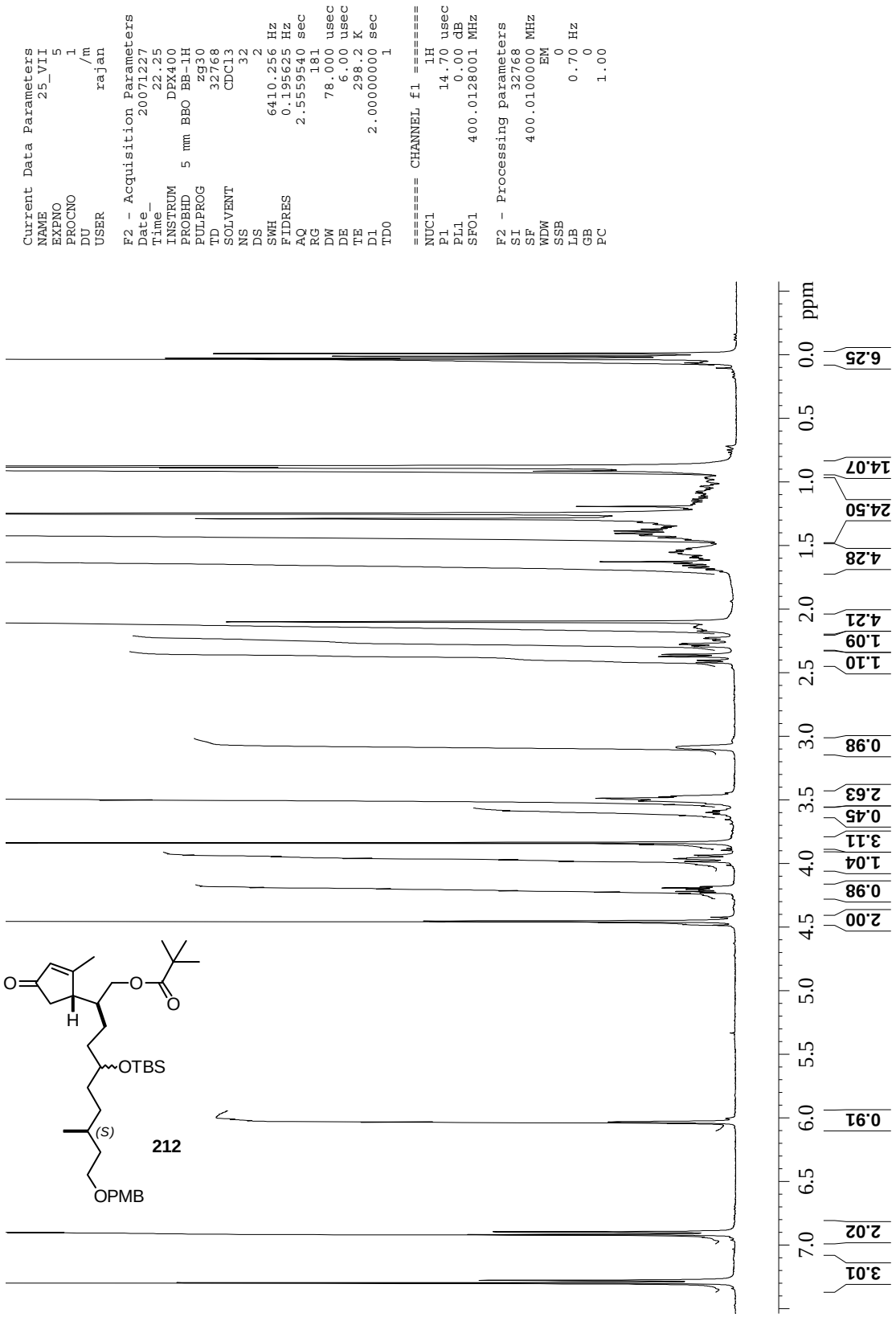
186

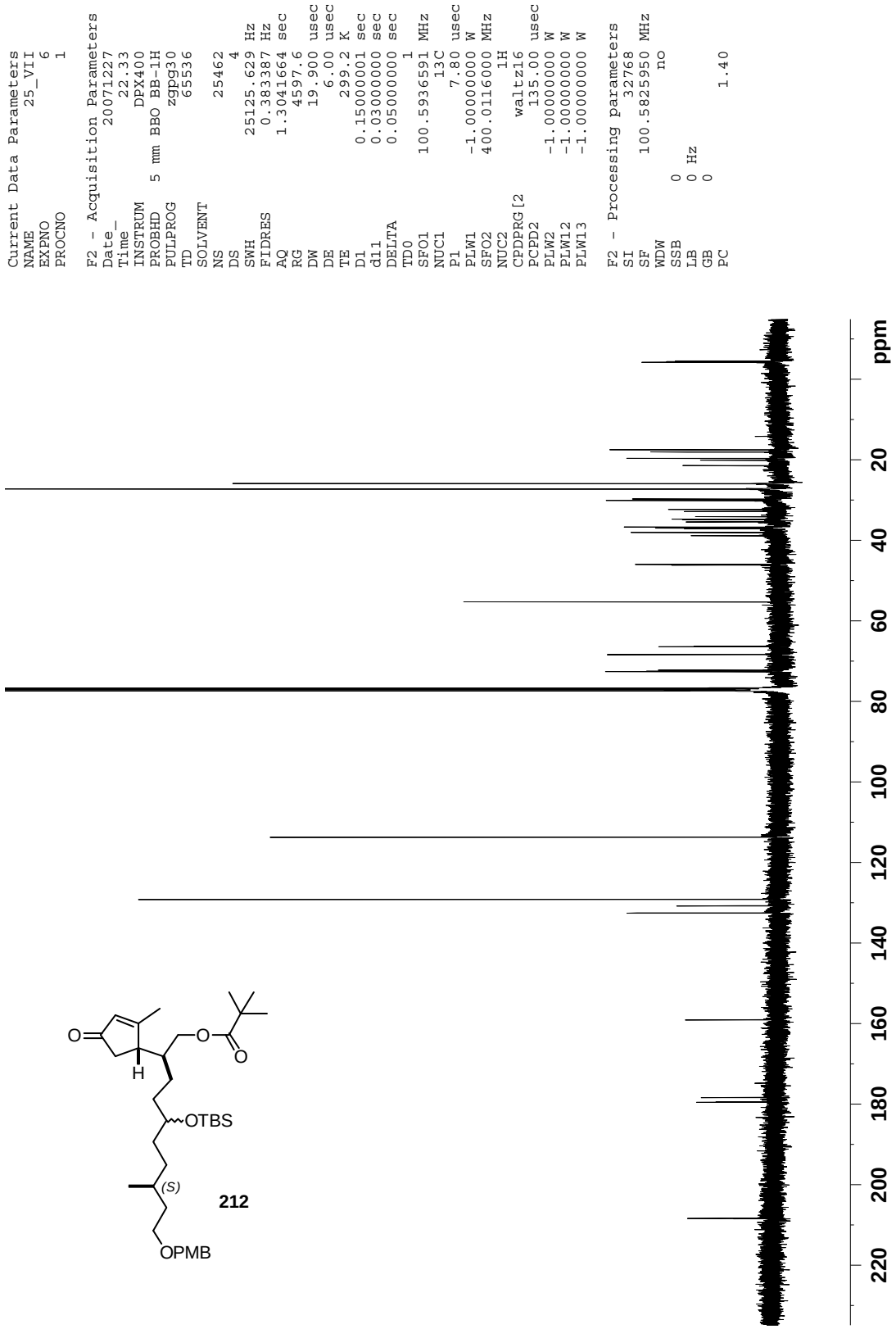

Current Data Parameters
NAME 16_VI
EXPNO 2
PROCNO 1
DU /m
USER rajan
F2 - Acquisition Parameters
Date_ 20070424
Time 17.10
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 512
DW 78.000 usec
DE 6.00 usec
TE 298.2 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
HO
OH
OH
H
OTBS
(S)
OPMB
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
0.5
6.18
13.04
2.42
6.62
8.29
3.22
5.44
1.62
1.19
1.29
2.20
2.13
1.12
2.89
0.96
2.00
1.81
4.57

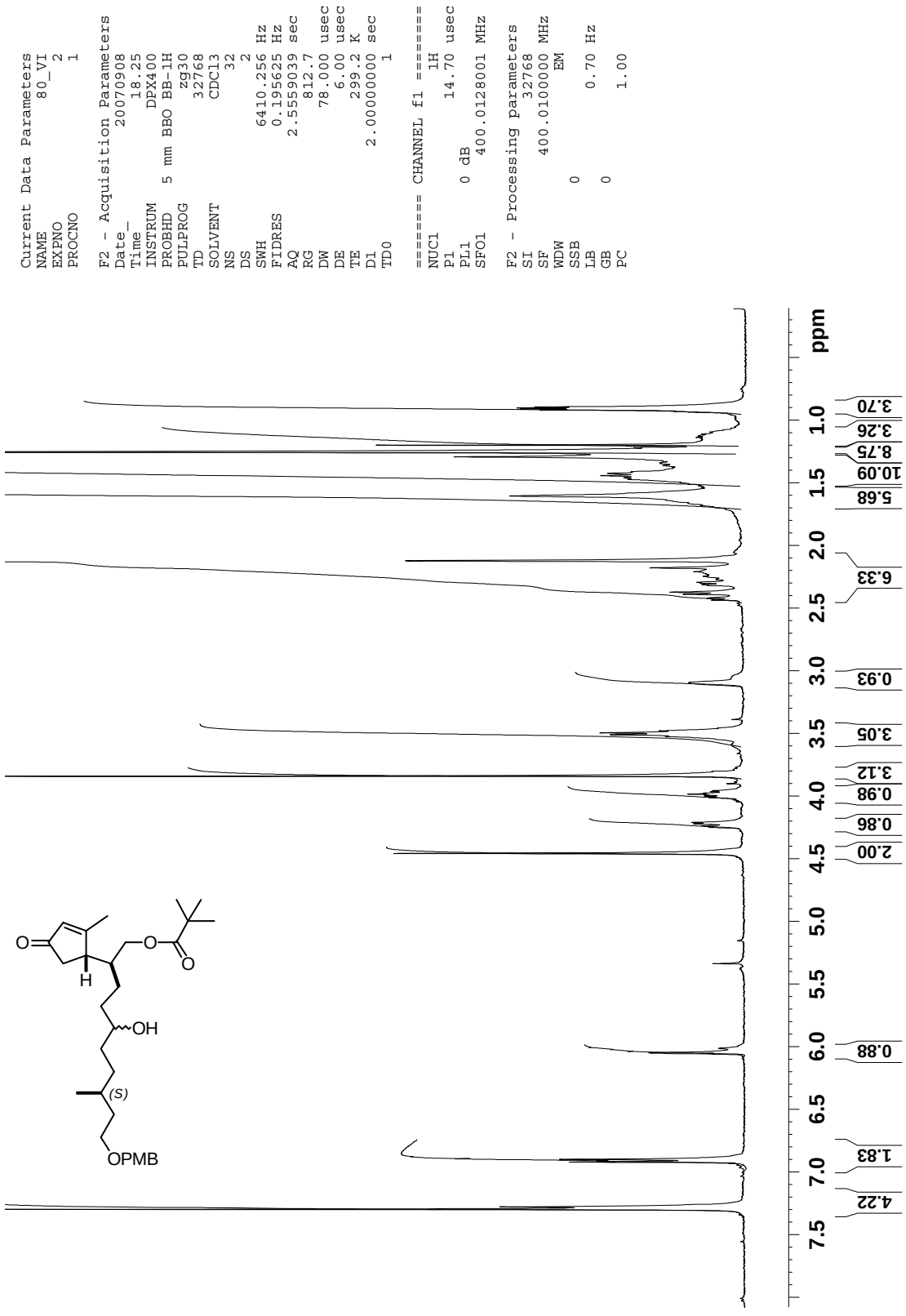

Current Data Parameters
NAME 16_VI
EXPNO 4
PROCNO 1
DU /m
USER rajan
F2 - Acquisition Parameters
Date_ 20070424
Time 22.17
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 24051
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3042164 sec
RG 4597.6
DW 19.900 usec
DE 6.00 usec
TE 298.2 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
HO
OH
OH
H
OTBS
(S)
OPMB
0 ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180

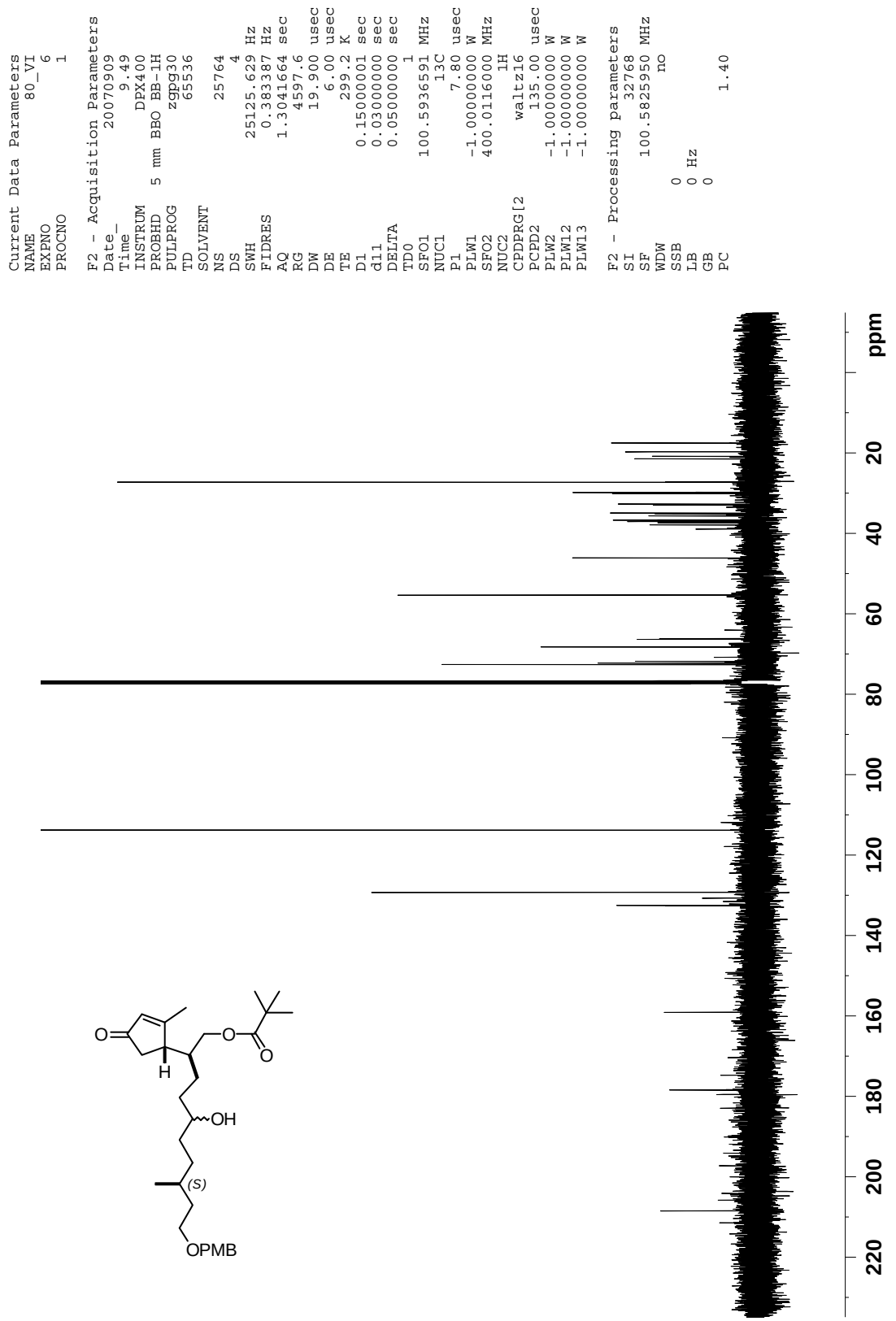

Current Data Parameters
NAME 58_VI
EXPNO 3
PROCNO 1
DU /m
USER rajan
F2 - Acquisition Parameters
Date_ 20070723
Time 14.59
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 512
DW 78.000 usec
DE 6.00 usec
TE 298.2 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
ppm
6.13
13.08
10.12
2.09
4.23
5.10
2.48
6.14
2.62
2.10
1.02
0.86
0.88
2.09
1.03
3.07
1.96
0.97
2.00
1.97
3.49
HO
OH
O
O
H
OTBS
(S)
OPMB
211

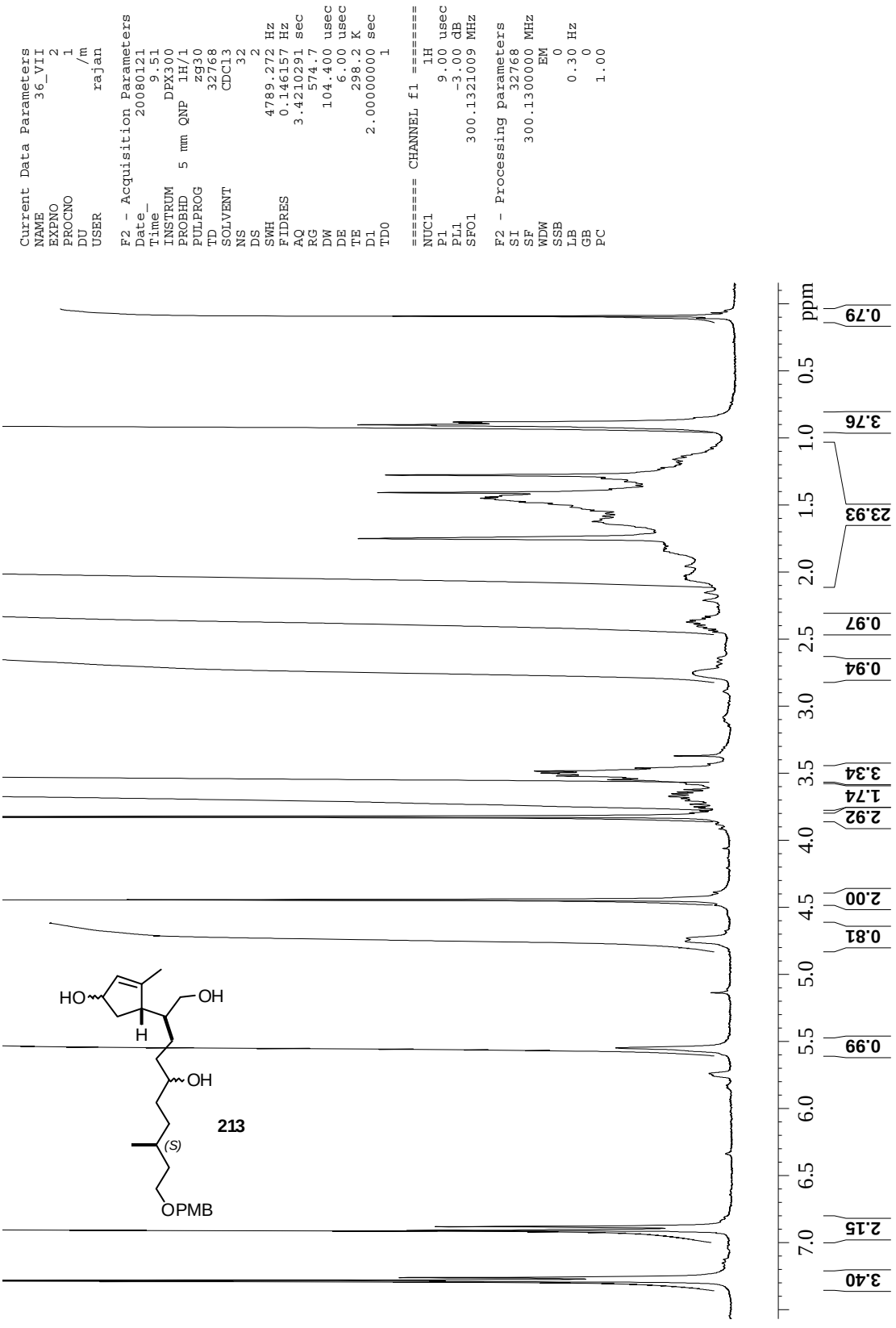

Current Data Parameters
NAME 20_VII
EXPNO 7
PROCNO 1
F2 - Acquisition Parameters
Date_ 20071219
Time_ 22.40
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 20983
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3041664 sec
RG 4597.6
DW 19.900 usec
DE 6.00 usec
TE 299.2 K
D1 0.15000001 sec
d11 0.03000000 sec
DELTA 0.05000000 sec
TD0 1
SFO1 100.5936591 MHz
NUC1 13C
P1 7.80 usec
PLW1 -1.00000000 W
SFO2 400.0116000 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 135.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 32768
SF 100.5825950 MHz
WDW no
SSB 0
LB 0 Hz
GB 0
PC 1.40
HO
OH
O
O
H
OTBS
(S)
OPMB
211
0 ppm
20
40
60
80
100
120
140
160
180

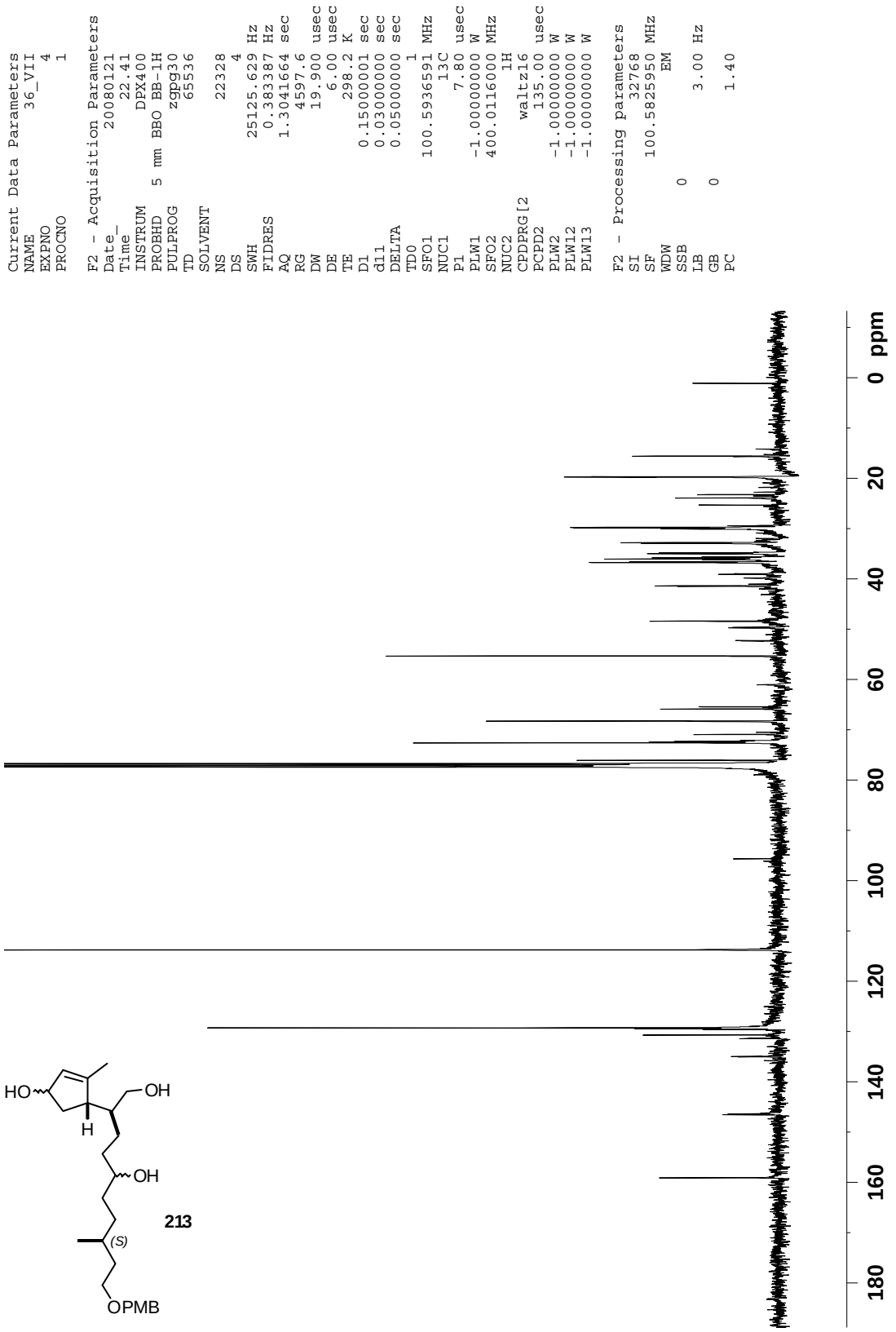

Current Data Parameters
NAME 25_VII
EXPNO 5
PROCNO 1
DU /m
USER rajan
F2 - Acquisition Parameters
Date_ 20071227
Time 22.25
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 181
DW 78.000 usec
DE 6.00 usec
TE 298.2 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
ppm
6.25
14.07
24.50
4.28
4.21
1.09
1.10
0.98
2.63
0.45
3.11
1.04
0.98
2.00
0.91
2.02
3.01
O
O
O
H
OTBS
(S)
OPMB
212

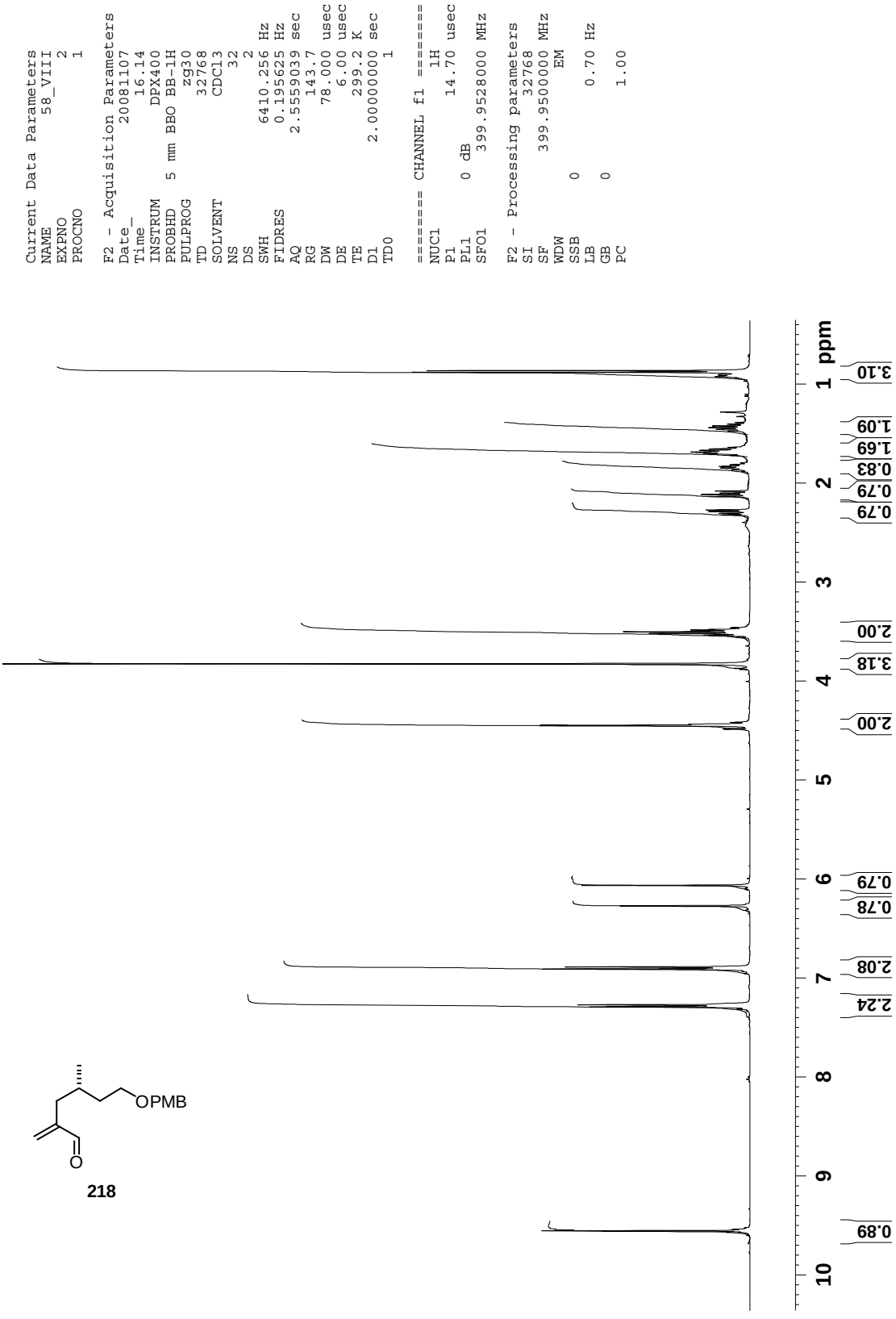

Current Data Parameters
NAME 25_VII
EXPNO 6
PROCNO 1
F2 - Acquisition Parameters
Date_ 20071227
Time 22.33
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 25462
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3041664 sec
RG 4597.6
DW 19.900 usec
DE 6.00 usec
TE 299.2 K
D1 0.15000001 sec
d11 0.03000000 sec
DELTA 0.05000000 sec
TD0 1
SFO1 100.5936591 MHz
NUC1 13C
P1 7.80 usec
PLW1 -1.00000000 W
SFO2 400.0116000 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 135.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 32768
SF 100.5825950 MHz
WDW no
SSB 0
LB 0 Hz
GB 0
PC 1.40
O
O
O
H
OTBS
(S)
OPMB
212
ppm
220
200
180
160
140
120
100
80
60
40
20

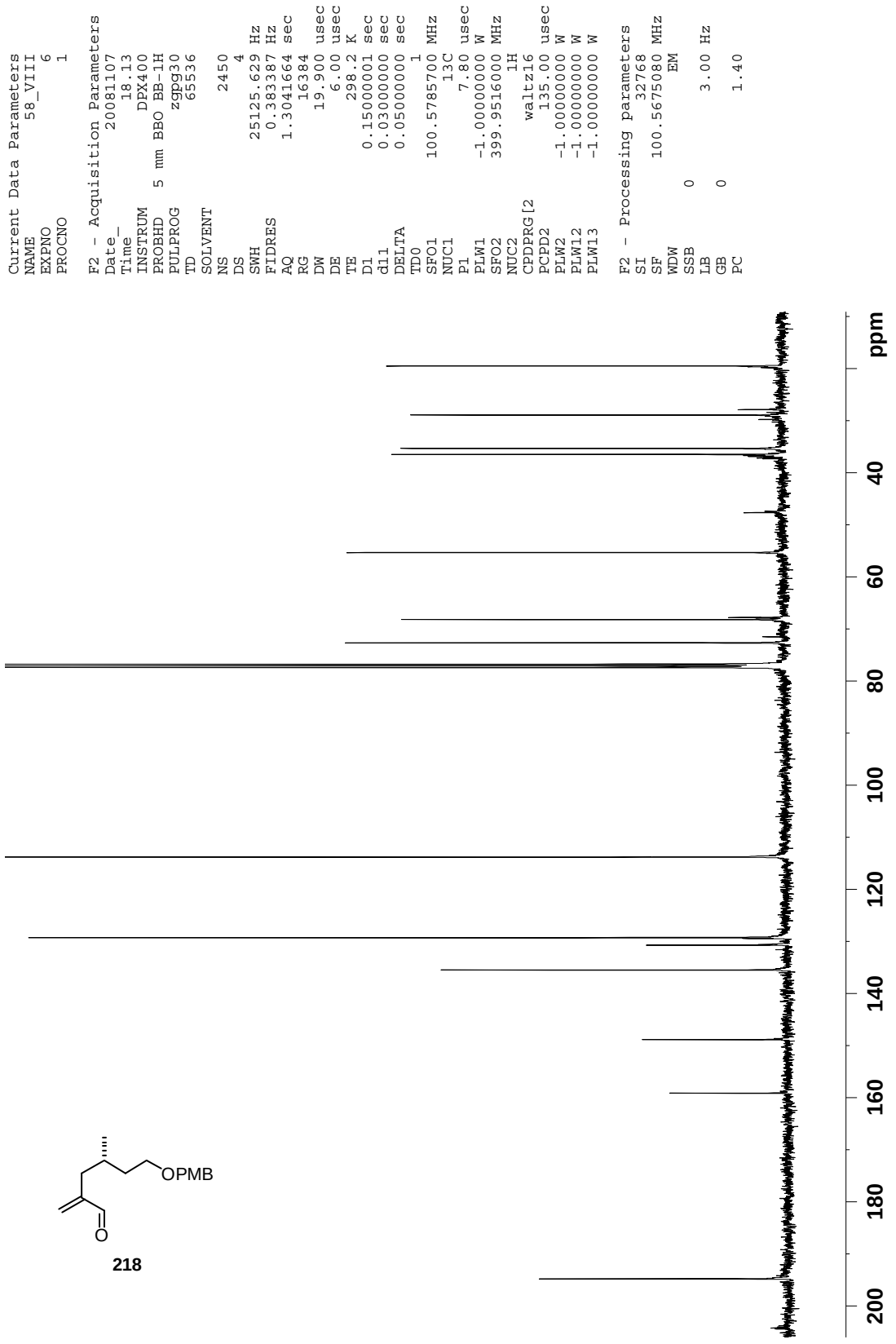

Current Data Parameters
NAME 80_VI
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20070908
Time 18.25
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559039 sec
RG 812.7
DW 78.000 usec
DE 6.00 usec
TE 299.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0 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
O
O
O
H
OH
(S)
OPMB
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
4.22
1.83
0.88
2.00
0.86
0.98
3.12
3.05
0.93
6.33
5.68
10.09
8.75
3.26
3.70

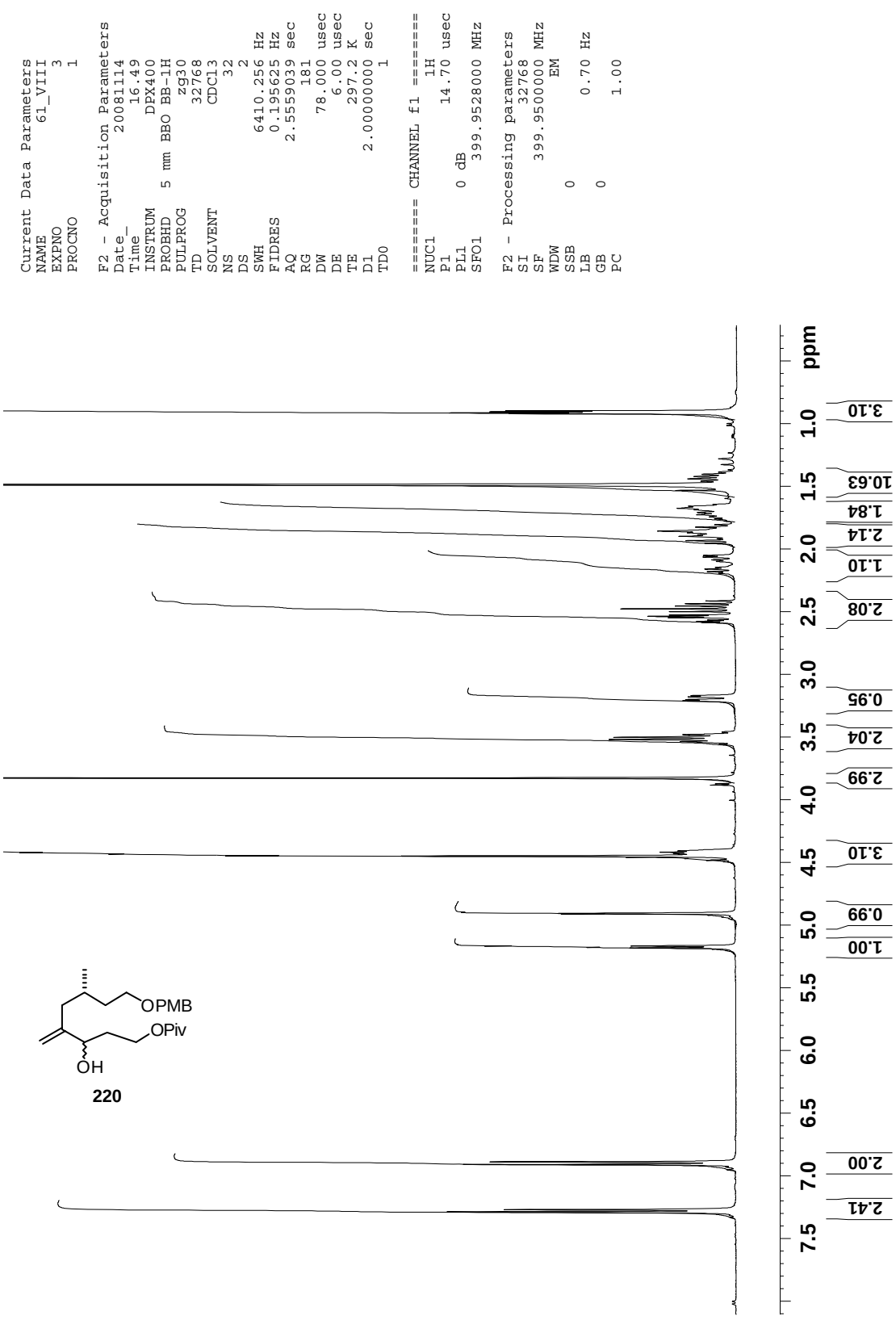

Current Data Parameters
NAME 80_VI
EXPNO 6
PROCNO 1
F2 - Acquisition Parameters
Date_ 20070909
Time_ 9.49
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 25764
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3041664 sec
RG 4597.6
DW 19.900 usec
DE 6.00 usec
TE 299.2 K
D1 0.15000001 sec
d11 0.03000000 sec
DELTA 0.05000000 sec
TD0 1
SFO1 100.5936591 MHz
NUC1 13C
P1 7.80 usec
PLW1 -1.00000000 W
SFO2 400.0116000 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 135.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 32768
SF 100.5825950 MHz
WDW no
SSB 0
LB 0 Hz
GB 0
PC 1.40
O
O
O
H
OH
(S)
OPMB
220
200
180
160
140
120
100
80
60
40
20
ppm

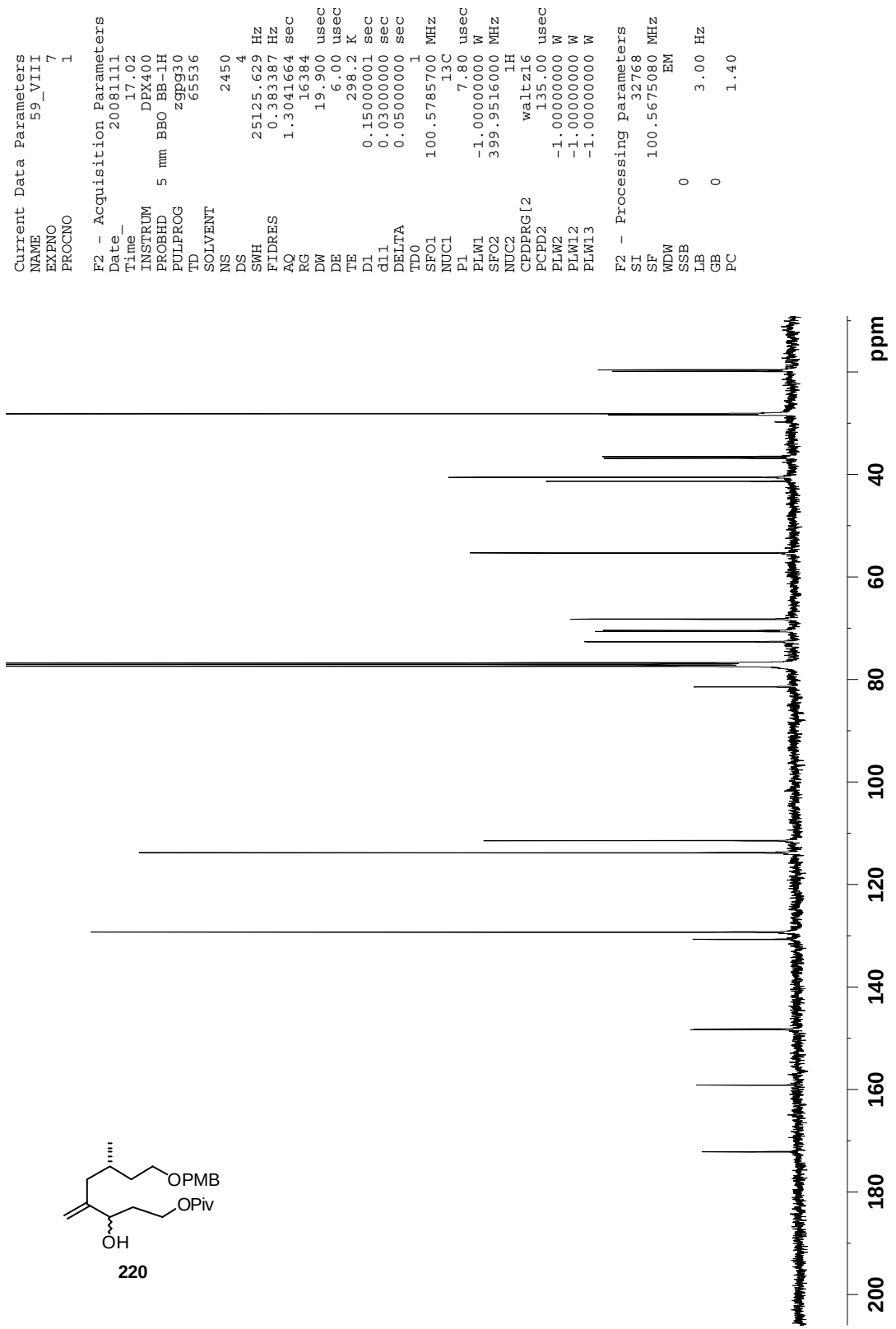

Current Data Parameters
NAME 36_VII
EXPNO 2
PROCNO 1
DU /m
USER rajan
F2 - Acquisition Parameters
Date_ 20080121
Time 9.51
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.42102912 sec
RG 574.7
DW 104.400 usec
DE 6.00 usec
TE 298.2 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 EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
HO
OH
H
OH
(S)
OPMB
213
ppm
0.79
3.76
23.93
0.97
0.94
3.34
1.74
2.92
2.00
0.81
0.99
2.15
3.40


Current Data Parameters
NAME 36_VII
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20080121
Time_ 22.41
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 22328
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3041664 sec
RG 4597.6
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
SFO1 100.5936591 MHz
NUC1 13C
P1 7.80 usec
PLW1 -1.00000000 W
SFO2 400.0116000 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 135.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 32768
SF 100.5825950 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
HO
OH
H
OH
(S)
OPMB
213
0 ppm
20
40
60
80
100
120
140
160
180

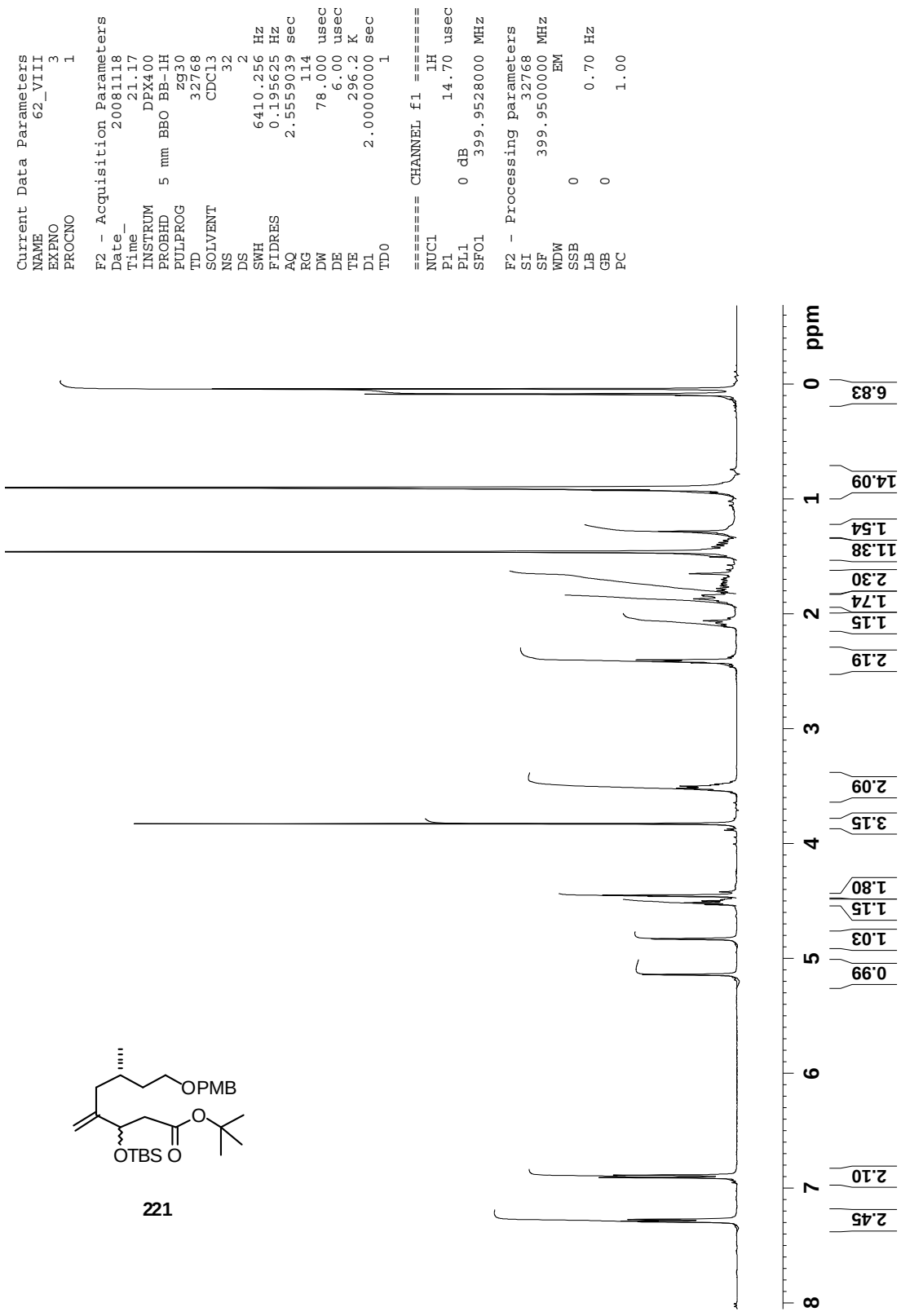

Current Data Parameters
NAME 58_VIII
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20081107
Time_ 16.14
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559039 sec
RG 143.7
DW 78.000 usec
DE 6.00 usec
TE 299.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0 dB
SFO1 399.9528000 MHz
F2 - Processing parameters
SI 32768
SF 399.9500000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00
OPMB
O
218
3.10
1.09
1.69
0.83
0.79
0.79
2.00
3.18
2.00
0.79
0.78
2.08
2.24
0.89
1 ppm
2
3
4
5
6
7
8
9
10


Current Data Parameters
NAME 58_VIII
EXPNO 6
PROCNO 1
F2 - Acquisition Parameters
Date_ 20081107
Time_ 18.13
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 1.3041664 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
SFO1 100.5785700 MHz
NUC1 13C
P1 7.80 usec
PLW1 -1.00000000 W
SFO2 399.9516000 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 135.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 32768
SF 100.5675080 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
OPMB
O
218
200
180
160
140
120
100
80
60
40
ppm

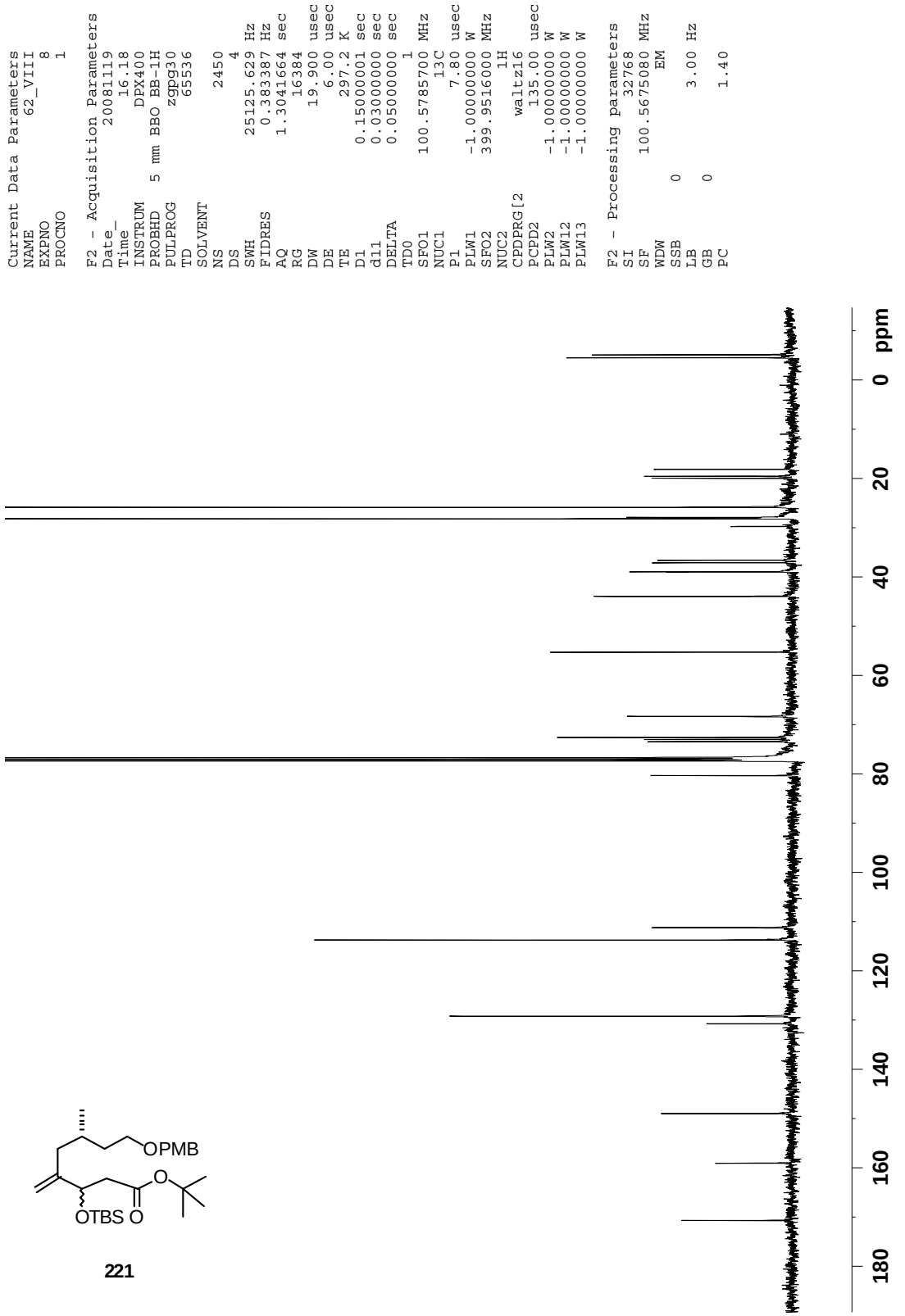

Current Data Parameters
NAME 61_VIII
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20081114
Time 16.49
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDC13
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559039 sec
RG 181
DW 78.000 usec
DE 6.00 usec
TE 297.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0 dB
SFO1 399.9528000 MHz
F2 - Processing parameters
SI 32768
SF 399.9500000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00
OPMB
OPiv
OH
220
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
2.41
2.00
1.00
0.99
3.10
2.99
2.04
0.95
2.08
1.10
2.14
1.84
10.63
3.10

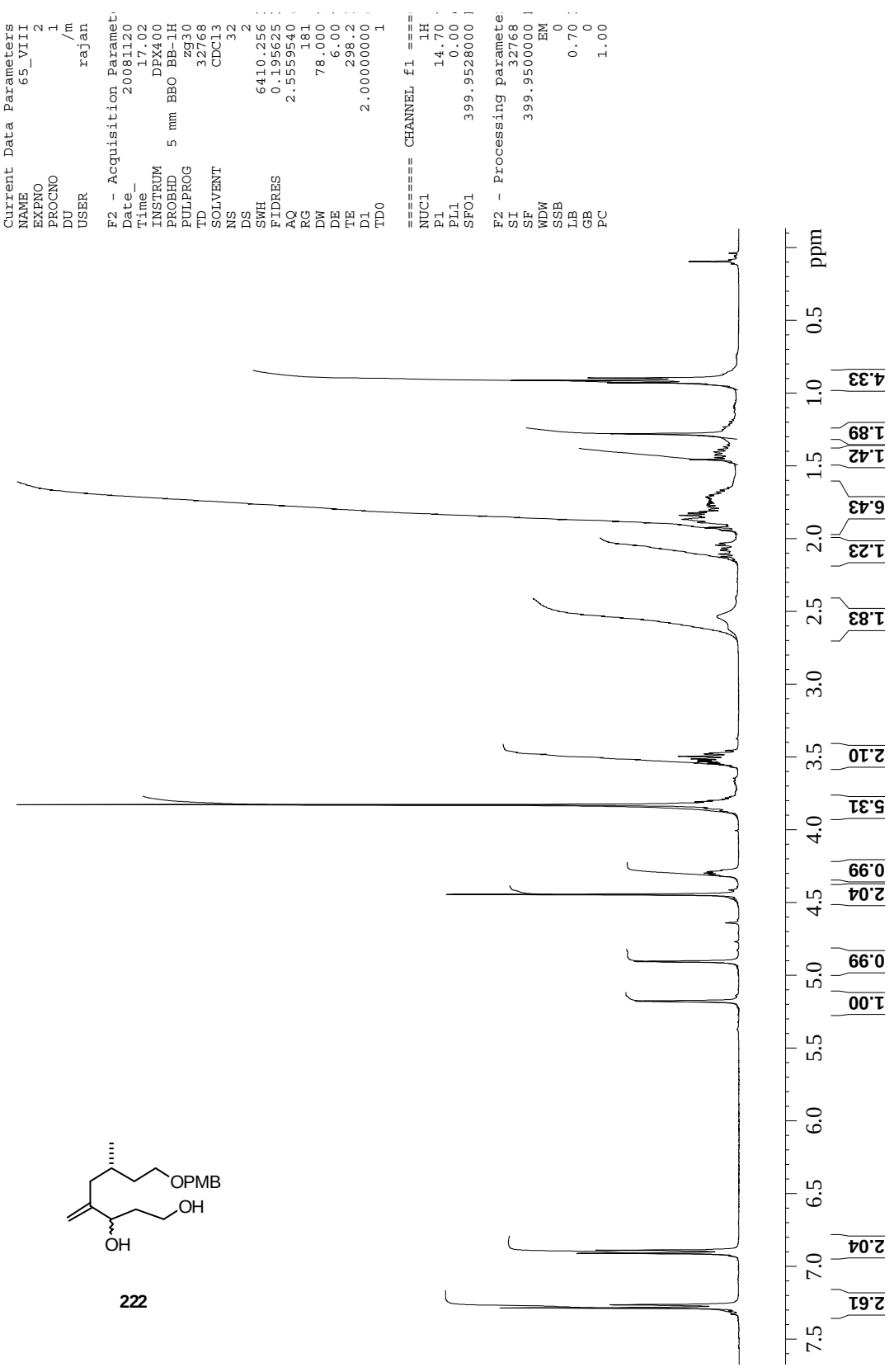

Current Data Parameters
NAME 59_VIII
EXPNO 7
PROCNO 1
F2 - Acquisition Parameters
Date_ 20081111
Time_ 17.02
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 2450
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.30041664 sec
RG 16384
DW 19.900 usec
DE 6.00 usec
TE 298.2 K
D1 0.15000001 sec
d11 0.03000000 sec
DELTA 0.05000000 sec
TD0 1
SFO1 100.5785700 MHz
NUC1 13C
P1 7.80 usec
PLW1 -1.00000000 W
SFO2 399.9516000 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 135.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 32768
SF 100.5675080 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
ppm
200
180
160
140
120
100
80
60
40
OPMB
OPiv
OH

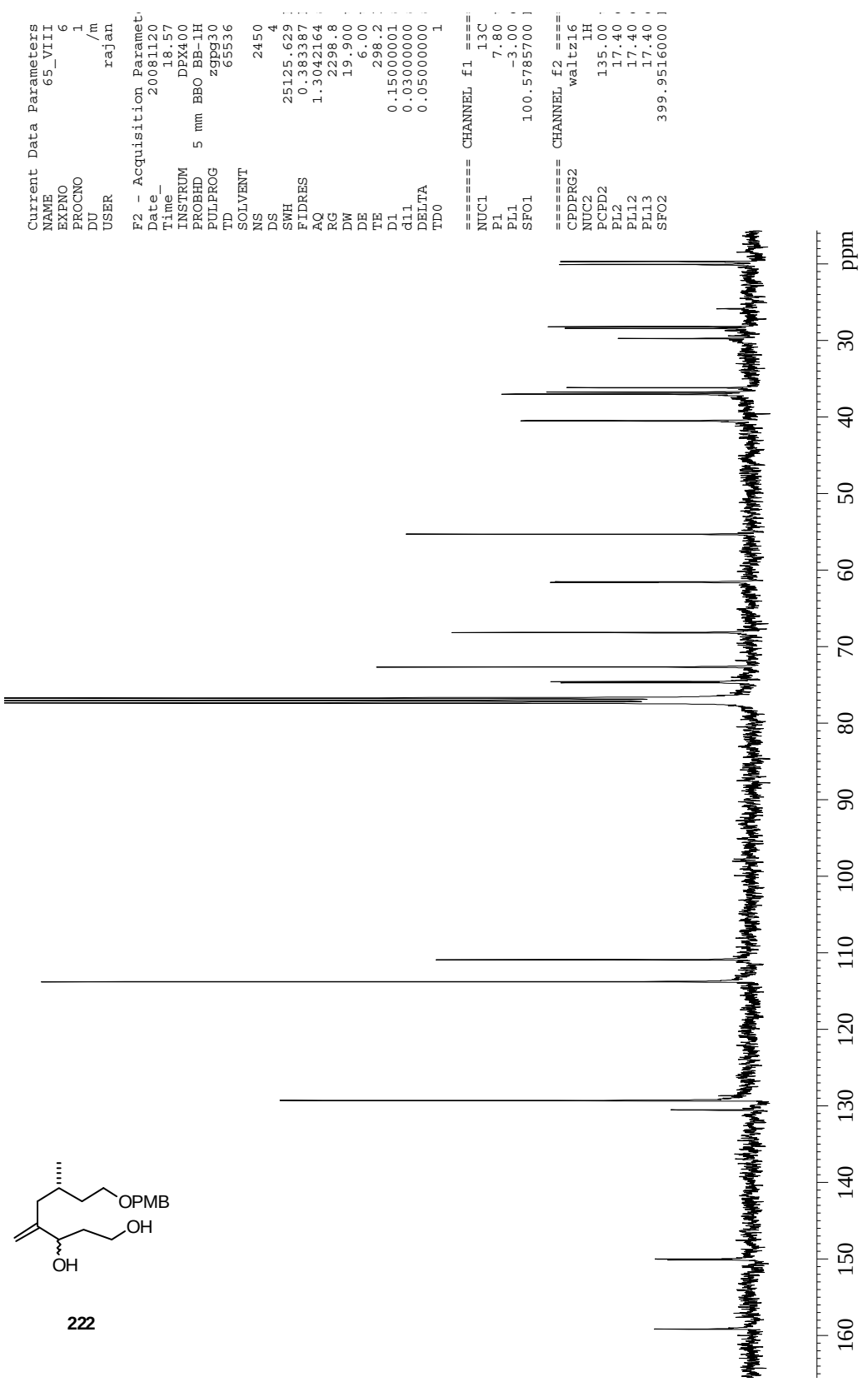
220

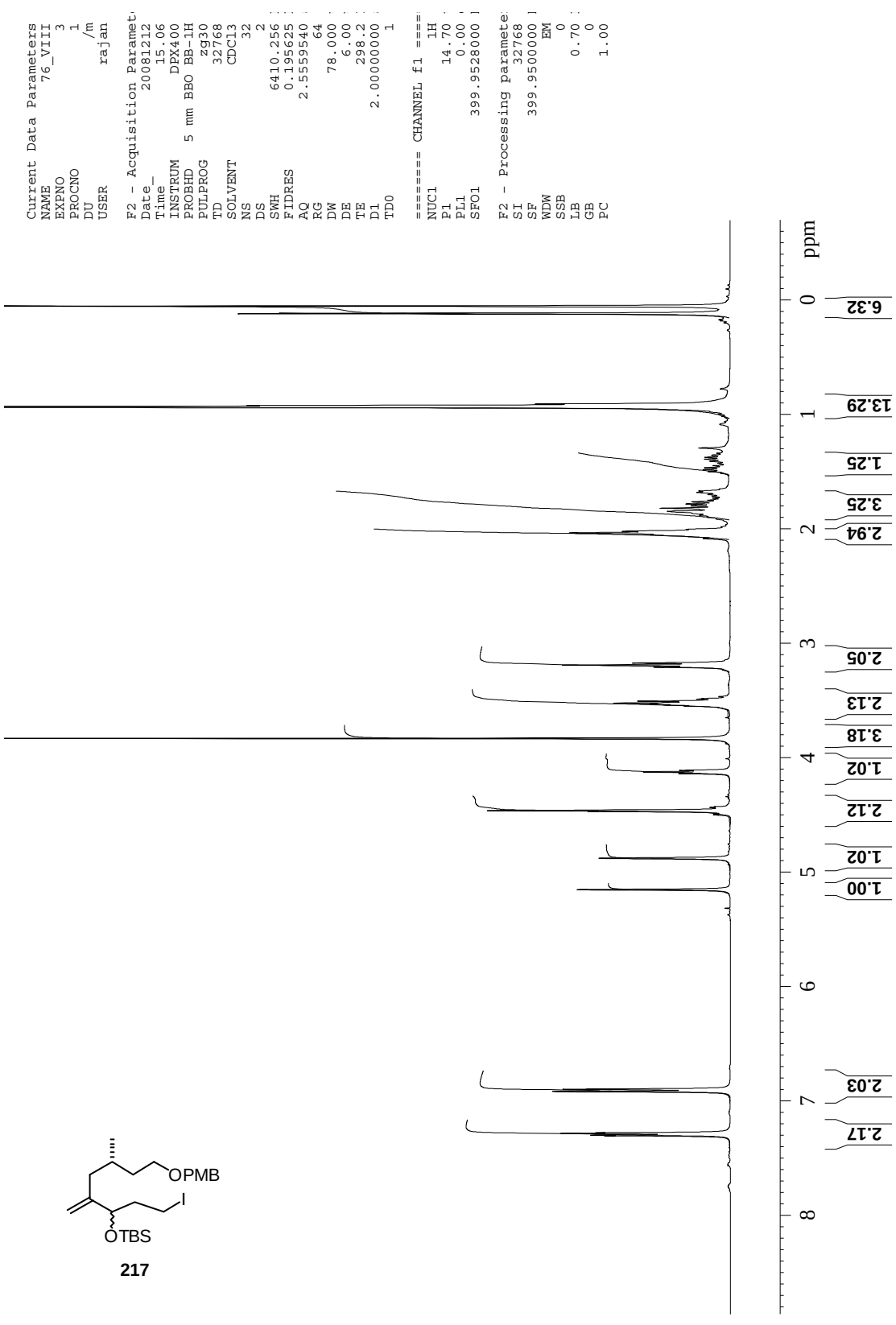

Current Data Parameters
NAME 62_VIII
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20081118
Time 21.17
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.55590039 sec
RG 114
DW 78.000 usec
DE 6.00 usec
TE 296.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0 dB
SFO1 399.9528000 MHz
F2 - Processing parameters
SI 32768
SF 399.9500000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00
ppm
0
1
2
3
4
5
6
7
8
6.83
14.09
1.54
11.38
2.30
1.74
1.15
2.19
2.09
3.15
1.80
1.15
1.03
0.99
2.10
2.45
OPMB
O
OTBS
O

221

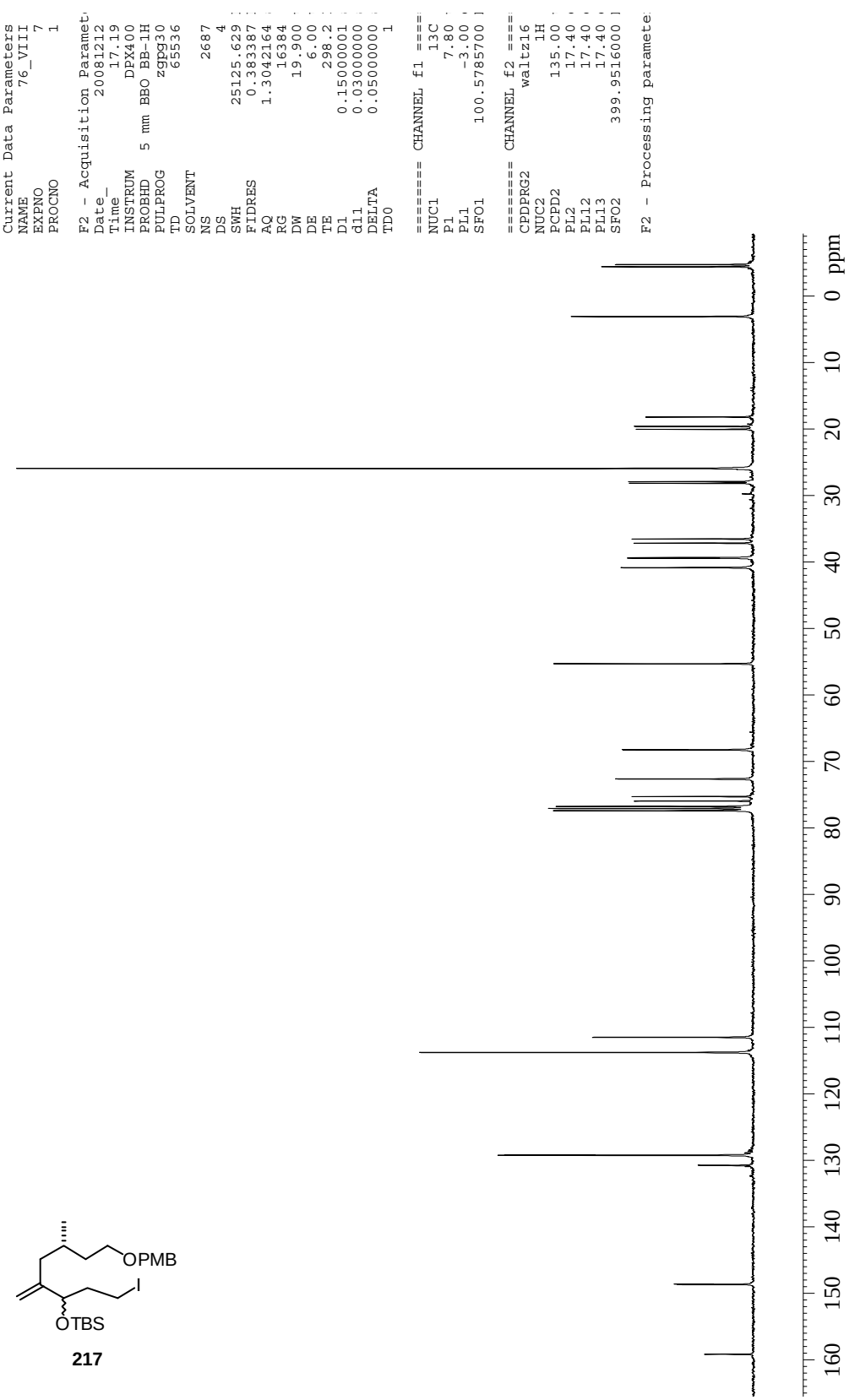

Current Data Parameters
NAME 62_VIII
EXPNO 8
PROCNO 1
F2 - Acquisition Parameters
Date_ 20081119
Time 16.18
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 2450
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3041664 sec
RG 16384
DW 19.900 usec
DE 6.00 usec
TE 297.2 K
D1 0.15000001 sec
d11 0.03000000 sec
DELTA 0.05000000 sec
TD0 1
SFO1 100.5785700 MHz
NUC1 13C
P1 7.80 usec
PLW1 -1.00000000 W
SFO2 399.9516000 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 135.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 32768
SF 100.5675080 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
OPMB
O
OTBS O
221
180
160
140
120
100
80
60
40
20
0
ppm

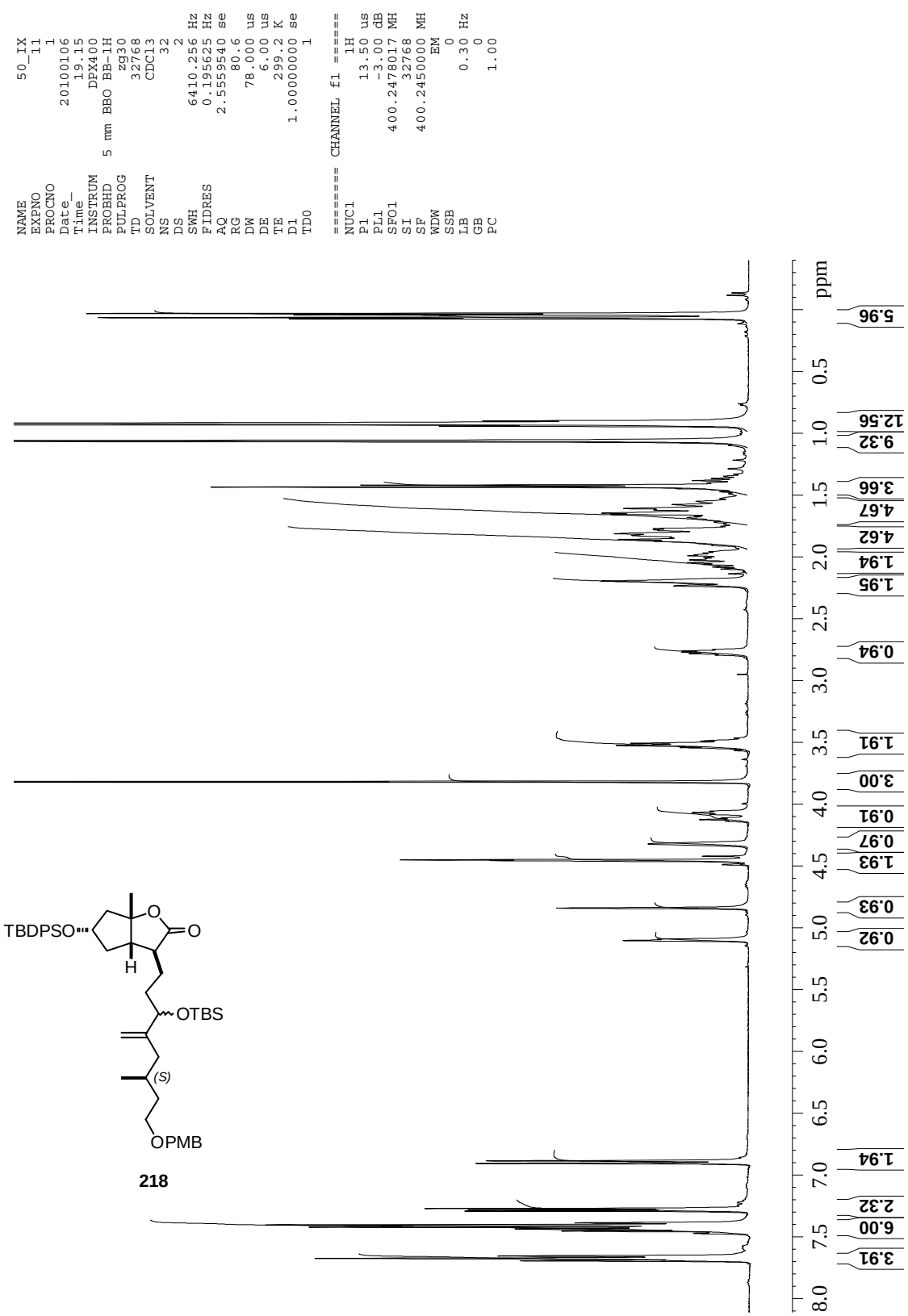

Current Data Parameters
NAME 65_VIII
EXPNO 2
PROCNO 1
DU /m
USER rajan
P2 - Acquisition Paramet
Date_ 20081120
Time_ 17.02
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDC13
NS 32
DS 2
SWH 6410.256
FIDRES 0.195625
AQ 2.5559540
RG 181
DW 78.000
DE 6.00
TE 298.2
D1 2.00000000
TD0 1
======== CHANNEL f1 ====
NUC1 1H
P1 14.70
PL1 0.00
SFO1 399.9528000
F2 - Processing parame
SI 32768
SF 399.9500000
WDW EM
SSB 0
LB 0.70
GB 0
PC 1.00
ppm
4.33
1.89
1.42
6.43
1.23
1.83
2.10
5.31
0.99
2.04
0.99
1.00
2.04
2.61
OPMB
OH
OH
222


Current Data Parameters
NAME 65_VIII
EXPNO 6
PROCNO 1
DU /m
USER rajan
F2 - Acquisition Paramet
Date_ 20081120
Time_ 18.57
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 2450
DS 4
SWH 25125.629
FIDRES 0.383387
AQ 1.3042164
RG 2298.8
DW 19.900
DE 6.00
TE 298.2
D1 0.15000001
d11 0.03000000
DELTA 0.05000000
TD0 1
======== CHANNEL f1 ====
NUC1 13C
P1 7.80
PL1 -3.00
SFO1 100.5785700
======== CHANNEL f2 ====
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00
PL2 17.40
PL12 17.40
PL13 17.40
SFO2 399.9516000
OPMB
OH
OH
222
ppm

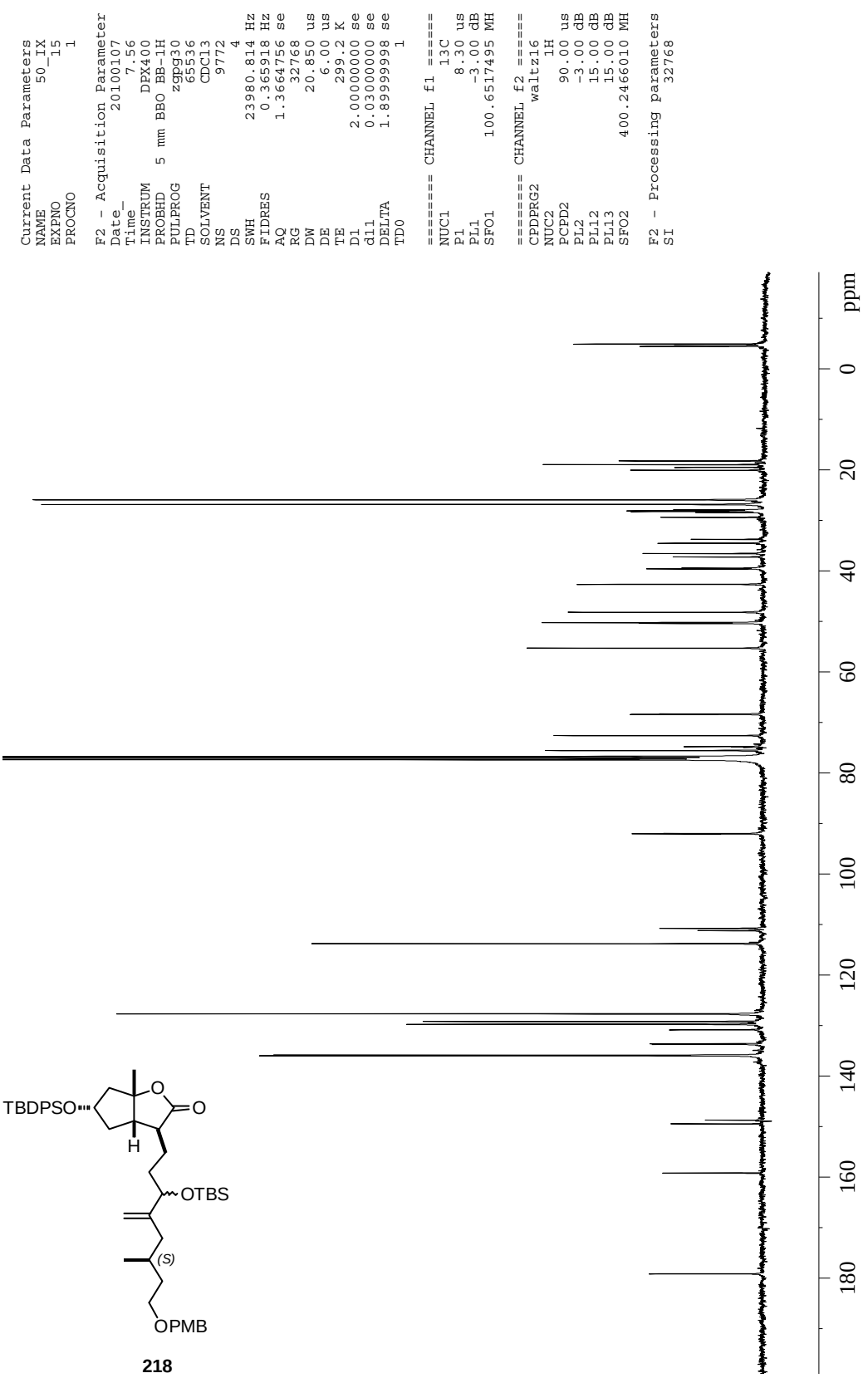

Current Data Parameters
NAME 76_VIII
EXPNO 3
PROCNO 1
DU /m
USER rajan
F2 - Acquisition Paramet
Date_ 20081212
Time 15.06
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256
FIDRES 0.195625
AQ 2.5559540
RG 64
DW 78.000
DE 6.00
TE 298.2
D1 2.00000000
TDO 1
========== CHANNEL f1 ====
NUC1 1H
P1 14.70
PL1 0.00
SFO1 399.9528000
F2 - Processing parameter
SI 32768
SF 399.9500000
WDW EM
SSB 0
LB 0.70
GB 0
PC 1.00
ppm
0
1
2
3
4
5
6
7
8
6.32
13.29
1.25
3.25
2.94
2.05
2.13
3.18
1.02
2.12
1.02
1.00
2.03
2.17
OPMB
I
OTBS

217

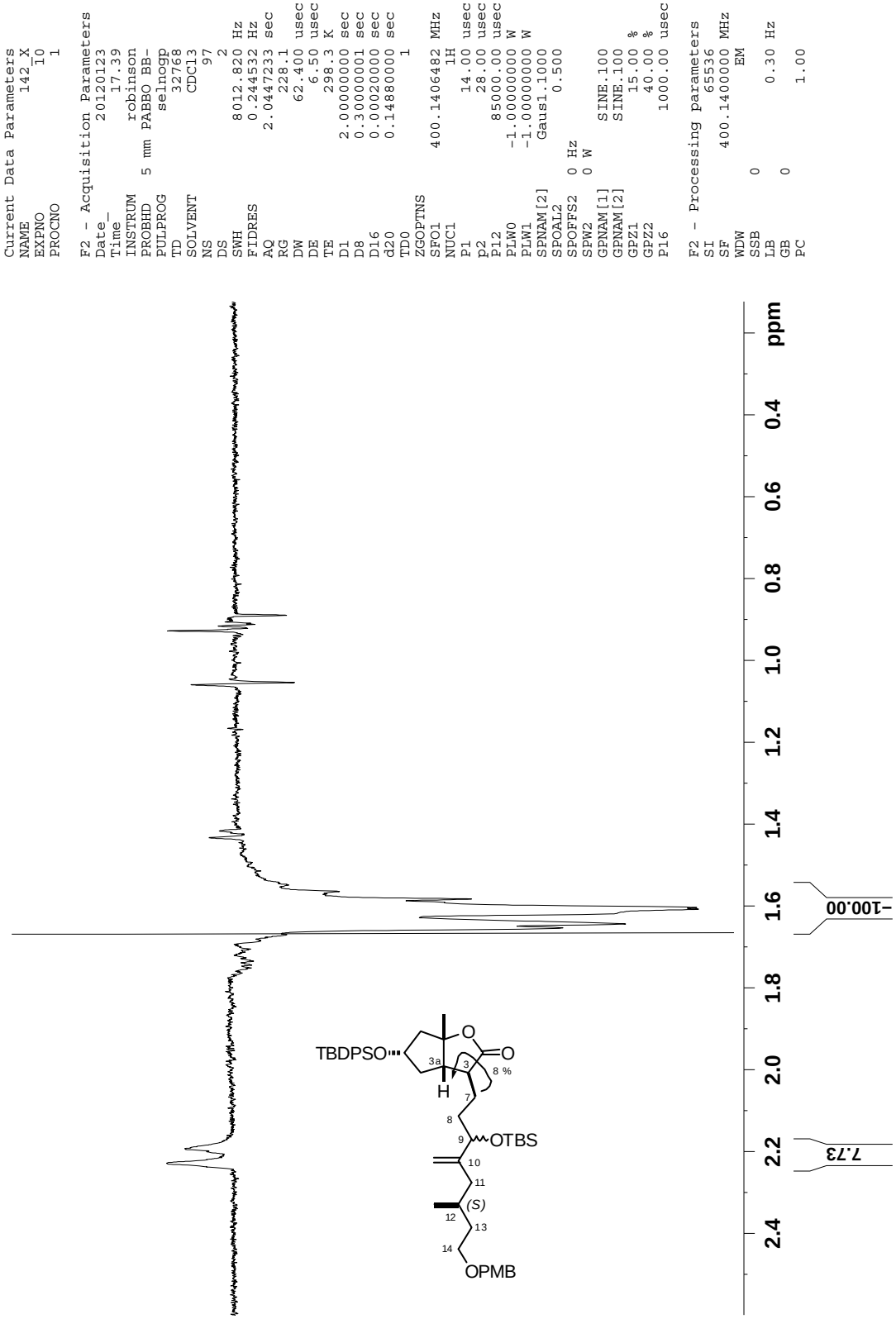

Current Data Parameters
NAME 76_VIII
EXPNO 7
PROCNO 1
F2 - Acquisition Paramet
Date_ 20081212
Time 17.19
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 2687
DS 4
SWH 25125.629
FIDRES 0.383387
AQ 1.3042164
RG 16384
DW 19.900
DE 6.00
TE 298.2
D1 0.15000001
d11 0.03000000
DELTA 0.05000000
TD0 1
======== CHANNEL f1 ====
NUC1 13C
P1 7.80
PL1 -3.00
SFO1 100.5785700
======== CHANNEL f2 ====
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00
PL2 17.40
PL12 17.40
PL13 17.40
SFO2 399.9516000
F2 - Processing paramete
OPMB
I
OTBS
217
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

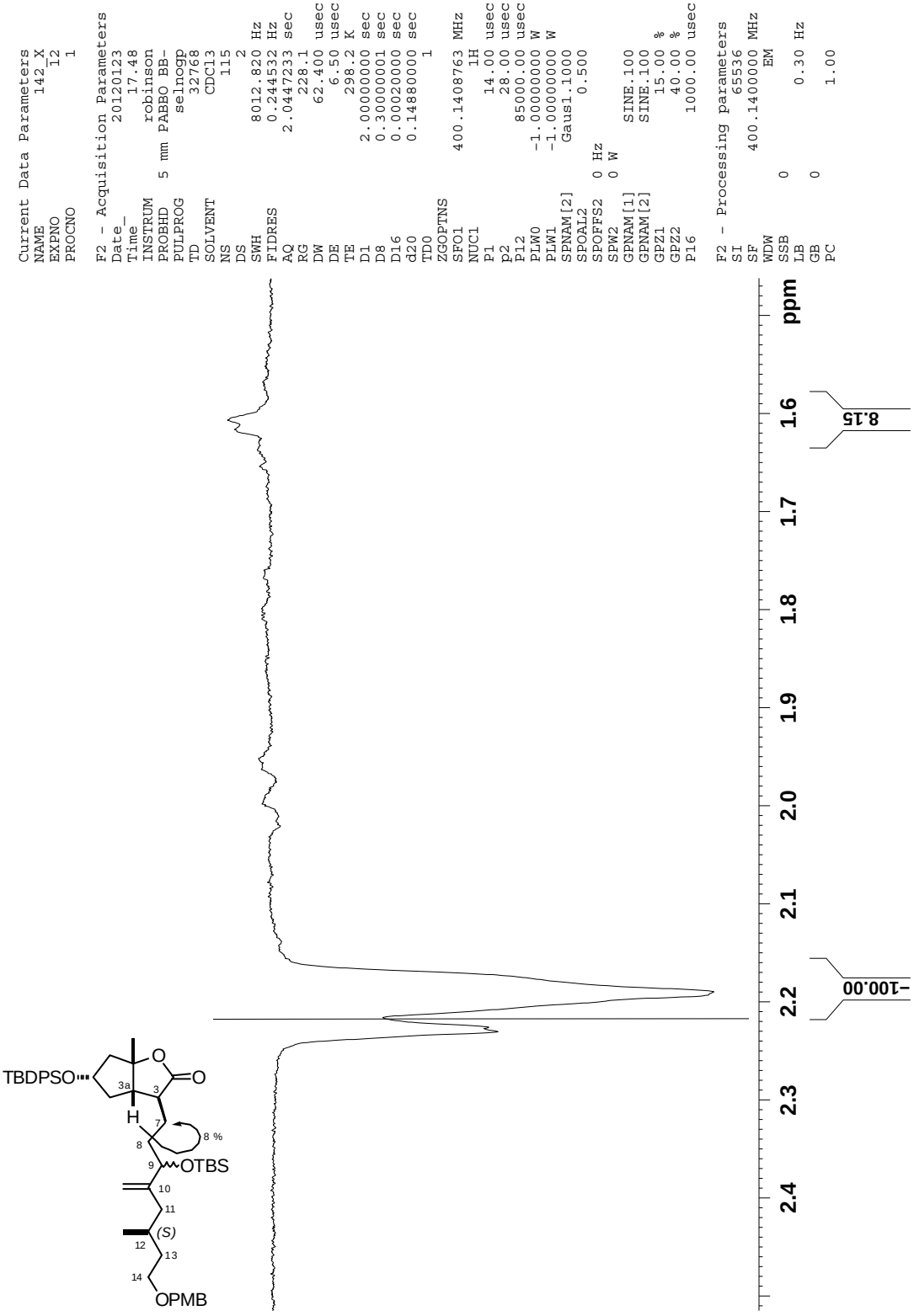

NAME 50_IX
EXPNO 11
PROCNO 1
Date_ 20100106
Time 19.15
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 se
RG 80.6
DW 78.000 us
DE 6.00 us
TE 299.2 K
D1 1.00000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 13.50 us
PL1 -3.00 dB
SFO1 400.2478017 MH
SI 32768
SF 400.2450000 MH
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
2.0
1.5
1.0
0.5
5.96
12.56
9.32
3.66
4.67
4.62
1.94
1.95
0.94
1.91
3.00
0.91
0.97
1.93
0.93
0.92
1.94
2.32
6.00
3.91
TBDPSO
O
O
H
OTBS
(S)
OPMB

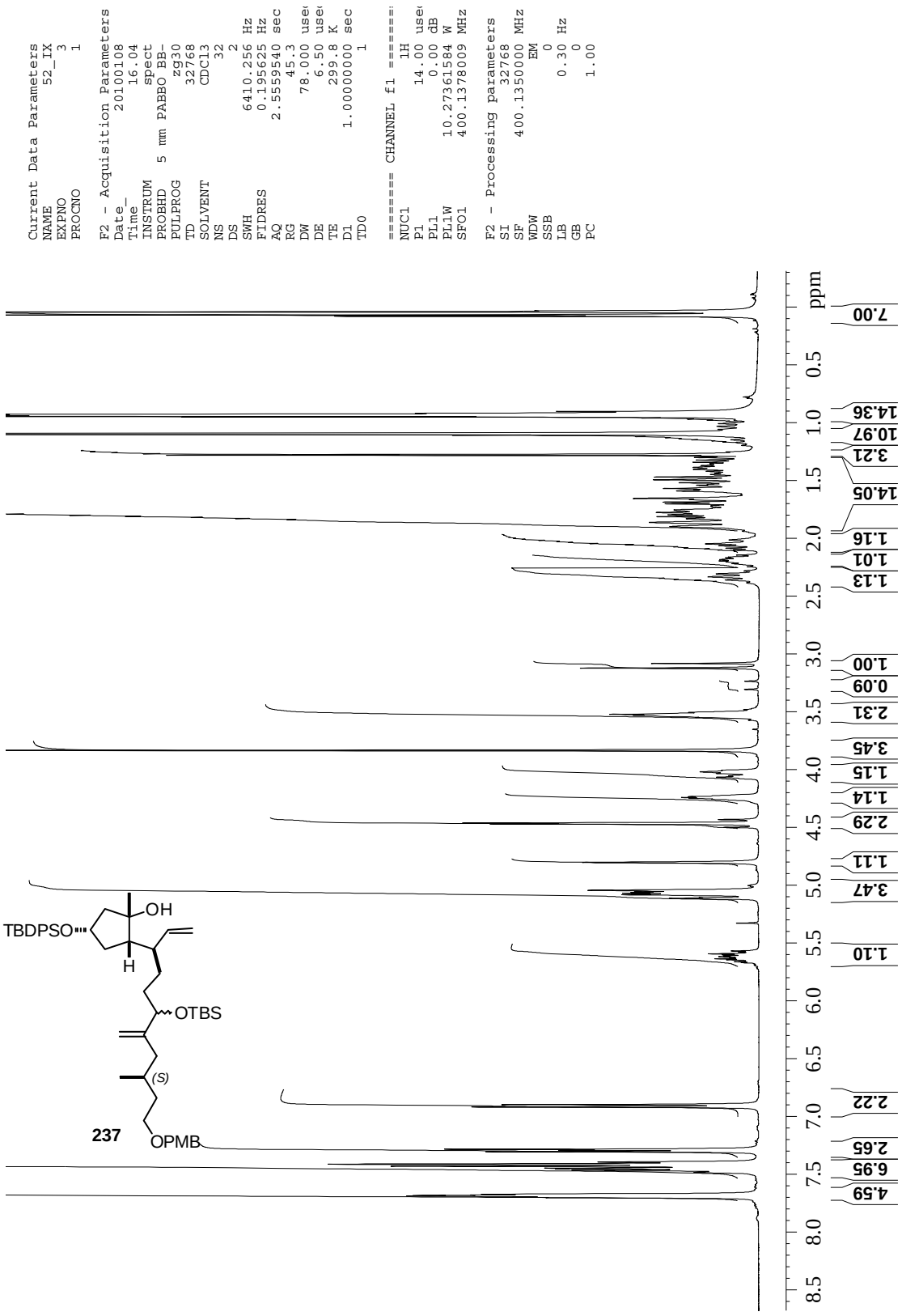
218

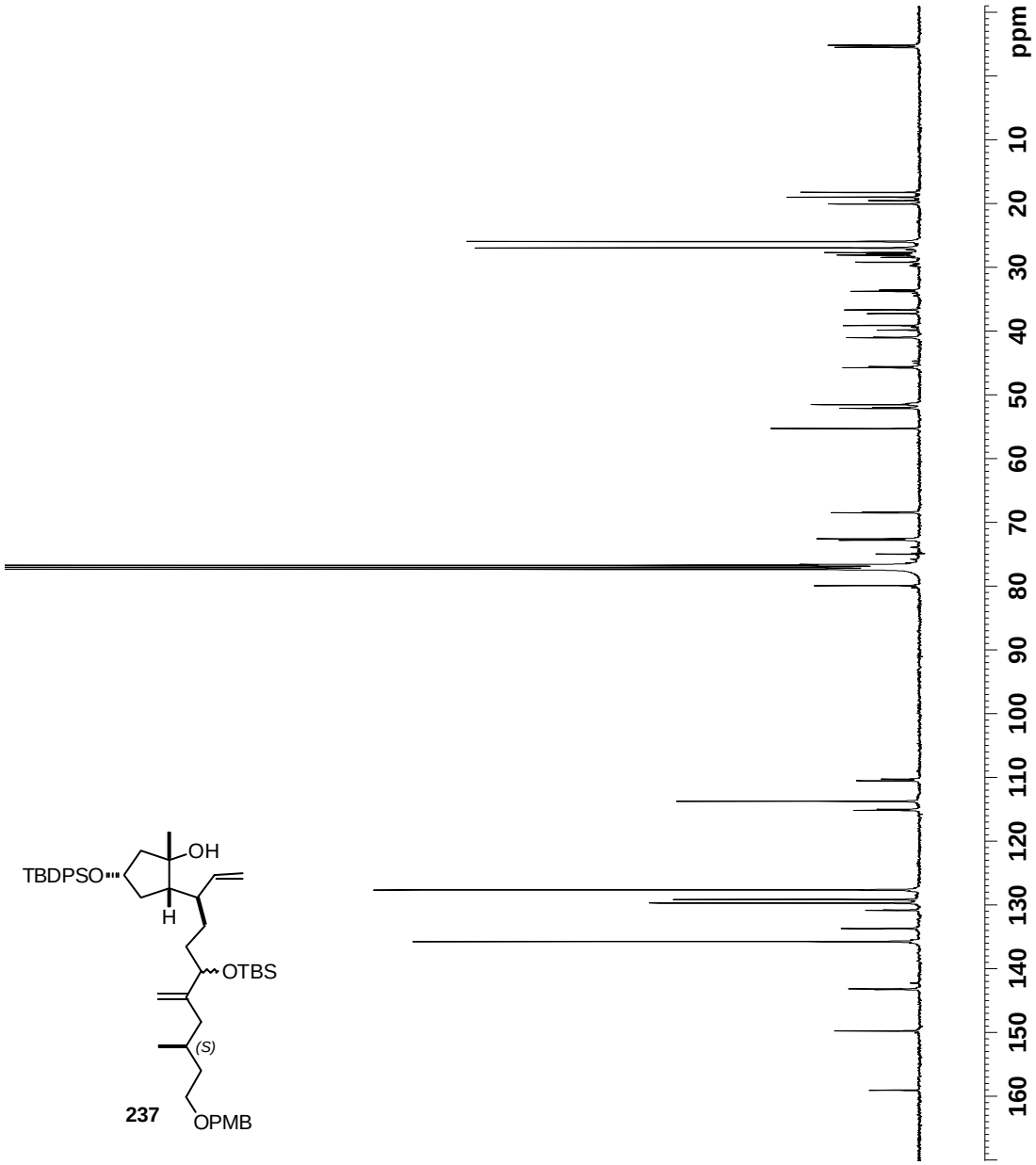

Current Data Parameters
NAME 50_IX
EXPNO 15
PROCNO 1
F2 - Acquisition Parameter
Date_ 20100107
Time_ 7.56
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 9772
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 32768
DW 20.850 usec
DE 6.00 usec
TE 299.2 K
D1 2.00000000 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
ppm
0
20
40
60
80
100
120
140
160
180
TBDPSO
O
O
H
OTBS
(S)
OPMB

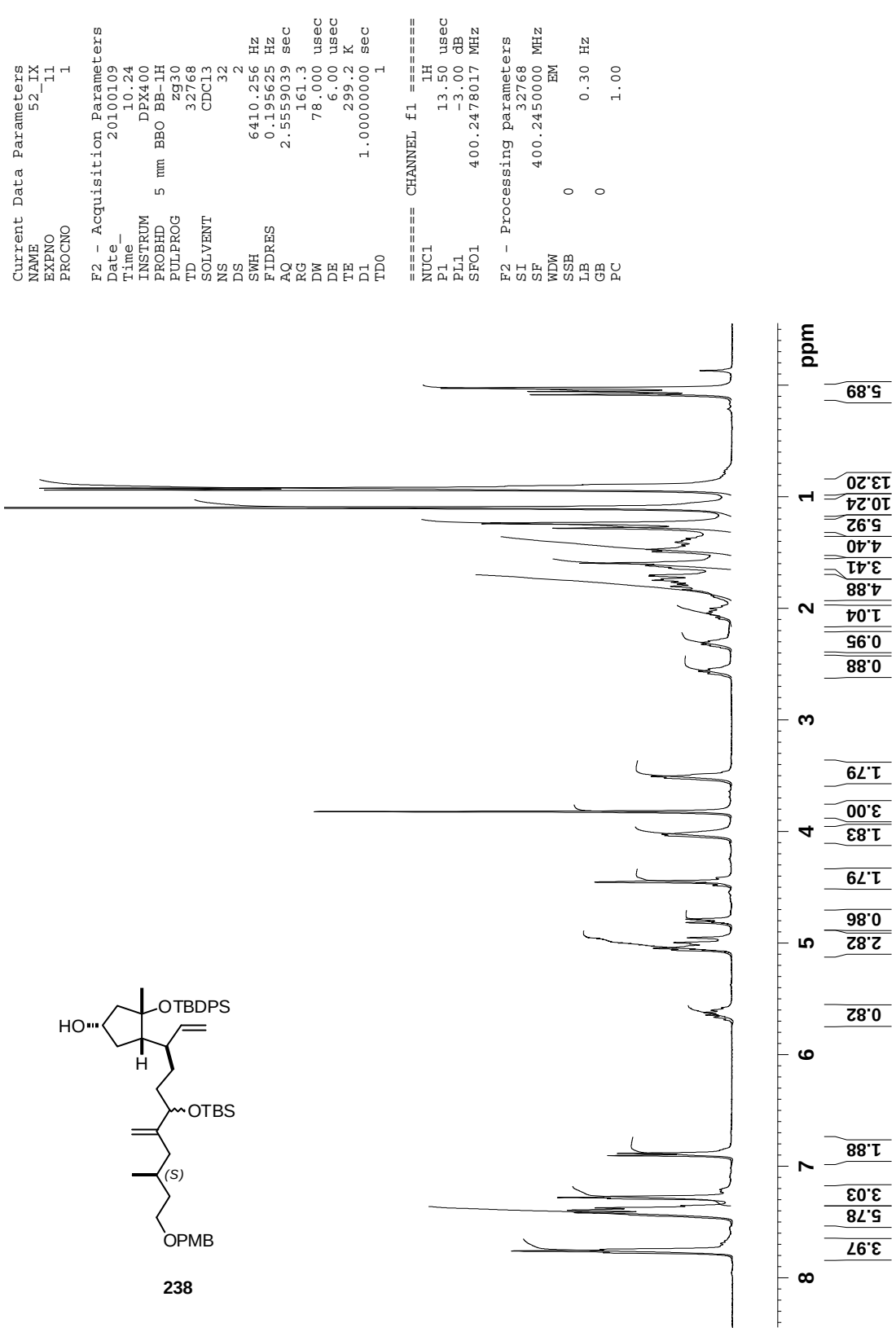
218


Current Data Parameters
NAME 142_X
EXPNO 10
PROCNO 1
F2 - Acquisition Parameters
Date_ 20120123
Time 17.39
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG selnogp
TD 32768
SOLVENT CDC13
NS 97
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 2.0447233 sec
RG 228.1
DW 62.400 usec
DE 6.50 usec
TE 298.3 K
D1 2.00000000 sec
D8 0.30000001 sec
D16 0.00020000 sec
d20 0.14880000 sec
TD0 1
ZGOPTNS
SFO1 400.1406482 MHz
NUC1 1H
P1 14.00 usec
p2 28.00 usec
P12 85000.00 usec
PLW0 -1.00000000 W
PLW1 -1.00000000 W
SPNAM[2] Gaus1.1000
SPOAL2 0.500
SPOFFS2 0 Hz
SPW2 0 W
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPZ1 15.00 %
GPZ2 40.00 %
P16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 400.1400000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
TBDPSO
O
O
3a
3
8 %
H
7
8
9
OTBS
10
11
(S)
12
13
14
OPMB
7.73
-100.00
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
0.4
ppm

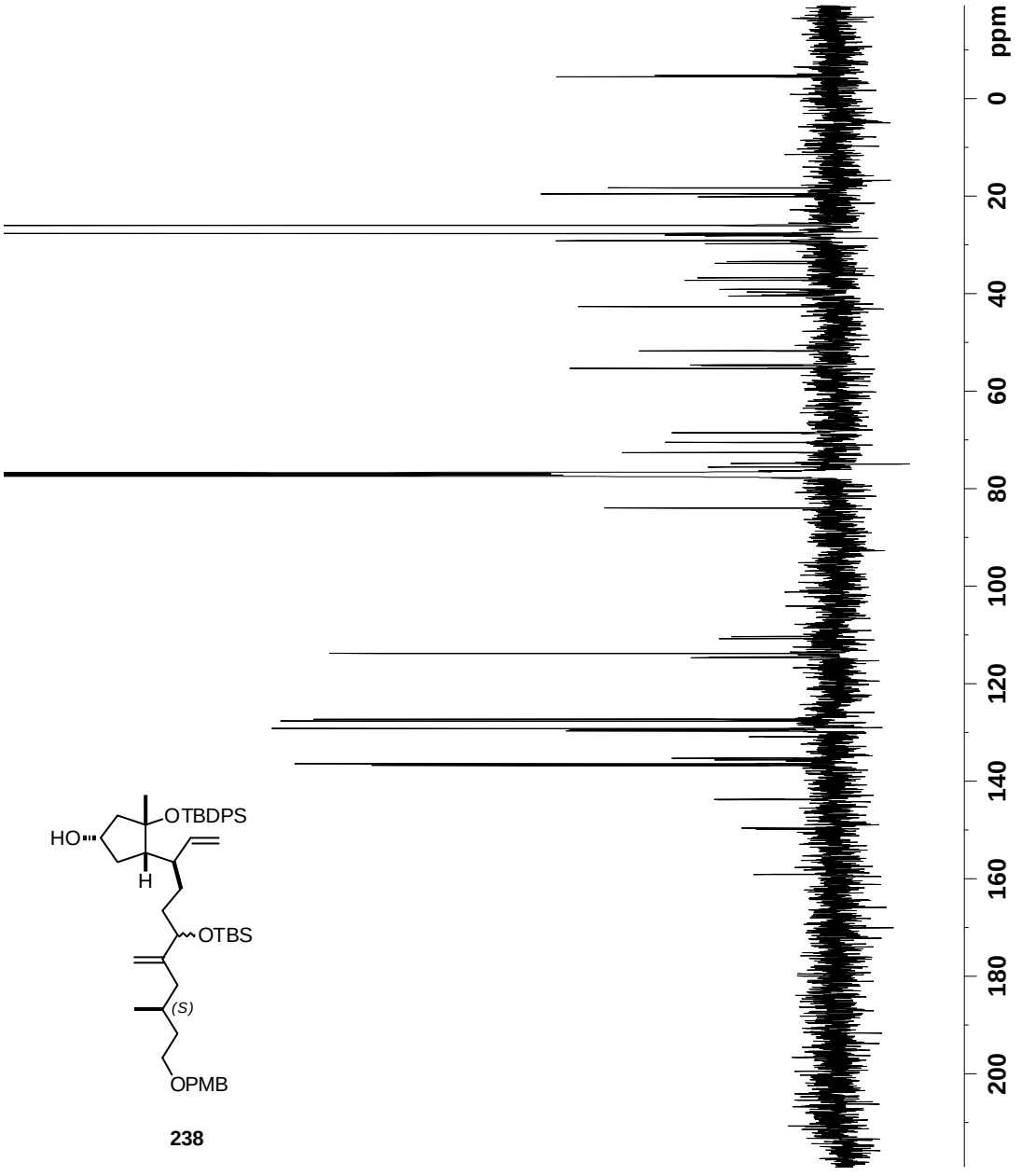

Current Data Parameters
NAME 142_X
EXPNO 12
PROCNO 1
F2 - Acquisition Parameters
Date_ 20120123
Time 17.48
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG selnogp
TD 32768
SOLVENT CDC13
NS 115
DS 2
SWH 8012.820 Hz
FIDRES 0.244532 Hz
AQ 2.0447233 sec
RG 228.1
DW 62.400 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
D8 0.30000001 sec
D16 0.00020000 sec
d20 0.14880000 sec
TD0 1
ZGOPTNS
SFO1 400.1408763 MHz
NUC1 1H
P1 14.00 usec
p2 28.00 usec
P12 85000.00 usec
PLW0 -1.00000000 W
PLW1 -1.00000000 W
SPNAM[2] Gaus1.1000
SPOAL2 0.500
SPOFFS2 0 Hz
SPW2 0 W
GPNAM[1] SINE.100
GPNAM[2] SINE.100
GPZ1 15.00 %
GPZ2 40.00 %
P16 1000.00 usec
F2 - Processing parameters
SI 65536
SF 400.1400000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
8.15
100.00
ppm
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
TBDPSO
O
O
3a
3
H
7
8
8 %
9
OTBS
10
11
(S)
12
13
14
OPMB

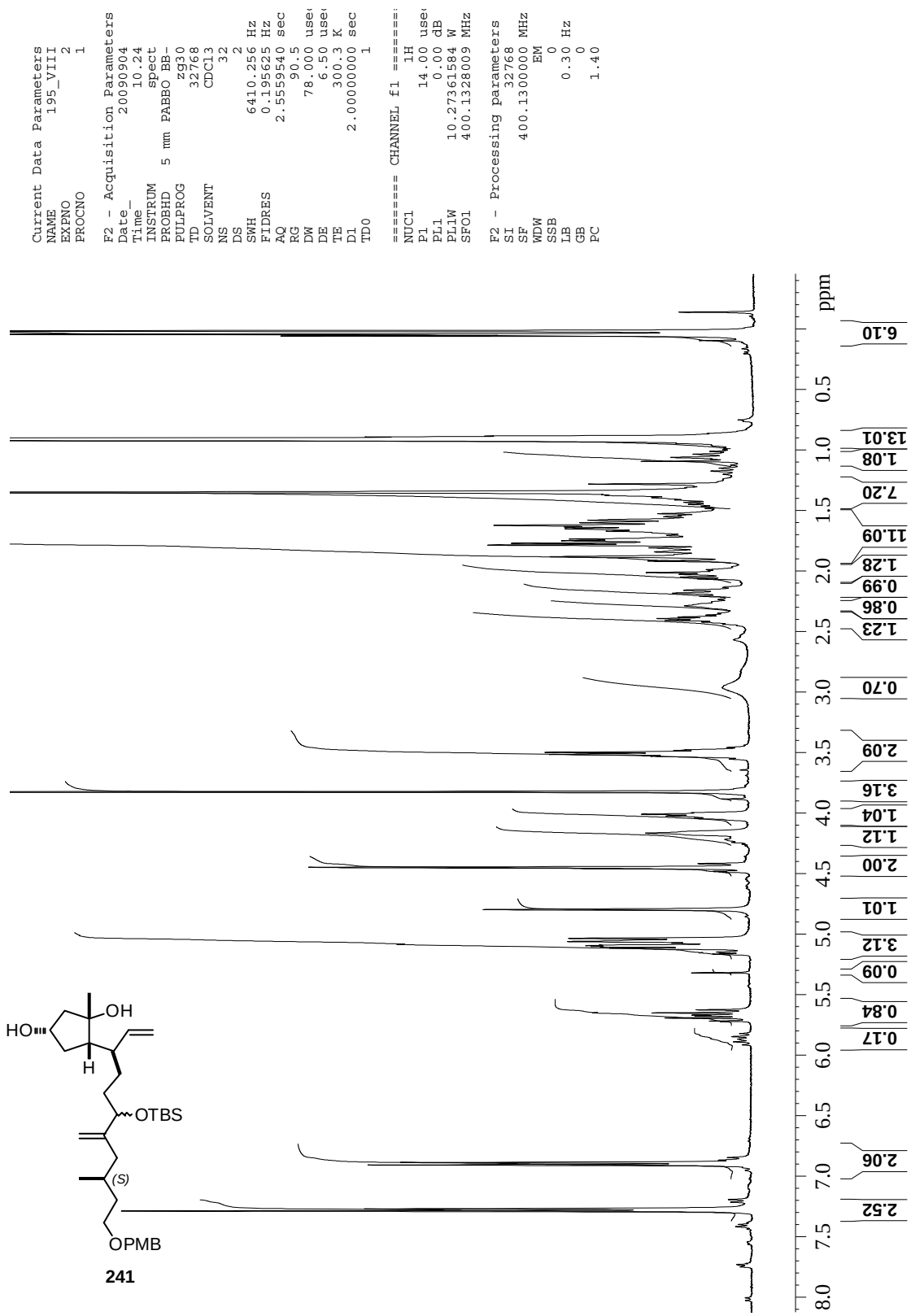

Current Data Parameters
NAME 52_IX
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20100108
Time_ 16.04
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDC13
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.55595540 sec
RG 45.3
DW 78.000 use
DE 6.50 use
TE 299.8 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 use
PL1 0.00 dB
PL1W 10.27361584 W
SFO1 400.1378009 MHz
F2 - Processing parameters
SI 32768
SF 400.1350000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
ppm
7.00
4.59
6.95
2.65
2.22
1.10
3.47
1.11
2.29
1.14
1.15
3.45
2.31
0.09
1.00
1.13
1.01
1.16
14.05
3.21
10.97
14.36
TBDPSO
OH
H
OTBS
(S)
OPMB
237


Current Data Parameters
NAME 52_IX
EXPNO 10
PROCNO 1
F2 - Acquisition Parameters
Date_ 20100109
Time 9.34
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 13402
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664256 sec
RG 13004
DW 20.850 usec
DE 6.00 usec
TE 300.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
SFO1 100.6517495 MHz
NUC1 13C
P1 8.30 usec
PLW1 -1.00000000 W
SFO2 400.2466010 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 32768
SF 100.6416850 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
TBDPSO
OH
H
OTBS
(S)
OPMB
237
ppm
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

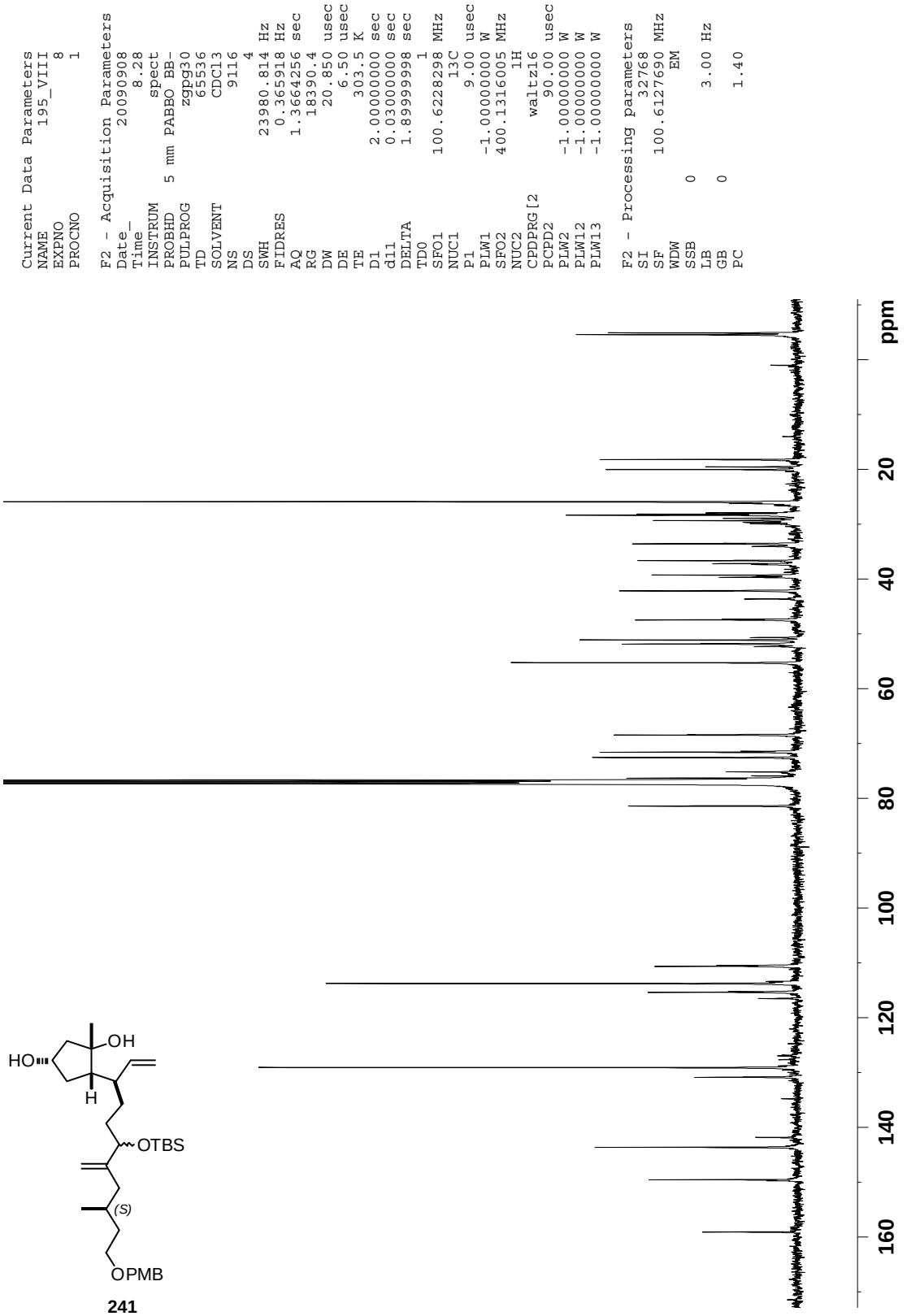

Current Data Parameters
NAME 52_IX
EXPNO 11
PROCNO 1
F2 - Acquisition Parameters
Date_ 20100109
Time 10.24
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559039 sec
RG 161.3
DW 78.000 usec
DE 6.00 usec
TE 299.2 K
D1 1.00000000 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 EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
ppm
8
7
6
5
4
3
2
1
3.97
5.78
3.03
1.88
0.82
2.82
0.86
1.79
1.83
3.00
1.79
0.88
0.95
1.04
4.88
3.41
4.40
5.92
10.24
13.20
5.89
HO
OTBDPS
H
OTBS
(S)
OPMB

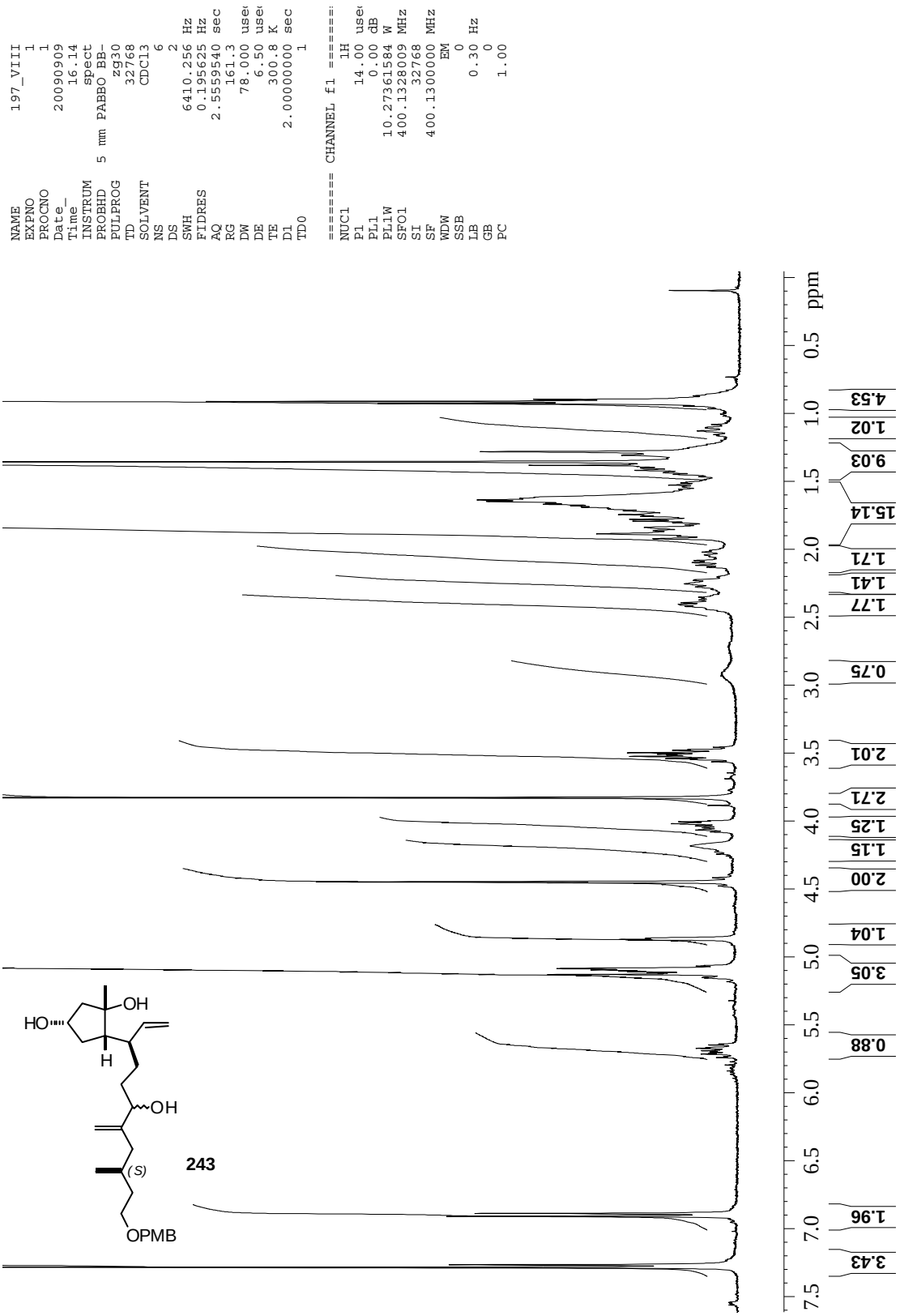
238

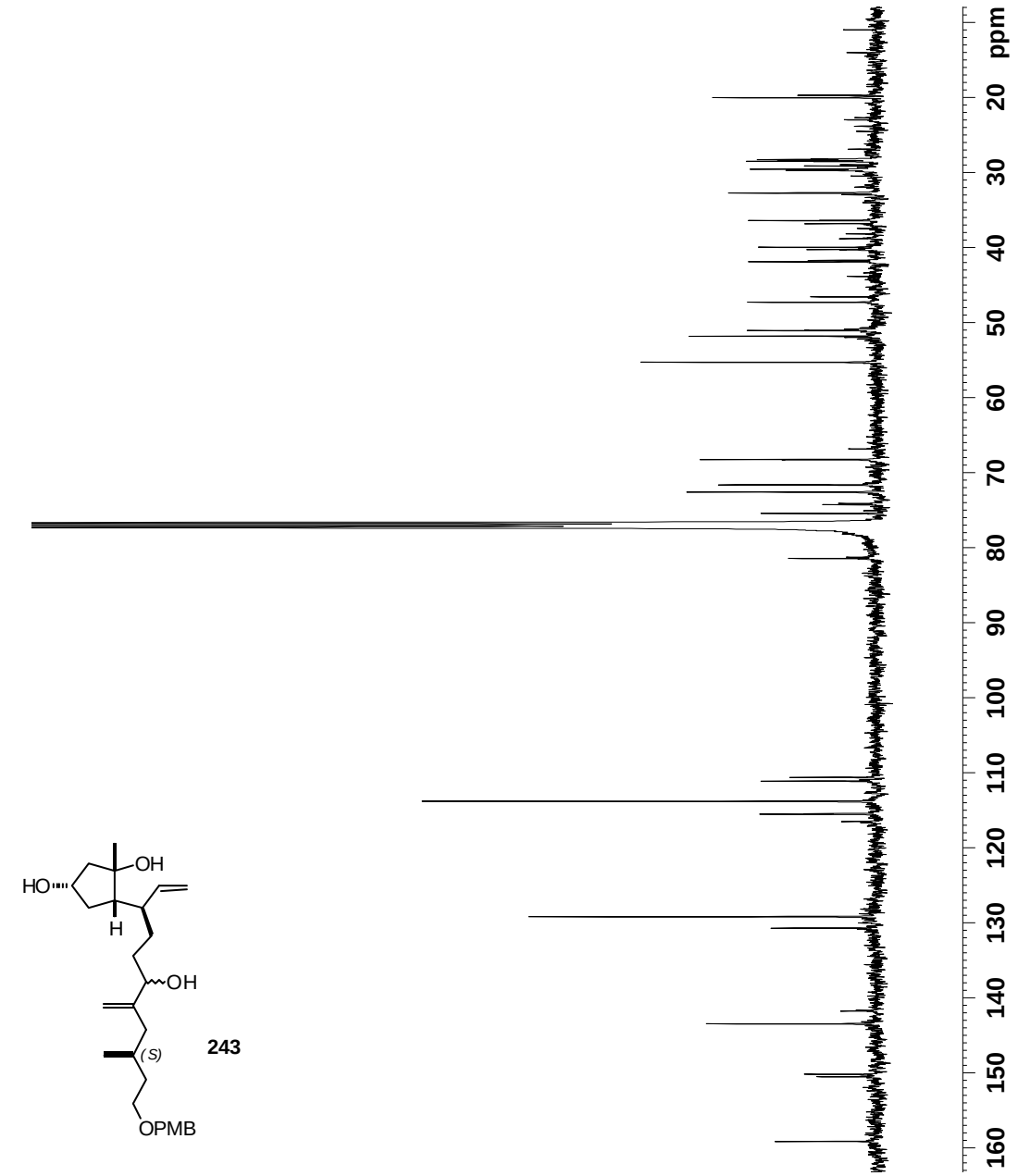

Current Data Parameters
NAME 52_IX
EXPNO 15
PROCNO 1
F2 - Acquisition Parameters
Date_ 20100109
Time_ 12.17
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1024
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664256 sec
RG 3251
DW 20.850 usec
DE 6.00 usec
TE 300.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
SFO1 100.6517495 MHz
NUC1 13C
P1 8.30 usec
PLW1 -1.00000000 W
SFO2 400.2466010 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 32768
SF 100.6416850 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
HO
OTBDPS
H
OTBS
(S)
OPMB
238
200
180
160
140
120
100
80
60
40
20
0
ppm

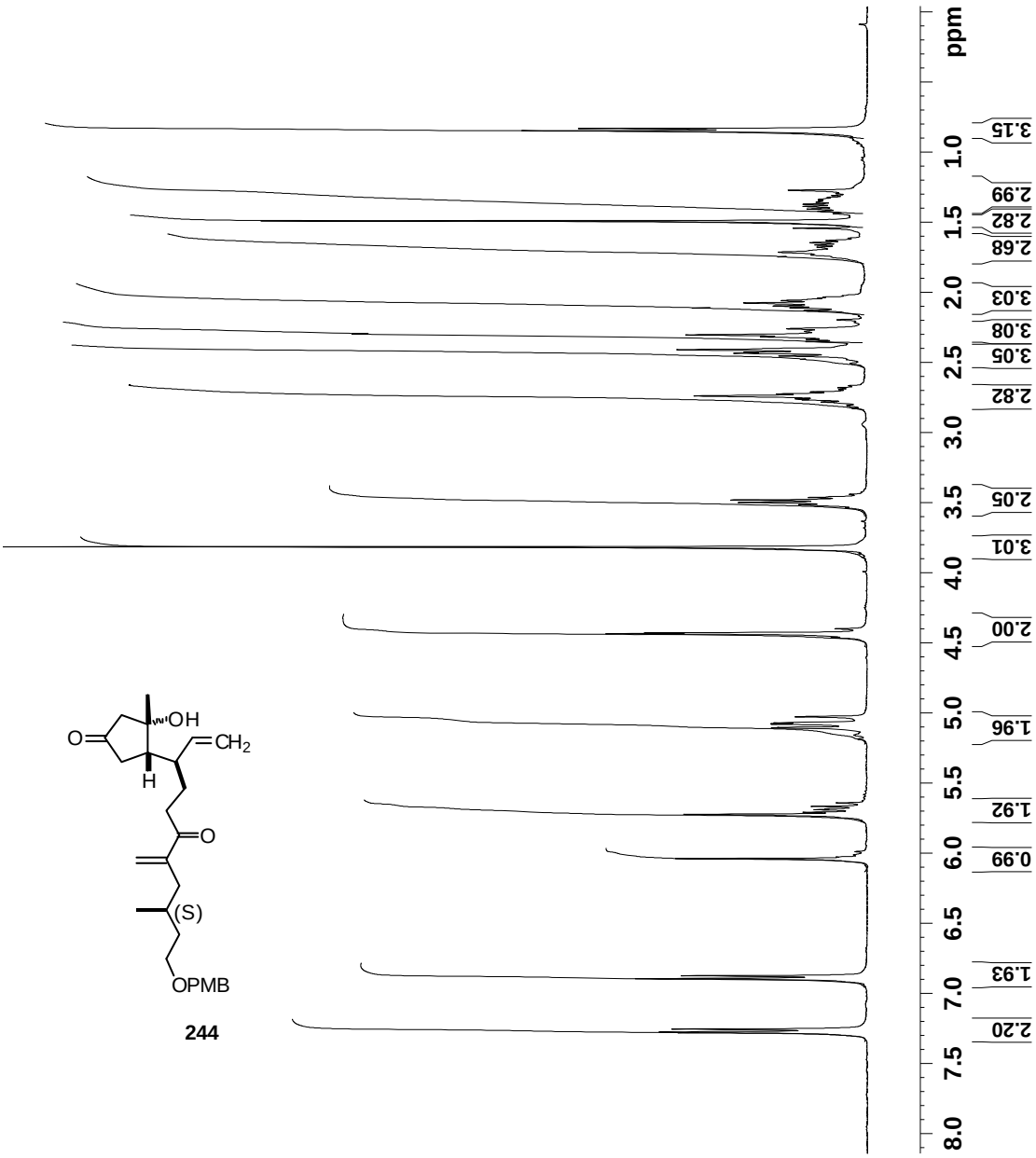

Current Data Parameters
NAME 195_VIII
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20090904
Time_ 10.24
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 90.5
DW 78.000 use
DE 6.50 use
TE 300.3 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 use
PL1 0.00 dB
PL1W 10.27361584 W
SFO1 400.1328009 MHz
F2 - Processing parameters
SI 32768
SF 400.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40
ppm
6.10
13.01
1.08
7.20
11.09
1.28
0.99
0.86
1.23
0.70
2.09
3.16
1.04
1.12
2.00
1.01
3.12
0.09
0.84
0.17
2.06
2.52
OH
HO
H
OTBS
(S)
OPMB

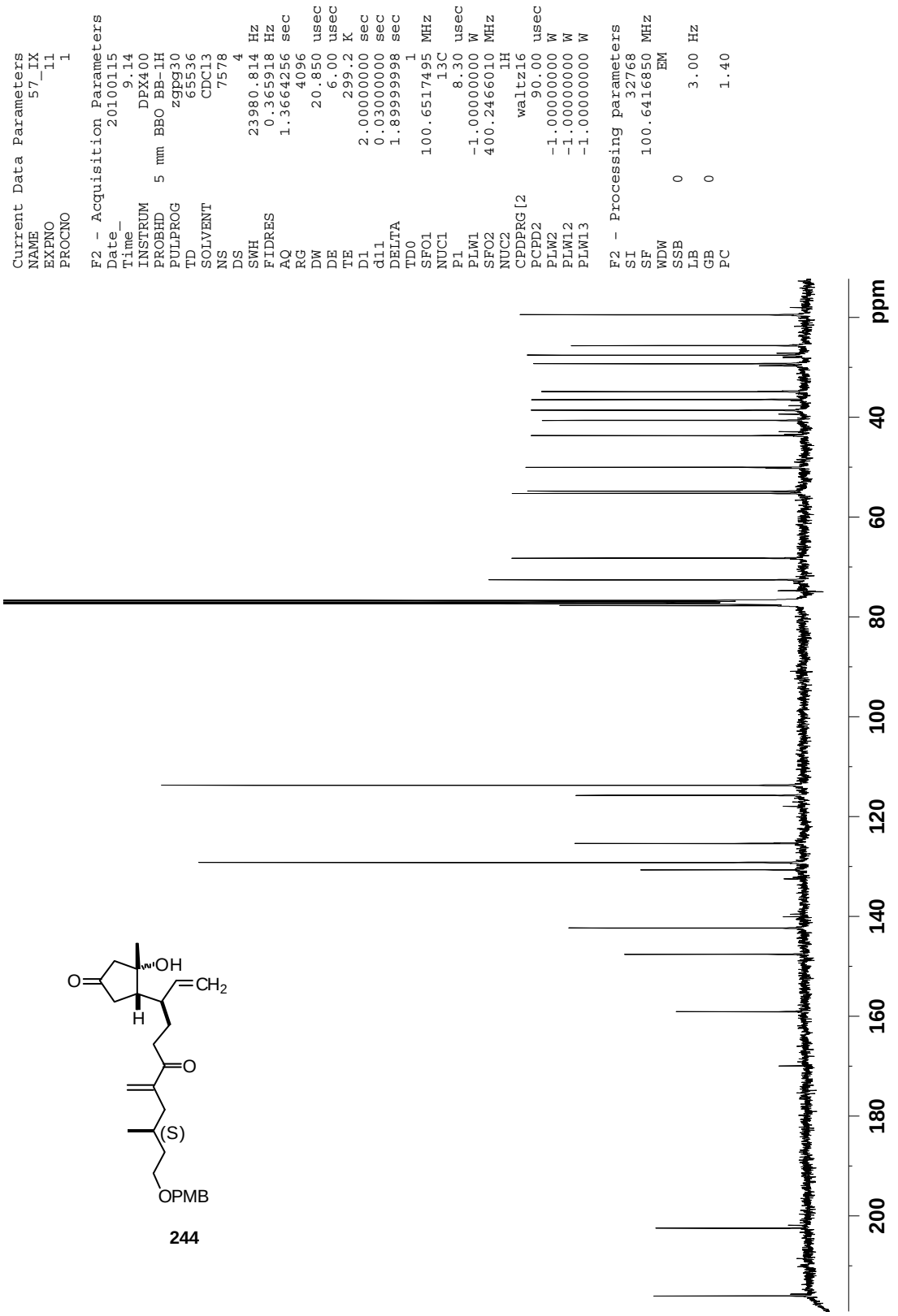
241


Current Data Parameters
NAME 195_VIII
EXPNO 8
PROCNO 1
F2 - Acquisition Parameters
Date_ 20090908
Time 8.28
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 9116
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664256 sec
RG 18390.4
DW 20.850 usec
DE 6.50 usec
TE 303.5 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
SFO1 100.6228298 MHz
NUC1 13C
P1 9.00 usec
PLW1 -1.00000000 W
SFO2 400.1316005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 32768
SF 100.6127690 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
HO
OH
H
OTBS
(S)
OPMB
241
ppm
20
40
60
80
100
120
140
160

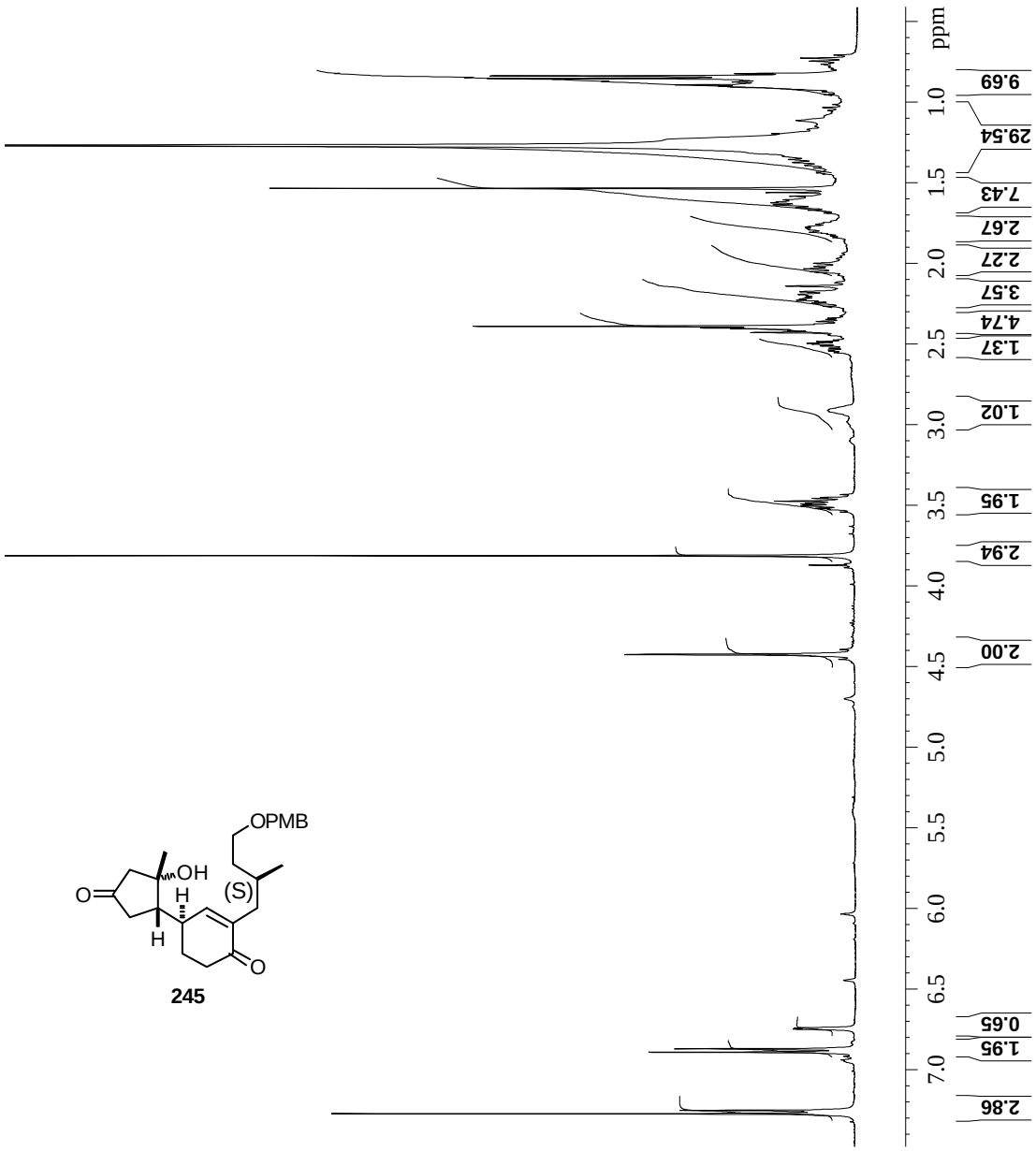

197_VIII
1
1
20090909
16.14
spect
5 mm PABBO BB-
zg30
32768
CDC13
6
2
6410.256 Hz
0.195625 Hz
2.5559540 sec
161.3
78.000 use
6.50 use
300.8 K
2.00000000 sec
1
CHANNEL f1
1H
14.00 use
0.00 dB
10.27361584 W
400.1328009 MHz
32768
400.1300000 MHz
EM
0
0.30 Hz
0
1.00
NAME
EXPNO
PROCNO
Date_
Time_
INSTRUM
PROBHD
PULPROG
TD
SOLVENT
NS
DS
SWH
FIDRES
AQ
RG
DW
DE
TE
D1
TD0
NUC1
P1
PL1
PL1W
SFO1
SI
SF
WDW
SSB
LB
GB
PC
OH
HO
H
OH
(S)
OPMB
243
ppm
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5
7.0
7.5
4.53
1.02
9.03
15.14
1.71
1.41
1.77
0.75
2.01
2.71
1.25
1.15
2.00
1.04
3.05
0.88
1.96
3.43

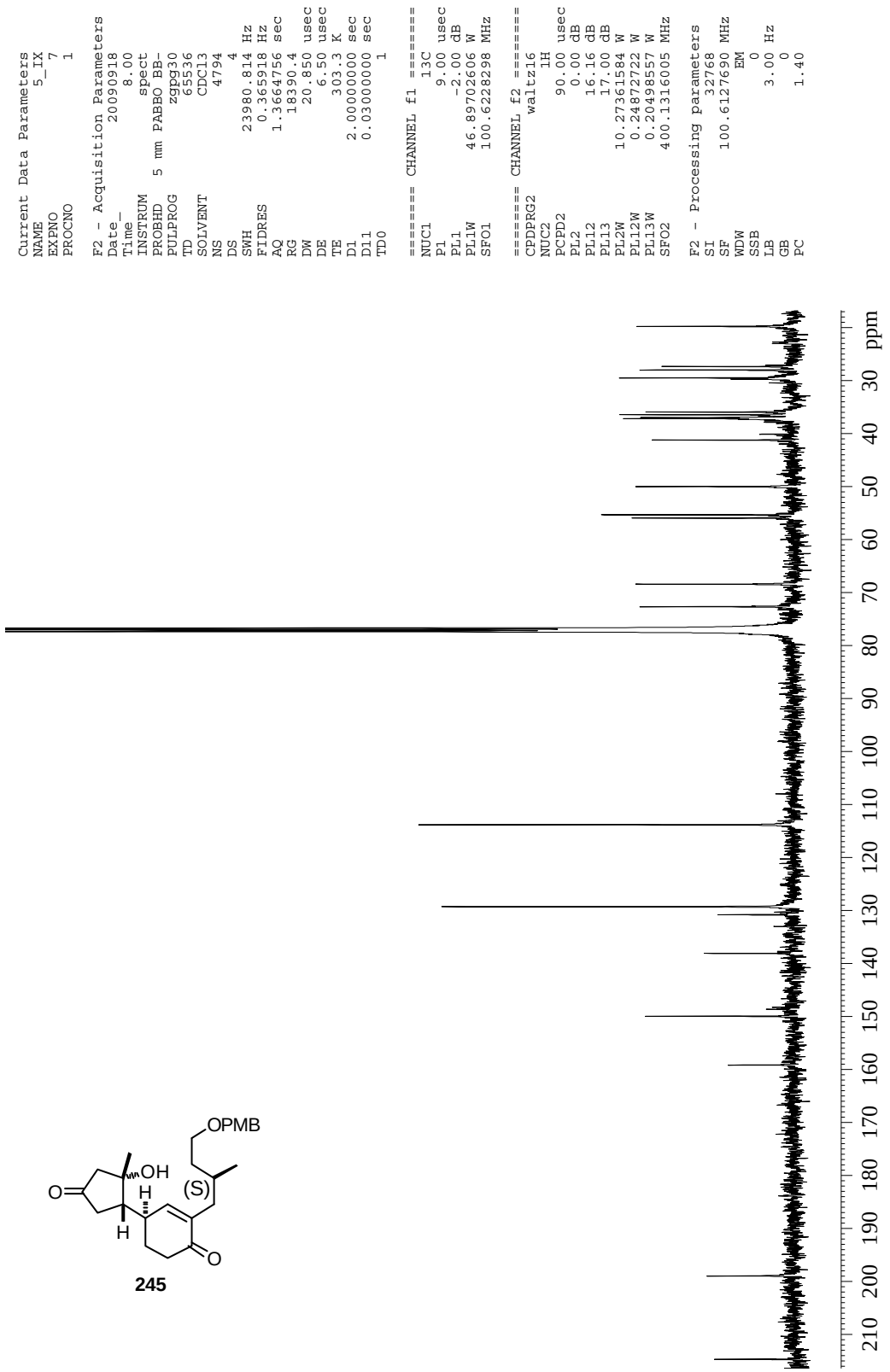

Current Data Parameters
NAME 197_VIII
EXPNO 6
PROCNO 1
F2 - Acquisition Parameters
Date_ 20090910
Time_ 8.49
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 9314
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664256 sec
RG 18390.4
DW 20.850 usec
DE 6.50 usec
TE 303.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
SFO1 100.6228298 MHz
NUC1 13C
P1 9.00 usec
PLW1 -1.00000000 W
SFO2 400.1316005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 32768
SF 100.6127690 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
HO
OH
H
OH
(S)
OPMB
243
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

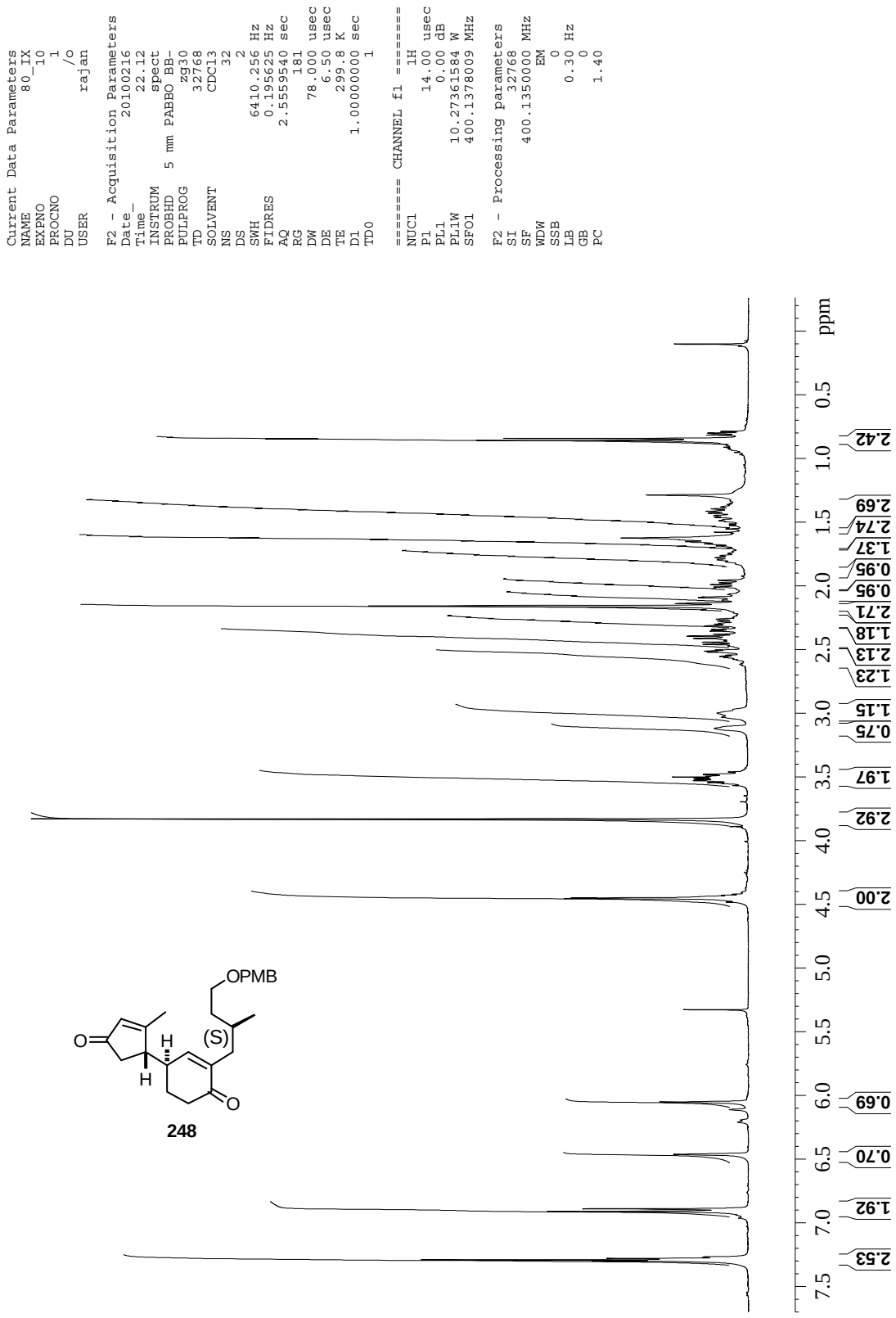

Current Data Parameters
NAME 57_IX
EXPNO 7
PROCNO 1
F2 - Acquisition Parameters
Date_ 20100114
Time_ 22.35
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDC13
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559039 sec
RG 256
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 1.00000000 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 EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
O
OH
CH2
H
O
(S)
OPMB
244
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
2.0
1.5
1.0
3.15
2.99
2.82
2.68
3.03
3.08
3.05
2.82
2.05
3.01
2.00
1.96
1.92
0.99
1.93
2.20

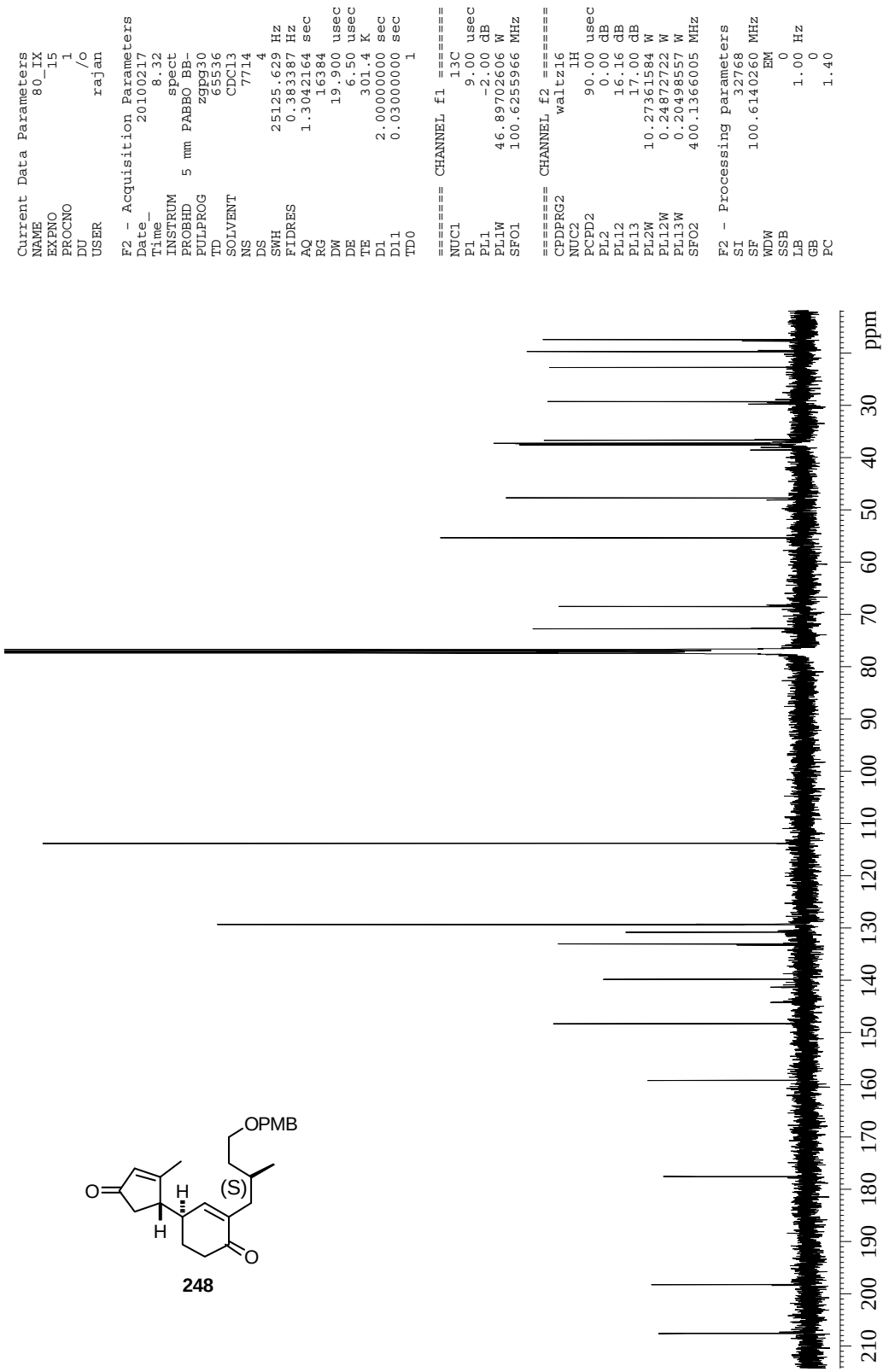

Current Data Parameters
NAME 57_IX
EXPNO 11
PROCNO 1
F2 - Acquisition Parameters
Date_ 20100115
Time 9.14
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 7578
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664256 sec
RG 4096
DW 20.850 usec
DE 6.00 usec
TE 299.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
SFO1 100.6517495 MHz
NUC1 13C
P1 8.30 usec
PLW1 -1.00000000 W
SFO2 400.2466010 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 32768
SF 100.6416850 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
ppm
200
180
160
140
120
100
80
60
40
OH
CH2
O
H
O
(S)
OPMB

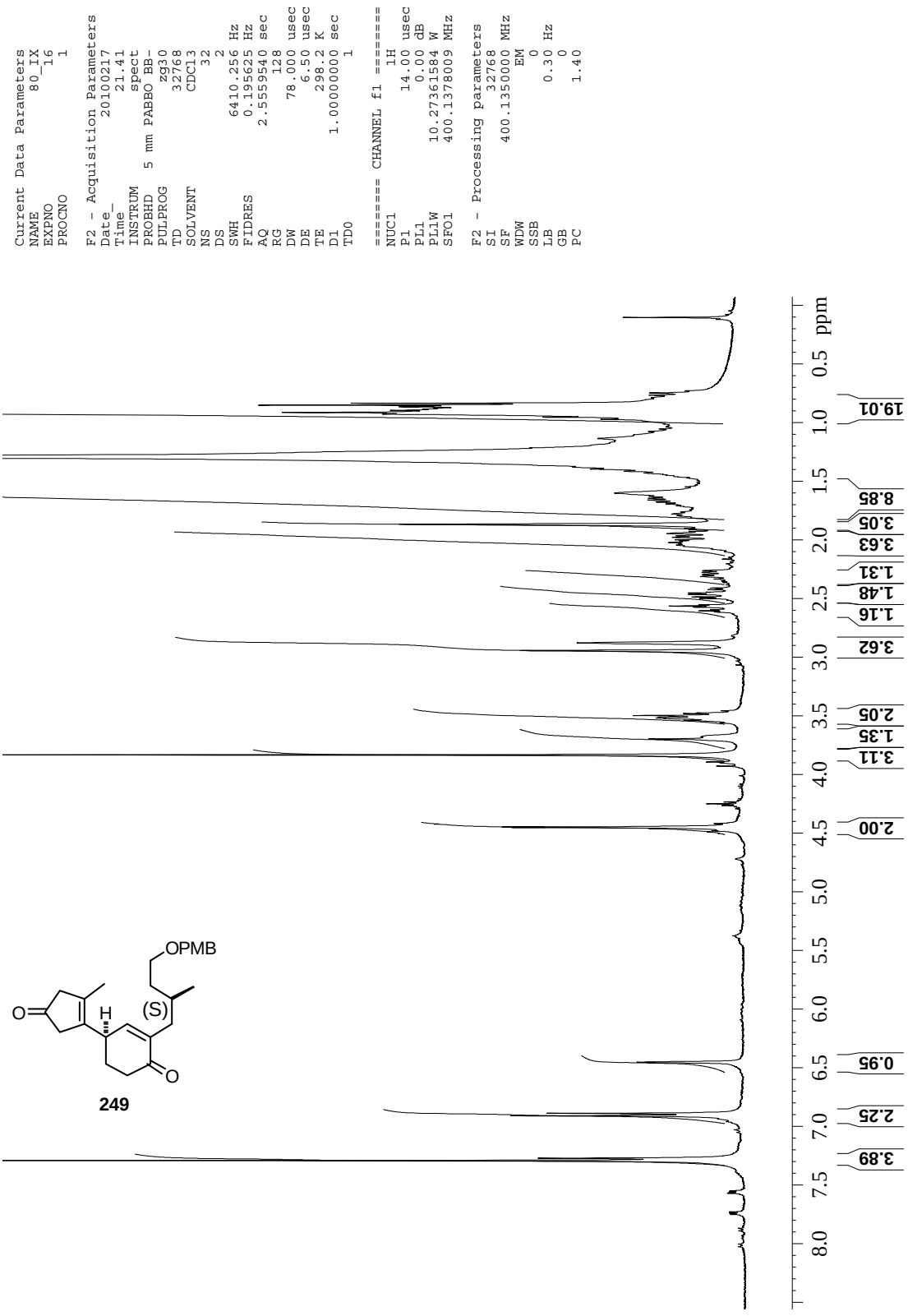
244

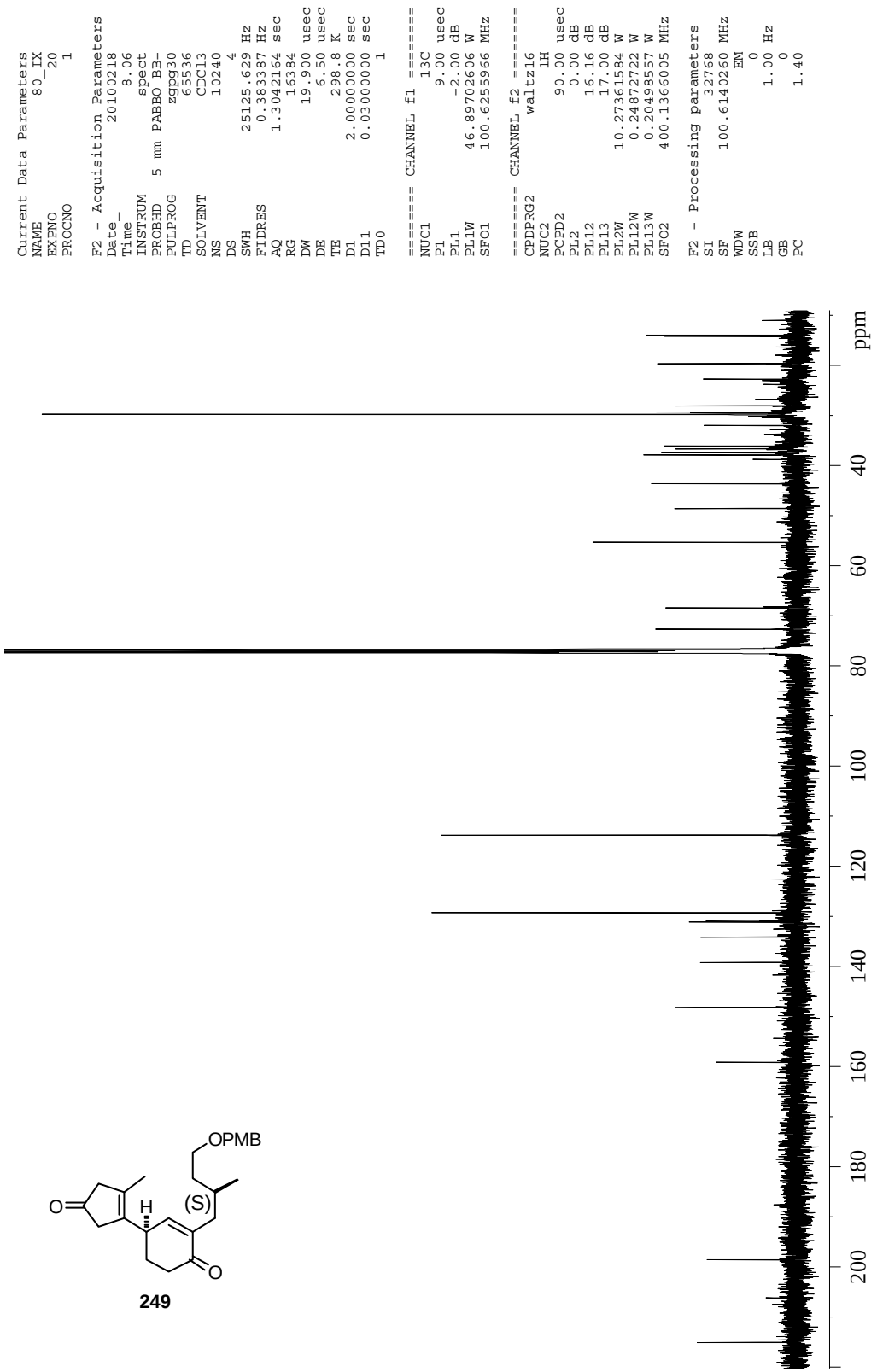

Current Data Parameters
NAME 10_IX
EXPNO 4
PROCNO 1
DU /m
USER rajan
F2 - Acquisition Parameters
Date_ 20090926
Time_ 14.20
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 256
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.50 usec
PL1 -3.00 dB
SFO1 400.2428017 MHz
F2 - Processing parameters
SI 32768
SF 400.2400000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
OPMB
OH
H
(S)
O
H
O
245
ppm
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
2.86
1.95
0.65
2.00
2.94
1.95
1.02
1.37
4.74
3.57
2.27
2.67
7.43
29.54
9.69


Current Data Parameters
NAME 5_IX
EXPNO 7
PROCNO 1
F2 - Acquisition Parameters
Date_ 20090918
Time 8.00
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 4794
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 18390.4
DW 20.850 usec
DE 6.50 usec
TE 303.3 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 100.6228298 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 400.1316005 MHz
F2 - Processing parameters
SI 32768
SF 100.6127690 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
OPMB
OH
H
(S)
O
H
O
245
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 ppm

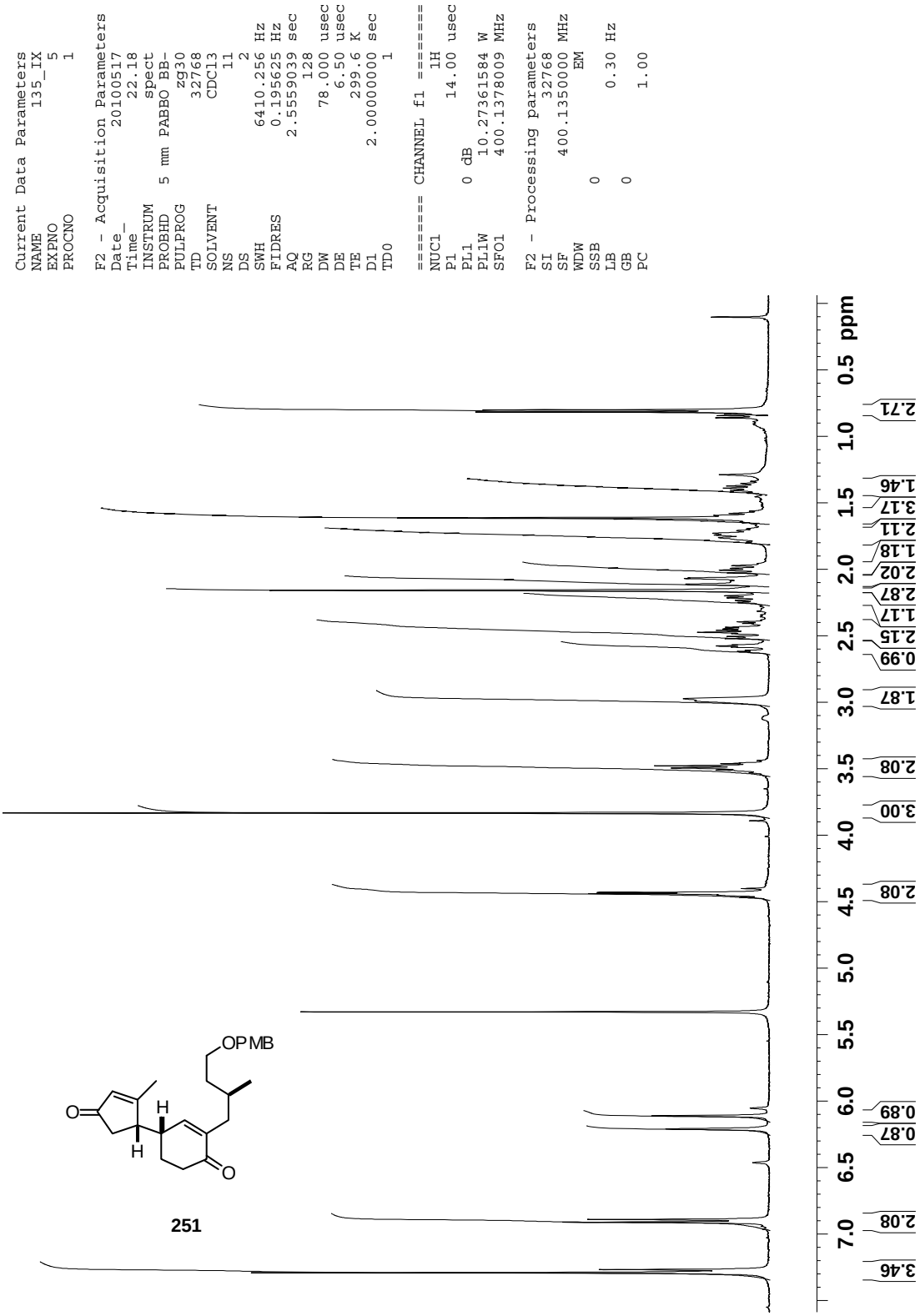

Current Data Parameters
NAME 80_IX
EXPNO 10
PROCNO 1
DU /o
USER rajan
F2 - Acquisition Parameters
Date_ 20100216
Time_ 22.12
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 181
DW 78.000 usec
DE 6.50 usec
TE 299.8 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 usec
PL1 0.00 dB
PL1W 10.27361584 W
SFO1 400.1378009 MHz
F2 - Processing parameters
SI 32768
SF 400.1350000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40
OPMB
O
H
(S)
H
O
248
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
0.5
2.53
1.92
0.70
0.69
2.00
2.92
1.97
0.75
1.15
1.23
2.13
1.18
2.71
0.95
0.95
1.37
2.74
2.69
2.42

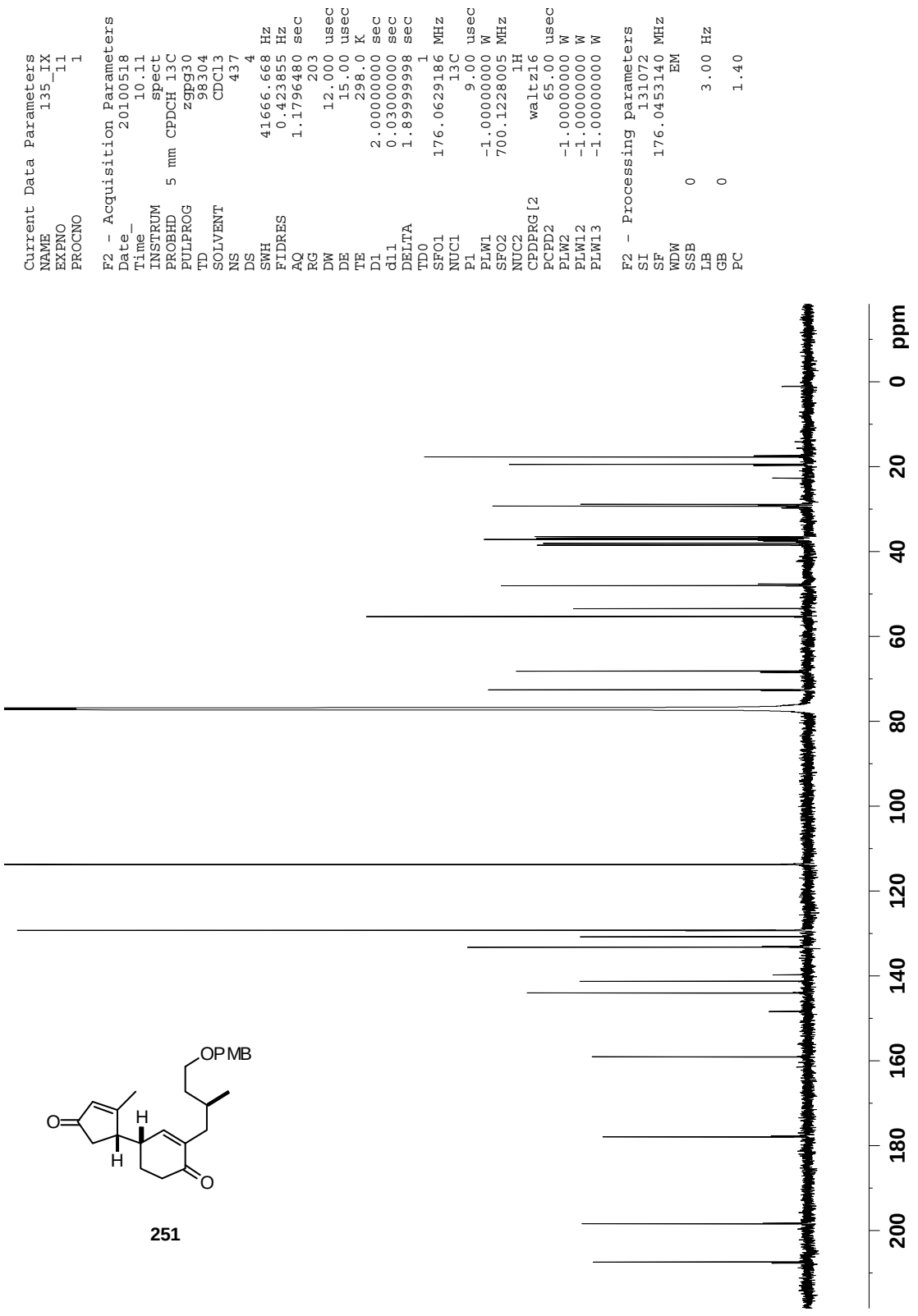

Current Data Parameters
NAME 80_IX
EXPNO 15
PROCNO 1
DU /o
USER rajan
F2 - Acquisition Parameters
Date_ 20100217
Time_ 8.32
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 7714
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.30442164 sec
RG 16384
DW 19.900 usec
DE 6.50 usec
TE 301.4 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 100.6255966 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
OPMB
(S)
O
H
H
O
248
ppm

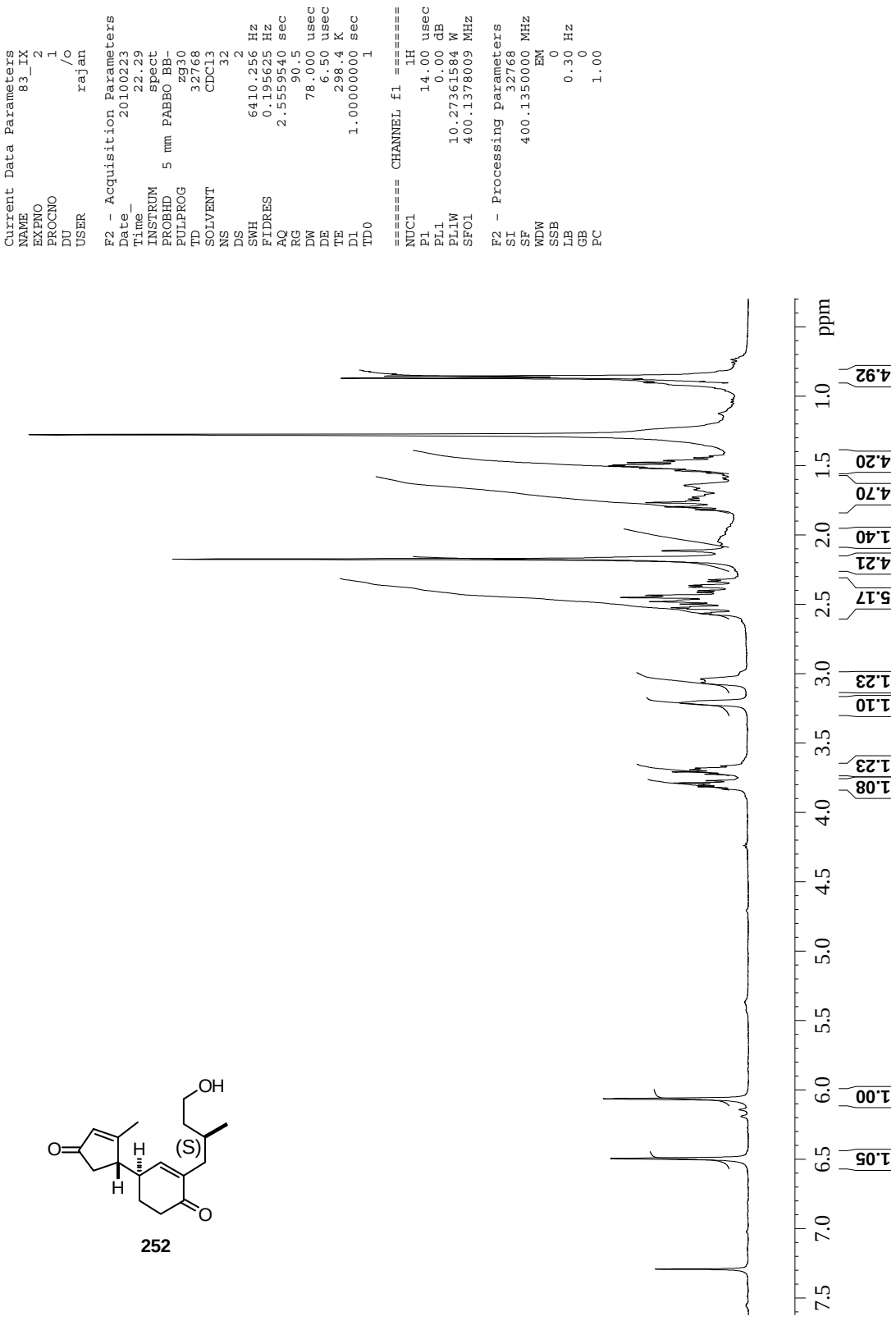

Current Data Parameters
NAME 80_IX
EXPNO 16
PROCNO 1
F2 - Acquisition Parameters
Date_ 20100217
Time 21.41
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 128
DW 78.000 usec
DE 6.50 usec
TE 298.2 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 usec
PL1 0.00 dB
PL1W 10.27361584 W
SFO1 400.1378009 MHz
F2 - Processing parameters
SI 32768
SF 400.1350000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40
OPMB
O
H
(S)
O
249
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
19.01
8.85
3.05
3.63
1.31
1.48
1.16
3.62
2.05
1.35
3.11
2.00
0.95
2.25
3.89


Current Data Parameters
NAME 80_IX
EXPNO 20
PROCNO 1
F2 - Acquisition Parameters
Date_ 20100218
Time 8.06
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 10240
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3042164 sec
RG 16384
DW 19.900 usec
DE 6.50 usec
TE 298.8 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 100.6255966 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
200
180
160
140
120
100
80
60
40
ppm
OPMB
O
H
(S)
O

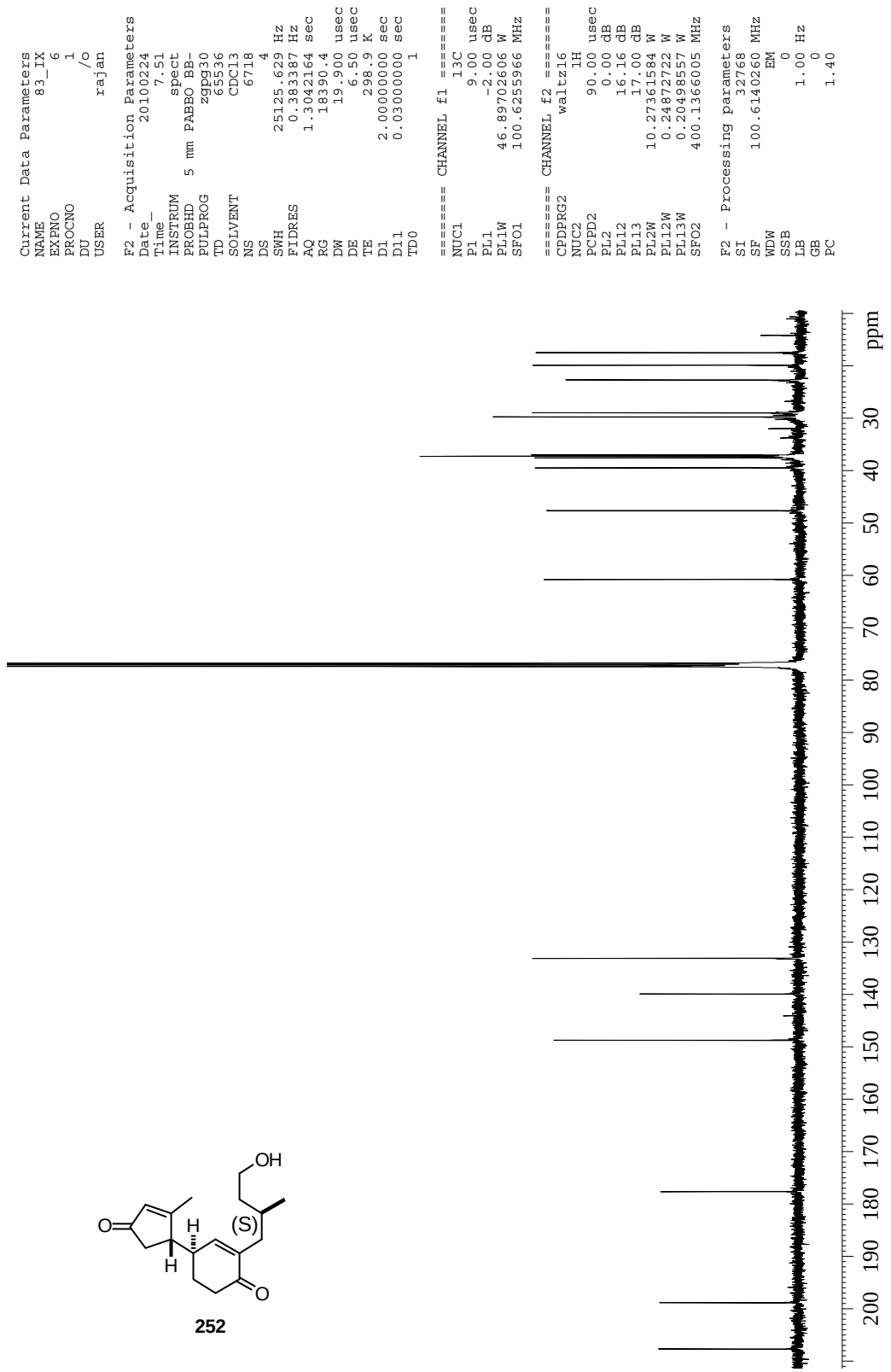
249


Current Data Parameters
NAME 135_IX
EXPNO 5
PROCNO 1
F2 - Acquisition Parameters
Date_ 20100517
Time 22.18
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 11
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559039 sec
RG 128
DW 78.000 usec
DE 6.50 usec
TE 299.6 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 usec
PL1 0 dB
PL1W 10.27361584 W
SFO1 400.1378009 MHz
F2 - Processing parameters
SI 32768
SF 400.1350000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
OPMB
O
H
H
O
251
ppm
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
3.46
2.08
0.87
0.89
2.08
3.00
2.08
1.87
0.99
2.15
1.17
2.87
2.02
1.18
2.11
3.17
1.46
2.71

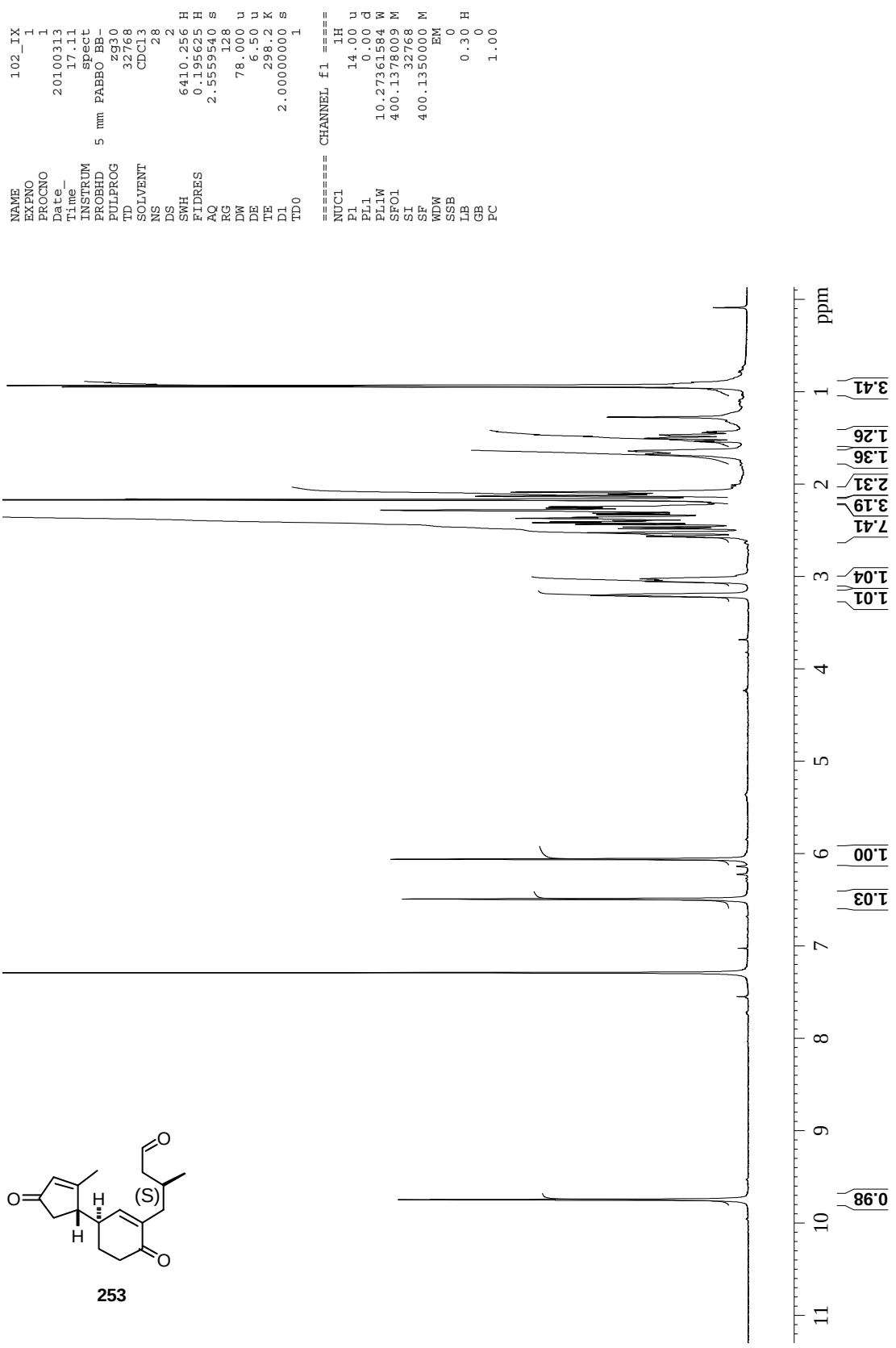

Current Data Parameters
NAME 135_IX
EXPNO 11
PROCNO 1
F2 - Acquisition Parameters
Date_ 20100518
Time_ 10.11
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDCl3
NS 437
DS 4
SWH 41666.668 Hz
FIDRES 0.423855 Hz
AQ 1.1796480 sec
RG 203
DW 12.000 usec
DE 15.00 usec
TE 298.0 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
SFO1 176.0629186 MHz
NUC1 13C
P1 9.00 usec
PLW1 -1.00000000 W
SFO2 700.1228005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 65.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 131072
SF 176.0453140 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
OPMB
O
H
H
O
251
ppm
0
20
40
60
80
100
120
140
160
180
200


Current Data Parameters
NAME 83_IX
EXPNO 2
PROCNO 1
DU /o
USER rajan
F2 - Acquisition Parameters
Date_ 20100223
Time_ 22.29
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 90.5
DW 78.000 usec
DE 6.50 usec
TE 298.4 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 usec
PL1 0.00 dB
PL1W 10.27361584 W
SFO1 400.1378009 MHz
F2 - Processing parameters
SI 32768
SF 400.1350000 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
1.05
1.00
1.23
1.08
1.23
1.10
1.23
5.17
4.21
1.40
4.70
4.20
4.92
OH
O
H
(S)
H
O

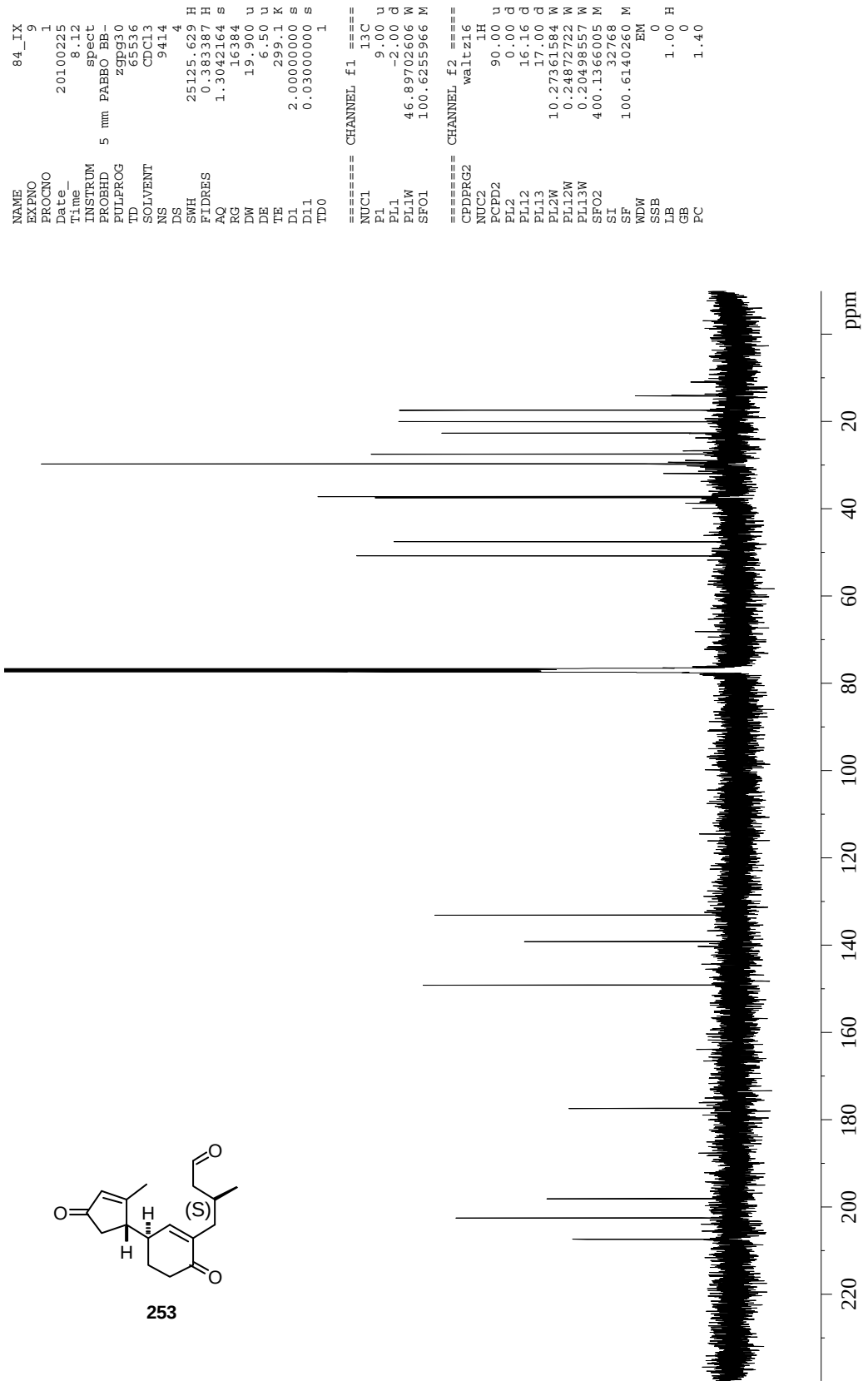
252


Current Data Parameters
NAME 83_IX
EXPNO 6
PROCNO 1
DU /o
USER rajan
F2 - Acquisition Parameters
Date_ 20100224
Time_ 7.51
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 6718
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3042164 sec
RG 18390.4
DW 19.900 usec
DE 6.50 usec
TE 298.9 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 100.6255966 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
ppm
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30
O
H
(S)
H
OH
O

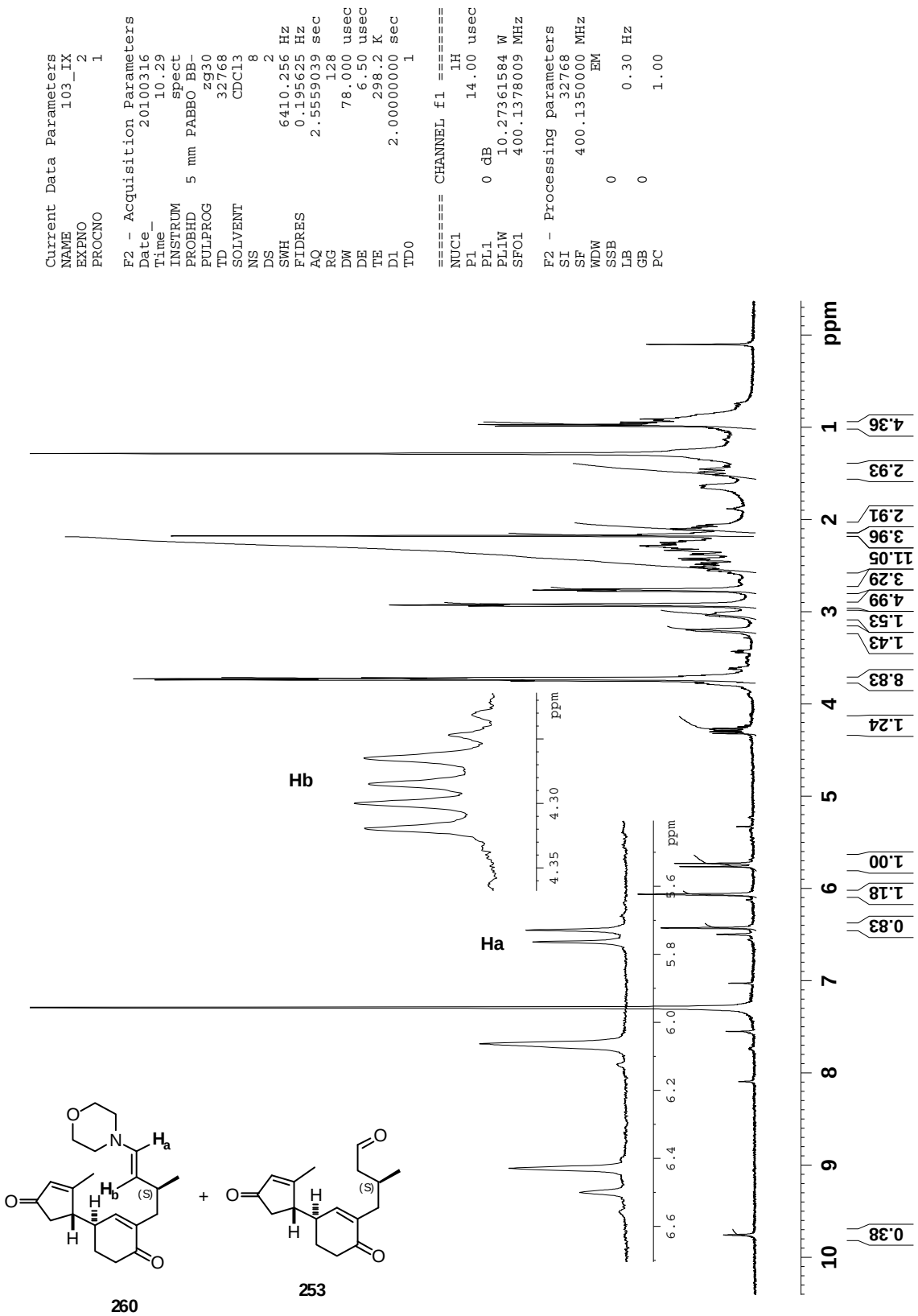
252

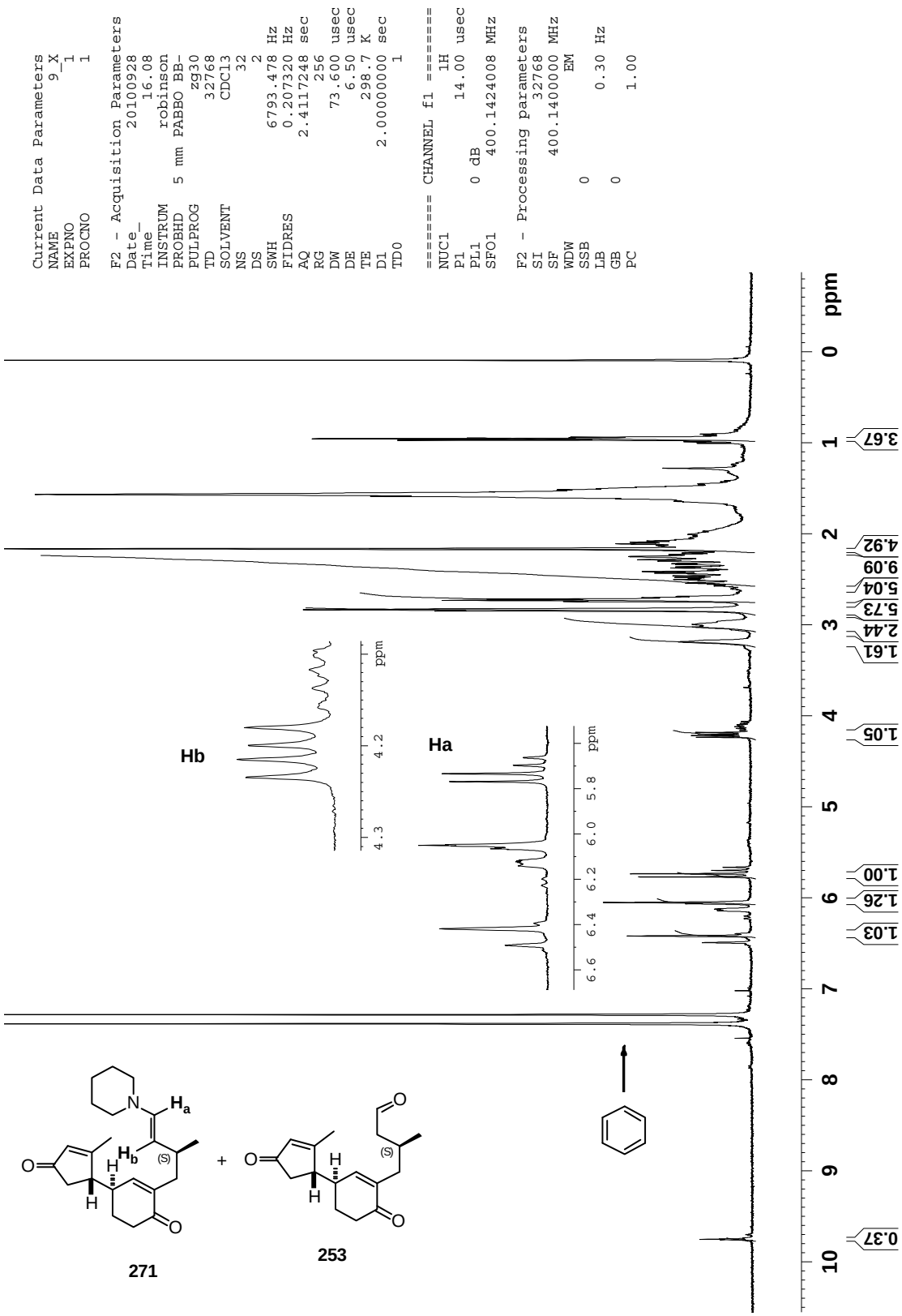

102_IX
1
1
20100313
17.11
spect
5 mm PABBO BB-
zg30
32768
CDCl3
28
2
6410.256 H
0.195625 H
2.5559540 s
128
78.000 u
6.50 u
298.2 K
2.00000000 s
1
======== CHANNEL f1 =====
1H
14.00 u
0.00 d
10.27361584 W
400.13780009 M
32768
400.13500000 M
EM
0
0.30 H
0
1.00
NAME
EXPNO
PROCNO
Date_
Time_
INSTRUM
PROBHD
PULPROG
TD
SOLVENT
NS
DS
SWH
FIDRES
AQ
RG
DW
DE
TE
D1
TD0
NUC1
P1
PL1
PL1W
SFO1
SI
SF
WDW
SSB
LB
GB
PC
ppm
3.41
1.26
1.36
2.31
3.19
7.41
1.04
1.01
1.00
1.03
0.98
O
H
(S)
H
O
O

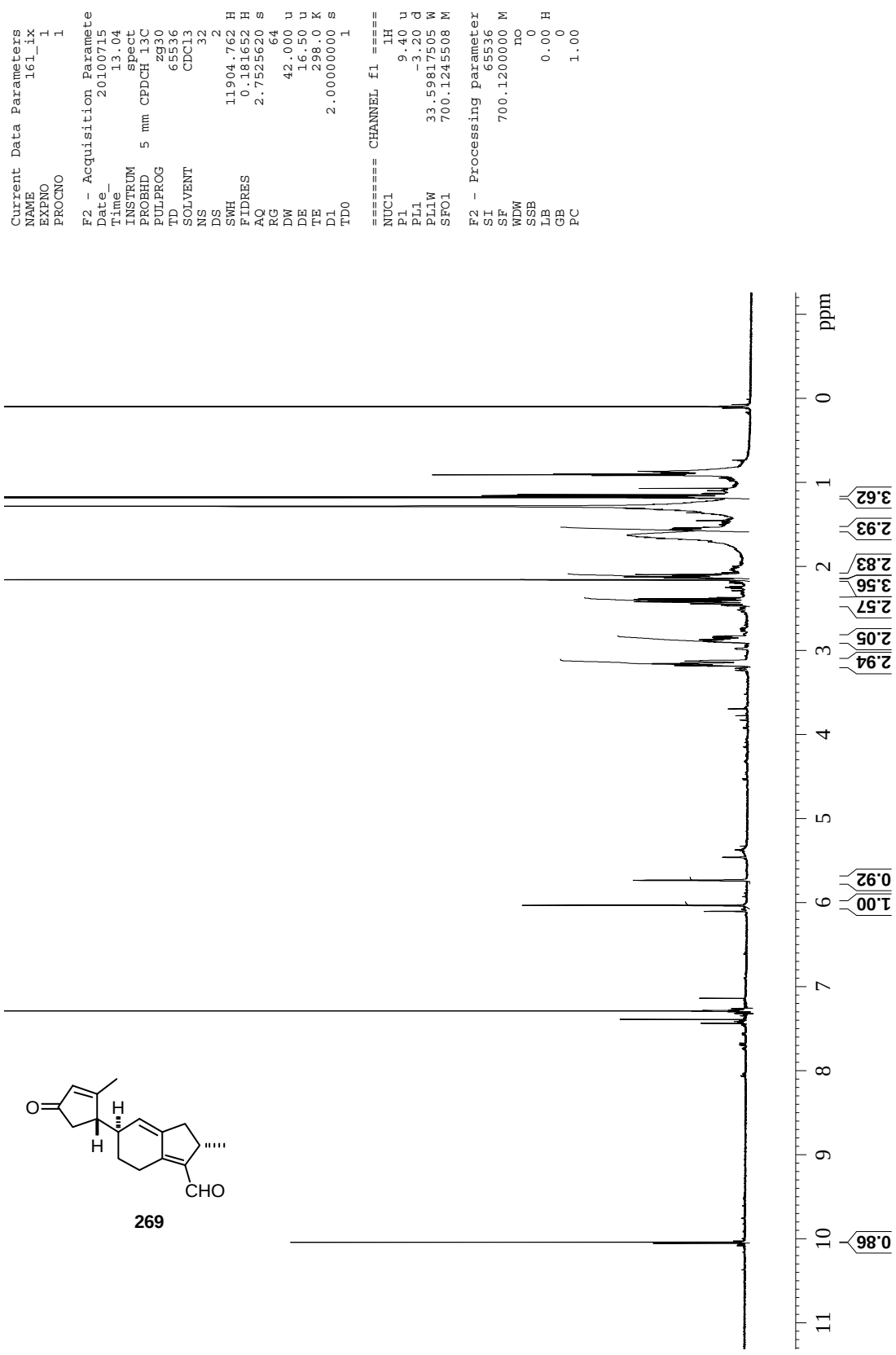
253


NAME 84_IX
EXPNO 9
PROCNO 1
Date_ 20100225
Time_ 8.12
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 9414
DS 4
SWH 25125.629 H
FIDRES 0.383387 H
AQ 1.3042164 s
RG 16384
DW 19.900 u
DE 6.50 u
TE 299.1 K
D1 2.00000000 s
D11 0.03000000 s
TD0 1
======== CHANNEL f1 =====
NUC1 13C
P1 9.00 u
PL1 -2.00 d
PL1W 46.89702606 W
SFO1 100.6255966 M
======== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 u
PL2 0.00 d
PL12 16.16 d
PL13 17.00 d
PL2W 10.27361584 W
PL12W 0.24872722 W
PL13W 0.20498557 W
SFO2 400.1366005 M
SI 32768
SF 100.6140260 M
WDW EM
SSB 0
LB 1.00 H
GB 0
PC 1.40
ppm
20
40
60
80
100
120
140
160
180
200
220
O
H
H
(S)
O
O

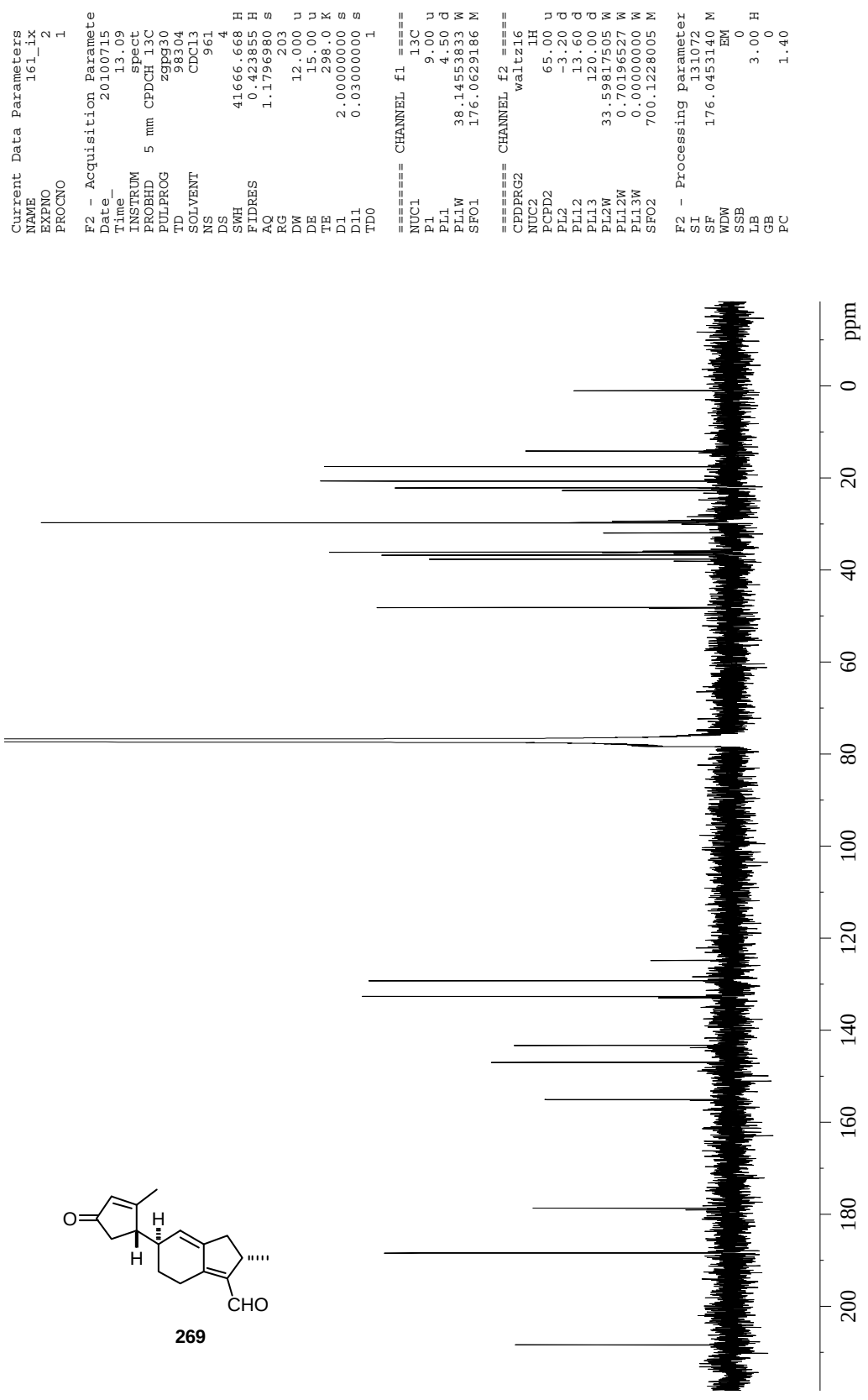
253


Current Data Parameters
NAME 103_IX
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20100316
Time_ 10.29
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 8
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559039 sec
RG 128
DW 78.000 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 usec
PL1 0 dB
PL1W 10.27361584 W
SFO1 400.1378009 MHz
F2 - Processing parameters
SI 32768
SF 400.1350000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
Hb
Ha
ppm
4.35
4.30
5.6
5.8
6.0
6.2
6.4
6.6
4.36
2.93
2.91
3.96
11.05
3.29
4.99
1.53
1.43
8.83
1.24
1.00
1.18
0.83
0.38
1
2
3
4
5
6
7
8
9
10
ppm
O
N
Ha
Hb
H
(S)
O
O
H
+
O
H
(S)
O
O
H
260
253

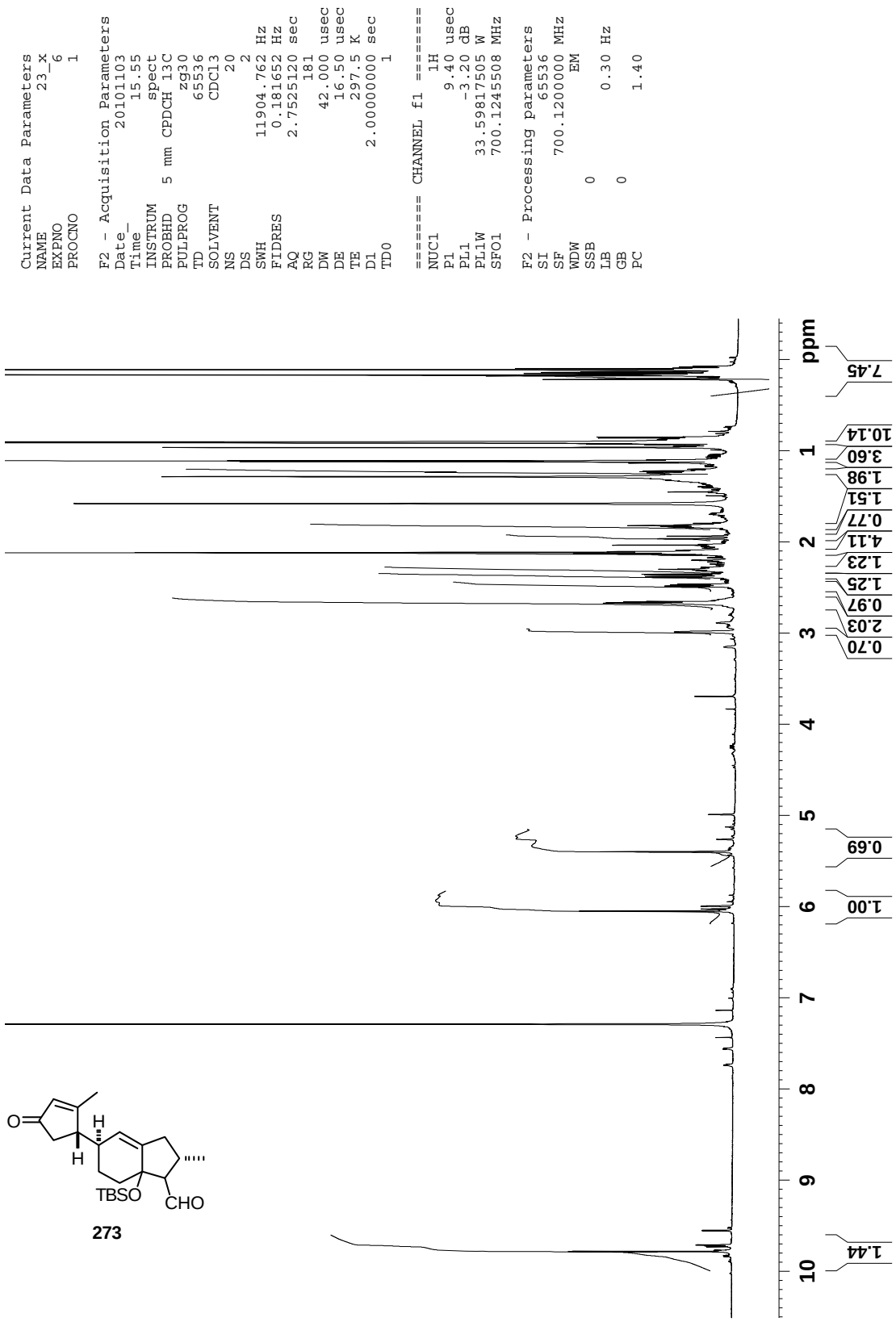

Current Data Parameters
NAME 9_X
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20100928
Time 16.08
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6793.478 Hz
FIDRES 0.207320 Hz
AQ 2.4117248 sec
RG 256
DW 73.600 usec
DE 6.50 usec
TE 298.7 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 usec
PL1 0 dB
SFO1 400.1424008 MHz
F2 - Processing parameters
SI 32768
SF 400.1400000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
Hb
Ha
ppm
0.37
1.03
1.26
1.00
1.05
1.61
2.44
5.73
5.04
9.09
4.92
3.67
271
253

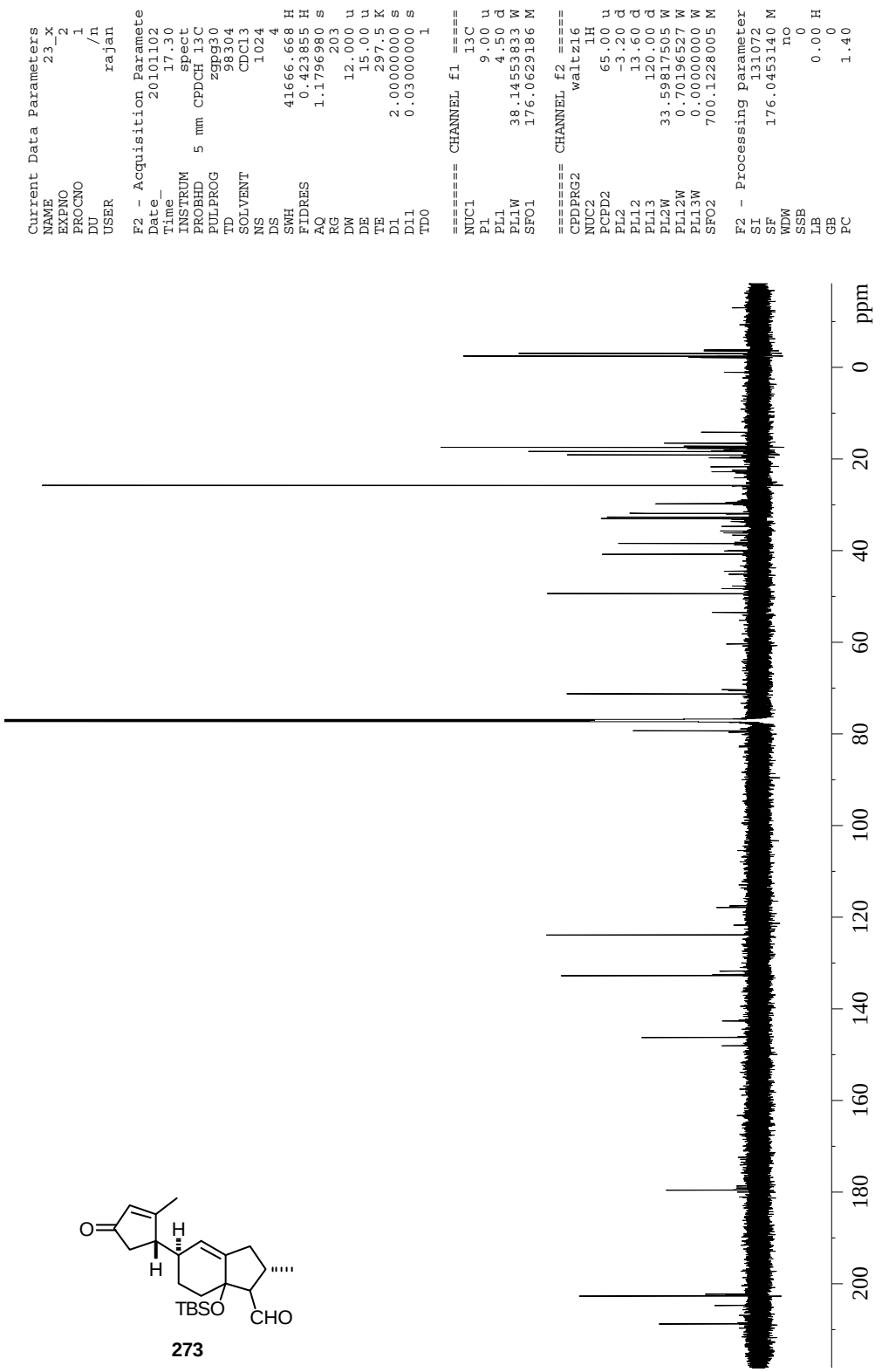

Current Data Parameters
NAME 161_ix
EXPNO 1
PROCNO 1
F2 - Acquisition Paramete
Date_ 20100715
Time_ 13.04
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 H
FIDRES 0.181652 H
AQ 2.7525620 s
RG 64
DW 42.000 u
DE 16.50 u
TE 298.0 K
D1 2.00000000 s
TD0 1
======== CHANNEL f1 =====
NUC1 1H
P1 9.40 u
PL1 -3.20 d
PL1W 33.59817505 W
SFO1 700.1245508 M
F2 - Processing parameter
SI 65536
SF 700.1200000 M
WDW no
SSB 0
LB 0.00 H
GB 0
PC 1.00
ppm
0
1
2
3
4
5
6
7
8
9
10
11
3.62
2.93
2.83
3.56
2.57
2.05
2.94
1.00
0.92
0.86
O
H
H
CHO

269

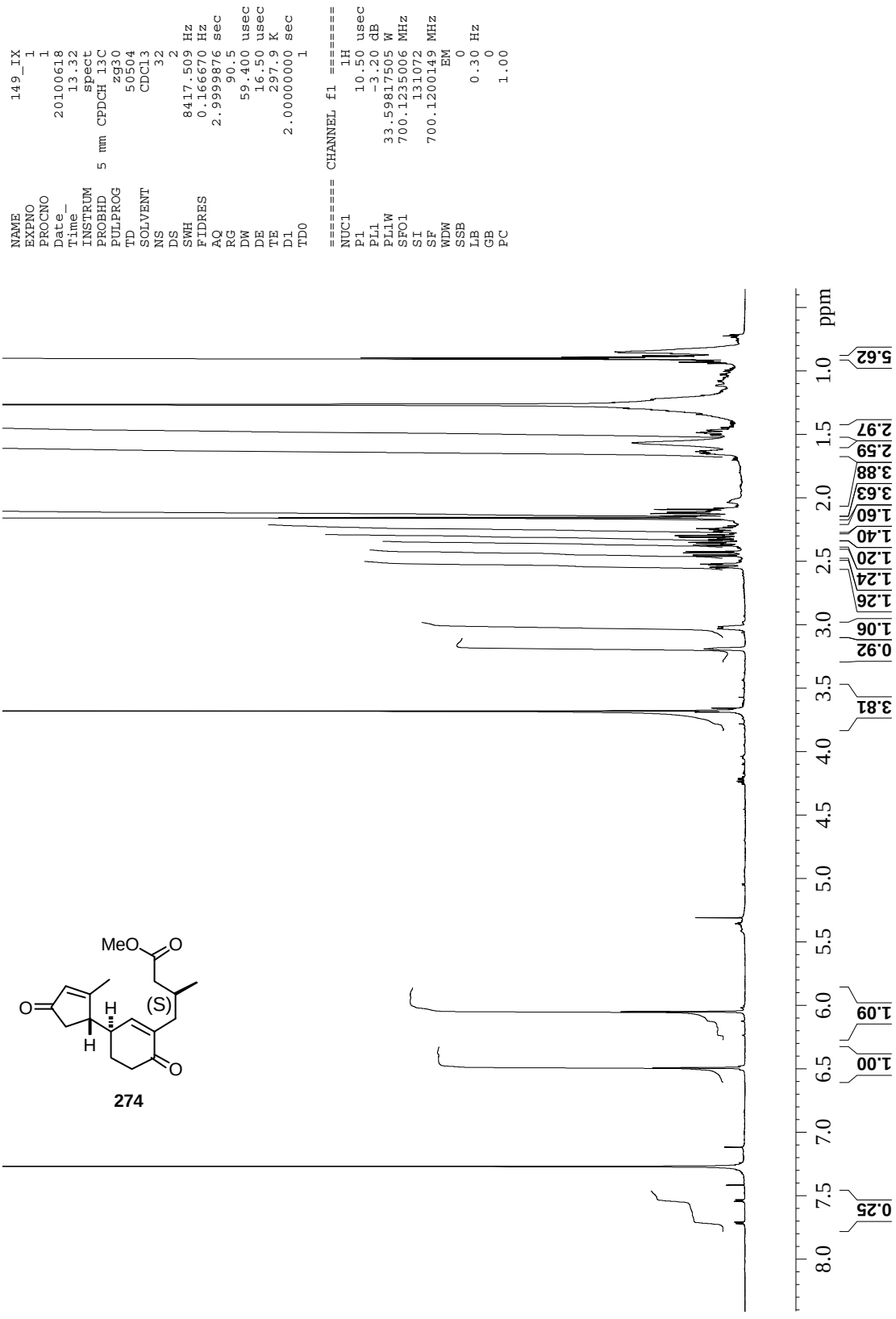

Current Data Parameters
NAME 161_ix
EXPNO 2
PROCNO 1
F2 - Acquisition Paramete
Date_ 20100715
Time_ 13.09
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDCl3
NS 961
DS 4
SWH 41666.668 H
FIDRES 0.423855 H
AQ 1.1796980 s
RG 203
DW 12.000 u
DE 15.00 u
TE 298.0 K
D1 2.00000000 s
D11 0.03000000 s
TD0 1
======== CHANNEL f1 =====
NUC1 13C
P1 9.00 u
PL1 4.50 d
PL1W 38.14553833 W
SFO1 176.0629186 M
======== CHANNEL f2 =====
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 u
PL2 -3.20 d
PL12 13.60 d
PL13 120.00 d
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1228005 M
F2 - Processing parameter
SI 131072
SF 176.0453140 M
WDW EM
SSB 0
LB 3.00 H
GB 0
PC 1.40
ppm
0
20
40
60
80
100
120
140
160
180
200
O
H
H
CHO

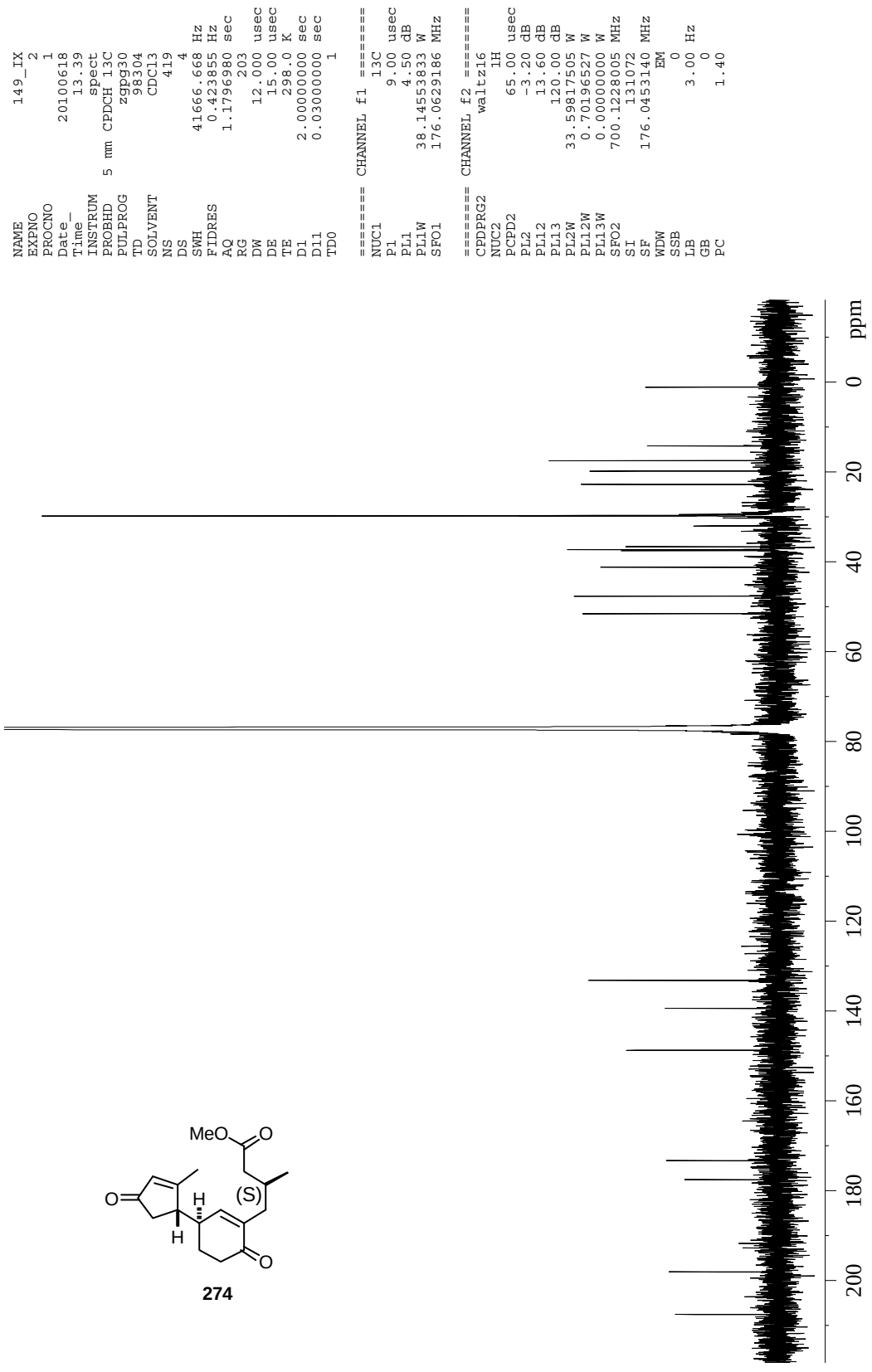
269


Current Data Parameters
NAME 23_x
EXPNO 6
PROCNO 1
F2 - Acquisition Parameters
Date_ 20101103
Time 15.55
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 20
DS 2
SWH 11904.762 Hz
FIDRES 0.181652 Hz
AQ 2.7525120 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
F2 - Processing parameters
SI 65536
SF 700.1200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40
ppm
7.45
10.14
3.60
1.98
1.51
0.77
4.11
1.23
1.25
0.97
2.03
0.70
0.69
1.00
1.44
O
H
H
TBSO
CHO
273

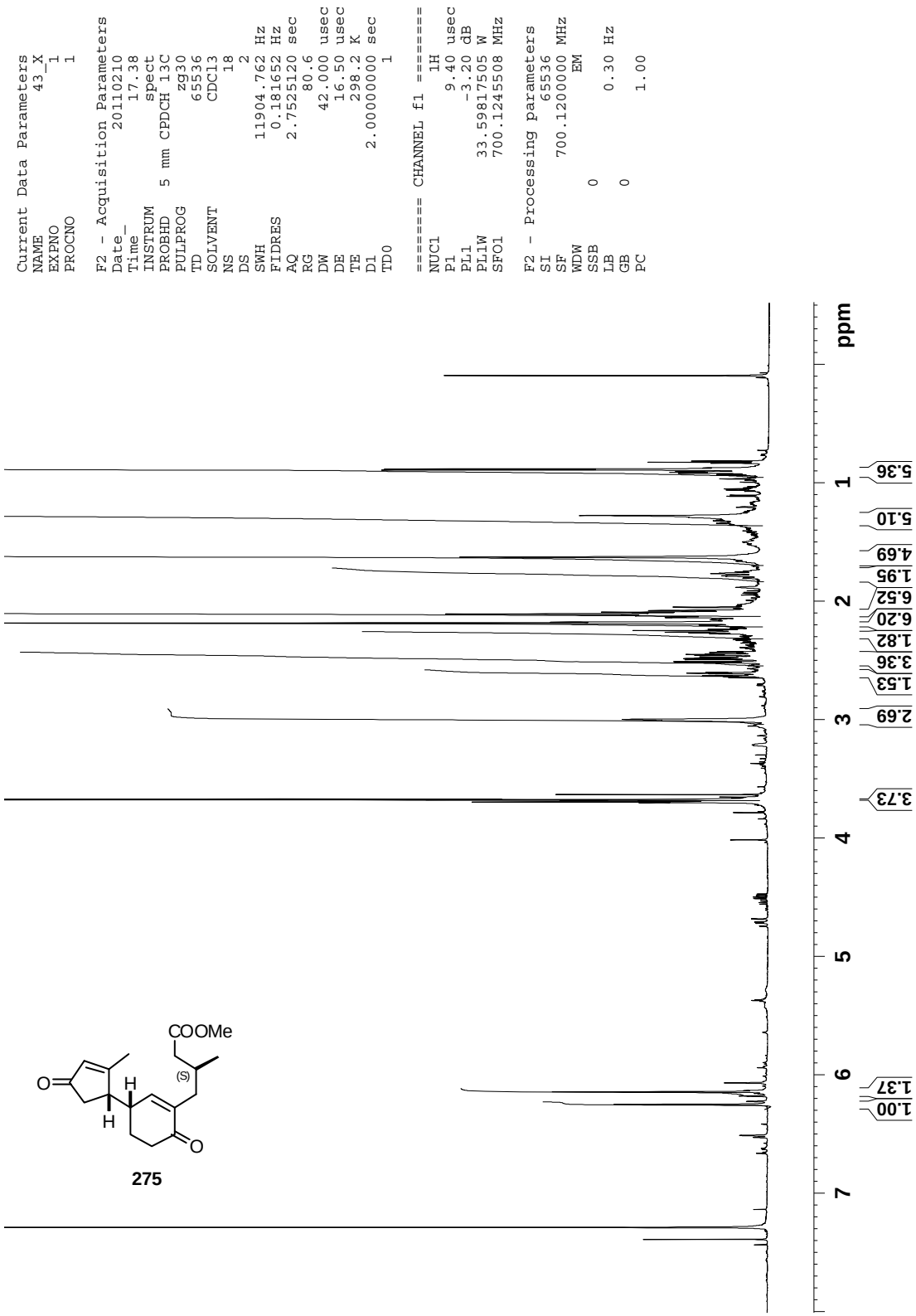

Current Data Parameters
NAME 23_x
EXPNO 2
PROCNO 1
DU /n
USER rajan
F2 - Acquisition Parameters
Date_ 20101102
Time 17.30
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDCl3
NS 1024
DS 4
SWH 41666.668 Hz
FIDRES 0.423855 Hz
AQ 1.1796980 sec
RG 203
DW 12.000 usec
DE 15.00 usec
TE 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
F2 - Processing parameters
SI 131072
SF 176.0453140 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.40
ppm
200
180
160
140
120
100
80
60
40
20
0
O
H
H
TBSO
CHO

273

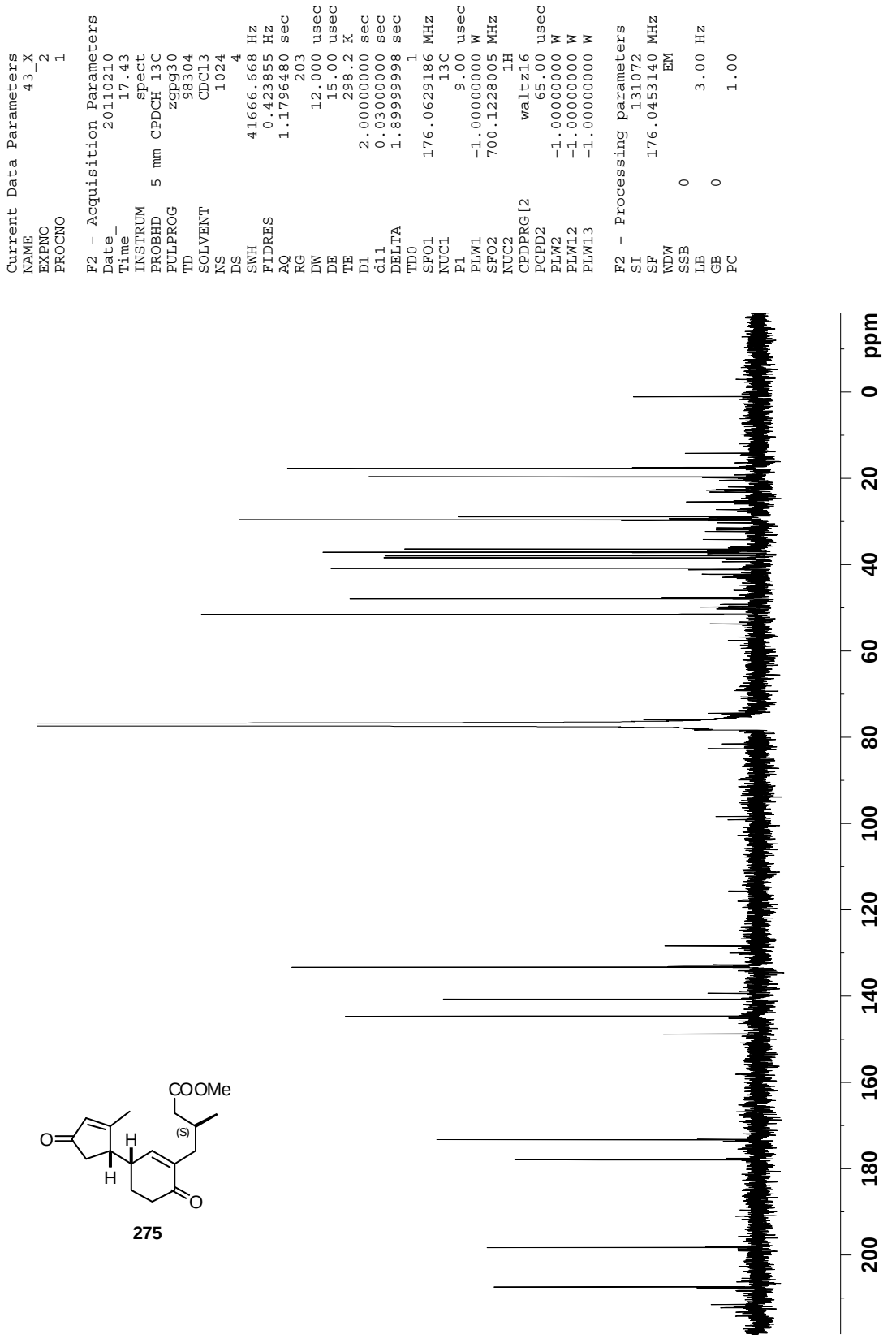

NAME 149_IX
EXPNO 1
PROCNO 1
Date_ 20100618
Time_ 13.32
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 50504
SOLVENT CDCl3
NS 32
DS 2
SWH 8417.509 Hz
FIDRES 0.166670 Hz
AQ 2.9999876 sec
RG 90.5
DW 59.400 usec
DE 16.50 usec
TE 297.9 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 10.50 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1235006 MHz
SI 131072
SF 700.1200149 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
MeO
O
O
H
(S)
H
O
O
274
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
2.0
1.5
1.0
0.25
1.00
1.09
3.81
0.92
1.06
1.26
1.24
1.20
1.40
1.60
3.63
3.88
2.59
2.97
5.62

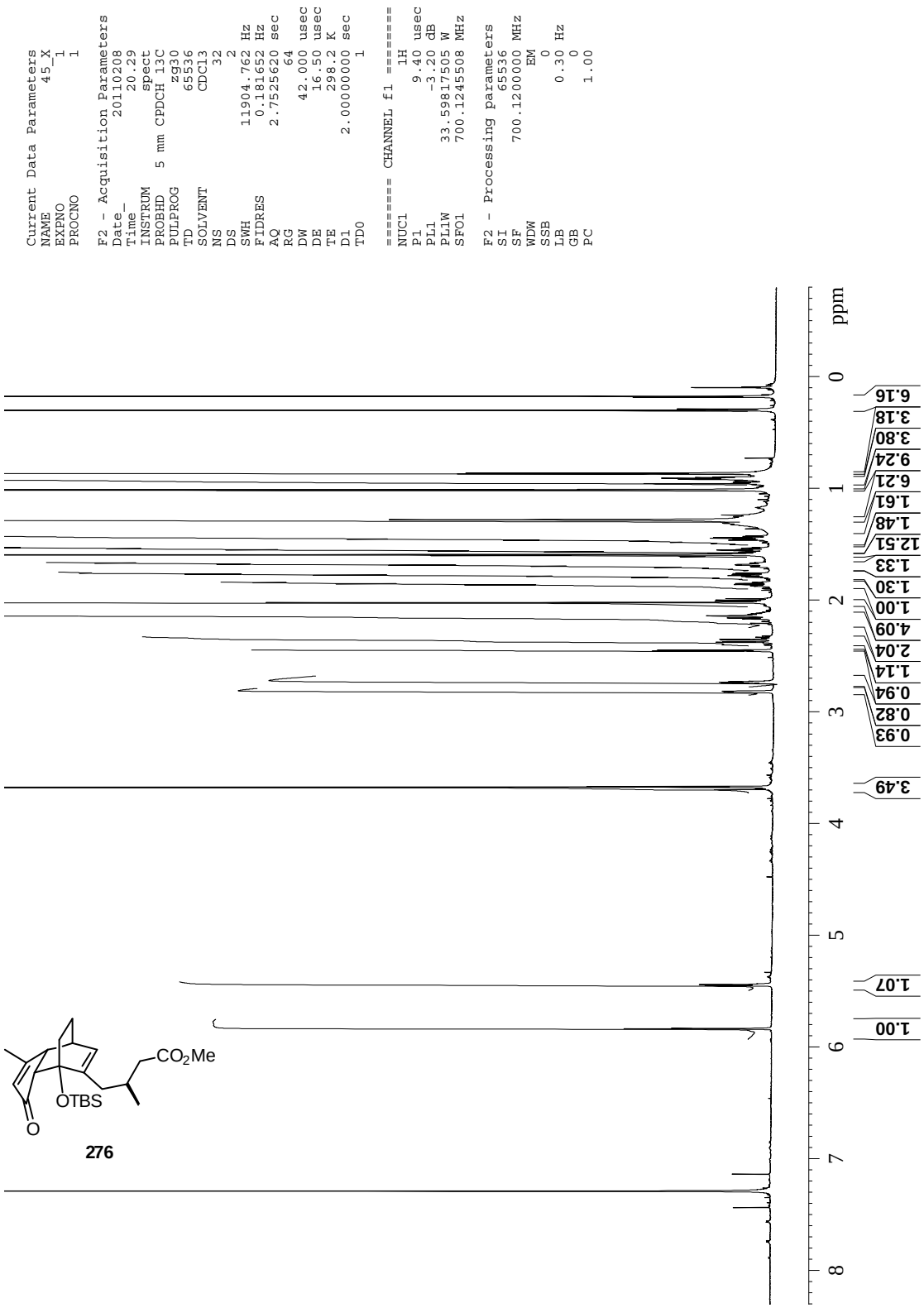

NAME 149_IX
EXPNO 2
PROCNO 1
Date_ 20100618
Time_ 13.39
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDCl3
NS 419
DS 4
SWH 41666.668 Hz
FIDRES 0.423855 Hz
AQ 1.1796980 sec
RG 203
DW 12.000 usec
DE 15.00 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL 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
ppm
0
20
40
60
80
100
120
140
160
180
200
MeO
O
O
H
(S)
H
O

274

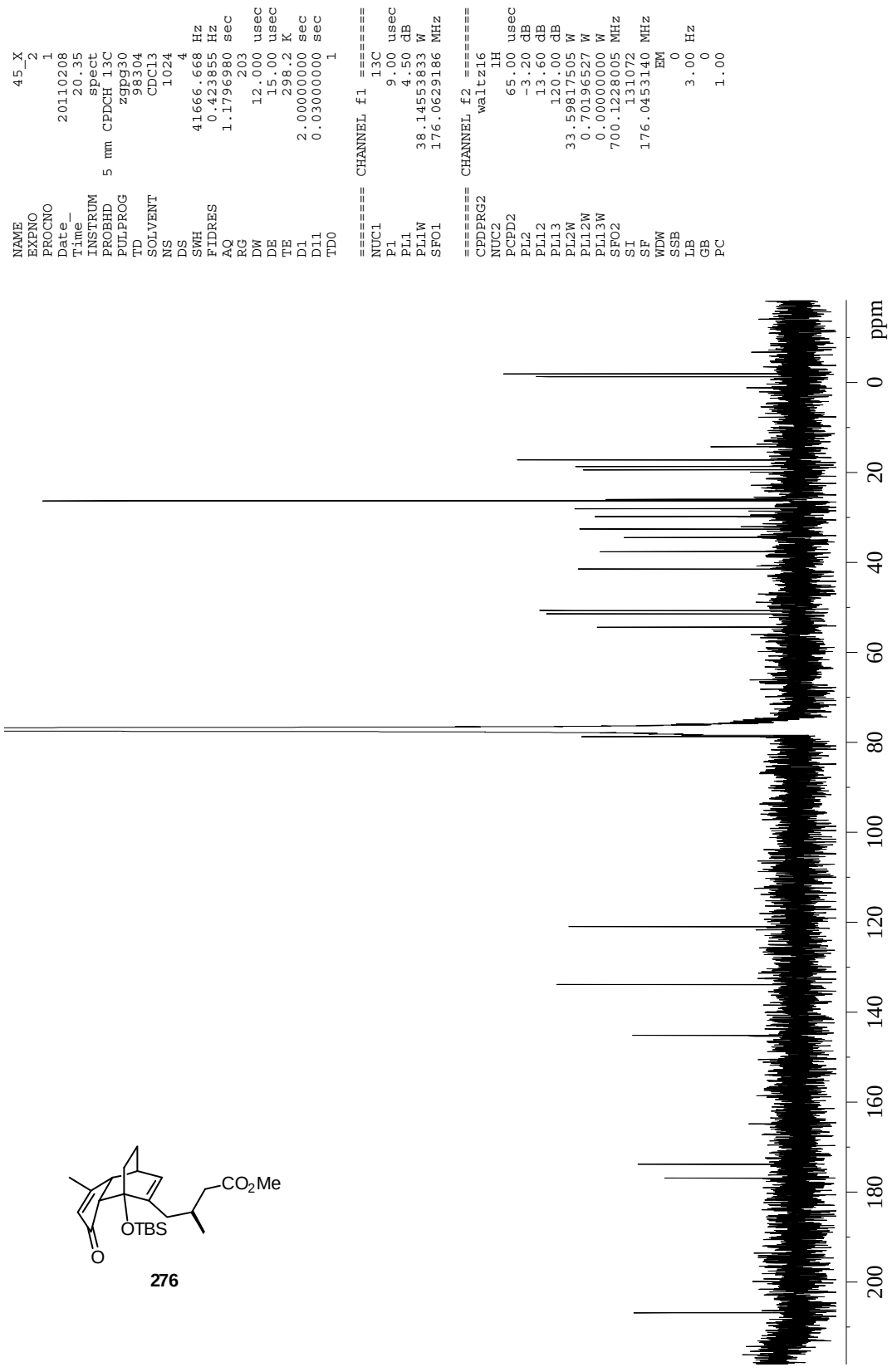

Current Data Parameters
NAME 43_X
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20110210
Time 17.38
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 18
DS 2
SWH 11904.762 Hz
FIDRES 0.181652 Hz
AQ 2.7525120 sec
RG 80.6
DW 42.000 usec
DE 16.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1245508 MHz
F2 - Processing parameters
SI 65536
SF 700.1200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
ppm
1
2
3
4
5
6
7
5.36
5.10
4.69
1.95
6.52
6.20
1.82
3.36
1.53
2.69
3.73
1.37
1.00
COOMe
(S)
O
H
H
O

275

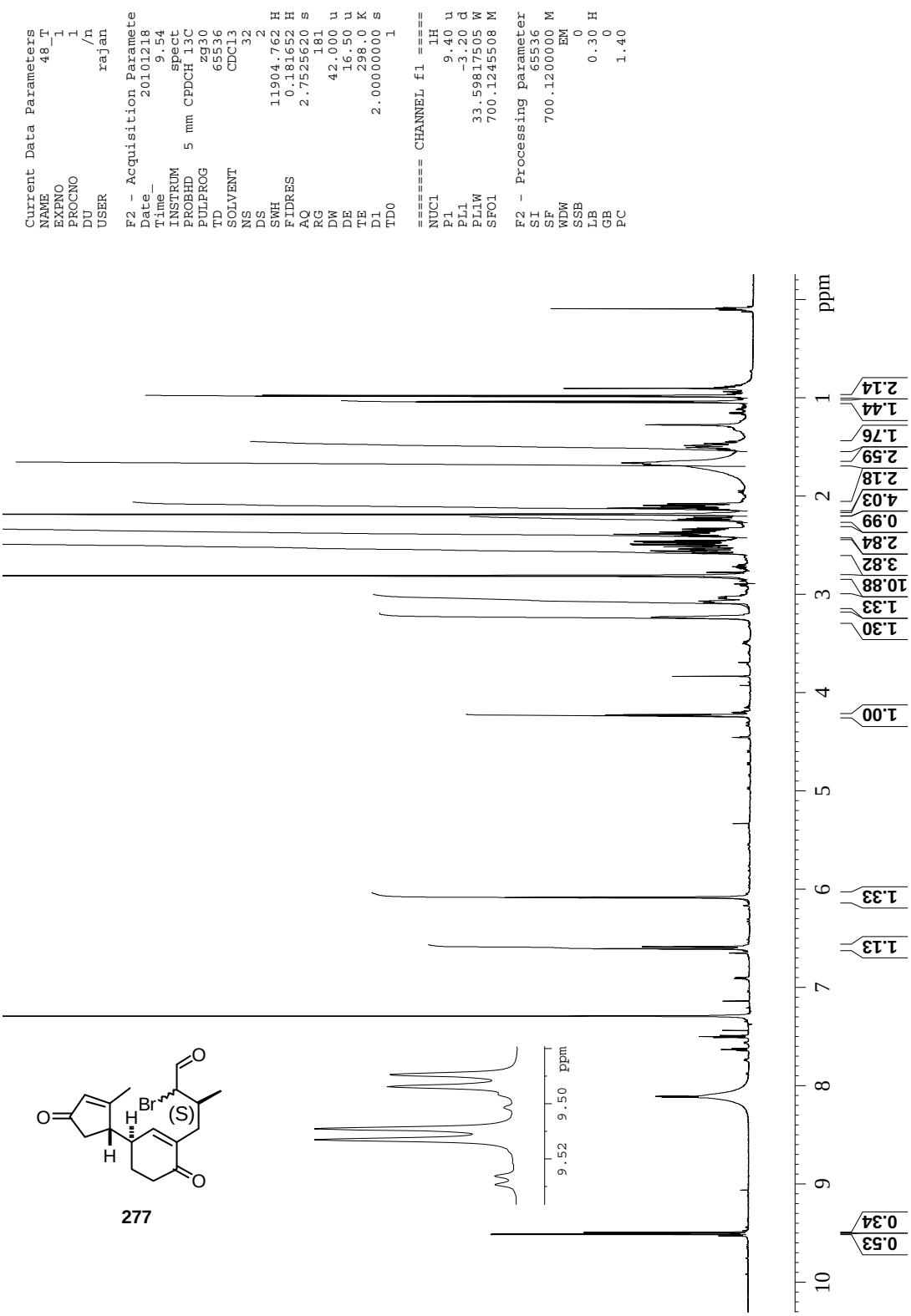

Current Data Parameters
NAME 43_X
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20110210
Time_ 17.43
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDCl3
NS 1024
DS 4
SWH 41666.668 Hz
FIDRES 0.423855 Hz
AQ 1.1796480 sec
RG 203
DW 12.000 usec
DE 15.00 usec
TE 298.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
SFO1 176.0629186 MHz
NUC1 13C
P1 9.00 usec
PLW1 -1.00000000 W
SFO2 700.1228005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 65.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 131072
SF 176.0453140 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.00
COOMe
(S)
O
H
H
O
275
200
180
160
140
120
100
80
60
40
20
0
ppm


Current Data Parameters
NAME 45_X
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20110208
Time_ 20.29
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
F2 - Processing parameters
SI 65536
SF 700.1200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
ppm
0
1
2
3
4
5
6
7
8
6.16
3.18
3.80
9.24
6.21
1.61
1.48
12.51
1.33
1.30
1.00
4.09
2.04
1.14
0.94
0.82
0.93
3.49
1.07
1.00
CO2Me
OTBS
O

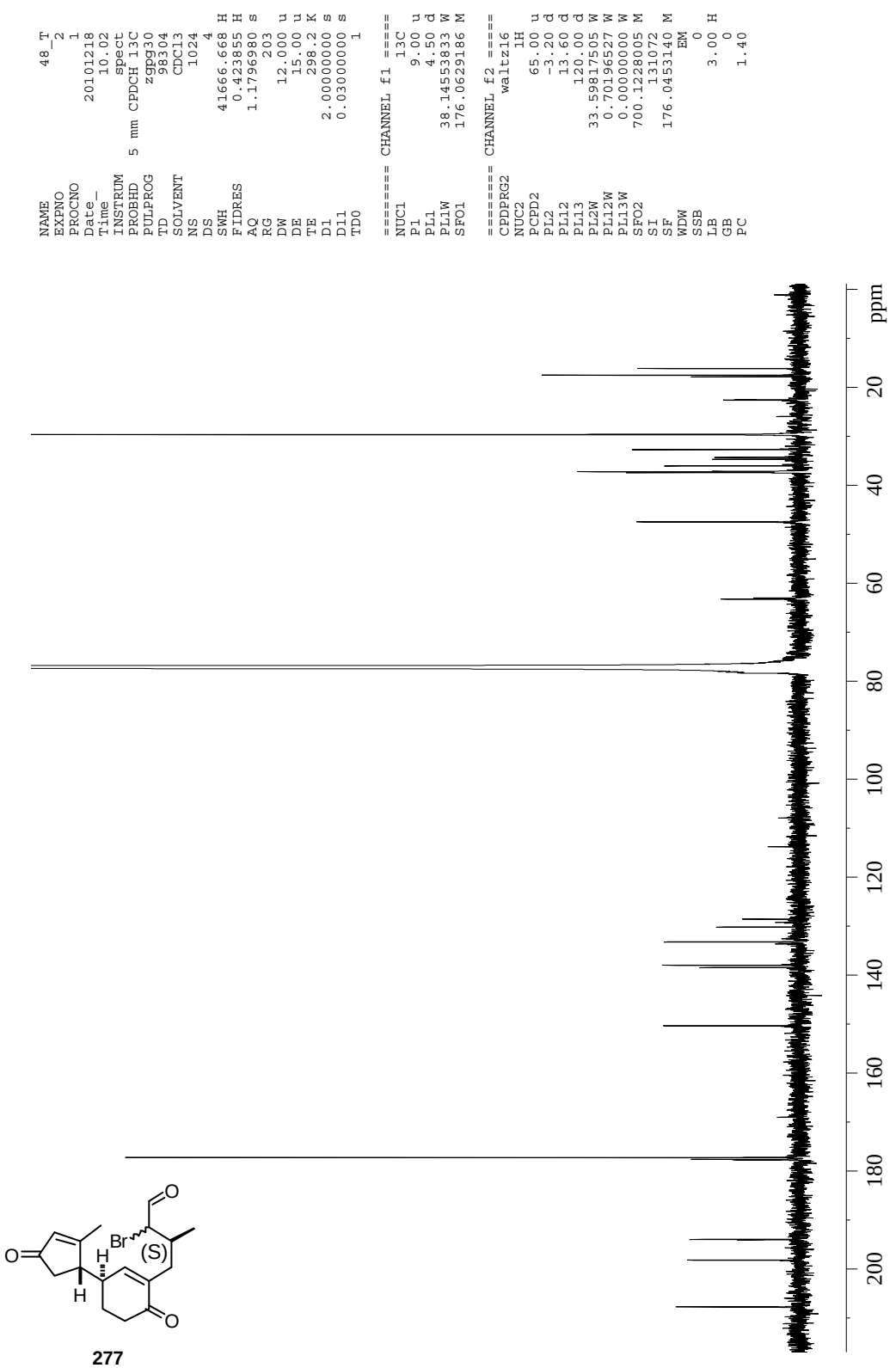
276


NAME 45_X
EXPNO 2
PROCNO 1
Date_ 20110208
Time_ 20.35
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 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 1.00
ppm
0
20
40
60
80
100
120
140
160
180
200
CO2Me
OTBS
O

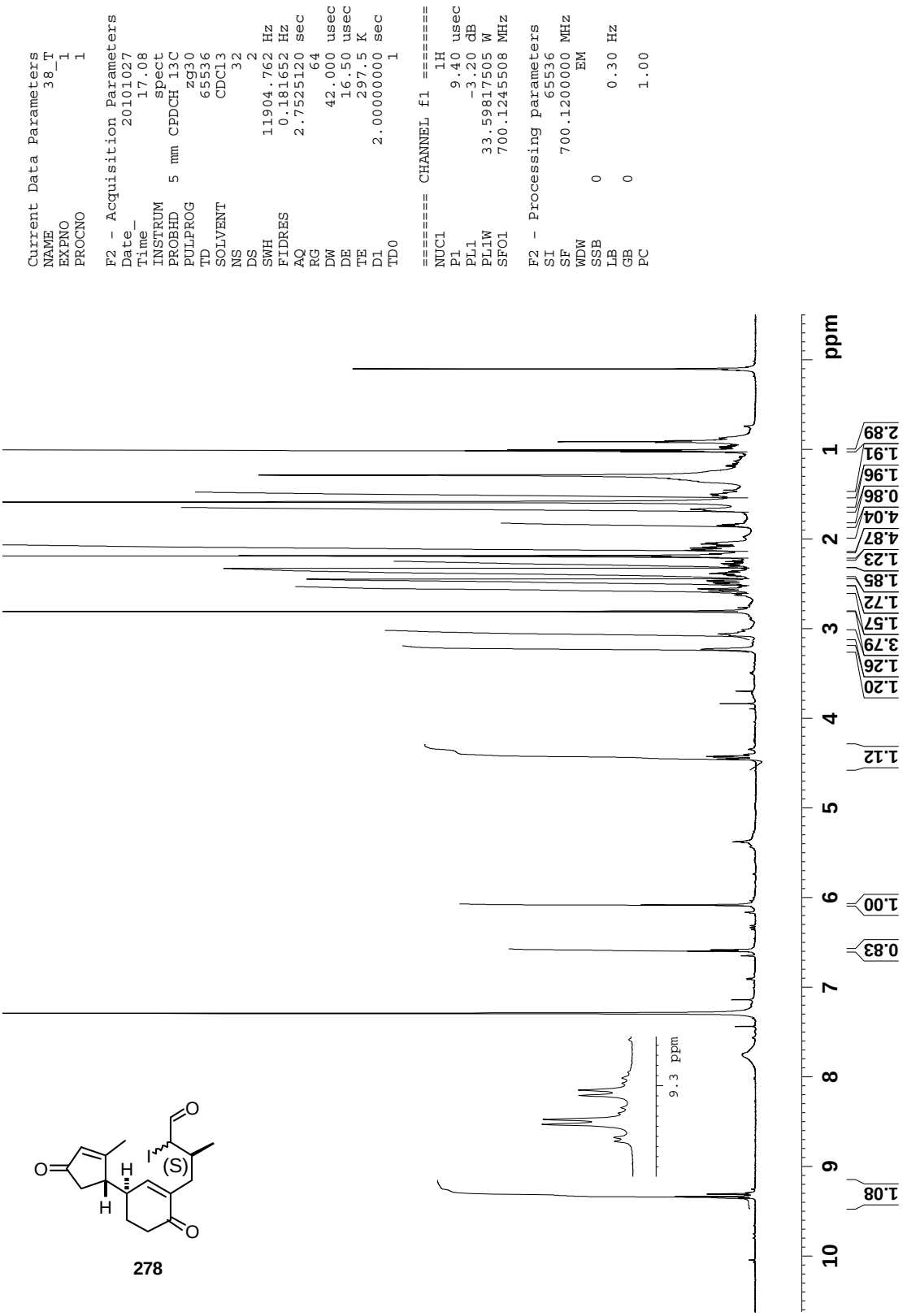
276

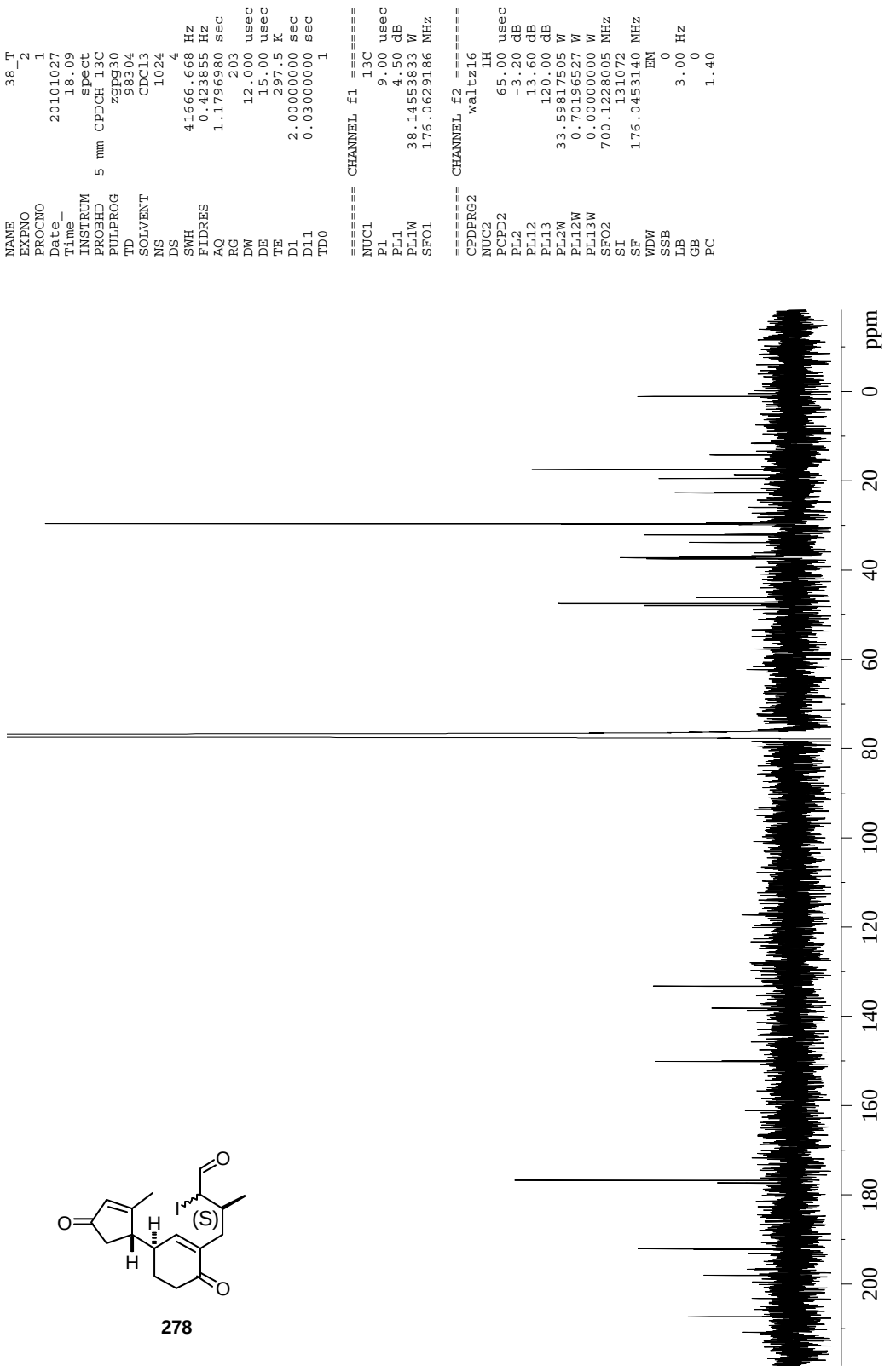

Current Data Parameters
NAME 48_T
EXPNO 1
PROCNO 1
DU /n
USER rajan
F2 - Acquisition Paramete
Date_ 20101218
Time_ 9.54
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 H
FIDRES 0.181652 H
AQ 2.7525620 s
RG 181
DW 42.000 u
DE 16.50 u
TE 298.0 K
D1 2.00000000 s
TD0 1
======== CHANNEL f1 =====
NUC1 1H
P1 9.40 u
PL1 -3.20 d
PL1W 33.59817505 W
SFO1 700.1245508 M
F2 - Processing parameter
SI 65536
SF 700.1200000 M
WDW EM
SSB 0
LB 0.30 H
GB 0
PC 1.40
ppm
0.53
0.34
1.13
1.33
1.00
1.30
1.33
10.88
3.82
2.84
0.99
4.03
2.18
2.59
1.76
1.44
2.14
9.52
9.50
ppm
O
O
Br
(S)
H
H
O

277

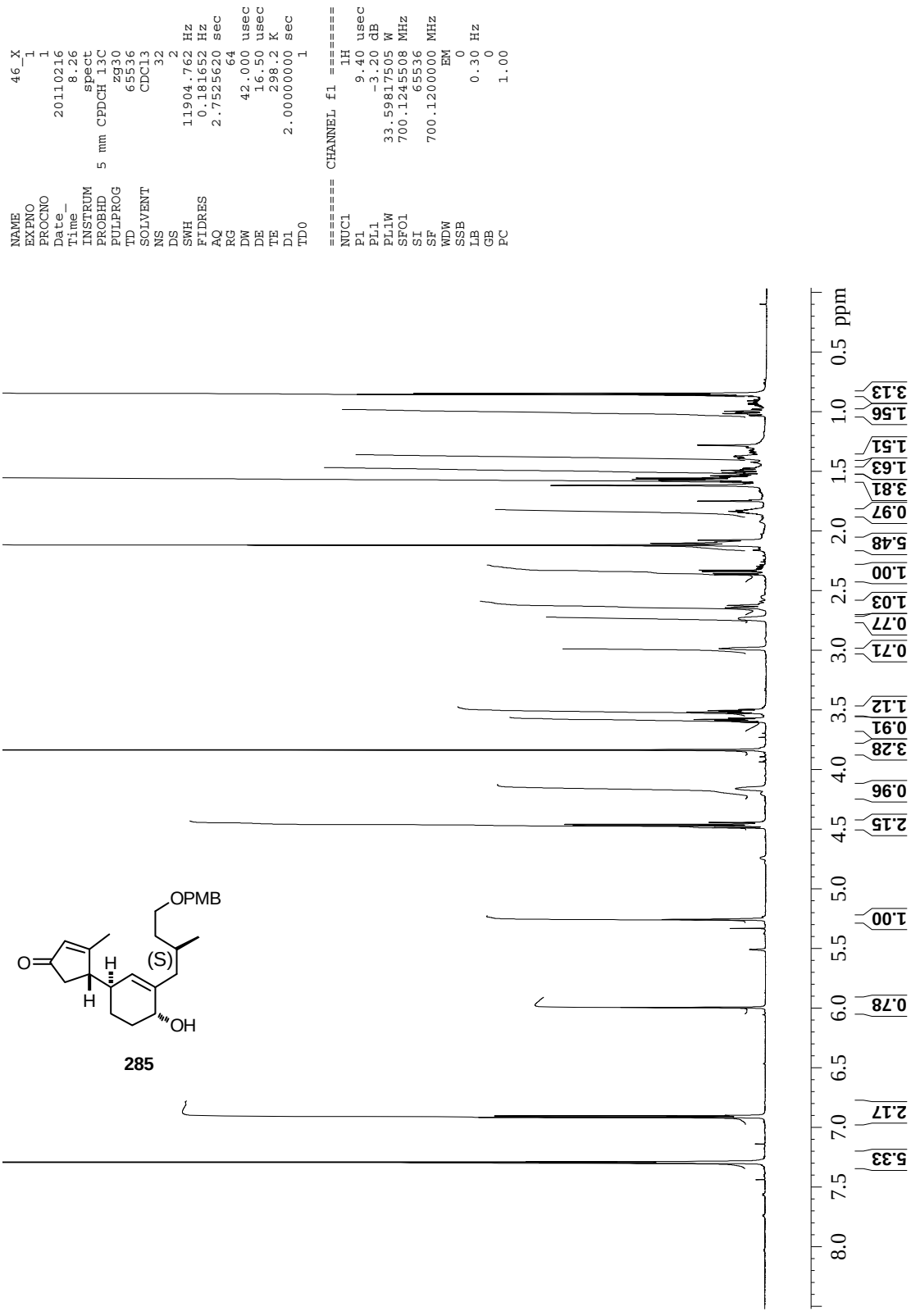

48_T
2
1
20101218
10.02
spect
5 mm CPDCH 13C
zgpg30
98304
CDCl3
1024
4
41666.668 H
0.423855 H
1.1796980 s
203
12.000 u
15.00 u
298.2 K
2.00000000 s
0.03000000 s
1
======== CHANNEL f1 =====
13C
9.00 u
4.50 d
38.14553833 W
176.0629186 M
======== CHANNEL f2 =====
waltz16
1H
65.00 u
-3.20 d
13.60 d
120.00 d
33.59817505 W
0.70196527 W
0.00000000 W
700.1228005 M
131072
176.0453140 M
EM
0
3.00 H
0
1.40
NAME
EXPNO
PROCNO
Date_
Time_
INSTRUM
PROBHD
PULPROG
TD
SOLVENT
NS
DS
SWH
FIDRES
AQ
RG
DW
DE
TE
D1
D11
TD0
NUC1
P1
PL1
PL1W
SFO1
CPDPRG2
NUC2
PCPD2
PL2
PL12
PL13
PL2W
PL12W
PL13W
SFO2
SI
SF
WDW
SSB
LB
GB
PC
ppm
20
40
60
80
100
120
140
160
180
200
O
Br
(S)
H
H
O
O

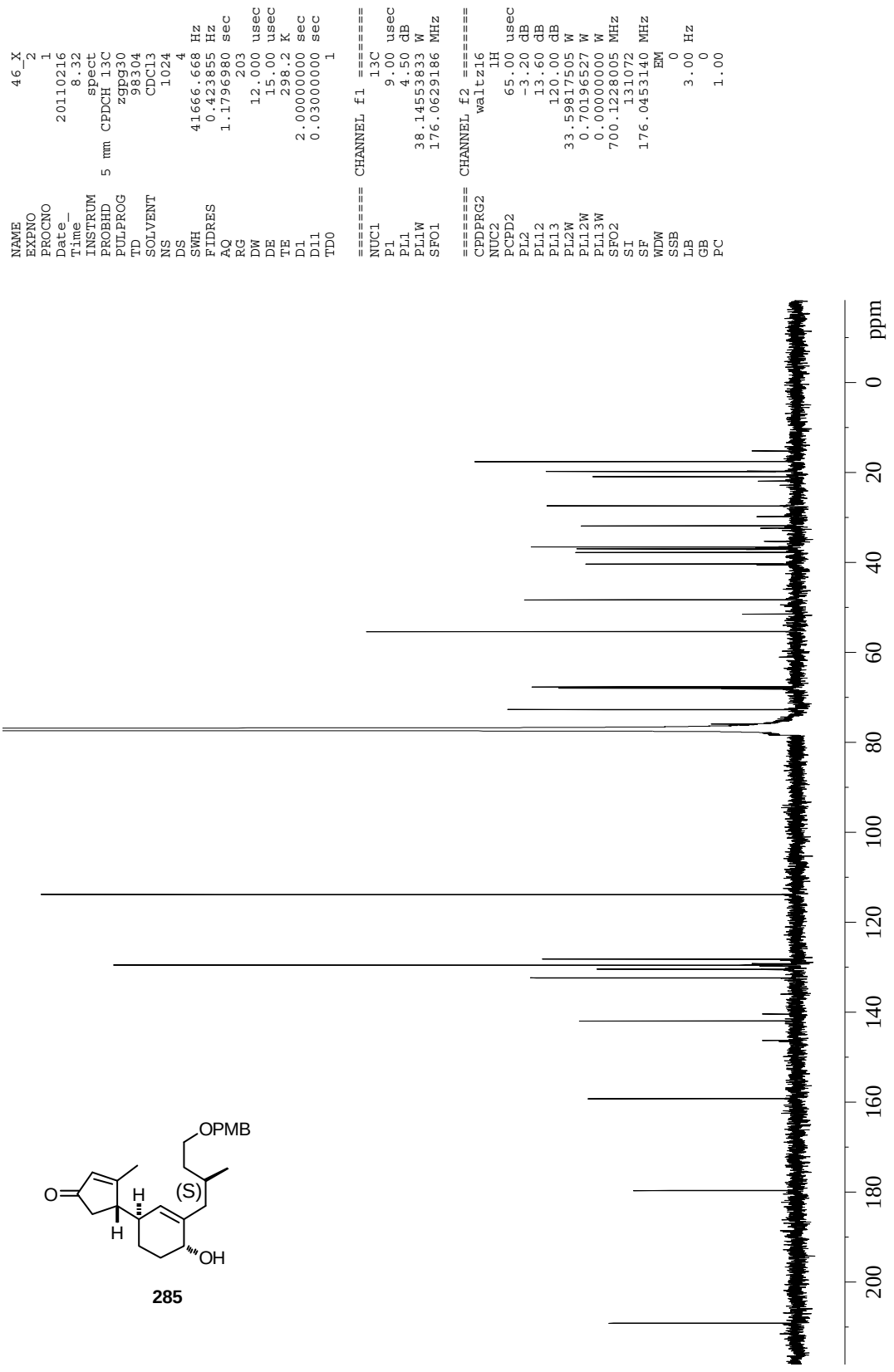
277


Current Data Parameters
NAME 38_T
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20101027
Time_ 17.08
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 2.7525120 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
F2 - Processing parameters
SI 65536
SF 700.1200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
9.3 ppm
1.08
0.83
1.00
1.12
1.20
1.26
3.79
1.57
1.72
1.85
1.23
4.87
4.04
0.86
1.96
1.91
2.89
ppm
278

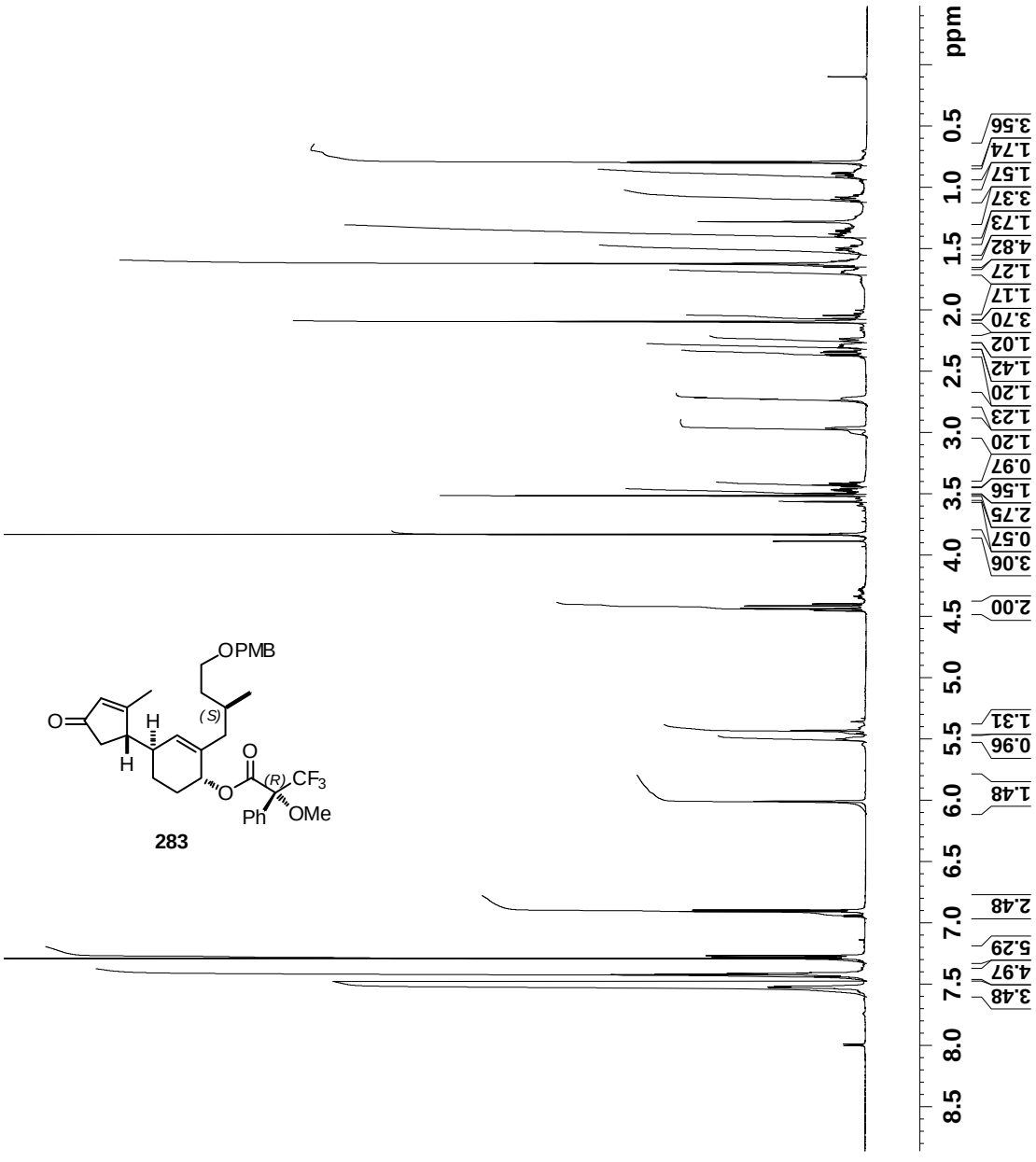

NAME 38_T
EXPNO 2
PROCNO 1
Date_ 20101027
Time_ 18.09
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDC13
NS 1024
DS 4
SWH 41666.668 Hz
FIDRES 0.423855 Hz
AQ 1.1796980 sec
RG 203
DW 12.000 usec
DE 15.00 usec
TE 297.5 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL 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
ppm
0
20
40
60
80
100
120
140
160
180
200
O
O
H
H
(S)
O
O

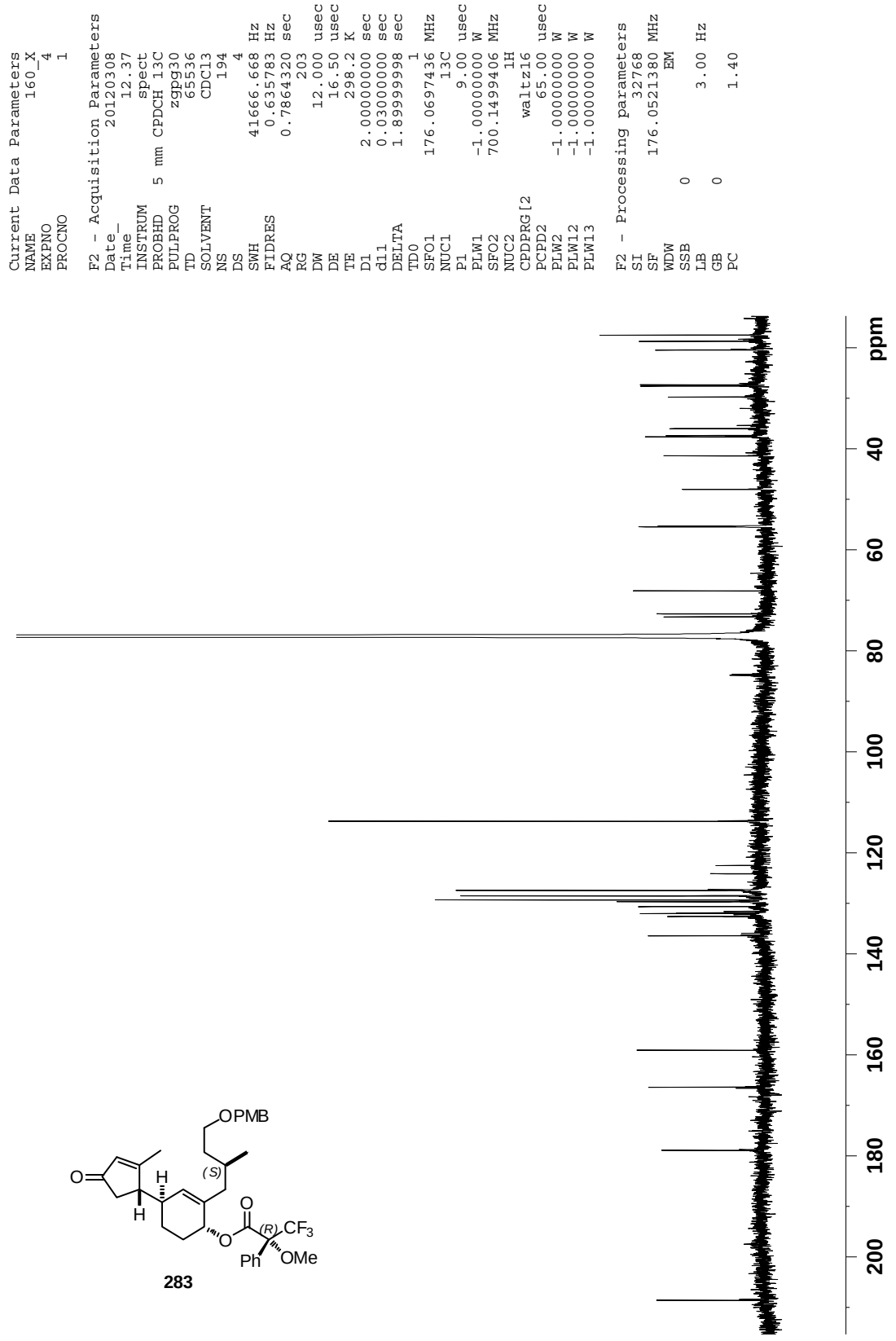
278


NAME 46_X
EXPNO 1
PROCNO 1
Date_ 20110216
Time_ 8.26
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
OPMB
O
H
(S)
H
OH
285
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
5.33
2.17
0.78
1.00
2.15
0.96
3.28
0.91
1.12
0.71
0.77
1.03
1.00
5.48
0.97
3.81
1.63
1.51
1.56
3.13

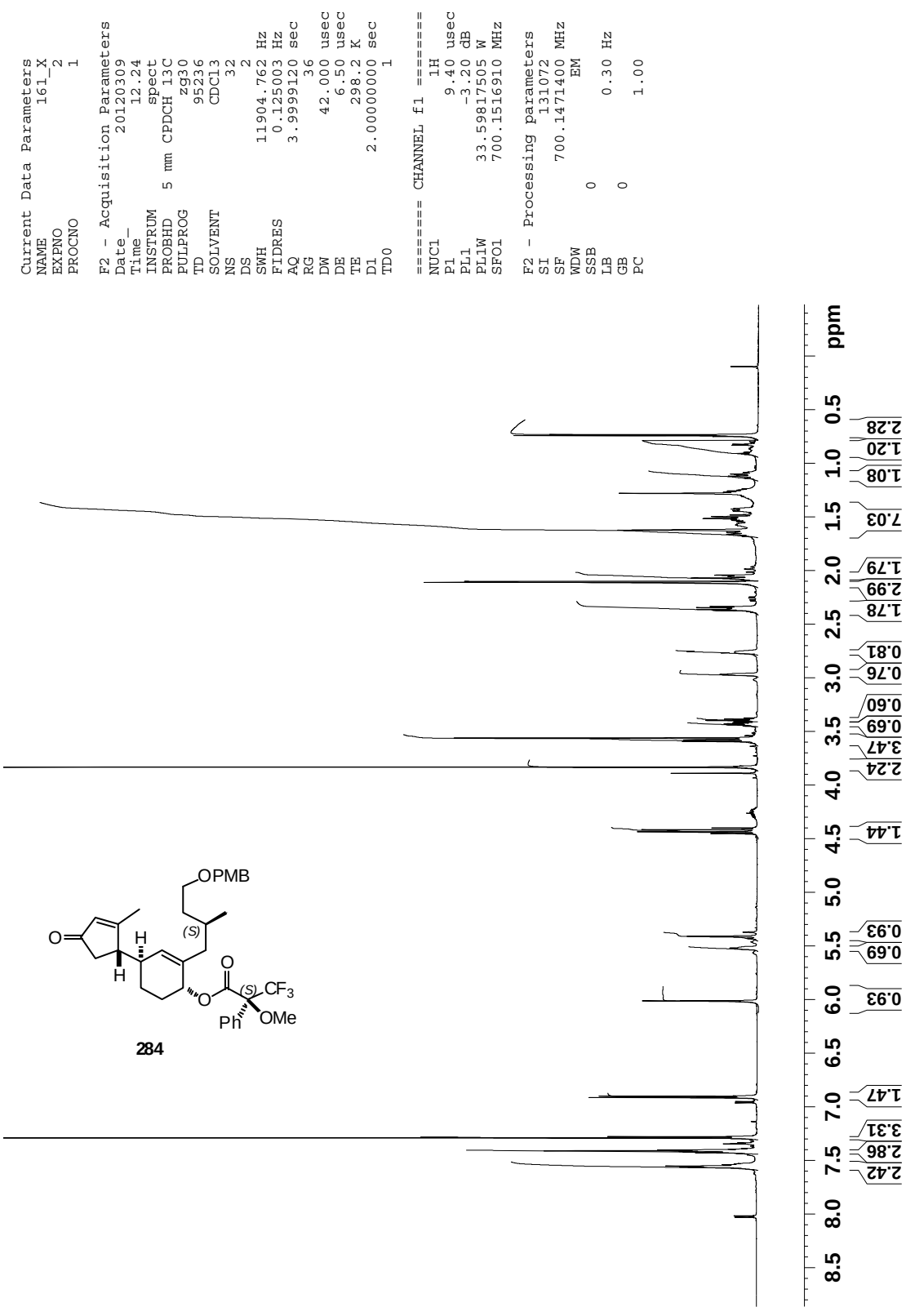

NAME 46_X
EXPNO 2
PROCNO 1
Date_ 20110216
Time_ 8.32
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDCl3
NS 1024
DS 4
SWH 41666.668 Hz
FIDRES 0.423855 Hz
AQ 1.1796980 sec
RG 203
DW 12.000 usec
DE 15.00 usec
TE 298.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
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 1.00
ppm
0
20
40
60
80
100
120
140
160
180
200
OPMB
O
H
(S)
H
OH

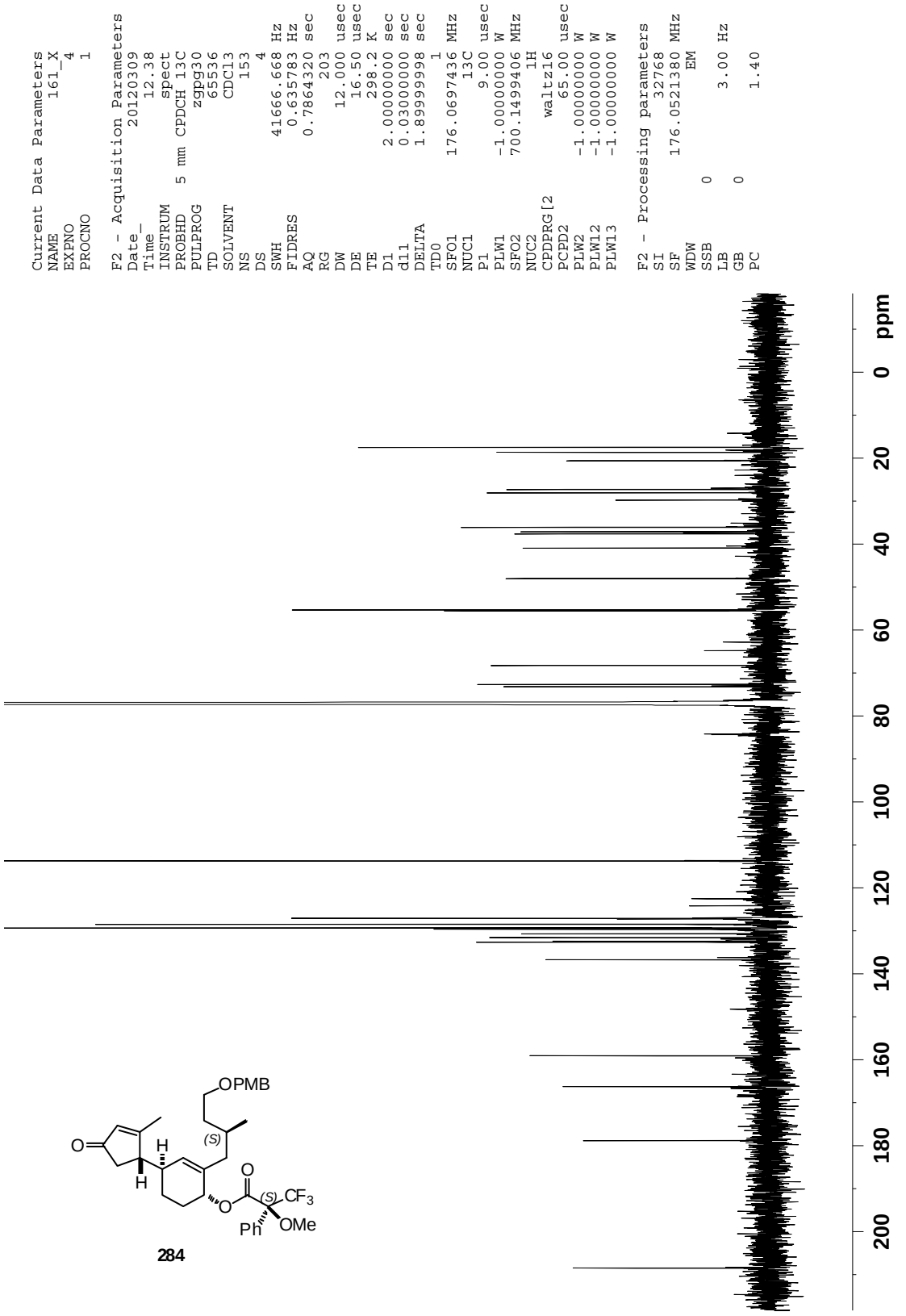
285


Current Data Parameters
NAME 160_X
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20120308
Time 12.18
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 3.9999120 sec
RG 36
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
F2 - Processing parameters
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
OPMB
(S)
H
H
O
O
O
(R)
CF3
Ph
OMe
283
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
3.48
4.97
5.29
2.48
1.48
0.96
1.31
2.00
3.06
0.57
2.75
1.56
0.97
1.20
1.23
1.20
1.42
1.02
3.70
1.17
1.27
4.82
1.73
3.37
1.57
1.74
3.56

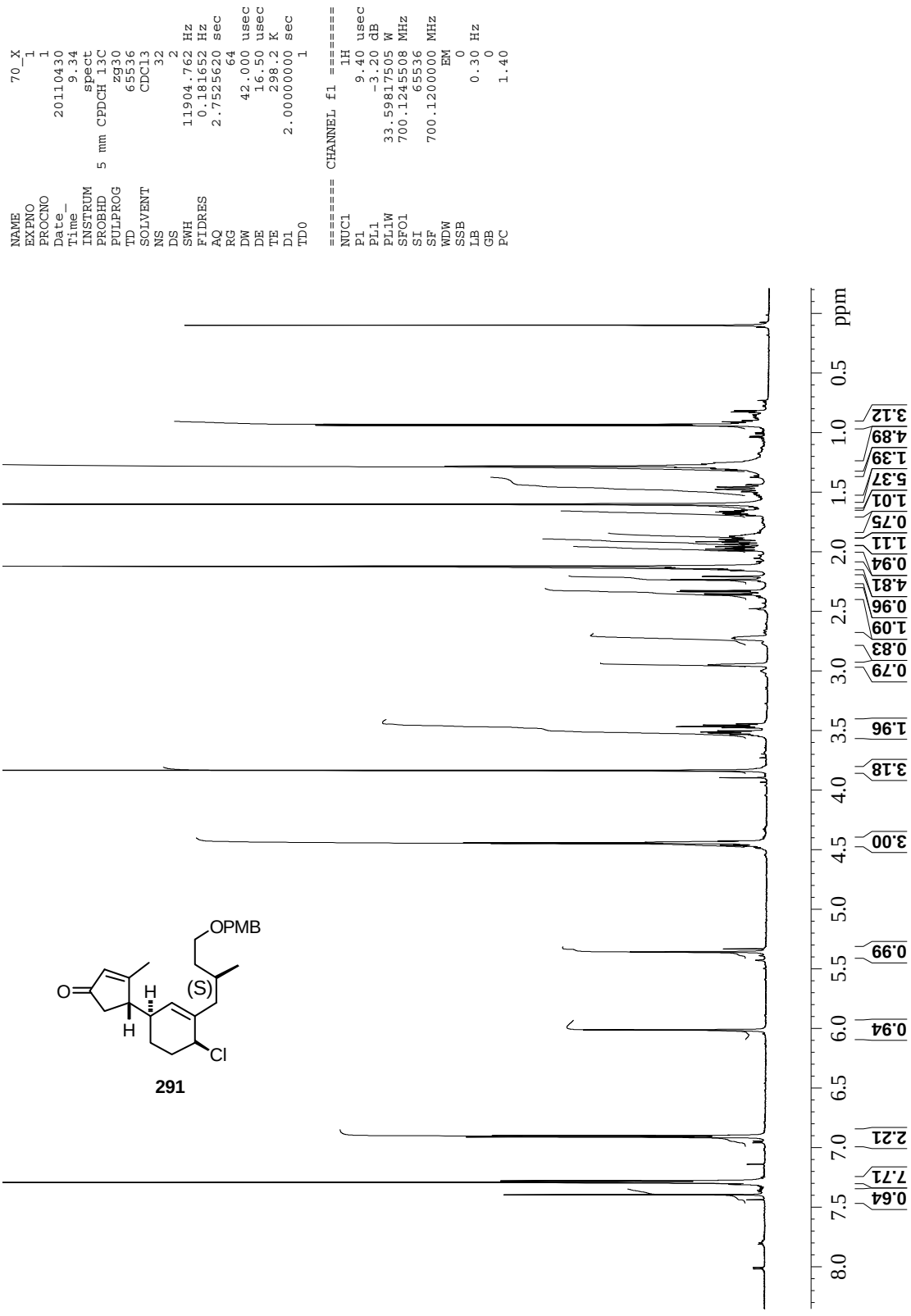

Current Data Parameters
NAME 160_X
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20120308
Time_ 12.37
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 194
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864320 sec
RG 203
DW 12.000 usec
DE 16.50 usec
TE 298.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
SFO1 176.0697436 MHz
NUC1 13C
P1 9.00 usec
PLW1 -1.00000000 W
SFO2 700.1499406 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 65.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 32768
SF 176.0521380 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
ppm
200
180
160
140
120
100
80
60
40
OPMB
(S)
H
H
O
O
O
(R)
CF3
Ph
OMe

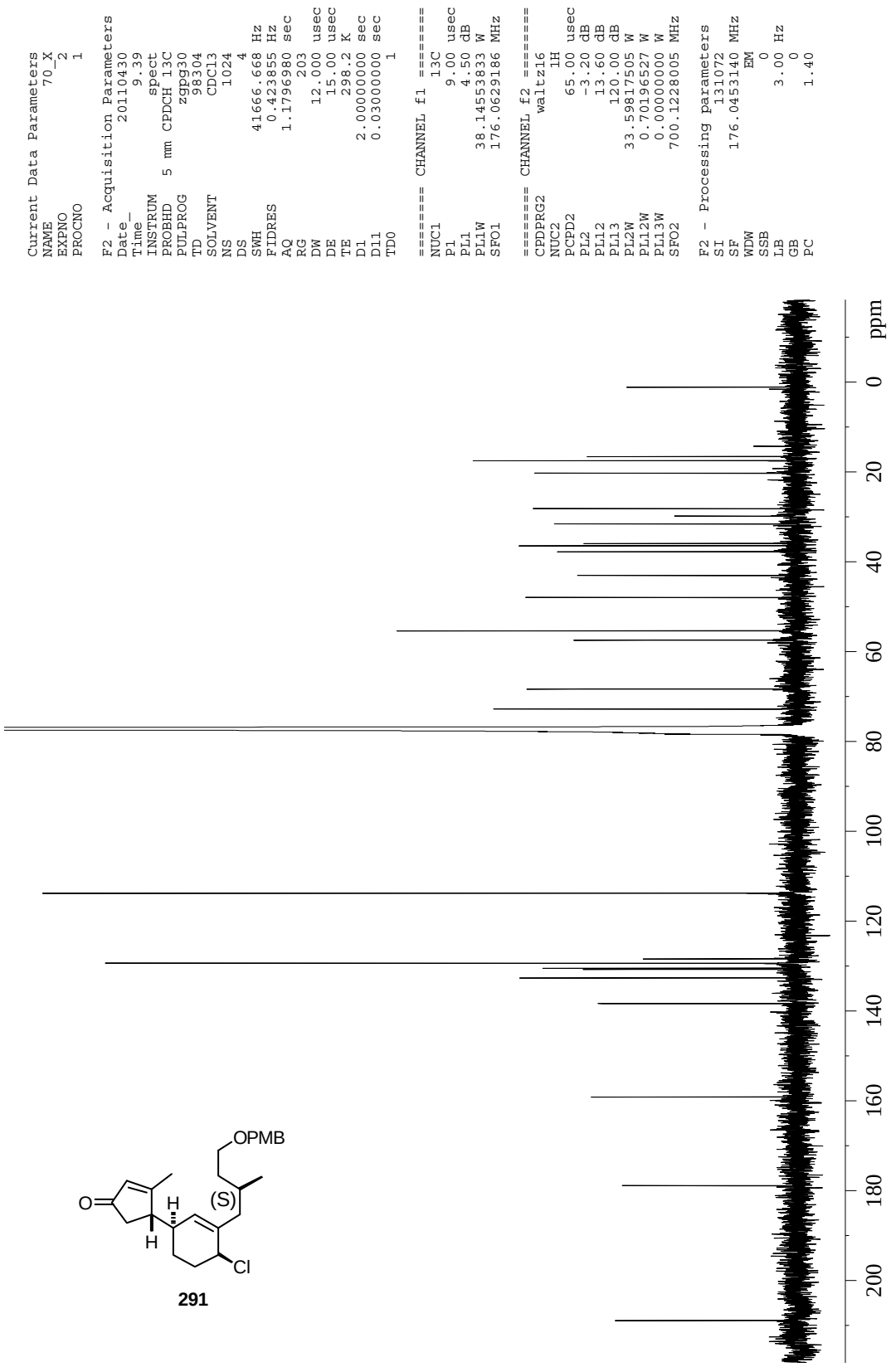
283

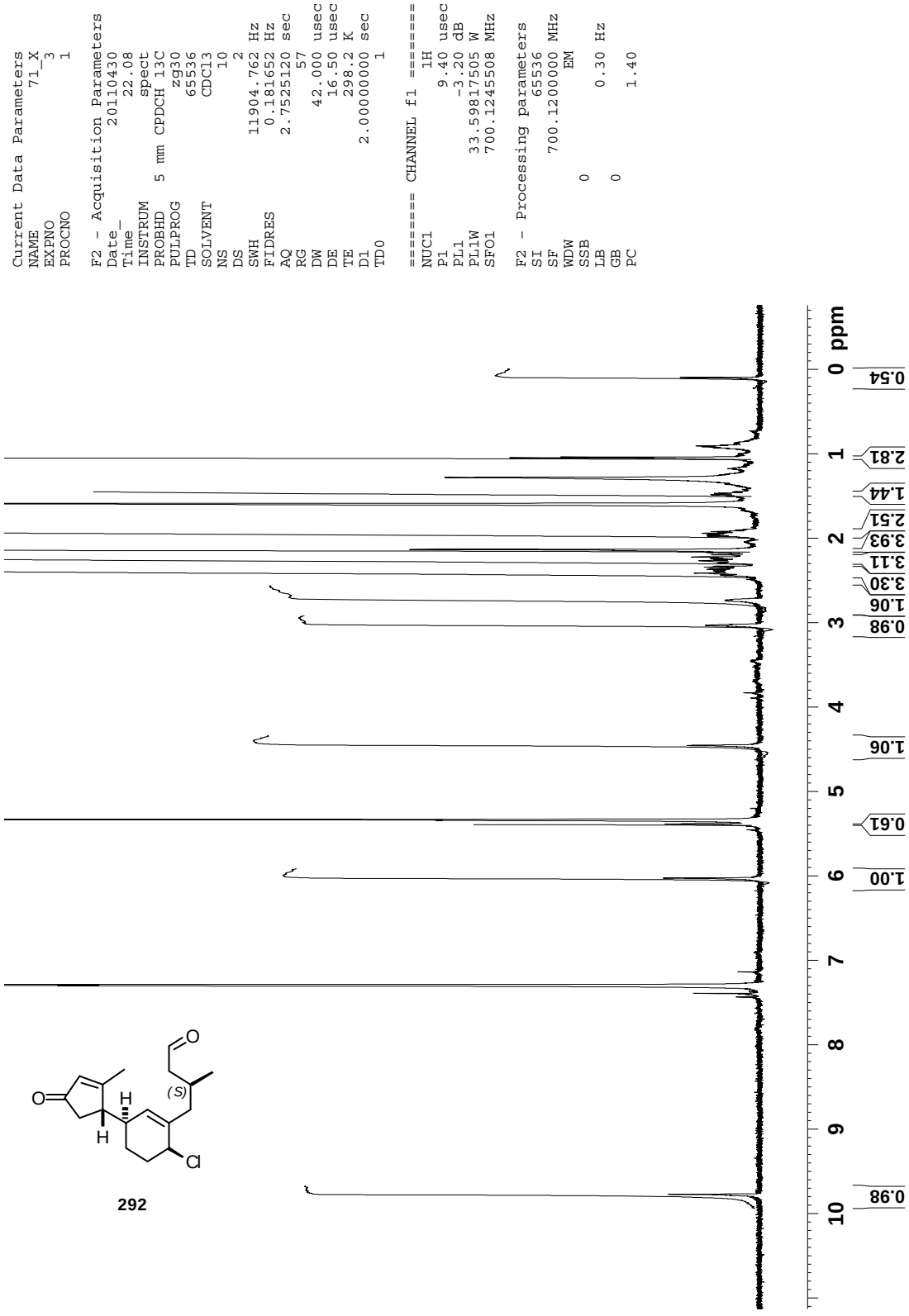

Current Data Parameters
NAME 161_X
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20120309
Time 12.24
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999120 sec
RG 36
DW 42.000 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
F2 - Processing parameters
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
OPMB
(S)
H
H
O
O
(S)
CF3
O
Ph
OMe
284
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
2.42
2.86
3.31
1.47
0.93
0.69
0.93
1.44
2.24
3.47
0.69
0.60
0.76
0.81
1.78
2.99
1.79
7.03
1.08
1.20
2.28


Current Data Parameters
NAME 161_X
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20120309
Time 12.38
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 153
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864320 sec
RG 203
DW 12.000 usec
DE 16.50 usec
TE 298.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
SFO1 176.0697436 MHz
NUC1 13C
P1 9.00 usec
PLW1 -1.00000000 W
SFO2 700.1499406 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 65.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 32768
SF 176.0521380 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
ppm
200
180
160
140
120
100
80
60
40
20
0
OPMB
(S)
H
H
O
O
O
(S)
CF3
Ph
OMe

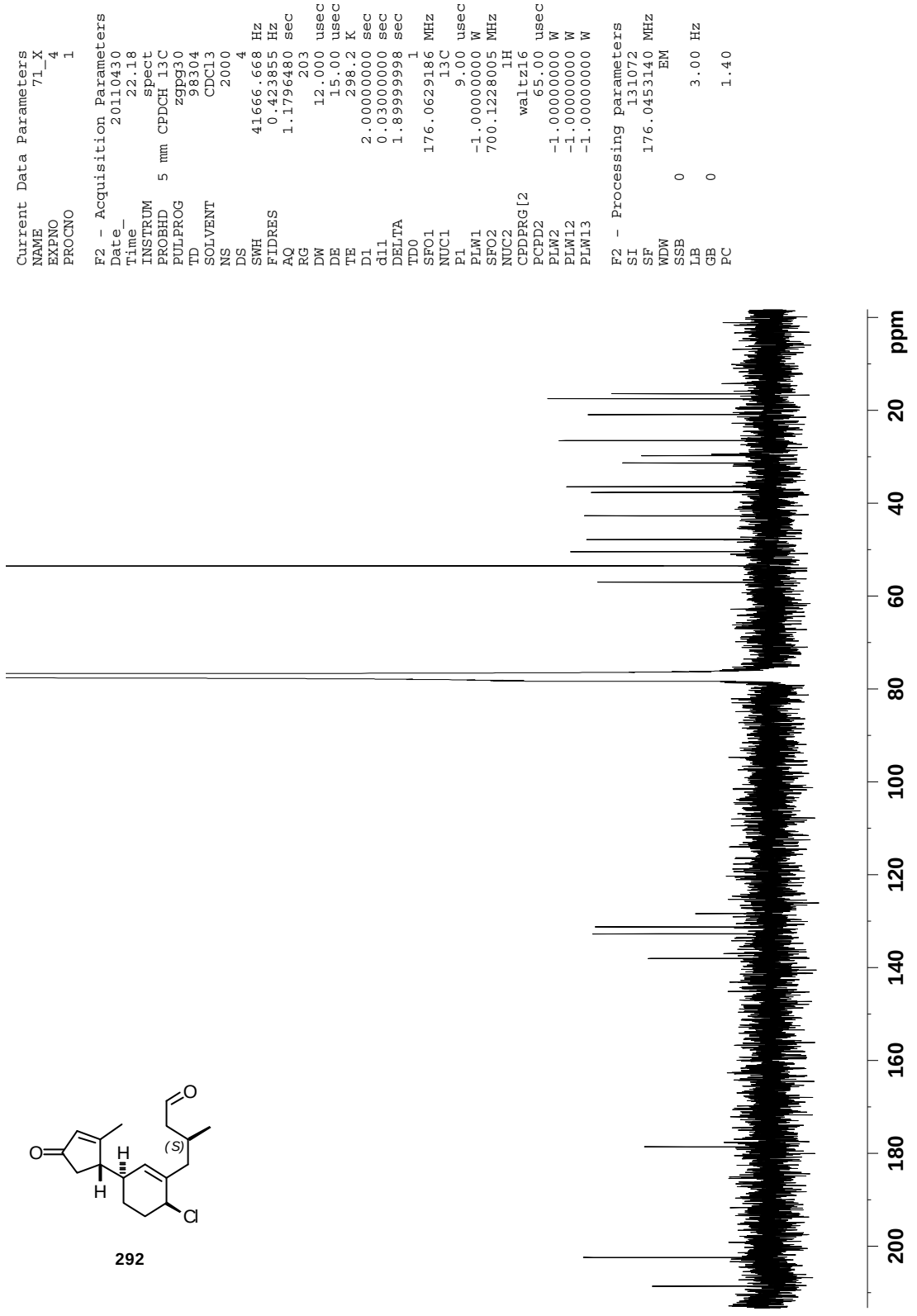
284


70_X
1
20110430
9.34
spect
5 mm CPDCH 13C
zg30
65536
CDCl3
32
2
11904.762 Hz
0.181652 Hz
2.7525620 sec
64
42.000 usec
16.50 usec
298.2 K
2.00000000 sec
1
CHANNEL f1
1H
9.40 usec
-3.20 dB
33.59817505 W
700.12445508 MHz
65536
700.1200000 MHz
EM
0
0.30 Hz
0
1.40
OPMB
O
H
H
(S)
Cl
291
ppm
3.12
4.89
1.39
5.37
1.01
0.75
1.11
0.94
4.81
0.96
1.09
0.83
0.79
1.96
3.18
3.00
0.99
0.94
2.21
7.71
0.64

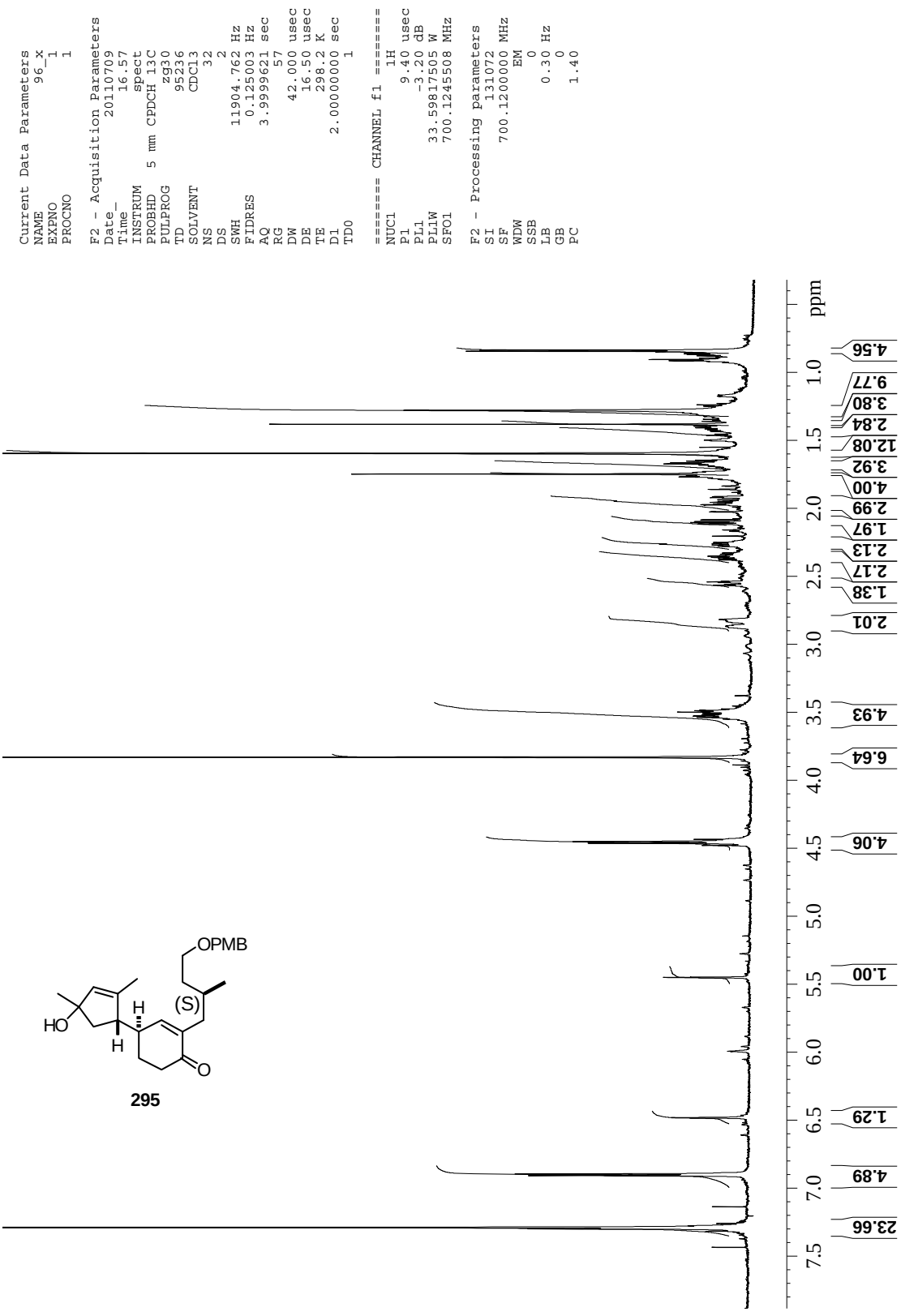

Current Data Parameters
NAME 70_X
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20110430
Time_ 9.39
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDCl3
NS 1024
DS 4
SWH 41666.668 Hz
FIDRES 0.423855 Hz
AQ 1.1796980 sec
RG 203
DW 12.000 usec
DE 15.00 usec
TE 298.2 K
D1 2.00000000 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
F2 - Processing parameters
SI 131072
SF 176.0453140 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
200
180
160
140
120
100
80
60
40
20
0
ppm
O
H
(S)
OPMB
H
Cl
291

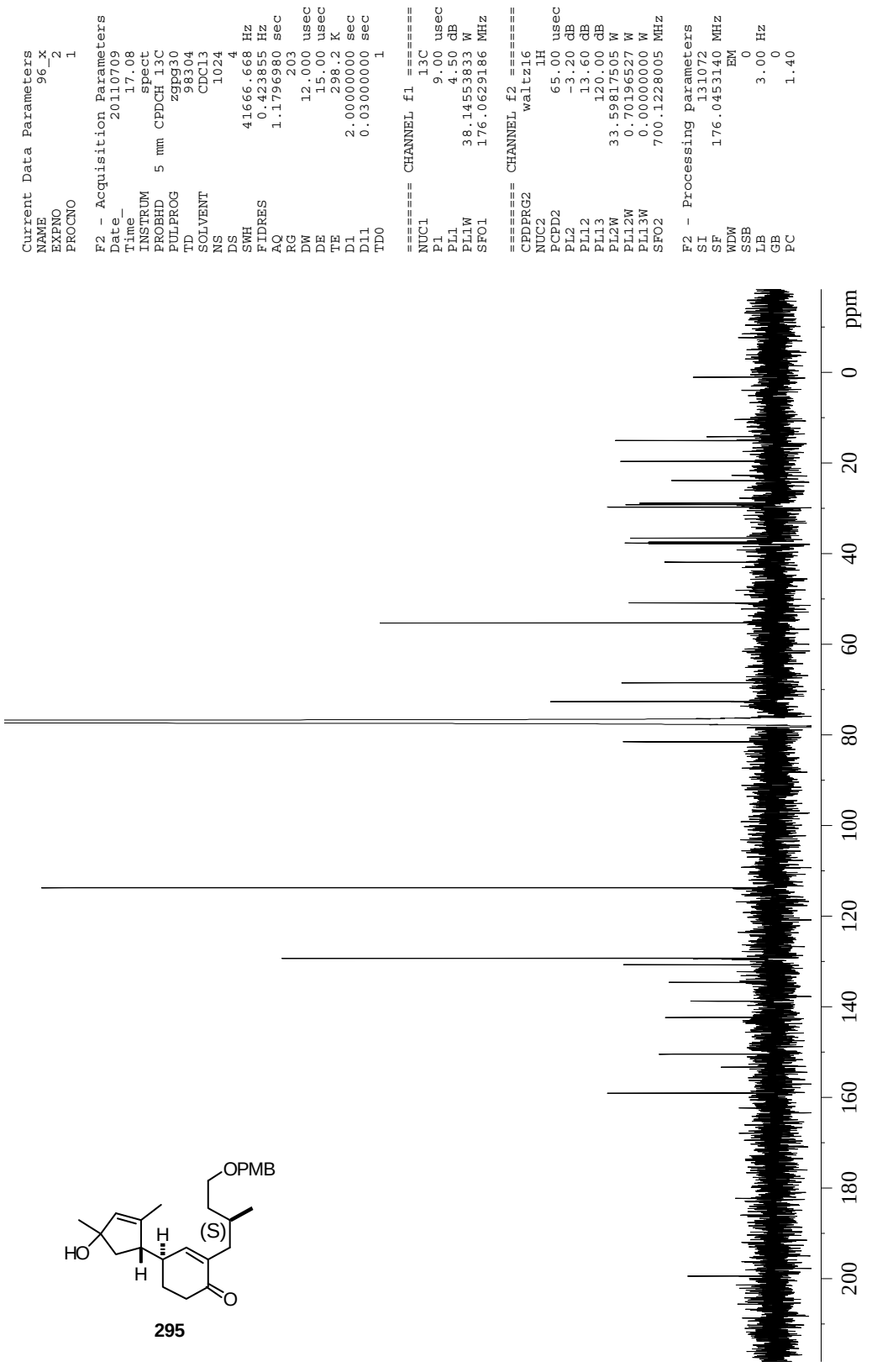

Current Data Parameters
NAME 71_X
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20110430
Time 22.08
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 10
DS 2
SWH 11904.762 Hz
FIDRES 0.181652 Hz
AQ 2.7525120 sec
RG 57
DW 42.000 usec
DE 16.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1245508 MHz
F2 - Processing parameters
SI 65536
SF 700.1200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40
0.54
2.81
1.44
2.51
3.93
3.11
3.30
1.06
0.98
1.06
0.61
1.00
0.98
ppm
O
O
H
H
(S)
Cl

292

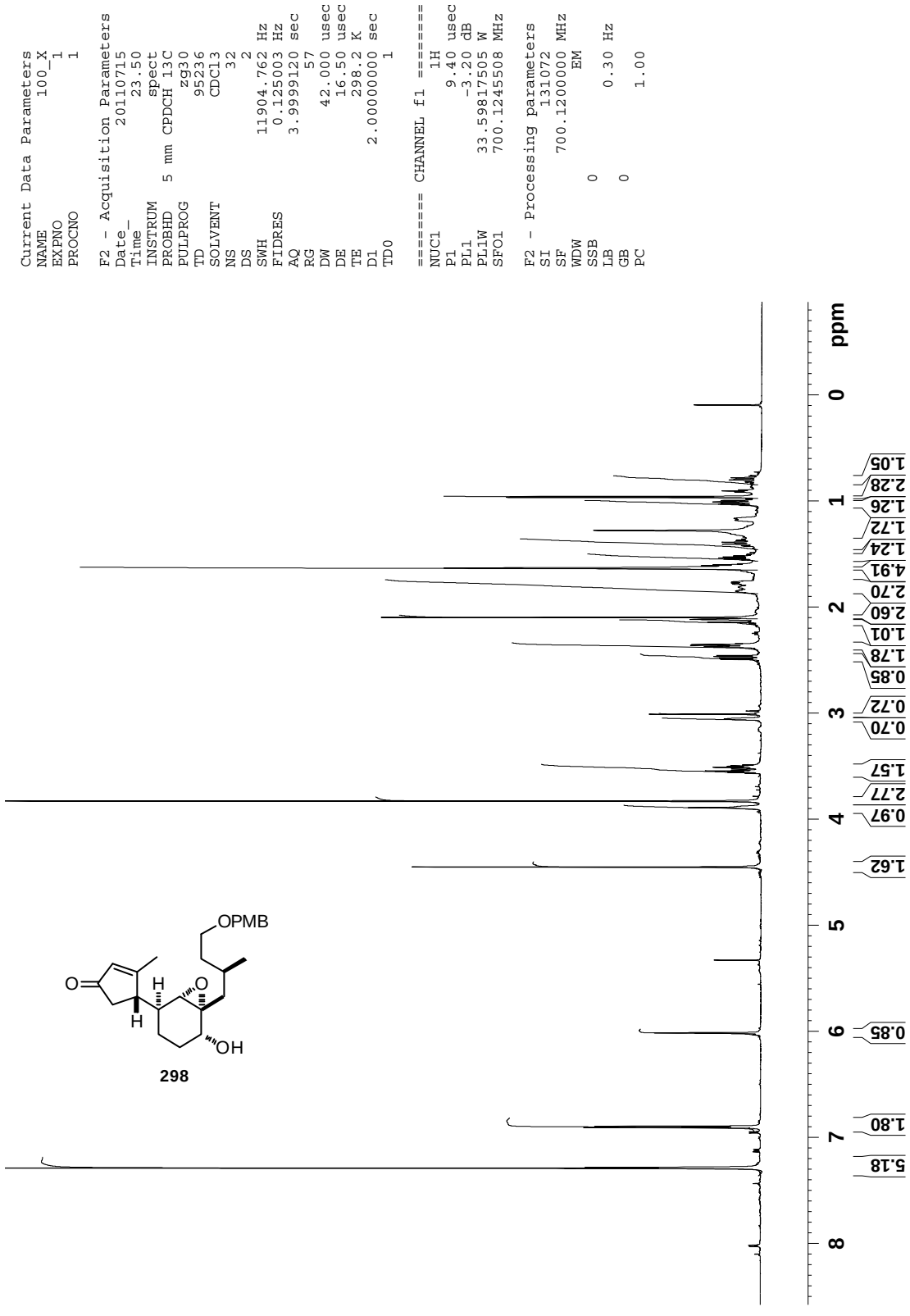

Current Data Parameters
NAME 71_X
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20110430
Time 22.18
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDCl3
NS 2000
DS 4
SWH 41666.668 Hz
FIDRES 0.423855 Hz
AQ 1.1796480 sec
RG 203
DW 12.000 usec
DE 15.00 usec
TE 298.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
SFO1 176.0629186 MHz
NUC1 13C
P1 9.00 usec
PLW1 -1.00000000 W
SFO2 700.1228005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 65.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 131072
SF 176.0453140 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
ppm
200
180
160
140
120
100
80
60
40
20
O
H
H
(S)
O
Cl

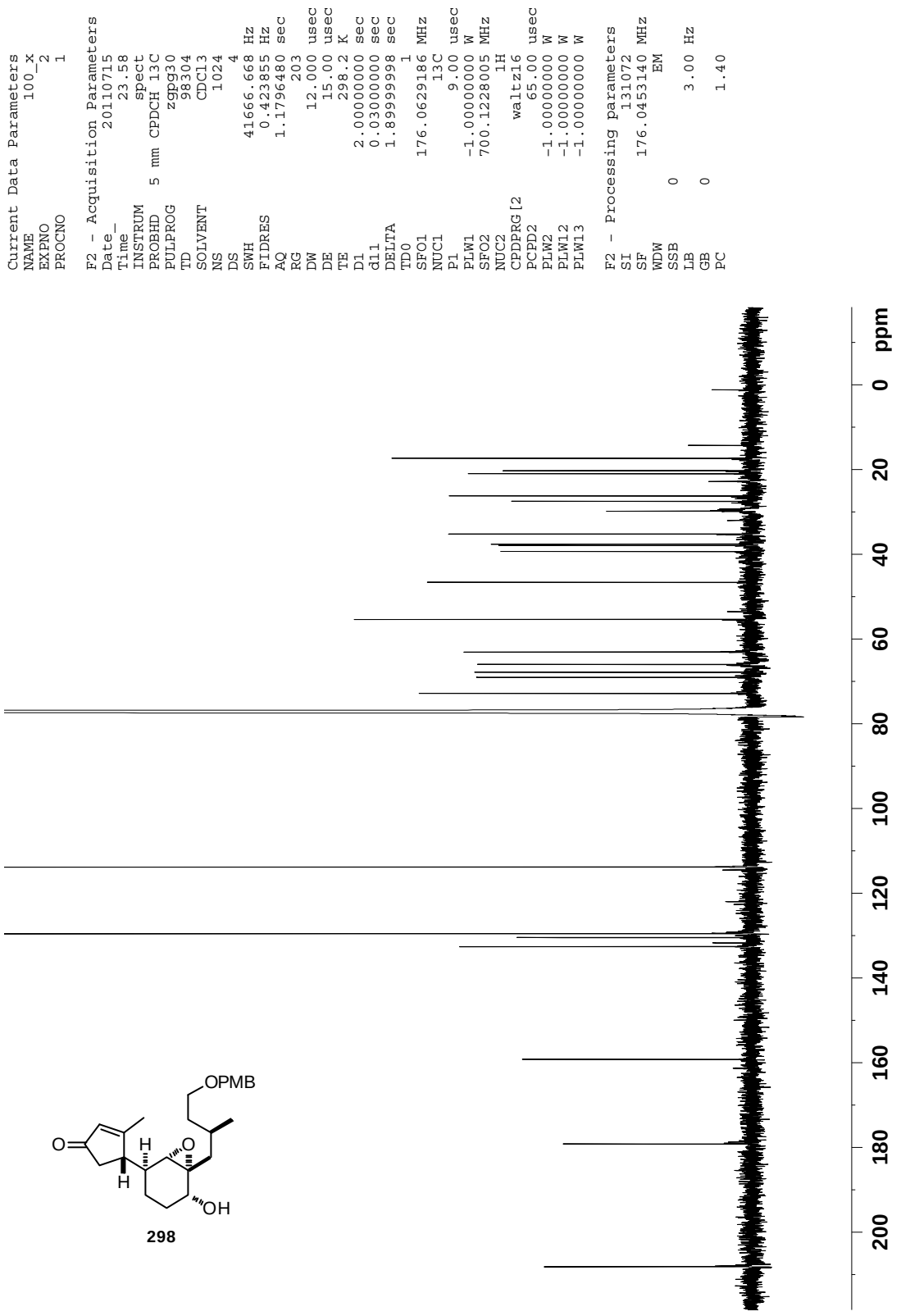
292

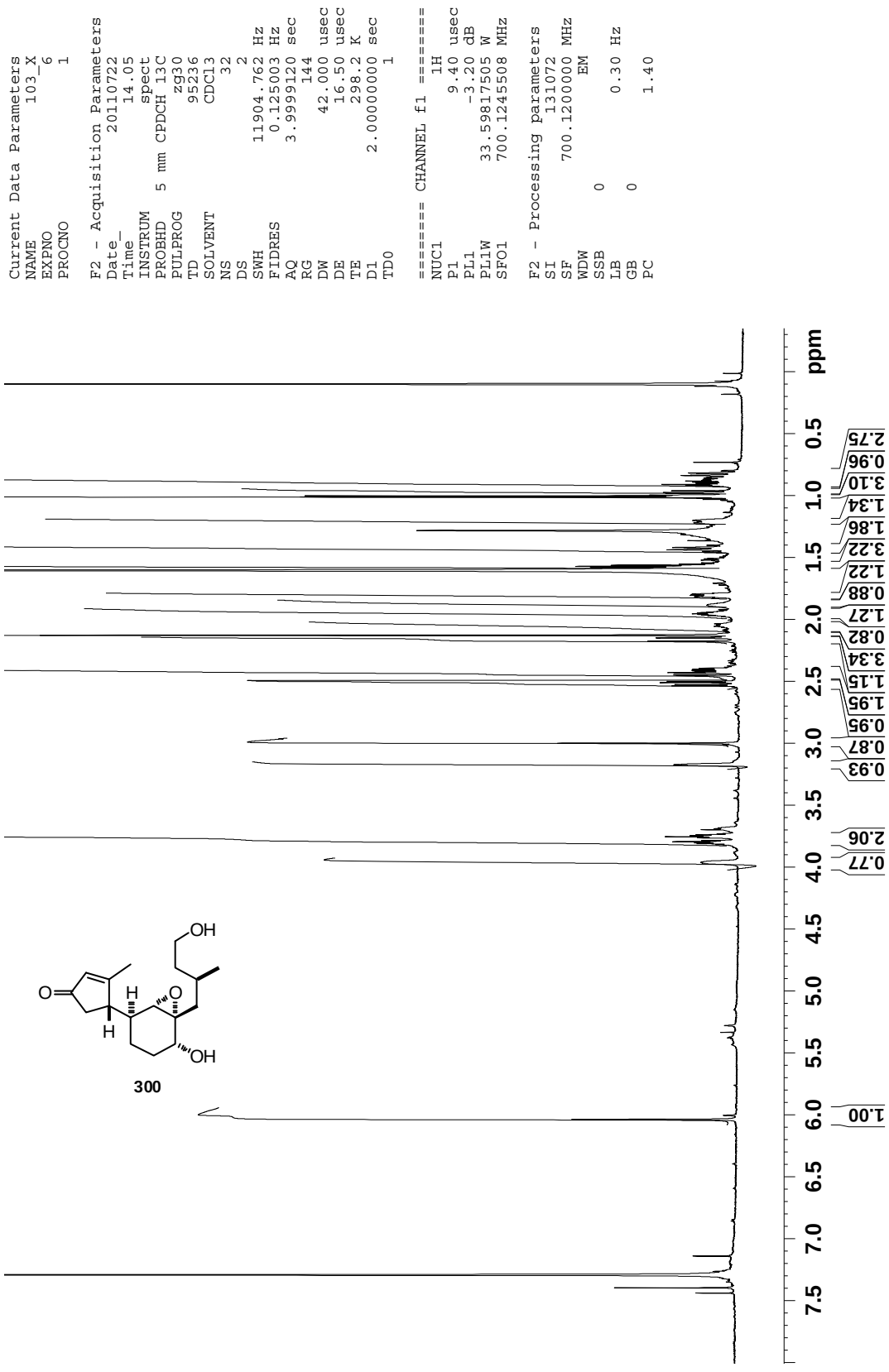

Current Data Parameters
NAME 96_x
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20110709
Time_ 16.57
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 57
DW 42.000 usec
DE 16.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1245508 MHz
F2 - Processing parameters
SI 131072
SF 700.1200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40
OPMB
(S)
H
HO
H
O
295
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
23.66
4.89
1.29
1.00
4.06
6.64
4.93
2.01
1.38
2.17
2.13
1.97
2.99
4.00
3.92
12.08
2.84
3.80
9.77
4.56


Current Data Parameters
NAME 96_x
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20110709
Time 17.08
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDC13
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 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
F2 - Processing parameters
SI 131072
SF 176.0453140 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
200
180
160
140
120
100
80
60
40
20
0
ppm
OPMB
(S)
H
HO
H
O

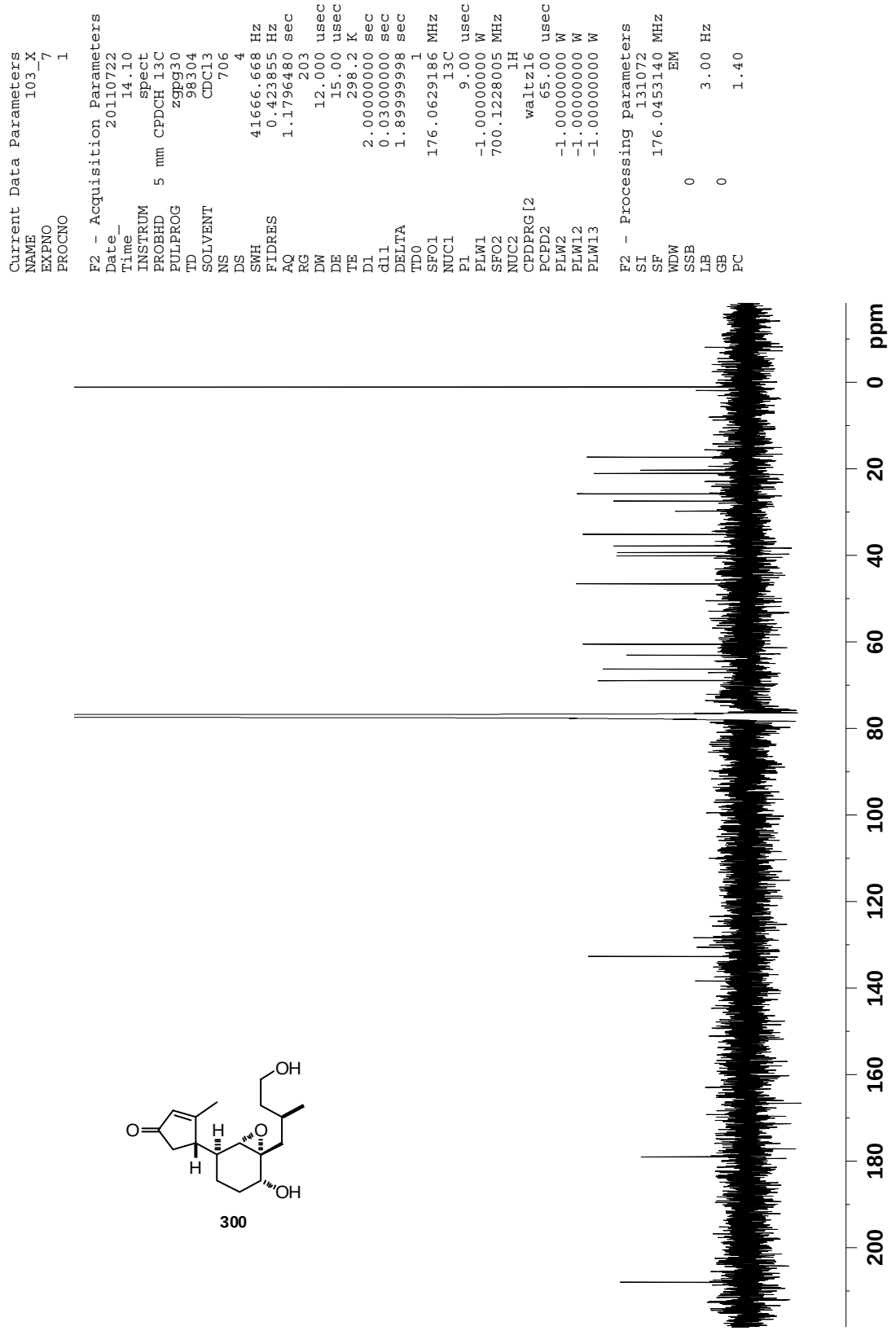
295

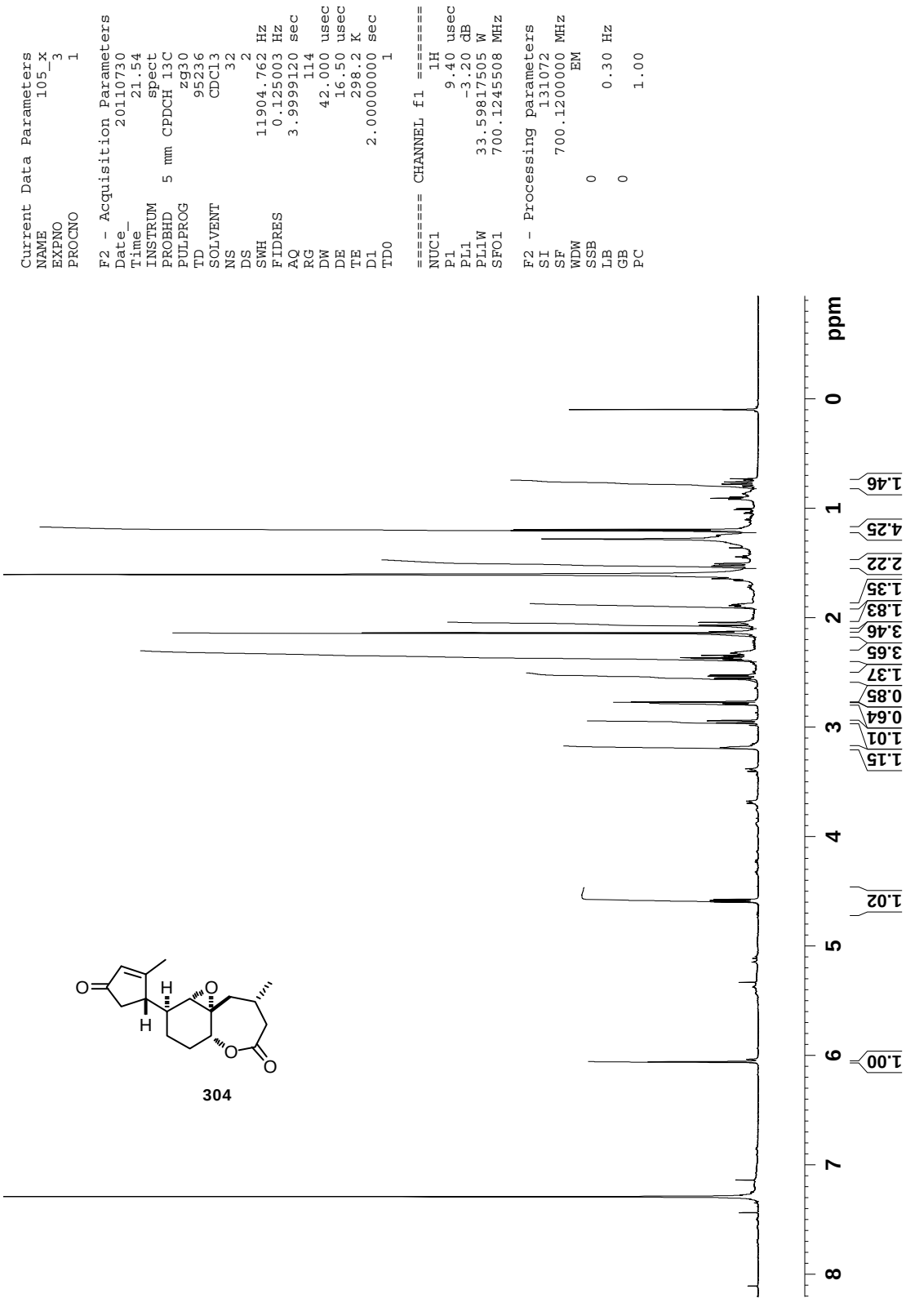

Current Data Parameters
NAME 100_X
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20110715
Time 23.50
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999120 sec
RG 57
DW 42.000 usec
DE 16.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1245508 MHz
F2 - Processing parameters
SI 131072
SF 700.1200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
OPMB
O
H
O
H
OH
298
ppm
0
1
2
3
4
5
6
7
8
5.18
1.80
0.85
1.62
0.97
2.77
1.57
0.72
0.70
0.85
1.78
1.01
2.60
2.70
4.91
1.24
1.72
1.26
2.28
1.05


Current Data Parameters
NAME 100_x
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20110715
Time 23.58
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 1.1796480 sec
RG 203
DW 12.000 usec
DE 15.00 usec
TE 298.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
SFO1 176.0629186 MHz
NUC1 13C
P1 9.00 usec
PLW1 -1.00000000 W
SFO2 700.1228005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 65.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 131072
SF 176.0453140 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
OPMB
O
H
O
H
OH
298
200
180
160
140
120
100
80
60
40
20
0
ppm

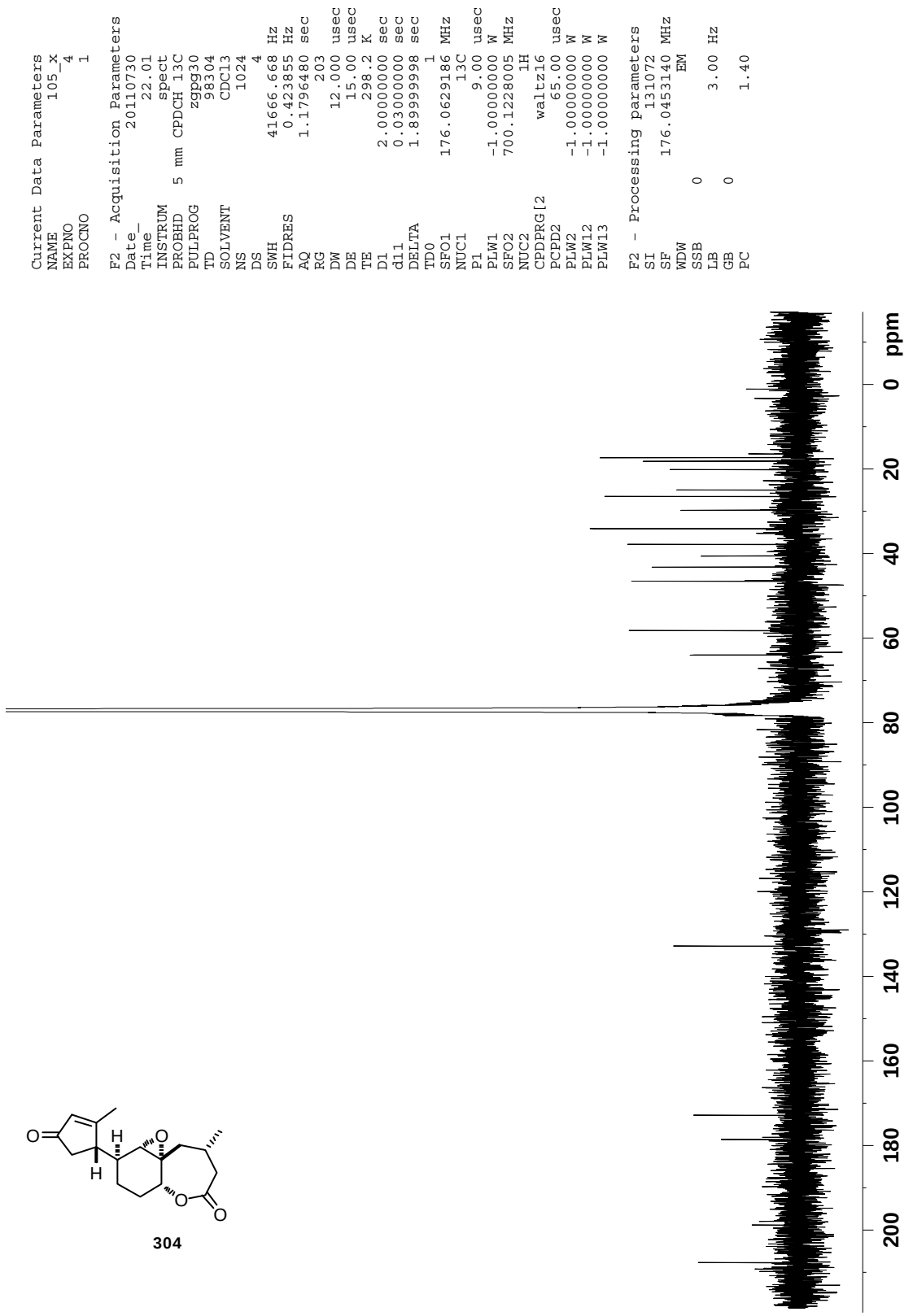

Current Data Parameters
NAME 103_X
EXPNO 6
PROCNO 1
F2 - Acquisition Parameters
Date_ 20110722
Time_ 14.05
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999120 sec
RG 144
DW 42.000 usec
DE 16.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1245508 MHz
F2 - Processing parameters
SI 131072
SF 700.1200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.40
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
0.5
1.00
2.06
0.77
0.93
0.87
0.95
1.95
1.15
3.34
0.82
1.27
0.88
1.22
3.22
1.86
1.34
3.10
0.96
2.75
OH
O
H
H
O
OH

300

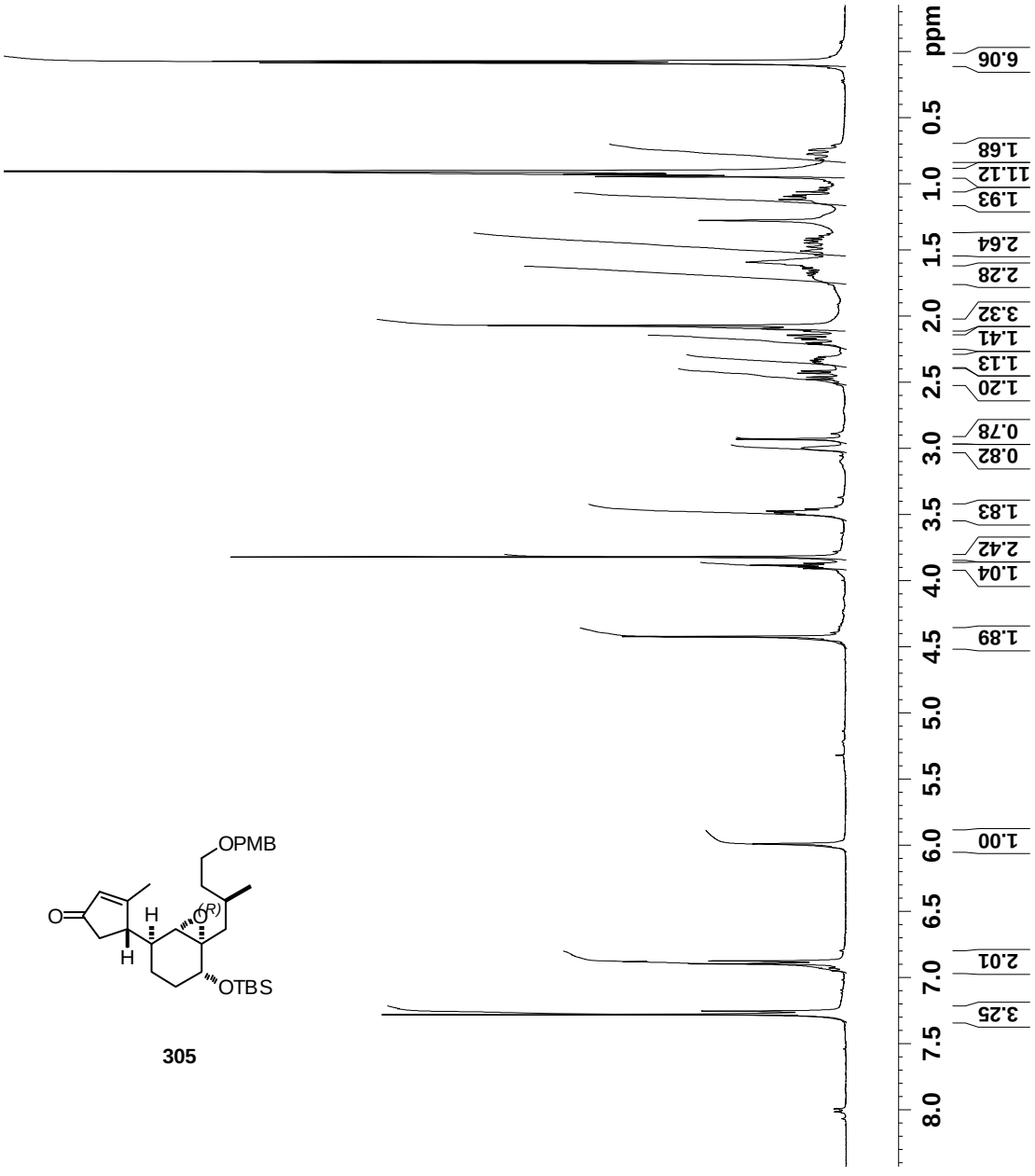

Current Data Parameters
NAME 103_X
EXPNO 7
PROCNO 1
F2 - Acquisition Parameters
Date_ 20110722
Time_ 14.10
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDCl3
NS 706
DS 4
SWH 41666.668 Hz
FIDRES 0.423855 Hz
AQ 1.1796480 sec
RG 203
DW 12.000 usec
DE 15.00 usec
TE 298.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
SFO1 176.0629186 MHz
NUC1 13C
P1 9.00 usec
PLW1 -1.00000000 W
SFO2 700.1228005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 65.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 131072
SF 176.0453140 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
200
180
160
140
120
100
80
60
40
20
0
ppm
OH
O
H
H
O
OH
300


Current Data Parameters
NAME 105_x
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20110730
Time 21.54
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 3.9999120 sec
RG 114
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
F2 - Processing parameters
SI 131072
SF 700.1200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1.46
4.25
2.22
1.35
1.83
3.46
3.65
1.37
0.85
0.64
1.01
1.15
1.02
1.00
ppm
0
1
2
3
4
5
6
7
8
O
H
H
O
O
O

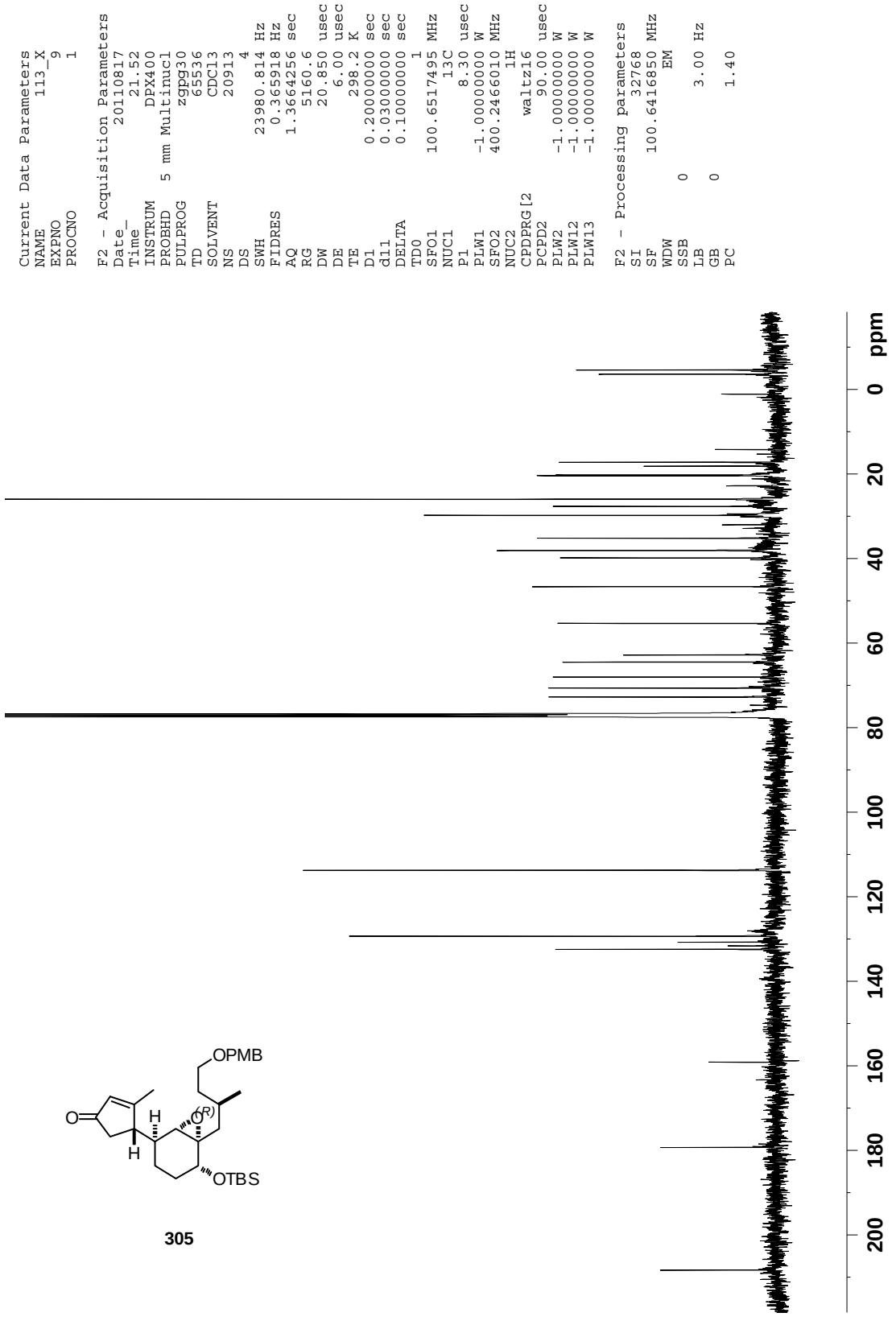
304

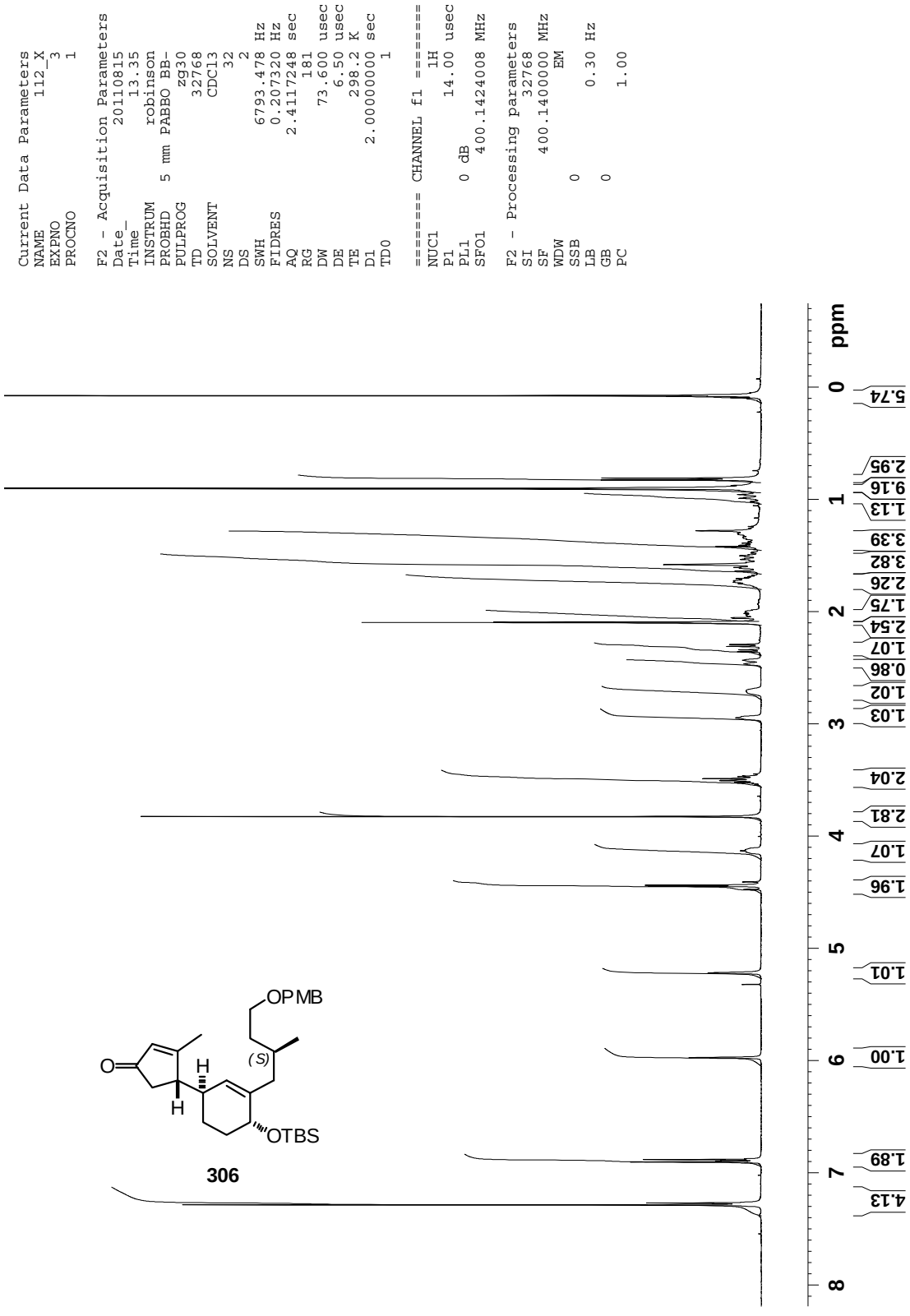

Current Data Parameters
NAME 105_x
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20110730
Time_ 22.01
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDCl3
NS 1024
DS 4
SWH 41666.668 Hz
FIDRES 0.423855 Hz
AQ 1.1796480 sec
RG 203
DW 12.000 usec
DE 15.00 usec
TE 298.2 K
D1 2.00000000 sec
d11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
SFO1 176.0629186 MHz
NUC1 13C
P1 9.00 usec
PLW1 -1.00000000 W
SFO2 700.1228005 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 65.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 131072
SF 176.0453140 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
200
180
160
140
120
100
80
60
40
20
0 ppm
O
H
H
O
O
O

304

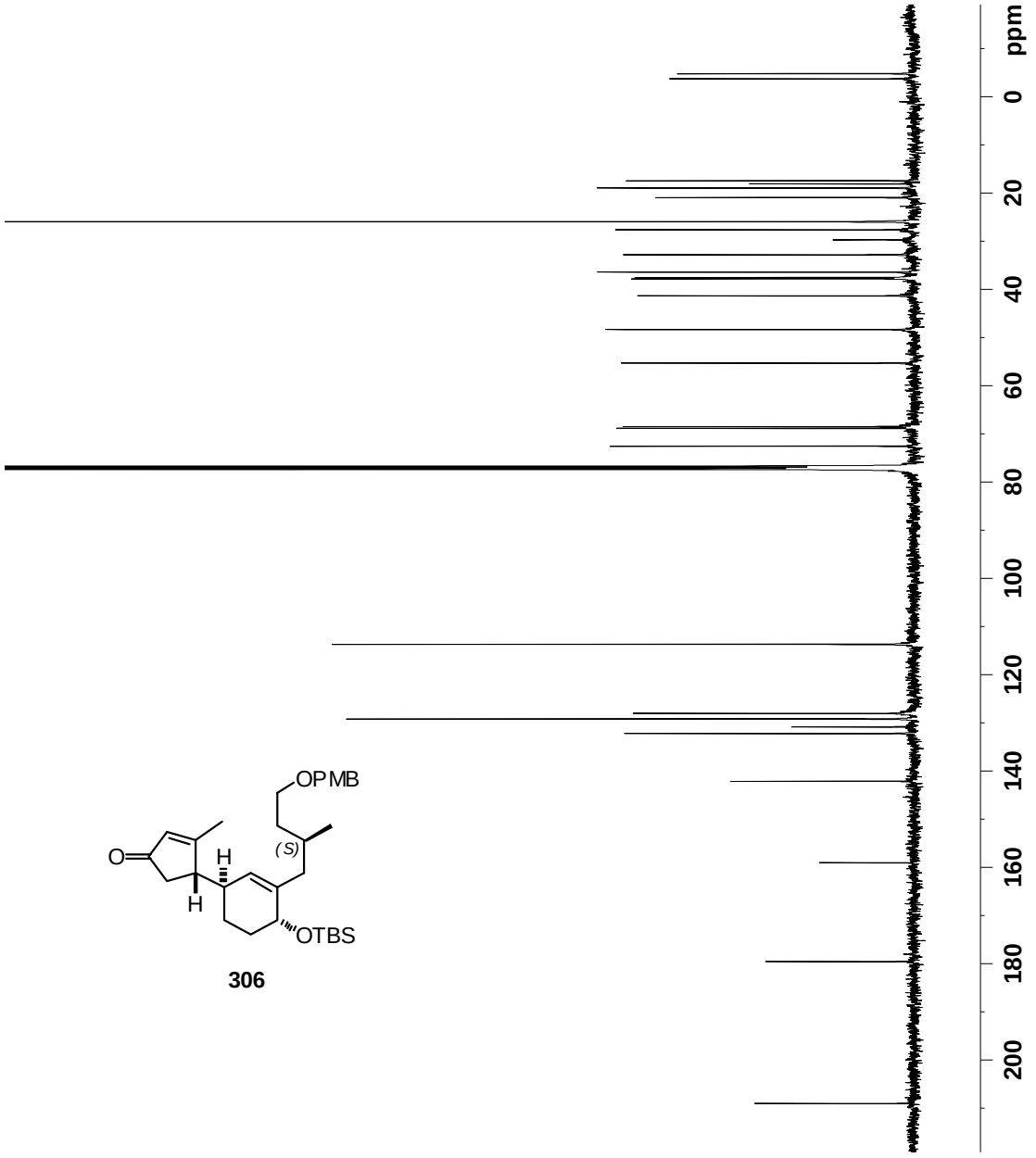

Current Data Parameters
NAME 113_X
EXPNO 4
PROCNO 1
F2 - Acquisition Parameters
Date_ 20110816
Time 22.21
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6793.478 Hz
FIDRES 0.207320 Hz
AQ 2.4117248 sec
RG 161.3
DW 73.600 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 usec
PL1 0 dB
SFO1 400.1424008 MHz
F2 - Processing parameters
SI 32768
SF 400.1400000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
ppm
6.06
1.68
11.12
1.93
2.64
2.28
3.32
1.41
1.13
1.20
0.78
0.82
1.83
2.42
1.04
1.89
1.00
2.01
3.25
OPMB
O
H
H
O
(R)
OTBS

305

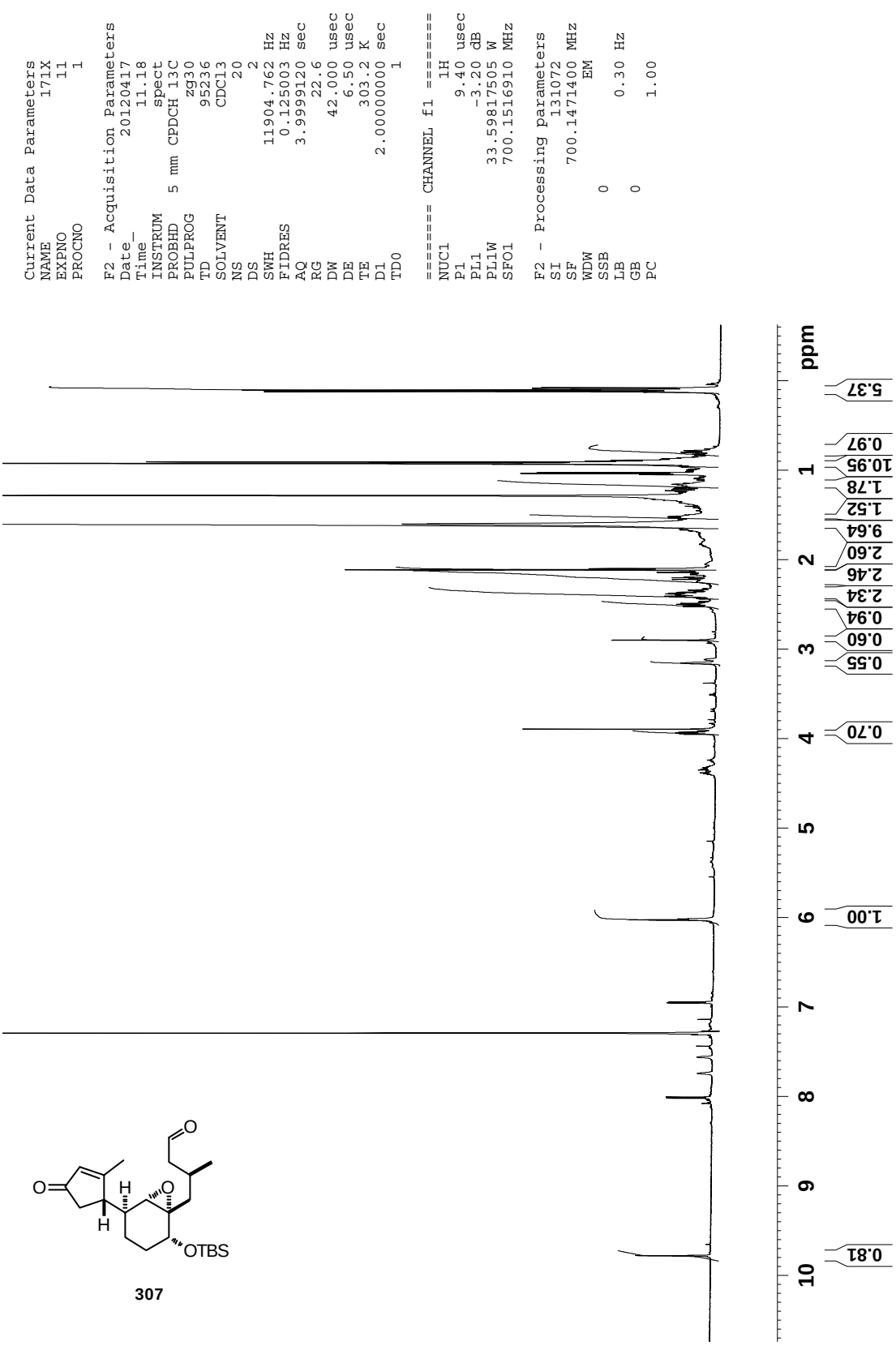

Current Data Parameters
NAME 113_X
EXPNO 9
PROCNO 1
F2 - Acquisition Parameters
Date_ 20110817
Time_ 21.52
INSTRUM DPX400
PROBHD 5 mm Multinucl
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 20913
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664256 sec
RG 5160.6
DW 20.850 usec
DE 6.00 usec
TE 298.2 K
D1 0.20000000 sec
d11 0.03000000 sec
DELTA 0.10000000 sec
TD0 1
SFO1 100.6517495 MHz
NUC1 13C
P1 8.30 usec
PLW1 -1.00000000 W
SFO2 400.2466010 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 32768
SF 100.6416850 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
OPMB
O
H
H
(R)
OTBS
305
200
180
160
140
120
100
80
60
40
20
0
ppm


Current Data Parameters
NAME 112_X
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20110815
Time 13.35
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDC13
NS 32
DS 2
SWH 6793.478 Hz
FIDRES 0.207320 Hz
AQ 2.4117248 sec
RG 181
DW 73.600 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 usec
PL1 0 dB
SFO1 400.1424008 MHz
F2 - Processing parameters
SI 32768
SF 400.1400000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
ppm
0
1
2
3
4
5
6
7
8
5.74
2.95
9.16
1.13
3.39
3.82
2.26
1.75
2.54
1.07
0.86
1.02
1.03
2.04
2.81
1.07
1.96
1.01
1.00
1.89
4.13
OPMB
O
H
H
(S)
OTBS

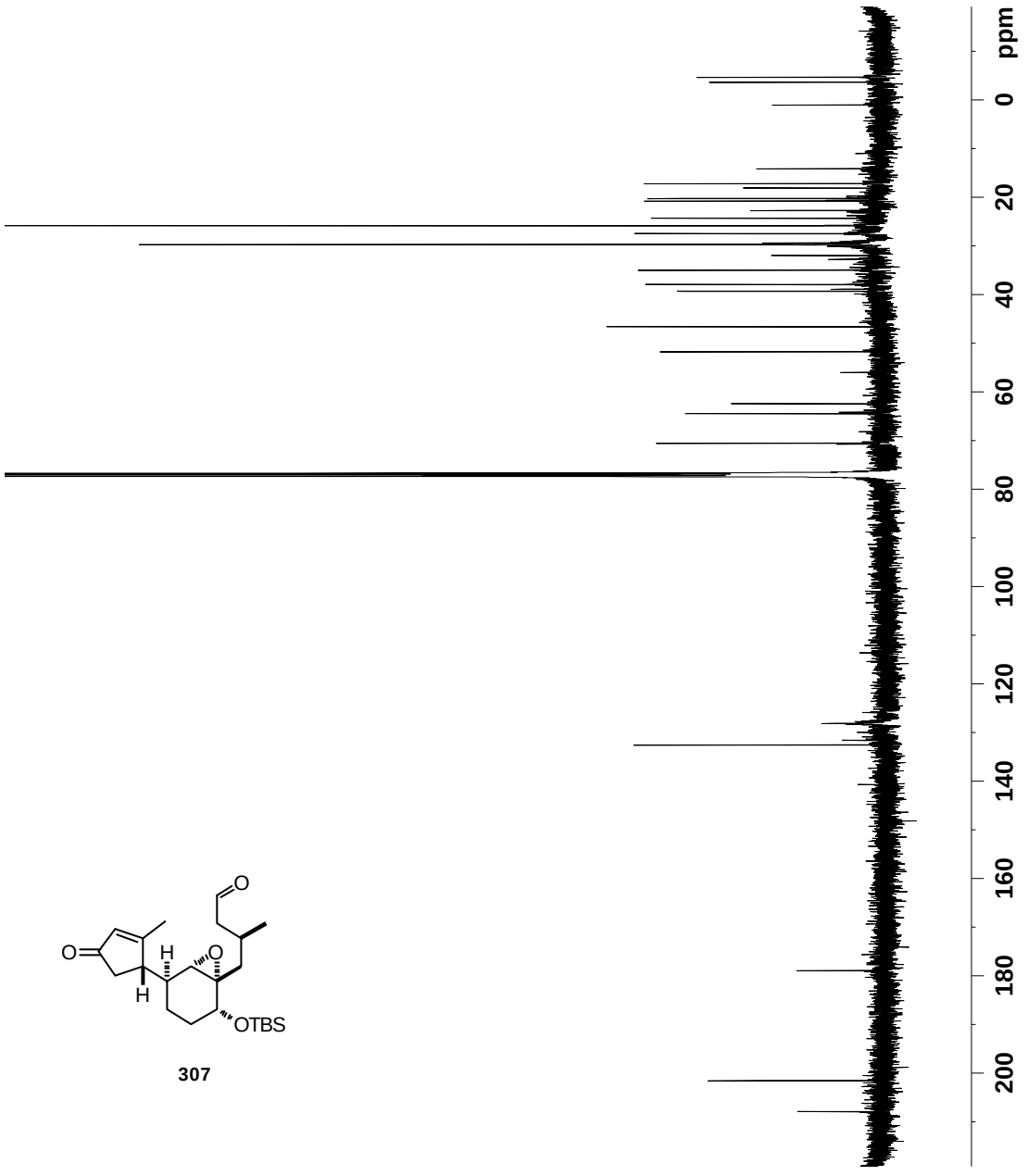
306


Current Data Parameters
NAME 112_X
EXPNO 12
PROCNO 1
F2 - Acquisition Parameters
Date_ 20110816
Time_ 21.57
INSTRUM DPX400
PROBHD 5 mm Multinucl
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 21276
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664256 sec
RG 6502
DW 20.850 usec
DE 6.00 usec
TE 298.2 K
D1 0.20000000 sec
d11 0.03000000 sec
DELTA 0.10000000 sec
TD0 1
SFO1 100.6517495 MHz
NUC1 13C
P1 8.30 usec
PLW1 -1.00000000 W
SFO2 400.2466010 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 32768
SF 100.6416850 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
ppm
0
20
40
60
80
100
120
140
160
180
200
OPMB
(S)
H
H
O
OTBS

306

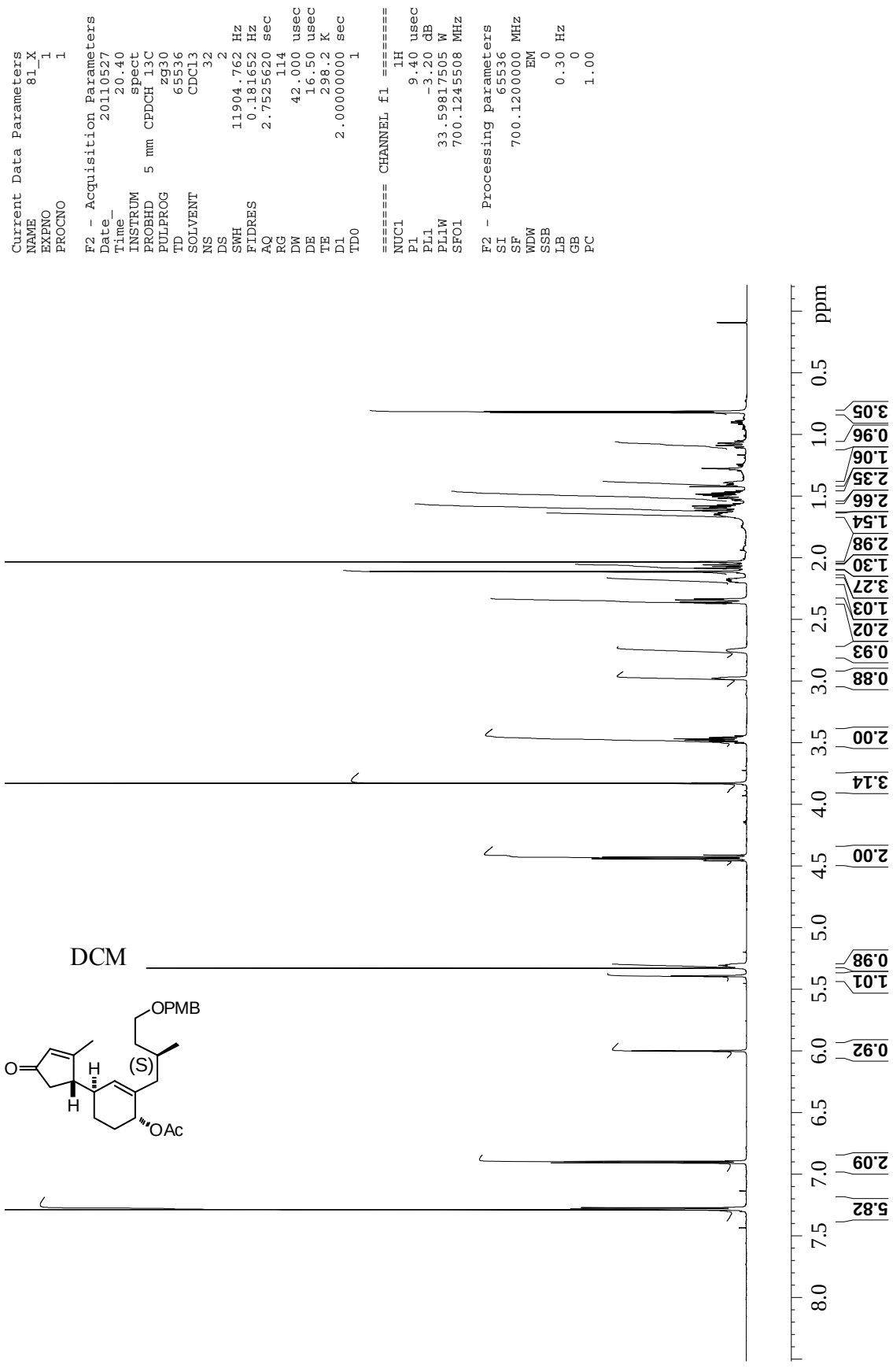

Current Data Parameters
NAME 171X
EXPNO 11
PROCNO 1
F2 - Acquisition Parameters
Date_ 20120417
Time_ 11.18
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 20
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999120 sec
RG 22.6
DW 42.000 usec
DE 6.50 usec
TE 303.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
F2 - Processing parameters
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
ppm
5.37
0.97
10.95
1.78
1.52
9.64
2.60
2.46
2.34
0.94
0.60
0.55
0.70
1.00
0.81
O
H
O
H
OTBS
O

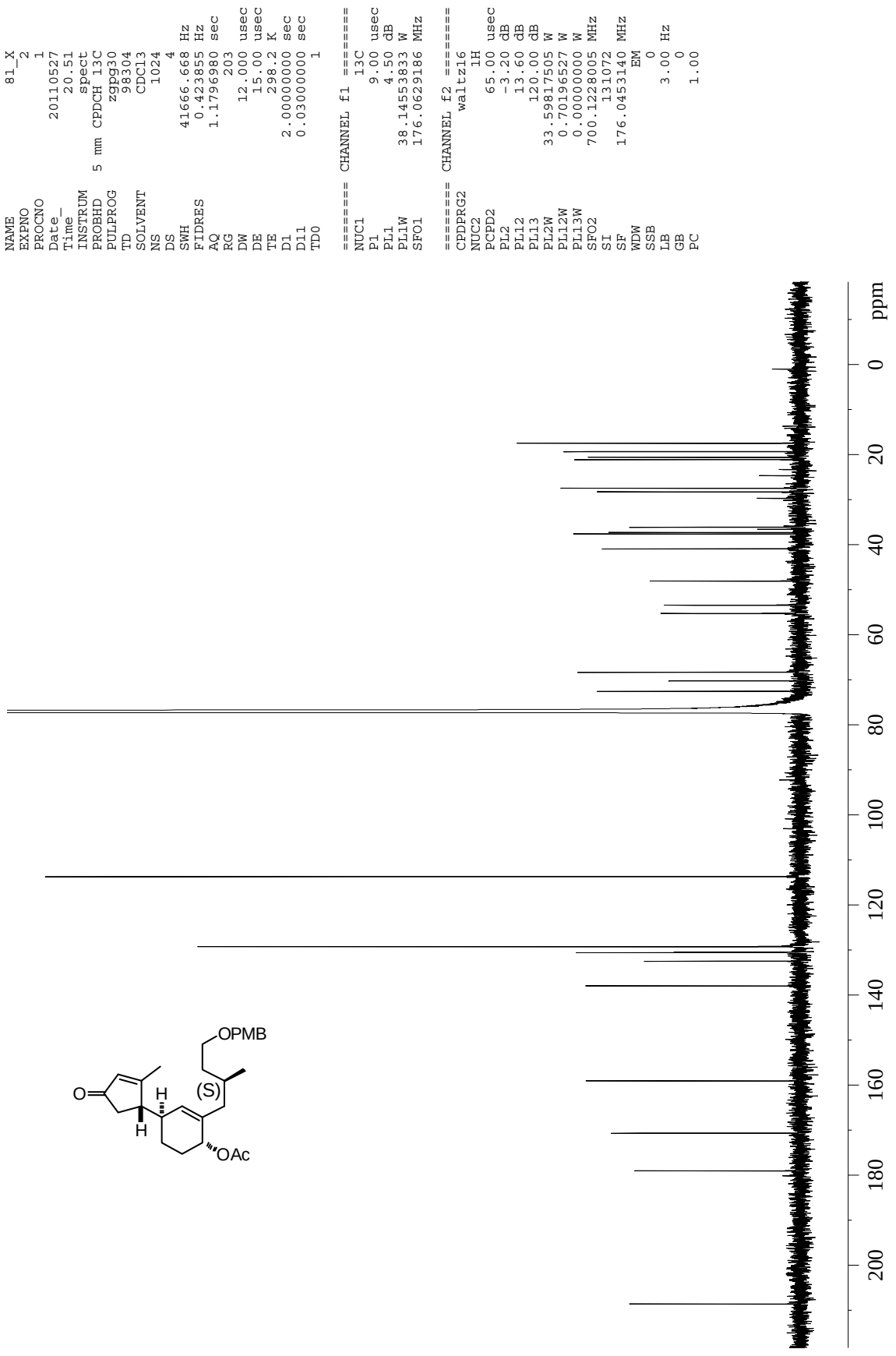
307

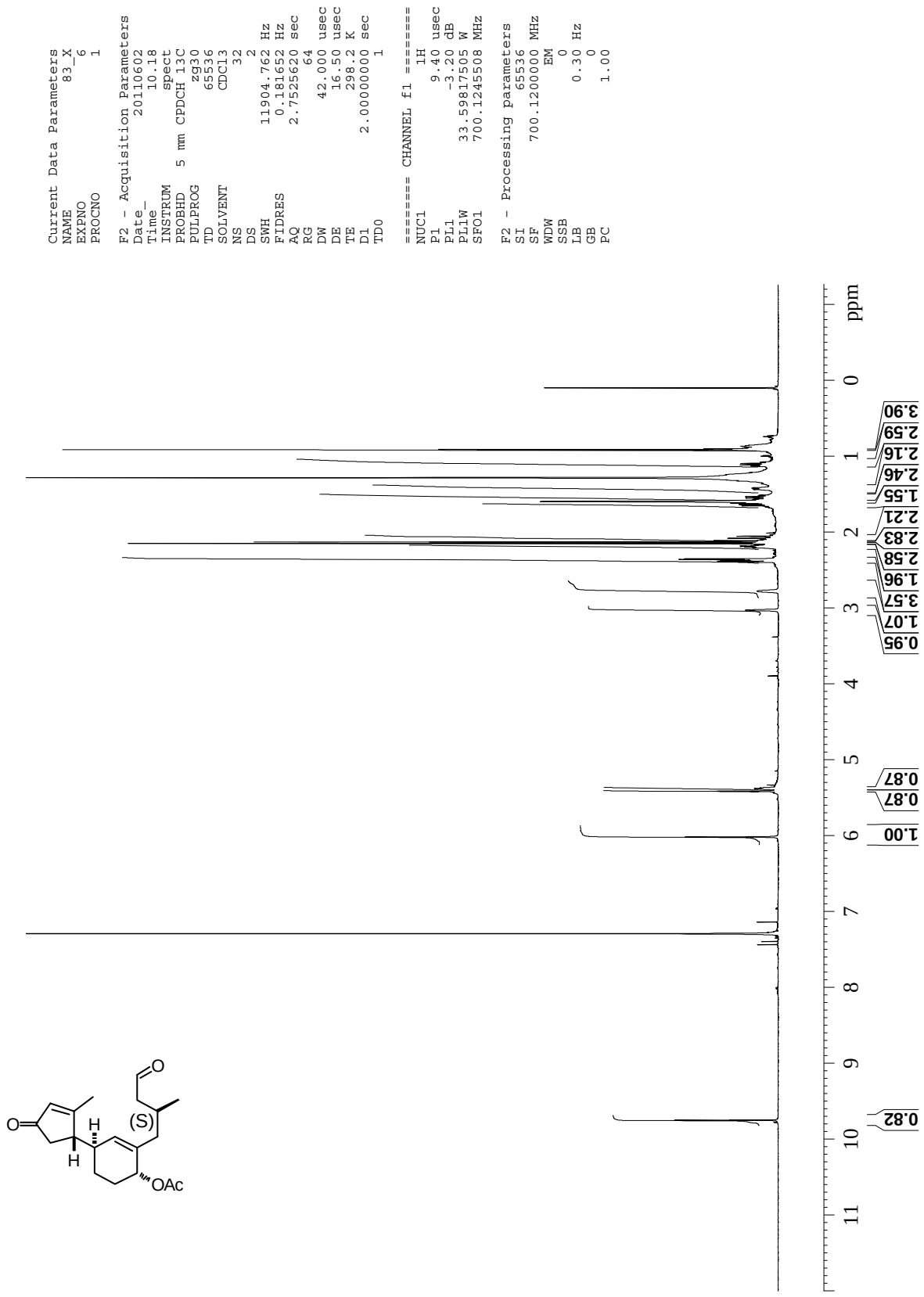

Current Data Parameters
NAME 115_X
EXPNO 12
PROCNO 1
F2 - Acquisition Parameters
Date_ 20110819
Time_ 22.17
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 37321
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664256 sec
RG 32768
DW 20.850 usec
DE 6.50 usec
TE 298.7 K
D1 0.20000000 sec
d11 0.03000000 sec
DELTA 0.10000000 sec
TD0 1
SFO1 100.6253446 MHz
NUC1 13C
P1 9.00 usec
PLW1 -1.00000000 W
SFO2 400.1416006 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 90.00 usec
PLW2 -1.00000000 W
PLW12 -1.00000000 W
PLW13 -1.00000000 W
F2 - Processing parameters
SI 32768
SF 100.6152830 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
200
180
160
140
120
100
80
60
40
20
0
ppm

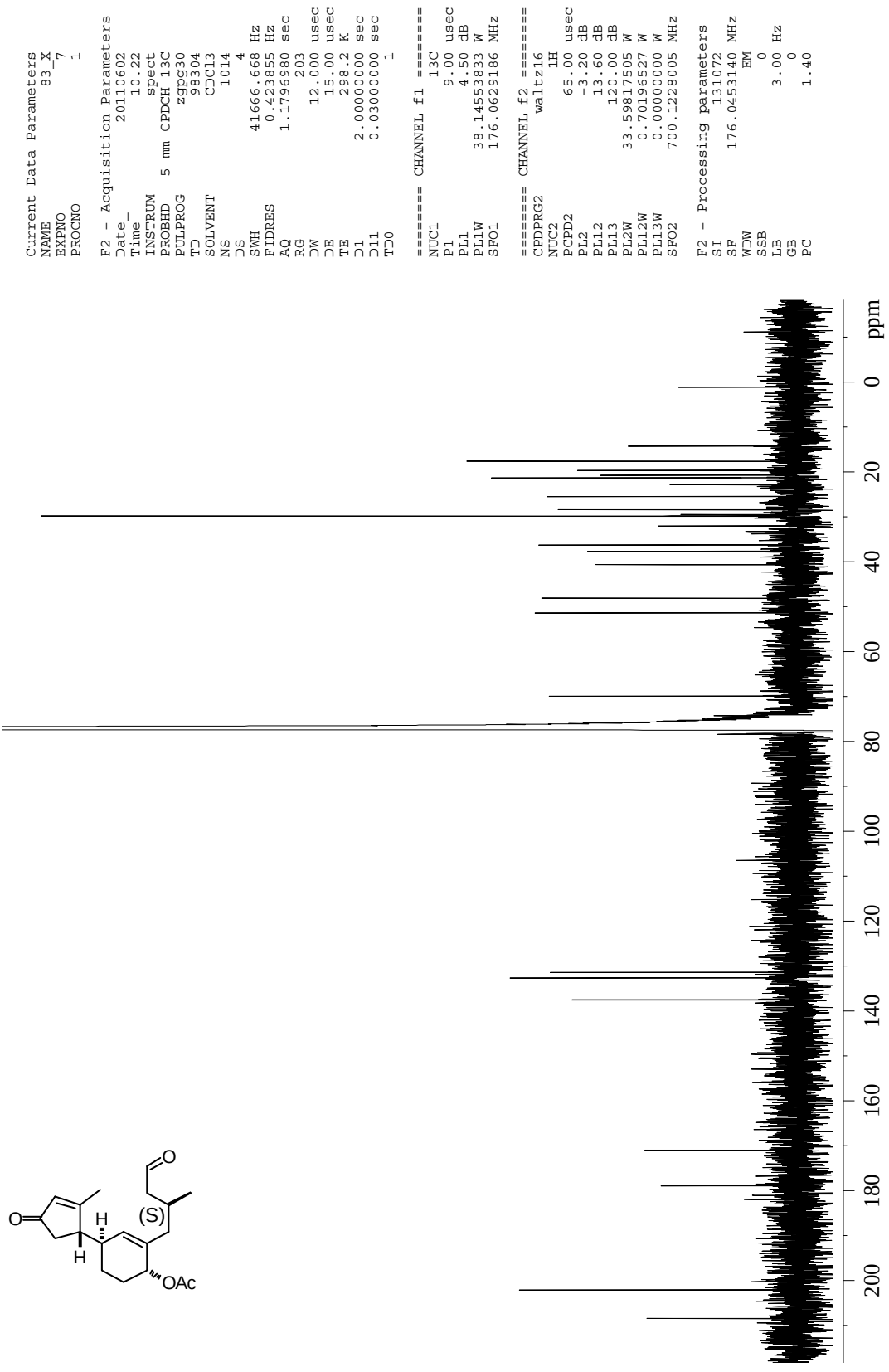
O
O
H
H
O
OTBS

307


Current Data Parameters
NAME 81_X
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20110527
Time 20.40
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 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
F2 - Processing parameters
SI 65536
SF 700.1200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
DCM
OPMB
O
H
(S)
H
OAc
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
2.0
1.5
1.0
0.5
5.82
2.09
0.92
1.01
0.98
2.00
3.14
2.00
0.88
0.93
2.02
1.03
3.27
1.30
2.98
1.54
2.66
2.35
1.06
0.96
3.05


81_X
2
1
20110527
20.51
spect
5 mm CPDCH 13C
zgpg30
98304
CDCl3
1024
4
41666.668 Hz
0.423855 Hz
1.1796980 sec
203
12.000 usec
15.00 usec
298.2 K
2.00000000 sec
0.03000000 sec
1
======== CHANNEL f1 ========
13C
9.00 usec
4.50 dB
38.14553833 W
176.0629186 MHz
======== CHANNEL f2 ========
waltz16
1H
65.00 usec
-3.20 dB
13.60 dB
120.00 dB
33.59817505 W
0.70196527 W
0.00000000 W
700.1228005 MHz
131072
176.0453140 MHz
EM
0
3.00 Hz
0
1.00
OPMB
O
H
(S)
H
OAc
ppm
0
20
40
60
80
100
120
140
160
180
200


Current Data Parameters
NAME 83_X
EXPNO 6
PROCNO 1
F2 - Acquisition Parameters
Date_ 20110602
Time_ 10.18
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
F2 - Processing parameters
SI 65536
SF 700.1200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
ppm
0.82
1.00
0.87
0.87
3.90
2.59
2.16
2.46
1.55
2.21
2.83
2.58
1.96
3.57
1.07
0.95
O
O
H
(S)
H
OAc


Current Data Parameters
NAME 83_X
EXPNO 7
PROCNO 1
F2 - Acquisition Parameters
Date_ 20110602
Time_ 10.22
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDCl3
NS 1014
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
F2 - Processing parameters
SI 131072
SF 176.0453140 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
200
180
160
140
120
100
80
60
40
20
0
ppm
O
O
H
H
(S)
OAc