AN ABSTRACT OF THE THESIS OF

Yi Lu for the degree of Doctor of Philosophy in Chemistry presented on August 6, 2018.

Title: Strategies for the Synthesis of Nitrogeous Compounds:
Aminal Radical Reactions and Pyridinium Oxide Cycloadditions

Abstract approved:

_____

Christopher M. Beaudry

Pharmaceuticals, molecular catalysts, and secondary metabolites often contain nitrogen. The problems faced synthesizing compounds which contain nitrogen was because of the Lewis base reactivity of nitrogen lone pairs, and the acidic protons of some nitrogenous functional groups. We developed two methods for the synthesis of nitrogeous compounds. Additionally, we successfully constructed the heterotetracyclic core of himgaline.

The aminal radicals were generated by reduction of the corresponding amidine or amidinium ion. The intermediate radicals participate in C−C bond- forming reactions to produce fully substituted aminal stereocenters. No toxic additives or reagents are required.

The regioselectivity and diastereoselectivity was investigated in pyridinium oxide cycloadditions using complex substrates. The reaction is reversible under the reaction conditions. High levels of diastereoselectivity and regioselectivty are observed, which can be attributed to minimization of *syn*-pentane interactions in the products.

The stereo- and region-selective intramoleculer pyridinium oxide cycloaddition successfully forms two bonds and builds four stereocenters in a single step. These key cycloaddition reactions are particularly suitable to the challenge of preparing multiple rings with control of stereochemistry. It has been shown that the new methodology replacing acid-base strategy would enhance the efficiency of alkaloid synthesis.

Strategies for the Synthesis of Nitrogeous Compounds: Aminal Radical Reaction and Pyridinium Oxide Cycloadditions

by
Yi Lu

A THESIS

submitted to

Oregon State University

in partial fulfillment of
the requirements for the
degree of

Doctor of Philosophy

Presented August 6, 2018

Commencement June 2019

Doctor of Philosophy thesis of Yi Lu presented on August 6, 2018

APPROVED:

Major Professor, representing Chemistry

Head of the Department of Chemistry

Dean of the Graduate School

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

Yi Lu, Author

ACKNOWLEDGEMENTS

I would like to express my thanks to my wife, Wanyu, for all of her support to complete my degree. I would also like to thank my family for the encouragement during my time in Oregon. I would like to thank my mentor, Cem Celik, for all of the help from first to the end. I would like to thank David Schiedler for teaching me in lab and helping with the chapter 1 and 2. I would also like to thank the members of the Beaudry research group, both past and present for their support. I am appreciated for all my friends here. In the end, I would like to thank my advisor, Professor Chris Beaudry, for his guidance over the last six years. Professor Beaudry led me to the field of chemistry, taught me to think critically about chemistry.

CONTRIBUTION OF AUTHORS

David A. Schiedler assisted with the data collection for chapter 2 and the writing of chapters 2.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF SCHEMES

Strategies for the Synthesis of Nitrogeous Compounds: Aminal Radical Reactions and Pyridinium Oxide Cycloadditions.

by

Yi Lu

August 6, 2018

LPSC 2pm

1. Introduction

Nitrogenous molecules are abundant in nature. Pharmaceuticals, molecular catalysts, and secondary metabolites often contain nitrogen.[1] Some examples of nitrogen containing natural products are morphine, saxitoxin, vallesine, noscapine, daphmanidin E, and strychnine (Figure1.1).

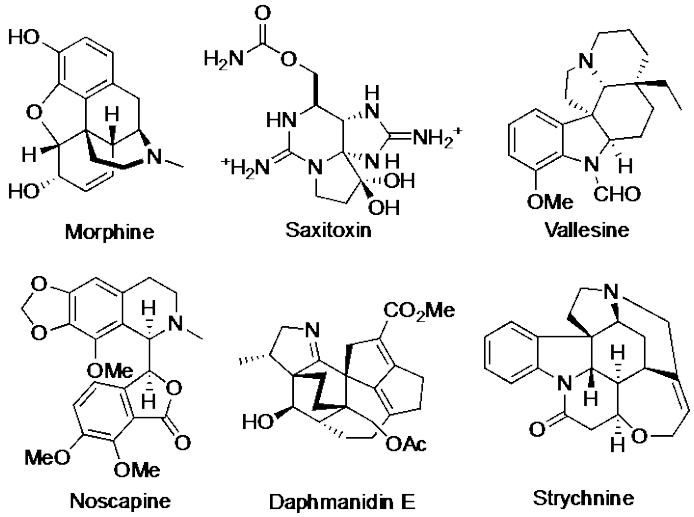
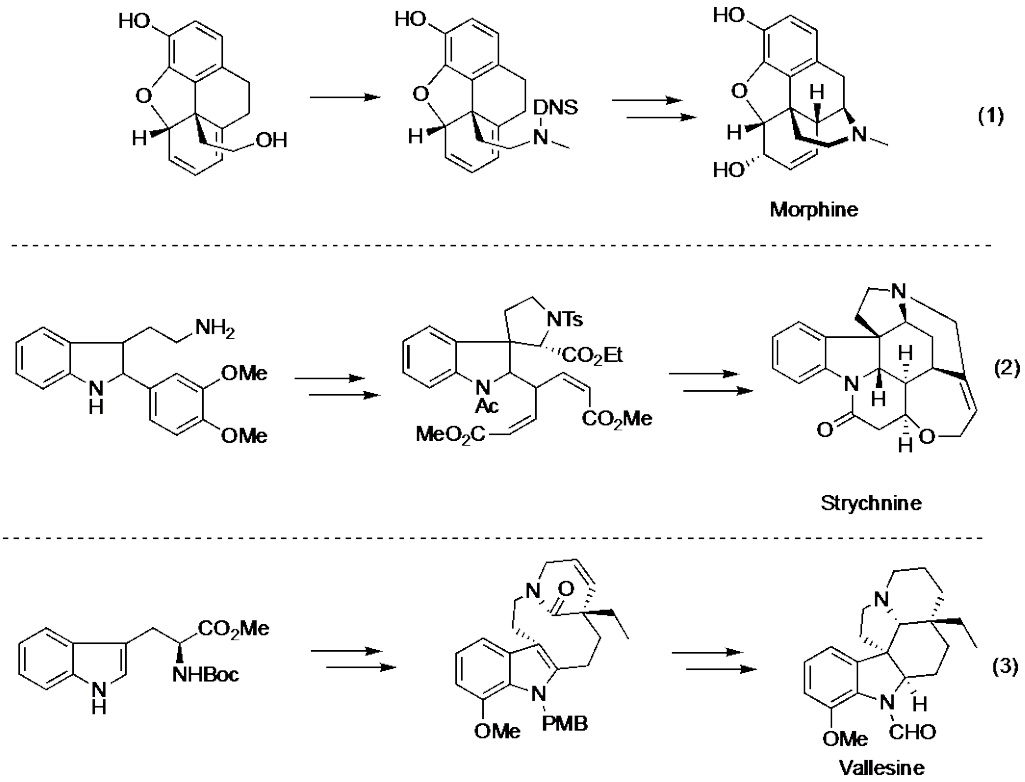


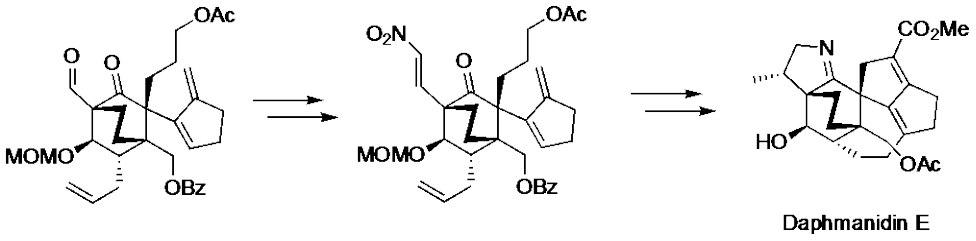
Figure 1.1 Well-known natural products containing nitrogen.

It is difficult to synthesize nitrogen rich compounds. The problems faced synthesizing compounds which contain nitrogen are the Lewis base reactivity of nitrogen lone pairs and the acidic protons of some nitrogenous functional groups.[2] Solubility and reactivity can sometimes become the major difficulty in synthesizing nitrogen-containing compounds. Overcoming these challenges with the development and application of new methods for synthesis of nitrogen rich compounds is necessary and relevant to the improvement of human health. There are different ways to work with nitrogen in organic molecules. The most common way protection.[3] Examples in which nitrogen protection have been used are dinitrobenzene sulfonyl (DNs) of nitrogen in morphine synthesis of Fukuyama (Scheme1.1, entry 1),[4] Woodward's nitrogen protection with toluenesulfonyl (Ts) in the strychnine synthesis (Scheme1.1, entry 2),[5] or *tert*-butyloxycarbonyl (Boc) protection of nitrogen in the vallesine synthesis by Movasagghi (Scheme1.1, entry 3).[6]



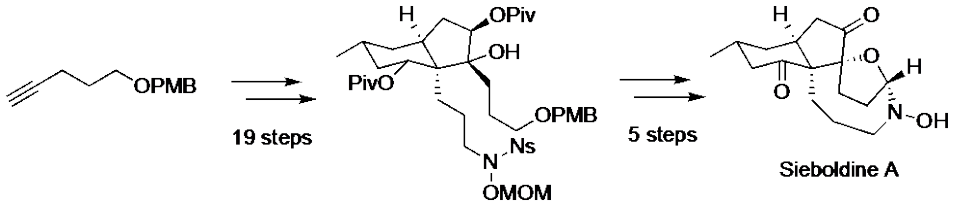
Scheme 1.1 Alkaloid synthesis utilizing the protecting group strategies.

Another similar idea to protection is to incorporate unreactive nitrogenous groups and convert them to the final desired functional group later. These methods work well but take additional steps and cause lower yields. One example is daphmanidin E synthesis by Weiss and Carreira (Scheme1.2), where a nitro group was used to install the nitrogen.[7]



Scheme 1.2 Alkaloid synthesis utilizing the strategy of unreactive nitrogenous groups.

Another common approach is to introduce the nitrogen in at a late stage of synthesis. This strategy usually limits flexibility of the synthetic route and might also increase step count. An example is sieboldine A synthesis by Mukai and co-workers. In this synthesis, it took 19 steps to reach the intermediate which had the nitrogen atom, and only took 5 steps to finish this synthesis (Scheme1.3).[8]

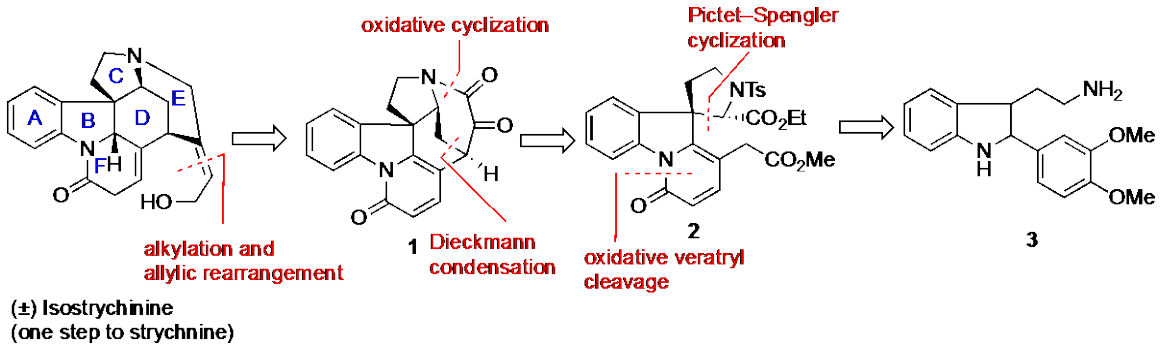


Scheme 1.3 Alkaloid synthesis utilizing the strategy of late stage nitrogen installation.

Alkaloids are difficult to synthesize due to the mentioned properties of nitrogen atom(s) found in the molecule. Therefore chemists have pursued different strategies to overcome this challenge. The earliest and most followed strategy is based on Lewis acid-base reactions. Recently developed and frequently used strategies are radical- and pericyclic reactions, which have proven to reduce the number of Lewis acid-base manipulations and step count because it forms C-C bonds directly. This outcome requests the need for the development of new methodologies to decrease the step count and improve the yield further. The relevant support is provided by the study of strychnine done by famous synthetic chemists.

The application and importance of radical and pericyclic reactions in the alkaloid syntheses is elaborated in the strychnine synthesis. The first racemic synthesis of strychnine was published by Woodward et al in 1954.[9] The retrosynthetic analysis is shown in Scheme 1.4. Strychnine has hexacyclic ring system with two nitrogen atoms and six stereocenters. At that time it was thought that it is extremely difficult to synthesize an alkaloid such as strychnine's structural complexity. By the standards of the time, the first synthesis is impressive, with a longest linear step count of 28 and an overall yield of 0.0002 %. To overcome the difficulty of alkaloid synthesis, Woodward has used Lewis acid-base type reactions in the strychnine synthesis. The

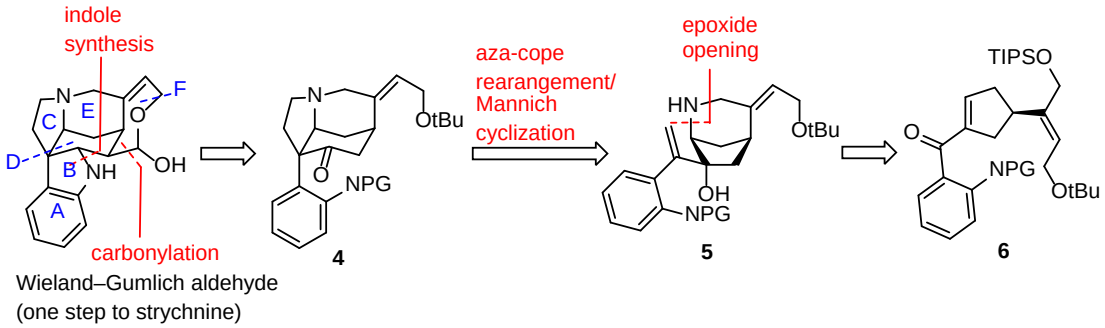
rings needed to be fused consecutively in Woodward's synthesis, because there were no reactions involved that form multiple C-C bonds in the single step. It is noticeable that Woodward did not use any reactions belonging to the radical or pericyclic reaction type which could have probably decreased the step count and led also to a higher yield. According to their analysis, (±)-strychnine could be obtained from compound **1** via alkylation and allylic rearrangement. The hexacyclic ring system in compound **1** could be yielded from compound **2** by oxidative cyclization which closes ring E and the Dieckmann condensation which forms ring D. The spiro tetracyclic compound **2** should be formed from indole **3**, by which ring F would form by a oxidative veratryl cleavage and the spiro cycle C should be obtained via a Pictet-Spengler cyclization.



Scheme 1.4 Woodward's retrosynthetic analysis of strychnine.

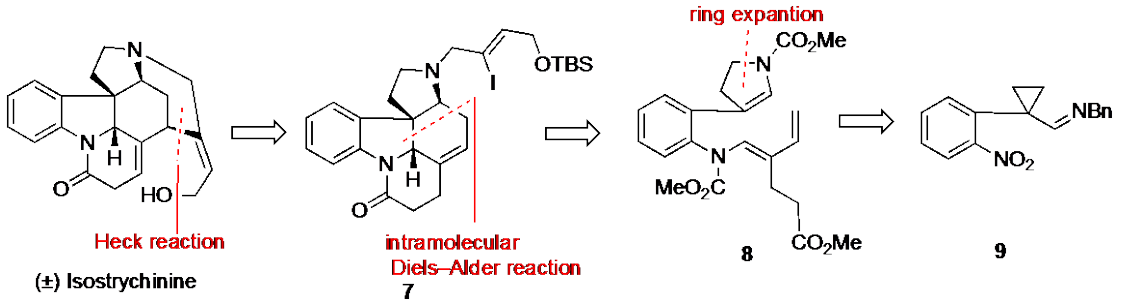
The Overman group reported their enantioselective synthesis of strychnine in 1993.[9] The retrosynthetic analysis of Overman's strychnine synthesis is outlined in Scheme 1.5. The strategy that Overman used to overcome the difficulty of alkaloid synthesis was to set the radical and pericyclic reactions as their key step and to avoid Lewis acid-base reactions. For this purpose, Overman made use of aza-cope rearrangement / Mannich cyclization reactions as their key step. The use the radical and pericyclic reactions in their synthesis resulted in decrease of the step count and increased yield. Based on Overman's retrosynthetic analysis, the hexacyclic Wieland-Gumlich aldehyde should be obtained from the tricyclic compound **4,** installing rings B and G by indole synthesis and carbonylation respectively. Tricyclic compound **4** would be yielded from bicyclic compound **5** through a sequential aza-cope rearrangement and

Mannich cyclization accordingly forming ring C and D. Compound **5** would be obtained from cyclopentene **6** via an epoxide opening reaction which could form ring E.



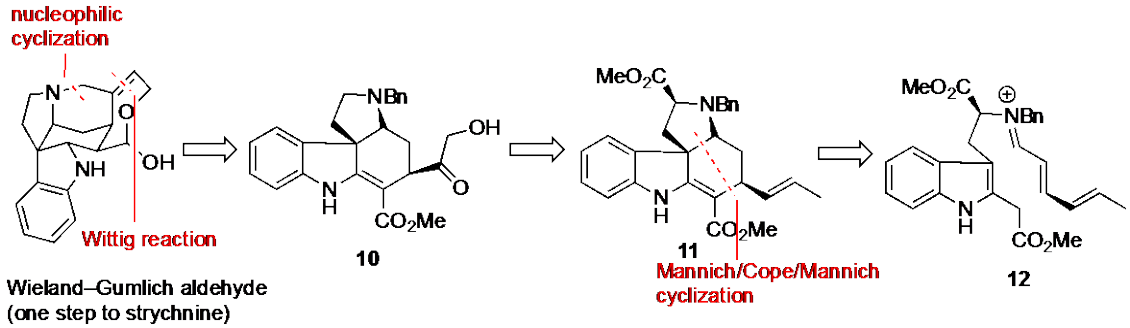
Scheme 1.5 Overman's retrosynthetic analysis of strychnine.

In 1994, Rawal et al published their racemic synthesis of strychnine.[9] Their retrosynthetic analysis of strychnine is depicted in Scheme 1.6. Rawal's strategy to overcome the challenge linked with alkaloid synthesis was also to employ the radical and pericyclic reactions as a key step in order to avoid Lewis acid-base reactions. The further improvement in yield and decrease in the overall step count in Rawal and coworkers synthesis was due to their Diels-Alder key step, belonging to the category of pericyclic reactions. More and more well-known chemists are using radical and pericyclic reaction in their strategies for the syntheses of alkaloids, to avoid the Lewis acid-base reaction disadvantages. Considering Rawal's retrosynthetic analysis, (±)-isostrychnine would be yielded from pentacyclic compound **7** by a Heck reaction which installs ring E. The pentacyclic compound **7** should be obtained from diene **8** via Diels-Alder reaction that installs ring B and D. Pyrroline **8** could be obtained from construction of ring C via ring expansion of cyclopropane **9**.



Scheme 1.6 Rawal's retrosynthetic analysis of strychnine.

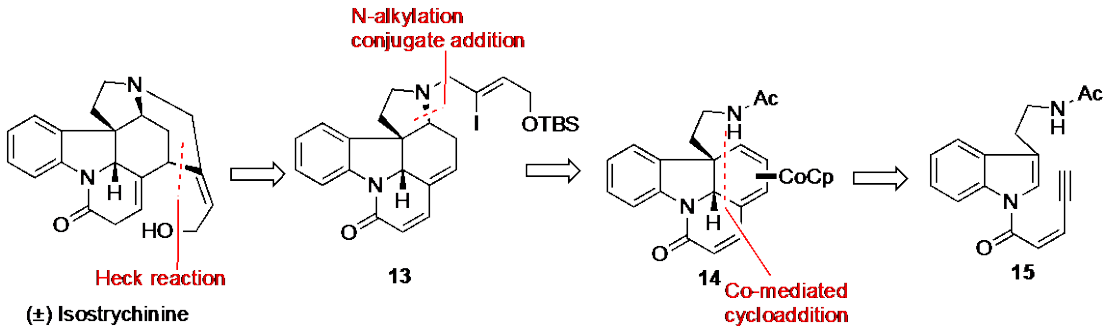
Kuehne's group reported their strychnine synthesis in 1998.[9] Their retrosynthetic analysis is shown in Scheme 1.7. They also avoided Lewis acid base reactions and have used in their key step Mannich / Cope / Mannich cyclization to improve yield and step count. According to Kuehne's analysis, Wieland-Gumlich aldehyde would be generated from tetracyclic compound **10** through a nucleophilic cyclization to close ring E and a Wittig reaction to form ring G. Compound **10** could be yielded from compound **11**. This tetracyclic compound **11** should be obtained from iminium ion **12** by Mannich / Cope / Mannich cyclization reactions thereby forming ring C and D.



Scheme 1.7 Kuehne's retrosynthetic analysis of strychnine.

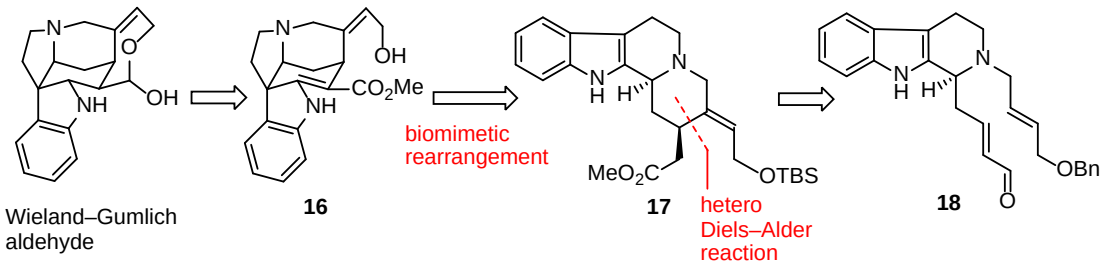
In 2000, Vollhardt and coworkers published their strychnine synthesis (Scheme 1.8).[9] The group used the radical and pericyclic reaction strategy as a key step. Their key step involved a Co-mediated cycloaddition reaction, which is a pericyclic reaction. Vollhardt's retrosynthesis indicates (±)-isostrychnine could be obtained from compound **13** via a Heck reaction with the formation of ring E. The pentacyclic

compound **13** should be obtained through an N-alkylation conjugate addition from tetracyclic compound **14**, which in turn would be yielded from indole **15** by a Co-mediated cycloaddition reaction whereby rings D and F are installed.



Scheme 1.8 Vollhardt's retrosynthetic analysis of strychnine.

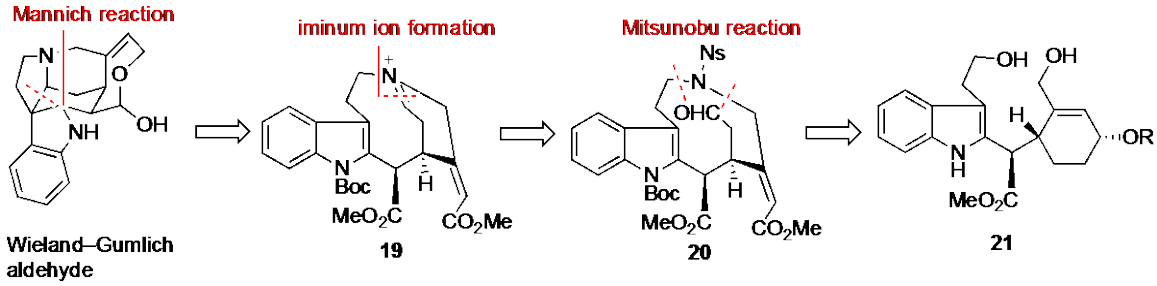
Martin and coworkers synthesized strychnine in 2001.[9] Their retrosynthesis is shown in Scheme 1.9. The same trend in favoring radical and pericyclic reactions over Lewis acid-base reactions is also recognizable in their work. Martin group's choice of pericyclic reaction was the hetero Diels-Alder reaction. Considering Martin's retrosynthetic analysis, the Wieland-Gumlich aldehyde could be obtained from pentacyclic compound **16** via functional group manipulations, which could be yielded from biomimetic rearrangement that results in the C and D ring formation from tetracyclic compound **17**. Compound **17** should result diene **18** via a hetero Diels-Alder reaction which installs ring E.



Scheme 1.9 Martin's retrosynthetic analysis of strychnine.

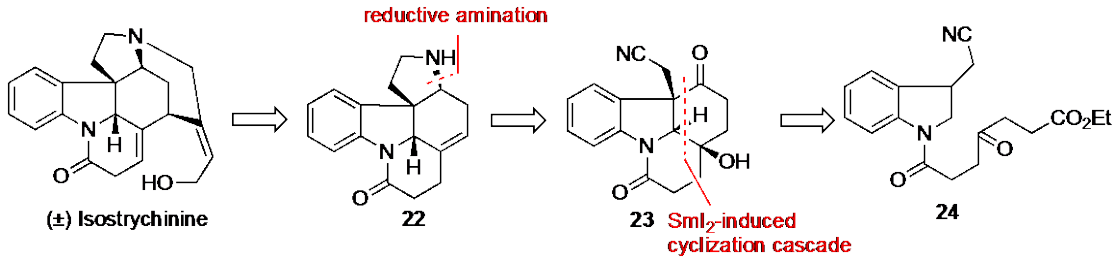
Fukuyama et al. published their strychnine synthesis in 2004.[9] The retrosynthetic analysis is outlined in Scheme 1.10. Their analysis indicates that the Wieland-

Gumlich aldehyde could be obtained from iminium ion **19** via a Mannich reaction that forms ring C and D. Coumpound **19** should yield from aldehyde **20** through an iminium ion formation which closes ring E. Amine **20** would result from alcohol **21** by a Mitsunobu reaction that installs the amine. The interesting feature about Fukuyama's synthesis is that no radical or pericyclic reaction was used.



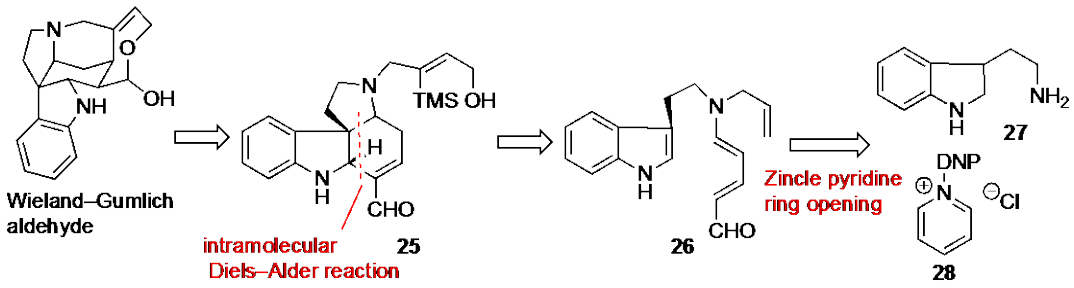
Scheme 1.10 Fukuyama's retrosynthetic analysis of strychnine.

In 2010 Reissig et al. reported their strychnine synthesis.[9] Scheme 1.11 depicts their retrosynthetic analysis. Similarly, a radical reaction, SmI_2 induced cyclization cascade reaction, was involved as a key step instead of a Lewis acid-base reaction. Reissig's retrosynthetic analysis indicates that (±)-isostrychnine could be obtained from pentacyclic compound **22**, which should be yielded from tetracyclic compound **23** by installation of ring C through a reductive amination reaction. The tetracyclic compound **23** would be obtained from indole **24** via SmI_2 induced cyclization cascade which results in the formation of ring D and F.



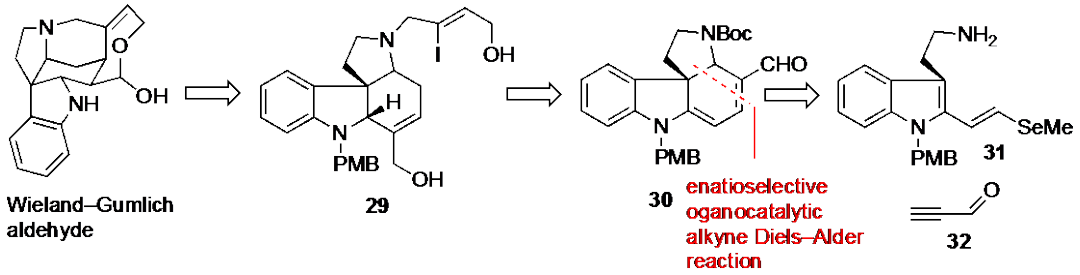
Scheme 1.11 Reissig's retrosynthetic analysis of strychnine.

Vanderwal's strychnine synthesis was published in 2011,[9] and Scheme 1.12 shows the retrosynthetic analysis. The group used an intramolecular Diels-Alder reaction to avoid the Lewis acid-base reaction to obtain a better yield and shorter route. In Vanderwal's analysis, the Wieland-Gumlich aldehyde could be obtained from tetracyclic compound **25** via an intramolecular Diels-Alder reaction which installs rings C and D. Compound **25** should be yielded from Diels-Alder precursor **26,** which should be formed from indole **27** and pyridinium **28** through a Zincle pyridine ring opening reaction.



Scheme 1.12 Vanderwal's retrosynthetic analysis of strychnine.

MacMillan and coworkers published their strychnine synthesis in 2011.[9] The retrosynthetic analysis is outlined in Scheme 1.13. The latest trend of favoring radical and pericyclic reactions over Lewis acid-base reactions is also the case in MacMillan's synthesis. To shorten the route and increase the yield their choice was to employ the enantioselective organo-catalytic alkyne Diels-Alder reaction as their key step, which belongs to the pericyclic reactions. According to MacMillan's retrosynthetic analysis, the Wieland-Gumlich aldehyde should be yielded from tetracyclic compound **29**, which would be obtained from compound **30**. Tetracyclic compound **30** could result diene **31** and alkyne **32** via an enantioselective organocatalytic alkyne Diels-Alder reaction, thereby forming ring C and D.



Scheme 1.13 MacMillan's retrosynthetic analysis of strychnine.

As elaborated on the strychnine example, the total synthesis has gradually been improved over the past 65 years. The first synthesis of strychnine was reported in 1954 with overall 28 steps and 0.0002 % yield. Whereas, the last outlined synthesis was made in 2011 with overall 12 steps and 6 % yield. The strategy to overcome the challenge linked with alkaloid synthesis was also in to use more radical and pericyclic reactions which decreased the step count and increased the yield. Essentially, for the further improvement in yield and decrease in the overall steps, more and more chemists are using radical and pericyclic reaction in their strategies for the syntheses of alkaloids with the aim to avoid the disadvantages of Lewis acid-base reaction. The first strychnine syntheses used more strategies based on Lewis acid-base reactions, whereas the recent strychnine syntheses have avoided this strategy by using more radical or pericyclic reactions.

Figure 1.2 shows the racemic strychnine synthesis made by different research groups. The diagram shows the synthesis step count over the course of time, the red numbers show the amount of newly formed C-C sigma bonds resulted from a single radical or pericyclic reaction step. The figure shows clearly how the step count decreases as the amount of C-C bonds formed by radical or pericyclic reaction increases.

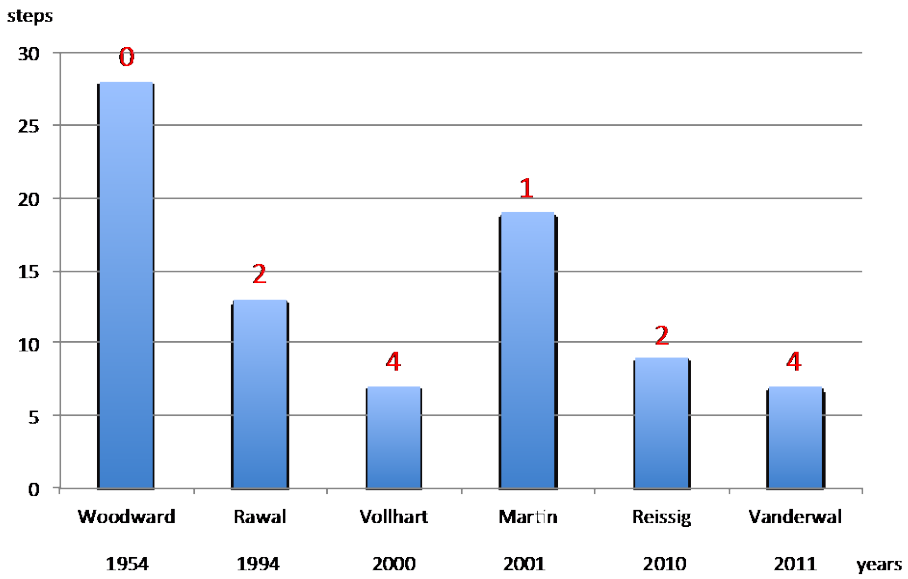


Figure 1.2 Racemic strychnine syntheses over the course of time.

Figure 1.3 shows the enantioselective strychnine synthesis published by different research groups. The racemic and enantioselective syntheses were analyzed separately to obtain a better comparison. The diagram shows the synthesis step count over the course of time, the red numbers show the amount of newly formed C-C sigma bonds resulted from a single radical or pericyclic reaction step. The figure gives the same conclusion as the racemic strychnine synthesis and confirms that the step count decreases as the amount of C-C bonds formed by radical or pericyclic reaction increases.

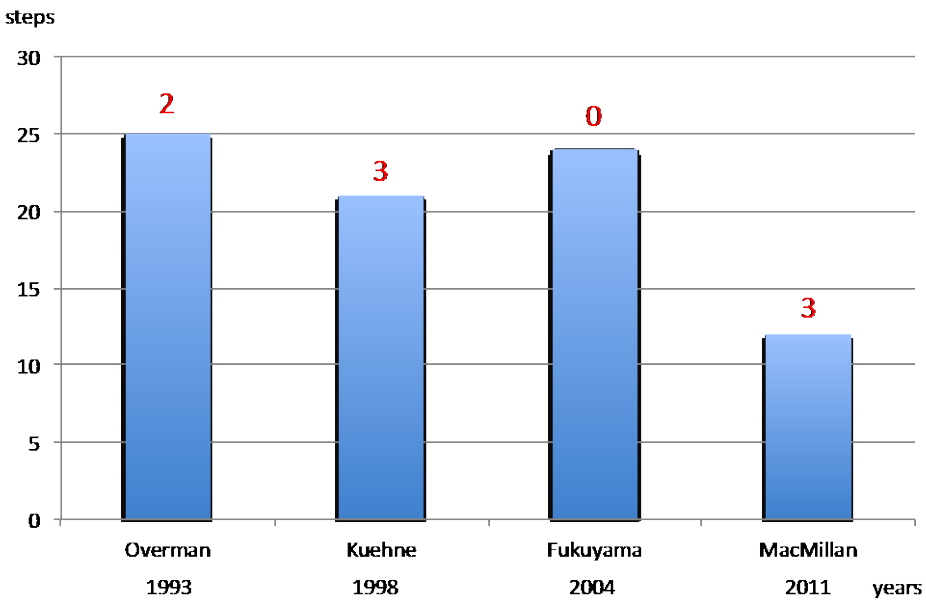


Figure 1.3 Enantioselective strychnine syntheses over the course of time.

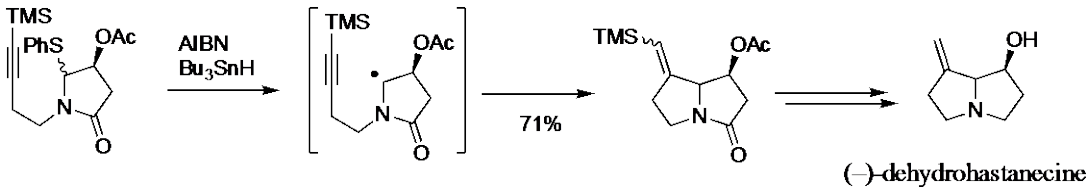
In conclusion, alkaloids have been known for many years as difficult targets. The difficulty in synthesizing them is mainly due to the properties of the nitrogen atom(s) in the compound. Therefore, the common strategies that chemists have pursued to overcome this challenge was to use Lewis acid-base strategy. This approach to the alkaloid syntheses either involved the protection of nitrogen atoms, or the employment of unreactive nitrogen groups, or the installation of the nitrogen atom in the late stage of the total synthesis. This approach resulted in high step counts and low yields. Better solutions were provided by the use of radical or pericylic reactions instead of Lewis acid-base reactions, which led to shorter synthesis and higher yields.

In addition, the reduction in step count and improvement in yield is due to the development of new methodologies and reagents by organic chemists such as the radical and pericyclic reactions. These new C-C bond formation reactions, based on radical and pericyclic reactions, made the cascade possible and enabled the installation of two rings in one step. Besides the traditional ways to overcome alkaloid syntheses the new methodologies have enriched the toolbox with more alternatives. Therefore, it is worthwhile to discover new methodologies or expand on existing strategies that can overcome the limitations and difficulties in the synthesis of alkaloids.

2. Reductive Synthesis of Aminal Radicals for Carbon–Carbon Bond Formation

2.1. Radicals in the Synthesis of Nitrogen Containing Molecules

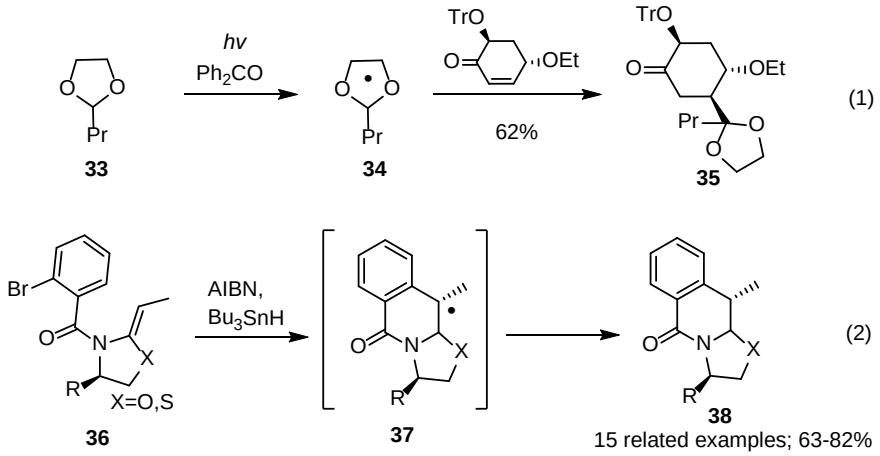
In order to mask the Lewis acid-base reactivity of nitrogen while progressing towards the target compound, synthetic chemists often resort to the use of protecting groups. One efficient way to avoid this is single-electron processes, such as radical reactions, which can be used to prevent the interference of the acid−base reactivity of nitrogen.[10] Radical reactions are generally tolerant of N–H bonds, O–H bonds, and heteroatom lone pairs; they are ideally suited to the synthesis of heteroatom-rich substrates. The method of incorporating carbon-centered radicals containing heteroatoms to C–C multiple bonds was introduced more than 50 years ago.[11] Hart and coworkers reported that N,S acetal was converted to the α-amido radical intermediate, which subsequently formed the bicycle through a 5-exodig radical reaction yielding the formal synthesis of (–)-dehydrohastanecine (Scheme 2.1).[12] The effect of the lone pair on the adjacent nitrogen is to increase the stability of α-aminoalkyl and α-amido radicals and forming C-C bonds with the unsaturated carbon atoms.[9] The advantage of this approach is the key disconnection of bonds that would be challenging to be formed with classic cationic or anionic reaction conditions and it has already been demonstrated in the synthesis of heterocycles and alkaloid natural products.



Scheme 2.1 C-C bond formation of α-aminoalkyl radical.

It is known that carbon-centered radicals having two adjacent heteroatoms form C–C bond after reacting with C–C multiple bonds. The acetal radical **34** was obtained from

acetal **33** by a homolytic C-H bond cleavage with photosensitized benzophenone. Compound **35** forms after the propagation step in which the radical **34** adds across the unsaturated enone system (Scheme 2.2, entry 1). The reaction between 2-bromobenzoyl enamides **36** and AIBN and Bu_3SnH is thought to form via N,S- and N,O- acetal radical intermediates **37** while the C–C bond forms to yield the ring fused compound **38** (Scheme 2.2, entry 2). [12]



Scheme 2.2 C-C bond formation of acetal radical.

Since the reactivity of acetal and α-aminoalkyl radicals are well known, the observation of a new reaction was thought to be formed in which the aminal radical adds to alkenes yielding a C-C bond. Based on findings of computational chemistry the aminal radicals are 1–2 kcal/mol lower in energy compared to the analogous α-aminoalkyl radicals.[13] This result suggested a promising selectivity in favor of aminal radical formation over carbon atoms containing a single nitrogen atom.

Carbon-centered radical reactions of nitrogen-rich functional groups, such as the aminal, would enjoy useful application in synthesis. Aminals can be conveniently prepared from condensation reactions, and also can functionalize several nitrogen atoms in the same step of carbon-centered radical reactions. Thus, the aminal functional group was identified as a particularly attractive substrate for radical-based bond-forming reactions. It illustrates some biologically active pharmaceuticals

bearing aminal(Figure 2.1), that are in the focus of many synthetic organic chemists.[14] Additionally, quinethazone and metolazone are some commercial pharmaceuticals that contain the aminal functionality.

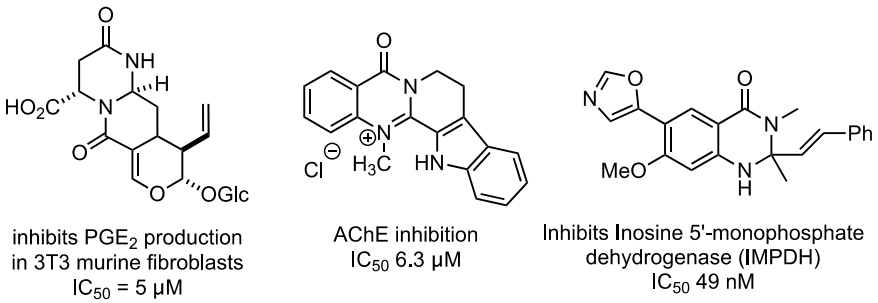
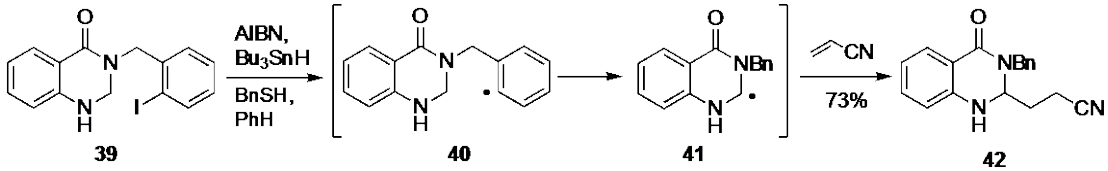


Figure 2.1 Nitrogen-rich pharmaceuticals which contain aminal.

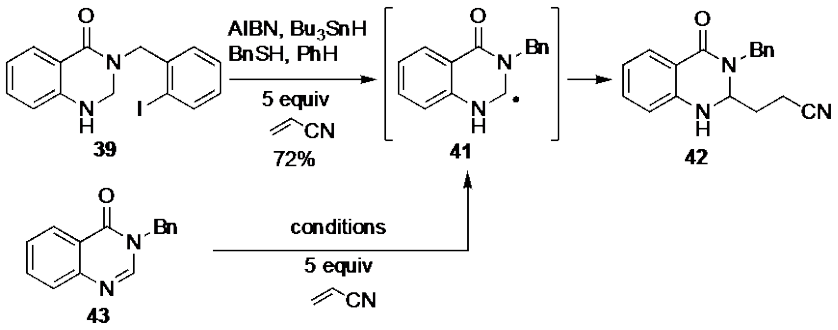
Previously, our lab reported the formation of C–C bonds using aminal radical intermediates.[15] The hydrogen atom abstraction of iodobenzyl-substituted aminals **39** undergo radical translocation **40** to generate aminal radical intermediates **41**. The aminal radicals add to a radical acceptor, such as an electron poor alkene to give products **42** with carbon−carbon bond formation (Scheme 2.3). It demonstrates a new methodology to construct an aminal group by forming a carbon−carbon bond allowing new strategies for synthesizing nitrogen-rich compounds.



Scheme 2.3 C-C bond formation of aminal radical by our lab

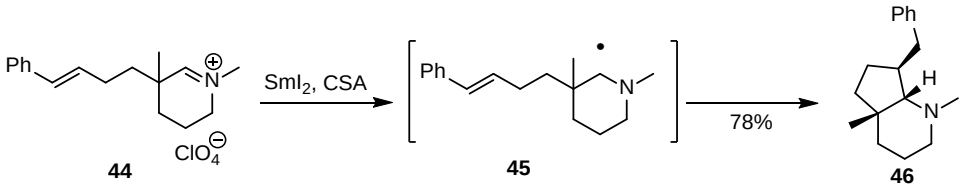
Despite the effectiveness of the radical translocation method to obtain aminal radical intermediates, it requires foul smelling or toxic reagents, leading us to develop alternative methods. Ideally, the starting materials should be easy to be obtained and should not need a 2-iodobenzyl substituent. Due to the success of starting material **39** in the radical translocation reaction product **41** should be formed if aminal radical **41** is obtained through an alternative radical acceptor (Scheme 2.4). It was expected that

the reaction of known[16] amidine **43** by protonation and single electron reduction should yield intermediate **41**.



Scheme 2.4 Alternative method to generate aminal radicals.

For many years, α-amino radicals have been formed from iminium ions by single electron reduction with the aid of a proton source.[17] Imminium ion **44** was converted by Martin to the fused bicyclic compound **46** via α-amino radical **45** (Scheme 2.5).
This strategy had the potential to be widened for the formation of aminal radicals because it was an alternative way to obtain an aminal radical in a regioselective fashion without a poor atom economy in contract to the C–X bond homolysis method.

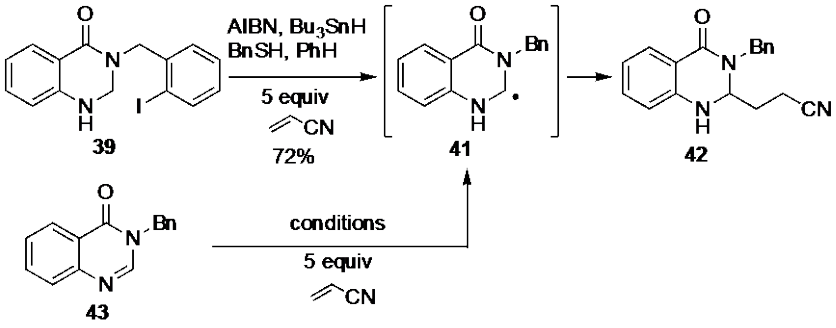


Scheme 2.5 Generation of α-amino radicals by single electron reduction of iminium ions

2.2. Result

Searching different conditions for this conversion, amidine **43** was produced with reductive condition in the presence of acrylonitrile (Table2.1). The use of Zn metal yielded no reaction and LiDBB induced the decomposition (entries 1–4). We found that aminal radical **41** could be generated by protonation and single electron reduction

of **43** with samarium(II) iodide and camphor sulfonic acid (entry 5). Although the reaction worked in the absence of a proton source, yields were significantly lower and some starting material remained unreacted (entry 6). Ammonium chloride was the best choice as proton source because it is mild, cheap, and provided high yields (entry 7). In comparison, the amidine reduction strategy had several advantages over the translocation strategy; it formed quickly at room temperature, no toxic or foul smelling additives were necessary, easy to handle, and higher yields were obtained.



entry	conditions	result
1	Zn (2.2 equiv), HOAc (0.1 M), rt	no reaction
2	Zn (2.2 equiv), HOAc (0.1 M), 118 °C	no reaction
3	LiDBB (2.5 equiv), CSA (1.1 equiv), THF (0.3 M), rt	decomposition
4	LiDBB (2.5 equiv), THF (0.3M), rt	decomposition
5	SmI_2 (2.5 equiv), CSA (1.1 equiv), THF (0.3 M), rt	90%
6	SmI_2 (2.5 equiv), THF (0.3 M), rt	57%
7	SmI_2 (2.5 equiv), NH_4Cl (1.1 equiv), THF (0.3 M), rt	99%

Table 2.1 Development of the amidine reduction reaction.

After determining the optimal reaction conditions, different substrate combinations were investigated. Quinazolinones which have the N-acyl amidine incorporated in the structure, show interesting biological activities,[18] and can be obtained from the corresponding aminobenzamide derivatives. The reaction between amidine, methyl and tertbutyl acrylates yielded **47b** and **47c** (Table 2.2). The quinazolinone containing a tethered alkene would still react with acrylonitrile **49a**, tert-butyl acrylate **49b**, and methyl acrylate **49c** in a bimolecular radical fashion disfavoring the unimolecular 5-exo-trig radical cyclization that contained the tethered alkene.

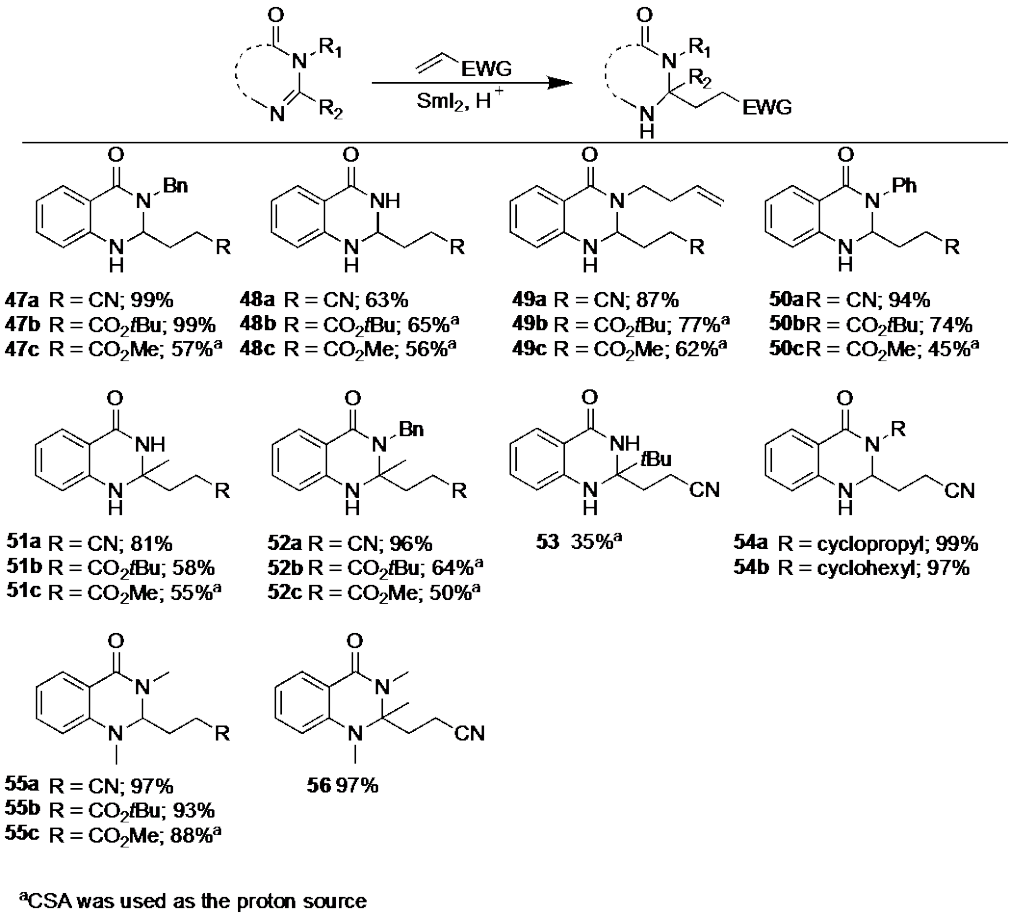


Table 2.2 Scope of the amidine and amidinium reduction reaction.

The execution of the amidine reduction strategy does not require a benzyl substituent and substrates that contain N-alkyl **54a,b**, N-aryl **54a-c**, and unprotected nitrogen **54a-c** all participated in the reaction. However, for the translocation alternative, completely substituted aminals needed to be formed in high yield through a reductive alkylation of the relevant amidines (**51a-c**, **52a-c**). Interestingly, the amidine containing an even more sterically demanding tert-butyl moiety reacted also to form the desired aminal (**53**). The reaction of dihydroquinazolinone-derived amidinium ion gave an excellent yield with methyl acrylate **55a**, tert-butyl acrylate **55b**, and acrylonitrile **55c**, and this condition also reacted perfectly with amidinium ion to produce fully substituted aminal **56**.

In summary, aminal radicals are obtained through the reduction of the relevant amidine and amidinium ions with the employment of a proton source. The C–C bonds are formed by the reaction of radical intermediates and radical acceptors in good yields, without using heavy metal hydrides or thiols. The reaction is versatile and can be used inter- and intramolecularly with high yields. Moreover, this methodology enables fully substituted aminal stereocenters formation in good yields.

3. Cycloadditions of Pyridinium Oxide

3.1. Intramolecular Pyridinium Oxide Cycloadditions: Regioselectivity, and Diastereoselectivity.

Polycyclic nitrogenous architectures are widespread in biologically active natural products. For example, the tropane alkaloids, exemplified by cocaine, are characterized by a 8-aza-bicyclo[3.2.1]octane structure,[19] **57**. Amaryllidaceae alkaloids such as siculine display a topologically distinct 1-azabicyclo[3.2.1]octane (**58**) core.[20] Homopumiliotoxin 223G is a quinolizidine (**59**) alkaloid isolated from poison dart frogs.[21] Finally, the intriguing structure of the galubalimima alkaloid,[22] himgaline, displays all of these component aza-bicyclic fragments in a 2-azatricyclo[4.4.1.$0^{2,7}$]undecane architecture (**60**) (Figure 3.1.1).

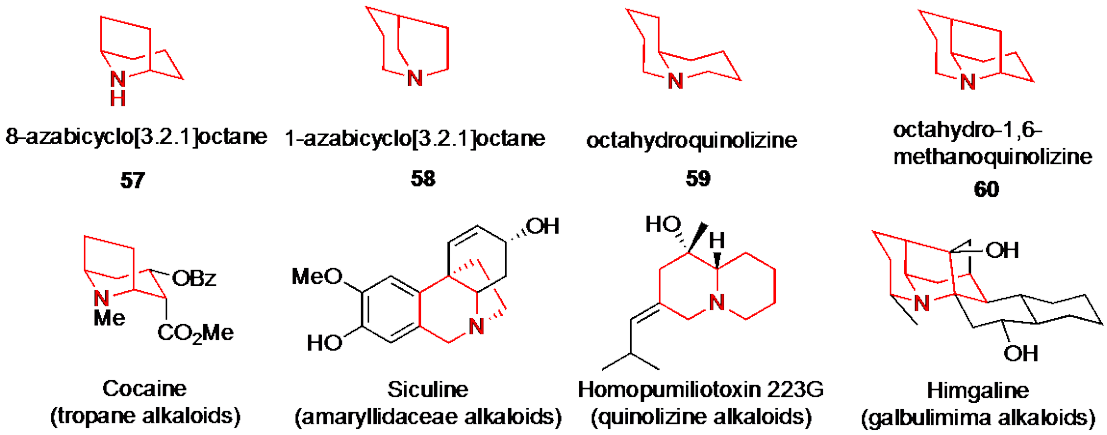
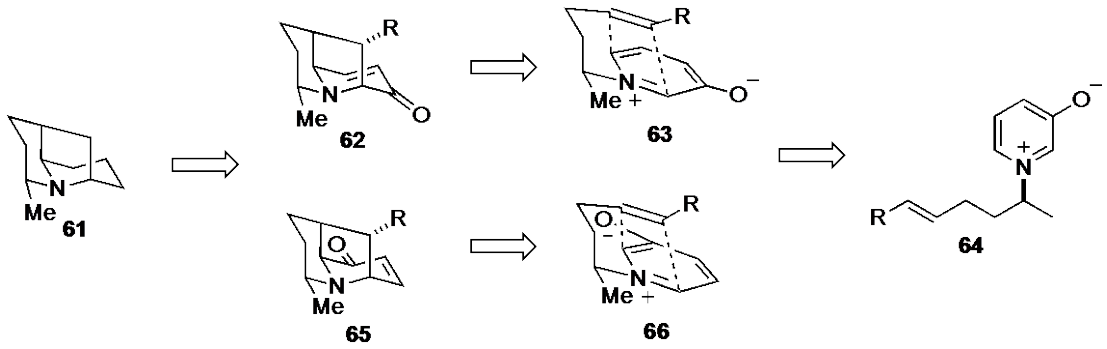


Figure 3.1.1 Polycyclic architecture featuring bridgehead nitrogen atoms.

Such bridged polycyclic alkaloids represent enduring challenges for synthetic chemists. A notable difficulty associated with the synthesis of the natural products shown are the stereogenic carbons bearing nitrogen; the himgaline structure displays stereogenic carbon atoms at all three adjacent positions. Many synthetic strategies have appeared to access nitrogenous bicycles, and particularly successful approaches create multiple rings in a single transformation with control of stereochemical configuration of the substituents.

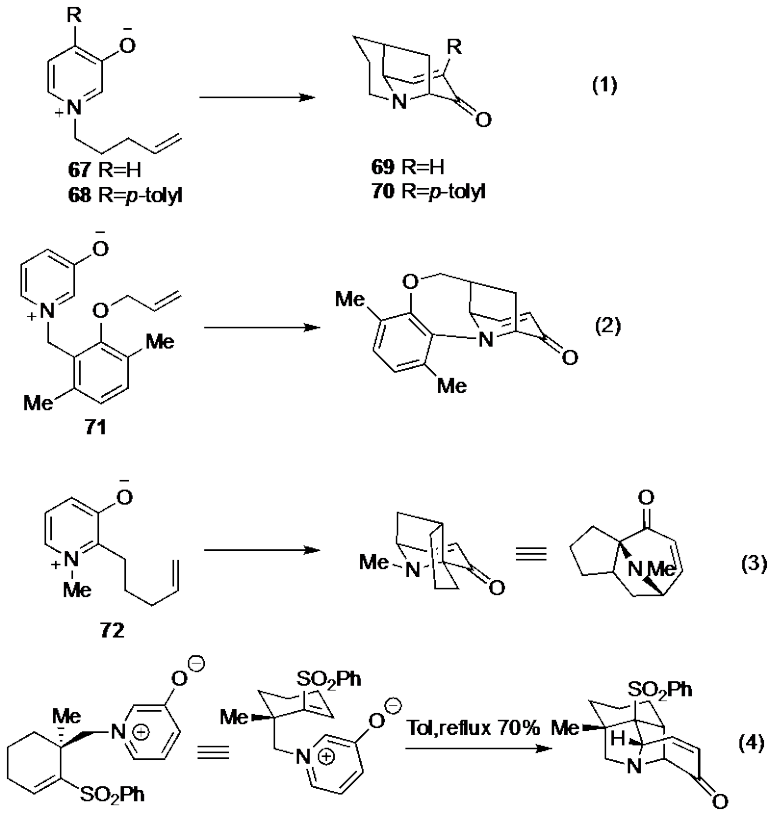
Cycloaddition reactions are particularly well-suited to the challenge of preparing multiple rings with control of stereochemistry, and we wondered if such polycyclic nitrogenous frameworks could be prepared using a suitable cycloaddition. We decided to focus on the tricyclic motif found in himgaline, complete with the equatorial methyl substituent (**60**). Any method capable of preparing this tricyclic architecture could, at least in principle, be used to construct any of the component bicyclic structures (**57**–**59**).

We envisioned tricyclic molecules such as **61** arising from a molecule such as enone **62**, which contains functional handles suitable for the construction of additional C–C bonds. Consideration of the topology of **62** suggested that an intramolecular dipolar cycloaddition of a pyridinium oxide with a tethered alkene dipolarophile (**63**) would give the required molecular connectivity. Moreover, it appeared that the diastereoselectivity of the cycloaddition may be controlled by a favored orientation of the molecular tether, which positions the methyl substituent in an equatorial position. The starting material for this cycloaddition would be the relatively simple pyridinium oxide **64** (Scheme 3.1.1). One question was the regiochemistry of the cycloaddition; specifically, regioisomeric tricycle **65** would arise from cycloaddition of conformer **66**, and it was unclear to us which pathway would be favored.



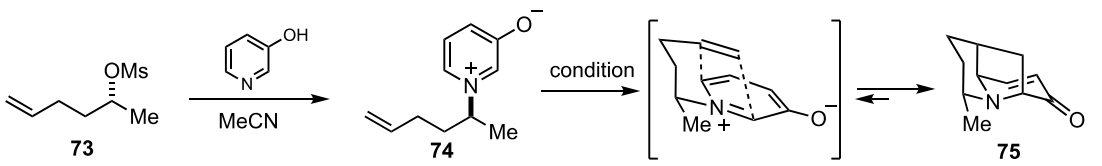
Scheme 3.1.1 Retrosynthetic analysis of azatricyclo[4.4.1.$0^{2,7}$]undecanes.

Pyridinium oxide cycloadditions are well known in the literature. Since the first report by Katrizky in 1988,[23] there have been dozens of intermolecular examples. Intermolecular pyridinium oxide cycloadditions require electron-poor alkene dipolarophiles (e.g. acrylonitrile, maleamide) for successful reactivity. Conversely, intramolecular pyridinium oxide cycloadditions are much fewer in number (Scheme 3.2). Simple *N*-pentenyl pyridinium oxide **67** and tolyl-substituted substrate **68** react to form **69** and **70**, respectively (Scheme 3.2, entry 1).[23] Substrate **71** featured a substituted tether between the dipole and dipolarophile (Scheme 3.2, entry 2).[24] Pyridinium oxide **72** featured a tethered dipolarophile linked to the pyridinium ring, rather than the nitrogen atom (Scheme 3.1.2, entry 3).[25] It is notable that these intramolecular examples do not require a polarized dipolarophile, and simple terminal alkenes participate in the reaction. Gin published an intramolecular cycloaddition where stereochemistry in the tether lead to good diasterofacial discrimination of the dipolarophile (Scheme 3.2, entry 4).[26] However, there has been no systematic study of substitution in such systems.



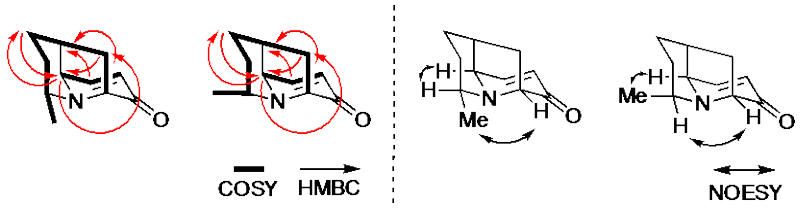
Scheme 3.1.2 Intramolecular pyridinium oxide cycloaddition.

We began our investigations by preparing cycloaddition substrate **74**. There are multiple synthetic strategies for preparing pyridinium oxides; however, we found the most convenient method was the substitution of alkyl mesylates with 3-hydroxypyridines. The pyridinium oxides was subjected under the published cycloaddition reaction conditions with no reaction in refluxing toluene, while heating to 210ºC in different solvents resulted in either no reaction or decomposition (Table 3.1.1, entry 1-3). Under the catalytic acid and base condition, there was no consumption of the starting material (Table 3.1.1, entry 4, 5). With the strong base, substrate was decomposed, and no desired product was obtained in the reaction with Lewis acid. (Table 3.1.1, entry 6,7). Under the condition which was heat the IRX-78 (OH form), we were able to yield cycloaddition product **75** in 60% yield with dr=4:1(Table 3.1.1, entry 8). The major product of the reaction was the anticipated product, which positions the tether methyl substituent in an equatorial orientation. The structure of the major and minor diastereomers was confirmed by 2D–NMR methods (Scheme 3.1.3). This result is consistent with our prediction, in which substrate control arises from the methyl substituent in an equatorial position. After screening basic reaction conditions, we found that K_2CO_3 is a suitable reagent in this cycloaddition reaction to give the 83% yield dr=5:1, whereby the decomposition may happen because of the basicity of Cs_2CO_3 (Table 3.1.1, entry 9-13). Sequestration of the potassium counterion had no effect on the reaction yield (Table 3.1.1, entry 14). The reaction was largely insensitive to the carbonate counter-cation, and both Ag_2CO_3 (93% yiel dr=6:1) and K_2CO_3 were effective in promoting the reaction (Table 3.1.1, entry 16,17). We found that polar solvents such as acetonitrile gave the best reaction rates, limited the formation of unwanted by products, and gave good selectivities for the major product. The best yields were obtained in butyronitrile at 130 ºC, and we settled on these as our standard conditions.



Entry	Reagent	Solvent	Tempearture	Result
1	-	Toluene	210°C	no Reaction
2	-	ACN	210°C	no Reaction
3	-	DMSO	150°C	decomposition
4	cat. HCl	ACN	160°C	no Reaction
5	cat. NaOH	ACN	160°C	no Reaction
6	NaOH	ACN	130-150°C	decomposition
7	$TiCl_4$	ACN	130-150°C	no Reaction
8	IRX-78 OH form	ACN	130°C	60%, dr=4:1
9	TBAI	ACN	130°C	57%, dr=4:1
10	NEt_3	ACN	130°C	38%, dr=4:1
11	K_2CO_3	ACN	130°C	83%, dr=5:1
12	Cs_2CO_3	ACN	130°C	decomposition
13	K_2HPO_4	ACN	130°C	82%, dr=5:1
14	K_2CO_3, 18-C-6	ACN	130°C	75%, dr=5:1
15	K_2CO_3, AgOAc	ACN	130°C	88%, dr=5:1
16	Ag_2CO_3	ACN	130°C	93%, dr=6:1
17	Ag_2CO_3	BuCN	130°C	87%, dr=7:1

Table 3.1.1 Development of the intramolecular pyridinium oxide cycloaddition reaction.



Scheme 3.1.3 Conformation of the cycloaddition product

We next evaluated additional substrates to investigate the ability of the intramolecular cycloaddition to create other complex bicyclic products. Substitution on the dipolarophile and the pyridinium oxide dipole was well tolerated (Table 3.1.2). Halogen substituents as well as alkyl substitution are tolerated on the pyridinium oxide. Substrate **77** features an additional carbocycle and leads to polycyclic product **78**. Moving the methyl substituent on the tether was possible, and **76** reacted to give good yields of the major product resulting from positioning of the methyl equatorial in the product. Substrate **92** includes two methyl substituents on the tether and cycloaddition leads to product **93**, where both methyl groups are equatorial. In this

case the product ratio was very high, and we could not detect (NMR, TLC) a minor isomer. Conversely, diastereomeric substrate **94** reacts and is required to position one methyl group axial. The reaction was successful; however, as expected, the product isomer ratio was low (~3:1). These result deomonstrate that the substitution on the molecular tether can control the stereochemistry of the cycloaddition. Unfortunately, cyclization of trisubstituted alkene dipolarophiles such as **96** and **98** were unsuccessful.

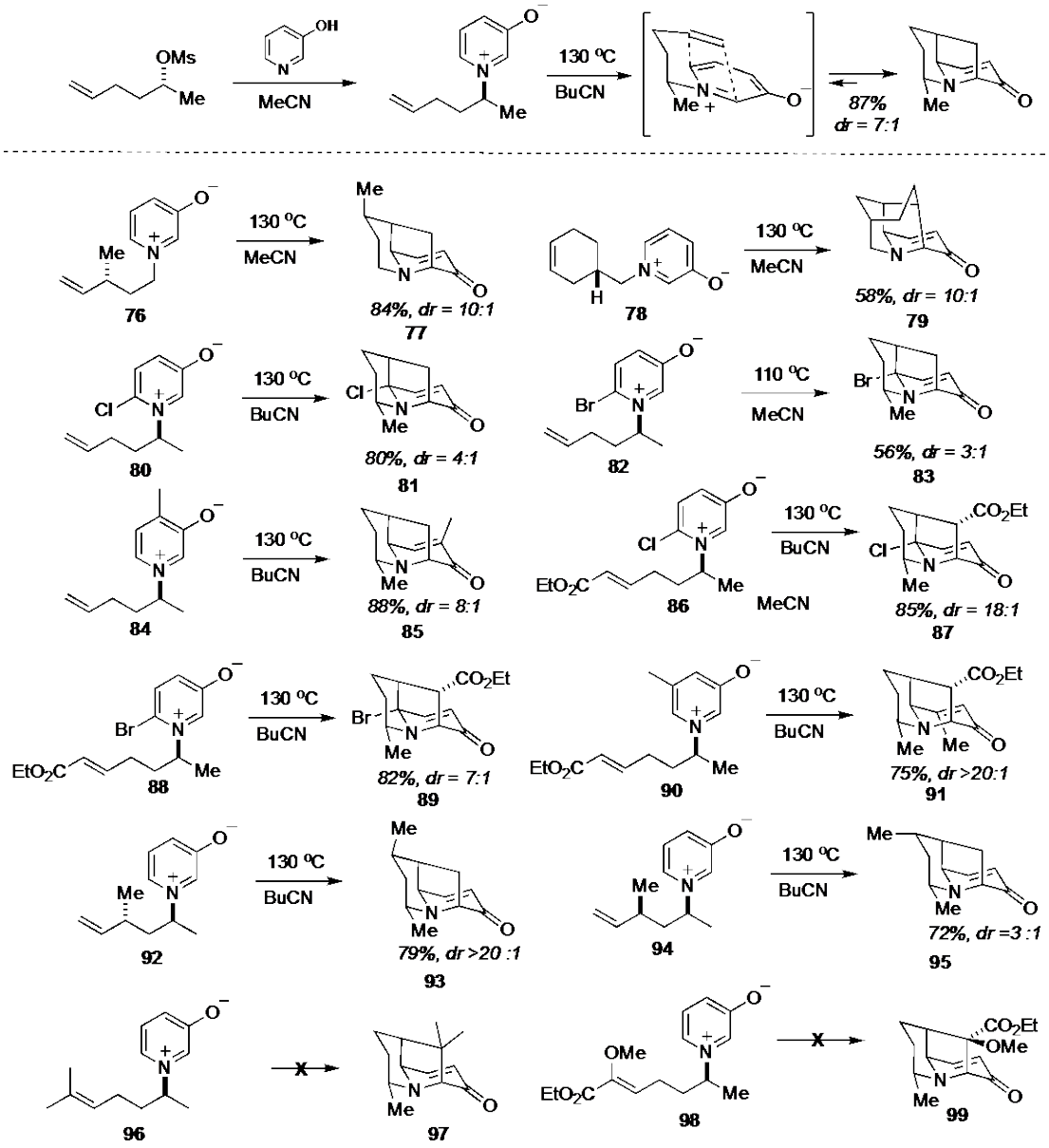
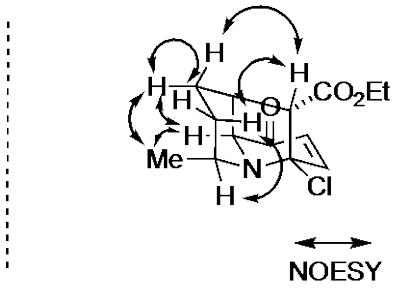


Table 3.1.2 Scope of the intramolecular pyridinium oxide cycloaddition reaction.

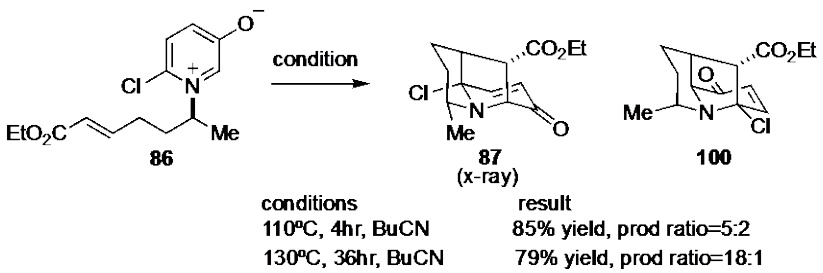
In all cases the product ratio was usually quite high, favoring a single major product with equatorial methyl substituent. All major products were separated and the isomer was characterized by 2D–NMR methods. In the case of **86**, we were able to obtain x-ray crystallographic confirmation of the major product structure **87 (**Scheme 3.1.4). Additionally, we isolated the minor product of the reaction, and found that it was structure **100**, which is the result of the regioisomeric bond formation and positioning of the methyl substituent axial. Presumably, this avoids *syn*-pentane interactions between the halogen and methyl groups. Other than these two cases, we did not characterize the minor component of the product mixture.



X-ray stucture of **87** NOESY correlation of **100**

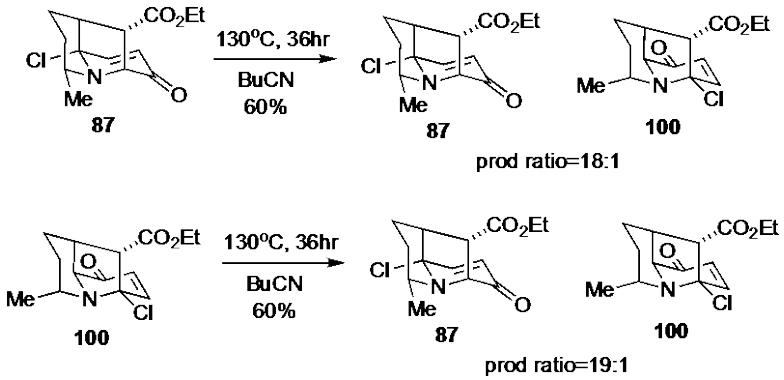
Scheme 3.1.4 Structure conformation of **87** and **100**.

Our original hypothesis was that the stereochemical outcome of the reaction was a result of kinetic control. Specifically, we anticipated that the transition state leading to the major product would be favored if the tether methyl was equatorial. This follows from Katritsky's analysis in his seminal publication on the intermolecular reaction. However, we began to suspect the reaction may actually be under thermodynamic control. We noticed that the product ratios were somewhat variable, and more forcing conditions (higher temperatures, longer reaction times) generally gave superior product ratios. Finally, when the reaction was stopped prior to full consumption of the starting material, the product ratios tended to be lower.



Scheme 3.1.5 Study of the minor product in the cycloaddition reaction.

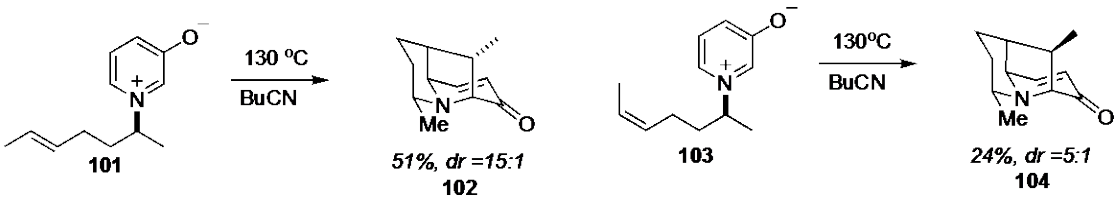
To unequivocally test whether the reaction was reversible, we isolated major product **87** and minor product **100**, and resubjected it to the reaction conditions respectively. Resubjecting compound **87** and compound **100** to the reaction conditions respectively resulted in equilibration to the same product ratio. This clearly demonstrates that this reaction is under thermodynamic control (Scheme 3.1.6).



Scheme 3.1.6 Study of the mechanism in the cycloaddition I.

We also wondered if the reaction was stereospecific with respect to dipolarophile substituents. We prepared geometrical isomers **101** and **103** and subjected them to our standard conditions (Scheme 3.7). *E*-Isomer **101** reacted to give product **102**, and *Z*-alkene isomer **103** gave **104**; the reaction is stereospecific with respect to the alkene substituents. This also suggests that although the reaction is reversible, it is likely proceeds with concerted bond formation. We observed that the cycloaddition of *E*-configured **101** was a smooth transformation that occurred under our normal conditions. However, *Z*-isomer **103** required longer reaction times. Moreover, the reaction yield was low, likely a result of the production of numerous other by

products. Analysis of crystal structure data for the related product **87** and models of **104** suggested that the pyrrolidine methyl substituent projects directly into the concave bicyclic structure leading to sever steric interactions. Such interactions would destabilize the transition state leading to this molecule, which in turn, would explain why more forcing conditions are required. Furthermore, these steric interactions would also explain the reluctance of trisubstituted alkenes in the cycloaddition reaction.



101 **102** **103** **104**

Scheme 3.1.7 Study of the mechanism in the cycloaddition II.

In conclusion, polycyclic nitrogenous architectures can be constructed by the regioselectivity and diastereoselectivity intramolecular pyridiniun oxide cycloaddition reaction. In our investigation, the selectivity arises from the substrate control induced by the orientation of the molecular tether. Furthermore, this cycloaddition is concerted and under thermodynamic control. This methodology will be useful for the alkaloid synthesis to build up multiple bonds and control stereocenters in one step.

3.2. Application of cycloaddition of pyridinium oxide in total synthesis: Progress towards the total synthesis of himgaline

The rainforest tree *Galbulimima belgraveana* is distributed in Northern Astralgonistia and Papua New Guinea. In Papua New Guinea, people used Galbulimima bark as a traditional medicine.[27] The bark was chewed and then swallowed with salt to reduce pain and fever, or it was mixed with leaves of *Homalomena* sp. to induce visions and a dream-like state. Likewise, people used Galbulimima bark in combination with tobacco leaves for the treatment of hair lice. The Galbulimima bark was found as a rich source of several complex alkaloids since 1965.[22] A total of 28 Galbulimima

alkaloids have been isolated, of which 22 have structures which have been elucidated.[28] According to their structural properties, Galbulimima alkaloids are divided into four classes (Figure 3. 2.1): (1) Class I can be represented by himbacine, which has shown potent muscarinic antagonist activity.[29] Based on series structure-activity relationships (SAR) studies, derivatives of himbacine have been developed.[30] Vorapaxar (SCH530348) was approved by FDA in 2014 as a treatment of acute coronary syndrome. Another class I compound (SCH205831) has shown strong antispasmodic activity.[31, 32] (2) Class II can be represented by himandrine (15 members). (3) Class III is represented by GB13 and himgaline. (4) Some miscellaneous compounds belong to Class IV, like GB17. Synthetic chemists are interested in class I began with the biological properties. Despite the potentially high activity of class I, the pharmacological properties of class II－IV remain unexplored. We speculate that the difficulty to screen bioactivity of class II－IV Galbulimima alkaloids was due to the trace amount of these compounds. Although the more structurally complex molecules of class II－IV have received attention from synthetic chemists, the number of steps leads to low yields of these alkaloids. Based on the high potential of class I, the pharmacological properties are possible to be explored if the efficient synthetic route of class II－IV can be found. Himgaline has one of the most complicated structures of the Galbulimima alkaloids. The challenges include a hexacyclic ring system, nine contiguous chiral centers, a tertiary amine attached to three chiral centers, and few funtional groups; these features make it the most difficult synthetic target of the Galbulimima alkaloids.

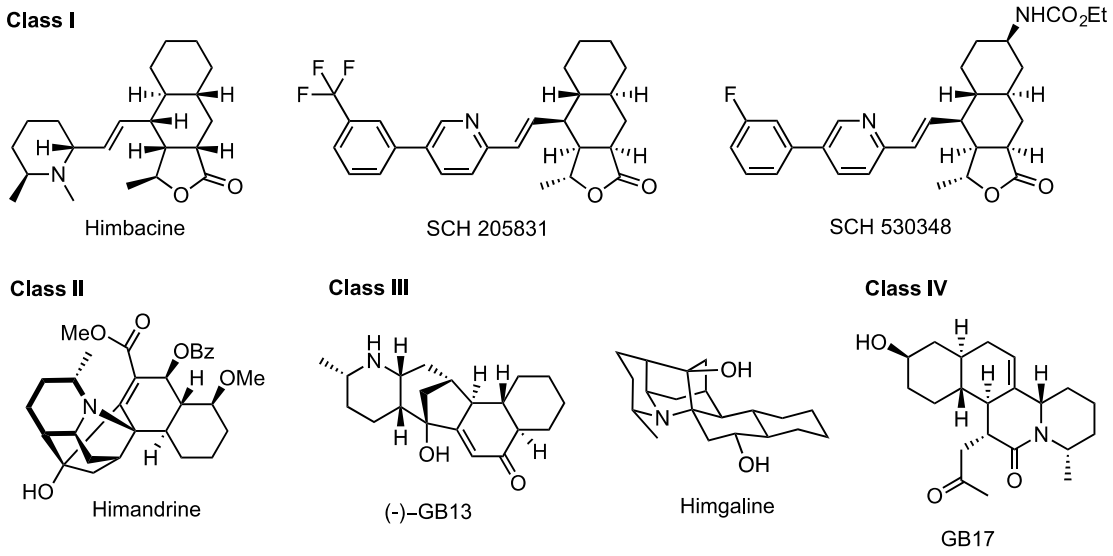
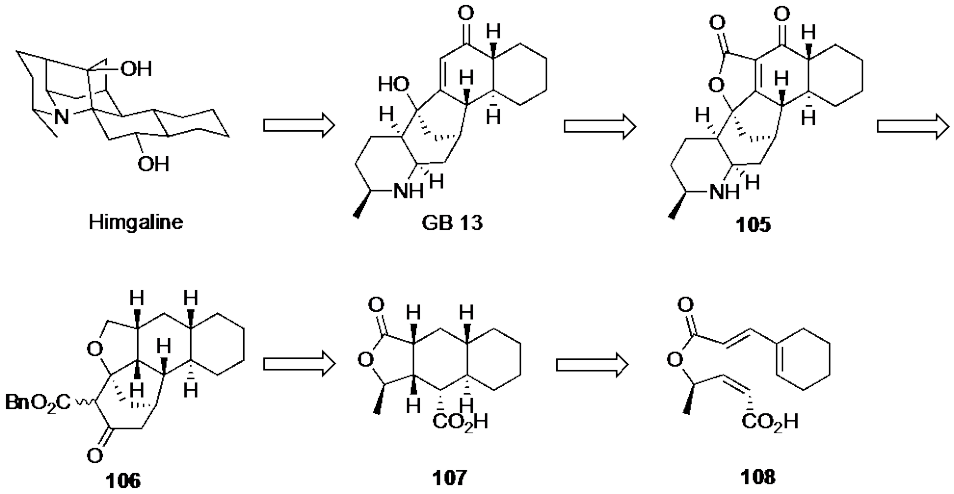


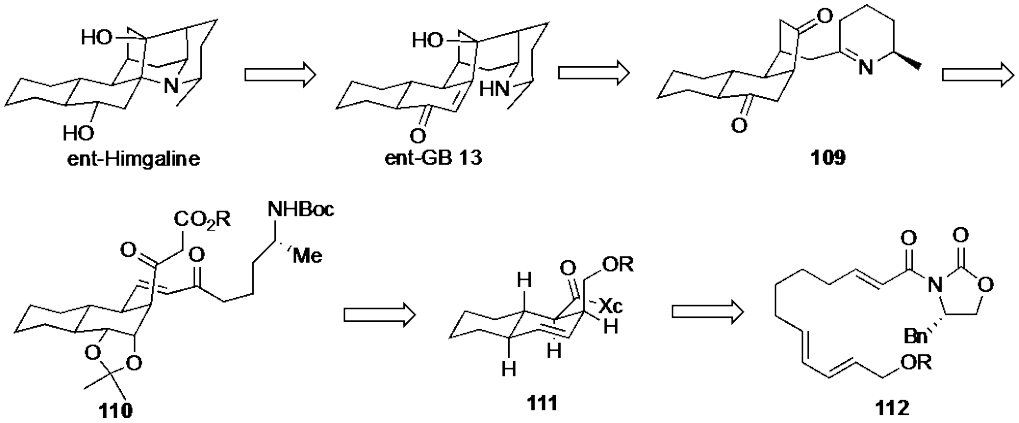
Figure 3.2.1 Representative Galbulimima alkaloids by class.

Shah and co-workers reported the first total synthesis of (–)-himgaline in 2006 (Scheme 3.2.1). [33] Himgaline could be converted from GB13 by conjugate addition and hydrogenation. Hexacyclic intermediate **105** would be converted to GB13 via a decarboxylative intramolecular conjugate addition reaction, followed by a retro conjugate reaction. The intermediate **105** could be built from the pentacyclic intermediate **106**, which was from the tricyclic carboxylic acid **107**. Pentacyclic intermediate **106** was built from a diastereoselective intramolecular Diels-Alder reaction of precursor **108**. This route took 33 steps to finish and the overall yield was 0.3%.



Scheme 3.2.1 Retrosynthetic analysis of himgaline by Shah.

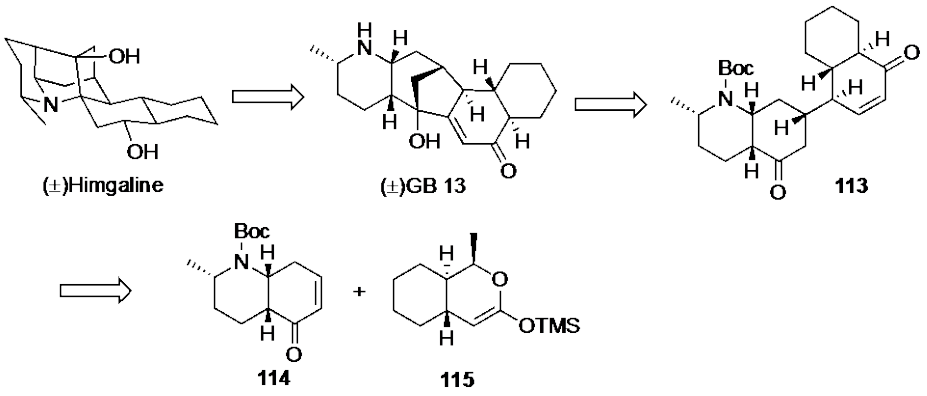
Evans and co-workers reported a total synthesis of ent-himgaline at about the same time (Scheme 3.2.2). [34] As in Shah's synthetic route, they converted ent-GB13 to ent-himgaline. The ent-GB13 was made from imine **109** by enamine aldol cyclization. Multiple steps were required to convert imine **108** from **110**, which was made by enantiopure *trans* decalin **111**. The Evans auxiliary controlled the enantioselective intramolecular Diels–Alder reaction to give *trans* decalin **111** from the triene **112**. Synthesizing the unnatural enantiomer, the Evans group was able to elucidate the absolute stereochemistry of himgaline, which was previously unknown. This route is still a beautiful synthesis, although it took them 32 steps to finish and the unnatural enantiomer of himgaline was obtained in 0.9% yield.



Scheme 3.2.2 Retrosynthetic analysis of ent-himgaline by Evans.

Ma and co-workers reported a racemic synthesis of himgaline in 2011 (Scheme 3.2.3). [35] As before, himgaline could be produed from GB13. Several steps including the key step, SmI_2-mediated carbonyl–alkene reductive coupling reaction of ketone **113**, gave the GB13 from the pentacyclic intermediate. The carbonyl–alkene reductive coupling precursor **113** was made from silyl enol ether **115** and α,β-unsaturated ketone **114**. This route took 25 steps to finish and the overall yield was 1.2%. It is a good strategy to build the pentacyclic intermediate by using a reductive coupling reaction.

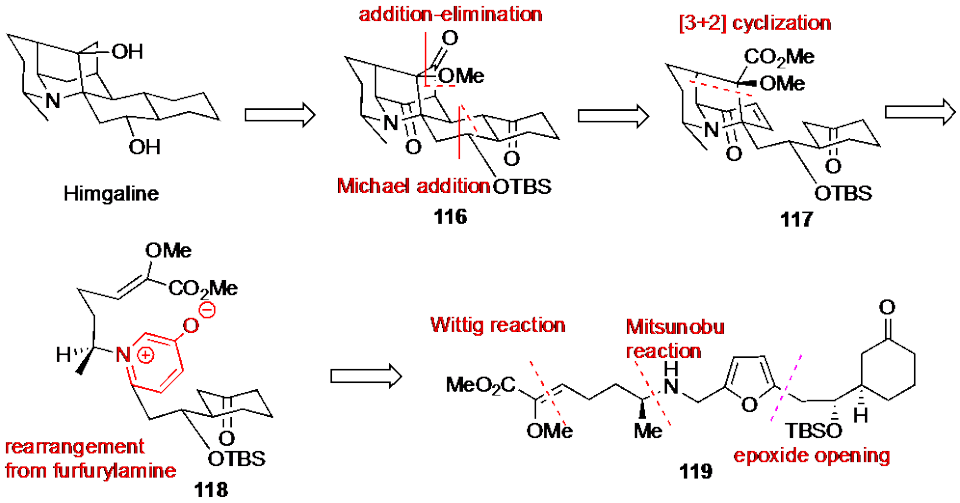
The advantage of our strategy to synthesize himgaline is the use of our intramolecular oxide cycloaddition which could reduce the synthesis steps significantly.



Scheme 3.2.3 Retrosynthetic analysis of ent-himgaline by Ma.

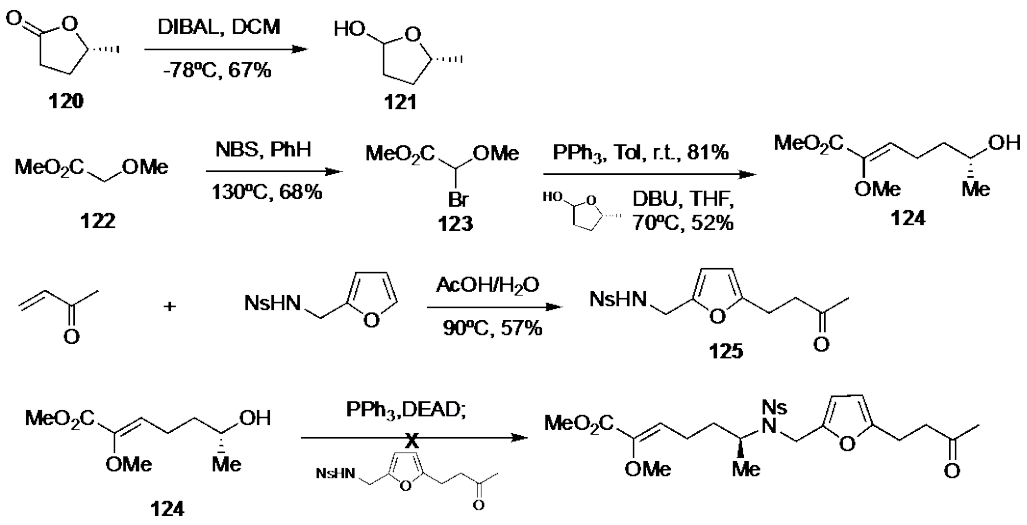
Our first generation retrosynthetic plan is described in Scheme 3.2.4. Himgaline could be broken down to triketone **116** by global deoxygenation and deprotection. The hexacyclic ring **116** could be constructed by the keto enone ester **117** by Michael addition and reductive Claisen condensation. The intramolecular pyridinium oxide cycloaddition, which is the key step of this synthetic route, is expected to selectively give heterotricyclic intermediate **117**. Br_2-mediated oxidative rearrangement of furanylamine **119** would form the 1,3-dipole **118**, which is the pyridinium oxide cycloaddition precursor. The linear product **119** could be made by Wittig reaction,

Mitsunobu reaction and the epoxide opening reaction. Minimization of $A^{1,3}$ strain would give the selective addition and condensation of the trisubstituted alkene. The only stereogenic center in the linear product **119** would be installed by Mitsunobu reaction of sulfonamide. 2,5- disubstituted furan could be installed by epoxide opening reaction.



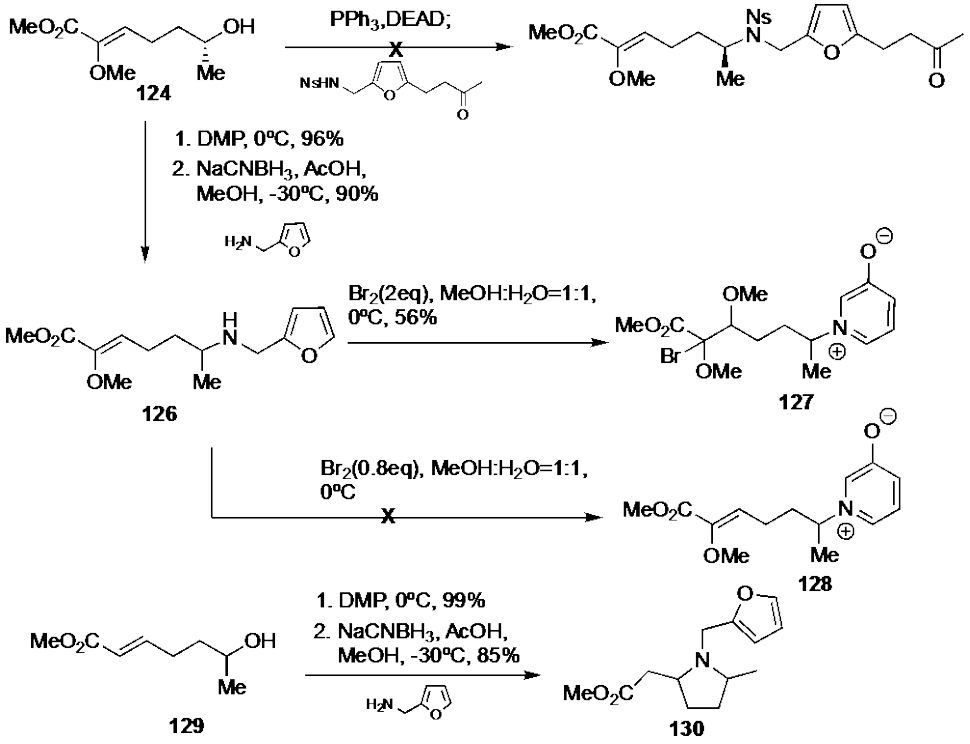
Scheme 3.2.4 The first generation of himgaline synthesis.

According to our plan, we prepared the starting material for the Wittig reaction as depicted in Scheme 3.2.5. We reduced the lactone **120** to the acetal **121** with DIBAL. Bromination of methyl 2-methoxyacetate **122** by NBS gave bromide **123**, and followed by the Wittig reaction with acetal **121** yielded the Mitsunobu reaction precursor **124** as an alcohol. For the other Mitsunobu reaction partner, we took the Ns protected furanylamine in the acidic condition in presence of methyl vinyl ketone to functionalize the C5 position of the furanylamine to obtain ketone **125**. With this two reaction partners in hand, we tried this reaction with several Mitsunobu reaction conditions, but we did not identify suitable conditions.



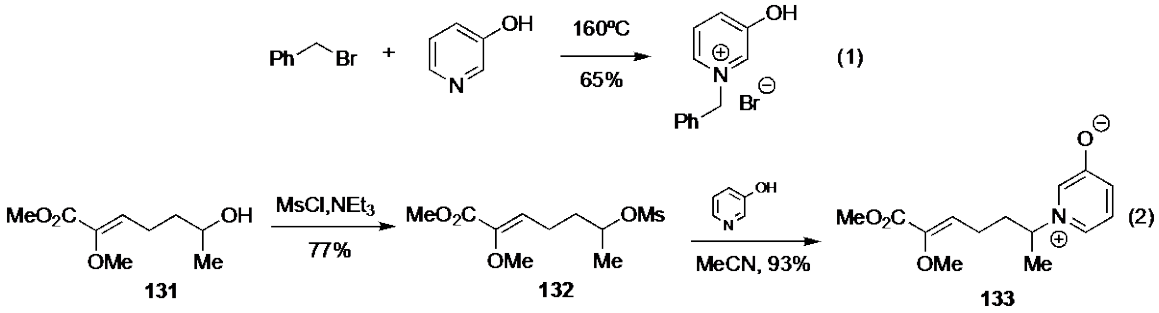
Scheme 3.2.5 Attempted amination by Mitsunobu reaction.

Because of this result, we investigated other ways to form the C-N bond such as reductive amination. (Scheme 3.2.6) We treated alcohol **124** with Dess-Martin periodinane (DMP) to gain the corresponding ketone and followed by reductive amination with furanylamine in the presence of sodium cyanoborohydride to generate the anime **126** as a pyridinium oxide formation precursor. We tried to set up pyridinium oxide formation using Gin's method, [26] but it only showed the brominated compound **127**. We thought that the second equivalent of bromine in Gin's conditions could cause this undesired reaction, so we changed the reaction condition to only 0.8 equivalents of bromine. However, we were not able to observe our desired product. We also suspected that the relative electron rich alkene in amine **126** causes the undesired bromination reaction, so we tried to start with the simpler alkene which is the vinyl ester. The reaction was set up with vinyl ester **129** under the same reaction condition as we installed the furanylamine, but we obtained the undesired conjugated addition product **130** back. At this point, we were facing the problem that the previous chemists did not deal with, so it was important to find other ways to form the pyridinium oxide in our system.



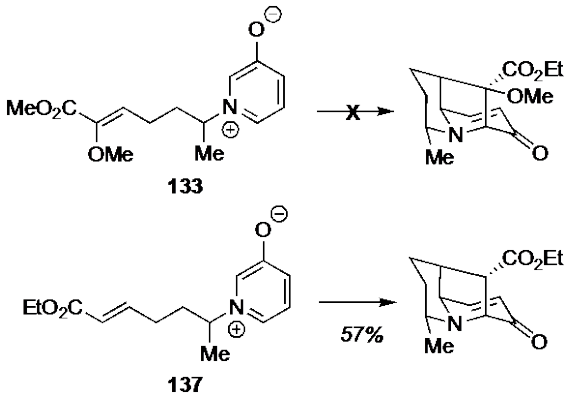
Scheme 3.2.6 Attempt to synthesize pyridinium oxide.

Aggarwal mixed benzyl bromide with 3-hydroxypyridine to yield the pyridinium oxide bromine salt[36] (Scheme 3.2.7, entry 1). Coming up with a similar idea, we treated the alcohol **131** under mesylation condition to yield mesylate **132**. The mesylate was stirred with 3-hydroxypyridine in acetonitrile at 130ºC to obtain the corresponding pyridinium oxide **133** successfully in good yield (Scheme 4.7, entry 2).



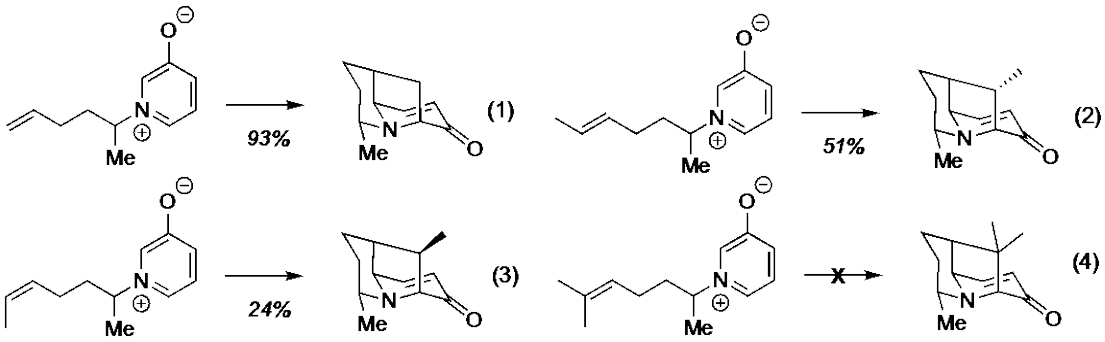
Scheme 3.2.7 Pyridinium oxide formation.

After having the pyridinium oxide **133** in hand, we started to run the key step of himgaline synthesis. The cycloaddition precursor **133** was treated under the standard reaction condition, but the starting material decomposed (Scheme 3.2.8). This result pushed us to investigate this intermolecular pyridinium cycloaddition reaction more in depth. First, we simplified the alkene and checked what the result was. The desired product was formed if the vinyl ester **137** was the starting material. This result showed that the diastereoselectivity and the regeoselectivity of this intramolecular pyridinium oxide cycloaddition matched our expectations.



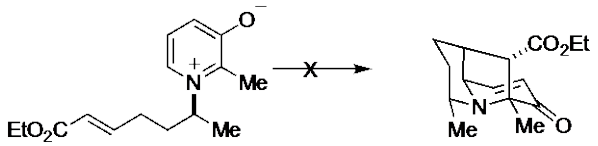
Scheme 3.2.8 Study of the cycloaddition of the trisubstituted alkene I.

In order to figure out the intramolecular pyridinium oxide cycloaddition, more cycloaddition reactions were attempted. The monosubstituted alkene reacted very well in this reaction in 93% yield (Scheme 3.2.9). The 1,2-disubstituted alkene under the cycloaddition reaction condition only gave 51% yield. The 1,1,2-trisubstituted alkene was decomposed slowly under reaction condition. These results indicated the hindrance of the alkene played a very important rule in the intramolecular pyridinium oxide cycloaddition, and also implied the 1,1,2-trisubstituted alkene might not work in this reaction.



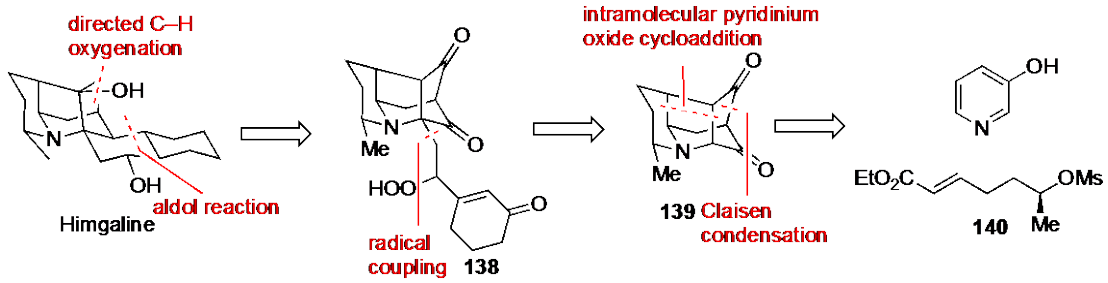
Scheme 3.2.9 Study of the cycloaddition of the trisubstituted alkene II.

We found that the trisubstituted alkene does not generate the intramolecular dipolar pyridinium oxide cycloaddition product. We also found that the substitution of the pyridinium ring at position 2 does not yield cycloaddition product (Scheme 3.2.10). Based on these results we proposed our third generation retrosynthesis of himgaline. This new route has the tricyclic core structure of himgaline already installed and the end game is the functionalization of both α ester α keto-amino methynes.



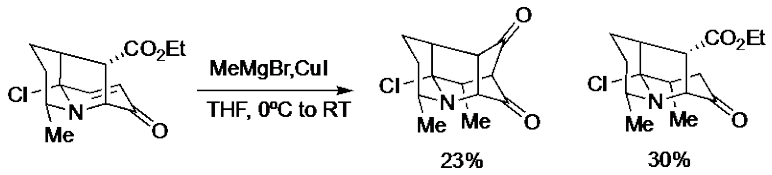
Scheme 3.2.10 Study of the cycloaddition of the 2-substituted pyridinium oxide.

Our retrosynthetic analysis of himgaline is outlined in Scheme 3.2.11. Himgaline could be obtained from peroxide **138** through aldol reaction and directed C-H oxygenation. The peroxide **138** should be available from the α-amino carbonyl **139** via a radical coupling reaction. Tetracyclic compound **139** should arise from hydroxypyridine and mesylate **140**.



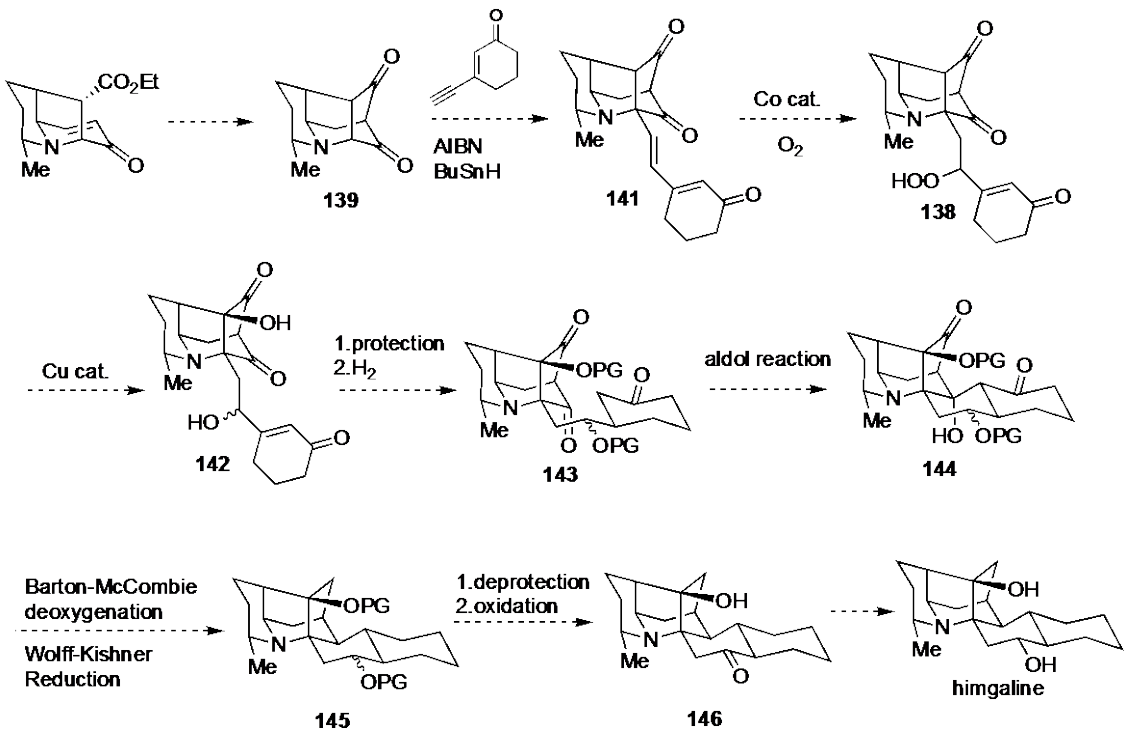
Scheme 3.2.11 The second generation of himgaline synthesis.

After the core structure of himgaline was successfully installed by the key step, we tried to construct the heterotetracyclic core of himgaline through Claisen condensation. The first successful reaction was the methylcuprate conjugate addition to the enone followed by Claisen condensation to give the heterotetracyclic core of himgaline (Scheme 3.2.12).



Scheme 3.2.12 Synthesis of heterotetracyclic core of himgaline.

In the future, the funtionalization of himgaline heterotetracyclic core to yield the natural product precursor is proposed in Scheme 3.2.13. The Claisen condensation will yield tetracyclic compound **139**, followed by the radical coupling with alkyne-enone to form dienone **141**.[37] The treatment of **141** with oygen with Co catalyst would produce peroxide **138**[38] and the treatment with Cu catalyst should result in hydroxyenone **142**.[39] After its protection and reduction, we should obtain the aldol precursor **143** which would lead under basic condition to the hexacyclic compound **144**. After the Barton-McCombie deoxygenation and Wolff-Kishner reduction compound **145** would be obtained. The subsequent deprotection and oxidation should yield himgaline precursor **146**, whereas the conversion of it to himgaline is a known reaction.

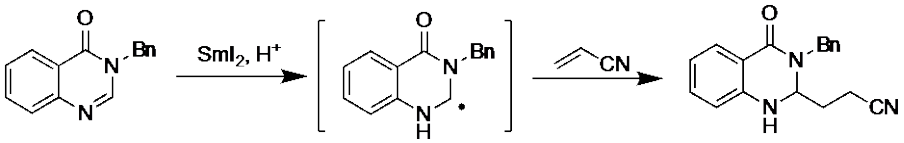


Scheme 3.2.13 Future work on the himgaline synthesis.

If this route succeeds as we expect, we would be able to reduce the step count to 16. This is because of the methodology we discovered that belongs to a pericyclic reaction. The stereo and regio-selective intramoleculer pyridinium oxide cycloaddition successfully forms two bonds and builds four stereocenters in a single step. This key cycloaddition reactions are particularly suitable to the challenge of preparing multiple rings with control of stereochemistry. It has been shown that the new methodology avoiding acid-base strategy would enhance the efficiency of the alkaloid synthesis.

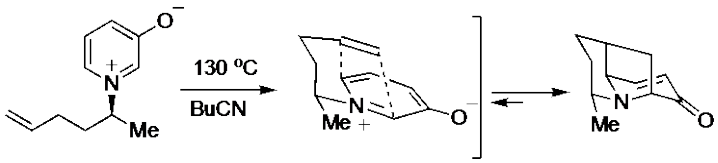
4. Conclusion

In conclusion, alkaloids have been known for many years as difficult targets. They are important for human health and are difficult to synthesize. The difficulty in synthesizing them is mainly due to the properties of the nitrogen atom(s) in the compound. Hence, the common strategies that chemists have pursued to overcome this challenge was to use Lewis acid-base strategy. This strategy to the alkaloid syntheses either involved the protection of nitrogen atoms, the employment of unreactive nitrogen groups, or the installation of the nitrogen atom in the late stage of the total synthesis. It resulted in high step counts and low yields. Better solutions were provided by the use of radical or pericyclic reactions instead of Lewis acid-base reactions, which led to shorter synthesis and higher yields. As supportive evidence, the investigation of development in the strychnine syntheses over the years clearly shows the conclusion that the step count decreases as the amount of C-C bonds formed by radical or pericyclic reaction increases. This application of this feature is noticeable in the latest alkaloid synthetic approaches made by well-known chemists, which have the following two common features. Using radical or pericyclic reactions (avoiding Lewis acid-base reactions) leads to shorter routes and higher yields. In addition, the reduction in step count and improvement in yield is due to the development of new methodologies and reagents by organic chemists such as the radical and pericyclic reactions. These new C-C bond formation reactions, based on radical and pericyclic reactions, made the cascade possible and enabled the installation of two rings in one step.

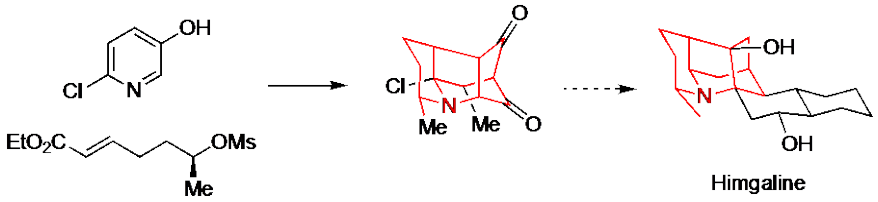


In order to further expand the synthetic strategies for the alkaloid syntheses, we also developed a methodology in which the reductive synthesis of aminal radicals were utilized for the Carbon-Carbon bond formation. In our methodology we showed that the C-C bond formation by aminal radicals were successfully obtained from amidine or amidinium. Besides the traditional ways to overcome alkaloid syntheses, the new

methodologies have enriched the toolbox with more alternatives. Hence, it is important to develop new methodologies based on radical and pericyclic reactions to expand the toolbox for synthetic organic chemists. It is worthwhile to discover new methodologies or expand on existing strategies that can overcome the limitations and difficulties in the synthesis of alkaloids even further.



Furthermore, we were also interested in another alkaloid known as himgaline. For its synthesis we developed a pyridnium oxide cycloaddition reaction. We investigated the intramolecular pyridinium oxide cycloaddition reactions on its regioselectivity and diastereoselectivity and were able to successfully showcase the cycloaddition of pyridinium oxide in the progress towards the total synthesis of himgaline core structure.



We have successfully installed the himgaline core, which is the aza-tetracyclic ring system, in four steps. Our key step of the himgaline synthesis is the intramolecular pyridinium oxide cycloaddition which controlled four new stereocenters and formed two bonds in a single step. In addition, polycyclic nitrogenous architectures can be constructed by the regioselectivity and diastereoselectivity intramolecular pyridiniun oxide cycloaddition reaction. These intramolecular pyridinium oxide cycloadditions have proven to be a useful tool for the successful polycyclic architecture construction such as in azatricyclo[4.4.1.$0^{2,7}$]undecanes. In our investigation, the selectivity arises from the substrate control induced by the orientation of the molecular tether. Furthermore, this cycloaddition is concerted and under thermodynamic control. This methodology will be useful for the alkaloid synthesis to build up multiple bonds and control stereocenters in one step. The facial diastereoselectivity and the

regioselectivity of the cycloaddition were described, and the cycloaddition was shown to be under thermodynamic control and stereospecific.

1. McGrath, N. A.; Brichacek, M.; Njardarson, J. T. “A Graphical Journey of Innovative Organic Architectures That Have Improved Our Lives” *J. Chem. Ed.* **2010,** *87*, 1348.
2. Hesse, M. *Alkaloid Chemistry*, Wiley, New York, **1981,** pp. 175–200.
3.Wuts, P. G. M.; Greene, T. W. *Protective Groups in Organic Sythesis.* 4th ed.: Wiley: Hoboken, NJ, **2007**, pp. 696–926.
4. Gates, M.; Woodward, R. B.; Newhall, W. F.; Künzli, R. *Org. React.* **1950**, *72*, 1141–1146.
5. Umihara, H.; Yokoshima, S.; Inoue, M.; Fukuyama, T. *Chem. Eur. J.* **2017**, *23*, 6993–6995.
6. Antropow, A. H.; Garcia, N. R.; White, K. L.; Movassaghi, M. *Org. Lett.* **2018**, *20*, 3647−3650.
7. Weiss, M.; Carreira, E. M. *Angew. Chem. Int. Ed.* **2011**, *50*, 11501 –11505.
8. Abd El-Gaber, M. K.; Yasuda, S., Iida, E., Mukai, C. *Org. Lett.* **2017**, *19*, 320−323.
9. Cannon, J. S.; Overman, L. E. *Angew. Chem. Int. Ed.* **2012**, *51*, 4288 – 4311.
10. Selected recent examples of radical reactions in alkaloid synthesis: (a) Baran, P. S.; Hafensteiner, B. D.; Ambhaikar, N. B.; Guerrero, C. A.; Gallagher, J. D. *J. Am. Chem. Soc.* **2006**, *128*, 8678−8693. (b) Movassaghi, M.; Schmidt, M. A. *Angew. Chem., Int. Ed.* **2007**, *46*, 3725−3728. (c) Zhang, H.; Curran, D. P. *J. Am. Chem. Soc.* **2011**, *133*, 10376−10378. (d) Palframan, M. J.; Parsons, A. F.; Johnson, P. *Tetrahedron Lett.* **2011**, *52*, 1154−1156.
11. Walling, C.; Huyser, E. S. *Org. React.* **1963**, *13*, 91–149. 12. Zhou, A.; Njogu, M. N.; Pittman, C. U. *Tetrahedron* **2006**, *62*, 4093–4102.
12. Choi, J. K.; Hart, D. J. *Tetrahedron.* **1985**, *41*, 3959–3971.
13. Urry, W. H.; Juveland, O. O. *J. Am. Chem. Soc.* **1958**, *80*, 3322–3328.
14. a) Bhonde, V. R.; Looper, R. E. *J. Am. Chem. Soc.* **2011**, *133*, 20172–20174; (b) Iwamoto, O.; Shinohara, R.; Nagasawa, K. Chem. Asian J. **2009**, 4, 277–285; (c) Fleming, J. J.; McReynolds, M. D.; Du Bois, J. *J. Am. Chem. Soc.* **2007**, *129*, 9964–9975; (d) Jacobi, P. A.; Martinelli, M. J.; Polanc, S. *J. Am. Chem. Soc.* **1984**, *106*, 5594–5598; (e) Tanino, H.; Nakata, T.; Kaneko, T.; Kishi, Y. *J. Am. Chem. Soc.* **1977**, *99*, 2818–2819; (f) Yang, J.; Wu, H.; Shen, L.; Qin, Y. *J. Am. Chem. Soc.* **2007**, *129*, 13794–13795; (g) Zuo, Z.; Xie, W.; Ma, D. *J. Am. Chem. Soc.* **2010**, *132*, 13226–13228; (h) Seo, J. H.; Liu, P.; Weinreb, S. M. *J. Org. Chem.* **2010**, *75*, 2667–2680; (i) Liu, P.; Seo, J. H.; Weinreb, S. M. *Angew. Chem., Int. Ed.* **2010**, *49*, 2000–2003; (j) Belmar, J.; Funk, R. L. *J. Am. Chem. Soc.* **2012**, *134*, 16941–16943; (k) Takano, S.; Sato, T.; Inomata, K.; Ogasawara, K. *J. Chem. Soc.*, Chem. Commun. **1991**, 462–464; (l) Morales, C. L.; Pagenkopf, B. L. *Org. Lett.* **2008**, *10*, 157–159; (m) Simone, F. D.;

Gertsch, J. *Angew. Chem., Int. Ed.* **2010**, *49*, 5767–5770; (n) Simone, F. D.; Gertsch, J.; Waser, J. *Angew. Chem., Int. Ed.* **2010**, *49*, 5767–5770; (o) Mizutani, M.; Inagaki, F.; Nakanishi, T.; Yanagihara, C.; Tamai, I.; Mukai, C. *Org. Lett.* **2011**, *13*, 1796–1799; (p) Xu, Z.; Wang, Q.; Zhu, J. *Angew. Chem., Int. Ed.* **2013**, *52*, 3272–3276.

15. Schiedler, D. A.; Vellucci, J. K.; Beaudry, C. M. *Org. Lett.* **2012,** *14*, 6092–6095.

16. Qin, F.; Wang, L.; Xia, J.; Qian, C.; Sun, J. *Synthesis* **2003**, 1241–1247.

17. Martin, S. F.; Yang, C. P.; Laswell, W. L.; Rüger, H. *Tetrahedron Lett.* **1988**, *29*, 6685–6687.

18. (a)Chawla, A.;Batra, C. *Int.Res. J.Pharm.***2013**, *4*, 49–58;(b)Rajput, R.; Mishra, A. P. *Int. J. Pharm. Pharm. Sci.* **2012**, *4*, 66–70; (c) Rajput, C. S.; Bora, P. S. *Int. J. Pharm. Bio Sci.* **2012**, *3*, 119–132.

19. Fodor, G.; Dharanipragada, R. *Nat. Prod. Rep.* **1994**, *11*, 443–450.

20. Jin, Z. *Nat. Prod. Rep.* **2013**, *30*, 849–868.

21. Michael, J. P. *Nat. Prod. Rep.* **2008**, *25*, 139–165.

22. (a) Binns, S. V.; Dunstan, P. J.; Guise, G. B.; Holder, G. M.; Hollis, A. F.; McCredie, R. S.; Pinhey, J. T.; Prager, R. H.; Rasmussen, M.; Ritchie, E.; Taylor, W. C. *Aust. J.* Chem. **1965**, *18*, 469-573. (b) Mander, L. N.; Prager, R. H. ; Rasmussen, M.; Ritchie, E.; Taylor, W. C. *Aust. J.* Chem. **1967**, *20*, 1473-1491. (c) Mander, L. N.; Prager, R. H. ; Rasmussen, M.; Ritchie, E.; Taylor, W. C. *Aust. J.* Chem. **1967**, *20*, 1705-1718. (d) Mander, L. N.; Willis, A. C. ; Herlt, A. J.; Taylor, W. C. *Tetrahedron Lett.* **2009**, *50*, 7089-7092.

23. Sammes, P. G.; Watt, R. A. *J. Chem. Soc., Chem. Commun.* **1976**, *13*, 367–368.

24. Orlek, B. S.; Sammes, P. G.; Weller, D. J. *J. Chem. Soc., Chem. Commun.* **1993**, 1412–1413.

25. Bromidge, S. M.; Archer, D. A. *J. Chem. Soc., Perkin Trans. 1* **1990**, 353–359.

26. Peese, K. M.; Gin, D. Y. *Chem. Eur. J.* **2008**, *14*, 1654 – 1665.

27. Thomas, B. *PNG. Med. J.* **2006**, *49*, 57-59.

28. Rinner, U.; Lentsch, C.; Aichinger, C. *Synthesis*. **2010**, *22*, 3763-3784.

29. Anwar-Ul, S.; Gilani, H.; Cobbin, L. B. *Naunyn-Schmiedebergs Arch. Pharmacol.* **1986**, *332*, 16-20.

30. (a) Darroch, S. A.; Taylor, W. C.; Choo, L. K.; Mitchelson, F. *Eur. J. Pharmacol.* **1990**, *182*, 131-136. (b) Malaska, M. J.; Fauq, A. H.; Kozikowski, A. P.; Aagaard, P. J.; McKinney, M. *Bioorg. Med. Chem. Lett.* **1995**, *5*, 61-66.

31. Chackalamannil, S.; Xia, Y.; Greenlee, W. J.; Clasby, M.; Doller, D; Tsai, H.; Asberom, T.; Czarniecki, M., Ahn, H.; Boykow, G.; Foster, C., Agans-Fantuzzi, J.; Bryant, M.; Lau, J.; Chintala, M. *J. Med. Chem*. **2005**, *48*, 5884-5887.

32. Siller-Matula, J. M.; Krumphuber, J.; Jilma, B. *Brit. J. Pharmacol.* **2010**, *159*, 502-517.

33. Shah, U.; Chackalamannil, S.; Ganguly, A. K.; Chelliah, M.; Kolotuchin, S.; Buevich, A.; McPhail, A. *J. Am. Chem. Soc.* **2006**, *128*, 12654-12655.

34. Evans, D. A.; Adams, D. J. *J. Am. Chem. Soc.* **2007**, *129*, 1048-1049.

35. Zi, W.; Yu, S.; Ma, D. *Chem. Asian. J.* **2011**, *6*, 573-579.

36. Aggarwal, V.K.; Grainger, R.S.; Newton, G.K.; Spargo, P.L.; Hobson, A.D.; Adams, H. *Org. Biomol. Chem.,* **2003**, *1*, 1884–1893.

37. P. J. Crick, N.S. Simpkins, A. Highton *Org. Lett. ,* **2011**, Vol. 13, No. 24, 6472-6475.
38. P. C. Too, Y. L. Tnay, S. Chiba, *Beilstein J. Org. Chem.* **2013**, 9, 1217-1225.
39. K. Sugamoto, Y. Matsushita, T. Matsui, *J. Chem. Soc., Perkin Trans. 1*, **1998**, 3989-3998.
40.Tauber, J; Rohr M; Walter, T; Erkel, G; Opatz, Till, *Org. Biomol. Chem.*, **2015**. 13. 7813-7821.
41.Hay, M. B.; Hardin, A. R.; Wolfe, J. P.; *J. Org. Chem.*, **2005**, 70, 3099-3107
42. Commercially available
43.Stangeland, E. L.; Sammakia, T.; *J. Org. Chem.*, **2004**, 69, 2381-2385
44.Tannert, R.; Milroy, L. G.; Ellinger, B.; Hu, T. S.; Arndt, H. D.; Waldmann, H.; *J. Am. Chem. Soc.*, **2010**, 132, 3063-3077
45.Warner, M. C.; Backvall, J. E.; *Eur. J. Org. Chem.*, **2015**, 2388-2393
46. Paradine, S. M.; Whit, M. C.; *J. Am. Chem. Soc.*, **2012**, 134, 2036-2039

General Experimental Details:

All reactions were carried out under an inert Ar atmosphere in oven-dried glassware. Flash column chromatography was carried out with SiliaFlash P60, 60 Å silica gel. Reactions and column chromatography were monitored with EMD silica gel 60 F254 plates and visualized with potassium permanganate, iodine, or vanillin stains. Toluene (PhMe) and methylene chloride (DCM) were dried by passage through activated alumina columns. Tetrahydrofuran (THF) was distilled from sodium and benzophenone and stored under an atmosphere of Ar. Butyl nitrite (BuCN) was distilled and stored under an atmosphere of Ar. Methyl acrylate and tert-butyl acrylate were purified by washing with aqueous NaOH, drying over MgSO4, and calcium hydride. These reagents were then distilled under vacuum prior to use. Acrylonitrile was distilled under vacuum prior to use. Samarium iodide solutions were prepared with THF distilled from sodium and benzophenone and were stored under an atmosphere of argon with vigorous stirring. The concentrations of the samarium iodide solutions were determined by iodometirc titration. All other reagents and solvents were used without further purification from commercial sources.
Instrumentation: FT-IR spectra were obtained on NaCl plates with a PerkinElmer Spectrum Vision spectrometer. Proton and carbon NMR spectra (^{1}H NMR and ^{13}C NMR) were recorded in deuterated chloroform ($CDCl_3$) unless otherwise noted on a Bruker 700 MHz Avance III Spectrometer with carbon-optimized cryoprobe and Bruker 400 MHz DPX-400 spectrometer and calibrated to residual solvent peaks. Multiplicities are abbreviated as follows: s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, sept = septet, br = broad, m = multiplet. FCC: flash column chromatography. Melting points were determined with a Cole–Parmer instrument and are uncorrected.

3-(3-benzyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanenitrile (47b) (general reductive alkylation procedure). To a solution of 3-benzylquinazolin-4(3H)-one75 (0.0327 g, 0.1390 mmol), NH_4Cl (0.0089g, 0.166 mmol), and acrylonitrile (0.05 mL, 0.76 mmol) in THF (0.46 mL, 0.3 M) was added a THF solution of SmI_2 (3.7 mL, 0.35 mmol) via syringe pump over a period of 1 hour. At this time, TLC indicated the consumption of 3-benzylquinazolin-4(3H)-one. The reaction mixture was diluted with half-saturated aqueous Rochelle salt. This biphasic mixture was extracted with ethyl acetate. The combined extracts were dried over MgSO4 and concentrated to give known adduct **47b** (0.0403 g, 0.1383 mmol, 99%) as a colorless oil.

methyl 3-(3-benzyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanoate (47c). *Following the general reductive alkylation procedure*, 3-benzylquinazolin-4(3H)-one (0.0332 g, 0.141 mmol), CSA (0.0358g, 0.154 mmol), methyl acrylate (0.065 mL, 0.70 mmol) in THF (0.50 mL, 0.3 M) were reacted with a THF solution of SmI_2 (3.45 mL, 0.35 mmol) to give known adduct 66 (0.0261 g, 0.080 mmol, 57%) as a colorless oil after purification by FCC (4:1 hexanes:EtOAc).

3-(4-oxo-3-phenyl-1,2,3,4-tetrahydroquinazolin-2-yl)propanenitrile(50a).
Following the general reductive alkylation procedure, 3-phenylquinazolin-4(3H)-one76 (0.0320 g, 0.144 mmol), NH_4Cl (0.0086g, 0.158 mmol), acrylonitrile (0.05 mL, 0.76 mmol) in THF (0.50 mL, 0.3 M) were reacted with a THF solution of SmI_2 (4.4 mL, 0.36 mmol) to give **50a** (0.0375 g, 0.135 mmol, 94%) as a colorless oil.

Data for **50a**: R*f* 0.40 (1:1 hexanes:EtOAc); mp = 155–156 ºC; IR (thin film) 2929, 2246, 1638, 1496, 1154, 757 cm-1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (dd, *J* = 7.7, 1.2 Hz, 1 H), 7.41 (m, 5 H), 7.33 (t, *J* = 7.7 Hz, 1 H), 7.01 (t, *J* = 7.7 Hz, 1 H), 6.84 (d, *J* = 8.1 Hz, 1 H), 5.20 (dt, *J* = 9.0, 4.5 Hz, 1 H), 4.72 (d, *J* = 4.5 Hz, 1 H), 2.36 (m, 2 H), 2.10 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT) δ *C* 161.8, 143.6, 140.1, 118.5, 118.2; *C*H 134.0, 128.9, 129.5, 129.2, 127.4, 127.0, 121.0, 117.0; *C*H2 28.5, 13.7; HRMS (EI) calcd for C17H15N3O [M+]: 277.1215, found 277.1227.

Methyl 3-(4-oxo-3-phenyl-1,2,3,4-tetrahydroquinazolin-2-yl)propanoate (50c).
Following the general reductive alkylation procedure, 3-phenylquinazolin-4(3H)-one (0.0312 g, 0.140 mmol), CSA (0.0358 g, 0.154 mmol), methyl acrylate (0.07 mL, 0.70 mmol) in THF (0.50 mL, 0.3 M) were reacted with a THF solution of SmI_2 (4.6 mL, 0.35 mmol) to give **50c** (0.0195 g, 0.0629 mmol, 45%) as a colorless oil after purification by FCC (4:1 hexanes:EtOAc).

Data for **50c**: R*f* 0.44 (1:1 hexanes:EtOAc); mp = 79–80 ºC; IR (thin film) 2951, 1732, 1634, 1496, 1169, 756 cm-1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 7.8 Hz, 1 H), 7.42 (m, 4 H), 7.34 (t, *J* = 7.6 Hz, 1 H), 7.29 (m, 1 H), 6.91 (t, *J* = 7.6 Hz, 1 H), 6.72 (d, *J* = 8.1 Hz, 1 H), 5.19 (dd, *J* = 8.5, 3.8 Hz, 1 H), 3.60 (s, 3 H), 2.35 (m, 2 H),

2.22 (m, 1 H), 2.13 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT) δ *C* 173.3, 162.3, 144.8, 140.4, 117.4; *C*H 133.7, 129.3, 129.1, 127.1, 127.0, 119.8, 115.7, 71.3; *C*H2 29.7, 28.5; *C*H3 51.8; HRMS (ESI) calcd for C18H18N2O3 [M+H]: 310.1318, found 310.1304.

***tert*-butyl 3-(4-oxo-3-phenyl-1,2,3,4-tetrahydroquinazolin-2-yl)propanoate 50b** .
Following the general reductive alkylation procedure, 3-phenylquinazolin-4(3H)-one (0.0313 g, 0.141 mmol), NH_4Cl (0.0083 g, 0.155 mmol), *tert*-butyl acrylate (0.11 mL, 0.71 mmol) in THF (0.50 mL, 0.3 M) were reacted with a THF solution of SmI_2 (4.3 mL, 0.35 mmol) to give **50b** (0.0367 g, 0.104 mmol, 74%) as a colorless oil after purification by FCC (3:1 hexanes:EtOAc).

Data for **50b**: R*f* 0.65 (1:1 hexanes:EtOAc); IR (thin film) 2977, 1724, 1685, 1495, 1152, 753 cm-1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (dd, *J* = 7.7, 1.6 Hz, 1 H), 7.42 (m, 4 H), 7.34 (ddd, *J* = 8.1, 7.6, 1.6 Hz, 1 H), 7.29 (tt, *J* = 6.6, 2.1 Hz, 1 H), 6.91 (t, *J* = 7.8 Hz, 1 H), 6.73 (d, *J* = 8.1 Hz, 1 H), 5.18 (dd, *J* = 8.4, 4.2 Hz, 1 H), 2.28 (m, 2 H), 2.14 (m, 2 H), 1.37 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT) δ *C* 172.1, 162.3, 145.0, 140.5, 117.2, 81.0; *C*H 133.7, 129.3, 129.1, 127.2, 127.0, 119.7, 115.5, 71.4; *C*H2 31.1, 28.5; *C*H3 28.0; HRMS (ESI) calcd for C21H24N2O3Na[M+Na]: 375.1685, found 375.1674.

methyl 3-(4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanoate 48b.
Following the general reductive alkylation procedure, quinazolin-4(3H)-one (0.0218 g, 0.149 mmol), CSA (0.0381g, 0.164 mmol), methyl acrylate (0.08 mL, 0.89 mmol) in THF (0.50 mL, 0.3 M) were reacted with a THF solution of SmI_2 (3.8 mL, 0.37 mmol) to give **48b** (0.0195 g, 0.083 mmol, 56%) as a colorless oil.

Data for **48b**: R*f* 0.25 (1:4 hexanes:EtOAc); IR (thin film) 2951, 1725, 1653, 1438, 1382, 1155, 756 cm-1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (dd, *J* = 7.7, 1.4 Hz, 1 H), 7.30 (ddd, *J* = 8.1, 7.3, 1.5 Hz, 1 H), 6.85 (td, *J* = 7.5 1.0 Hz, 1 H), 6.66 (d, *J* = 8.0 Hz, 1 H), 6.46 (s, 1 H), 5.05 (t, *J* = 4.6 Hz, 1 H), 3.71 (s, 3 H), 2.64 (dt, *J* = 17.1, 6.6 Hz, 1 H), 2.57 (dt, *J* = 17.1, 6.6, Hz, 1 H), 2.12 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT) δ *C* 173.9, 165.3, 147.2, 115.6, 81.1; *C*H 133.9, 128.5, 119.4, 114.8, 64.7; *C*H2 29.9, 28.1, *C*H3 52.1; HRMS (EI) calcd for C12H14N2O3 [M+]: 234.1005, found 234.1016.

***tert*-butyl 3-(4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanoate 48c**.
Following the general reductive alkylation procedure, quinazolin-4(3H)-one (0.0238 g, 0.162 mmol), NH_4Cl (0.0096 g, 0.178 mmol), *tert*-butyl acrylate (0.12 mL, 0.81 mmol) in THF (0.50 mL, 0.3 M) were reacted with a THF solution of SmI_2 (5.0 mL, 0.41 mmol) to give **48c** (0.0289 g, 0.105 mmol, 65%) as a colorless oil after purification by FCC (1:3 hexanes:EtOAc).

Data for **48c**: R*f* 0.48 (1:2 hexanes:EtOAc); mp = 114–115 ^{o}C; IR (thin film) 2978, 2830, 1728, 1677, 1469, 1367, 1154, 757 cm-1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86

(dd, *J* = 7.7, 1.4 Hz, 1 H), 7.28 (td, *J* = 7.6, 1.6 Hz, 1 H), 6.96 (s, 1 H), 6.82 (td, *J* =7.5 1.0 Hz, 1 H), 6.64 (d, *J* = 8.0 Hz, 1 H), 5.01 (t, *J* = 4.6 Hz, 1 H), 4.56 (s, 1 H), 2.55 (dt, *J* = 17.0, 7.0 Hz, 1 H), 2.45 (dt, *J* = 17.0, 6.7, Hz, 1 H), 2.01–2.13 (m, 2 H), 1.44 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT) δ *C* 172.8, 165.5, 147.4, 115.5, 81.1; *C*H 133.8, 128.4, 119.1, 114.7, 64.8; *C*H2 29.9, 29.6, *C*H3 28.3; HRMS (EI) calcd for C15H20N2O3Na [M+Na]: 299.1372, found 299.1379.

3-(3-(but-3-en-1-yl)-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanenitrile 49a. *Following the general reductive alkylation procedure*, 3-(but-3-en-1-yl)quinazolin-4(3H)-one (0.0276 g, 0.138 mmol), NH_4Cl (0.0086 g, 0.160 mmol), acrylonitrile (0.05 mL, 0.76 mmol) in THF (0.46 mL, 0.3 M) were reacted with a THF solution of SmI_2 (3.7 mL, 0.35 mmol) to give **49a** (0.0307 g, 0.120 mmol, 87%) as a colorless oil after purification by FCC (1:1 hexanes:EtOAc).

Data for **49a**: R*f* 0.31 (1:1 hexanes:EtOAc); IR (thin film) 2916, 2246, 1632, 1469, 1394, 759 cm-1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (dd, *J* = 7.7, 1.4 Hz, 1 H), 7.32 (td, *J* = 7.6, 1.5 Hz, 1 H), 6.93 (t, *J* = 7.5, 1.0 Hz, 1 H), 6.77 (d, *J* = 8.1 Hz, 1 H), 5.84 (ddt, *J* = 17.0, 10.2, 6.8 Hz, 1 H), 5.12 (dd, *J* = 17.1, 1.6 Hz, 1 H), 5.07 (d, *J* = 10.3 Hz, 1 H), 4.75 (dd, *J* = 9.2, 3.6 Hz, 1 H), 4.20 (dt, *J* = 13.7, 6.9 Hz, 1 H), 2.92 (dt, *J* =14.0, 7.1 Hz, 1 H), 2.50–2.36 (m, 1 H), 2.15 (m, 1 H), 1.94 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT) δ *C* 162.0, 143.2, 118.5; *C*H 134.8, 133.5, 128.6, 120.9, 117.1; *C*H2 117.5, 44.9, 32.9, 28.5, 13.6; HRMS (ESI) calcd for C15H18 N3O [M+H]: 256.1450, found 256.1446.

methyl3-(3-(but-3-en-1-yl)-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanoate 49c. *Following the general reductive alkylation procedure,* 3-(but-3-en-1-yl) quinazolin-4(3H)-one (0.0295 g, 0.147 mmol), CSA (0.0375 g, 0.162 mmol), methyl acrylate (0.07 mL, 0.78 mmol) in THF (0.50 mL, 0.3 M) were reacted with a THF solution of SmI_2 (3.6 mL, 0.37 mmol) to give **17** (0.0264 g, 0.0916 mmol, 62%) as a colorless oil after purification by FCC (3:1 hexanes:EtOAc).

Data for **49c**: R*f* 0.42 (2:1 hexanes:EtOAc); IR (thin film) 2976, 2926, 1733, 1632, 1468, 1370, 1168, 754 cm-1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (dd, *J* = 7.8, 1.4 Hz, 1 H), 7.28 (td, *J* = 7.6, 1.5 Hz, 1 H), 6.87 (t, *J* = 7.5, 1.0 Hz, 1 H), 6.65 (d, *J* = 8.1 Hz, 1 H), 5.84 (ddt, *J* = 17.1, 10.2, 6.9 Hz, 1 H), 5.12 (dd, *J* = 17.2, 1.6 Hz, 1 H), 5.05 (d, *J* = 10.1 Hz, 1 H), 4.72 (dd, *J* = 8.9, 3.8 Hz, 1 H), 4.54 (brs, 1 H), 4.19 (dt, *J* = 13.9, 7.0 Hz, 1 H), 3.67 (s, 3 H), 2.92 (dt, *J* = 13.7, 7.1 Hz, 1 H), 2.40 (m, 4 H), 2.40 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT) δ *C* 173.3, 162.2, 144.3, 117.5; *C*H 135.1, 133.2, 128.5, 119.6, 115.7, 68.4; *C*H2 117.0, 44.8, 32.7, 29.6, 28.5; *C*H3 51.8; HRMS (ESI) calcd for C16H21N2O3 [M+H]: 289.1541, found 289.1552.

***tert*-butyl 3-(3-(but-3-en-1-yo)-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanoate 49b.** *Following the general reductive alkylation procedure*, 3-(but-3-en-1-yl)quinazolin-4(3H)-one (0.0289 g, 0.144 mmol), CSA (0.0368 g, 0.158 mmol), *tert*-butyl acrylate (0.11 mL, 0.76 mmol) in THF (0.50 mL, 0.3 M) were reacted with

a THF solution of SmI_2 (3.5 mL, 0.36 mmol) to give **49b** (0.0364 g, 0.110 mmol, 77%) as a colorless oil after purification by FCC (3:2 hexanes:EtOAc).

Data for **49b**: R*f* 0.68 (1:1 hexanes:EtOAc); IR (thin film) 2977, 2930, 1726, 1631, 1470, 1367, 1152, 754 cm-1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (dd, *J* = 7.8, 1.3 Hz, 1 H), 7.27 (td, *J* = 7.7, 1.4 Hz, 1 H), 6.85 (t, *J* = 7.7 Hz, 1 H), 6.65 (d, *J* = 7.9 Hz, 1 H), 5.84 (ddt, *J* = 17.1, 10.2, 6.9 Hz, 1 H), 5.11 (dd, *J* = 17.1, 1.5 Hz, 1 H), 5.05 (d, *J* = 10.7 Hz, 1 H), 4.70 (dd, *J* = 8.8, 3.9 Hz, 1 H), 4.59 (brs, 1 H), 4.20 (dt, *J* = 13.9, 7.0 Hz, 1 H), 2.90 (dt, *J* = 14.1, 7.2 Hz, 1 H), 2.41 (q, *J* = 7.4 Hz, 1 H), 2.28 (t, *J* = 6.9 Hz, 1 H), 2.09–1.91 (m, 2 H), 1.44 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT) δ *C* 172.0, 162.2, 144.5, 117.3, 81.0; *C*H 135.1, 133.2, 128.4, 119.4, 115.4; *C*H2 117.0, 44.7, 32.7, 31.0, 28.6; *C*H3 28.0; HRMS (ESI) calcd for C19H27N2O3 [M+H]: 331.2022, found 331.2015.

3-(2-methyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanenitrile 51a.
Following the general reductive alkylation procedure, 2-methylquinazolin-4(3H)-one (0.0229 g, 0.141 mmol), NH_4Cl (0.0085 g, 0.155 mmol), acrylonitrile (0.05 mL,0.76 mmol) in THF (0.50 mL, 0.3 M) were reacted with a THF solution of SmI_2 (3.6 mL, 0.35 mmol) to give **51a** (0.0247 g, 0.115 mmol, 81%) as a white solid.

Data for **51a**: R*f* 0.26 (1:2 hexanes:EtOAc); mp = 113–114 °C; IR (thin film) 2927, 2249, 1655, 1486, 754 cm-1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (dd, *J* = 7.8, 1.4 Hz, 1 H), 7.66 (s, 1 H), 7.33 (td, *J* = 7.6, 1.5 Hz, 1 H), 6.85 (t, *J* = 7.5 Hz, 1 H), 6.66 (d, *J*= 8.0 Hz, 1 H), 4.22 (s, 1 H), 2.67 (ddd, *J* = 17.4, 8.7, 6.3 Hz, 1 H), 2.55 (ddd, *J* =17.3, 8.7, 6.5 Hz, 1 H), 2.20 (ddd, *J* = 14.5, 8.7, 6.5 Hz, 1 H), 2.09 (ddd, *J* = 14.5, 8.7, 6.3 Hz, 1 H), 1.60 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT) δ *C* 164.8, 145.4, 119.6, 113.9, 69.4; *C*H 134.4, 128.2, 119.3, 114.9; *C*H2 37.3, 12.3; *C*H3 28.5; HRMS (ESI) calcd for C12H14N3O [M+H]: 216.1137, found 216.1129.

methyl3-(2-methyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2yl) propanoate 51c.
Following the general reductive alkylation procedure, 2-methylquinazolin-4(3H)-one (0.0211 g, 0.130 mmol), CSA (0.0333 g, 0.143 mmol), methyl acrylate (0.04 mL, 0.65 mmol) in THF (0.50 mL, 0.3 M) were reacted with a THF solution of SmI_2 (4.9 mL, 0.33 mmol) to give know adduct (0.0179 g, 0.115 mmol, 55%).

***tert*-butyl 3-(2-methyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanoate 51b.**
Following the general reductive alkylation procedure, 2-methylquinazolin-4(3H)-one (0.0220 g, 0.136 mmol), CSA (0.0348 g, 0.150 mmol), *tert*-butyl acrylate (0.10 mL,0.68 mmol) in THF (0.50 mL, 0.3 M) were reacted with a THF solution of SmI_2 (3.3 mL, 0.34 mmol) to give **51b** (0.0227 g, 0.0782 mmol, 58%) as a white solid after purification by FCC (1:1 hexanes:EtOAc).

Data for **51b**: R*f* 0.53 (1:2 hexanes:EtOAc); mp = 116–117 °C; IR (thin film) 2976, 2929, 1709, 1656, 1486, 1368, 1155, 753 cm-1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (dd, *J* = 7.9, 1.2 Hz, 1 H), 7.27 (td, *J* = 7.7, 1.4 Hz, 1 H), 6.79 (t, *J* = 7.6 Hz, 1 H),

6.57 (d, *J* = 8.0 Hz, 1 H), 6.30 (s, 1 H), 4.23 (s, 1 H), 2.55 (dt, *J* = 16.9, 7.1 Hz, 1 H), 2.44 (dt, , *J* = 16.9, 6.8 Hz, 1 H), 2.11 (dt, *J* = 14.7, 6.9 Hz, 1 H), 1.99 (dt, *J* = 14.8, 6.9 Hz, 1 H), 1.53 (s, 3 H), 1.42 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT) δ *C* 173.2, 164.4, 145.9, 114.0, 80.9, 70.0; *C*H 134.0, 128.3, 118.5, 114.5; *C*H2 36.4, 30.0; *C*H3 29.1, 28.0; HRMS (ESI) calcd for C16H23N2O3 [M+H]: 291.1709, found 291.1697.

3-(3-benzyl-2-methyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanenitrile 52a.

Following the general reductive alkylation procedure, 3-benzyl-2-methylquinazolin-4(3H)-one (0.0356 g, 0.142 mmol), NH_4Cl (0.0093 g, 0.174 mmol), acrylonitrile (0.05 mL, 0.76 mmol) in THF (0.47 mL, 0.3 M) were reacted with a THF solution of SmI_2 (4.7 mL, 0.36 mmol) to give **52a** (0.0416 g, 0.136 mmol, 96%) as a white solid.

Data for **52a**: R*f* 0.45 (1:1 hexanes:EtOAc); mp = 148–149 ºC; IR (thin film) 3013, 2249, 1625, 1489, 1397, 1158, 754 cm-1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (dd, *J* = 8.0, 1.2 Hz, 1 H), 7.36–7.25 (m, 6 H), 6.91 (dt, *J* = 7.6, 1.0 Hz, 1 H), 6.68 (d, *J* = 8.0 Hz, 1 H), 4.85 (d, *J* = 16.0 Hz, 1 H), 4.35 (d, *J* = 16.0 Hz, 1 H), 4.35 (s, 1 H), 2.36 (m,2 H), 2.12 (m, 1 H), 1.86 (m, 1 H), 1.55 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT) δ *C* 163.9, 143.8, 138.7, 119.2, 115.5, 73.4; *C*H 134.0, 128.9, 128.8, 127.4, 127.3, 119.8, 115.1; *C*H2 45.4, 34.5, 12.3; *C*H3 25.6; HRMS (ESI) calcd for C19H19N3ONa [M+Na]: 328.1426, found 328.1415.

methyl 3-(3-benzyl-2-methyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanoate 52c. *Following the general reductive alkylation procedure,* 3-benzyl-2-methylquinazolin-4(3H)-one (0.0321 g, 0.128 mmol), CSA (0.0328 g, 0.141 mmol), methyl acrylate (0.06 mL, 0.92 mmol) in THF (0.50 mL, 0.3 M) were reacted with a THF solution of SmI_2 (4.2 mL, 0.32 mmol) to give **52c** (0.0199 g, 0.0588 mmol, 46%) as a white solid after purification by FCC (5:1 hexanes:EtOAc).

Data for **52c**: R*f* 0.66 (1:1 hexanes:EtOAc); mp = 136–137 ºC; IR (thin film) 2950, 1734, 1624, 1489, 1397, 754 cm-1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 7.7 Hz, 1 H), 7.35–7.20 (m, 6 H), 6.85 (t, *J* = 7.7 Hz, 1 H), 6.57 (d, *J* = 8.1 Hz, 1 H), 4.96 (d, *J* = 15.8 Hz, 1 H), 4.60 (d, *J* = 15.8 Hz, 1 H), 4.27 (s, 1 H), 3.59 (s, 3 H), 2.34 (m, 2 H), 2.12 (dt, *J* = 14.7, 5.2 Hz, 1 H), 2.02 (td, *J* = 10.0, 5.1 Hz, 1 H), 1.46 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT) δ *C* 173.8, 164.2, 144.5, 139.1, 115.2, 74.1; *C*H 133.6, 128.9, 128.5, 127.4, 127.0, 119.0, 114.4; *C*H2 45.3, 34.0, 28.9; *C*H3 51.8, 26.4; HRMS (ESI) calcd for C20H23N2O3 [M+H]: 339.1709, found 339.1693.

***tert*-butyl 3-(3-benzyl-2-methyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanoate 52b.** *Following the general reductive alkylation procedure,* 3-benzyl-2-methylquinazolin-4(3H)-one (0.0331 g, 0.132 mmol), NH_4Cl (0.0080 g, 0.145 mmol), *tert*-butyl acrylate (0.10 mL, 0.66 mmol) in THF (0.50 mL, 0.3 M) were reacted with a THF solution of SmI_2 (3.4 mL, 0.33 mmol) to give **52b** (0.0322 g, 0.0847 mmol, 64%) as a white solid.

Data for **52b**: R*f* 0.40 (3:1 hexanes:EtOAc); mp = 142–143 °C; IR (thin film) 2977, 2930, 1726, 1625, 1489, 1394, 1154, 754 cm-1; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.7 Hz, 1 H), 7.33–7.20 (m, 5 H), 7.22 (t, *J* = 7.3 Hz, 1 H), 6.83 (t, *J* = 7.5 Hz, 1 H), 6.56 (d, *J* = 7.7 Hz, 1 H), 5.00 (d, *J* = 15.8 Hz, 1 H), 4.54 (d, *J* = 15.9 Hz, 1 H), 4.40 (s, 1 H), 2.27 (m, 2 H), 2.10–1.99 (m, 1 H), 1.42 (s, 3 H), 1.38 (s, 9 H); ^{13}C NMR (175 MHz, $CDCl_3$, DEPT) δ *C* 172.7, 164.2, 144.6, 139.0, 115.0, 80.8, 74.1; *C*H 133.6, 128.8, 128.5, 127.3, 126.9, 118.7, 114.2; *C*H2 45.2, 33.8, 30.2; *C*H3 27.9, 26.4; HRMS (ESI) calcd for C20H23N2O3 [M+H]: 339.1709, found 339.1693.

3-(2-(*tert*-butyl)-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanenitrile 53. *Following the general reductive alkylation procedure,* 2-(*tert*−butyl)quinazolin-4(3H)-one (0.0280 g, 0.138 mmol), CSA (0.0366 g, 0.158 mmol), acrylonitrile (0.05 mL, 0.76 mmol) in THF (0.46 mL, 0.3 M) were reacted with a THF solution of SmI_2 (3.7 mL, 0.35 mmol) to give **153** (0.0124 g, 0.0482 mmol, 35%) as a white solid along with 0.0099g of 2-(*tert*-butyl)quinazolin-4(3H)-one after purification by FCC (1:1 hexanes:EtOAc).

Data for **53**: R*f* 0.65 (1:2 EtOAc: Hexanes); IR (thin film) 3356, 2921, 2246, 1655 cm-1; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.79 (dd, *J* = 8.4, 1.4 Hz, 1 H), 6.73 (t, *J* = 7.7 Hz, 1 H), 6.55 (d, *J* = 8.4 Hz, 1 H), 6.10 (s, 1 H), 4.09 (s, 1 H), 2.61-2.66 (m, 1 H), 2.53-2.58 (m, 1 H), 2.03-2.11 (m, 2 H), 1.03 (s, 9 H); ^{13}C (176 MHz, $CDCl_3$) δ *C* 164.1, 146.5, 134.9, 128.3, 120.0, 118.2, 12.8, 111.6, 43.2, 33.5, 29.9, 24.6, 12.8; HRMS (TOF MS ES+) calcd for C15H20N3O [M+H]: 258.1606, found 258.1599.

3-(3-cyclopropyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanenitrile 54a. *Following the general reductive alkylation procedure,* 3-cyclopropylquinazolin-4(3H)-one (0.0261 g, 0.140 mmol), NH_4Cl (0.0086 g, 0.158 mmol), acrylonitrile (0.05 mL, 0.76 mmol) in THF (0.47 mL, 0.3 M) were reacted with a THF solution of SmI_2 (3.7 mL, 0.35 mmol) to give **54a** (0.0340 g, 0.140 mmol, 99%) as a colorless oil.

Data for **54a**: R*f* 0.24 (1:1 EtOAc: Hexanes); IR (thin film) 3294, 2929, 2246, 1636 cm-1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (dd, *J* = 8.0, 1.6 Hz, 1 H), 7.32 (td, *J* = 8.0,1.6 Hz, 1 H), 6.90 (ddd, *J* = 8.0, 8.0, 0.8 Hz, 1 H), 6.73 (d, *J* = 8.0 Hz, 1 H), 4.81 (dd, *J* = 9.6, 4.0 Hz,1 H), 2.69 (ddd, *J* = 9.6, 6.8, 4.0 Hz, 1 H), 2.46 (ddd, *J* = 8.0, 6.4, 4.4 Hz, 2 H), 2.15-2.24 (m, 1 H) 2.01-2.10 (m, 1 H), 1.09-1.17 (m, 1 H), 0.79-0.89 (m, 2 H), 0.61-0.68 (m, 2 H); ^{13}C (100 MHz, $CDCl_3$) δ *C* 164.4, 143.4, 134.0, 128.6, 120.3, 118.9, 117.4, 116.4, 68.9, 28.5, 27.9, 13.8, 10.2, 6.0; HRMS (EI+) calcd for C14H15N3O [M+]: 241.12152, found 241.12128.

3-(3-cyclohexyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanenitrile 54b *Following the general reductive alkylation procedure,* 3-cyclohexylquinazolin-4(3H)-one (0.0338 g, 0.148 mmol), NH_4Cl (0.0089 g, 0.166 mmol), acrylonitrile (0.05 mL,0.76 mmol) in THF (0.49 mL, 0.3 M) were reacted with a THF solution of SmI_2

(4.9 mL, 0.37 mmol) to give **54b** (0.0409 g, 0.144 mmol, 97%) as a colorless oil after purification by FCC (3:1 hexanes:EtOAc).

Data for **54b**: R*f* 0.38 (1:1 EtOAc: Hexanes); IR (thin film) 3284, 2932, 2856, 2245, 1622 cm-1; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.94 (dd, *J* = 7.7, 1.4 Hz, 1 H), 7.32 (td, *J* = 8.4, 1.4 Hz, 1 H), 6.95 (ddd, *J* = 8.4, 8.4, 1.4 Hz, 1 H), 6.77 (d, *J* = 7.7 Hz, 1 H), 4.82 (dd, *J* = 10.5, 2.8 Hz,1 H), 4.46 (tt, *J* = 11.9, 3.5 Hz, 1 H), 2.34-2.44 (m, 2 H), 2.23-2.29 (m, 1 H) 1.78-1.92 (m, 6 H), 1.69 (d, *J* = 13.3 Hz, 1 H), 1.54 (qd, *J* = 11.9, 3.5 Hz, 1 H), 1.37-1.45 (m, 3 H), 1.14 (qt, *J* = 9.1, 4.2 Hz, 1 H); ^{13}C (176 MHz, $CDCl_3$) δ *C* 161.8, 142.9, 133.4, 128.9, 120.8, 119.6, 118.9, 117.1, 63.2, 53.4, 31.8, 31.6, 30.2, 26.1, 25.9, 25.5, 14.0; HRMS (EI+) calcd for C17H21N3O [M+]: 283.16847, found 283.16723.

3-(3-cyclopropyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanenitrile (54a). Following the general reductive alkylation procedure, 3-cyclopropylquinazolin-4(3H)-one (0.0261 g, 0.140 mmol), NH_4Cl (0.0086 g, 0.158 mmol), acrylonitrile (0.05 mL, 0.76 mmol) in THF (0.47 mL, 0.3 M) were reacted with a THF solution of SmI_2 (3.7 mL, 0.35 mmol) to give **54a** (0.0340 g, 0.140 mmol, 99%) as a colorless oil.

Data for **54a**: Rf 0.24 (1:1 EtOAc: Hexanes); IR (thin film) 3294, 2929, 2246, 1636 cm-1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (dd, J = 8.0, 1.6 Hz, 1 H), 7.32 (td, J = 8.0, 1.6 Hz, 1 H), 6.90 (ddd, J = 8.0, 8.0, 0.8 Hz, 1 H), 6.73 (d, J = 8.0 Hz, 1 H), 4.81 (dd, J = 9.6, 4.0 Hz,1 H), 2.69 (ddd, J = 9.6, 6.8, 4.0 Hz, 1 H), 2.46 (ddd, J = 8.0, 6.4, 4.4 Hz, 2 H), 2.15-2.24 (m, 1 H) 2.01-2.10 (m, 1 H), 1.09-1.17 (m, 1 H), 0.79-0.89 (m, 2 H), 0.61-0.68 (m, 2 H); ^{13}C (100 MHz, $CDCl_3$) δ *C* 164.4, 143.4, 134.0, 128.6, 120.3, 118.9, 117.4, 116.4, 68.9, 28.5, 27.9, 13.8, 10.2, 6.0; HRMS (EI+) calcd for C14H15N3O [M+]: 241.12152, found 241.12128.

3-(3-cyclohexyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanenitrile (54b). Following the general reductive alkylation procedure, 3-cyclohexylquinazolin-4(3H)-one (0.0338g,0.148mmol),NH_4Cl(0.0089g,0.166mmol),acrylonitrile(0.05mL, 0.76 mmol) in THF (0.49 mL, 0.3 M) were reacted with a THF solution of SmI_2 (4.9 mL, 0.37 mmol) to give **54b** (0.0409 g, 0.144 mmol, 97%) as a colorless oil after purification by FCC (3:1 hexanes:EtOAc).

Data for **54b**: Rf 0.38 (1:1 EtOAc: Hexanes); IR (thin film) 3284, 2932, 2856, 2245, 1622 cm-1; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.94 (dd, J = 7.7, 1.4 Hz, 1 H), 7.32 (td, J = 8.4, 1.4 Hz, 1 H), 6.95 (ddd, J = 8.4, 8.4, 1.4 Hz, 1 H), 6.77 (d, J = 7.7 Hz, 1 H), 4.82 (dd, J = 10.5, 2.8 Hz,1 H), 4.46 (tt, J = 11.9, 3.5 Hz, 1 H), 2.34-2.44 (m, 2 H), 2.23- 2.29 (m, 1 H) 1.78-1.92 (m, 6 H), 1.69 (d, J = 13.3 Hz, 1 H), 1.54 (qd, J = 11.9, 3.5 Hz, 1 H), 1.37-1.45 (m, 3 H), 1.14 (qt, J = 9.1, 4.2 Hz, 1 H); ^{13}C (176 MHz, $CDCl_3$) δ *C* 161.8, 142.9, 133.4, 128.9, 120.8, 119.6, 118.9, 117.1, 63.2, 53.4, 31.8, 31.6, 30.2, 26.1, 25.9, 25.5, 14.0; HRMS (EI+) calcd for C17H21N3O [M+]: 283.16847, found 283.16723.

General procedure for synthesizing pyridinium oxide:

To a solution of the corresponding alcohol(1eq) in DCM (0.2M) at 0 °C was added Et_3N (1.5eq) and then methanesulfonyl chloride (1.5eq). The mixture was stirred for 1 h at 0 °C and slowly warming up to room temperature for 3hr before saturated aqueous NH_4Cl solution was added. This mixture was extracted with DCM three times. The combined extracts were washed with brine and dried over Na_2SO_4 and concentrated. The mixture of the crude corresponding methylate (1eq), 3-hydroxypyridine (2eq) in BuCN(20M) were heated up to 130 °C for 6 hr in sealed tube to give pyridinium oxide after purification by FCC (DCM:10%NH_4OH in MeOH=1:0.08 to 1:0.15).

1-(hex-5-en-2-yl)pyridin-1-ium-3-olate (74) *Following the general reductive alkylation procedure,* hex-5-en-2-ol[40] (1g, 10 mmol) in DCM (20 mL) at 0 °C was added Et_3N (2.07 mL, 15 mmol) and then methanesulfonyl chloride (1.17 mL, 15 mmol). The mixture of the crude methylate (89mg, 0.5 mmol), 3-hydroxypyridine (95mg, 1 mmol) in BuCN(2 drops) were heated up to 130 °C for 6 hr in sealed tube to give **74**(68mg, 67% two steps) after purification by FCC (DCM:10%NH_4OH in MeOH=1:0.06 to 1:0.12).

Data for **74**: R_f 0.20 (1:0.1 DCM: 10%NH_4OH in MeOH); IR (thin film) 3368, 3077, 2931, 1588, 1507, 1379 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.75 (t, *J* = 2.1, 1 H), 7.15 (dd, *J* = 8.8, 1.8 Hz, 1 H), 7.12 (dd, *J* = 8.8, 5.3 Hz, 1 H), 7.00 (d, *J* = 5.3 Hz, 1 H), 5.60 (ddt, *J* = 16.7, 10.5, 6.7 Hz, 1 H), 4.92 (d, *J* = 10.5 Hz, 1 H), 4.89 (d, *J* = 16.7 Hz, 1 H), 4.06 (dq, *J* = 8.8, 6.8 Hz, 1 H), 1.79–1.91 (m, 4 H), 1.48 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 170.1, 135.7, 134.5, 131.5, 126.8, 119.8, 116.7, 66.6, 35.6, 29.7, 21.8; HRMS (EI) calcd for $C_{11}H_{16}NO$ [M+]: 178.1232, found 277.1238.

1-(3-methylpent-4-en-1-yl)pyridin-1-ium-3-olate (76) *Following the general reductive alkylation procedure,* 3-methylpent-4-en-1-ol[41] (500 mg, 5 mmol) in DCM (25 mL) at 0 °C was added Et_3N (1.05mL, 7.5 mmol) and then methanesulfonyl chloride (0.6 mL, 75 mmol). The mixture of the crude methylate (165mg, 1 mmol), 3-hydroxypyridine (340mg, 4 mmol) in ACN(2 ml) were heated up to 100 °C for 10 hr in sealed tube to give **76** (165mg, 75% two steps) after purification by FCC (DCM:10%NH_4OH in MeOH=1:0.1 to 1:0.12).

Data for **76**: R_f 0.20 (1:0.1 DCM: 10%NH_4OH in MeOH); IR (thin film) 3367, 3072, 2966, 1566, 1506 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.43 (s, 1 H), 7.30 (d, *J* = 9.3 Hz, 1 H), 7.23 (dd, *J* = 8.9, 4.9 Hz, 1 H), 7.00 (d, *J* = 4.9 Hz, 1 H), 5.67 (ddd, *J* = 17.3, 10.9, 7.7 Hz, 1 H), 5.12 (d, *J* = 11.1 Hz, 1 H), 5.01 (d, *J* = 17.3 Hz, 1 H), 4.11 (ddd, *J* = 13.3, 8.5, 5.2 Hz, 1 H), 4.02 (dd, *J* = 13.3, 7.9 Hz, 1 H), 2.20 (brs, 1 H), 2.00 (dtd, *J* = 16.3, 8.8, 5.2 Hz, 1 H), 1.92–1.85 (m, 4 H), 1.10 (d, *J* = 6.9 Hz, 3 H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 160.0, 141.0, 133.0, 131.8, 130.5, 128.0, 115.5, 68.4, 43.8, 36.0, 21.5, 21.2; HRMS (EI) calcd for $C_{11}H_{16}NO$ [M+]: 178.1232, found 277.1236.

1-(cyclohex-3-en-1-ylmethyl)pyridin-1-ium-3-olate (78) *Following the general reductive alkylation procedure,* cyclohex-3-en-1-ylmethanol[42] (1g, 10 mmol) in DCM (20 mL) at 0 °C was added Et_3N (2.07 mL, 15 mmol) and then methanesulfonyl chloride (1.17 mL, 15 mmol). The mixture of the crude methylate (89mg, 0.5 mmol), 3-hydroxypyridine (95mg, 1 mmol) in BuCN (2 drops) were heated up to 130 °C for 6 hr in sealed tube to give **78**(68mg, 67% two steps) after purification by FCC (DCM:10%NH_4OH in MeOH=1:0.06 to 1:0.12).

Data for **78**: R_f 0.20 (1:0.1 DCM:10%NH_4OH in MeOH); IR (thin film) 3368, 3077, 2931, 1588, 1563, 1507, 1379 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.75 (t, *J* = 2.1, 1 H), 7.15 (dd, *J* = 8.8, 1.8 Hz, 1 H), 7.12 (dd, *J* = 8.8, 5.3 Hz, 1 H), 7.00 (d, *J* = 5.3 Hz, 1 H), 5.60 (ddt, *J* = 16.7, 10.5, 6.7 Hz, 1 H), 4.92 (d, *J* = 10.5 Hz, 1 H), 4.89 (d, *J* = 16.7 Hz, 1 H), 4.06 (dq, *J* = 8.8, 6.8 Hz, 1 H), 1.79–1.91 (m, 4 H), 1.48 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 170.1, 135.7, 134.5, 131.5, 126.8, 119.8, 116.7, 66.6, 35.6,29.7,21.8; HRMS (EI) calcd for $C_{11}H_{15}NOCl$ [M+]: 178.1232, found 177.1238.

6-chloro-1−(hex-5-en-2-yl)pyridin-1-ium-3-olate (80) *Following the general reductive alkylation procedure,* hex-5-en-2-ol[40] (1g, 10 mmol) in DCM (20 mL) at 0 °C was added Et_3N (2.07 mL, 15 mmol) and then methanesulfonyl chloride (1.17 mL, 15 mmol). The mixture of the crude methylate (60mg, 0.34 mmol), 6-chloropyridin-3-ol (88mg, 0.68 mmol) in BuCN(2 drops) were heated up to 130 °C for 6 hr in sealed tube to give **80**(49mg, 48% two steps) after purification by FCC (DCM:10%NH_4OH in MeOH=1:0.06 to 1:0.08).

Data for **80** in acid: R_f 0.28 (1:0.1 DCM:10%NH_4OH in MeOH); IR (thin film) 3390, 3076, 2934, 1581, 1499, 1374 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 9.47 (d, *J* = 2.3, 1 H), 8.07 (dd, *J* = 8.6, 2.3 Hz, 1 H), 7.72 (d, *J* = 8.6 Hz, 1 H), 7.00 (d, *J* = 5.3 Hz, 1 H), 5.71 (ddt, *J* = 16.4, 10.4, 6.4 Hz, 1 H), 5.30 (tq, *J* = 6.8, 6.3 Hz, 1 H), 5.03 (d, *J* = 11.6 Hz, 1 H), 5.01 (d, *J* = 16.9 Hz, 1 H), 2.07–2.22 (m, 4 H), 1.73 (d, *J* = 6.3 Hz, 3 H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 158.9, 135.0, 134.9, 133.6, 132.1, 129.6, 117.3, 65.2, 35.4, 29.9, 21.0; HRMS (EI) calcd for $C_{11}H_{15}NOCl$ [M+]: 212.0842, found 212.0832.

6-bromo-1−(hex-5-en-2-yl)pyridin-1-ium-3-olate (82) *Following the general reductive alkylation procedure,* hex-5-en-2-ol[40] (1g, 10 mmol) in DCM (20 mL) at 0 °C was added Et_3N (2.07 mL, 15 mmol) and then methanesulfonyl chloride (1.17 mL, 15 mmol). The mixture of the crude methylate (45mg, 0.25 mmol), 6-bromopyridin-3-ol (89mg, 0.51 mmol) in BuCN(2 drops) were heated up to 130 °C for 6 hr in sealed tube to give **82**(mg, 46% two steps) after purification by FCC (DCM:10%NH_4OH in MeOH=1:0.08 to 1:0.15).

Data for **82** in acid: R_f 0.22 (1:0.1 DCM:10%NH_4OH in MeOH); IR (thin film) 3404, 2978, 1578, 1494, 1374 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.76 (d, *J* = 2.5, 1 H), 7.43 (d, *J* = 9.3 Hz, 1 H), 7.72 (d, *J* = 8.6 Hz, 1 H), 7.24 (dd, *J* = 9.6, 3.2 Hz, 1 H),

5.72 (ddt, *J* = 16.6, 10.4, 6.3 Hz, 1 H), 5.03-5.01 (m, 3 H), 1.92–2.10 (m, 4 H), 1.67 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 168.3, 136.5, 135.5, 133.2, 132.4, 116.9, 109.7, 65.6, 35.8, 29.8, 21.3; HRMS (EI) calcd for $C_{11}H_{15}NOBr$ [M+]: 256.0337, found 256.0324.

1-(hex-5-en-2-yl)-4-methylpyridin-1-ium-3-olate (84) *Following the general reductive alkylation procedure,* hex-5-en-2-ol[40] (1g, 10 mmol) in DCM (20 mL) at 0 °C was added Et_3N (2.07 mL, 15 mmol) and then methanesulfonyl chloride (1.17 mL, 15 mmol). The mixture of the crude methylate (89mg, 0.5 mmol), 4-methylpyridin-3-ol (220mg, 2 mmol) in BuCN(2 drops) were heated up to 130 °C for 6 hr in sealed tube to give **84**(50mg, 48% two steps) after purification by FCC (DCM:10%NH_4OH in MeOH=1:0.08 to 1:0.12).

Data for **84** in acid: R_f 0.22 (1:0.1 DCM:10%NH_4OH in MeOH); IR (thin film) 3384, 3079, 2980, 1506, 1361 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.26 (s, 1 H), 7.04 (d, *J* = 5.5 Hz, 1 H), 6.94 (d, *J* = 5.2 Hz, 1 H), 5.58 (ddt, *J* = 16.6, 10.6, 6.3 Hz, 1 H), 4.89 (d, *J* = 10.6 Hz, 1 H), 4.87 (d, *J* = 16.6 Hz, 1 H), 3.99 (tq, *J* = 7.3, 6.8, 1 H), 2.19 (s, 3 H), 1.75–1.87 (m, 4 H), 1.44 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 169.3, 137.5, 135.8, 134.8, 129.3, 120.9, 116.7, 66.6, 35.7, 29.8, 21.8, 18.6; HRMS (EI) calcd for $C_{12}H_{18}NO$ [M+]: 192.1388, found 192.1378.

(*E*)-6-chloro-1−(7-ethoxy-7-oxohept-5-en-2-yl)pyridin-1-ium-3-olate (86) *Following the general reductive alkylation procedure*, ethyl (*E*)-6-hydroxyhept-2-enoate[43] (1g, 5.8 mmol) in DCM (11.6 mL) at 0 °C was added Et_3N (1.21 mL, 8.7 mmol) and then methanesulfonyl chloride (0.68 mL, 8.7 mmol). The mixture of the crude methylate (511 mg, 2.04 mmol), 6-chloropyridin-3-ol (531 mg, 4.09 mmol) in BuCN(0.1 mL) were heated up to 130 °C for 6 hr in sealed tube to give **86** (55mg, 44% two steps) after purification by FCC (DCM:10%NH_4OH in MeOH=1:0.06 to 1:0.012).

Data for **86** in acid: R_f 0.36 (1:0.1 DCM:10%NH_4OH in MeOH); IR (thin film) 3388, 2983, 1713, 1588, 1506, 1371 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 9.53 (S, 1 H), 8.05 (d, *J* = 8.6, Hz, 1 H), 7.73 (d, *J* = 8.6 Hz, 1 H), 6.82 (dt, *J* = 14.4, 6.5 Hz, 1 H), 5.80 (d, *J* = 15.5 Hz, 1 H), 5.27 (quint, *J* = 6.7 Hz, 1 H), 4.17 (q, *J* = 7.0 Hz, 2 H), 2.33 (quint, *J* = 7.3 Hz, 1 H), 2.27 (q, *J* = 6.4 Hz, 2 H), 2.21 (quint, *J* = 7.3 Hz, 1 H), 1.76 (d, *J* = 6.8 Hz, 3 H), 1.27 (d, *J* = 7.4 Hz, 3 H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 165.8, 158.8, 144.5, 135.1, 133.6, 132.1, 129.7, 123.7, 65.0, 60.6, 34.7, 28.3, 21.0, 14.2; HRMS (EI) calcd for $C_{14}H_{19}NO_3Cl$ [M+]: 284.1053, found 284.1048.

(*E*)-6-bromo-1−(7-ethoxy-7-oxohept-5-en-2-yl)pyridin-1-ium-3-olate (88) *Following the general reductive alkylation procedure,* ethyl (*E*)-6-hydroxyhept-2-enoate[43] (1g, 5.8 mmol) in DCM (11.6 mL) at 0 °C was added Et_3N (1.21 mL, 8.7 mmol) and then methanesulfonyl chloride (0.68 mL, 8.7 mmol). The mixture of the crude methylate (25 mg, 0.1 mmol), 6-bromopyridin-3-ol (34 mg, 0.2 mmol) in BuCN(0.2 mL) were heated up to 130 °C for 6 hr in sealed tube to give **88** (14.4 mg, 37% two steps) after purification by FCC (DCM:10%NH_4OH in MeOH=1:0.06).

Data for **88** in acid: R_f 0.36 (1:0.1 DCM:10%NH_4OH in MeOH); IR (thin film) 3396, 3056, 2981, 1711, 1493, 1369 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 9.62 (S, 1 H), 7.96 (d, *J* = 8.7, Hz, 1 H), 7.90 (d, *J* = 8.7 Hz, 1 H), 6.83 (dt, *J* = 15.7, 6.8 Hz, 1 H), 5.80 (d, *J* = 15.9 Hz, 1 H), 5.25 (quint, *J* = 7.0 Hz, 1 H), 4.17 (q, *J* = 7.0 Hz, 2 H), 2.35 (quint, *J* = 7.3 Hz, 1 H), 2.27 (q, *J* = 6.4 Hz, 2 H), 2.21 (quint, *J* = 7.3 Hz, 1 H), 1.76 (d, *J* = 6.8 Hz, 3 H), 1.27 (d, *J* = 7.4 Hz, 3 H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 165.7, 159.2, 144.5, 134.6, 133.7, 133.2, 123.6, 123.3, 68.2, 60.5, 34.8, 28.2, 21.1, 14.2; HRMS (EI) calcd for $C_{14}H_{19}NO_3Br$ [M+]: 328.5048, found 328.5055.

1-((2*S*,4*R*)-4-methylhex-5-en-2-yl)pyridin-1-ium-3-olate (92) *Following the general reductive alkylation procedure,* (4*R*)-4-methylhex-5-en-2-ol[44] (120 mg, 1.05 mmol) in DCM (5mL) at 0 °C was added Et_3N (0.22 mL, 1.58 mmol) and then methanesulfonyl chloride (0.13 mL, 1.58 mmol). The mixture of the crude methylate (165 mg, 0.86 mmol), 3-hydroxypyridine (164 mg, 1.72 mmol) in BuCN (2 drops) were heated up to 130 °C for 6 hr in sealed tube to give **92** (105mg, 55% two steps) after purification by FCC (DCM:10%NH_4OH in MeOH=1:0.06 to 1:0.1).

Data for **92**: R_f 0.25 (1:0.1 DCM: 10%NH_4OH in MeOH); IR (thin film) 3388, 2979, 2935, 1728, 1579, 1496, 1374 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 8.95 (s, *J* = 1 H), 8.39 (d, *J* = 5.0 Hz 1 H), 7.80 (d, *J* = 6.8 Hz, 1 H), 7.99 (d, *J* = 5.3 Hz, 1 H), 5.36 (m 1 H), 5.26 (m, 1 H), 4.72 (quint, *J* = 7.6 Hz, 1 H), 4.10 (quint, *J* = 7.2 Hz, 1 H), 1.98–2.05 (m, 2 H), 1.95–1.89 (m, 2 H), 1.67 (d, *J* = 6.4 Hz, 3 H), 1.57 (d, *J* = 6.6 Hz, 3 H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 160.0, 141.0, 133.0, 131.9, 130.5, 128.0, 115.5, 68.4, 43.8, 36.0, 21.5, 21.2; HRMS (EI) calcd for $C_{12}H_{18}NO$ [M+]: 192.1388, found 192.1384.

(*E*)-1-(hept-5-en-2-yl)pyridin-1-ium-3-olate (101) *Following the general reductive alkylation procedure,* (*E*)-hept-5-en-2-ol[45] (400mg, 3.5 mmol) in DCM (17mL) at 0 °C was added Et_3N (0.74 mL, 5.3 mmol) and then methanesulfonyl chloride (0.41 mL, 5.3 mmol). The mixture of the crude methylate (38 mg, 0.2 mmol), 3-hydroxypyridine (38 mg, 0.4 mmol) in BuCN (2 drops) were heated up to 130 °C for 6 hr in sealed tube to give **101** (27.5mg, 55% two steps) after purification by FCC (DCM:10%NH_4OH in MeOH=1:0.08 to 1:0.15).

Data for **101**: R_f 0.20 (1:0.1 DCM:10%NH_4OH in MeOH); IR (thin film) 3390, 3059, 2936, 1586, 1493, 1384 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 8.95 (s, *J* = 1 H), 8.39 (d, *J* = 5.0 Hz 1 H), 7.80 (d, *J* = 6.8 Hz, 1 H), 7.99 (d, *J* = 5.3 Hz, 1 H), 5.36 (m 1 H), 5.26 (m, 1 H), 4.72 (quint, *J* = 7.6 Hz, 1 H), 4.10 (quint, *J* = 7.2 Hz, 1 H), 1.98–2.05 (m, 2 H), 1.95–1.89 (m, 2 H), 1.67 (d, *J* = 6.4 Hz, 3 H), 1.57 (d, *J* = 6.6 Hz, 3 H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 159.1, 132.9, 132.6, 130.7, 128.5, 127.8, 127.7, 69.0, 36.5, 28.8, 21.8, 12.9; HRMS (EI) calcd for $C_{12}H_{18}NO$ [M+]: 192.1388, found 192.1384.

（*Z*)-1-(hept-5-en-2-yl)pyridin-1-ium-3-olate (103) *Following the general reductive alkylation procedure,* （*Z*)-hept-5-en-2-ol[46] (140mg, 1.23 mmol) in DCM (6.2 mL) at 0 °C was added Et_3N (0.26 mL, 1.84 mmol) and then methanesulfonyl chloride (0.145 mL, 1.84 mmol). The mixture of the crude methylate (100 mg, 0.52 mmol), 3-hydroxypyridine (99 mg, 1.04 mmol) in BuCN (3 drops) were heated up to 130 °C for 6 hr in sealed tube to give **103**(75mg, 62% two steps) after purification by FCC (DCM:10%NH_4OH in MeOH=1:0.06 to 1:0.12).

Data for **103**: R_f 0.20 (1:0.1 DCM:10%NH_4OH in MeOH); IR (thin film) 3382, 3024, 2919, 1567, 1505, 1507, 1372 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.44 (s, *J* = 1 H), 7.27 (m, 1 H), 7.20 (d, *J* = 8.8 Hz, 1 H), 7.99 (d, *J* = 5.3 Hz, 1 H), 5.52 (dq, *J* = 13.3, 7.0 Hz, 1 H), 5.27 (m, 1 H), 4.89 (d, *J* = 16.7 Hz, 1 H), 4.10 (quint, *J* = 7.2 Hz, 1 H), 1.83–1.98 (m, 4 H), 1.58 (d, *J* = 6.8 Hz, 3 H), 1.50 (d, *J* = 7.2 Hz, 3 H); ^{13}C NMR (175 MHz, $CDCl_3$） δ 170.3, 134.6, 134.6, 131.9, 127.3, 126.7, 126.5, 119.3, 66.8, 36.4, 23.0, 21.9, 12.9; HRMS (EI) calcd for $C_{12}H_{18}NO$ [M+]: 192.1388, found 192.1386.

General procedure for the pyridinium oxide cycloaddition:

Procedure A: The mixture of the corresponding pyridinium oxide (1eq) and Ag_2CO_3 (1.1eq) in BuCN (0.1mL) was heated up to 130 °C for 36 hr in sealed tube and filtered by celite to give cycloaddition product after purification by FCC (DCM:10%NH_4OH in MeOH=1:0.04).

Procedure B: The mixture of the corresponding pyridinium oxide (1eq) and Ag_2CO_3 (1.1eq) in ACN (0.1M) was heated up to 130 °C for 24 hr in sealed tube and filtered by celite to give cycloaddition product after purification by FCC (DCM:10%NH_4OH in MeOH=1:0.04).

* Unstable compound, directly to next step.
** assigned by 2D-NMR (COSY, HSQC, HMBC).

(1S,4S,5S,6R,9aS)-4-methyl-1,3,4,9a-tetrahydro-2H-1,6-methanoquinolizin -7(6H)-one (75) *Following the general reductive alkylation procedure A,* 1-(hex-5-en-2-yl)pyridin-1-ium-3-olate (35.4mg, 0.2 mmol) and Ag_2CO_3 (83mg, 0.22mmol) in BuCN (2 mL) was heated up to 130 °C for 36 hr in sealed tube to give **75** (30.8 mg, 87% product ratio=7:1) after purification by FCC (pure EtOAc).

Data for **75**: R_f 0.50 (1:0.1 DCM: 10%NH_4OH in MeOH); IR (thin film) 2933, 2860, 1694, 1507, 1386 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.10 (dd, *J* = 9.5, 5.7 1 H), 5.87 (d, *J* = 9.5 Hz, 1 H), 3.75 (d, *J* = 7.4Hz, 1 H), 3.55 (d, *J* = 5.6 Hz, 1 H), 2.92 (tq, *J* = 11.6, 6.4 Hz, 1 H), 2.35 (t, *J* = 3.4 Hz, 1 H), 1.83 (dd, *J* = 13.5, 7.5 1 H), 1.77–1.71 (m, 2 H), 1.59 (ddd, *J* = 13.8, 6.7, 1.5 1 H), 1.47 (dt, *J* = 13.8, 5.3 1 H), 1.18–1.13 (m, 1 H), 1.04 (d, *J* = 6.4 Hz, 3 H); ^{13}C NMR (175 MHz, $CDCl_3$） δ 199.4, 151.2,

126.8, 69.1, 64.4, 34.8, 30.4, 30.2, 25.9, 20.0; HRMS (EI) calcd for $C_{11}H_{16}NO$ [M+]: 178.1232, found 178.1223.

(1*R*,2*R*,5*S*,6*R*,9a*R*)-2-methyl-1,3,4,9a-tetrahydro-2*H*-1,6-methanoquinolizin -7(6*H*)-one (77) *Following the general reductive alkylation procedure B,* 1-(3-methylpent-4-en-1-yl)pyridin-1-ium-3-olate (60 mg, 0.34 mmol) and Ag_2CO_3 (103 mg, 0.37 mmol) in BuCN (3.4 mL) was heated up to 130 °C for 36 hr in sealed tube to give **77** (50 mg, 84% product ratio=10:1) after purification by FCC (DCM:10%NH_4OH in MeOH=1:0.02 to 0.04).

Data for **77**: R_f 0.4 (1:0.1 DCM: 10%NH_4OH in MeOH); IR (thin film) 2954, 2924, 1695, 1381 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.10 (dd, *J* = 9.9, 6.1 1 H), 5.88 (d, *J* = 9.9 1 H), 3.54 (d, *J* = 7.6 Hz, 1 H), 3.51 (d, *J* = 6.1 Hz 1 H), 2.92-2.88 (m, 2 H), 2.12 (d, *J* = 6.8 Hz, 1 H), 1.92 (dd, *J* = 13.7, 7.6 Hz, 1 H), 1.87 (dt, *J* = 11.8, 5.7 Hz, 1 H), 1.41 (dd, *J* = 13.6, 6.8 Hz, 1 H), 1.37-1.33 (m, 1 H), 1.12-1.07 (m, 1 H), 0.88 (d, *J* = 6.5 1 H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 199.3, 151.5, 126.3, 69.8, 68.6, 53.4, 42.1, 35.0, 26.7, 26.2, 20.9; HRMS (EI) calcd for $C_{11}H_{16}NO$ [M+]: 178.1232, found 178.1224.

(2*S*,5*R*,9*R*,9a*S*,10*S*)-1,2,3,4,4a,5,9,9a-octahydro-6*H*-5,9,2-(epinitrilomethano)benzo[7]annulen-6-one (79) *Following the general reductive alkylation procedure B,* (S)-1-(cyclohex-3-en-1-ylmethyl)pyridin-1-ium-3-olate (19 mg, 0.1 mmol) and Ag_2CO_3 (30 mg, 0.11 mmol) in ACN (1 mL) was heated up to 130 °C for 24 hr in sealed tube to give **79** (11 mg, 58% product ratio=10:1) after purification by FCC (DCM:10%NH_4OH in MeOH=1:0.03 to 0.1).

Data for **79**: R_f 0.45 (DCM:10%NH_4OH in MeOH=1:0.1); IR (thin film) 2960, 2922, 1696 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.17 (dd, *J* = 9.7, 6.2 1 H), 5.96 (d, *J* = 9.7 1 H), 3.60 (s, 1 H), 3.58 (d, *J* = 6.2 Hz, 1 H), 3.35 (s, 1 H), 3.22 (dd, *J* = 14.4, 4.0 Hz, 1 H), 2.79 (d, *J* = 14.0 Hz, 1 H), 2.32 (t, *J* = 6.3 Hz, 1 H), 2.25 (m, 1 H), 1.97 (dt, *J* = 13.1, 7.7 1 H), 1.86-1.81 (m, 2 H), 1.74-1.69 (m, 3 H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 199.5, 152.3, 126.2, 76.2, 69.0, 61.9, 38.8, 37.0, 30.4, 27.8, 27.2, 20.8; HRMS (EI) calcd for $C_{12}H_{18}NO$ [M+]: 190.1230, found 190.1232.

(1*S*,4*S*,5*R*,6*R*,9a*R*)-9a-chloro-4-methyl-1,3,4,9a-tetrahydro-2*H*-1,6-methanoquinolizin-7(6*H*)-one (81) *Following the general reductive alkylation procedure A,* 6-chloro-1-(hex-5-en-2-yl)pyridin-1-ium-3-olate (27 mg, 0.13 mmol) and Ag_2CO_3 (39 mg, 0.14 mmol) in BuCN (1.3 mL) was heated up to 130 °C for 12 hr in sealed tube to give **81** (21.9 mg, 80% product ratio=4:1) after purification by FCC (DCM:10%NH_4OH in MeOH=1:0.04 to 1:0.06).

Data for **81**: R_f 0.48 (1:0.1 DCM: 10%NH_4OH in MeOH); IR (thin film) 2940, 1710, 1606 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.11 (d, *J* = 9.7 1 H), 5.92 (dd, *J* = 9.3, 1.4 Hz, 1 H), 3.80 (d, *J* = 8.6Hz, 1 H), 3.38 (dq, *J* = 13.5, 6.5 Hz, 1 H), 2.48 (brs, 1 H), 2.34 (td, *J* = 13.2, 5.2 Hz, 1 H), 2.05 (dd, *J* = 13.6, 8.6 1 H), 1.80 (ddd, *J* = 13.6, 6.6,

2.2 1 H), 1.62 (dt, *J* = 13.6, 5.2 1 H), 1.49 (dt, *J* = 14.8, 5.5 1 H), 1.19 (dd, *J* = 14.4, 6.0 1 H), 1.08 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 197.4, 153.8, 125.8, 89.9, 62.3, 51.0, 38.8, 30.8, 25.2, 24.5, 19.7; HRMS (EI) calcd for $C_{11}H_{15}NOCl$ [M+]: 212.0842, found 212.0842.

(1*S*,4*S*,5*R*,6*R*,9a*R*)-9a-bromo-4-methyl-1,3,4,9a-tetrahydro-2*H*-1,6-methanoquinolizin-7(6*H*)-one (83) *Following the general reductive alkylation procedure B,* 6-bromo-1-(hex-5-en-2-yl)pyridin-1-ium-3-olate (9.5 mg, 0.037 mmol) and Ag_2CO_3 (11.5 mg, 0.041 mmol) in ACN (0.4 mL) was heated up to 110 °C for 24 hr in sealed tube to give **82**(5.3 mg, 56% product ratio=3:1) after purification by FCC (DCM:10%NH_4OH in MeOH=1:0.03).

Data for **83**: R_f 0.42 (1:0.075 DCM: 10%NH_4OH in MeOH); IR (thin film) 2934, 2870, 1707, 1378 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.29 (d, *J* = 9.8 1 H), 5.82 (d, *J* = 9.5 Hz, 1 H), 3.73 (d, *J* = 8.5Hz, 1 H), 3.92 (tq, *J* = 13.1, 6.2 Hz, 1 H), 3.48 (q, *J* = 7 Hz, 1 H), 2.52 (t, *J* = 3.7 Hz, 1 H), 2.34 (td, *J* = 13.5, 7.5 1 H), 1.98 (dd, *J* = 14.7, 9.2 1 H), 1.78 (dd, *J* = 13.5, 7.0 1 H), 1.67 (dt, *J* = 13.8, 4.6 1 H), 1.56 (dt, *J* = 14.6, 5.4 1 H), 1.16 (dd, *J* = 13.2, 6.2 1 H), 1.07 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 198.0, 154.8, 125.3, 62.4, 53.4, 39.2, 30.3, 29.7, 26.9, 24.5, 20.0; HRMS (EI) calcd for $C_{11}H_{15}NOBr$ [M+]: 254.0337, found 256.0341.

(1*S*,4*S*,5*S*,6*R*,9a*S*)-4,8-dimethyl-1,3,4,9a-tetrahydro-2*H*-1,6-methanoquinolizin-7(6*H*)-one (85) *Following the general reductive alkylation procedure A,* 1-(hex-5-en-2-yl)-4-methylpyridin-1-ium-3-olate (19 mg, 0.1 mmol) and Ag_2CO_3 (31 mg, 0.11 mmol) in BuCN (1 mL) was heated up to 130 °C for 36 hr in sealed tube to give **85** (16.8 mg, 88% product ratio=8:1) after purification by FCC (pure EtOAc).

Data for **85**: R_f 0.23 (pure EtOAc); IR (thin film) 2931, 1789, 1380 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 6.82 (d, *J* = 6.2 1 H), 3.78 (d, *J* = 7.6 Hz, 1 H), 3.51 (d, *J* = 6.0 Hz, 1 H), 2.90 (dt, *J* = 12.3, 7.0 1 H), 2.30 (t, *J* = 3.1 Hz, 1 H), 1.81 (dd, *J* = 13.2, 7.2 1 H), 1.73 (s, 3 H), 1.51 (dd, *J* = 13.7, 6.8 1 H), 1.43 (dt, *J* = 14.0, 4.5 1 H), 1.19-1.12 (m, 1 H), 1.05 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 199.7, 146.7, 133.1, 69.1, 63.4, 57.6, 34.7, 30.4, 30.2, 25.9, 20.0, 14.6; HRMS (EI) calcd for $C_{12}H_{18}NO$ [M+]: 192.1388, found 192.1385.

ethyl (1*S*,4*S*,5*R*,6*R*,9a*S*,10*S*)-9a-chloro-4-methyl-7-oxo-1,3,4,6,7,9a-hexahydro-2*H*-1,6-methanoquinolizine-10-carboxylate (87) *Following the general reductive alkylation procedure A,* (*E*)-6-chloro-1-(7-ethoxy-7-oxohept-5-en-2-yl)pyridin-1-ium-3-olate (75mg, 0.017 mmol), Ag_2CO_3 (86 mg, 0.019mmol) was heated up to 130 °C for 36 hr in sealed tube to give **87** (64 mg, 85% product ratio=15:1) after purification by FCC (hexanes:EtOAc =1:3).

Data for **87**: R_f 0.55 (1:0.1 DCM: 10%NH_4OH in MeOH); IR (thin film) 2966, 2935, 1728, 1370 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.04 (d, *J* = 9.6 1 H), 5.86 (d, *J* = 9.6 Hz, 1 H), 4.11 (d, *J* = 9.6 Hz, 1 H), 4.09-4.00 (m, 2H), 3.68 (tq, *J* = 12.8, 7.0 Hz,

1 H), 3.23 (d, *J* = 9.0 Hz, 1 H), 3.13 (s 1 H), 2.36 (td, *J* = 15.5 , 8.0 Hz, 1 H), 1.68 (dt, *J* = 12.8 , 4.2 Hz, 1 H), 1.57 (dt, *J* = 14.9 , 5.3 Hz, 1 H), 1.18 (t, *J* = 7.5 Hz, 3 H), 1.08 (d, *J* = 6.4 Hz, 3 H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 193.8, 171.0, 153.6, 126.7, 89.1, 65.3, 61.5, 51.2, 48.4, 42.0, 25.1, 24.8, 19.6, 13.9; HRMS (EI) calcd for $C_{14}H_{19}NO_3Cl$ [M+]: 284.1053, found 284.1048.

ethyl (1*S*,4*S*,5*R*,6*R*,9a*S*,10*S*)-9a-bromo-4-methyl-7-oxo-1,3,4,6,7,9a-hexahydro-2*H*-1,6-methanoquinolizine-10-carboxylate (89) *Following the general reductive alkylation procedure A,* (*E*)-6-bromo-1-(7-ethoxy-7-oxohept-5-en-2-yl)pyridin-1-ium-3-olate (23mg, 0.07 mmol), Ag_2CO_3 (21 mg, 0.077mmol) was heated up to 130 °C for 4 hr in sealed tube to give **89** (18.6 mg, 82% product ratio=7:1) after purification by FCC (DCM:10%NH_4OH in MeOH=1:0.02 to 0.04).

Data for **89**: R_f 0.52 (1:0.1 DCM: 10%NH_4OH in MeOH); IR (thin film) 2969, 2939, 1730, 1372 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.23 (d, *J* = 9.6 1 H), 5.76 (d, *J* = 9.6 Hz, 1 H), 4.09-4.00 (m, 3H), 3.66 (tq, *J* = 12.9, 6.6 Hz, 1 H), 3.20-3.17 (m, 2H), 2.40 (td, *J* = 13.9 , 5.8 Hz, 1 H), 1.75 (dt, *J* = 13.8 , 5.3 Hz, 1 H), 1.58-1.56 (m, 1 H), 1.18 (t, *J* = 7.5 Hz, 3 H), 1.09 (d, *J* = 6.4 Hz, 3 H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 193.6, 170.9, 154.6, 126.0, 85.3, 65.3, 61.5, 53.4, 48.9, 42.5, 26.5, 25.1, 19.9, 13.8; HRMS (EI) calcd for $C_{14}H_{19}NO_3Br$ [M+]:328.5048, found 328.5037.

ethyl (1*S*,4*S*,5*S*,6*R*,9a*S*,10*S*)-4,9-dimethyl-7-oxo-1,3,4,6,7,9a-hexahydro-2*H*-1,6-methanoquinolizine-10-carboxylate (91) To a solution of the ethyl (*E*)-6-hydroxyhept-2-enoate[43] (1g, 5.8 mmol) in DCM (11.6 mL) at 0 °C was added Et_3N (1.21 mL, 8.7 mmol) and then methanesulfonyl chloride (0.68 mL, 8.7 mmol). The mixture was stirred for 1 h at 0 °C and slowly warming up to room temperature for 3hr before saturated aqueous NH_4Cl solution was added. This mixture was extracted with DCM three times. The combined extracts were washed with brine and dried over Na_2SO_4 and concentrated. The mixture of the crude corresponding methylate (50mg, 0.2 mmol), 5-methylpyridin-3-ol (48mg, 0.4 mmol) in BuCN(2drops) were heated up to 130 °C for 6 hr in sealed tube to give pyridinium oxide after purification by FCC (DCM:10%NH_4OH in MeOH=1:0.06 to 0.12). The corresponding pyridinium oxide (13.2 mg, 0.05 mmol), Ag_2CO_3 (15 mg, 0.055 mmol) was heated up to 130 °C for 12 hr in sealed tube to give **90** (18.6 mg, 75% product ratio>20:1) after purification by FCC (hexanes:EtOAc =1:3).

Data for **91**: R_f 0.55 (1:0.1 DCM: 10%NH_4OH in MeOH); IR (thin film) 2966, 2931, 1723, 1699, 1371 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 5.65 (s, 1 H), 4.09 (d, *J* = 8.2 Hz, 1 H), 4.05-4.00 (m, 2H), 3.34 (s, 1 H), 3.07 (d, *J* = 7.9 Hz, 1 H), 3.01-2.97 (m, 2H), 2.00 (s, 1H), 1.86-1.82 (m, 2 H), 1.58-1.57 (m, 1 H), 1.18 (t, *J* = 7.1 Hz, 3 H), 1.10 (d, *J* = 6.4 Hz, 3 H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 195.1, 171.8, 164.3, 124.3, 67,0, 61.1, 57.6, 49.3, 38.1, 30.1, 26.7, 20.9, 20.0, 13.9; HRMS (EI) calcd for $C_{15}H_{22}NO_3$ [M+]:264.1600, found 264.1589.

(1*R*,2*R*,4*S*,5*S*,6*R*,9a*R*)-2,4-dimethyl-1,3,4,9a-tetrahydro-2*H*-1,6-methanoquinolizin -7(6*H*)-one (93) *Following the general reductive alkylation procedure A,* 1-((2*S*,4*R*)-4-methylhex-5-en-2-yl)pyridin-1-ium-3-olate (10mg, 0.052 mmol) and Ag_2CO_3 (16 mg, 0.059mmol) in BuCN (0.4 mL) was heated up to 130 °C for 36 hr in sealed tube to give **93** (7.9 mg, 79% product ratio>20:1) after purification by FCC (pure EtOAc).

Data for **93**: R_f 0.50 (1:0.1 DCM: 10%NH_4OH in MeOH); IR (thin film) 2954, 2927, 2871, 1699, 1507, 1386 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.11 (dd, *J* = 9.5, 6.0 1 H), 5.90 (d, *J* = 9.5 Hz, 1 H), 3.66 (d, *J* = 7.8 Hz, 1 H), 3.54 (d, *J* = 5.6 Hz, 1 H), 2.92 (tq, *J* = 11.9, 6.6 Hz, 1 H), 2.11 (d, *J* = 7.0 Hz, 1 H), 1.90 (tq, *J* = 12.0, 6.7 Hz, 1 H), 1.78 (dd, *J* = 13.4, 7.4 1 H), 1.46 (dt, *J* = 13.8, 4.2 1 H), 1.40 (ddd, *J* = 13.4, 6.7, 1.5 1 H), 1.06 (d, *J* = 6.7 Hz, 3 H), 0.88 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 199.4, 151.6, 126.6, 69.6, 64.1, 57.2, 41.3, 35.0, 34.8, 25.9, 20.5, 19.6; HRMS (EI) calcd for $C_{12}H_{18}NO$ [M+]: 192.1388, found 192.1389.

(1*R*,2*S*,4*S*,5*S*,6*R*,9a*R*)-2,4-dimethyl-1,3,4,9a-tetrahydro-2*H*-1,6-methanoquinolizin-7(6*H*)-one (95) To a solution of the (4*S*)-4-methylhex-5-en-2-ol[44] (62.6 mg, 0.55 mmol) in DCM (1.1 mL) at 0 °C was added Et_3N (0.12 mL, 0.83 mmol) and then methanesulfonyl chloride (0.06 mL, 0.83 mmol). The mixture was stirred for 1 h at 0 °C and slowly warming up to room temperature for 1hr before saturated aqueous NH_4Cl solution was added. This mixture was extracted with DCM three times. The combined extracts were washed with brine and dried over Na_2SO_4 and concentrated. The mixture of the crude corresponding methylate (90mg, 0.47 mmol), 3-hydroxypyridine (94 mg, 0.94 mmol) in BuCN(2drops) were heated up to 130 °C for 6 hr in sealed tube to give pyridinium oxide **94*** (53 mg, 53% two steps) after purification by FCC (DCM:10%NH_4OH in MeOH=1:0.08 to 0.15). The corresponding pyridinium oxide (45 mg, 0.24 mmol), Ag_2CO_3 (72 mg, 0.26 mmol) was heated up to 130 °C for 36 hr in sealed tube to give **95** (32.3 mg, 72% product ratio=3:1:1) after purification by FCC (DCM:10%NH_4OH in MeOH =1:0.05)

Data for **95**: R_f 0.48 (1:0.1 DCM: 10%NH_4OH in MeOH); IR (thin film) 2955, 2922, 1694, 1381 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.08 (dd, *J* = 9.6, 5.9 1 H), 5.90 (dd, *J* = 9.5, 1.1 Hz, 1 H), 3.81 (d, *J* = 6.2 Hz, 1 H), 3.56 (d, *J* = 8.0 Hz, 1 H), 2.99 (tq, *J* = 14.2, 7.4 Hz, 1 H), 2.06 (d, *J* = 7.0 Hz, 1 H), 1.96 (dd, *J* = 14.0, 7.9 Hz, 1 H), 1.37 (ddd, *J* = 13.6, 6.7, 2.0 1 H), 1.21 (d, *J* = 7.1 Hz, 3 H), 0.86 (d, *J* = 6.7 Hz, 3 H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 199.4, 151.4, 126.7, 71.3, 61.8, 55.8, 41.9, 31.4, 31.3, 24.8, 20.8, 20.0; HRMS (EI) calcd for $C_{12}H_{18}NO$ [M+]: 192.1388, found 192.1384.

ethyl (1S,4S,5S,6R,9aS,10R)-6-chloro-4-methyl-9-oxo-1,3,4,6,9,9a-hexahydro-2H-1,6-methanoquinolizine-10-carboxylate (100) *Following the general reductive alkylation procedure A,* (*E*)-6-chloro-1-(7-ethoxy-7-oxohept-5-en-2-yl)pyridin-1-ium-3-olate (75mg, 0.017 mmol), Ag_2CO_3 (86 mg, 0.019mmol) was heated up to 130 °C for 36 hr in sealed tube to give **100** (48 mg, 64% product ratio=2:1) after purification by FCC (hexanes:EtOAc =1:3).

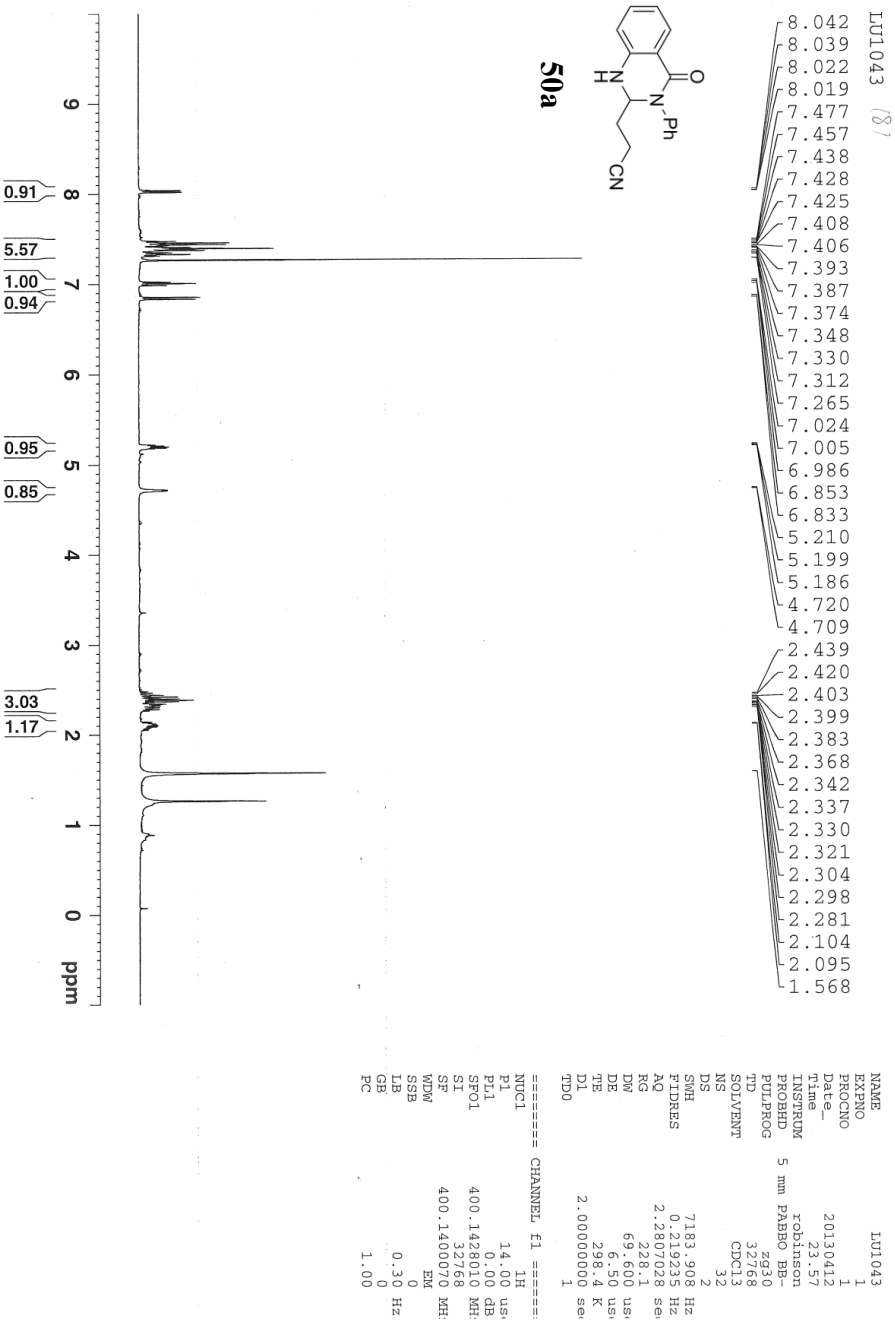
Data for **100**: R_f 0.55 (1:0.1 DCM: 10%NH_4OH in MeOH); IR (thin film) 3039, 1714, 1601, 1369 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.37 (d, *J* = 9.8 1 H), 5.88 (d, *J* = 9.8 Hz, 1 H), 4.14-4.09 (m, 2H), 3.92 (s, 1 H), 3.75 (dq, *J* = 13.0, 6.7 Hz, 1 H), 3.46 (dq, *J* = 14.4 Hz, 1 H), 2.84 (s, 1 H), 2.05 (ddd, *J* =13.0, 5.8, 2.0 Hz, 1 H), 1.86-1.75 (m, 5H), 1.30 (dd, *J* = 14.4 , 5.9 Hz, 1 H), 1.25 (t, *J* = 6.8 Hz, 3 H), 1.23 (d, *J* = 7.2 Hz, 3 H); ^{13}C NMR (175 MHz, $CDCl_3$) δ 195.8, 169.9, 157.8, 126.9, 87.3, 72.4, 62.7, 61.5, 51.2, 39.0, 27.1, 22.2, 19.6, 14.1; HRMS (EI) calcd for $C_{14}H_{19}NO_3Cl$ [M+]: 284.1053, found 284.1048.

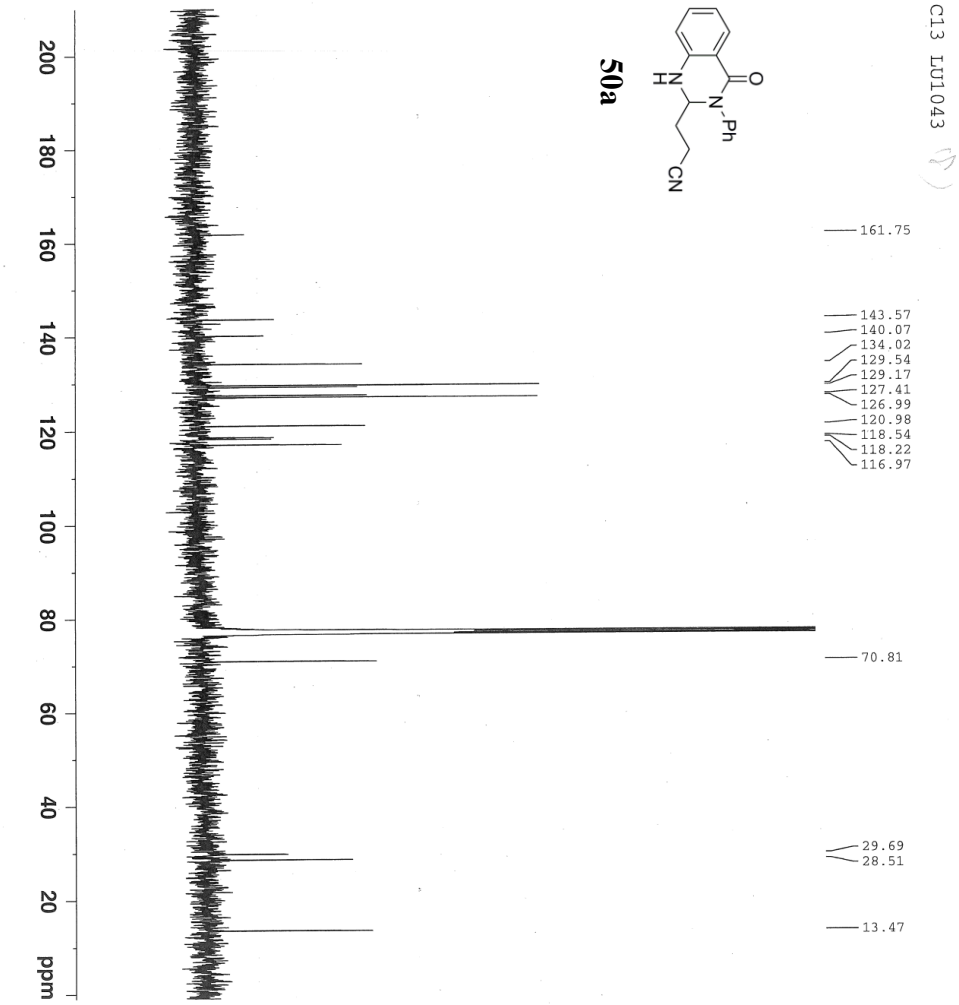
(1*S*,4*S*,5*S*,6*R*,9a*R*,10*S*)-4,10-dimethyl-1,3,4,9a-tetrahydro-2*H*-1,6-methanoquinolizin-7(6*H*)-one (102) *Following the general reductive alkylation procedure A,* (*E*)-1-(hept-5-en-2-yl)pyridin-1-ium-3-olate (9mg, 0.05 mmol), Ag_2CO_3 (15 mg, 0.055mmol), and trace of BHT in BuCN (0.5 mL) was heated up to 130 °C for 24 hr, then 150 °C for 24 hr in sealed tube to give **102** (4.6 mg, 51% product ratio=15:1) after purification by FCC (DCM:10%NH_4OH in MeOH=1:0.04 to 0.06).

Data for **102**: R_f 0.55 (1:0.1 DCM: 10%NH_4OH in MeOH); IR (thin film) 2966, 2931, 2862, 1693, 1507, 1383 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.17 (dd, *J* = 9.6, 5.9 1 H), 5.99 (dd, *J* = 9.8, 1.0 Hz, 1 H), 3.86 (d, *J* = 7.9 Hz, 1 H), 3.42 (d, *J* = 6.2 Hz, 1 H), 2.99 (tq, *J* = 12.4, 7.0 Hz, 1 H), 2.34 (dq, *J* = 15.5, 8.0 Hz, 1 H), 2.03 (s, 1 H), 1.78 (dd, *J* = 13.4, 7.4 1 H), 1.83-1.72 (m, 1H), 1.51 (dtd, *J* = 13.8, 5.7, 1.2 1 H), 1.24-1.19 (m, 1H), 1.09 (d, *J* = 6.4 Hz, 3 H), 0.96 (d, *J* = 7.7 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.5, 152.1, 129.2, 69.9, 69.4, 57.5, 42.0, 37.1, 30.9, 27.0, 20.0, 17.5; HRMS (EI) calcd for $C_{12}H_{18}NO$ [M+]: 192.1388, found 192.1382.

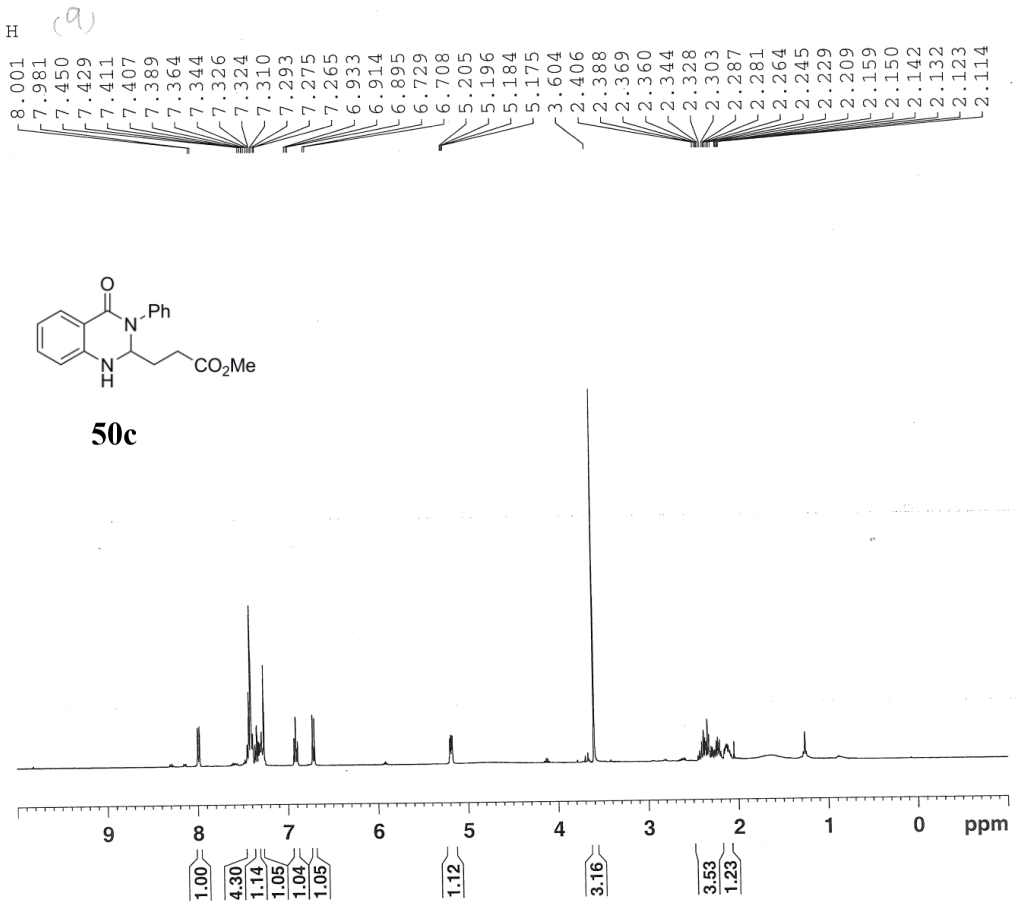
(1*S*,4*S*,5*S*,6*R*,9a*R*,10*R*)-4,10-dimethyl-1,3,4,9a-tetrahydro-2*H*-1,6-methanoquinolizin-7(6*H*)-one (104) *Following the general reductive alkylation procedure A,* (*Z*)-1-(hept-5-en-2-yl)pyridin-1-ium-3-olate (9mg, 0.05 mmol), Ag_2CO_3 (15 mg, 0.055mmol), and trace of BHT in BuCN (0.5 mL) was heated up to 130 °C for 24 hr, then 150 °C for 24 hr in sealed tube to give **104** (2.1 mg, 23% product ratio=8:1) after purification by FCC (DCM:10%NH_4OH in MeOH=1:0.04 to 0.06).

Data for **104**: R_f 0.55 (1:0.1 DCM: 10%NH_4OH in MeOH); IR (thin film) 2964, 2927, 2862, 1715, 1370 cm^{-1}; ^1H NMR (800 MHz, $CDCl_3$) δ 7.03 (dd, *J* = 9.6, 5.8 1 H), 5.90 (d, *J* = 9.4 Hz, 1 H), 3.62 (d, *J* = 5.6 Hz, 1 H), 3.26 (brs, 1 H), 3.06 (tq, *J* = 13.4, 6.8 Hz, 1 H), 2.27 (m, 1 H), 2.04 (brs, 1H), 1.91-179 (m, 2H), 1.52 (m, 1H), 1.14 (m, 1H), 1.28 (d, *J* = 7.4 Hz, 3 H), 1.06 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR** (200 MHz, $CDCl_3$) δ 199.5, 150.4, 127.0, 70.5, 70.1, 57.3, 36.4, 35.6, 30.9, 27.2, 26.4, 20.1, 11.2; HRMS (EI) calcd for $C_{12}H_{18}NO$ [M+]: 192.1388, found 192.1384.


LU1043 (8)
8.042
8.039
8.022
8.019
7.477
7.457
7.438
7.428
7.425
7.408
7.406
7.393
7.387
7.374
7.348
7.330
7.312
7.265
7.024
7.005
6.986
6.853
6.833
5.210
5.199
5.186
4.720
4.709
2.439
2.420
2.403
2.399
2.383
2.368
2.342
2.337
2.330
2.321
2.304
2.298
2.281
2.104
2.095
1.568
50a
0.91
5.57
1.00
0.94
0.95
0.85
3.03
1.17
9
8
7
6
5
4
3
2
1
0
ppm
NAME LU1043
EXPNO 1
PROCNO 1
Date_ 20130412
Time_ 23.57
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 7183.908 Hz
FIDRES 0.219235 Hz
AQ 2.2807028 se
RG 228.1
DW 69.600 us
DE 6.50 us
TE 298.4 K
D1 2.00000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.00 us
PL1 0.00 dB
SFO1 400.1428010 MH
SI 32768
SF 400.1400070 MH
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

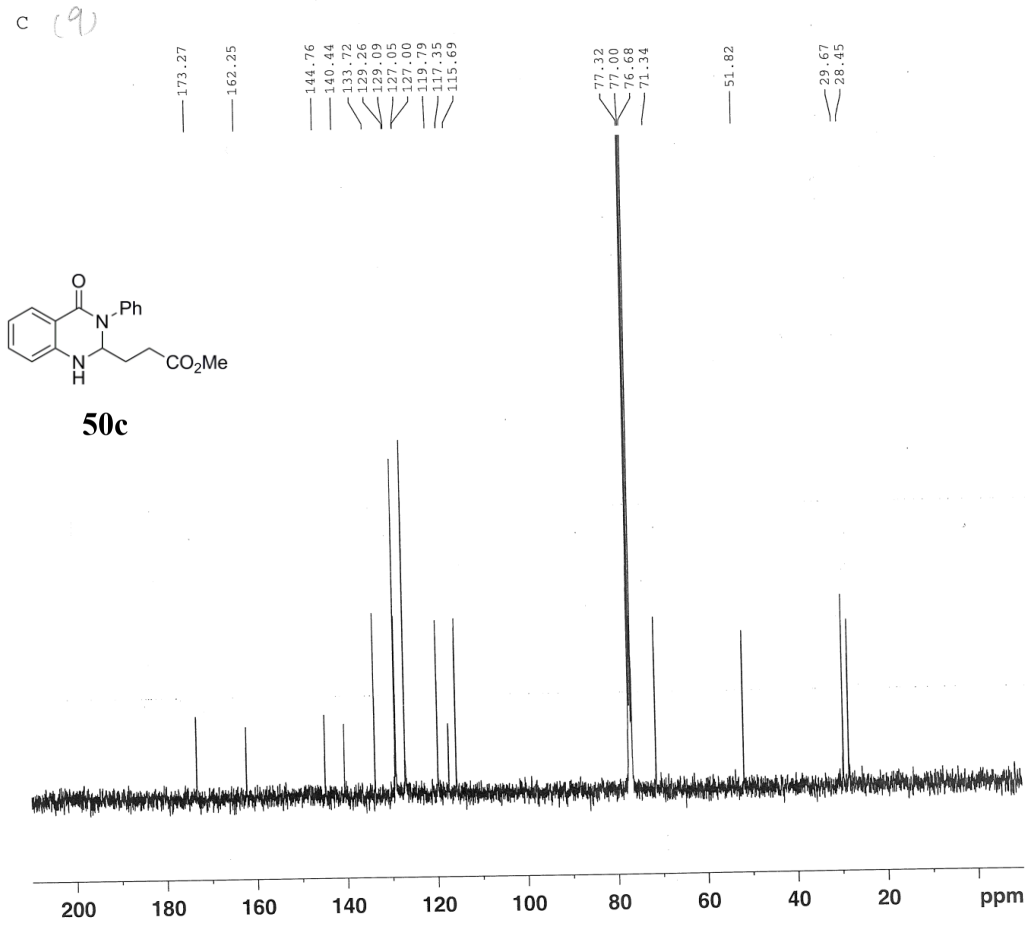



```
NAME                                LU1043
EXPNO                                    3
PROCNO                                   1
Date_                             20130413
Time                                 4.36
INSTRUM                      robinson
PROBHD                5 mm PABBO BB-
PULPROG                          zgpg30
TD                                  65536
SOLVENT                           CDCl3
NS                                    4000
DS                                       4
SWH                           23980.814 Hz
FIDRES                         0.365918 Hz
AQ                             1.3664756 sec
RG                                   32768
DW                                20.850 usec
DE                                 6.50 usec
TE                                 300.3 K
D1                          1.00000000 sec
D11                         0.03000000 sec
TD0                                      1

========== CHANNEL f1 =======
NUC1                                  13C
P1                                  9.00 usec
PL1                                -2.00 dB
SFO1                    100.6253446 MHz

========== CHANNEL f2 =======
CPDPRG2                       waltz16
NUC2                                  1H
PCPD2                              90.00 usec
PL2                                 0.00 dB
PL12                               16.16 dB
PL13                               17.00 dB
SFO2                    400.1416006 MHz
SI                                   32768
SF                      100.6152841 MHz
WDW                                   EM
SSB                                    0
LB                                  3.00 Hz
GB                                     0
PC                                  1.40
```



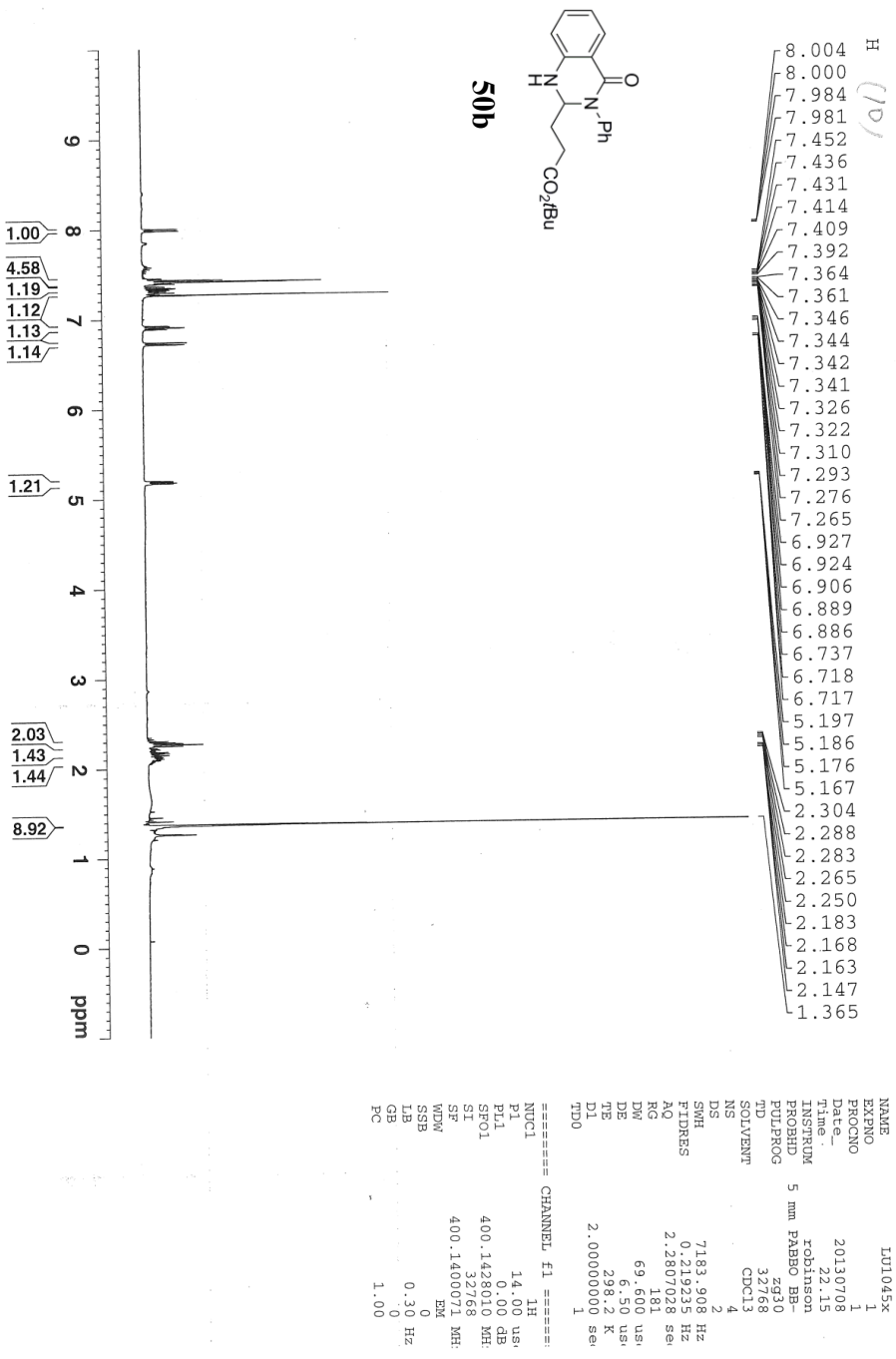
50c

NAME	LU1044
EXPNO	2
PROCNO	1
Date_	20130709
Time	23.33
INSTRUM	robinson
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	32768
SOLVENT	CDCl3
NS	8
DS	2
SWH	7183.908 Hz
FIDRES	0.219235 Hz
AQ	2.2807028 se
RG	18
DW	69.600 us
DE	6.50 us
TE	298.2 K
D1	2.00000000 se
TD0	1
======== CHANNEL f1 ======	
NUC1	1H
P1	14.00 us
PL1	0.00 dB
SFO1	400.1428010 MH
SI	32768
SF	400.1400070 MH
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00



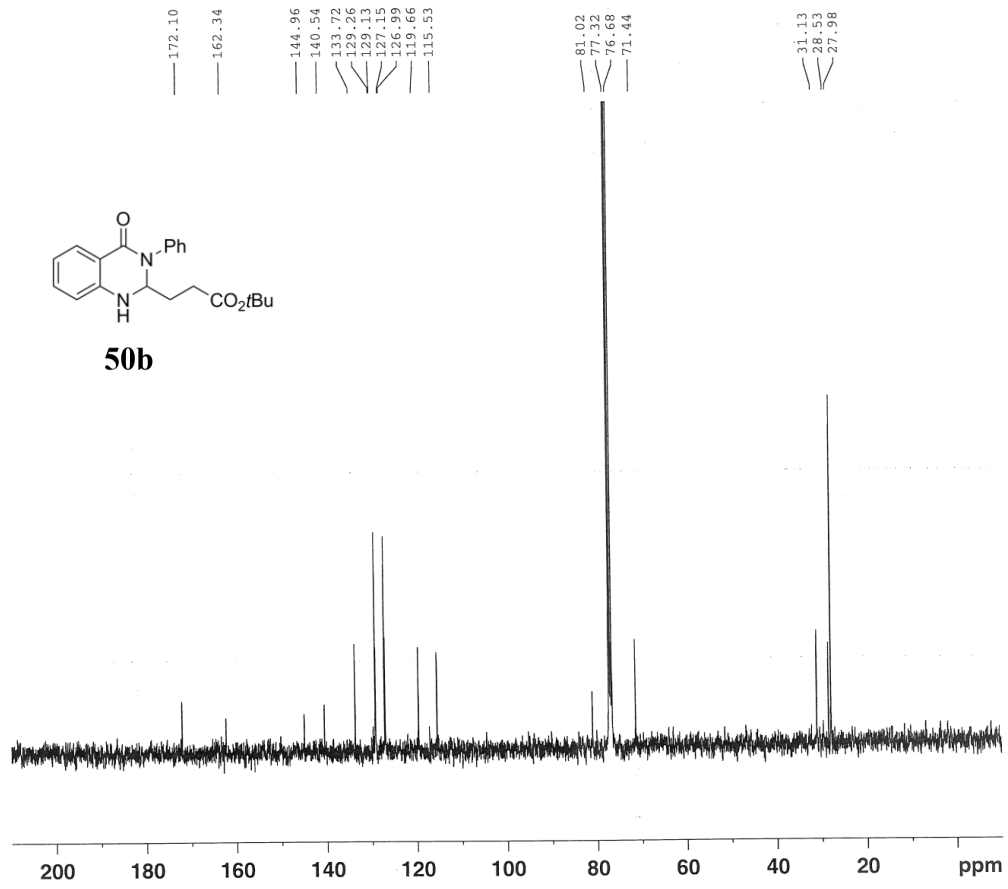
50c

NAME	LU1044
EXPNO	3
PROCNO	1
Date_	20130710
Time	2.24
INSTRUM	robinson
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	800
DS	4
SWH	23980.814 Hz
FIDRES	0.365918 Hz
AQ	1.3664756 sec
RG	20642.5
DW	20.850 use
DE	6.50 use
TE	299.8 K
D1	1.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 =======	
NUC1	13C
P1	9.00 use
PL1	-2.00 dB
SFO1	100.6253446 MHz
======== CHANNEL f2 =======	
CPDPRG2	waltz16
NUC2	1H
PCPD2	90.00 use
PL2	0.00 dB
PL12	16.16 dB
PL13	17.00 dB
SFO2	400.1416006 MHz
SI	32768
SF	100.6152857 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40



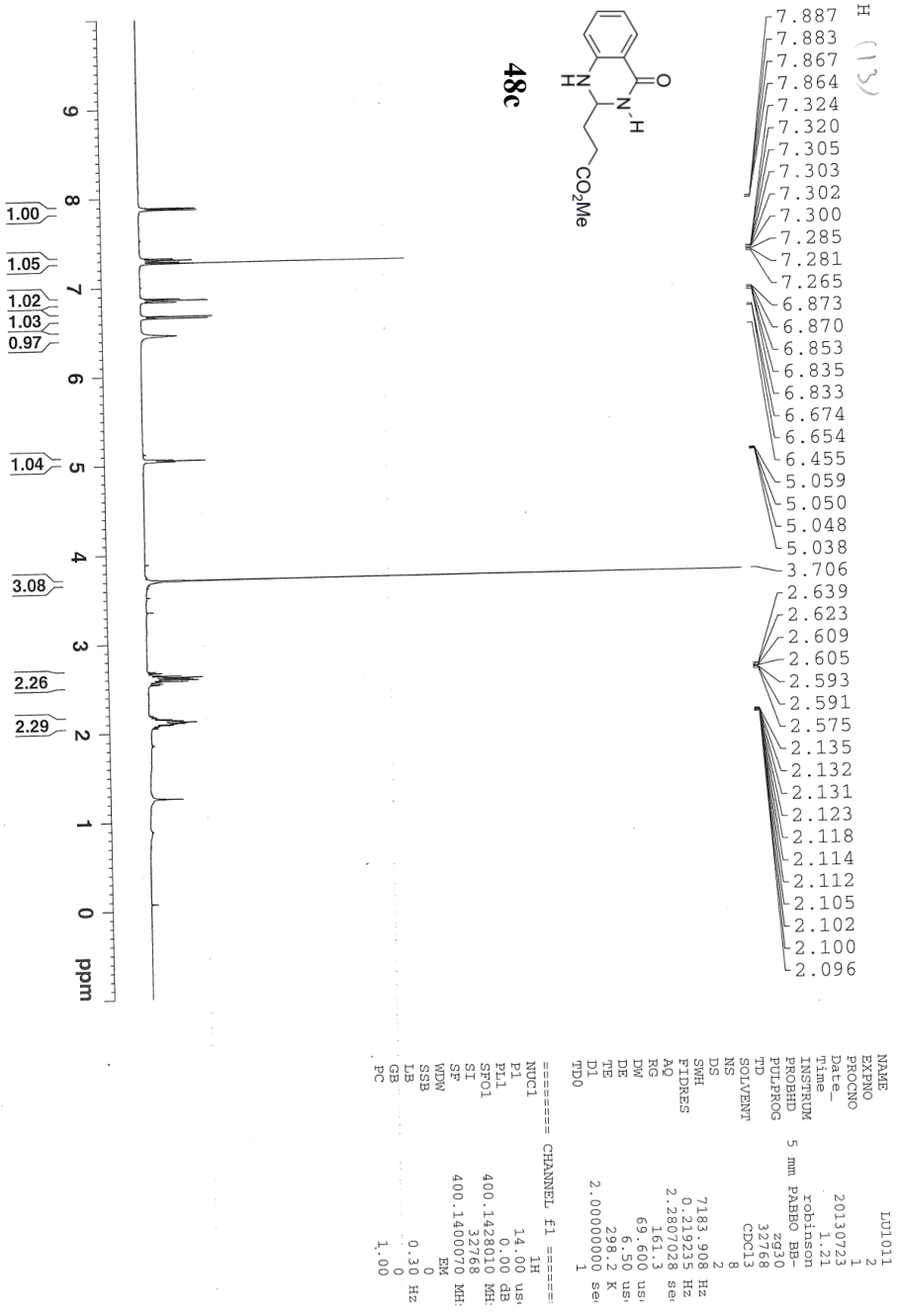

```
NAME                  LU1045x
EXPNO                       1
PROCNO                      1
Date_              20130708
Time               22.15
INSTRUM            robinson
PROBHD     5 mm PABBO BB-
PULPROG            zg30
TD                 32768
SOLVENT            CDCl3
NS                  4
DS                  2
SWH                7183.908 Hz
FIDRES             0.219235 Hz
AQ                 2.2807028 se
RG                 181
DW                 69.600 us
DE                 6.50 us
TE                 298.2 K
D1                 2.00000000 se
TD0                1

======== CHANNEL f1 ========
NUC1               1H
P1                 14.00 us
PL1                0.00 dB
SFO1               400.1428010 MH
SI                 32768
SF                 400.1400071 MH
WDW                EM
SSB                0
LB                 0.30 Hz
GB                 0
PC                 1.00
```

C (10)

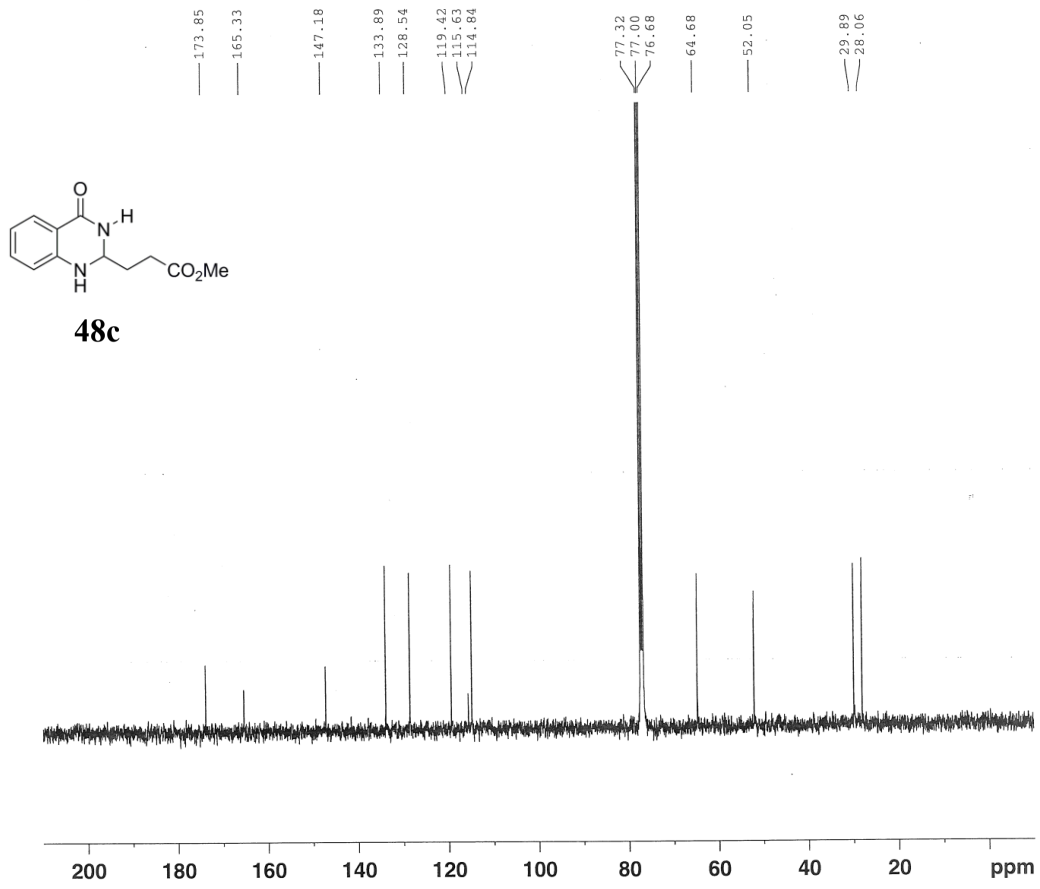


50b

NAME	LU1045
EXPNO	3
PROCNO	1
Date_	20130708
Time	23.07
INSTRUM	robinson
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	1200
DS	4
SWH	23980.814 Hz
FIDRES	0.365918 Hz
AQ	1.3664756 sec
RG	13004
DW	20.850 use
DE	6.50 use
TE	299.8 K
D1	1.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 =======	
NUC1	13C
P1	9.00 use
PL1	-2.00 dB
SFO1	100.6253446 MHz
======== CHANNEL f2 =======	
CPDPRG2	waltz16
NUC2	1H
PCPD2	90.00 use
PL2	0.00 dB
PL12	16.16 dB
PL13	17.00 dB
SFO2	400.1416006 MHz
SI	32768
SF	100.6152836 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40

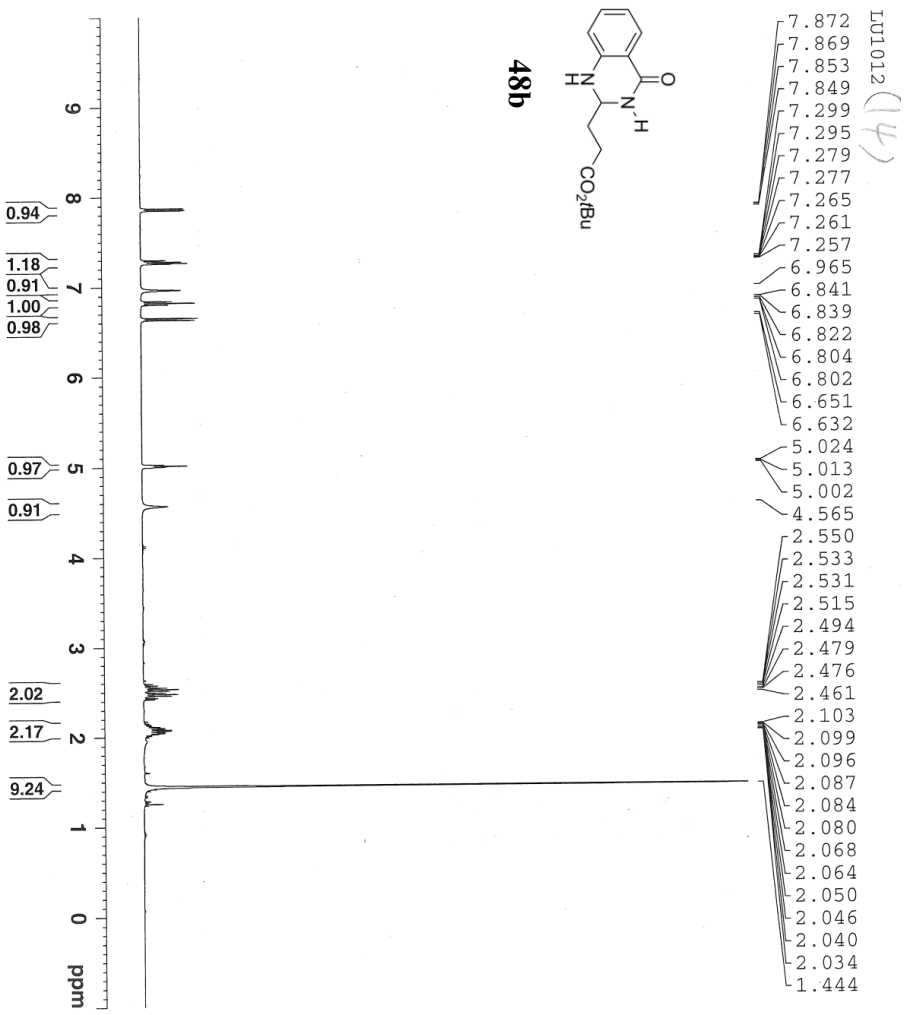

48c
CO2Me
7.887
7.883
7.867
7.864
7.324
7.320
7.305
7.303
7.302
7.300
7.285
7.281
7.265
6.873
6.870
6.853
6.835
6.833
6.674
6.654
6.455
5.059
5.050
5.048
5.038
3.706
2.639
2.623
2.609
2.605
2.593
2.591
2.575
2.135
2.132
2.131
2.123
2.118
2.114
2.112
2.105
2.102
2.100
2.096
1.00
1.05
1.02
1.03
0.97
1.04
3.08
2.26
2.29
ppm
NAME LU1011
EXPNO 2
PROCNO 1
Date_ 20130723
Time_ 1.21
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 8
DS 2
SWH 7183.908 Hz
FIDRES 0.219235 Hz
AQ 2.2807028 se
RG 161.3
DW 69.600 us
DE 6.50 us
TE 298.2 K
D1 2.00000000 se
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 us
PL1 0.00 dB
SFO1 400.1428010 MH
SI 32768
SF 400.1400070 MH
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

C 113

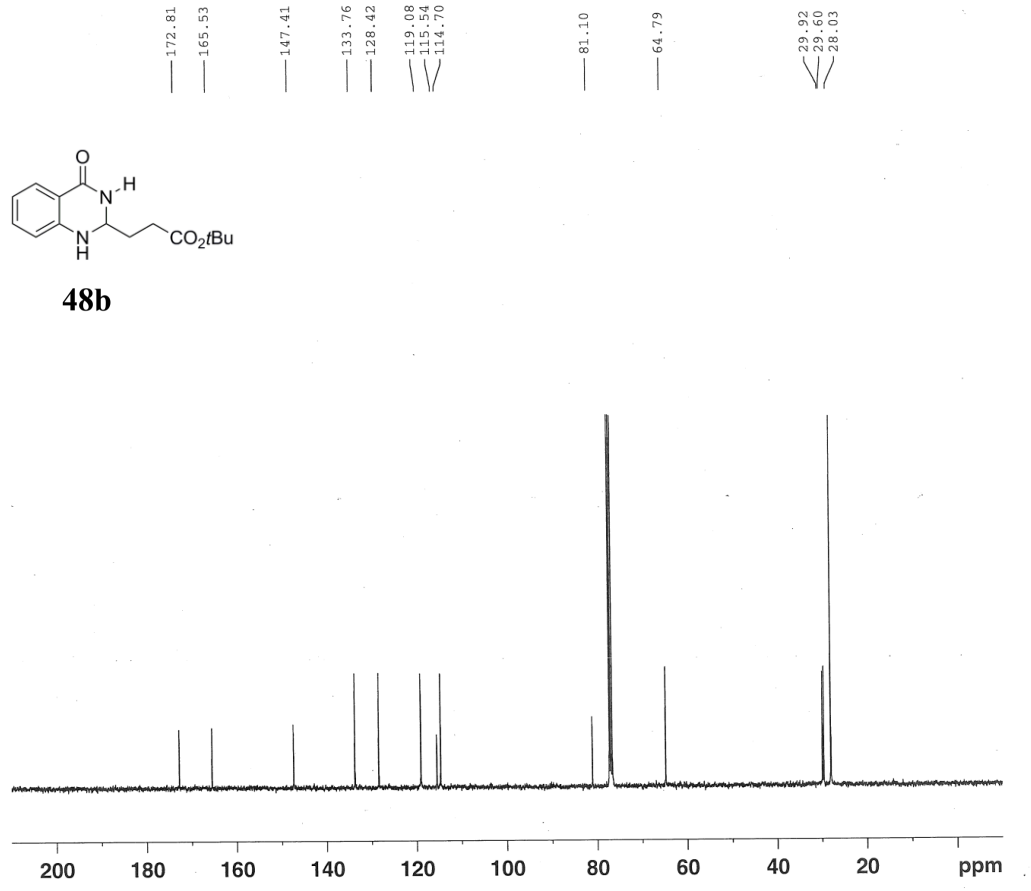


48c

NAME	LU1011
EXPNO	3
PROCNO	1
Date_	20130723
Time	2.10
INSTRUM	robinson
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	1200
DS	4
SWH	23980.814 Hz
FIDRES	0.365918 Hz
AQ	1.3664756 sec
RG	8192
DW	20.850 use
DE	6.50 use
TE	299.5 K
D1	1.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 =======	
NUC1	13C
P1	9.00 use
PL1	-2.00 dB
SFO1	100.6253446 MHz
======== CHANNEL f2 =======	
CPDPRG2	waltz16
NUC2	1H
PCPD2	90.00 use
PL2	0.00 dB
PL12	16.16 dB
PL13	17.00 dB
SFO2	400.1416006 MHz
SI	32768
SF	100.6152847 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40

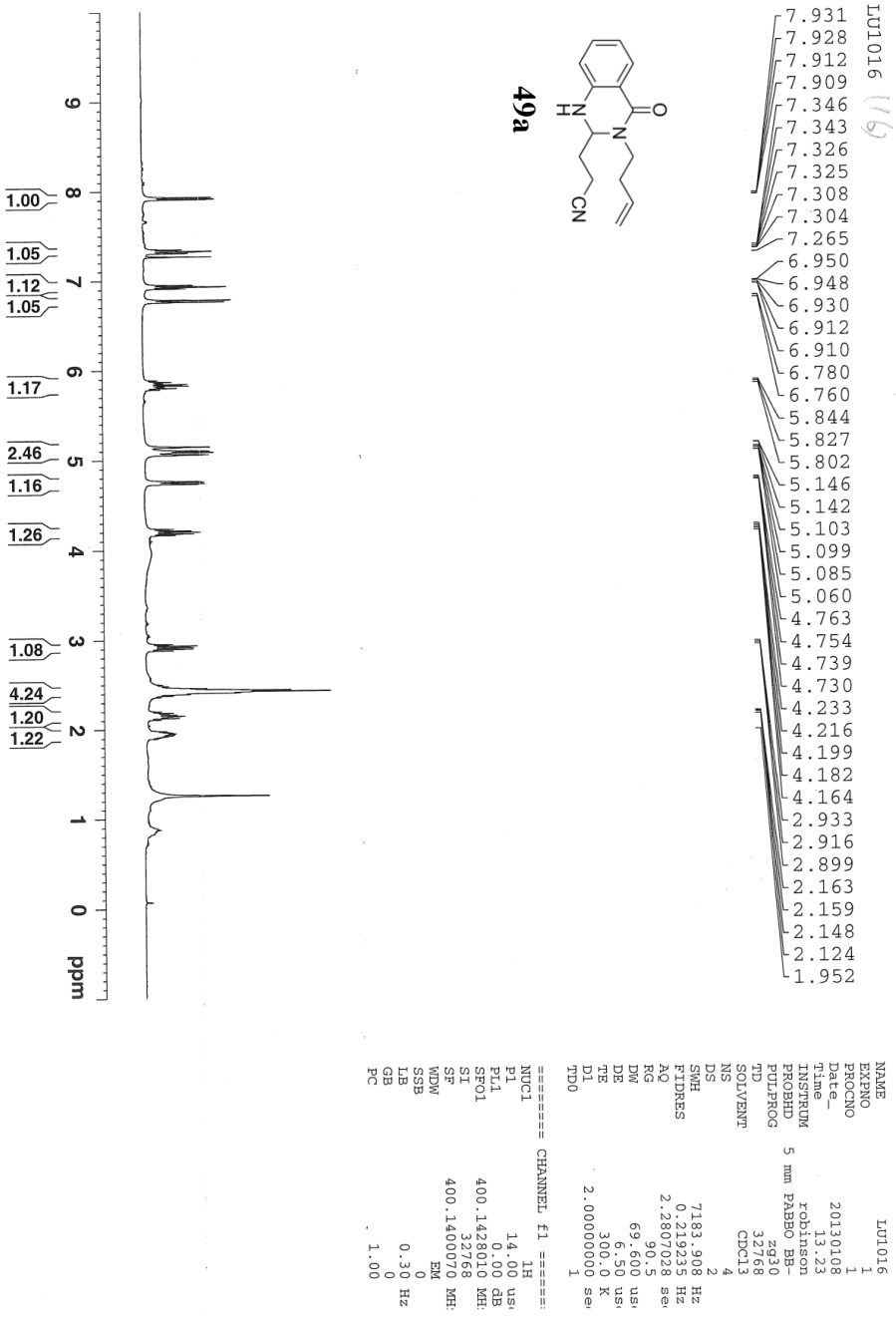

LU1012 (14)
7.872
7.869
7.853
7.849
7.299
7.295
7.279
7.277
7.265
7.261
7.257
6.965
6.841
6.839
6.822
6.804
6.802
6.651
6.632
5.024
5.013
5.002
4.565
2.550
2.533
2.531
2.515
2.494
2.479
2.476
2.461
2.103
2.099
2.096
2.087
2.084
2.080
2.068
2.064
2.050
2.046
2.040
2.034
1.444
48b
CO2tBu
0.94
1.18
0.91
1.00
0.98
0.97
0.91
2.02
2.17
9.24
ppm
NAME LU1012
EXPNO 1
PROCNO 1
Date_ 20130413
Time 21.41
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 7183.908 Hz
FIDRES 0.219235 Hz
AQ 2.2807028 se
RG 64
DW 69.600 us
DE 6.50 us
TE 298.7 K
D1 2.00000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.00 us
PL1 0.00 dB
SFO1 400.1428010 MH
SI 32768
SF 400.1400070 MH
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

C13 LU1012 (14)

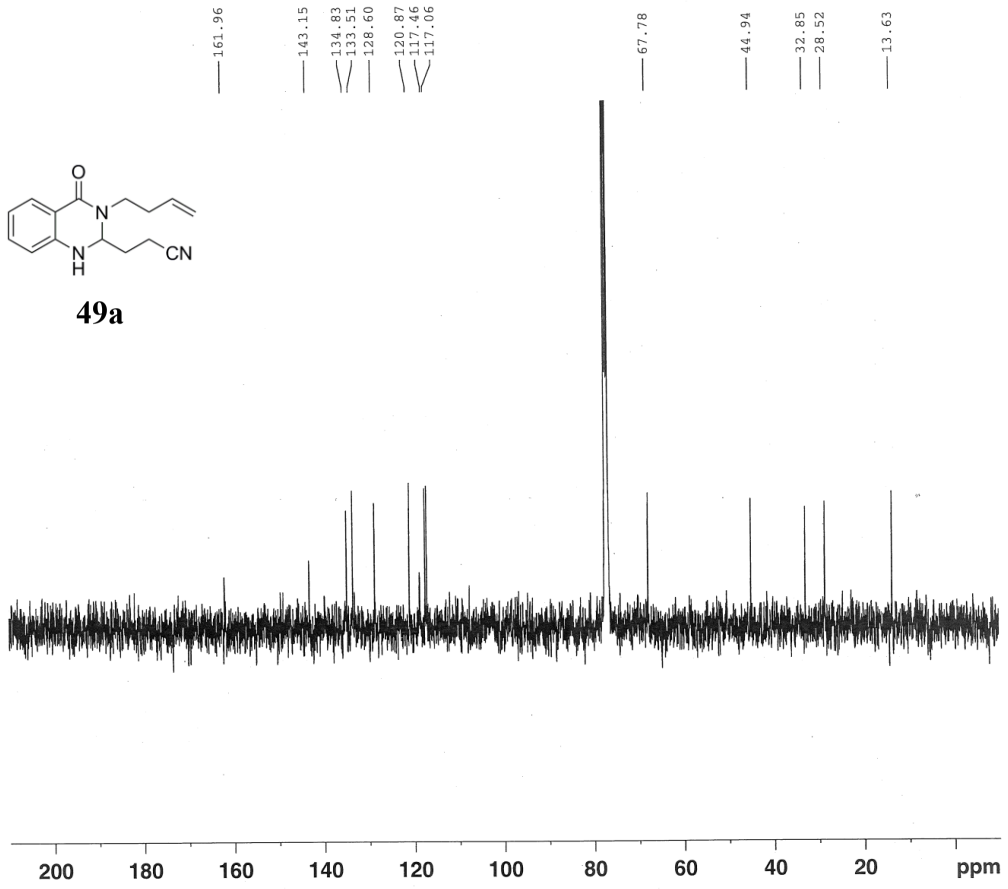


48b

NAME	LU1012
EXPNO	3
PROCNO	1
Date_	20130413
Time	22.06
INSTRUM	robinson
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	600
DS	4
SWH	23980.814 Hz
FIDRES	0.365918 Hz
AQ	1.3664756 sec
RG	11585.2
DW	20.850 use
DE	6.50 use
TE	300.3 K
D1	1.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 =======	
NUC1	13C
P1	9.00 use
PL1	-2.00 dB
SFO1	100.6253446 MHz
======== CHANNEL f2 =======	
CPDPRG2	waltz16
NUC2	1H
PCPD2	90.00 use
PL2	0.00 dB
PL12	16.16 dB
PL13	17.00 dB
SFO2	400.1416006 MHz
SI	32768
SF	100.6152874 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40

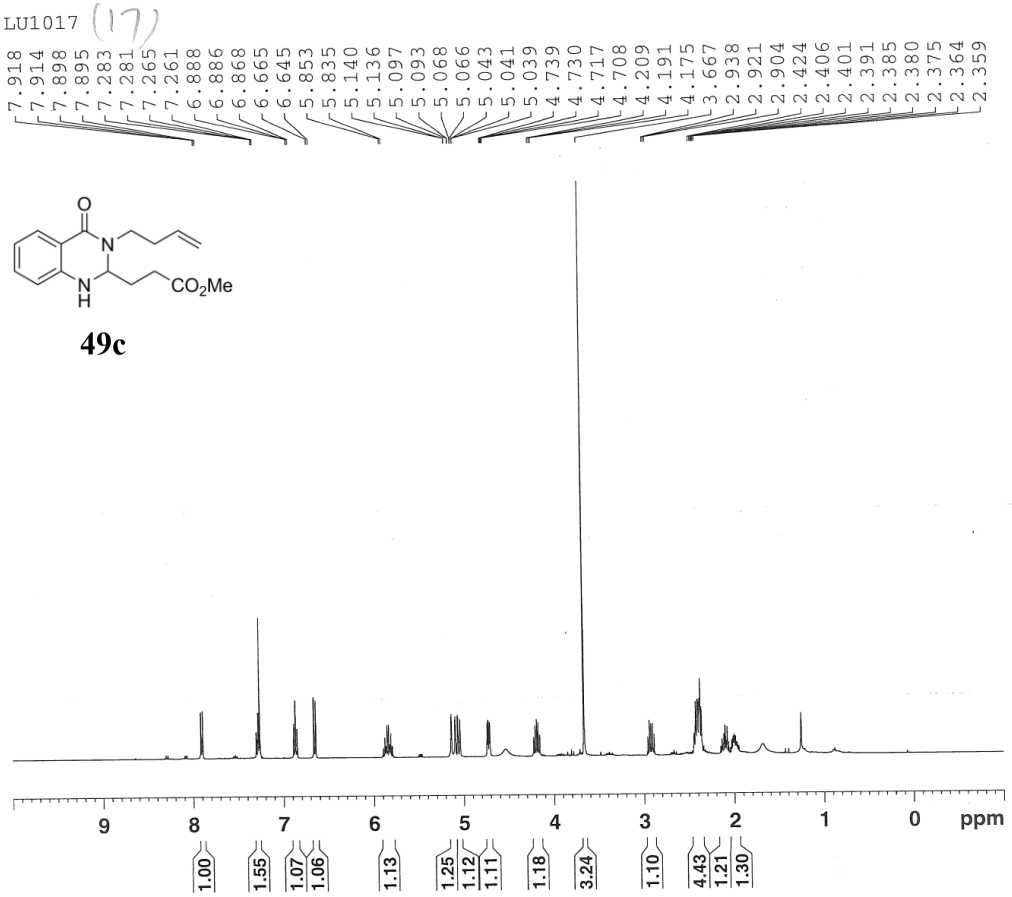

LU1016 (16)
7.931
7.928
7.912
7.909
7.346
7.343
7.326
7.325
7.308
7.304
7.265
6.950
6.948
6.930
6.912
6.910
6.780
6.760
5.844
5.827
5.802
5.146
5.142
5.103
5.099
5.085
5.060
4.763
4.754
4.739
4.730
4.233
4.216
4.199
4.182
4.164
2.933
2.916
2.899
2.163
2.159
2.148
2.124
1.952
49a
NAME LU1016
EXPNO 1
PROCNO 1
Date_ 20130108
Time 13.23
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 4
DS 2
SWH 7183.908 Hz
FIDRES 0.219235 Hz
AQ 2.2807028 se
RG 90.5
DW 69.600 us
DE 6.50 us
TE 300.0 K
D1 2.00000000 se
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 us
PL1 0.00 dB
SFO1 400.1428010 MH
SI 32768
SF 400.1400070 MH
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1.00
1.05
1.12
1.05
1.17
2.46
1.16
1.26
1.08
4.24
1.20
1.22
9 8 7 6 5 4 3 2 1 0 ppm

C13 LU1016 (16)



49a

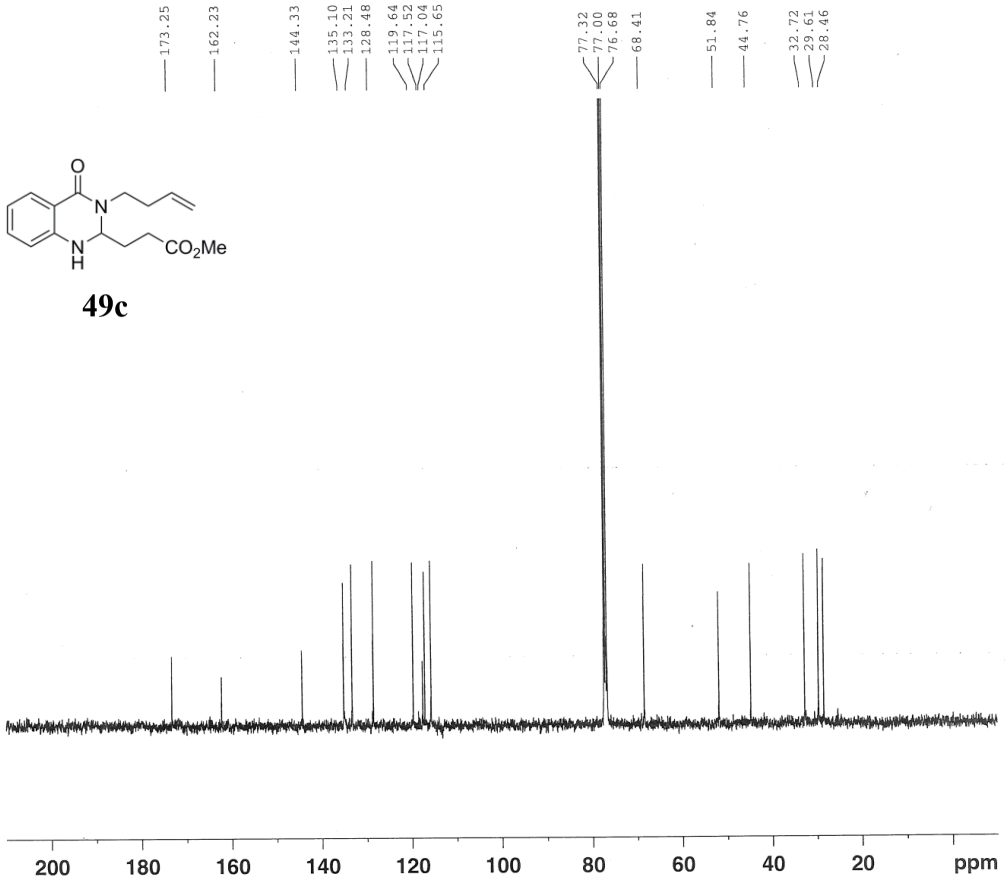
NAME	LU1016x
EXPNO	3
PROCNO	1
Date_	20130404
Time	22.58
INSTRUM	robinson
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	2000
DS	4
SWH	23980.814 Hz
FIDRES	0.365918 Hz
AQ	1.3664756 sec
RG	18390.4
DW	20.850 use
DE	6.50 use
TE	300.5 K
D1	1.00000000 sec
D11	0.03000000 sec
TD0	1
========	CHANNEL f1 =======
NUC1	13C
P1	9.00 use
PL1	-2.00 dB
SFO1	100.6253446 MHz
========	CHANNEL f2 =======
CPDPRG2	waltz16
NUC2	1H
PCPD2	90.00 use
PL2	0.00 dB
PL12	16.16 dB
PL13	17.00 dB
SFO2	400.1416006 MHz
SI	32768
SF	100.6152835 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40



49c

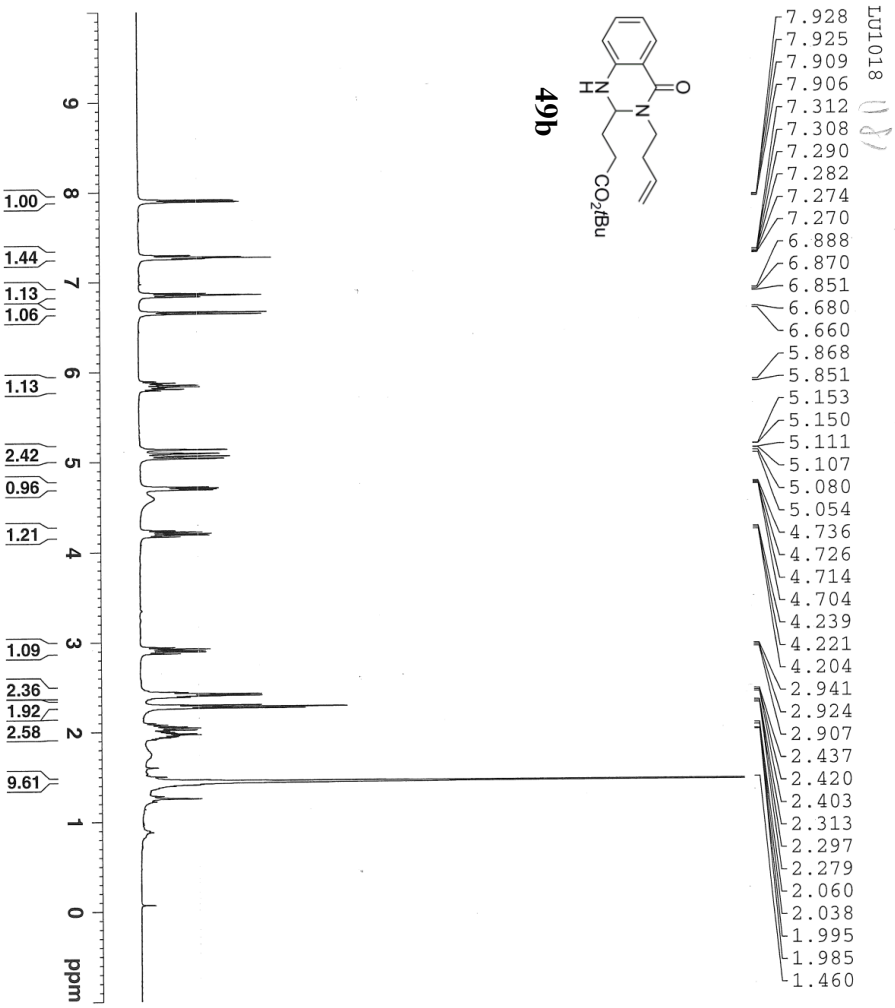
```
NAME                LU1017
EXPNO                    1
PROCNO                   1
Date_             20130528
Time                 0.24
INSTRUM           robinson
PROBHD    5 mm PABBO BB-
PULPROG               zg30
TD                   32768
SOLVENT              CDCl3
NS                      16
DS                       2
SWH               7183.908 Hz
FIDRES            0.219235 Hz
AQ                2.2807028 se
RG                    90.5
DW                 69.600 us
DE                  6.50 us
TE                 298.8 K
D1              2.00000000 se
TD0                      1

======== CHANNEL f1 ======
NUC1                    1H
P1                 14.00 us
PL1                 0.00 dB
SFO1          400.1428010 MH
SI                   32768
SF            400.1400069 MH
WDW                     EM
SSB                      0
LB                  0.30 Hz
GB                       0
PC                    1.00
```

C13 LU1017 (17)



49c

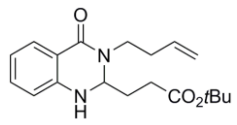
NAME	LU1017
EXPNO	3
PROCNO	1
Date_	20130528
Time	1.05
INSTRUM	robinson
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	1000
DS	4
SWH	23980.814 Hz
FIDRES	0.365918 Hz
AQ	1.3664756 sec
RG	8192
DW	20.850 use
DE	6.50 use
TE	301.0 K
D1	1.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 =======	
NUC1	13C
P1	9.00 use
PL1	-2.00 dB
SFO1	100.6253446 MHz
======== CHANNEL f2 =======	
CPDPRG2	waltz16
NUC2	1H
PCPD2	90.00 use
PL2	0.00 dB
PL12	16.16 dB
PL13	17.00 dB
SFO2	400.1416006 MHz
SI	32768
SF	100.6152849 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40



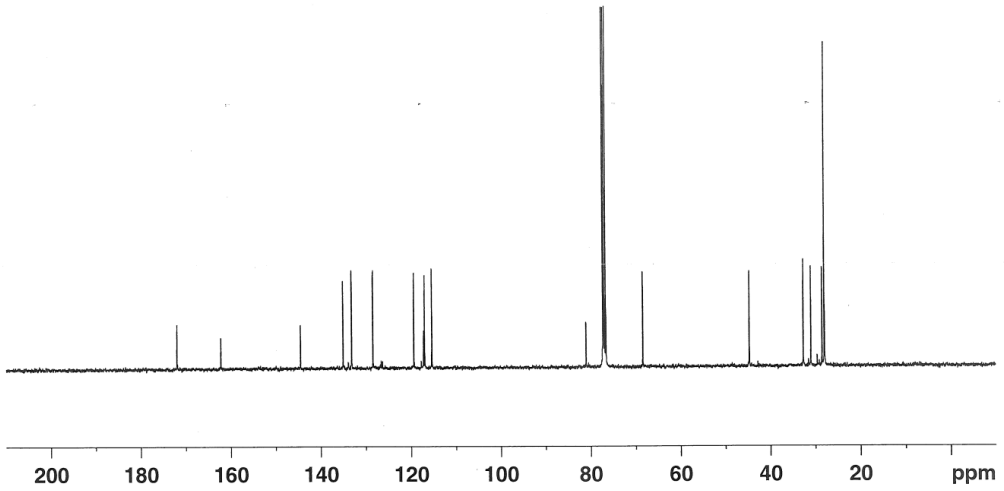

```
NAME                  LU1018
EXPNO                      1
PROCNO                     1
Date_              20130108
Time                   13.37
INSTRUM          robinson
PROBHD     5 mm PABBO BB-
PULPROG              zg30
TD                  32768
SOLVENT             CDCl3
NS                         4
DS                         2
SWH              7183.908 Hz
FIDRES           0.219235 Hz
AQ               2.2807028 se
RG                      90.5
DW                    69.600 us
DE                     6.50 us
TE                    300.0 K
D1               2.00000000 se
TD0                        1

========== CHANNEL f1 ========
NUC1                     1H
P1                   14.00 us
PL1                   0.00 dB
SFO1          400.1428010 MH
SI                     32768
SF            400.1400070 MH
WDW                       EM
SSB                        0
LB                  0.30 Hz
GB                         0
PC                      1.00
```

C13 LU1018 (18)

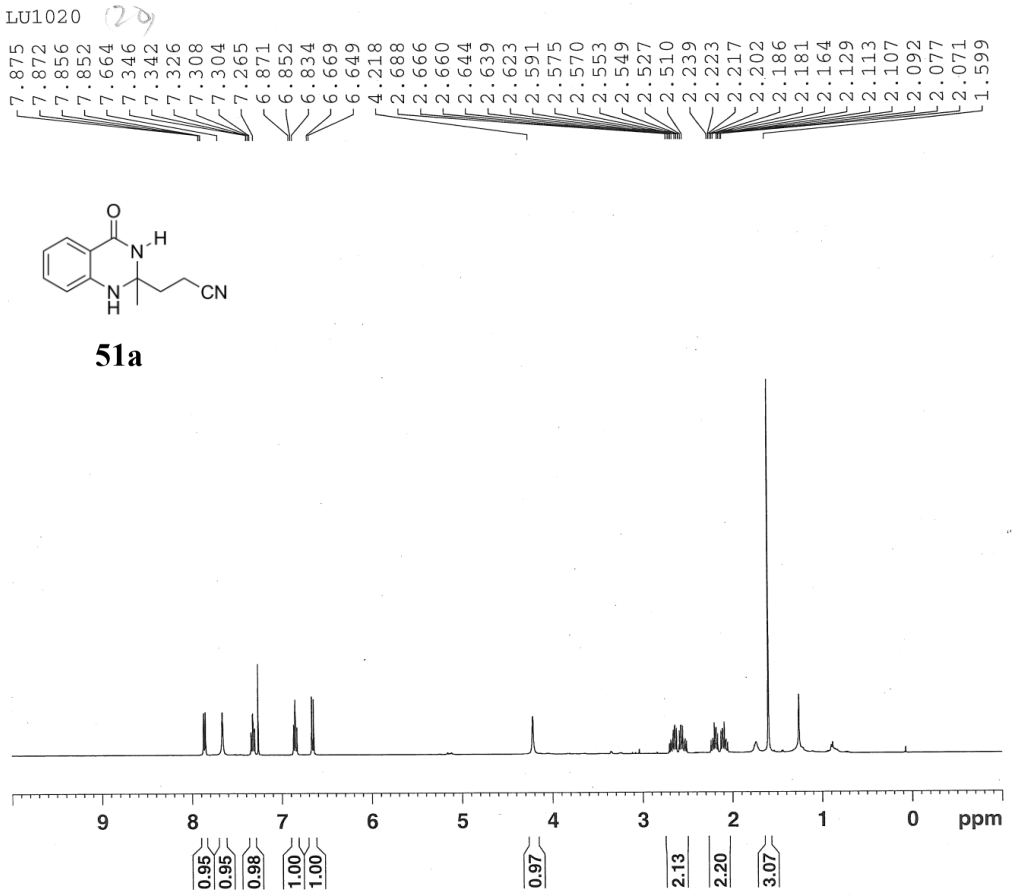
171.99
162.23
144.51
135.06
133.16
128.43
119.38
116.99
115.41
81.01
77.29
76.97
76.65
44.71
32.70
31.01
28.55
28.03



49b



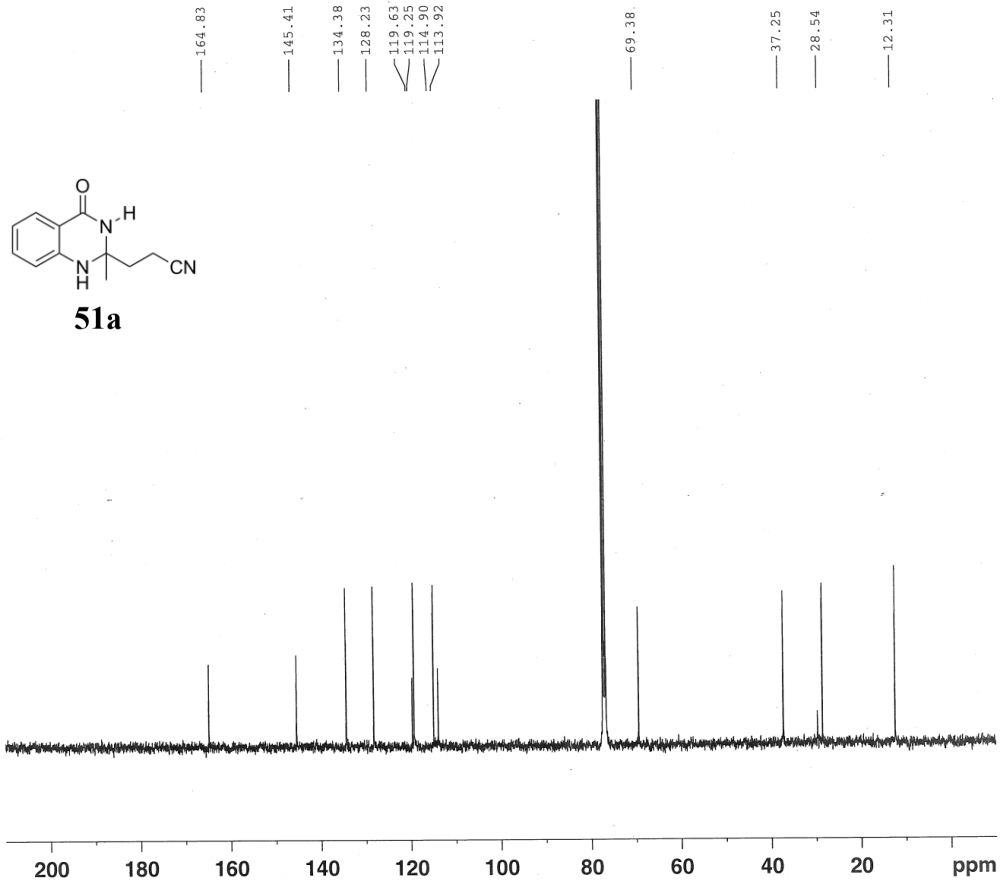
NAME	LU1018
EXPNO	3
PROCNO	1
Date_	20130227
Time	2.48
INSTRUM	robinson
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	3000
DS	4
SWH	23980.814 Hz
FIDRES	0.365918 Hz
AQ	1.3664756 sec
RG	18390.4
DW	20.850 use
DE	6.50 use
TE	299.1 K
D1	1.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 =======	
NUC1	13C
P1	9.00 use
PL1	-2.00 dB
SFO1	100.6253446 MHz
======== CHANNEL f2 =======	
CPDPRG2	waltz16
NUC2	1H
PCPD2	90.00 use
PL2	0.00 dB
PL12	16.16 dB
PL13	17.00 dB
SFO2	400.1416006 MHz
SI	32768
SF	100.6152893 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40



51a

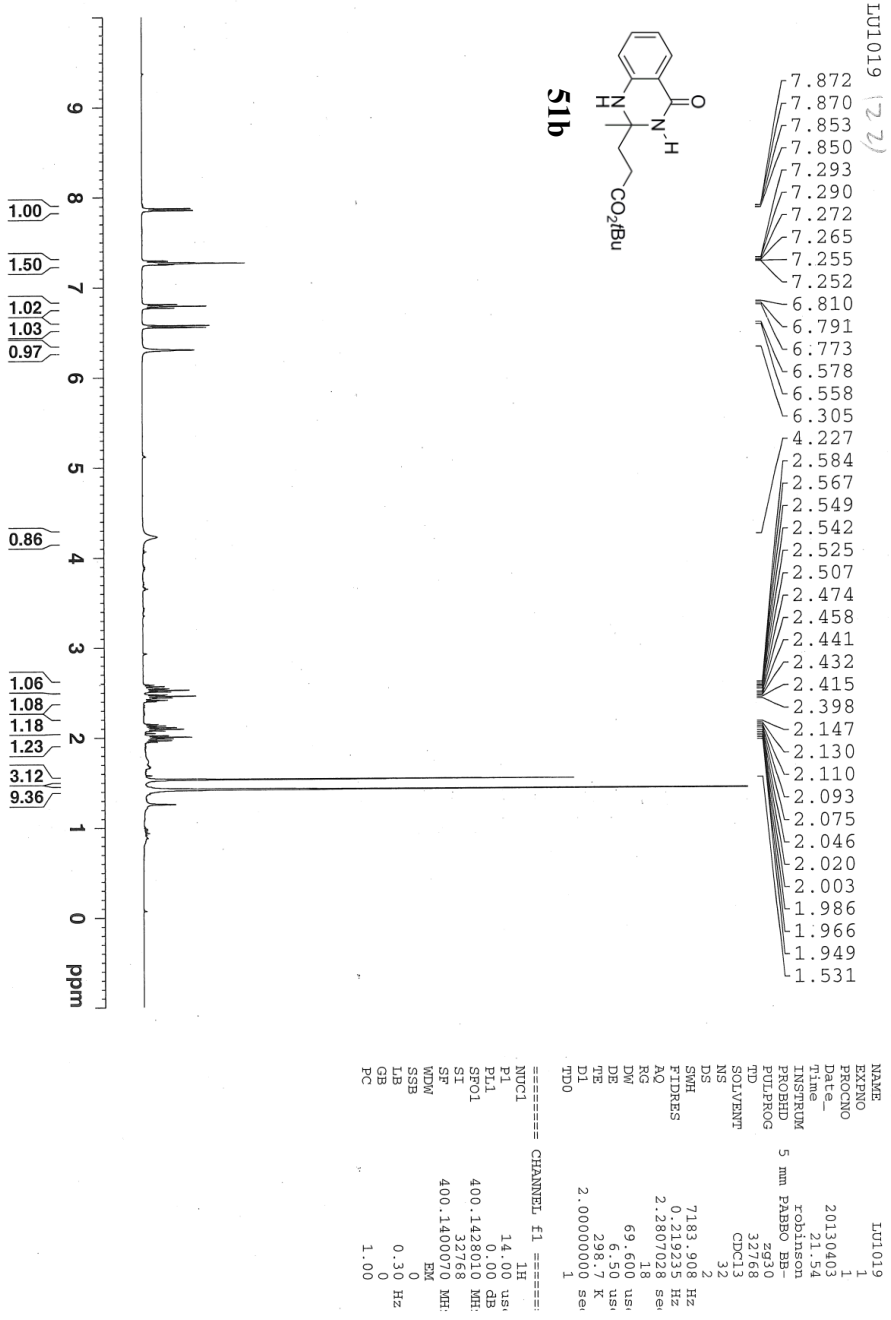
NAME	LU1020
EXPNO	1
PROCNO	1
Date_	20130413
Time	18.02
INSTRUM	robinson
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	32768
SOLVENT	CDCl3
NS	32
DS	2
SWH	7183.908 Hz
FIDRES	0.219235 Hz
AQ	2.2807028 se
RG	128
DW	69.600 us
DE	6.50 us
TE	298.7 K
D1	2.00000000 se
TD0	1
======== CHANNEL f1 =======	
NUC1	1H
P1	14.00 us
PL1	0.00 dB
SFO1	400.1428010 MH
SI	32768
SF	400.1400070 MH
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

C13 LU1020 129

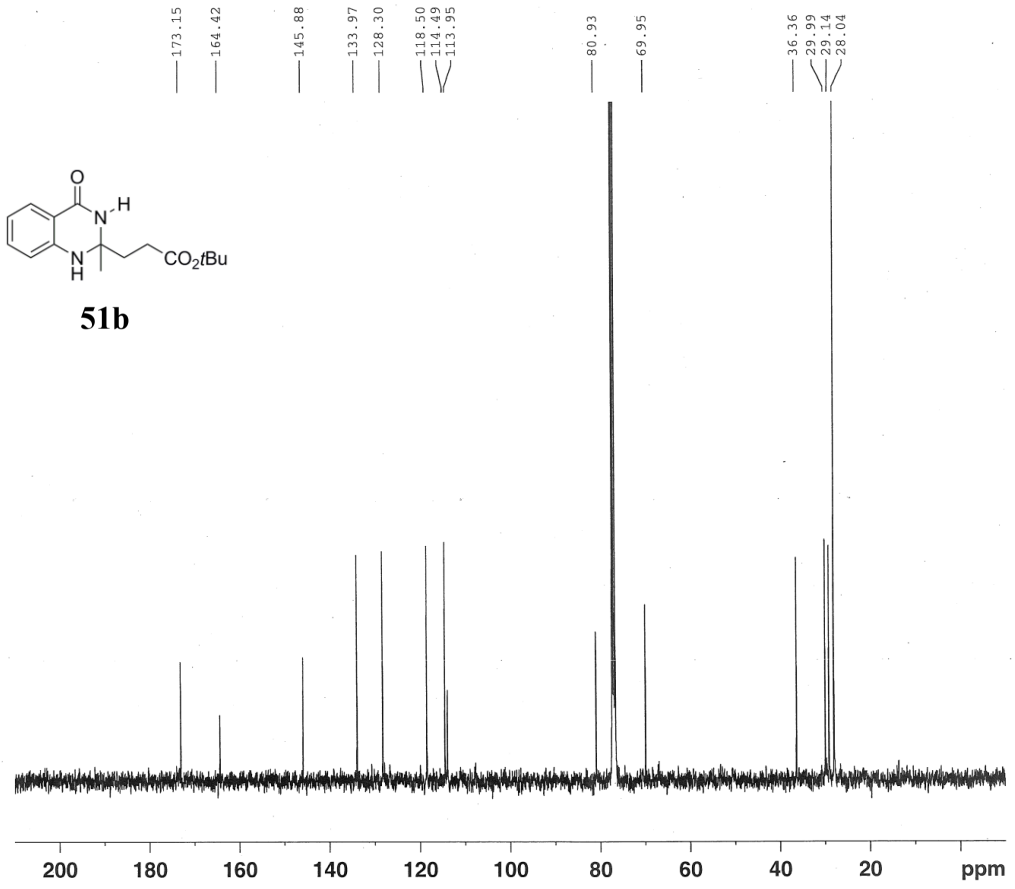


51a

```
NAME                LU1020
EXPNO                    3
PROCNO                   1
Date_             20130413
Time                19.07
INSTRUM           robinson
PROBHD   5 mm PABBO BB-
PULPROG             zgpg30
TD                   65536
SOLVENT              CDCl3
NS                    1600
DS                       4
SWH             23980.814 Hz
FIDRES          0.365918 Hz
AQ              1.3664756 sec
RG                 9195.2
DW                20.850 use
DE                 6.50 use
TE                300.6 K
D1          1.00000000 sec
D11         0.03000000 sec
TD0                      1

======== CHANNEL f1 =======
NUC1                   13C
P1                  9.00 use
PL1                -2.00 dB
SFO1          100.6253446 MHz

======== CHANNEL f2 =======
CPDPRG2            waltz16
NUC2                   1H
PCPD2              90.00 use
PL2                 0.00 dB
PL12               16.16 dB
PL13               17.00 dB
SFO2          400.1416006 MHz
SI                   32768
SF            100.6152855 MHz
WDW                    EM
SSB                     0
LB                 3.00 Hz
GB                      0
PC                   1.40
```

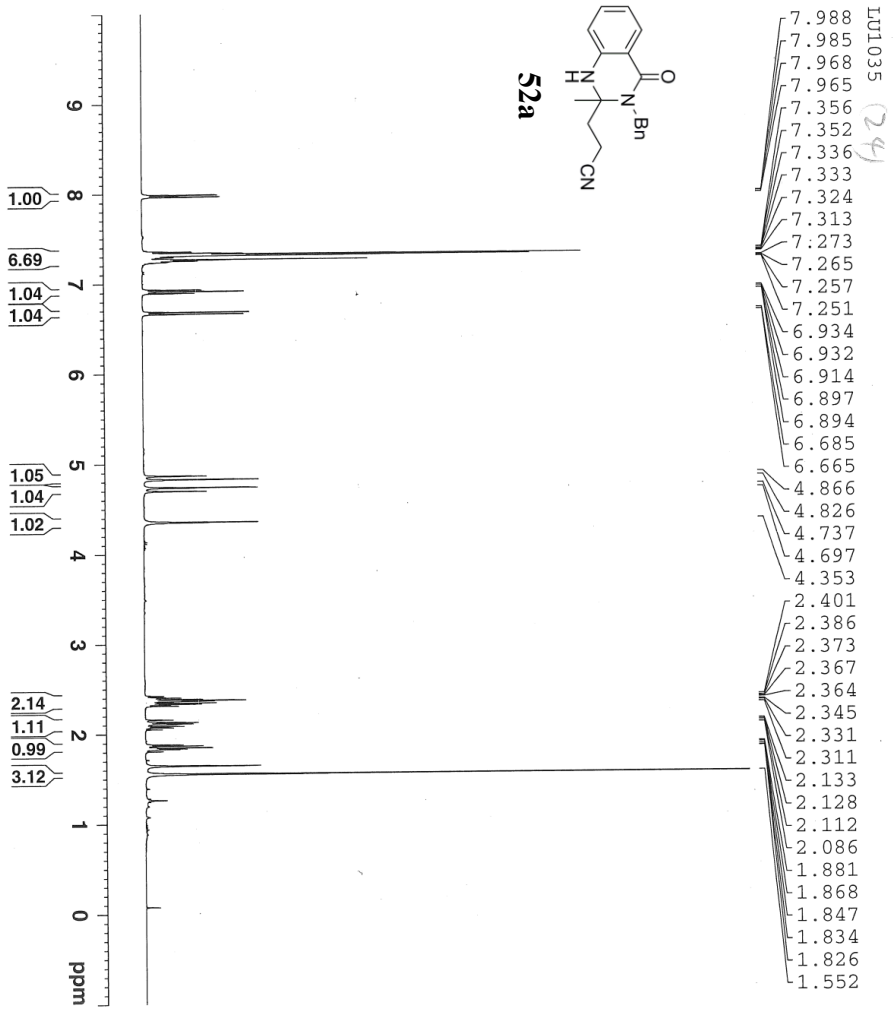

LU1019 (2 2)
7.872
7.870
7.853
7.850
7.293
7.290
7.272
7.265
7.255
7.252
6.810
6.791
6.773
6.578
6.558
6.305
4.227
2.584
2.567
2.549
2.542
2.525
2.507
2.474
2.458
2.441
2.432
2.415
2.398
2.147
2.130
2.110
2.093
2.075
2.046
2.020
2.003
1.986
1.966
1.949
1.531
51b
1.00
1.50
1.02
1.03
0.97
0.86
1.06
1.08
1.18
1.23
3.12
9.36
ppm
NAME LU1019
EXPNO 1
PROCNO 1
Date_ 20130403
Time 21.54
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 7183.908 Hz
FIDRES 0.219235 Hz
AQ 2.2807028 se
RG 18
DW 69.600 us
DE 6.50 us
TE 298.7 K
D1 2.00000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 14.00 us
PL1 0.00 dB
SFO1 400.1428010 MH
SI 32768
SF 400.1400070 MH
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

C13 LU1019 (22)



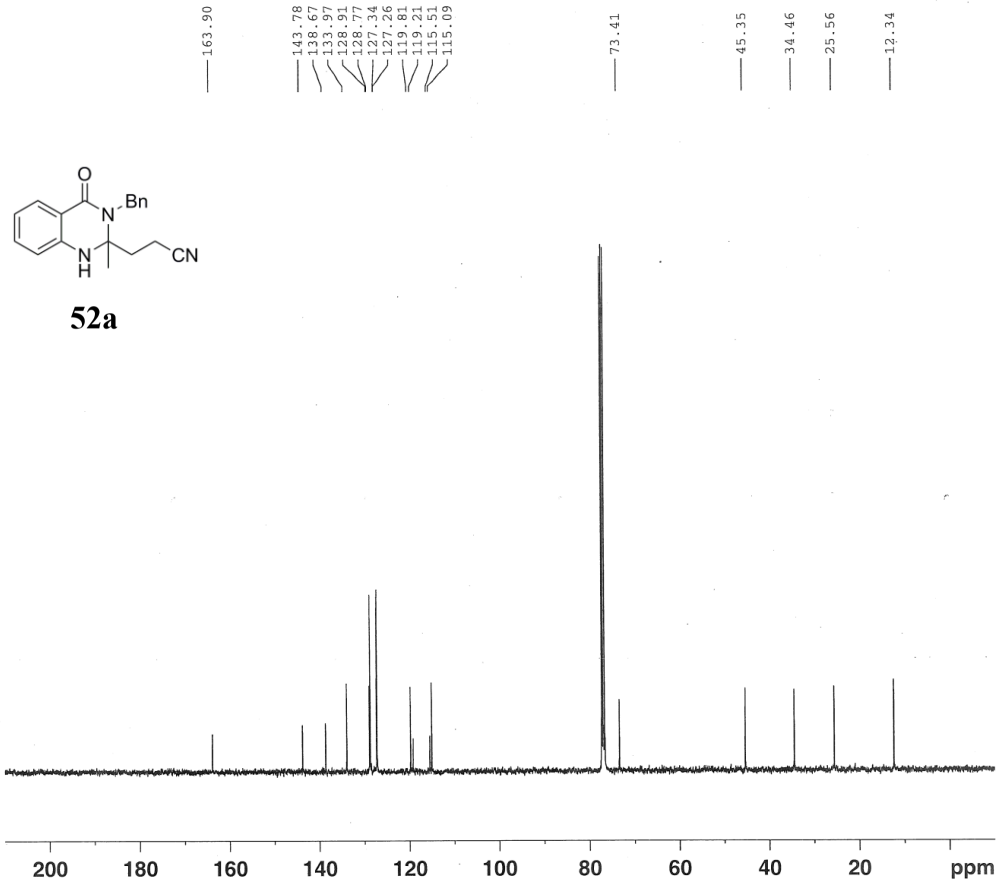
51b

NAME	LU1019
EXPNO	3
PROCNO	1
Date_	20130403
Time	22.42
INSTRUM	robinson
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDC13
NS	1000
DS	4
SWH	23980.814 Hz
FIDRES	0.365918 Hz
AQ	1.3664756 sec
RG	16384
DW	20.850 use
DE	6.50 use
TE	300.4 K
D1	1.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 =======	
NUC1	13C
P1	9.00 use
PL1	-2.00 dB
SFO1	100.6253446 MHz
======== CHANNEL f2 =======	
CPDPRG2	waltz16
NUC2	1H
PCPD2	90.00 use
PL2	0.00 dB
PL12	16.16 dB
PL13	17.00 dB
SFO2	400.1416006 MHz
SI	32768
SF	100.6152848 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40




```
NAME                  LU1035
EXPNO                      1
PROCNO                     1
Date_              20130411
Time                   21.53
INSTRUM                robinson
PROBHD     5 mm PABBO BB-
PULPROG                zg30
TD                    32768
SOLVENT               CDCl3
NS                        32
DS                         2
SWH                7183.908 Hz
FIDRES                0.219235 Hz
AQ                 2.2807028 se
RG                       114
DW                    69.600 us
DE                     6.50 us
TE                   298.5 K
D1                 2.00000000 se
TD0                        1

======== CHANNEL f1 ========
NUC1                     1H
P1                    14.00 us
PL1                    0.00 dB
SFO1           400.1428010 MH
SI                    32768
SF             400.1400070 MH
WDW                       EM
SSB                        0
LB                      0.30 Hz
GB                         0
PC                      1.00
```

C13 LU1035 (24)

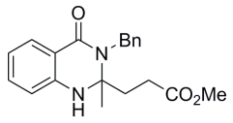


52a

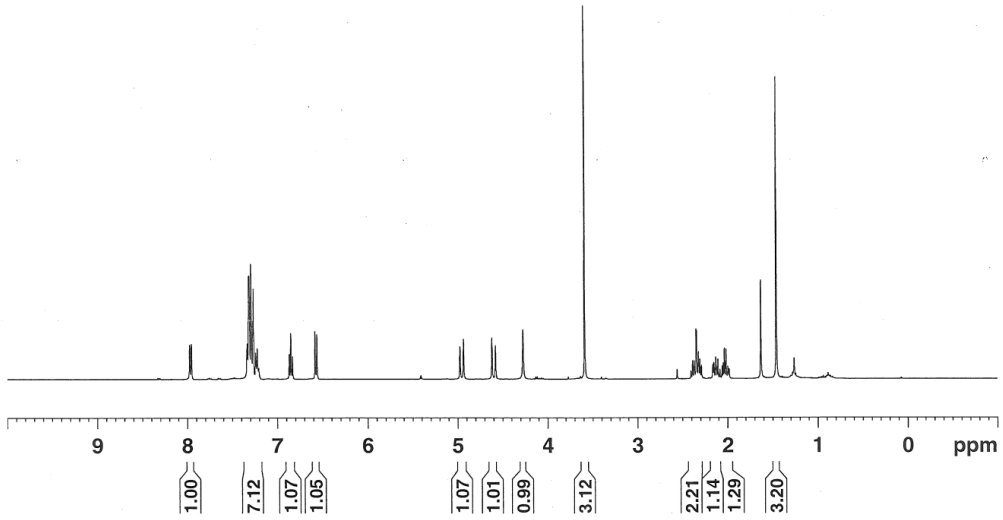
```
NAME                LU1035
EXPNO                    3
PROCNO                   1
Date_             20130412
Time                 0.48
INSTRUM            robinson
PROBHD    5 mm PABBO BB-
PULPROG              zgpg30
TD                   65536
SOLVENT              CDCl3
NS                    1000
DS                       4
SWH              23980.814 Hz
FIDRES            0.365918 Hz
AQ                1.3664756 sec
RG                  11585.2
DW                   20.850 use
DE                    6.50 use
TE                   300.2 K
D1             1.00000000 sec
D11            0.03000000 sec
TD0                      1

======== CHANNEL f1 =======
NUC1                   13C
P1                    9.00 use
PL1                  -2.00 dB
SFO1          100.6253446 MHz

======== CHANNEL f2 =======
CPDPRG2            waltz16
NUC2                   1H
PCPD2                90.00 use
PL2                   0.00 dB
PL12                 16.16 dB
PL13                 17.00 dB
SFO2          400.1416006 MHz
SI                   32768
SF            100.6152863 MHz
WDW                    EM
SSB                     0
LB                   3.00 Hz
GB                      0
PC                   1.40
```

LU1036 (25)

7.976 7.957 7.335 7.318 7.311 7.292 7.272 7.265 7.241 7.224 6.871 6.851 6.833 6.584 6.564 4.975 4.936 4.618 4.579 4.273 3.590 2.406 2.388 2.371 2.348 2.343 2.322 2.307 2.289 2.164 2.153 2.131 2.125 2.107 2.084 2.060 2.048 2.035 2.016 1.998 1.992 1.981

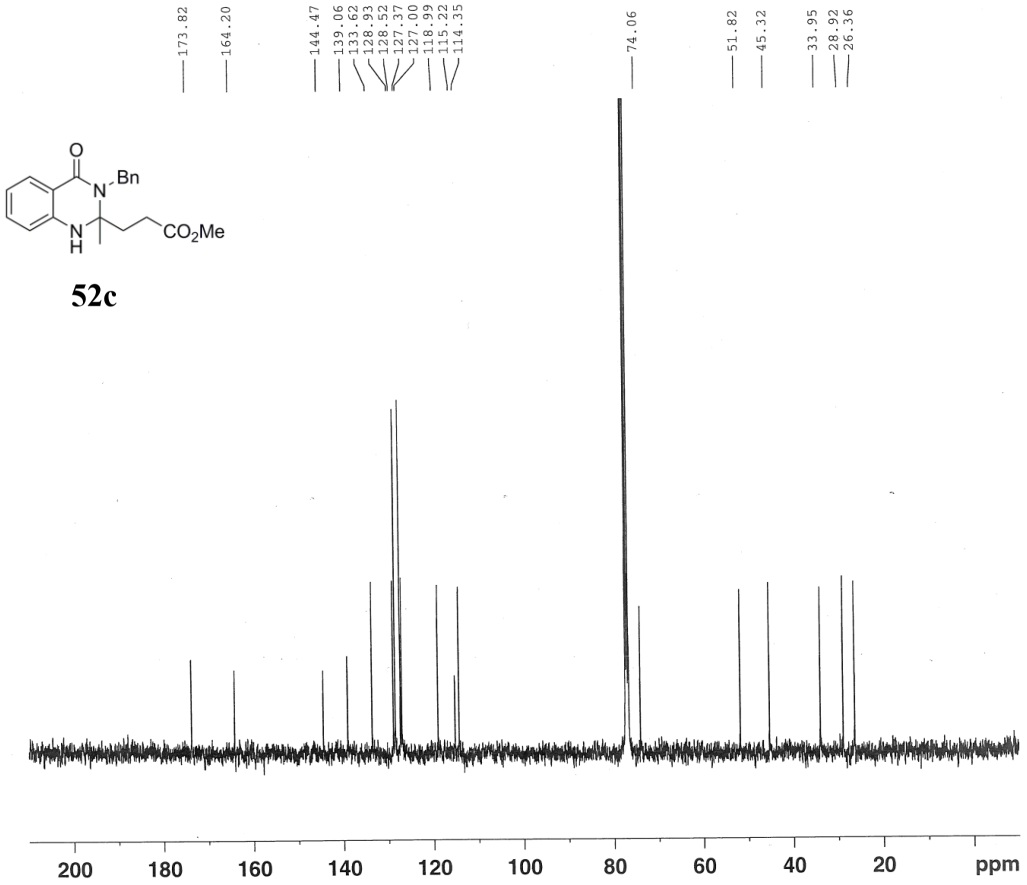


52c



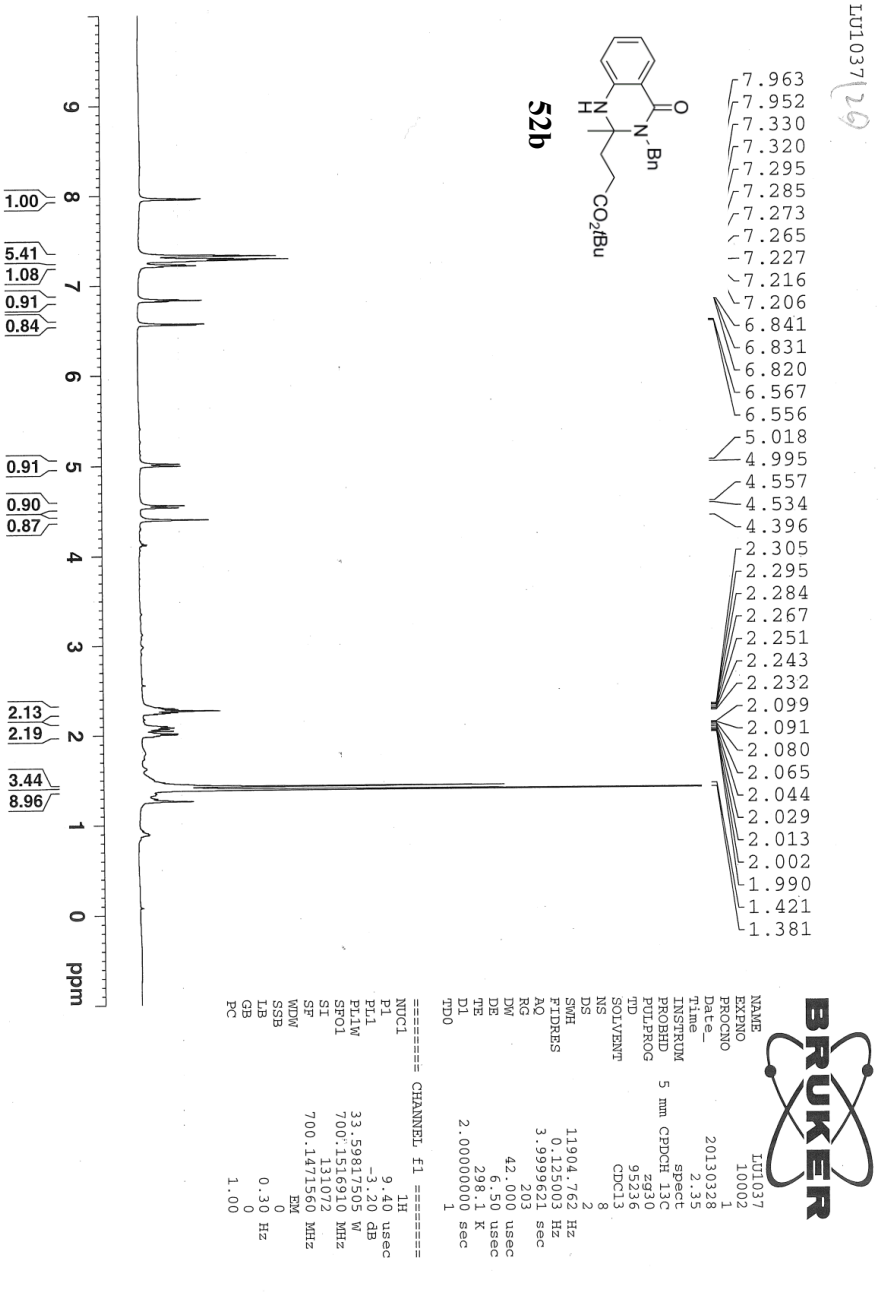
NAME	LU1036
EXPNO	1
PROCNO	1
Date_	20130410
Time	22.20
INSTRUM	robinson
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	32768
SOLVENT	CDCl3
NS	32
DS	2
SWH	7183.908 Hz
FIDRES	0.219235 Hz
AQ	2.2807028 se
RG	128
DW	69.600 us
DE	6.50 us
TE	300.0 K
D1	2.00000000 se
TD0	1
======== CHANNEL f1 =======	
NUC1	1H
P1	14.00 us
PL1	0.00 dB
SFO1	400.1428010 MH
SI	32768
SF	400.1400071 MH
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

C13 LU1036 (25)

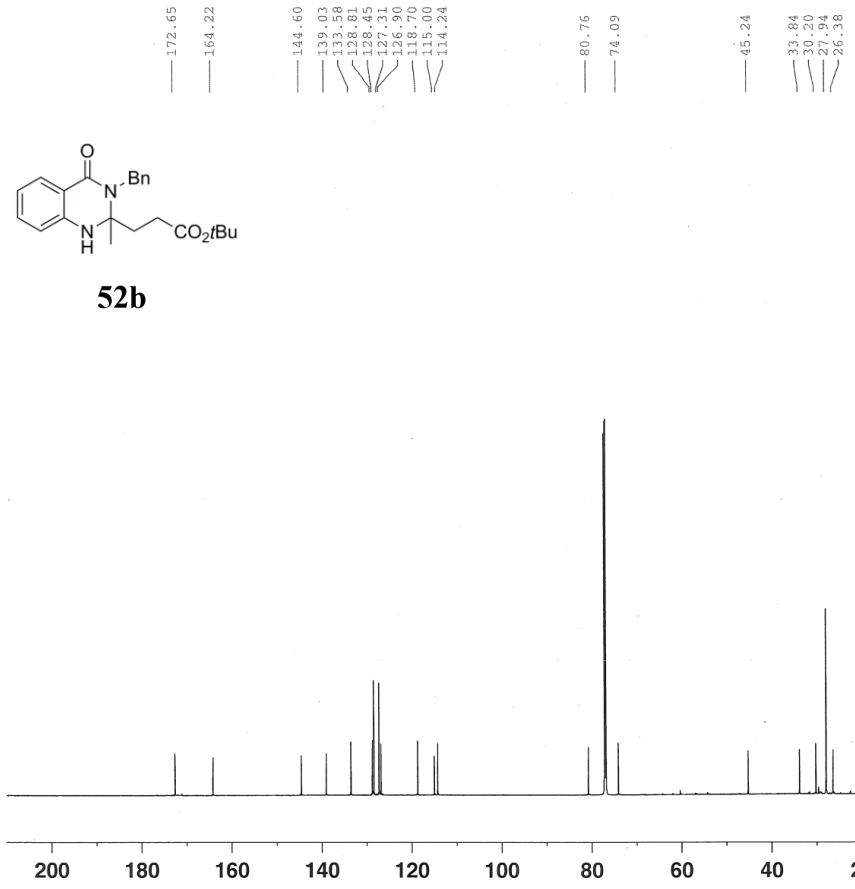


52c

NAME	LU1036
EXPNO	3
PROCNO	1
Date_	20130410
Time	23.03
INSTRUM	robinson
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	1000
DS	4
SWH	23980.814 Hz
FIDRES	0.365918 Hz
AQ	1.3664756 sec
RG	18390.4
DW	20.850 use
DE	6.50 use
TE	300.8 K
D1	1.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 =======	
NUC1	13C
P1	9.00 use
PL1	-2.00 dB
SFO1	100.6253446 MHz
======== CHANNEL f2 =======	
CPDPRG2	waltz16
NUC2	1H
PCPD2	90.00 use
PL2	0.00 dB
PL12	16.16 dB
PL13	17.00 dB
SFO2	400.1416006 MHz
SI	32768
SF	100.6152850 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40


LU1037(2)
7.963
7.952
7.330
7.320
7.295
7.285
7.273
7.265
7.227
7.216
7.206
6.841
6.831
6.820
6.567
6.556
5.018
4.995
4.557
4.534
4.396
2.305
2.295
2.284
2.267
2.251
2.243
2.232
2.099
2.091
2.080
2.065
2.044
2.029
2.013
2.002
1.990
1.421
1.381
52b
1.00
5.41
1.08
0.91
0.84
0.91
0.90
0.87
2.13
2.19
3.44
8.96
ppm
BRUKER
NAME LU1037
EXPNO 10002
PROCNO 1
Date_ 20130328
Time_ 2.35
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 8
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 203
DW 42.000 usec
DE 6.50 usec
TE 298.1 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471560 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

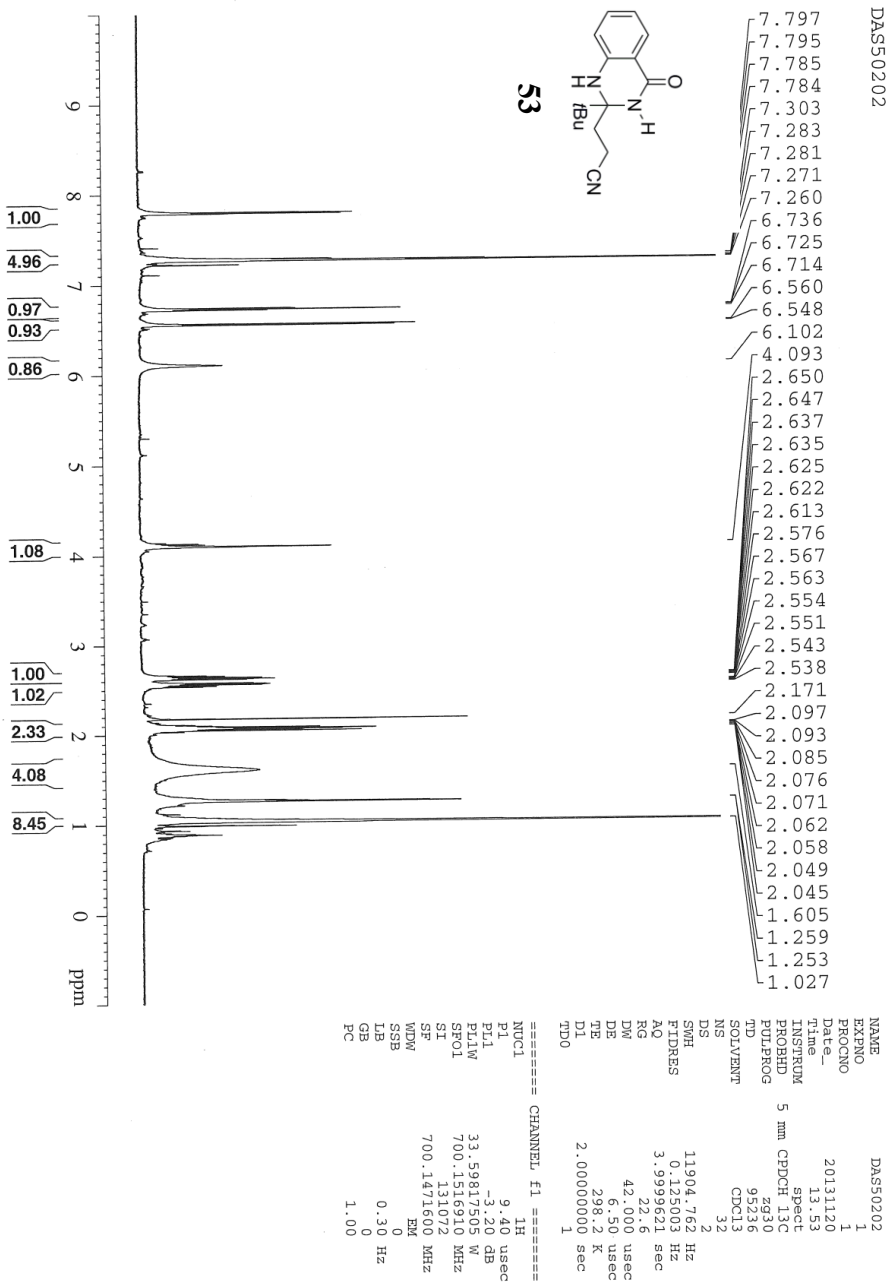
C13 LU1037 (24



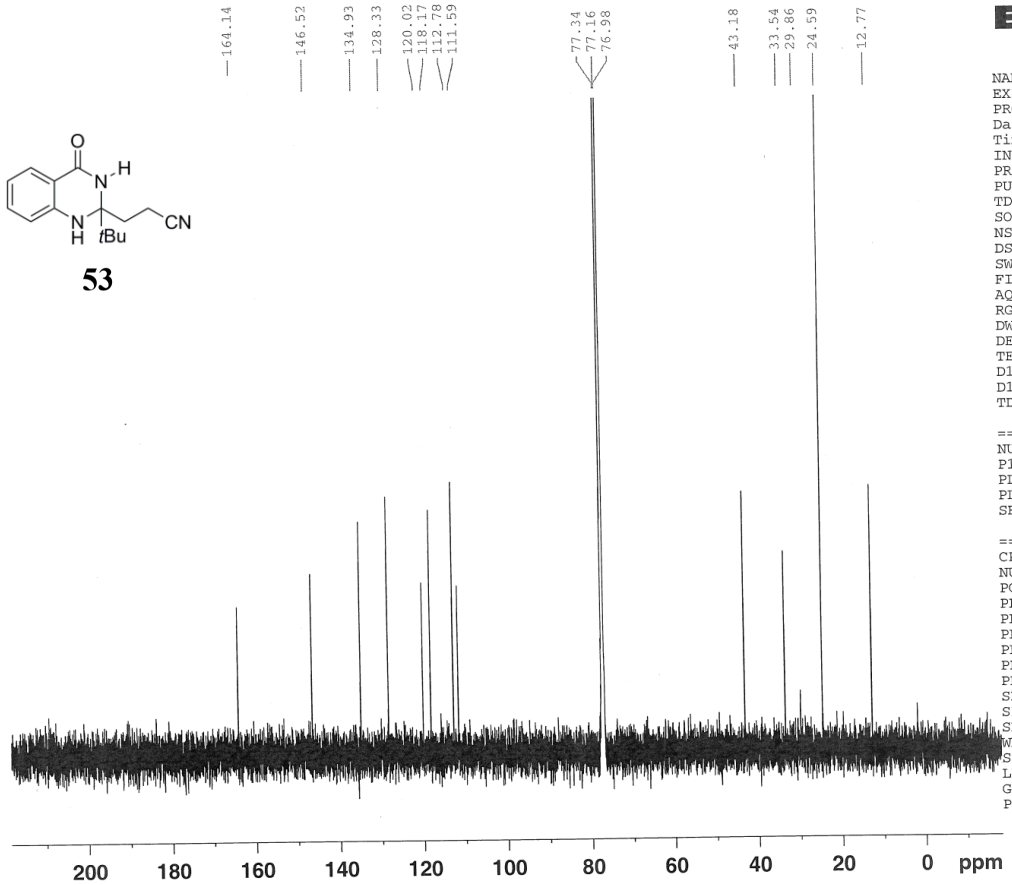
52b

BRUKER

NAME	LU1037
EXPNO	3
PROCNO	1
Date_	20130327
Time	22.19
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	65536
SOLVENT	CDC13
NS	500
DS	4
SWH	41666.668 Hz
FIDRES	0.635783 Hz
AQ	0.7864820 sec
RG	203
DW	12.000 usec
DE	16.50 usec
TE	298.1 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 usec
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0697436 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 usec
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1499406 MHz
SI	32768
SF	176.0521541 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40


DAS50202
7.797
7.795
7.785
7.784
7.303
7.283
7.281
7.271
7.260
6.736
6.725
6.714
6.560
6.548
6.102
4.093
2.650
2.647
2.637
2.635
2.625
2.622
2.613
2.576
2.567
2.563
2.554
2.551
2.543
2.538
2.171
2.097
2.093
2.085
2.076
2.071
2.062
2.058
2.049
2.045
1.605
1.259
1.253
1.027
53
1.00
4.96
0.97
0.93
0.86
1.08
1.00
1.02
2.33
4.08
8.45
ppm
NAME DAS50202
EXPNO 1
PROCNO 1
Date_ 20131120
Time 13.53
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 3.9995621 sec
RG 22.6
DW 42.000 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471600 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

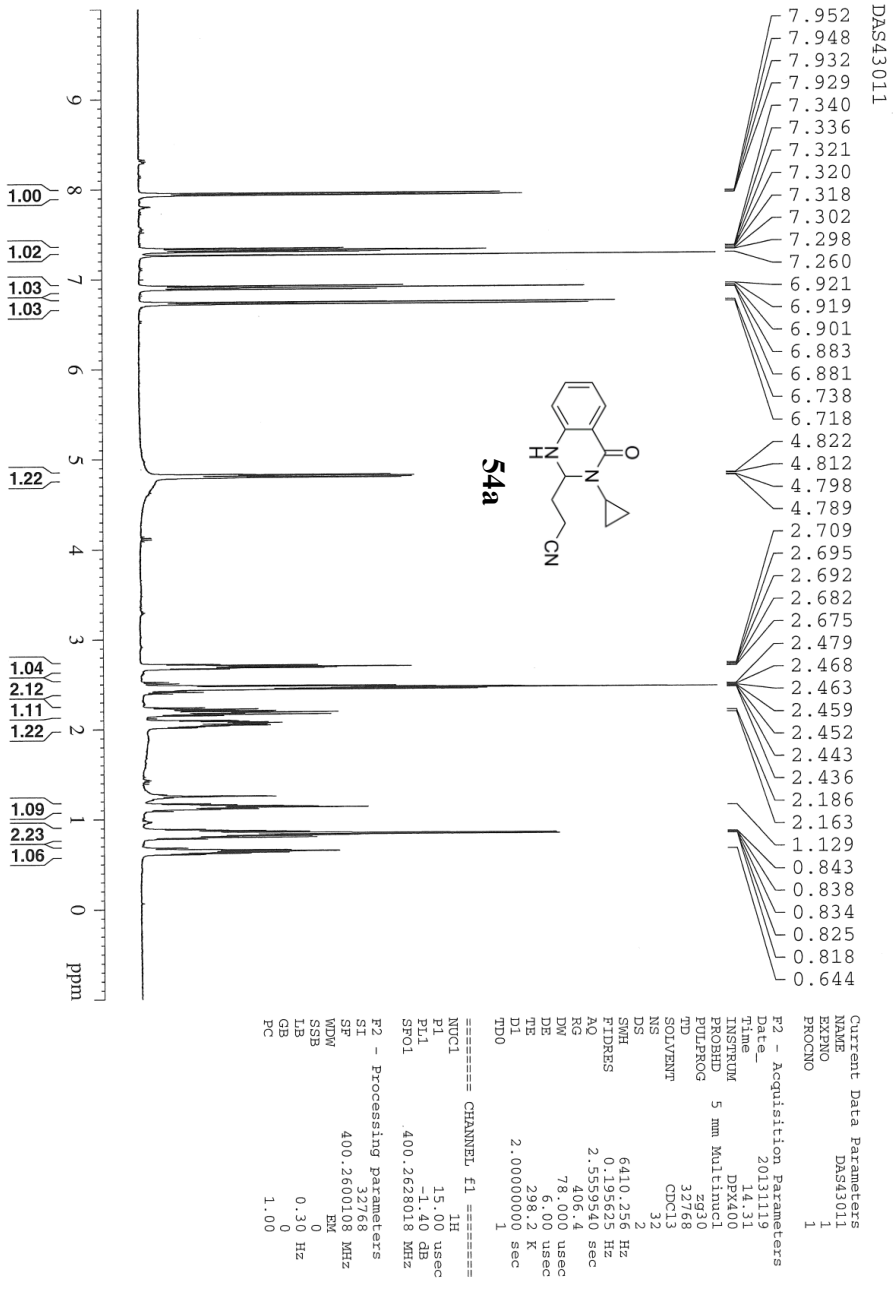
DAS50202

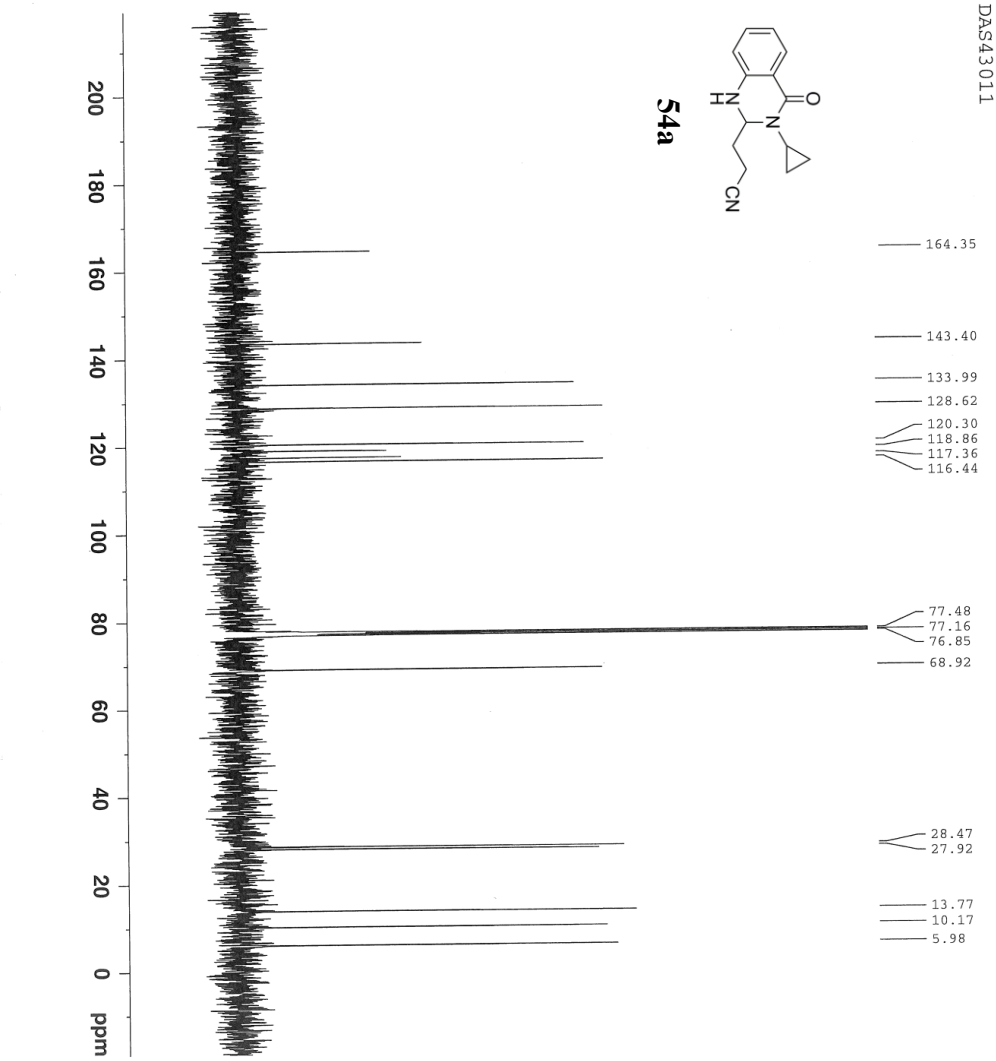


53

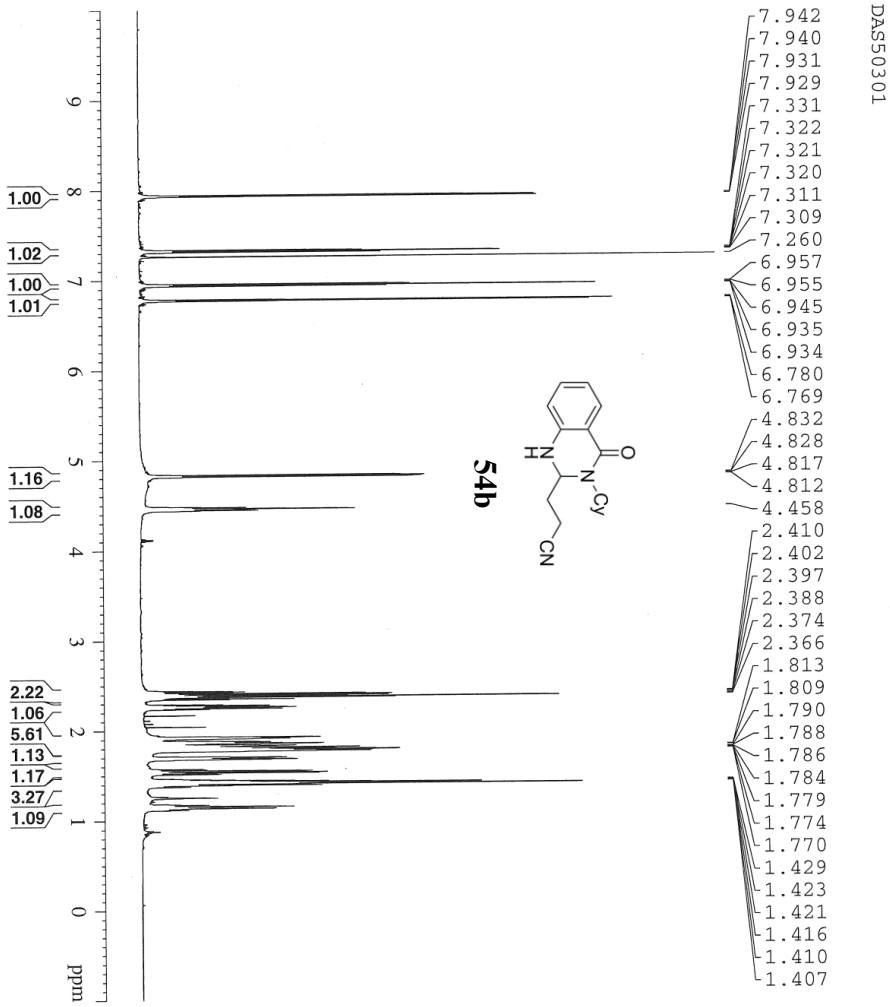
BRUKER

NAME	DAS50202
EXPNO	2
PROCNO	1
Date_	20131120
Time	13.57
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	65536
SOLVENT	CDC13
NS	194
DS	4
SWH	41666.668 Hz
FIDRES	0.635783 Hz
AQ	0.7864820 sec
RG	203
DW	12.000 usec
DE	16.50 usec
TE	298.2 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 usec
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0697436 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 usec
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1499406 MHz
SI	32768
SF	176.0521140 MHz
WDW	EM
SSB	0
LB	1.50 Hz
GB	0
PC	1.40

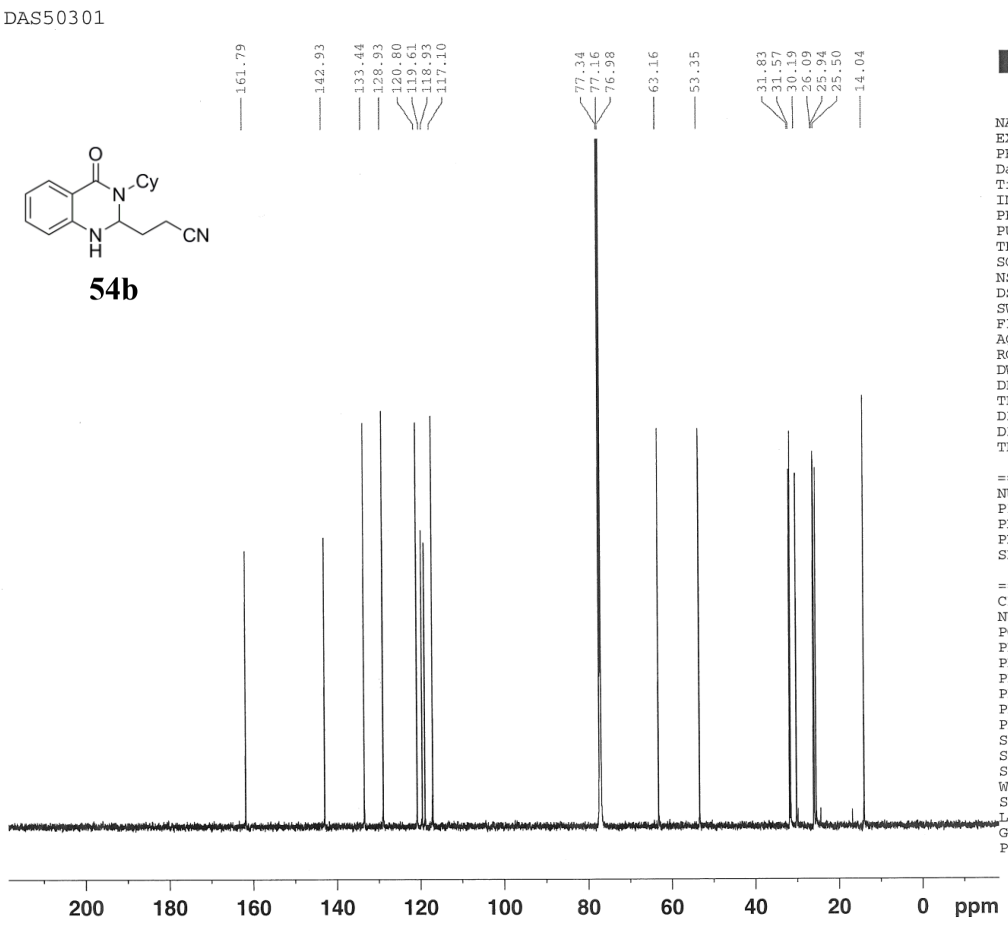

DAS43011
7.952
7.948
7.932
7.929
7.340
7.336
7.321
7.320
7.318
7.302
7.298
7.260
6.921
6.919
6.901
6.883
6.881
6.738
6.718
4.822
4.812
4.798
4.789
2.709
2.695
2.692
2.682
2.675
2.479
2.468
2.463
2.459
2.452
2.443
2.436
2.186
2.163
1.129
0.843
0.838
0.834
0.825
0.818
0.644
54a
1.00
1.02
1.03
1.03
1.22
1.04
2.12
1.11
1.22
1.09
2.23
1.06
ppm
Current Data Parameters
NAME DAS43011
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20131119
Time_ 14.31
INSTRUM DPX400
PROBHD 5 mm Multinucl
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 406.4
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 15.00 usec
PL1 1.40 dB
SFO1 400.2628018 MHz
F2 - Processing parameters
SI 32768
SF 400.2600108 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00




```
Current Data Parameters
NAME                  DAS43011
EXPNO                        2
PROCNO                       1

F2 - Acquisition Parameters
Date_               20131119
Time                   14.38
INSTRUM                DPX400
PROBHD   5 mm Multinucl
PULPROG                zgpg30
TD                      65536
SOLVENT                 CDCl3
NS                        300
DS                          4
SWH                23980.814 Hz
FIDRES                 0.365918 Hz
AQ                     1.3664756 sec
RG                      1625.5
DW                     20.850 usec
DE                      6.00 usec
TE                     298.2 K
D1                     1.00000000 sec
D11                    0.03000000 sec
DELTA                  0.89999998 sec
TD0                         1

========== CHANNEL f1 =======
NUC1                      13C
P1                     8.30 usec
PL1                    -3.00 dB
SFO1          100.6555216 MHz

========== CHANNEL f2 =======
CPDPRG2                waltz16
NUC2                       1H
PCPD2                  90.00 usec
PL2                    -3.00 dB
PL12                   15.00 dB
PL13                   15.00 dB
SFO2          400.2620013 MHz

F2 - Processing parameters
SI                      32768
SF            100.6454458 MHz
WDW                        EM
SSB                         0
LB                     3.00 Hz
GB                          0
PC                     1.40
```


DAS50301
7.942
7.940
7.931
7.929
7.331
7.322
7.321
7.320
7.311
7.309
7.260
6.957
6.955
6.945
6.935
6.934
6.780
6.769
4.832
4.828
4.817
4.812
4.458
2.410
2.402
2.397
2.388
2.374
2.366
1.813
1.809
1.790
1.788
1.786
1.784
1.779
1.774
1.770
1.429
1.423
1.421
1.416
1.410
1.407
54b
1.00
1.02
1.00
1.01
1.16
1.08
2.22
1.06
5.61
1.13
1.17
3.27
1.09
ppm
NAME DAS50301
EXPNO 1
PROCNO 1
Date_ 20131119
Time 13.26
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 25.4
DW 42.000 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471608 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

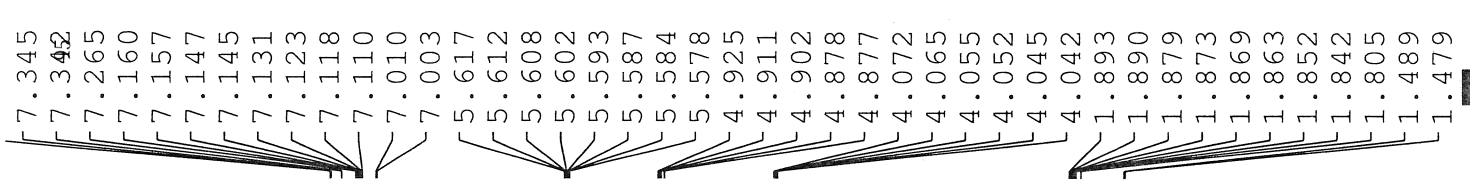
DAS50301

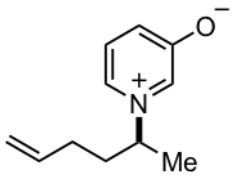


54b

BRUKER

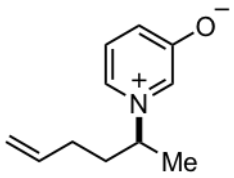
NAME	DAS50301
EXPNO	2
PROCNO	1
Date_	20131119
Time	13.32
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	135
DS	4
SWH	41666.668 Hz
FIDRES	0.635783 Hz
AQ	0.7864820 sec
RG	203
DW	12.000 usec
DE	16.50 usec
TE	298.2 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 usec
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0697436 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 usec
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1499406 MHz
SI	32768
SF	176.0521203 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40





74

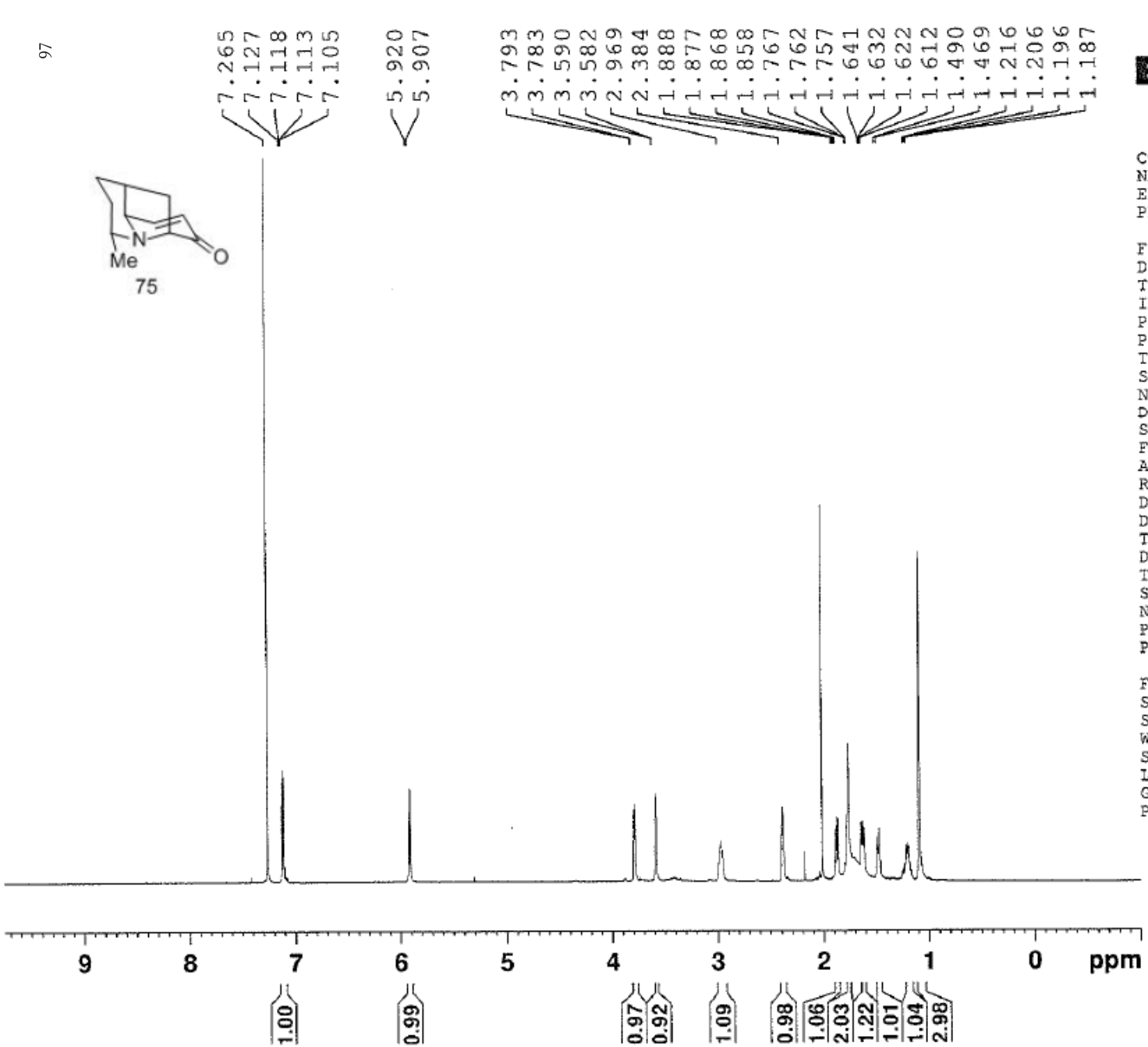

```
Current Data Parameters
NAME      LU5036_OX_mono_0
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_           20180102
Time                8.17 h
INSTRUM            spect
PROBHD   Z151340_0001 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH            10504.202 Hz
FIDRES          0.320563 Hz
AQ             3.1195135 sec
RG                  11.3
DW                47.600 usec
DE                20.00 usec
TE                298.2 K
D1           1.00000000 sec
TD0                    1
SFO1         700.0115500 MHz
NUC1                  1H
P1                 11.00 usec
PLW1         13.00000000 W

F2 - Processing parameters
SI                131072
SF           700.0070169 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```



74

BRUKER

```
Current Data Parameters
NAME      LU5036_OX_mono_0
EXPNO                    3
PROCNO                   1

F2 - Acquisition Parameters
Date_           20180102
Time                8.18 h
INSTRUM            spect
PROBHD   Z151340_0001 (
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                    8
DS                    4
SWH           42613.637 Hz
FIDRES         1.300465 Hz
AQ            0.7689557 sec
RG                  203
DW               11.733 usec
DE                18.00 usec
TE                298.2 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1        176.0362620 MHz
NUC1               13C
P1                11.00 usec
PLW1        29.00000000 W
SFO2        700.0098000 MHz
NUC2               1H
CPDPRG[2        waltz16
PCPD2             65.00 usec
PLW2        13.00000000 W
PLW12        0.37231001 W
PLW13        0.18747000 W

F2 - Processing parameters
SI                131072
SF          176.0169002 MHz
WDW                 EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```



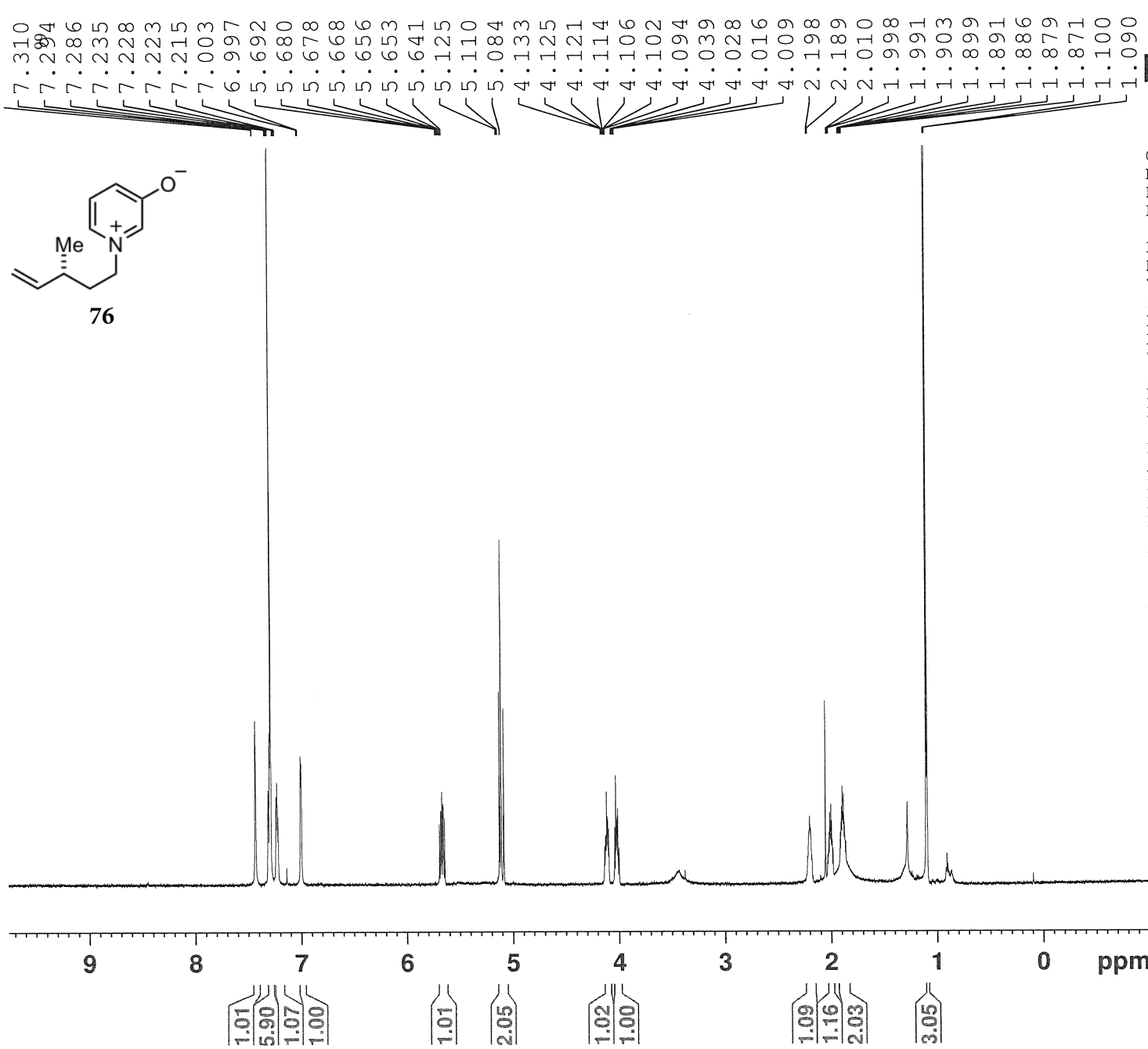
BRUKER

```
Current Data Parameters
NAME                  check4
EXPNO                  50391
PROCNO                     1

F2 - Acquisition Parameters
Date_              20180818
Time                  17.42 h
INSTRUM                spect
PROBHD    Z566801_0015 (
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       14
DS                        2
SWH               10504.202 Hz
FIDRES             0.320563 Hz
AQ                 3.1195135 sec
RG                      203
DW                   47.600 usec
DE                    6.50 usec
TE                   294.6 K
D1                1.00000000 sec
TD0                       1
SFO1            700.0115500 MHz
NUC1                     1H
P1                   12.88 usec
PLW1           40.00000000 W

F2 - Processing parameters
SI                   131072
SF              700.0070132 MHz
WDW                      EM
SSB          0
LB                    0.30 Hz
GB           0
PC                    1.00
```

75

BRUKER

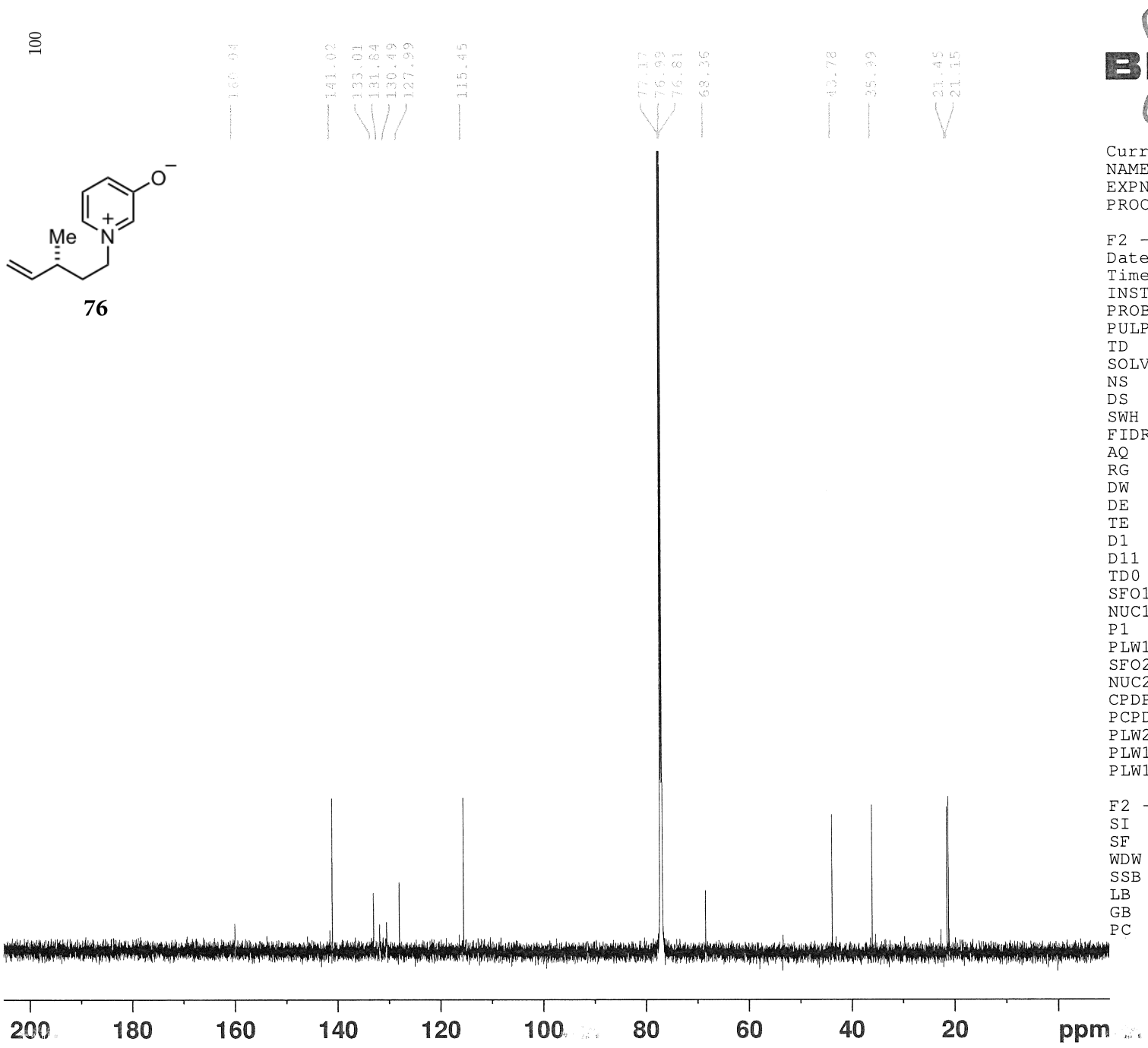
```
Current Data Parameters
NAME       LU5039_mono_0
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180104
Time               13.17 h
INSTRUM             spect
PROBHD   Z151340_0001 (
PULPROG           zgpg30
TD                 65536
SOLVENT            CDCl3
NS                    11
DS                     4
SWH            42613.637 Hz
FIDRES          1.300465 Hz
AQ             0.7689557 sec
RG                   203
DW                11.733 usec
DE                18.00 usec
TE                298.2 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                    1
SFO1       176.0362620 MHz
NUC1                13C
P1                11.00 usec
PLW1        29.00000000 W
SFO2       700.0098000 MHz
NUC2                1H
CPDPRG[2         waltz16
PCPD2             65.00 usec
PLW2        13.00000000 W
PLW12        0.37231001 W
PLW13        0.18747000 W

F2 - Processing parameters
SI                131072
SF         176.0169002 MHz
WDW                 EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```



76

BRUKER

```
Current Data Parameters
NAME        PURE_eqme_OX
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180726
Time                7.38 h
INSTRUM            spect
PROBHD   Z566801_0015 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH            10504.202 Hz
FIDRES          0.320563 Hz
AQ              3.1195135 sec
RG                   203
DW                47.600 usec
DE                 6.50 usec
TE                294.2 K
D1           1.00000000 sec
TD0                    1
SFO1        700.0115500 MHz
NUC1                  1H
P1                12.88 usec
PLW1        40.00000000 W

F2 - Processing parameters
SI                131072
SF            700.0070000 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```



76

BRUKER

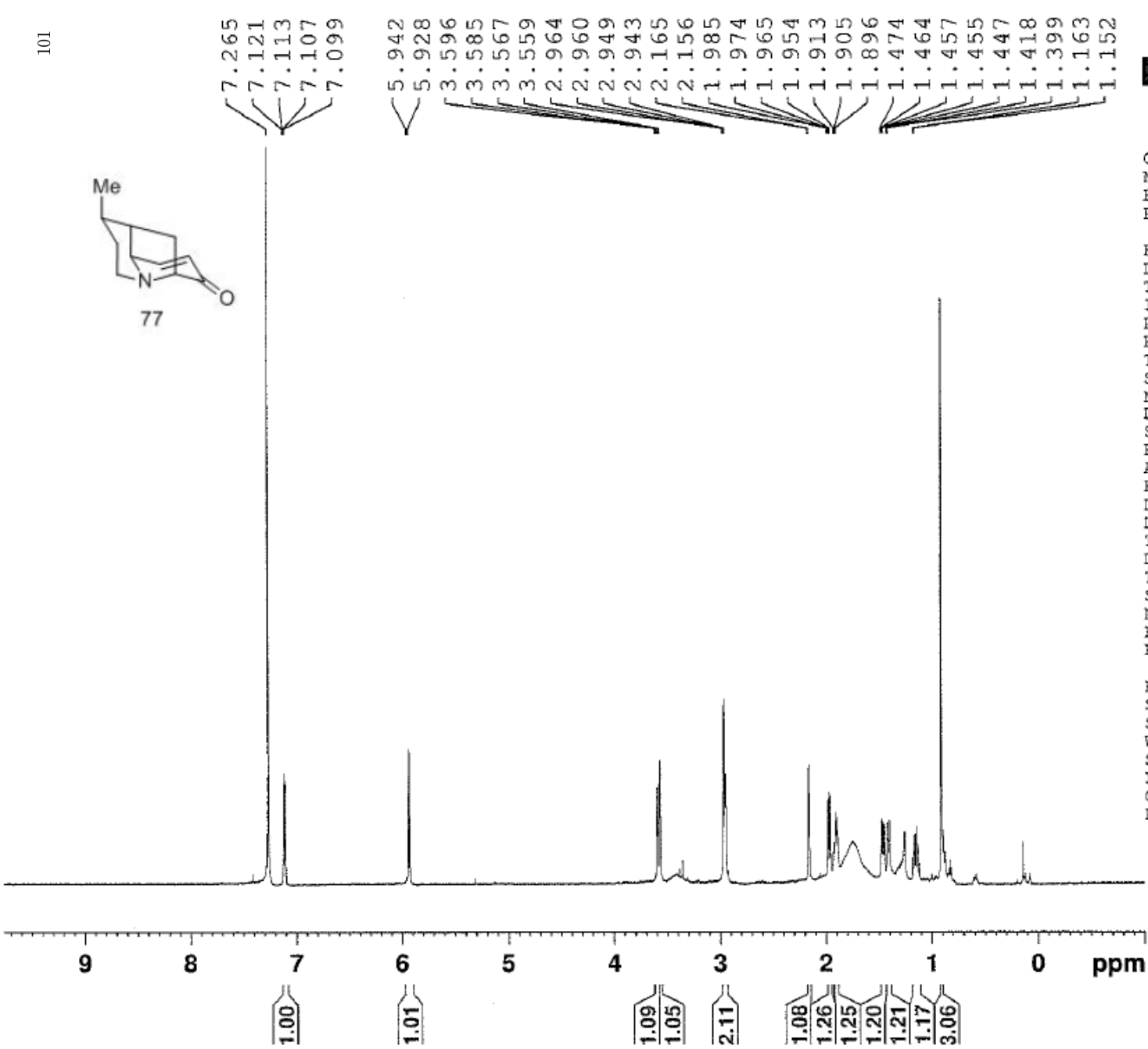
Current Data Parameters
NAME LU4292_PURE_2Me_ox
EXPNO 3
PROCNO 1

F2 - Acquisition Parameters

Date_	20180701	
Time	5.35	h
INSTRUM	spect	
PROBHD	Z566801_0015 (	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	6000	
DS	4	
SWH	42613.637	Hz
FIDRES	1.300465	Hz
AQ	0.7689557	sec
RG	203	
DW	11.733	usec
DE	6.50	usec
TE	301.4	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
SFO1	176.0362620	MHz
NUC1	13C	
P1	8.95	usec
PLW1	100.00000000	W
SFO2	700.0098000	MHz
NUC2	1H	
CPDPRG[2	waltz16	
PCPD2	65.00	usec
PLW2	40.00000000	W
PLW12	1.57060003	W
PLW13	0.79086000	W

F2 - Processing parameters

SI	131072	
SF	176.0169002	MHz
WDW	EM	
SSB	0	
LB	1.00	Hz
GB	0	
PC	1.40	

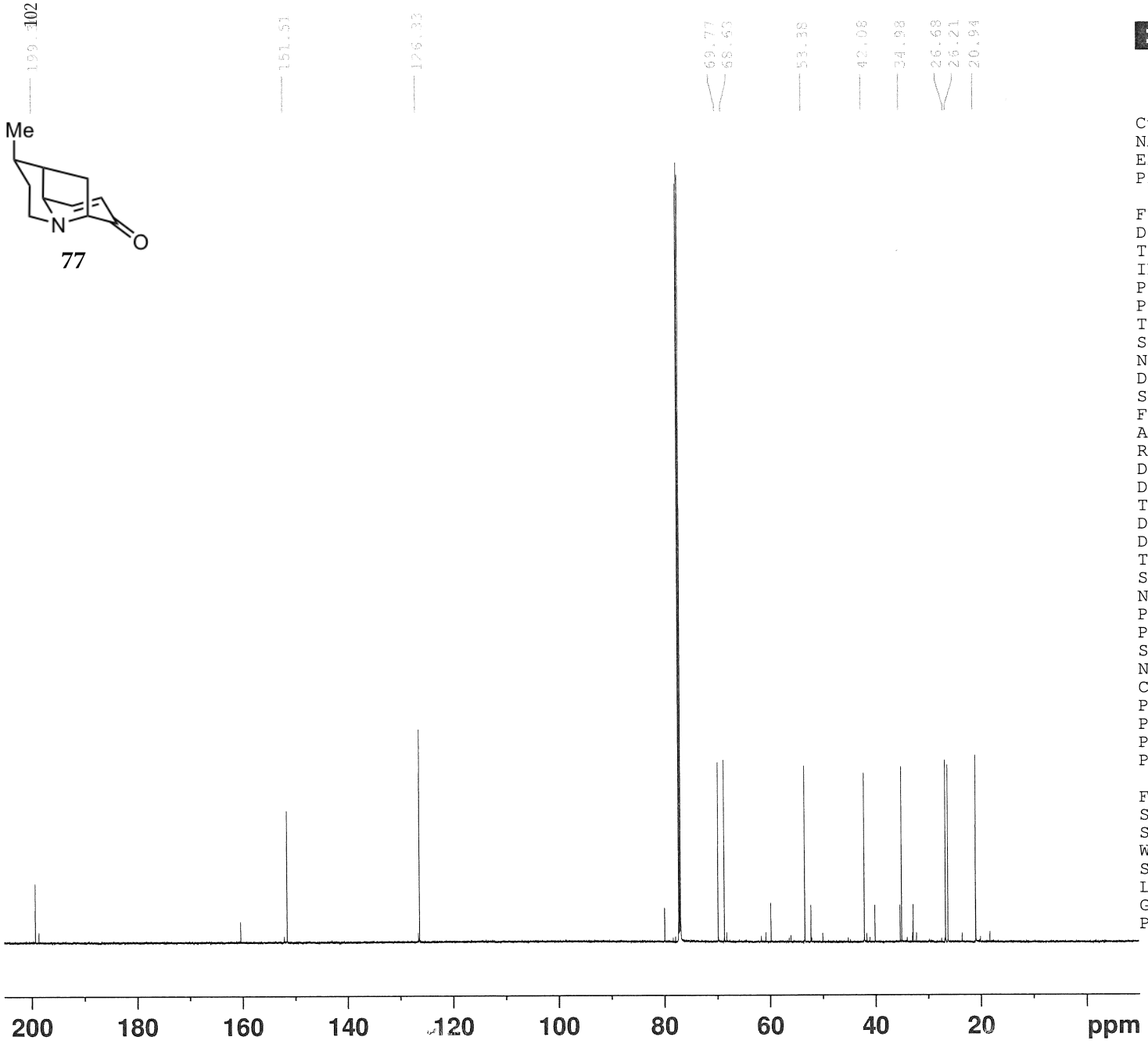


BRUKER

Current Data Parameters
NAME eqme_cy
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20180819
Time 6.50 h
INSTRUM spect
PROBHD Z566801_0015 (
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 10504.202 Hz
FIDRES 0.320563 Hz
AQ 3.1195135 sec
RG 203
DW 47.600 usec
DE 6.50 usec
TE 294.4 K
D1 1.00000000 sec
TD0 1
SFO1 700.0115500 MHz
NUC1 1H
P1 12.88 usec
PLW1 40.00000000 W

F2 - Processing parameters
SI 131072
SF 700.0070132 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

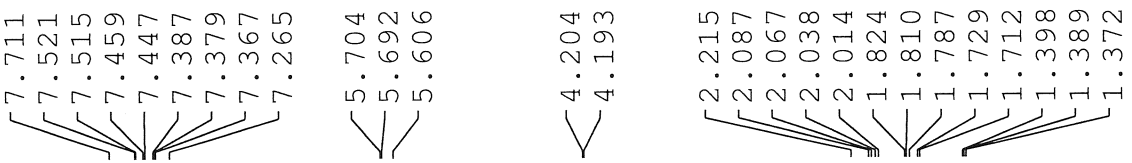


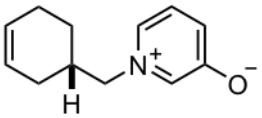
Current Data Parameters
NAME LU4001_Monome_0_
EXPNO 3
PROCNO 1

F2 - Acquisition Parameters
Date_ 20170328
Time 13.51 h
INSTRUM spect
PROBHD Z151340_0001 (
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 44
DS 4
SWH 42613.637 Hz
FIDRES 1.300465 Hz
AQ 0.7689557 sec
RG 203
DW 11.733 usec
DE 18.00 usec
TE 298.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
SFO1 176.0362620 MHz
NUC1 13C
P1 11.75 usec
PLW1 29.00000000 W
SFO2 700.0098000 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 65.00 usec
PLW2 13.00000000 W
PLW12 0.38942000 W
PLW13 0.19609000 W

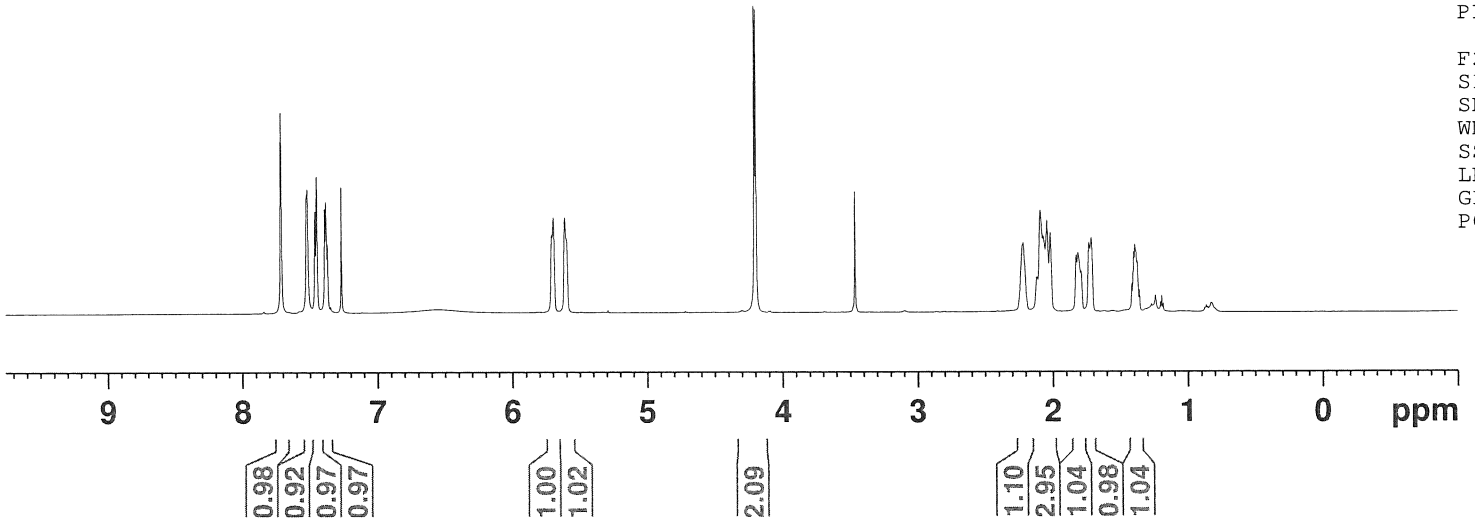
F2 - Processing parameters
SI 131072
SF 176.0169002 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

103





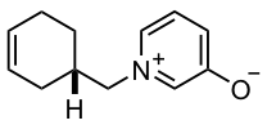
78



BRUKER

```
Current Data Parameters
NAME      LU3246_Pure_CYH_ox
EXPNO                      1
PROCNO                     1

F2 - Acquisition Parameters
Date_              20180607
Time                  14.45 h
INSTRUM               spect
PROBHD    Z151340_0001 (
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       13
DS                        2
SWH              10504.202 Hz
FIDRES            0.320563 Hz
AQ               3.1195135 sec
RG                      5.6
DW                 47.600 usec
DE                 10.00 usec
TE                 303.2 K
D1              1.00000000 sec
TD0                       1
SFO1           700.0115500 MHz
NUC1                    1H
P1                 11.00 usec
PLW1           13.00000000 W

F2 - Processing parameters
SI                   131072
SF             700.0070152 MHz
WDW                     EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

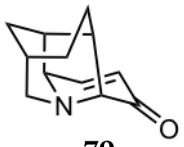
104



78

BRUKER

```
Current Data Parameters
NAME      LU3246_Pure_CYH_ox
EXPNO                      3
PROCNO                     1

F2 - Acquisition Parameters
Date_              20180607
Time                 14.48 h
INSTRUM              spect
PROBHD    Z151340_0001 (
PULPROG            zgpg30
TD                  65536
SOLVENT             CDCl3
NS                     43
DS                      4
SWH             42613.637 Hz
FIDRES           1.300465 Hz
AQ               0.7689557 sec
RG                    203
DW                 11.733 usec
DE                 18.00 usec
TE                 303.2 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                    1
SFO1          176.0362620 MHz
NUC1                  13C
P1                 11.00 usec
PLW1           29.00000000 W
SFO2           700.0098000 MHz
NUC2                   1H
CPDPRG[2          waltz16
PCPD2              65.00 usec
PLW2           13.00000000 W
PLW12           0.37231001 W
PLW13           0.18747000 W

F2 - Processing parameters
SI                  131072
SF            176.0169002 MHz
WDW                    EM
SSB       0
LB                  1.00 Hz
GB        0
PC                  1.40
```

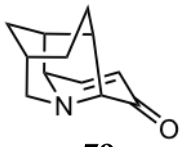


79

BRUKER

```
Current Data Parameters
NAME        LU3260_CYH_0
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20171219
Time               15.32 h
INSTRUM            spect
PROBHD   Z151340_0001 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    13
DS                     2
SWH            10504.202 Hz
FIDRES          0.320563 Hz
AQ             3.1195135 sec
RG                    32
DW                47.600 usec
DE                20.00 usec
TE                298.2 K
D1             1.00000000 sec
TD0                    1
SFO1         700.0115500 MHz
NUC1                  1H
P1                11.00 usec
PLW1         13.00000000 W

F2 - Processing parameters
SI                131072
SF         700.0070133 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

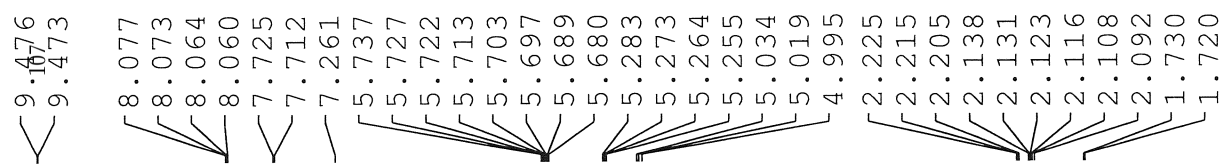
106

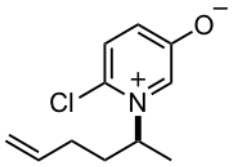


79

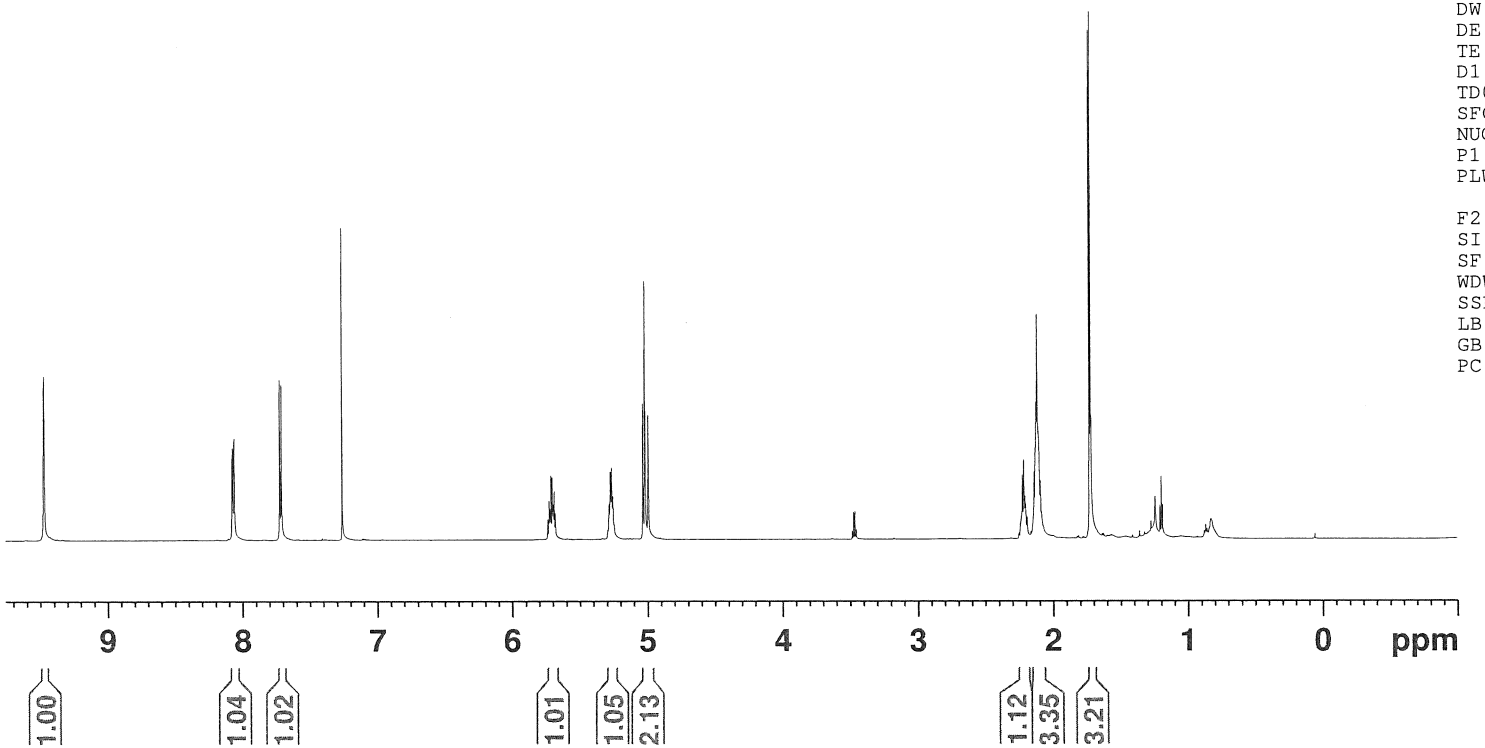
BRUKER

```
Current Data Parameters
NAME      check_cyclohexene_(
EXPNO                    3
PROCNO                   1

F2 - Acquisition Parameters
Date_          20171219
Time               15.45 h
INSTRUM             spect
PROBHD    Z151340_0001 (
PULPROG           zgpg30
TD                65536
SOLVENT           CDCl3
NS                  256
DS                    4
SWH           42613.637 Hz
FIDRES         1.300465 Hz
AQ            0.7689557 sec
RG                  203
DW                11.733 usec
DE                18.00 usec
TE                298.2 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1        176.0362620 MHz
NUC1                13C
P1                11.00 usec
PLW1        29.00000000 W
SFO2        700.0098000 MHz
NUC2                1H
CPDPRG[2         waltz16
PCPD2             65.00 usec
PLW2        13.00000000 W
PLW12        0.37231001 W
PLW13        0.18747000 W

F2 - Processing parameters
SI                131072
SF          176.0169002 MHz
WDW                 EM
SSB       0
LB                 1.00 Hz
GB        0
PC                 1.40
```





80



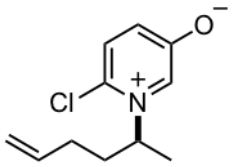
Current Data Parameters
NAME LU5053_Pure Mono_Cl_OX
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20180531
Time 19.40 h
INSTRUM spect
PROBHD Z151340_0001 (
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 10
DS 2
SWH 10504.202 Hz
FIDRES 0.320563 Hz
AQ 3.1195135 sec
RG 28.5
DW 47.600 usec
DE 20.00 usec
TE 303.2 K
D1 1.00000000 sec
TD0 1
SFO1 700.0115500 MHz
NUC1 1H
P1 11.00 usec
PLW1 13.00000000 W

F2 - Processing parameters
SI 131072
SF 700.0070169 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

108

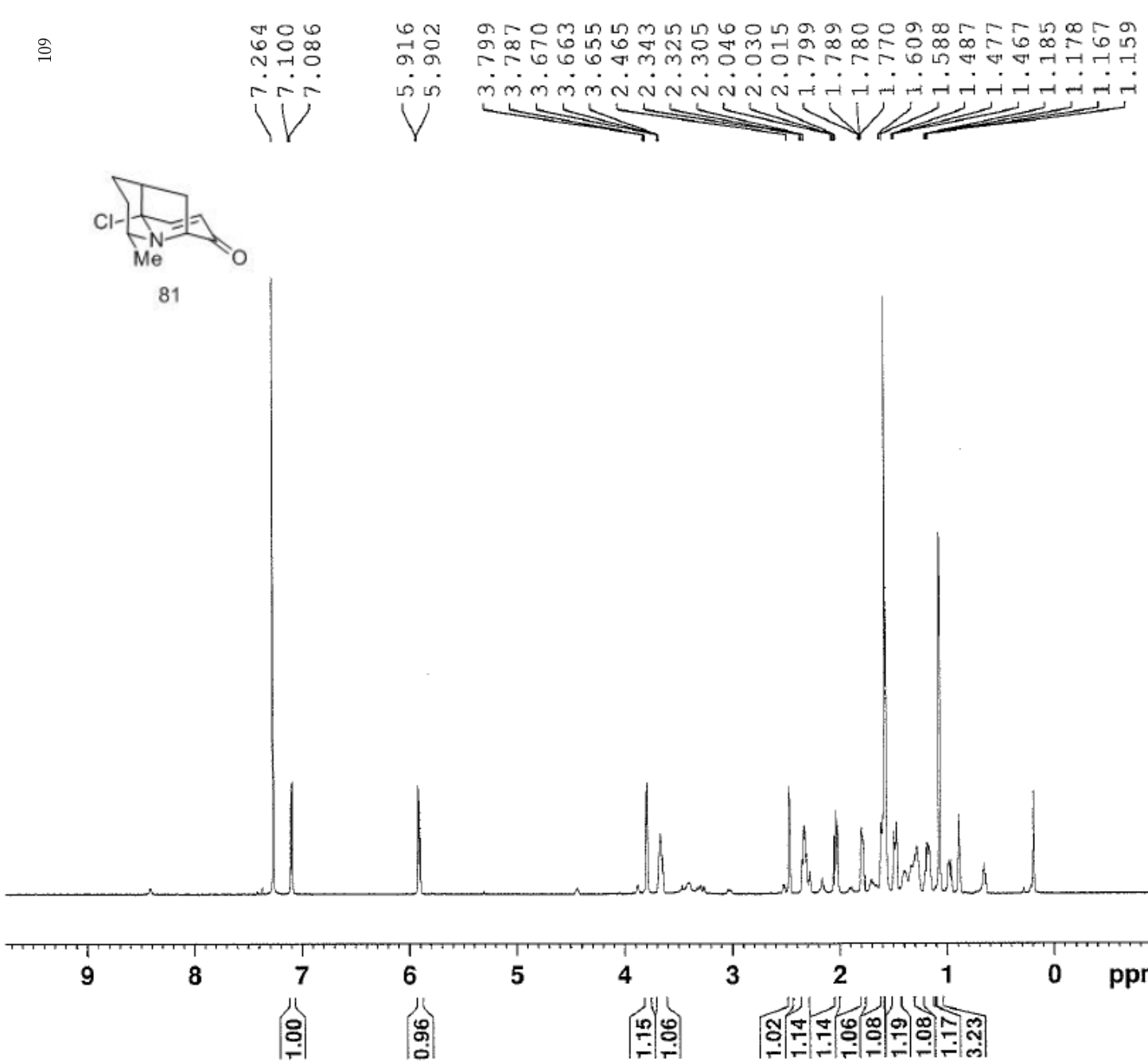
158.69
135.04
134.92
133.58
132.12
129.60
117.31
77.23
77.05
76.87
65.16
35.45
29.90
20.99



80

BRUKER

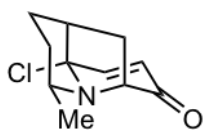
```
Current Data Parameters
NAME      LU5053_Pure Mono_Cl_OX
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180531
Time              19.44 h
INSTRUM           spect
PROBHD   Z151340_0001 (
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                   44
DS                    4
SWH           42613.637 Hz
FIDRES         1.300465 Hz
AQ             0.7689557 sec
RG                  203
DW               11.733 usec
DE                18.00 usec
TE                303.2 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1        176.0362620 MHz
NUC1               13C
P1               11.00 usec
PLW1        29.00000000 W
SFO2        700.0098000 MHz
NUC2               1H
CPDPRG[2        waltz16
PCPD2            65.00 usec
PLW2        13.00000000 W
PLW12        0.37231001 W
PLW13        0.18747000 W

F2 - Processing parameters
SI               131072
SF          176.0169002 MHz
WDW                 EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```



BRUKER

```
Current Data Parameters
NAME                  check4
EXPNO                   5238
PROCNO                     1

F2 - Acquisition Parameters
Date_              20180819
Time                  11.22 h
INSTRUM               spect
PROBHD    Z566801_0015 (
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       32
DS                        2
SWH               10504.202 Hz
FIDRES             0.320563 Hz
AQ                3.1195135 sec
RG                      203
DW                   47.600 usec
DE                    6.50 usec
TE                   294.6 K
D1                1.00000000 sec
TD0                       1
SFO1            700.0115500 MHz
NUC1                    1H
P1                   12.88 usec
PLW1           40.00000000 W

F2 - Processing parameters
SI                   131072
SF              700.0070130 MHz
WDW                     EM
SSB          0
LB                    0.30 Hz
GB           0
PC                    1.00
```

PURE_MONO_CL



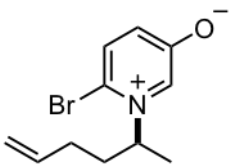
81

BRUKER

```
Current Data Parameters
NAME      LU4246_PURE_MONO_C
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameter
Date_           20180626
Time              11.22 h
INSTRUM            spect
PROBHD   Z161768_0001 (
PULPROG           zgig30
TD                65536
SOLVENT           CDCl3
NS                 1165
DS                    4
SWH           48076.922 Hz
FIDRES         1.467191 Hz
AQ            0.6815744 sec
RG               192.59
DW               10.400 usec
DE               18.00 usec
TE               298.1 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1        201.2330858 MHz
NUC1               13C
P1               12.00 usec
PLW1       138.64999390 W
SFO2        800.2132008 MHz
NUC2               1H
CPDPRG[2         waltz16
PCPD2             60.00 usec
PLW2         9.66049957 W
PLW12        0.13911000 W

F2 - Processing parameters
SI                131072
SF          201.2129645 MHz
WDW                EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```

111

7.762
7.757
7.433
7.420
7.263
7.245
7.241
7.232
7.227
5.738
5.732
5.729
5.723
5.714
5.708
5.705
5.699
5.035
5.021
4.997
2.095
2.085
2.072
2.061
2.053
2.042
2.025
2.014
1.957
1.948
1.939
1.574
1.565



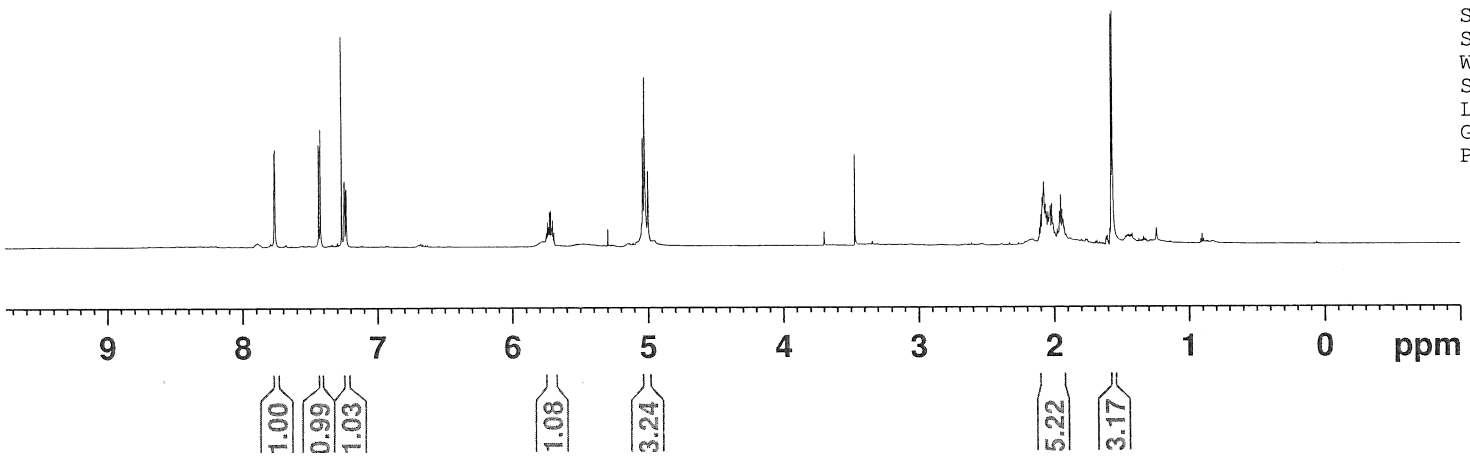
82

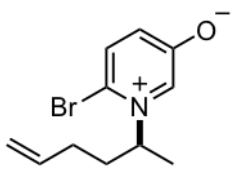
BRUKER

Current Data Parameters
NAME LU5049_OX_mono_Br
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20180108
Time 14.27 h
INSTRUM spect
PROBHD Z151340_0001 (
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 10504.202 Hz
FIDRES 0.320563 Hz
AQ 3.1195135 sec
RG 25.4
DW 47.600 usec
DE 20.00 usec
TE 298.2 K
D1 1.00000000 sec
TD0 1
SFO1 700.0115500 MHz
NUC1 1H
P1 11.00 usec
PLW1 13.00000000 W

F2 - Processing parameters
SI 131072
SF 700.0070169 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

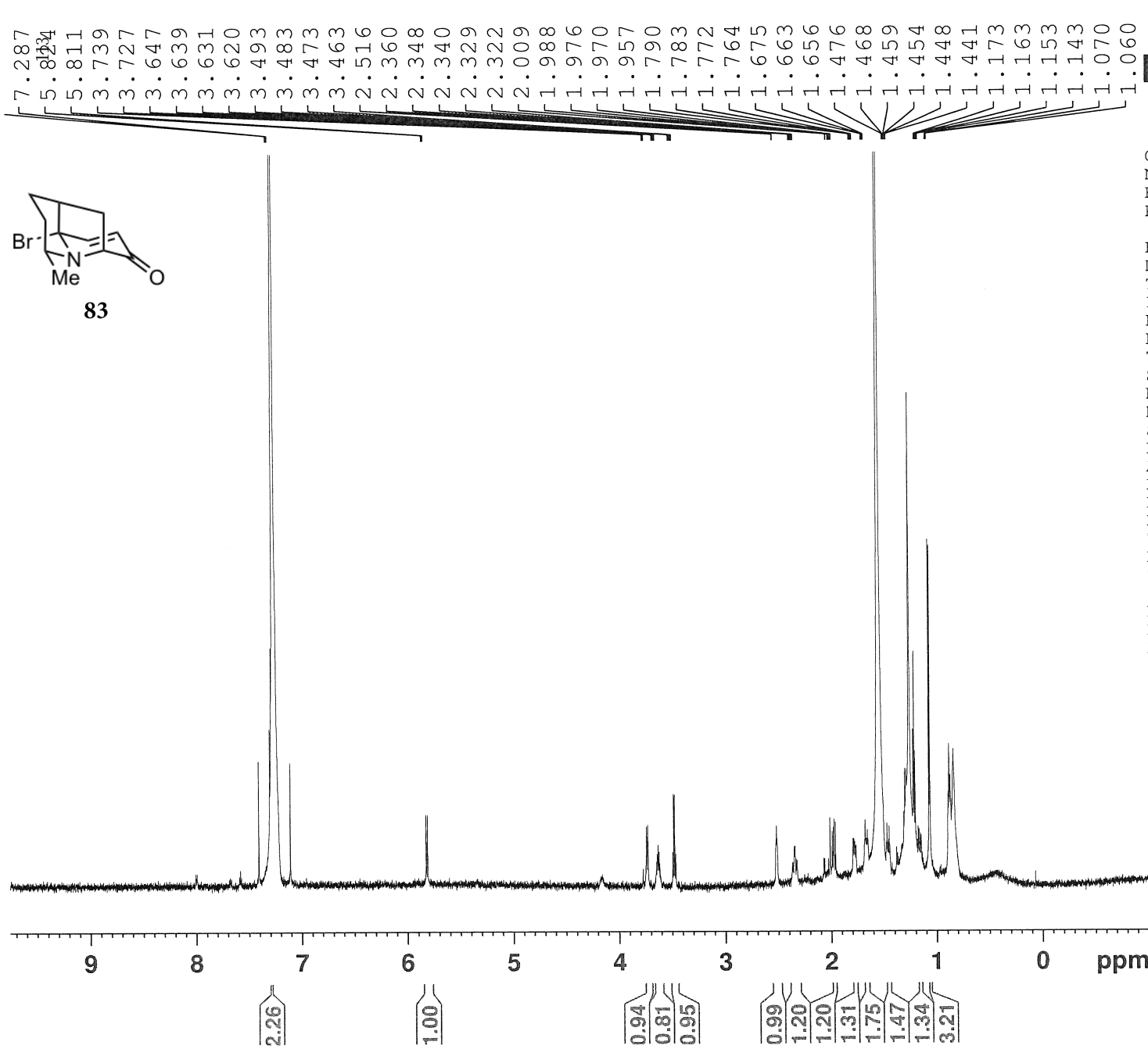




82

BRUKER

```
Current Data Parameters
NAME      LU5049_OX_mono_Br
EXPNO                    3
PROCNO                   1

F2 - Acquisition Parameters
Date_           20180108
Time              14.33 h
INSTRUM             spect
PROBHD   Z151340_0001 (
PULPROG           zgpg30
TD                65536
SOLVENT           CDCl3
NS                   73
DS                    4
SWH           42613.637 Hz
FIDRES         1.300465 Hz
AQ            0.7689557 sec
RG                  203
DW               11.733 usec
DE                18.00 usec
TE                298.2 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                  1
SFO1       176.0362620 MHz
NUC1               13C
P1               11.00 usec
PLW1        29.00000000 W
SFO2       700.0098000 MHz
NUC2               1H
CPDPRG[2        waltz16
PCPD2             65.00 usec
PLW2        13.00000000 W
PLW12        0.37231001 W
PLW13        0.18747000 W

F2 - Processing parameters
SI               131072
SF         176.0169002 MHz
WDW                EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```



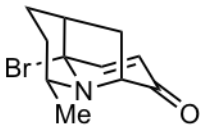
83

BRUKER

Current Data Parameters
NAME LU5258_mono_br
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20180521
Time 2.50 h
INSTRUM spect
PROBHD Z151340_0001 (
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 10504.202 Hz
FIDRES 0.320563 Hz
AQ 3.1195135 sec
RG 32
DW 47.600 usec
DE 20.00 usec
TE 303.3 K
D1 1.00000000 sec
TD0 1
SFO1 700.0115500 MHz
NUC1 1H
P1 11.00 usec
PLW1 13.00000000 W

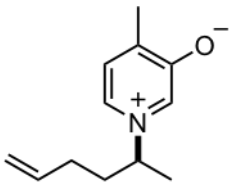
F2 - Processing parameters
SI 131072
SF 700.0070169 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



83

BRUKER

```
Current Data Parameters
NAME      LU5258_mono_br
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180521
Time                7.38 h
INSTRUM            spect
PROBHD   Z151340_0001 (
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 6000
DS                    4
SWH           42613.637 Hz
FIDRES         1.300465 Hz
AQ            0.7689557 sec
RG                  203
DW               11.733 usec
DE               18.00 usec
TE               303.2 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1        176.0362620 MHz
NUC1               13C
P1               11.00 usec
PLW1        29.00000000 W
SFO2        700.0098000 MHz
NUC2               1H
CPDPRG[2        waltz16
PCPD2            65.00 usec
PLW2        13.00000000 W
PLW12        0.37231001 W
PLW13        0.18747000 W

F2 - Processing parameters
SI               131072
SF          176.0169002 MHz
WDW                EM
SSB       0
LB               1.00 Hz
GB        0
PC               1.40
```



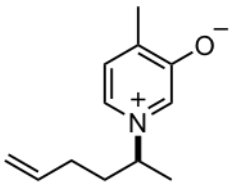
84

BRUKER

Current Data Parameters
NAME LU5045_mono_me4
EXPNO 1
PROCNO 1

F2 - Acquisition Parameter
Date_ 20180105
Time 18.08 h
INSTRUM spect
PROBHD Z151340_0001 (
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 11
DS 2
SWH 10504.202 Hz
FIDRES 0.320563 Hz
AQ 3.1195135 sec
RG 9
DW 47.600 usec
DE 20.00 usec
TE 298.2 K
D1 1.00000000 sec
TD0 1
SFO1 700.0115500 MHz
NUC1 1H
P1 11.00 usec
PLW1 13.00000000 W

F2 - Processing parameters
SI 131072
SF 700.0070169 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

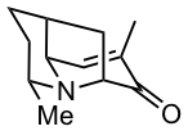


84

Current Data Parameters
NAME LU5045_mono_me4
EXPNO 3
PROCNO 1

F2 - Acquisition Parameter
Date_ 20180105
Time 18.10 h
INSTRUM spect
PROBHD Z151340_0001 (
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 6
DS 4
SWH 42613.637 Hz
FIDRES 1.300465 Hz
AQ 0.7689557 sec
RG 203
DW 11.733 usec
DE 18.00 usec
TE 298.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
SFO1 176.0362620 MHz
NUC1 13C
P1 11.00 usec
PLW1 29.00000000 W
SFO2 700.0098000 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 65.00 usec
PLW2 13.00000000 W
PLW12 0.37231001 W
PLW13 0.18747000 W

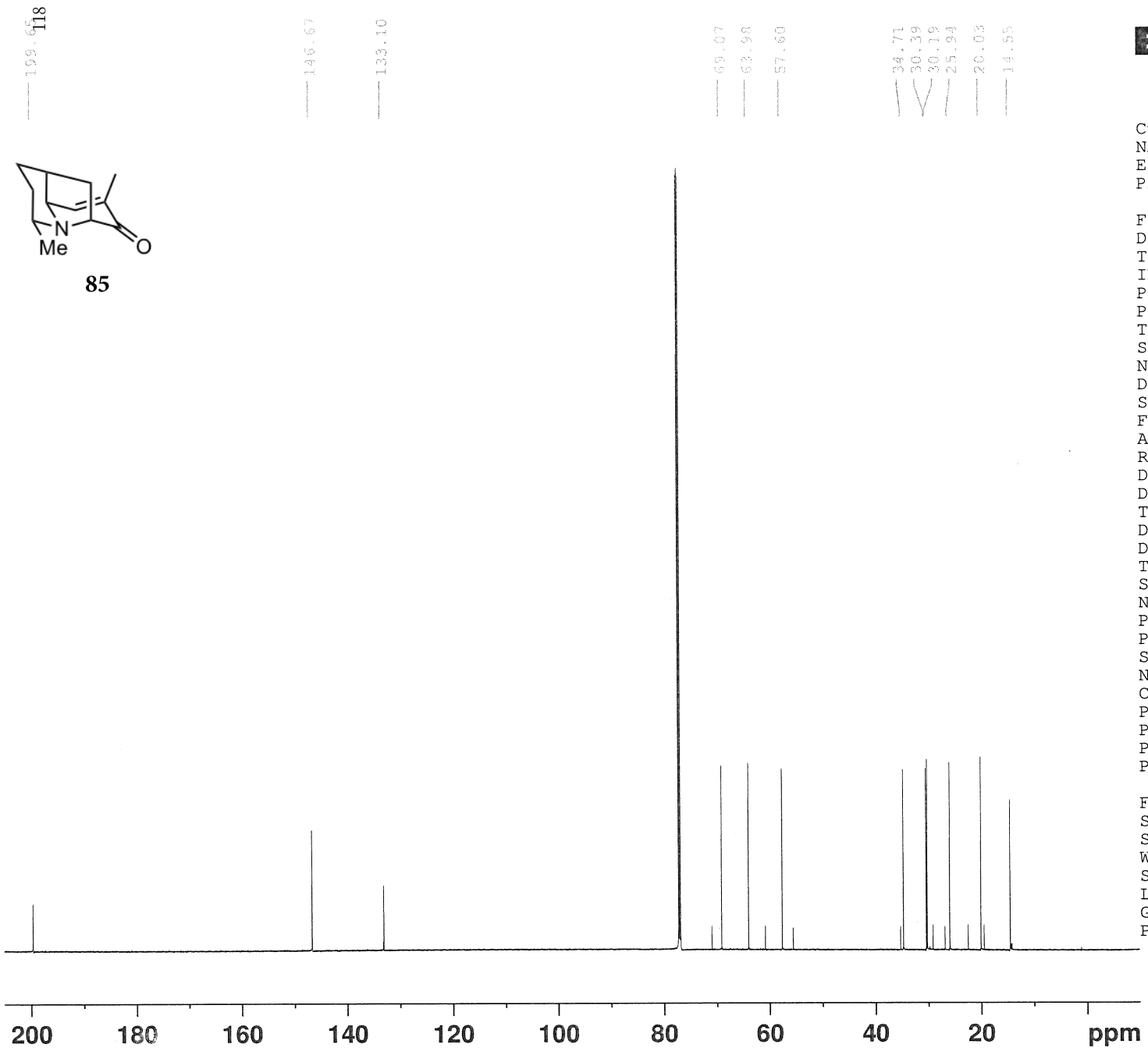
F2 - Processing parameters
SI 131072
SF 176.0169002 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.00



85

BRUKER

```
Current Data Parameters
NAME      LU5055_mono_Me4
EXPNO                   1
PROCNO                  1

F2 - Acquisition Parameters
Date_           20180112
Time                9.35 h
INSTRUM            spect
PROBHD   Z151340_0001 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH            10504.202 Hz
FIDRES          0.320563 Hz
AQ             3.1195135 sec
RG                  25.4
DW                47.600 usec
DE                20.00 usec
TE                298.2 K
D1           1.00000000 sec
TD0                    1
SFO1         700.0115500 MHz
NUC1                  1H
P1                 11.00 usec
PLW1        13.00000000 W

F2 - Processing parameters
SI                131072
SF           700.0070169 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

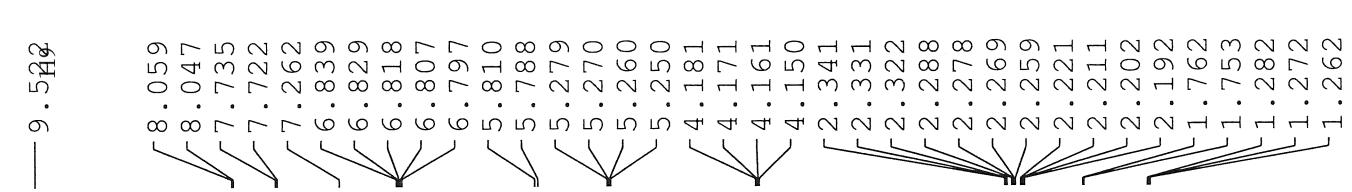


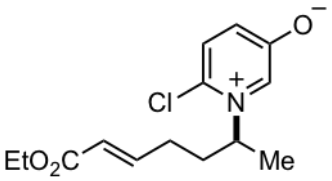
85

Current Data Parameters
NAME LU5055_mono_Me4
EXPNO 3
PROCNO 1

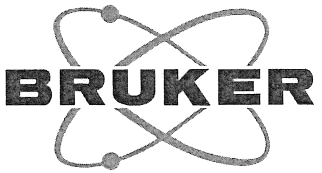
F2 - Acquisition Parameters
Date_ 20180112
Time 9.40 h
INSTRUM spect
PROBHD Z151340_0001 (
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 53
DS 4
SWH 42613.637 Hz
FIDRES 1.300465 Hz
AQ 0.7689557 sec
RG 203
DW 11.733 usec
DE 18.00 usec
TE 298.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
SFO1 176.0362620 MHz
NUC1 13C
P1 11.00 usec
PLW1 29.00000000 W
SFO2 700.0098000 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 65.00 usec
PLW2 13.00000000 W
PLW12 0.37231001 W
PLW13 0.18747000 W

F2 - Processing parameters
SI 131072
SF 176.0169002 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

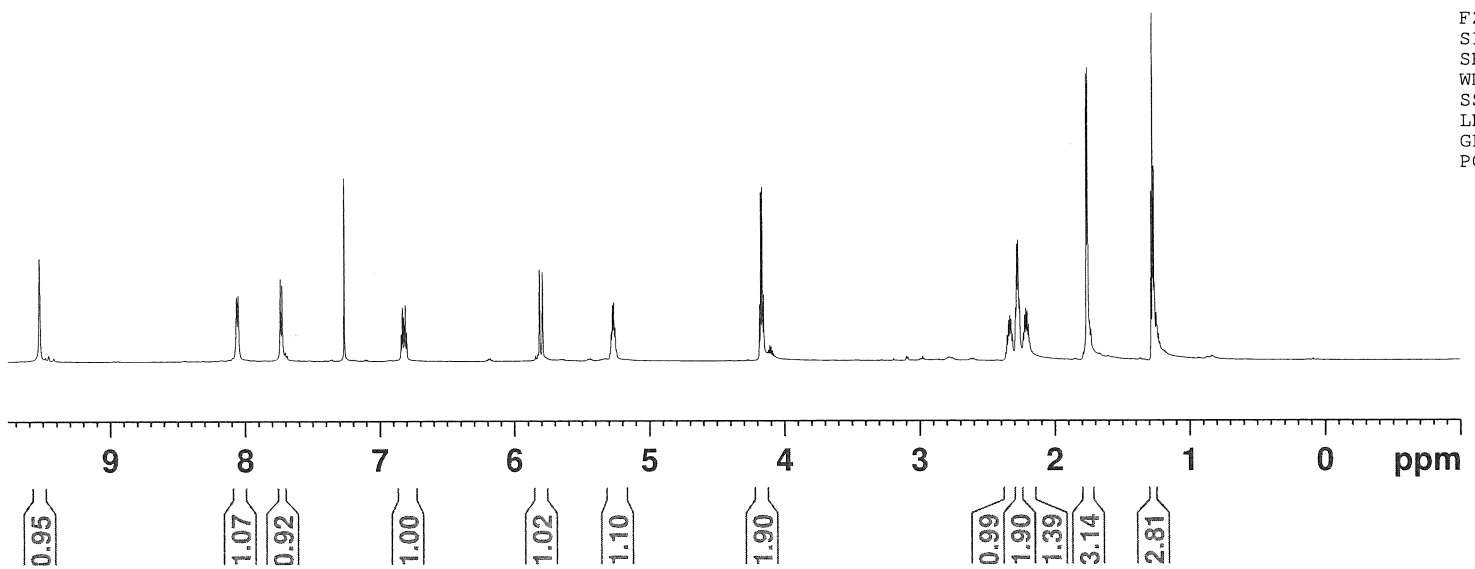


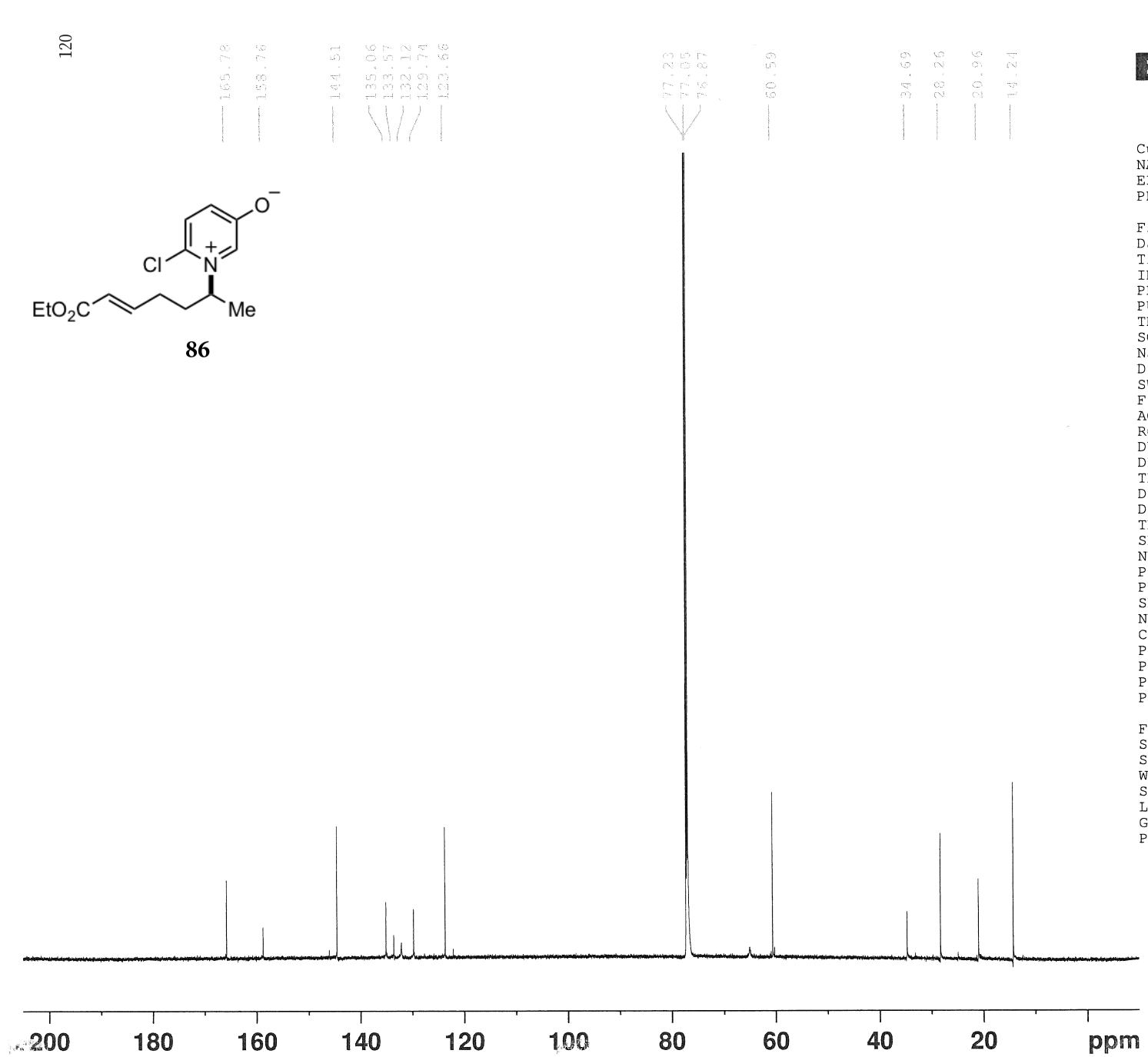


86



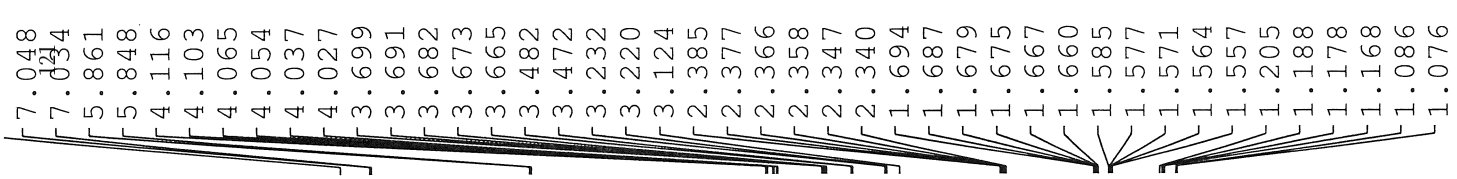

```
Current Data Parameters
NAME      LU4068_PURE_Ester_Cl_OX
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180531
Time              19.51 h
INSTRUM             spect
PROBHD   Z151340_0001 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    13
DS                     2
SWH           10504.202 Hz
FIDRES         0.320563 Hz
AQ            3.1195135 sec
RG                  28.5
DW                47.600 usec
DE                20.00 usec
TE                303.2 K
D1           1.00000000 sec
TD0                    1
SFO1        700.0115500 MHz
NUC1                  1H
P1                 11.00 usec
PLW1        13.00000000 W

F2 - Processing parameters
SI                131072
SF          700.0070169 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

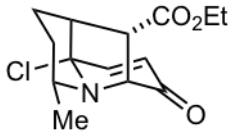




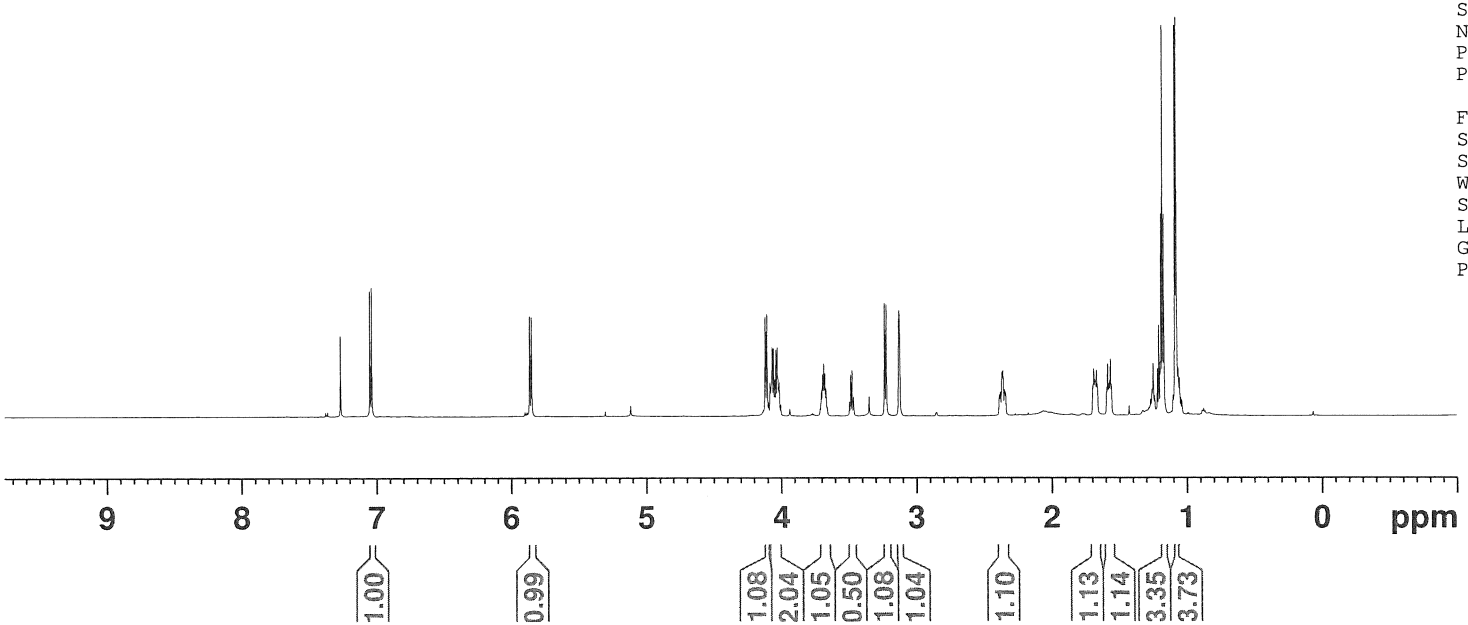
BRUKER

```
Current Data Parameters
NAME      LU4068_PURE_Ester_Cl_OX
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180531
Time              19.56 h
INSTRUM           spect
PROBHD   Z151340_0001 (
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                   96
DS                    4
SWH           42613.637 Hz
FIDRES         1.300465 Hz
AQ            0.7689557 sec
RG                  203
DW               11.733 usec
DE               18.00 usec
TE               303.2 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1        176.0362620 MHz
NUC1               13C
P1              11.00 usec
PLW1        29.00000000 W
SFO2        700.0098000 MHz
NUC2               1H
CPDPRG[2        waltz16
PCPD2             65.00 usec
PLW2        13.00000000 W
PLW12        0.37231001 W
PLW13        0.18747000 W

F2 - Processing parameters
SI                131072
SF          176.0169002 MHz
WDW                 EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```

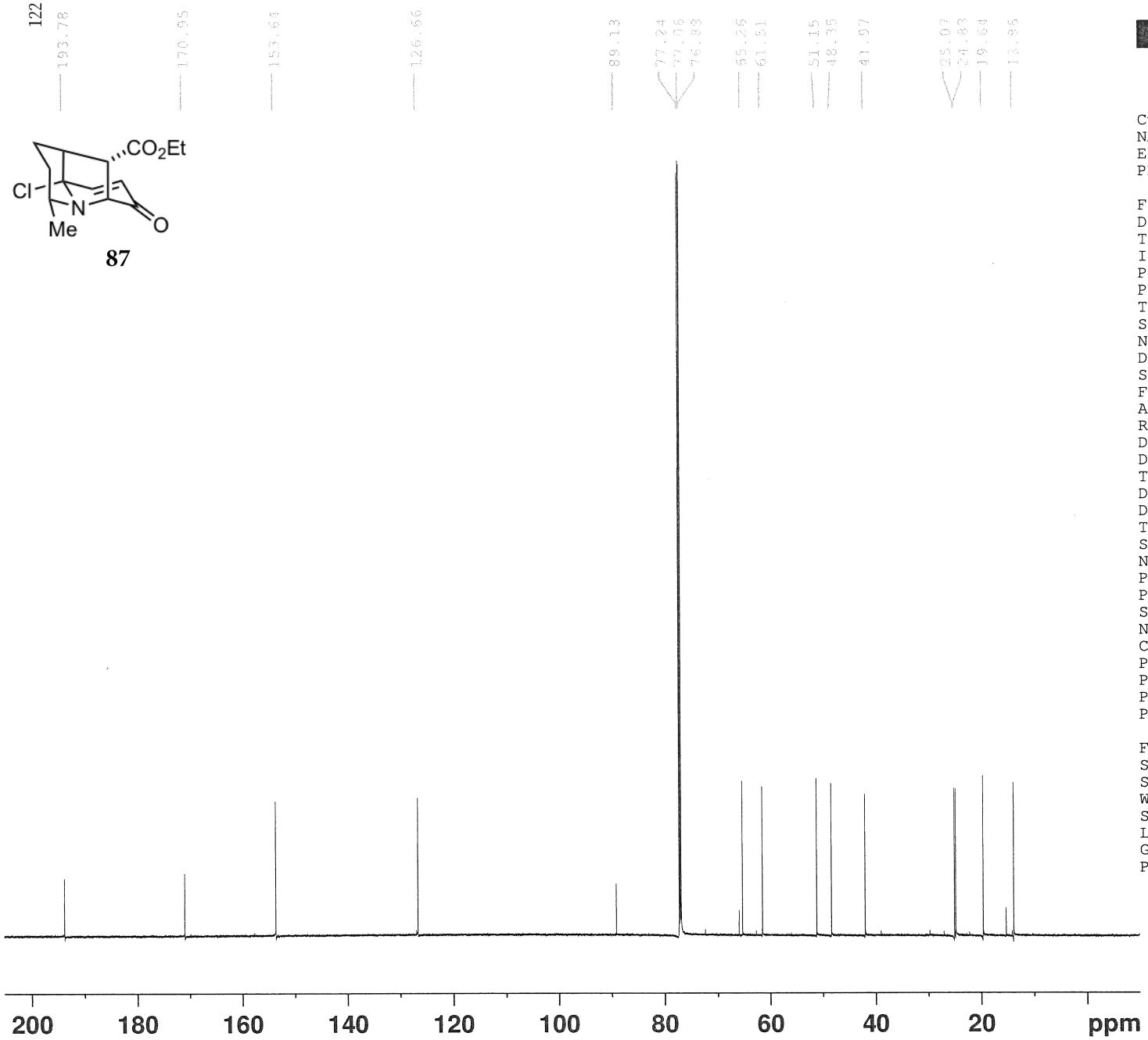




87




```
Current Data Parameters
NAME      LU43762_pure_ester_Cl
EXPNO                        1
PROCNO                       1

F2 - Acquisition Parameters
Date_              20171106
Time                  17.35 h
INSTRUM               spect
PROBHD    Z151340_0001 (
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                        6
DS                        2
SWH               10504.202 Hz
FIDRES             0.320563 Hz
AQ                3.1195135 sec
RG                     25.4
DW                   47.600 usec
DE                   20.00 usec
TE                   299.4 K
D1              1.00000000 sec
TD0                       1
SFO1           700.0115500 MHz
NUC1                    1H
P1                   11.00 usec
PLW1           13.00000000 W

F2 - Processing parameters
SI                    131072
SF             700.0070142 MHz
WDW                      EM
SSB       0
LB                    0.30 Hz
GB        0
PC                    1.00
```

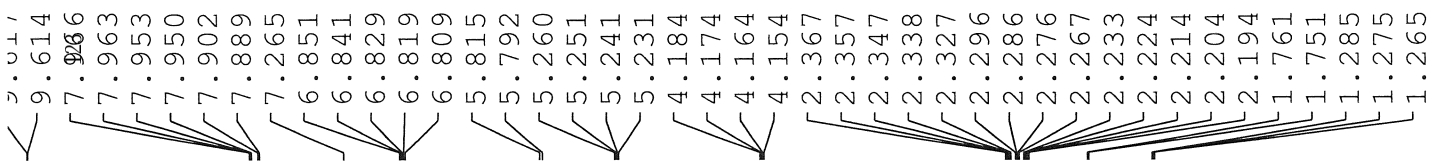


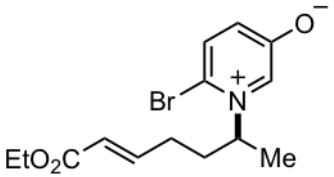
BRUKER

Current Data Parameters
NAME LU43762_pure_ester_Cl
EXPNO 3
PROCNO 1

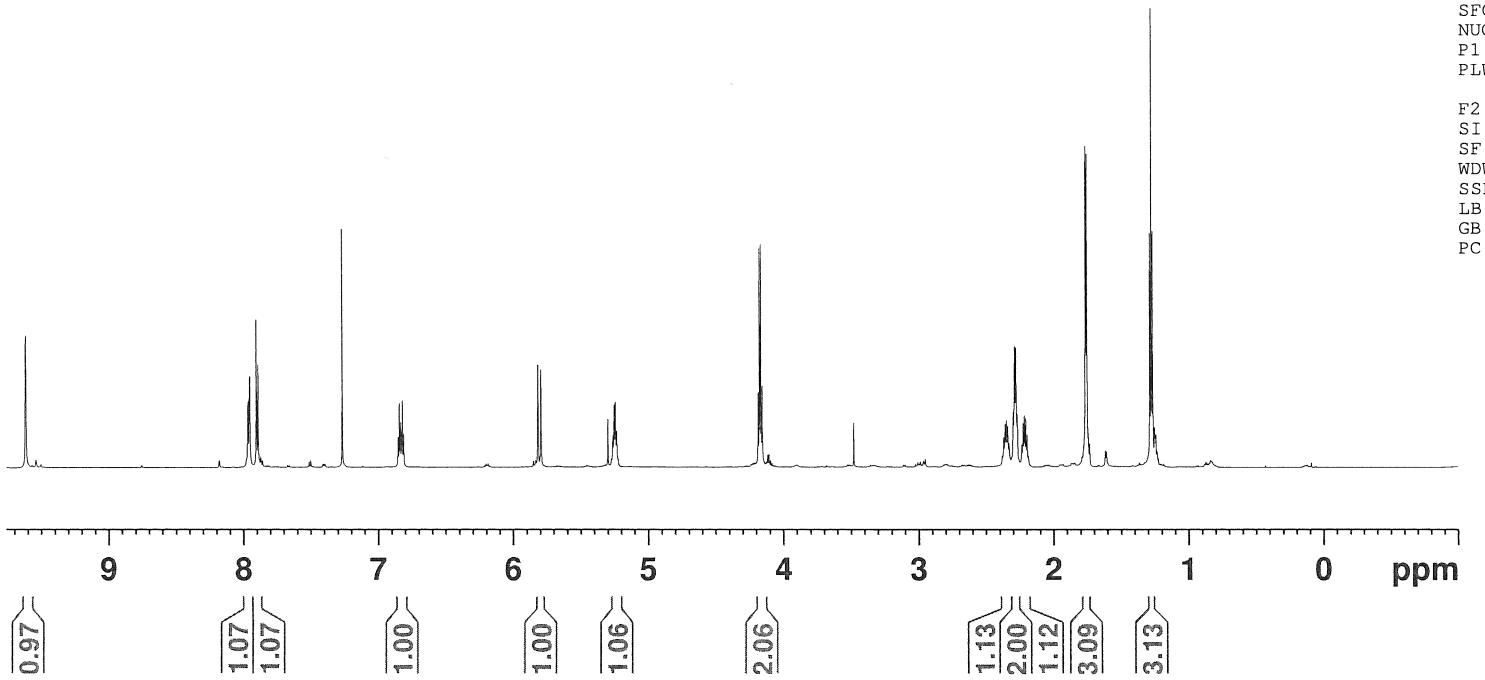
F2 - Acquisition Parameters
Date_ 20171106
Time 17.37 h
INSTRUM spect
PROBHD Z151340_0001 (
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 32
DS 4
SWH 42613.637 Hz
FIDRES 1.300465 Hz
AQ 0.7689557 sec
RG 203
DW 11.733 usec
DE 18.00 usec
TE 298.5 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
SFO1 176.0362620 MHz
NUC1 13C
P1 11.00 usec
PLW1 29.00000000 W
SFO2 700.0098000 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 65.00 usec
PLW2 13.00000000 W
PLW12 0.37231001 W
PLW13 0.18747000 W

F2 - Processing parameters
SI 131072
SF 176.0169002 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40



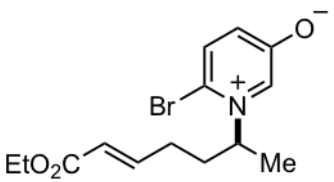


88



BRUKER

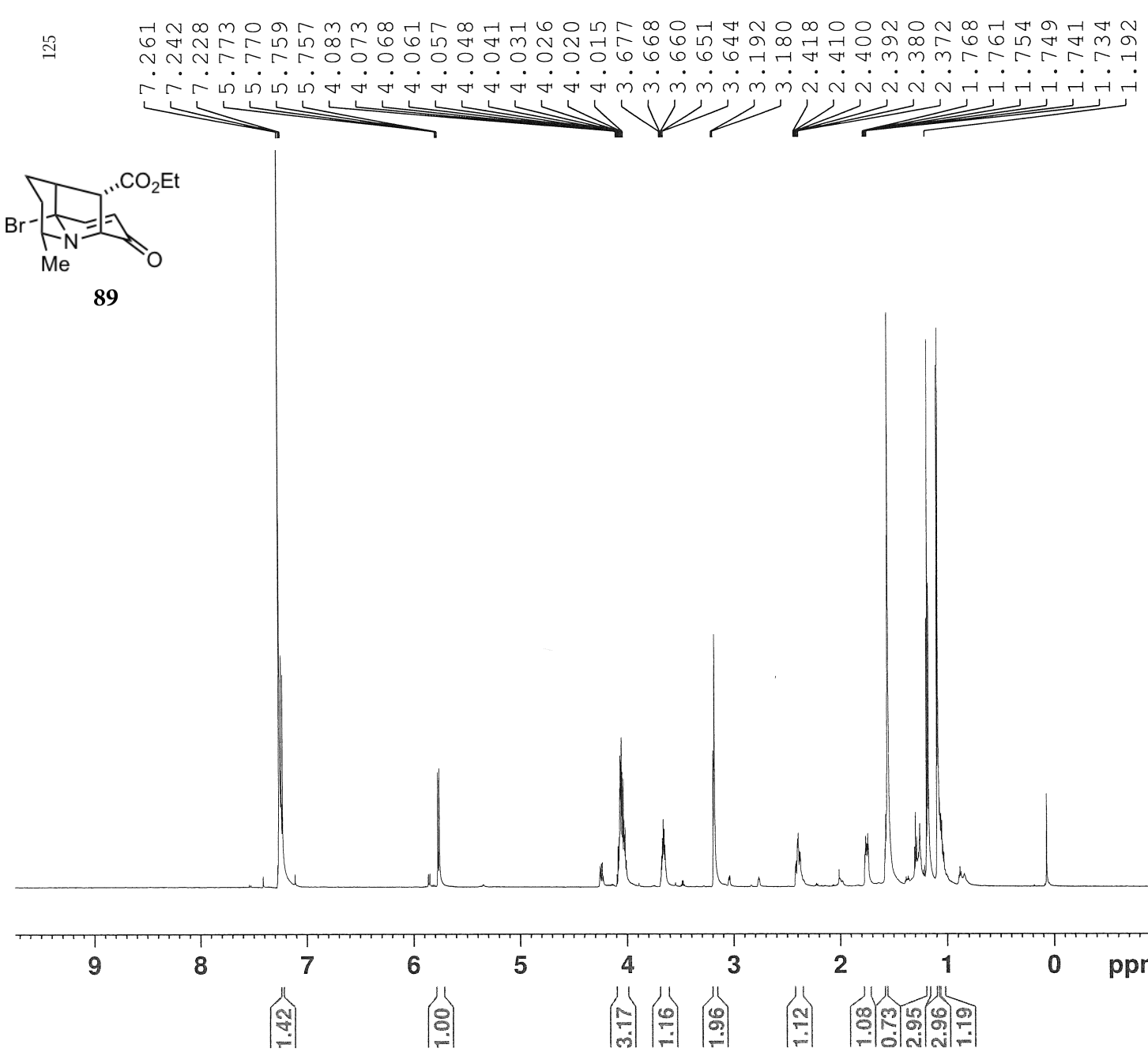
```
Current Data Parameters
NAME      LU4255_Pure_Estrer_Br_OX
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180528
Time              18.02 h
INSTRUM           spect
PROBHD   Z151340_0001 (
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    16
DS                     2
SWH           10504.202 Hz
FIDRES         0.320563 Hz
AQ            3.1195135 sec
RG                 25.4
DW                47.600 usec
DE                20.00 usec
TE                303.2 K
D1           1.00000000 sec
TD0                    1
SFO1         700.0115500 MHz
NUC1                  1H
P1                11.00 usec
PLW1         13.00000000 W

F2 - Processing parameters
SI                131072
SF          700.0070140 MHz
WDW                   EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```



88

BRUKER

```
Current Data Parameters
NAME      LU4255_Pure_Estrer_Br_OX
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20180528
Time              18.06 h
INSTRUM            spect
PROBHD   Z151340_0001 (
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                   37
DS                    4
SWH           42613.637 Hz
FIDRES         1.300465 Hz
AQ            0.7689557 sec
RG                  203
DW               11.733 usec
DE                18.00 usec
TE                303.2 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1        176.0362620 MHz
NUC1               13C
P1                11.00 usec
PLW1        29.00000000 W
SFO2        700.0098000 MHz
NUC2               1H
CPDPRG[2        waltz16
PCPD2             65.00 usec
PLW2        13.00000000 W
PLW12        0.37231001 W
PLW13        0.18747000 W

F2 - Processing parameters
SI               131072
SF          176.0169099 MHz
WDW                 EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```



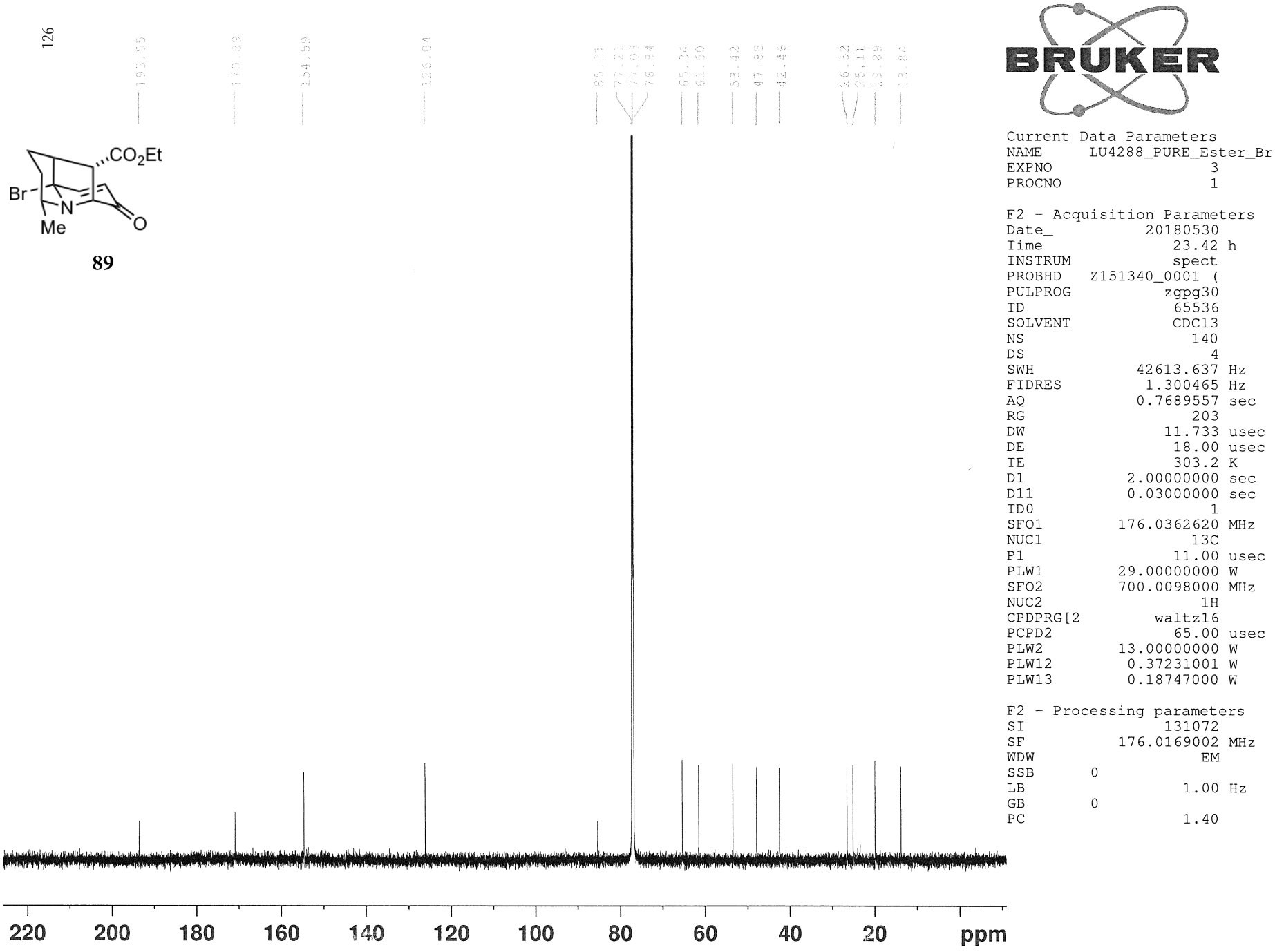
89

BRUKER

Current Data Parameters
NAME LU4288_PURE_Ester_Br
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20180530
Time 23.34 h
INSTRUM spect
PROBHD Z151340_0001 (
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 10504.202 Hz
FIDRES 0.320563 Hz
AQ 3.1195135 sec
RG 28.5
DW 47.600 usec
DE 20.00 usec
TE 303.2 K
D1 1.00000000 sec
TD0 1
SFO1 700.0115500 MHz
NUC1 1H
P1 11.00 usec
PLW1 13.00000000 W

F2 - Processing parameters
SI 131072
SF 700.0070169 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

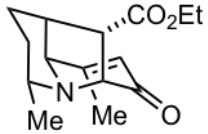


BRUKER

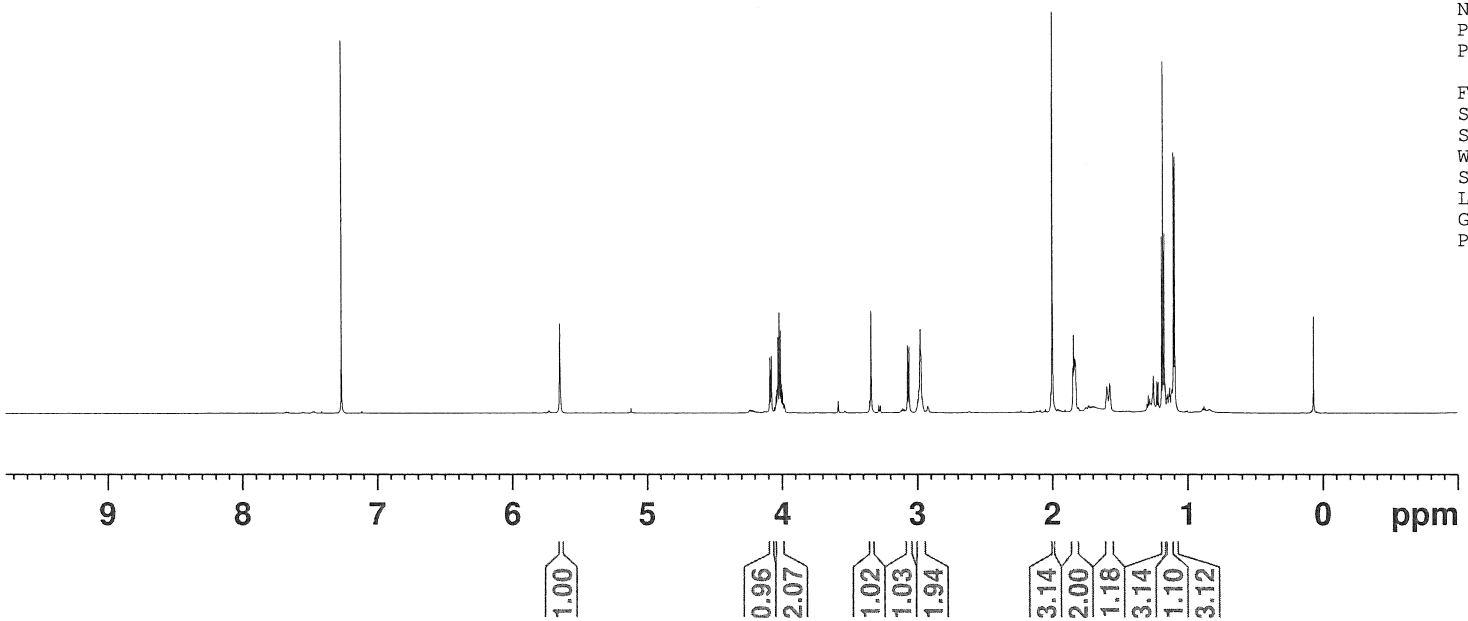
```
Current Data Parameters
NAME      LU4288_PURE_Ester_Br
EXPNO                        3
PROCNO                       1

F2 - Acquisition Parameters
Date_              20180530
Time                  23.42 h
INSTRUM               spect
PROBHD    Z151340_0001 (
PULPROG             zgpg30
TD                    65536
SOLVENT               CDCl3
NS                      140
DS                        4
SWH               42613.637 Hz
FIDRES             1.300465 Hz
AQ                0.7689557 sec
RG                      203
DW                   11.733 usec
DE                   18.00 usec
TE                   303.2 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                       1
SFO1           176.0362620 MHz
NUC1                    13C
P1                   11.00 usec
PLW1           29.00000000 W
SFO2           700.0098000 MHz
NUC2                    1H
CPDPRG[2           waltz16
PCPD2                65.00 usec
PLW2           13.00000000 W
PLW12           0.37231001 W
PLW13           0.18747000 W

F2 - Processing parameters
SI                   131072
SF             176.0169002 MHz
WDW                     EM
SSB       0
LB                    1.00 Hz
GB        0
PC                    1.40
```

127

7.265
5.648
4.088
4.077
4.044
4.039
4.034
4.029
4.019
4.009
4.004
3.999
3.994
3.340
3.070
3.059
2.975
2.971
1.999
1.998
1.846
1.841
1.836
1.831
1.828
1.825
1.596
1.592
1.581
1.576
1.570
1.191
1.180
1.170



91



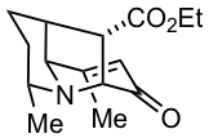
Current Data Parameters
NAME LU5023_PURE_Ester_me51
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20171212
Time 18.07 h
INSTRUM spect
PROBHD Z151340_0001 (
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 12
DS 2
SWH 10504.202 Hz
FIDRES 0.320563 Hz
AQ 3.1195135 sec
RG 22.6
DW 47.600 usec
DE 20.00 usec
TE 298.2 K
D1 1.00000000 sec
TD0 1
SFO1 700.0115500 MHz
NUC1 1H
P1 11.00 usec
PLW1 13.00000000 W

F2 - Processing parameters
SI 131072
SF 700.0070131 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

128

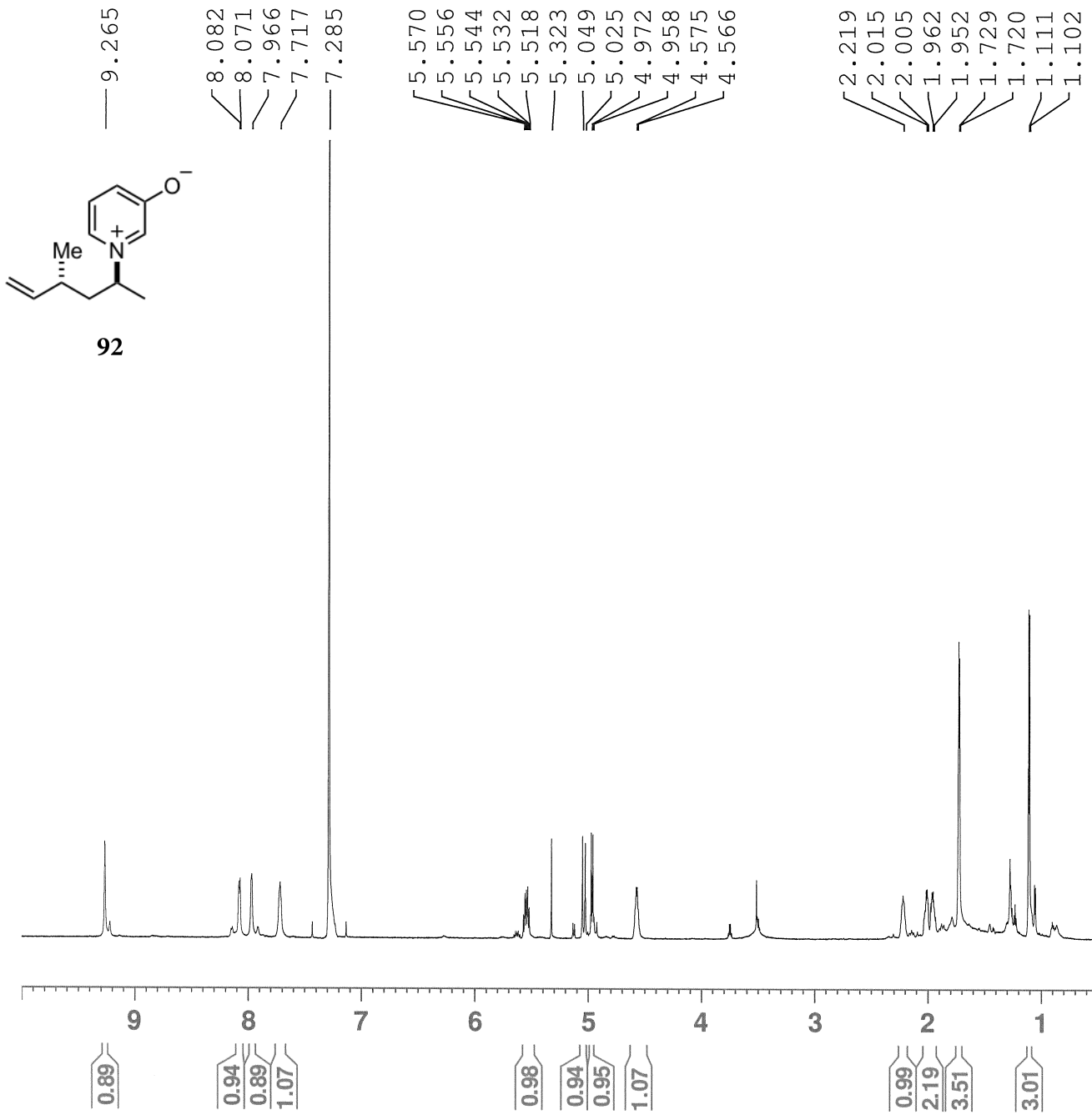
195.10
171.94
164.29
124.32
77.23
77.05
76.87
74.25
68.97
61.11
57.59
49.29
38.03
30.05
26.69
20.90
19.67
13.94



91

BRUKER

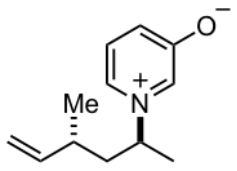
```
Current Data Parameters
NAME      LU5023_PURE_Ester_me51
EXPNO                          3
PROCNO                         1

F2 - Acquisition Parameters
Date_              20171212
Time                  18.13 h
INSTRUM               spect
PROBHD    Z151340_0001 (
PULPROG              zgpg30
TD                    65536
SOLVENT               CDCl3
NS                      102
DS                        4
SWH               42613.637 Hz
FIDRES             1.300465 Hz
AQ                0.7689557 sec
RG                      203
DW                   11.733 usec
DE                   18.00 usec
TE                   298.2 K
D1              2.00000000 sec
D11             0.03000000 sec
TD0                       1
SFO1           176.0362620 MHz
NUC1                    13C
P1                   11.00 usec
PLW1           29.00000000 W
SFO2           700.0098000 MHz
NUC2                    1H
CPDPRG[2             waltz16
PCPD2                65.00 usec
PLW2           13.00000000 W
PLW12           0.37231001 W
PLW13           0.18747000 W

F2 - Processing parameters
SI                    131072
SF             176.0169002 MHz
WDW                      EM
SSB       0
LB                    1.00 Hz
GB        0
PC                    1.40
```



92

BRUKER

```
Current Data Parameters
NAME      LU4292_PURE_2Me_o:
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameter
Date_          20180701
Time               0.43 h
INSTRUM           spect
PROBHD   Z566801_0015 (
PULPROG           zg30
TD               65536
SOLVENT          CDCl3
NS                  32
DS                   2
SWH          10504.202 Hz
FIDRES        0.320563 Hz
AQ           3.1195135 sec
RG                 203
DW              47.600 usec
DE               6.50 usec
TE               294.3 K
D1          1.00000000 sec
TD0                  1
SFO1        700.0115500 MHz
NUC1                1H
P1               12.88 usec
PLW1        40.00000000 W

F2 - Processing parameters
SI               131072
SF          700.0070000 MHz
WDW                 EM
SSB      0
LB                0.30 Hz
GB       0
PC                1.00
```

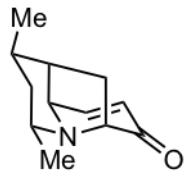


92

BRUKER

```
Current Data Parameters
NAME      LU4292_PURE_2Me_o:
EXPNO                    3
PROCNO                   1

F2 - Acquisition Parameter
Date_           20180701
Time                5.35 h
INSTRUM             spect
PROBHD    Z566801_0015 (
PULPROG           zgpg30
TD                65536
SOLVENT            CDCl3
NS                 6000
DS                    4
SWH           42613.637 Hz
FIDRES          1.300465 Hz
AQ             0.7689557 sec
RG                  203
DW                11.733 usec
DE                 6.50 usec
TE                301.4 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                   1
SFO1         176.0362620 MHz
NUC1                13C
P1                 8.95 usec
PLW1        100.00000000 W
SFO2         700.0098000 MHz
NUC2                1H
CPDPRG[2         waltz16
PCPD2             65.00 usec
PLW2         40.00000000 W
PLW12         1.57060003 W
PLW13         0.79086000 W

F2 - Processing parameters
SI                131072
SF          176.0169002 MHz
WDW                 EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```

7.126
7.118
7.112
7.104
5.910
5.908
5.896
5.894
3.662
3.651
3.540
3.532
2.924
2.914
2.117
2.108
1.906
1.896
1.889
1.801
1.790
1.781
1.770
1.473
1.467
1.459
1.453
1.446
1.417
1.414
1.407
1.404
1.397
1.395
1.387
1.385
1.068
1.058
0.884
0.874
0.734
0.716
0.696

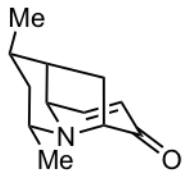


93

Current Data Parameters
NAME LU5028_PURE_ 2me_0
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20180531
Time 9.34 h
INSTRUM spect
PROBHD Z151340_0001 (
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 10504.202 Hz
FIDRES 0.320563 Hz
AQ 3.1195135 sec
RG 28.5
DW 47.600 usec
DE 20.00 usec
TE 303.2 K
D1 1.00000000 sec
TD0 1
SFO1 700.0115500 MHz
NUC1 1H
P1 11.00 usec
PLW1 13.00000000 W

F2 - Processing parameters
SI 131072
SF 700.0070143 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

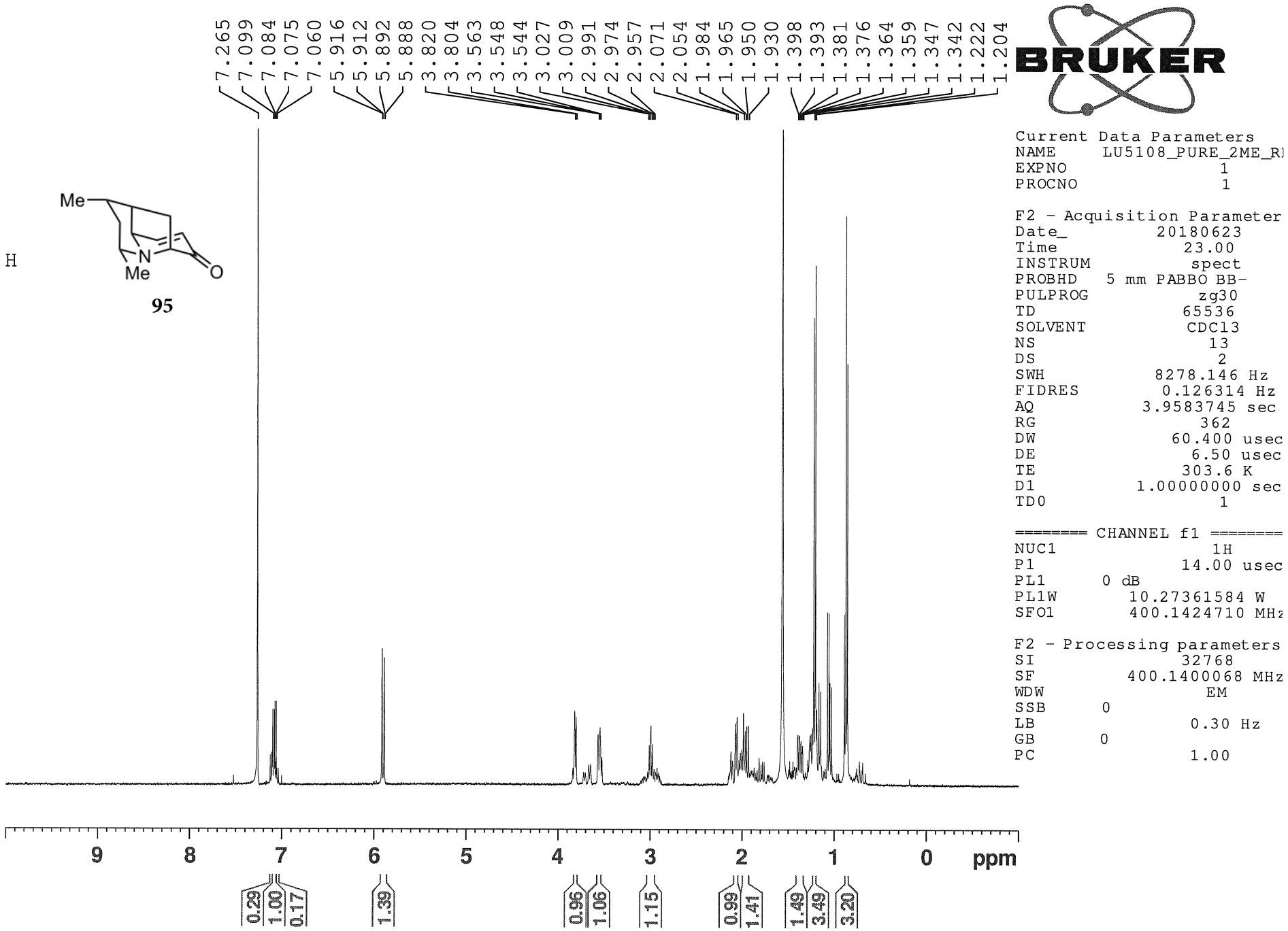


93

Current Data Parameters
NAME LU5028_PURE_ 2me_0
EXPNO 3
PROCNO 1

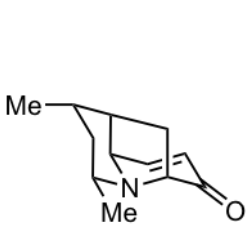
F2 - Acquisition Parameters
Date_ 20180531
Time 9.41 h
INSTRUM spect
PROBHD Z151340_0001 (
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 96
DS 4
SWH 42613.637 Hz
FIDRES 1.300465 Hz
AQ 0.7689557 sec
RG 203
DW 11.733 usec
DE 18.00 usec
TE 303.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
SFO1 176.0362620 MHz
NUC1 13C
P1 11.00 usec
PLW1 29.00000000 W
SFO2 700.0098000 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 65.00 usec
PLW2 13.00000000 W
PLW12 0.37231001 W
PLW13 0.18747000 W

F2 - Processing parameters
SI 131072
SF 176.0169002 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40




```
Current Data Parameters
NAME      LU5108_PURE_2ME_R
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameter
Date_           20180623
Time              23.00
INSTRUM            spect
PROBHD   5 mm PABBO BB-
PULPROG             zg30
TD                 65536
SOLVENT            CDCl3
NS                    13
DS                     2
SWH             8278.146 Hz
FIDRES           0.126314 Hz
AQ              3.9583745 sec
RG                   362
DW                60.400 usec
DE                 6.50 usec
TE                303.6 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 14.00 usec
PL1       0 dB
PL1W         10.27361584 W
SFO1         400.1424710 MHz

F2 - Processing parameters
SI                 32768
SF          400.1400068 MHz
WDW                  EM
SSB       0
LB                 0.30 Hz
GB        0
PC                 1.00
```

This exp uses qsim mode. it has inherent lower S/N
The SW is 240 ppm



95

BRUKER

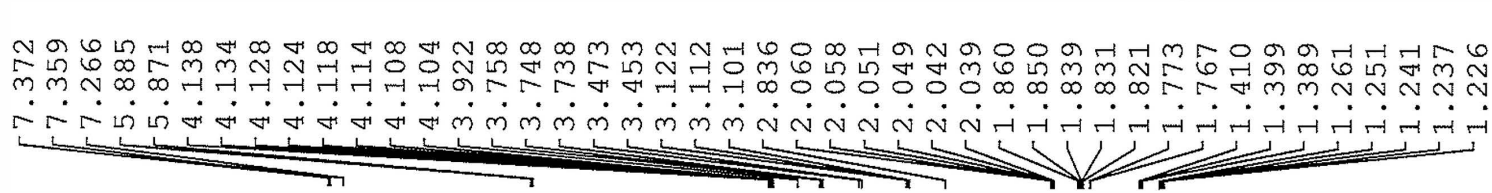
Current Data Parameters
NAME LU5108_PURE_2ME_RE
EXPNO 3
PROCNO 1

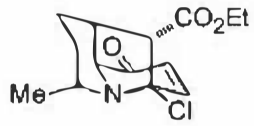
F2 - Acquisition Parameters
Date_ 20180624
Time 0.54
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 2429
DS 4
SWH 24154.590 Hz
FIDRES 0.368570 Hz
AQ 1.3565952 sec
RG 14596.5
DW 20.700 usec
DE 6.50 usec
TE 303.5 K
D1 2.70000005 sec
D11 0.03000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 -2.00 dB
PL1W 46.89702606 W
SFO1 100.6263507 MHz

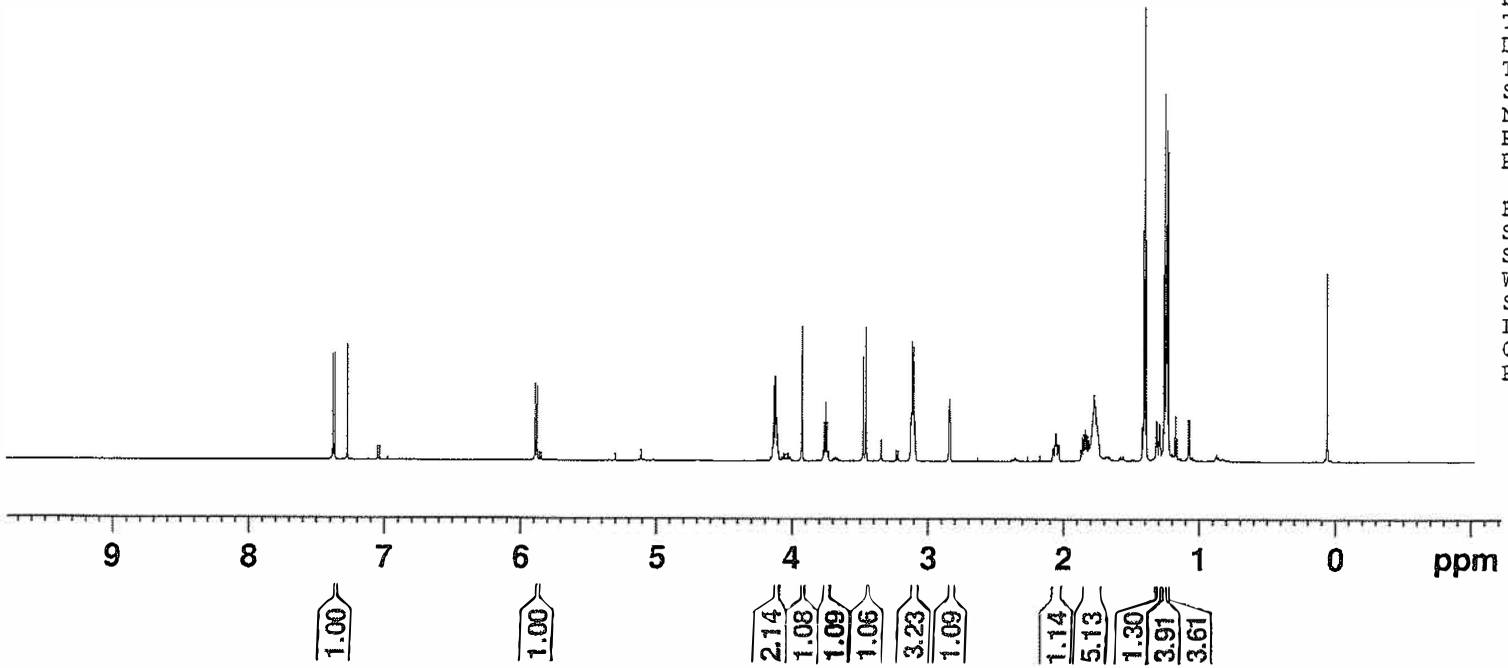
======== CHANNEL f2 ========
CPDPRG[2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 0 dB
PL12 16.16 dB
PL13 17.00 dB
PL2W 10.27361584 W
PL12W 0.24872722 W
PL13W 0.20498557 W
SFO2 400.1416006 MHz

F2 - Processing parameters
SI 131072
SF 100.6152830 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40





100

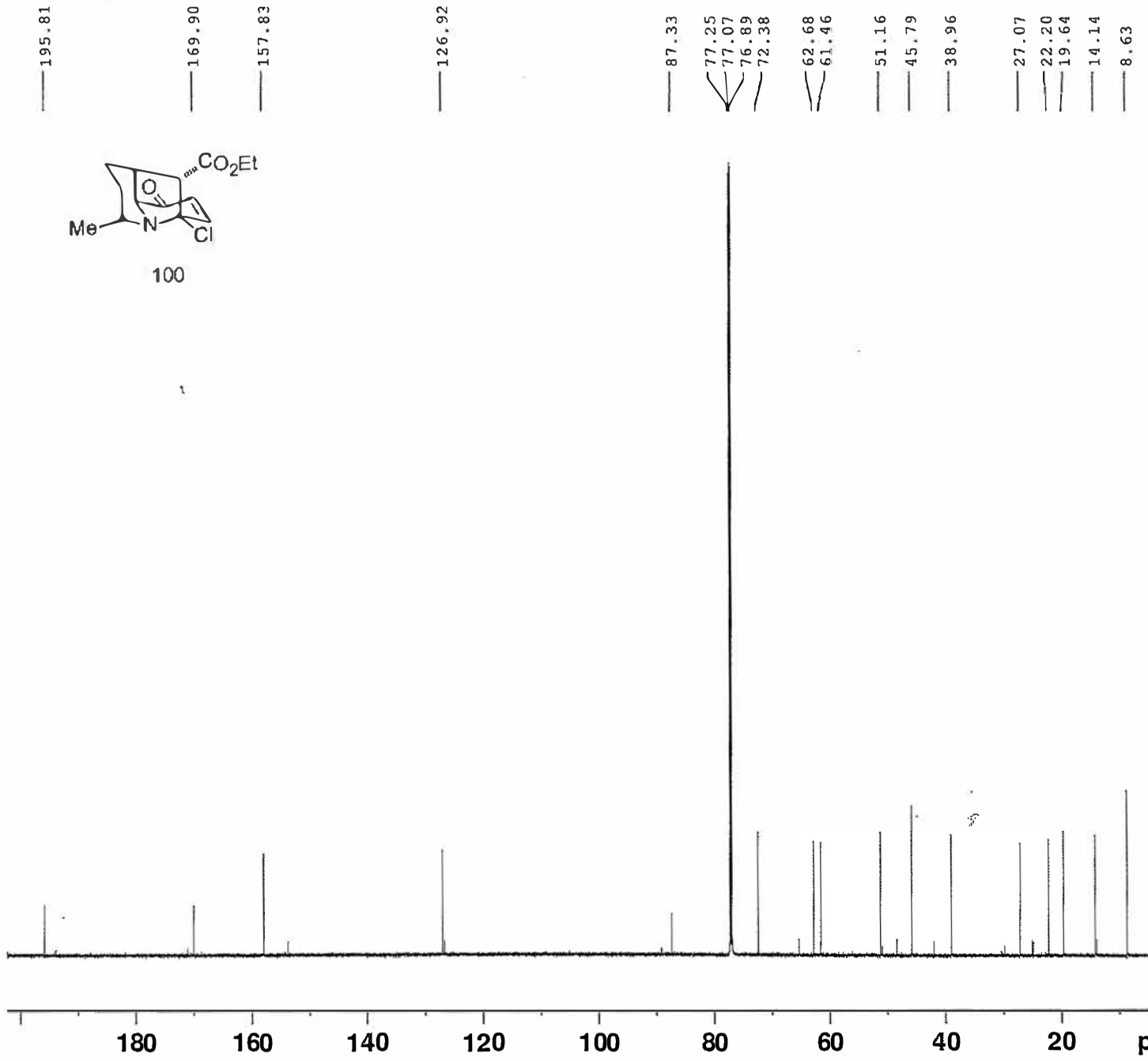


BRUKER

Current Data Parameters
NAME LU43761
EXPNO 1
PROCNO 1

F2 - Acquisition Parameter
Date_ 20171106
Time 16.33 h
INSTRUM spect
PROBHD Z151340_0001 (
PULPROG zg30
TD 65536
SOLVENT CDC13
NS 8
DS 2
SWH 10504.202 Hz
FIDRES 0.320563 Hz
AQ 3.1195135 sec
RG 18
DW 47.600 usec
DE 20.00 usec
TE 299.5 K
D1 1.00000000 sec
TD0 1
SFO1 700.0115500 MHz
NUC1 1H
P1 11.00 usec
PLW1 13.00000000 W

F2 - Processing parameters
SI 131072
SF 700.0070137 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

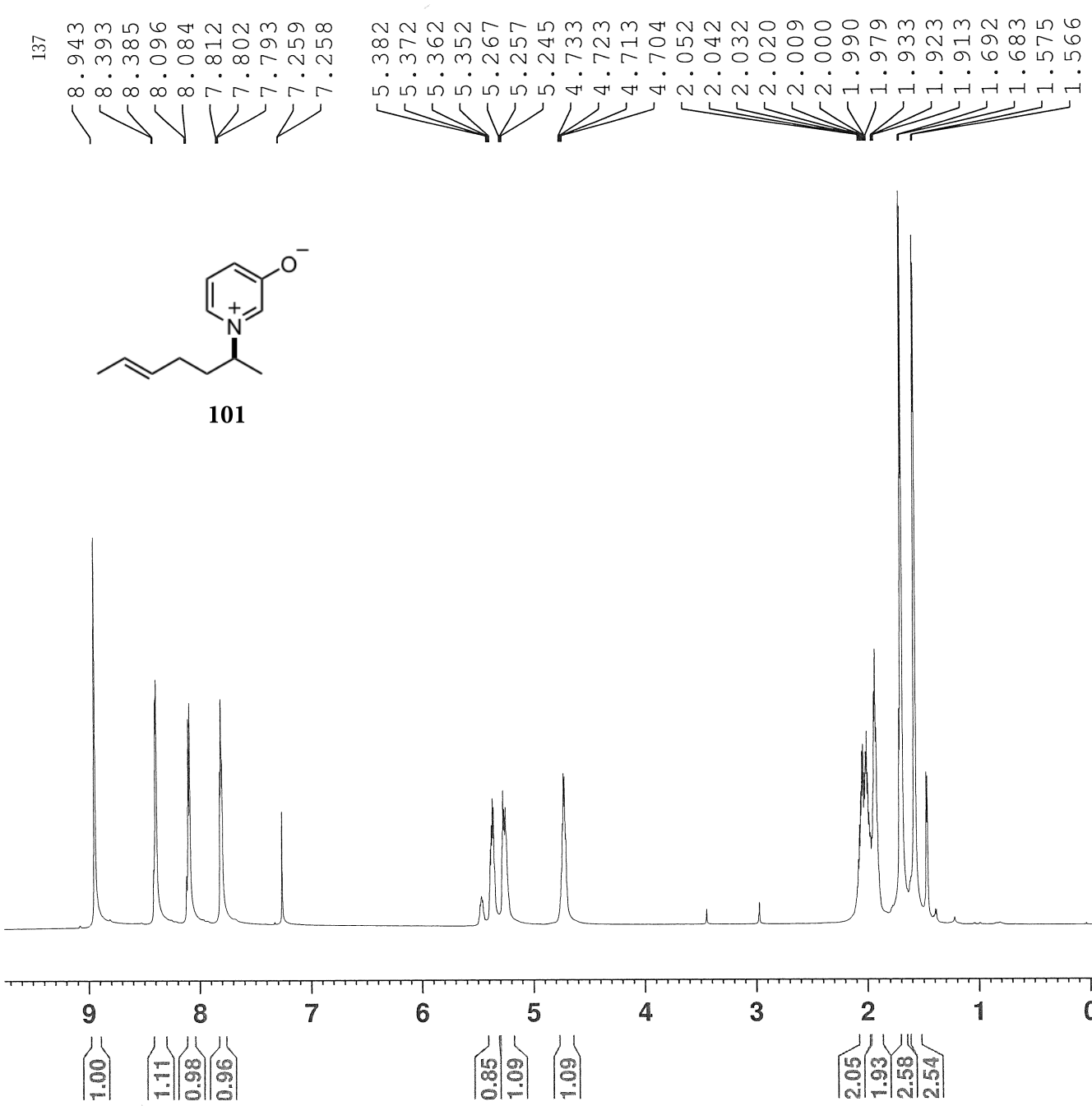


BRUKER

Current Data Parameters
NAME LU43761
EXPNO 3
PROCNO 1

F2 - Acquisition Parameter
Date_ 20171106
Time 16.44 h
INSTRUM spect
PROBHD Z151340_0001 (
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 17
DS 4
SWH 42613.637 Hz
FIDRES 1.300465 Hz
AQ 0.7689557 sec
RG 203
DW 11.733 usec
DE 18.00 usec
TE 298.4 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
SFO1 176.0362620 MHz
NUC1 13C
P1 11.00 usec
PLW1 29.00000000 W
SFO2 700.0098000 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 65.00 usec
PLW2 13.00000000 W
PLW12 0.37231001 W
PLW13 0.18747000 W

F2 - Processing parameters
SI 131072
SF 176.0169002 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

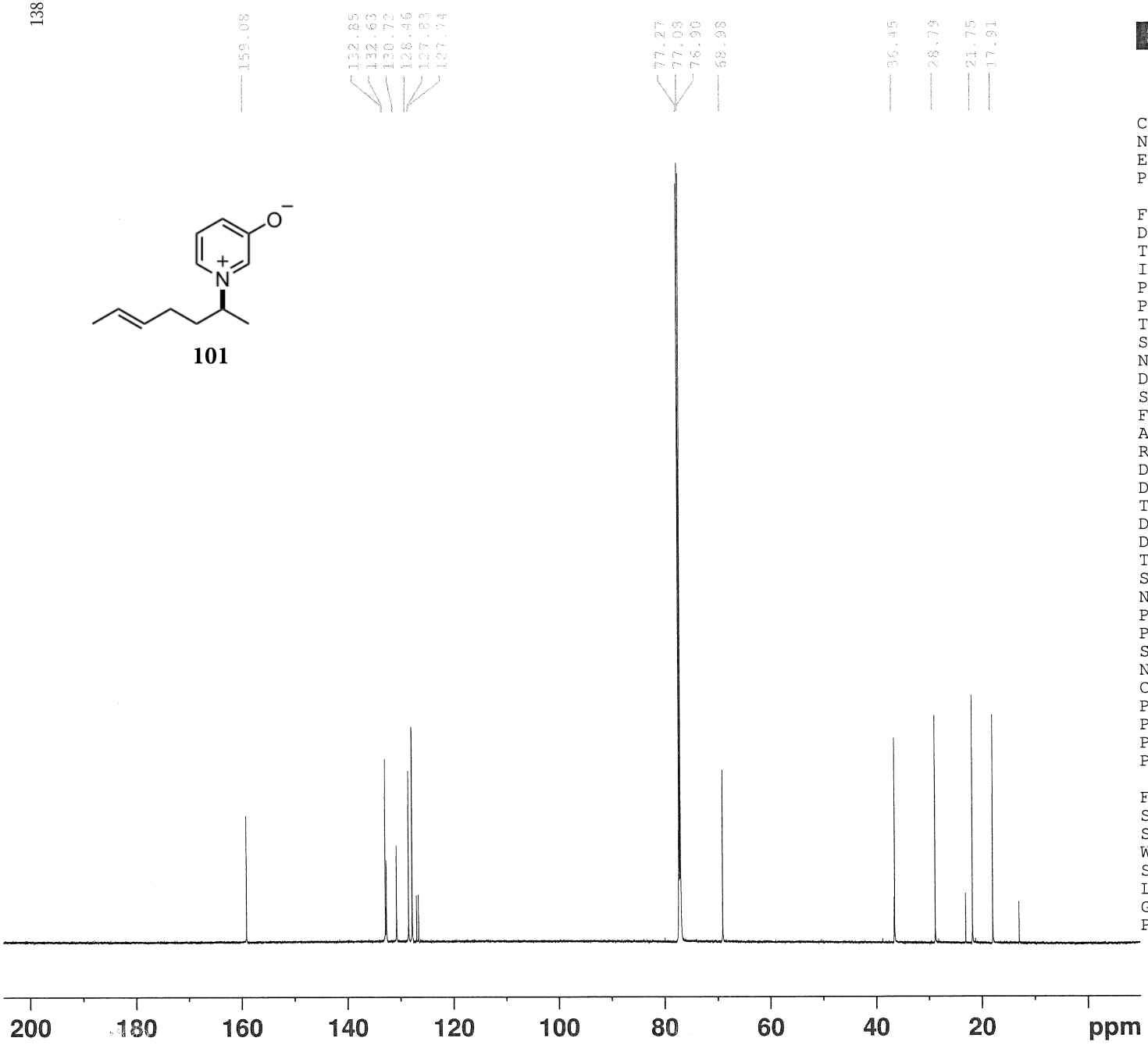


101

Current Data Parameters
NAME LU5193_E_OX
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20180607
Time 2.52 h
INSTRUM spect
PROBHD Z151340_0001 (
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 15
DS 2
SWH 10504.202 Hz
FIDRES 0.320563 Hz
AQ 3.1195135 sec
RG 5.6
DW 47.600 usec
DE 10.00 usec
TE 303.2 K
D1 1.00000000 sec
TD0 1
SFO1 700.0115500 MHz
NUC1 1H
P1 11.00 usec
PLW1 13.00000000 W

F2 - Processing parameters
SI 131072
SF 700.0070169 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



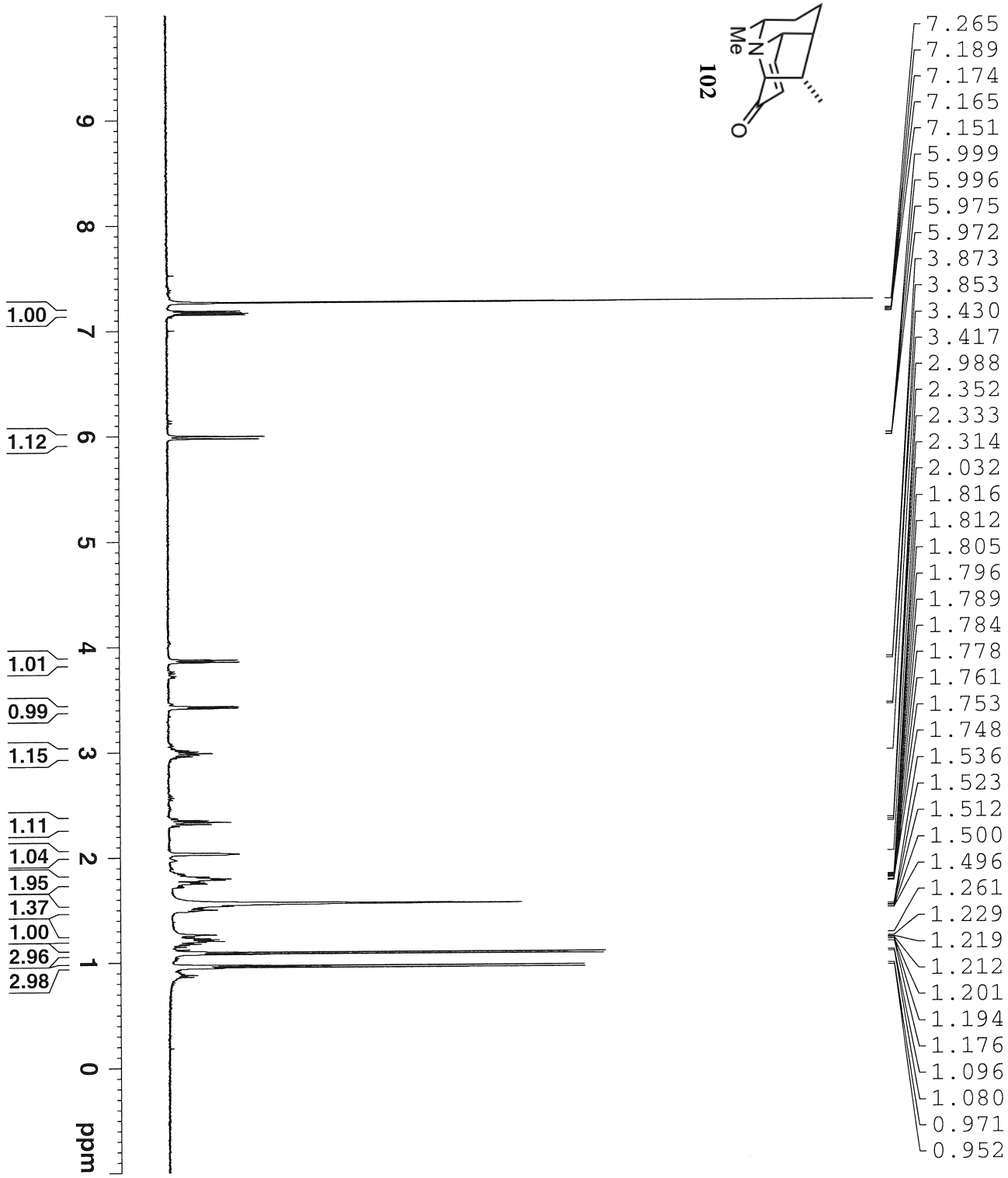
101

BRUKER

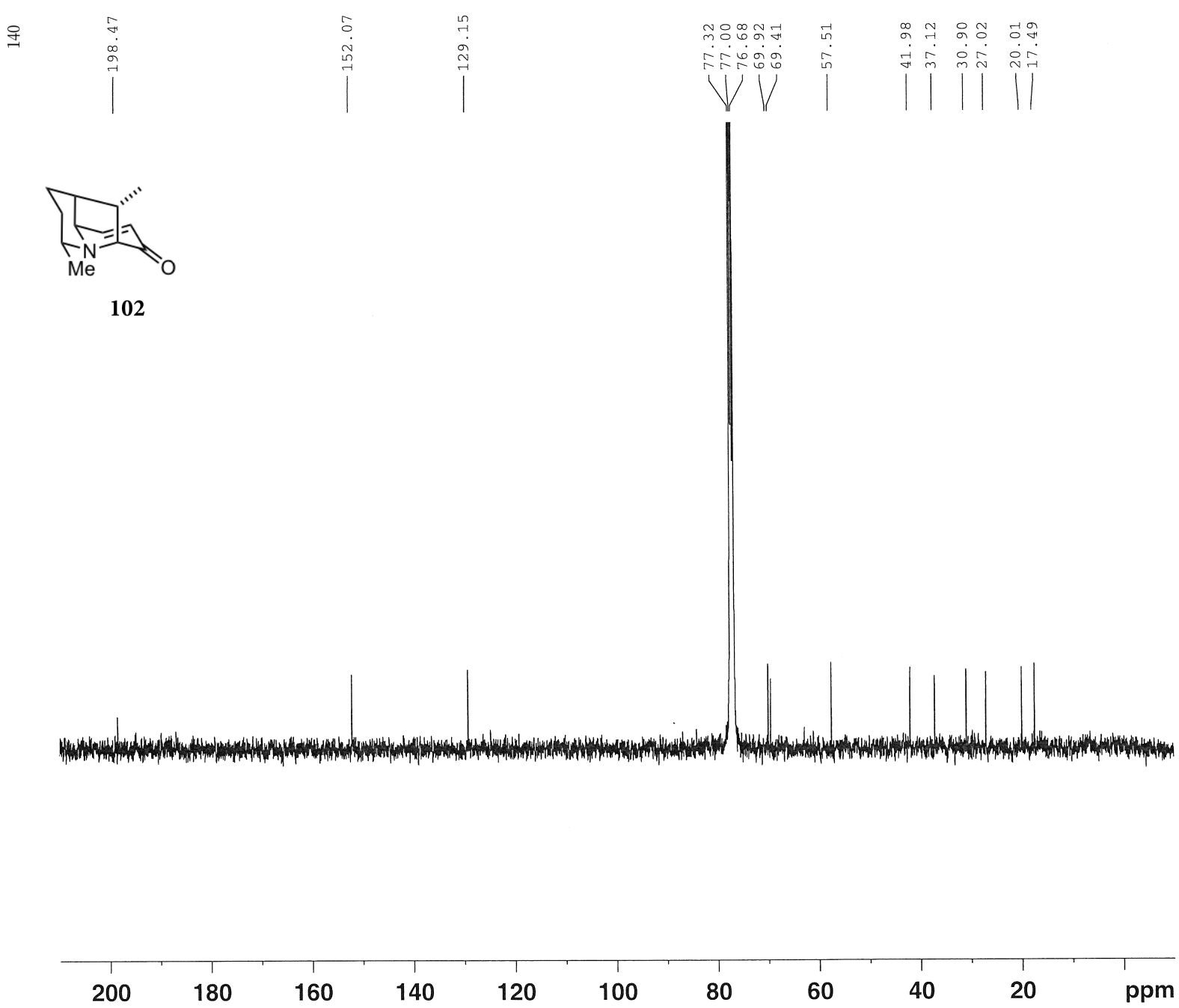
Current Data Parameters
NAME LU5193_E_OX
EXPNO 3
PROCNO 1

F2 - Acquisition Parameters
Date_ 20180607
Time 2.57 h
INSTRUM spect
PROBHD Z151340_0001 (
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 83
DS 4
SWH 42613.637 Hz
FIDRES 1.300465 Hz
AQ 0.7689557 sec
RG 203
DW 11.733 usec
DE 18.00 usec
TE 303.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
SFO1 176.0362620 MHz
NUC1 13C
P1 11.00 usec
PLW1 29.00000000 W
SFO2 700.0098000 MHz
NUC2 1H
CPDPRG[2 waltz16
PCPD2 65.00 usec
PLW2 13.00000000 W
PLW12 0.37231001 W
PLW13 0.18747000 W

F2 - Processing parameters
SI 131072
SF 176.0169002 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40




```
NAME                  LU51761_Pure_E_0
EXPNO                          1
PROCNO                         1
Date_                   20180624
Time                       2.20
INSTRUM                    spect
PROBHD     5 mm PABBO BB-
PULPROG                    zg30
TD                        65536
SOLVENT                   CDC13
NS                           13
DS                            2
SWH                    8278.146 Hz
FIDRES                 0.126314 Hz
AQ                     3.9584243 se
RG                          362
DW                     60.400 us
DE                      6.50 us
TE                     303.2 K
D1                     1.00000000 se
                               1
TD0

======== CHANNEL f1 ========
NUC1                       1H
P1                     14.00 us
PL1                     0.00 dB
PL1W                10.27361584 W
SFO1               400.1424710 MH
SI                        32768
SF                 400.1400068 MH
WDW                        EM
SSB                         0
LB                     0.30 Hz
GB                          0
PC                     1.00
```

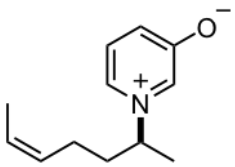


102

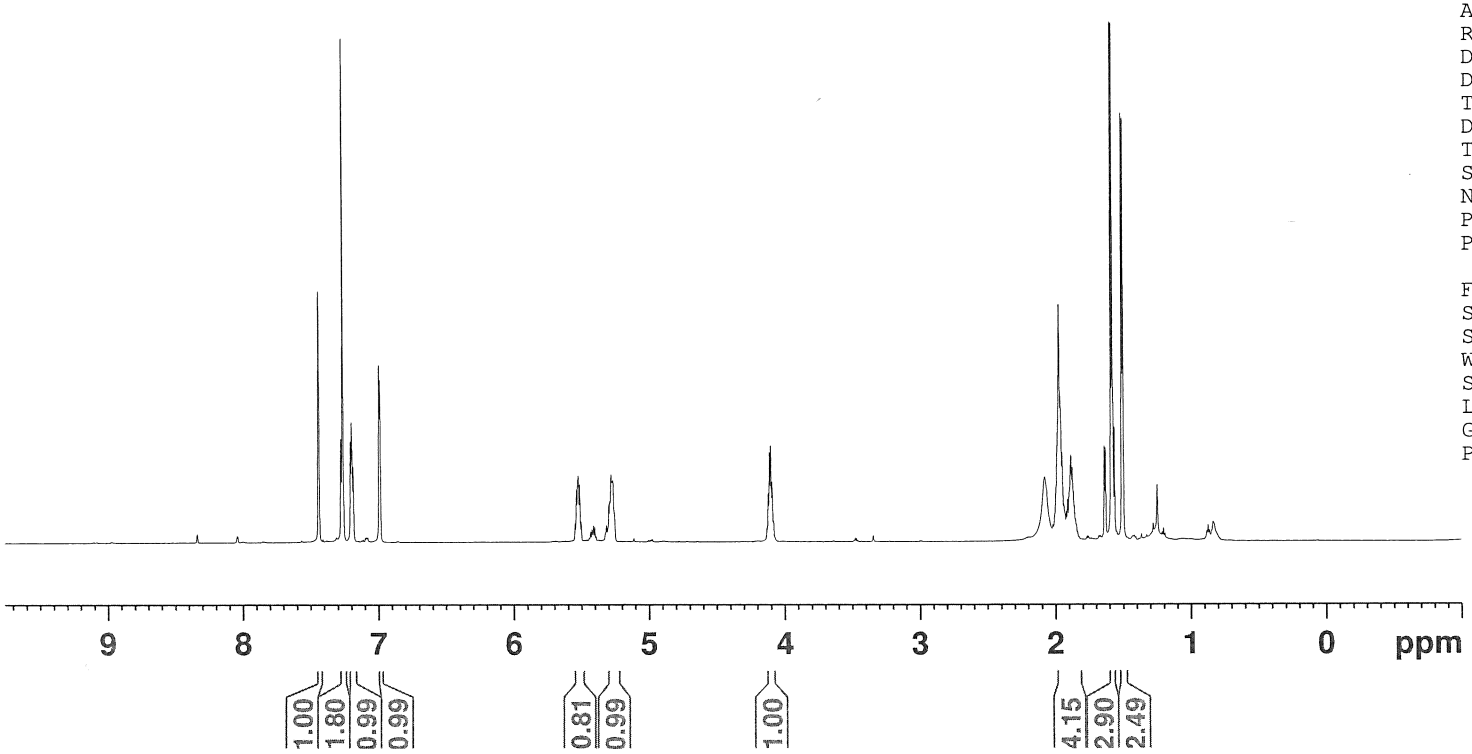
NAME	LU51761_Pure_E_0
EXPNO	3
PROCNO	1
Date_	20180624
Time	9.14
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	6000
DS	4
SWH	24154.590 Hz
FIDRES	0.368570 Hz
AQ	1.3566452 sec
RG	14596.5
DW	20.700 use
DE	6.50 use
TE	303.2 K
D1	2.70000005 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 =======	
NUC1	13C
P1	9.00 use
PL1	-2.00 dB
PL1W	46.89702606 W
SFO1	100.6263507 MHz
======== CHANNEL f2 =======	
CPDPRG2	waltz16
NUC2	1H
PCPD2	90.00 use
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	400.1416006 MHz
SI	131072
SF	100.6152830 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40

141

7.438
7.274
7.261
7.204
7.196
7.184
6.993
6.985
5.544
5.534
5.519
5.510
5.500
5.294
5.277
5.263
4.118
4.108
4.099
4.090
1.969
1.960
1.948
1.907
1.883
1.873
1.587
1.577
1.507
1.497



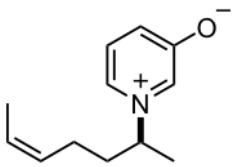
103



BRUKER

```
Current Data Parameters
NAME      LU5179_oure_Z_ox
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_           20180503
Time               18.19 h
INSTRUM             spect
PROBHD   Z151340_0001 (
PULPROG              zg30
TD                  65536
SOLVENT             CDCl3
NS                     13
DS                      2
SWH            10504.202 Hz
FIDRES          0.320563 Hz
AQ             3.1195135 sec
RG                     18
DW                47.600 usec
DE                20.00 usec
TE                303.2 K
D1            1.00000000 sec
TD0                     1
SFO1         700.0115500 MHz
NUC1                   1H
P1                 11.00 usec
PLW1         13.00000000 W

F2 - Processing parameters
SI                 131072
SF          700.0070169 MHz
WDW                    EM
SSB       0
LB                  0.30 Hz
GB        0
PC                  1.00
```

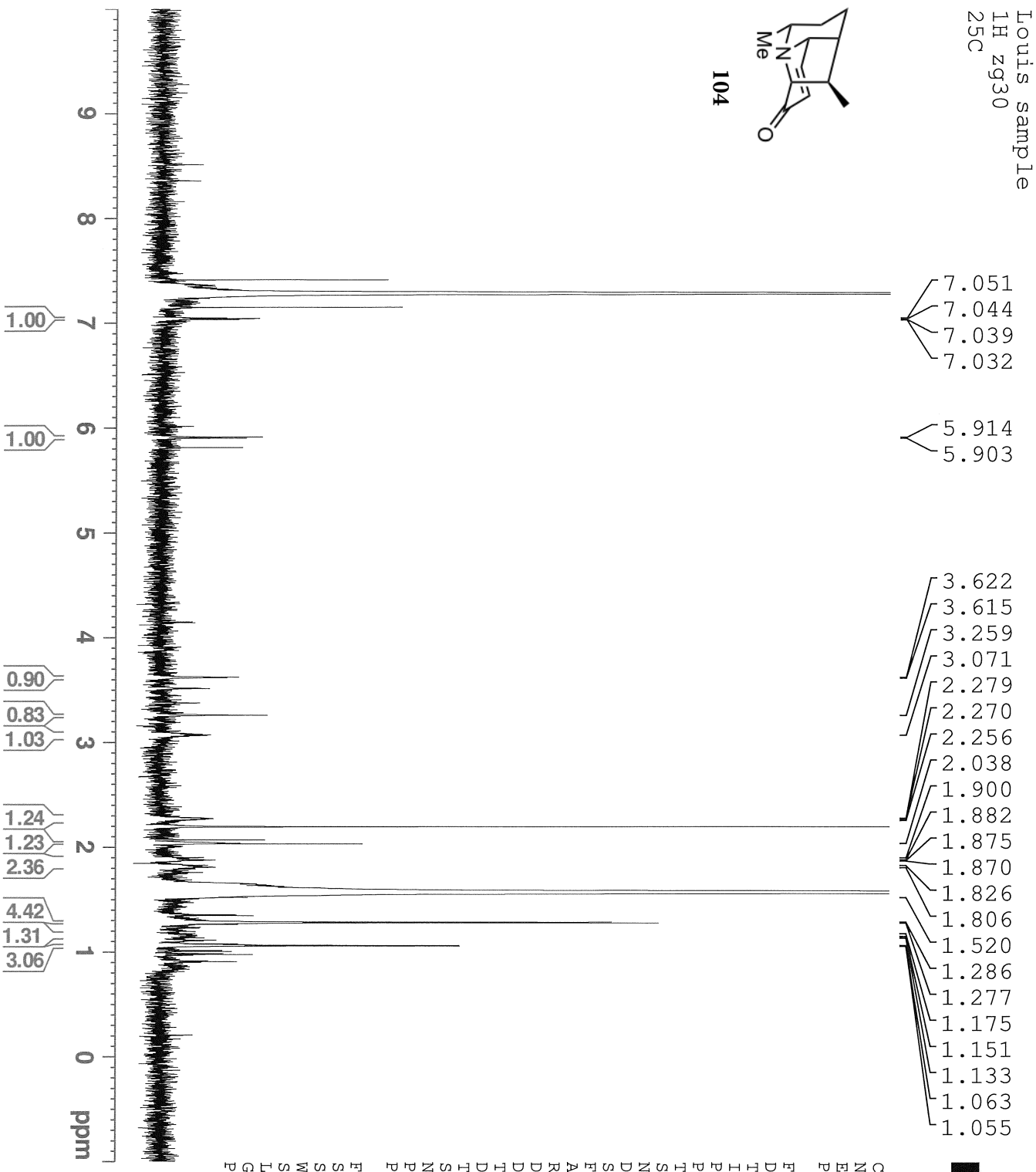
142



103

BRUKER

```
Current Data Parameters
NAME      LU5179_oure_Z_ox
EXPNO                    3
PROCNO                   1

F2 - Acquisition Parameters
Date_           20180503
Time              18.22 h
INSTRUM             spect
PROBHD   Z151340_0001 (
PULPROG           zgpg30
TD                65536
SOLVENT           CDCl3
NS                   40
DS                    4
SWH           42613.637 Hz
FIDRES         1.300465 Hz
AQ             0.7689557 sec
RG                  203
DW                11.733 usec
DE                18.00 usec
TE                303.2 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1
SFO1        176.0362620 MHz
NUC1                13C
P1                11.00 usec
PLW1        29.00000000 W
SFO2        700.0098000 MHz
NUC2                1H
CPDPRG[2         waltz16
PCPD2             65.00 usec
PLW2        13.00000000 W
PLW12        0.37231001 W
PLW13        0.18747000 W

F2 - Processing parameters
SI                131072
SF          176.0169002 MHz
WDW                 EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
```


Louis sample
1H zg30
25C
104
Me
N
O
7.051
7.044
7.039
7.032
5.914
5.903
3.622
3.615
3.259
3.071
2.279
2.270
2.256
2.038
1.900
1.882
1.875
1.870
1.826
1.806
1.520
1.286
1.277
1.175
1.151
1.133
1.063
1.055
1.00
1.00
0.90
0.83
1.03
1.24
1.23
2.36
4.42
1.31
3.06
9
8
7
6
5
4
3
2
1
0
ppm
BRUKER
Current Data Parameters
NAME louis_07022018
EXPNO 1
PROCNO 1
F2 - Acquisition Parameter
Date_ 20180702
Time 17.34 h
INSTRUM spect
PROBHD z161768_0001 (
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 12820.513 Hz
FIDRES 0.782502 Hz
AQ 1.2779520 sec
RG 6.3
DW 39.000 usec
DE 10.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
SFO1 800.2137610 MHz
NUC1 1H
P1 7.19 usec
PLW1 9.66800022 W
F2 - Processing parameters
SI 32768
SF 800.2100000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

The Crystal data of compound 87

```
    cu_osu41_0m.res created by SHELXL-2014/7

TITL cu_osu41_0m in P2(1)/c
CELL 1.54178 6.4248 10.6067 20.8894 90.000 94.550 90.000
ZERR 4.00 0.0002 0.0003 0.0006 0.000 0.002 0.000
LATT 1
SYMM -x, y+1/2, -z+1/2
SFAC C  H  N  O  Cl
UNIT 56  72  4  12  4
L.S. 10
ACTA
BOND $H
FMAP 2
PLAN 20
EQIV $1 -x+1, y+1/2, -z+1/2
HTAB C7 O1_$1
EQIV $2 -x, y-1/2, -z+1/2
HTAB C10 O2_$2
CONF
HTAB
SIZE 0.020 0.040 0.040
TEMP -100.000
WGHT    0.064800    0.430300
FVAR       0.16073
CL1   5    0.232430    0.254902    0.442254    11.00000    0.04015    0.03346 =
         0.02804   -0.00749    0.00095   -0.00095
O1    4    0.546234    0.002240    0.237209    11.00000    0.02652    0.03695 =
         0.04593   -0.00731    0.01357    0.00183
O2    4   -0.067373    0.205627    0.206522    11.00000    0.03832    0.03492 =
         0.03022    0.00618    0.00129    0.00959
O3    4    0.081347    0.024128    0.178154    11.00000    0.04783    0.03549 =
         0.02265    0.00212    0.00212    0.00913
N1    3    0.317354    0.046685    0.373198    11.00000    0.01937    0.02449 =
         0.02359    0.00043   -0.00010   -0.00030
C1    1    0.213380    0.170698    0.366949    11.00000    0.02305    0.02531 =
         0.02347   -0.00319    0.00146    0.00099
C2    1   -0.012580    0.137285    0.341770    11.00000    0.02097    0.02978 =
         0.02408    0.00048    0.00214    0.00374
C3    1   -0.119706    0.066302    0.394109    11.00000    0.01859    0.04282 =
         0.02607    0.00034    0.00297   -0.00196
C4    1   -0.001422   -0.055019    0.413250    11.00000    0.02883    0.03562 =
         0.02399    0.00392    0.00383   -0.00757
C5    1    0.234555   -0.033892    0.423911    11.00000    0.02753    0.03028 =
         0.02253    0.00291   -0.00048   -0.00326
C6    1    0.355491   -0.156846    0.429415    11.00000    0.03387    0.03467 =
         0.03427    0.00968   -0.00336    0.00116
C7    1    0.323289    0.251050    0.320566    11.00000    0.02398    0.02298 =
         0.03265    0.00013    0.00074   -0.00288
C8    1    0.431592    0.199221    0.275925    11.00000    0.02198    0.02826 =
         0.03543    0.00384    0.00534   -0.00334
C9    1    0.428854    0.060629    0.268977    11.00000    0.01850    0.02951 =
         0.02760    0.00014    0.00154    0.00062
C10   1    0.263787   -0.001021    0.306948    11.00000    0.01923    0.02076 =
```

```
          0.02588   -0.00003    0.00051    0.00018
C11   1    0.034603    0.047197    0.286814    11.00000    0.01873    0.02524 =
          0.02467    0.00106    0.00148   -0.00090
C12   1    0.007619    0.104469    0.220476    11.00000    0.01890    0.03097 =
          0.02582    0.00051   -0.00037    0.00018
C13   1    0.082967    0.066437    0.111999    11.00000    0.07931    0.05157 =
          0.02343    0.00686    0.00703    0.02118
C14   1    0.237895   -0.011623    0.080175    11.00000    0.07601    0.06209 =
          0.03644    0.00220    0.01778    0.00900
H2    2   -0.094570    0.212244    0.325395    11.00000    0.02576
H3A   2   -0.129425    0.123293    0.430674    11.00000    0.03178
H3B   2   -0.252887    0.048688    0.380051    11.00000    0.02370
H4A   2   -0.051138   -0.090565    0.452975    11.00000    0.03571
H4B   2   -0.032322   -0.114700    0.381345    11.00000    0.02882
H5    2    0.265526    0.010512    0.464810    11.00000    0.02253
H6A   2    0.318085   -0.200312    0.466930    11.00000    0.04077
H6B   2    0.332212   -0.210518    0.391125    11.00000    0.03220
H6C   2    0.501533   -0.141965    0.434038    11.00000    0.05303
H7    2    0.308647    0.340351    0.325211    11.00000    0.02943
H8    2    0.507163    0.248688    0.247729    11.00000    0.03704
H10   2    0.271308   -0.087640    0.304171    11.00000    0.01921
H11   2   -0.058661   -0.024372    0.285725    11.00000    0.02442
H13A  2   -0.054998    0.061897    0.093935    11.00000    0.06948
H13B  2    0.129278    0.149036    0.110572    11.00000    0.06971
H14A  2    0.207135   -0.105608    0.083051    11.00000    0.08440
H14B  2    0.244959    0.021120    0.034066    11.00000    0.08284
H14C  2    0.371780    0.012693    0.101737    11.00000    0.07268
HKLF 4 1 1 0 0 0 1 0 0 0 1

REM  cu_osu41_0m in P2(1)/c
REM R1 =  0.0371 for    2222 Fo > 4sig(Fo)  and  0.0422 for all    2498 data
REM    244 parameters refined using      0 restraints

END

WGHT      0.0632      0.4528

REM Instructions for potential hydrogen bonds
HTAB C7 O1_$1
HTAB C10 O2_$2

REM Highest difference peak  0.288,  deepest hole -0.200,  1-sigma level  0.047
Q1    1   0.1482  0.0245  0.2949  11.00000  0.05    0.29
Q2    1   0.0108  0.0903  0.3131  11.00000  0.05    0.27
Q3    1   0.2776  0.0034  0.3978  11.00000  0.05    0.26
Q4    1   0.2835  0.2129  0.3456  11.00000  0.05    0.25
Q5    1   0.1188 -0.0399  0.4226  11.00000  0.05    0.24
Q6    1   0.2726  0.1125  0.3742  11.00000  0.05    0.24
Q7    1   0.3359  0.0319  0.2890  11.00000  0.05    0.23
Q8    1   0.0936  0.1676  0.3603  11.00000  0.05    0.23
Q9    1  -0.0652  0.1013  0.3657  11.00000  0.05    0.22
Q10   1   0.3133  0.2192  0.2815  11.00000  0.05    0.21
Q11   1   0.4355  0.0504  0.3777  11.00000  0.05    0.20
Q12   1   0.4379  0.1299  0.2780  11.00000  0.05    0.20
Q13   1   0.0181  0.0778  0.2577  11.00000  0.05    0.19
```

Q14	1	0.2914	0.0232	0.3449	11.00000	0.05	0.19
Q15	1	-0.0662	0.0024	0.3976	11.00000	0.05	0.17
Q16	1	0.2113	0.2081	0.4002	11.00000	0.05	0.16
Q17	1	0.2714	0.0818	0.1012	11.00000	0.05	0.16
Q18	1	0.0075	0.1316	0.1024	11.00000	0.05	0.15
Q19	1	0.2772	-0.0985	0.4211	11.00000	0.05	0.15
Q20	1	0.2973	0.1401	0.1130	11.00000	0.05	0.15