AN ABSTRACT OF THE DISSERTATION OF

David A. Schiedler for the degree of Doctor of Philosophy in Chemistry presented on December 2, 2014.

Title: The Development of Aminal Radicals for the Synthesis of Nitrogen-Rich Natural Products.

Abstract approved:

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Christopher M. Beaudry

Abstract

Organic compounds which contain one or more nitrogen atoms are especially important as they are disproportionately represented among biologically active molecules. As a result, significant effort has been focused on the development of methods for the synthesis of nitrogenous molecules. We identified the aminal as an under-explored functional group. Despite the presence of the aminal functional group in several biologically active natural products which have attracted the attention of the synthetic community, no bond forming reactions of the aminal functional group had been described in the literature.

This dissertation describes the development of two new carbon-carbon bond forming reactions utilizing aminal radical intermediates (carbon-centered radicals wherein the radical bearing carbon atom has two nitrogen substituents). Additionally, this document describes progress towards the application of aminal radicals in the context of the total synthesis of the alkaloid leuconoxine.

The preliminary investigations centered on the generation of aminal radicals under peroxide initiated conditions similar to those previously reported for the generation of α-aminoalkyl radicals. The treatment of aminal containing molecules with di-*tert*-butyl peroxide in the presence of a radical acceptor (e.g. 1-octene) produced either a complex mixture of products, or no reaction.

Aminal radicals were successfully formed from 2-iodobenzyl substituted *N*-acyl aminals by radical translocation reactions using AIBN and either Bu_3SnH or $(TMS)_3SiH$ as a stoichiometric hydrogen atom donor. It was found that aminal radicals participate in inter- and intramolecular C–C bond forming reactions with electron deficient alkenes. Reactions in the presence of electron rich or unactivated alkenes did not lead to the desired bond formation, instead giving products of dehalogenation. The reaction of *N*-acyl aminals which contained carbon atoms bearing only one nitrogen atom were shown to selectively give the product of bond formation at the aminal carbon. Chemical yields of the radical translocation reactions were as high as 91%.

It was demonstrated that the SmI_2 reduction of *N*-acyl amidines or amidinium ions in the presence of a proton source and an electron deficient alkene yielded products of C–C bond formation. Chemical yields of these transformations were as high as 99% and can lead to diastereoselectivities in excess of 20:1. Mechanistic investigations of this reactivity indicated that the reactions likely proceed through an aminal radical intermediate.

The application of aminal radicals to the total synthesis of the alkaloid natural product leuconoxine has been investigated. It was envisioned that the SmI_2 induced reductive alkylation reaction of a simple bicyclic *N*-acyl amidine would rapidly construct the fully substituted aminal stereocenter present in the natural product. While similar amidines have been reported in the literature, no general strategy to access amidines

of this type was known. Three distinct synthetic strategies towards the preparation of the desired bicyclic *N*-acyl amidine substrate were developed and investigated.

The first strategy relied on the formation of the amidine using the intramolecular aza-Wittig reaction of an imide and an azide. Unexpectedly, these reactions produced a bis-amide product. Attempts to induce an intramolecular condensation reaction of the bis-amide to give the desired amidine were unsuccessful. The second strategy disconnected the desired bicyclic *N*-acyl amidine through an intramolecular *N*-acylaiton reaction of an *N*-aryl amidine. It was envisioned that the amidine could be prepared from a bimolecular condensation reaction of an aniline and a lactam derivative. All attempts to form the desired amidine functionality were unsuccessful. The third strategy depended upon an *N*-arylation reaction for the conversion of a known bicyclic *N*-acyl amidine to the desired substrate for the synthesis of leuconoxine. While the desired substrate has remained elusive, a model system of the key *N*-arylation reaction has successfully given the desired *N*-aryl-*N*-acyl bicyclic amidine product.

The Development of Aminal Radicals for the Synthesis of Nitrogen-Rich Natural Products.

by
David A. Schiedler

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APPROVED:

Major Professor, representing Chemistry

Chair of the Department of Chemistry

Dean of the Graduate School

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David A. Schiedler, Author

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CONTRUBUTION OF AUTHORS

Jessica Vellucci assisted with data collection for chapter 2 and with the writing of chapters 1 and 2. Yi Lu assisted with the data collection for chapter 3 and the writing of chapters 1 and 3.

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The Development of Aminal Radicals for the Synthesis of Nitrogen-Rich Natural Products

Chapter 1: Introduction, Background, and Preliminary Investigations

1.1 Nitrogen Rich Natural Product Synthesis

Many biologically active molecules, including pharmaceuticals, contain one or more nitrogen atoms. As a result, nitrogen rich compounds, such as alkaloids and pharmaceuticals, make compelling synthetic targets (Figure 1.1, **1**-**7**).[1] However, the complex reactivity of nitrogen can be problematic in synthesis. The ability to quaternize, the Lewis basic lone pair, and the weakly acidic N–H protons found in nitrogen-containing molecules often give rise to undesired reactivity.

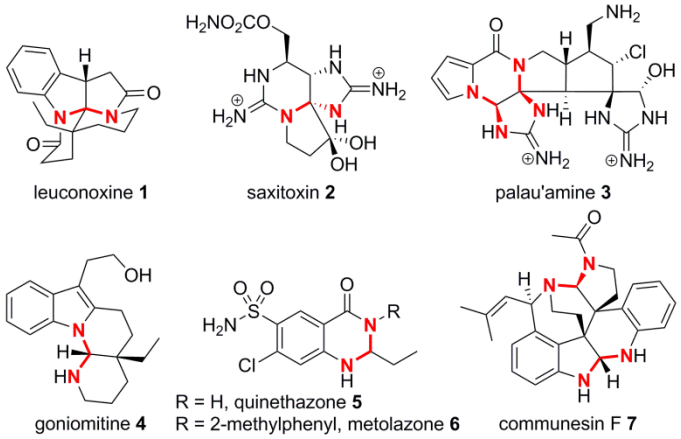
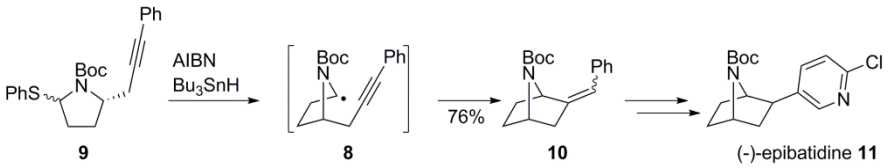


Figure 1.1. Nitrogen-rich natural products and pharmaceuticals which contain aminals

In order to mask the complex Lewis acid-base reactivity of nitrogen, synthetic chemists often resort to the use of protective groups.[2] Other strategies which have proven successful for the synthesis of nitrogen-containing structures include opting to install nitrogen late in the synthesis[3] or in the form of a less reactive functional group (e.g., as a nitro[4] or nitrile[5] group).

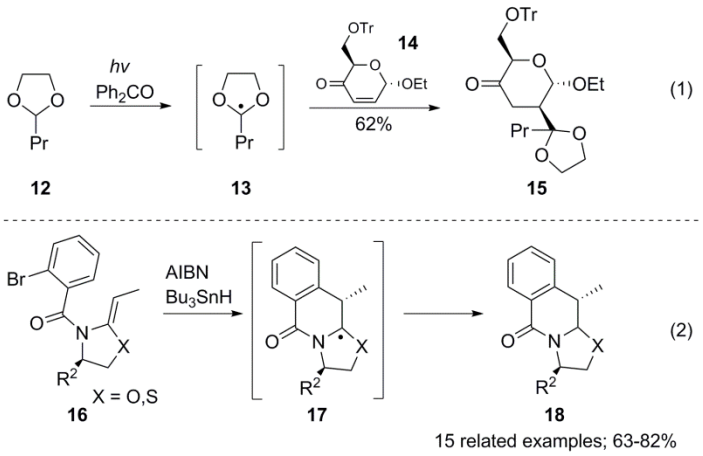
1.2 Radicals in the Synthesis of Heteroatom Containing Molecules

An alternative means to circumvent the pitfalls of alkaloid synthesis is the use of single electron reactivity (i.e., free radical reactions). Free radicals are known to tolerate heteroatom lone pairs, and N–H bonds are resistive to homolytic cleavage.[6] The addition of carbon-centered radicals bearing heteroatoms to C–C multiple bonds has been known for over fifty years.[7] For example, Clive and coworkers generated the α-amido radical intermediate **8** from the *N,S*-acetal **9** to construct the bicycle **10** in their formal synthesis of (–)-epipatidine **11** (Scheme 1.1).[8] α-Aminoalkyl and α-amido radicals, such as **8**, gain stability from the electron lone pair on the adjacent nitrogen atom and react with unsaturated carbon atoms to give products of C–C bond formation.[9] This reactivity has proven useful for the synthesis of heterocycles and alkaloid natural products as it allows for the strategic disconnection of bonds which would be difficult to form using standard cationic or anionic reaction conditions.[10]



Scheme 1.1. Clive's formal synthesis of (–)-epibatidine

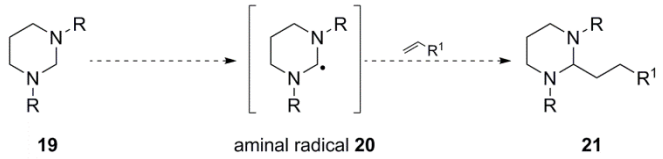
Carbon-centered radicals bearing two adjacent heteroatoms are also known to undergo C–C bond forming reactions with C–C multiple bonds. Homolytic C–H bond cleavage of acetal **12** was induced by photosensitized benzophenone to give the aceal radical **13**. Radical **13** then added across the enone **14** to give the observed product **15** after propagation (Scheme 1.2, eq. 1). Reactions of 2-bromobenzoyl enamides **16** with AIBN and Bu_3SnH were presumed to proceed through *N,S*- and *N,O*- acetal radical intermediates (**17**) during C–C bond forming reactions to give the ring-fused products **18** (Scheme 1.2, eq. 2).[11]



Scheme 1.2. C–C bond forming reactions of acetal radicals

Carbon-centered radicals bearing two adjacent nitrogen atoms (i.e. aminal radicals) have been implicated as intermediates in the free radical and radiative damage of DNA nucleotide bases,[12] they have been experimentally generated and studied spectroscopically,[13] and long-lived aminal radicals have been isolated.[14] Applications of aminal radicals include their use as photochromic dyes[15] and as tools for mechanistic investigations.[16] Although there are reports of fragmentation,[17] protonation,[18] and dimerization reactions of aminal radicals, there had been no reports of their synthetic utility prior to recent work from our laboratory.[19]

1.3 Aminal Radicals as Synthetic Intermediates



Scheme 1.3. Proposed reaction of an aminal radical with an alkene

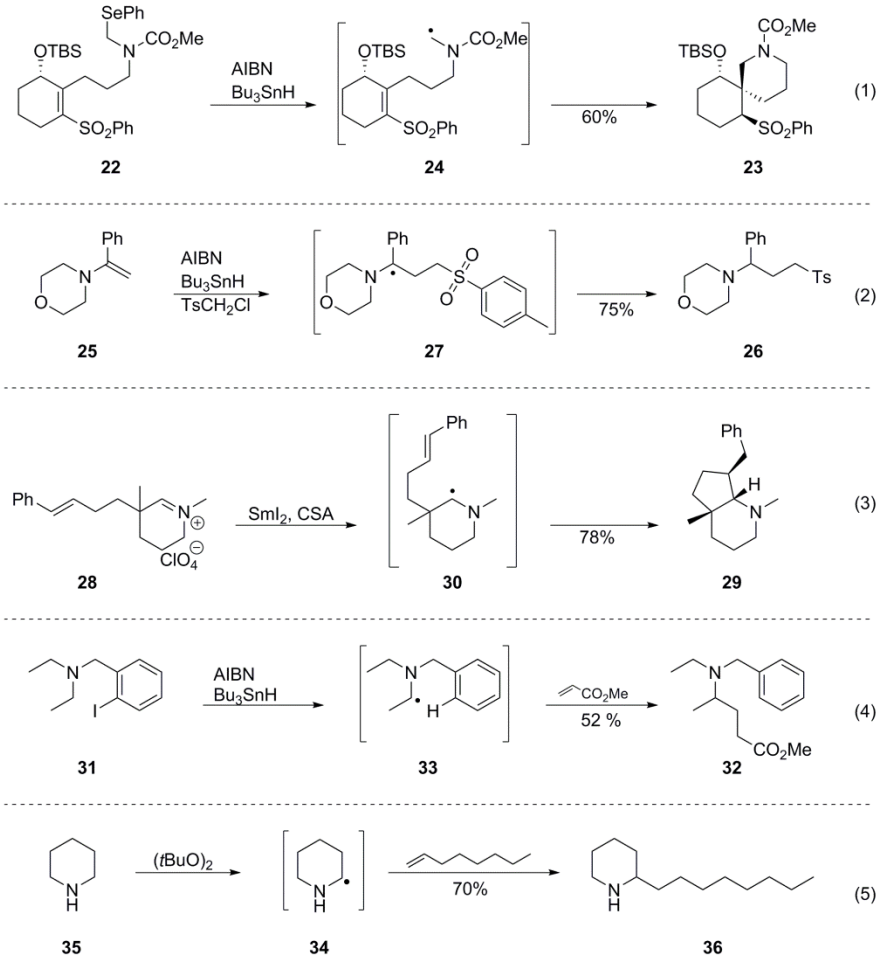
Having considered the known reactivity of acetal and α-aminoalkyl radicals, the creation of a new reaction was envisioned wherein a nitrogen-rich starting material

(**19**) would be converted into an aminal radical intermediate (**20**) and would undergo addition to an alkene to give the product of C–C bond formation (**21**, Scheme 1.3). Computational studies predicted that aminal radicals are 1-2 kcal/mol more stable than analogous α-aminoalkyl radicals.[20] This suggested that it would be possible to selectively generate aminal radicals in the presence of carbon atoms bearing a single nitrogen atom as depicted in Scheme 1.3. Based on these considerations, we postulated that aminal radical intermediates would be well suited for the construction of the carbon framework in nitrogen-rich molecules.

It was predicted that aminal radical intermediates would react in a manner similar to α-aminoalkyl and α-amido radicals. Following from this prediction, it was reasoned that aminal radicals might be accessible by an extension of a method previously reported for the generation of α-amino radicals. Scheme 1.4 gives a summary of the known methods for the generation of α-amino radicals. One of the most common ways in which α-amino radicals have been generated is by the homolytic cleavage of a C–X bond on the carbon which bears nitrogen (X = SR, SeR, Cl, Br, $SiMe_3$, or C(O)R). For example, Zhang reported the conversion of the selenide **22** to the spirocyclic compound **23** which presumably results from the 6-*exo*-trig radical cyclization of the aminal radical **24** (eq. 1).[21] While this strategy allows for completely regioselective radical generation, it was deemed unattractive for the extension to the generation of aminal radicals as it required the synthesis of pre-functionalized aminal substrates.

Another means to generate α-amino radicals involves the addition of a carbon-centered radical to an enamine. Renaud reported the conversion of enamine **25** to the alkylated product **26** by addition of an alkyl radical to give the α-amino radical intermediate **27** followed by hydrogen atom abstraction from Bu_3SnH (eq. 2).[22] The single electron reduction of iminium ions in the presence of a proton source has been reported for the generation of α-amino radicals. Martin reported the conversion of the

iminium ion **28** to the fused bicyclic compound **29** by way of the α-amino radical **30** (eq. 3).[23] This method was attractive for extension to the generation of aminal radicals as it had the potential to generate an aminal radical in a regioselective manner without the poor atom economy exhibited by the C–X bond homolysis strategy.



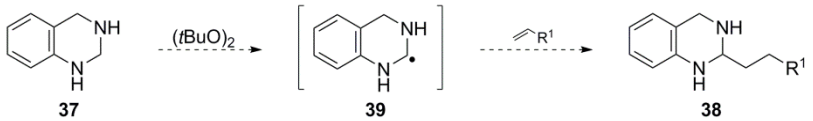
Scheme 1.4. Methods for the generation of α-amino radicals

α-Amino radicals have also been obtained from the homolysis of a C–H bond on the carbon bearing nitrogen. One such method, termed protective radical translocation,[24] involves the use of a halogen-substituted protecting group. Undheim reported the conversion of 2-iodobenzyl protected amine **31** to the alkylated amine product **32** (eq. 4).[25] The reaction proceeded through a phenyl radical which then underwent a 1,5-

hydrogen atom abstraction to produce the aminal radical intermediate **33**. In 1958, Juveland reported the generation of α-aminoalkyl radical intermediate **34** under peroxide initiated conditions (eq. 5).[26] Treatment of piperidine (**35**) with di-*tert*-butylperoxide in the presence of 1-octene yielded 2-octyl piperidine (**36**). Similar transformations using Et_3B / O_2[27] or a transition-metal catalyzed photo-redox process[28] to generate the radical species have also been reported. Reactions of this type were particularly attractive for extension to the generation of aminal radicals because they would not require any pre-functionalization of the aminal substrates.

1.4 Preliminary Investigations Using Peroxide Initiated Conditions

Extension of Juveland's peroxide initiated method for the generation of α-amino radicals to the generation of aminal radicals was chosen for the preliminary investigations. This extension could involve the treatment of an aminal with di-*tert*-butylperoxide in the presence of a suitable radical acceptor (Scheme 1.5). Tetrahydroisoquinazoline (**37**) was chosen because it was easy to prepare, it was chromatographically stable, and it contained a chromophore which allowed for facile monitoring of reaction progress.

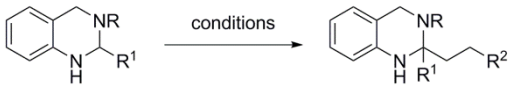


37 39 38

Scheme 1.5. The attempted extension of Juveland's method

Following Juveland's procedure, **37** was heated in the presence of di-*tert*-butylperoxide and 1-octene in a sealed tube (Table 1, entry 1). The reaction produced an intractable mixture of products and none of the desired product **40** was observed. The ^{1}NMR spectrum of the product mixture showed additional aryl protons with no additional signals in the alkyl region of the spectrum. In an effort to affect cleaner reactivity, modified reaction conditions were investigated. Increasing the equivalents

of the radical acceptor and adding benzene as a solvent had no effect (entry 2). The benzyl protected aminal **41** was subjected to the reaction conditions with methyl acrylate as a radical acceptor, but also gave a mixture of products and none of the desired compound **42** was observed (entry 3). The ^{1}H NMR spectrum of the product mixture showed new peaks in the aryl region. Lowering the reaction temperature resulted in no reaction (entry 4). The aminal substrate **43** was prepared and subjected to the reaction conditions with carbon tetrachloride, benzene, or solventless conditions (entries 5-7). None of the desired spirocycle **44** was obtained in any case. ^{1}H NMR analysis of the product mixture revealed that a number of new compounds containing alkenyl signals had formed. This indicated that the newly formed products were not the result of the desired radical cyclization event.



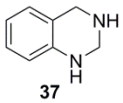
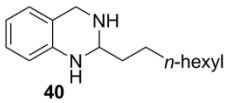
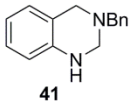
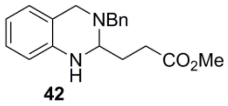
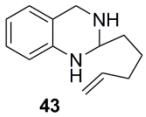
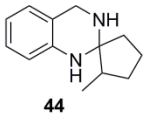
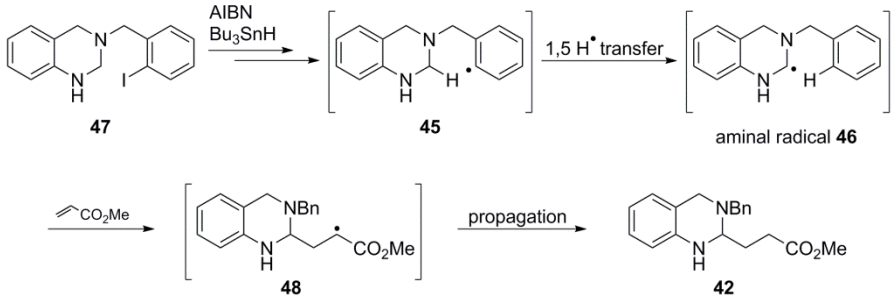
entry	aminal	desired product	conditions	result
1	 **37**	 **40**	1 equiv. 1-octene 0.22 equiv. (tBuO)$_2$ neat, 120 °C	decomp.
2	**37**	**40**	10 equiv. 1-octene 0.95 equiv. (tBuO)$_2$ 0.5M in PhH 120 °C	decomp.
3	 **41**	 **42**	3 equiv. acrylate 4 equiv. (tBuO)$_2$ 0.02M in PhH 120 °C	decomp.
4	**41**	**42**	3 equiv. acrylate 4 equiv. (tBuO)$_2$ 0.01M in PhH 80 °C	no reaction
5	 **43**	 **44**	7 equiv. (tBuO)$_2$ 0.01M in CCl_4 120 °C	decomp.
6	**43**	**44**	7 equiv. (tBuO)$_2$ 0.01M in PhH 120 °C	decomp.
7	**43**	**44**	0.63 equiv. (tBuO)$_2$ neat, 120 °C	decomp.

Table 1.1. Reactions using peroxide-initiated conditions

Based on these results, two plausible explanations were formulated. Either the desired aminal radical **39** was generated, and it was reacting in an unselective manner to give the observed decomposition, or aminal radical **39** had not been generated and the observed degradation was arising from other reaction pathways. Unable to easily distinguish between these possibilities, an alternative method for the generation of aminal radicals was sought. Ideally, this method would incorporate a functional handle that could be used to determine whether aminal radicals were being generated.

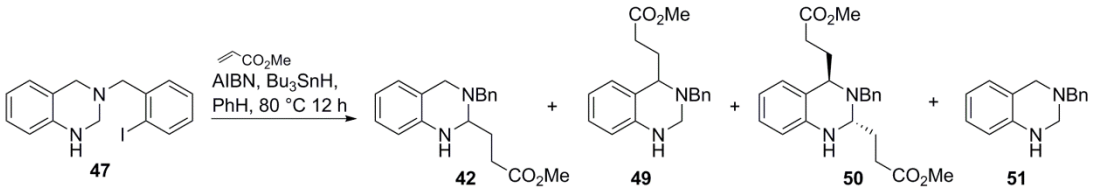
1.5 Radical Translocation Reactions of Non-Acylated Aminals

Evaluation of the known methods for the generation of α-amino radicals previously discussed led us to consider a radical translocation strategy for the generation of aminal radicals.[29] The application of radical translocation as a means to generate aminal radicals was particularly attractive because it would provide a functional handle through which problematic reactivity might be diagnosed. Specifically, the loss of iodide is diagnostic for the formation of a phenyl radical (**45**) (Scheme 1.6). Deuteration experiments could be used to determine whether the desired 1,5-H atom abstraction event had occurred to yield the desired aminal radical **46.** Additionally, the necessary 2-iodobenzyl substituted starting material **47** could be easily prepared by alkylation of **37**. The product of the reaction, proceeding through the radical intermediate **48** after addition to methyl acrylate and subsequent propagation, would be a benzyl protected aminal (**42**).



Scheme 1.6. Extension of radical translocation for the generation of aminal radicals

N-2-Iodobenzyl-tetrahydroquinazoline (**47**) was prepared from **37** and 2-iodobenzyl iodide. Treatment of the protected aminal with AIBN and Bu_3SnH in the presence of methyl acrylate yielded some of the desired aminal radical product **42** (Table 1.2, entry 1). This indicated that the desired aminal radical is synthetically competent. However, in addition to the desired product, isomeric product **49**,[30] over addition product **50**, and dehalogenated product **51** were also observed. Formation of the undesired product **49** is competitive with the formation of desired product **42** as a result of the stability of the α-aminobenzylic radical from which it presumably arises. The formation of dehalogenated **51** was not surprising given that similar reaction conditions have been used to perform radical dehalogenation.[31] Although Curran reported the oxidation of 2-iodobenzyl ethers under similar reaction conditions,[32] no amidine formation was observed.



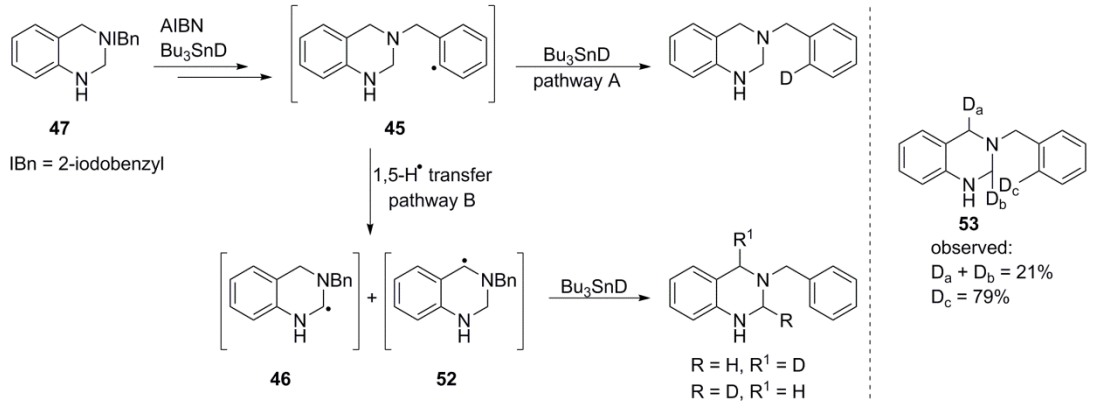
entry	Bu_3SnH	acrylate	addition time	concentration	solvent	**42** + **49** (%)	**50** (%)	**51** (%)
1	3.9 equiv.	3 equiv.	10 h	0.1 M	PhH	32	18	24
2	2.0 equiv.	3 equiv.	1 h	0.1 M	PhH	28	9	37
3	0.9 equiv.	3 equiv.	1 h	0.1 M	PhH	12	8	14
4	2.0 equiv.	1 equiv.	1 h	0.1 M	PhH	4	0	34
5	2.0 equiv.	3 equiv.	1 h	0.1 M	PhH	28	9	37
6	2.0 equiv.	5 equiv.	1 h	0.1 M	PhH	16	8	17
7	2.0 equiv.	10 equiv.	1 h	0.1 M	PhH	6	4	18
8	3.9 equiv.	3 equiv.	10 h	0.1 M	PhH	32	18	24
9	3.9 equiv.	3 equiv.	1 h	0.1 M	PhH	12	0	23
10	3.9 equiv.	3 equiv.	10 h	0.01 M	PhH	16	19	9
11	2.0 equiv.	3 equiv.	1 h	0.1 M	PhH	28	9	37
12	2.0 equiv.	3 equiv.	1 h	0.5 M	PhH	14	5	25
13	2.0 equiv.	3 equiv.	1 h	0.1 M	CyH	6	3	12
14	2.0 equiv.	3 equiv.	1 h	0.1 M	PhMe	12	6	18
15	2.0 equiv.	3 equiv.	1 h	0.1 M	CCl_4	decomposition		

Table 1.2. Attempted optimization of radical translocation

Having successfully demonstrated that aminal radical intermediates are generated and add to alkenes using the radical translocation method, efforts were turned to reaction optimization. Variation of the Bu_3SnH equivalents had little effect on the product distribution; however, the yield of **42** decreased when less than two equivalents were added (Table 1, entries 1-3). Adjustment of the acrylate equivalents showed that only trace amounts of the desired products were formed when less than two equivalents were used (entry 4). Increasing the stoichiometry of the acrylate up to five equivalents showed little effect on the product distribution or isolated yield (entries 5, 6). However, using a large excess of the acceptor resulted in a decrease in yield (entry 7). Decreasing the time of addition from 10 hours to 1 hour was found to partially suppress the formation of the over addition product **50** (entries 8, 9). Systematic variation of the reaction concentration showed that the optimal yield was obtained with a concentration of 0.1 M with respect to the aminal, but the reaction remained unselective (entries 10-12). A solvent screen showed that toluene and cyclohexane were also amenable to the desired reactivity while use of carbon tetrachloride resulted in decomposition (entries 13-15). Benzene was chosen as the optimal solvent as it was easily removed by rotary evaporation, provided superior yields, and possessed favorable solubility properties. In total, more than one hundred conditions were screened but all failed to cleanly produce **42** in high chemical yield.

Of the undesired side products formed in the reaction of **47**, the dehalogenation product **51** was always the most abundant. Presumably, **51** results from the reaction of either the phenyl radical **45** or the aminal radical **46** with Bu_3SnH before it has had sufficient opportunity to react with the acrylate. A deuteration experiment was performed in order to probe whether this undesired reduction was occurring before or after the 1,5-H atom transfer event. After homolysis of the C–I bond, the phenyl radical **45** is generated. If the 1,5-H atom transfer is slow and **45** radical reacts with Bu_3SnD[33], then a deuterium atom should be incorporated at the *ortho*-position of the benzyl group (Scheme 1.7, pathway A). However, if the 1,5-H atom transfer event occurs rapidly, then the deuterium would be incorporated on the aminal containing

ring after reaction of either the aminal radical **46** or the α-amino radical **52** with Bu_3SnD (pathway B).



Scheme 1.7. Deuterium incorporation in the dehalotenated side product

A solution of aminal **47** and methyl acrylate was heated to reflux while a solution of Bu_3SnD and AIBN in benzene was added over a period of one hour. Deuterium NMR analysis of the dehalogenated product (**53**) revealed that 79% of the deuterium was incorporated at the *ortho* position of the benzyl group while only 21% was incorporated on the tetrahydroquinazoline ring. Assuming that the 1,5-H atom transfer is irreversible, this result suggested that the aminal radical, once formed, reacted smoothly with the acrylate acceptor and proceeded to the desired product. However, the rate of D atom abstraction from Bu_3SnD was competitive with that of 1,5-H atom abstraction from the aminal.

Based on this result, it was reasoned that the use of a terminal reductant which undergoes H-atom abstraction at a slower rate than Bu_3SnH would likely decrease the amount of undesired dehalogenation observed. $(TMS)_3SiH$, a common substitute for tin hydrides in radical processes,[34] is known to undergo H-atom abstraction at a rate approximately one fifth than that of Bu_3SnH.[35] Unfortunately, substitution of $(TMS)_3SiH$ for Bu_3SnH in the reaction mixture resulted in no reaction. It was reasoned that the rate of H atom abstraction from $(TMS)_3SiH$ may have been

insufficient to sustain the radical chain. Ph_3GeH is known to undergo H-atom abstraction at a rate slower than that of Bu_3SnH and faster than that of $(TMS)_3SiH$.[36] However, use of Ph_3GeH as a terminal reductant also failed to give any product formation.

1.6 Experimental Section

General Experimental Details:

All reactions were carried out under an inert Ar atmosphere in oven-dried glassware. Flash column chromatography (FCC) 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, ninhydrin, or vanillin stains. Tetrahydrofuran (THF) was dried by passage through an activated alumina column. Benzene (PhH) was dried over CaH_2, distilled under an atmosphere of argon, and degassed by three freeze - pump - thaw cycles. Methyl acrylate was purified by washing with aqueous NaOH, drying over $MgSO_4$, and calcium hydride. It was then distilled under vacuum prior to use. Bu_3SnH and BnSH were dried over CaH_2 and distilled under vacuum prior to use. All other reagents and solvents were used without further purification from commercial sources. FT-IR spectra were measured using NaCl plates. Multiplicities are abbreviated as follows: s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, br = broad, m = multiplet. Melting points are uncorrected.

2-(pent-4-en-1-yl)-1,2,3,4-tetrahydroquinazoline (43). To a solution of hex-5-enal[37] (0.2041 g, 2.08 mmol) and NH_4Cl (0.0185 g, 0.346 mmol) in EtOAc (10 mL, 0.1 M) was added 2-aminobenzylamine (0.2109 g, 1.7262 mmol). The mixture was stirred at room temperature for 0.5 h. At this time, TLC indicated the consumption of 2-aminobenzylamine. The reaction mixture was filtered through celite and was then concentrated. A light yellow oil resulted. Flash column chromatography (3:1 Hexanes : EtOAc) gave **43** (0.2501 g, 1.236 mmol, 72%) as a colorless oil.

Data for **43**: R_f 0.16 (1:1 hexanes : EtOAc); IR (thin film) 2928, 2849, 1607 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.01 (td, *J* = 8.0, 0.4 Hz, 1 H), 6.89 (d, *J* = 7.2 Hz, 1 H), 6.68 (td, *J* = 7.2, 0.8 Hz, 1 H), 6.51 (d, *J* = 8.0 Hz, 1 H), 5.83 (dddd, *J* = 23.6, 10.0, 6.4, 6.4 Hz, 1 H), 4.97-5.07 (m, 2 H), 4.11-4.16 (m, 2 H), 3.95 (d, *J* = 16.8 Hz, 1 H), 3.88 (br s, 1 H), 2.13 (q, *J* = 6.8 Hz, 2 H), 1.54-1.66 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$,) δ 143.8, 138.4, 127.3, 126.3, 121.7, 118.1, 115.1, 66.9, 46.7, 46.7, 36.1, 33.7, 24.3; HRMS (EI+) calcd for $C_{13}H_{18}N_2$ [M+]: 202.14700, found 202.14632.

3-(2-iodobenzyl)-1,2,3,4-tetrahydroquinazoline (47). To a solution of 2-iodobenzyliodide[38] (0.2301 g, 0.690 mmol) and K_2CO_3 (0.1819 g, 1.32 mmol) in a mixture of water (0.5 mL, 1.4 M) and THF (2 mL, 0.35 M) was added 1,2,3,4-tetrahydroquinazoline[39] (0.1800 g, 1.34 mmol). The mixture was stirred at room temperature for 12 h. At this time, TLC indicated the consumption of 2-iodobenzyliodide. The reaction mixture was concentrated. Flash column chromatography (9:1 Hexanes : EtOAc) gave **47** (0.2202 g, 0.629 mmol, 91%) as a yellow oil.

Data for **47**: R_f 0.36 (4:1 hexanes : EtOAc); IR (thin film) 2928, 2847, 1606 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (dd, *J* = 7.6, 0.8 Hz, 1 H), 7.47 (dd, *J* = 7.6, 1.6 Hz, 1 H), 7.34 (td, *J* = 7.2, 0.8 Hz, 1 H), 7.06 (td, *J* = 7.6, 1.2 Hz, 1 H), 6.98 (td, *J* = 7.6, 1.6 Hz, 1 H), 6.73 (td, *J* = 7.2, 1.2 Hz, 1 H), 6.61 (d, *J* = 8.0 Hz, 1 H), 4.13 (s, 2 H), 3.94 (s, 2 H), 3.79 (s, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$,) δ 142.8, 141.0, 139.6, 130.4, 128.9, 128.2, 127.7, 127.3, 120.1, 118.4, 115.3, 100.7, 63.0, 61.0, 53.2; HRMS (TOF MS ES+) calcd for $C_{15}H_{16}N_2I$ [M+H]: 351.0358, found 351.0347.

methyl 3-(3-benzyl-1,2,3,4-tetrahydroquinazolin-2-yl)propanoate (42), methyl 3-(3-benzyl-1,2,3,4-tetrahydroquinazolin-4-yl)propanoate (49), dimethyl 3,3'-(3-benzyl-1,2,3,4-tetrahydroquinazoline-2,4-diyl)dipropionate (50), and 3-benzyl-

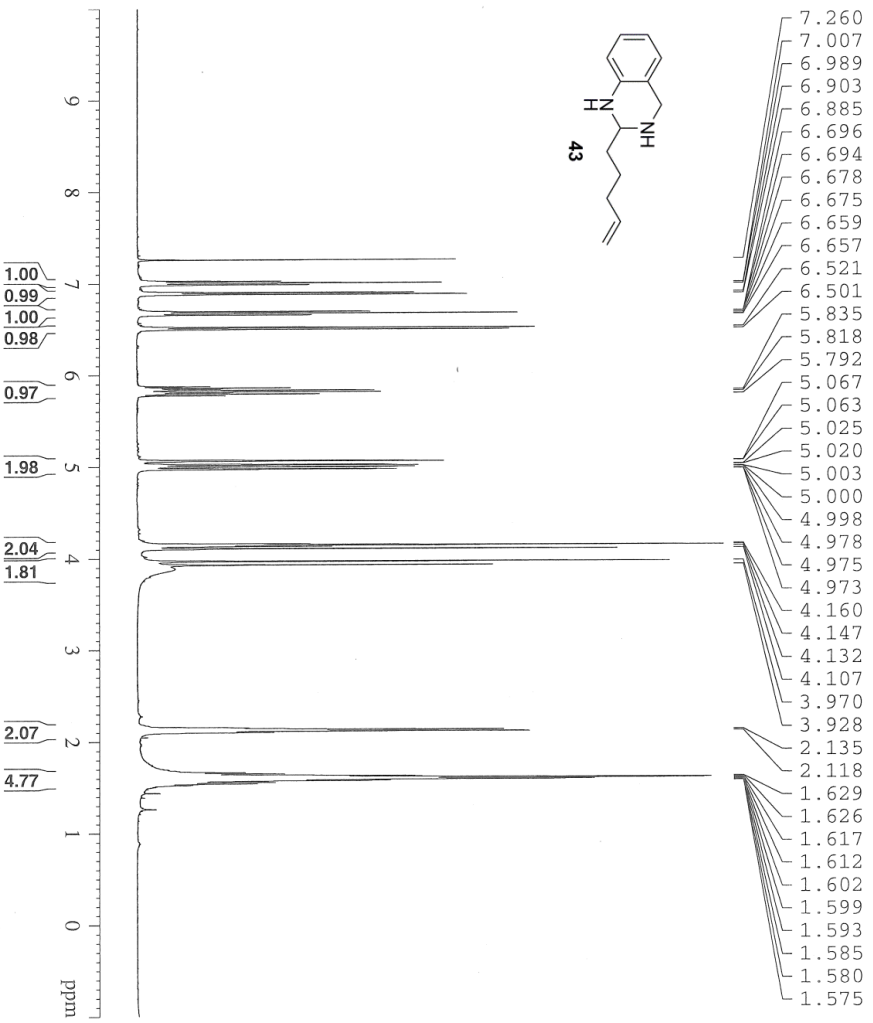
1,2,3,4-tetrahydroquinazoline (51). (*Representative procedure for the radical translocation reactions of* **47***).* **47** (0.2030 g, 0.580 mmol) and methyl acrylate (0.16 mL, 1.8 mmol) were dissolved in PhH (4.6 mL, 0.13 M) and the mixture was heated to reflux. A PhH solution (1.2 mL) containing AIBN (0.0198 g, 0.121 mmol) and Bu_3SnH (0.31 mL, 1.2 mmol) was added by syringe pump to the refluxing solution over a period of 1.2 h. After 15 h, the mixture was cooled to rt, concentrated, and re-dissolved in MeCN. The MeCN solution was washed with hexanes, concentrated, and purified by flash column chromatography (8:1 Hexanes : EtOAc) to give a 1:1 mixture of **42** and **49** (0.0542 g, 0.1748 mmol, 30%) as a colorless oil, **50** (0.0155 g, 0.0391 mmol, 6.7%) as a colorless oil, and 3-benzyl-1,2,3,4-tetrahydroquinazoline (**51**) (0.0462 g, 0.206 mmol, 36%).

Data for **42**: R_f 0.28 (4:1 hexanes:EtOAc); IR (thin film) 2920, 1732 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.23-7.34 (m, 5 H), 7.04 (t, *J* = 7.7 Hz, 1 H), 6.86 (d, *J* = 7.0 Hz, 1 H), 6.67 (t, *J* = 7.7 Hz, 1 H), 6.53 (d, *J* = 7.7 Hz, 1 H), 4.09 (t, *J* = 7.7 Hz, 1 H), 4.03 (br s, 1 H), 3.97 (d, *J* = 16.8 Hz, 1 H), 3.60-3.73 (m, 6 H), 2.44-2.53 (m, 2 H), 2.04-2.09 (m, 1 H), 1.89-1.94 (m, 1 H); ^{13}C NMR (176 MHz, $CDCl_3$,) δ 174.1, 142.2, 139.4, 128.9, 128.4, 127.9, 127.4, 127.1, 118.3, 117.8, 114.4, 69.4, 55.2, 51.8, 48.1, 30.0, 29.7; HRMS (TOF MS ES+) calcd for $C_{19}H_{23}N_2O_2$ [M+H]: 311.1760, found 311.1770.

Data for **49**: R_f 0.28 (4:1 hexanes : EtOAc); IR (thin film) 2950, 1732, 1607 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.03-7.35 (m, 4 H), 7.25-7.27 (m, 1 H), 7.05 (td, *J* = 7.7, 1.4 Hz, 1 H), 6.98 (dd, *J* = 7.7, 1.4 Hz, 1 H), 6.71 (td, *J* = 7.0, 1.4 Hz, 1 H), 6.57 (dd, *J* = 8.4, 1.4 Hz, 1 H), 4.33 (d, *J* = 11.9 Hz, 1 H), 3.90 (br s, 1 H), 3.83 (d, *J* = 13.3 Hz, 1 H), 3.81 (dd, *J* = 11.9, 1.4 Hz, 1 H), 3.63 (s, 3 H), 3.56 (d, *J* = 13.3 Hz, 1 H), 3.50 (dd, *J* = 11.2, 4.9 Hz, 1 H), 2.55 (ddd, *J* = 16.8, 7.7, 6.3 Hz, 1 H), 2.46 (ddd, *J* = 14.7, 7.7, 7.7 Hz, 1 H) 1.99-2.08 (m, 2 H); ^{13}C NMR (176 MHz, $CDCl_3$,) δ 174.5, 142.6, 139.3, 129.3, 128.9, 128.3, 127.4, 127.2, 122.9, 117.9, 114.8, 59.0, 57.1, 56.0, 51.6,

33.0, 30.92; HRMS (TOF MS ES+) calcd for $C_{19}H_{23}N_2O_2$ [M+H]: 311.1760, found 311.1750.

Data for **50**: R_f 0.14 (4:1 hexanes : EtOAc); IR (thin film) 2950, 2851, 1735, 1692, 1493 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.23-7.34 (m, 5 H), 6.99 (td, *J* = 8.4, 1.6 Hz, 1 H), 6.95 (d, *J* = 7.2 Hz, 1 H), 6.32 (t, *J* = 7.6 Hz, 1 H), 5.31 (s, 1 H), 4.37 (t, *J* = 6.0 Hz, 1 H), 3.94 (d, *J* = 14.0 Hz, 1 H), 3.66 (s, 3 H), 3.54 (s, 3 H), 3.09 (d, *J* = 14.0 Hz, 1 H), 2.63 (t, *J* = 8.0 Hz, 2 H), 2.44 (dt, *J* = 16.8, 6.8 Hz, 1 H), 2.24-2.32 (m 1 H), 2.09 (q, *J* = 7.2 Hz, 2 H), 2.93 (q, *J* = 7.2 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$,) δ 174.1, 173.7, 143.2, 139.5, 129.1, 128.9, 128.3, 127.1, 126.1, 123.0, 118.4, 114.7, 64.1, 58.0, 51.8, 51.4, 49.1, 32.2, 30.4, 29.4, 27.6; HRMS (CI+) calcd for $C_{23}H_{29}N_2O_4$ [M+H]: 397.2127, found 397.2129.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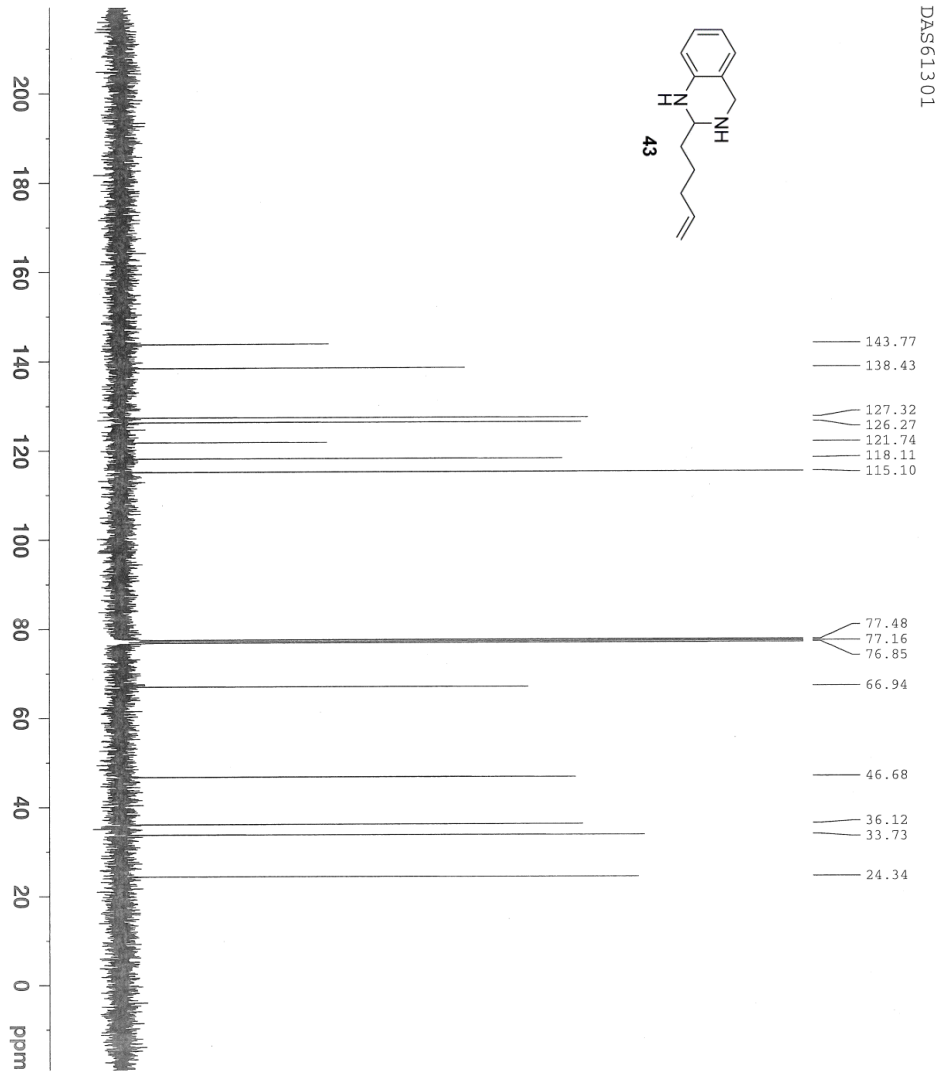


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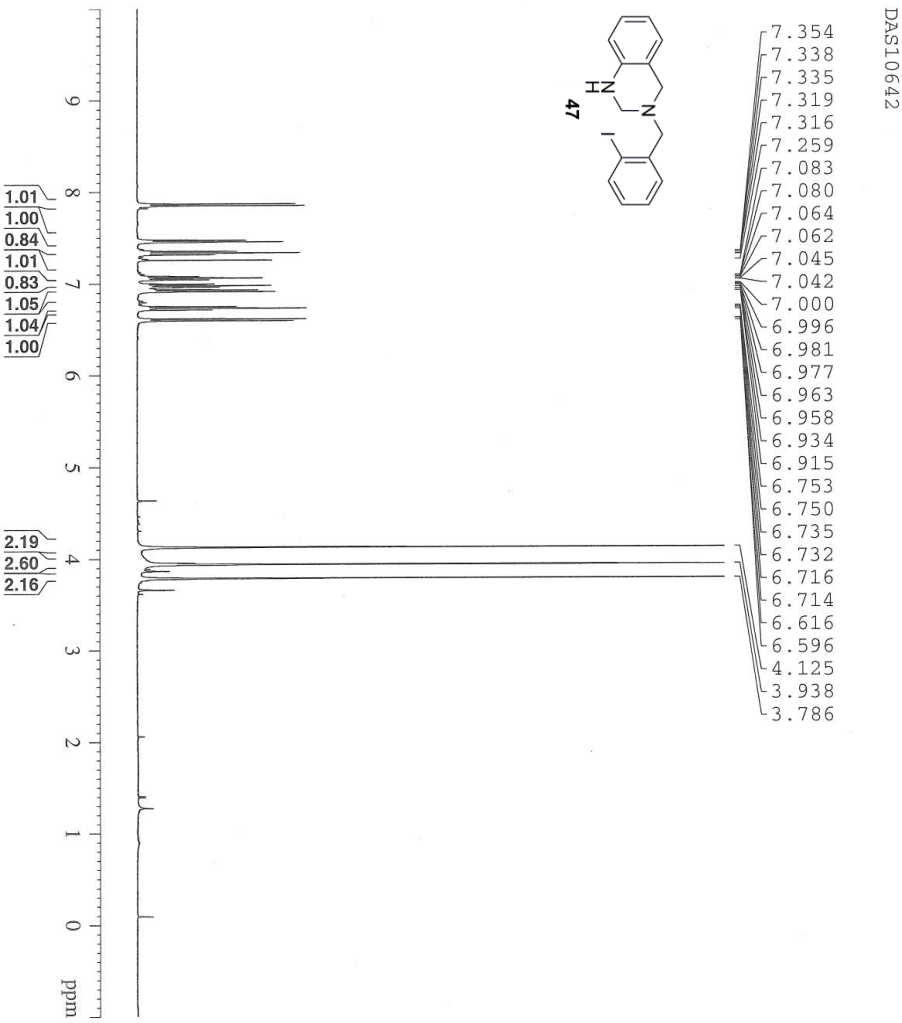
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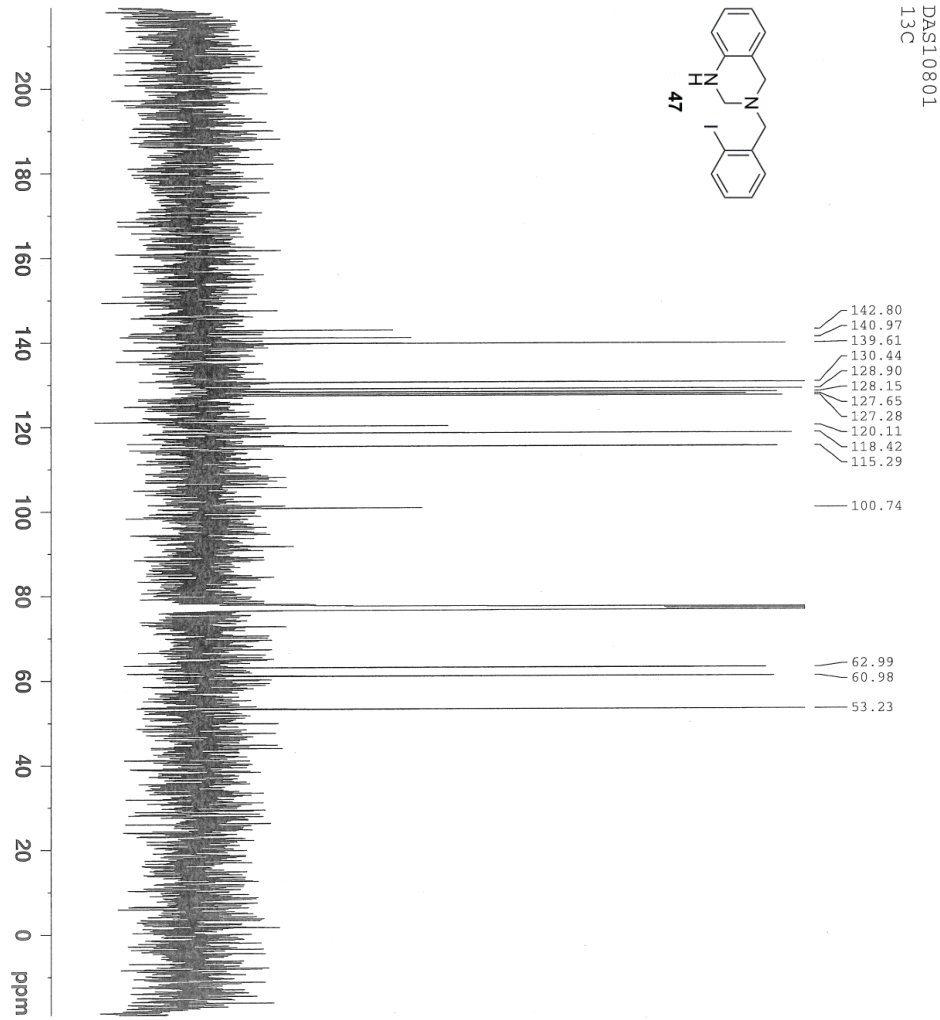


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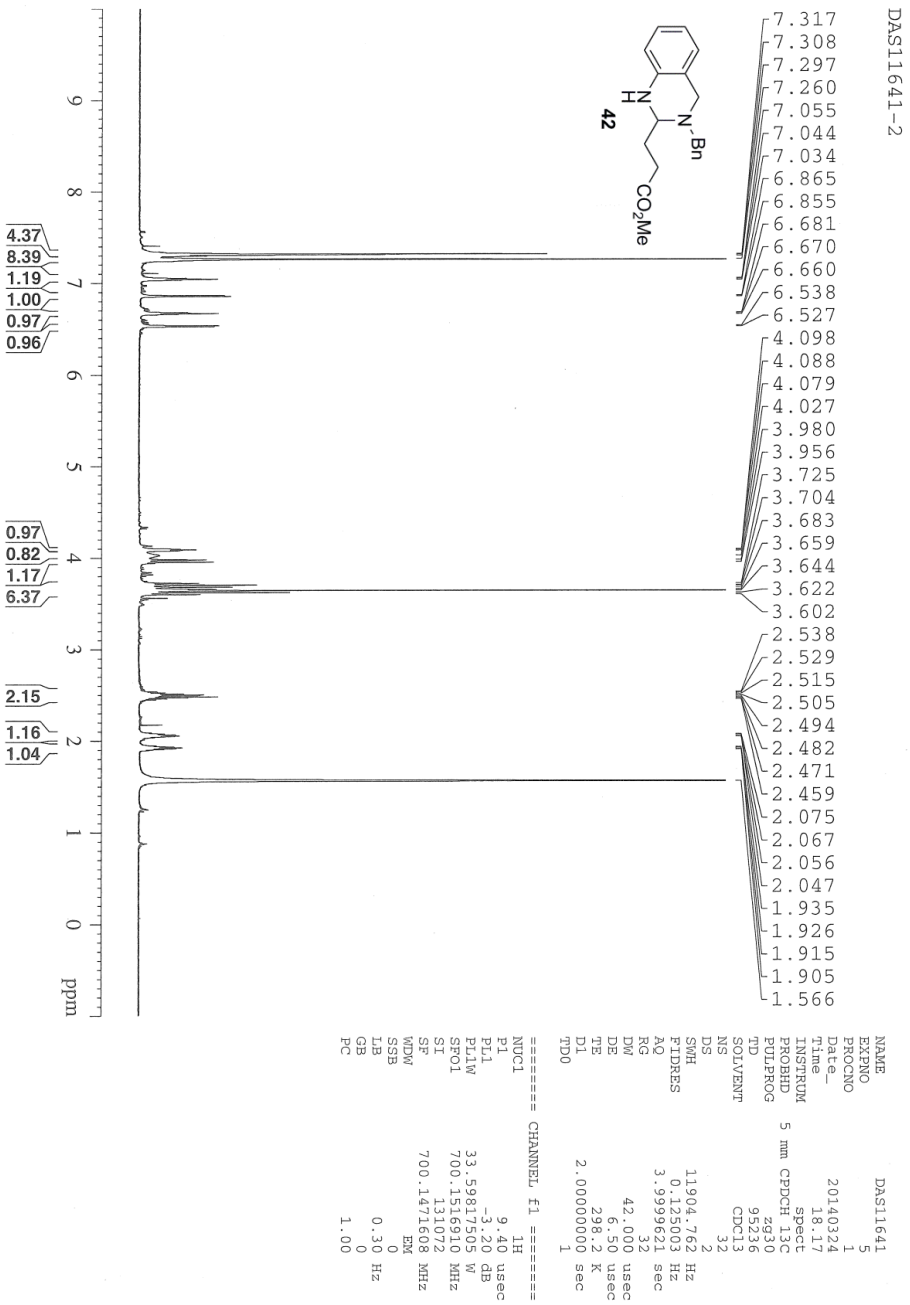
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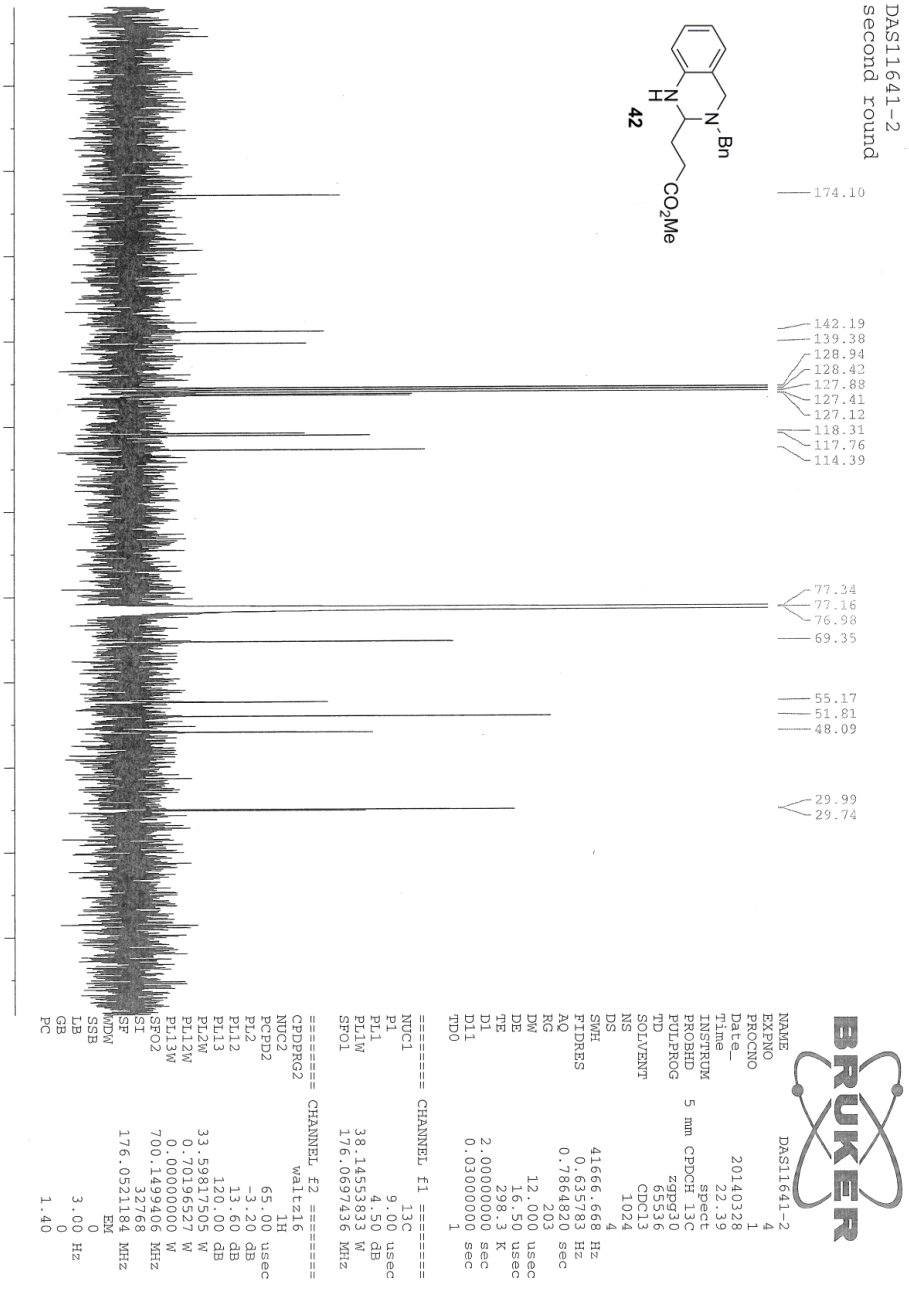
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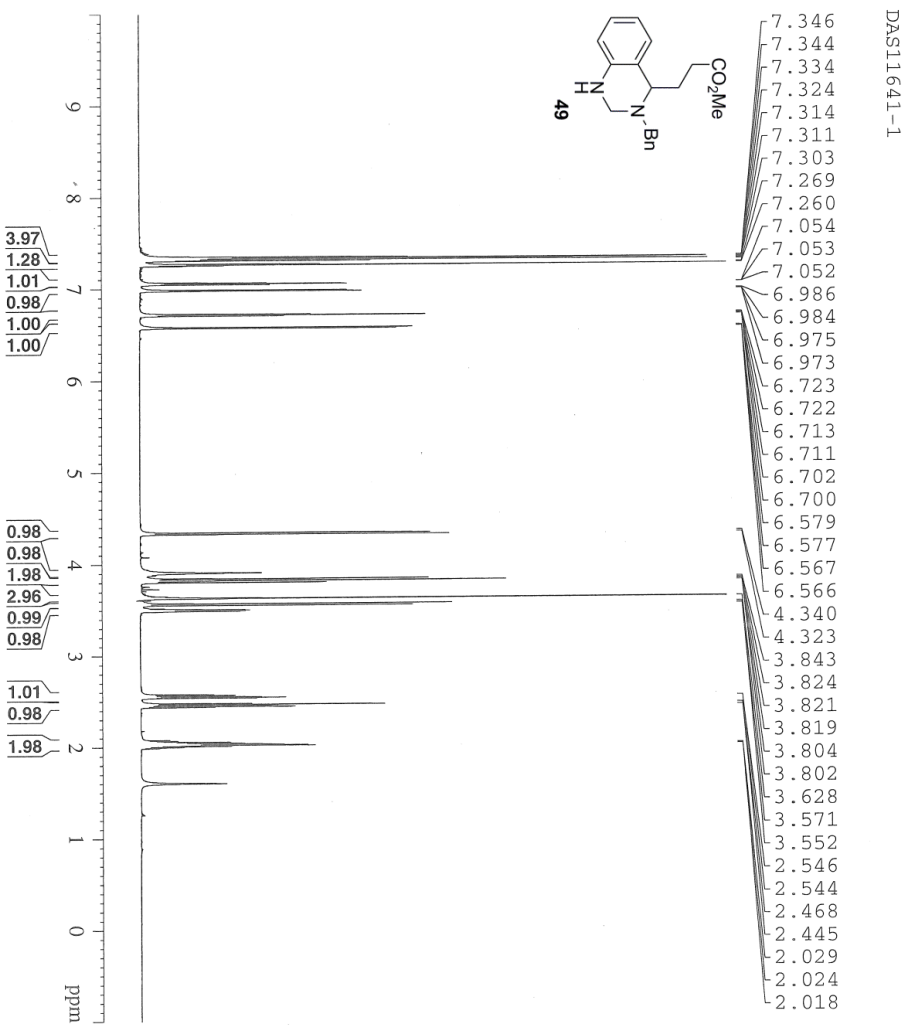
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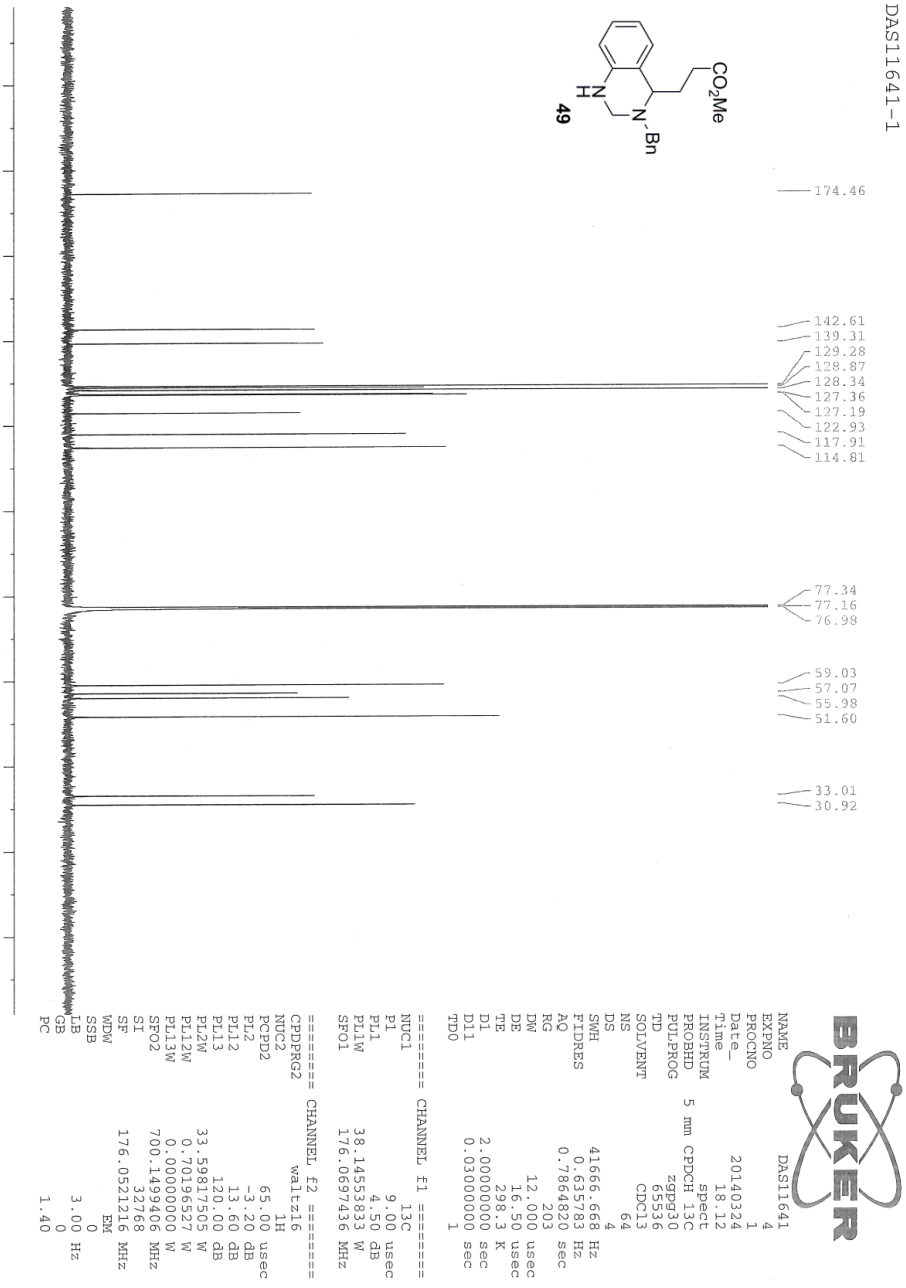
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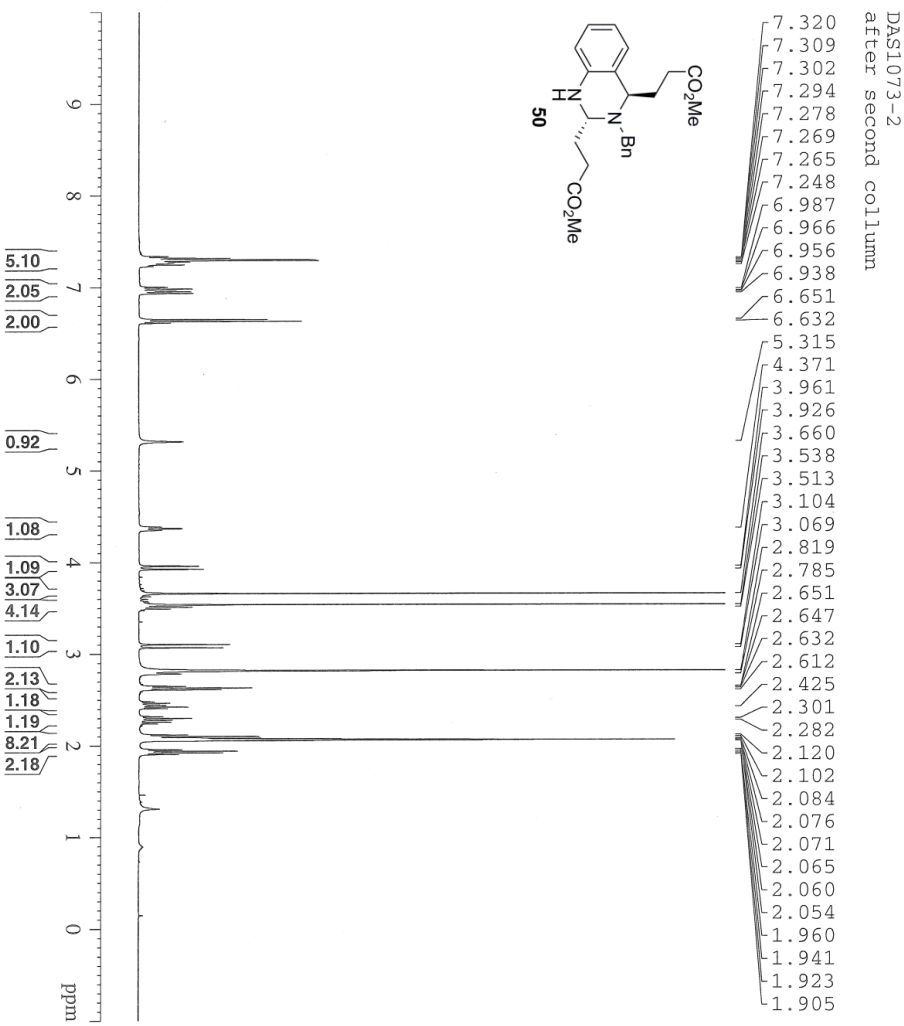
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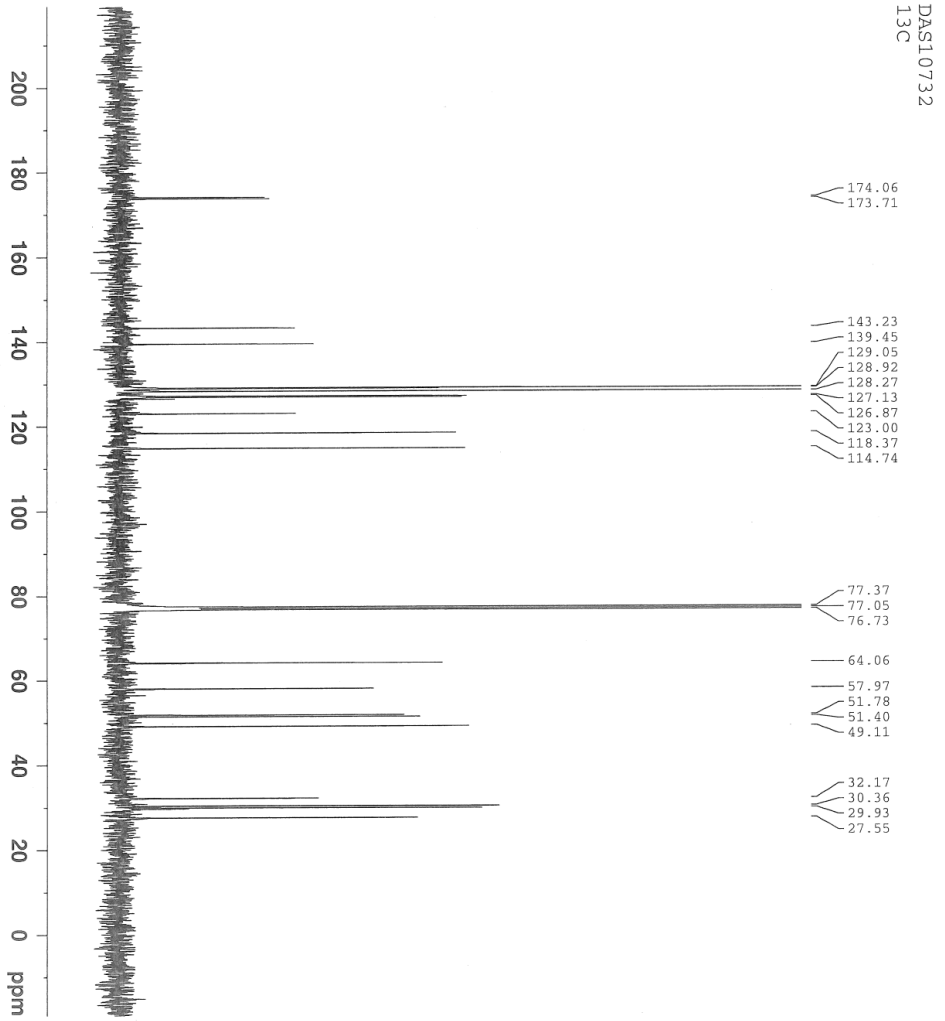


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Chapter 2: Formation of Carbon–Carbon Bonds Using Aminal Radicals

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Issue 23

2.1 Introduction

Nitrogenous molecules are ubiquitous in Nature. Pharmaceuticals, molecular catalysts, and secondary metabolites often contain nitrogen. As a result, nitrogenous molecules, such as alkaloids, make compelling targets for synthesis. However, alkaloid synthesis is inherently complicated by the nitrogen atom.[40] The Lewis basic lone pair found on amines, the presence of weakly acidic N–H hydrogens, and the readiness of amines to quaternize often lead to undesired reactivity. These factors conspire against the synthetic chemist.

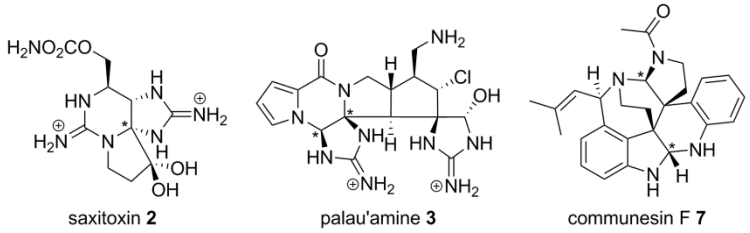


Figure 2.1. Selected nitrogen-rich alkaloids; aminals indicated by *

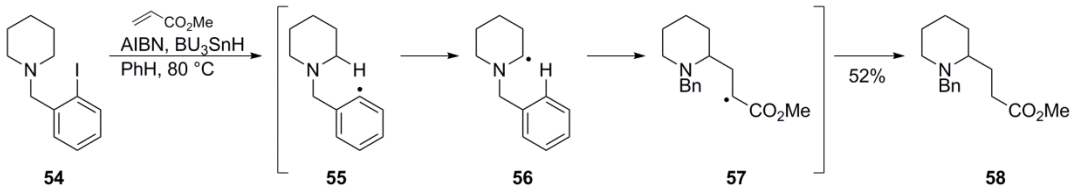
Traditional strategies used to circumvent the Lewis acid-base reactivity of nitrogen include: using protecting groups,[41] installing nitrogen at the end of a synthesis,[42] or packaging the nitrogen in a less reactive functional group (e.g. as a nitrile[43] or nitro[44] group). Such strategies have enjoyed widespread success in synthesis. However, a conceptually different approach to avoid the acid-base properties of nitrogen is to use single electron processes (i.e. radical reactions) to build the C–C bonds of alkaloid molecular architectures.[45]

Figure 2.1 shows a selection of alkaloids that has attracted considerable interest from the synthetic community.[46,47] Although more than half of the 55 carbons depicted in Figure 2.1 bear heteroatoms, only five are disubstituted with nitrogen (i.e. diamino- or aminal carbons). Harnessing reactivity specific to the aminal carbon in the presence of heteroatom-bearing carbons could be useful in alkaloid synthesis. Toward this end,

we envisioned creating an aminal radical intermediate that could be used in the formation of C–C bonds. We expected such a radical would be unreactive toward acidic N–H bonds and Lewis basic lone pairs,[48] and it would be well suited to forging C–C bonds in nitrogen-rich molecular architectures. Aminal radicals have been generated, and their spectral and physical properties have been studied.[49] However, to the best of our knowledge, they have not been used in synthesis.[50] Herein, we describe bond-forming reactions of aminal radicals for the first time.

2.2 α-Amino Radicals and Protective Radical Translocation

Carbon-centered radicals bearing one nitrogen (α-amino radicals) are well known.[51] A convenient method for their generation is by radical translocation (Scheme 2.1). For example, homolytic cleavage of a C–I bond in **54** generates intermediate **55**, which undergoes hydrogen-atom transfer to generate stabilized α-amino radical **56**.[52] The stability provided by the neighboring nitrogen atom is 11 kcal/mol.[53] Addition to a radical acceptor such as methyl acrylate leads to **57**, which receives a hydrogen atom from Bu_3SnH to form the product (**58**). Use of iodobenzyl to initiate radical translocation results in a benzyl-protected amine product.

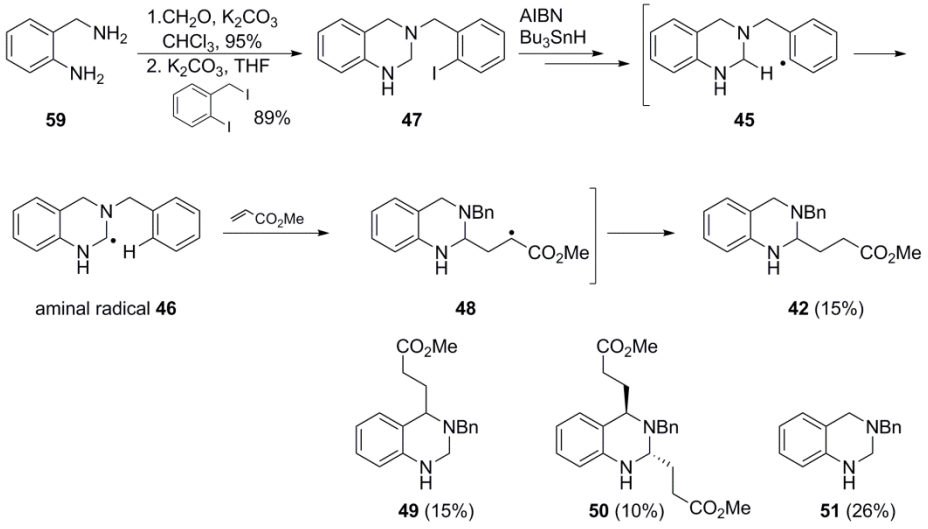


Scheme 2.1. Radical Translocation

Computational methods estimate the stabilization of an aminal radical to be approximately 2 kcal/mol relative to the α-amino radical.[53] Thus, it should be possible to selectively form an aminal radical in the presence of other nitrogen-bearing carbons.

2.3 Results and Discussion

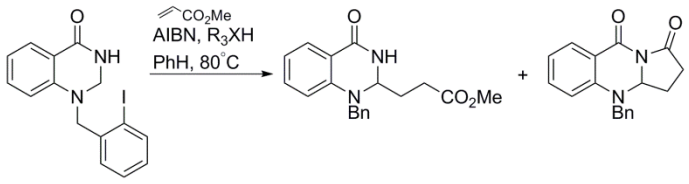
The first substrate chosen to evaluate this hypothesis was aminal **47**, prepared in two steps from diamine **59** (Scheme 2.2). Reaction of aminal **47** with methyl acrylate as a radical acceptor led to the formation of the desired addition product **42**, presumably via the route shown. Unreacted starting material, isomer **49**, over-addition product **50**, and the product of deiodination (**51**) were present in the reaction mixture. Attempts to improve the yield of **42** by adjusting reagent stoichiometry, concentration, or hydrogen-atom source were unsuccessful. We suspect that competitive formation of **49** is the result of the additional stabilization at the benzylic position (*vide infra*).



Scheme 2.2. Initial Investigations of Aminal Radical Reactivity

We next prepared substrate **60** in order to block reactivity at the benzylic position and simplify the product mixture (Table 2.1, entry 1). Substrate **60** is prepared in two steps and 70% overall yield from inexpensive anthranilamide. Gratifyingly, **60** showed cleaner reactivity giving 61% yield of the desired products (49% yield of **61**, accompanied by 12% of the corresponding lactam **62**). The increased yield may be

partially attributable to the capto-dative effect: one nitrogen is relatively electron poor, and one nitrogen is relatively electron rich.[54]



60 **61** **62**

entry	R−H	additive	combined yield (**61**:**62**)
1	2 equiv Bu_3SnH	none	61% (80:20)
2[a]	2 equiv Bu_3SnH	0.1 equiv BnSH	86% (30:70)
3	2 equiv Bu_3SnH	0.9 equiv BnSH	75% (100:0)
4	none	0.9 equiv BnSH	0%
5[b]	2 equiv Bu_3SnH	0.9 equiv BnSH	18% (100:0)
6	2 equiv $(TMS)_3SiH$	none	48% (48:52)
7[a]	2 equiv $(TMS)_3SiH$	0.1 equiv BnSH	91% (77:23)
8	2 equiv $(TMS)_3SiH$	0.9 equiv BnSH	89% (81:19)

Table 2.1. Reactivity of aminal **60.** [a] 5 equiv of methyl acrylate used. [b] AIBN was omitted from the reaction mixture.

Thiols are used as polarity-reversal catalysts in radical reactions, and may assist in hydrogen atom transfer events,[55] and the addition of BnSH increased reaction yields (entry 2). Further increasing the stoichiometry of the thiol had little effect on the overall yield (entry 3), but **61** was formed as the sole product. No product formation occurs in the absence of stannane (entry 4), suggesting the thiol is not the terminal hydrogen atom donor. We also performed a control experiment by omitting the AIBN and observed only modest product formation (entry 5). We speculate that in hot benzene some homolytic cleavage of the C–I bond may occur. The aminal radical reaction is also successful using $(TMS)_3SiH$ as a hydrogen atom donor (entry 6). The yield of the reaction is improved by adding BnSH (entries 7 and 8).

Based on a comparison of the data in entries 2, 3, 6, 7, and 8, it appears that BnSH may also serve to suppress the formation of the imide product **62**. As the loading of BnSH was increased, the ratio of the **61**:**62** also increased. This hypothesis is

bolstered by the fact that the result shown in entry 3 was obtained after heating at reflux for 15 hours while the result shown in entry 2 was obtained after just 4 hours of heating at reflux. This suggested that the increased formation of **62** observed was not simply the result of increased heating times.

The aminal radical reaction was examined with various aminals and radical acceptors. The aminals were made by condensing the corresponding amino amide with formalin (see Experimental Section). Use of acrylonitrile, *tert*-butyl acrylate, and acrolein as radical acceptors in the reaction with **60** results in good yields of the addition products **63**, **64**, and **65**, respectively (Figure 2.2). Use of Bu_3SnH as a hydrogen atom source gives superior yields compared with $(TMS)_3SiH$. However, use of the silane often gives synthetically useful yields without the use of heavy metals, and we report yields with both reagents. Attachment of the iodobenzyl group at the amide nitrogen also resulted in productive reactions with methyl acrylate, acrylonitrile, or *tert*-butyl acrylate to give products **66**, **67**, and **68**, respectively.

Aliphatic six-membered ring aminals participated in the reaction, provided one nitrogen bears an electron-withdrawing group. The acetamide-derived aminal added to methyl acrylate to give **69** in good yield. We found that trifluoroacetamides also participate in the reaction giving **70**. Note that the aminal radical is generated in the presence of the amino-substituted carbon. In these cases, products derived from formation of the α-amino radicals are not observed. It appears that in the absence of benzylic stabilization (vis-à-vis with substrate **47**), aminal radicals selectively form in the presence of amino-substituted carbons. Substrates that lacked electron-withdrawing carbonyl groups did not participate in the reaction; they gave only complex intractable product mixtures.

Intramolecular reactions were possible, and compound **71** was produced as a single diastereomer, whereas **72** was formed as a diastereomeric mixture. Bicyclic 5-

membered aminals are competent substrates in the reaction. Pipecolic acid-derived aminals react with methyl acrylate and acrylonitrile in good yields and selectivities to form **73** and **74**, respectively. Finally, proline-derived aminals undergo diastereoselective reactions giving **75** and **76**, respectively.

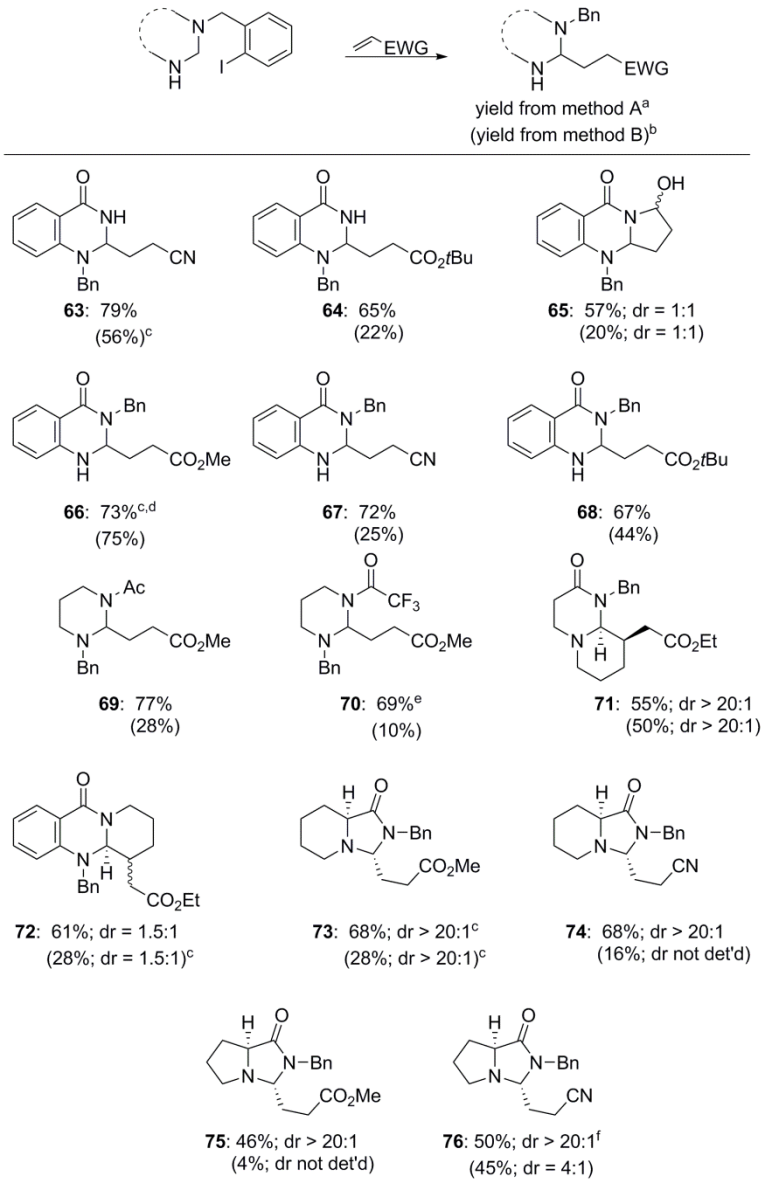
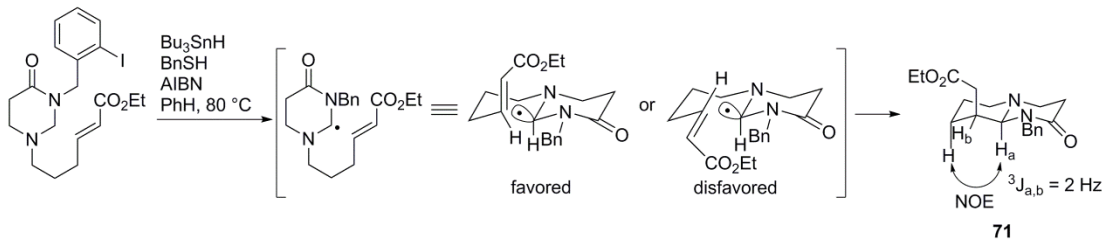


Figure 2.2. Scope of the aminal radical reaction. [a] Method A: 5.0 equiv alkene, 2.0 equiv Bu_3SnH, 0.1 equiv BnSH, 0.2 equiv AIBN, 0.10 M PhH, reflux, 3 h; [b] Method B: 5.0 equiv alkene, 2.0 equiv $(TMS)_3SiH$, 0.1 equiv BnSH, 0.2 equiv AIBN, 0.10 M PhH, reflux, 12 h; [c] 0.9 equiv BnSH; [d] 3.0 equiv of methyl acrylate; [e] 10 equiv methyl acrylate; [f] 0.2 equiv BnSH.

The relative stereochemistry of **71** was determined by ^{1}H NMR methods. First, methyne hydrogen H_a is positioned axial as evidenced by NOESY crosspeaks to the indicated hydrogens (Scheme 2.3). The small (2 Hz) coupling constant between H_a and H_b suggests H_b is equatorial. The diastereoselectivity in the formation of **71** may be a result of the model shown in Scheme 2.3. The favored conformation positions the ester away from the benzyl substituent, giving rise to **71**. As the aminal-containing ring becomes more planar, the benzyl substituent should block both faces of the aminal radical equally and the selectivity should decrease. This hypothesis is consistent with the observation that the bicyclic product **72** was produced with only modest diastereoselectivity.[56] The favored diastereomer of the bicyclic aminal products **73**–**76** likely results from addition to the convex face of the bicycle. The relative stereochemistry was confirmed using NOESY methods.



Scheme 2.3. Plausible model for formation of **71**

2.4 Conclusion

In conclusion, aminal radicals are formed via radical translocation reactions. These carbon-centered radicals react with radical acceptors in C–C bond-forming reactions in good yields with both Bu_3SnH and $(TMS)_3SiH$ as hydrogen atom donors. Aminals can be formed from aromatic or aliphatic diamines, provided that one nitrogen bears an electron-withdrawing carbonyl group. The reactivity of the aminal radical is different than the α-amino radical; specifically it can be formed in the presence of amino-substituted carbon atoms. We believe this reactivity will be useful in the

synthesis of nitrogen-rich alkaloids, and efforts to apply this chemistry in synthesis are underway in our laboratory.

2.5 Experimental Section

General Experimental Details:

All reactions were carried out under an inert Ar atmosphere in oven-dried glassware. Flash column chromatography (FCC) 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, ceric ammonium molybdate, molybdate, ninhydrin, or iodine stains. Tetrahydrofuran (THF), methylene chloride (CH_2Cl_2), acetonitrile (MeCN), benzene (PhH), dimethylformamide (DMF), ethanol (EtOH), and methanol (MeOH) were dried by passage through activated columns. Dimethylsulfoxide (DMSO) was stored over 3 Å molecular sieves. Acrylonitrile, acrolein, methyl acrylate, *tert*-butyl acrylate were distilled under reduced pressure to remove BHT and stored under inert atmosphere. Tributyltin hydride (Bu_3SnH) was dried over calcium hydride, distilled under reduced pressure and stored under inert atmosphere. 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, br = broad, m = multiplet. Melting points were determined with a Cole-Parmer instrument and are uncorrected.

1-(2-iodobenzyl)-2,3-dihydroquinazolin-4(1H)-one (**60**). To a solution of known 2,3-dihydroquinazolin-4(1H)-one[57] (2.77 g, 18.7 mmol) in THF (43 mL, 0.4 M) were added K_2CO_3 (7.07 g, 51.1 mmol) and known 1-iodo-2-(iodomethyl)benzene (5.86 g, 17.0 mmol). The reaction mixture was heated to reflux for 25 hours. At this time, TLC indicated the consumption of the iodide. The reaction mixture was cooled to rt, diluted with EtOAc, washed with saturated aqueous NaCl, dried over $MgSO_4$, and concentrated. The resulting solids were recrystallized from EtOAc (30 mL) to give **60** (4.45 g, 12.2 mmol, 72%) as a white solid.

Data for **60**: R_f 0.31 (3:1 EtOAc:Hexanes); mp = 149.9-151.1 ℃; IR (thin film) 3207, 3057, 2885, 1669, 1606, 1494, 750 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 8.03 (d, *J* = 7.7 Hz, 1 H), 7.92 (d, *J* = 7.7 Hz, 1 H), 7.34-7.39 (m, 3 H), 7.05 (t, *J* = 7.0 Hz, 1 H), 6.95 (t, *J* = 7.0 Hz, 1 H), 6.64 (d, *J* = 8.4 Hz, 1 H), 6.48 (br s, 1 H), 4.65 (s, 2 H), 4.44 (s, 2 H); ^{13}C (176 MHz, $CDCl_3$) δ 165.4, 148.5, 139.8, 138.1, 134.1, 129.5, 129.1, 128.7, 128.5, 119.4, 117.5, 113.4, 98.2, 60.7, 58.5; HRMS (TOF MS ES+) calcd for $C_{15}H_{14}N_2OI$ [M+H]: 365.0151, found 365.0138.

methyl 3-(1-benzyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanoate (**61**) and **4-benzyl-2,3,3a,4-tetrahydropyrrolo[2,1-b]quinazoline-1,9-dione** (**62**). To a solution of **60** (0.168 g, 0.461 mmol) in benzene (4.9 mL, 0.1 M) were added methyl acrylate (0.13 mL, 1.4 mmol), benzyl thiol (0.05 mL, 0.4 mmol), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilane (0.30 mL, 0.97 mmol), and AIBN (0.0168 g, 0.102 mmol). The reaction mixture was heated to reflux for 16 hours. At this time, TLC indicated the consumption of **60**. The reaction mixture was cooled to rt, diluted with MeCN, washed with hexanes, and concentrted. Purification by FCC to give **61** (0.108 g, 0.333 mmol, 72%) as a white foam and **62** (0.0233g, 0.0797 mmol, 17%) as a yellow solid.

Data for **61**: R_f 0.50 (3:1 EtOAc:Hexanes); IR (thin film) 2951, 1733, 1665, 1492, 753 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.96 (dd, *J* = 7.7, 1.4 Hz, 1 H), 7.36-7.38 (m, 5 H), 7.31-7.36 (m, 1 H), 6.90 (td, *J* = 7.7, 1.4 Hz, 1 H), 6.75 (d, *J* = 7.7 Hz, 1 H), 6.43 (br s, 1 H) 4.72 (dt, *J* = 7.7, 4.9 Hz, 1 H), 4.66 (d, *J* = 15.4 Hz, 1 H), 4.35 (d, *J* = 16.1 Hz, 1 H), 3.63 (s, 3 H), 2.36-2.43 (m, 2 H), 2.11 (sextet, *J* = 7.0 Hz, 1 H), 1.98-2.02 (m, 1 H); ^{13}C (176 MHz, $CDCl_3$) δ 173.2, 164.3, 146.6, 136.9, 134.1, 128.9, 128.6, 127.7, 127.5, 119.1, 117.5, 115.0, 68.5, 53.9, 51.8, 29.0, 28.9; HRMS (TOF MS ES+) calcd for $C_{19}H_{21}N_2O_3$ [M+H]: 325.15523, found 325.15497.

Data for **62**: R_f 0.21 (2:1 EtOAc:Hexanes); mp = 146-147℃; IR (thin film) 2926, 1768, 1385, 754 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 8.15 (dd, *J* = 7.7, 1.4 Hz, 1 H), 7.37-7.40 (m, 3 H), 7.31-7.34 (m, 3 H), 6.96 (td, *J* = 7.7, 0.7 Hz, 1 H), 6.71 (d, *J* = 8.4 Hz, 1 H), 5.40 (dd, *J* = 8.4, 5.6 Hz, 1 H), 4.72 (d, *J* = 17.5 Hz, 1 H), 4.48 (d, *J* = 17.5 Hz, 1 H), 2.67 (ddd, *J* = 17.5, 9.8, 1.4 Hz 1 H), 2.55-2.60 (m, 1 H), 2.45-2.49 (m, 1 H), 2.24-2.30 (m, 1 H); ^{13}C (176 MHz, $CDCl_3$) δ 172.4, 160.8, 149.1, 136.6, 135.5, 130.4, 129.1, 127.7, 126.2, 119.8, 116.7, 113.7, 72.6, 49.0, 30.6, 25.3: HRMS (TOF MS ES+) calcd for $C_{18}H_{17}N_2O_2$ [M+H]: 293.12901, found 293.12867.

methyl 3-(1-benzyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanoate (**61**)**.** To a solution of **60** (0.167 g, 0.459 mmol) in benzene (3.9 mL, 0.12 M) were added methyl acrylate (0.13 mL, 1.4 mmol), benzyl thiol (0.05 mL, 0.4 mmol). This solution was heated to reflux. In a separate flask were combined tributyltin hydride (0.26 mL, 0.97 mmol), AIBN (0.0155 g, 0.0944 mmol), and benzene (0.9 mL, 1.1 M). The tributyltin hydride solution was then added to the refluxing mixture via syringe pump over a period of 1 hour. The mixture was heated at reflux for an additional 14 hours. At this time, TLC indicated the consumption of **60**. After cooling to rt, the mixture was diluted with MeCN, washed with hexanes, and concentrated. Purification by FCC (2:3 hexanes:EtOAc) to give **61** (0.112 g, 0.344 mmol, 75%) as a white foam.

3-(1-benzyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanenitrile (63). To a solution of **60** (0.176 g, 0.482 mmol) in benzene (2.9 mL, 0.17 M) were added acrylonitrile (0.16 mL, 2.4 mmol), 10% benzyl thiol in benzene (0.06 mL, 0.05 mmol). This solution was heated to reflux. In a separate flask were combined tributyltin hydride (0.26 mL, 0.97 mmol), AIBN (0.0177 g, 0.108 mmol), and benzene (1.9 mL, 0.51 M). The tributyltin hydride solution was then added to the refluxing mixture via syringe pump over a period of 3 hours. At this time, TLC indicated the consumption of **60**. After cooling to rt, the mixture was diluted with MeCN, washed with hexanes, and concentrated. Purification by FCC (1:2 hexanes:EtOAc) to give **63** (0.110 g, 0.378 mmol, 79%) as a white foam.

Data for **63**: R_f 0.44 (3:1 EtOAc:hexanes); IR (thin film) 2928, 2250, 1666, 1606, 1492, 755 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.98 (dd, *J* = 7.7, 1.4 Hz, 1 H), 7.52, (s, 1 H), 7.44 (dddd, *J* = 9.1, 8.4, 7.7, 2.1 Hz, 1 H), 7.39-7.41 (m, 4 H), 7.34-7.36 (m, 1 H), 7.00 (td, *J* = 8.4, 1.4 Hz, 1 H), 6.91 (d, *J* = 7.7 Hz, 1 H), 4.70 (dddd, *J* = 10.5, 7.0, 6.3, 4.9 Hz, 1 H), 4.66 (d, *J* = 14.7 Hz, 1 H), 4.37 (d, *J* = 14.7, 1 H), 2.37 (td, *J* = 8.4, 1.4 Hz, 2 H), 2.08 (sextet, *J* = 7.0, 1 H), 2.02 (sextet, *J* = 7.7 Hz, 1 H); ^{13}C (176 MHz, $CDCl_3$) δ 164.6, 146.5, 136.5, 134.4, 129.0, 128.5, 128.0, 127.7, 120.1, 118.9, 117.9, 116.3, 67.9, 55.1, 30.0, 13.0 HRMS (TOF MS ES+) calcd for $C_{18}H_{18}N_3O$ [M+H]: 292.1450, found 292.1448.

3-(1-benzyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanenitrile (63). To a solution of **60** (0.162 g, 0.446 mmol) in benzene (4.5 mL, 0.1 M) were added acrylonitrile (0.15 mL, 2.3 mmol), a 10% solution of benzyl thiol in benzene (0.04 mL, 0.034 mmol), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilane (0.28 mL, 0.91 mmol), and AIBN (0.0165 g, 0.100 mmol). The reaction mixture was heated to reflux for 16 hours. At this time, TLC indicated the consumption of **60**. The reaction mixture was cooled to rt, diluted with MeCN, washed with hexanes, and concentrted.

Purification by FCC (1:2 hexanes:EtOAc) to give **63** (0.0727 g, 0.250 mmol, 56%) as a white foam.

***tert*-butyl 3-(1-benzyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanoate (64).** To a solution of **60** (0.165 g, 0.453 mmol) in benzene (2.5 mL, 0.18 M) were added *tert*-butyl acrylate (0.33 mL, 2.3 mmol), 5% benzyl thiol in benzene (0.10 mL, 0.043 mmol). This solution was heated to reflux. In a separate flask were combined tributyltin hydride (0.24 mL, 0.89 mmol), AIBN (0.0155 g, 0.0944 mmol), and benzene (2.0 mL, 0.45 M). The tributyltin hydride solution was then added to the refluxing mixture via syringe pump over a period of 3 hours. At this time, TLC indicated the consumption of **60**. After cooling to rt, the mixture was diluted with MeCN, washed with hexanes, and concentrated. Purification by FCC (1:2 hexanes:EtOAc) to give **64** (0.108 g, 0.295 mmol, 65%) as a white foam.

Data for **64**: R_f 0.63 (3:1 EtOAc:hexanes); IR (thin film) 2977, 1724, 1668, 1492, 752 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (dd, *J* = 8.0, 1.6 Hz, 1 H), 7.29-7.40 (m, 6 H), 6.89 (t, *J* = 7.6 Hz, 1 H), 6.74 (d, *J* = 8.4 Hz, 1 H), 6.49 (d, *J* = 4.0 Hz, 1 H), 4.66-4.72 (m, 2 H), 4.33 (d, *J* = 15.6 Hz, 1 H), 2.29 (t, *J* = 7.2 Hz, 1 H), 1.99-2.10 (m, 1 H), 1.19-1.99 (m, 1 H), 1.41 (s, 9 H); ^{13}C (176 MHz, $CDCl_3$) δ 172.1, 164.4, 146.6, 136.9, 134.0, 128.9, 128.6, 127.7, 127.3, 118.7, 117.3, 114.5, 80.8, 68.9, 53.5, 30.3, 29.0, 28.1; HRMS (TOF MS ES+) calcd for $C_{22}H_{27}N_2O_3$ [M+H]: 367.2022, found 367.2012.

***tert*-butyl 3-(1-benzyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanoate (64).** To a solution of **60** (0.164 g, 0.450 mmol) in benzene (4.5 mL, 0.1 M) were added *tert*-butyl acrylate (0.33 mL, 2.3 mmol), a 5% solution of benzyl thiol in benzene (0.10 mL, 0.043 mmol), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilane (0.28 mL, 0.91 mmol), and AIBN (0.0147 g, 0.0895 mmol). The reaction mixture was heated to reflux for 23 hours. At this time, TLC indicated the consumption of **60**. The reaction

mixture was cooled to rt, diluted with MeCN, washed with hexanes, and concentrted. Purification by FCC (2:1 hexanes:EtOAc) to give **64** (0.0369 g, 0.101 mmol, 22%) as a white foam.

4-benzyl-1-hydroxy-2,3,3a,4-tetrahydropyrrolo[2,1-*b*]quinazolin-9(1*H*)-one (**65a** and **65b**)**.** To a solution of **60** (0.160 g, 0.440 mmol) in benzene (2.4 mL, 0.18 M) were added acrolein (0.15 mL, 2.2 mmol), 5% benzyl thiol in benzene (0.10 mL, 0.043 mmol). This solution was heated to reflux. In a separate flask were combined tributyltin hydride (0.24 mL, 0.89 mmol), AIBN (0.0150 g, 0.0913 mmol), and benzene (2.0 mL, 0.45 M). The tributyltin hydride solution was then added to the refluxing mixture via syringe pump over a period of 3 hours. At this time, TLC indicated the consumption of **60**. After cooling to rt, the mixture was diluted with MeCN, washed with hexanes, and concentrated. Purification by FCC (2:3 hexanes:EtOAc) to give a 1:1 mixture of **65a** and **65b** (0.0735 g, 0.250 mmol, 57%) as a colorless oil.

Data for **65a** and **65b**: R_f 0.25 and R_f 0.43 (3:1 EtOAc:Hexanes); IR (thin film) as a mixture of diastereomers 2949, 1645, 1605, 1485, 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.97 (td, *J* = 6.4 1.2 Hz, 2 H), 7.27-7.36 (m, 12 H), 6.85-6.89 (m, 2 H), 6.66 (d, *J* = 8.4 Hz, 1 H), 6.61 (d, *J* = 8.4 Hz, 1 H), 5.98 (td, *J* = 6.0, 1.6 Hz, 1 H), 5.89 (dd, *J* = 5.6, 1.2 Hz, 1 H), 5.34 (dd, *J* = 9.2, 4.8 Hz, 1 H), 5.05 (dd, *J* = 10.0, 5.2 Hz, 1 H), 4.39-4.71 (m, 3 H), 4.09 (br s, 1 H), 2.36-2.54 (m, 3 H), 2.25 (quintet, *J* = 5.6 Hz, 1 H), 1.95-2.13 (m, 3 H), 1.80-1.90 (m, 1 H); ^{13}C (126 MHz, $CDCl_3$) δ 163.4, 163.0, 149.0, 148.8, 137.0, 136.9, 134.1, 133.9, 128.9, 128.4, 127.4, 127.3, 126.6, 126.4, 118.9, 118.8, 117.9, 117.1, 113.0, 112.9, 112.8, 81.9, 80.2, 73.9, 73.8, 72.5, 72.4, 50.2, 31.3, 29.6, 29.3; HRMS (TOF MS ES+) calcd for $C_{18}H_{19}N_2O_2Na$ [M+Na]: 317.1266, found 317.1277.

***tert*-butyl 3-(1-benzyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanoate** (**65a** and **65b**)**.** To a solution of **60** (0.166 g, 0.456 mmol) in benzene (4.6 mL, 0.1 M) were added acrolein (0.15 mL, 2.2 mmol), a 5% solution of benzyl thiol in benzene (0.10 mL, 0.043 mmol), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilane (0.28 mL, 0.91 mmol), and AIBN (0.0151 g, 0.0920 mmol). The reaction mixture was heated to reflux for 5.5 hours. At this time, TLC indicated the consumption of **60**. The reaction mixture was cooled to rt, diluted with MeCN, washed with hexanes, and concentrted. Purification by FCC (2:3 hexanes:EtOAc) to give a mixture of **65a** and **65b** (0.0265 g, 0.0900 mmol, 20%) as a colorless oil.

3-(2-iodobenzyl)-2,3-dihydroquinazolin-4(1H)-one (**S1**). To a solution of known 2,3-dihydroquinazolin-4(1H)-one (2.84 g, 19.2 mmol) in THF (58 mL, 0.3 M) were added NaOH (0.806 g, 20.2 mmol) and known 1-iodo-2-(iodomethyl)benzene (5.97 g, 17.4 mmol). The reaction mixture was heated to reflux for 34 hours. At this time, TLC indicated the consumption of the iodide. The reaction mixture was cooled to rt, diluted with EtOAc, washed with saturated aqueous NaCl, dried over $MgSO_4$, and concentrated. The resulting solids were recrystallized from EtOAc (20 mL) to give **S1** (3.01 g, 8.27 mmol, 48%) as a white solid.

Data for **S1**: R_f 0.45 (1:2 EtOAc:Hexanes); mp = 134.5-135.5℃; IR (thin film)3295, 1636, 1462, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (dd, *J* = 8.0, 1.6 Hz, 1 H), 7.87 (dd, *J* = 8.0, 1.2 Hz, 1 H), 7.45 (dd, *J* = 8.0, 1.6 Hz, 1 H), 7.34 (td, *J* = 8.8, 1.6 Hz, 2 H), 7.00 (td, *J* = 8.0, 1.6 Hz, 1 H), 6.94 (td, *J* = 8.0, 1.2 Hz, 1 H), 6.72 (dd, *J* = 8.0, 0.4 Hz, 1 H), 4.80 (s, 1H), 4.61 (s, 1H), 4.35 (br s, 1 H); ^{13}C (100 MHz, $CDCl_3$) δ 163.8, 147.5, 139.6, 138.7, 133.4, 129.3, 129.2, 128.7, 128.6, 119.6, 117.4, 115.0, 98.8, 59.3, 53.1; HRMS (TOF MS ES+) calcd for $C_{15}H_{14}N_2OI$ [M+H]: 365.0151, found 365.0139.

methyl 3-(3-benzyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanoate (66). To a solution of **S1** (0.195 g, 0.534 mmol) in benzene (4.5 mL, 0.12 M) were added methyl acrylate (0.15 mL, 1.7 mmol), benzyl thiol (0.06 mL, 0.5 mmol). This solution was heated to reflux. In a separate flask were combined tributyltin hydride (0.30 mL, 1.1 mmol), AIBN (0.0186 g, 0.113 mmol), and benzene (1.1 mL, 1.0 M). The tributyltin hydride solution was then added to the refluxing mixture via syringe pump over a period of 1 hour. The mixture was heated at reflux for an additional 13 hours. At this time, TLC indicated the consumption of **S1**. After cooling to rt, the mixture was diluted with MeCN, washed with hexanes, and concentrated. Purification by FCC (3:1 hexanes:EtOAc) to give **66** (0.126 g, 0.387 mmol, 72%) as a colorless oil.

Data for **66**: R_f 0.21 (3:1 EtOAc:hexanes); IR (thin film) 2950, 1733, 1628, 1495, 756 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.99 (dd, *J* = 7.6, 1.2 Hz, 1 H), 7.29-7.39 (m, 6 H), 6.91 (td, *J* = 8.0, 0.8 Hz, 1 H), 6.57 (d, *J* = 8.0 Hz, 1 H), 5.58 (d, *J* = 15.2 Hz, 1 H), 4.66 (dt, *J* = 9.2, 3.6 Hz, 1 H), 4.48 (d, *J* = 2.8 Hz, 1 H), 4.05 (d, *J* = 15.2 Hz, 1 H), 3.65 (s, 3 H), 2.34-2.38 (m, 2 H), 2.11-2.20 (m, 1 H), 1.96-2.04 (m, 1 H); ^{13}C (176 MHz, $CDCl_3$) δ 173.2, 162.5, 144.5, 137.1, 133.5, 128.8, 128.7, 128.0, 127.6, 119.6, 117.0, 115.6, 67.1, 51.9, 47.4, 29.7, 27.9; HRMS (TOF MS ES+) calcd for $C_{19}H_{21}N_2O_3$ [M+H]: 325.1552, found 325.1554.

methyl 3-(3-benzyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanoate (66). To a solution of **S1** (0.168 g, 0.461 mmol) in benzene (4.6 mL, 0.1 M) were added methyl acrylate (0.21 mL, 2.3 mmol), a 5% solution of benzyl thiol in benzene (0.10 mL, 0.043 mmol), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilane (0.28 mL, 0.91 mmol), and AIBN (0.0154 g, 0.0938 mmol). The reaction mixture was heated to reflux for 18 hours. At this time, TLC indicated the consumption of **S1**. The reaction mixture was cooled to rt, diluted with MeCN, washed with hexanes, and concentrted. Purification by FCC (3:1 hexanes:EtOAc) to give **66** (0.111 g, 0.342 mmol, 75%) as a colorless oil.

3-(3-benzyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanenitrile (67). To a solution of **S1** (0.160 g, 0.439 mmol) in benzene (2.4 mL, 0.18 M) were added acrylonitrile (0.14 mL, 2.1 mmol), 10% benzyl thiol in benzene (0.05 mL, 0.04 mmol). This solution was heated to reflux. In a separate flask were combined tributyltin hydride (0.24 mL, 0.89 mmol), AIBN (0.0143 g, 0.0871 mmol), and benzene (2.0 mL, 0.45 M). The tributyltin hydride solution was then added to the refluxing mixture via syringe pump over a period of 3 hours. At this time, TLC indicated the consumption of **S1**. After cooling to rt, the mixture was diluted with MeCN, washed with hexanes, and concentrated. Purification by FCC (2:1 hexanes:EtOAc) to give **67** (0.0916 g, 0.314 mmol, 72%) as a colorless oil.

Data for **67**: R_f 0.16 (1:2 EtOAc:hexanes); IR (thin film) 2930, 2250, 1632, 1497, 756 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 8.03 (dd, *J* = 8.4, 1.4 Hz, 1 H), 7.36-7.39 (m, 5 H), 7.31-7.34 (m, 1 H), 7.00 (td, *J* = 7.7, 1.4 Hz, 1 H), 6.78 (dd, *J* = 7.7, 0.7 Hz, 1 H), 5.42 (d, *J* = 14.7 Hz, 1 H), 4.72 (ddd, *J* = 9.8, 4.9, 3.5 Hz, 1 H), 4.50 (br s, 1 H), 4.17 (d, *J* = 15.4 Hz, 1 H), 2.33-2.43 (m, 2 H), 2.16-2.21 (m, 1 H), 1.86-1.90 (m, 1 H); ^{13}C (176 MHz, $CDCl_3$) δ 162.2, 143.3, 136.8, 133.8, 129.0, 128.9, 128.1, 127.9, 120.7, 118.7, 117.9, 116.9, 66.5, 47.8, 28.2, 13.6; HRMS (TOF MS ES+) calcd for $C_{18}H_{18}N_3O$ [M+H]: 292.1450, found 292.1436.

3-(3-benzyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanenitrile (67). To a solution of **S1** (0.169 g, 0.464 mmol) in benzene (4.6 mL, 0.1 M) were added acrylonitrile (0.15 mL, 2.3 mmol), a 5% solution of benzyl thiol in benzene (0.11 mL, 0.047 mmol), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilane (0.29 mL, 0.94 mmol), and AIBN (0.0160 g, 0.0974 mmol). The reaction mixture was heated to reflux for 23 hours. At this time, TLC indicated the consumption of **S1**. The reaction mixture was cooled to rt, diluted with MeCN, washed with hexanes, and concentrted.

Purification by FCC (2:1 hexanes:EtOAc) to give **67** (0.0342 g, 0.117 mmol, 25%) as a colorless oil.

***tert*-butyl 3-(3-benzyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanoate (68)**. To a solution of **S1** (0.159 g, 0.437 mmol) in benzene (2.4 mL, 0.18 M) were added *tert*-butyl acrylate (0.32 mL, 2.2 mmol), 5% benzyl thiol in benzene (0.10 mL, 0.043 mmol). This solution was heated to reflux. In a separate flask were combined tributyltin hydride (0.24 mL, 0.89 mmol), AIBN (0.0147 g, 0.0895 mmol), and benzene (2.0 mL, 0.45 M). The tributyltin hydride solution was then added to the refluxing mixture via syringe pump over a period of 3 hours. At this time, TLC indicated the consumption of **S1**. After cooling to rt, the mixture was diluted with MeCN, washed with hexanes, and concentrated. Purification by FCC (4:1 hexanes:EtOAc) to give **68** (0.1071 g, 0.292 mmol, 67%) as a colorless oil.

Data for **68**: R_f 0.52 (1:1 EtOAc:hexanes); IR (thin film) 3305, 2978, 1722, 1632, 755 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 8.00 (dd, *J* = 7.7, 1.4 Hz, 1 H), 7.28-7.39 (m, 6 H), 6.91 (td, *J* = 7.7, 0.7 Hz, 1 H), 6.66 (dd, *J* = 8.4, 0.7 Hz, 1 H), 5.58 (d, *J* = 14.7 Hz, 1 H), 4.65 (dt, *J* = 9.1, 3.5 Hz, 1 H), 4.51 (br s,1 H), 4.04 (d, *J* = 15.4 Hz, 1 H), 2.23-2.29 (m, 2 H), 2.10-2.14 (m, 1 H), 1.96-2.01 (m, 1 H), 1.43 (s, 9 H); ^{13}C (176 MHz, $CDCl_3$) δ 172.0, 162.6, 144.8, 137.2, 133.5, 128.8, 128.7, 127.9, 127.5, 119.3, 116.7, 115.4, 81.0, 67.3, 47.4, 31.1, 28.1, 26.0; HRMS (TOF MS ES+) calcd for $C_{22}H_{27}N_2O_3$ [M+H]: 367.2022, found 367.2026.

***tert*-butyl 3-(3-benzyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanoate (68)**. To a solution of **S1** (0.166 g, 0.457 mmol) in benzene (4.6 mL, 0.1 M) were added *tert*-butyl acrylate (0.33 mL, 2.3 mmol), a 5% solution of benzyl thiol in benzene (0.11 mL, 0.047 mmol), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilane (0.28 mL, 0.91 mmol), and AIBN (0.0155 g, 0.0944 mmol). The reaction mixture was heated to reflux for 19 hours. At this time, TLC indicated the consumption of **S1**. The reaction

mixture was cooled to rt, diluted with MeCN, washed with hexanes, and concentrted. Purification by FCC (4:1 hexanes:EtOAc) to give **68** (0.0731 g, 0.199 mmol, 44%) as a colorless oil.

***N*^{1}-(2-iodobenzyl)propane-1,3-diamine** (**S2**). To a solution of known 1,3-propanediamine (10 mL, 120 mmol) in THF (20 mL, 6.0 M) were added K_2CO_3 (3.30 g, 23.9 mmol), and 1-iodo-2-(iodomethyl)benzene (4.09 g, 11.9 mmol) dropwise as a solution in THF (20 mL, 0.60 M). The reaction mixture was stirred at rt for 0.5 hours. At this time, TLC indicated the consumption of the iodide. The reaction mixture was diluted with EtOAc, washed with saturated aqueous NaCl, dried over $MgSO_4$, and concentrated to give **S2** (3.36 g, 11.6 mmol, 97%) as a colorless oil.

Data for **S2**: R_f 0.31 (4:1 EtOAc:10% NH_4OH in MeOH); IR (thin film) 2933,1464, 749 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.81 (dd, *J* = 8.4, 1.4 Hz, 1 H), 7.37 (dd, *J* = 7.0, 1.4 Hz, 1 H), 7.31 (dd, *J* = 7.7, 0.7 Hz, 1 H), 6.95 (td, *J* = 7.7, 1.4 Hz, 1 H), 3.79 (s, 2 H), 2.85 (t, *J* = 7.0 Hz, 2 H), 2.71 (t, *J* = 7.0 Hz, 2 H), 1.72 (quintet, *J* = 7.0 Hz, 2 H); ^{13}C (176 MHz, $CDCl_3$) δ 141.9, 139.5, 129.8, 128.9, 128.4, 99.8, 58.2, 47.1, 40.3, 32.0; HRMS (TOF MS ES+) calcd for $C_{10}H_{15}F_3IN_2$ [M+H]: 291.03585, found 291.03462.

1-(2-iodobenzyl)hexahydropyrimidine (**S3**). To a solution of **S2** (3.98 g, 13.7 mmol) in 95% EtOH (35 mL, 0.4 M) were added 30% aqueous NaOH (0.36 mL, 2.7 mmol), and 36% aqueous formaldehyde (1.95 g, 23.4 mmol). The reaction mixture was heated to reflux for 1 hour. At this time, TLC indicated the consumption of the diamine. After cooling to rt, the reaction mixture was diluted with EtOAc, washed with saturated aqueous NaCl, dried over $MgSO_4$, and concentrated. Purification by FCC (9:1 EtOAc:10% NH_4OH in MeOH) to give **S3** (2.86 g, 9.48 mmol, 69%) as a colorless oil.

Data for **S3**: R_f 0.48 (4:1 EtOAc:10% NH_4OH in MeOH); IR (thin film) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 8.0, 0.8 Hz, 1 H), 7.42 (dd, *J* = 7.6, 1.2 Hz, 1 H), 7.33 (td, *J* = 7.6, 0.8 Hz, 1 H), 6.95 (td, *J* = 7.6, 1.6 Hz, 1 H), 3.50 (s, 2 H), 3.45 (s, 2 H), 2.87 (t, *J* = 5.2 Hz, 2 H), 2.67 (t, *J* = 4.6 Hz, 2 H) 1.63 (quintet, *J* = 5.2 Hz, 2 H); ^{13}C (100 MHz, $CDCl_3$) δ 140.6, 139.5, 130.2, 128.7, 128.0, 100.6, 69.6, 63.6, 53.1, 45.2, 27.2; HRMS (TOF MS ES+) calcd for $C_{11}H_{16}F_3IN_2$ [M+H]:3030358 , found 303.0353.

1-(3-(2-iodobenzyl)tetrahydropyrimidin-1(2*H*)-yl)ethanone (**S4**). To a solution of **S3** (0.112 g, 0.369 mmol) in CH_2Cl_2 (1.25 mL, 0.3 M) were added pyridine (0.06 mL, 0.7 mmol), and acetic anhydride (0.10 mL, 1.1 mmol). The reaction mixture was stirred at rt for 22 hours. At this time, TLC indicated the consumption of **S3**. The reaction mixture was concentrated. Purification by FCC (1:3 hexanes:EtOAc) to give **S4** (0.119 g, 0.344 mmol, 93%) as a clear colorless oil.

Data for **S4**: R_f 0.46 (EtOAc); IR (thin film) 2945, 2812, 1646, 1433, 753 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) as a 1.7:1 mixture of rotational isomers δ 7.85 (dd, *J* = 7.7, 1.4 Hz, 0.6 of 1 H), 7.81 (dd, *J* = 7.7, 1.4 Hz, 0.4 of 1 H), 7.47 (dd, *J* = 7.7, 2.1 Hz, 0.4 of 1 H), 7.41 (dd, *J* = 7.7, 1.4 Hz, 0.4 of 1 H), 7.33 (qd, *J* = 8.4, 1.4 Hz, 1 H), 6.98 (td, *J* = 7.7, 1.4 Hz, 0.6 of 1 H), 6.94 (td, *J* = 7.7, 1.4 Hz, 0.4 of 1 H), 4.33 (s, 0.7 of 2 H), 4.05 (s, 1.3 of 2 H), 3.63 (t, *J* = 5.6 Hz, 1.3 of 2 H), 3.59 (s, 2 H), 3.53 (t, *J* = 5.6 Hz, 0.7 of 2 H), 2.82 (t, *J* = 5.6 Hz, 0.7 of 2 H), 2.79 (t, *J* = 5.6 Hz, 1.3 of 2 H), 2.13 (s, 1.1 of 3 H), 1.95 (s, 1.9 of 3 H), 1.72-1.74 (m, 0.7 of 2 H), 1.68 (quintet, *J* = 5.6 Hz, 1.3 of 2 H), ; ^{13}C (176 MHz, $CDCl_3$) δ 169.4 (0.6 of 1 C), 169.1 (0.4 of 1 C), 140.3 (0.4 of 1 C), 119.9 (0.6 of 1 C), 139.7 (0.6 of 1 C), 139.4 (0.4 of 1 C), 130.4 (0.4 of 1 C), 130.1 (0.6 of 1 C), 129.2 (0.6 of 1 C), 128.9 (0.4 of 1 C), 128.3 (0.4 of 1 C), 128.2 (0.4 of 1 C), 100.6 (0.4 of 1 C), 100.5 (0.6 of 1 C), 67.6 (0.6 of 1 C), 62.7 (0.4 of 1 C), 61.9 (0.6 of 1 C), 61.4 (0.4 of 1 C), 52.5 (0.6 of 1 C), 51.6 (0.4 of 1 C), 46.2 (0.4 of 1 C), 41.7 (0.4 of 1 C), 23.7 (0.4 of 1 C), 23.6 (0.6 of 1 C), 21.5 (0.4 of 1

C), 21.2 (0.6 of 1 C); HRMS (TOF MS ES+) calcd for $C_{13}H_{17}IN_2O$ [M+]: 344.03860, found 344.03787.

methyl 3-(1-acetyl-3-benzylhexahydropyrimidin-2-yl)propanoate (**69**)**.** To a solution of **S4** (0.172 g, 0.501 mmol) in benzene (3.0 mL, 0.17 M) were added methyl acrylate (0.22 mL, 2.4 mmol), 10% benzyl thiol in benzene (0.06 mL, 0.05 mmol). This solution was heated to reflux. In a separate flask were combined tributyltin hydride (0.27 mL, 1.0 mmol), AIBN (0.0163 g, 0.0993 mmol), and benzene (2.0 mL, 0.50 M). The tributyltin hydride solution was then added to the refluxing mixture via syringe pump over a period of 3 hours. The mixture was heated at reflux for an additional 10 hours. At this time, TLC indicated the consumption of **S4**. After cooling to rt, the mixture was diluted with MeCN, washed with hexanes, and concentrated. Purification by FCC (1:4 hexanes:EtOAc) to give **69** (0.118 g, 0.386 mmol, 77%) as a colorless oil.

Data for **69**: R_f 0.43 (EtOAc); IR (thin film) 2949, 1736, 1641 cm^{-1}; ^1H NMR (700 MHz, DMSO D_6) δ 7.34-7.52 (m, 5 H), 3.91 (d, *J* = 4 Hz, 1 H), 3.69-3.79 (m, 4 H), 3.25-3.31 (m, 1 H), 2.90 (s, 3 H), 2.77-2.83 (m, 1 H), 2.65-2.67 (m, 2 H), 2.37-2.45 (m, 2 H), 2.03-2.12 (m, 4 H), 1.44-1.47 (m, 1 H); ^{13}C (176 MHz, $CDCl_3$) δ 174.0 (0.5 of 1 C), 173.4 (0.5 of 1 C), 169.5, 139.1 (0.5 of 1 C), 138.7 (0.5 of 1 C), 129.0 (0.5 of 1 C), 128.7 (0.5 of 1 C), 128.5 (0.5 of 1 C), 128.3 (0.5 of 1 C), 127.5 (0.5 of 1 C), 127.1 (0.5 of 1 C), 70.4 (0.5 of 1 C), 67.3 (0.5 of 1 C), 57.2 (0.5 of 1 C), 56.8 (0.5 of 1 C), 51.6, 44.0 (0.5 of 1 C), 42.4 (0.5 of 1 C), 41.4 (0.5 of 1 C), 35.8 (0.5 of 1 C), 30.7 (0.5 of 1 C), 29.9 (0.5 of 1 C), 24.6 (0.5 of 1 C), 24.0 (0.5 of 1 C), 21.6 (0.5 of 1 C), 21.1 (0.5 of 1 C), 20.0 (0.5 of 1 C), 19.6 (0.5 of 1 C); HRMS (TOF MS ES+) calcd for $C_{17}H_{25}N_2O_3$ [M+H]: 305.1865, found 305.1876.

methyl 3-(1-acetyl-3-benzylhexahydropyrimidin-2-yl)propanoate (**69**)**.** To a solution of **S4** (0.188 g, 0.545 mmol) in benzene (5.4 mL, 0.1 M) were added methyl

acrylate (0.25 mL, 2.8 mmol), a 5% solution of benzyl thiol in benzene (0.13 mL, 0.055 mmol), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilane (0.34 mL, 1.1 mmol), and AIBN (0.0178 g, 0.108 mmol). The reaction mixture was heated to reflux for 18 hours. At this time, TLC indicated the consumption of **S4**. The reaction mixture was cooled to rt, diluted with MeCN, washed with hexanes, and concentrted. Purification by FCC (1:4 hexanes:EtOAc) to give **69** (0.0471 g, 0.155 mmol, 28%) as a colorless oil.

2,2,2-trifluoro-1-(3-(2-iodobenzyl)tetrahydropyrimidin-1(2*H*)-yl)ethanone (**S5**). To a solution of **S3** (0.126 g, 0.417 mmol) in dry Et_2O (1.5 mL, 0.3 M) were added triethylamine (0.07 mL, 0.5 mmol), and trifluoroacetic anhydride (0.07 mL, 0.5 mmol). The reaction mixture was stirred at rt for 10 minutes. At this time, TLC indicated the consumption of **S3**. The reaction mixture was concentrated. Purification by FCC (4:1 hexanes:EtOAc) to give **S5** (0.126 g, 0.316 mmol, 76%) as a colorless oil.

Data for **S5**: R_f 0.61 (1:2 EtOAc:hexanes); IR (thin film) 2952, 1694, 752 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) as a 1.2:1 mixture of rotational isomers δ 7.86 (ddd, *J* = 7.7, 3.5, 0.7 Hz, 1 H), 7.44 (dd, *J* = 7.7, 1.4 Hz, 0.6 of 1 H), 7.35-7.39 (m, 1.4 of 2 H), 7.00 (qd, *J* = 7.7, 1.4 Hz, 1 H), 4.46 (s, 1.2 of 2 H), 4.35 (s, 0.8 of 2 H), 3.76 (t, *J* = 5.6 Hz, 0.8 of 2 H), 3.74 (t, *J* = 5.6 Hz, 1.2 of 2 H), 3.72 (s, 1.2 of 2 H), 3.70 (s, 0.8 of 2 H), 2.96 (t, *J* = 5.6 Hz, 1.2 of 2 H), 2.85 (t, *J* = 5.6 Hz, 0.8 of 2 H), 1.82 (sextet, *J* = 5.6 Hz, 2 H); ^{13}C (176 MHz, $CDCl_3$) δ 155.8 (q, *J* = 35.2 Hz, 0.6 of 1 C), 155.6 (q, *J* = 35.2 Hz, 0.4 of 1 C), 139.8 (0.4 of 1 C), 139.7 (0.6 of 1 C), 139.6 (0.6 of 1 C), 139.4 (0.4 of 1 C), 130.4 (0.6 of 1 C), 130.1 (0.4 of 1 C), 129.2 (0.4 of 1 C), 129.1 (0.6 of 1 C), 128.3 (0.6 of 1 C), 128.2 (0.4 of 1 C), 116.5 (q, *J* = 288.6 Hz, 0.6 of 1 C), 116.3 (q, *J* = 288.6 Hz, 0.4 of 1 C), 100.6 (0.6 of 1 C), 100.3 (0.4 of 1 C), 66.8 (q, *J* = 3.52 Hz, 0.4 of 1 C), 64.1 (0.6 of 1 C), 61.2 (0.4 of 1 C), 60.7 (0.6 of 1 C), 51.7 (0.6 of 1 C), 50.9 (0.4 of 1 C), 45.9 (0.4 of 1 C), 45.8 (0.6 of 1 C), 45.3 (1 C), 23.2

(0.6 of 1 C), 22.6 (0.4 of 1 C); HRMS (TOF MS ES+) calcd for $C_{13}H_{14}F_3IN_2O$ [M+]: 398.01033, found 398.00872.

methyl 3-(1-benzyl-3-(2,2,2-trifluoroacetyl)hexahydropyrimidin-2-yl)propanoate (70). To a solution of **S5** (0.1902 g, 0.478 mmol) in benzene (2.8 mL, 0.17 M) were added methyl acrylate (0.43 mL, 4.8 mmol), 10% benzyl thiol in benzene (0.05 mL, 0.04 mmol). This solution was heated to reflux. In a separate flask were combined tributyltin hydride (0.27 mL, 1.0 mmol), AIBN (0.0158 g, 0.0962 mmol), and benzene (2.0 mL, 0.50 M). The tributyltin hydride solution was then added to the refluxing mixture via syringe pump over a period of 3 hours. At this time, TLC indicated the consumption of **S5**. After cooling to rt, the mixture was diluted with MeCN, washed with hexanes, and concentrated. Purification by FCC (7:1 hexanes:EtOAc) to give **70** (0.118 g, 0.329 mmol, 69%) as a colorless oil.

Data for **70**: R_f 0.46 (1:2 EtOAc:hexanes); IR (thin film) 2955, 1738, 1693, 1437, 756 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) as a mixture of rotational isomers δ 7.19-7.36 (m, 5 H), 6.22 (d, *J* = 2.1 Hz, 1 H), 5.62 (d, *J* = 2.1 Hz, 1 H), 4.27-4.64 (m, 2 H), 3.78 (s, 1.5 H), 3.70-3.68 (m, 2 H), 3.67 (m, 1.5 H) 3.02 (td, *J* = 13.3 4.2 Hz; 0.5 H), 2.32-2.84 (m, 3.5 H), 1.89-1.97 (m, 0.5 H), 1.28-1.78 (m, 0.5 H), 0.89-0.96 (m, 2 H); ^{13}C (176 MHz, $CDCl_3$) δ 175.1, 173.9, 173.2, 167.0, 138.1, 137.5, 130.5, 129.5, 129.0, 128.5, 128.4, 128.4, 128.0, 127.4, 127.2, 129.3, 126.2, 64.3, 60.0, 56.2, 56.1, 55.5, 55.3, 52.0, 51.7, 51.6, 51.1, 50.9, 43.8, 43.4, 40.5, 35.5, 35.8, 34.7, 31.6, 30.6, 30.5, 29.1, 27.8, 27.6, 27.0, 26.6, 25.6, 24.7, 23.3, 23.0; HRMS (TOF MS ES+) calcd for $C_{17}H_{22}F_3N_2O_3$ [M+H]: 359.1583, found 359.1575.

methyl 3-(1-benzyl-3-(2,2,2-trifluoroacetyl)hexahydropyrimidin-2-yl)propanoate (70). To a solution of **S5** (0.2001 g, 0.504 mmol) in benzene (5.0 mL, 0.1 M) were added methyl acrylate (0.23 mL, 2.6 mmol), a 5% solution of benzyl thiol in benzene (0.12 mL, 0.051 mmol), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilane (0.31 mL,

1.0 mmol), and AIBN (0.0168 g, 0.102 mmol). The reaction mixture was heated to reflux for 19 hours. At this time, TLC indicated the consumption of **S5**. The reaction mixture was cooled to rt, diluted with MeCN, washed with hexanes, and concentrted. Purification by FCC (7:1 hexanes:EtOAc) to give **70** (0.0176 g, 0.0491 mmol, 10%) as a colorless oil.

tert-butyl (3-((2-iodobenzyl)amino)-3-oxopropyl)carbamate (**S6**). To a solution of known 3-((tert-butoxycarbonyl)amino)propanoic acid[58] (0.332 g, 1.75 mmol) in DCM (4.4 mL, 0.4 M) were added HOBt (2.66 g, 1.97 mmol), DCC (0.398 g, 1.93 mmol), and known (2-iodophenyl)methanamine (0.451 g, 1.94 mmol). The reaction mixture was stirred at rt for 7 hours. After filtration though celite to remove the solids, the reaction mixture was washed with 1 M aqueous citric acid, saturated aqueous $NaHCO_3$, and saturated aqueous NaCl. The organics were dried over $MgSO_4$ and concentrated. Purification by FCC (1:1 EtOAc:hexanes) to give **S7** (0.289 g, 0.715 mmol, 41%) as a white solid.

Data for **S6**: R_f 0.44 (2:1 EtOAc:Hexanes); mp = 147.8-149.0 ℃; IR (thin film) 3308, 3062, 2975, 2930, 1693, 1651, 1525, 1169, 748 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.85 (d, *J* = 7.7 Hz, 1 H), 7.34-7.39 (m, 1 H), 7.01 (t, *J* = 7.7 Hz, 1 H), 6.13 (bs, 1 H), 5.18 (br s, 1 H), 4.49 (d, *J* = 5.6 Hz, 2 H), 3.45 (q, *J* = 6.3 Hz 2 H), 2.48 (t, *J* = 4.9 Hz 2 H), 1.44 (s, 9 H); ^{13}C (176 MHz, $CDCl_3$) δ 171.3, 156.1, 140.2, 139.6, 129.8, 129.5, 128.7, 99.1, 79.4, 48.3, 36.7, 36.2, 28.4: HRMS (TOF MS ES+) calcd for $C_{10}H_{14}IN_2O$ [M-Cl+H]: 305.0151, found 305.0155.

3-((2-iodobenzyl)amino)-3-oxopropan-1-aminium chloride (**S7**). To a solution of **S6** (0.156 g, 0.512 mmol) in MeOH (6 mL, 0.1 M) was added TMSCl (0.40 mL, 3.2 mmol). The reaction mixture was stirred at rt for 47 hours. At this time, TLC indicated the consumption of **S6**. The reaction mixture was concentrated to give **S7** (0.156 g, 0.512 mmol, 82%) as a white solid.

Data for **S7**: R_f 0.58 (10% NH_4OH in MeOH); mp = 161-163 ℃; IR (thin film) 1627, 1108, 748 cm^{-1}; ^1H NMR (700 MHz, CD_4O) δ 7.89 (dd, *J* = 7.7, 0.7 Hz, 1 H), 7.36-7.41 (m, 2 H), 7.04 (td, *J* = 7.7, 2.1 Hz, 1 H), 4.44 (s, 2 H), 3.24 (t, *J* = 7.0 Hz, 2 H), 2.72 (t, *J* = 7.0 Hz, 2 H); ^{13}C (176 MHz, $CDCl_3$) δ 170.7, 140.0, 139.3, 128.9, 128.5, 128.2, 97.8, 48.1, 35.7, 31.2; HRMS (TOF MS ES+) calcd for $C_{10}H_{14}IN_2O$ [M+]: 305.0151, found 305.0155.

3-(2-iodobenzyl)tetrahydropyrimidin-4(1H)-one (**S8**). To a solution of 3-((2-iodobenzyl)amino)-3-oxopropan-1-aminium chloride (**S7**) (0.322 g, 0.946 mmol) in EtOH (3.2 mL, 0.3 M) were added 30% aqueous NaOH (0.20 mL, 1.5 mmol), and 36% aqueous formaldehyde (0.993 g, 1.19 mmol). This mixture was heated to reflux for 22 hours. After cooling to rt, the mixture was diluted with EtOAc and washed with saturated aqueous NaCl prior to drying with $MgSO_4$. Purification by FCC (19:1 EtOAc:10% NH_4OH in MeOH) to give **S8** (0.180g, 0.510 mmol, 54%) as a colorless oil.

Data for **S8**: R_f 0.52 (EtOAc:10% NH_4OH in MeOH); IR (thin film) 2924, 2855, 1634, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.87 (dd, *J* = 8.0, 1.2 Hz, 1 H), 7.34 (dt, *J* = 7.6, 1.2 Hz, 1 H), 7.24 (dd, *J* = 7.6, 1.2 Hz, 1 H), 6.96 (dt, *J* = 7.6, 1.6 Hz, 1 H), 4.66 (s, 2 H), 4.20 (s, 2 H), 3.20 (t, *J* = 6.4 Hz, 2 H), 2.52 (t, *J* = 6.4 Hz 2 H); ^{13}C (176 MHz, $CDCl_3$) δ 168.2, 139.7, 138.7, 129.2, 128.7, 128.4, 99.0, 63.2, 52.0, 42.6, 33.4; HRMS (TOF MS ES+) calcd for $C_{11}H_{14}N_2OI$ [M+H]: 317.0151, found 317.0138.

(*E*)-ethyl 6-(3-(2-iodobenzyl)-4-oxotetrahydropyrimidin-1(2*H*)-yl)hex-2-enoate (**S9**). To a solution of **S7** (0.426 g, 1.35 mmol) in DMF (4.0 mL, 0.3 M) were added K_2CO_3 (0.510 g, 3.69 mmol), tetrabutylammonium iodide (0.0894 g, 0.242 mmol), and known (*E*)-ethyl 6-bromohex-2-enoate[59] (0.827 g, 7.74 mmol). The reaction

mixture was heated to 80℃ 17 hours. At this time, TLC indicated the consumption of **S7**. The reaction mixture was cooled to rt, diluted with EtOAc, washed with saturated aqueous LiCl, washed with saturated aqueous NaCl, dried over $MgSO_4$, and concentrated. Purification by FCC (EtOAc) to give **S9** (0.3836 g, 0.0841 mmol, 62%) as a colorless oil.

Data for **S9**: R_f 0.50 (9:1 EtOAc:10% NH_4OH in MeOH); IR (thin film) 2951, 1733, 1666, 1492, 753 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.85 (dd, *J* = 7.7, 0.7 Hz, 1 H), 7.35 (td, *J* = 7.7, 0.7 Hz, 1 H), 7.25 (d, *J* = 7.0 Hz, 1 H), 7.00 (td, *J* = 7.7, 2.1 Hz, 1 H), 6.91 (dt, *J* = 15.4, 7.0 Hz,1 H), 4.64 (s, 2 H), 4.20 (q, *J* = 7.0 Hz, 2 H), 3.94 (s, 2 H), 2.98 (t, *J* = 7.0 Hz, 2 H), 2.58 (t, *J* = 6.3 Hz, 2 H), 2.53 (t, *J* = 7.0 Hz, 2 H), 2.21 (qd, *J* = 8.4, 0.7 Hz, 2 H), 1.54 (quintet, *J* = 7.7 Hz, 2 H), 1.30 (t, *J* = 7.0 Hz, 3 H); ^{13}C (176 MHz, $CDCl_3$) δ 168.1, 166.5, 148.1, 139.6, 138.6, 129.2, 128.7, 128.4, 121.9, 98.9, 67.9. 60.3, 52.3, 51.7, 48.4, 29.7, 29.6, 25.8, 14.3 HRMS (TOF MS ES+) calcd for $C_{19}H_{26}N_2O_3I$ [M+H]: 457.0988, found 457.0999.

ethyl 2-(1-benzyl-2-oxooctahydro-1*H*-pyrido[1,2-*a*]pyrimidin-9-yl)acetate (71). To a solution of **S9** (0.1884 g, 0.413 mmol) in benzene (2.1 mL, 0.20 M) were added 10% benzyl thiol in benzene (0.05 mL, 0.04 mmol). This solution was heated to reflux. In a separate flask were combined tributyltin hydride (0.22 mL, 0.82 mmol), AIBN (0.0133 g, 0.081 mmol), and benzene (2.0 mL, 0.41 M). The tributyltin hydride solution was then added to the refluxing mixture via syringe pump over a period of 3 hours. At this time, TLC indicated the consumption of **S9**. After cooling to rt, the mixture was diluted with MeCN, washed with hexanes, and concentrated. Purification by FCC (4:1 hexanes:EtOAc) to give **71** (0.0737 g, 0.223 mmol, 54%) as a colorless oil.

Data for **71**: R_f 0.42 (EtOAc); IR (thin film) 2938, 2812, 1729, 1654, 1447, 703 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.33-7.34 (m, 2 H), 7.26-7.28 (m, 3 H), 5.50 (d, *J* =

15.4 Hz, 1 H), 4.12 (q, *J* = 7.7 Hz, 2 H), 3.99 (d, *J* = 15.4, 1 H), 3.41 (d, *J* = 2.1 Hz, 1 H), 2.88 (dt, *J* = 11.2, 2.1 Hz, 1 H), 2.70-2.77 (m, 2 H), 2.64-2.66 (m, 1 H), 2.46-2.51 (m, 3 H), 2.33 (ddd, *J* = 16.8, 2.8, 1.4 Hz, 1 H), 2.19 (ddd, *J* = 23.8, 11.9, 2.8 Hz, 1 H), 1.72-1.79 (m, 2 H), 1.34-1.42 (m, 2 H), 1.28 (t, *J* = 7.7 Hz, 3 H); ^{13}C (176 MHz, $CDCl_3$) δ 173.3, 169.9, 136.8, 128.6, 128.1, 127.2, 60.4, 55.5, 49.7, 44.2, 33.2, 32.0, 30.6, 26.5, 19.8, 14.3; HRMS (TOF MS ES+) calcd for $C_{19}H_{27}N_2O_3$ [M+]: 331.2022, found 331.2006.

ethyl 2-(5-benzyl-11-oxo-5a,6,7,8,9,11-hexahydro-5*H*-pyrido[2,1-*b*]quinazolin-6-yl)acetate (**71**)**.** To a solution of **S9** (0.155 g, 0.340 mmol) in benzene (3.4 mL, 0.1 M) were added 10% benzyl thiol in benzene (0.04 mL, 0.03 mmol), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilane (0.21 mL, 0.68 mmol), and AIBN (0.0120 g, 0.0730 mmol). The reaction mixture was heated to reflux for 2 hours. At this time, TLC indicated the consumption of **S9**. The reaction mixture was cooled to rt, diluted with MeCN, washed with hexanes, and concentrated. Purification by FCC (4:1 hexanes:EtOAc) to give **71** (0.0556 g, 0.168 mmol, 50%) as a colorless oil.

(*E*)-ethyl 6-(1-(2-iodobenzyl)-4-oxo-1,2-dihydroquinazolin-3(4*H*)-yl)hex-2-enoate (**S10**). To a solution of **60** (1.00 g, 2.75 mmol) in DMF (9.0 mL, 0.3 M) were added 57% NaH in mineral oil (0.234 g, 5.55 mmol) and known (*E*)-ethyl 6-bromohex-2-enoate (1.22 g, 5.50 mmol). The reaction mixture was heated to 80℃ 46 hours. The reaction mixture was cooled to rt, diluted with EtOAc, washed with saturated aqueous LiCl, washed with saturated aqueous NaCl, dried over $MgSO_4$, and concentrated. Purification by FCC (4:1 EtOAc:hexanes) to give **S10** (0.2212 g, 0.439 mmol, 16%) as a colorless oil.

Data for **S10**: R_f 0.43 (1:1 EtOAc:Hexanes); IR (thin film) 2929, 1714, 1651, 1494, 751 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.05 (dd, *J* = 7.7, 1.4 Hz, 1 H), 7.93 (d, *J* = 8.4 Hz, 1 H), 7.34-7.37 (m, 3 H), 7.04-7.07 (m, 1 H), 6.92-6.96 (m, 2 H), 6.67 (d, *J* =

8.4 Hz, 1 H), 5.83 (dt, *J* = 15.4, 1.4 Hz, 1 H), 4.53 (s, 2 H), 4.44 (s, 2 H), 4.19 (q, *J* = 7.0 Hz, 2 H), 3.53 (t, *J* = 7.0 Hz, 2 H), 2.26 (qd, *J* = 8.4, 1.4 Hz, 2 H), 1.71 (quintet, *J* = 7.0 Hz, 2 H), 1.30 (t, *J* = 7.0 Hz, 3 H); ^{13}C (176 MHz, $CDCl_3$) δ 166.6, 136.7, 148.0, 147.8, 140.0, 138.1, 133.4, 129.6, 129.3, 128.7, 128.6, 121.9, 119.6, 118.3, 113.05, 98.4, 64.3, 60.3, 58.2, 44.7, 29.5, 26.2, 14.3; HRMS (TOF MS ES+) calcd for $C_{23}H_{26}N_2O_3I$ [M+H]: 505.0988, found 505.0984.

ethyl 2-(5-benzyl-11-oxo-5a,6,7,8,9,11-hexahydro-5*H*-pyrido[2,1-*b*]quinazolin-6-yl)acetate (**72a and 72b**)**.** To a solution of **S10** (0.0520 g, 0.103 mmol) in benzene (0.40 mL, 0.26 M) were added 5% benzyl thiol in benzene (0.03 mL, 0.01 mmol). This solution was heated to reflux. In a separate flask were combined tributyltin hydride (0.06 mL, 0.2 mmol), AIBN (0.0039 g, 0.024 mmol), and benzene (0.6 mL, 0.3 M). The tributyltin hydride solution was then added to the refluxing mixture via syringe pump over a period of 3 hours. At this time, TLC indicated the consumption of **S10**. After cooling to rt, the mixture was diluted with MeCN, washed with hexanes, and concentrated. Purification by FCC (3:1 hexanes:EtOAc) to give a 1:1.6 mixture of **72a** (minor isomer) and **72b** (major isomer) (0.0238 g, 0.0629 mmol, 61%) as a colorles oil.

Data for **72a**: R_f 0.11 (2:1 Hexanes:EtOAc); IR (thin film) 2935, 1728, 1647, 754 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.97 (dd, *J* = 8.4, 2.1 Hz, 1 H), 7.30-7.37 (m, 5 H), 7.20 (ddd, *J* = 8.4, 7.7, 2.1 Hz, 1 H), 6.73 (td, *J* = 8.4, 1.4 Hz, 1 H), 6.45 (d, *J* = 8.4 Hz, 1 H), 5.03 (d, *J* = 2.8 Hz, 1 H), 4.94-4.96 (m, 1 H), 4.68 (d, *J* = 17.5 Hz, 1 H), 4.40 (d, *J* = 16.8 Hz, 1 H), 4.00-4.04 (m, 1 H), 3.86-3.91 (m, 1 H), 2.63-2.65 (m, 1 H), 2.57-2.61 (m, 2 H), 2.33 (dd, *J* = 7.7 Hz, 1 H), 1.87-1.88 (m, 1 H), 1.75-1.77 (m, 1 H), 1.48-1.52 (m, 1 H), 1.11 (t, *J* = 7.7 Hz, 3 H); ^{13}C (176 MHz, $CDCl_3$) δ 171.7, 163.5, 145.9, 137.2, 133.5, 128.8, 128.7, 127.7, 127.6, 120.0, 118.6, 117.0, 78.9, 60.6,

57.7, 45.5, 38.7, 37.3, 31.4, 24.5, 14.1; HRMS (TOF MS ES+) calcd for $C_{23}H_{27}N_2O_3$ [M+H]: 379.2022, found 379.2015.

Data for **72b**: R_f 0.11 (2:1 Hexanes:EtOAc); IR (thin film) 2933, 1730, 1646, 750.3 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.08 (dd, *J* = 7.6, 1.6 Hz, 1 H), 7.25-7.35 (m, 6 H), 6.92 (t, *J* = 7.2 Hz, 1 H), 6.78 (d, *J* = 8.4 Hz, 1 H), 4.80 (d, *J* = 15.6 Hz, 1 H), 4.69-4.74 (m, 1 H), 4.34-4.38 (m, 2 H), 3.97-4.15 (m, 2 H), 2.58 (td, *J* = 12.8, 3.2 Hz, 1 H), 2.38-2.50 (m, 2 H), 2.11 (dd, *J* = 6.0 Hz, 1 H), 1.95-2.01 (m, 1 H), 1.67-1.78 (m, 1 H), 1.60-1.63 (m, 1 H), 1.33-1.44 (m, 1 H), 1.15 (t, *J* = 7.2 Hz, 3 H); ^{13}C (176 MHz, $CDCl_3$) δ 172.5, 161.5, 145.8, 136.5, 133.8, 129.0, 128.9, 127.5, 126.6, 117.2, 113.8, 110.9, 77.3, 60.6, 50.6, 44.1, 36.2, 31.2, 31.4, 29.2, 19.9, 14.0; HRMS (TOF MS ES+) calcd for $C_{23}H_{27}N_2O_3$ [M+H]: 379.2022, found 379.2015.

ethyl 2-(5-benzyl-11-oxo-5a,6,7,8,9,11-hexahydro-5*H*-pyrido[2,1-*b*]quinazolin-6-yl)acetate (**72a and 72b**)**.** To a solution of **S10** (0.0619 g, 0.123 mmol) in benzene (1.2 mL, 0.1 M) were added benzyl thiol (0.01 mL, 0.1 mmol), 1,1,1,3,3,3-hexamethyl-2-(trimethylsilyl)trisilane (0.08 mL, 0.3 mmol), and AIBN (0.0059 g, 0.036 mmol). The reaction mixture was heated to reflux for 18 hours. At this time, TLC indicated the consumption of **S10**. The reaction mixture was cooled to rt, diluted with MeCN, washed with hexanes, and concentrted. Purification by FCC (3:2 hexanes:EtOAc) to give a 1:1.6 mixture of **72a** and **72b** (0.0227 g, 0.0600 mmol, 49%) as a colorless oil.

(*S*)-*tert*-butyl-2-((2-iodobenzyl)carbamoyl)piperidine-1-carboxylate (S11). To a solution of commercially available (*S*)-1-(*tert*-butoxycarbonyl)piperidine-2-carboxylic acid (700 mg, 3.06 mmol) in CH_2Cl_2 (6.1 mL) at 0 °C were added Et_3N (0.90 mL, 6.42 mmol) and isobutylchloroformate (0.44 mL, 3.36 mmol) dropwise. The mixture was stirred at 0 °C for one hour then 2-iodobenzylamine (783 mg, 3.36 mmol) was added. The solution was warmed to rt and stirred for 10 hours. The

mixture was washed with 1 M HCl, saturated sodium bicarbonate solution, and brine and dried over Na_2SO_4. Purification by FCC (8:1 Hexanes:EtOAc) afforded **S11** (1.26 g, 2.83 mmol, 93%) as a white foam.

Data for **S11**: R_f 0.24 (6:1 Hexanes:EtOAc); IR (thin film) 3327, 2975, 2937, 1684, 1665, 1410, 1366, 1161 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$), δ 7.85 (d, *J* = 7.7 Hz, 1 H), 7.35 (m, 2 H), 7.01 (t, *J* = 7.35 Hz, 1 H), 6.56 (br s, 1 H), 4.80 (br s, 1 H), 4.50 (br s, 2 H), 4.08 (br s, 1 H), 2.80 (br s, 1 H), 2.36 (br s, 1 H), 1.60 (m, 5 H), 1.46 (s, 9 H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 171.1, 156.0, 140.4, 139.5, 129.6, 129.4, 128.6, 99.0, 80.7, 55.9, 54.0, 48.2, 42.6, 41.5, 28.4, 25.3, 24.9, 20.6; HRMS (TOF MS ES+) calcd for [M+Na]: $C_{18}H_{25}IN_2O_3$ 467.0802, found 467.0808; $[\alpha]_D^{24}$ = –60.5 (*c* 1.0, $CHCl_3$).

(*S*)-*tert*-butyl 2-((2-iodobenzyl)carbamoyl)piperidine-1-carboxylate (S12). S11 (1.25 g, 2.82 mmol) was dissolved in 20% TFA in CH_2Cl_2 (5.9 mL, 0.48 M). The mixture was stirred at rt for 17 hours and diluted with 2 mL CH2Cl2. The mixture was made basic with 1 M NaOH until pH > 9. The aqueous layer was extracted with CH_2Cl_2, dried over Na2SO4, and concentrated to give **S12** (929 mg, 2.70 mmol, 96%) as a yellow oil.

Data for **S12**: R*f* 0.19 (EtOAc); IR (thin film) 3283 (br), 3058, 2934, 1662, 1552, 1523, 1013 cm-1; ^1H NMR (700 MHz, $CDCl_3$), δ 7.83 (d, *J* = 7.7 Hz, 1 H), 7.77 (s, 1 H), 7.31 (m, 2 H), 6.97 (m, 1 H), 4.48 (dd, *J* = 15.4, 6.3 Hz, 1 H), 4.37 (dd, *J* = 15.4, 5.6 Hz, 1 H), 3.62 (s, 1 H), 3.11 (d, *J* = 11.9 Hz, 1 H), 2.91 (t, *J* = 10.9 Hz, 1 H), 1.99 (d, *J* = 10.5 Hz, 1 H), 1.70 (m, 1 H), 1.62 (m, 1 H), 1.52 (m, 2 H), 1.35 (m, 1 H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 172.4, 140.2, 139.4, 129.1, 128.8, 128.5, 98.5, 59.2, 48.0, 44.8, 29.3, 24.4, 23.0; HRMS (EI+) calcd for [M+]: $C_{13}H_{17}IN_2O$ 344.0373, found 344.0386; $[\alpha]_D^{24}$ = –27.0 (*c* 1.0, $CHCl_3$).

(*S*)-2-(2-iodobenzyl)hexahydroimidazo[1,5-*a*]pyridin-1(5*H*)-one (**S13**)**.** To a solution of (*S*)-*N*-(2-iodobenzyl)piperidine-2-carboxamide (**S12**) (928 mg, 2.70 mmol) in formalin (36% in water, 11 mL, 0.668 M) was added K_2CO_3 (447 mg, 5.6 mmol) and stirred for 12 hours at rt. The mixture was diluted with EtOAc and washed with $NaHSO_3$ and brine and dried over sodium sulfate. Purification via FCC (10:1 EtOAc:MeOH) afforded **S13** (1.39g, 4.06 mmol, 87%) as a yellow oil.

Data for **S13**: R_f 0.58 (10:1 EtOAc:MeOH); IR (thin film) 2936, 1707, 1438, 1012 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$), 7.84 (dd, *J* = 7.9, 1 Hz, 1 H), 7.34 (ddd, *J* =8.4, 7.6, 1.1 Hz, 1 H), 7.29 (dd, *J* = 7.6, 1.4 Hz, 1 H), 7.00 (ddd, *J* = 9.1, 7.7, 1.7 Hz, 1 H), 4.59 (dd, *J* = 52.5, 15.4 Hz, 2 H), 4.11 (d, *J* = 5.4 Hz, 1 H), 3.84 (dd, *J* = 5.4, 2.1 Hz, 1 H), 2.85 (m, 2 H), 2.42 (m, 1 H), 2.01 (m, 1 H), 1.80 (m, 1 H), 1.70 (s, 1 H), 1.63 (m, 3 H), 1.40 (m, 1 H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 173.0, 139.6, 138.5, 129.5, 129.3, 128.8, 98.9, 67.7, 63.2, 49.9, 49.6, 24.8, 24.3, 23.2; HRMS (TOF MS ES+) calcd for $C_{14}H_{17}IN_2O$ [M+H]: 357.0458, found 357.0464; $[\alpha]_D^{24}$ = +13.9 (*c* 1.0, $CHCl_3$).

Methyl-3-((8a*S*)-2-benzyl-1-oxooctahydroimidazo[1,5-*a*]pyridin-3-yl)-propanoate (**73**)**.** To a solution of **S13** (105 mg, 0.296 mmol) in PhH (1.5 mL, 0.2 M) were added methyl acrylate (0.13 mL, 1.478 mmol) and benzyl thiol (5% solution in PhH, 0.62 mL, 0.266 mmol) and heated to reflux. To the refluxing miture was added a solution of AIBN (9.7 mg, 0.059 mmol) and Bu_3SnH (0.16 mL, 0.591 mmol) in PhH (1.5 mL, 0.2 M) via syringe pump over 3 hours. After the addition was complete, the mixture was cooled to room temperature and the solvent evaporated. Purification via FCC (3:2 Hex:EtOAc then EtOAc only) afforded **73** (64 mg, 0.201 mmol, 68% as a single diastereomer) as a yellow oil.

Data for **73**: R_f 0.48 (1:1 CH_2Cl_2:EtOAc); IR (thin film) 2924, 2849, 1735, 1553, 1440 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$), δ 7.36 (m, 2 H), 7.31 (m, 3 H), 5.06 (d, *J* =

15.4 Hz, 1 H), 4.08 (t, *J* = 8.4 Hz, 1 H), 3.88 (d, *J* = 14.7 Hz, 1 H), 3.68 (s, 3 H), 3.55 (m, 1 H), 2.68 (m, 1 H), 2.57 (m, 1 H), 2.38 (m, 1 H), 2.24 (m, 1 H), 1.93 (m, 2 H), 1.83 (m, 1 H), 1.66 (m, 2 H), 1.49 (m, 1 H), 1.39 (m, 2 H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 173.9, 173.8, 136.3, 128.8, 128.3, 127.8, 74.3, 58.5, 51.7, 46.6, 43.8, 27.9, 24.4, 24.0, 22.5, 22.2; HRMS (TOF MS ES+) calcd for $C_{18}H_{24}N_2O_3$ [M+H]: 317.1858, found 317.1865; $[\alpha]_D^{24}$ = +13.6 (*c* 0.45, $CHCl_3$).

Methyl-3-((8a*S*)-2-benzyl-1-oxooctahydroimidazo[1,5-*a*]pyridin-3-yl)-propanoate (**73**)**.** To a solution of **S13** (97 mg, 0.272 mmol) in PhH (2.7 mL, 0.1 M) were added AIBN (9 mg, 0.054 mmol), methyl acrylate (0.12 mL, 1.360 mmol) and benzyl thiol (5% solution in PhH, 0.57 mL, 0.245 mmol) and $(TMS)_3SiH$ (0.17 mL, 0.544 mmol) and heated to reflux. After the reaction was complete, the mixture was cooled to room temperature and the solvent evaporated. Purification via FCC (3:2 Hex:EtOAc then EtOAc only) afforded **73** (24 mg, 0.075 mmol, 28% as a single diastereomer) as a yellow oil.

3-((8a*S*)-2-benzyl-1-oxooctahydroimidazo[1,5-*a*]pyridin-3-yl)propanenitrile (**74**)**.** To a solution of **S13** (99 mg, 0.278 mmol) in PhH (1.3 mL, 0.21 M) were added acrylonitrile (0.09 mL, 1.391 mmol) and benzyl thiol (5% solution in PhH, 0.07 mL, 0.028 mmol) and heated to reflux. To the refluxing mixture was added a solution of AIBN (9 mg, 0.0556 mmol) and Bu_3SnH (0.15 mL, 0.556 mmol) in PhH (1.5 mL, 0.2 M) via syringe pump over 3 hours. After the addition was complete, the mixture was cooled to room temperature and the ! S23! solvent evaporated. Purification via FCC (1:1 EtOAc:CH_2Cl_2) afforded **74** (53 mg, 0.188 mmol, 68% as a single diastereomer) as a yellow oil.

Data for **74**: R_f 0.52 (1:1 CH_2Cl_2:EtOAc); IR (thin film) 2939, 2860, 2248, 1702, 1439 cm^{-1}; $_1$H NMR (400 MHz, $CDCl_3$), δ 7.36 (m, 5 H), 4.94 (d, *J* = 15 Hz, 1 H), 4.19 (t, *J* = 3.4 Hz, 1 H), 4.0 (d, *J* = 15 Hz, 1 H), 3.59 (dd, *J* = 8.4, 4.9 Hz, 1 H), 2.8

(m, 1 H), 2.60 (m, 1 H), 2.41 (m, 1 H), 2.17 (m, 1 H), 1.87 (m, 2 H), 1.57 (m, 4 H), 1.40 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0, 136.0, 129.0, 128.2, 128.1, 119.6, 73.3, 58.4, 46.1, 44.2, 24.9, 24.3, 22.2, 22.1, 10.8; HRMS (TOF MS ES+) calcd for $C_{17}H_{21}N_3O$ [M+H]: 284.1763, found 284.1763; $[\alpha]_D^{24}$ = +5.4 (*c* 0.5, $CHCl_3$).

3-((8a*S*)-2-benzyl-1-oxooctahydroimidazo[1,5-*a*]pyridin-3-yl)propanenitrile (**74**)**.** To a solution of **S13** (85 mg, 0.238 mmol) in PhH (2.4 mL, 0.1 M) were added, acrylonitrile (0.08 mL, 1.189 mmol), benzyl thiol (10% solution in PhH, 0.02 mL, 0.024 mmol), AIBN (8 mg, 0.048 mmol), and $(TMS)_3SiH$ (0.15 mL, 0.476 mmol) and heated to reflux. After the reaction was complete, the mixture was cooled to room temperature and the solvent evaporated. Purification via FCC (1:1 EtOAc:CH_2Cl_2) afforded **74** (11 mg, 0.039 mmol, 16%, dr not determined) as a yellow oil.

(*S*)-2-(2-iodobenzyl)hexahydro-1*H*-pyrrolo[1,2-*c*]imidazol-1-one (**S14**)**.** To a solution of known (*S*)-*N*-(2-iodobenzyl)pyrrolidine-2-carboxamide (1.54 g, 4.67 mmol) in formalin (36% in water, 19 mL, 0.668 M) was added K_2CO_3 (774 mg, 5.6 mmol) and stirred for 12 hours at room temperature. The mixture was diluted with EtOAc and washed with $NaHSO_3$ and brine and dried over sodium sulfate. Purification via FCC (10:1 EtOAc:MeOH) afforded **S14** (1.39g, 4.06 mmol, 87%) as a light yellow oil.

Data for **S14**: R_f 0.17 (10:1 EtOAc:MeOH); IR (thin film) 3464 (br), 2966, 2874, 1693, 1443, 1287 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$), δ 7.88 (dd, *J* = 7.9, 1.2 Hz, 1 H), 7.36 (ddd, *J* = 8.7, 7.6, 1.2 Hz, 1 H), 7.26 (dd, *J* = 7.7, 1.6 Hz, 1 H), 7.02 (ddd, *J* = 9.3, 7.7, 1.7, 1 H), 4.74 (d, *J* = 15.2 Hz, 1 H), 4.45 (d, *J* = 8.2 Hz, 1 H), 4.38 (d, *J* = 15.2 Hz, 1 H), 3.97 (d, *J* = 8.2 Hz, 1 H), 3.82 (dd, *J* = 8.8, 4.6 Hz, 1 H), 3.16 (m, 1 H), 2.56 (m, 1 H), 2.14 (m, 2 H), 1.82 (m, 2 H); ^{13}C NMR (100 MHz, CDCl3) δ 175.0,

139.8, 138.3, 129.6, 129.2, 128.8, 98.9, 69.9, 65.2, 56.3, 50.0, 27.7, 25.3; HRMS (TOF MS ES+) calcd for $C_{13}H_{15}IN_2O$ [M+H]: 343.0315, found 343.0307; $[\alpha]_D^{24}$ = –14.3 (*c* 1.0, $CHCl_3$).

Methyl-3-((3*R*,7a*S*)-2-benzyl-1-oxohexahydro-1*H*-pyrrolo[1,2-*c*]imidazol-3-yl)propanoate (**75**)**.** To a solution of **S14** (101 mg, 0.295 mmol) in PhH (1.5 mL, 0.2 M) were added methyl acrylate (0.13 mL, 1.48 mmol) and benzyl thiol (5% solution in PhH, 0.07 mL, 0.0295 mmol) and heated to reflux. To the refluxing mixture was added a solution of AIBN (9.7 mg, 0.059 mmol) and Bu_3SnH (0.16 mL, 0.591 mmol) in PhH (1.5 mL, 0.2 M) via syringe pump over 3 hours. After the addition was complete, the mixture was cooled to room temperature and the solvent evaporated. Purification via FCC (10:1 EtOAc:MeOH) afforded **75** (41 mg, 0.135 mmol, 46% as a single diastereomer) as a yellow oil.

Data for **75**: R_f 0.32 (4:1 EtOAc:CH2Cl2); IR (thin film) 2944, 1735, 1694, 1438, 1259, 1166 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$), δ 7.36 (m, 2 H), 7.32 (m, 1H), 7.25 (m, 2 H), 5.04 (d, J = 14.7 Hz, 1 H), 3.90 (m, 1 H), 3.88 (d, J = 15.4 Hz, 1 H), 3.83 (dd, J = 9.1, 4.9 Hz, 1 H), 3.67 (s, 3 H), 3.03 (dd, J = 9.8, 5.6 Hz, 1 H), 2.42 (t, J = 7.4 Hz, 2 H), 2.40 (m, 1 H), 2.15 (m, 1 H), 2.02 (m, 2 H), 1.75 (m, 2 H), 1.68 (m, 1 H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 174.6, 173.6, 136.1, 128.8, 128.1, 127.8, 78.8, 64.0, 56.2, 51.7, 44.0, 29.0, 29.0, 28.1, 25.1; HRMS (TOF MS ES+) calcd for $C_{17}H_{22}N_2O_3$ [M+H]: 303.1715, found 303.1709; $[\alpha]_D^{24}$ = +10.9 (*c* 0.55, $CHCl_3$).

Methyl-3-((3*R*,7a*S*)-2-benzyl-1-oxohexahydro-1*H*-pyrrolo[1,2-*c*]imidazol-3-yl)propanoate (**75**)**.** To a solution of **S14** (102 mg, 0.299 mmol) in PhH (1.5 mL, 0.1 M) were added AIBN (9 mg, 0.060 mmol), methyl acrylate (0.13 mL, 1.49 mmol) and benzyl thiol (5% solution in PhH, 0.07 mL, 0.030 mmol), and $(TMS)_3SiH$ (0.18 mL, 0.60 mmol) and heated to reflux. After the reaction was complete, the mixture was cooled to room temperature and the solvent evaporated. Purification via FCC

(10:1 EtOAc:MeOH) afforded **75** (13 mg, 0.041 mmol, 4%, dr not determined) as a yellow oil.

3-((7a*S*)-2-benzyl-1-oxohexahydro-1*H*-pyrrolo[1,2-*c*]imidazol-3-yl)propanenitrile (76). To a solution of **S14** (107 mg, 0.311 mmol) in PhH (1.5 mL, 0.2 M) were added acrylonitrile (0.10 mL, 1.56 mmol) and benzyl thiol (10% solution in PhH, 0.06 mL, 0.062 mmol) and heated to reflux. To the refluxing mixture was added a solution of AIBN (10 mg, 0.062 mmol) and Bu_3SnH (0.17 mL, 0.623 mmol) in PhH (1.6 mL, 0.2 M) via syringe pump over 3 hours. After the addition was complete, the mixture was cooled to room temperature and the solvent evaporated. Purification via FCC (10:1 EtOAc:MeOH) afforded **76** (59 mg, 0.219 mmol, 50% as a single diastereomer) as a yellow oil.

Data for **76**: R_f 0.29 (1:1 CH_2Cl_2:EtOAc); IR (thin film) 2956, 2925, 2246, 1690, 1444 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$), δ 7.38 (m, 2 H), 7.34 (m, 1 H), 7.25 (d, *J* = 7.0 Hz, 2 H), 4.97 (d, *J* = 15.4 Hz, 1 H), 3.98 (m, 1 H), 3.97 (d, *J* = 15.4 Hz, 1 H), 3.83 (dd, *J* = 9.1, 4.9 Hz, 1 H), 3.09 (m, 1 H), 2.51 (m, 2 H), 2.43 (m, 1 H), 2.17 (m, 1 H), 2.08 (m, 1 H), 1.99 (m, 1 H), 1.78 (m, 1 H), 1.71 (m, 2 H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 174.4, 135.7, 129.0, 128.1, 128.0, 119.1, 78.3, 64.0, 56.4, 44.3, 29.9, 28.2, 25.1, 12.4; HRMS (TOF MS ES+) calcd for $C_{16}H_{19}N_3O$ [M+H]: 270.1595, found 270.1606; $[\alpha]_D^{24}$ = +14.4 (*c* 1.0, $CHCl_3$).

3-((7a*S*)-2-benzyl-1-oxohexahydro-1*H*-pyrrolo[1,2-*c*]imidazol-3-yl)propanenitrile (76). To a solution of **S14** (132 mg, 0.386 mmol) in PhH (3.9 mL, 0.1 M) were added acrylonitrile (0.13 mL, 1.93 mmol) and benzyl thiol (10% solution in PhH, 0.04 mL, 0.039 mmol), AIBN (13 mg, 0.077 mmol), and $(TMS)_3SiH$ (0.24 mL, 0.772 mmol) and heated to reflux. After the reaction was complete, the mixture was cooled to room temperature and the solvent evaporated. Purification via FCC

(10:1 EtOAc:MeOH) afforded **76** (56 mg, 0.208 mmol, 45% as a 4:1 mixture of diastereomers) as a yellow oil.

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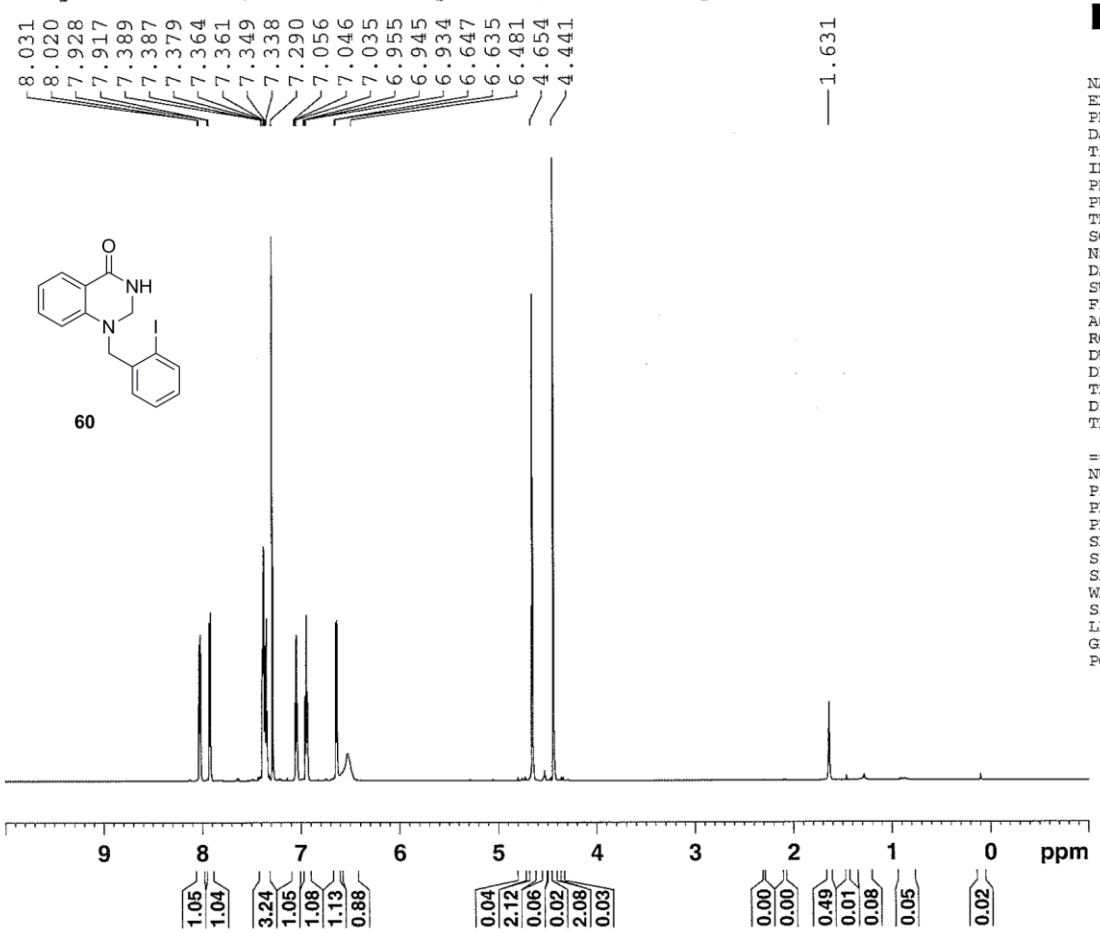
recrystallized 3x, washed with pentane, and rotovaped form CDCl3



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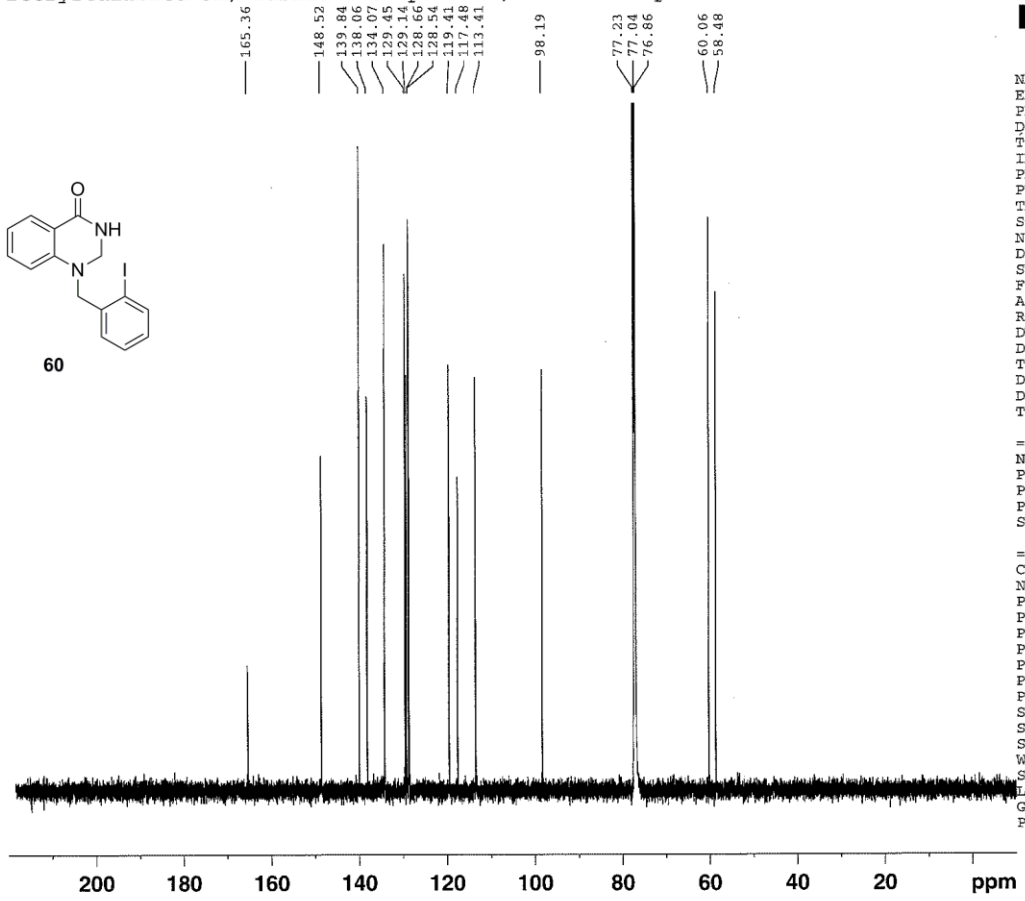
DAS32082
recrystallized 3x, washed with pentane, and rotovaped form CDCl3



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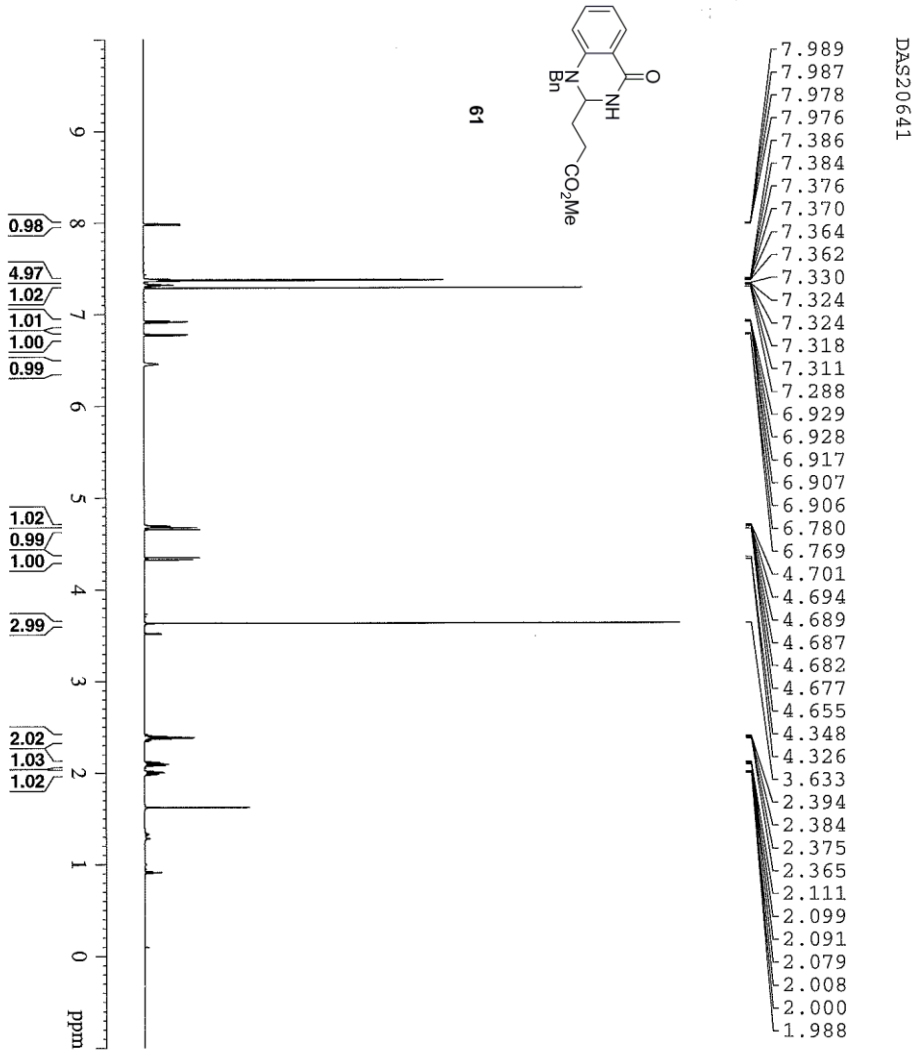
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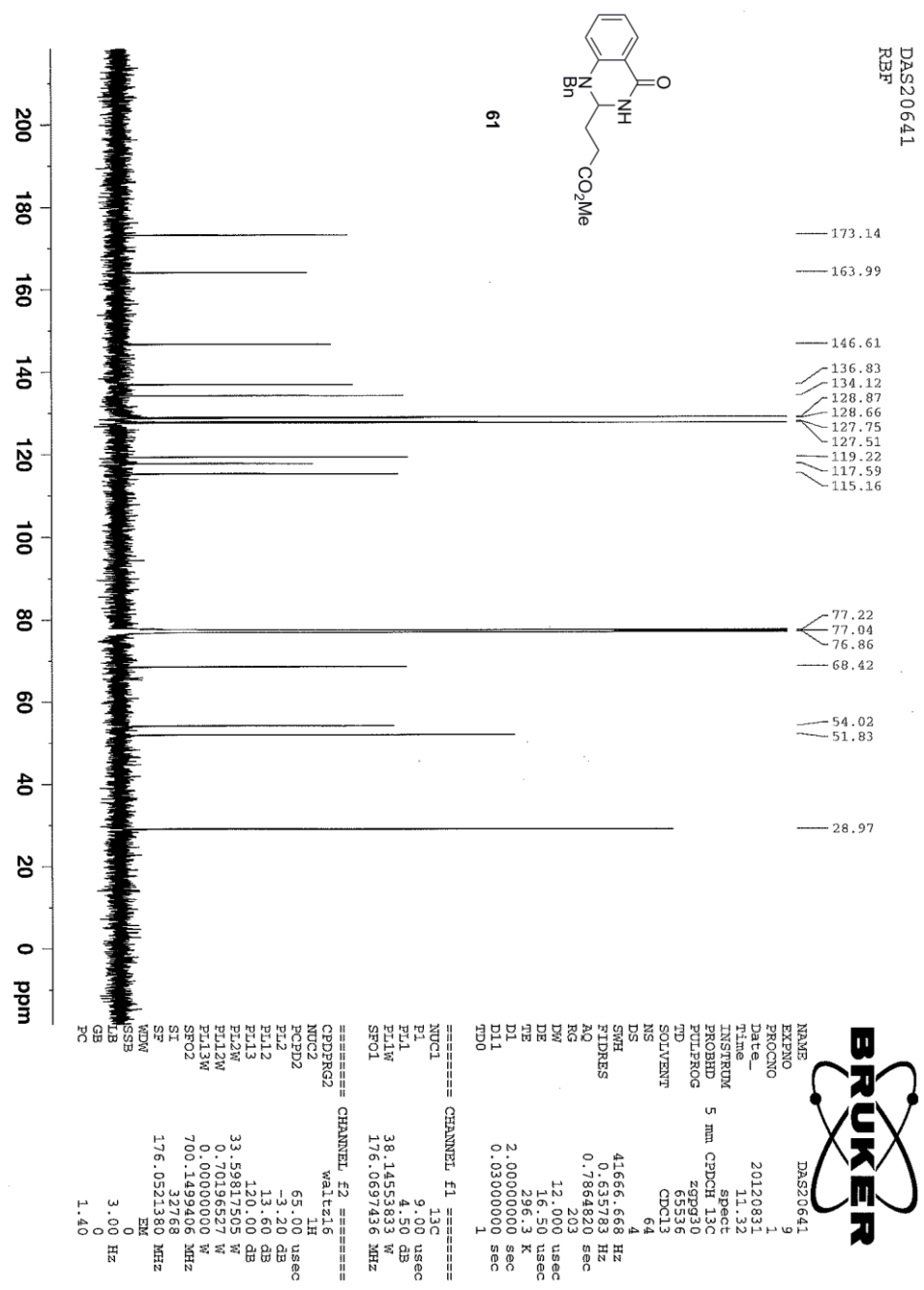
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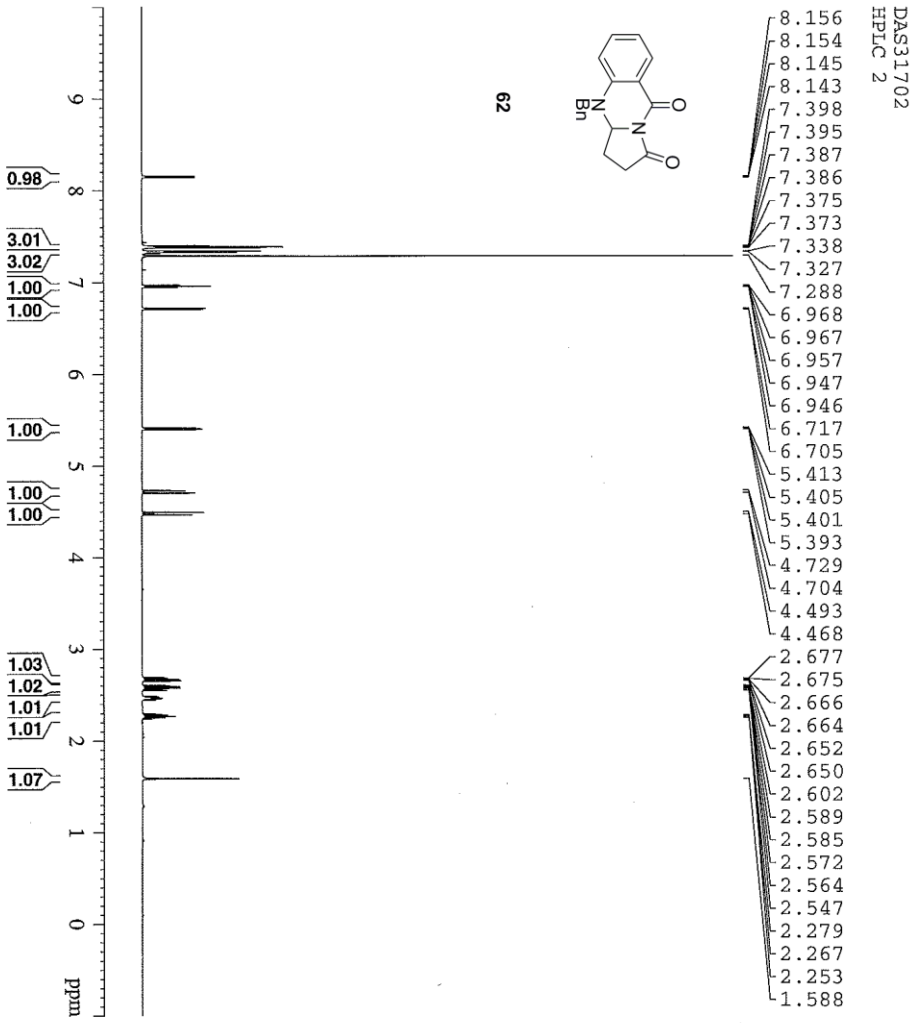
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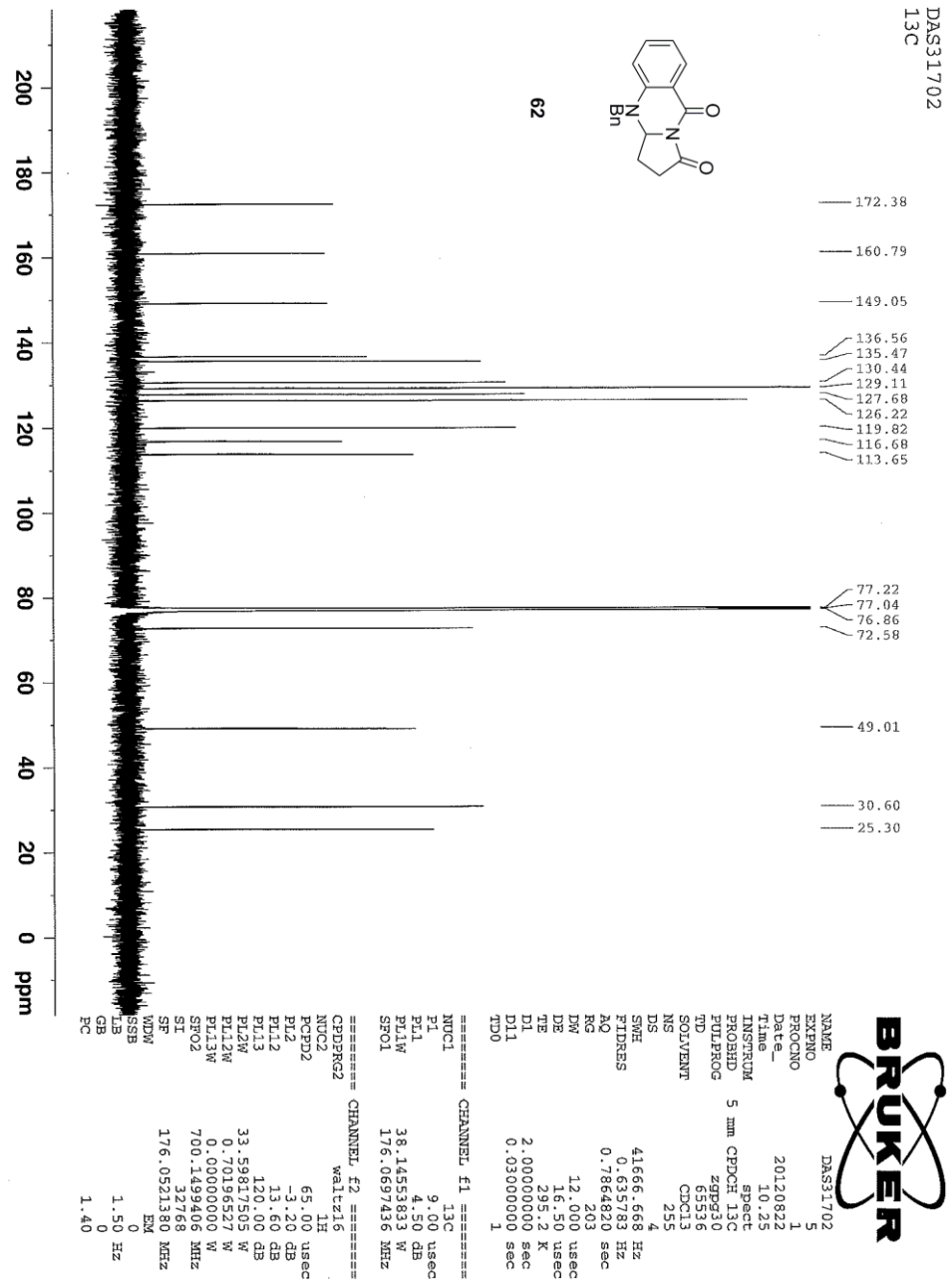
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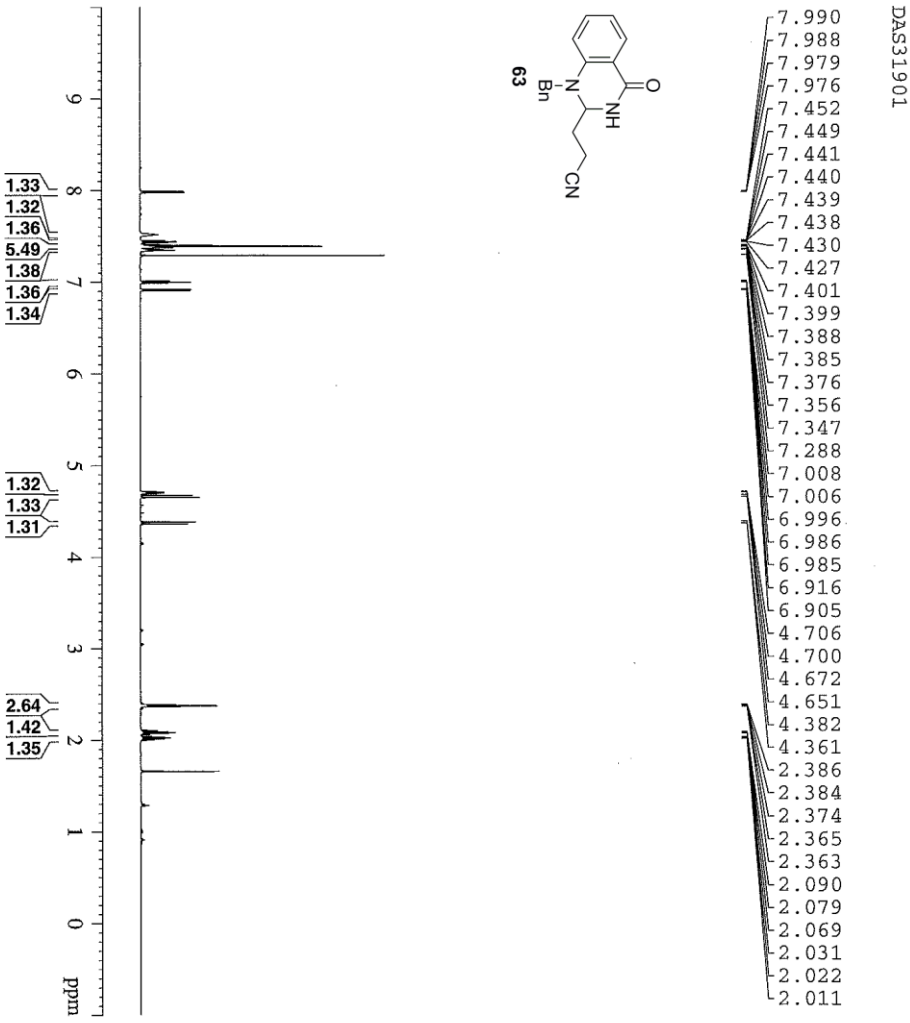
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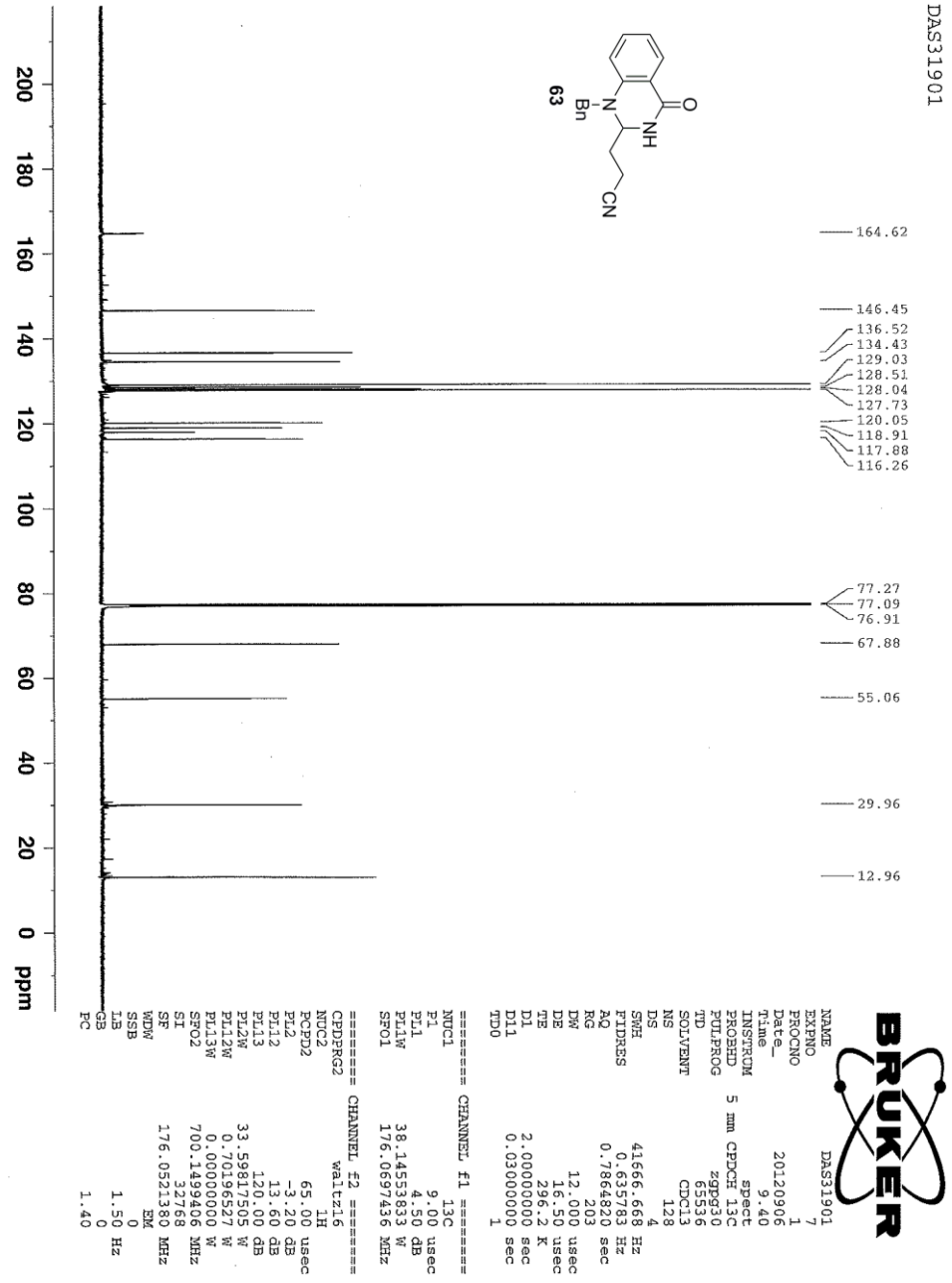
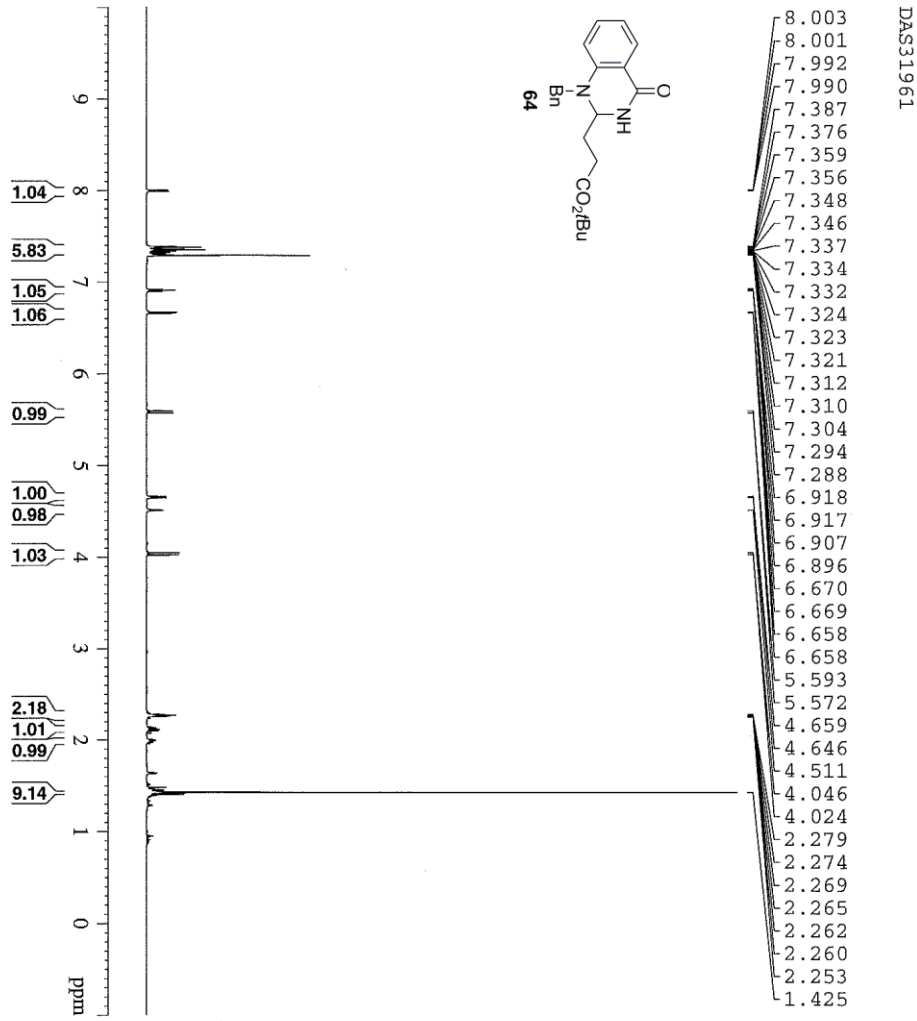
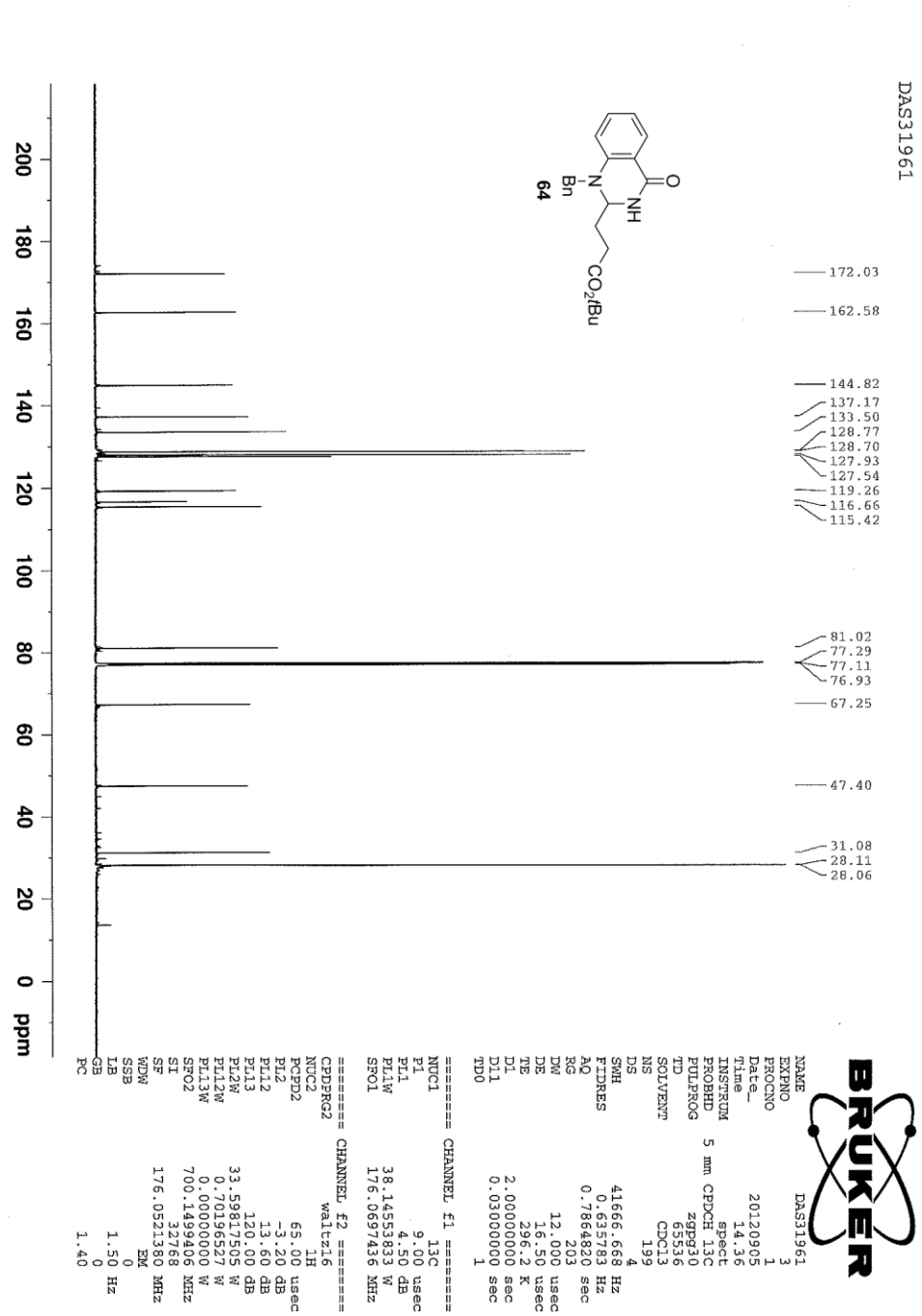
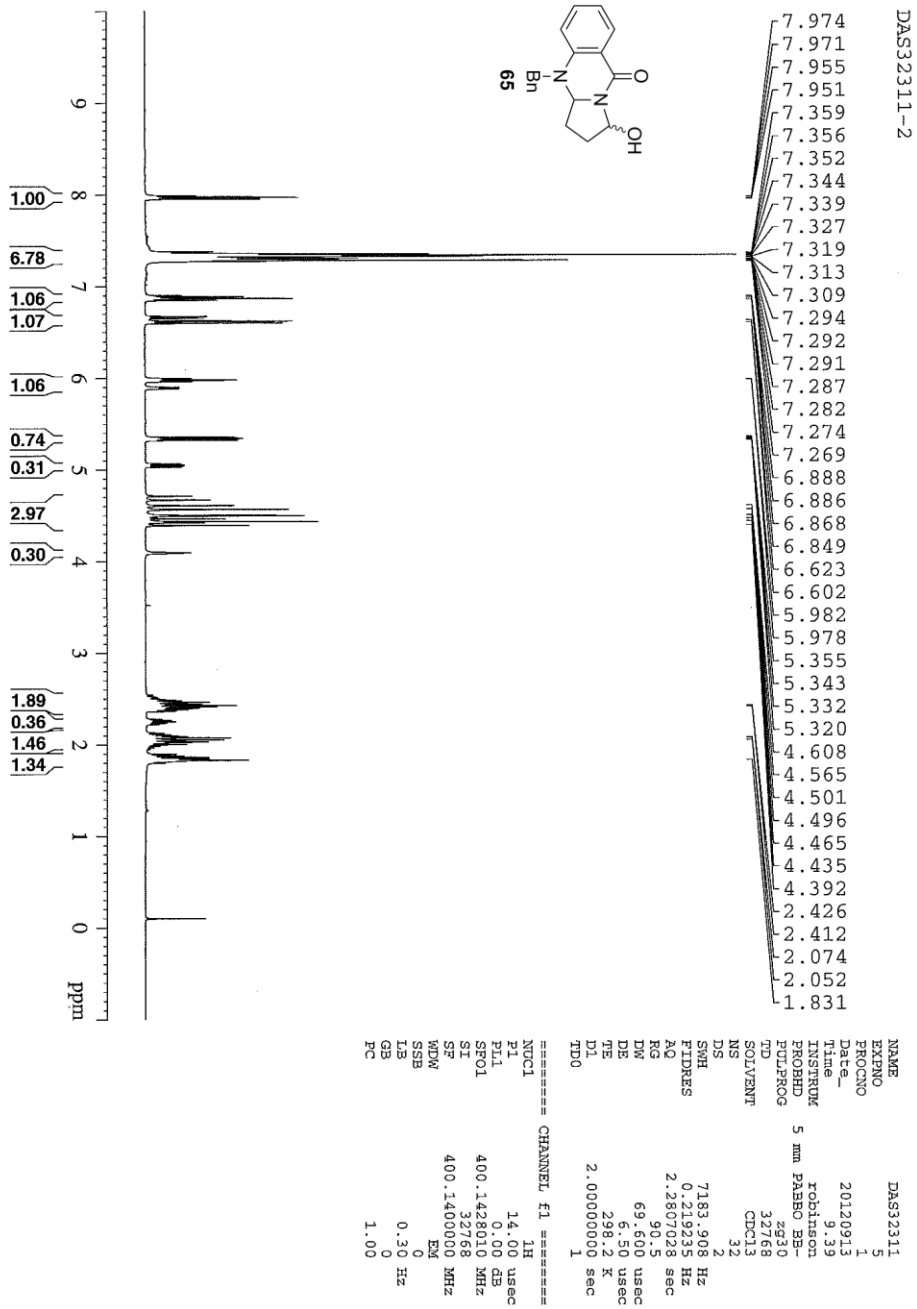
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

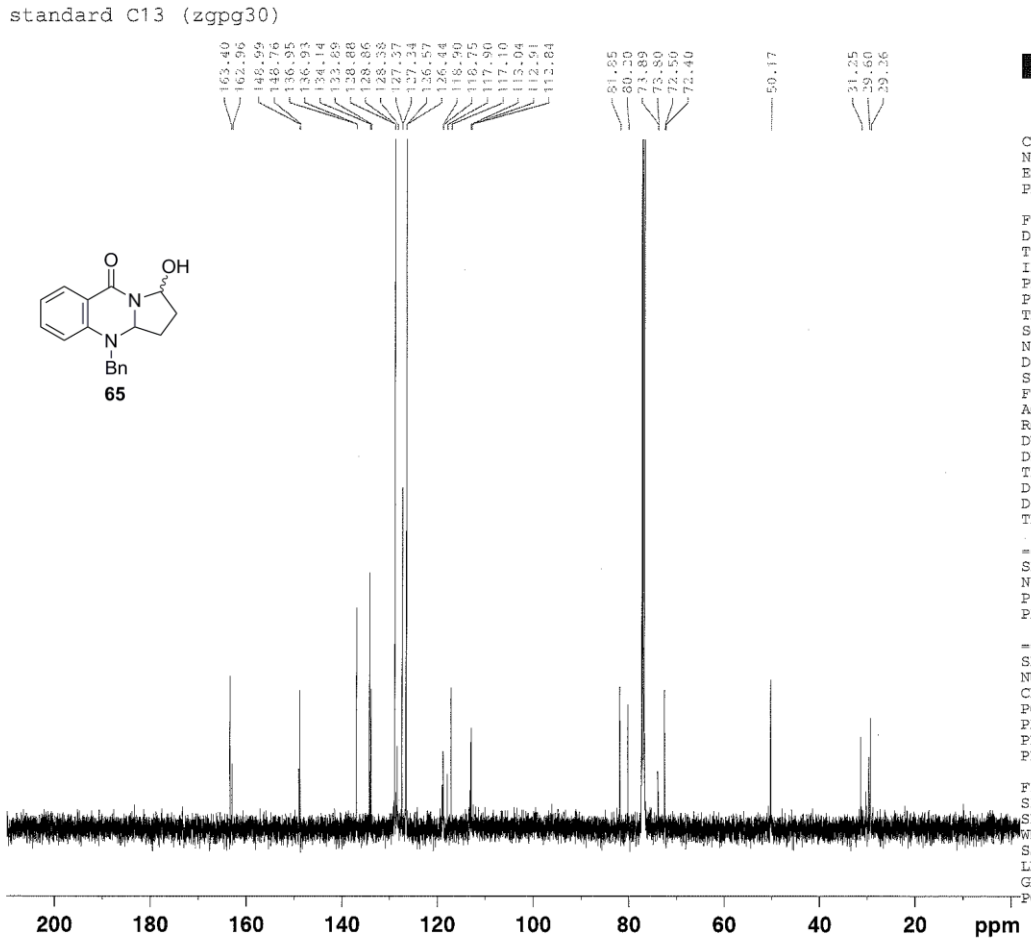

DAS31901
63
164.62
146.45
136.52
134.43
129.03
128.51
128.04
127.73
120.05
118.91
117.88
116.26
77.27
77.09
76.91
67.88
55.06
29.96
12.96
200
180
160
140
120
100
80
60
40
20
0
ppm
BRUKER
NAME DAS31901
EXPNO 7
PROCNO 1
Date_ 20120906
Time_ 9.40
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 128
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864820 sec
RG 203
DW 12.000 usec
DE 16.50 usec
TE 296.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0697436 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 usec
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1499406 MHz
SI 32768
SF 176.0521380 MHz
WDW EM
SSB 0
LB 1.50 Hz
GB 0
FC 1.40


DAS31961
8.003
8.001
7.992
7.990
7.387
7.376
7.359
7.356
7.348
7.346
7.337
7.334
7.332
7.324
7.323
7.321
7.312
7.310
7.304
7.294
7.288
6.918
6.917
6.907
6.896
6.670
6.669
6.658
6.658
5.593
5.572
4.659
4.646
4.511
4.046
4.024
2.279
2.274
2.269
2.265
2.262
2.260
2.253
1.425
O
NH
N
Bn
Bn
CO2tBu
64
1.04
5.83
1.05
1.06
0.99
1.00
0.98
1.03
2.18
1.01
0.99
9.14
9
8
7
6
5
4
3
2
1
0
ppm
NAME DAS31961
EXPNO 1
PROCNO 1
Date_ 20120905
Time 14.26
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 64
DW 42.000 usec
DE 6.50 usec
TE 296.1 K
D1 2.00000000 sec
TD0 1
========== CHANNEL f1 ==========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00


DAS31961
64
172.03
162.58
144.82
137.17
133.50
128.77
128.70
127.93
127.54
119.26
116.66
115.42
81.02
77.29
77.11
76.93
67.25
47.40
31.08
28.11
28.06
BRUKER
NAME DAS31961
EXPNO 3
PROCNO 1
Date_ 20120905
Time 14.36
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 199
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864820 sec
RG 203
DW 12.000 usec
DE 16.50 usec
TE 296.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0697436 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 usec
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1499406 MHz
SI 32768
SF 176.0521380 MHz
WDW EM
SSB 0
LB 1.50 Hz
GB 0
PC 1.40
200 180 160 140 120 100 80 60 40 20 0 ppm


DAS32311-2
7.974
7.971
7.955
7.951
7.359
7.356
7.352
7.344
7.339
7.327
7.319
7.313
7.309
7.294
7.292
7.291
7.287
7.282
7.274
7.269
6.888
6.886
6.868
6.849
6.623
6.602
5.982
5.978
5.355
5.343
5.332
5.320
4.608
4.565
4.501
4.496
4.465
4.435
4.392
2.426
2.412
2.074
2.052
1.831
Bn
65
OH
1.00
6.78
1.06
1.07
1.06
0.74
0.31
2.97
0.30
1.89
0.36
1.46
1.34
ppm
NAME DAS32311
EXPNO 5
PROCNO 1
Date_ 20120913
Time 9.39
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 sec
RG 90.5
DW 69.600 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 usec
PL1 0.00 dB
SFO1 400.1428010 MHz
SI 32768
SF 400.1400000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

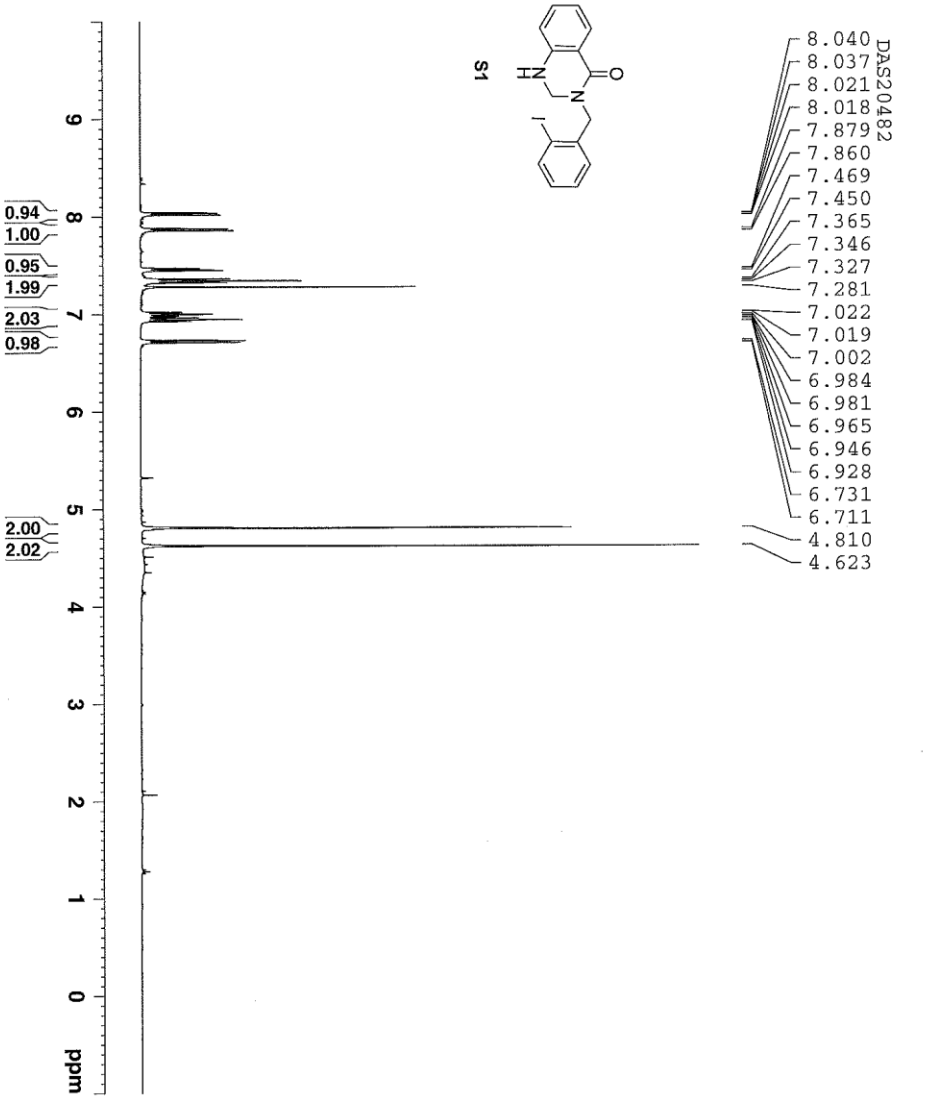
standard C13 (zgpg30)



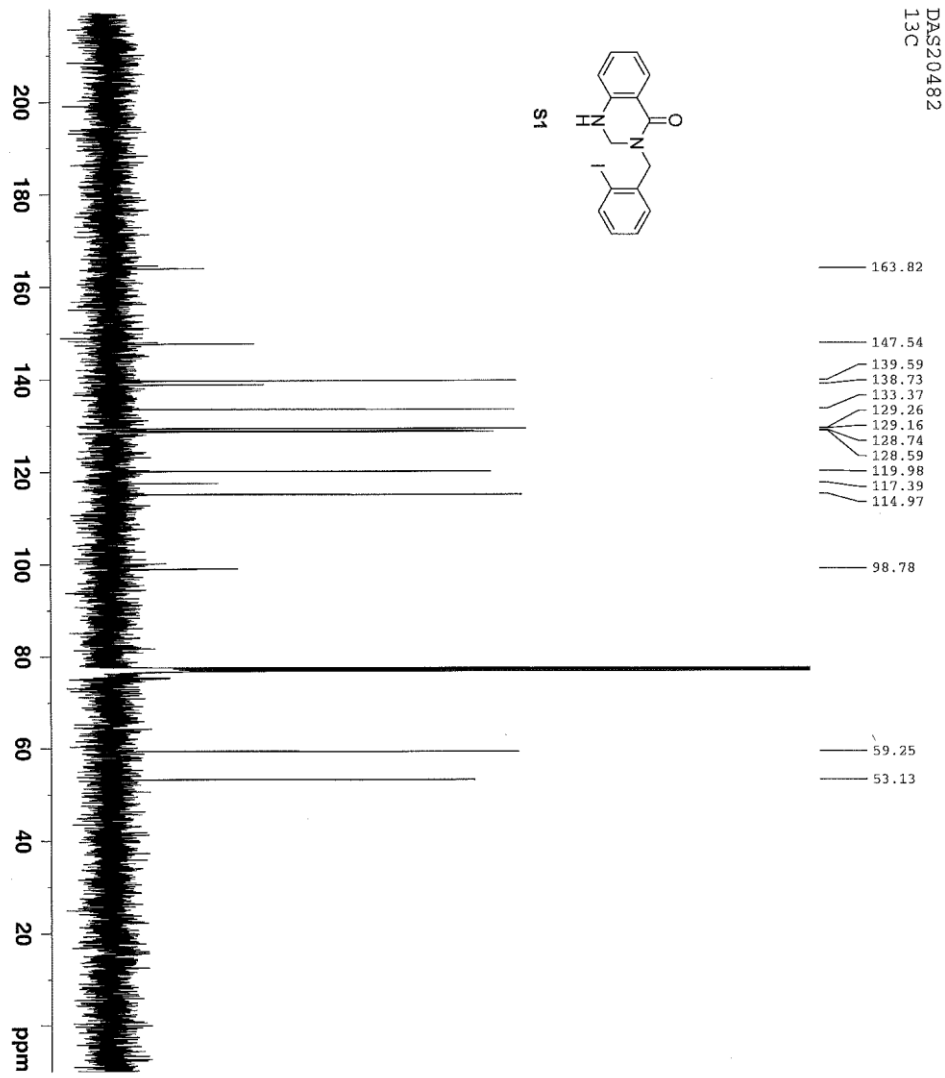
65

BRUKER

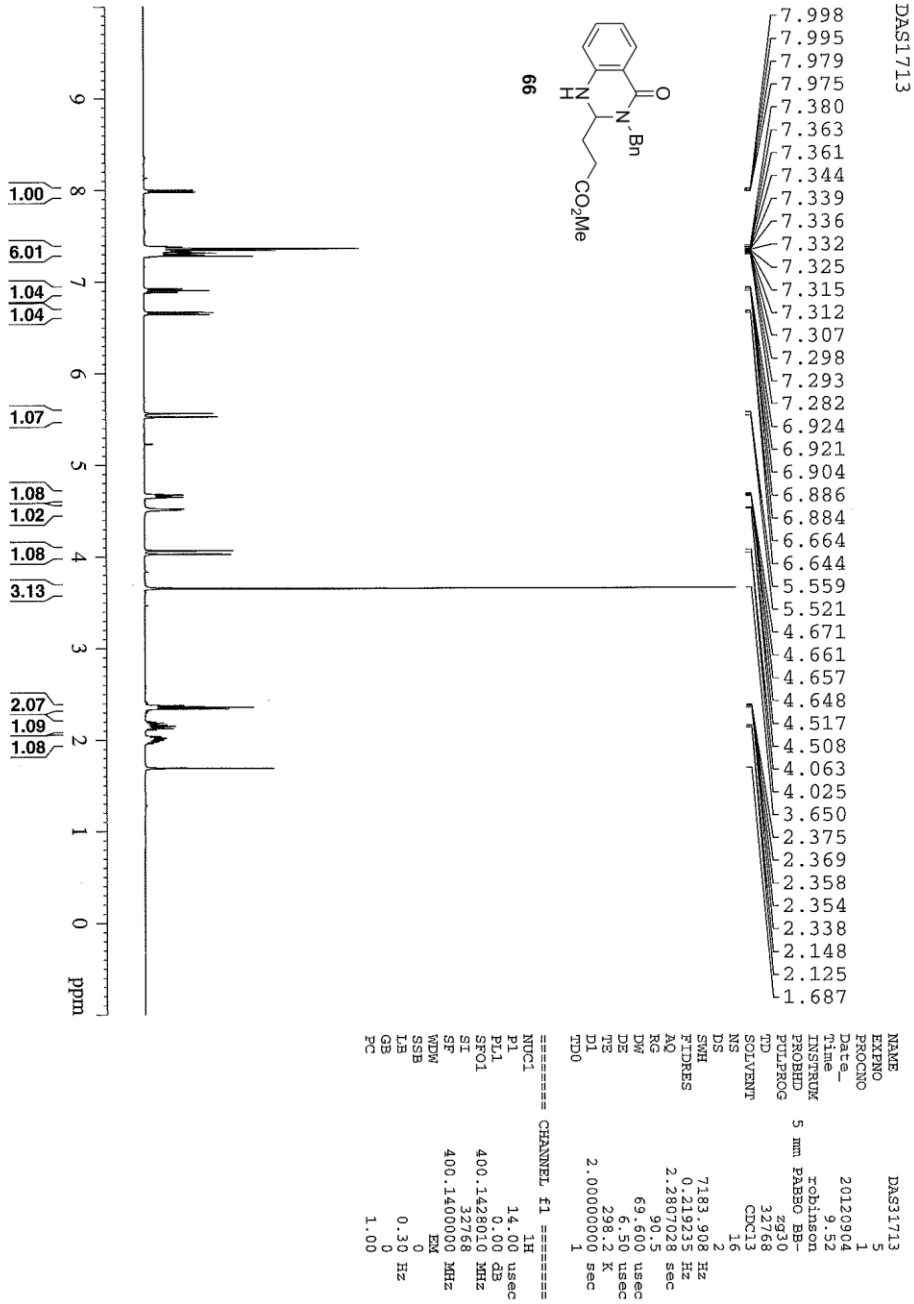
```
Current Data Parameters
NAME            DAS32311
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameters
Date_           20120913
Time               13.27
INSTRUM            spect
PROBHD   5 mm PATXI 1H/
PULPROG          zgpg30
TD                65536
SOLVENT           CDC13
NS                 2425
DS                    2
SWH           35714.285 Hz
FIDRES        0.544957 Hz
AQ            0.9175040 sec
RG               190.98
DW               14.000 usec
DE                6.50 usec
TE                298.0 K
D1           2.00000000 sec
D11          0.03000000 sec
TD0                   1

======== CHANNEL f1 ========
SFO1        125.7753951 MHz
NUC1                13C
P1                12.00 usec
PLW1       160.00000000 W

======== CHANNEL f2 ========
SFO2        500.1320005 MHz
NUC2                1H
CPDPRG[2         waltz16
PCPD2             80.00 usec
PLW2       12.00000000 W
PLW12       0.11408000 W
PLW13       0.07300800 W

F2 - Processing parameters
SI                 32768
SF          125.7577890 MHz
WDW                EM
SSB       0
LB               1.00 Hz
GB        0
PC               1.40
```

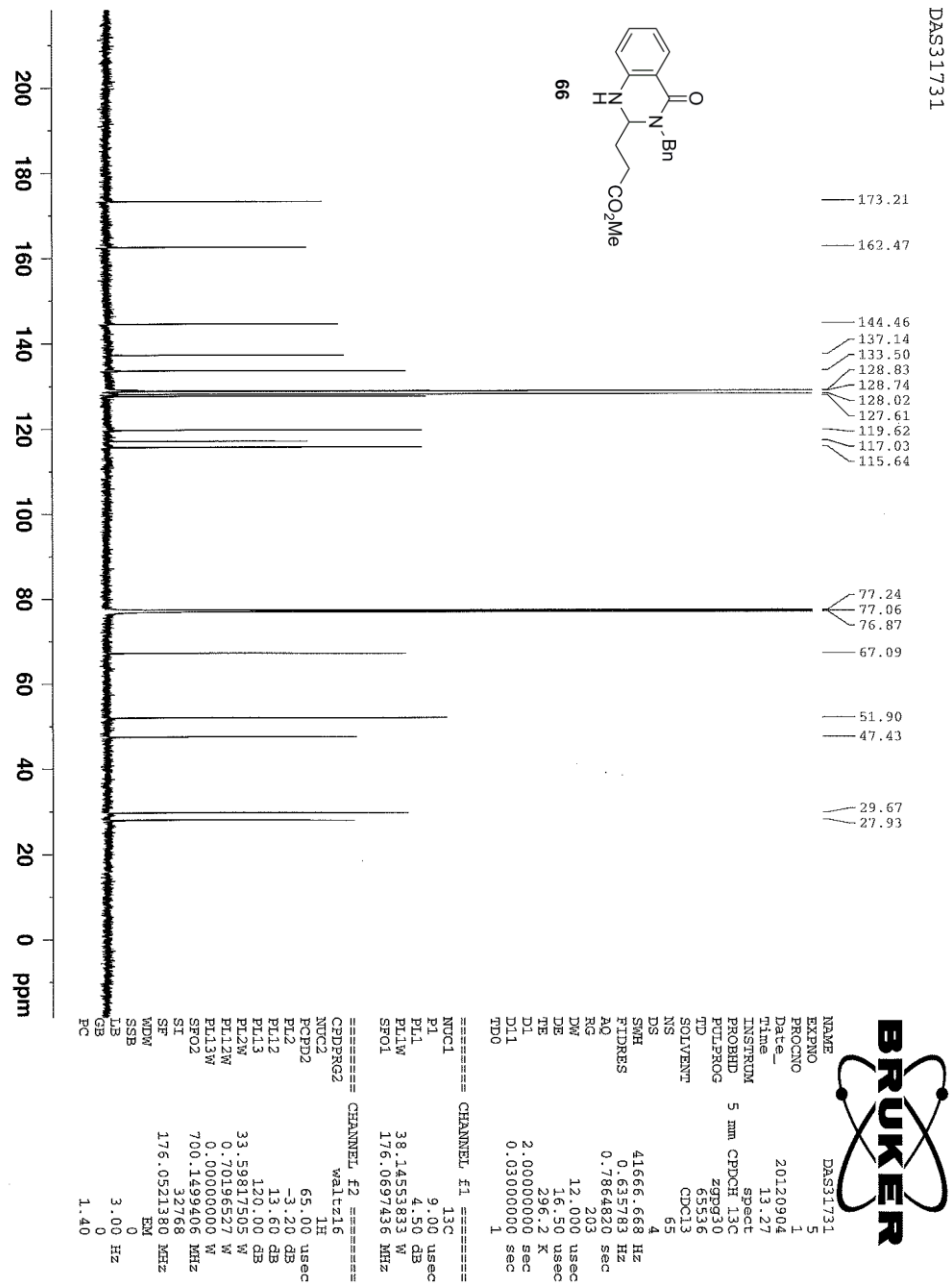



```
Current Data Parameters
NAME                  DAS20482
EXPNO                        1
PROCNO                       1
DU                          /m
USER                    davids

F2 - Acquisition Parameters
Date_                20110601
Time_                   15.14
INSTRUM                DPX400
PROBHD  5 mm BBO BB-1H
PULPROG                 zg30
TD                     32768
SOLVENT                CDCl3
NS                        32
DS                         2
SWH                6410.256 H
FIDRES             0.195625 H
AQ                 2.5559540 s
RG                     812.7
DW                  78.000 u
DE                   6.00 u
TE                    298.2 K
D1                 2.00000000 s
TD0                        1

======== CHANNEL f1 ========
NUC1                     1H
P1                   13.50 u
PL1                  -3.00 d
SFO1          400.2478017 M

F2 - Processing parameter
SI                     32768
SF            400.2450000 M
WDW                       EM
SSB                        0
LB                      0.30 H
GB                         0
PC                      1.00
```

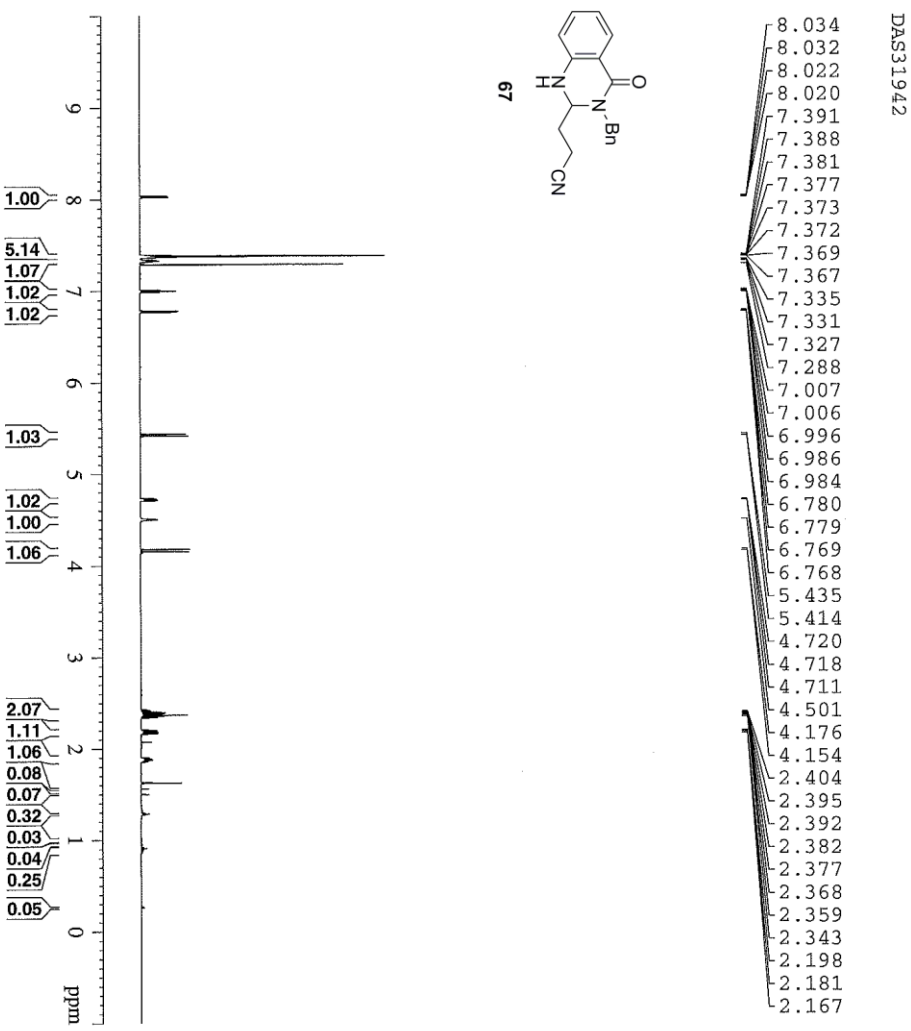


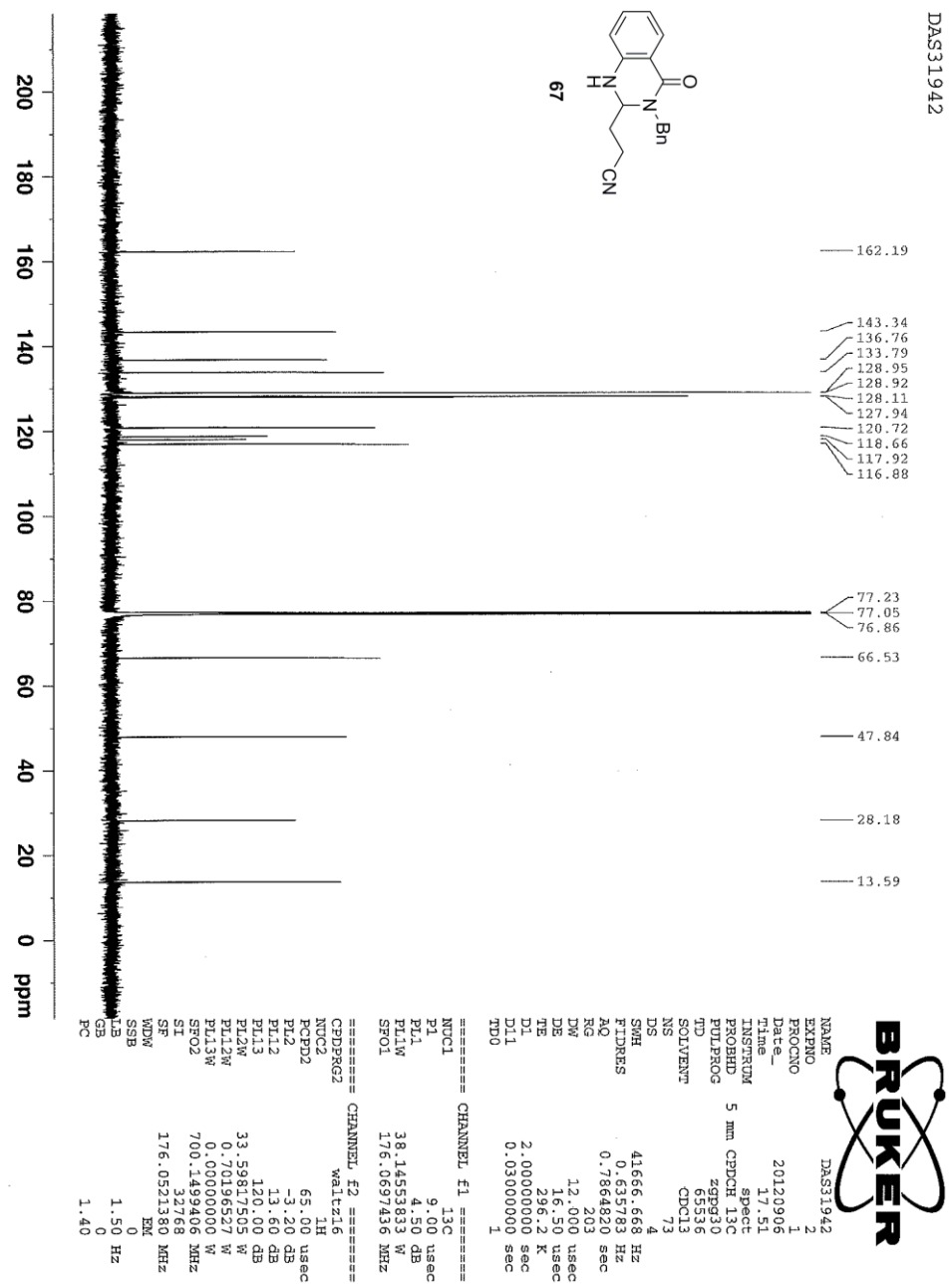

```
Current Data Parameters
NAME                  DAS20482
EXPNO                        2
PROCNO                       1

F2 - Acquisition Parameters
Date_              20110601
Time                   15.19
INSTRUM                DPX400
PROBHD  5 mm BBO BB-1H
PULPROG                zgpg30
TD                     65536
SOLVENT                CDCl3
NS                      1024
DS                         4
SWH                23980.814 Hz
FIDRES                 0.365918 Hz
AQ                 1.3664756 sec
RG                     20642.5
DW                      20.850 use
DE                      6.00 use
TE                     298.2 K
D1                  0.20000000 sec
D11                 0.03000000 sec
DELTA               0.10000000 sec
TD0                        1

========== CHANNEL f1 ========
NUC1                      13C
P1                       8.30 use
PL1                     -3.00 dB
SFO1           100.6517495 MHz

========== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                      1H
PCPD2                   90.00 use
PL2                     -3.00 dB
PL12                    15.00 dB
PL13                    15.00 dB
SFO2           400.2466010 MHz

F2 - Processing parameters
SI                         32768
SF             100.6416850 MHz
WDW                           EM
SSB                            0
LB                          1.50 Hz
GB                             0
PC                          1.40
```

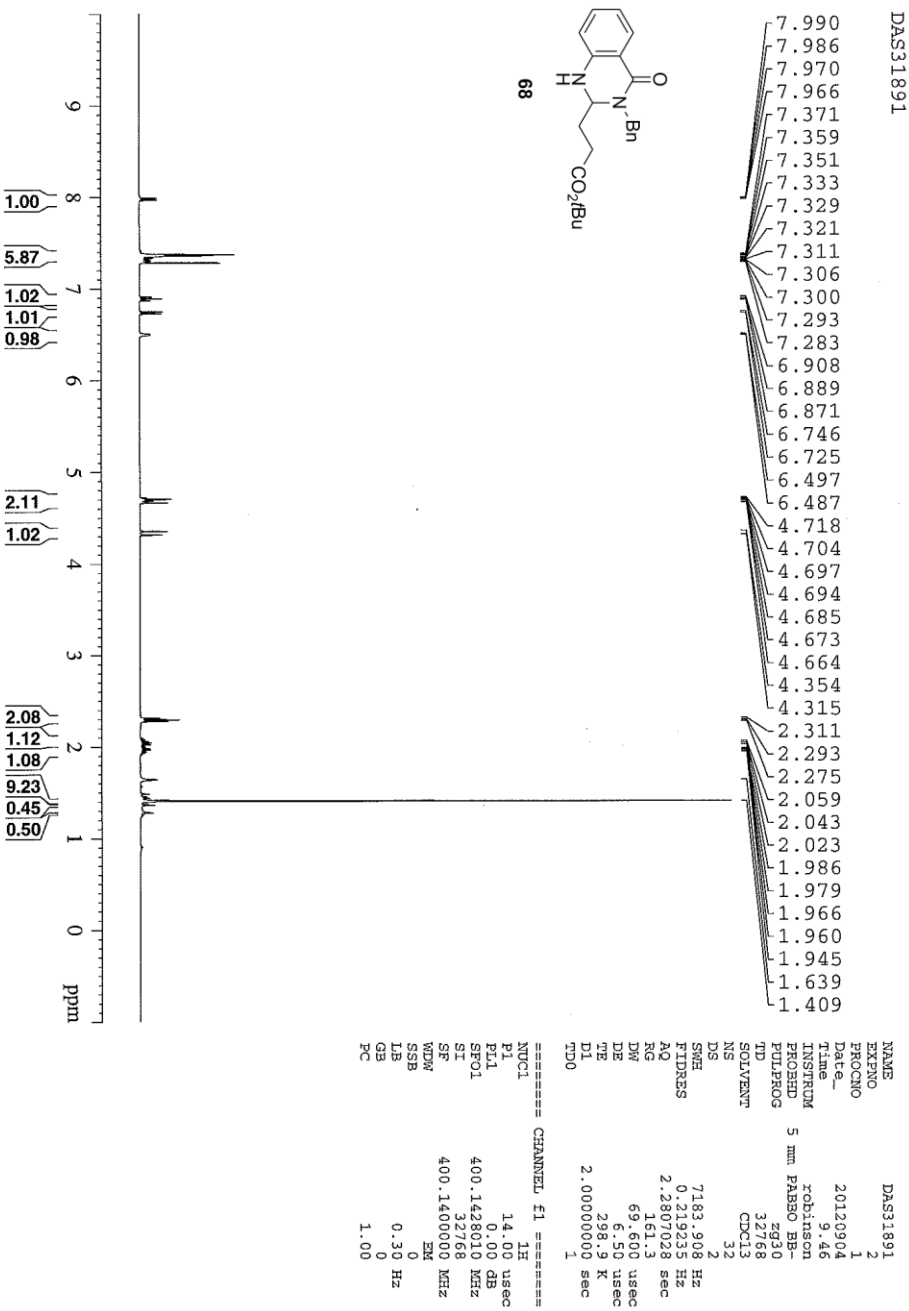

DAS1713
7.998
7.995
7.979
7.975
7.380
7.363
7.361
7.344
7.339
7.336
7.332
7.325
7.315
7.312
7.307
7.298
7.293
7.282
6.924
6.921
6.904
6.886
6.884
6.664
6.644
5.559
5.521
4.671
4.661
4.657
4.648
4.517
4.508
4.063
4.025
3.650
2.375
2.369
2.358
2.354
2.338
2.148
2.125
1.687
66
1.00
6.01
1.04
1.04
1.07
1.08
1.02
1.08
3.13
2.07
1.09
1.08
ppm
NAME DAS31713
EXPNO 5
PROCNO 1
Date_ 20120904
Time 9.52
INSTRUM rcbinson
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 sec
RG 90.5
DW 69.600 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
========== CHANNEL f1 ==========
NUC1 1H
P1 14.00 usec
PL1 0.00 dB
SFO1 400.1428010 MHz
SI 32768
SF 400.1400000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

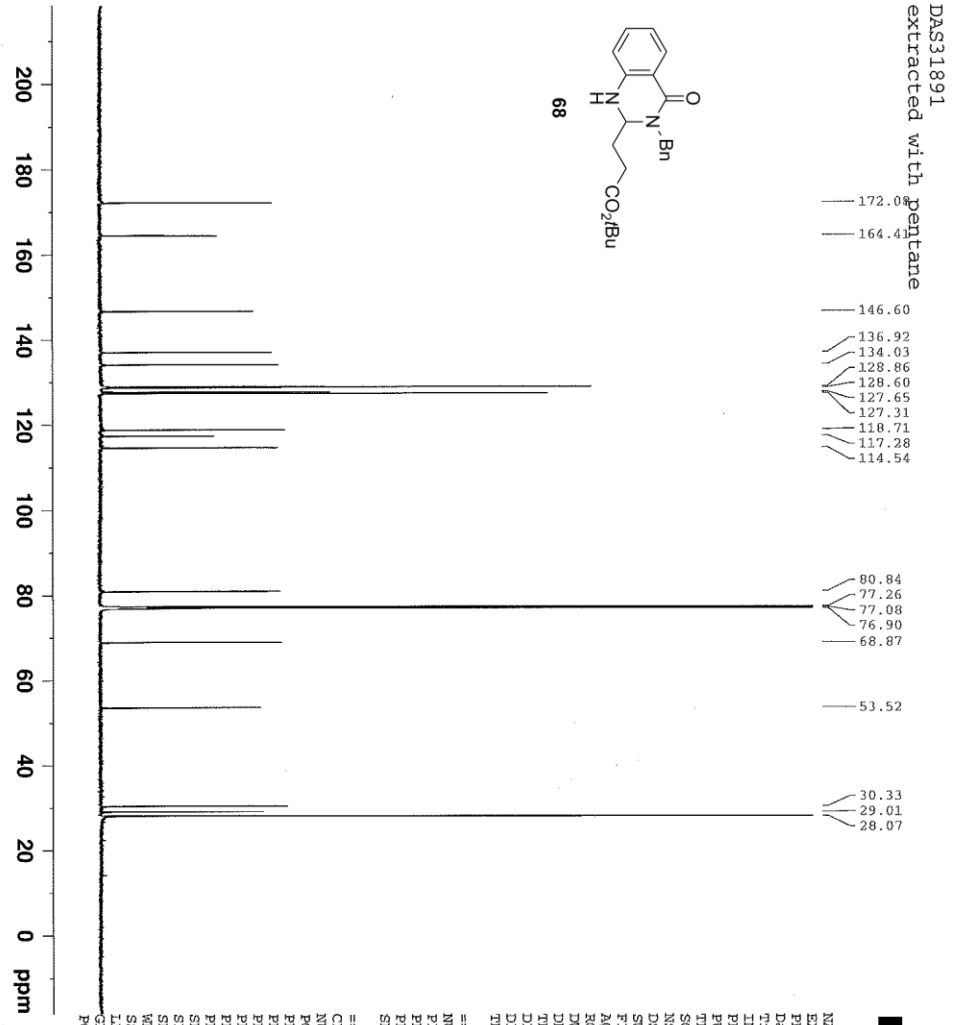



```
NAME                 DAS31731
EXPNO                       5
PROCNO                      1
Date_             20120904
Time_                 13.27
INSTRUM                spect
PROBHD     5 mm CPDCH 13C
PULPROG             zgpg30
TD                   65536
SOLVENT              CDCl3
NS                      65
DS                       4
SWH                41666.668 Hz
FIDRES                0.635783 Hz
AQ                    0.7864820 sec
RG                      203
DW                   12.000 usec
DE                    16.50 usec
TE                   296.2 K
D1                    2.00000000 sec
D11                   0.03000000 sec
TD0                         1

========== CHANNEL f1 ==========
NUC1                       13C
P1                    9.00 usec
PL1                   4.50 dB
PL1W            38.14553833 W
SFO1            176.0697436 MHz

========== CHANNEL f2 ==========
CPDPRG2                waltz16
NUC2                        1H
PCPD2                 65.00 usec
PL2                   -3.20 dB
PL12                  13.60 dB
PL13                 120.00 dB
PL2W            33.59817505 W
PL12W            0.70196527 W
PL13W            0.00000000 W
SFO2            700.1499406 MHz
SI                      32768
SF              176.0521380 MHz
WDW                        EM
SSB                         0
LB                   3.00 Hz
GB                          0
PC                   1.40
```

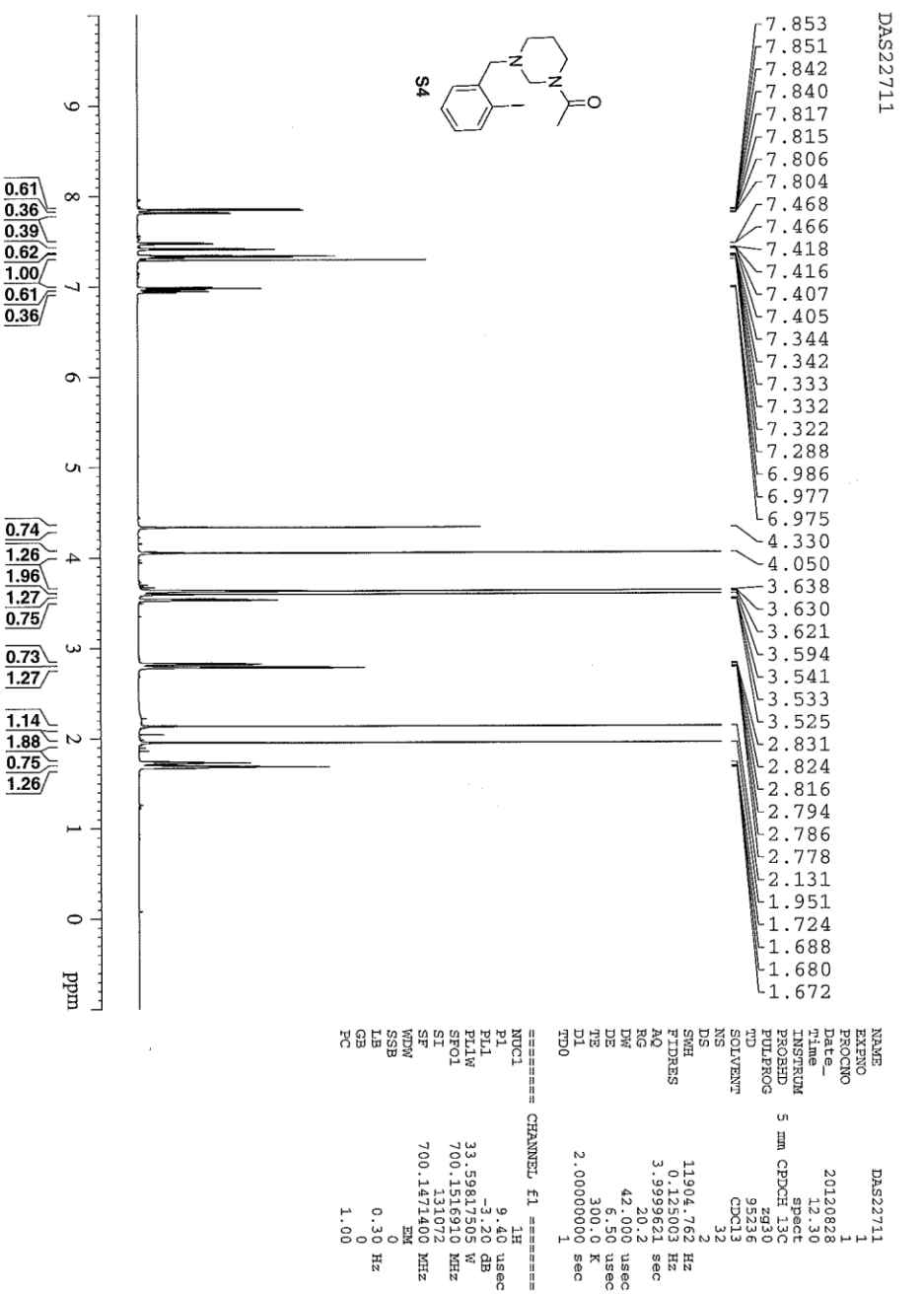

DAS31942
8.034
8.032
8.022
8.020
7.391
7.388
7.381
7.377
7.373
7.372
7.369
7.367
7.335
7.331
7.327
7.288
7.007
7.006
6.996
6.986
6.984
6.780
6.779
6.769
6.768
5.435
5.414
4.720
4.718
4.711
4.501
4.176
4.154
2.404
2.395
2.392
2.382
2.377
2.368
2.359
2.343
2.198
2.181
2.167
67
1.00
5.14
1.07
1.02
1.02
1.03
1.02
1.00
1.06
2.07
1.11
1.06
0.08
0.07
0.32
0.03
0.04
0.25
0.05
9
8
7
6
5
4
3
2
1
0
ppm
NAME DAS31942
EXPNO 1
PROCNO 1
Date_ 20120906
Time 17.46
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 45.2
DW 42.000 usec
DE 6.50 usec
TE 296.1 K
D1 2.00000000 sec
TD0 1
========== CHANNEL f1 ==========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

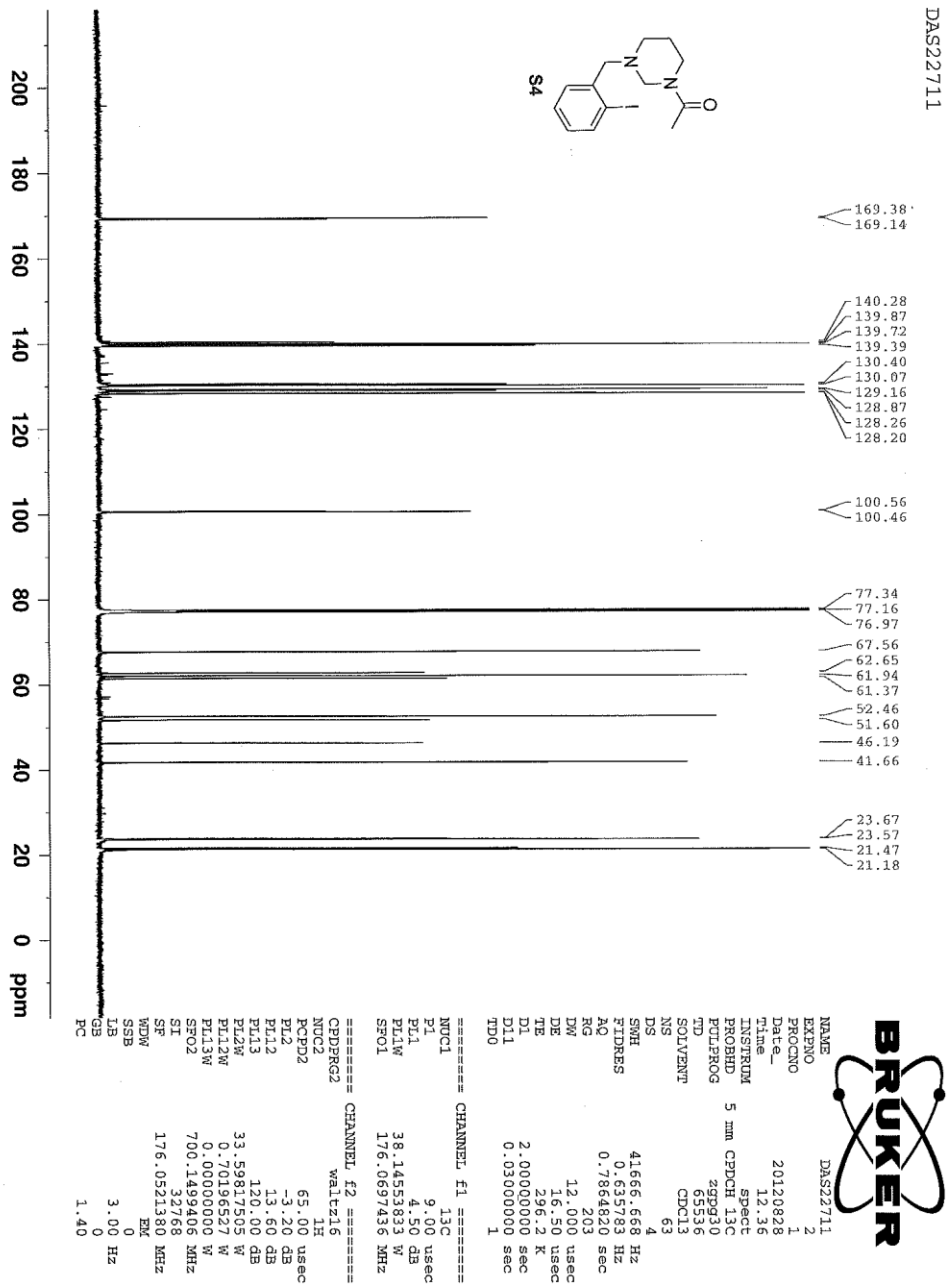

DAS31942
67
162.19
143.34
136.76
133.79
128.95
128.92
128.11
127.94
120.72
118.66
117.92
116.88
77.23
77.05
76.86
66.53
47.84
28.18
13.59
200
180
160
140
120
100
80
60
40
20
0
ppm
BRUKER
NAME DAS31942
EXPNO 2
PROCNO 1
Date_ 20120906
Time_ 17.51
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 73
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864820 sec
RG 203
DW 12.000 usec
DE 16.50 usec
TE 296.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0697436 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 usec
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1499406 MHz
SI 32768
SF 176.0521380 MHz
WDW EM
SSB 0
LB 1.50 Hz
GB 0
PC 1.40

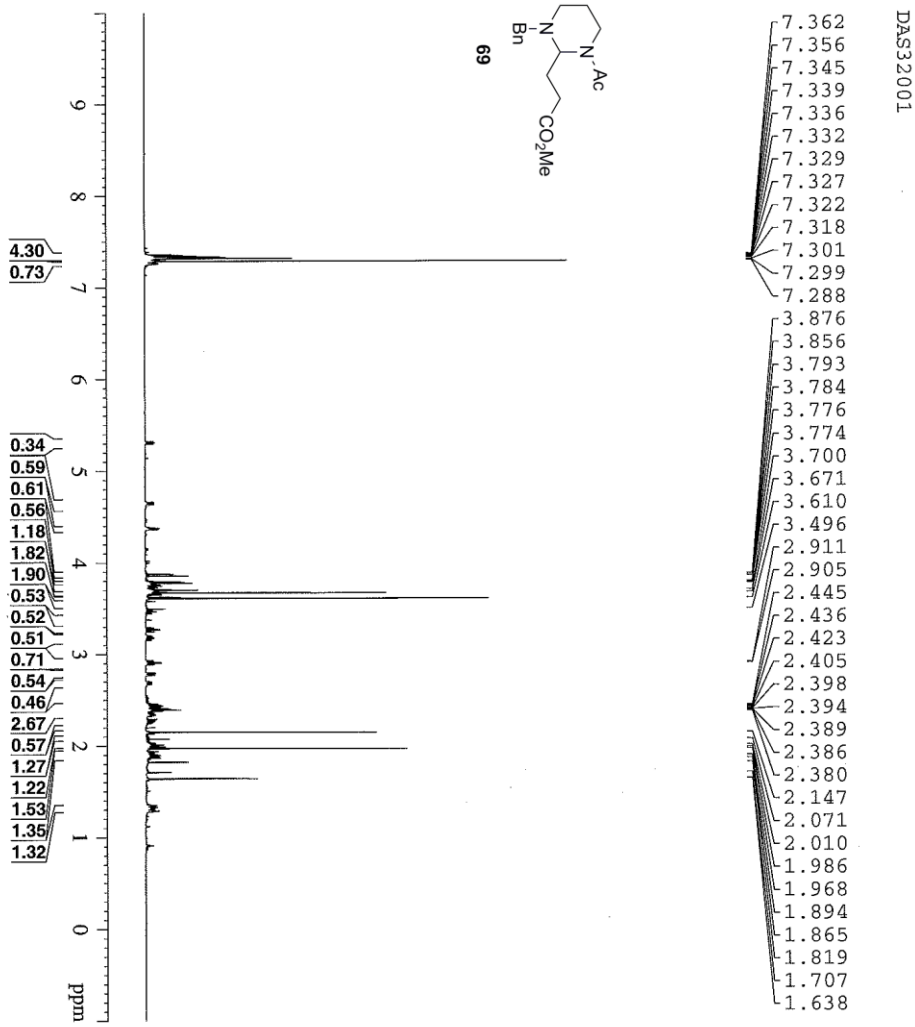

DAS31891
7.990
7.986
7.970
7.966
7.371
7.359
7.351
7.333
7.329
7.321
7.311
7.306
7.300
7.293
7.283
6.908
6.889
6.871
6.746
6.725
6.497
6.487
4.718
4.704
4.697
4.694
4.685
4.673
4.664
4.354
4.315
2.311
2.293
2.275
2.059
2.043
2.023
1.986
1.979
1.966
1.960
1.945
1.639
1.409
68
Bn
CO2tBu
1.00
5.87
1.02
1.01
0.98
2.11
1.02
2.08
1.12
1.08
9.23
0.45
0.50
ppm
NAME DAS31891
EXPNO 2
PROCNO 1
Date_ 20120904
Time 9.46
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 sec
RG 161.3
DW 69.600 usec
DE 6.50 usec
TE 298.9 K
D1 2.00000000 sec
TD0 1
========== CHANNEL f1 ==========
NUC1 1H
P1 14.00 usec
PL1 0.00 dB
SFO1 400.1428010 MHz
SI 32768
SF 400.1400000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

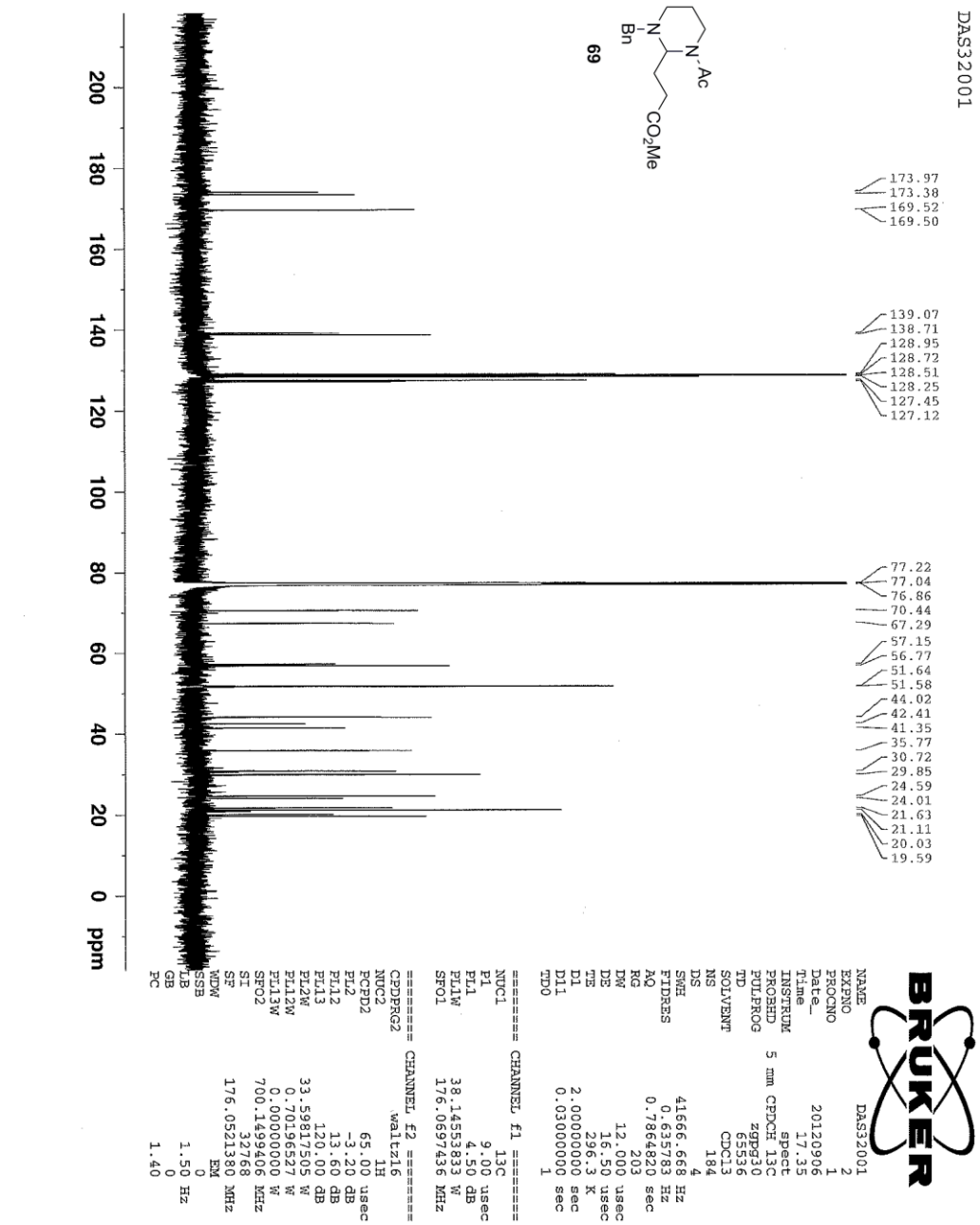


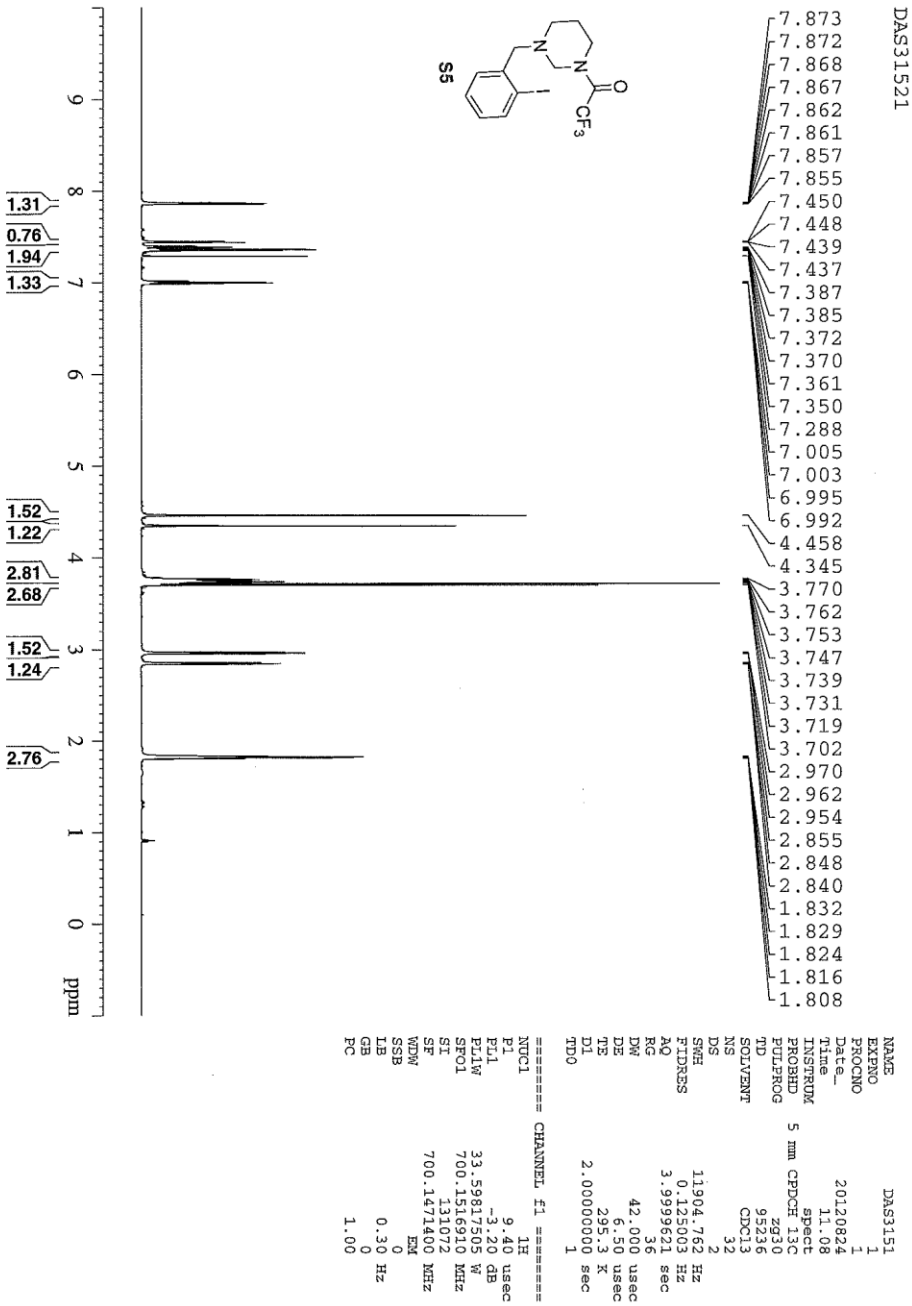

```
NAME                 DAS31891
EXPNO                       3
PROCNO                      1
Date_                20120904
Time_                   13.09
INSTRUM                  spect
PROBHD     5 mm CPDCH 13C
PULPROG                 zgpg30
TD                       65536
SOLVENT                  CDCl3
NS                          63
DS                           4
SWH                  41666.668 Hz
FIDRES                0.635783 Hz
AQ                    0.7864820 sec
RG                         203
DW                      12.000 usec
DE                      16.50 usec
TE                      296.2 K
D1                    2.00000000 sec
D11                   0.03000000 sec
TD0                          1

========== CHANNEL f1 ==========
NUC1                       13C
P1                        9.00 usec
PL1                       4.50 dB
PL1W                38.14553833 W
SFO1                176.0697436 MHz

========== CHANNEL f2 ==========
CPDPRG2                waltz16
NUC2                        1H
PCPD2                    65.00 usec
PL2                      -3.20 dB
PL12                     13.60 dB
PL13                    120.00 dB
PL2W                33.59817505 W
PL12W                0.70196527 W
PL13W                0.00000000 W
SFO2                700.1499406 MHz
SI                         32768
SF                  176.0521380 MHz
WDW                        EM
SSB                         0
LB                       3.00 Hz
GB                          0
PC                       1.40
```

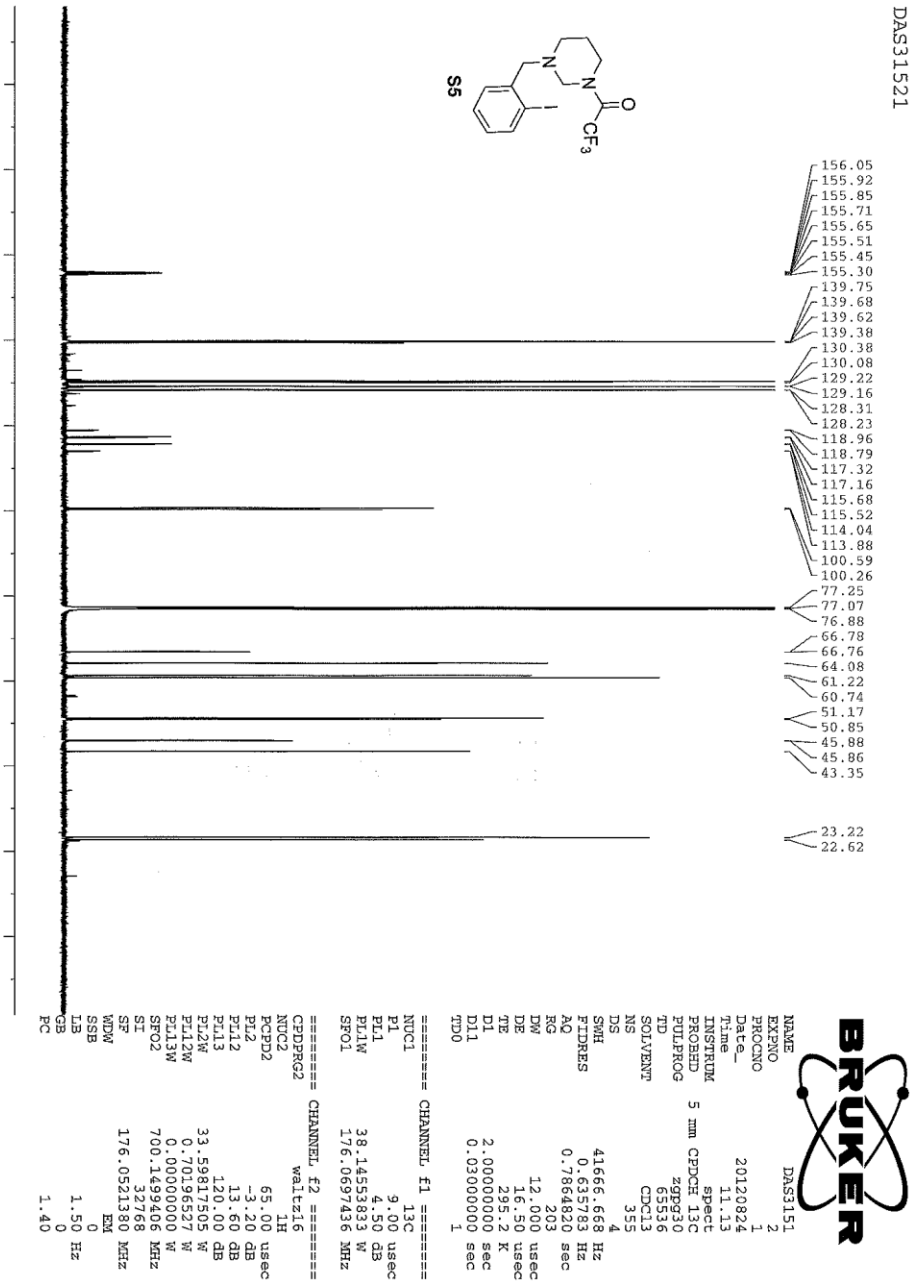

DAS22711
S4
7.853
7.851
7.842
7.840
7.817
7.815
7.806
7.804
7.468
7.466
7.418
7.416
7.407
7.405
7.344
7.342
7.333
7.332
7.322
7.288
6.986
6.977
6.975
4.330
4.050
3.638
3.630
3.621
3.594
3.541
3.533
3.525
2.831
2.824
2.816
2.794
2.786
2.778
2.131
1.951
1.724
1.688
1.680
1.672
0.61
0.36
0.39
0.62
1.00
0.61
0.36
0.74
1.26
1.96
1.27
0.75
0.73
1.27
1.14
1.88
0.75
1.26
ppm
NAME DAS22711
EXPNO 1
PROCNO 1
Date_ 20120828
Time 12.30
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 3.9996621 sec
RG 20.2
DW 42.000 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
TD0 1
========== CHANNEL f1 ==========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

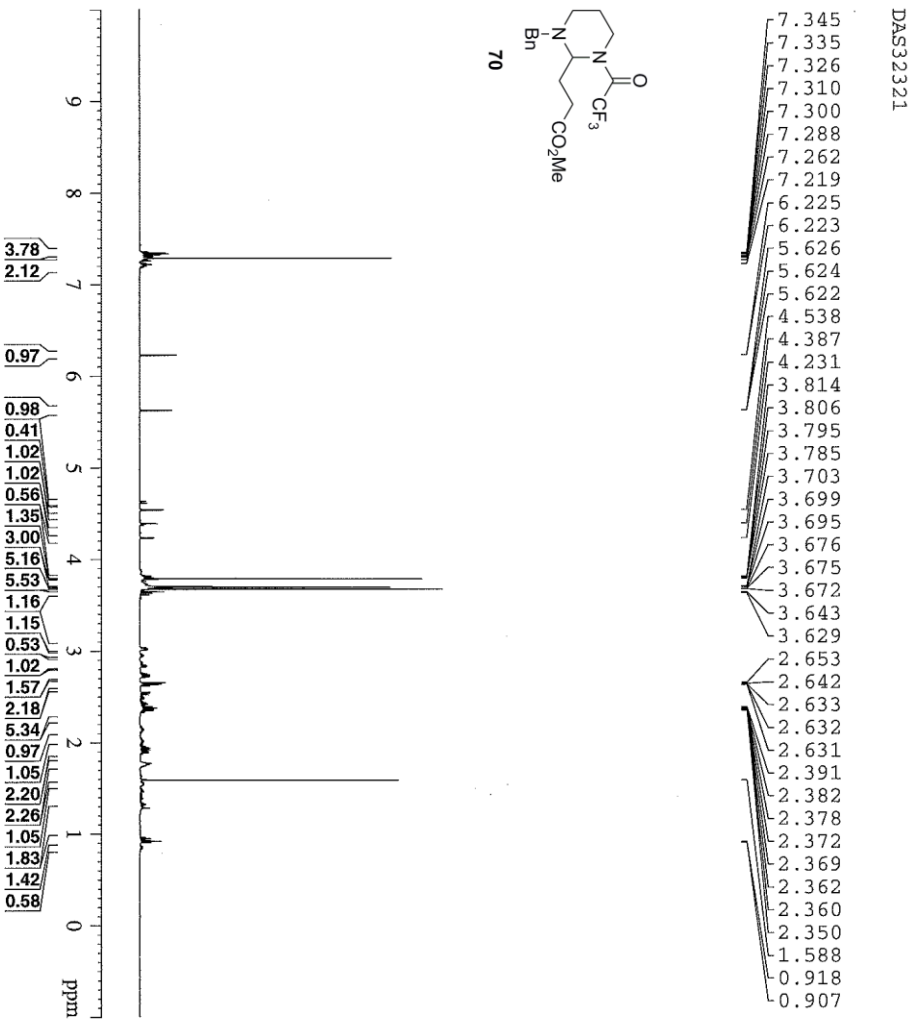

DAS22711
S4
169.38
169.14
140.28
139.87
139.72
139.39
130.40
130.07
129.16
128.87
128.26
128.20
100.56
100.46
77.34
77.16
76.97
67.56
62.65
61.94
61.37
52.46
51.60
46.19
41.66
23.67
23.57
21.47
21.18
200
180
160
140
120
100
80
60
40
20
0
ppm
BRUKER
NAME DAS22711
EXPNO 2
PROCNO 1
Date_ 20120828
Time 12.36
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 63
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864820 sec
RG 203
DW 12.000 usec
DE 16.50 usec
TE 296.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0697436 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 usec
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1499406 MHz
SI 32768
SF 176.0521380 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40

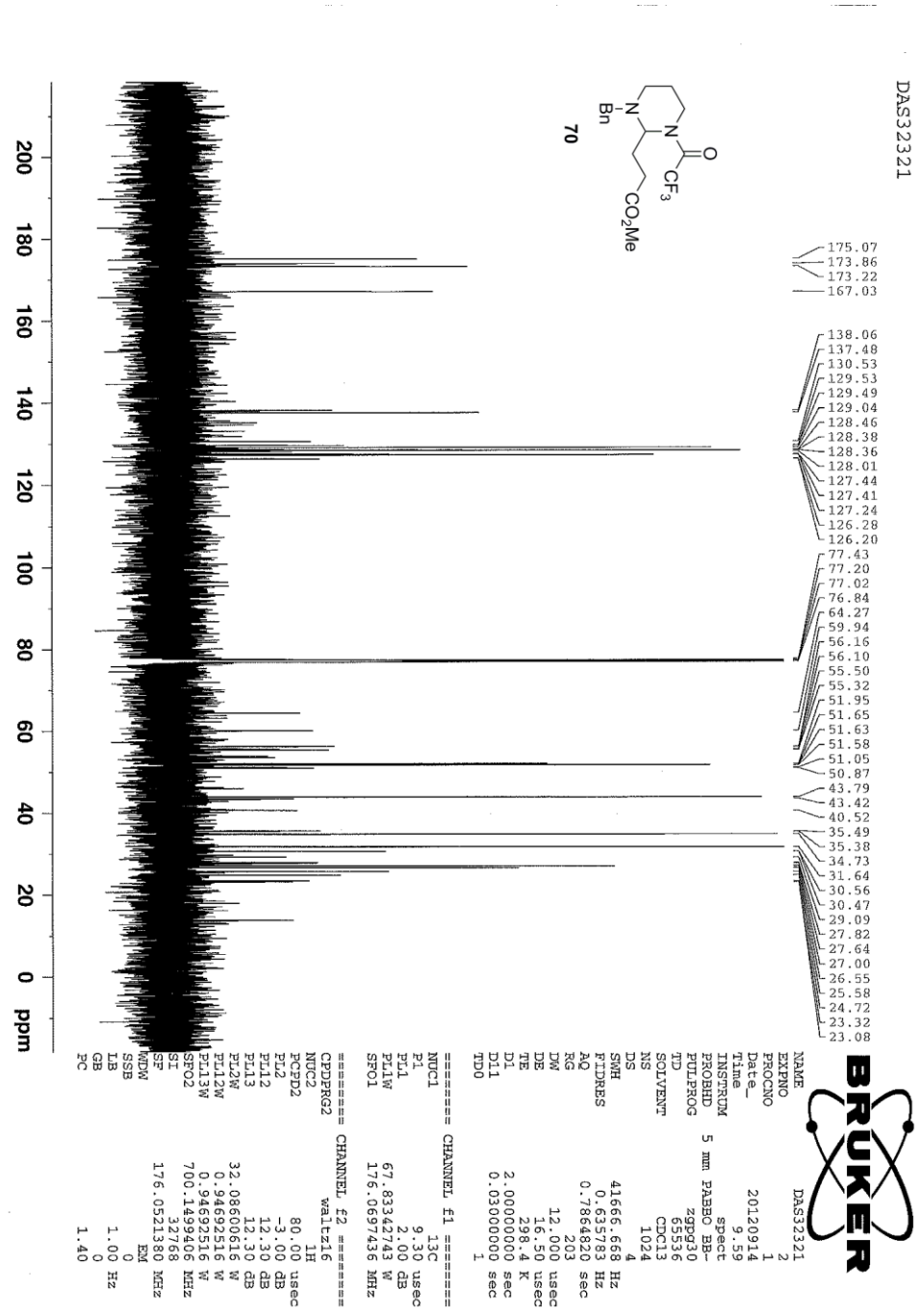

DAS32001
7.362
7.356
7.345
7.339
7.336
7.332
7.329
7.327
7.322
7.318
7.301
7.299
7.288
3.876
3.856
3.793
3.784
3.776
3.774
3.700
3.671
3.610
3.496
2.911
2.905
2.445
2.436
2.423
2.405
2.398
2.394
2.389
2.386
2.380
2.147
2.071
2.010
1.986
1.968
1.894
1.865
1.819
1.707
1.638
NAME DAS32001
EXPNO 1
PROCNO 1
Date_ 20120906
Time 17.31
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 17
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 50.8
DW 42.000 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
69
4.30
0.73
0.34
0.59
0.61
0.56
1.18
1.82
1.90
0.53
0.52
0.51
0.71
0.54
0.46
2.67
0.57
1.27
1.22
1.53
1.35
1.32
ppm

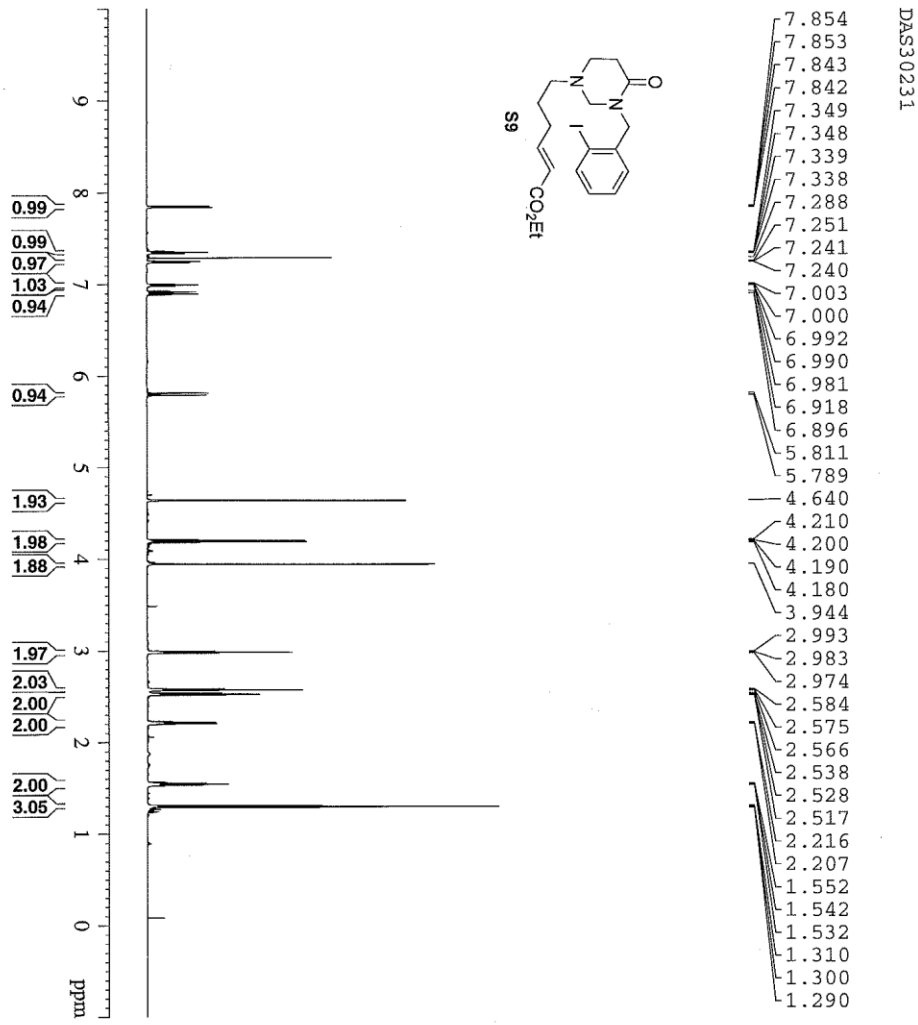

DAS32001
69
Ac
N
N
Bn
CO2Me
173.97
173.38
169.52
169.50
139.07
138.71
128.95
128.72
128.51
128.25
127.45
127.12
77.22
77.04
76.86
70.44
67.29
57.15
56.77
51.64
51.58
44.02
42.41
41.35
35.77
30.72
29.85
24.59
24.01
21.63
21.11
20.03
19.59
BRUKER
NAME DAS32001
EXPNO 2
PROCNO 1
Date_ 20120906
Time 17.35
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 184
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864820 sec
RG 203
DW 12.000 usec
DE 16.50 usec
TE 296.3 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0697436 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 usec
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1499406 MHz
SI 32768
SF 176.0521380 MHz
WDW EM
SSB 0
LB 1.50 Hz
GB 0
PC 1.40
200
180
160
140
120
100
80
60
40
20
0
ppm

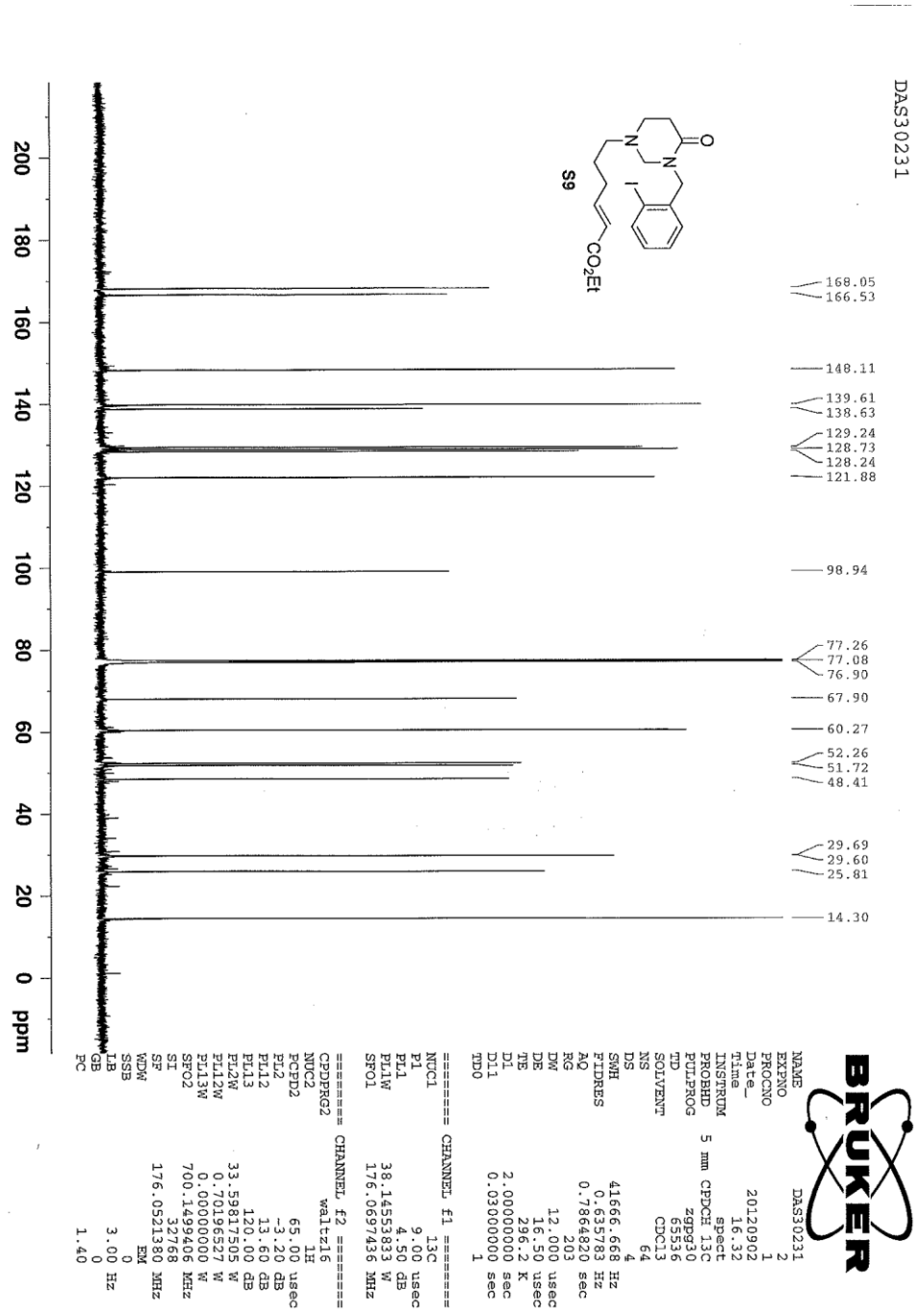

DAS31521
7.873
7.872
7.868
7.867
7.862
7.861
7.857
7.855
7.450
7.448
7.439
7.437
7.387
7.385
7.372
7.370
7.361
7.350
7.288
7.005
7.003
6.995
6.992
4.458
4.345
3.770
3.762
3.753
3.747
3.739
3.731
3.719
3.702
2.970
2.962
2.954
2.855
2.848
2.840
1.832
1.829
1.824
1.816
1.808
S5
1.31
0.76
1.94
1.33
1.52
1.22
2.81
2.68
1.52
1.24
2.76
ppm
NAME DAS3151
EXPNO 1
PROCNO 1
Date_ 20120824
Time 11.08
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 36
DW 42.000 usec
DE 6.50 usec
TE 295.3 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

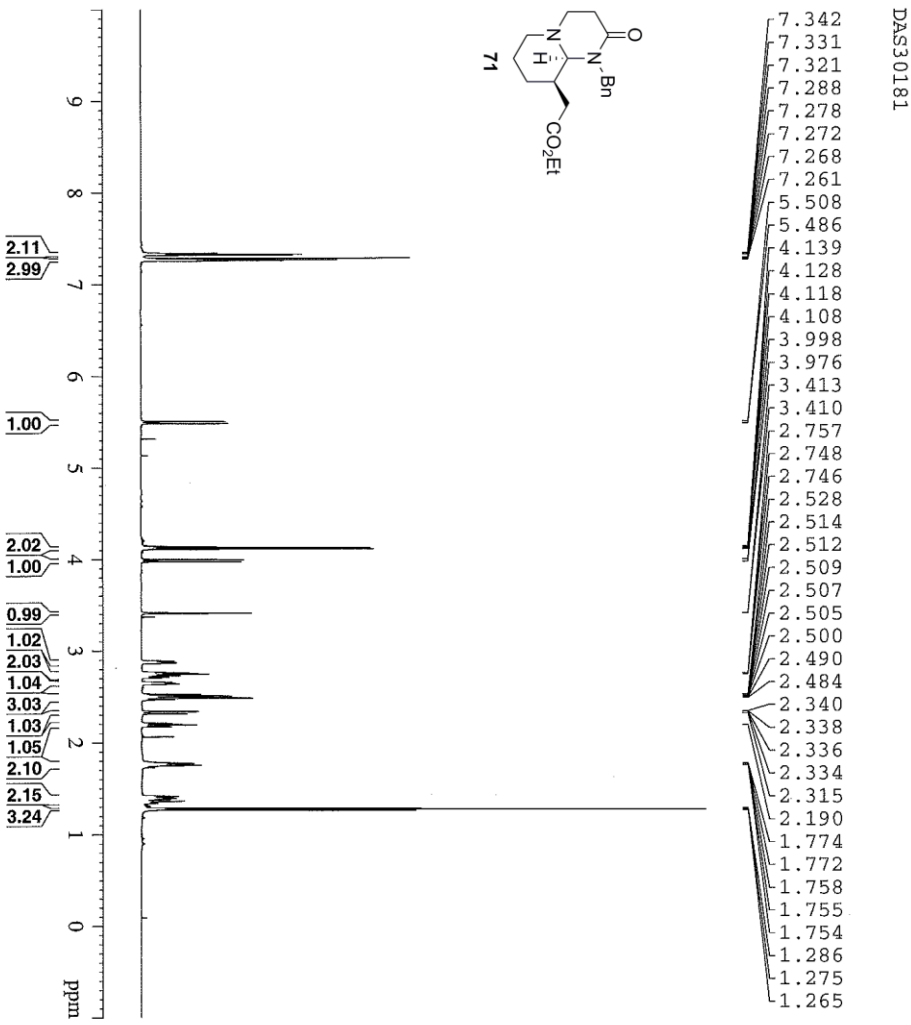

DAS31521
S5
156.05
155.92
155.85
155.71
155.65
155.51
155.45
155.30
139.75
139.68
139.62
139.38
130.38
130.08
129.22
129.16
128.31
128.23
118.96
118.79
117.32
117.16
115.68
115.52
114.04
113.88
100.59
100.26
77.25
77.07
76.88
66.78
66.76
64.08
61.22
60.74
51.17
50.85
45.88
45.86
43.35
23.22
22.62
BRUKER
NAME DAS31521
EXPNO 2
PROCNO 1
Date_ 20120824
Time 11.13
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 355
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864820 sec
RG 203
DW 12.000 usec
DE 16.50 usec
TE 295.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
========== CHANNEL f1 ==========
NUC1 13C
P1 9.00 usec
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0697436 MHz
========== CHANNEL f2 ==========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 usec
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1499406 MHz
SI 32768
SF 176.0521380 MHz
WDW EM
SSB 0
LB 1.50 Hz
GB 0
FC 1.40
200
180
160
140
120
100
80
60
40
20
0
ppm


DAS32321
7.345
7.335
7.326
7.310
7.300
7.288
7.262
7.219
6.225
6.223
5.626
5.624
5.622
4.538
4.387
4.231
3.814
3.806
3.795
3.785
3.703
3.699
3.695
3.676
3.675
3.672
3.643
3.629
2.653
2.642
2.633
2.632
2.631
2.391
2.382
2.378
2.372
2.369
2.362
2.360
2.350
1.588
0.918
0.907
Bn
CF3
CO2Me
70
3.78
2.12
0.97
0.98
0.41
1.02
1.02
0.56
1.35
3.00
5.16
5.53
1.16
1.15
0.53
1.02
1.57
2.18
5.34
0.97
1.05
2.20
2.26
1.05
1.83
1.42
0.58
ppm
NAME DAS32321
EXPNO 1
PROCNO 1
Date_ 20120914
Time 9.50
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 203
DW 42.000 usec
DE 6.50 usec
TE 298.3 K
D1 2.00000000 sec
TD0 1
========== CHANNEL f1 ==========
NUC1 1H
P1 13.75 usec
PL1 -3.00 dB
PL1W 32.08600616 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

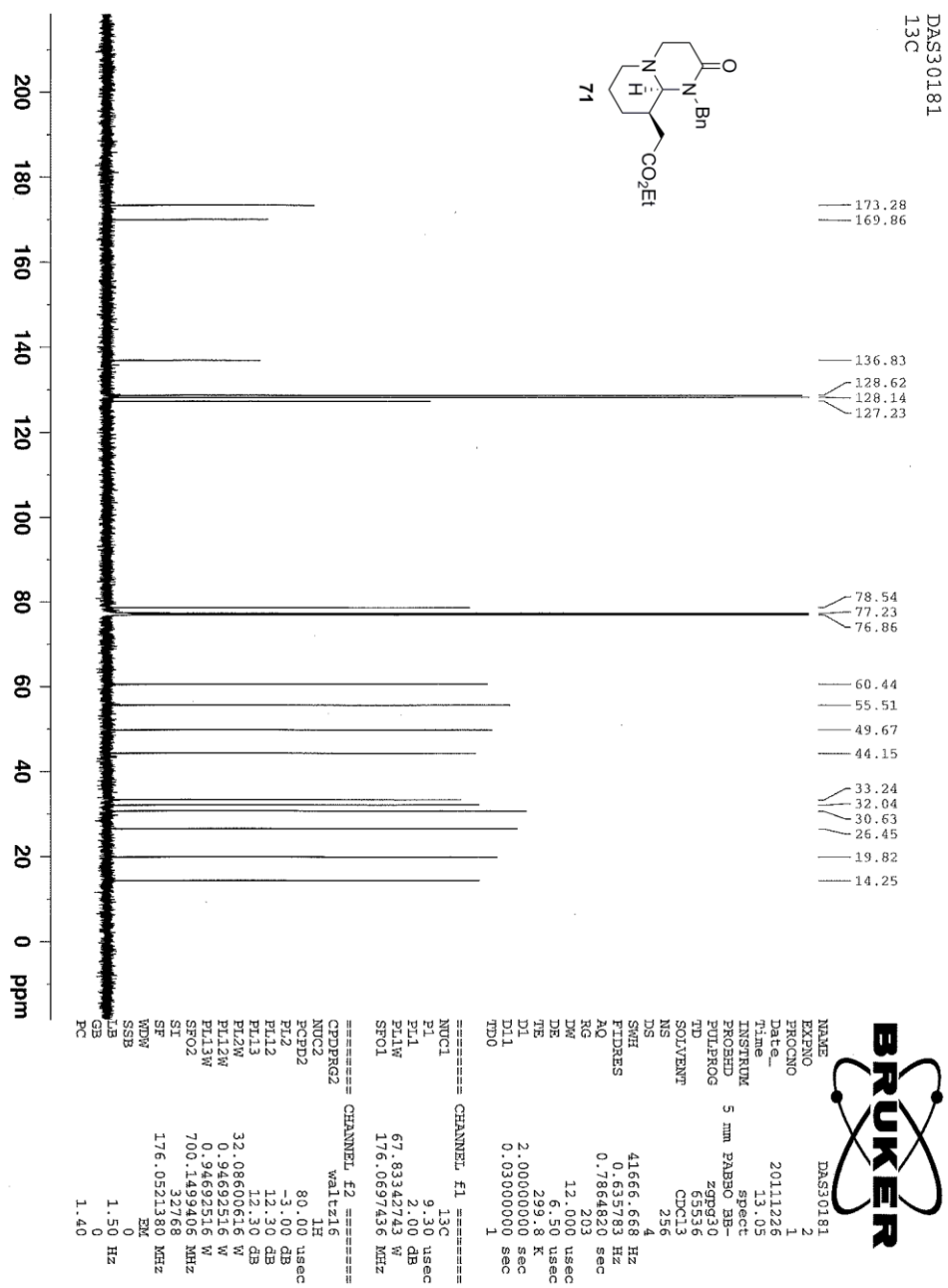

DAS32321
70
175.07
173.86
173.22
167.03
138.06
137.48
130.53
129.53
129.49
129.04
128.46
128.38
128.36
128.01
127.44
127.41
127.24
126.28
126.20
77.43
77.20
77.02
76.84
64.27
59.94
56.16
56.10
55.50
55.32
51.95
51.65
51.63
51.58
51.05
50.87
43.79
43.42
40.52
35.49
35.38
34.73
31.64
30.56
30.47
29.09
27.82
27.64
27.00
26.55
25.58
24.72
23.32
23.08
200
180
160
140
120
100
80
60
40
20
0
ppm
BRUKER
NAME DAS32321
EXPNO 2
PROCNO 1
Date_ 20120914
Time 9.59
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1024
DS 4
SWH 41665.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864820 sec
RG 203
DW 12.000 usec
DE 16.50 usec
TE 298.4 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.30 usec
PL1 2.00 dB
PL1W 67.83342743 W
SFO1 176.0697436 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -3.00 dB
PL12 12.30 dB
PL13 12.30 dB
PL2W 32.08600616 W
PL12W 0.94692516 W
PL13W 0.94692516 W
SFO2 700.1499406 MHz
SI 32768
SF 176.0521380 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

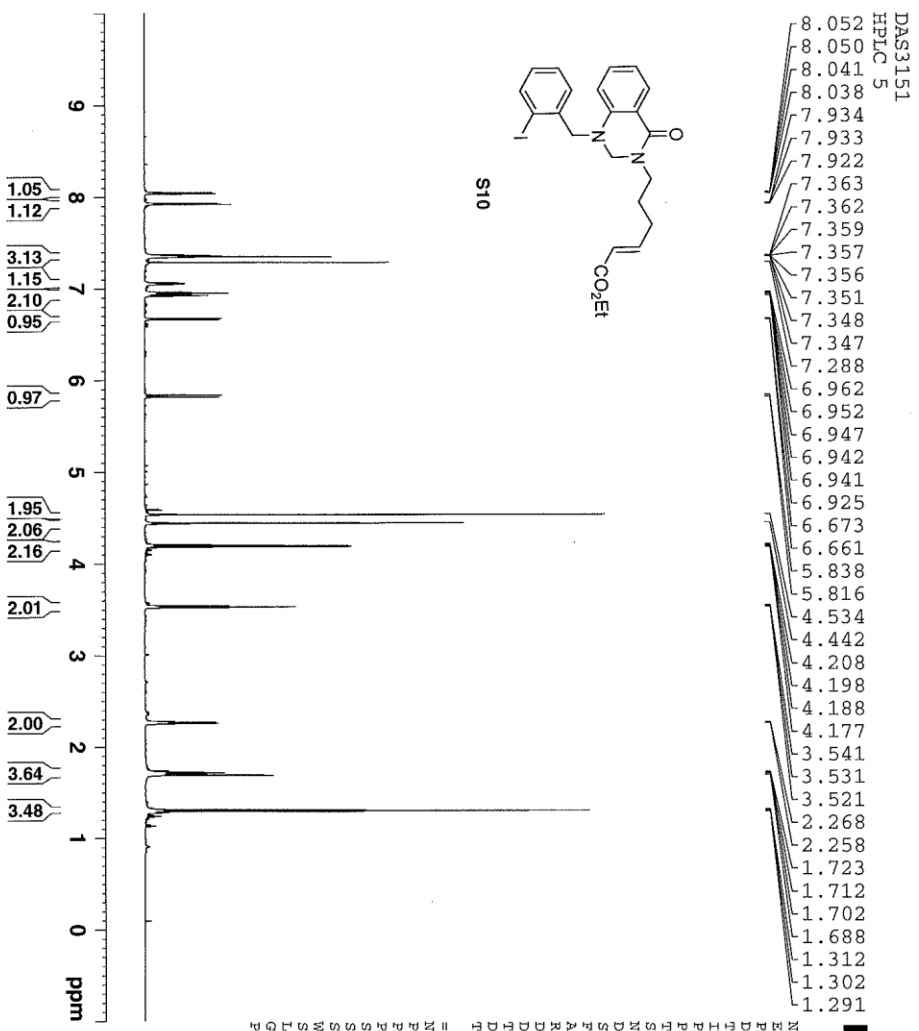

DAS30231
7.854
7.853
7.843
7.842
7.349
7.348
7.339
7.338
7.288
7.251
7.241
7.240
7.003
7.000
6.992
6.990
6.981
6.918
6.896
5.811
5.789
4.640
4.210
4.200
4.190
4.180
3.944
2.993
2.983
2.974
2.584
2.575
2.566
2.538
2.528
2.517
2.216
2.207
1.552
1.542
1.532
1.310
1.300
1.290
S9
CO2Et
0.99
0.99
0.97
1.03
0.94
0.94
1.93
1.98
1.88
1.97
2.03
2.00
2.00
2.00
3.05
ppm
NAME DAS30231
EXPNO 1
PROCNO 1
Date_ 20120902
Time 16.25
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 296.1 K
D1 2.00000000 sec
TD0 1
========== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

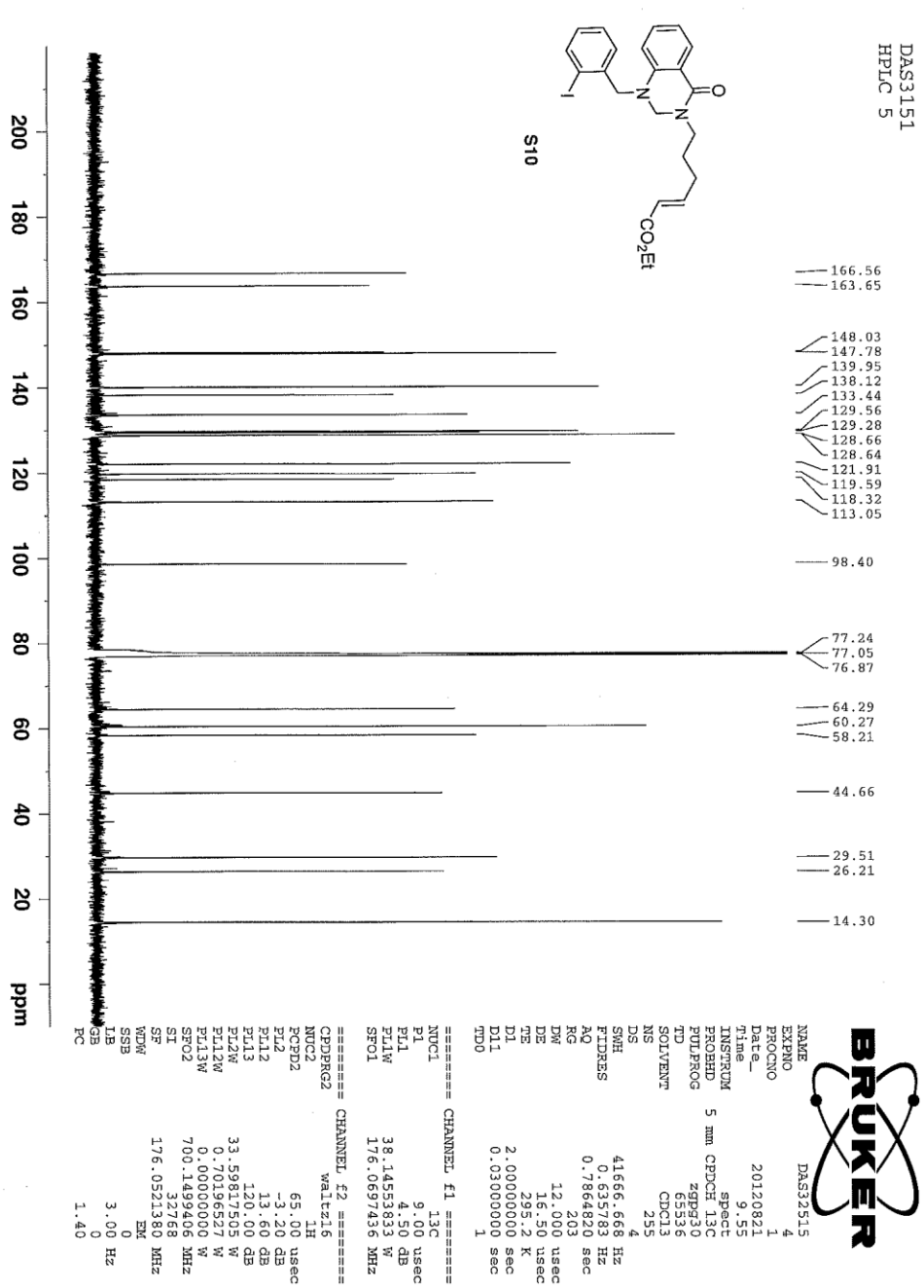

DAS30231
S9
CO2Et
168.05
166.53
148.11
139.61
138.63
129.24
128.73
128.24
121.88
98.94
77.26
77.08
76.90
67.90
60.27
52.26
51.72
48.41
29.69
29.60
25.81
14.30
200
180
160
140
120
100
80
60
40
20
0
ppm
BRUKER
NAME DAS30231
EXPNO 2
PROCNO 1
Date_ 20120902
Time_ 16.32
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 64
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864820 sec
RG 203
DW 12.000 usec
DE 16.50 usec
TE 296.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
========== CHANNEL f1 ==========
NUC1 13C
P1 9.00 usec
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0697436 MHz
========== CHANNEL f2 ==========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 usec
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1499406 MHz
SI 32768
SF 176.0521380 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40

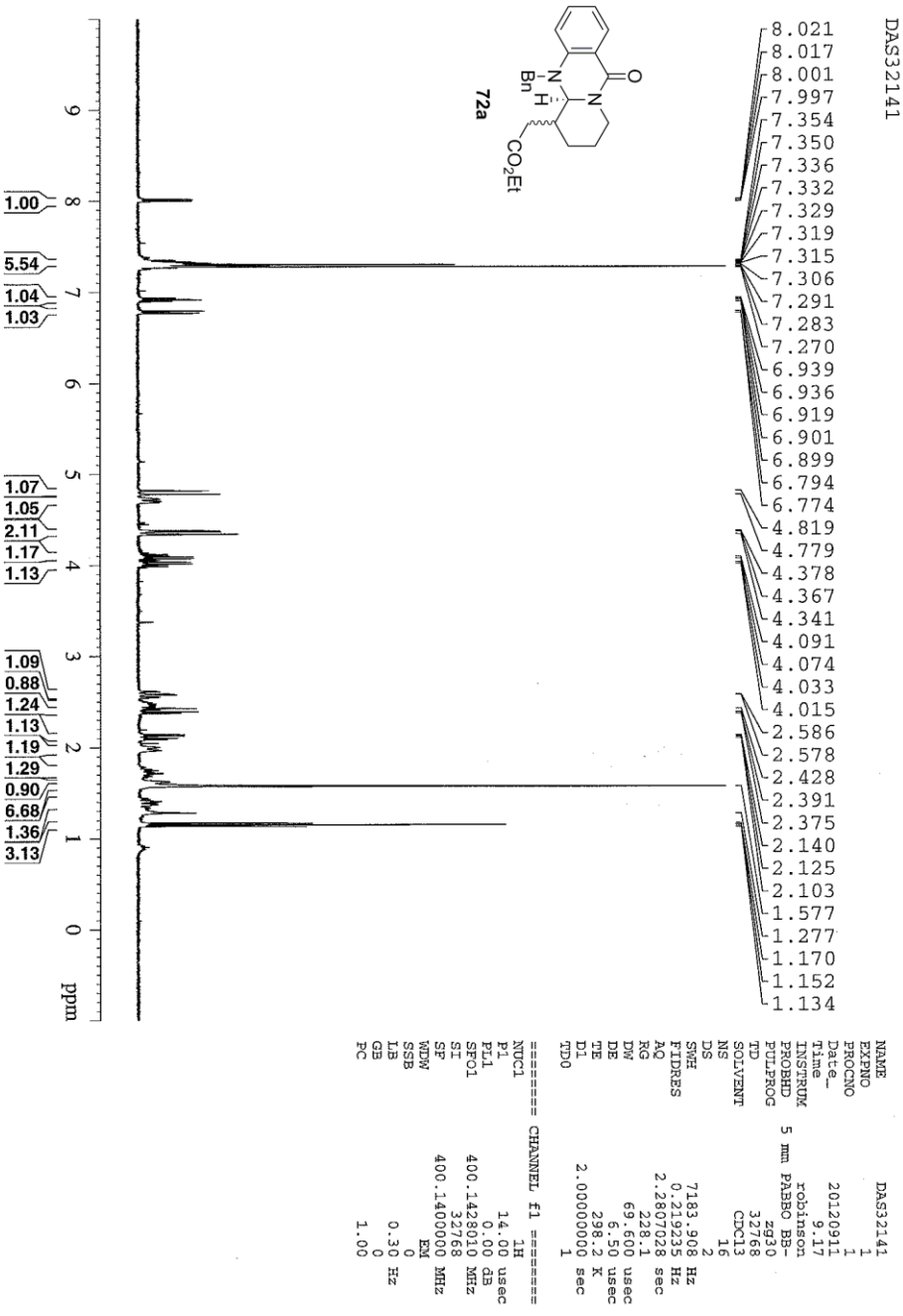


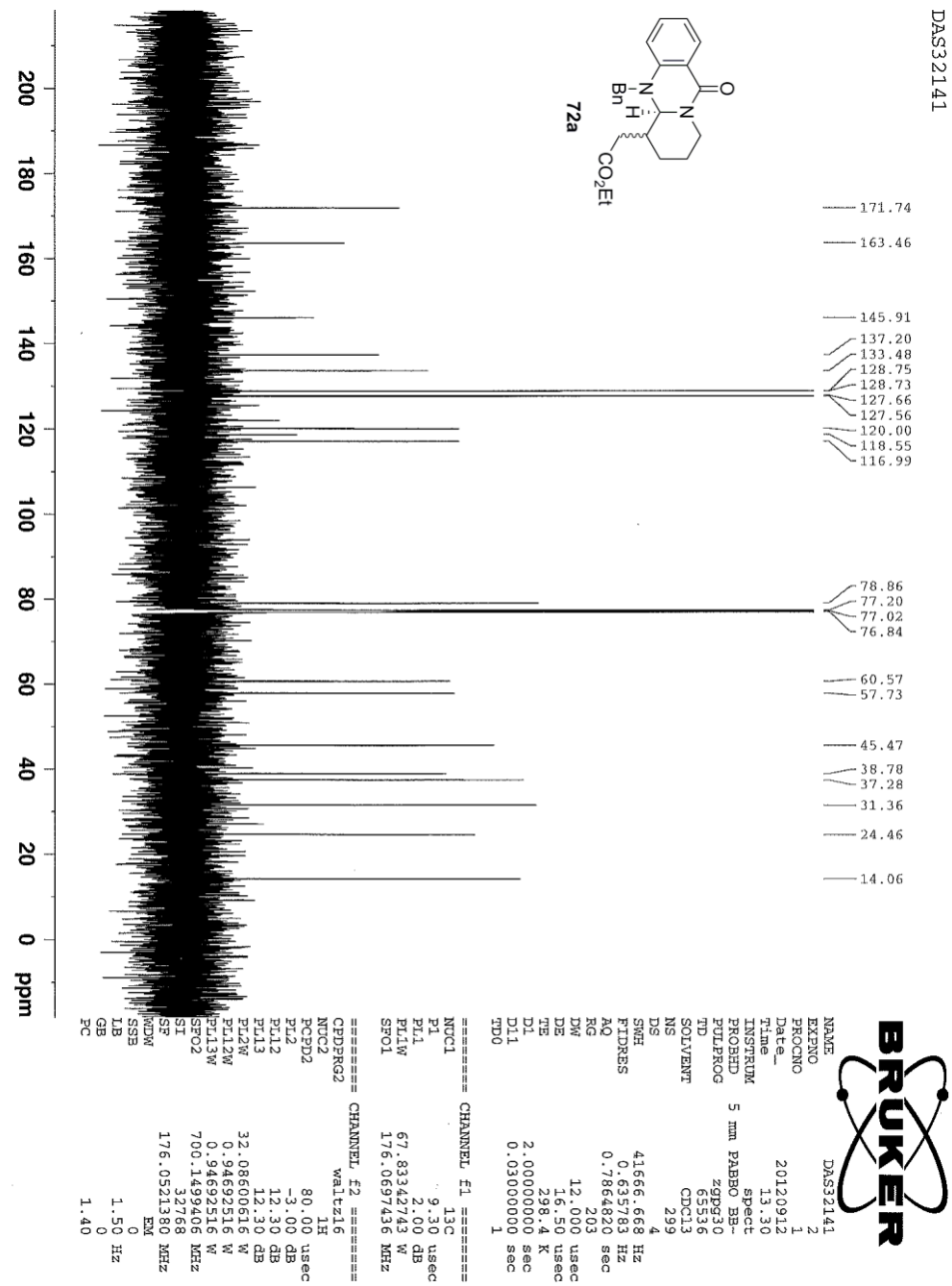

```
NAME                  DAS30181
EXPNO                        1
PROCNO                       1
Date_              20111226
Time                    12.58
INSTRUM                 spect
PROBHD     5 mm PABBO BB-
PULPROG                 zg30
TD                      95236
SOLVENT                 CDCl3
NS                         32
DS                          2
SWH                11904.762 Hz
FIDRES             0.125003 Hz
AQ                 3.9999621 sec
RG                        144
DW                     42.000 usec
DE                      6.50 usec
TE                     298.8 K
D1                 2.00000000 sec
TD0                          1

========== CHANNEL f1 ==========
NUC1                       1H
P1                      13.75 usec
PL1                     -3.00 dB
PL1W               32.08600616 W
SFO1              700.1516910 MHz
SI                        131072
SF                700.1471400 MHz
WDW                         EM
SSB                          0
LB                        0.30 Hz
GB                           0
PC                        1.00
```

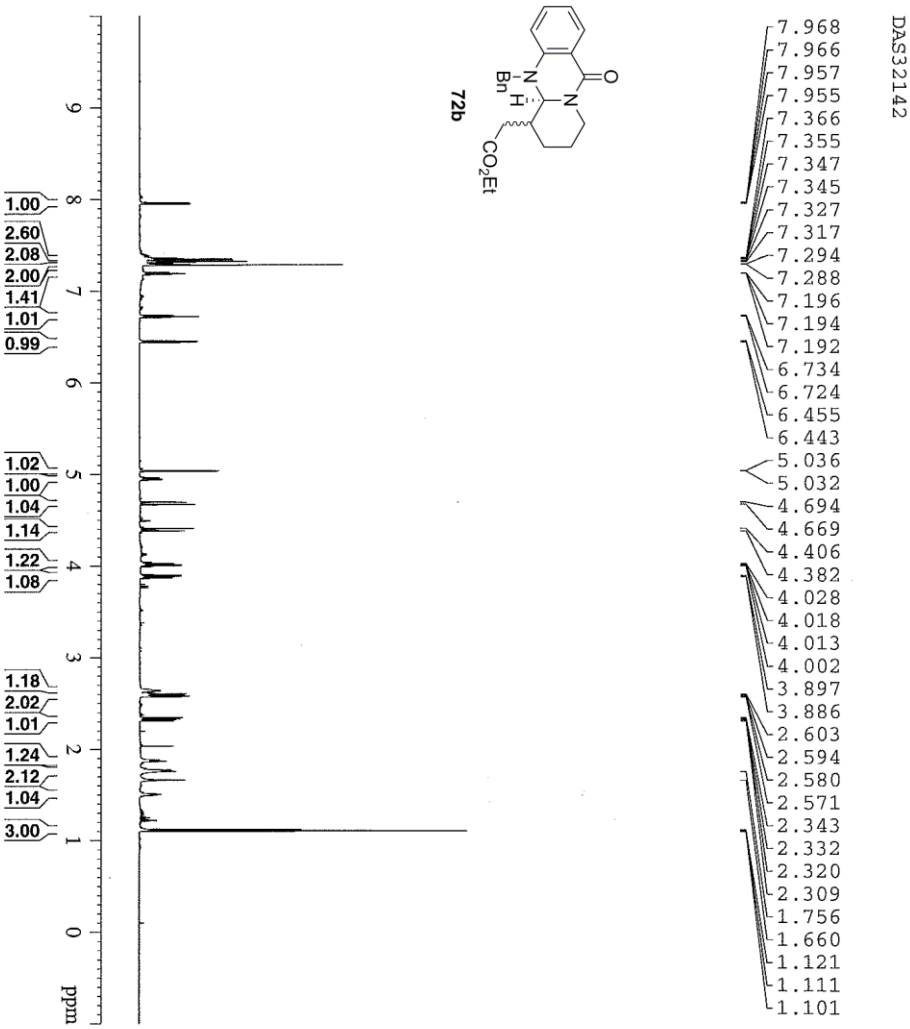

DAS30181
13C
71
Bn
CO2Et
173.28
169.86
136.83
128.62
128.14
127.23
78.54
77.23
76.86
60.44
55.51
49.67
44.15
33.24
32.04
30.63
26.45
19.82
14.25
200
180
160
140
120
100
80
60
40
20
0
ppm
BRUKER
NAME DAS30181
EXPNO 2
PROCNO 1
Date_ 20111226
Time 13.05
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 256
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864820 sec
RG 203
DW 12.000 usec
DE 6.50 usec
TE 299.8 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.30 usec
PL1 2.00 dB
PL1W 67.83342743 W
SFO1 176.0697436 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -3.00 dB
PL12 12.30 dB
PL13 12.30 dB
PL2W 32.08600616 W
PL12W 0.94692516 W
PL13W 0.94692516 W
SFO2 700.1499406 MHz
SI 32768
SF 176.0521380 MHz
WDW EM
SSB 0
LB 1.50 Hz
GB 0
PC 1.40

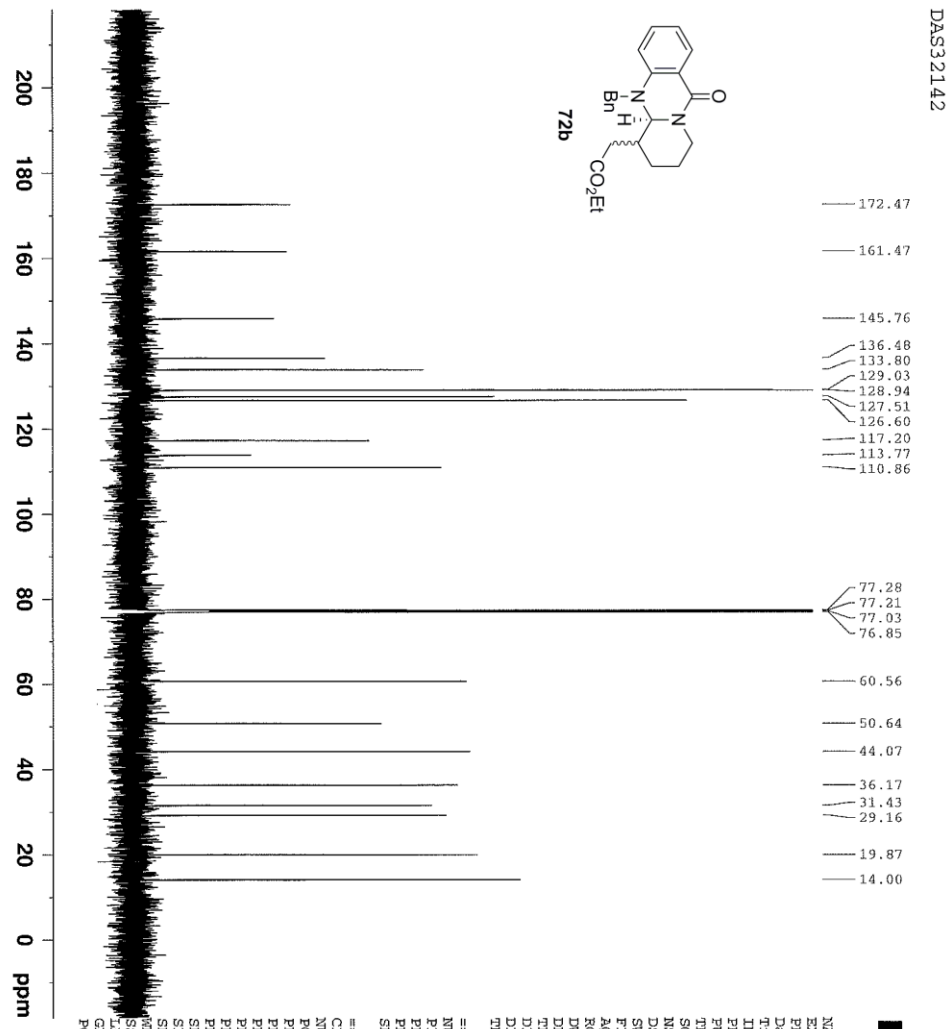

DAS3151
HPLC 5
8.052
8.050
8.041
8.038
7.934
7.933
7.922
7.363
7.362
7.359
7.357
7.356
7.351
7.348
7.347
7.288
6.962
6.952
6.947
6.942
6.941
6.925
6.673
6.661
5.838
5.816
4.534
4.442
4.208
4.198
4.188
4.177
3.541
3.531
3.521
2.268
2.258
1.723
1.712
1.702
1.688
1.312
1.302
1.291
S10
CO2Et
1.05
1.12
3.13
1.15
2.10
0.95
0.97
1.95
2.06
2.16
2.01
2.00
3.64
3.48
9
8
7
6
5
4
3
2
1
0
ppm
NAME DAS32515
EXPNO 3
PROCNO 1
Date_ 20120821
Time_ 9.46
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 295.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00


DAS3151
HPLC 5
S10
CO2Et
166.56
163.65
148.03
147.78
139.95
138.12
133.44
129.56
129.28
128.66
128.64
121.91
119.59
118.32
113.05
98.40
77.24
77.05
76.87
64.29
60.27
58.21
44.66
29.51
26.21
14.30
200
180
160
140
120
100
80
60
40
20
ppm
BRUKER
NAME DAS32515
EXPNO 4
PROCNO 1
Date_ 20120821
Time_ 9.55
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDC13
NS 255
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864820 sec
RG 203
DW 12.000 usec
DE 16.50 usec
TE 295.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0697436 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 usec
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1499406 MHz
SI 32768
SF 176.0521380 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40

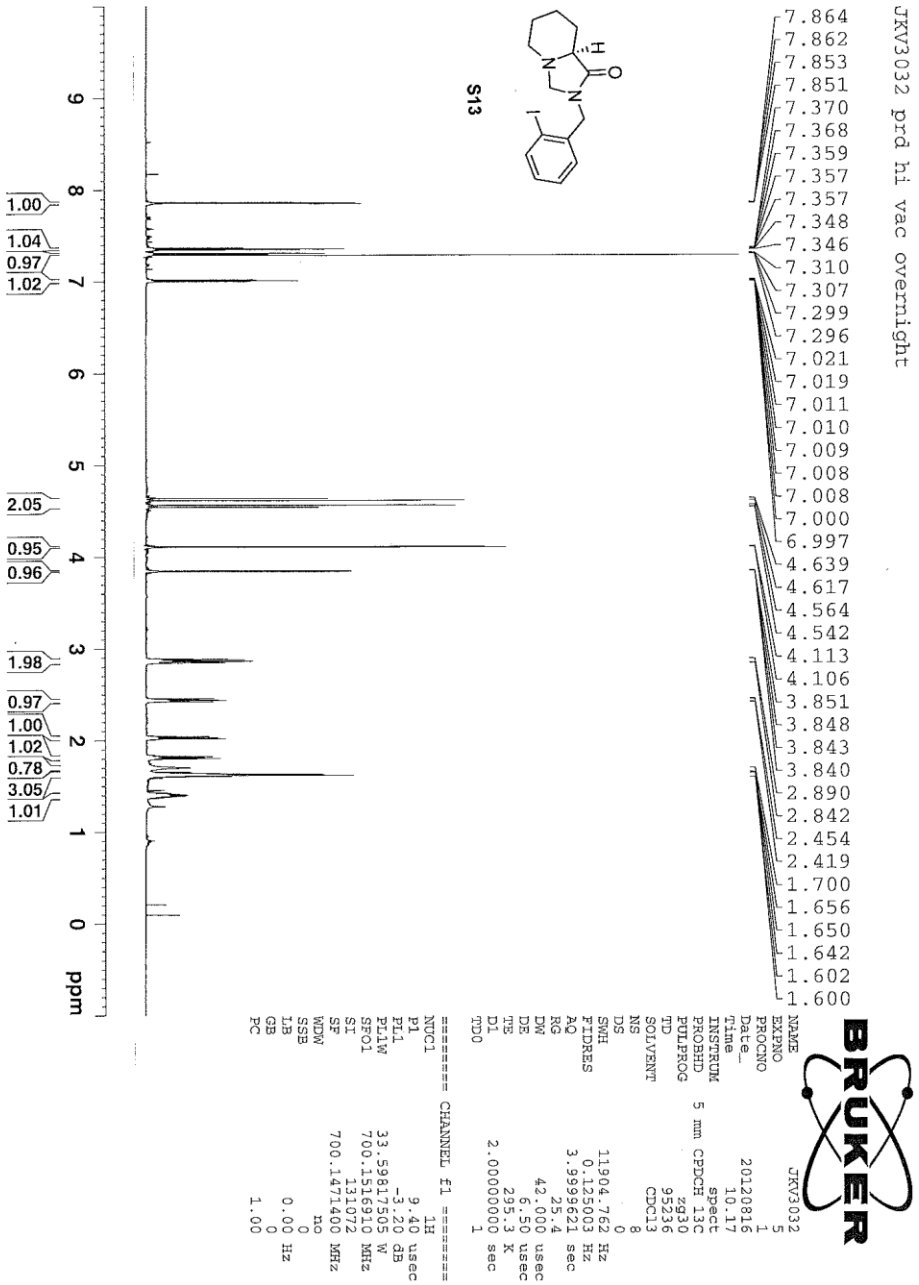

DAS32141
8.021
8.017
8.001
7.997
7.354
7.350
7.336
7.332
7.329
7.319
7.315
7.306
7.291
7.283
7.270
6.939
6.936
6.919
6.901
6.899
6.794
6.774
4.819
4.779
4.378
4.367
4.341
4.091
4.074
4.033
4.015
2.586
2.578
2.428
2.391
2.375
2.140
2.125
2.103
1.577
1.277
1.170
1.152
1.134
72a
1.00
5.54
1.04
1.03
1.07
1.05
2.11
1.17
1.13
1.09
0.88
1.24
1.13
1.19
1.29
0.90
6.68
1.36
3.13
ppm
NAME DAS32141
EXPNO 1
PROCNO 1
Date_ 20120911
Time 9.17
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 sec
RG 228.1
DW 69.600 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
========== CHANNEL f1 ==========
NUC1 1H
P1 14.00 usec
PL1 0.00 dB
SFO1 400.1428010 MHz
SI 32768
SF 400.1400000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

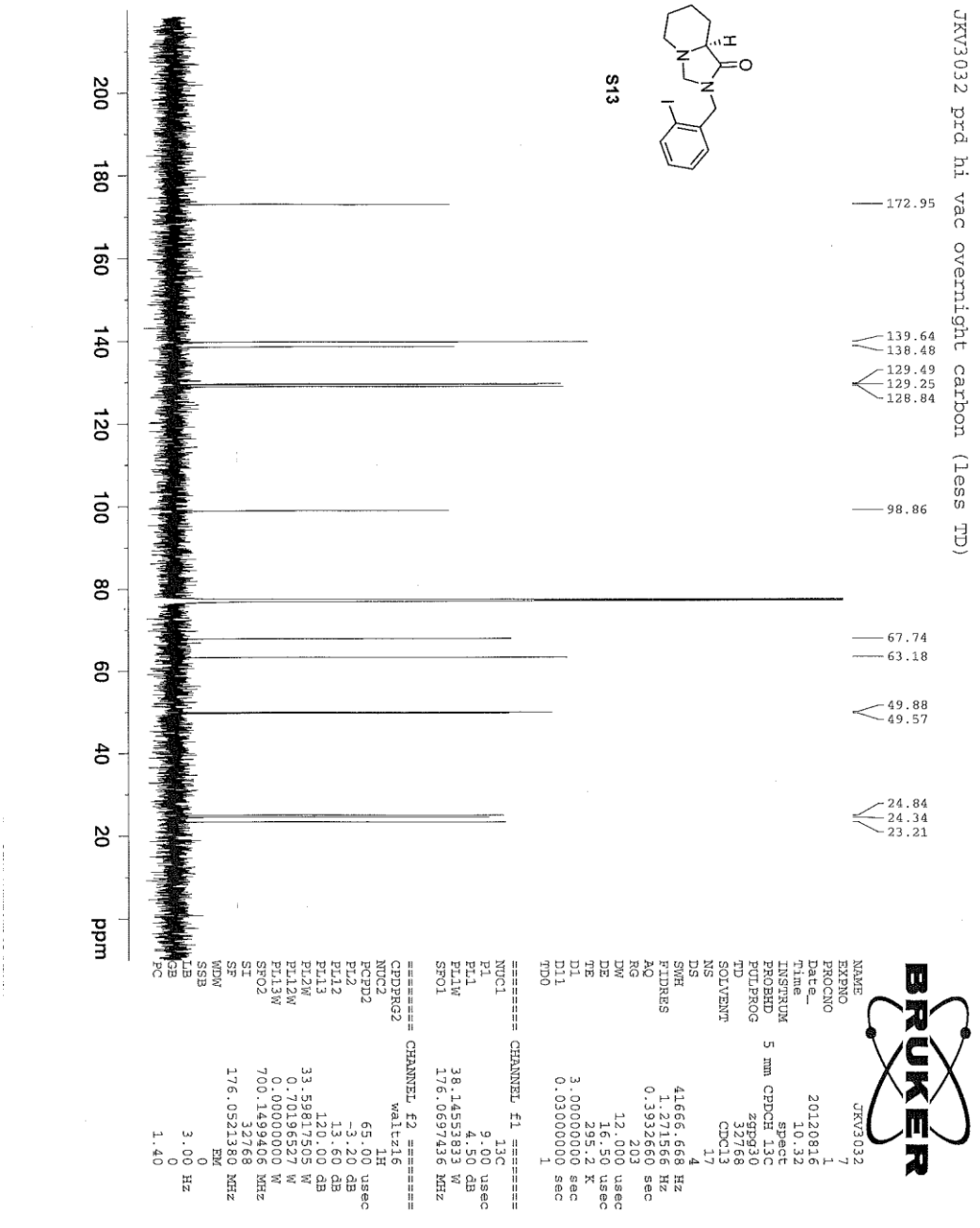

DAS32141
72a
171.74
163.46
145.91
137.20
133.48
128.75
128.73
127.66
127.56
120.00
118.55
116.99
78.86
77.20
77.02
76.84
60.57
57.73
45.47
38.78
37.28
31.36
24.46
14.06
200
180
160
140
120
100
80
60
40
20
0
ppm

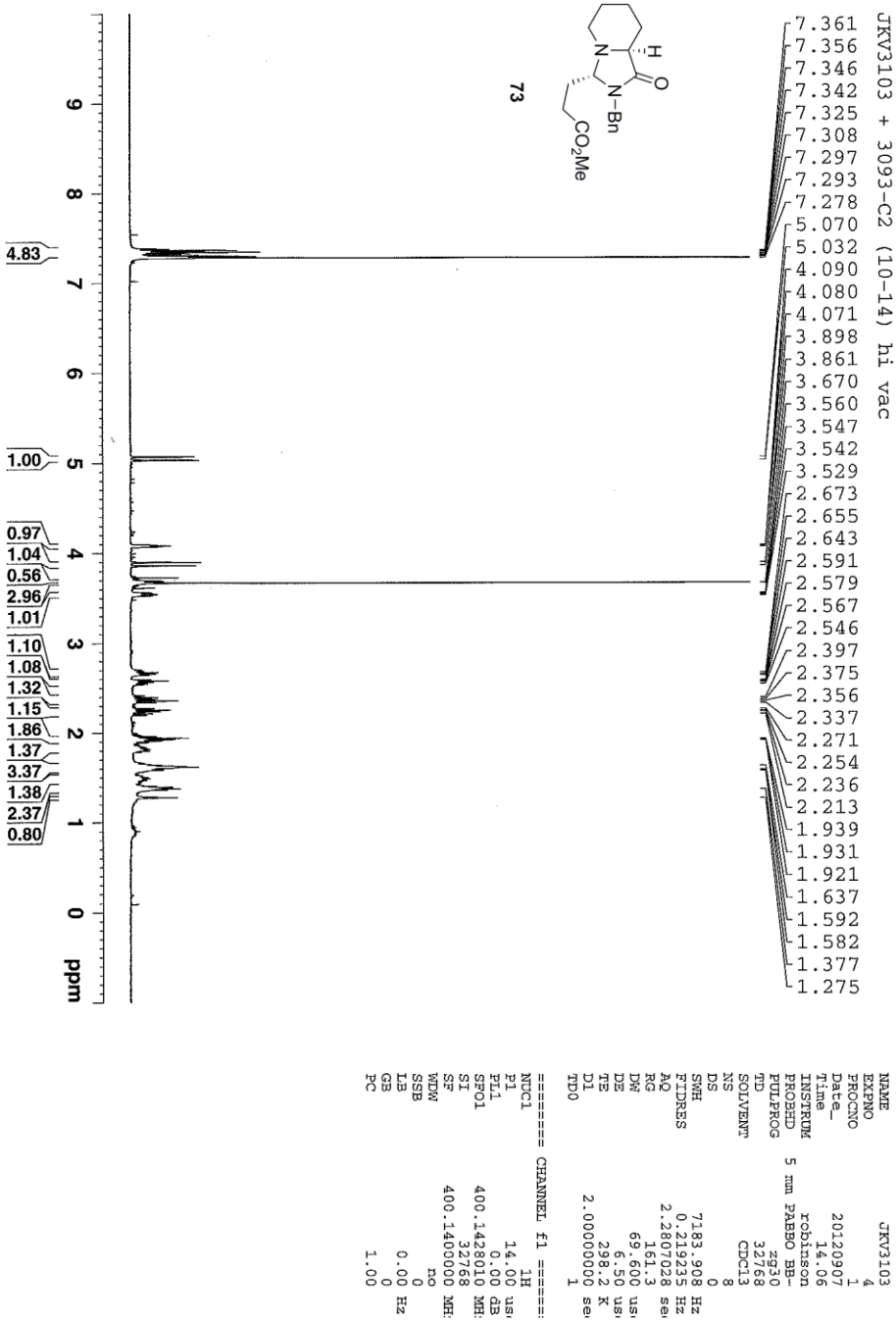

DAS32142
7.968
7.966
7.957
7.955
7.366
7.355
7.347
7.345
7.327
7.317
7.294
7.288
7.196
7.194
7.192
6.734
6.724
6.455
6.443
5.036
5.032
4.694
4.669
4.406
4.382
4.028
4.018
4.013
4.002
3.897
3.886
2.603
2.594
2.580
2.571
2.343
2.332
2.320
2.309
1.756
1.660
1.121
1.111
1.101
72b
1.00
2.60
2.08
2.00
1.41
1.01
0.99
1.02
1.00
1.04
1.14
1.22
1.08
1.18
2.02
1.01
1.24
2.12
1.04
3.00
ppm
NAME DAS32142
EXPNO 3
PROCNO 1
Date_ 20120912
Time 12:09
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 203
DW 42.000 usec
DE 6.50 usec
TE 300.0 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.75 usec
PL1 -3.00 dB
PL1W 32.08600616 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



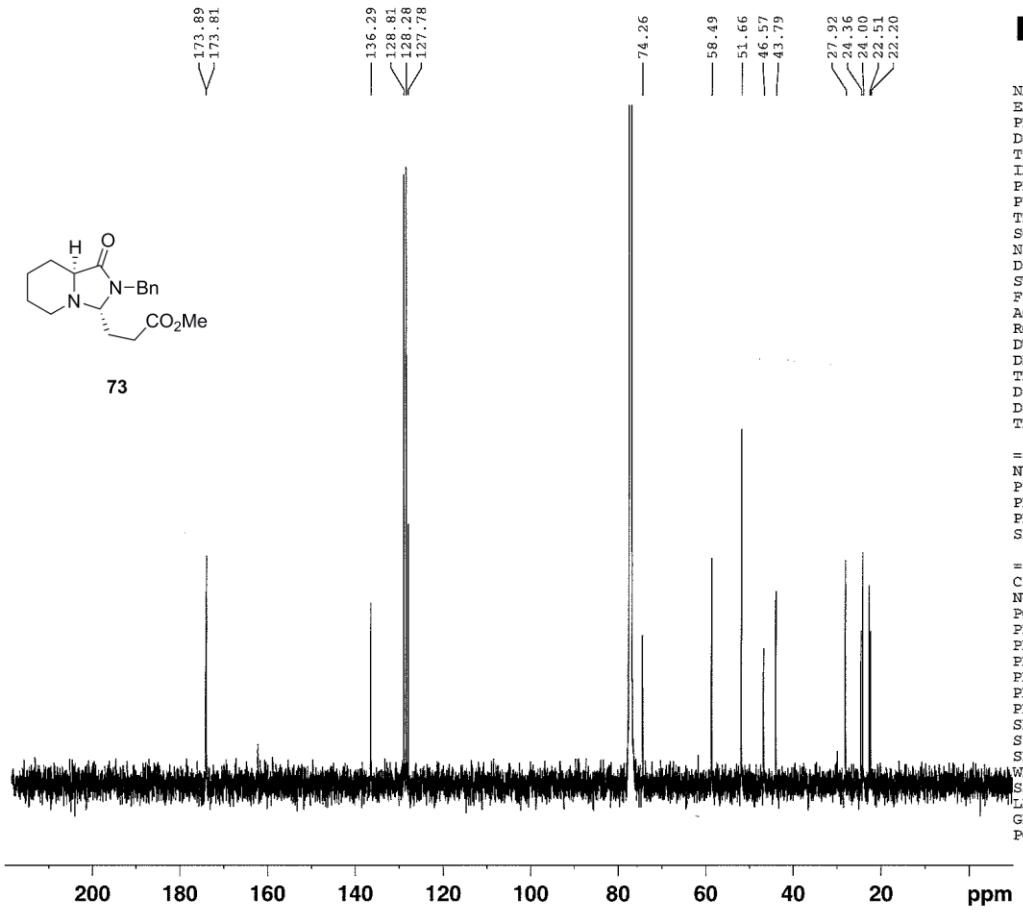

```
NAME                 DAS32142
EXPNO                       4
PROCNO                      1
Date_              20120912
Time_                  12.16
INSTRUM                spect
PROBHD     5 mm PABBO BB-
PULPROG             zgpg30
TD                       65536
SOLVENT                 CDCl3
NS                        179
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                      299.3 K
D1                    2.00000000 sec
D11                   0.03000000 sec
TD0                         1

========== CHANNEL f1 ==========
NUC1                      13C
P1                       9.30 usec
PL1                      2.00 dB
PL1W               67.83342743 W
SFO1              176.0697436 MHz

========== CHANNEL f2 ==========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                   80.00 usec
PL2                     -3.00 dB
PL12                    12.30 dB
PL13                    12.30 dB
PL2W               32.08600616 W
PL12W               0.94692516 W
PL13W               0.94692516 W
SFO2              700.1499406 MHz
SI                       32768
SF                176.0521380 MHz
WDW                        EM
SSB                         0
LB                       1.50 Hz
GB                          0
PC                       1.40
```


JKV3032 prd hi vac overnight
S13
7.864
7.862
7.853
7.851
7.370
7.368
7.359
7.357
7.357
7.348
7.346
7.310
7.307
7.299
7.296
7.021
7.019
7.011
7.010
7.009
7.008
7.008
7.000
6.997
4.639
4.617
4.564
4.542
4.113
4.106
3.851
3.848
3.843
3.840
2.890
2.842
2.454
2.419
1.700
1.656
1.650
1.642
1.602
1.600
1.00
1.04
0.97
1.02
2.05
0.95
0.96
1.98
0.97
1.00
1.02
0.78
3.05
1.01
ppm
NAME JKV3032
EXPNO 5
PROCNO 1
Date_ 20120816
Time_ 10.17
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 8
DS 0
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 25.4
DW 42.000 usec
DE 6.50 usec
TE 295.3 K
D1 2.00000000 sec
TD0 1
========== CHANNEL f1 ==========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 1311072
SF 700.1471400 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
BRUKER


JKV3032 prd hi vac overnight carbon (less TD)
S13
172.95
139.64
138.48
129.49
129.25
128.84
98.86
67.74
63.18
49.88
49.57
24.84
24.34
23.21
200
180
160
140
120
100
80
60
40
20
ppm

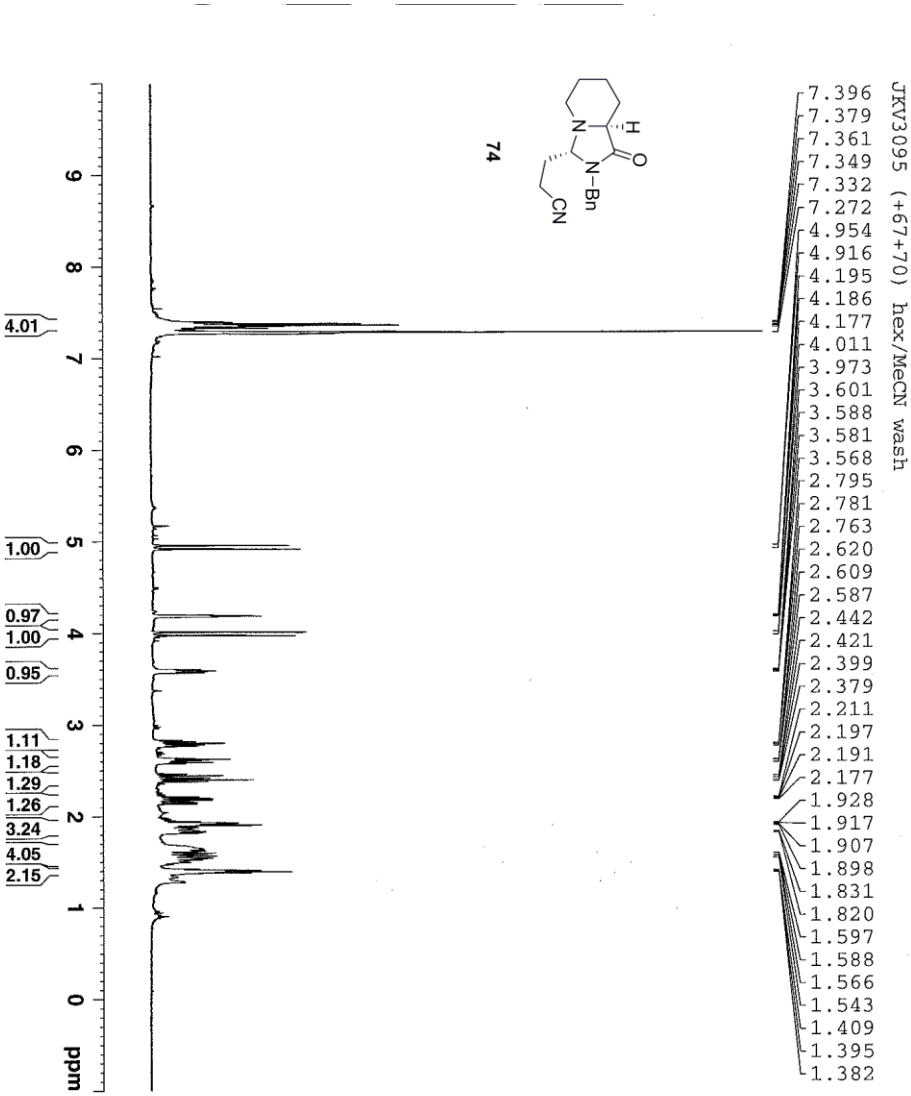

JKV3103 + 3093-C2 (10-14) hi vac
7.361
7.356
7.346
7.342
7.325
7.308
7.297
7.293
7.278
5.070
5.032
4.090
4.080
4.071
3.898
3.861
3.670
3.560
3.547
3.542
3.529
2.673
2.655
2.643
2.591
2.579
2.567
2.546
2.397
2.375
2.356
2.337
2.271
2.254
2.236
2.213
1.939
1.931
1.921
1.637
1.592
1.582
1.377
1.275
N-Bn
CO2Me
73
4.83
1.00
0.97
1.04
0.56
2.96
1.01
1.10
1.08
1.32
1.15
1.86
1.37
3.37
1.38
2.37
0.80
ppm
NAME JKV3103
EXPNO 4
PROCNO 1
Date_ 20120907
Time 14.06
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 8
DS 0
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 400.1400000 MH
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00

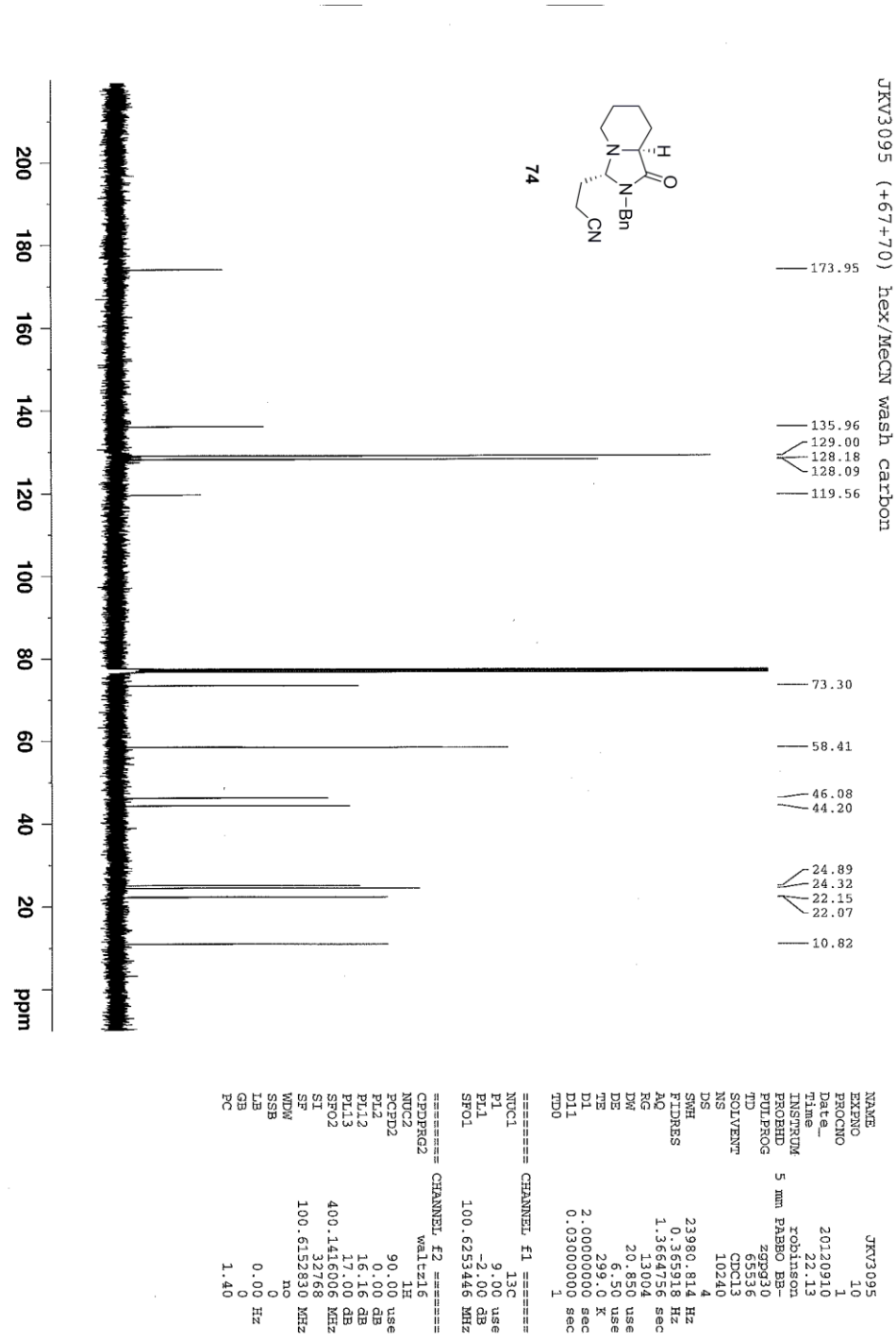
JKV3093 + 3103-C2 (10-12) carbon



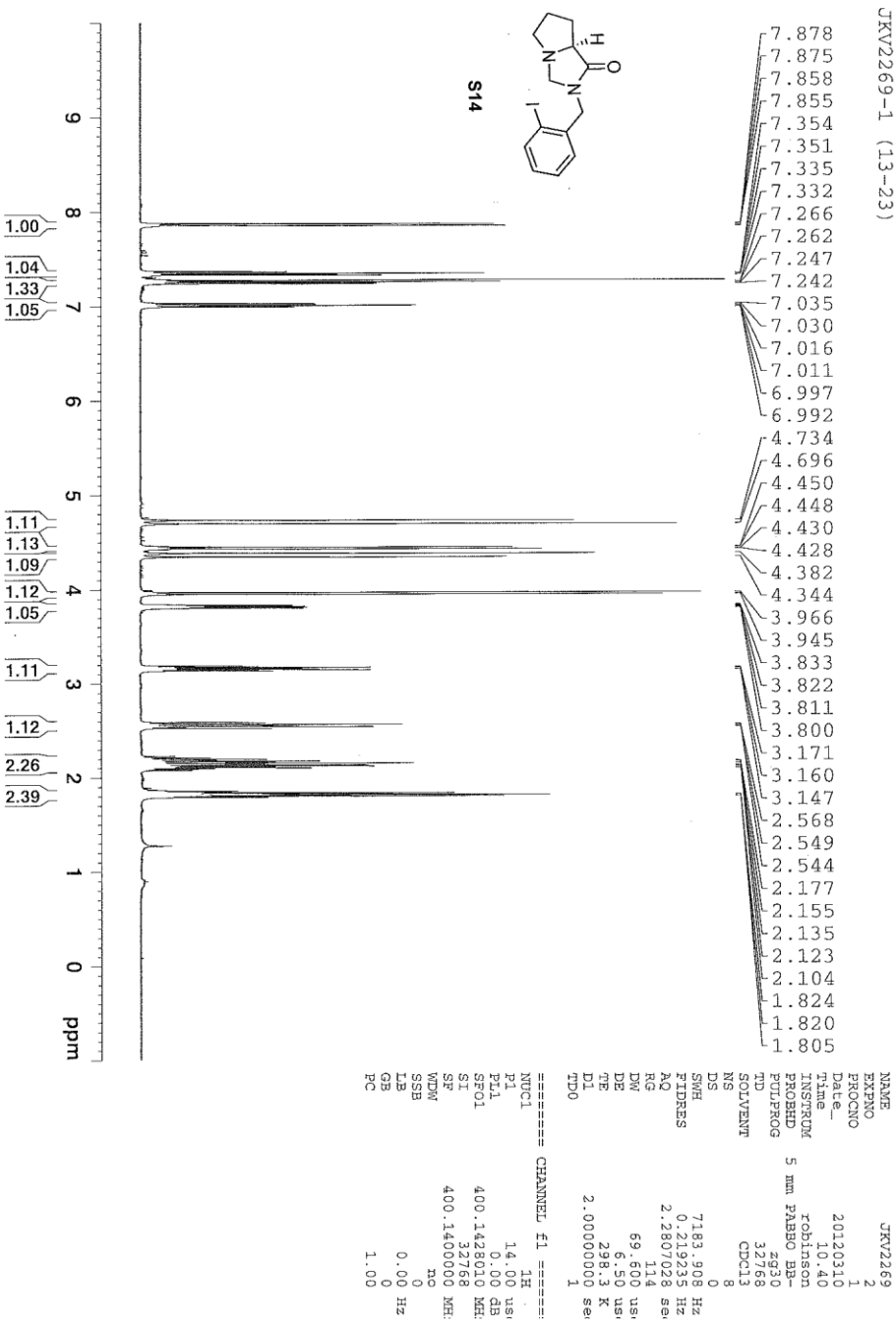
73

NAME	JKV3093	
EXPNO	4	
PROCNO	1	
Date_	20120906	
Time	18.24	
INSTRUM	spect	
PROBHD	5 mm CPDCH 13C	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	184	
DS	4	
SWH	41666.668	Hz
FIDRES	0.635783	Hz
AQ	0.7864820	sec
RG	203	
DW	12.000	usec
DE	16.50	usec
TE	296.2	K
D1	4.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	9.00	usec
PL1	4.50	dB
PL1W	38.14553833	W
SFO1	176.0697436	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	65.00	usec
PL2	-3.20	dB
PL12	13.60	dB
PL13	120.00	dB
PL2W	33.59817505	W
PL12W	0.70196527	W
PL13W	0.00000000	W
SFO2	700.1499406	MHz
SI	32768	
SF	176.0521380	MHz
WDW	EM	
SSB	0	
LB	3.00	Hz
GB	0	
PC	1.40	


JKV3095 (+67+70) hex/MeCN wash
7.396
7.379
7.361
7.349
7.332
7.272
4.954
4.916
4.195
4.186
4.177
4.011
3.973
3.601
3.588
3.581
3.568
2.795
2.781
2.763
2.620
2.609
2.587
2.442
2.421
2.399
2.379
2.211
2.197
2.191
2.177
1.928
1.917
1.907
1.898
1.831
1.820
1.597
1.588
1.566
1.543
1.409
1.395
1.382
74
N
H
O
N
N–Bn
CN
4.01
1.00
0.97
1.00
0.95
1.11
1.18
1.29
1.26
3.24
4.05
2.15
9
8
7
6
5
4
3
2
1
0
ppm
NAME JKV3095
EXPNO 8
PROCNO 1
Date_ 20120910
Time 10.50
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 19
DS 0
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 400.1400000 MH
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.00




```
NAME                    JKV3095
EXPNO                        10
PROCNO                        1
Date_               20120910
Time                    22.13
INSTRUM                 robinson
PROBHD     5 mm PABBO BB-
PULPROG                 zgpg30
TD                      65536
SOLVENT                 CDCl3
NS                      10240
DS                          4
SWH                 23980.814 Hz
FIDRES                0.365918 Hz
AQ                    1.3664756 sec
RG                      13004
DW                     20.850 usec
DE                      6.50 usec
TE                     299.0 K
D1                    2.00000000 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                 100.6152830 MHz
WDW                          no
SSB                           0
LB                         0.00 Hz
GB                            0
PC                         1.40
```


JKV2269-1 (13-23)
S14
7.878
7.875
7.858
7.855
7.354
7.351
7.335
7.332
7.266
7.262
7.247
7.242
7.035
7.030
7.016
7.011
6.997
6.992
4.734
4.696
4.450
4.448
4.430
4.428
4.382
4.344
3.966
3.945
3.833
3.822
3.811
3.800
3.171
3.160
3.147
2.568
2.549
2.544
2.177
2.155
2.135
2.123
2.104
1.824
1.820
1.805
1.00
1.04
1.33
1.05
1.11
1.13
1.09
1.12
1.05
1.11
1.12
2.26
2.39
ppm
NAME JKV2269
EXPNO 2
PROCNO 1
Date_ 20120310
Time 10.40
INSTRUM robinson
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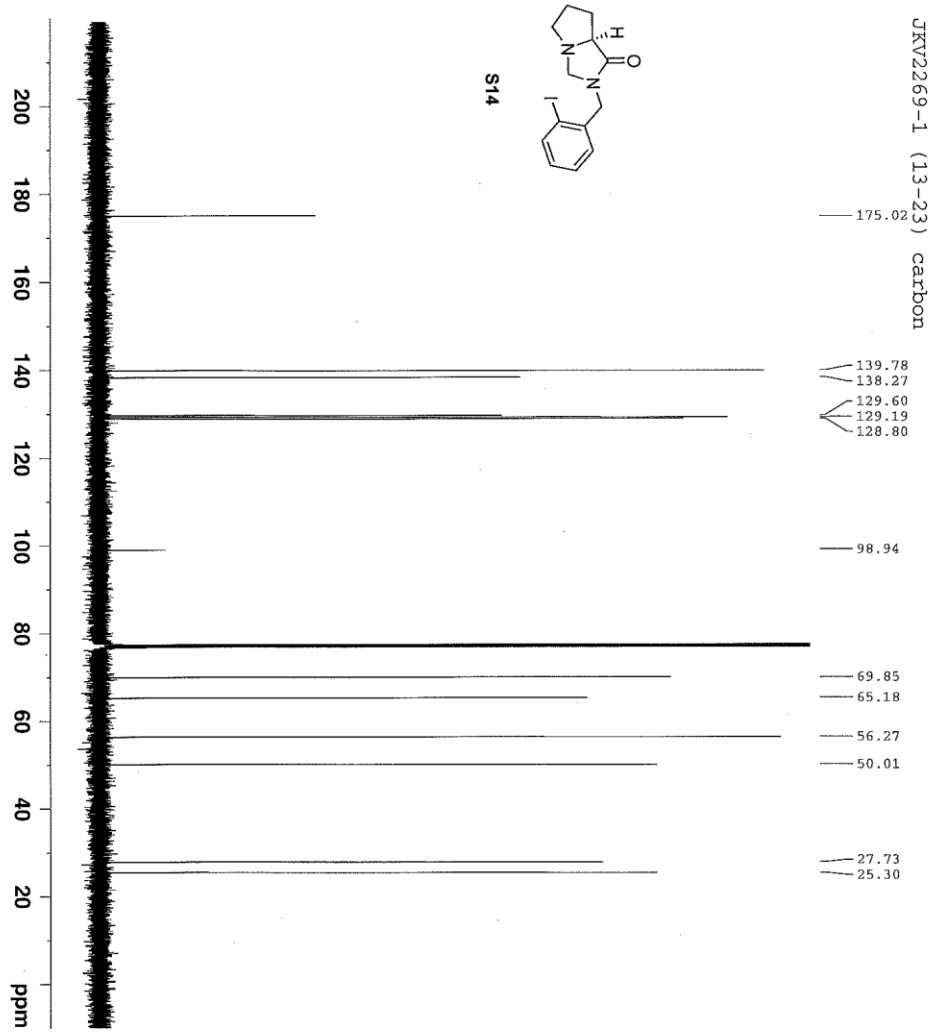


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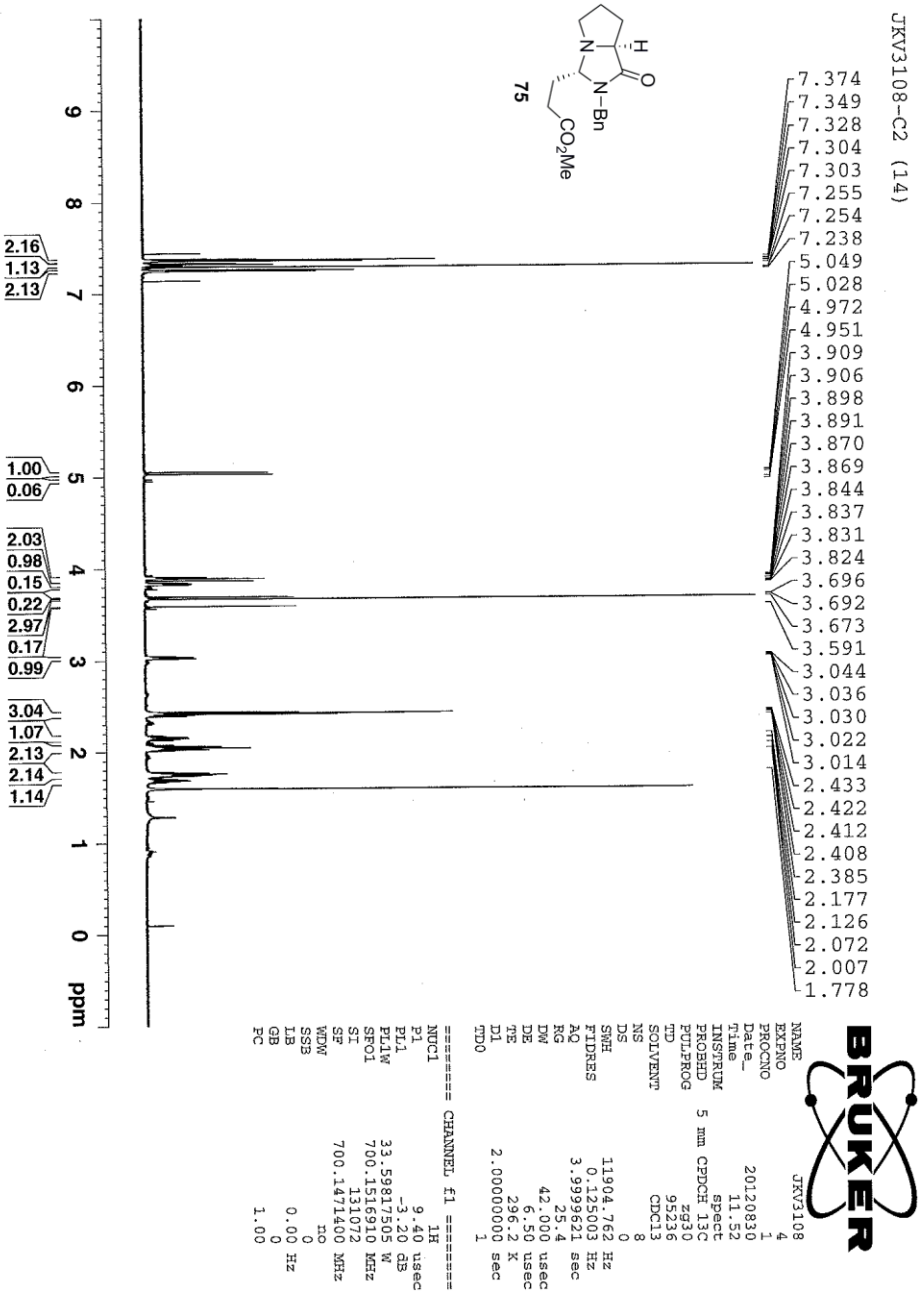
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4.951
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3.906
3.898
3.891
3.870
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3.844
3.837
3.831
3.824
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3.591
3.044
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3.014
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N-Bn
CO2Me
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2.03
0.98
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0.22
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0.17
0.99
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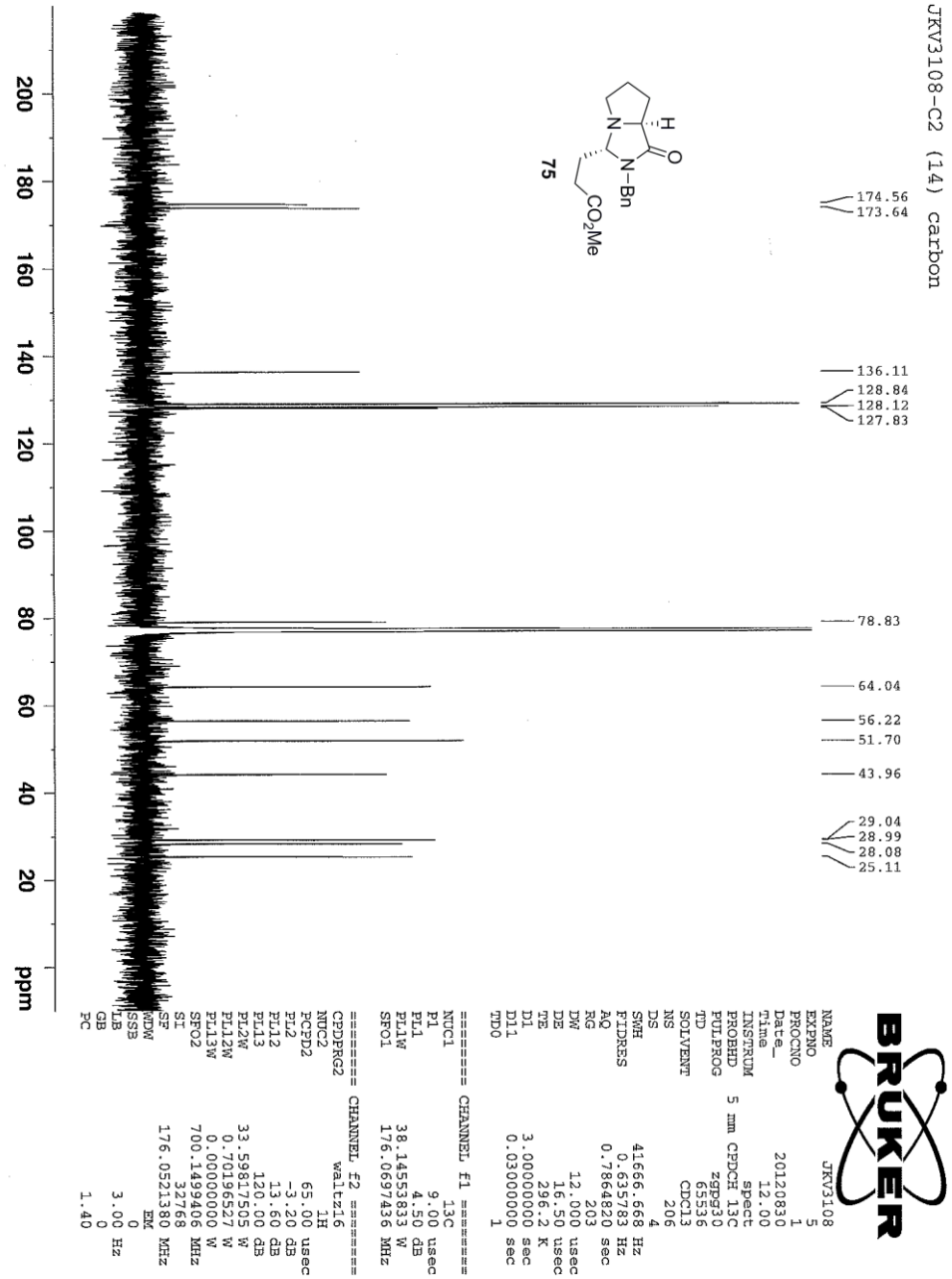
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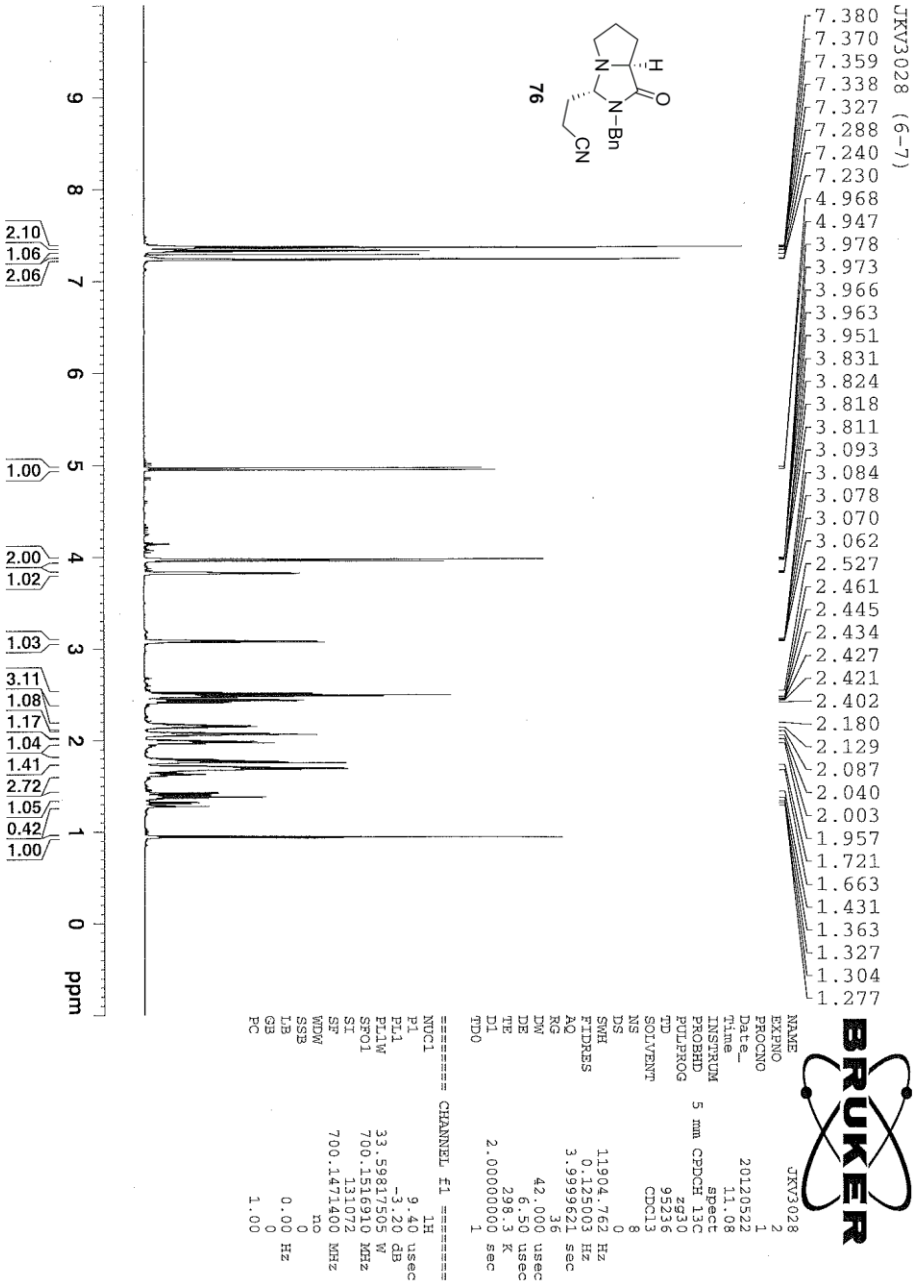
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3.824
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3.811
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3.084
3.078
3.070
3.062
2.527
2.461
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2.434
2.427
2.421
2.402
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2.040
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76
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CN
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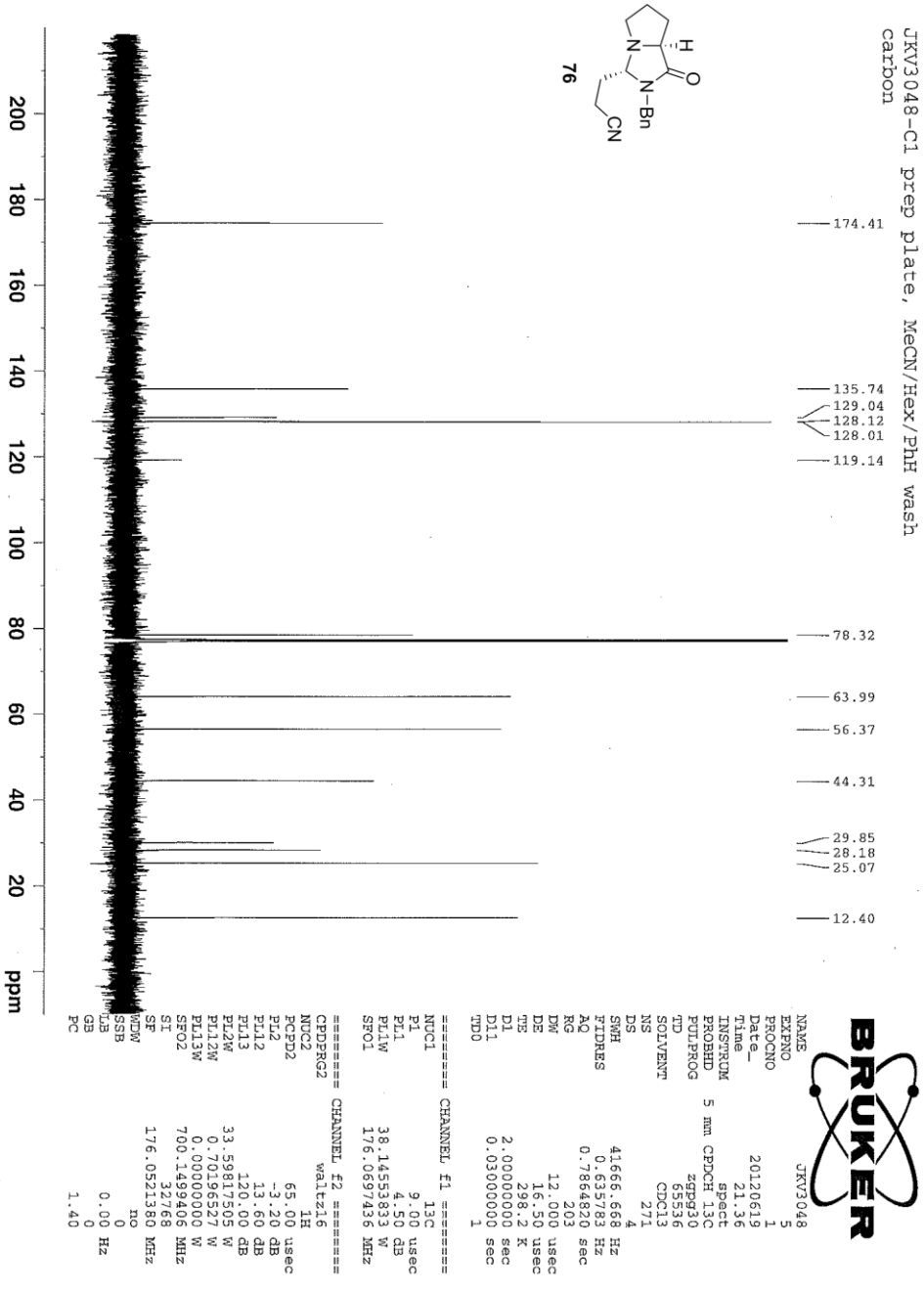
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Chapter 3: Reductive Synthesis of Aminal Radicals for Carbon–Carbon Bond Formation

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Organic Letters

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Issue 4

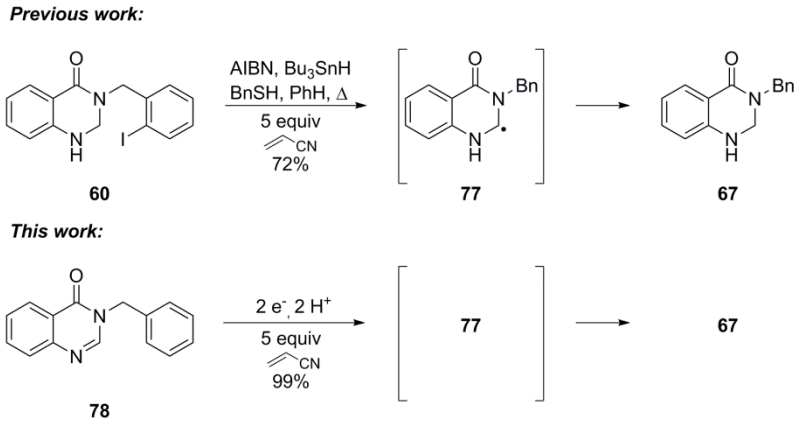
3.1 Introduction

Biologically active molecules commonly contain one or more nitrogen atoms. As a result, nitrogenous molecules, such as alkaloids, make compelling targets for synthesis.[60] However, synthesis of molecules containing Lewis basic nitrogen atoms or Bronsted acidic nitrogenous functional groups is not trivial. For example, the Lewis basic reactivity of amines, the weakly acidic N–H hydrogens, and the ability of amines to quaternize represent considerable challenges for the synthetic chemist.

Single electron processes (i.e. radical reactions) can be used to circumvent the acid-base reactivity of nitrogen.[61] Carbon-centered radicals are generally tolerant of heteroatom lone pairs and N–H bonds. Thus, chemoselective reactions of nitrogen-rich functional groups would enjoy useful application in synthesis. The aminal functional group was identified as a particularly attractive substrate for radical-based bond forming reactions.

Aminals are conveniently prepared from condensation reactions of readily available starting materials. Furthermore, calculations suggested that carbon-centered aminal radicals could be prepared in the presence of other nitrogen-containing carbon atoms.[62]

We recently reported the first use of aminal radical intermediates in synthetic reactions (Scheme 3.1).[63] Iodobenzyl-substituted aminals (**60**) undergo radical translocation[64] (i.e. hydrogen atom abstraction) to give aminal radical intermediates such as **77**. The aminal radicals add to electron poor alkenes to give products of carbon-carbon bond formation (**67**). Radical translocation selectively activates the aminal position in the presence of carbons bearing only one nitrogen atom. Intermolecular and intramolecular reactions are possible, and diastereoselectivities can be quite high.



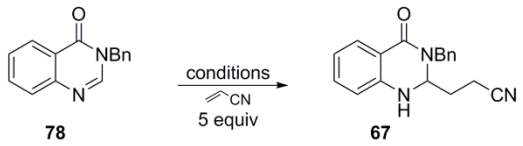
Scheme 3.1. Formation of C–C bonds with aminal radicals

Despite the potential of the aminal radical reaction in synthesis, a complementary approach for the formation of the aminal radical intermediates was desired. Such a reaction would avoid the use of toxic or foul-smelling reagents. Starting materials that are convenient to prepare and do not require an iodobenzyl group would be particularly useful. An amidine reduction reaction (Scheme 3.1; **78** → **67**) satisfies these criteria and was selected for further study.

3.2 Results and Discussion

The success of substrate **60** in the translocation reaction indicated that if presumptive intermediate radical **77** was produced under different conditions, then the desired product **67** could be formed. Amidine **78** was prepared and subjected to reductive conditions in the presence of acrylonitrile (Table 3.1). Reductions with Zn and LiDBB[65] did not give the desired product (entries 1-4). Gratifyingly, treatment of **78** with the single-electron reducing agent SmI_2,[66] camphor sulfonic acid (CSA), and acrylonitrile as a radical acceptor gave product **67** (entry 5). The reaction is operationally easy, requires no noxious reagents, is high yielding, and occurs rapidly at rt. The reaction yield decreased if an acid was not present (entry 6). After a screen

of several acids, ammonium chloride was identified as a convenient and effective proton source that generally gives higher yields than CSA (entry 7).[67]



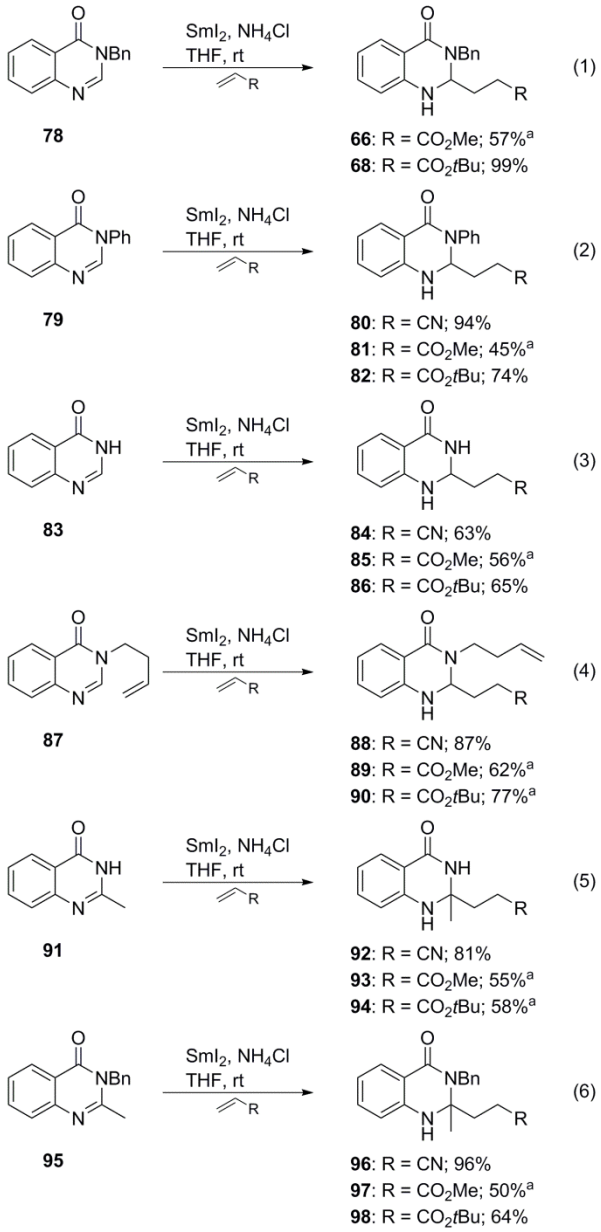
entry	conditons	result
1	Zn (2.2 equiv), HOAc (0.1 M), rt	no reaction
2	Zn (2.2 equiv), HOAc (0.1 M), 118 °C	no reaction
3	LiDBB (2.5 equiv), CSA (1.1 equiv), THF (0.3 M), rt	decomposition
4	LiDBB (2.5 equiv), THF (0.3 M), rt	decomposition
5	SmI_2 (2.5 equiv), CSA (1.1 equiv), THF (0.3 M), rt	90%
6	SmI_2 (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 3.1. Development of the Amidine Reduction Reaction

The amidine reduction reaction was examined with various substrates and acceptors (Scheme 3.2). Quinazolinones have important medicinal properties,[68] are easy to prepare,[69] and have an acyl amidine substructure. Substrate **78** reacted with acrylates to form products **66** and **68**, respectively. In the amidine reduction reaction a benzyl group is not required. Thus, phenyl substitution is tolerated, and **79** reacts with acrylonitrile, methyl acrylate, and *tert*-butyl acrylate to give **80**, **81**, and **82**, respectively. Unsubstituted quinazolinone **83** reacted to give **84**, **85**, and **86** in good yield. The presumptive aminal radical intermediate does not add to unactivated alkenes. Thus, substrate **87** preferentially undergoes bimolecular addition to acrylonitrile and acrylates giving **88**, **89**, and **90** rather than unimolecular 5-*exo*-trig cyclizations of the pendent alkene.

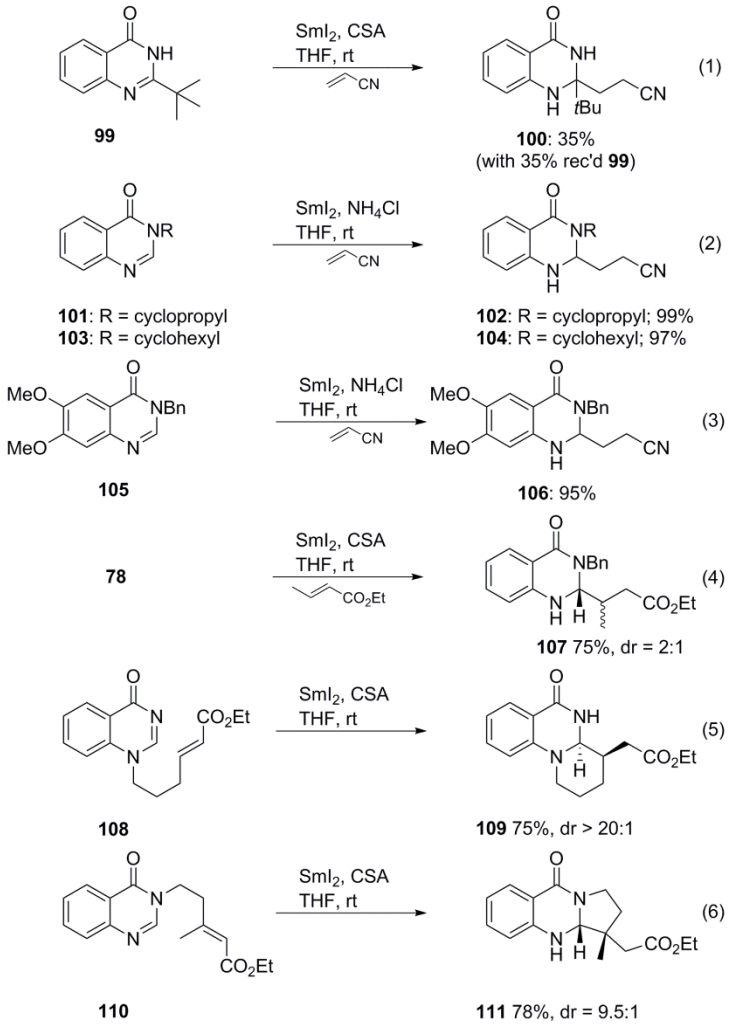
Gratifyingly, substituted amidines also participate in the reaction in good yields. Substrate **91** gave products **92**–**94** which contain fully-substitued carbon stereocenters. Benzyl-substituted amidine **95** reacted to give fully-substituted aminals **96**–**98**. Even the *tert*-butyl substituted amidine **99** (Scheme 3.3) reacts to give product **100**, which contains vicinal fully-substituted carbon atoms. Cyclopropyl groups are

tolerated in the substrate (**101**), provided they are distant from the carbon-centered radicals, to give product **102**. A sterically hindered amidine appended with a cyclohexyl group (**103**) participated giving product **104**. Electron rich arenes are tolerated in the reaction, and **105** reacts to form **106** in high yield.



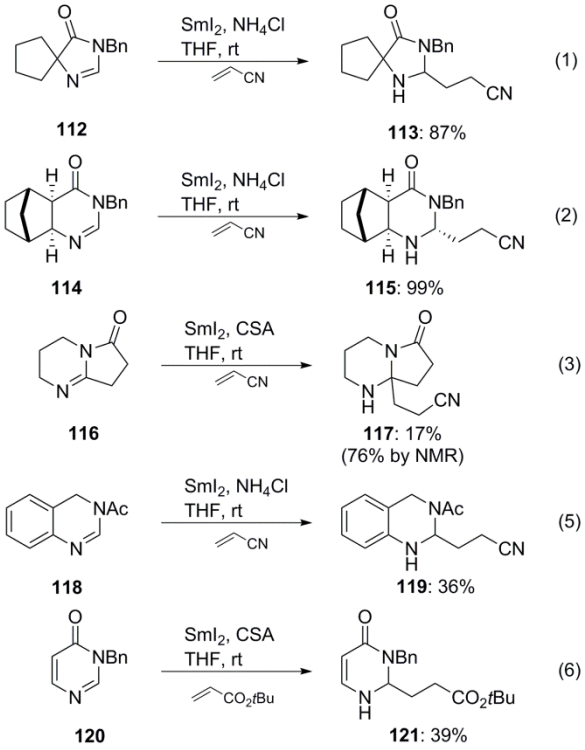
Scheme 3.2. Scope of the amidine reduction reaction. [a] Reaction was preformed with CSA.

Disubstituted alkenes are reactive acceptors, and **78** added to ethyl crotonate to give **107** in good yield, but the diastereoselectivity was modest.[70] However, intramolecular reactions proceeded in good yield and high diastereocontrol. Substrate **108** reacted to form a six-membered ring product **109**. This reaction also demonstrates that the amidine can be substituted at either nitrogen atom. Compound **110** contains a trisubstituted alkene acceptor, and it reacts smoothly in high yield and high diastereoselectivity to give **111**, which contains a quaternary carbon stereocenter. The relative stereochemistry was confirmed by NOE methods.



Scheme 3.3. Scope of the amidine reduction reaction (continued).

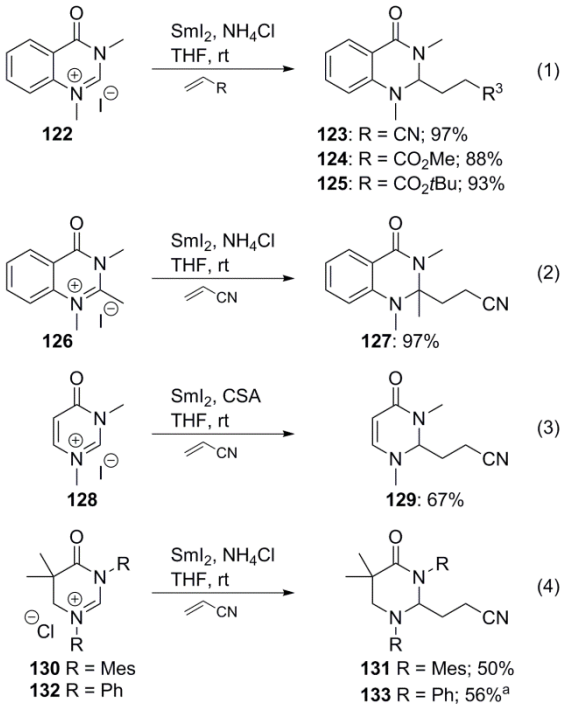
Acyl amidines that are not quinazolinones are suprisingly rare in the literature. Nevertheless, we found that they also participate in the reaction (Scheme 4). Spiro-fused amidine **112** reacted to produce **113**. Substituted amidine substrate **114** reacted under the conditions to give **115**. Bicyclic amidine **116** gave **117**, which contains a fully-substituted stereocenter. The acyl substiutent may be present as an acetyl group on the amidine, and substrate **118** reacted with acrylonitrile to give **119**. Pyrimidinone **120** underwent dearomatizative reductive bond formation to give substituted product **121**.



Scheme 3.4. Scope of amidine substrates

The mechanism of the amidine reduction reaction may involve initial protonation of the amidine to form an amidinium ion, followed by single-electron reduction to give the aminal radical. If this is the case, then amidinium ions should participate in the reaction.

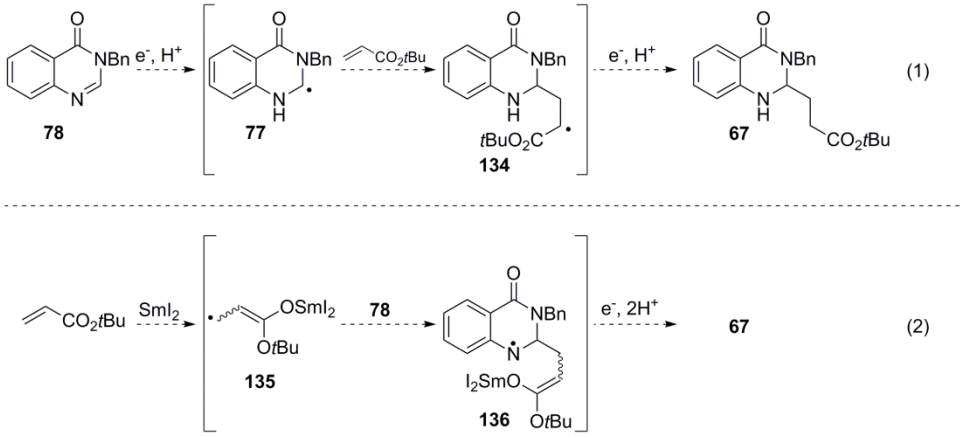
Various amidinium ions were formed using standard transformations of the corresponding amidine.[10] Subjection of the amidinium ions to SmI_2, acid, and a radical acceptor led to carbon-carbon bond formation in good yields (Scheme 3.5).[71] Quinazolinone-derived amidinium ion **122** participated in the reaction with standard radical acceptors to give **123**–**125**. Substituted amidinium ion **126** also particpated in the reduction, giving a product (**127**) with a fully substituted carbon stereocenter. The monocyclic amidinium substrate **128** also participated in the reaction giving good yield of the desired product (**129**). Aliphatic amidinium ions also participated in the reduction. Known amidinium **130** underwent reductive bond formation with acryonitrile to form product **131**. Phenyl-substituted amidinium **132** reacted to form **133**.



Scheme 3.5. Amidinum reduction. [a] Reaction was preformed with CSA.

Mechanistically, amidine **78** may receive a proton and an electron to form neutral aminal radical **77** (Scheme 3.6, eq. 1). The aminal radical could react with the electron poor acceptor to give radical **134**. This radical would be further reduced and

protonated to give the product (**67**). Alternatively, the acrylate may be reduced to radical **135** (eq. 2). Addition to the amidine would give intermediate **136**. This intermediate could be reduced and protonated to give the product (**67**). Related radical mechanisms have been proposed in the literature.[72]

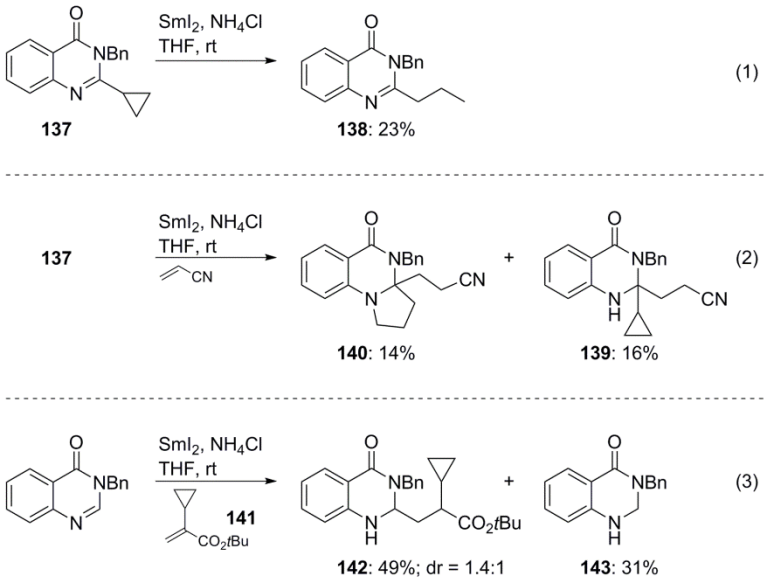


Scheme 3.6. Mechanistic investigation

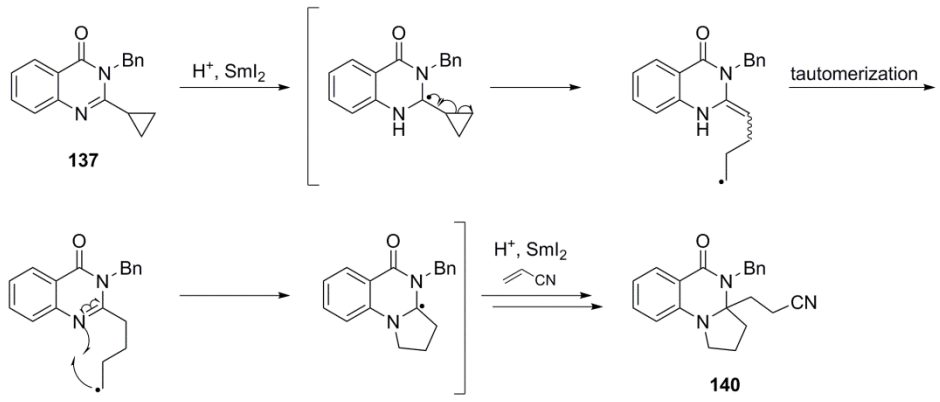
To distinguish between these mechanistic possibilities, amidine substrate **137** was prepared, which contains a cyclopropyl group attached directly to the amidine. Reduction of **137** by SmI_2 in the absence of a radical acceptor leads to fragmentation of the cyclopropane and formation of **138** (Scheme 3.7, eq. 1). Reduction of **137** in the presence of an acceptor gave addition product **139** and formation of ring-fragmentation product **140** (eq. 2).[73] This product may arise by the mechanism given in Scheme 3.8 wherein the cyclopropane ring fragmented to give a primary radical which could then undergo tautomerization followed by radical cyclization to give an aminal radical. After addition to acrylonitrile, the product **140** was obtained.

Cyclopropyl-containing radical acceptors were also investigated. Amidine **78** reacted with cyclopropyl acrylate **141** to form addition product **142** (Scheme 3.7, eq. 3). The balance of the material was the reduction product **143** and unreacted starting material. Control experiments indicated the acrylate acceptors (acrylonitrile, methyl acyrlate, *tert*-butyl acrylate, and **141**) did not react under the reaction conditions in the absence

of the amidine. This suggests that the amidine is reduced prior to reactions with the alkene acceptor. Reduction of the aminal radical such as **77** to carbanion intermediates is unlikely in the presence of strong acids (CSA and NH_4Cl). On the basis of these experiments, we believe the first mechanism is operative (i.e. **78** → **77** → **134** → **67**, Scheme 3.6, eq. 1).



Scheme 3.7. Mechanistic investigation (continued)



Scheme 3.8. A possible mechanism for the formation of the product **140**

3.3 Conclusion

In conclusion, aminal radicals are formed via reduction of the corresponding amidine and amidinium ions in the presence of a proton source. The putative radical intermediates react with radical acceptors in C–C bond-forming reactions in good yields without the use of heavy metal hydrides or thiols. The reaction can be performed in inter- and intramolecular contexts in high yield. Furthermore, fully substituted aminal stereocenters are formed in good yields with this chemistry. We believe this reactivity will be useful in the synthesis of nitrogen-rich alkaloids, and efforts to apply this chemistry in synthesis are underway in our laboratory.

3.4 Experimental Section

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. Methyl acrylate and *tert*-butyl acrylate were purified by washing with aqueous NaOH, drying over $MgSO_4$, 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.[74] 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. 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 (67) (*general reductive alkylation procedure)*. To a solution of 3-benzylquinazolin-4(3H)-one[75] (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 $MgSO_4$ and concentrated to give known adduct **67** (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 (66). *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 (80). *Following the general reductive alkylation procedure,* 3-phenylquinazolin-4(3H)-

one[76] (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 **80** (0.0375 g, 0.135 mmol, 94%) as a colorless oil.

Data for **80**: R_f 0.40 (1:1 hexanes:EtOAc); mp = 155–156 ^oC; IR (thin film) 2929, 2246, 1638, 1496, 1154, 757 cm^{-1}; ^1H 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*H_2 28.5, 13.7; HRMS (EI) calcd for $C_{17}H_{15}N_3O$ [M+]: 277.1215, found 277.1227.

methyl 3-(4-oxo-3-phenyl-1,2,3,4-tetrahydroquinazolin-2-yl)propanoate (81). *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 **81** (0.0195 g, 0.0629 mmol, 45%) as a colorless oil after purification by FCC (4:1 hexanes:EtOAc).

Data for **81**: R_f 0.44 (1:1 hexanes:EtOAc); mp = 79–80 ^oC; IR (thin film) 2951, 1732, 1634, 1496, 1169, 756 cm^{-1}; ^1H 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*H_2 29.7, 28.5; *C*H_3 51.8; HRMS (ESI) calcd for $C_{18}H_{18}N_2O_3$ [M+H]: 310.1318, found 310.1304.

***tert*-butyl 3-(4-oxo-3-phenyl-1,2,3,4-tetrahydroquinazolin-2-yl)propanoate (82)**. *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 **10** (0.0367 g, 0.104 mmol, 74%) as a colorless oil after purification by FCC (3:1 hexanes:EtOAc).

Data for **82**: R_f 0.65 (1:1 hexanes:EtOAc); IR (thin film) 2977, 1724, 1685, 1495, 1152, 753 cm^{-1}; ^1H 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*H_2 31.1, 28.5; *C*H_3 28.0; HRMS (ESI) calcd for $C_{21}H_{24}N_2O_3Na$[M+Na]: 375.1685, found 375.1674.

3-(4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanenitrile (84). *Following the general reductive alkylation procedure,* 3-phenylquinazolin-4(3H)-one[77] (0.0191 g, 0.131 mmol), NH_4Cl (0.0079 g, 0.144 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 (4.0 mL, 0.33 mmol) to give known[78] adduct **84** (0.0169 g, 0.0832 mmol, 63%) as a colorless oil.

methyl 3-(4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanoate (85). *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 **85** (0.0195 g, 0.083 mmol, 56%) as a colorless oil.

Data for **85**: R_f 0.25 (1:4 hexanes:EtOAc); IR (thin film) 2951, 1725, 1653, 1438, 1382, 1155, 756 cm^{-1}; ^1H 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*H_2 29.9, 28.1, *C*H_3 52.1; HRMS (EI) calcd for $C_{12}H_{14}N_2O_3$ [M+]: 234.1005, found 234.1016.

***tert*-butyl 3-(4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanoate (86)**. *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 **86** (0.0289 g, 0.105 mmol, 65%) as a colorless oil after purification by FCC (1:3 hexanes:EtOAc).

Data for **86**: R_f 0.48 (1:2 hexanes:EtOAc); mp = 114–115 ^oC; IR (thin film) 2978, 2830, 1728, 1677, 1469, 1367, 1154, 757 cm^{-1}; ^1H 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*H_2 29.9, 29.6, *C*H_3 28.3; HRMS (EI) calcd for $C_{15}H_{20}N_2O_3Na$ [M+Na]: 299.1372, found 299.1379.

3-(3-(but-3-en-1-yl)-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanenitrile (88). *Following the general reductive alkylation procedure,* 3-(but-3-en-1-yl)quinazolin-4(3H)-one[79] (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 **88** (0.0307 g, 0.120 mmol, 87%) as a colorless oil after purification by FCC (1:1 hexanes:EtOAc).

Data for **88**: R_f 0.31 (1:1 hexanes:EtOAc); IR (thin film) 2916, 2246, 1632, 1469, 1394, 759 cm^{-1}; ^1H 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*H_2 117.5, 44.9, 32.9, 28.5, 13.6; HRMS (ESI) calcd for $C_{15}H_{18}N_3O$ [M+H]: 256.1450, found 256.1446.

methyl 3-(3-(but-3-en-1-yl)-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanoate (89). *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 **89**: R_f 0.42 (2:1 hexanes:EtOAc); IR (thin film) 2976, 2926, 1733, 1632, 1468, 1370, 1168, 754 cm^{-1}; ^1H 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*H_2 117.0, 44.8, 32.7, 29.6, 28.5; *C*H_3 51.8; HRMS (ESI) calcd for $C_{16}H_{21}N_2O_3$ [M+H]: 289.1541, found 289.1552.

***tert*-butyl 3-(3-(but-3-en-1-yl)-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanoate (90).** *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 **90** (0.0364 g, 0.110 mmol, 77%) as a colorless oil after purification by FCC (3:2 hexanes:EtOAc).

Data for **90**: R_f 0.68 (1:1 hexanes:EtOAc); IR (thin film) 2977, 2930, 1726, 1631, 1470, 1367, 1152, 754 cm^{-1}; ^1H 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*H_2 117.0, 44.7, 32.7, 31.0, 28.6; *C*H_3 28.0; HRMS (ESI) calcd for $C_{19}H_{27}N_2O_3$ [M+H]: 331.2022, found 331.2015.

3-(2-methyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanenitrile (92). *Following the general reductive alkylation procedure*, 2-methylquinazolin-4(3H)-one[80] (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 **92** (0.0247 g, 0.115 mmol, 81%) as a white solid.

Data for **92**: R_f 0.26 (1:2 hexanes:EtOAc); mp = 113–114 ^oC; IR (thin film) 2927, 2249, 1655, 1486, 754 cm^{-1}; ^1H 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*H_2 37.3, 12.3; *C*H_3 28.5; HRMS (ESI) calcd for $C_{12}H_{14}N_3O$ [M+H]: 216.1137, found 216.1129.

methyl 3-(2-methyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanoate (93). *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 **93** (0.0179 g, 0.115 mmol, 55%).

***tert*-butyl 3-(2-methyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanoate (94).** *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 **94** (0.0227 g, 0.0782 mmol, 58%) as a white solid after purification by FCC (1:1 hexanes:EtOAc).

Data for **94**: R_f 0.53 (1:2 hexanes:EtOAc); mp = 116–117 ^{o}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*H_2 36.4, 30.0; *C*H_3 29.1, 28.0; HRMS (ESI) calcd for $C_{16}H_{23}N_2O_3$ [M+H]: 291.1709, found 291.1697.

3-(3-benzyl-2-methyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanenitrile (96). *Following the general reductive alkylation procedure*, 3-benzyl-2-methylquinazolin-4(3H)-one[81] (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 **96** (0.0416 g, 0.136 mmol, 96%) as a white solid.

Data for **96**: R_f 0.45 (1:1 hexanes:EtOAc); mp = 148–149 ^oC; IR (thin film) 3013, 2249, 1625, 1489, 1397, 1158, 754 cm^{-1}; ^1H 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*H_2 45.4, 34.5, 12.3; *C*H_3 25.6; HRMS (ESI) calcd for $C_{19}H_{19}N_3ONa$ [M+Na]: 328.1426, found 328.1415.

methyl 3-(3-benzyl-2-methyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanoate (97). *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 **97** (0.0199 g, 0.0588 mmol, 46%) as a white solid after purification by FCC (5:1 hexanes:EtOAc).

Data for **97**: R_f 0.66 (1:1 hexanes:EtOAc); mp = 136–137 ^oC; IR (thin film) 2950, 1734, 1624, 1489, 1397, 754 cm^{-1}; ^1H 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*H_2 45.3, 34.0, 28.9; *C*H_3 51.8, 26.4; HRMS (ESI) calcd for $C_{20}H_{23}N_2O_3$ [M+H]: 339.1709, found 339.1693.

***tert*-butyl 3-(3-benzyl-2-methyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanoate (98).** *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 **98** (0.0322 g, 0.0847 mmol, 64%) as a white solid.

Data for **98**: R_f 0.40 (3:1 hexanes:EtOAc); mp = 142–143 ^oC; IR (thin film) 2977, 2930, 1726, 1625, 1489, 1394, 1154, 754 cm^{-1}; ^1H 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*H_2 45.2, 33.8, 30.2; *C*H_3 27.9, 26.4; HRMS (ESI) calcd for $C_{20}H_{23}N_2O_3$ [M+H]: 339.1709, found 339.1693.

3-(2-(*tert*-butyl)-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanenitrile (100). *Following the general reductive alkylation procedure,* 2-(*tert*-butyl)quinazolin-4(3H)-one[82] (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 **100** (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 **100**: R_f 0.65 (1:2 EtOAc: Hexanes); IR (thin film) 3356, 2921, 2246, 1655 cm^{-1}; ^1H 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 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 $C_{15}H_{20}N_3O$ [M+H]: 258.1606, found 258.1599.

3-(3-cyclopropyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanenitrile (102). *Following the general reductive alkylation procedure,* 3-cyclopropylquinazolin-4(3H)-one[83] (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 **102** (0.0340 g, 0.140 mmol, 99%) as a colorless oil.

Data for **102**: R_f 0.24 (1:1 EtOAc: Hexanes); IR (thin film) 3294, 2929, 2246, 1636 cm^{-1}; ^1H 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 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 $C_{14}H_{15}N_3O$ [M+]: 241.12152, found 241.12128.

3-(3-cyclohexyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanenitrile (104). *Following the general reductive alkylation procedure,* 3-cyclohexylquinazolin-4(3H)-one[84] (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 **104** (0.0409 g, 0.144 mmol, 97%) as a colorless oil after purification by FCC (3:1 hexanes:EtOAc).

Data for **104**: R_f 0.38 (1:1 EtOAc: Hexanes); IR (thin film) 3284, 2932, 2856, 2245, 1622 cm^{-1}; ^1H 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 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 $C_{17}H_{21}N_3O$ [M+]: 283.16847, found 283.16723.

3-(3-benzyl-6,7-dimethoxy-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanenitrile (106). *Following the general reductive alkylation procedure,* 3-benzyl-6,7-dimethoxyquinazolin-4(3H)-one[85] (0.0425 g, 0.143 mmol), NH_4Cl (0.0092 g, 0.172 mmol), acrylonitrile (0.05 mL, 0.76 mmol) in THF (0.48 mL, 0.3 M) were reacted with a THF solution of SmI_2 (4.7 mL, 0.36 mmol) to give **106** (0.0481 g, 0.137 mmol, 95%) as a white foam after purification by FCC (1:2 hexanes:EtOAc).

Data for **106**: R_f 0.36 (4:1 EtOAc: Hexanes); IR (thin film) 3326, 2930, 2247, 1674, 1613, 1502 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.47 (s, 1 H), 7.28-7.34 (m, 5 H), 6.30 (s, 1 H), 5.32 (d, 14.8 Hz, 1 H), 4.62 (dd, *J* = 17.5, 5.6 Hz, 1 H), 4.13 (d, *J* = 14.8 Hz, 1 H), 3.88 (s, 3 H), 3.85 (s, 3 H), 2.28-2.43 (m, 2 H), 2.09-2.18 (m, 1 H), 1.74-1.82 (m, 1 H); ^{13}C (100 MHz, $CDCl_3$) δ 162.1, 154.2, 144.7, 138.1, 137.2, 129.0, 128.2, 128.0, 119.0, 111.3, 110.1, 101.5, 67.0, 56.4, 56.2, 47.9, 27.7, 13.8; HRMS (TOF MS ES+) calcd for $C_{20}H_{21}N_3O_3$ [M+H]: 352.1661, found 352.1660.

(±)-ethyl 3-((R)-3-benzyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)butanoate (107) *Following the general reductive alkylation procedure,* 3-benzylquinazolin-4(3H)-one (0.0327 g, 0.139 mmol), NH_4Cl (0.0085g, 0.159 mmol), ethyl crotylate

(0.86 mL, 6.9 mmol) in THF (0.46 mL, 0.3 M) were reacted with a THF solution of SmI_2 (4.8 mL, 0.35 mmol) to give adduct **107** (0.0369 g, 0.105 mmol, 76%) as a light yellow oil.

Data for **107**: R_f 0.51 (1:1 hexanes:EtOAc); IR (thin film) 2919, 1730, 1630 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.93 (dd, *J* = 7.7, 0.7 Hz, 1 H), 7.27-7.33 (m, 6 H), 6.84 (td, *J* = 7.7, 0.7 Hz, 1 H), 6.59 (dd, *J* = 0.7, 8.4 Hz, 1 H), 5.74 (d, *J* = 15.4 Hz, 1 H), 4.55 (d, *J* = 6.3 Hz, 1 H), 4.05-4.10 (m, 2 H), 3.96 (d, *J* = 15.4 Hz, 1 H), 2.58-2.63 (m, 1 H), 2.38 (dd, *J* = 15.4, 4.9 Hz, 1 H), 2.15 (dd, *J* = 15.4, 8.4 Hz, 1 H), 1.19 (t, *J* = 7.0 Hz, 3 H), 1.05 (d, *J* = 7.0 Hz, 3 H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 172.4, 162.8, 145.3, 137.1, 133.7, 129.0, 128.9, 127.9, 127.7, 119.2, 116.6, 114.5, 71.6, 60.8, 49.0, 37.1, 35.5, 16.5, 14.3; HRMS (ES+) calcd for $C_{21}H_{25}N_2O_3$ [M+H]: 353.1865, found 353.1870.

ethyl (E)-6-((2-carbamoylphenyl)amino)hex-2-enoate (S15). To a DMF (5.4 mL, 0.3 M) solution of 2-aminobenzamide (0.6663 g, 4.89 mmol) was added K_2CO_3 (0.4556 g, 3.30 mmol), tetrabutylammonium iodide (0.1808g, 0.490mmol), and the known[86] bromo ester (0.3608 g, 1.63 mmol). This mixture was heated to 50℃ with stirring for a period of 16 hours. After cooling, the reaction mixture was diluted with ethyl acetate and washed with half-saturated aqueous LiCl. The organics were dried over $MgSO_4$, concentrated, and purified by FCC (2:1 hexanes:EtOAc) to give **S15** (0.2425 g, 0.878 mmol, 54%) as a colorless oil.

Data for **S15**: R_f 0.57 (2:1 EtOAc: Hexanes); IR (thin film) 3345, 2936, 1711, 1648 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38 (dd, *J* = 7.6, 1.2 Hz, 1 H), 7.30 (ddd, *J* = 8.4, 8.4, 1.2 Hz, 1 H), 6.96 (dt, *J* = 15.6, 6.8 Hz, 1 H), 6.66 (d, *J* = 8.4 Hz, 1 H), 6.56 (t, *J* = 7.6 Hz, 1 H), 5.92 (bs, 2 H), 5.85 (d, *J* = 15.6 Hz, 1 H), 4.17 (q, *J* = 7.2 Hz, 2 H), 3.19 (t, *J* = 6.8 Hz, 2 H), 2.32 (q, *J* = 6.8 Hz, 2 H), 1.82 (quin. *J* = 7.2 Hz, 2 H), 1.27 (t, *J* = 7.2 Hz, 3 H); ^{13}C (100 MHz, $CDCl_3$) δ 172.4, 166.7, 150.3, 148.2, 133.6,

128.5, 122.1, 114.6, 113.0, 111.8, 60.3, 42.2, 29.8, 27.6, 14.4; HRMS (EI+) calcd for $C_{15}H_{20}N_2O_3$ [M+]: 276.14740, found 276.14666.

ethyl (E)-6-(4-oxoquinazolin-1(4H)-yl)hex-2-enoate (108). To a THF (0.75 mL, 0.3 M) solution of **S15** (0.0621 g, 0.255 mmol) were added trimethyl orthoformate (0.12 mL, 1.097 mmol), and one drop of trifluoroacetic acid. The mixture was heated to reflux for 65 minutes. At this time, TLC indicated the consumption of **S15**. After cooling, the reaction mixture was concentrated and purified by FCC (19:1 hexanes:EtOAc) to give **108** (0.0559g, 0.195 mmol, 86%) as a colorless oil.

Data for **108**: R_f 0.75 (4:1 EtOAc: 10% NH_4OH in MeOH); IR (thin film) 2981, 1713, 1648, 1606, 1546 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.39 (dd, *J* = 8.0, 0.8 Hz, 1 H), 8.32 (bs, 1 H), 7.77 (td, *J* = 7.2, 1.6 Hz, 1 H), 7.52 (td, *J* = 7.6, 0.4 Hz, 1 H), 7.33 (d, *J* = 8.4 Hz, 1 H), 7.92 (dt, *J* = 15.6, 6.8 Hz, 1 H), 5.90 (dt, *J* = 15.6, 1.6 Hz, 1 H), 4.18 (quin, *J* = 7.2 Hz, 2 H), 2.35 (q, *J* = 6.8 Hz, 2 H), 2.07 (quin, *J* = 7.2 Hz, 2 H), 1.28 (t, *J* = 6.8 Hz, 3 H); ^{13}C (100 MHz, $CDCl_3$) δ 169.0, 166.0, 153.0, 145.5, 138.8, 134.0, 129.5, 126.7, 123.4, 12.09, 114.4, 60.5, 49.6, 28.8, 27.0, 14.2; HRMS (TOF MS ES+) calcd for $C_{16}H_{19}N_2O_3$ [M+H]: 287.1396, found 287.1392.

ethyl 2-((4R,4aR)-6-oxo-2,3,4,4a,5,6-hexahydro-1H-pyrido[1,2-a]quinazolin-4-yl)acetate (109). To a solution of **108** (0.0458 g, 0.1594 mmol) and CSA (0.0412g, 0.177 mmol) in THF (0.53 mL, 0.3 M) was added a THF solution of SmI_2 (4.3 mL, 0.40 mmol) via syringe pump over a period of 1 hour. At this time, TLC indicated the consumption of **108**. 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 $MgSO_4$ and concentrated. Purification by FCC (1:1 hexanes:EtOAc) gave **109** (0.0343 g, 0.119 mmol, 75%) as a white solid.

Data for **109**: R_f 0.71 (4:1 EtOAc: 10% NH_4OH in MeOH); IR (thin film) 3201, 2939, 1730, 1675 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.96 (dd, *J* = 7.7 1.4 Hz, 1 H), 7.39 (ddd, *J* = 8.4, 7.0, 1.4 Hz, 1 H), 6.91 (t, *J* = 7.0 Hz, 1 H), 6.85 (d, *J* = 8.4 Hz, 1 H), 4.67 (d, *J* = 3.5 Hz, 1 H), 4.14-4.21 (m, 2 H), 3.74 (d, *J* = 10.5 Hz, 1 H), 3.05 (dd, *J* = 7.0, 17.5 Hz, 1 H), 2.59 (td, *J* = 3.5, 11.9 Hz, 1 H), 2.53 (sept. *J* = 3.5 Hz, 1 H), 2.36 (dd, *J* = 16.8, 2.8 Hz, 1 H), 1.75-1.82 (m, 2 H), 1.66-1.73 (m, 2 H), 1.26 (t, *J* = 7.0 Hz, 3 H); ^{13}C (176 MHz, $CDCl_3$) δ 174.1, 164.2, 149.9, 134.1, 128.9, 119.9, 117.6, 113.2, 71.0, 61.2, 46.0, 34.0, 33.0, 27.5, 20.1, 14.3; HRMS (TOF MS ES+) calcd for $C_{16}H_{21}N_2O_3$ [M+H]: 289.1552, found 289.1556.

ethyl (E)-5-(2-aminobenzamido)-3-methylpent-2-enoate (S16). To a DCM (4.1 mL, 0.5M) solution of the known[87] ester (0.5275 g, 2.05 mmol) was added trifluoroacetic acid (0.80 mL, 10.4 mmol). The solution was stirred at room temperature for 18 hours. At this time, TLC indicated the consumption of the ester. The reaction was quenched with excess solid K_2CO_3, filtered, and concentrated to give the free aminoester. The aminoester was dissolved in THF (7 mL, 0.3M). To this solution were added Isatoic anhydride (0.2787 g, 1.71 mmol) along with DMAP (0.0420 g, 0.342 mmol) and the mixture was heated to reflux for 24 hours. At this time, TLC indicated the consumption of the isatoic anhydride. The reaction mixture was diluted with EtOAc, washed with brine, the organics were dried over $MgSO_4$, and concentrated. Purification by FCC (3:1 hexanes:EtOAc) gave **S16** (0.4703 g, 1.70 mmol, 99%) as a colorless oil.

Data for **S16**: R_f 0.44 (4:1 EtOAc : Hexanes); IR (thin film) 3461, 3353, 2981, 1707, 1693 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.28 (dd, *J* = 7.6, 1.2 Hz, 1 H), 7.23 (dd, *J* = 7.6, 1.2 Hz, 1 H), 7.74 (d, *J* = 8.0 Hz, 1 H), 6.68 (t, *J* = 7.2 Hz, 1 H), 6.10 (bs, 1 H), 5.74 (d, *J* = 1.2 Hz, 1 H), 4.16 (q, *J* = 7.2 Hz, 2 H), 2.45 (t, *J* = 6.8 Hz, 2 H), 2.22 (d, *J* = 1.2 Hz, 3 H), 1.28 (t, *J* = 7.2 Hz, 3 H); ^{13}C (100 MHz, $CDCl_3$) δ 169.3, 133.5,

156.1, 148.0, 132.5, 127.2, 118.0, 117.9, 117.4, 116.6, 59.9, 40.7, 37.4, 18.8, 14.4; HRMS (TOF MS ES+) calcd for $C_{15}H_{21}N_2O_3$ [M+H]: 277.1552, found 277.1547.

ethyl (E)-3-methyl-5-(4-oxoquinazolin-3(4H)-yl)pent-2-enoate (110). To a THF (2.0 mL, 0.3 M) solution of **S16** (0.1613 g, 0.584 mmol) was added one drop of trifluoroacetic acid and trimethyl orthoformate (0.32 mL, 2.92 mmol). This mixture was heated to reflux for 30 hours. The reaction mixture was concentrated and purified by FCC (1:1 hexanes:EtOAc) to give **110** (0.0384 g, 0.134 mmol, 23%) along with 0.0904 g of recovered **S16**.

Data for **110**: R_f 0.42 (1:1 EtOAc : Hexanes); IR (thin film) 2981, 1714, 1676 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 8.31 (dd, *J* = 7.7, 0.7 Hz, 1 H), 7.96 (s, 1 H), 7.77 (ddd, *J* = 8.4, 8.4, 1.4 Hz, 1 H), 7.71 (d, *J* = 8.4 Hz, 1 H), 7.52 (ddd, *J* = 7.7, 7.7, 0.7 Hz, 1 H), 5.67 (d, *J* = 0.7 Hz, 1 H), 4.13 (quin, *J* = 7.7 Hz, 4 H), 2.62 (t, *J* = 7.7 Hz, 2 H), 2.26 (d, *J* = 0.7 Hz, 3 H), 1.24 (t, *J* = 7.0 Hz, 3 H); ^{13}C (176 MHz, $CDCl_3$) δ 166.2, 161.1, 154.2, 148.2, 146.2, 134.5, 127.7, 127.6, 126.8, 122.2, 118.8, 59.9, 45.3, 40.1, 18.9, 14.4; HRMS (TOF MS ES+) calcd for $C_{16}H_{19}N_2O_3$ [M+H]: 287.1396, found 287.1387.

ethyl 2-((3R,3aR)-3-methyl-9-oxo-1,2,3,3a,4,9-hexahydropyrrolo[2,1-b]quinazolin-3-yl)acetate (111). To a solution of **110** (0.0390 g, 0.136 mmol) and NH_4Cl (0.0080g, 0.150 mmol) in THF (0.45 mL, 0.3 M) was added a THF solution of SmI_2 (4.5 mL, 0.34 mmol) via syringe pump over a period of 1 hour. At this time, TLC indicated the consumption of **110**. 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 $MgSO_4$ and concentrated. Purification by FCC (2:1 hexanes:EtOAc) gave **111** (0.0308 g, 0.107 mmol, 78%, 9.5:1 dr) as a white solid.

Data for **111** (major diastereomer): R_f 0.29 (1:1 EtOAc: Hexanes); IR (thin film) 3284, 2976, 1726, 1637 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.88 (dd, *J* = 7.7, 1.4 Hz, 1 H), 7.28 (d, *J* = 1.4 Hz, 1 H), 7.27-7.27 (m, 2 H), 6.86 (td, *J* = 7.7, 0.7 Hz, 1 H), 6.68 (dd, *J* = 7.7, 0.7 Hz, 1 H), 4.84 (bs, 1 H), 4.76 (s, 1 H), 4.16 (qd, *J* = 7.0, 1.4 Hz, 2 H), 3.76 (dt, *J* = 11.9, 8.4 Hz, 1 H), 3.64 (dd, *J* = 12.6, 9.1, 4.2 Hz, 1 H), 2.73 (d, *J* = 15.4 Hz, 1 H), 2.43 (d, *J* = 15.4 Hz, 1 H), 2.06 (ddd, *J* = 13.3, 7.7, 4.2 Hz, 1 H), 1.73 (dt, *J* = 12.6, 1.4 Hz, 1 H), 1.31 (s, 3 H), 1.27 (t, *J* = 7.0 Hz, 3 H); ^{13}C (176 MHz, $CDCl_3$) δ 172.7, 162.6, 147.4, 133.2, 128.3, 119.8, 117.3, 115.0, 77.7, 60.9, 44.3, 42.2, 38.7, 35.6, 22.4, 14.4; HRMS (EI+) calcd for $C_{16}H_{21}N_2O_3$ [M+H]: 289.1552, found 289.1539.

3-(3-benzyl-4-oxo-1,3-diazaspiro[4.4]nonan-2-yl)propanenitrile (113). *Following the general reductive alkylation procedure*, 3-benzyl-1,3-diazaspiro[4.4]non-1-en-4-one[88] (0.0294 g, 0.129 mmol), NH_4Cl (0.0078 g, 0.146 mmol), acrylonitrile (0.04 mL, 0.61 mmol) in THF (0.43 mL, 0.3 M) were reacted with a THF solution of SmI_2 (4.2 mL, 0.32 mmol) to give **113** (0.0319 g, 0.113 mmol, 87%) as a yellow oil after purification by FCC (3:2 hexanes:EtOAc).

Data for **113**: R_f 0.68 (EtOAc); IR (thin film) 3326, 2947, 2246, 1689 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 4.87 (d, *J* = 15.4 Hz, 1 H), 4.36 (dd, *J* = 8.4, 2.8 Hz, 1 H), 4.09 (d, *J* = 15.4 Hz, 1 H), 2.41-2.46 (m, 1 H) 2.34-2.39 (m, 1 H), 2.07-2.14 (m, 2 H), 2.01 (dddd, *J* = 16.8, 14.0, 8.4, 2.8 Hz, 1 H), 1.82-1.84 (m, 2 H) 1.74-1.80 (m, 2 H), 1.67-1.71 (m, 1 H), 1.60-1.65 (m, 1 H), 1.55-1.59 (m, 1 H); ^{13}C (176 MHz, $CDCl_3$) δ 177.9, 136.1, 129.1, 128.2, 128.0, 128.0, 119.2, 69.5, 68.8, 44.7, 39.3, 38.5, 37.4, 29.9, 25.5, 25.3, 12.2; HRMS (TOF MS ES+) calcd for $C_{17}H_{22}N_3O$ [M+H]: 284.1763, found 284.1767.

(±) *tert*-butyl (1S,2S,5R,6R)-4-oxo-3-azatricyclo[4.2.1.02,5]nonane-3-carboxylate (S17). To a THF (5.0 mL, 0.3 M) solution of known[89] (1S,2S,5R,6R)-3-

azatricyclo[4.2.1.02,5]nonan-4-one was added Boc_2O (0.35 mL, 1.52 mmol) and DMAP (0.0180 g, 0.147 mmol). This mixture was stirred at rt for 20 hours. At this time, TLC indicated the consumption of the (1S,2S,5R,6R)-3-azatricyclo[4.2.1.02,5]nonan-4-one. The mixture was diluted with EtOAc, washed with brine, dried over $MgSO_4$, and concentrated. Purification by FCC (9:1 hexanes:EtOAc) gave **S17** (0.0874 g, 0.368 mmol, 26%) as a white solid.

Data for **S17**: R_f 0.34 (1:1 EtOAc: Hexanes); IR (thin film) 2973, 2877, 1796, 1720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.70 (d, *J* = 7.7 Hz, 1 H), 2.92 (d, *J* = 7.7 Hz, 1 H), 2.67 (d, *J* = 6.3 Hz, 1 H), 2.48 (d, *J* = 4.2 Hz, 1 H), 1.53-1.68 (m, 3 H), 1.50 (s, 9 H), 1.24-1.28 (m, 1 H), 1.07-1.13 (m, 2 H); ^{13}C (100 MHz, $CDCl_3$) δ 166.5, 147.8, 83.0, 56.6, 56.5, 37.1, 34.8, 31.2, 28.2, 27.2, 24.5; HRMS (TOF MS ES+) calcd for $C_{13}H_{19}NO_3$ [M+Na]: 260.1263, found 260.1255.

(±) *tert*-butyl ((1S,2S,3R,4R)-3-(benzylcarbamoyl)bicyclo[2.2.1]heptan-2-yl)carbamate (S18). To a THF (0.40 mL, 0.3 M) solution of **S17** (0.0297 g, 0.125 mmol) was added benzylamine (0.02 mL, 0.183 mmol). The mixture was stirred at rt for 22 hours. At this time, TLC indicated the consumption of **S17**. The mixture was concentrated to give **S18** (0.0430 g, 0.125 mmol, 99%) as a white solid.

Data for **S18**: R_f 0.28 (3:1 Hexanes : EtOAc); IR (thin film) 3292, 2952, 1643, 1555 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.32 (t, *J* = 7.7 Hz, 2 H), 7.25–7.27 (m, 3 H), 5.94 (bs, 1 H), 5.36 (d, *J* = 9.1 Hz, 1 H), 4.53 (dd, *J* = 14.7, 6.3 Hz, 1 H), 4.23 (dd, *J* = 14.7, 4.9 Hz, 1 H), 3.88 (t, *J* = 8.4 Hz, 1 H), 2.46 (d, *J* = 2.1 Hz, 1 H), 2.39 (d, *J* = 8.4 Hz, 1 H), 2.15 (d, *J* = 4.2 Hz, 1 H), 1.98 (d, *J* = 10.5 Hz, 1 H), 1.57 (dddd, *J* = 16.1, 12.6, 4.2, 4.2 Hz, 1 H), 1.45–1.51 (m, 1 H), 1.42, (s, 9 H), 1.22–1.26 (m, 2 H), 1.12 (dddd, *J* = 14.0, 8.4, 2.8, 2.8); ^{13}C (176 MHz, $CDCl_3$) δ 172.5, 156.0, 138.3, 128.8, 127.9, 127.6, 79.4, 56.4, 53.9, 43.7, 42.6, 40.7, 35.3, 28.8, 28.6, 26.7; HRMS (TOF MS ES+) calcd for $C_{20}H_{29}N_2O_3$ [M+H]: 345.2178, found 345.2164.

(±) (4aR,5R,8S,8aS)-3-benzyl-4a,5,6,7,8,8a-hexahydro-5,8-methanoquinazolin-4(3H)-one (114). Gaseous HCl was bubbled through a DCM (7.0 mL, 0.1 M) solution of **S4** (0.2404 g, 0.698 mmol) while stirring at rt for a period of 1 hour. At this time, TLC indicated the consumption of **S18**. The reaction mixture was concentrated to give the HCl salt of the Boc-deprotected **S18** (0.2006 g, 0.714 mmol, 99%). This salt (0.0846 g, 0.301 mmol) was dissolved in triethyl orthoformate (3.0 mL, 0.1 M) and heated to reflux for 19 hours. The reaction mixture was concentrated and purified by FCC (1:1 hexanes:EtOAc to give **114** (0.0270 g, 0.0762 mmol, 35%) as a white solid.

Data for **114**: R_f 0.38 (2:1 EtOAc: Hexanes); IR (thin film) 3377, 2959, 2873, 1671 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.23-7.36 (m, 6 H), 4.80 (d, *J* = 26.6 Hz, 1 H), 4.62 (d, *J* = 26.6 Hz, 1 H), 3.84 (d, *J* = 15.4 Hz, 1 H), 2.74 (s,1 H), 2.62 (d, *J* = 15.4 Hz, 1 H), 2.51 (s, 1 H), 1.58-1.69 (m, 2 H) 1.22-1.46 (m, 4 H); ^{13}C (176 MHz, $CDCl_3$) δ 168.4, 144.0, 136.4, 129.1, 128.1, 127.8, 65.0, 48.7, 48.1, 46.1, 43.7, 34.6, 29.9, 26.4; HRMS (TOF MS ES+) calcd for $C_{16}H_{19}N_2O$ [M+H]: 255.1497, found 255.1493.

(±) 3-((2R,4aR,5R,8S,8aS)-3-benzyl-4-oxodecahydro-5,8-methanoquinazolin-2-yl)propanenitrile (115). *Following the general reductive alkylation procedure*, **114** (.0234 g, 0.0920 mmol), NH_4Cl (0.0056 g, 0.105 mmol), acrylonitrile (0.03 mL, 0.46 mmol) in THF (0.31 mL, 0.3 M) were reacted with a THF solution of SmI_2 (3.0 mL, 0.23 mmol) to give **115** (0.0283 g, 0.0915 mmol, 99%, single diastereomer) as a yellow oil.

Data for **115**: R_f 0.50 (2:1 EtOAc: Hexanes); IR (thin film) 3317, 2953, 2246, 1633 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.27-7.36 (m, 5 H), 5.00 (bs, 1 H), 4.17 (bs, 2 H), 3.24 (d, 7.6 Hz, 1 H), 3.09 (s, 1 H), 2.41-2.45 (m, 2 H), 2.19 (d, *J* = 6.8 Hz, 2 H), 1.98-2.07 (m, 1 H), 1.77-1.86 (m, 1 H), 1.59-1.70 (m, 2 H), 1.47 (d, *J* = 10.4 Hz, 1 H), 1.21-1.34 (m, 4 H); ^{13}C (176 MHz, $CDCl_3$) δ 169.4, 137.3, 129.1, 128.2, 127.9,

119.0, 68.6, 57.2, 49.4, 48.2, 42.6, 41.1, 34.2, 28.4, 27.7, 27.2, 14.3; HRMS (TOF MS ES+) calcd for $C_{19}H_{24}N_3O$ [M+H]: 310.1919, found 310.1933.

3-(6-oxohexahydropyrrolo[1,2-a]pyrimidin-8a(6H)-yl)propanenitrile (117). *Following the general reductive alkylation procedure,* known[90] 3,4,7,8-tetrahydropyrrolo[1,2-a]pyrimidin-6(2H)-one (.0187 g, 0.135 mmol), CSA (0.0343 g, 0.148 mmol), acrylonitrile (0.04 mL, 0.61 mmol) in THF (0.45 mL, 0.3 M) were reacted with a THF solution of SmI_2 (4.5 mL, 0.34 mmol) to give **117** (0.0044 g, 0.0228 mmol, 17%) as a colorless oil after purification by FCC (6:1 EtOAc:10% NH_4OH in MeOH).

Data for **117**: R_f 0.40 (4:1 EtOAc: 10% NH_4OH in MeOH); IR (thin film) 3358, 2933, 2247, 1674 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 4.17 (dd, *J* = 14.0, 4.2 Hz, 1 H), 2.92-3.04 (m, 3 H), 2.34-2.50 (m, 5 H), 2.25 (t, *J* = 12.6 Hz, 1 H), 1.87 (bs, 1 H), 1.53-1.69 (m, 4 H); ^{13}C (176 MHz, $CDCl_3$) δ 171.8, 119.5, 75.0, 40.0, 36.1, 31.9, 28.9, 28.1, 25.5, 12.5; HRMS (TOF MS ES+) calcd for $C_{10}H_{16}N_3O$ [M+H]: 194.1293, found 194.1294.

3-(3-acetyl-1,2,3,4-tetrahydroquinazolin-2-yl)propanenitrile (119). *Following the general reductive alkylation procedure,* known[91] 1-(quinazolin-3(4H)-yl)ethan-1-one (.0248 g, 0.142 mmol), NH_4Cl (0.0087 g, 0.16 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 **119** (0.0116 g, 0.0506 mmol, 36%) as a colorless oil after purification by FCC (3:2 EtOAc:hexanes).

Data for **119**: R_f 0.14 (2:1 EtOAc: Hexanes); IR (thin film) 3346, 2930, 2245, 1639 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) as a 3:1 mixture of rotational isomers δ 7.13 (t, *J* = 7.7 Hz, 1 H), 7.03 (d, *J* = 7.7 Hz, 1 H), 6.85 (t, *J* = 7.7 Hz, 1 H), 6.71 (d, *J* = 7.7 Hz, 1 H), 5.90 (t, *J* = 7.7 Hz, 1 H), 4.66 (d, *J* = 16.1 Hz, 1 H), 4.57 (d, *J* = 16.1 Hz, 1 H),

2.39-2.52 (m, 2 H), 2.00 (s, 3 H), 1.96-2.06 (m, 2 H); ^{13}C (176 MHz, $CDCl_3$) δ 169.9, 140.1, 128.5, 126.6, 120.1, 119.4, 118.7, 117.8, 59.4, 43.5, 29.0, 22.2, 13.7; HRMS (EI+) calcd for $C_{13}H_{15}N_3O$ [M+]: 229.12152, found 229.12141.

***tert*-butyl 3-(3-benzyl-4-oxo-1,2,3,4-tetrahydropyrimidin-2-yl)propanoate (121)**. *Following the general reductive alkylation procedure*, known[92] 3-benzylpyrimidin-4(3H)-one (.0293 g, 0.157 mmol), CSA (0.0419 g, 0.180 mmol), *tert*-butyl acrylate (0.11 mL, 0.75 mmol) in THF (0.52 mL, 0.3 M) were reacted with a THF solution of SmI_2 (5.0 mL, 0.39 mmol) to give **121** (0.0195 g, 0.0616 mmol, 39%) as a colorless oil along with 0.0046g of recovered starting material after purification by FCC (2:1 hexanes:EtOAc).

Data for **121**: R_f 0.45 (EtOAc); IR (thin film) 3283, 2977, 2920, 1726, 1616 cm^{-1}; ^{1}H NMR (700 MHz, D_3COD) δ 7.32-7.35 (m, 4 H), 7.26-7.29 (m, 1 H), 6.92 (dd, *J* = 7.0, 0.7 Hz, 1 H), 5.20 (d, *J* = 15.4 Hz, 1 H), 4.75 (d, *J* = 7.0 Hz, 1 H), 4.72-4.74 (m, 1 H), 4.06 (d, *J* = 15.4 Hz, 1 H), 2.23-2.29 (m, 3 H), 1.77-1.81 (m, 1 H), 1.44 (s, 9 H); ^{13}C (176 MHz, $CDCl_3$) δ 172.4, 166.0, 143.9, 137.7, 128.2, 127.9, 127.1, 90.1, 80.4, 66.9, 46.5, 29.8, 26.9, 25.7; HRMS (TOF MS ES+) calcd for $C_{18}H_{24}N_2O_3Na$ [M+Na]: 339.1685, found 339.1688.

3-(1,3-dimethyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanenitrile (123). *Following the general reductive alkylation procedure*, known[93] 1,3-dimethyl-4-oxo-3,4-dihydroquinazolin-1-ium iodide (.0430 g, 0.142 mmol), NH_4Cl (0.0085 g, 0.156 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 **123** (0.0335 g, 0.138 mmol, 97%) as a colorless oil.

Data for **123**: R_f 0.18 (1:2 hexanes:EtOAc); IR (thin film) 2938, 2245, 1646, 1495, 756 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (dd, *J* = 8.0, 1.3 Hz, 1 H), 7.40 (td, *J* =

8.0, 1.6 Hz, 1 H), 6.93 (t, *J* = 7.7 Hz, 1 H), 6.75 (d, *J* = 7.7 Hz, 1 H), 4.61 (t, *J* = 6.5 Hz, 1 H), 3.16 (s, 3 H), 3.06 (s, 3 H), 2.36 (t, *J* = 7.2 Hz, 2 H), 2.02 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT) δ *C* 162.2, 146.1, 118.5, 118.2; *C*H 133.7, 128.5, 120.0, 115.3, 76.6; *C*H_2 27.2, 13.4; *C*H_3 39.4, 33.7; HRMS (ESI) calcd for $C_{13}H_{15}N_3O$ [M+H]: 229.1215, found 229.1220.

methyl 3-(1,3-dimethyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanoate (124). *Following the general reductive alkylation procedure,* known 1,3-dimethyl-4-oxo-3,4-dihydroquinazolin-1-ium iodide (.0412 g, 0.136 mmol), NH_4Cl (0.0089 g, 0.166 mmol), methyl acrylate (0.06 mL, 0.68 mmol) in THF (0.50 mL, 0.3 M) were reacted with a THF solution of SmI_2 (3.5 mL, 0.34 mmol) to give **124** (0.0331 g, 0.120 mmol, 88%) as a colorless oil.

Data for **124**: R_f 0.27 (1:2 hexanes:EtOAc); IR (thin film) 2950, 1735, 1648, 1494, 1162, 753 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (dd, *J* = 7.8, 1.5 Hz, 1 H), 7.36 (td, *J* = 7.8, 1.5 Hz, 1 H), 6.85 (t, *J* = 7.5 Hz, 1 H), 6.63 (d, *J* = 8.1 Hz, 1 H), 4.62 (t, *J* = 5.9 Hz, 1 H), 3.64 (s, 3 H), 3.13 (s, 3 H), 2.99 (s, 3 H), 2.33 (t, *J* = 7.5 Hz, 2 H), 2.02 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT) δ *C* 173.0, 162.5, 146.5, 117.4; *C*H 133.5, 128.5, 118.7, 113.3, 77.3; *C*H_2 29.2, 26.5; *C*H_3 51.8, 37.9, 33.8; HRMS (ESI) calcd for $C_{14}H_{18}N_2O_3$ [M+H]: 262.1318, found 262.1323.

***tert*-butyl 3-(1,3-dimethyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanoate (125).** *Following the general reductive alkylation procedure,* known 1,3-dimethyl-4-oxo-3,4-dihydroquinazolin-1-ium iodide (.0442 g, 0.146 mmol), NH_4Cl (0.0088 g, 0.161 mmol), *tert*-butyl acrylate (0.11 mL, 0.73 mmol) in THF (0.50 mL, 0.3 M) were reacted with a THF solution of SmI_2 (4.5 mL, 0.37 mmol) to give **125** (0.0434 g, 0.136 mmol, 93%) as a colorless oil.

Data for **125**: R_f 0.51 (1:2 hexanes:EtOAc); IR (thin film) 2975, 1726, 1649, 1494, 1152, 754 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (dd, *J* = 7.6, 1.2 Hz, 1 H), 7.36 (td, *J* = 7.7, 1.6 Hz, 1 H), 6.85 (t, *J* = 7.8 Hz, 1 H), 6.64 (d, *J* = 8.1 Hz, 1 H), 4.63 (t, *J* = 6.0 Hz, 1 H), 3.14 (s, 3 H), 3.00 (s, 3 H), 2.45 (t, *J* = 7.4 Hz, 2 H), 1.97 (m, 2 H), 1.43 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT) δ *C* 171.9, 162.6, 146.5, 117.4, 80.9; *C*H 133.5, 128.5, 118.5, 113.1, 77.2; *C*H_2 30.6, 26.5; *C*H_3 37.7, 33.9, 28.1; HRMS (ESI) calcd for $C_{17}H_{24}N_2O_3$ [M+H]: 304.1787, found 304.1796.

3-(1,2,3-trimethyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanenitrile (127). *Following the general reductive alkylation procedure*, known[94] 1,2,3-trimethyl-4-oxo-3,4-dihydroquinazolin-1-ium iodide (.0450 g, 0.142 mmol), NH_4Cl (0.0089 g, 0.166 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 **127** (0.0334 g, 0.137 mmol, 97%) as a colorless oil.

Data for **127**: R_f 0.77 (4:1 EtOAc: 10% NH_4OH in MeOH); IR (thin film) 2952, 2247, 1644 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (dd, *J* = 7.6, 1.2 Hz, 1 H), 7.40 (ddd, *J* = 8.4, 7.2, 1.6 Hz, 1 H), 6.92 (ddd, *J* = 8.4, 8.4, 0.8 Hz, 1 H), 6.79 (d, *J* = 8.4 Hz, 1 H), 3.10 (s, 3 H), 2.86 (s, 3 H) 2.35-2.50 (m, 2 H), 2.22-2.34 (m, 2 H), 1.58 (s, 3 H); ^{13}C (176 MHz, $CDCl_3$) δ 163.3, 146.9, 134.1, 128.7, 119.9, 119.1, 117.0, 114.6, 33.7, 33.0, 28.6, 20.8, 12.1; HRMS (EI+) calcd for $C_{14}H_{17}N_3O$ [M+]: 243.13717, found 243.13734.

3-(1,3-dimethyl-4-oxo-1,2,3,4-tetrahydropyrimidin-2-yl)propanenitrile (129). *Following the general reductive alkylation procedure*, known[95] 1,3-dimethyl-4-oxo-3,4-dihydropyrimidin-1-ium iodide (.0343 g, 0.144 mmol), CSA (0.0376 g, 0.162 mmol), acrylonitrile (0.05 mL, 0.76 mmol) in THF (0.48 mL, 0.3 M) were reacted with a THF solution of SmI_2 (3.9 mL, 0.36 mmol) to give **129** (0.0173 g, 0.0965

mmol, 67%) as a yellow oil after purification by FCC (9:1 EtOAc:10% NH_4OH in MeOH).

Data for **129**: R_f 0.45 (4:1 EtOAc: 10% NH_4OH in MeOH); IR (thin film) 2927, 2246, 1627 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 6.53 (dd, *J* = 7.7, 1.4 Hz, 1 H), 4.82 (d, *J* = 7.7 Hz, 1 H), 4.66 (td, *J* = 6.3, 1.4 Hz, 1 H), 3.05 (s, 3 H), 2.99 (s, 3 H), 2.43-2.53 (m, 2 H), 2.16-2.21 (m, 1 H), 2.10-2.14 (m, 1 H); ^{13}C (176 MHz, $CDCl_3$) δ 163.6, 145.7, 118.9, 93.9, 75.3, 40.9, 33.2, 25.6, 13.0; HRMS (EI+) calcd for $C_9H_{13}N_3O$ [M+]: 179.10587, found 179.10647.

3-(1,3-dimesityl-5,5-dimethyl-4-oxohexahydropyrimidin-2-yl)propanenitrile (131). *Following the general reductive alkylation procedure,* known[96] 1,3-dimesityl-5,5-dimethyl-4-oxo-3,4,5,6-tetrahydropyrimidin-1-ium chloride (.0569 g, 0.143 mmol), CSA (0.0401 g, 0.173 mmol), acrylonitrile (0.05 mL, 0.76 mmol) in THF (0.48 mL, 0.3 M) were reacted with a THF solution of SmI_2 (3.8 mL, 0.36 mmol) to give **131** (0.0301 g, 0.0721 mmol, 50%) as a white solid after purification by FCC (9:1 EtOAc:10% NH_4OH in MeOH).

Data for **131**: R_f 0.65 (1:1 EtOAc:hexanes); IR (thin film) 2959, 2244, 1651 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.00 (s, 1 H), 6.99 (s, 1 H), 6.93 (s, 1 H), 6.89 (s, 1 H), 5.29 (t, *J* = 5.6 Hz, 1 H), 3.60 (d, *J* = 12.6 Hz, 1 H), 3.23 (d, *J* = 12.6 Hz, 1 H), 2.48 (s, 3 H), 2.45 (s, 3 H) 2.34 (s, 3 H), 2.29 (s, 3 H), 2.25 (s, 3 H), 2.19 (s, 3 H), 1.95-2.00 (m, 1 H), 1.78-1.83 (m, 1 H), 1.54-1.62 (m, 2 H), 1.48 (s, 3 H), 1.26 (s, 3 H); ^{13}C (176 MHz, $CDCl_3$) δ 177.7, 142.7, 139.4, 138.6, 138.5, 137.9, 137.7, 136.1, 135.6, 132.1, 131.3, 131.1, 130.6, 119.9, 76.7, 61.0, 49.4, 49.2, 49.1, 49.0, 48.9, 48.8, 48.6, 42.0, 28.7, 26.5, 24.8, 21.0, 20.9, 20.7, 20.5, 19.0, 18.9, 14.7; HRMS (EI+) calcd for $C_{27}H_{36}N_3O$ [M+H]: 418.2858, found 418.2842.

5,5-dimethyl-4-oxo-1,3-diphenyl-3,4,5,6-tetrahydropyrimidin-1-ium chloride (132). To a DCM (4 mL, 0.5 M) solution of known[97] chloropivalic acid (0.2537 g, 1.86 mmol) and 1 drop of DMF was added oxalyl chloride (0.17 mL, 1.98 mmol). This solution was stirred at rt for 2 h. At this time, the solution of the acid chloride was added dropwise to a DCM (3.7 mL, 0.2 M) solution of known[98] (E)-*N*,*N'*-diphenylformimidamide (0.3004 g, 1.53 mmol) and triethylamine (0.28 mL, 2.00 mmol). After stirring at rt for 0.5 hours, the mixture was concentrated and extracted with PhMe. The PhMe extracts were filtered through celite and then refluxed for 28 hours. Filtration of the white precipitate gave **132** (0.2815 g, 0.08941 58%) as a white solid.

Data for **132**: R_f 0.64 (4:1 EtOAc: 10% NH_4OH in MeOH); IR (thin film) 2972, 2873, 1671, 1594 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.44 (s, 1 H), 7.71-7.30 (m, 2 H), 7.59-7.68 (m, 6 H), 7.51-7.54 (m, 2 H), 4.54 (s, 2 H), 1.57 (s, 6 H); ^{13}C (100 MHz, $CDCl_3$) δ 170.0, 156.1, 140.8, 135.3, 130.4, 130.4, 130.3, 128.2, 123.5, 60.4, 38.1, 22.8; HRMS (TOF MS ES+) calcd for $C_{18}H_{19}N_2O$ [M+]: 279.1497, found 279.1487.

3-(5,5-dimethyl-4-oxo-1,3-diphenylhexahydropyrimidin-2-yl)propanenitrile (133). *Following the general reductive alkylation procedure,* **132** (.0418 g, 0.133 mmol), NH_4Cl (0.0081 g, 0.151 mmol), acrylonitrile (0.04 mL, 0.61 mmol) in THF (0.44 mL, 0.3 M) were reacted with a THF solution of SmI_2 (4.4 mL, 0.33 mmol) to give **61** (0.0247 g, 0.0741 mmol, 56%) as a colorless oil after purification by FCC (2:1 hexanes:EtOAc).

Data for **133**: R_f 0.37 (4:1 EtOAc: 10% NH_4OH in MeOH); IR (thin film) 3364, 2926, 2245, 1651 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.48 (t, *J* = 7.6 Hz, 2 H), 7.32-7.38 (m, 5 H), 7.15 (d, *J* = 8.0 Hz, 2 H), 6.97 (t, *J* = 7.6 Hz, 1 H), 5.43-5.46 (m, 1 H), 3.73 (dd, *J* = 14.4, 1.2 Hz, 1 H), 3.58 (d, *J* = 14.4 Hz, 1 H), 2.16-2.29 (m,4 H), 1.28

(s, 3 H), 1.11 (s, 3 H); ^{13}C (176 MHz, $CDCl_3$) δ 174.8, 149.6, 140.2, 130.0, 129.9, 128.0, 127.9, 121.5, 118.8, 117.6, 74.7, 54.5, 40.6, 28.3, 27.4, 25.0, 13.5; HRMS (TOF MS ES+) calcd for $C_{21}H_{23}N_3O$ [M+H]: 334.1919, found 334.1904.

3-benzyl-2-propylquinazolin-4(3H)-one (138). To a stirring THF (0.48 mL, 0.3M) solution of known[99] amidine **137** (0.0396 g, 0.143 mmol) and NH_4Cl (0.0091 g, 0.170 mmol) was added a THF solution of SmI_2 (4.7 mL, 0.36 mmol) via syringe pump over 1 hour. The reaction mixture was then diluted with half-saturated aqueous Rochelle salt. This biphasic mixture was extracted with ethyl acetate. The combined extracts were dried over $MgSO_4$ and concentrated to give known[100] amidine **138** (0.0114 g, 0.041 mmol, 23%) as a white solid along with 0.0179 g of recovered **137**.

3-(3-benzyl-2-cyclopropyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)propanenitrile (139) and 3-(4-benzyl-5-oxo-2,3,4,5-tetrahydropyrrolo[1,2-a]quinazolin-3a(1H)-yl)propanenitrile (140). *Following the general reductive alkylation procedure,* known[101] amidine **137** (.0391 g, 0.141 mmol), CSA (0.0371 g, 0.160 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 (3.8 mL, 0.36 mmol) to give **139** (0.0074 g, 0.0224 mmol, 16%) as a colorless oil and **140** (0.0069 g, 0.0208 mmol, 15%) as a colorless oil after purification by FCC (2:1 hexanes:EtOAc) along with 0.0136 g of **137**.

Data for **139**: R_f 0.52 (1:1 Hexanes: EtOAc); IR (thin film) 3330, 2929, 2247, 1625 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.96 (dd, *J* = 7.7, 1.4 Hz, 1 H), 7.35 (d, *J* = 7.0 Hz, 1 H), 7.31 (td, *J* = 7.7, 2.1 Hz, 2 H), 7.24-7.25 (m,3 H), 6.87 (td, *J* = 7.7, 0.7 Hz, 1 H), 6.62 (dd, *J* = 7.7, 0.7 Hz, 1 H), 5.10 (d, *J* = 15.4 Hz, 1 H), 4.79 (d, *J* = 15.4 Hz, 1 H), 3.90 (s, 1 H), 2.32-2.37 (m, 2 H), 2.09-2.14 (m, 1 H), 1.69-1.73 (m, 1 H), 1.30 (dddd, *J* = 10.5, 8.4, 5.6, 5.6 Hz, 1 H), 0.69-.73 (m, 1 H), 0.60-.64 (m, 1 H), 0.50-.54 (m, 1 H), .37-.41 (m, 1 H); ^{13}C (176 MHz, $CDCl_3$) δ 163.9, 144.3, 139.2, 134.2,

129.0, 128.8, 127.8, 127.5, 119.6, 119.5, 114.4, 114.3, 75.8, 45.5, 34.2, 19.7, 12.5, 4.0, 1.9; HRMS (TOF MS ES+) calcd for $C_{21}H_{22}N_3O$ [M+H]: 332.1763, found 332.1773.

Data for **140**: R_f 0.42 (1:1 Hexanes: EtOAc); IR (thin film) 3356, 2963, 2247, 1660 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.99 (dd, *J* = 7.7, 1.4 Hz, 1 H), 7.41 (ddd, *J* = 8.4, 7.7, 2.1 Hz, 1 H), 7.23-7.32 (m, 5 H), 7.88 (td, *J* = 8.4, 1.4 Hz, 1 H), 6.68 (d, *J* = 8.4 Hz, 1 H), 5.21 (d, *J* = 16.1 Hz, 1 H), 4.34 (d, *J* = 16.1 Hz, 1 H), 3.73 (td, *J* = 9.1, 3.5 Hz, 1 H), 3.47 (q, *J* = 7.7 Hz, 1 H), 2.35 (ddd, *J* = 11.2, 8.4, 4.2 Hz, 1 H), 2.29 (ddd, *J* = 8.4, 7.7, 2.1 Hz, 2 H), 2.22 (ddd, *J* = 12.6, 7.0, 2.8 Hz, 1 H), 2.11 (ddd, *J* = 14.7, 8.4, 8.4, 2.11 Hz, 1 H), 1.95-2.06 (m, 3 H); ^{13}C (176 MHz, $CDCl_3$) δ 163.6, 144.7, 138.6, 134.4, 129.3, 128.9, 127.4, 127.2, 119.0, 118.9, 115.4, 114.4, 81.4, 49.0, 47.1, 37.2, 34.4, 21.9, 12.9; HRMS (TOF MS ES+) calcd for $C_{21}H_{21}N_3NaO$ [M+Na]: 354.1582, found 354.1587.

***tert*-butyl 2-cyclopropylacrylate (141).** To a dry THF (10.2 mL, 0.4 M) solution of (iPr)$_2$NH (0.06 mL, 0.43 mmol) and methyltriphenylphosphonium bromide (1.6034 g, 4.49 mmol) stirring at -78℃, was added a solution of *n*-butyl lithium in hexanes (2.8 mL, 4.11 mmol). The mixture was allowed to warm to rt. Once the solution had stirred at rt for 1 h, the solution was again cooled to -78℃ and the known[102] *tert*-butyl 2-cyclopropyl-2-oxoacetate (0.6970 g, 4.10 mmol) was added in a dropwise fashion. The solution was allowed to warm to rt over 16 hours. At this time, TLC indicated the consumption of the ketoester and the reaction was quenched with the addition of 5% aqueous H_2SO_4. The mixture was then diluted with brine, extracted with EtOAc, and the organic extracts were dried over $MgSO_4$. After concentration, the oil was purified by FCC (19:1 hexanes:EtOAc) to give **141** (0.4426 g, 2.65 mmol, 64%) as a colorless oil.

Data for **141**: R_f 0.80 (1:1 hexanes: EtOAc); IR (thin film) 2926, 1716, 1629 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 5.19 (d, *J* = 0.7 Hz, 1 H), 5.21 (t, *J* = 1.4 Hz, 1 H), 1.69-1.73 (m, 1 H), 1.51 (s, 9 H), 0.76 (ddd, *J* = 6.3, 4.2, 4.2 Hz, 2 H), 5.21 (ddd, *J* = 5.63,

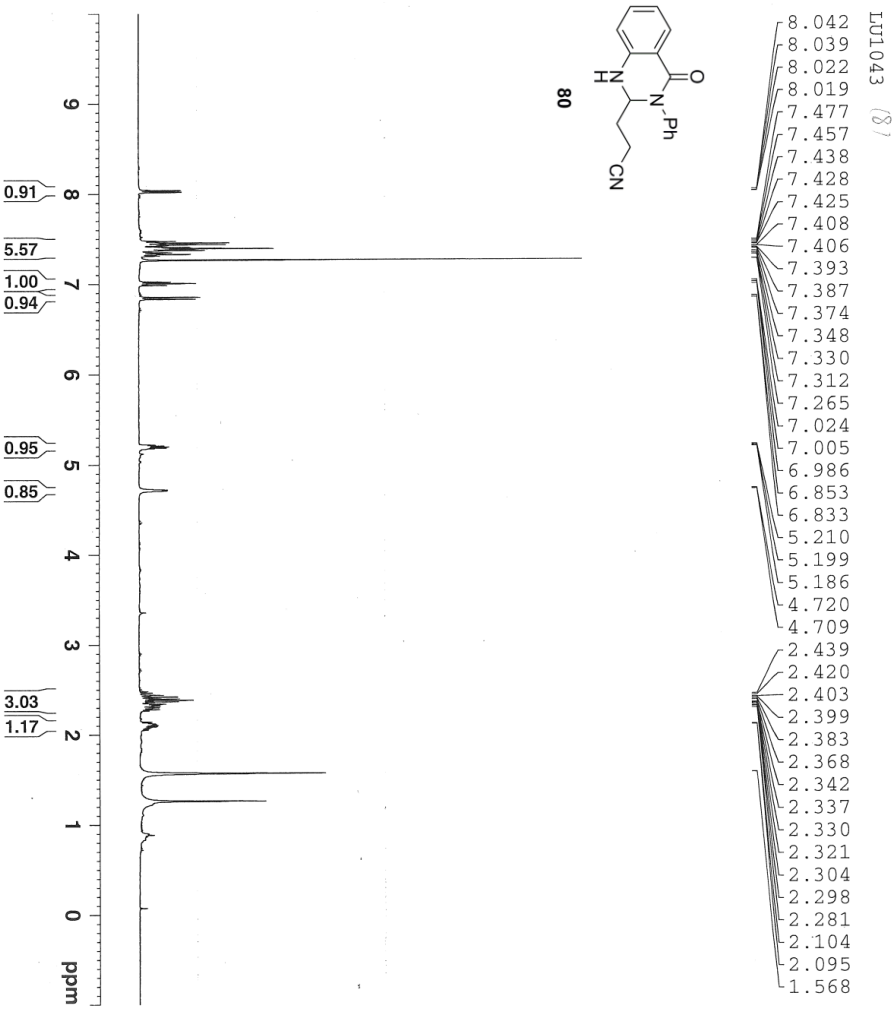
4.2, 4.2 Hz, 2 H); ^{13}C (176 MHz, $CDCl_3$) δ 166.7, 144.2, 119.5, 80.7, 28.2, 12.0, 7.5; HRMS (EI+) calcd for $C_6H_8O_2$ [M-*t*Bu]: 112.05243, found 112.05274.

tert-butyl 3-(3-benzyl-4-oxo-1,2,3,4-tetrahydroquinazolin-2-yl)-2-cyclopropylpropanoate (142) and 3-benzyl-2,3-dihydroquinazolin-4(1H)-one (143). *Following the general reductive alkylation procedure,* **78** (.0347 g, 0.148 mmol), NH_4Cl (0.0088 g, 0.164 mmol), **141** (0.1242 g, 0.7382 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 **142** (0.0291 g, 0.0716 mmol, 49%, 1.4:1 dr) as a colorless oil, **143**[103] (0.0109 g, 0.0460 mmol, 31%) as a colorless oil, and 0.0055 g of recovered **78** after purification by FCC (4:1 hexanes:EtOAc).

Data for **142a**: R_f 0.81 (1:1 EtOAc:hexanes); IR (thin film) 3301, 2926, 2246, 1718, 1629 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.97 (dd, *J* = 7.7, 1.4 Hz, 1 H), 7.25-7.36 (m, 6 H), 6.88 (td, *J* = 8.4, 1.4 Hz, 1 H), 6.60 (dd, *J* = 7.7, 0.7 Hz, 1 H), 5.58 (d, *J* = 15.4 Hz, 1 H), 4.52 (dd, *J* = 10.5, 2.8 Hz, 1 H), 3.95 (d, *J* = 15.4 Hz, 1 H), 2.19 (ddd, *J* = 14.7, 11.2, 4.2 Hz, 1 H), 1.98 (ddd, *J* = 14.0, 11.2, 2.1 Hz, 1 H) 1.50 (ddd, *J* = 11.2, 9.8, 4.2 Hz, 1 H), 1.38 (s, 9 H), 0.81-0.86 (m, 1 H), 0.46-0.50 (m, 1 H), 0.42-0.46 (m, 1 H), 0.26 (sextet, *J* = 4.2 Hz, 1 H), -0.08 (sextet, *J* = 4.9 Hz, 1 H); ^{13}C (176 MHz, $CDCl_3$) δ 174.3, 162.6, 144.6, 137.2, 133.6, 129.0, 128.8, 128.2, 127.7, 119.6, 117.0, 115.4, 81.4, 66.2, 48.1, 47.1, 34.4, 28.2, 13.7, 4.3, 4.0; TOF MS ES+) calcd for $C_{25}H_{30}N_2O_3Na$ [M+H]: 407.2335, found 407.2339.

Data for **142b**: R_f 0.77 (1:1 EtOAc:hexanes); IR (thin film) 3320, 2917, 2248, 1722, 1630 m^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.97 (dd, *J* = 7.7, 1.4 Hz, 1 H), 7.27-7.35 (m, 6 H), 6.89 (td, *J* = 8.4, 1.4 Hz, 1 H), 6.61 (dd, *J* = 8.4, 0.7 Hz, 1 H), 5.49 (d, *J* = 15.4 Hz, 1 H), 4.69 (dd, *J* = 8.4, 3.5 Hz, 1 H), 4.05 (d, *J* = 15.4 Hz, 1 H), 2.27 (dt, *J* = 14.7, 7.7 Hz, 1 H), 1.94 (ddd, *J* = 9.8, 6.3, 4.2 Hz, 1 H) 1.46 (ddd, *J* = 9.8, 7.7, 5.6 Hz, 1 H), 1.41 (s, 9 H), 0.86-0.90 (m, 1 H), 0.74-0.79 (m, 1 H), 0.43-0.52 (m, 2 H),

0.28 (sextet, J = 4.9 Hz, 1 H), 0.00 (sextet, J = 4.9 Hz, 1 H); ^{13}C (176 MHz, $CDCl_3$) δ 174.3, 162.6, 144.9, 137.3, 133.5, 128.9, 128.9, 128.2, 127.8, 119.6, 117.0, 115.8, 81.2, 67.2, 48.4, 47.9, 35.9, 28.3, 14.2, 4.9, 3.5; (TOF MS ES+) calcd for $C_{25}H_{30}N_2O_3Na$ [M+Na]: 429.2154, found 429.2134.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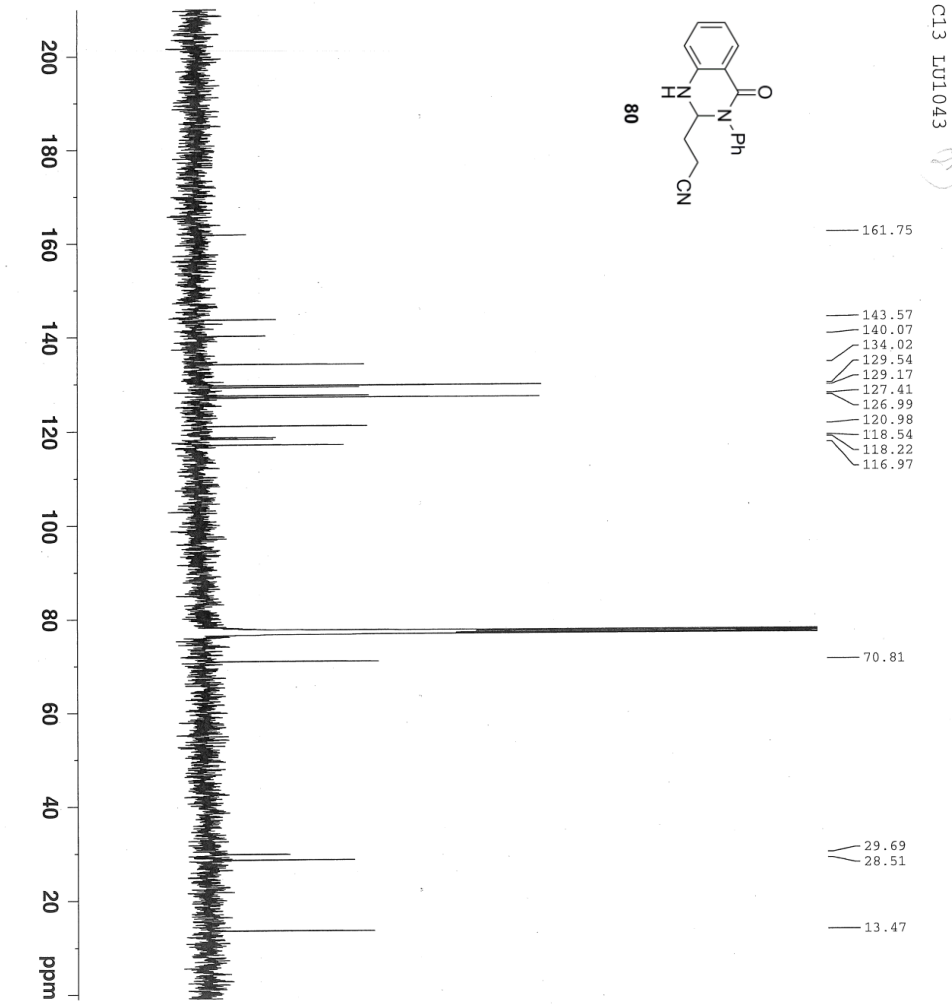


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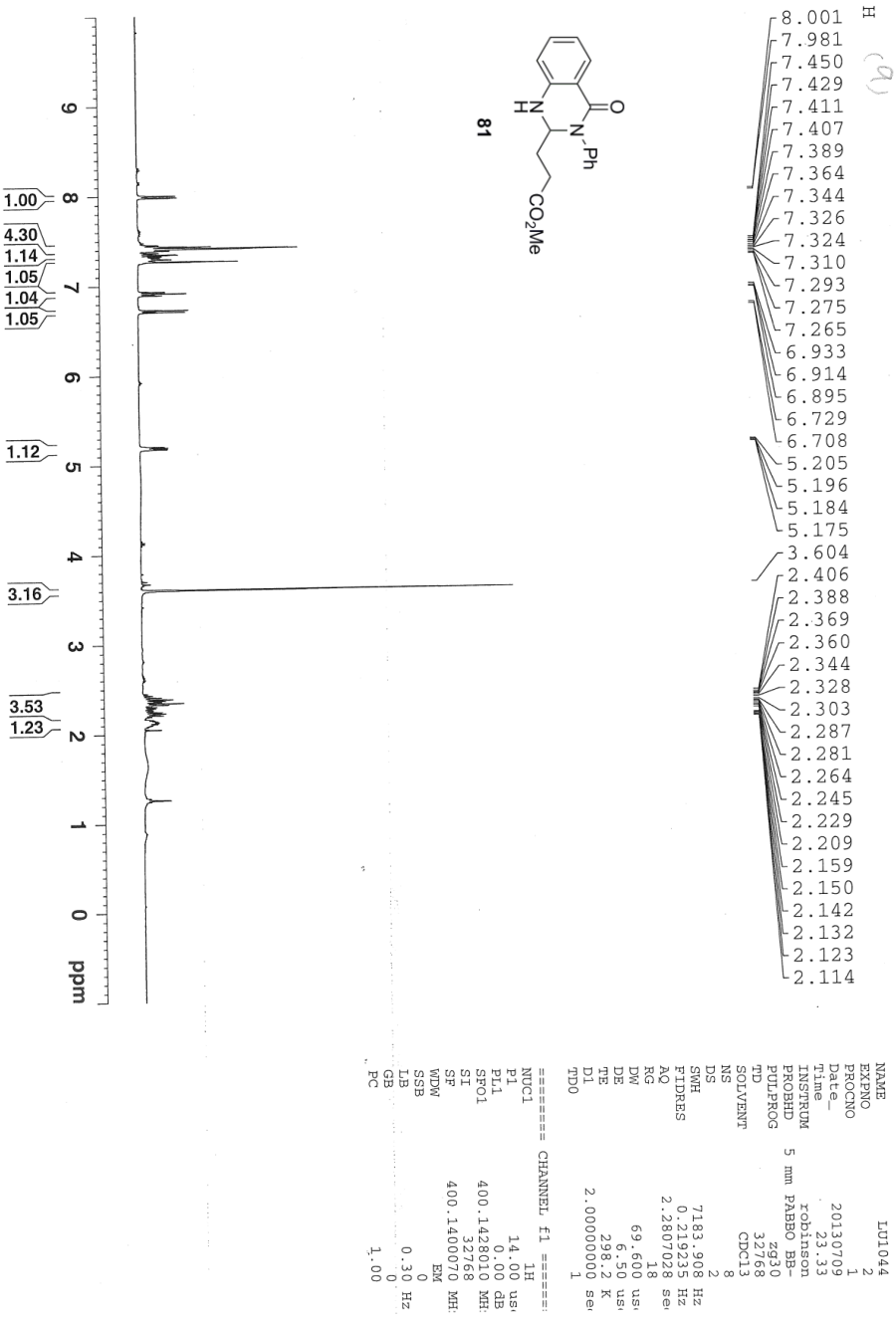
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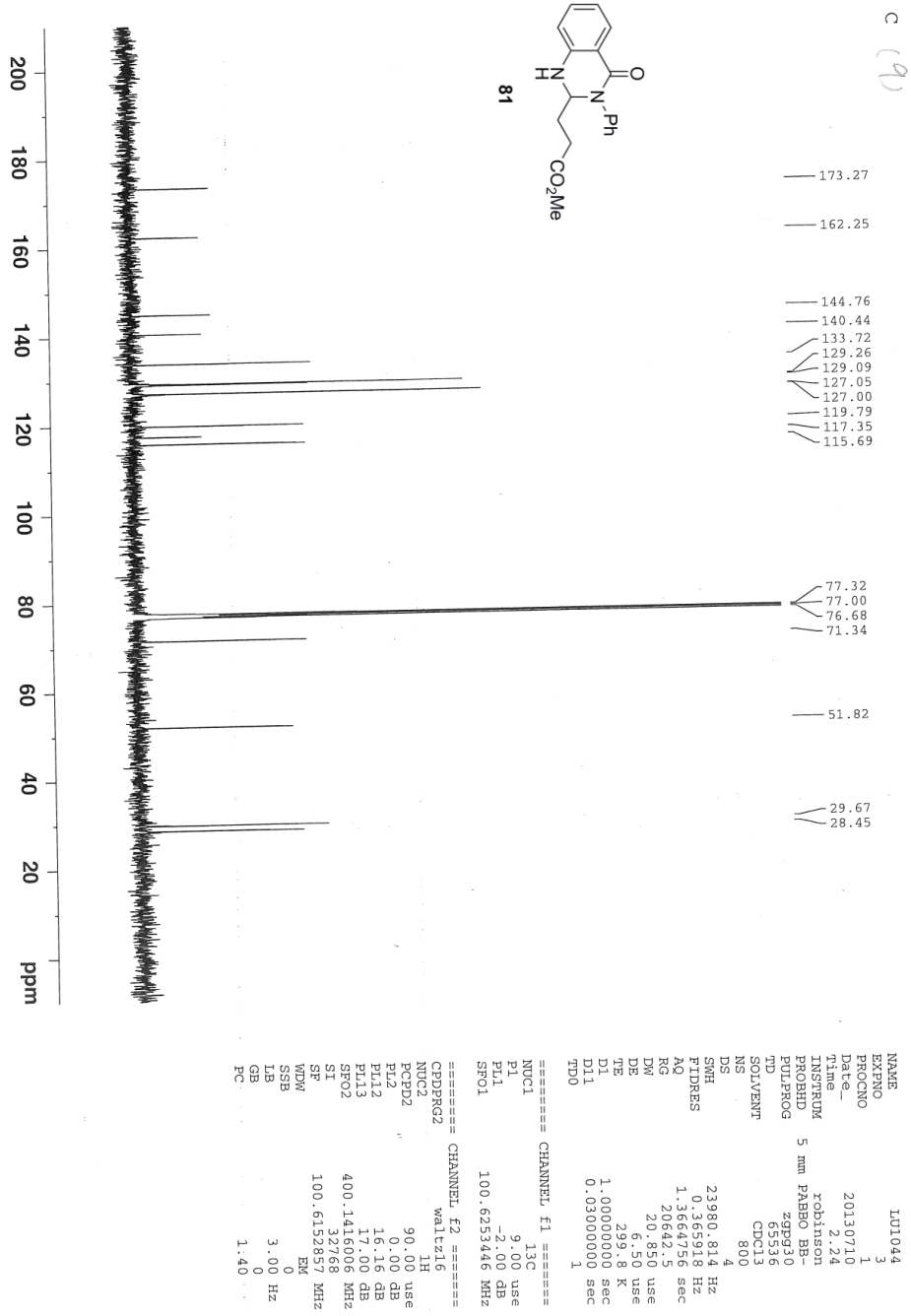
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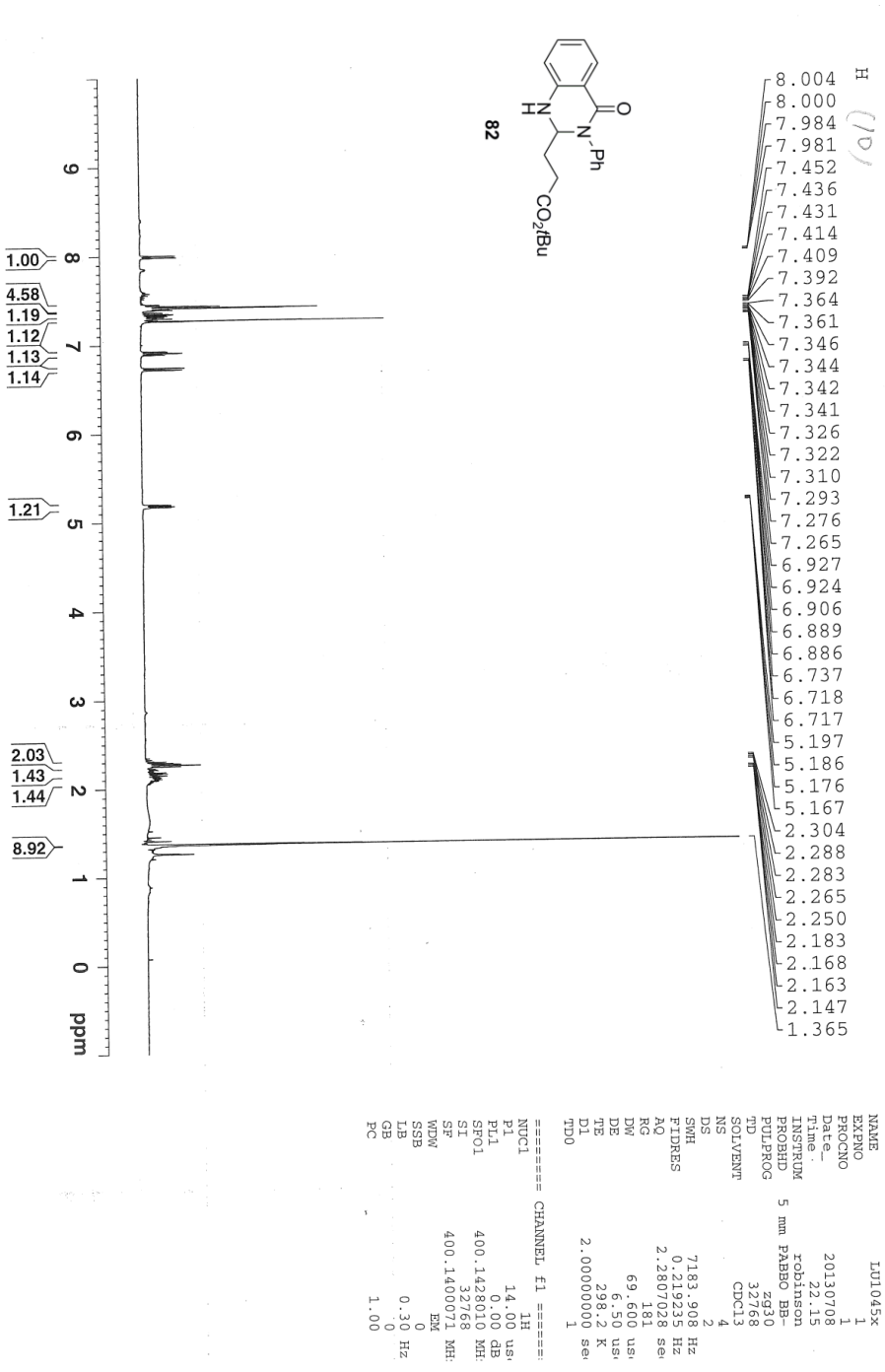
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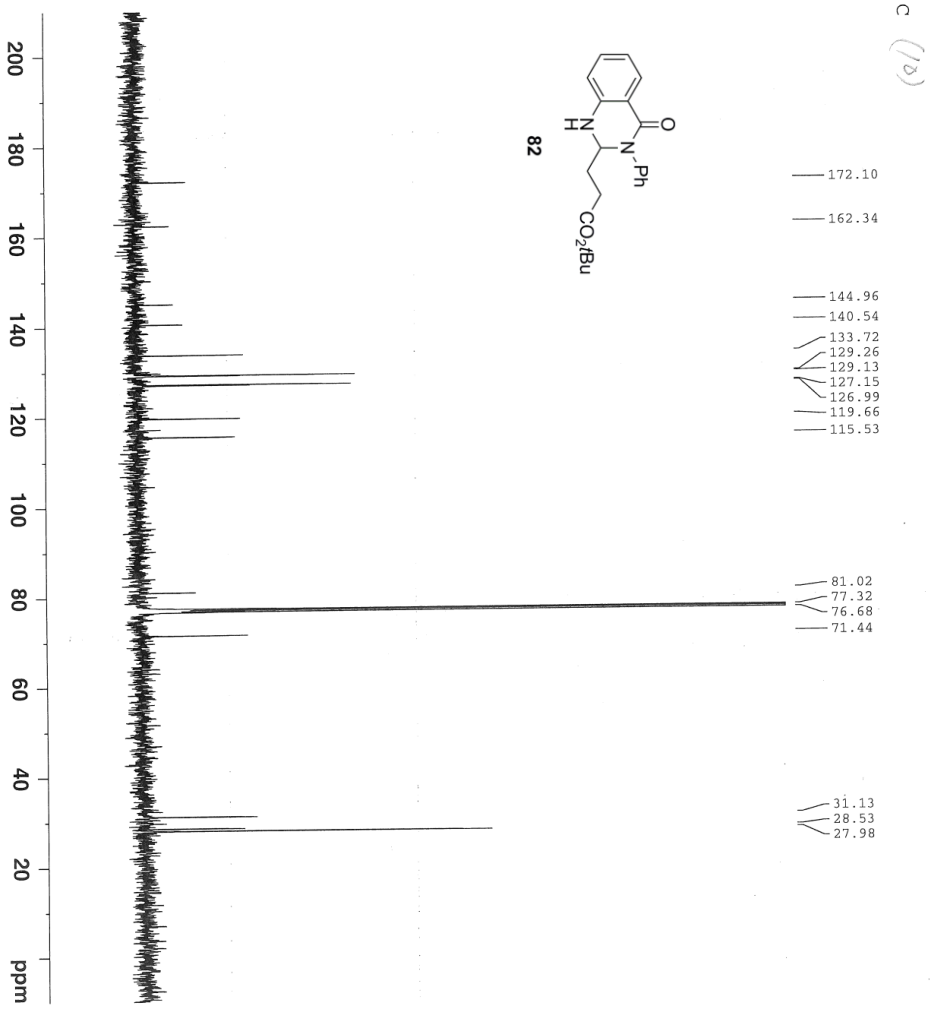
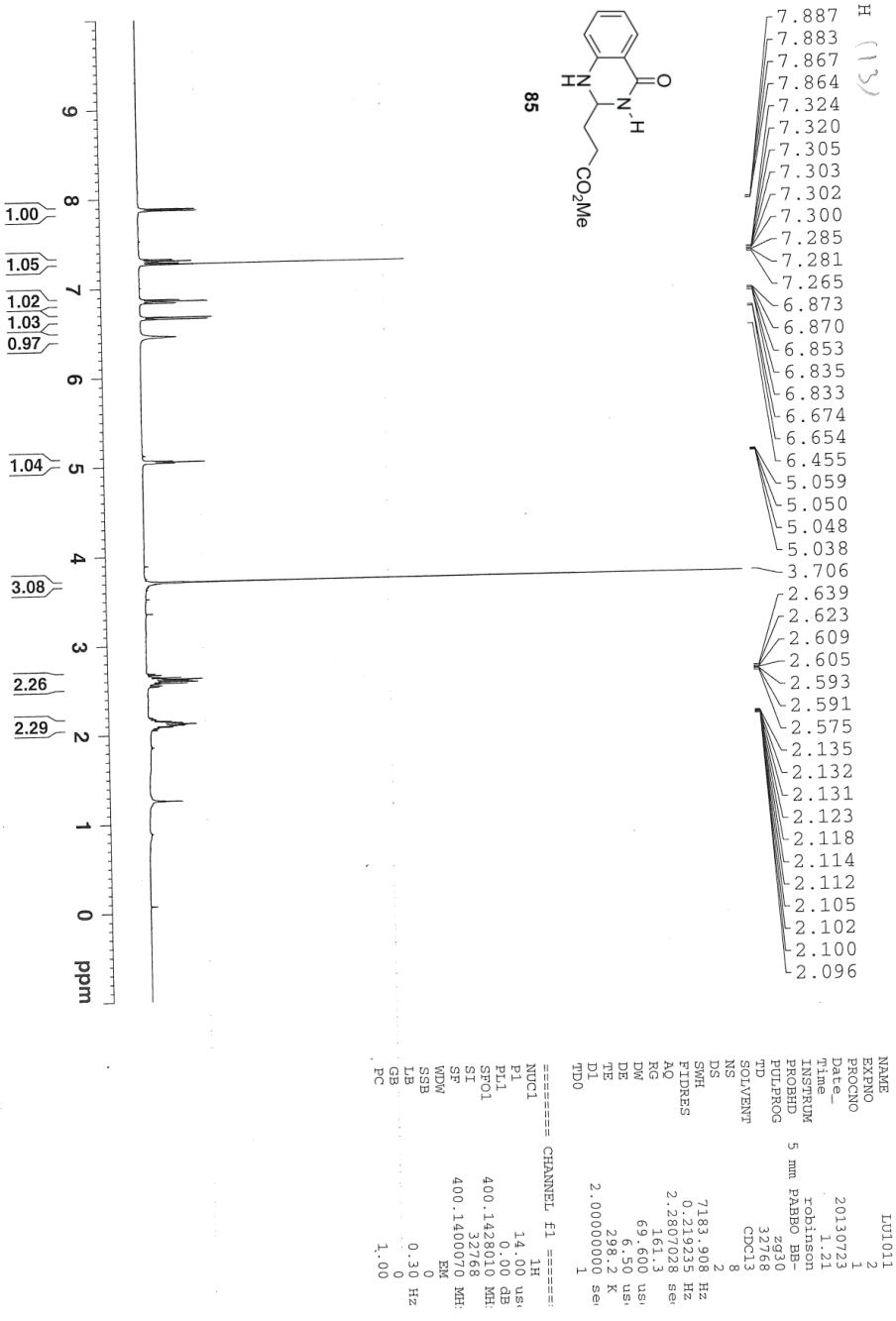
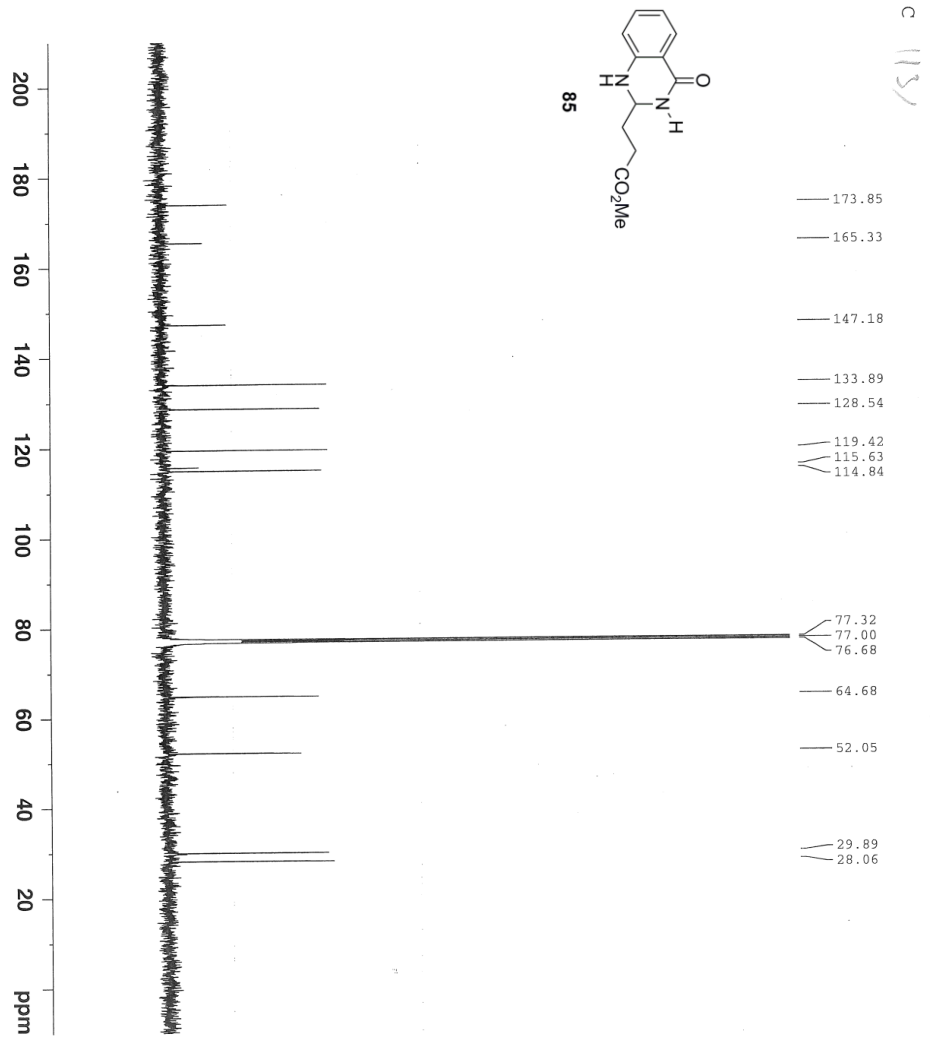
GB 0
PC 1.00

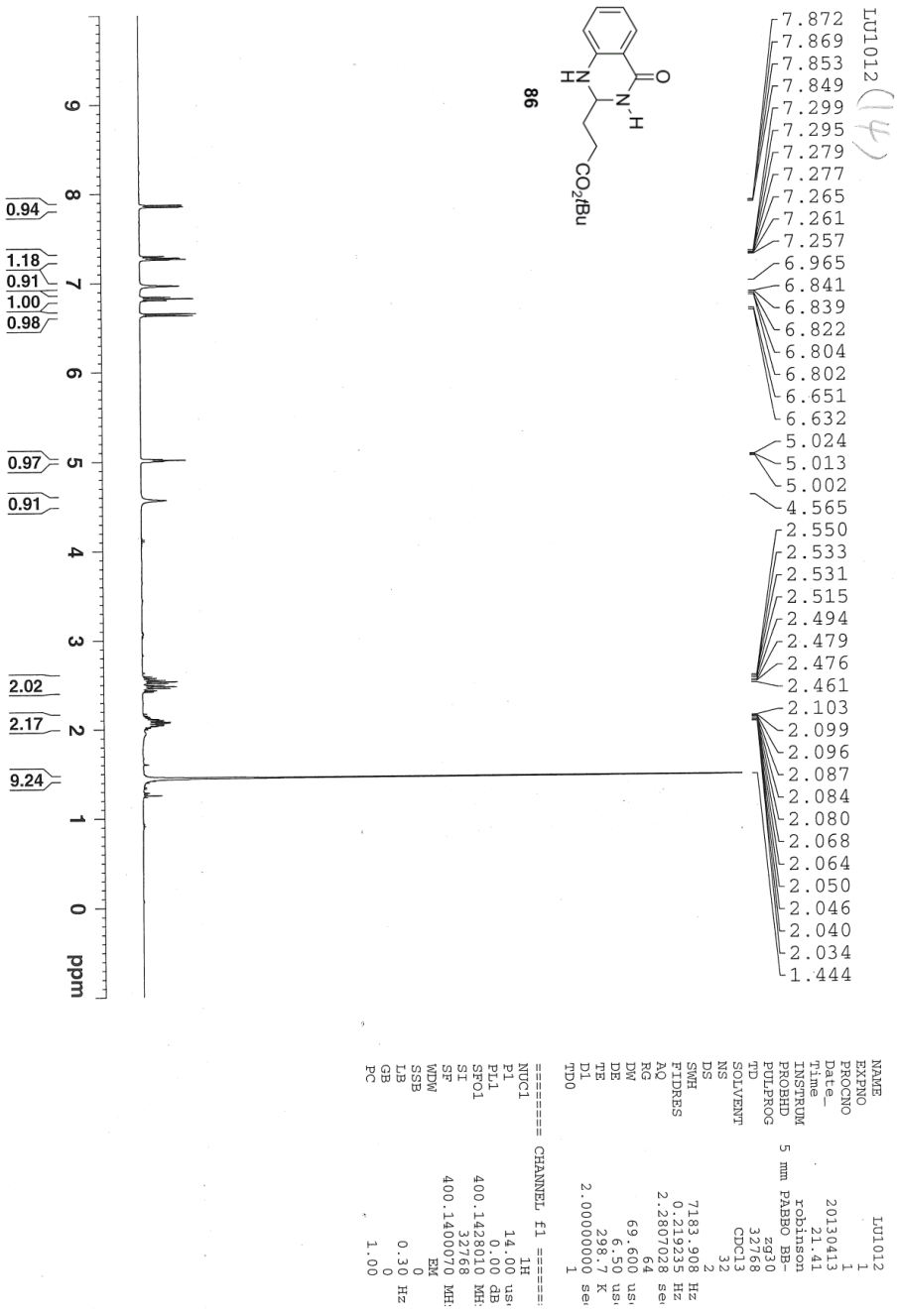



```
NAME                                   LU1045
EXPNO                                       3
PROCNO                                      1
Date_                               20130708
Time                                    23.07
INSTRUM                                robinson
PROBHD                     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 usec
DE                                      6.50 usec
TE                                     299.8 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                            100.6152836 MHz
WDW                                        EM
SSB                                         0
LB                                      3.00 Hz
GB                                          0
PC                                      1.40
```

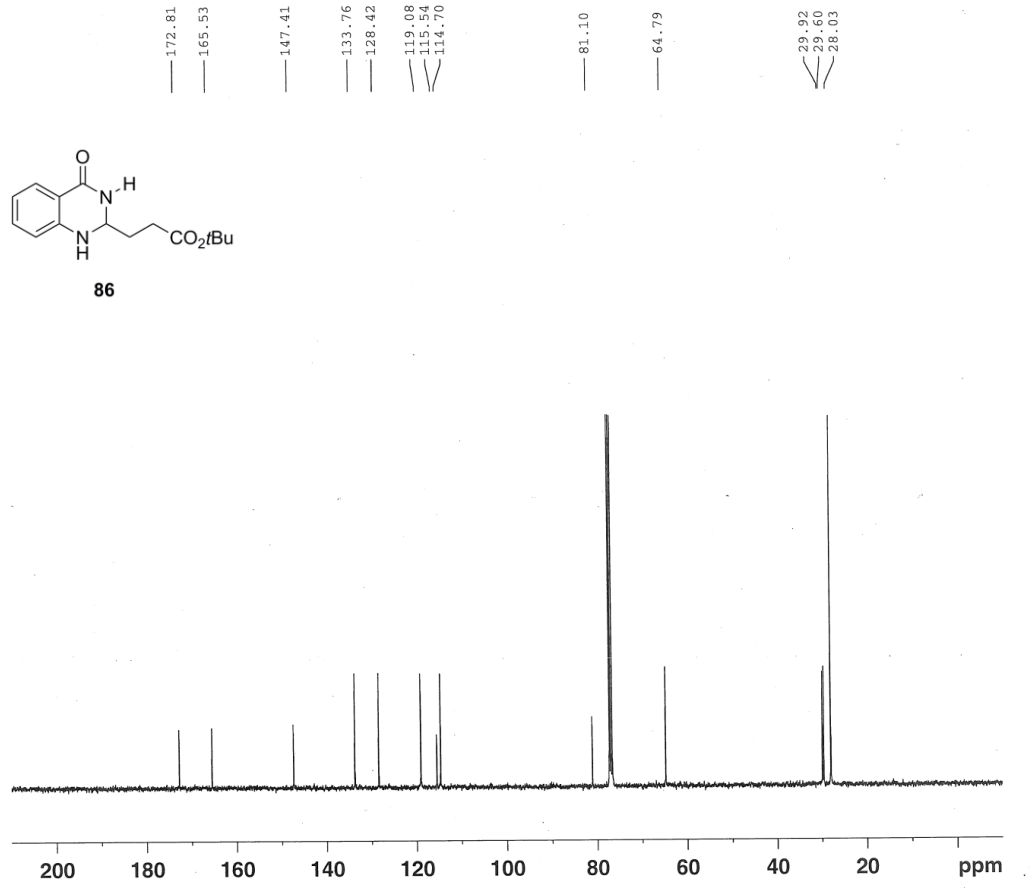

H (13)
7.887
7.883
7.867
7.864
7.324
7.320
7.305
7.303
7.302
7.300
7.285
7.281
7.265
6.873
6.870
6.853
6.835
6.833
6.674
6.654
6.455
5.059
5.050
5.048
5.038
3.706
2.639
2.623
2.609
2.605
2.593
2.591
2.575
2.135
2.132
2.131
2.123
2.118
2.114
2.112
2.105
2.102
2.100
2.096
85
CO2Me
1.00
1.05
1.02
1.03
0.97
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



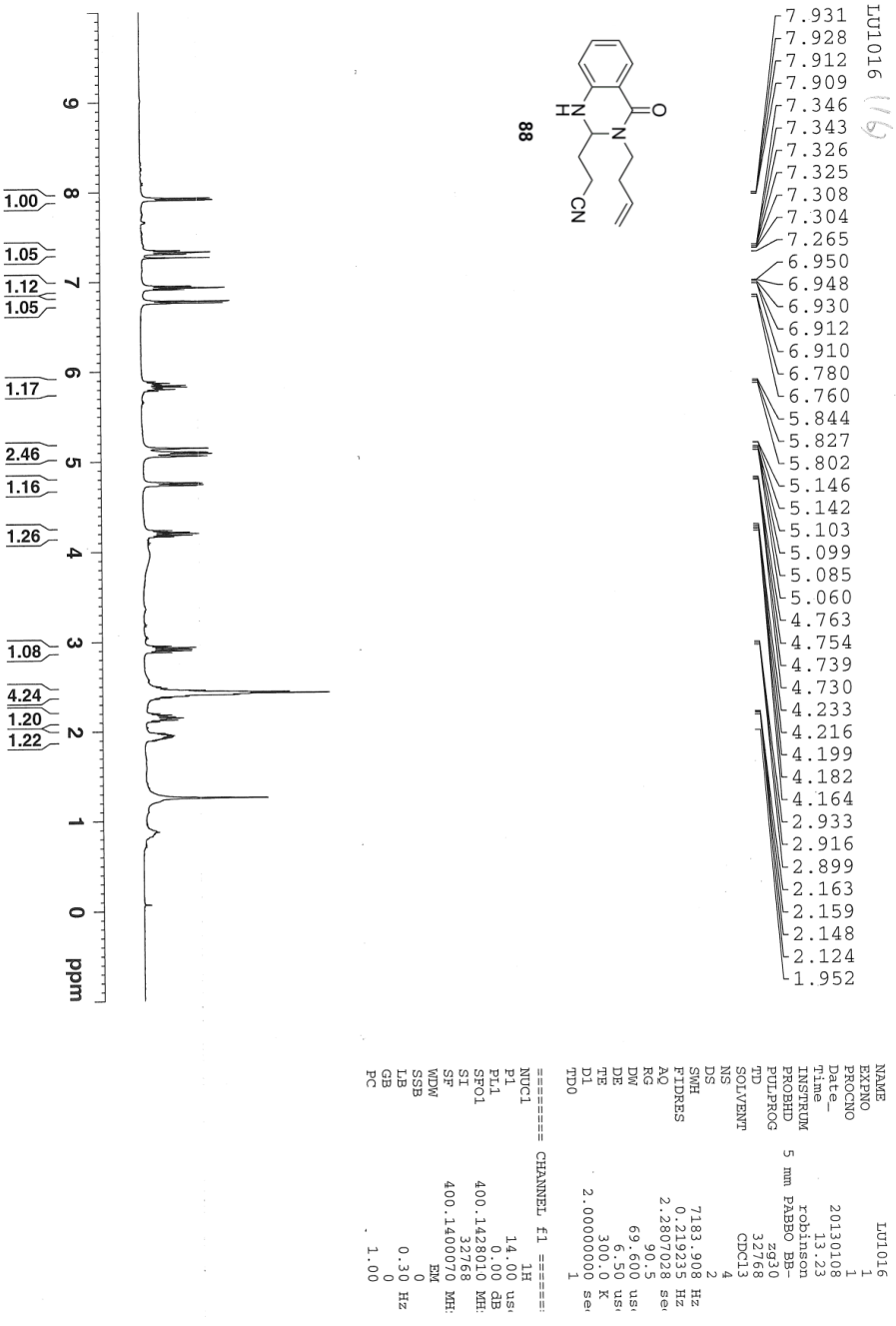

```
NAME                                    LU1011
EXPNO                                        3
PROCNO                                       1
Date_                               20130723
Time_                                    2.10
INSTRUM                                  robinson
PROBHD                    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 usec
DE                                      6.50 usec
TE                                     299.5 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                       100.6152847 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
86
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

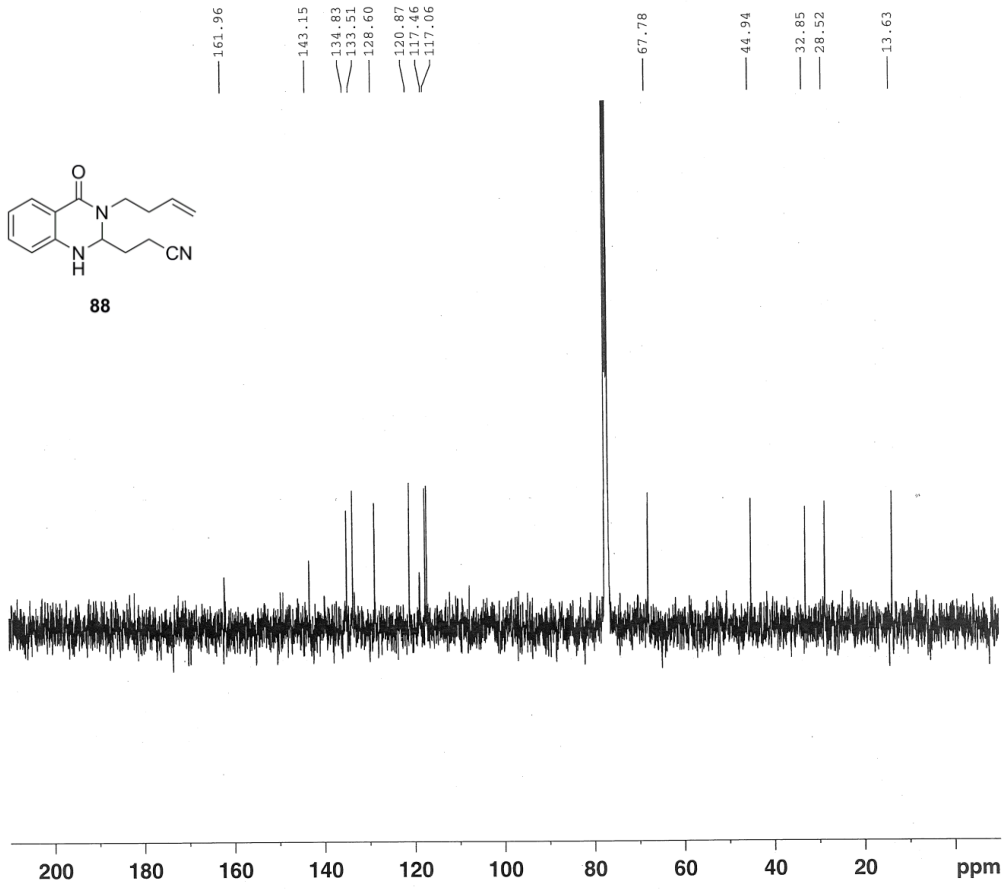
C13 LU1012 (14)



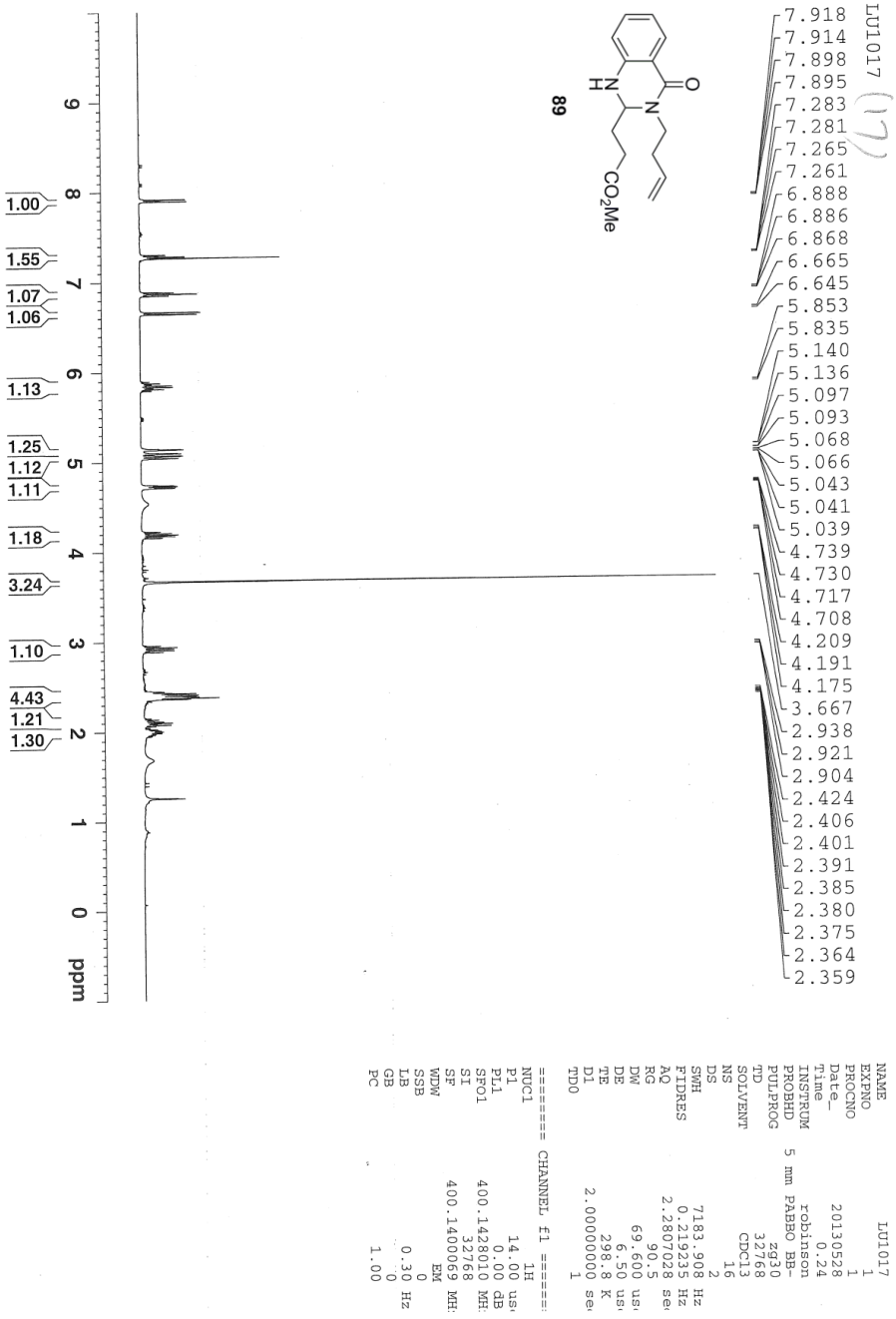
NAME	LU1012
EXPNO	3
PROCNO	1
Date_	20130413
Time	22.06
INSTRUM	robinson
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	600
DS	4
SWH	23980.814 Hz
FIDRES	0.365918 Hz
AQ	1.3664756 sec
RG	11585.2
DW	20.850 use
DE	6.50 use
TE	300.3 K
D1	1.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL 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

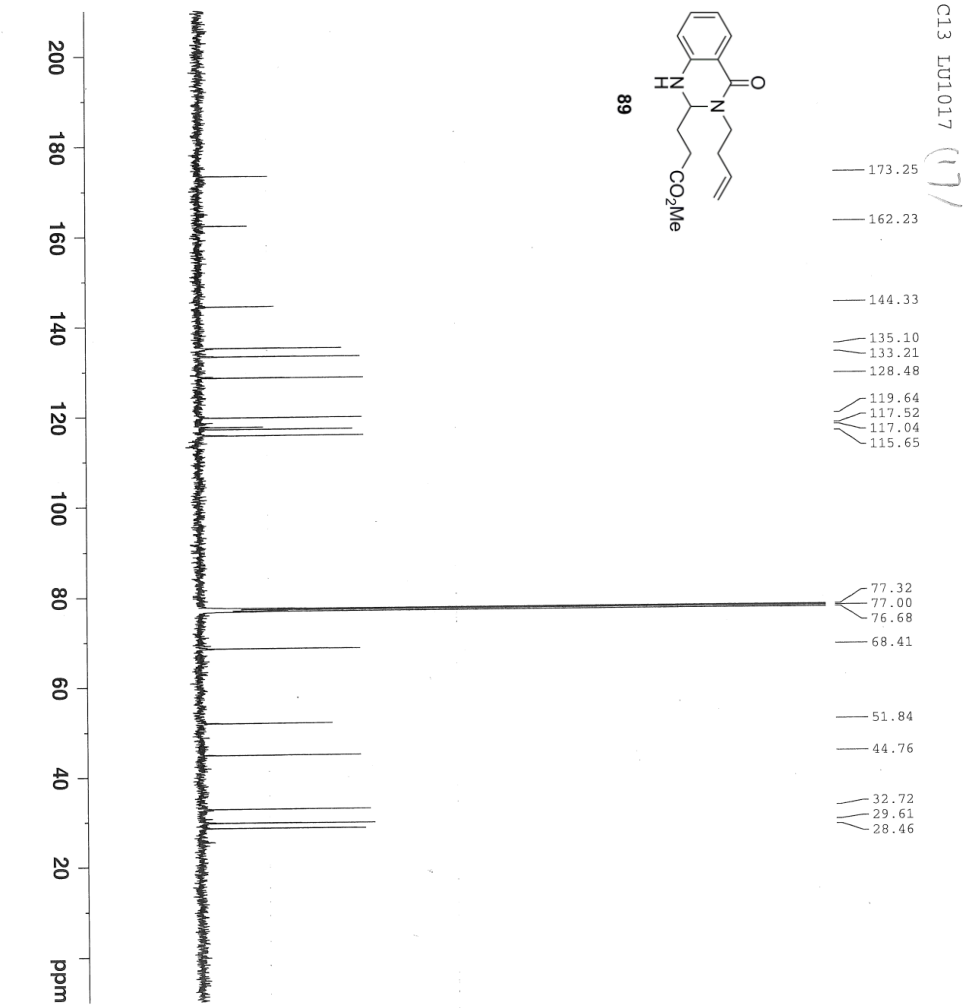

LU1016 (16)
7.931
7.928
7.912
7.909
7.346
7.343
7.326
7.325
7.308
7.304
7.265
6.950
6.948
6.930
6.912
6.910
6.780
6.760
5.844
5.827
5.802
5.146
5.142
5.103
5.099
5.085
5.060
4.763
4.754
4.739
4.730
4.233
4.216
4.199
4.182
4.164
2.933
2.916
2.899
2.163
2.159
2.148
2.124
1.952
88
1.00
1.05
1.12
1.05
1.17
2.46
1.16
1.26
1.08
4.24
1.20
1.22
ppm
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

C13 LU1016 (16)

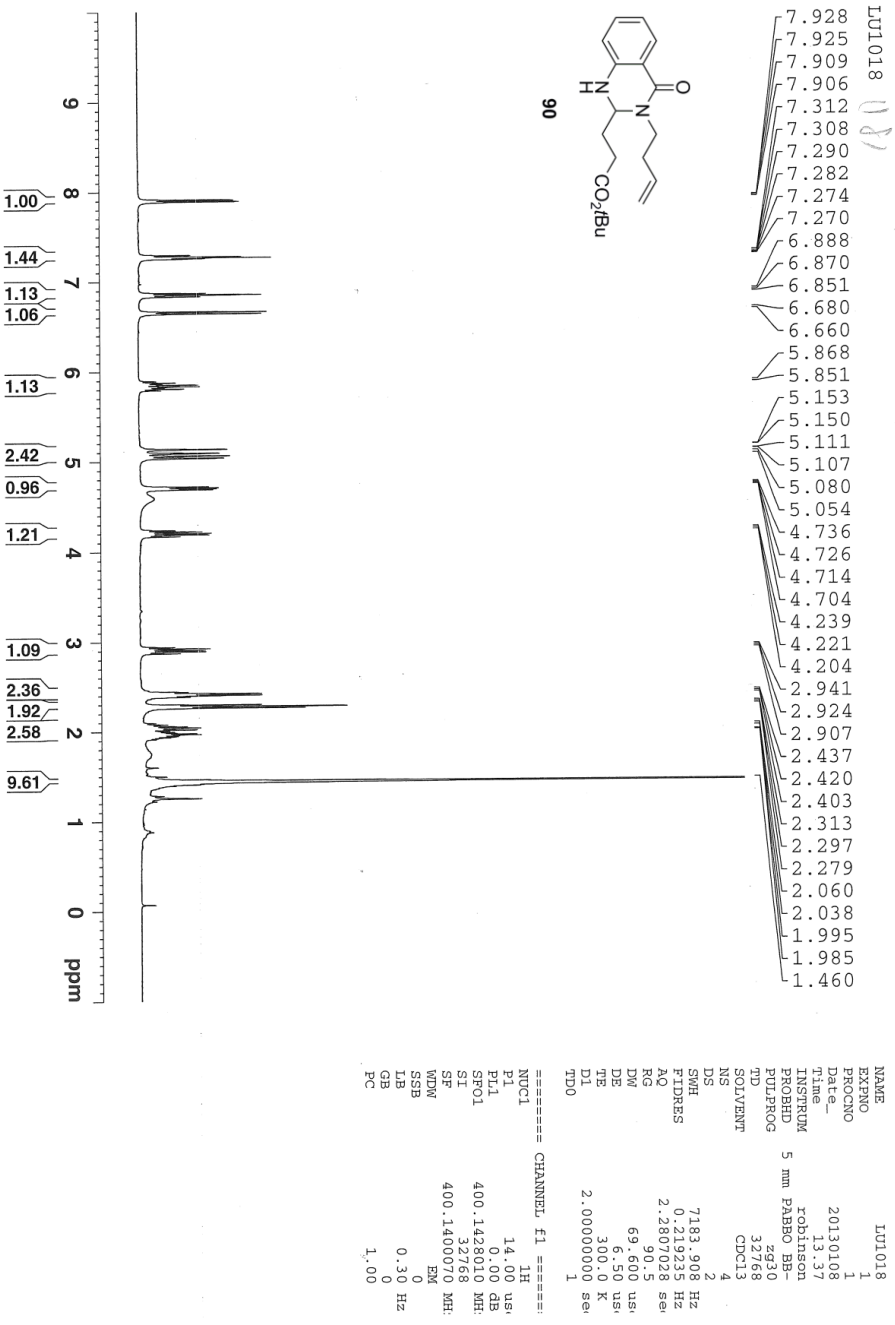


NAME	LU1016x
EXPNO	3
PROCNO	1
Date_	20130404
Time	22.58
INSTRUM	robinson
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	2000
DS	4
SWH	23980.814 Hz
FIDRES	0.365918 Hz
AQ	1.3664756 sec
RG	18390.4
DW	20.850 use
DE	6.50 use
TE	300.5 K
D1	1.00000000 sec
D11	0.03000000 sec
TD0	1
========	CHANNEL 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


LU1017 (17)
7.918
7.914
7.898
7.895
7.283
7.281
7.265
7.261
6.888
6.886
6.868
6.665
6.645
5.853
5.835
5.140
5.136
5.097
5.093
5.068
5.066
5.043
5.041
5.039
4.739
4.730
4.717
4.708
4.209
4.191
4.175
3.667
2.938
2.921
2.904
2.424
2.406
2.401
2.391
2.385
2.380
2.375
2.364
2.359
89
1.00
1.55
1.07
1.06
1.13
1.25
1.12
1.11
1.18
3.24
1.10
4.43
1.21
1.30
ppm
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

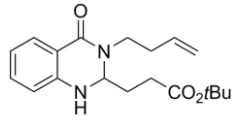



```
NAME                                    LU1017
EXPNO                                        3
PROCNO                                       1
Date_                               20130528
Time                                     1.05
INSTRUM                          robinson
PROBHD                 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 usec
DE                                       6.50 usec
TE                                     301.0 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                                  100.6152849 MHz
WDW                                        EM
SSB                                         0
LB                                       3.00 Hz
GB                                          0
PC                                       1.40
```

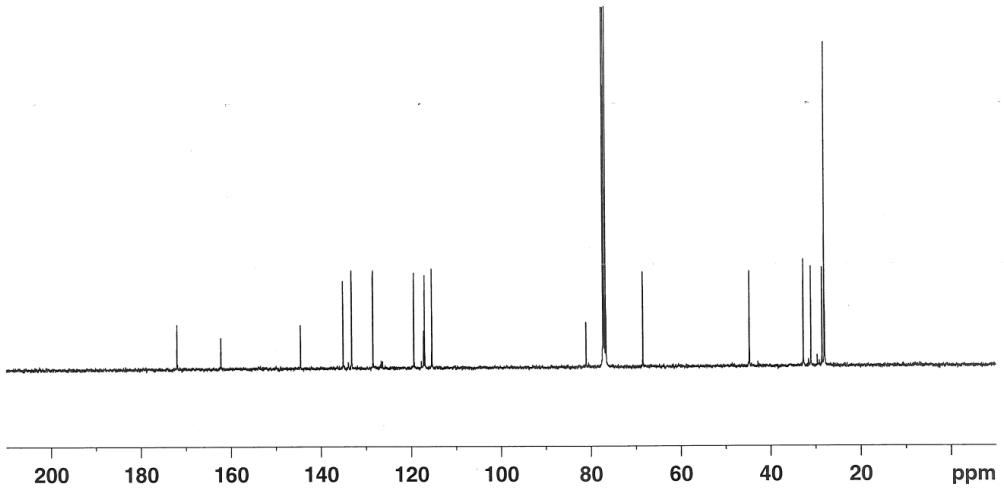

LU1018
7.928
7.925
7.909
7.906
7.312
7.308
7.290
7.282
7.274
7.270
6.888
6.870
6.851
6.680
6.660
5.868
5.851
5.153
5.150
5.111
5.107
5.080
5.054
4.736
4.726
4.714
4.704
4.239
4.221
4.204
2.941
2.924
2.907
2.437
2.420
2.403
2.313
2.297
2.279
2.060
2.038
1.995
1.985
1.460
90
CO2tBu
1.00
1.44
1.13
1.06
1.13
2.42
0.96
1.21
1.09
2.36
1.92
2.58
9.61
ppm
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)

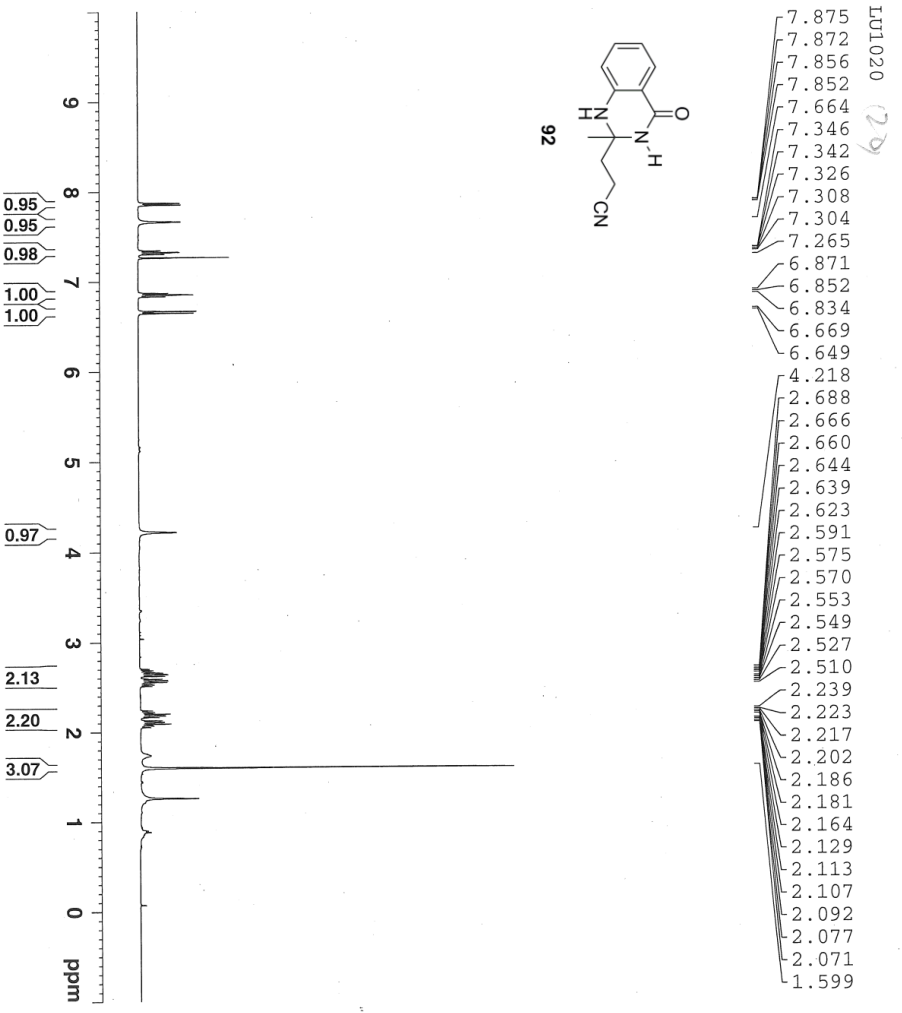
171.99
162.23
144.51
135.06
133.16
128.43
119.38
116.99
115.41
81.01
77.29
76.97
76.65
44.71
32.70
31.01
28.55
28.03



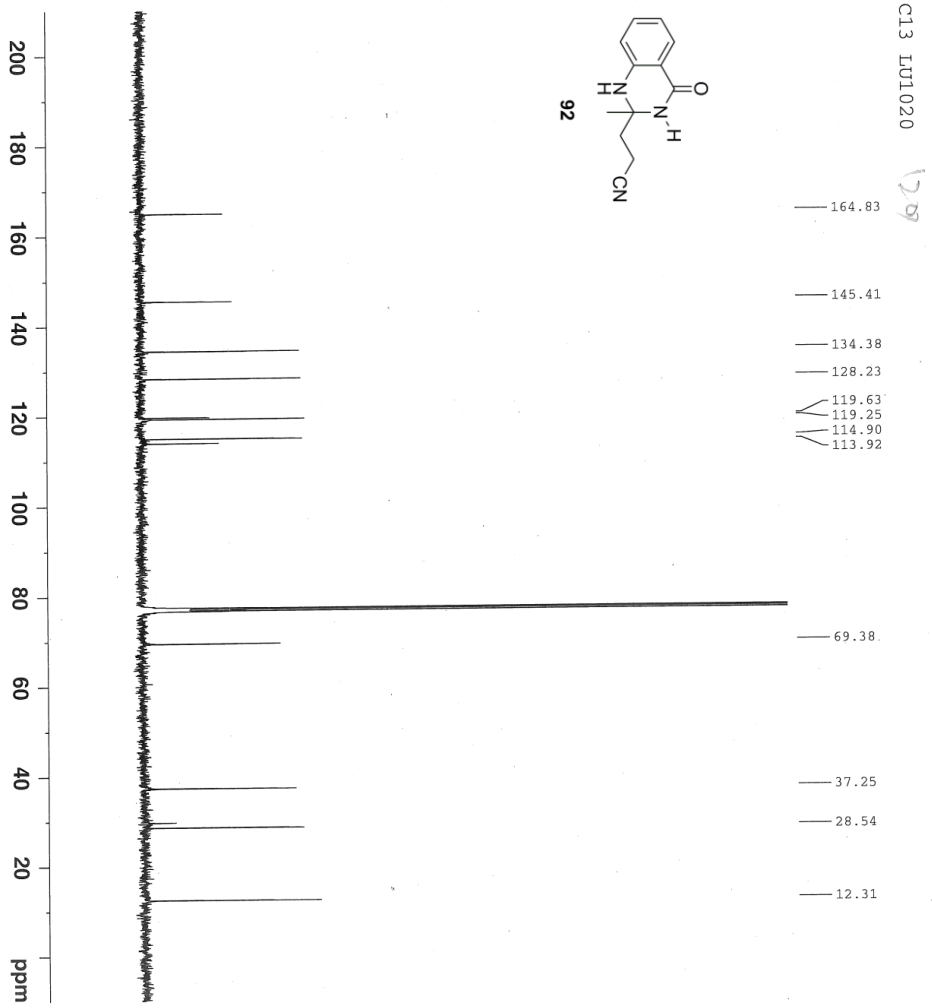
90



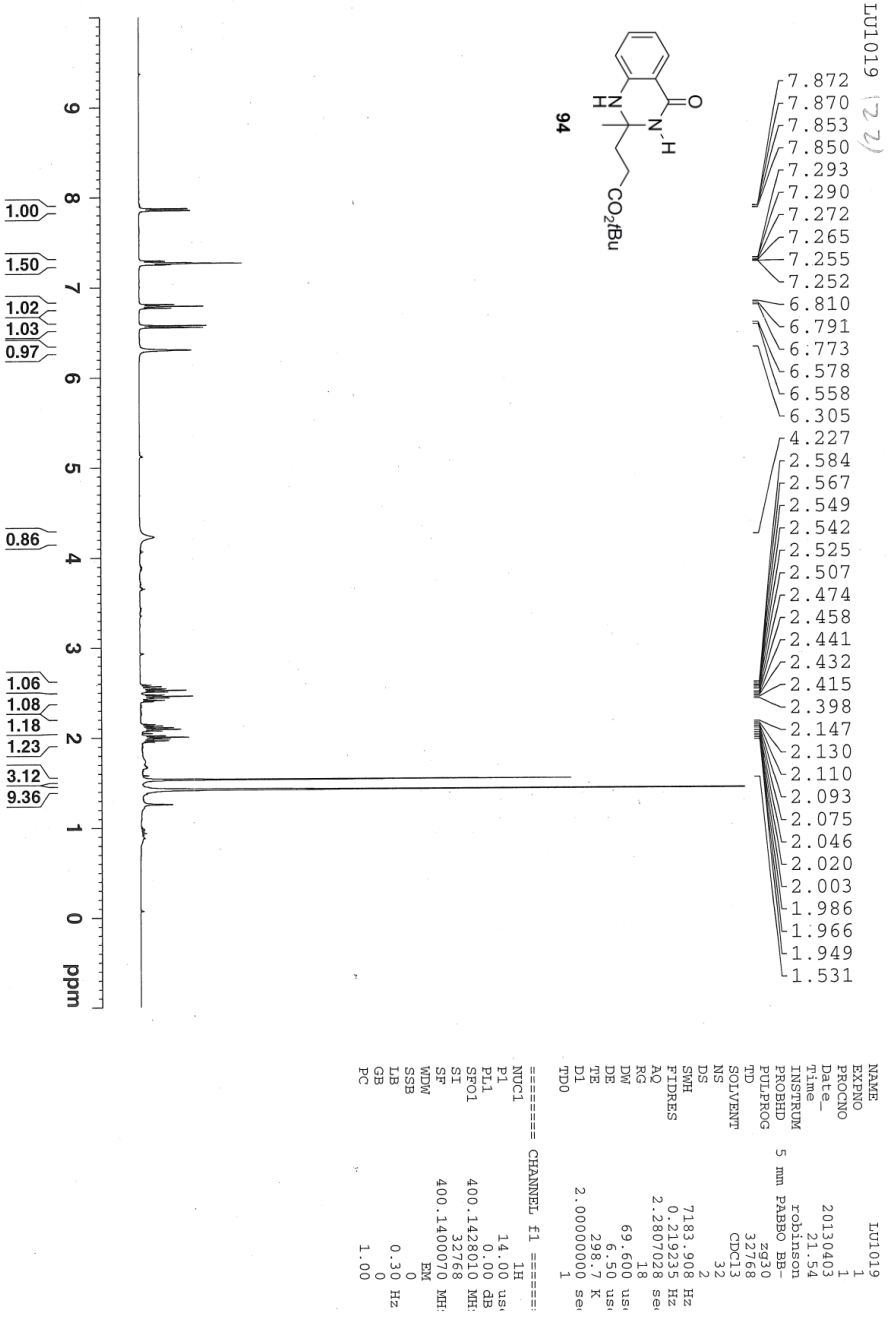
NAME	LU1018
EXPNO	3
PROCNO	1
Date_	20130227
Time	2.48
INSTRUM	robinson
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	3000
DS	4
SWH	23980.814 Hz
FIDRES	0.365918 Hz
AQ	1.3664756 sec
RG	18390.4
DW	20.850 use
DE	6.50 use
TE	299.1 K
D1	1.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL 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



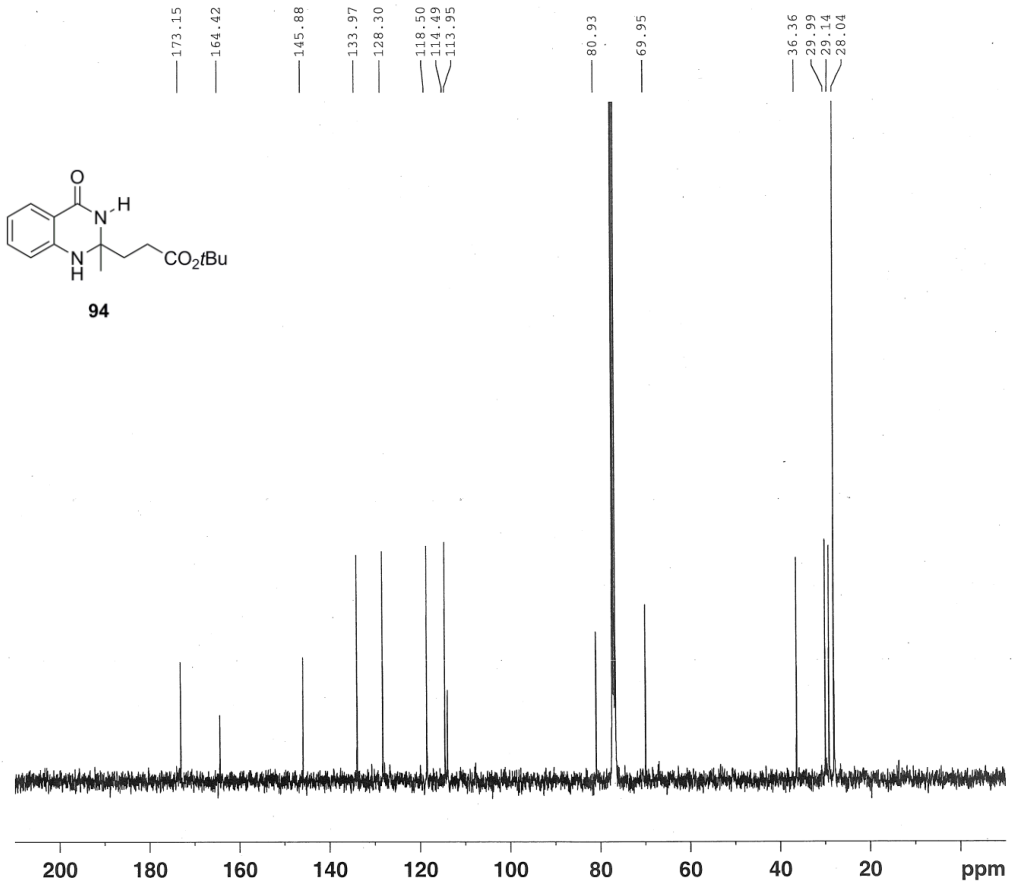

```
NAME                   LU1020
EXPNO                       1
PROCNO                      1
Date_              20130413
Time                   18.02
INSTRUM                robinson
PROBHD     5 mm PABBO BB-
PULPROG                zg30
TD                     32768
SOLVENT                CDCl3
NS                         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
```



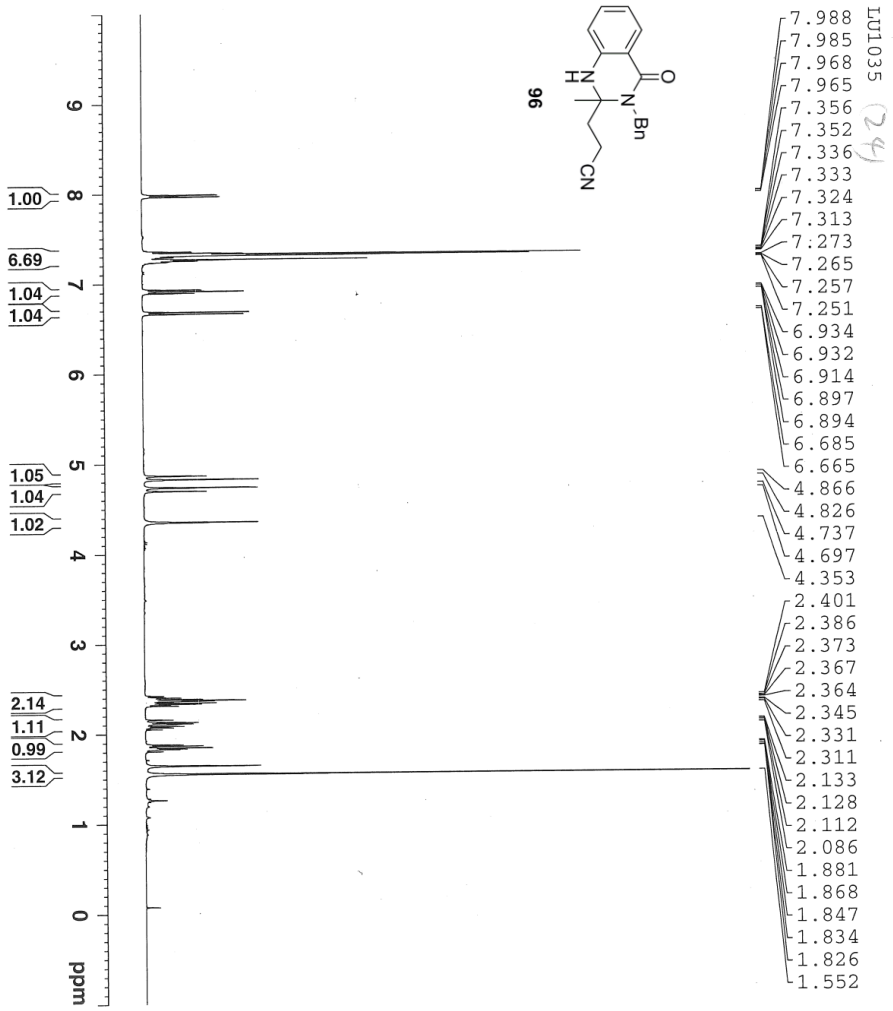

```
NAME                  LU1020
EXPNO                      3
PROCNO                     1
Date_              20130413
Time                   19.07
INSTRUM           robinson
PROBHD     5 mm PABBO BB-
PULPROG            zgpg30
TD                      65536
SOLVENT                 CDCl3
NS                       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
94
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)

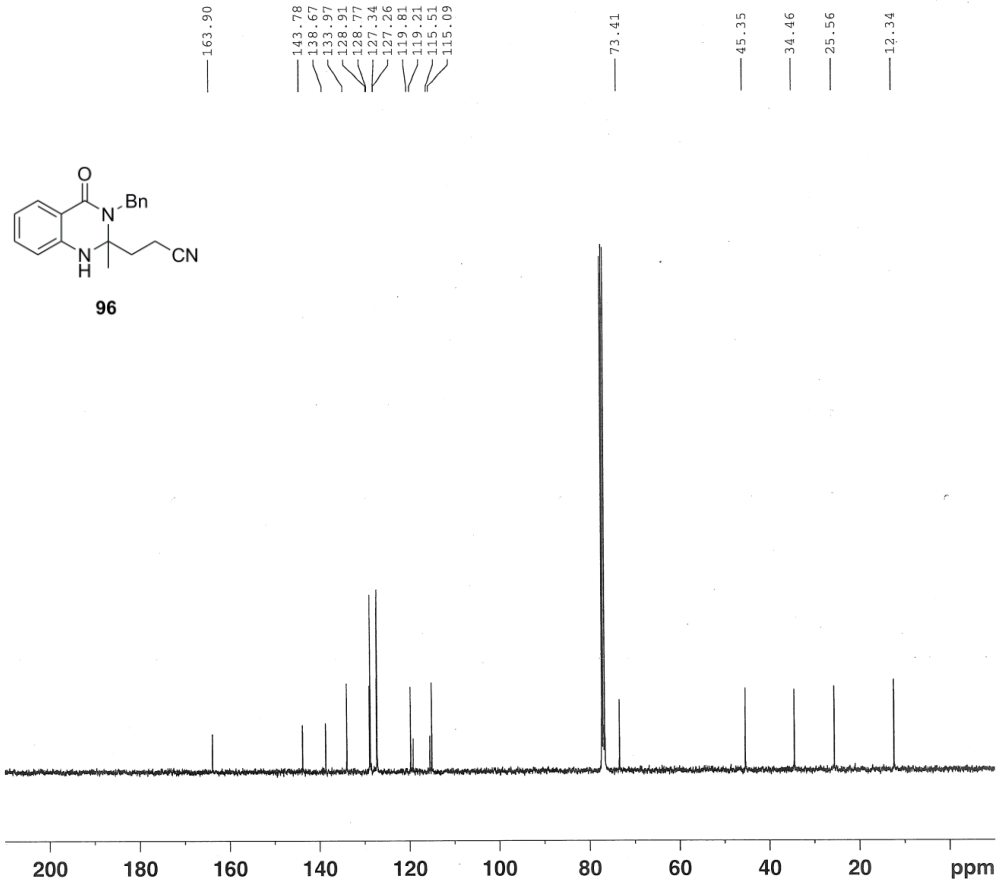


NAME	LU1019
EXPNO	3
PROCNO	1
Date_	20130403
Time	22.42
INSTRUM	robinson
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDC13
NS	1000
DS	4
SWH	23980.814 Hz
FIDRES	0.365918 Hz
AQ	1.3664756 sec
RG	16384
DW	20.850 use
DE	6.50 use
TE	300.4 K
D1	1.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL 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

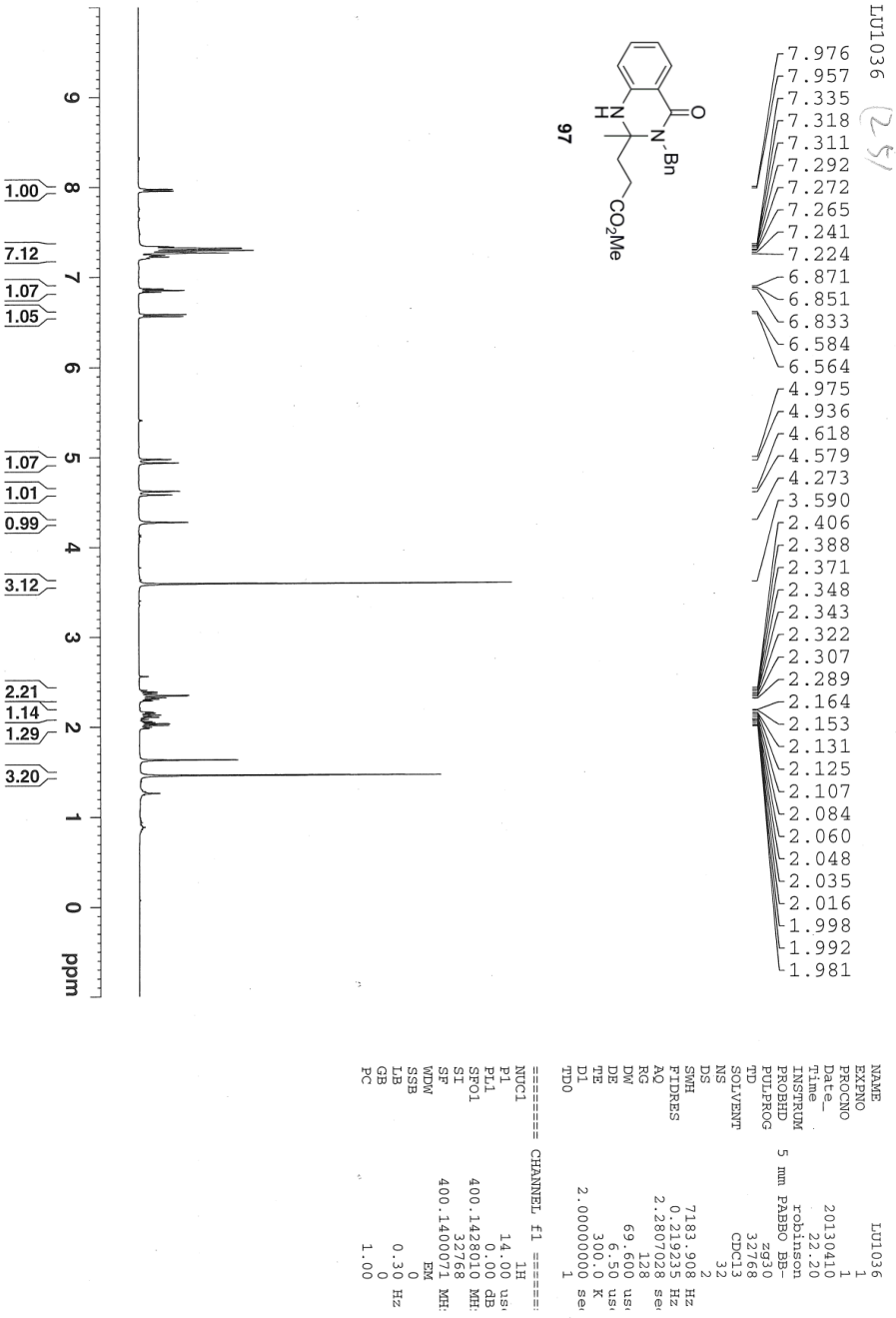



```
NAME                                    LU1035
EXPNO                                        1
PROCNO                                       1
Date_                               20130411
Time                                    21.53
INSTRUM                                robinson
PROBHD                 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
```

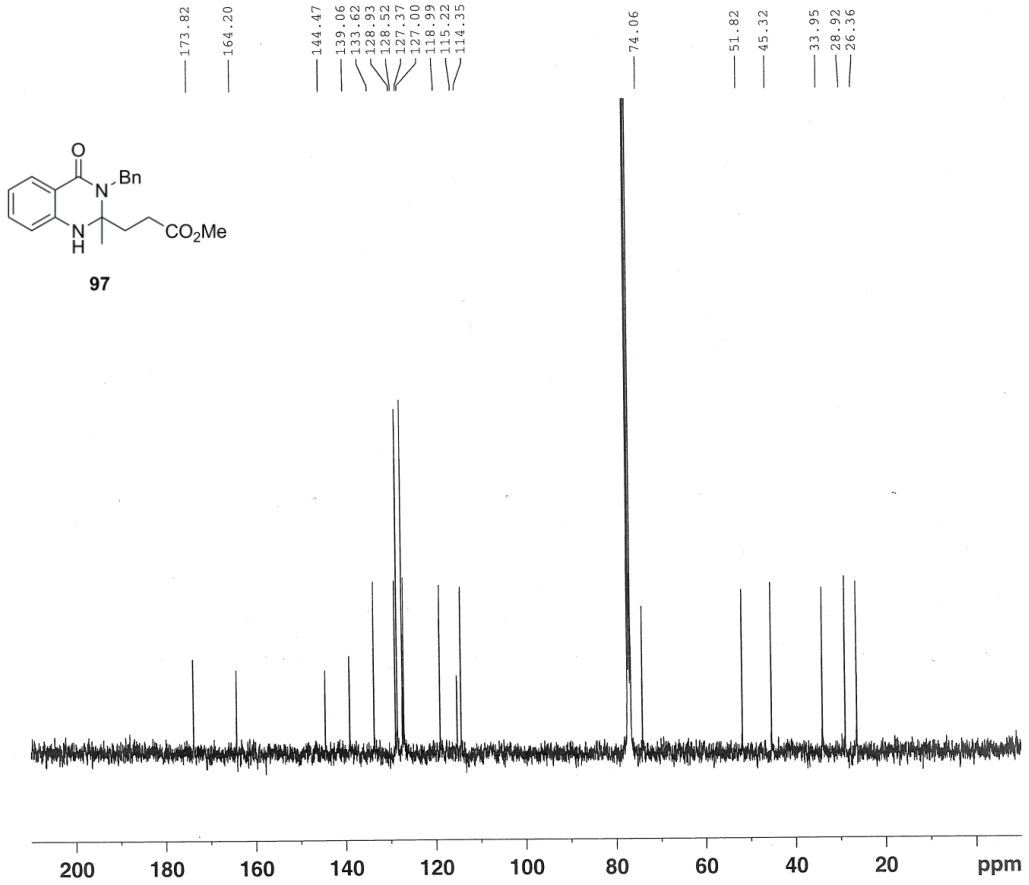
C13 LU1035 (24)



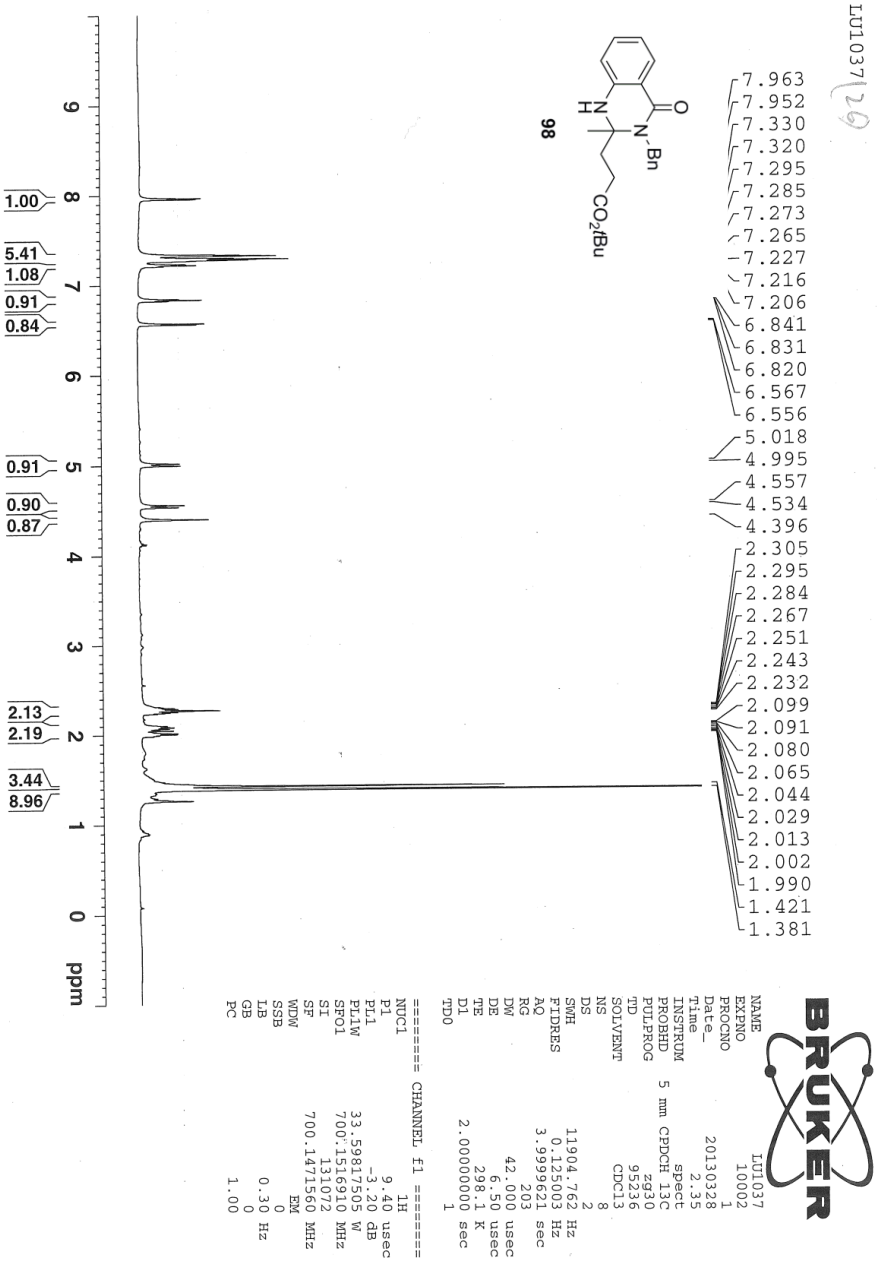
NAME	LU1035
EXPNO	3
PROCNO	1
Date_	20130412
Time	0.48
INSTRUM	robinson
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	1000
DS	4
SWH	23980.814 Hz
FIDRES	0.365918 Hz
AQ	1.3664756 sec
RG	11585.2
DW	20.850 use
DE	6.50 use
TE	300.2 K
D1	1.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL 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
97
1.00
7.12
1.07
1.05
1.07
1.01
0.99
3.12
2.21
1.14
1.29
3.20
ppm
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

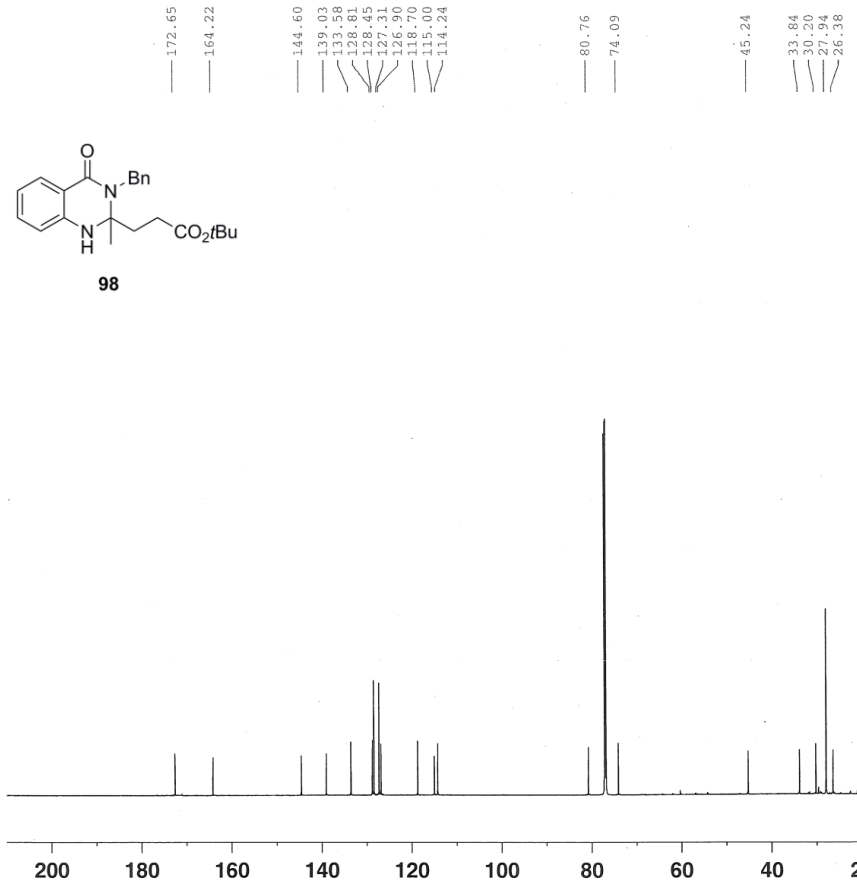
C13 LU1036 (25)



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
98
Bn
CO2tBu
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
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



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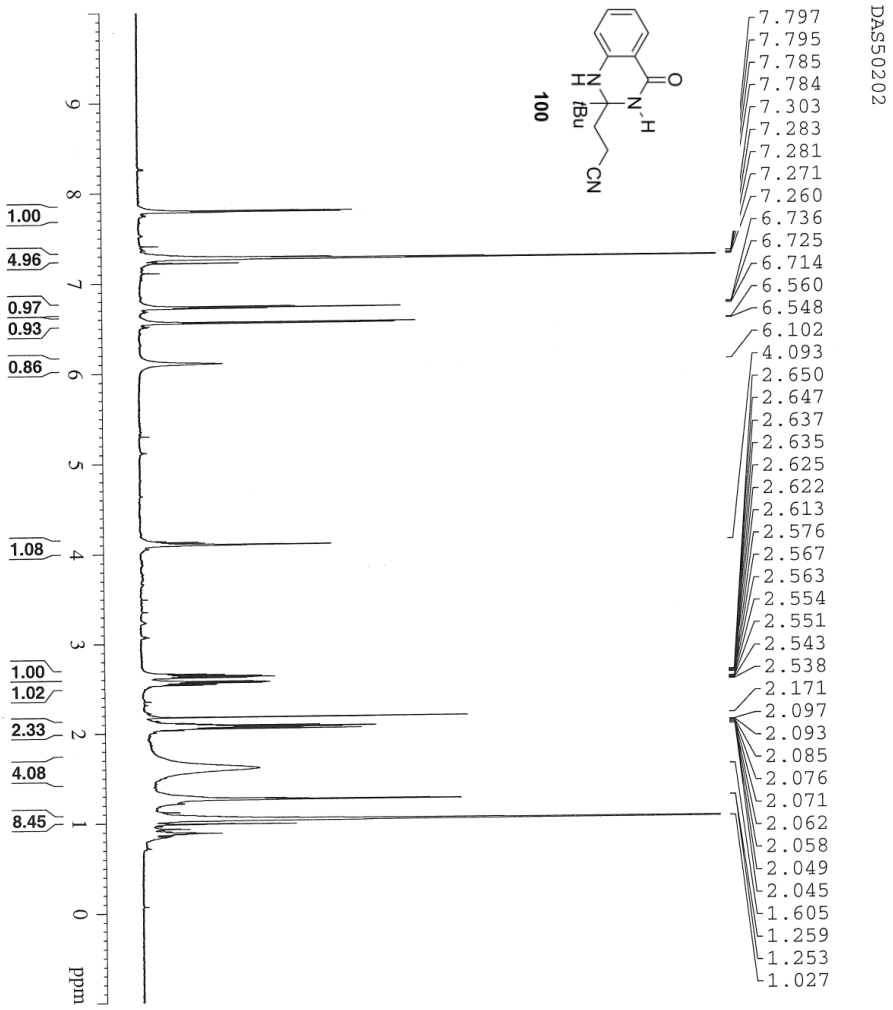
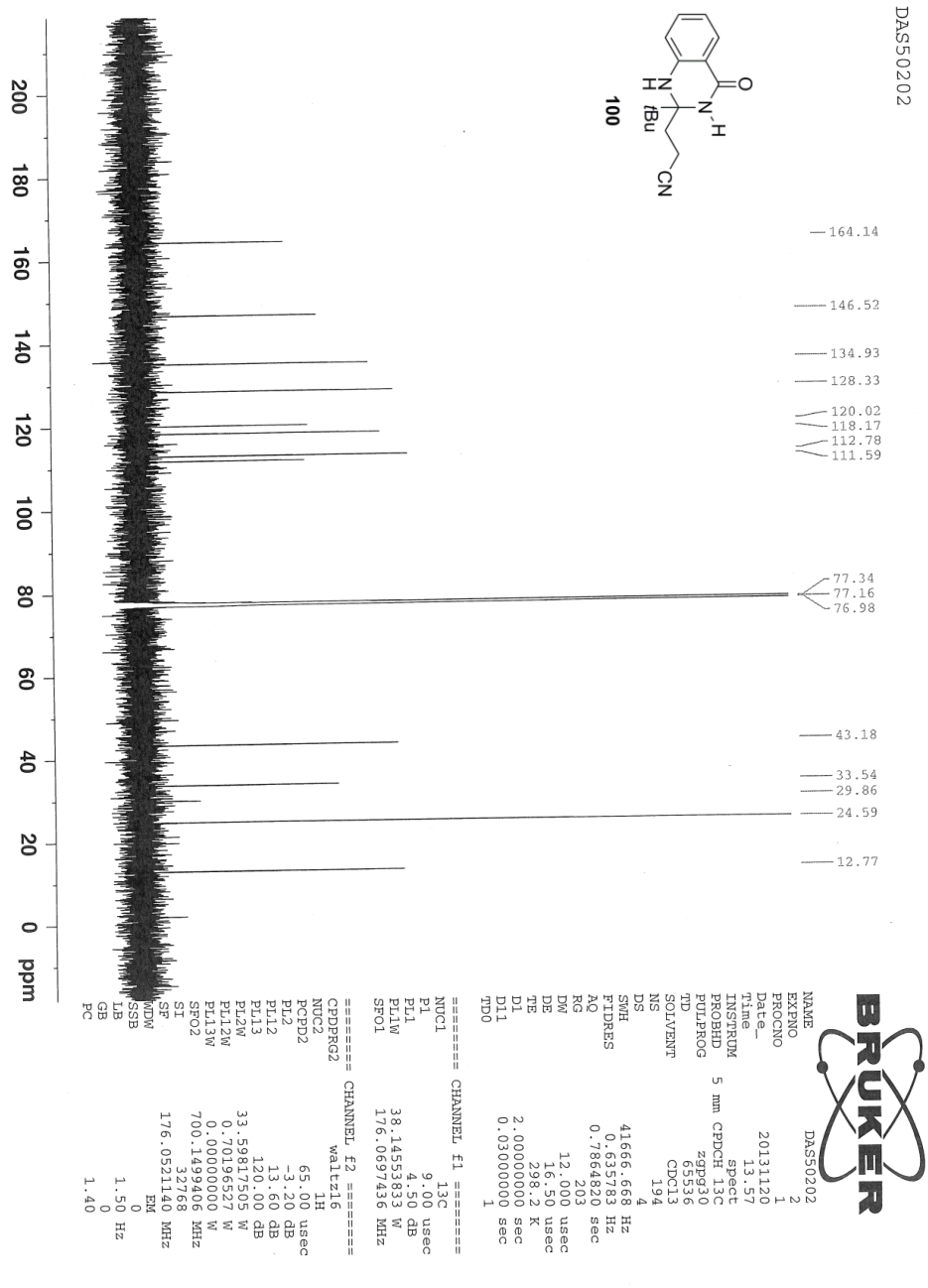
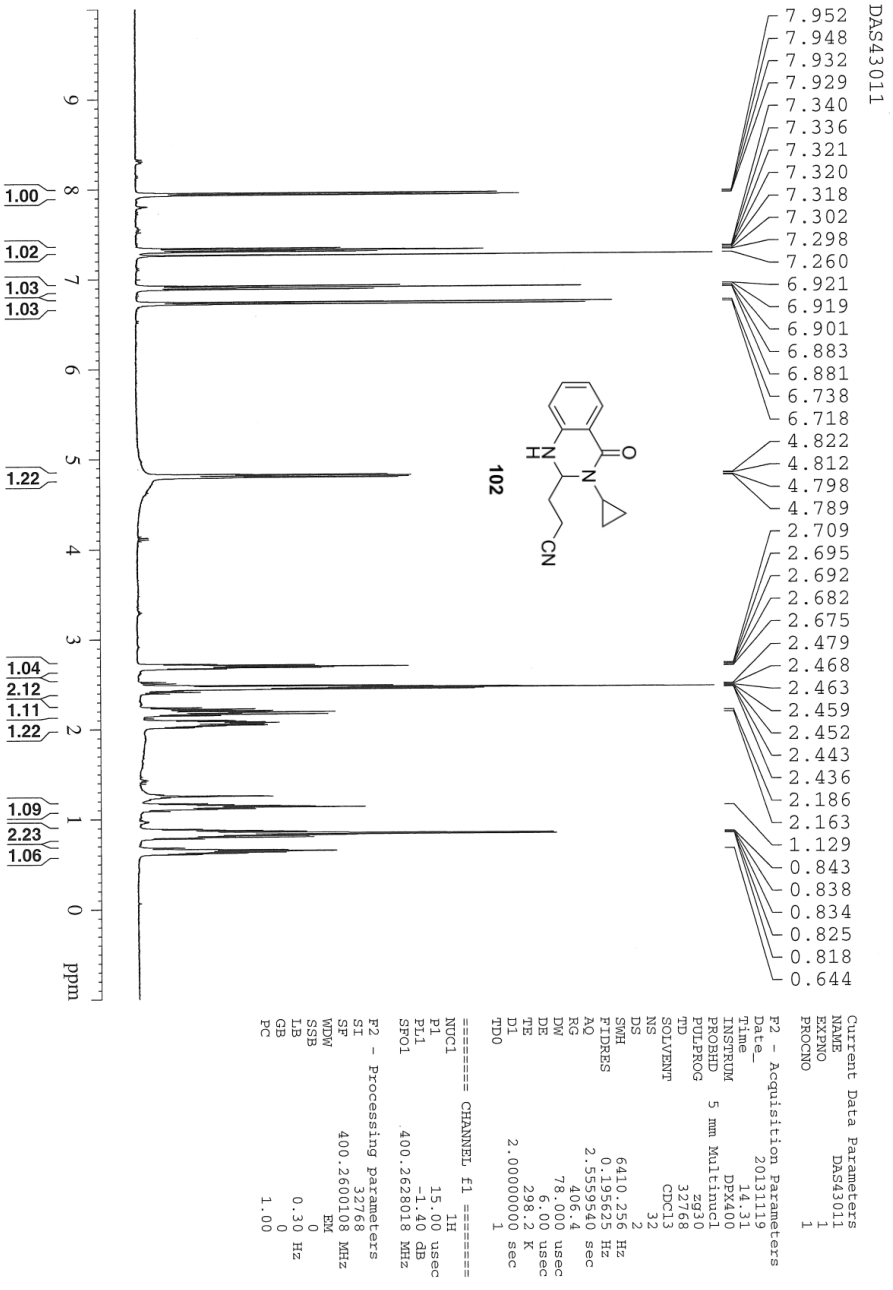
BRUKER

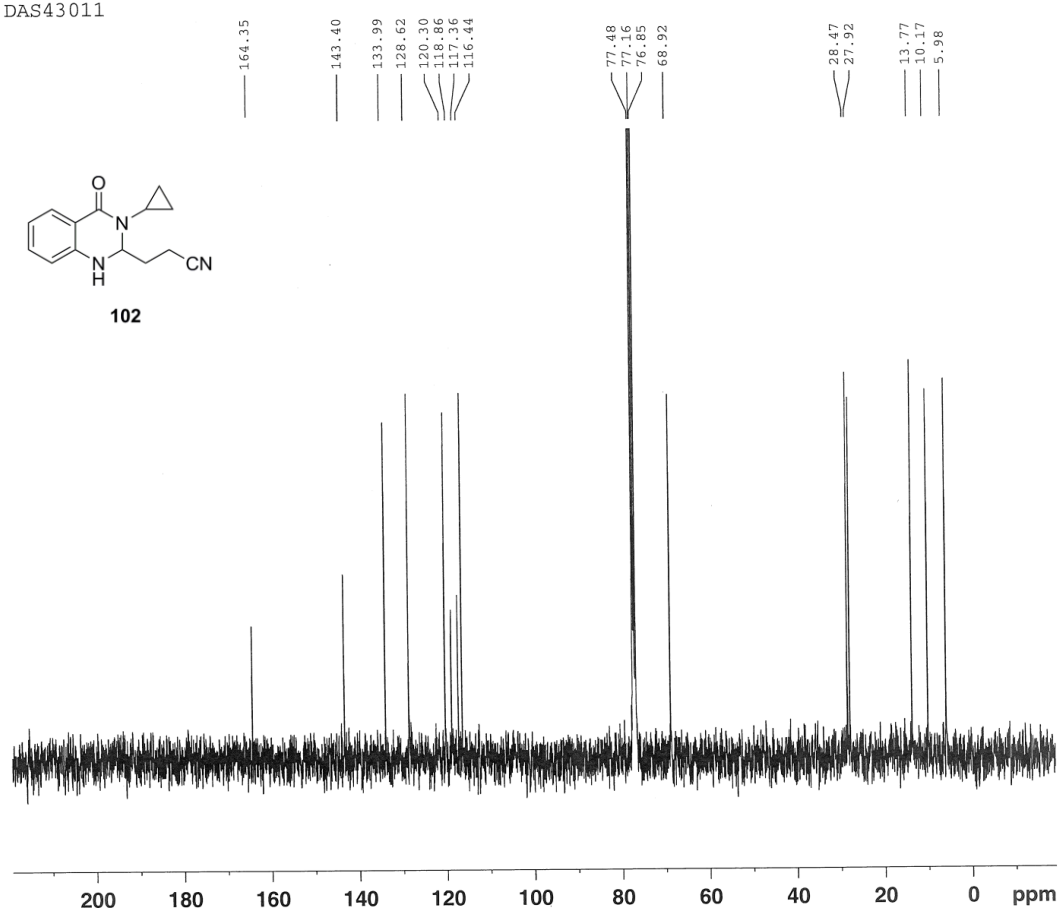
NAME	LU1037
EXPNO	3
PROCNO	1
Date_	20130327
Time	22.19
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	65536
SOLVENT	CDC13
NS	500
DS	4
SWH	41666.668 Hz
FIDRES	0.635783 Hz
AQ	0.7864820 sec
RG	203
DW	12.000 usec
DE	16.50 usec
TE	298.1 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL 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
100
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
100
164.14
146.52
134.93
128.33
120.02
118.17
112.78
111.59
77.34
77.16
76.98
43.18
33.54
29.86
24.59
12.77
200
180
160
140
120
100
80
60
40
20
0
ppm
BRUKER
NAME DAS50202
EXPNO 2
PROCNO 1
Date_ 20131120
Time_ 13.57
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 194
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864820 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
102
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

DAS43011



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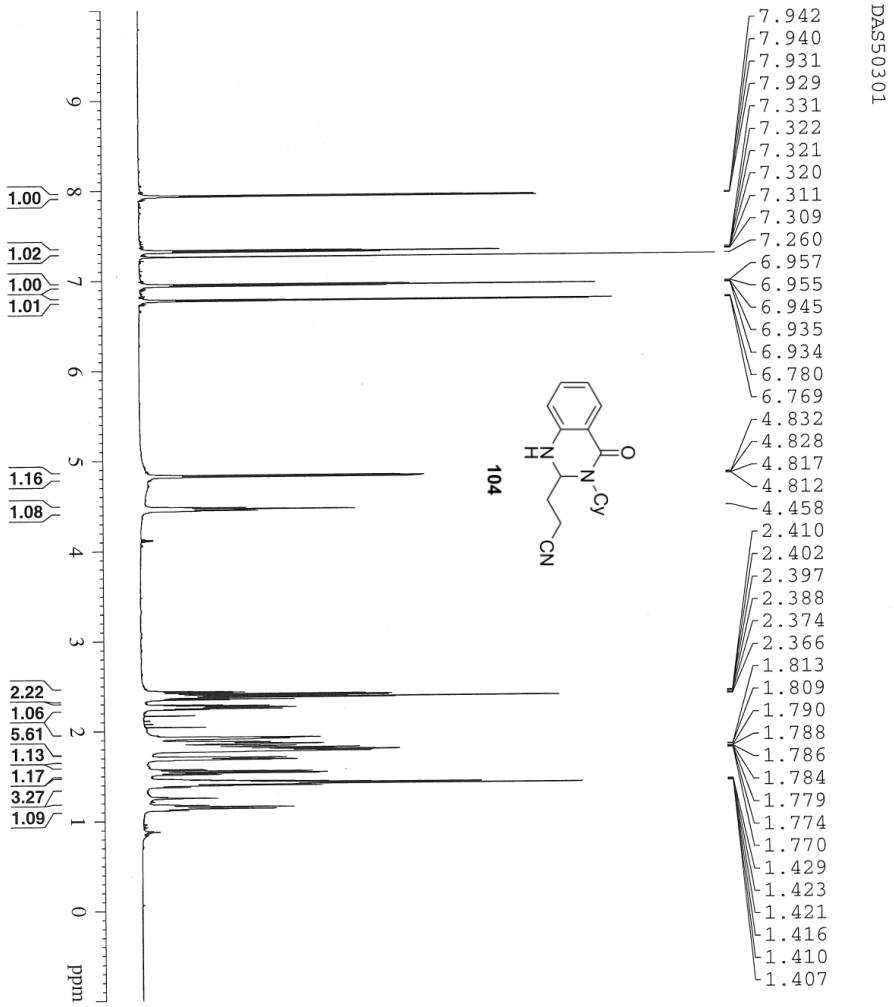
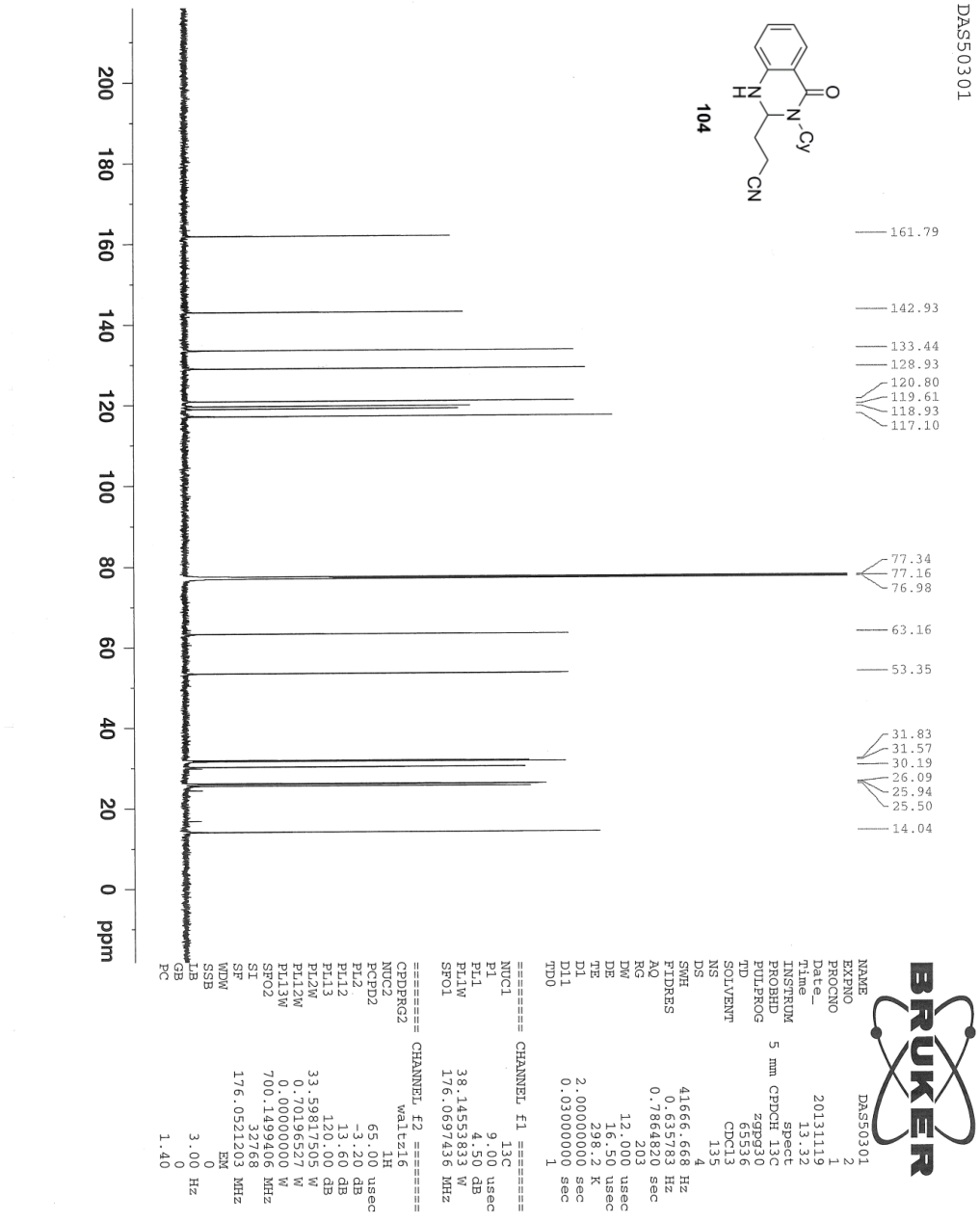
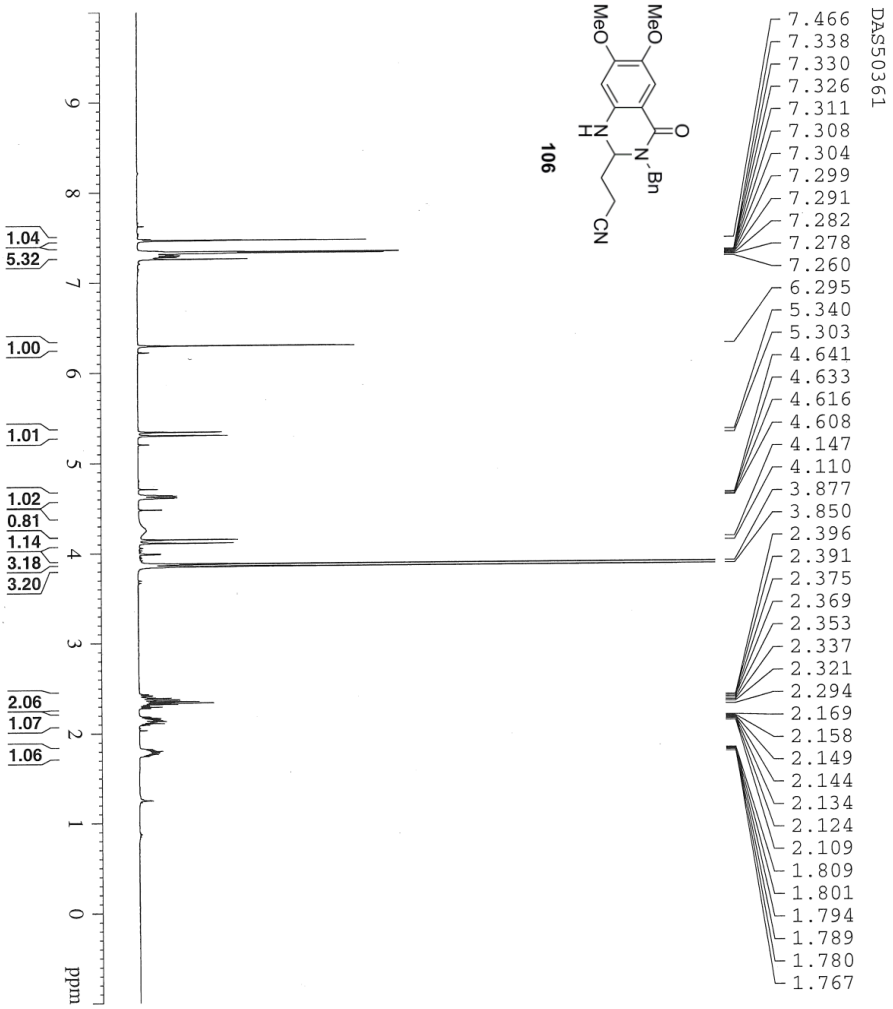
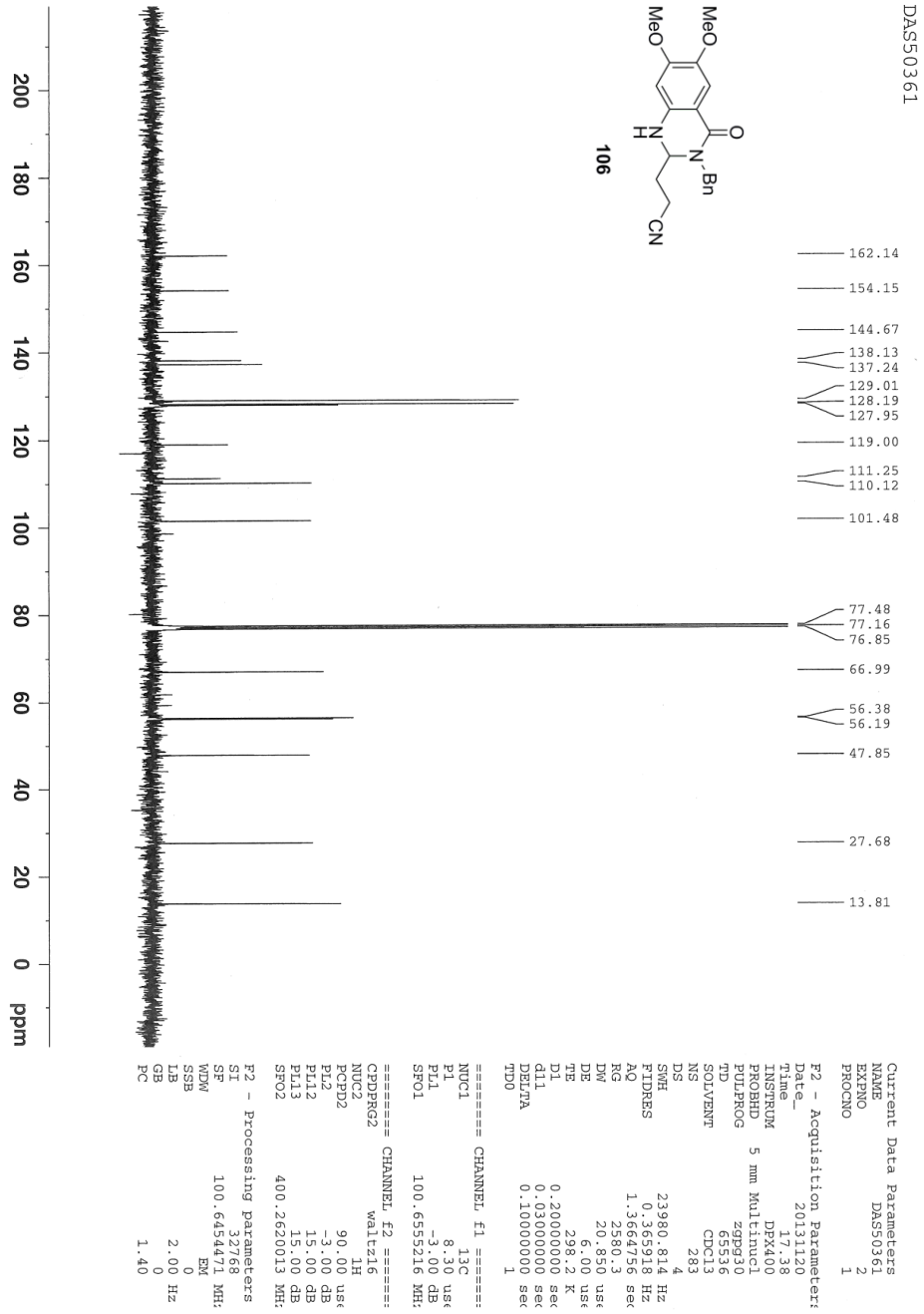
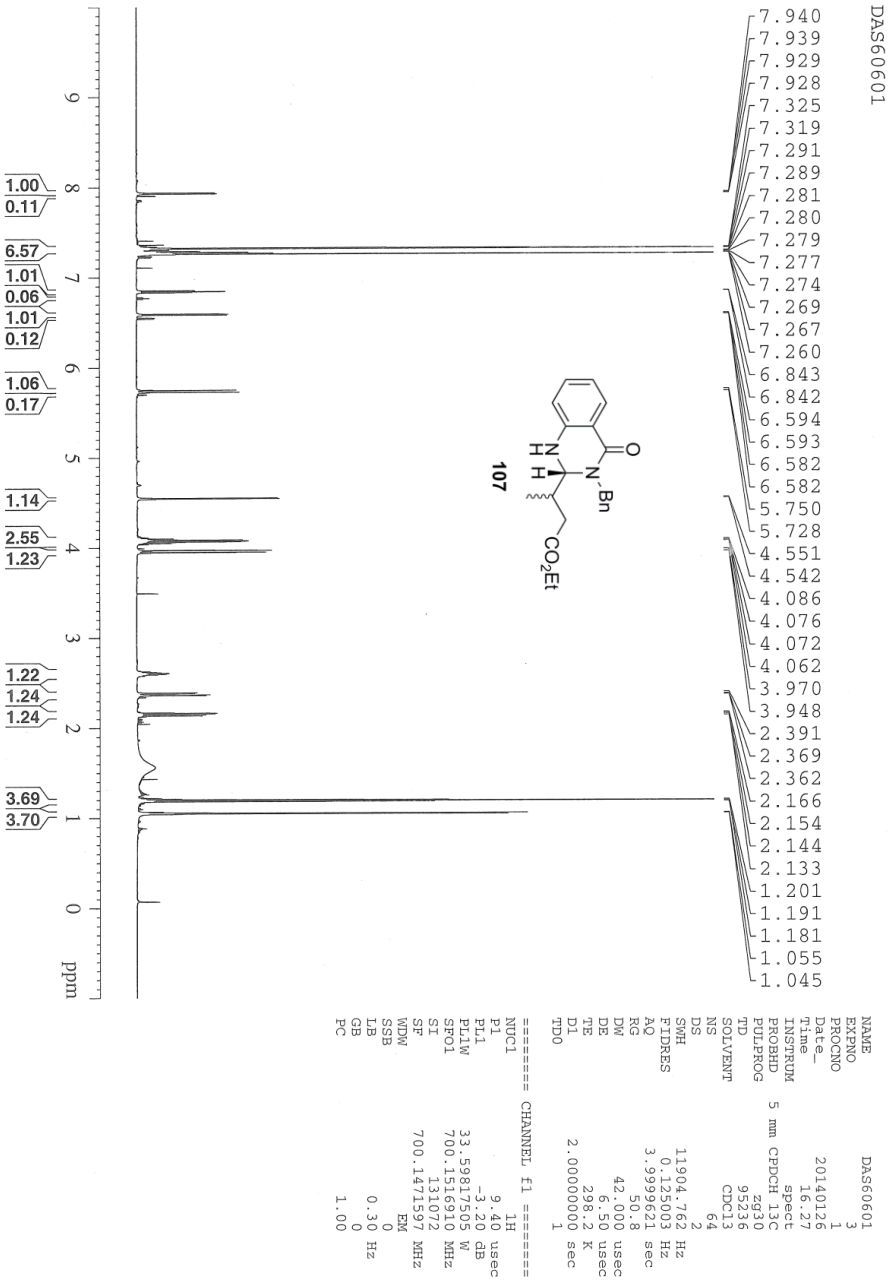
```
Current Data Parameters
NAME                  DAS43011
EXPNO                        2
PROCNO                       1

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 use
DE                    6.00 use
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 use
PL1                  -3.00 dB
SFO1           100.6555216 MHz

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

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

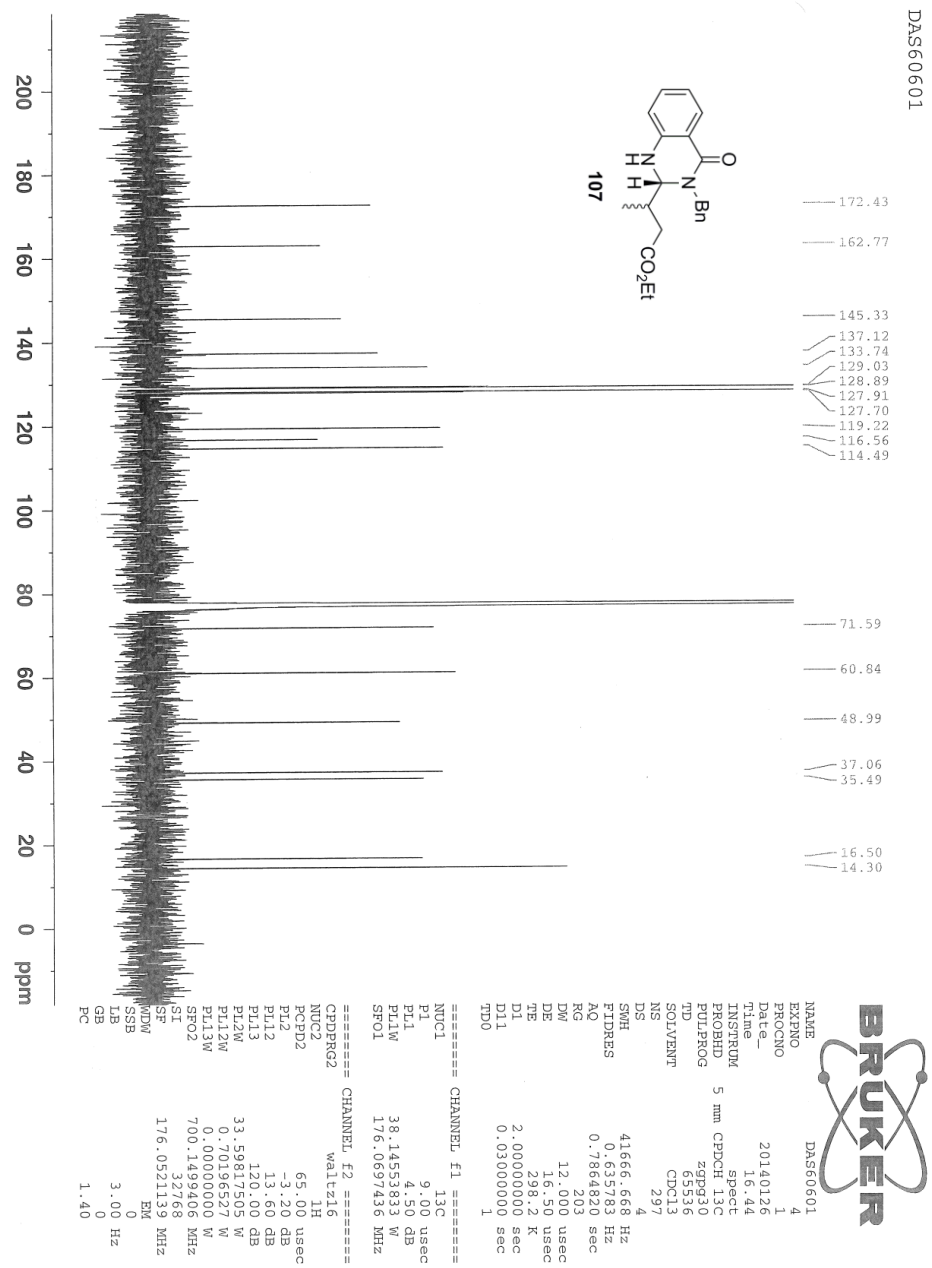

DAS50301
7.942
7.940
7.931
7.929
7.331
7.322
7.321
7.320
7.311
7.309
7.260
6.957
6.955
6.945
6.935
6.934
6.780
6.769
4.832
4.828
4.817
4.812
4.458
2.410
2.402
2.397
2.388
2.374
2.366
1.813
1.809
1.790
1.788
1.786
1.784
1.779
1.774
1.770
1.429
1.423
1.421
1.416
1.410
1.407
104
1.00
1.02
1.00
1.01
1.16
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

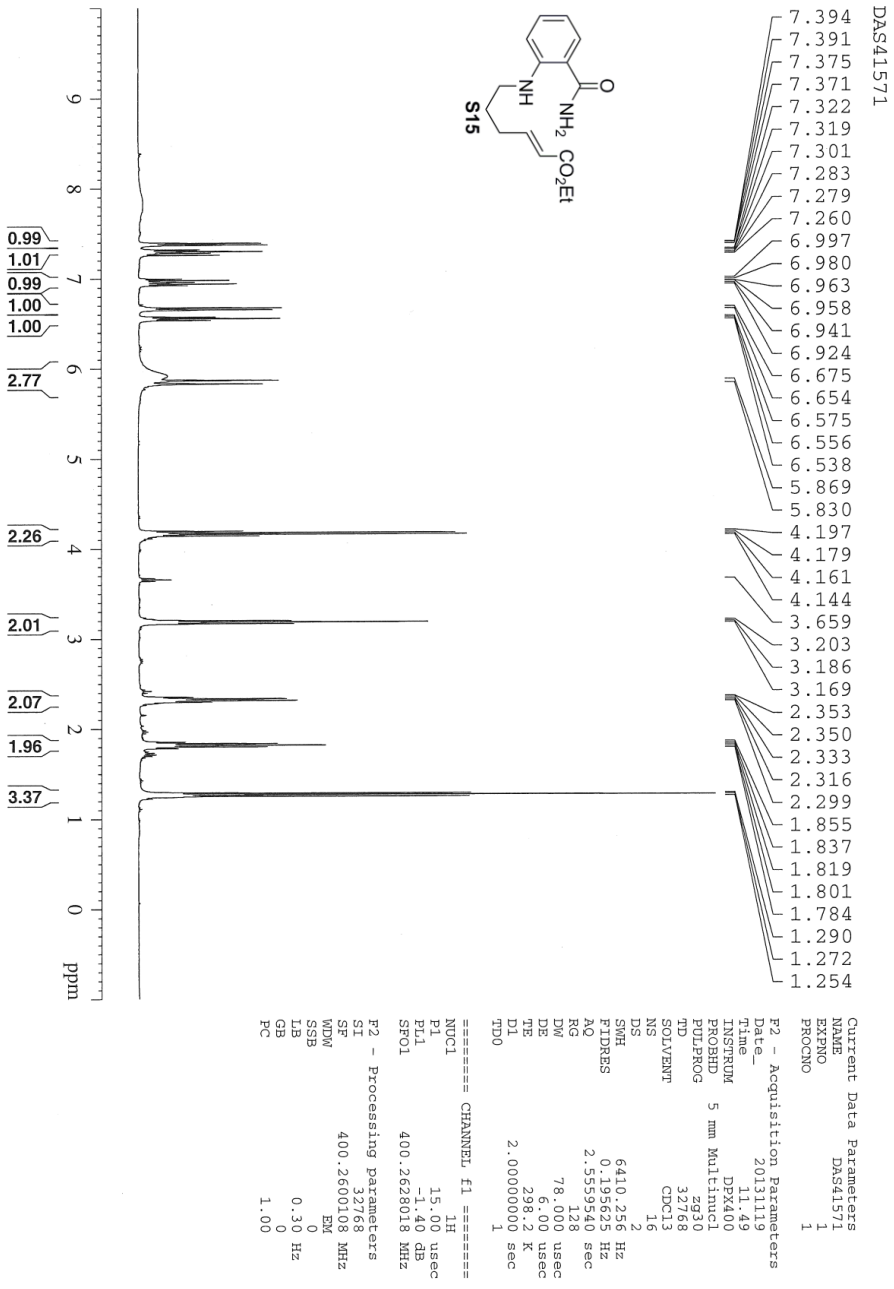

DAS50301
104
161.79
142.93
133.44
128.93
120.80
119.61
118.93
117.10
77.34
77.16
76.98
63.16
53.35
31.83
31.57
30.19
26.09
25.94
25.50
14.04
200
180
160
140
120
100
80
60
40
20
0
ppm
BRUKER
NAME DAS50301
EXPNO 2
PROCNO 1
Date_ 20131119
Time 13.32
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 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

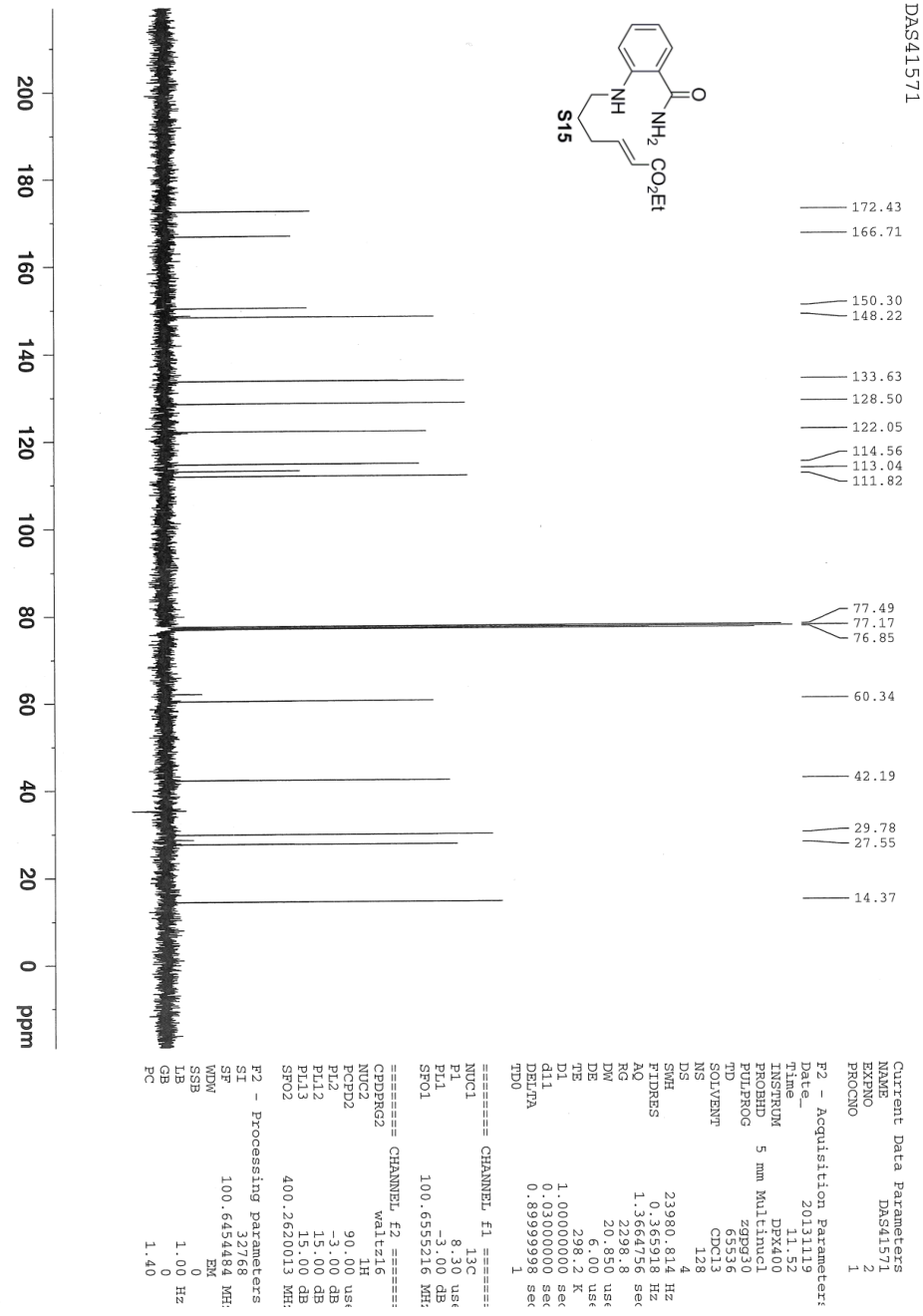

DAS50361
7.466
7.338
7.330
7.326
7.311
7.308
7.304
7.299
7.291
7.282
7.278
7.260
6.295
5.340
5.303
4.641
4.633
4.616
4.608
4.147
4.110
3.877
3.850
2.396
2.391
2.375
2.369
2.353
2.337
2.321
2.294
2.169
2.158
2.149
2.144
2.134
2.124
2.109
1.809
1.801
1.794
1.789
1.780
1.767
MeO
MeO
N
H
O
N
Bn
CN
106
1.04
5.32
1.00
1.01
1.02
0.81
1.14
3.18
3.20
2.06
1.07
1.06
ppm
Current Data Parameters
NAME DAS50361
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20131120
Time 17.30
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 228.11
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 400.2600111 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00


DAS50361
MeO
MeO
N
H
O
N
Bn
CN
106
162.14
154.15
144.67
138.13
137.24
129.01
128.19
127.95
119.00
111.25
110.12
101.48
77.48
77.16
76.85
66.99
56.38
56.19
47.85
27.68
13.81
200
180
160
140
120
100
80
60
40
20
0
ppm
Current Data Parameters
NAME DAS50361
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20131120
Time 17.38
INSTRUM DPX400
PROBHD 5 mm Multinucl
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 283
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 se
RG 2580.3
DW 20.850 us
DE 6.00 us
TE 298.2 K
D1 0.20000000 se
D11 0.03000000 se
DELTA 0.10000000 se
TD0 1
======== CHANNEL f1 ======
NUC1 13C
P1 8.30 us
PL1 -3.00 dB
SFO1 100.6555216 MH
======== CHANNEL f2 ======
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 us
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2620013 MH
F2 - Processing parameters
SI 32768
SF 100.6454471 MH
WDW EM
SSB 0
LB 2.00 Hz
GB 0
PC 1.40

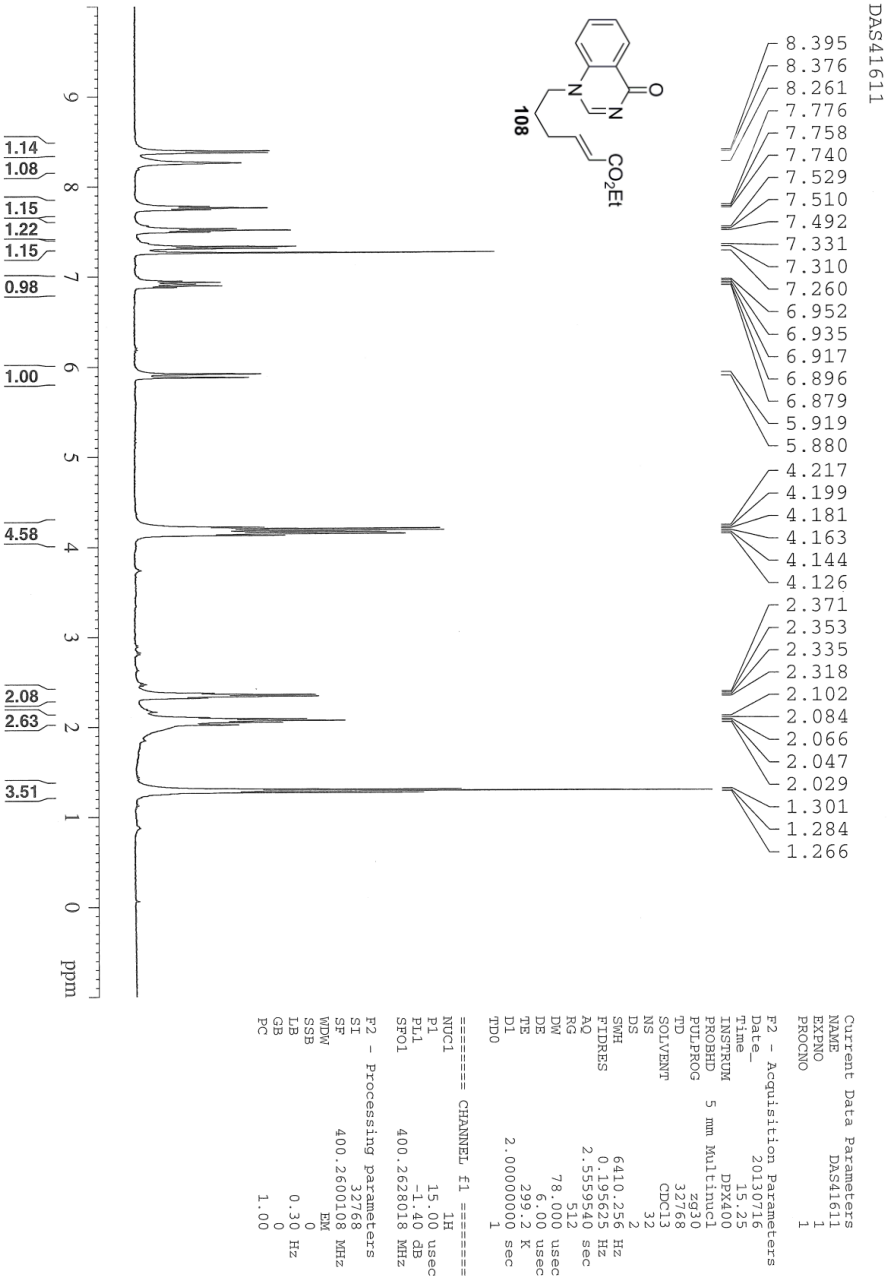

DAS60601
7.940
7.939
7.929
7.928
7.325
7.319
7.291
7.289
7.281
7.280
7.279
7.277
7.274
7.269
7.267
7.260
6.843
6.842
6.594
6.593
6.582
6.582
5.750
5.728
4.551
4.542
4.086
4.076
4.072
4.062
3.970
3.948
2.391
2.369
2.362
2.166
2.154
2.144
2.133
1.201
1.191
1.181
1.055
1.045
107
Bn
CO2Et
1.00
0.11
6.57
1.01
0.06
1.01
0.12
1.06
0.17
1.14
2.55
1.23
1.22
1.24
1.24
3.69
3.70
ppm
NAME DAS60601
EXPNO 3
PROCNO 1
Date_ 20140126
Time_ 16.27
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 64
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 50.8
DW 42.000 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471597 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

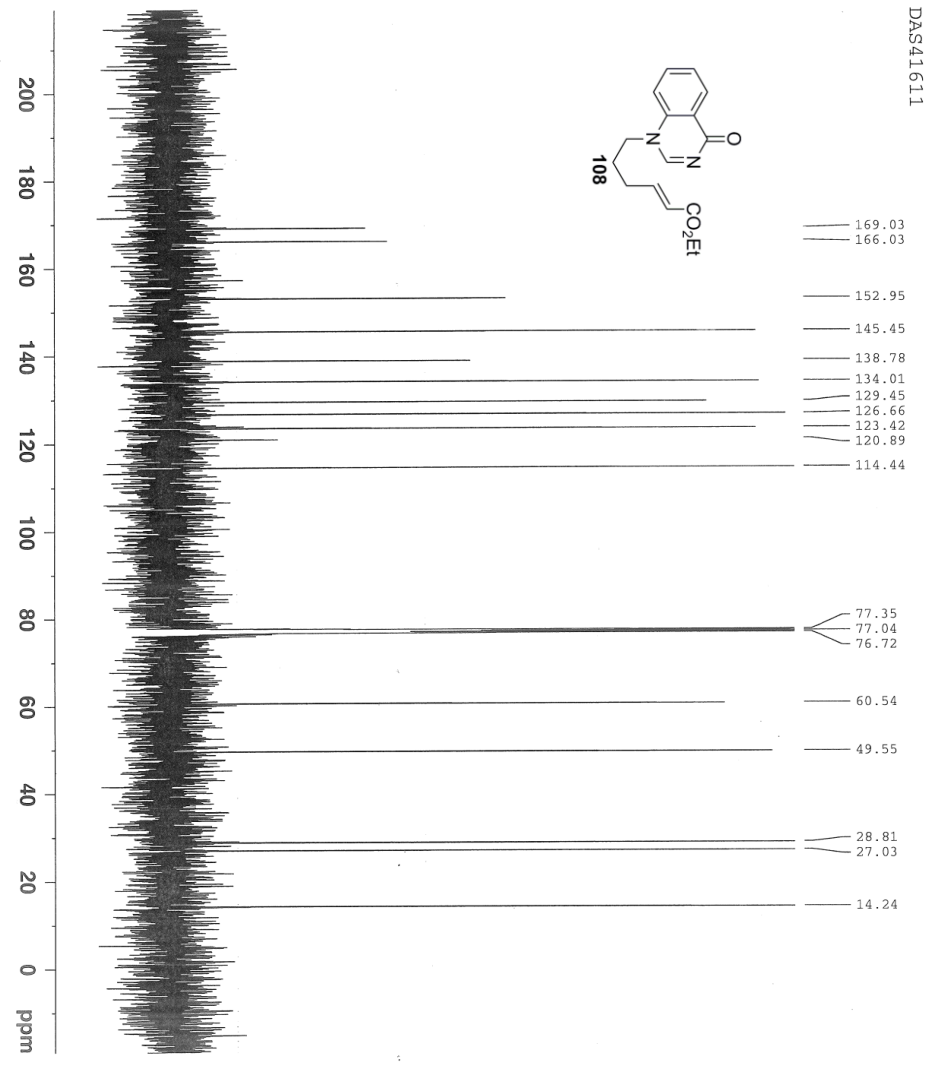

DAS60601
107
172.43
162.77
145.33
137.12
133.74
129.03
128.89
127.91
127.70
119.22
116.56
114.49
71.59
60.84
48.99
37.06
35.49
16.50
14.30
200
180
160
140
120
100
80
60
40
20
0
ppm


DAS41571
7.394
7.391
7.375
7.371
7.322
7.319
7.301
7.283
7.279
7.260
6.997
6.980
6.963
6.958
6.941
6.924
6.675
6.654
6.575
6.556
6.538
5.869
5.830
4.197
4.179
4.161
4.144
3.659
3.203
3.186
3.169
2.353
2.350
2.333
2.316
2.299
1.855
1.837
1.819
1.801
1.784
1.290
1.272
1.254
S15
NH
NH2
CO2Et
0.99
1.01
0.99
1.00
1.00
2.77
2.26
2.01
2.07
1.96
3.37
ppm
Current Data Parameters
NAME DAS41571
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20131119
Time 11.49
INSTRUM DPX400
PROBHD 5 mm Multinucl
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 16
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 128
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

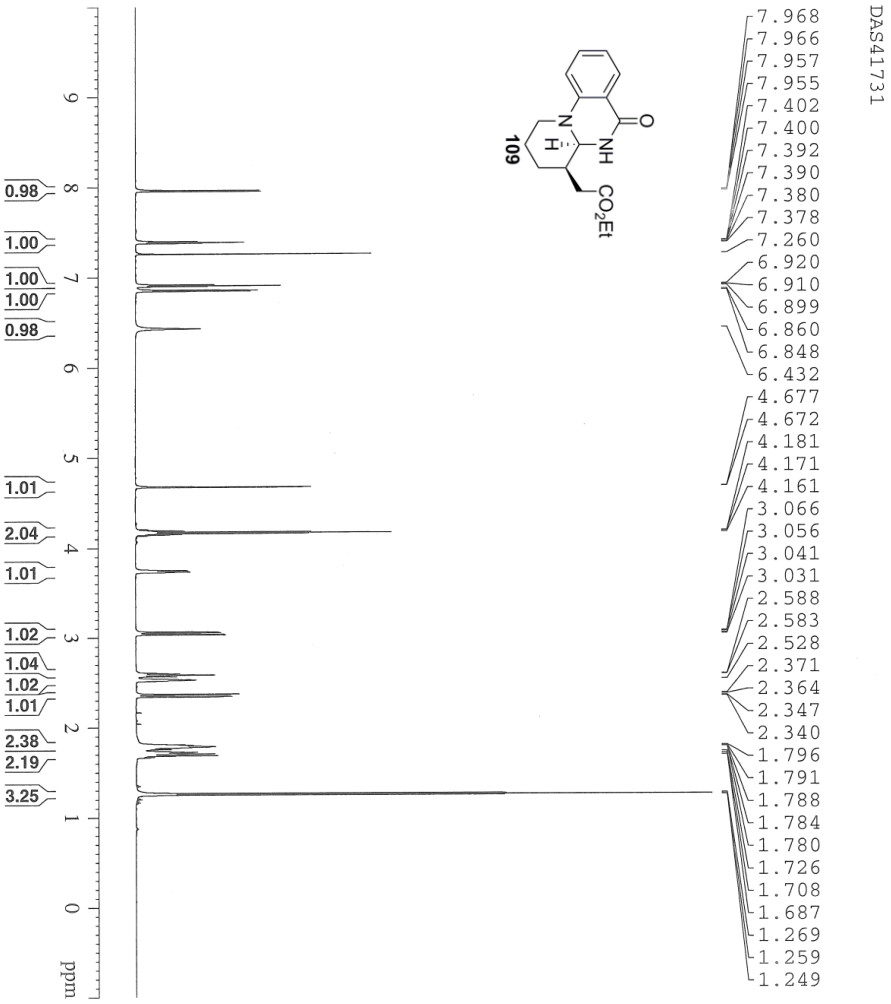


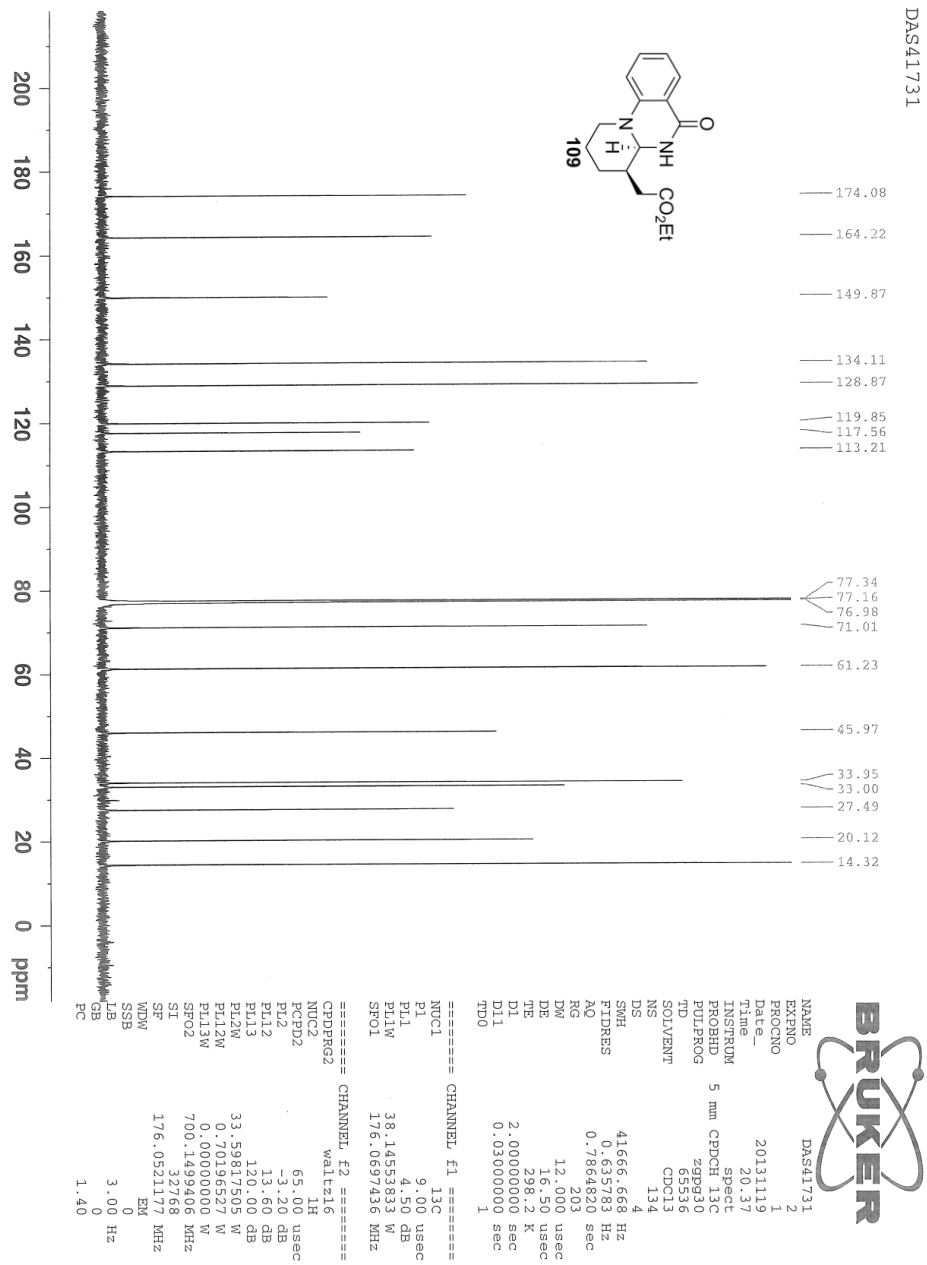

```
Current Data Parameters
NAME                  DAS41571
EXPNO                        2
PROCNO                       1

F2 - Acquisition Parameter
Date_               20131119
Time                    11.52
INSTRUM                DPX400
PROBHD  5 mm Multinucl
PULPROG               zgpg30
TD                     65536
SOLVENT                CDCl3
NS                       128
DS                         4
SWH                23980.814 Hz
FIDRES              0.365918 Hz
AQ                  1.3664756 sec
RG                     2298.8
DW                    20.850 use
DE                     6.00 use
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 use
PL1                  -3.00 dB
SFO1        100.6555216 MHz

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

F2 - Processing parameters
SI                       32768
SF          100.6454484 MHz
WDW                         EM
SSB                          0
LB                    1.00 Hz
GB                           0
PC                    1.40
```

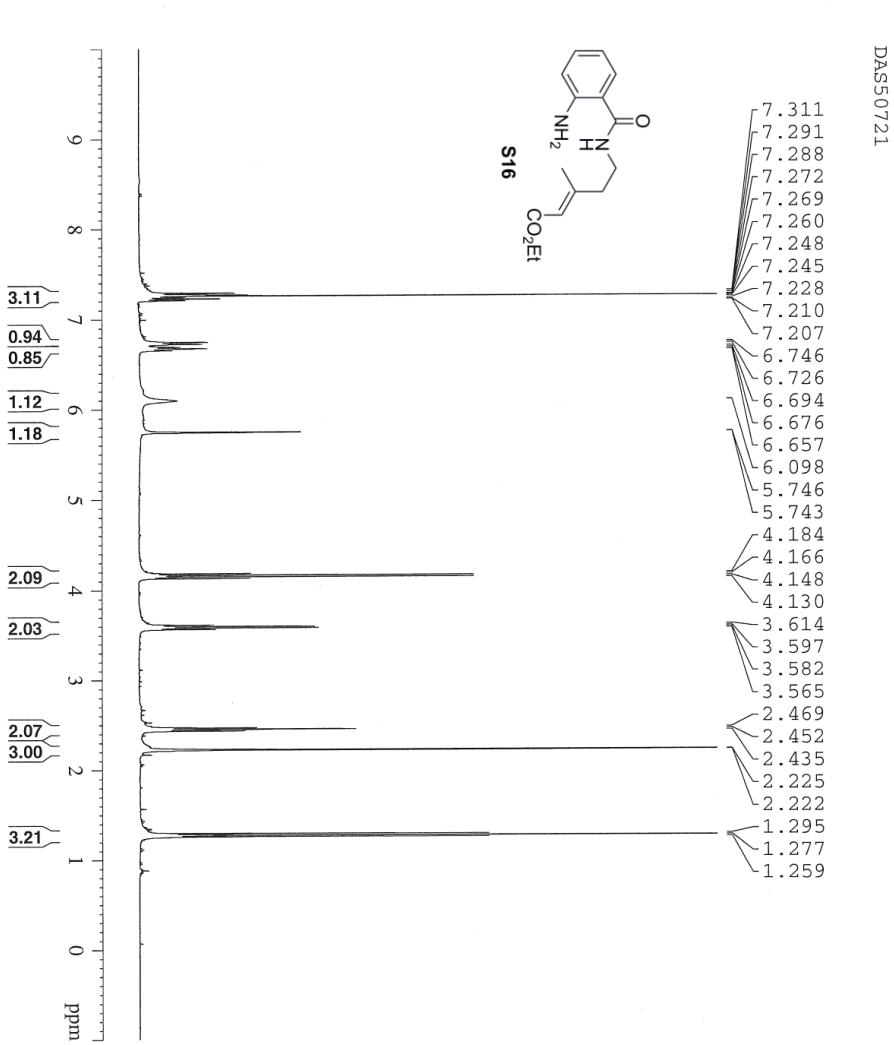

DAS41611
8.395
8.376
8.261
7.776
7.758
7.740
7.529
7.510
7.492
7.331
7.310
7.260
6.952
6.935
6.917
6.896
6.879
5.919
5.880
4.217
4.199
4.181
4.163
4.144
4.126
2.371
2.353
2.335
2.318
2.102
2.084
2.066
2.047
2.029
1.301
1.284
1.266
108
CO2Et
1.14
1.08
1.15
1.22
1.15
0.98
1.00
4.58
2.08
2.63
3.51
ppm
Current Data Parameters
NAME DAS41611
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20130716
Time_ 15.25
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 512
DW 78.000 usec
DE 6.00 usec
TE 299.2 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

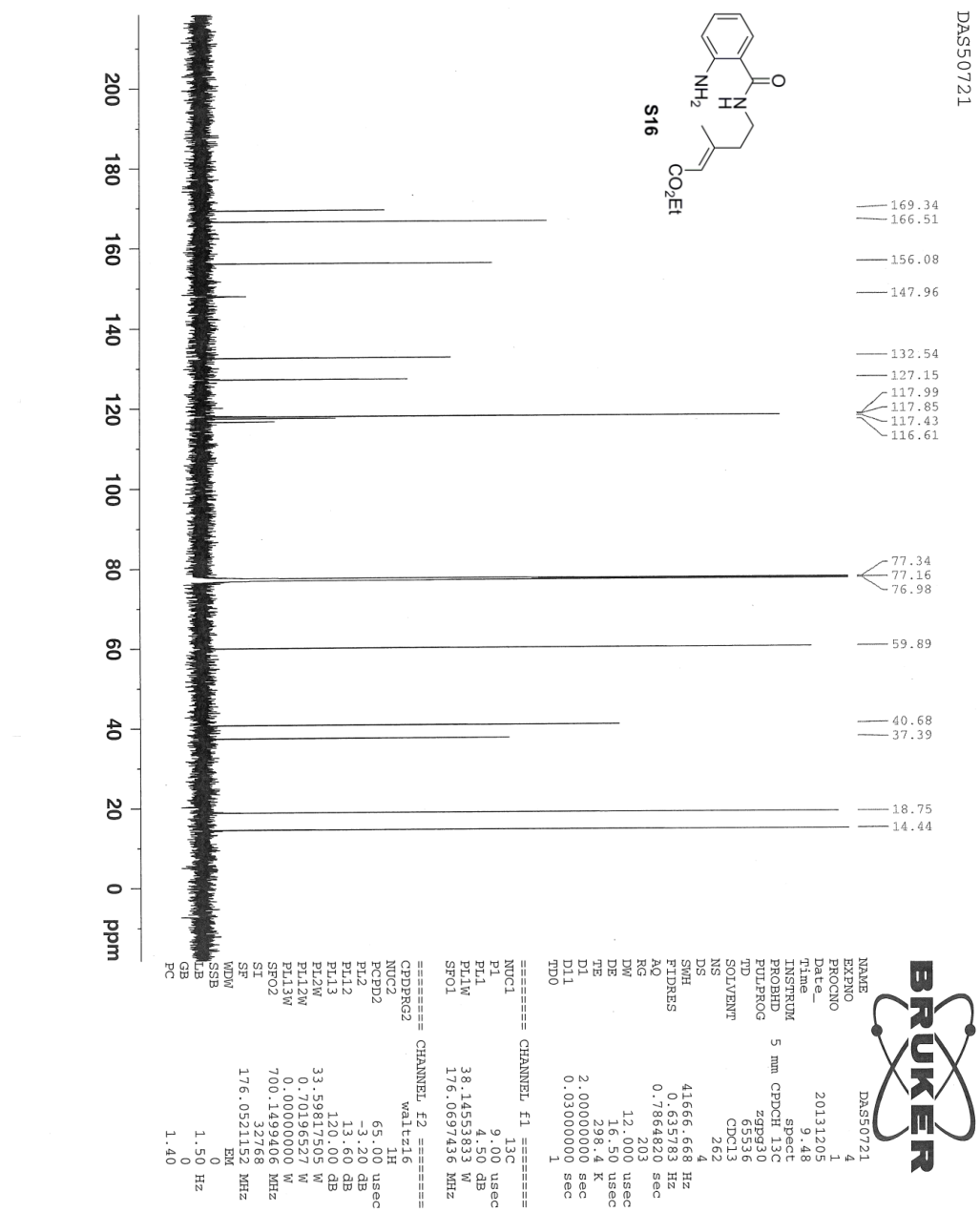


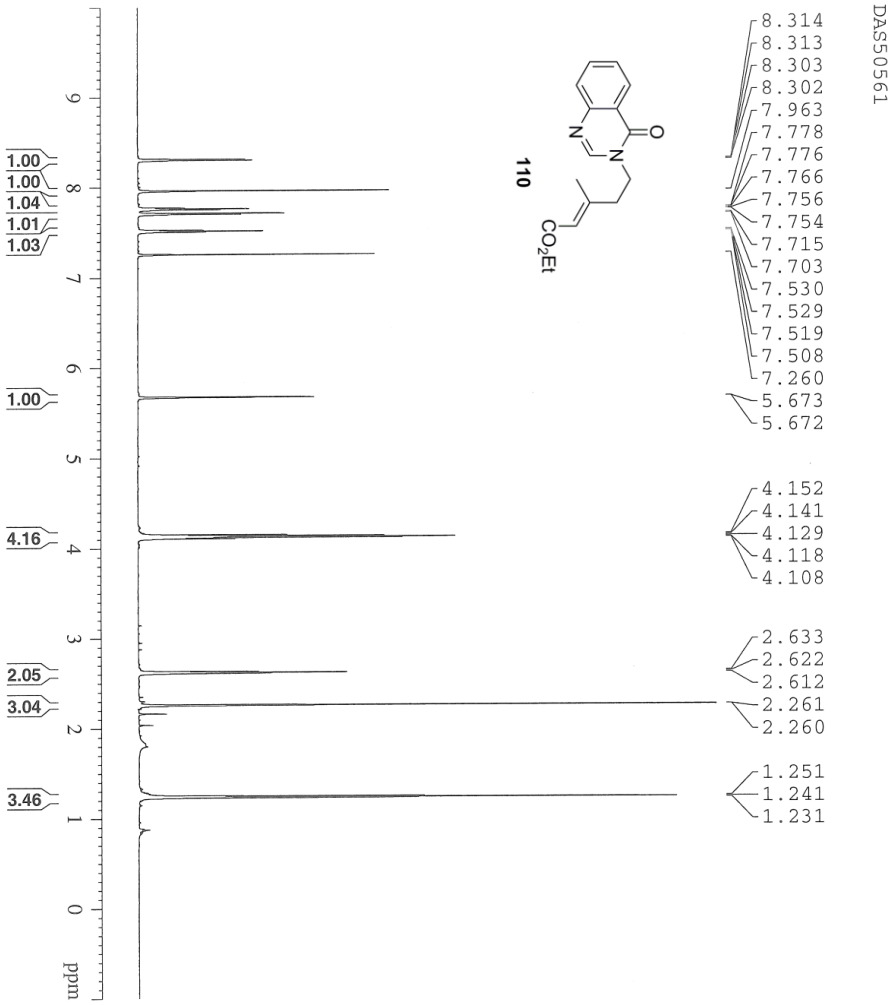

```
Current Data Parameters
NAME                  DAS41611
EXPNO                        2
PROCNO                       1

F2 - Acquisition Parameters
Date_               20130716
Time                    15.30
INSTRUM                DPX400
PROBHD    5 mm Multinucl
PULPROG              zgpg30
TD                       65536
SOLVENT                CDCl3
NS                        2048
DS                           4
SWH                23980.814 Hz
FIDRES              0.365918 Hz
AQ                  1.3664756 sec
RG                        3251
DW                     20.850 use
DE                      6.00 use
TE                     299.2 K
D1                  0.50000000 sec
D11                 0.03000000 sec
DELTA               0.40000001 sec
TD0                          1

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

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

F2 - Processing parameters
SI                       32768
SF            100.6454570 MHz
WDW                         EM
SSB                          0
LB                    1.50 Hz
GB                           0
PC                    1.40
```


DAS41731
7.968
7.966
7.957
7.955
7.402
7.400
7.392
7.390
7.380
7.378
7.260
6.920
6.910
6.899
6.860
6.848
6.432
4.677
4.672
4.181
4.171
4.161
3.066
3.056
3.041
3.031
2.588
2.583
2.528
2.371
2.364
2.347
2.340
1.796
1.791
1.788
1.784
1.780
1.726
1.708
1.687
1.269
1.259
1.249
109
0.98
1.00
1.00
1.00
0.98
1.01
2.04
1.01
1.02
1.04
1.02
1.01
2.38
2.19
3.25
ppm
NAME DAS41731
EXPNO 1
PROCNO 1
Date_ 20131119
Time 20.30
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 40.3
DW 42.000 usec
DE 6.50 usec
TE 298.4 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 700.1471601 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00


DAS41731
109
174.08
164.22
149.87
134.11
128.87
119.85
117.56
113.21
77.34
77.16
76.98
71.01
61.23
45.97
33.95
33.00
27.49
20.12
14.32
200
180
160
140
120
100
80
60
40
20
0
ppm
BRUKER
NAME DAS41731
EXPNO 2
PROCNO 1
Date_ 20131119
Time 20.37
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 134
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 176.0521177 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40

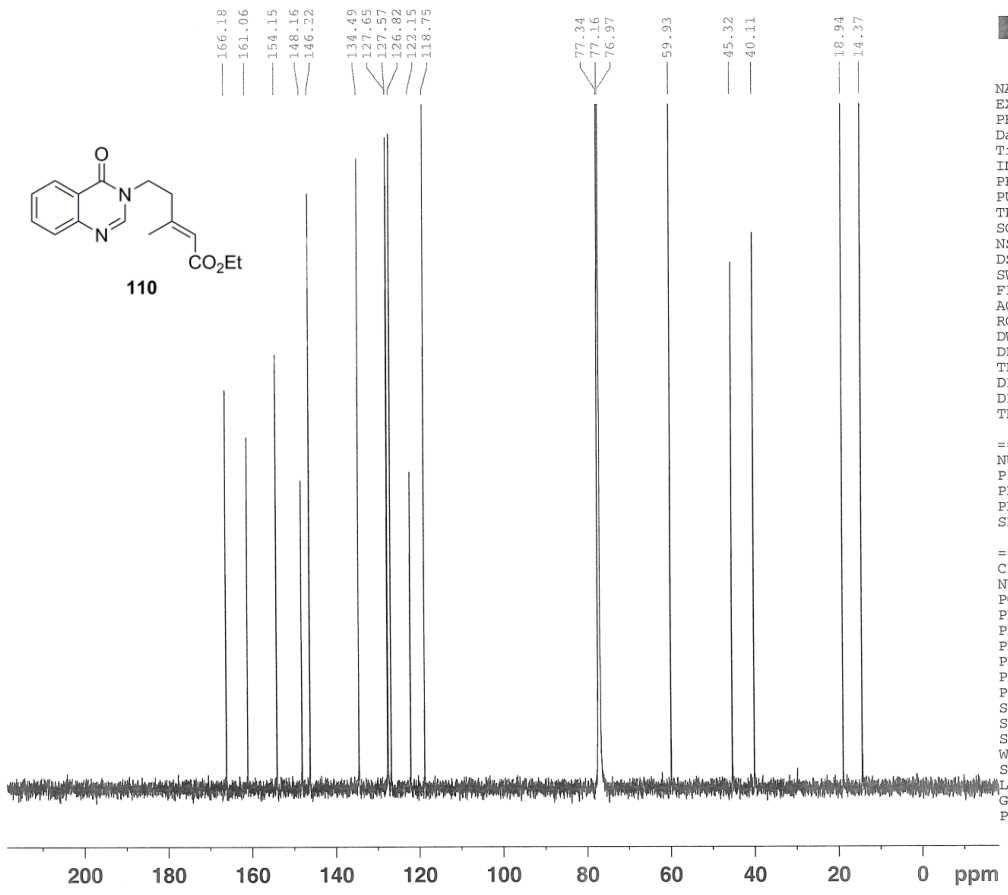

DAS50721
7.311
7.291
7.288
7.272
7.269
7.260
7.248
7.245
7.228
7.210
7.207
6.746
6.726
6.694
6.676
6.657
6.098
5.746
5.743
4.184
4.166
4.148
4.130
3.614
3.597
3.582
3.565
2.469
2.452
2.435
2.225
2.222
1.295
1.277
1.259
S16
3.11
0.94
0.85
1.12
1.18
2.09
2.03
2.07
3.00
3.21
9
8
7
6
5
4
3
2
1
0
ppm
NAME DAS50721
EXPNO 2
PROCNO 1
Date_ 20131204
Time 22.09
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 sec
RG 228.1
DW 69.600 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 usec
PL1 0.00 dB
SFO1 400.1428010 MHz
SI 32768
SF 400.1400089 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00


DAS50721
S16
169.34
166.51
156.08
147.96
132.54
127.15
117.99
117.85
117.43
116.61
77.34
77.16
76.98
59.89
40.68
37.39
18.75
14.44
200
180
160
140
120
100
80
60
40
20
0
ppm



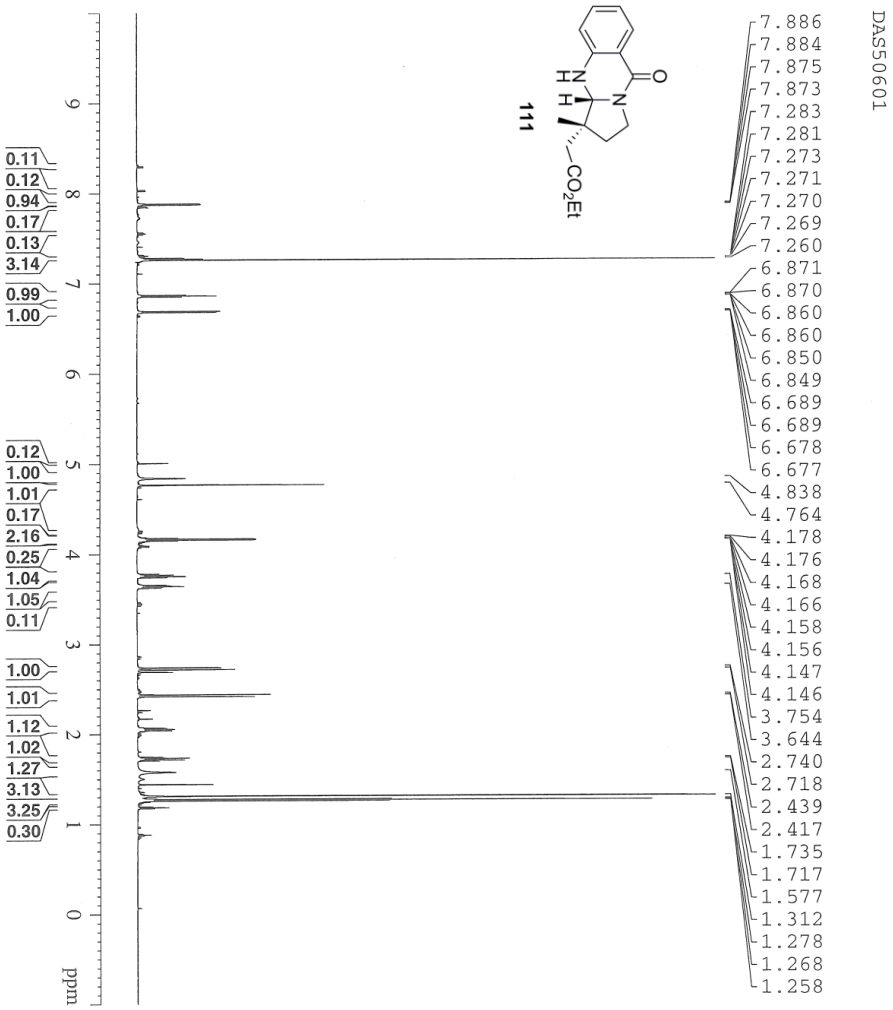

```
NAME                    DAS50561
EXPNO                          1
PROCNO                         1
Date_                   20131121
Time                       14.11
INSTRUM                     spect
PROBHD     5 mm CPDCH 13C
PULPROG                 zg30
TD                         95236
SOLVENT                    CDCl3
NS                            32
DS                             2
SWH                    11904.762 Hz
FIDRES                     0.125003 Hz
AQ                     3.9999621 sec
RG                            20.2
DW                          42.000 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                  700.1471607 MHz
WDW                           EM
SSB                            0
LB                          0.30 Hz
GB                             0
PC                          1.00
```

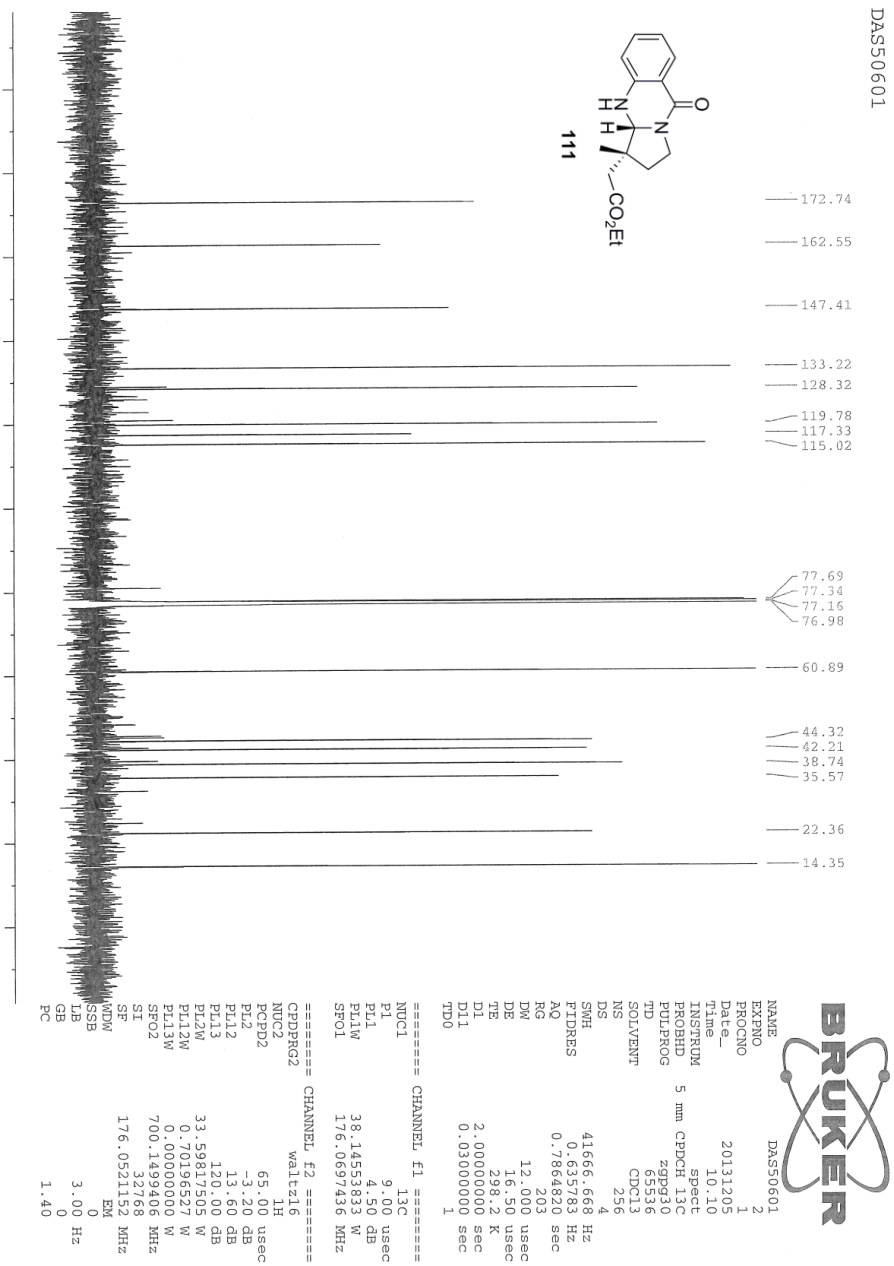
DAS50561

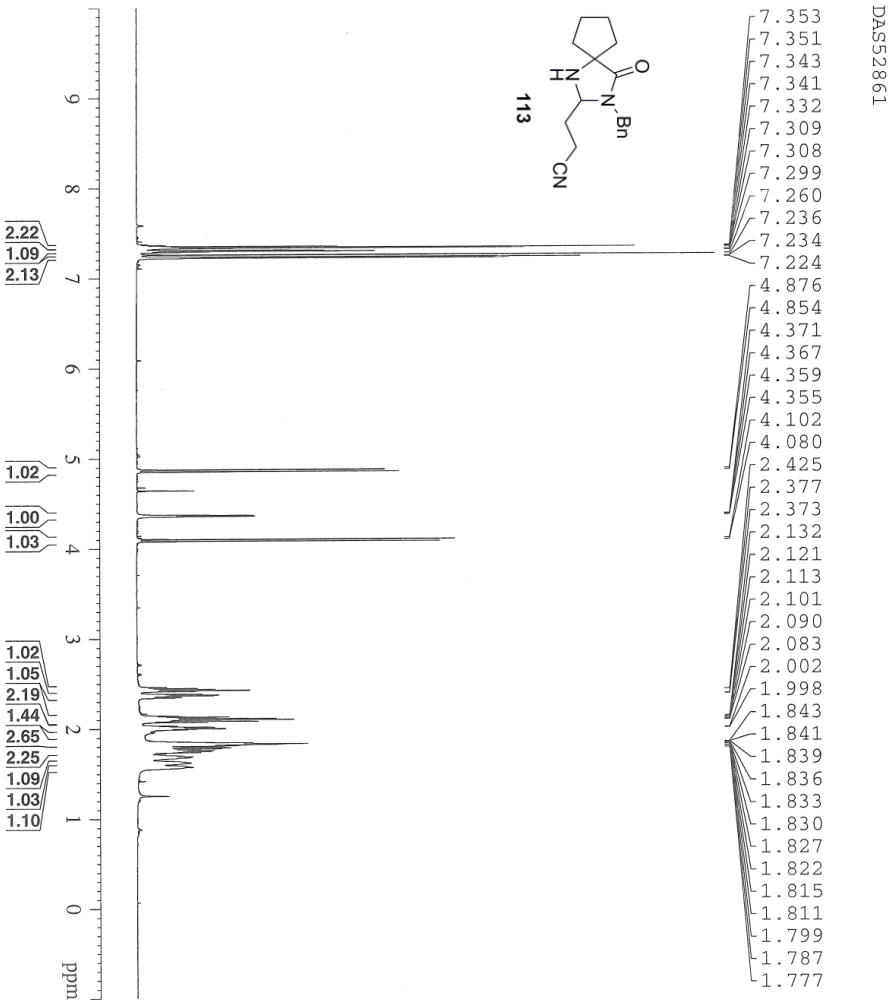


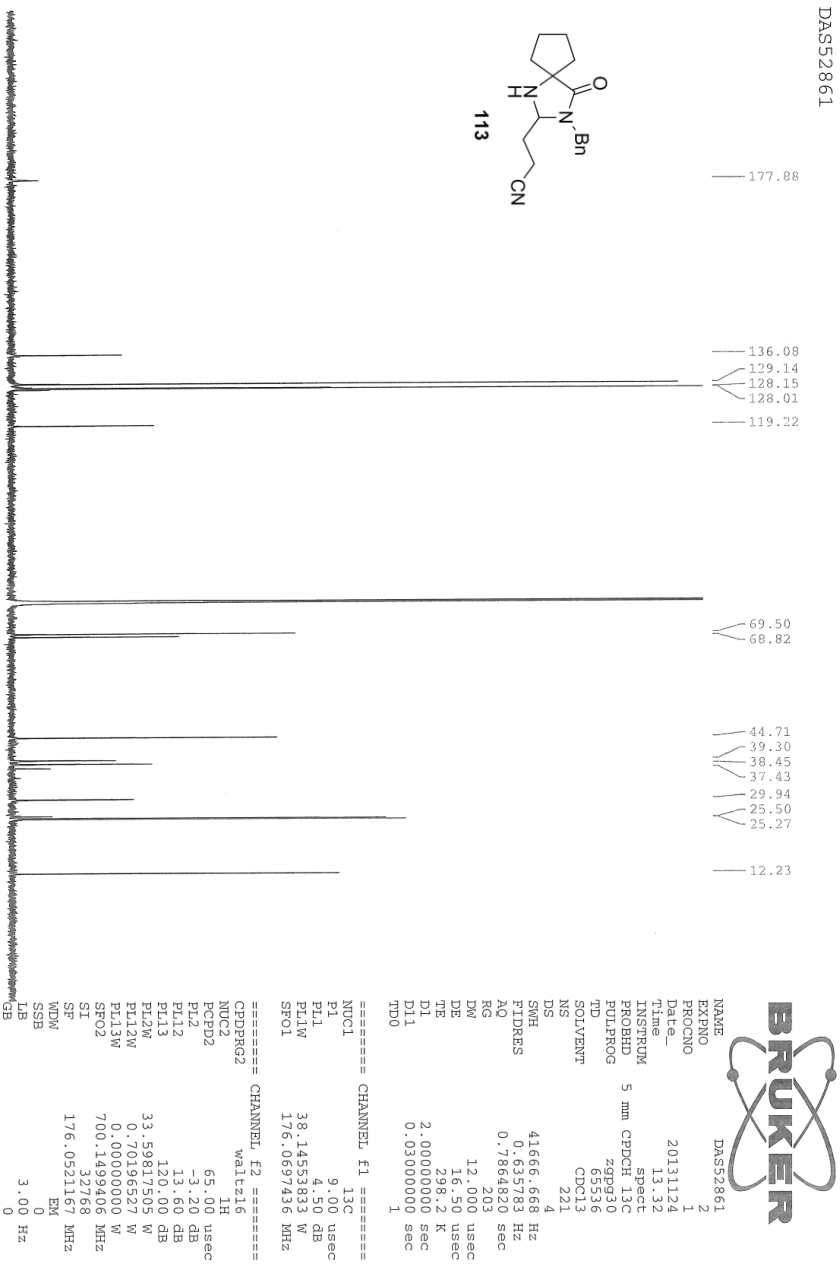
BRUKER

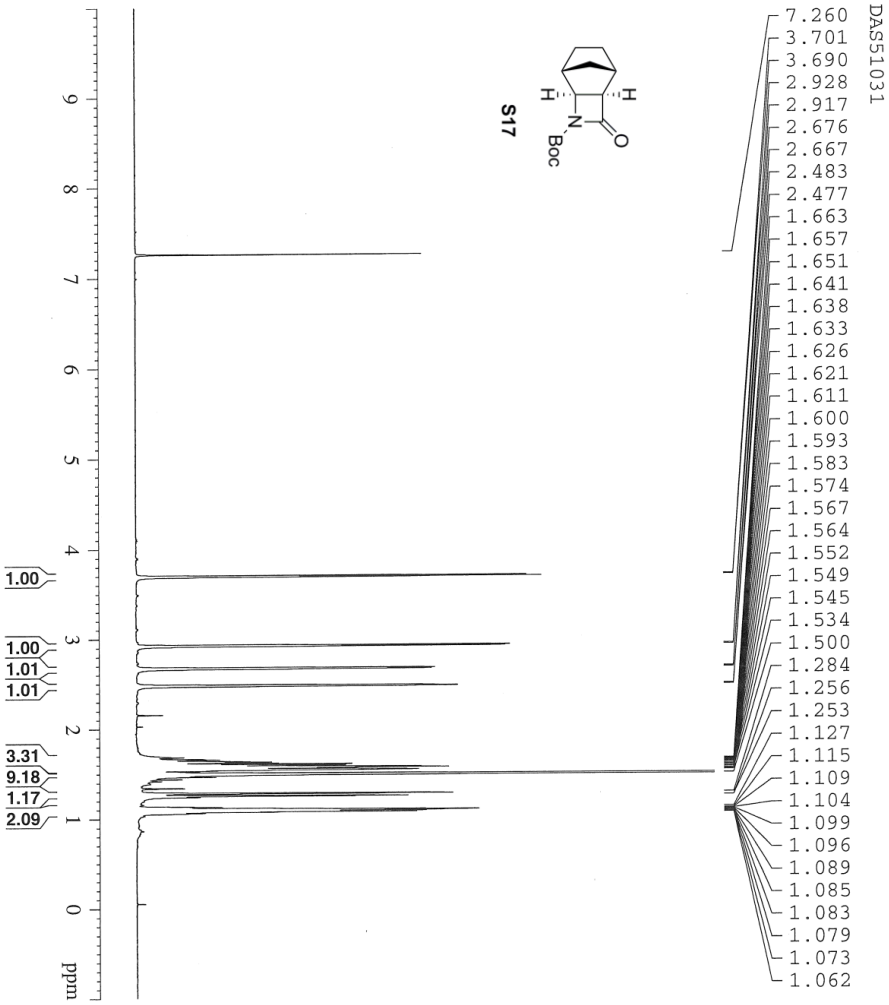
NAME	DAS50561
EXPNO	2
PROCNO	1
Date_	20131121
Time	14.16
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	128
DS	4
SWH	41666.668 Hz
FIDRES	0.635783 Hz
AQ	0.7864820 sec
RG	203
DW	12.000 usec
DE	16.50 usec
TE	298.2 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL 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	176.0521168 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40


DAS50601
7.886
7.884
7.875
7.873
7.283
7.281
7.273
7.271
7.270
7.269
7.260
6.871
6.870
6.860
6.860
6.850
6.849
6.689
6.689
6.678
6.677
4.838
4.764
4.178
4.176
4.168
4.166
4.158
4.156
4.147
4.146
3.754
3.644
2.740
2.718
2.439
2.417
1.735
1.717
1.577
1.312
1.278
1.268
1.258
111
CO2Et
0.11
0.12
0.94
0.17
0.13
3.14
0.99
1.00
0.12
1.00
1.01
0.17
2.16
0.25
1.04
1.05
0.11
1.00
1.01
1.12
1.02
1.27
3.13
3.25
0.30
ppm
NAME DAS50601
EXPNO 1
PROCNO 1
Date_ 20131205
Time 10.03
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 32
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 700.1471598 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

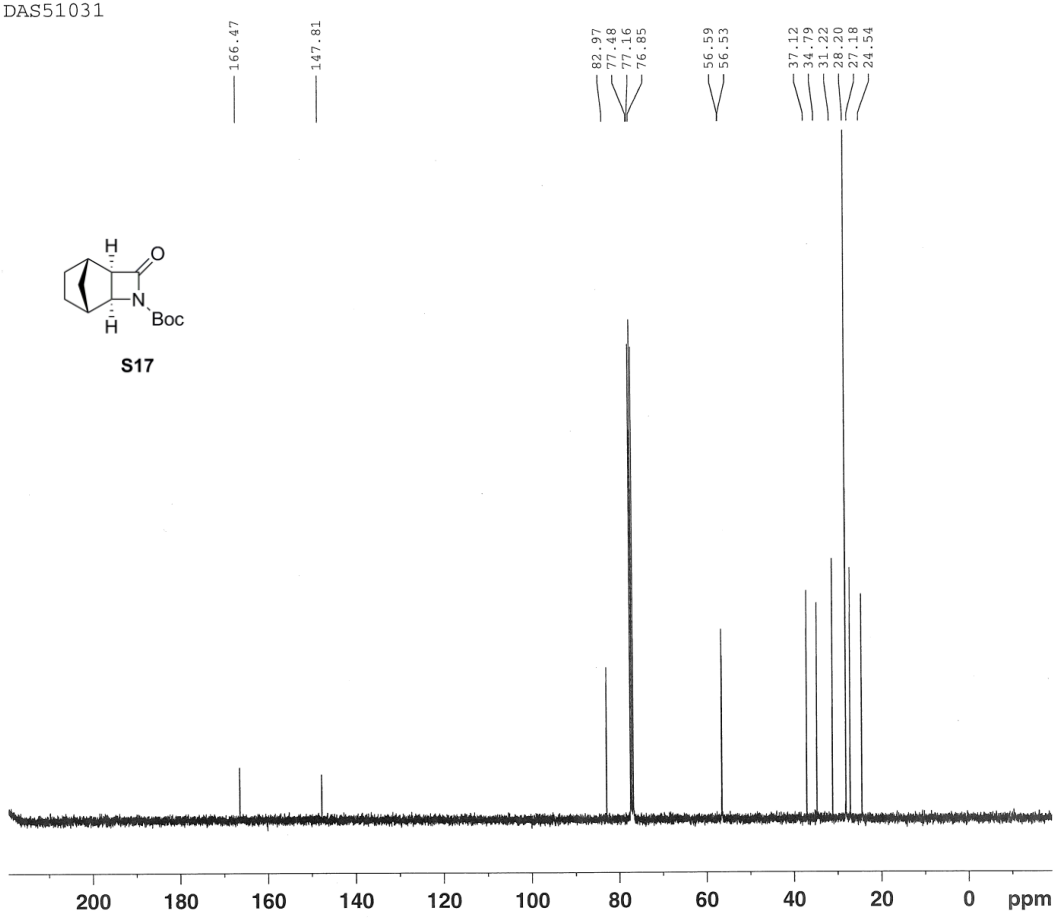

DAS50601
111
CO2Et
172.74
162.55
147.41
133.22
128.32
119.78
117.33
115.02
77.69
77.34
77.16
76.98
60.89
44.32
42.21
38.74
35.57
22.36
14.35
200
180
160
140
120
100
80
60
40
20
0
ppm
BRUKER
NAME DAS50601
EXPNO 2
PROCNO 1
Date_ 20131205
Time 10.10
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 256
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 176.0521152 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40


DAS52861
7.353
7.351
7.343
7.341
7.332
7.309
7.308
7.299
7.260
7.236
7.234
7.224
4.876
4.854
4.371
4.367
4.359
4.355
4.102
4.080
2.425
2.377
2.373
2.132
2.121
2.113
2.101
2.090
2.083
2.002
1.998
1.843
1.841
1.839
1.836
1.833
1.830
1.827
1.822
1.815
1.811
1.799
1.787
1.777
113
2.22
1.09
2.13
1.02
1.00
1.03
1.02
1.05
2.19
1.44
2.65
2.25
1.09
1.03
1.10
9
8
7
6
5
4
3
2
1
0
ppm
NAME DAS52861
EXPNO 1
PROCNO 1
Date_ 20131124
Time 13.27
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDC13
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 32
DW 42.000 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
========== CHANNEL f1 ==========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471609 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00


DAS52861
113
177.88
136.08
129.14
128.15
128.01
119.22
69.50
68.82
44.71
39.30
38.45
37.43
29.94
25.50
25.27
12.23
200
180
160
140
120
100
80
60
40
20
0
ppm
NAME DAS52861
EXPNO 2
PROCNO 1
Date_ 20131124
Time 13.32
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 221
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 176.0521167 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40

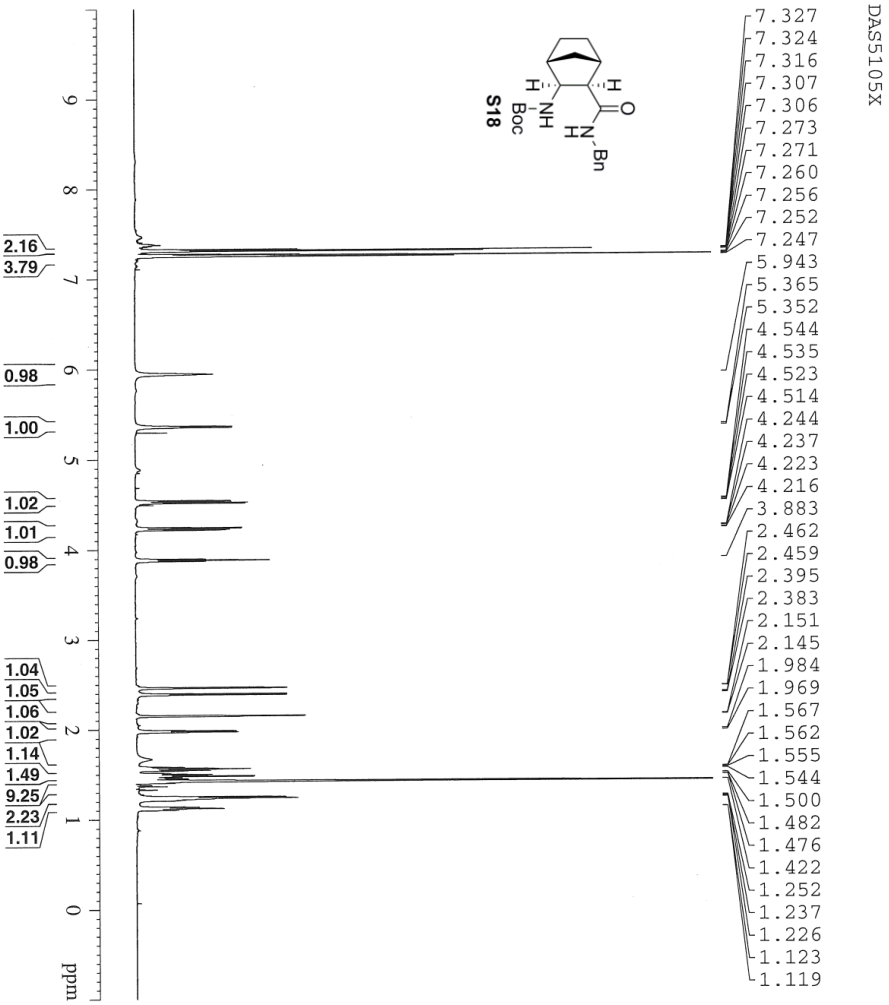

DAS51031
7.260
3.701
3.690
2.928
2.917
2.676
2.667
2.483
2.477
1.663
1.657
1.651
1.641
1.638
1.633
1.626
1.621
1.611
1.600
1.593
1.583
1.574
1.567
1.564
1.552
1.549
1.545
1.534
1.500
1.284
1.256
1.253
1.127
1.115
1.109
1.104
1.099
1.096
1.089
1.085
1.083
1.079
1.073
1.062
H
H
N
Boc
O
S17
1.00
1.00
1.01
1.01
3.31
9.18
1.17
2.09
ppm
Current Data Parameters
NAME DAS51031
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20131120
Time_ 20.23
INSTRUM DPX400
PROBHD 5 mm Multinucl
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 16
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 128
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 400.2600109 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

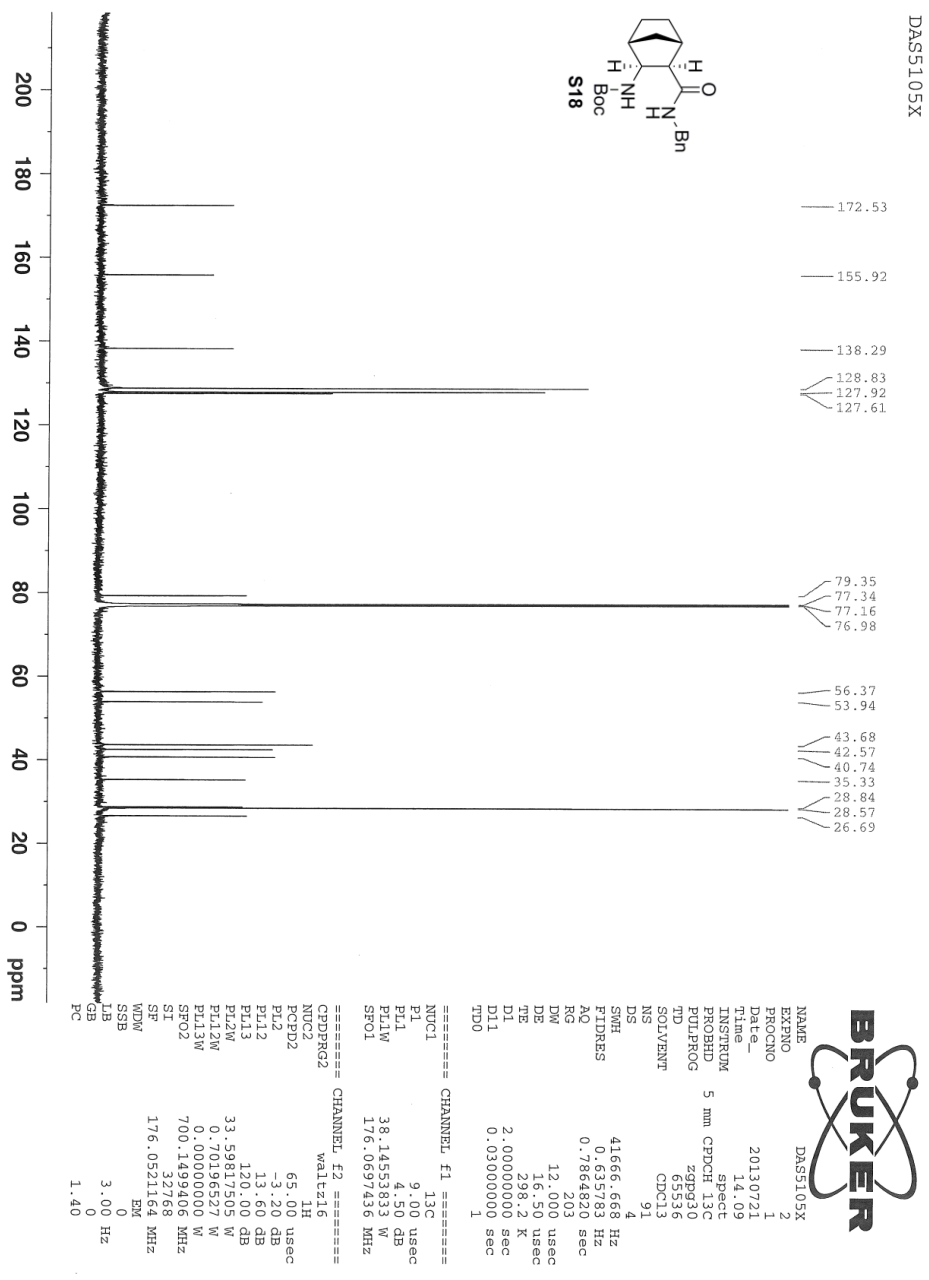
DAS51031

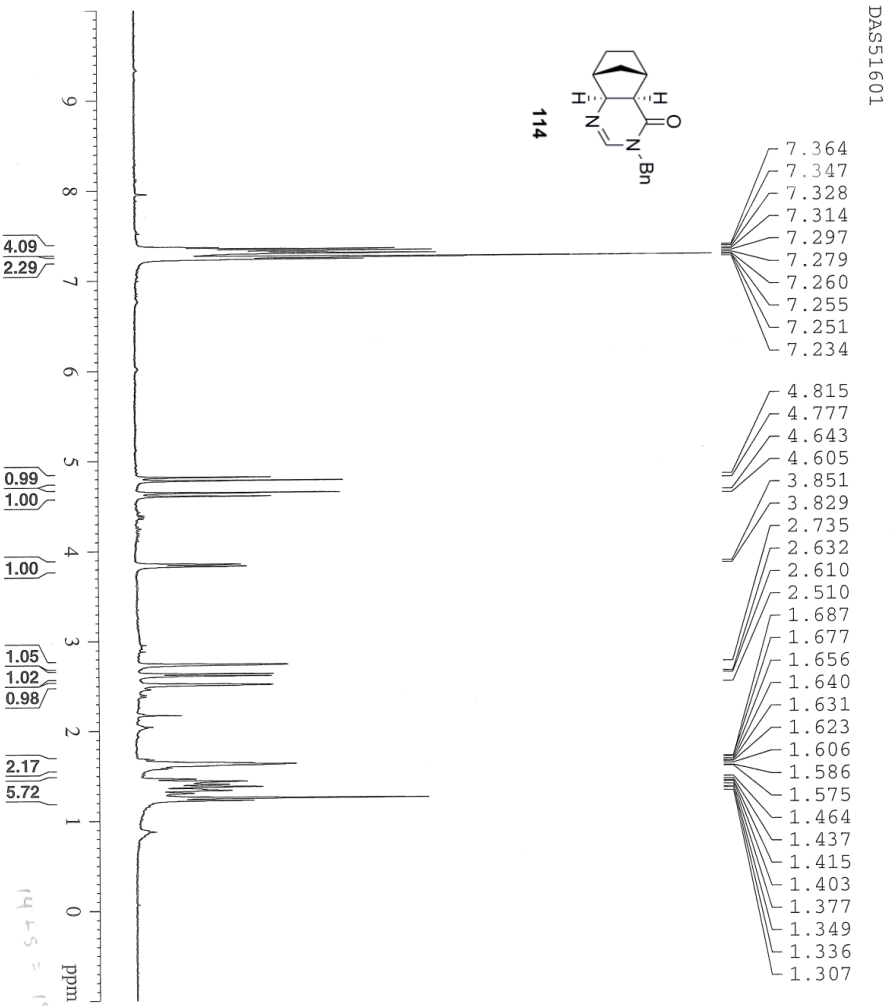


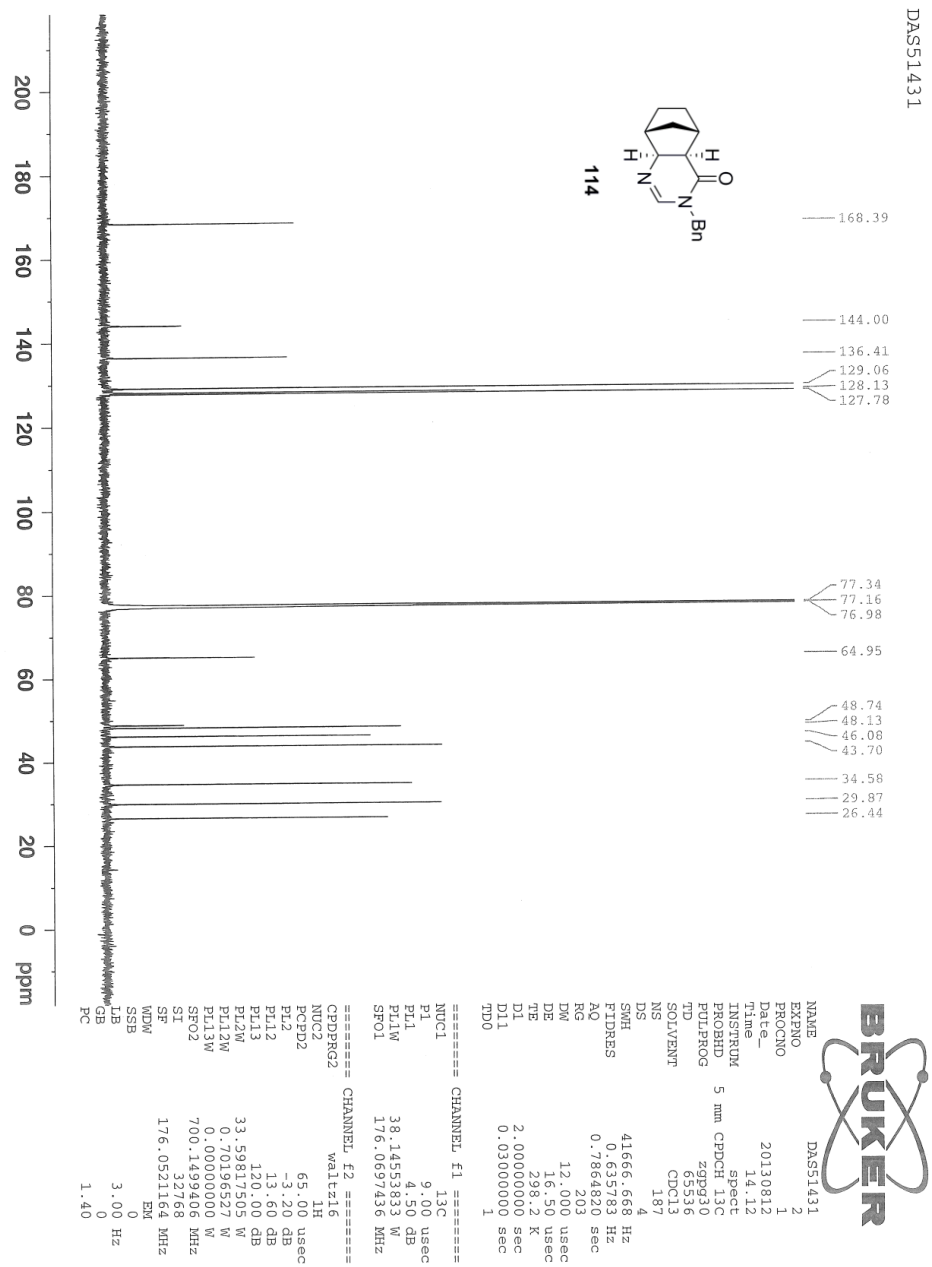
S17

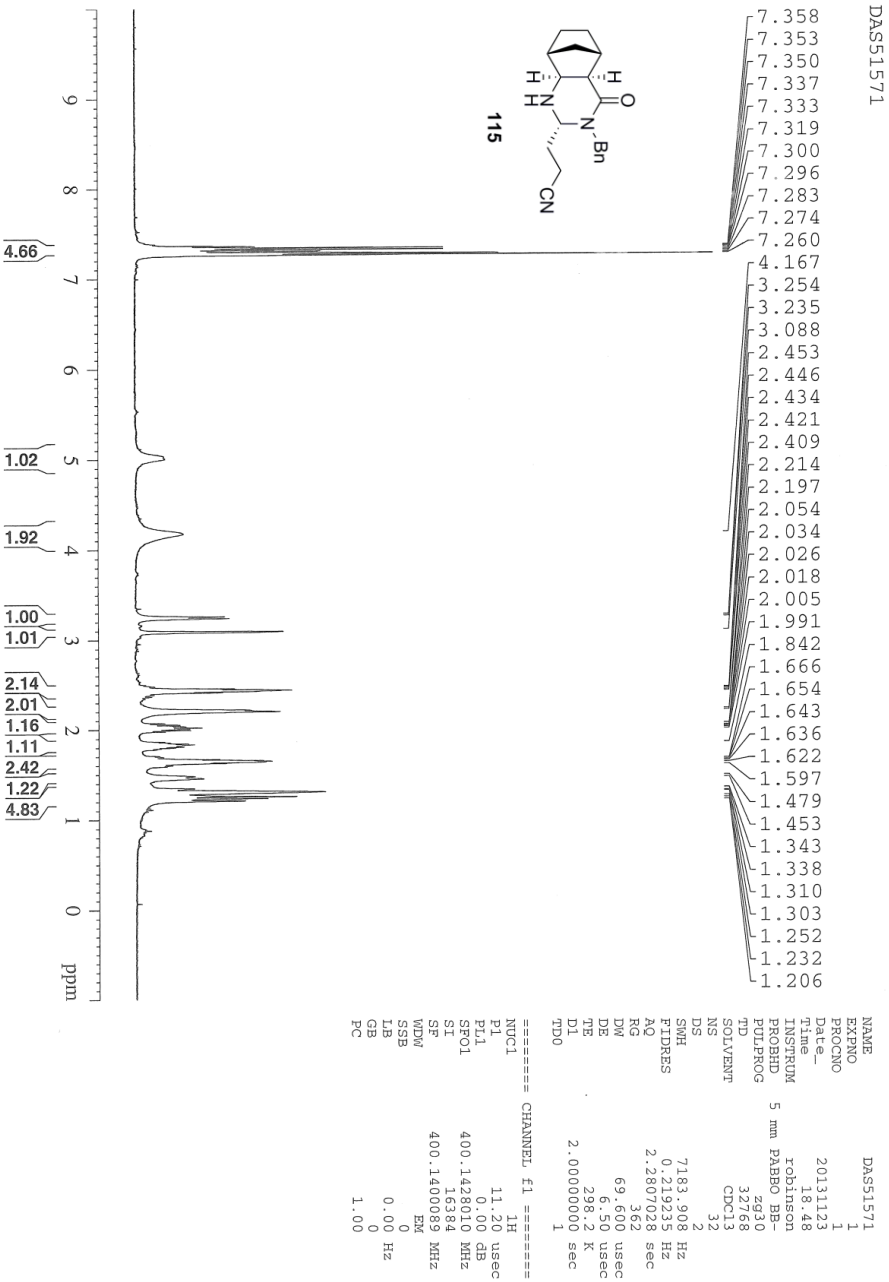
```
Current Data Parameters
NAME                  DAS51031
EXPNO                        2
PROCNO                       1

F2 - Acquisition Parameters
Date_              20131120
Time                   20.27
INSTRUM                DPX400
PROBHD   5 mm Multinucl
PULPROG                zgpg30
TD                      65536
SOLVENT                 CDCl3
NS                        257
DS                          4
SWH                23980.814 Hz
FIDRES             0.365918 Hz
AQ                 1.3664756 sec
RG                    2298.8
DW                    20.850 use
DE                     6.00 use
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 use
PL1                     -3.00 dB
SFO1              100.6555216 MHz

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

F2 - Processing parameters
SI                       32768
SF                100.6454465 MHz
WDW                         EM
SSB                          0
LB                        1.00 Hz
GB                           0
PC                        1.40
```

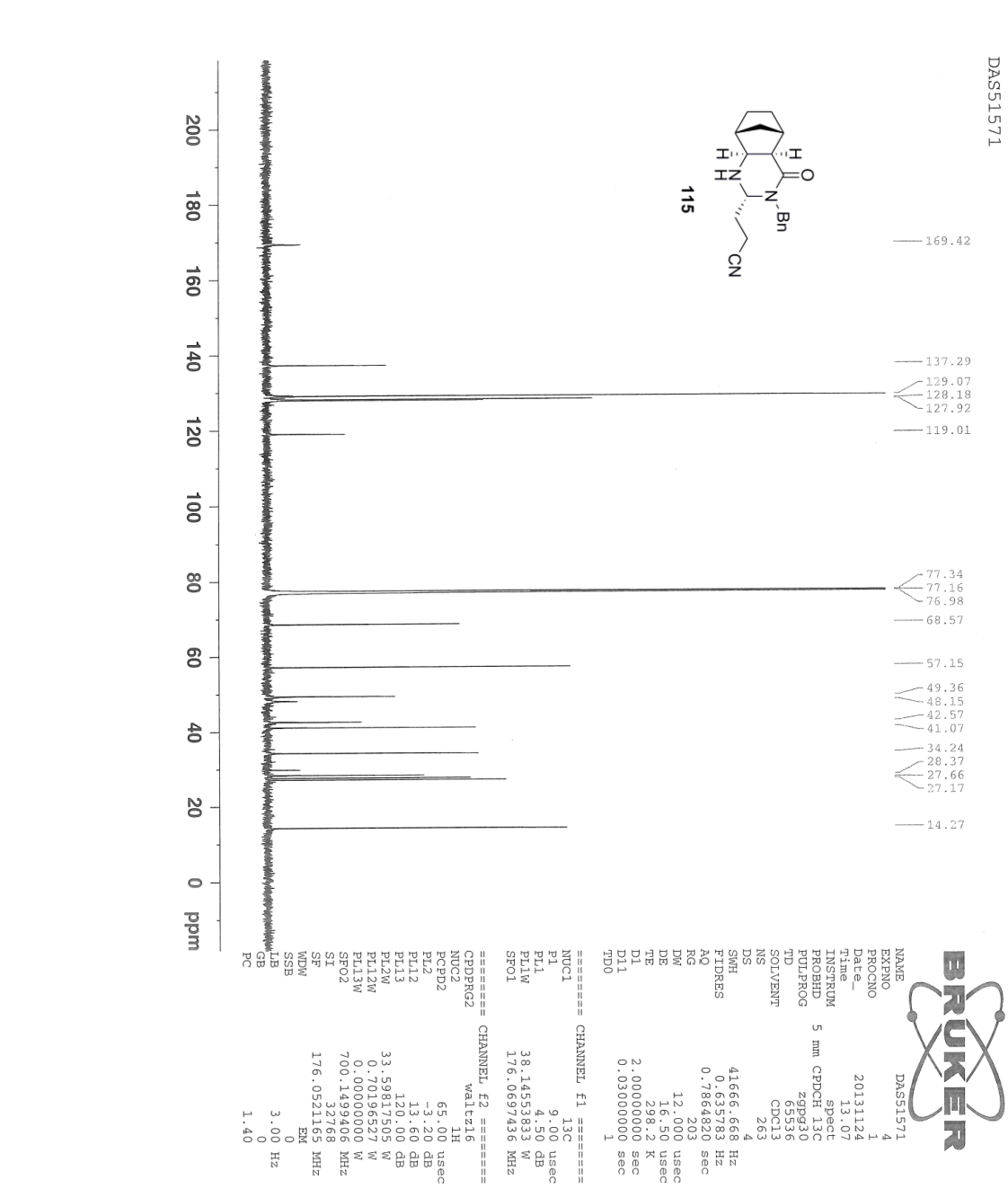

DAS5105X
7.327
7.324
7.316
7.307
7.306
7.273
7.271
7.260
7.256
7.252
7.247
5.943
5.365
5.352
4.544
4.535
4.523
4.514
4.244
4.237
4.223
4.216
3.883
2.462
2.459
2.395
2.383
2.151
2.145
1.984
1.969
1.567
1.562
1.555
1.544
1.500
1.482
1.476
1.422
1.252
1.237
1.226
1.123
1.119
S18
Boc
Bn
2.16
3.79
0.98
1.00
1.02
1.01
0.98
1.04
1.05
1.06
1.02
1.14
1.49
9.25
2.23
1.11
ppm
NAME DAS5105X
EXPNO 1
PROCNO 1
Date_ 20130721
Time 14.05
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 16
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 25.4
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 700.1471596 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

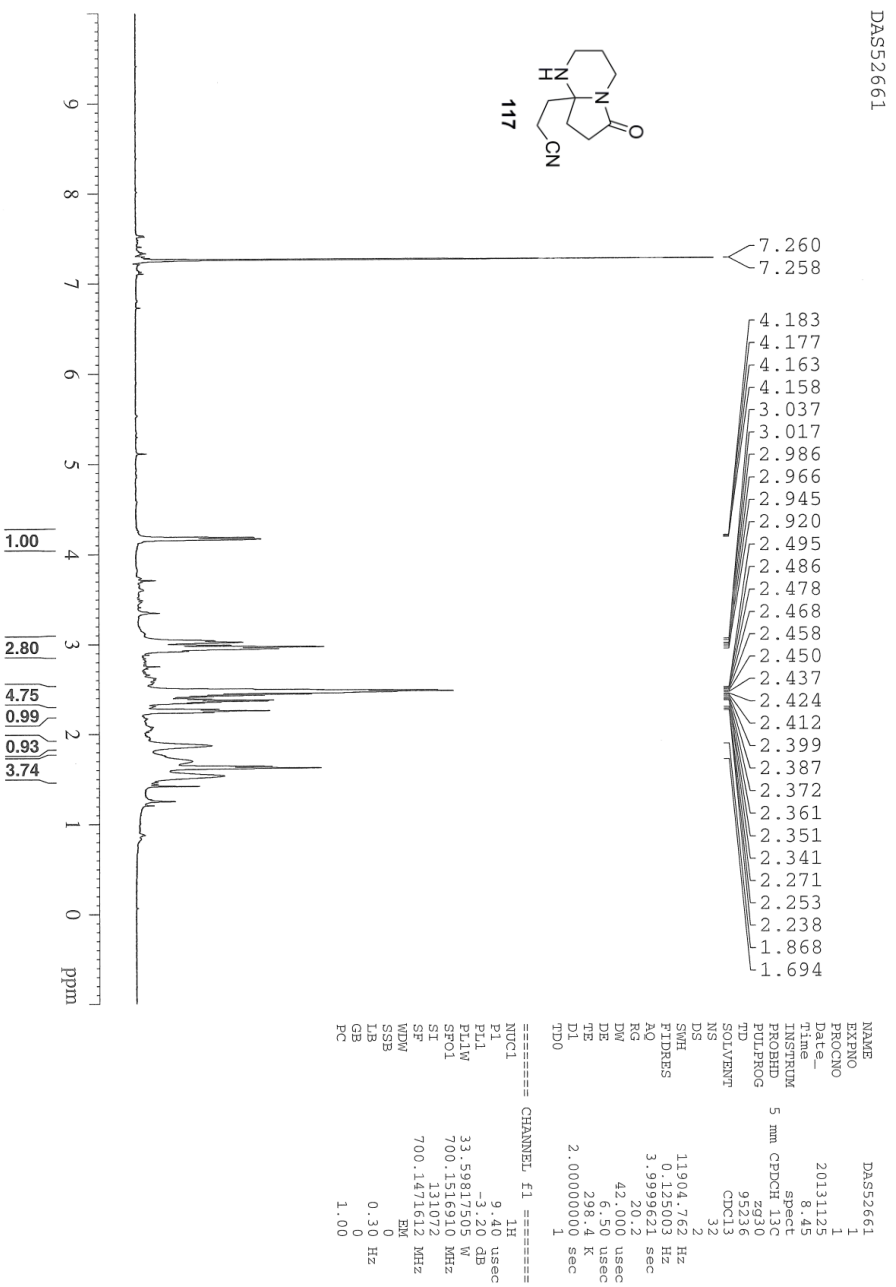

DAS5105X
S18
172.53
155.92
138.29
128.83
127.92
127.61
79.35
77.34
77.16
76.98
56.37
53.94
43.68
42.57
40.74
35.33
28.84
28.57
26.69
200
180
160
140
120
100
80
60
40
20
0
ppm
NAME DAS5105X
EXPNO 2
PROCNO 1
Date_ 20130721
Time_ 14.09
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 91
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 176.0521164 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40

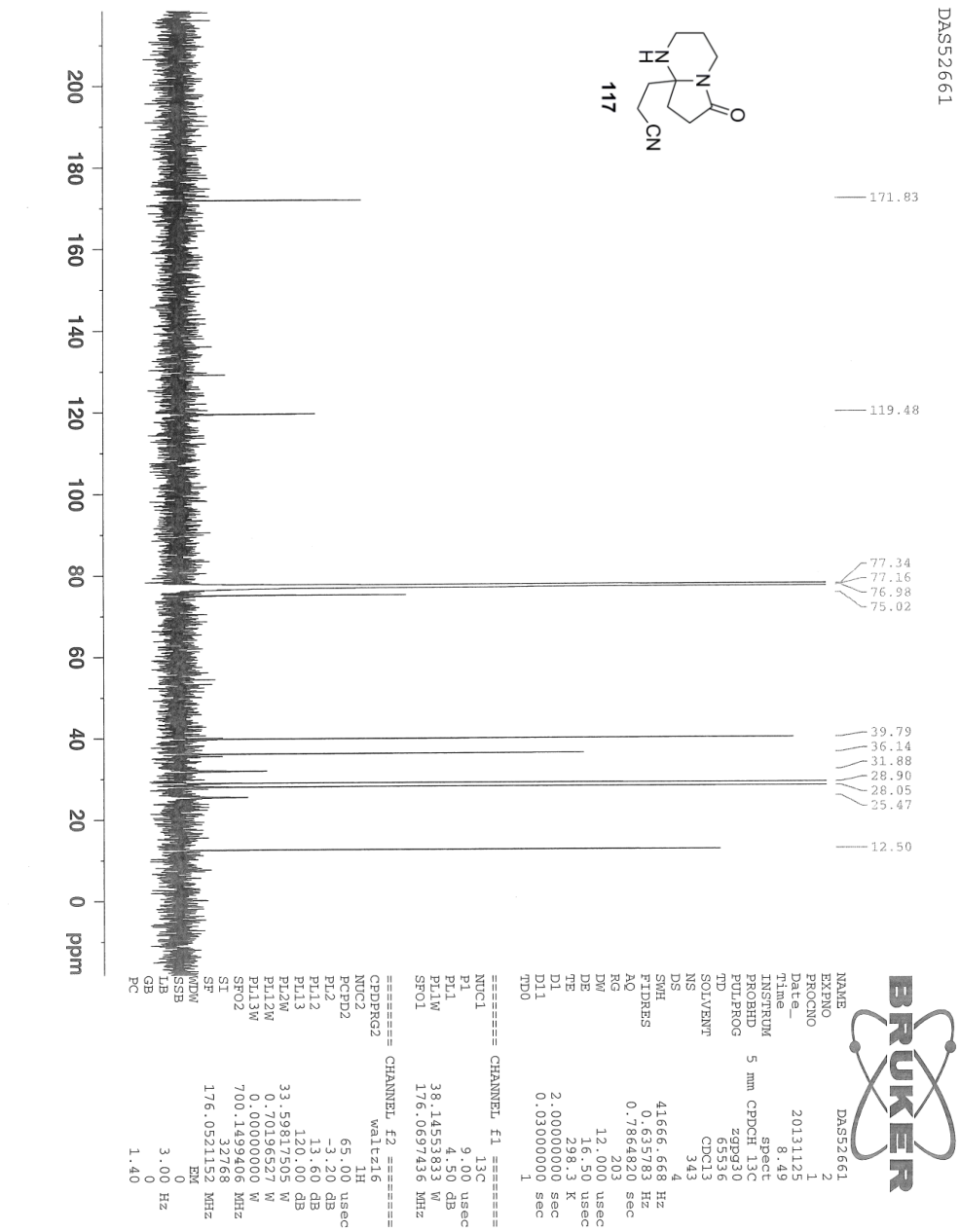

DAS51601
7.364
7.347
7.328
7.314
7.297
7.279
7.260
7.255
7.251
7.234
4.815
4.777
4.643
4.605
3.851
3.829
2.735
2.632
2.610
2.510
1.687
1.677
1.656
1.640
1.631
1.623
1.606
1.586
1.575
1.464
1.437
1.415
1.403
1.377
1.349
1.336
1.307
114
4.09
2.29
0.99
1.00
1.00
1.05
1.02
0.98
2.17
5.72
ppm
Current Data Parameters
NAME DAS51601
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20131120
Time_ 17.48
INSTRUM DPX400
PROBHD 5 mm Multinuc1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 362
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 400.2600110 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

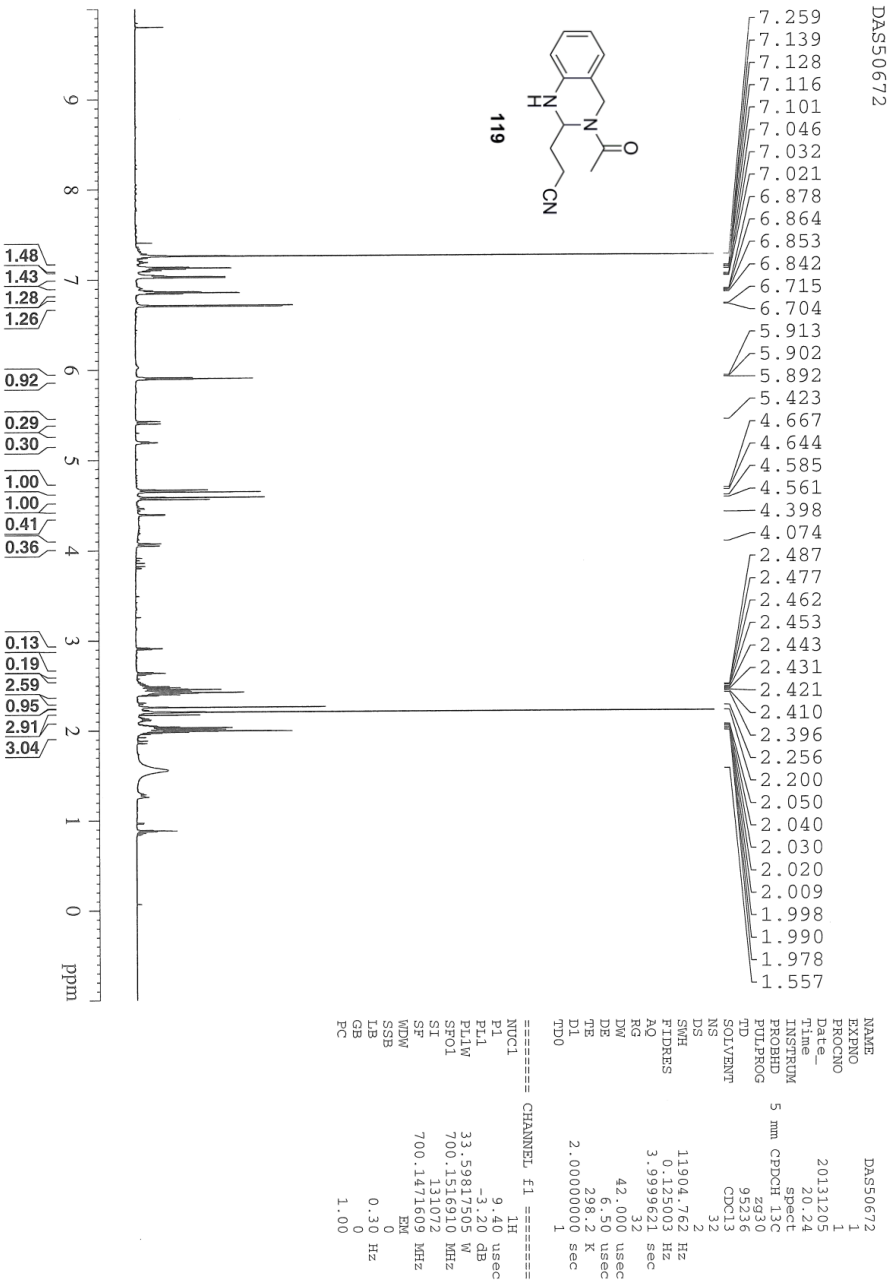

DAS51431
114
168.39
144.00
136.41
129.06
128.13
127.78
77.34
77.16
76.98
64.95
48.74
48.13
46.08
43.70
34.58
29.87
26.44
200
180
160
140
120
100
80
60
40
20
0
ppm
NAME DAS51431
EXPNO 2
PROCNO 1
Date_ 20130812
Time 14.12
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 187
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 176.0521164 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40

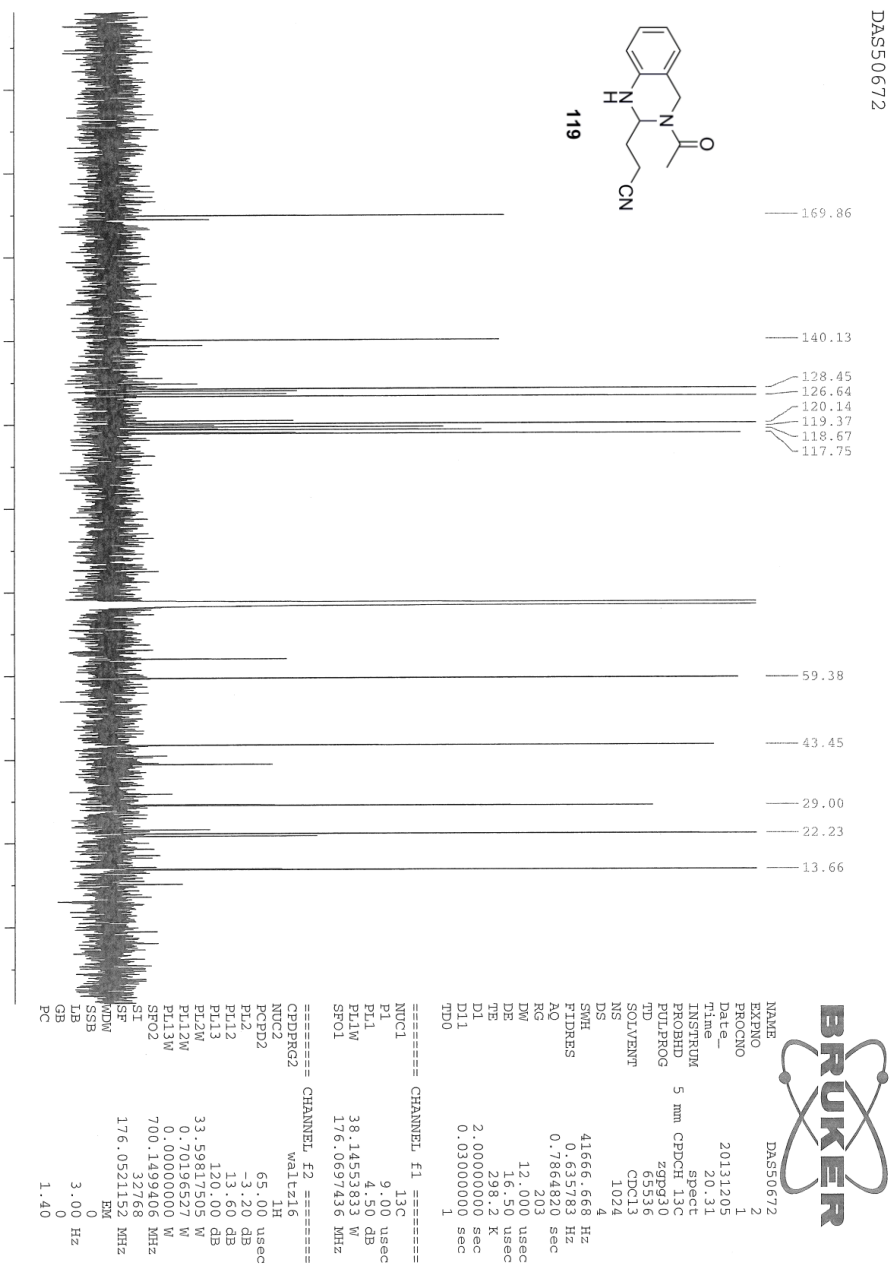

DAS51571
7.358
7.353
7.350
7.337
7.333
7.319
7.300
7.296
7.283
7.274
7.260
4.167
3.254
3.235
3.088
2.453
2.446
2.434
2.421
2.409
2.214
2.197
2.054
2.034
2.026
2.018
2.005
1.991
1.842
1.666
1.654
1.643
1.636
1.622
1.597
1.479
1.453
1.343
1.338
1.310
1.303
1.252
1.232
1.206
115
4.66
1.02
1.92
1.00
1.01
2.14
2.01
1.16
1.11
2.42
1.22
4.83
9 8 7 6 5 4 3 2 1 0 ppm
NAME DAS51571
EXPNO 1
PROCNO 1
Date_ 20131123
Time 18.48
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 sec
RG 362
DW 69.600 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 11.20 usec
PL1 0.00 dB
SFO1 400.1428010 MHz
SI 16384
SF 400.1400089 MHz
WDW EM
SSB 0
LB 0.00 Hz
GB 0
PC 1.00

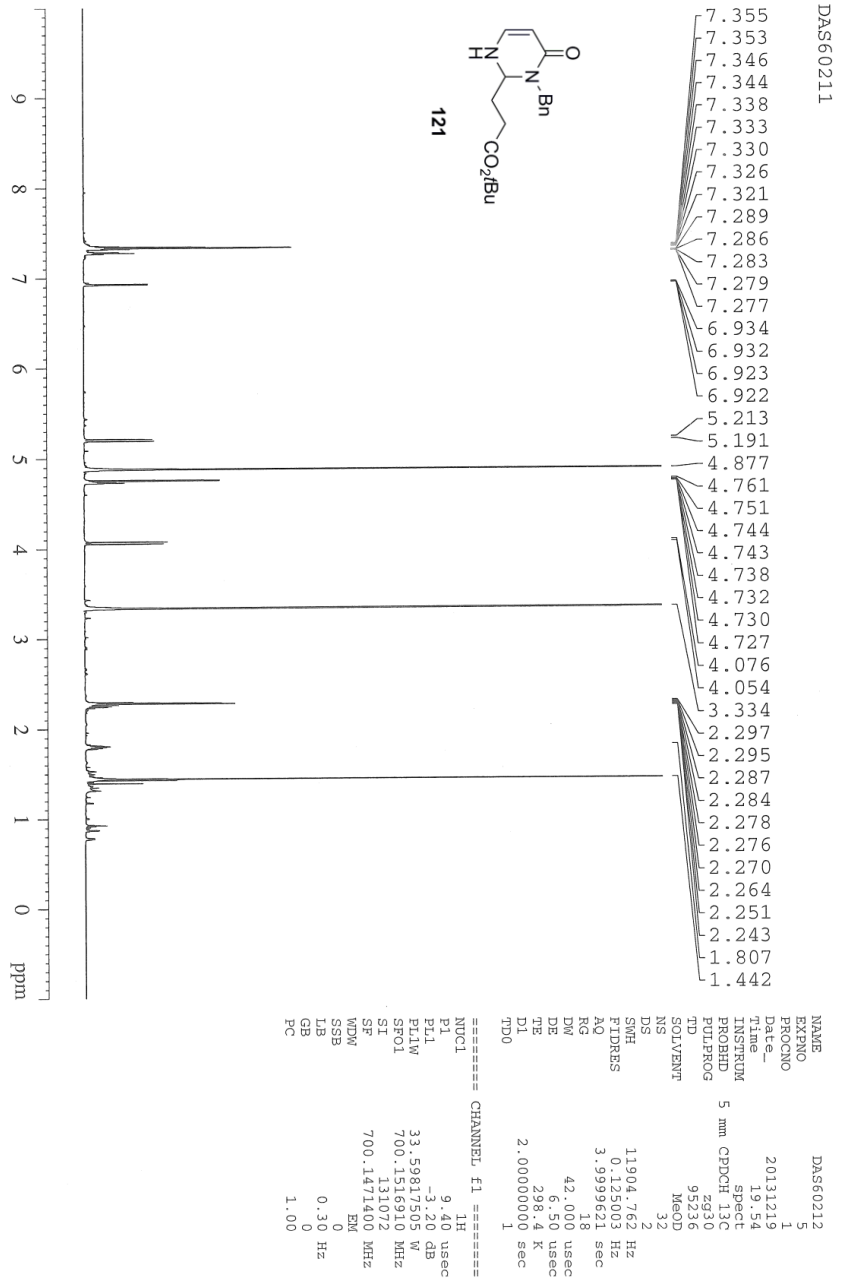

DAS51571
115
169.42
137.29
129.07
128.18
127.92
119.01
77.34
77.16
76.98
68.57
57.15
49.36
48.15
42.57
41.07
34.24
28.37
27.66
27.17
14.27
200
180
160
140
120
100
80
60
40
20
0
ppm

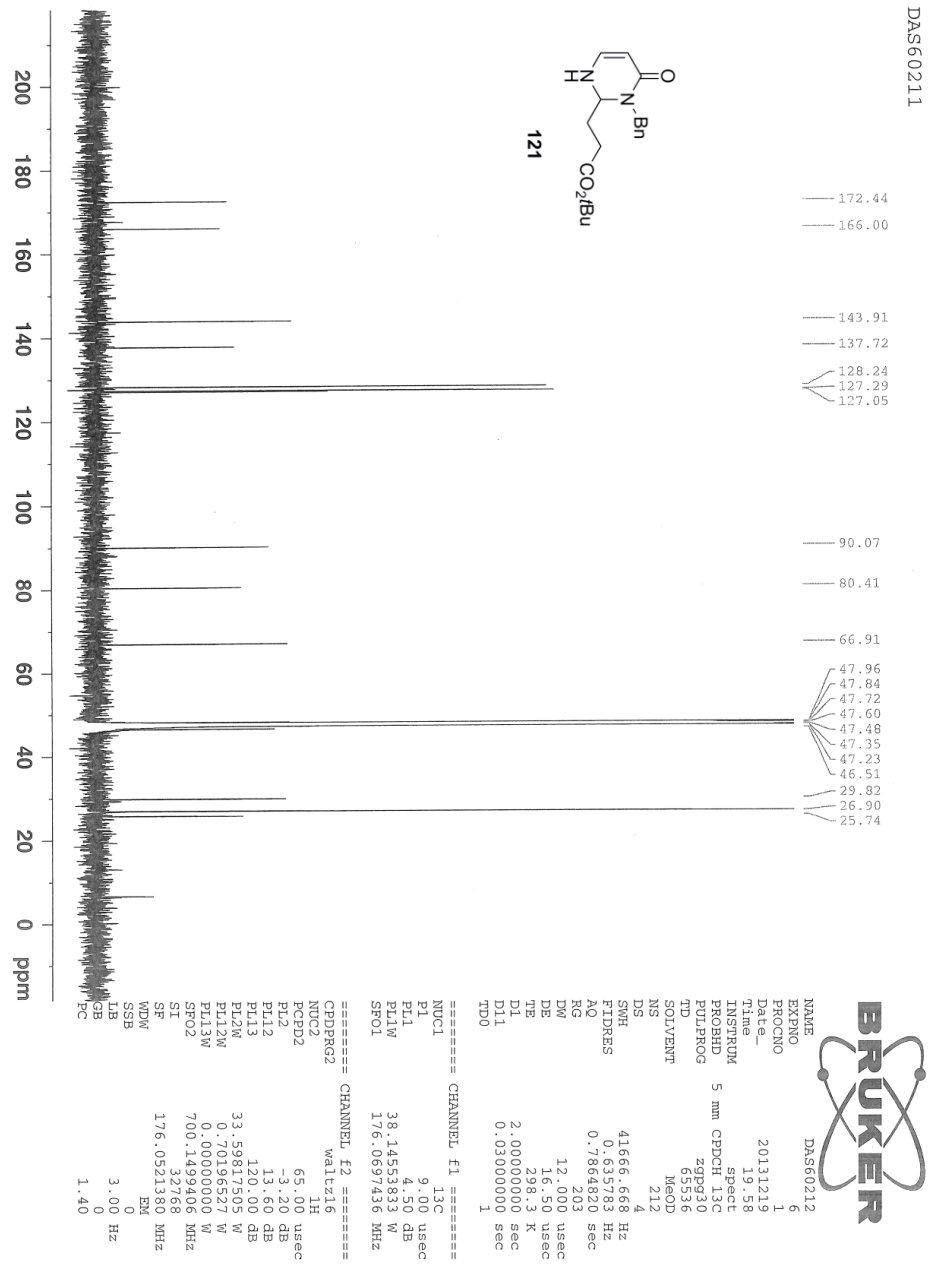

DAS52661
117
7.260
7.258
4.183
4.177
4.163
4.158
3.037
3.017
2.986
2.966
2.945
2.920
2.495
2.486
2.478
2.468
2.458
2.450
2.437
2.424
2.412
2.399
2.387
2.372
2.361
2.351
2.341
2.271
2.253
2.238
1.868
1.694
1.00
2.80
4.75
0.99
0.93
3.74
ppm
NAME DAS52661
EXPNO 1
PROCNO 1
Date_ 20131125
Time 8.45
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 20.2
DW 42.000 usec
DE 6.50 usec
TE 298.4 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 700.1471612 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00


DAS52661
117
171.83
119.48
77.34
77.16
76.98
75.02
39.79
36.14
31.88
28.90
28.05
25.47
12.50
BRUKER
NAME DAS52661
EXPNO 2
PROCNO 1
Date_ 20131125
Time 8.49
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 343
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864820 sec
RG 203
DW 12.000 usec
DE 16.50 usec
TE 298.3 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0697436 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 usec
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1499406 MHz
SI 32768
SF 176.0521152 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
200 180 160 140 120 100 80 60 40 20 0 ppm

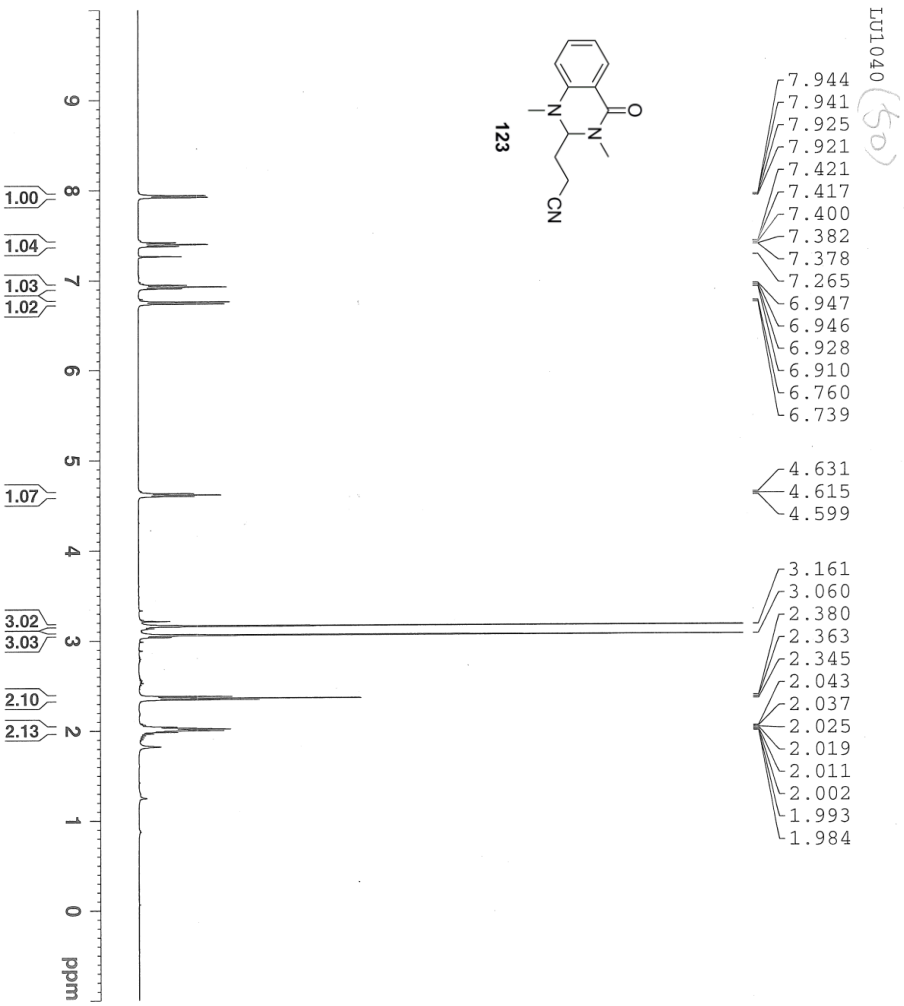

DAS50672
7.259
7.139
7.128
7.116
7.101
7.046
7.032
7.021
6.878
6.864
6.853
6.842
6.715
6.704
5.913
5.902
5.892
5.423
4.667
4.644
4.585
4.561
4.398
4.074
2.487
2.477
2.462
2.453
2.443
2.431
2.421
2.410
2.396
2.256
2.200
2.050
2.040
2.030
2.020
2.009
1.998
1.990
1.978
1.557
119
1.48
1.43
1.28
1.26
0.92
0.29
0.30
1.00
1.00
0.41
0.36
0.13
0.19
2.59
0.95
2.91
3.04
ppm
NAME DAS50672
EXPNO 1
PROCNO 1
Date_ 20131205
Time 20.24
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 32
DW 42.000 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
========== CHANNEL f1 ==========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471609 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00


DAS50672
119
169.86
140.13
128.45
126.64
120.14
119.37
118.67
117.75
59.38
43.45
29.00
22.23
13.66
200
180
160
140
120
100
80
60
40
20
0
ppm
BRUKER
NAME DAS50672
EXPNO 2
PROCNO 1
Date_ 20131205
Time 20.31
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1024
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864820 sec
RG 203
DW 12.000 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 176.0521152 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40


DAS60211
7.355
7.353
7.346
7.344
7.338
7.333
7.330
7.326
7.321
7.289
7.286
7.283
7.279
7.277
6.934
6.932
6.923
6.922
5.213
5.191
4.877
4.761
4.751
4.744
4.743
4.738
4.732
4.730
4.727
4.076
4.054
3.334
2.297
2.295
2.287
2.284
2.278
2.276
2.270
2.264
2.251
2.243
1.807
1.442
121
9
8
7
6
5
4
3
2
1
0
ppm
NAME DAS60212
EXPNO 5
PROCNO 1
Date_ 20131219
Time 19.54
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT MeOD
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 18
DW 42.000 usec
DE 6.50 usec
TE 298.4 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

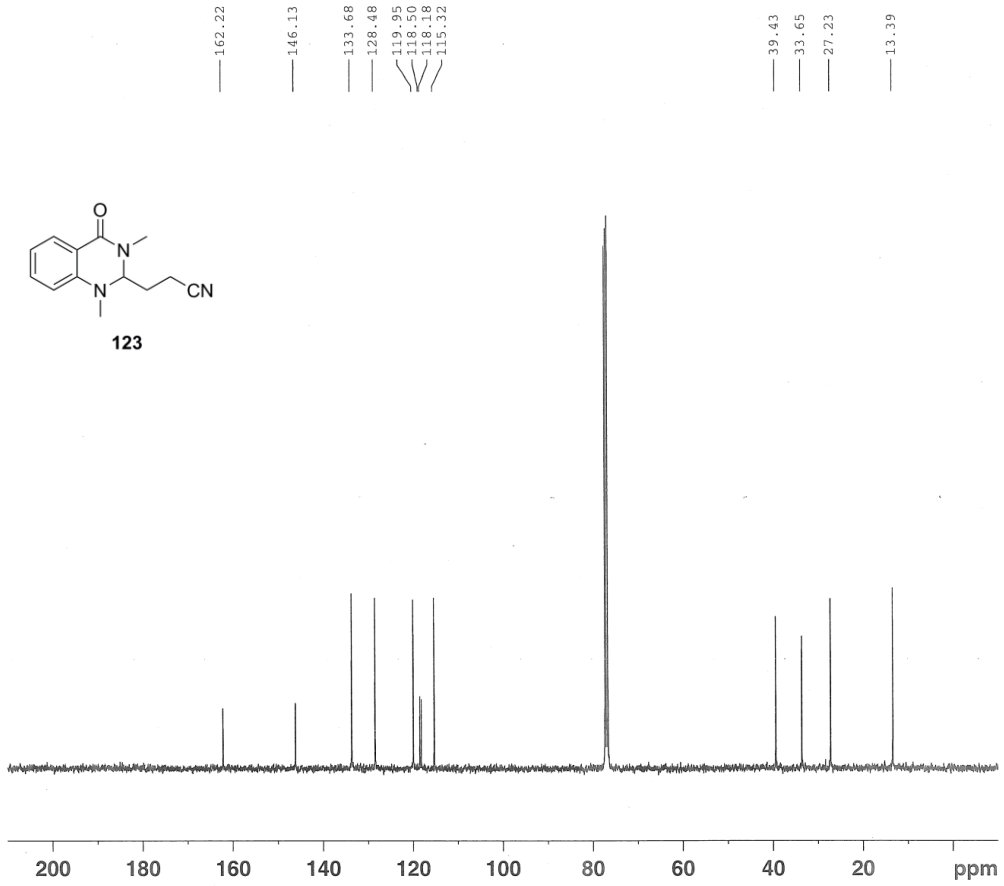



```
NAME                 DAS60212
EXPNO                        6
PROCNO                       1
Date_             20131219
Time_                    19.58
INSTRUM                  spect
PROBHD     5 mm CPDCH 13C
PULPROG              zgpg30
TD                        65536
SOLVENT                   MeOD
NS                          212
DS                            4
SWH                  41666.668 Hz
FIDRES                0.635783 Hz
AQ                    0.7864820 sec
RG                          203
DW                       12.000 usec
DE                       16.50 usec
TE                       298.3 K
D1                    2.00000000 sec
D11                   0.03000000 sec
TD0                          1

========== CHANNEL f1 ==========
NUC1                        13C
P1                        9.00 usec
PL1                       4.50 dB
PL1W               38.14553833 W
SFO1              176.0697436 MHz

========== CHANNEL f2 ==========
CPDPRG2                 waltz16
NUC2                         1H
PCPD2                     65.00 usec
PL2                       -3.20 dB
PL12                      13.60 dB
PL13                     120.00 dB
PL2W               33.59817505 W
PL12W               0.70196527 W
PL13W               0.00000000 W
SFO2              700.1499406 MHz
SI                       32768
SF                176.0521380 MHz
WDW                         EM
SSB                          0
LB                        3.00 Hz
GB                           0
PC                        1.40
```



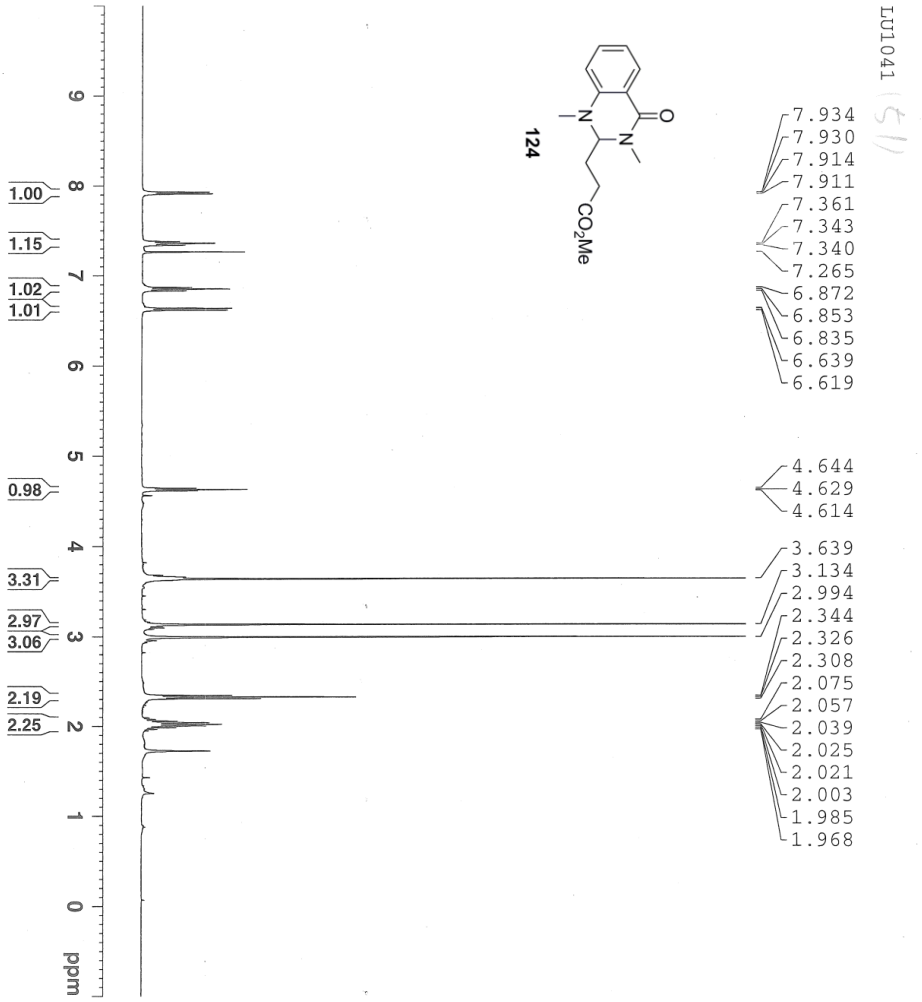

```
NAME                                    LU1040
EXPNO                                        1
PROCNO                                       1
Date_                                 20130407
Time_                                    20.31
INSTRUM                                robinson
PROBHD                 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                                        71.8
DW                                      69.600 us
DE                                       6.50 us
TE                                      298.6 K
D1                                   2.00000000 se
TD0                                          1

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

C13 LU1040 (50)



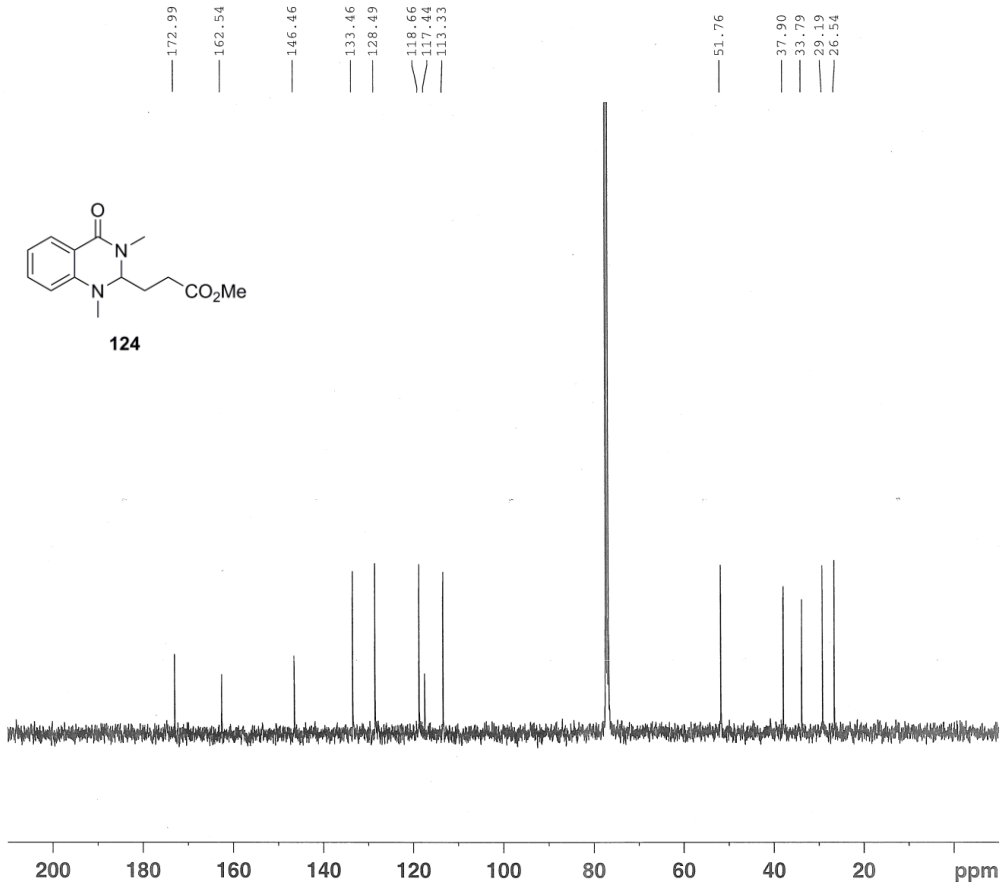
123

NAME	LU1040
EXPNO	3
PROCNO	1
Date_	20130407
Time	21.59
INSTRUM	robinson
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDC13
NS	600
DS	4
SWH	23980.814 Hz
FIDRES	0.365918 Hz
AQ	1.3664756 sec
RG	23170.5
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	100.6152900 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40



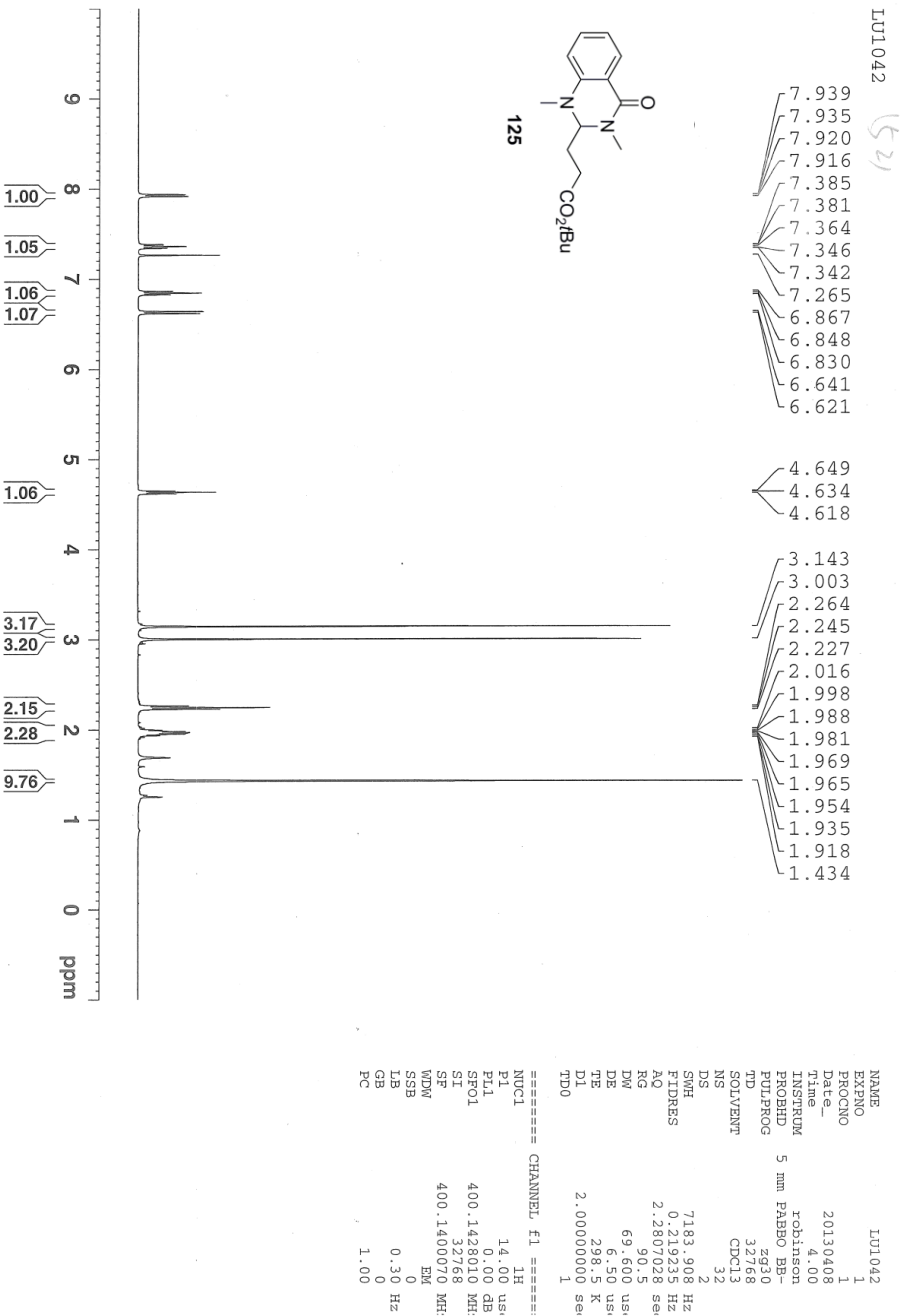

```
NAME                                    LU1041
EXPNO                                        1
PROCNO                                       1
Date_                                 20130407
Time_                                    23.55
INSTRUM                                robinson
PROBHD                 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                                        90.5
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 LU1041 (5')



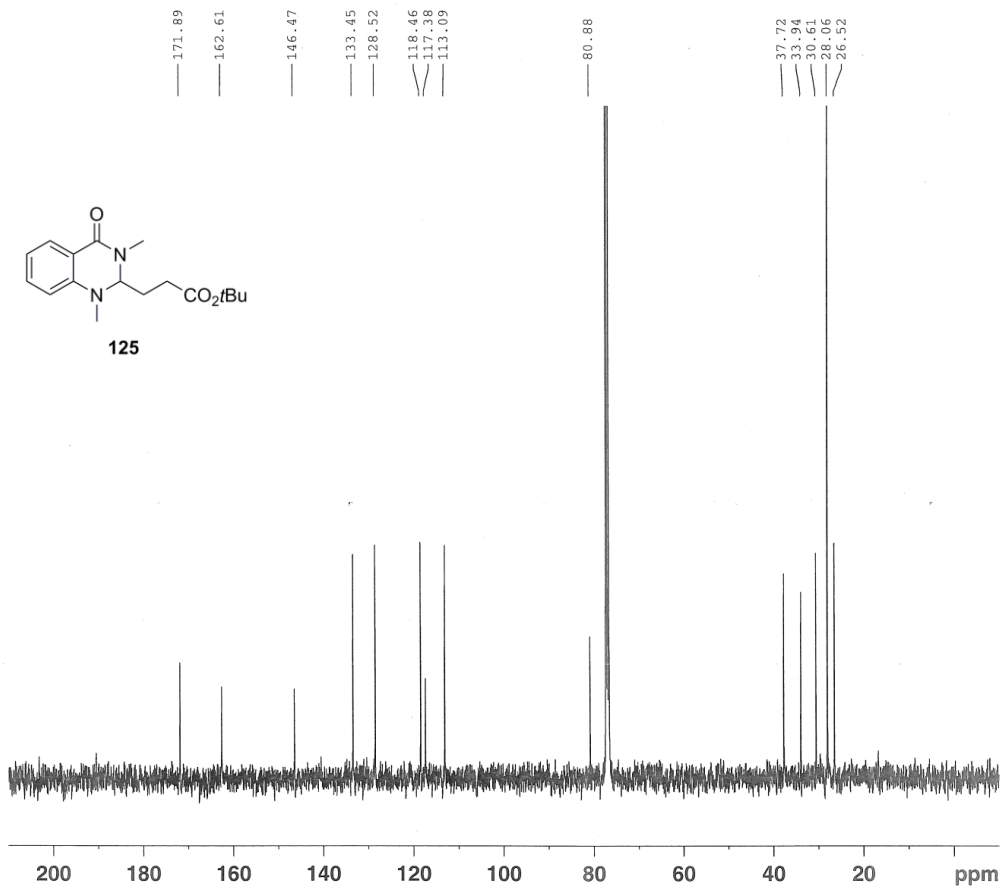
124

NAME	LU1041
EXPNO	3
PROCNO	1
Date_	20130408
Time	3.53
INSTRUM	robinson
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	500
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	300.0 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	100.6152861 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40



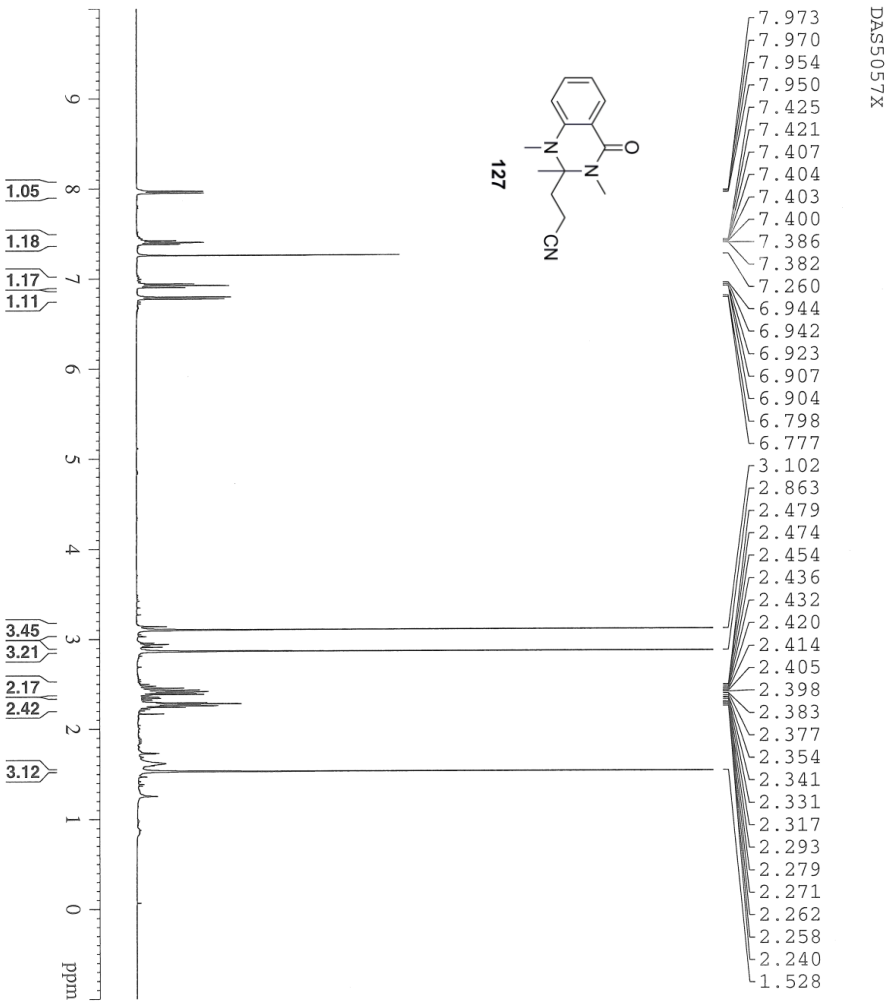

```
NAME                  LU1042
EXPNO                      1
PROCNO                     1
Date_               20130408
Time_                  4.00
INSTRUM                robinson
PROBHD     5 mm PABBO BB-
PULPROG                zg30
TD                     32768
SOLVENT                CDCl3
NS                        32
DS                         2
SWH                7183.908 Hz
FIDRES             0.219235 Hz
AQ                 2.2807028 se
RG                        90.5
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 LU1042



125

NAME	LU1042
EXPNO	3
PROCNO	1
Date_	20130408
Time	4.23
INSTRUM	robinson
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	500
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	300.0 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	100.6152853 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40


DAS5057X
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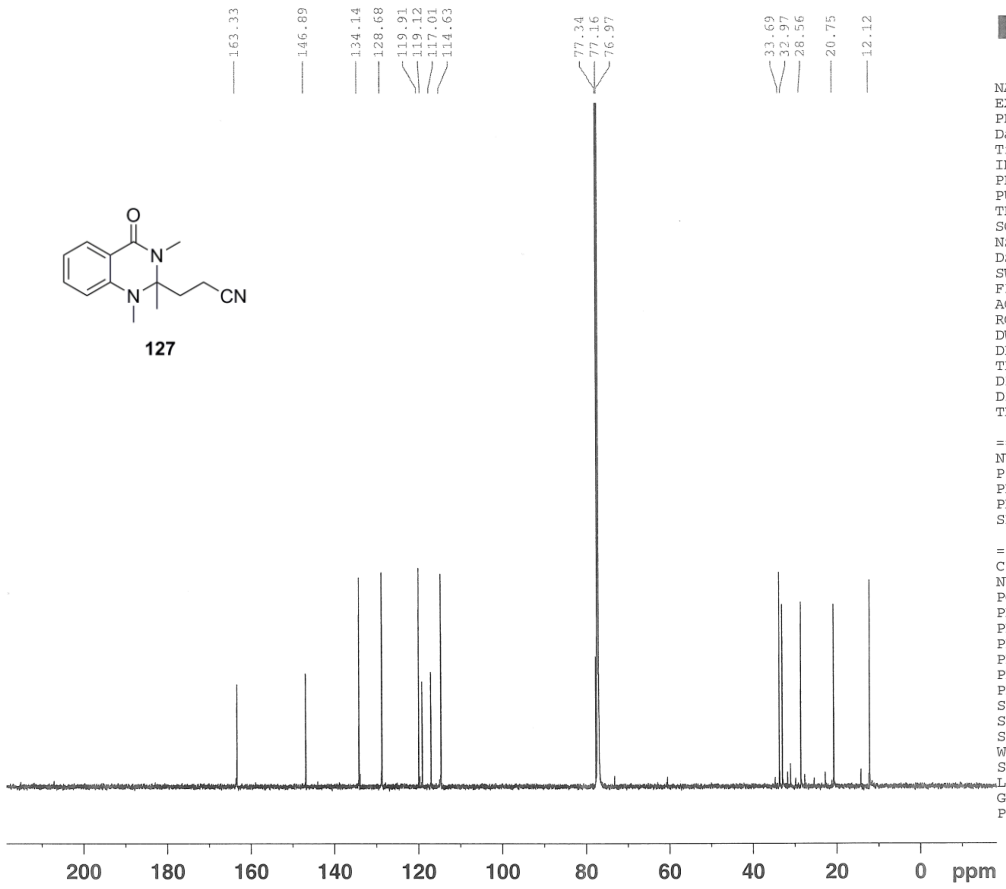
7.970
7.954
7.950
7.425
7.421
7.407
7.404
7.403
7.400
7.386
7.382
7.260
6.944
6.942
6.923
6.907
6.904
6.798
6.777
3.102
2.863
2.479
2.474
2.454
2.436
2.432
2.420
2.414
2.405
2.398
2.383
2.377
2.354
2.341
2.331
2.317
2.293
2.279
2.271
2.262
2.258
2.240
1.528
127
CN
1.05
1.18
1.17
1.11
3.45
3.21
2.17
2.42
3.12
ppm
NAME DAS5057X
EXPNO 1
PROCNO 1
Date_ 20130624
Time 13.59
INSTRUM robinson
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 24
DS 2
SWH 7183.908 Hz
FIDRES 0.219235 Hz
AQ 2.2807028 sec
RG 161.3
DW 69.600 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 usec
PL1 0.00 dB
SFO1 400.1428010 MHz
SI 32768
SF 400.1400092 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

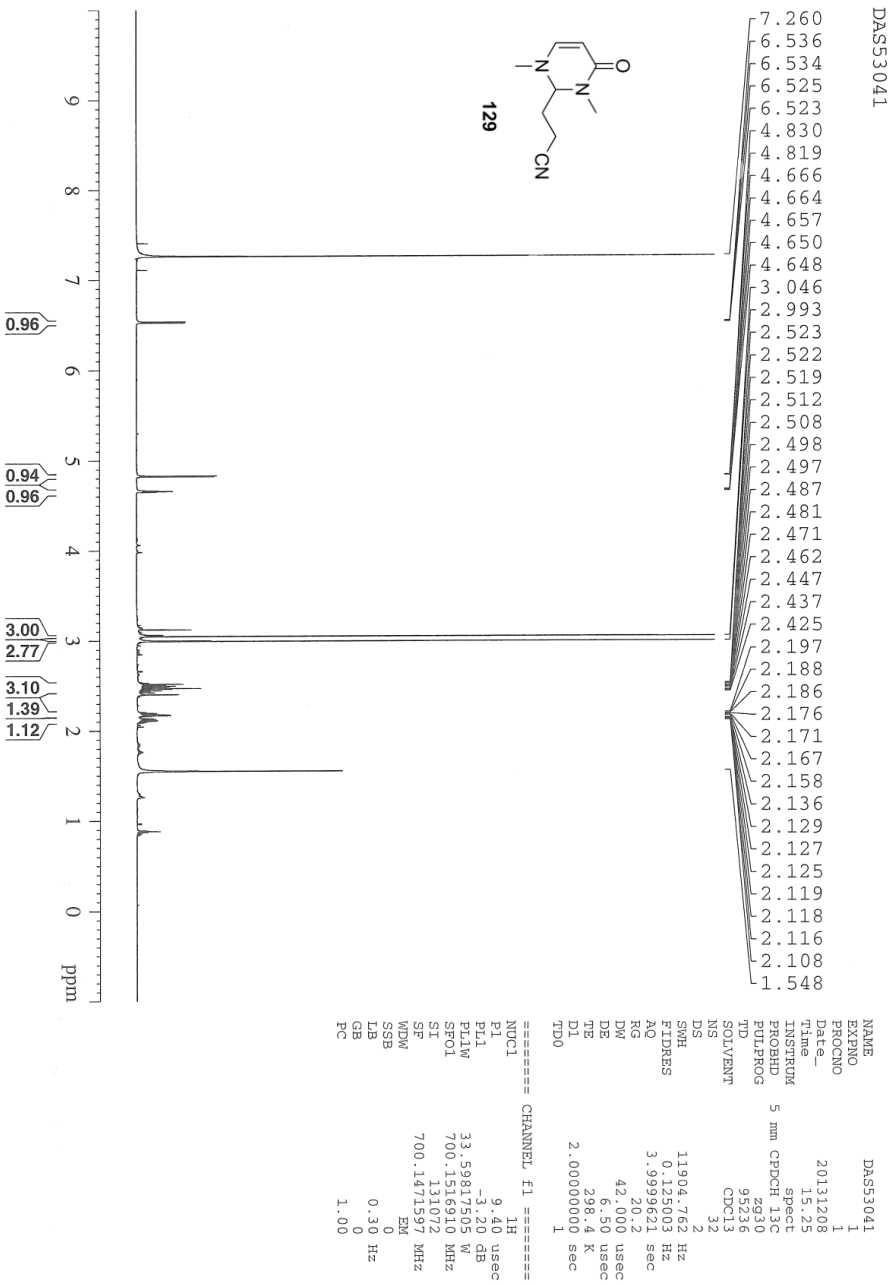
DAS33121



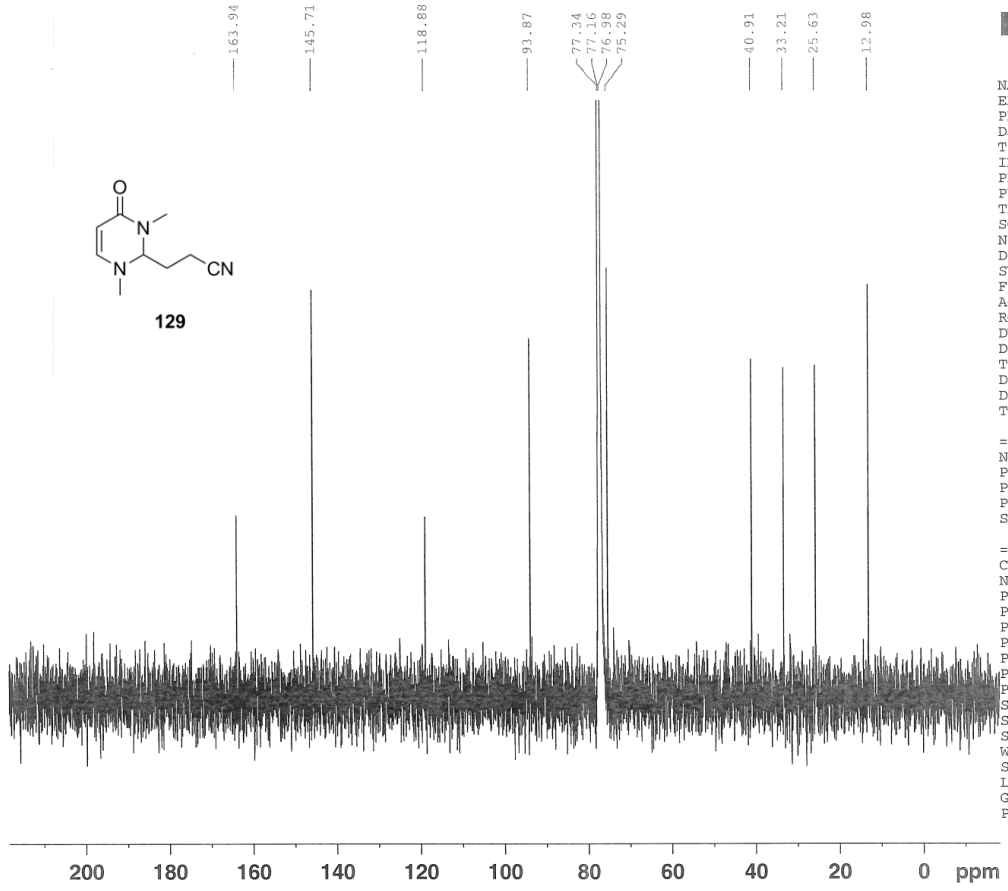
127

BRUKER

NAME	DAS33121
EXPNO	2
PROCNO	1
Date_	20131119
Time	16.57
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	160
DS	4
SWH	41666.668 Hz
FIDRES	0.635783 Hz
AQ	0.7864820 sec
RG	203
DW	12.000 usec
DE	16.50 usec
TE	298.3 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.00 usec
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0697436 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 usec
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1499406 MHz
SI	32768
SF	176.0521178 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40

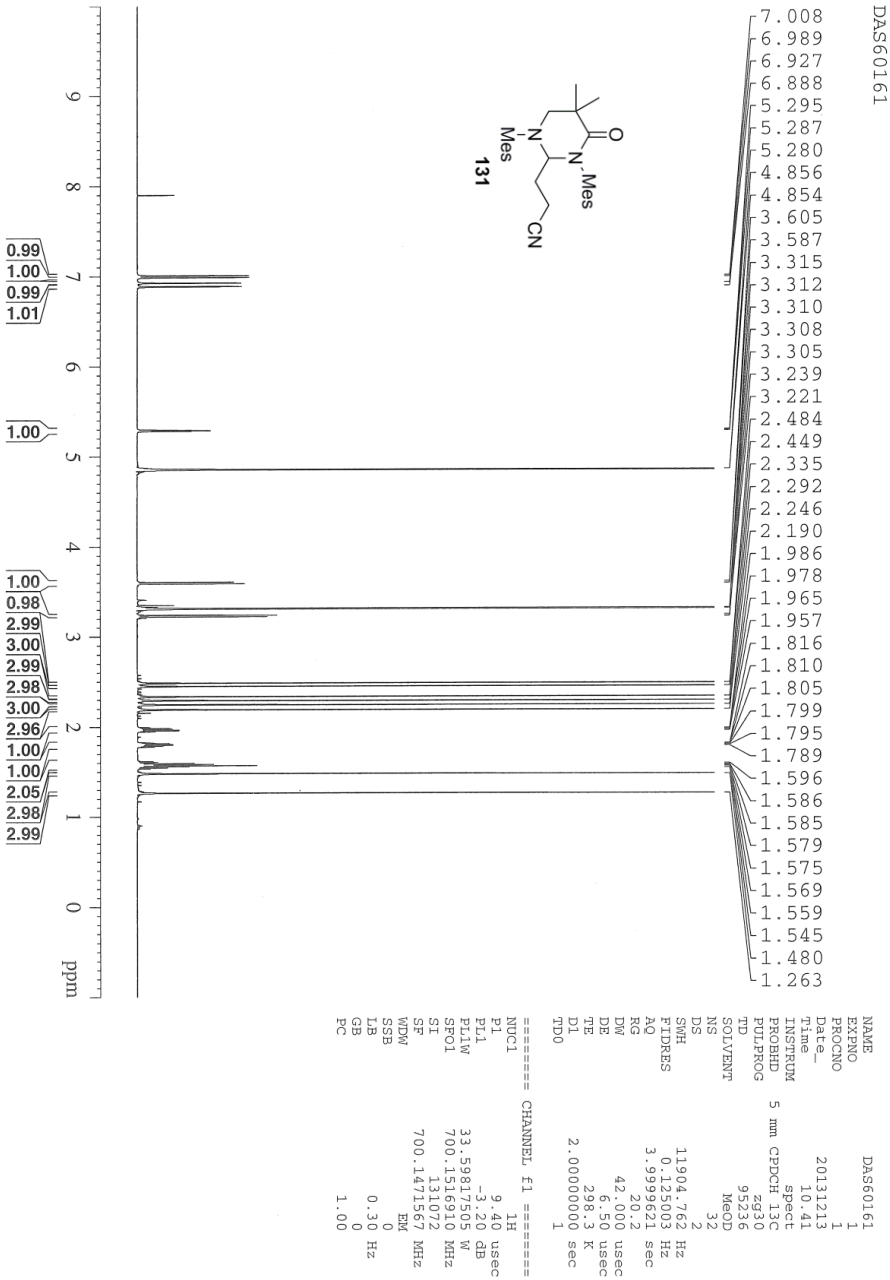

DAS53041
7.260
6.536
6.534
6.525
6.523
4.830
4.819
4.666
4.664
4.657
4.650
4.648
3.046
2.993
2.523
2.522
2.519
2.512
2.508
2.498
2.497
2.487
2.481
2.471
2.462
2.447
2.437
2.425
2.197
2.188
2.186
2.176
2.171
2.167
2.158
2.136
2.129
2.127
2.125
2.119
2.118
2.116
2.108
1.548
129
0.96
0.94
0.96
3.00
2.77
3.10
1.39
1.12
ppm
NAME DAS53041
EXPNO 1
PROCNO 1
Date_ 20131208
Time 15.25
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 95236
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 20.2
DW 42.000 usec
DE 6.50 usec
TE 298.4 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 700.1471597 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

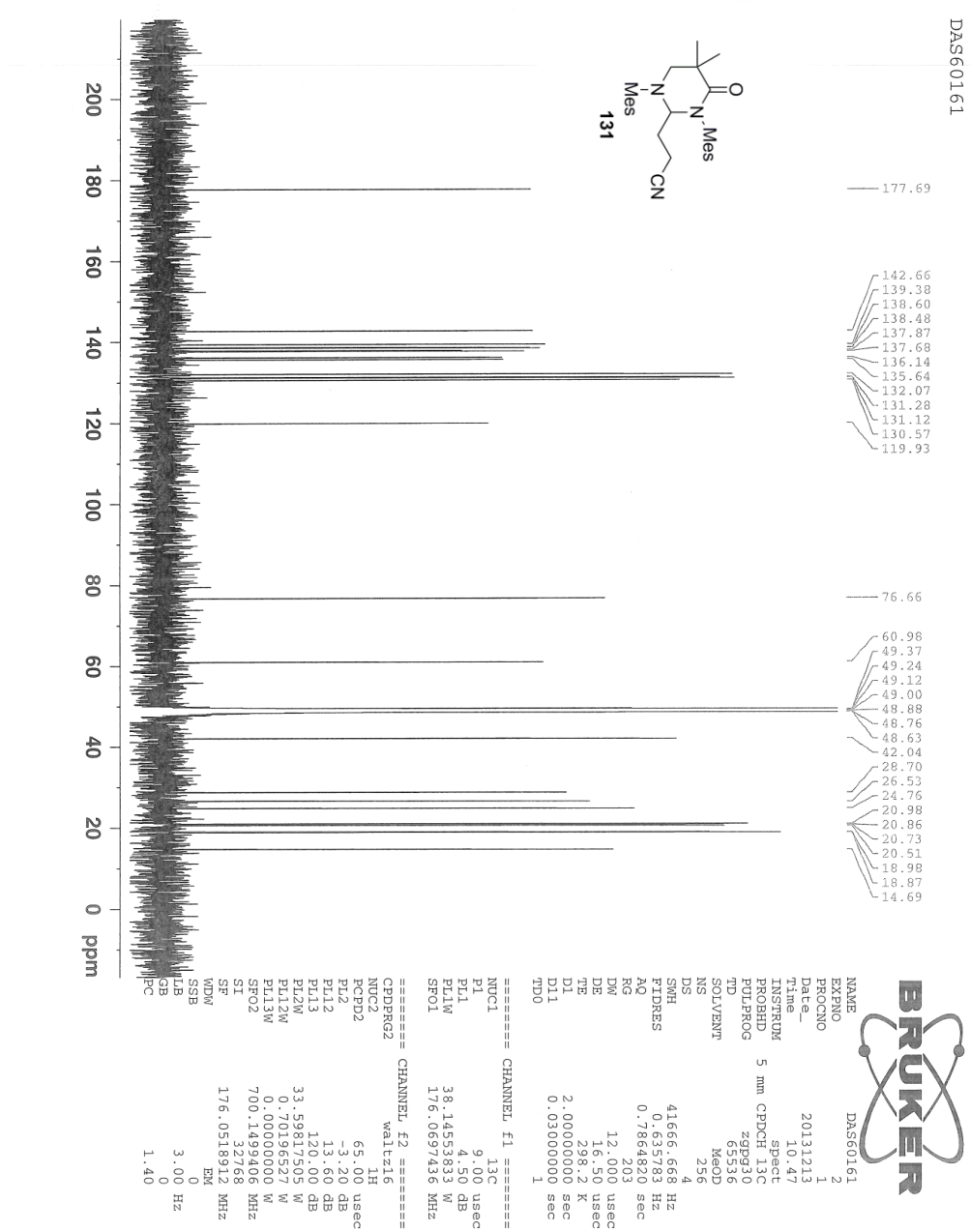
DAS53041

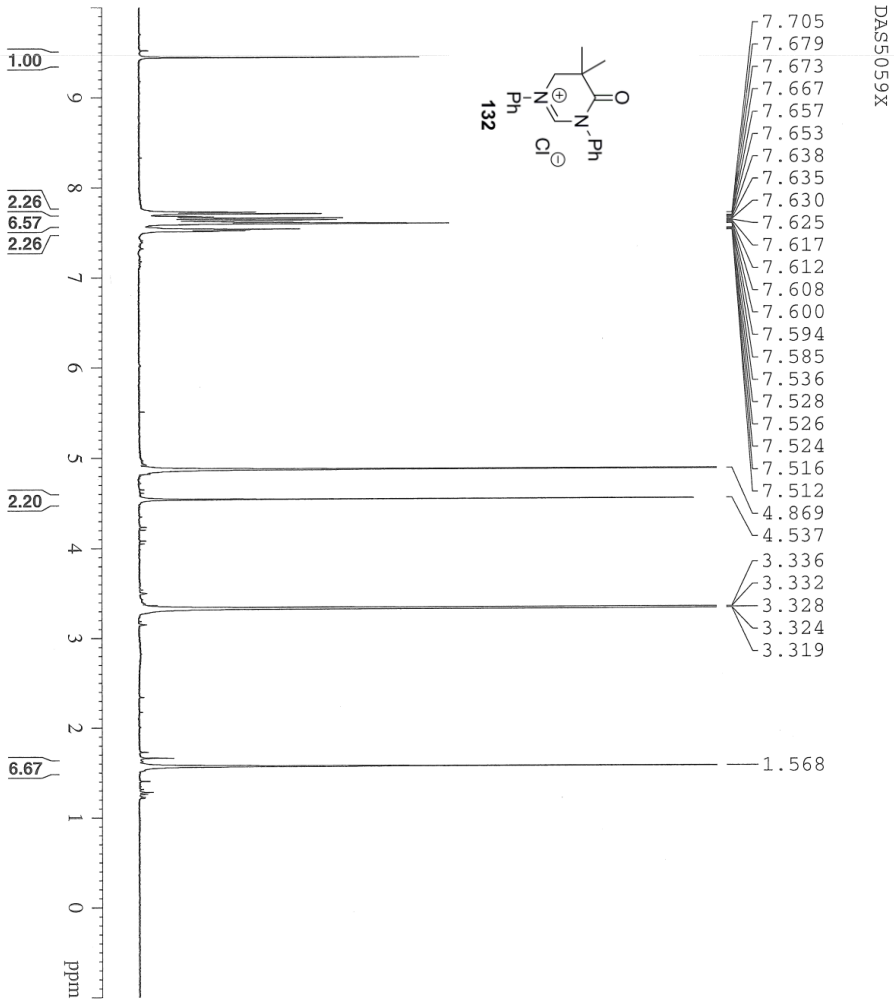


129

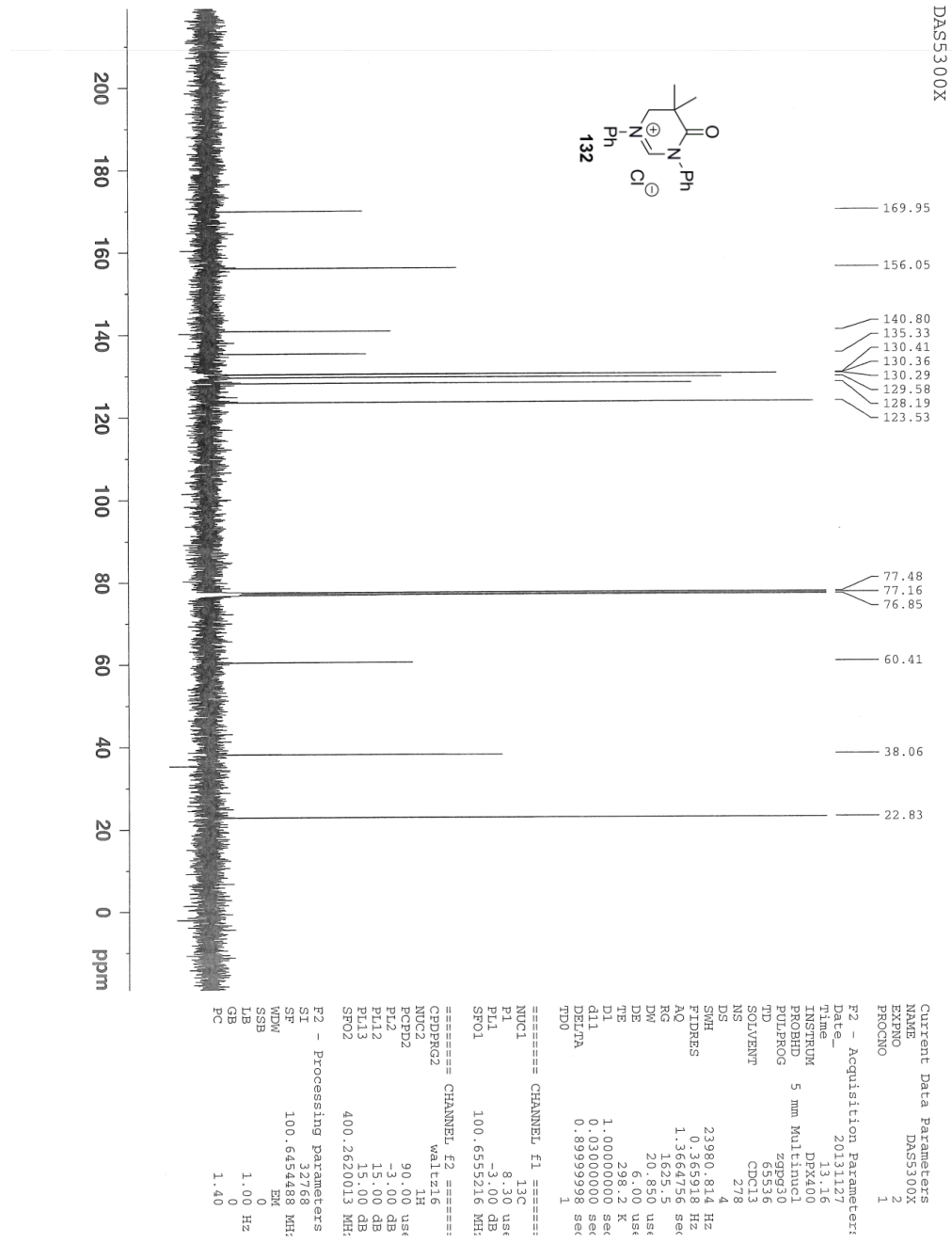
NAME	DAS53041
EXPNO	2
PROCNO	1
Date_	20131208
Time	15.31
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	446
DS	4
SWH	41666.668 Hz
FIDRES	0.635783 Hz
AQ	0.7864820 sec
RG	203
DW	12.000 usec
DE	16.50 usec
TE	298.2 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL 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	176.0521139 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40


DAS60161
7.008
6.989
6.927
6.888
5.295
5.287
5.280
4.856
4.854
3.605
3.587
3.315
3.312
3.310
3.308
3.305
3.239
3.221
2.484
2.449
2.335
2.292
2.246
2.190
1.986
1.978
1.965
1.957
1.816
1.810
1.805
1.799
1.795
1.789
1.596
1.586
1.585
1.579
1.575
1.569
1.559
1.545
1.480
1.263
Mes
N
N
O
CN
Mes
131
0.99
1.00
0.99
1.01
1.00
1.00
0.98
2.99
3.00
2.99
2.98
3.00
2.96
1.00
1.00
2.05
2.98
2.99
9
8
7
6
5
4
3
2
1
0
ppm
NAME DAS60161
EXPNO 1
PROCNO 1
Date_ 20131213
Time_ 10.41
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT MeOD
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 20.2
DW 42.000 usec
DE 6.50 usec
TE 298.3 K
D1 2.00000000 sec
TD0 1
========== CHANNEL f1 ==========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471567 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

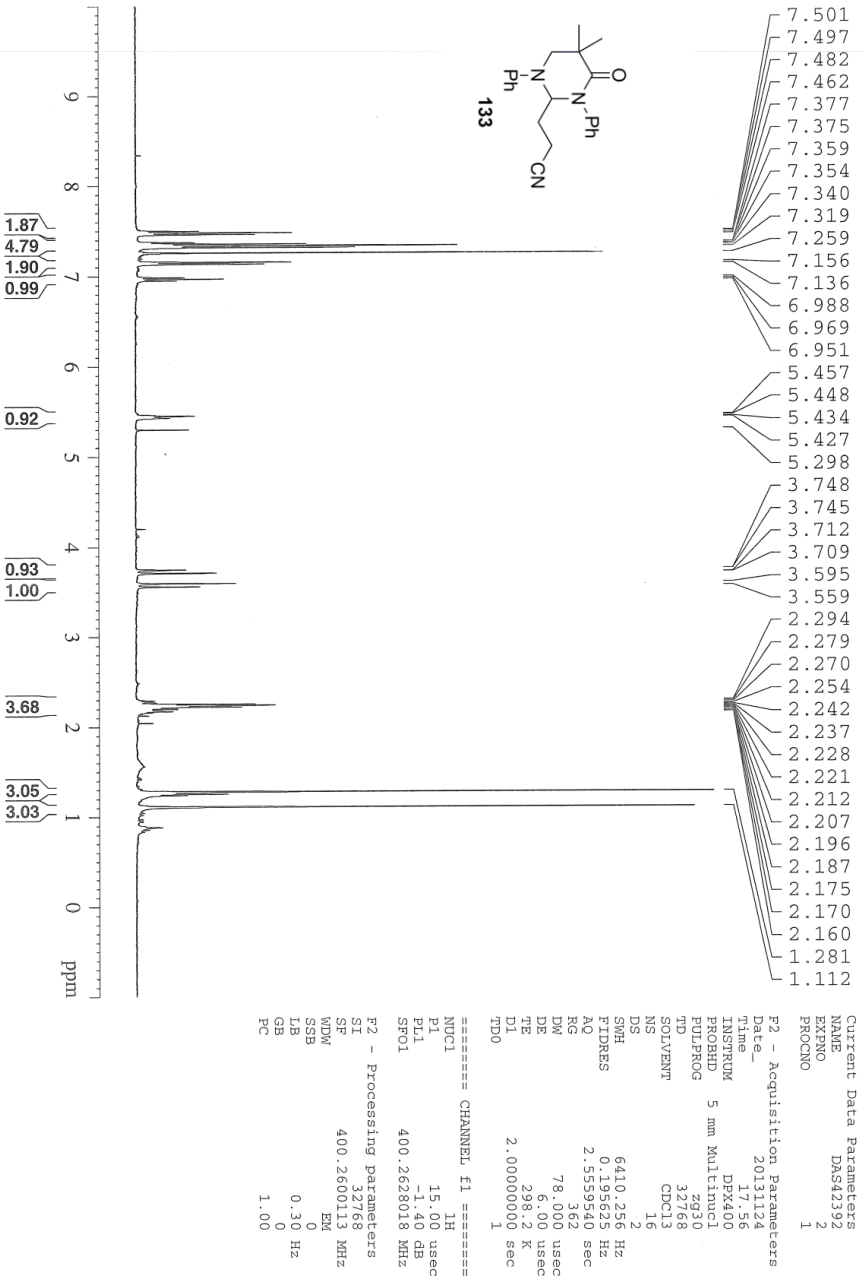

DAS60161
O
N
Mes
N
Mes
CN
131
177.69
142.66
139.38
138.60
138.48
137.87
137.68
136.14
135.64
132.07
131.28
131.12
130.57
119.93
76.66
60.98
49.37
49.24
49.12
49.00
48.88
48.76
48.63
42.04
28.70
26.53
24.76
20.98
20.86
20.73
20.51
18.98
18.87
14.69
BRUKER
NAME DAS60161
EXPNO 2
PROCNO 1
Date_ 20131213
Time_ 10.47
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT MeOD
NS 256
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 176.0518912 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
200 180 160 140 120 100 80 60 40 20 0 ppm

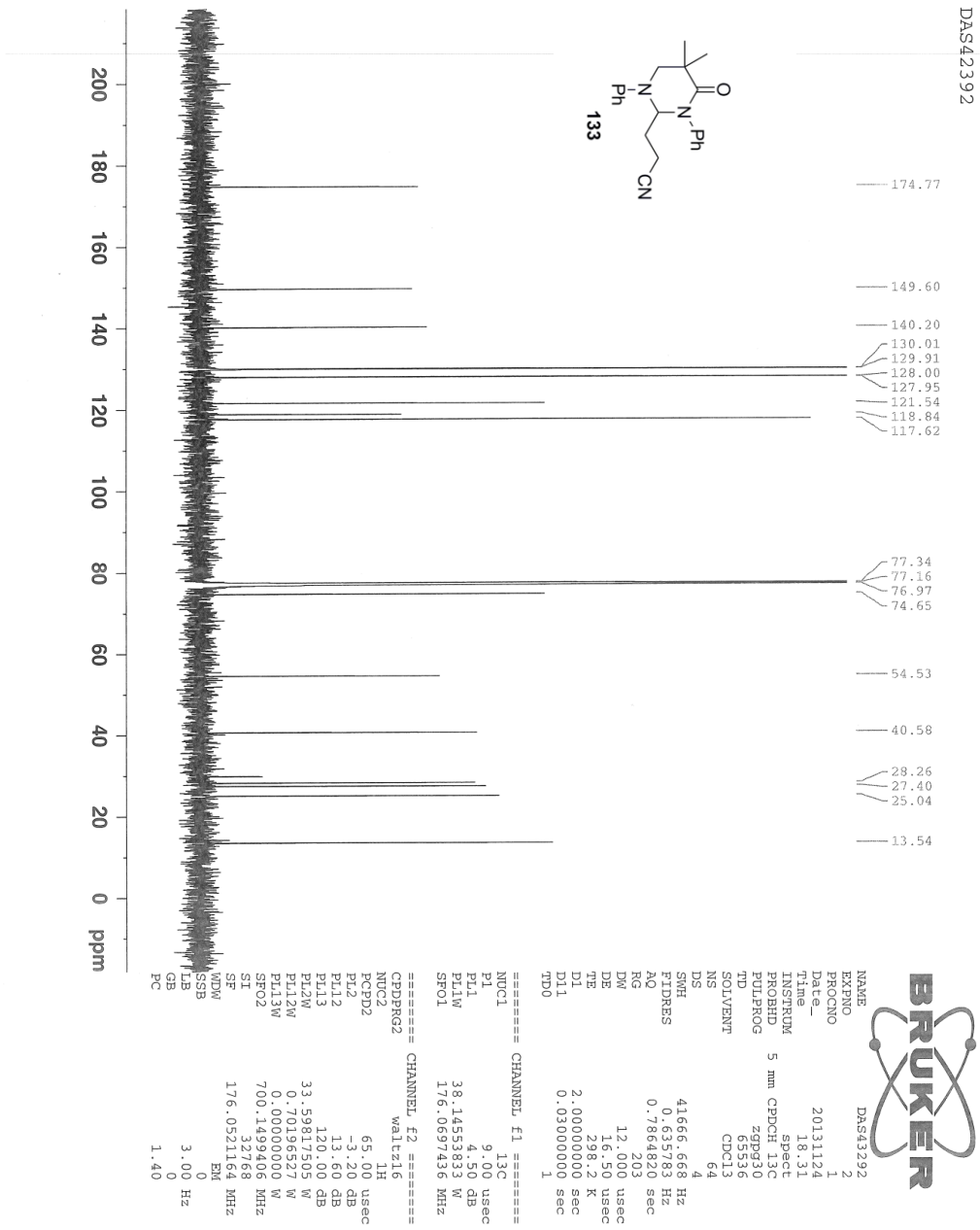


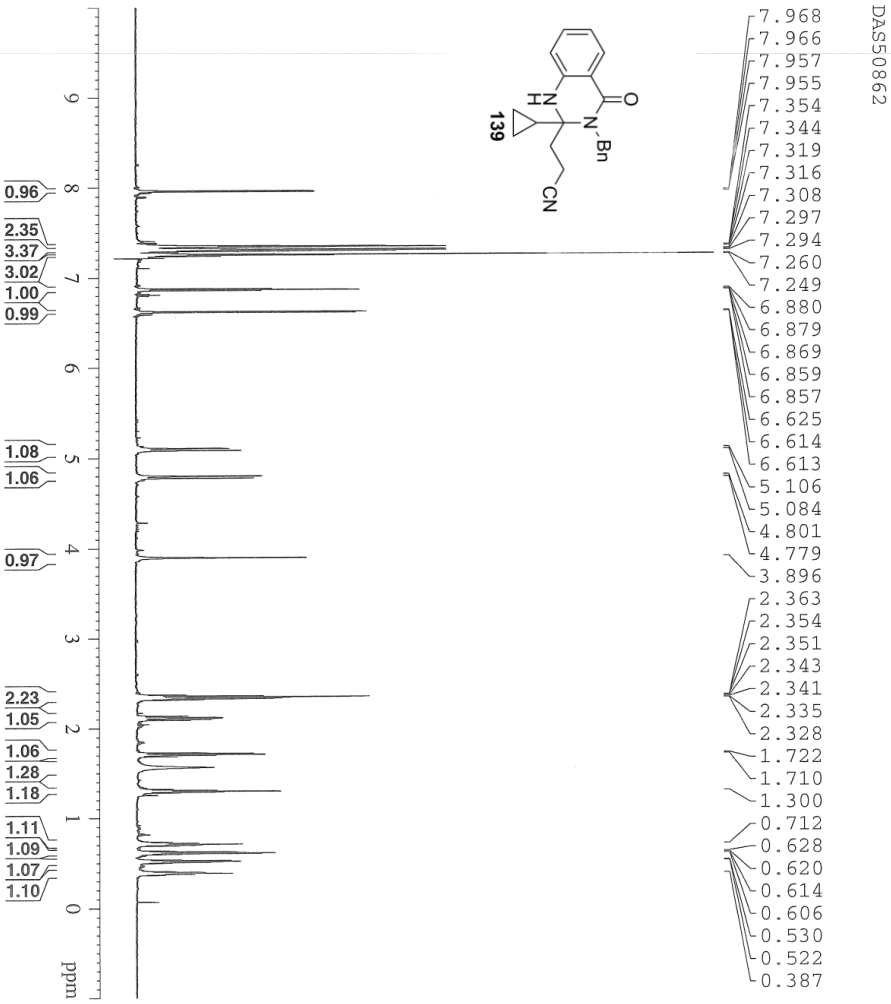

```
NAME                  DAS5059X
EXPNO                        1
PROCNO                       1
Date_              20130626
Time                    10.17
INSTRUM          robinson
PROBHD     5 mm PABBO BB-
PULPROG              zg30
TD                  32768
SOLVENT              MeOD
NS                     16
DS                      2
SWH              7183.908 Hz
FIDRES           0.219235 Hz
AQ               2.2807028 sec
RG                   228.1
DW                  69.600 usec
DE                   6.50 usec
TE                  298.3 K
D1               2.00000000 sec
TD0                          1

======== CHANNEL f1 ========
NUC1                      1H
P1                     14.00 usec
PL1                     0.00 dB
SFO1           400.1428010 MHz
SI                      32768
SF             400.1400000 MHz
WDW                        EM
SSB                         0
LB                       0.30 Hz
GB                          0
PC                       1.00
```

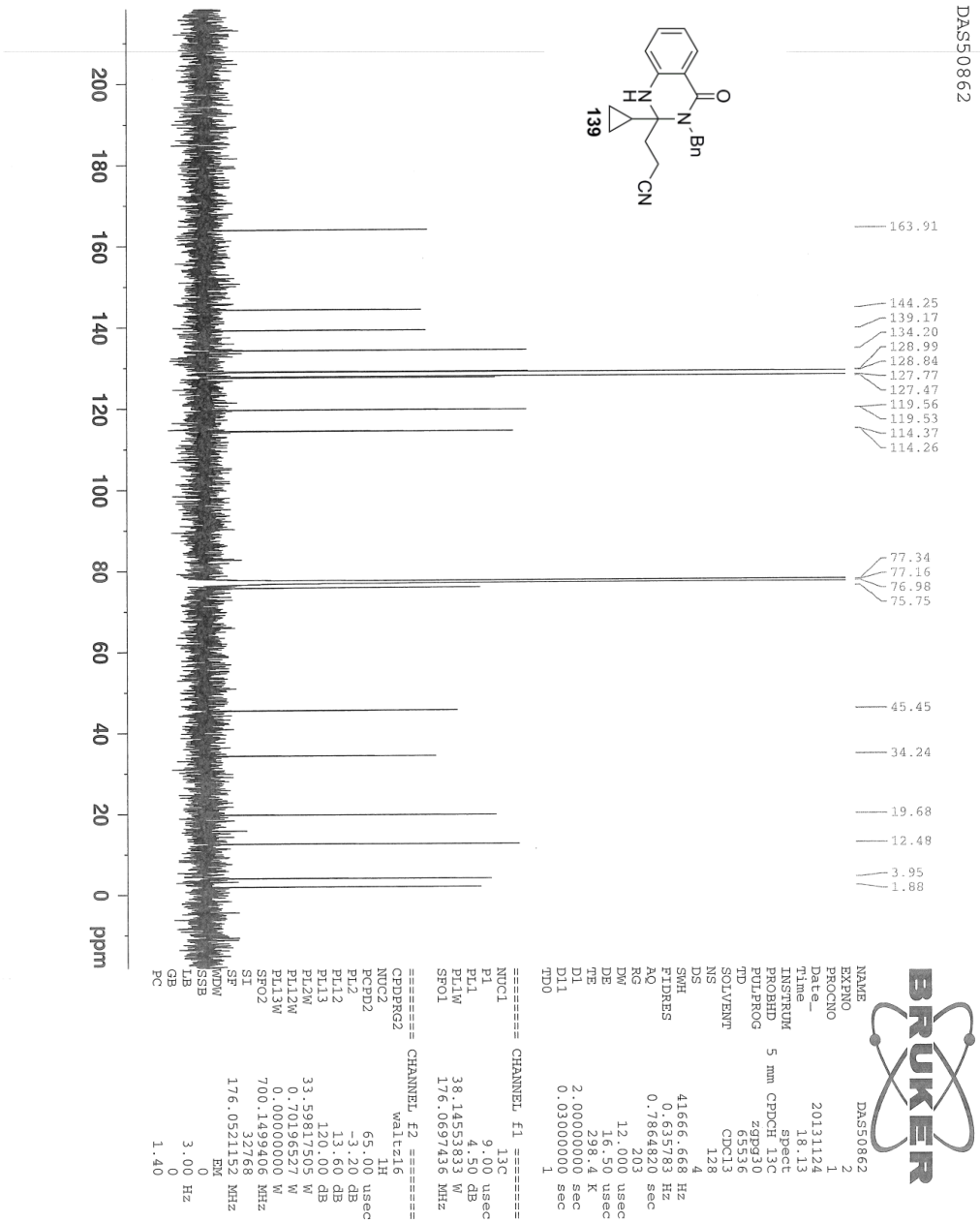


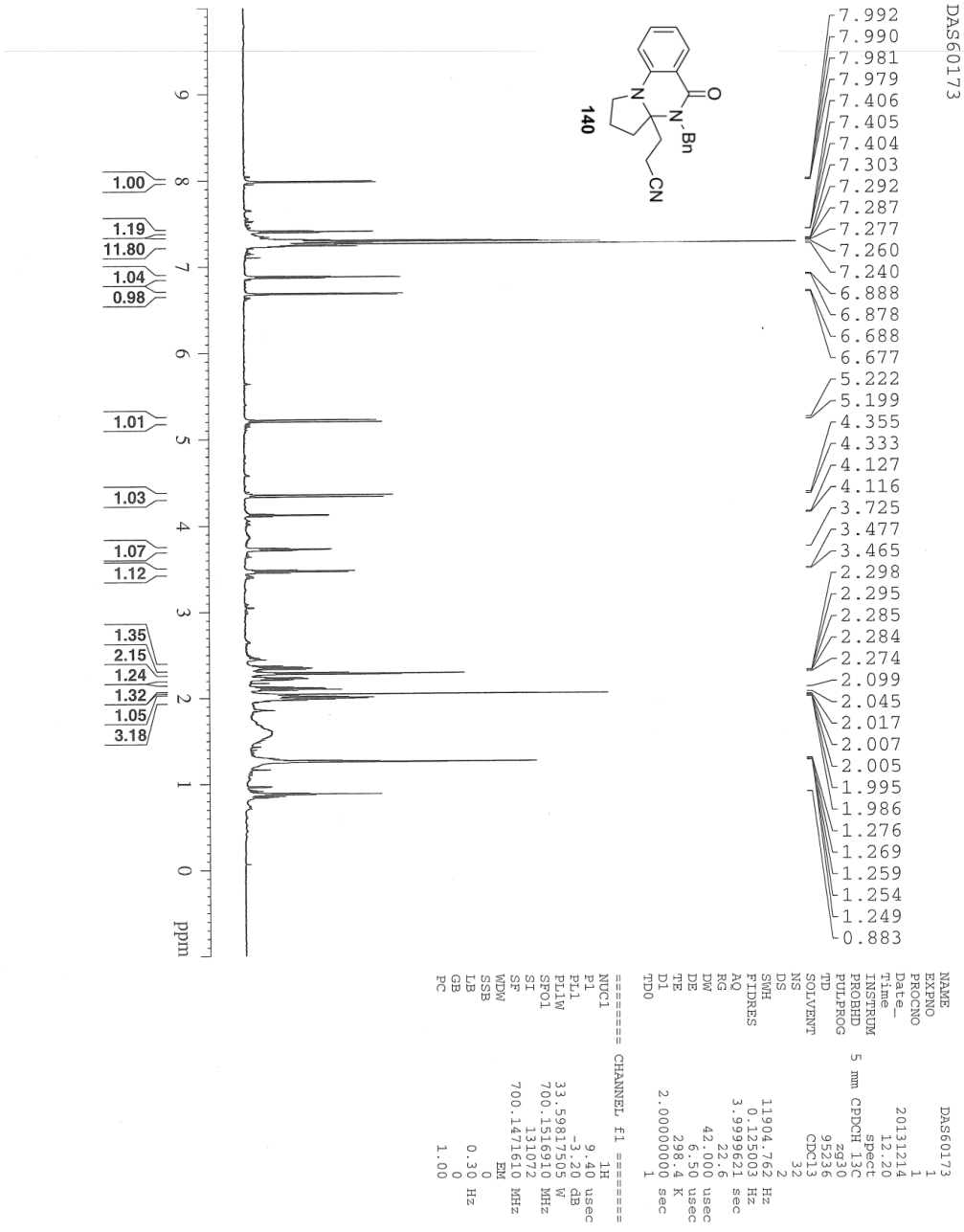

```
Current Data Parameters
NAME                  DAS5300X
EXPNO                        2
PROCNO                       1

F2 - Acquisition Parameters
Date_               20131127
Time                   13.16
INSTRUM                DPX400
PROBHD   5 mm Multinucl
PULPROG                zgpg30
TD                     65536
SOLVENT                CDCl3
NS                       278
DS                         4
SWH                23980.814 Hz
FIDRES             0.365918 Hz
AQ                 1.3664756 se
RG                      1625.5
DW                     20.850 us
DE                      6.00 us
TE                     298.2 K
D1                  1.00000000 se
D11                 0.03000000 se
DELTA               0.89999998 se
TD0                          1

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

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

F2 - Processing parameters
SI                       32768
SF            100.6454488 MHz
WDW                         EM
SSB                          0
LB                        1.00 Hz
GB                           0
PC                        1.40
```

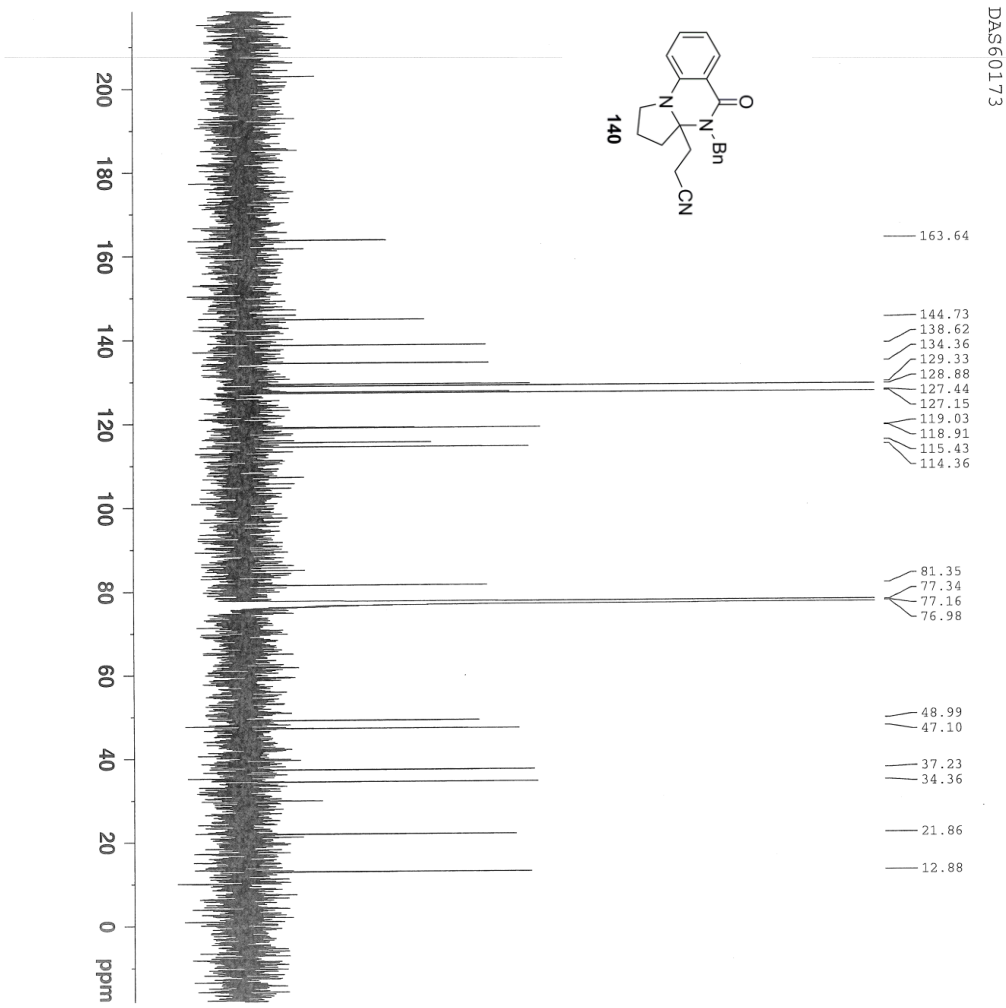

DAS42392
7.501
7.497
7.482
7.462
7.377
7.375
7.359
7.354
7.340
7.319
7.259
7.156
7.136
6.988
6.969
6.951
5.457
5.448
5.434
5.427
5.298
3.748
3.745
3.712
3.709
3.595
3.559
2.294
2.279
2.270
2.254
2.242
2.237
2.228
2.221
2.212
2.207
2.196
2.187
2.175
2.170
2.160
1.281
1.112
133
1.87
4.79
1.90
0.99
0.92
0.93
1.00
3.68
3.05
3.03
ppm
Current Data Parameters
NAME DAS42392
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20131124
Time_ 17.56
INSTRUM DPX400
PROBHD 5 mm Multinucl
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 16
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 362
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 400.2600113 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00


DAS42392
133
174.77
149.60
140.20
130.01
129.91
128.00
127.95
121.54
118.84
117.62
77.34
77.16
76.97
74.65
54.53
40.58
28.26
27.40
25.04
13.54
200
180
160
140
120
100
80
60
40
20
0
ppm

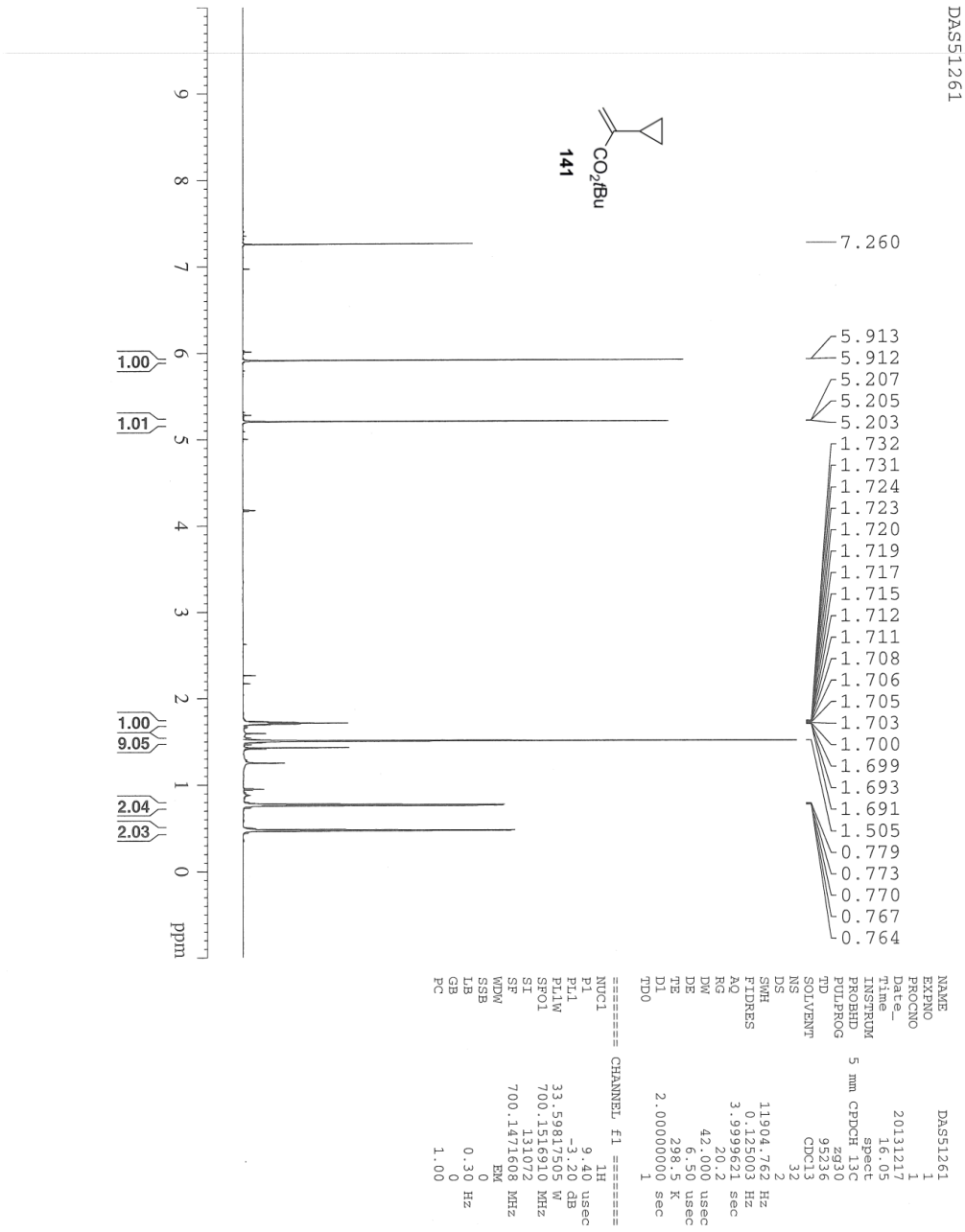

DAS50862
7.968
7.966
7.957
7.955
7.354
7.344
7.319
7.316
7.308
7.297
7.294
7.260
7.249
6.880
6.879
6.869
6.859
6.857
6.625
6.614
6.613
5.106
5.084
4.801
4.779
3.896
2.363
2.354
2.351
2.343
2.341
2.335
2.328
1.722
1.710
1.300
0.712
0.628
0.620
0.614
0.606
0.530
0.522
0.387
NAME DAS50862
EXPNO 3
PROCNO 1
Date_ 20131125
Time 9.12
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 32
DW 42.000 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
========== CHANNEL f1 ==========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471598 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
139
0.96
2.35
3.37
3.02
1.00
0.99
1.08
1.06
0.97
2.23
1.05
1.06
1.28
1.18
1.11
1.09
1.07
1.10
ppm

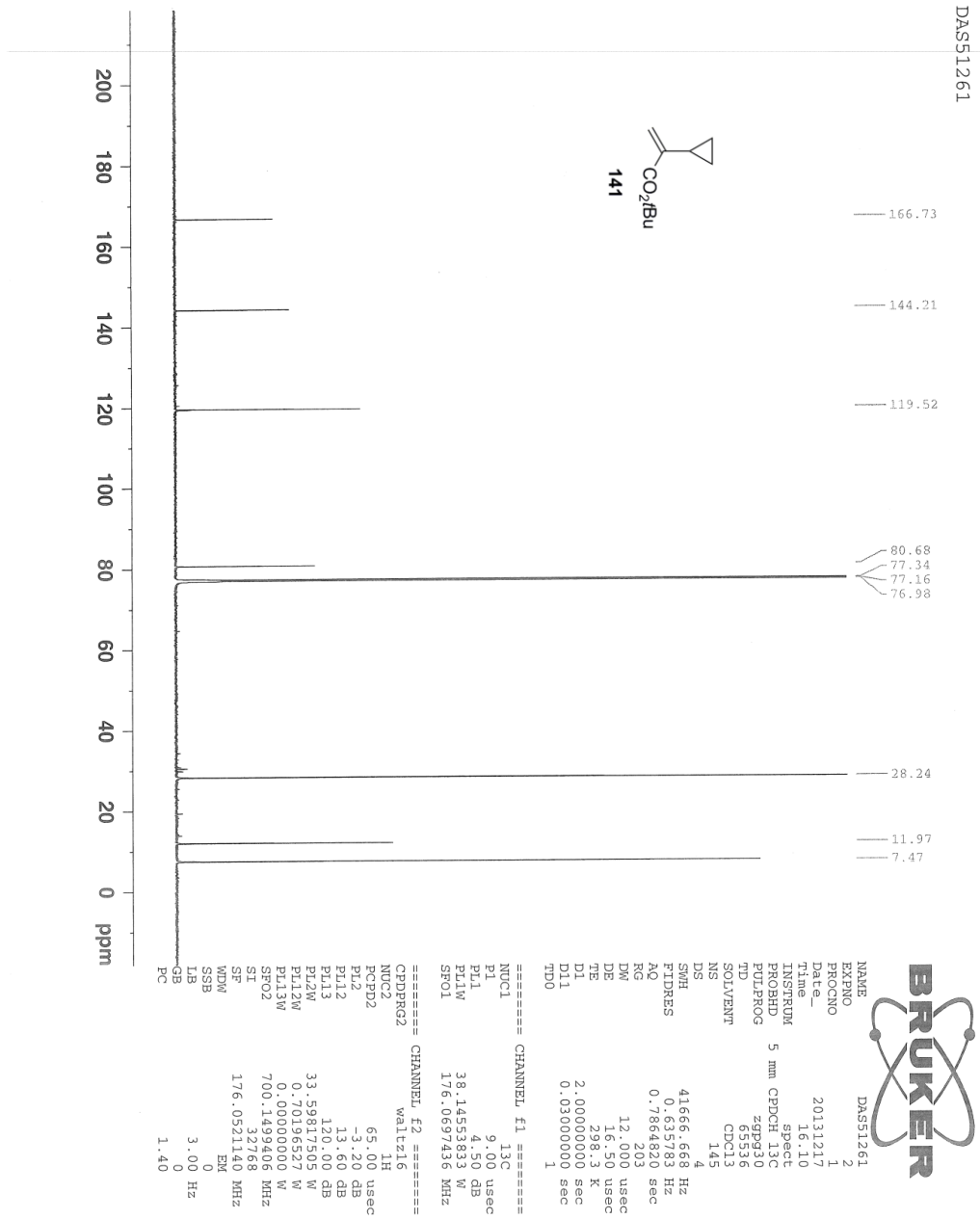

DAS50862
139
Bn
CN
163.91
144.25
139.17
134.20
128.99
128.84
127.77
127.47
119.56
119.53
114.37
114.26
77.34
77.16
76.98
75.75
45.45
34.24
19.68
12.48
3.95
1.88
NAME DAS50862
EXPNO 2
PROCNO 1
Date_ 20131124
Time 18.13
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 128
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864820 sec
RG 203
DW 12.000 usec
DE 16.50 usec
TE 298.4 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 176.0521152 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
200 180 160 140 120 100 80 60 40 20 0 ppm

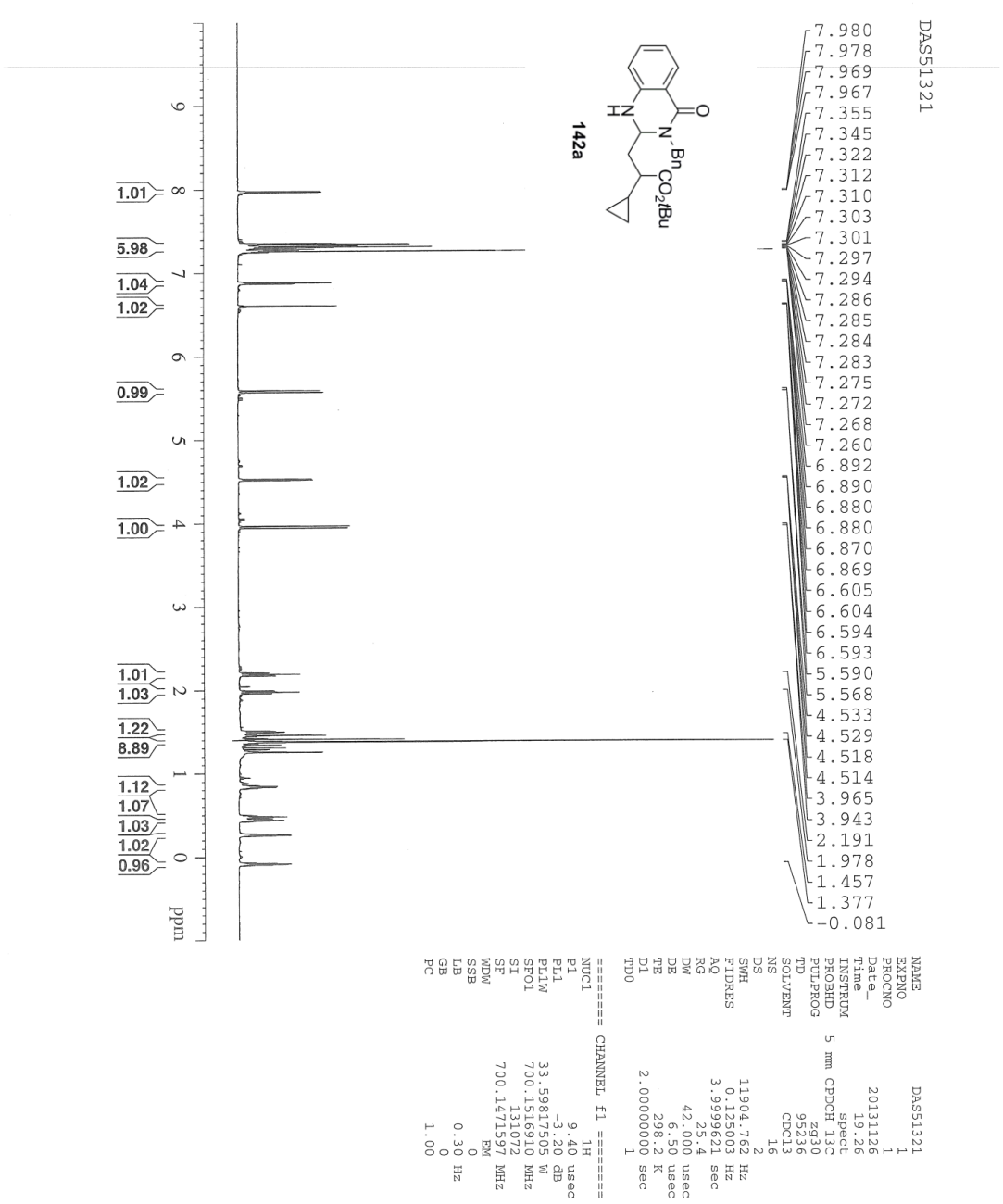

DAS60173
7.992
7.990
7.981
7.979
7.406
7.405
7.404
7.303
7.292
7.287
7.277
7.260
7.240
6.888
6.878
6.688
6.677
5.222
5.199
4.355
4.333
4.127
4.116
3.725
3.477
3.465
2.298
2.295
2.285
2.284
2.274
2.099
2.045
2.017
2.007
2.005
1.995
1.986
1.276
1.269
1.259
1.254
1.249
0.883
O
N
N
Bn
CN
140
1.00
1.19
11.80
1.04
0.98
1.01
1.03
1.07
1.12
1.35
2.15
1.24
1.32
1.05
3.18
9
8
7
6
5
4
3
2
1
0
ppm
NAME DAS60173
EXPNO 1
PROCNO 1
Date_ 20131214
Time 12.20
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 22.6
DW 42.000 usec
DE 6.50 usec
TE 298.4 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 700.1471610 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

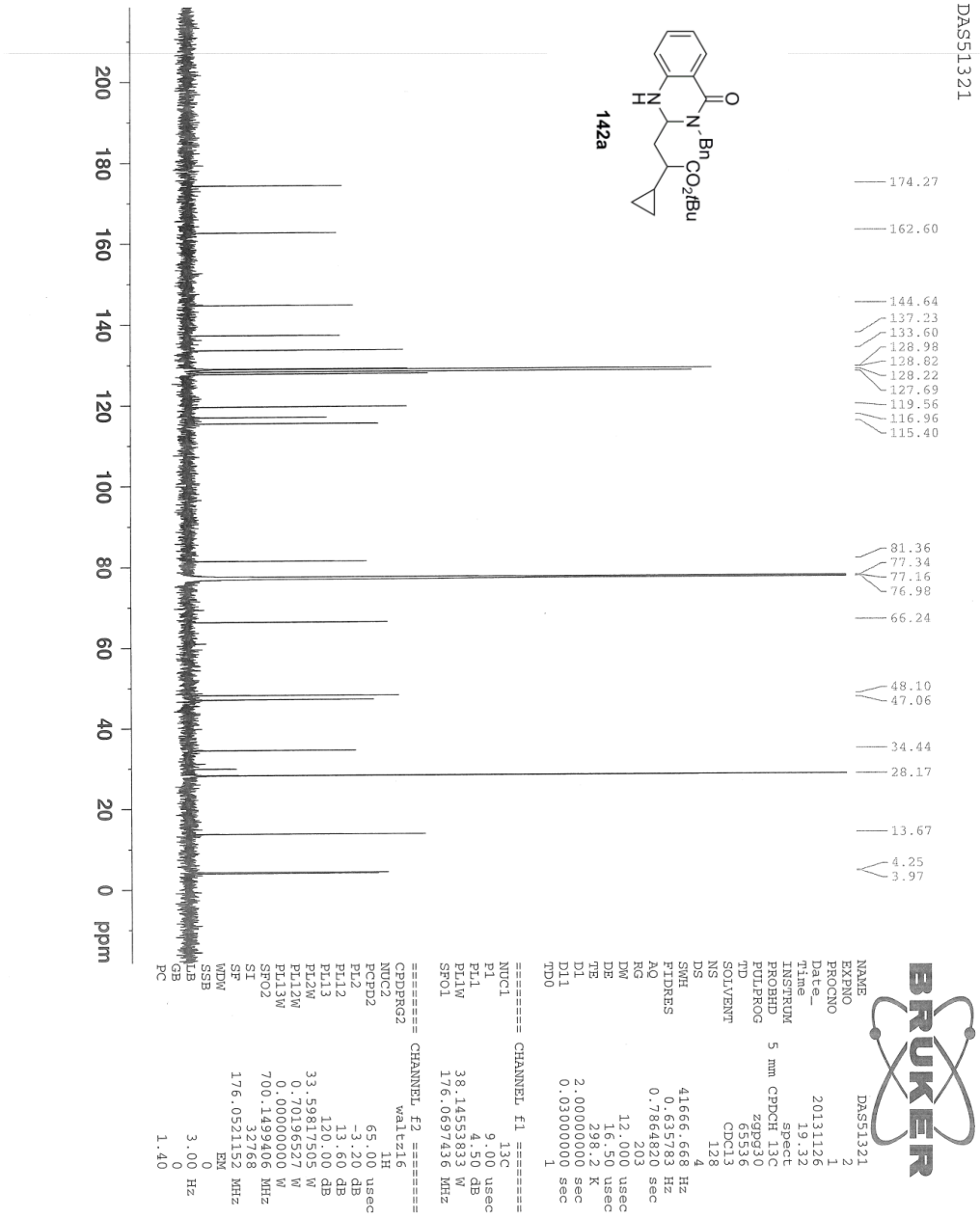



```
NAME                    DAS60173
EXPNO                          3
PROCNO                         1
Date_               20131216
Time                      10.12
INSTRUM                    spect
PROBHD     5 mm CPDCH 13C
PULPROG                zgpg30
TD                        65536
SOLVENT                   CDCl3
NS                          261
DS                            4
SWH                   41666.668 Hz
FIDRES                0.635783 Hz
AQ                    0.7864820 sec
RG                          203
DW                       12.000 usec
DE                       16.50 usec
TE                       298.3 K
D1                    2.00000000 sec
D11                   0.03000000 sec
TD0                            1

======== CHANNEL f1 ========
NUC1                        13C
P1                         9.00 usec
PL1                        4.50 dB
PL1W                 38.14553833 W
SFO1                 176.0697436 MHz

======== CHANNEL f2 ========
CPDPRG2                  waltz16
NUC2                         1H
PCPD2                     65.00 usec
PL2                       -3.20 dB
PL12                      13.60 dB
PL13                     120.00 dB
PL2W                 33.59817505 W
PL12W                 0.70196527 W
PL13W                 0.00000000 W
SFO2                 700.1499406 MHz
SI                         32768
SF                   176.0521139 MHz
WDW                           EM
SSB                            0
LB                          3.00 Hz
GB                             0
PC                          1.40
```


DAS51261
CO2tBu
141
7.260
5.913
5.912
5.207
5.205
5.203
1.732
1.731
1.724
1.723
1.720
1.719
1.717
1.715
1.712
1.711
1.708
1.706
1.705
1.703
1.700
1.699
1.693
1.691
1.505
0.779
0.773
0.770
0.767
0.764
1.00
1.01
1.00
9.05
2.04
2.03
ppm
NAME DAS51261
EXPNO 1
PROCNO 1
Date_ 20131217
Time_ 16.05
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 20.2
DW 42.000 usec
DE 6.50 usec
TE 298.5 K
D1 2.00000000 sec
TD0 1
========== CHANNEL f1 ==========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471608 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00


DAS51261
CO2tBu
141
166.73
144.21
119.52
80.68
77.34
77.16
76.98
28.24
11.97
7.47
200
180
160
140
120
100
80
60
40
20
0
ppm
BRUKER
NAME DAS51261
EXPNO 2
PROCNO 1
Date_ 20131217
Time 16.10
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 145
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864820 sec
RG 203
DW 12.000 usec
DE 16.50 usec
TE 298.3 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0697436 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 usec
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1499406 MHz
SI 32768
SF 176.0521140 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40


DAS51321
7.980
7.978
7.969
7.967
7.355
7.345
7.322
7.312
7.310
7.303
7.301
7.297
7.294
7.286
7.285
7.284
7.283
7.275
7.272
7.268
7.260
6.892
6.890
6.880
6.880
6.870
6.869
6.605
6.604
6.594
6.593
5.590
5.568
4.533
4.529
4.518
4.514
3.965
3.943
2.191
1.978
1.457
1.377
-0.081
142a
1.01
5.98
1.04
1.02
0.99
1.02
1.00
1.01
1.03
1.22
8.89
1.12
1.07
1.03
1.02
0.96
ppm
NAME DAS51321
EXPNO 1
PROCNO 1
Date_ 20131126
Time 19.26
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 16
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 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 700.1471597 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00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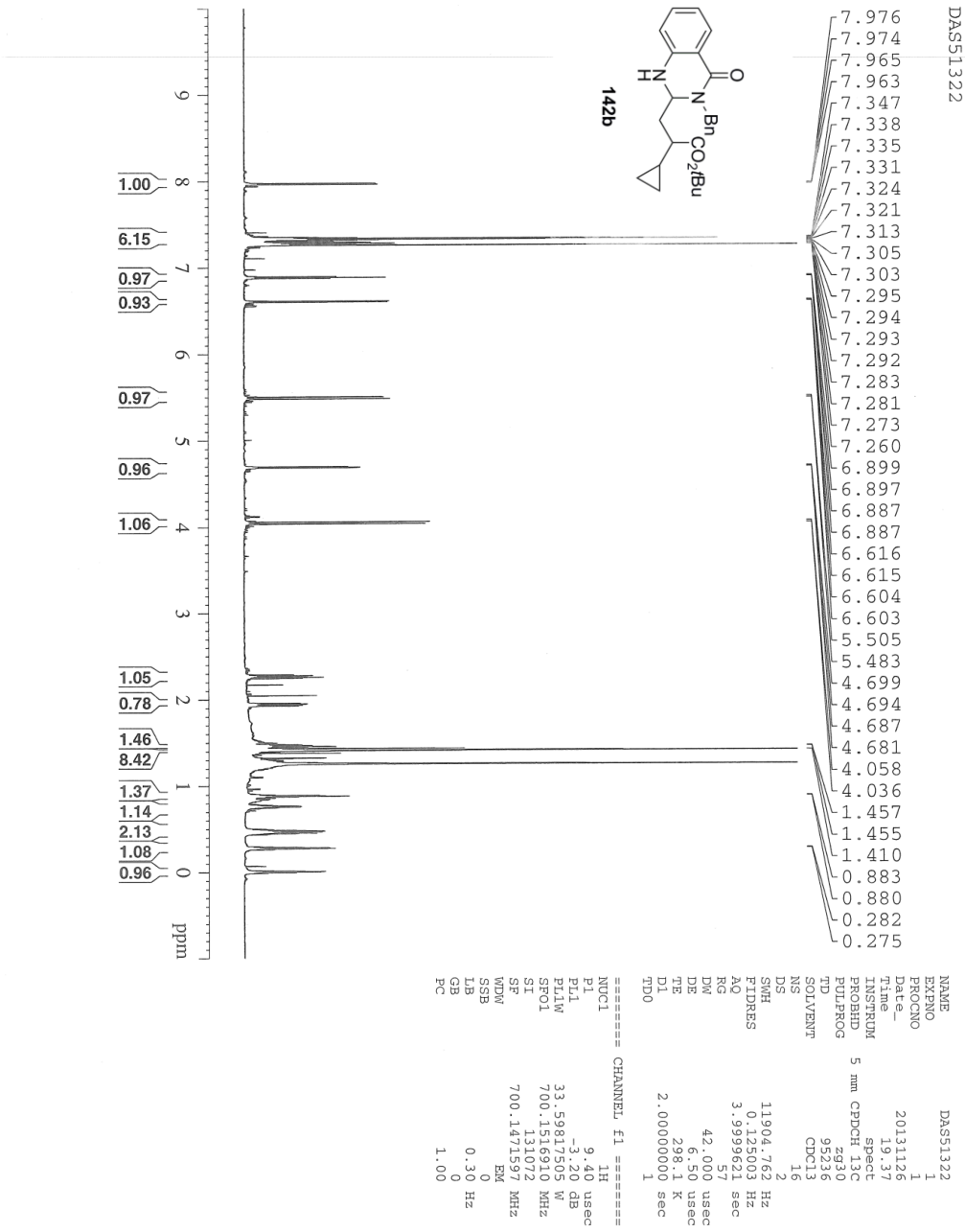
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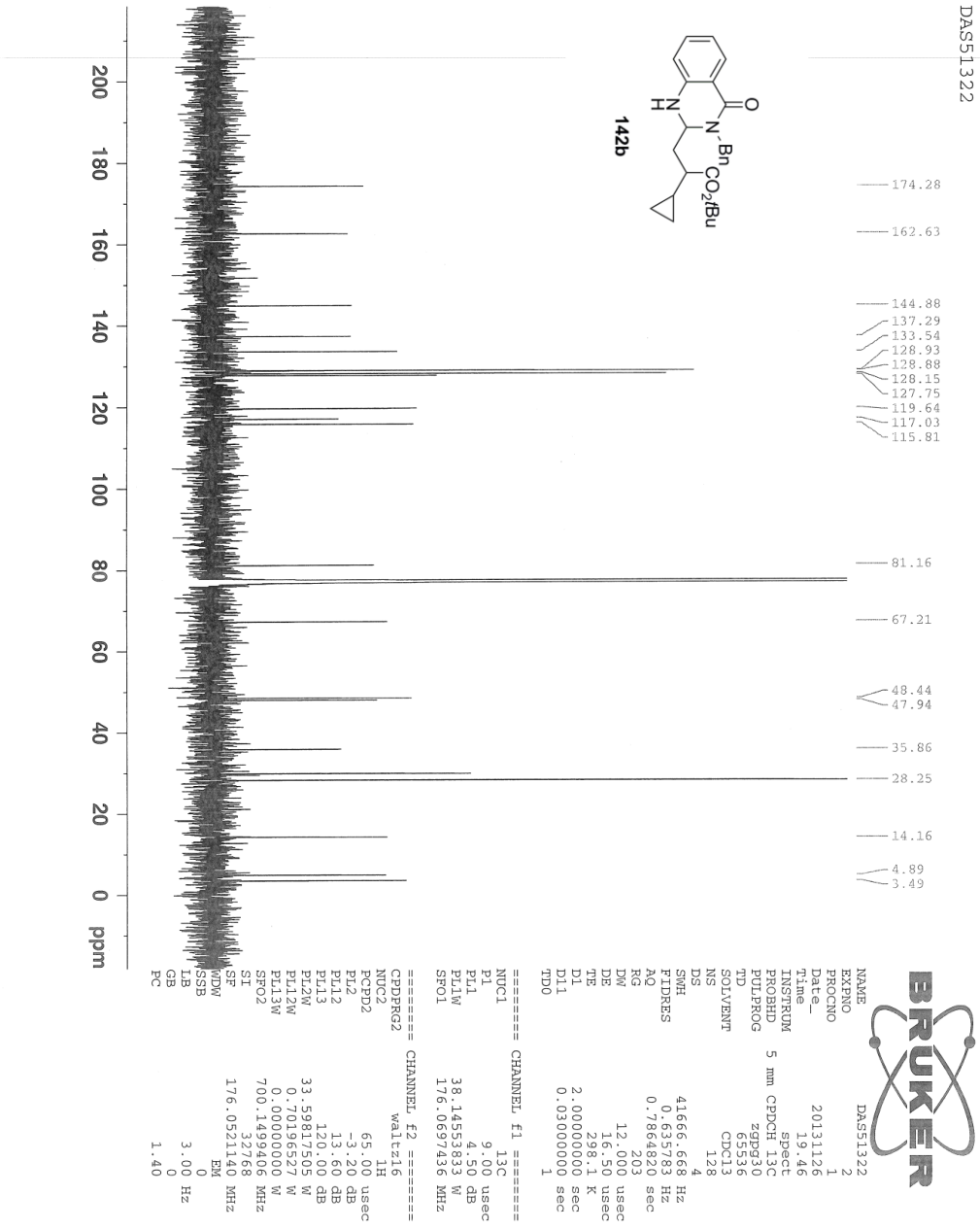
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PC 1.40

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69 See Expermintal Section.

70 The configuration of the major diastereomer was not determined.

71 The amidinium reduction stoichiometry requires one equivalent of acid, and the reaction yield drops substantially if acid is omitted.

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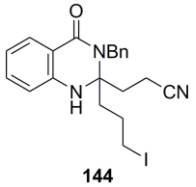

144

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Chapter 4: Application of Aminal Radicals in Total Synthesis: Progress Towards the Total Synthesis of Leuconoxine

4.1 Isolation and Previous Syntheses

(–)-Leuconoxine (**1**), a monoterpene indole alkaloid, was isolated from the stems of *Leuconotis eugenifolius*, a leafy plant indigenous to Malaysia and Indonesia.[104] While there have been no reports on the biological activity of **1**, the latex of *L. eugenifolius* has been used in traditional medicine for the treatment of yaws. A number of structurally related natural products **145**–**147** (Figure 4.1) have been found to exhibit cytotoxicity toward human cancer cell lines.[105]

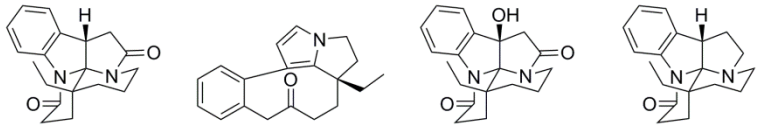
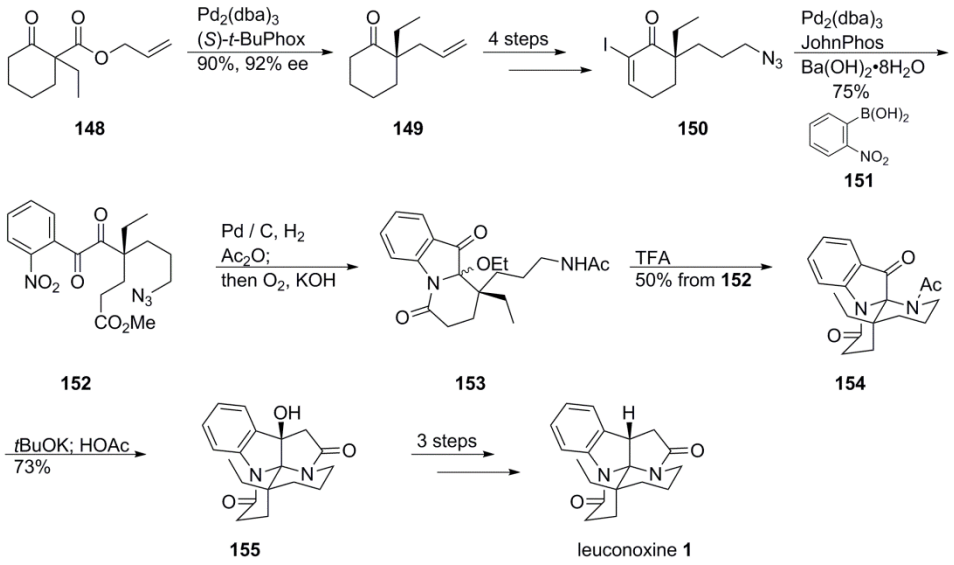


Figure 4.1. Leuconoxine and its biological active congeners

The structure of **1** features a pentacyclic [5.5.6.6]diazafenestrane skeleton which contains three contiguous stereogenic centers including an all-carbon quaternary stereocenter and a fully substituted aminal stereocenter. The structural complexity of **1** has garnered the interest of the synthetic community resulting in two recent total syntheses from the groups of Zhu and Tokuyama.[106]

Zhu's enantioselective synthesis of **1** is outlined in Scheme 4.1. The sequence begins from the substituted cyclohexanone **148** which can be prepared in three steps from commercially available 1,7-heptanedioic acid.[107] Using a procedure developed by Stoltz, **148** was converted to the enantioenriched ketone **149** bearing the necessary all-carbon quaternary stereocenter.[108] Functional group manipulation of **149** yielded

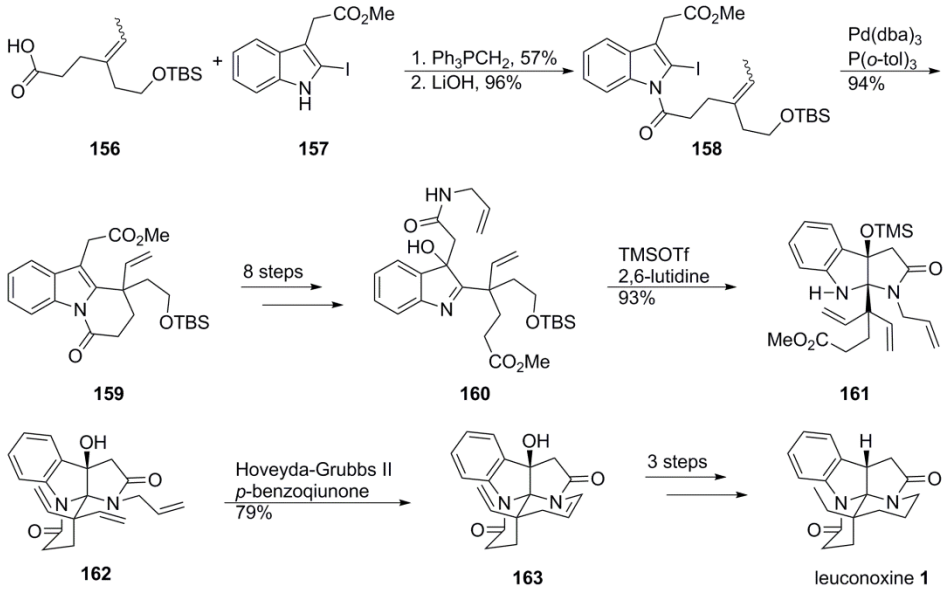
the vinyl iodide **150** in 4 steps. Suzuki cross coupling of **150** with 2-nitrophenyl boronic acid (**151**) followed by oxidative cleavage gave the 1,2-dione **152**. Hydrogenation of the nitro group in the presence of acetic anhydride followed by oxidation with molecular oxygen and subsequent treatment with KOH in ethanol resulted in the formation of the *N,O*-ketal **153**. The fully substituted aminal stereocenter present in **1** was then constructed in an intramolecular iminium ion trapping event by treatment of **153** with acidic conditions to give the aminal **154**. The pyrrolidinone ring was closed by an intramolecular aldolization reaction to give **155**. Mesylation of the resulting tertiary alcohol followed by elimination and hydrogenation gave (–)-leuconoxine (**1**) in 16 steps (longest linear sequence) and 4.2% overall yield.



Scheme 4.1. Zhu's enantioselective total synthesis of (–)-leuconoxine

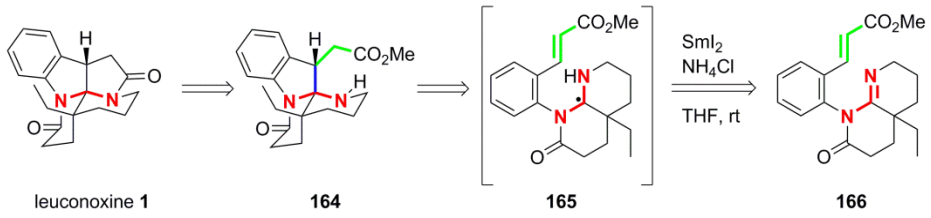
Tokuyama's synthesis of (±)-**1** is outlined in Scheme 4.2. The carboxylic acid **156** was prepared in five steps. The acid was coupled with the known iodoindole **157** to give the Mizoroki–Heck substrate **158**.[109] Intramolecular Heck reaction of **158** formed the necessary all–carbon quaternary stereocenter yielding the annulated product **159**. Functional group manipulation gave the hydroxyindolenine **160** in eight steps. Treatment of **160** with TMSOTf and 2,6-lutidine induced an intramolecular aminal

formation to provide **161**. Formation of the δ-lactam ring was accomplished under basic conditions to give the divinylallyl compound **162**. Diastereoselective ring closing metathesis gave **163**. Hydrogenation of the alkene and Barton–McCombie deoxygenaiton completed the synthesis of (±)-leuconoxine in 21 steps (longest linear sequence) and 5.7% overall yield.



Scheme 4.2. Tokuyama's synthesis of (±)-**1**

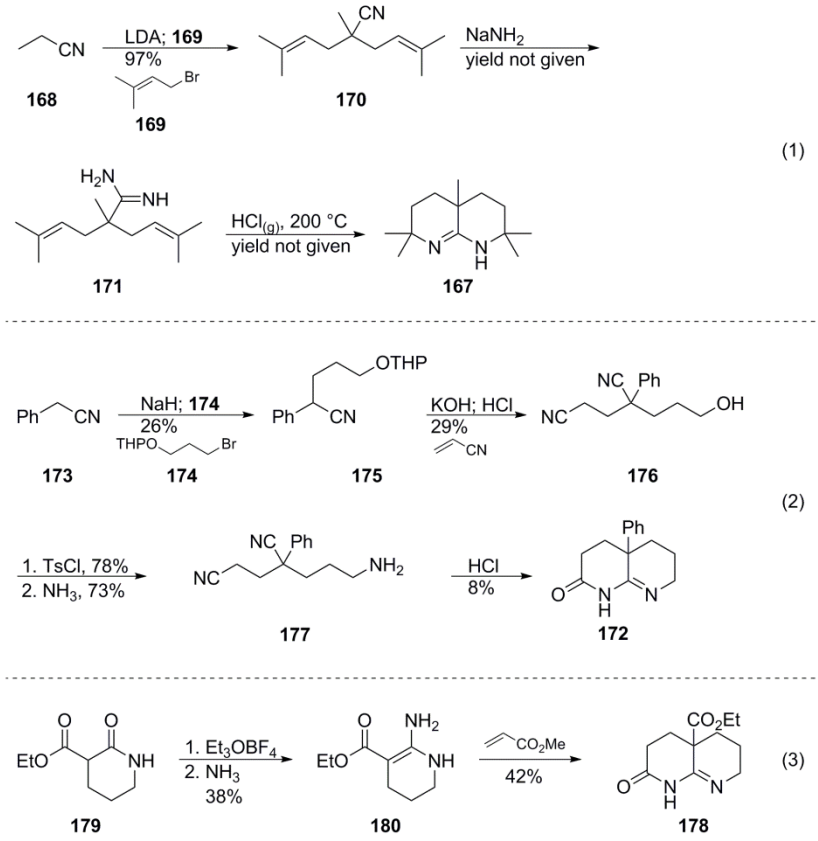
4.2 Retrosynthetic Analysis



Scheme 4.3. Retrosynthetic analysis of **1** with an aminal radical disconnection

While the previously reported routes to **1** all involved the late-stage installation of the aminal functional group by way of an intramolecular condensation reaction, we

envisioned the early installation of the aminal functionality and. In a retrosynthetic sense, the opening of the pyrrolidinone ring gives the amino ester **164** (Scheme 4.3). The structure of **164** exhibits all of the features found in the product of an aminal radical reaction. Specifically, the aminal is acylated and bears an electron withdrawing substituent located three carbon atoms away from the aminal stereocenter. We envisioned that **164** could be easily prepared by the 5-*exo*-trig radical cyclization of the aminal radical intermediate **165** with the appended cinnamate. The necessary aminal radical **165** could be accessed by the reaction of SmI_2 with the bicyclic *N*-acyl amidine **166** under the conditions previously developed in our laboratory. Enticed by the simplifying nature of this synthetic strategy, we chose to pursue the total synthesis of **1** as a means to demonstrate the utility of aminal radicals in the synthesis of complex alkaloid synthesis.



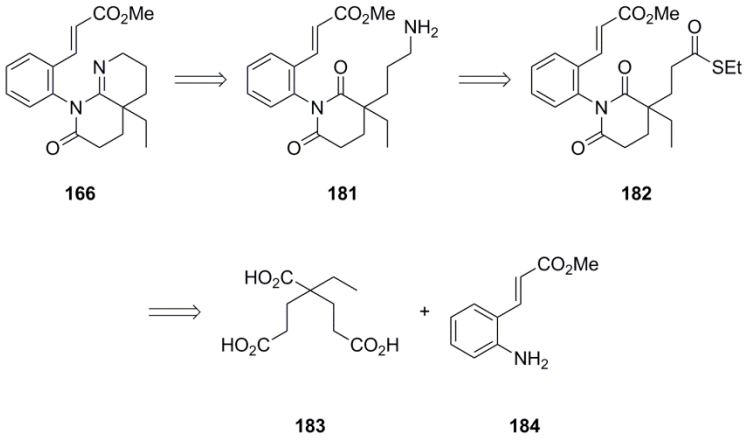
Scheme 4.4. Known methods for the preparation of bicyclo[4.4.0]amidines

We next turned our attention to the retrosynthetic analysis of the key intermediate **166**. A search of the literature revealed there have been no reports of bicyclo[4.4.0]-*N*-aryl-amidines. However, methods for the preparation of unsubstituted amidines of this type were known. The three methods for the preparation of bicyclo[4.4.0]amidines are detailed in Scheme 4.4. Amidines of the type reported by Leffek (eq. 1, **167**) were prepared by the double alkylation of propionitrile (**168**) with an allyl bromide (**169**) to give the all-carbon quaternary stereocenter containing nitrile prodouct **170**.[110] Subsequent addition of sodium amide to the nitrile produced the amidine **171**. Heating **171** in the presence of gaseous HCl resulted in the formation of **167**. While this method allowed for the preparation of a bicyclo[4.4.0]amidine bearing a quaternary stereocenter at the bridgehead position as is present in structure of **166**, the method does not appear to be general. The cyclization was carried out under harsh reaction conditions and would likely be unsuccessful for a substrate that did not contain a functional group capable of forming a tertiary carbocation intermediate.

Smissman reported the synthesis of bicyclo[4.4.0]amidines such as **172** (eq. 2).[111] These amidines contain both the desired quaternary stereocenter and the acyl substitution found in **166**. The first step in the synthesis of **172** was the alkylation of phenyl acetonitrile **173** with the THP protected alcohol **174** to give the bis-nitrile **175**. Selective alkylation of **175** at the benzylic position with acrylonitrile produced the quaternary stereocenter containing product **176**. Deprotection of the alcohol followed by formation of the tosylate and displacement with ammonia gave the amine **177**. Treatment of **177** with ethanolic HCl yielded the bicyclic amidine **172**. This method relies on the phenyl substituent to provide selectivity in the second alkylation reaction, and an analogous sequence using butyronitrile as the substrate would likely be unsuccessful.

The third method was reported by Wamhoff to give amidines such as **178** (eq. 3).[112] The synthesis of **178** began from the known δ-lactam **179**, which was prepared in two steps from diethylmalonate.[113] Imidate formation followed by addition of ammonia gave the ketene aminal **180**. Treatment of **180** with methyl acrylate yielded the amidine **178**. While this amidine bears the desired acyl substitution and the necessary quaternary stereocenter, the method of its preparation likely relied upon the presence of the electron-withdrawing ethyl ester functionality in order to successfully prepare the ketene aminal **180**. An analogous reaction sequence beginning from 3-ethylpiperidin-2-one would likely fail to produce the necessary ketene aminal functionality

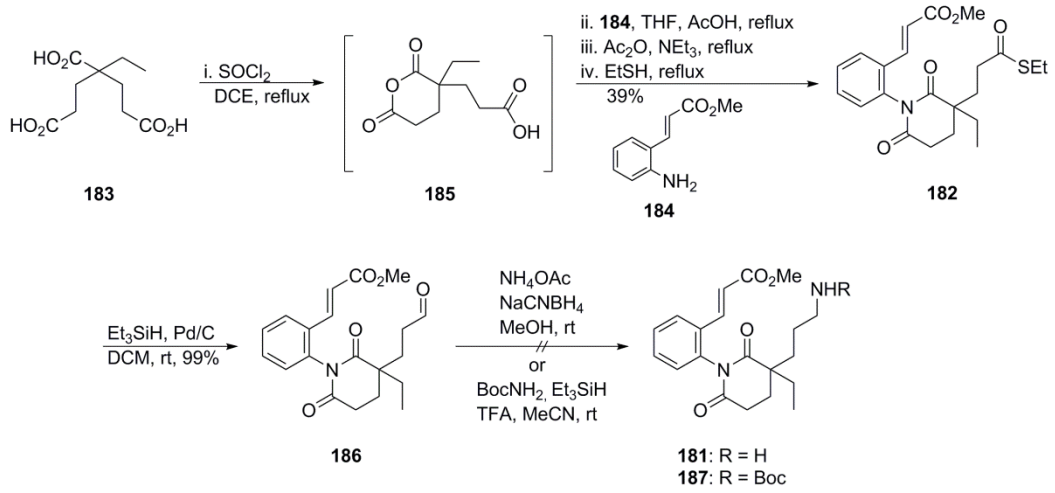
Having found no suitable procedure among the known methods for the synthesis of bicyclo[4.4.0]amidines, a new synthetic strategy was devised. We envisioned that **166** might be accessible from the intramolecular condensation of the amino imide **181** (Scheme 4.5). The amine could then be obtained from the thioester **182** by way of Fukkuyama reduction and reductive amination.[114] The thioester **182** could then be prepared from the known tri-carboxylic acid **183** and the known ester **184**.[115]



Scheme 4.5. The first generation retrosynthetic analysis of **166**

4.3 Progress Towards the Synthesis of Leuconoxine

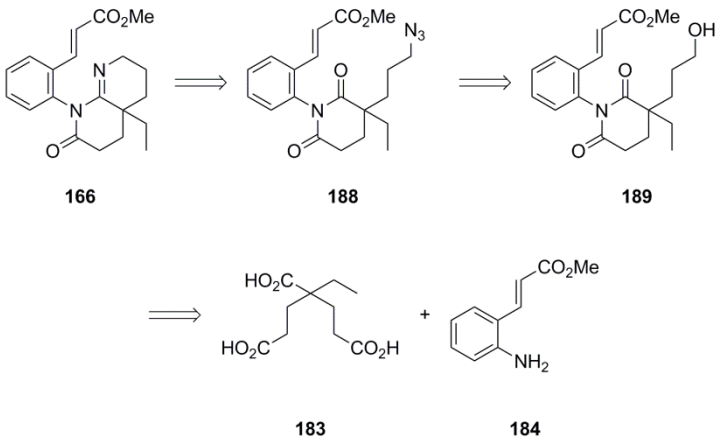
The thioester **182** was rapidly constructed using a one-pot sequence starting from the known tri-acid **183**. Treatment of the acid with thionyl chloride resulted in the formation of the anhydride **185** (Scheme 4.6, not isolated).[116] The solvent was exchanged for THF and AcOH was added in addition to the aniline **184**. After refluxing the mixture for several hours, excess acetic anhydride and triethylamne were added and heating was continued to give a mixed acyl carbonate intermediate. Finally, the addition of ethane thiol gave the desired thioester **182** in 39% yield.



Scheme 4.6. Attempted synthesis of the amine **181**

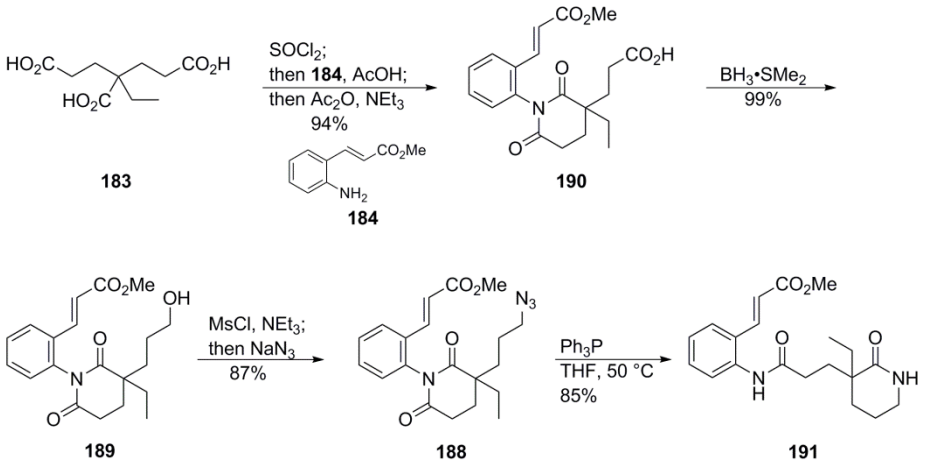
Reduction of the thioester proceeded cleanly in the presence of stoichiometric palladium to give the aldehyde **186**. However, attempts to synthesize the amine **181** by reductive amination using $NaCNBH_4$ / NH_4OAc resulted in decomposition, presumably by reduction of the imide. Reductive amination of **186** with *tert*-butyl carbamate and triethyl silane as described by Dubé also failed to install the desired nitrogen functionality (**187**).[117]

Unable to prepare the amine **181**, we modified our retrosynthetic analysis (Scheme 4.7). We envisioned that **166** could be prepared by the aza-Wittig reaction of the imido azide **188**.[118] Intramolecular aza-Wittig reactions of imides were well precedented, and the necessary azido imide **188** might be easily prepared from the alcohol **189**.[119] The alcohol could likely be prepared from the tri-acid **183** and the ester **184**.



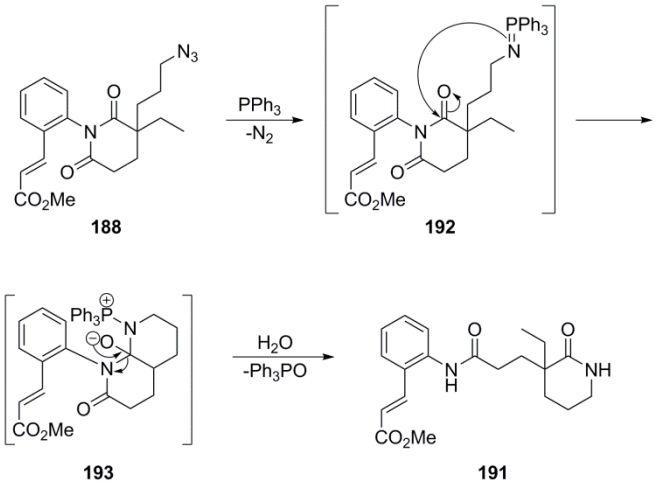
Scheme 4.7. Second-Generation retrosynthetic analysis of the key intermediate **166**

Preparation of the desired alcohol commenced with an analogous one-pot sequence from the known tri-acid **183** to give the carboxylic acid **190** (Scheme 4.8). Selective reduction of the carboxylic acid in the presence of the imide was accomplished by treatment with BH_3•SMe_2 furnishing the alcohol **189** in 99% yield. While attempts to convert the alcohol directly to the azide **188** with DPPA were unsuccessful, the azide was readily obtained from a one-pot mesylation / displacement sequence.



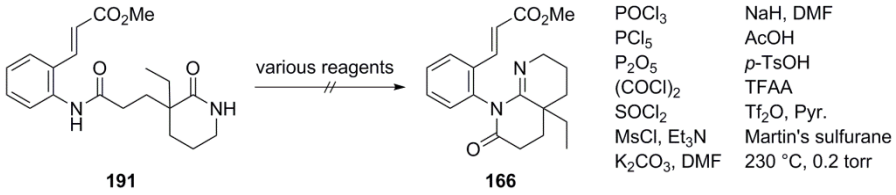
Scheme 4.8. Synthesis of the amido lactam **191**

With the azide in hand, we attempted the key intramolecular aza-Wittig reaction (Scheme 4.8). Unexpectedly, treatment of **188** with triphenylphosphine in anhydrous THF resulted in the formation of the amido lactam **191** as the sole isolable product. The same result was obtained upon treatment of the azide with zinc metal in methanol. We speculate that the amido lactam may form by the mechanism shown in Scheme 4.9. Staudinger reduction of the azide **188** with triphenylphospine gave the aza-ylide **192**. Upon intramolecular addition of the aza-ylide to the imide carbonyl, the tetrahedral intermediate **193** was formed. Collapse of the tetrahedral intermediate to eject an aryl-amide anion followed by hydrolysis upon aqueous workup resulted in the formation of the amido lactam **191**.



Scheme 4.9. Plausible mechanism for the formation of the amido lactam **191**

A wide variety of conditions were examined in order to induce an intramolecular condensation reaction between the δ-lactam and the aryl amide (Scheme 4.10). Treatment with dehydrating reagents including Martin's sulfurane, phosphoryl chloride, phosphorus pentachloride, diphosphorus pentoxide, oxalyl chloride, thionyl chloride, mesyl chloride, and triflic anhydride[120] all failed to produce the desired bicyclo[4.4.0]amidine. Heating **191** under acidic (AcOH or *p*-TsOH) or basic[121] (K_2CO_3) conditions also failed to yield any of the amidine. Heating **191** at 230 °C and 0.2 torr, for an extended period gave no reaction. It is likely that both the poor nucleophilicity of the electron-poor aryl amide and the sterically hindered nature of the neopentylic lactam carbonyl conspire against this transformation.

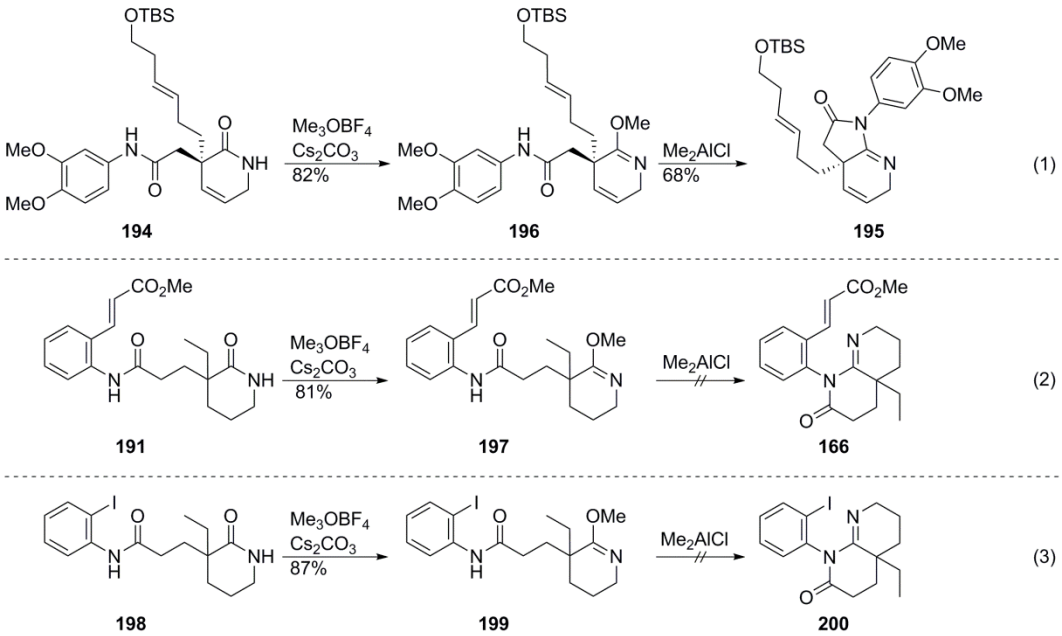


Scheme 4.10. The attempted dehydration of the amido lactam **191**

An expanded literature search indicated that it might be possible to induce the desired condensation reaction under Lewis-acidic conditions. In 2007, Zhou reported the total

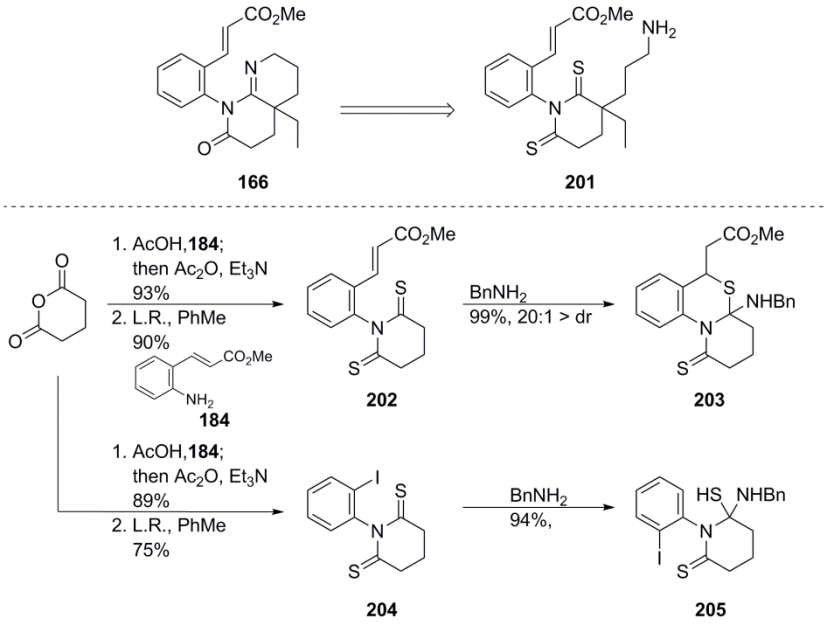
synthesis of the alkaloid isoshizogamine wherein the amido lactam **194** was dehydrated to form an *N*-aryl-*N*-acyl bicyclo[4.3.0]amidine (**195**) by way of the imidate **196** (Scheme 4.11, eq. 1).[122] Following this precedent, the lactam was selectively converted to the imidate **197** (eq.2). However, upon treatment with Me_2AlCl, the substrate decomposed yielding none of the desired amidine. Reasoning that the methyl ester may be the source of the observed decomposition, the analogous 2-iodo aryl compound **198** was prepared (eq. 3, see the Experimental Section for details). After selective imidate formation, the cyclization substrate **199** was obtained. Unfortunately, none of the desired amidine **200** was observed upon treatment of **199** with Zhou's conditions.

It was envisioned that the desired amidine **166** might accessible from the intramolecular condensation reaction of an amine onto a dithioimide (**201**, Scheme 4.12). While dithioimides are relatively rare in the literature and only a few reactions for the formation of an *N*-thioacyl amidine from a dithioimide were known, the condensation reactions of thioamides with amines have been well studied.[123]



Scheme 4.11. Lewis-acid catalyzed amidine formation

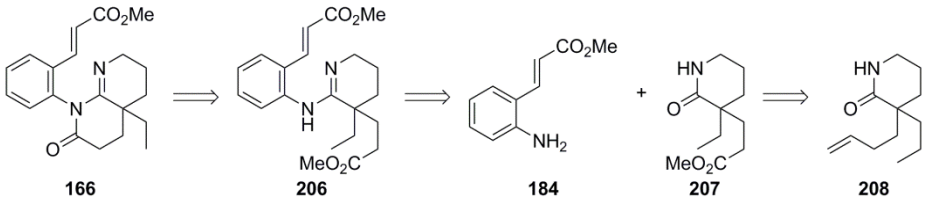
In order to probe this possibility, the model imido ester **202** was prepared from glutarimide and the aniline **184**. Upon treatment of the dithioimide **202** with benzyl amine as a generic primary amine nucleophile, the cyclized product **203** was formed as a single diastereomer (relative stereochemistry not determined). Reasoning that removal of the unsaturated ester would prevent the intramolecular trapping of the presumed thiolate anion intermediate, the analogous iodo compound **204** was prepared (eq. 3). However, treatment of **204** with benzyl amine also resulted in the formation of a sulfur containing addition product (**205**). Reaction conditions with mercuric chloride or NBS also failed to produce the desired addition products. Based on these results, this line of research has suspended.



Scheme 4.12. Reactions of the dithioimide model systems

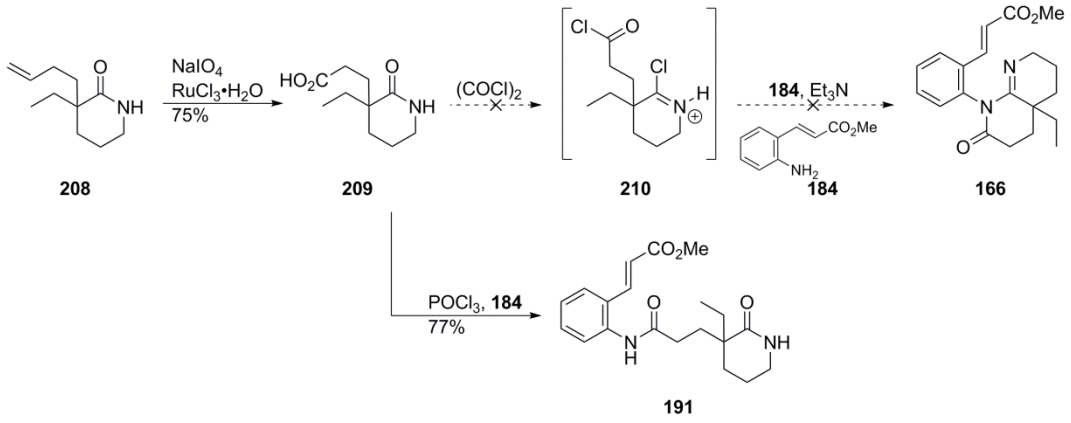
Having been unsuccessful in achieving the synthesis of **166**, an alternate retrosynthetic analysis was performed. Disconnection of the *N*-acyl bond of the amidine through an intramolecular *N*-acylation reaction of an *N*-aryl amidine gave **206** (Scheme 4.13). It was envisioned that the amidine could be prepared from a

bimolecular condensation reaction of the aniline **184** and a δ-lactam derivative (**207**). The δ-lactam derivative could then be prepared from the known δ-lactam **208**.[124]



Scheme 4.13. An alternate retrosynthetic analysis of **166**

Starting from the known alkenyl lactam **208**, the carboxylic acid **209** was synthesized by oxidative cleavage (Scheme 4.14).[125] It was envisioned that **166** might be prepared by the treatment of **209** with oxalyl chloride to first give the chloroiminium ion **210** followed by the addition of the aniline **184**. This reaction failed to produce the desired amidine, instead giving adducts of oxalyl chloride. Treatment of **209** with phosphoryl chloride gave only the amido lactam **191**.

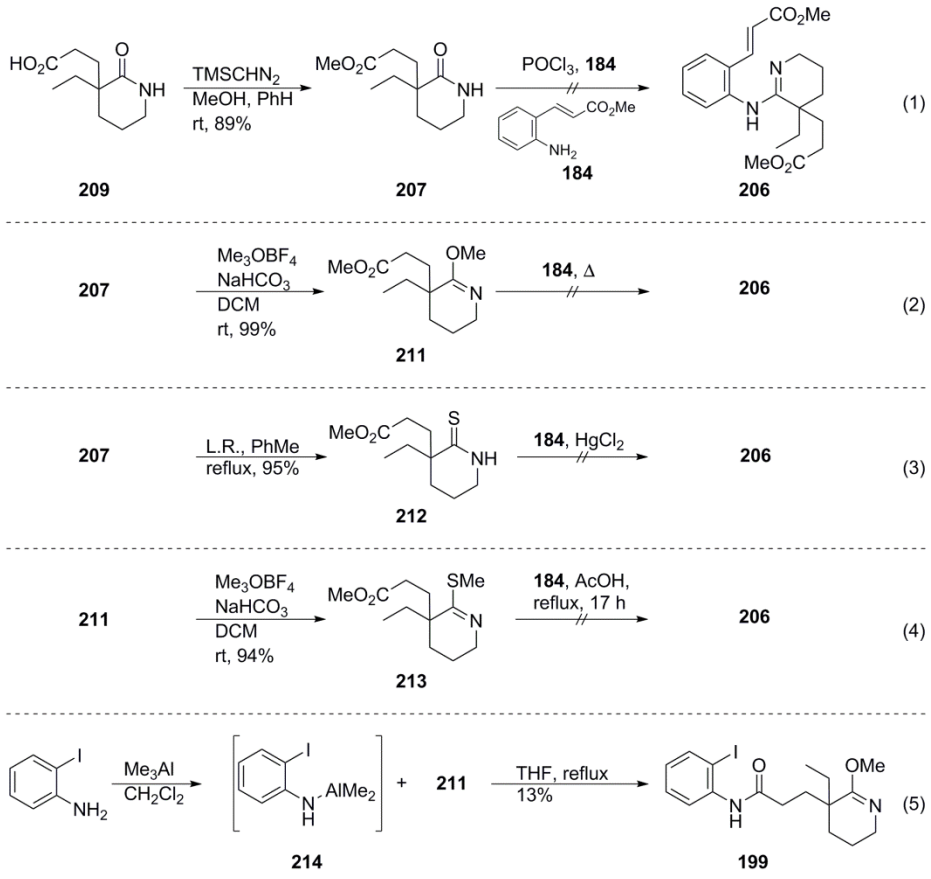


Scheme 4.14. Attempts to form the desired amidine from **209**

In order to prevent the amide formation previously observed, the carboxylic acid **209** was protected as the ester **211** by methylation with $TMSCHN_2$ (Scheme 4.15, eq. 1). Subsequent treatment of **211** with phosphoryl chloride followed by addition of the aniline **184** gave no reaction. Treatment of **211** with a variety of other reagents known

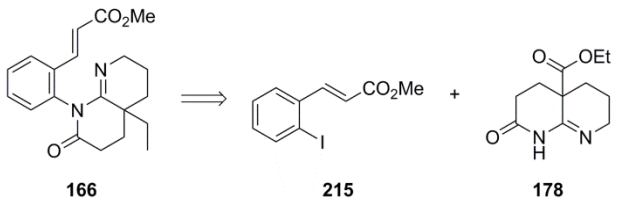
to give chloroiminium ions by their reactions with amides also failed to give amidine formation.

In order to activate the carbonyl carbon toward nucleophilic addition, the imidate **211** was prepared (eq. 2). Heating a 1:1 mixture of the imidate **211** and the aniline **184** to reflux in toluene resulted in no reaction. Analogous reaction conditions using AcOH resulted in decomposition. The thiolactam **212** was prepared by treatment of **207** with Lawesson's reagent (L.R.) (eq. 3).[126] Treatment of the thiolactam **212** with mercuric chloride or NBS in the presence of **184** resulted in decomposition of **212** and no reaction respectively. The corresponding thioimidate **213** was prepared and treated with the aniline **184**. However, its reactions also failed to produce the desired amidine **206** (eq. 4).



Scheme 4.15. Attempted addition of anilines to activated lactams

It was postulated that poor the nucleophilicity of **184** coupled with the steric hindrance provided by the quaternary stereocenter on the lactam, thiolactam, imidate, and thioimidate substrates were responsible for the of the lack of desired reactivity. Dimethylaluminium amides are known to have enhanced nucleophilic character when compared with their amine counterparts.[127] While dimethylaluminium amides were known to react with esters, there had been no reports on their addition to imidates. However, other amine nucleophiles were known to react with imidates in the presence methyl esters. The dimethylaluminium amide of 2-iodoaniline (**214**) was generated *in situ* by the method reported by Weinreb in 1977 (eq. 5).[128] Addition of a solution of **214** to the imidate **211** gave only the imidate **199** resulting from the selective addition to the methyl ester. The addition of a solution of **214** to mixture of the thiolactam **212** and mercuric chloride (not shown) gave no reaction.

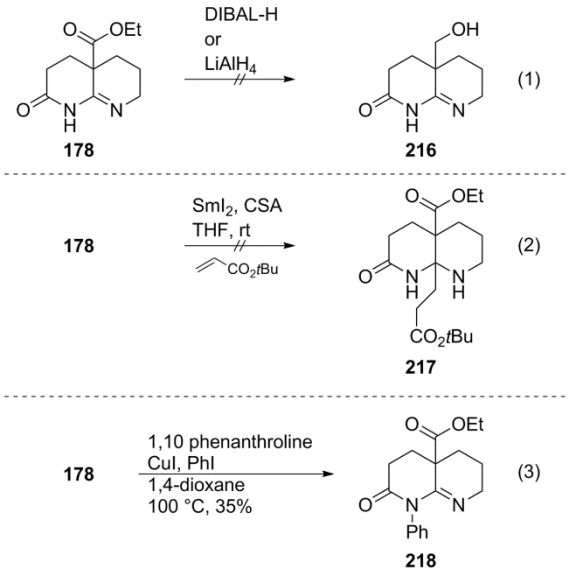


Scheme 4.16. Retrosynthetic analysis of **166** from Wamhoff's amidine **178**

Concluding that the bimolecular amidine formation strategy would be unsuccessful, we again revised our retrosynthetic analysis of **166** (Scheme 4.16). It was envisioned that the *N*-aryl bond could be forged by the coupling of the amidine previously reported by Wamhoff (**178**) and an aryl iodide, such as the known acyrlate **215** using cross coupling conditions.[129] This strategy required the conversion of the undesired ethyl ester to the required ethyl substituent.

Preliminary investigations of this chemistry are currently under way and are detailed in Scheme 4.17. Attempts to selectively reduce the ester to the alcohol **216** in the presence of the amidine by treatment with diisobutylaluminium hydride or with

lithium aluminum hydride have resulted in no reaction (eq. 1). Using **178** as a model substrate, investigations on the reductive alkylation with samarium iodide have been carried out (eq. 2). Using ammonium chloride as the proton source and methyl acrylate or *trans*-methyl cinnamate as the radical acceptor, only starting material was recovered. Using CSA as the proton source in the presence of *tert*-butyl acrylate gave none of the desired addition product **217**, instead yielding the corresponding aminal.



Scheme 4.17. Reactions of Wamhoff's amidine **178**

Examining the *N*-arylation reaction, **178** was treated with Ullman coupling conditions using a variety of aryl iodides (eq. 3).[130] The reactions with 2-iodophenyl methyl acrylate, 2-iodobenzaldehyde, and 2-iodostyrene all resulted in partial decomposition of the starting materials and no coupling products were detected. However, the reaction of iodobenzene gave the coupling product **218** in 35% yield.

4.4 Experimental Section

General Experimental Details:

All reactions were carried out under an inert Ar atmosphere in oven-dried glassware. Flash column chromatography (FCC) 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, ninhydrin, or vanillin stains. Tetrahydrofuran (THF), methylene chloride (DCM), benzene (PhH), and toluene (PhMe) were dried by passage through an activated alumina column. 1,4-dioxanne and 1,2-dichloroethane (1,2-DCE) were dried over calcium hydride and distilled under argon prior to use. *N*,*N*-dimethylfomamide (DMF) was dried over 3 Å molecular sieves prior to use. Methyl acrylate was purified by washing with aqueous NaOH, drying over $MgSO_4$, and calcium hydride. It was then distilled under vacuum prior to use. *tert*-Butyl acrylate was distilled prior to use. All other reagents and solvents were used without further purification from commercial sources. FT-IR spectra were measured using NaCl plates. Multiplicities are abbreviated as follows: s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, br = broad, m = multiplet. Melting points are uncorrected.

methyl (E)-3-(2-(3-ethyl-3-(3-(ethylthio)-3-oxopropyl)-2,6-dioxopiperidin-1-yl)phenyl)acrylate (182). To a solution of the known acid **183** (0.1185 g, 0.510 mmol) suspended in 1,2-dichloroethane (1.0 mL, 0.5 M) stirring at room temperature was added thionyl chloride (0.04 mL, 0.55 mmol). The mixture was heated to reflux. After 11 hours, the solvent was removed under vacuum and the resulting anhydride was dissolved in THF. To this solution were added 2-iodoaniline (0.0747 g, 0.422 mmol) and AcOH (0.03 mL, 0.52 mmol). This mixture was heated to reflux. After 8 hours, the mixture was cooled to room temperature and Ac_2O (0.16 mL, 1.70 mmol) and Et_3N (0.26 mL, 1.9 mmol) were added. The mixture was heated to reflux again. After 12.5 hours, the mixture was again cooled to room temperature and ethane thiol (0.12 mL, 1.7 mmol) was added prior to heating to reflux. After an additional 2 hours, the mixture was cooled to room temperature, concentrated, diluted with EtOAc, washed with saturated sodium chloride solution, dried over $MgSO_4$, filtered, and concentrated. The resulting mixture was purified by flash column chromatography (1:2 EtOAc : hexanes) to give **182** (0.0679g, 0.163 mmol, 39%) as a light yellow oil.

Data for **182**: R_f 0.35 (1:1 EtOAc : hexanes); IR (thin film) 2950, 1716, 1668, 1639 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) as a 1:1 mixture of rotational isomers δ 7.70 (d, *J* = 7.7 Hz, 1 H), 7.45–7.49 (m, 1 H), 7.42–7.44 (m, 1 H), 7.39 (dd, *J* = 16.1, 4.2 Hz, 1 H), 7.09 (dd, *J* = 7.0, 1.4 Hz, 0.5 H), 7.02 (dd, *J* = 7.7, 0.7 Hz, 0.5 H), 6.39 (dd, *J* = 15.4, 6.3 Hz, 1 H), 3.77 (d, *J* = 14.0 Hz, 3 H), 2.84–2.98 (m, 4 H), 2.56–2.68 (m, 2 H), 1.96–2.22 (m, 4 H), 1.86–1.92 (m, 0.5 H), 1.75–1.85 (m, 1.5 H), 1.24 (t, *J* = 7.0 Hz, 3 H), 0.98 (t, *J* = 7.0 Hz, 3 H); ^{13}C NMR (176 MHz, $CDCl_3$) as a 1:1 mixture of rotational isomers δ 199.1, 198.9, 176.2, 176.1, 171.89, 171.85, 167.0, 166.8, 138.9, 138.8, 135.44, 135.36, 132.46, 132.42, 131.2, 131.1, 129.7, 129.5, 129.38, 129.36, 127.3, 127.2, 121.0, 120.7, 52.0, 51.9, 45.2, 45.1, 38.7, 30.4, 30.3, 29.32, 29.30, 28.48, 48.45, 25.7, 25.3, 23.6, 23.5, 14.8, 8.13, 8.10; HRMS (TOF MS ES+) calcd for $C_{22}H_{27}NO_5NaS$ [M+Na]: 440.1508, found 440.1492.

methyl (E)-3-(2-(3-ethyl-2,6-dioxo-3-(3-oxopropyl)piperidin-1-yl)phenyl)acrylate (186). To a solution of **182** (0.0369 g, 0.0884 mmol) dissolved in DCM (0.9 mL, 0.1 M) stirring at room temperature were added triethylsilane (0.10 mL, 0.63 mmol) and 10% Pd / C (0.0911 g, 0.086 mmol). The mixture was stirred at room temperature. After 0.5 hours, the reaction mixture was filtered through celite 535 and concentrated. The resulting mixture was purified by flash column chromatography (1:1 EtOAc : hexanes) to give **186** (0.03115 g, 0.087 mmol, 99%) as a colorless oil.

Data for **186**: R_f 0.37 (2:1 EtOAc : hexanes); IR (thin film) 295, 1717, 1687 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) as a 1:1 mixture of rotational isomers δ 9.77 (d, *J* = 14.7 Hz, 1 H), 7.71 (ddd, *J* = 9.8, 8.4, 1.4 Hz, 1 H), 7.48 (td, *J* = 7.0, 0.7 Hz, 1 H), 7.43–7.45 (m, 1 H), 7.38 (dd, *J* = 16.1, 10.5 Hz, 1 H), 7.05 (ddd, *J* = 26.6, 7.7, 1.4 Hz, 1 H), 6.40 (dd, *J* = 16.1, 13.3 Hz, 1 H), 3.76 (d, *J* = 1.4 Hz, 3 H), 2.88–3.00 (m, 2 H), 2.50–2.69 (m, 2 H), 2.08–2.18 (m, 1.5 H), 2.03–2.08 (m, 2 H), 1.89–2.01 (m, 1.5 H), 1.74–1.87 (m, 2 H), 0.97 (q, *J* = 7.7 Hz, 3 H); ^{13}C NMR (176 MHz, $CDCl_3$) as a 1:1

mixture of rotational isomers δ 201.3, 176.3, 171.9, 167.01, 166.95, 138.8, 135.4, 132.3, 132.2, 131.2, 129.6, 129.5, 129.42, 129.40, 127.2, 127.1, 120.71, 120.66, 52.0, 51.9, 44.9, 38.9, 38.7, 29.3, 28.7, 28.4, 27.0, 26.9, 25.9, 25.6, 8.09, 8.05; HRMS (TOF MS ES+) calcd for $C_{20}H_{24}NO_5$ [M+H]: 358.1654, found 358.1659.

(*E*)-3-(3-ethyl-1-(2-(3-methoxy-3-oxoprop-1-en-1-yl)phenyl)-2,6-dioxopiperidin-3-yl)propanoic acid (190). To a suspension of the known tri-acid **183** (3.1230 g, 13.4 mmol) in 1,2-dichloroethane (27 mL, 0.5 M) stirring at room temperature was added thionyl chloride (1.10 mL, 15.1 mmol). The mixture was heated to reflux. After 22 hours, an additional portion of thionyl chloride (0.10 mL, 1.4 mmol) was added. After an additional 2 hours, thionyl chloride (0.10 mL, 1.4 mmol) was added. After an additional 12 hours, the reaction mixture was cooled and concentrated to give a white solid. This material was dissolved in THF (45 mL, 0.25 M) and 2-iodoaniline (1.9890 g, 11.2 mmol) along with AcOH (0.77 mL, 13.5 mmol) were added prior to heating at reflux. After 17 hours, the reaction mixture was cooled to room temperature and Ac_2O (3.2 mL, 33.9 mmol) along with Et_3N (4.7 mL, 33.7 mmol) were added. The mixture was again heated to reflux for one additional hour prior to cooling to room temperature and concentrating the mixture. Purification by flash column chromatography (1:1 hexanes:EtOAc with 2% AcOH) gave **190** (3.9317 g, 10.5 mmol, 94%) as a colorless oil.

Data for **190**: R_f 0.60 (1:2 hexanes:EtOAc); IR (thin film) 3201, 2971, 1715, 1686 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) as a mixture of rotational isomers δ 7.71 (ddd, *J* = 9.2, 5.6, 2.0 Hz, 1 H), 7.37–7.49 (m,3 H), 7.03 (ddd, *J* = 12.8, 7.2, 0.8 Hz, 1 H), 6.40 (dd, *J* = 16.0, 10.0 Hz, 1 H), 3.76 (d, *J* = 0.4 Hz, 3 H), 2.84–3.03 (m, 2 H), 2.37–2.53 (m, 2 H), 1.93–2.18 (m, 4 H), 1.71–1.91 (m, 2 H), 0.97 (ddd, *J* = 7.6, 7.6, 0.4 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) as a mixture of rotational isomers δ 178.4, 177.5, 176.3, 176.1, 172.1, 172.0, 167.6, 167.0, 139.3, 138.9, 135.5, 135.4, 132.42, 132.38, 131.24. 131.15, 129.6, 129.5, 129.4, 127.17, 127.15, 120.7, 120.6, 52.2, 51.9, 45.1,

45.0, 30.0, 29.6, 29.3, 29.2, 29.04, 28.96, 28.7, 28.4, 25.7, 25.5, 8.11, 8.05; HRMS (TOF MS ES+) calcd for $C_{20}H_{23}NO_6Na$ [M+Na]: 396.1423, found 396.1415.

methyl (E)-3-(2-(3-ethyl-3-(3-hydroxypropyl)-2,6-dioxopiperidin-1-yl)phenyl)acrylate (189). To a solution of the acid **190** (0.2743 g, 0.735 mmol) dissolved in THF (2.5 mL, 0.3 M) stirring at room temperature was added borane dimethyl sulfide complex (2 M in THF 0.74 mL, 1.48 mmol). After 0.5 hours, the reaction mixture was diluted with EtOAc, washed with saturated aqueous sodium chloride, dried over $MgSO_4$, filtered, and concentrated. The resulting mixture was purified by flash column chromatography (2:1 EtOAc : hexanes) to give **189** (0.2483g, 0.691 mmol, 94%) as a colorless oil.

Data for **189**: R_f 0.31 (4:1 EtOAc : hexanes); IR (thin film) 2951, 1716, 1683 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) as a 1:1 mixture of rotational isomers δ 7.72 (ddd, *J* = 7.7, 1.4 Hz, 1 H), 7.39–7.49 (m, 3 H), 7.04 (ddd, *J* = 7.7, 4.2, 1.4 Hz, 1 H), 6.42 (dd, *J* = 29.4, 16.1 Hz, 1 H), 3.76 (d, *J* = 6.3 Hz, 3 H), 3.73 (quintet, *J* = 5.6 Hz, 0.5 H), 3.62–3.66 (m, 1 H), 3.58–3.61 (m, 0.5 H), 2.86–3.03 (m, 2 H), 2.00–2.11 (m, 2 H), 1.93–1.98 (m, 0.5 H), 1.81–1.89 (m, 2.5 H), 1.72–1.77 (m, 1 H), 1.59–1.65 (m, 2 H), 1.52–1.57 (m, 0.5 H), 0.95 (dt, *J* = 14.7, 7.7 Hz, 3 H); ^{13}C NMR (176 MHz, $CDCl_3$) as a 1:1 mixture of rotational isomers δ 176.9, 176.7, 172.4, 172.2, 167.8, 167.0, 139.6, 138.9, 135.8, 135.8, 135.5, 132.4, 132.2, 131.4, 131.2, 129.5, 129.33, 129.29, 127.2, 127.0, 120.6, 120.1, 62.8, 62.7, 52.2, 51.9, 45.3, 31.9, 31.2, 29.43, 29.35, 28.6, 28.5, 27.5, 27.1, 25.5, 25.3, 8.3, 8.2; HRMS (TOF MS ES+) calcd for $C_{20}H_{25}NO_5Na$ [M+Na]: 382.1630, found 382.1638.

methyl (*E*)-3-(2-(3-(3-azidopropyl)-3-ethyl-2,6-dioxopiperidin-1-yl)phenyl)acrylate (188). To a solution of the alcohol **189** (0.0976 g, 0.272 mmol) dissolved in THF (2.7 mL, 0.1 M) stirring at room temperature were added MsCl (10% in THF, 0.25 mL, 0.32 mmol) and Et_3N (10% in THF, 0.45 mL, 0.32 mmol).

After 1.5 h, the solvent was exchanged for DMF (2.7 mL, 0.1 M) and NaN_3 (0.0893 g, 1.37 mmol) was added. After 17 hours, the reaction mixture was diluted with Et_2O and washed three times with saturated aqueous LiCl. The Et_2O solution was then dried over $MgSO_4$, filtered, and concentrated. The resulting oil was purified by flash column chromatography (7:3 hexanes: EtOAc) to give **188** (0.0906g, 0.236 mmol, 87%) as a colorless oil.

Data for **188**: R_f 0.85 (1:4 hexanes:EtOAc); IR (thin film) 2950, 2097, 1717, 1686 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) as a mixture of rotational isomers δ 7.72 (dd, *J* = 7.7, 1.4 Hz, 1 H), 7.47 (td, *J* = 7.0, 2.1 Hz, 1 H), 7.43 (td, *J* = 7.7, 1.4 Hz, 1 H), 7.38 (d, *J* = 16.1 Hz, 1 H), 7.04 (dd, *J* = 7.7, 1.4 Hz, 1 H), 6.41 (d, *J* = 16.1 Hz, 1 H), 3.77 (s, 3 H), 3.30–3.38 (m, 2 H), 2.87–2.97 (m, 2 H), 2.01–2.10 (m, 2 H), 1.75–1.87 (m, 4 H), 1.57–1.67 (m, 2 H), 0.96 (t, *J* = 7.7 Hz, 3 H); ^{13}C NMR (176 MHz, $CDCl_3$) as a mixture of rotational isomers δ 176.48. 176.45, 172.0, 167.0, 166.9, 138.83, 138.77, 135.5, 135.4, 132.4, 132.3, 131.2, 129.5, 129.38, 129.36, 127.2, 120.7, 120.6, 51.97, 51.91, 51.74, 51.69, 45.34, 45.31, 32.5, 32.2, 29.3, 28.43, 28.40, 25.5, 23.7, 23.6, 8.2; HRMS (TOF MS ES+) calcd for $C_{20}H_{24}N_4O_4Na$ [M+Na]: 407.1695, found 407.1704.

methyl (E)-3-(2-(3-(3-ethyl-2-oxopiperidin-3-yl)propanamido)phenyl)acrylate (191). To a solution of the azide **188** (0.0210 g, 0.0546 mmol) dissolved in THF (0.55 mL, 0.1 M) stirring at room temperature was added triphenyl phosphine (0.0246 g, 0.094 mmol). The mixture was heated to 50 °C. After 3 hours, the reaction mixture was cooled to room temperature and concentrated. The resulting mixture was purified by flash column chromatography (1:49 10% NH_4OH in MeOH : EtOAc) to give **191** (0.0166g, 0.0463 mmol, 85%) as a white solid.

Data for **191**: R_f 0.50 (9:1 EtOAc : 10% NH_4OH in MeOH); mp = 150–151 ^oC; IR (thin film) 2925, 1717, 1683 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 8.44 (br s, 1 H), 7.96 (d, *J* = 16.1 Hz, 1 H), 7.74 (d, *J* = 7.7 Hz, 1 H), 7.56 (d, *J* = 7.7 Hz, 1 H), 7.37 (t,

J = 7.0 Hz, 1 H), 7.16 (t, *J* = 7.7 Hz, 1 H), 6.58 (br s, 1 H), 6.40 (d, *J* = 16.1 Hz, 1 H), 3.79 (s, 3 H), 3.32 (t, *J* = 3.5 Hz, 2 H), 2.68 (quintet, *J* = 7.7 Hz, 1 H), 2.43 (quintet, *J* = 7.7 Hz, 1 H), 2.04 (quintet, *J* = 7.0 Hz, 1 H), 1.96 (quintet, *J* = 7.7 Hz, 1 H), 1.77–1.84 (m, 4 H), 1.59–1.67 (m, 2 H), 0.90 (t, *J* = 7.0 Hz, 3 H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 177.6, 172.8, 167.9, 140.5, 136.7, 130.9, 127.2, 127.0, 125.4, 125.1, 119.5, 52.0, 44.8, 42.9, 33.6, 33.3, 30.5, 29.8, 19.5, 8.4; HRMS (TOF MS ES+) calcd for $C_{20}H_{26}N_2O_4Na$ [M+Na]: 381.1790, found 381.1787.

methyl (E)-3-(2-(3-(3-ethyl-2-methoxy-3,4,5,6-tetrahydropyridin-3-yl)propanamido)phenyl)acrylate (197). To a solution of **191** (0.0500 g, .140 mmol) dissolved in DCM (1.4 mL, 0.1 M) were added Cs_2CO_3 (0.1346 g, 0.419 mmol) and Me_3OBF_4 (0.0325 g, 0.220 mmol). The mixture was stirred at room temperature. After 80 minutes, the reaction mixture was diluted with DCM, washed with saturated aqueous $NaHCO_3$, dried over $MgSO_4$, filtered, and concentrated. The resulting mixture was purified by flash column chromatography (1:1 hexanes: EtOAc) to give **197** (0.0422 g, 0.113 mmol, 81%) as a colorless oil.

Data for **197**: R_f 0.33 (1:2 hexanes : EtOAc); IR (thin film) 2943, 1717, 1667cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 15.6 Hz, 1 H), 7.65–7.71 (m, 1 H), 7.51 (d, *J* = 7.6 Hz, 1 H), 7.35 (t, *J* = 7.6 Hz, 1 H), 7.16 (t, *J* = 7.2 Hz, 1 H), 6.36 (d, *J* = 15.6 Hz, 1 H), 3.77 (s, 3 H), 3.57 (br s, 3 H), 3.43 (br s, 2 H), 2.36–2.46 (m, 1 H), 2.24–2.34 (m, 1 H), 1.94–2.05 (m, 1 H), 1.81–1.91 (m, 1 H), 1.64–1.72 (m, 2 H), 1.51–1.63 (m, 3 H), 1.47–1.42 (m, 1 H), 0.82 (t, *J* = 7.2 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 167.3, 166.2, 139.8, 136.1, 130.9, 127.6, 127.2, 125.8, 125.3, 120.1, 52.1, 51.9, 47.3, 41.3, 34.1, 33.0, 31.4, 29.9, 20.7, 8.8; HRMS (TOF MS ES+) calcd for $C_{21}H_{29}N_2O_4$ [M+H]: 373.2127, found 373.2145.

3-(3-ethyl-2-oxopiperidin-3-yl)-N-(2-iodophenyl)propanamide (198). To a solution of the acid **209** (0.2102 g, 1.06 mmol) dissolved in THF (2.1 mL, 0.5 M) stirring at

room temperature were added freshly chromatographed 2-iodoaniline (0.4670 g, 2.13 mmol) and $POCl_3$ (0.1 mL, 1.07 mmol). The mixture was heated to 60 °C. After 0.5 hours, the reaction mixture was cooled to room temperature and concentrated. The solids were extracted with chloroform and the combined organic extracts were washed with saturated aqueous sodium bicarbonate, saturated aqueous sodium chloride, dried over $MgSO_4$, filtered, and concentrated. The resulting oil was purified by flash column chromatography (1:4 hexanes: EtOAc) to give **198** (0.2964g, 0.741 mmol, 70%) as a white solid.

Data for **198**: R_f 0.37 (EtOAc); mp = 125–126 ^oC; IR (thin film) 2962, 1644 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 8.16 (d, *J* = 7.7 Hz, 1 H), 7.77 (dd, *J* = 8.4, 1.4 Hz, 1 H), 7.56 (br s, 1 H), 7.32 (td, *J* = 8.4, 0.7 Hz, 1 H), 6.83 (td, *J* = 7.7, 1.4 Hz, 1 H), 5.72 (br s, 1 H), 3.31 (td, *J* = 3.5, 2.1 Hz, 2 H), 2.52–2.57 (m, 1 H), 2.47–2.51 (m, 1 H), 2.06 (ddd, *J* = 14.0, 11.2, 5.6 Hz, 1 H), 1.99 (ddd, *J* = 14.0, 10.5, 5.6 Hz, 1 H), 1.82–1.87 (m, 2 H), 1.78–1.82 (m, 2 H), 1.66–1.70 (m, 1 H), 1.61 (sextet, *J* = 7.7 Hz, 1 H), 0.92 (t, *J* = 7.7 Hz, 3 H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 176.6, 171.6, 139.0, 138.5, 129.3, 126.0, 122.5, 90.3, 44.5, 42.9, 33.5, 33.2, 30.5, 29.8, 19.5, 8.5; HRMS (TOF MS ES+) calcd for $C_{16}H_{22}N_2O_2I$ [M+H]: 401.0726, found 401.0739.

3-(3-ethyl-2-methoxy-3,4,5,6-tetrahydropyridin-3-yl)-N-(2-iodophenyl)propanamide (199). To a solution of the lactam **198** (0.0296 g, 0.0740 mmol) dissolved in DCM (0.75 mL, 0.1 M) stirring at room temperature were added Cs_2CO_3 (0.0741 g, 0.227 mmol) and Me_3OBF_4 (0.0170g, 0.115 mmol). After 2 hours, the reaction mixture was diluted with DCM and washed with saturated aqueous sodium bicarbonate. The DCM solution was then dried over $MgSO_4$, filtered, and concentrated. The resulting solids were purified by flash column chromatography (1:1 hexanes: EtOAc) to give **199** (0.0266g, 0.0642 mmol, 87%) as a white solid.

Data for **199**: R_f 0.67 (9:1 EtOAc : 10% NH_4OH in MeOH); mp = 74–76 ^oC; IR (thin film) 2938, 1668, 1519 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 8.21 (d, *J* = 7.7 Hz, 1 H), 7.77 (d, *J* = 7.7 Hz, 1 H), 7.42 (br s, 1 H), 7.33 (td, *J* = 8.4, 1.4 Hz, 1 H), 6.83 (t, *J* = 7.7 Hz, 1 H), 3.61 (s, 3 H), 3.47 (t, *J* = 5.6 Hz, 2 H), 2.43 (td, *J* = 15.4, 5.6 Hz, 1 H), 2.29 (ddd, *J* = 15.4, 11.9, 4.9 Hz, 1 H), 2.03 (ddd, *J* = 13.3, 11.9, 4.9 Hz, 1 H), 1.89 (ddd, *J* = 13.3, 11.2, 4.9 Hz, 1 H), 1.68–1.75 (m, 2 H), 1.54–1.66 (m, 3 H), 1.49 (sextet, *J* = 7.0 Hz, 1 H), 0.85 (t, *J* = 7.7 Hz, 3 H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 171.3, 165.9, 138.9, 138.3, 129.4, 126.0, 122.0, 90.0, 52.2, 47.5, 41.3, 34.2, 33.9, 31.4, 30.0, 20.8, 8.9; HRMS (TOF MS ES+) calcd for $C_{17}H_{24}N_2O_2I$ [M+H]: 415.0883, found 415.0894.

methyl (E)-3-(2-(2,6-dioxopiperidin-1-yl)phenyl)acrylate (S19). To a solution of 2-aminophenyl methylcinamate **184** (0.9930 g, 5.77 mmol) dissolved in THF (19 mL, 0.3 M) were added AcOH (0.07 mL, 1.22 mmol) and glutaric anhydride (0.9838 g, 8.62 mmol). The mixture was heated to reflux. After 20 hours, the reaction mixture was cooled to room temperature and Ac_2O (1.1 mL, 11.7 mmol) and Et_3N (2.4 mL, 17.2 mmol) were added. The mixture was heated to reflux again for an additional 20 minutes. After cooling, the reaction was dilluted with EtOAc, washed with saturated aqueous sodium chloride, dried over $MgSO_4$, filtered, and concentrated. The resulting mixture was purified by flash column chromatography (1:1 hexanes: EtOAc) to give **S19** (1.3983 g, 5.12 mmol, 89%) as a white solid.

Data for **S19**: R_f 0.47 (3:1 hexanes : EtOAc); mp = 125–126.5 ^oC; IR (thin film) 2952, 1715, 1689 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (dd, *J* = 7.6, 1.6 Hz, 1 H), 7.40–7.50 (m, 3 H), 7.09 (dd, *J* = 8.0, 1.6 Hz, 1 H), 6.41 (d, *J* = 16.0 Hz, 1 H), 3.77 (s, 3 H), 2.94–2.78 (m, 4 H), 2.10–2.22 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 167.1, 138.9, 134.9, 132.5, 131.1, 129.6, 129.5, 127.4, 120.8; HRMS (TOF MS ES+) calcd for $C_{15}H_{16}NO_4$ [M+H]: 274.1079, found 274.1082.

methyl (E)-3-(2-(2,6-dithioxopiperidin-1-yl)phenyl)acrylate (202). To a solution of the imide **S19** (0.4122 g, 1.51 mmol) dissolved in toluene (5 mL, 0.3 M) stirring at room temperature was added Laweson's reagent (0.6730 g, 1.66 mmol). The mixture was heated to reflux. After 3 hours, the reaction mixture was cooled to room temperature and concentrated. The resulting mixutre was purified by flash column chromatography (9:1 hexanes: EtOAc) to give **202** (0.4165 g, 1.36 mmol, 90%) as a bright red solid.

Data for **202**: R_f 0.27 (3:1 hexanes : EtOAc); mp = 108–110 ^oC; IR (thin film) 2949, 1715, 1637 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.69 (dd, *J* = 7.2, 1.6 Hz, 1 H), 7.41–7.49 (,m 2 H), 7.34 (d, *J* = 16.0 Hz, 1 H), 7.04 (dd, *J* = 8.0, 1.6 Hz, 1 H), 3.77 (s, 3 H), 3.46 (qdd, *J* = 18.0, 6.8, 5.2 4 H), 2.09–2.21 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.6, 167.1, 144.0, 138.6, 131.6, 131.3, 129.2, 129.1, 127.5, 120.9, 52.0, 44.9, 19.8; HRMS (TOF MS ES+) calcd for $C_{11}H_{11}NS_2I$ [M+H]: 347.9378, found 347.9390.

methyl 2-(4a-(benzylamino)-1-thioxo-2,3,4,4a-tetrahydro-1H,6H-benzo[d]pyrido[2,1-b][1,3]thiazin-6-yl)acetate (203). To a solution of **202** (0.0491 g, .161 mmol) dissolved in THF (0.5 mL, 0.3 M) was added $BnNH_2$ (0.04 mL, 0.37 mmol). The mixture was stirred at room temperature. After 25 minutes, the reaction mixture was concentrated. The resulting mixture was purified by flash column chromatography (2:1 hexanes: EtOAc) to give **203** (0.0608 g, 0.147 mmol, 92%) as a yellow solid.

Data for **203**: R_f 0.11 (3:1 hexanes : EtOAc); mp = 96.5–98.5 ^oC; IR (thin film) 3318, 3206, 2948, 1737 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 9.34 (br s, 1 H), 7.34–7.42 (m, 5 H), 7.22 (td, *J* = 7.0, 1.4 Hz, 1 H), 7.18 (td, *J* = 7.7, 1.4 Hz, 1 H), 7.10 (dd, *J* = 7.7, 1.4 Hz, 1 H), 6.61 (d, *J* = 7.7 Hz, 1 H), 4.84 (qd, *J* = 14.7, 4.9 Hz, 2 H), 4.43 (dd, *J* = 9.1, 7.0 Hz, 1 H), 3.64 (s, 3 H), 2.88–2.91 (m, 1 H), 2.81–2.85 (m, 1 H), 2.70 (ddd, *J*

= 14.7, 10.5, 4.9 Hz, 1 H), 2.54–2.60 (m, 3 H), 2.28–2.35 (m, 1 H), 2.13–2.19 (m, 1 H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 203.9, 170.3, 164.3, 141.4, 136.4, 129.0, 128.9, 128.3, 128.1, 126.9, 126.8, 121.3, 52.2, 50.9, 44.4, 43.0, 38.9, 38.2, 27.6; HRMS (TOF MS ES+) calcd for $C_{22}H_{25}N_2O_2S_2$ [M+H]: 413.1357, found 413.1345.

1-(2-iodophenyl)piperidine-2,6-dione (S20). To a solution of 2-aminophenyl methylcinamate **184** (0.9930 g, 5.77 mmol) dissolved in THF (19 mL, 0.3 M) were added AcOH (0.07 mL, 1.22 mmol) and glutaric anhydride (0.9838 g, 8.62 mmol). The mixture was heated to reflux. After 20 hours, the reaction mixture was cooled to room temperature and Ac_2O (1.1 mL, 11.7 mmol) and Et_3N (2.4 mL, 17.2 mmol) were added. The mixture was heated to reflux again for an additional 20 minutes. After cooling, the reaction was dilluted with EtOAc, washed with saturated aqueous sodium chloride, dried over $MgSO_4$, filtered, and concentrated. The resulting mixture was purified by flash column chromatography (1:1 hexanes: EtOAc) to give **S20** (1.3983 g, 5.12 mmol, 89%) as a white solid.

Data for **S20**: R_f 0.41 (1:1 hexanes : EtOAc); mp = 134–135 ^{o}C; IR (thin film) 1727, 1683 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (dd, *J* = 11.6, 1.6 Hz, 1 H), 7.44 (td, *J* = 8.0, 1.6 Hz, 1 H), 7.10–7.16 (m, 2 H), 2.73–2.91 (m, 4 H), 2.17–2.27 (m, 1 H), 2.04–2.14 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 139.7, 138.5, 130.4, 129.7, 129.5, 99.1, 33.2, 17.2; HRMS (TOF MS ES+) calcd for $C_{11}H_{11}NO_2I$ [M+H]: 315.9835, found 315.9836.

1-(2-iodophenyl)piperidine-2,6-dithione (204). To a solution of the imide **S20** (0.3203 g, 1.02 mmol) dissolved in toluene (3.4 mL, 0.3 M) stirring at room temperature was added Laweson's reagent (0.4574 g, 1.13 mmol). The mixture was heated to reflux. After 3.5 hours, the reaction mixture was cooled to room temperature and concentrated. The resulting mixture was purified by flash column

chromatography (9:1 hexanes: EtOAc) to give **204** (0.2638 g, 0.760 mmol, 75%) as a bright red solid.

Data for **204**: R_f 0.41 (6:1 hexanes : EtOAc); mp = 150–151 ^{o}C; IR (thin film) 2929, 1268, 1260, 1146 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.88 (dd, *J* = 8.4, 1.4 Hz, 1 H), 7.44 (td, *J* = 7.7, 0.7 Hz, 1 H), 7.14 (dd, *J* = 7.7, 1.4 Hz, 1 H), 7.09 (ddd, *J* = 8.4, 7.7, 2.1 Hz, 1 H), 3.44 (qq, *J* = 18.2, 4.2 Hz, 4 H), 2.16–2.21 (m, 1 H), 2.06–2.11 (m, 1 H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 205.4, 146.5, 140.0, 129.7, 129.6, 129.5, 98.2, 44.8, 19.5; HRMS (TOF MS ES+) calcd for $C_{11}H_{11}NS_2I$ [M+H]: 347.9378, found 347.9390.

6-(benzylamino)-1-(2-iodophenyl)-6-mercaptopiperidine-2-thione (205). To a solution of **204** (0.0498 g, .143 mmol) dissolved in THF (0.7 mL, 0.2 M) was added benzylamine (0.02 mL, 0.183 mmol). The mixture was stirred at room temperature. After 22 hours, the reaction mixture was concentrated. The resulting mixture was purified by flash column chromatography (3:1 hexanes : EtOAc) to give **205** (0.0565 g, 0.134 mmol, 94%) as a colorless oil.

Data for **205**: R_f 0.14 (3:1 hexanes : EtOAc); IR (thin film) 3204, 2970, 1521, 1390cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.99 (br s, 1 H), 7.93 (dd, *J* = 7.7, 1.4 Hz, 2 H), 7.89 (dd, *J* = 7.7, 0.7 Hz, 1 H), 7.40 (td, *J* = 7.0, 0.7 Hz, 1 H), 7.31–7.36 (m, 5 H), 7.03 (td, *J* = 7.7, 0.7 Hz, 1 H), 4.85 (d, *J* = 4.9 Hz, 2 H), 3.01 (t, *J* = 7.0 Hz, 2 H), 2.92 (t, *J* = 7.0 Hz, 2 H), 2.42 (quin., *J* = 7.0 Hz, 2 H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 205.0, 204.2, 139.8, 139.5, 136.1, 129.2, 129.1, 128.9, 128.6, 128.3, 127.6, 95.5, 50.6, 45.8, 44.3, 28.6; HRMS (TOF MS ES+) calcd for $C_{18}H_{20}N_2S_2I$ [M+H]:455.0113, found 455.0134.

3-(3-ethyl-2-oxopiperidin-3-yl)propanoic acid (209). To a solution of the known lactam **208** (0.5461 g, 3.01 mmol) dissolved in 1,4-dioxane (10 mL, 0.3 M) and water (10 mL, 0.3 M) stirring at room temperature were added $NaIO_4$ (2.5785 g, 0.12.1 mmol) and $RuCl_3 \bullet H_2O$ (0.0311g, 0.150 mmol). After 6 hours, the reaction mixture was concentrated. The resulting solids were extracted with EtOAc, filtered through celite 535, and concentrated. The resulting oil was purified by flash column chromatography (1:20:79 AcOH : hexanes: EtOAc) to give **209** (0.4406g, 2.21 mmol, 73%) as a lightly colored oil which produced colorless crystals upon standing.

Data for **209**: R_f 0.37 (49:1 EtOAc : AcOH); mp = 124–125 ^oC; IR (thin film) 2944, 1697, 1626 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 12.76 (br s, 1 H), 7.75 (br s, 1 H), 3.23–3.31 (m, 2 H), 2.44 (ddd, *J* = 16.1, 8.4, 7.0 Hz, 1 H), 2.34 (ddd, *J* = 14.7, 7.7, 6.3 Hz, 1 H), 1.93 (ddd, *J* = 14.0, 7.7, 7.0 Hz, 1 H), 1.82–1.88 (m, 2 H), 1.72–1.80 (m, 3 H), 1.63 (ddd, *J* = 14.0, 8.4, 4.2 Hz, 1 H), 1.51 (sextet, *J* = 7.0 Hz, 1 H), 0.87 (t, 3 H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 178.4, 178.3, 43.7, 24.5, 32.4, 30.8, 30.1, 29.4, 19.5, 8.5; HRMS (TOF MS ES+) calcd for $C_{10}H_{17}NO_3Na$ [M+Na]: 222.1106, found 222.1116.

methyl 3-(3-ethyl-2-oxopiperidin-3-yl)propanoate (207). To a solution of the carboxylic acid **209** (0.7505 g, 3.77 mmol) dissolved in PhH (7.5 mL, 0.5 M) and MeOH (3.8 mL, 1M) stirring at room temperature was added $TMSCHN_2$ (2M in hexanes, 2.8 mL, 5.6 mmol). After 10 minutes, the reaction was quenched by addition of glacial acetic acid until the yellow color was no longer visible. The reaction mixture was then concentrated. Purification by flash column chromatography (1:2 hexanes : EtOAc) gave **207** (0.7141g, 3.35 mmol, 89%) as a white solid.

Data for **207**: R_f 0.31 (EtOAc); mp = 48–50 ^oC; IR (thin film) 2950, 1737, 1655 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 6.11 (br s, 1 H), 3.64 (s, 3 H), 3.25 (td, *J* = 6.3, 2.8 Hz, 2 H), 2.40 (ddd, *J* = 21.0, 10.5, 4.9 Hz, 1 H), 2.34 (ddd, *J* = 16.1, 11.2, 5.6 Hz, 1 H),

1.92 (ddd, *J* = 14.0, 11.2, 5.6 Hz, 1 H), 1.84 (ddd, *J* = 14.0, 11.2, 5.6 Hz, 1 H), 1.77–1.81 (m, 2 H), 1.70–1.75 (m, 2 H), 1.59 (ddd, *J* = 11.9, 7.7, 4.9 Hz, 1 H), 1.51 (sextet, *J* = 7.7 Hz, 1 H), 0.87 (t, *J* = 7.7 Hz, 3 H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 176.5, 174.4, 51.7, 44.1, 42.7, 32.8, 30.5, 29.7, 29.5, 19.7, 8.5; HRMS (TOF MS ES+) calcd for $C_{11}H_{19}NO_3Na$ [M+Na]: 236.1263, found 236.1272.

methyl 3-(3-ethyl-2-methoxy-3,4,5,6-tetrahydropyridin-3-yl)propanoate (211). To a solution of the lactam **207** (0.106 g, 0.498 mmol) dissolved in DCM (1.7 mL, 0.3 M) stirring at room temperature were added $NaHCO_3$ (0.252 g, 3.00 mmol) and Me_3OBF_4 (0.222g, 1.50 mmol). After 70 minutes, the reaction mixture was diluted with DCM and washed with saturated aqueous sodium chloride. The DCM solution was then dried over $MgSO_4$, filtered, and concentrated to give **211** (0.1132g, 0.498 mmol, 99%) as a colorless oil.

Data for **211**: R_f 0.52 (2:3 EtOAc : hexanes); IR (thin film) 2942, 2860, 1739, 1671 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 3.65 (s, 3 H), 3.55 (s, 3 H), 3.42 (t, *J*= 5.6 Hz, 2 H), 2.32 (ddd, *J* = 16.1, 11.9, 4.9 Hz, 1 H), 2.20 (ddd, *J* = 16.1, 11.9, 4.9 Hz, 1 H), 1.89 (td, *J* = 12.6, 4.9 Hz, 1 H), 1.74 (td, *J* = 12.6, 5.6 Hz, 1 H), 1.63–1.69 (m, 2 H), 1.54–1.61 (m, 2 H), 1.47–1.52 (m, 1 H), 1.41 (sextet, *J* = 7.0 Hz, 1 H), 0.81 (t, *J* = 7.7 Hz, 3 H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 174.3, 165.9, 52.0, 51.7, 47.4, 41.1, 33.6, 31.2, 29.99, 29.95, 20.8, 8.9; HRMS (TOF MS ES+) calcd for $C_{12}H_{22}NO_3$ [M+H]: 228.1600, found 228.1596.

methyl 3-(3-ethyl-2-thioxopiperidin-3-yl)propanoate (212). To a solution of the lactam **207** (0.4291 g, 2.01 mmol) dissolved in PhMe (6.7 mL, 0.3 M) stirring at room temperature was added Laweson's reagent (0.9018 g, 2.23 mmol). The mixture was heated to reflux. After 2 hours, the reaction mixture was cooled to room temperature and concentrated. Purification by flash column chromatography (3:1 hexanes : EtOAc) gave **212** (0.4394g, 1.92 mmol, 95%) as a white solid.

Data for **212**: R_f 0.56 (2:3 EtOAc : hexanes); mp = 85–87 ^{o}C; IR (thin film) 2952, 1735 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.67 (br s, 1 H), 3.66 (s, 3 H), 3.29 (ddd, *J* = 5.6, 5.6, 2.8 Hz, 2 H), 2.47 (ddd, *J* = 15.4, 11.2, 4.9 Hz, 1 H), 2.36 (ddd, *J* = 15.4, 11.9, 4.9 Hz, 1 H), 2.28 (ddd, *J* = 13.3, 11.9, 5.6 Hz, 1 H), 1.91–1.98 (m, 2 H), 1.81–1.89 (m, 2 H), 1.77 (ddd, *J* = 11.9, 7.0, 4.2 Hz, 1 H), 1.73 (sextet, *J* = 7.7 Hz, 1 H), 1.63 (ddd, *J* = 14.7, 8.4, 3.5 Hz, 1 H), 0.91 (t, *J* = 7.7 Hz, 3 H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 210.5, 174.2, 51.8, 48.2, 45.4, 36.4, 35.0, 29.8, 27.6, 19.4, 8.7; HRMS (TOF MS ES+) calcd for $C_{11}H_{20}NO_2S$ [M+H]: 230.1215, found 230.1207.

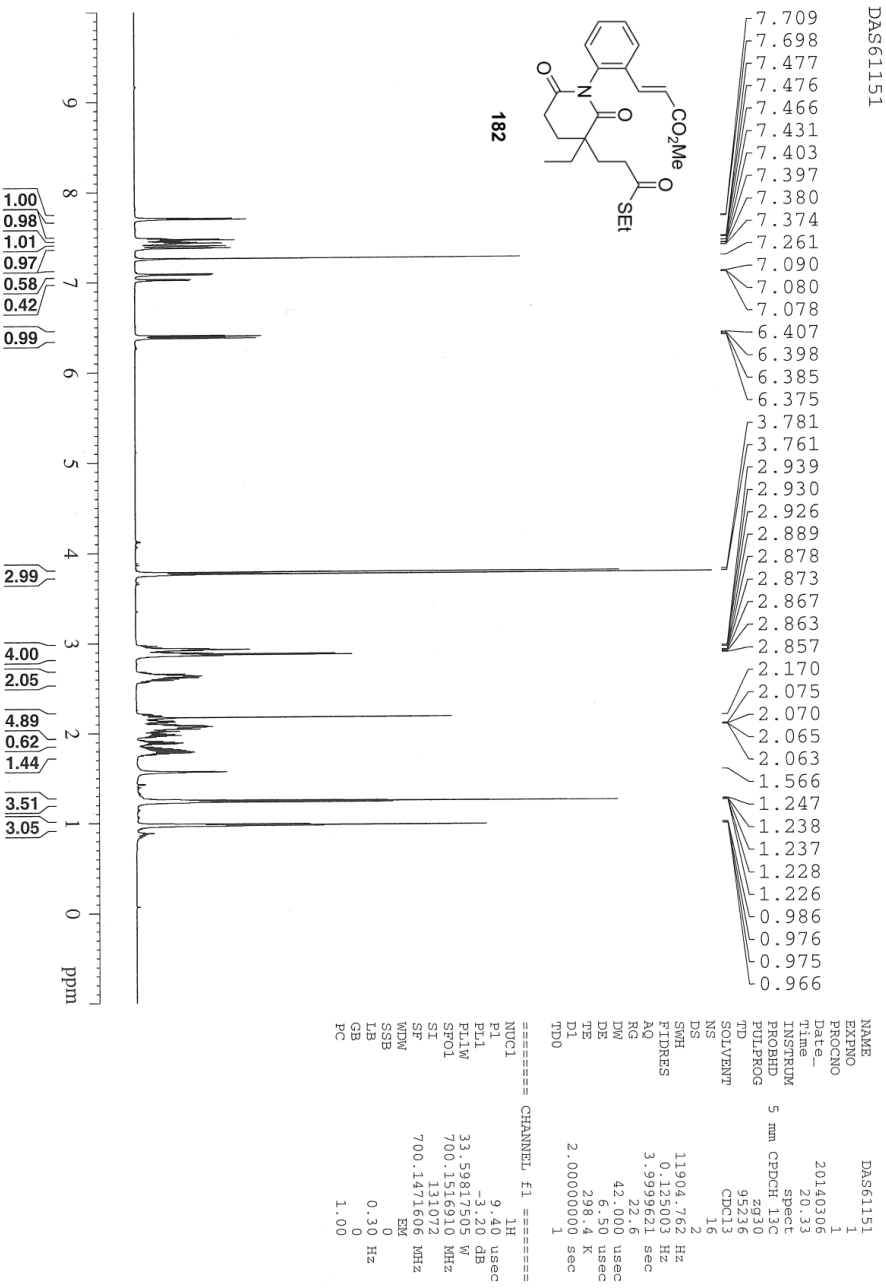
methyl 3-(3-ethyl-2-(methylthio)-3,4,5,6-tetrahydropyridin-3-yl)propanoate (213). To a solution of the thiolactam **212** (0.0486 g, 0.212 mmol) dissolved in DCM (0.7 mL, 0.3 M) stirring at room temperature were added $NaHCO_3$ (0.0361 g, 0.430 mmol) and MeI (0.13mL, 2.09 mmol). After 4.5 hours, the reaction mixture was diluted with DCM and washed with saturated aqueous sodium bicarbonate. The DCM solution was then dried over $MgSO_4$, filtered, and concentrated to give **213** (0.0485g, 0.200 mmol, 94%) as a colorless oil.

Data for **213**: R_f 0.44 (1:3 EtOAc : hexanes); IR (thin film) 2933, 1739, 1618 cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 3.66 (s, 3 H), 3.58 (qt, *J*= 16.8, 6.3 Hz, 2 H), 2.28–2.36 (m, 2 H), 2.20 (s, 3 H), 1.98 (ddd, *J* = 14.0, 11.2, 6.3 Hz, 1 H), 1.67–1.79 (m, 3 H), 1.48–1.62 (m, 4 H), 0.86 (t, *J* = 7.7 Hz, 3 H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 174.2, 172.1, 51.8, 50.9, 44.4, 35.2, 33.4, 29.7, 29.1, 20.6, 12.1, 8.8; HRMS (TOF MS ES+) calcd for $C_{12}H_{22}NO_2S$ [M+H]: 244.1371, found 244.1360.

ethyl 2-oxo-1-phenyl-1,3,4,5,6,7-hexahydro-1,8-naphthyridine-4a(2H)-carboxylate (218). To a solution of **178** (0.0309 g, .138 mmol), Cs_2CO_3 (0.0980 g, 301 mmol), 1,10-phenanthroline (0.0110 g, 0.056 mmol), and CuI (0.0055 g, 0.029 mmol) dissolved in dry, degassed 1,4-dioxane (0.6 mL, 0.25 M) was added

iodobenzene (0.04 mL, 0.36 mmol). The mixture was sealed in a bomb and heated to 100 °C. After 24 hours, the reaction mixture was diluted with $CHCl_3$, filtered through celite 353, and concentrated. The resulting mixture was purified by preparative TLC (1:9 10% NH_4OH in MeOH: EtOAc) to give **218** (0.0144 g, 0.048 mmol, 35%) as a colorless oil.

Data for **218**: R_f 0.30 (1:9 10% NH_4OH in MeOH : EtOAc); IR (thin film) 2958, 1730, 1661, 1521cm^{-1}; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.40 (t, *J* = 7.7 Hz, 2 H), 7.26–7.29 (m, 1 H), 7.21 (d, *J* = 7.7 Hz, 2 H), 4.24–4.33 (m, 2 H), 3.73–3.77 (m, 1 H), 3.65–3.68 (m, 1 H), 2.53–2.57 (m, 1 H), 2.44–2.47 (m, 1 H), 2.35–2.40 (m, 2 H), 1.95–2.03 (m, 2 H), 1.86–1.94 (m, 2 H), 1.82 (td, *J* = 12.6, 4.9 Hz, 1 H), 1.32 (t, *J* = 7.0 Hz, 3 H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 180.6, 171.9, 170.0, 143.9, 129.7, 127.7, 126.3, 62.5, 52.0, 47.4, 32.2, 31.6, 30.6, 19.9, 14.3, ; HRMS (TOF MS ES+) calcd for $C_{17}H_{21}N_2O_3$ [M+H]: 301.1552, found 301.1561.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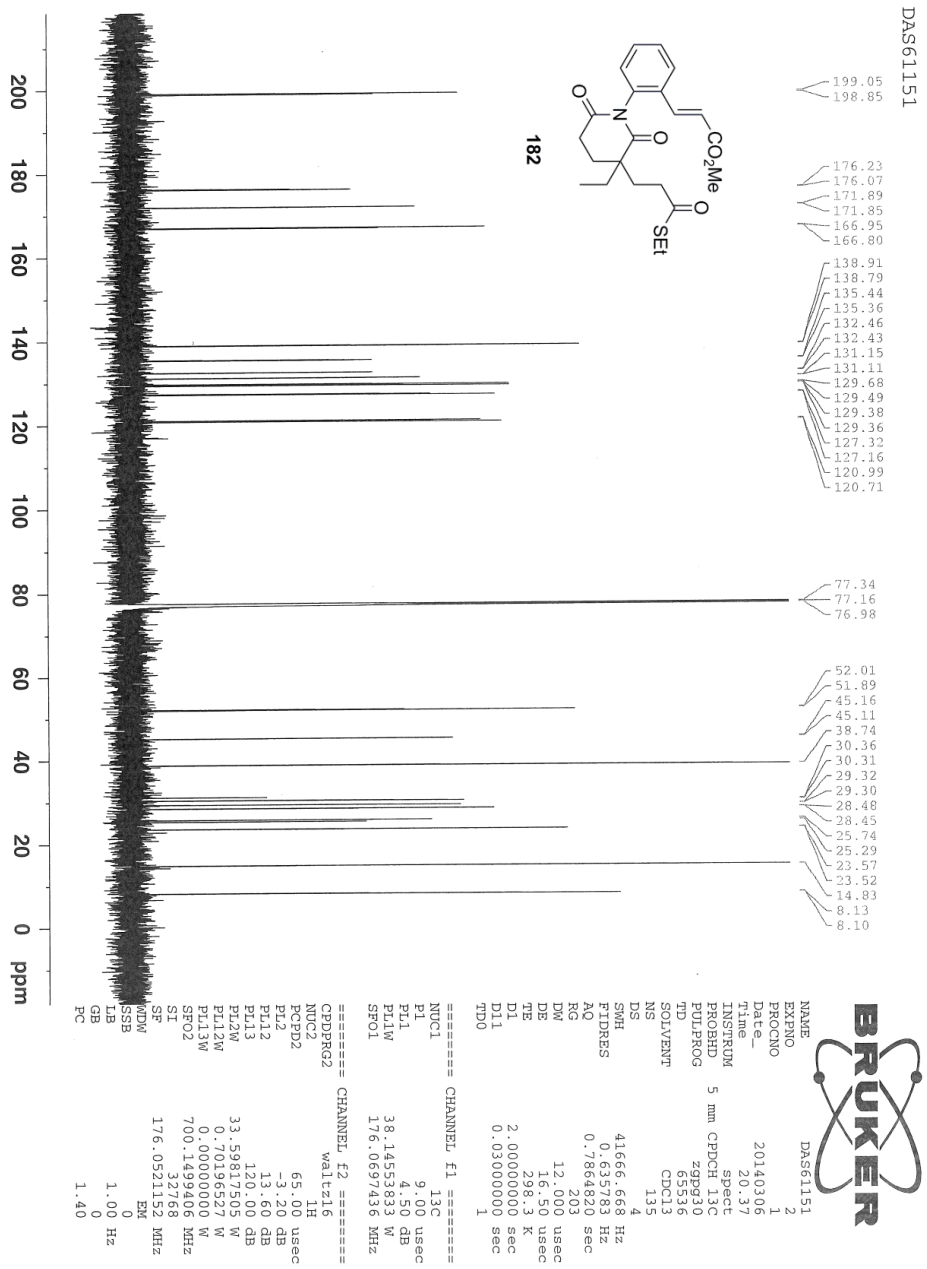
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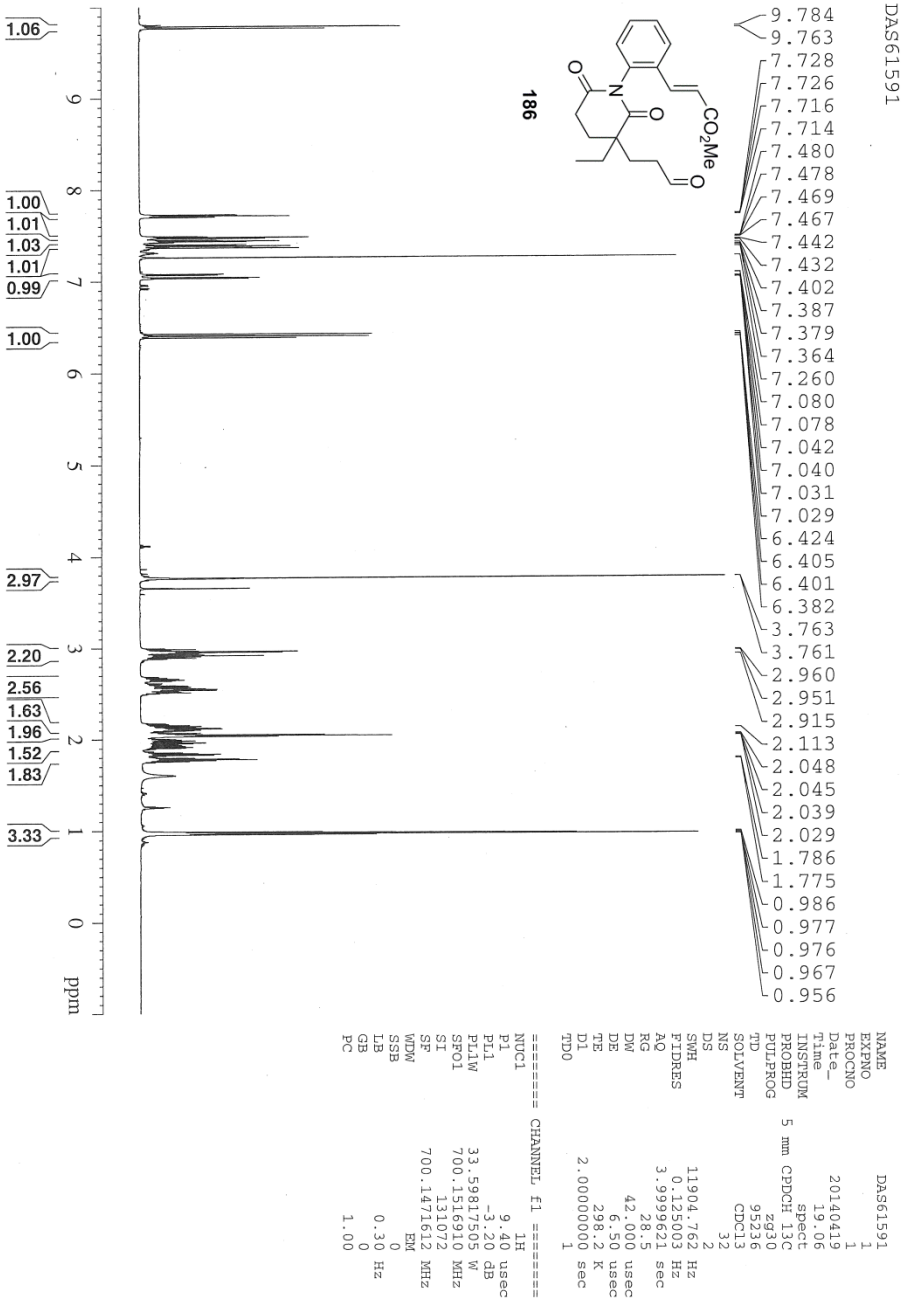
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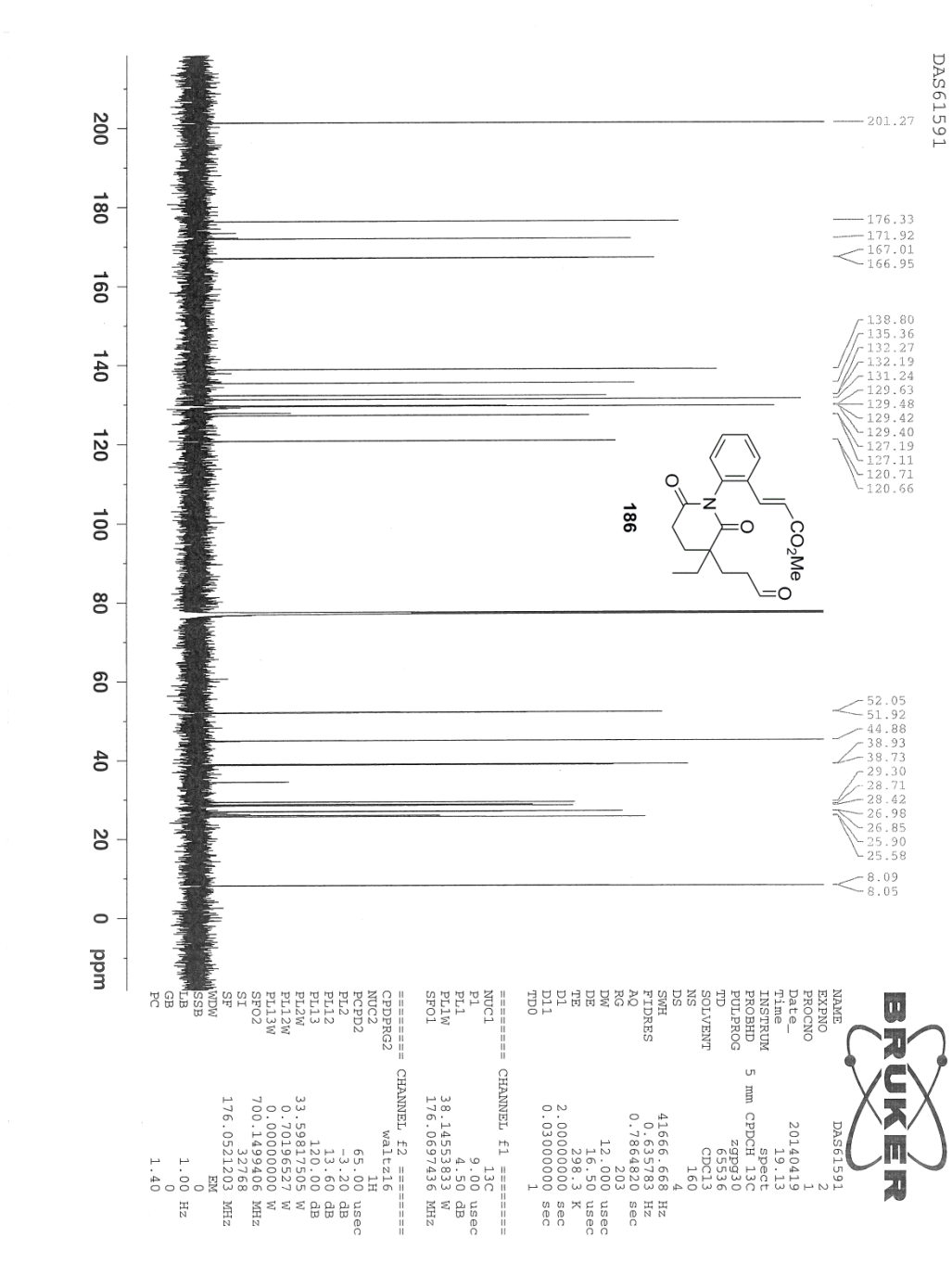
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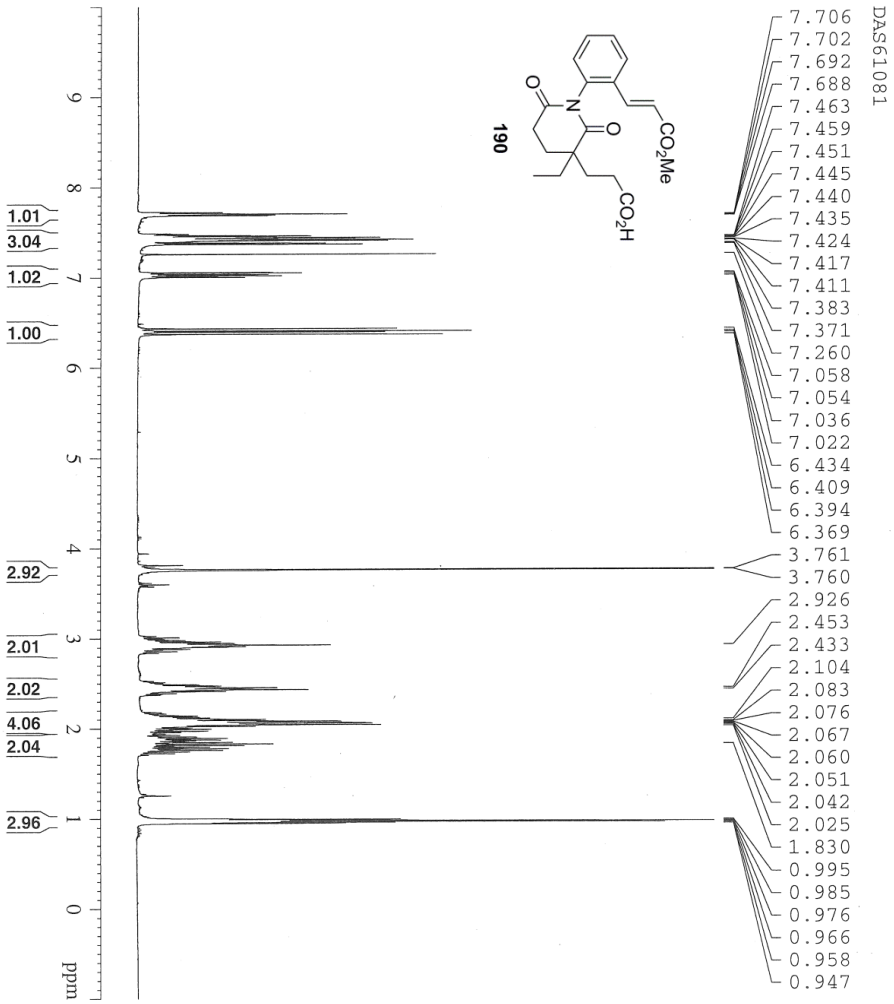
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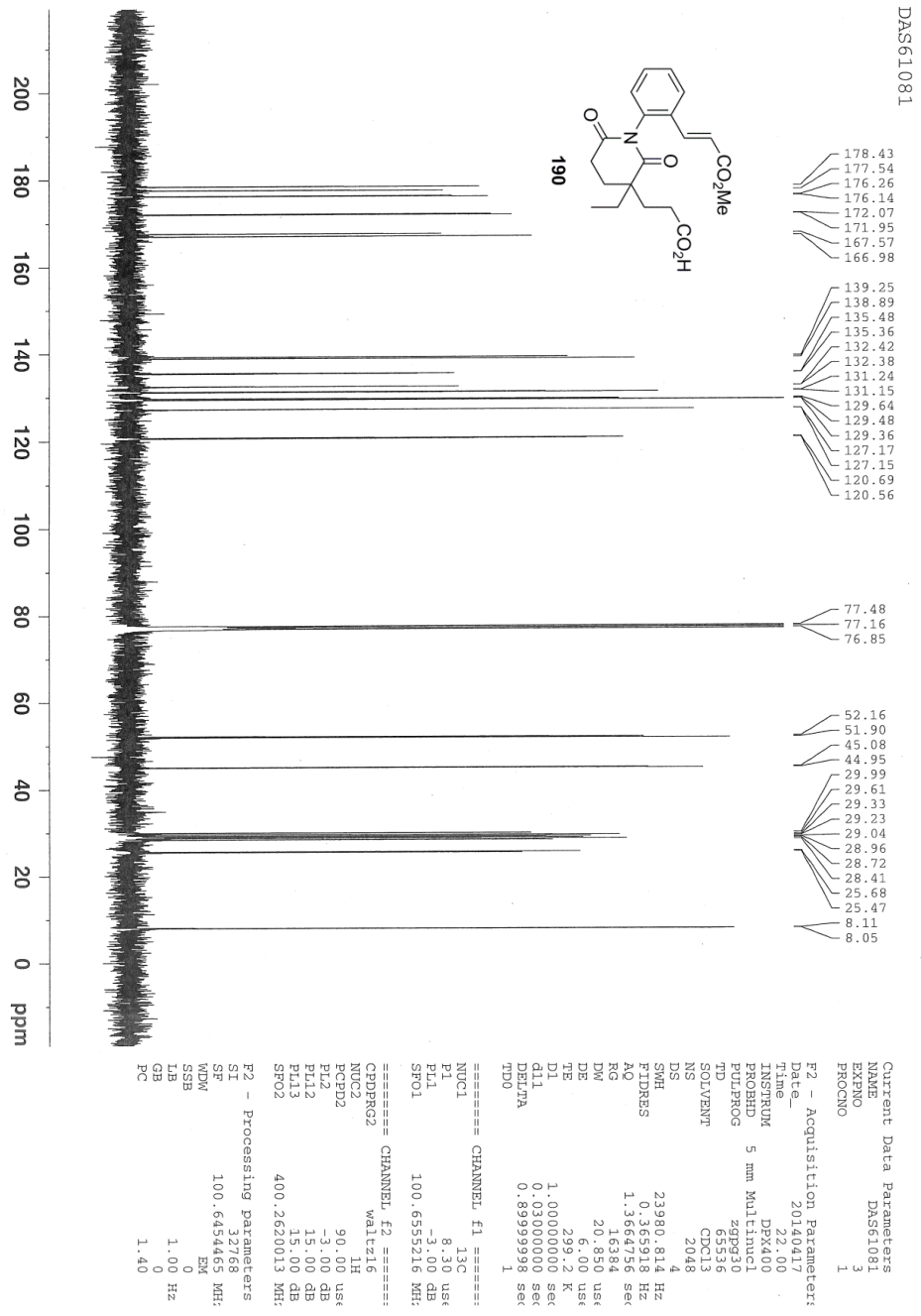


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SFO2          400.2620013 MHz

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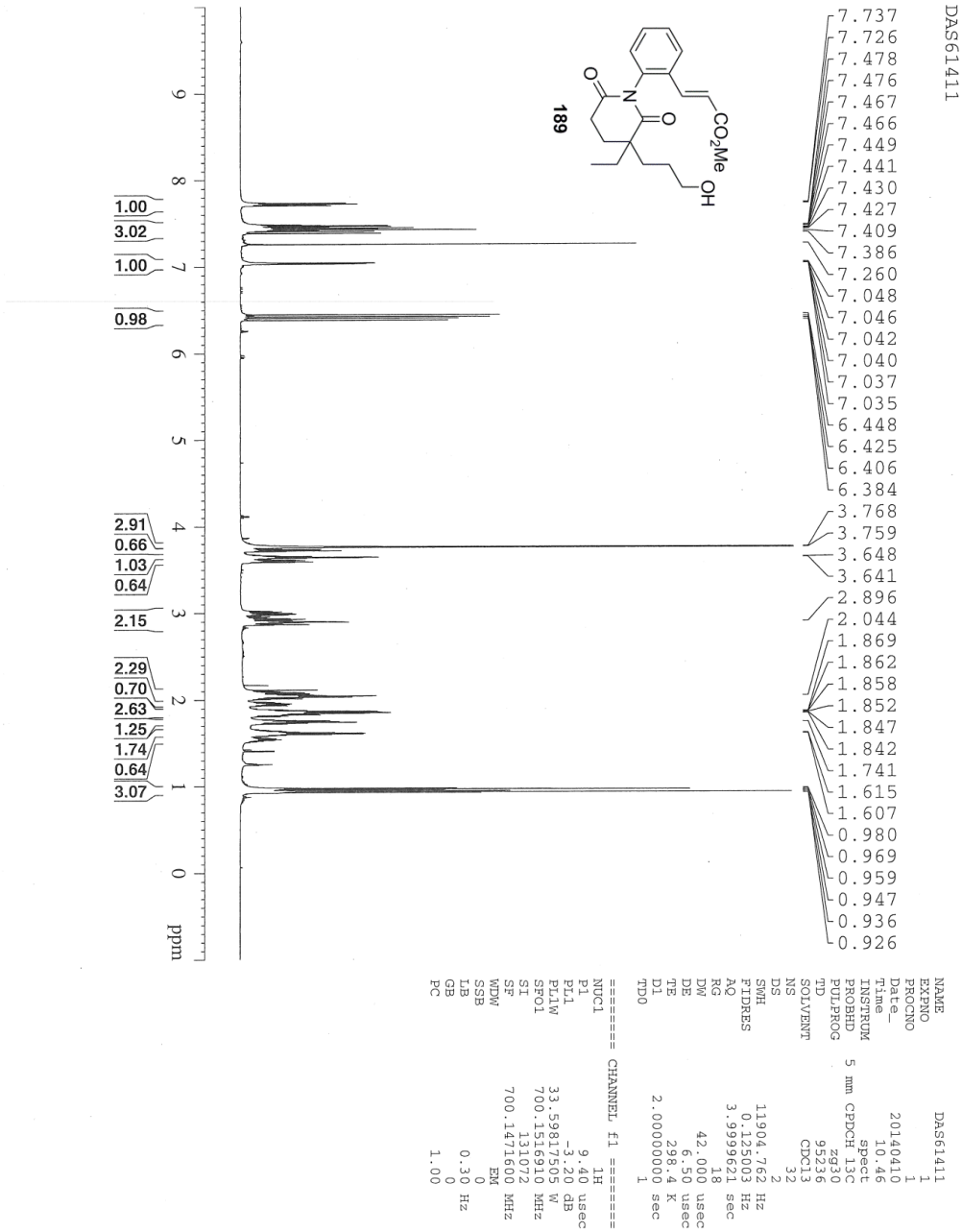
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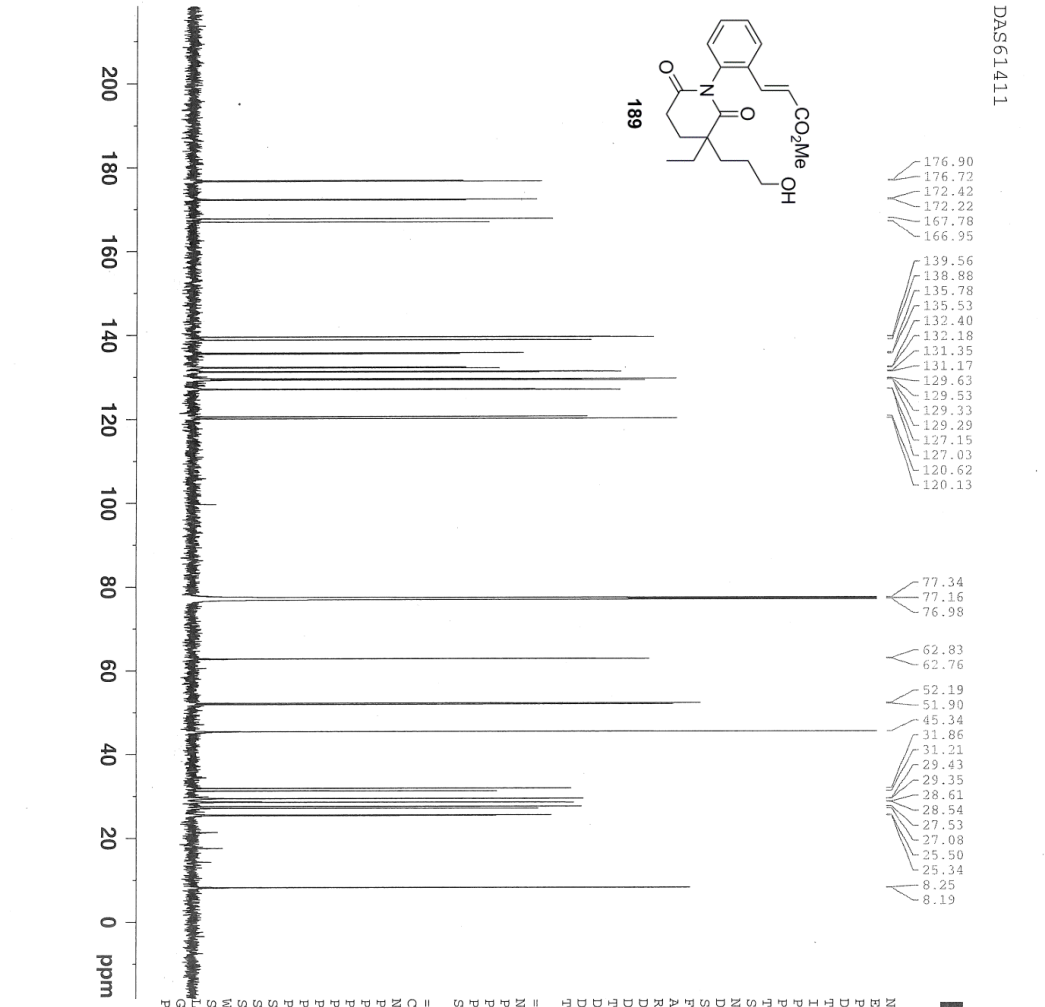
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PL12 13.60 dB
PL13 120.00 dB
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PL12W 0.70196527 W
PL13W 0.00000000 W
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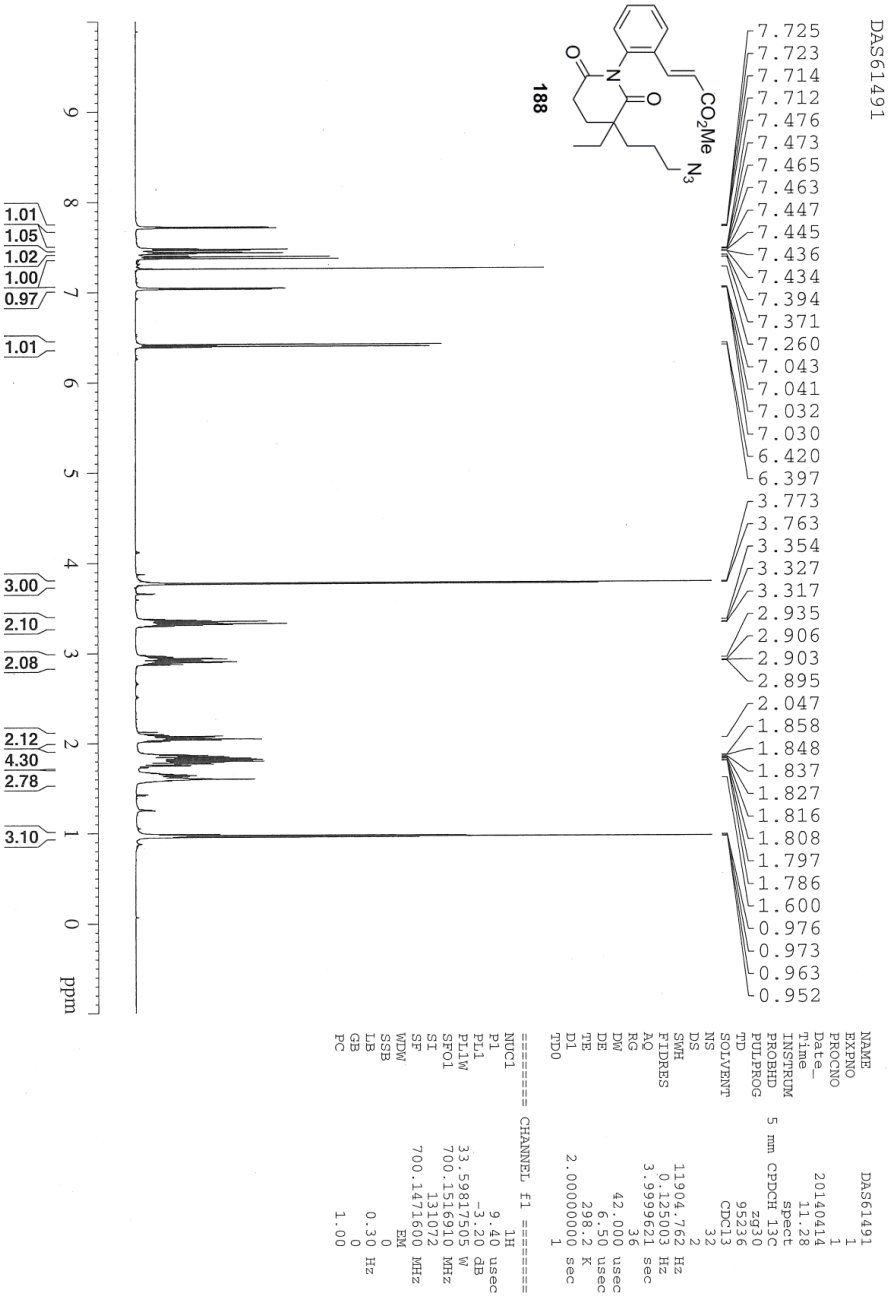
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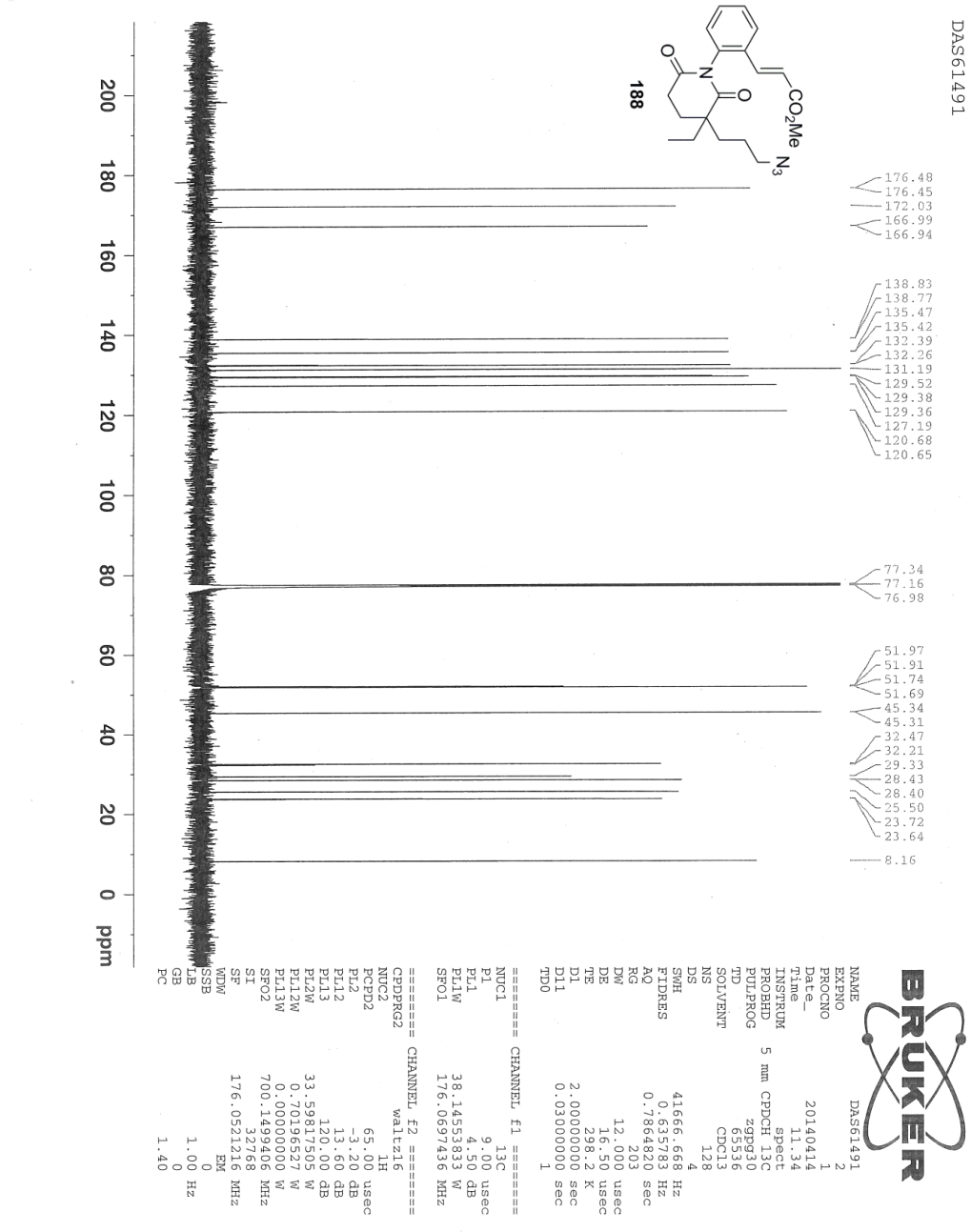
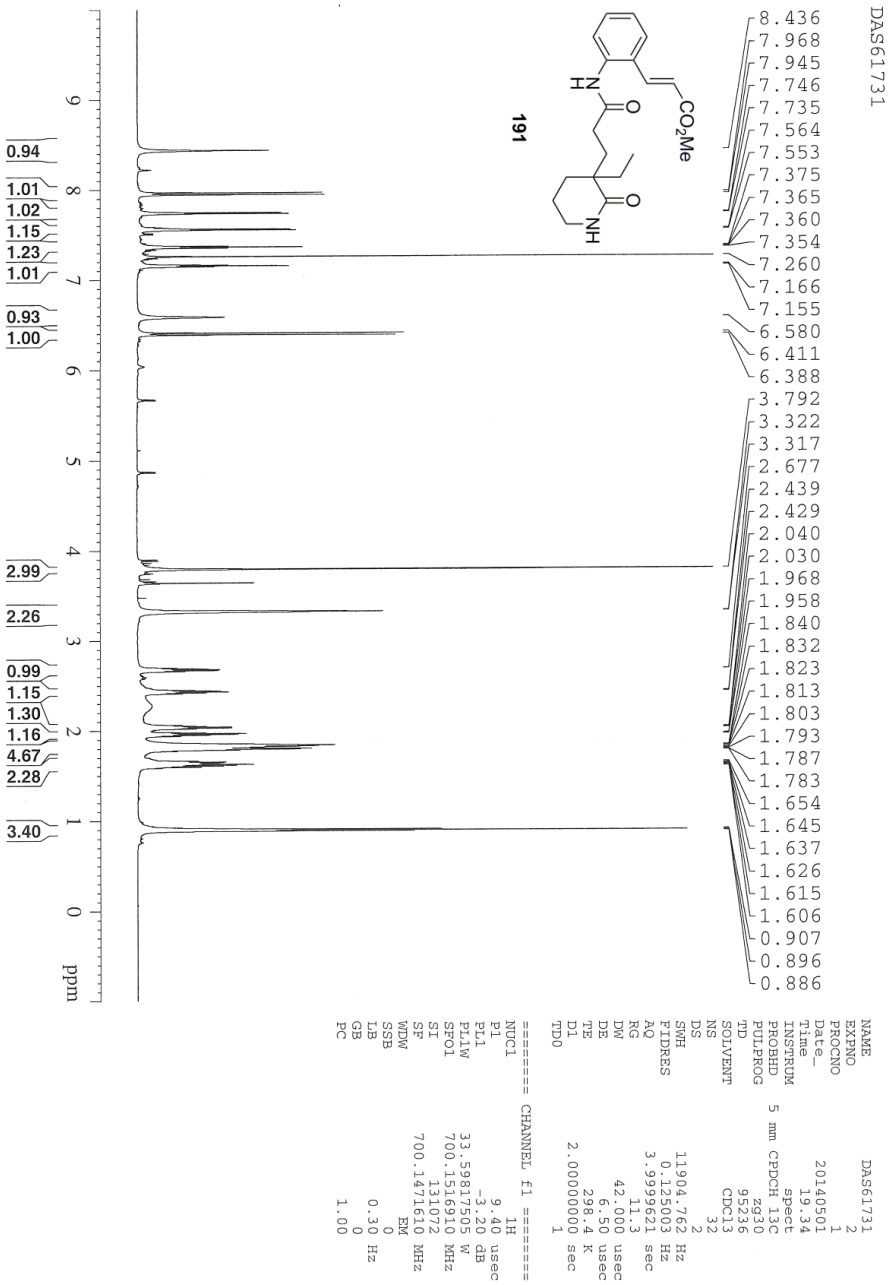
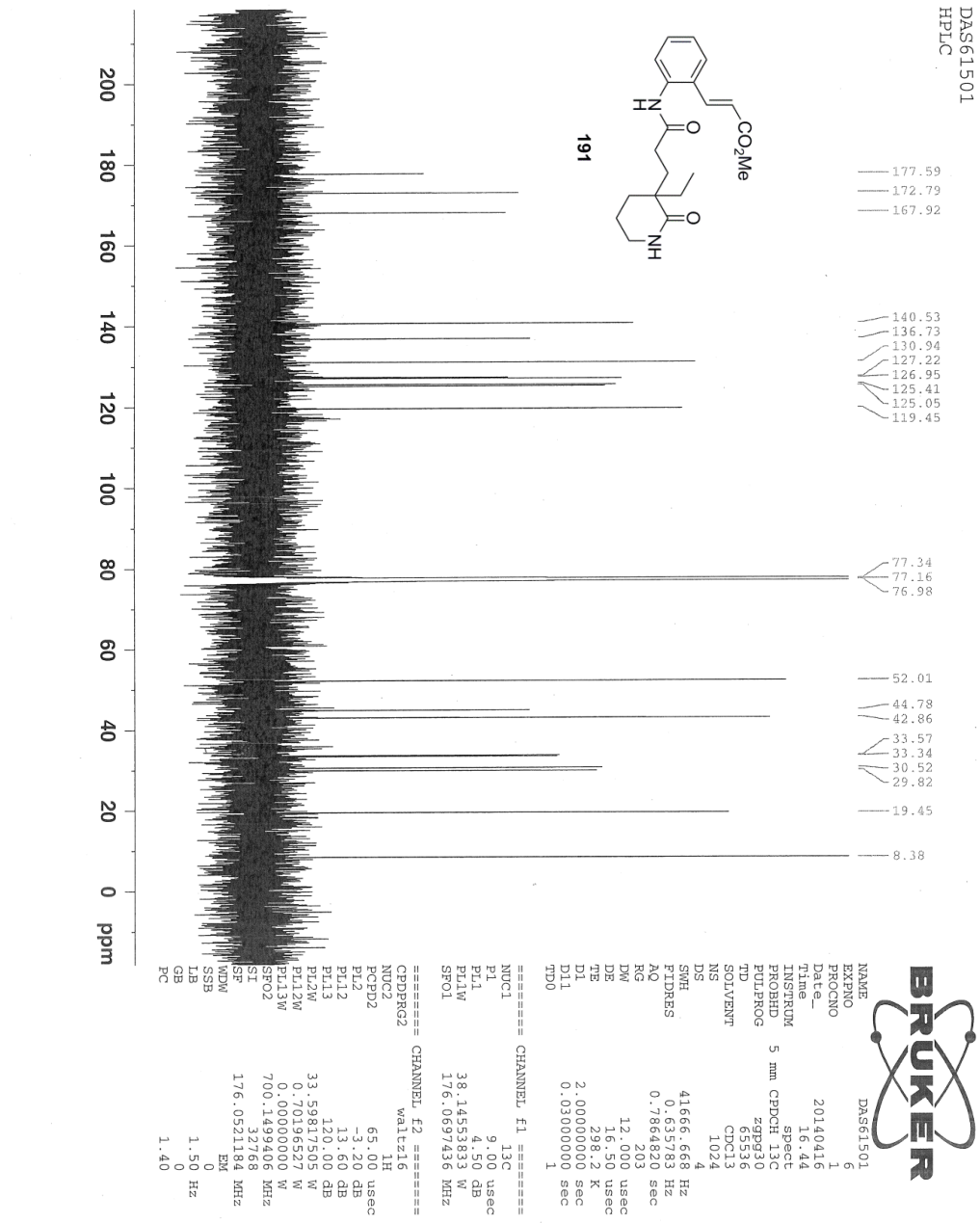
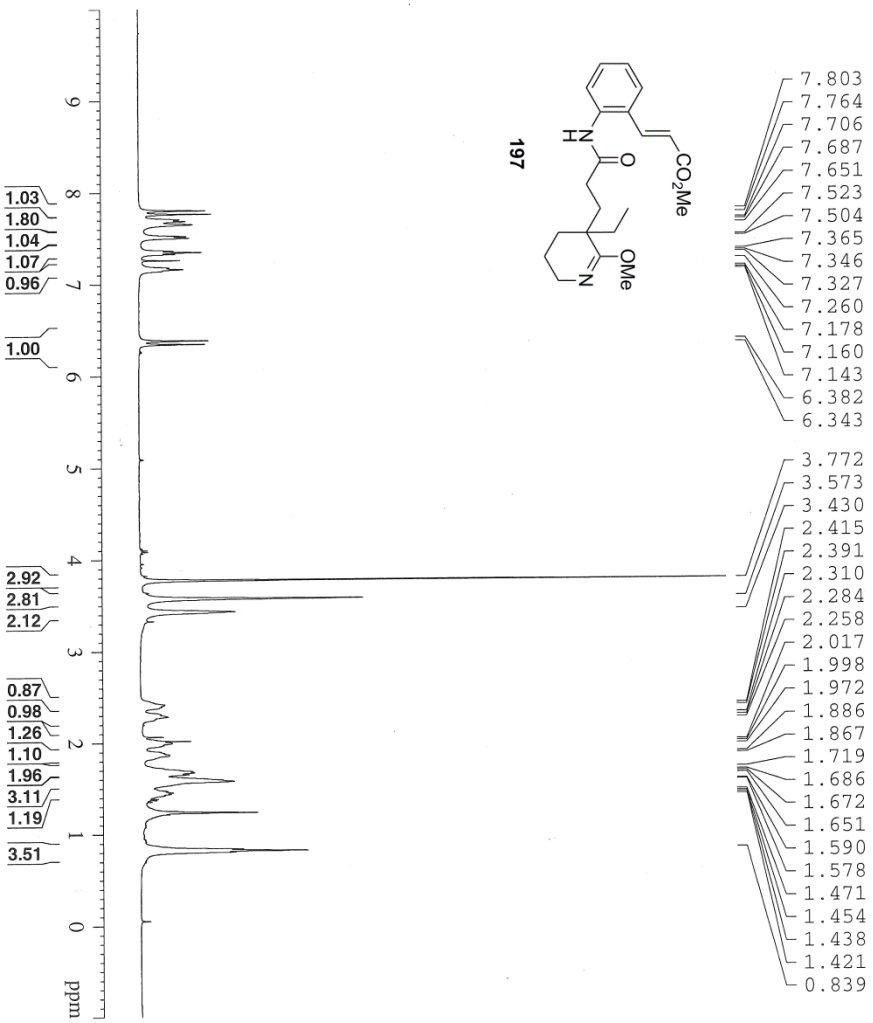
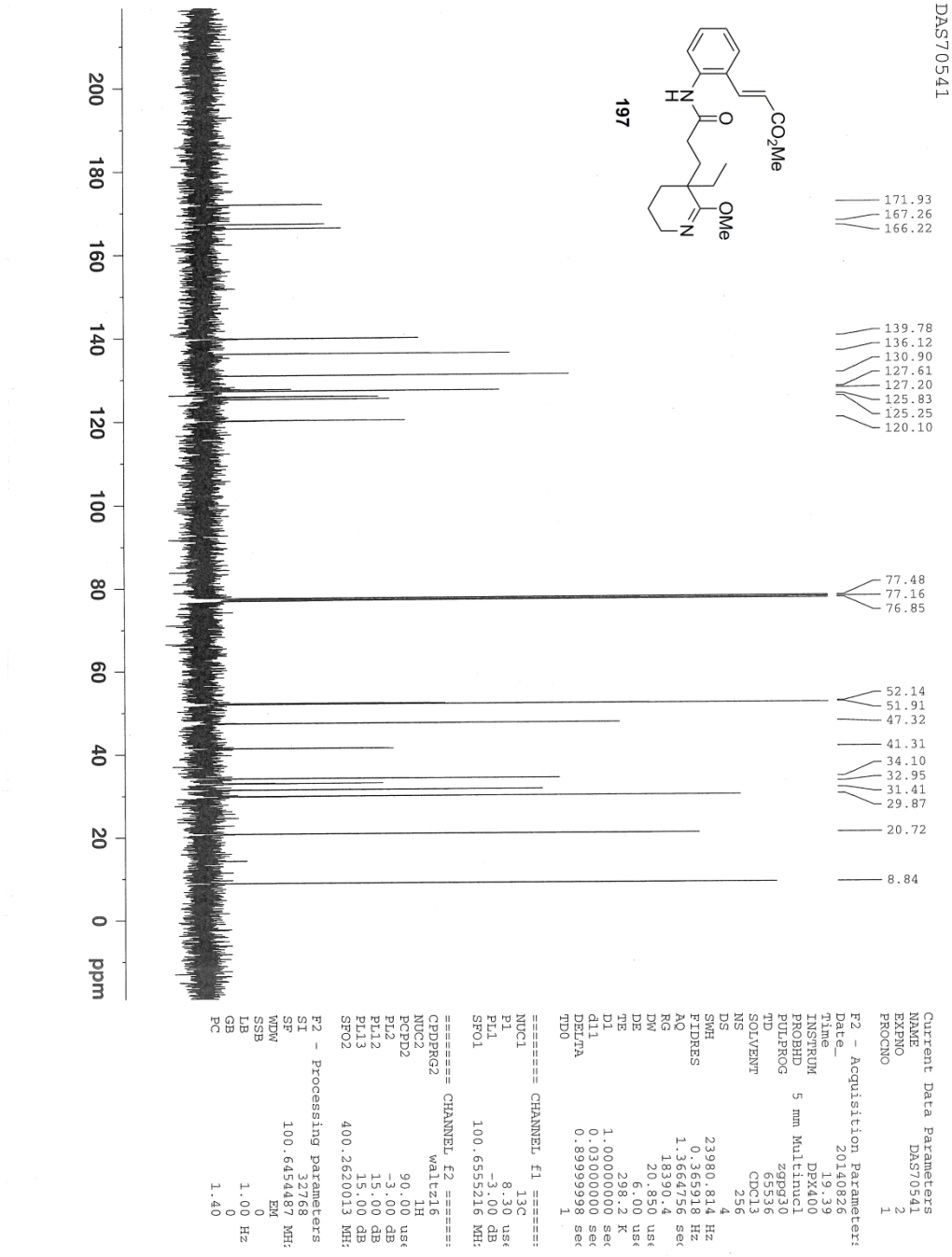
1.827
1.816
1.808
1.797
1.786
1.600
0.976
0.973
0.963
0.952
188
1.01
1.05
1.02
1.00
0.97
1.01
3.00
2.10
2.08
2.12
4.30
2.78
3.10
ppm
NAME DAS61491
EXPNO 1
PROCNO 1
Date_ 20140414
Time 11.28
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 36
DW 42.000 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
========== CHANNEL f1 ==========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471600 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00


DAS61491
188
CO2Me
N3
176.48
176.45
172.03
166.99
166.94
138.83
138.77
135.47
135.42
132.39
132.26
131.19
129.52
129.38
129.36
127.19
120.68
120.65
77.34
77.16
76.98
51.97
51.91
51.74
51.69
45.34
45.31
32.47
32.21
29.33
28.43
28.40
25.50
23.72
23.64
8.16
200
180
160
140
120
100
80
60
40
20
0
ppm
BRUKER
NAME DAS61491
EXPNO 2
PROCNO 1
Date_ 20140414
Time 11.34
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 128
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 176.0522116 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

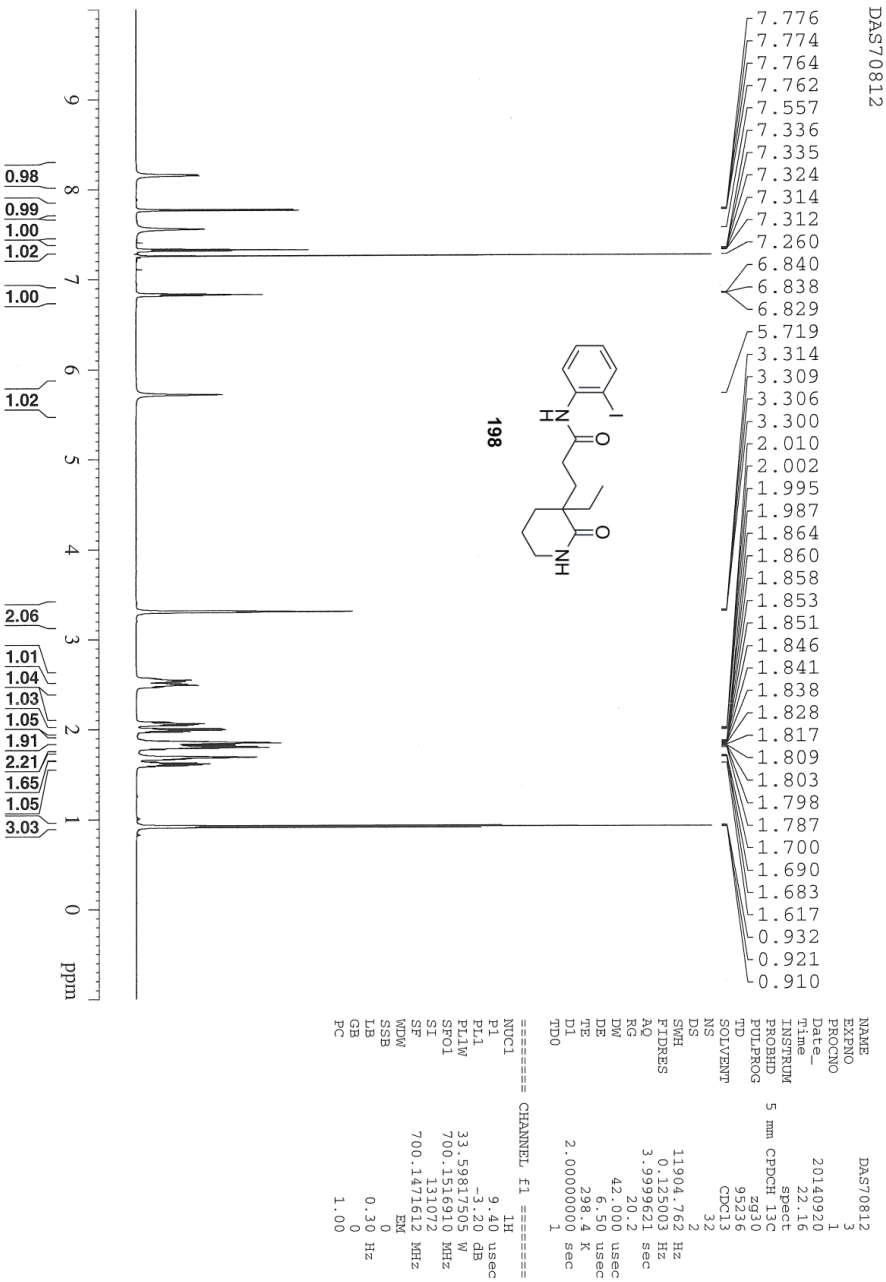

DAS61731
8.436
7.968
7.945
7.746
7.735
7.564
7.553
7.375
7.365
7.360
7.354
7.260
7.166
7.155
6.580
6.411
6.388
3.792
3.322
3.317
2.677
2.439
2.429
2.040
2.030
1.968
1.958
1.840
1.832
1.823
1.813
1.803
1.793
1.787
1.783
1.654
1.645
1.637
1.626
1.615
1.606
0.907
0.896
0.886
CO2Me
NH
O
O
NH
191
0.94
1.01
1.02
1.15
1.23
1.01
0.93
1.00
2.99
2.26
0.99
1.15
1.30
1.16
4.67
2.28
3.40
ppm
NAME DAS61731
EXPNO 2
PROCNO 1
Date_ 20140501
Time 19.34
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 11.3
DW 42.000 usec
DE 6.50 usec
TE 298.4 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 700.1471610 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

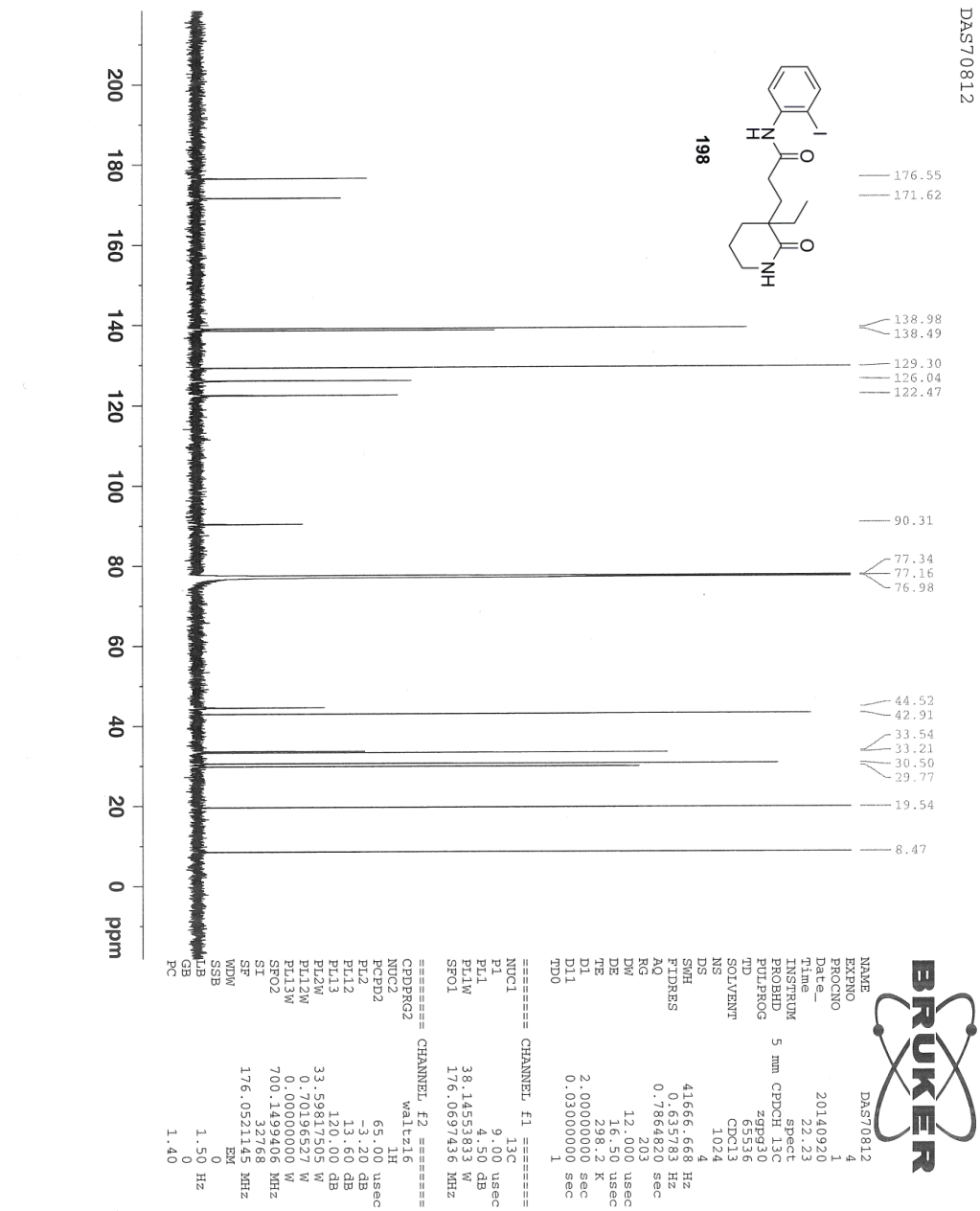

DAS61501
HPLC
191
177.59
172.79
167.92
140.53
136.73
130.94
127.22
126.95
125.41
125.05
119.45
77.34
77.16
76.98
52.01
44.78
42.86
33.57
33.34
30.52
29.82
19.45
8.38
200
180
160
140
120
100
80
60
40
20
0
ppm
BRUKER
NAME DAS61501
EXPNO 6
PROCNO 1
Date_ 20140416
Time 16.44
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1024
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864820 sec
RG 203
DW 12.000 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 176.0521184 MHz
WDW EM
SSB 0
LB 1.50 Hz
GB 0
PC 1.40

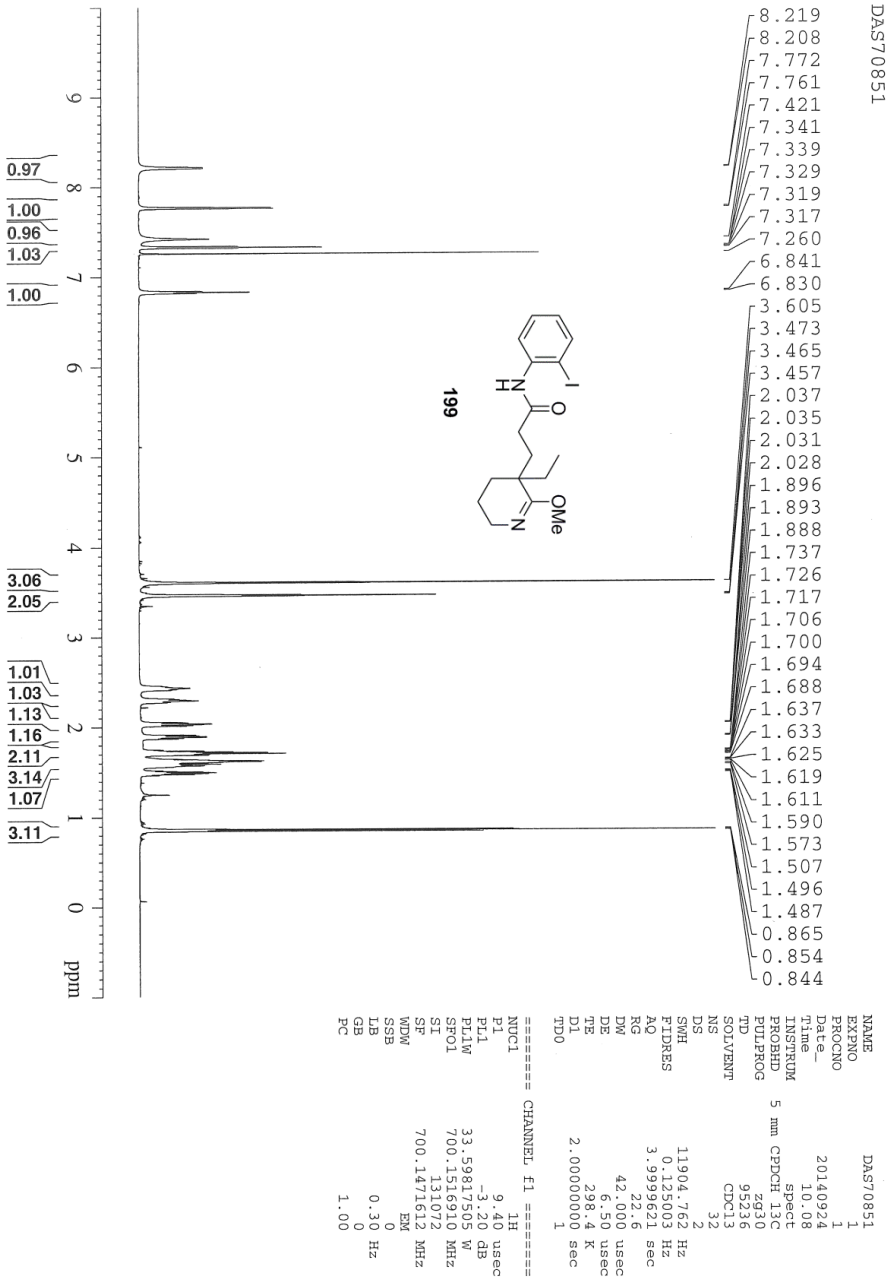

DAS70541
7.803
7.764
7.706
7.687
7.651
7.523
7.504
7.365
7.346
7.327
7.260
7.178
7.160
7.143
6.382
6.343
3.772
3.573
3.430
2.415
2.391
2.310
2.284
2.258
2.017
1.998
1.972
1.886
1.867
1.719
1.686
1.672
1.651
1.590
1.578
1.471
1.454
1.438
1.421
0.839
CO2Me
OMe
197
1.03
1.80
1.04
1.07
0.96
1.00
2.92
2.81
2.12
0.87
0.98
1.26
1.10
1.96
3.11
1.19
3.51
ppm
Current Data Parameters
NAME DAS70541
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20140826
Time 19.35
INSTRUM DPX400
PROBHD 5 mm Multinuc1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 16
DS 2
SWH 6410.256 Hz
FTDRES 0.195625 Hz
AQ 2.5559540 sec
RG 71.8
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 400.2600109 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

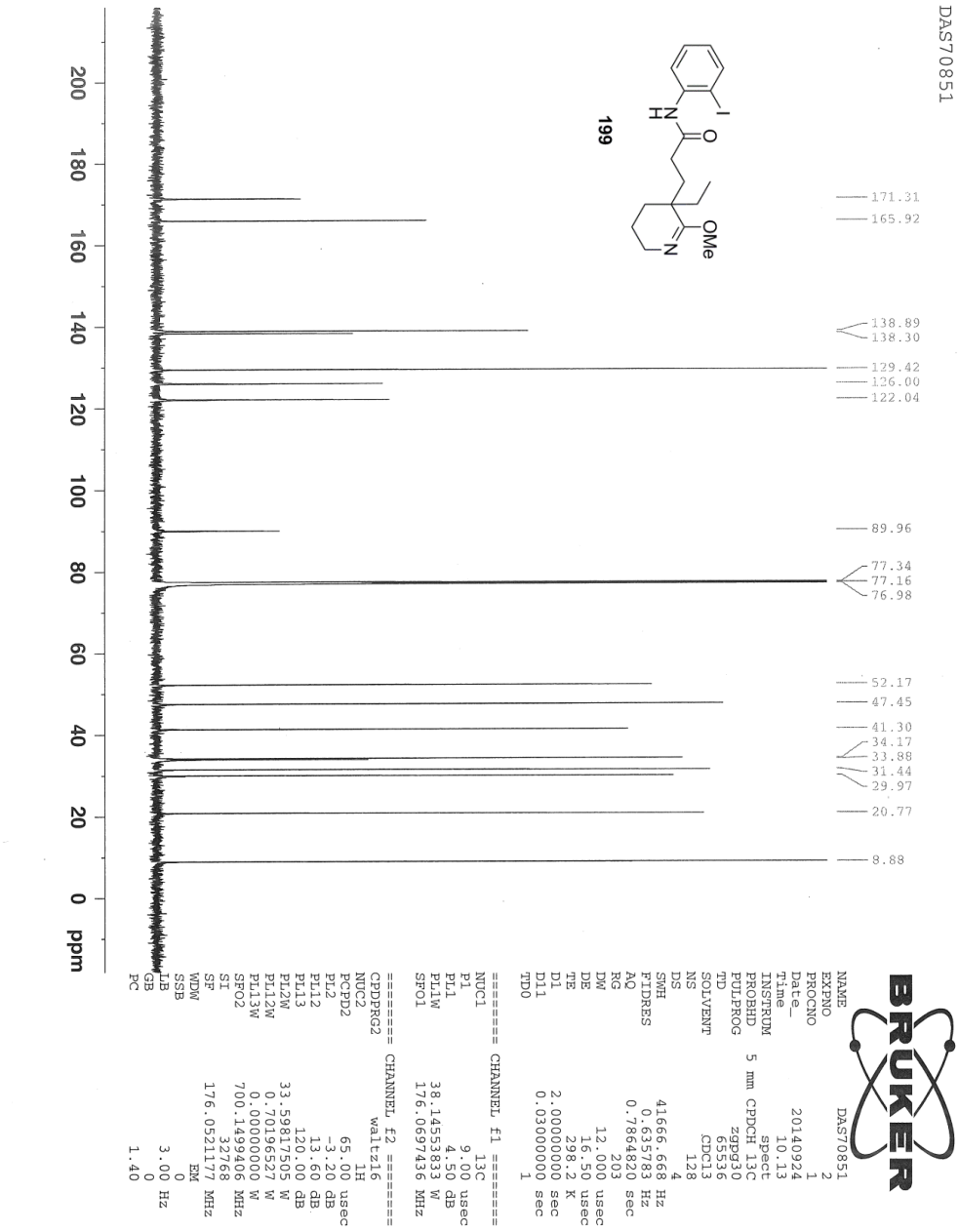


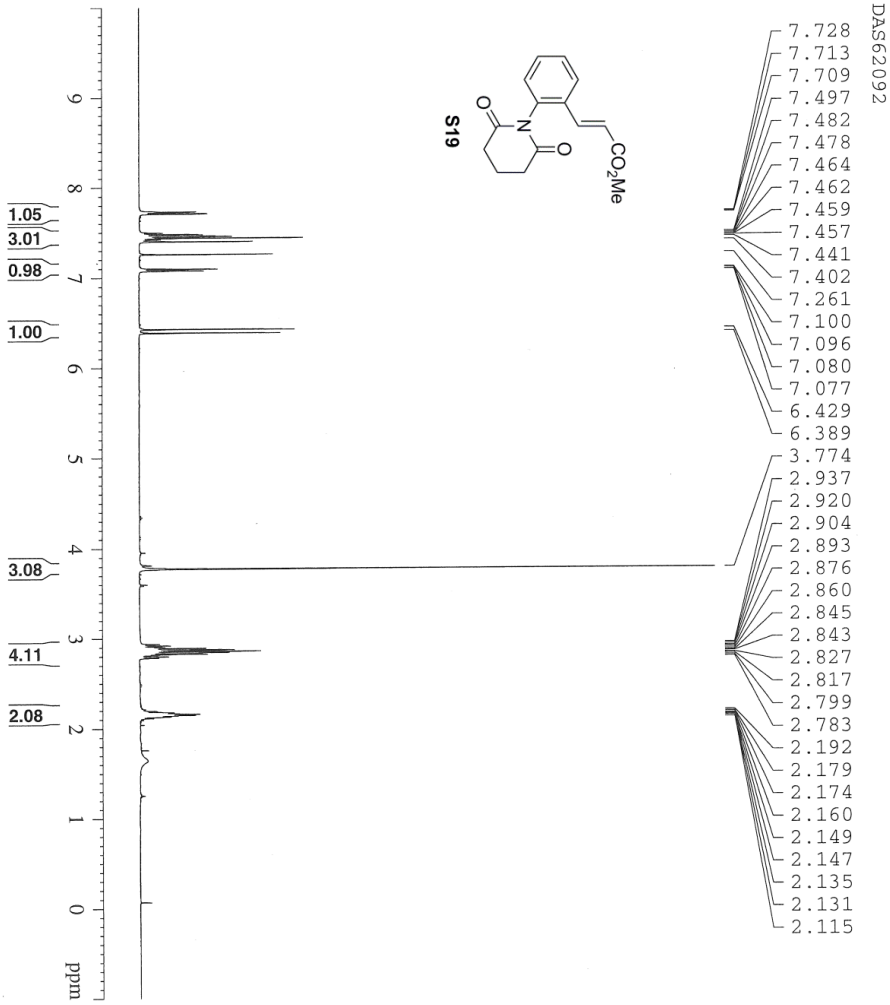

```
Current Data Parameters
NAME                  DAS70541
EXPNO                        2
PROCNO                       1

F2 - Acquisition Parameters
Date_               20140826
Time                    19.39
INSTRUM                DPX400
PROBHD  5 mm Multinucl
PULPROG             zgpg30
TD                       65536
SOLVENT                CDCl3
NS                         256
DS                           4
SWH                23980.814 Hz
FIDRES              0.365918 Hz
AQ                  1.3664756 sec
RG                       18390.4
DW                       20.850 use
DE                        6.00 use
TE                         298.2 K
D1                  1.00000000 sec
D11                 0.03000000 sec
DELTA               0.89999998 sec
TD0                          1

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

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

F2 - Processing parameters
SI                       32768
SF             100.6454487 MHz
WDW                         EM
SSB                          0
LB                        1.00 Hz
GB                           0
PC                        1.40
```

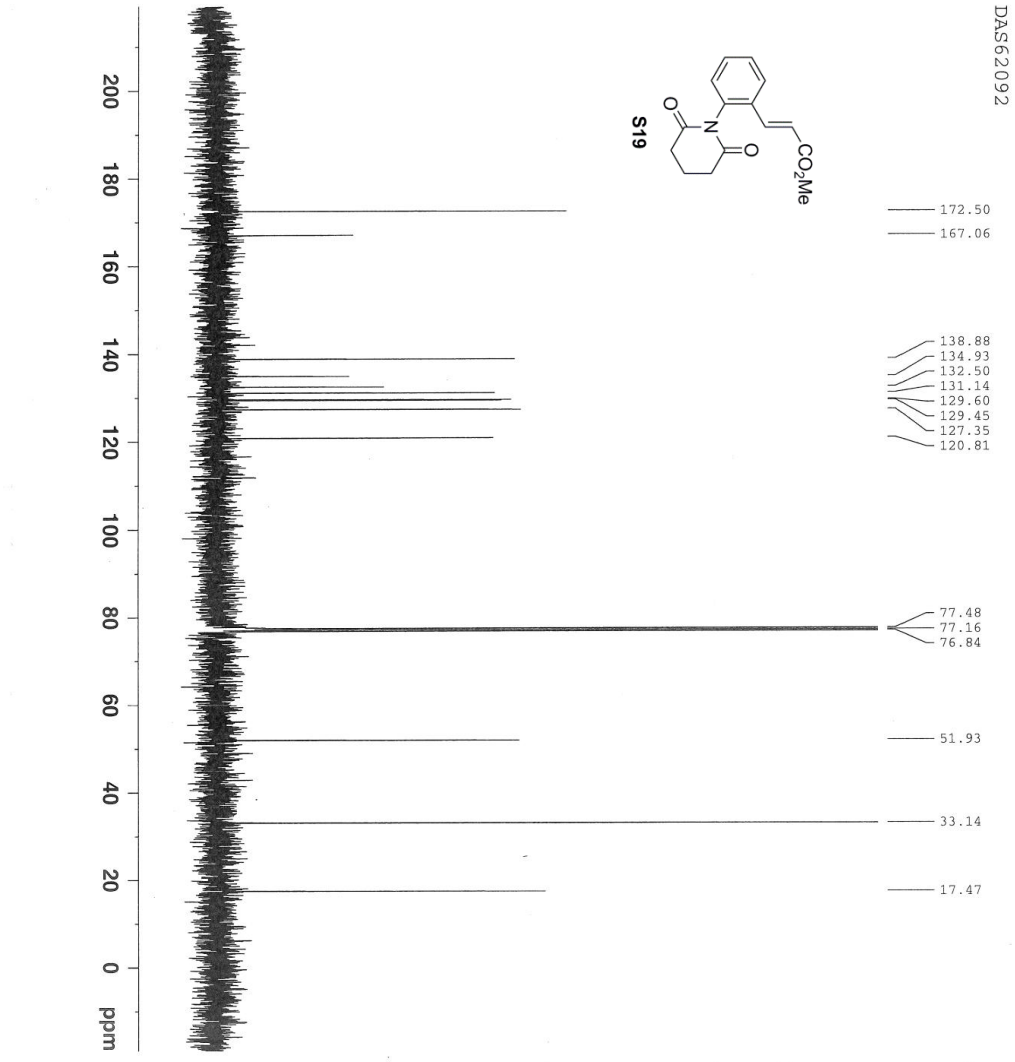

DAS70812
7.776
7.774
7.764
7.762
7.557
7.336
7.335
7.324
7.314
7.312
7.260
6.840
6.838
6.829
5.719
3.314
3.309
3.306
3.300
2.010
2.002
1.995
1.987
1.864
1.860
1.858
1.853
1.851
1.846
1.841
1.838
1.828
1.817
1.809
1.803
1.798
1.787
1.700
1.690
1.683
1.617
0.932
0.921
0.910
198
0.98
0.99
1.00
1.02
1.00
1.02
2.06
1.01
1.04
1.03
1.05
1.91
2.21
1.65
1.05
3.03
ppm
NAME DAS70812
EXPNO 3
PROCNO 1
Date_ 20140920
Time 22.16
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 20.2
DW 42.000 usec
DE 6.50 usec
TE 298.4 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 700.1471612 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00


DAS70812
198
176.55
171.62
138.98
138.49
129.30
126.04
122.47
90.31
77.34
77.16
76.98
44.52
42.91
33.54
33.21
30.50
29.77
19.54
8.47
200
180
160
140
120
100
80
60
40
20
0
ppm
BRUKER
NAME DAS70812
EXPNO 4
PROCNO 1
Date_ 20140920
Time 22.23
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1024
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864820 sec
RG 203
DW 12.000 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 176.0521145 MHz
WDW EM
SSB 0
LB 1.50 Hz
GB 0
PC 1.40

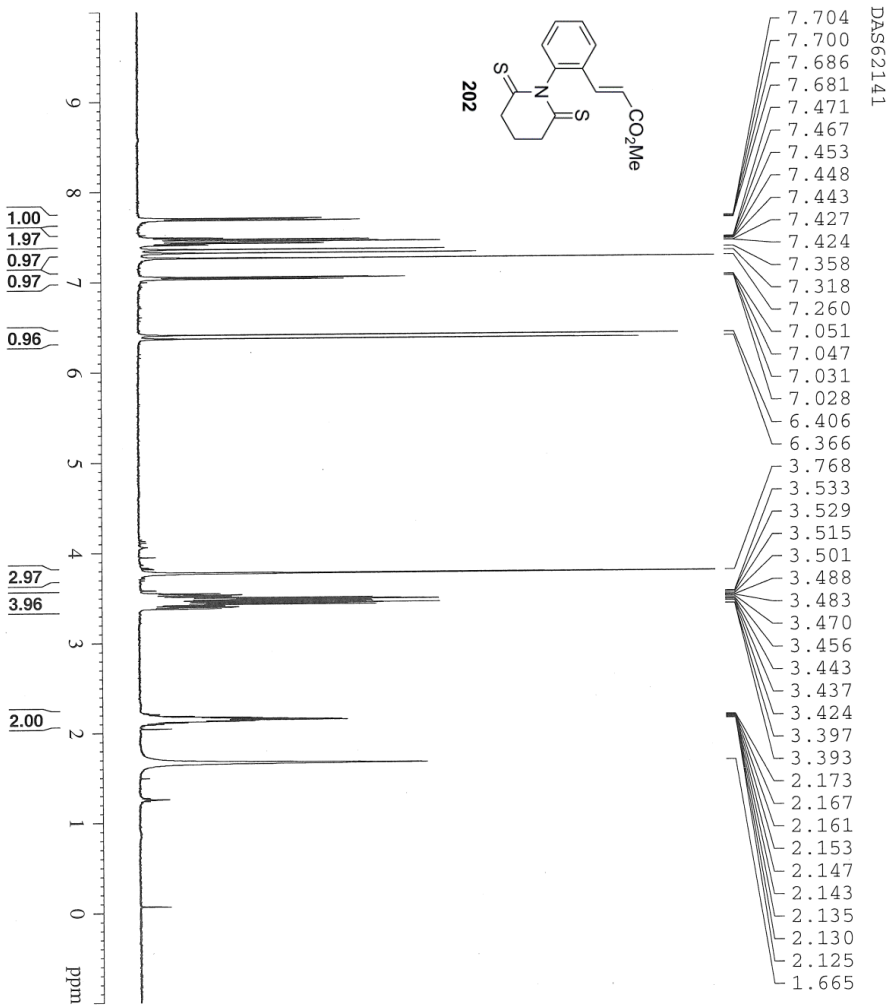

DAS70851
8.219
8.208
7.772
7.761
7.421
7.341
7.339
7.329
7.319
7.317
7.260
6.841
6.830
3.605
3.473
3.465
3.457
2.037
2.035
2.031
2.028
1.896
1.893
1.888
1.737
1.726
1.717
1.706
1.700
1.694
1.688
1.637
1.633
1.625
1.619
1.611
1.590
1.573
1.507
1.496
1.487
0.865
0.854
0.844
199
0.97
1.00
0.96
1.03
1.00
3.06
2.05
1.01
1.03
1.13
1.16
2.11
3.14
1.07
3.11
9
8
7
6
5
4
3
2
1
0
ppm
NAME DAS70851
EXPNO 1
PROCNO 1
Date_ 20140924
Time_ 10.08
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 22.6
DW 42.000 usec
DE 6.50 usec
TE 298.4 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 700.1471612 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00


DAS70851
199
171.31
165.92
138.89
138.30
129.42
126.00
122.04
89.96
77.34
77.16
76.98
52.17
47.45
41.30
34.17
33.88
31.44
29.97
20.77
8.88
200
180
160
140
120
100
80
60
40
20
0
ppm
BRUKER
NAME DAS70851
EXPNO 2
PROCNO 1
Date_ 20140924
Time_ 10.13
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 128
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 176.0521177 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40

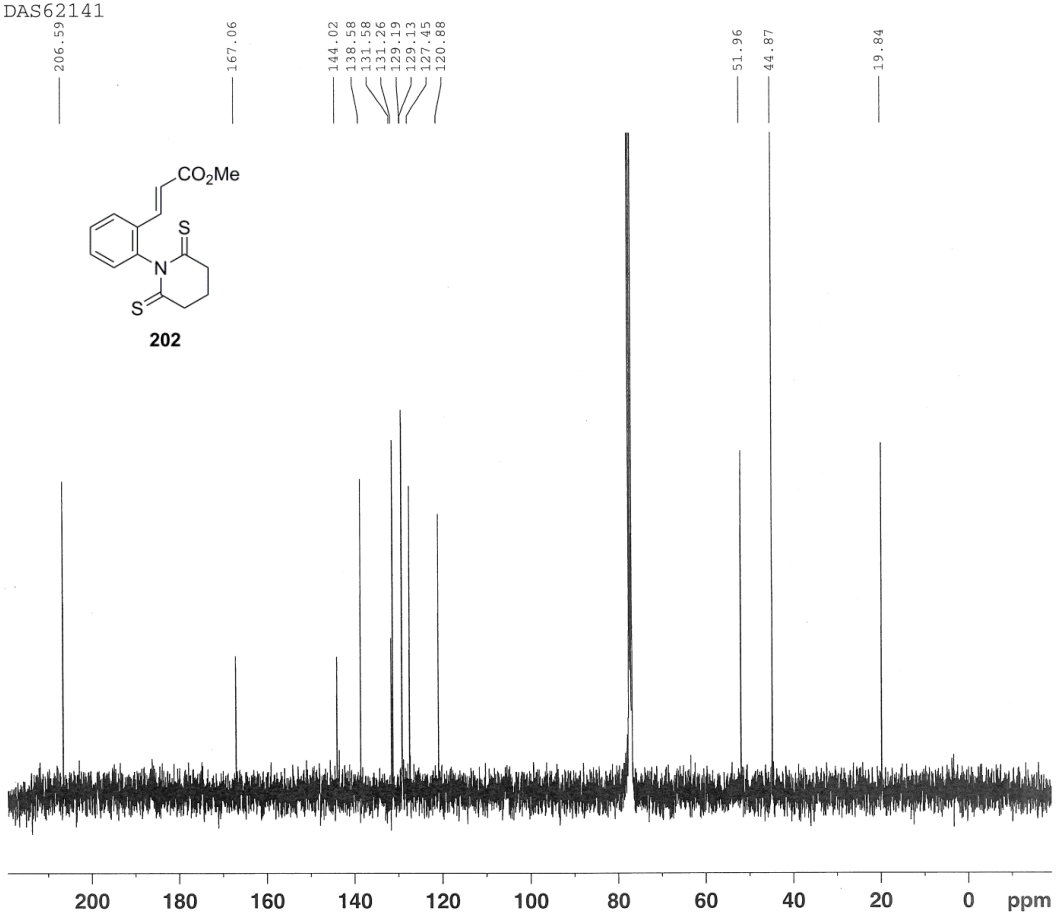

DAS62092
7.728
7.713
7.709
7.497
7.482
7.478
7.464
7.462
7.459
7.457
7.441
7.402
7.261
7.100
7.096
7.080
7.077
6.429
6.389
3.774
2.937
2.920
2.904
2.893
2.876
2.860
2.845
2.843
2.827
2.817
2.799
2.783
2.192
2.179
2.174
2.160
2.149
2.147
2.135
2.131
2.115
S19
CO2Me
O
N
O
1.05
3.01
0.98
1.00
3.08
4.11
2.08
9
8
7
6
5
4
3
2
1
0
ppm
Current Data Parameters
NAME DAS62092
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20141110
Time_ 14.13
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 256
DW 78.000 usec
DE 6.00 usec
TE 299.2 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 400.2600109 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00




```
Current Data Parameters
NAME                  DAS62092
EXPNO                        2
PROCNO                       1

F2 - Acquisition Parameters
Date_               20141110
Time                    14.17
INSTRUM                DPX400
PROBHD   5 mm Multinucl
PULPROG               zgpg30
TD                     65536
SOLVENT                CDCl3
NS                       258
DS                         4
SWH                23980.814 Hz
FIDRES                0.365918 Hz
AQ                 1.3664756 sec
RG                      7298.2
DW                     20.850 usec
DE                      6.00 usec
TE                     299.2 K
D1                  1.00000000 sec
D11                 0.03000000 sec
DELTA               0.89999998 sec
TD0                          1

========== CHANNEL f1 ========
NUC1                       13C
P1                        9.00 usec
PL1                       0.00 dB
SFO1          100.6555216 MHz

========== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                  80.00 usec
PL2                    -1.40 dB
PL12                   13.14 dB
PL13                   14.00 dB
SFO2          400.2620013 MHz

F2 - Processing parameters
SI                       32768
SF            100.6454456 MHz
WDW                         EM
SSB                          0
LB                        1.50 Hz
GB                           0
PC                        1.40
```

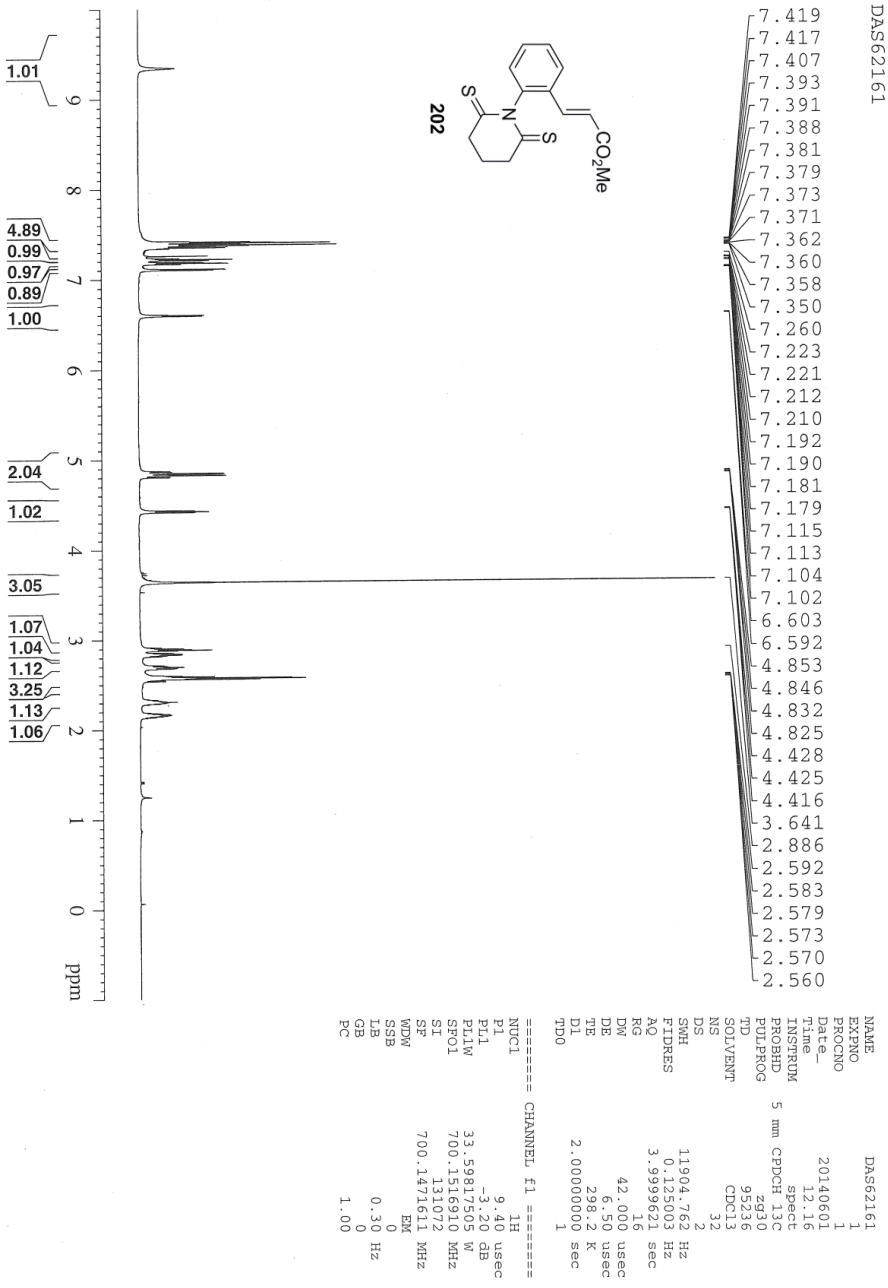

DAS62141
7.704
7.700
7.686
7.681
7.471
7.467
7.453
7.448
7.443
7.427
7.424
7.358
7.318
7.260
7.051
7.047
7.031
7.028
6.406
6.366
3.768
3.533
3.529
3.515
3.501
3.488
3.483
3.470
3.456
3.443
3.437
3.424
3.397
3.393
2.173
2.167
2.161
2.153
2.147
2.143
2.135
2.130
2.125
1.665
202
CO2Me
1.00
1.97
0.97
0.97
0.96
2.97
3.96
2.00
ppm
Current Data Parameters
NAME DAS62141
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20141108
Time_ 12.22
INSTRUM DPX400
PROBHD 5 mm Multinuc1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 16
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 645.1
DW 78.000 usec
DE 6.00 usec
TE 299.2 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 400.2600109 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

DAS62141

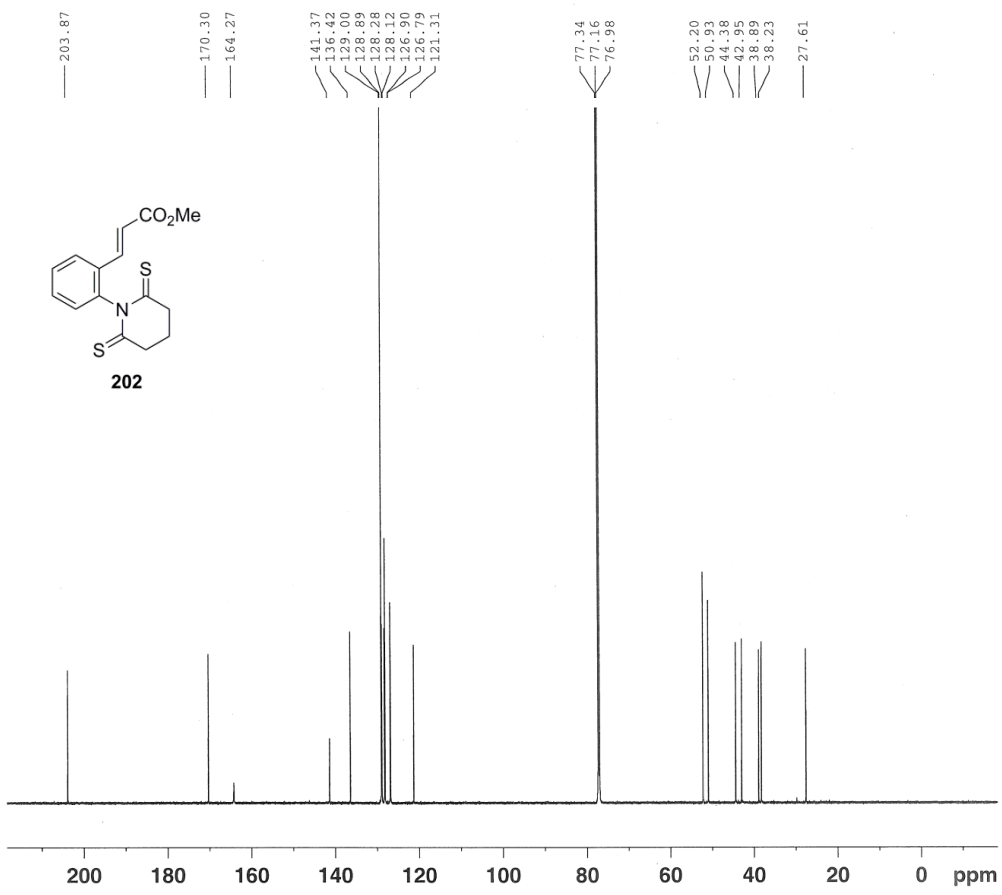


202

```
Current Data Parameters
NAME            DAS62141
EXPNO                  2
PROCNO                 1

F2 - Acquisition Parameter
Date_           20141108
Time               12.29
INSTRUM          DPX400
PROBHD   5 mm Multinucl
PULPROG          zgpg30
TD                65536
SOLVENT           CDCl3
NS                 2048
DS                    4
SWH           23980.814 Hz
FIDRES         0.365918 Hz
AQ            1.3664756 sec
RG               4597.6
DW               20.850 use
DE                6.00 use
TE               300.2 K
D1           1.00000000 sec
d11          0.03000000 sec
DELTA        0.89999998 sec
TD0                   1

======== CHANNEL f1 =======
NUC1                 13C
P1                8.30 use
PL1              -3.00 dB
SFO1        100.6555216 MH

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

F2 - Processing parameters
SI                32768
SF          100.6454436 MH
WDW                  EM
SSB                   0
LB                1.50 Hz
GB                    0
PC                1.40
```

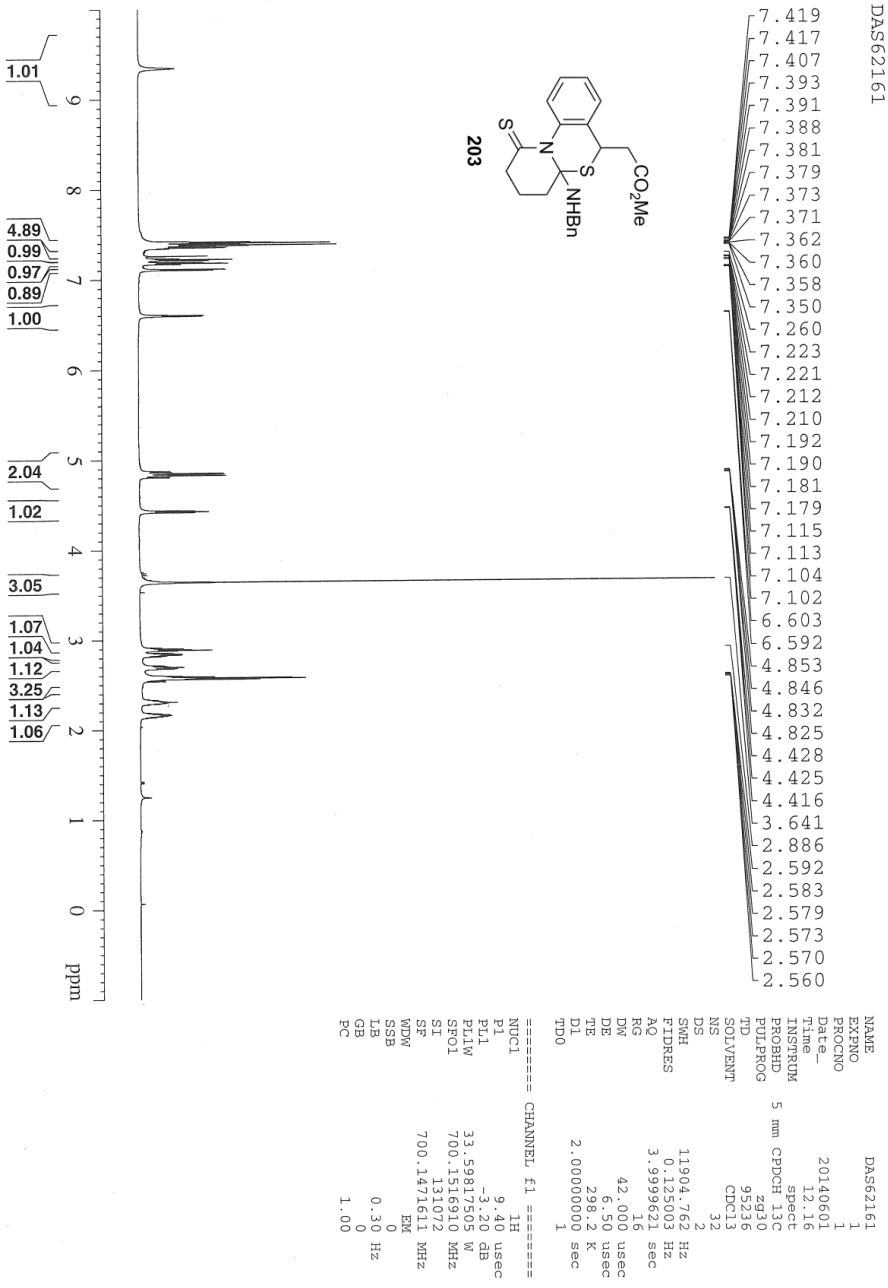

DAS62161
7.419
7.417
7.407
7.393
7.391
7.388
7.381
7.379
7.373
7.371
7.362
7.360
7.358
7.350
7.260
7.223
7.221
7.212
7.210
7.192
7.190
7.181
7.179
7.115
7.113
7.104
7.102
6.603
6.592
4.853
4.846
4.832
4.825
4.428
4.425
4.416
3.641
2.886
2.592
2.583
2.579
2.573
2.570
2.560
202
CO2Me
1.01
4.89
0.99
0.97
0.89
1.00
2.04
1.02
3.05
1.07
1.04
1.12
3.25
1.13
1.06
ppm
NAME DAS62161
EXPNO 1
PROCNO 1
Date_ 20140601
Time_ 12.16
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 16
DW 42.000 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PLIW 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471611 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

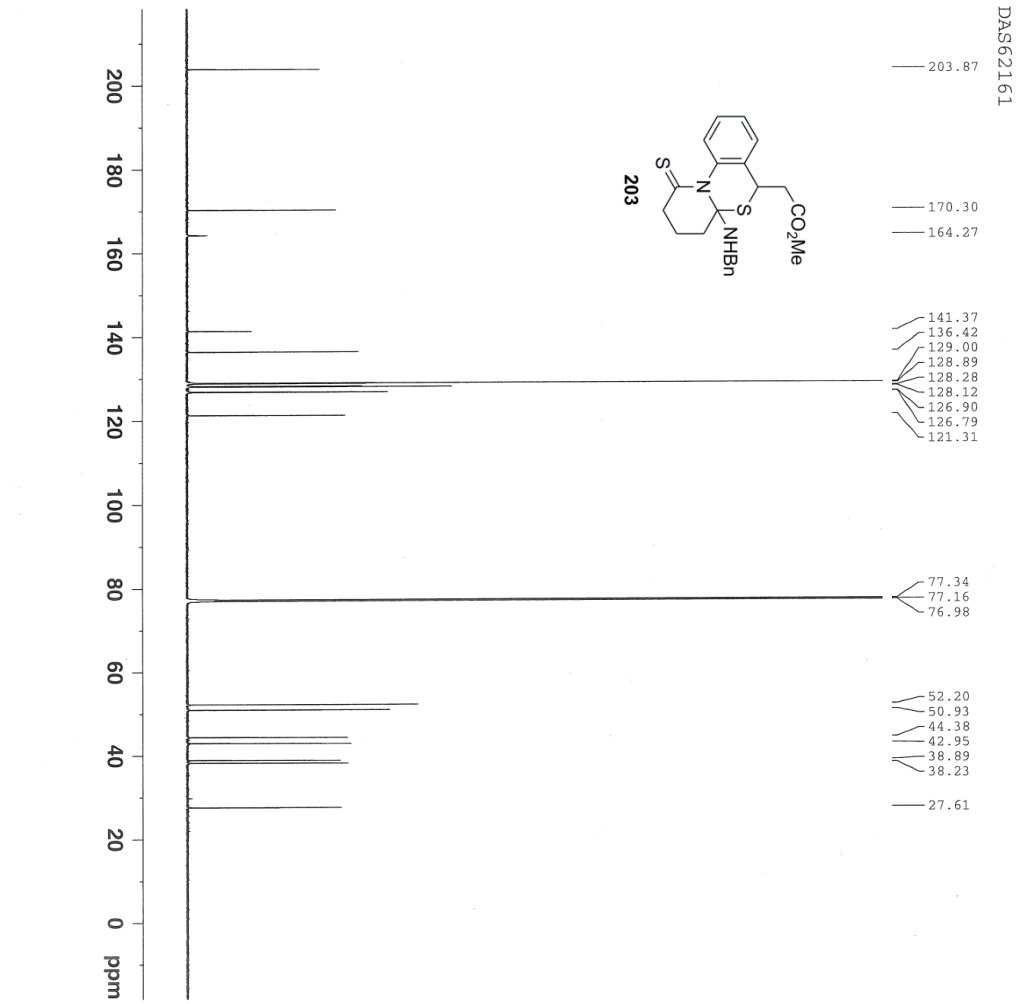
DAS62161



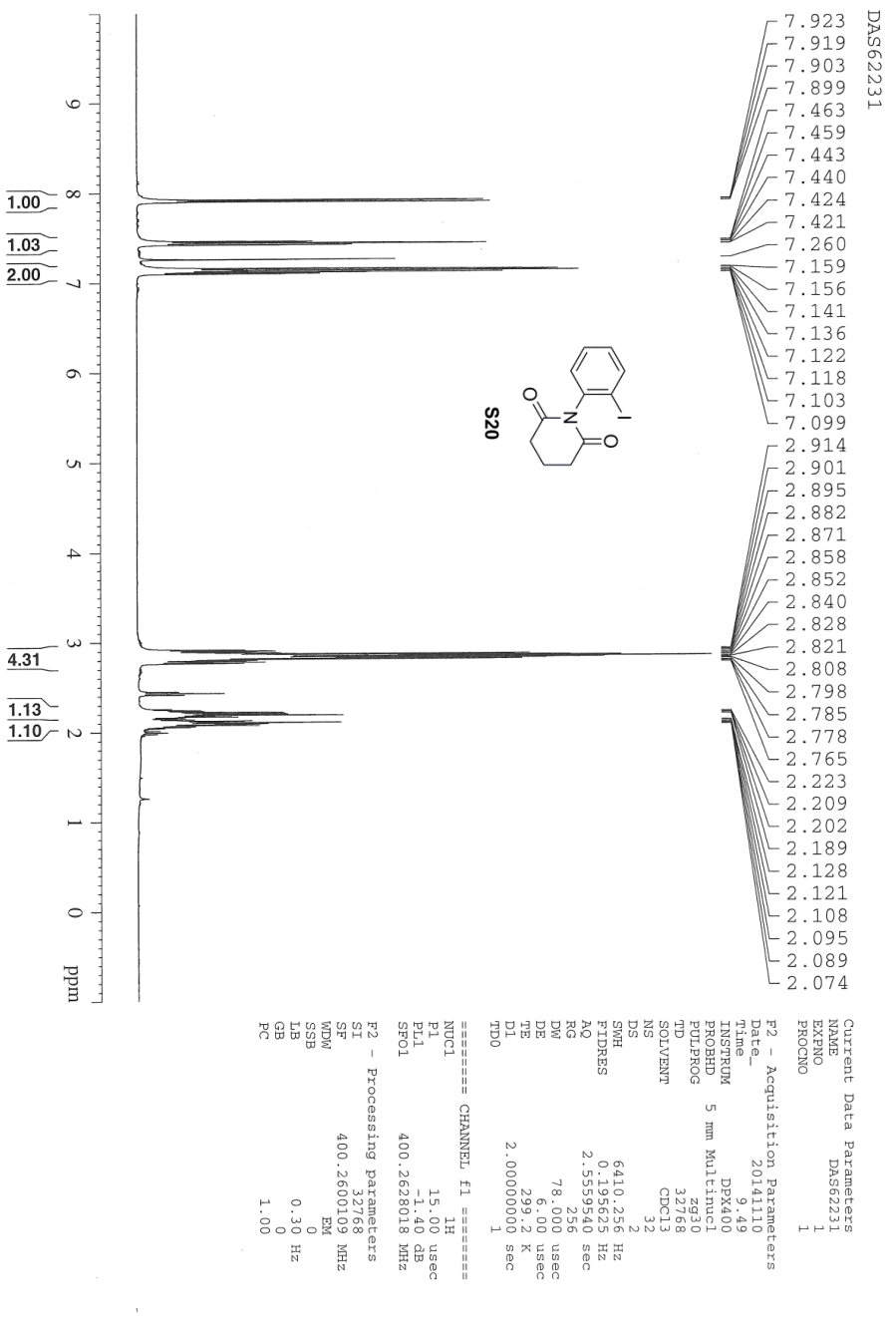
202

NAME	DAS62161
EXPNO	2
PROCNO	1
Date_	20140601
Time	12.24
INSTRUM	spect
PROBHD	5 mm CPDCH 13C
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	256
DS	4
SWH	41666.668 Hz
FIDRES	0.635783 Hz
AQ	0.7864820 sec
RG	203
DW	12.000 use
DE	16.50 use
TE	298.2 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 =======	
NUC1	13C
P1	9.00 use
PL1	4.50 dB
PL1W	38.14553833 W
SFO1	176.0697436 MHz
======== CHANNEL f2 =======	
CPDPRG2	waltz16
NUC2	1H
PCPD2	65.00 use
PL2	-3.20 dB
PL12	13.60 dB
PL13	120.00 dB
PL2W	33.59817505 W
PL12W	0.70196527 W
PL13W	0.00000000 W
SFO2	700.1499406 MHz
SI	32768
SF	176.0521291 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

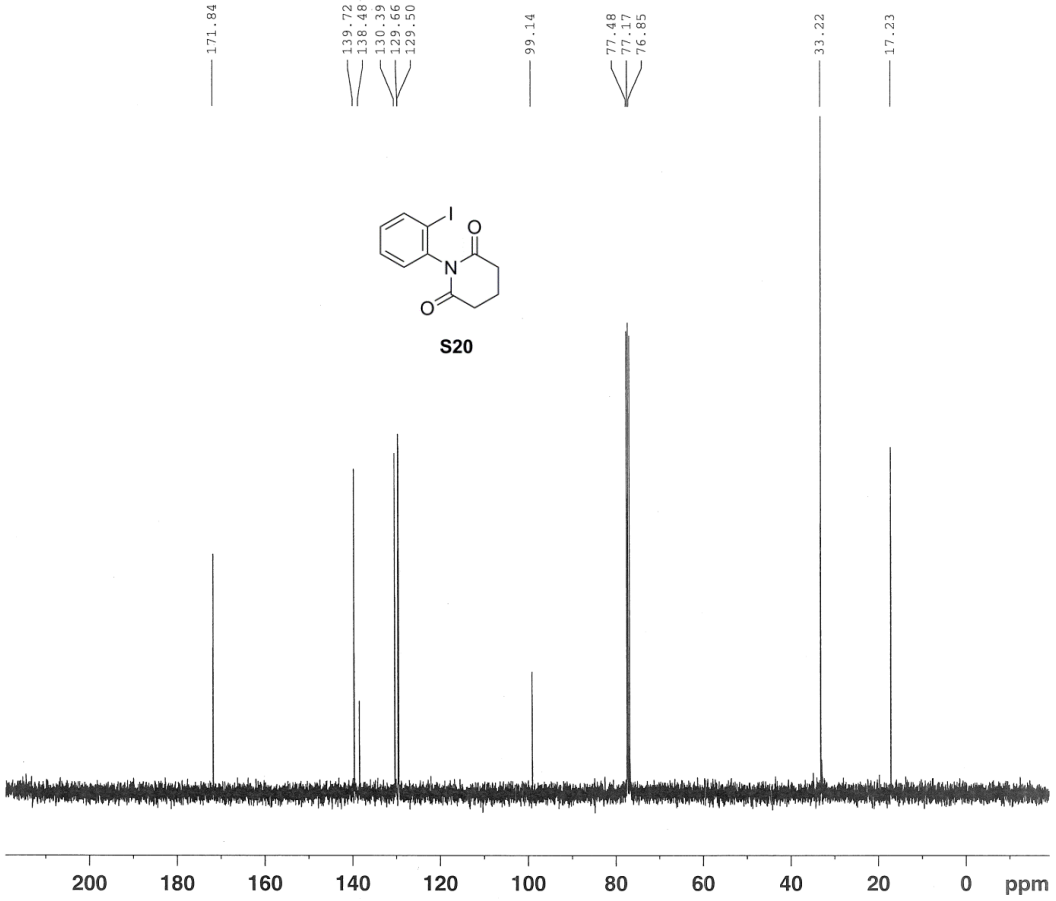

DAS62161
7.419
7.417
7.407
7.393
7.391
7.388
7.381
7.379
7.373
7.371
7.362
7.360
7.358
7.350
7.260
7.223
7.221
7.212
7.210
7.192
7.190
7.181
7.179
7.115
7.113
7.104
7.102
6.603
6.592
4.853
4.846
4.832
4.825
4.428
4.425
4.416
3.641
2.886
2.592
2.583
2.579
2.573
2.570
2.560
CO2Me
NHBn
S
N
S
203
1.01
4.89
0.99
0.97
0.89
1.00
2.04
1.02
3.05
1.07
1.04
1.12
3.25
1.13
1.06
9
8
7
6
5
4
3
2
1
0
ppm
NAME DAS62161
EXPNO 1
PROCNO 1
Date_ 20140601
Time_ 12.16
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 16
DW 42.000 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PLIW 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471611 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00



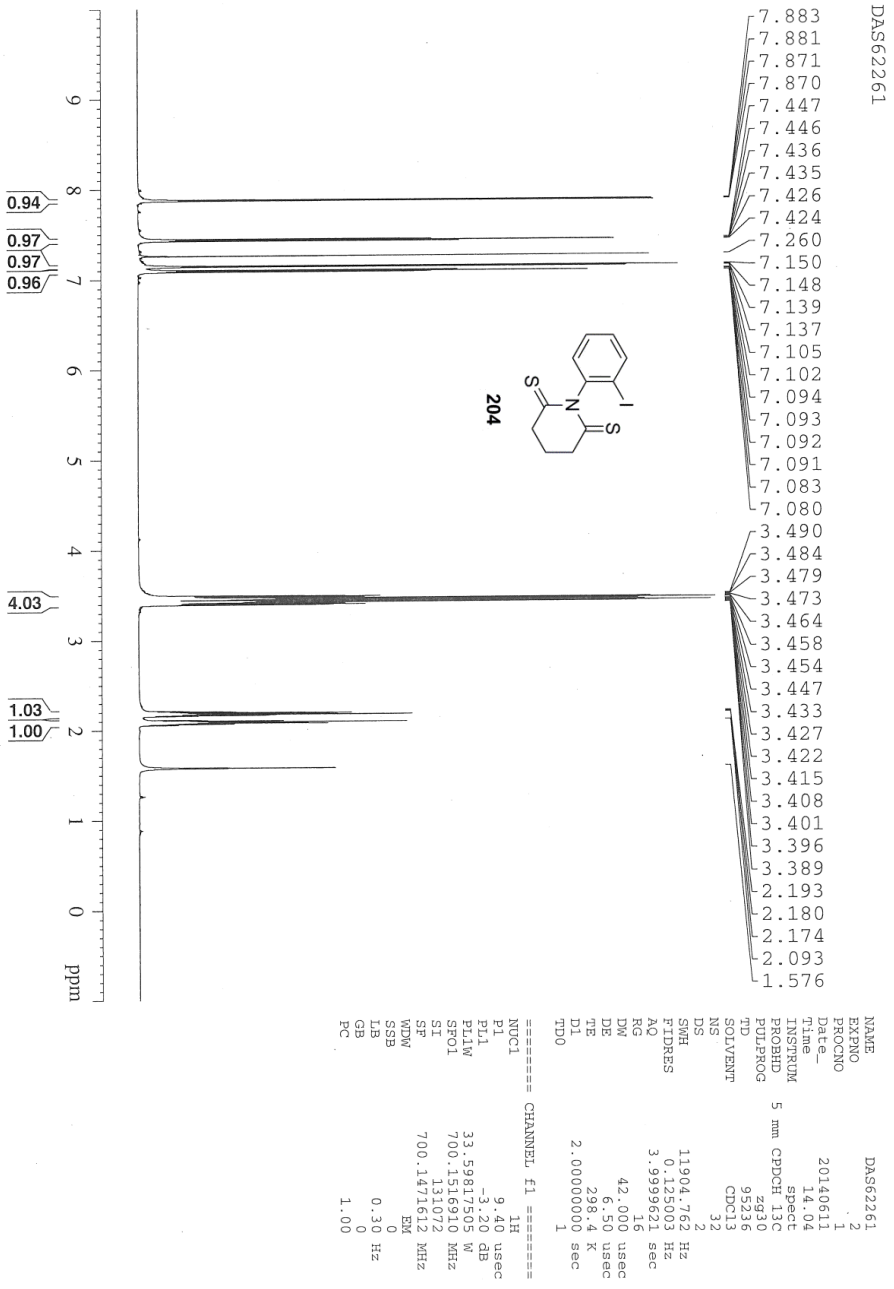

```
NAME                    DAS62161
EXPNO                          2
PROCNO                         1
Date_                   20140601
Time                       12.24
INSTRUM                     spect
PROBHD     5 mm CPDCH 13C
PULPROG                 zgpg30
TD                         65536
SOLVENT                    CDCl3
NS                           256
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                    176.0521291 MHz
WDW                           EM
SSB                            0
LB                          1.00 Hz
GB                             0
PC                          1.40
```

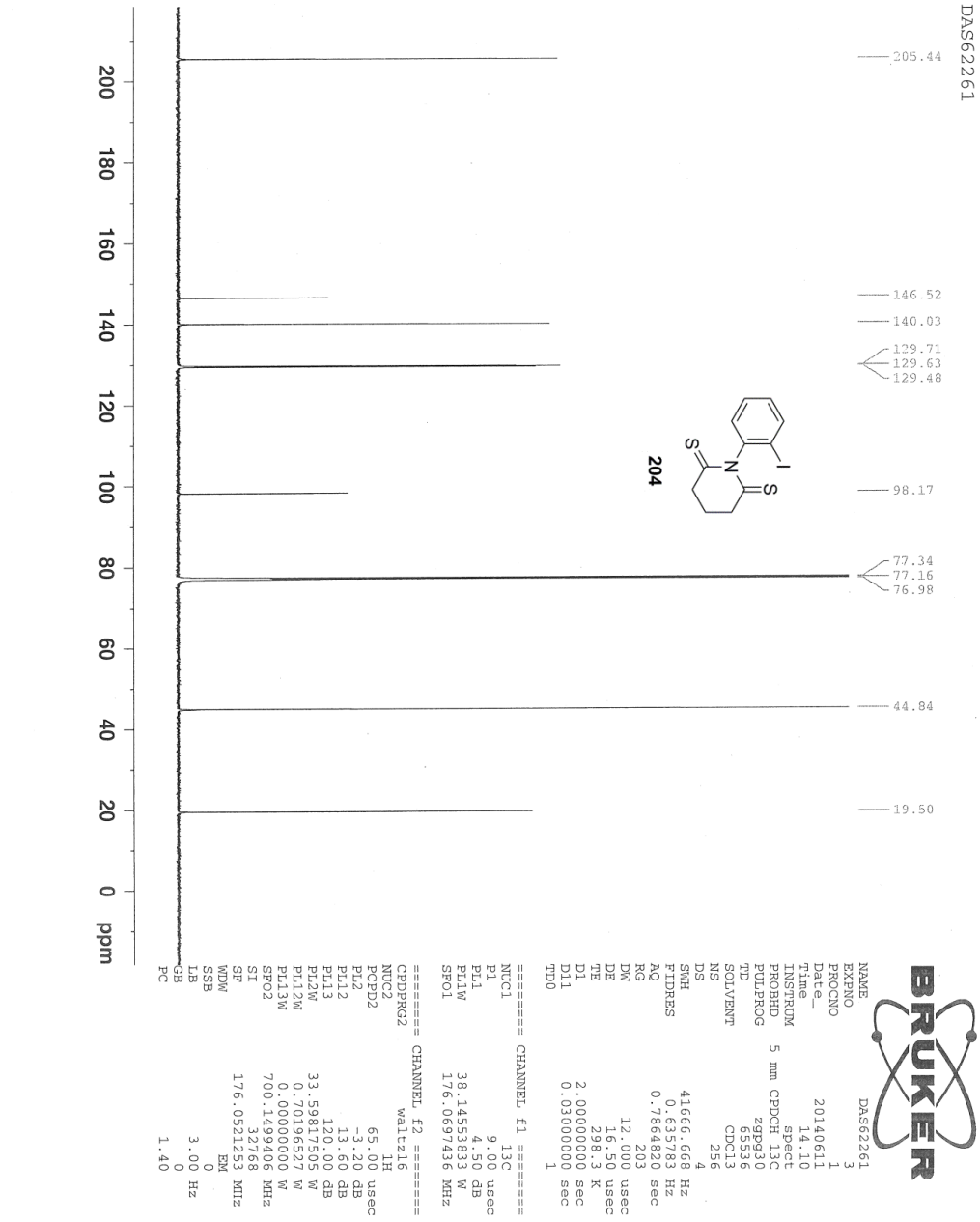

DAS62231
7.923
7.919
7.903
7.899
7.463
7.459
7.443
7.440
7.424
7.421
7.260
7.159
7.156
7.141
7.136
7.122
7.118
7.103
7.099
2.914
2.901
2.895
2.882
2.871
2.858
2.852
2.840
2.828
2.821
2.808
2.798
2.785
2.778
2.765
2.223
2.209
2.202
2.189
2.128
2.121
2.108
2.095
2.089
2.074
S20
1.00
1.03
2.00
4.31
1.13
1.10
ppm
Current Data Parameters
NAME DAS62231
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20141110
Time 9.49
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 256
DW 78.000 usec
DE 6.00 usec
TE 299.2 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 400.2600109 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

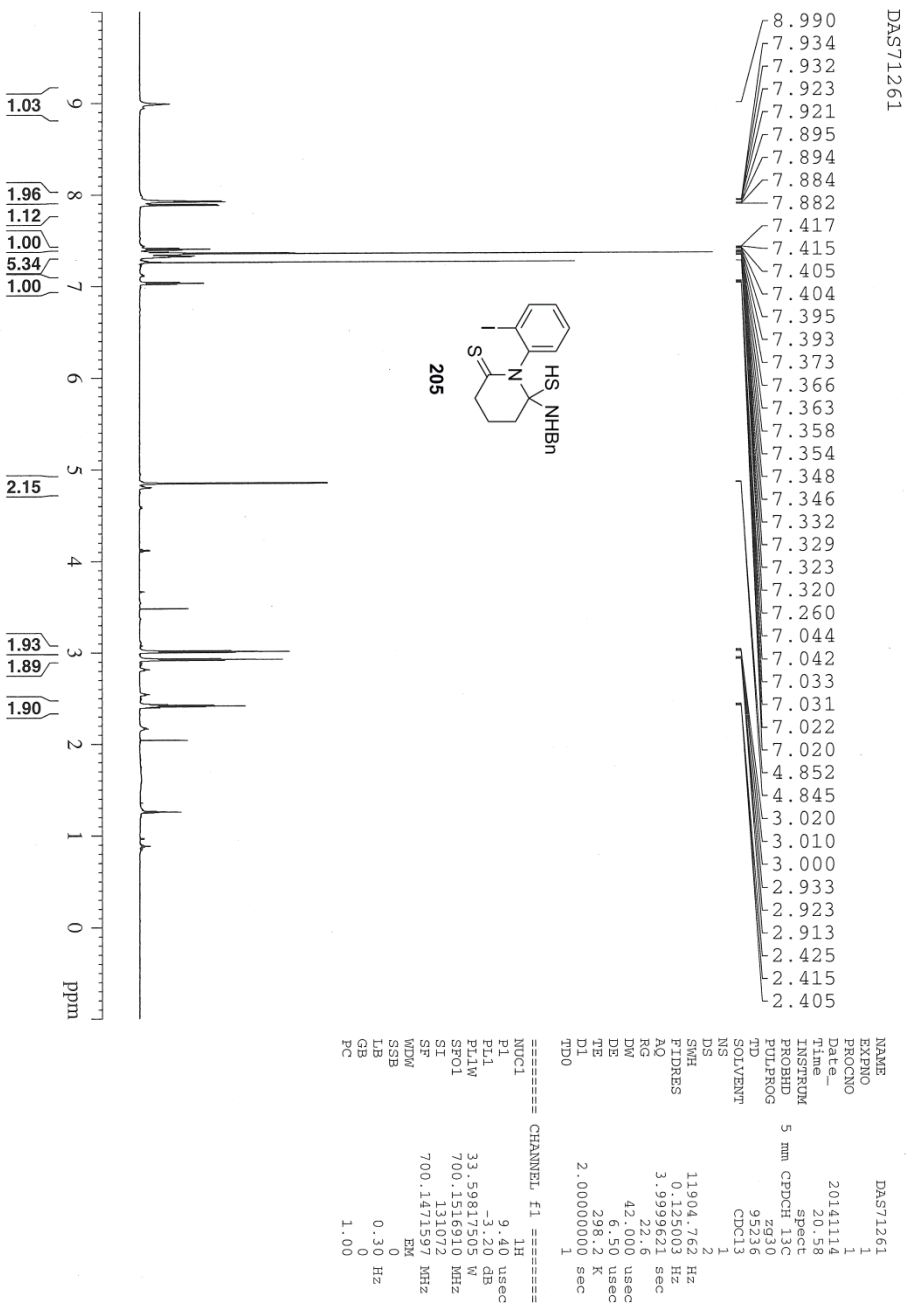
DAS62231

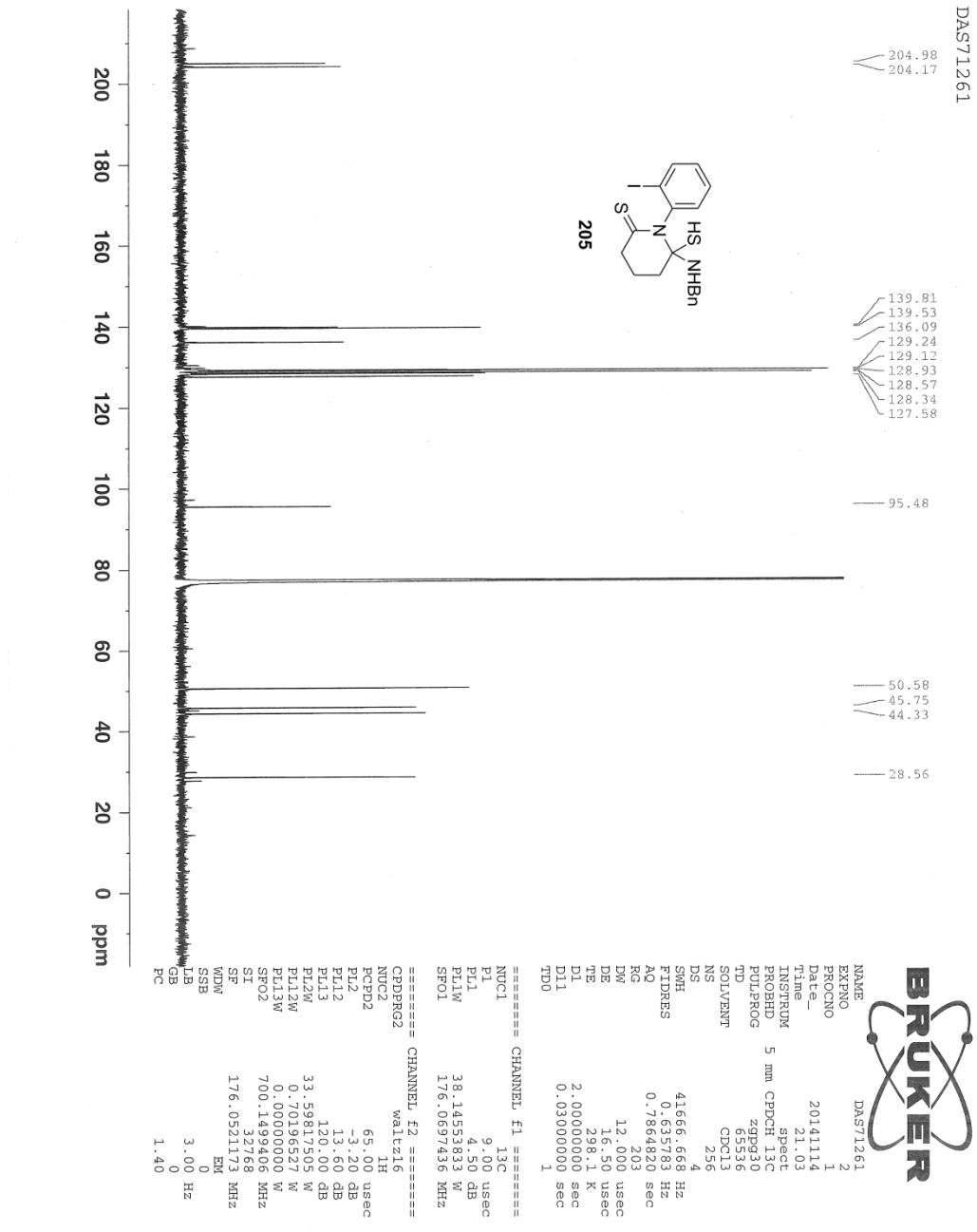


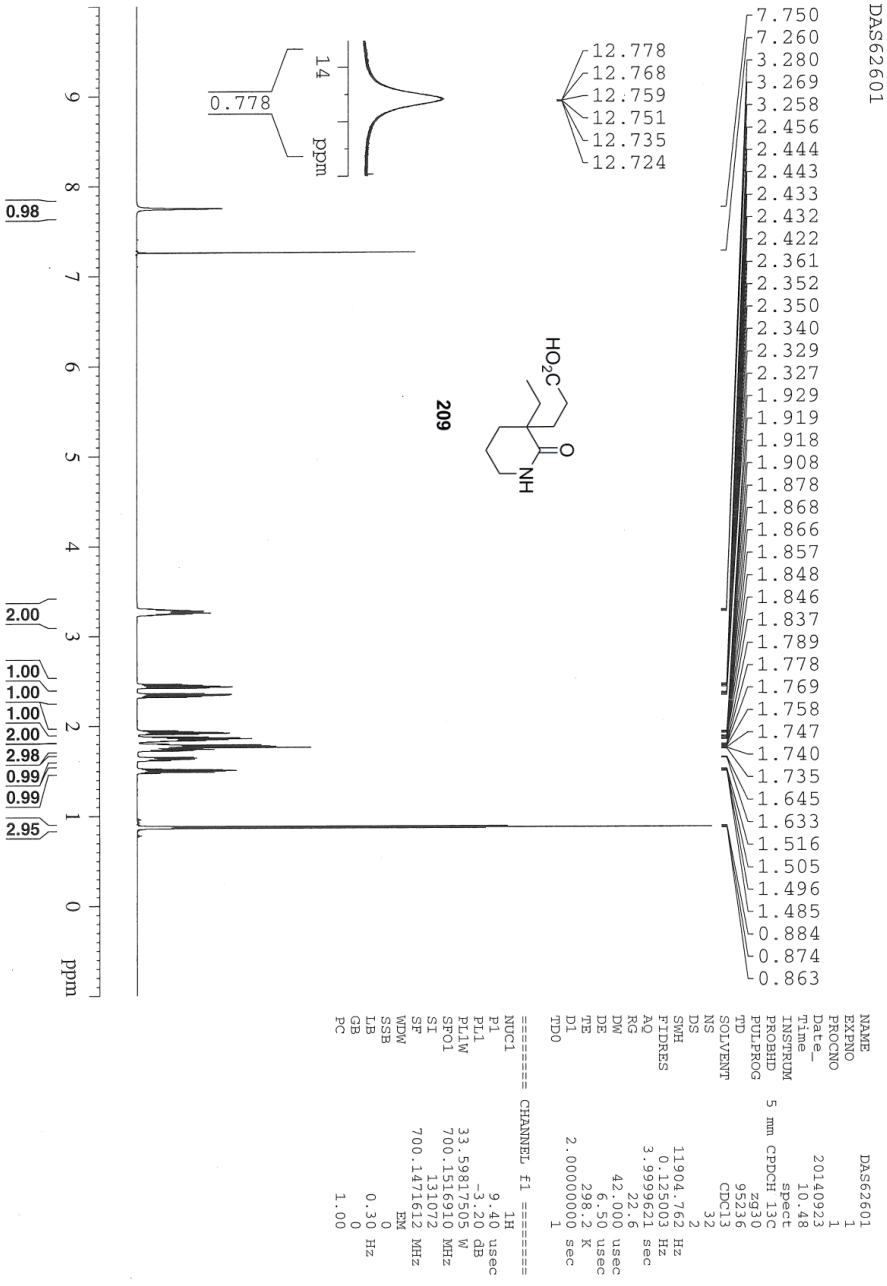

```
Current Data Parameters
NAME                  DAS62231
EXPNO                        3
PROCNO                       1

F2 - Acquisition Parameters
Date_                 20141110
Time                     14.32
INSTRUM                DPX400
PROBHD   5 mm Multinucl
PULPROG                zgpg30
TD                      65536
SOLVENT                 CDCl3
NS                        129
DS                          4
SWH                 23980.814 Hz
FIDRES               0.365918 Hz
AQ                   1.3664756 sec
RG                        4096
DW                      20.850 use
DE                       6.00 use
TE                      299.2 K
D1                 1.00000000 sec
d11                0.03000000 sec
DELTA              0.89999998 sec
TD0                          1

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

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

F2 - Processing parameters
SI                       32768
SF                 100.6454493 MHz
WDW                         EM
SSB                          0
LB                        1.00 Hz
GB                           0
PC                        1.40
```

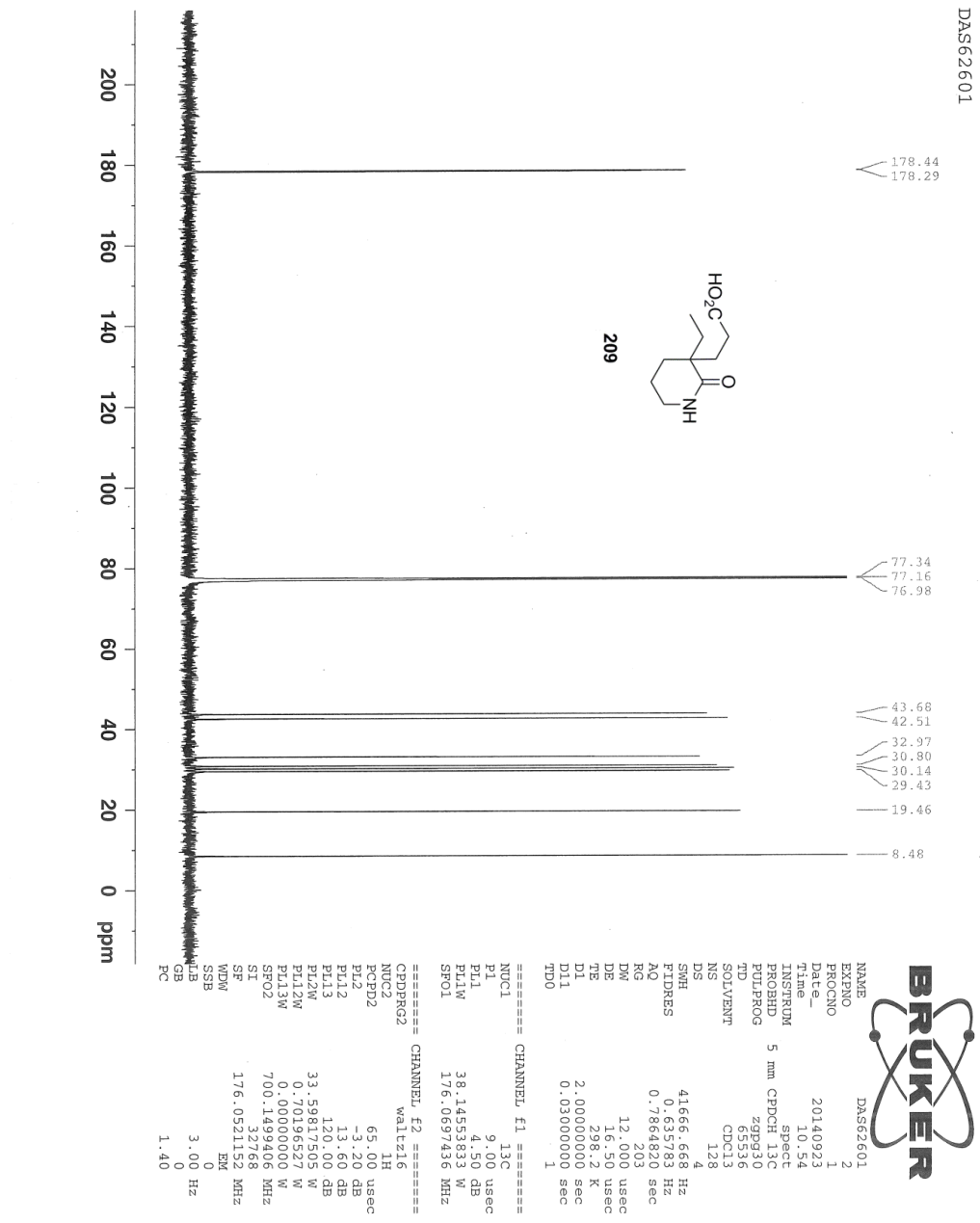

DAS62261
7.883
7.881
7.871
7.870
7.447
7.446
7.436
7.435
7.426
7.424
7.260
7.150
7.148
7.139
7.137
7.105
7.102
7.094
7.093
7.092
7.091
7.083
7.080
3.490
3.484
3.479
3.473
3.464
3.458
3.454
3.447
3.433
3.427
3.422
3.415
3.408
3.401
3.396
3.389
2.193
2.180
2.174
2.093
1.576
204
0.94
0.97
0.97
0.96
4.03
1.03
1.00
ppm
NAME DAS62261
EXPNO 2
PROCNO 1
Date_ 20140611
Time 14.04
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95336
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 16
DW 42.000 usec
DE 6.50 usec
TE 298.4 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 700.1471612 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

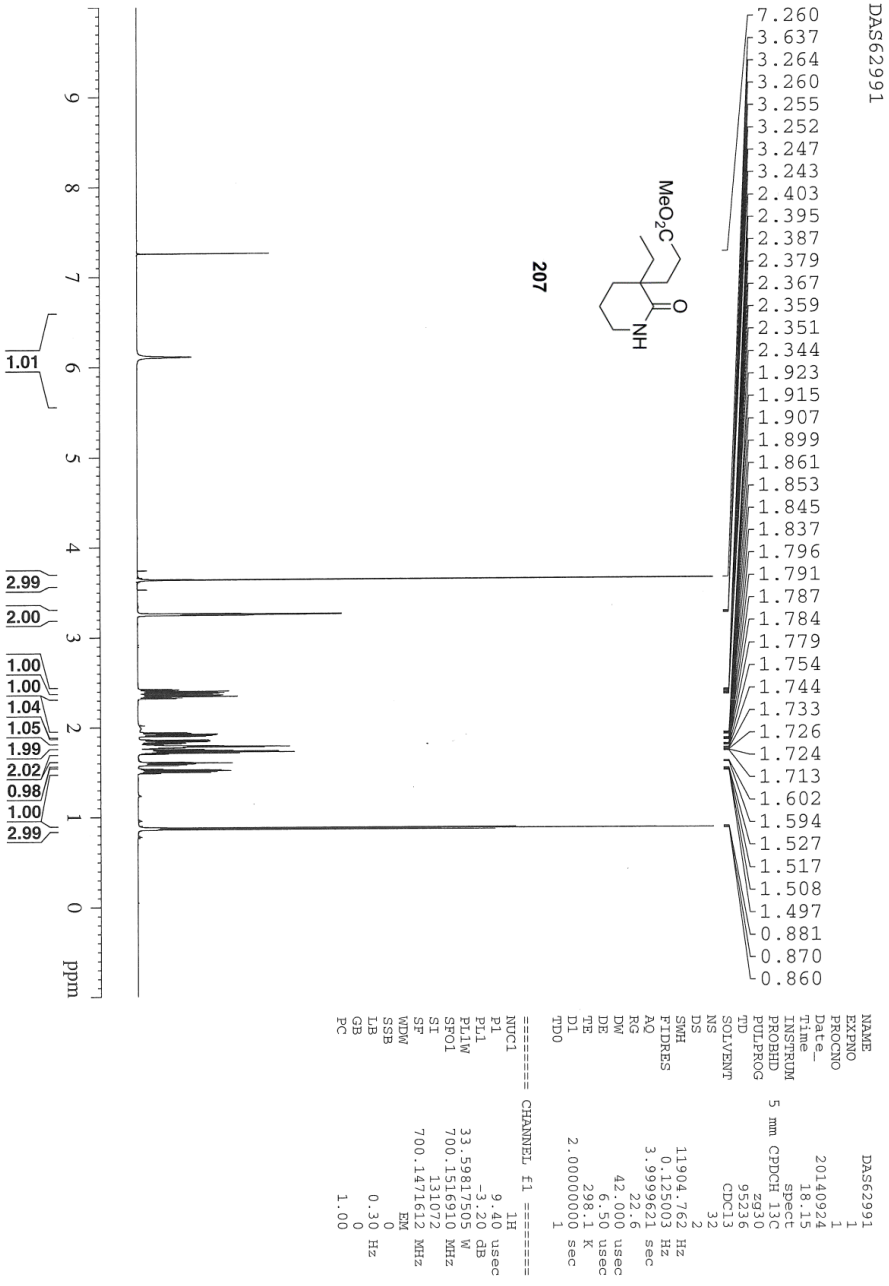

DAS62261
205.44
146.52
140.03
129.71
129.63
129.48
98.17
77.34
77.16
76.98
44.84
19.50
204
BRUKER
NAME DAS62261
EXPNO 3
PROCNO 1
Date_ 20140611
Time 14.10
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 256
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864820 sec
RG 203
DW 12.000 usec
DE 16.50 usec
TE 298.3 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0697436 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 usec
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1499406 MHz
SI 32768
SF 176.0521253 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
200 180 160 140 120 100 80 60 40 20 0 ppm


DAS71261
8.990
7.934
7.932
7.923
7.921
7.895
7.894
7.884
7.882
7.417
7.415
7.405
7.404
7.395
7.393
7.373
7.366
7.363
7.358
7.354
7.348
7.346
7.332
7.329
7.323
7.320
7.260
7.044
7.042
7.033
7.031
7.022
7.020
4.852
4.845
3.020
3.010
3.000
2.933
2.923
2.913
2.425
2.415
2.405
HS
NHBn
N
S
I
205
1.03
1.96
1.12
1.00
5.34
1.00
2.15
1.93
1.89
1.90
9
8
7
6
5
4
3
2
1
0
ppm
NAME DAS71261
EXPNO 1
PROCNO 1
Date_ 20141114
Time_ 20.58
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 1
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 22.6
DW 42.000 usec
DE 6.50 usec
TE 298.2 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 700.1471597 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00


DAS71261
204.98
204.17
139.81
139.53
136.09
129.24
129.12
128.93
128.57
128.34
127.58
95.48
50.58
45.75
44.33
28.56
205
HS NHBn
N
S
I
200
180
160
140
120
100
80
60
40
20
0
ppm
BRUKER
NAME DAS71261
EXPNO 2
PROCNO 1
Date_ 20141114
Time 21.03
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 256
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 176.0521173 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40


DAS62601
7.750
7.260
3.280
3.269
3.258
2.456
2.444
2.443
2.433
2.432
2.422
2.361
2.352
2.350
2.340
2.329
2.327
1.929
1.919
1.918
1.908
1.878
1.868
1.866
1.857
1.848
1.846
1.837
1.789
1.778
1.769
1.758
1.747
1.740
1.735
1.645
1.633
1.516
1.505
1.496
1.485
0.884
0.874
0.863
12.778
12.768
12.759
12.751
12.735
12.724
HO2C
O
NH
209
0.778
14
ppm
0.98
2.00
1.00
1.00
1.00
2.00
2.98
0.99
0.99
2.95
9
8
7
6
5
4
3
2
1
0
ppm
NAME DAS62601
EXPNO 1
PROCNO 1
Date_ 20140923
Time 10.48
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 22.6
DW 42.000 usec
DE 6.50 usec
TE 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 700.1471612 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00


DAS62601
178.44
178.29
77.34
77.16
76.98
43.68
42.51
32.97
30.80
30.14
29.43
19.46
8.48
200
180
160
140
120
100
80
60
40
20
0
ppm
209
NH
O
HO_2C
BRUKER
NAME DAS62601
EXPNO 2
PROCNO 1
Date_ 20140923
Time 10.54
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 128
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 176.0521152 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40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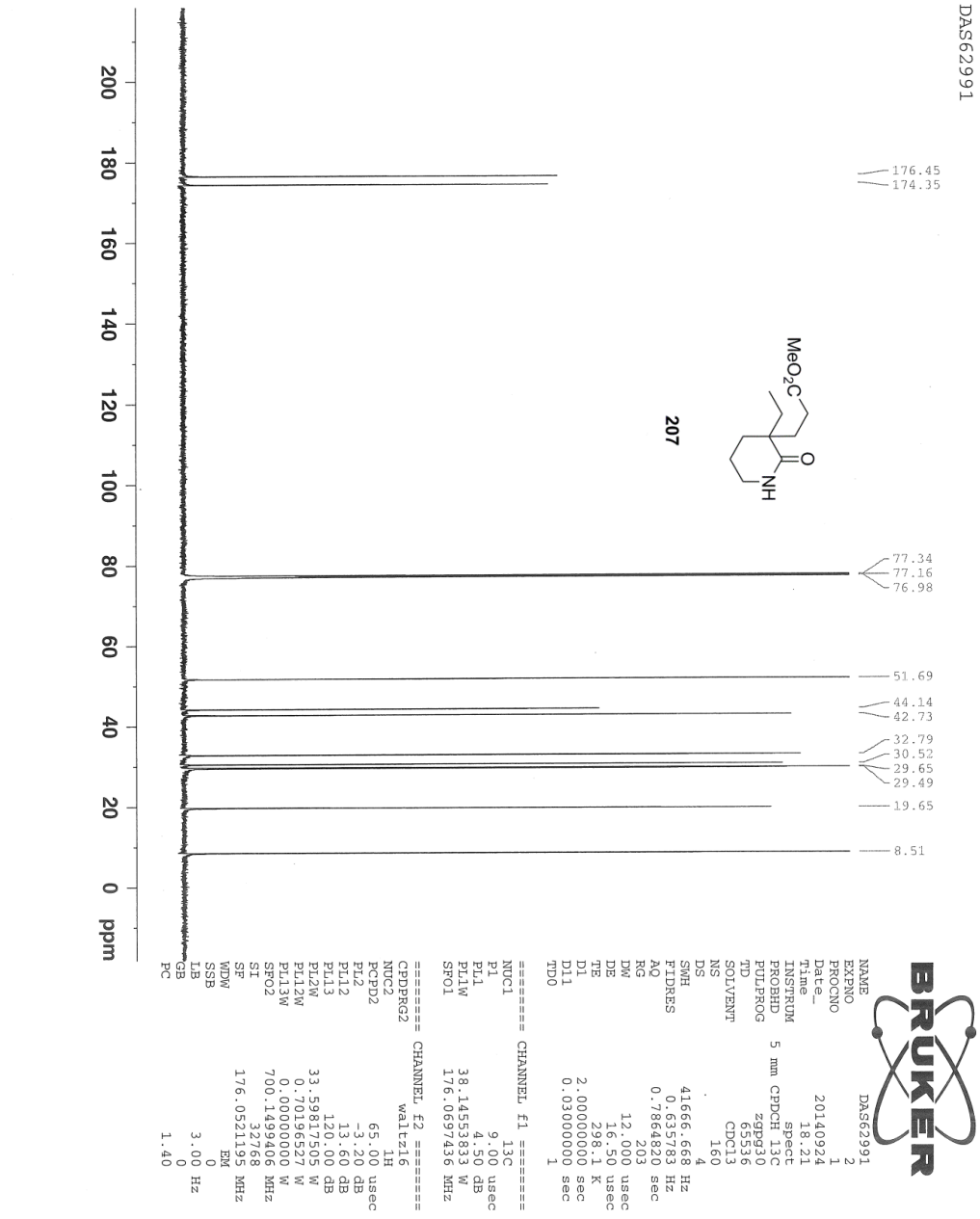
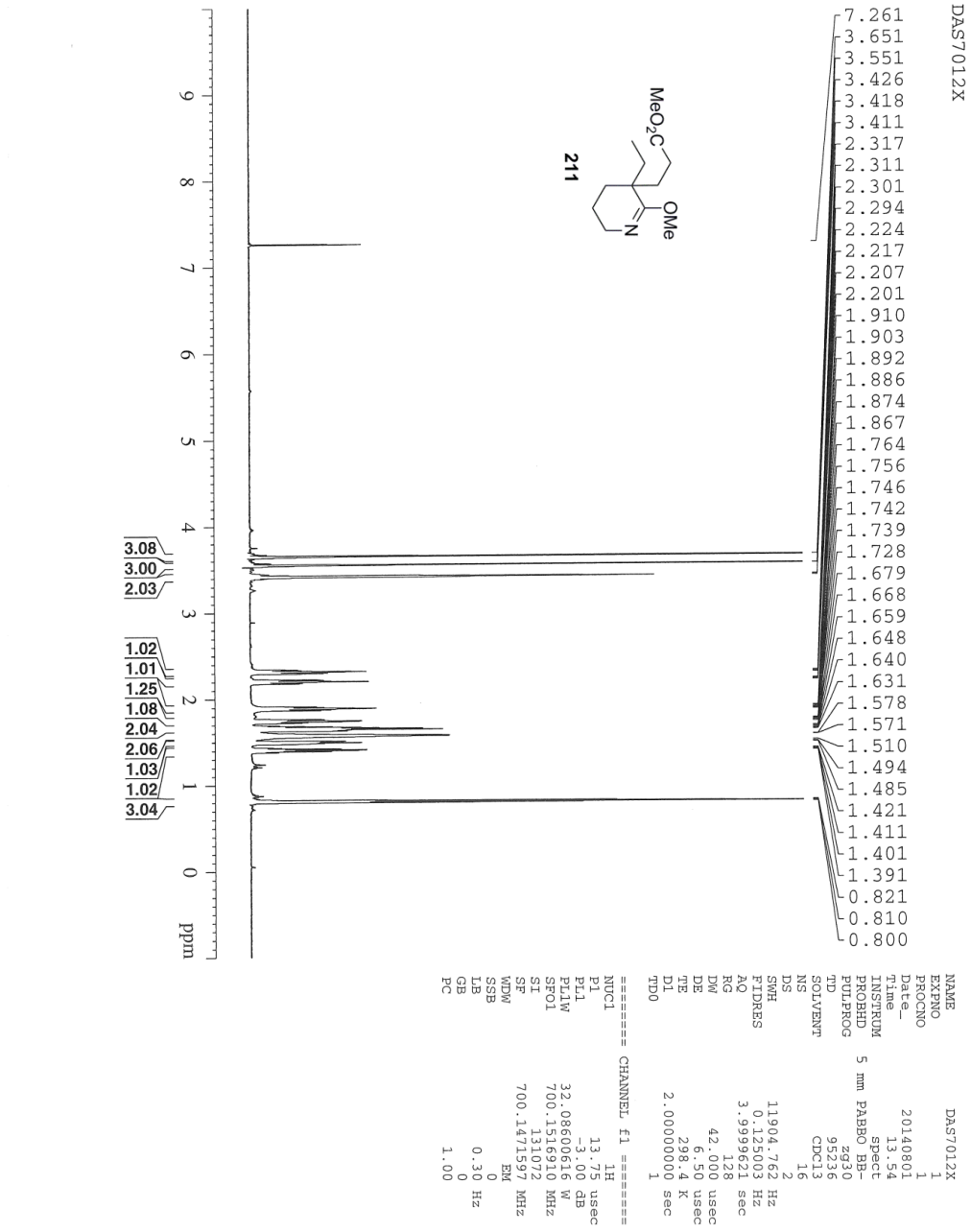
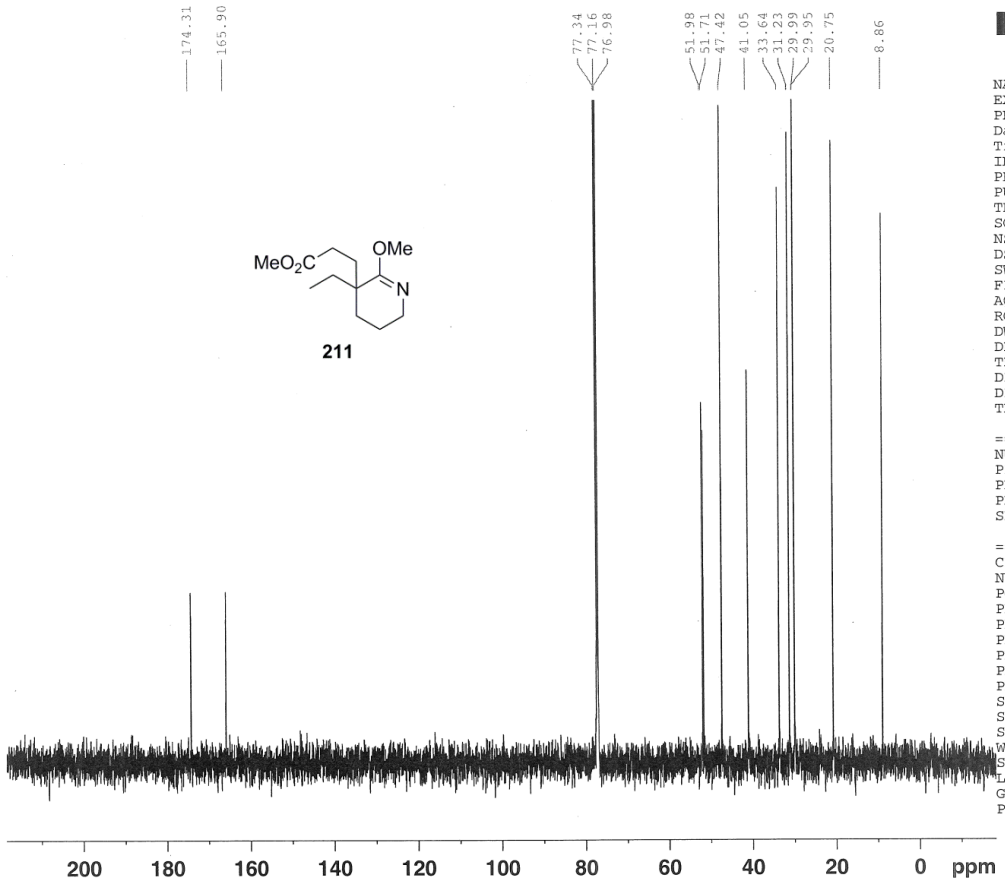
7.260
3.637
3.264
3.260
3.255
3.252
3.247
3.243
2.403
2.395
2.387
2.379
2.367
2.359
2.351
2.344
1.923
1.915
1.907
1.899
1.861
1.853
1.845
1.837
1.796
1.791
1.787
1.784
1.779
1.754
1.744
1.733
1.726
1.724
1.713
1.602
1.594
1.527
1.517
1.508
1.497
0.881
0.870
0.860
MeO2C
O
NH
207
1.01
2.99
2.00
1.00
1.00
1.04
1.05
1.99
2.02
0.98
1.00
2.99
ppm
NAME DAS62991
EXPNO 1
PROCNO 1
Date_ 20140924
Time 18.15
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDC13
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 22.6
DW 42.000 usec
DE 6.50 usec
TE 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 700.1471612 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00


DAS62991
176.45
174.35
77.34
77.16
76.98
51.69
44.14
42.73
32.79
30.52
29.65
29.49
19.65
8.51
MeO2C
O
NH
207
BRUKER
NAME DAS62991
EXPNO 2
PROCNO 1
Date_ 20140924
Time 18.21
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 160
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864820 sec
RG 203
DW 12.000 usec
DE 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 176.0521195 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
200
180
160
140
120
100
80
60
40
20
0
ppm

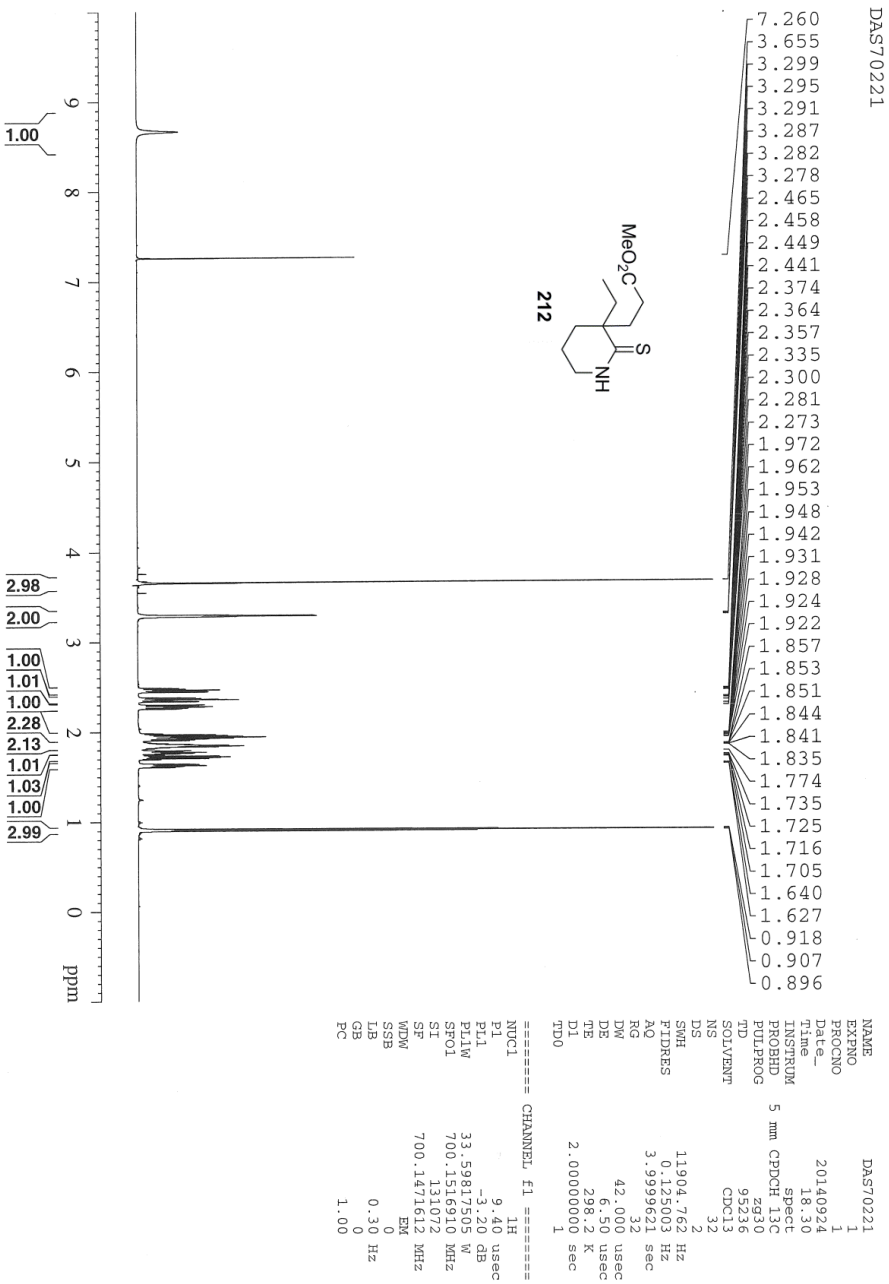

DAS7012X
7.261
3.651
3.551
3.426
3.418
3.411
2.317
2.311
2.301
2.294
2.224
2.217
2.207
2.201
1.910
1.903
1.892
1.886
1.874
1.867
1.764
1.756
1.746
1.742
1.739
1.728
1.679
1.668
1.659
1.648
1.640
1.631
1.578
1.571
1.510
1.494
1.485
1.421
1.411
1.401
1.391
0.821
0.810
0.800
MeO2C
OMe
N
211
3.08
3.00
2.03
1.02
1.01
1.25
1.08
2.04
2.06
1.03
1.02
3.04
9 8 7 6 5 4 3 2 1 0 ppm
NAME DAS7012X
EXPNO 1
PROCNO 1
Date_ 20140801
Time 13.54
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 16
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 128
DW 42.000 usec
DE 6.50 usec
TE 298.4 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.75 usec
PL1 -3.00 dB
PL1W 32.08600616 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471597 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

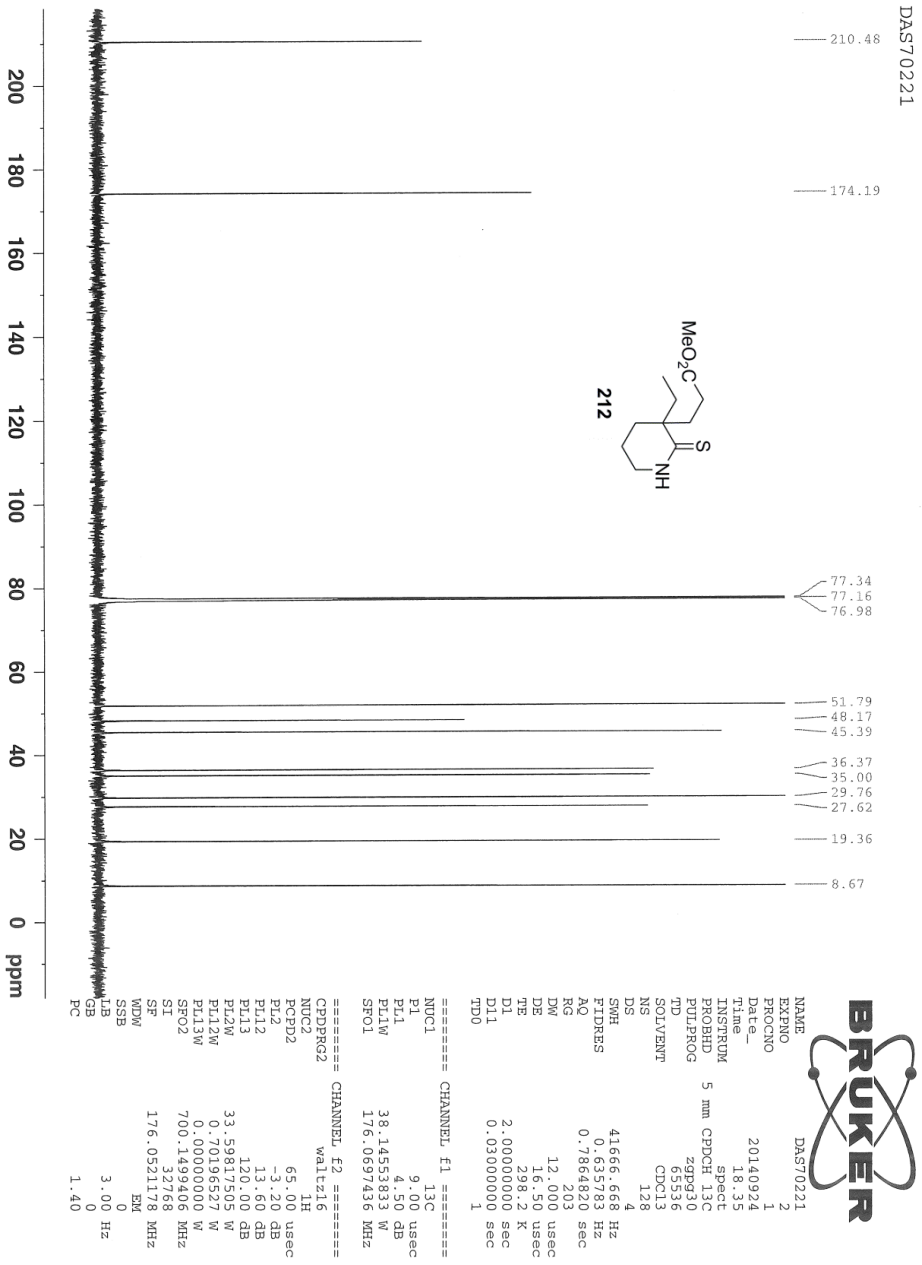
DAS7012X

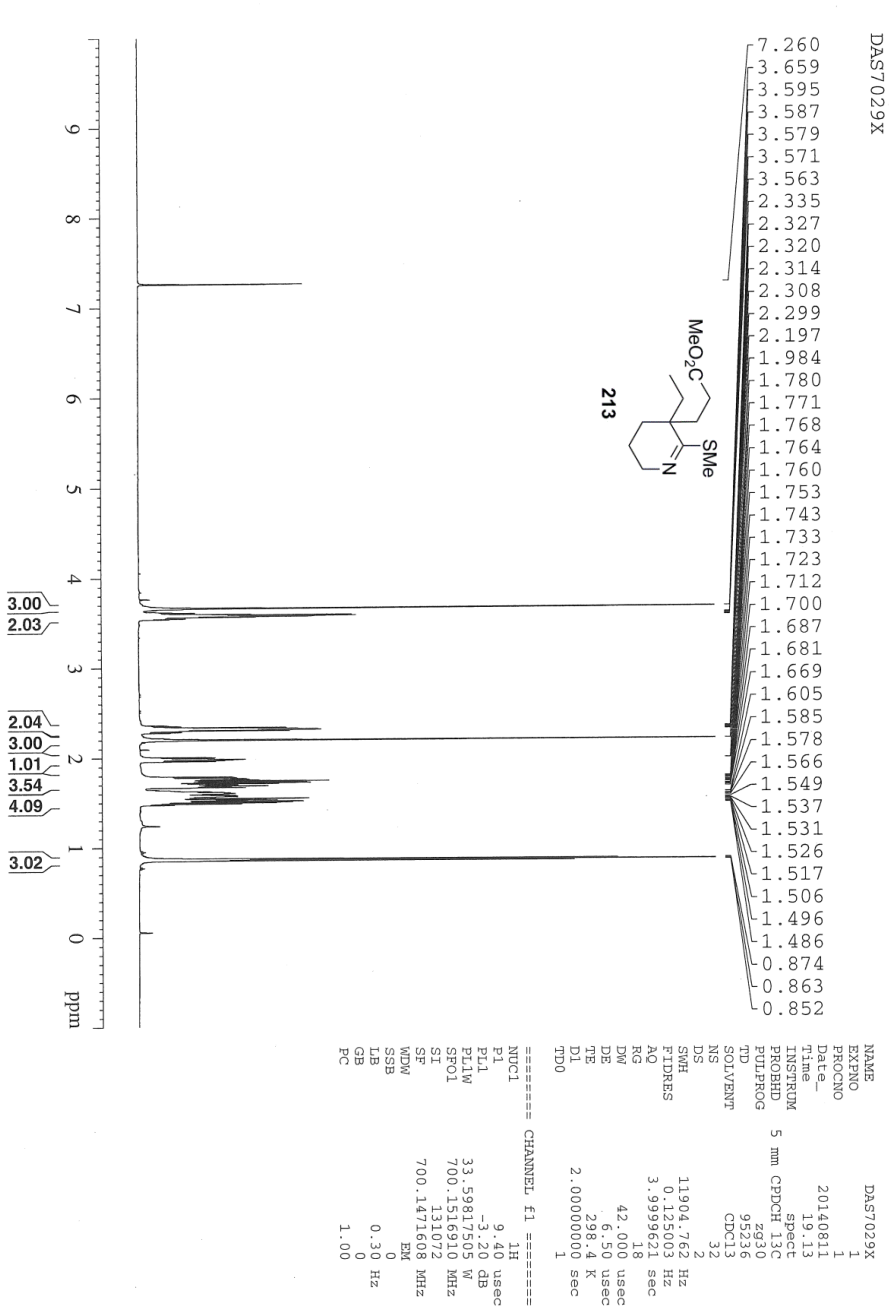


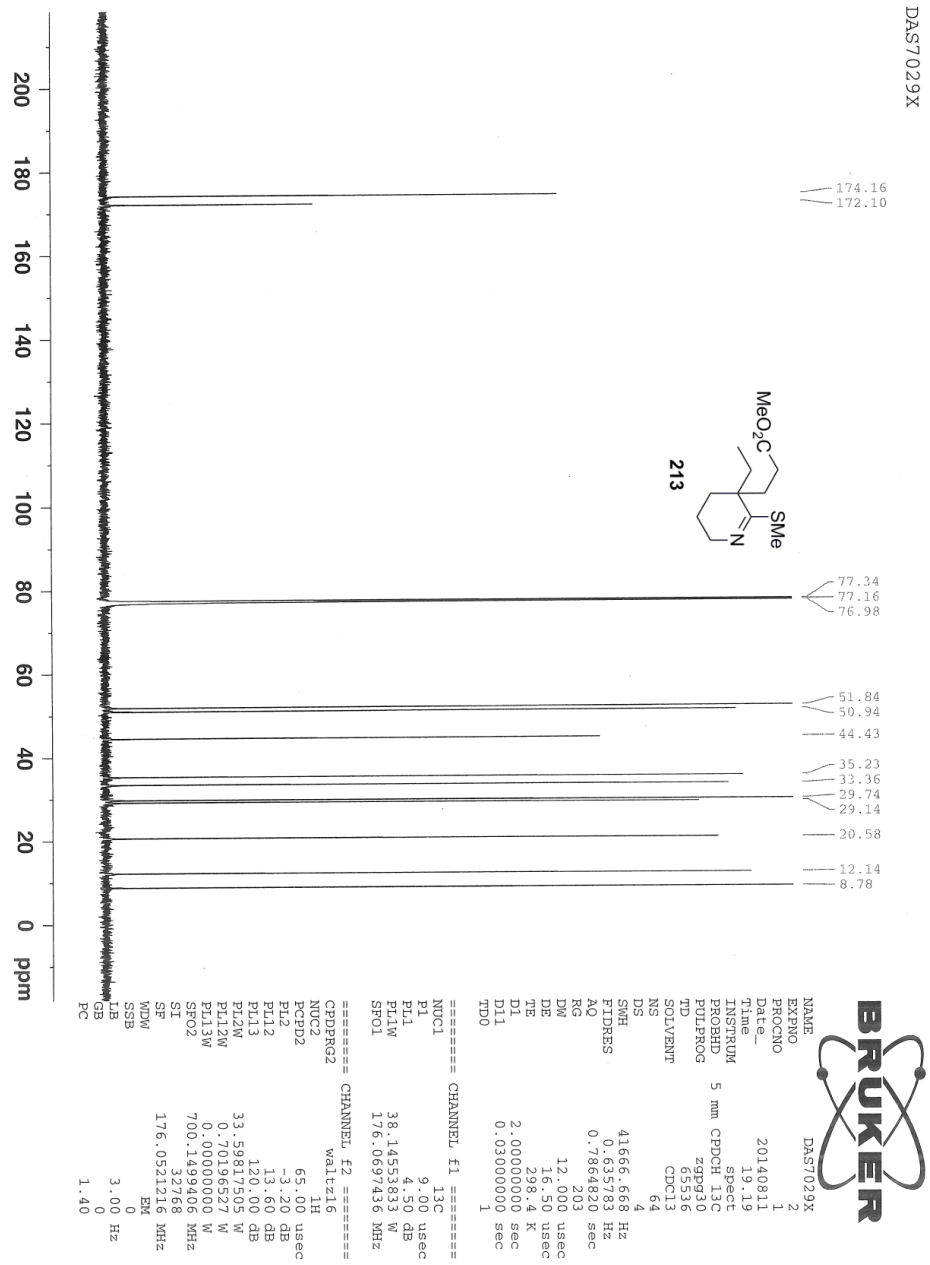
BRUKER

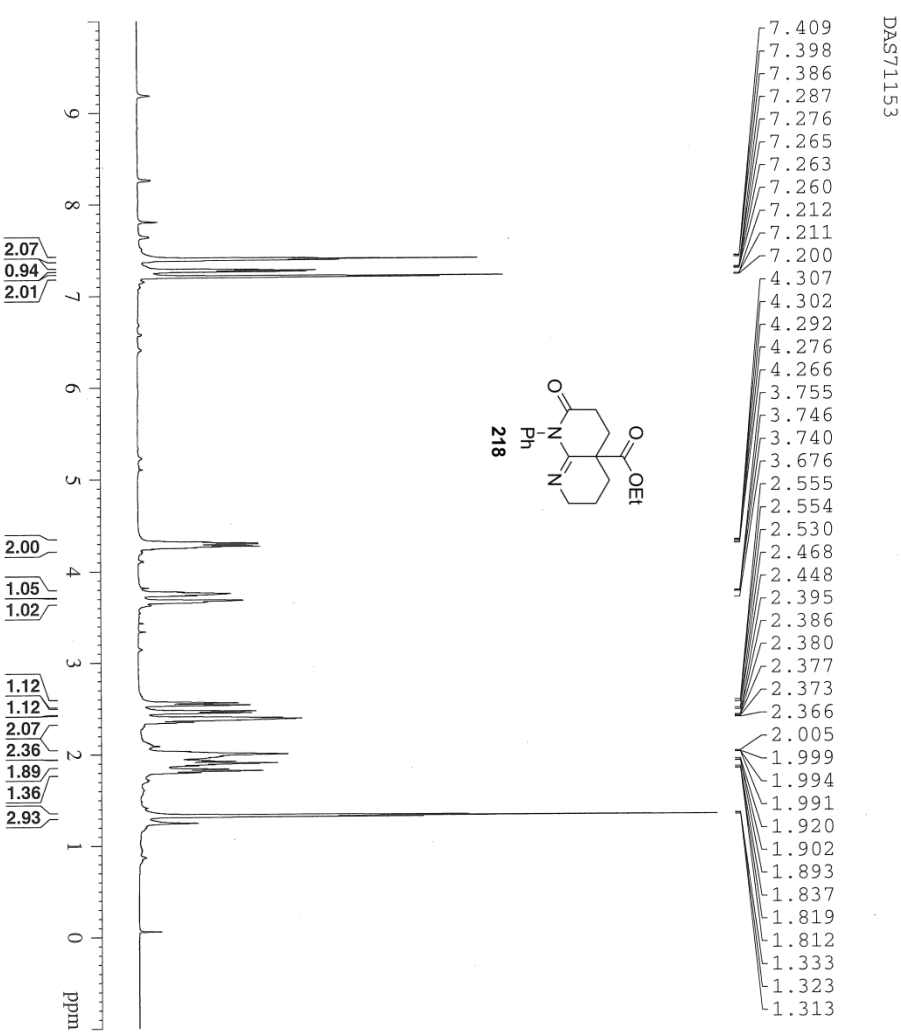
NAME	DAS7012X
EXPNO	2
PROCNO	1
Date_	20140801
Time	13.59
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	64
DS	4
SWH	41666.668 Hz
FIDRES	0.635783 Hz
AQ	0.7864820 sec
RG	203
DW	12.000 usec
DE	16.50 usec
TE	300.3 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.30 usec
PL1	2.00 dB
PL1W	67.83342743 W
SFO1	176.0697436 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	-3.00 dB
PL12	12.30 dB
PL13	12.30 dB
PL2W	32.08600616 W
PL12W	0.94692516 W
PL13W	0.94692516 W
SFO2	700.1499406 MHz
SI	32768
SF	176.0521140 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40

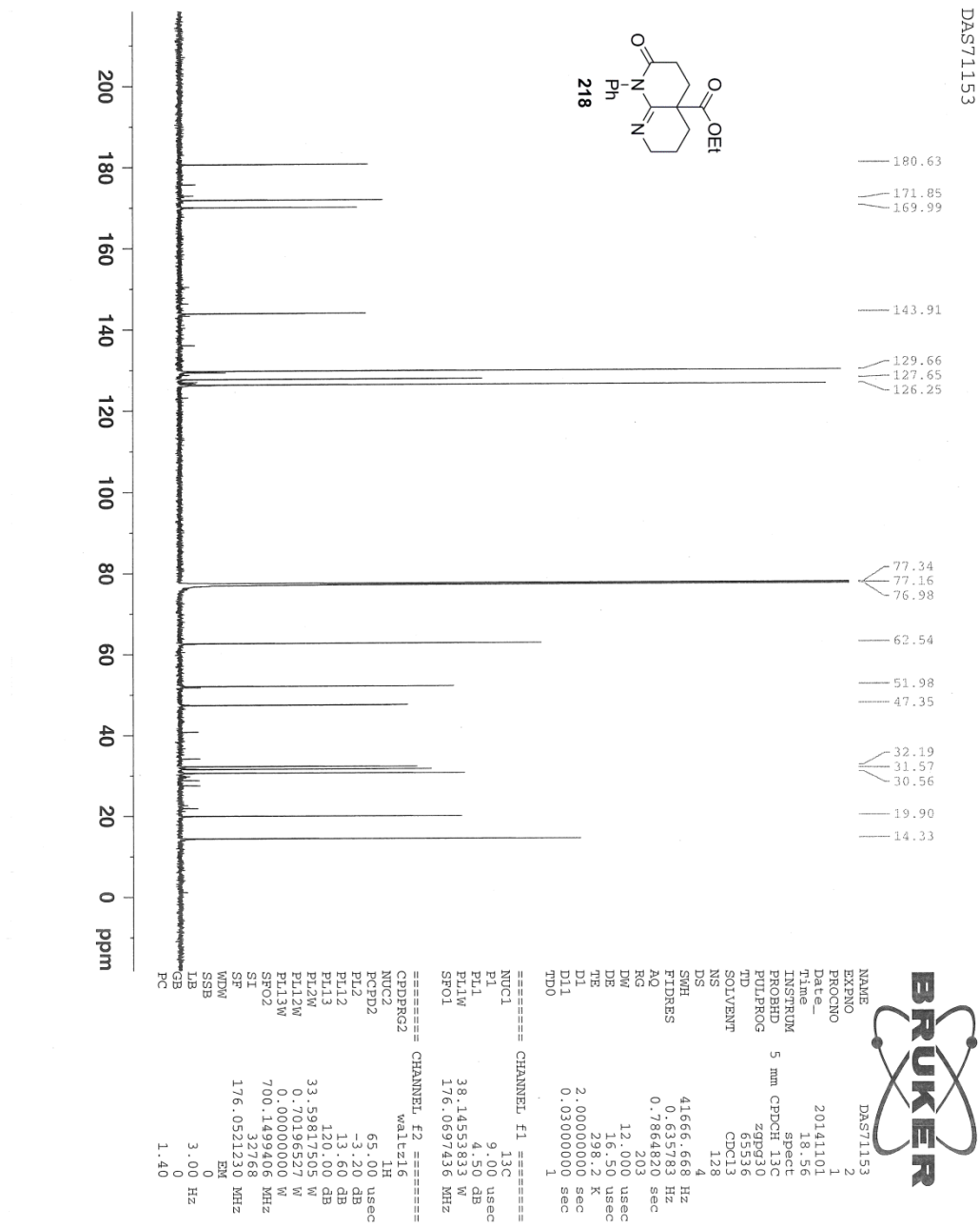

DAS70221
7.260
3.655
3.299
3.295
3.291
3.287
3.282
3.278
2.465
2.458
2.449
2.441
2.374
2.364
2.357
2.335
2.300
2.281
2.273
1.972
1.962
1.953
1.948
1.942
1.931
1.928
1.924
1.922
1.857
1.853
1.851
1.844
1.841
1.835
1.774
1.735
1.725
1.716
1.705
1.640
1.627
0.918
0.907
0.896
MeO2C
S
NH
212
1.00
2.98
2.00
1.00
1.01
1.00
2.28
2.13
1.01
1.03
1.00
2.99
ppm
NAME DAS70221
EXPNO 1
PROCNO 1
Date_ 20140924
Time 18.30
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 32
DW 42.000 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471612 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00


DAS70221
210.48
174.19
77.34
77.16
76.98
51.79
48.17
45.39
36.37
35.00
29.76
27.62
19.36
8.67
MeO2C
S
NH
212
200
180
160
140
120
100
80
60
40
20
0
ppm
NAME DAS70221
EXPNO 2
PROCNO 1
Date_ 20140924
Time 18.35
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 128
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 176.0521178 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40


DAS7029X
7.260
3.659
3.595
3.587
3.579
3.571
3.563
2.335
2.327
2.320
2.314
2.308
2.299
2.197
1.984
1.780
1.771
1.768
1.764
1.760
1.753
1.743
1.733
1.723
1.712
1.700
1.687
1.681
1.669
1.605
1.585
1.578
1.566
1.549
1.537
1.531
1.526
1.517
1.506
1.496
1.486
0.874
0.863
0.852
MeO2C
SMe
N
213
3.00
2.03
2.04
3.00
1.01
3.54
4.09
3.02
ppm
NAME DAS7029X
EXPNO 1
PROCNO 1
Date_ 20140811
Time 19.13
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDC13
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.999621 sec
RG 18
DW 42.000 usec
DE 6.50 usec
TE 298.4 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


DAS7029X
174.16
172.10
77.34
77.16
76.98
51.84
50.94
44.43
35.23
33.36
29.74
29.14
20.58
12.14
8.78
MeO2C
SMe
N
213
200
180
160
140
120
100
80
60
40
20
0
ppm
BRUKER
NAME DAS7029X
EXPNO 2
PROCNO 1
Date_ 20140811
Time 19.19
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 64
DS 4
SWH 41666.668 Hz
FIDRES 0.635793 Hz
AQ 0.7864820 sec
RG 203
DW 12.000 usec
DE 16.50 usec
TE 298.4 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 176.0521216 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40


DAS71153
7.409
7.398
7.386
7.287
7.276
7.265
7.263
7.260
7.212
7.211
7.200
4.307
4.302
4.292
4.276
4.266
3.755
3.746
3.740
3.676
2.555
2.554
2.530
2.468
2.448
2.395
2.386
2.380
2.377
2.373
2.366
2.005
1.999
1.994
1.991
1.920
1.902
1.893
1.837
1.819
1.812
1.333
1.323
1.313
218
2.07
0.94
2.01
2.00
1.05
1.02
1.12
1.12
2.07
2.36
1.89
1.36
2.93
ppm
NAME DAS71153
EXPNO 1
PROCNO 1
Date_ 20141101
Time 18.51
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 18
DW 42.000 usec
DE 6.50 usec
TE 298.4 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PLIW 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471594 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00


DAS71153
218
180.63
171.85
169.99
143.91
129.66
127.65
126.25
77.34
77.16
76.98
62.54
51.98
47.35
32.19
31.57
30.56
19.90
14.33
200
180
160
140
120
100
80
60
40
20
0
ppm
BRUKER
NAME DAS71153
EXPNO 2
PROCNO 1
Date_ 20141101
Time 18.56
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 128
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 176.0521230 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40

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Chapter 5: Conclusion and Future Direction

5.1 Conclusion

The advancement of medicine relies greatly on the ability to efficiently construct new molecules for screening and derivatization. Because many biologically active molecules contain one or more nitrogen atoms, the development of new methods for their synthesis is an important endeavor. However, the complex reactivity of nitrogen can be problematic in synthesis. The ability to quaternize, the Lewis basic lone pair, and the weakly acidic N–H protons found in nitrogen-containing molecules often give rise to undesired reactivity.

As a means to mute the reactivity of nitrogen, synthetic chemists often employ protective groups. Other strategies which have proven successful for the synthesis of nitrogen-containing structures include opting to install nitrogen late in the synthesis or in the form of a less reactive functional group.

Free radical reactivity avoids the complications inherent in the synthesis of nitrogen-rich molecules. Radicals are known to tolerate heteroatom lone pairs, and N–H bonds are resistive to homolytic cleavage. Free radical reactivity has proven useful for the synthesis of heterocycles and alkaloid natural products. This reactivity also allows for the strategic disconnection of bonds which would be difficult to form using standard cationic or anionic reaction conditions. For these reasons, free radical based methods are ideally suited to the synthesis of nitrogen containing molecules.

Despite the presence of the aminal functional group in several nitrogen-rich natural products which had attracted the attention of the synthetic community, very little

attention had been given to the development of reactions specific to the aminal. Although there were reports of fragmentation, protonation, and dimerization reactions of aminal radicals, there had been no reports of their synthetic utility prior to the work described in this dissertation. The goal of this work was to develop the reactivity of the aminal radical intermediate as a new tool for the construction of C–C bonds in the context of nitrogen-rich molecular architectures.

As detailed in the first chapter of this dissertation, preliminary investigations centered on the generation of aminal radicals under peroxide initiated conditions similar to those previously reported for the generation of α-amino radicals. The treatment of aminal containing molecules with di-*tert*-butyl peroxide in the presence of a radical acceptor produced either a complex mixture of products, or no reaction. Unable to determine if aminal radicals were being generated, a new method was sought.

Treatment of 2-iodobenzyl substituted aminals with AIBN and a hydrogen atom donor in the presence of an electron-poor alkene resulted in the formation of the desired aminal radical addition product. However, efforts to optimize this reactivity with non-acylated aminals were unsuccessful.

The second chapter was taken from the published paper Formation of Carbon–Carbon Bonds Using Aminal Radicals, Schiedler, D. A.; Vellucci, J. K.; Beaudry, C. M. *Org. Lett.* **2012,** *14*, 6092–6095. This chapter described the further development of this reactivity. Aminal radicals were successfully formed from 2-iodobenzyl substituted *N*-acyl aminals by radical translocation reactions using AIBN and a either Bu_3SnH or $(TMS)_3SiH$ as a stoichiometric hydrogen atom donor. It was discovered that the installation of an acyl substituent on the aminal greatly enhances the reactivity of the aminal radical species, resulting in cleaner reactivity, increased reaction yields, and the ability to form aminal radicals in the presence of carbon atoms bearing a single

nitrogen atom substituent. Chemical yields of the radical translocation reactions were as high as 91%.

The third chapter was taken from the published paper Reductive Synthesis of Aminal Radicals for Carbon–Carbon Bond Formation, Schiedler, D. A.; Lu, Y.; Beaudry, C. M. *Org. Lett.* **2014,** *16,* 1160–1163. This chapter described the development of an alternative means to access aminal radicals. It was demonstrated that the SmI_2 reduction of *N*-acyl amidines or amidinium ions in the presence of CSA or NH_4Cl and an electron deficient alkene yielded products of C–C bond formation. Chemical yields of these transformations were as high as 99% and diastereoselectivities were as high as 20:1. Mechanistic investigations of this reactivity indicated that these reactions likely proceed through an aminal radical intermediate.

The fourth chapter described our current investigations on the application of aminal radicals to the total synthesis of the alkaloid natural product leuconoxine. It was envisioned that the SmI_2 induced reductive alkylation reaction of a simple bicyclic *N*-acyl amidine would rapidly construct the fully substituted aminal stereocenter present in the natural product and could lead to an efficient synthesis of the target.

While similar amidines have been reported in the literature, no general strategy to access amidines of this type was known. Three distinct synthetic strategies towards the preparation of the desired bicyclic *N*-acyl amidine substrate were developed and investigated.

The first strategy relied on the formation of the amidine using the intramolecular aza-Wittig reaction of an imide and an azide. Unexpectedly, this reaction produced a amido lactam product rather than the desired *N*-acyl amidine. Attempts to induce an intramolecular condensation reaction of the amido lactam to give the desired amidine

were unsuccessful. It was concluded that the poor nucleophilicity of the electron-poor aryl amide and the sterically congested nature of the desired site of attack were to blame for the lack of desired reactivity.

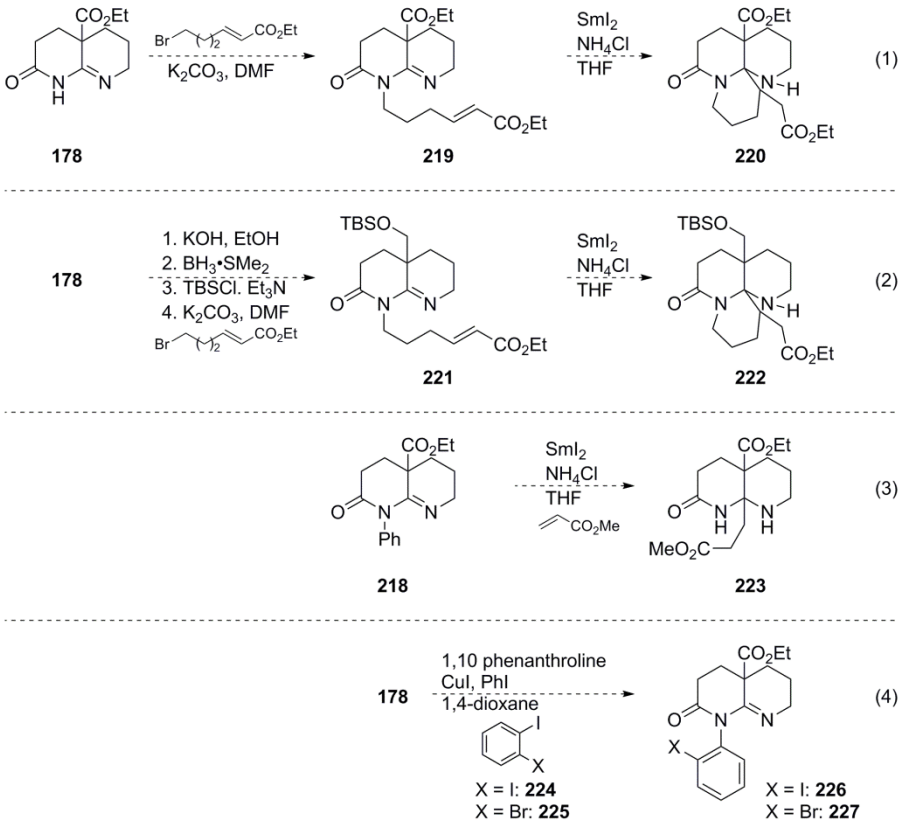
The second strategy disconnected the desired bicyclic *N*-acyl amidine through an intramolecular *N*-acylation reaction of an *N*-aryl amidine. It was envisioned that the amidine could be prepared from a bimolecular condensation reaction of an aniline and a lactam derivative. All attempts to form the desired amidine functionality were unsuccessful. It was again concluded that the poor nucleophilicity of the electron-poor aryl nucleophile coupled with the sterically congested nature of the desired site of attack were to blame for the lack of desired reactivity.

The third strategy depended upon an *N*-arylation reaction for the conversion of the bicyclic *N*-acyl amidine reported by Wamhoff into the desired substrate for the synthesis of leuconoxine (**1**). While the key intermediate for the synthesis of leuconoxine (**1**) utilizing an aminal radical disconnection has remained elusive, a model system of the key *N*-arylation reaction has successfully produced an *N*-aryl-*N*-acyl bicyclic amidine product. The investigation of this synthetic route is still underway.

5.2 Future Directions

The immediate goals for the future of this project are related to the total synthesis of leuconoxine (**1**). In order to determine if the key aminal radical cyclization reaction is likely to be successful, it would be instructive to perform a few model reactions (Scheme 5.1). The amidine reported by Wamhoff (**178**) has not successfully participated in an aminal radical reaction (see chapter 4). However, the reactions investigated do not closely resemble the key aminal radical cyclization reaction

proposed for the synthesis of **1**. The preparation of the alkylated amidine **219** and the investigation of its reactivity under the SmI_2 reaction conditions will be performed (eq. 1). If **220** is not obtained from this reaction, then the reaction of analogous TBS-protected alcohol **221** to give the product **222** will be investigated to determine if the electron-withdrawing nature of the ester functional group is the cause of the problematic reactivity (eq. 2). Similarly, the bimolecular aminal radical reactions of **218** to give **223** will be examined (eq. 3). Additionally, the reactions **178** with the 1,2-dihalogenated arenes (**224** and **225**) will be investigated in order to prepare the substrates **226** and **227** for further study (eq. 4).

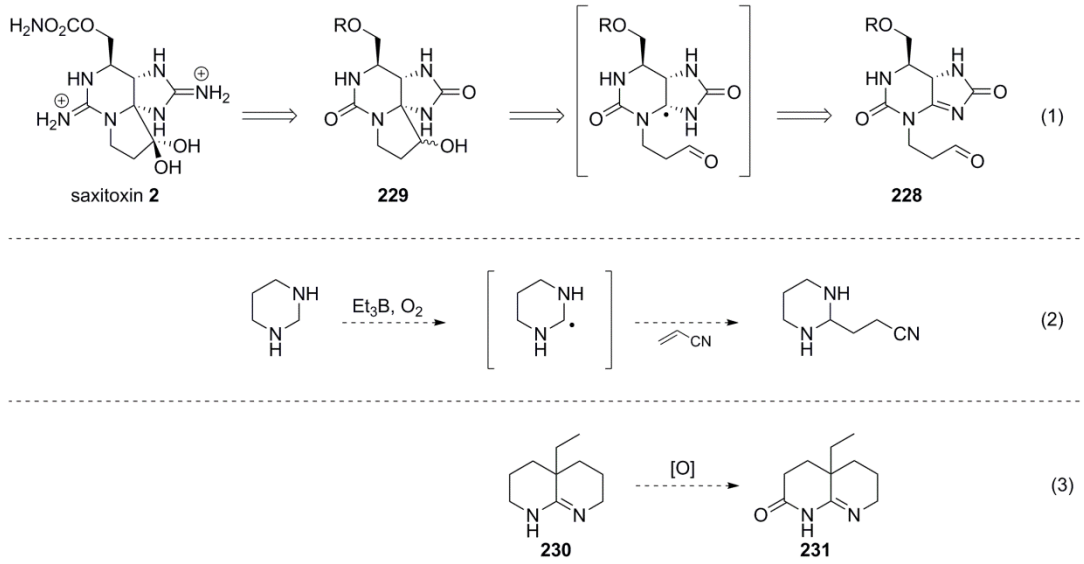


Scheme 5.1. Future work on the synthesis of **1**

The long-term goals of the project include the development of new modes of reactivity and their application in total synthesis (Scheme 5.2). The development of the reaction between aminal radicals and a C-1 radical acceptor, such as the aldehyde

228, to give the alcoholic product **229** is currently being investigated by Mr. Yi Lu (eq. 1). Once successfully developed, this reactivity will be applied in the total synthesis of saxitoxin (**2**).

The reactions of aminal radicals described in this dissertation both require pre-functionalization of the reaction substrate. It would be advantageous to develop a means to access aminal radicals directly from unsubstituted aminal substrates. For example, the extension of the method developed by Tanaka using triethylborane and molecular oxygen for the formation of α-amino radicals to the generaton of aminal radicals (eq 2) would be particularly useful.



Scheme 5.2. Additional reactions to be developed

The main limitation of the amidine reduction method we have developed is the lack of general and robust methods for the synthesis of *N*-acyl amidines. We envision the development of an oxidation reaction wherein an amidine (**230**) is oxidized to give an *N*-acyl amidine (**231**). Reactions of this type have been reported, but have not been investigated systematically.[131] If fully realized, this reactivity could greatly increase

the utility of the amidine reduction chemistry described in chapter 3 of this dissertation.

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