AN ABSTRACT OF THE DISSERTATION OF

Nathan D. Collett for the degree of Doctor of Philosophy in Chemistry presented on September 26, 2013.
Title: Himeradine A: Synthetic Efforts Towards Himeradine A and Related Natural Products, a Michael Reaction Focused Approach.

Abstract approved:

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Rich G. Carter

Lycopodium alkaloids have generated enormous amounts of interest from the scientific community, both as synthetic targets and for their medicinal properties. Herein is described work towards a unifying approach to large segments of the *Lycopodium* family.

An organocatalyzed intramolecular heteroatom Michael reaction method, for the construction of piperidine and piperizine rings has been developed. The method, described herein, has been utilized in the construction of pelletierine and homopipecolic acid.

An initial route to the $C_{1'}$-$C_{11'}$ quinolizidine fragment of himeradine A utilized a scope expanded version of our heteroatom Michael method to construct the $C_{10'}$-$N_{1'}$ ring. The $C_{1'}$-$C_{10'}$ quinolizidine portion was synthesized by intramolecular amide alkylation. Numerous routes were explored for the formation of the $C_{10'}$-$C_{11'}$ bond.

A second generation route to the $C_{1'}$-$C_{11'}$ quinolizidine fragment of himeradine A was developed. The $C_{10'}$-$N_{1'}$ ring was formed by Lewis acid-catalyzed diastereocontrolled intramolecular Michael reaction. The

$C_{6'}$-$C_{2'}$ ring was formed by Wittig reaction and subsequent lactam bond formation. A model system for the installation of the C_{17}-C_{15} portion of himeradine A containing the stereodefined N_{18} was demonstrated.

With a viable synthesis of $C_{1'}$-$C_{11'}$ quinolizidine fragment, the C_1-C_{17} fragment was developed. Several routes were explored for the functionalization of the C_1-C_{14} fragment, a Mander's reagent strategy successfully installed C_{15}.

A modified approach to the $C_{1'}$-$C_{11'}$ quinolizidine was explored. The C_{17}-C_{16} portion was installed using a Wittig reaction. Potential coupling strategies with the C_1-C_{15} fragment were developed.

Himeradine A: Synthetic Efforts Towards Himeradine A and Related Natural Products, a Michael Reaction Focused Approach

By
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APPROVED:

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Major Professor, representing Chemistry

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Chair of the Department of Chemistry

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Dean of the Graduate School

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

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Nathan D. Collett, Author

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Chapter 1 Introduction

1.1: *Lycopodium* Alkaloids and Their Uses.

The *lycopodium* alkaloids are a large and diverse family isolated from the club mosses of North and South America, Eurasia and Africa (Figure 1.1).[1] Many club mosses and their extracts have been used in the traditional medicines of countless cultures of the world to treat various ailments, from headaches to nausea, dementia, and in the treatment of skin conditions.[2] In modern times, the powder of *lycopodium* spores has been used to coat pills, as a lubricant, and to create pyrotechnic flashes for photography. The ignition of *lycopodium* powder is a common demonstration in general chemistry classes. Use in traditional medicine has led to intensive investigation of the medicinal properties of the various natural products produced by the many species of *lycopodium*.[3] This potential use in modern medicine, as well as highly novel and interesting structures has led to the interest of our group and many others in the *lycopodium* alkaloid family as targets of total synthesis.[4]

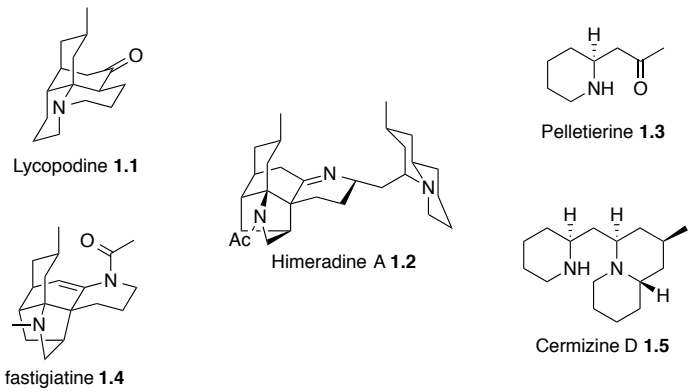
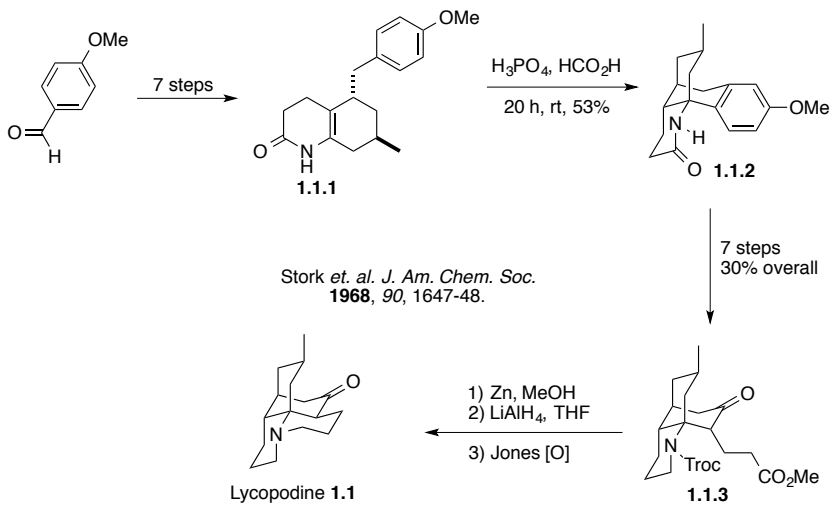


Figure 1.1: Various Representative *Lycopodium* Alkaloids.

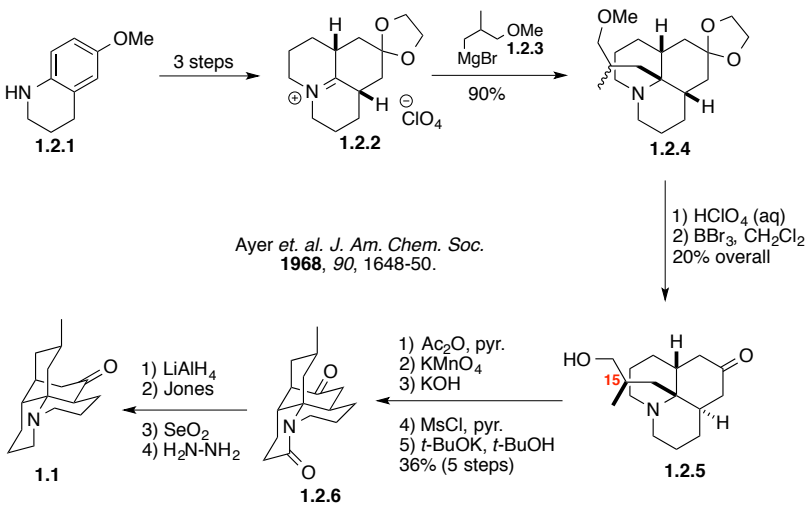
1.2: Prior Work on Lycopodine **1.1**.

The first total syntheses of lycopodine **1.1**, the parent member of the family were achieved concurrently by Stork and co-workers and Ayer and co-workers in 1968 (Scheme 1.1).[5] Stork's synthesis began with the elaboration of anisaldehyde to bicyclic amide **1.1.1**. Bicyclic amide **1.1.1** was treated with strong acid to first cause tautomerization of the enamine to the acyl iminium and subsequent intramolecular electrophilic aromatic substitution to form the tricyclic lycopodine skeleton **1.1.2**. Amide **1.1.2** was elaborated to keto ester **1.1.3** in seven steps. The remaining ring of lycopodine **1.1** was formed by the cleavage of the Troc group of keto ester **1.1.3** to allow for intramolecular amide formation; subsequent reduction and oxidation yielded lycopodine in racemic form.



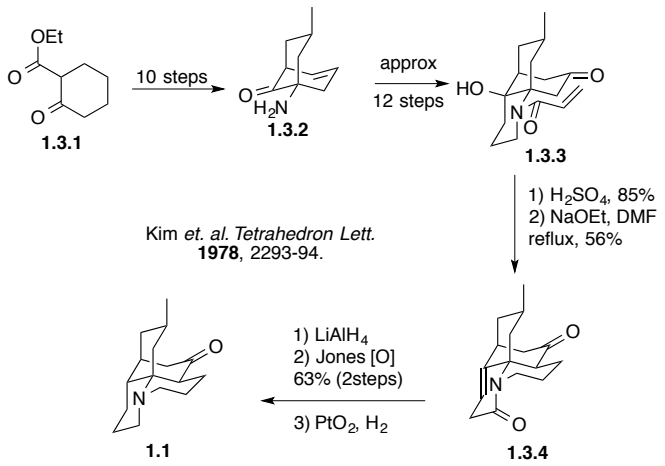
Scheme 1.1: Stork's Synthesis of Lycopodine **1.1**.

The Ayer group reported their concurrent synthesis of lycopodine **1.1** from thalline derivative **1.2.1** (Scheme 1.2).[6] Iminium **1.2.2** was reacted with Grignard reagent **1.2.3** to form the tricyclic skeleton **1.2.4**. The tricyclic compound **1.2.4** was deprotected in a two-step sequence, after which the two epimers were separated to give keto alcohol **1.2.5**. The formation of the final ring of the natural product was achieved by alcohol protection, followed by $KMnO_4$ oxidation to the amide, alcohol deprotection and activation, to form the final ring via intramolecular alkylation (**1.2.6**). The endgame of the synthesis necessitated the migration of the ketone and the reduction amide to form lycopodine **1.1**.



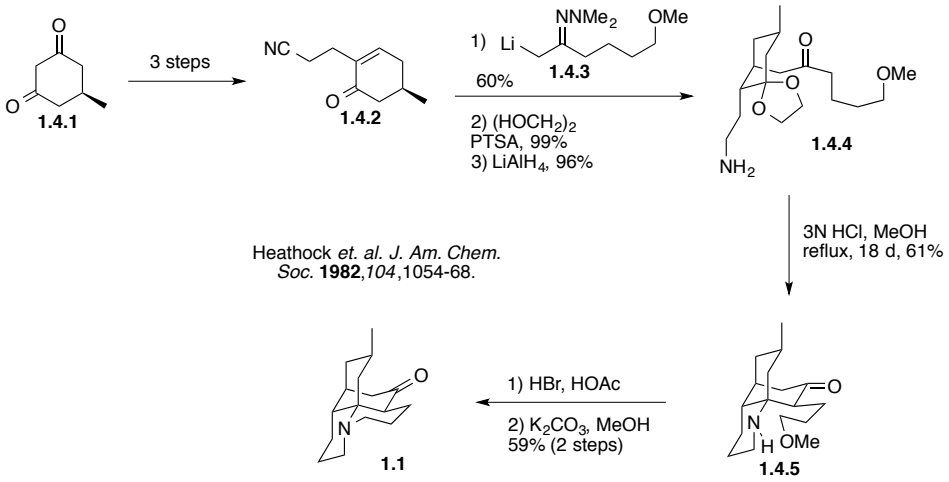
Scheme 1.2: Ayer's Synthesis of Lycopodine **1.1**.

Kim's group was the next to accomplish the total synthesis of lycopodine **1.1** (Scheme 1.3).[7] Beginning from readily available keto ester **1.3.1**, primary amine **1.3.2** was synthesized in 10 steps. Amino ketone **1.3.2** was elaborated in 12 steps to tricycle **1.3.3**. Alcohol **1.3.3** was eliminated to the alkene and subsequent intramolecular Michael reaction was achieved by treatment with NaOEt. With the carbon skeleton of lycopodine in hand (**1.3.4**), Kim's group completed the total synthesis of lycopodine **1.1** by a reduction / oxidation / reduction sequence.



Scheme 1.3: Kim's Synthesis of Lycopodine **1.1**.

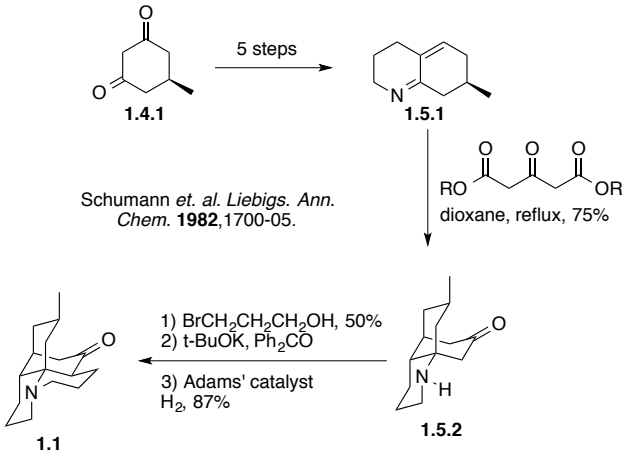
The next completed total synthesis of lycopodine **1.1** was the Heathcock group's seminal multi-route effort on the synthesis of various *lycopodium* alkaloids (Scheme 1.4).[8] Heathcock's synthesis was initiated from 5-Me-1,3-cyclohexandione **1.4.1**, which was elaborated to cyano hexanone **1.4.2** in three steps. Cyano hexanone **1.4.2** was then reacted with lithiated hydrazine **1.4.3** to give the 1,4-addition product. The ketone was then protected as the ketal to allow for subsequent reduction by $LiAlH_4$ of the cyanide to form the primary amine **1.4.4**. The key step of Heathcock's synthesis was the acid-catalyzed Mannich reaction deprotection cascade to form the tricyclic core **1.4.5** of lycopodine. The endgame of Heathcock's synthesis necessitated the formation of the final ring via intramolecular alkylation, triggered by HBr / HOAc and subsequent deprotonation of the resulting tertiary amine salt to give lycopodine **1.1**.



Scheme 1.4: Heathcock's Synthesis of Lycopodine **1.1**.

In the same year that Heathcock reported his extensive work on the *lycopodium* alkaloids, Schuman's group reported a total synthesis of lycopodine **1.1** (Scheme 1.5).[9] This approach was similar in broad strokes to Heathcock's approach, even beginning with the same starting material 5-Me-1,3-cyclohexandione **1.4.1**. Schuman elaborated dione **1.4.1** to bicyclic imine **1.5.1** in five steps. The tricyclic skeleton **1.5.2** of lycopodine was formed by reacting imine **1.5.1** with ambident nucleophile acetonedicarboxylate, to give the double addition product. Schuman's endgame for the synthesis of lycopodine **1.1** was similar to Heathcock's approach (though it was not in the shortest route summarized prior). The tricylic skeleton **1.4.5** was alkylated with 3-bromo-1-propanol, subjected to Oppenauer oxidation, wherein concontaminent aldol

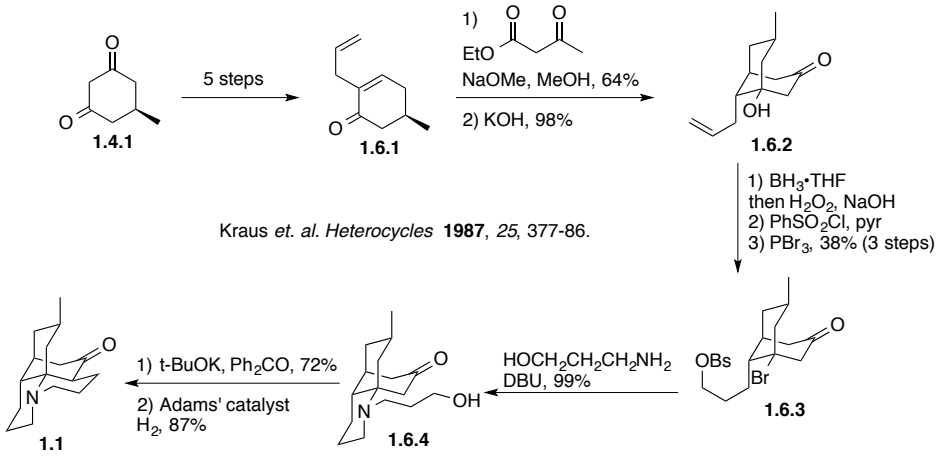
condensation/cylcization occurred to give a hexenone intermediate that could be reduced to lycopodine **1.1** by treatment with PtO_2 / H_2.



Scheme 1.5: Schuman's Total Synthesis of Lycopodine **1.1**.

In 1987, the Kraus group reported their synthesis of lycopodine **1.1**, again utilizing 5-Me-1,3-cyclohexandione **1.4.1** as the starting material (Scheme 1.6).[10] 5-Me-1,3-cyclohexandione **1.4.1** was elaborated in five steps to cyclohexenone **1.6.1**. An ambident nucleophile strategy, similar to that employed by Schuman and co-workers, was used on cyclohexenone **1.6.1** to form the first two rings of the lycopodine skeleton, **1.6.2**. Alcohol **1.6.2** was converted in a three-step sequence to bis-electrophile **1.6.3**. The third ring of the lycopodine skeleton was formed by an impressive bis-nitrogen alkylation strategy to converge on Heathcock / Schuman's

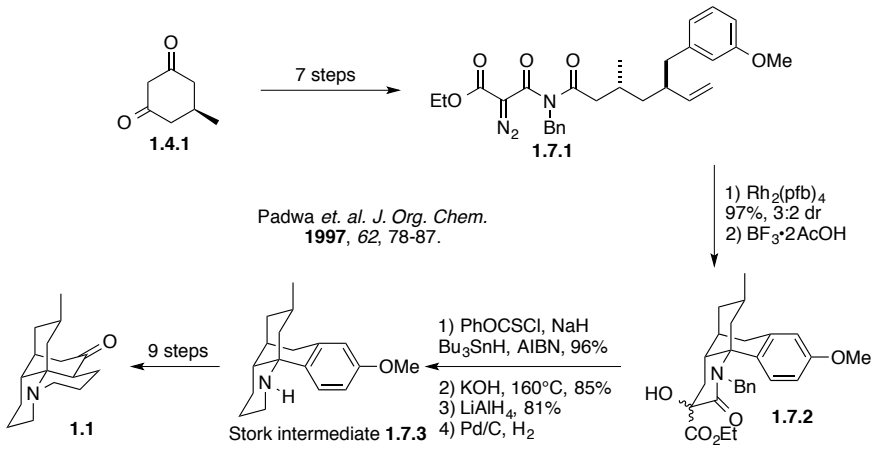
advanced primary alcohol intermediate **1.6.4**. Heathcock's endgame was utilized to achieve total synthesis of lycopodine **1.1**.



Scheme 1.6: Kraus Group's Synthesis of Lycopodine **1.1**.

In the mid nineties, Padwa used the total synthesis of lycopodine **1.1**, as a proving ground for his group's rhodium ylide chemistry, (Scheme 1.7).[11] Padwa's group again utilized 5-Me-1, 3-cyclohexandione **1.4.1** as starting material and converted it to diazo compound **1.7.1** in seven steps. Diazo compound **1.7.1** was treated with rhodium to from an ylide intermediate, which underwent a dipolar cycloaddition. The mixture of products was treated with $BF_3 \cdot 2AcOH$ to form the fourth ring via intramolecular nucleophilic aromatic substitution, providing tetracyclic intermediate **1.7.2**. The tetracyclic intermediate **1.7.2** could be converted

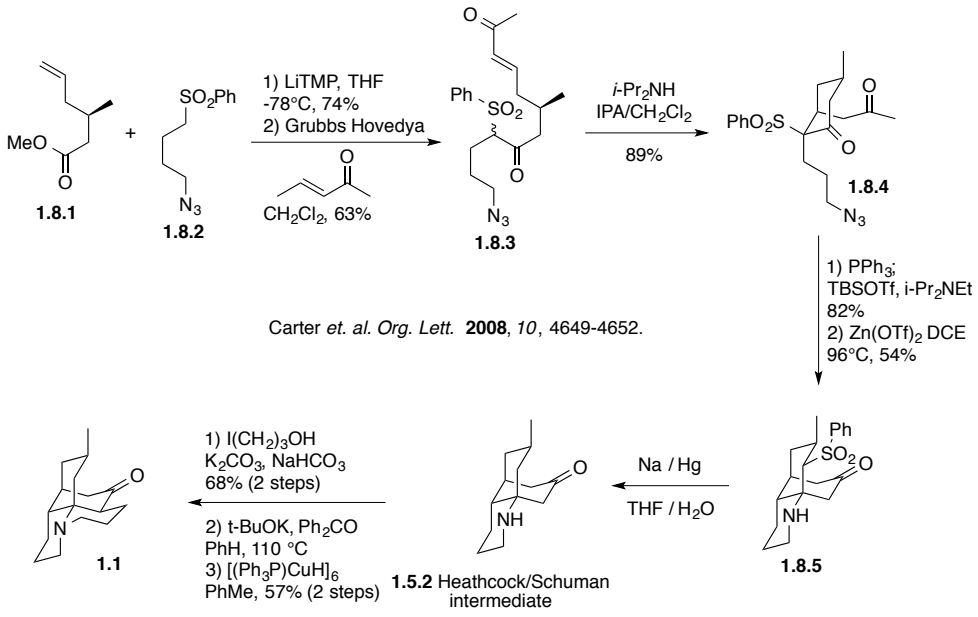
to Stork's advanced intermediate **1.7.3** via a four-step sequence of functional group interconversions.



Scheme 1.7: Padwa's Synthesis of Lycopodine **1.1**.

In 2008, our own group reported the first enantioselective synthesis of lycopodine **1.1** (Scheme 1.8).[12] This approach is the basis of our strategy for the synthesis of the western fragment of himeradine. Our group's synthesis began with coupling of ester **1.8.1** and sulfone **1.8.2**, followed by Grubbs cross metathesis with pentenone to yield keto sulfone **1.8.3**. Treatment of keto sulfone **1.8.3** with *i*-Pr_2NH triggered an intramolecular enamine Michael reaction to form cyclohexanone **1.8.4**. Cyclohexanone **1.8.4** was subjected to Staudinger reduction / TBS enol ether formation / $Zn(OTf)_2$ promoted Mannich reaction to form sulfone rearranged tricycle **1.8.5**. A four-step sequence similar to Heathcock's

endgame was used to complete our group's synthesis of lycopodine **1.1**. In addition to our own work on lycopodine **1.1** several other groups have published syntheses of lycopodine **1.1** and work towards its synthesis that is not covered in this summary.[13,14]

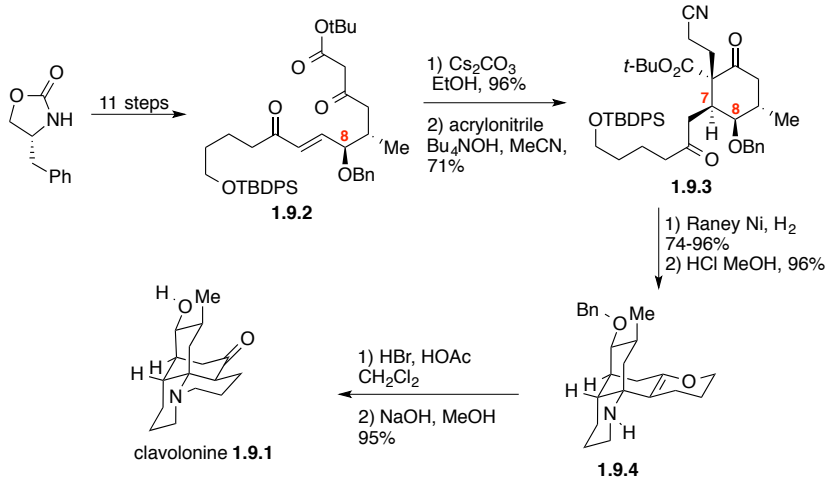


Scheme 1.8: Carter Group Synthesis of Lycopodine **1.1**.

1.3: Other Lycopodine-Related Natural Products.

In 2005, Evans and co-workers disclosed the synthesis of clavolonine **1.9.1**, a hydroxylated *lycopodium* alkaloid (Scheme 1.9).[15] Evans synthesized advanced di-ketone intermediate **1.9.2** utilizing his own chiral oxazolidinone chemistry in 11 steps. The di-ketone intermediate

1.9.2 was cyclized to give the first ring of the natural product, followed by an intermolecular Michael reaction with acroylnitrile to give highly functionalized cyano ketone **1.9.3**. Cyano ketone **1.9.3** could be converted to the cyclic imine by reduction with Raney nickel. Subsequent treatment of the imine with HCl triggered a decarboxylative Mannich cascade with concontaminant cyclic enol ether formation to give tetracycle **1.9.4**. Enol ether **1.9.4** could then be treated with HBr to liberate the ketone and form the bromide which promptly alkylativley cyclized onto the nitrogen. The resulting HBr salt was deprotonated with NaOH to give clavolonine **1.9.1**.

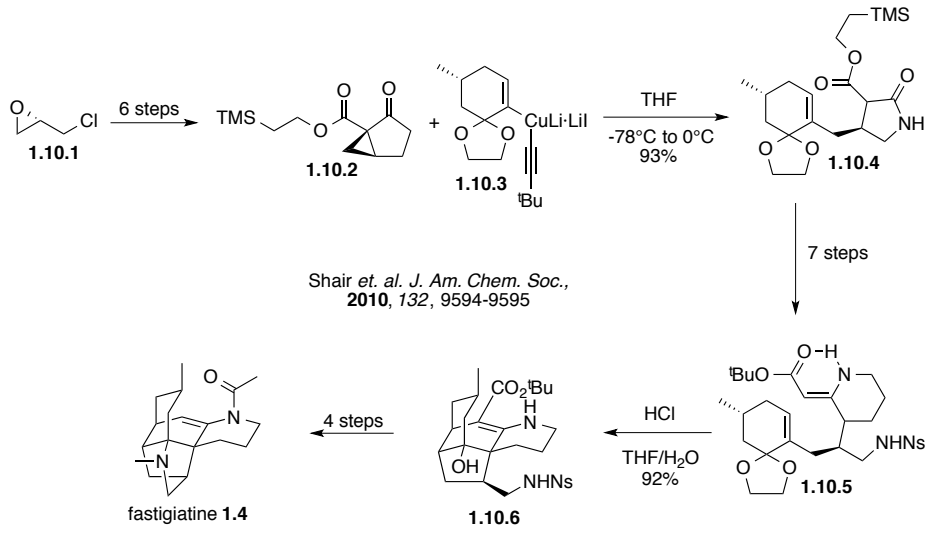


Evans, D. A. *et. al. Angew. Chem. Int. Ed.* **2005**, *44*, 6038-42.

Scheme 1.9: Evans' Synthesis of Clavolonine **1.9.1**.

In 2010, Shair and coworkers accomplished the total synthesis of fastigiatine **1.4**, a natural product with high structural similarity to the

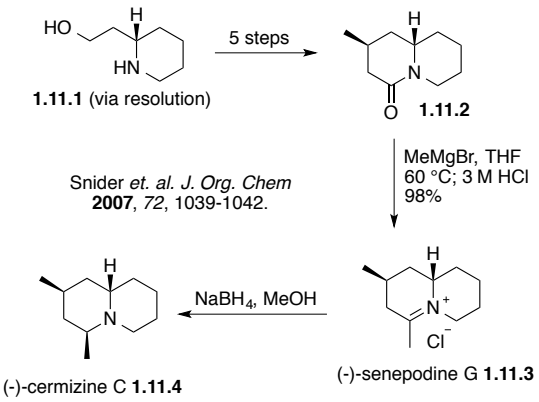
western portion of himeradine A **1.2** (Scheme 1.10).[16] Shair's synthesis was initiated by the coupling of two modestly complex fragments by the addition of cuprate **1.10.3** into cyclopropane **1.10.2** (synthesized from (S)-epichlorohydrin **1.10.1**) to give keto ester **1.10.4**. Keto ester **1.10.4** was elaborated in 7 steps to vinylogous urethane **1.10.5**. A di-enamine addition cascade was initiated by treating vinylogous urethane **1.10.5** with HCl producing tertiary alcohol **1.10.6**, which contains the carbon skeleton of fastigiatine **1.4**. The endgame of Shair's synthesis hinged on mono-methylation of the terminal amine and subsequent functional group interconversion to provide the natural product **1.4** in four-steps.



Scheme 1.10: Shair's Total Synthesis of Fastigiatine **1.4**.

1.4: Quinolizidine Containing *Lycopodium* Alkaloids.

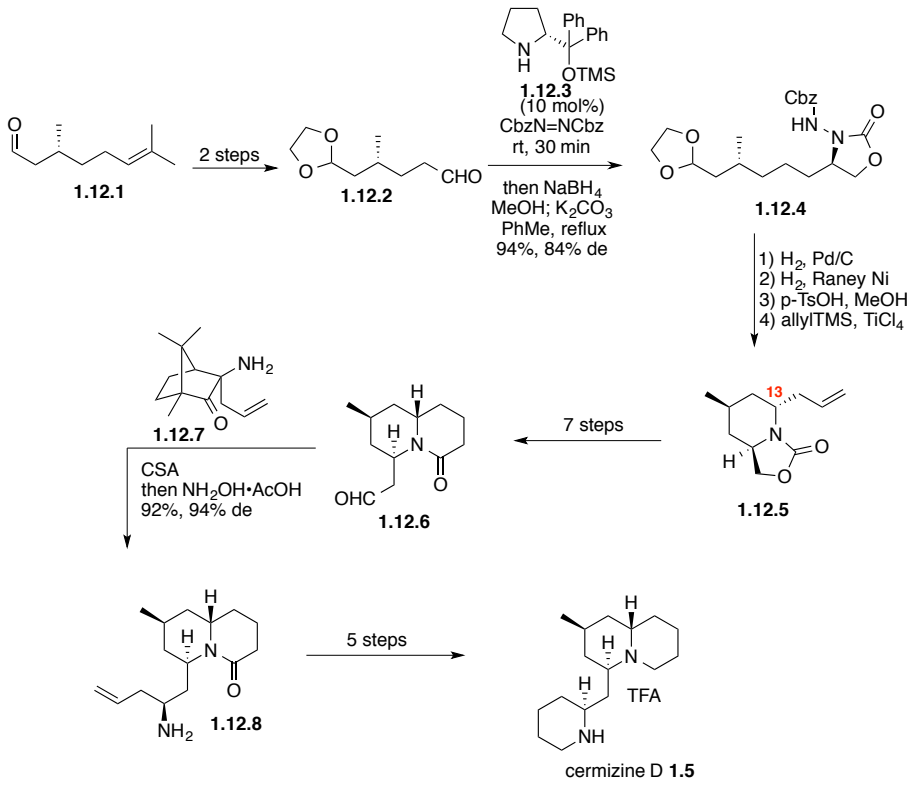
In 2007, Snider and co-workers published a synthesis of several quinolizidine containing *lycopodium* alkaloids (Scheme 1.11).[17] Snider utilized 2-piperidineethanol **1.11.1** as starting material (after classical resolution), elaborating it to quinolizidine amide **1.11.2** in 5 steps. The quinolizidine amide could be converted to (-)-senepodine G **1.11.3** by treatment with MeMgBr followed by HCl. Reduction of (-)-senepodine G **1.11.3** with $NaBH_4$ provided (-)-cermizine C **1.11.4**.



Scheme 1.11: Snider's Syntheses of (-)-senepodine G **1.11.3** and (-)-cermizine C **1.11.4**.

Takayama and coworkers published the synthesis of the lycopodium alkaloid cermizine D **1.5** in 2008; it bears significant structural similarities to the eastern portion of himeradine A **1.2** (Scheme 1.12).[18]

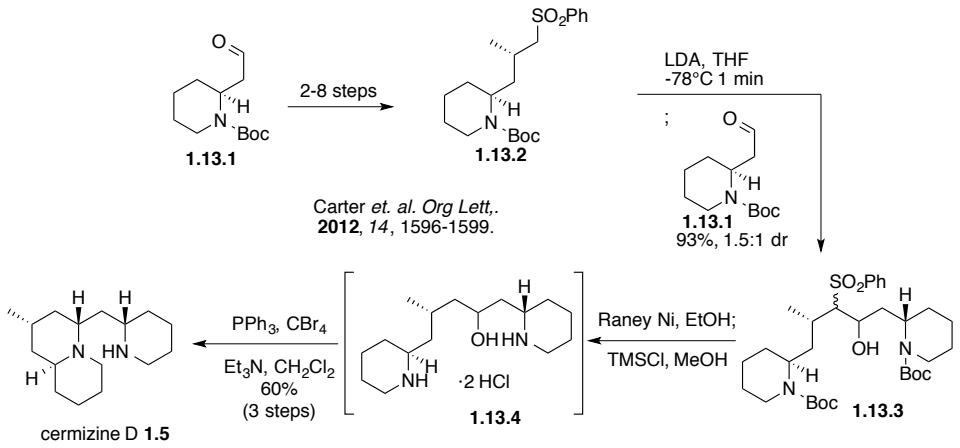
Takayama's key step utilized citronellal **1.12.1** derivative **1.12.2**, subjecting the aldehyde to organocatalyzed reductive Mannich cascade to form hydrazine oxazolidinone **1.12.4**. The first ring of the quinolizidine portion of the natural product was formed by a reduction / reduction / iminium formation / Sakurai reaction sequence to give bicyclic oxazolidinone **1.12.5**. The second ring of the quinolizidine was formed by ring closing metathesis as part of a seven-step sequence to provide lactam aldehyde **1.12.6**. Aldehyde **1.12.6** was transfer amino allylated with reagent **1.12.7** to give primary amine **1.12.8**. The endgame of the synthesis utilized another ring closing metathesis reaction form the remaining ring and a global reduction to yield cermizine D **1.5**.



Scheme 1.12: Takayama's Approach to Cermizine D **1.5**.

In 2012, our group disclosed our own approach to the synthesis of cermizine D **1.5** (Scheme 1.13).[19] Piperadine aldehyde **1.13.1** was utilized as the starting material, serving as the source of two of the three ring of cermizine D **1.5** (the development of our groups methodology for contrasting such rings is disclosed in this thesis, as this author was one of the contributing researchers)[20]. Several routes were developed for the conversion of aldehyde **1.13.1** to sulfone **1.13.2**, the shortest being two steps the longest eight steps. Sulfone **1.13.2** was Julia coupled with

another unit of aldehyde **1.13.1** to provide sulfone alcohol **1.13.3**. Treatment of sulfone **1.13.3** with Raney Ni, followed by treatment with HCl formed amino alcohol **1.13.4**. Cermizine D **1.5** was formed by Appel reaction of amino alcohol **1.13.4**.



Scheme 1.13: Carter Group Synthesis of Cermizine D **1.5**.

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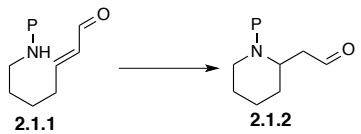
Chapter 2 Development of Intramolecular Heteroatom Michael Reaction

2.1. Overview of Methodological Strategy.

The initial goal of this project was to develop a method for the construction of enantioenriched piperidine and piperizine rings via an organocatalyzed intramolecular heteroatom Michael reaction (Scheme 2.1). We hoped to use such compounds as building blocks in the synthesis of several lycopodine natural products, specifically the quinolizidine-containing members of the family. There are several challenges with such a methodology. First, the nucleophilicty of the nitrogen must be moderated to prevent spontaneous cyclization.[1] Second, a suitable chiral secondary amine catalyst must be found to impart enantioselectivity in the cyclization via the formation of a chiral iminium ion, which will both increase the electrophilicity of the enal and control the stereochemical outcome. Lastly, the requisite cyclization precursors must be synthesized. It should be noted that Lauren Rathbone and Eric Carlson were the lead researchers on this project with this author working in support

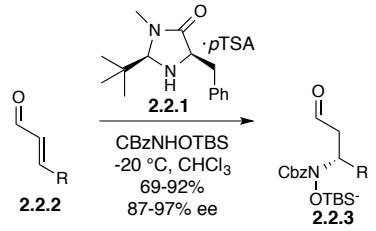


2.1.1 2.1.2

Scheme 2.1: Overall Reaction Manifold Goal.

2.2. Background on Organocatalyzed Heteroatom Michael Reactions.

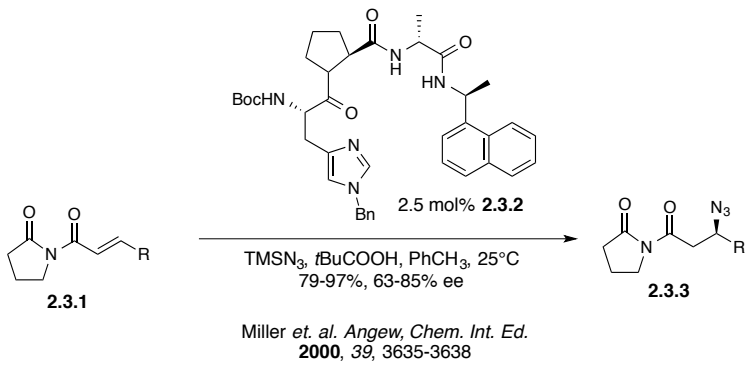
Prior to our work on the development of our intramolecular organocatalyzed heteroatom Michael methodology, related work had been done by several groups but only in the intermolecular sense (Scheme 2.2). The MacMillan group had developed an intermolecular organocatalyzed heteroatom Michael methodology based on their imidazolidinone catalyst **2.2.1**[2,3] In the MacMillan methodology, CbzNHOTBS was used as the nitrogen nucleophile. This choice is interesting because typically a hydroxylamine is more nucleophilic than its corresponding amine, whereas a Cbz amine is less nucleophilic. The interplay of these two things presumably modulates the nucleophilicity of CbzNHOTBS, which is key for this type of reaction manifold. Too strong a nucleophile would allow the background reaction of the nucleophile with the enal to dominate, too weak a nucleophile would obviously not allow the reaction to occur at all.



MacMillan *et. al. J. Am. Chem. Soc* **2006**, *128* , 9328

Scheme 2.2: MacMillan Organocatalyzed Intramolecular Heteroatom Michael Methodology.

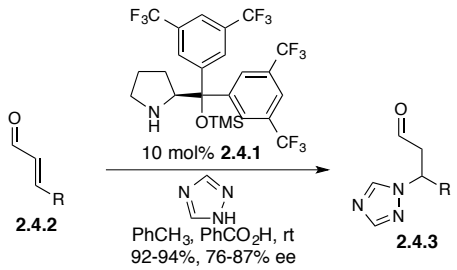
In 2000, Scott Miller's group disclosed a methodology for the enantioselective Michael addition of azide to acrylamides (Scheme 2.3).[4] The Miller group's methodology utilized an artificial peptide[5] scaffold **2.3.2** as its chirality source, and $TMSN_3$ as its nitrogen source. The methodologies enantioselectivity was somewhat variable depending on substrate (63-85% ee). Another limitation of the methodology is the toxicity of $TMSN_3$.[6] Lastly the catalyst loading was impressively low for an organocatalytic process.



Scheme 2.3: Scott Miller's Azide Addition Technique.

Jorgensen's group developed an intermolecular nitrogen nucleophile methodology in 2007 utilizing their own catalyst **2.4.1**[7] (Scheme 2.4).[8] Jorgensen's methodology used triazole as its nitrogen source and is highly efficient, proceeding in high yield and good enantioselectivity. The largest limitation of this methodology is the triazole

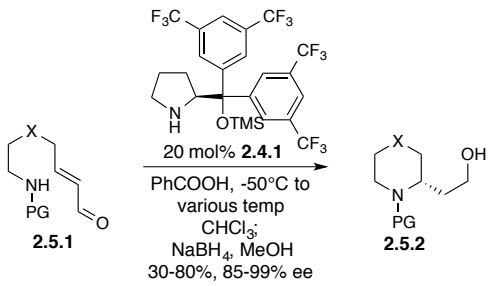
nucleophile; conversion to another functional group is challenging, as triazoles are relatively stable.[9]



Jorgensen *et. al. Angew. Chem. Int. Ed.* **2007**, *46*, 1983-1987.

Scheme 2.4: Jorgensen Triazole Addition Methodology.

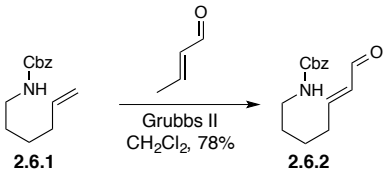
Concurrent to our own reaction methodology development, the Fustero group developed a similar organocatalyzed intramolecular Michael methodology (Scheme 2.5).[10] The Fustero group's methodology utilized Jorgensen catalyst **2.4.1** with Cbz and Boc carbamate enals. The Fustero group's methodology required an acidic additive (PhCOOH), which could potentially be problematic with substrates containing sensitive functional groups; secondly the reaction required warming from -50°C to various temperatures (-30°C to -10°C) over periods that varied by substrate (24-48 h).



Scheme 2.5: Fustero Intramolecular Michael Reaction Manifold.

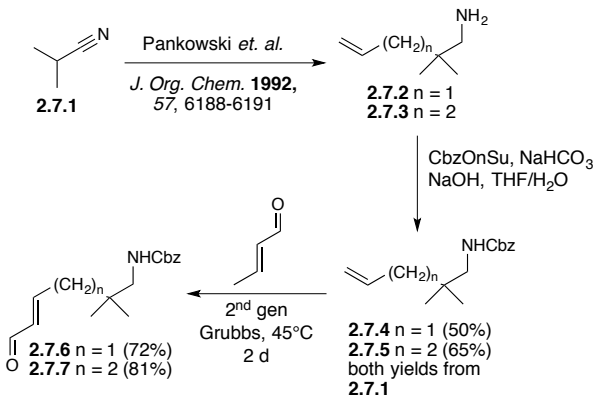
2.3. Synthesis of Carbamate / Enal Starting Materials.

Our general strategy for synthesizing the key cyclization precursors employed a cross metathesis strategy involving a mono substituted alkene and an enal (Scheme 2.6). The simplest example of our substrate synthesis strategy is shown beginning with known Cbz amino alkene **2.6.1**.[11] Our cross metathesis strategy utilized 2nd generation Grubbs catalyst and crotonaldehyde to form carbamate / enal **2.6.2** in 78% yield. We found while optimizing this reaction that crotonaldehyde was consistently more effective at these types of cross metathesis than acrolien. We speculated this higher efficacy was due to the lower propensity of the crotonaldehyde to polymerize or to undergo deleterious side reaction including polymerization.



Scheme 2.6: Synthesis of Carbamate / Enal **2.6.2**.

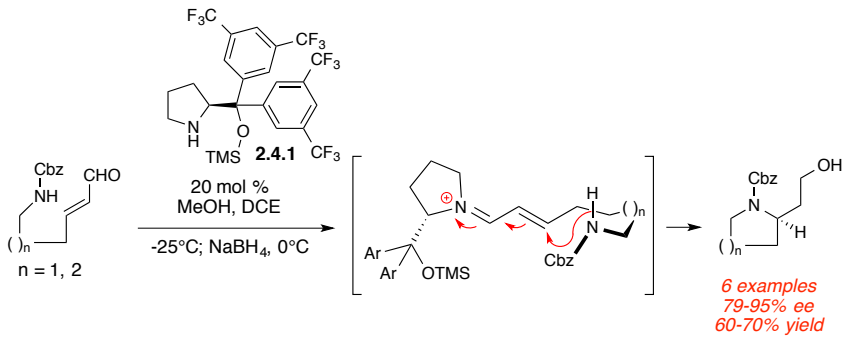
The substrates synthesized by this author are shown in Scheme 2.7. My focus was on the β-di-methyl series (relative to the amine functionality), which were synthesized from known β-di-methyl amines **2.7.2** and **2.7.3**,[12] both available in two steps from isopropylcyanide **2.7.1**. β-Di-methyl amines **2.7.2** and **2.7.3** were protected as the Cbz carbamates by treatment with CbzOnSu.[13] Interestingly, standard CbzCl conditions were entirely ineffective on these substrates. These CbzOnSu reactions proceeded in 50% and 65% yield respectively to form Cbz carbamates **2.7.4** and **2.7.5**. Next, Grubbs cross metathesis reactions of Cbz amines **2.7.4** and **2.7.5** with crotonaldehyde provided enals **2.7.6** and **2.7.7** in 72% and 81% yield respectively.



Scheme 2.7: Synthesis of Carbamate / Enals **2.7.6** and **2.7.7**.

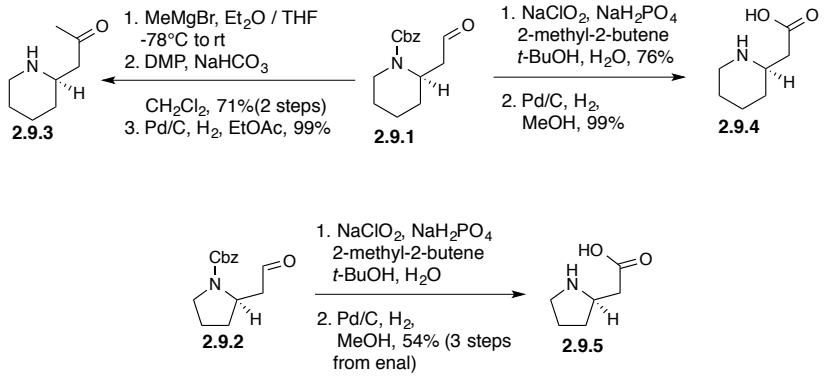
2.4. Intramolecular Heteroatom Michael Reaction and Future Directions in Natural Product Synthesis.

The optimized protocol for our intramolecular heteroatom Michael reaction was arrived at after screening several catalyst and solvent systems (Scheme 2.8).[11] The optimized conditions utilized catalyst **2.4.1**[14] developed by Jorgenson in DCE / MeOH. A possible diastereocontrol model is shown in Scheme 2.8 wherein the chiral iminium ion is blocked form nucleophilic attack from one side by the bulky aryl and OTMS group of the catalyst **2.4.1**. In order to assay the enantioselectivity of the Michael products, we reduced the product aldehydes to the alcohol to minimize the possibility of a retro Michael pathway potentially eroding our enantioselectivity during HPLC analysis.



Scheme 2.8: Heteroatom Michael Reaction Conditions.

With our intramolecular heteroatom Michael reaction developed, we now had access to enantiopure carbamate / aldehyde **2.9.1** and the five membered analog **2.9.2**. These intermediates should be ideal for the synthesis of numerous natural products (Scheme 2.9). In our initial publication on our intramolecular heteroatom Michael reaction, we disclosed the synthesis of two minor natural products, both previously synthesized, homopipecolic acid **2.9.4**, pelletierine **2.9.3** and non-natural amino acid homoproline **2.9.5**. In addition, another member of our group, Mr. Naga Veersamy employed the Boc-protected version of **2.9.1** to synthesize the natural product cermizine D **1.5** which is covered in detail in chapter 1.[15]



Scheme 2.9: Intramolecular Heteroatom Michael Reactions Use in Synthesis.

2.5. Conclusion.

In summary, our group has successfully developed an intramolecular heteroatom Michael reaction for the construction of enantiopure piperidine and piperazine rings. We have successfully leveraged such piperidine rings towards numerous natural products. Future work will focus on the expansion of this intramolecular heteroatom Michael reaction to amide substrates. This reaction manifold would appear to be ideally suited for accessing more complicated lycopodium alkaloids including the quinolizidine portion of himeradine A.

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Chapter 3: Studies Towards the Synthesis of the Eastern Fragment of Himeradine A **1.2**.

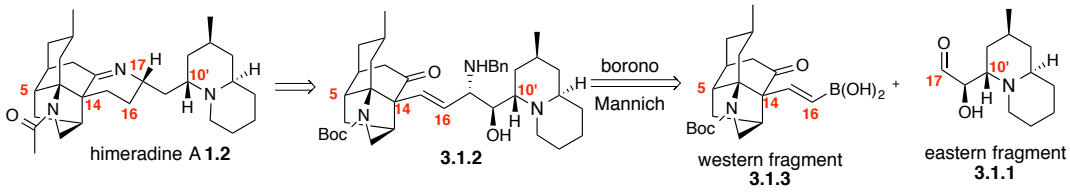
3.1: Himeradine A **1.2** Background and Isolation.

Himeradine A **1.2** is a highly complex member of the lycopodium alkaloid family, isolated in 2003 by Kobayashi and coworkers from *lycopodium chinense*, one of the most common alpine club mosses in China (Scheme 3.1).[2] Himeradine A **1.2** contains a complex heptacyclic structure, possessing three nitrogen atoms, a quaternary center and a fully substituted carbon. The stereochemical relationship between the two domains of himeradine A **1.2**, the western and eastern domains was not unambiguously determined, and appeared to be assigned based on the assumption that the pelletierine units utilized to form the two domains were of the same stereochemical origin. In addition to its complex structure himeradine A **1.2** possess nano-molar cytotoxicity against murine lymphoma L1210 cells (IC_{50}, 10 μg/mL) in vitro. These features combine to make himeradine A **1.2** an attractive candidate for total synthesis. To date no other group has published work towards himeradine A, though Shair's group has published work on a related natural product fastigiatine **1.4**[1] that is structurally similar to the western domain of himeradine A **1.2**. No work

has been done to date towards quinolizidines with the stereochemical arrangement of the western domain.

3.2: General Retrosynthetic Strategy.

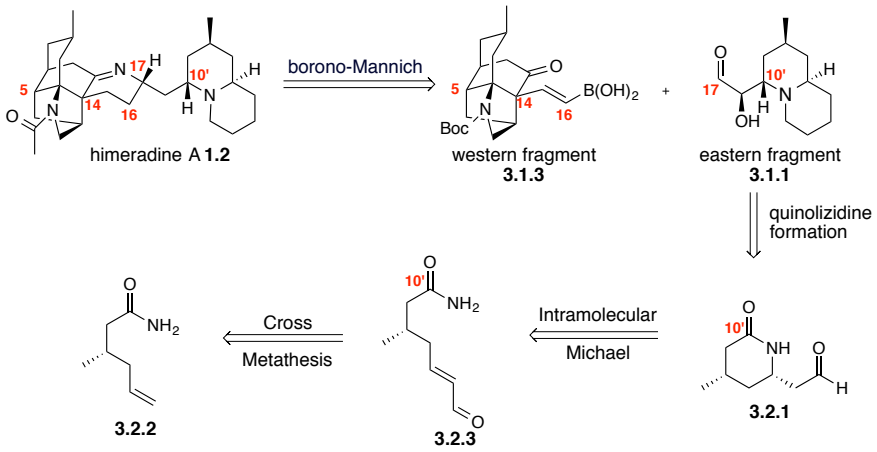
Our strategy for the synthesis of himeradine A **1.2**[2] envisioned dividing the molecule into two major domains, an eastern quinolizidine fragment and a western pentacyclic amino ketone fragment as outlined in Scheme 3.1. Our initial synthetic undertakings focused on synthesizing the α-hydroxyl aldehyde **3.1.1** and its uniquely substituted quinolizidine core (as compared to related quinolizidine containing lycopodium alkaloids, see cermizine D **1.5**), in order to couple the two fragments via a borono Mannich reaction[3,4,5]. The borono Mannich reaction, also called the Petasis-Borono-Mannich reaction was developed by the Petasis group and is the extension of the traditional Mannich reaction to the acceptance of vinyl or aryl boronic acids as the nucleophile. This general strategy of breaking himeradine A into two domains allows for a great deal of programmability in our hypothetical coupling strategies as carbons C_{15}-C_{17} could potentially be delivered as components of the eastern or western fragments. Such flexibility is desirable when the coupling of two large and complex fragments is planned late in the synthesis. Herein, the studies towards the eastern fragment will be discussed.



Scheme 3.1: Borono-Mannich Retrosynthetic Strategy.

3.3: First Generation Retro-Synthesis of Eastern Fragment.

Our first generation approach to the synthesis of α-hydroxyl aldehyde **3.1.1** is outlined in Scheme 3.2. We imagined the α-hydroxyl aldehyde **3.1.1** as potentially resulting from the Sharpless dihydroxylation of a vinyl sulfone, a strategy developed by Evans.[6] The quinolizidine ring of α-hydroxyl aldehyde **3.1.1** would be formed through the elaboration of aldehyde **3.2.1** via a Wittig reaction and a subsequent intramolecular nitrogen alkylation. The first piperidine ring of the quinolizidine might be accessible via an amide nucleophile-expanded version of our organocatalyzed intramolecular heteroatom Michael reaction.[7] Amide **3.2.2** could be constructed from the corresponding known methyl ester.[8]

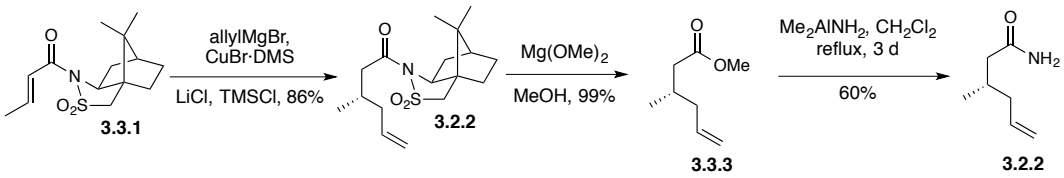


Scheme 3.2: First Generation Retro-synthesis of Eastern Fragment.

3.4: Synthesis of Amide **3.2.2**.

Synthesis of the requisite amide **3.2.2** began with known cuprate addition into Oppolzer's sultam **3.3.1** to yield sulfonamide **3.3.2** (Scheme 3.3).[8] Our group has previously prepared the enantiomer of this compound during our synthesis of lycopodine.[8] Although no precedent exists in the literature for the direct cleavage of the Oppolzer's sultam chiral auxiliary to a primary amide, it was hypothesized that this reaction should be feasible due to the strong thermodynamic driving force of forming a primary amide.[9] While treatment with $NH_4OH_{(aq)}$ / dioxane conditions did produce the desired amide **3.2.2** in modest yield (100 °C, sealed tube, 3 d, 32%), this reaction could not be driven to completion and scaled poorly. Alternate conditions for the formation of amides were screened (methanolic ammonia and $(Me)_2AlNH_2$) and proved ineffective even under forcing

conditions (e.g. reflux for extended periods). Fortunately, a two-step method from known methyl ester **3.3.3**,[8] followed by treatment with $(Me)_2AlNH_2$[10] cleanly produced the amide in 60% yield. The modest yield is likely due to the loss of volatile methyl ester **3.3.3** during the reaction.

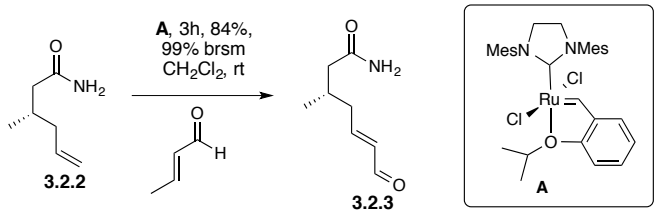


Scheme 3.3: Synthesis of Amide **3.2.2**.

3.5: Synthesis of Enal **3.2.3** and Cyclization Reaction to Form Aldehyde **3.2.1**.

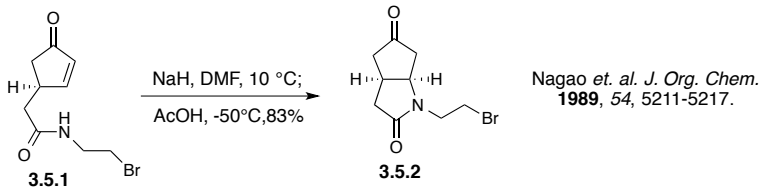
After obtaining amide **3.2.2**, we set out to form enal **3.2.3** via Grubbs cross metathesis (Scheme 3.4). The synthesis of enal **3.2.3** was initially accomplished using 2nd generation Grubbs catalyst, (rt, 18 h, 80%). Upon further optimization, it was discovered that the newly available (at the time) and more active 2nd generation Hovedya-Grubbs catalyst proved more advantageous. While the yield for these new conditions was comparable (84%), the yield based on recovered starting material (BRSM 99%) allowed us to recycle the recovered starting material. As mentioned in chapter 2, our group had previously discovered that use of the β-substituted enals and enones often provides increased

yield in cross metathesis. Enal **3.2.3** proved modestly stable (as long as 2 months at -25°C); however, **3.2.3** was more prone to spontaneous cyclization than the previously synthesized carbamate-protected amines at room temperature.[7]



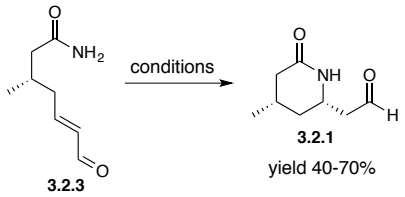
Scheme 3.4: Synthesis of Enal **3.2.3.**

Prior to this work, amides have seen some use as Michael nucleophiles, a typical example by Nagao and co-workers is shown in Scheme 3.5.[11,12] The vast majority of literature precedent in this area is with secondary amides like secondary amide **3.5.1**. Many of the literature examples involve deprotonation of the amide and are typically substrate controlled.



Scheme 3.5: Example of Typical Amide Nucleophile Michael Reaction by Nagao.

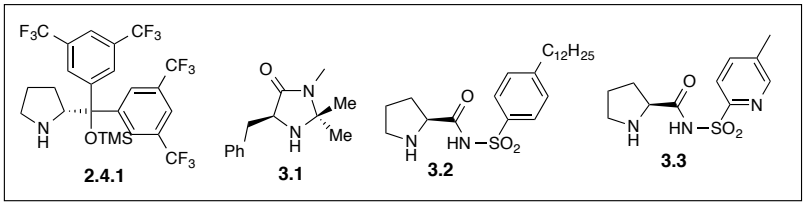
With enal **3.2.3** in hand, we set out to explore the proposed expansion of our organocatalyzed intramolecular heteroatom Michael reaction (scheme 3.6). Several possible challenges exist with the use of an amide as the nucleophile of an intramolecular Michael reaction. Firstly, amides are inherently ambident nucleophiles capable of reacting with both oxygen and nitrogen lone pairs nucleophilicly.[13] Secondly, amides tend to be weak nucleophiles unless deprotonated, a possible incompatibility with organocatalysis.[14] Lastly, we had not yet explored the effect of existing stereochemistry on our intramolecular Michael reactions. The potential for matched / mismatched scenarios clearly existed as well.



Scheme 3.6: Intramolecular Heteroatom Michael Reaction.

The investigation of the intramolecular heteroatom Michael addition is shown in Table 3.1. We initially explored the inherent selectivity of the substrate (sans external chiral catalysis). $BF_3{\cdot}Et_2O$ was specifically selected due to the prior success it achieved in our carbamate heteroatom Michael additions.[7] This Lewis acid produced the desired isomer in modest diastereoselectivity (Entry 1, 1.3:1 d.r. 40%) with no oxygen cyclization products (lactones) observed. Hu and co-workers as well as Eschenmoser and co-workers have observed lactone formation via the oxygen of the amide acting as the nucleophile in related reactions.[15,16] Next, we screened the Jorgenson catalyst **2.4.1** using our established protocol (entry 2), which proved ineffective at the standard -25 °C. Fortunately, at ambient temperature, this transformation proceeded in acceptable yield 50% and stereoselectivity (10:1 dr). The slightly lower yield obtained as compared to the carbamate examples seemed to be

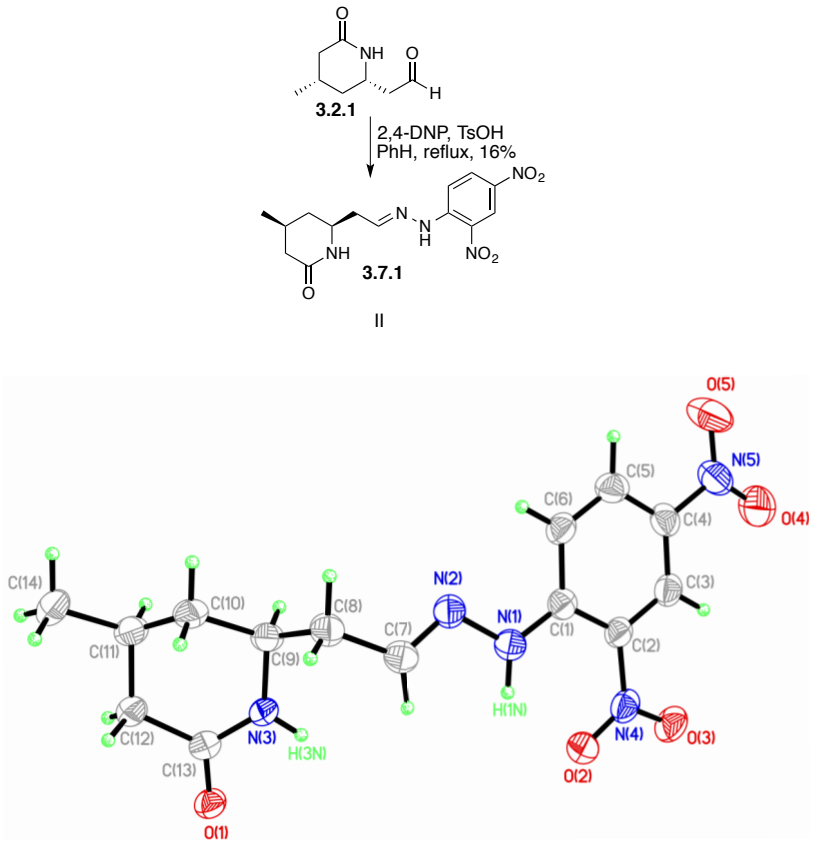
caused by side reactions of the product to form acetals and hemiacetals that were observed by crude NMR; this problem was partially overcome by utilizing a strong acid (HCl) workup to hydrolyze these products to the aldehyde. Interestingly, a pronounced mismatch relationship was observed when the enantiomeric form of catalyst **2.4.1** was screened (entry 3, 1:1 d.r.). The MacMillan catalyst **3.1** was screened as well though it produced essentially no selectivity (entry 4, 1:1 d.r.) Two catalysts developed in our lab were screened Hua Cat **3.2**[17] (entries 5 and 6).[18] One of these conditions (entry 6) produced higher yield in the cyclization, but with significantly lower diastereoselectivity, the sulfonamide catalysts were however somewhat faster. The enantiomers of catalysts **3.1**, **3.2** and **3.3** were not screened.



Entry	Catalyst	Conditions	Time	Yield
1	$BF_3{\cdot}Et_2O$	CH_3CN, rt	1 d	40% (1.3:1)
2	**2.4.1**	DCE/MeOH (1:1), rt	6 d	50% (10:1)
3	*ent*-**2.4.1**	DCE/MeOH (1:1), rt	5 d	n/d (1:1)
4	**3.1**	DCE/MeOH (1:1), rt	4 d	45% (1:1)
5	**3.2**	DCE/MeOH (1:1), rt	3 d	45% (2:1)
6	**3.3**	DCE/MeOH (1:1), rt	14 h	70% (4:1)

Table 3.1: Screening Cyclization of Conditions.

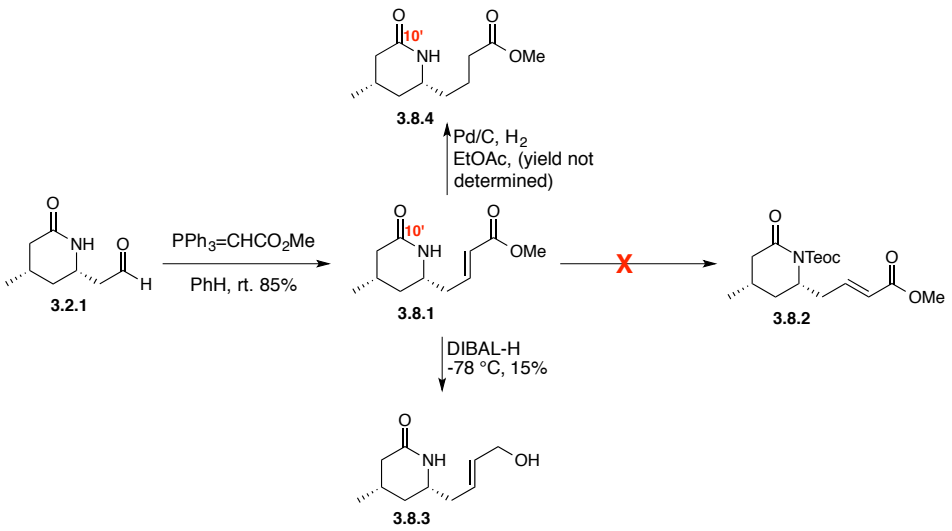
The diastereomeric outcome of the cyclization was ascertained by the conversion of aldehyde **3.2.1** to the 2,4-DNP derivative **3.7.1**, which produced crystalline solid suitable for single crystal x-ray crystallographic analysis (Scheme 3.7). The X-ray data, combined with the known configuration of the methyl group,[8] unambiguously established that the diasteromeric outcome of the cyclization is analogous to the prior carbamate examples.[7]



Scheme 3.7: Synthesis of 2,4-DNP Derivative **3.7.1.**

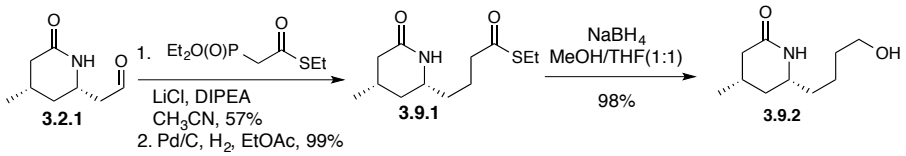
3.6: Wittig Reaction and Attempted Elaboration of Aldehyde **3.2.1**.

With aldehyde **3.2.1** in hand, we shifted focus to the incorporation of the remaining carbons of the quinolizidine ring and the functionalization of the $C_{10'}$ amide carbonyl carbon (scheme 3.8). Aldehyde **3.2.1** was reacted with stabilized Wittig reagent $Ph_3P{=}CHCO_2Me$ to produce unsaturated methyl ester **3.8.1** in good yield (85%). Working based on a protocol developed by Greico,[19] Teoc protection of the amide **3.8.1** was screened to convert of the amide to the imine. Both TeocCl[20] and $PNP(CO_2)$Teoc[21] proved ineffective, with indications that protection on oxygen was occurring as the starting material was consumed but reappeared on aqueous work up. Efforts to reduce the ester sidearm to the primary alcohol proved fruitless, as hydrogenation with Pd/C and H_2 was slow, could not be driven to completion and the starting material was inseparable from the product. Attempted reduction of the ester **3.8.1** with DIBAL-H also proved low yielding (<15%), with both potential reduction routes appeared blocked to us. We suspected that both reductions were problematic due to the presence of the lactam moiety in **3.8.1**.



Scheme 3.8: Wittig Reaction and Attempted Elaboration of Aldehyde **3.2.1**.

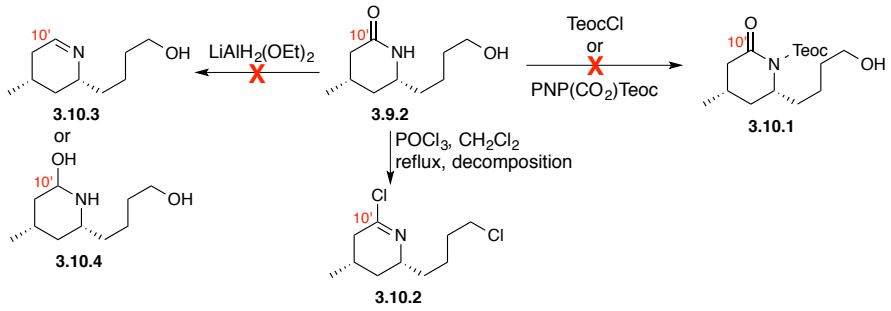
In order to ameliorate our difficulties with the selective reduction in the presence of the lactam, a thioester analog was chosen (Scheme 3.9). The thioester was installed using the Masamune-Roush[22] modification of the HWE reaction.[23] Subsequent hydrogenation of the thioester with Pd/C proceeded smoothly (99% yield) to provide thioester **3.9.1**. The hydrogenation reaction proved far more effective than the analogous methyl ester, possibly due to an advantageous coordination by the sulfur atom of the thioester. With thioester **3.9.1** in hand, reduction to the alcohol **3.9.2** proved facile with $NaBH_4$ (98% yield).



Scheme 2.9: Synthesis of Alcohol **3.9.2**.

Efforts now shifted to the formation of the $C_{10'}$-$C_{11'}$ bond (Scheme 3.10). Teoc protection was again explored in the hopes of using the imine formation technique developed by Greico.[19] Unfortunately, alcohol **3.9.2** was unamenable to Teoc protection using both standard protocols (TeocCl and PNP(CO_2)Teoc). Apparently, O-alkylation of the amide was again occurring, causing us to abandon this strategy. Another approach that was explored was the formation of chloro imine **3.10.1** by reaction with $POCl_3$.[24] The rationale in this approach was to exploit the inherent oxygen reactivity of the substrate to our advantage. Additionally, we had also hoped for the concontaminent conversion of the primary alcohol to the chloride by the reaction with $POCl_3$. Unfortunately, treatment of amide **3.9.2** with $POCl_3$ resulted in only decomposition. Partial reduction either to the imine or the aminal was also explored, both having limited precedent in the literature, though typically on Boc protected amides.[25] Treatment of amide **3.9.2** with a single equivalent of $LiAlH_2(OEt)_2$ (the di-ethoxy version was utilized rather than the tri-ethoxy because our substrate amide / alcohol **3.9.2** contained a primary alcohol that would

react with one of the hydride positions on the aluminum center) led only to complex mixtures of reduction products.[26]

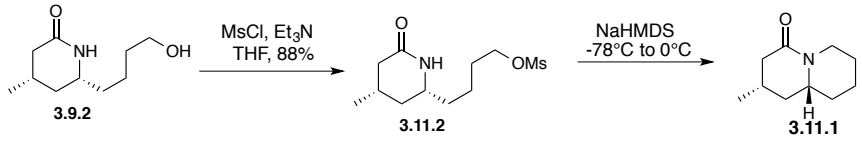


Scheme 3.10: Attempted Functionalization of $C_{10'}$.

3.7: Bicyclic Lactam **3.11.1** Synthesis.

With functionalization of $C_{10'}$ apparently untenable on structures such as secondary amide **3.9.2**, we explored a reordering of the quinolizidine formation and $C_{10'}$ functionalization (Scheme 3.11). Formation of the bicyclic lactam was achieved by mesylation of alcohol **3.9.2** to form primary mesylate **3.11.2**, followed by reaction with NaHMDS to produce bicycle **3.11.1**. We initially converted mesylate **3.11.2** to the corresponding iodide and treated the iodide with NaHMDS, but later found this additional activation to be superfluous. Snider and co-workers have previously reported bicycle **3.11.1** in racemic form and our spectra match nicely with the reported data (this serves as further confirmation of our

stereochemcial configuration).[27] The bicyclic lactam **3.11.1** proved to be highly unstable to purification, congruent with Snider's reported synthesis of **3.11.1**. In fact lactam **3.11.1** decomposes upon being frozen in PhH at -25 C° overnight. We speculate that poor amide resonance must be the origin of this instability though specific mechanism was not able to be ascertained as the decomposition of lactam **3.11.1** appeared to be via some sort of volatilization pathway, as **3.11.1** not only decomposed but the crude mass of the decomposition products was significantly lower. This instability necessitated performing the cyclization reaction immediately prior to utilizing lactam **3.11.1** in any subsequent chemistry. A DIBAL-H reduction and $POCl_3$ activation were both screened on lactam **3.11.1** but neither proved fruitful, likely due to the compounds inherent reactivity. Given the difficulties with the handling of lactam **3.11.1**, this route was abandoned.[28]



Scheme 3.11: Synthesis of lactam **3.11.1**.

3.8: Formal Synthesis of C_5-epi-senepodine G.

As mentioned previously, bicyclic lactam **3.11.1** was synthesized by Snider and co-workers, but only as a racemate during their work on the synthesis of cermizine C **1.11.4** and senepodine G **1.11.3**.[27] Snider's synthesis was from racemic pelletierine and thus could be rendered enantioselective by utilizing enantiopure pelletierine **2.9.3**. Our lactam could be carried on to C_5-*epi*-senepodine G (the ring junction epimer) by treatment with excess MeMgBr and quenching with HCl. While C_5-*epi*-senepodine G is not a natural product as yet discovered, the fact that it bears the quinolizidine stereochemical relationship present in himeradine A **1.2**, implies that Nature at some point likely builds a senepodine-like structure in order to synthesize himeradine A. Most senepodines are speculated to be intermediates in the synthesis of more complicated lycopodium alkaloid natural products.[29]

3.9: Conclusion.

In summary, the successful extension of our group's organocatalyzed heteroatom Michael process to primary amides has been achieved. Unfortunately, our efforts to leverage the lactam aldehyde product **3.2.1** towards himeradine A were stymied by our inability to

functionalize $C_{10'}$. Gratifyingly, conversion of lactam product into the required quinolizidine was accomplished; however, $C_{10'}$ functionalization again proved an insurmountable challenge. Our construction of quinolizidine lactam **3.11.1** represents a formal synthesis of C_5-*epi*-senopodine. Future work on the eastern fragment of himeradine A **1.2** will seek to avoid the pitfalls of this strategy, including functionalization on $C_{10'}$.

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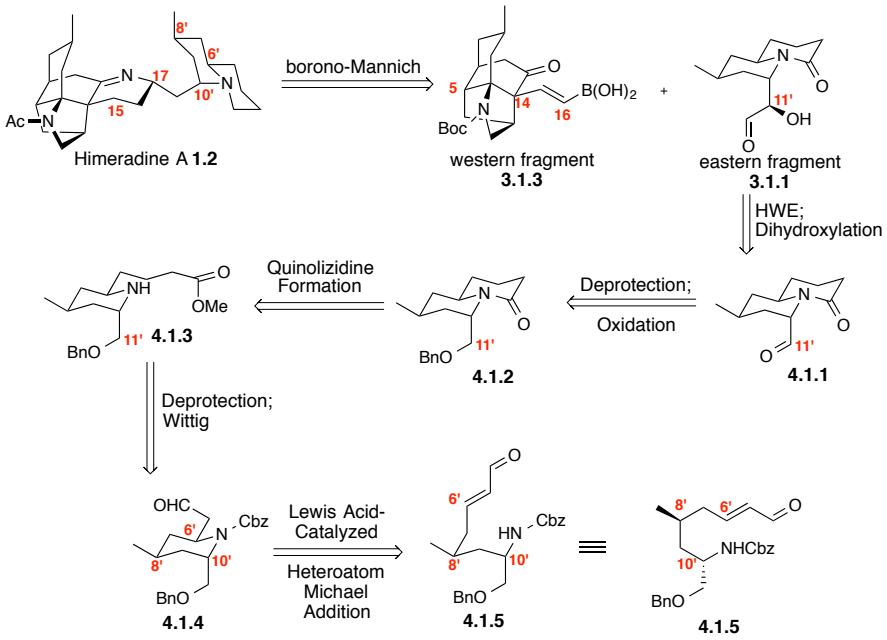
Chapter 4: Second Generation Approach to Eastern Half of Himeradine A **1.2**.

4.1: Second Generation Revised Retrosynthesis.

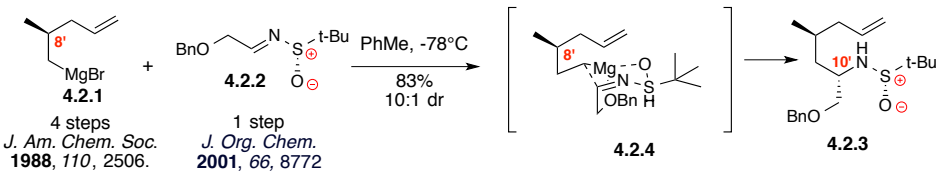
Given the challenges we faced in completing the eastern half of himeradine A **1.2** with our first generation route (e.g. functionalizing $C_{10'}$ and appending the sidearm), our second-generation route sought to overcome these issues (Scheme 4.1). Specifically this route functionalizes the $C_{10'}$ carbon earlier in the synthesis, thereby circumventing our previously encountered challenges. Our retrosynthesis proposed to synthesize α-hydroxyl aldehyde **3.1.1** from lactam aldehyde **4.1.1** via a HWE reaction and subsequent dihydroxylation as in our prior Scheme.[1] Lactam aldehyde **4.1.1** would be synthesized from benzyl ether **4.1.2**. The benzyl ether would be formed from cyclization of the amino ester **4.1.3** which itself would be formed by Wittig reaction of aldehyde **4.1.4**. Aldehyde **4.1.4** would be derived from the substrate-controlled version of our previous intramolecular heteroatom Michael methodology on Cbz amine enal **4.1.5**.[2]



Scheme 4.1: Second Generation Retrosynthesis.

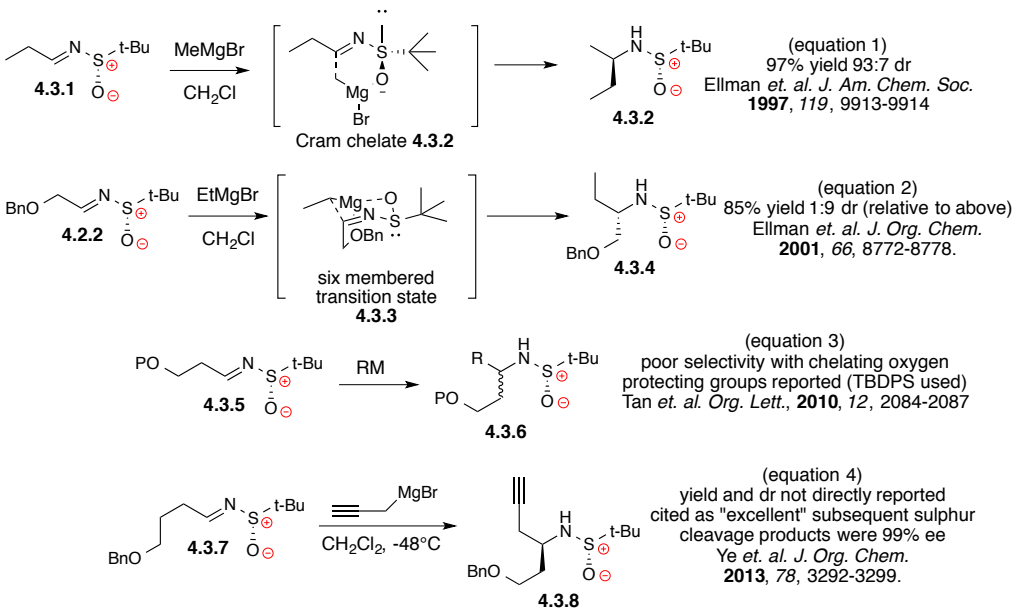
4.2: Synthesis of Cbz Amine Enal **4.1.5**.

Our synthesis of Cbz amine enal **4.1.5** began with known Grignard reagent **4.2.1**[3] and known Ellman sulfinimine **4.2.2**[4] being combined to produce sulfinamide **4.2.3** in a 10:1 diastereomeric ratio and 83% yield (Scheme 4.2). This Ellman sulfinimine addition produces the selectivity shown because of the proposed six-membered transition state **4.2.4**, this is not the typical selectivity for these types of reactions. The stereochemical outcome was confirmed by x-ray crystallography of a later intermediate.



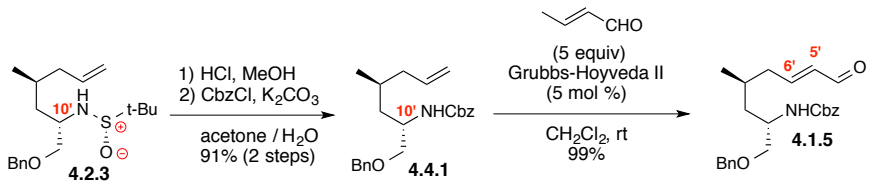
Scheme 4.2: Synthesis of Sulfinamide **4.2.3**.

The stereo control model for this transformation is worthy of further discussion (Scheme 4.3).[5] Equation 1 shows the typical selectivities for these types of sulfinimines not bearing an oxygenated substituent on a simple substrate. Interestingly, as shown previously in Scheme 4.2 the product of additions into sulfinimine **4.2.2** show an inverted stereochemical product (Equation 2). The distance of the oxygen from the imine has pronounced impact on the selectivity. Note that Equation 3 illustrates that when the oxygen is two atoms away the selectivity is poor, though not precisely reported. Interestingly, when the oxygen is three atoms (equation 4) away the selectivity returns to the normal mode as indicated by the eventual sulfur cleavage products being of high yield (99% ee), indicating the cyclic transition state is no longer in play.[4]



Scheme 4.3: Effect of Oxygen Bearing substituents on Ellman Sulfinimine Additions.

Synthesis of our key cyclization substrate is shown in Scheme 4.4. Treatment of sulfinamide **4.2.3** with HCl produced the amine hydrochloride, which was converted directly to the Cbz protected amine **4.4.1** by treatment with CbzCl and K_2CO_3 in acetone / H_2O mixture (91% yield over two steps). Alkene **4.4.1** was then converted to enal **4.1.5** by cross metathesis with crotonaldehyde utilizing second-generation Grubbs-Hoyveda II catalyst. The synthesis of enal **4.1.5** again benefited from our group's observation that β-methyl substituted unsaturated carbonyls provide improved outcomes for these types of cross metathesis.[2, 6]

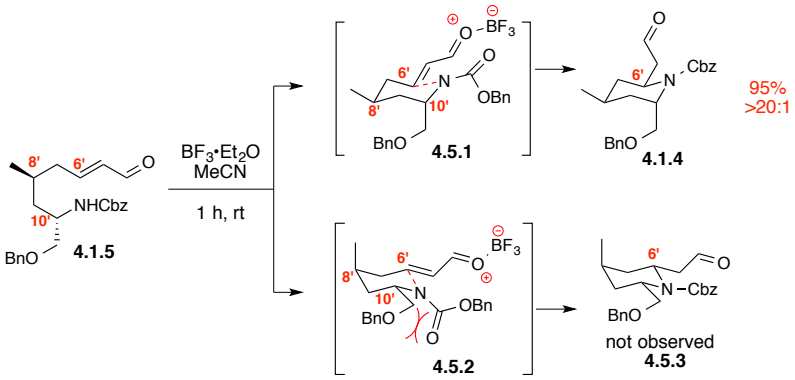


Scheme 4.4: Synthesis of Enal **4.1.5**.

4.3: Substrate Controlled Intramolecular Heteroatom Michael Reaction of Cbz Amine Enal **4.1.5**.

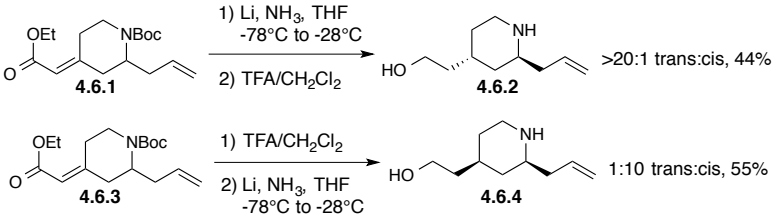
With Cbz enal **4.1.5** in hand, we set out to explore our intramolecular heteroatom Michael reaction (Scheme 4.5). Given the poor substrate control exhibited in the amide example of our first generation synthetic route, we anticipated that chiral catalysis might be required to afford good stereoselectivity in the Michael cyclization. The possibility also existed that substrate control would produce our desired isomer based on our postulated transition state **4.5.1**; however, the effect of the interplay of the two stereocenters present in **4.1.5** was unknown. We were pleased to find that treatment of Cbz enal **4.1.5** with $BF_3{\cdot}Et_2O$ provided the desired piperadine ring system in excellent diastereoselectivity (>20: 1) and yield (95%). Our diastereocontrol model, depicting both the productive transition state **4.5.1** and the nonproductive one **4.5.2** for the minor diastereoisomer are both shown in Scheme 4.5. Transition state **4.5.2** highlights the disadvantageous interaction that is presumably the basis for the high diastereoinduction of the cyclization. The planar nature of the Cbz group

forces itself into a pseudo equatorial position while the benzyloxy sidearm is forced into a psuedo axial position.



Scheme 4.5: Substrate Controlled Intramolecular Heteroatom Michael Reaction of Cbz Amine Enal **4.1.5**.

Such an effect wherein a carbamate group bonded to a piperadine ring exhibits pseudo equatorial behavior has some precedent in the literature (Scheme 4.6).[7] In this example radically divergent chemical outcomes occur based on whether the nitrogen is carbamate protected or a free amine. The outcomes are consistent with Li° metal reduction occurring via a transition state like for our reaction wherein the group in the two position of the piperidine ring is forced into an axial position by the carbamate protecting group.

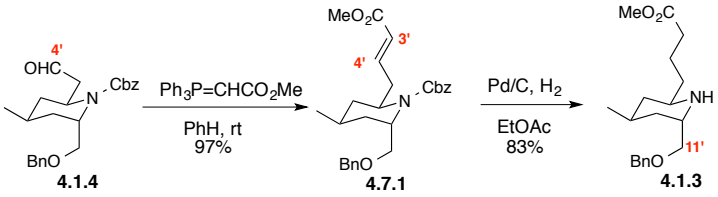


Watson *et. al. Org. Lett.* **2000**, *2*, 3679-3681.

Scheme 4.6: Carbamate Protecting Groups Acting in a Psuedo Equatorial Fashion.

4.4: Elaboration of Aldehyde **4.1.4** and Formation of Amino Ester **4.1.3**.

Our next goal was the synthesis of the amino ester **4.1.3** (Scheme 4.7). Wittig reaction of Cbz aldehyde **4.1.4** with stabilized Wittig reagent $Ph_3P{=}CHCO_2Me$ produced the α, β-unsaturated methyl ester **4.7.1** in 83% yield. With Cbz ester **4.7.1** in hand, we next required the removal of the benzyl ether, the Cbz moiety as well as the $C_{3'}$-$C_{4'}$ π bond to produce a precursor suitable for lactam cyclization. We had initially hoped the hydrogenation of Cbz ester **4.7.1** with Pd/C would achieve all of the set goals in addition to the lactam formation. Interestingly, hydrogenation of **4.7.1** yielded only two of the desired reactions: the cleavage of the Cbz group and the reduction of the double bond to form amino ester **4.1.3**. One possible explanation is that the free amine liberated by the Cbz cleavage poisoned the Pd catalyst and prevented the cleavage of the benzyl ether. Such deactivation of Pd by amines is known in the literature.[8]



Scheme 4.7: Elaboration of 4.1.4 and Formation of Amino Ester **4.13**.

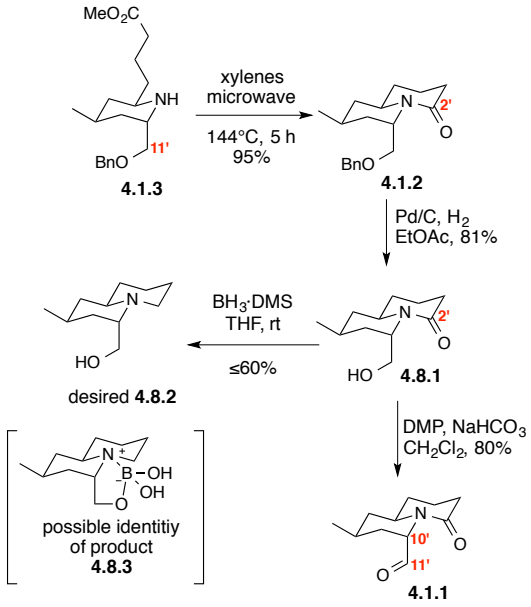
4.5: Formation of the Quinolizidine Core and Synthesis of Aldehyde **4.1.1**.

Our strategy for the formation of the quinolizidine core **4.1.2** is outlined in Scheme 4.8. At first glace the formation of the lactam bond and thus the quinolizidine core would appear to be straightforward, in fact, δ amino ester have been known to spontaneously produce the δ lactam.[9] To our dismay, the difficulty of overcoming the enthalpic penalty to form the ring appears to make the process significantly higher in energy. Cyclization of amino ester **4.1.3** was initially attempted via traditional thermal processes (in an oil bath with a water cooled reflux condenser). Reflux of amino ester **4.1.3** in xylenes overnight produced only modest amount of the cyclized product **4.1.2** (~15%). We also screened several Lewis acids ($AlMe_3$,[10] $AlMe_2Cl$ and $Ti(OiPr)_4$) which proved similarly unsuccessful (only token amount of cyclized material was obtained and

the mass recovery was typically poor with the Lewis acid conditions). Saponification of the ester was accomplished by treatment with LiOH / H_2O_2 / THF to allow for peptide type coupling reactions. This strategy has a wealth of precedent for accessing highly challenging lactam bonds; in fact DCC was developed by Sheehan during the synthesis of Penicillin to form strained β-lactam bonds.[11] Efforts to couple the crude amino acid with DCC or HATU[12] were met with frustration and complex mixtures of products, none of which were lactam **4.1.2**. Part of the logistical challenge posed by this strategy was the result of the difficulty with isolation of the amino acid; non-crystalline amino acids are often challenging to purify. At this point, we revisited thermolysis as a possible method to access lactam **4.1.2**. Our group had recently purchased a microwave synthesizer and we elected to explore the feasibility of utilizing it to cyclize amino ester **4.1.3**. Anecdotal evidence shows that microwave reactions are at times uniquely capable of achieving some reactions, though more rigorous studies seem to imply that such a “microwave effect” is merely the result of highly efficient heating.[13] We were pleased to find clean and rapid conversion to the desired lactam **4.1.2** in 95% yield, at temperatures where traditional thermal conditions were almost an order of magnitude slower (a side by side reaction was run with the microwave being complete after 5 h, the thermal reaction being only ~10% complete in the same time frame). We attributed this marked difference to the highly

efficient heating provided by the microwave synthesizer. With lactam **4.1.2** in hand, our next objective was the cleavage of the benzyl ether. Interestingly, we had previously attempted this transformation unsuccessfully on the Cbz-protected amine **4.7.1**. Hydrogenative cleavage of the benzyl ether, utilizing essentially identical Pd/C hydrogenation conditions, which previously led to the conversion of Cbz protected amine **4.7.1** to piperidine **4.1.3**, smoothly yielded alcohol **4.8.1**. This outcome provides credence to our suspicion that the free amine poisoned the Pd catalyst and prevented the cleavage of the benzyl ether in the previous hydrogenation. Alcohol **4.8.1** was converted to the aldehyde **4.1.1** by oxidation with DMP[14]. At this point, we also explored the possibility of reducing the lactam and carrying the amino alcohol **4.8.2** forward. The reduction of the lactam carbonyl was achieved with BH_3·DMS, however the amino alcohol synthesized behaved rather oddly, being soluble in no common organic solvents but MeOH (the compound was characterized in D_3COD). In retrospect, we surmised that we had isolated an amino borate (tenetivley **4.8.3**) of some type, as amino alcohols of much lower molecular weight are soluble in common organic solvents ie. 2-Piperidineethanol. At the time of isolation all characterization data in MeOD was consistent with amino alcohol but the compound isolated was un-amenable to all attempts at further reaction. If the amino alcohol route were attempted again a more vigorous work up (eg. 4M NaOH) would

likely be required to liberate the boron from the amino alcohol. Alternatively, formation of the HCl salt could also alleviate this problem with the borate.

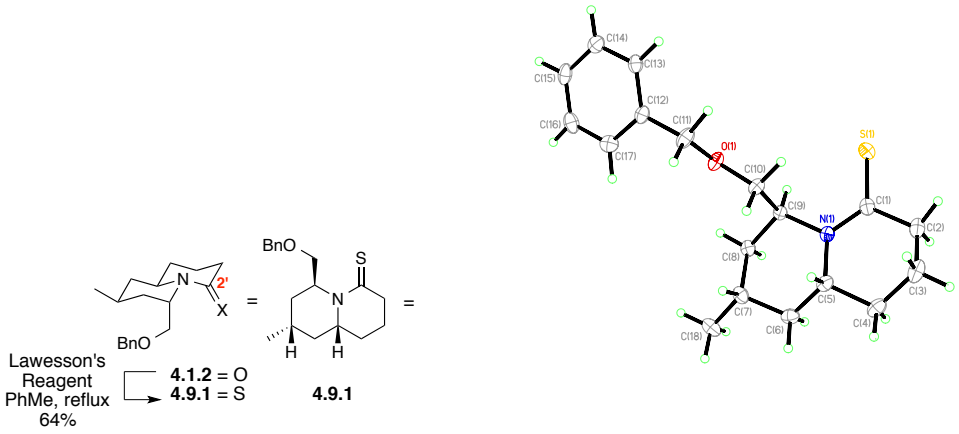


Scheme 4.8: Cyclization of Amino Ester **2.3.x** and Synthesis of Aldehyde **4.1.1**.

4.6: Confirmation of Stereochemistry Via Derivitization and X-ray Crystallographic Analysis.

We had hoped that the bicyclic nature of lactam **4.1.2** presented a possible method for the confirmation of the stereochemical outcome of the intramolecular Michael reaction via crystallization and x-ray diffraction. We

converted lactam **4.1.2** to the corresponding thiolactam **4.9.1** by treatment with Lawesson's reagent[15] (Scheme 4.9). Gratifyingly, thiolactam **4.9.1** proved highly crystalline and single crystal x-ray analysis was undertaken. The x-ray crystal structure of thiolactam **4.9.1** confirmed the stereochemical assignment required for himeradine A had been achieved. Unfortunately, the x-ray structure offered no significant insight into difficulty in forming the lactam ring beyond the highly planar nature of the ring fusion nitrogen forcing five atoms into planarity.



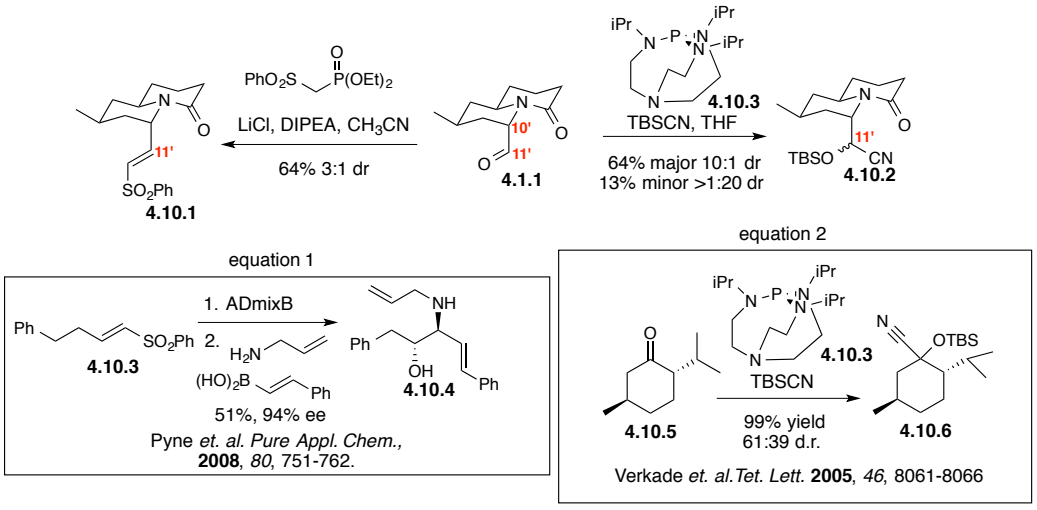
Scheme 4.9: Confirmation of Stereochemistry Via Derivitization and X-ray Crystallographic Analysis.

4.7: Attempted Functionalization Strategies Towards α-Hydroxy Aldehyde **3.1.1**.

With aldehyde **4.1.1** in hand and its stereochemical configuration confirmed, we set out to synthesize the α-hydroxyl aldehyde **3.1.1** (Scheme 4.10). Our first strategy hinged on the synthesis of unsaturated sulfone **4.10.1**, which proceeded in serviceable yield utilizing the Masamune-Roush modified version of the Horner Wadsworth Emmons reaction.[16] Next, unsaturated sulfone **4.10.1** was subjected to various dihydroxylation conditions, to attempt to form the α-hydroxyl aldehyde **3.1.1**. This approach was based on prior work be Pyne[17] and co-workers. They had employed an unsaturated sulfone in a Sharpless dihydroxylation to afford the α-hydroxyl aldehyde that was then utilized in a boron-Mannich reaction (an example is shown equation 1). Both Sharpless variants and OsO_4 / pyridine type conditions were screened. Unfortunately, sulfone **4.10.1** proved completely resistant to a variety of conditions (ADmix α, ADmix α*[†] in both acetone / H_2O and tBuOH / H_2O, with extended reaction times at elevated temperatures).[1] Our second strategy for the synthesis of α-hydroxyl aldehyde **3.1.1** hinged on the synthesis of silyl cyanohydrin **4.10.2**. Treatment of aldehyde **4.1.1** with TBSCN in the presence of Verkade's[18] phosphorous reagent **4.10.3** produced the silyl

[†] AD mix α* = $(DHQ)_2PHAL$ (100 mg), $K_2OsO_2 \cdot H_2O$ (14.2 mg), K_2CO_3 (478 mg), $K_3Fe(CN)_6$ (1.22 g).

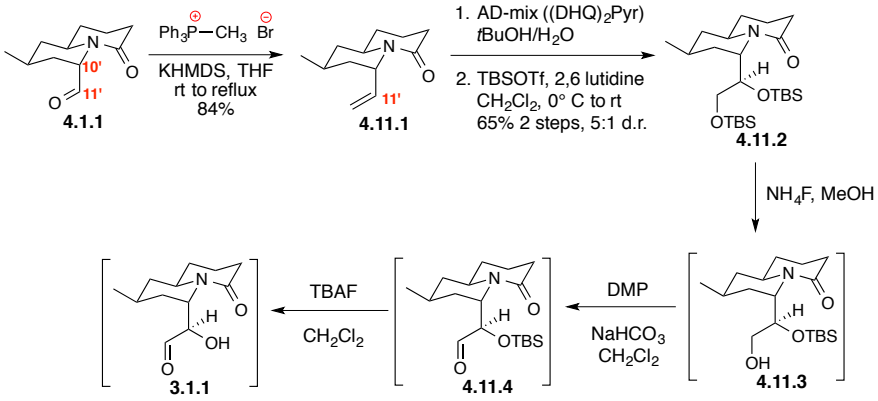
cyanohydrin **4.10.2** in good yield but in modest (3:1) dr. The poor diastereoselectivty exhibited was not wholly unexpected, as cyanohydrin formations using this technique are not typically highly selective; the only literature example with potential Felkin selectivity is shown in equation 2, though it is a ketone example not an aldehyde. Unfortunately, attempted reduction of the silyl cyanohydrin **4.10.2** with DIBAL-H proved fruitless as a complex mixture of reduction products was observed, leading us to explore an alternate stratagem.



Scheme 4.10: Attempted Synthesis of α Hydroxy Aldehyde **3.1.1**.

Our third and final effort to synthesize α-hydroxyl aldehyde **3.1.1** hinged on the conversion of aldehyde **4.1.1** to terminal alkene **4.11.1** via Wittig homologation (Scheme 4.11). The Wittig reaction of aldehyde **4.1.1** proceeded in 84% yield to produce alkene **4.11.1**. Alkene **4.11.1** was subjected to Sharpless dihydroxylation with the non-standard $(DHQ)_2Pyr$

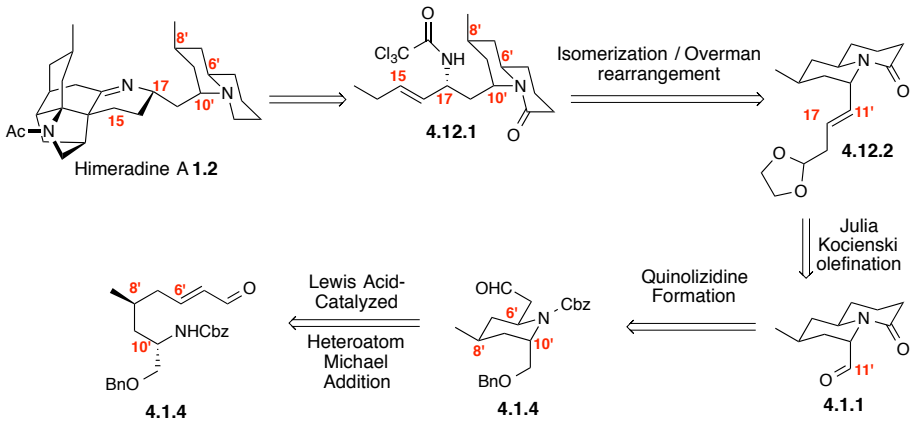
ligand, as the standard ligand set proved sluggish.[19] While the oxidation proceeded smoothly, the resulting diol was highly polar and purification required exhaustive TBS protection to produce di TBS ether **4.11.2** in 65% yield over two steps. The stereochemistry of TBS diol **4.11.2** was assigned based on literature precedent, but not independently verified. Di-TBS ether **4.11.2** was then treated with NH_4F to selectively cleave the primary TBS group;[20] however, the resulting product proved highly prone to silyl ether migration. Crude NMR data clearly showed the disappearance of one of the silyl ethers. With the unstable primary alcohol in hand, oxidation to the aldehyde was accomplished by treatment with DMP but the resulting aldehyde was unstable and appeared to be two compounds by crude NMR (two aldehydic protons were apparent), possibly due to epimerization of the unstable α silyl ether aldehyde. The α-silyl ether aldehyde was treated with TBAF, crude NMR showed evidence of a new aldehyde compound; however, it too proved unstable and too impure to carry on. The difficulty of carrying forth three discreet chemical steps in order to explore the reactivity of a highly unstable intermediate led us to abandon this route as a coupling strategy.



Scheme 4.11: Evident Synthesis of Alpha Hydroxy Aldehyde **3.1.1**.

4.8: Revised Coupling Strategy and Retrosynthesis.

With the difficulties encountered with our borono-Mannich reaction strategy, we endeavored to craft a new approach for coupling the two domains of himeradine A **1.2** (Scheme 4.12). Our revised approach utilized a Julia-Kocienski[21] / isomerization strategy which set the stage for an Overmann rearrangement[26] or a heteroatom Michael addition to install the central nitrogen atom bonded to C_{17}. In the model system, an ethyl group would be used to convert the enal to the allyl alcohol oxidation state instead of the western fragment of himeradine A **1.2**.

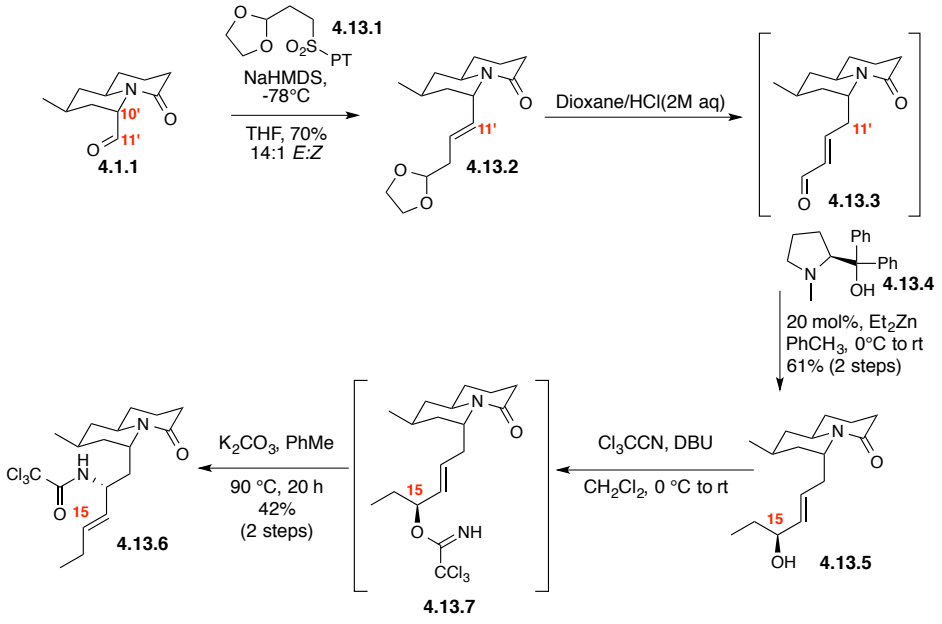


Scheme 4.12: Revised Coupling Strategy Retrosynthesis.

4.9: Execution of Overmann Strategy and Synthesis of Trichloro Acid Amide **4.12.1**.

Utilizing previously synthesized aldehyde **4.1.1**, we began by performing a Julia-Kocienski[21] coupling with known PT sulfone **4.13.1**[22] to yield β-γ-unsaturated acetal **4.13.2** in 70% yield (Scheme 4.13). With β-γ-unsaturated acetal **4.13.2** in hand, we then attempted to achieve simultaneous de-protection / isomerization to form enal **4.13.3**. Treatment with HCl in dioxane[23] proved effective, though enal **4.13.3** was highly unstable and had to be carried on crude. Initially, we attempted to install the C_{17} nitrogen via Michael addition of a nitrogen nuclephile. See chapter 2 for background on intermolecular nitrogen nucleophile reactions. Unfortunately, enal **4.13.3** proved unstable under a range of conditions

(NaN_3 / HOAc or TBSONHCbz / piperadine) and we suspected that amide oxygen could be attacking the enal and leading to a fragmentation pathway. We next explored a 1,2-addition to the enal **4.13.3** followed by an Overmann rearrangement. Treatment of enal **4.13.3** with Et_2Zn and proline derivative **4.13.4**[24] provided allylic alcohol **4.13.5** as a single isomer in 61% yield over two steps. The stereochemistry of allylic alcohol **4.13.5** was confirmed via the advanced Mosher ester method.[25] Allylic alcohol **4.13.5** was subjected to two-step Overmann rearrangement[26] to yield trichloro acid amide **4.13.6** in 42% yield (over two steps) with no apparent erosion of diastereoselectivity.



Scheme 4.13: Synthesis of Trichloro Acid Amide **4.13.6** via Overmann Rearrangement.

4.10: Conclusion.

Our second-generation approach demonstrated the feasibility of utilizing an Overmann rearrangement to diastereoselectively install the C_{17} nitrogen. In addition, the intramolecular heteroatom Michael reaction was applied in a diasteroselective process, which provided further knowledge of how existing stereochemistry influences the reaction outcome. Lastly, aldehyde **4.1.1** contains all the stereochemistry of the eastern domain of himeradine A with a functional handle that could potentially lend itself to numerous coupling strategies, for completion of the total synthesis of himeradine A **1.2**.[27]

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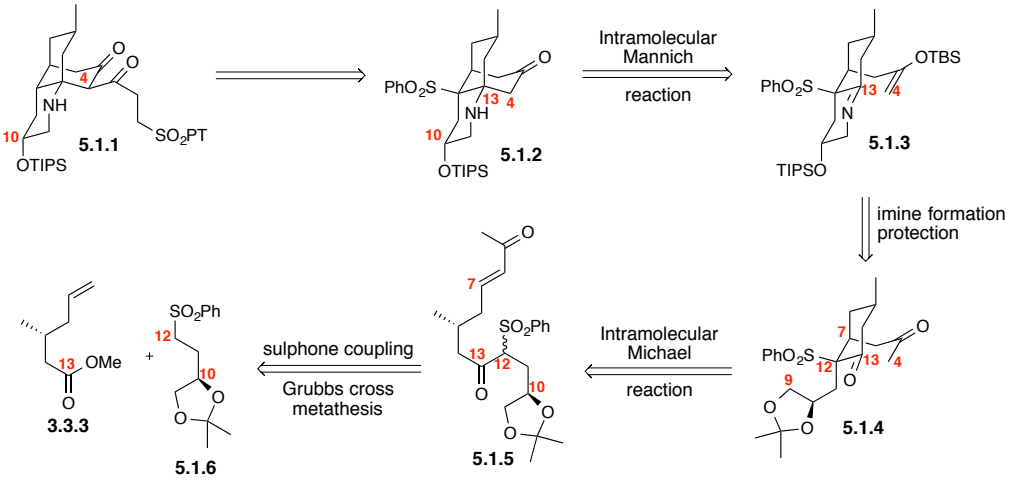
Chapter 5 Studies Towards the Western Fragment of Himeradine A **1.2**

5.1. Retrosynthetic Strategy and General Outline.

Our strategy for the synthesis of the western domain of himeradine A **1.2** follows the same overall path as our group's synthesis of lycopodine **1.1** (Scheme 5.1).[1] This work was started by another student in the group, Mr. Mrinmoy Saha, as such portions of the route were already established when the author of this thesis joined this portion of the project. Consequently, it will be covered in considerably less detail, with this author's work being the primary focus. Mr. Mrinmoy Saha's work will be given as necessary for context (e.g. multiple routes were being explored with one being abandoned because the other researcher and had been successful). Our retrosynthesis targeted PT sulfone **5.1.1** as it is the extension of our previously modeled Julia-Kocienski / Overmann rearrangement strategy with the eastern half of the natural product.[2] Our initial strategy envisioned appending the PT sulfone-containing sidearm via nitrogen chelation directed enolate chemistry. The tricyclic amine **5.1.2** would be synthesized via an intramolecular sulfone enhanced Mannich reaction of TBS enol ether/imine **5.1.3**. TBS enol ether / imine **5.1.3** could be synthesized via intramolecular aza-Wittig reaction from protected diol **5.1.4**. Cyclohexanone **5.1.4** could be synthesized via the organocatalyzed,

intramolecular keto sulfone Michael reaction of enone **5.1.5**. Keto sulfone **5.1.5** would be synthesized via a sulfone ester coupling of ester **3.3.3**[1] and sulfone **5.1.6**.

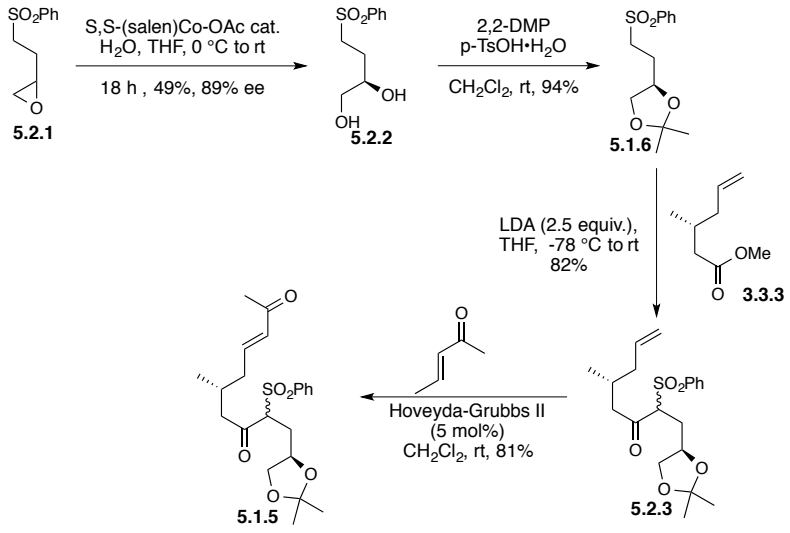


Scheme 5.1: Retrosynthetic Strategy for the Western Domain of Himeradine A **1.2**.

5.2. State of Western Domain Chemistry Upon Joining the Project.

Working in parallel to this author's efforts, Mr. Mrinmoy Saha accomplished a considerable fraction of the synthesis of the western portion of himeradine A (Scheme 5.2). Epoxy sulfone **5.2.1** was subjected to Jacobsen hydrolytic kinetic resolution [3] to yield enantiomerically enriched known diol **5.2.2**[4] in 49% yield. It should be noted in a resolution reaction of this type is effectively a 98% yield as 50% is the theoretical

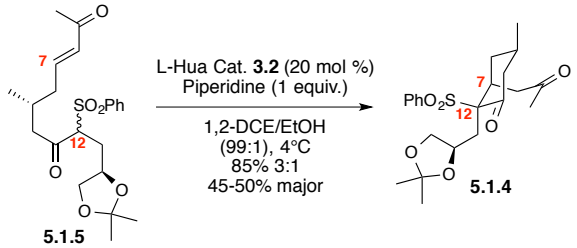
maximum. With diol **5.2.2** in hand, protection as the acetonide was achieved by treatment with 2,2-DMP and acid in 94% yield. Sulfone **5.1.6** was then coupled with known ester **3.3.3**[1] (the enantiomer of the ester utilized in our first generation approach to the eastern fragment), to yield keto ester **5.2.3**. Conversion of the terminal alkene **5.2.3** to the enone **5.1.5** by Grubbs cross metathesis with pentenone proceeded smoothly in 81% yield.



Scheme 5.2: Synthesis of Keto Sulfone/Enone **5.1.5**.

The organocatalyzed intramolecular Michael reaction of keto sulfone, to form the first ring of the western fragment of himeradine A **1.2** was achieved after considerable screening by Mr. Mrinmoy Saha (Scheme 5.3). The reaction proceeded well, utilizing our group's Hua Cat[5]

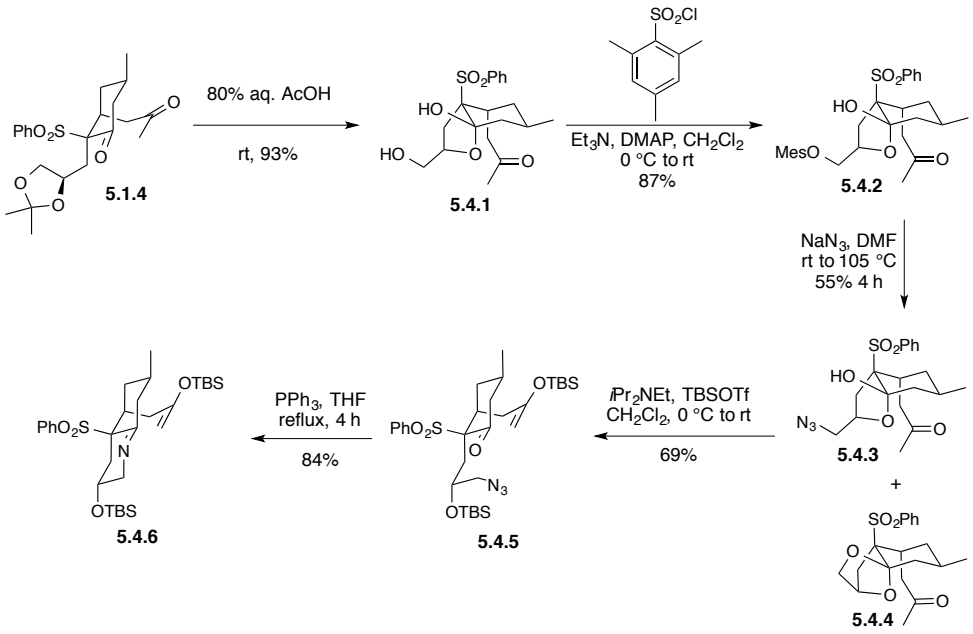
catalyst **3.2**, though in modest diastereoselectivity (3:1). The reaction had the additional complication of requiring a recrystallization after column chromotography to separate the major diastereoisomer from the minor diastereoisomer. Unfortunately, this protocol left a considerable amount of the desired isomer behind in the mother liquor and was a non-ideal purification protocol.



Scheme 5.3: Organocatalyzed Intramolecular Keto Sulfone Michael Synthesis of Cyclohexanone **5.1.4**.

Our next goal was to accomplish the formation of the first ring of the western portion of the natural product (Scheme 5.4). Cyclohexanone **5.1.4** could be successfully converted to hemiketal **5.4.1** by treatment with AcOH. Hemiketal **5.4.1** was converted to primary mesetylate **5.4.2** by treatment with mesetylate chloride and DMAP. Subsequent treatment of mesetylate **5.4.2** with NaN_3 in DMF yielded the primary azide **5.4.3** along with non-trivial amounts of ketal **5.4.4** (which could be converted to hemiketal **5.4.2** by treatment with HCl). Hemiketal / azide **5.4.3** was

treated with TBSOTf facilitate silyation of the open hydroxyl ketone at the C_{11} alcohol and the methyl ketone as the silyl enol ether **5.4.5**. Staudinger reduction and concontaminent aza-Wittig reaction provided the imine **5.4.6**. Unfortunately, bicyclic imine **5.4.6** could not yet be successfully cyclized using any Lewis acid type conditions. This was the status of the synthesis of when this author joined this portion of project, the western fragment.



Scheme 5.4: Synthesis of Bicyclic Imine **5.4.6**.

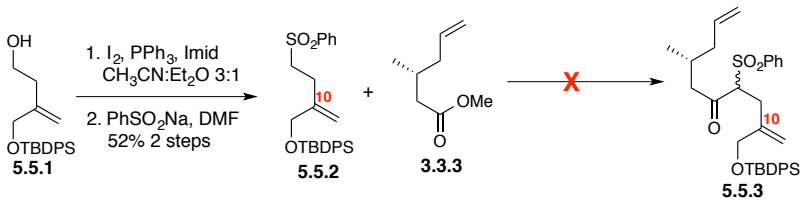
The key remaining challenges left to be addressed to complete the western fragment were the formation of the two remaining rings as well the installation of the three remaining carbons of the central ring of himeradine

A **1.2**. Specifically efforts to cyclize di-TBS ether **5.4.6** with Lewis acid-type conditions invariably caused cleavage of the C_{10} silyl ether. Some method for modulating this deleterious reactivity would be required for the Mannich reaction to proceed effectively. In addition, the functionality utilized to facilitate the intramolceular Mannich reaction would need to allow for an intramolcular alkylation reaction to form the fourth ring. We also desired to improve the selectivity of the Michael reaction to improve the yield and ease purification.

5.3. Intramolecular Mannich Reaction Studies.

At this juncture, the Mannich reaction had not yet been executed and we took a two-pronged approach to solving this issue. Based on our group's previous synthesis of lycopodine[1] **1.1**, we knew that our intramolecular Mannich reaction is successful on the compound not containing the TBS ether. Unfortunately, the TBS ether was prone to cleavage under the Lewis acid conditions we had explored. Our two approaches to solving this problem were (a) a different protecting group would be installed at the front lines (pursued by Mr. Mrinmoy Saha) and (b) installation of a different functional group much earlier in the synthesis (pursued by this author). We elected to attempt to install an exo-methylene subunit at C_{10} as it could be readily converted to many potential functional

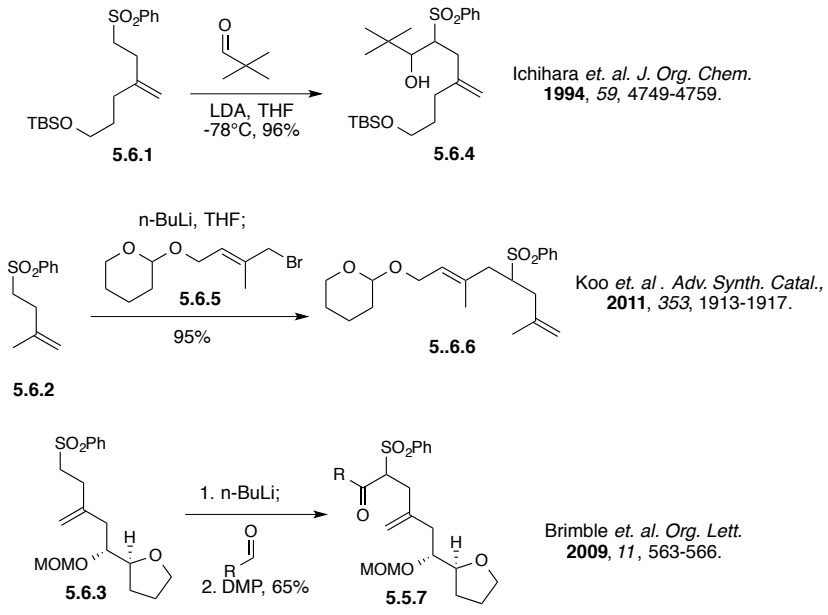
groups and should be inert to the problematic Lewis acid cyclization conditions. Scheme 5.5 shows our efforts to install an exomethylene earlier in the synthesis. Known alcohol **5.5.1**[6] was converted to sulfone **5.5.2** by an Appel reaction,[7] followed by displacement of the resulting iodide with $PhSO_2Na$ (52% 2 steps). Unfortunately, attempts to couple sulfone **5.5.2** with ester **3.3.3** utilizing various equivalencies of LDA and LiTMP (1 eq, 2 eq and 2.5 eq with both bases) proved fruitless. Interestingly, quenching the presumed sulfone di-anion with D_3COD at both -78 °C and 0 °C to measure deuterium incorporation showed only modest incorporation (~10%).



Scheme 5.5: Attempted Exomethylene Incorporation.

These results are difficult to explain, we searched the literature for homoallylic sulfones that are differentially substituted from **5.5.1** to see if they were capable of being deprotonated, as we desired (Scheme 5.6). We found several similar examples that were competent nucleophiles, TBS sulfone **5.6.1** was competent in Julia chemistry,[8] the un-substituted

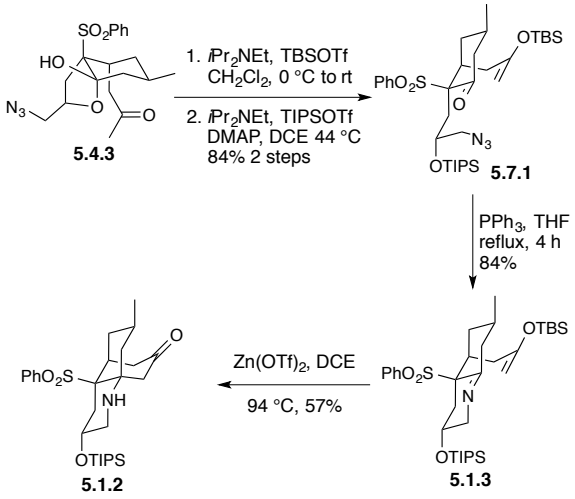
sulfone **5.6.2** was competent in alkylation chemistry[9] and lastly the oxygenated sulfone **5.6.3** was competent in Julia chemistry (the aldehyde partner is not depicted in its entirety as it is quite large).[10] Given the plethora of literature examples, running the gamut of steric bulk and coordinating and non coordinating functional groups all being competent as nucleophiles, the inability of our sulfone **5.5.2** to be effectively deprotonated and act as a nucleophile would seem to be difficult to explain and to have no prior explanation in the literature.



Scheme 5.6: Literature Examples of Homoallylic Sulfone as Nucleophiles.

Concurrently to this author's investigation, Mr. Mrinmoy Saha developed a viable Mannich cyclization approach via a redesigned

protecting group strategy (Scheme 5.7). Previously synthesized hemiketal **5.4.3** was treated with TBSOTf, but at lower temperatures and equivalancies to allow for selective silyl enol ether formation. Next, the hemiketal was protected as the TIPS ether to reveal the ketone and produce the fully protected ketone **5.7.1**. Ketone **5.7.1** was converted to the bicyclic imine **5.1.3** by Staudinger reduction with PPh_3. Mannich reaction of imine **5.1.3** was successful with $Zn(OTf)_2$ to yield tricyclic amine **5.1.2**. This development made further investigation of early incorporation of a different functional group moot.

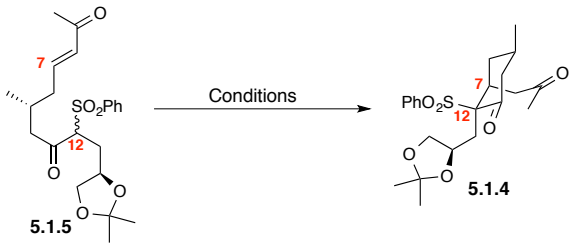


Scheme 5.7: Synthesis of Tricyclic Amine **5.1.2**.

5.4. Optimization of Keto Sulfone Michael Reaction

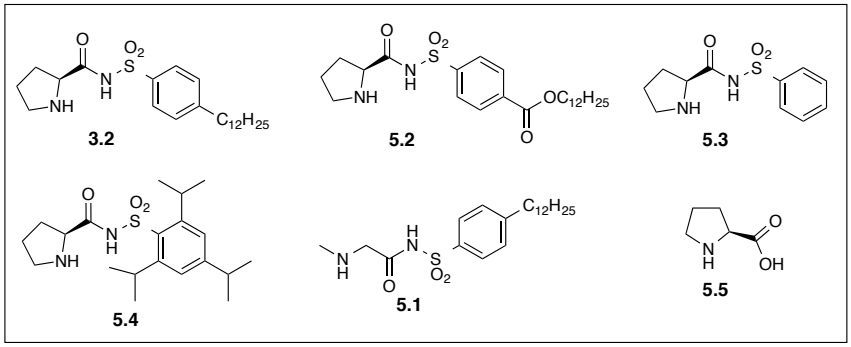
The next key challenge in our work on the western fragment was the optimization of the keto sulfone Michael reaction, shown in generic

form in Scheme 5.8. Our current conditions were somewhat problematic, with modest diastereoselectivity and poor efficacy in the recrystalization. We believed a modest improvement in diastereoselectivity could make recrystallization unnecessary and thus set out to further optimize the cyclization.



Scheme 5.8: Keto Sulfone Michael Reaction Outline.

Consequently, we explored a range of conditions for the cyclization (Table 5.1). The three main axes of investigation were (a) the catalyst used, (b) the solvent and (c) the protic additive. The reaction proved highly resistant to changes of reaction conditions, which led us to believe that perhaps the reactions selectivity was being controlled by the stereochemistry of the starting material. To investigate this possibility an achiral version of our group's sulfonamide catalyst **5.1** was synthesized from N-methyl glycine, though as indicated it was not a competent catalyst. We did however discover that proline **5.5** was a competent catalyst in this transformation allowing us to circumvent the four-step synthesis required for **3.2** and the related catalysts.

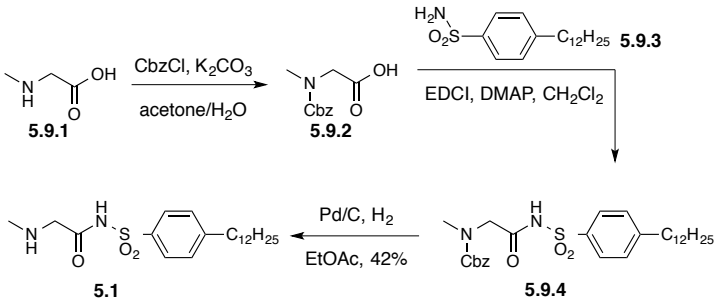


Entry	Catalyst/CoCatalyst	Conditions	dr (by NMR)
1	**3.2** / piperadine	DCE/EtOH (99:1)	3:1
2	**3.2** / piperadine	DCE/EtOH (98:2)	2.6:1
3	**3.2**·HCl / piperadine	DCE/EtOH (99:1)	2.7:1
4	**3.2**·PhCOOH / piperadine	DCE/EtOH (99:1)	2.5:1
5	**5.2** / piperadine	DCE/EtOH (99:1)	2.2:1
6	**5.3** / piperadine	DCE/EtOH (99:1)	2.1:1
7	**5.4** / piperadine	DCE/EtOH (99:1)	1.8:1
8	**5.1** / piperadine	DCE/EtOH (99:1)	Ineffective
9	**5.5** / piperadine	DMF	3:1

Table 5.1: Summary of Keto Sulfone Michael Reaction Screening.

An achiral version of our sulfonamide catalyst **3.2** was synthesized from N-methylglycine **5.1** (Scheme 5.9). Commercially available N-methylglycine **5.9.1** was protected as the Cbz carbamate **5.9.2**, which was carried on crude. Crude Cbz carbamate **5.9.2** was EDCI coupled with sulfonamide **5.9.3** to provide sulfonamide **5.9.4**, which was again carried on crude. Crude sulfonamide **5.9.4** was deprotected by hydrogenation with Pd/C and H_2 to provide the secondary amine sulfonamide catalyst **5.1** in 42% yield (with sulfonamide **5.9.3** as the limiting reagent) over three steps. While this catalyst has not yet proven competent in any of the reactions

screened, it is part of our group's catalyst library and we hope to find reactions in the future for which it is more effective.

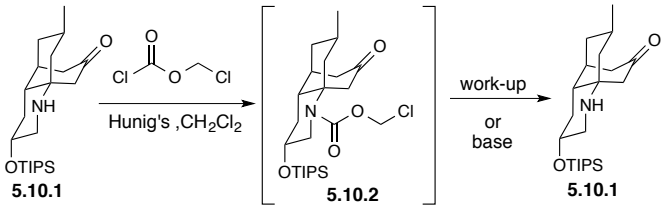


Scheme 5.9: Synthesis of Sulfonamide Catalyst **5.1**.

5.5. Acyl Transfer Strategies.

The next challenge in our synthesis was the installation of the remaining three carbons of the himeradine A **1.2** (Scheme 5.10). We explored the possibility of utilizing a nitrogen acylation/transfer strategy to functionalize the C_4 position of tricyclic amino ketone **5.10.1** (obtained by treatment of amine **5.4.6**). We envisioned acylating the secondary nitrogen of tricycle **5.10.1** with chloromethylchloroformate, which could be treated with a base to form the enolate that would react intramolecularly with the chloride. Unfortunately, our acylation strategy was ineffective, under DIPEA and chloromethylchloroformate conditions. The acylation event appeared to occur, as the starting amine **5.10.1** was consumed by TLC analysis; however, no new compounds were evident by TLC analysis.

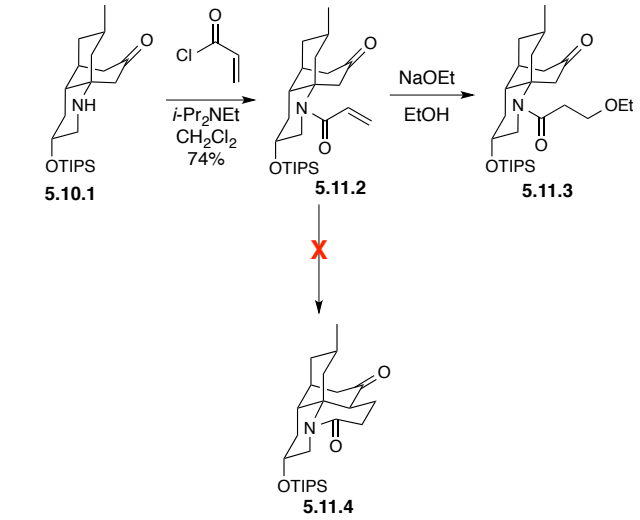
Work-up conditions (even as mild as filtration through celite) returned only unaltered starting amine **5.10.1**, implying a highly labile acyl group. Experiments in $CDCl_3$ did give credence to our speculation the acylation event was occurring, crude NMR showed a clear downfield shift for one of the alpha amino methylene signals (to ~3.1 from 2.68ppm, total disappearance of this signal was evident) indicating the likely formation of a carbamate. Unfortunately, efforts to treat the crude carbamate with stronger base (KO*t*Bu), capable of enolizing the ketone and causing cyclization by chloride displacement, were ineffective only yielding up tricyclic amine **5.10.1**. We chose this base due to its effectiveness at triggering a similar cyclization in many syntheses of lycopodine.



Scheme 5.10: Chloromethylchloroformate Transfer Strategy.

Our second acyl transfer strategy was based on work by Kim[11] and co-workers in their synthesis of anhydrolycodoline and lycopodine (Scheme 5.11). In their approach, the nitrogen of the lycopodine skeleton was converted to the acrylamide and the fourth ring of the lycopodine

skeleton was formed via intramolecular Michael reaction (the literature example also produced quantities of the solvolyitc Michael reaction product). While this reaction manifold was precedented a key difference between this example and our substrate was the bridgehead alkene. Inspection of models comparing alkene **5.11.1** with our substrate acrylamide **5.11.2** showed both compounds to be of similar conformational space and flexibility. Both structures appeared to have access to similar transition states for the intramolcular Michael reaction (if anything the precedented example of alkene acrylamide **5.11.1**'s transition state appeared to be more strained than our substrate). Tricylic amine **5.10.1** was converted to the acrylamide **5.11.2** by treatment with acryloyl chloride and Et_3N in 74% yield. Our efforts to achieve the cyclization reaction followed the precedent example, using NaOEt in EtOH; however, the only product evident by crude NMR was a trace amount of ether **5.11.3** (yield not determined), disappearance of the alkene signals and appearance of a new CH_3 unit led us to this assignment. Acidic cyclization conditions (PTSA, THF, reflux) produced complex mixtures of products that were globular, possibly indicating the formation of acrylamide polymers.

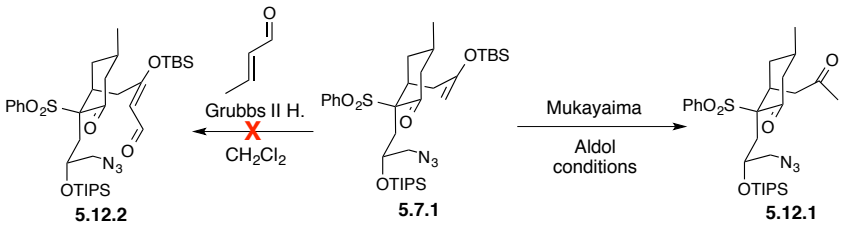


Scheme 5.11: Acrylamide Cyclization Strategy.

5.6. TBS Enol Ether Functionalization Strategies.

With our inability to affect any of our acyl transfer strategies, we changed our focus towards two potential functionalization methods for TBS enol ether **5.7.1** (Scheme 5.12). The first strategy explored was to use the enol ether of **5.7.1** as a functional handle for a cross metathesis reaction. Literature precedent shows that enol ethers are competent cross metathesis partners, but only to our knowledge for ring closing metathesis reactions to form five and six membered rings. [12] This low reactivity to

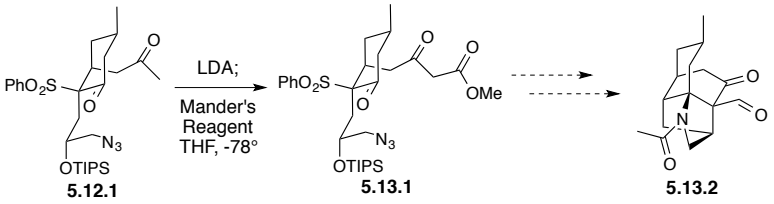
cross metathesis chemistry is likely due to the fact that a silyl enol ether is in the least substituted case still a Type III (1,1 di-substituted) alkene and more substituted enol ethers are Type IV alkenes (typically considered inert to cross metathesis).[13] TBS enol ether **5.7.1** was treated with crotonaldehyde and Grubbs Hovedya II in CH_2Cl_2 at reflux (reaction was begun at rt but no reaction occurred), but proved to be a poor cross metathesis partner, yielding only slow decomposition of starting material. The second strategy we attempted to functionalize the silyl enol ether **5.7.1** was a Mukayaima[14] type activation. Multiple electrophilic acceptors could potentially be useful with this approach. A battery of Lewis acids were screened ($BF_3{\cdot}Et_2O$, $TiCl_4$ and $Zn(OTf)_2$); with butanal and monomeric formaldehyde, but unfortunately all conditions yielded only the deprotected methyl ketone **5.12.1**.



Scheme 5.12: Attempted TBS Enol Ether Functionalization Strategies.

5.7. Formation of Ester Using Mander's Reagent.

Given our challenges with functionalization, Mr. Mrinmoy Saha attempted yet another carbon-carbon bond formation strategy Mander's[15] reagent homologation of methyl ketone **5.12.1** (scheme 5.13). The reaction of methyl ketone with **5.12.1** LDA and Mander's reagent provided the β-keto ester **5.13.1** in 70% yield. With this development, it became clear that a slightly modified coupling strategy might be required as the western fragment of himeradine A would only be providing one of the three central carbons of the natural product (eg. Tetracyclic aldehyde **5.13.2**).



Scheme 5.13: Mander's Reagent Homologation of Methyl Ketone **5.12.1**.

5.8. Conclusion.

The successful synthesis of keto methyl ester **5.13.1** has been achieved by Mr. Mrinmoy Saha. Our work on the western fragment of himeradine A has informed us as to what chemistry would be most

capable of coupling the two fragments of the natural product. Future work on this portion of the natural product will seek to synthesize keto aldehyde **5.13.2** and will be pursued primarily by Mr. Mrinmoy Saha.

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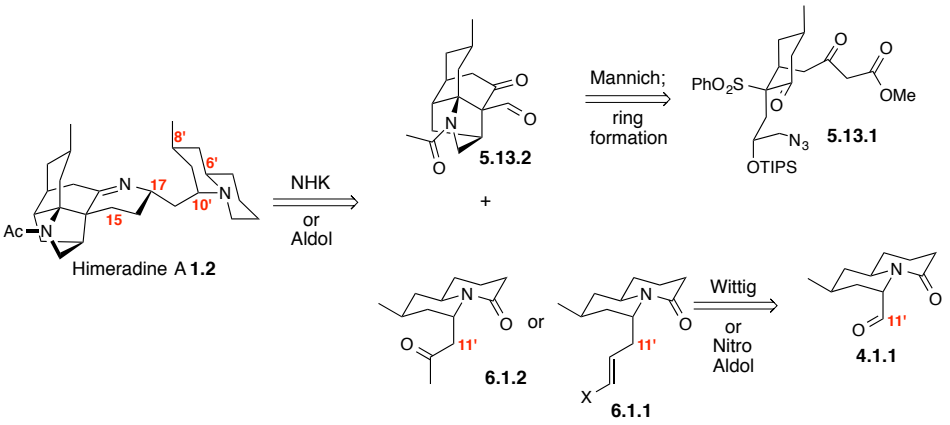
Chapter 6: Modification of Eastern Fragment Coupling Strategy.

6.1: Modified Retrosynthetic Strategy.

With our recent acylation of our methyl ketone intermediate **5.12.1**, we decided that a slightly modified retrosynthetic strategy would be required in our efforts to synthesize himeradine A **1.2** (Scheme 6.1). Our goal was to find a viable coupling strategy utilizing aldehyde **5.13.2**, which should be available from synthesized keto ester **5.13.1**. We hoped to elaborate previously synthesized lactam / aldehyde **4.1.1** to either vinyl halide **6.1.1** to enable an NHK[1] coupling strategy or to methyl ketone **6.1.2** for an aldol coupling approach. The impetus for this change of strategy was not for a lack of faith in our prior Julia[2] coupling strategy, but rather to increase the convergency of the approach. Elaborating the western fragment to the necessary PT sulfone **5.1.1** would involve significantly more synthetic operations than utilizing the proposed aldehyde **5.13.2**.

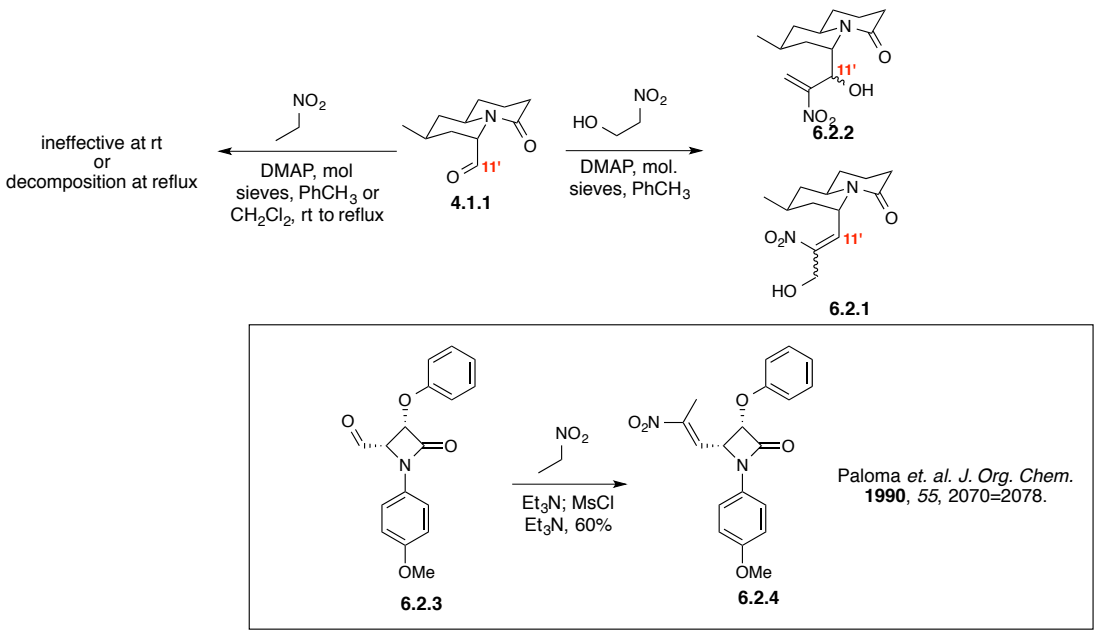


Scheme 6.1: Revised Retrosynthetic Coupling Strategy.

6.2: Attempted Synthesis of Methyl Ketone **6.1.2**.

With our new target of methyl ketone **6.1.2** in mind, we endeavored to achieve its synthesis (Scheme 6.2). We had hoped that a nitro aldol[3] / Nef reaction[4] sequence would be able to convert aldehyde **4.1.1** to methyl ketone **6.1.2**. A nitro aldol reaction has the advantage of typically being mild (an example is shown below of a substrate that contains a β-lactam)[5], and (in combination with a Nef reaction) allows umpolong type reactivity of the ultimate ketone carbon. Our initial reaction screening was of one-pot condensation conditions (DMAP, nitroethane, molecular sieves, rt to reflux, in $PhCH_3$ or CH_2Cl_2); however, neither set of conditions proved effective. Lower temperature conditions (rt and slightly above) were insufficient to facilitate condensation (returning starting materials) and higher temperatures caused decomposition. The next strategy we

explored was a two-step Henry reaction[6] / elimination protocol. Use of DMAP with nitroethane as the solvent did not induce C-C bond formation, even under such forcing conditions. To further explore the possibility of this Henry / nitro aldol reaction manifold, we utilized a more active nitro compound 2-nitroethanol, based on examples in the literature where it precedes in nitro aldol chemistry at lower temperatures than nitroethane (the reaction with cyclohexanal proceeds at rt).[7] Using catalytic DMAP and molecular sieves in refluxing $PhCH_3$, the nitro aldol reaction was apparently achieved (lower temperatures were ineffective), though unfortunately as a mixture of at least four compounds. We hypothesized this complex mixture of products was the result of the two possible elimination reactions and the two possible Henry products (**6.2.1** and **6.2.2**). The lack of success here lead us to abandon our Henry / nitro aldol strategy.

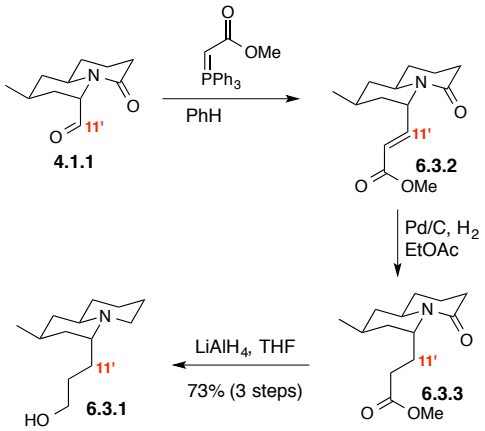


Scheme 6.2: Attempted Synthesis of Methyl Ketone **6.1.2**.

6.3: Efforts Towards the Synthesis of Vinyl Halide **6.1.1**.

For the synthesis of vinyl halide **6.1.1**, our approach hinged on the synthesis of amino alcohol **6.3.1** (Scheme 6.3). Wittig olefination of aldehyde **4.1.1** using the stabilized Wittig reagent $Ph_3P{=}CHCO_2Me$ gave α,β-unsaturated ester **6.3.2**. α,β-Unsaturated ester **6.3.2** was hydrogenated with Pd/C to provide ester **6.3.3**. For both **6.3.2** and **6.3.3**, the compound had to be carried on crude due to the inability to separate either compound from the triphenylphospineoxide side products. Our next

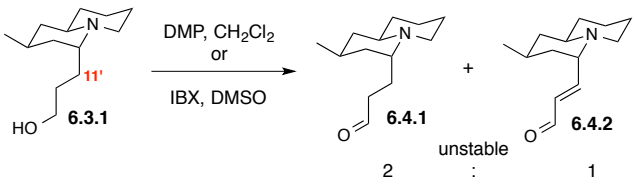
challenge was to achieve global reduction of ester **6.3.3** to amino alcohol **6.3.1**, which was accomplished by treatment with $LiAlH_4$. Interestingly, the reduction proceeded in good yield (73%), but a rather exhaustive work up (stirring with $NaOH_{(aq)}$ for several days) was required to liberate the amino alcohol **6.3.1** from the aluminum. We speculated that the difficulty of the work up was due to a possible chelation of each aluminum center by two molecules of amino alcohol **6.3.1**. The alcohol **6.3.1** could be readily purified by column chromatography or by conversion to the HCl salt, trituration and reformation of the free base.



Scheme 6.3: Synthesis of Amino Alcohol **6.3.1**.

With amino alcohol **6.3.1** in hand, we set out to synthesize a vinyl halide equivilant for our NHK[1] coupling strategy (Scheme 6.4). We believed that oxidation of the terminal alcohol of **6.3.1** would be quite

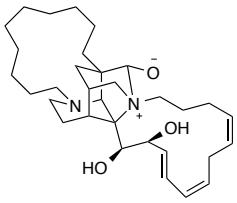
simple, as amino alcohols have precedent in the literature for ready oxidation.[8] (In retrospect we noted an absence of examples with a 1,6 relationship between the amine and the alcohol). When we explored this transformation however some interesting reactivity arose. Treatment of alcohol **6.3.1** with either DMP[9] in CH_2Cl_2, or IBX in DMSO produced a 2:1 mixture of what was tentatively assigned based on crude NMR to be the aldehyde **6.4.1** and enal **6.4.2**. Unfortunately, attempted purification of the mixture of aldehydes resulted only in decomposition. The high instability of aldehyde **6.4.1** led us to believe that something somewhat unexpected was occurring, as DMP is not to this author's knowledge capable of oxidizing a primary alcohol to the enal oxidation state.



Scheme 6.4: Oxidation of Amino Alcohol **6.3.1**.

We next set out to explore how hypervalent iodine oxidizing-reagents were converting amino alcohol **6.3.1** to the enal. We believed that the oxidation to the enal was related to the instability of the aldehyde product. Interestingly, Overmann and co-workers have reported the synthesis of (-)-sarain A **6.1** a natural product containing a 1-6 relationship

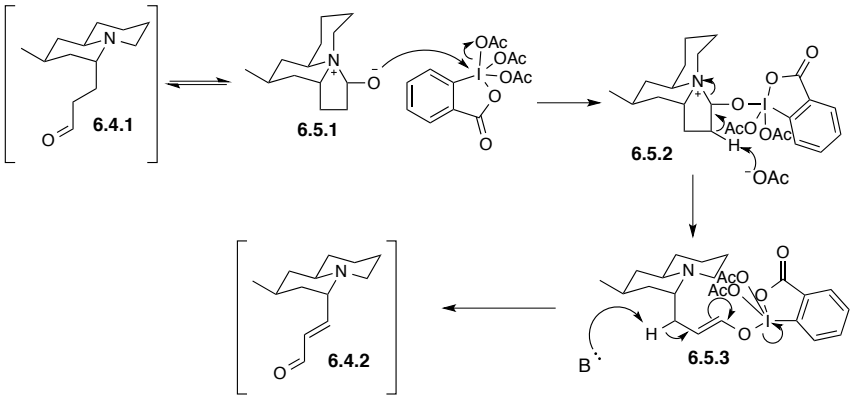
between a tertiary amine and an aldehyde, wherein the compound exists as a zwiterionic aminal (Figure 6.1). We believed that a zwiterioninc aminal similar to (-)-sarain A **6.1** could be responsible for the unusual reactivity of amino aldehyde **6.4.1**.



(-)-sarain A **6.1**

Figure 6.1: (-)-Sarain A **6.1**.

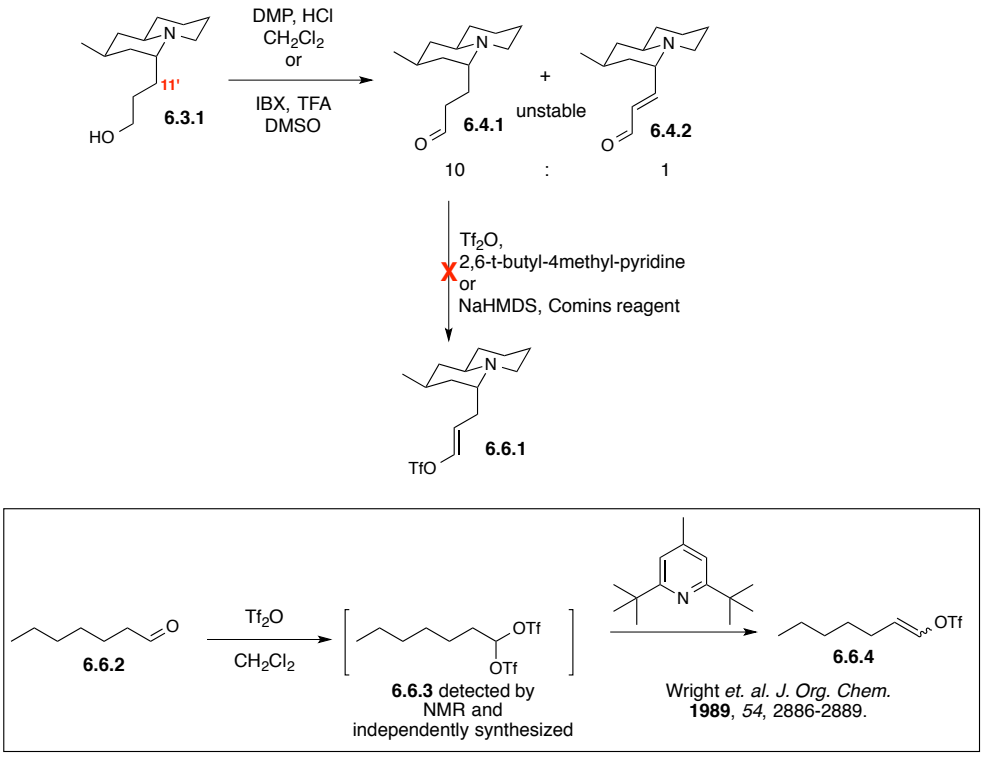
A possible mechanism whereby the zwiterionic aminal could facilitate the DMP oxidation to the enal is outlined below (Scheme 6.5). Our mechanism begins with the open form of aldehyde **6.4.1** being in equilibrium with the zwiterionic aminal **6.5.1**. The oxygen of zwiterion **6.5.1** could attack the iodine of DMP to form activated aminal **6.5.2**. Aminal **6.5.2** could be restored to electronic neutrality by elimination of the tertiary amine to form activated enol **6.5.3**. Activated enol **6.3.3** could then be eliminated in a 1,4-sense to form enal **6.4.2**.



Scheme 6.5: Proposed Mechanism of Enal **6.4.2** Formation.

We next explored the feasibility of our proposed mechanism by modifying our oxidation reaction conditions (Scheme 6.6). We speculated that our proposed enal formation mechanism would not be possible if the tertiary amine of amino alcohol **6.3.1** were protonated. [eg. attempted oxidation of amino alcohol in the presence of acid (DMP and HCl or IBX and TFA)]. Gratifyingly, both reactions produced much higher ratios of aldehyde to enal (10:1), as measured by crude NMR. With a more serviceable aldehyde ratio in hand, we moved our efforts towards the conversion of the aldehyde to the vinyl triflate **6.6.1**. Consulting the literature, there are relatively limited numbers of examples of triflation of aldehydes (all with Tf_2O),[10] and the mechanism proceeds differently than triflation of ketones. Triflation of aldehydes proceeds via formation of a di-triflated acetal, which is then eliminated to the vinyl triflate (Scheme 6.6).[11] Unfortunately, efforts to form the corresponding vinyl triflate utilizing the

Stang[12] triflation conditions (Tf_2O and 2,6-di-tertbutyl-4-methylpyridine in DCE), led to decomposition. We next screened triflation conditions that were effective with ketones (NaHMDS and Comins reagent in THF at -78°C), [13] which again led to decomposition. We attributed the ineffectiveness of our triflation chemistry to the high instability of aldehyde **6.4.1**, the instability likely being due to the postulated intramolecular aminal and we abandoned further efforts to employ the unstable aldehyde **6.4.1**.

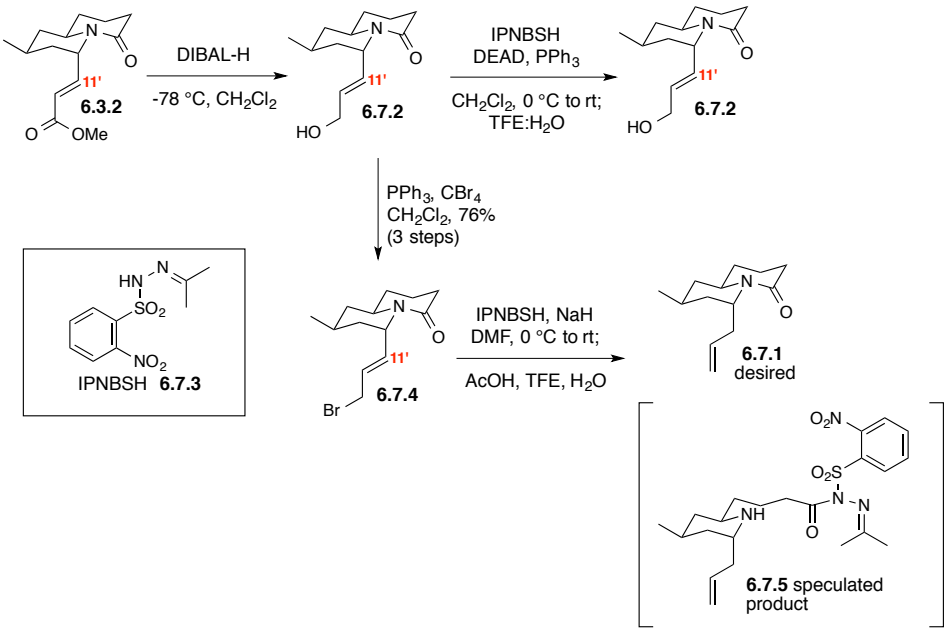


Scheme 6.6: Modified Oxidation of Amino Alcohol **6.3.1**.

6.4: Synthesis of Allylic Bromide **6.7.4** and Attempted Synthesis of Alkene **6.7.1**.

With our vinyl triflate route untenable, we endeavored to synthesize terminal alkene **6.7.1** (Scheme 6.7). We believed that terminal alkene **6.7.1** could be converted to a vinyl halide by Grubbs cross metathesis,[14] or potentially be used to couple the western and eastern fragments via a direct cross metathesis reaction.[15] Our route began with α,β-unsaturated ester **6.3.2**, which was reduced with DIBAL-H at -78°C to the allylic alcohol **6.7.2** in 95% yield over two steps. We hoped to utilize an allylic transposition reduction reaction developed by Movassaghi and co-workers to convert allylic alcohol **6.7.2** to the desired terminal alkene **6.7.1**.[16] Unfortunately, attempts to utilize the Mitsunobu protocol (IPNBSH **6.7.3**, DEAD and PPh_3 followed by treatment with TFE : H_2O) were ineffective, returning only the starting allylic alcohol **6.7.2** despite the apparent consumption of starting material by TLC. We hypothesized a deceptively encumbered environment around the alcohol may have inhibited the Mitsunobu reaction. With the Mitsunobu strategy ineffective, we elected to attempt a two-step protocol. The allylic alcohol **6.7.2** was converted into the allylic bromide **6.7.4** via an Appel[17] reaction in 68% yield. Next, displacement of the bromide with the anion derived from IPNBSH **6.7.3** and subsequent fragmentation with TFE / H_2O appeared to provide

terminal alkene **6.7.1** by NMR. The terminal alkene signal was evident but column chromatography appeared incapable of separating the alkene containing compound from an impurity, while the impurity appeared by NMR to be IPNBSH **6.7.3** the instability of the alkene containing compound to storage at -5 C° (decomposition to a complex mixture over 5 days) led us to speculate that perhaps a second equivalent of IPNBSH **6.7.3** had reacted with the amide moiety and created an unstable hydrazine amide that slowly decomposed (**6.7.5**). We speculated, that such a deleterious reaction pathway could be ameliorated by reducing the lactam moiety prior to the reductive isomerization.



Scheme 6.7: Synthesis of Allylic Bromide **6.7.4** and Attempted Synthesis of Alkene **6.7.1**.

6.5: Conclusions and Future Work.

The successful synthesis of allylic bromide **6.7.4** has been achieved and it should be easily converted to alkene **6.7.1.** Future work will focus on the conversion of allylic bromide **6.7.4 to** terminal alkene **6.7.1** and then finally to the corresponding vinyl halide by Grubbs cross metathesis. The vinyl halide will be utilized to NHK couple the two domains of the natural product.

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[1] (a) Okude, Y.; Hirano, S.; Hiyama, T.; Nozaki, H. *J. Am. Chem. Soc.* **1977**, *99*, 3179-3181. (b) Jin, H.; Uenishi, J.; Christ, W. J.; Kishi, Y. *J. Am. Chem. Soc.* **1986**, *108*, 5644-5646.

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Chapter 7: Conclusion.

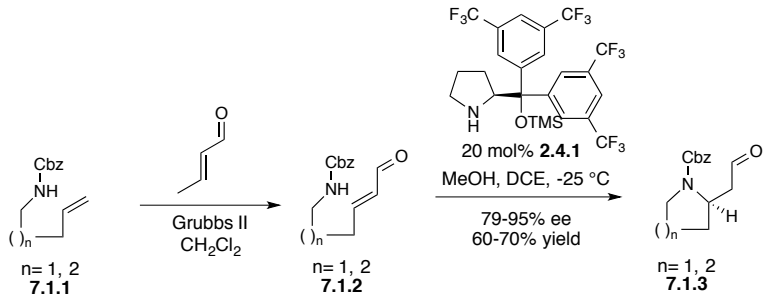
7.1: General Conclusion.

In our efforts to synthesize himeradine A **1.2** we have made significant strides, being well down the path towards a completed synthesis. We have synthesized aldehyde **4.1.1**, which represents all of the stereochemistry of the eastern fragment of himeradine A **1.2**, after a failed first generation route. We now are able to synthesize intermediates allowing for two potential coupling strategies, a Julia / Kocienski[1] coupling strategy already developed with a model system and an advanced intermediate for a potential NHK[2] coupling strategy. We are also well positioned with regards to the western fragment **5.13.1** with many of the challenges overcome with regards to its synthesis, the remaining challenges include the formation of the two remaining rings and the functional group interconversion of the methyl ester to allow for our coupling strategies.

7.2: Development of Organocatalyzed Heteroatom Michael Reaction.

We have successfully developed an organocatalyzed heteroatom Michael methodology for the construction of piperidine and piperizine rings

(Scheme 7.1).[3] Beginning with carbamate alkenes like **7.1.1** a Grubbs cross metathesis efficiently converts the alkene to the corresponding one carbon homologated enal like **7.1.2**. With the enals like **7.1.2** in hand treatment with Jorgenson catalyst **2.4.1** provides piperidine and piperizine aldehydes like **7.1.3** in good yield and enantioselectivity for a variety of substrates. This methodology was successfully leveraged to synthesize several natural products, pelletierine **2.9.3**, homopipecolic acid **2.9.4** and cermizine D **1.5** by another group member Mr. Naga Veerasamy.

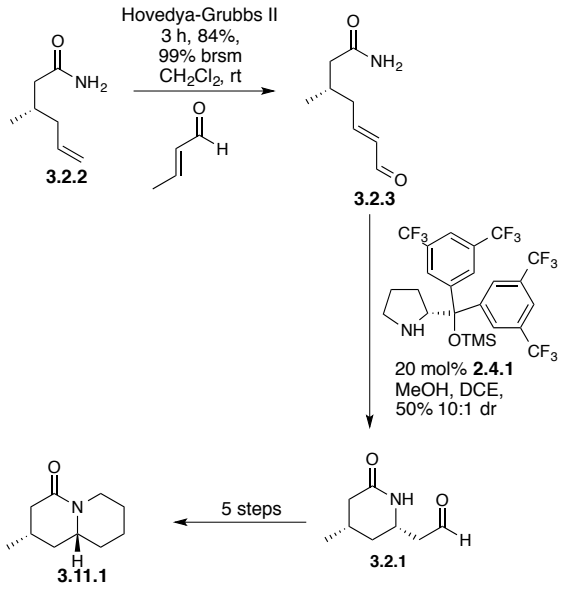


Scheme 7.1: Summary of Intramolecular Organocatalytic Michael Methodology.

7.3: First Generation Approach to the Eastern Fragment of Himeradine A **1.2**.

Our first generation approach to the eastern fragment of himeradine A **1.2** expanded our Intramolecular Organocatalytic Michael reaction to

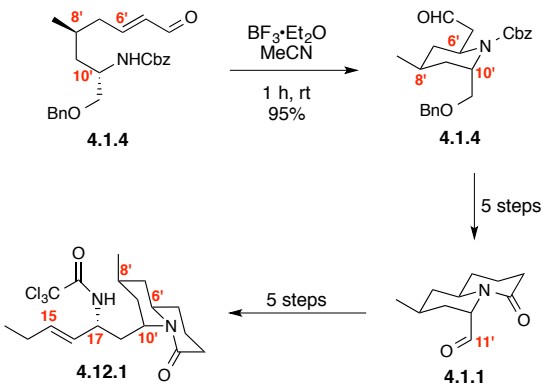
include amide nucleophiles and successfully formed the quinolizidine core of the eastern fragment of himeradine A **1.2** (Scheme 7.2).[4] Beginning with amide **3.2.2** we utilized a sequence similar to our prior intramolecular Michael work to form enal **3.2.3**, on which our Michael methodology was successful in forming aldehyde **3.2.1** though at higher temperatures. Further elaboration of aldehyde **3.2.1** formed the quinolizidine skeleton **3.11.1** in 5 steps however none of our routes were capable of functionalizing $C_{10'}$ leading us to abandon this route and attempt a new strategy. The synthesis of lactam **3.11.1** also represents the successful completion of a formal synthesis of C_5-*epi*-senepodine.



Scheme 7.2: Expansion of Intramolecular Organocatalytic Michael Methodology in Efforts Towards the Eastern Fragment of Himeradine A **1.2**.

7.4: Second Generation Approach to the Eastern Fragment of Himeradine A **1.2**.

Our successful second-generation approach to the eastern fragment of himeradine A **1.2** utilized a substrate controlled variant of our group's intramolecular heteroatom Michael reaction (Scheme 7.3).[1] Enal **4.1.5** was efficiently and selectively cyclized by Lewis acid catalysis to form piperidine ring aldehyde **4.1.4**. A five-step sequence elaborated aldehyde **4.1.4** to key quinolizidine aldehyde **4.1.1**, which contains all of the stereocenters of the eastern fragment of himeradine A **1.2** as well as a functional handle (aldehyde) that allows for several possible coupling strategies. A model coupling strategy was demonstrated on aldehyde **4.1.1** via a five step Julia / Kocienski, ethyl addition and Overmann rearrangement sequence to yield trichloro acid amide **4.12.1**. This accomplishment demonstrated the feasibility of our coupling strategy and the subsequent setting of the C_{17} stereochemistry, while aldehyde **4.1.1** could potentially be elaborated to allow for other coupling strategies.

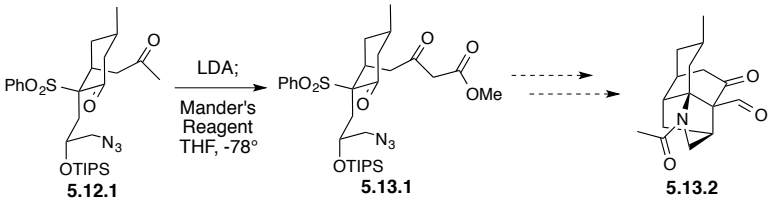


Scheme 7.3: Summary of Our Synthesis of the Eastern Fragment of Himeradine A **1.2**.

7.5: Synthetic Work Towards the Western Fragment of Himeradine A **1.2**.

Considerable effort was made in the continuation of the chemistry accomplished by Mr. Mrinmoy Saha on the western fragment, ultimately culminating in the synthesis of keto ester **5.13.1** (Scheme 7.4).[5] An effort was made to optimize the keto sulphone Michael reaction of **5.1.5**, where the modest improvement of utilizing proline **5.5** was discovered. We investigated the possibility of installing an alternate functional group at C_{10} but the necessary sulphone proved inactive as a nucleophile. We also explored several nitrogen acylation transfer strategies, as well as Mukayaima aldol coupling type strategies to poor results. Ultimately Mr. Mrinmoy Saha discovered that a Mander's reagent could effectively install the desired carbon on the alpha keto C_4 forming keto ester **5.13.1** that

should be able to be elaborated to aldehyde **5.13.2**. The key remaining challenge is the formation of the quaternary center of himeradine A **1.2**

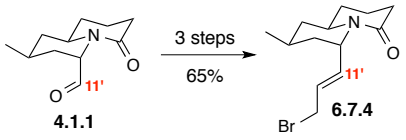


Scheme 7.4: Synthesis of Advanced Intermediate **5.13.1** in Our Work Towards Himeradine A **1.2**.

7.6: Modification of the Eastern Fragment of Himeradine A **1.2**.

With the synthesis of keto ester **5.13.1** we elected to slightly modify our coupling strategy to increase the convergency of our synthesis, imagining a possible NHK [6] coupling (Scheme 7.5). Beginning from previously synthesized aldehyde **4.1.1** we attempted to synthesize the two carbon extended aldehyde **6.4.1** but encountered an interesting zwiterionic aminal intermediate that was found to be quite unstable. We did succeed in the synthesis of allylic bromide **6.7.4** but unfortunately it could not be effectively allylicly transposed / reduced in isolation as it appeared that a second equivalent of IPNBSH **6.7.3** or possibly the eliminated *m*-nitrosulfinic acid further reacting with the amide. We believed this

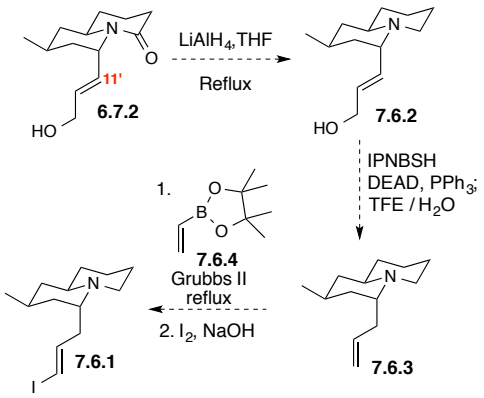
challenge could be overcome by reduction of the lactam prior to the reduction isomerization protocol.



Scheme 7.5: Modification of Aldehyde **4.1.1** to Allylic Bromide **6.7.4**.

7.7: Future Work.

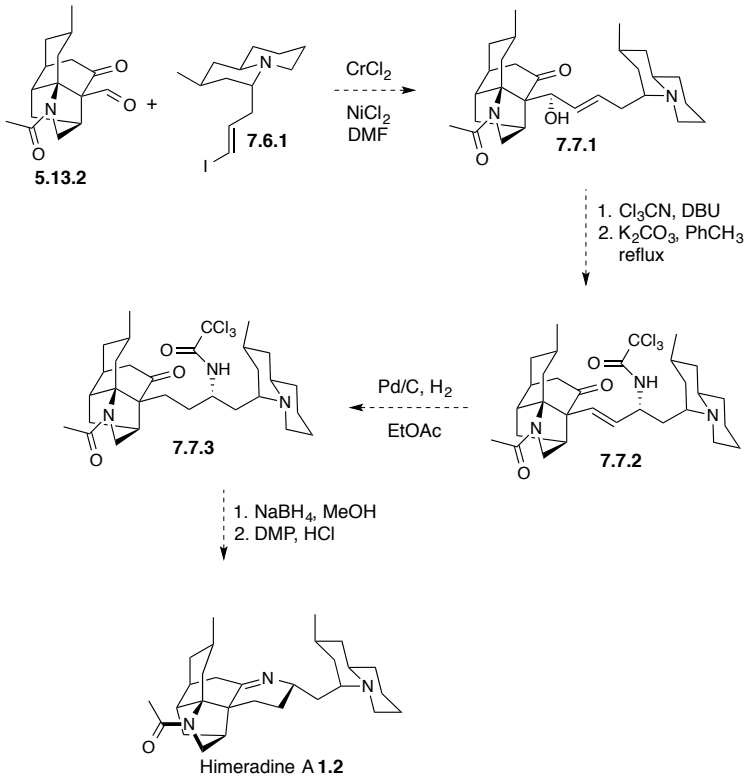
With the successful synthesis of allylic bromide **6.7.4** future work will focus on its elaboration towards vinyl iodide **7.6.1** (Scheme 7.6). Starting with previously synthesized allylic alcohol **6.7.2** reduction with $LiAlH_4$ should provide amino alcohol **7.6.2**. Use of the Movassaghi[7] protocol should convert amino alcohol **7.6.2** to terminal alkene **7.6.3**. Conversion of terminal alkene **7.6.3** to vinyl iodide **7.6.1** should be possible by Grubbs cross metathesis (the salt of the amine may be required to achieve effective cross metathesis) with vinyl pinacol boronate **7.6.4** followed by treatment with I_2 and NaOH.[8]



Scheme 7.6: Proposed Synthesis of Vinyl Iodide **7.6.1**.

With vinyl iodide **7.6.1** synthesized it should be a competent coupling partner for the proposed eastern domain fragment keto aldehyde **5.13.2** (Scheme 7.7). NHK[2] coupling of aldehyde **5.13.2** with vinyl iodide **7.6.1** should provide allylic alcohol **7.7.1**, we speculate that a chelation between the lone pairs of the aldehyde and the ketone should force the nucleophilic attack on the aldehyde to come from the bottom and desired face. Two-step Overmann[9] rearrangement of allylic alcohol **7.7.1** will yield allylic amide **7.7.2**. From allylic amide **7.7.2** completion of himeradine A should be relatively simple as the entire carbon skeleton will be assembled, hydrogenation (Pd/C, H_2) of allylic amide **7.7.2** will provide amide **7.7.3**. Completion of himeradine A **1.2** could be accomplished from amide **7.7.3** by reduction with $NaBH_4$, followed by acidic oxidation DMP / HCl; the $NaBH_4$ would cleave the trichloro acid amide and reduce the ketone moiety and the subsequent oxidation will return the alcohol to the ketone oxidation state, where upon intramolecular imine formation

should rapidly form himeradine A **1.2** and thus complete our synthetic effort.



Scheme 7.7: Proposed Strategy for the Completion of the Synthesis of Himeradine A **1.2**.

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[1] Collett, N. D.; Carter, R. G. *Org. Lett.,* **2011**, *13*, 4144-4147.

[2] (a) Okude, Y.; Hirano, S.; Hiyama, T.; Nozaki, H. *J. Am. Chem. Soc.* **1977**, *99*, 3179-3181. (b) Jin, H.; Uenishi, J.; Christ, W. J.; Kishi, Y. *J. Am. Chem. Soc.,* **1986**, *108*, 5644-5646.

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[6] (a) Okude, Y.; Hirano, S.; Hiyama, T.; Nozaki, H. *J. Am. Chem. Soc.* **1977**, *99*, 3179-3181. (b) Jin, H.; Uenishi, J.; Christ, W. J.; Kishi, Y. *J. Am. Chem. Soc.,* **1986**, *108*, 5644-5646.

[7] Movassaghi, M.; Ahmad, O. K. *J. Org. Chem.* **2007**, *72*, 1838-1841.

[8] Morrill, C.; Grubbs, R. H. *J. Org. Chem.,* **2003**, *68*, 6031-6034.

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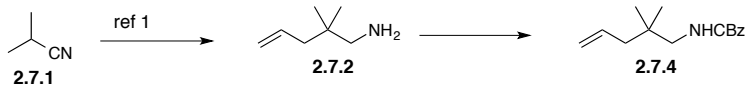
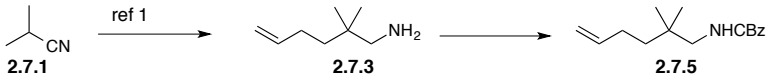
Chapter 8 Experimentals

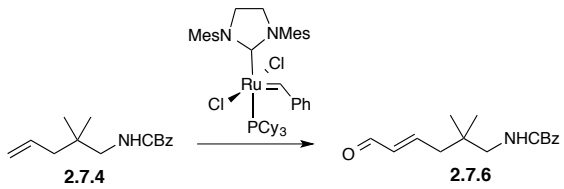


2.7.1 2.7.2 2.7.4

Carbamate 2.7.4: To a stirred solution of the crude known amine **2.7.2** (7.24 mmol) in THF (12 mL) and H_2O (12 mL) was added sequentially $NaHCO_3$ (563 mg, 7.24 mmol), NaOH (3 mL, 10% aq.) and Cbz-OnSu (1.67 mg, 7.24 mmol).[1] After 16 h, the organic solvent was removed in vacuo and the residual aqueous solution was extracted with Et_2O (3 X 30 mL). The combined organic layers were washed with sat. aq. NaCl (30 mL) and the dried extract ($MgSO_4$) was concentrated in vacuo. The crude product was purified by chromatography over silica gel, eluting with 0-20% EtOAc / Hexanes to yield **2.7.4** (1.22 g, 4.69 mmol, 65% over 3 steps) as a light yellow oil. IR (neat) 3432, 3341, 3062, 2959, 2916, 1733, 1533 cm^{-1}; NMR (400 MHz, $CDCl_3$) δ 7.33-7.39 (m, 5H), 5.76-5.83 (m, 1H), 5.13 (s, 2H), 4.94-5.05 (m, 2H), 4.79 (bs, 1H), 3.06 (d, *J* = 6.6 Hz, 2H), 2.03-2.06 (m, 2H), 1.28-1.40 (m, 4H), 0.90 (s, 6H); NMR (300 MHz, $CDCl_3$) δ 156.7, 139.2, 128.6, 128.4, 128.2, 114.2, 69.7, 66.7, 51.0, 38.8, 34.3, 28.3, 24.7; HRMS (EI+) calcd. For $C_{16}H_{23}NO_2$ (M+) 261.1729, found 261.1732.



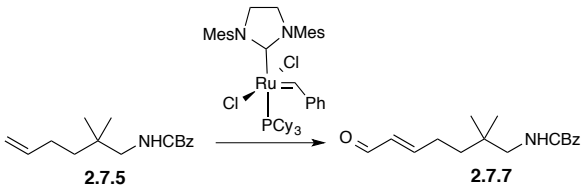
Carbamate 2.7.5: To a stirred solution of the crude known amine **2.7.3** (3.62 mmol) in THF (6 mL) and H_2O (6 mL) was added sequentially $NaHCO_3$ (304 mg, 3.62 mmol), NaOH (2 mL, 10% aq.) and Cbz-OnSu (902 mg, 3.62 mmol).[1] After 16 h, the organic solvent was removed in vacuo and the residual aqueous solution was extracted with Et_2O (3 X 30 mL). The combined organic layers were washed with sat. aq. NaCl (30 mL) and the dried extract ($MgSO_4$) was concentrated in vacuo. The crude product was purified by chromatography over silica gel, eluting with 0-20% EtOAc / Hexanes to yield **2.7.5** (444.5 mg, 1.81 mmol, 50% over 3 steps) as a light yellow oil. IR (neat) 3343, 3071, 3033, 2960, 1698, 1639 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.33-7.39 (m, 5H), 5.74-5.90 (m, 1H), 5.13 (s, 2H), 5.03-5.10 (m, 2H), 4.87 (bs, 1H), 3.05 (d, *J* = 6.6 Hz, 2H), 2.00 (d, *J* = 7.5 Hz, 2H), 0.90 (s, 6H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 156.7, 136.7, 134.7, 128.5, 128.4, 128.2, 117.6, 66.7, 50.9, 44.3, 34.8, 24.7; HRMS (EI+) calcd. For $C_{15}H_{21}O_2N$ (M+) 247.1572, found 247.1580.



2.7.4 **2.7.6**

Enal 2.7.6: To a stirred pressure vessel containing a solution of **2.7.4** (100 mg, 0.383 mmol) in CH_2Cl_2 (10 mL) was added sequentially crotonaldehyde (134 mg, 0.32 mL, 1.92 mmol) and aged[†] 2nd generation Grubbs catalyst (16 mg, 0.019 mmol, 5 mol %). The vessel was sealed and heated to 45 °C. After 48 h, the solution was cooled to rt and concentrated in vacuo. The crude product was purified by chromatography over silica gel, eluting with 0-30% EtOAc / Hexanes to yield **2.7.6** (89.8 mg, 0.310 mmol, 81%) as a brownish oil. IR (neat) 3344, 2959, 2864, 2722, 1689, 1653, 1539, 1455, 1242 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.49 (d, J = 8.1 Hz, 1H), 7.30-7.30 (m, 5H), 6.82 (m, 1H), 6.12 (dd, J = 8.4, 15.6 Hz, 1H), 5.11 (s, 2H), 4.80-4.90 (m, 1H), 3.06 (d, J = 6.6 Hz, 2H), 2.30-2.30 (m, 2H), 1.36-1.42 (m, 2H), 0.92 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.1, 159.0, 156.7, 136.5, 132.7, 128.6, 128.2, 66.8, 50.6, 37.2, 34.5, 27.5, 24.7; HRMS (EI+) calcd. For $C_{17}H_{23}NO_3$ (M+) 289.1678, found 289.1688.

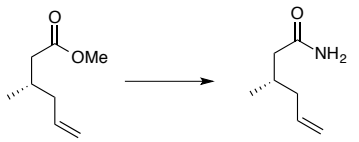
[†] Catalyst was left open to the air for approximately one week.



2.7.5 **2.7.7**

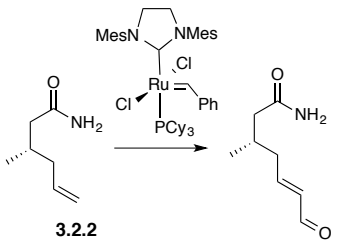
Enal 2.7.7: To a stirred pressure vessel containing a solution of **2.7.5** (200 mg, 0.796 mmol) in CH_2Cl_2 (20 mL) was added sequentially aldehyde crotonaldehyde (279 mg, 3.98 mmol, 0.324 mL) and aged[‡] 2nd generation Grubbs catalyst (33.8 mg, 0.040 mmol, 5 mol %). The vessel was sealed and heated to 45 °C. After 48 h, the solution was cooled to rt and concentrated in vacuo. The crude product was purified by chromatography over silica gel, eluting with 0-30% EtOAc / Hexanes to yield **2.7.7** (160 mg, 0.573 mmol, 72%) as a brownish oil. IR (neat) 3354, 2958, 2864, 2713, 1699, 1455, 1417, 1280 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.53 (d, J = 7.8 Hz, 1H), 7.30- 7.38 (m, 5H), 6.90 (m, 1H), 6.13 (dd, J =7.8, 15.3 Hz, 1H), 5.12 (s, 2H), 4.93 (bs, NH), 3.10 (d, J = 6.6 Hz, 2H), 2.26 (d, J = 7.8 Hz, 2H), 1.03 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 193.7, 156.7, 154.7, 136.4, 135.5, 128.6, 128.2, 66.9, 50.9, 42.7, 35.8, 24.9; HRMS (EI+) calcd. For $C_{16}H_{21}NO_3$ (M+) 275.1522, found 275.1513.

[‡] Catalyst was left open to the air for approximately one week.



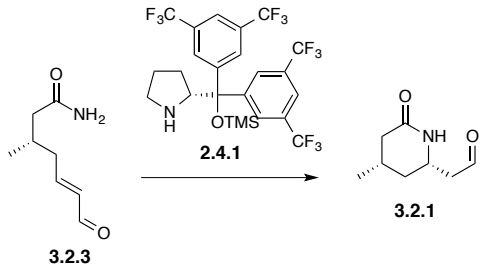
3.3.3 3.2.2

Amide 3.2.2: To a stirred solution of **7** (0.140 g, 0.986 mmol) in CH_2Cl_2 (5 mL) was added di-methylaluminumamide (0.733 mL, 1.13 mmol, 1.5 M in CH_2Cl_2). The reaction was warmed to 30 °C and stirred 16 h, di-methylaluminumamide (0.30 mL, 0.45 mmol, 1.5 M in CH_2Cl_2) was added. After 24 h, the reaction was quenched with MeOH (0.5 mL) and allowed to stir for ten min, sat. aq. Rochelle's salt (5 mL) was added and stirred 10 min to form two clear layers. The reaction was extracted with CH_2Cl_2 (3 x 15 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10-50% EtOAc / hexanes, to give **3.2.2** (105 mg, 0.83 mmol, 85%) as a white solid. Mp 91.7-93.2 $^{\circ}$C; $[\alpha]_D^{23}$ = +5.98° (c = 1.07, $CHCl_3$); IR (neat) 3352, 3183, 2954, 2911, 1664, 1631, 1413, 1152,988, 906 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.48-5.83 (m, 3H), 5.05 (d, J = 12.4 Hz, 2H), 2.28 (dd, J_1 = 13.6, J_2 = 5.2 Hz, 1H), 1.97-2.13 (m, 4H), 1.00 (d, J = 6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 136.5, 116.6, 42.8, 41.0, 30.4, 19.5; HRMS (EI+) calcd. for $C_7H_{13}NO$ (M+) 127.0997, found 127.0993.

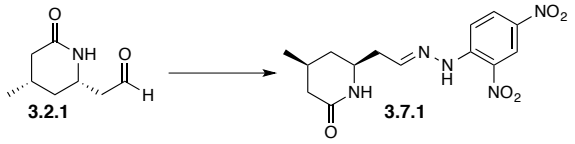


3.2.2 **3.2.3**

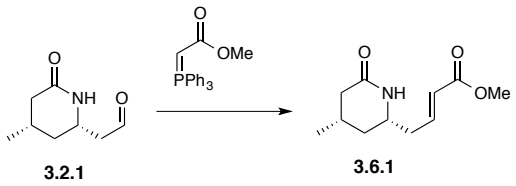
Enal 3.2.3: To a stirred solution of **3.2.2** (0.100 g, 0.79 mmol) in CH_2Cl_2 (15 mL) was added crotonaldehyde (0.4 mL, 280 mg, 3.968 mmol), and 2nd Gen. Grubbs catalyst (33 mg, 0.0389 mmol). After 3 d, the reaction was concentrated *in vacuo* and loaded directly onto silica gel and purified by chromatography, eluting with 50-100% EtOAc / hexanes, to give **3.2.3** (0.096 g, 0.67 mmol, 84%) as a brown oil: $[\alpha]_D^{23} = -7.93^{\circ}$ (c =1.35, $CHCl_3$); IR (neat) 3350, 3198, 2960, 1684, 1405, 1149, 978 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.48 (d, *J* = 7.8 Hz, 1H), 6.77-6.87 (m, 1H), 6.07-6.14 (m, 2H), 5.88 (brs, 1H), 2.39-2.44 (m, 1H), 2.17-2.30 (m, 3H), 2.06-2.12 (m, 1H) 1.00 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.9, 173.9, 156.2, 134.6, 42.5, 39.6, 29.9, 19.8; HRMS (EI+) calcd. for $C_8H_{13}NO_2$ (M+) 155.0946, found 155.0944.



Aldehyde 3.2.1: To a stirred solution of **3.2.3** (0.0574 g, 0.401 mmol) in MeoH (2 mL) was added **2.4.1** (0.0479 g, 0.080 mmol) in DCE (1.9 mL). After 4 d, the reaction was concentrated *in vacuo* and filtered through a pad of silica gel, eluting in 100% EtOAc which was concentrated *in vacuo*. This crude mixture was dissolved in CH_2Cl_2 (2 mL) and stirred with 10% aq. HCl (3 mL). After 2 h, extracted with CH_2Cl_2 (10 mL x 2). The combined organic layers are dried ($MgSO_4$) and concentrated *in vacuo* to give **3.2.1** (10:1 dr) (0.034 mg, 0.238 mmol, 59%) as a greenish oil: $[\alpha]_D^{23}$ = +10.43° (c = 1.63, $CHCl_3$); IR (neat) 3213, 2955, 1722, 1660, 1457, 1408, 1338, 1280, 1173, 1137, 1098, 1049, 682 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.80 (s, 1H), 6.14 (brs, 1H), 3.90-3.97 (m, 1H), 2.75-2.82 (dd, J_1 = 18.6, J_2 = 3.9 Hz, 1H), 2.56-2.65 (dd, J_1 = 18.6, J_2 = 8.7 Hz, 1H), 2.44-2.49 (dd, J_1 = 13.2, J_2 = 2.4 Hz, 1H), 1.86-2.01 (m, 4H), 1.06 (d, J = 12.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.0, 172.4, 50.5, 47.5, 39.6, 37.1, 27.4, 21.3; HRMS (EI+) calcd. For $C_8H_{13}NO_2$ (M+) 155.0946, found 155.0921.

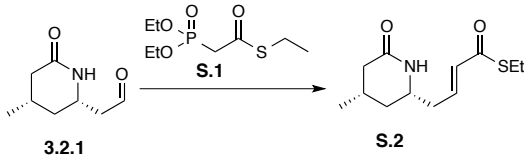


2,4-DNP: (Partial characterization) To a stirred solution of **3.2.1** (0.020 g, 0.14 mmol) in PhH (1.5 mL) was added sequentially 2,4-DNP (0.066 g, 0.34 mmol) and $TsOH \cdot H_2O$ (5 mg, 0.028 mmol). The reaction was refluxed 10 min then concentrated *in vacuo* and loaded onto a pad of silica gel, purified by chromatography eluting in 30-40% EtOAc / Hexanes to give to give **3.7.1** (7 mg, 0.021 mmol, 16%) as orange/red crystals: ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.15 (s, 1H), 9.15 (d, J = 2.7 Hz, 1H), 8.35 (dd, J_1 = 9.6 Hz, J_2 = 2.4 Hz, 1H), 7.91 (d, J = 9.3, 1H), 7.59 (m, 1H), 6.27 (bs, 1H), 3.88 (m, 1H), 2.71-2.52 (m, 3H), 2.06-1.90 (m, 3H), 1.10 (m, 4H); HRMS (EI+) calcd. For $C_{14}H_{17}N_5O_5$ (M+) 335.12297, found 335.12352.

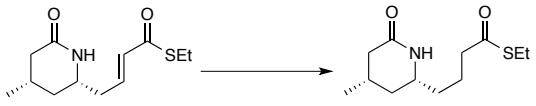


3.2.1 3.6.1

Methyl Ester 3.6.1: To a stirred solution of **3.2.1** (0.020 g, 0.140 mmol) in PhH (2 mL) at room temperature was added $Ph_3P{=}CHCO_2Me$ (0.057 g, 0.147 mmol). After 18 h, the reaction was concentrated *in vacuo* and loaded directly onto silica gel and purified by chromatography, eluting with 60-100% EtOAc / hexanes, to give **3.6.1** (0.0251 g, 0.119 mmol, 85%) as a white solid. Mp 106.5-109 $^{\circ}$C; $[\alpha]_D^{23}$ = -13.44° (c = 0.9, $CHCl_3$); IR (neat) 3194, 3074, 2949, 2927, 2845, 1723, 1658, 1560, 1435, 1408, 1320, 1217, 1173, 1135, 994, 819, 716 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.83-6.88 (m, 1H), 6.40 (brs, 1H), 5.94 (d, *J* = 15.6 Hz, 1H), 3.75 (s, 3H), 3.54-3.57 (m, 1H), 2.36-2.45 (m, 3H), 1.86-1.92 (m, 3H), 1.02 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 166.3, 143.1, 124.7, 51.6, 39.6, 39.5, 37.1, 27.5, 21.4; HRMS (EI+) calcd. For $C_{11}H_{17}NO_3$ (M+) 211.1209, found 211.1192.

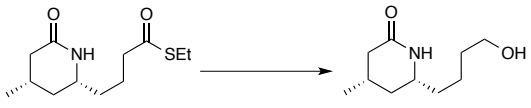


Thioester S.2: To a stirred solution of **3.2.1** (0.280 g, 1.16 mmol) in CH_3CN (5.8 mL) was added sequentially LiCl (0.059 g, 1.39 mmol), DIPEA (0.150 g, 1.16 mmol). After 10 min, the solution was cooled to 0°C. After 5 min, a precooled (0°C) solution of **S.1**[2] (0.18 g, 1.16 mmol) in CH_3CN (6 mL) was cannulated into the reaction (2 X 0.5 mL MeCN rinse). The reaction was allowed to warm to r.t over 10 min. After an additional 30 min, the reaction was quenched with aq. HCl (2 mL, 1.22 M) and extracted with EtOAc (3 X 20 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 95% EtOAc / Hexanes to give **S.2** (0.160 g, 0.66 mmol, 57%) as a white solid. Mp 91.7-93.2 °C; $[\alpha]_D^{23}$ = -34.3° (c = 0.525, $CHCl_3$); IR (neat) 2954, 2927, 2862, 1662 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.76 (m, 1H), 6.20 (d, *J* = 18.8 Hz, 1H), 5.97 (bs, 1H), 3.56 (m, 1H), 2.97 (m, 2H), 2.50-2.25 (m, 3H), 2.00-1.80 (m, 3H) 1.30 (t, 3H), 1.05 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.4, 172.9, 138.8, 131.7, 51.6, 39.5, 39.0, 36.8, 27.4, 23.1, 21.4, 14.7; HRMS (EI+) calcd. for $C_{12}H_{20}O_2SN$ (M+) 242.1215, found 242.1414.



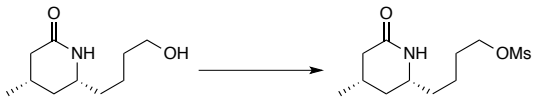
S.2 **3.9.1**

Thioester 3.9.1: To a stirred solution of **S.2** (0.615 g, 2.54 mmol) in EtOAc (60 mL) at rt was added Pd/C (10 wt % palladium on carbon) (0.490 g, 8 wt %), the reaction flask was purged with a balloon of H_2 gas for 10 min, a second balloon of H_2 gas was added. After 2 d, the H_2 atmosphere is purged with argon for 5 min. The reaction was then filtered through celite, rinsed with EtOAc (200 mL), concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10% MeOH / EtOAc, to give **3.9.1** (0.615 g, 2.54 mmol, 99%) as a white wax: $[\alpha]_D^{23}$ = -2.46° (c = 0.65, $CHCl_3$); IR (neat) 3215, 2954, 2927, 1684, 1653 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.7 (bs, 1H), 3.39 (m, 1H), 2.88 (m, 2H), 2.57 (m, 2H), 2.43 (bd, 1H), 1.50 (m, 2H), 1.27 (t, 3H) 1.05 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.0, 172.4, 52.6, 43.5, 39.7, 37.1, 36.1, 27.6, 23.3, 21.5, 21.0, 14.8. HRMS (EI+) calcd for $C_{12}H_{20}O_2SN$ (M+) 242.1215, found 242.1214.



3.9.1 3.9.2

Alcohol 3.9.2: To a stirred solution of **3.9.1** (0.082 g, 0.34 mmol) in MeoH/THF 1:1 (4 mL) at rt was added $NaBH_4$ (0.100 g, 2.63 mmol) in small portions over 30 min. After 1 h, the reaction was quenched with sat. aq. $NaHCO_3$ (6 mL) and extracted with EtOAc (3 X 10 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel eluting in 20% MeOH / EtOAc to give **3.9.2** (0.061 g, 0.328 mmol, 98%) as a white wax: $[\alpha]_D^{23}$ = -21.6° (c = 0.37, $CHCl_3$); IR (neat) 3286, 2933, 1653 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.8 (bs, 1H), 3.67 (m, 2H), 3.39 (m, 1H), 2.44 (bd, 2H), 1.95-1.84 (m, 4H), 1.66-1.55 (m, 7H), 1.28 (m, 2H), 1.06 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 61.9, 52.9, 39.5, 37.5, 36.2, 32.2, 27.6, 21.5, 21.2; HRMS (EI+) calcd. For $C_{10}H_{19}NO_2$ (M+) 185.14158, found 155.14196.

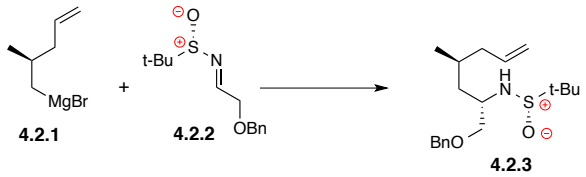


3.9.2 **3.11.2**

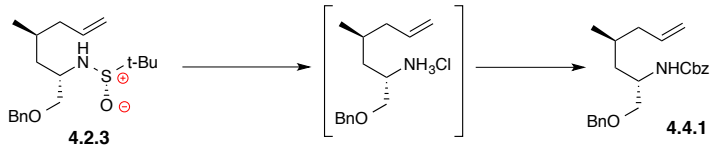
Mesylate 3.11.2: To a stirred solution of **3.9.2** (0.120 g, 0.648 mmol) in THF (30 mL) at 0 °C was added sequentially Et_3N (0.131 g, 1.296 mmol) and MsCl (0.118 g, 1.038 mmol). After 15 min, the ice bath was removed and the reaction was allowed to warm to rt. After 45 min, the reaction was quenched with H_2O (15 mL) and extracted with EtOAc (3 X 15 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10% MeOH / EtOAc, to give **3.11.2** (0.150 g, 0. mmol, 88%) as a white solid. Mp 90.0-91.5 $^{\circ}$C; $[\alpha]_D^{23}$ = -33.41° (c = 0.82, $CHCl_3$); IR (neat) 3177, 2943, 2916, 1653 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.45 (bs, 1H), 4.24 (t, *J* = 6.4 Hz, 2H), 3.39 (m, 1H), 3.02 (s, 3H), 3.54-3.57 (m, 1H), 2.41 (m, 2H), 1.92-1.84 (m, 3H), 1.83-1.73 (m, 2H), 1.60-1.49 (m, 4H), 1.02 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 69.5, 52.7, 39.7, 37.4, 37.1, 36.3, 29.0, 27.6, 21.5, 21.1; HRMS (EI+) calcd. For $C_{11}H_{21}NO_4S$ (M+) 263.1191, found 263.1197.

3.11.2 S.3

Iodide S.3: To a stirred solution of **3.11.2** (0.070 g, 0.268 mmol) in acetone (10 mL) was added NaI (0.321 g, 2.144 mmol) and the reaction was heated to reflux. After 2 h, the reaction was concentrated *in vacuo*, and diluted with 9:1 EtOAc:Hexanes (50 mL). This organic solution washed with sat. aq. $NaSO_4$ (15 mL), sat. aq. $NaHCO_3$ (15 mL) and sat. aq. NaCl (15 mL). The dried extract ($MgSO_4$) was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10% MeOH / EtOAc, to give **S.3** (0.071 g, 0.236 mmol, 88%) as a yellow wax: $[\alpha]_D^{23}$ = -10.58° (c = 1.55, $CHCl_3$); IR (neat) 2925, 2854, 1653 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.1 (bs, 1H), 3.40 (m, 1H), 3.20 (m, 2H), 2.43 (m, 2H), 1.92-1.80 (m, 6H), 1.52-1.47 (m, 4H), 1.02 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 52.8, 39.7 37.3, 35.9, 33.0, 27.6, 26.0, 21.5, 6.4; HRMS (EI+) calcd. For $C_{10}H_{18}NOI$ (M+) 295.0433, found 295.0422.



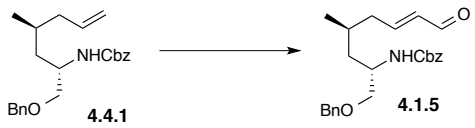
Sulfinamide 4.2.3: To a stirred solution of sulfinimine **4.2.1**[3] (0.780 g, 3.0 mmol) in $PhCH_3$ (45 mL) at -78 °C was added Grignard reagent **4.2.2**[4] (8.0 mL, ~3.0 mmol, 0.375 M in THF). After 3.5 h, the reaction was quenched by sat. aq. Na_2SO_4 (0.1 mL) and then dried by addition of solid $MgSO_4$. The resulting slurry was filtered through celite (EtOAc, 150 mL), concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 50-70% EtOAc / hexanes, to give sulfinamide **4.2.3** (0.900 g, 2.67 mmol, 89%) as an oil. $[\alpha]_D^{23}$ = +16.6° (*c* = 2.2, $CHCl_3$); IR (neat) 2959, 2927, 2861, 1324 1195 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.25-7.33 (m, 5H), 5.72 (m, 1H), 5.01 (d, *J* = 2.4 Hz, 2H), 4.59 (d, *J* = 11.4 Hz, 1H), 4.47 (d, *J* = 12.0 Hz, 1H), 3.63-3.75 (m, 2H), 3.47-3.51 (m, 2H), 2.09 (m, 1H), 1.87 (m, 1H), 1.64 (m, 1H), 1.47 (m, 2H), 1.45 (s, 9H), 0.9 (d, *J* = 6.4 Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.2, 136.7, 128.4, 127.7, 127.6, 116.1, 73.3, 73.1, 55.7, 54.1, 40.5, 40.0, 29.3, 22.7, 20.0 ppm; HRMS (CI+) calcd. for $C_{19}H_{32}NO_2S$ (M+H) 338.2154, found 338.2145.



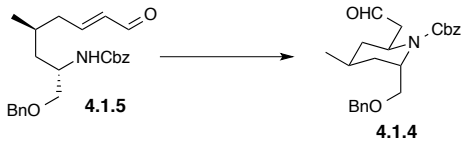
Cbz-amine 4.4.1: To stirred solution of sulfinimine **4.2.3** (3.35 g, 9.94 mmol) in MeOH (100 mL) was added HCl (1.67 mL, 19.88 mmol, 12 M in H_2O). After 2 h, the reaction was concentrated *in vacuo* and filtered through a plug of silica gel washing first with EtOAc (500 mL) then 10% MeOH / CH_2Cl_2 (500 mL). all MeOH / CH_2Cl_2 filtrate was concentrated *in vacuo* to yield ~2.69g of the crude amine hydrochloride, the material was carried on crude.

To a stirred solution of crude amine hydrochloride (~2.69 g, ~9.94 mmol) in acetone / H_2O (1:1) (80 mL) at r.t. was added sequentially K_2CO_3 (4.14 g, 29.98 mmol) and CbzCl (12.0 mL, 19.98 mmol, 33% in $PhCH_3$). After 1 h, the reaction was quenched by sat. aq. $NaHCO_3$ (180 mL) and extracted with CH_2Cl_2 (3 X 200 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 15-20% EtOAc / hexanes, to give Cbz-amine **4.4.1** (3.33 g, 9.05 mmol, 91%) as a colorless oil. $[\alpha]_D^{23}$ = -9.0° (*c* = 0.5, $CHCl_3$); IR (neat) 2958, 2853, 2758, 1747 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29-7.42 (m, 10H), 5.79-5.54 (m, 1H), 5.07-5.18 (m, 5H), 4.51-4.61 (m, 2H), 4.00 (bs, 1H), 3.53 (bm, 2H), 2.19 (bm, 1H), 1.99 (bm, 1H), 1.63 (m, 2H), 1.43 (m, 1H), 0.99 (d, *J* = 5.6 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.1, 138.2, 136.9, 136.8, 128.5, 128.4, 128.1, 127.7, 127.7, 116.2, 73.2, 71.8, 66.6, 49.2, 41.0,

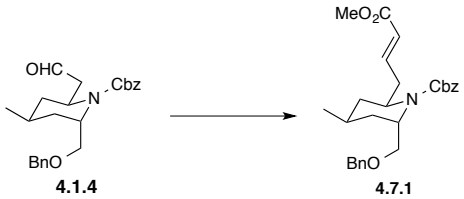
38.7, 29.6, 19.8 ppm; HRMS (CI+) calcd. for $C_{23}H_{30}NO_3$ (M+H) 368.2226, found 368.2227.



Enal 4.1.5: To a stirred solution of Cbz-amine **4.4.1** (0.460 g, 1.25 mmol) in CH_2Cl_2 (12.5 mL) at r.t was added sequentially crotonaldehyde (0.439 g, 0.52 mL, 6.26 mmol) and Grubbs Hoveyda II (15.6 mg, 0.025 mmol). After 60 min, the reaction was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 25-35% EtOAc / hexanes, to give enal **4.1.5** (0.491 g, 1.23 mmol, 98%) as a brown oil. $[\alpha]_D^{23}$ = -21.9° (*c* = 1.3, $CHCl_3$); IR (neat) 3336, 2954, 2922, 2856, 1718, 1696 cm^{-1}; ^1H NMR (400 MHz, $CHCl_3$) δ 9.51 (d, *J* = 8.0 Hz, 1H), 7.29-7.39 (m, 10H), 6.76 (m, 2H), 6.14 (m, 1H), 5.13 (s, 2H), 5.06 (d, *J* = 9.2 Hz, 1H), 4.48-4.58 (m, 2H), 3.92-3.98 (bs, 1H), 3.51 (m, 2H), 2.48 (m, 1H), 2.17 (m, 1H), 1.75 (m, 1H), 1.51-1.60 (m, 2H), 0.98 (d, *J* = 6.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.8, 157.0, 156.0, 137.9, 136.6, 134.4, 128.5, 128.5, 128.1, 128.1, 128.1, 127.8, 127.7, 73.3, 71.8, 66.7, 48.9, 39.5, 39.2, 29.4, 20.0 ppm; HRMS (CI+) calcd. for $C_{24}H_{30}NO_4$ (M+H) 396.2175, found 396.2157.

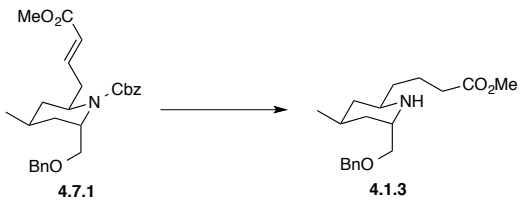


Aldehyde 4.1.4: To a stirred solution of enal **4.1.5** (0.319 g, 0.80 mmol) in CH_3CN (12 mL) at r.t. was added $BF_3{\cdot}Et_2O$ (0.22 g, 0.20 mL, 1.58 mmol). After 60 min, the reaction was quenched by sat. aq. $NaHCO_3$ (30 mL) and extracted with CH_2Cl_2 (3 X 40 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 30% EtOAc / hexanes, to give aldehyde **4.1.4** (0.311 g, 1.0 mmol, 98%) as a light brown / yellow oil. $[\alpha]_D^{23}$ = -17.8° (*c* = 0.9, $CHCl_3$); IR (neat) 2949, 2916, 2862, 1734 cm^{-1}; ^1H NMR (400 MHz, $CHCl_3$) δ 9.74 (s, 1H), 7.29-7.38 (m, 10H), 5.09 (s, 2H), 4.49-4.57 (m, 3H), 3.95-3.99 (s, 1H), 3.65-3.69 (m, 1H), 3.56-3.60 (m, 1H), 3.12-3.24 (m, 1H), 2.58 (dd, J_1 = 17.2, J_2 = 5.6, 1H), 1.80-1.98 (m, 2H), 1.70-2.80 (m, 2H), 1.19-1.36 (m, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.6, 156.1, 138.2, 136.6, 128.5, 128.4, 128.0, 128.0, 127.7, 127.6, 73.1, 69.3, 67.0, 52.3, 67.0, 52.7, 49.2, 48.1, 39.1, 33.2, 24.9, 22.5 ppm; HRMS (CI+) calcd. for $C_{24}H_{30}NO_4$ (M+H) 396.2175, found 396.2180.



4.1.4 **4.7.1**

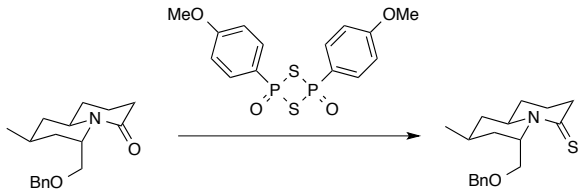
Ester 4.7.1: To a stirred solution of aldehyde **4.1.4** (0.206 g, 0.52 mmol) in PhH (13 mL) at r.t. was added $Ph_3P{=}CO_2Me$ (0.182 g, 0.54 mmol). After 16 h, the reaction was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 30-40% EtOAc / hexanes, to give ester **4.7.1** (0.232 g, 0.51 mmol, 99%) as a milky oil. $[\alpha]_D^{23}$ = -21.5° (*c* = 0.8, $CHCl_3$); IR (neat) 2943, 2867, 1718, 1696 cm^{-1}; ^1H NMR (400 MHz, $CHCl_3$) δ 7.29-7.40 (m, 10H), 6.93 (m, 1H), 5.89 (d, *J* = 15.6 Hz, 1H), 5.14 (s, 2H), 4.53 (m, 2H), 4.33 (m, 1H), 3.75 (s, 3H), 3.67-3.72 (m, 2H), 3.53 (m, 1H), 2.83-2.91 (m, 1H), 2.54-2.68 (m, 1H), 2.00 (bd, 1H), 1.79-1.86 (m, 2H), 1.43 (m, 1H), 1.01-1.30 (m, 1H), 1.01 (d, *J* = 6.4 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 156.0, 146.2, 138.3, 136.7, 128.5, 128.4, 128.0, 127.6, 122.9, 73.0, 69.9, 67.0, 52.2, 52.1, 67.0, 38.4, 34.5, 32.2, 23.4, 23.2 ppm; HRMS (CI+) calcd. for $C_{27}H_{34}NO_5$ (M+H) 452.2437, found 452.2437.



Aminoester 4.1.3: To a stirred solution of ester **4.7.1** (0.213 g, 0.483 mmol) in EtOAc (18 mL) at r.t. under argon was added Pd/C (0.218 g, 10 wt%), the argon was then removed by flushing with a balloon of H_2 gas. After 5 min, the balloon was replaced with a new baloon. After 18 h, the hydrogen was removed by flushing with argon and filtered through celite washing with 10% MeOH / EtOAc (150 mL). The filtered extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10% MeOH / EtOAc, to give aminoester **4.1.3** (0.133 g, 0.483 mmol, 86%) as a colorless oil. $[\alpha]_D^{23}$ = +3.0° (*c* = 1.0, $CHCl_3$); IR (neat) 2949, 2916, 1734 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29-7.38 (m, 5H), 4.56 (m, 2H), 3.68-3.71 (m, 1H), 3.68 (s, 3H), 3.28-3.32 (m, 2H), 2.55-2.67 (m, 2H), 2.32 (t, *J* = 14.8, 2H), 1.60-1.67 (m, 3H), 1.52-1.55 (m, 2H), 1.31-1.36 (m, 3H), 0.88 (d, *J* = 4.8 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.9, 138.3, 128.4, 127.8, 127.6, 75.1, 73.4, 56.2, 55.7, 51.5, 41.0, 37.1, 36.6, 34.2, 30.9, 22.3, 21.5 ppm; HRMS (CI+) calcd. for $C_{19}H_{30}NO_3$ (M+H) 320.2226, found 320.2220.

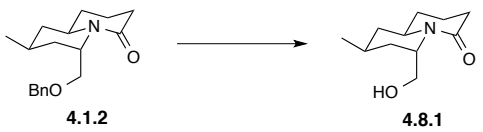
4.1.3 4.1.2

Lactam 4.1.2: To a stirred solution of aminoester **4.1.3** (0.600 g, 0.1.88 mmol) in xylenes (7 mL) in a sealed tube was applied microwave radiation elevating the vessel to a temperature of 144°C. After 12 h, the reaction was cooled to r.t., the reaction was then concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 0-10% MeOH / EtOAc, to give lactam **4.1.2** (0.513 g, 1.78 mmol, 95%) as a brown oil. $[\alpha]_D^{23}$ = -22.3° (*c* = 0.8, $CHCl_3$); IR (neat) 2954, 2922, 2862, 1636 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.26-7.34 (m, 5H), 5.14 (m, 1H), 4.53 (m, 2H), 3.54 (d, *J* = 7.2 Hz, 2H), 3.33 (m, 1H), 2.42-2.51 (m, 1H), 2.28-2.36 (m, 1H), 1.63-1.89 (m, 6H), 1.39-1.42 (m, 1H), 1.17 (m, 1H), 0.85-0.94 (m, 4h) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 138.5, 128.3, 127.6, 127.5, 72.7, 68.6, 52.6, 47.0, 42.6, 33.9, 33.3, 31.1, 25.7, 22.1, 19.3 ppm; HRMS (EI+) calcd. for $C_{18}H_{25}NO_2$ (M+) 287.1885, found 287.1894.



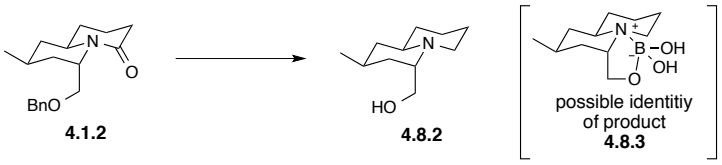
4.1.2 **4.9.1**

Thiolactam 4.9.1: To a stirred solution of lactam **4.1.2** (0.02 g, 0.070 mmol) in $PhCH_3$ (0.8 mL) at r.t. under argon was added Lawesson's reagent (0.016g, 0.083 mmol). The reaction was heated to 60 °C. After 1 h, the reaction was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 0-10% MeOH / EtOAc, to give thiolactam **4.9.1** (0.013 g, 0.045 mmol, 64%) as a colorless oil. $[\alpha]_D^{23}$ = -59.4° (*c* = 1.4, $CHCl_3$); IR (neat) 2921, 2867, 1456, 1450 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38-7.29 (m, 5H), 6.35 (m, 1H), 4.61 (s, 2H), 3.70 (m, 2H), 3.51 (m, 1H), 3.19 (d, J = 17.2 Hz, 2H), 2.99-2.95 (m, 1H), 2.04-1.94 (m, 3H), 1.75-1.67 (m, 2H), 1.62-1.55 (m, 2H), 1.04 (dt, J_1 = 13.2 Hz, J_2 = 12.0 Hz, 1H), 0.94 (d, J = 6.4 Hz, 3H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 200.7, 138.2, 128.4, 127.8, 127.7, 68.1, 56.2, 55.6, 43.3, 42.5, 33.8, 31.0, 25.9, 21.7, 18.7 ppm; HRMS (EI+) calcd. for $C_{18}H_{25}NOS$ (M+) 303.1657, found 303.1664.

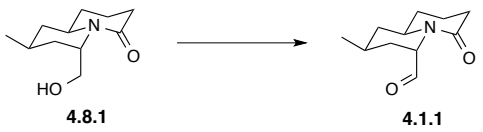


4.1.2 4.8.1

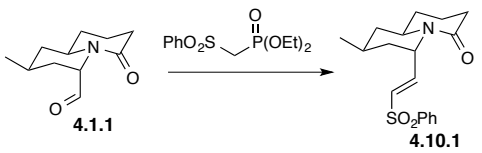
Alcohol 4.8.1: To a stirred solution of lactam **4.1.2** (0.114 g, 0.396 mmol) in EtOAc (3 mL) at r.t. under argon was added Pd/C (0.413 g, 10 wt%), the argon was then removed by flushing with a balloon of H_2 gas. After 5 min, the balloon was replaced with a new baloon. After 18 h, the hydrogen balloon was removed and the reaction flushed with argon and subsequently filtered through celite washing with 10% MeOH / EtOAc (80 mL). The filtered extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 0-10% MeOH / EtOAc, to give alcohol **4.8.1** (0.067 g, 0.34 mmol, 86%) as a colorless oil. $[\alpha]_D^{23}$ = -17.1° (*c* = 1.0, $CHCl_3$); IR (neat) 3374, 2949, 2867, 1615 cm^{-1}; ^1H NMR (400 MHz, MeOD) δ 3.60-3.67 (m, 2H), 3.32-3.49 (m, 1H), 2.31-2.47 (m, 2H), 1.60-2.07 (m, 6H), 1.45-1.53 (m, 1H), 1.09-1.17 (m, 2H), 0.91-0.97 (m, 4H) ppm; ^{13}C NMR (100 MHz, CD_3OD) δ 171.4, 59.8, 52.4, 50.2, 42.2, 33.0, 32.6, 30.4, 25.2, 21.0, 18.5 ppm; HRMS (EI+) calcd. for $C_{11}H_{19}NO_2$ (M+) 197.1416, found 197.1409.



Amino Alcohol 4.8.2 or 4.8.3: (partial characterization) To a stirred solution of amide **4.1.2** (0.036 g, 0.18 mmol) in THF (3 mL) at 0 °C was added BH_3·DMS (69 mg, 90 µL, 0.91 mmol), the reaction was then warmed slowly to ambient temperature. After 14 h, the reaction was quenched by sat. aq. Rochelle's salt (5 mL) and extracted with EtOAc (3 X 5 mL). The combined organics were washed with aq. NaOH (1 mL, 5.4 M). The dried ($MgSO_4$) extract was concentrated *in vacuo* to give amino alcohol **4.8.2 / 4.8.3** (0.31 g, 0.175 mmol, 95% based on amino alcohol molecular weight, 60% based on double borate) as an oil. $[\alpha]_D^{23}$ = -36.2° (*c* = 0.9, MeOH); IR (not collected compound was only soluble in MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.99 (dd, J_1 = 11.6 Hz, J_2 = 5.2 Hz, 1H), 3.69 (dd, J_1 = 11.2 Hz, J_2 = 6.8, 1H), 3.33-2.92 (bm, 2H), 2.83-2.78 (bt, 1H), 2.69 (bs, 1H) 1.75-1.58 (m, 6H), 1.40-1.21 (m, 4H), 0.94-0.99 (m, 4H) ppm; ^{13}C NMR (100 MHz, D_3COD) δ 61.9, 57.0, 54.7, 51.9, 41.9, 35.2, 33.6, 25.6, 24.8, 23.7, 21.4 ppm; HRMS (CI+) calcd. for $C_{11}H_{22}NO$ (M+H) 184.1701, found 184.1703.



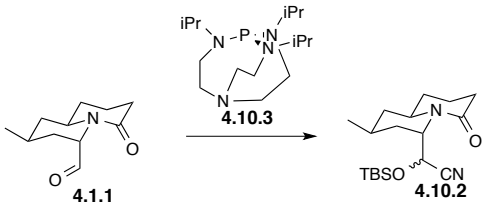
Aldehyde 4.1.1: To a stirred solution of alcohol **4.8.1** (0.108 g, 0.55 mmol) in CH_2Cl_2 (9 mL) at r.t. was added sequentially $NaHCO_3$ (0.184 g, 2.2 mmol) and DMP (0.464 g, 1.10 mmol). After 60 min, the reaction was quenched by sat. aq. $Na_2S_2O_3$ (7 mL) and extracted with CH_2Cl_2 (3 X 20 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 100% EtOAc, to give aldehyde **4.1.1** (0.101 g, 0.518 mmol, 95%) as a milky oil. $[\alpha]_D^{23}$ = +88.0° (*c* = 1.0, MeOH); IR (neat) 2949, 2922, 2862, 1734, 1636 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.55 (s, 1H), 5.47 (m, 1H), 3.36 (m, 1H), 2.56 (bd, *J* = 15.6 Hz, 1H), 2.32-2.43 (m, 2H) 1.87-2.05 (m, 1H), 1.62-1.87 (m, 4H), 1.47-1.53 (m, 2H), 1.27-1.32 (m, 1H), 0.94-0.99 (m, 4H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.7, 170.8, 58.7, 54.8, 41.7, 32.9, 31.3, 30.9, 27.6, 21.8, 19.5 ppm; HRMS (ES+) calcd. for $C_{11}H_{17}NO_2Na$ (M+Na) 218.1157, found 218.1163.



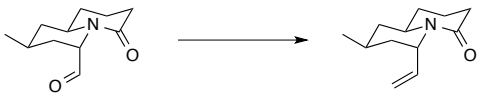
4.1.1 4.10.1

Sulfone 4.10.1: To a stirred solution of LiCl (7.8 mg, 0.185 mmol) in CH_3CN was added $PhSO_2CH_2P(O)(OEt)_2$ (0.129 mL, 0.129 mmol, 1 M in CH_3CN). After 10 min, DIPEA (22 µL, 0.129 mmol) was added followed by cannulation of aldehyde **4.1.1** (24 mg, 0.123 mmol) in CH_3CN (1 mL). After 6 h, the reaction was diluted with H_2O (5 mL) and extracted with CH_2Cl_2 (3 X 5 mL). The dried ($MgSO_4$) organic extract was concentrated *in vacuo* and purified by column chromatography over silica gel, eluting with 100% EtOAc to give sulfone **4.10.1** (26 mg, 0.078 mmol, 64% 3:1 E/Z) as a milky oil. $[\alpha]_D^{23}$ = +72.0° (*c* = 1.0, $CHCl_3$); IR (neat) 2951, 2815, 1457 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 8.17 (m, 2H (min)), 8.00 (m, 1H (min)), 7.89 (m, 2H (maj)), 7.64 (m, 1H (maj)), 7.63 (m, 2H (min)), 7.57 (m, 2H (maj)), 6.93 (d, J = 15.4 Hz, 1H (maj)), 6.57 (bs, 1H (min)), 6.40 (m, 1H (min)), 6.29 (dd, J_1 = 15.4 Hz, J_2 = 2.1 Hz, 1H (maj)), 6.22 (m, 1H (min)), 5.75 (m, 1H (maj)), 4.19 (m, 1H (min)), 4.18 (m, 1H (maj)), 3.49 (s, 1H (min)), 3.41 (s, 1H (maj)), 2.45-2.33 (m, 2H (maj), 2.19 (m, 1H (min)), 2H (min)), 2.02 (m, 1H (maj)), 1.87 (m, 2H (maj), 2H (min)), 1.73-1.66 (m, 3H (maj), 3H (min)), 1.58 (m, 1H (maj), 1H (min)), 1.52 (m, 1H (maj), 1H (min)), 0.98-0.95 (m, 4H (maj), 4H (min)) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 170.6 (min), 169.9, 146.2, 146.1, 140.1, 140.1, 133.7, 133.6, 131.7, 129.9, 129.4, 129.4, 129.3, 129.2, 128.4, 128.1, 127.7, 127.7, 63.5, 60.4, 52.6, 52.5,

46.9, 42.2, 40.5, 36.9, 33.4, 33.1, 30.6, 26.6, 26.5, 22.0, 21.8, 19.7 19.1 ppm; HRMS (EI+) calcd. for $C_{18}H_{23}NO_3S$ (M+) 333.13987, found 333.13987.

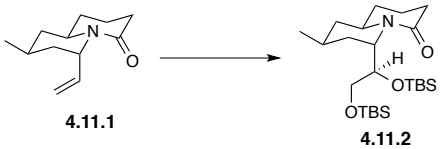


TBS Cyano Hydrin 4.10.2: To a stirred solution of aldehyde **4.1.1** (22.7 mg, 0.116 mmol) in THF (0.8 mL) at -78 °C was added TBSCN (19.8 mg, 0.14 mmol) and phosphamine **4.10.3** (3.3 mg, 0.012 mmol) in THF (0.4 mL) at -78 °C via cannula. The reaction was allowed to warm slowly. After 1.5 h, the reaction was passed through a plug of silica gel, concentrated *in vacuo* and purified by column chromatography over silica gel eluting with 50-60% EtOAc / Hexanes to give **4.10.2** (major diastereomer) (25 mg, 0.074 mmol, 64% 5 : 1 dr) and **4.10.2** (minor diastereomer) (5 mg, 0.015 mmol, 13% >1 : 20 dr). Data for minor diastereomer listed $[\alpha]_D^{23}$ = -27.5° (*c* = 1.0, $CHCl_3$); IR (neat) 2954, 2875, 2253, 1443 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 4.93 (m, 1H), 4.68 (m, 1H), 3.65 (m, 1H), 2.50 (m, 1H), 2.40 (m, 1H), 2.26-2.24 (m, 1H), 2.13 (bs, 1H), 2.02 (m, 1H), 1.84 (m, 1H), 1.79 (m, 1H), 1.70 (m, 1H), 1.48 (m, 1H), 1.27 (m, 1H), 0.99-0.98 (m, 4H), 0.95 (s, 9H), 0.24 (s, 3H), 0.19 (s, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ (minor diastereomer) 170.6, 120.5, 60.4, 53.1, 51.5, 42.0, 33.3, 31.4, 31.2, 25.5, 25.5, 25.5, 25.4, 22.2, 19.2, 18.0, -5.2, -5.3 ppm; HRMS (ES+) calcd. for $C_{18}H_{33}N_2O_2SI$ (M+) 337.2311, found 337.2300.



4.1.1 4.11.1

Alkene 4.11.1: To a stirred solution of Ph_3PMeBr (0.270 g, 0.756 mmol) in THF (3 mL) at r.t. was added KHMDS (1.51 mL, 0.756 mmol, 0.5 M in $PhCH_3$). After 30 min, the reaction was cannulated into a stirred solution of aldehyde **4.1.1**. After 5 min, the reaction was fitted with a reflux condenser and heated to reflux. After 2 h, the reaction was cooled to r.t and diluted with H_2O (10 mL) and extracted with Et_2O (3 X 15 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo,* dissolved in 9:1 pentane / Et_2O (10 mL) and cooled to at -20°C. After 16 h, the supernatant was concentrated *in vacuo* purified by chromatography over silica gel, eluting with 40-50% EtOAc / hexanes, to give **4.11.1** (0.049 g, 0.252 mmol, 84%) as a light brown oil. $[\alpha]_D^{23}$ = -10.8° (*c* = 1.0, $CDCl_3$); IR (neat) 2949, 2922, 2867, 1653, 1647, 1636 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 5.76 (m, 1H), 5.51 (s, 1H), 5.20 (m, 1H), 5.04 (m, 1H), 3.47 (m, 1H), 2.49 (m, 1H), 2.38 (m, 1H), 1.94 (m, 1H), 1.76-1.85 (m, 5H), 1.67 (m, 2H), 1.49 (m, 1H) 1.31 (m, 1H), 0.93-0.97 (m, 4H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 169.8, 136.9, 115.7, 52.0, 50.0, 42.7, 37.1, 33.2, 30.8, 26.0, 22.0, 19.3 ppm; HRMS (CI+) calcd. for $C_{12}H_{20}NO$ (M+H) 194.1545, found 194.1541.

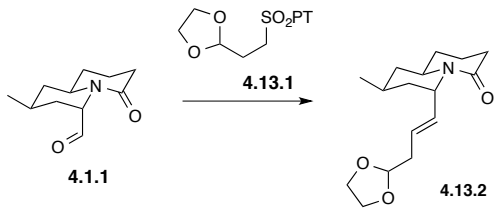


4.11.1 4.11.2

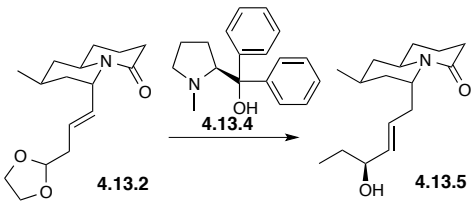
Di-TBS Ether 4.11.1: To a stirred solution of alkene **4.11.1** (41 mg, 0.213 mmol) in t-BuOH / H_2O (2 mL, 1 : 1) at r.t. was added AD-mix ($(DHQ)_2Pyr$) (340 mg)[§] After 3 d, the reaction was diluted with H_2O (10 mL) and extracted with EtOAc (3 X 10 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and carried on crude. To a stirred solution of the crude diol in CH_2Cl_2 (x mL) at 0°C was added sequentially 2,6-lutidine (223 mg, 246 µL, 2.13 mmol) and TBSOTf (237 mg, 243 µL, 1.065 mmol). The reaction was warmed to r.t. After 2 h, the reaction was quenched with sat aq. $NaHCO_3$ (10 mL) and extracted with CH_2Cl_2 (3 X 10 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* purified by chromatography over silica gel, eluting with 40-50% EtOAc / hexanes, to give **4.11.2** (0.049 g, 0.252 mmol, 84%, 5:1 dr) as an oil. $[\alpha]_D^{23}$ = -39.8° (*c* = 0.7, $CDCl_3$); IR (neat) 2941, 2852, 1654, 1649, 1627 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 4.77 (m, 1H), 3.96 (m, 1H), 3.62 (m, 1H), 3.51 (m, 1H), 2.40-2.36 (m, 2H), 2.13 (m, 1H), 1.95 (m, 1H), 1.84 (m, 1H), 1.78 (m, 2H), 1.71 (m, 1H), 1.63 (m, 1H) 1.45 (m, 1H), 1.05-8.88 (m, 23H), 0.13-0.06 (m, 12H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 169.7, 169.6, 72.8, 72.5, 67.1, 66.9, 52.5, 52.1, 51.7, 50.6, 42.7, 42.5, 33.7, 33.3, 32.8, 31.9, 30.7, 30.3, 29.7, 29.7, 26.2,

[§] AD mix α* = $(DHQ)_2PHAL$ (100 mg), $K_2OsO_2 \cdot H_2O$ (14.2 mg), K_2CO_3 (478 mg), $K_3Fe(CN)_6$ (1.22 g).

26.0, 26.0, 25.9, 25.9, 25.7, 22.3, 22.0, 18.6, 18.5, 18.2, -3.7, -4.9, -5.0, -5.1 ppm; HRMS (CI+) calcd. for $C_{12}H_{20}NO$ (M+H) 194.1545, found 194.1541.

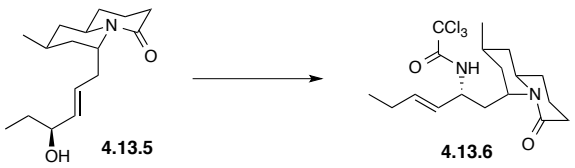


Acetal 4.13.2: To a stirred solution of PT-Sulfone[5] **4.13.1** (0.047 g, 0.152 mmol) in THF (0.1 mL) at -78 °C was added NaHMDS (0.075 mL, 0.152 mmol, 2.0 M in THF). After 30 min, the reaction was cannulated into a stirred solution of aldehyde **4.1.1** (0.020 g, 0.101 mmol) in THF (0.1 mL) at -78 °C. After 60 min, the reaction was warmed briefly by removal of the bath, quenched by the addition of sat. aq. $NaHCO_3$ (5 mL) and extracted with CH_2Cl_2 (3 X 15 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 100% EtOAc, to give acetal **4.13.2** (0.020 g, 0.071 mmol, 70%, 14:1 E:Z) as a colorless oil. $[\alpha]_D^{23}$ = -46.8° (*c* = 0.8, $CHCl_3$); IR (neat) 2943, 2922, 2867, 1636, cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 5.46 (m, 3H), 4.86 (t, J_1 = 9.1 Hz, J_2 = 4.9 Hz, 1H), 3.95-3.93 (m, 2H), 3.84-3.83 (m, 2H), 3.47 (m, 1H), 2.39-2.33 (m, 4H), 1.93 (m, 1H) 1.78 (m, 3H), 1.63 (m, 2H), 1.45 (m, 1H), 1.23 (m, 1H), 0.93-0.88 (m, 4H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 169.6, 132.3, 125.1, 103.8, 64.9, 51.8, 49.3, 42.7, 37.4, 33.2, 30.8, 25.9, 22.0, 19.2 ppm; HRMS (CI+) calcd. for $C_{12}H_{20}NO$ (M+H) 280.1913, found 280.1927.



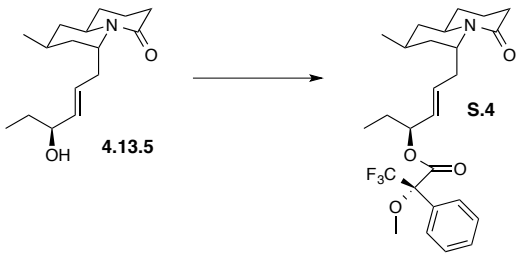
Alcohol 4.13.5: To a stirred solution of acetal **4.13.2** (0.020 g, 0.071 mmol) in dioxane (0.9 mL) at r.t was added aq. HCl (0.180 ml, 2 *N*). After 16 h, the reaction was quenched by the addition of sat. aq. $NaHCO_3$ (3 mL) and extracted with EtOAc (3 X 3 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and carried on crude. To a stirred solution of the crude enal in $PhCH_3$ (0.85 mL) was added catalyst **4.13.4** (0.078 g, 0.017mmol). After 15 min, the reaction is cooled to 0 °C and Et_2Zn (0.127 mL, 0.255 mmol, 2 M in $PhCH_3$) is added, the reaction is let warm slowly. After 16 h, the reaction is quenched with sat. aq. $NaHCO_3$ (3 mL) and extracted with EtOAc (3 X 3 mL). The combined organics were washed with aq HCl (2 mL, 1 *N*). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 5% MeOH / EtOAc, to give alcohol **4.13.5** (11.5 mg, 0.043 mmol, 61%, 10:1 dr) as a colorless oil. $[\alpha]_D^{23}$ = -25.8° (*c* = 0.54, $CHCl_3$); IR (neat) 3397, 2926, 2870, 1618, cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 5.62-5.59 (m, 1H), 5.52-5.48 (m, 1H), 5.01 (m, 1H), 3.98 (m, 1H), 3.40 (m, 1H), 2.44-2.35 (m, 2H), 2.33-2.30 (m, 1H), 2.26-2.21 (m, 1H), 1.97 (m, 1H), 1.86-1.76 (m, 3H), 1.74-1.67 (m, 2H), 1.60-1.54 (m, 2H), 1.52-1.45 (m, 2H), 1.25-1.21 (m, 1h), 0.95-0.90 (m, 7H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 169.8,

135.2, 128.7, 74.1, 51.2, 47.8, 42.8, 36.3, 33.8, 33.3, 30.9, 30.0, 25.2, 22.0, 19.0, 9.8 ppm; HRMS (CI+) calcd. for $C_{16}H_{27}NO_2Na$ (M+Na) 288.1939, found 288.1966.

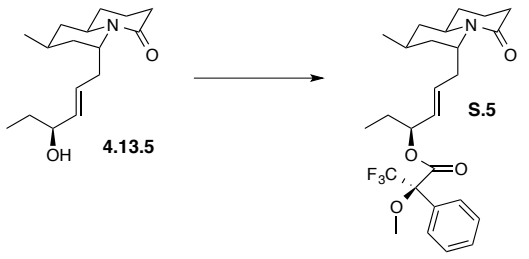


Amide 4.13.6: To a stirred solution of alcohol **4.13.5** (0.045 g, 0.016 mmol) in CH_2Cl_2 (0.4 mL) at 0 °C was added Cl_3CCN (0.006 mL, 0.06 mmol). After 15 min, DBU (4 mg, 0.003 mL, 0.027 mmol) was added. After 16 h, the reaction was quenched by the addition of sat. aq. NH_4Cl (2 mL) and extracted with CH_2Cl_2 (3 X 3 mL). Et_3N (1 mL) was added to the combined organics which were eluted through a small plug of silica gel. The dried ($MgSO_4$) extract was concentrated *in vacuo* and carried on crude. To a stirred solution of crude imidate in $PhCH_3$ (1 mL) was added K_2CO_3 (0.014 g, 0.10 mmol). The reaction was heated to 90 °C. After 18 h, the reaction is diluted with EtOAc (10 mL) and washed with H_2O (1 mL) then sat. aq. NaCl (1 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 5% MeOH / EtOAc, to give amide **4.13.6** (3.4 mg, 0.0083 mmol, 52%) as a colorless oil. $[\alpha]_D^{23}$ = -12.1° (*c* = 0.34, $CHCl_3$); IR (neat) 2927, 1710, 1620, cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.79 (s, 1H), 5.79-5.77 (m, 1H), 5.64-5.61 (m, 1H), 4.93 (m, 1H), 4.26 (m, 1H), 3.40 (m, 1H), 2.44 (m, 1H), 2.38 (m, 1H), 2.11 (m, 2H), 1.98 (m, 2H), 1.87-1.84 (m, 3H), 1.73 (m, 1H), 1.53 (m, 1H), 1.28-1.24 (m, 3H), 1.04-0.97 (m, 7H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 170.5, 161.3, 135.3, 126.1, 93.01, 51.9, 51.7, 45.0, 42.4, 38.3,

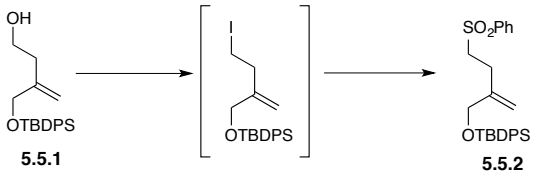
35.7, 33.3, 30.7, 25.4, 25.4, 22.0, 19.0, 13.4 ppm; HRMS (ES+) calcd. for $C_{18}H_{28}N_2O_2Cl_3$ (M+H) 409.1216, found 409.1222.



(*S*)-mosher ester S.4: To a stirred solution of alcohol **4.13.5** (3.6 mg, 0.013 mmol) in CH_2Cl_2 (0.2 mL) at r.t. was added sequentially DMAP (8 mg, 0.065 mmol) and (*R*)-mosher acid chloride (8.6 mg, 6.4 µL, 0.034 mmol). After 2 h, the reaction was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 70% EtOAc / Hexanes, to give (*S)*-mosher ester **S.4** (3.4 mg, 0.007 mmol, 54%) as a colorless oil. $[\alpha]_D^{23}$ = -75.6° (*c* = 0.34, $CHCl_3$); IR (neat) 2926, 1746, 1636 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.55-7.54 (m, 2H), 7.43-7.41 (m, 3H), 5.83-5.81 (m, 1H), 5.51-5.47 (m, 1H), 5.38 (m, 1H), 5.02 (m, 1H), 3.57 (m, 3H) 2.41-2.32 (m, 4H), 1.94 (m, 1H), 1.83-1.78 (m, 2H) 1.72-1.64 (m, 5H), 1.43 (m, 1H), 1.21 (m, 1H), 0.90-0.88 (m, 4H), 0.84-0.82 (t, J_1 = 14.7 Hz, J_2 = 7.0 Hz, 3H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 169.5, 165.9, 133.0, 132.5, 129.5, 129.3, 128.4, 127.4, 79.0, 55.5, 51.4, 47.4, 42.7, 35.8, 33.7, 33.2, 30.9, 27.3, 25.1, 22.0, 19.1, 9.4 ppm; HRMS (ES+) calcd. for $C_{26}H_{35}NO_4F_3$ (M+H) 482.2518, found 482.2525.

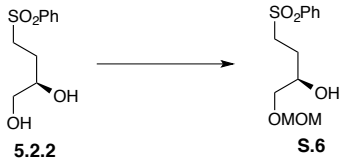


(*R*)-mosher ester S.5: To a stirred solution of alcohol **4.13.5** (2.4 mg, 0.009 mmol) in CH_2Cl_2 (0.15 mL) at r.t. was added sequentially DMAP (5.5 mg, 0.045 mmol) and (*S*)-mosher acid chloride (5.6 mg, 4.1 µL, 0.022 mmol). After 2 h, the reaction was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 70% EtOAc / Hexanes, to give (*R*)-mosher ester **S.5** (1.7 mg, 0.004 mmol, 40%) as a colorless oil. $[\alpha]_D^{23}$ = -64.0° (*c* = 0.1, $CHCl_3$); IR (neat) 2926, 1746, 1635 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.53-7.52 (m, 2H), 7.43-7.41 (m, 3H), 5.77-5.75 (m, 1H), 5.38-5.33 (m, 2H), 4.98 (m, 1H), 3.58 (s, 3H), 3.33 (m, 1H), 2.41-2.39 (m, 1H), 2.32-2.30 (m, 3H), 1.94 (m, 1H), 1.78-1.62 (m, 7H), 1.45 (m, 1H), 1.18 (m, 1H), 0.94-0.89 (m, 7H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 169.5, 165.8, 132.7, 132.4, 129.5, 129.0, 128.34, 127.5, 79.1, 55.5, 51.3, 47.4, 42.7, 35.7, 33.6, 33.3, 30.9, 29.8, 27.4, 25.1, 22.0, 19.0, 9.7 ppm; HRMS (ES+) calcd. for $C_{26}H_{35}NO_4F_3$ (M+H) 482.2518, found 482.2521.

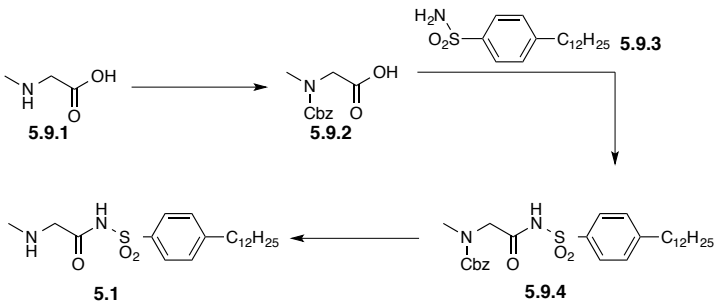


Sulfone 5.5.2: To a stirred solution of alcohol **5.5.1**[6] (0.65 g, 1.91 mmol) in CH_3CN:Et_2O 3:1 (20 mL) at ambient temperature was added sequentially imidazole (0.39 g, 5.73 mmol), PPh_3 (0.55 g, 2.10 mmol) and I_2 (0.53 g, 2.10 mmol). After 60 min, the reaction was quenched by sat. aq. NH_4Cl (20 mL) and extracted with EtOAc (3 X 25 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and carried on crude.

To a stirred solution of the crude iodide in DMF (1 mL) at ambient temperature was added $PhSO_2Na$ (0.38 g, 2.29 mmol). After 18 h, the reaction was diluted with water (50 mL) and extracted with CH_2Cl_2 (3 X 25 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 15-30% EtOAc / hexanes, to give sulfone **43** (0.46 g, 0.98 mmol, 51%) as a clear colorless oil. IR (neat) 2930, 2856, 1471, 1447, 1427, 1313 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.93 (m, 2H), 7.64-7.68 (m, 4H), 7.59 (m, 2H), 7.46 (m, 2H), 7.39-7.42 (m, 5H), 5.15 (s, 1H), 4.87 (s, 1H), 4.08 (s, 2H), 3.25 (m, 2H), 2.49 (m, 2H), 1.06 (s, 9H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 144.2, 139.0, 135.5, 133.8, 133.2, 129.8, 129.3, 128.1, 127.8, 111.5, 66.4, 54.9, 26.8, 26.0, 19.2 ppm; HRMS (ES+) calcd. for $C_{27}H_{33}O_3SSi$ (M+H) 465.1920, found 465.1909.



Alcohol S.6: To a stirred solution of alcohol **5.2.2** (11 mg, 0.048 mmol) in CH_2Cl_2 (0.1 mL) at 0°C was added sequentially DIPEA (37.2 mg, 50.0 µL, 0.29 mmol) and MOMCl (3.6 mg, 3.4 uL, 0.045 mmol). After 16 h, the reaction was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 70-80% EtOAc / hexanes, to give **S.6** (5 mg, 0.018 mmol, 38%) as a brown oil. $[\alpha]_D^{23}$ = -13.3° (*c* = 1.2, $CHCl_3$); IR (neat) 3500, 2931, 1447, 1304, 1147 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.94 (m, 2H), 7.68 (m, 1H), 7.60 (m, 2H), 4.65 (m, 2H), 3.85 (bs, 1H), 3.62-3.63 (m, 1H), 4.51-4.53 (m, 1H), 3.38 (s, 3H), 3.22-3.26 (m, 2H), 2.80 (m, 1H), 1.93-1.97 (m, 2H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 133.8, 129.4, 129.3, 128.0, 97.2, 72.8, 68.8, 55.6, 53.0, 26.3 ppm; HRMS (ES+) calcd. for $C_{12}H_{18}NaS$ (M+Na) 297.0773, found 297.0761.

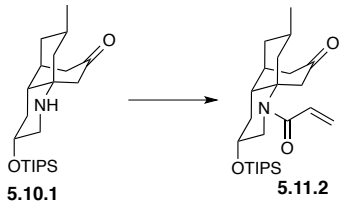


Sulfonamide 5.1: To a stirred solution of N-methyl glycine **5.9.1** (2.00 g, 22.44) in H_2O (29 mL) was added sat. aq. NaOH (10 mL) followed by dropwise addition of CbzCl (20.6 mL, 33% in $PhCH_3$). After 2 h, the organic layer was collected and the aqueous layer extracted with EtOAc (2 X 20 mL). The dried ($MgSO_4$) organic extract was concentrated *in vacuo* to provide crude Cbz-amino acid **5.9.2**.

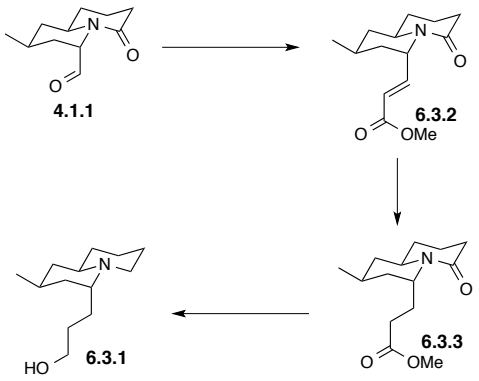
To a stirred solution of crude Cbz-amino acid **5.9.2** and sulfonamide **5.9.3** (3.725 g, 11.36 mmol) in CH_2Cl_2 (40 mL) was added sequentially DMAP (0.548 g, 4.488 mmol) and EDC (3.483 g, 22.44 mmol). After 24 h, the reaction was quenched by the addition of aq. HCl (20 mL, 1 M) and extracted with EtOAc (3 X 25 mL). The dried ($MgSO_4$) organic extract was concentrated *in vacuo* to provide crude Cbz-sulfonamide **5.9.4**.

To a stirred solution of crude Cbz-sulfonamide **5.9.4** in EtOAc (27 mL) was added Pd/C (312 mg, 10 wt%). the reaction flask was purged with a balloon of H_2 gas for 10 min, a second balloon of H_2 gas was added. After 36 h, the reaction was flushed with argon, filtered through celite with EtOAc rinse (200mL). The organic extract was concentrated *in vacuo* and

purified by chromatography on silica gel eluting with 10% MeOH / CH_2Cl_2 to give **5.1** (2.00 g, 5.05 mmol, 42% based on sulfonamide **5.9.3**, product is isolated as a mixture of $C_{12}H_{25}$ chain isomers). IR (neat) 3500, 2931, 2905, 2871, 1431, 1294, 1102 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 7.88 (bs, 2H), 7.41-7.36 (m, 2H), 3.78 (bs, 2H), 2.72 (bs, 3H), 1.83-1.56 (m, 4H), 1.33-1.08 (m, 9H), 0.90-0.74 (m, 13H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 171.2, 154.1, 139.8, 126.8, 126.7, 126.3, 126.2, 53.2, 41.4, 38.0, 33.8, 29.3, 28.9, 28.8, 27.2, 26.7, 22.6, 19.7, 14.1, 8.7 ppm; HRMS (ES+) calcd. for $C_{21}H_{37}N_2O_3S$ (M+H) 397.2525, found 397.2506.



Acrylamide 5.11.2: To a stirred solution of amine **5.10.1** (14.4 mg, 0.037 mmol) in CH_2Cl_2 (0.37 mL) at 0°C was added sequentially DIPEA (14.7 mg, 19.8 uL, 0.12 mmol) and acroyl chloride (4.6 uL, 0.057 mmol). After 30 min, the reaction was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 60-80% EtOAc / hexanes, to give **5.11.2** (12 mg, 0.028 mmol, 75%, an amide rotomer is also present in trace amounts) as a colorless oil. $[\alpha]_D^{23}$ = -27.1° (*c* = 1.0, $CHCl_3$); IR (neat) 2965, 1442, 1298, 1147 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 6.48 (dd, J_1 = 10.5 Hz, J_2 = 16.8 Hz, 1H), 6.13 (dd, J_1 = 1.4 Hz, J_2 = 16.8 Hz, 1H), 5.60 (dd, J_1 = 2.1 Hz, J_2 = 10.5 1H), 4.21 (m, 1H), 3.65 (m, 2H), 3.43 (m, 1H), 3.27 (m, 1H), 2.82 (m, 1H), 2.54 (m, 1H), 2.20-2.04 (m, 3H), 1.86 (m, 1H), 1.73 (m, 2H), 1.31-1.27 (m, 4H), 1,11-1.05 (m, 21H), 0.90 (d, *J* = 6.3 Hz, 3H) ppm; ^{13}C NMR (176 MHz, $CDCl_3$) δ 210.6 168.44, 131.8, 126.3, 67.0, 60.6, 49.3, 44.8, 44.4, 42.0, 41.8, 40.1, 35.0, 34.7, 29.7, 25.9, 22.3, 18.1, 18.0, 18.0, 12.2, 12.1, 12.1 ppm; HRMS (ES+) calcd. for $C_{25}H_{44}O_3Si$ (M+H) 434.3090, found 434.3104.

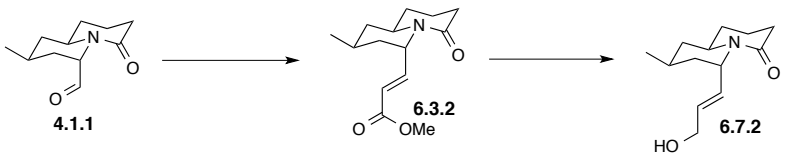


Amino Alcohol 6.3.1: To a stirred solution of **4.1.1** (50 mg, 0.25 mmol) in PhH (2.5 mL) was added $Ph_3P{=}CHCO_2Me$ (90 mg, 0.269 mmol). After 18 h, the reaction was concentrated *in vacuo* and passed through a plug of silica to yield crude ester **6.3.2**.

To a stirred solution of crude ester **6.3.2** in EtOAc (6.8 mL) was added Pd/C (59 mg, 10 wt%). the reaction flask was purged with a balloon of H_2 gas for 10 min, a second balloon of H_2 gas was added. After 16 h, the reaction was flushed with argon, filtered though celite with EtOAc rinse (100 mL), concentrated *in vacuo* and passed through a plug of silica eluting with EtOAc to yield crude ester **6.3.3**.

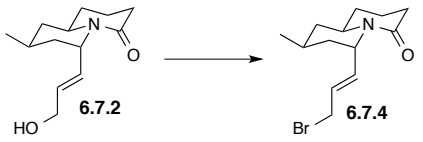
To a stirred solution of crude ester **6.3.3** in THF (2.9 mL) at 0 C° was added $LiAlH_4$ (22 mg, 0.581 mmol). The reaction was heated to reflux. After 2 h, the reaction was cooled to rt and quenched with sat. aq. NaOH (5 mL). After 3 d, the reaction was extracted with EtOAc (3 X 10 mL). The dried ($MgSO_4$) organic extract was concentrated *in vacuo* and purified by chromatography over silica gel eluting with 70-90% EtOAc / Hexanes to provide amino alcohol **6.3.1** (29 mg, 0.14 mmol, 73% over three steps) as

an oil. $[\alpha]_D^{23}$ = -4.66° (*c* = 0.6, MeOH); IR (neat) 3413, 2928, 1641, 1455, cm^{-1}; ^1H NMR (700 MHz, D_3COD) δ 3.59 (m, 2H), 2.78 (bs, 1H), 2.65-2.61 (m, 2H), 2.46 (m, 1H), 1.75-1.55 (m, 9H), 1.35-1.29 (m, 6H), 0.93-0.90 (m, 4H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 61.7, 60.5, 53.5, 51.2, 41.6, 36.0 33.5, 30.5, 29.4, 25.4, 24.2, 23.7, 21.3 ppm; HRMS (ES+) calcd. for $C_{13}H_{26}NOCl$ (M+H) 212.2013, found 212.2014.



Allylic Alchol 6.7.2: To a stirred solution of aldehyde **4.1.1** (16 mg, 0.0.82 mmol) in PhH (2 mL) at rt was added $Ph_3P{=}CHCO_2Me$ (28 mg, 0.0.86 mmol). After 17 h, the reaction was concentrated *in vacuo* and passed through a plug of silica gel to yield crude ester **6.3.2**, 50% of this crude material was carried on.

To a stirred solution of crude ester **6.3.2** in CH_2Cl_2 (0.4 mL) at -78 C° was added DIBAL-H (0.123 mL, 0.123 mmol, 1 M in Hexanes). After 1 h, the reaction was quenched by dropwise addition of MeOH (5 drops) followed by sat. aq. Rochelle's salt (1 mL). After 2 h, the reaction was extracted with CH_2Cl_2 (3 X 3 mL). The dried ($MgSO_4$) extract was concentrated *in vacuo* and purified by column chromatography over silica gel to yield amino alcohol **6.3.1** (Data reported for material containing triphenyphospineoxide) as an oil. $[\alpha]_D^{23}$ = -5.3° (*c* = 1.0, $CHCl_3$); IR (neat) 3334, 2923, 1617, 1437, 1120 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 5.66 (m, 2H), 5.53 (m, 1H), 4.18 (m, 2H), 3.55 (m, 1H), 2.59 (m, 1H), 2.73 (m, 1H), 1.97 (m, 1H), 1-.81-1.65 (m, 7H), 1.53 (m, 1H), 0.93 (m, 4H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 169.8, 130.4 (triphenyphosphine oxide peaks omitted), 130.3, 63.3, 52.1, 49.1, 42.7, 37.5, 33.2, 30.9, 26.0, 21.9, 19.3 ppm; HRMS (ES+) calcd. for $C_{13}H_{21}NO_2Na$ (M+Na) 246.1470, found 246.1477.



Allylic Bromide 6.7.4: To a stirred solution of crude allylic alcohol **6.7.2** (~ 0.072 mmol from previous entry) in CH_2Cl_2 (0.7 mL) at rt was added sequentially CBr_4 (35.5 mg, 0.107 mmol) and PPh_3 (26 mg, 0.101 mmol). After 1 h, CBr_4 (8 mg, 0.024 mmol) and PPh_3 (6 mg, 0.023 mmol) was added to the reaction. After 1 h, the reaction was diluted with H_2O (3 mL) and extracted with CH_2Cl_2 (3 X 5 mL). The dried ($MgSO_4$) organic extract was concentrated *in vacuo* and purified by column chromatography over silica gel eluting with 60-70% EtOAc / Hexanes to provide allylic bromide **6.7.4** (15.6 mg, 0.055 mmol, 76% over three steps) as a colorless oil. $[\alpha]_D^{23}$ = -34.8° (*c* = 0.35, $CHCl_3$); IR (neat) 2922, 2856, 1635, 1453 cm^{-1}; ^1H NMR (700 MHz, $CDCl_3$) δ 5.72 (m, 2H), 5.56 (m, 1H), 3.99 (m, 2H), 3.44 (m, 1H), 2.50 (m, 1H), 2.39 (m, 1H), 1.97 (m, 1H), 1.84-1.81 (m, 3H), 1.71-1.68 (m, 2H), 1.31 (m, 1H), 1.34-1.31 (m, 2H), 0.98-0.90 (m, 4H) ppm; ^{13}C NMR (175 MHz, $CDCl_3$) δ 169.8, 134.5, 127.8, 52.2, 48.8, 42.6, 37.2, 33.2, 32.5, 30.8, 29.7, 26.0, 21.9, 19.3 ppm; HRMS (ES+) calcd. for $C_{13}H_{21}NOBr$ (M+H) 286.0807, found 286.0808.

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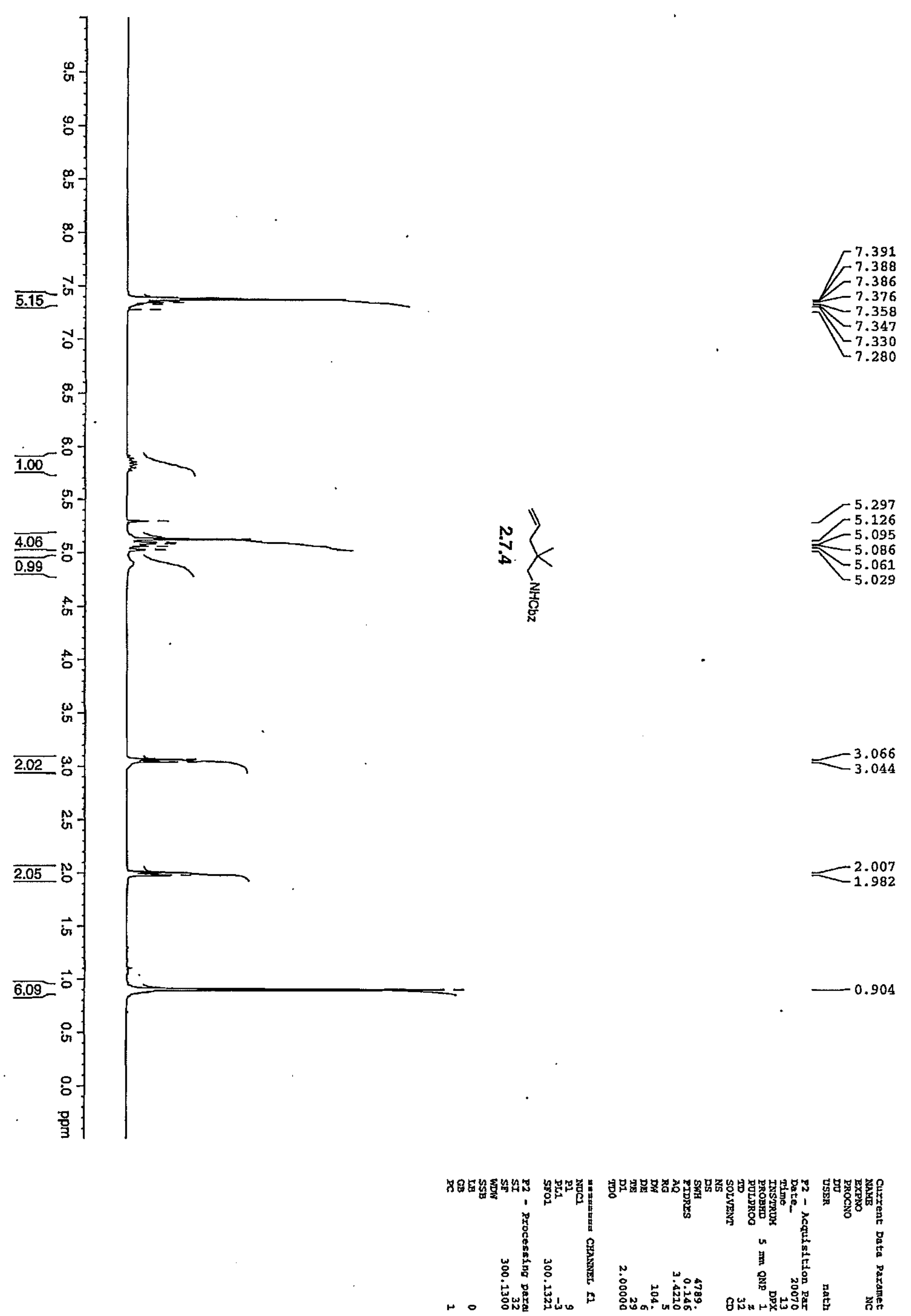

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2.02
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6.09
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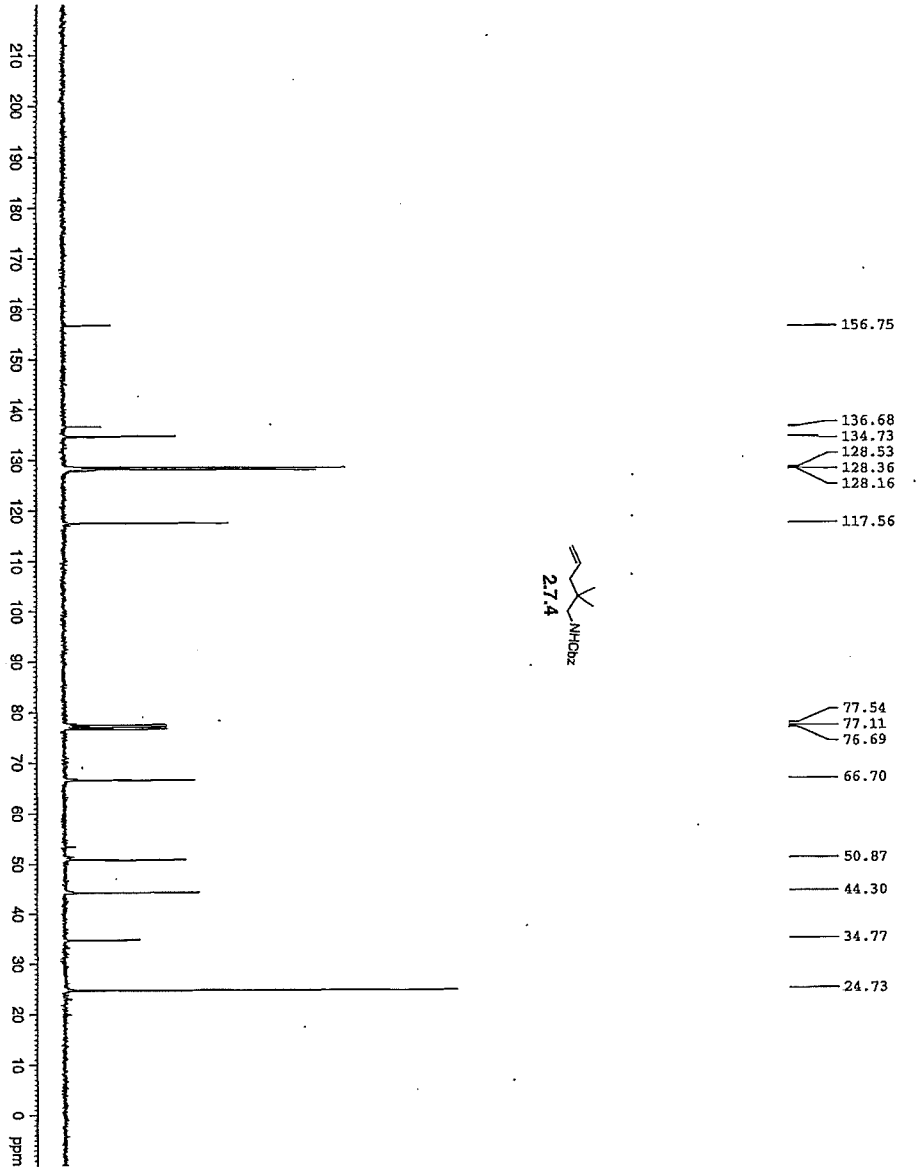


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NUC2                    1H
PCPD2                 80.00
PL2                   -3.00
PL12                  17.55
PL13                  17.55
SFO2              300.1312005

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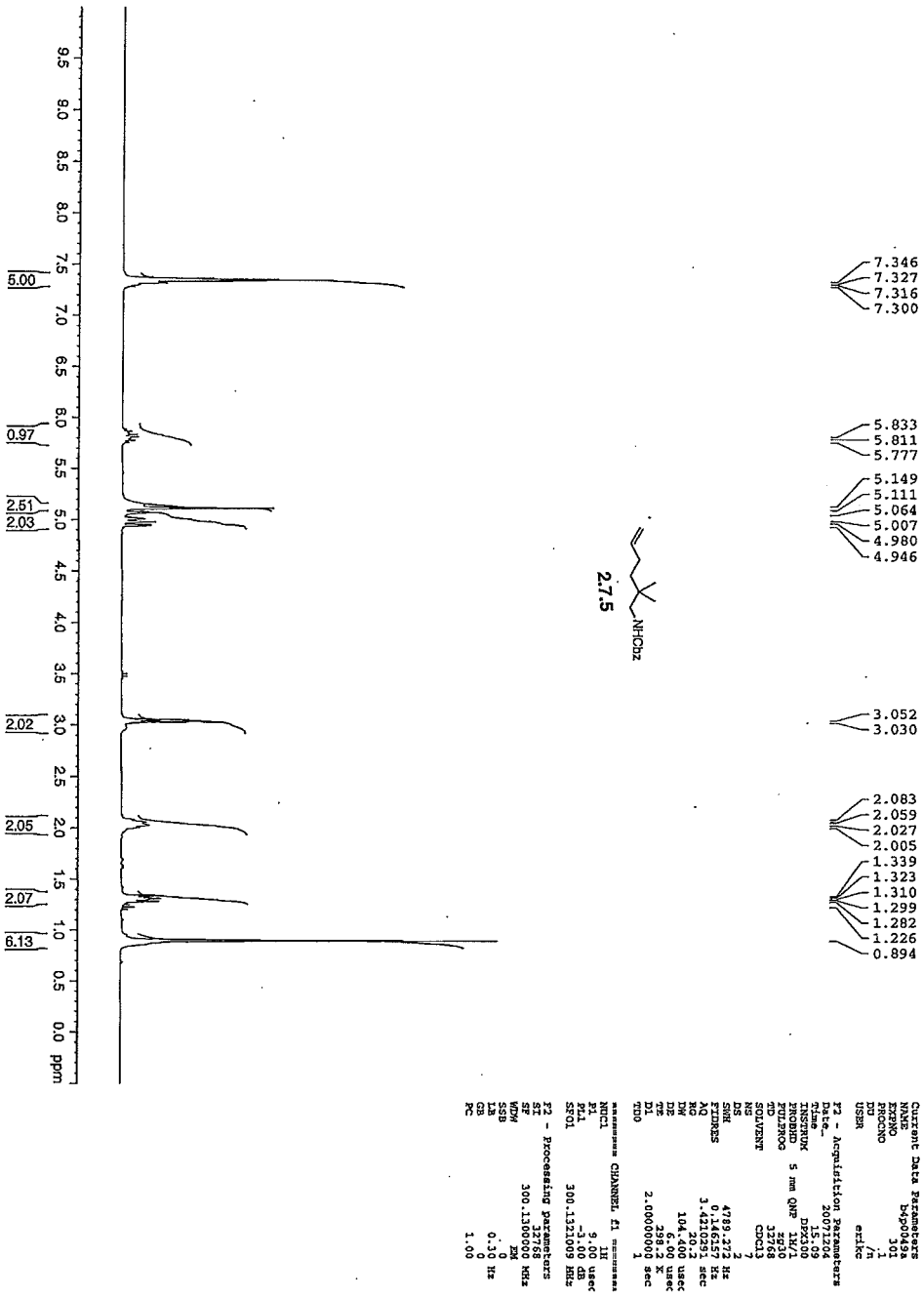


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DS                     2
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FIDRES          0.146137 Hz
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PL1               -3.00 dB
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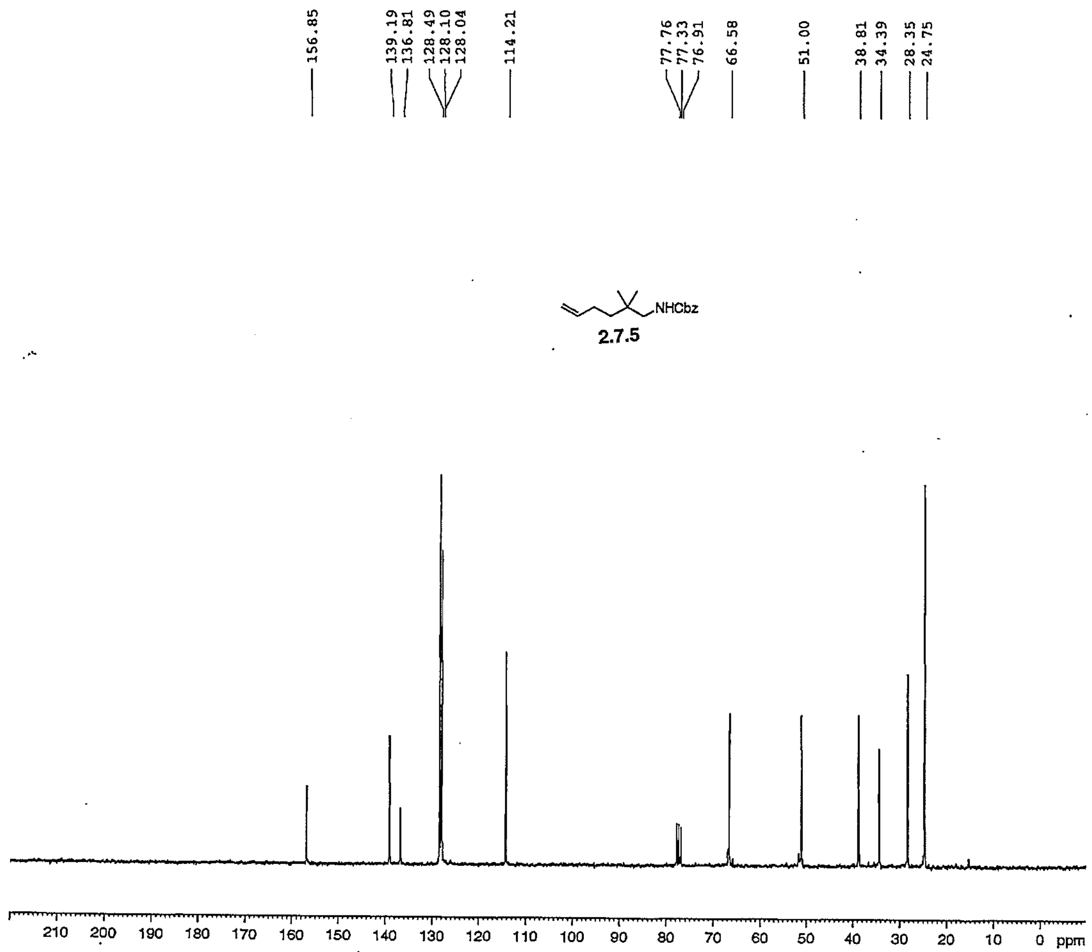


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SOLVENT           CDCl3
NS                  111
DS                    4
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FIDRES        0.287360 Hz
AQ           1.7400308 sec
RG               9195.2
DW              26.550 usec
DE                6.00 usec
TE               298.2 K
D1          0.15000001 sec
d11         0.03000000 sec
DELTA       0.05000000 sec
TD0                   1

======== CHANNEL f1 ========
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P1                 8.80 usec
PL1               -3.00 dB
SFO1        75.4760505 MHz

======== CHANNEL f2 ========
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NUC2                 1H
PCPD2             80.00 usec
PL2               -3.00 dB
PL12              17.55 dB
PL13              17.55 dB
SFO2       300.1312005 MHz

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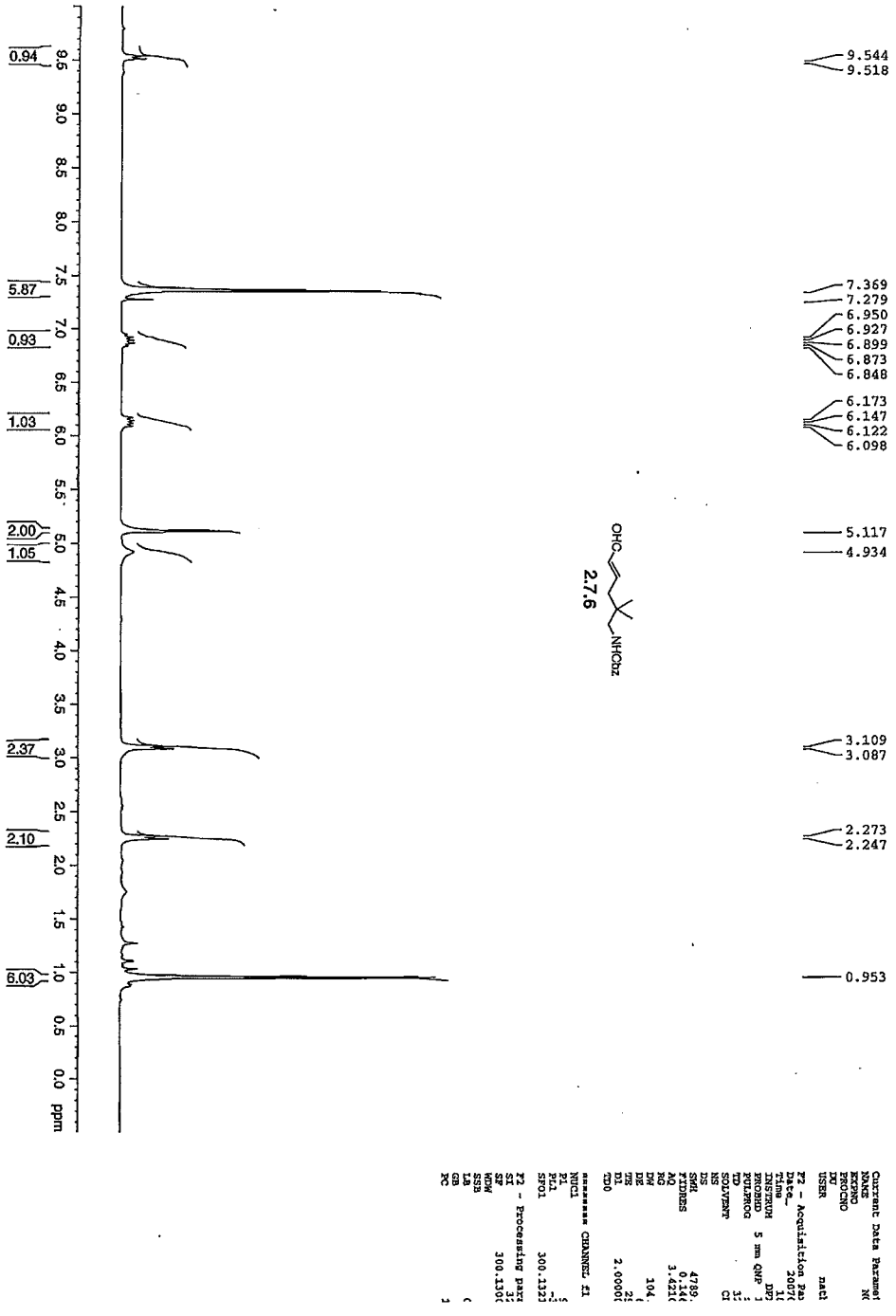
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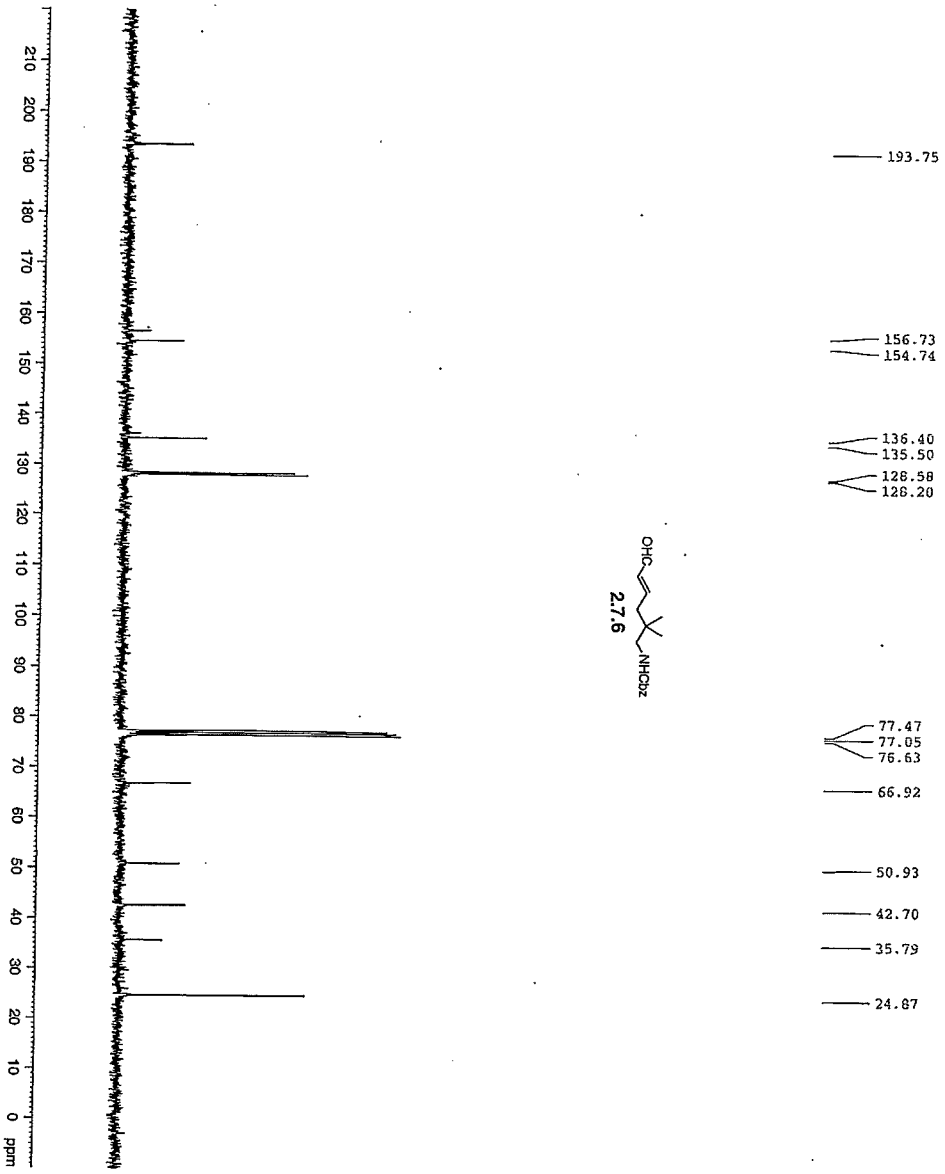

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PL1 -3.0
SFO1 75.4760505

======== CHANNEL f2 ===
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PL12 17.5
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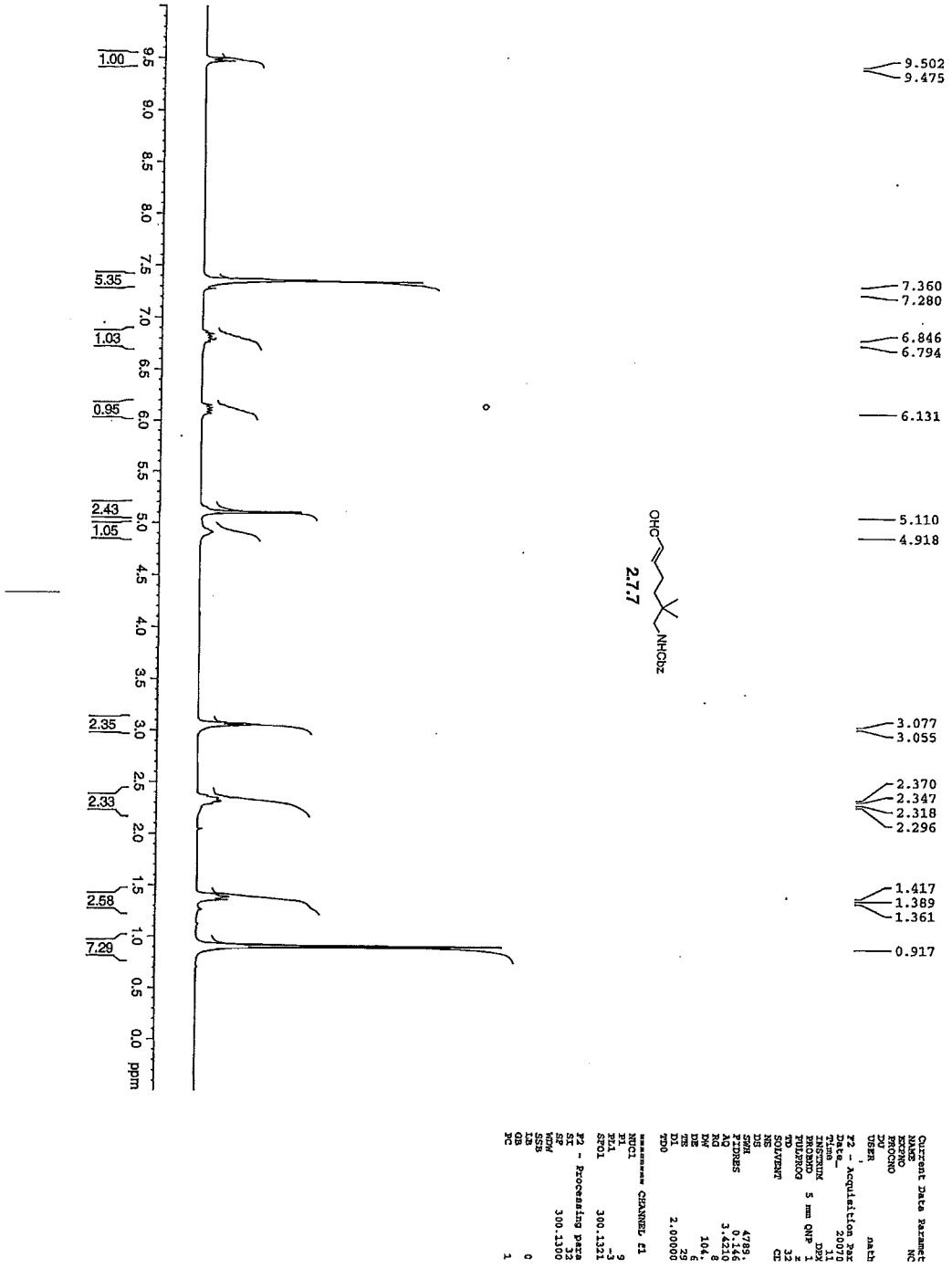

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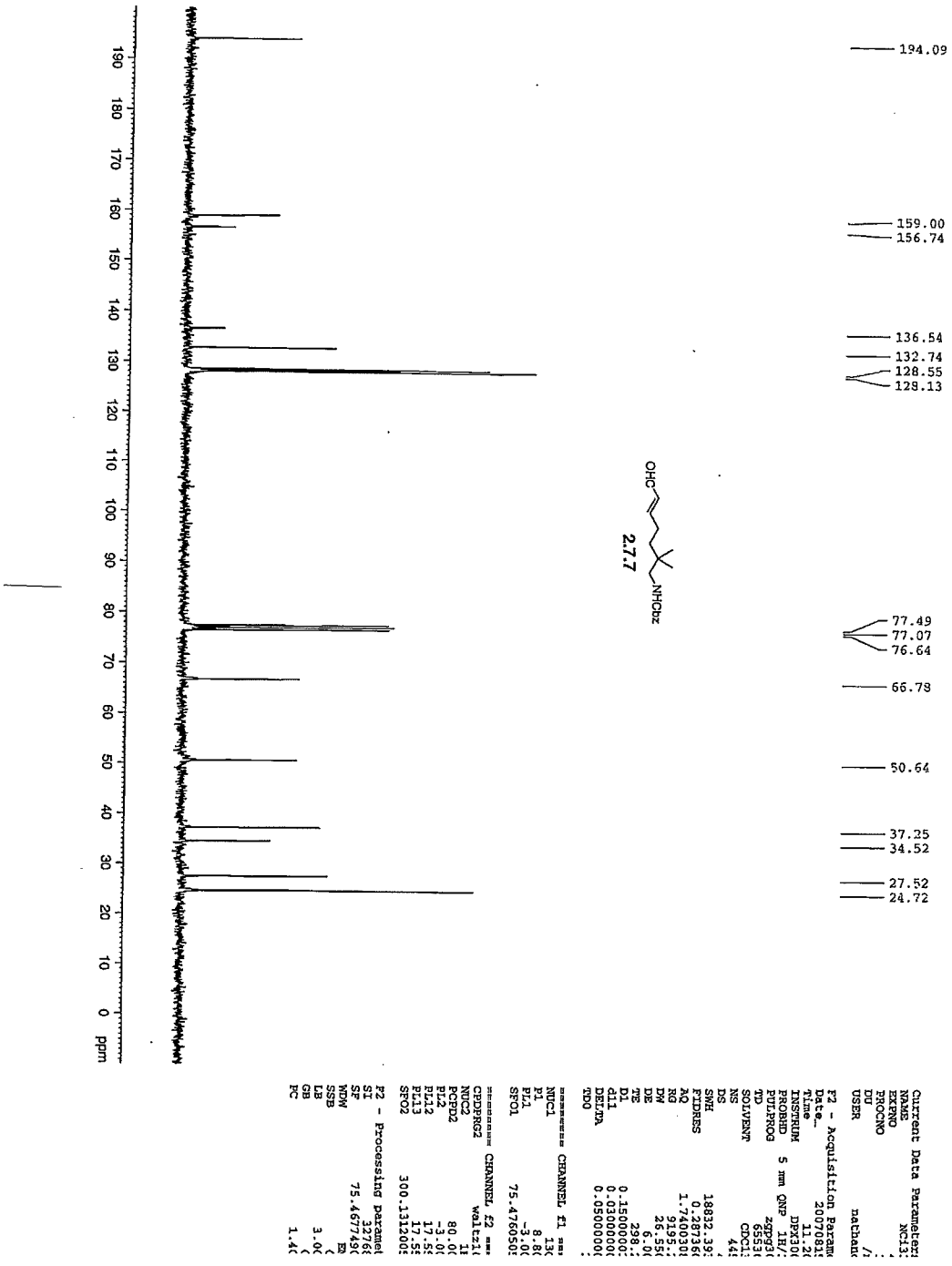

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SFO1 75.4760500

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PCPD2 80.00
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PL12 17.55
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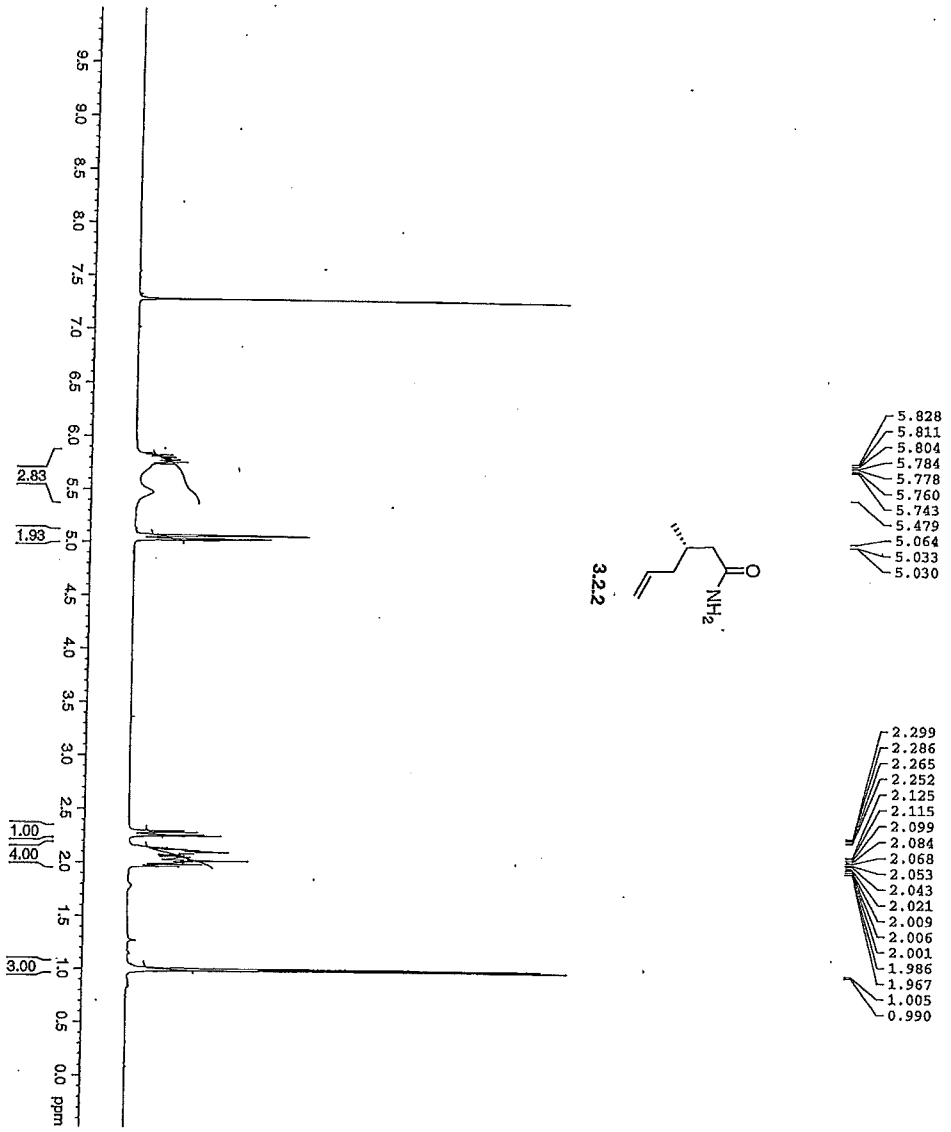
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5.479
5.064
5.033
5.030
2.299
2.286
2.265
2.252
2.125
2.115
2.099
2.084
2.068
2.053
2.043
2.021
2.009
2.006
2.001
1.986
1.967
1.005
0.990
3.2.2
2.83
1.93
1.00
4.00
3.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
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DW 15.000 usec
DE 298.0 K
TE 2.00000000 sec
D1 1
TDO
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P1 14.70 usec
PL1 0.00 dB
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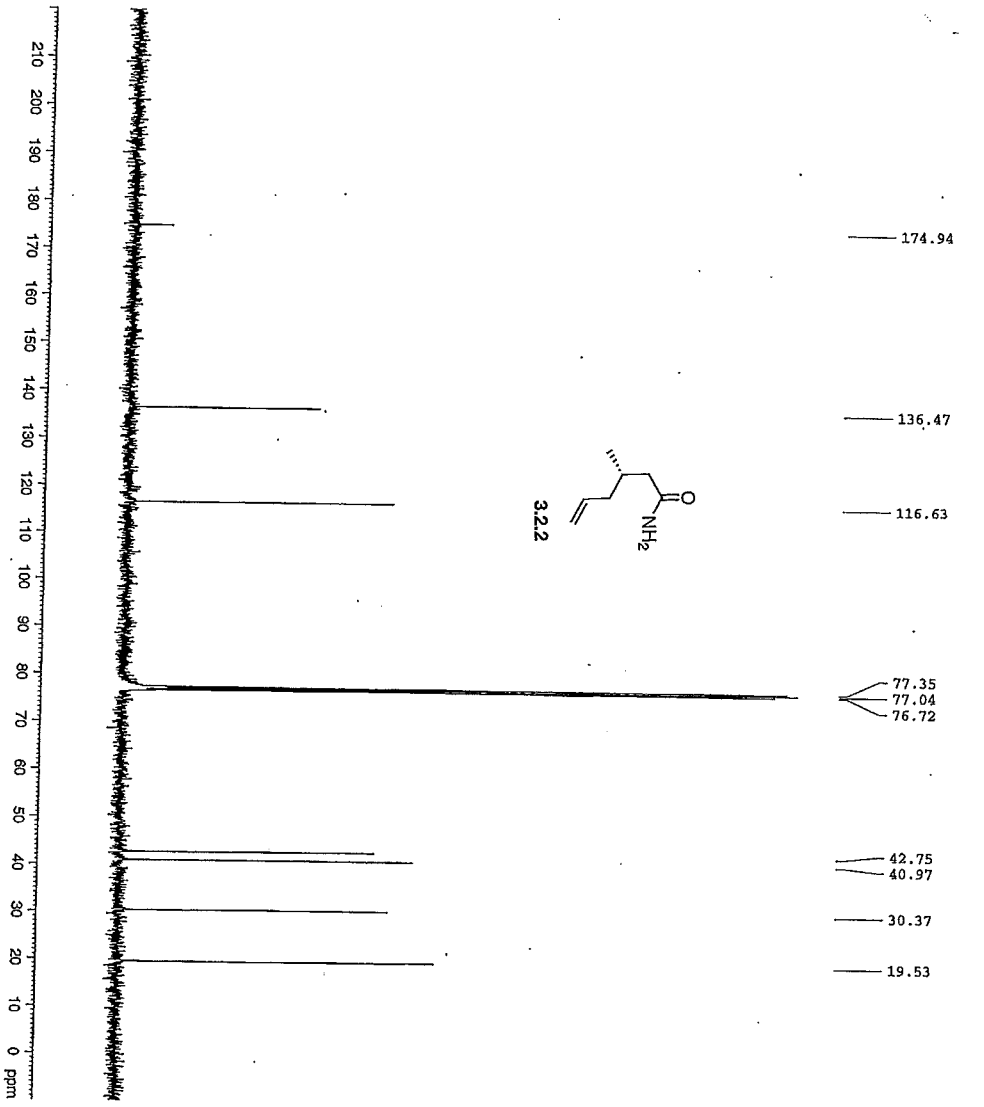
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3.2.2
NH2
O
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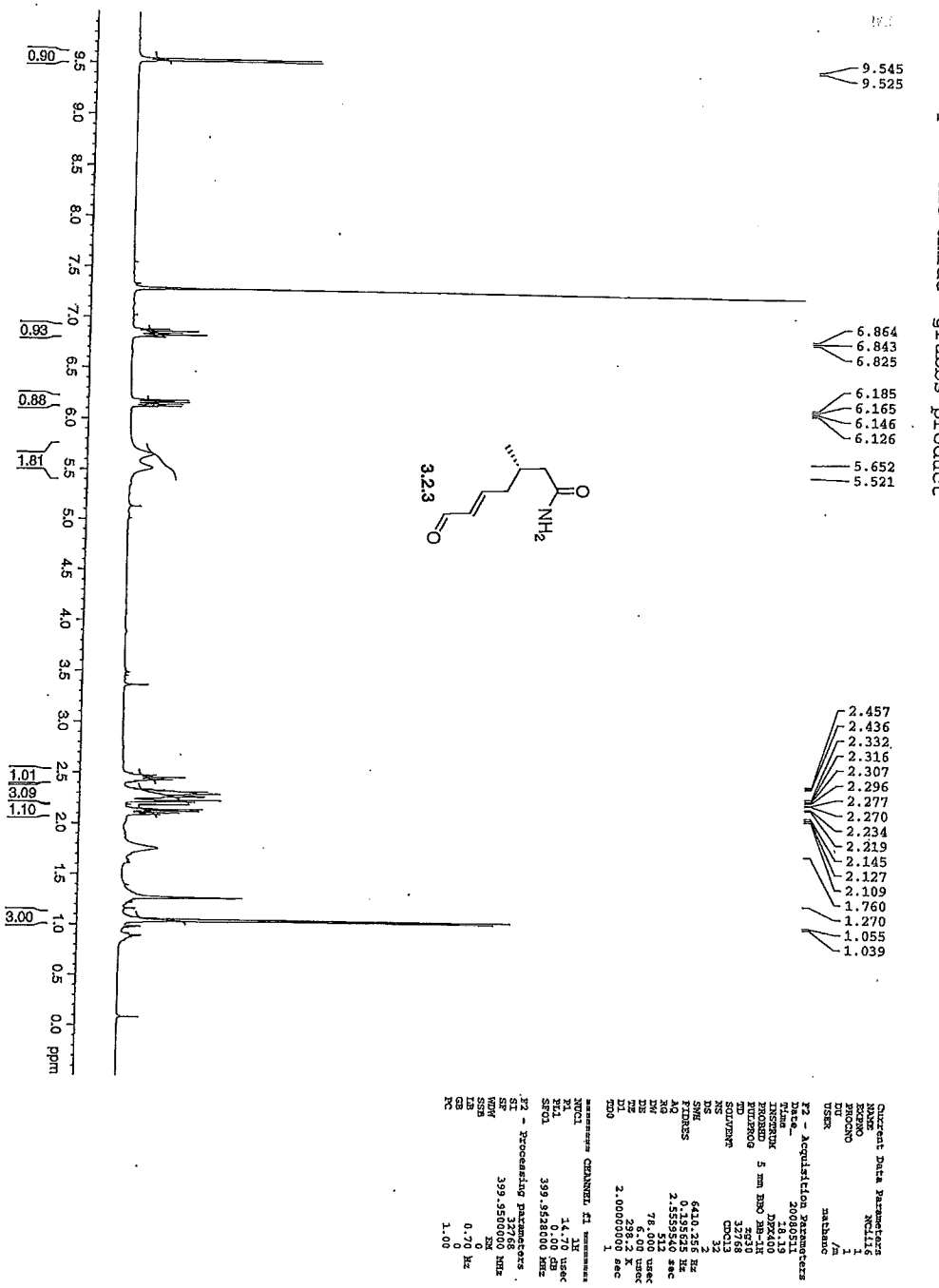
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6.185
6.165
6.146
6.126
5.652
5.521
2.457
2.436
2.332
2.316
2.307
2.296
2.277
2.270
2.234
2.219
2.145
2.127
2.109
1.760
1.270
1.055
1.039
3.2.3
NH2
O
O
0.90
0.93
0.88
1.81
1.01
3.09
1.10
3.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
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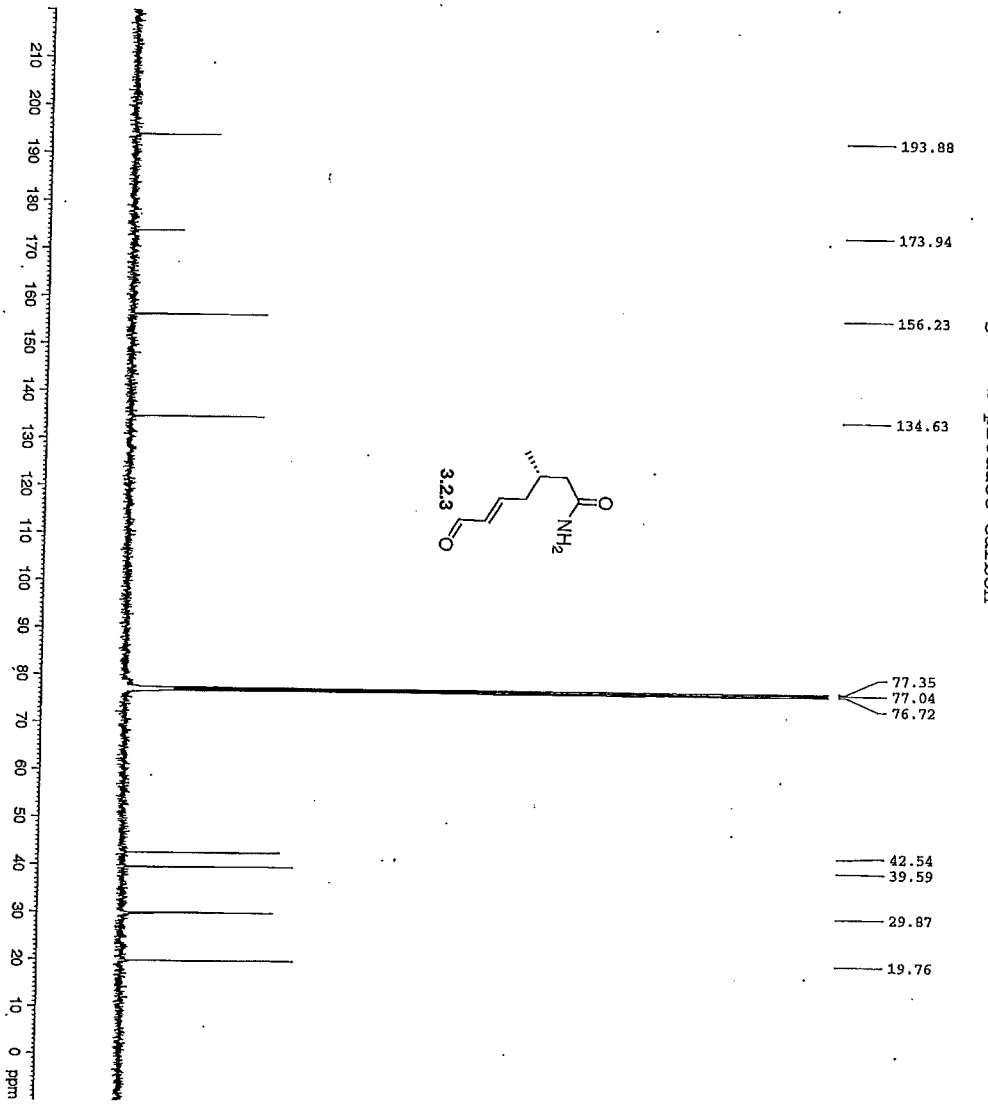
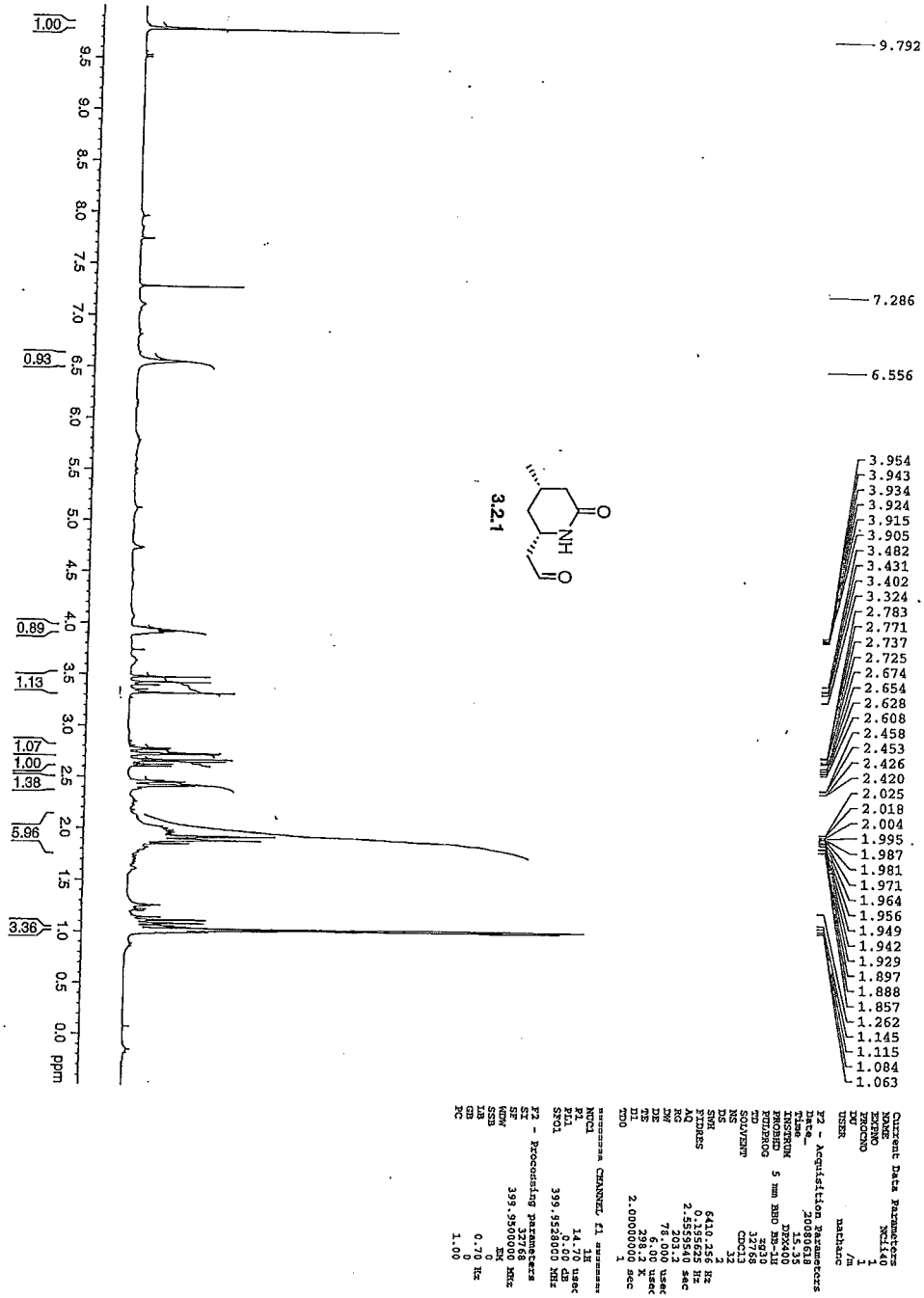
RG 512
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 399.9528000 MHz
F2 - Processing parameters
SI 32768
SF 399.9500000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB
PC 1.00

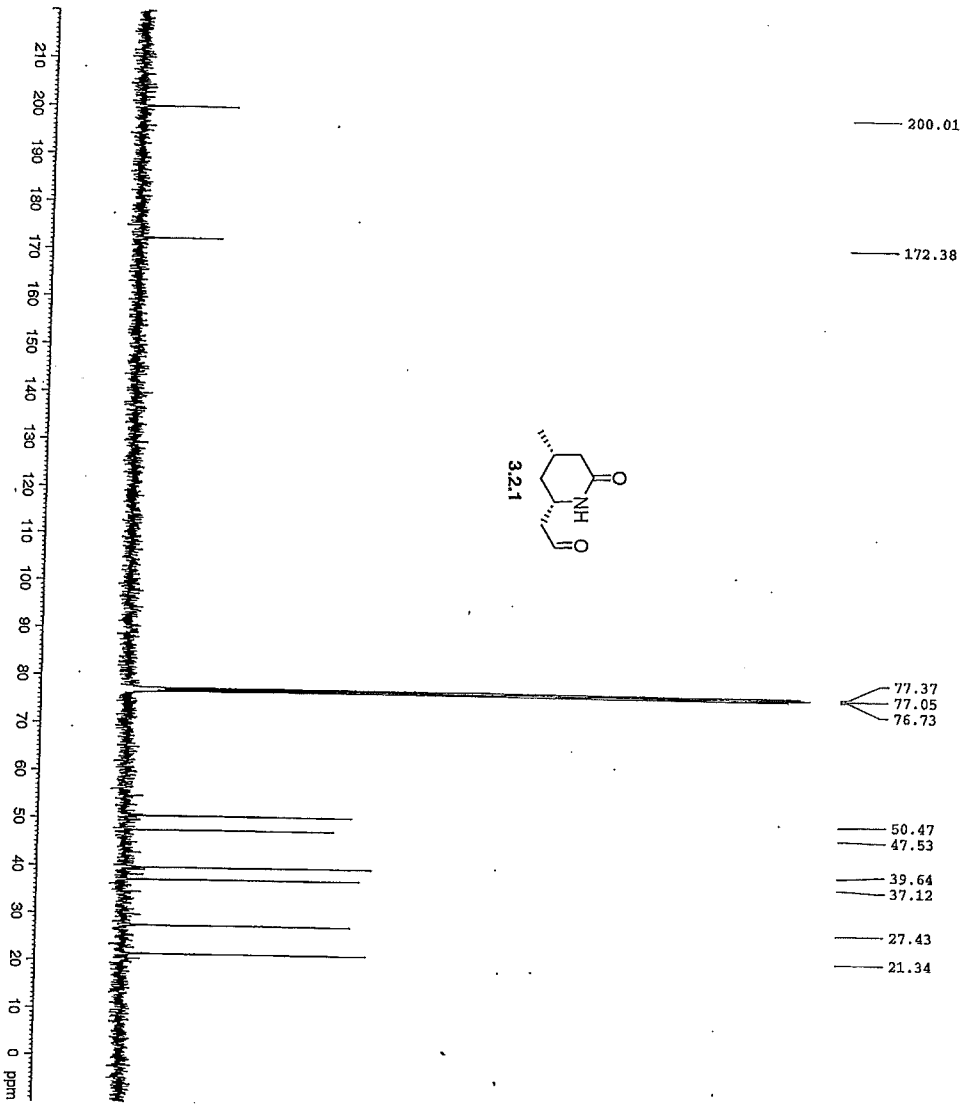
3-methyl-5-ene-amide grubbs product carbon



Current Data Parameters
NAME NC1116
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20080511
Time 15.42
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 2363
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3041184 sec
RG 19.900
DW 6.00 usec
DE 6.00 usec
TE 298.2 K
D1 0.15000001 sec
D11 0.03000000 sec
DELTA 0.05000000 sec
TD0 1
========== CHANNEL f1 ==========
NUC1 1H
P1 7.80 usec
PL1 -3.00 dB
SFO1 100.5785700 MHz
========== CHANNEL f2 ==========
CPDPRG2 waltz16
NUC2 13C
PCPD2 135.00 usec
PL2 17.40 dB
PL12 17.40 dB
PL13 17.40 dB
SFO2 399.9516000 MHz
F2 - Processing parameters
SI 32768
SF 100.5675080 MHz
WDW 0
SSB 0
LB 3.00 Hz
GB 0
PC 1.40


TMS jorgonson cyclization
9.792
7.286
6.556
3.954
3.943
3.934
3.924
3.915
3.905
3.482
3.431
3.402
3.324
2.783
2.771
2.737
2.725
2.674
2.654
2.628
2.608
2.458
2.453
2.426
2.420
2.025
2.018
2.004
1.995
1.987
1.981
1.971
1.964
1.956
1.949
1.942
1.929
1.897
1.888
1.857
1.262
1.145
1.115
1.084
1.063
3.2.1
1.00
0.93
0.89
1.13
1.07
1.00
1.38
5.96
3.36
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
Current Data Parameters
NAME mc1140
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20080618
Time 15.35
INSTRUM spect
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 203.2
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 399.9528000 MHz
F2 - Processing parameters
SI 32768
SF 399.9500000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00

TMS jorgonson cyclization carbon



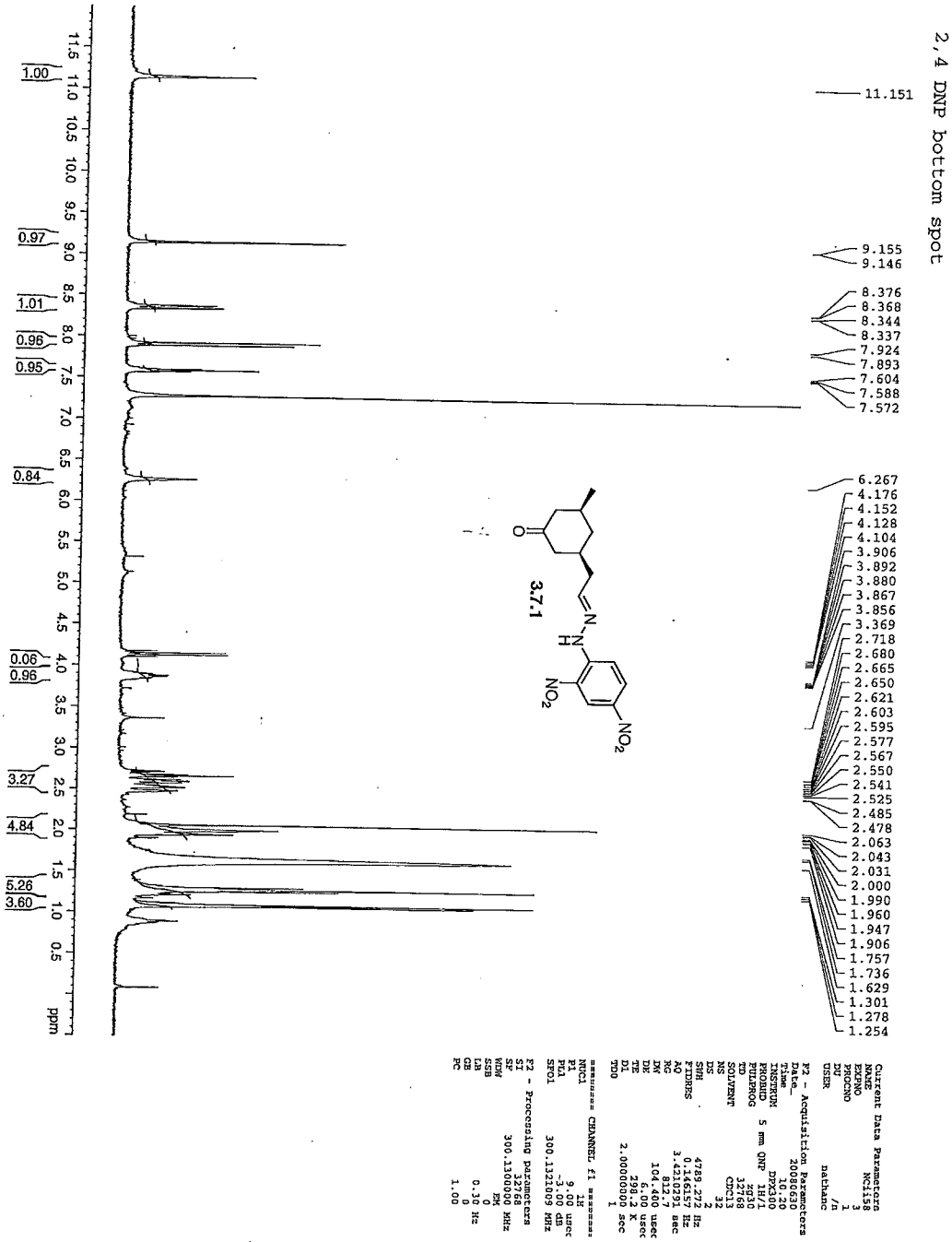
Current Data Parameters
NAME Nci140
EXPNO 2
PROCNO 1
USER matthesc

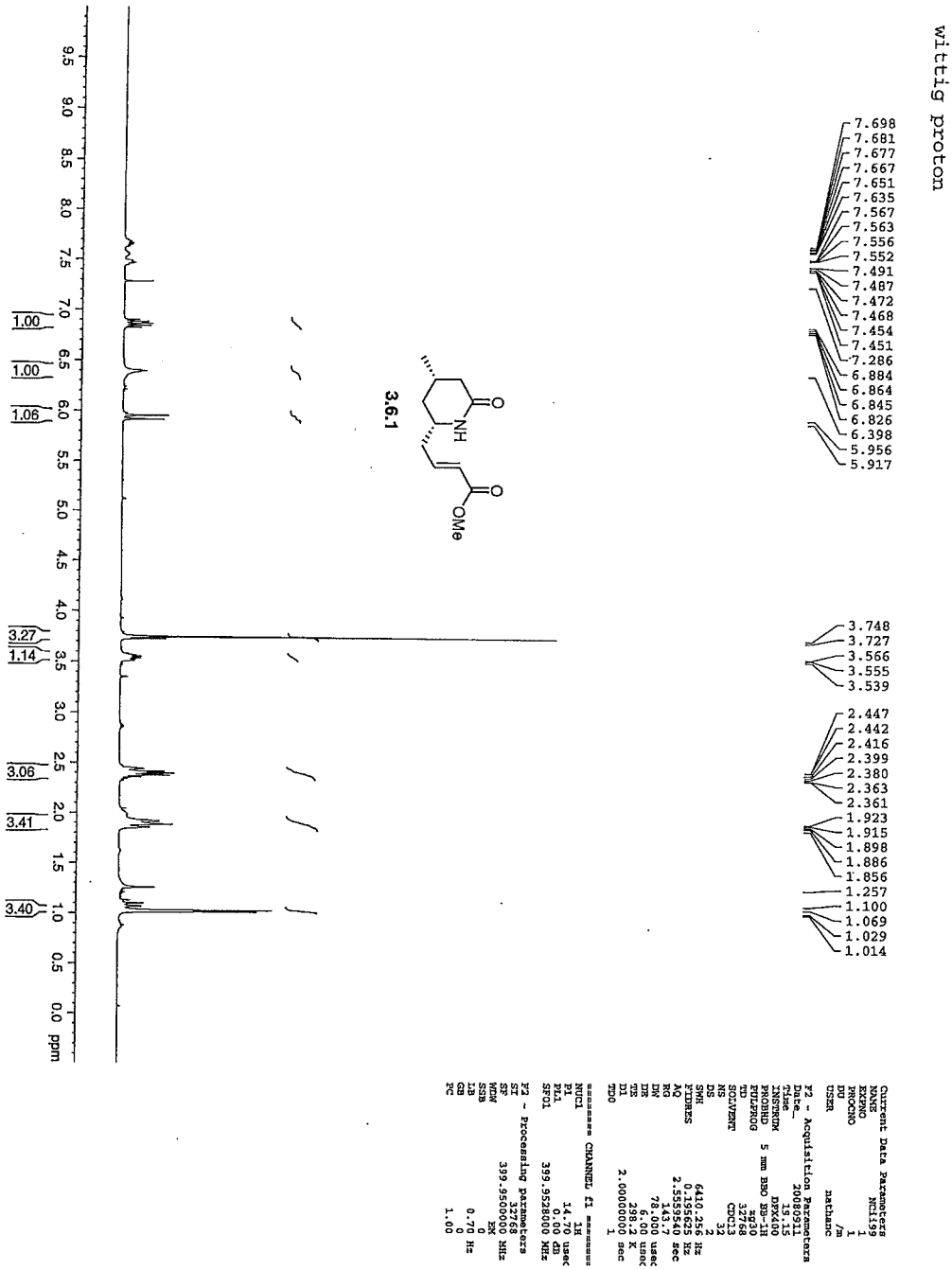
F2 - Acquisition Parameters
Date_ 20080618
Time 15.52
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 606
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3042164 sec
RG 16384
DW 19.900 usec
DE 6.00 usec
TE 298.2 K
D1 0.15000001 sec
D11 0.03000000 sec
DELAY 0.05000000 sec
TD0 1

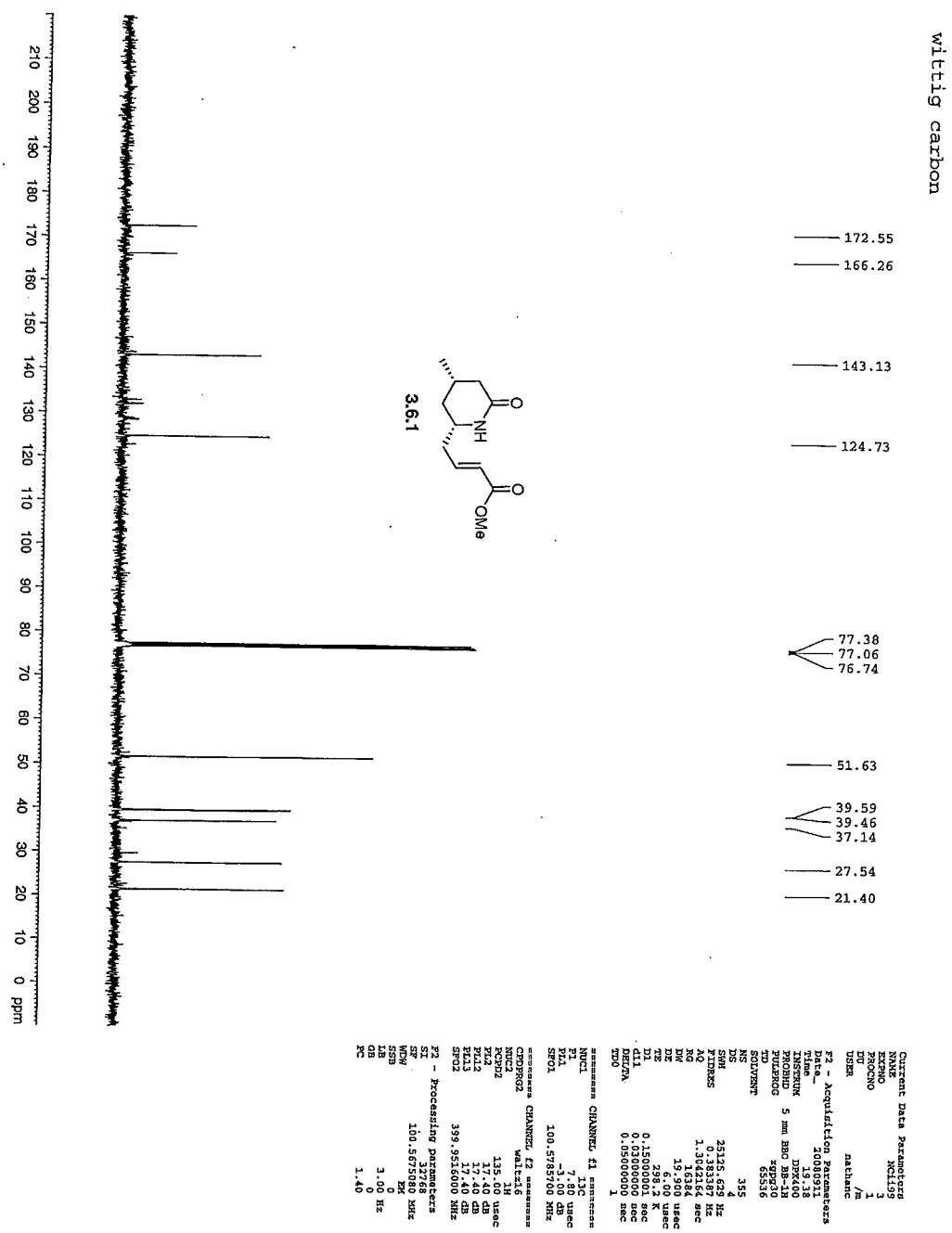
========== CHANNEL f1 ==========
NUC1 13C
P1 7.10 usec
PL1 -3.00 dB
SFO1 100.5785700 MHz

========== CHANNEL f2 ==========
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 usec
PL2 17.40 dB
PL12 17.40 dB
SFO2 399.9516000 MHz

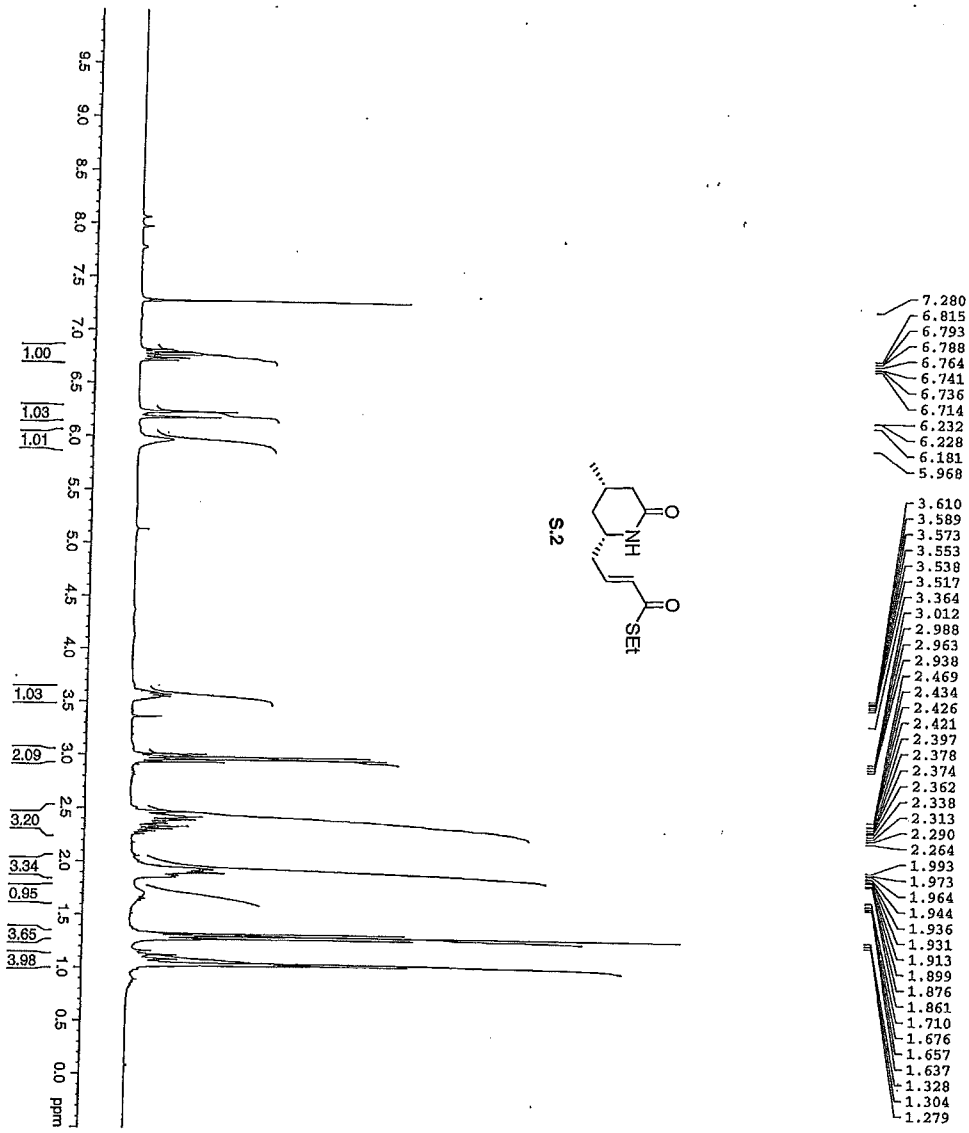
F2 - Processing parameters
SI 32768
SF 100.5675080 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40


2,4 DNP bottom spot
11.151
9.155
9.146
8.376
8.368
8.344
8.337
7.924
7.893
7.604
7.588
7.572
6.267
4.176
4.152
4.128
4.104
3.906
3.892
3.880
3.867
3.856
3.369
2.718
2.680
2.665
2.650
2.621
2.603
2.595
2.577
2.567
2.550
2.541
2.525
2.485
2.478
2.063
2.043
2.031
2.000
1.990
1.960
1.947
1.906
1.757
1.736
1.629
1.301
1.278
1.254
3.7.1
1.00
0.97
1.01
0.96
0.95
0.84
0.06
0.96
3.27
4.84
5.26
3.60
ppm


wittig proton
7.698
7.681
7.677
7.667
7.651
7.635
7.567
7.563
7.556
7.552
7.491
7.487
7.472
7.468
7.454
7.451
7.286
6.884
6.864
6.845
6.826
6.398
5.956
5.917
3.748
3.727
3.566
3.555
3.539
2.447
2.442
2.416
2.399
2.380
2.363
2.361
1.923
1.915
1.898
1.886
1.856
1.257
1.100
1.069
1.029
1.014
3.6.1
1.00
1.00
1.06
3.27
1.14
3.06
3.41
3.40
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
Current Data Parameters
NAME NC1199
EXPNO 1
PROCNO 1
DU /m
USER nschanc
F2 - Acquisition Parameters
Date_ 20000511
Time 15.15
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559040 sec
RG 78.000
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
========== CHANNEL f1 ==========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 399.9528000 MHz
F2 - Processing parameters
SI 32768
SF 399.9500000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00


wittig carbon
172.55
166.26
143.13
124.73
77.38
77.06
76.74
51.63
39.59
39.46
37.14
27.54
21.40
3.6.1
NH
O
O
OMe
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
Current Data Parameters
NAME NC1199
EXPNO 3
PROCNO 1
F2 - Acquisition Parameters
Date_ 20080511
Time 19.38
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 355
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3041284 sec
RG 19.900
DW 19.900 usec
DE 6.00 usec
TE 298.2 K
D1 0.15000001 sec
D11 0.03000000 sec
DELTA 0.05000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 7.10 usec
PL1 -3.00 dB
SFO1 100.5785700 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 usec
PL2 17.40 dB
PL12 17.40 dB
PL13 17.40 dB
SFO2 399.9516000 MHz
F2 - Processing parameters
SI 32768
SF 100.5675080 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40

HWE columed check



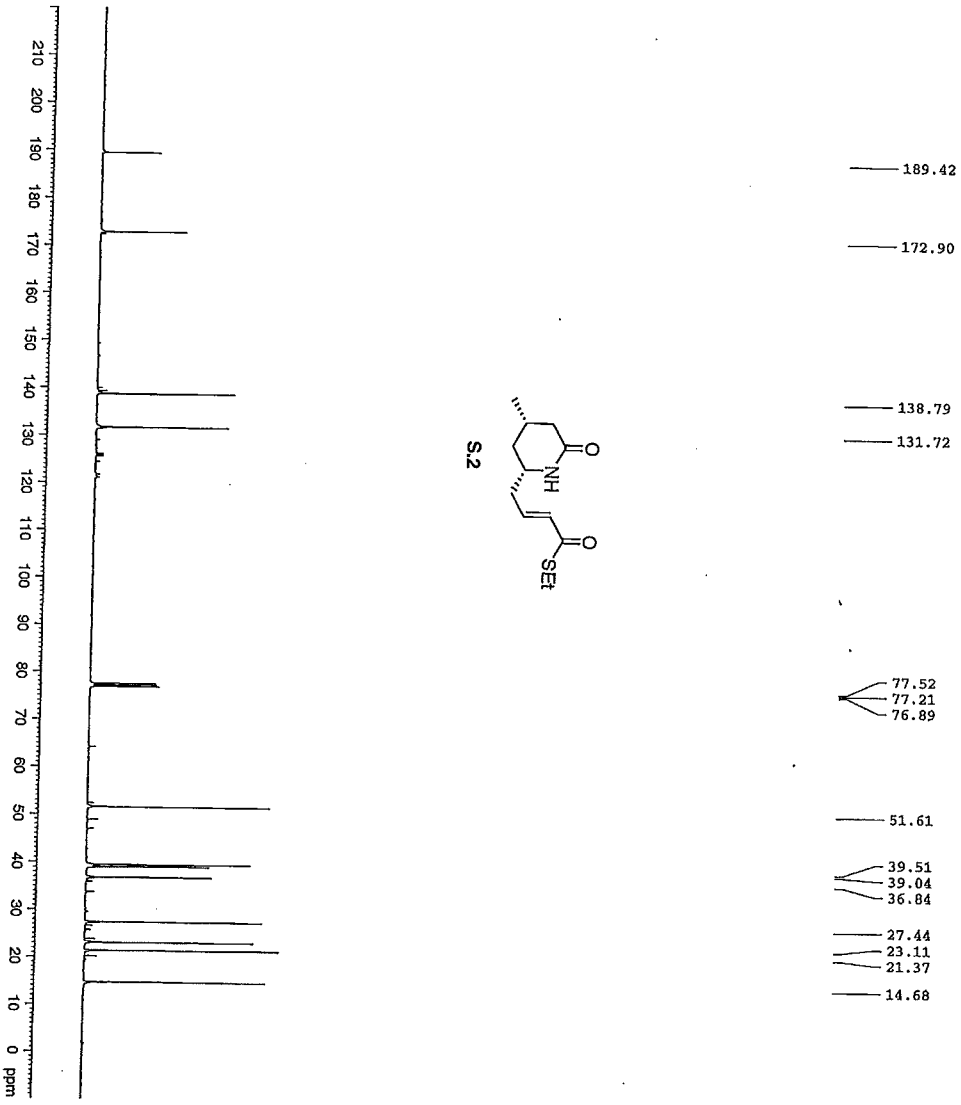
Current Data Parameters
NAME NCLv36
EXPNO 2
PROCNO 1
USER mathanz

F2 - Acquisition Parameters
Date_ 20090216
Time 14.23.06
INSTRUM DPX300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 4789.272 Hz
FIDRES 0.146157 Hz
AQ 3.4406591 sec
RG 456.1
DW 104.400 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1

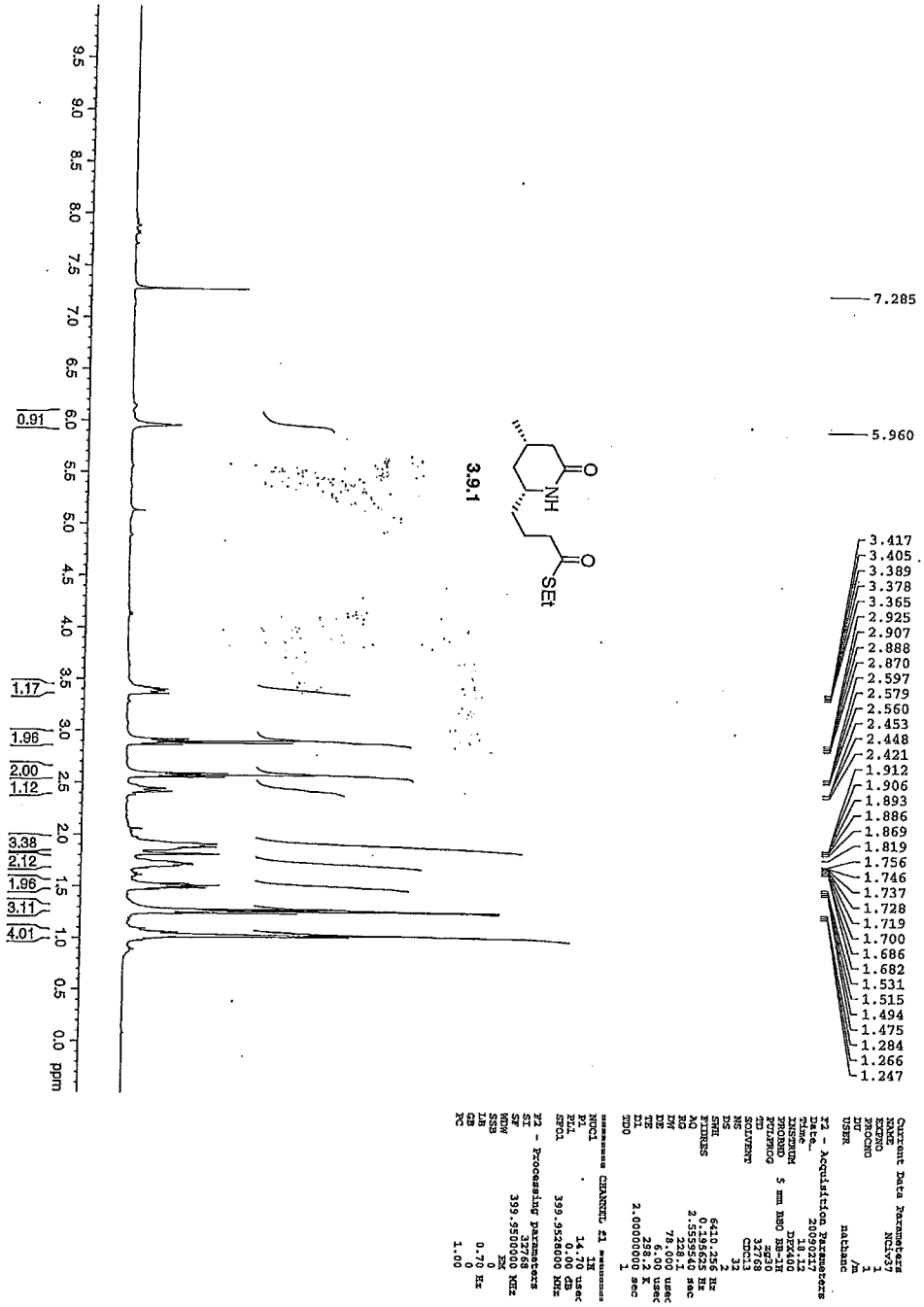
======== CHANNEL f1 ========
NUC1 1H
P1 9.00 usec
PL1 -3.00 dB
SFO1 300.1321009 MHz

F2 - Processing parameters
SI 32768
SF 300.1500000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

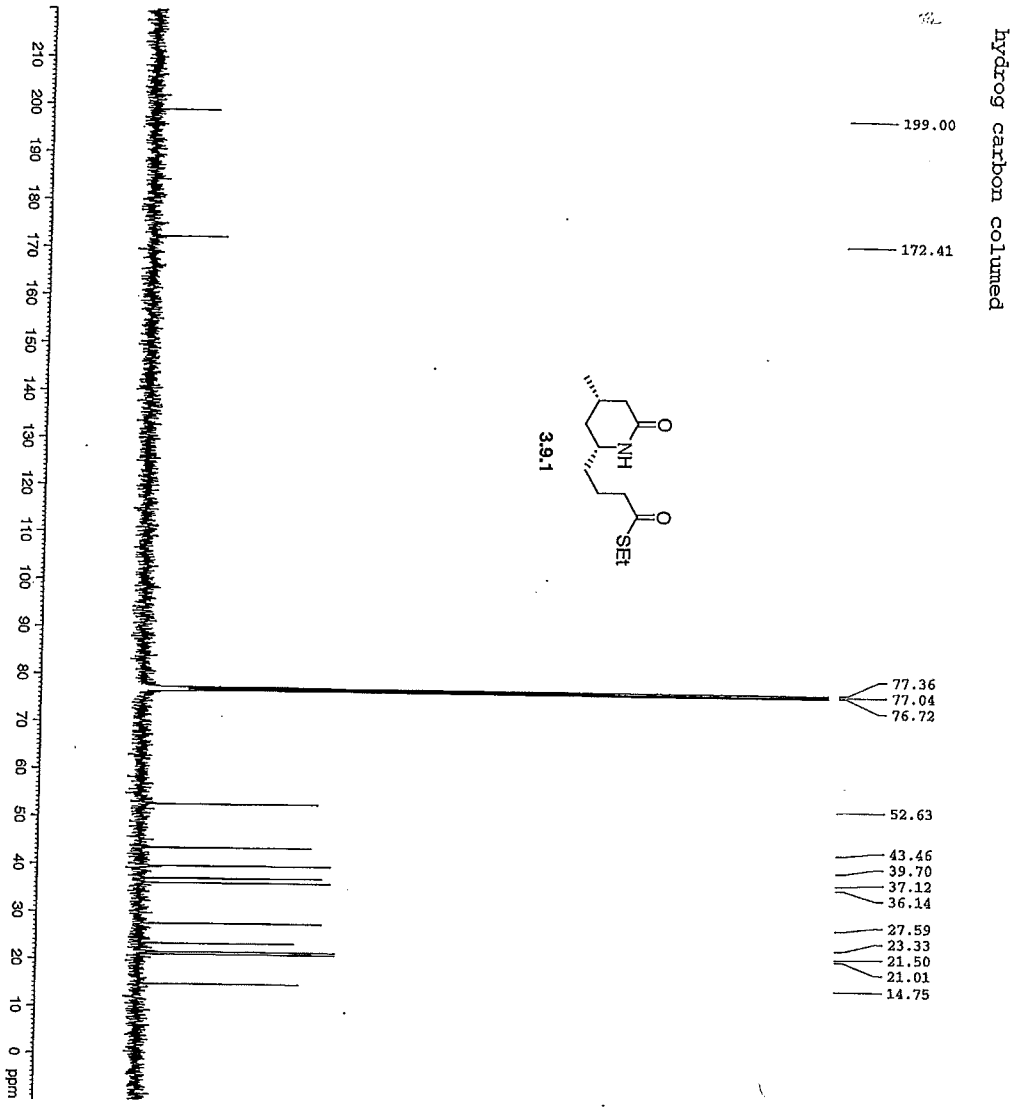
HWE carbon thioester



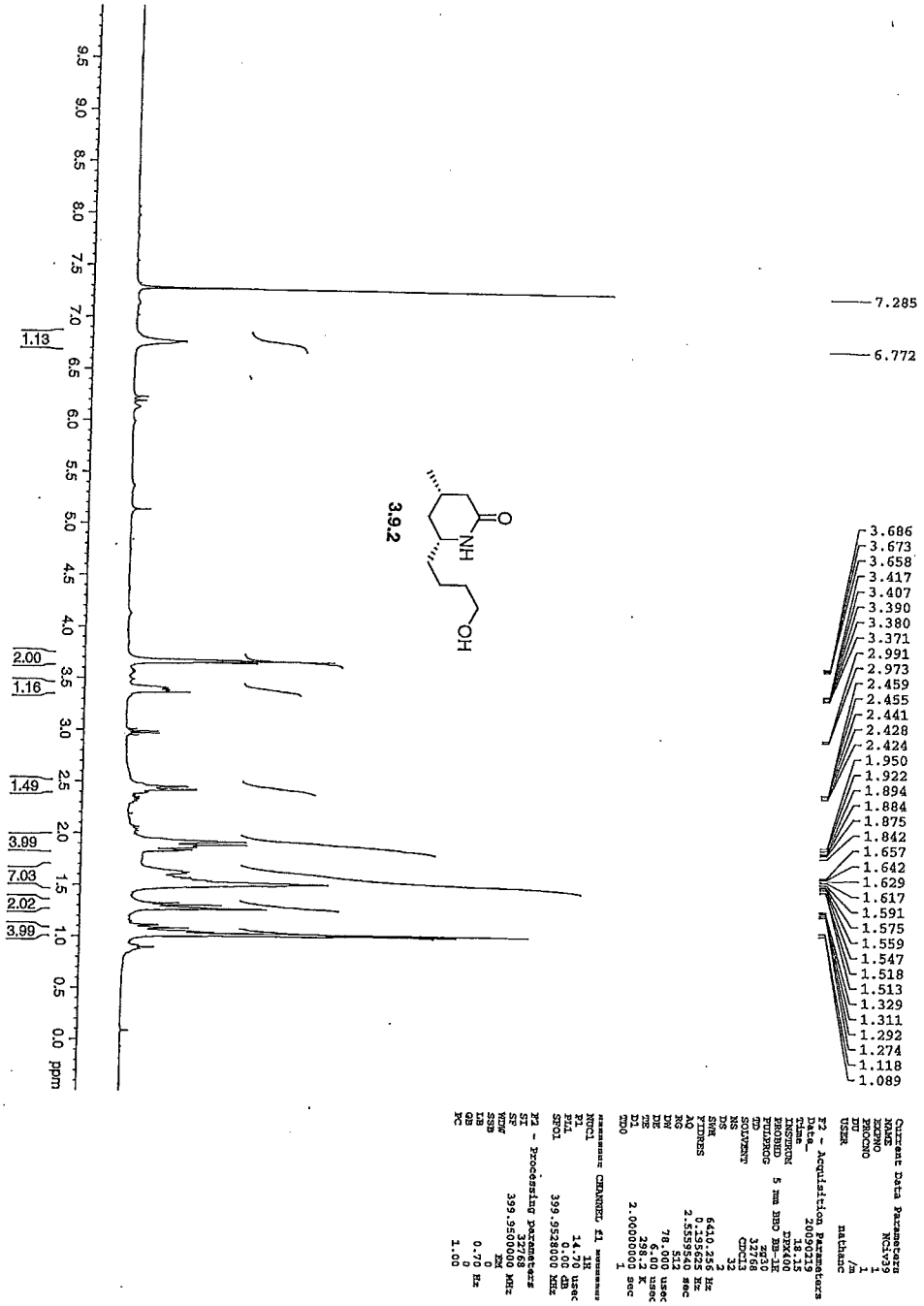
hydrog proton columed



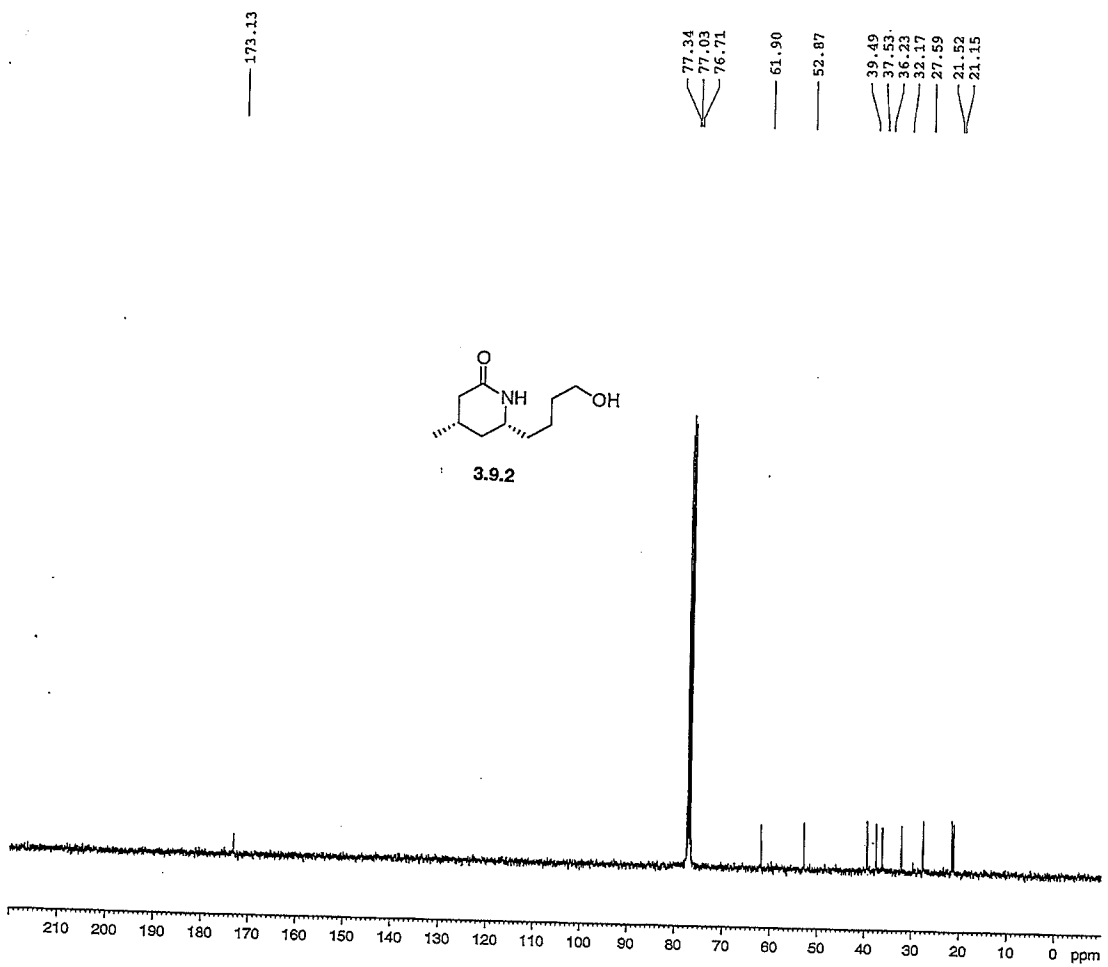
Current Data Parameters
NAME NCLv37
EXPNO 1
PROCNO 1
USER nathanc /A
F2 - Acquisition Parameters
Date_ 20060217
Time 18.12
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5555540 sec
RG 228.1
DW 78.000 usec
DE 6.00 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
========== CHANNEL f1 ==========
NUC1 1H
P1 14.70 usec
PL1 0.00 dB
SFO1 399.9528000 MHz
F2 - Processing parameters
SI 32768
SF 399.9500000 MHz
WDW EM
SSB 0
LB 0.70 Hz
GB 0
PC 1.00


hydrog carbon columed
199.00
172.41
77.36
77.04
76.72
52.63
43.46
39.70
37.12
36.14
27.59
23.33
21.50
21.01
14.75
NH
O
O
SEt
3.9.1
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
Current Data Parameters
NAME NCLV97
EXPNO 1
PROCNO 1
USER nathanc
F2 - Acquisition Parameters
Date_ 20050217
Time 18.51
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 818
DS 4
SWH 25125.628 Hz
FIDRES 0.383387 Hz
AQ 1.3042164 sec
RG 16384
DW 19.900 usec
DE 6.00 usec
TE 298.1 K
D1 0.15000001 sec
D11 0.03000000 sec
DELTA 0.05000000 sec
TD0 1
CHANNEL f1
NUC1 13C
P1 7.80 usec
PL1 -3.00 dB
SFO1 100.5785700 MHz
CHANNEL f2
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 usec
PL2 17.40 dB
PL12 17.40 dB
PL13 17.40 dB
SFO2 399.9516000 MHz
F2 - Processing parameters
SI 327680
SF 100.5675080 MHz
WDW EM
SSB 0
LB 3.0 Hz
GB 0
PC 1.40

columed borohydride



columed borohydride carbon



Current Data Parameters
NAME NCiv39
EXPNO 2
PROCNO 1
DU /m
USER nathanc

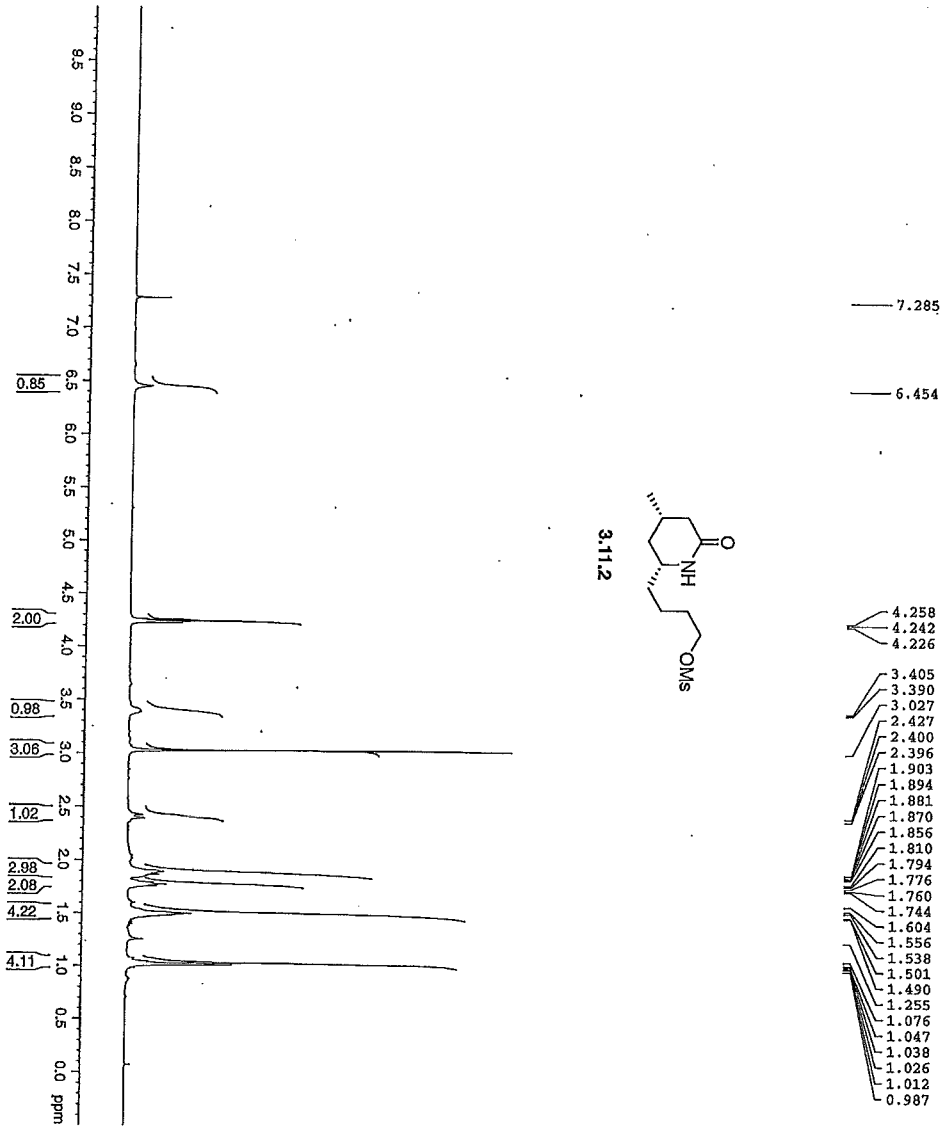
F2 - Acquisition Parameters
Date_ 20090219
Time 19.03
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 1751
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3042164 sec
RG 16384
DW 19.900 usec
DE 6.00 usec
TE 298.2 K
D1 0.15000001 sec
d11 0.03000000 sec
DELTA 0.05000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 13C
P1 7.80 usec
PL1 -3.00 dB
SFO1 100.5785700 MHz

======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 usec
PL2 17.40 dB
PL12 17.40 dB
PL13 17.40 dB
SFO2 399.9516000 MHz

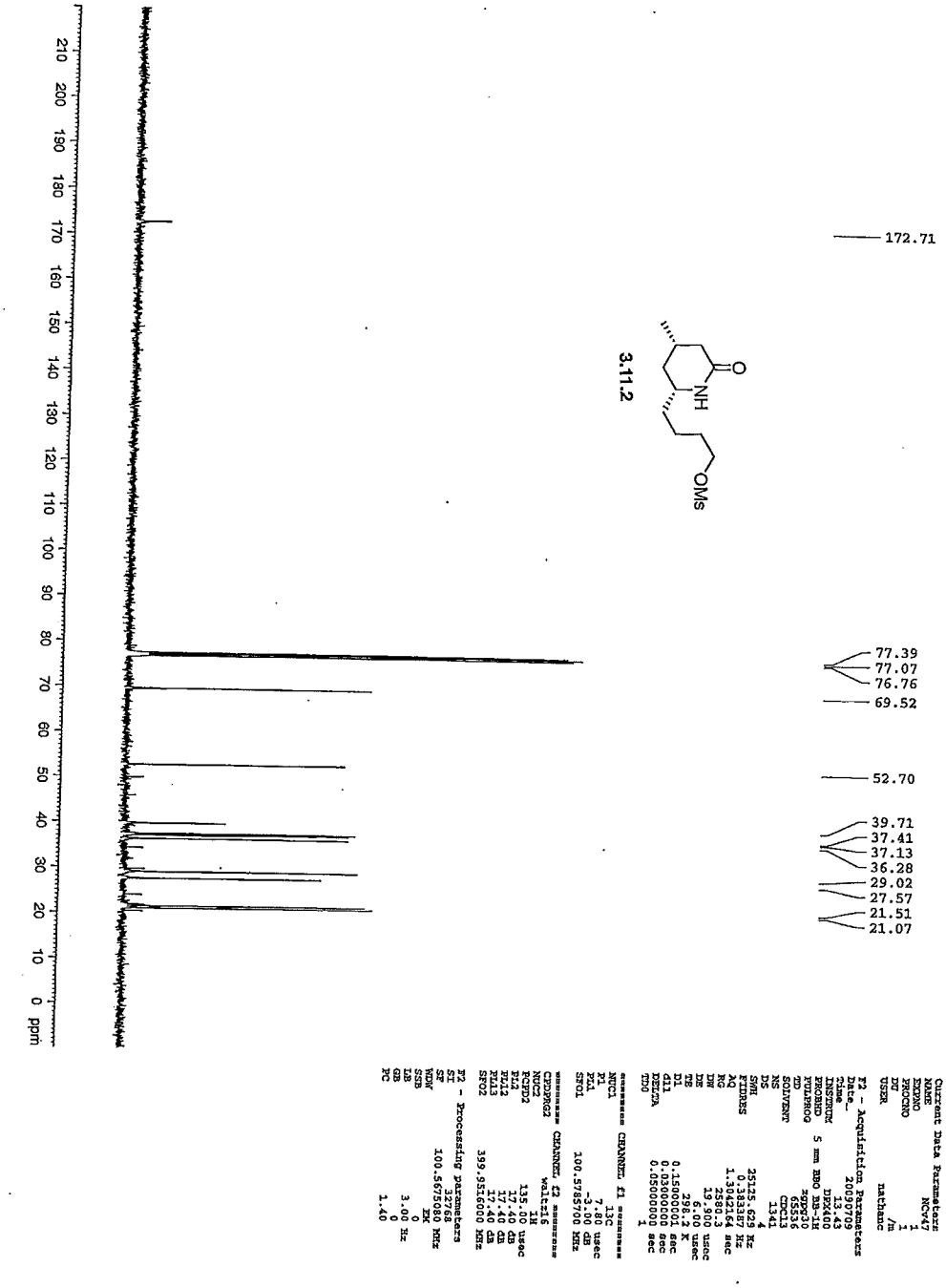
F2 - Processing parameters
SI 32768
SF 100.5675080 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40

mesylate proton



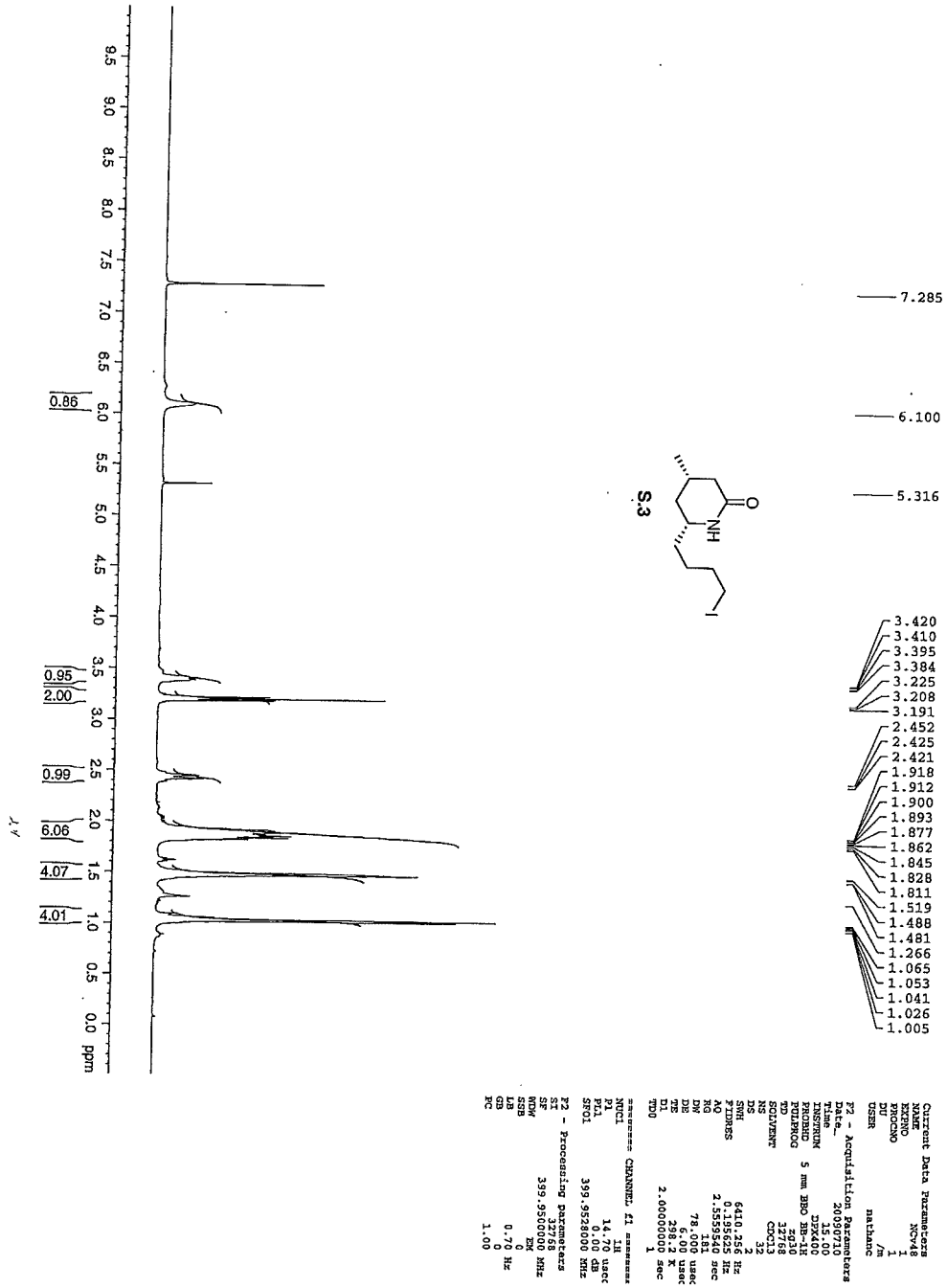

```
Current Data Parameters
NAME                  NCY47
EXPNO                     2
PROCNO                    1
USER                    /n
                      nathanc

F2 - Acquisition Parameters
Date_              20090709
Time              13.47.47
INSTRUM             DPX400
PROBHD  5 mm BBO BB-1H
PULPROG                zg30
TD                    32768
SOLVENT
NS                       32
DS                        2
SWH               6410.256 Hz
FIDRES            0.195625 Hz
AQ                2.5559540 sec
RG                     5211
DW                 78.000 usec
DE                  6.00 usec
TE                 298.2 K
D1                 2.00000000 sec
TD0                       1

========== CHANNEL f1 ==========
NUC1                    1H
P1                   14.70 usec
PL1                  0.00 dB
SFO1          399.9528000 MHz

F2 - Processing parameters
SI                    32768
SF                399.9500000 MHz
WDW                       EM
SSB                        0
LB                   0.70 Hz
GB                         0
PC                      1.00
```

mesylate proton

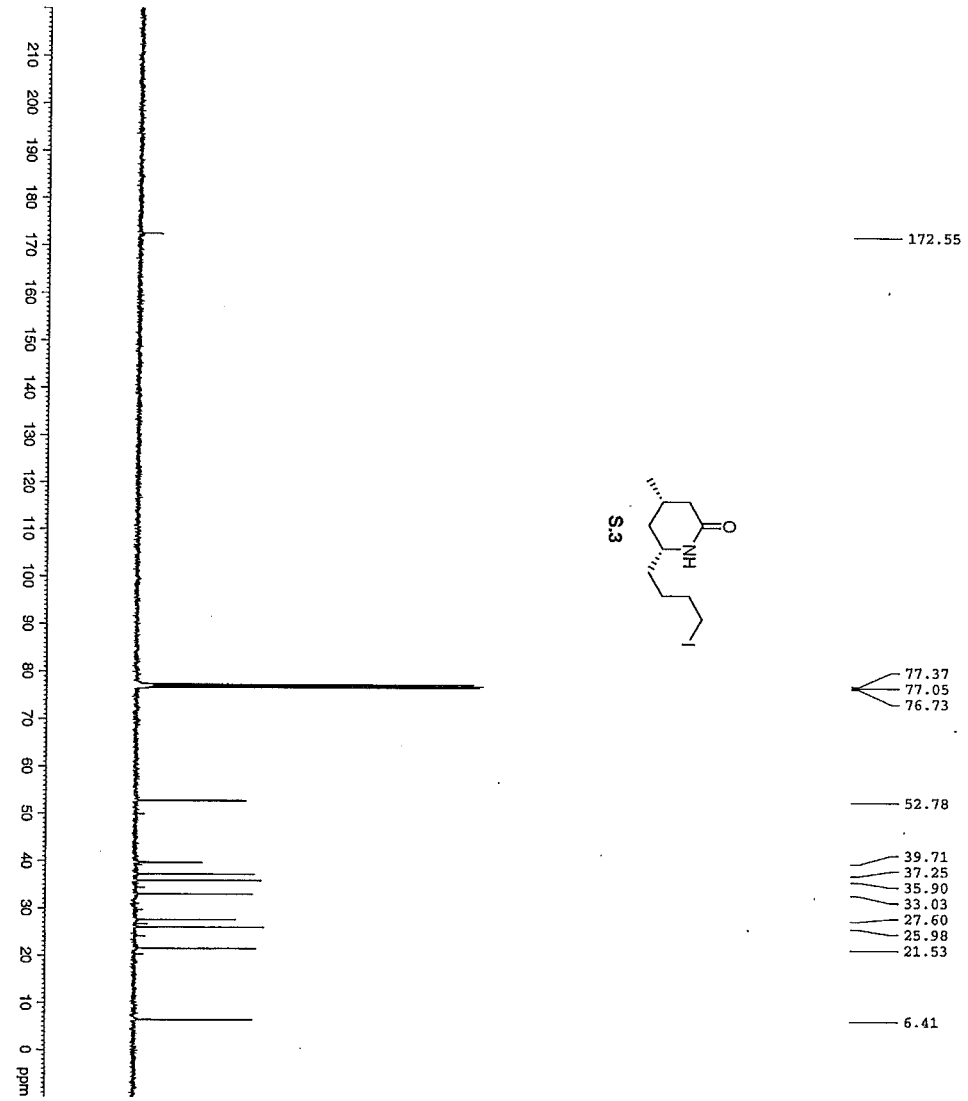


Current Data Parameters
NAME NC-47
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20090709
Time 13.43
INSTRUM DPX400
PROBHD 5 mm BBO
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1341
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3042164 sec
RG 2580.3
DW 19.900 usec
DE 6.00 usec
TE 298.2 K
D1 0.15000001 sec
D11 0.03000000 sec
MCREVA 0.05000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 7.80 usec
PL1 -2.00 dB
SFO1 100.5785700 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 usec
PL2 17.40 dB
PL12 17.40 dB
PL13 17.40 dB
SFO2 399.9516000 MHz
F2 - Processing parameters
SI 32768
SF 100.5675080 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40

iodide proton



iodide carbon



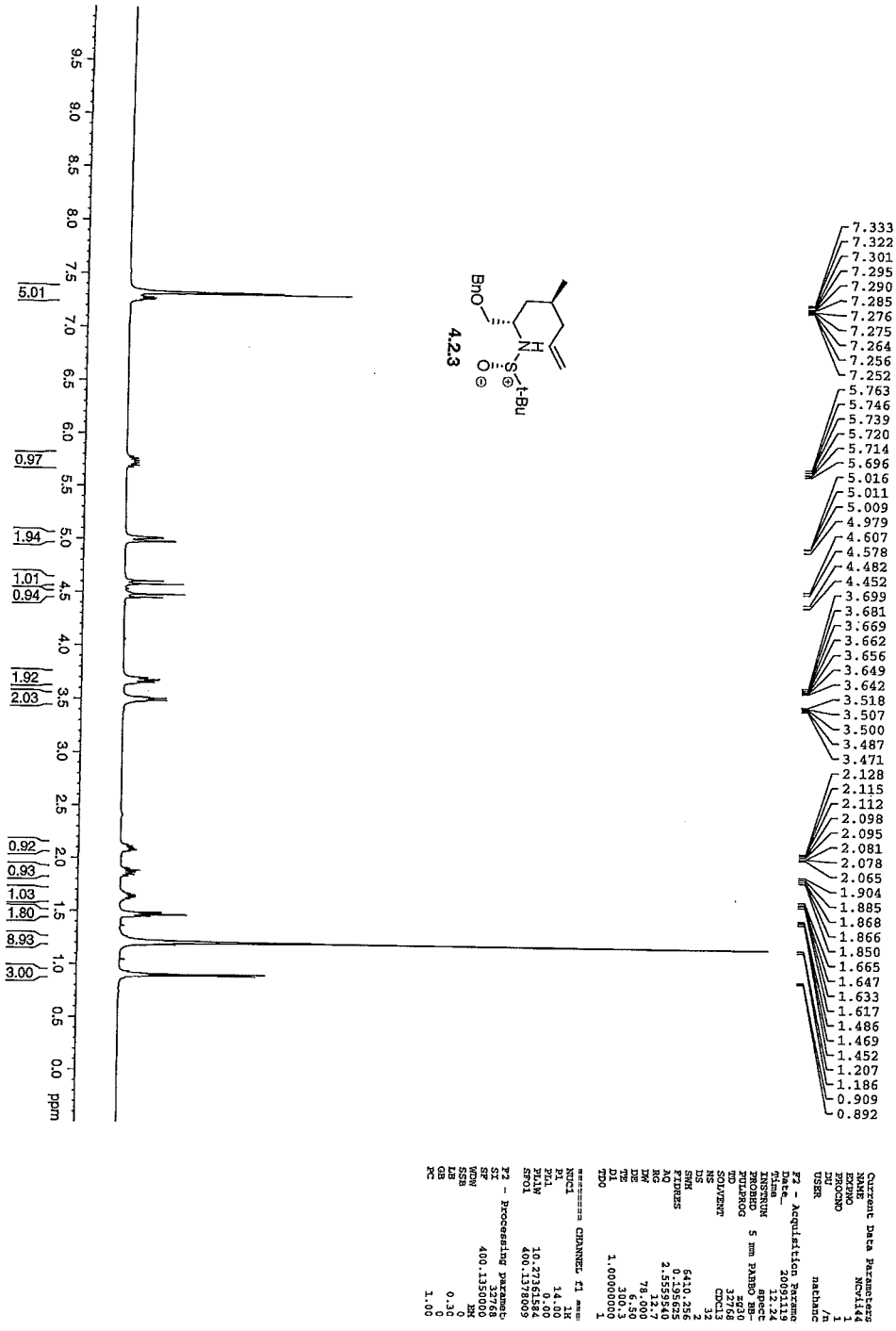
Current Data Parameters
NAME NCv48
EXPNO 3
PROCNO 1
DU /n
USER nathanc

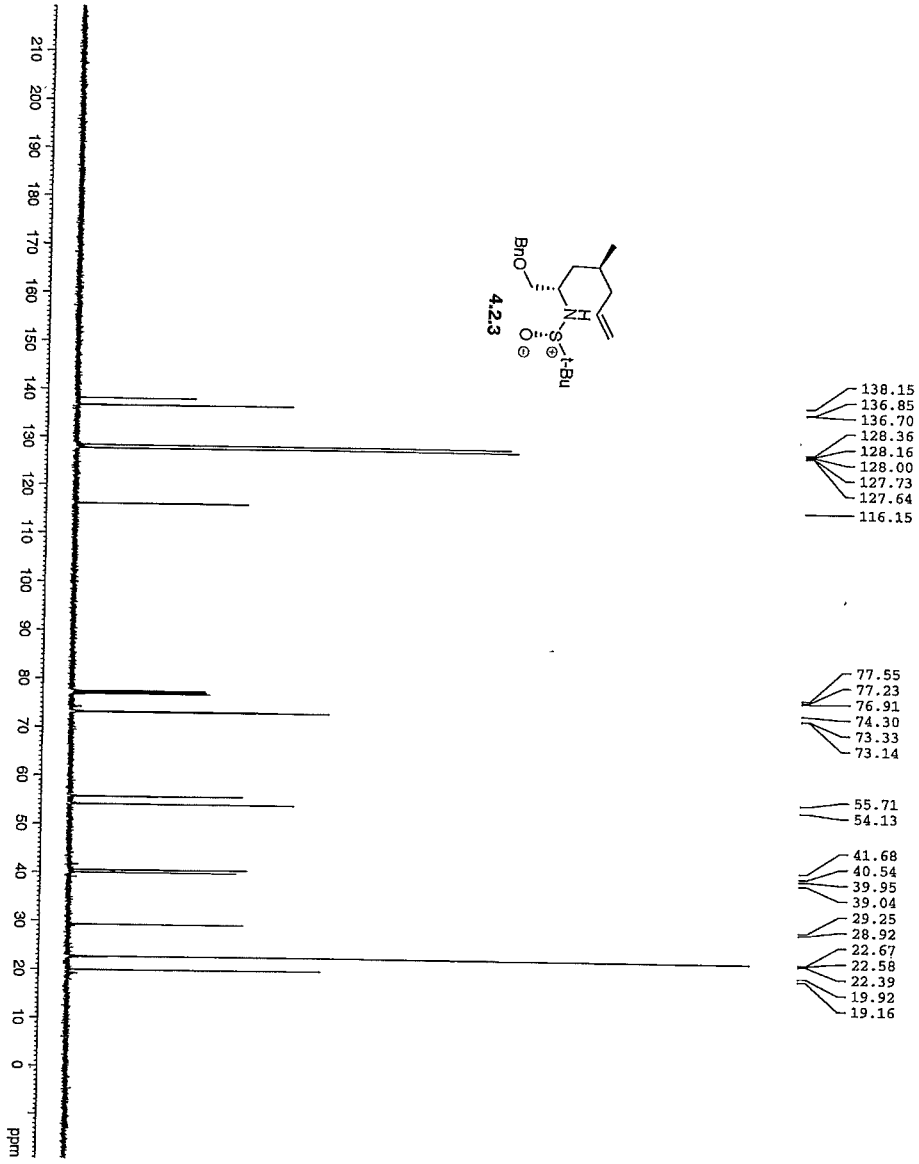
F2 - Acquisition Parameters
Date_ 20050710
Time 14:56
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT
NS 2450
DS 4
SWH 25125.629 Hz
FIDRES 0.383387 Hz
AQ 1.3042564 sec
RG 143.84
DW 19.900 usec
DE 6.00 usec
TE 299.2 K
D1 0.15000001 sec
D11 0.03000000 sec
DELTA 0.05000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 13C
P1 7.10 usec
PL1 -3.00 dB
SFO1 100.5785700 MHz

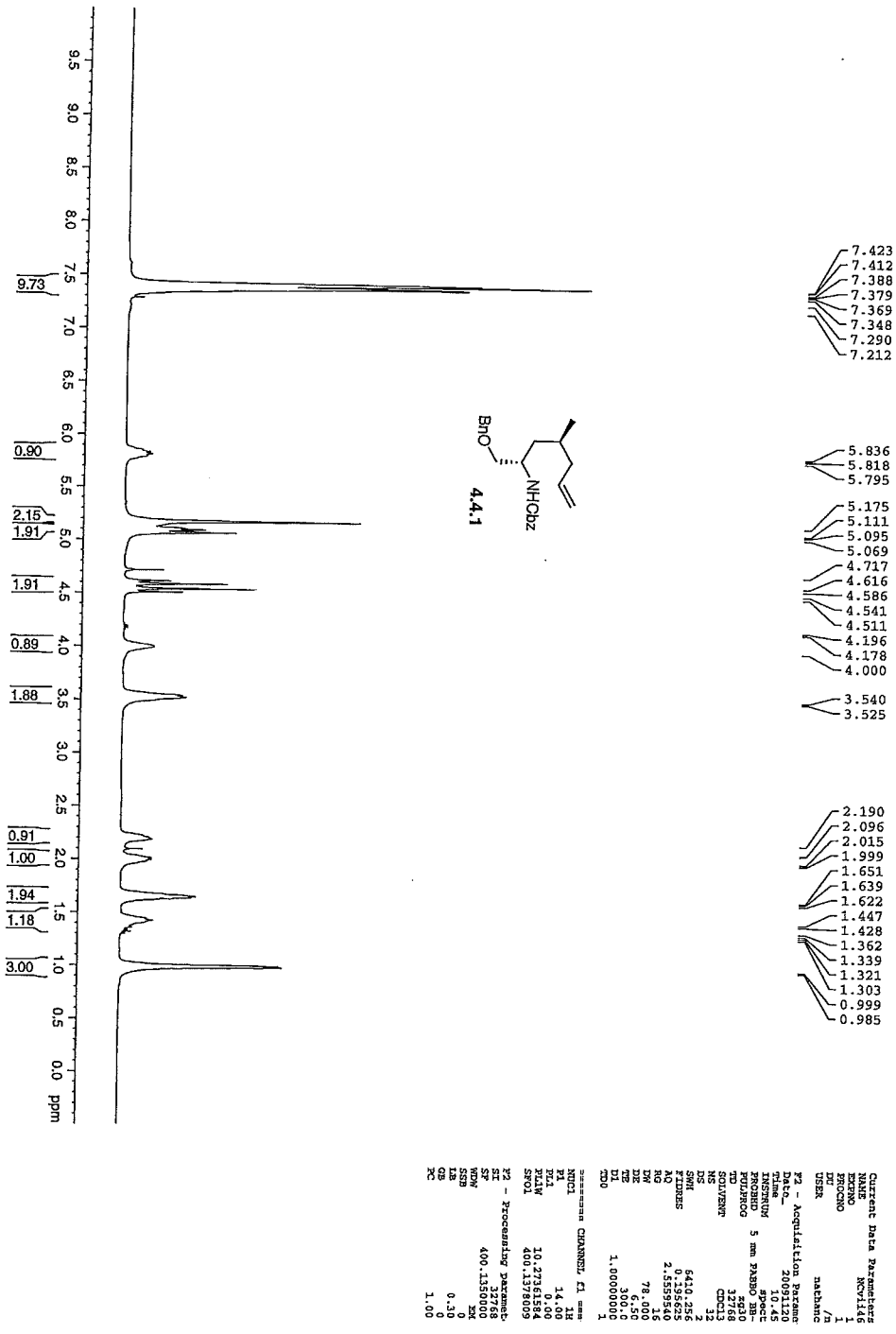
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 135.00 usec
PL2 17.40 dB
PL12 17.40 dB
PL13 17.40 dB
SFO2 399.9516000 MHz

F2 - Processing parameters
SI 32768
SF 100.5675080 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40

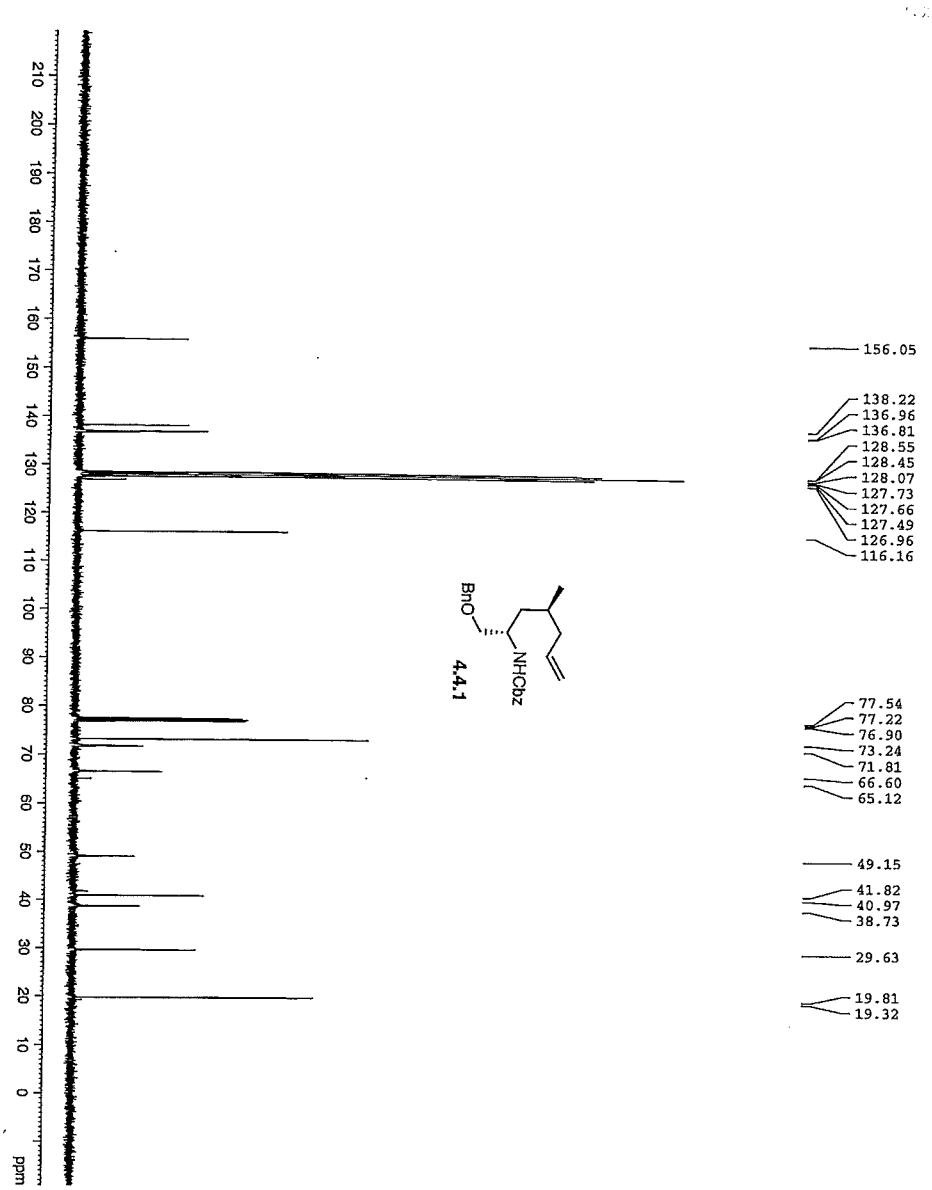

4.2.3
BnO
H
N
S
t-Bu
O
5.01
0.97
1.94
1.01
0.94
1.92
2.03
0.92
0.93
1.03
1.80
8.93
3.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
7.333
7.322
7.301
7.295
7.290
7.285
7.276
7.275
7.264
7.256
7.252
5.763
5.746
5.739
5.720
5.714
5.696
5.016
5.011
5.009
4.979
4.607
4.578
4.482
4.452
3.699
3.681
3.669
3.662
3.656
3.649
3.642
3.518
3.507
3.500
3.487
3.471
2.128
2.115
2.112
2.098
2.095
2.081
2.078
2.065
1.904
1.885
1.868
1.866
1.850
1.665
1.647
1.633
1.617
1.486
1.469
1.452
1.207
1.186
0.909
0.892
Current Data Parameters
NAME NCV1144
EXPNO 1
PROCNO 1
F2 - Acquisition Parame
Date_ 20091119
Time 12.24
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 2
DS 2
SWH 6410.256
FIDRES 0.195625
AQ 2.5559240
RG 128
DW 78.000
DE 6.50
TE 300.3
D1 1.00000000
TD0 1
======== CHANNEL f1 ====
NUC1 1H
P1 14.00
PLW1 0.0000
PLW1 10.27161598
SFO1 400.1378009
F2 - Processing paramet
SI 32768
SF 400.1350000
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00



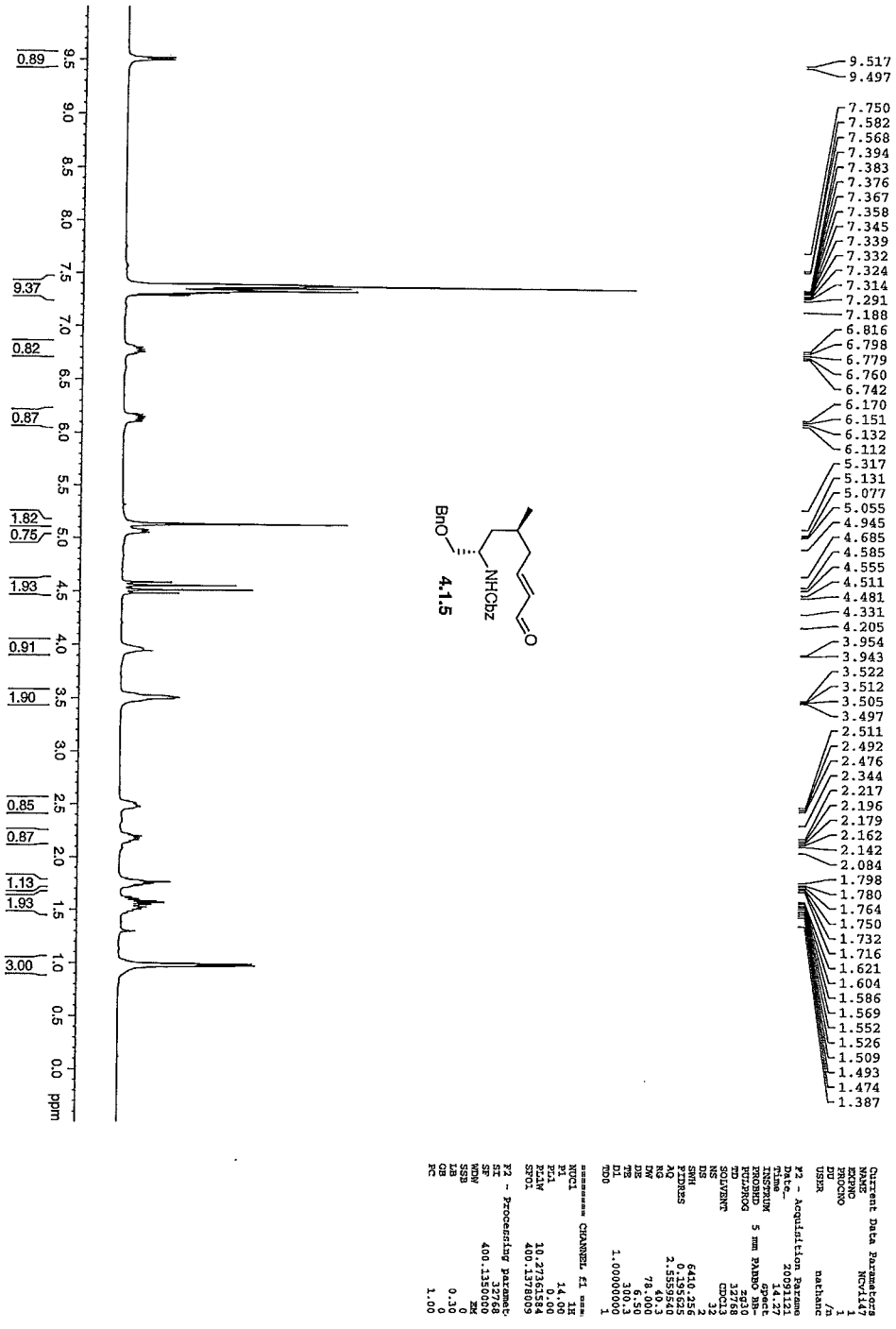

```
Current Data Parameters
NAME                  NCV1144
EXPNO                       3
PROCNO                      1
DIR                        /n
USER                 nathanc

F2 - Acquisition Parameter
Date_              20051119
Time                   12.43
INSTRUM                spect
PROBHD     5 mm PABBO BB/
PULPROG             zgpg30
TD                     65536
SOLVENT               CDCl3
NS                       101
DS                         4
SWH                23980.814 Hz
FIDRES                 0.365918 Hz
AQ                     1.3664756 sec
RG                       32768
DW                     20.850 usec
DE                      6.50 usec
TE                     301.4 K
D1                     2.00000000 sec
D11                    0.03000000 sec
TD0                           1

======== CHANNEL f1 ========
NUC1                       13C
P1                        9.00 usec
PL1                      -2.00 dB
PL1W               46.89702606 W
SFO1               100.6240872 MHz

======== CHANNEL f2 ========
CPDPRG2                 waltz16
NUC2                        1H
PCPD2                    90.00 usec
PL2                       0.00 dB
PL12                     16.16 dB
PL13                     17.00 dB
PL2W               10.27361584 W
PL12W               0.24872722 W
PL13W               0.20498557 W
SFO2               400.1366005 MHz

F2 - Processing parameters
SI                         32768
SF                 100.6140260 MHz
WDW                           EM
SSB                            0
LB                          1.00 Hz
GB                             0
PC                          1.40
```

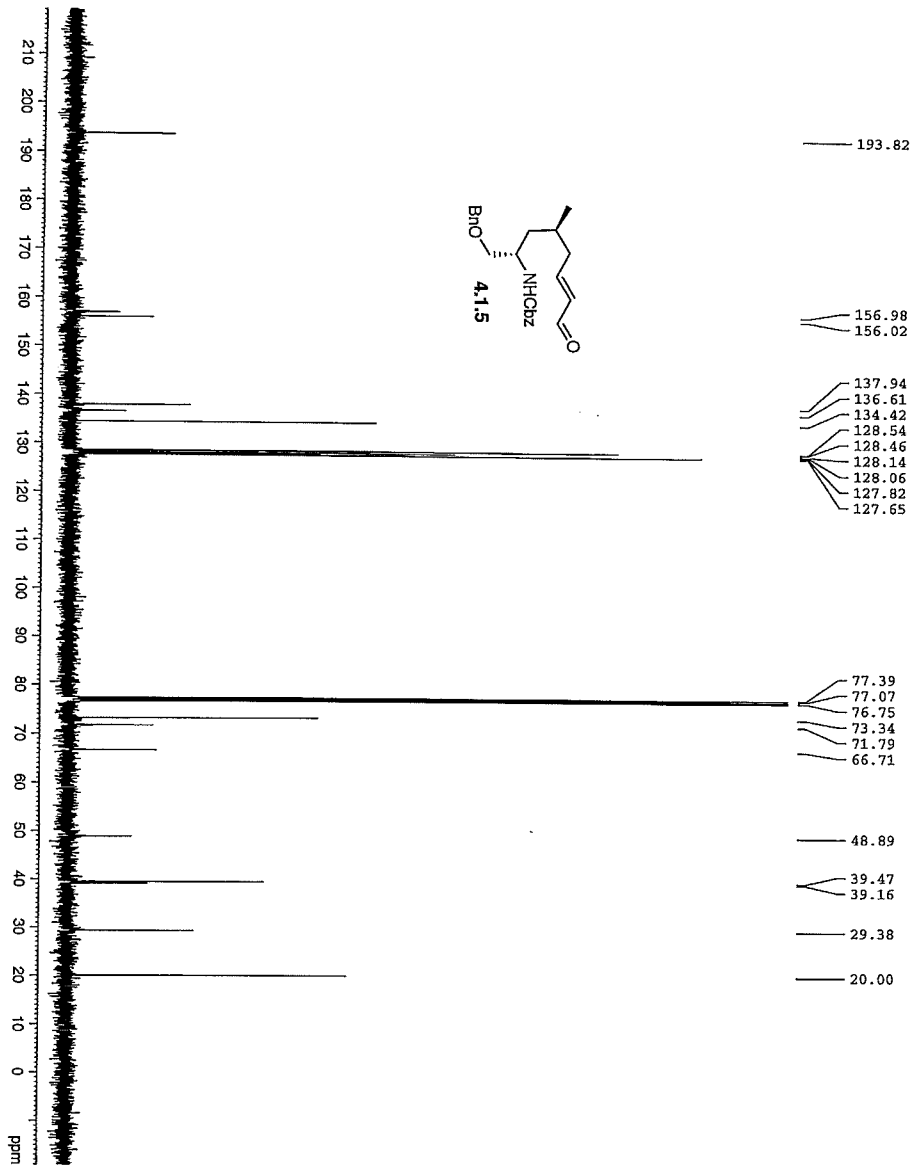



```
Current Data Parameters
NAME                  NCY1146
EXPNO                      1
PROCNO                     1
F2 - Acquisition Parameters
Date_              20091120
Time                   10.45
INSTRUM                spect
PROBHD     5 mm PABBO BB-
PULPROG                zg30
TD                    32768
SOLVENT               CDCl3
NS                        32
DS                         2
SWH                64210.256
FIDRES             1.959540
AQ                 2.5559540
RG                       156
DW                  78.000
DE                   6.50
TE                  300.0
D1                  1.00000000
TD0                        1
======== CHANNEL f1 ========
NUC1                     1H
P1                    14.00
PL1                    0.00
PL1W          10.27161584
SFO1          400.1378009
F2 - Processing parameters
SI                    32768
SF                400.1350000
WDW                       EM
SSB                        0
LB                      0.30
GB                         0
PC                      1.00
```

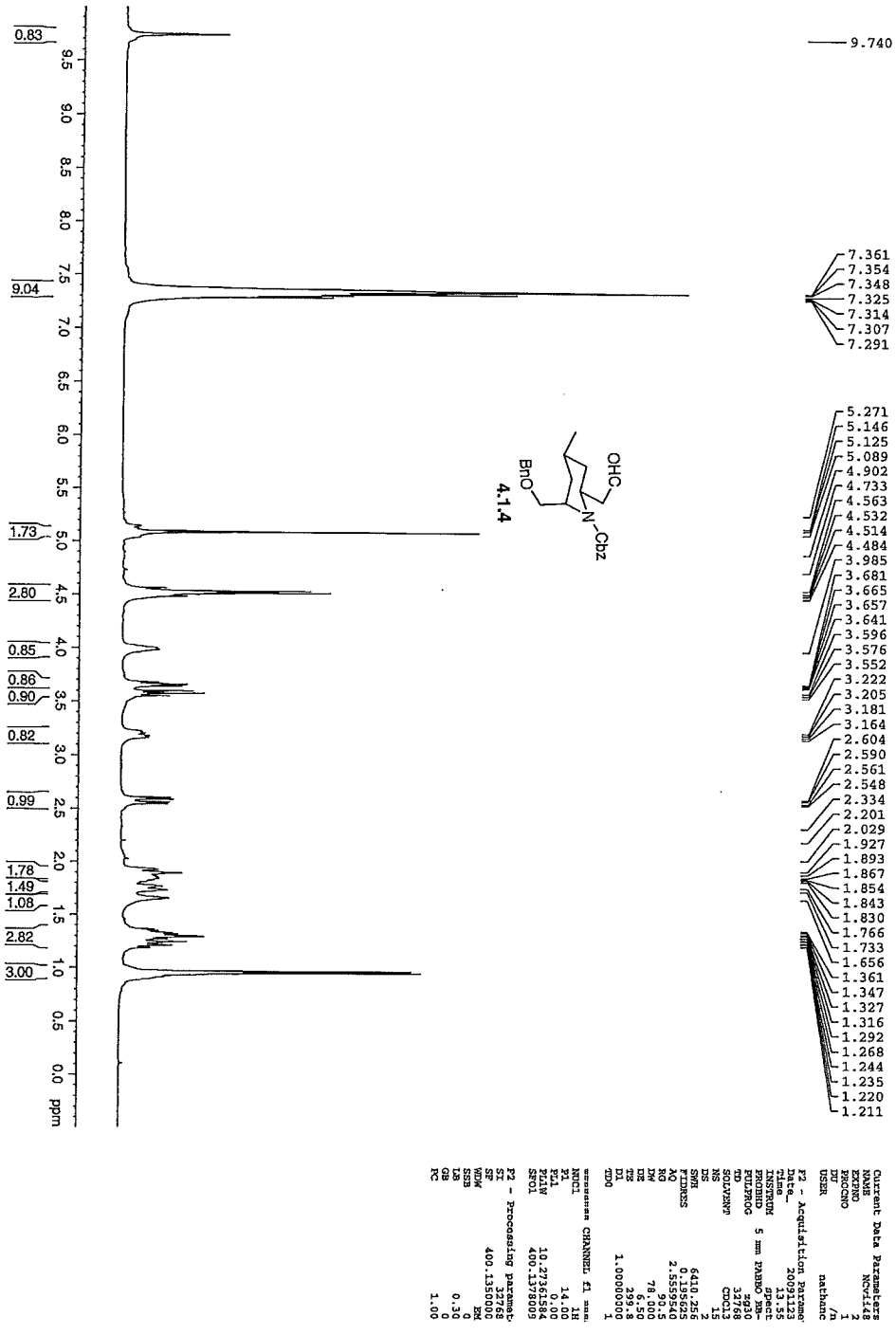


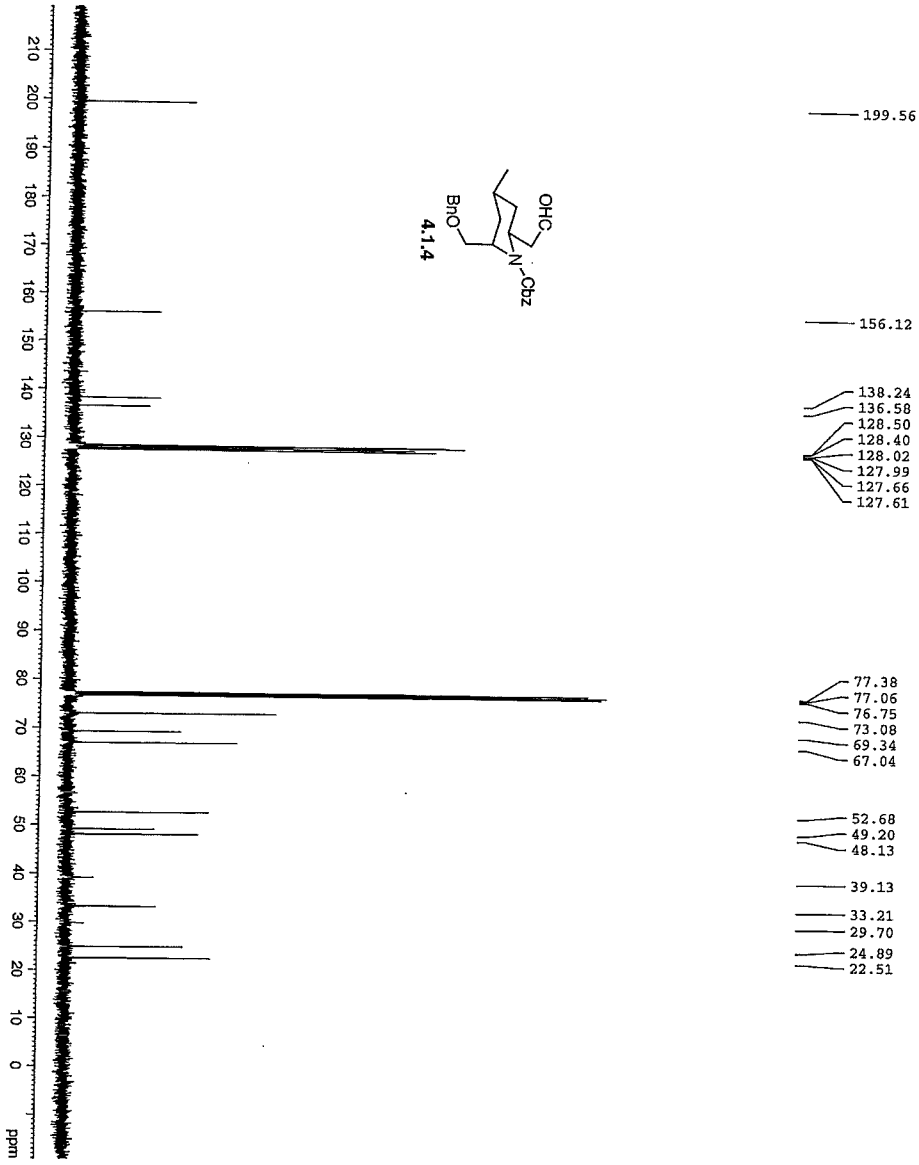

```
Current Data Parameters
NAME                  NCY1146
EXPNO                       2
PROCNO                      1
DU                          /n
USER                  nathanc

F2 - Acquisition Parameter
Date_              20091120
Time                   10.53
INSTRUM                spect
PROBHD  5 mm PABBO BB-
PULPROG                zgpg30
TD                      65536
SOLVENT                CDCl3
NS                        101
DS                          4
SWH                23980.814 Hz
FIDRES              1.366475 Hz
AQ                  1.365918 sec
RG                      32768
DW                     20.850 us
DE                      6.50 us
TE                     301.1 K
D1                  2.0000000 sec
D11                 0.0300000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                      13C
P1                       9.00 us
PL1                     -2.00 dB
PL1W               46.89702606 W
SFO1               100.6240872 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                        1H
PCPD2                   90.00 us
PL2                      0.00 dB
PL12                    16.16 dB
PL13                    17.00 dB
PL2W               10.27361584 W
PL12W               0.24872722 W
PL13W               0.20498557 W
SFO2               400.1366005 MHz

F2 - Processing parameters
SI                      32768
SF                 100.6140260 MHz
WDW                        EM
SSB                         0
LB                       1.00 Hz
GB                          0
PC                       1.40
```


9.517
9.497
7.750
7.582
7.568
7.394
7.383
7.376
7.367
7.358
7.345
7.339
7.332
7.324
7.314
7.291
7.188
6.816
6.798
6.779
6.760
6.742
6.170
6.151
6.132
6.112
5.317
5.131
5.077
5.055
4.945
4.685
4.585
4.555
4.511
4.481
4.331
4.205
3.954
3.943
3.522
3.512
3.505
3.497
2.511
2.492
2.476
2.344
2.217
2.196
2.179
2.162
2.142
2.084
1.798
1.780
1.764
1.750
1.732
1.716
1.621
1.604
1.586
1.569
1.552
1.526
1.509
1.493
1.474
1.387
BnO
NHCbz
O
4.1.5
0.89
9.37
0.82
0.87
1.82
0.75
1.93
0.91
1.90
0.85
0.87
1.13
1.93
3.00
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
Current Data Parameters
NAME NCv1147
EXPNO 1
PROCNO 1
DU /n
USER nathanc
f2 - Acquisition Parame
Date_ 20091111
Time 14.27
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 128788
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256
FIDRES 0.199542
AQ 2.5559545
RG 40.3
DW 78.000
DE 6.50
TE 300.3
D1 1.0000000
TD0 1
========== CHANNEL f1 ===
NUC1 1H
P1 14.00
PL1 0.00
PL1W 10.27361584
SFO1 400.1378009
F2 - Processing paramet
SI 131072
SF 400.1350000
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00

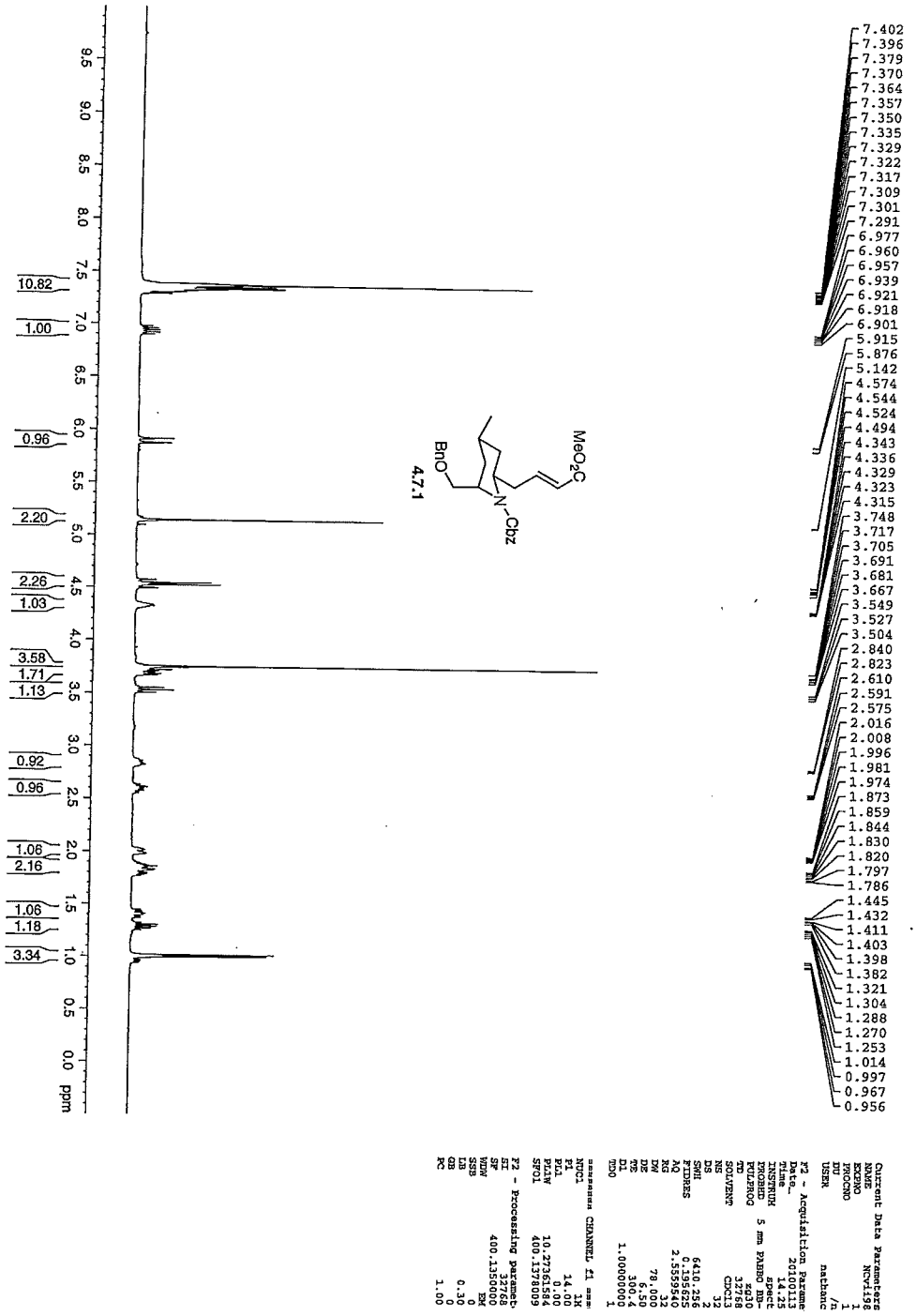


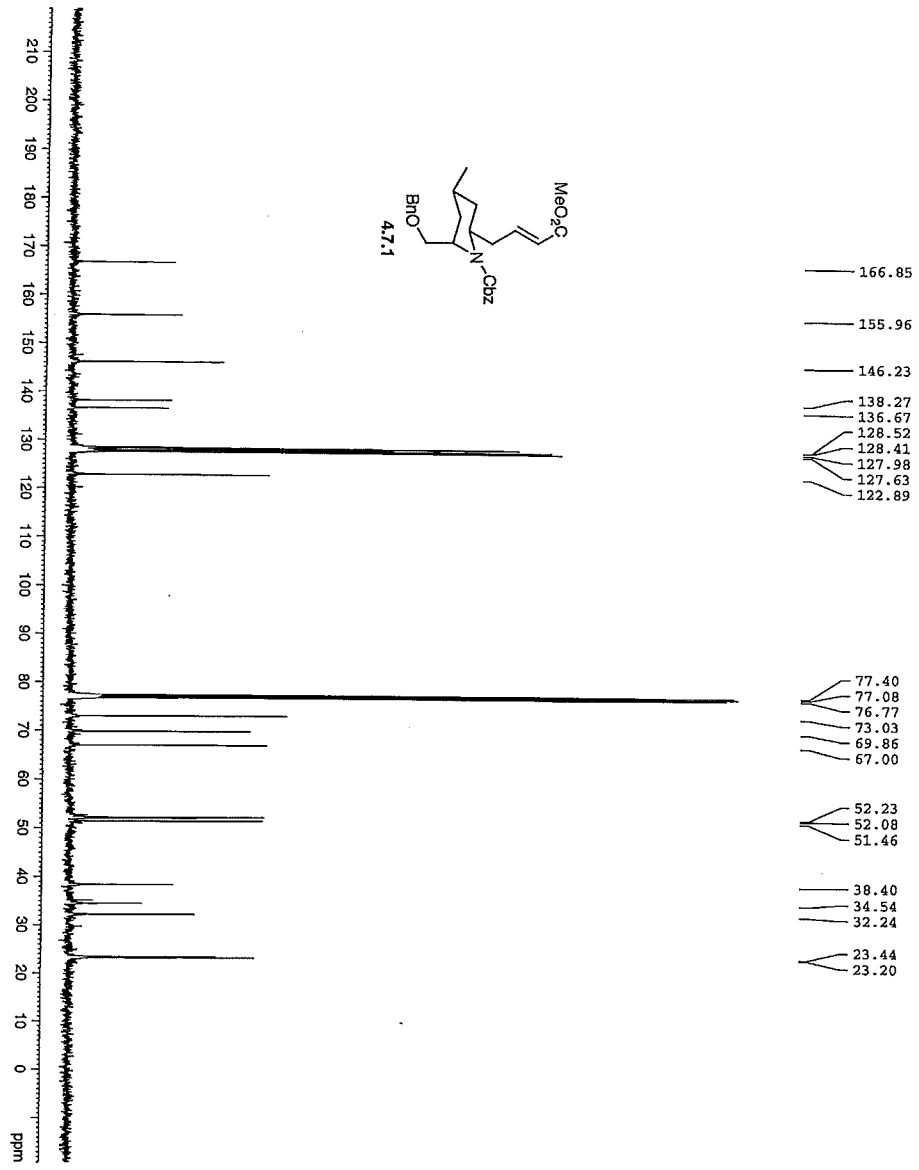

```
Current Data Parameters
NAME                  NCval47
EXPNO                        2
PROCNO                       1
DU                          /n
USER                 nathanc

F2 - Acquisition Parameters
Date_              20091121
Time                   14.32
INSTRUM                spect
PROBHD     5 mm PABBO BB-
PULPROG            zgpg30
TD                 65536
SOLVENT            CDCl3
NS                   212
DS                     4
SWH            23980.814 Hz
FIDRES         0.365918 Hz
AQ             1.3664736 sec
RG                  287.56
DW                 20.850 usec
DE                  6.50 usec
TE                 300.9 K
D1                 2.00000000 sec
D11                0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  13C
P1                   9.00 usec
PL1                 -2.00 dB
PL1W           46.89702606 W
SFO1           100.6240872 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                  1H
PCPD2              90.00 usec
PL2                 0.00 dB
PL12               16.16 dB
PL13               17.00 dB
PL2W           10.27361584 W
PL12W          0.24872722 W
PL13W          0.20498557 W
SFO2           400.1366005 MHz

F2 - Processing parameters
SI                 131072
SF             100.6140280 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   1.40
```


9.740
7.361
7.354
7.348
7.325
7.314
7.307
7.291
5.271
5.146
5.125
5.089
4.902
4.733
4.563
4.532
4.514
4.484
3.985
3.681
3.665
3.657
3.641
3.596
3.576
3.552
3.222
3.205
3.181
3.164
2.604
2.590
2.561
2.548
2.334
2.201
2.029
1.927
1.893
1.867
1.854
1.843
1.830
1.766
1.733
1.656
1.361
1.347
1.327
1.316
1.292
1.268
1.244
1.235
1.220
1.211
OHC
BnO
N
Obz
4.1.4
0.83
9.04
1.73
2.80
0.85
0.86
0.90
0.82
0.99
1.78
1.49
1.08
2.82
3.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
Current Data Parameters
NAME NCV1148
EXPNO 1
PROCNO 1
DU nathanc /n
USER
F2 - Acquisition Parameters
Date_ 20091123
Time 13.55
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 16
DS 2
SWH 6410.256
FIDRES 0.195595
AQ 2.5559540
RG 90.5
DW 78.000
DE 6.50
TE 295.1
D1 1.00000000
TDO 1
========== CHANNEL f1 ===
NUC1 1H
P1 14.00
PL1 0.00
PL1W 10.27361584
SFO1 400.1378009
F2 - Processing parameters
SI 32768
SF 400.1350000
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00

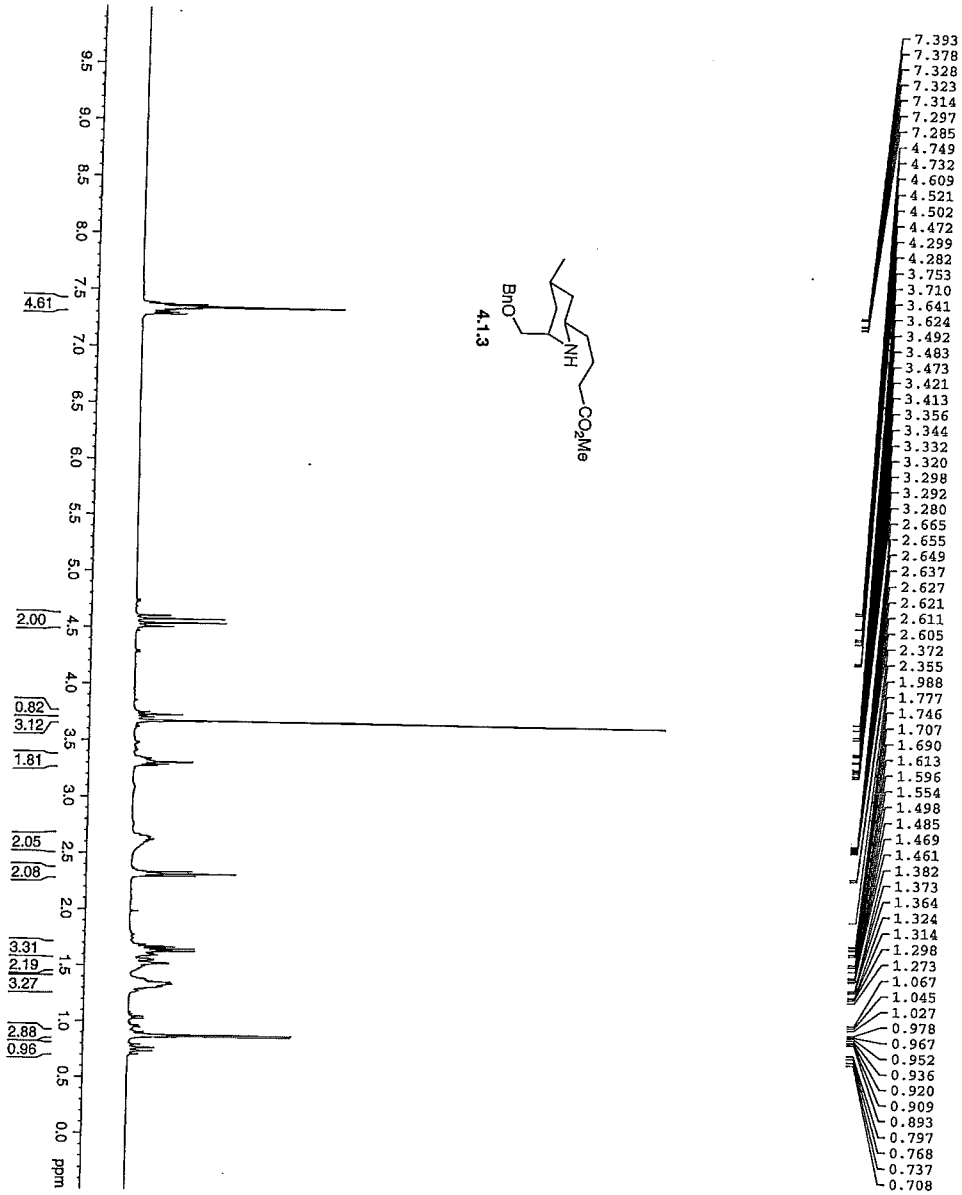


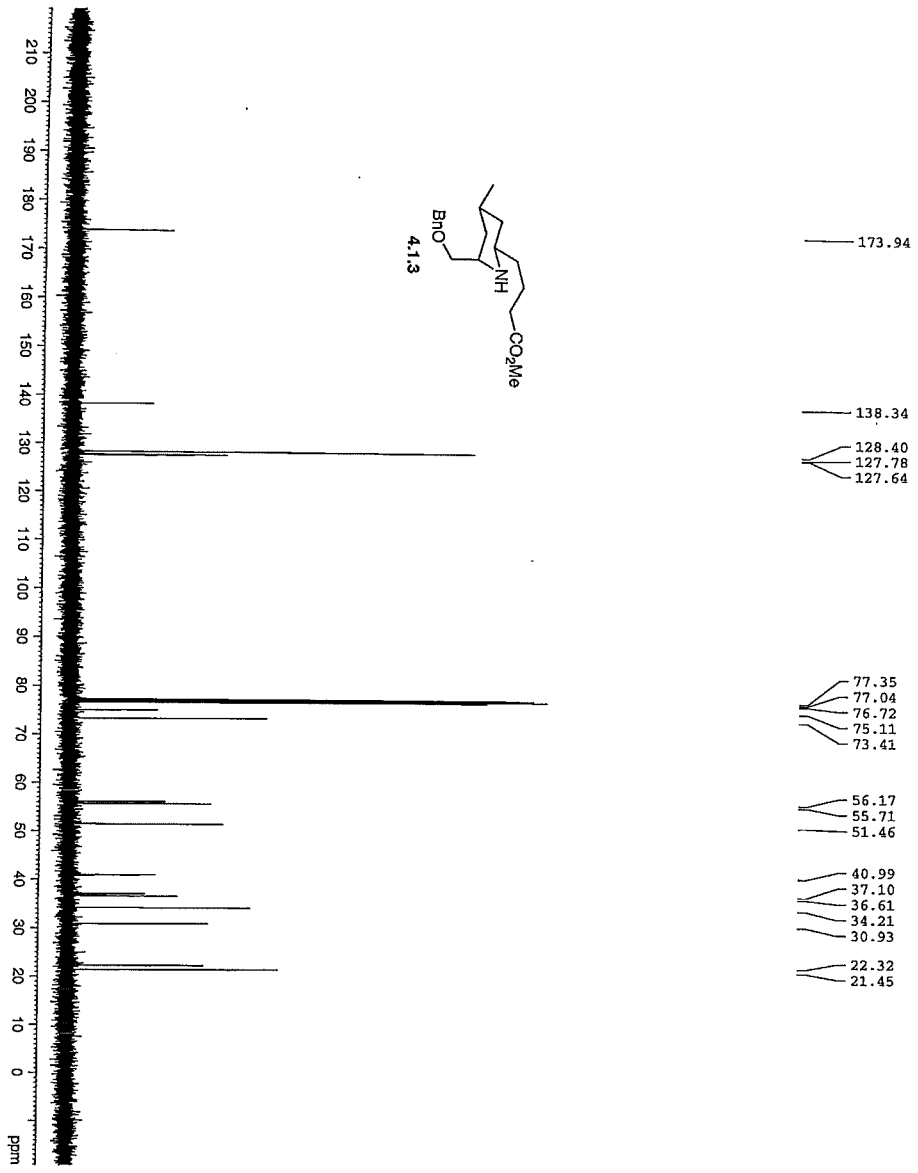

```
Current Data Parameters
NAME                  NCV1151
EXPNO                        2
PROCNO                       1
DU                           /n
USER                 nathanc

F2 - Acquisition Parameter
Date_              20091124
Time                   18.04
INSTRUM                spect
PROBHD  5 mm PABBO BB-
PULPROG                zgpg30
TD                      65536
SOLVENT                CDCl3
NS                        305
DS                          4
SWH                23980.814 Hz
FIDRES              0.365918 Hz
AQ                  1.3664756 sec
RG                      32768
DW                     20.850 us
DE                      6.50 us
TE                     301.0 K
D1                  2.00000000 sec
D11                 0.03000000 sec
TD0                         1

======== CHANNEL f1 ========
NUC1                      13C
P1                       9.00 us
PL1                     -2.00 dB
PL1W               46.89702606 W
SFO1               100.6240872 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                   90.00 us
PL2                      0.00 dB
PL12                    16.16 dB
PL13                    17.00 dB
PL2W               10.27361584 W
PL12W               0.24872722 W
PL13W               0.20498557 W
SFO2               400.1366005 MHz

F2 - Processing parameters
SI                      32768
SF                100.6140260 MHz
WDW                        EM
SSB                         0
LB                       1.00 Hz
GB                          0
PC                       1.40
```


MeO2C
BnO
N
Cbz
4.7.1
10.82
1.00
0.96
2.20
2.26
1.03
3.58
1.71
1.13
0.92
0.96
1.06
2.16
1.06
1.18
3.34
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
7.402
7.396
7.379
7.370
7.364
7.357
7.350
7.335
7.329
7.322
7.317
7.309
7.301
7.291
6.977
6.960
6.957
6.939
6.921
6.918
6.901
5.915
5.876
5.142
4.574
4.544
4.524
4.494
4.343
4.336
4.329
4.323
4.315
3.748
3.717
3.705
3.691
3.681
3.667
3.549
3.527
3.504
2.840
2.823
2.610
2.591
2.575
2.016
2.008
1.996
1.981
1.974
1.873
1.859
1.844
1.830
1.820
1.797
1.786
1.445
1.432
1.411
1.403
1.398
1.382
1.321
1.304
1.288
1.270
1.253
1.014
0.997
0.967
0.956
Current Data Parameters
NAME NCY4159
EXPNO 1
PROCNO 1
DU /n
USER nathanc
F2 - Acquisition Parame
Date_ 20100113
Time 14.25
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256
FIDRES 0.195625
AQ 2.5559540
RG 78.000
DW 32
DE 6.50
TE 300.4
D1 1.00000000
TD0 1
======== CHANNEL f1 ====
NUC1 1H
P1 14.00
PL1 0.00
PL1W 10.27361584
SFO1 400.1378009
F2 - Processing paramet
SI 32768
SF 400.1350000
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00

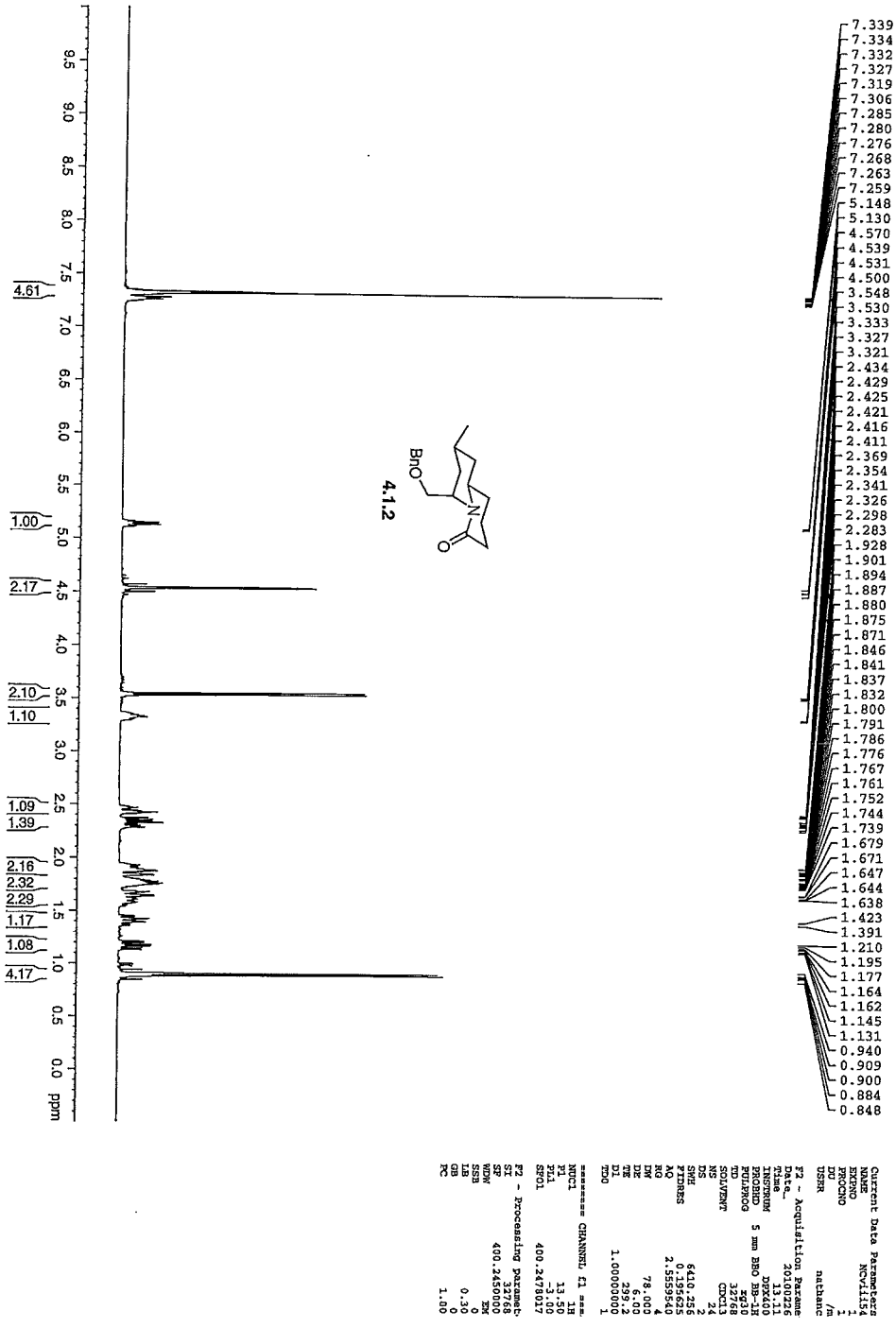


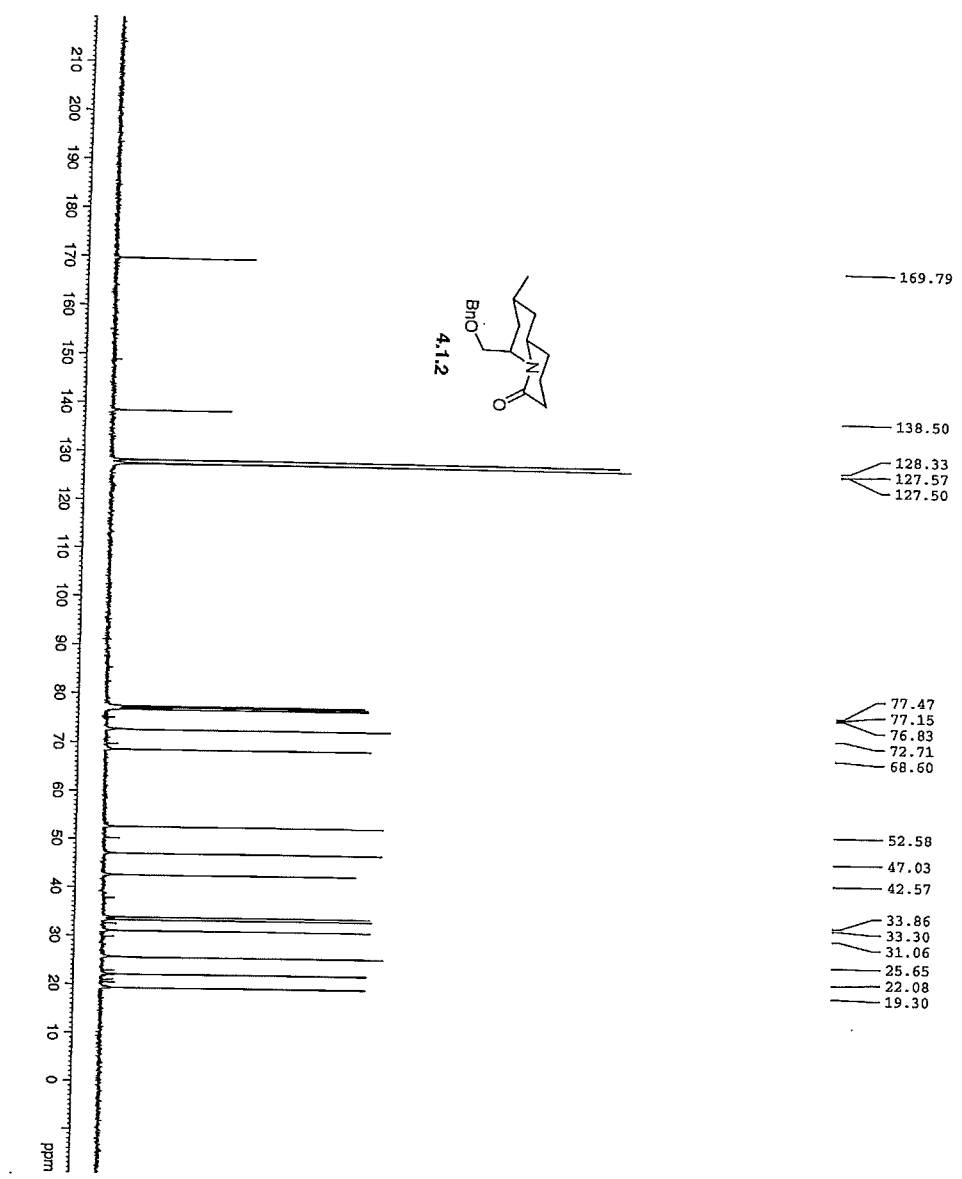

```
Current Data Parameters
NAME                 NCV155
EXPNO                     3
PROCNO                    1
DU                       /m
USER                 nathanc

F2 - Acquisition Parameter
Date_              20091202
Time                  10.18
INSTRUM             DPX400
PROBHD  5 mm BBO BB-1H
PULPROG             zgpg30
TD                   65536
SOLVENT              CDCl3
NS                     845
DS                       4
SWH             23980.814 H
FIDRES           0.365918 H
AQ               1.3664756 s
RG                    20.85
DW                   32768
DE                       6
TE                   297.2 K
D1                2.000000
D11               0.030000 s
DELTA             1.899999 s
TD0                      1

========== CHANNEL f1 ======
NUC1                   13C
P1                    8.30 u
PL1                  -3.00 d
SFO1          100.6517495 M

========== CHANNEL f2 ======
CPDPRG2          waltz16
NUC2                   1H
PCPD2                90.00 u
PL2                  -3.00 d
PL12                 15.00 d
PL13                 15.00 d
SFO2          400.2466010 M

F2 - Processing parameter
SI                   32768
SF            100.6416850 M
WDW                     EM
SSB                      0
LB                    3.00 H
GB                       0
PC                    1.40
```


4.61
2.00
0.82
3.12
1.81
2.05
2.08
3.31
2.19
3.27
2.88
0.96
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
BnO
NH
CO2Me
4.1.3
7.393
7.378
7.328
7.323
7.314
7.297
7.285
4.749
4.732
4.609
4.521
4.502
4.472
4.299
4.282
3.753
3.710
3.641
3.624
3.492
3.483
3.473
3.421
3.413
3.356
3.344
3.332
3.320
3.298
3.292
3.280
2.665
2.655
2.649
2.637
2.627
2.621
2.611
2.605
2.372
2.355
1.988
1.777
1.746
1.707
1.690
1.613
1.596
1.554
1.498
1.485
1.469
1.461
1.382
1.373
1.364
1.324
1.314
1.298
1.273
1.067
1.045
1.027
0.978
0.967
0.952
0.936
0.920
0.909
0.893
0.797
0.768
0.737
0.708
Current Data Parameters
NAME NCV1126
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20110126
Time 10.43
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256 Hz
FIDRES 0.195625 Hz
AQ 2.5559540 sec
RG 40.3
DW 78.000 usec
DE 6.50 usec
TE 295.7 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.00 usec
PL1 0.00 dB
PL1W 10.27361584 W
SFO1 400.1378009 MHz
F2 - Processing parameters
SI 32768
SF 400.1350000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

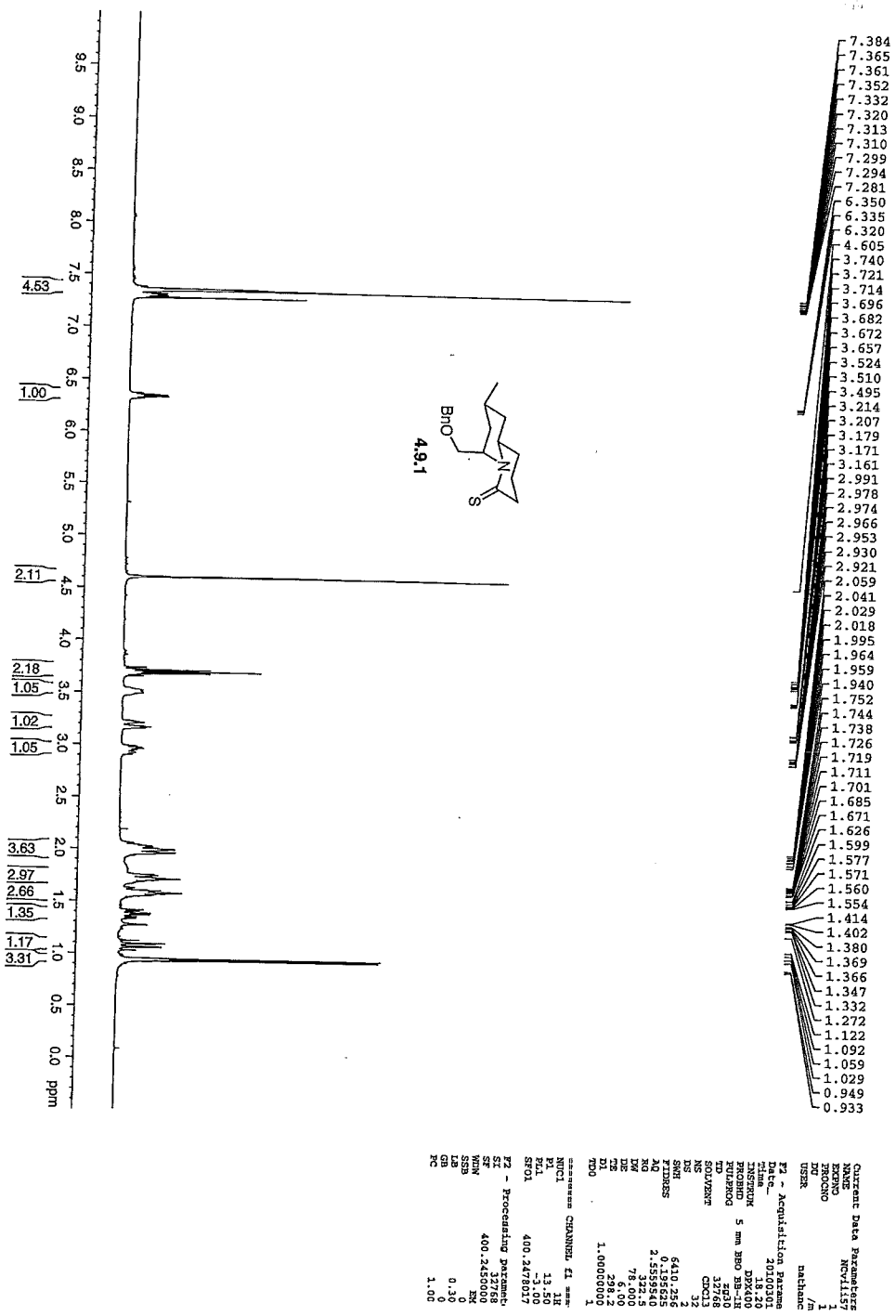


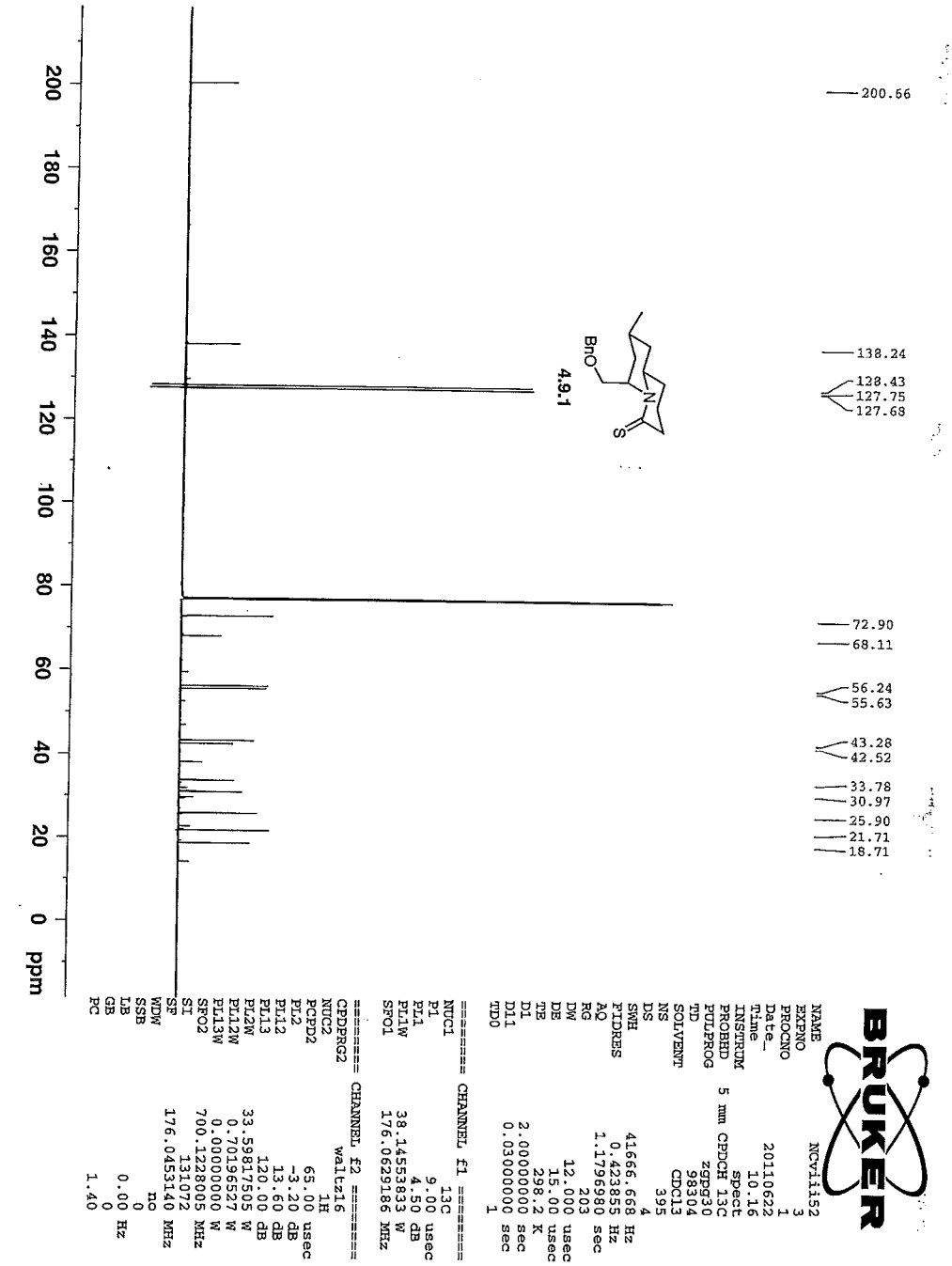

```
Current Data Parameters
NAME                  NCvi130
EXPNO                      3
PROCNO                     1
DATA                    /n
USER                    nathanc

F2 - Acquisition Parameter
Date_              20091108
Time               14.06
INSTRUM                spect
PROBHD     5 mm PABBO BB-
PULPROG                zgpg30
TD                     65536
SOLVENT                CDCl3
NS                       286
DS                         4
SWH              23980.814 H
FIDRES            0.365918 H
AQ                1.3664756 s
RG                     32768
DW                20.850 u
DE                 6.50 u
TE                 301.1 K
D1                 2.00000000 s
D11                0.03000000 s
TD0                        1

========== CHANNEL f1 ======
NUC1                     13C
P1                      9.00 u
PL1                    -2.00 d
PL1W             46.89702606 W
SFO1             100.6240872 M

========== CHANNEL f2 ======
CPDPRG2             waltz16
NUC2                     1H
PCPD2                 90.00 u
PL2                    0.00 d
PL12                  16.16 d
PL13                  17.00 d
PL2W             10.27361584 W
PL12W             0.24872722 W
PL13W             0.20498557 W
SFO2             400.1366005 M

F2 - Processing parameter
SI                     32768
SF               100.6140260 M
WDW                       no
SSB                        0
LB                      0.00 H
GB                         0
PC                      1.40
```

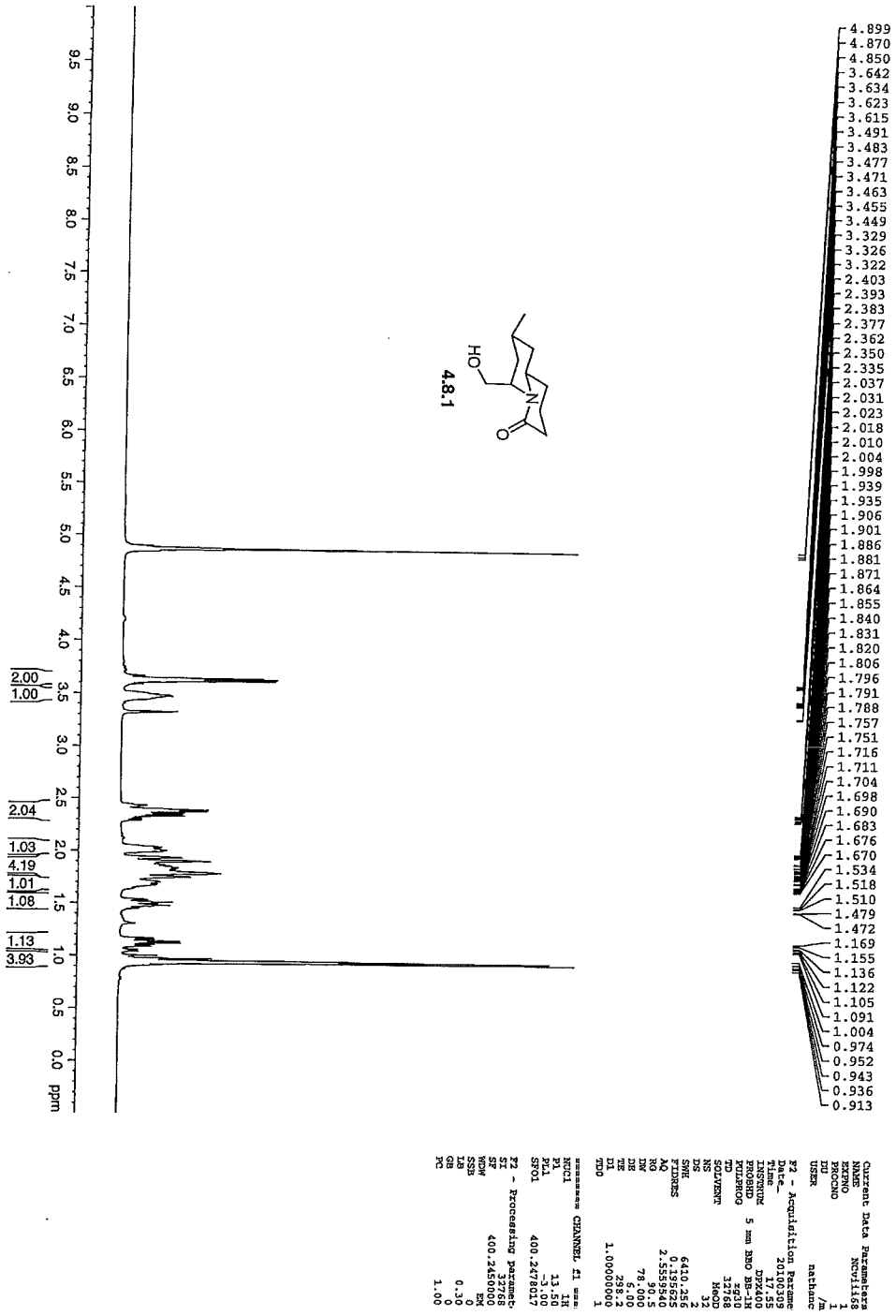

4.1.2
BnO
N
O
4.61
1.00
2.17
2.10
1.10
1.09
1.39
2.16
2.32
2.29
1.17
1.08
4.17
ppm
7.339
7.334
7.332
7.327
7.319
7.306
7.285
7.280
7.276
7.268
7.263
7.259
5.148
5.130
4.570
4.539
4.531
4.500
3.548
3.530
3.333
3.327
3.321
2.434
2.429
2.425
2.421
2.416
2.411
2.369
2.354
2.341
2.326
2.298
2.283
1.928
1.901
1.894
1.887
1.880
1.875
1.871
1.846
1.841
1.837
1.832
1.800
1.791
1.786
1.776
1.767
1.761
1.752
1.744
1.739
1.679
1.671
1.647
1.644
1.638
1.423
1.391
1.210
1.195
1.177
1.164
1.162
1.145
1.131
0.940
0.909
0.900
0.884
0.848
Current Data Parameters
NAME NCV11154
EXPNO 1
PROCNO 1
USER natbanc
F2 - Acquisition Parame
Date_ 20100226
Time 13.11
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 24
DS 2
SWH 6410.256
FIDRES 0.195544
AQ 2.5559540
RG 4
DW 78.000
DE 6.00
TE 298.2
D1 1.00000000
TD0 1
========== CHANNEL f1 ===
NUC1 1H
P1 13.50
PL1 -3.00
SFO1 400.2478017
F2 - Processing parame
SI 32768
SF 400.2450000
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00

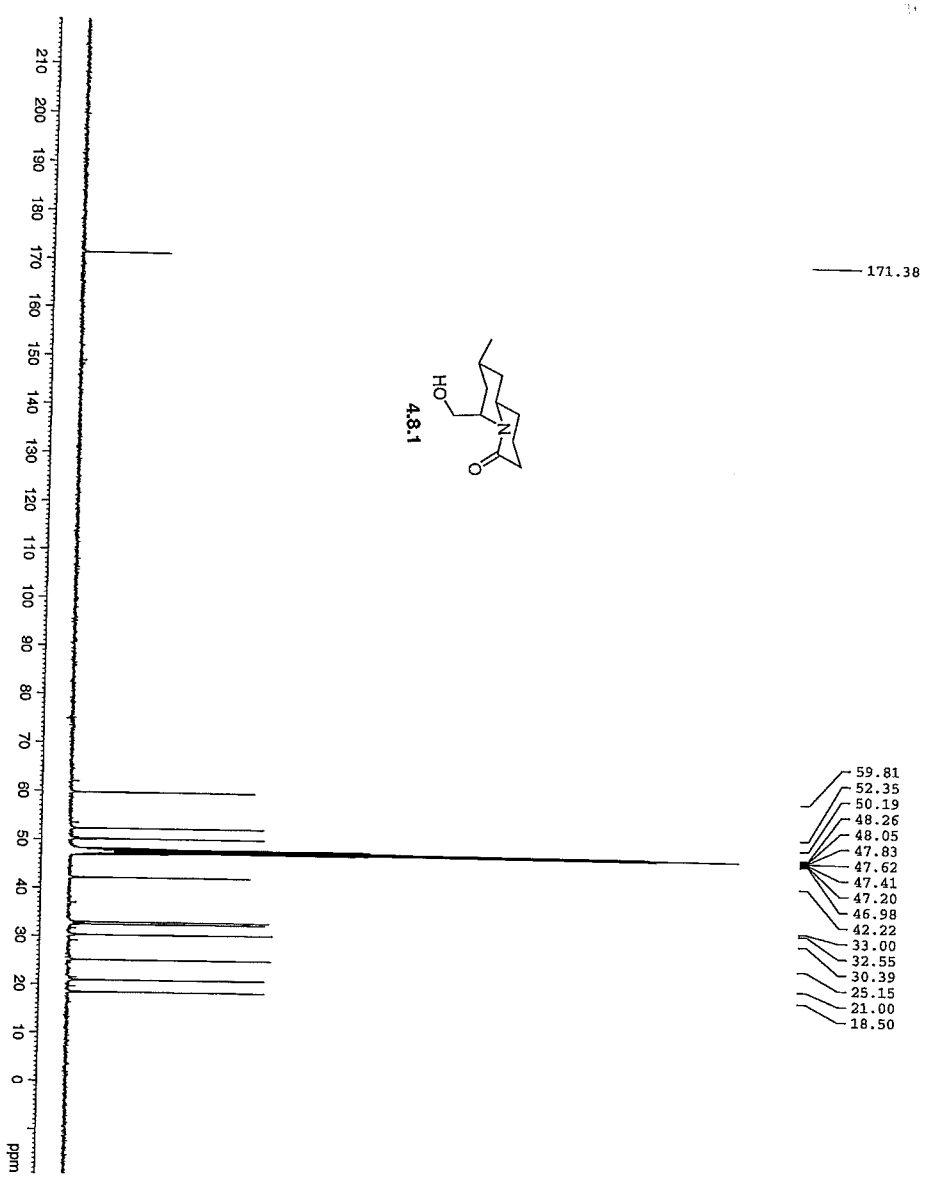



```
Current Data Parameters
NAME                  NCv1154
EXPNO                       2
PROCNO                      1
DU                         /m
USER                 nathanc

F2 - Acquisition Parameter
Date_              20100226
Time                   13:45
INSTRUM                DPX400
PROBHD  5 mm BBO BB-1H
PULPROG              zgpg30
TD                     65536
SOLVENT                CDCl3
NS                       562
DS                         4
SWH                23980.814 Hz
FIDRES              0.365918 Hz
AQ                  1.3664756 sec
RG                        256
DW                     20.850 usec
DE                      6.00 usec
TE                     299.2 K
D1                  2.00000000 sec
D11                 0.03000000 sec
DELTA               1.89999998 sec
TD0                        1

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

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

F2 - Processing parameter
SI                        32768
SF              100.6416850 MHz
WDW                          EM
SSB                           0
LB                         3.00 Hz
GB                            0
PC                         1.40
```


BnO
N
S
4.9.1
4.53
1.00
2.11
2.18
1.05
1.02
1.05
3.63
2.97
2.66
1.35
1.17
3.31
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
7.384
7.365
7.361
7.352
7.332
7.320
7.313
7.310
7.299
7.294
7.281
6.350
6.335
6.320
4.605
3.740
3.721
3.714
3.696
3.682
3.672
3.657
3.524
3.510
3.495
3.214
3.207
3.179
3.171
3.161
2.991
2.978
2.974
2.966
2.953
2.930
2.921
2.059
2.041
2.029
2.018
1.995
1.964
1.959
1.940
1.752
1.744
1.738
1.726
1.719
1.711
1.701
1.685
1.671
1.626
1.599
1.577
1.571
1.560
1.554
1.414
1.402
1.380
1.369
1.366
1.347
1.332
1.272
1.122
1.092
1.059
1.029
0.949
0.933
Current Data Parameters
NAME MCY1157
EXPNO 1
PROCNO 1
F2 - Acquisition Parame
Date_ 20100301
Time 19.20
INSTRUM DRX400-0
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256
FIDRES 0.195625
AQ 2.5559540
RG 128.5
DW 78.000
DE 6.00
TE 298.2
D1 1.00000000
TD0 1
======== CHANNEL f1 ===
NUC1 1H
P1 13.50
PL1 -3.00
SFO1 400.2478017
F2 - Processing paramet
SI 32768
SF 400.2450000
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00

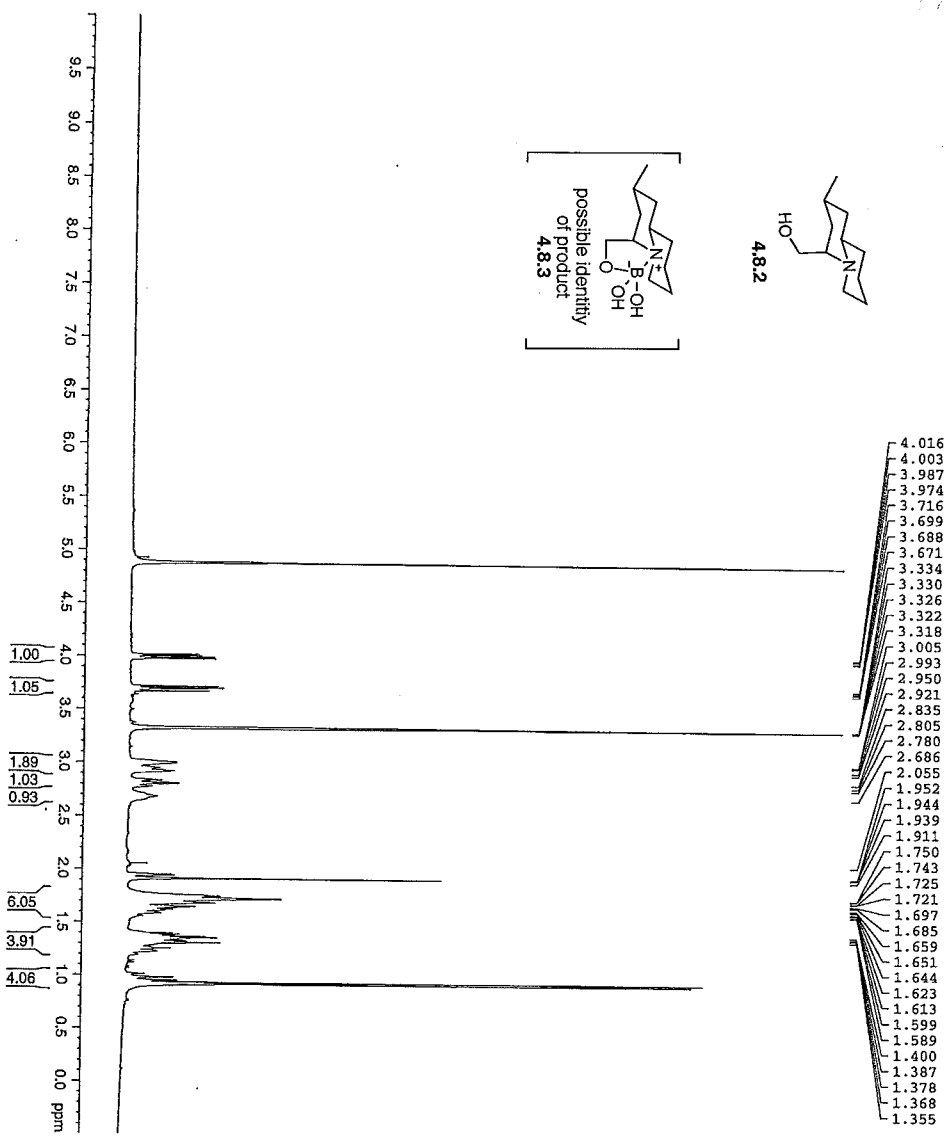

200.66
138.24
128.43
127.75
127.68
72.90
68.11
56.24
55.63
43.28
42.52
33.78
30.97
25.90
21.71
18.71
BnO
N
S
4.9.1
200
180
160
140
120
100
80
60
40
20
0
ppm
BRUKER
NAME NCvili52
EXPNO 3
PROCNO 1
Date_ 20110622
Time 10.16
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDCl3
NS 395
DS 4
SWH 41666.668 Hz
FIDRES 0.423855 Hz
AQ 1.1796980 sec
RG 203
DW 12.000 usec
DE 15.00 usec
TE 298.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0629186 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 usec
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1228005 MHz
SI 131072
SF 176.0453140 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.40


4.8.1
HO
N
O
2.00
1.00
2.04
1.03
4.19
1.01
1.08
1.13
3.93
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
4.899
4.870
4.850
3.642
3.634
3.623
3.615
3.491
3.483
3.477
3.471
3.463
3.455
3.449
3.329
3.326
3.322
2.403
2.393
2.383
2.377
2.362
2.350
2.335
2.037
2.031
2.023
2.018
2.010
2.004
1.998
1.939
1.935
1.906
1.901
1.886
1.881
1.871
1.864
1.855
1.840
1.831
1.820
1.806
1.796
1.791
1.788
1.757
1.751
1.716
1.711
1.704
1.698
1.690
1.683
1.676
1.670
1.534
1.518
1.510
1.479
1.472
1.169
1.155
1.136
1.122
1.105
1.091
1.004
0.974
0.952
0.943
0.936
0.913
Current Data Parameters
NAME RCV1168
EXPNO 1
PROCNO 1
F2 - Acquisition Parame
Date_ 20100309
Time 17.55
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zg30
TD 32768
SOLVENT MeOD
NS 32
DS 2
SWH 6410.256
FIDRES 0.195650
AQ 2.5559540
RG 90.5
DW 78.000
DE 6.00
TE 298.2
D1 1.00000000
TD0 1
========== CHANNEL f1 ===
NUC1 1H
P1 13.50
PL1 -3.00
SFO1 400.2478017
F2 - Processing paramet
SI 131072
SF 400.2450000
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00

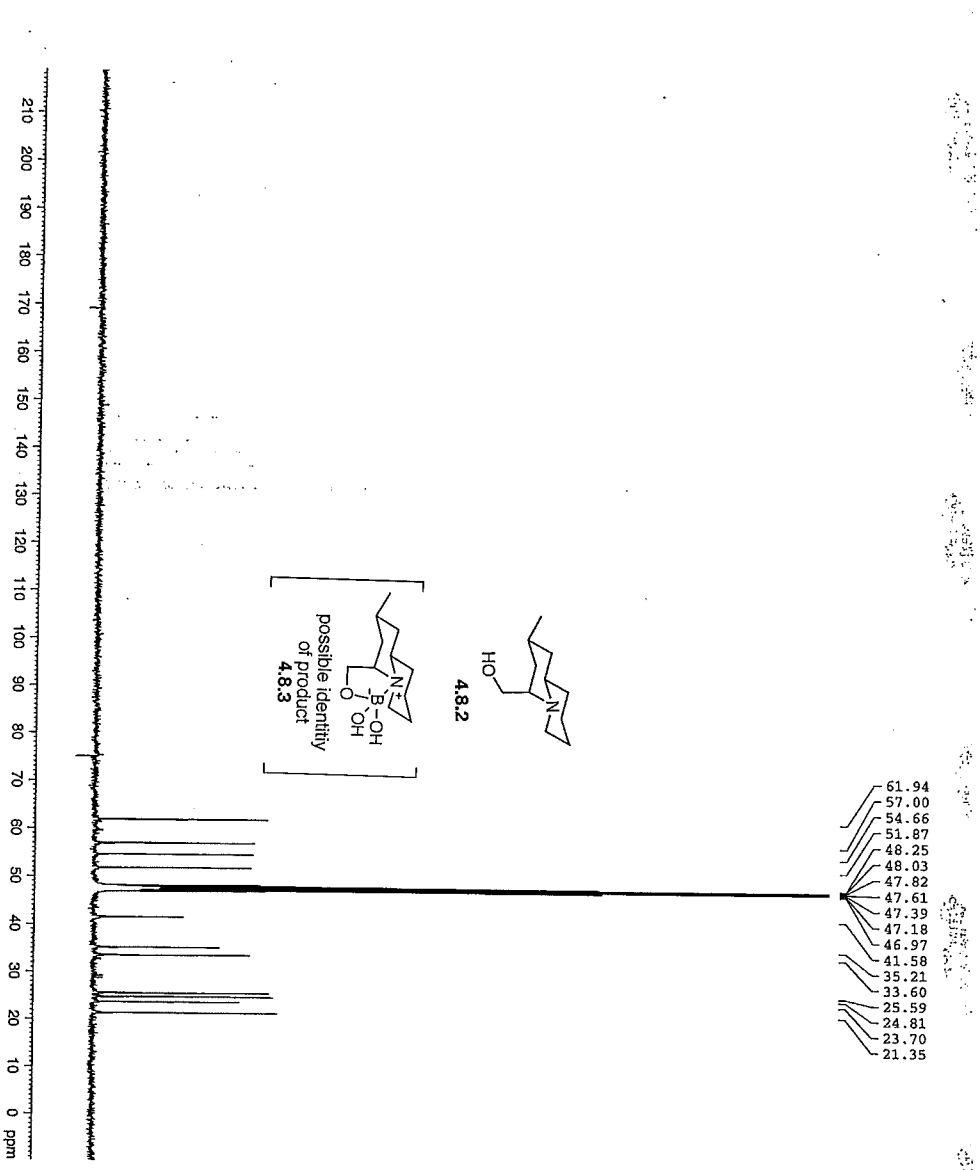


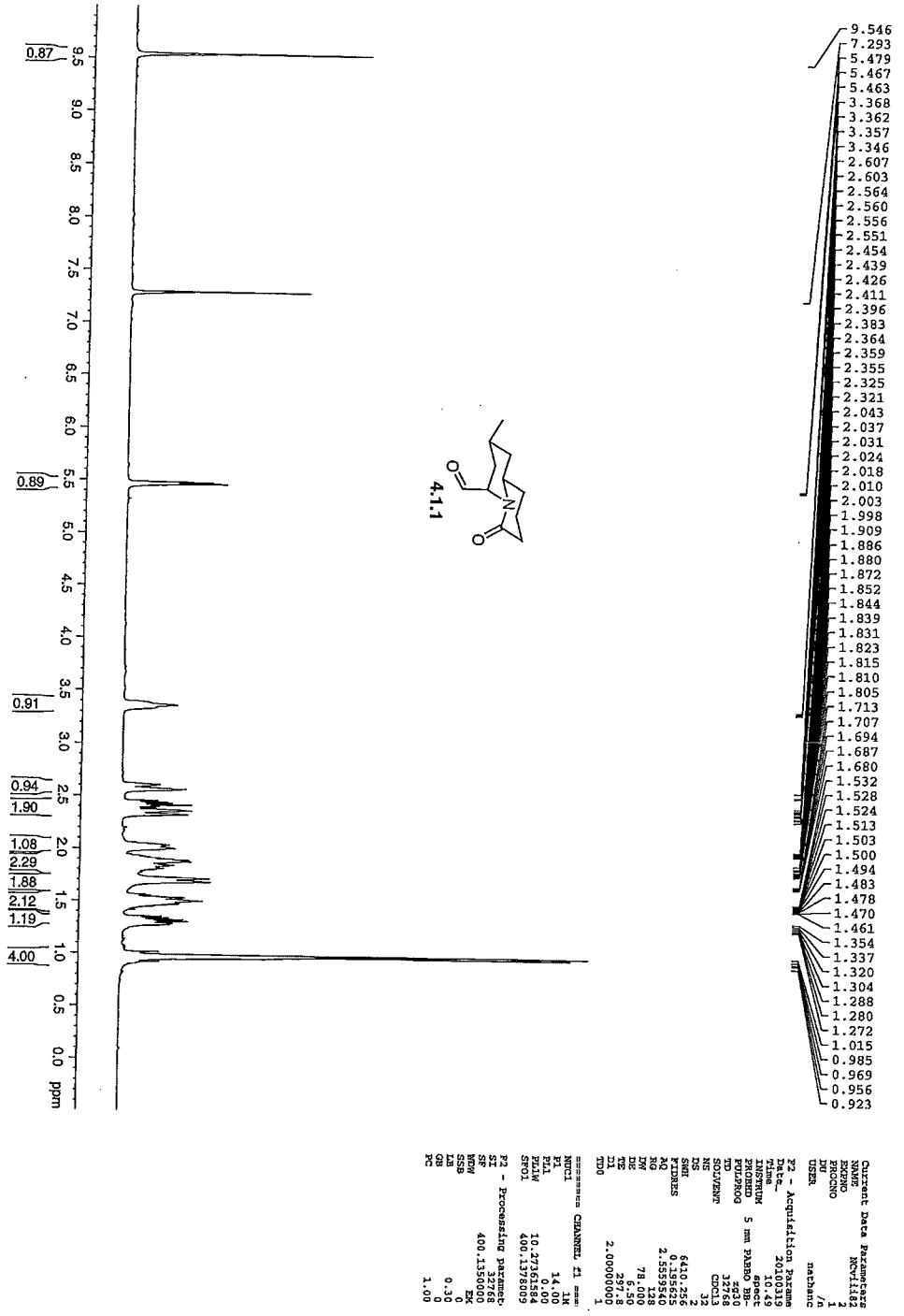

```
Current Data Parameters
NAME                  NCyi168
EXPNO                        2
PROCNO                       1
DU                          /m
USER                 nathanc

F2 - Acquisition Parameter
Date_              20100309
Time                   18.52
INSTRUM              DPX400
PROBHD     5 mm BBO BB-1H
PULPROG              zg30
TD                    65536
SOLVENT              CDCl3
NS                      963
DS                        4
SWH               23980.814 Hz
FIDRES                0.365918 Hz
AQ                    1.3664756 sec
RG                      332768
DW                     20.850 usec
DE                      6.00 usec
TE                     299.2 K
D1                     2.00000000 sec
D11                    0.03000000 sec
DELTA                  1.89999998 sec
TD0                           1

======== CHANNEL f1 ========
NUC1                       13C
P1                        8.30 usec
PL1                      -3.00 dBm
SFO1          100.6517495 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                       1H
PCPD2                    90.00 usec
PL2                      -9.00 dBm
PL12                     15.00 dBm
PL13                     15.00 dBm
SFO2          400.2466010 MHz

F2 - Processing parameters
SI                       32768
SF            100.6416850 MHz
WDW                        EM
SSB                         0
LB                       3.00 Hz
GB                          0
PC                       1.40
```

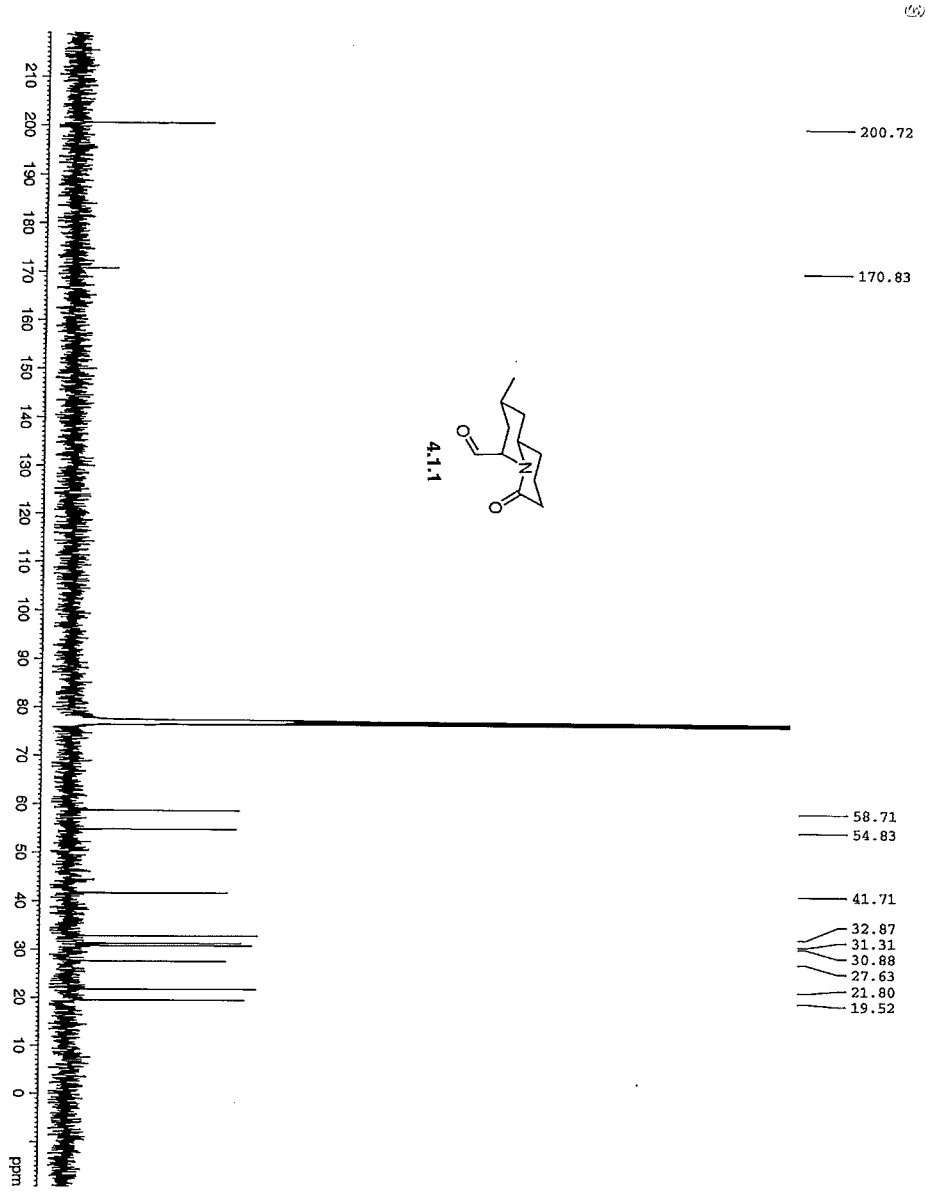
BH3 crude amino alcohol check



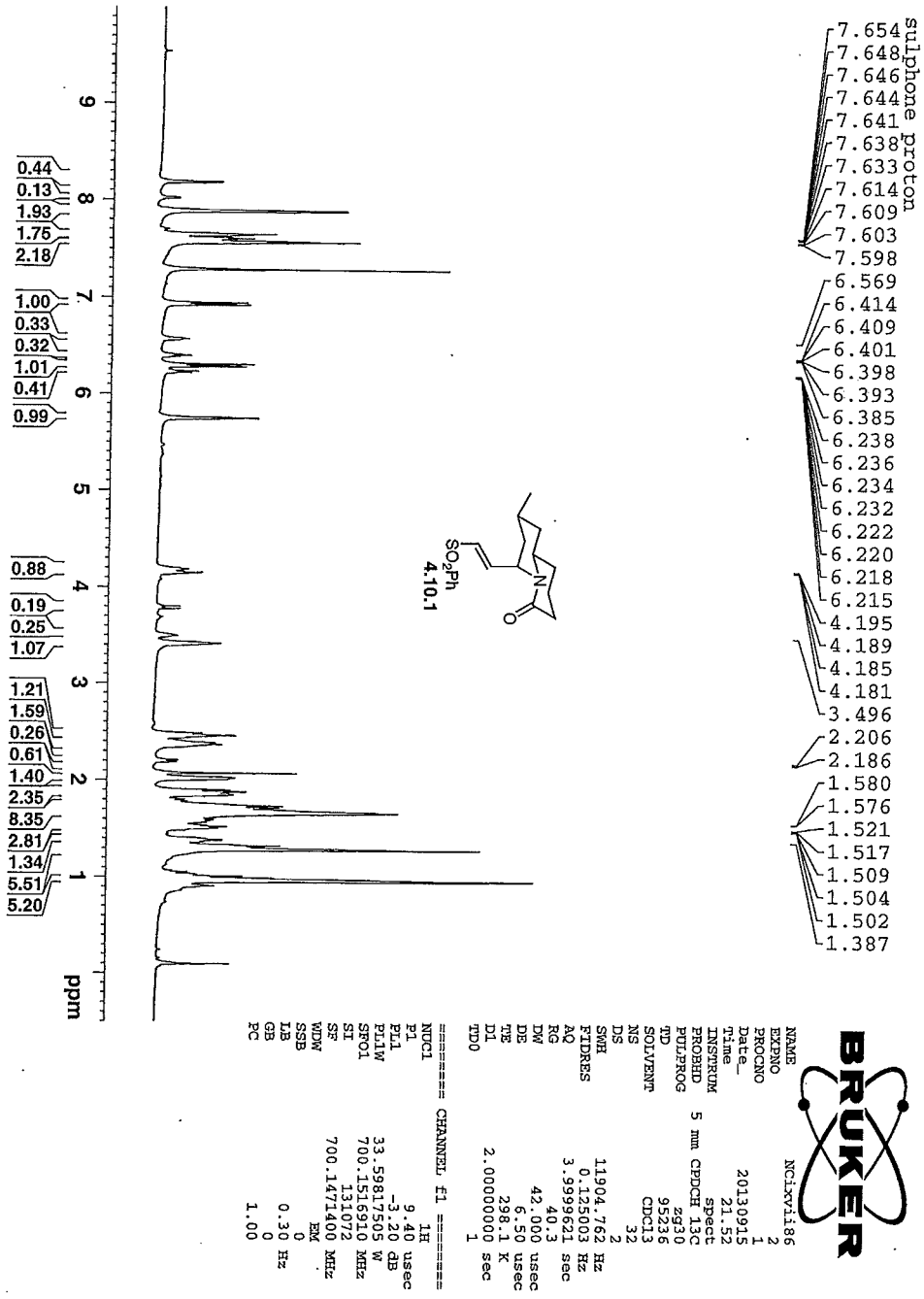
amino alcohol Carbon

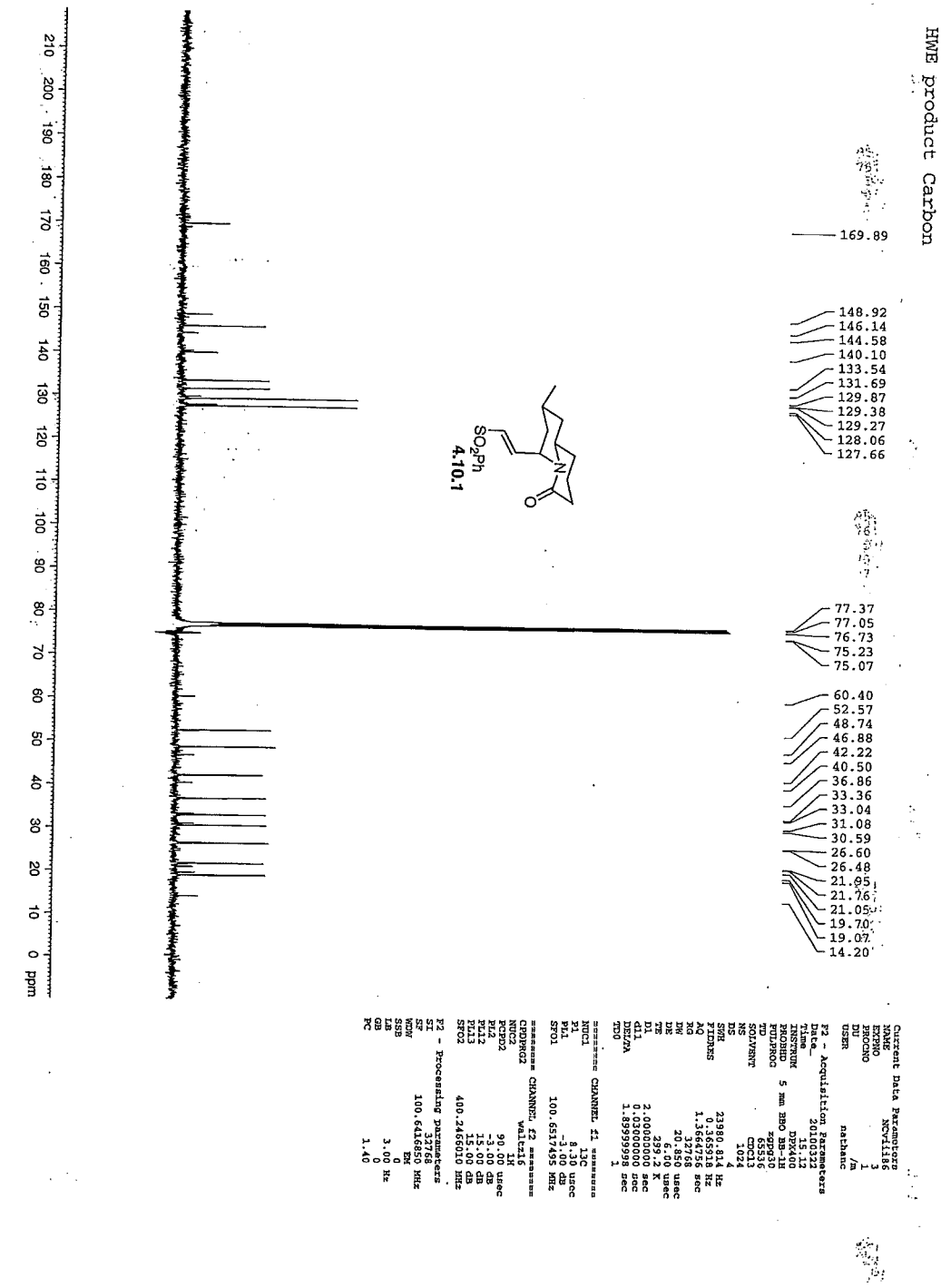


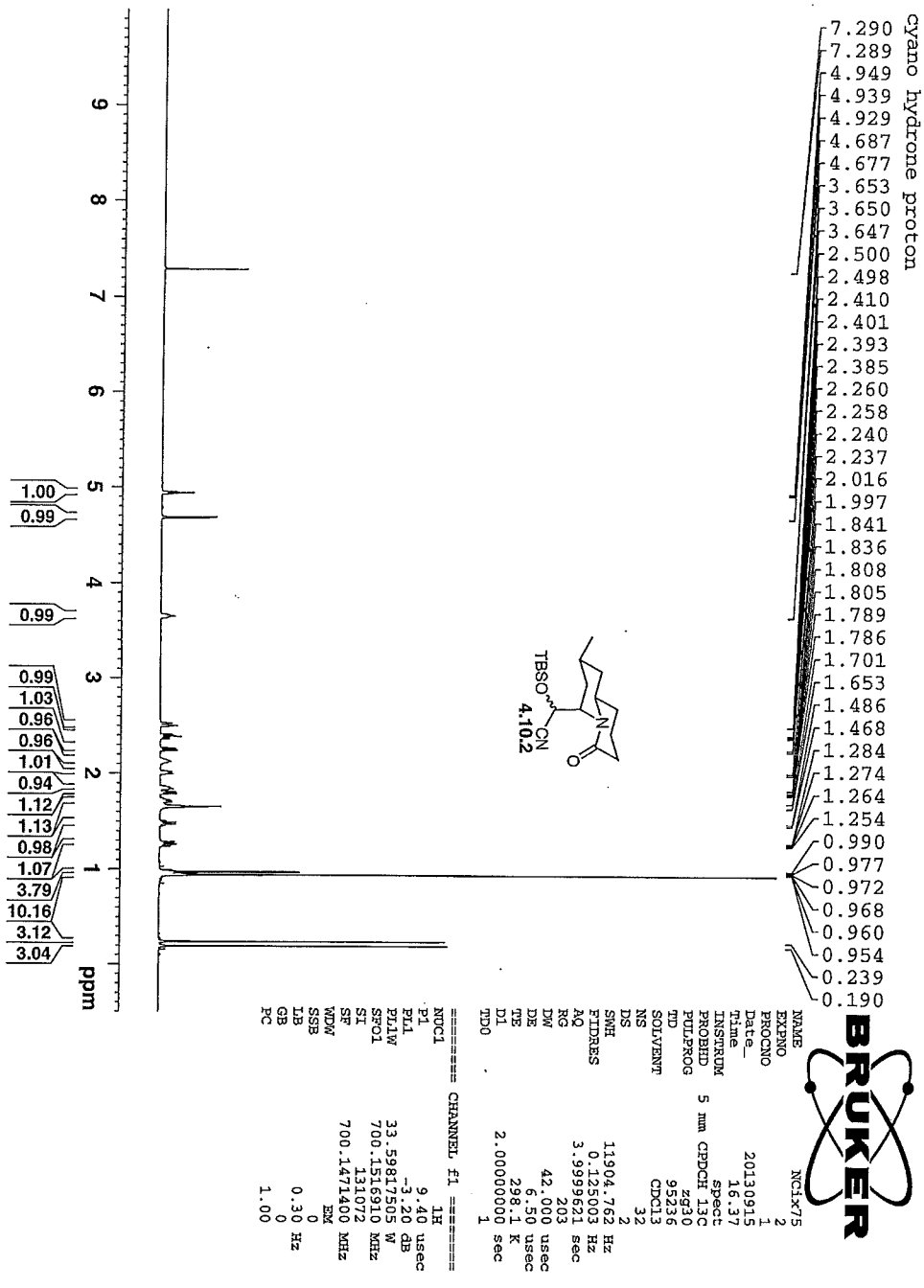

4.1.1
0.87
0.89
0.91
0.94
1.90
1.08
2.29
1.88
2.12
1.19
4.00
ppm
9.546
7.293
5.479
5.467
5.463
3.368
3.362
3.357
3.346
2.607
2.603
2.564
2.560
2.556
2.551
2.454
2.439
2.426
2.411
2.396
2.383
2.364
2.359
2.355
2.325
2.321
2.043
2.037
2.031
2.024
2.018
2.010
2.003
1.998
1.909
1.886
1.880
1.872
1.852
1.844
1.839
1.831
1.823
1.815
1.810
1.805
1.713
1.707
1.694
1.687
1.680
1.532
1.528
1.524
1.513
1.503
1.500
1.494
1.483
1.478
1.470
1.461
1.354
1.337
1.320
1.304
1.288
1.280
1.272
1.015
0.985
0.969
0.956
0.923
Current data Parameters
NAME NCY1182
EXPNO 1
PROCNO 1
USER nathanc
/n
F2 - Acquisition Parame
Date_ 20100119
Time 10.49
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
SOLVENT CDCl3
NS 32
DS 2
SWH 6410.256
FIDRES 0.195625
AQ 2.5559680
RG 128
DW 78.000
DE 6.50
TE 297.8
D1 2.00000000
TD0 1
======== CHANNEL f1 ===
NUC1 1H
P1 14.00
PL1 0.00
PLW1 10.27161584
SFO1 400.1378009
F2 - Processing parame
SI 32768
SF 400.1350000
WDW EM
SSB 0
LB 0.30
GB 0
PC 1.00

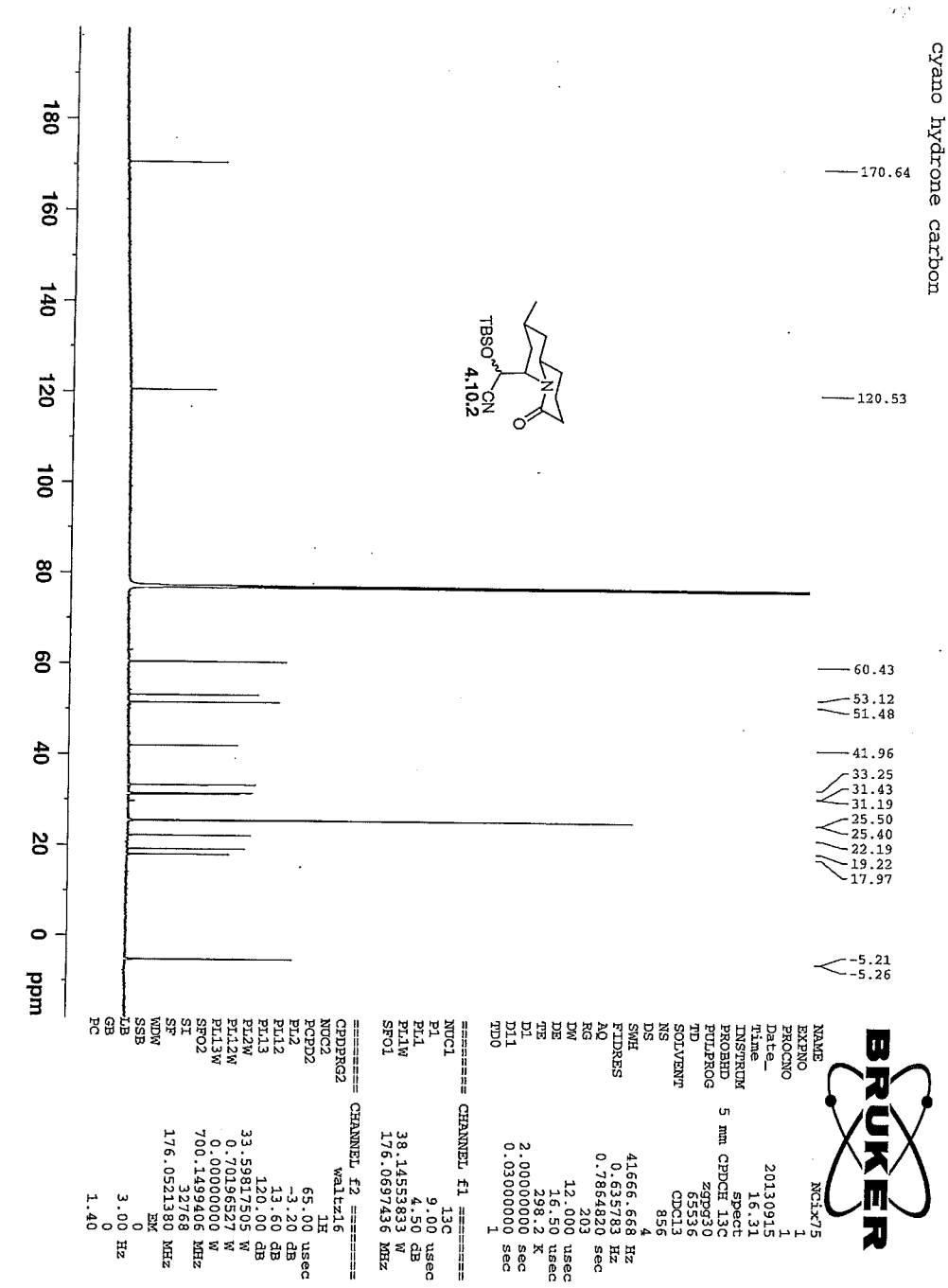


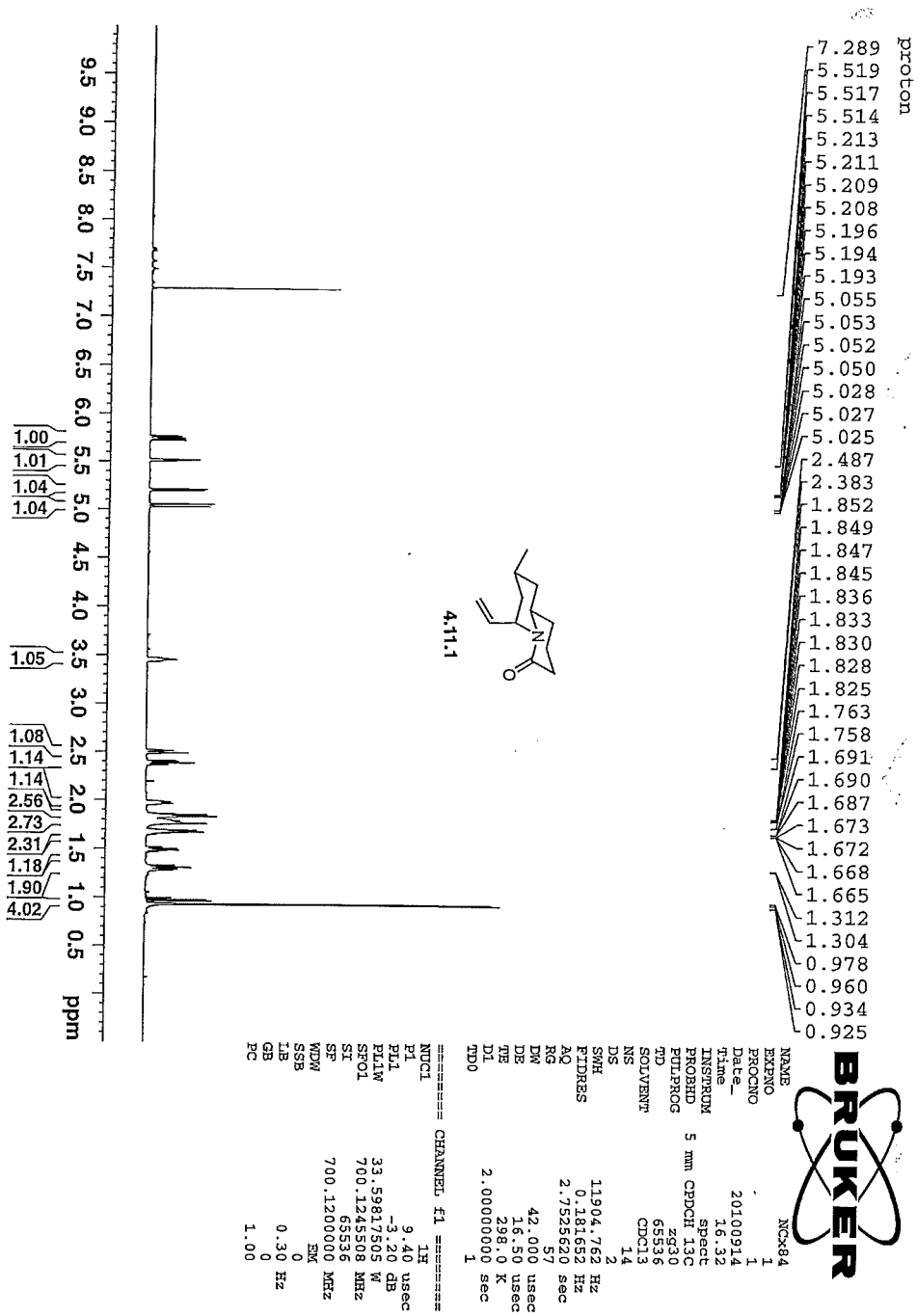

```
Current Data Parameters
NAME                  NCix72
EXPNO                      1
PROCNO                     1
DU                        /m
USER              nathanc

F2 - Acquisition Parameter
Date_              20100525
Time                  23.21
INSTRUM             DPX400
PROBHD   5 mm BBO BB-1H
PULPROG           zgpg30
TD                 65536
SOLVENT            CDCl3
NS                  3000
DS                     4
SWH              23980.814 Hz
FIDRES               0.365518 Hz
AQ                1.3664756 sec
RG                  51470.5
DW                 20.856 usec
DE                  6.00 usec
TE                 300.2 K
D1                 0.20000000 sec
d11                0.03000000 sec
DELTA              0.10000000 sec
MD0                        1

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

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

F2 - Processing parameter
SI                    32768
SF            100.6416850 MHz
WDW                      EM
SSB                       0
LB                     3.00 Hz
GB                        0
PC                     1.40
```

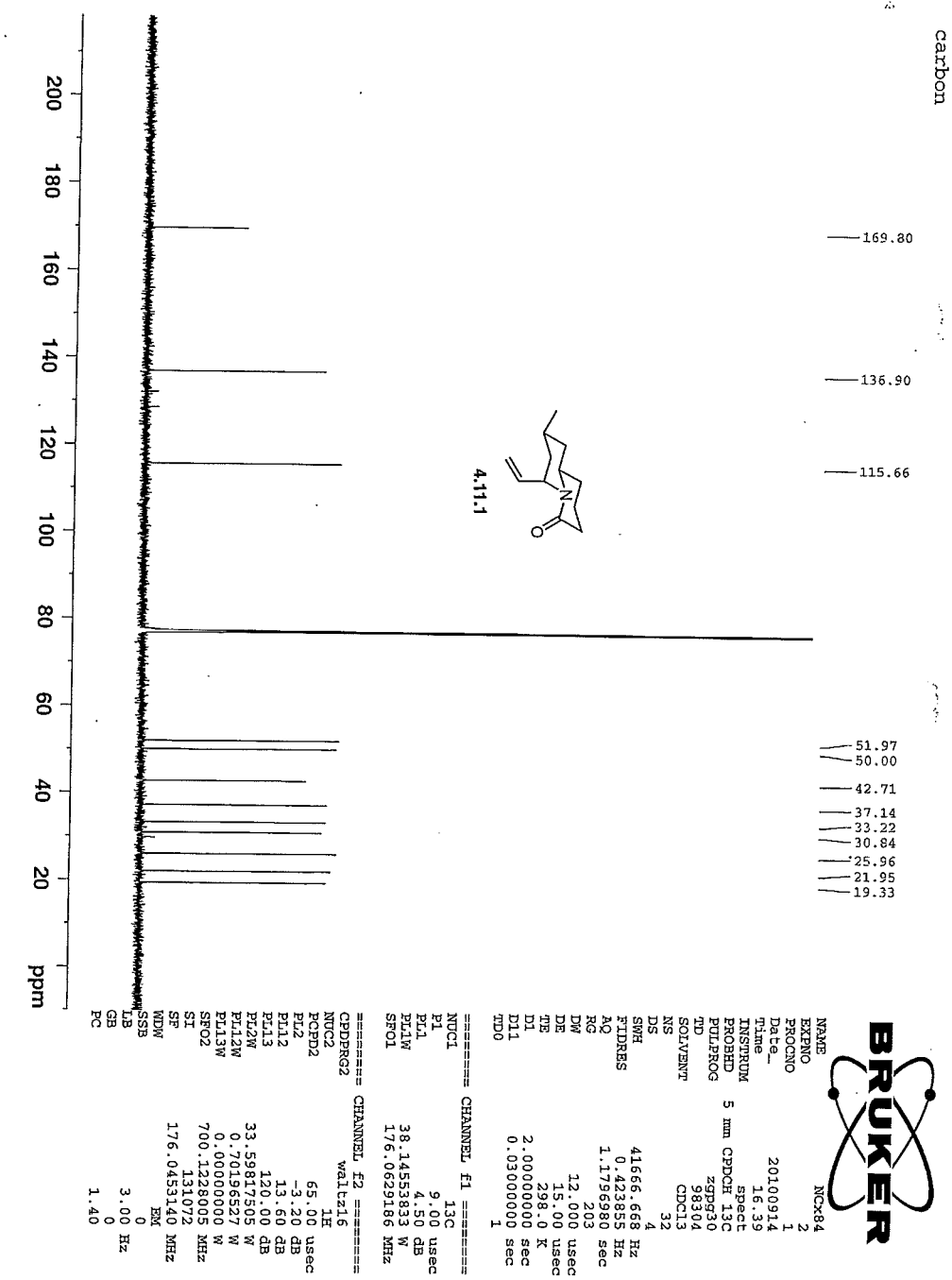

sulphone proton
7.654
7.648
7.646
7.644
7.641
7.638
7.633
7.614
7.609
7.603
7.598
6.569
6.414
6.409
6.401
6.398
6.393
6.385
6.238
6.236
6.234
6.232
6.222
6.220
6.218
6.215
4.195
4.189
4.185
4.181
3.496
2.206
2.186
1.580
1.576
1.521
1.517
1.509
1.504
1.502
1.387
NAME NCixvi186
EXPNO 2
PROCNO 1
Date_ 20130915
Time 21.52
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 298.1 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
SO2Ph
4.10.1
0.44
0.13
1.93
1.76
2.18
1.00
0.33
0.32
1.01
0.41
0.99
0.88
0.19
0.25
1.07
1.21
1.59
0.26
0.61
1.40
2.35
8.35
2.81
1.34
5.51
5.20
ppm

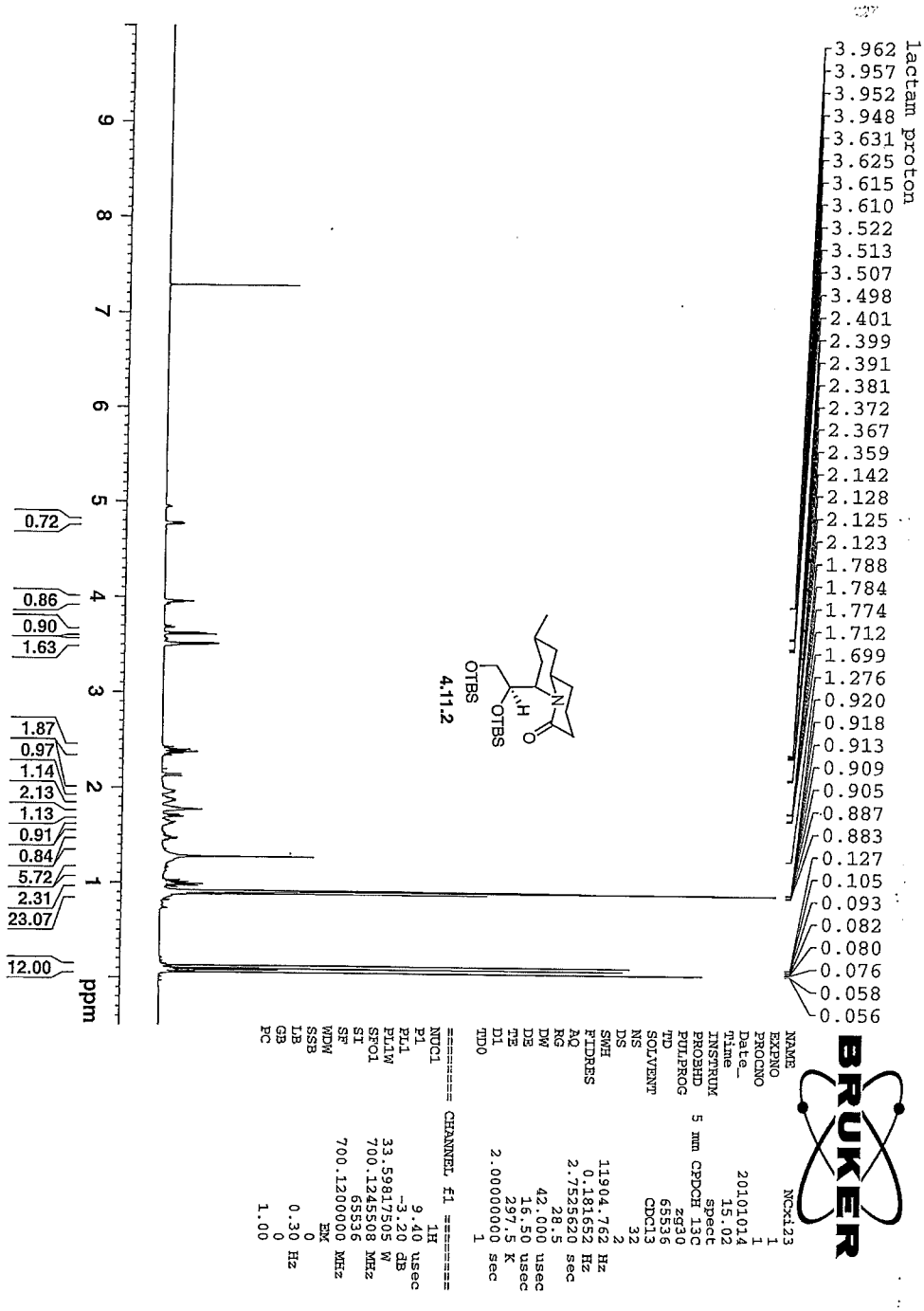

HWE product Carbon
4.10.1
169.89
148.92
146.14
144.58
140.10
133.54
131.69
129.87
129.38
129.27
128.06
127.66
77.37
77.05
76.73
75.23
75.07
60.40
52.57
48.74
46.88
42.22
40.50
36.86
33.36
33.04
31.08
30.59
26.60
26.48
21.95
21.76
21.05
19.70
19.07
14.20
Current Data Parameters
NAME NCV1186
EXPNO 3
PROCNO 1
USER /m
natbasic
F2 - Acquisition Parameters
Date_ 20110322
Time 15.12
INSTRUM DPX400
PROBHD 5 mm BBO BB-1H
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 1024
DS 4
SWH 23980.814 Hz
FIDRES 0.365918 Hz
AQ 1.3664756 sec
RG 32768
DW 20.850 usec
DE 6.00 usec
TE 299.2 K
D1 2.00000000 sec
D11 0.03000000 sec
DELTA 1.89999998 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.30 usec
PL1 -3.00 dB
SFO1 100.6517495 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -3.00 dB
PL12 15.00 dB
PL13 15.00 dB
SFO2 400.2466010 MHz
F2 - Processing parameters
SI 32768
SF 100.6416850 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

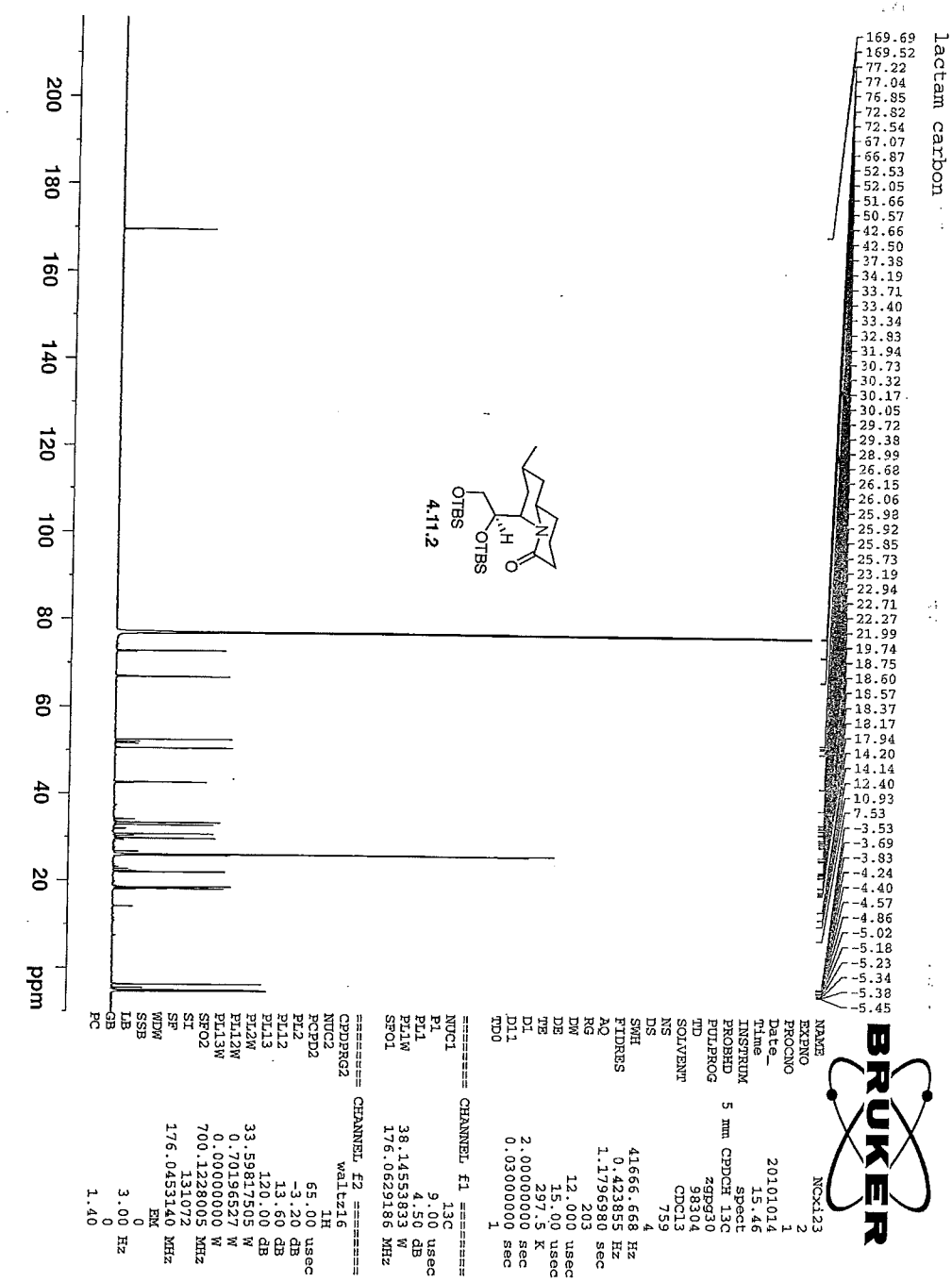

cyano hydrone proton
7.290
7.289
4.949
4.939
4.929
4.687
4.677
3.653
3.650
3.647
2.500
2.498
2.410
2.401
2.393
2.385
2.260
2.258
2.240
2.237
2.016
1.997
1.841
1.836
1.808
1.805
1.789
1.786
1.701
1.653
1.486
1.468
1.284
1.274
1.264
1.254
0.990
0.977
0.972
0.968
0.960
0.954
0.239
0.190
TBSO
CN
4.10.2
N
O
1.00
0.99
0.99
0.99
1.03
0.96
0.96
1.01
0.94
1.12
1.13
0.98
1.07
3.79
10.16
3.12
3.04
ppm
NAME NCix75
EXPNO 2
PROCNO 1
Date_ 20130915
Time 16.37
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 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 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
BRUKER

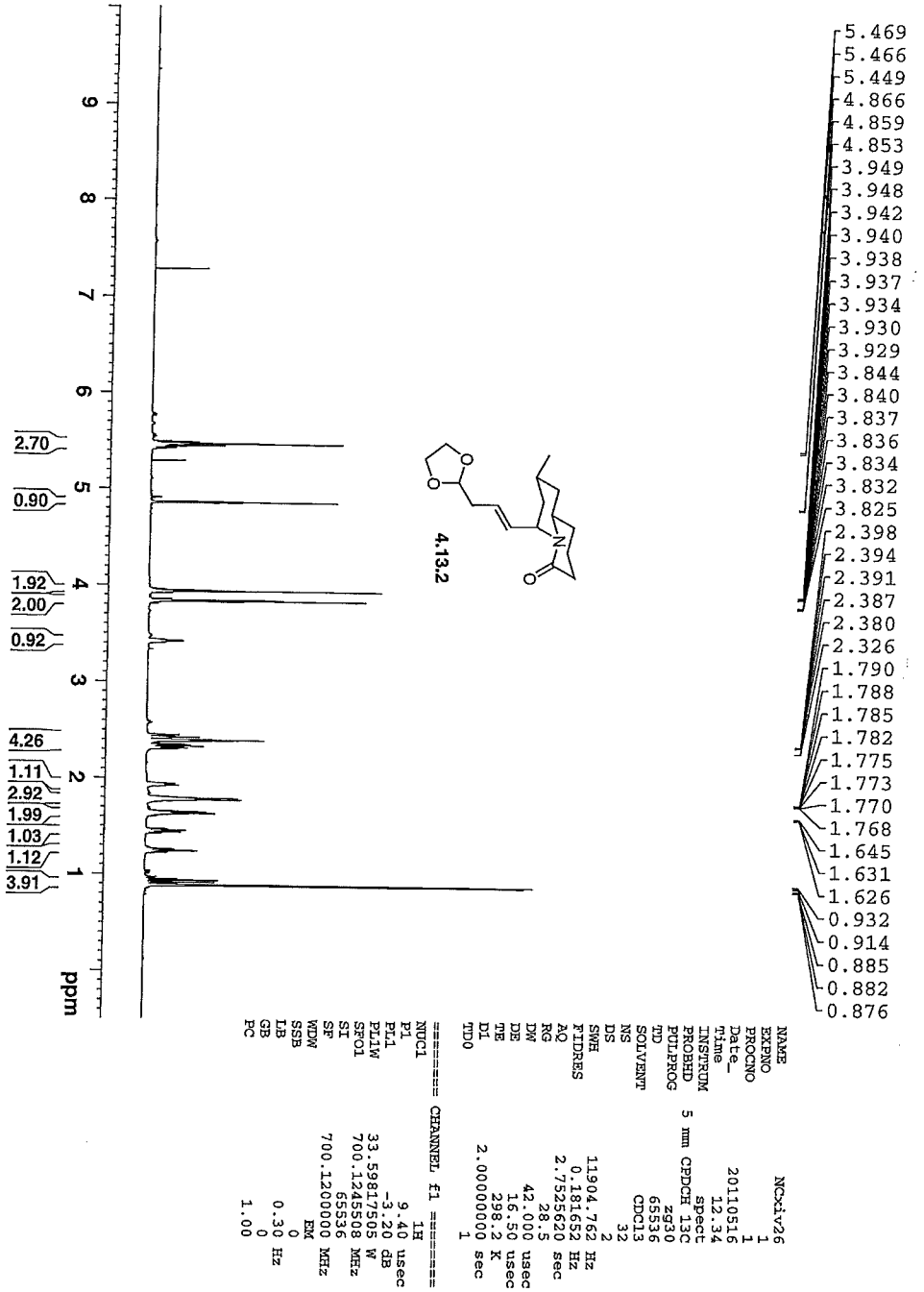

cyano hydrone carbon
170.64
120.53
60.43
53.12
51.48
41.96
33.25
31.43
31.19
25.50
25.40
22.19
19.22
17.97
-5.21
-5.26
TBSO
CN
4.10.2
N
O
BRUKER
NCix75
NAME
EXPNO
PROCNO
Date_
Time
INSTRUM
PROBHD
PULPROG
TD
SOLVENT
NS
DS
SWH
FIDRES
AQ
RG
DW
DE
TE
D1
D11
TD0
5 mm CPDCH 13C
20130915
16.31
spect
zgpg30
65536
CDCl3
856
4
41666.668 Hz
0.635783 Hz
0.7864820 sec
203
12.000 usec
16.50 usec
298.2 K
2.00000000 sec
0.03000000 sec
1
======== CHANNEL f1 ========
NUC1
P1
PL1
PL1W
SFO1
13C
9.00 usec
4.50 dB
38.14553833 W
176.0697436 MHz
======== CHANNEL f2 ========
CPDPRG2
NUC2
PCPD2
PL2
PL12
PL13
PL2W
PL12W
PL13W
SFO2
SI
SF
WDW
SSB
LB
GB
PC
waltz16
1H
65.00 usec
-3.20 dB
13.60 dB
120.00 dB
33.59817505 W
0.70196527 W
0.00000000 W
700.1499406 MHz
32768
176.0521380 MHz
EM
0
3.00 Hz
0
1.40
180
160
140
120
100
80
60
40
20
0
ppm

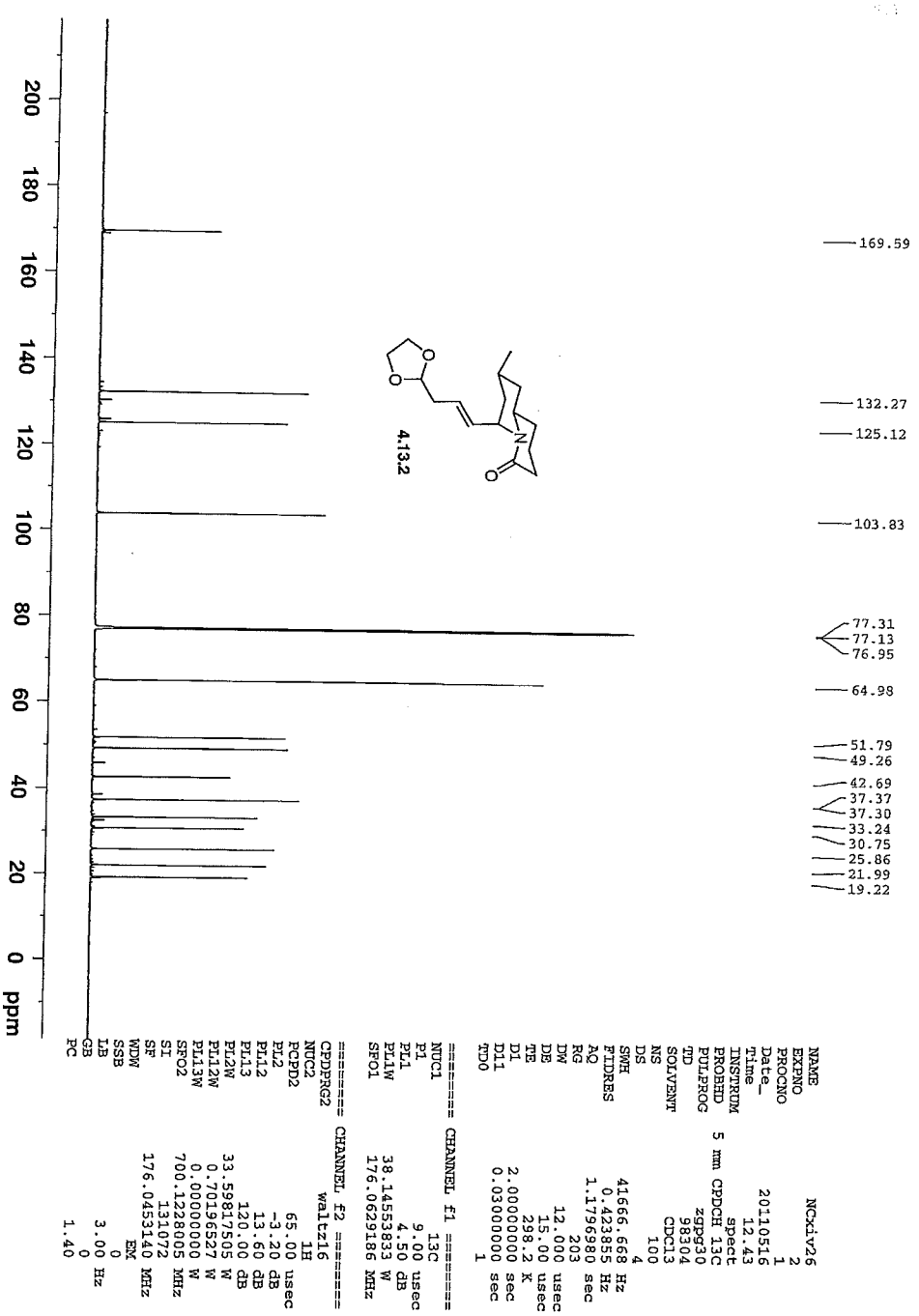

proton
7.289
5.519
5.517
5.514
5.213
5.211
5.209
5.208
5.196
5.194
5.193
5.055
5.053
5.052
5.050
5.028
5.027
5.025
2.487
2.383
1.852
1.849
1.847
1.845
1.836
1.833
1.830
1.828
1.825
1.763
1.758
1.691
1.690
1.687
1.673
1.672
1.668
1.665
1.312
1.304
0.978
0.960
0.934
0.925
NAME NCx84
EXPNO 1
PROCNO 1
Date_ 20100914
Time 16.32
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 14
DS 2
SWH 11904.762 Hz
FIDRES 0.181652 Hz
AQ 2.7525620 sec
RG 57
DW 42.000 usec
DE 16.50 usec
TE 298.0 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PLIW 33.59817505 W
SFO1 700.1245508 MHz
SI 65536
SF 700.1200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
4.11.1
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.00
1.01
1.04
1.04
1.05
1.08
1.14
1.14
2.56
2.73
2.31
1.18
1.90
4.02

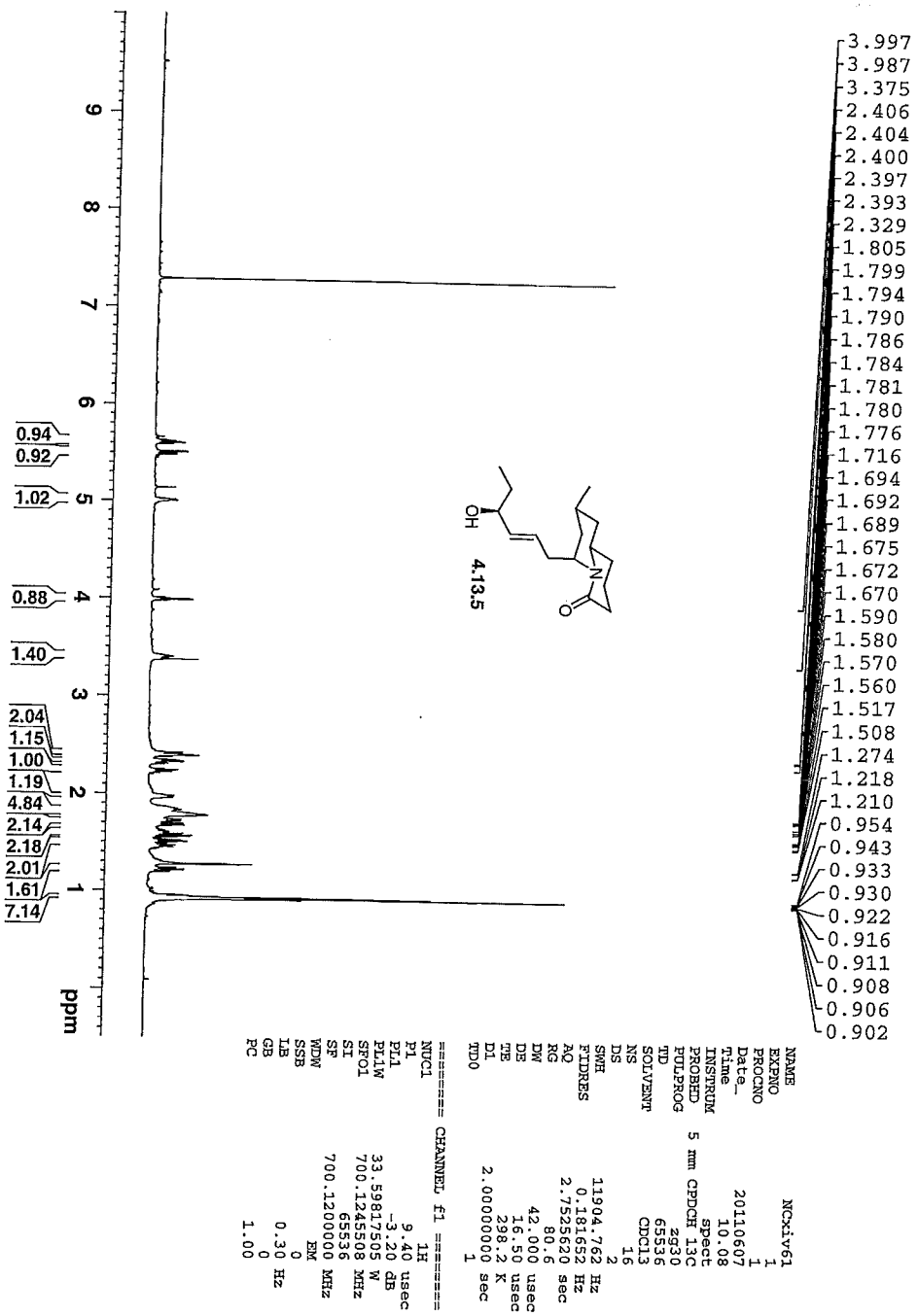

carbon
169.80
136.90
115.66
51.97
50.00
42.71
37.14
33.22
30.84
25.96
21.95
19.33
4.11.1
BRUKER
NAME NCx84
EXPNO 2
PROCNO 1
Date_ 20100914
Time 16.39
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDCl3
NS 32
DS 4
SWH 41666.668 Hz
FIDRES 0.423855 Hz
AQ 1.1796980 sec
RG 203
DW 12.000 usec
DE 15.00 usec
TE 298.0 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0629186 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 usec
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1228005 MHz
SI 131072
SF 176.0453140 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
200
180
160
140
120
100
80
60
40
20
ppm

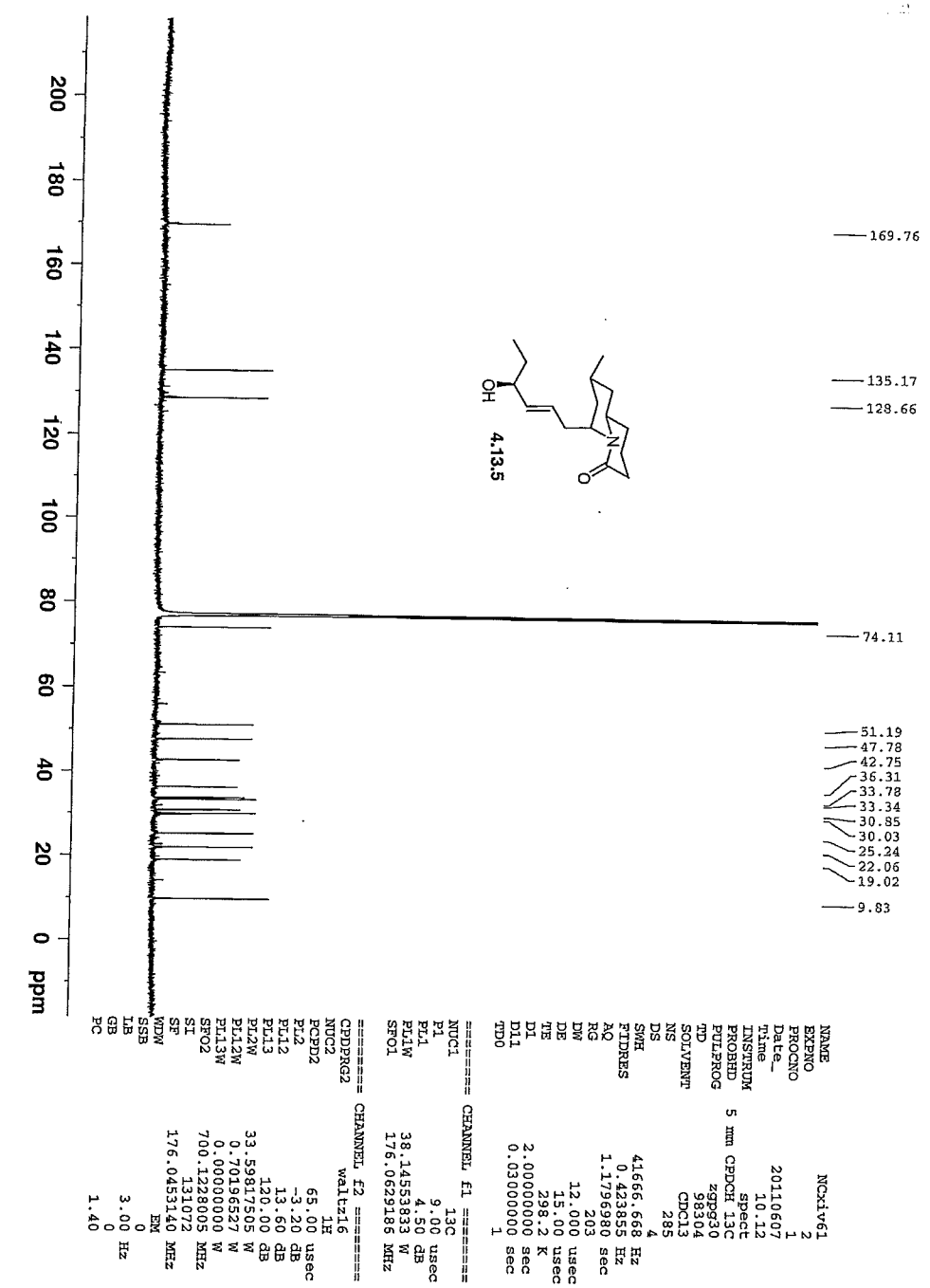

lactam proton
3.962
3.957
3.952
3.948
3.631
3.625
3.615
3.610
3.522
3.513
3.507
3.498
2.401
2.399
2.391
2.381
2.372
2.367
2.359
2.142
2.128
2.125
2.123
1.788
1.784
1.774
1.712
1.699
1.276
0.920
0.918
0.913
0.909
0.905
0.887
0.883
0.127
0.105
0.093
0.082
0.080
0.076
0.058
0.056
NAME NCxi23
EXPNO 1
PROCNO 1
Date_ 20101014
Time 15.02
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.181652 Hz
AQ 2.7525620 sec
RG 28.5
DW 42.000 usec
DE 16.50 usec
TE 297.5 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1245508 MHz
SI 65536
SF 700.1200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
OTBS
OTBS
4.11.2
0.72
0.86
0.90
1.63
1.87
0.97
1.14
2.13
1.13
0.91
0.84
5.72
2.31
23.07
12.00
ppm
9
8
7
6
5
4
3
2
1

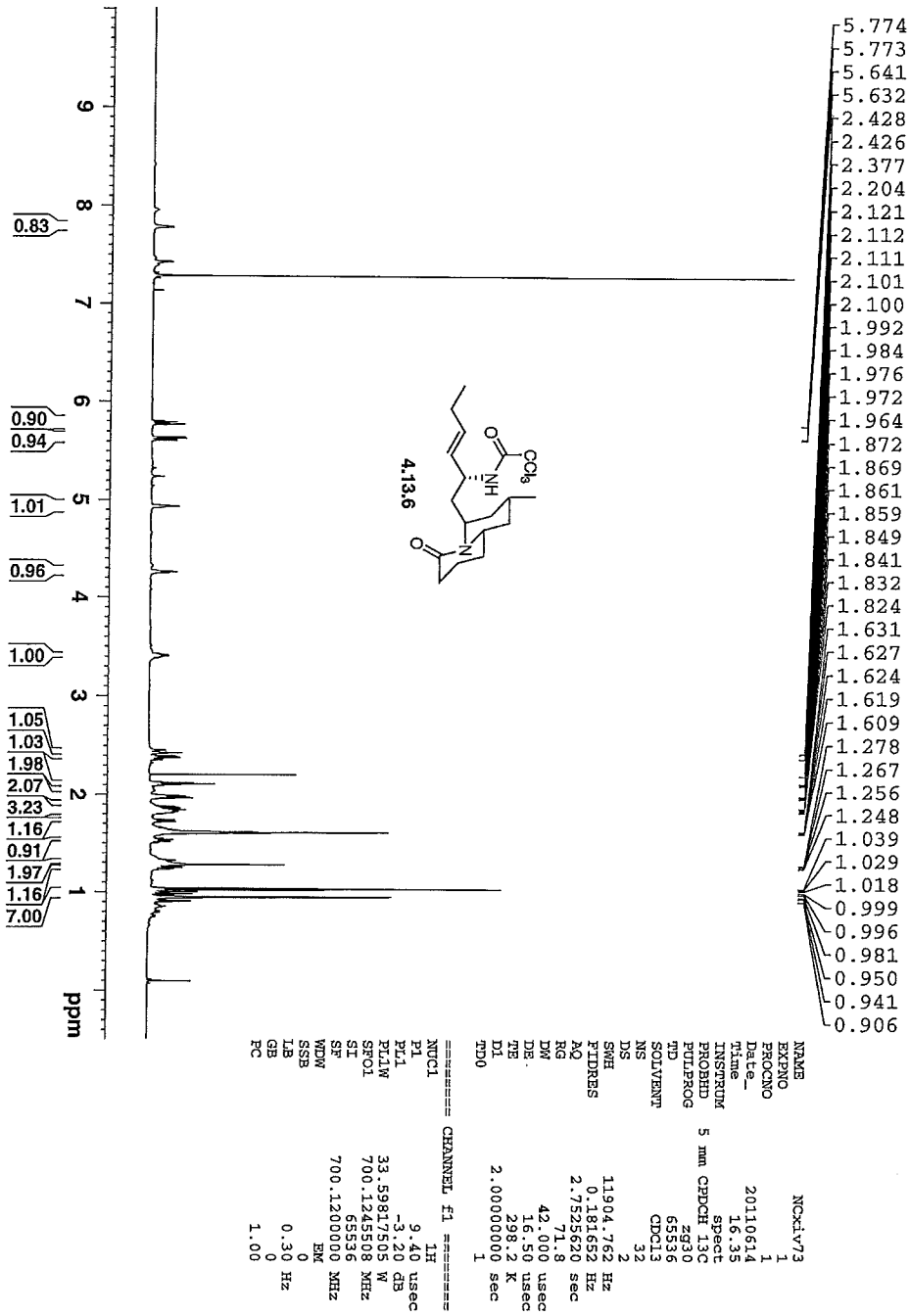

lactam carbon
4.11.2
OTBS
OTBS
ppm
200
180
160
140
120
100
80
60
40
20
BRUKER

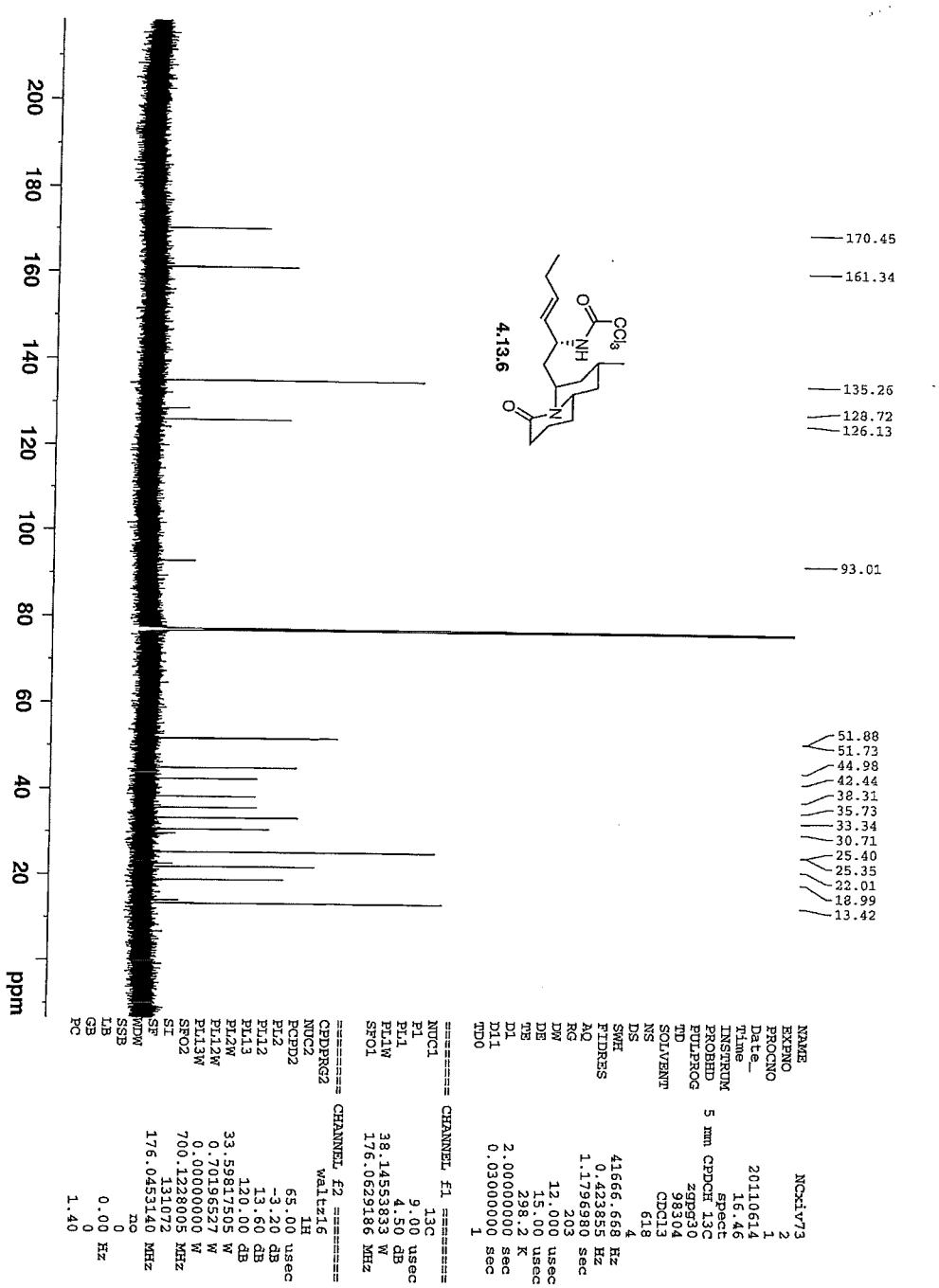

5.469
5.466
5.449
4.866
4.859
4.853
3.949
3.948
3.942
3.940
3.938
3.937
3.934
3.930
3.929
3.844
3.840
3.837
3.836
3.834
3.832
3.825
2.398
2.394
2.391
2.387
2.380
2.326
1.790
1.788
1.785
1.782
1.775
1.773
1.770
1.768
1.645
1.631
1.626
0.932
0.914
0.885
0.882
0.876
NAME NCxiv26
EXPNO 1
PROCNO 1
Date_ 20110516
Time 12.34
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.181652 Hz
AQ 2.7525620 sec
RG 28.5
DW 42.000 usec
DE 16.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PLW 33.59817505 W
SFO1 700.1245508 MHz
SI 65536
SF 700.1200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
4.13.2
2.70
0.90
1.92
2.00
0.92
4.26
1.11
2.92
1.99
1.03
1.12
3.91
ppm

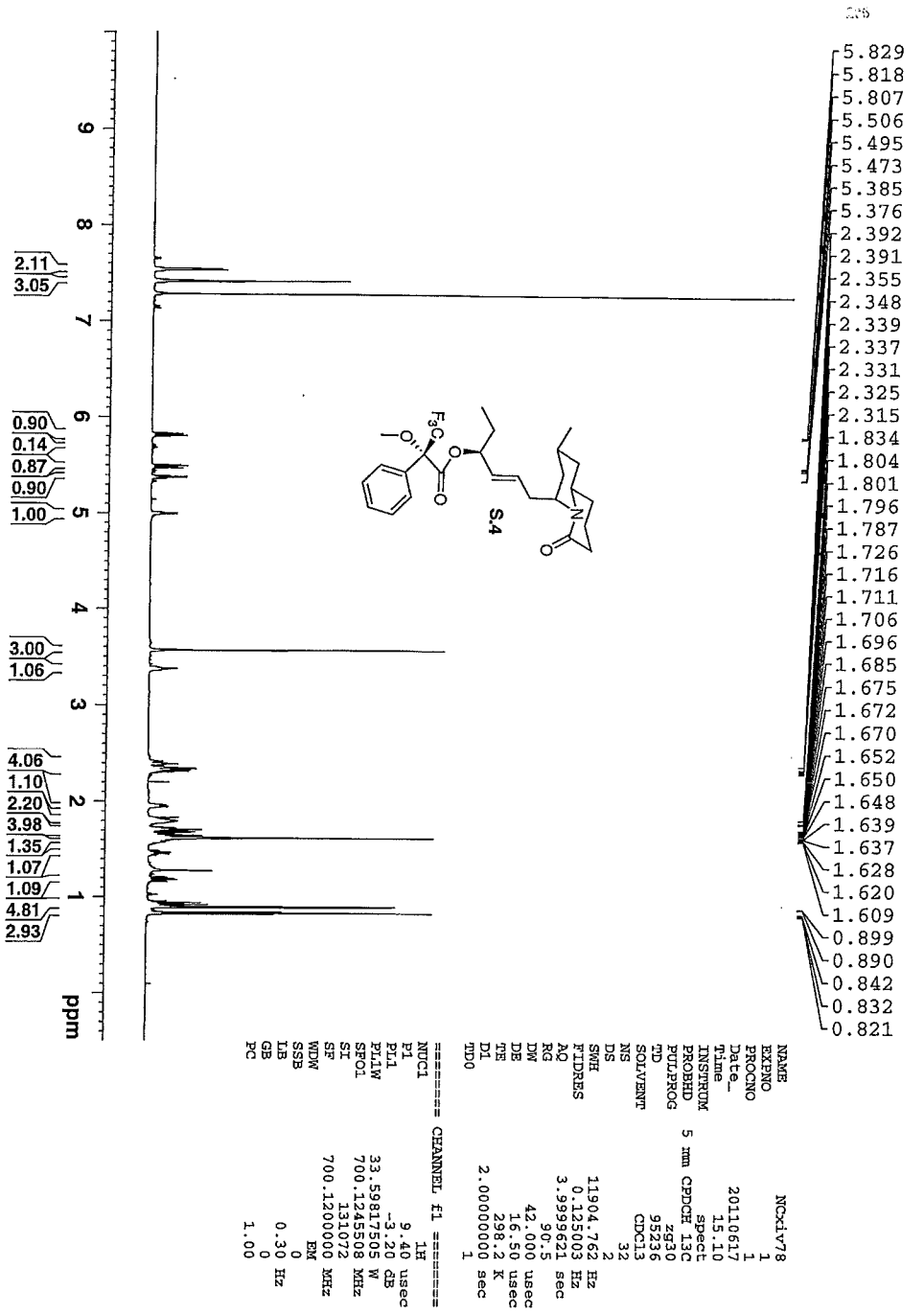

169.59
132.27
125.12
103.83
77.31
77.13
76.95
64.98
51.79
49.26
42.69
37.37
37.30
33.24
30.75
25.86
21.99
19.22
4.13.2
200
180
160
140
120
100
80
60
40
20
0
ppm
NAME NCxiv26
EXPNO 2
PROCNO 1
Date_ 20110516
Time 12.43
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDCl3
NS 100
DS 4
SWH 41666.668 Hz
FIDRES 0.423855 Hz
AQ 1.1796980 sec
RG 203
DW 12.000 usec
DE 15.00 usec
TE 298.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
========== CHANNEL f1 ==========
NUC1 13C
P1 9.00 usec
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0629186 MHz
========== CHANNEL f2 ==========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 usec
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1228005 MHz
SI 131072
SF 176.0453140 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40

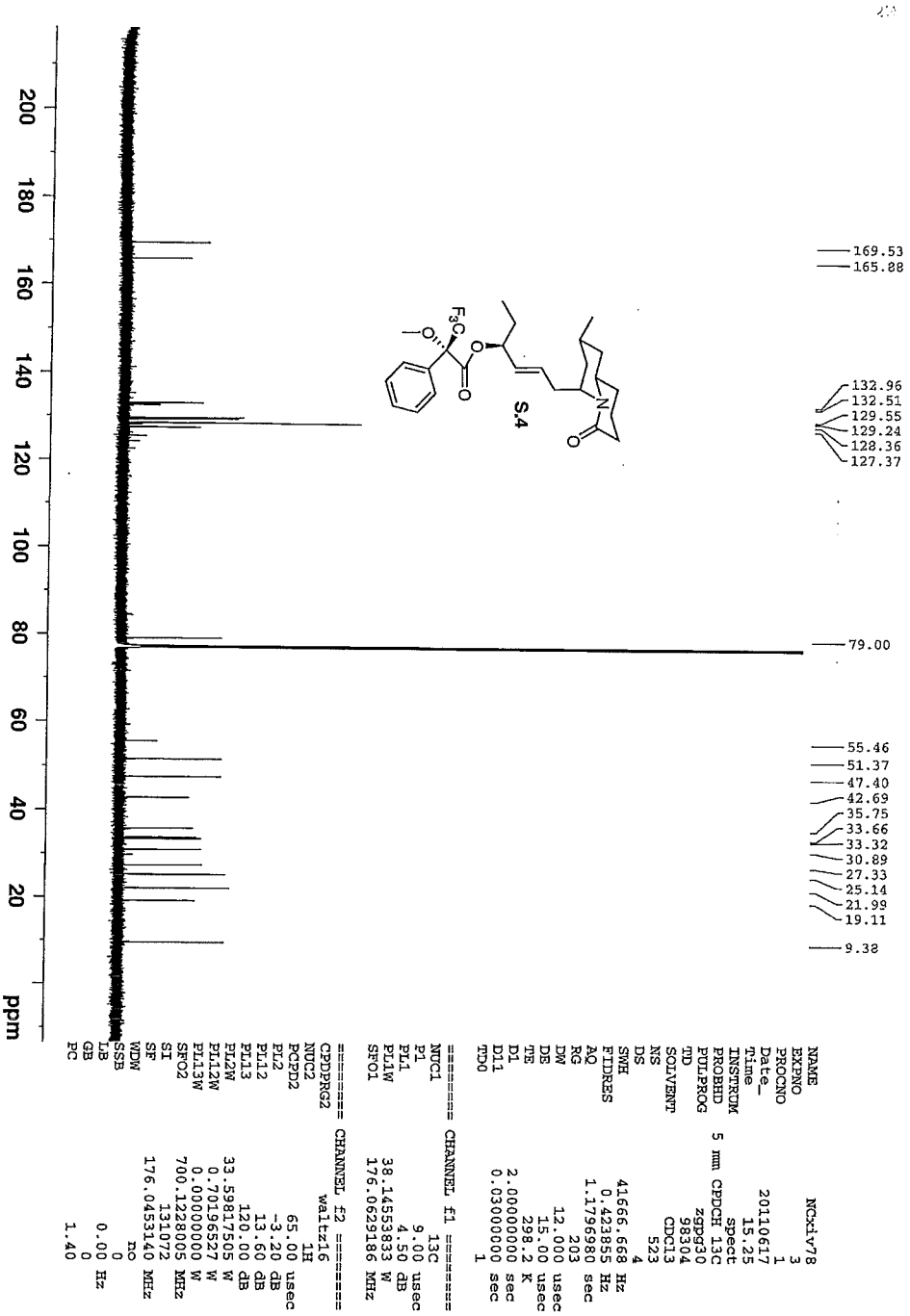

3.997
3.987
3.375
2.406
2.404
2.400
2.397
2.393
2.329
1.805
1.799
1.794
1.790
1.786
1.784
1.781
1.780
1.776
1.716
1.694
1.692
1.689
1.675
1.672
1.670
1.590
1.580
1.570
1.560
1.517
1.508
1.274
1.218
1.210
0.954
0.943
0.933
0.930
0.922
0.916
0.911
0.908
0.906
0.902
NAME NCxiv61
EXPNO 1
PROCNO 1
Date_ 20110607
Time 10.08
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 11904.762 Hz
FIDRES 0.181652 Hz
AQ 2.7525620 sec
RG 80.6
DW 42.000 usec
DE 16.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1245508 MHz
SI 65536
SF 700.1200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
OH 4.13.5
0.94
0.92
1.02
0.88
1.40
2.04
1.15
1.00
1.19
4.84
2.14
2.18
2.01
1.61
7.14
ppm

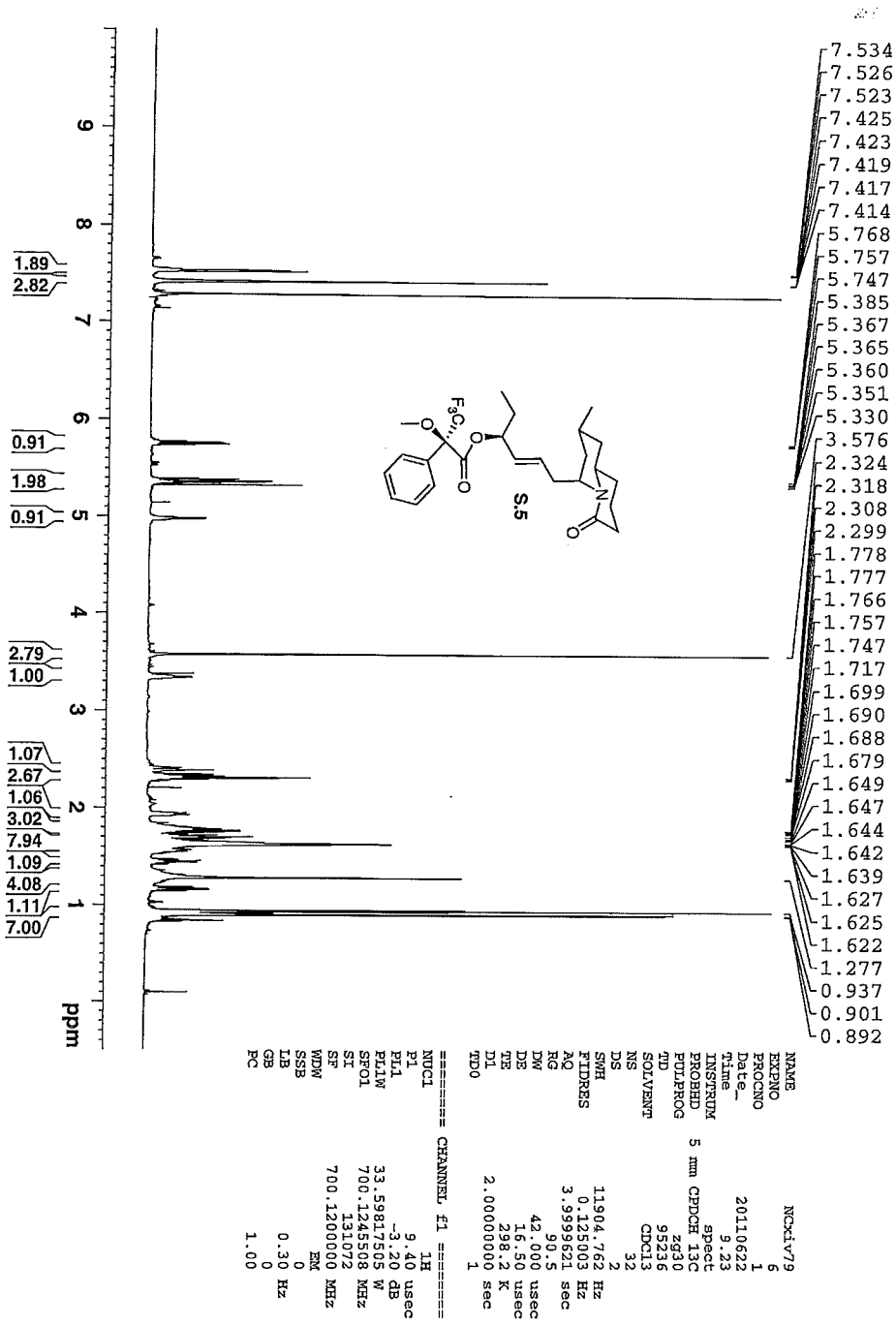

OH
4.13.5
N
O
169.76
135.17
128.66
74.11
51.19
47.78
42.75
36.31
33.78
33.34
30.85
30.03
25.24
22.06
19.02
9.83
200
180
160
140
120
100
80
60
40
20
0
ppm
NAME NCxiv61
EXPNO 2
PROCNO 1
Date_ 20110607
Time 10.12
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDCl3
NS 285
DS 4
SWH 41666.668 Hz
FIDRES 0.423855 Hz
AQ 1.1796980 sec
RG 203
DW 12.000 usec
DE 15.00 usec
TE 298.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.06229186 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 usec
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1228005 MHz
SI 131072
SF 176.0453140 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40

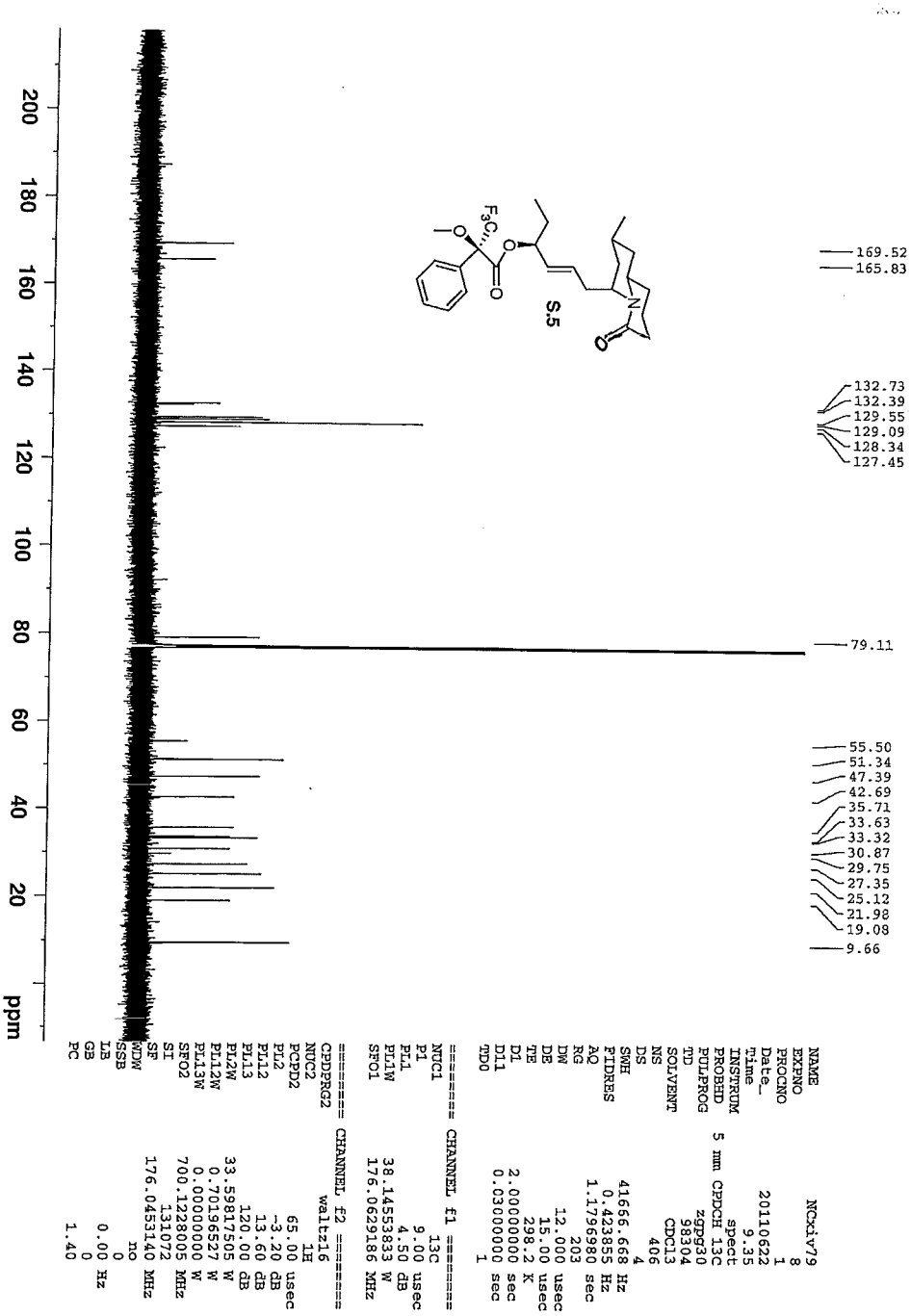

5.774
5.773
5.641
5.632
2.428
2.426
2.377
2.204
2.121
2.112
2.111
2.101
2.100
1.992
1.984
1.976
1.972
1.964
1.872
1.869
1.861
1.859
1.849
1.841
1.832
1.824
1.631
1.627
1.624
1.619
1.609
1.278
1.267
1.256
1.248
1.039
1.029
1.018
0.999
0.996
0.981
0.950
0.941
0.906
NAME NCxiv73
EXPNO 1
PROCNO 1
Date_ 20110614
Time_ 16.35
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.181652 Hz
AQ 2.7525620 sec
RG 71.8
DW 42.000 usec
DE 16.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1245508 MHz
SI 65536
SF 700.1200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
4.13.6
NH
O
CCl3
N
O
0.83
0.90
0.94
1.01
0.96
1.00
1.05
1.03
1.98
2.07
3.23
1.16
0.91
1.97
1.16
7.00
ppm
9
8
7
6
5
4
3
2
1

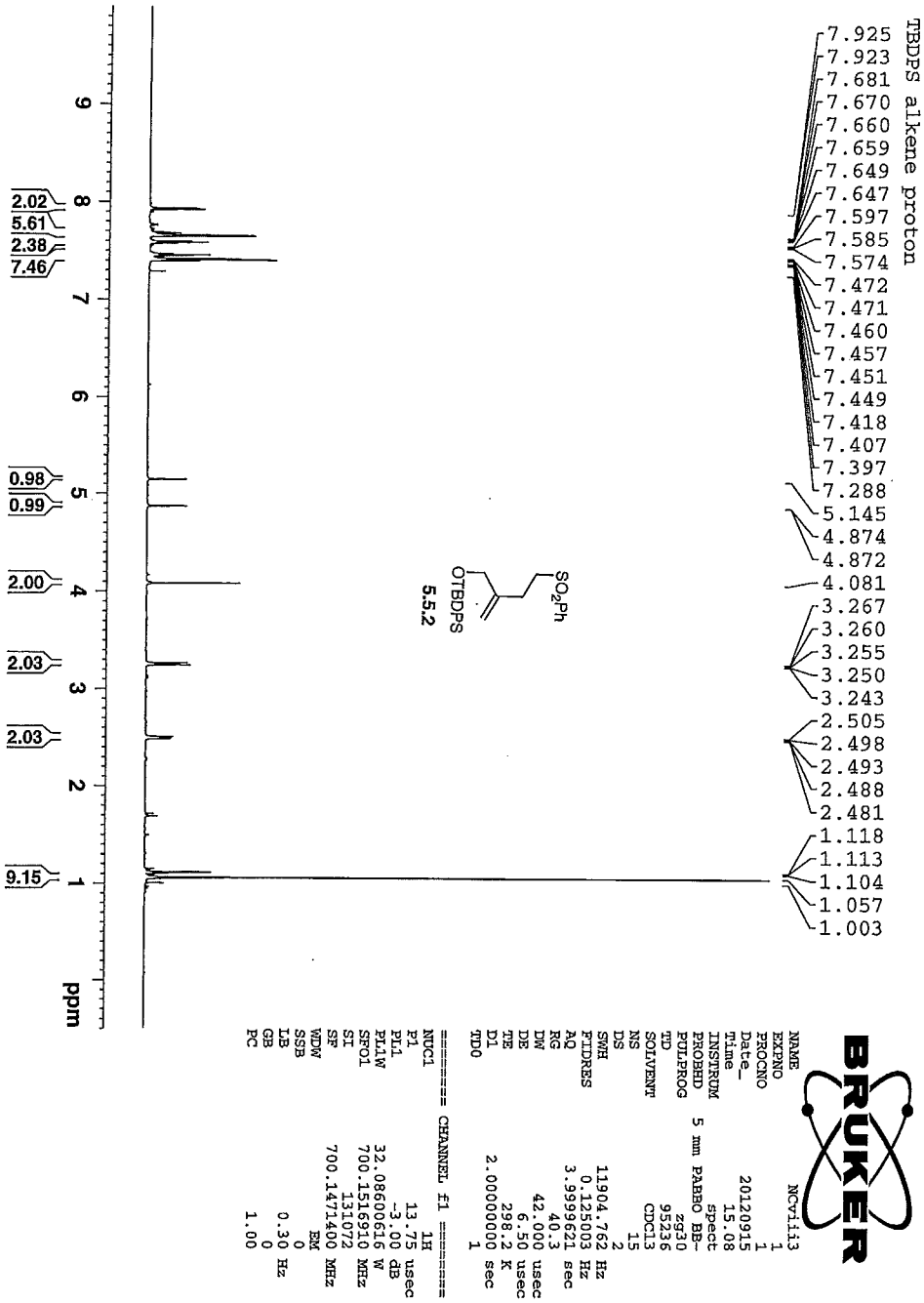

4.13.6
170.45
161.34
135.26
128.72
126.13
93.01
51.88
51.73
44.98
42.44
38.31
35.73
33.34
30.71
25.40
25.35
22.01
18.99
13.42
ppm
200
180
160
140
120
100
80
60
40
20
NAME NCxiv73
EXPNO 2
PROCNO 1
Date_ 20110614
Time 16.46
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDCl3
NS 618
DS 4
SWH 41666.668 Hz
FIDRES 0.423855 Hz
AQ 1.1796980 sec
RG 203
DW 12.000 usec
DE 15.00 usec
TE 298.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0629186 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 usec
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70195527 W
PL13W 0.00000000 W
SFO2 700.1228005 MHz
SI 131072
SF 176.0453140 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.40


5.829
5.818
5.807
5.506
5.495
5.473
5.385
5.376
2.392
2.391
2.355
2.348
2.339
2.337
2.331
2.325
2.315
1.834
1.804
1.801
1.796
1.787
1.726
1.716
1.711
1.706
1.696
1.685
1.675
1.672
1.670
1.652
1.650
1.648
1.639
1.637
1.628
1.620
1.609
0.899
0.890
0.842
0.832
0.821
NAME NCxiv78
EXPNO 1
PROCNO 1
Date_ 20110617
Time 15.10
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 90.5
DW 42.000 usec
DE 16.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1245508 MHz
SI 131072
SF 700.1200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
S.4
2.11
3.05
0.90
0.14
0.87
0.90
1.00
3.00
1.06
4.06
1.10
2.20
3.98
1.35
1.07
1.09
4.81
2.93
ppm

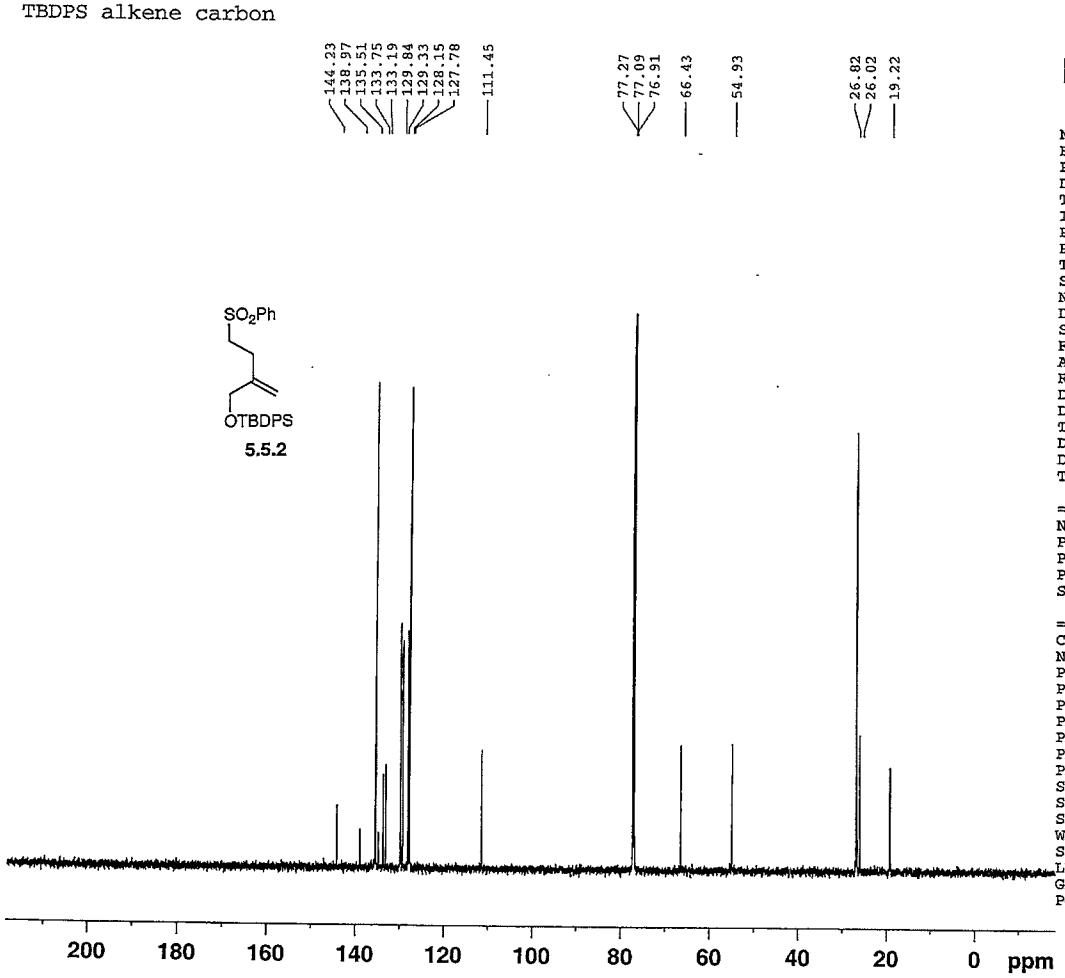

169.53
165.88
132.96
132.51
129.55
129.24
128.36
127.37
79.00
55.46
51.37
47.40
42.69
35.75
33.66
33.32
30.89
27.33
25.14
21.99
19.11
9.38
S.4
200
180
160
140
120
100
80
60
40
20
ppm
NAME NCxiv78
EXPNO 3
PROCNO 1
Date_ 20110617
Time 15.25
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDCl3
NS 523
DS 4
SWH 41666.668 Hz
FIDRES 0.423855 Hz
AQ 1.1796980 sec
RG 203
DW 12.000 usec
DE 15.00 usec
TE 298.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0629186 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 usec
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1228005 MHz
SI 131072
SF 176.0453140 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.40


7.534
7.526
7.523
7.425
7.423
7.419
7.417
7.414
5.768
5.757
5.747
5.385
5.367
5.365
5.360
5.351
5.330
3.576
2.324
2.318
2.308
2.299
1.778
1.777
1.766
1.757
1.747
1.717
1.699
1.690
1.688
1.679
1.649
1.647
1.644
1.642
1.639
1.627
1.625
1.622
1.277
0.937
0.901
0.892
1.89
2.82
0.91
1.98
0.91
2.79
1.00
1.07
2.67
1.06
3.02
7.94
1.09
4.08
1.11
7.00
S.5
ppm
NAME NCxiv79
EXPNO 6
PROCNO 1
Date_ 20110622
Time 9.23
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 90.5
DW 42.000 usec
DE 16.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1245508 MHz
SI 131072
SF 700.1200000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00


S.5
169.52
165.83
132.73
132.39
129.55
129.09
128.34
127.45
79.11
55.50
51.34
47.39
42.69
35.71
33.63
33.32
30.87
29.75
27.35
25.12
21.98
19.08
9.66
200
180
160
140
120
100
80
60
40
20
ppm
NAME NCxiv79
EXPNO 8
PROCNO 1
Date_ 20110622
Time 9.35
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 98304
SOLVENT CDCl3
NS 406
DS 4
SWH 41666.668 Hz
FIDRES 0.423855 Hz
AQ 1.1796980 sec
RG 203
DW 12.000 usec
DE 15.00 usec
TE 298.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0629186 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 usec
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70136527 W
PL13W 0.00000000 W
SFO2 700.1228005 MHz
SI 131072
SF 176.0453140 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 1.40

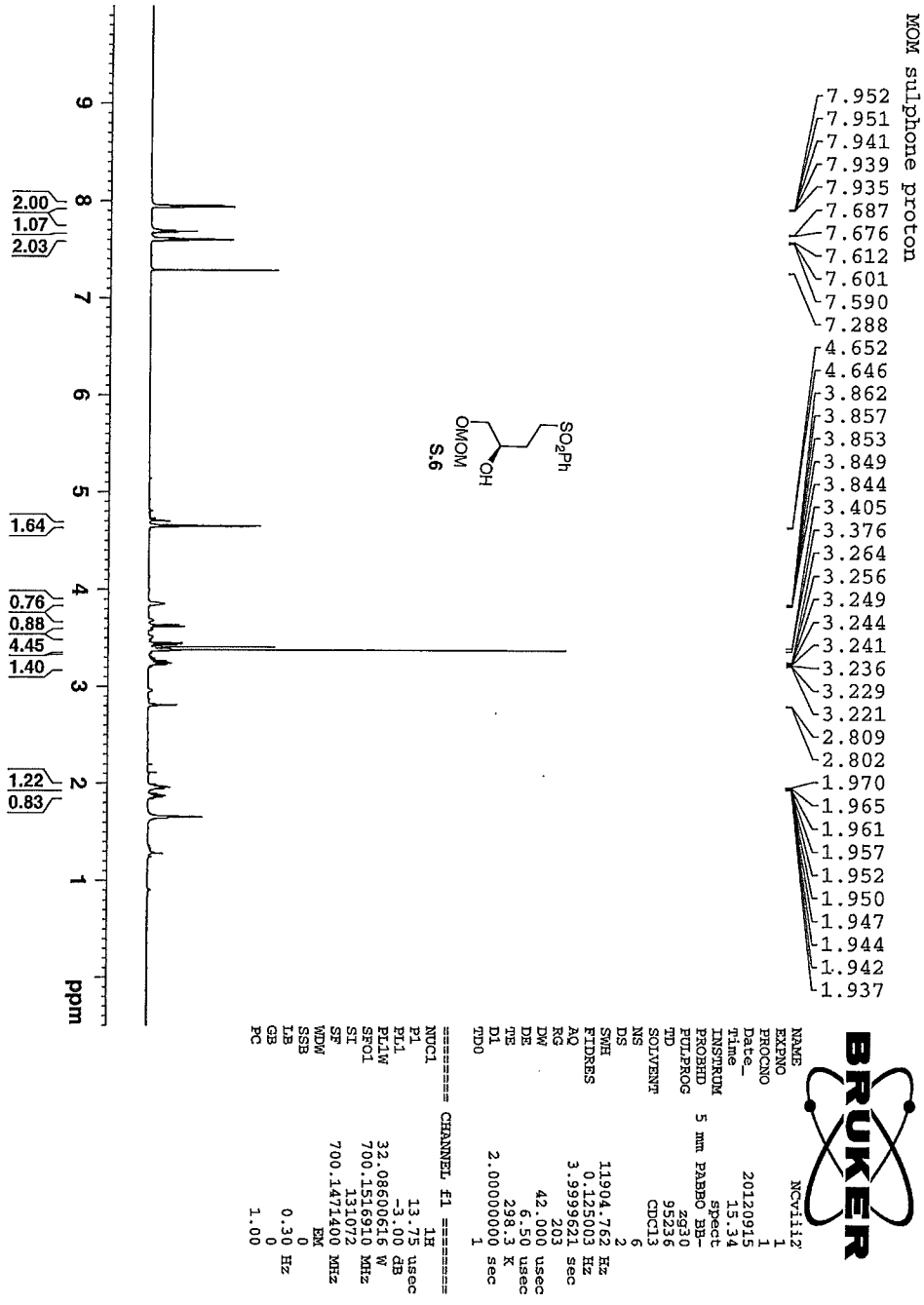

TBDPS alkene proton
7.925
7.923
7.681
7.670
7.660
7.659
7.649
7.647
7.597
7.585
7.574
7.472
7.471
7.460
7.457
7.451
7.449
7.418
7.407
7.397
7.288
5.145
4.874
4.872
4.081
3.267
3.260
3.255
3.250
3.243
2.505
2.498
2.493
2.488
2.481
1.118
1.113
1.104
1.057
1.003
OTBDPS
SO2Ph
5.5.2
2.02
5.61
2.38
7.46
0.98
0.99
2.00
2.03
2.03
9.15
ppm
NAME NCY113
EXPNO 1
PROCNO 1
Date_ 20120915
Time 15.08
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 40.3
DW 42.000 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.75 usec
PL1 -3.00 dB
PL1W 32.08600616 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

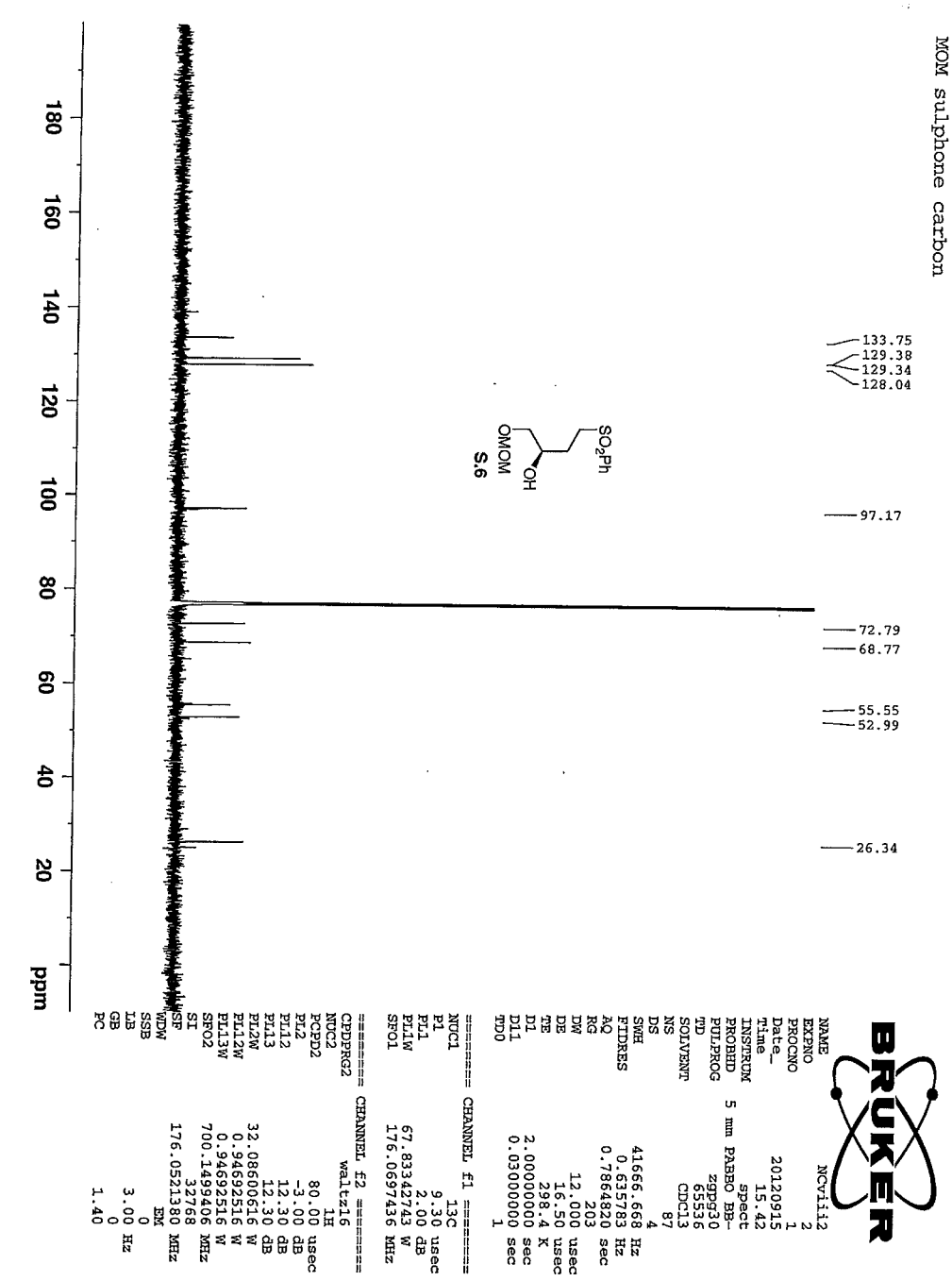
TBDPS alkene carbon

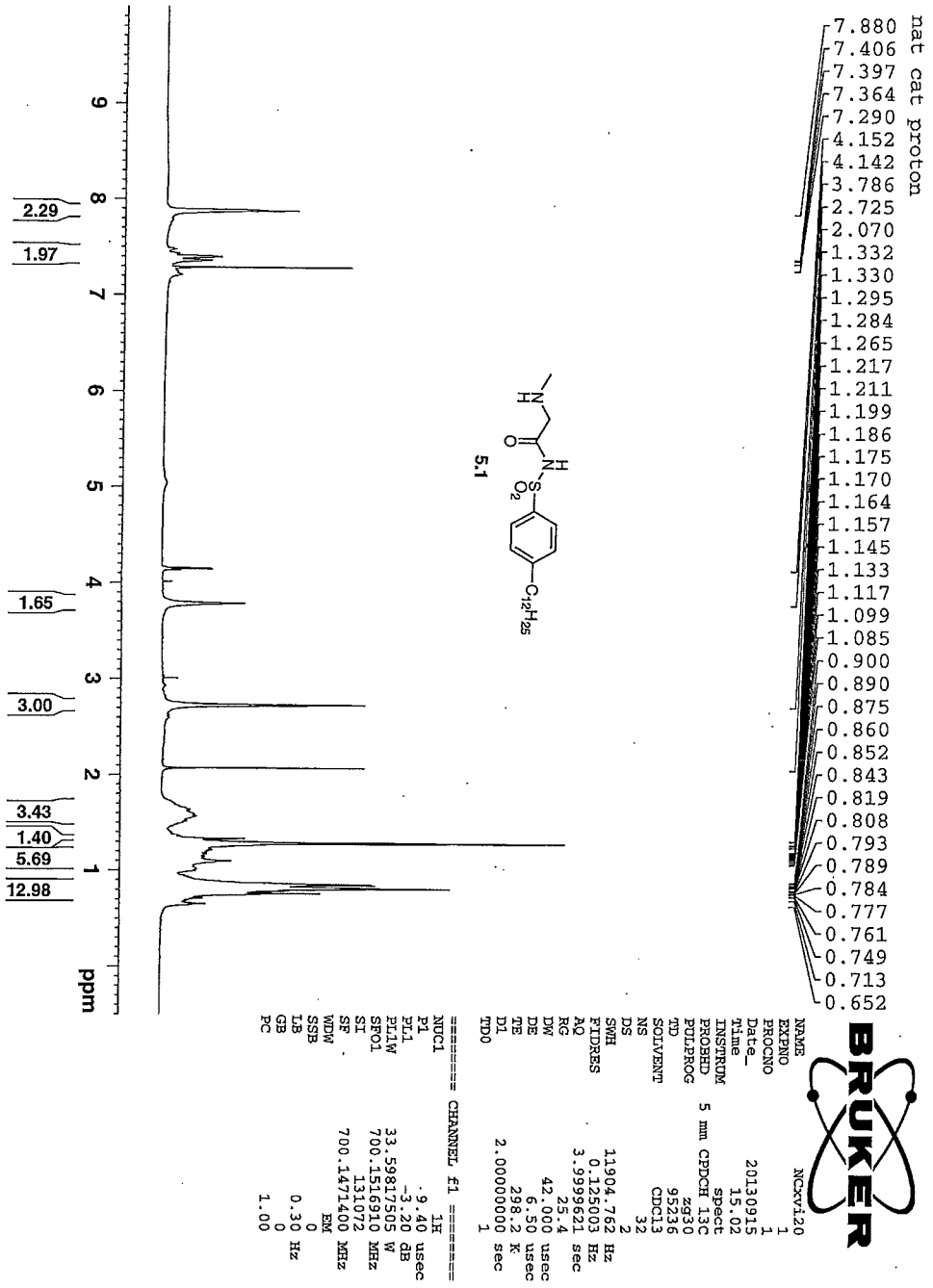


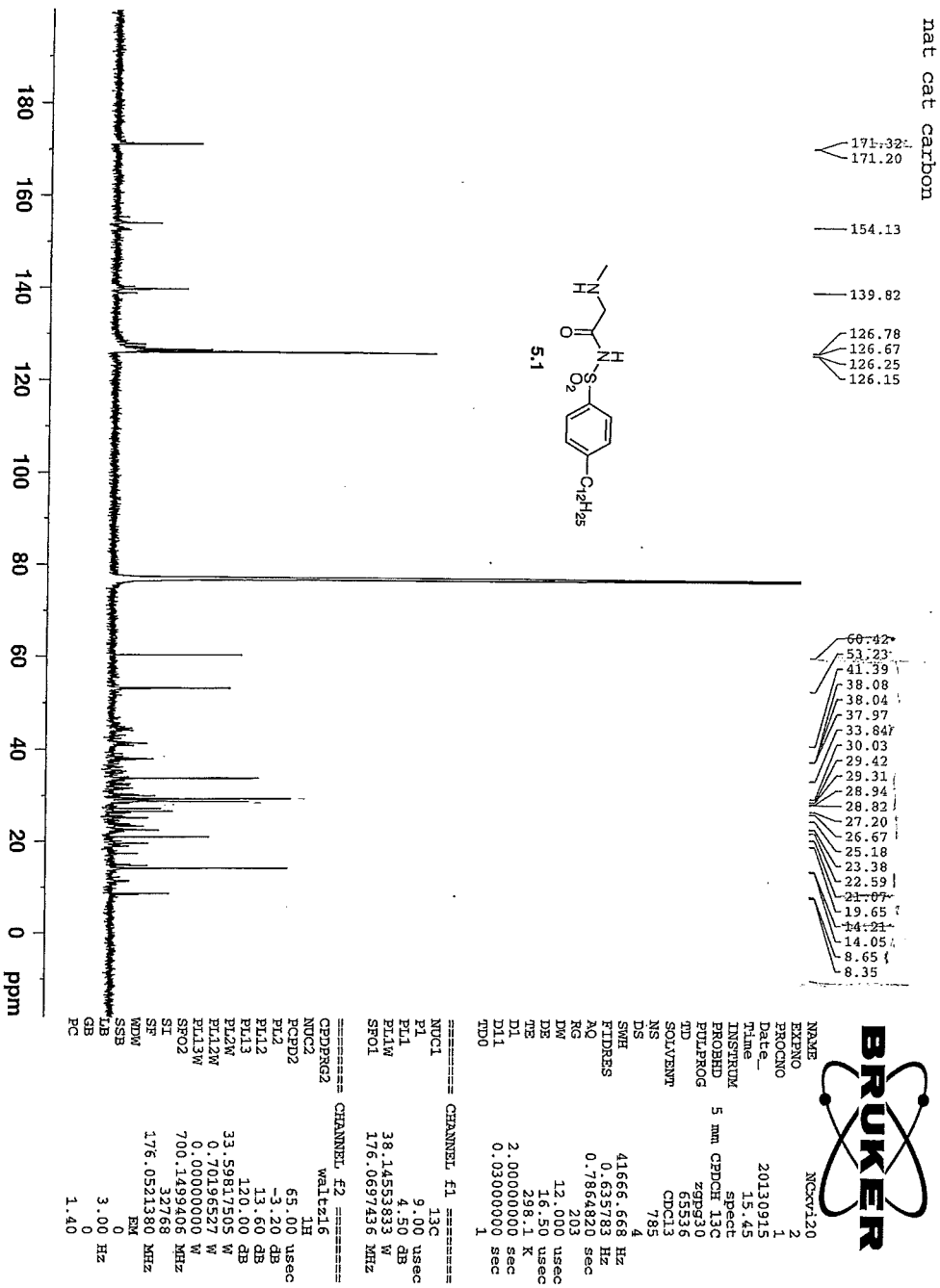
BRUKER

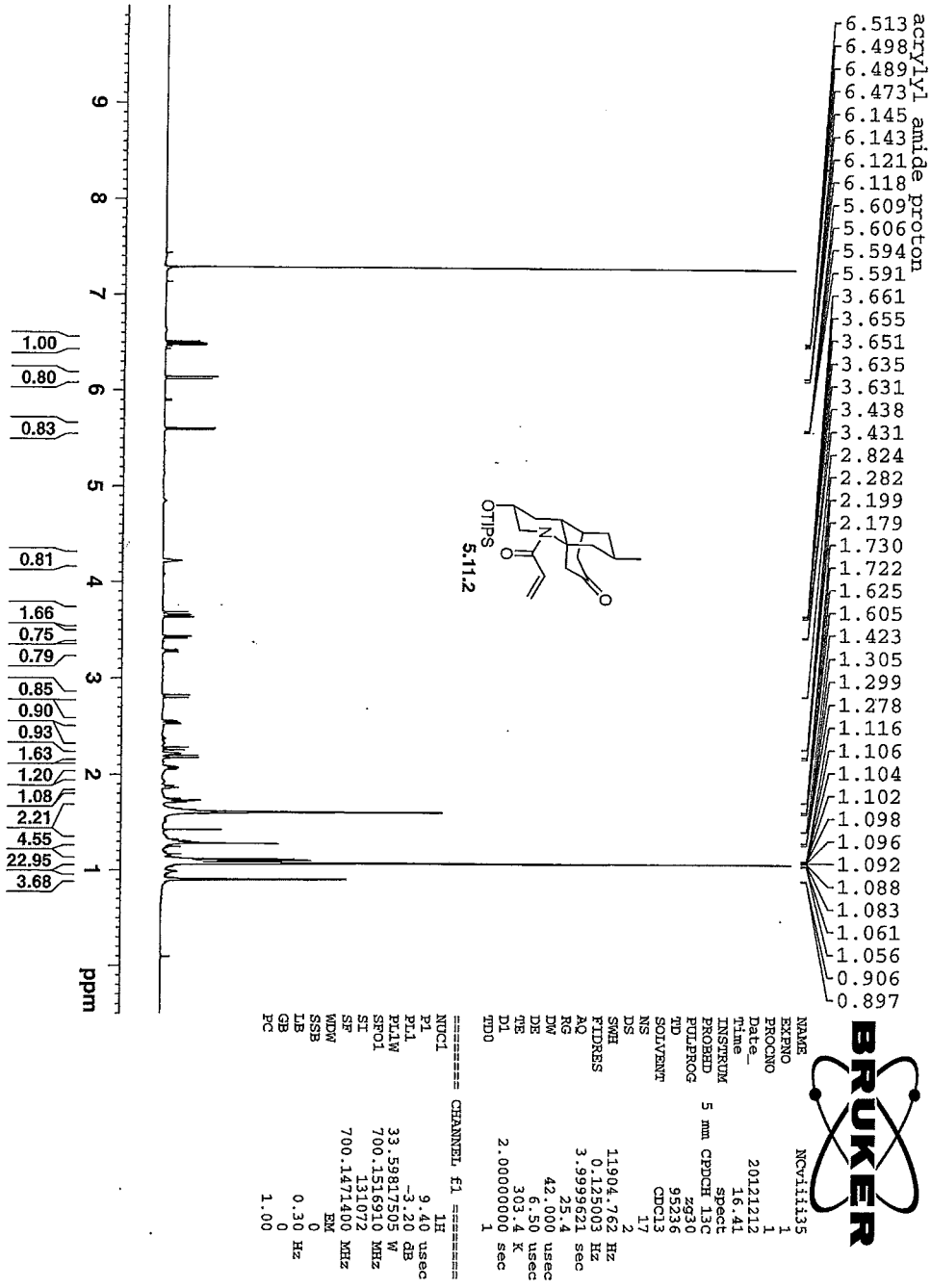
NAME	NCviii3
EXPNO	2
PROCNO	1
Date_	20120915
Time	15.14
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	31
DS	4
SWH	41666.668 Hz
FIDRES	0.635783 Hz
AQ	0.7864820 sec
RG	203
DW	12.000 usec
DE	16.50 usec
TE	299.0 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.30 usec
PL1	2.00 dB
PL1W	67.83342743 W
SFO1	176.0697436 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	-3.00 dB
PL12	12.30 dB
PL13	12.30 dB
PL2W	32.08600616 W
PL12W	0.94692516 W
PL13W	0.94692516 W
SFO2	700.1499406 MHz
SI	32768
SF	176.0521380 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40

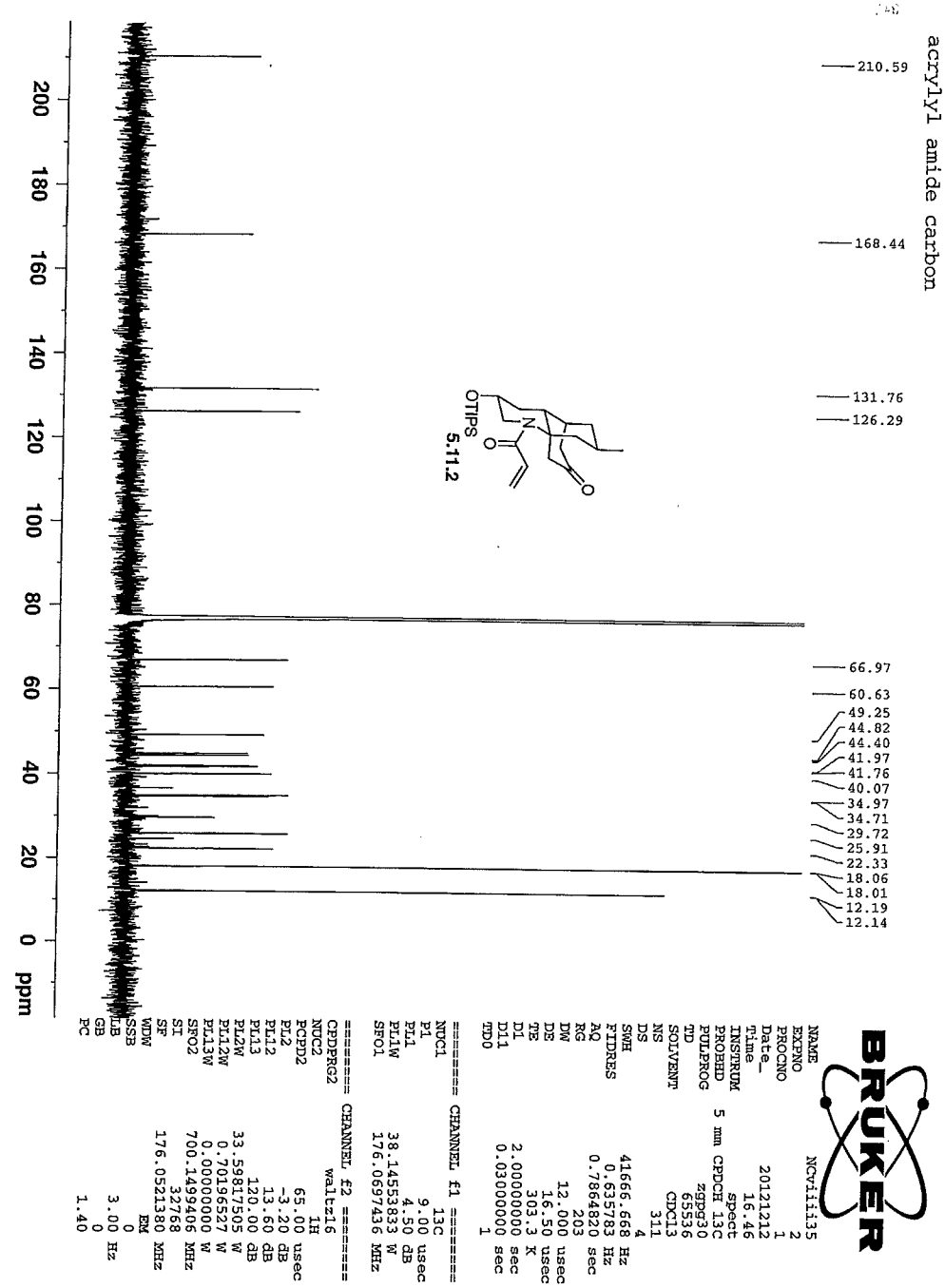

MOM sulphone proton
7.952
7.951
7.941
7.939
7.935
7.687
7.676
7.612
7.601
7.590
7.288
4.652
4.646
3.862
3.857
3.853
3.849
3.844
3.405
3.376
3.264
3.256
3.249
3.244
3.241
3.236
3.229
3.221
2.809
2.802
1.970
1.965
1.961
1.957
1.952
1.950
1.947
1.944
1.942
1.937
NAME NCvili2'
EXPNO 1
PROCNO 1
Date_ 20120915
Time 15.34
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG 2g30
TD 95236
SOLVENT CDCl3
NS 6
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
SO2Ph
OMOM
OH
S.6
2.00
1.07
2.03
1.64
0.76
0.88
4.45
1.40
1.22
0.83
9
8
7
6
5
4
3
2
1
ppm

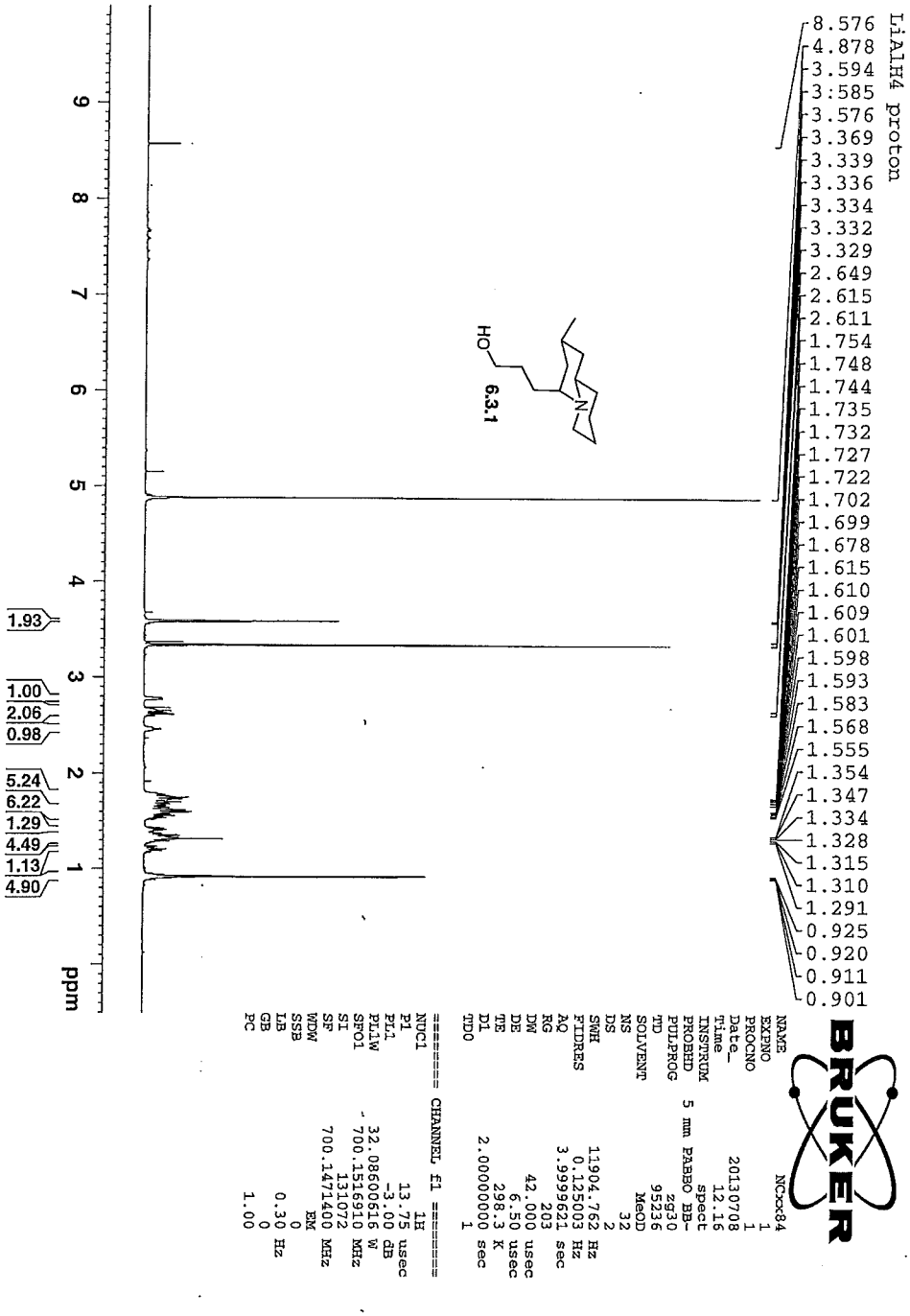

MOM sulphone carbon
133.75
129.38
129.34
128.04
97.17
72.79
68.77
55.55
52.99
26.34
SO2Ph
OMOM
OH
S.6
180
160
140
120
100
80
60
40
20
ppm
NAME NCvii2
EXPNO 2
PROCNO 1
Date_ 20120915
Time_ 15.42
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 87
DS 4
SWH 41666.668 Hz
FIDRES 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 9.30 usec
PL1 2.00 dB
PL1W 67.83342743 W
SFO1 176.0697436 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -3.00 dB
PL12 12.30 dB
PL13 12.30 dB
PL2W 32.08600616 W
PL12W 0.94692516 W
PL13W 0.94692516 W
SFO2 700.1499406 MHz
SI 32768
SF 176.0521380 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40


nat cat proton
7.880
7.406
7.397
7.364
7.290
4.152
4.142
3.786
2.725
2.070
1.332
1.330
1.295
1.284
1.265
1.217
1.211
1.199
1.186
1.175
1.170
1.164
1.157
1.145
1.133
1.117
1.099
1.085
0.900
0.890
0.875
0.860
0.852
0.843
0.819
0.808
0.793
0.789
0.784
0.777
0.761
0.749
0.713
0.652
NAME NCxvi20
EXPNO 1
PROCNO 1
Date_ 20130915
Time 15.02
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 25.4
DW 42.000 usec
DE 6.50 usec
TE 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PL1W 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
5.1
2.29
1.97
1.65
3.00
3.43
1.40
5.69
12.98
ppm

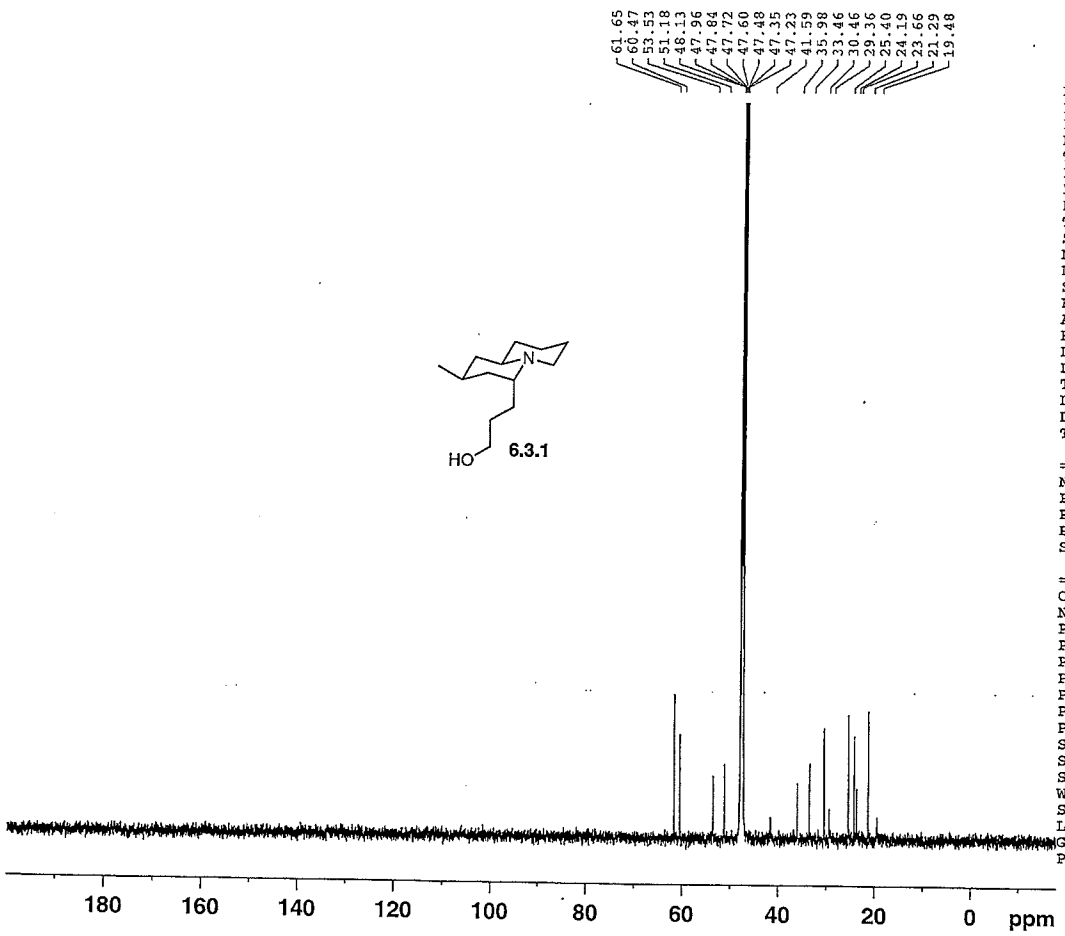

nat cat carbon
171.32
171.20
154.13
139.82
126.78
126.67
126.25
126.15
60.42
53.23
41.39
38.08
38.04
37.97
33.84
30.03
29.42
29.31
28.94
28.82
27.20
26.67
25.18
23.38
22.59
21.07
19.65
14.21
14.05
8.65
8.35
5.1
180
160
140
120
100
80
60
40
20
0
ppm
NAME NCsvi20
EXPNO 2
PROCNO 1
Date_ 20130915
Time 15.45
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 785
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864820 sec
RG 203
DW 12.000 usec
DE 16.50 usec
TE 298.1 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0697436 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 usec
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1499406 MHz
SI 32768
SF 176.0521380 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40


acrylyl amide proton
6.513
6.498
6.489
6.473
6.145
6.143
6.121
6.118
5.609
5.606
5.594
5.591
3.661
3.655
3.651
3.635
3.631
3.438
3.431
2.824
2.282
2.199
2.179
1.730
1.722
1.625
1.605
1.423
1.305
1.299
1.278
1.116
1.106
1.104
1.102
1.098
1.096
1.092
1.088
1.083
1.061
1.056
0.906
0.897
OTIPS
5.11.2
1.00
0.80
0.83
0.81
1.66
0.75
0.79
0.85
0.90
0.93
1.63
1.20
1.08
2.21
4.55
22.95
3.68
ppm
NAME NCvili135
EXPNO 1
PROCNO 1
Date_ 20121212
Time 16.41
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 17
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 25.4
DW 42.000 usec
DE 6.50 usec
TE 303.4 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
BRUKER


acrylyl amide carbon
210.59
168.44
131.76
126.29
66.97
60.63
49.25
44.82
44.40
41.97
41.76
40.07
34.97
34.71
29.72
25.91
22.33
18.06
18.01
12.19
12.14
OTIPS
5.11.2
200
180
160
140
120
100
80
60
40
20
0
ppm
BRUKER
NAME NCvilii35
EXPNO 2
PROCNO 1
Date_ 20121212
Time 16.46
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 311
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864820 sec
RG 203
DW 12.000 usec
DE 16.50 usec
TE 303.3 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 13.20 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

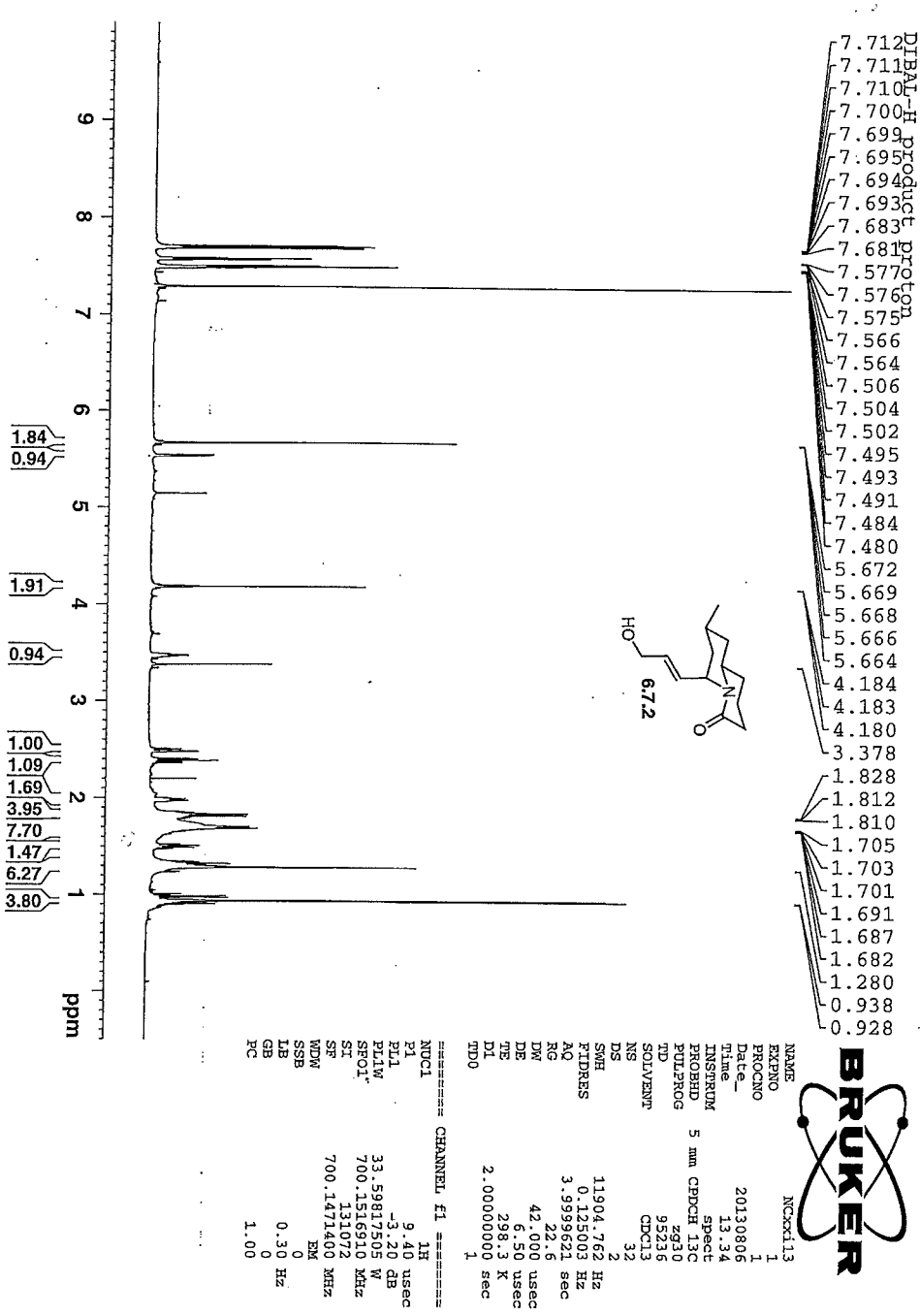

LiAlH4 proton
8.576
4.878
3.594
3:585
3.576
3.369
3.339
3.336
3.334
3.332
3.329
2.649
2.615
2.611
1.754
1.748
1.744
1.735
1.732
1.727
1.722
1.702
1.699
1.678
1.615
1.610
1.609
1.601
1.598
1.593
1.583
1.568
1.555
1.354
1.347
1.334
1.328
1.315
1.310
1.291
0.925
0.920
0.911
0.901
HO
6.3.1
N
1.93
1.00
2.06
0.98
5.24
6.22
1.29
4.49
1.13
4.90
ppm
NAME NCxx84
EXPNO 1
PROCNO 1
Date_ 20130708
Time 12.16
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 95336
SOLVENT MeOD
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

LiAlH4 carbon



BRUKER

NAME	NCxx84
EXPNO	3
PROCNO	1
Date_	20130708
Time	12.31
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	MeOD
NS	1024
DS	4
SWH	41666.668 Hz
FIDRES	0.635783 Hz
AQ	0.7864820 sec
RG	203
DW	12.000 usec
DE	16.50 usec
TE	298.9 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.30 usec
PL1	2.00 dB
PL1W	67.83342743 W
SFO1	176.0697436 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	-3.00 dB
PL12	12.30 dB
PL13	12.30 dB
PL2W	32.08600616 W
PL12W	0.94692516 W
PL13W	0.94692516 W
SFO2	700.1499406 MHz
SI	32768
SF	176.0521380 MHz
WDW	EM
SSB	0
LB	3.00 Hz
GB	0
PC	1.40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7.711
7.710
7.700
7.699
7.695
7.694
7.693
7.683
7.681
7.577
7.576
7.575
7.566
7.564
7.506
7.504
7.502
7.495
7.493
7.491
7.484
7.480
5.672
5.669
5.668
5.666
5.664
4.184
4.183
4.180
3.378
1.828
1.812
1.810
1.705
1.703
1.701
1.691
1.687
1.682
1.280
0.938
0.928
HO
6.7.2
1.84
0.94
1.91
0.94
1.00
1.09
1.69
3.95
7.70
1.47
6.27
3.80
ppm
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EXPNO 1
PROCNO 1
Date_ 20130806
Time 13.34
INSTRUM spect
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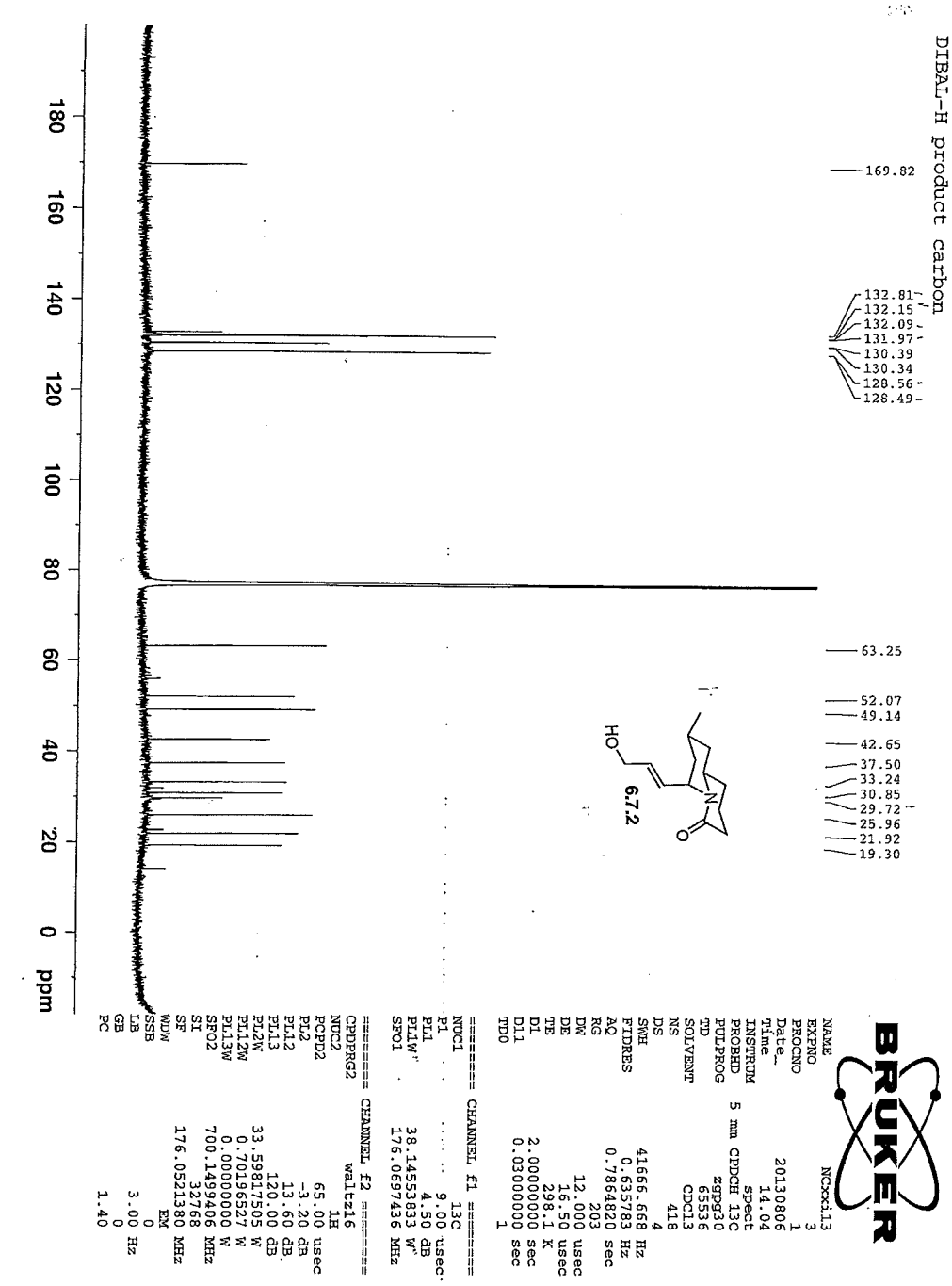
PULPROG zg30
TD 95236
SOLVENT CDCl3
NS 32
DS 2
SWH 11904.762 Hz
FIDRES 0.125003 Hz
AQ 3.9999621 sec
RG 22.6
DW 42.000 usec
DE 6.50 usec
TE 298.3 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 9.40 usec
PL1 -3.20 dB
PLIW 33.59817505 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
BRUKER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132.15
132.09
131.97
130.39
130.34
128.56
128.49
63.25
52.07
49.14
42.65
37.50
33.24
30.85
29.72
25.96
21.92
19.30
HO
N
O
6.7.2
BRUKER
NAME NCxxi13
EXPNO 3
PROCNO 1
Date_ 20130806
Time 14.04
INSTRUM spect
PROBHD 5 mm CPDCH 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 418
DS 4
SWH 41666.668 Hz
FIDRES 0.635783 Hz
AQ 0.7864820 sec
RG 203
DW 12.000 usec
DE 16.50 usec
TE 298.1 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.00 usec
PL1 4.50 dB
PL1W 38.14553833 W
SFO1 176.0697436 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 65.00 usec
PL2 -3.20 dB
PL12 13.60 dB
PL13 120.00 dB
PL2W 33.59817505 W
PL12W 0.70196527 W
PL13W 0.00000000 W
SFO2 700.1499406 MHz
SI 32768
SF 176.0521380 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
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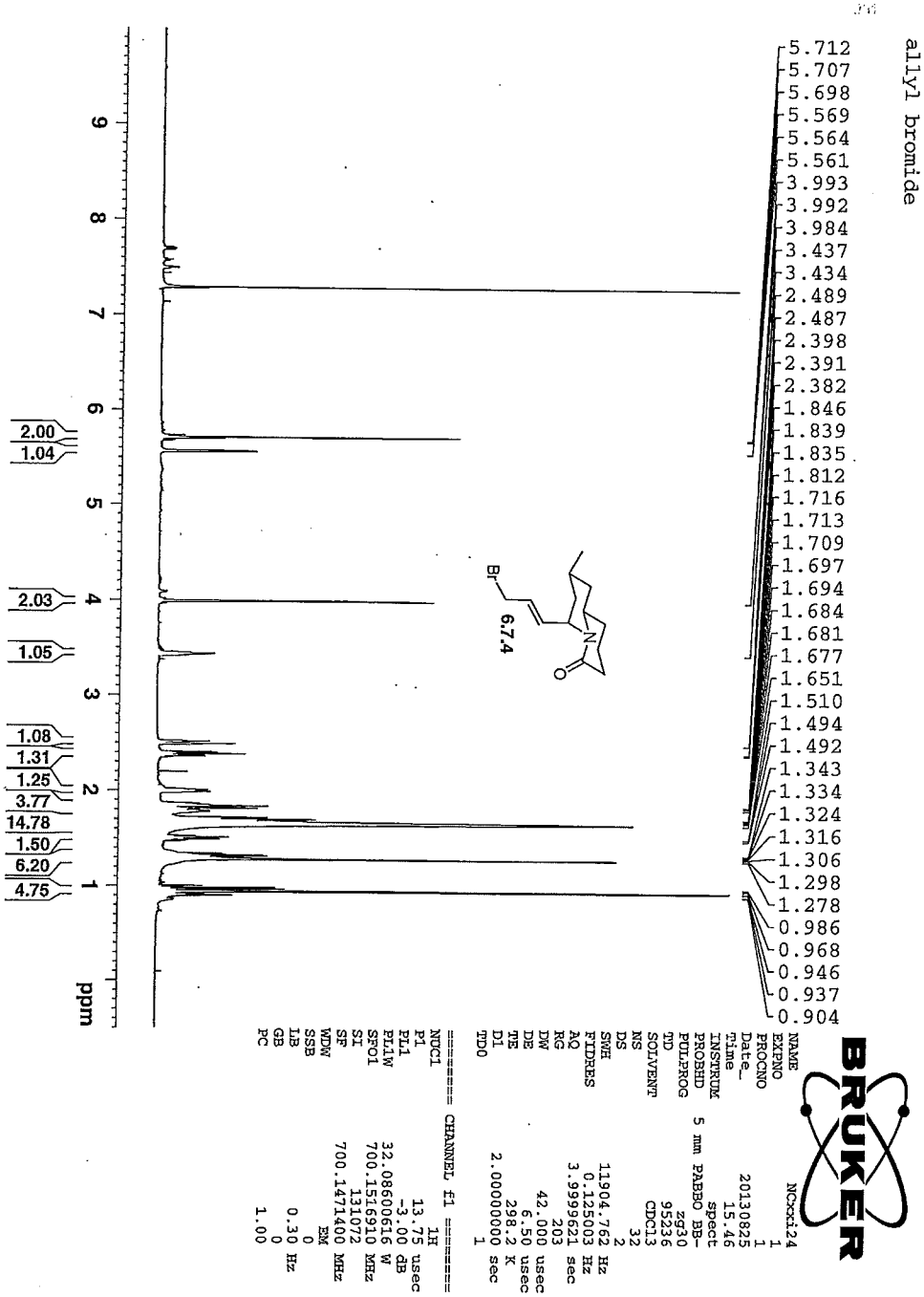
160
140
120
100
80
60
40
20
0
ppm


allyl bromide
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5.707
5.698
5.569
5.564
5.561
3.993
3.992
3.984
3.437
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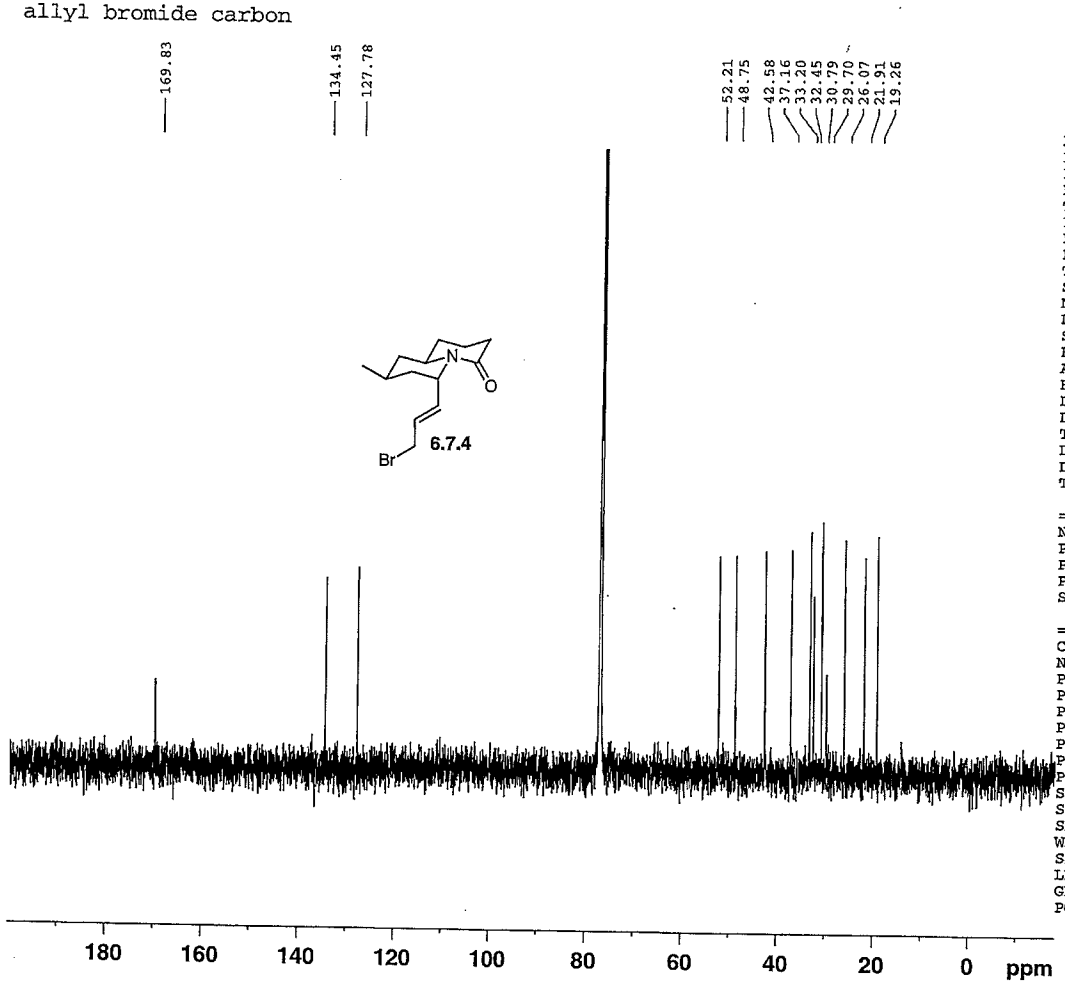
2.487
2.398
2.391
2.382
1.846
1.839
1.835
1.812
1.716
1.713
1.709
1.697
1.694
1.684
1.681
1.677
1.651
1.510
1.494
1.492
1.343
1.334
1.324
1.316
1.306
1.298
1.278
0.986
0.968
0.946
0.937
0.904
2.00
1.04
2.03
1.05
1.08
1.31
1.25
3.77
14.78
1.50
6.20
4.75
ppm
Br
6.7.4
N
O
NAME NCxxi24
EXPNO 1
PROCNO 1
Date_ 20130825
Time 15.46
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 298.2 K
D1 2.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 13.75 usec
PL1 -3.00 dB
PL1W 32.08600616 W
SFO1 700.1516910 MHz
SI 131072
SF 700.1471400 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
BRUKER

allyl bromide carbon

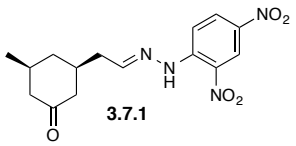


BRUKER

NAME	NCxxi24
EXPNO	3
PROCNO	1
Date_	20130825
Time	16.10
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	920
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	298.8 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	3.00 Hz
GB	0
PC	1.40

X-ray Crystal Structure Determination. X-ray diffraction intensity data were collected with a Bruker Smart Apex CCD diffractometer using MoKa – radiation (0.71073 Å). Crystallographic data and some details of data collections and refinements for the investigated structures are given in Tables A1-A4. The structures were solved using direct methods, completed by subsequent difference Fourier syntheses, and refined by full matrix least-squares procedures on F2. The non-hydrogen atoms in all structures were refined with anisotropic thermal parameters. Highly disordered solvent molecules were treated by SQUEEZE (Van der Sluis, P. & Spek, A. L. (1990) Acta Cryst. Sect. A, A46, 194-201). All software and scattering factor sources are contained in the SHELXTL (5.10) program package (G. Sheldrick, Bruker XRD, Madison, WI).

2,4-DNP Derivative **3.7.1.**



3.7.1

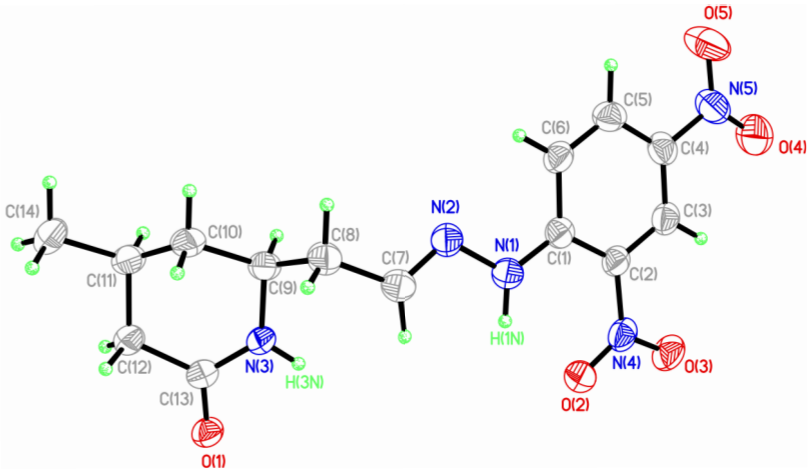


Table A1. Crystal data and structure refinement for rc38.

Identification code	rc38	
Empirical formula	C14 H17 N5 O5	
Formula weight	335.33	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 7.3537(8) Å	a= 90°.
	b = 15.6169(18) Å	b= 90°.
	c = 27.771(3) Å	g = 90°.
Volume	3189.3(6) $Å^3$	
Z	8	
Density (calculated)	1.397 Mg/m^3	
Absorption coefficient	0.108 mm^{-1}	
F(000)	1408	
Crystal size	0.32 x 0.20 x 0.14 mm^3	
Theta range for data collection	1.47 to 27.00°.	
Index ranges	-9<=h<=9, -19<=k<=19, -35<=l<=35	
Reflections collected	35830	
Independent reflections	6968 [R(int) = 0.0585]	

Completeness to theta = 27.00°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9850 and 0.9661
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6968 / 0 / 569
Goodness-of-fit on F^2	1.076
Final R indices [I>2sigma(I)]	R1 = 0.0469, wR2 = 0.1019
R indices (all data)	R1 = 0.0818, wR2 = 0.1328
Absolute structure parameter	0.1(12)
Largest diff. peak and hole	0.334 and -0.241 e.Å^{-3}

Table A2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3)
for rc38. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	3040(3)	660(1)	5576(1)	39(1)
O(2)	3114(3)	2869(1)	3315(1)	47(1)
O(3)	4506(3)	3635(1)	2781(1)	50(1)
O(4)	7441(4)	2447(2)	1432(1)	72(1)
O(5)	7603(4)	1076(2)	1340(1)	70(1)
N(1)	3163(3)	1192(2)	3268(1)	38(1)
N(2)	2969(3)	358(1)	3435(1)	39(1)
N(3)	2903(3)	45(2)	4843(1)	31(1)
N(4)	4023(3)	2939(2)	2941(1)	41(1)
N(5)	7087(4)	1719(2)	1557(1)	52(1)
C(1)	4110(4)	1337(2)	2857(1)	34(1)
C(2)	4537(4)	2169(2)	2684(1)	35(1)
C(3)	5498(4)	2287(2)	2257(1)	39(1)
C(4)	6044(4)	1589(2)	2000(1)	40(1)
C(5)	5670(4)	761(2)	2156(1)	40(1)
C(6)	4736(4)	641(2)	2575(1)	38(1)
C(7)	2062(4)	298(2)	3825(1)	41(1)
C(8)	1825(5)	-543(2)	4070(1)	42(1)
C(9)	3088(4)	-667(2)	4502(1)	35(1)
C(10)	2664(5)	-1510(2)	4754(1)	39(1)
C(11)	3652(4)	-1611(2)	5227(1)	38(1)
C(12)	3171(5)	-868(2)	5557(1)	37(1)
C(13)	3052(4)	-1(2)	5323(1)	33(1)
C(14)	3184(5)	-2455(2)	5474(1)	48(1)
O(1')	7382(3)	-3155(1)	10513(1)	36(1)
O(2')	6543(3)	-5412(1)	8281(1)	53(1)
O(3')	5268(3)	-6178(1)	7730(1)	56(1)

O(4')	2317(4)	-4970(2)	6384(1)	65(1)
O(5')	1766(4)	-3613(2)	6365(1)	70(1)
N(1')	6502(3)	-3738(2)	8232(1)	39(1)
N(2')	6820(3)	-2905(1)	8382(1)	37(1)
N(3')	7290(3)	-2565(1)	9776(1)	29(1)
N(4')	5680(4)	-5478(2)	7902(1)	44(1)
N(5')	2504(4)	-4243(2)	6540(1)	48(1)
C(1')	5604(4)	-3875(2)	7816(1)	35(1)
C(2')	5156(4)	-4709(2)	7646(1)	37(1)
C(3')	4185(4)	-4823(2)	7223(1)	39(1)
C(4')	3626(4)	-4121(2)	6967(1)	38(1)
C(5')	4089(4)	-3292(2)	7113(1)	38(1)
C(6')	5069(4)	-3181(2)	7523(1)	37(1)
C(7')	7836(4)	-2846(2)	8754(1)	36(1)
C(8')	8201(4)	-2000(2)	8981(1)	35(1)
C(9')	7026(4)	-1858(2)	9433(1)	30(1)
C(10')	7453(4)	-1007(2)	9668(1)	35(1)
C(11')	6558(4)	-930(2)	10156(1)	31(1)
C(12')	7334(5)	-1625(2)	10479(1)	33(1)
C(13')	7329(3)	-2499(2)	10255(1)	29(1)
C(14')	6788(5)	-47(2)	10380(1)	43(1)

Table A3. Bond lengths [Å] and angles [°] for rc38.

O(1)-C(13)	1.248(3)
O(2)-N(4)	1.241(3)
O(3)-N(4)	1.227(3)
O(4)-N(5)	1.217(3)
O(5)-N(5)	1.231(3)
N(1)-C(1)	1.354(3)
N(1)-N(2)	1.391(3)
N(1)-H(1N)	0.89(3)
N(2)-C(7)	1.276(4)
N(3)-C(13)	1.340(3)
N(3)-C(9)	1.465(3)
N(3)-H(3N)	0.84(3)
N(4)-C(2)	1.449(3)
N(5)-C(4)	1.463(4)
C(1)-C(6)	1.417(4)
C(1)-C(2)	1.421(4)
C(2)-C(3)	1.392(4)
C(3)-C(4)	1.363(4)
C(3)-H(3)	0.95(3)
C(4)-C(5)	1.392(4)
C(5)-C(6)	1.364(4)
C(5)-H(5)	0.97(3)
C(6)-H(6)	0.94(2)
C(7)-C(8)	1.490(4)
C(7)-H(7)	0.95(3)
C(8)-C(9)	1.529(4)
C(8)-H(8A)	0.98(3)
C(8)-H(8B)	0.96(3)
C(9)-C(10)	1.523(4)
C(9)-H(9)	0.98(3)
C(10)-C(11)	1.509(4)
C(10)-H(10A)	0.94(3)
C(10)-H(10B)	1.02(3)
C(11)-C(12)	1.520(4)

C(11)-C(14)	1.525(4)
C(11)-H(11)	0.98(3)
C(12)-C(13)	1.506(4)
C(12)-H(12A)	0.90(3)
C(12)-H(12B)	0.96(3)
C(14)-H(14A)	0.89(3)
C(14)-H(14B)	0.99(3)
C(14)-H(14C)	1.05(3)
O(1')-C(13')	1.251(3)
O(2')-N(4')	1.232(3)
O(3')-N(4')	1.232(3)
O(4')-N(5')	1.222(3)
O(5')-N(5')	1.225(3)
N(1')-C(1')	1.349(4)
N(1')-N(2')	1.386(3)
N(1')-H(1N')	1.00(3)
N(2')-C(7')	1.278(3)
N(3')-C(13')	1.332(3)
N(3')-C(9')	1.473(3)
N(3')-H(3N')	0.83(2)
N(4')-C(2')	1.449(4)
N(5')-C(4')	1.457(4)
C(1')-C(6')	1.412(4)
C(1')-C(2')	1.424(4)
C(2')-C(3')	1.386(4)
C(3')-C(4')	1.369(4)
C(3')-H(3')	0.92(3)
C(4')-C(5')	1.399(4)
C(5')-C(6')	1.357(4)
C(5')-H(5')	0.88(3)
C(6')-H(6')	0.90(3)
C(7')-C(8')	1.489(4)
C(7')-H(7')	0.99(3)
C(8')-C(9')	1.540(4)
C(8')-H(8C)	1.07(3)
C(8')-H(8D)	0.94(3)

C(9')-C(10')	1.515(4)
C(9')-H(9')	0.98(3)
C(10')-C(11')	1.511(4)
C(10')-H(10C)	1.00(3)
C(10')-H(10D)	0.90(3)
C(11')-C(12')	1.519(4)
C(11')-C(14')	1.522(4)
C(11')-H(11')	0.97(3)
C(12')-C(13')	1.501(4)
C(12')-H(12C)	0.96(3)
C(12')-H(12D)	0.82(3)
C(14')-H(14D)	0.90(4)
C(14')-H(14E)	1.02(3)
C(14')-H(14F)	0.93(3)

C(1)-N(1)-N(2)	119.4(2)
C(1)-N(1)-H(1N)	123.0(18)
N(2)-N(1)-H(1N)	116.8(17)
C(7)-N(2)-N(1)	114.0(2)
C(13)-N(3)-C(9)	126.5(2)
C(13)-N(3)-H(3N)	110.9(17)
C(9)-N(3)-H(3N)	121.8(17)
O(3)-N(4)-O(2)	122.6(2)
O(3)-N(4)-C(2)	118.7(2)
O(2)-N(4)-C(2)	118.7(2)
O(4)-N(5)-O(5)	123.8(3)
O(4)-N(5)-C(4)	118.8(3)
O(5)-N(5)-C(4)	117.3(3)
N(1)-C(1)-C(6)	120.2(3)
N(1)-C(1)-C(2)	123.5(2)
C(6)-C(1)-C(2)	116.3(3)
C(3)-C(2)-C(1)	121.4(3)
C(3)-C(2)-N(4)	116.3(2)
C(1)-C(2)-N(4)	122.3(3)
C(4)-C(3)-C(2)	119.4(3)
C(4)-C(3)-H(3)	120.8(17)

C(2)-C(3)-H(3) 119.8(17)
C(3)-C(4)-C(5) 121.4(3)
C(3)-C(4)-N(5) 118.9(3)
C(5)-C(4)-N(5) 119.7(3)
C(6)-C(5)-C(4) 119.6(3)
C(6)-C(5)-H(5) 123.0(17)
C(4)-C(5)-H(5) 117.4(17)
C(5)-C(6)-C(1) 122.0(3)
C(5)-C(6)-H(6) 120.2(15)
C(1)-C(6)-H(6) 117.8(15)
N(2)-C(7)-C(8) 120.9(3)
N(2)-C(7)-H(7) 119.3(18)
C(8)-C(7)-H(7) 118.9(18)
C(7)-C(8)-C(9) 113.5(3)
C(7)-C(8)-H(8A) 110.0(17)
C(9)-C(8)-H(8A) 107.6(16)
C(7)-C(8)-H(8B) 110.5(15)
C(9)-C(8)-H(8B) 105.4(16)
H(8A)-C(8)-H(8B)110(2)
N(3)-C(9)-C(10) 109.9(2)
N(3)-C(9)-C(8) 110.7(2)
C(10)-C(9)-C(8) 110.2(2)
N(3)-C(9)-H(9) 106.4(16)
C(10)-C(9)-H(9) 108.5(16)
C(8)-C(9)-H(9) 111.0(15)
C(11)-C(10)-C(9)113.0(2)
C(11)-C(10)-H(10A)112.3(17)
C(9)-C(10)-H(10A)108.9(16)
C(11)-C(10)-H(10B)108.2(16)
C(9)-C(10)-H(10B)105.7(15)
H(10A)-C(10)-H(10B)
C(10)-C(11)-C(12)109.4(2)
C(10)-C(11)-C(14)111.9(3)
C(12)-C(11)-C(14)109.7(3)
C(10)-C(11)-H(11)105.5(16)
C(12)-C(11)-H(11)109.7(15)

C(14)-C(11)-H(11)110.6(16)
C(13)-C(12)-C(11)116.1(2)
C(13)-C(12)-H(12A)109(2)
C(11)-C(12)-H(12A)110(2)
C(13)-C(12)-H(12B)102.6(15)
C(11)-C(12)-H(12B)110.0(16)
H(12A)-C(12)-H(12B)
O(1)-C(13)-N(3) 121.1(2)
O(1)-C(13)-C(12)120.1(2)
N(3)-C(13)-C(12)118.8(2)
C(11)-C(14)-H(14A)111.6(19)
C(11)-C(14)-H(14B)110.4(18)
H(14A)-C(14)-H(14B)
C(11)-C(14)-H(14C)109.3(16)
H(14A)-C(14)-H(14C)
H(14B)-C(14)-H(14C)
C(1')-N(1')-N(2') 119.3(2)
C(1')-N(1')-H(1N')115.9(19)
N(2')-N(1')-H(1N')124.7(18)
C(7')-N(2')-N(1') 114.1(2)
C(13')-N(3')-C(9')126.2(2)
C(13')-N(3')-H(3N')114.7(16)
C(9')-N(3')-H(3N')118.5(16)
O(3')-N(4')-O(2') 122.2(3)
O(3')-N(4')-C(2') 118.7(3)
O(2')-N(4')-C(2') 119.2(2)
O(4')-N(5')-O(5') 123.8(3)
O(4')-N(5')-C(4') 118.3(3)
O(5')-N(5')-C(4') 117.9(2)
N(1')-C(1')-C(6') 120.6(3)
N(1')-C(1')-C(2') 122.9(3)
C(6')-C(1')-C(2') 116.5(3)
C(3')-C(2')-C(1') 121.2(3)
C(3')-C(2')-N(4') 116.6(2)
C(1')-C(2')-N(4') 122.2(3)
C(4')-C(3')-C(2') 119.5(3)

C(4')-C(3')-H(3') 123.3(19)
C(2')-C(3')-H(3') 117.2(19)
C(3')-C(4')-C(5') 121.1(3)
C(3')-C(4')-N(5') 119.2(3)
C(5')-C(4')-N(5') 119.7(3)
C(6')-C(5')-C(4') 119.3(3)
C(6')-C(5')-H(5') 120.5(19)
C(4')-C(5')-H(5') 119.9(19)
C(5')-C(6')-C(1') 122.2(3)
C(5')-C(6')-H(6') 119.9(17)
C(1')-C(6')-H(6') 117.9(17)
N(2')-C(7')-C(8') 120.7(3)
N(2')-C(7')-H(7') 121.6(16)
C(8')-C(7')-H(7') 117.6(16)
C(7')-C(8')-C(9') 111.8(2)
C(7')-C(8')-H(8C)107.5(15)
C(9')-C(8')-H(8C)108.5(14)
C(7')-C(8')-H(8D)110.5(16)
C(9')-C(8')-H(8D)107.2(16)
H(8C)-C(8')-H(8D)111(2)
N(3')-C(9')-C(10')110.5(2)
N(3')-C(9')-C(8') 110.3(2)
C(10')-C(9')-C(8')111.2(2)
N(3')-C(9')-H(9') 105.8(15)
C(10')-C(9')-H(9')110.2(15)
C(8')-C(9')-H(9') 108.7(15)
C(11')-C(10')-C(9')111.5(2)
C(11')-C(10')-H(10C)
C(9')-C(10')-H(10C)108.9(15)
C(11')-C(10')-H(10D)
C(9')-C(10')-H(10D)109.8(16)
H(10C)-C(10')-H(10D)
C(10')-C(11')-C(12')108.0(2)
C(10')-C(11')-C(14')113.0(2)
C(12')-C(11')-C(14')111.4(2)
C(10')-C(11')-H(11')110.6(15)

C(12')-C(11')-H(11')109.3(15)
C(14')-C(11')-H(11')104.6(15)
C(13')-C(12')-C(11')113.8(2)
C(13')-C(12')-H(12C)
C(11')-C(12')-H(12C)
C(13')-C(12')-H(12D)
C(11')-C(12')-H(12D)
H(12C)-C(12')-H(12D)
O(1')-C(13')-N(3')120.6(2)
O(1')-C(13')-C(12')120.4(2)
N(3')-C(13')-C(12')119.0(2)
C(11')-C(14')-H(14D)
C(11')-C(14')-H(14E)
H(14D)-C(14')-H(14E)
C(11')-C(14')-H(14F)
H(14D)-C(14')-H(14F)
H(14E)-C(14')-H(14F)

Symmetry transformations used to generate equivalent atoms:

Table A4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for rc38. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}	
O(1)	51(1)	30(1)	36(1)	-4(1)	-4(1)	4(1)	
O(2)	64(2)	40(1)	36(1)	-3(1)	-2(1)	8(1)	
O(3)	68(2)	27(1)	55(1)	4(1)	-6(1)	-2(1)	
O(4)	105(2)	56(2)	57(1)	14(1)	20(2)	-5(2)	
O(5)	93(2)	64(2)	53(1)	-19(1)	24(1)	-14(2)	
N(1)	49(2)	33(1)	34(1)	-3(1)	-3(1)	1(1)	
N(2)	51(2)	31(1)	34(1)	-1(1)	-4(1)	-3(1)	
N(3)	37(1)	24(1)	33(1)	-1(1)	0(1)	1(1)	
N(4)	49(2)	34(1)	40(1)	1(1)	-14(1)	4(1)	
N(5)	65(2)	53(2)	37(1)	-4(1)	4(1)	-6(1)	
C(1)	35(2)	34(2)	32(1)	-2(1)	-9(1)	0(1)	
C(2)	43(2)	31(2)	32(1)	-2(1)	-12(1)	3(1)	
C(3)	48(2)	33(2)	36(2)	2(1)	-11(2)	0(1)	
C(4)	47(2)	41(2)	32(2)	0(1)	-6(1)	-5(1)	
C(5)	43(2)	39(2)	39(2)	-7(1)	-3(1)	2(1)	
C(6)	47(2)	28(2)	38(2)	1(1)	-7(1)	0(1)	
C(7)	53(2)	35(2)	34(2)	-8(1)	-5(2)	-3(1)	
C(8)	57(2)	34(2)	34(2)	-5(1)	0(2)	-3(2)	
C(9)	38(2)	32(2)	36(2)	-4(1)	5(1)	1(1)	
C(10)	48(2)	29(2)	41(2)	-7(1)	4(2)	-1(1)	
C(11)	41(2)	32(2)	43(2)	-3(1)	2(1)		

	4(1)					
C(12)	41(2)	34(2)	37(2)	1(1)	-1(2)	
	7(1)					
C(13)	31(1)	30(1)	37(2)	-3(1)	-2(1)	
	1(1)					
C(14)	60(2)	31(2)	52(2)	6(2)	-2(2)	
	6(2)					
O(1')	43(1)	33(1)	33(1)	6(1)	1(1)	
	4(1)					
O(2')	72(2)	40(1)	48(1)	-2(1)	-2(1)	
	2(1)					
O(3')	76(2)	29(1)	62(1)	-11(1)	7(1)	-
3(1)						
O(4')	84(2)	60(1)	50(1)	-26(1)	-2(1)	-
10(1)						
O(5')	101(2)	58(2)	51(1)	8(1)	-28(1)	-
21(2)						
N(1')	48(2)	31(1)	39(1)	-3(1)	1(1)	-
5(1)						
N(2')	45(2)	32(1)	35(1)	-4(1)	1(1)	-
7(1)						
N(3')	35(1)	22(1)	31(1)	-1(1)	1(1)	-
2(1)						
N(4')	52(2)	37(2)	42(2)	-6(1)	10(1)	
	2(1)					
N(5')	60(2)	52(2)	33(1)	-7(1)	7(1)	-
15(2)						
C(1')	35(2)	34(2)	35(2)	-4(1)	9(1)	-
2(1)						
C(2')	42(2)	33(2)	35(2)	-2(1)	11(1)	-
4(1)						
C(3')	45(2)	33(2)	38(2)	-10(1)	15(1)	-
7(1)						
C(4')	43(2)	46(2)	26(1)	-7(1)	6(1)	-
10(1)						
C(5')	49(2)	33(2)	32(2)	-1(1)	9(1)	-

7(1)						
C(6')	43(2)	33(2)	35(2)	-4(1)	5(1)	-8(1)
C(7')	41(2)	34(2)	32(1)	4(1)	7(1)	-2(1)
C(8')	41(2)	34(2)	31(2)	4(1)	-1(1)	-3(1)
C(9')	30(2)	28(1)	32(1)	3(1)	-3(1)	0(1)
C(10')	42(2)	26(1)	35(2)	5(1)	0(1)	-4(1)
C(11')	29(1)	26(1)	39(2)	-3(1)	-2(1)	1(1)
C(12')	34(2)	34(2)	30(2)	0(1)	2(1)	-1(1)
C(13')	23(1)	31(1)	33(1)	1(1)	0(1)	2(1)
C(14')	46(2)	32(2)	50(2)	-7(1)	-6(2)	1(2)

Table A5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3)
for rc38.

	x	y	z	U(eq)
H(1N)	2810(40)	1612(17)	3466(10)	41(8)
H(1N')	6820(50)	-4260(20)	8421(11)	68(11)
H(3N)	2870(30)	556(16)	4750(9)	23(7)
H(3N')	7280(40)	-3065(16)	9673(8)	23(7)
H(3)	5750(40)	2849(19)	2146(10)	43(8)
H(3')	3930(40)	-5375(19)	7133(10)	54(9)
H(5)	6050(40)	294(19)	1952(10)	47(8)
H(5')	3820(40)	-2850(18)	6928(10)	42(9)
H(6)	4520(30)	86(16)	2691(9)	28(7)
H(6')	5400(40)	-2652(17)	7614(9)	33(8)
H(7)	1710(40)	800(20)	3989(10)	57(9)
H(7')	8390(40)	-3361(17)	8906(10)	42(8)
H(8A)	570(40)	-602(18)	4185(9)	41(8)
H(8B)	2110(40)	-1005(17)	3854(9)	35(7)
H(8C)	9610(40)	-1990(17)	9086(9)	44(8)
H(8D)	7930(40)	-1554(17)	8765(9)	38(8)
H(9)	4370(40)	-675(17)	4401(9)	37(7)
H(9')	5750(40)	-1880(16)	9339(9)	31(7)
H(10A)	2900(40)	-1963(18)	4542(9)	37(8)
H(10B)	1300(40)	-1498(17)	4823(10)	36(7)
H(10C)	8800(40)	-952(16)	9703(9)	36(8)
H(10D)	7150(40)	-574(17)	9468(9)	34(7)
H(11)	4950(40)	-1589(16)	5146(9)	37(7)
H(11')	5250(40)	-1006(16)	10129(9)	33(7)
H(12A)	3980(50)	-840(20)	5800(11)	57(10)
H(12B)	1960(40)	-945(16)	5685(9)	30(7)
H(12C)	6640(40)	-1625(16)	10772(9)	31(7)
H(12D)	8410(40)	-1498(17)	10518(10)	35(8)
H(14A)	3820(40)	-2528(18)	5744(10)	42(9)

H(14B)	3420(40)	-2940(20)	5255(11)	54(9)
H(14C)	1790(40)	-2459(19)	5564(10)	51(9)
H(14D)	7970(50)	90(20)	10420(11)	61(11)
H(14E)	6190(40)	-2(16)	10709(10)	36(7)
H(14F)	6230(40)	357(19)	10183(11)	51(9)

Table A6. Torsion angles [°] for rc38.

C(1)-N(1)-N(2)-C(7)	179.6(2)
N(2)-N(1)-C(1)-C(6)	6.5(4)
N(2)-N(1)-C(1)-C(2)	-173.4(2)
N(1)-C(1)-C(2)-C(3)	-179.3(3)
C(6)-C(1)-C(2)-C(3)	0.8(4)
N(1)-C(1)-C(2)-N(4)	1.4(4)
C(6)-C(1)-C(2)-N(4)	-178.5(3)
O(3)-N(4)-C(2)-C(3)	-2.5(4)
O(2)-N(4)-C(2)-C(3)	177.7(2)
O(3)-N(4)-C(2)-C(1)	176.9(2)
O(2)-N(4)-C(2)-C(1)	-3.0(4)
C(1)-C(2)-C(3)-C(4)	-0.1(4)
N(4)-C(2)-C(3)-C(4)	179.2(3)
C(2)-C(3)-C(4)-C(5)	-0.4(4)
C(2)-C(3)-C(4)-N(5)	-178.7(3)
O(4)-N(5)-C(4)-C(3)	0.2(4)
O(5)-N(5)-C(4)-C(3)	178.0(3)
O(4)-N(5)-C(4)-C(5)	-178.1(3)
O(5)-N(5)-C(4)-C(5)	-0.3(4)
C(3)-C(4)-C(5)-C(6)	0.1(4)
N(5)-C(4)-C(5)-C(6)	178.4(3)
C(4)-C(5)-C(6)-C(1)	0.7(4)
N(1)-C(1)-C(6)-C(5)	179.0(3)
C(2)-C(1)-C(6)-C(5)	-1.2(4)
N(1)-N(2)-C(7)-C(8)	-176.2(3)
N(2)-C(7)-C(8)-C(9)	101.2(3)
C(13)-N(3)-C(9)-C(10)	24.4(4)
C(13)-N(3)-C(9)-C(8)	146.4(3)
C(7)-C(8)-C(9)-N(3)	53.9(3)
C(7)-C(8)-C(9)-C(10)	175.8(3)
N(3)-C(9)-C(10)-C(11)	-48.8(3)
C(8)-C(9)-C(10)-C(11)	-171.0(3)
C(9)-C(10)-C(11)-C(12)	57.6(4)
C(9)-C(10)-C(11)-C(14)	179.3(3)

C(10)-C(11)-C(12)-C(13)	-40.5(4)
C(14)-C(11)-C(12)-C(13)	-163.5(3)
C(9)-N(3)-C(13)-O(1)	173.2(2)
C(9)-N(3)-C(13)-C(12)	-8.9(4)
C(11)-C(12)-C(13)-O(1)	-165.2(3)
C(11)-C(12)-C(13)-N(3)	16.9(4)
C(1')-N(1')-N(2')-C(7')	-173.3(2)
N(2')-N(1')-C(1')-C(6')	3.1(4)
N(2')-N(1')-C(1')-C(2')	-177.4(2)
N(1')-C(1')-C(2')-C(3')	178.1(3)
C(6')-C(1')-C(2')-C(3')	-2.4(4)
N(1')-C(1')-C(2')-N(4')	-1.7(4)
C(6')-C(1')-C(2')-N(4')	177.8(2)
O(3')-N(4')-C(2')-C(3')	1.2(4)
O(2')-N(4')-C(2')-C(3')	-179.8(2)
O(3')-N(4')-C(2')-C(1')	-179.0(3)
O(2')-N(4')-C(2')-C(1')	0.0(4)
C(1')-C(2')-C(3')-C(4')	-0.8(4)
N(4')-C(2')-C(3')-C(4')	179.1(2)
C(2')-C(3')-C(4')-C(5')	2.9(4)
C(2')-C(3')-C(4')-N(5')	-176.0(2)
O(4')-N(5')-C(4')-C(3')	-10.5(4)
O(5')-N(5')-C(4')-C(3')	167.7(3)
O(4')-N(5')-C(4')-C(5')	170.6(3)
O(5')-N(5')-C(4')-C(5')	-11.1(4)
C(3')-C(4')-C(5')-C(6')	-1.7(4)
N(5')-C(4')-C(5')-C(6')	177.2(3)
C(4')-C(5')-C(6')-C(1')	-1.7(5)
N(1')-C(1')-C(6')-C(5')	-176.8(3)
C(2')-C(1')-C(6')-C(5')	3.7(4)
N(1')-N(2')-C(7')-C(8')	-175.7(2)
N(2')-C(7')-C(8')-C(9')	100.9(3)
C(13')-N(3')-C(9')-C(10')	19.9(4)
C(13')-N(3')-C(9')-C(8')	143.3(3)
C(7')-C(8')-C(9')-N(3')	55.3(3)
C(7')-C(8')-C(9')-C(10')	178.3(2)

N(3')-C(9')-C(10')-C(11')	-47.1(3)
C(8')-C(9')-C(10')-C(11')	-169.9(2)
C(9')-C(10')-C(11')-C(12')	62.6(3)
C(9')-C(10')-C(11')-C(14')	-173.8(3)
C(10')-C(11')-C(12')-C(13')	-49.2(3)
C(14')-C(11')-C(12')-C(13')	-173.8(3)
C(9')-N(3')-C(13')-O(1')	172.9(2)
C(9')-N(3')-C(13')-C(12')	-7.9(4)
C(11')-C(12')-C(13')-O(1')	-157.9(2)
C(11')-C(12')-C(13')-N(3')	22.9(4)

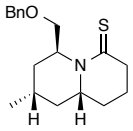
Symmetry transformations used to generate equivalent atoms:

Table A7. Hydrogen bonds for rc38 [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)	
N(1)-H(1N)...O(2)	0.89(3)	2.02(3)	2.621(3)	124(2)	
N(3)-H(3N)...O(1')#1		0.84(3)	2.15(3)	2.987(3)	176(2)
N(1')-H(1N')...O(2')	1.00(3)	1.85(3)	2.618(3)	131(3)	
N(3')-H(3N')...O(1)#2		0.83(2)	2.12(3)	2.949(3)	174(3)

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

Thiolactam **4.9.1**



4.9.1

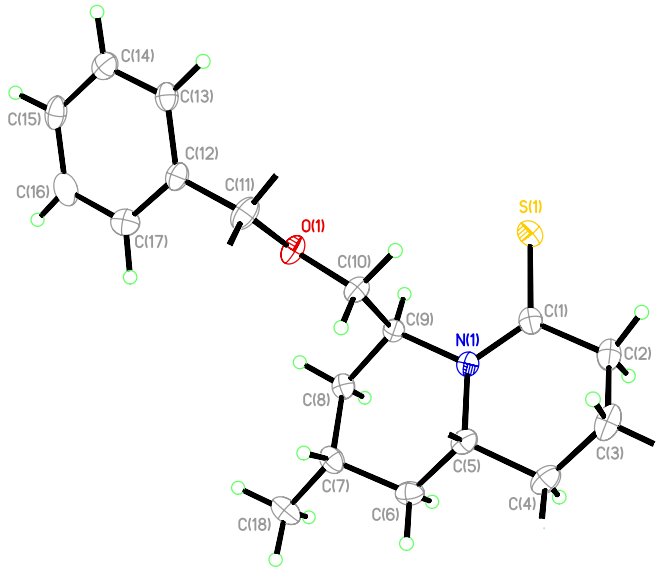


Table A8: Crystal date and structure refinement for thiolactam **4.9.1.**

Identification code	rc58	
Empirical formula	C18 H25 N O S	
Formula weight	303.45	
Temperature	173(2) K	
Wavelength	0.71073 ≈	
Crystal system	Hexagonal	
Space group	P6(1)	
Unit cell dimensions	a = 8.3672(6) ≈	a= 90∞.
	b = 8.3672(6) ≈	b= 90∞.
	c = 41.378(6) ≈	g = 120∞.
Volume	2508.8(4) $\approx^3$	
Z	6	
Density (calculated)	1.205 Mg/m^3	

Absorption coefficient	0.193 mm^{-1}
F(000)	984
Crystal size	0.37 x 0.16 x 0.12 mm^3
Theta range for data collection	2.81 to 26.00∞.
Index ranges	-10<=h<=9, -10<=k<=10, -50<=l<=42
Reflections collected	14757
Independent reflections	3160 [R(int) = 0.0391]
Completeness to theta = 26.00∞	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9772 and 0.9320
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3160 / 1 / 290
Goodness-of-fit on F^2	1.055
Final R indices [I>2sigma(I)]	R1 = 0.0327, wR2 = 0.0699
R indices (all data)	R1 = 0.0384, wR2 = 0.0737
Absolute structure parameter	0.00(6)
Largest diff. peak and hole	0.150 and -0.123 e.$≈^{-3}$

Table A9: Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($≈^2$x 10^3)
for rc58. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
S(1)	7572(1)	3933(1)	526(1)	41(1)
N(1)	8356(2)	2793(2)	1076(1)	27(1)
O(1)	11103(2)	7732(2)	1260(1)	33(1)
C(1)	7874(2)	2477(3)	763(1)	32(1)
C(2)	7545(3)	680(3)	613(1)	41(1)
C(3)	8549(3)	-184(3)	775(1)	46(1)
C(4)	8192(3)	-272(3)	1133(1)	40(1)
C(5)	8906(3)	1647(3)	1275(1)	32(1)
C(6)	8296(3)	1536(3)	1623(1)	36(1)
C(7)	8941(3)	3394(3)	1780(1)	35(1)
C(8)	8239(3)	4415(3)	1575(1)	31(1)

C(9)	8789(2)	4591(2)	1221(1)	27(1)
C(10)	10813(3)	5985(3)	1162(1)	32(1)
C(11)	12984(3)	9100(3)	1249(1)	41(1)
C(12)	13228(2)	10900(3)	1373(1)	31(1)
C(13)	13868(3)	12415(3)	1173(1)	33(1)
C(14)	14165(3)	14087(3)	1290(1)	37(1)
C(15)	13798(3)	14249(3)	1607(1)	40(1)
C(16)	13135(3)	12744(3)	1810(1)	42(1)
C(17)	12854(3)	11064(3)	1694(1)	39(1)
C(18)	8242(4)	3201(4)	2124(1)	51(1)

Table A10. Bond lengths [≈] and angles [∞] for rc58.

S(1)-C(1)	1.678(2)
N(1)-C(1)	1.342(2)
N(1)-C(9)	1.485(2)
N(1)-C(5)	1.500(2)
O(1)-C(11)	1.410(2)
O(1)-C(10)	1.417(2)
C(1)-C(2)	1.519(3)
C(2)-C(3)	1.511(3)
C(2)-H(2A)	0.95(3)
C(2)-H(2B)	1.00(2)
C(3)-C(4)	1.507(3)
C(3)-H(3A)	1.01(3)
C(3)-H(3B)	0.94(2)
C(4)-C(5)	1.523(3)
C(4)-H(4A)	0.96(2)
C(4)-H(4B)	0.93(2)
C(5)-C(6)	1.515(3)
C(5)-H(5)	1.00(2)
C(6)-C(7)	1.513(3)
C(6)-H(6A)	0.98(2)
C(6)-H(6B)	0.99(2)
C(7)-C(8)	1.514(3)
C(7)-C(18)	1.517(3)
C(7)-H(7)	0.98(2)
C(8)-C(9)	1.522(3)
C(8)-H(8A)	0.92(3)
C(8)-H(8B)	0.95(2)
C(9)-C(10)	1.521(3)
C(9)-H(9)	0.91(2)
C(10)-H(10A)	1.01(2)
C(10)-H(10B)	0.97(2)
C(11)-C(12)	1.505(3)
C(11)-H(11A)	0.96(3)
C(11)-H(11B)	1.06(3)

C(12)-C(13)	1.380(3)
C(12)-C(17)	1.388(3)
C(13)-C(14)	1.382(3)
C(13)-H(13)	0.97(2)
C(14)-C(15)	1.368(3)
C(14)-H(14)	0.94(2)
C(15)-C(16)	1.377(3)
C(15)-H(15)	0.95(2)
C(16)-C(17)	1.389(3)
C(16)-H(16)	0.91(2)
C(17)-H(17)	0.97(3)
C(18)-H(18A)	0.93(3)
C(18)-H(18B)	0.98(3)
C(18)-H(18C)	0.95(2)

C(1)-N(1)-C(9)	119.00(16)
C(1)-N(1)-C(5)	124.10(16)
C(9)-N(1)-C(5)	115.43(15)
C(11)-O(1)-C(10)	111.96(14)
N(1)-C(1)-C(2)	118.48(18)
N(1)-C(1)-S(1)	124.02(15)
C(2)-C(1)-S(1)	117.49(16)
C(3)-C(2)-C(1)	115.08(19)
C(3)-C(2)-H(2A)	112.7(16)
C(1)-C(2)-H(2A)	106.2(15)
C(3)-C(2)-H(2B)	108.3(12)
C(1)-C(2)-H(2B)	104.7(12)
H(2A)-C(2)-H(2B)	109.4(19)
C(4)-C(3)-C(2)	108.32(19)
C(4)-C(3)-H(3A)	110.8(14)
C(2)-C(3)-H(3A)	107.7(14)
C(4)-C(3)-H(3B)	110.9(13)
C(2)-C(3)-H(3B)	108.8(13)
H(3A)-C(3)-H(3B)	110(2)
C(3)-C(4)-C(5)	111.34(18)
C(3)-C(4)-H(4A)	110.9(12)

C(5)-C(4)-H(4A) 108.3(12)
C(3)-C(4)-H(4B) 111.2(14)
C(5)-C(4)-H(4B) 106.5(14)
H(4A)-C(4)-H(4B)108.5(18)
N(1)-C(5)-C(6) 111.03(16)
N(1)-C(5)-C(4) 112.27(17)
C(6)-C(5)-C(4) 111.04(17)
N(1)-C(5)-H(5) 105.2(11)
C(6)-C(5)-H(5) 109.3(11)
C(4)-C(5)-H(5) 107.7(11)
C(7)-C(6)-C(5) 114.10(17)
C(7)-C(6)-H(6A) 110.5(12)
C(5)-C(6)-H(6A) 107.1(12)
C(7)-C(6)-H(6B) 107.7(12)
C(5)-C(6)-H(6B) 108.4(12)
H(6A)-C(6)-H(6B)108.9(17)
C(6)-C(7)-C(8) 107.49(17)
C(6)-C(7)-C(18) 111.9(2)
C(8)-C(7)-C(18) 110.36(18)
C(6)-C(7)-H(7) 109.5(11)
C(8)-C(7)-H(7) 110.9(11)
C(18)-C(7)-H(7) 106.8(12)
C(7)-C(8)-C(9) 114.18(16)
C(7)-C(8)-H(8A) 111.2(15)
C(9)-C(8)-H(8A) 105.0(14)
C(7)-C(8)-H(8B) 107.5(12)
C(9)-C(8)-H(8B) 108.3(12)
H(8A)-C(8)-H(8B)110.6(18)
N(1)-C(9)-C(10) 109.10(15)
N(1)-C(9)-C(8) 112.38(16)
C(10)-C(9)-C(8) 113.28(16)
N(1)-C(9)-H(9) 106.6(12)
C(10)-C(9)-H(9) 105.5(12)
C(8)-C(9)-H(9) 109.6(12)
O(1)-C(10)-C(9) 107.24(15)
O(1)-C(10)-H(10A)109.2(11)

C(9)-C(10)-H(10A)109.6(11)
O(1)-C(10)-H(10B)111.6(11)
C(9)-C(10)-H(10B)110.2(11)
H(10A)-C(10)-H(10B)
O(1)-C(11)-C(12)109.82(16)
O(1)-C(11)-H(11A)111.5(15)
C(12)-C(11)-H(11A)110.7(15)
O(1)-C(11)-H(11B)107.3(13)
C(12)-C(11)-H(11B)111.8(13)
H(11A)-C(11)-H(11B)
C(13)-C(12)-C(17)119.22(18)
C(13)-C(12)-C(11)120.69(19)
C(17)-C(12)-C(11)120.1(2)
C(12)-C(13)-C(14)120.6(2)
C(12)-C(13)-H(13)120.5(12)
C(14)-C(13)-H(13)118.9(12)
C(15)-C(14)-C(13)120.2(2)
C(15)-C(14)-H(14)118.4(14)
C(13)-C(14)-H(14)121.4(14)
C(14)-C(15)-C(16)120.0(2)
C(14)-C(15)-H(15)121.1(14)
C(16)-C(15)-H(15)118.9(14)
C(15)-C(16)-C(17)120.2(2)
C(15)-C(16)-H(16)122.7(14)
C(17)-C(16)-H(16)117.0(14)
C(12)-C(17)-C(16)119.8(2)
C(12)-C(17)-H(17)120.0(15)
C(16)-C(17)-H(17)120.1(15)
C(7)-C(18)-H(18A)110.9(17)
C(7)-C(18)-H(18B)109.8(16)
H(18A)-C(18)-H(18B)
C(7)-C(18)-H(18C)115.2(14)
H(18A)-C(18)-H(18C)
H(18B)-C(18)-H(18C)

Symmetry transformations used to generate equivalent atoms:

Table A11. Anisotropic displacement parameters ($\approx^2$x 10^3)for rc58. The anisotropic
displacement factor exponent takes the form: $-2p^2[h^2a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
S(1)48(1)	43(1)	31(1)	-1(1)	-4(1)	21(1)
N(1)21(1)	28(1)	31(1)	-2(1)	0(1)	11(1)
O(1)	24(1)	25(1)	49(1)	-7(1)	0(1)
11(1)					
C(1)23(1)	35(1)	32(1)	-4(1)	2(1)	10(1)
C(2)39(1)	38(1)	42(1)	-10(1)	0(1)	15(1)
C(3)37(1)	35(1)	63(2)	-15(1)	0(1)	16(1)
C(4)33(1)	30(1)	60(2)	0(1)	-1(1)	17(1)
C(5)23(1)	27(1)	43(1)	1(1)	-3(1)	11(1)
C(6)29(1)	36(1)	42(1)	8(1)	0(1)	16(1)
C(7)25(1)	44(1)	33(1)	-2(1)	-4(1)	15(1)
C(8)24(1)	35(1)	32(1)	-2(1)	0(1)	13(1)
C(9)25(1)	26(1)	30(1)	-2(1)	-3(1)	14(1)
C(10)	28(1)	26(1)	39(1)	-1(1)	4(1)
13(1)					
C(11)	27(1)	29(1)	63(2)	-6(1)	5(1)
12(1)					
C(12)	22(1)	29(1)	41(1)	-6(1)	-1(1)
11(1)					
C(13)	25(1)	36(1)	35(1)	-7(1)	-3(1)
15(1)					
C(14)	29(1)	34(1)	49(2)	1(1)	-9(1)
15(1)					
C(15)	33(1)	37(1)	56(1)	-18(1)	-16(1)
22(1)					
C(16)	38(1)	58(1)	35(1)	-14(1)	-4(1)
28(1)					

C(17)	34(1)	44(1)	41(1)	4(1)	4(1)
21(1)					
C(18)	56(2)	66(2)	32(1)	4(1)	-4(1)
32(1)					

Table A12. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (≈^{2}x 10^3)
for rc58.

	x	y	z	U(eq)
H(2A)	7850(30)	930(30)	390(7)	55(7)
H(2B)	6180(30)	-190(30)	637(5)	31(5)
H(3A)	9910(40)	620(30)	727(6)	56(7)
H(3B)	8110(30)	-1370(30)	690(5)	41(6)
H(4A)	6890(30)	-1000(30)	1178(5)	28(5)
H(4B)	8790(30)	-790(30)	1243(5)	45(7)
H(5)	10290(30)	2310(30)	1265(4)	29(5)
H(6A)	8760(30)	840(30)	1742(5)	31(5)
H(6B)	6940(30)	850(30)	1629(5)	32(5)
H(7)	10300(30)	4080(30)	1791(5)	34(5)
H(8A)	8700(30)	5610(40)	1646(5)	47(7)
H(8B)	6920(30)	3750(30)	1588(5)	34(6)
H(9)	8150(30)	5010(30)	1106(5)	23(5)
H(10A)	11100(30)	6030(30)	923(5)	35(5)
H(10B)	11590(30)	5640(20)	1281(5)	21(5)
H(11A)	13740(30)	8740(30)	1370(6)	59(7)
H(11B)	13420(30)	9210(30)	1006(6)	50(7)
H(13)	14150(30)	12330(30)	948(5)	34(6)
H(14)	14610(30)	15140(30)	1156(6)	46(6)
H(15)	14000(30)	15390(30)	1692(6)	42(6)
H(16)	12810(30)	12780(30)	2017(6)	40(6)
H(17)	12470(30)	10030(40)	1841(6)	58(7)
H(18A)	6960(40)	2570(40)	2129(6)	59(8)
H(18B)	8680(30)	4430(30)	2218(7)	59(7)
H(18C)	8620(30)	2560(30)	2268(6)	44(6)

Table A13. Torsion angles [∞] for rc58.

C(9)-N(1)-C(1)-C(2)	176.43(16)
C(5)-N(1)-C(1)-C(2)	10.9(3)
C(9)-N(1)-C(1)-S(1)	-4.8(2)
C(5)-N(1)-C(1)-S(1)	-170.30(14)
N(1)-C(1)-C(2)-C(3)	-25.5(3)
S(1)-C(1)-C(2)-C(3)	155.60(17)
C(1)-C(2)-C(3)-C(4)	49.9(3)
C(2)-C(3)-C(4)-C(5)	-60.9(2)
C(1)-N(1)-C(5)-C(6)	-146.56(17)
C(9)-N(1)-C(5)-C(6)	47.4(2)
C(1)-N(1)-C(5)-C(4)	-21.6(2)
C(9)-N(1)-C(5)-C(4)	172.39(16)
C(3)-C(4)-C(5)-N(1)	46.7(2)
C(3)-C(4)-C(5)-C(6)	171.63(18)
N(1)-C(5)-C(6)-C(7)	-53.8(2)
C(4)-C(5)-C(6)-C(7)	-179.46(17)
C(5)-C(6)-C(7)-C(8)	56.9(2)
C(5)-C(6)-C(7)-C(18)	178.20(18)
C(6)-C(7)-C(8)-C(9)	-54.8(2)
C(18)-C(7)-C(8)-C(9)	-177.04(19)
C(1)-N(1)-C(9)-C(10)	-86.37(19)
C(5)-N(1)-C(9)-C(10)	80.41(19)
C(1)-N(1)-C(9)-C(8)	147.13(16)
C(5)-N(1)-C(9)-C(8)	-46.1(2)
C(7)-C(8)-C(9)-N(1)	50.6(2)
C(7)-C(8)-C(9)-C(10)	-73.6(2)
C(11)-O(1)-C(10)-C(9)	173.54(18)
N(1)-C(9)-C(10)-O(1)	171.64(16)
C(8)-C(9)-C(10)-O(1)	-62.4(2)
C(10)-O(1)-C(11)-C(12)	-176.89(18)
O(1)-C(11)-C(12)-C(13)	-116.0(2)
O(1)-C(11)-C(12)-C(17)	65.6(3)
C(17)-C(12)-C(13)-C(14)	1.2(3)

C(11)-C(12)-C(13)-C(14)	-177.23(18)
C(12)-C(13)-C(14)-C(15)	-1.1(3)
C(13)-C(14)-C(15)-C(16)	0.2(3)
C(14)-C(15)-C(16)-C(17)	0.7(3)
C(13)-C(12)-C(17)-C(16)	-0.4(3)
C(11)-C(12)-C(17)-C(16)	178.08(19)
C(15)-C(16)-C(17)-C(12)	-0.6(3)

Symmetry transformations used to generate equivalent atoms: