TOTAL SYNTHESIS OF CYCLOOROIDIN AND STUDIES TOWARDS SOME OROIDIN DIMERS

by

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The years I spent here will be with me throughout my life and I cherish that.

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ABSTRACT

TOTAL SYNTHESIS OF CYCLOOROIDIN AND STUDIES TOWARDS SOME OROIDIN DIMERS

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The University of Texas at Arlington, 2010

Supervising Professor: Dr. Carl J. Lovely

This dissertation consists of two parts. The first part describes the synthesis of northern fragment of nagelamide R and the enantioselective total synthesis of cyclooroidin. The oroidin family of marine natural products is a growing group of marine sponge-derived alkaloids which contain 2-aminoimidazole and pyrrolecarboxamide fragments as their signature features. The structural complexity, and in many cases interesting biological profiles, of these compounds has rendered several of these natural products as targets of interest. In the context of nagelamide R, the key transformation involves the intramolecular cyclization of a pyrrolecarboxamide via the carbonyl oxygen leading to the formation of oxazoline, whose subsequent elaboration by pyrrole

bromination and imidazole azidation provides the fully functionalized northern fragment of the natural product. This chemistry suggests a possible biosynthetic pathway to the formation of nagelamide R through nagelamide B via activation and substitution of the amide carbonyl.

The key steps en route to the enantioselective total synthesis of cyclooroidin involve a coupling reaction between an imidazole chlorohydrin and pyrrole 2-carboxylic acid followed by intramolecular cyclization to form an oxazine ring. Conversion into the corresponding pyrazine, followed by bromination of the pyrrole and introduction of the azide group at the C-2 position of the imidazole provided the complete natural product framework. Removal of the protecting group and reduction of the azide to amine provide synthetic enantioselective cyclooroidin.

The second part of this dissertation describes studies towards some oroidin dimers including palau'amine and ageliferin. These studies have resulted in a concise entry into the all *trans*-substituted spiro cyclopentyl imidazolone system found in palau'amine and related natural products. These structures are accessed through an intramolecular Diels-Alder reaction of an enyne followed by an oxidative rearrangement. The final section describes a preliminary investigation of methods for the stereoselective incorporation of the chloro moiety, which is present in several oroidin dimers, including palau'amine.

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INTRODUCTION

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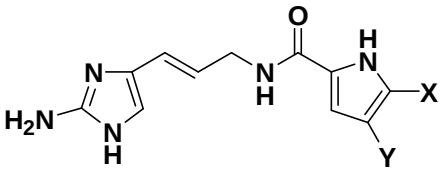
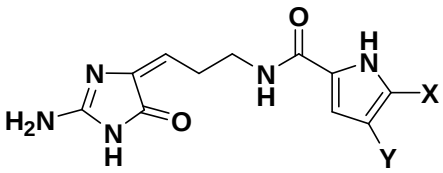


1a: Oroidin (X = Y = Br)
1b: Hymenidin (X = H, Y = Br)
1c: Clathrodin (X = Y = H)



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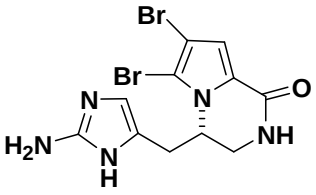

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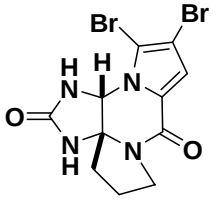

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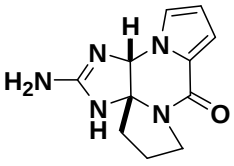

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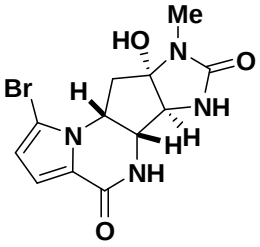

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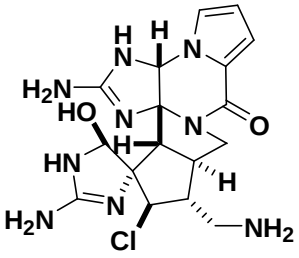
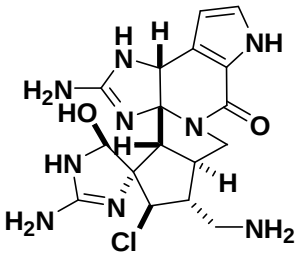
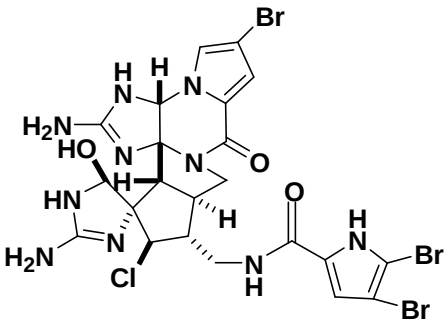


7: Palau'amine



8: Styloguanidine



9: Konbu'acidin A

Figure 1.1 Pyrrole-imidazole marine alkaloids

Marine sponges have been, and continue to be, a rich source of structurally diverse pyrrole-imidazole alkaloids.[1-3] Over the past thirty years, many pyrrole-imidazole alkaloids with unprecedented skeletal diversity and a broad range of biological activities have been isolated and characterized.[1-3] The first member of

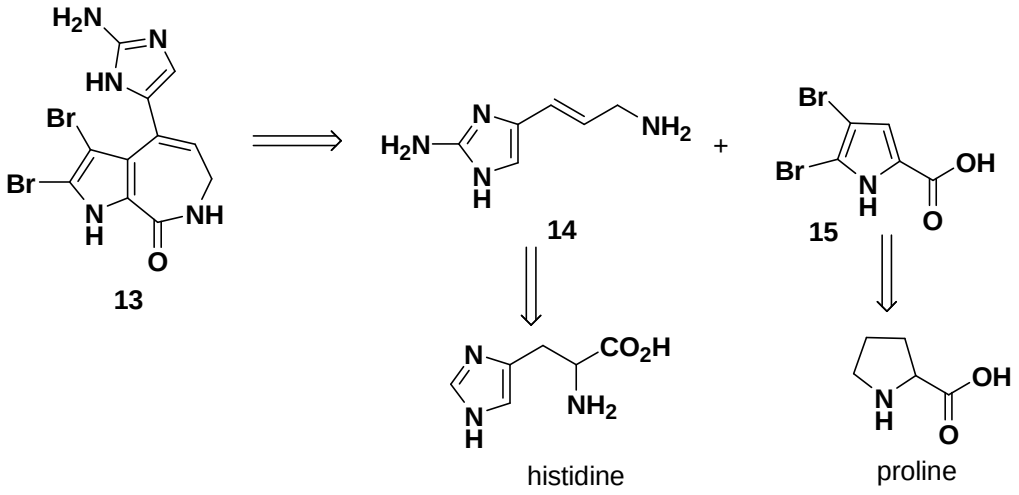
this family of alkaloids to be isolated was oroidin (**1a**), initially from *Agelas oroides* in 1971, and subsequently from a variety of other sponges.[1-3] Over the years, more elaborate and complex derivatives have been isolated and the whole family is frequently referred to either as the oroidin alkaloids or the pyrrole-imidazole alkaloids. Furthermore, these natural products are frequently characterized by the number of oroidin subunits and thus are described as oroidin monomers, dimmers or tetramers. The more elaborate members of this family of natural products arise from various modes of functionalization, cyclization, and in some cases dimerization or tetramerization of the parent heterocycles **1a-c**, leading to the production of **2-9** (Figure 1.1).[4]

Inspired in large part by this family of natural products, our research group has been interested in the development of new and efficient synthetic methods for the elaboration of simple imidazole derivatives into highly functionalized polycyclic systems as key intermediates *en route* to the total synthesis of a number of the imidazole-containing natural products, including several illustrated in Figure 1.1. These approaches include: the inter- and intramolecular Diels-Alder reactions of 4-vinylimidazoles;[5,6] the intramolecular radical cyclization reactions of imidazoles;[7] ring-closing metathesis of dienylimidazoles and enynes;[8] and oxidative chemistry.[9,10a,10b] The work described in this dissertation represents a continuation of this effort and the development of a number of new reactions.

1.2 Biosynthetic pathways

Several groups have proposed biogenetic pathways for the assembly of pyrrole-imidazole alkaloids. Baran et al. recently proposed that several of the dimeric

members of the family come from a single precursor.[11] This proposal bears some resemblance to the more comprehensive hypothesis of Al Mourabit and Potier.[3] However, despite numerous proposals in the literature there is very little described in terms of experimental work to support these hypotheses. Kerr et al. reported the first, and to date only biosynthetic study using cell culture of the sponge *Teichaxinella morchella*.[12] Using ^{14}C-labeled proline and histidine they demonstrated that these amino acids are precursors of the monomer stevensine (**13**) through 2-aminoimidazolylprop-1-ene (**14**) and 4,5-dibromopyrrole carboxylic acid (**15**) (scheme 1.1). Unfortunately, this study did not reveal any details of the transformations involved.

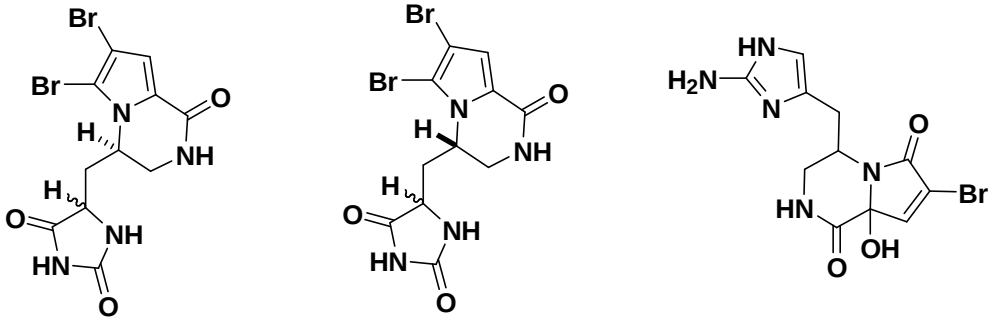


Scheme 1.1

1.3 Cyclooroidin

In 2000, Fattorusso et al. isolated a new alkaloid belonging to the pyrrole-imidazole alkaloid family from the Mediterranean sponge *Agelas oroides*, collected in the Bay of Naples, which they termed (-)-cyclooroidin (**3**).[14] It exhibited a negative optical rotation $[\alpha]_D$ -12 (c 0.02, MeOH) and the absolute stereochemistry was established to be *S* by comparison of its CD spectrum with

the one reported for dibromophakellin. This alkaloid was also detected in an extract obtained from the Okinawan marine sponge *Agelas sp* (Figure 1.2).[15] In 2006 three more natural products structurally related to cyclooroidin (**3**) were isolated. Agesamide A (**10**) and B (**11**) were obtained from the Okinawan marine sponge *Agelas sp*.[16] Oxocyclostylidol **12** was extracted from the Caribbean derived sponge *Stylissa caribica*.[17]

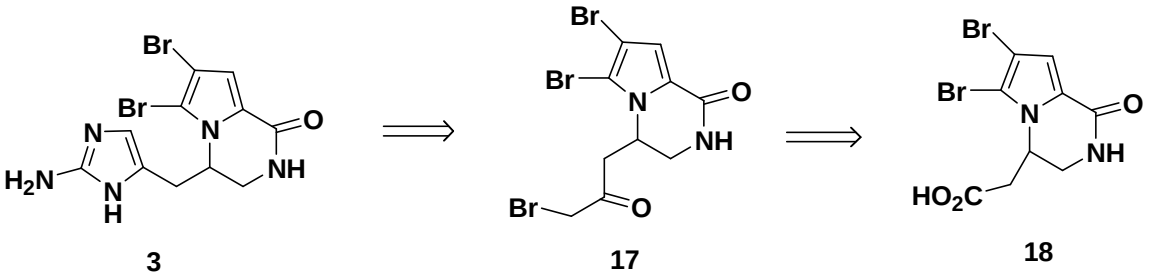


10. Agesamide A **11. Agesamide B** **12. Oxocyclostylidol**

Figure 1.2 Pyrrole-imidazole marine alkaloids

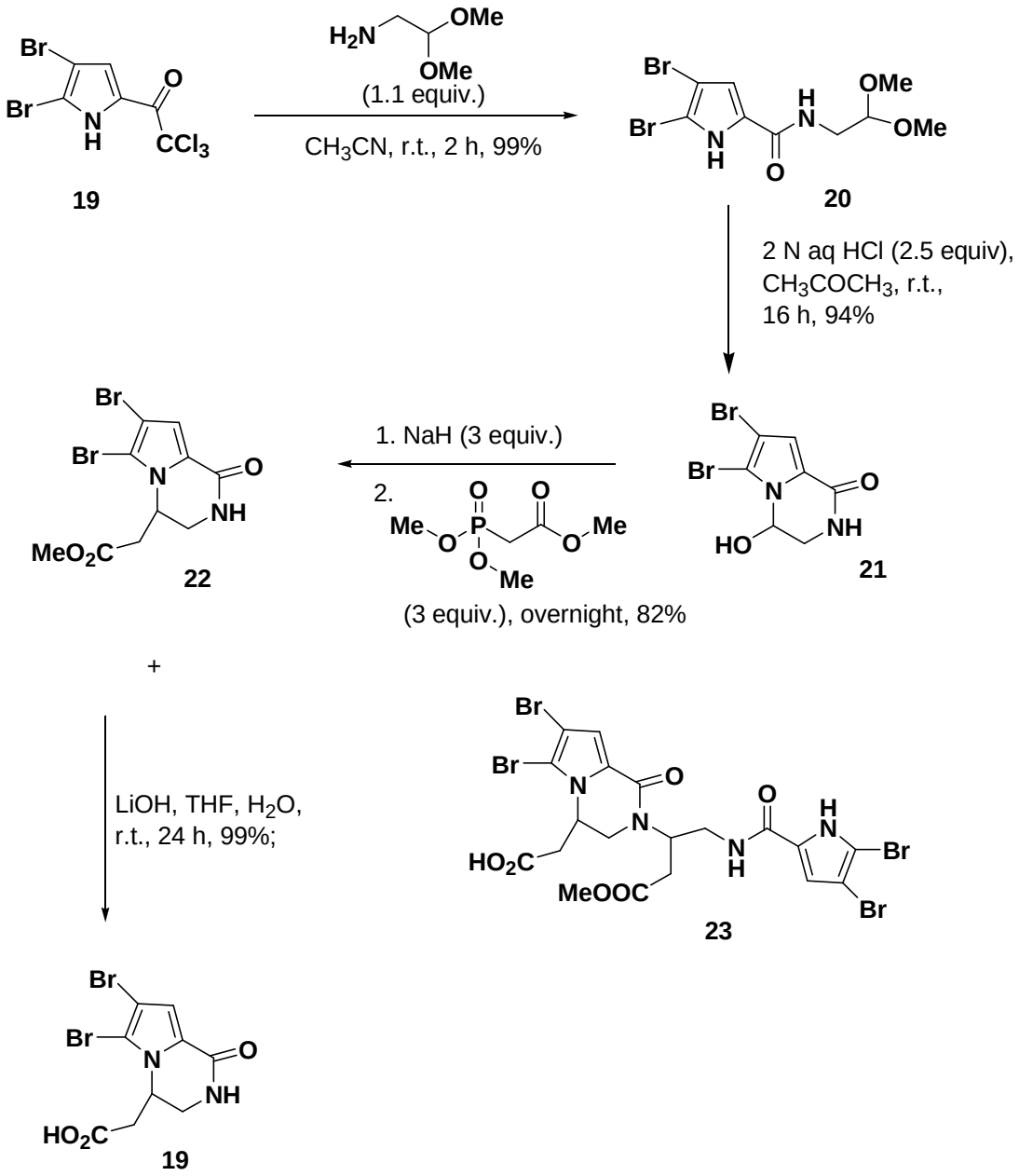
1.4 (±)-cyclooroidin by Papeo

As might be expected cyclooroidin has attracted attention from the synthetic community and very recently, two racemic syntheses have been described. The first one, published by Papeo et al.[18] was achieved in nine steps with an overall yield of 10%. As depicted in (Scheme 1.2) the 2-aminoimidazole ring **16** was constructed from the corresponding α-bromoketone **17**, which was in turn derived from previously prepared from racemic longamide B (**18**)[19] through a Wolff bromoketone synthesis.[20]



Scheme 1.2

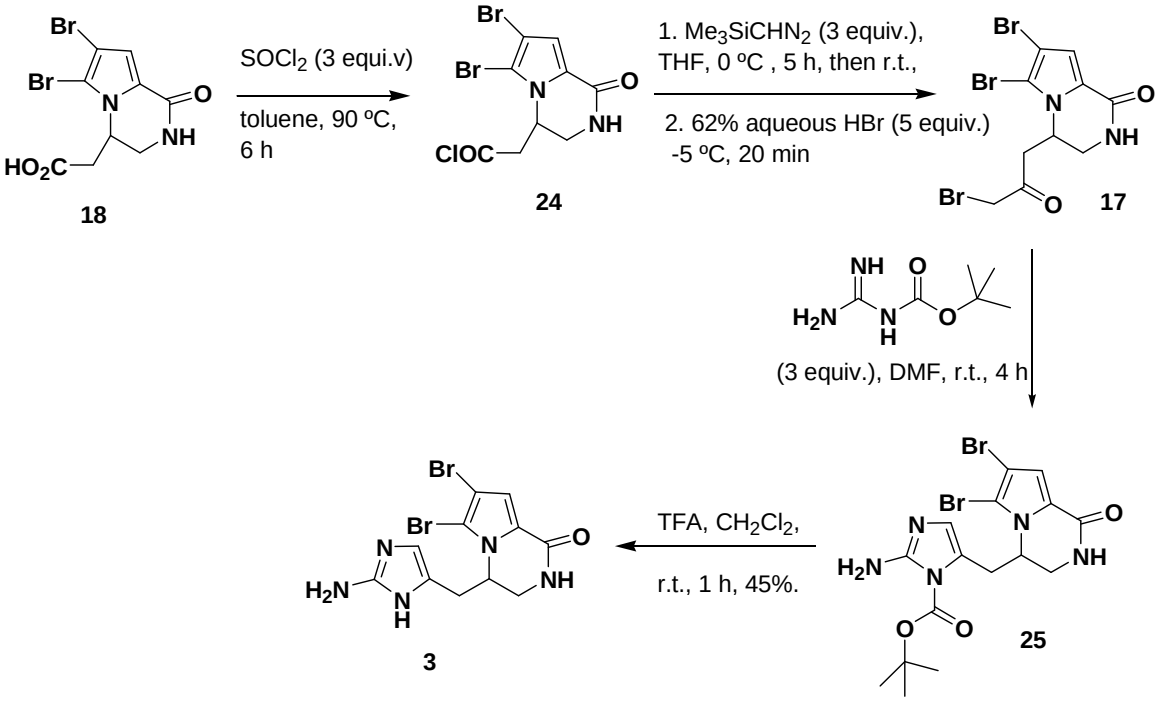
Their synthetic efforts started (Scheme 1.3) by following the previously disclosed protocol[19] for the synthesis of racemic longamide B (**18**). 4,5-Dibromo-trichloroacetylpyrrole (**19**)[21] was used as a starting material, which upon treatment with commercially available aminoacetaldehyde dimethyl acetal delivered amido-acetal **20**. Treating this amido-acetal with 2 N HCl resulted in the formation of intermediate **21** in quantitative yield.[19,22] Then they attempted to convert the racemic carbinolamine **21** to longamide B methyl ester (**22**) by a published procedure using (MeONa/MeOH/methyl diethylphosphonoacetate).[19] However, they obtained a complex reaction mixture, in which the amount of the desired product (**22**) was minor due to the presence of by-products, most of them arising from hydrolysis and competitive conjugate addition of methanol. Eventually longamide B methyl ester (**22**) was obtained by a modification of the reaction conditions and using NaH/trimethylphosphonoacetate in THF in 82% yield. Along with the expected product, they obtained a diastereomeric mixture (15/85 ratio based on HPLC analysis) of dimer **23**, arising from an intermolecular aza-Michael reaction. The yield of this diastereomeric mixture was up to 15%, depending on reaction time and reactant concentration.



Scheme 1.3

In the presence of LiOH in a mixture of THF/water at r.t. longamide B methyl ester (**22**) was then converted quantitatively into longamide B (**18**). Subsequently longamide B (**18**) was converted into the corresponding acyl chloride **24** through standard $SOCl_2$ treatment (Scheme 1.4). Reacting **24** with Me_3SiCHN_2[24] followed by exposure of the resulting α-diazoketone solution to aqueous HBr at 5 ºC

delivered the α-bromoketone **17**. The crude α-bromoketone was immediately reacted with Boc protected guanidine, yielding the 15-Boc-protected cyclooroidin **25** (30% over four steps).[25] It was purified by extensive chromatography (AcOEt/MeOH) in order to remove unreacted Boc-guanidine. They postulated that the migration of the *tert*-butoxycarbonyl group from the exo- to the endocyclic nitrogen atom could occur during the purification step.[25] Removal of the protecting group, followed by column chromatography with a basic mobile phase (CH_2Cl_2/MeOH/NH_3 aq) delivered (±)-cyclooroidin (**16**) as the free base in 45% yield from **25**.

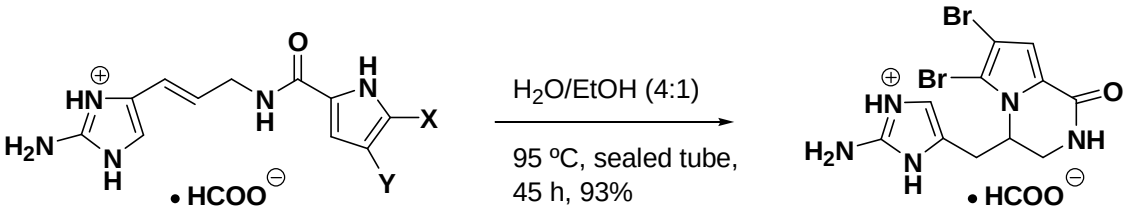


Scheme 1.4

1.5 (±)-cyclooroidin by Lindel

The second racemic syntheses was disclosed by Lindel and co-workers[26] which involved the intramolecular cyclization of oroidin formate in protic solvents (Scheme 1.5). The authors suggested that the biosynthesis of optically active

cyclooroidin from the major marine metabolite oroidin (**1a**) may be a related but enzyme-assisted process.



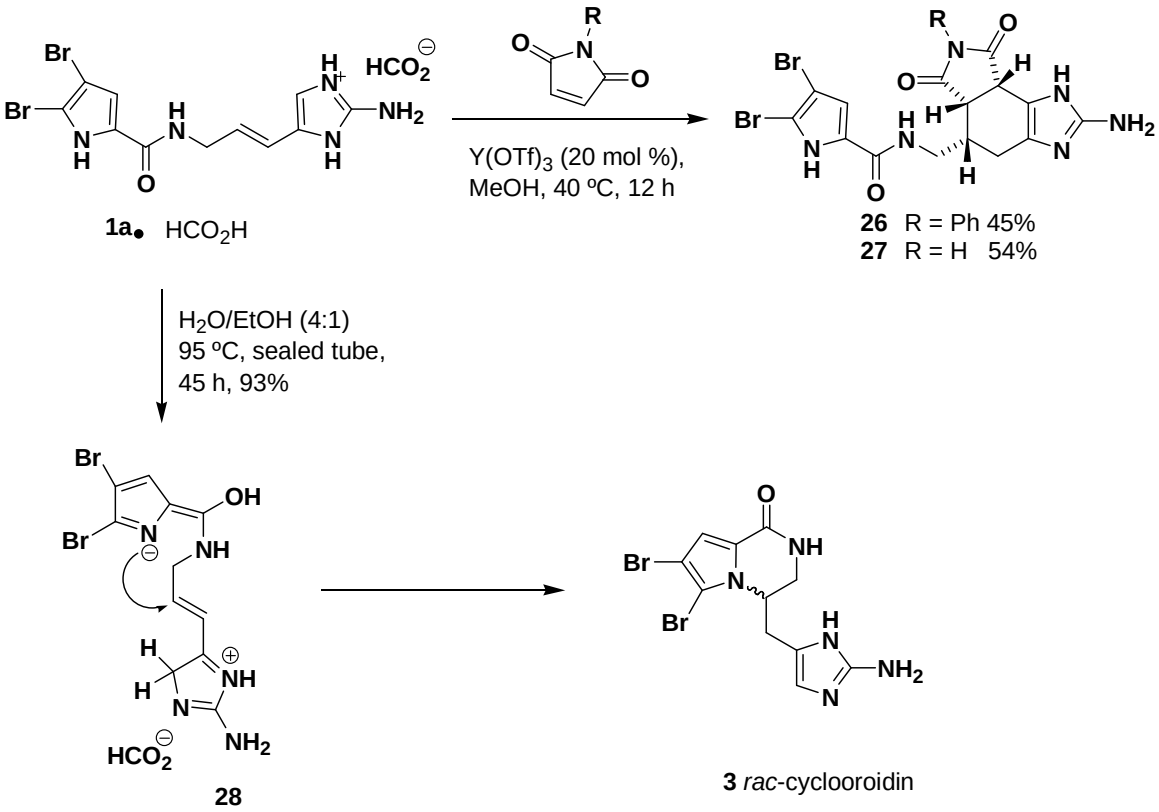
1a: Oroidin

3: *rac*-Cyclooroidin

Scheme 1.5

It should be noted that Lindel and co-workers were actually exploring [4 + 2] cycloaddition reactions of oroidin itself and related 4(5)-alkenylimidazoles bearing an 2-amino substituent rather than attempting a total synthesis of cyclooroidin.[27] In this study they found natural product oroidin itself starts to react with *N*-phenylmaleimide and maleimide at room temperature. Addition of $Y(OTf)_3$ (20 mol%) led to acceleration of the Diels-Alder reactions of oroidin, providing the *endo* cycloadducts **26** and **27** in good yields (Scheme 1.6).[28] During this study they attempted a [4+2]-dimerization of oroidin (**1a**) and they noticed a new product was forming on heating **1a**.HCO_2H (in the absence of maleimides) above 65 ℃ in protic solvents. They discovered that the doub le bond had disappeared, whereas the product had similar molecular formula as oroidin. They concluded that instead of a Diels-Alder reaction, a cyclization had taken place affording *rac*-cyclooroidin formate **3** in almost quantitative yield. They proposed an azafulvene tautomer **28** as an intermediate which reacts via the pyrrole nitrogen. It is of note, that the enolic oxygen does not engage in cyclization to give an oxazole, a pathway which has recently been described by Al-Mourabit[43b] and by our lab.[29]

Although we would note in the case of Al-Mourabit report they describe the use of slightly different conditions (CH_3SO_3H, 80 ºC, 3h) and thus the products obtained may simply reflect kinetic verses thermodynamic preferences in the cyclization.

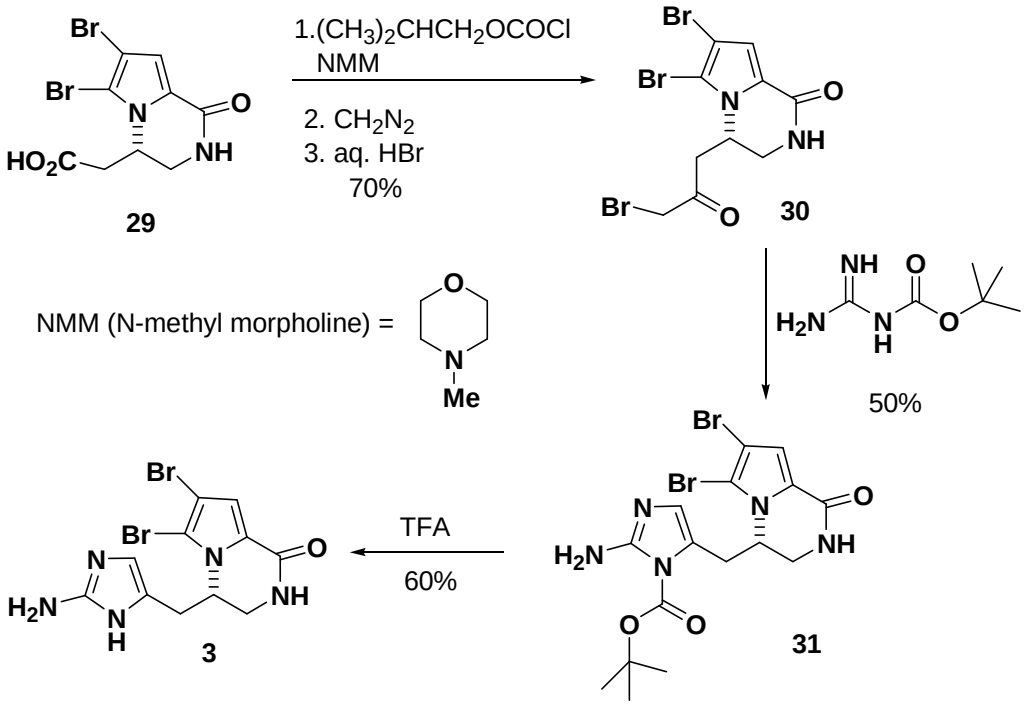


Scheme 1.6

1.6 (*S*)-cyclooroidin by Pelloux-Léon

In 2006 Pelloux-Léon et al.[32] (Scheme 1.7) first synthesized non-racemic (*S*)-(-)-cyclooroidin (**3**)[14] taking advantage of their earlier synthesis of (*S*)-(-)-longamide B.[30] Starting from enantiopure sample of (*S*)-(-)-longamide B (**29**), the carboxylic acid was transformed into a mixed anhydride with isobutyl chloroformate,[31] which was then treated with CH_2N_2 and aqueous HBr[31] to furnish optically active bromoketone **30**. The α-bromoketone was converted to 15-*N*-Boc protected

cyclooroidin **31**. Finally enantiopure cyclooroidin was obtained by adding trifluroacetic acid to (**3**).



Scheme 1.7

The CD spectra of synthetic cyclooroidin (**3**) and of (*S*)-longamide B methyl ester were compared and they observed no difference in the positions of the positive and negative Cotton effects. Their results therefore suggest that these two alkaloids have the same stereochemistry at C9.

Finally, they measured specific rotation. In the first attempt, they mimicked the conditions used for the natural product.[14] In that regard, their synthetic sample exhibited the same value as the one described for natural cyclooroidin (-12.5 (c 0.02, MeOH)). The second measurement was performed using a more concentrated solution ($[\alpha]_D^{25}$ - 33.0 (c 1, MeOH)). These experiments confirmed that natural cyclooroidin has an (*S*)-configuration at C-9 as it was postulated by Taglialatela-Scafati and co-workers.[14]

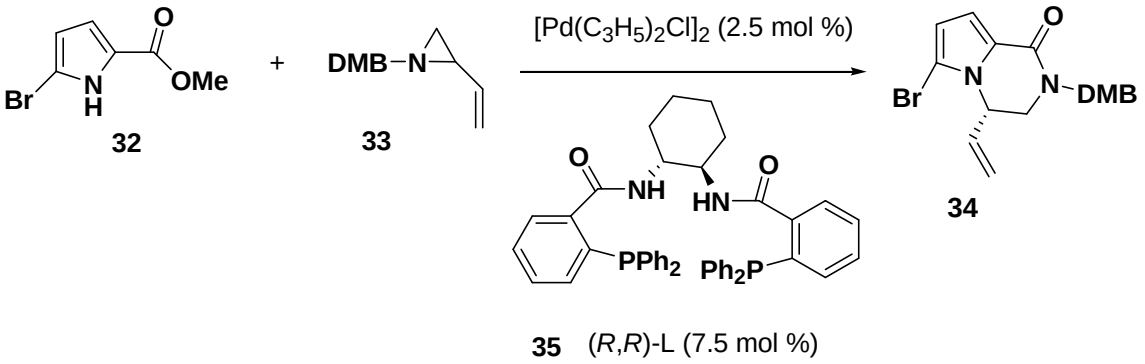
1.7 (*S*)-cyclooroidin by Trost

Recently Trost et al.[33] (Scheme 1.8) have developed an enantioselective, Pd-catalyzed alkylation-annulation reaction to construct a pyrrolopiperazinone from a 5-bromopyrrole-2-carboxylate ester and a vinyl aziridine. Application of this protocol leads to the concise asymmetric synthesis of longamide B in five steps from **32** and **33**, while cyclooroidin can be synthesized in four additional steps from longamide B based on the work of Papeo et al.[18] and Pelloux-Léon et al described in (scheme 1.7).[32]

They envisioned that by using a 5-bromopyrrole-2-carboxylate derivative, the nitrogen on the pyrrole would behave as a good nucleophile to open the aziridine ring regioselectively during the AAA (asymmetric allylic alkylation), while the ester group on the pyrrole would act as a nitrogen acceptor to form a 6-membered lactam. Thus, the pyrrolopiperazinone skeleton can be formed in single step.

Initially they examined the reaction between methyl 5-bromopyrrole-2-carboxylate **32** and vinyl aziridine **33**[34] (Table 1.1) in the presence of 2.5 mol % of $[Pd(C_3H_5)Cl]_2$ and 7.5 mol % of (*R*,*R*)-L. It had been shown previously that enantioselectivity in the Pd-catalyzed cycloadditions of isocyanates to vinyl aziridines was enhanced greatly by the addition of catalytic amount of HOAc.[35] By using 10 mol % of HOAc they obtained the desired pyrrolopiperazinone **34** in 71% ee but very low yield due to the decomposition of starting materials. Addition of 50 mol % of Cs_2CO_3 gave much higher ee (89%) but only slightly improved the

yield (41%). However, they found that without any additives, the annulation product **34** was obtained in 72% yield and 95% ee.



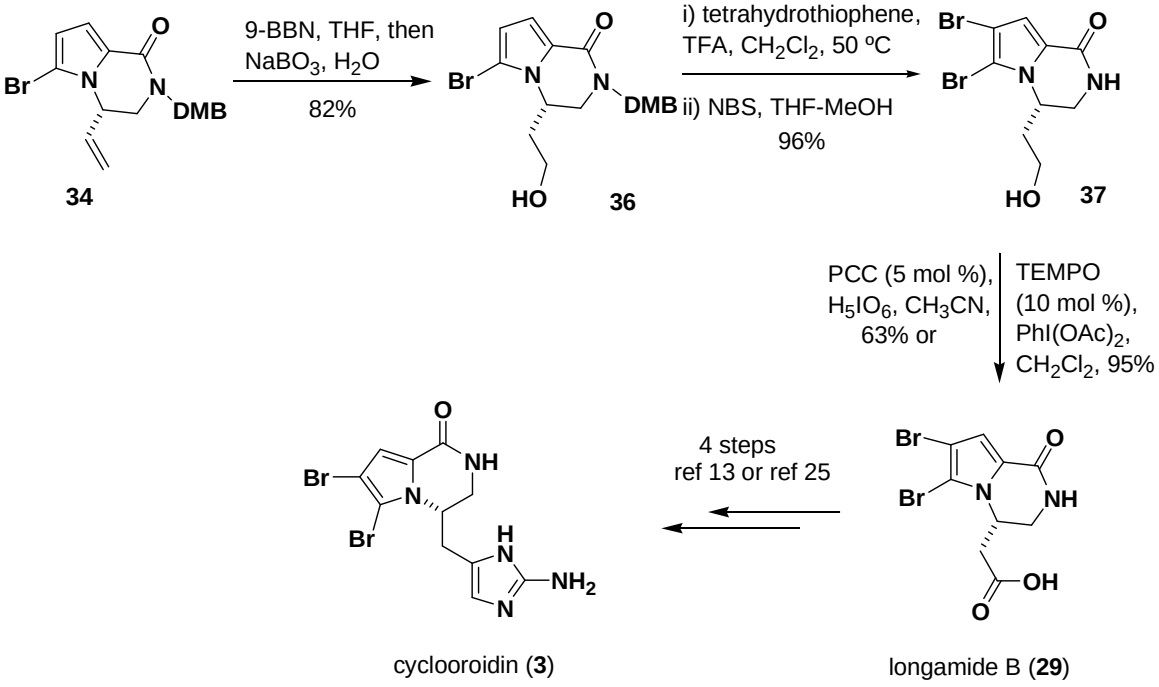
Scheme 1.8

Table 1.1 Effect of additives in Pd-catalyzed asymmetric allylic alkylation

entry	Additives	% yield	% ee
1	10 mol % HOAc	19	71
2	50 mol % Cs_2CO_3	41	89
3	None	72	95

As depicted in (Scheme 1.9) primary alcohol **36** was obtained in high yield and excellent regioselectivity by hydroboration of **34** with 9-BBN followed by oxidation with sodium perborate. The DMB group was cleaved by treating **36** with 5 equiv of tetrahydrothiophene in TFA/DCM (1:1). The deprotected amide **30** was contaminated with its protiodebrominated counterpart product, however they obtained dibromo alcohol **37** in 96% yield over two steps by NBS-mediated bromination of **36**. They screened conditions for oxidizing primary alcohol **30** to the carboxylic acid, and determined the PCC-catalyzed oxidation with H_5IO_6 [36] gave (*S*)-(-)-longamide B (**29**) in 63% (brsm 90%) yield. A more effective

oxidation was found later in an attempt to oxidize **37** to the corresponding aldehyde. They found that treatment of **37** with 10 mol% of TEMPO and 2.5 equiv of $PhI(OAc)_2$ in CH_2Cl_2[37] produced carboxylic acid **29** instead of the aldehyde in 95% yield. The total synthesis of (*S*)-(-)-longamide B also confirmed the absolute configuration of the Pd-catalyzed asymmetric annulation reaction. As indicated above cyclooroidin (**3**) can be synthesized in four steps from longamide B based on the work of Papeo et al.[18] and Pelloux-Léon et al.[32]



Scheme 1.9

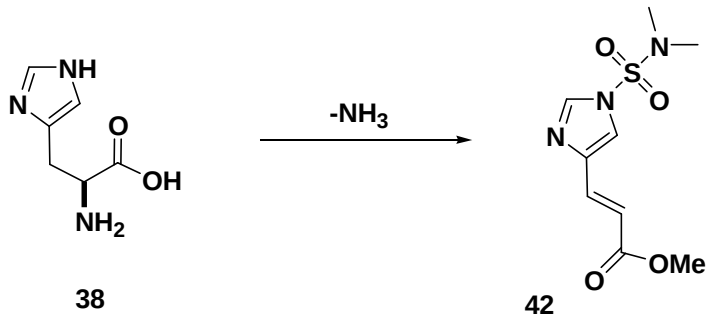
In the next chapter, we will delineate our own asymmetric total synthesis of cyclooroidin, which adopts a strategically different approach to the previously reported syntheses. In the chemistry to be outline below, we will use histidine as both our source of chirality and also to provide one of the heterocyclic rings.

CHAPTER 2

RESULTS AND DISCUSSION

2.1 Initial efforts

Our group uses large amounts of urocanic acid as a starting material, and while this is commercially available, it is relatively expensive and its supply was sometimes unreliable. Driven by these concerns, we set out to develop a more cost effective approach to urocanic acid (Scheme 2.1)[38] and it was in the course of this study that an approach to the cyclooroidin problem evolved.



38 **42**

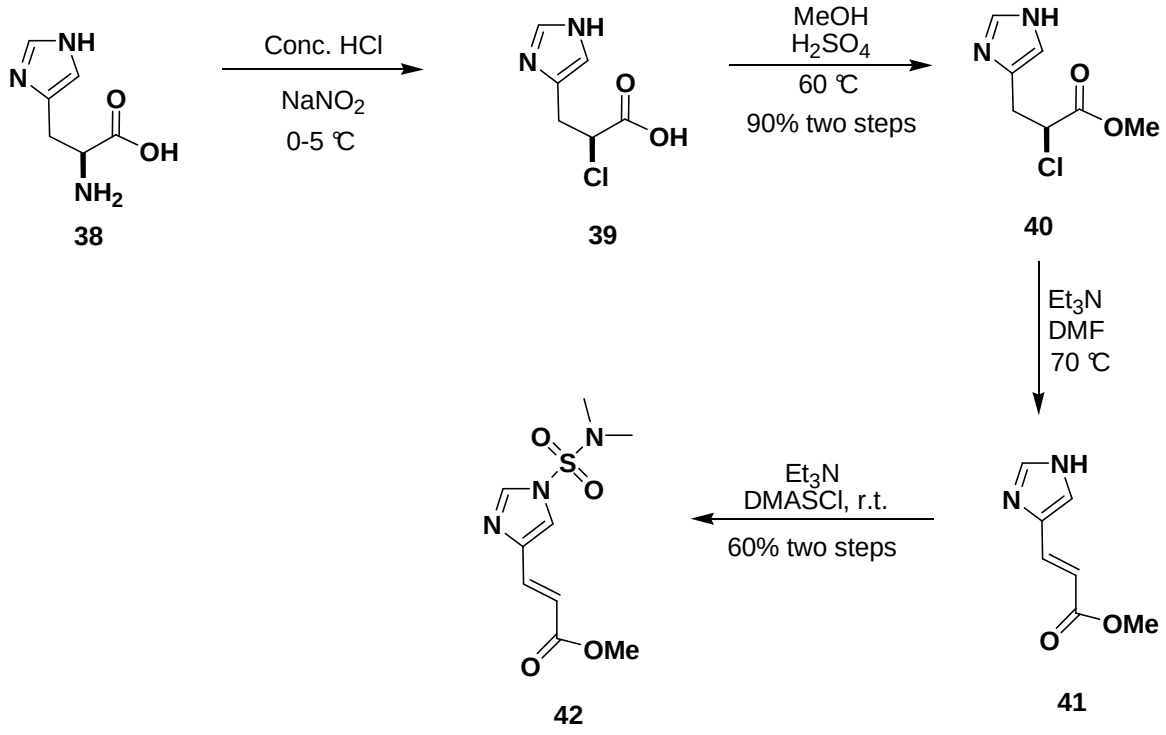
Scheme 2.1

2.2 Preparation of the methyl ester of Urocanic acid.

When the structures of histidine and urocanic acid are compared, the net loss of ammonia from **38** provides urocanic acid. In practice, such a direct conversion is not straightforward and therefore, we converted the amino group into a better leaving group through the incorporation of a chloro moiety.

Diazotization was carried out on L-histidine **38** using a mixture of concentrated hydrochloric acid and sodium nitrate at 0-5 ºC according to the report of

Edlbacher (Scheme 2.2).[38] The α-chloro acid **39** was then esterified using methanol and sulfuric acid with heating at 40 ºC providing **40**, which was more convenient to work with. The α-chloro ester **40** was dissolved in DMF and then triethylamine was added and the solution was heated to around 70 ºC under N_2 atmosphere to effect dehydrochlorination. The desired urocanoate ester **41** was then protected using dimethylaminosulfonyl chloride (DMASCl) and triethylamine at room temperature to give compound **42**.[39a-j]

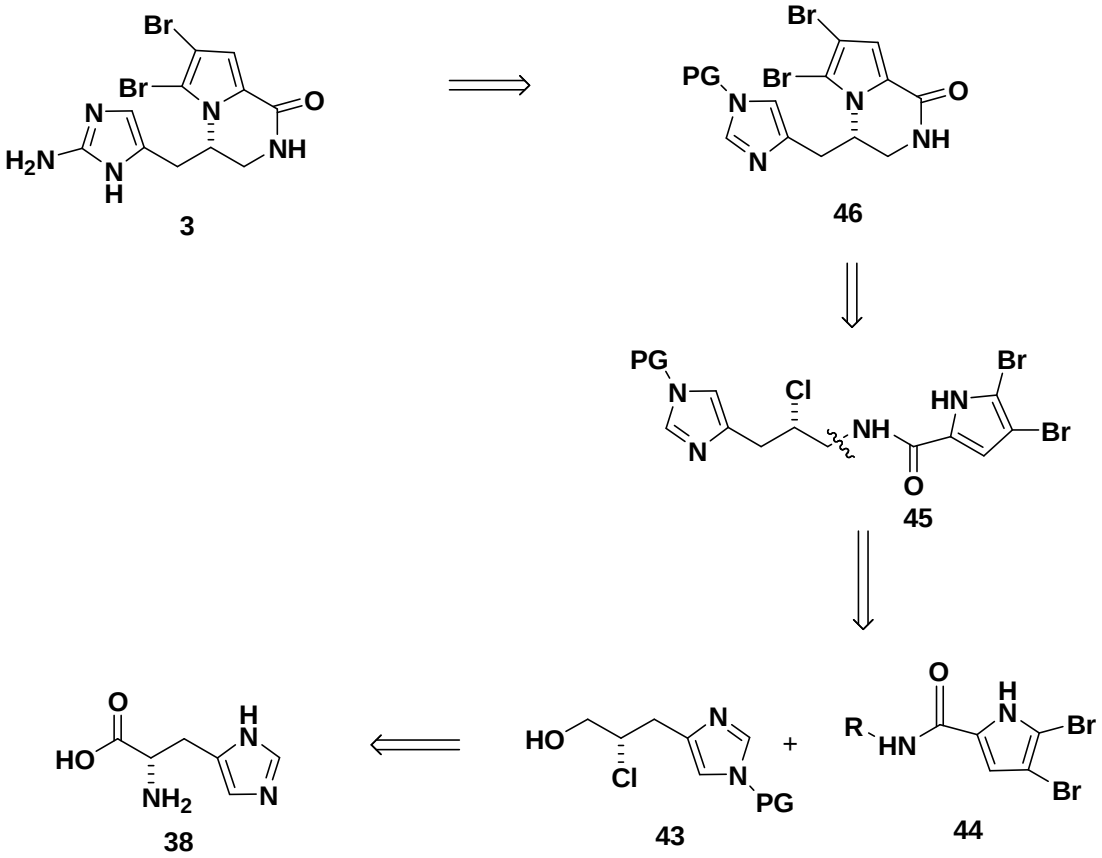


Scheme 2.2

2.3 Retrosynthesis of cyclooroidin

It was at this point that α-chloro ester **40** caught our attention as a potentially attractive precursor for the construction of several oroidin alkaloids, including cyclooroidin (**3**). Conversion of α-chloro ester to chloroalcohol **43** followed by alkylation with imide **44** would provide **45**. Subsequent intramolecular

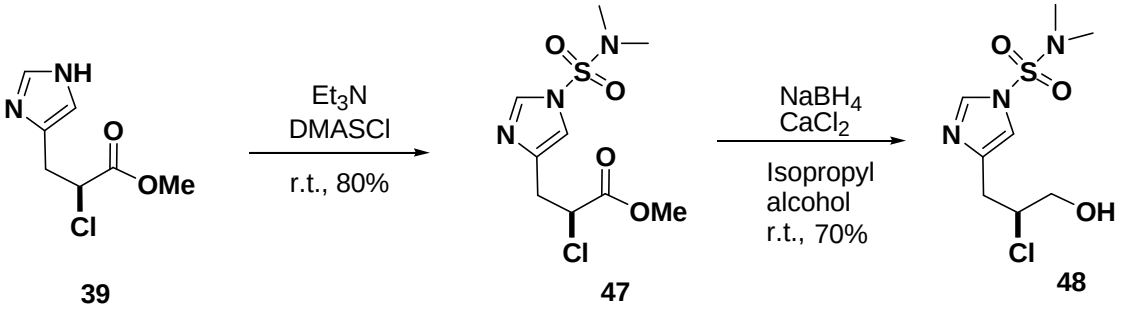
displacement of the chloride with the pyrrole nitrogen would give the basic skeleton of cyclooroidin (Scheme 2.3)**.** In a forward sense, the key steps involve a Mitsunobu reaction between alcohol **43** and a novel cyclic pyrrole imide **49** followed by basecatalyzed cyclization to form the core skeleton of the molecule. Once the basic core of the molecule is assembled, the next goal is to introduce two bromines into the pyrrole of the molecule **46**. Finally an azide needs to be introduced at the C-2 position of the imidazole of the molecule **46**. Synthetic cyclooroidin can be obtained by reducing the azide **46** to amine first and then ultimately removing off the protecting group.



Scheme 2.3

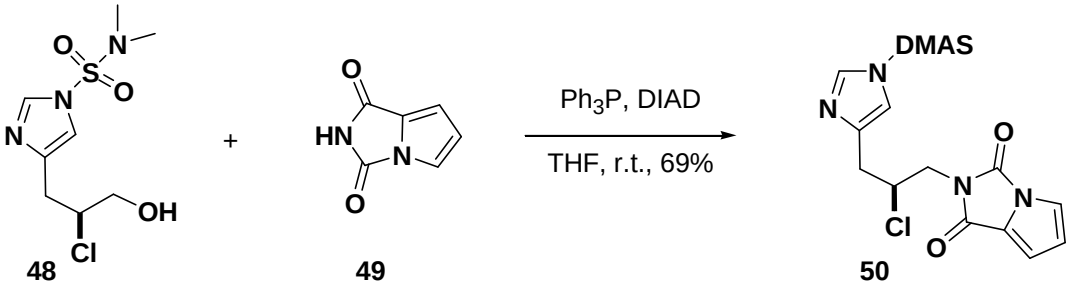
2.4 Efforts towards synthesis of cyclooroidin

The α-chloro ester **39** was protected with dimethylaminosulfonyl chloride at room temperature to obtain **47** which was then reduced to alcohol **48** (Scheme 2.4) using sodium borohydride, calcium chloride and isopropyl alcohol as solvent (at room temperature).[40]

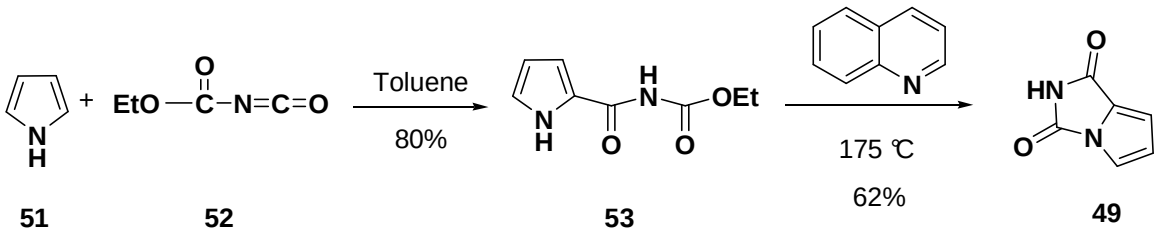


Scheme 2.4

After screening several nucleophiles or pronucleophiles including *N*-(1*H*-pyrrole-2-carbonyl)- benzenesulfonamide,[41a] 4-methyl-*N*-(1*H*-pyrrole-2-carbonyl)benzene sulfonamide,[41b] diphenyl phosphoryl azide,[41b] it was found that the alcohol **48** underwent Mitsunobu reaction[41] with imide **49** to obtain **50** (Scheme 2.5). Imide **49**[42] was obtained by reacting ethoxycarbonyl isocyanate (**52**)[42] with pyrrole (**51**) to provide *N*-ethoxycarbonylpyrrole-2-carboxamide (**53**) (Scheme 2.6)**.**[42] Cyclization occurred on heating a quinoline solution of **53** at 175 ºC affording the known compound **49**.[42]

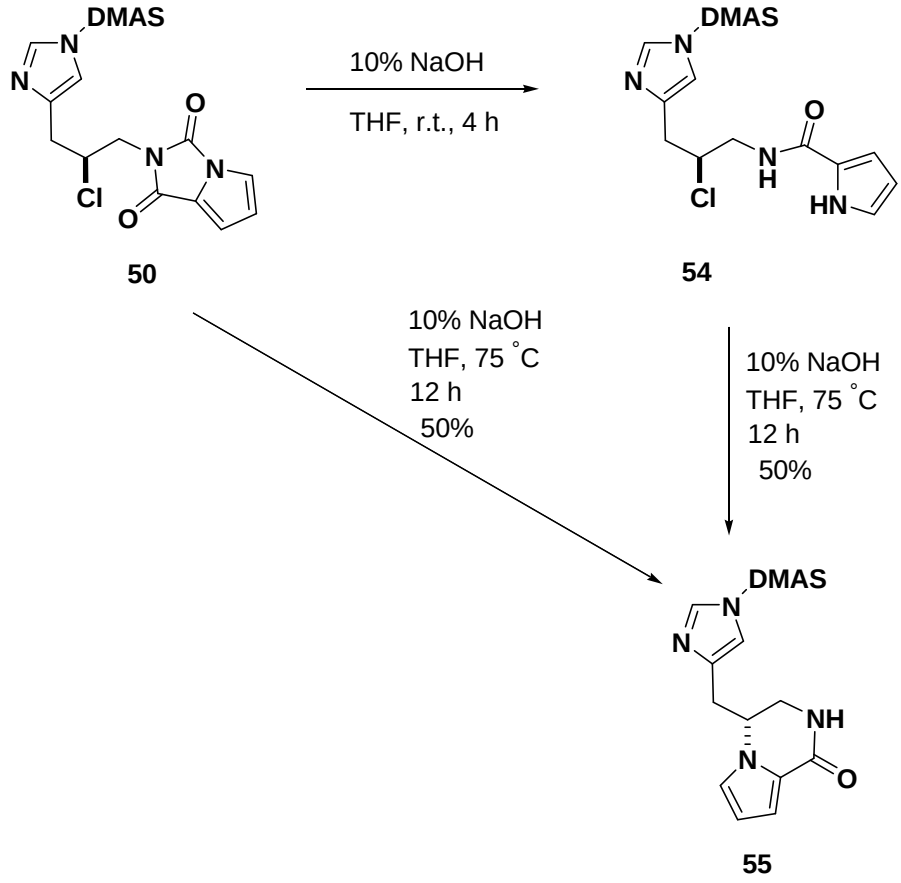


Scheme 2.5



Scheme 2.6

Stirring a solution **50** in THF and 10% NaOH solution for about 4 h, led to hydrolytic opening of hydantoin moiety and affording compound **54** (Scheme 2.7).[42]



Scheme 2.7

When compound **54** (contaminated with triphenylphosphine oxide) was heated for an additional period time under the same reaction conditions it underwent

cyclization to form what we initially believed was compound **55**. We also found that **50** undergoes tandem hydrolysis and cyclization by simply running the reaction for 12 h at 75 ºC. While we initially thought that we had constructed the basic core ring system of cyclooroidin **55**, there were some troubling discrepancies between the spectroscopic data of the isolated natural product (Table 2.1) and with our synthetically prepared compound **55**. It was found that although it was largely similar, there were inconsistensies in the ^{13}C NMR spectrum, in particular a signal due to one of the aliphatic carbons corresponding to C9 in cyclooroidin did not match well with the natural product. The particular signal in question was 19.0 ppm further downfield than anticipated, suggesting that this carbon may be bonded to oxygen rather than with nitrogen i.e., an oxazoline had been formed rather than a pyrazine. Comparison of the NMR data of similar compounds from the literature (Table 2.1) suggested that instead of forming a C-N bond, the cyclization has occurred through formation of a C-O bond.[43a-b, 44]

Table 2.1 Comparison of ^{13}C NMR studies of C9 for cyclooroidin and several related oxazolines.

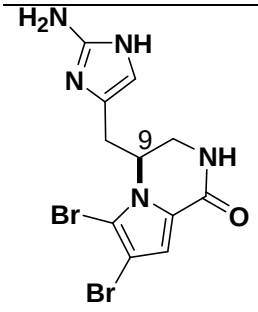
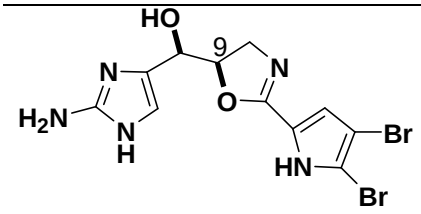
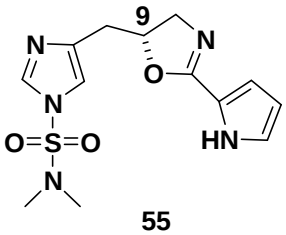
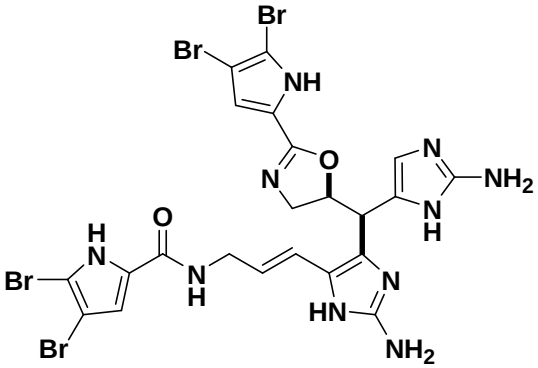
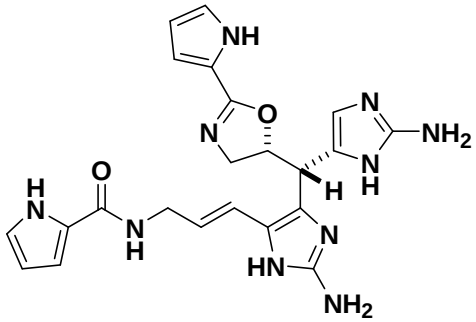
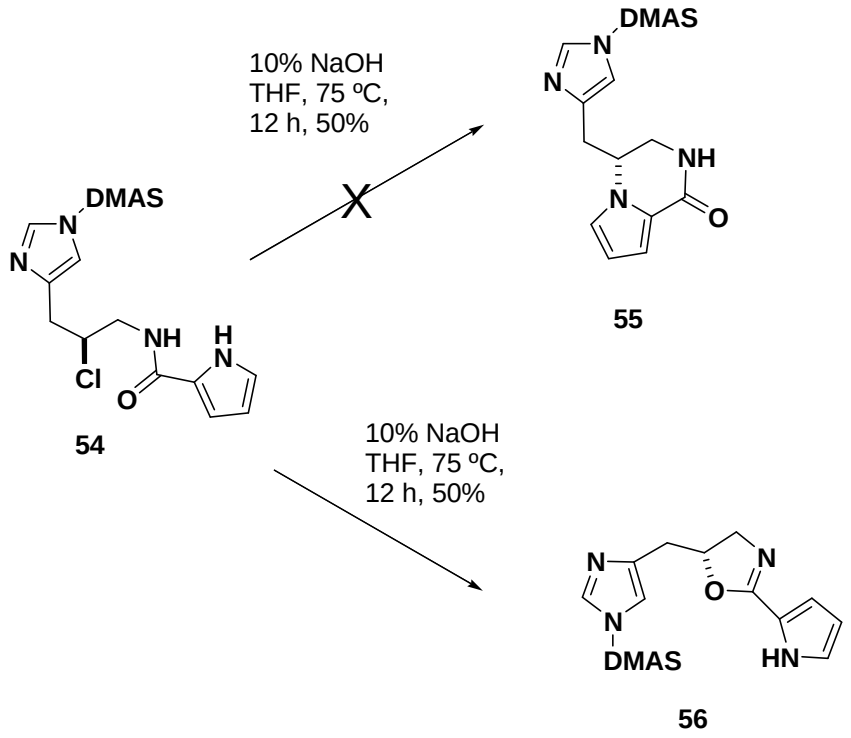
Compound	**δ_{C9}**
 **3**	57.9

Table 2.1-continued

 **57**	89.0
 **55**	77.6
 **Nagelamide R**	79.5
 **Nagelamide T**	80.2

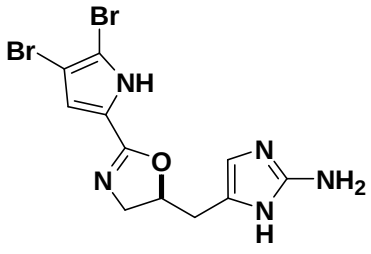
So when a THF solution of compound **54** was heated under basic condition (10% NaOH solution) it underwent cyclization through the amide oxygen instead

of pyrrole nitrogen to give an oxazole ring, thus resulting in the formation of compound **56** (Scheme 2.8)**.**

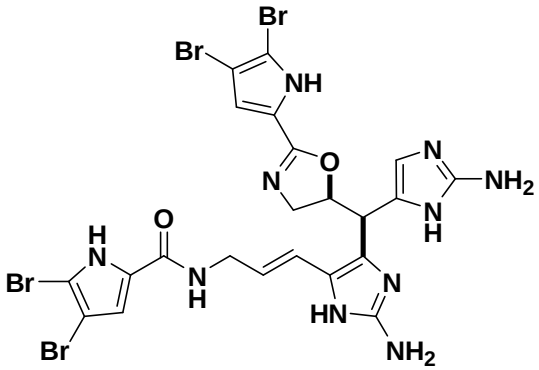


Scheme 2.8

Compound **56** has the appropiate structural fragments as the northern sector of the natural product nagelamide R.[44] So we decided to continue our investigation to establish whether **56** could be further elaborated to **57**, which would be useful in the pursuit of a total synthesis of nagelamide R.

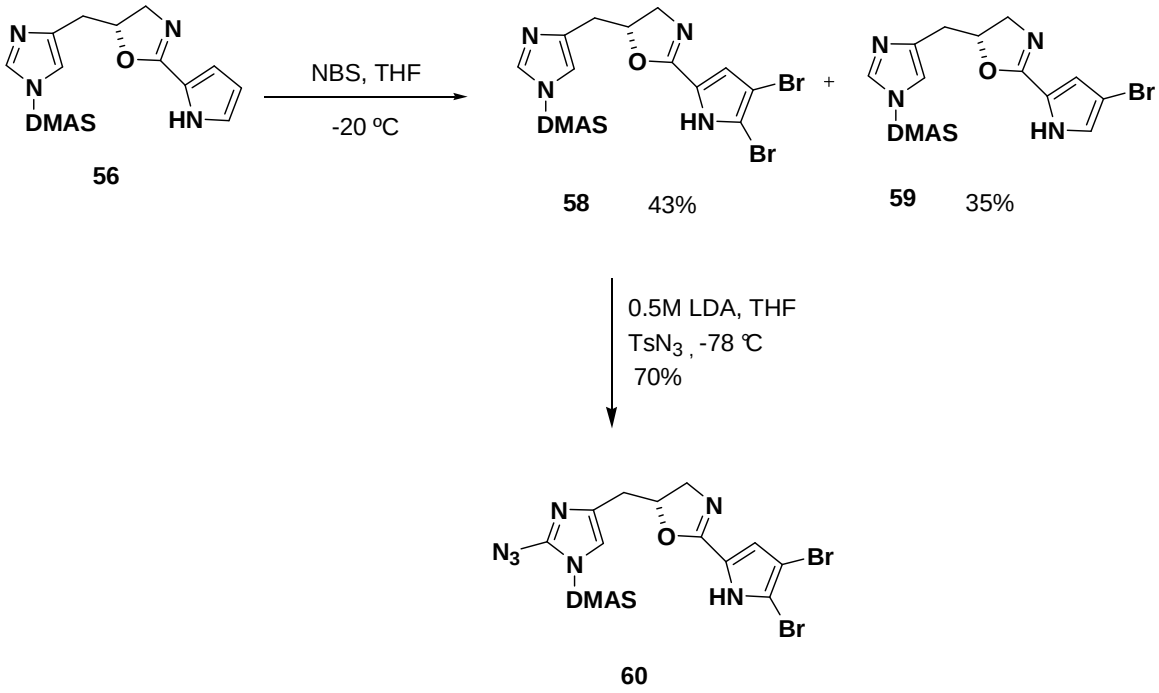


57: Northern fragment



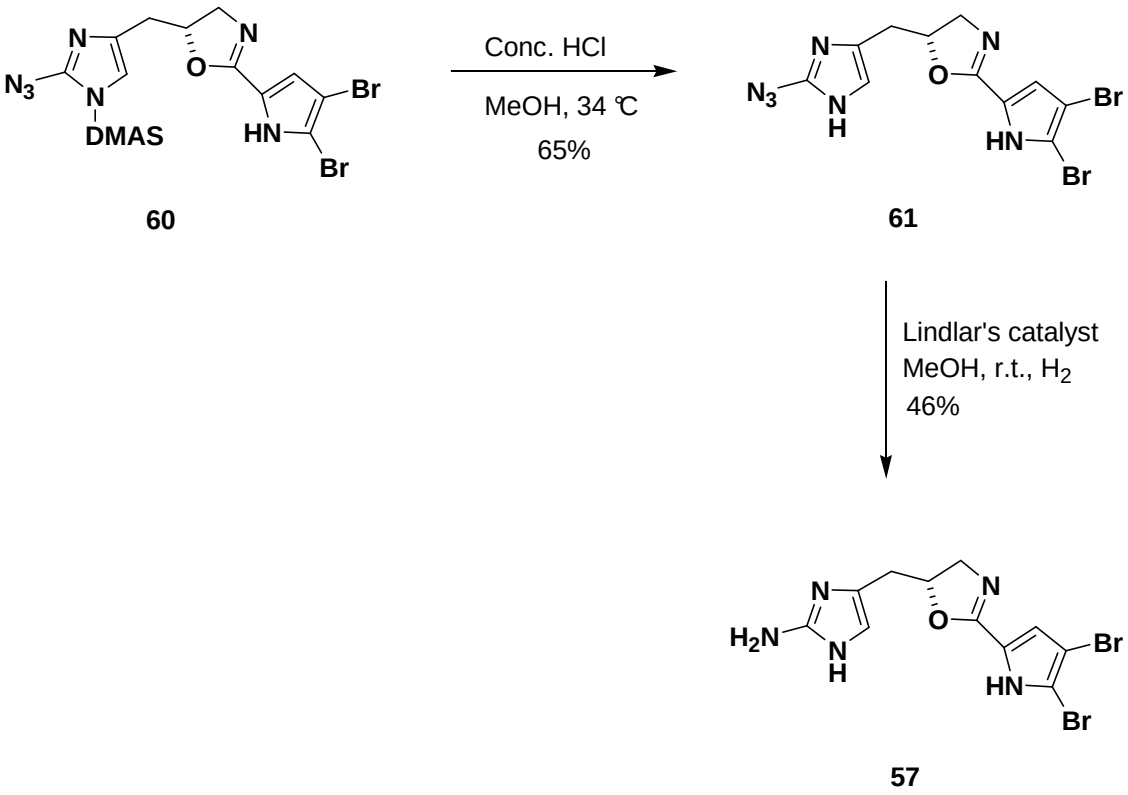
Nagelamide R

The cyclic compound **56** was subjected to bromination with NBS at -20 ℃ leading to the formation of compound **58** in modest yield.[45] The yield of the bromination was reatively low due to competitive formation of mono brominated compound **59** in 35%. Subsequently the azide moiety was introduced to the brominated compound **58** by generating the anion at C-2 position with 4.1 equiv. of LDA and adding TsN_3 while maintaining the reaction temperature throughout at -78 ℃, thus leading to formation of compound **60** (Scheme 2.9).[46]



Scheme 2.9

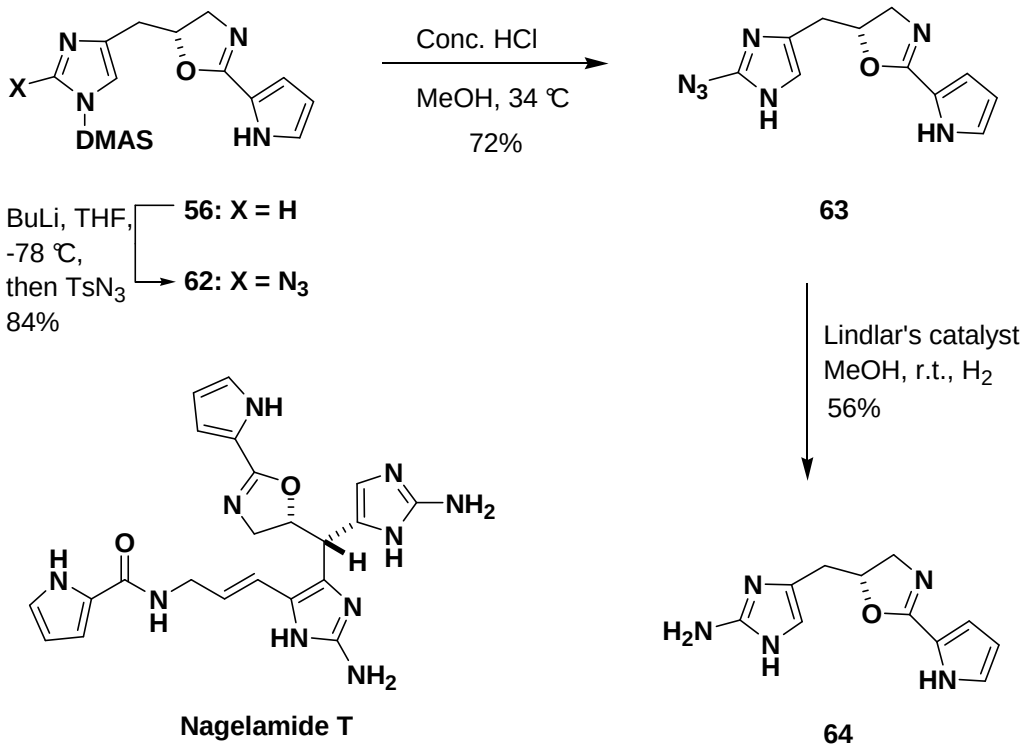
The dimethylsulfamoyl protecting group was removed by adding conc. HCl to the compound **60** dissolved in methanol and heating the resulting mixture to 34 ℃ to provide compound **61**.[47] Finally the azide was reduced to amine **61** in the of Lindlar's catalyst and hydrogen atmosphere to give **62** (Scheme 2.10).[47]



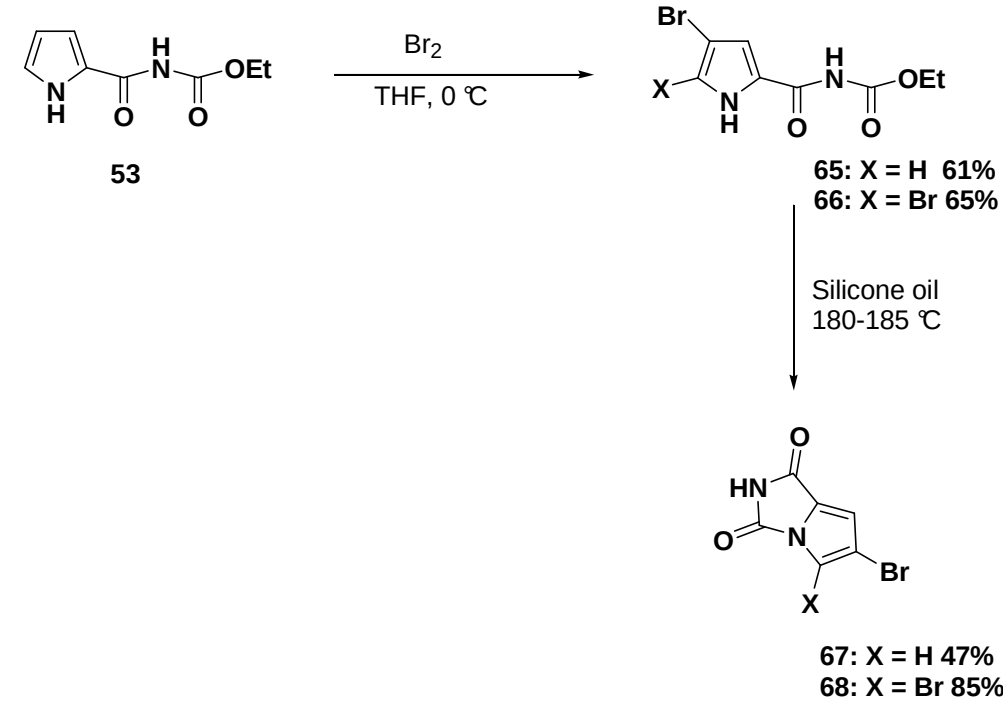
60 61 57

Scheme 2.10

We would note that initial studies on the final few steps were conducted on the non-brominated congener to determine viability of the deprotective and reduction steps. This sequence of reactions provides the oxazoline portion of the nagelamide T, although at the time these reactions were conducted, nagelamide T had not been described. The azidation in this case can be performed with n-BuLi rather than LDA, this chemistry is depicted in (Scheme 2.11).



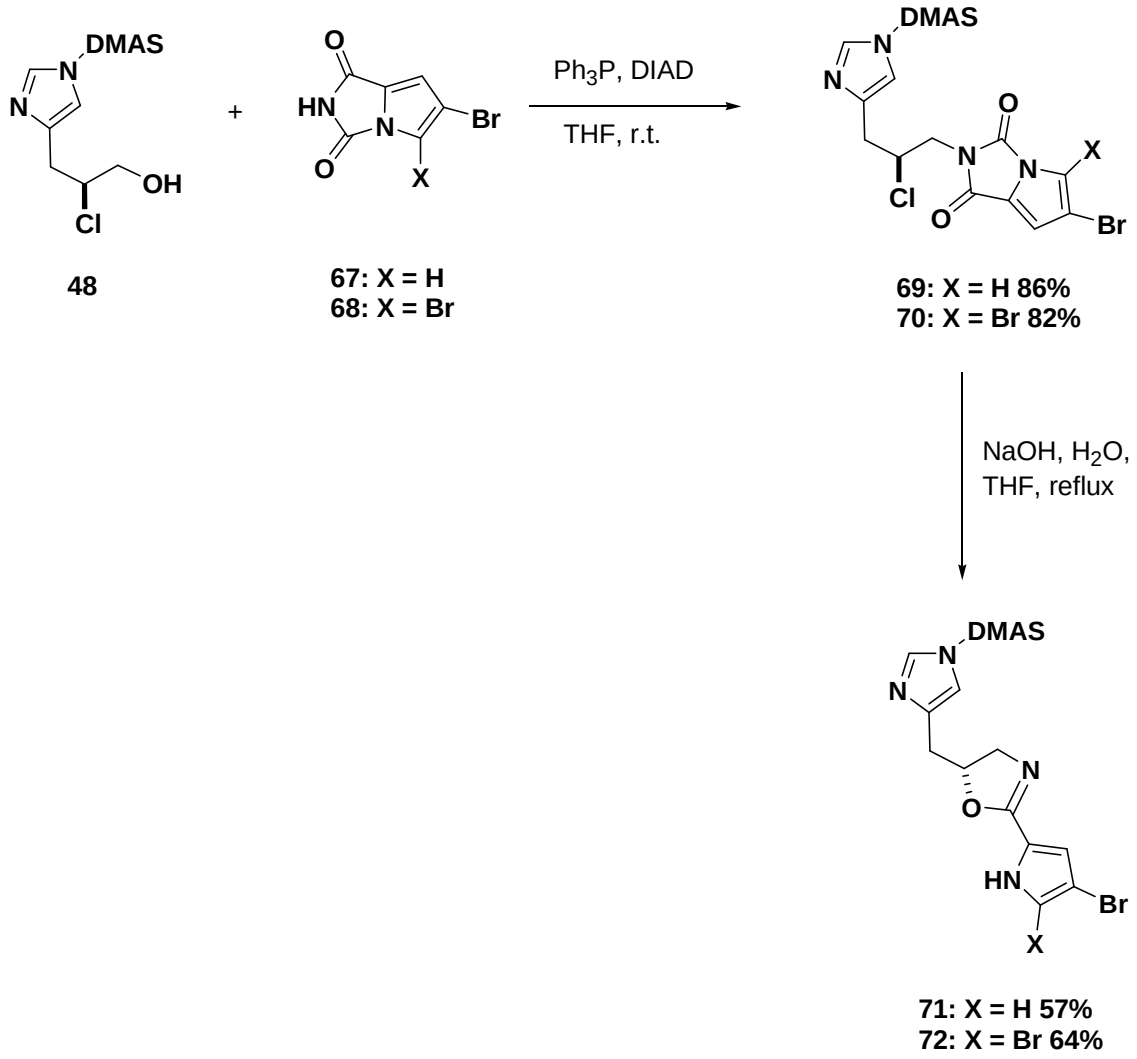
Scheme 2.11



Scheme 2.12

We were somewhat disappointed with the efficiency of the bromination step in the earlier sequence (Scheme 2.9, **56**→**58**) due to the formation of the monobromo product. We reasoned that if the bromo substituents were introduced prior to the Mitsunobu reaction, this issue would be less of a problem. Accordingly we have examined the use of other pyrrole hydantoin derivatives, specifically brominated derivatives (**67** and **68)**, in the Mitsunobu sequence as mono- and dibrominated pyrrole substituents are widely distributed among the oroidin alkaloids. It is well known that the corresponding pyrrole trichloro ketones can be brominated in a controlled fashion and thus it was reasoned that imide **53** should behave similarly. Gratifyingly, treatment of **53** with 1 or 2 equiv of Br_2 provided the correspondoing mono- and dibrominated derivatives. Monobromopyrrole **65** was mixed with silicone oil in a round bottom flask which was evacuated (40 mm, Hg) and heated to 180-185 ºC.[48] using a procedure adapted from Spoering's dissertation.[48] After 4 h, the reaction was cooled and then the residue was crushed. Hexane was added and the solids were collected by filtration and washed repeatedly with hexane. The procedure was repeated and the resulting product was purified by chromatography, providing **67** in 47% yield. The dibrominated hydantoin **68** was also prepared in a similar fashion as described above. We have found that both the mono and the dibrominated derivatives **67** and **68** participate in the substitution reaction (Scheme 2.12).[27,47] These alkylated hydantoin derivatives **69** and **70** were subjected to hydrolysis under basic conditions, and in a similar fashion to **54** underwent concomittent hydrolysis, cyclization to provide the corresponding oxazoles **71** and **72** (Scheme

2.13). In the case of the dibrominated derivative **72**, this provides a more efficient preparation of the oxazoline than bromination of the parent system **56**. It is challenging to unequivocally prove the location of the bromine atoms on the pyrroles, but fortunately both **69** and **72** were nice crystalline solids that provide good X-ray crystal structures.



Scheme 2.13

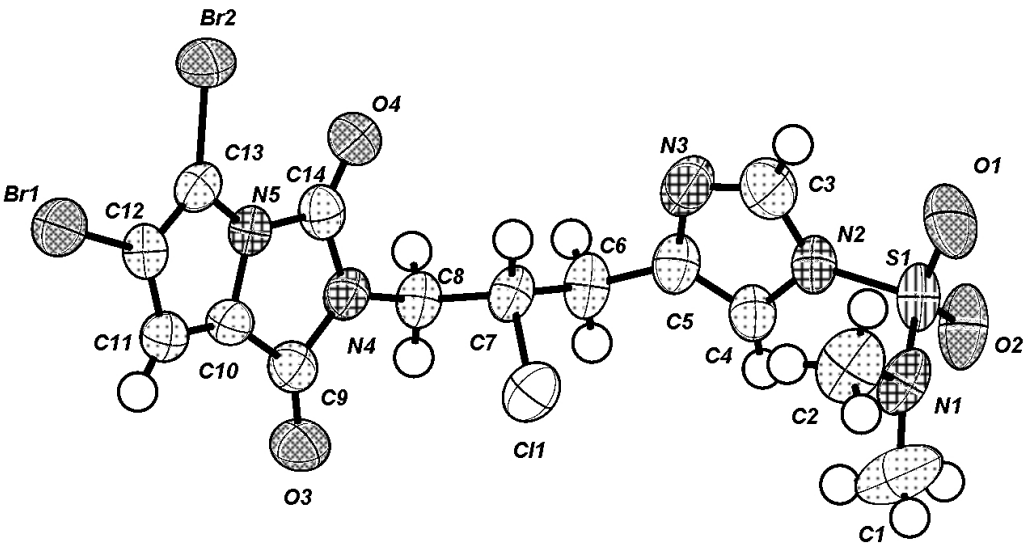


Figure 2.1 X-ray Crystal structure of compound **70**

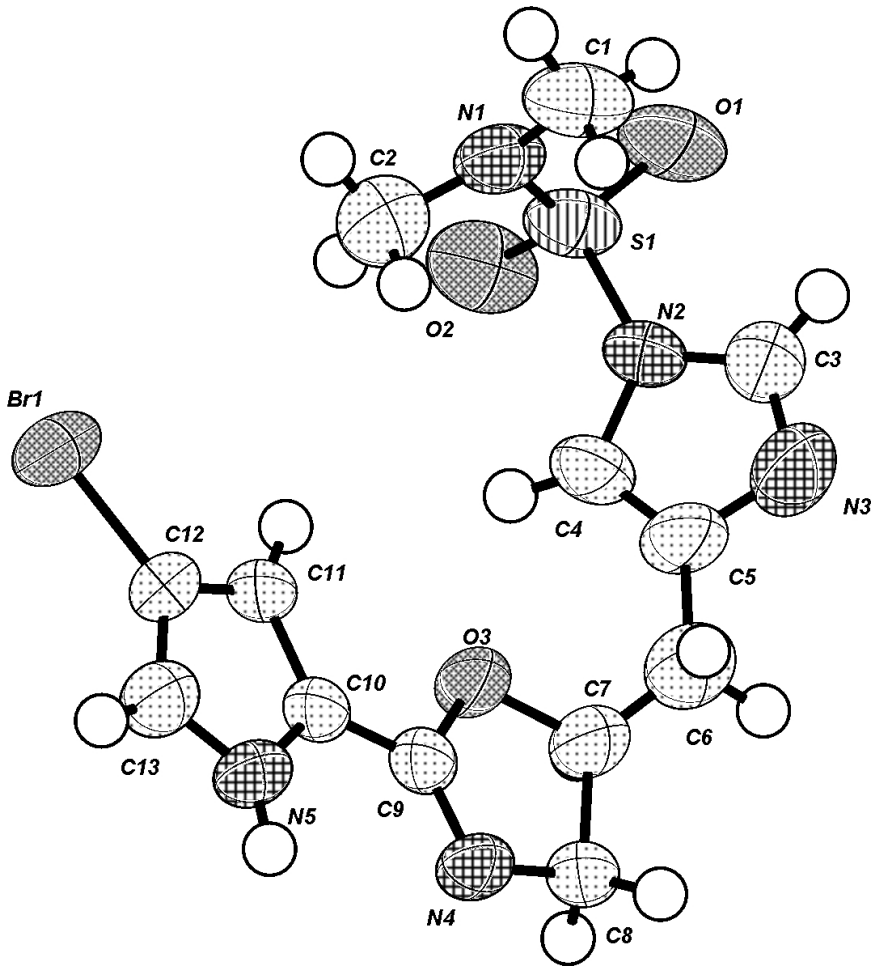
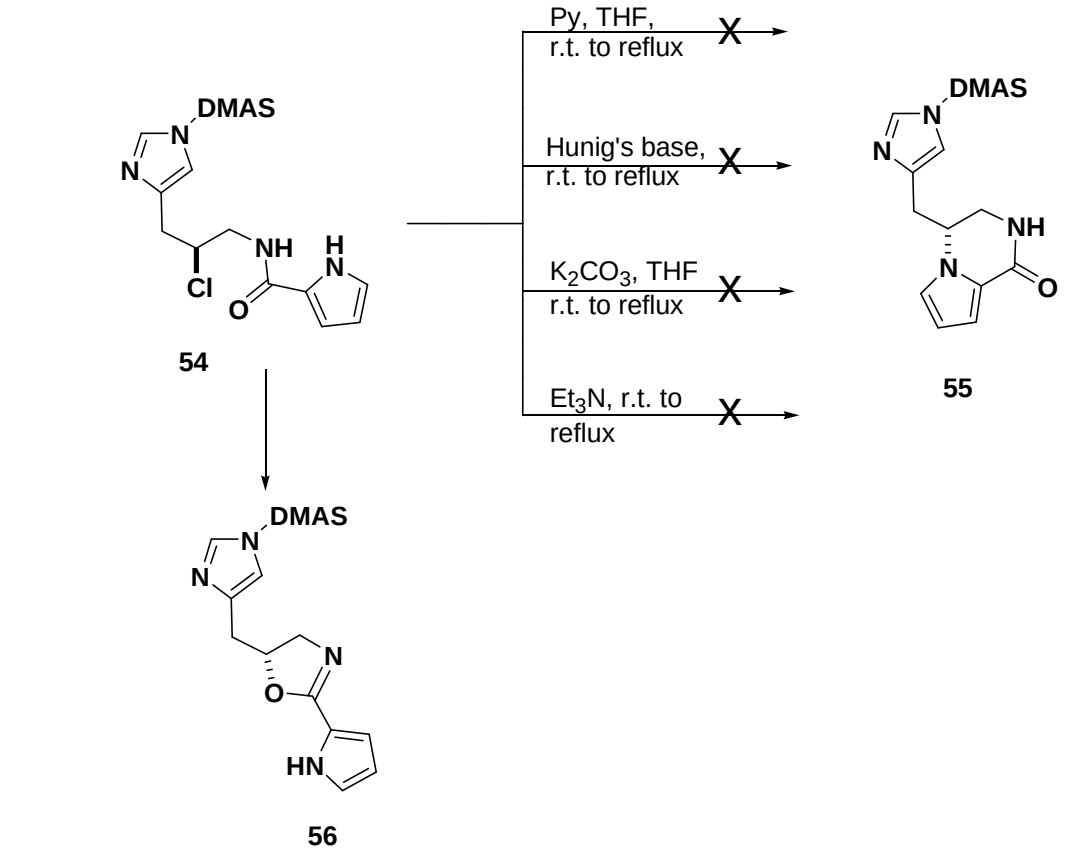


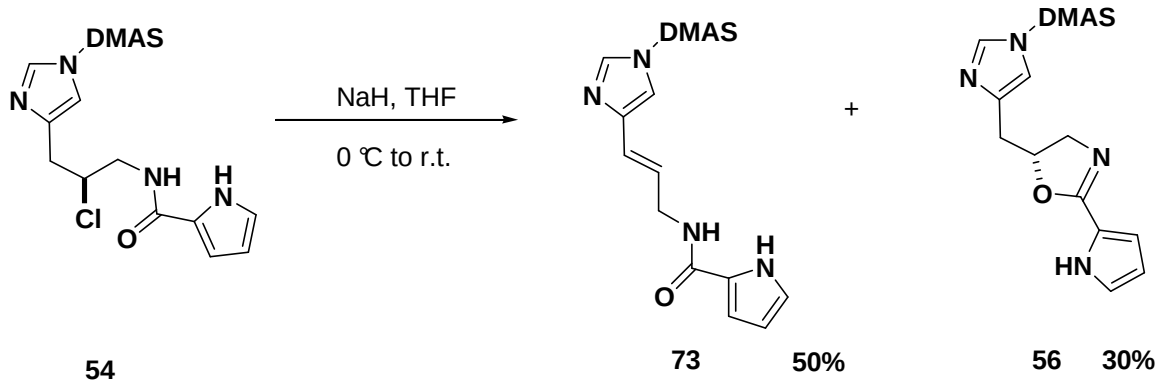
Figure 2.2 X-ray Crystal structure of compound **71**

In regards to advancing the total synthesis of cyclooroidin we attempted to determine conditions leading to the cyclization of compound **54** via the pyrrole nitrogen. A variety of different bases such as pyridine, Hunig's base, Et_3N, K_2CO_3 were evaluated however cyclization only occurred through the amide oxygen instead of pyrrole nitrogen (Scheme 2.14).



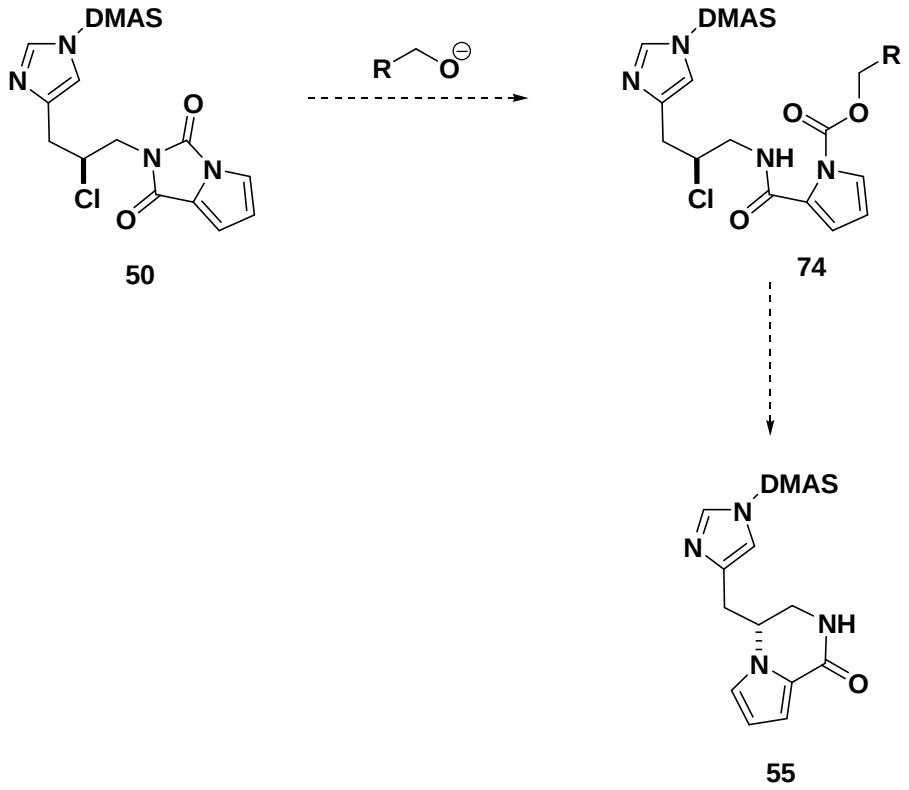
Scheme 2.14

Then we tried to cyclize compound **54** via the pyrrole nitrogen using a stronger base like NaH but a mixture of two compounds was obtained one of them being compound **56** and the other one was dehydrochlorinated compound **73** (Scheme 2.15).



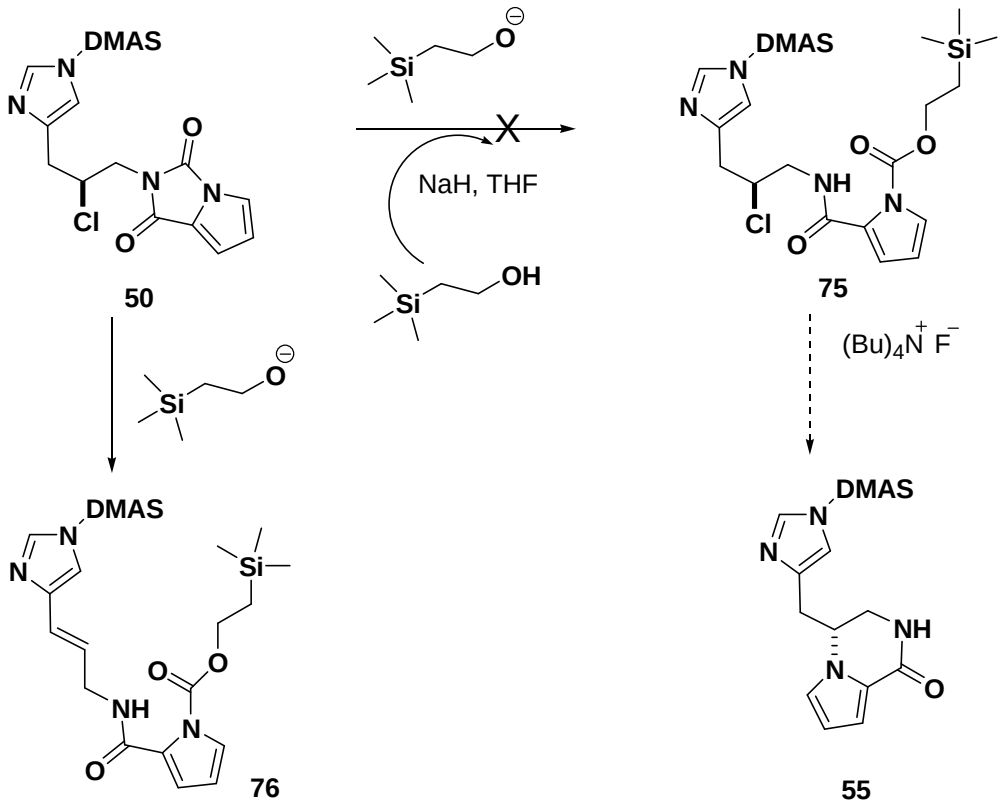
Scheme 2.15

Since our initial attempt to cyclize compound **54** directly via the pyrrole nitrogen had failed we considered using alternative nucleophiles to cleave the urea in compound **50**. This would result in the pyrrole nitrogen being protected; subsequent amide protection would then provide a differentially protected substrate. Addition of an appropriate reagent to the reaction mixture we can generate the pyrrole anion rather than the amide N-H (Scheme 2.16).[49]



Scheme 2.16

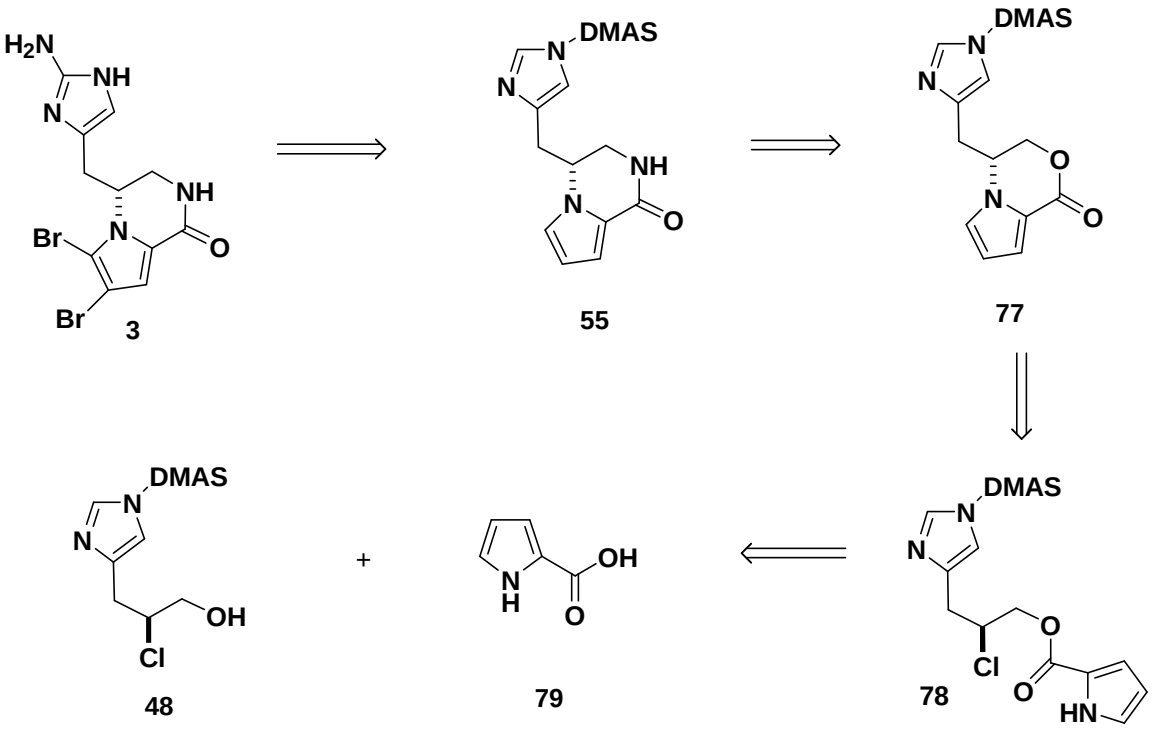
Unfortunately, attempts to execute this strategy using the anion generated from 2-trimethylsilyl alcohol were not successful. Instead of obtaining compound **75**, compound **77** was isolated which represents a dead end for synthesis of cyclooroidin (Scheme 2.17).



Scheme 2.17

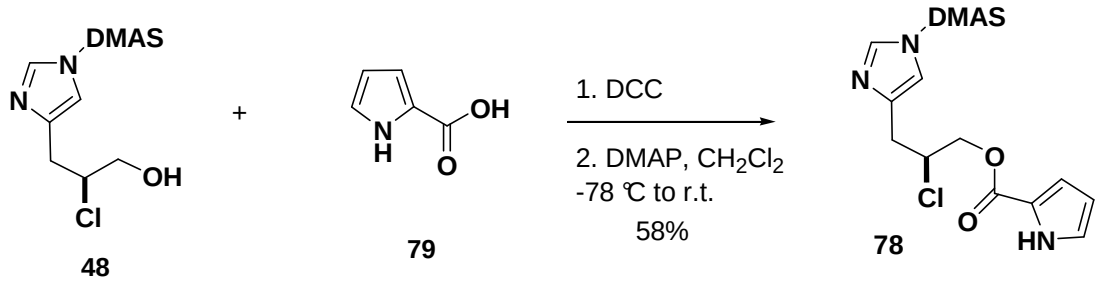
In order to address the incorrect cyclization manifold, the synthetic strategy was redesigned to avoid this pitfall and thus we developed the idea of replacing the amide with an ester. The advantage with oxygen atom as a linker is that there is no longer a problem of wrong cyclization through the amide oxygen instead of pyrrole nitrogen (Scheme 2.18). An alternative pathway involving protection of the amide nitrogen was considered, but this approach appeared to be lengthy.

2.5 Modified retrosynthetic analysis



Scheme 2.18

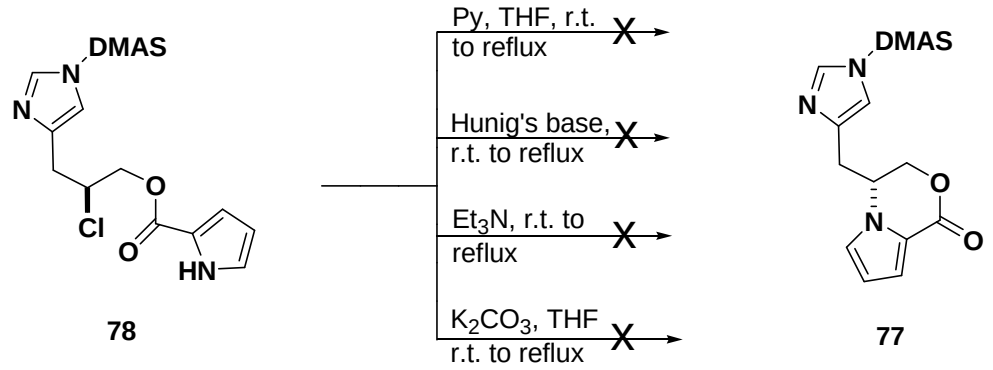
Accordingly, we esterified chloro alcohol **48** with pyrrole-2-carboxylic acid **79** in the presence of DCC,[50] obtaining ester **78** in 58% yield (Scheme 2.19).



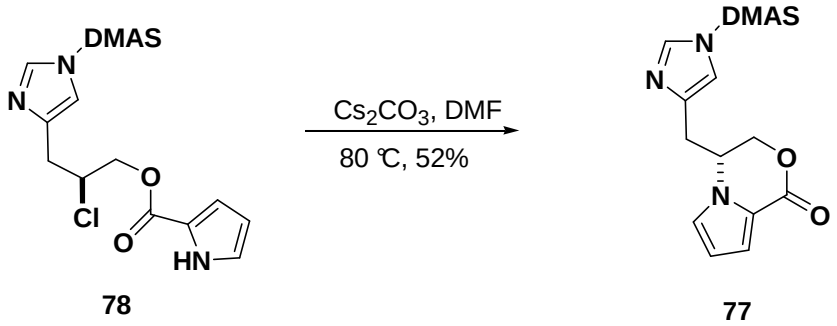
Scheme 2.19

Once we had compound **78** our next aim was to cyclize the molecule via pyrrole nitrogen. In this respect we tried mild conditions (Scheme 2.20) to remove the pyrrole N-H which in turn will cyclize intramolecularly in a S_N2 fashion. We already knew that strong bases like NaH should be avoided as they promote

dehydrochlorination. Initial studies with amine bases and K_2CO_3 were not successful. However, finally the desired cyclization was achieved by dissolving compound **78** in dry DMF and adding cesium carbonate[51] to the reaction mixture and heating the reaction mixture to 80 ºC for 12 h (Scheme 2.21).



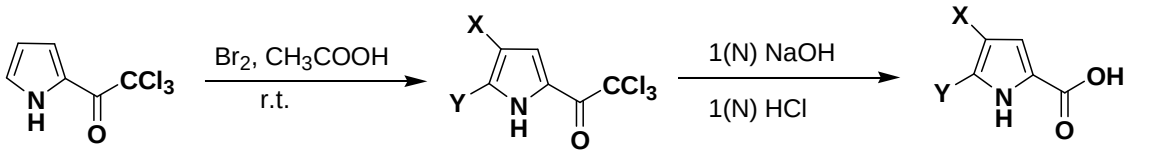
Scheme 2.20



Scheme 2.21

Once compound **77** was in hand our next goal was to introduce the bromine group into the pyrrole moiety as our target molecule cyclooroidin (**3**) has two bromine atom on the pyrrole moiety. In this regard we started with trichloroacetylpyrrole **80** and selectively performed either mono and dibromination on it and obtained known compounds **81** and **82**[52] which were further transformed to mono **83** and dibrominated pyrrole carboxylic acid **84** by

hydrolysis with NaOH[52] and finally neutralizing the solution with HCl (Scheme 2.22).



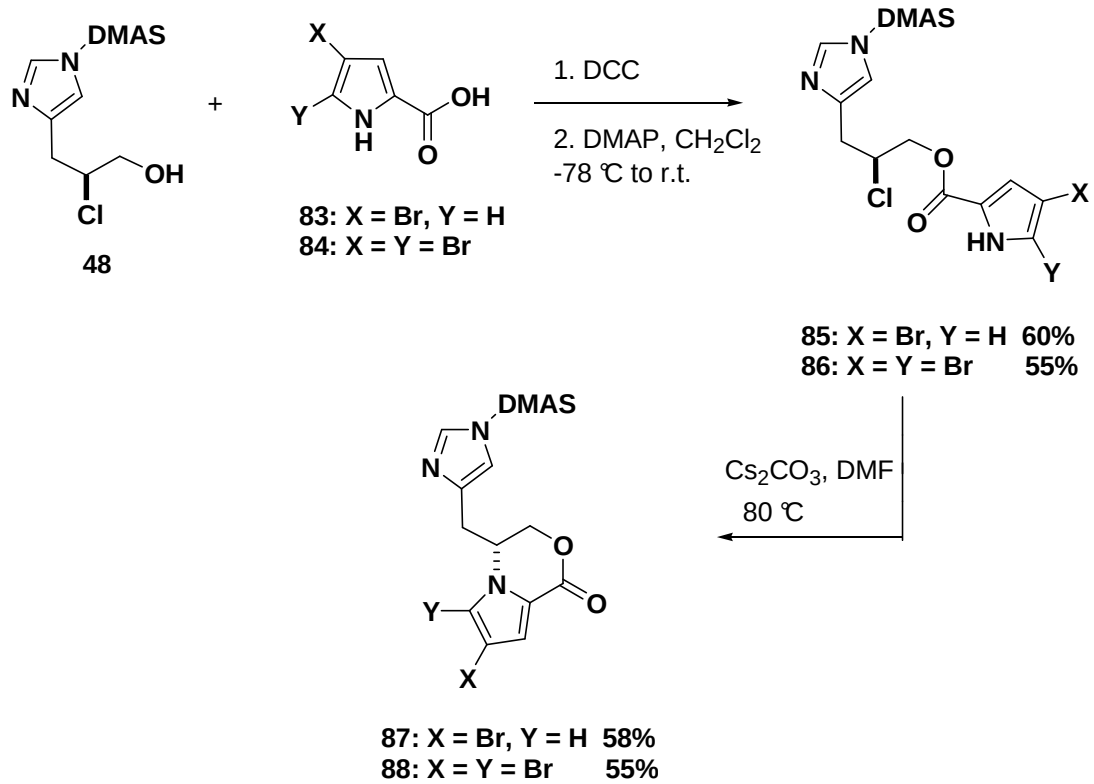
80

81: X = Br, Y = H 90%
82: X = Y = Br 90%

83: X = Br, Y = H 68%
84: X = Y = Br 60%

Scheme 2.22

Once the mono- and dibromocarboxylic acids **83** and **84** were prepared they were coupled with chloro alcohol **48** in presence of DCC[50] at -78 ºC to obtain the compound **85** and **86**. Subjection of both esters to cyclization by in DMF in the presence of cesium carbonate and then heating it to 80 ºC (Scheme 2.23) led to the formation of **87** and **88**.



48

83: X = Br, Y = H
84: X = Y = Br

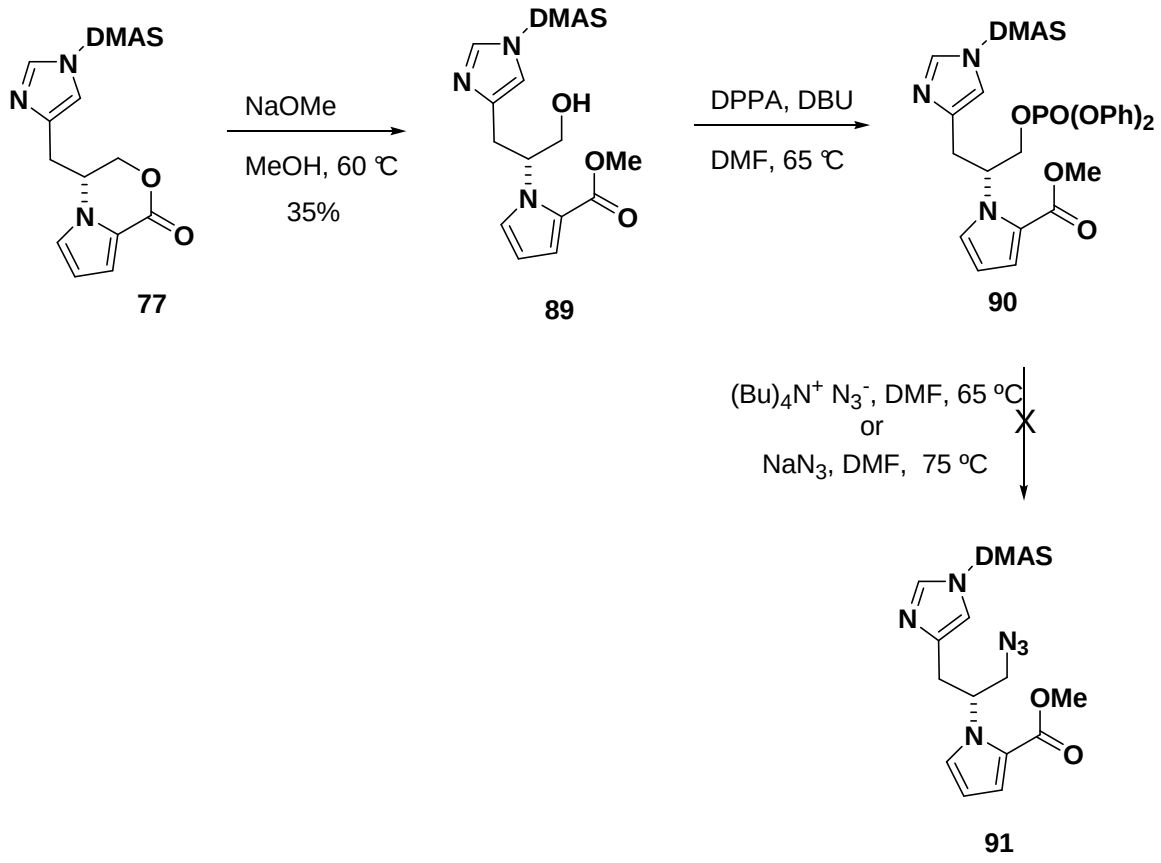
85: X = Br, Y = H 60%
86: X = Y = Br 55%

87: X = Br, Y = H 58%
88: X = Y = Br 55%

Scheme 2.23

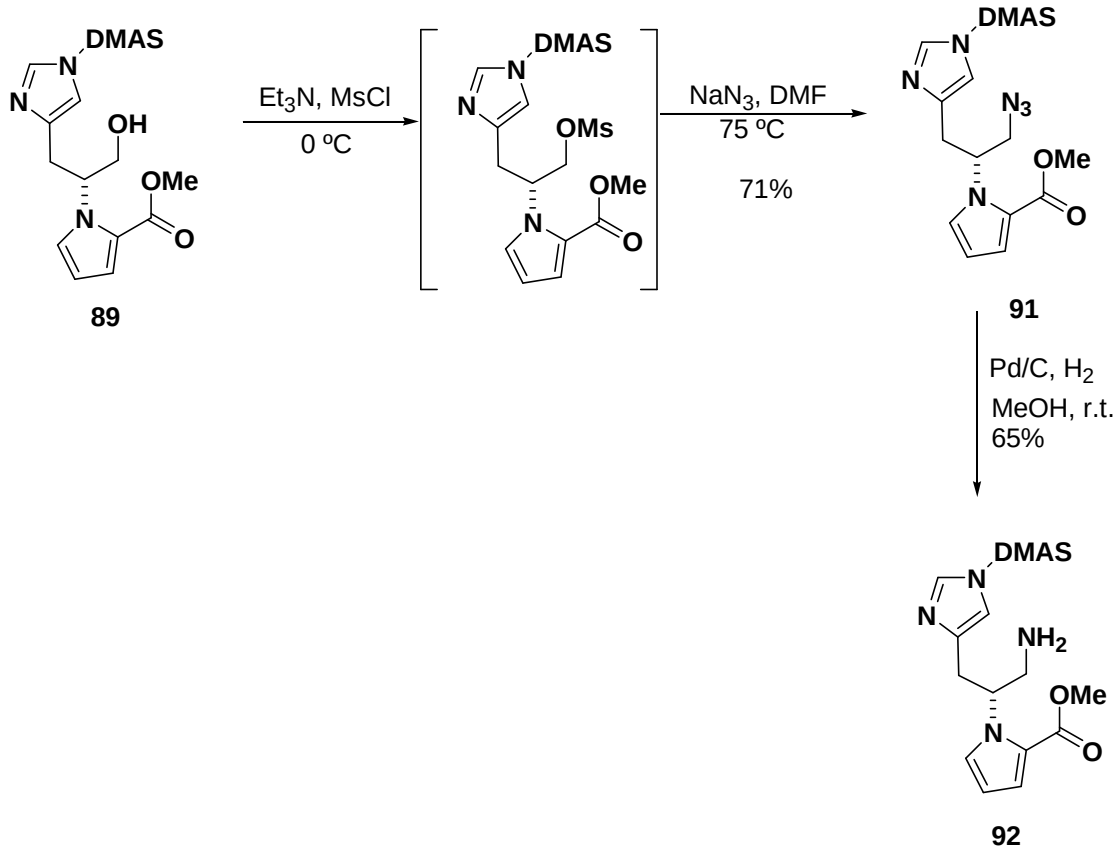
With the correct cyclized products in hand our next task was to replace the oxygen atom of the six membered lactone ring with a nitrogen atom. In order to achieve this transformation, it was decided to ring-open the lactone ring with sodium methoxide[53] to provide the hydroxy ester. Conversion of free alcohol to primary azide[54] and subsequent reduction of the azide to primary amine[55] should allow construction of the six membered ring.

The ring-opening of the lactone ring with sodium methoxide was achieved but the yield of the reaction was relatively low, providing the hydroxy ester **89** in 35% yield, with the remainder being recovered starting material (55%). The extent of conversion could not be improved suggesting that an equilibrium distribution has been reached between **89** and **77**. While this was not optimal, the two components can be separated and **77** can be resubjected to the ring-opening reaction. Compound **89** was subjected to DPPA and DBU in order to obtain the azide with the ultimate goal to covert this intermediate to the primary azide.[54] Interestingly the primary azide was not obtained rather only the phosphoryl intermediate **90** was isolated. Attempts to convert this phosporyl intermediate to the primary azide with an external nucleophile like sodium azide and heating the reaction mixture to 75 ºC were unsuccessful (Scheme 2.24).



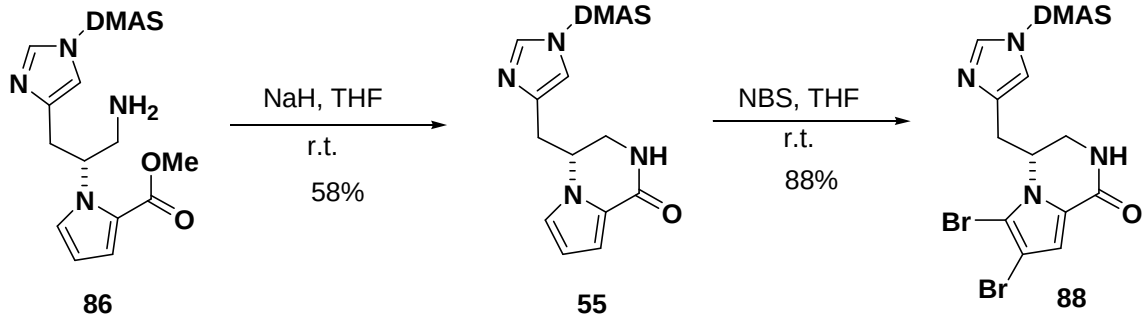
Scheme 2.24

Since this initial reaction sequence did not yield the primary azide, we decided to convert the primary alcohol to mesylate[56] and then displace the mesylate with azide ion to obtain the alkyl azide. Using this sequence the desired primary azide **91** was formed in 71% yield. The resulting azide was reduced to the primary amine[55] by using Pd/C under a hydrogen atmosphere at room temperature in 65% yield (Scheme 2.25).



Scheme 2.25

The primary amine **86** was cyclized by using NaH in THF at room temperature to obtain pyrazine **55** in 58% yield. Bromination of compound **55** using *N*-bromosuccinimide at room temperature provided dibrominated compound **93** in 88% yield (Scheme 2.26).[31] Note here the improved efficiency compared to the oxazolines described earlier in (scheme 2.9).



Scheme 2.26

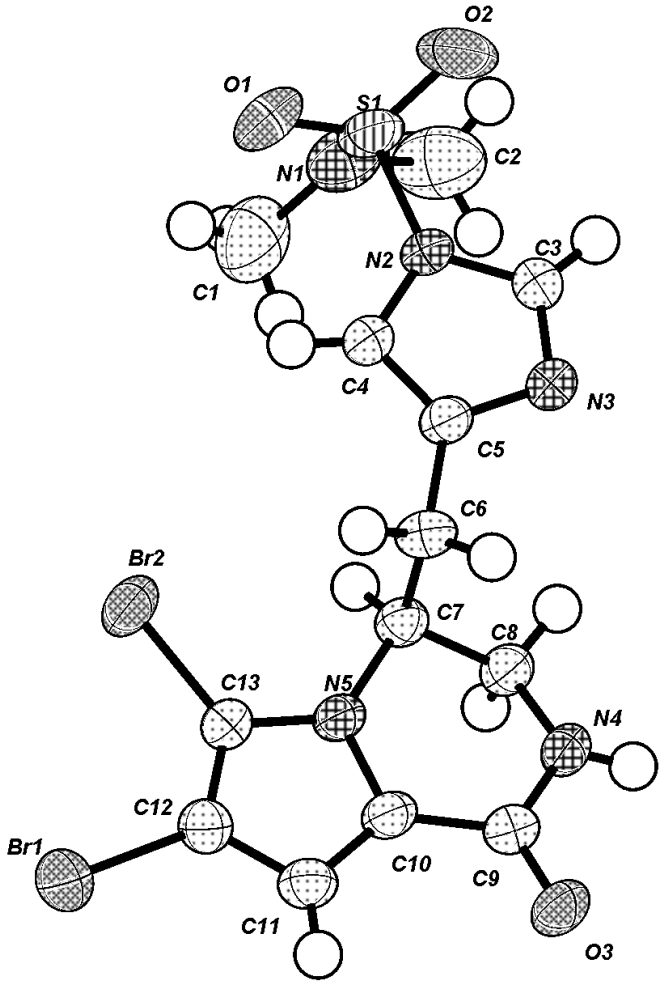
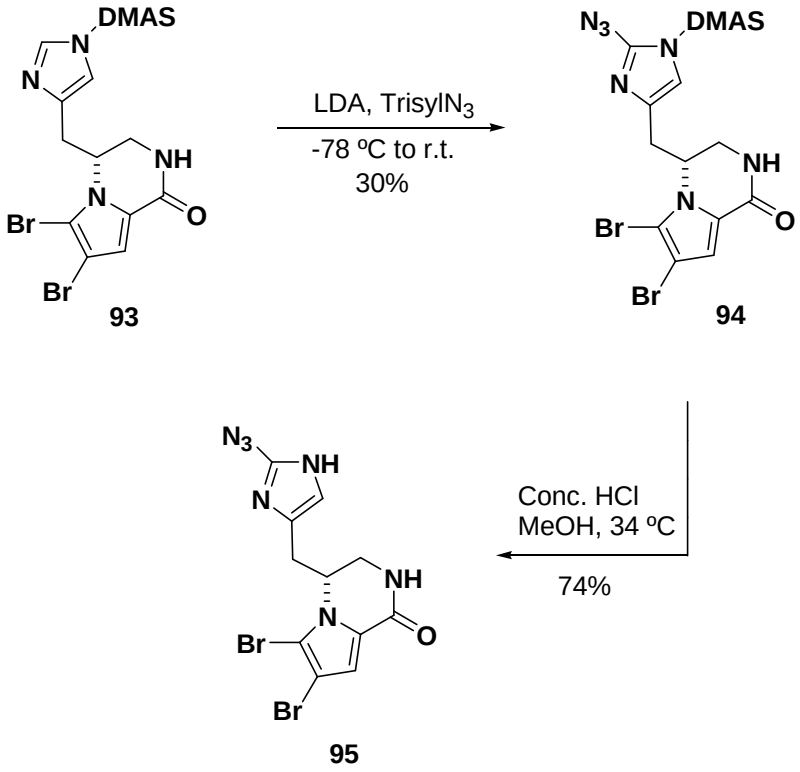


Figure 2.3 X-ray crystal structure of compound **88**

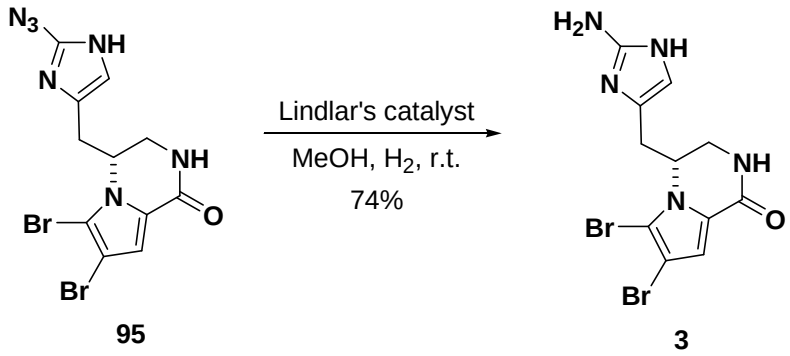
At this stage, all that remained to complete the synthesis was the incorporation of the C-2 amino group and removal of protecting group. Accordingly azide group was introduced at the C-2 position of the compound **93** by LDA at -78 ºC to generate the anion at the C-2 position and then treatment with TrisylN_3.[46] Attempts to improve the efficiency of the C-2 azidation were not successful. The

imidazole protecting group was removed by using conc. HCl in MeOH at 34 ºC to produce compound **94** (Scheme 2.27).[47]



Scheme 2.27

Azide reduction with Lindlar's catalyst at the C-2 position provided the primary amine, which was achieved in 74% yield (Scheme 2.28).[47] Finally the NMR data of our synthetically cyclooroidin matched with the isolated cyclooroidin and the specific rotation in our synthetic version was of correct magnitude ($[\alpha]_D$ = 10.6 (*c* = 0.02, MeOH)) but of opposite direction compared to the natural product ($[\alpha]_D$ -12 (c 0.02, MeOH)).



Scheme 2.28

2.6 Summary

In summary, we have developed an approach to the oxazoline-containing fragment of the oroidin dimer nagelamide R and the recently isolated nagelamide T. The key transformation involves the intramolecular cyclization of a pyrrolecarboxamide via the carbonyl oxygen leading to the formation of oxazoline, whose subsequent elaboration by bromination and azidation provides the fully functionalized northern fragment of nagelamide R. This chemistry suggests a possible biosynthetic pathway to the formation of nagelamide R through nagelamide B via activation and substitution of the amide carbonyl.

We have also developed a concise enantioselective route for total synthesis of cyclooroidin. The key steps here involved a coupling reaction between alcohol **48** and pyrrole 2-carboxylic acid followed by an intramolecular cyclization to form lactone ring **77**. The lactone was then converted to pyrazine **55**. Bromine was introduced into the pyrrole ring of the molecule **55** and finally azide was introduced at the C-2 position of the imidazole of the molecule **93**. Synthetic, cyclooroidin was obtained by removing the protecting group and finally reducing the C-2 azide to the amine.

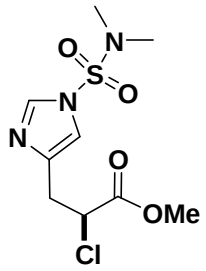
CHAPTER 3

EXPERIMENTAL DETAILS

3.1 General procedures

All reagents were purchased from commercial suppliers and were used as received unless otherwise noted. ^{1}H and ^{13}C NMR (δ in ppm) spectra were recorded in $CDCl_3$ (unless otherwise noted) at 300 and 75 MHz, respectively; using a JEOL Eclipse+ 300 spectrometer unless otherwise noted using residual $CHCl_3$ as reference (^{1}H NMR and carbon absorption of $CDCl_3$ for ^{13}C NMR). Infrared spectra were recorded either as neat films or as KBr pellets using a Bruker Vector 22 spectrometer. Elemental analyses were performed using a Perkin-Elmer 2400 CHN analyzer. Optical rotation was measured on a Perkin-Elmer 241MC polarimeter (*c* = g/100 mL) and the observed value was an average of 2-3 runs. The solvent used for optical rotation was MeOH unless otherwise noted. High resolution mass spectra (HR-MS) were obtained by Dr. Powell through the mass spectrometry service at the University of Florida, Gainesville, Florida.

(*S*)-methyl2-chloro-3-(1-(*N*,*N*-dimethylsulfamoyl)-1H-imidazol-4-yl)propanoate (47):

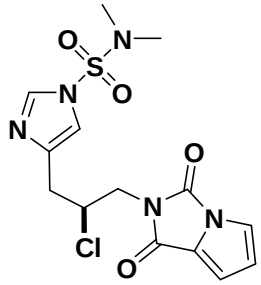


In a round bottom flask containing dry DMF (100 mL) chloroester **45**[1] (10.0 g, 0.05 mol) was added under N_2 atmosphere. The reaction mixture was stirred and to it triethylamine (11.1 mL, 0.08 mol) was added dropwise. Then the reaction mixture was cooled to 0 ºC and DMASCl (8.4 mL, 0.08 mol) was added dropwise. The reaction mixture was allowed to come to r.t. and then the reaction mixture was heated to 57 ºC and stirred for 9 h. Aqueous sat. $NaHCO_3$ (100 mL) and water (100 mL) were added to the reaction mixture and then the aqueous layer was repeatedly washed with ethyl acetate. The combined organic layer was dried using anhydrous Na_2SO_4 and concentrated to afford the crude product, which was purified by chromatography (hexane/EtOAc: 1/1) to give a colorless solid (11.1 g, 71%). $[\alpha]_D$ = -19.6 (*c* = 0.4, MeOH). m.p. 75-77 ºC. ^{1}H NMR: δ = 7.81 (s, 1H), 7.09 (s, 1H), 4.59 (t, *J* = 7.2 Hz, 1H), 3.75 (s, 3H), 3.30 (dd, *J* = 15.1, 6.9 Hz, 1H), 3.15 (dd, *J* = 15.1, 7.2 Hz, 1H), 2.82 (s, 6H); ^{13}C NMR: δ = 169.5, 138.4, 136.6, 115.7, 55.4, 53.1, 38.2, 33.7; FT-IR (neat, cm^{-1}): 3125, 2955, 1747, 1391, 1274, 1174, 1083, 963, 728, 594; HR-MS (*m/z*): calc for $[M+H]^+$ $C_9H_{15}ClN_3O_4S$ is 296.0472 found 296.0466.

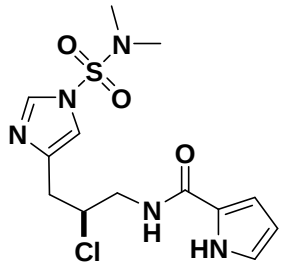
(*S*)-4-(2-chloro-3-hydroxypropyl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide

(48): The chloro ester **47** (2.00 g, 6.75 mmol) was dissolved in dry isopropyl alcohol (30 mL) under N_2 atmosphere. The reaction mixture was stirred and to it was added anhydrous $CaCl_2$ (2.24 g, 2.0 mmol) followed by the addition of anhydrous $NaBH_4$ (0.50 g, 1.3 mmol). The resulting reaction mixture was stirred 24 h. After completion of the reaction, water (40 mL) was added and then dil. HCl was added until the solution pH becomes ~ 4 and finally $NaHCO_3$ was added to reaction mixture to make the pH 8. Then the aqueous layer was repeatedly extracted with CH_2Cl_2. The combined organic solutions were dried using anhydrous Na_2SO_4 and concentrated. Purification of the crude product by chromatography (EtOAc) provided the product as a colorless liquid (1.4 g, 70%). $[\alpha]_D$ = -5.0 (*c* = 0.4, MeOH) ^{1}H NMR: δ = 7.84 (s, 1H), 7.12 (s, 1H), 4.31-4.28 (m, 1H), 3.74-3.72 (m, 2H), 3.70 (brs, 1H), 3.10 (d, *J* = 5.8 Hz, 2H), 2.84 (s, 6H). ^{13}C NMR ($CDCl_3$, 125.8 MHz): δ = 139.1, 136.5, 115.8, 65.8, 61.4, 38.3, 33.2. FT-IR (neat, cm^{-1}): 3127, 2927, 1647, 1570, 1473, 1391, 964, 837, 675. HR-MS (*m/z*): calc for $[M+H]^+$ $C_8H_{15}ClN_3O_3S$ 268.0523 Found 268.0528.

(*S*)-4-(2-chloro-3-(1,3-dioxo-1H-pyrrolo[1,2-c]imidazol-2(3H)-yl)propyl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide (50): In a round bottom flask containing hydantoin[2] **49** (0.61 g, 4.5 mmol), triphenylphosphine (1.18 g, 4.5 mmol), were dissolved in dry THF (32 mL) under an N_2 atmosphere. The reaction mixture was cooled to (0 ºC) and DIAD (1.06 g, 5.25 mmol) was added dropwise. After 30 min, chloroalcohol **48** (1.00 g, 3.75 mmol) dissolved in THF (5 mL) was added to the reaction mixture dropwise. The reaction mixture was stirred for 12 h and then concentrated. The crude product was purified by chromatography (hexane/EtOAc, 3:7) to provide **50** as a yellow oil (0.98 g, 68%). ^{1}H NMR: δ = 7.81 (s, 1H), 7.26 (s, 1H), 7.17 (s, 1H), 6.79 (d, *J* = 3.4 Hz, 1H), 6.47 (t, *J* = 3.4 Hz, 1H), 4.59 (quint, *J* = 7.6 Hz, 1H), 3.96–3.92 (m, 2H), 3.15 (dd, *J* = 15.1, 5.2 Hz, 1H), 3.04 (dd, *J* = 15.1, 7.6, Hz, 1H), 2.84 (s, 6H); ^{13}C NMR: δ = 158.1, 148.6, 139.1, 136.5, 125.1, 119.5, 117.8, 115.8, 114.2, 57.3, 44.5, 38.3, 34.9; FT-IR (neat, cm^{-1}): 2969, 2926, 1793, 1733, 1373, 1339, 1266. HR-MS (*m/z*): calc for $[M+H]^+$ $C_{14}H_{17}ClN_5O_4S$ 386.0690 Found 386.0681.

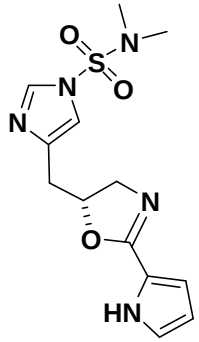


(*S*)-N-(2-chloro-3-(1-(*N*,*N*-dimethylsulfamoyl)-1H-imidazol-4-yl)propyl)-1H-pyrrole-2-carboxamide (54):



The Mitsunobu product **50** (0.90 g, 2.3 mmol) was dissolved in THF (10 mL) and to it was added 20% NaOH (7 mL, 1.40 g, 3.5 mmol). The reaction mixture was stirred at r.t. for 1 h. The organic solution was separated and the aqueous solution was extracted with EtOAc (3x100 mL). The combined organic solutions were dried with anhydrous Na_2SO_4 and concentrated, and the crude product was purified by chromatography ($CHCl_3$/MeOH, 99:1) to afford a colorless liquid (0.58 g, 70%). ^{1}H NMR: δ = 9.45 (bs, 1H), 7.86 (s, 1H), 7.15 (s, 1H), 6.93 (s, 1H), 6.70 (t, *J* = 6.5 Hz, 1H), 6.65 (d, *J* = 2.4 Hz, 1H), 6.25 (d, *J* = 3.1 Hz, 1H), 4.43 (m, 1H), 3.78 (m, 1H), 3.66 (m, 1H), 3.08 (d, *J* = 5.8 Hz, 2H), 2.85 (s, 6H); ^{13}C NMR: δ = 161.0, 139.0, 136.5, 125.6, 121.8, 115.9, 110.1, 109.4, 59.7, 44.3, 38.3, 34.6; FT-IR (neat, cm^{-1}): 2969, 2926, 1620, 1450, 1392, 1272, 1166, 1074, 953, 732. HR-MS (*m/z*): calc for $[M+H]^+$ $C_{13}H_{19}ClN_5O_3S$ 360.0897 Found 360.0887.

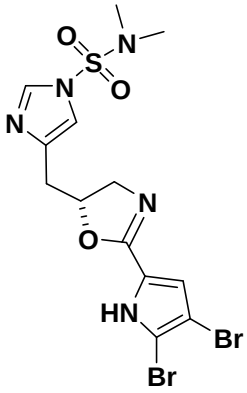
(*R*)-4-((2-(1H-pyrrol-2-yl)-4,5-dihydrooxazol-5-yl)methyl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide (56): The Mitsunobu product **50** (0.90 g, 2.0 mmol) was dissolved in THF (10 mL) and to it was added 20% NaOH (7 mL, 1.40 g, 3.5 mmol). The reaction mixture was heated at 75 ºC for 12 h. After cooling to r.t. the organic solution was separated and the aqueous solution was extracted with EtOAc (3x100 mL). The combined organic solutions were dried with anhydrous Na_2SO_4 and concentrated, and the crude product was purified by chromatography ($CHCl_3$/MeOH, 98:2) to afford a white solid (0.45 g, 60%). $[\alpha]_D$ = -18.0 (*c* = 0.6, MeOH). m.p. 155-157 ºC. ^{1}H NMR: δ = 9.71 (bs, 1H), 7.82 (s, 1H), 7.05 (s, 1H), 6.88 (s, 1H), 6.70 (d, *J* = 3.4 Hz, 1H), 6.23 (t, *J* = 3.1 Hz, 1H), 5.02 (m, 1H), 4.06 (dd, *J* = 14.4, 9.3 Hz, 1H), 3.85 (dd, *J* = 14.4, 6.9 Hz, 1H), 2.98 (d, *J* = 5.5 Hz, 2H), 2.69 (s, 6H); ^{13}C NMR: δ = 158.9, 138.8, 136.8, 122.5, 119.9, 115.4, 112.9, 109.7, 77.6, 58.3, 37.9, 33.6; FT-IR (neat, cm^{-1}): 2969, 2926, 1793, 1733, 1373, 1339, 1266. HR-MS (*m/z*): calc for $[M+H]^+$ $C_{13}H_{18}N_5O_3S$ 324.1130 Found 324.1120.



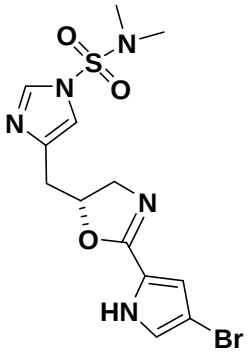
(*R*)-4-((2-(4,5-dibromo-1H-pyrrol-2-yl)-4,5-dihydrooxazol-5-yl)methyl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide (58) and (*R*)-4-((2-(4-bromo-1H-pyrrol-2-yl)-4,5-dihydrooxazol-5-yl)methyl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide (59): The cyclized compound **56** (400 mg, 1.23 mol) was dissolved in THF (12 mL). The reaction mixture was cooled to -20 ºC, NBS (330 mg, 1.83 mmol) was added and then stirred at -20 ºC for 8 h. The reaction mixture was

quenched by addition of aq. $NaHCO_3$ and then the organic layer was separated. The aqueous layer was extracted with EtOAC (3x50 mL), then the combined organic solutions were dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by chromatography ($CHCl_3$/MeOH, 98:2) providing **58** as a white solid (240 mg, 43%). $[\alpha]_D$ = -22.1 (*c* = 0.04, MeOH)

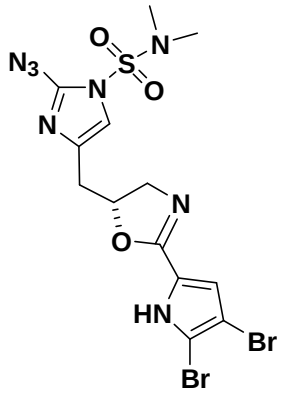
m.p. 62-64 ºC. ^{1}H NMR: δ = 7.84 (s, 1H), 7.07 (s, 1H), 6.69 (s, 1H), 5.05 (quint, *J* = 5.9 Hz, 1H), 4.12 (dd, *J* = 14.4, 7.6 Hz, 1H), 3.92 (dd, *J* = 14.2, 6.9 Hz, 1H), 3.02 (dd, *J* = 15.1, 6.4 Hz, 1H), 2.95 (dd, *J* = 14.7, 5.9 Hz, 1H), 2.79 (s, 6H); ^{13}C NMR: δ = 157.8, 138.7, 136.6, 121.4, 115.9, 115.3, 105.8, 99.6, 79.3, 58.1, 37.8, 33.6; FT-IR (neat, cm^{-1}): 1701, 1645, 1433, 1389, 1177, 1086, 962, 826, 738. HR-MS (*m/z*): calc for $[M+H]^+$ $C_{13}H_{16}Br_2N_5O_3S$ is 479.9341 found 479.9335.



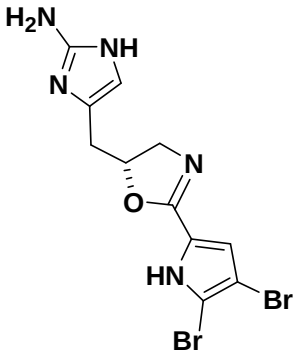
Further elution provided the monobrominated product **59** as a white solid (150 mg, 34%). $[\alpha]_D$ = -35.2 (*c* = 0.04, MeOH). m.p 145-147 ºC. ^{1}H NMR: δ = 7.81 (s, 1H), 7.05 (s, 1H), 6.85 (s, 1H), 6.66 (s, 1H), 5.04–5.02 (m, 1H), 4.06 (dd, *J* = 13.8, 9.6 Hz, 1H), 3.87 (dd, *J* = 14.7, 6.9 Hz, 1H), 2.98–2.94 (m, 2H) 2.71 (s, 6H); ^{13}C NMR: δ = 157.9, 138.9, 136.6, 122.2, 120.5, 115.3, 114.7, 97.4, 78.6, 58.3, 38.0, 33.6; FT-IR (neat, cm^{-1}): 1649, 1559, 1537, 1504, 1457, 1398, 1173, 1078, 962. HR-MS (*m/z*): calc for $[M+H]^+$ $C_{13}H_{17}BrN_5O_3S$ 402.0235 Found 402.0229.



(*R*)-2-azido-4-((2-(4,5-dibromo-1H-pyrrol-2-yl)-4,5-dihydrooxazol-5-yl)methyl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide (60): Dibrromopyrrole **58** (160 mg, 0.31 mmol) was dissolved in anhydrous THF (8 mL) and the reaction mixture was cooled to -78 ºC and 0.5 M LDA (2.72 mL, 4.1 eq) in THF was added dropwise to the reaction mixture. The reaction mixture was left stirring for 30 min at -78 °C and then TsN_3 (0.28 g, 1.07 mmol) was added. The reaction mixture was allowed to come to r.t. and then stirred for an additional 1 h, followed by addition of aqueous NH_4Cl to quench the reaction mixture. The organic layer was separated and the aqueous layer was extracted with EtOAC (3x50 mL). The organic solutions were combined, dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by chromatography ($CHCl_3$/MeOH, 98:2) giving **22** as a white solid (120 mg, 71%). $[\alpha]_D$ = -36.5 (*c* = 0.04, MeOH). m.p. 70-72 ºC. ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 6.93 (s, 1H), 6.69 (s, 1H), 5.01 (quint, *J* = 6.4 Hz, 1H), 4.11 (dd, *J* = 14.5, 7.6 Hz, 1H), 3.87 (dd, *J* = 14.2, 6.8 Hz, 1H), 2.93(s, 6H), 2.91- 2.88 (m, 2H); ^{13}C NMR: δ = 143.7, 139.8, 135.1, 129.4, 126.3, 121.3, 116.5, 116.3, 78.9, 57.8, 38.8, 33.3; FT-IR (neat, cm^{-1}): 2145, 1649, 1534, 1509, 1457, 1398, 1336, 1181, 1086, 990. HR-MS (*m/z*): calc for $[M+H]^+$ $C_{13}H_{15}Br_2N_8O_3S$ is 520.9355 found 520.9355.

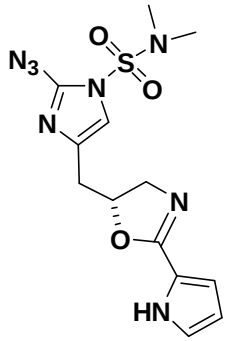


4-(((*R*)-2-(4,5-dibromo-1H-pyrrol-2-yl)-4,5-dihydrooxazol-5-yl)methyl)-2,3-dihydro-1H-imidazol-2-amine (57):[47]



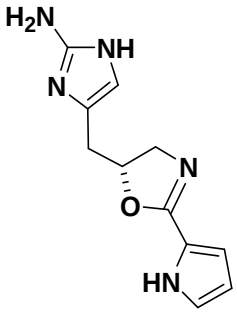
Conc. HCl (0.003 mL) was added to the solution of compound **60** (100 mg, 0.19 mmol) in methanol (3.5 mL) and then stirred at 34 ºC for 12 h. Then the mixture was concentrated under vacuum and the residue was neutralized with $NaHCO_3$ and extracted with EtOAc (3 times). The organic extracts were combined, concentrated and purified by column chromatography ($CHCl_3$/methanol/NH_3, 94:5:1) to give the free imidazole (50 mg, 63%) as yellow thick liquid. This compound (30 mg, 0.05 mmol) was dissolved in methanol (2 mL) and Lindlar catalyst (20 mg) was added and the reaction mixture was stirred for 8 h under a hydrogen atmosphere (balloon). Finally the reaction mixture was filtered through a bed of Celite and then the crude reaction mixture was loaded onto a column as a solid, preadsorbed on silica gel. Then the crude product was purified by chromatography (CH_2Cl_2/MeOH/NH_4OH: 85/14/1). A colorless thick liquid was obtained (13 mg, 46%). $[\alpha]_D$ = -8.5 (*c* = 0.04, MeOH) ^{1}H NMR (CD_3OD): δ = 6.73 (s, 1H), 6.37 (s, 1H), 4.94–4.87 (m, 1H), 3.99 (dd, *J* = 15.2, 10.3 Hz, 1H), 3.69 (dd, *J* = 14.4, 5.8 Hz, 1H), 2.78–2.72 (m , 2H); ^{13}C NMR (CD_3OD): δ = 157.7, 149.6, 128.4, 121.5, 115.0, 111.1, 104.9, 99.1, 79.6, 58.4, 32.1. This compound has been recently been described in the literature.[43b]

(*R*)-4-((2-(1H-pyrrol-2-yl)-4,5-dihydrooxazol-5-yl)methyl)-2-azido-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide (62):



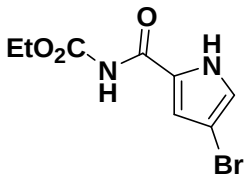
The cyclized compound **56** (160 mg, 0.49 mmol) was dissolved in anhydrous THF (8 mL) and the reaction mixture was cooled to -78 ºC and 0.5 M LDA (2.06 mL, 2.1 eq) was added dropwise to the reaction mixture. The reaction mixture was left stirring for 30 min at -78 °C and then TsN_3 (0.30 g, 1.56 mmol) was added. The reaction mixture was allowed to come to r.t. and then stirred for an additional 1 h, followed by addition of aqueous NH_4Cl to quench the reaction mixture. The organic layer was separated and the aqueous layer was extracted with EtOAC (3x50 mL). The organic solutions were combined, dried with anhydrous Na_2SO_4 and concentrated. Then the crude product was purified by chromatography ($CHCl_3$/MeOH, 98:2) giving **62** as a yellow liquid (150 mg, 84%). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 6.92 (s, 1H), 6.89 (s, 1H), 6.72 (d, *J* = 4.1 Hz, 1H), 6.23 (t, *J* = 3.7 Hz, 1H), 4.96 (quint, *J* = 5.9 Hz, 1H), 4.05 (dd, *J* = 15.1, 8.7 Hz, 1H), 3.78 (dd, *J* = 13.3, 7.3 Hz, 1H), 2.93 (s, 6H), 2.89- 2.82 (m, 2H); ^{13}C NMR: δ = 158.5, 134.8, 121.9, 120.6, 116.8, 112.6, 110.0, 78.7, 58.7, 38.4, 33.8; FT-IR (neat, cm^{-1}): 2971, 2145, 1651, 1534, 1509, 1457, 1394, 1342, 1170, 1067, 950. HR-MS (*m/z*): calc for $[M+H]^+$ $C_{13}H_{17}N_8O_3S$ is 365.1139 found 365.1143.

4-(((*R*)-2-(1H-pyrrol-2-yl)-4,5-dihydrooxazol-5-yl)methyl)-2,3-dihydro-1H-imidazol-2-amine (64):



Conc. HCl (0.004 mL) was added to the solution of compound **62** (150 mg, 0.41 mmol) in methanol (3.5 mL) and stirred at 34 ºC for 12 h. Then the mixture was concentrated under vacuum and the residue was neutralized with $NaHCO_3$ and extracted with EtOAc (3 times). The organic layer were combined, concentrate and purified by column chromatography ($CHCl_3$/methanol/NH_4OH, 92:7:1) to give DMAS-deprotected product (76 mg, 72%) as yellow thick liquid. This compound (50 mg, 0.19 mmol) was dissolved in methanol (3 mL) and Lindlar catalyst (30 mg) was added and the reaction mixture was stirred for 8 h under a hydrogen atmosphere (balloon). Finally the reaction mixture was filtered through a bed of Celite and then the crude reaction mixture was loaded onto a column as a solid, preadsorbed on silica gel. Then the crude product was purified by chromatography (CH_2Cl_2/MeOH/NH_3: 82/17/1). A colorless thick liquid **64** was obtained (26 mg, 56%). ^{1}H NMR (CD_3OD): δ = 6.89 (s, 1H), 6.72 (d, *J* = 3.7 Hz, 1H), 6.37 (s, 1H), 6.12 (t, *J* = 3.4 Hz, 1H), 4.95–4.90 (m, 1H), 3.94 (dd, *J* = 13.7, 9.4 Hz, 1H), 3.69 (dd, *J* = 14.1, 6.8 Hz, 1H), 2.82 (dd, *J* = 14.8, 5.8 Hz, 1H), 2.74 (dd, *J* = 14.8, 6.5 Hz, 1H); ^{13}C NMR (CD_3OD): δ = 159.5, 149.5, 128.5, 121.8, 119.2, 112.8, 111.3, 109.1, 78.9, 58.8, 32.2.; FT-IR (neat, cm^{-1}): 3050, 2887, 1601, 1407, 1364, 1260, 1164, 1054, 927. HR-MS (*m/z*): calc for $[M+H]^+$ $C_{11}H_{14}N_5O$ is 232.1198 found 232.1193.

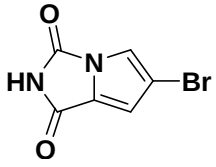
Ethyl 4-bromo-1H-pyrrole-2-carbonylcarbamate (65):



Ethyl-1-pyrrole-2-carbonylcarbamate (3.0 g, 0.02 mol, 1 eq) was dissolved in AcOH (59 mL). A solution of bromine (0.76 mL, 0.01 mol, 0.9 eq) in AcOH (6.4 mL) was added dropwise at r.t. The reaction mixture was stirred for 30 mins, after which a white precipitate appeared in the reaction flask. The resulting mixture was filtered and the collected solids were washed with cold dichloromethane (10 mL). Then dried under vacuum to give white solid (2.4 g, 56%). m.p. 193-195 ºC. ^{1}H NMR (DMSO-d_6): δ = 12.14 (b, 1H), 10.56 (s, 1H), 7.21 (s, 1H), 7.13 (s, 1H), 4.10 (q, *J* = 7.3 Hz, 2H) 1.22 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (DMSO): δ = 157.8, 151.8, 125.9, 124.8, 115.5, 96.1, 61.5, 14.8; FT-IR (neat, cm^{-1}): 3126, 2975, 2931, 1707, 1681, 1370, 1187, 1002, 979, 919, 736. HR-MS (*m/z*): calc for $[M+H]^+$ $C_8H_{10}BrN_2O_3$ is 260.9875 found 260.9869.

6-bromo-1H-pyrrolo[1,2-c]imidazole-1,3(2H)-dione (67):

Monobromopyrrole **65** (2.0 g, 9.3 mmol) was mixed with silicone oil (2 mL) in a

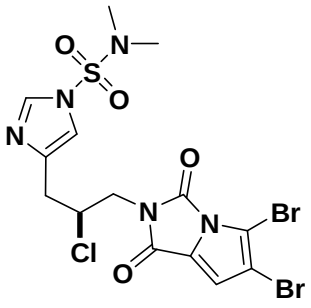


round bottom flask which was evacuated (40 mmHg) and heated to 180-185 ºC. After 4 h, the reaction was cooled and then the residue was crushed. Hexane was added and the solids were collected by filtration and washed repeatedly with hexane. The procedure was repeated with (1.5 mL) silicone oil. The product was purified by chromatography (hexane/EtOAc: 8/2). A yellow solid was thus obtained (750 mg, 47%). m.p. 216-218 ºC. ^{1}H NMR (DMSO-d_6, 500 MHz): δ = 11.60 (b, 1H), 7.81

(s, 1H), 7.01 (s, 1H); ^{13}C NMR (DMSO- d_6, 125.8 MHz): δ = 159.2, 148.7, 126.9, 119.1, 113.9, 104.7; FT-IR (neat, cm^{-1}): 3285, 1801, 1733, 1558, 1452, 1409, 1371, 1311. Anal. Calcd. for $C_6H_3BrN_2O_2$: C, 33.52; H, 1.41; N, 13.03. Found: C, 33.62; H, 1.54; N, 12.62.

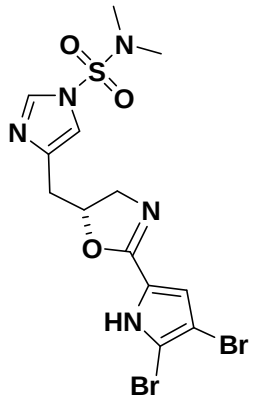
(*S*)-4-(3-(6-bromo-1,3-dioxo-1H-pyrrolo[1,2-c]imidazol-2(3H)-yl)-2-chloropropyl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide (69): In a round bottom flask containing the bromohydantoin **67** (120 mg, 0.56 mmol), triphenylphosphine (150 mg, 0.56 mmol), was dissolved in dry THF (5 mL) under N_2 atmosphere. The mixture was cooled to (0 ºC) and DEAD (0.26 mL, 0.56 mmol, 40% wt in toluene) was added dropwise. After 30 min, the chloroalcohol **48** (100 mg, 0.37 mmol) dissolved in THF (2 mL) was added to the reaction mixture was dropwise. The reaction mixture was stirred for 12 h, concentrated and then the crude product was purified by chromatography (hexane/EtOAc, 6:4) providing a colorless solid (0.15 g, 86%). $[\alpha]_D$ = -5.0 (*c* = 0.04, MeOH). m.p. 154-156 ºC. ^{1}H NMR: δ = 7.82 (s, 1H), 7.29 (s, 1H), 7.16 (s, 1H), 6.79 (s, 1H), 4.60–4.56 (m, 1H), 3.96–3.93 (m, 2H), 3.10 (dd, *J* = 15.1, 5.5 Hz, 1H), 3.06 (dd, *J* = 14.8, 7.6 Hz, 1H), 2.85 (s, 6H); ^{13}C NMR: δ = 157.4, 147.6, 138.9, 136.5, 124.8, 118.7, 115.8, 115.7, 105.9, 57.2, 44.7, 38.2, 34.9; FT-IR (neat, cm^{-1}): 1797, 1733, 1562, 1392, 1272, 1166, 1074, 953, 732. HR-MS (*m/z*): calc for $[M+H]^+$ $C_{14}H_{16}BrClN_5O_4S$ is 463.9795 found 463.9789.

(*S*)-4-(2-chloro-3-(5,6-dibromo-1,3-dioxo-1H-pyrrolo[1,2-c]imidazol-2(3H)-yl)propyl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide (70):



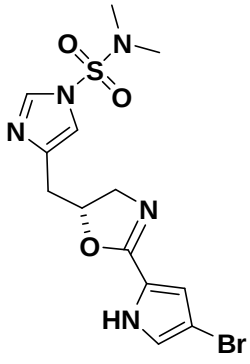
Dibromohydantoin[3] **68** (100 mg, 0.34 mmol) and triphenylphosphine (90 mg, 0.33 mmol) were dissolved in dry THF (5 mL) under N_2 atmosphere and cooled to 0 ºC. DEAD (0.15 mL, 0.33 mmol, 40% wt in toluene) was added dropwise then stirred for 30 min. Chloroalcohol **48** (60 mg, 0.22 mmol) dissolved in THF (3 mL) was added to the reaction mixture was dropwise. The reaction mixture was stirred for 12 h and then concentrated. The crude product was purified by chromatography (hexane/EtOAc, 7:3) affording a yellow liquid (0.10 g, 82%). $[\alpha]_D$ = -3.0 (*c* = 0.04, MeOH). ^{1}H NMR: δ = 7.82 (s, 1H), 7.16 (s, 1H), 6.85 (s, 1H), 4.61–4.56 (m, 1H), 3.96–3.94 (m, 2H), 3.10 (dd, *J* = 15.1, 5.5 Hz, 1H), 3.04 (dd, *J* = 14.8, 7.6 Hz, 1H), 2.84 (s, 6H); ^{13}C NMR: δ = 156.1, 146.8, 139.1, 136.6, 125.3, 115.9, 115.7, 109.4, 105.0, 57.1, 44.5, 38.0, 34.8; FT-IR (neat, cm^{-1}): 2907, 2359, 1796, 1734, 1423, 1388, 1260, 1167, 1093, 953, 736. HR-MS (*m/z*): calc for $[M+H]^+$ $C_{14}H_{15}Br_2ClN_5O_4S$ is 541.8900 found 541.9506.

(*R*)-4-((2-(4,5-dibromo-1H-pyrrol-2-yl)-4,5-dihydrooxazol-5-yl)methyl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide (58):



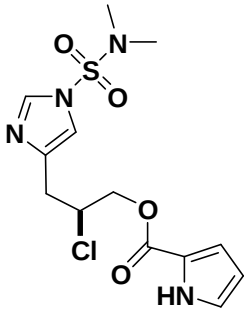
The Mitsunobu product (80 mg, 0.15 mmol) was dissolved in THF (6 mL) and to it (0.4 mL, 80 mg, 2.2 mmol) of 20% NaOH was added. The reaction mixture was heated to 75 ºC for 6 h. After cooling to r.t., the organic solution was separated and the aqueous solution was extracted with EtOAc (3x50 mL) times. The organic solutions were combined and dried with anhydrous Na_2SO_4 and concentrated. Then the crude product was purified by chromatography ($CHCl_3$/MeOH, 98:2) providing a white solid (40 mg, 57%) which was identical in all respects to that described above.

(*R*)-4-((2-(4-bromo-1H-pyrrol-2-yl)-4,5-dihydrooxazol-5-yl)methyl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide (59): The Mitsunobu product (110 mg, 0.24 mmol) was dissolved in THF (6 mL) and 20% NaOH (0.7 mL) was added. The reaction mixture was heated to 75 ºC for 8 h. After cooling to r.t., the organic solution was separated and the aqueous solution was extracted with EtOAc (3x50 mL). The organic solutions were combined together, dried with anhydrous Na_2SO_4 and concentrated.



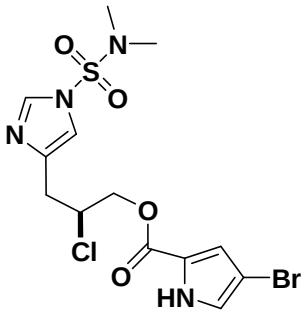
The crude product was purified by chromatography ($CHCl_3$/MeOH, 98:2) providing a white solid (60 mg, 64%) that was identical in all respects to the material described above.

(*S*)-2-chloro-3-(1-(*N*,*N*-dimethylsulfamoyl)-1H-imidazol-4-yl)propyl 1H-pyrrole-2-carboxylate (78):



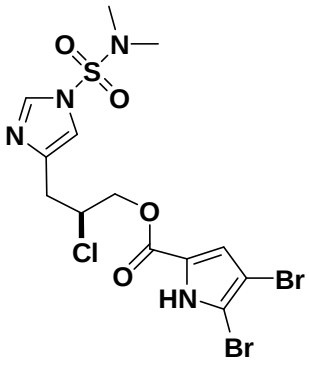
In a round bottom flask the alcohol **48** (2.60 g, 9.73 mmol), acid **79** (1.60 g, 14.4 mmol), DMAP (120 mg, 0.98 mmol) and camphorsulfonic acid (140 mg, 0.60 mmol) were dissolved in dry CH_2Cl_2 (150 mL). The mixture was cooled to (-78 ºC) and DCC (2.80 g, 13.6 mmol) in dry CH_2Cl_2 (8 mL) was added dropwise. The reaction mixture was allowed to warm up to r.t. and stirred for an additional 8 h. The resulting mixture was filtered through Celite and the filter cake was washed with CH_2Cl_2. Concentration of the filtrate provided the crude product, which was purified by chromatography (hexane/EtOAc, 1:9) to provide **78** as a thick colorless liquid (2.04 g, 58%). $[\alpha]_D$ = -2.0 (*c* = 0.04, MeOH). ^{1}H NMR: δ = 9.36 (b, 1H), 7.85 (d, *J* = 1.0 Hz, 1H), 7.14 (s, 1H), 7.00-6.96 (m, 2H), 6.28 (q, *J* = 3.1 Hz, 1H), 4.55-4.44 (m, 3H), 3.21 (dd, *J* = 14.4, 4.8 Hz, 1H), 3.02 (dd, *J* = 14.4, 7.6 Hz, 1H), 2.84 (s, 6H); ^{13}C NMR: δ = 160.4, 139.3, 136.6, 123.5, 122.0, 116.2, 115.7, 110.8, 66.5, 57.6, 38.3, 33.9; FT-IR (neat, cm^{-1}): 3150, 2928, 1695, 1422, 1396, 1173, 1074, 959, 722, 599; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{13}H_{18}ClN_4O_4S$ 361.0737 found 361.0747.

(*S*)-2-chloro-3-(1-(*N*,*N*-dimethylsulfamoyl)-1H-imidazol-4-yl)propyl 4-bromo-1H-pyrrole-2-carboxylate (85):



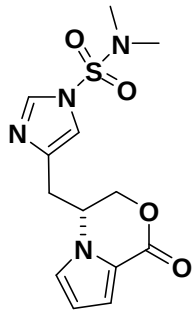
In a round bottom flask the alcohol **48** (1.00 g, 3.74 mmol), acid **83** (1.06 g, 5.61 mmol), DMAP (45 mg, 0.37 mmol) and camphorsulfonic acid (52 mg, 0.22 mmol) were dissolved in dry CH_2Cl_2 (100 mL). The mixture was cooled (-78 ºC) and DCC (1.16 g, 5.61 mmol) in dry CH_2Cl_2 (4 mL) was added dropwise. The reaction mixture was allowed to warm up to r.t. and stirred for an additional 8 h. The resulting mixture was filtered through Celite and the filter cake was washed with CH_2Cl_2. Concentration of the filtrate provided the crude product, which was purified by chromatography (hexane/EtOAc, 1:9) to provide **85** as a thick colorless liquid (0.88 g, 54%). $[\alpha]_D$ = -1.5 (*c* = 0.06, MeOH). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 9.80 (b, 1H), 7.96 (s, 1H), 7.17 (s, 1H), 6.97-6.95 (m, 2H), 4.50-4.41 (m, 3H), 3.22 (dd, *J* = 15.1, 4.1 Hz, 1H), 3.06 (dd, *J* = 15.1, 7.3 Hz, 1H), 2.86 (s, 6H); ^{13}C NMR ($CDCl_3$ 125.8 MHz): δ = 159.5, 138.6, 136.4, 123.4, 122.4, 118.7, 117.8, 116.0, 98.1, 66.9, 57.2, 38.3, 33.6; FT-IR (neat, cm^{-1}): 3095, 2915, 1712, 1540, 1393, 1311, 1173, 1079, 969, 725, 590; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{13}H_{17}BrClN_4O_4S$ 438.9837 found 438.9843.

(*S*)-2-chloro-3-(1-(*N*,*N*-dimethylsulfamoyl)-1H-imidazol-4-yl)propyl 4,5-dibromo-1H-pyrrole-2-carboxylate (86):



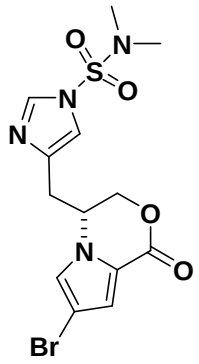
In a round bottom flask the alcohol **48** (200 mg, 0.75 mmol), acid **84** (300 mg, 1.12 mmol), DMAP (10 mg, 0.07 mmol) and camphorsulfonic acid (10 mg, 0.04 mmol) were dissolved in dry CH_2Cl_2 (20 mL). The mixture was cooled to (-78 ºC) and DCC (230 mg, 1.12 mmol) in dry CH_2Cl_2 (4 mL) was added dropwise. The reaction mixture was allowed to warm up to r.t. and stirred for an additional 8 h. The resulting mixture was filtered through Celite and the filter cake was washed with CH_2Cl_2. Concentration of the filtrate provided the crude product, which was purified by chromatography (hexane/EtOAc, 1:9) to provide **86** as a thick colorless liquid (210 mg, 55%). $[\alpha]_D$ = -1.4 (*c* = 0.06, MeOH). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 10.68 (b, 1H), 7.90 (s, 1H), 7.16 (s, 1H), 6.94 (s, 1H), 4.50-4.41 (m, 3H), 3.21 (dd, *J* = 15.1, 4.6 Hz, 1H), 3.06 (dd, *J* = 15.1, 6.9 Hz, 1H), 2.86 (s, 6H); ^{13}C NMR: δ = 158.8, 138.8, 136.6, 123.2, 118.7, 116.1, 107.7, 100.9, 66.8, 57.0, 38.3, 33.7; FT-IR (neat, cm^{-1}): 3085, 2890, 1706, 1405, 1323, 1182, 1082, 959, 907, 722, 584; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{13}H_{16}Br_2ClN_4O_4S$ 516.8948 found 516.8997.

(*R*)-*N*,*N*-dimethyl-4-((1-oxo-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazin-4-yl)methyl)-1H-imidazole-1-sulfonamide (77):



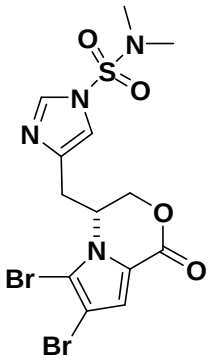
In a round bottom flask compound **78** (350 mg, 0.97 mmol) was dissolved in DMF (10 mL) and cesium carbonate (3.16 g, 9.70 mmol) was added to the reaction mixture. The reaction mixture was heated at 80 ºC for 12 h. Water was added to the reaction mixture and it was extracted with EtOAc. The organic extract was dried with anhydrous Na_2SO_4, concentrated, and the residue was purified by chromatography (EtOAc) providing **77** as a thick colorless liquid (163 mg, 52%). $[\alpha]_D$ = -16.0 (*c* = 0.02, MeOH). ^{1}H NMR: δ = 8.01 (d, *J* = 1.0 Hz, 1H), 7.20 (dd, *J* = 3.8, 1.4 Hz, 1H), 6.99 (d, *J* = 0.7 Hz, 1H), 6.80 (t, *J* = 1.7 Hz, 1H), 6.33 (dd, *J* = 2.4, 1.7 Hz, 1H), 4.81-4.77 (m, 2H), 4.61 (dd, *J* = 12.7, 3.1 Hz, 1H), 3.23 (d, *J* = 7.2 Hz, 2H), 2.95 (s, 6H); ^{13}C NMR: δ = 158.7, 138.5, 137.0, 124.3, 118.8, 117.9, 115.8, 110.7, 68.3, 52.6, 38.0, 31.8; FT-IR (neat, cm^{-1}): 3204, 2885, 1665, 1551, 1478, 1390, 1334, 1173, 1079, 734, 596; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{13}H_{17}N_4O_4S$ 325.0971 found 325.0986.

(*R*)-4-((7-bromo-1-oxo-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazin-4-yl)methyl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide (87):



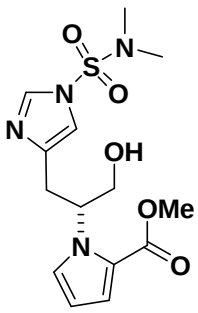
In a round bottom flask compound **85** (50 mg, 0.11 mmol) was dissolved in DMF (2 mL) and cesium carbonate (0.37 g, 1.13 mmol) was added to the reaction mixture. The reaction mixture was heated at 80 ºC for 12 h. Water was added to the reaction mixture and it was extracted with EtOAc. The organic extract was dried with anhydrous Na_2SO_4, concentrated, and the residue was purified by chromatography on silica gel (EtOAc) providing **87** as a thick colorless liquid (25 mg, 55%). $[\alpha]_D$ = -6.0 (*c* = 0.02, MeOH). ^{1}H NMR: δ = 7.85 (d, *J* = 1.0 Hz, 1H), 7.08 (d, *J* = 4.1 Hz, 1H), 6.91 (s, 1H), 6.35 (d, *J* = 4.1 Hz, 1H), 4.75-4.68 (m, 1H), 4.59 (d, *J* = 1.7 Hz, 2H), 3.15-3.06 (m, 2H), 2.87 (s, 6H); ^{13}C NMR: δ = 157.6, 138.1, 137.0, 119.8, 118.5, 115.8, 113.6, 107.3, 68.3, 51.8, 38.2, 30.8; FT-IR (neat, cm^{-1}): 3121, 2926, 1711, 1387, 1172, 1080, 1007, 962, 726, 590; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{13}H_{16}BrN_4O_4S$ 403.0069 found 403.0069.

(*R*)-4-((6,7-dibromo-1-oxo-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazin-4-yl)methyl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide (88):



In a round bottom flask compound **86** (70 mg, 0.13 mmol) was dissolved in DMF (2.5 mL) and cesium carbonate (430 mg, 1.34 mmol) was added to the reaction mixture. The reaction mixture was heated at 80 ºC for 12 h. Water was added to the reaction mixture and it was extracted with EtOAc. The organic extract was dried with anhydrous Na_2SO_4, concentrated, and the residue was purified by chromatography on silica gel (EtOAc) providing **86** as a thick colorless liquid (35 mg, 52%). $[\alpha]_D$ = -6.4 (*c* = 0.12, MeOH). ^{1}H NMR: δ = 7.85 (s, 1H), 7.12 (s, 1H), 6.95 (s, 1H), 4.71-4.61 (m, 1H), 4.60-4.56 (m, 2H), 3.20-2.99 (m, 2H), 2.86 (s, 6H); ^{13}C NMR: δ = 156.3, 137.7, 137.1, 120.2, 119.7, 115.7, 108.9, 102.0, 68.3, 52.8, 38.3, 30.4; FT-IR (neat, cm^{-1}): 3130, 2950, 1733, 1399, 1331, 1170, 1085, 959, 910, 740, 584; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{13}H_{15}Br_2N_4O_4S$ 480.9181 found 480.9178.

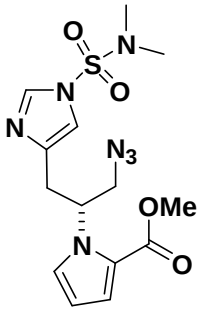
(*R*)-methyl 1-(1-(1-(*N*,*N*-dimethylsulfamoyl)-1H-imidazol-4-yl)-3-hydroxypropan-2-yl)-1H-pyrrole-2-carboxylate (89):



In a round bottom flask compound **77** (160 mg, 0.49 mmol) was dissolved in anhydrous methanol (10 mL) under N_2 atmosphere and to the reaction mixture freshly generated 0.23 M sodium methoxide (10.7 mL, 0.23 mmol) was added. The reaction mixture was stirred at r.t. for 8 h. Finally NH_4Cl and water were

added to the reaction mixture and it was repeatedly extracted with EtOAc. The organic layer was dried with anhydrous Na_2SO_4 concentrated and the residue was purified by chromatography on silica gel (CH_2Cl_2/MeOH, 98:2) providing **89** as a thick colorless liquid (61 mg, 35%). In addition recovered starting material (80 mg, 50%) was obtained. $[\alpha]_D$ = -14.1 (*c* = 0.04, MeOH). ^{1}H NMR: δ = 7.80 (s, 1H), 7.24 (t, *J* = 2.4 Hz, 1H), 6.93 (dd, *J* = 3.8, 1.7 Hz, 1H), 6.86 (s, 1H), 6.15 (t, *J* = 3.8 Hz, 1H), 5.60-5.52 (m, 1H), 3.95 (d, *J* = 5.2 Hz, 2H), 3.79 (s, 3H), 3.16-3.13 (dd, *J* = 7.4, 2.4 Hz 2H), 2.80 (s, 6H); ^{13}C NMR: δ = 162.0, 139.9, 136.4, 126.3, 122.1, 118.3, 114.9, 108.8, 64.8, 57.8, 51.2, 38.2, 31.1; FT-IR (neat, cm^{-1}): 3290, 3121, 1698, 1399, 1176, 1106, 1079, 959, 734, 590; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{14}H_{21}N_4O_5S$ 357.1233 found 357.1242.

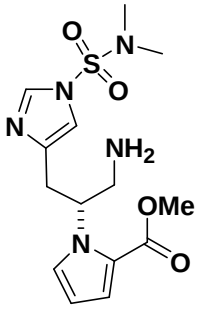
(*R*)-methyl 1-(1-azido-3-(1-(*N*,*N*-dimethylsulfamoyl)-1H-imidazol-4-yl)propan-2-yl)-1H-pyrrole-2-carboxylate (91):



In a round bottom flask compound **89** (40 mg, 0.11 mmol) was dissolved in anhydrous CH_2Cl_2 (5 mL) under N_2 atmosphere and to the reaction mixture triethylamine (0.02 mL, 0.13 mmol) was added dropwise after cooling the reaction mixture to 0 ºC. Then to the resulting reaction mixture CH_3SO_2Cl (0.02 mL, 0.13 mmol) was added dropwise. The reaction mixture was stirred at 0 ºC for 2 h. Then the solvent was concentrated under vaccum and the crude reaction mixture was dissolved in DMF (2 mL) and to it was added NaN_3 (90 mg, 1.40 mmol). The reaction mixture was heated at 80 ºC for 8 h. After cooling to r.t. water was added

to the reaction mixture and it was extracted with EtOAc. The organic extract was dried with anhydrous Na_2SO_4, concentrated, and the residue was purified by chromatography on silica gel (CH_2Cl_2/MeOH, 99:1) providing **91** (30 mg, 71%) as a thick yellow liquid. $[\alpha]_D$ = -3.8 (*c* = 0.02, MeOH). ^{1}H NMR: δ = 7.77 (s, 1H), 7.01 (s, 1H), 6.94 (s,1H), 6.75 (s, 1H), 6.16 (t, *J* = 3.8 Hz, 1H), 5.84-5.68 (m, 1H), 3.79 (s, 3H), 3.75-3.66 (m, 2H), 3.17 (d, *J* = 7.2 Hz 2H), 2.73 (s, 6H); ^{13}C NMR: δ = 161.7, 139.5, 136.5, 122.6, 118.7, 114.9, 109.1, 77.3, 54.9, 51.3, 38.1, 31.5; FT-IR (neat, cm^{-1}): 2950, 2108, 1695, 1387, 1220, 1173, 1106, 959, 725, 593; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{14}H_{20}N_7O_4S$ 382.1297 found 382.1303.

(*R*)-methyl 1-(1-amino-3-(1-(*N*,*N*-dimethylsulfamoyl)-1H-imidazol-4-yl)propan-2-yl)-1H-pyrrole-2-carboxylate (92):



Compound **91** (50 mg, 0.13 mmol) was dissolved in dry methanol (3 mL). To the reaction mixture 10% Pd/C (50 mg) was added. The heterogeneous reaction mixture was stirred at r.t. for 8 h under a hydrogen atmosphere (balloon). The reaction mixture was filtered over Celite and the filter cake was repeatedly washed with hot methanol. The filtrate was evaporated under reduced pressure followed by purification of the residue by chromatography on silica gel ($CHCl_3$/MeOH, 92:8) furnishing the primary amine compound **92** (30 mg, 65%) as a thick colorless liquid. $[\alpha]_D$ = 29.7 (*c* = 0.2, MeOH). ^{1}H NMR: δ = 7.75 (s, 1H), 7.00 (t, *J* = 1.7 Hz, 1H), 6.88 (dd, *J* = 1.7, 3.8 Hz, 1H), 6.66 (s, 1H), 6.16 (t, *J* = 3.4 Hz, 1H), 5.66-5.55 (m, 1H), 3.78 (s, 3H),

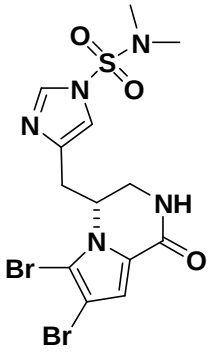
3.18-2.97 (m, 4H), 2.71 (s, 6H); ^{13}C NMR: δ = 162.0, 140.1, 136.3, 123.0, 118.3, 118.1, 114.2, 109.1, 103.8, 77.3, 51.2, 46.8, 37.9, 32.3; FT-IR (neat, cm^{-1}): 3250, 2366, 2334, 1720, 1502, 1449, 1207, 1144, 1010, 737, 708. HR-MS (*m/z*): calc for $[M+H]^+$ $C_{14}H_{21}N_5O_4S$ 356.1393 the expected molecular ion was not observed, but that for the cyclized product (**55**) $[M+H]^+$ $C_{13}H_{18}N_5O_3S$ 324.1126 was found 324.1123.

(*R*)-*N*,*N*-dimethyl-4-((1-oxo-1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazin-4-yl)methyl)-1H-imidazole-1-sulfonamide (55):

In a round bottom flask **92** (50 mg, 0.14 mmol) was dissolved in dry THF (4 Ml) under N_2 atmosphere. The reaction mixture was cooled to 0 ºC and to it 60% sodium hydride (30 mg, 1.4 mmol) was added. The reaction mixture was stirred at r.t. for 8 h. NH_4Cl solution was added and the reaction mixture was repeatedly extracted with EtOAc. The combined extracts were dried with anhydrous Na_2SO_4, concentrated, and the residue was purified by chromatography (CH_2Cl_2/MeOH, 94:6) providing **55** as a thick colorless solid (34 mg, 58%). m.p 192-194 ºC. $[\alpha]_D$ = 17.0 (*c* = 0.4, MeOH). ^{1}H NMR: δ = 7.86 (d, *J* = 1.4 Hz, 1H), 6.90 (dd, *J* = 4.1, 1.4 Hz, 1H), 6.76 (s, 1H), 6.55 (t, *J* = 2.4 Hz, 1H), 6.20 (b, 1H), 6.11 (dd, *J* = 2.7, 2.4 Hz, 1H), 4.64-4.62 (m, 1H), 3.92 (dd, *J* = 12.7, 4.1 Hz, 1H), 3.53 (dd, *J* = 12.7, 2.4 Hz, 1H), 3.06 (dd, *J* = 14.4, 6.9 Hz, 2H), 2.81 (s, 6H); ^{13}C NMR: δ = 161.0, 139.1, 136.9, 128.4, 123.2, 115.6, 114.0, 109.4, 53.6, 44.3, 38.2, 32.3; FT-IR (neat, cm^{-1}): 3140, 2934, 1674, 1551, 1460, 1387, 1170, 1088,

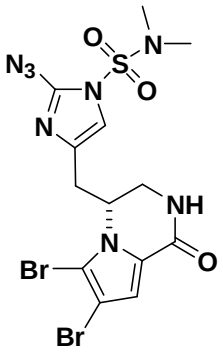
962, 722, 602; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{13}H_{18}N_5O_3S$ 324.1126 found 324.1130.

(*R*)-4-((6,7-dibromo-1-oxo-1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazin-4-yl)methyl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide (93):



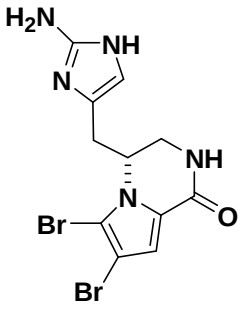
The cyclized compound **55** (90 mg, 0.27 mmol) was dissolved in THF (3.5 mL). The reaction mixture was cooled to 0 ºC and to it NBS (100 mg, 0.58 mmol) was added. The reaction mixture was stirred at r.t. for 1 h. The reaction mixture was quenched by addition of aq. $NaHCO_3$ and then the organic layer was separated. The aqueous layer was extracted with EtOAC (3x50 mL), then the combined organic solutions were dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by chromatography (CH_2Cl_2/MeOH, 97:3) providing **93** as a brown solid (117 mg, 88%). m.p 183-185 ºC. $[\alpha]_D$ = 14.0 (*c* = 0.004, MeOH). ^{1}H NMR: δ = 7.86 (s, 1H), 7.00 (s, 1H), 6.85 (s, 1H), 5.90 (b, 1H), 4.68-4.63 (m, 1H), 3.91-3.85 (dd, *J* = 13.1, 4.1 Hz, 1H), 3.67-3.61 (dd, *J* = 13.1, 5.2 Hz, 1H), 3.11-3.03 (dd, *J* = 14.4, 7.9 Hz, 1H), 3.02-2.94 (dd, *J* = 14.4, 5.8 Hz, 1H), 2.87 (s, 6H); ^{13}C NMR: δ = 158.8, 138.6, 137.1, 124.9, 116.1, 115.5, 107.1, 100.6, 53.5, 43.4, 38.2, 31.2; FT-IR (neat, cm^{-1}): 3180, 2960, 1680, 1545, 1480, 1350, 1210, 1070, 972, 725, 635. HR-MS (*m/z*): calc for $[M+H]^+$ $C_{13}H_{16}Br_2N_5O_3S$ 479.9341 found 479.9355.

(*R*)-2-azido-4-((6,7-dibromo-1-oxo-1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazin-4-yl)methyl)-*N*,*N*-dimethyl-1H-imidazole- 1-sulfonamide (94):



Dibromopyrrole **93** (60 mg, 0.12 mmol) was dissolved in anhydrous THF (3 mL) and the reaction mixture was cooled to -78 ºC and 0.5 M LDA (1.22 mL, 4.2 equiv) was added dropwise to the reaction mixture. The reaction mixture was brought to 0 ºC and then left stirring for 45 min at 0 °C and then again the reaction mixture was cooled to -78 ºC and TrisylN_3 (0.28 g, 1.07 mmol) was added. The reaction mixture was allowed to come to r.t. and then stirred for an additional 1 h, followed by addition of aqueous NH_4Cl (3 mL) to quench the reaction mixture. The organic layer was separated and the aqueous layer was extracted with EtOAC (3x50 mL). The organic solutions were combined, dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by chromatography ($CHCl_3$/MeOH, 98:2) giving **94** as a yellow liquid (17 mg, 30%). In addition 30 mg, (50%) of recovered starting material was obtained. ^{1}H NMR: δ = 7.00 (s, 1H), 6.77 (s, 1H), 5.76 (b, 1H), 4.63-4.60 (m, 1H), 3.86 (dd, *J* = 13.8, 4.1 Hz, 1H), 3.66 (d, *J* = 13.8 Hz, 1H), 2.94 (s, 6H), 2.86 (d, *J* = 7.6 Hz 2H); ^{13}C NMR: δ = 158.5, 140.7, 134.4, 124.5, 117.1, 115.9, 107.4, 100.6, 53.8, 42.7, 38.0, 30.7; FT-IR (neat, cm^{-1}): 2985, 2145, 1649, 1534, 1509, 1457, 1398, 1336, 1181, 1086, 990; HR-MS (*m/z*): calc for $[M+Na]^+$ $C_{13}H_{14}Br_2N_8O_3SNa$ is 542.9169 found 542.9177.

(*ent*)-Cyclooroidin (3):



Conc. HCl (0.003 mL) was added to the solution of compound **94** (22 mg, 0.04 mmol) in methanol (1.2 mL) and stirred at 34 ºC for 12 h. Then the mixture was concentrated under vacuum and the residue was neutralized with $NaHCO_3$ and extracted with EtOAc (3 times). The organic layer were combined, concentrate and purified by column chromatography ($CHCl_3$/methanol/NH_4OH, 92:5:3) to give the free imidazole (13 mg, 76%) as a thick yellow liquid. This compound (10 mg, 0.02 mmol) was dissolved in methanol (1 mL) and Lindlar catalyst (10 mg) was added and the reaction mixture was stirred for 8 h under a hydrogen atmosphere (balloon). Finally the reaction mixture was filtered through a bed of Celite and then the crude reaction mixture was loaded onto a column as a solid, preadsorbed on silica gel. Then the crude product was purified by chromatography (CH_2Cl_2/MeOH/NH_4OH: 80/15/5). A colorless thick liquid was obtained (5 mg, 74%). $[\alpha]_D$ = 10.6 (*c* = 0.02, MeOH). ^{1}H NMR (CD_3OD) : δ = 6.92 (s, 1H), 6.28 (s, 1H), 4.60-4.56 (m, 1H), 3.75 (dd, *J* = 13.4, 4.1 Hz, 1H), 3.52 (dd, *J* = 13.4, 4.1 Hz, 1H), 2.80 (d, *J* = 7.2 Hz, 2H); ^{13}C NMR (CD_3OD): δ = 159.6, 149.6, 127.9, 124.3, 115.2, 111.3, 107.3, 100.0, 54.2, 42.1, 29.3; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{11}H_{11}Br_2N_5O$ 387.9403 found 387.9404.

Part II STUDIES TOWARDS SOME OROIDIN DIMERS

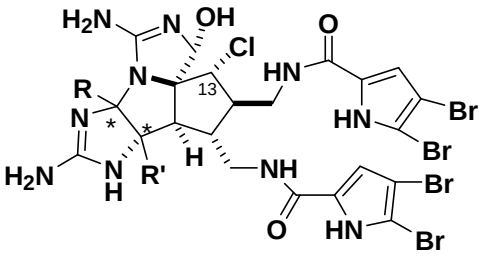
CHAPTER 4

INTRODUCTION

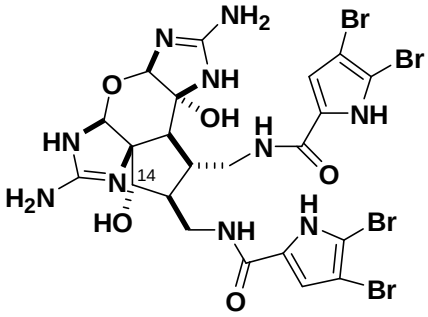
4.1 Introduction

During the last few years the oroidin class of polyheterocyclic, nitrogen-rich alkaloids has received much attention as they rank among the most challenging synthetic targets. [4,11,56-60] In addition, several family members exhibit substantial biological activity in particular several of the dimeric congeners. Examples of these alkaloids include sceptrin (**103**), the axinellamines A (**99**) and B (**100**), palau'amine (**105**), and ageliferin (**104**). These marine natural products appear to arise from one precursor, oroidin (**1a**) which was first identified in 1971.[60] These densely functionalized, highly oxidized, polycyclic alkaloids are believed to obtain from dimerization of oroidin and then followed by consecutive functionalizations (Figure 4.1). [3,11,62,63] However, to date there is only one reported biosynthetic study and so the precise origin of these alkaloids remains to be fully elucidated.[12] Recently the palau'amine (**105**) structure was revised and thus as a consequence, the synthetic approaches to this molecule required redesign. In the original report the stereochemistry of the junction of the two fused five-membered rings had been assigned as *cis*.[64] However, a thorough spectroscopic re-investigation[11,65] was recently complemented by synthesis (vide infra),[66,67] suggesting that the C-11/C-12 ring fusion in **105** to be in the thermodynamically less stable *trans* configuration (Figure 4.1). In addition the stereochemistry of C-

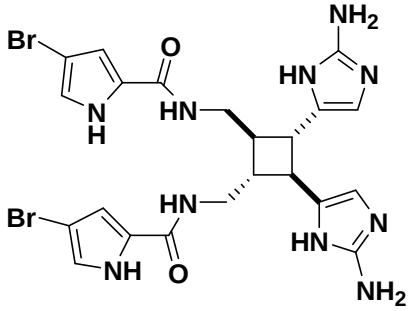
17 chloro bearing center was revised such that palau'amine now shares a common stereochemical arrangement around the carbocyclic E ring with the axinellamines and massadine families. As a result, it appears that all of these systems, **99**-**101** and **105** may be derived from a common, late stage biosynthetic intermediate.



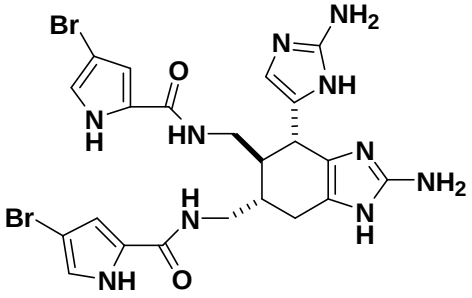
99: Axinellamine A
(R = β–OH, R' = β–OH)
100: (R = –OH, R' = α–OH) B



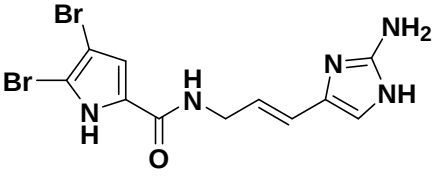
101: Massadine



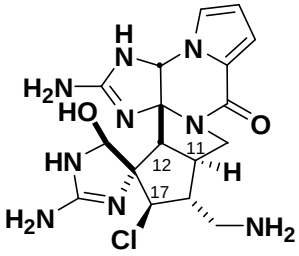
103: Sceptrin



104: Ageliferin



1a: Oroidin

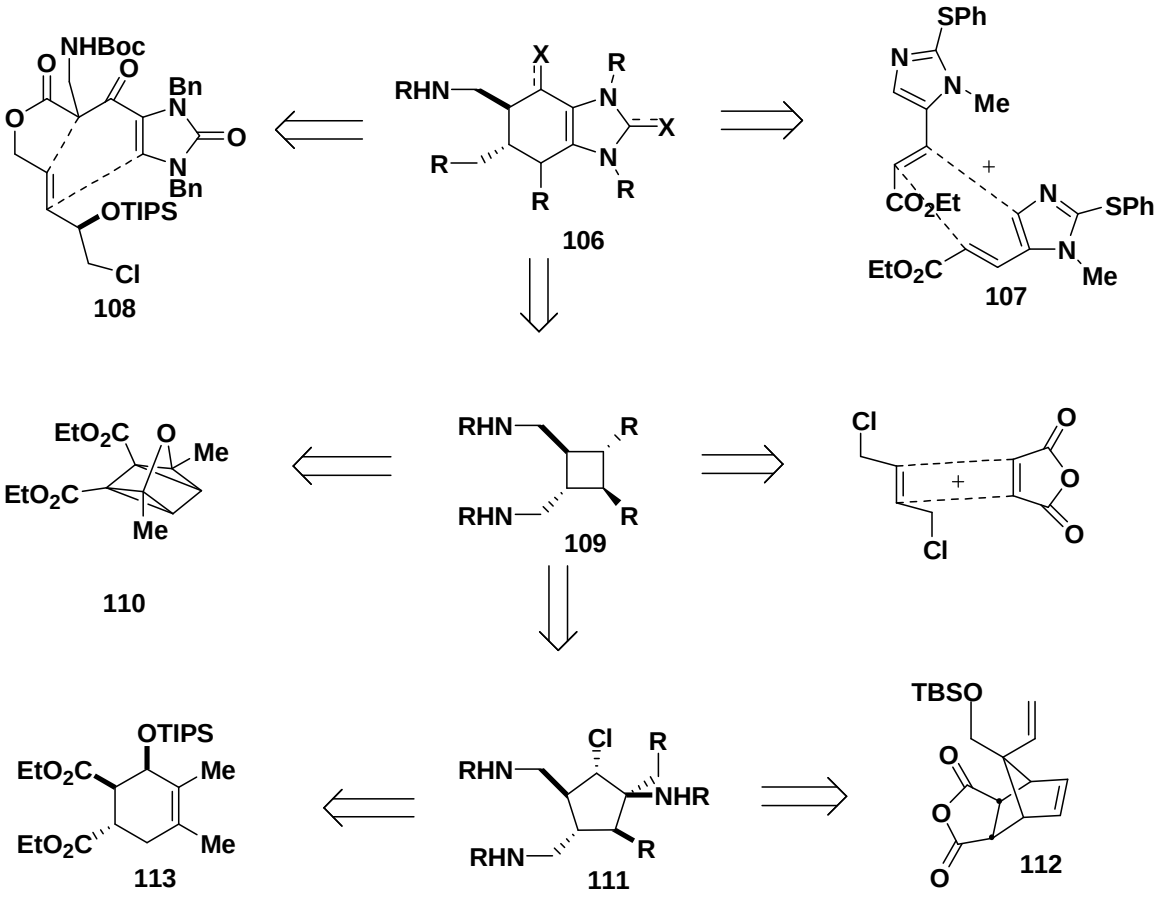


105: Palau'amine

Figure 4.1 Selected Oroidin alkaloids of marine origin.

All of these pyrrole–imidazole alkaloids feature a central four-, five-, or six-membered carbocyclic ring decorated with different arrangements of the remaining heterocycles. Due to their unique structural patterns many synthetic efforts have been pursued which in turn have led to distinct solutions for assembly of each of the scaffolds (Scheme 4.1).[59] The six-membered ring of the ageliferins **106** was proposed to arise from a [4+2] cycloaddition in one early biosynthetic hypothesis.[62] This was first implemented by Ohta et al. (**107**→**106**) although this results in the synthesis of a non-natural occurring material.[70] Our group has pursued a related, but intramolecular strategy, towards the ageliferins.[10a] Chen and Tan developed a Mn(III)-promoted radical cascade annulation from the imidazolone **108**.[71] Baran et al. successfully demonstrated that ageliferin **104** can be obtained from sceptrin (**103**) through a double ring-enlargement through a vinylcyclobutane rearrangement of sceptrin (**103**) under high temperature conditions in their total synthesis of **104.**[72] Starting from (*E*)-1,4-dichloro-2-butene and maleic anhydride[73] or by fragmentation of the photochemically accessible oxaquadricyclane **110** the sceptrin scaffold **109** has been synthesised by [2+2] photocycloadditions.[24,74] The fully substituted five-membered-ring scaffolds **111** present in the axinellamines and palau'amines is the biggest challenge as of now. For these molecules, many linear biomimetic pathways have been proposed, including ring enlargements of a four-membered sceptrin-like precursor **109**, or oxidative ring contractions of six-membered ageliferin-like precursors **106**.[3,4,11,56-59, 62,63] Experimentally the ring-enlargement of **109**→**111** still waits to be realized whereas ring-contractions **106**→**111** have

been executed with considerable success.[10b,76] However, “abiotic” syntheses of scaffolds **111** have proven to be the most successful to date.[4,11,56-59] The first enantioselective synthesis of the axinellamine core **111** by desymmetrization of anhydride **112** was reported by Carreira et al. in 2000.[4,76,77,63] The first total synthesis of the axinellamines was completed by Baran et al.[78] (**99**, **100**) in racemic form by using a ring opening-ring-contraction of the cyclohexene **113**.[78]

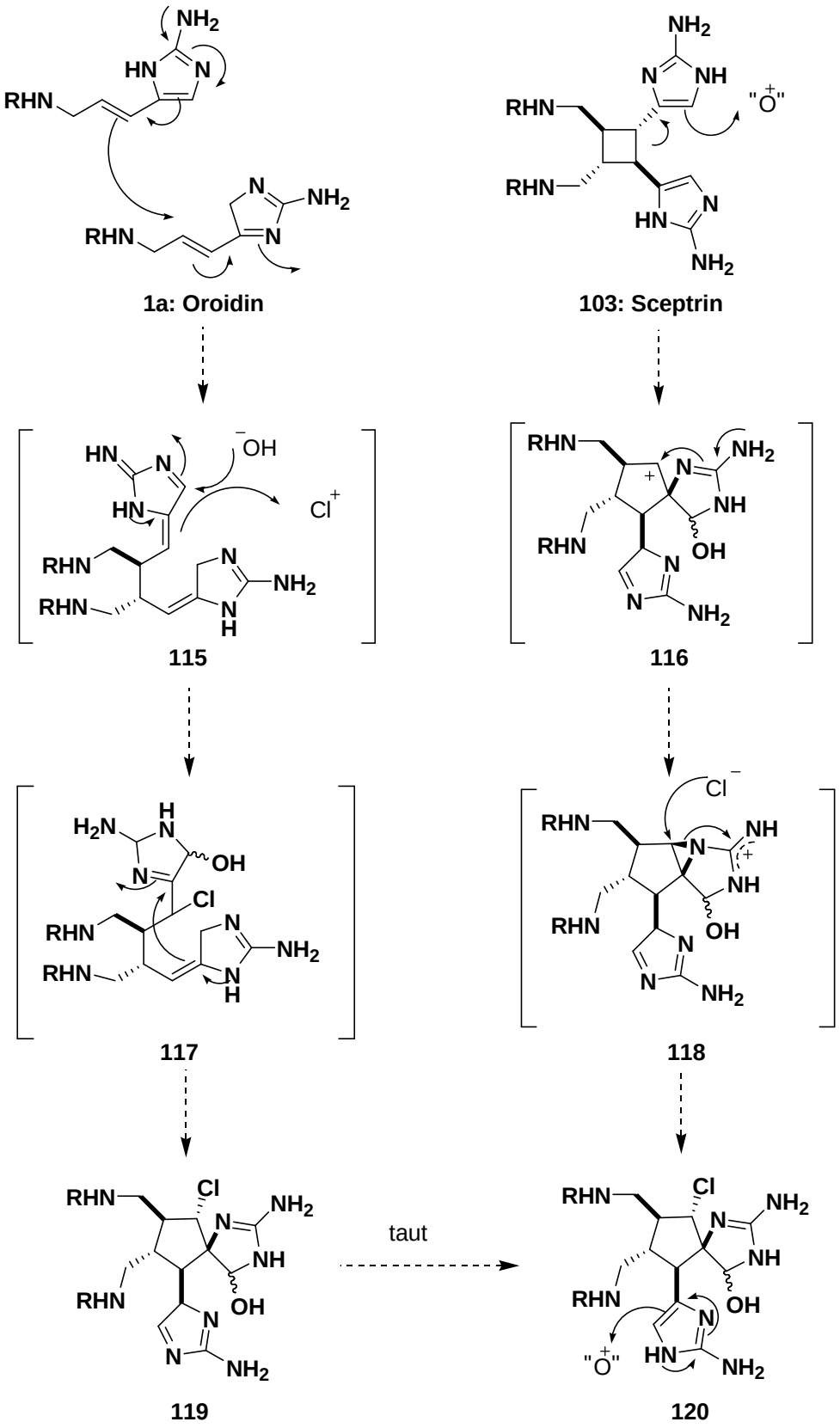


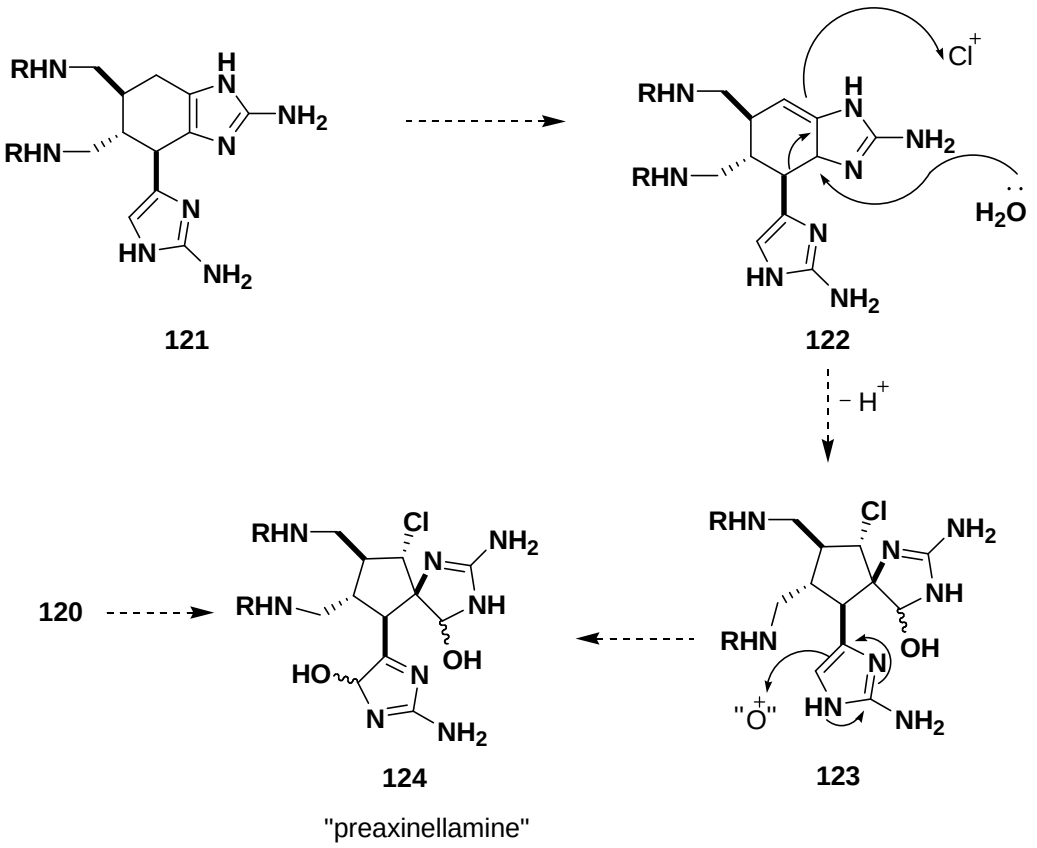
Scheme 4.1 Synthetic routes to the core structures of related oroidin alkaloids.

4.2 Three possible biosynthetic pathways to “preaxinellamine”

Scheme 4.2 depicts three possible biosynthetic pathways to “preaxinellamine” (**124**). In the first proposal (linear), oroidin-like molecules **1a** undergo an enantio- and diastereocontrolled dimerization to form **115**.[3,11] **119** was formed by reacting

with an electrophilic chlorine source, a hydration reaction and then cyclization via **117**. After tautomerization and oxidation of the remaining aminoimidazole, “preaxinellamine” (**124**) is formed. An alternative proposal was recently put forth which involves a ring expansion of the cyclobutane nucleus of sceptrin (**103**).[72] Since extremely high concentrations of **103** have been found in many of the organisms that produce ageliferin (**104**)[80,81] (compound **103** has also been isolated from the same organism as palau’amine (**105**)[62]) has led to the proposition that **103** is a possible biosynthetic precursor of the other more-complex members of this family. The proposal was that exposure of **103** to an oxidant leads to the formation cation **116**. Cation-initiated expansions of cyclobutanes to cyclopentanes have good precedent in the literature,[82] and have been implicated in the biosynthesis of hirsutene terpenes from illudanes.[83] Compound **120** can be formed by attack of a chloride ion, possibly through the intermediacy of aziridine **118**. The third pathway (ring contraction) bears its conceptual roots in the earlier hypothesis for the genesis of palau’amine (**7**).[62] **124** can be obtained by tautomerization of ageliferin (**104**) followed by reaction with an electrophilic chlorine source, ring contraction, and hydration. Both baran et al. and our lab have recently demonstrated that the ring-contraction pathway can lead to axinellamine-like structures from **104** but with the incorrect stereochemistry.[75,94]


1a: Oroidin
103: Sceptrin
115
116
117
118
119
120
taut



Scheme 4.2 Biosynthetic pathways of marine Oroidin alkaloids

4.3 Carreira's approach towards Massadine

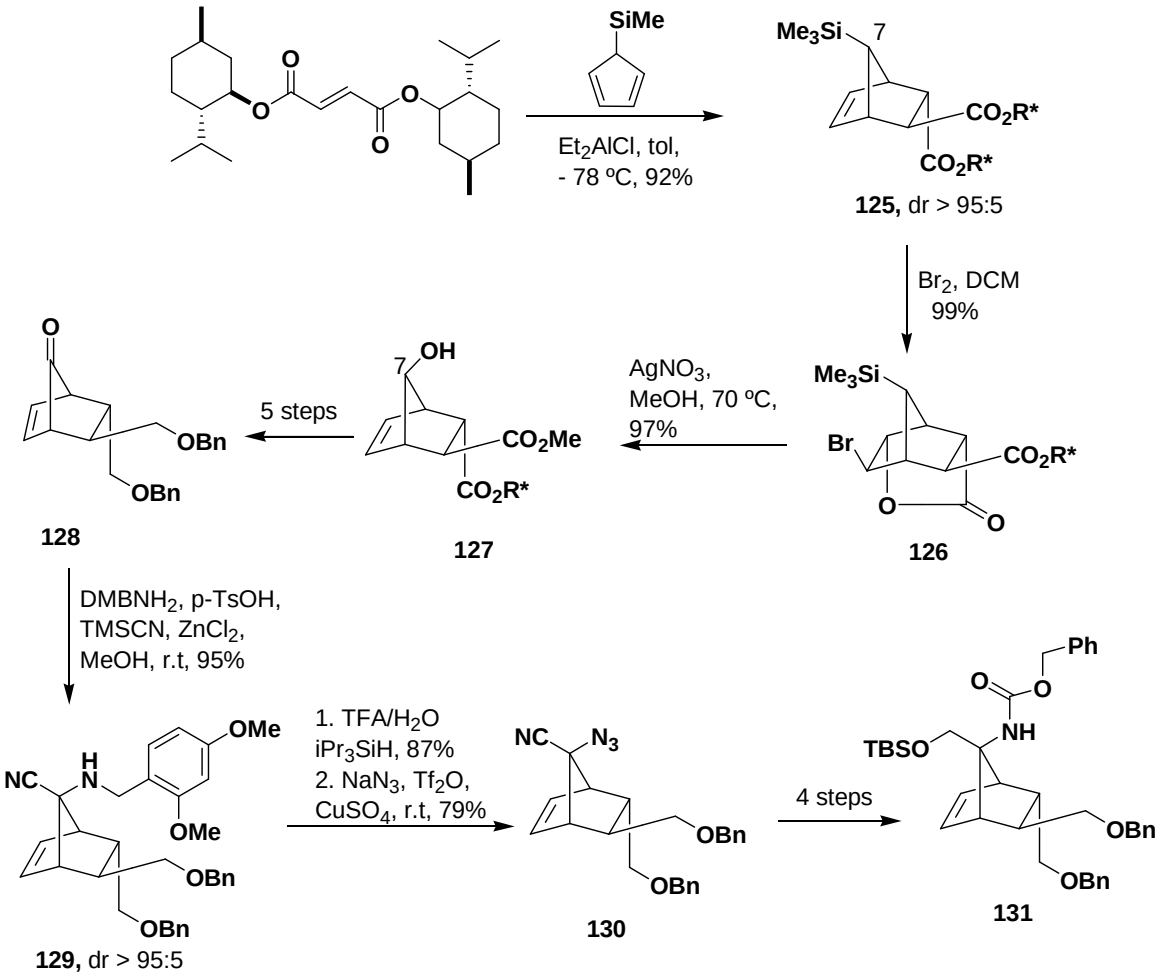
Carreira et al. have developed a synthetic route[77,84] to access the fully substituted cyclopentane ring of the massadine-type alkaloids.[84] The goal was to produce an enantiopure norbornene intermediate as a conformationally rigid precursor to the cyclopentane and then to elaborate functionality at the C7 position (norbornene numbering) in a chemo- and diastereoselective manner followed by oxidative cleavage of the olefin to provide the polysubstituted cyclopentane. Their synthesis started (Scheme 4.3)[77,84] with a diastereoselective cycloaddition of 5-(trimethysilyl)cyclopentadiene with a chiral, non-racemic fumarate to obtain the bicyclo[2.2.1]heptane efficiently. The C7 position is then oxygenated through bromo-lactonization of **125**, and then followed by an Ag (I)-

mediated rearrangement of the C7-silane to generate the inverted alcohol **127** via methanolysis of the putative lactone intermediate. The alcohol was converted to ketone **128** over 5 steps from which a single amino-nitrile isomer **129** was obtained by Strecker reaction. The diastereoselectivity was achieved due to steric shielding of one diastereoface of the iminium ion by the bulky *exo*-oriented benzyloxymethylene. The silyl ether **131** was obtained by reduction of azidonitrile **130,** which was in turn generated by by Cu (II)-catalyzed diazotransfer. Repeated attempts at reduction of variously protected amino-nitrile substrates led to decomposition.

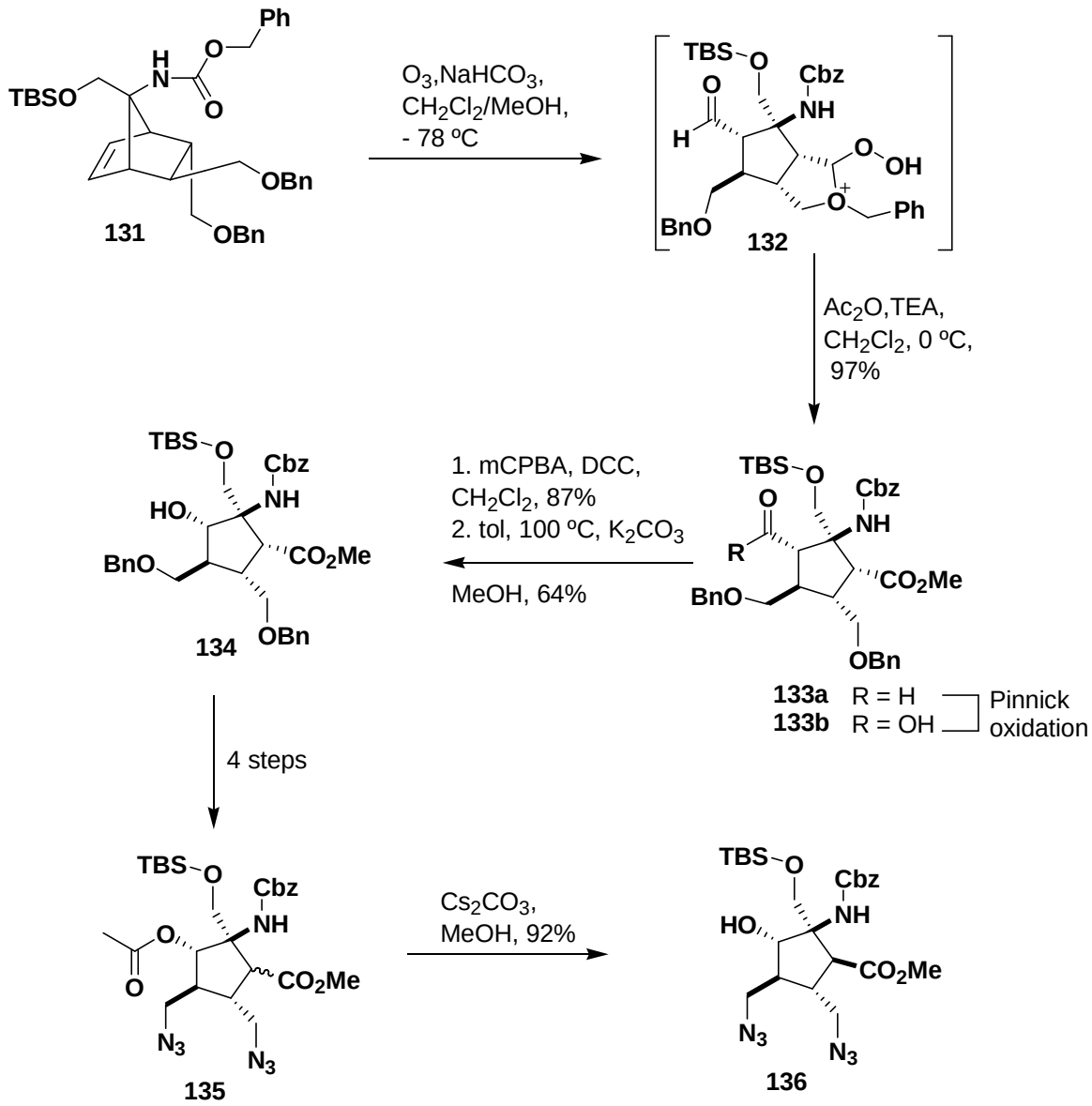
In (Scheme 4.4), ozonolysis provided regioselectively the ester/aldehyde **133a** in excellent yield. The putative oxonium species **132** was generated by anchimeric participation of one benzyloxy group in the rearrangement of the primary ozonide followed by methanolysis and dehydration to **133a**.

By generating the unsymmetrical diacyl peroxide from carboxylic acid **133b** using DCC and peracid, "carboxy-inversion" (**133b→134**, Scheme 4.4)[86] was realized. The alcohol **134** was obtained by heating the intermediate to promote rearrangement to the mixed carbonate and then subsequent methanolysis. A diastereomeric mixture of diazides **135** was obtained in four additional steps.

The massadine core fragment **136** was obtained in an enantioselective fashion by using tandem acetate saponification/ester epimerization with Cs_2CO_3 (the massadine intermediate was synthesized by 24 linear steps).



Scheme 4.3 Carreira's enantioselective synthesis of a massadine D ring precursor.

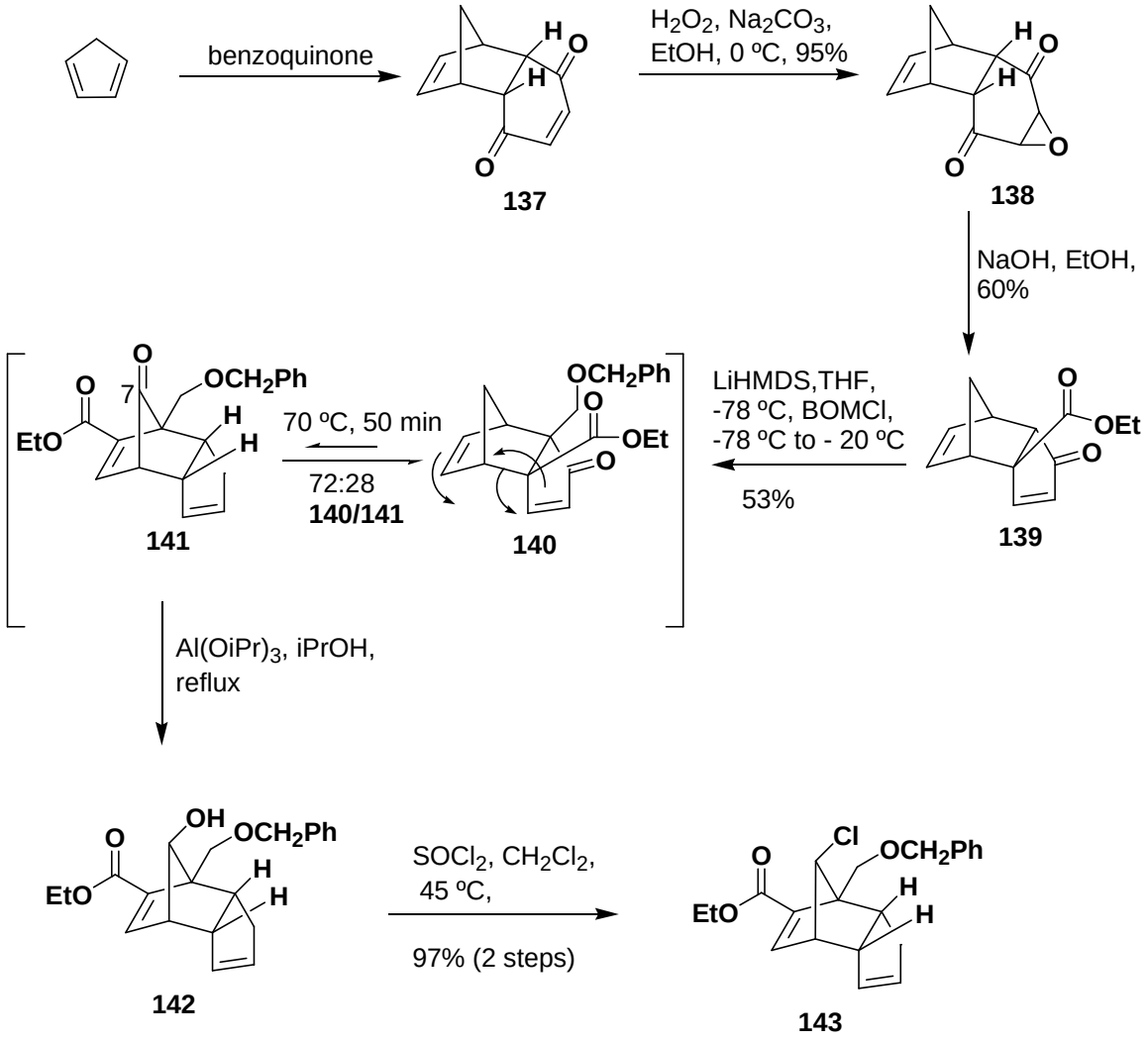


Scheme 4.4 Completion of D-ring-core fragment of massadine.

4.4 Gin's approach towards Palau'amine

Gin and co-workers synthesized the chlorocyclopentane core palau'amine by using a known [3,3]-sigmatropic rearrangement of bridged tricyclodecadienes (e.g. **140**, Scheme 4.5)[87] in order to obtain a C7-functionalized norbornene intermediate suitable for elaboration to the chlorocyclopentane core of **105**. The racemic Diels–Alder adduct **137** was epoxidized chemoselectively providing a

keto-epoxide which can be subjected to a Favorskii-type ring-contraction. The rearrangement proceeds by enolization followed by intramolecular oxirane ring-opening and finally dehydrative ring-contraction to provide the enone/ester **139** in good yield.

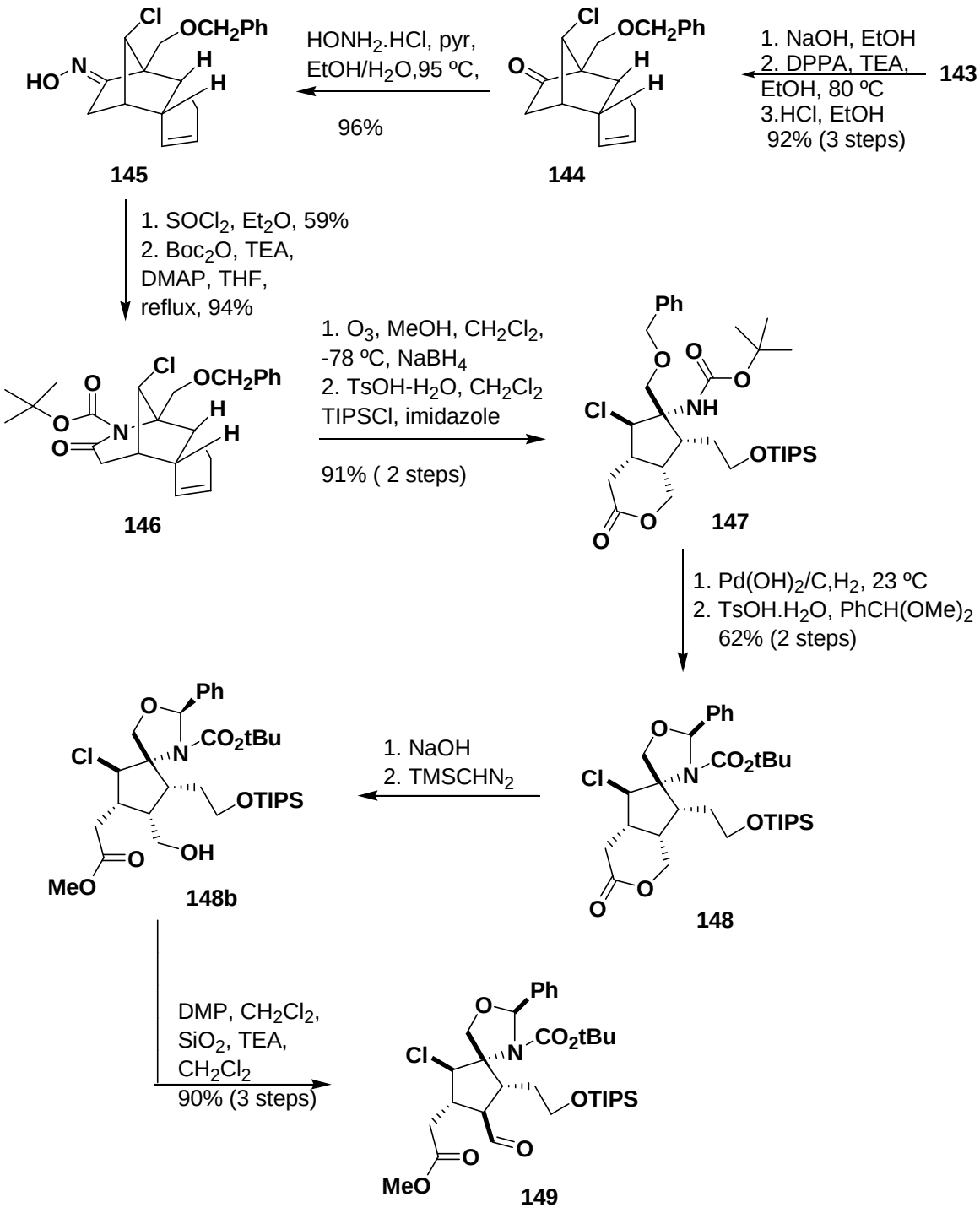


Scheme 4.5 Gin's synthesis of bridged lactam intermediate

Ketone **140**, that bears the 1,5-diene system, and can equilibrate via a [3,3]-sigmatropic rearrangement (**140→141**) was obtained by α-alkylation as described by Woodward.[88] This process provides a latent chloride functionality at C7 of norbornene **141** in the form of a ketone. The **140**/**141** mixture in a

thermodynamic ratio of 72:28 was reduced under Meerwein–Verley–Pondorf conditions, advancing selectively intermediate **141** through rearrangement and reduction. The efficiency of the above reaction depends on exploitation of the Curtin–Hammett principal of the dynamic **140**/**141** system. The alcohol **142** was chlorinated with net retention of configuration providing chloride **143**.

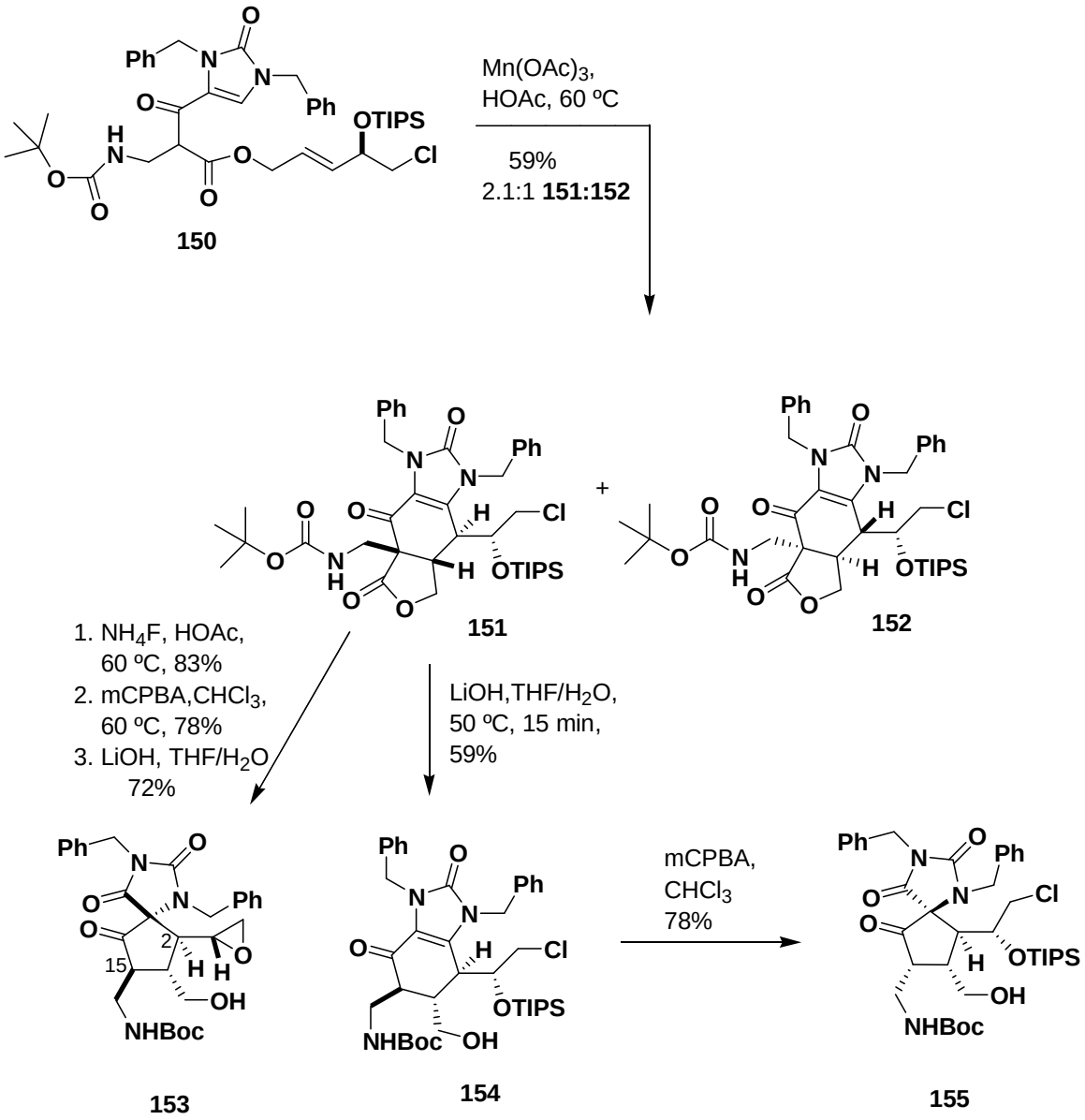
The ketone **144** was generated by an ene-carbamate Curtius rearrangement. Beckmann ring expansion of the oxime initiated with thionyl chloride was completely regioselective resulting from migration of the more substituted alkyl group to provide the lactam **146** after Boc protection. Reductive ozonolysis (Scheme 4.6) of the cyclopentene **146** and subsequent intramolecular alcoholysis of the imide gave **147** after protection of the primary alcohol as the silyl ether. In two additional steps oxazoline **148** was generated and then the lactone moiety was chemoselectively hydrolyzed and esterified with $TMSCHN_2$ to afford **148b**. Finally, aldehyde **149** was obtained by oxidation of the alcohol followed by a epimerization as a single diastereomer (19 steps from cyclopentadiene).



Scheme 4.6 Synthesis of diastereomeric Palau'amine chlorocyclopentane core.

4.5 Chen's Mn(III) mediated oxidative strategy towards oroidin alkaloids.

A $Mn(OAc)_3$ promoted oxidative radical heterobicyclization of β-keto esters tethered to unsaturated N-heterocyclic ring systems was developed by Chen and coworkers (Scheme 4.7).[71] By a cascade bicyclization reaction imidazolone **150** undergoes single electron oxidation to provide an electrophilic α-radical[91,92] that cyclizes by a 5-*exo*/6-*endo* pathway to generate **151** and **152** when it is treated with $Mn(OAc)_3$ in warm acetic acid. In this single step two C–C bonds and three contiguous stereocenters are established; as only two of a possible eight diastereomers are obtained. The alcohol **154** was then obtained by decarboxylation of the lactone **151**. This intermediate was converted to the spirocyclic cyclopentanone-hydantoin **155** by oxidative rearrangement with concomitant epimerization of the methylene amino-bearing stereocenter. Starting from **151** diastereomeric cyclopentanone **153** can also be prepared by deprotection of the TIPS group and then the resulting lactone was oxidized with mCPBA. The relative stereochemistry of C2 and C15 of **153** was epimeric to the massadine/palau'amine core-ring fragment.



Scheme 4.7 Chen's Mn(III) mediated strategy to acess core skeleton of oroidin alkaloids.

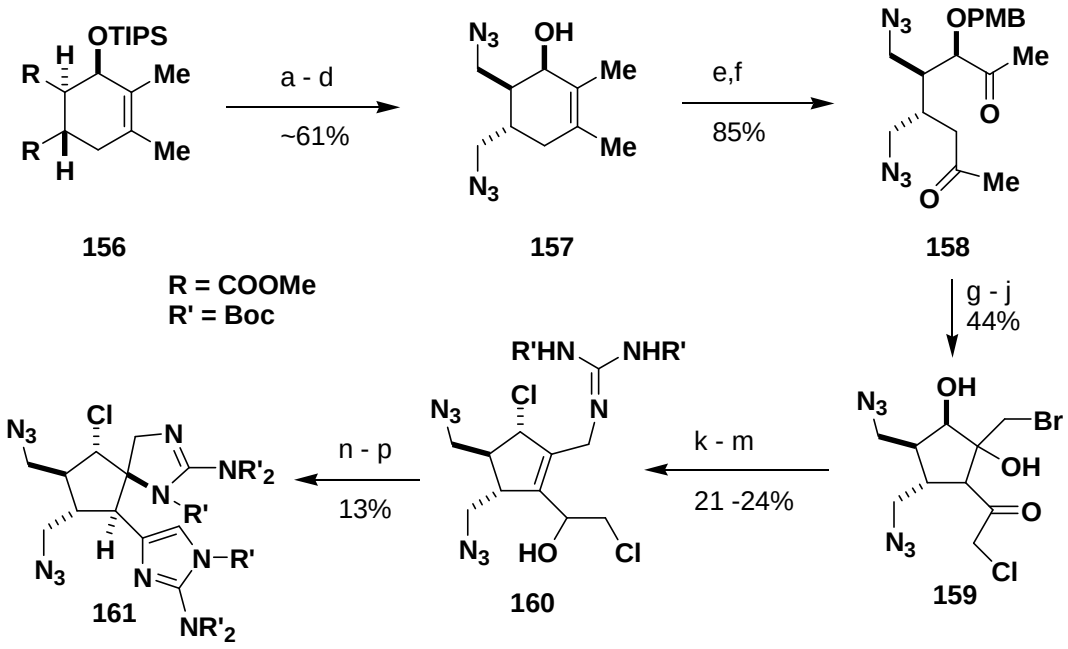
4.6 Baran's total synthesis of the axinellamines

The first total synthesis of the axinellamines was reported by Baran et al. in 2008 (Scheme 4.8).[78] First, the racemic Diels–Alder product **156** was transformed to diazide **157** in four standard conversions.[79] Protection of the secondary alcohol as the PMB ether was followed by ozonolysis provided diketone **158**, which was

α,ω-dibrominated via the bis-silylenol ether. Intramolecular aldol reaction under solvent-free conditions provided the cyclopentane derivative. Exchange of the more reactive bromide for a more stable chloride was achieved by treatment with LiCl, and deprotection of the PMB-ether gave diol **159**. The C17-chloro substituent was installed by eliminating the tertiary hydroxy group and the secondary hydroxy group was displaced by Cl^- using SO_2Cl_2 in a one-pot reaction. After Luche reduction of the enone, chemoselective displacement of the bromide substituents was achieved with protected guanidine (**159**→**160**). Upon reoxidation to the enone, spirocyclization occurred produced two diastereomers (1.3:1). Formation of the major (and correct) diastereomer was favored by high temperatures. The 2-aminoimidazole moiety was then introduced by displacement and in situ condensation with Boc-guanidine, providing spirocycle **161** after derivatization (Boc_2O) and purification. The protected axinellamine precursor **161** with two heterocycles already installed was achieved in 16 steps from **156** (overall yield 0.7%).

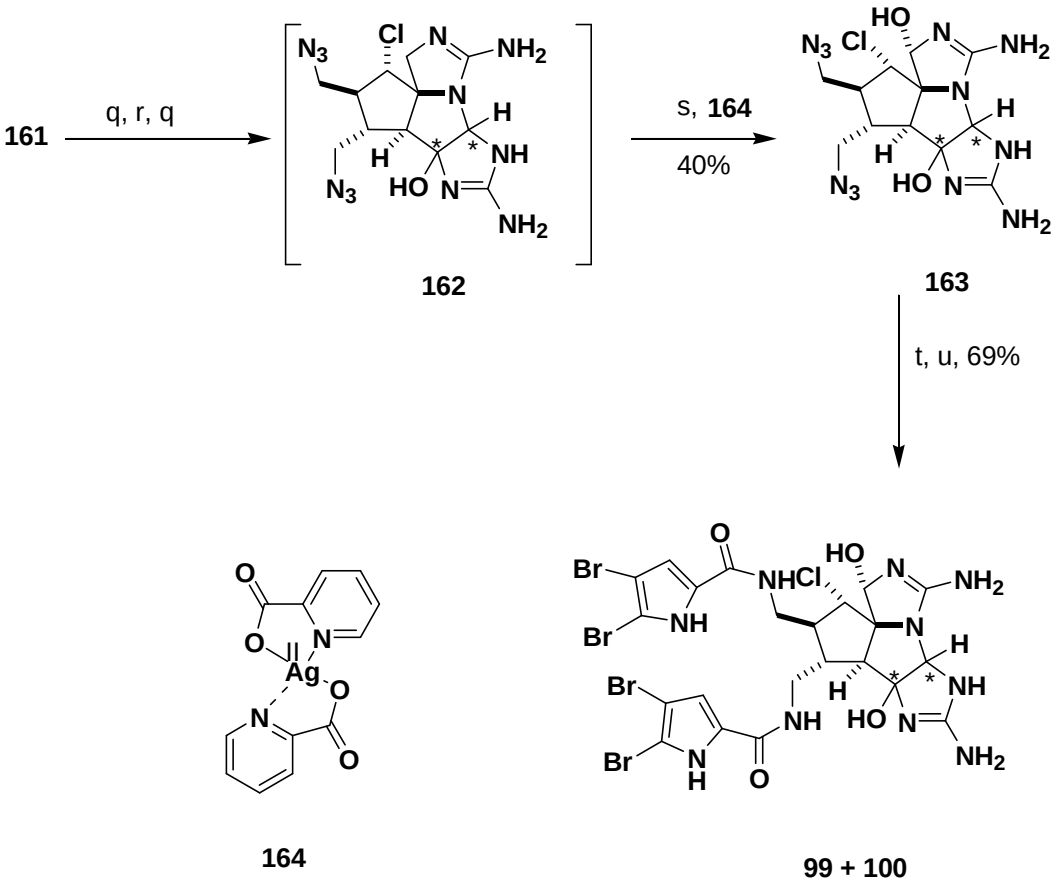
Compound **161** was separated from the axinellamine target connectivity by only two oxidations (Scheme 4.9).[78] Baran et al. realized that the aminoimidazole 4,5-double bond might be selectively oxidized,[57] and indeed found that after Boc deprotection of **161** the respective diol could be formed by DMDO oxidation, which on treatment with TFA condensed to carbinolamine **162**. The tetracycle **163** was obtained by chemoselective oxidation with the Ag (II) complex **164**, in only four steps and 40% yield from **161**. Finally the axinellamines **99** and **100** were obtained by reduction of the azide groups followed by acylation with

suitable pyrrole building blocks. The first total synthesis of **99** and **100** was thereby completed in 22 steps from **156** (overall yield 0.2%).



Scheme 4.8 Diastereoselective synthesis of the axinellamine core.

a) $LiAlH_4$, THF; b) MsCl, pyridine; c) NaN_3, DMF, 100 ºC; d) TBAF; e) PMBCl, NaH, DMF; f) O_3, MeOH; g) TMSOTf, $EtNiPr_2$, then NBS; h) SiO_2, no solvent, 47 ºC; i) LiCl, DMF; j) 10% TFA; k) SO_2Cl_2, 2,6-lutidine, CH_2Cl_2; l) $NaBH_4$, $CeCl_3$, MeOH; m) N,N'-bis-Boc-guanidine, DBU, DMF; n) IBX, benzene, reflux; o) Boc-guanidine,THF, reflux; p) Boc_2O, NEt_3, cat. DMAP, CH_2Cl_2. R = COOMe, R' = Boc, PMB = para-methoxybenzyl, MsCl = methylsulfonyl chloride, TBAF = tetrabutylammoniumfluoride, TMS = trimethylsilyl, NBS = N-bromosuccinimide, TFA = trifluoroacetic acid, DBU = 1,8-diazabicyclo-[5.4.0]undec-7-ene, IBX = o-iodoxybenzoic acid.



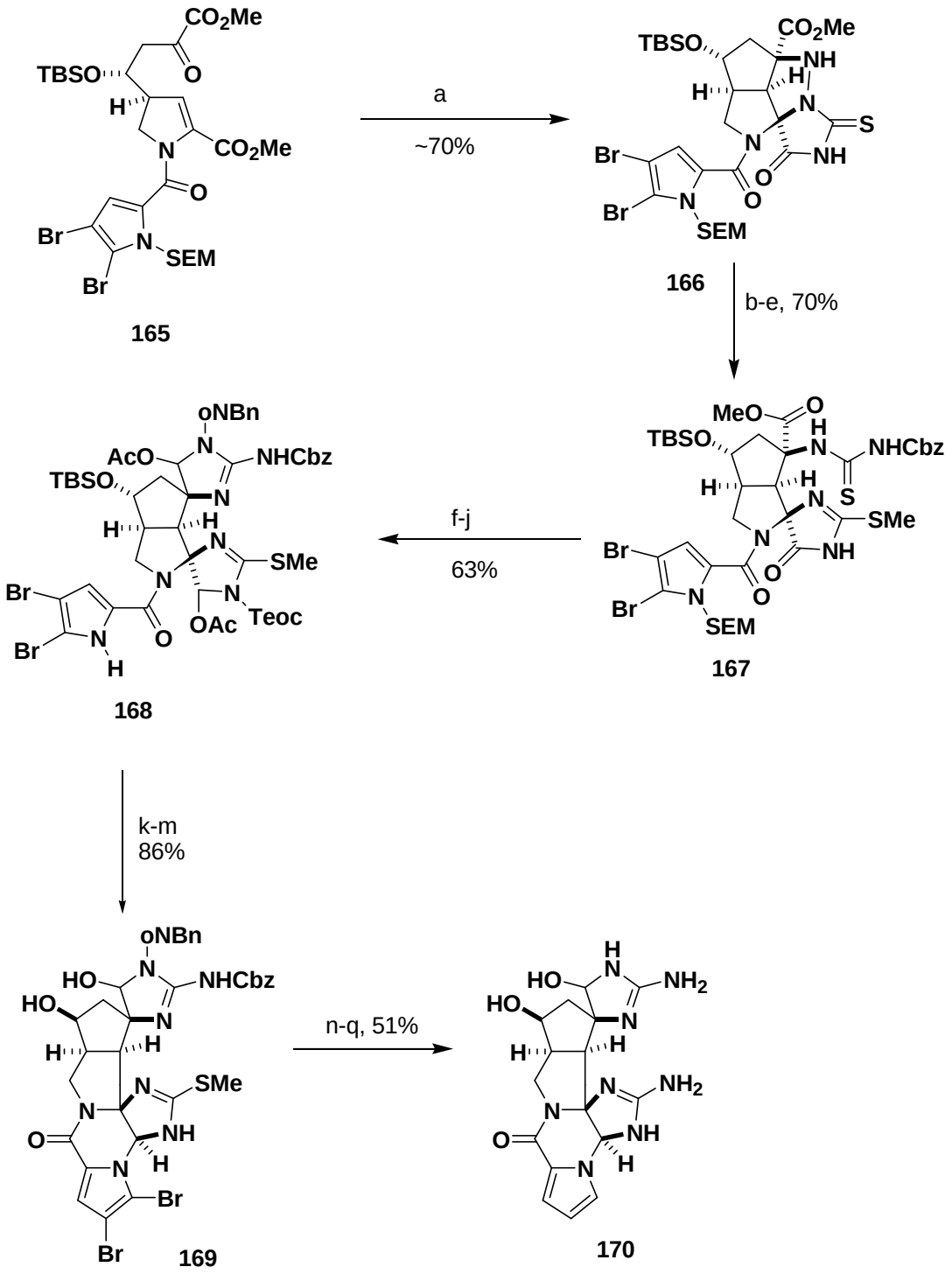
Scheme 4.9 Completion of the axinellamine total synthesis

q) 67% TFA; r) DMDO, H_2O, 0 ºC; s) H_2O, 50 ºC; t) 1,3-propanedithiol, NEt_3, MeOH; u) 4,5-dibromopyrrole-2-yl-trichloromethyl ketone, $EtNiPr_2$, DMF, 45 ºC. DMDO = 2, 2-dimethyldioxirane.

4.7 Synthetic studies towards Palau'amine by Overman

Overman et al. recently provided a synthetic strategy towards the original stereochemistry of **105** (Scheme 4.10). The key steps towards the synthesis[67] of the *epi*-palau'amine scaffold **170** include a bicyclization, which was achieved by an intramolecular 1,3-dipolar cycloaddition, providing tetracycle **166** from the dihydropyrrole **165** in 70% yield.[66] Three contiguous stereocenters were fixed by this elegant transformation, two of them quaternary. The thiourea **167** was obtained by cleaving the N-N bond, thiohydantoin protection and amine acylation.

Compound **167** was then transformed into protected imidazolone, doubly reduced, and protected to give the bisaminal **168**. The Teoc and TBS protecting groups were removed by using TBAF and also closure of the ketopiperazine ring was obtained. The hemiaminal **169** was obtained by inversion of the secondary alcohol followed by an oxidation–reduction sequence. Conversion of the isothiourea into the guanidine and deprotection yielded the *cis*-configured compound **170** in 17 steps and 14% total yield from **165** (ca. 31 steps and 2.4% yield from monoprotected 2-butene-diol), which was found by NMR spectroscopy to differ significantly from natural palau'amine (**105**).



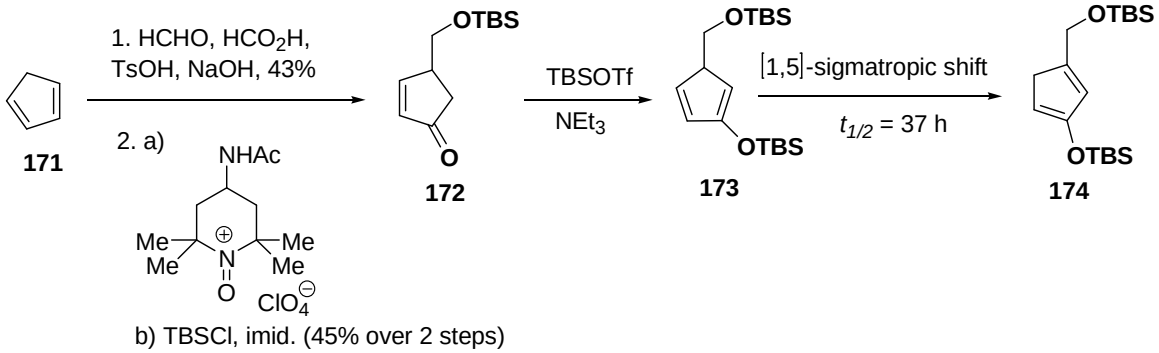
Scheme 4.10 Synthesis of the fully elaborated *epi*-palau'amine scaffold.

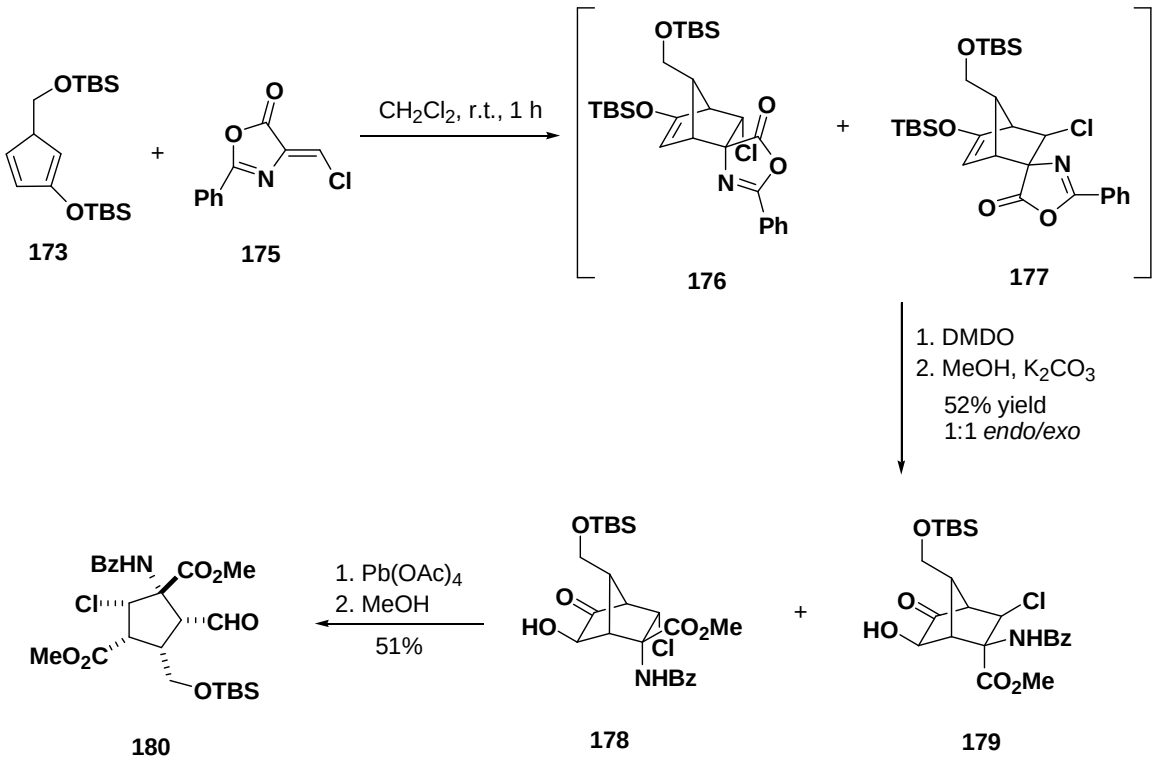
a) Thiosemicarbazide, EtOH, 110 ºC; b) SmI_2, THF/MeOH; c) MeI, $EtNiPr_2$, DMAP, CH_2Cl_2; d) TeocCl, $EtNiPr_2$, CH_2Cl_2; e) Cbz-NCS, CH_2Cl_2; f) EDC, oNBn-NH_2, $EtNiPr_2$, CH_2Cl_2; g) 10% TFA; h) TeocCl, $EtNiPr_2$, CH_2Cl_2; i) $NaBH_4$, MeOH/THF; j) Ac_2O, pyridine, DMAP; k) TBAF, THF; l) IBX,

DMSO; m) $NaBH_4$, MeOH, 0 ºC; n) mCPBA, CH_2Cl_2; o) NH_3, CH_2Cl_2, -78 ºC; p) hν, dioxane; q) H_2, Pd/C, aq dioxane. SEM = 2-(trimethylsilyl)ethoxymethyl, Teoc = trimethylsilylethyloxycarbonyl, oNBn = ortho-nitrobenzyl, NCS = N-chlorosuccinimide, MCPBA = m-chloroperoxybenzoic acid.

4.8 Synthetic studies towards Palau'amine by Gleason

Gleason and co-workers have demostrated that 2-siloxy substitution markedly stabilizes 5-substituted cyclopentadienes almost by 30-fold at 23 ºC relative to 5-methylcyclopentadienes[68] towards [1,5]-sigmatropic shifts (e.g. **173→174**, Scheme 4.11). This allows for productive application of similar dienes in Diels-Alder cycloaddition reactions performed at room temperature. They showed that diene **173** undergoes a variety of [4+2] reactions exhibiting different levels of *endo/exo* selectivity.[68,69] Cycloaddition reaction between diene **173** and **175** at room temperature gave 1:1 mixture of cycloadducts (**176** and **177**) which were directly subjected to DMDO oxidation followed by methanolysis to give hydroxy ketones **178** and **179**. After separating **178** from **179**, it was oxidatively ring-opened to deliver fully substituted cyclopentane **180**.



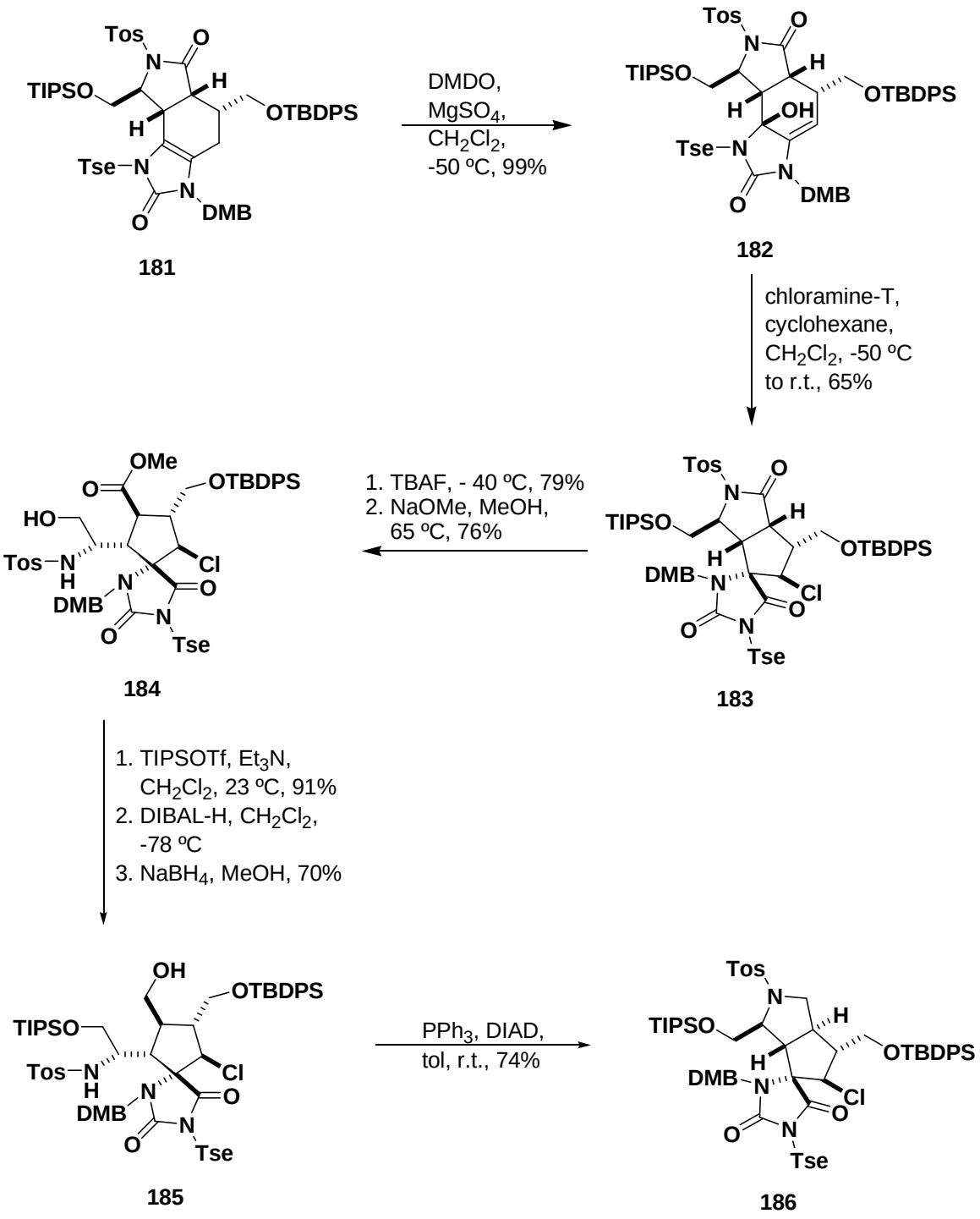


Scheme 4.11 Highly functionalized chloropentane core of palau'amine

4.9 Synthetic studies towards Palau'amine by Romo

Romo and co-workers[52,76,93] have demonstrated that the palau'amine core skeleton can be obtained from Diels–Alder adducts such as **181** (Scheme 4.12) by a two-step oxidation/chlorination/ring-contraction sequence.[75,96] In this sequence the imidazolone **181** (prepared via a Diels-Alder reaction) is first subjected to DMDO oxidation at low temperature providing the allylic alcohol **182** in excellent yield as a single diastereomer. Treating **182** with an electrophilic chlorinating agent resulted in the incorporation of the key chlorine atom on the convex face of the tricyclic systems. Then a 1,2-alkyl migration on this iminium species yielded the ring-contracted spirocycle **183** in good yield on a gram scale.[93] The use of cyclohexene as a HOCl buffer suppresses formation of aromatized over-oxidation by-products. The all *trans* relative stereochemistry

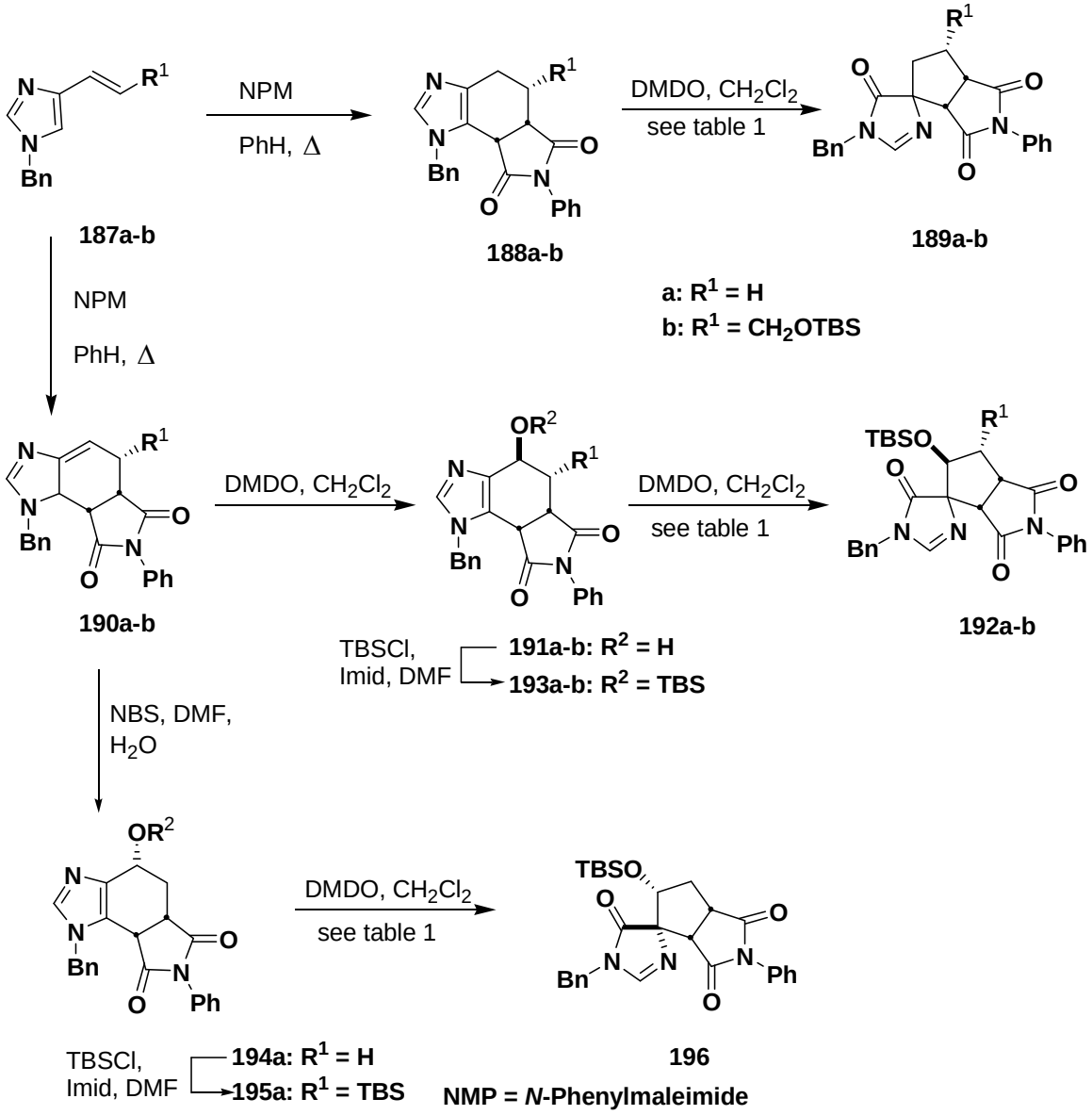
common to oroidin alkaloids **101** and **105** was achieved by cleaving the lactam with concomitant epimerization of the methoxy carbonyl-containing stereocenter. The relative configuration of this *anti*-chlorocyclopentane **184** was verified crystallographically.[52] The azabicyclooctane **186** was obtained by employing Mitsunobu conditions at room temperature in 74% yield.[52] The coupling constants of several key protons in this core substructure correlate well with the revised structure of palau'amine. For eventual total synthesis of **105** demonstration of the feasibility of this intramolecular cyclization to obtain the D–E *trans*-fused 5,5 ring system of the revised palau'amine structure is a critical achievement.



Scheme 4.12 Romo's Diels-Alder/oxidation/tandem chlorination-1,2-alkyl shift sequence for synthesis of core structure of Palau'amine.

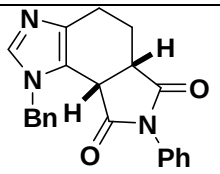
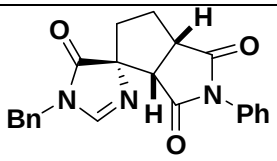
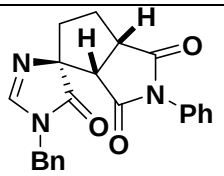
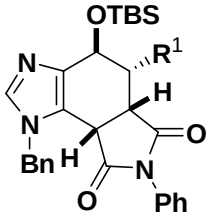
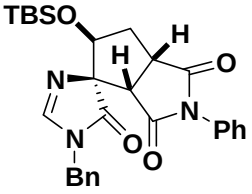
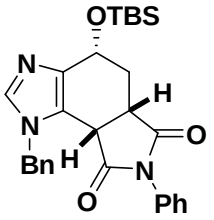
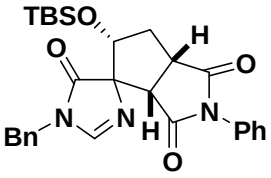
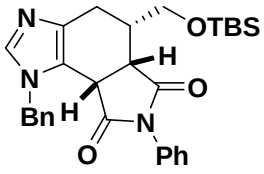
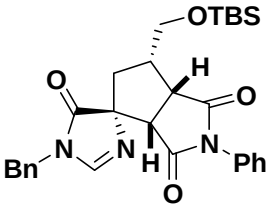
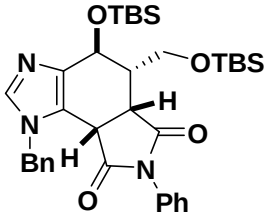
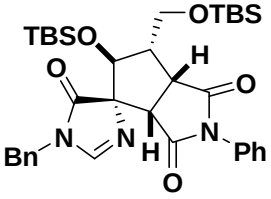
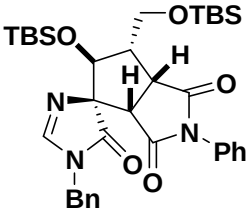
Our own group has explored approaches to palau'amine based on a similar strategy to the Romo lab. The first generation plan focused on the construction of

the DEF-rings of palau'amine through elaboration of the succinimide-containing substrates related to **192** (Scheme 4.13),[10b] which were assembled *via* an *inter*molecular DA reaction between a vinylimidazole and subsequent oxidative rearrangement to obtain the spiro ring using DMDO or Davis' oxaziridine.

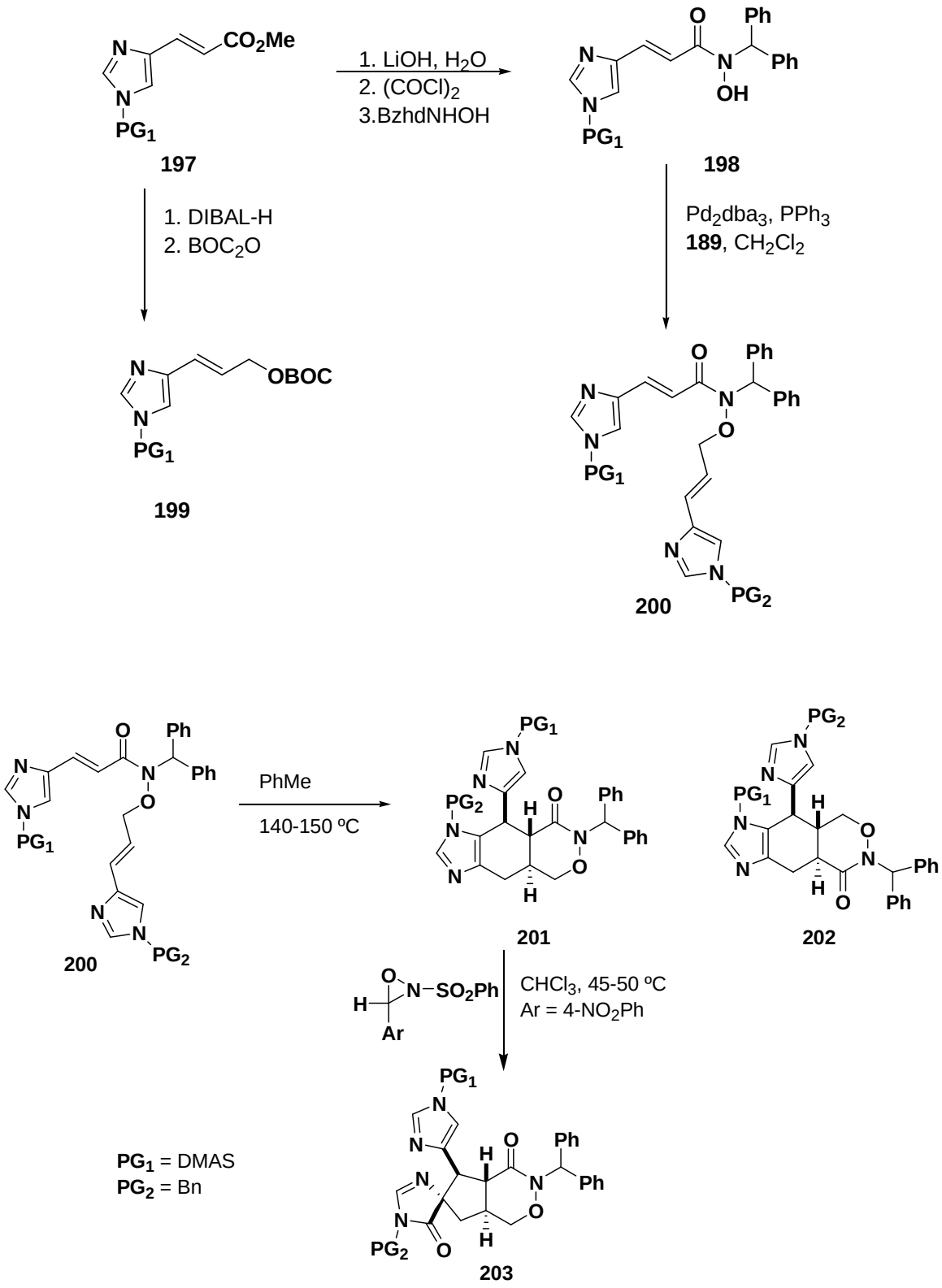


Scheme 4.13

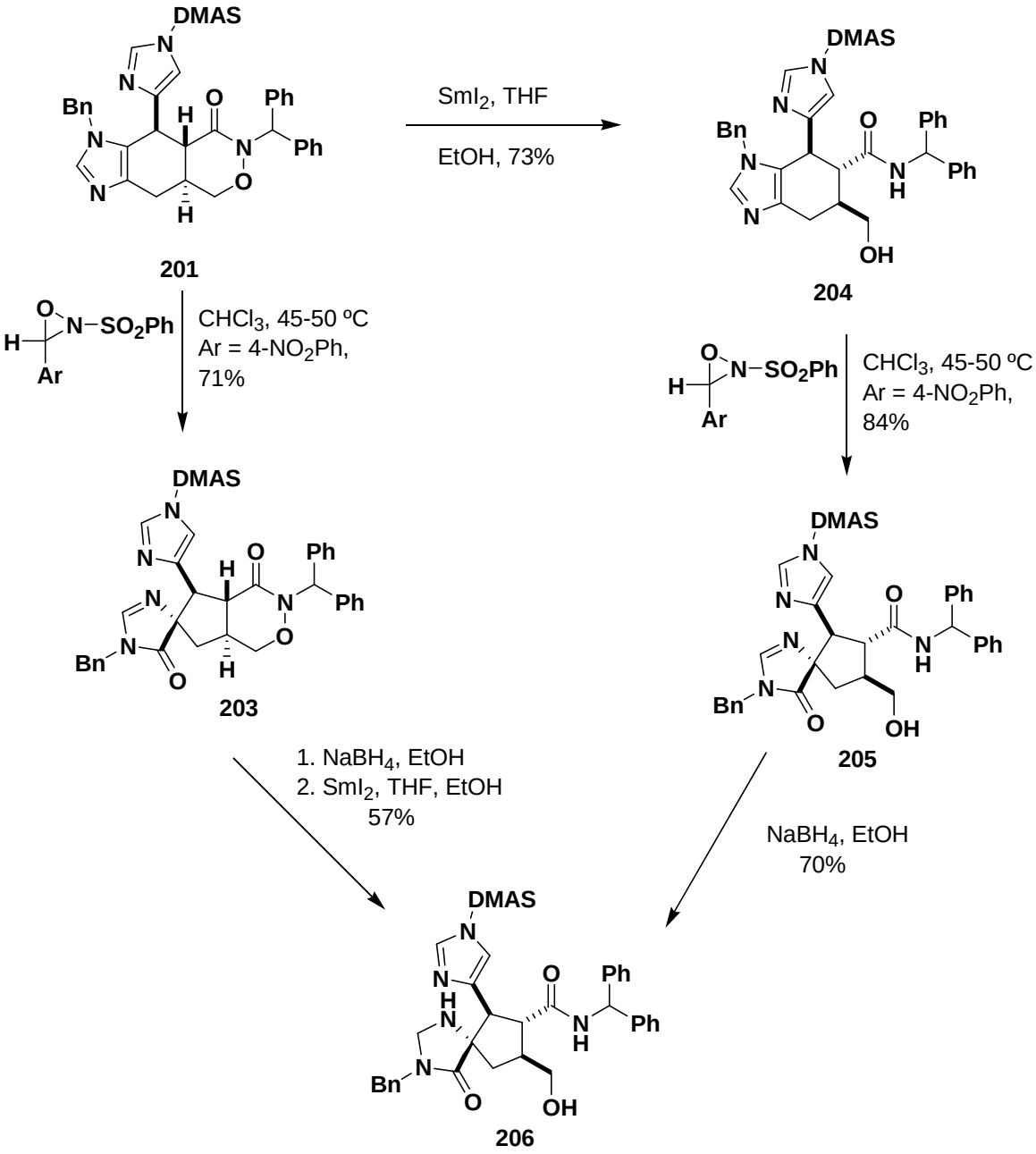
Table 4.1 Yields and products from the oxidative Rearrangement

entry	substrate	Product-yield%	Product-yield%
1	 **188a**	 **exo-189a 56**	 **endo-189b 27**
2	 **193**	 **endo-192a 82**	
3	 **195a**	 **exo-196 44**	
4	 **188b**	 **exo-189b 60**	
5	 **193b**	 **exo-192b 56**	 **endo-192b 14**

However, several aspects of this approach became less attractive in light of developments in a parallel investigation in our lab on the *intra*molecular DA (IMDA) reaction and as a result of the structural revision of palau'amine.[94] It was found in the course of these studies that fairly elaborate systems, *e.g.*, **200** (Scheme 4.14) could be assembled extremely rapidly and these substrates would engage in cycloadditions with reasonable efficiencies. Most notable were systems that potentially allowed access into the ageliferin[94] and axinellamine[94] families through the cyclization of pseudo dimeric substrates such as **200** which afford the all *trans* substituted tetrahydrobenzimidazoles **201** on IMDA reaction (Scheme 4.15). Subsequent reductive cleavage of the hydroxamate and oxidative rearrangement with an *N*-sulfonyloxaziridine provided the spiro fused imidazolone **203**. Unfortunately, the rearranged product was epimeric at the spiro fused center preventing the further use of this particular intermediate en route to axinellamine A (**99**) or palau'amine (**105**).



Scheme 4.14 Cycloaddition and Oxidative Rearrangement

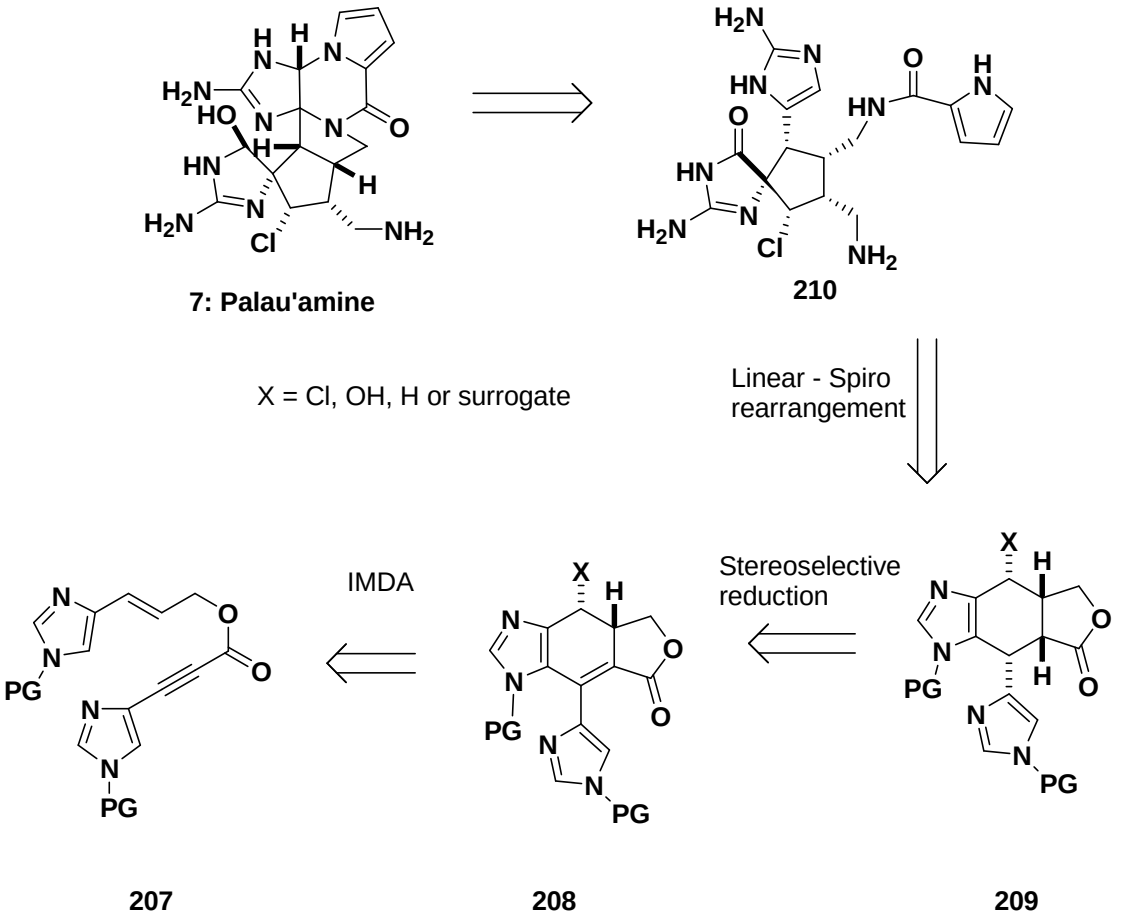


Scheme 4.15 Elaboration of the Cycloadduct

However, if the stereochemical issue of the rearrangement could be corrected, a concise approach for the construction of the key EF-ring system of palau'amine would be possible.

At the time these studies were initiated they were directed toward the original structure of palau'amine, *i.e.*, **7** (Fig. 1.1) but required modification of the strategy

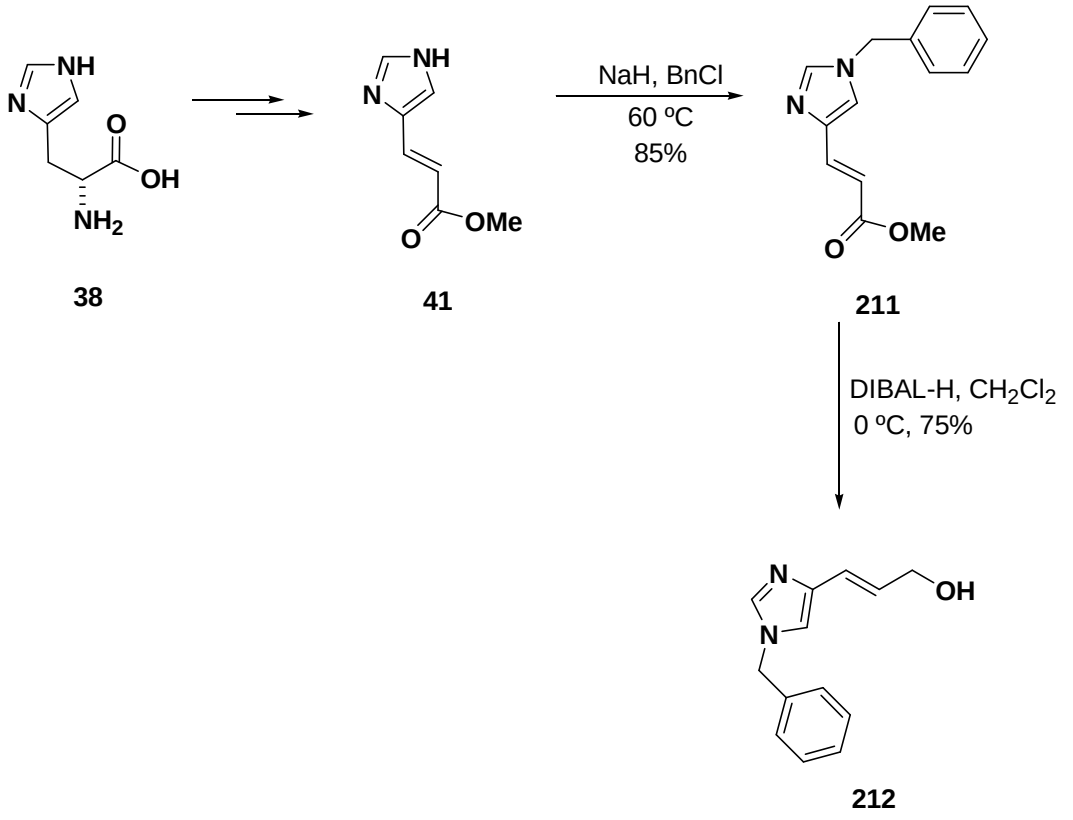
when the structural revision appeared. As indicated above, the use of bis imidazole substrates potentially would increase convergency, and would provide substrates that could utilize chemistries related to those used for the construction of the monomeric oroidin alkaloid phakellin for the formation of the BD-rings (**210** to **7**, Scheme 4.15).[94] Thus, if an all *cis* analog of **206**, *i.e.*, **210** could be constructed, access to a palau'amine-like precursor could be envisioned. However, rather than use a *cis* substituted dienophile in our bis-imidazole approach delineated in Scheme 4.15, we chose to employ a propiolic acid derivative in the cycloaddition and perform a diastereocontrolled hydrogenation on the resulting cycloalkene to establish the relative stereochemistry (**207** to **208** to **209**). This strategy was adopted as we reasoned that this would circumvent any potential issues associated with epimerization post-cycloaddition. Furthermore, based on earlier studies from our lab with aryl propiolate derivatives we were confident that the cycloaddition strategy would be successful.[47] We were able to propose an approach to **207** and **208** depicted retrosynthetically in (Scheme 4.16), which involves an intramolecular DA reaction and its subsequent rearrangement and elaboration of lactone **208 to 209** as we have already developed key transformations like the Diels-Alder reactions of vinyl imidazoles[5-10] and the oxidative rearrangement of tetrahydrobenzimidazoles.[10b]



Scheme 4.16 Retrosynthetic ananlysis

CHAPTER 5

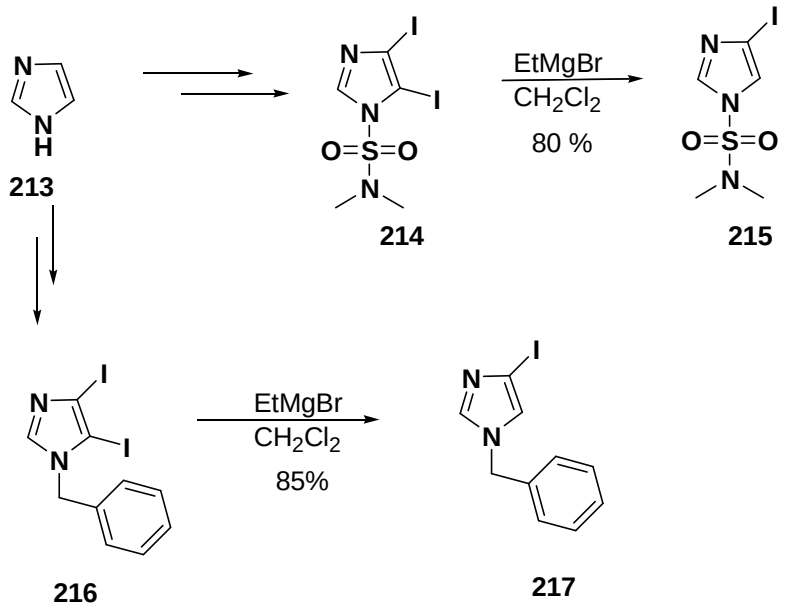
RESULTS AND DISCUSSION



Scheme 5.1

Our studies began by converting L-histidine (**38**) to the desired urocanate ester **41** and then the free imidazole N-H was protected using NaH and benzyl chloride in dry THF to give benzyl protected urocanic ester **211**.[95] The ester was reduced to allylic alcohol **212** by using DIBAL-H (Scheme 5.1). The benzyl protecting group was used since previous work from our group has shown that an electron

donating group at this position is critical in the formation of spiro ring in the oxidative rearrangement.[96]

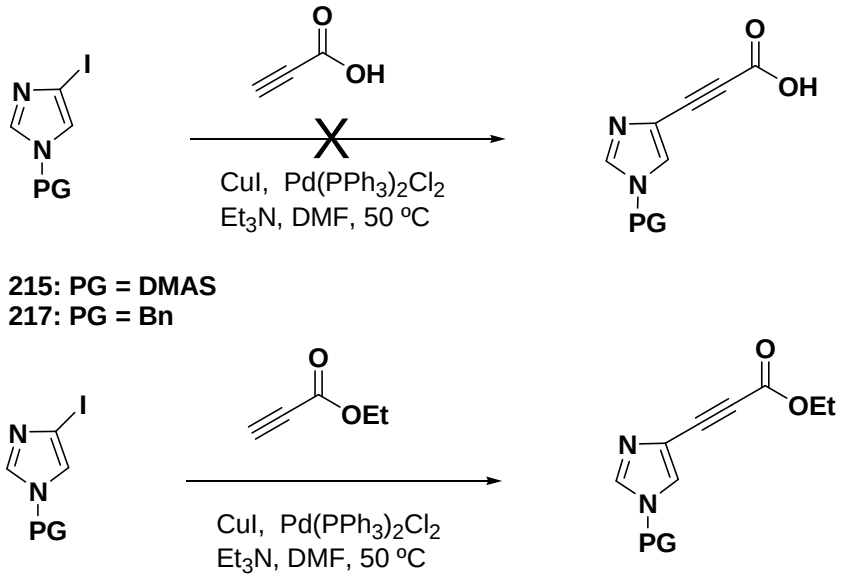


213 **214** **215** **216** **217**

Scheme 5.2

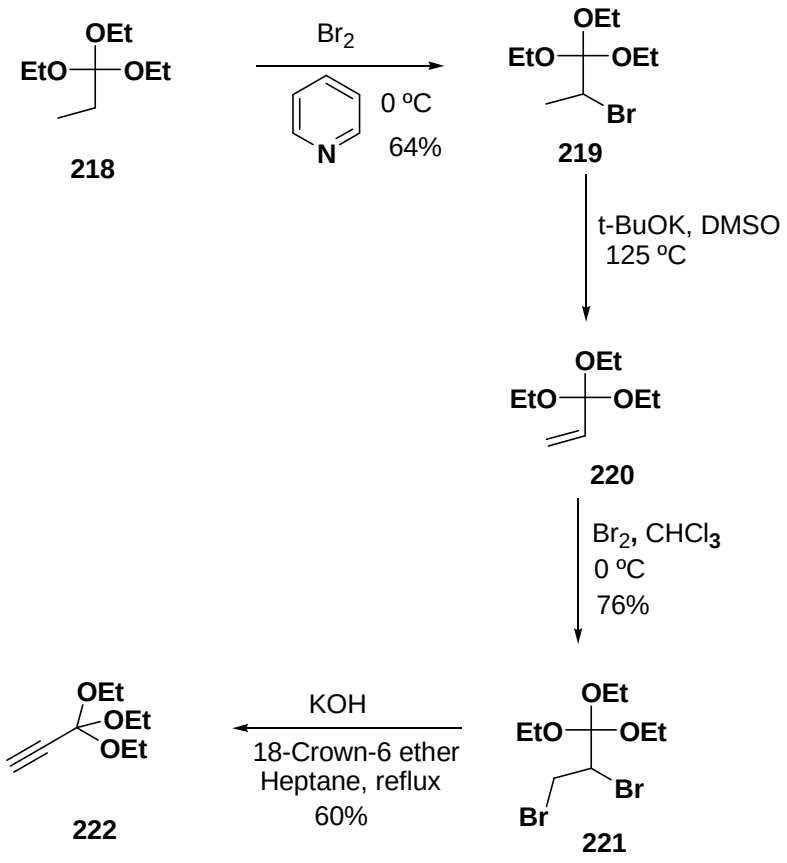
The second fragment was prepared from imidazole **213** by diiodination[97] with molecular iodine and potassium iodide in the presence of 4M NaOH (Scheme 5.2). The nitrogen atom of imidazole was protected with one the two different protecting groups so that we had flexibility at later stages of the synthesis. The iodine at the C-5 position of imidazole was removed by treatment with ethylmagnesium bromide to give **215** and **217**. With the mono iodoimidazoles in hand (**215** and **217**), our aim was to perform a Sonogashira reaction between the iodoimidazoles and a suitable alkyne coupling partner. In this regard we screened many alkynes including propiolic acid and propiolic esters (Scheme 5.3). In the case of propiolic acid we did not observe any desired Sonagashira reaction. However with propiolic ester, the desired product was obtained but the

yield was rather low (10%) as it can also act as a Michael acceptor leading to the formation many side products and scalibity was also an issue with the ester.



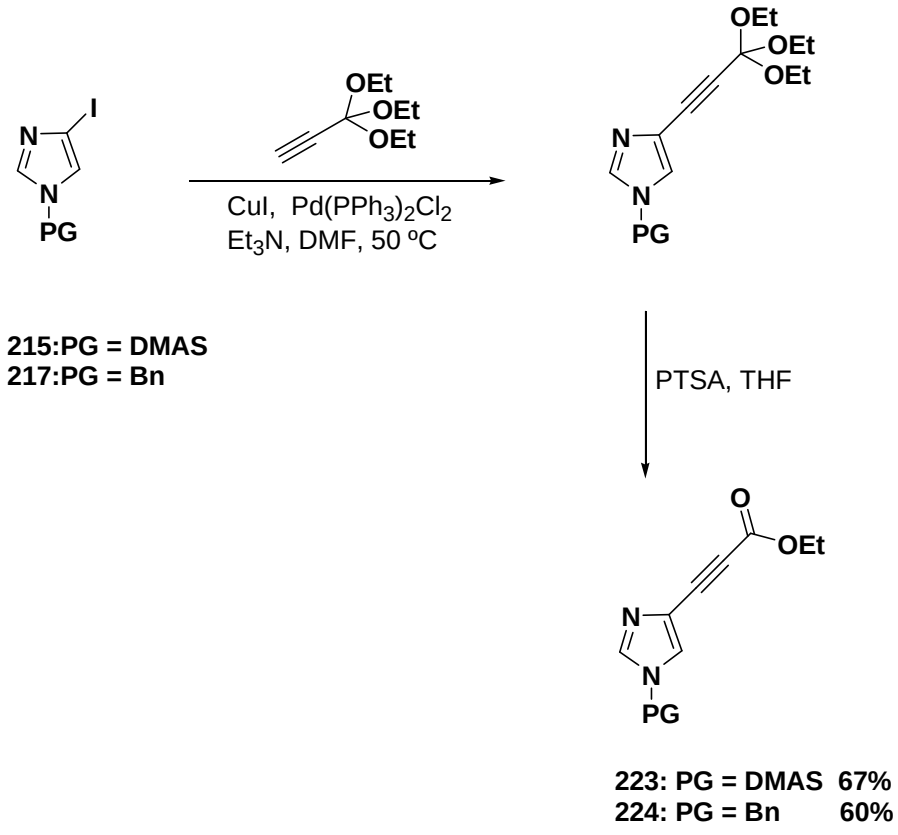
Scheme 5.3

To address this problem we decided to use 3,3,3-triethoxy-1-propyne (**222**)[98] as our other partner for the Sonagashira reaction as it is a masked propiolic ester and so it will not act as a Michael acceptor. In order to prepare this intermediate we started with the ortho ester **207**, brominated it with bromine and pyridine as a solvent (Scheme 5.4). Then compound **208** was dissolved in dry DMSO and t-BuOK was added, heating to 125 ºC led to the formation of the alkene **209**. The resulting alkene was dibrominated by treatment with bromine in chloroform to provide the dibrominated compound **210**. To obtain compound **211**, we performed a double elimination hydrogen bromide which was achieved by using KOH in the presence of 18-crown-6 and heating the reaction mixture to 115 ºC.



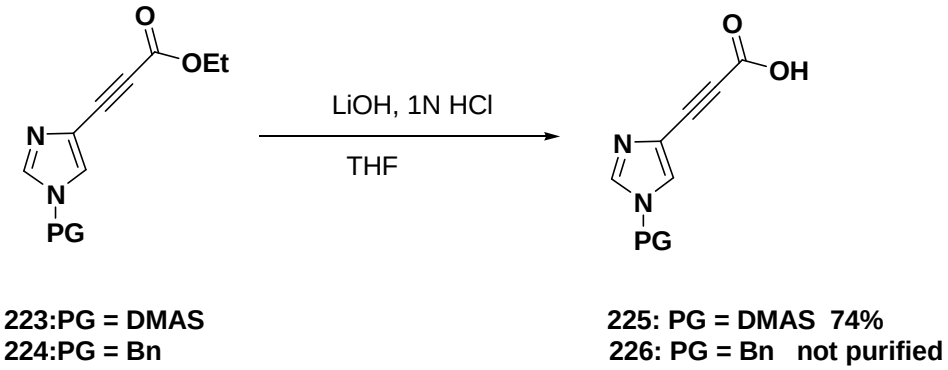
Scheme 5.4

Next a Sonogashira reaction was performed between 4-iodoimidazole (**215** and **217**) and 3,3,3-triethoxy-1-propyne (**222**) using a Pd(II) precatalyst in the presence of CuI and triethylamine and heating the reaction mixture to 50 ºC (Scheme 5.5).[99] Some hydrolysis of the ortho ester occurred on purification and so the Sonagashira product was subjected directly to in situ hydrolysis using PTSA (catalytic) to give compounds **223** and **224** in 67% and 60% yield respectively.



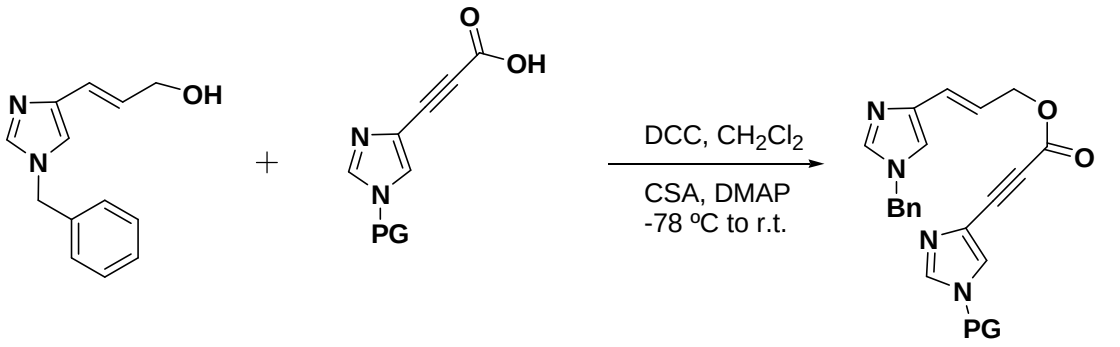
Scheme 5.5

Compounds **223** and **224** were converted into the corresponding acids **225** and **226** using aqueous lithium hydroxide and then neutralized with 1N HCl (Scheme 5.6).



Scheme 5.6

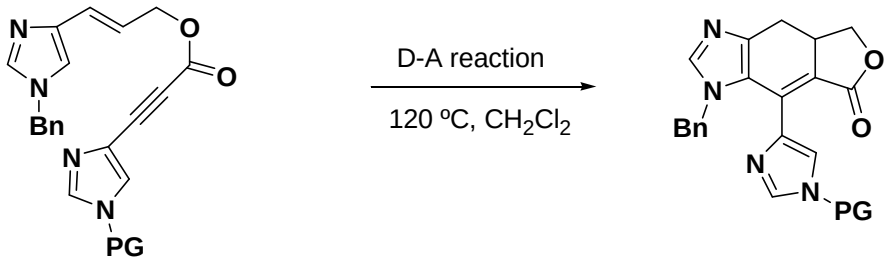
The resulting acids **225** and **226** were coupled with alcohol **212** mediated by DCC in the presence of a catalytic amount of camphorsulfonic acid (CSA) and 4-dimethylaminopyridine (DMAP) at -78 ºC to obtain the enyne compounds **227** and **228** (Scheme 5.7).[49]



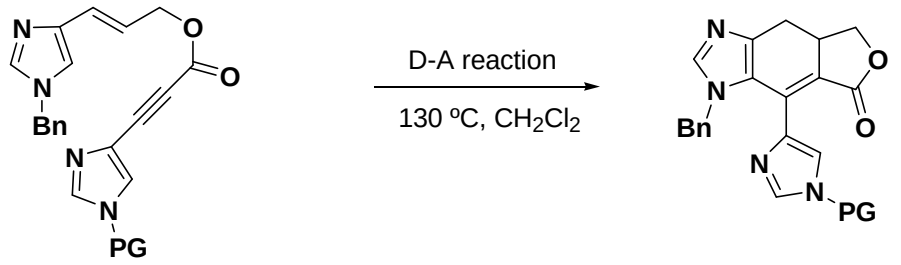
212 **225: PG = DMAS** **226: PG = Bn** **227: PG = DMAS** 67% **228: PG = Bn** 60%

Scheme 5.7

The ene-yne compounds **227** and **228** were dissolved in dichloromethane and heated to ~ 120 ºC in a sealed tube to provide the dihydrobenzimidazole Diels-Alder products **229** and **230** (Scheme 5.8). To obtain this Diels-Alder product we screened other solvents like benzene and toluene but the desired Diels-Alder product was obtained only when we used dichlromethane as solvent.



227:PG = DMAS **229: PG = DMAS 82%**

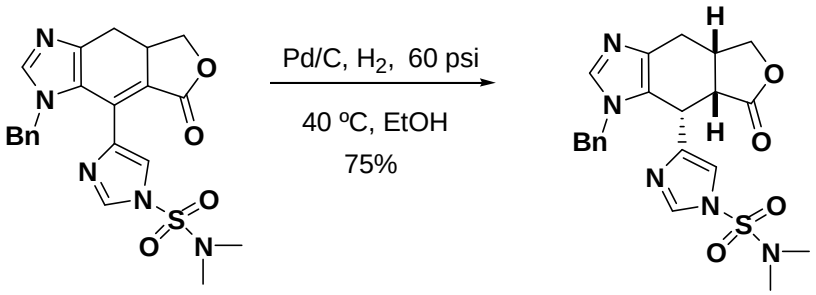


228:PG = Bn **230: PG = Bn** **70%**

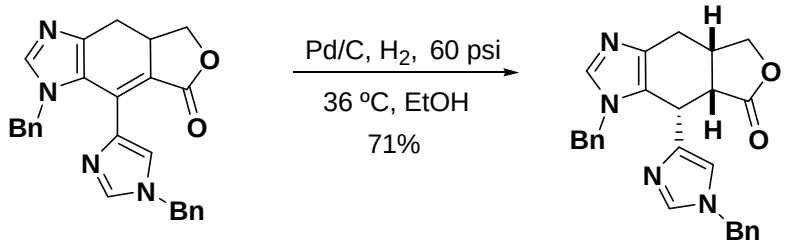
Scheme 5.8

The alkene in the six membered ring of the cycloadducts **229**, **230** was saturated using Pd/C under a hydrogen atmosphere (60 psi) with heating of the reaction mixture to 40 ºC (Scheme 5.9).

The initial assignment of the relative stereochemistry of the reduction product was obtained by examination of the relevant coupling constants of the bridgehead and benzylic protons. It has been determined that $J_{4a,7a}$ = 8.7 Hz and $J_{7a,8}$ = 8.7 Hz, which are completely consistent with the indicated stereochemistry. We have prepared a large number of cycloadducts related to **229** and **230** with the exception that they are all *trans* substituted, and in these cases the corresponding coupling constants are substantially larger $J_{4a,7a}$ = 12.8-13.6 Hz, and $J_{7a,8}$ = 10.1-10.8 Hz.[10a] Further, in several cases the relative configurations of these all trans derivatives have been rigorously established by X-ray crystallography.[94]



229 **231**

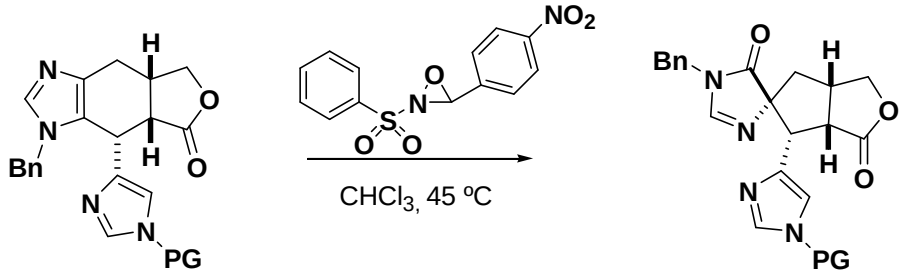


230 **232**

Scheme 5.9

With the all-*cis* cycloadducts **231** and **232** in hand, our next task involved their elaboration, including rearrangement into the spiro fused system. We have shown previously that this can be accomplished through an oxidative rearrangement using dimethyldioxirane,[10b] and while this works well in many cases some aspects of this chemistry were unattractive, in particular the need to prepare isolated reagent. It has been found (recently) that this same rearrangement can be performed using Davis' reagents (*N*-sulfonyloxaziridines).[100] Accordingly, when **231** and **232** were treated with two equivalents of Davis reagent in $CHCl_3$ at 40 °C, it undergoes a smooth oxidative rearrangement providing a single spiro imidazolone **233**, **234** in good yield

(Scheme 5.10). The exquisite chemoselectivity for the more substituted (and presumably more electron rich) imidazole in this reaction is noteworthy. We were also fortunate that both **233** and **234** were well-behaved crystalline solids, which gave crystals suitable for X-ray crystallography. This not only confirms the stereochemical sense of the spiro fusion, but also that the catalytic hydrogenation occurs *syn* to the hydrogen at the ring junction and leads to an all-*cis* fusion. Of particular note is the stereochemical outcome of this rearrangement. Our group previously reported studies with all *trans* substituted systems[94] and also one related substrate reported by Baran and coworkers[75] gives rise to an imidazolone with the opposite stereochemistry, and this seemingly subtle change in the relative stereochemistry of the substrate leads to a complete changeover in selectivity.

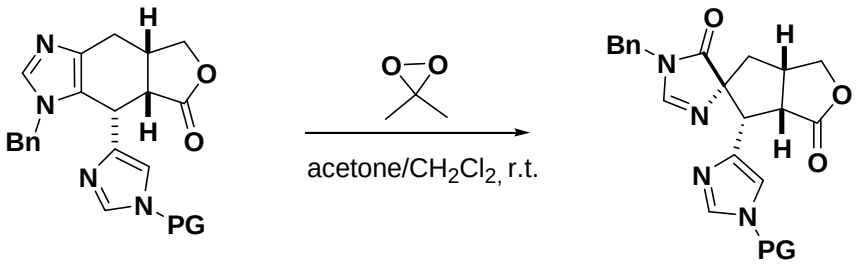


231: PG = DMAS
232: PG = Bn

233: PG = DMAS 60%
234: PG = Bn 65%

Scheme 5.10

For comparison, we also examined the rearrangement with DMDO and found that this proceded in marginally higher yield. The other advantage with DMDO is that the purification is substantially easier as the byproducts from the oxidant are readily removed.



231: PG = DMAS
232: PG = Bn

233: PG = DMAS 70%
234: PG = Bn 72%

Scheme 5.10

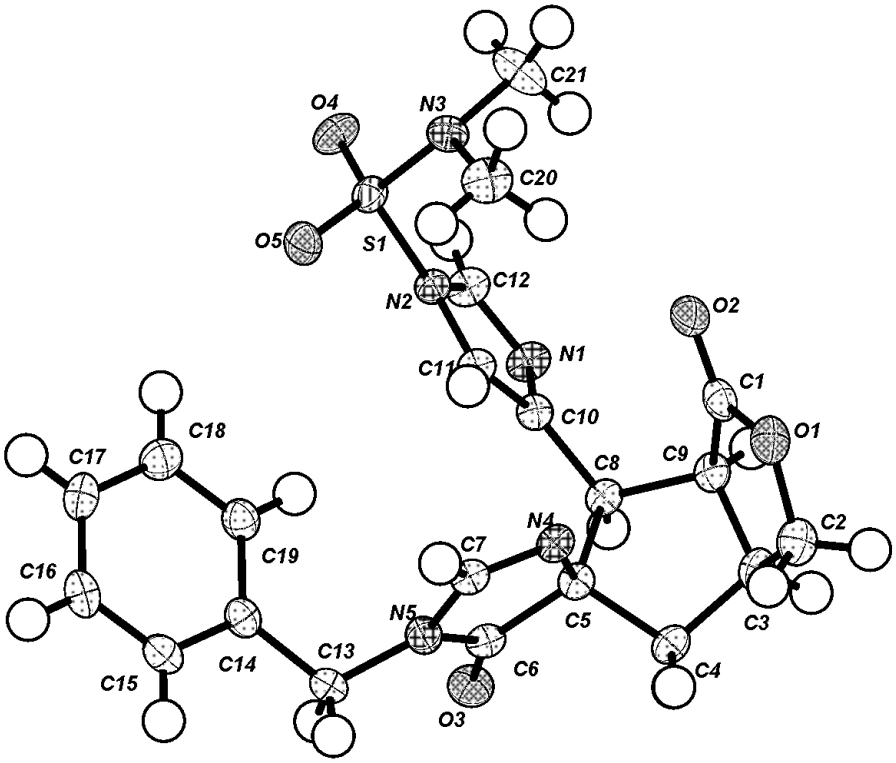
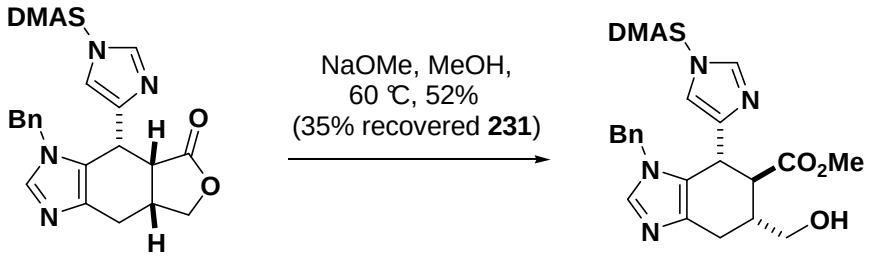
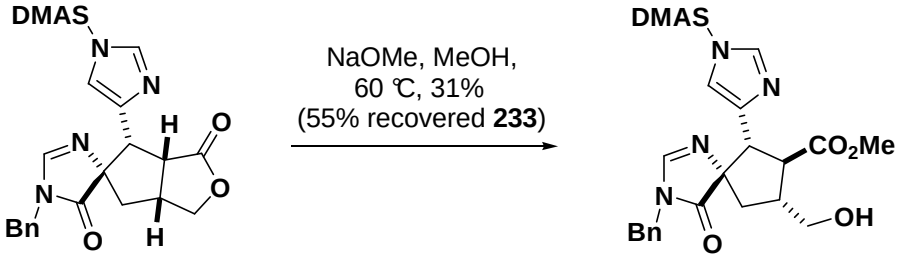


Figure 5.2 X-ray crystal structure of compound **233**

After some experimentation it was found that the lactone **233** underwent ring opening-epimerization on treatment with NaOMe in MeOH at 60 °C, providing the hydroxy ester in a modest 35% yield, with 55% recovered starting material (Scheme 5.11).[52] It was also determined that the tetrahydrobenzimidazole **231** would undergo ring-opening/epimerization, leading to an ageliferin-like stereochemical arrangement. Although both ring opening/epimerization reactions, require further optimization, access to the spiro fused core of palau'amine and related compounds has been developed. In addition, the cycloadducts **231** provide an entry to the ageliferin and potentially the related nagelamide family of natural products by suitable adjustments of the stereochemistry, and these efforts are underway in our lab.



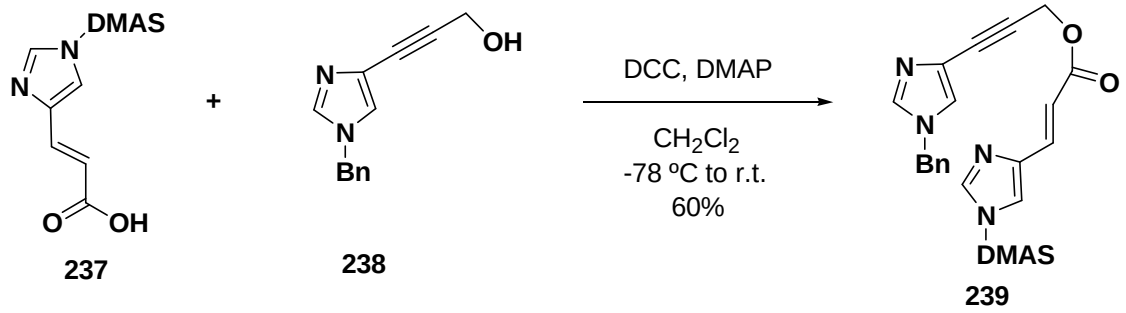
231 **235**



233 **236**

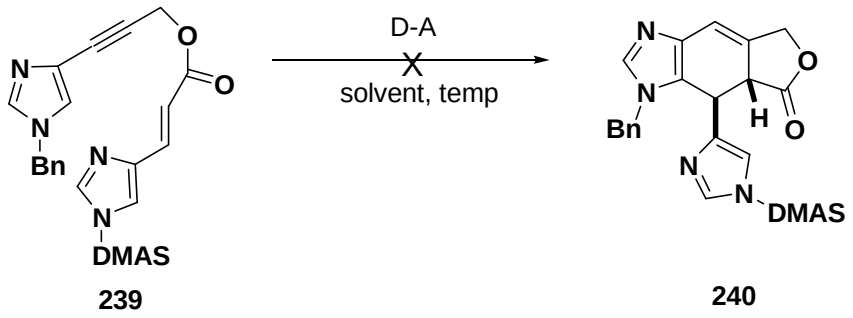
Scheme 5.11

After obtaining all *trans*-substituted spiro cyclopentyl imidazolone system found in palau'amine and related natural products, we turned our attention towards investigating methods for the stereoselective incorporation of the chloro moiety, and for the construction of the remaining rings. In order to incorporate the chloro or hydroxy moiety in the molecule, our initial stategy was to transpose the enyne part of the molecule **227** so that after the Diels-Alder reaction, the molecule will have a double bond in the six-membered ring which we can utilize to incorporate a chloro or a hydroxy group later. In order to prepare this substrate **239** compound **237** was coupled with **238** in presence of DCC (Scheme 5.12).[49]



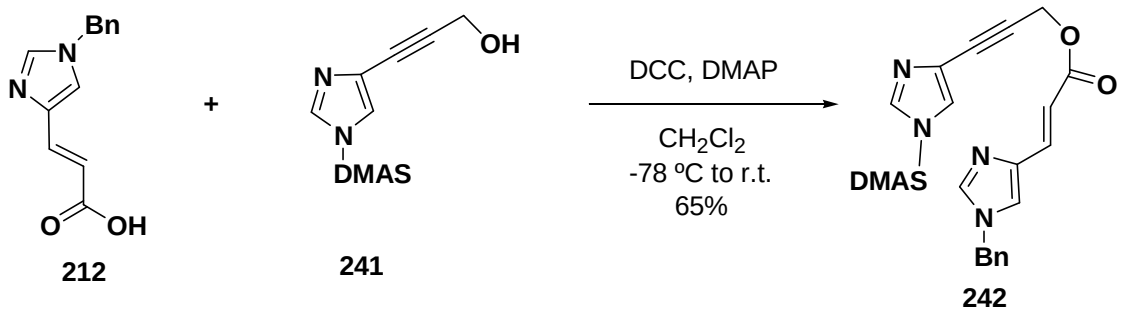
Scheme 5.12

Once we had compound **239**, we subjected it to Diels-Alder reaction under various solvent and at various reaction temperature starting from 90 to 120 ºC but the desired product **228** was never isolated and starting material was recovered (Scheme 5.13).



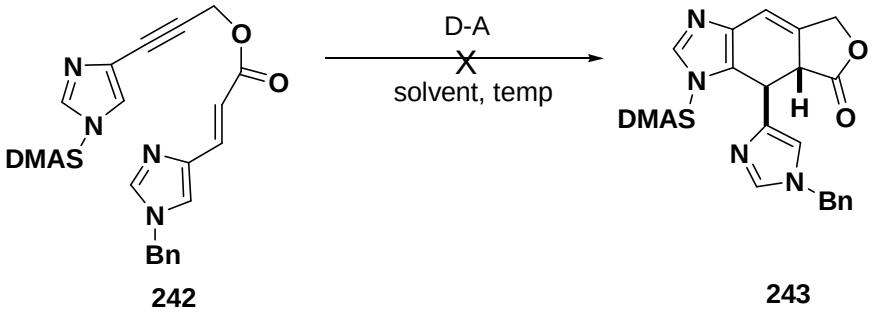
Scheme 5.13

Since compound **239** did not undergo Diels-Alder reaction, we wondered whether interchanging the protecting groups on the enyne compound **239** would lead to a productive D-A reaction (Scheme 5.14).



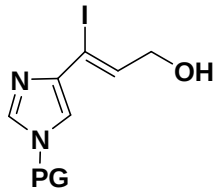
Scheme 5.14

Compound **242** was dissolved in dichloromethane in sealed tube and then it was subjected to Diels-Alder reaction at various reaction temperature starting from 90 to 120 ºC but the desired product **243** was never isolated (Scheme 5.15).



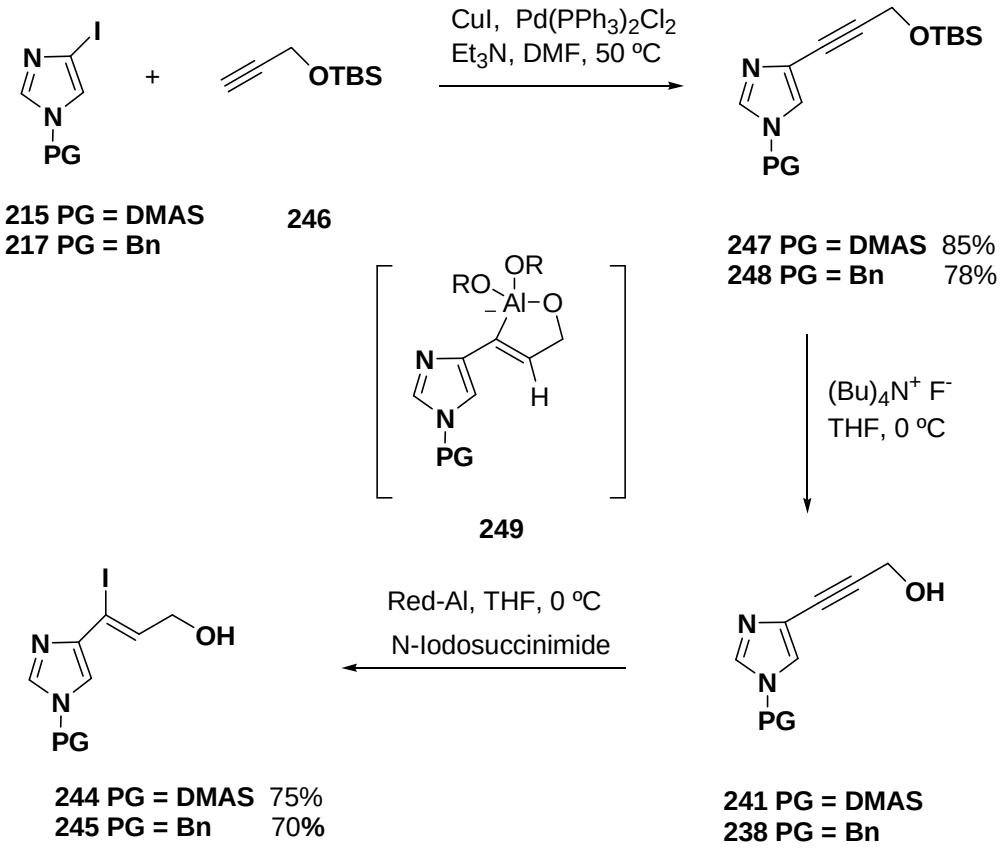
Scheme 5.15

Since compounds **239** and **242** did not undergo Diels-Alder reaction as expected, a change of strategy was necessary, specifically we chose to evaluate substrates in which the vinyl moiety was substituted. In this regard we considered using a halide, as it can be utilized either as a latent handle for incorporating other substitutents at this position or in the case of chlorine as the required substituent.



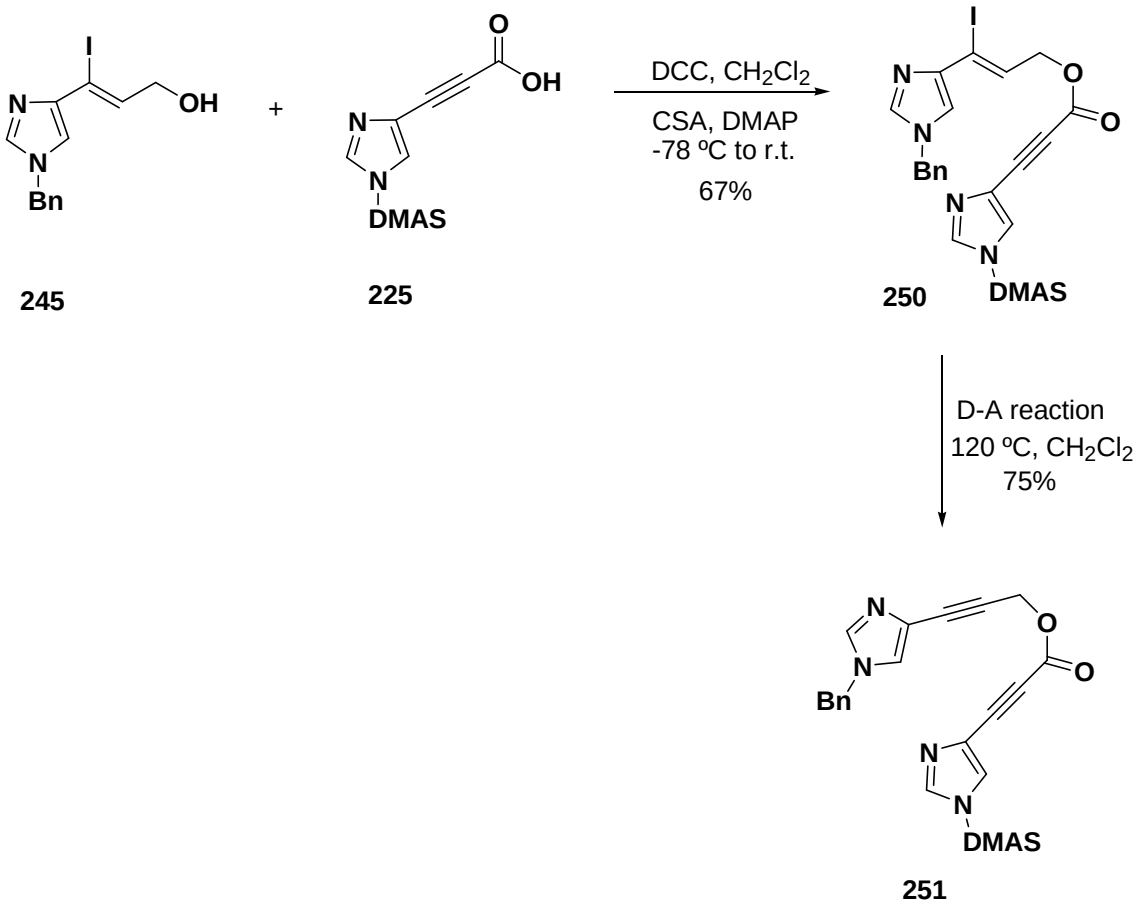
244 PG = DMAS
245 PG = Bn

First a Sonagashira reaction between iodoimidazoles **215** and **217** and the protected propargylic alcohol provided **247** and **248** (Scheme 5.16). Subsequent treatment of silyl ethers **247** and **248** with tetrabutylammonium fluoride provided alcohols **241** and **238**. The desired substituted alcohols **244** and **245** were obtained by hydroalumination with Red-Al[101] which upon addition of N-iodosuccinimide to the reaction mixture at 0 ºC provided the vinyliodides.



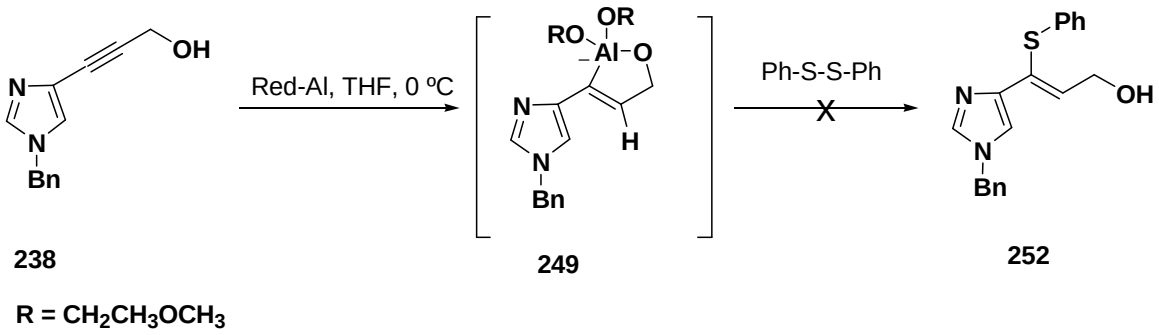
Scheme 5.16

Alcohol **245** was coupled with acid **225** mediated by DCC to obtain the enyne compound **237** (Scheme 5.17). Compound **250** was then subjected to an attempted Diels-Alder reaction at various temperatures ranging from 90 to 130 ºC. We observed that at 90 ºC the starting material does not react, so we inceased the temperature to 100 ºC still the starting material does not react. The same thing was observed as the temperature increased to 110 ºC and 115 ºC respectively. However, when the temperature was increased to 120 ºC, a new spot was observed developing on TLC plate which upon charactization was found to be compound **251** resulting from dehydroiodination.



Scheme 5.17

While we were not surprised that the iodine substitutent was somewhat labile under the Diels-Alder conditions, we were confident that the general strategy was worth pursuing and thus substitutents tolerant of the Diels-Alder reaction were required but that would function as latent halide equivalent. In this regard we tried to incorporate a thiophenyl moeity in place of iodine. Compound **238** was dissolved in THF and Red-Al was added at 0 ºC, then diphenyl disulfide was added to the mixture and was allowed to come to r.t. but we were unable to isolate compound **252**. Raising the reaction temperature to 50 ºC, also failed to lead to a productive reaction (Scheme 5.18).



238

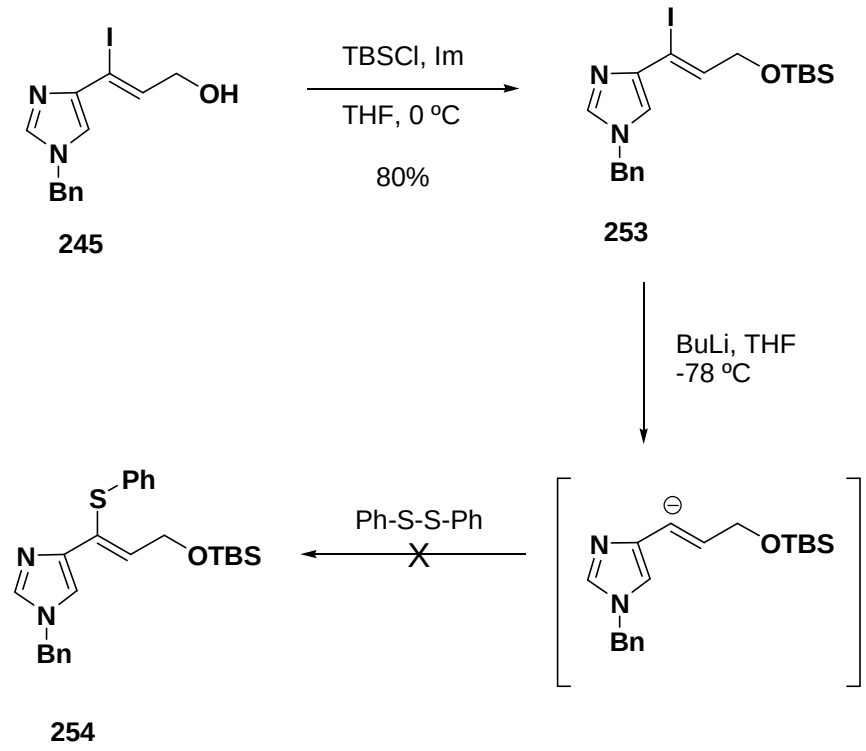
249

252

R = $CH_2CH_3OCH_3$

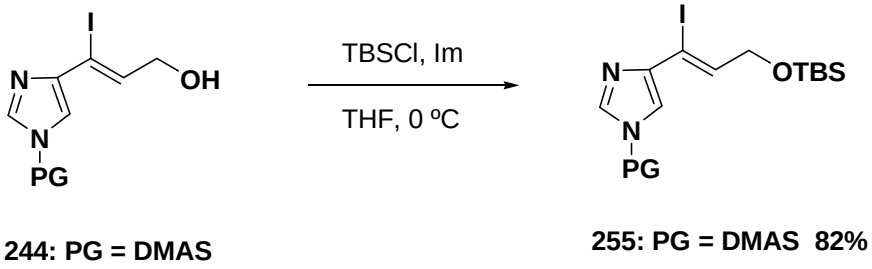
Scheme 5.18

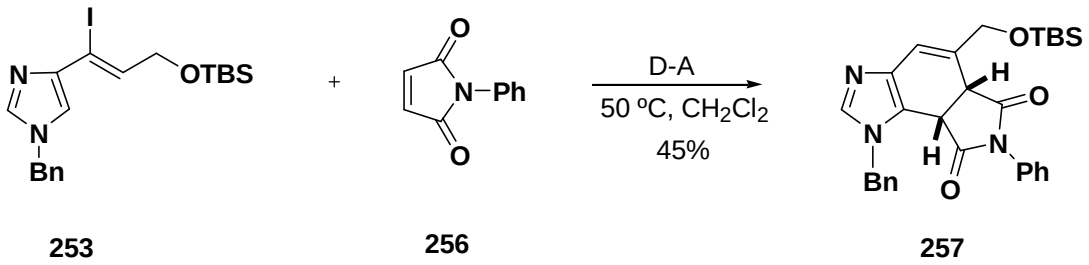
Presumably, we were not able to obtain the compound **252** because intermediate **249** is not sufficiently nucleophilic to attack the diphenyl disulfide. Therefore it was thought that generating the vinyl anion by iodine-lithium exchange and then adding diphenyl disulfide may provide a solution to the synthesis of **252**. The alcohol **245** was protected with TBSCl and then treatment of **253** in THF with BuLi at -78 ºC resulted in in iodine-lithium exchange to the desired anion. Diphenyl disulfide was added cooling the reaction mixture to -78 ºC. After allowing the reaction mixture to warm upto the r.t., it was found that the desired product has not formed. Even heating the reaction mixture to 50 ºC did not provide the desired product **254** (Scheme 5.19) instead we obtained the reduced allylic alcohol.



Scheme 5.19

Since we were not able to introduce the sulfur group at the vinyl position, we went back and protected the alcohols **244** and **245** with TBS group and then tried the intramolecular Diels-Alder reaction with the reactive *N*-phenylmaleimide at much lower temperature such as 50 ºC instead of 120 ºC. Even at 50 ºC we found that dehydroiodination was occurring, resulting in the formation of compound **257** (Scheme 5.20).[5,102]

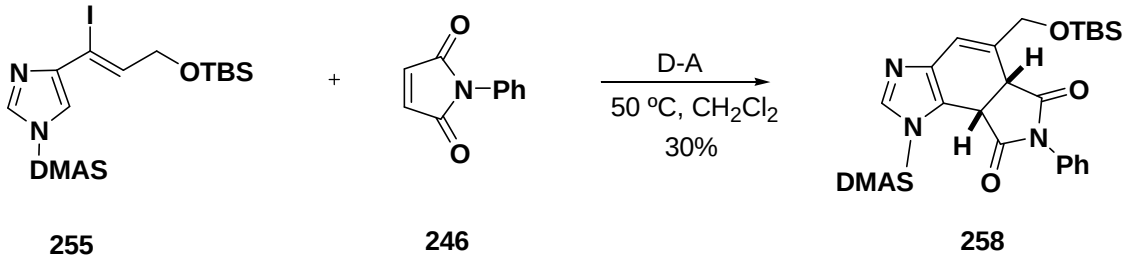




253 **256** **257**

Scheme 5.20

In order to stop this dehydroiodination we used $Y(OTf)_3$ as a Lewis acid since this Lewis acid has been reported to promote successful Diels-Alder reactions at much lower temperature including with vinylimidazoles.[103] So we dissolved compound **253** and **256** in dichloromethane and to the reaction mixture we added 0.01 equivalent of $Y(OTf)_3$ and then heated the reaction mixture in a sealed tube at 38 ºC. Even at this temperature we obtained the same compound **257**. A similar outcome was observed with compound **255** when subjected to Diels-Alder reaction (Scheme 5.21).

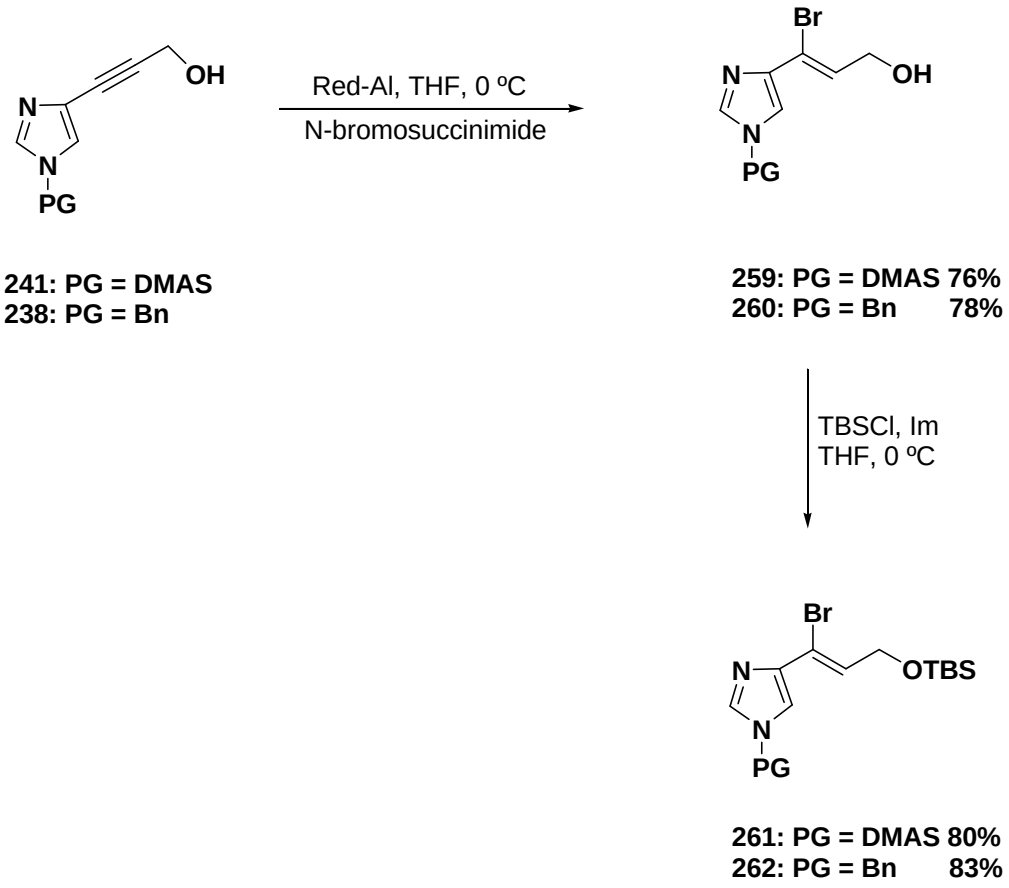


255 **246** **258**

Scheme 5.21

Since the iodo substituent was somewhat labile under the reaction conditions we thought that replacing iodine either with bromine or chlorine may provide more stable adducts under the Diels-Alder reaction conditions. Although the resulting 4-halo adducts are benzylic halides and thus be prone to elimination. In that

regard compound **259** and **260** were obtained by hydroalumination with Red-Al which upon treatment of *N*-bromosuccinimide to the reaction mixture at 0 ºC provided the vinylbromide. Alcohols **259** and **260** were then protected with TBS group to provide compounds **261** and **262** (Scheme 5.22).



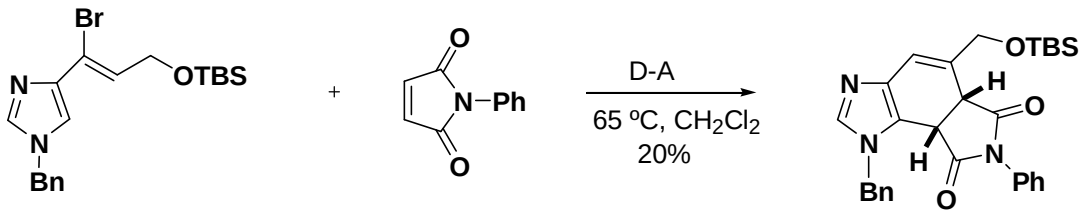
241: PG = DMAS
238: PG = Bn

259: PG = DMAS 76%
260: PG = Bn 78%

261: PG = DMAS 80%
262: PG = Bn 83%

Scheme 5.22

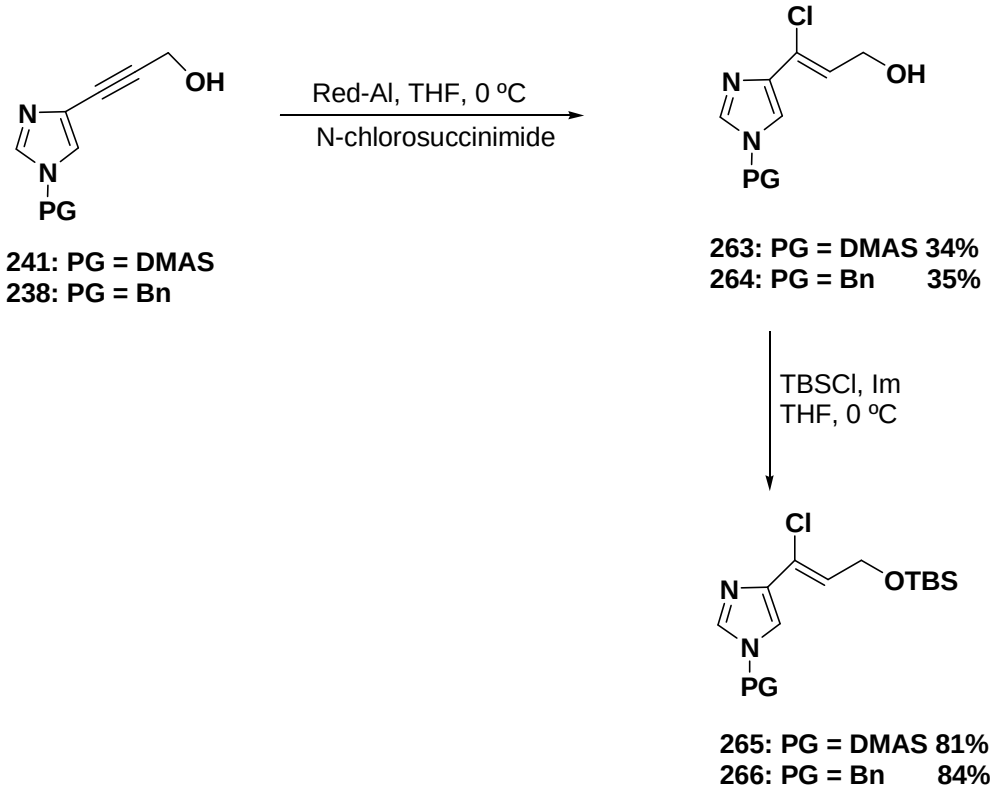
Compound **262** was subjected to the Diels-Alder reaction at various temperatures such as from 35 ºC to 65 ºC and it was determined that starting material remains intact up to 60 ºC. At around 65 ºC a new component was observed on TLC plate which upon charactization found to be compound **257** resulting from dehydrobromination in 20% yield (Scheme 5.23).



262 **246** **257**

Scheme 5.23

Since the Diels-Alder product derived from compound **262** also underwent dehydrobromination under the reaction conditions we decided to make the chloro version. Compound **263** and **264** were obtained by hydroalumination with Red-Al which upon treatment with *N*-chlorosuccinimide at 0 ºC provided the vinylchloride. Alcohols **263** and **264** were then protected with a TBS group to provide compound **265** and **266** (Scheme 5.24).



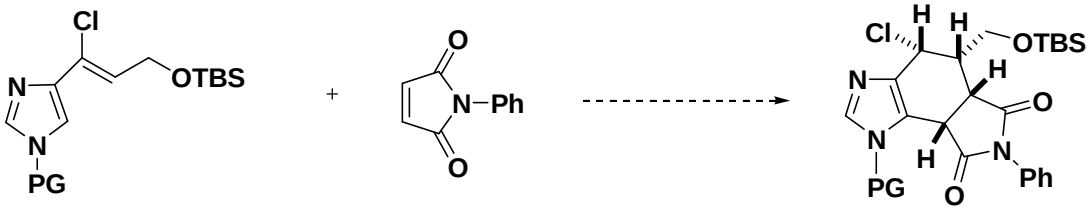
241: PG = DMAS
238: PG = Bn

263: PG = DMAS 34%
264: PG = Bn 35%

265: PG = DMAS 81%
266: PG = Bn 84%

Scheme 5.24

Compound **265** and **266** were dissolved in dichloromethane and to each of the reaction mixture **246** was added and then the resulting reaction mixture were subjected to the Diels-Alder reaction conditions. The reactions were monitored starting from around 40 to 75 ºC, but the desired product was not obtained instead starting materials were recovered (Scheme 5.25). It looks like the chloro atom is deactivating the diene and so to push this reaction towards forward direction we need to heat the reaction mixture at higher temperature. This reaction needs further investigation.



265: PG = DMAS
266: PG = Bn

246

267: PG = DMAS
268: PG = Bn

Scheme 5.25

In conclusion, we have developed a concise entry into the all *trans*-substituted spiro cyclopentyl imidazolone system found in palau'amine and related natural products *via* an IMDA reaction of an enyne followed by an oxidative rearrangement. Initial experiments aimed at elaborating this intermediate have demonstrated that precursors suitable for investigating various end-game strategies can be constructed by differentiating the two hydroxymethyl handles. Finally we have investigated a method for the stereoselective incorporation of the chloro moiety, which is present in parent molecule palau'amine.

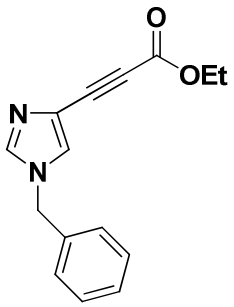
CHAPTER 6

EXPERIMENTAL DETAILS

3.1 General procedures

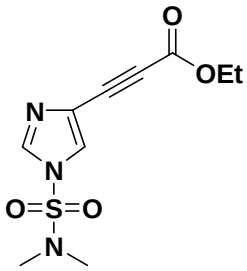
All reagents were purchased from commercial suppliers and were used as received unless otherwise noted. ^{1}H and ^{13}C NMR (δ in ppm) spectra were recorded in $CDCl_3$ (unless otherwise noted) at 500 and 125.8 MHz, respectively; using a JEOL Eclipse+ 500 spectrometer unless otherwise noted using residual $CHCl_3$ as reference (^{1}H NMR and carbon absorption of $CDCl_3$ for ^{13}C NMR). Infrared spectra were recorded either as neat films or as KBr pellets using a Bruker Vector 22 spectrometer. Elemental analyses were performed using a Perkin-Elmer 2400 CHN analyzer. Optical rotation was measured on a Perkin-Elmer 241MC polarimeter (*c* = g/100 mL) and the observed value was an average of 2-3 runs. The solvent used for optical rotation was MeOH unless otherwise noted. High resolution mass spectra (HR-MS) were obtained from Dr. Powell's lab in the University of Florida, Gainesville, Florida.

Ethyl 3-(1-benzyl-1H-imidazol-4-yl)propiolate (224):



DMF (50 mL) was first purged with N_2 then Bn-protected 4-iodoimidazole **217** (5.0 g, 0.02 mole) was added followed by $Pd(PPh_3)_2Cl_2$ (0.37 g, 0.53 mmol), copper (I) iodide (200 mg, 1.06 mmol), orthoester[98a] (4.54 mL, 26 mmol) and finally triethylamine (6.1 mL, 40 mmol) under a N_2 atmosphere. The reaction mixture was heated at 50 ºC for 8 h. *p*-TsOH (400 mg) was added to the above reaction mixture and then stirred at r.t. overnight. The organic solvent was washed with water (200 mL), the organic layer was dried with anhydrous Na_2SO_4 concentrated and the residue was purified by chromatography on silica gel (hexane/EtOAc, 3:2) providing **224** as a thick yellow liquid (2.68 g, 60%). ^{1}H NMR (300 MHz): δ = 7.38-7.36 (m, 4H), 7.19-7.17 (m, 3H), 5.11 (s, 2H), 4.24 (q, *J* = 7.6 Hz, 2H), 1.31 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (75 MHz): δ = 154.2, 138.4, 134.9, 129.3, 128.9, 127.6, 127.5, 121.9, 81.7, 80.8, 61.9, 51.5, 14.2; FT-IR (neat, cm^{-1}): 1749, 1716, 1699, 1497, 1489, 1473, 1457, 1436, 1419, 1396, 1374, 1362, 1339, 1318, 1094; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{15}H_{14}N_2O_2$ is 255.1128 found 255.1120.

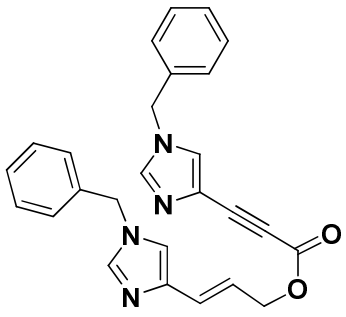
Ethyl 3-(1-(*N*,*N*-dimethylsulfamoyl)-1H-imidazol-4-yl)propiolate (223): DMF



(55 mL) was purged by bubbling N_2 through it for 10 min then DMAS-protected 4-iodoimidazole **215** (5.5 g, 18 mmol) was added followed by $Pd(PPh_3)_2Cl_2$ (0.38 g, 0.54 mmol), copper (I) iodide (0.21 g, 1.09 mmol), ortho ester (4.7 mL,

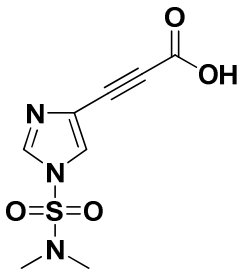
27 mmol) and triethylamine (6.3 mL, 45 mmol) under an N_2 atmosphere. The reaction mixture was heated at 45-50 ºC for 8 h. *p*-TsOH (500 mg) was added to the above reaction mixture followed by stirring at r.t. overnight. The organic solvent was washed with water (250 mL), the organic layer was dried with anhydrous Na_2SO_4 concentrated and the residue was purified by chromatography on silica gel (hexane/EtOAc, 3:2) to provided **223** as a yellow solid (3.30 g, 67%). m.p. 72-74 ºC. ^{1}H NMR: δ = 7.85 (s, 1H), 7.59 (s, 1H), 4.25 (q, *J* = 6.9 Hz, 2H), 2.87 (s, 6H), 1.31 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR: δ = 153.6, 137.1, 124.6, 123.4, 82.5, 78.2, 62.3, 38.3, 14.1; FT-IR (neat, cm^{-1}): 3131, 2984, 2223, 1706, 1474, 1421, 1396, 1332, 1288, 1218, 1176, 1080, 1024, 1010, 965, 856, 728; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{10}H_{13}N_3O_4S$ 272.0699, found 272.0700.

(*E*)-3-(1-benzyl-1H-imidazol-4-yl)allyl 3-(1-benzyl-1H-imidazol-4-yl)propiolate (228): Ester **224** (1.7 g, 6.6 mmol) was dissolved in a mixture of THF (17 mL) and LiOH (1N in water, 19.6 mL) and stirred at r.t. for 3 h. The pH of the solution was adjusted to pH = 4 through the addition of 1N HCl, then the resulting solution was extracted with EtOAc. The organic solvent was evaporated and a yellow solid (1.46 g) was obtained which consists of the corresponding acid and a trace of ester. The acid was not purified any further and was used directly in the preparation of the propiolate derivative. In a round bottom flask the crude acid **226** (0.90 g, 3.97 mmol), alcohol **212** (1.02 g, 4.77 mmol), DMAP (0.04 g, 0.39



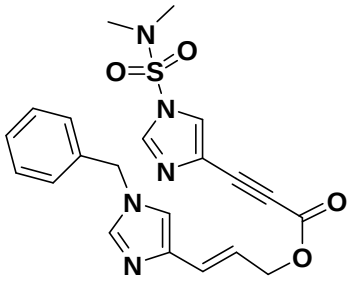
mmol) and camphorsulfonic acid (500 mg, 0.21 mmol) were dissolved in dry CH_2Cl_2 (30 mL). The mixture was cooled to (-78 ºC) and DCC (1.23 g, 5.96 mmol) in dry CH_2Cl_2 (8 mL) was added dropwise. The reaction mixture was allowed to warm up to r.t. and stirred for 2 h. The resulting mixture was filtered through Celite and the filter cake was washed with CH_2Cl_2. Concentration of the filtrate provided the crude product, which was purified by chromatography (hexane/EtOAc, 1:19) to provide **228** a thick colorless liquid (1.08 g, 60%) over two steps. ^{1}H NMR: δ = 7.50 (s, 1H), 7.46 (s, 1H), 7.37-7.31 (m, 6H), 7.28 (s, 1H), 7.17-7.12 (m, 4H), 6.84 (s, 1H), 6.56 (d, *J* = 15.6 Hz, 1H), 6.38 (td, *J* = 16.0, 6.4Hz, 1H), 5.11 (s, 2H), 5.05 (s, 2H), 4.79 (d, *J* = 6.4 Hz, 2H); ^{13}C NMR: δ = 153.9, 139.9, 138.3, 137.9, 135.9, 134.9, 129.3, 129.1, 128.9, 128.4, 127.6, 127.6, 127.4, 126.7, 121.9, 120.6, 117.9, 81.5, 81.2, 66.3, 51.4, 51.0; FT-IR (neat, cm^{-1}): 2988, 2215, 1701, 1540, 1496, 1455, 1377, 1292, 1219, 1148, 1044, 969, 940, 840, 727, 632; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{26}H_{22}N_4O_2$ 423.1816 found 423.1856.

3-(1-(*N*,*N*-dimethylsulfamoyl)-1H-imidazol-4-yl)propiolic acid (225): Ester **223** (3.10 g, 11.4 mmol) was dissolved in THF (20 mL) and LiOH (1N in water, 31 mL) and stirred at r.t. for 2.5 h. The pH of the basic solution was adjusted to pH = 4 by the addition of 1N HCl, and the resulting precipitate was collected by vacuum filtration and washed with small amount of cold water. After drying in vacuo, the corresponding acid **225** was



obtained as a colorless solid (2.00 g, 75%). m.p 138-140 ºC. ^{1}H NMR (DMSO, 300 MHz): δ = 8.32 (s, 1H), 8.29 (s, 1H), 2.81 (s, 6H); ^{13}C NMR (DMSO, 75 MHz): δ = 154.7, 138.7, 126.7, 122.1, 83.4, 78.6, 39.7; FT-IR (KBr, cm^{-1}): 3393, 3143, 2945, 1693, 1481, 1458, 1426, 1394, 1336, 1282, 1242, 1205, 1187, 1096, 999, 972, 727, 669, 618; HR-MS (*m/z*): calc for $[M+H]^{+}$ $C_8H_9N_3O_4S$ 244.0392 found 244.0387.

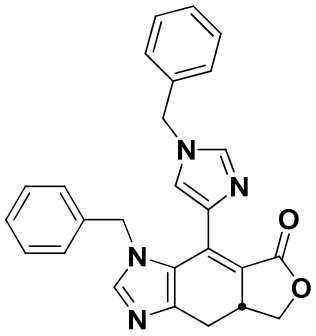
(*E*)-3-(1-benzyl-1H-imidazol-4-yl)allyl-3-(1-(*N*,*N*-dimethylsulfamoyl)-1H-imidazol-4-yl)propiolate (227): In a round bottom flask the acid **225** (2.00 g, 8.22 mmol), alcohol **212** (2.11 g, 9.86 mmol), DMAP (100mg, 0.82 mmol) and camphorsulfonic acid (110mg, 0.49 mmol) was dissolved in dry CH_2Cl_2 (40 mL) under N_2 atmosphere. The mixture was cooled to (-78 ºC) and DCC (2.54 g, 12.0 mmol) dissolved in dry CH_2Cl_2 (15 mL) was added dropwise. The reaction mixture was allowed to warm up to r.t. and stirred for 2 h. The mixture was filtered over Celite and the filter cake was washed with CH_2Cl_2. The filtrate was concentrated and the crude product was purified by chromatography (hexane/EtOAc, 1:19) affording **227** as a white solid (2.40 g, 68%). m.p 118-120 ºC. ^{1}H NMR (300 MHz): δ = 7.85 (d, *J* = 0.9 Hz, 1H), 7.73 (s, 1H), 7.60 (d, *J* = 0.9 Hz, 1H), 7.37-7.32 (m, 3H), 7.17 (d, *J* = 6.9 Hz, 2H), 6.88 (s, 1H), 6.53 (d, *J* = 15.6 Hz, 1H), 6.47 (td, *J* = 15.8, 6.4Hz 1H), 5.11 (s, 2H), 4.83 (d, *J* = 6.4 Hz, 2H), 2.88 (s, 6H); ^{13}C NMR (75 MHz): δ = 153.4, 138.7, 137.5, 137.1, 135.4, 129.2, 128.7, 127.6, 125.6, 124.7, 123.4,



121.6, 117.9, 82.3, 78.6, 66.5, 51.4, 38.3; FT-IR (neat, cm^{-1}): 3125, 2928, 2222, 1705, 1539, 1456, 1421, 1395, 1332, 1286, 1180, 1080, 1008, 967, 842, 728, 617; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{21}H_{21}N_5O_4S$ 440.1387 found 440.1409.

(*R)-1-benzyl-8-(1-benzyl-1H-imidazol-4-yl)-4a,5-dihydro-1H-isobenzofuro[5,6-d]imidazol-7(4H)-one (230):**

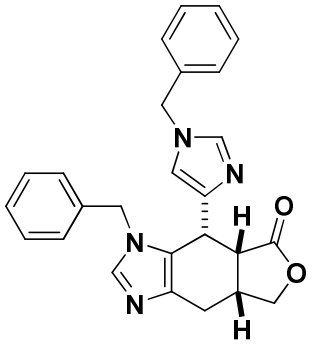
CH_2Cl_2 (75 mL) was placed in a resealable thick-walled tube and was purged with N_2 for 10 min, then ester **228** (0.70 g, 1.65 mmol) was added and again the reaction mixture was purged with N_2 for an additional 5 min. After sealing the tube with a Teflon screw cap, the reaction mixture was heated at 130 ºC for 12 h. The reaction mixture was cooled to r.t. and the CH_2Cl_2 was evaporated under vacuum. The crude product was purified by chromatography (acetone/EtOAc, 7:3) to provide **230** (490 mg, 70%) as a yellow solid. m.p 202-204 ºC. ^{1}H NMR: δ = 7.59 (s, 1H), 7.55 (s, 1H), 7.50 (s, 1H), 7.38-7.32 (m, 3H), 7.22 (d, *J* = 6.4 Hz, 2H), 7.15 (d, *J* = 7.3 Hz, 1H), 7.06 (t, *J* = 7.3 Hz, 2H), 6.59 (d, *J* = 7.3 Hz, 2H), 5.15-5.09 (m, 3H), 4.96 (d, *J* = 15.6 Hz, 1H), 4.62 (t, *J* = 9.2 Hz, 1H), 3.98 (t, *J* = 9.2 Hz, 1H), 3.55-3.49 (m, 1H), 2.98 (dd, *J* = 15.6, 8.3 Hz, 1H), 2.68 (t, *J* = 16.0 Hz, 1H); ^{13}C NMR: δ = 168.6, 144.5, 140.9, 136.5, 136.3, 135.7, 133.0, 131.5, 129.2, 128.6, 127.9, 127.7, 126.4, 125.4, 116.9, 70.9, 51.3, 51.0, 38.4, 27.7; FT-IR (neat, cm^{-1}): 1732, 1604, 1520, 1497,



1455, 1372, 1252, 1223, 1164, 1097, 1075, 1016, 913, 852, 766, 727; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{26}H_{22}N_4O_2$ 423.1816 found 423.1856.

(*R)-4-(1-benzyl-7-oxo-4,4a,5,7-tetrahydro-1H-isobenzofuro[5,6-d]imidazol-8-yl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide (229):** CH_2Cl_2 (80 mL) was placed in a thick-walled pressure tube and purged with N_2 for 10 min, then ester **227** (500 mg, 11.4 mmol) was added and again the reaction mixture was purged with N_2 for 5 min. After sealing the tube with a Teflon screw cap, the reaction mixture was heated to 120 ºC for 12 h. The reaction mixture was cooled to r.t., and then the reaction mixture was concentrated. The crude product was purified by chromatography (acetone/EtOAc, 7:3) to provide a yellow solid (410 mg, 82%). m.p 134-135 ºC. ^{1}H NMR: δ = 7.95 (d, *J* = 1.8 Hz, 1H), 7.52 (s, 1H), 7.34 (d, *J* = 1.4 Hz, 1H), 7.21-7.19 (m, 3H), 6.65 (d, *J* = 6.6 Hz, 2H), 4.99 (d, *J* = 15.6 Hz, 1H), 4.94 (d, *J* = 15.6 Hz, 1H), 4.66 (t, *J* = 8.7 Hz, 1H), 3.99 (t, *J* = 8.7 Hz, 1H), 3.59-3.55 (quintet, *J* = 8.7 Hz, 1H), 3.03 (dd, *J* = 8.7, 8.3 Hz, 1H), 2.88 (s, 6H), 2.70 (dd, *J* = 16.0, 15.6 Hz, 1H); ^{13}C NMR: δ = 168.4, 144.9, 141.4, 135.9, 135.8, 131.9, 131.2, 128.9, 128.1, 126.9, 126.1, 121.8, 118.6, 71.1, 50.9, 38.4, 38.2, 27.7; FT-IR (neat, cm^{-1}): 3122, 2926, 1736, 1615, 1557, 1521, 1457, 1420, 1392, 1334, 1255, 1176, 1083, 1011, 963, 848, 728, 702, 648; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{21}H_{22}N_5O_4S$ is 440.1387 found 440.1428.

(4a*R,7a*S**,8*R**)-1-benzyl-8-(1-benzyl-1H-imidazol-4-yl)-4a,5,7a,8-tetrahydro-1H-isobenzofuro[5,6-d]imidazol- 7(4H)-one (232):**



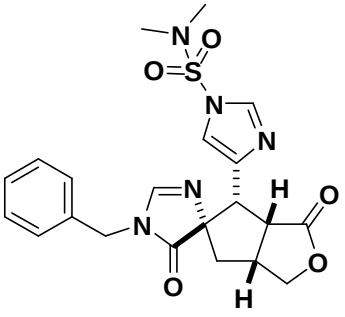
The Diels-Alder product **230** (160 mg, 0.37 mmol) was dissolved in dry ethanol (10 mL) and 10% Pd/C (100 mg) was added to the reaction mixture. The heterogeneous reaction mixture was stirred at 36 ºC for 8 h under a hydrogen atmosphere (60 psi). The reaction mixture was filtered over Celite and the filter cake was repeatedly washed with hot ethanol. The filtrate was evaporated under reduced pressure followed by purification of the residue by chromatography on silica gel ($CHCl_3$/MeOH, 49:1) furnished the hydrogenated compound **232** (110 mg, 71%) as a thick colorless liquid. ^{1}H NMR: δ = 7.45 (s, 1H), 7.37 (s, 1H), 7.34-7.30 (m, 3H), 7.25-7.21 (m, 3H), 7.07 (d, *J* = 7.3 Hz, 2H), 6.86 (d, *J* = 7.8 Hz, 2H), 6.53 (s, 1H), 4.98 (q, *J* = 15.1 Hz, 2H), 4.85 (d, *J* = 15.6 Hz, 1H), 4.57 (d, *J* = 16.0 Hz, 1H), 4.31-4.24 (m, 3H), 3.14-3.01 (m, 3H), 2.74 (d, *J* = 16.0 Hz, 1H); ^{13}C NMR (75 MHz): δ = 177.3, 139.8, 137.7, 137.4, 136.2, 136.1, 135.6, 129.1, 128.9, 128.4, 128.1, 127.2, 126.9, 124.5, 118.4, 72.5, 50.9, 48.7, 44.4, 34.9, 30.8, 22.4; FT-IR (neat, cm^{-1}): 2366, 2334, 1773, 1502, 1449, 1207, 1144, 1010, 737, 708. HR-MS (*m/z*): calc for $[M+H]^+$ $C_{26}H_{25}N_4O_2$ 425.1972 found 425.1999.

4-((4a*R,7a*S**,8*R**)-1-benzyl-7-oxo-4,4a,5,7,7a,8-hexahydro-1H-isobenzofuro[5,6-d]imidazol-8-yl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide (231):** The Diels-Alder product **229** (200 mg, 0.45 mmol) was dissolved in dry ethanol (15 mL) and then 10% Pd/C (120 mg) was added. The resulting heterogeneous reaction mixture was stirred at 40 ºC for 12 h under hydrogen atmosphere (60 psi). On completion of the reaction, the reaction mixture was filtered through Celite and the filter cake was washed repeatedly with hot ethanol. The filtrate was evaporated under reduced pressure followed by purification of the residue by chromatography on silica gel ($CHCl_3$/MeOH, 49:1) which furnished reduced compound **231** (150 mg, 75%) as yellow solid. m.p 158-160 ºC. ^{1}H NMR: δ = 7.68 (s, 1H), 7.54 (s, 1H), 7.27-7.26 (m, 3H), 6.92 (m, 2H), 6.91-6.90 (s, 1H), 4.94 (d, *J* = 15.6 Hz, 1H), 4.68 (d, *J* = 15.6 Hz, 1H), 4.28-4.22 (m, 2H), 4.21 (t, *J* = 8.7 Hz, 1H), 3.11-3.06 (m, 3H), 2.80 (d, *J* = 2.8 Hz, 1H), 2.77 (s, 6H); ^{13}C NMR: δ = 176.7, 140.6, 138.2, 136.6, 136.2, 135.6, 129.0, 128.3, 126.8, 123.1, 116.4, 72.3, 49.1, 43.8, 38.3, 34.8, 30.6, 22.7; FT-IR (neat, cm^{-1}): 2360, 1770, 1716, 1652, 1558, 1540, 1497, 1457, 1418, 1390, 1268, 1175, 1078, 1008, 962, 728; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{21}H_{24}N_5O_4S$ 442.1544 found 442.1581.

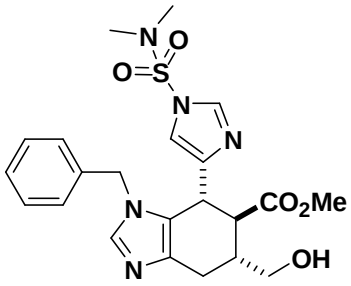
(3a*R,4'*S**,6*R**,6a*S**)-1'-benzyl-6-(1-benzyl-1H-imidazol-4-yl)-3a,4,6,6a-tetrahydrospiro[cyclopenta[c]furan-5,4'-imidazole]-1,5'(1'H,3H)-dione (234):**

The hydrogenated product **232** (90 mg, 0.21 mmol) was dissolved in chloroform (5 mL) and Davis' oxaziridine (160 mg, 0.53 mmol) was added to the reaction mixture. The reaction mixture was stirred at reflux for 8 h. The organic layer was washed with 2M NaOH solution and the organic layer was dried with anhydrous Na_2SO_4 concentrated and the residue was purified by chromatography on silica gel ($CHCl_3$/MeOH, 49:1) furnished rearranged product **234** (60 mg, 64%) as a yellow solid. ^{1}H NMR (300 MHz): δ = 7.43 (s, 1H), 7.32-7.22 (m, 9H), 7.05-6.99 (m, 2H), 6.85 (s, 1H), 4.93 (s, 2H), 4.59 (d, *J* = 15.1 Hz, 1H), 4.53 (d, *J* = 8.6 Hz, 1H), 4.41 (d, *J* = 15.5 Hz, 1H), 4.27 (dd, *J* = 9.3, 3.1 Hz, 1H), 4.07 (d, *J* = 8.3 Hz, 1H), 3.48-3.35 (m, 2H), 2.63 (dd, *J* = 13.4, 8.9 Hz, 1H), 1.86 (d, *J* = 13.4 Hz, 1H); ^{13}C NMR (75 MHz): δ = 181.7, 177.0, 152.6, 136.2, 135.7, 135.5, 133.8, 128.9, 128.2, 127.7, 127.3, 119.4, 79.5, 73.6, 52.0, 50.9, 46.3, 44.7, 43.4, 37.4; FT-IR (neat, cm^{-1}): 2363, 2336, 1770, 1733, 1651, 1557, 1542, 1508; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{22}H_{25}N_4O_3$ 441.1927 found 441.1936.

4-((3a*R,4'*S**,6R*,6a*S**)-1'-benzyl-1,5'-dioxo-1,1',3,3a,4,5',6,6a-octahydrospiro[cyclopenta[c]furan-5,4'-imidazole]-6-yl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide (233):** The tetrahydrobenzimidazole **231** (90 mg, 0.20 mmol) was dissolved in chloroform (3.5 mL) and Davis' oxaziridine (150 mg, 0.5 mmol) was added to the reaction mixture. The resulting mixture was stirred at reflux for 8 h. The organic layer was washed with 2M NaOH solution and the organic layer was dried with anhydrous Na_2SO_4 concentrated and the residue was purified by chromatography on silica gel ($CHCl_3$/MeOH, 49:1) to provide the spiro imidazolone **233** (50 mg, 60%) as a colorless solid. m.p 188–190 ºC. ^{1}H NMR: δ = 7.69 (d, *J* = 0.9 Hz, 1H), 7.60 (s, 1H), 7.29 – 7.25 (m, 3H), 7.09 (d, *J* = 1.4 Hz, 1H), 6.94 (d, *J* = 7.6 Hz, 2H), 4.72 (d, *J* = 15.6 Hz, 1H), 4.56 (t, *J* = 8.7 Hz, 1H), 4.42 (d, *J* = 15.1 Hz, 1H), 4.26 (dd, *J* = 9.2, 3.8 Hz, 1H), 4.06 (d, *J* = 8.3 Hz, 1H), 3.43-3.41 (m, 2H), 2.78 (s, 6H), 2.61 (dd, *J* = 15.3, 9.2 Hz, 1H), 1.88 (d, *J* = 13.7 Hz, 1H); ^{13}C NMR: δ = 181.1, 176.7, 153.4, 135.1, 134.9, 129.2, 128.4, 127.3, 117.2, 79.1, 73.7, 51.1, 46.1, 44.9, 43.7, 38.3, 37.2; FT-IR (neat, cm^{-1}): 2932, 1766, 1727, 1598, 1390, 1162, 1079, 954, 726; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{21}H_{23}N_5O_5S$ 458.1471 found 458.1471.

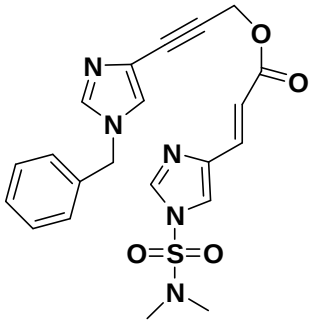


(5*R,6*R**,7*R**)-methyl-1-benzyl-7-(1-(*N*,*N*-dimethylsulfamoyl)-1H-imidazol-4-yl)-5-(hydroxymethyl)-4,5,6,7-tetrahydro-1H-benzo[d]imidazole-6-carboxylate (235):** The tetrahydrobenzimidazole **231** (200 mg, 0.42 mmol) was dissolved in MeOH (60 mL) under nitrogen atmosphere. To this reaction mixture 0.23 M sodium methoxide was added dropwise. After stirring this reaction at r.t. for 1 h it was heated to 60 ºC for 2 h. Then cooling this reaction mixture to room temperature, (20 mL) of saturated ammonium chloride solution was added followed by addition of equal amount of water. Then this aqueous solution was extracted repeatedly by EtOAc. The organic extracts were dried with anhydrous Na_2SO_4 concentrated and the residue was purified by chromatography on silica gel (CH_2Cl_2/MeOH, 4:1) furnishing the product **235** (120 mg, 52%) as a colorless oil. In addition, unreacted lactone **231** (70 mg, 35%) was recovered. ^{1}H NMR: δ = 7.74 (s, 1H), 7.40 (s, 1H), 7.31-7.25 (m, 3H), 6.85 (d, *J* = 7.3 Hz, 2H), 6.81 (s, 1H), 4.85 (d, *J* = 16.9 Hz, 1H), 4.48 (d, *J* = 18.3 Hz, 1H), 4.20 (d, *J* = 10.5 Hz, 1H), 3.64–3.59 (m, 2H), 3.57 (s, 3H), 3.00 (t, *J* = 9.2 Hz, 1H), 2.82–2.78 (m, 1H), 2.75 (s, 6H), 2.72–2.69 (m, 1H) 2.37–2.34 (m, 1H); ^{13}C NMR: δ = 174.5, 142.7, 137.9, 137.2, 136.1, 129.0, 127.9, 126.3, 115.4, 65.1, 51.9, 51.6, 49.2, 40.6, 38.1, 35.8, 26.8; FT-IR (neat, cm^{-1}): 3112, 2935, 1723, 1455, 1394, 1265, 1170, 1074, 953, 733, 603, 598; calc for $[M+H]^+$ $C_{22}H_{27}N_5O_5S$ 474.1806 found 474.1830.

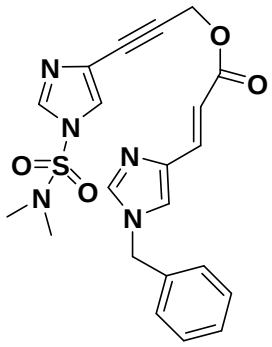


(5*S,6*R**,7*R**,8*R**)-methyl-3-benzyl-6-(1-(*N*,*N*-dimethylsulfamoyl)-1H-imidazol-4-yl)-8-(hydroxymethyl)-4-oxo-1,3-diazaspiro[4.4]non-1-ene-7-carboxylate (236):** The spiro imidazolone **233** (200 mg, 0.41 mmol) was dissolved in MeOH (60 mL) under a nitrogen atmosphere. To this reaction mixture 0.23 M sodium methoxide in MeOH (49 mL) was added dropwise. After stirring this reaction at r.t. for 1 h, it was heated to 60 ºC for 18 h. The reaction mixture was cooled to r.t., then saturated NH_4Cl solution (20 mL) was added followed by addition of equal amount of water. The resulting aqueous solution was extracted repeatedly with EtOAc. The organic extracts were dried with anhydrous Na_2SO_4 and concentrated and the residue was purified by chromatography on silica gel (CH_2Cl_2/MeOH; 44:6) furnished the desired product **236** (65 mg, 31%) as a colorless liquid. In addition, unreacted lactone **233** (110 mg, 55%) was recovered. ^{1}H NMR: δ = 7.60 (s, 1H), 7.39 (s, 1H), 7.34-7.28 (m, 3H), 7.15 (d, *J* = 7.2 Hz, 2H), 7.00 (s, 1H), 4.71 (d, *J* = 15.1 Hz, 1H), 4.50 (d, *J* = 15.1 Hz, 1H), 4.02 (d, *J* = 11.0 Hz, 1H), 3.80-3.78 (m, 2H), 3.68 (s, 3H), 3.66-3.62 (m, 1H), 2.93-2.91 (m, 1H), 2.74 (s, 6H), 2.65-2.63 (m, 1H), 1.74 (d, *J* = 13.8 Hz, 1H); ^{13}C NMR (75 MHz): δ = 180.9, 174.5, 152.6, 139.8, 135.8, 134.9, 129.1, 128.3, 127.9, 114.5, 79.0, 65.3, 52.2, 51.0, 48.6, 44.9, 43.8, 39.9, 38.2; FT-IR (neat, cm^{-1}): 2944, 1735, 1397, 1166, 1091, 962, 730; calc for $[M+H]^+$ $C_{22}H_{27}N_5O_6S$ 490.1755 found 490.1758.

(*E*)-3-(1-benzyl-1H-imidazol-4-yl)prop-2-ynyl-3-(1-(*N*,*N*-dimethylsulfamoyl)-1H-imidazol-4-yl)acrylate (239): In a round bottom flask the alcohol **238** (200 mg, 0.94 mmol), acid **237** (350 mg, 1.41 mmol), DMAP (10 mg, 0.09 mmol) and camphorsulfonic acid (13 mg, 0.06 mmol) was dissolved in dry CH_2Cl_2 (20 mL) under N_2 atmosphere. The mixture was cooled to (-78 ºC) and DCC (291 mg, 1.41 mmol) dissolved in dry CH_2Cl_2 (5 mL) was added dropwise. The reaction mixture was allowed to warm up to r.t. and stirred for 2 h. The mixture was filtered over Celite and the filter cake was washed with CH_2Cl_2. The filtrate was concentrated and the crude product was purified by chromatography (hexane/EtOAc, 1:19) affording **239** as a colorless thick liquid (240 mg, 60%). ^{1}H NMR (300 MHz): δ = 7.87 (s, 1H), 7.54 (d, *J* = 16.0 Hz, 1H), 7.46 (d, *J* = 0.9 Hz, 1H), 7.38-7.33 (m, 4H), 7.15 (dd, *J* = 1.8, 8.0 Hz, 2H), 7.10 (d, *J* = 1.4 Hz, 1H), 6.68 (d, *J* = 15.6 Hz, 1H), 5.07 (s, 2H), 4.99 (s, 2H), 2.88 (s, 6H); ^{13}C NMR (75 MHz): δ = 166.1, 139.4, 137.7, 137.5, 135.4, 135.2, 129.2, 128.7, 127.5, 124.1, 124.0, 118.9, 118.8, 83.2, 80.7, 52.7, 50.6, 38.3; FT-IR (neat, cm^{-1}): 3125, 2936, 2363, 1712, 1486, 1391, 1245, 1150, 1007, 775, 637, 592; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{21}H_{22}N_5O_4S$ 440.1393 found 440.1359.

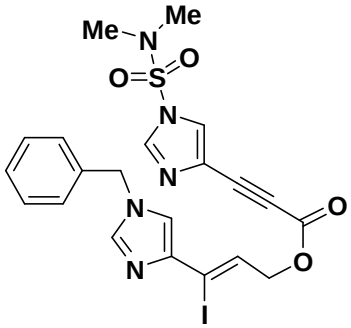


(*E*)-3-(1-(*N*,*N*-dimethylsulfamoyl)-1H-imidazol-4-yl)prop-2-ynyl-3-(1-benzyl-1H-imidazol-4-yl)acrylate (242):



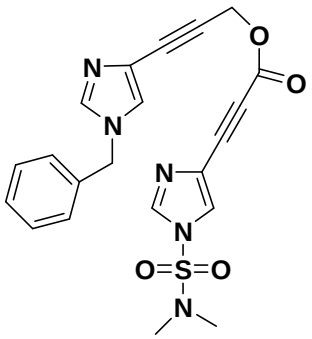
In a round bottom flask the alcohol **241** (200 mg, 0.87 mmol), acid **212** (290 mg, 1.31 mmol), DMAP (9 mg, 0.08 mmol) and camphorsulfonic acid (11 mg, 0.05 mmol) was dissolved in dry CH_2Cl_2 (20 mL) under N_2 atmosphere. The mixture was cooled to (-78 ºC) and DCC (270 mg, 1.31 mmol) dissolved in dry CH_2Cl_2 (5 mL) was added dropwise. The reaction mixture was allowed to warm up to r.t. and stirred for 2 h. The mixture was filtered over Celite and the filter cake was washed with CH_2Cl_2. The filtrate was concentrated and the crude product was purified by chromatography (hexane/EtOAc, 1:19) affording **242** as a colorless thick liquid (249 mg, 65%). ^{1}H NMR (300 MHz): δ =7.82 (s, 1H), 7.57 (d, *J* = 15.6 Hz, 1H), 7.55 (s, 1H), 7.39-7.36 (m, 4H), 7.18 (d, *J* = 7.8 Hz, 2H), 7.10 (s, 1H), 6.56 (d, *J* = 16.0 Hz, 1H), 5.10 (s, 2H), 4.98 (s, 2H), 2.87 (s, 6H); ^{13}C NMR (75 MHz): δ = 166.7, 138.9, 138.7, 137.3, 136.6, 135.4, 129.2, 128.7, 127.5, 125.5, 122.0, 121.3, 115.2, 85.6, 78.3, 52.4, 51.2, 38.3; FT-IR (neat, cm^{-1}): 3125, 2928, 2241, 1709, 1479, 1387, 1255, 1149, 1097, 1006, 961, 831, 728, 631; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{21}H_{22}N_5O_4S$ 440.1393 found 440.1358.

(*Z*)-3-(1-benzyl-1H-imidazol-4-yl)-3-iodoallyl-3-(1-(*N*,*N*-dimethylsulfamoyl)-1H-imidazol-4-yl)propiolate (250):



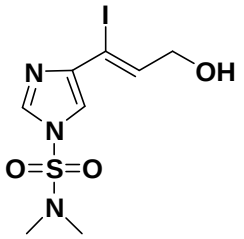
In a round bottom flask the alcohol **245** (200 mg, 0.58 mmol), acid **225** (210 mg, 0.88 mmol), DMAP (7 mg, 0.06 mmol) and camphorsulfonic acid (8 mg, 0.04 mmol) was dissolved in dry CH_2Cl_2 (15 mL) under N_2 atmosphere. The mixture was cooled to (-78 ºC) and DCC (180 mg, 0.88 mmol) dissolved in dry CH_2Cl_2 (5 mL) was added dropwise. The reaction mixture was allowed to warm up to r.t. and stirred for 8 h. The mixture was filtered over Celite and the filter cake was washed with CH_2Cl_2. The filtrate was concentrated and the crude product was purified by chromatography (hexane/EtOAc, 2:18) affording **250** as a white solid (230 mg, 68%). mp 135-137 ºC. ^{1}H NMR (300 MHz): δ = 7.86 (s, 1H), 7.61 (d, *J* = 0.9 Hz, 1H), 7.56 (s, 1H), 7.38-7.34 (m, 3H), 7.18 (d, *J* = 6.9 Hz, 2H), 7.11 (s, 1H), 6.83 (t, *J* = 15.6 Hz, 1H), 5.08 (s, 2H), 4.96 (d, *J* = 6.4 Hz, 2H), 2.90 (s, 6H); ^{13}C NMR (75 MHz): δ = 153.4, 140.9, 137.6, 137.2, 134.6, 129.9, 129.5, 129.2, 127.9, 124.9, 123.4, 122.1, 82.2, 79.2, 70.1, 52.1, 38.4; FT-IR (neat, cm^{-1}): 3138, 2849, 2219, 1703, 1453, 1386, 1333, 1212, 1167, 1086, 1048, 995, 850, 738, 617; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{21}H_{21}IN_5O_4S$ 566.0353 found 566.0352.

3-(1-benzyl-1H-imidazol-4-yl)prop-2-ynyl-3-(1-(*N*,*N*-dimethylsulfamoyl)-1H-imidazol-4-yl)propiolate (251):



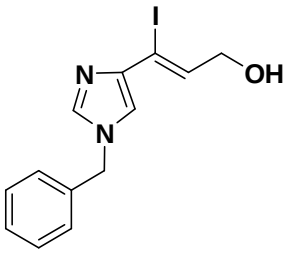
CH_2Cl_2 (10 mL) was placed in a thick-walled pressure tube and purged with N_2 for 10 min, then ester **250** (120 mg, 11.4 mmol) was added and again the reaction mixture was purged with N_2 for 5 min. After sealing the tube with a Teflon screw cap, the reaction mixture was heated to 120 ºC for 12 h. The reaction mixture was cooled to r.t., and then the reaction mixture was concentrated. The crude product was purified by chromatography (acetone/EtOAc, 7:3) to provide a yellow solid **251** (69 mg, 75%). m.p 209-211 ºC. ^{1}H NMR (300 MHz): δ = 8.14 (s, 1H), 8.00 (d, *J* = 0.9 Hz, 1H), 7.87 (s, 1H), 7.19-7.16 (m, 3H), 6.88 (d, *J* = 0.9 Hz, 1H), 6.58 (d, *J* = 6.9 Hz, 2H), 5.38 (s, 2H), 5.33 (s, 2H), 2.88 (s, 6H); ^{13}C NMR (75 MHz): δ = 170.0, 150.0, 149.2, 140.5, 135.8, 135.5, 133.4, 132.2, 128.9, 128.1, 125.3, 119.5, 118.5, 118.4, 113.7, 68.0, 50.7, 38.3; FT-IR (neat, cm^{-1}): 3101, 2927, 2241, 2219, 1759, 1501, 1456, 1390, 1264, 1167, 1077, 965, 734, 593; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{21}H_{20}N_5O_4S$ 438.1236 found 438.1241.

(*Z*)-4-(3-hydroxy-1-iodoprop-1-enyl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide (244):



In a round bottom flask compound **241** (1.0 g, 4.36 mmol) was dissolved under N_2 atmosphere in anhydrous THF (50 mL). The reaction mixture was colled to 0 ºC and then to it Red-Al (65 wt.% in toluene) (1.63 mL, 5.20 mmol) was added dropwise. After stirring the reaction mixture for 30 min, N-Iodosuccinimide (1.27 g, 5.60 mmol) dissolved in anhydrous THF (4 mL) was added. Then the reaction mixture was stirred for another 1 h at r.t. Finally the reaction was quenched with NH_4Cl (10 mL) then the organic layer was separated. The aqueous layer was extracted with EtOAC (3x50 mL), then the combined organic solutions were dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by chromatography (EtOAc/Hexane, 95:5) providing **244** as a yellow solid (1.27 g, 82%). The proton and carbon contains residual acetone impurity. m.p 94-96 ºC. ^{1}H NMR (300 MHz): δ = 7.95 (d, *J* = 1.4 Hz, 1H), 7.34 (d, *J* = 1.4 Hz, 1H), 6.99 (t, *J* = 5.8 Hz, 1H), 4.39 (d, *J* = 6.2 Hz, 2H), 2.89 (s, 6H); ^{13}C NMR (75 MHz): δ = 144.2, 137.1, 136.2, 118.5, 91.1, 67.2, 38.3; FT-IR (neat, cm^{-1}): 3250, 1392, 1167, 1079, 962, 599, 508; HR-MS (*m/z*): calc for $[M+H]^+$ $C_8H_{13}IN_3O_3S$ 357.9722 found 357.9723.

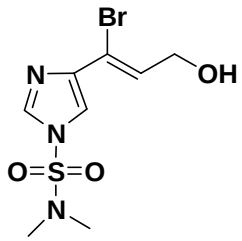
(*Z*)-3-(1-benzyl-1H-imidazol-4-yl)-3-iodoprop-2-en-1-ol (245):



In a round bottom flask compound **238** (1.2 g, 5.65 mmol) was dissolved under N_2 atmosphere in anhydrous THF (70 mL). The reaction mixture was colled to 0 ºC and then to it Red-Al (65 wt.% in toluene) (2.10 mL, 6.78 mmol) was added dropwise. After stirring the reaction mixture for 30 min, N-Iodosuccinimide (1.65 g, 7.35 mmol) dissolved in anhydrous THF (10 mL) was added. Then the reaction mixture was stirred for another 1 h at r.t. Finally the reaction was quenched with NH_4Cl (10 mL) then the organic layer was separated. The aqueous layer was extracted with EtOAC (3x50 mL), then the combined organic solutions were dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by chromatography (EtOAc 100%) providing **245** as a yellow solid (1.68 g, 88%). m.p 84-86 ºC. ^{1}H NMR (300 MHz): δ = 7.56 (d, *J* = 1.4 Hz, 1H), 7.37-7.32 (m, 3H), 7.18 (dd, *J* = 2.1, 7.4 Hz, 2H), 7.05 (d, *J* = 1.4 Hz, 1H), 6.83 (t, *J* = 6.2 Hz, 1H), 5.10 (s, 2H), 4.35 (d, *J* = 6.2 Hz, 2H), 2.95 (s, 1H); ^{13}C NMR (75 MHz): δ = 143.4, 137.9, 135.6, 133.4, 129.3, 128.6, 127.5, 121.2, 94.0, 67.3, 51.2; FT-IR (neat, cm^{-1}): 3192, 2850, 1633, 1493, 1457, 1355, 1156, 1041, 940, 840, 716; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{13}H_{14}IN_2O$ 341.0151 found 341.0146.

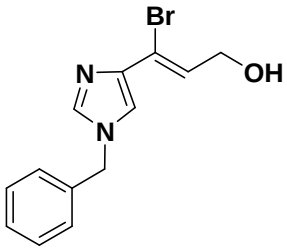
(*Z*)-4-(1-bromo-3-hydroxyprop-1-enyl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide (259):

In a round bottom flask compound **241** (300 mg, 1.31 mmol) was dissolved under



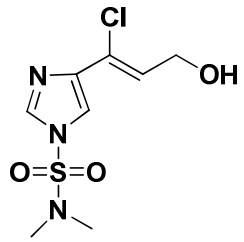
N_2 atmosphere in anhydrous THF (20 mL). The reaction mixture was colled to 0 ºC and then to it Red-Al (65 wt.% in toluene) (0.5 mL, 1.57 mmol) was added dropwise. After stirring the reaction mixture for 30 min, N-bromosuccinimide (310 mg, 1.70 mmol) dissolved in anhydrous THF (5 mL) was added. Then the reaction mixture was stirred for another 1 h at r.t. Finally the reaction was quenched with NH_4Cl (10 mL) then the organic layer was separated. The aqueous layer was extracted with EtOAC (3x50 mL), the combined organic solutions were dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by chromatography (EtOAc 100%) providing **259** as a yellow solid (315mg, 78%). m.p 101-103 ºC. ^{1}H NMR: δ = 7.88 (d, *J* = 1.4 Hz, 1H), 7.34 (s, 1H), 7.05 (t, *J* = 5.9 Hz, 1H), 4.43 (d, *J* = 5.5 Hz, 2H), 2.87 (s, 6H); ^{13}C NMR: δ = 142.1, 137.2, 129.9, 116.8, 114.9, 62.2, 38.3; FT-IR (neat, cm^{-1}): 2980, 2934, 1501, 1381, 1258, 1188, 1129, 839; HR-MS (*m/z*): calc for $[M+H]^+$ $C_8H_{13}BrN_3O_3S$ 309.9861 found 309.9870.

(*Z*)-3-(1-benzyl-1H-imidazol-4-yl)-3-bromoprop-2-en-1-ol (260):



In a round bottom flask compound **238** (200 mg, 0.94 mmol) was dissolved under N_2 atmosphere in anhydrous THF (20 mL). The reaction mixture was colled to 0 ºC and then to it Red-Al (65 wt.% in toluene) (0.35 mL, 1.13 mmol) was added dropwise. After stirring the reaction mixture for 30 min, N-bromosuccinimide (250 mg, 1.41 mmol) dissolved in anhydrous THF (2.5 mL) was added. Then the reaction mixture was stirred for another 1 hr at r.t. Finally the reaction was quenched with NH_4Cl (10 mL) then the organic layer was separated. The aqueous layer was extracted with EtOAC (3x50 mL), then the combined organic solutions were dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by chromatography (EtOAc 100%) providing **260** as a yellow thick liquid (220 mg, 81%). ^{1}H NMR (300 MHz): δ = 7.52 (d, *J* = 1.4 Hz, 1H), 7.39-7.33 (m, 3H), 7.18 (dd, *J* = 2.1, 7.4 Hz , 2H), 7.10 (*J* = 1.0 Hz 1H), 6.94 (t, *J* = 6.2 Hz, 1H), 5.08 (s, 2H), 4.43 (d, *J* = 6.2 Hz, 2H), 1.94 (b, 1H); ^{13}C NMR (75 MHz): δ = 141.7, 137.9, 135.6, 129.2, 128.6, 127.4, 126.2, 119.2, 117.2, 62.4, 51.2; FT-IR (neat, cm^{-1}): 3246, 2935, 1640, 1537, 1454, 1231, 1160, 1043, 830, 711; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{13}H_{14}BrN_2O$ 293.0284 found 293.0281.

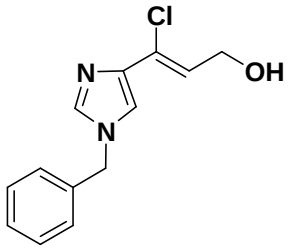
(*Z*)-4-(1-chloro-3-hydroxyprop-1-enyl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide (263):



In a round bottom flask compound **241** (300 mg, 1.31 mmol) was dissolved under N_2 atmosphere in anhydrous THF (25 mL). The reaction mixture was colled to 0 ºC and then to it Red-Al (65 wt.% in toluene) (0.50 mL, 1.57 mmol) was added dropwise. After stirring the reaction mixture for 30 min, N-chlorosuccinimide (250 mg, 1.70 mmol) dissolved in anhydrous THF (5 mL) was added. Then the reaction mixture was stirred for another 1 h at r.t. Finally the reaction was quenched with NH_4Cl (10 mL) then the organic layer was separated. The aqueous layer was extracted with EtOAC (3x50 mL), then the combined organic solutions were dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by chromatography (EtOAc 100%) providing **263** as a yellow solid (120 mg, 34%). ^{1}H NMR: δ = 7.85 (d, *J* = 1.4 Hz, 1H), 7.37 (d, *J* = 1.0 Hz, 1H), 6.84 (t, *J* = 6.2 Hz, 1H), 4.50 (d, *J* = 6.2 Hz, 2H), 2.90 (s, 6H), 5; ^{13}C NMR (75 MHz): δ = 141.3, 137.2, 125.9, 125.1, 115.6, 59.7, 38.3; FT-IR (neat, cm^{-1}): 3356, 2987, 1635, 1396, 1173, 1082, 968, 731, 599; HR-MS (*m/z*): calc for $[M+H]^+$ $C_8H_{13}ClN_3O_3S$ 266.0361 found 266.0357.

(*Z*)-3-(1-benzyl-1H-imidazol-4-yl)-3-chloroprop-2-en-1-ol (264):

In a round bottom flask compound **238** (250 mg, 1.17 mmol) was dissolved under



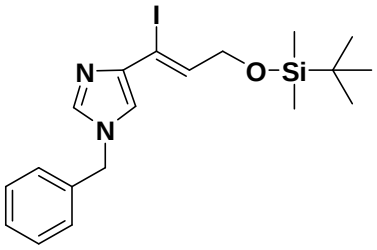
N_2 atmosphere in anhydrous THF (20 mL). The reaction mixture was colled to 0 ºC and then to it Red-Al (65 wt.% in toluene) (0.45 mL, 1.41 mmol) was added dropwise. After stirring the reaction mixture for 30 min, N-chlorosuccinimide (210 mg, 1.53 mmol) dissolved in anhydrous THF (2.5 mL) was added. Then the reaction mixture was stirred for another 1 hr at r.t. Finally the reaction was quenched with NH_4Cl (10 mL) then the organic layer was separated. The aqueous layer was extracted with EtOAC (3x50 mL), then the combined organic solutions were dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by chromatography (EtOAc 100%) providing **264** as a yellow thick liquid (102 mg, 35%). ^{1}H NMR (300 MHz): δ = 7.98 (s, 1H), 7.39-7.36 (m, 3H), 7.23 (dd, *J* = 2.1, 7.4 Hz, 2H), 7.01 (s, 1H), 6.85 (t, *J* = 6.2 Hz, 1H), 5.17 (s, 2H), 4.44 (d, *J* = 6.2 Hz, 2H), 4.03 (b, 1H); ^{13}C NMR (75 MHz): δ = 138.2, 137.5, 134.7, 129.3, 128.9, 127.9, 125.6, 124.1, 118.5, 59.6, 51.9; FT-IR (neat, cm^{-1}): 3230, 2948, 1610, 1512, 1415, 1331, 1140, 1080, 835, 712, 623; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{13}H_{14}ClN_2O$ 249.0797 found 249.0790.

(*Z*)-4-(3-(tert-butyldimethylsilyloxy)-1-iodoprop-1-enyl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide (255):

In a round bottom flask compound **244** (400 mg, 1.12 mmol) was dissolved in CH_2Cl_2 (20 mL) under nitrogen atmosphere. The solution was cooled to 0 ºC and then to the reaction mixture imidazole (110 mg, 1.68 mmol) and TBSCl (220 mg, 1.45 mmol) were added. The reaction mixture was stirred for 8 h, then NH_4Cl (5 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAC (3x50 mL), then the combined organic solutions were dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by chromatography (EtOAc 100%) providing **255** as a colorless solid (480 mg, 92%). m.p 75-77 ºC ^{1}H NMR (300 MHz): δ = 7.88 (d, *J* = 1.0 Hz, 1H), 7.31 (d, *J* = 1.4 Hz, 1H), 6.89 (t, *J* = 5.5 Hz, 1H), 4.39 (d, *J* = 5.5 Hz, 2H), 2.86 (s, 6H), 0.89 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (75 MHz): δ = 144.3, 137.4, 136.9, 117.9, 89.4, 68.4, 38.3, 26.0, 18.4, -5.1 ; FT-IR (neat, cm^{-1}): 2934, 2852, 1703, 1592, 1396, 1173, 1148, 1079, 833, 731, 596; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{14}H_{27}IN_3O_3SSi$ 472.0582 found 472.0596.

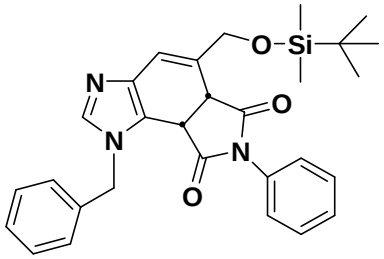
(*Z*)-1-benzyl-4-(3-(tert-butyldimethylsilyloxy)-1-iodoprop-1-enyl)-1H-imidazole (253):

In a round bottom flask compound **245** (0.77 g, 2.25 mmol) was dissolved in CH_2Cl_2 (25 mL) under a nitrogen atmosphere. The solution was cooled to 0 ºC



and then to the reaction mixture imidazole (240 mg, 3.60 mmol) and TBSCl (440, 2.94 mmol) was added. The reaction mixture was stirred for another 8 h, then NH_4Cl (10 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAC (3x50 mL), then the combined organic solutions were dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by chromatography (EtOAc 100%) providing **253** as a colorless thick liquid (920 mg, 90%). ^{1}H NMR (300 MHz): δ = 7.55 (d, *J* = 1.4 Hz, 1H), 7.40-7.33 (m, 3H), 7.16 (dd, *J* = 7.6, 1.4 Hz, 2H), 7.05 (*J* = 1.4 Hz, 1H), 6.73 (t, *J* = 5.5 Hz, 1H), 5.10 (s, 2H), 4.40 (d, *J* = 5.5 Hz, 2H), 0.92 (s, 9H), 0.10 (s, 6H); ^{13}C NMR (75 MHz): δ = 143.6, 137.7, 134.0, 129.2, 128.5, 127.4, 120.3, 92.3, 77.8, 68.1, 50.9, 25.9, 18.4, 17.9, -5.1; FT-IR (neat, cm^{-1}): 2928, 2849, 1498, 1449, 1258, 1097, 1065, 842, 769, 707; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{19}H_{28}IN_2OSi$ 455.1010 found 455.1014.

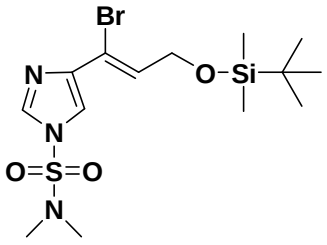
(5a*R,8a*S**)-1-benzyl-5-((tert-butyldimethylsilyloxy)methyl)-7-phenyl-7,8a-dihydroimidazo[4,5-e]isoindole-6,8(1H,5aH)-dione (257):**



CH_2Cl_2 (3 mL) was placed in a resealable thick-walled tube and was purged with N_2 for 5 minutes, then compound **253** (140 mg, 0.31 mmol) and compound **256** (65 mg, 0.37 mmol) was added and again the reaction mixture was purged with N_2 for an additional 5 minutes. After sealing the tube with a Teflon screw cap, the

reaction mixture was heated at 50 ºC for 12 h. The reaction mixture was cooled to r.t. and the CH_2Cl_2 was evaporated under vacuum. The crude product was purified by chromatography (EtOAc/Hexane, 1:1) to provide **257** (69 mg, 45%) as a yellow solid. m.p 202-204 ºC. ^{1}H NMR: δ = 7.52 (s, 1H), 7.49-7.46 (m, 2H), 7.42-7.32 (m, 4H), 7.24 (d, *J* = 7.8 Hz, 2H), 7.17 (d, *J* = 7.3 Hz, 2H), 6.67 (s, 1H), 5.77 (d, *J* = 15.6 Hz, 1H), 5.28 (d, *J* = 15.6 Hz, 1H), 4.53 (s, 2H), 4.20 (d, *J* = 11.4 Hz, 1H), 4.09 (d, *J* = 11.4 Hz, 1H), 0.92 (s, 9H), 0.10 (s, 6H); ^{13}C NMR: δ = 175.3, 175.1, 139.6, 137.3, 135.9, 131.7, 129.3, 129.2, 129.0, 128.8, 128.3, 127.5, 126.5, 119.1, 118.9, 64.6, 50.0, 43.4, 39.8, 26.1, 18.5, -5.2; FT-IR (neat, cm^{-1}): 2934, 2858, 1721, 1498, 1375, 1194, 1123, 839; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{29}H_{34}N_3O_3Si$ 500.2364 found 500.2371.

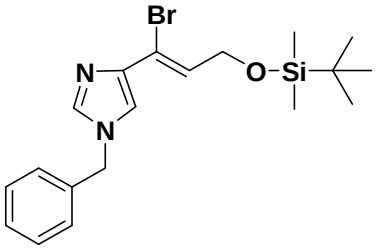
(*Z*)-4-(1-bromo-3-(tert-butyldimethylsilyloxy)prop-1-enyl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide (261):



In a round bottom flask compound **259** (280 mg, 0.90 mmol) was dissolved in CH_2Cl_2 (15 mL) under a nitrogen atmosphere. The solution was cooled to 0 ºC and then to the reaction mixture imidazole (90 mg, 1.35 mmol) and TBSCl (177 mg, 1.17 mmol) was added. The reaction mixture was stirred for 8 h, then NH_4Cl (5 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAC (3x50 mL), then the combined organic solutions were dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by chromatography (EtOAc 100%)

providing **261** as a colorless solid (336 mg, 88%). m.p 91-93 ºC. ^{1}H NMR: δ = 7.86 (d, *J* = 1.4 Hz, 1H), 7.34 (d, *J* = 1.4 Hz, 1H), 6.97 (t, *J* = 5.5 Hz, 1H), 4.48 (d, *J* = 5.5 Hz, 2H), 2.88 (s, 6H), 0.92 (s, 9H), 0.10 (s, 6H); ^{13}C NMR: δ = 142.4, 137.0, 130.9, 116.3, 113.3, 63.4, 38.3, 26.0, 18.4, -5.1; FT-IR (neat, cm^{-1}): 2938, 2845, 1592, 1397, 1165, 1150, 1085, 987, 840, 717, 590; HR-MS (*m/z*): calc for $[M+H]^{+}$ $C_{14}H_{27}BrN_3O_3SSi$ 424.0726 found.

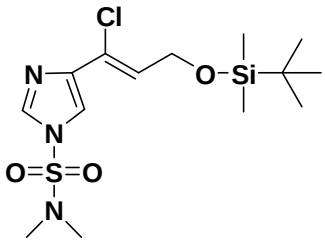
(*Z*)-1-benzyl-4-(1-bromo-3-(tert-butyldimethylsilyloxy)prop-1-enyl)-1H-imidazole (262):



In a round bottom flask compound **260** (170 mg, 0.58 mmol) was dissolved in CH_2Cl_2 (10 mL) under a nitrogen atmosphere. The solution was cooled to 0 ºC and then to the reaction mixture imidazole (60 mg, 3.60 mmol) and TBSCl (110 mg, 0.75 mmol) was added. The reaction mixture was stirred for 8 h, then NH_4Cl (5 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAC (3x50 mL), then the combined organic solutions were dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by chromatography (EtOAc 100%) providing **262** as a colorless thick liquid (210 mg, 91%). ^{1}H NMR (300 MHz): δ = 7.51 (d, *J* = 1.4 Hz, 1H), 7.37-7.34 (m, 3H), 7.16 (dd, *J* = 7.6, 1.4 Hz, 2H), 7.05 (*J* = 1.4 Hz, 1H), 6.83 (t, *J* = 5.5 Hz, 1H), 5.07 (s, 2H), 4.46 (d, *J* = 5.5 Hz, 2H), 0.90 (s, 9H), 0.09 (s, 6H); ^{13}C NMR (75 MHz): δ = 141.5, 137.8, 135.7, 129.2, 128.6, 127.6, 127.4, 119.1, 115.3, 63.6, 51.2, 26.0,

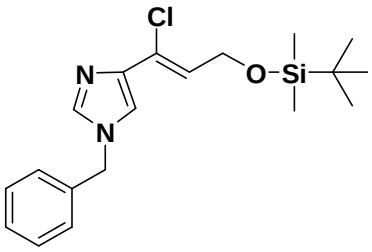
18.4, -5.1; FT-IR (neat, cm^{-1}): 2943, 2840, 1604, 1495, 1457, 1255, 1115, 1065, 781, 704; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{19}H_{28}BrN_2OSi$ 407.1149 found 407.1136 .

(*Z*)-4-(3-(tert-butyldimethylsilyloxy)-1-chloroprop-1-enyl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide (265):



In a round bottom flask compound **263** (130 mg, 0.49 mmol) was dissolved in CH_2Cl_2 (10 mL) under a nitrogen atmosphere. The solution was cooled to 0 ºC and then to the reaction mixture imidazole (50 mg, 0.73 mmol) and TBSCl (100 mg, 0.64 mmol) was added. The reaction mixture was stirred for 8 h, then NH_4Cl (5 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAC (3x50 mL), then the combined organic solutions were dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by chromatography (EtOAc 100%) providing **265** as a colorless solid (161 mg, 87%). m.p 88-90 ºC ^{1}H NMR (300 MHZ): δ = 7.84 (s, 1H), 7.34 (s, 1H), 6.76 (t, *J* = 5.9 Hz, 1H), 4.52 (d, *J* = 5.9 Hz, 2H), 2.89 (s, 6H), 0.91 (s, 9H), 0.10 (s, 6H); ^{13}C NMR (75 MHz): δ = 141.6, 137.1, 127.4, 123.2, 115.2, 60.7, 38.3, 26.0, 18.4, -5.1; FT-IR (neat, cm^{-1}): 2954, 2860, 1630, 1481, 1381, 1173, 1085, 827, 778, 754, 617; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{14}H_{26}ClN_3O_3SSi$ 380.1231 found 380.1231.

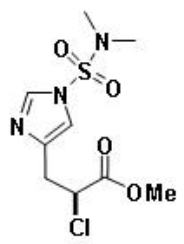
(*Z*)-1-benzyl-4-(3-(tert-butyldimethylsilyloxy)-1-chloroprop-1-enyl)-1H-imidazole (266):

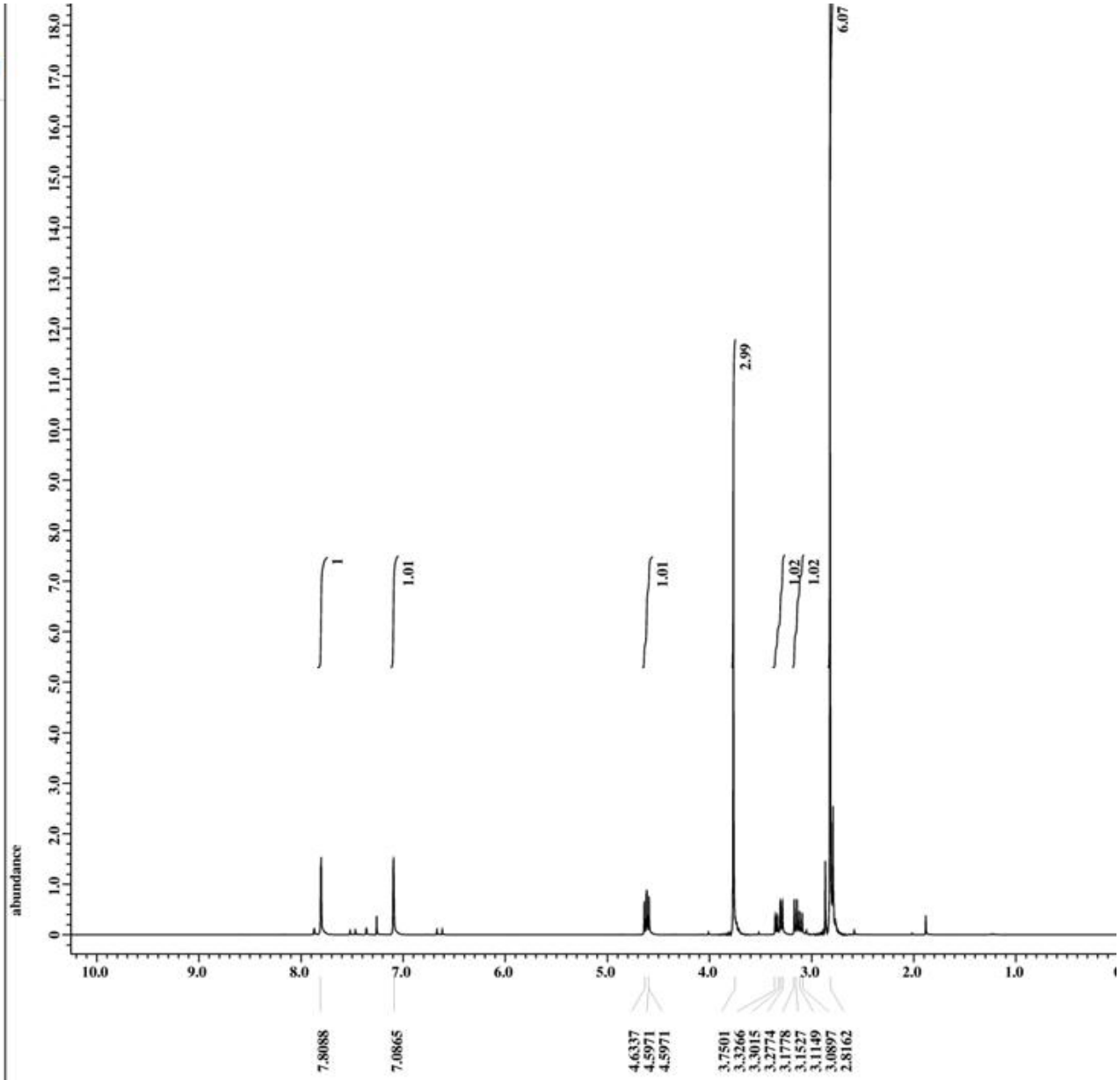


In a round bottom flask compound **264** (100 mg, 0.40 mmol) was dissolved in CH_2Cl_2 (10 mL) under a nitrogen atmosphere. The solution was cooled to 0 ºC and then to the reaction mixture imidazole (40 mg, 0.60 mmol) and TBSCl (78 mg, 0.52 mmol) was added. The reaction mixture was stirred for 8 h, then NH_4Cl (5 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAC (3x50 mL), then the combined organic solutions were dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by chromatography (EtOAc 100%) providing **266** as a colorless solid (135 mg, 92%). m.p 76-78 ºC ^{1}H NMR (300 MHz): δ = 7.54 (d, *J* = 1.4 Hz, 1H), 7.35-7.31 (m, 3H), 7.15 (dd, *J* = 7.4, 1.7 Hz, 2H), 7.03 (*J* = 1.0 Hz, 1H), 6.64 (t, *J* = 5.8 Hz, 1H), 5.06 (s, 2H), 4.49 (d, *J* = 5.8 Hz, 2H), 0.89 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (75 MHz): δ = 140.3, 137.8, 135.6, 129.2, 128.6, 127.5, 124.6, 124.4, 118.0, 60.8, 51.2, 26.2, 18.4, -5.1; FT-IR (neat, cm^{-1}): 2934, 2858, 1590, 1475, 1384, 1167, 1082, 822, 740, 596; HR-MS (*m/z*): calc for $[M+H]^+$ $C_{19}H_{27}ClN_2OSi$ 363.1659 found.

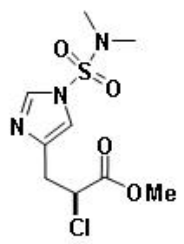
APPENDIX 1
^{1}H AND ^{13}C NMR SPECTRUM OF (*R*)-methyl-2-chloro-3-(1-(N,N-dimethylsulfamoyl)-1H-imidazol-4-yl)propanoate (47)

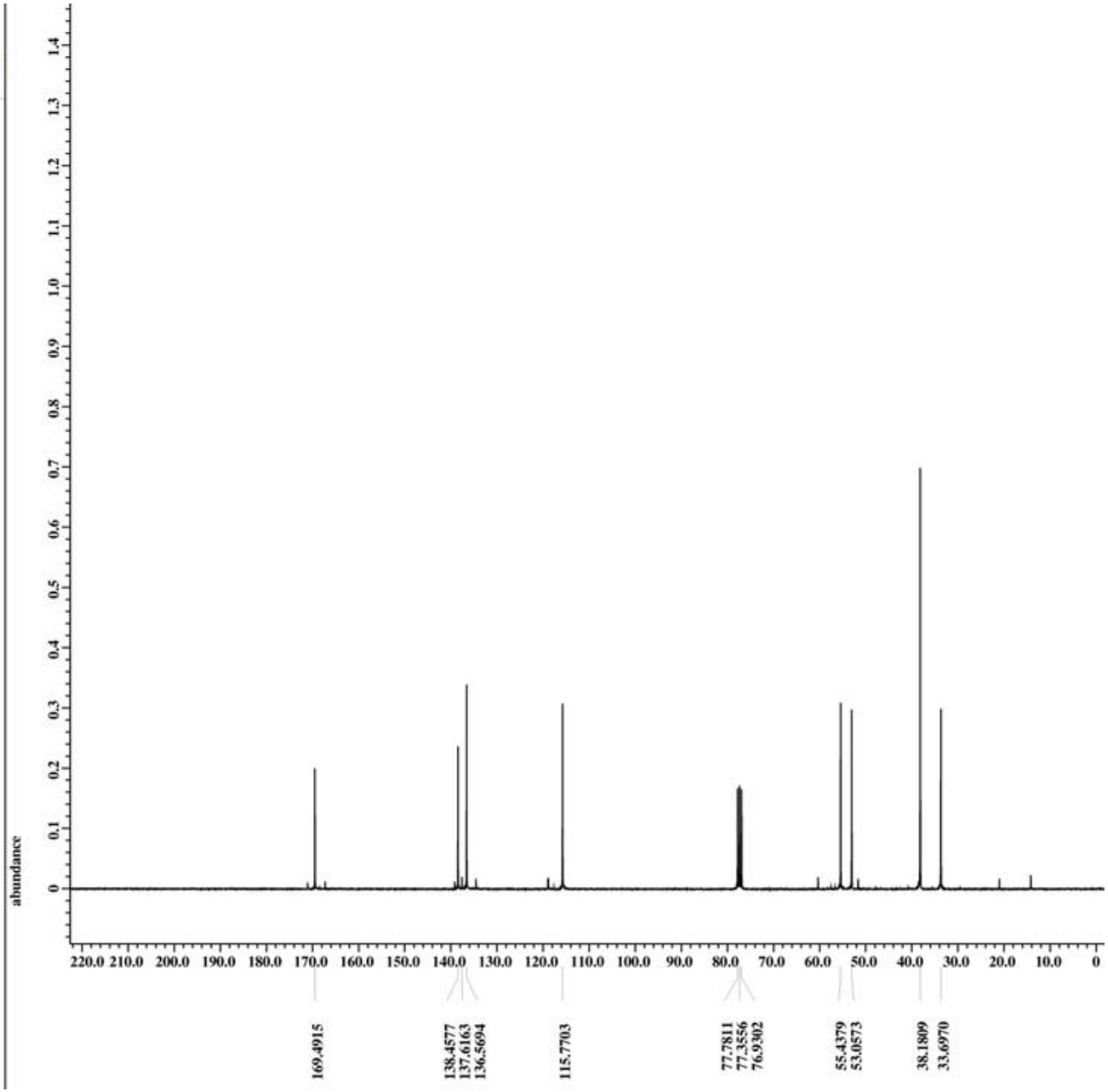
```
ilename          = sm_V_137_ii-4.jdf
uthor            = delta
xperiment        = single_pulse.ex2
ample_id         = S#659746
olvent           = CHLOROFORM-D
reation_time     = 11-JUN-2009 17:51:03
evision_time     = 19-APR-2010 23:49:14
urrent_time      = 20-APR-2010 19:36:39

omment           = single_pulse
ata_format       = 1D COMPLEX
im_size          = 13107
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.90717696[s]
_domain          = 1H
_freq            = 300.52965592[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.34397631[Hz]
_sweep           = 5.63570784[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
ri_domain        = 1H
ri_freq          = 300.52965592[MHz]
ri_offset        = 5[ppm]
lipped           = FALSE
od_return        = 1
cans             = 24
otal_scans       = 24

_90_width        = 13.01[us]
_acq_time        = 2.90717696[s]
_angle           = 45[deg]
_atn             = 4[dB]
_pulse           = 6.505[us]
rr_mode          = Off
ri_mode          = Off
ante_presat      = FALSE
nitial_wait      = 1[s]
ecvr_gain        = 38
elaxation_delay  = 5[s]
epetition_time   = 7.90717696[s]
emp_get          = 22.9[dC]
```





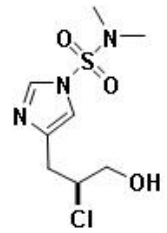
```
ilename          = sm_1_213_pure-4.jdf
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#778317
olvent           = CHLOROFORM-D
reation_time     = 10-JUN-2006 03:05:44
evision_time     = 10-JUN-2009 19:09:11
urrent_time      = 27-MAR-2010 16:21:11

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 52428
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.76824064[s]
_domain          = 13C
_freq            = 75.56823426[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.36124027[Hz]
_sweep           = 23.67424242[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
lipped           = FALSE
od_return        = 10
cans             = 3000
otal_scans       = 3000

_90_width        = 9.75[us]
_acq_time        = 2.76824064[s]
_angle           = 30[deg]
_atn             = 8[dB]
_pulse           = 3.25[us]
rr_atn_dec       = 25[dB]
rr_atn_noe       = 25[dB]
rr_noise         = WALTZ
ecoupling        = TRUE
nitial_wait      = 1[s]
oe               = TRUE
oe_time          = 3[s]
ecvr_gain        = 50
elaxation_delay  = 3[s]
epetition_time   = 5.76824064[s]
emp_get          = 22.2[dC]
```

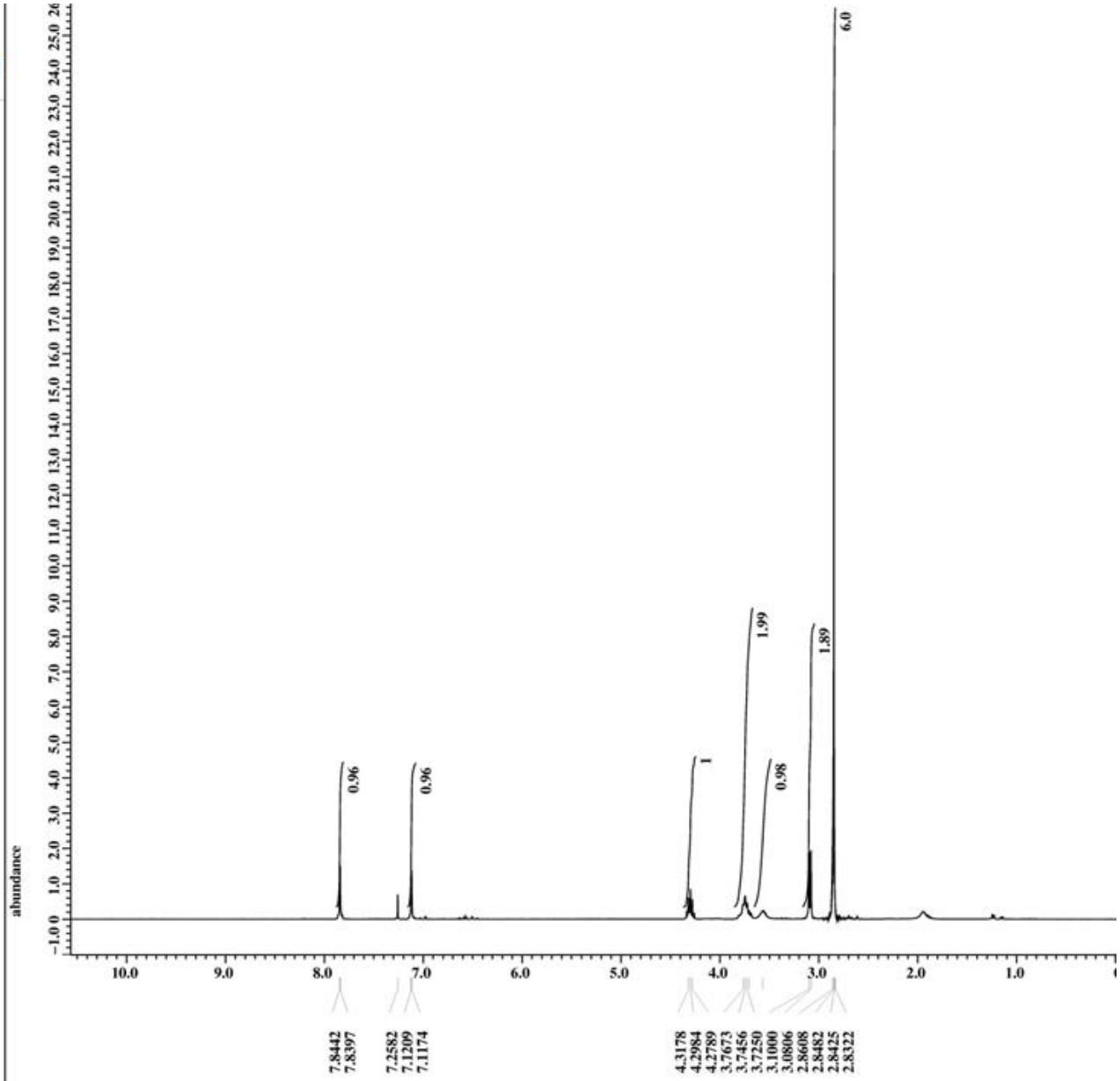




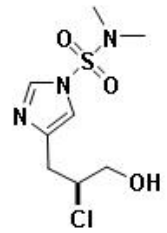
APPENDIX 2
^{1}H AND ^{13}C NMR SPECTRUM OF
(*R*)-4-(2-chloro-3-hydroxypropyl)-N,N-dimethyl-1H-imidazole-1-sulfonamide
(48)

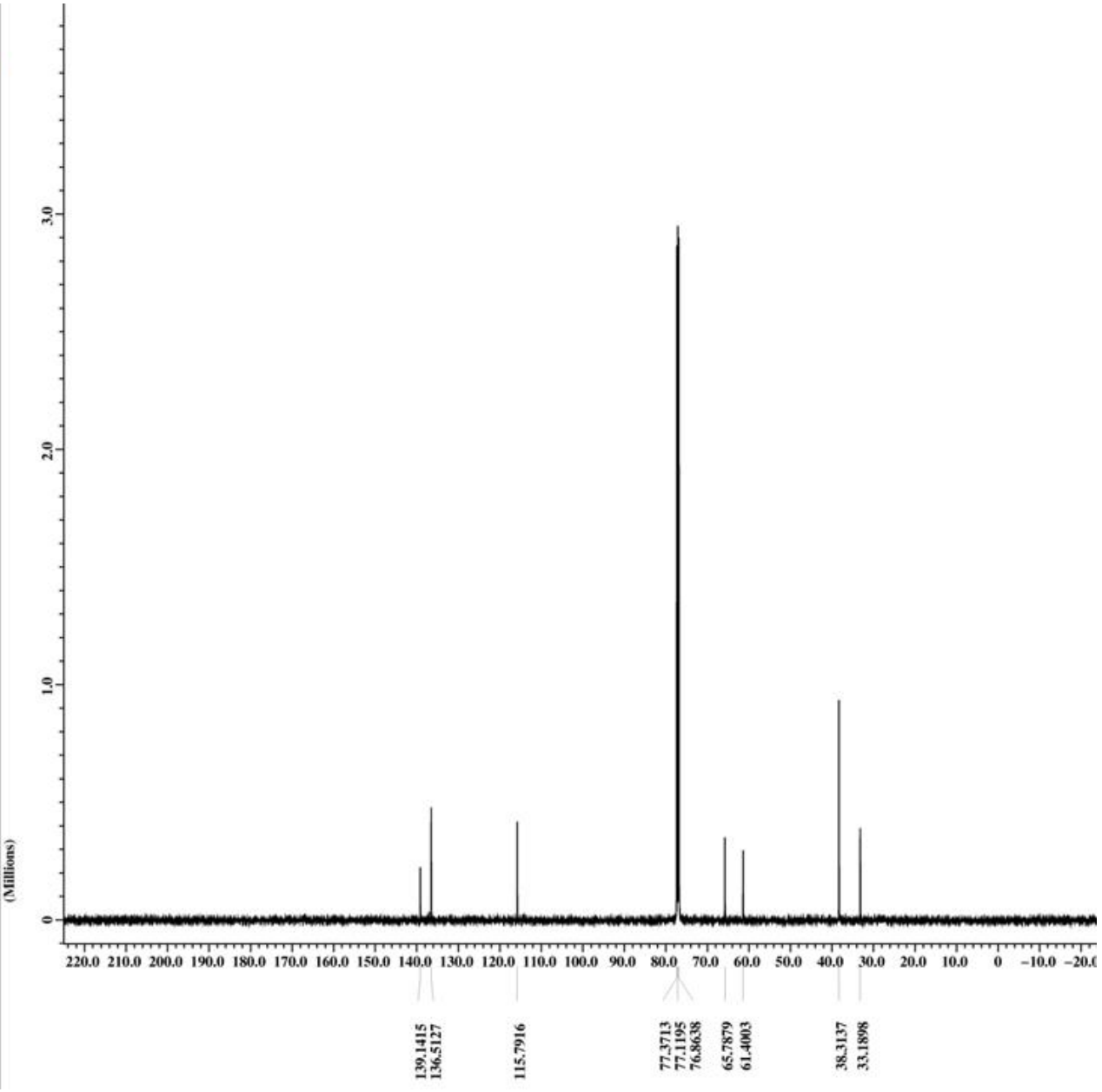
```
ilename          = sm_II_23_alcohol_pure
uthor            = delta
xperiment        = single_pulse.ex2
ample_id         = S#386706
olvent           = CHLOROFORM-D
reation_time     = 27-NOV-2006 11:33:17
evision_time     = 27-MAR-2010 16:29:19
urrent_time      = 27-MAR-2010 16:33:32

omment           = single_pulse
ata_format       = 1D COMPLEX
im_size          = 13107
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.90717696[s]
_domain          = 1H
_freq            = 300.52965592[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.34397631[Hz]
_sweep           = 5.63570784[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
ri_domain        = 1H
ri_freq          = 300.52965592[MHz]
ri_offset        = 5[ppm]
lipped           = FALSE
od_return        = 1
cans             = 24
otal_scans       = 24

_90_width        = 13.01[us]
_acq_time        = 2.90717696[s]
_angle           = 45[deg]
_atn             = 4[dB]
_pulse           = 6.505[us]
rr_mode          = Off
ri_mode          = Off
ante_presat      = FALSE
nitial_wait      = 1[s]
ecvr_gain        = 42
elaxation_delay  = 5[s]
epetition_time   = 7.90717696[s]
emp_get          = 23.5[dC]
```





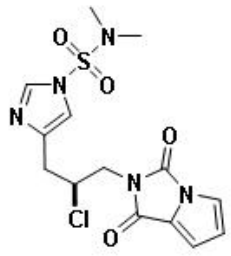
```
ilename          = sm_II_alcohol_pure-2.
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#708634
olvent           = CHLOROFORM-D
reation_time     = 10-DEC-2006 01:54:30
evision_time     = 10-DEC-2006 15:51:21
urrent_time      = 27-MAR-2010 16:38:46

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 65536
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7473579[T] (500[MH
_acq_duration    = 2.0840448[s]
_domain          = 13C
_freq            = 125.76529768[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.47983613[Hz]
_sweep           = 31.44654088[kHz]
rr_domain        = 1H
rr_freq          = 500.15991521[MHz]
rr_offset        = 5[ppm]
lipped           = TRUE
od_return        = 10
cans             = 3000
otal_scans       = 3000

_90_width        = 14.2[us]
_acq_time        = 2.0840448[s]
_angle           = 30[deg]
_pulse           = 4.73333333[us]
nitial_wait      = 1[s]
oe_time          = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 29
elaxation_delay  = 2[s]
emp_get          = 26.8[dC]
nblank_time      = 2[us]
```

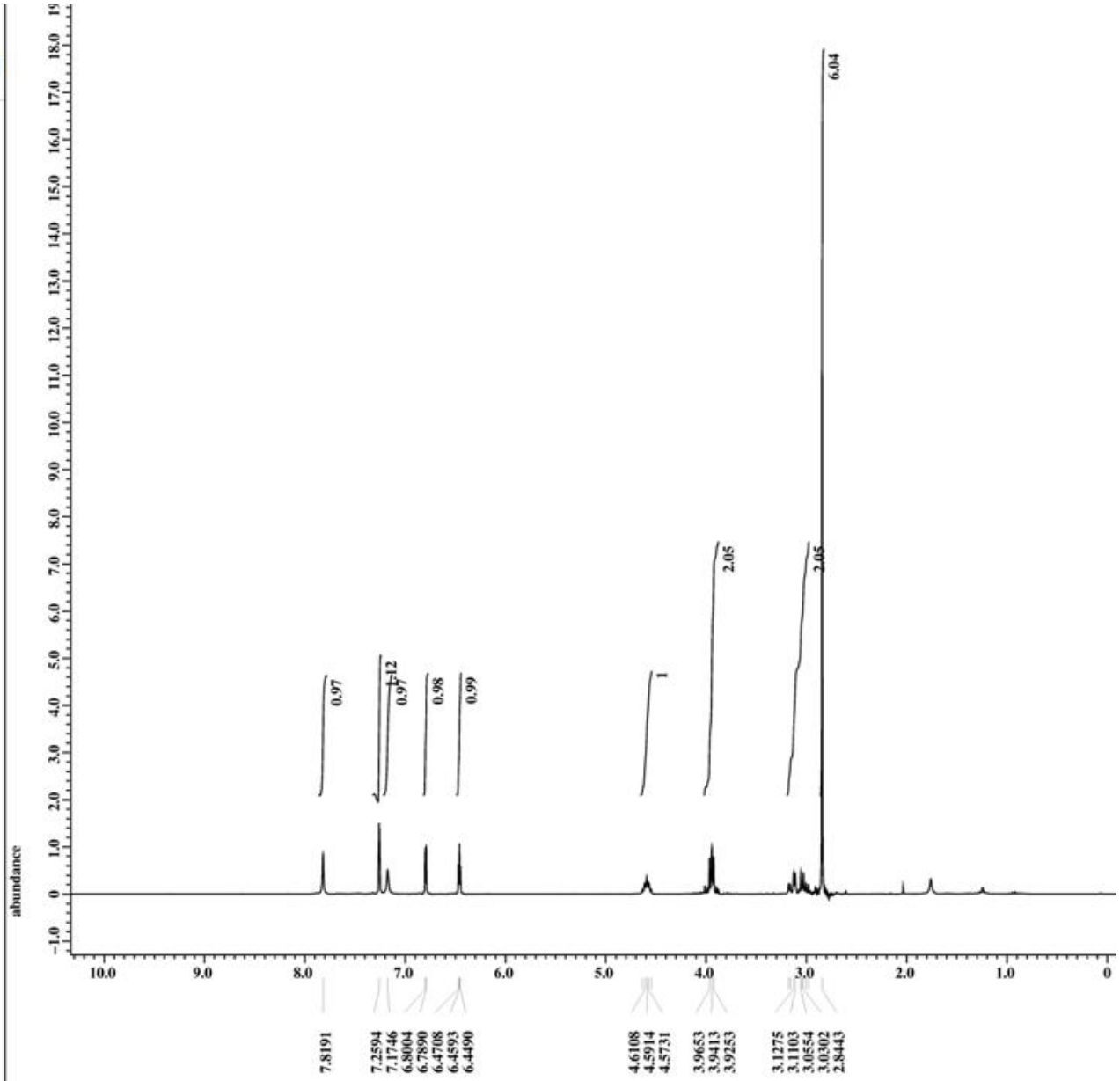




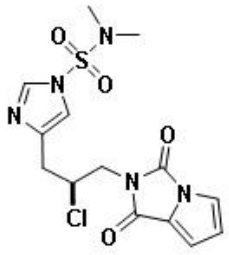
APPENDIX 3
^{1}H AND ^{13}C NMR SPECTRUM OF
(*R*)-4-(2-chloro-3-(1,3-dioxo-1H-pyrrolo[1,2-c]imidazol-2(3H)-yl)propyl)-N,N-dimethyl-1H-imidazole-1-sulfonamide (50)

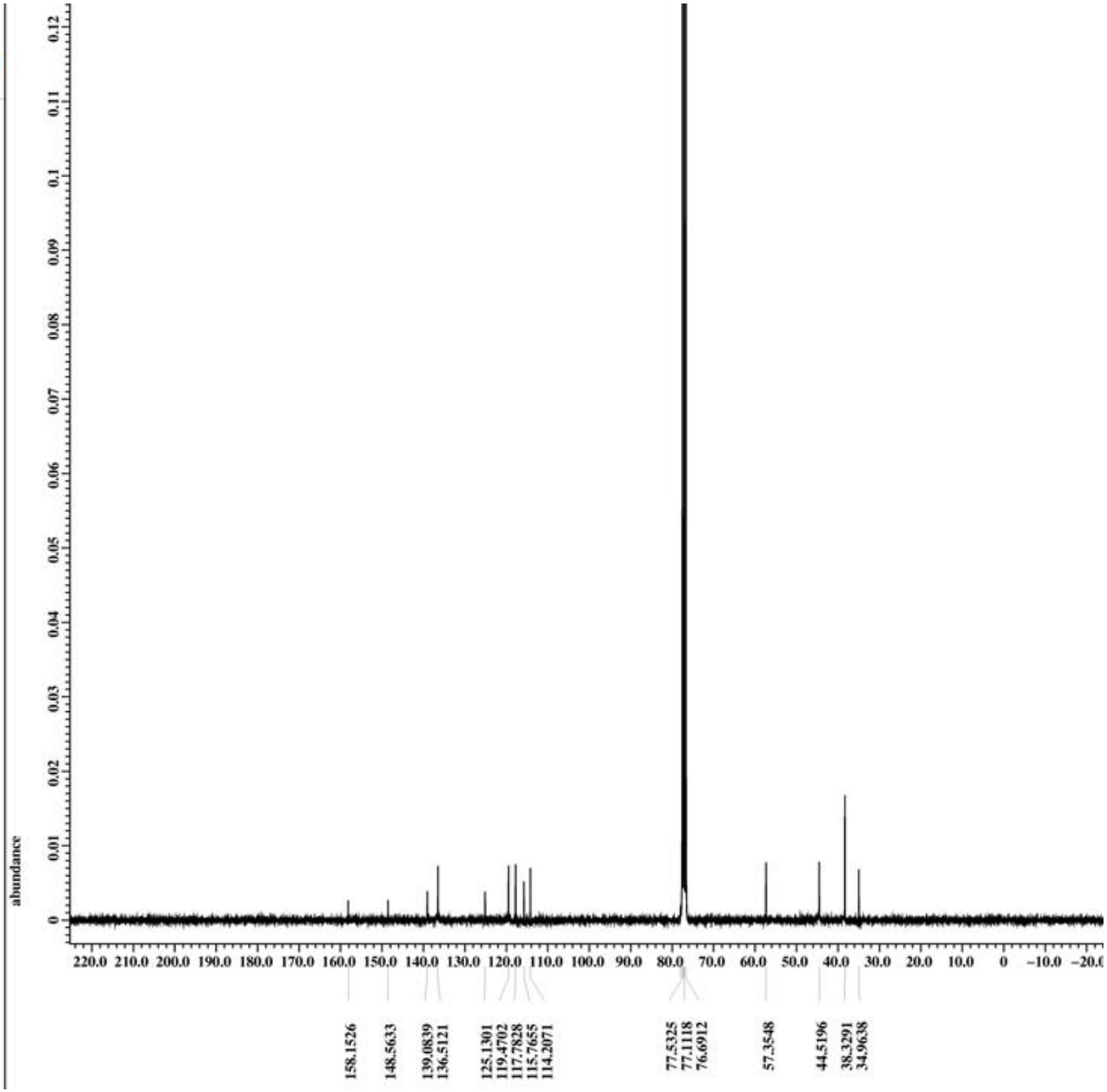
```
ilename          = sm_1_183_pure ii-4.jd
uthor            = delta
xperiment        = single_pulse.ex2
ample_id         = S#595971
olvent           = CHLOROFORM-D
reation_time     = 28-FEB-2006 17:30:58
evision_time     = 27-MAR-2010 16:46:52
urrent_time      = 27-MAR-2010 16:47:12

omment           = single_pulse
ata_format       = 1D COMPLEX
im_size          = 13107
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.90717696[s]
_domain          = 1H
_freq            = 300.52965592[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.34397631[Hz]
_sweep           = 5.63570784[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
ri_domain        = 1H
ri_freq          = 300.52965592[MHz]
ri_offset        = 5[ppm]
lipped           = FALSE
od_return        = 1
cans             = 14
otal_scans       = 14

_90_width        = 13.01[us]
_acq_time        = 2.90717696[s]
_angle           = 45[deg]
_atn             = 4[dB]
_pulse           = 6.505[us]
rr_mode          = Off
ri_mode          = Off
ante_presat      = FALSE
nitial_wait      = 1[s]
ecvr_gain        = 44
elaxation_delay  = 5[s]
epetition_time   = 7.90717696[s]
emp_get          = 21.6[dC]
```





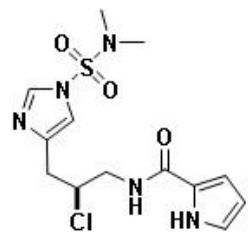
```
ilename          = sm_V_31_PURE-3.jdf
uthor            = delta
xperiment        = single_pulse_dec
mple_id          = S#502438
olvent           = CHLOROFORM-D
reation_time     = 23-DEC-2008 20:16:49
evision_time     = 23-DEC-2008 20:03:32
urrent_time      = 27-MAR-2010 16:52:08

omment           = single pulse decouple
ata_format       = 1D REAL
im_size          = 52428
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.76824064[s]
_domain          = 13C
_freq            = 75.56823426[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.36124027[Hz]
_sweep           = 23.67424242[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
lipped           = FALSE
od_return        = 10
cans             = 3775
otal_scans       = 3775

_90_width        = 9.75[us]
_acq_time        = 2.76824064[s]
_angle           = 30[deg]
_atn             = 8[dB]
_pulse           = 3.25[us]
rr_atn_dec       = 25[dB]
rr_atn_noe       = 25[dB]
rr_noise         = WALTZ
ecoupling        = TRUE
nitial_wait      = 1[s]
oe               = TRUE
oe_time          = 3[s]
ecvr_gain        = 50
elaxation_delay  = 3[s]
epetition_time   = 5.76824064[s]
emp_get          = 23.2[dC]
```

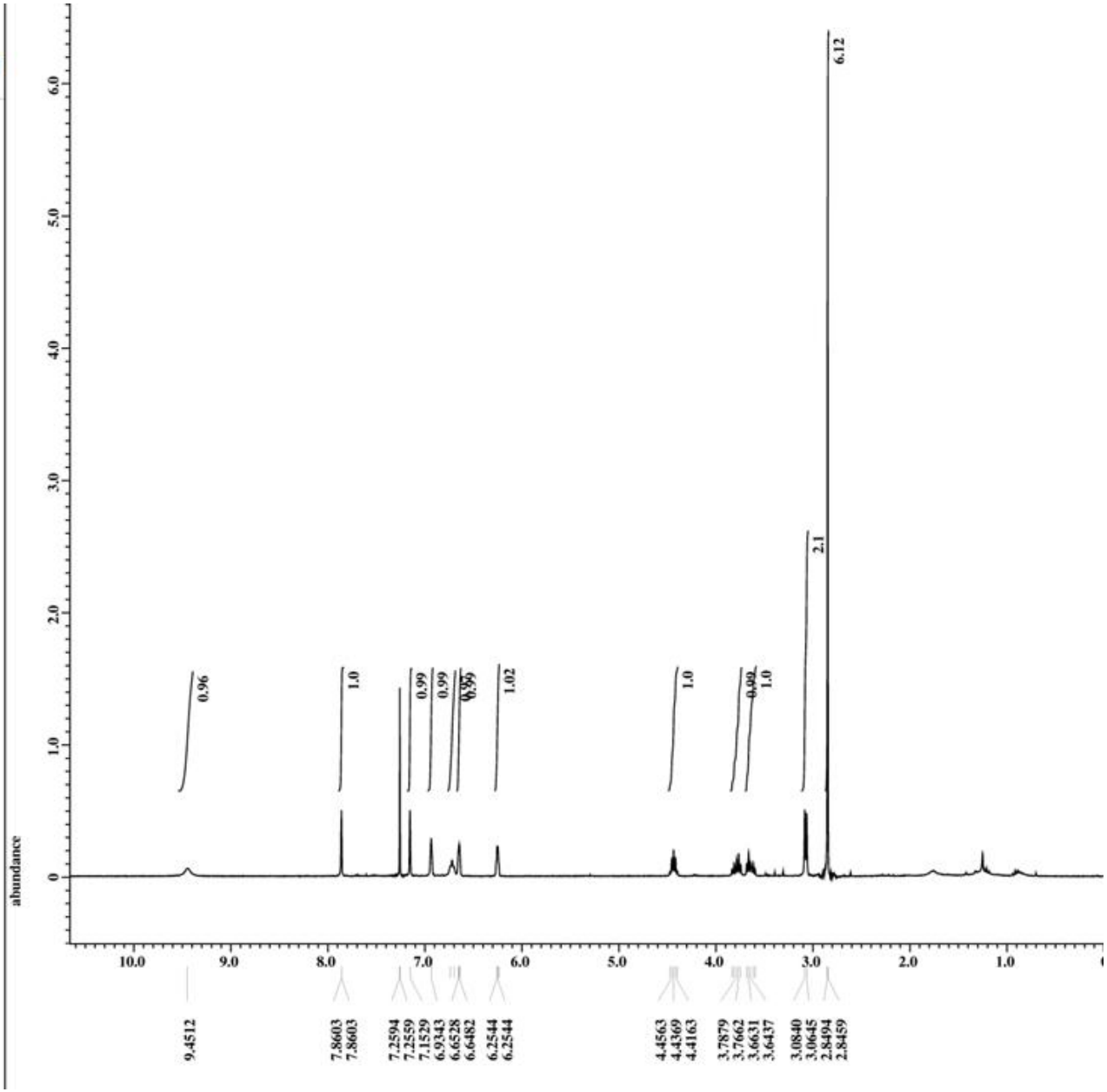




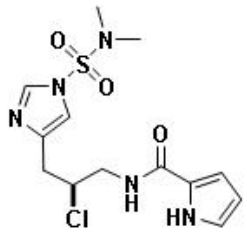
APPENDIX 4
^{1}H AND ^{13}C NMR SPECTRUM OF
(*R*)-N-(2-chloro-3-(1-(N,N-dimethylsulfamoyl)-1H-imidazol-4-yl)propyl)-1H-pyrrole-2-carboxamide (54)

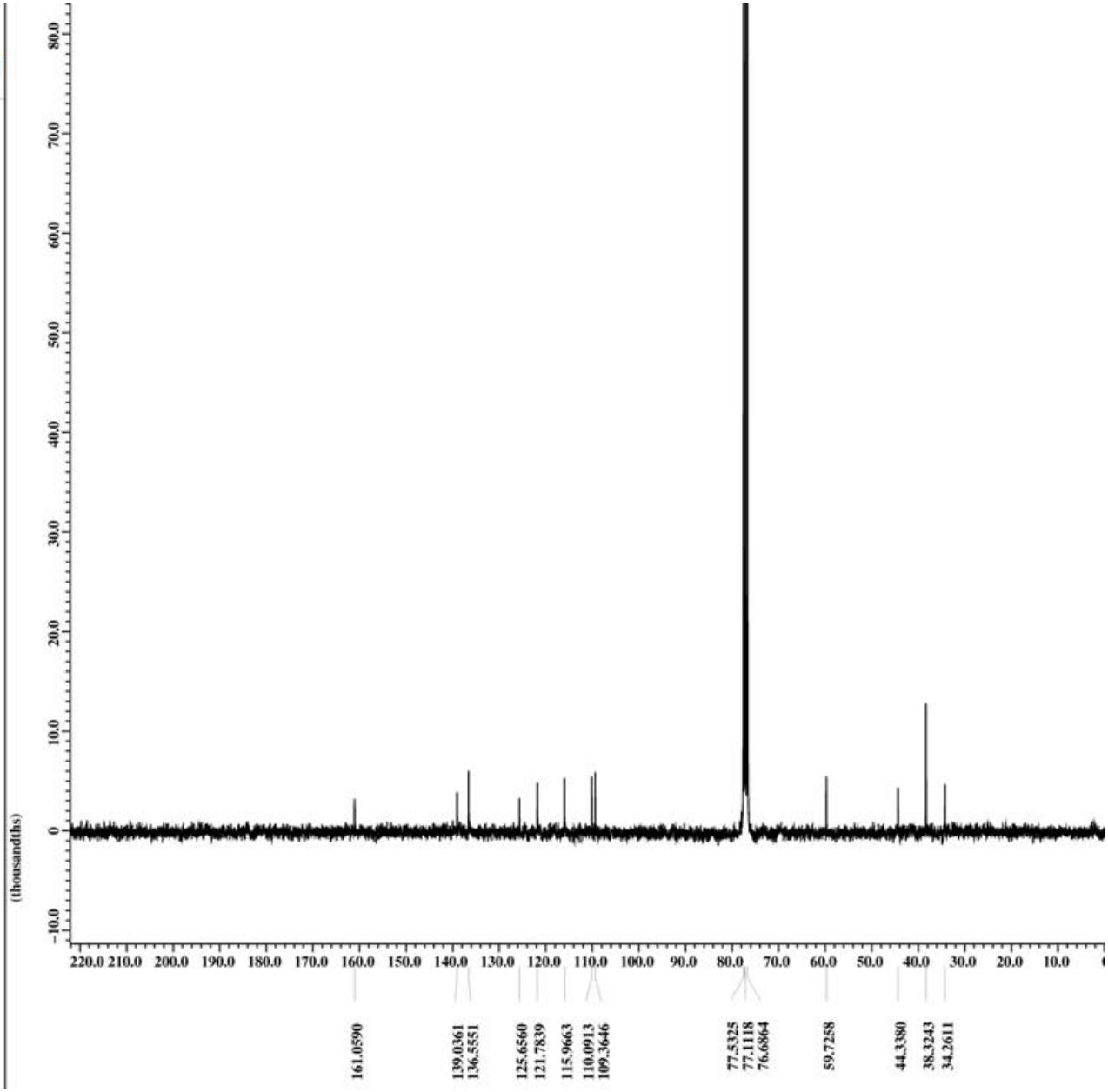
```
ilename          = sm_1_137_pure-5.jdf
uthor            = delta
xperiment        = single_pulse.ex2
mple_id          = S#463736
olvent           = CHLOROFORM-D
reation_time     = 17-NOV-2005 13:53:13
evision_time     = 27-MAR-2010 17:01:41
urrent_time      = 27-MAR-2010 17:03:16

omment           = single_pulse
ata_format       = 1D COMPLEX
im_size          = 13107
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.90717696[s]
_domain          = 1H
_freq            = 300.52965592[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.34397631[Hz]
_sweep           = 5.63570784[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
ri_domain        = 1H
ri_freq          = 300.52965592[MHz]
ri_offset        = 5[ppm]
lipped           = FALSE
od_return        = 1
cans             = 24
otal_scans       = 24

_90_width        = 13.01[us]
_acq_time        = 2.90717696[s]
_angle           = 45[deg]
_atn             = 4[dB]
_pulse           = 6.505[us]
rr_mode          = Off
ri_mode          = Off
ante_presat      = FALSE
nitial_wait      = 1[s]
ecvr_gain        = 46
elaxation_delay  = 5[s]
epetition_time   = 7.90717696[s]
emp_get          = 23[dC]
```





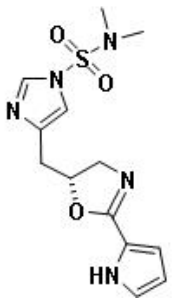
```
ilename          = sm_1_137_pure-2.jdf
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#617488
olvent           = CHLOROFORM-D
reation_time     = 17-NOV-2005 20:42:29
evision_time     = 17-NOV-2005 21:56:49
urrent_time      = 27-MAR-2010 17:08:07

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 52428
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.76824064[s]
_domain          = 13C
_freq            = 75.56823426[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.36124027[Hz]
_sweep           = 23.67424242[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
lipped           = FALSE
od_return        = 10
cans             = 1627
otal_scans       = 1627

_90_width        = 9.75[us]
_acq_time        = 2.76824064[s]
_angle           = 30[deg]
_atn             = 8[dB]
_pulse           = 3.25[us]
rr_atn_dec       = 25[dB]
rr_atn_noe       = 25[dB]
rr_noise         = WALTZ
ecoupling        = TRUE
nitial_wait      = 1[s]
oe               = TRUE
oe_time          = 3[s]
ecvr_gain        = 50
elaxation_delay  = 3[s]
epetition_time   = 5.76824064[s]
emp_get          = 23.3[dC]
```

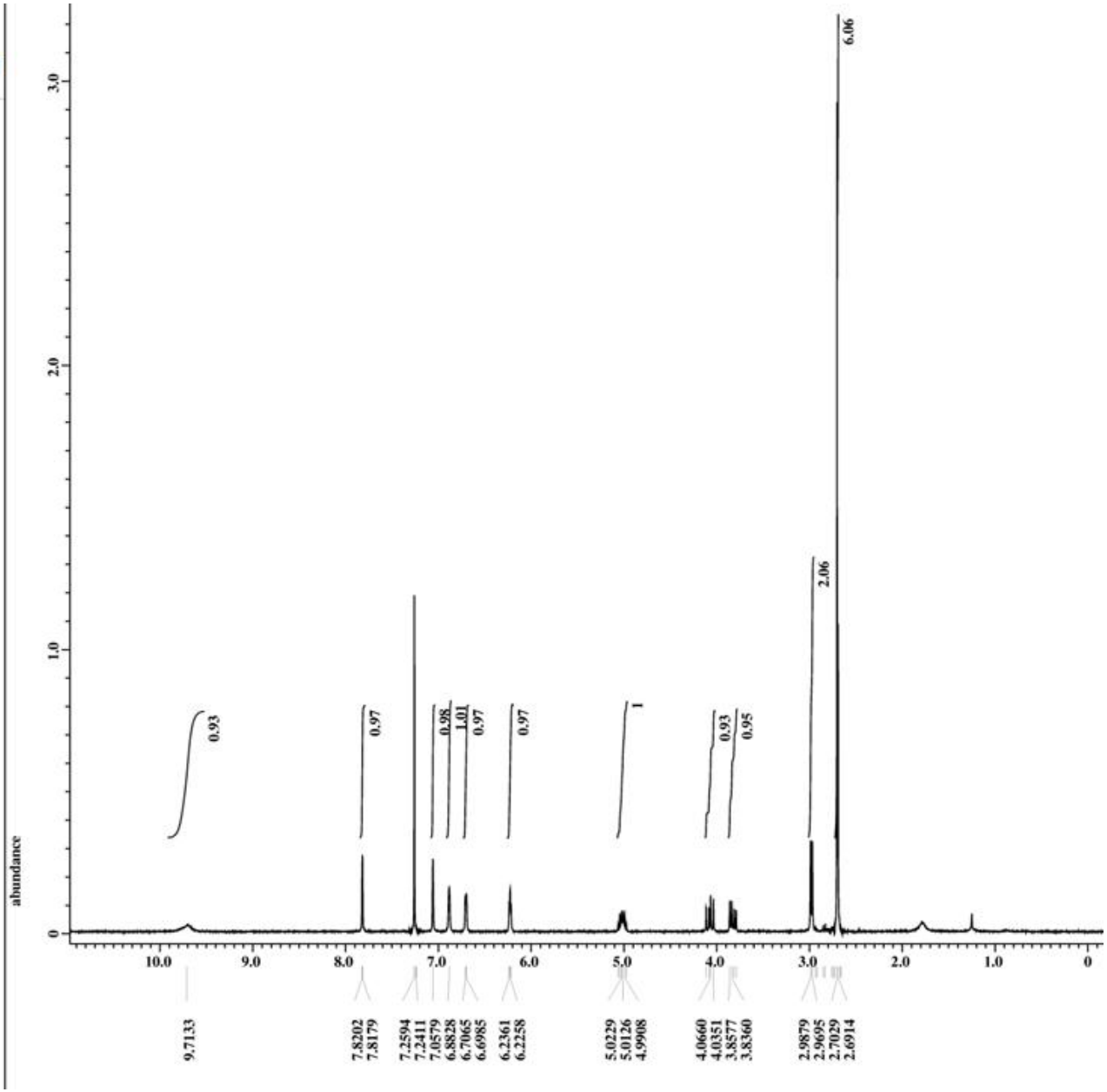




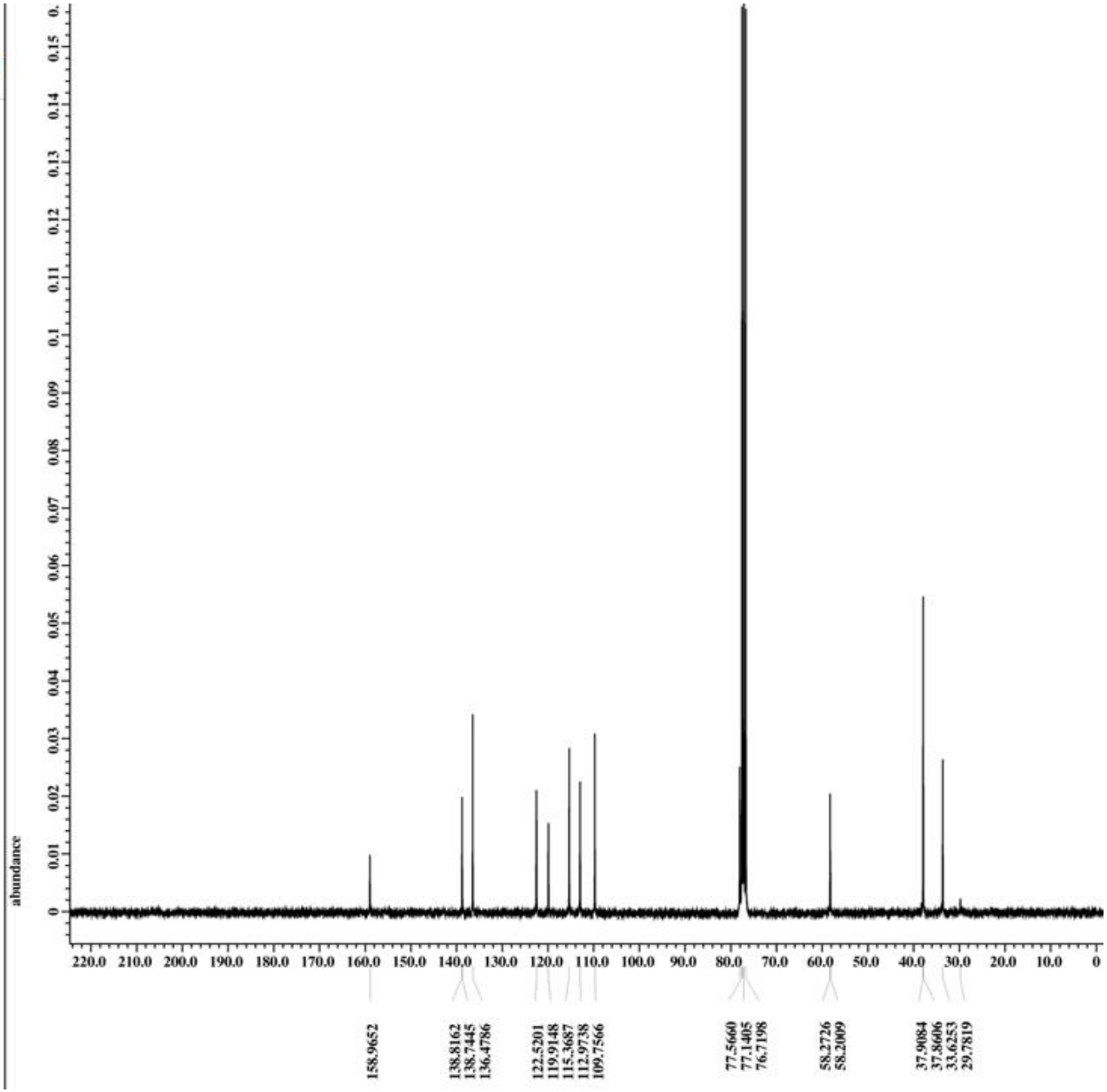
APPENDIX 5
^{1}H AND ^{13}C NMR SPECTRUM OF
(*S*)-4-((2-(1H-pyrrol-2-yl)-4,5-dihydrooxazol-5-yl)methyl)-N,N-dimethyl-1H-imidazole-1-sulfonamide (56)

```
ilename          = sm_precursor to azida
uthor            = delta
xperiment        = single_pulse.ex2
mple_id          = S#402502
olvent           = CHLOROFORM-D
reation_time     = 31-AUG-2006 11:53:19
evision_time     = 27-MAR-2010 17:13:30
urrent_time      = 27-MAR-2010 17:13:59

omment           = single_pulse
ata_format       = 1D COMPLEX
im_size          = 13107
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.90717696[s]
_domain          = 1H
_freq            = 300.52965592[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.34397631[Hz]
_sweep           = 5.63570784[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
ri_domain        = 1H
ri_freq          = 300.52965592[MHz]
ri_offset        = 5[ppm]
lipped           = FALSE
od_return        = 1
cans             = 19
otal_scans       = 19

_90_width        = 13.01[us]
_acq_time        = 2.90717696[s]
_angle           = 45[deg]
_atn             = 4[dB]
_pulse           = 6.505[us]
rr_mode          = Off
ri_mode          = Off
ante_presat      = FALSE
nitial_wait      = 1[s]
ecvr_gain        = 46
elaxation_delay  = 5[s]
epetition_time   = 7.90717696[s]
emp_get          = 22.8[dC]
```



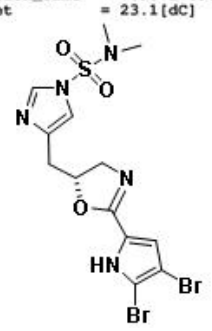


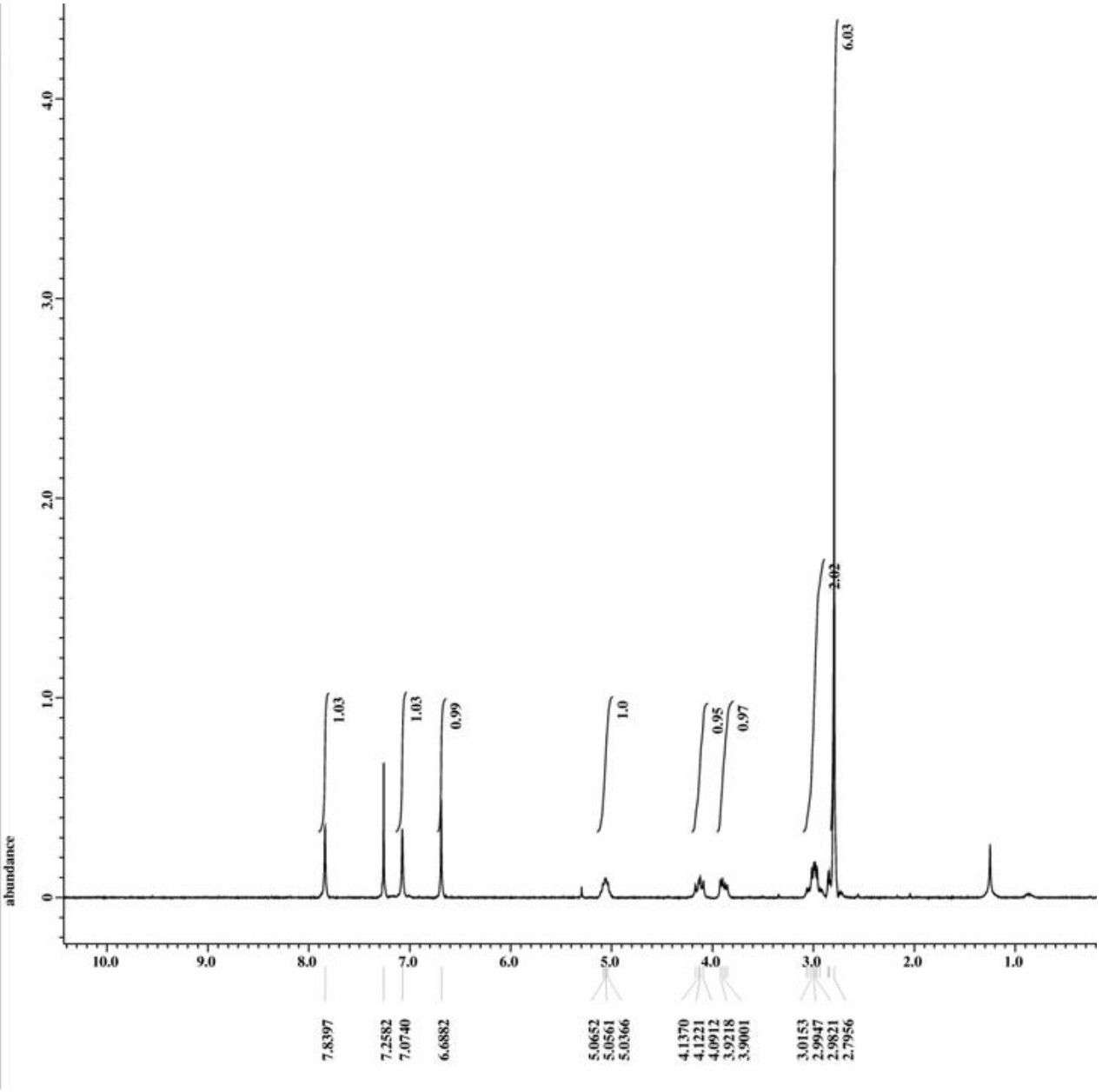
```
ilename          = sm_cyclic_int-2.jdf
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#781820
olvent           = CHLOROFORM-D
reation_time     = 16-JAN-2007 08:04:08
evision_time     = 16-JAN-2007 10:11:11
urrent_time      = 27-MAR-2010 17:17:35

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 52428
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.76824064[s]
_domain          = 13C
_freq            = 75.56823426[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.36124027[Hz]
_sweep           = 23.67424242[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
lipped           = FALSE
od_return        = 10
cans             = 6000
otal_scans       = 6000

_90_width        = 9.75[us]
_acq_time        = 2.76824064[s]
_angle           = 30[deg]
_atn             = 8[dB]
_pulse           = 3.25[us]
rr_atn_dec       = 25[dB]
rr_atn_noe       = 25[dB]
rr_noise         = WALTZ
ecoupling        = TRUE
nitial_wait      = 1[s]
oe               = TRUE
oe_time          = 3[s]
ecvr_gain        = 50
elaxation_delay  = 3[s]
epetition_time   = 5.76824064[s]
emp_get          = 23[dC]
```

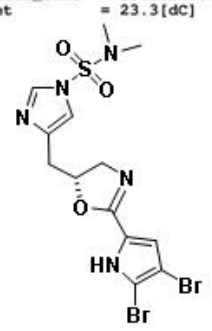
APPENDIX 6
^{1}H AND ^{13}C NMR SPECTRUM OF
(*S*)-4-((2-(4,5-dibromo-1H-pyrrol-2-yl)-4,5-dihydrooxazol-5-yl)methyl)-N,N-dimethyl-1H-imidazole-1-sulfonamide (58)

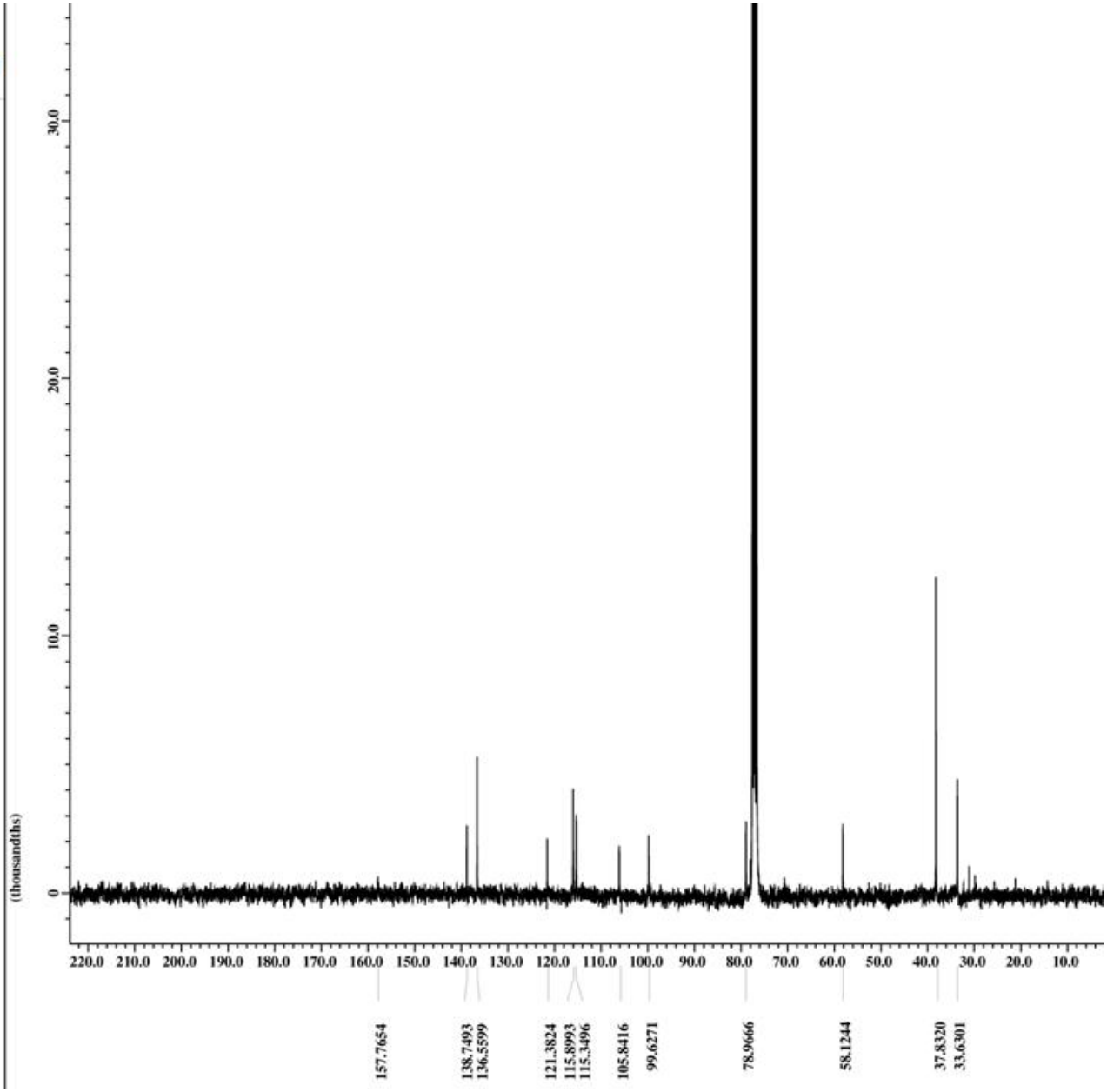
```
ilename          = sm_V_157_pure_iv-3.jd
uthor            = delta
xperiment        = single_pulse.ex2
ample_id         = S#832671
olvent           = CHLOROFORM-D
reation_time     =  9-JUL-2009 23:00:23
evision_time     =  9-JUL-2009 23:12:45
urrent_time      = 27-MAR-2010 17:21:21

omment           = single_pulse
ata_format       = 1D REAL
im_size          = 13107
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.90717696[s]
_domain          = 1H
_freq            = 300.52965592[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.34397631[Hz]
_sweep           = 5.63570784[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
ri_domain        = 1H
ri_freq          = 300.52965592[MHz]
ri_offset        = 5[ppm]
lipped           = FALSE
od_return        = 1
cans             = 16
otal_scans       = 16

_90_width        = 13.01[us]
_acq_time        = 2.90717696[s]
_angle           = 45[deg]
_atn             = 4[dB]
_pulse           = 6.505[us]
rr_mode          = Off
ri_mode          = Off
ante_presat      = FALSE
nitial_wait      = 1[s]
ecvr_gain        = 46
elaxation_delay  = 5[s]
epetition_time   = 7.90717696[s]
emp_get          = 23.1[dC]
```





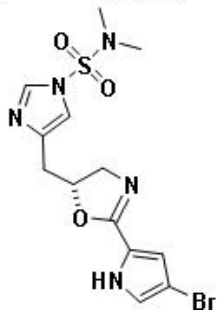
```
ilename          = sm_V_157_pure_iii-2.j
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#642639
olvent           = CHLOROFORM-D
reation_time     =  5-JUL-2009 04:53:39
evision_time     =  5-JUL-2009 16:04:38
urrent_time      = 27-MAR-2010 17:29:36

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 52428
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.76824064[s]
_domain          = 13C
_freq            = 75.56823426[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.36124027[Hz]
_sweep           = 23.67424242[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
lipped           = FALSE
od_return        = 10
cans             = 7000
otal_scans       = 7000

_90_width        = 9.75[us]
_acq_time        = 2.76824064[s]
_angle           = 30[deg]
_atn             = 8[dB]
_pulse           = 3.25[us]
rr_atn_dec       = 25[dB]
rr_atn_noe       = 25[dB]
rr_noise         = WALTZ
ecoupling        = TRUE
nitial_wait      = 1[s]
oe               = TRUE
oe_time          = 3[s]
ecvr_gain        = 50
elaxation_delay  = 3[s]
epetition_time   = 5.76824064[s]
emp_get          = 23.3[dC]
```

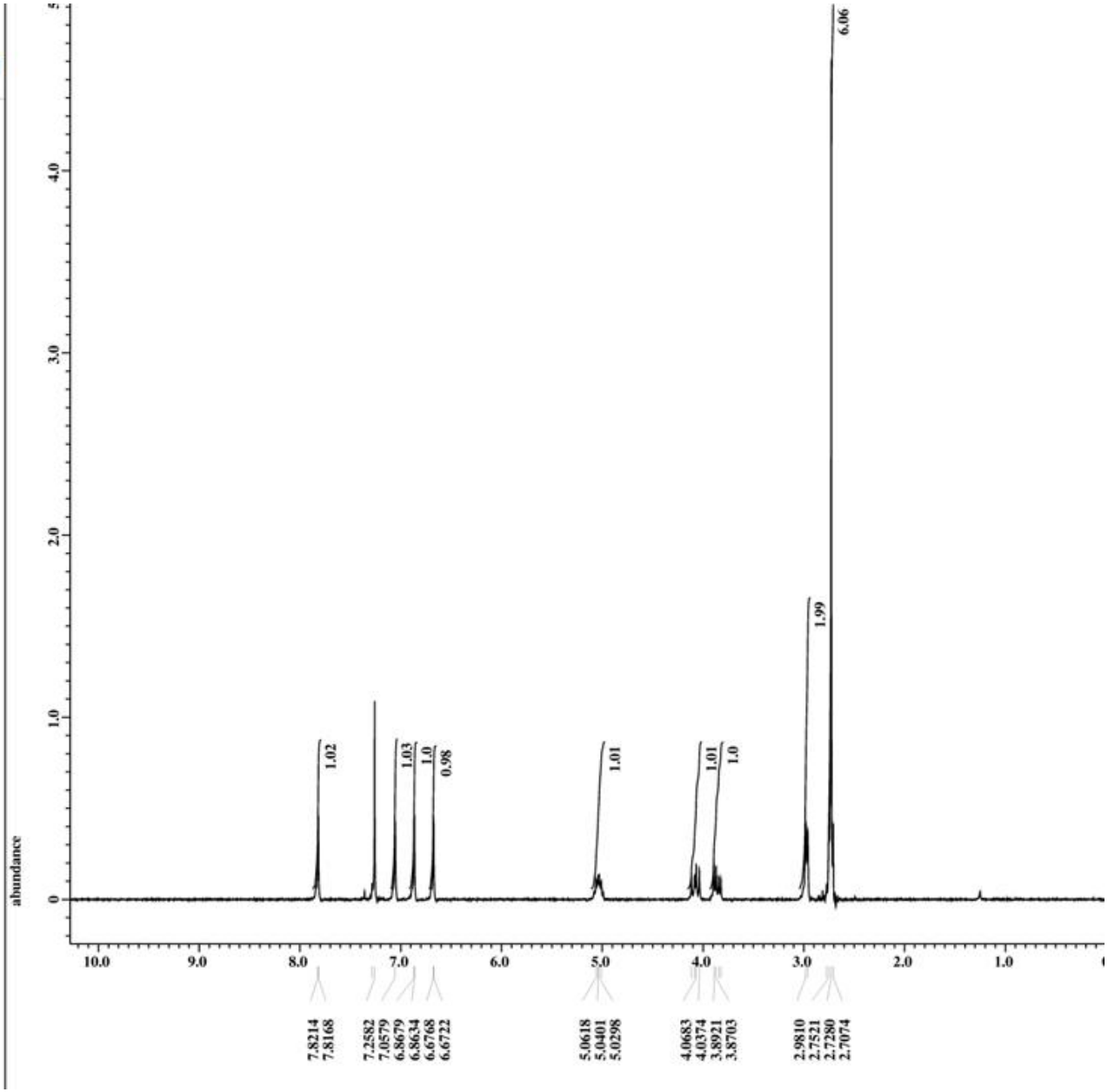


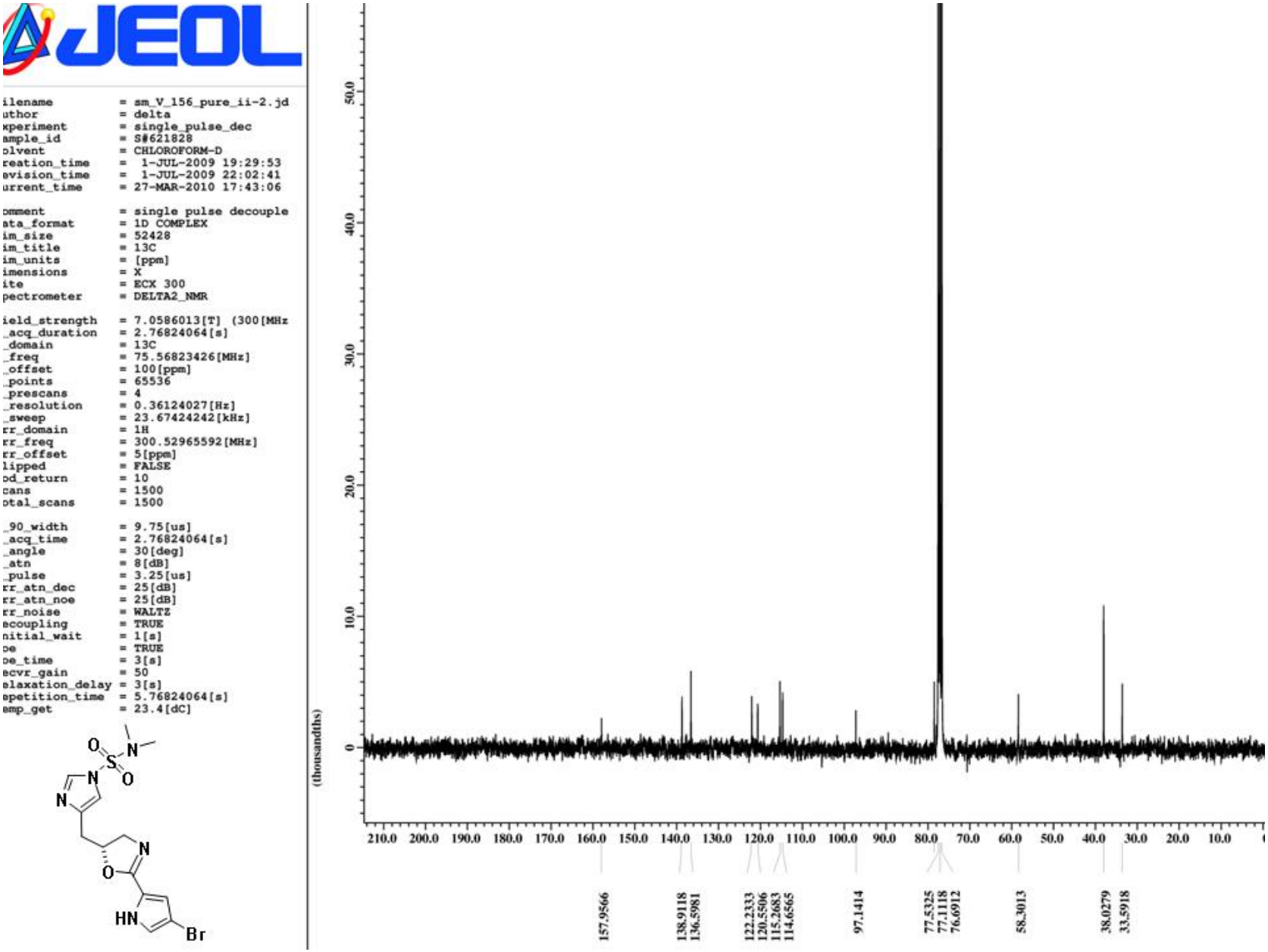


APPENDIX 7
^{1}H AND ^{13}C NMR SPECTRUM OF
(*S*)-4-((2-(4-bromo-1H-pyrrol-2-yl)-4,5-dihydrooxazol-5-yl)methyl)-N,N-dimethyl-1H-imidazole-1-sulfonamide (59)

```
ilename          = sm_V_156_pure_ii-4.jd
uthor            = delta
xperiment        = single_pulse.ex2
ample_id         = S#620333
olvent           = CHLOROFORM-D
reation_time     =  1-JUL-2009 17:05:04
evision_time     = 27-MAR-2010 17:38:18
urrent_time      = 27-MAR-2010 17:39:20

omment           = single_pulse
ata_format       = 1D REAL
im_size          = 13107
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.90717696[s]
_domain          = 1H
_freq            = 300.52965592[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.34397631[Hz]
_sweep           = 5.63570784[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
ri_domain        = 1H
ri_freq          = 300.52965592[MHz]
ri_offset        = 5[ppm]
lipped           = FALSE
od_return        = 1
cans             = 12
otal_scans       = 12

_90_width        = 13.01[us]
_acq_time        = 2.90717696[s]
_angle           = 45[deg]
_atn             = 4[dB]
_pulse           = 6.505[us]
rr_mode          = Off
ri_mode          = Off
ante_presat      = FALSE
nitial_wait      = 1[s]
ecvr_gain        = 48
elaxation_delay  = 5[s]
epetition_time   = 7.90717696[s]
emp_get          = 23.2[dC]
```



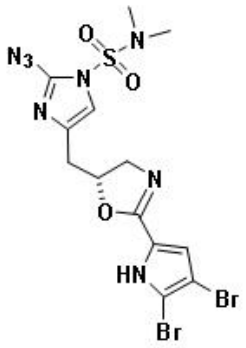


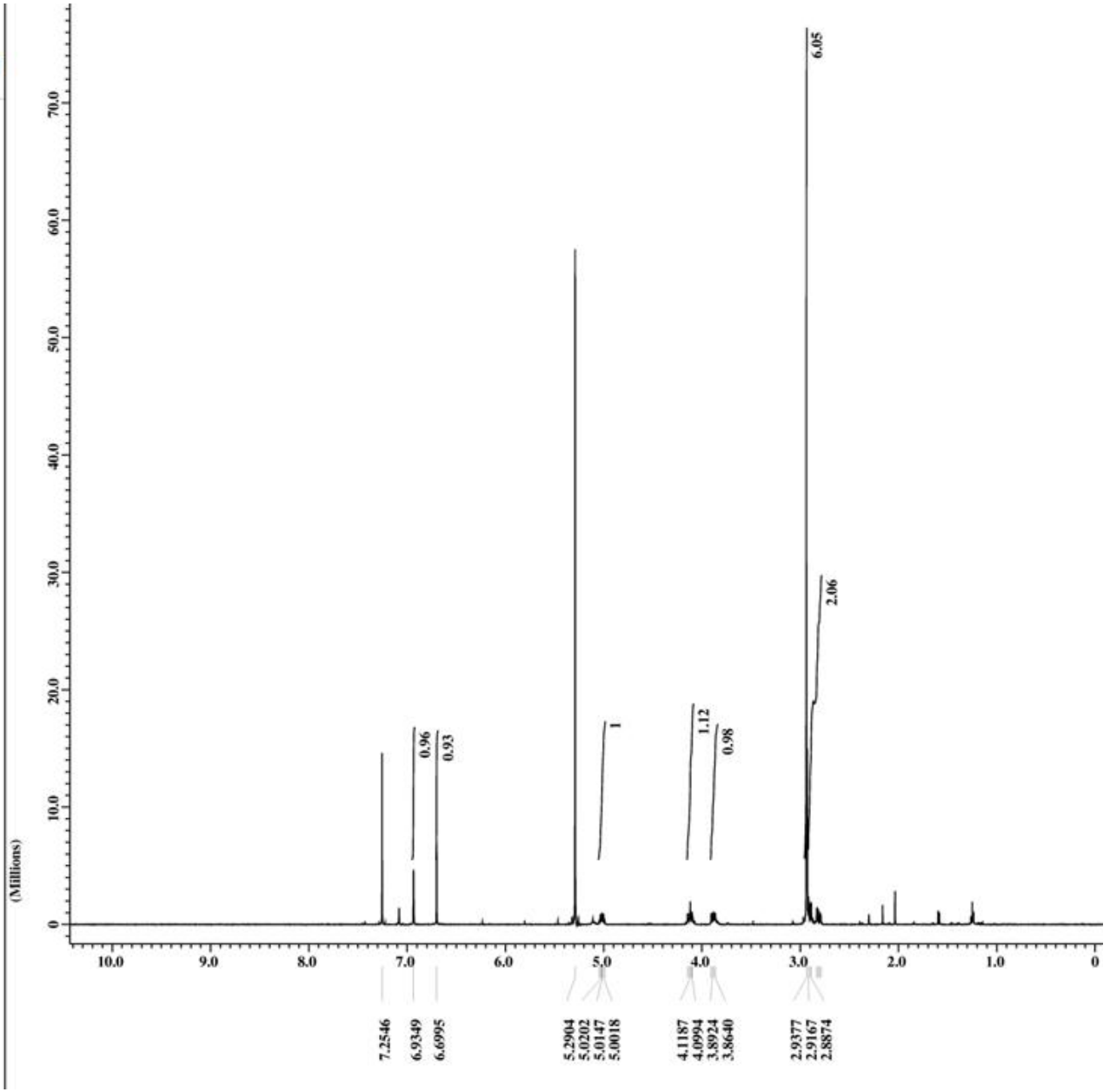


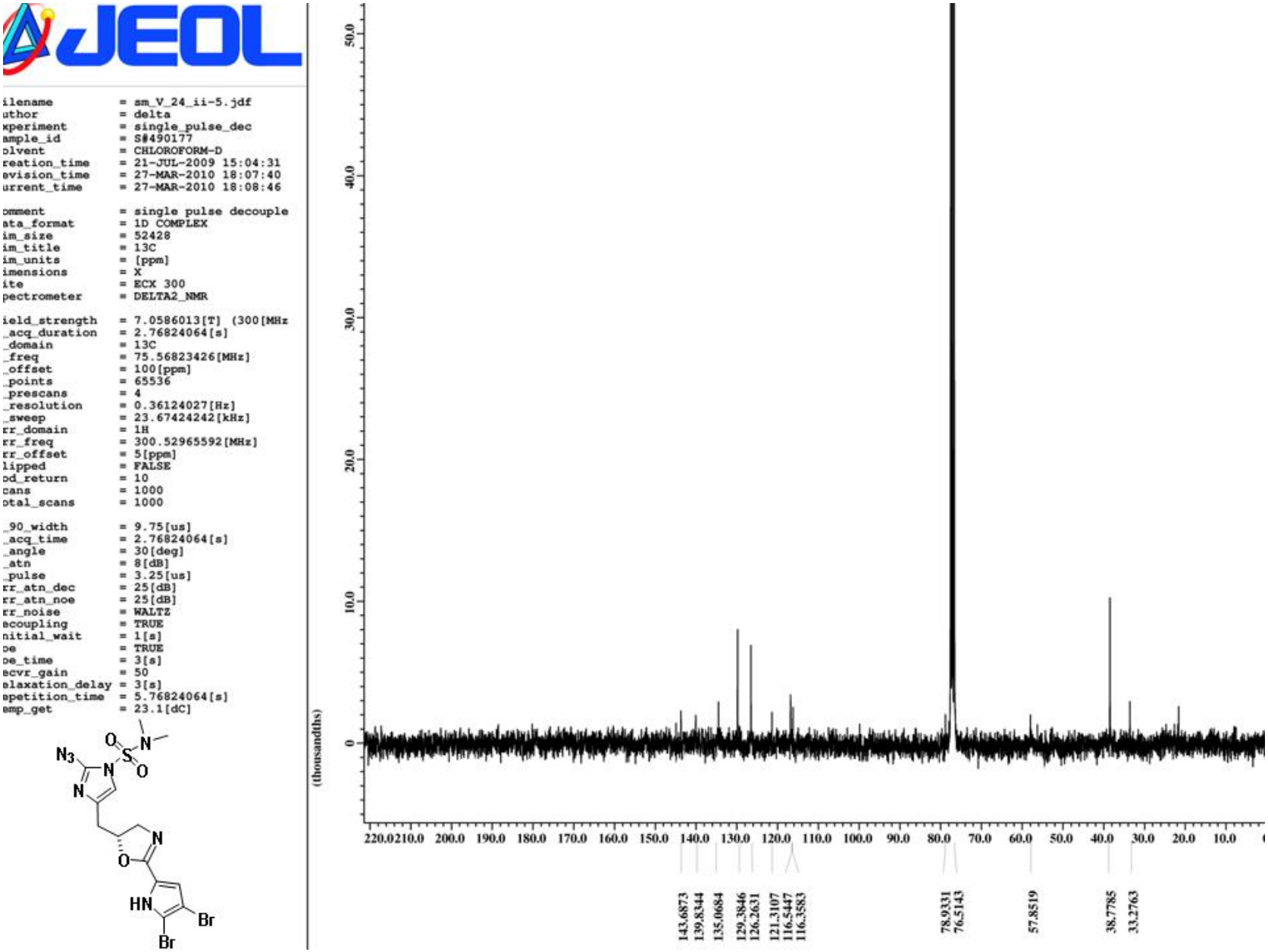
```
ilename          = sm_V_156_pure_ii-2.jd
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#621828
olvent           = CHLOROFORM-D
reation_time     =  1-JUL-2009 19:29:53
evision_time     =  1-JUL-2009 22:02:41
urrent_time      = 27-MAR-2010 17:43:06

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 52428
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.76824064[s]
_domain          = 13C
_freq            = 75.56823426[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.36124027[Hz]
_sweep           = 23.67424242[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
lipped           = FALSE
od_return        = 10
cans             = 1500
otal_scans       = 1500

_90_width        = 9.75[us]
_acq_time        = 2.76824064[s]
_angle           = 30[deg]
_atn             = 8[dB]
_pulse           = 3.25[us]
rr_atn_dec       = 25[dB]
rr_atn_noe       = 25[dB]
rr_noise         = WALTZ
ecoupling        = TRUE
nitial_wait      = 1[s]
oe               = TRUE
oe_time          = 3[s]
ecvr_gain        = 50
elaxation_delay  = 3[s]
epetition_time   = 5.76824064[s]
emp_get          = 23.4[dC]
```

APPENDIX 8
^{1}H AND ^{13}C NMR SPECTRUM OF
(*S*)-2-azido-4-((2-(4,5-dibromo-1H-pyrrol-2-yl)-4,5-dihydrooxazol-5-yl)methyl)-N,N-dimethyl-1H-imidazole-1-sulfonamide (60)

```
ilename          = sm_V_21_PURE-4.jdf
uthor            = delta
xperiment        = single_pulse.exp
ample_id         = S#31163
olvent           = CHLOROFORM-D
reation_time     =  9-DEC-2008 08:55:50
evision_time     = 27-MAR-2010 18:03:03
urrent_time      = 27-MAR-2010 18:04:01

omment           = Single Pulse Experime
ata_format       = 1D REAL
im_size          = 16384
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7473579[T] (500[MH
_acq_duration    = 2.1823488[s]
_domain          = 1H
_freq            = 500.15991521[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.45822189[Hz]
_sweep           = 7.50750751[kHz]
lipped           = FALSE
od_return        = 1
cans             = 8
otal_scans       = 8

_90_width        = 18.5[us]
_acq_time        = 2.1823488[s]
_angle           = 45[deg]
_pulse           = 9.25[us]
nitial_wait      = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 20
elaxation_delay  = 4[s]
mp_get           = 25.9[dC]
nblank_time      = 2[us]
```

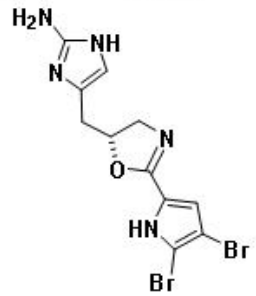


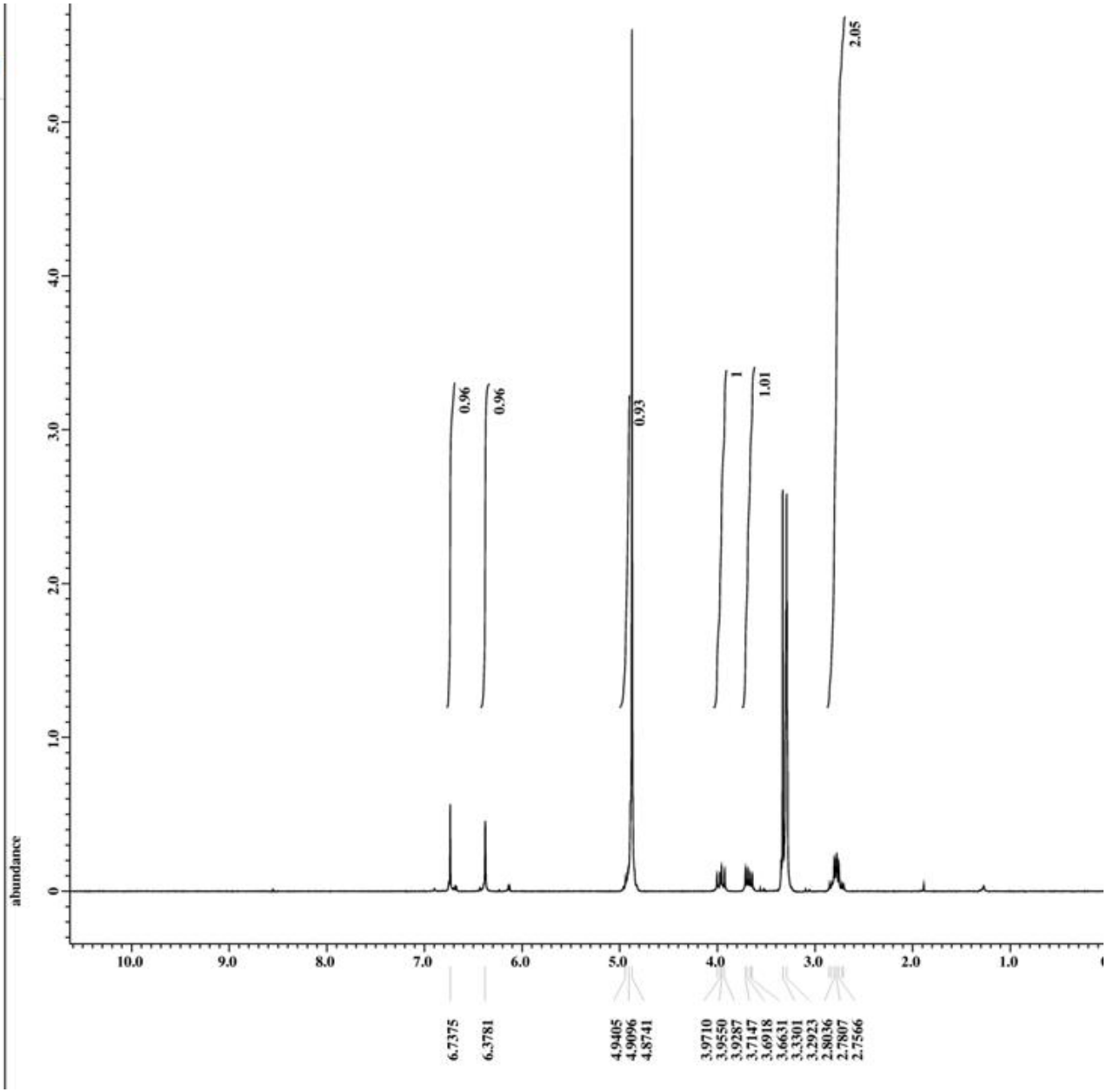



ilename = sm_V_24_ii-5.jdf
uthor = delta
xperiment = single_pulse_dec
ample_id = S#490177
olvent = CHLOROFORM-D
reation_time = 21-JUL-2009 15:04:31
evision_time = 27-MAR-2010 18:07:40
urrent_time = 27-MAR-2010 18:08:46
omment = single pulse decouple
ata_format = 1D COMPLEX
im_size = 52428
im_title = 13C
im_units = [ppm]
imensions = X
ite = ECX 300
pectrometer = DELTA2_NMR
ield_strength = 7.0586013[T] (300[MHz
_acq_duration = 2.76824064[s]
_domain = 13C
_freq = 75.56823426[MHz]
_offset = 100[ppm]
_points = 65536
_prescans = 4
_resolution = 0.36124027[Hz]
_sweep = 23.67424242[kHz]
rr_domain = 1H
rr_freq = 300.52965592[MHz]
rr_offset = 5[ppm]
lipped = FALSE
od_return = 10
cans = 1000
otal_scans = 1000
_90_width = 9.75[us]
_acq_time = 2.76824064[s]
_angle = 30[deg]
_atn = 8[dB]
_pulse = 3.25[us]
rr_atn_dec = 25[dB]
rr_atn_noe = 25[dB]
rr_noise = WALTZ
ecoupling = TRUE
nitial_wait = 1[s]
oe = TRUE
oe_time = 3[s]
ecvr_gain = 50
elaxation_delay = 3[s]
epetition_time = 5.76824064[s]
emp_get = 23.1[dC]
(thousandths)
50.0
40.0
30.0
20.0
10.0
0
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0
143.6873
139.8344
135.0684
129.3846
126.2631
121.3107
116.5447
116.3583
78.9331
76.5143
57.8519
38.7785
33.2763

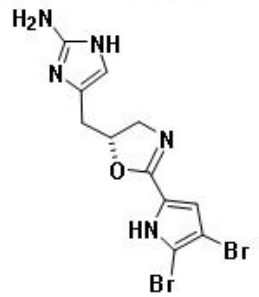
APPENDIX 9
^{1}H AND ^{13}C NMR SPECTRUM OF
4-(((*S*)-2-(4,5-dibromo-1H-pyrrol-2-yl)-4,5-dihydrooxazol-5-yl)methyl)-2,3-dihydro-1H-imidazol-2-amine (57)

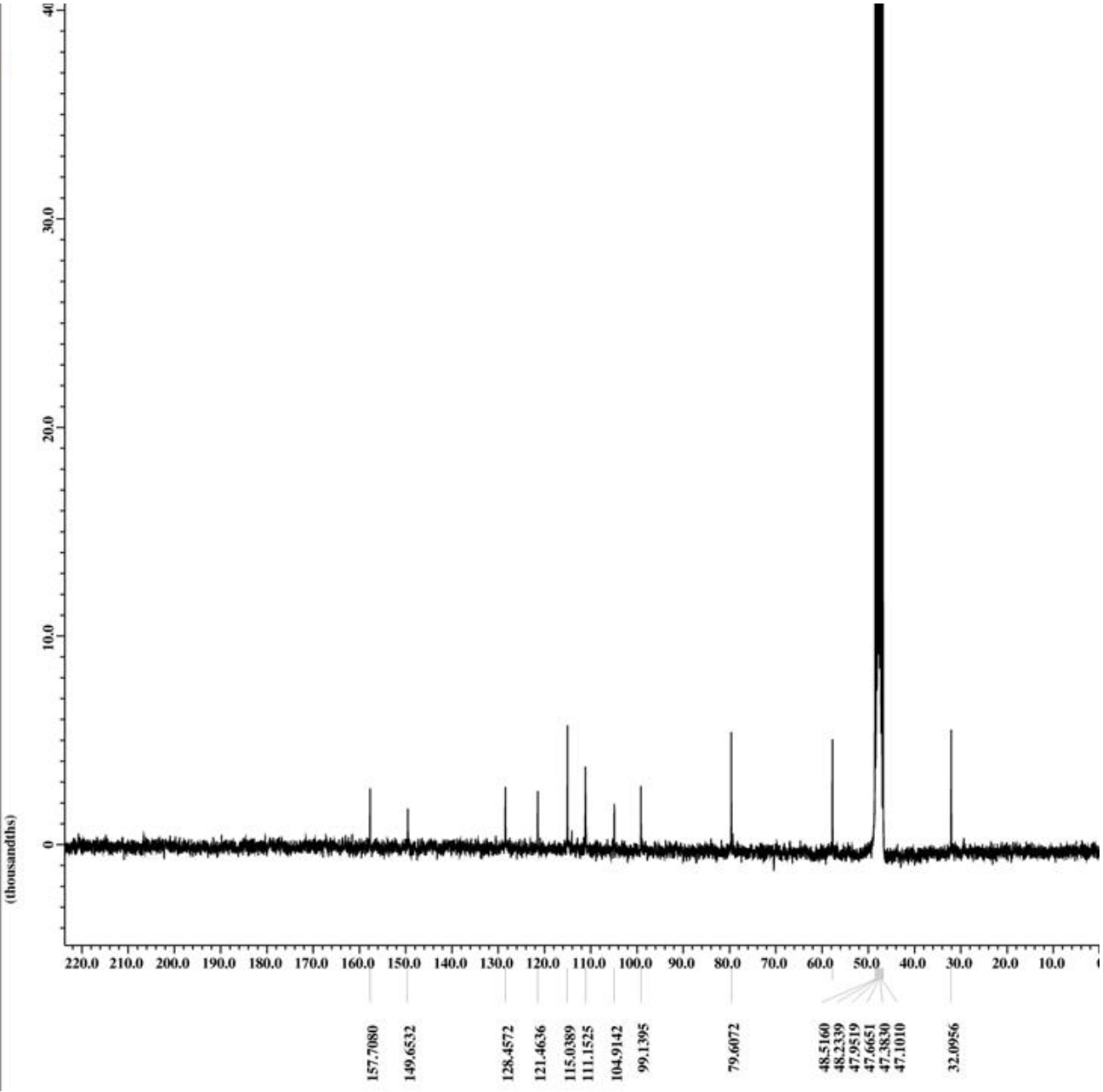
```
ilename          = sm_V_30_pure-5.jdf
uthor            = delta
xperiment        = single_pulse.ex2
mple_id          = S#754445
olvent           = METHANOL-D3
reation_time     = 12-DEC-2008 21:16:11
evision_time     = 12-DEC-2008 21:07:54
urrent_time      = 27-MAR-2010 18:16:17

omment           = single_pulse
ata_format       = 1D REAL
im_size          = 13107
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.90717696[s]
_domain          = 1H
_freq            = 300.52965592[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.34397631[Hz]
_sweep           = 5.63570784[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
ri_domain        = 1H
ri_freq          = 300.52965592[MHz]
ri_offset        = 5[ppm]
lipped           = FALSE
od_return        = 1
cans             = 24
otal_scans       = 24

_90_width        = 13.01[us]
_acq_time        = 2.90717696[s]
_angle           = 45[deg]
_atn             = 4[dB]
_pulse           = 6.505[us]
rr_mode          = Off
ri_mode          = Off
ante_presat      = FALSE
nitial_wait      = 1[s]
ecvr_gain        = 44
elaxation_delay  = 5[s]
epetition_time   = 7.90717696[s]
emp_get          = 23.2[dC]
```



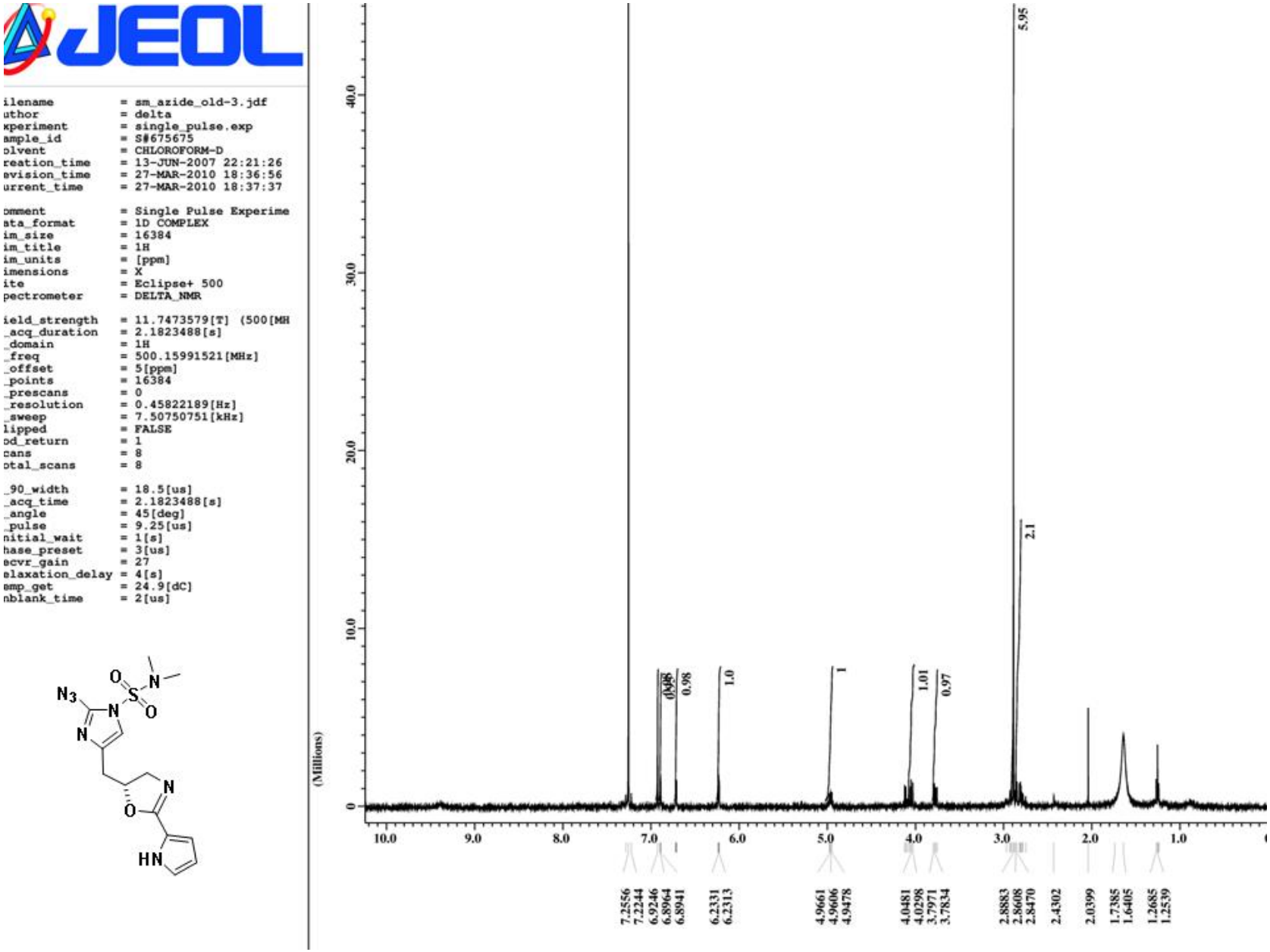


```
ilename          = sm_V_30_PURE-2.jdf
uthor            = delta
xperiment        = single_pulse_dec
mple_id          = S#757410
olvent           = METHANOL-D3
reation_time     = 13-DEC-2008 06:54:30
evision_time     = 13-DEC-2008 08:18:14
urrent_time      = 27-MAR-2010 18:19:24

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 52428
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.76824064[s]
_domain          = 13C
_freq            = 75.56823426[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.36124027[Hz]
_sweep           = 23.67424242[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
lipped           = FALSE
od_return        = 10
cans             = 6000
otal_scans       = 6000

_90_width        = 9.75[us]
_acq_time        = 2.76824064[s]
_angle           = 30[deg]
_atn             = 8[dB]
_pulse           = 3.25[us]
rr_atn_dec       = 25[dB]
rr_atn_noe       = 25[dB]
rr_noise         = WALTZ
ecoupling        = TRUE
nitial_wait      = 1[s]
oe               = TRUE
oe_time          = 3[s]
ecvr_gain        = 50
elaxation_delay  = 3[s]
epetition_time   = 5.76824064[s]
emp_get          = 23.3[dC]
```

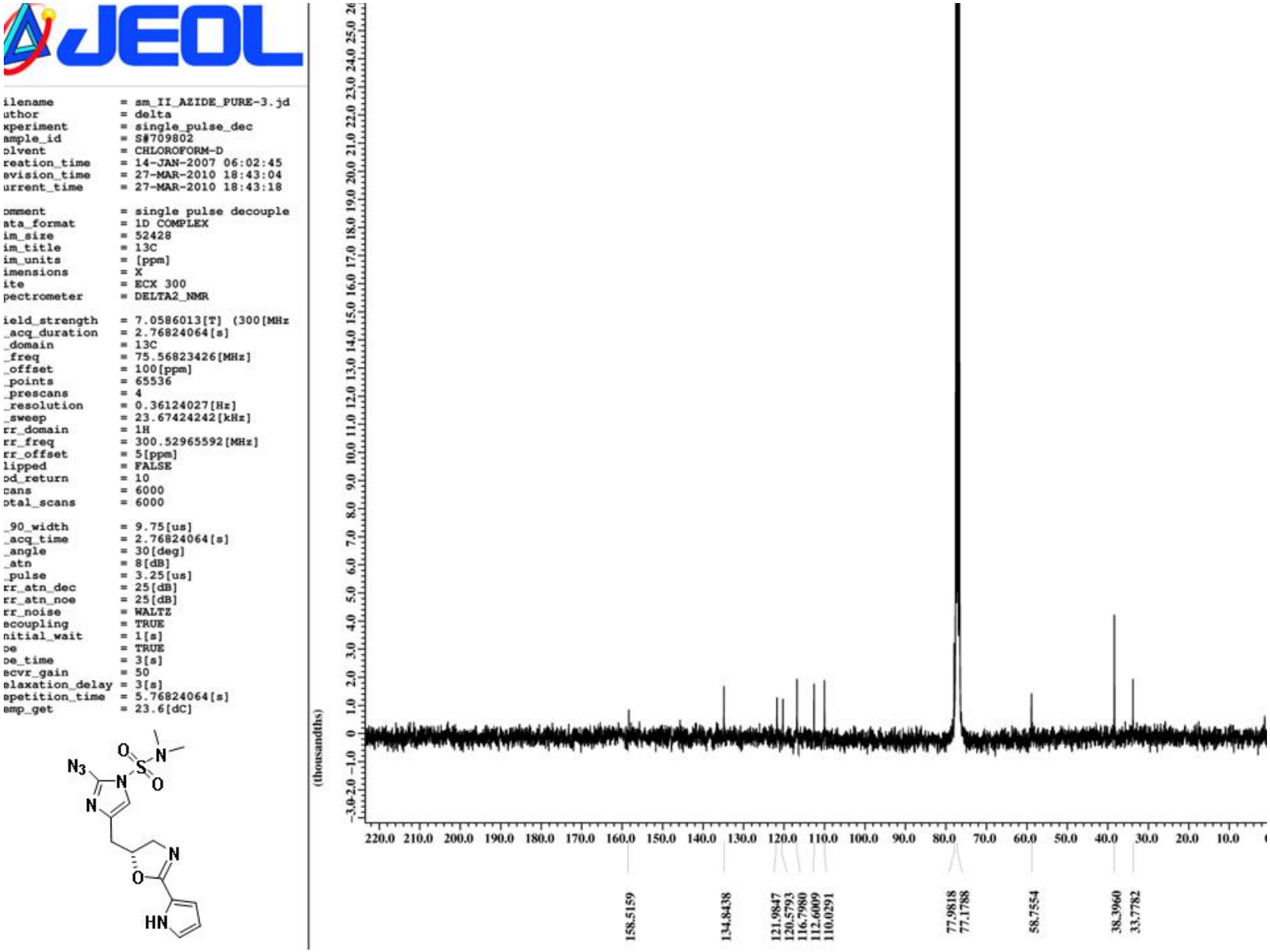




APPENDIX 10
^{1}H AND ^{13}C NMR SPECTRUM OF
(*S*)-4-((2-(1H-pyrrol-2-yl)-4,5-dihydrooxazol-5-yl)methyl)-2-azido-N,N-dimethyl-1H-imidazole-1-sulfonamide (62)



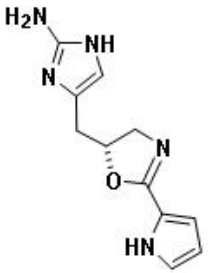
```
ilename          = sm_azide_old-3.jdf
uthor            = delta
xperiment        = single_pulse.exp
ample_id         = S#675675
olvent           = CHLOROFORM-D
reation_time     = 13-JUN-2007 22:21:26
evision_time     = 27-MAR-2010 18:36:56
urrent_time      = 27-MAR-2010 18:37:37

omment           = Single Pulse Experime
ata_format       = 1D COMPLEX
im_size          = 16384
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7473579[T] (500[MH
_acq_duration    = 2.1823488[s]
_domain          = 1H
_freq            = 500.15991521[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.45822189[Hz]
_sweep           = 7.50750751[kHz]
lipped           = FALSE
od_return        = 1
cans             = 8
otal_scans       = 8

_90_width        = 18.5[us]
_acq_time        = 2.1823488[s]
_angle           = 45[deg]
_pulse           = 9.25[us]
nitial_wait      = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 27
elaxation_delay  = 4[s]
emp_get          = 24.9[dC]
nblank_time      = 2[us]
```

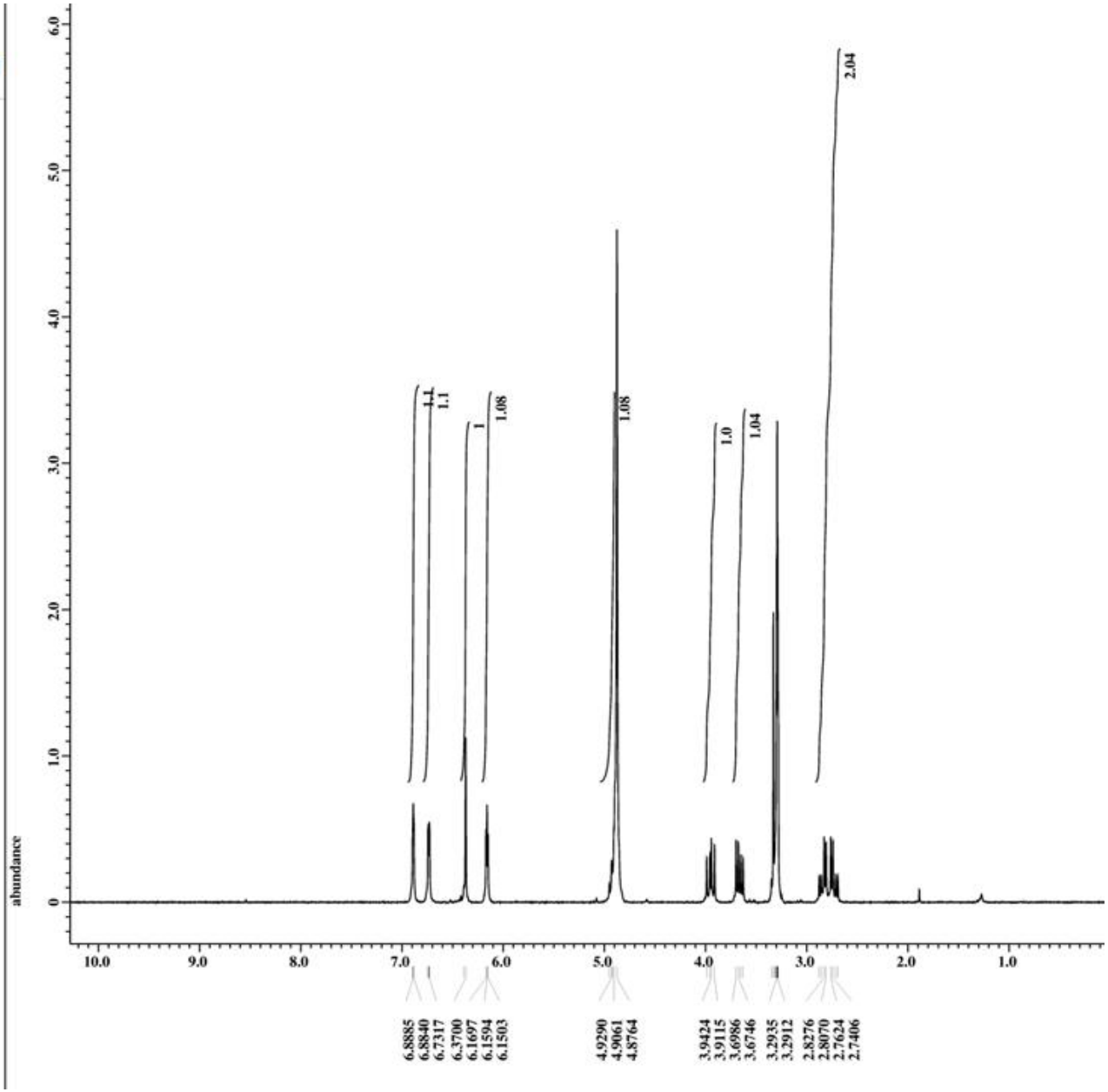


```
ilename          = sm_II_AZIDE_PURE-3.jd
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#709802
olvent           = CHLOROFORM-D
reation_time     = 14-JAN-2007 06:02:45
evision_time     = 27-MAR-2010 18:43:04
urrent_time      = 27-MAR-2010 18:43:18

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 52428
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.76824064[s]
_domain          = 13C
_freq            = 75.56823426[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.36124027[Hz]
_sweep           = 23.67424242[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
lipped           = FALSE
od_return        = 10
cans             = 6000
otal_scans       = 6000

_90_width        = 9.75[us]
_acq_time        = 2.76824064[s]
_angle           = 30[deg]
_atn             = 8[dB]
_pulse           = 3.25[us]
rr_atn_dec       = 25[dB]
rr_atn_noe       = 25[dB]
rr_noise         = WALTZ
ecoupling        = TRUE
nitial_wait      = 1[s]
oe               = TRUE
oe_time          = 3[s]
ecvr_gain        = 50
elaxation_delay  = 3[s]
epetition_time   = 5.76824064[s]
emp_get          = 23.6[dC]
```

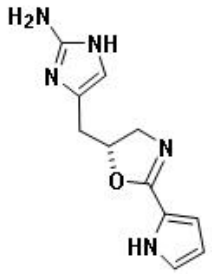
APPENDIX 11
^{1}H AND ^{13}C NMR SPECTRUM OF
4-(((*S*)-2-(1H-pyrrol-2-yl)-4,5-dihydrooxazol-5-yl)methyl)-2,3-dihydro-1H-imidazol-2-amine (64)

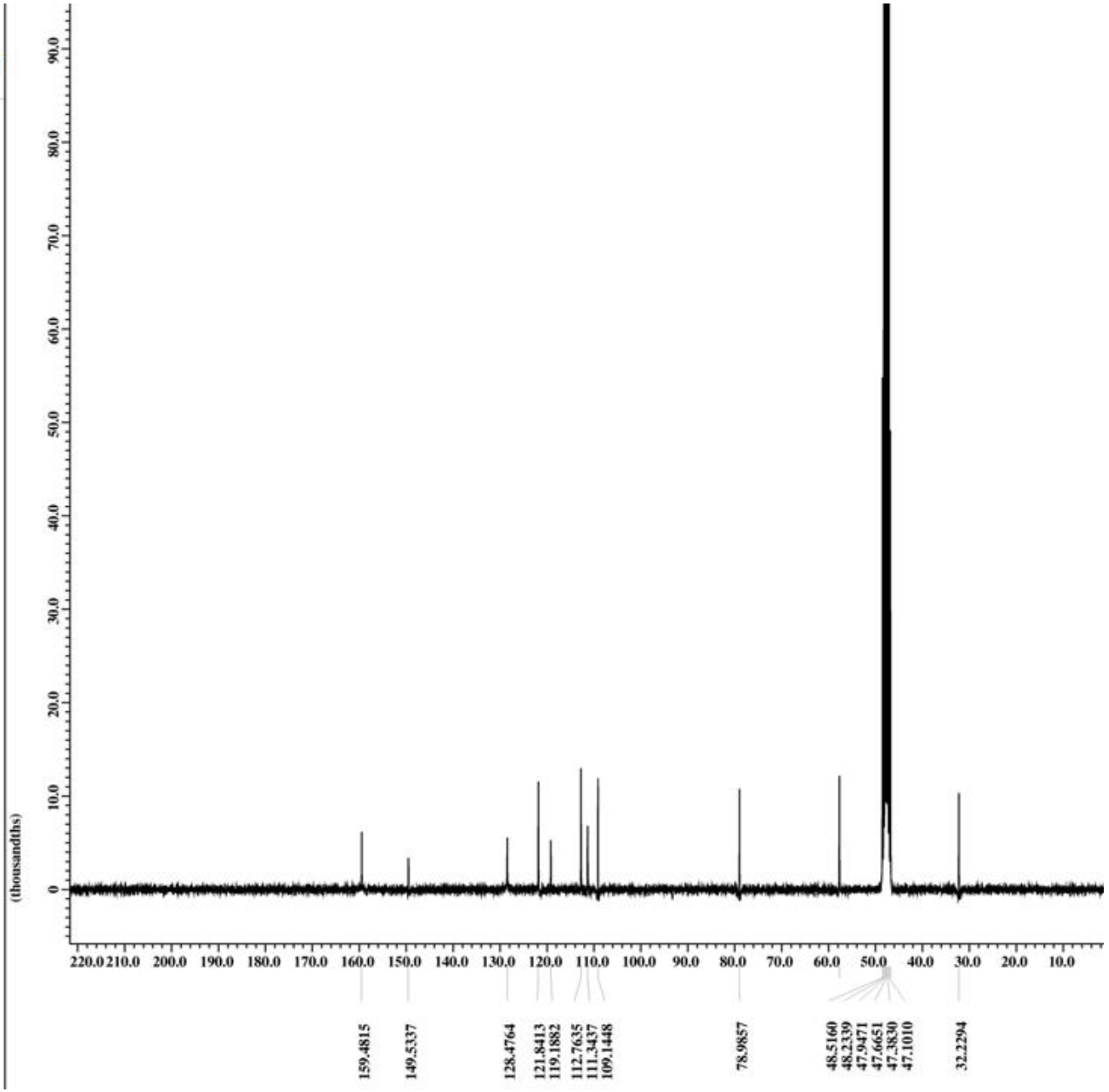
```
ilename          = sm_V_28_pure_2-3.jdf
uthor            = delta
xperiment        = single_pulse.ex2
ample_id         = _2
olvent           = METHANOL-D3
reation_time     = 11-DEC-2008 22:37:18
evision_time     = 11-DEC-2008 22:24:14
urrent_time      = 27-MAR-2010 18:47:18

omment           = single_pulse
ata_format       = 1D REAL
im_size          = 13107
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.90717696[s]
_domain          = 1H
_freq            = 300.52965592[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.34397631[Hz]
_sweep           = 5.63570784[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
ri_domain        = 1H
ri_freq          = 300.52965592[MHz]
ri_offset        = 5[ppm]
lipped           = FALSE
od_return        = 1
cans             = 11
otal_scans       = 11

_90_width        = 13.01[us]
_acq_time        = 2.90717696[s]
_angle           = 45[deg]
_atn             = 4[dB]
_pulse           = 6.505[us]
rr_mode          = Off
ri_mode          = Off
ante_presat      = FALSE
nitial_wait      = 1[s]
ecvr_gain        = 46
elaxation_delay  = 5[s]
epetition_time   = 7.90717696[s]
emp_get          = 23.1[dC]
```



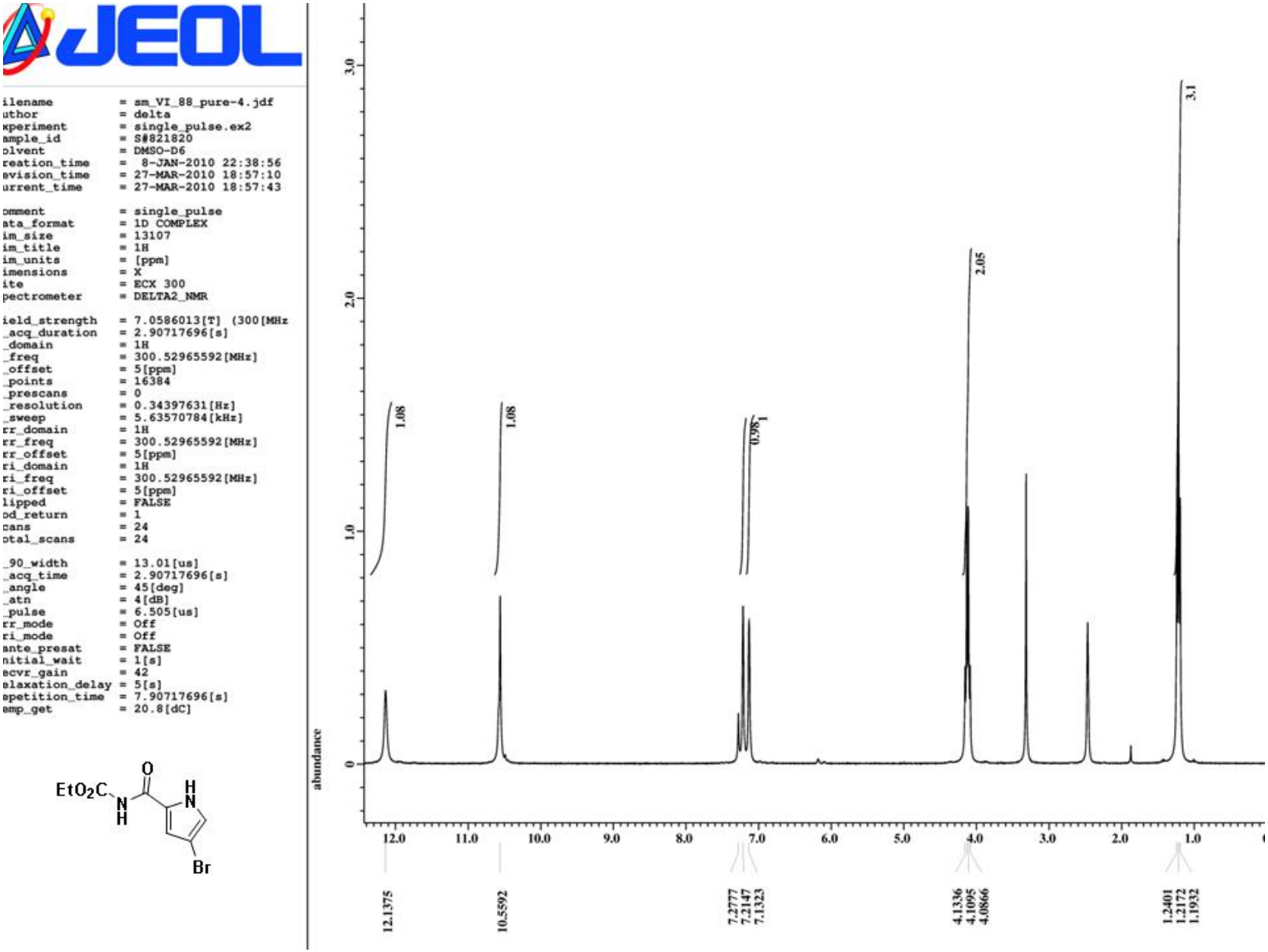


```
ilename          = sm_V_28_2-3.jdf
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#805616
olvent           = METHANOL-D3
reation_time     = 12-DEC-2008 05:02:27
evision_time     = 12-DEC-2008 14:21:39
urrent_time      = 27-MAR-2010 18:50:48

omment           = single pulse decouple
ata_format       = 1D REAL
im_size          = 52428
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.76824064[s]
_domain          = 13C
_freq            = 75.56823426[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.36124027[Hz]
_sweep           = 23.67424242[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
lipped           = FALSE
od_return        = 10
cans             = 4000
otal_scans       = 4000

_90_width        = 9.75[us]
_acq_time        = 2.76824064[s]
_angle           = 30[deg]
_atn             = 8[dB]
_pulse           = 3.25[us]
rr_atn_dec       = 25[dB]
rr_atn_noe       = 25[dB]
rr_noise         = WALTZ
ecoupling        = TRUE
nitial_wait      = 1[s]
oe               = TRUE
oe_time          = 3[s]
ecvr_gain        = 50
elaxation_delay  = 3[s]
epetition_time   = 5.76824064[s]
emp_get          = 23.5[dC]
```



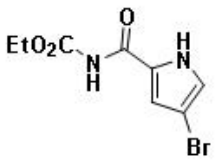


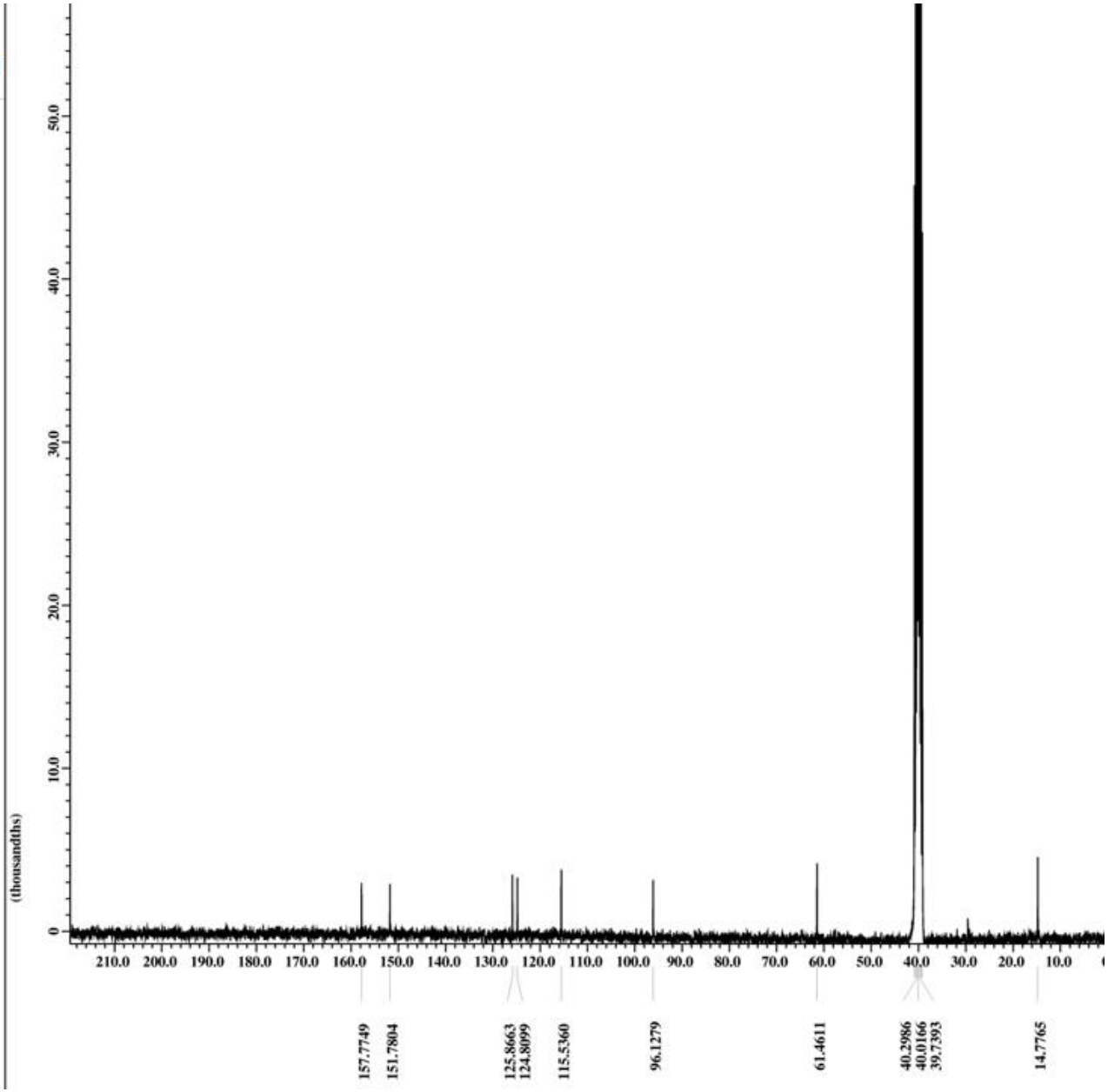
APPENDIX 12
^{1}H AND ^{13}C NMR SPECTRUM OF
Ethyl 4-bromo-1H-pyrrole-2-carbonylcarbamate (65)



```
ilename          = sm_VI_88_pure-4.jdf
uthor            = delta
xperiment        = single_pulse.ex2
ample_id         = S#821820
olvent           = DMSO-D6
reation_time     =  8-JAN-2010 22:38:56
evision_time     = 27-MAR-2010 18:57:10
urrent_time      = 27-MAR-2010 18:57:43

omment           = single_pulse
ata_format       = 1D COMPLEX
im_size          = 13107
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.90717696[s]
_domain          = 1H
_freq            = 300.52965592[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.34397631[Hz]
_sweep           = 5.63570784[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
ri_domain        = 1H
ri_freq          = 300.52965592[MHz]
ri_offset        = 5[ppm]
lipped           = FALSE
od_return        = 1
cans             = 24
otal_scans       = 24

_90_width        = 13.01[us]
_acq_time        = 2.90717696[s]
_angle           = 45[deg]
_atn             = 4[dB]
_pulse           = 6.505[us]
rr_mode          = Off
ri_mode          = Off
ante_presat      = FALSE
nitial_wait      = 1[s]
ecvr_gain        = 42
elaxation_delay  = 5[s]
epetition_time   = 7.90717696[s]
emp_get          = 20.8[dC]
```

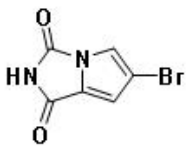
```
ilename          = sm_VI_precursor_monob
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#837678
olvent           = DMSO-D6
reation_time     =  4-FEB-2010 08:42:09
evision_time     =  4-FEB-2010 11:39:13
urrent_time      = 19-APR-2010 19:29:02

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 52428
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.76824064[s]
_domain          = 13C
_freq            = 75.56823426[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.36124027[Hz]
_sweep           = 23.67424242[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
lipped           = FALSE
od_return        = 10
cans             = 6000
otal_scans       = 6000

_90_width        = 9.75[us]
_acq_time        = 2.76824064[s]
_angle           = 30[deg]
_atn             = 8[dB]
_pulse           = 3.25[us]
rr_atn_dec       = 25[dB]
rr_atn_noe       = 25[dB]
rr_noise         = WALTZ
ecoupling        = TRUE
nitial_wait      = 1[s]
oe               = TRUE
oe_time          = 3[s]
ecvr_gain        = 50
elaxation_delay  = 3[s]
epetition_time   = 5.76824064[s]
emp_get          = 19.7[dC]
```

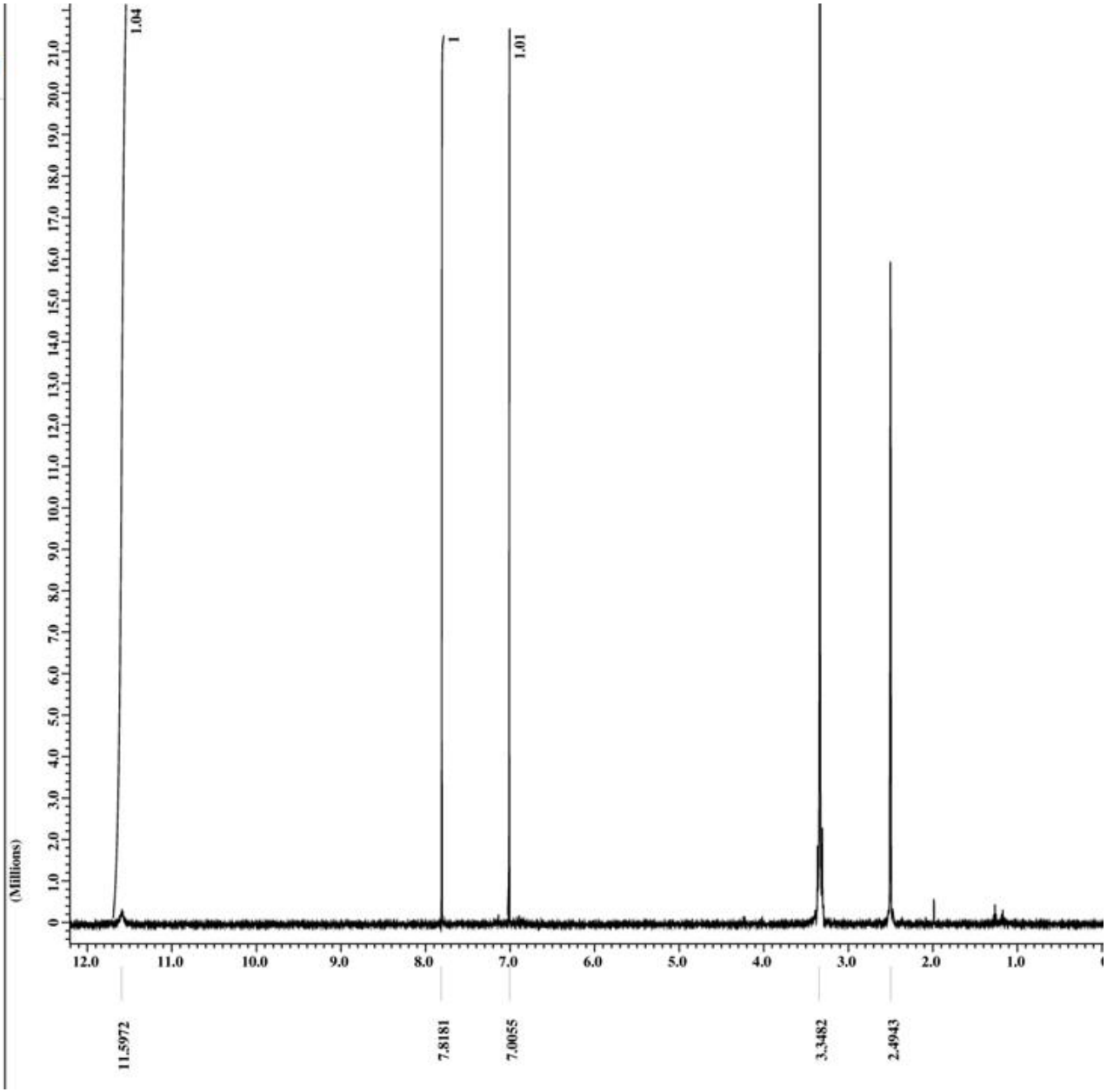




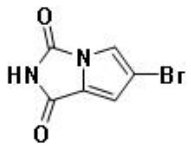
APPENDIX 13
^{1}H AND ^{13}C NMR SPECTRUM OF
6-bromo-1H-pyrrolo[1,2-c]imidazole-1,3(2H)-dione (67)

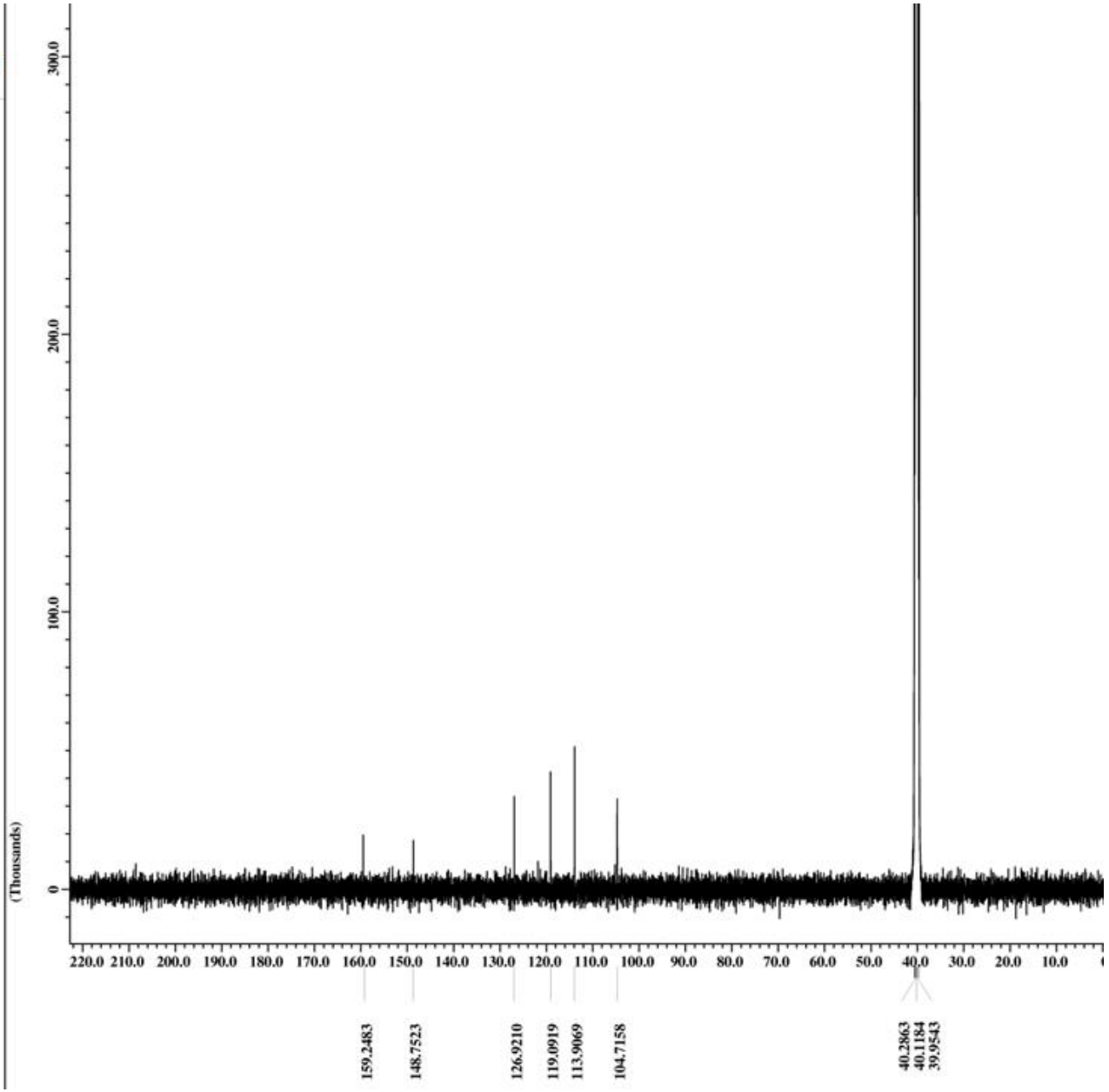
```
ilename          = sm_IV_98_pure-5.jdf
uthor            = delta
xperiment        = single_pulse.exp
ample_id         = S#767561
olvent           = DMSO-D6
reation_time     = 13-SEP-2008 04:47:28
evision_time     = 27-MAR-2010 19:17:27
urrent_time      = 27-MAR-2010 19:17:43

omment           = Single Pulse Experime
ata_format       = 1D COMPLEX
im_size          = 16384
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7473579[T] (500[MH
_acq_duration    = 2.1823488[s]
_domain          = 1H
_freq            = 500.15991521[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.45822189[Hz]
_sweep           = 7.50750751[kHz]
lipped           = FALSE
od_return        = 1
cans             = 3
otal_scans       = 3

_90_width        = 18.5[us]
_acq_time        = 2.1823488[s]
_angle           = 45[deg]
_pulse           = 9.25[us]
nitial_wait      = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 22
elaxation_delay  = 4[s]
mp_get           = 24.7[dC]
nblank_time      = 2[us]
```





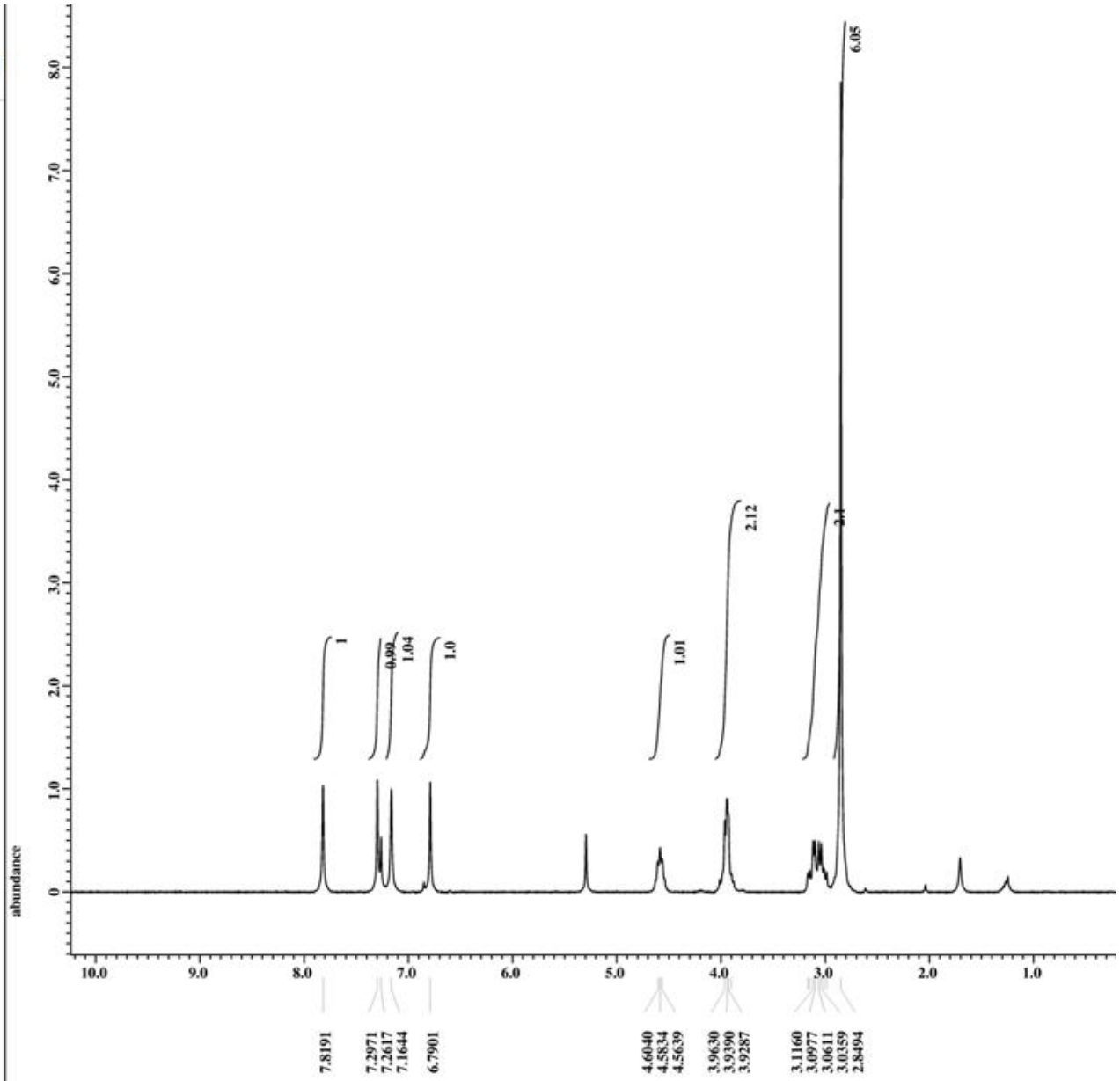
```
ilename          = sm_IV_98_pure-3.jdf
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#768816
olvent           = DMSO-D6
reation_time     = 13-SEP-2008 16:08:08
evision_time     = 13-SEP-2008 11:44:21
urrent_time      = 27-MAR-2010 19:20:43

omment           = single pulse decouple
ata_format       = 1D REAL
im_size          = 65536
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7473579[T] (500[MH
_acq_duration    = 2.0840448[s]
_domain          = 13C
_freq            = 125.76529768[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.47983613[Hz]
_sweep           = 31.44654088[kHz]
rr_domain        = 1H
rr_freq          = 500.15991521[MHz]
rr_offset        = 5[ppm]
lipped           = TRUE
od_return        = 10
cans             = 8000
otal_scans       = 8000

_90_width        = 14.2[us]
_acq_time        = 2.0840448[s]
_angle           = 30[deg]
_pulse           = 4.73333333[us]
nitial_wait      = 1[s]
oe_time          = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 30
elaxation_delay  = 2[s]
emp_get          = 28.8[dC]
nblank_time      = 2[us]
```



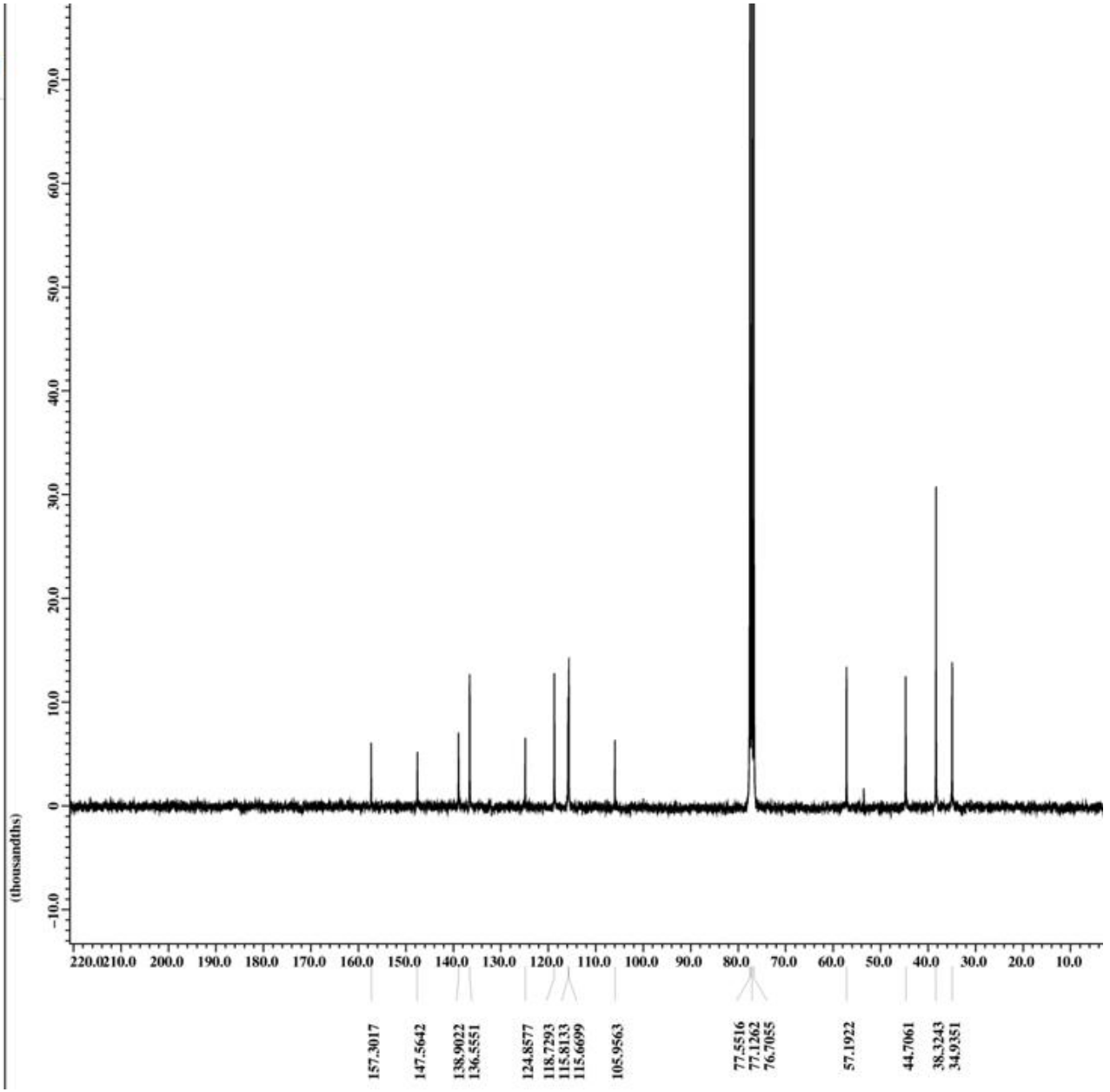


APPENDIX 14
^{1}H AND ^{13}C NMR SPECTRUM OF
(*R*)-4-(3-(6-bromo-1,3-dioxo-1H-pyrrolo[1,2-c]imidazol-2(3H)-yl)-2-chloropropyl)-N,N-dimethyl-1H-imidazole-1-sulfonamide (69)

```
ilename          = sm_V_154_pure_ii-4.jd
uthor            = delta
xperiment        = single_pulse.ex2
ample_id         = S#739199
olvent           = CHLOROFORM-D
reation_time     = 29-JUN-2009 20:23:34
evision_time     = 27-MAR-2010 19:24:06
urrent_time      = 27-MAR-2010 19:24:41

omment           = single_pulse
ata_format       = 1D REAL
im_size          = 13107
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.90717696[s]
_domain          = 1H
_freq            = 300.52965592[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.34397631[Hz]
_sweep           = 5.63570784[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
ri_domain        = 1H
ri_freq          = 300.52965592[MHz]
ri_offset        = 5[ppm]
lipped           = FALSE
od_return        = 1
cans             = 21
otal_scans       = 21

_90_width        = 13.01[us]
_acq_time        = 2.90717696[s]
_angle           = 45[deg]
_atn             = 4[dB]
_pulse           = 6.505[us]
rr_mode          = Off
ri_mode          = Off
ante_presat      = FALSE
nitial_wait      = 1[s]
ecvr_gain        = 50
elaxation_delay  = 5[s]
epetition_time   = 7.90717696[s]
emp_get          = 23.2[dC]
```

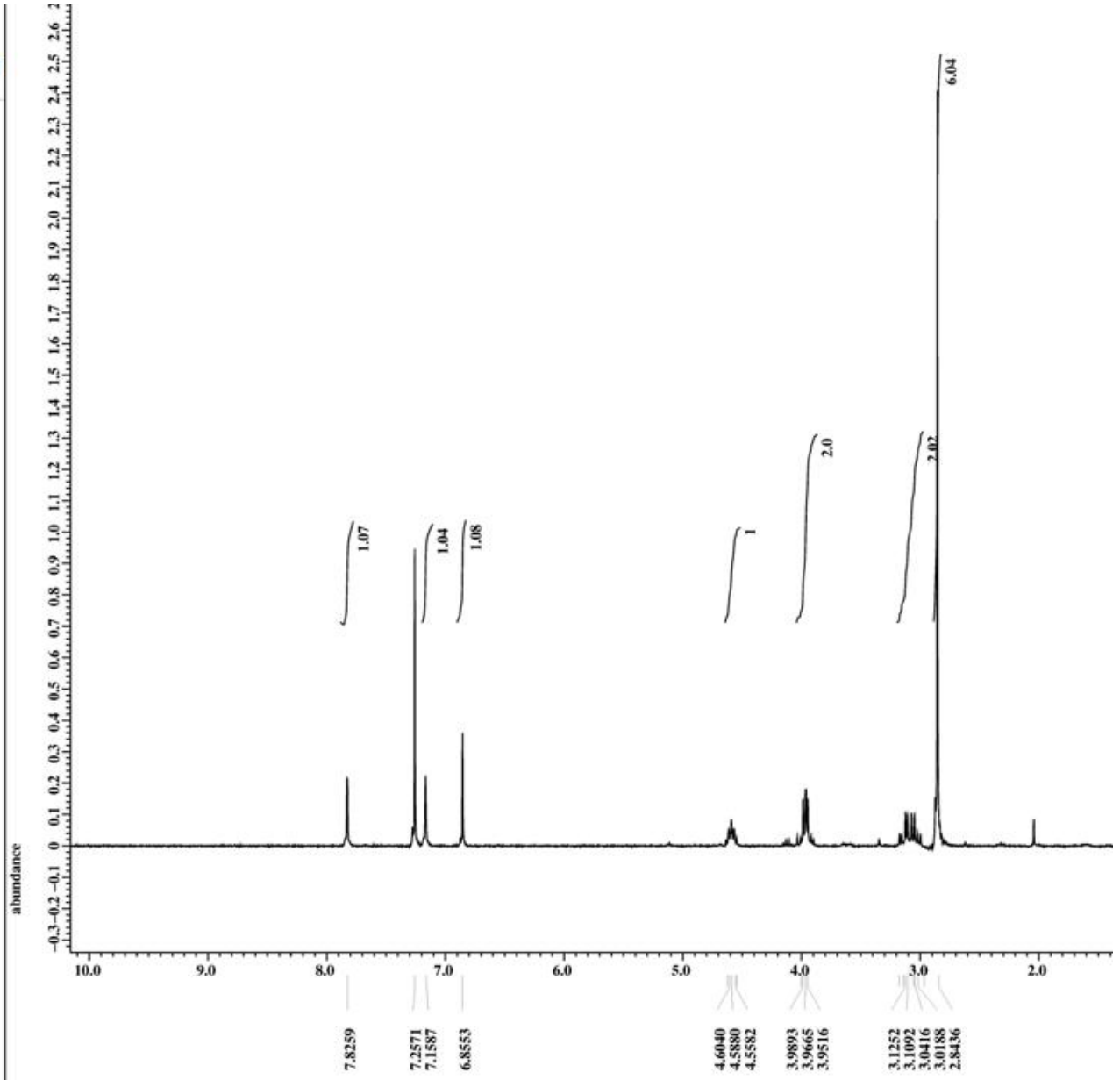


```
ilename          = sm_V_154_pure_ii-3.jd
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#741095
olvent           = CHLOROFORM-D
reation_time     = 30-JUN-2009 02:48:45
evision_time     = 30-JUN-2009 12:04:36
urrent_time      = 27-MAR-2010 19:27:23

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 52428
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.76824064[s]
_domain          = 13C
_freq            = 75.56823426[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.36124027[Hz]
_sweep           = 23.67424242[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
lipped           = FALSE
od_return        = 10
cans             = 4000
otal_scans       = 4000

_90_width        = 9.75[us]
_acq_time        = 2.76824064[s]
_angle           = 30[deg]
_atn             = 8[dB]
_pulse           = 3.25[us]
rr_atn_dec       = 25[dB]
rr_atn_noe       = 25[dB]
rr_noise         = WALTZ
ecoupling        = TRUE
nitial_wait      = 1[s]
oe               = TRUE
oe_time          = 3[s]
ecvr_gain        = 50
elaxation_delay  = 3[s]
epetition_time   = 5.76824064[s]
emp_get          = 23.3[dC]
```

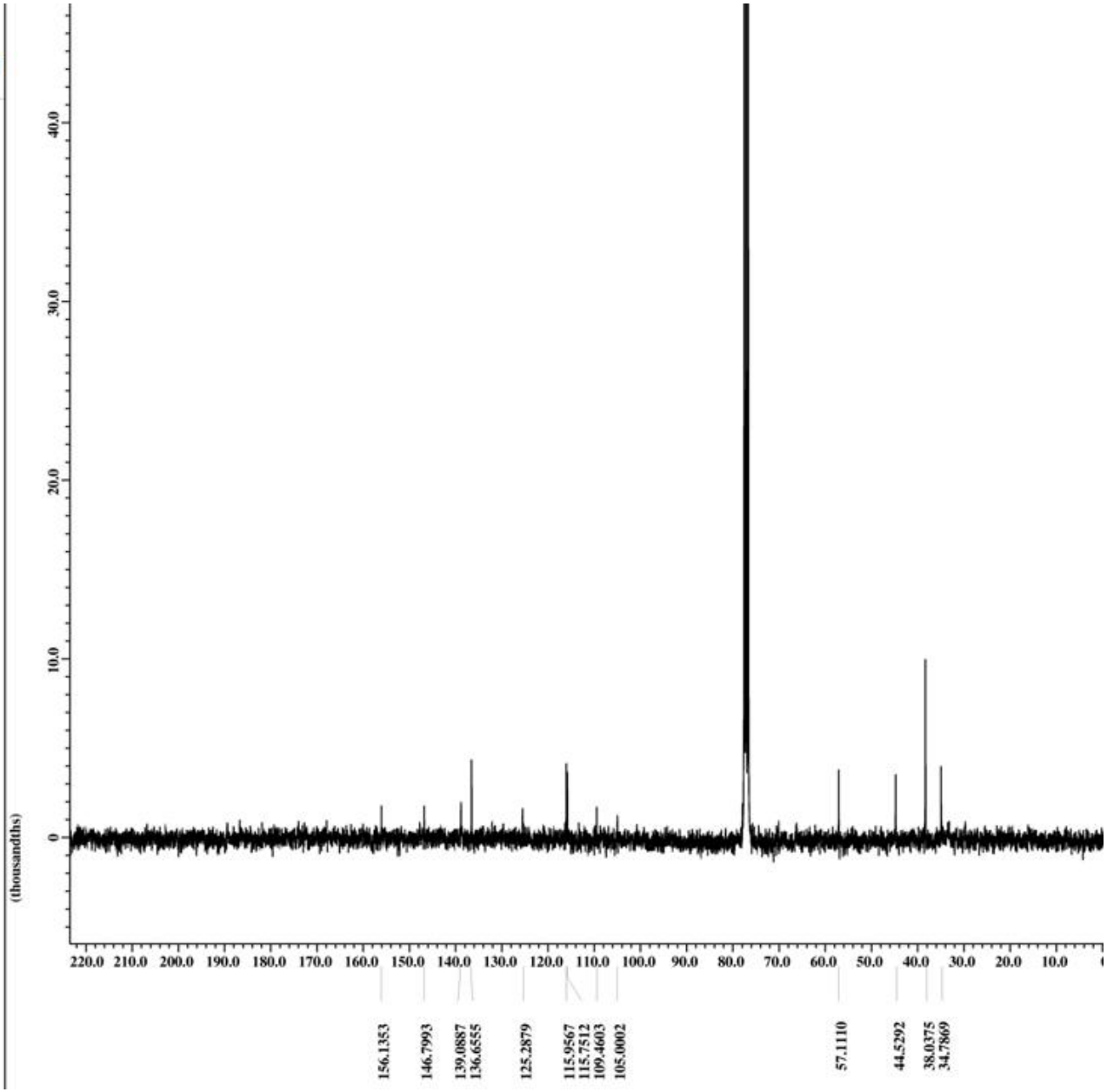


APPENDIX 15
^{1}H AND ^{13}C NMR SPECTRUM OF
(*R*)-4-(2-chloro-3-(5,6-dibromo-1,3-dioxo-1H-pyrrolo[1,2-c]imidazol-2(3H)-yl)propyl)-N,N-dimethyl-1H-imidazole-1-sulfonamide (70)

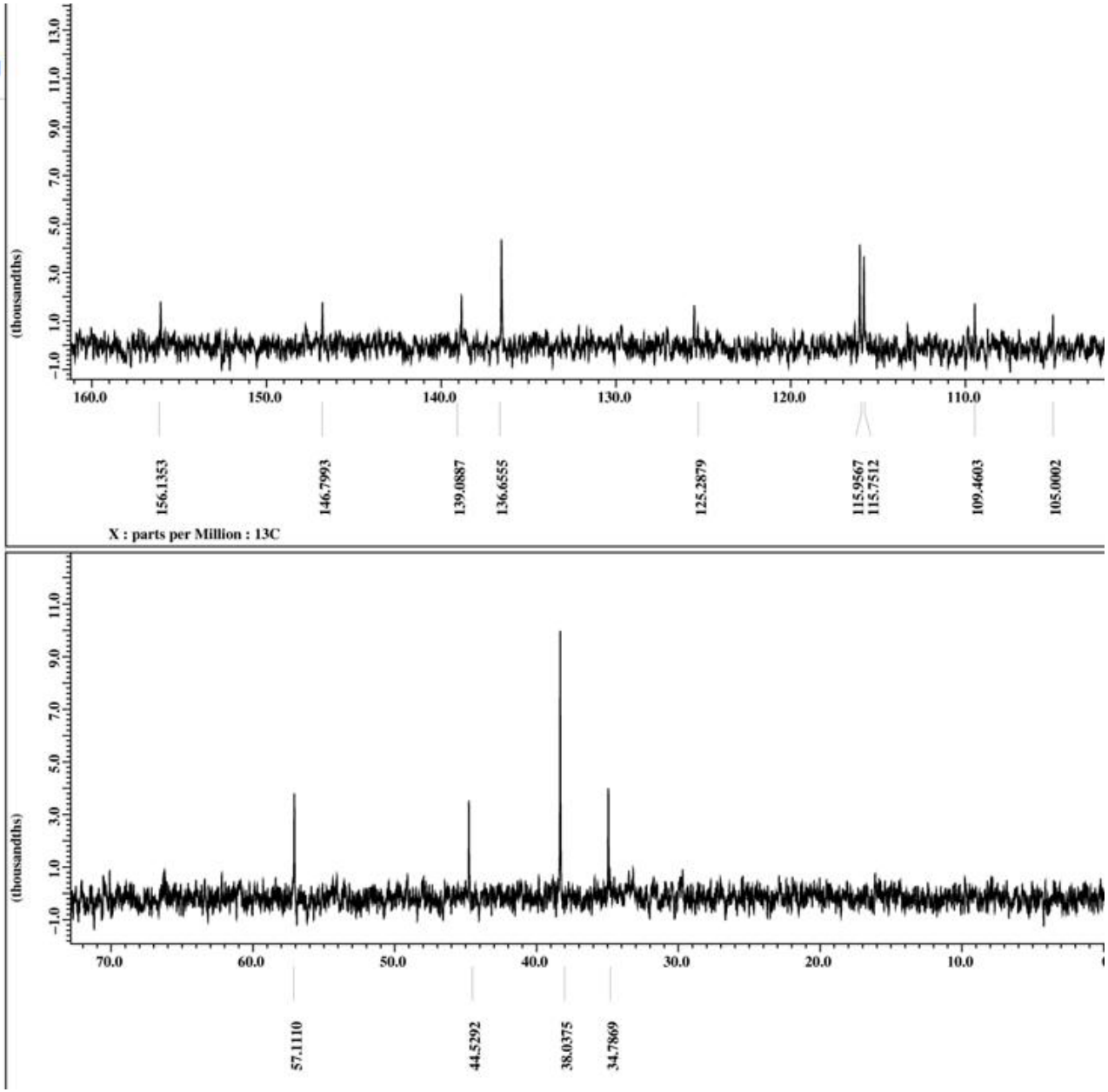
```
ilename          = sm_V_155_pure_ii-4.jd
uthor            = delta
xperiment        = single_pulse.ex2
ample_id         = S#596405
olvent           = CHLOROFORM-D
reation_time     = 17-JUL-2009 16:28:05
evision_time     = 27-MAR-2010 19:32:48
urrent_time      = 27-MAR-2010 19:33:02

omment           = single_pulse
ata_format       = 1D REAL
im_size          = 13107
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.90717696[s]
_domain          = 1H
_freq            = 300.52965592[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.34397631[Hz]
_sweep           = 5.63570784[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
ri_domain        = 1H
ri_freq          = 300.52965592[MHz]
ri_offset        = 5[ppm]
lipped           = FALSE
od_return        = 1
cans             = 21
otal_scans       = 21

_90_width        = 13.01[us]
_acq_time        = 2.90717696[s]
_angle           = 45[deg]
_atn             = 4[dB]
_pulse           = 6.505[us]
rr_mode          = Off
ri_mode          = Off
ante_presat      = FALSE
nitial_wait      = 1[s]
ecvr_gain        = 46
elaxation_delay  = 5[s]
epetition_time   = 7.90717696[s]
emp_get          = 23[dC]
```



```
ilename          = sm_V_32_pure-3.jdf
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#725973
olvent           = CHLOROFORM-D
reation_time     = 24-DEC-2008 00:00:03
evision_time     = 27-MAR-2010 19:36:10
urrent_time      = 27-MAR-2010 19:36:26

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 52428
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.76824064[s]
_domain          = 13C
_freq            = 75.56823426[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.36124027[Hz]
_sweep           = 23.67424242[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
lipped           = FALSE
od_return        = 10
cans             = 2221
otal_scans       = 2221

_90_width        = 9.75[us]
_acq_time        = 2.76824064[s]
_angle           = 30[deg]
_atn             = 8[dB]
_pulse           = 3.25[us]
rr_atn_dec       = 25[dB]
rr_atn_noe       = 25[dB]
rr_noise         = WALTZ
ecoupling        = TRUE
nitial_wait      = 1[s]
oe               = TRUE
oe_time          = 3[s]
ecvr_gain        = 50
elaxation_delay  = 3[s]
epetition_time   = 5.76824064[s]
emp_get          = 23.4[dC]
```

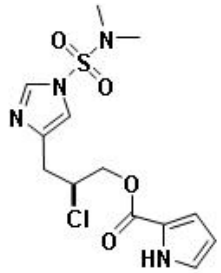


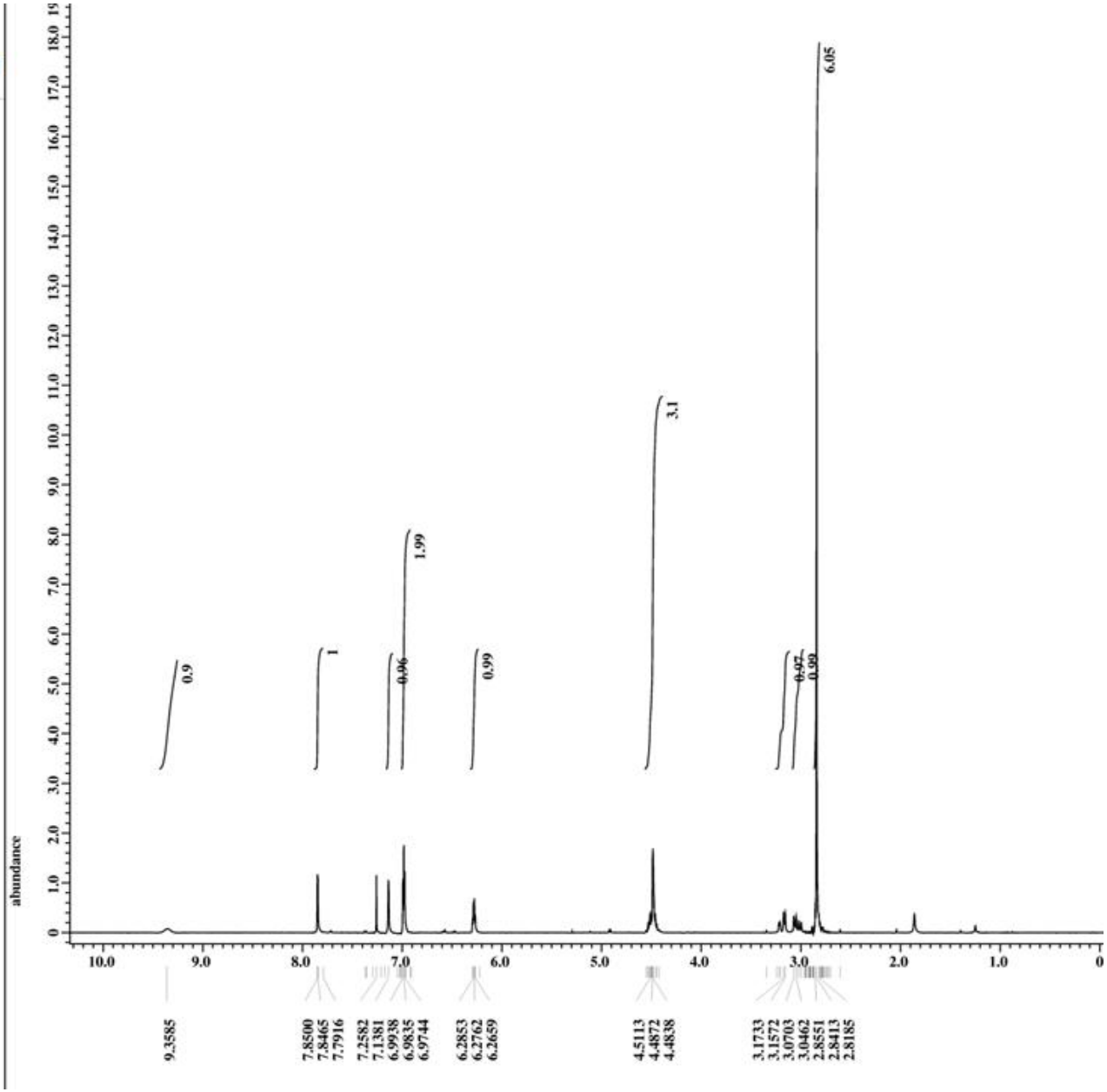
```
ilename          = sm_V_32_pure-3.jdf
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#725973
olvent           = CHLOROFORM-D
reation_time     = 24-DEC-2008 00:00:03
evision_time     = 27-MAR-2010 19:36:10
urrent_time      = 27-MAR-2010 19:39:27

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 52428
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.76824064[s]
_domain          = 13C
_freq            = 75.56823426[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.36124027[Hz]
_sweep           = 23.67424242[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
lipped           = FALSE
od_return        = 10
cans             = 2221
otal_scans       = 2221

_90_width        = 9.75[us]
_acq_time        = 2.76824064[s]
_angle           = 30[deg]
_atn             = 8[dB]
_pulse           = 3.25[us]
rr_atn_dec       = 25[dB]
rr_atn_noe       = 25[dB]
rr_noise         = WALTZ
ecoupling        = TRUE
nitial_wait      = 1[s]
oe               = TRUE
oe_time          = 3[s]
ecvr_gain        = 50
elaxation_delay  = 3[s]
epetition_time   = 5.76824064[s]
emp_get          = 23.4[dC]
```



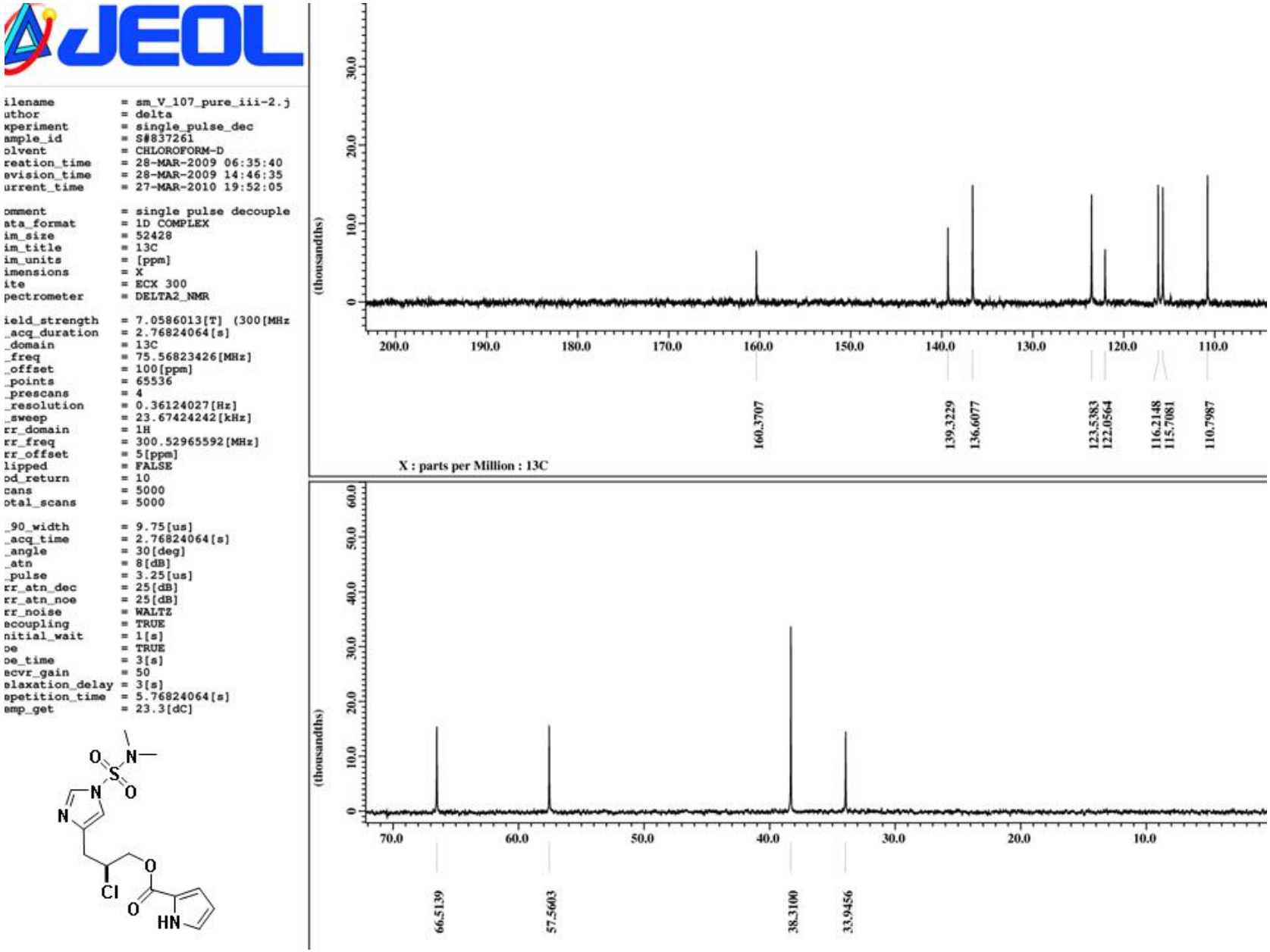
APPENDIX 16
^{1}H AND ^{13}C NMR SPECTRUM OF
(*R*)-2-chloro-3-(1-(N,N-dimethylsulfamoyl)-1H-imidazol-4-yl)propyl 1H-pyrrole-2-carboxylate (78)

```
ilename          = sm_V_107_pure_iii-5.j
uthor            = delta
xperiment        = single_pulse.ex2
ample_id         = S#835287
olvent           = CHLOROFORM-D
reation_time     = 27-MAR-2009 22:34:04
evision_time     = 27-MAR-2010 19:45:24
urrent_time      = 27-MAR-2010 19:47:25

omment           = single_pulse
ata_format       = 1D REAL
im_size          = 13107
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.90717696[s]
_domain          = 1H
_freq            = 300.52965592[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.34397631[Hz]
_sweep           = 5.63570784[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
ri_domain        = 1H
ri_freq          = 300.52965592[MHz]
ri_offset        = 5[ppm]
lipped           = FALSE
od_return        = 1
cans             = 18
otal_scans       = 18

_90_width        = 13.01[us]
_acq_time        = 2.90717696[s]
_angle           = 45[deg]
_atn             = 4[dB]
_pulse           = 6.505[us]
rr_mode          = Off
ri_mode          = Off
ante_presat      = FALSE
nitial_wait      = 1[s]
ecvr_gain        = 46
elaxation_delay  = 5[s]
epetition_time   = 7.90717696[s]
emp_get          = 23.3[dC]
```



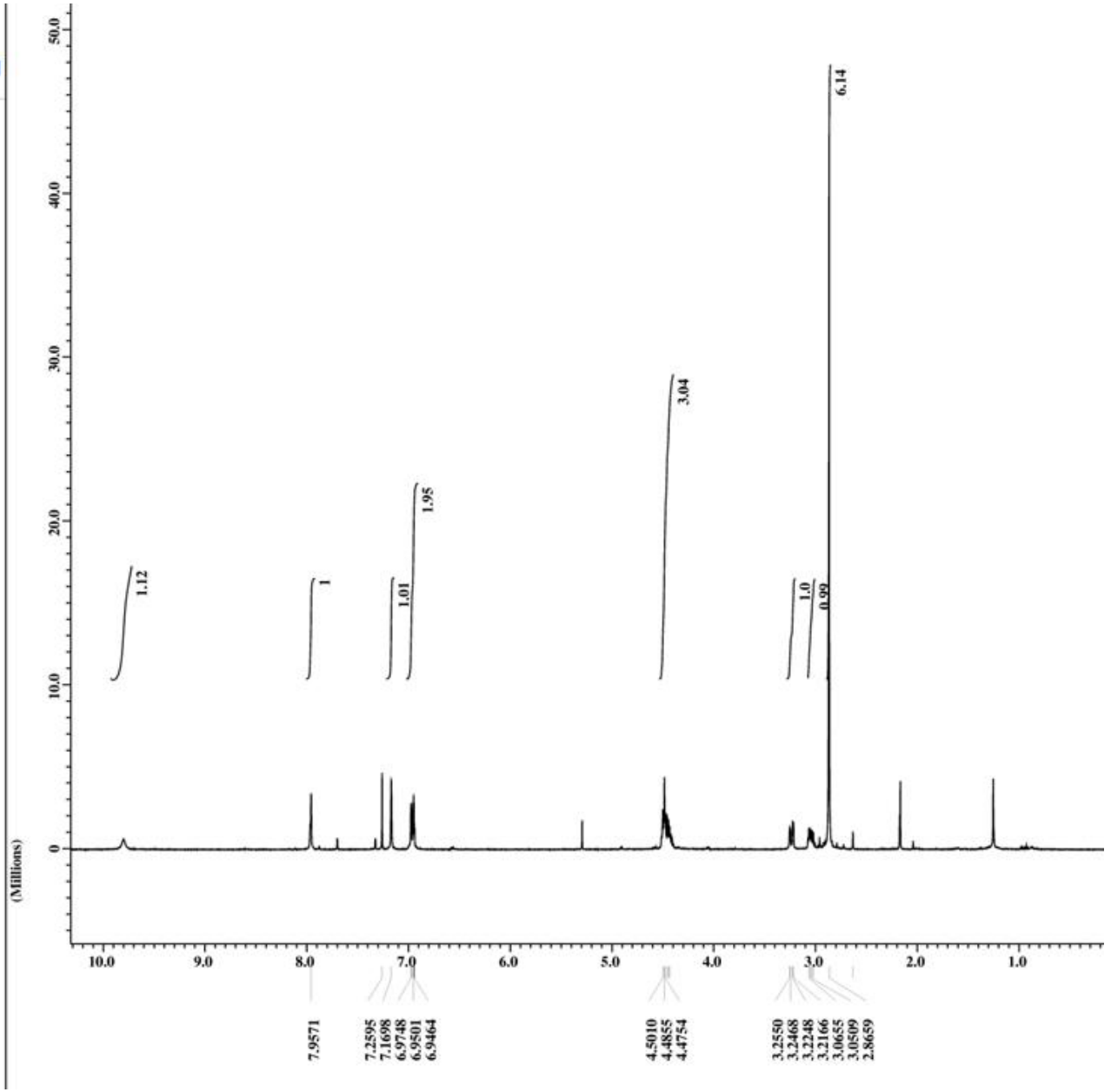


JEOL
ilename = sm_V_107_pure_iii-2.j
uthor = delta
xperiment = single_pulse_dec
ample_id = S#837261
olvent = CHLOROFORM-D
reation_time = 28-MAR-2009 06:35:40
evision_time = 28-MAR-2009 14:46:35
urrent_time = 27-MAR-2010 19:50:10
comment = single pulse decouple
ata_format = 1D COMPLEX
im_size = 52428
im_title = 13C
im_units = [ppm]
imensions = X
ite = ECX 300
pectrometer = DELTA2_NMR
ield_strength = 7.0586013[T] (300[MHz
_acq_duration = 2.76824064[s]
_domain = 13C
_freq = 75.56823426[MHz]
_offset = 100[ppm]
_points = 65536
_prescans = 4
_resolution = 0.36124027[Hz]
_sweep = 23.67424242[kHz]
rr_domain = 1H
rr_freq = 300.52965592[MHz]
rr_offset = 5[ppm]
lipped = FALSE
od_return = 10
cans = 5000
otal_scans = 5000
_90_width = 9.75[us]
_acq_time = 2.76824064[s]
_angle = 30[deg]
_atn = 8[dB]
_pulse = 3.25[us]
rr_atn_dec = 25[dB]
rr_atn_noe = 25[dB]
rr_noise = WALTZ
ecoupling = TRUE
nitial_wait = 1[s]
oe = TRUE
oe_time = 3[s]
ecvr_gain = 50
elaxation_delay = 3[s]
epetition_time = 5.76824064[s]
emp_get = 23.3[dC]
abundance
160.3707
139.3229
136.6077
123.5383
122.0564
116.2148
115.7081
110.7987
77.5421
77.3222
77.1214
76.6959
66.5139
57.5603
38.3100
33.9456
O
N
S
O
O
N
N
Cl
O
O
HN

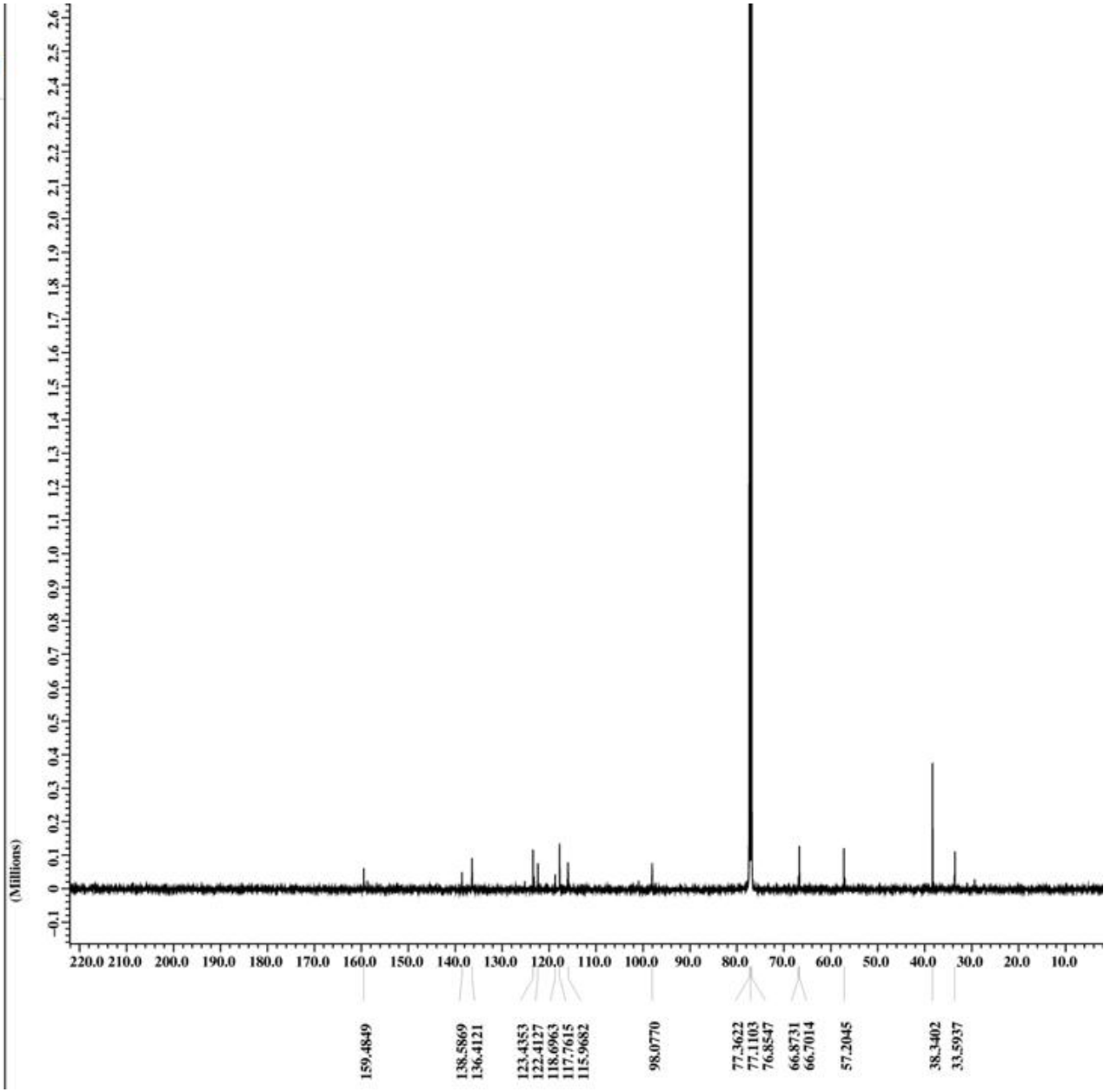

ilename = sm_V_107_pure_iii-2.j
uthor = delta
xperiment = single_pulse_dec
mple_id = S#837261
olvent = CHLOROFORM-D
reation_time = 28-MAR-2009 06:35:40
evision_time = 28-MAR-2009 14:46:35
urrent_time = 27-MAR-2010 19:52:05
omment = single pulse decouple
ata_format = 1D COMPLEX
im_size = 52428
im_title = 13C
im_units = [ppm]
imensions = X
ite = ECX 300
pectrometer = DELTA2_NMR
ield_strength = 7.0586013[T] (300[MHz
_acq_duration = 2.76824064[s]
_domain = 13C
_freq = 75.56823426[MHz]
_offset = 100[ppm]
_points = 65536
_prescans = 4
_resolution = 0.36124027[Hz]
_sweep = 23.67424242[kHz]
rr_domain = 1H
rr_freq = 300.52965592[MHz]
rr_offset = 5[ppm]
lipped = FALSE
od_return = 10
cans = 5000
otal_scans = 5000
_90_width = 9.75[us]
_acq_time = 2.76824064[s]
_angle = 30[deg]
_atn = 8[dB]
_pulse = 3.25[us]
rr_atn_dec = 25[dB]
rr_atn_noe = 25[dB]
rr_noise = WALTZ
ecoupling = TRUE
nitial_wait = 1[s]
oe = TRUE
oe_time = 3[s]
ecvr_gain = 50
elaxation_delay = 3[s]
epetition_time = 5.76824064[s]
emp_get = 23.3[dC]
(thousandths)
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
160.3707
139.3229
136.6077
123.5383
122.0564
116.2148
115.7081
110.7987
X : parts per Million : 13C
(thousandths)
70.0
60.0
50.0
40.0
30.0
20.0
10.0
66.5139
57.5603
38.3100
33.9456

APPENDIX 17
^{1}H AND ^{13}C NMR SPECTRUM OF
(*R*)-2-chloro-3-(1-(N,N-dimethylsulfamoyl)-1H-imidazol-4-yl)propyl 4-bromo-1H-pyrrole-2-carboxylate (85)

```
ilename          = sm_VI_49_pure-3.jdf
uthor            = delta
xperiment        = single_pulse.exp
ample_id         = S#855015
olvent           = CHLOROFORM-D
reation_time     = 11-DEC-2009 15:17:04
evision_time     = 27-MAR-2010 19:57:11
urrent_time      = 27-MAR-2010 19:57:28

omment           = Single Pulse Experime
ata_format       = 1D COMPLEX
im_size          = 16384
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7465928[T] (500[MH
_acq_duration    = 2.1839872[s]
_domain          = 1H
_freq            = 500.12734003[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.45787814[Hz]
_sweep           = 7.50187547[kHz]
lipped           = FALSE
od_return        = 1
cans             = 8
otal_scans       = 8

_90_width        = 18.5[us]
_acq_time        = 2.1839872[s]
_angle           = 45[deg]
_pulse           = 9.25[us]
nitial_wait      = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 20
elaxation_delay  = 4[s]
mp_get           = 25.8[dC]
nblank_time      = 2[us]
```

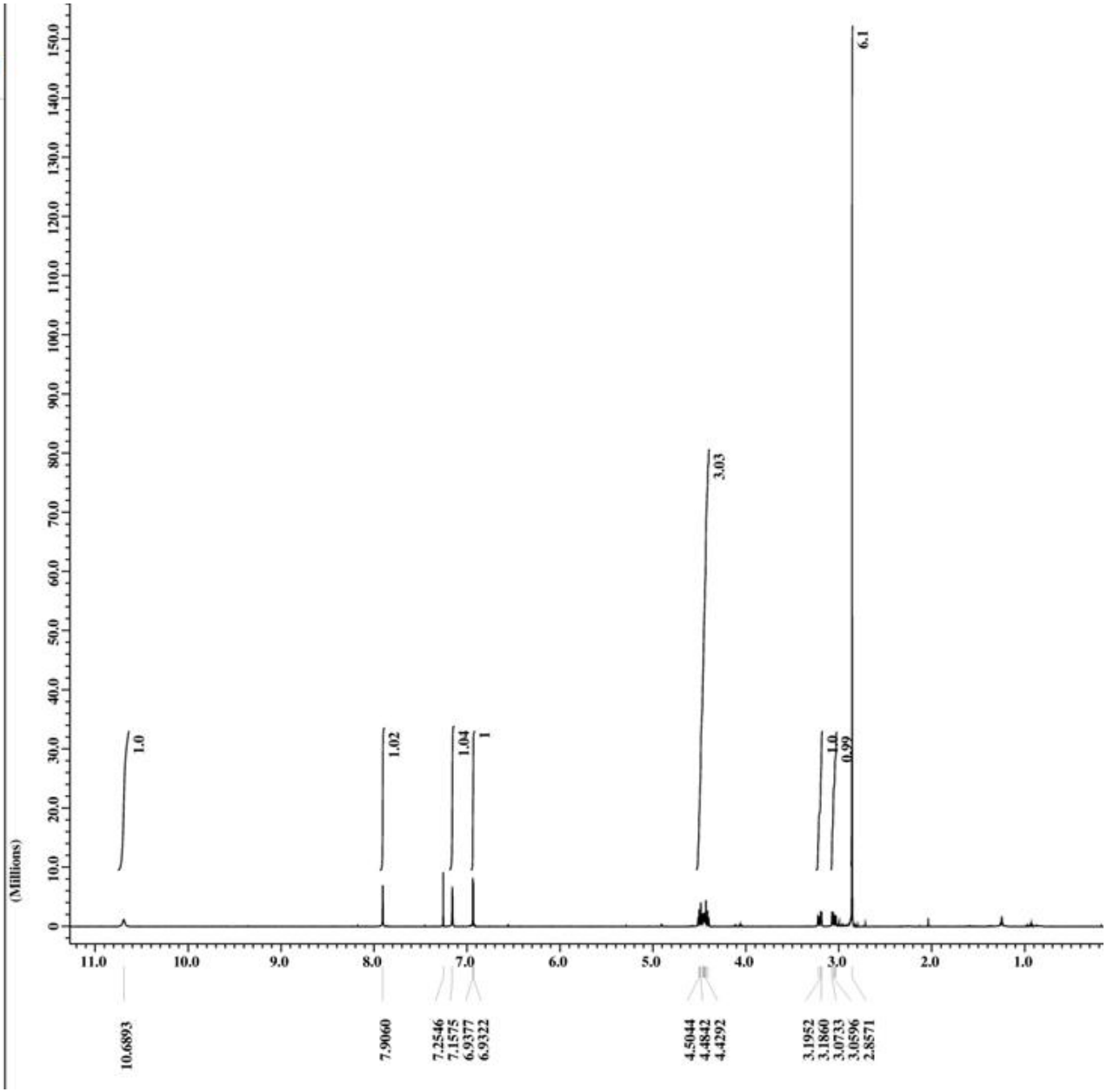


```
ilename          = sm_VI_49_pure-3.jdf
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#856074
olvent           = CHLOROFORM-D
reation_time     = 11-DEC-2009 22:22:59
evision_time     = 27-MAR-2010 20:00:11
urrent_time      = 27-MAR-2010 20:00:24

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 65536
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7465928[T] (500[MH
_acq_duration    = 2.0840448[s]
_domain          = 13C
_freq            = 125.75710665[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.47983613[Hz]
_sweep           = 31.44654088[kHz]
rr_domain        = 1H
rr_freq          = 500.12734003[MHz]
rr_offset        = 5[ppm]
lipped           = TRUE
od_return        = 10
cans             = 5000
otal_scans       = 5000

_90_width        = 14.2[us]
_acq_time        = 2.0840448[s]
_angle           = 30[deg]
_pulse           = 4.73333333[us]
nitial_wait      = 1[s]
pe_time          = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 30
elaxation_delay  = 2[s]
emp_get          = 28.3[dC]
nblank_time      = 2[us]
```



APPENDIX 18
^{1}H AND ^{13}C NMR SPECTRUM OF
(*R*)-2-chloro-3-(1-(N,N-dimethylsulfamoyl)-1H-imidazol-4-yl)propyl 4,5-dibromo-1H-pyrrole-2-carboxylate (86)

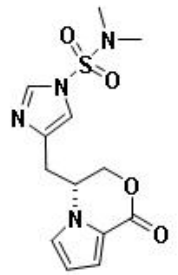
```
ilename          = sm_V_179_pure-4.jdf
uthor            = delta
xperiment        = single_pulse.exp
ample_id         = S#571802
olvent           = CHLOROFORM-D
reation_time     =  8-AUG-2009 05:59:14
evision_time     = 27-MAR-2010 20:12:14
urrent_time      = 27-MAR-2010 20:13:49

omment           = Single Pulse Experime
ata_format       = 1D REAL
im_size          = 16384
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7473579[T] (500[MH
_acq_duration    = 2.1823488[s]
_domain          = 1H
_freq            = 500.15991521[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.45822189[Hz]
_sweep           = 7.50750751[kHz]
lipped           = FALSE
od_return        = 1
cans             = 8
otal_scans       = 8

_90_width        = 18.5[us]
_acq_time        = 2.1823488[s]
_angle           = 45[deg]
_pulse           = 9.25[us]
nitial_wait      = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 21
elaxation_delay  = 4[s]
mp_get           = 27[dC]
nblank_time      = 2[us]
```

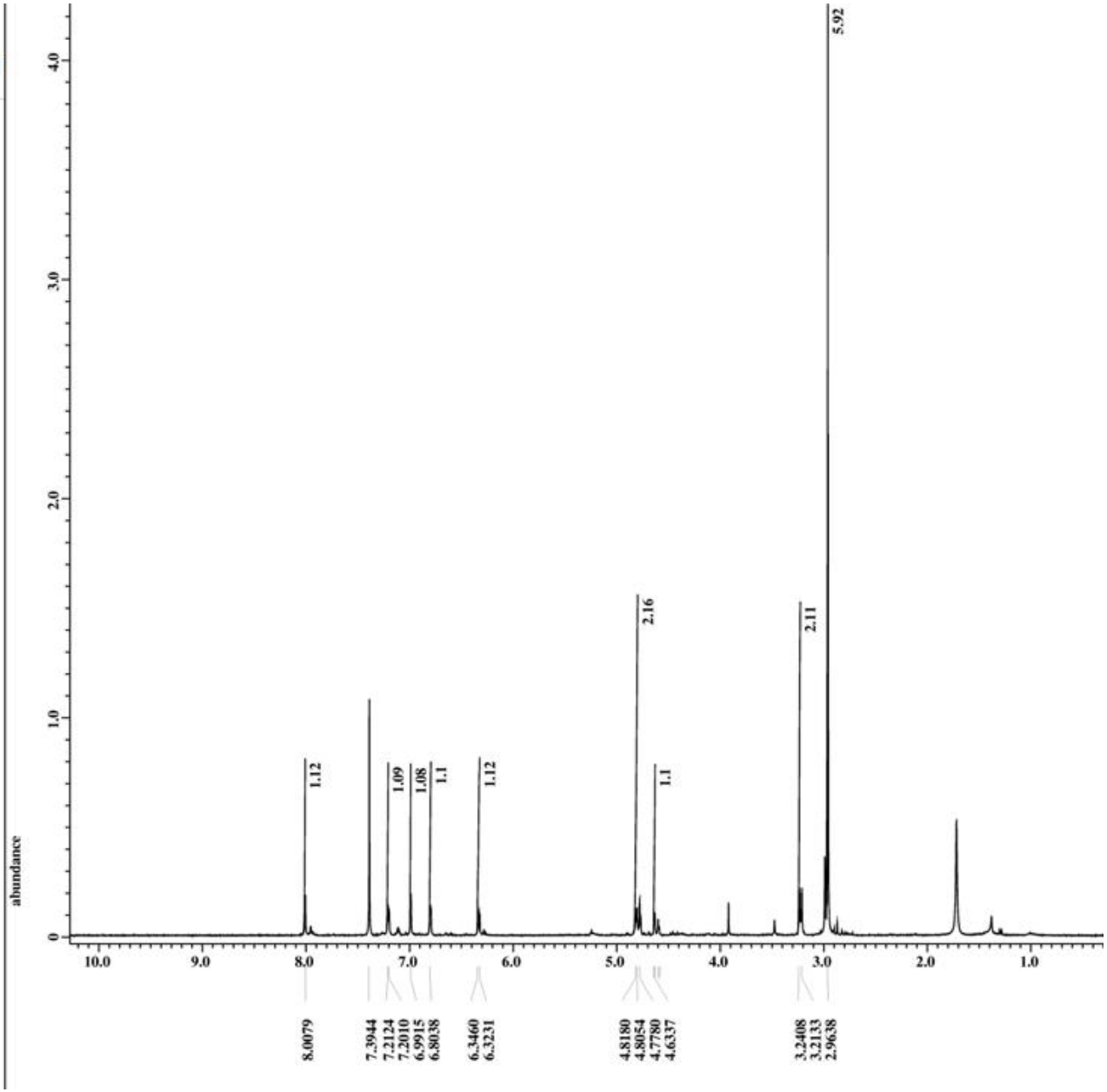


JEOL
ilename = sm_V_179_pure_ii-2.jd
uthor = delta
xperiment = single_pulse_dec
ample_id = S#553989
olvent = CHLOROFORM-D
reation_time = 9-AUG-2009 20:06:16
evision_time = 9-AUG-2009 23:00:22
urrent_time = 27-MAR-2010 20:16:48
comment = single pulse decouple
ata_format = 1D COMPLEX
im_size = 52428
im_title = 13C
im_units = [ppm]
imensions = X
ite = ECX 300
pectrometer = DELTA2_NMR
ield_strength = 7.0586013[T] (300[MHz
_acq_duration = 2.76824064[s]
_domain = 13C
_freq = 75.56823426[MHz]
_offset = 100[ppm]
_points = 65536
_prescans = 4
_resolution = 0.36124027[Hz]
_sweep = 23.67424242[kHz]
rr_domain = 1H
rr_freq = 300.52965592[MHz]
rr_offset = 5[ppm]
lipped = FALSE
od_return = 10
cans = 3000
otal_scans = 3000
_90_width = 9.75[us]
_acq_time = 2.76824064[s]
_angle = 30[deg]
_atn = 8[dB]
_pulse = 3.25[us]
rr_atn_dec = 25[dB]
rr_atn_noe = 25[dB]
rr_noise = WALTZ
ecoupling = TRUE
nitial_wait = 1[s]
oe = TRUE
oe_time = 3[s]
ecvr_gain = 50
elaxation_delay = 3[s]
epetition_time = 5.76824064[s]
emp_get = 22.9[dC]
abundance
158.8027
138.7827
136.6555
123.1893
118.7341
116.0714
107.6915
100.8844
77.5468
77.3270
77.1214
76.7007
66.8437
57.0584
38.3482
33.6922
Br
Br
HN
O
Cl
O
O
S
N
N
N

APPENDIX 19
^{1}H AND ^{13}C NMR SPECTRUM OF
(*S*)-N,N-dimethyl-4-((1-oxo-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazin-4-yl)methyl)-1H-imidazole-1-sulfonamide (77)

```
ilename          = sm_V_165_pure-3.jdf
uthor            = delta
xperiment        = single_pulse.ex2
mple_id          = S#508172
olvent           = CHLOROFORM-D
reation_time     = 12-JUL-2009 14:00:37
evision_time     = 27-MAR-2010 20:30:16
urrent_time      = 27-MAR-2010 20:32:44

omment           = single_pulse
ata_format       = 1D COMPLEX
im_size          = 13107
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.90717696[s]
_domain          = 1H
_freq            = 300.52965592[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.34397631[Hz]
_sweep           = 5.63570784[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
ri_domain        = 1H
ri_freq          = 300.52965592[MHz]
ri_offset        = 5[ppm]
lipped           = FALSE
od_return        = 1
cans             = 24
otal_scans       = 24

_90_width        = 13.01[us]
_acq_time        = 2.90717696[s]
_angle           = 45[deg]
_atn             = 4[dB]
_pulse           = 6.505[us]
rr_mode          = Off
ri_mode          = Off
ante_presat      = FALSE
nitial_wait      = 1[s]
ecvr_gain        = 46
elaxation_delay  = 5[s]
epetition_time   = 7.90717696[s]
emp_get          = 23[dC]
```

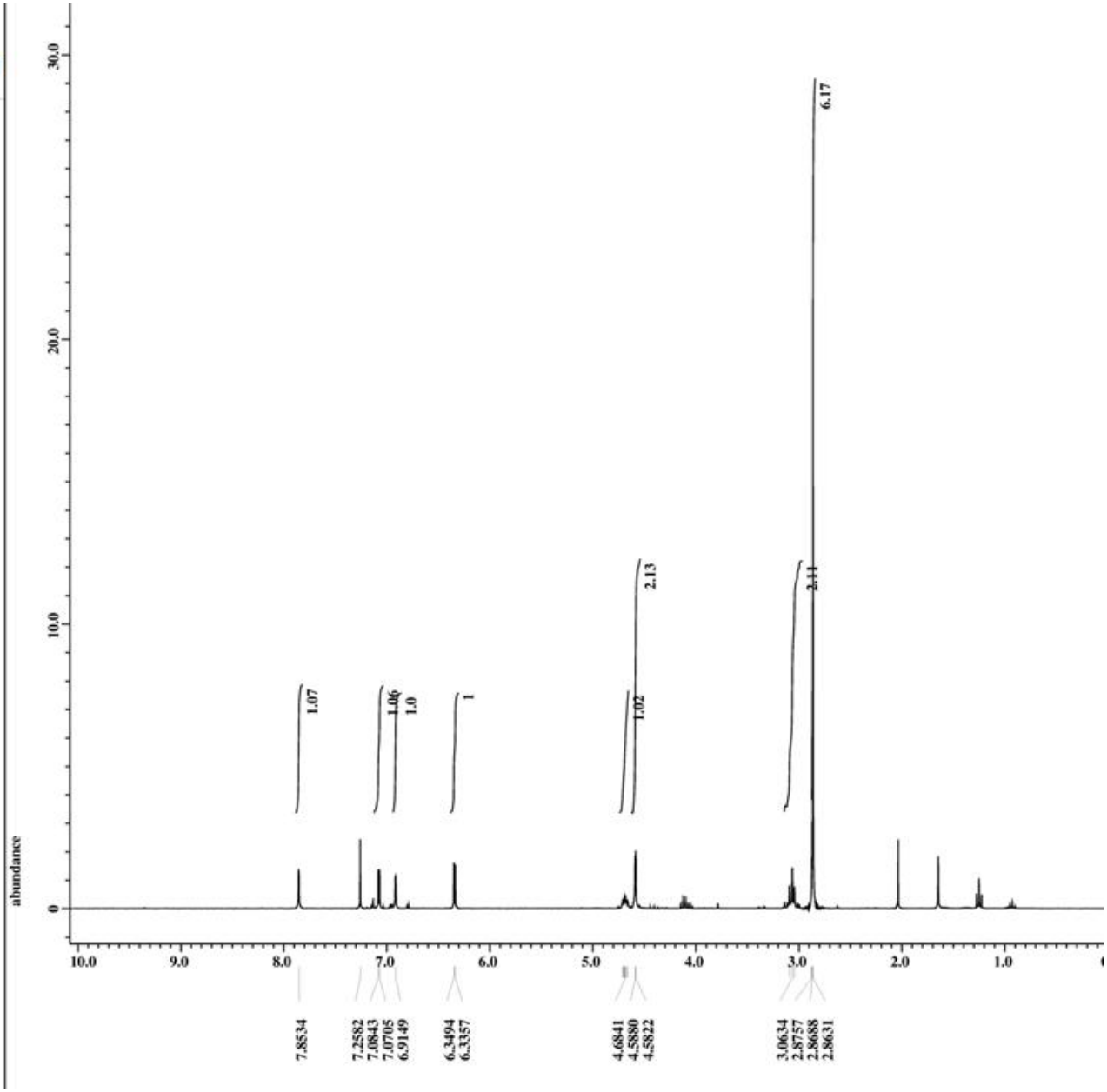




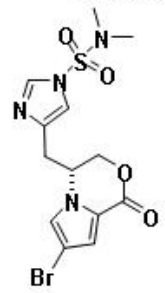
ilename = sm_V_108_pure-2.jdf
uthor = delta
xperiment = single_pulse_dec
ample_id = S#842009
olvent = CHLOROFORM-D
reation_time = 3-APR-2009 03:32:08
evision_time = 27-MAR-2010 20:36:38
urrent_time = 27-MAR-2010 20:36:49
omment = single pulse decouple
ata_format = 1D COMPLEX
im_size = 52428
im_title = 13C
im_units = [ppm]
imensions = X
ite = ECX 300
pectrometer = DELTA2_NMR
ield_strength = 7.0586013[T] (300[MHz
_acq_duration = 2.76824064[s]
_domain = 13C
_freq = 75.56823426[MHz]
_offset = 100[ppm]
_points = 65536
_prescans = 4
_resolution = 0.36124027[Hz]
_sweep = 23.67424242[kHz]
rr_domain = 1H
rr_freq = 300.52965592[MHz]
rr_offset = 5[ppm]
lipped = FALSE
od_return = 10
cans = 3000
otal_scans = 3000
_90_width = 9.75[us]
_acq_time = 2.76824064[s]
_angle = 30[deg]
_atn = 8[dB]
_pulse = 3.25[us]
rr_atn_dec = 25[dB]
rr_atn_noe = 25[dB]
rr_noise = WALTZ
ecoupling = TRUE
nitial_wait = 1[s]
oe = TRUE
oe_time = 3[s]
ecvr_gain = 50
elaxation_delay = 3[s]
epetition_time = 5.76824064[s]
emp_get = 23.4[dC]
(thousandths)
158.7692
138.4816
137.0570
124.2745
118.7962
117.9836
115.7512
110.6792
68.2682
52.6462
38.0375
31.7466

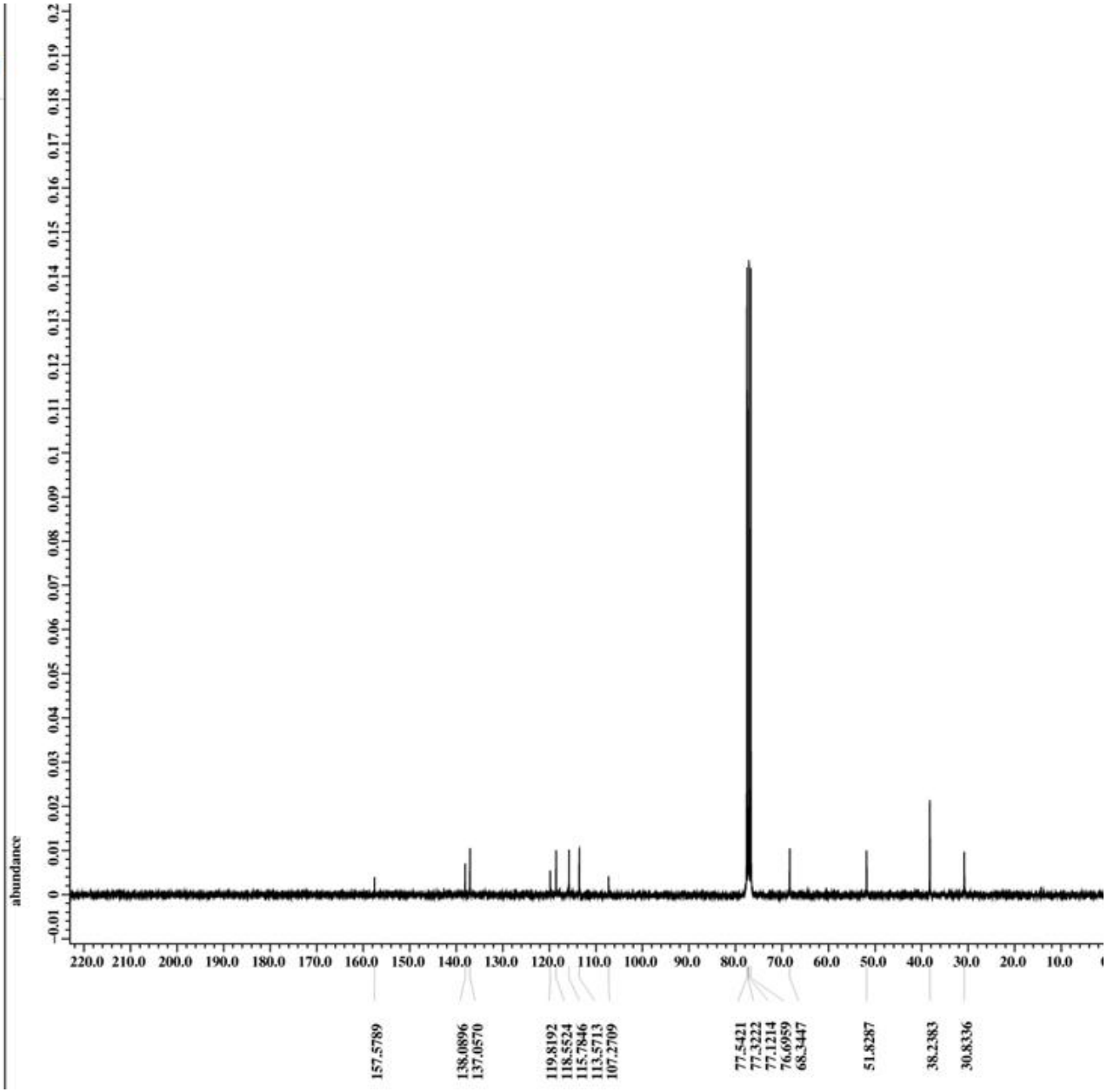
APPENDIX 20
^{1}H AND ^{13}C NMR SPECTRUM OF
(*S*)-4-((7-bromo-1-oxo-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazin-4-yl)methyl)-N,N-dimethyl-1H-imidazole-1-sulfonamide (87)


ilename = sm_VI_50_pure-2.jdf
uthor = delta
xperiment = single_pulse.ex2
mple_id = S#791896
olvent = CHLOROFORM-D
reation_time = 2-DEC-2009 22:09:25
evision_time = 2-DEC-2009 22:06:02
urrent_time = 27-MAR-2010 20:41:38
omment = single_pulse
ata_format = 1D COMPLEX
im_size = 13107
im_title = 1H
im_units = [ppm]
imensions = X
ite = ECX 300
pectrometer = DELTA2_NMR
ield_strength = 7.0586013[T] (300[MHz
_acq_duration = 2.90717696[s]
_domain = 1H
_freq = 300.52965592[MHz]
_offset = 5[ppm]
_points = 16384
_prescans = 0
_resolution = 0.34397631[Hz]
_sweep = 5.63570784[kHz]
rr_domain = 1H
rr_freq = 300.52965592[MHz]
rr_offset = 5[ppm]
ri_domain = 1H
ri_freq = 300.52965592[MHz]
ri_offset = 5[ppm]
lipped = FALSE
od_return = 1
cans = 24
otal_scans = 24
_90_width = 13.01[us]
_acq_time = 2.90717696[s]
_angle = 45[deg]
_atn = 4[dB]
_pulse = 6.505[us]
rr_mode = Off
ri_mode = Off
ante_presat = FALSE
nitial_wait = 1[s]
ecvr_gain = 50
elaxation_delay = 5[s]
epetition_time = 7.90717696[s]
emp_get = 23.2[dC]
O
N
S
O
N
N
O
N
O
Br


abundance
30.0
20.0
10.0
0
6.17
2.13
2.11
1.07
1.06
1.0
1
1.02
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
7.8534
7.2582
7.0843
7.0705
6.9149
6.3494
6.3357
4.6841
4.5880
4.5822
3.0634
2.8757
2.8688
2.8631

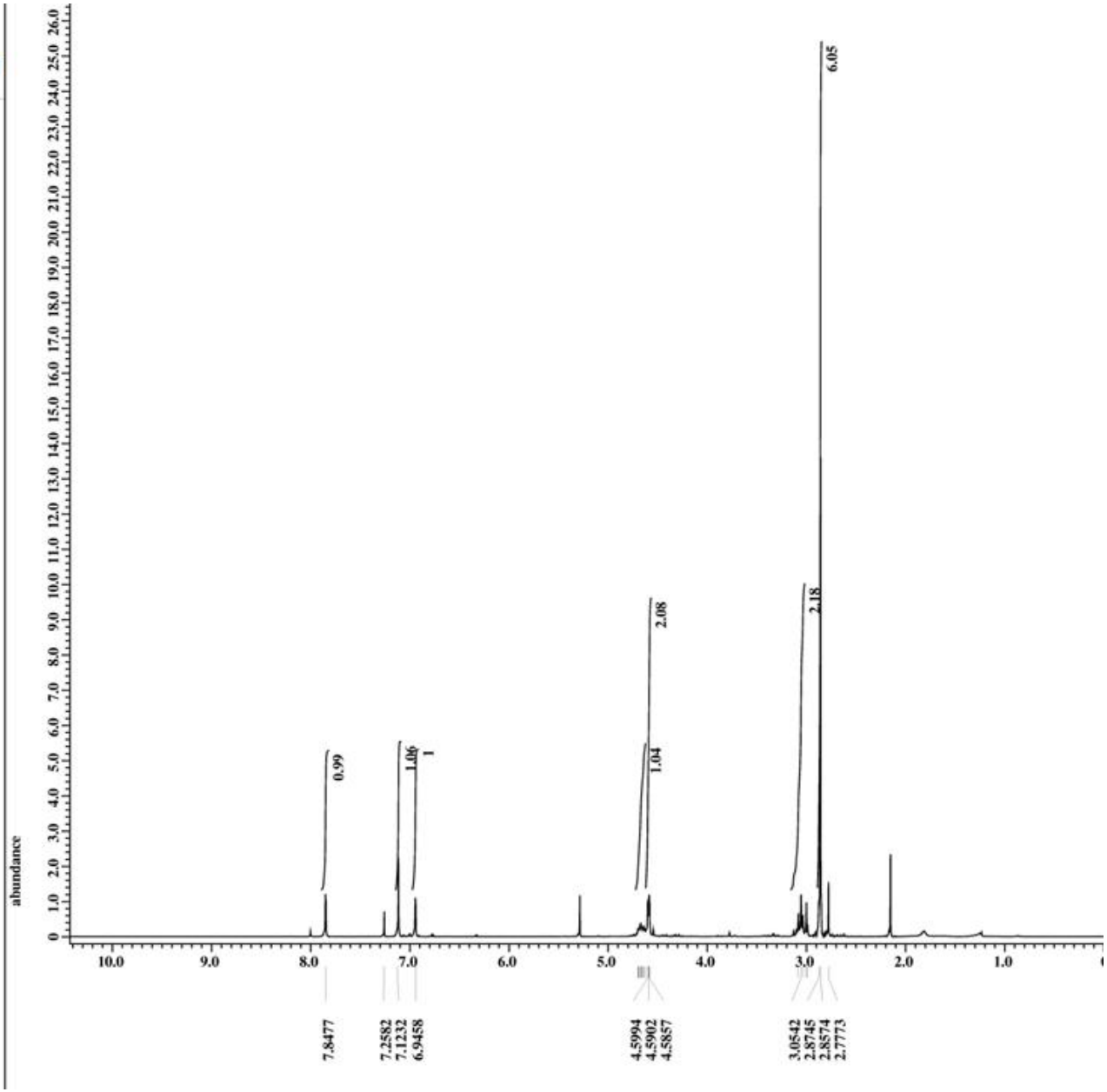
```
ilename          = sm_VI_50_pure-2.jdf
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#796170
olvent           = CHLOROFORM-D
reation_time     =  3-DEC-2009 06:14:17
evision_time     =  3-DEC-2009 15:55:51
urrent_time      = 27-MAR-2010 20:44:53

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 52428
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.76824064[s]
_domain          = 13C
_freq            = 75.56823426[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.36124027[Hz]
_sweep           = 23.67424242[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
lipped           = FALSE
od_return        = 10
cans             = 5000
otal_scans       = 5000

_90_width        = 9.75[us]
_acq_time        = 2.76824064[s]
_angle           = 30[deg]
_atn             = 8[dB]
_pulse           = 3.25[us]
rr_atn_dec       = 25[dB]
rr_atn_noe       = 25[dB]
rr_noise         = WALTZ
ecoupling        = TRUE
nitial_wait      = 1[s]
oe               = TRUE
oe_time          = 3[s]
ecvr_gain        = 50
elaxation_delay  = 3[s]
epetition_time   = 5.76824064[s]
emp_get          = 23.1[dC]
```



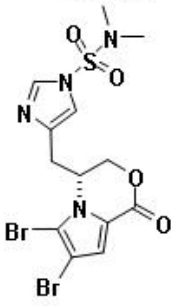


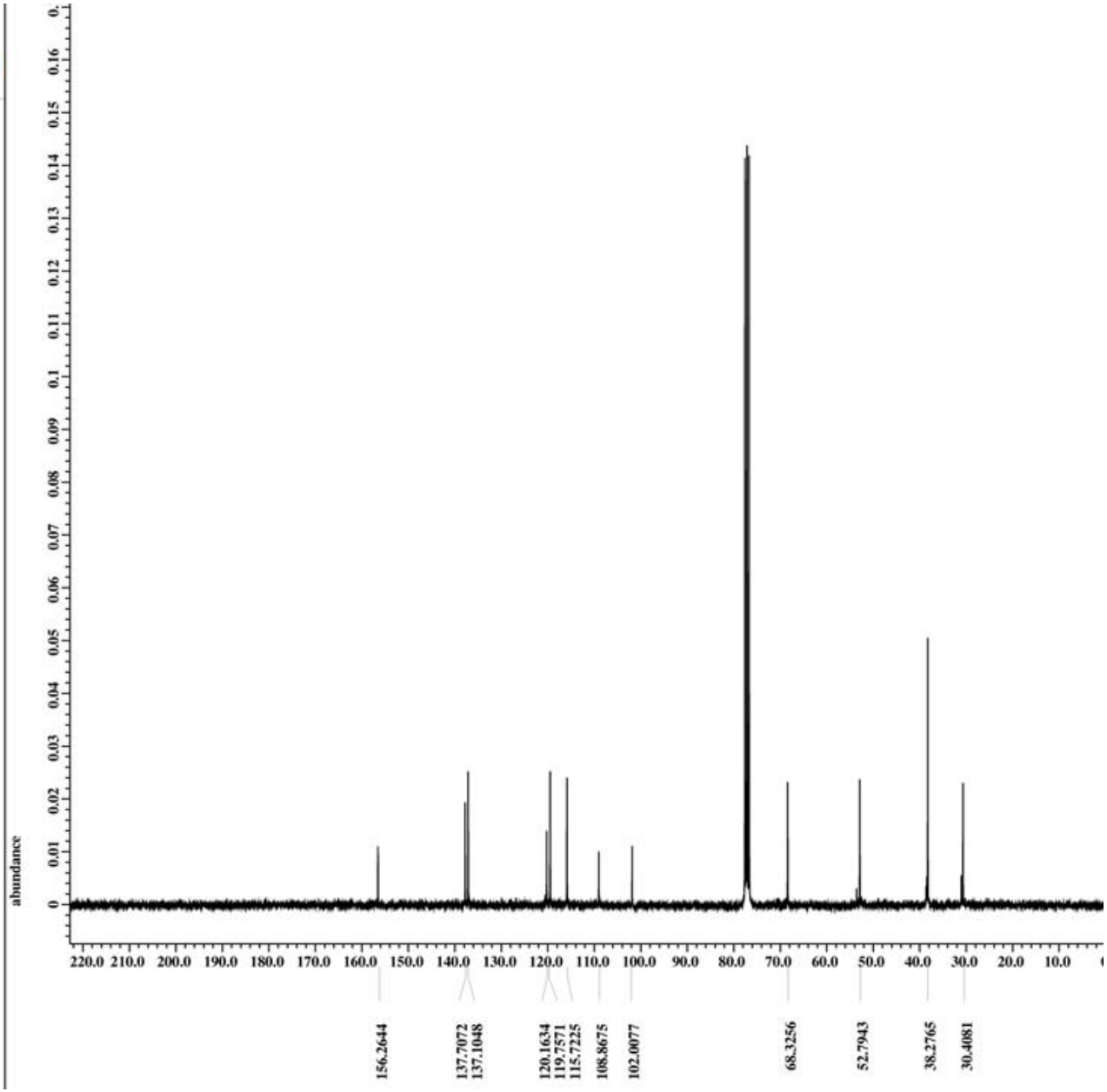
APPENDIX 21
^{1}H AND ^{13}C NMR SPECTRUM OF
(*S*)-4-((6,7-dibromo-1-oxo-3,4-dihydro-1H-pyrrolo[2,1-c][1,4]oxazin-4-yl)methyl)-N,N-dimethyl-1H-imidazole-1-sulfonamide (88)

```
ilename          = sm_VI_47_pure-3.jdf
uthor            = delta
xperiment        = single_pulse.ex2
ample_id         = S#833575
olvent           = CHLOROFORM-D
reation_time     =  1-DEC-2009 23:19:18
evision_time     = 27-MAR-2010 20:48:49
urrent_time      = 27-MAR-2010 20:49:20

omment           = single_pulse
ata_format       = 1D COMPLEX
im_size          = 13107
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.90717696[s]
_domain          = 1H
_freq            = 300.52965592[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.34397631[Hz]
_sweep           = 5.63570784[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
ri_domain        = 1H
ri_freq          = 300.52965592[MHz]
ri_offset        = 5[ppm]
lipped           = FALSE
od_return        = 1
cans             = 24
otal_scans       = 24

_90_width        = 13.01[us]
_acq_time        = 2.90717696[s]
_angle           = 45[deg]
_atn             = 4[dB]
_pulse           = 6.505[us]
rr_mode          = Off
ri_mode          = Off
ante_presat      = FALSE
nitial_wait      = 1[s]
ecvr_gain        = 42
elaxation_delay  = 5[s]
epetition_time   = 7.90717696[s]
emp_get          = 23.2[dC]
```

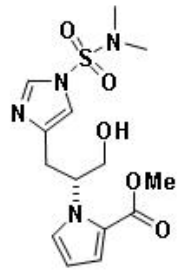
```
ilename          = sm_VI_47_pure-2.jdf
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#835989
olvent           = CHLOROFORM-D
reation_time     =  2-DEC-2009 07:20:39
evision_time     = 27-MAR-2010 20:52:22
urrent_time      = 27-MAR-2010 20:52:36

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 52428
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.76824064[s]
_domain          = 13C
_freq            = 75.56823426[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 5
_resolution      = 0.36124027[Hz]
_sweep           = 23.67424242[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
lipped           = FALSE
od_return        = 10
cans             = 5000
otal_scans       = 5000

_90_width        = 9.75[us]
_acq_time        = 2.76824064[s]
_angle           = 30[deg]
_atn             = 8[dB]
_pulse           = 3.25[us]
rr_atn_dec       = 25[dB]
rr_atn_noe       = 25[dB]
rr_noise         = WALTZ
ecoupling        = TRUE
nitial_wait      = 1[s]
oe               = TRUE
oe_time          = 3[s]
ecvr_gain        = 50
elaxation_delay  = 3[s]
epetition_time   = 5.76824064[s]
emp_get          = 23.3[dC]
```

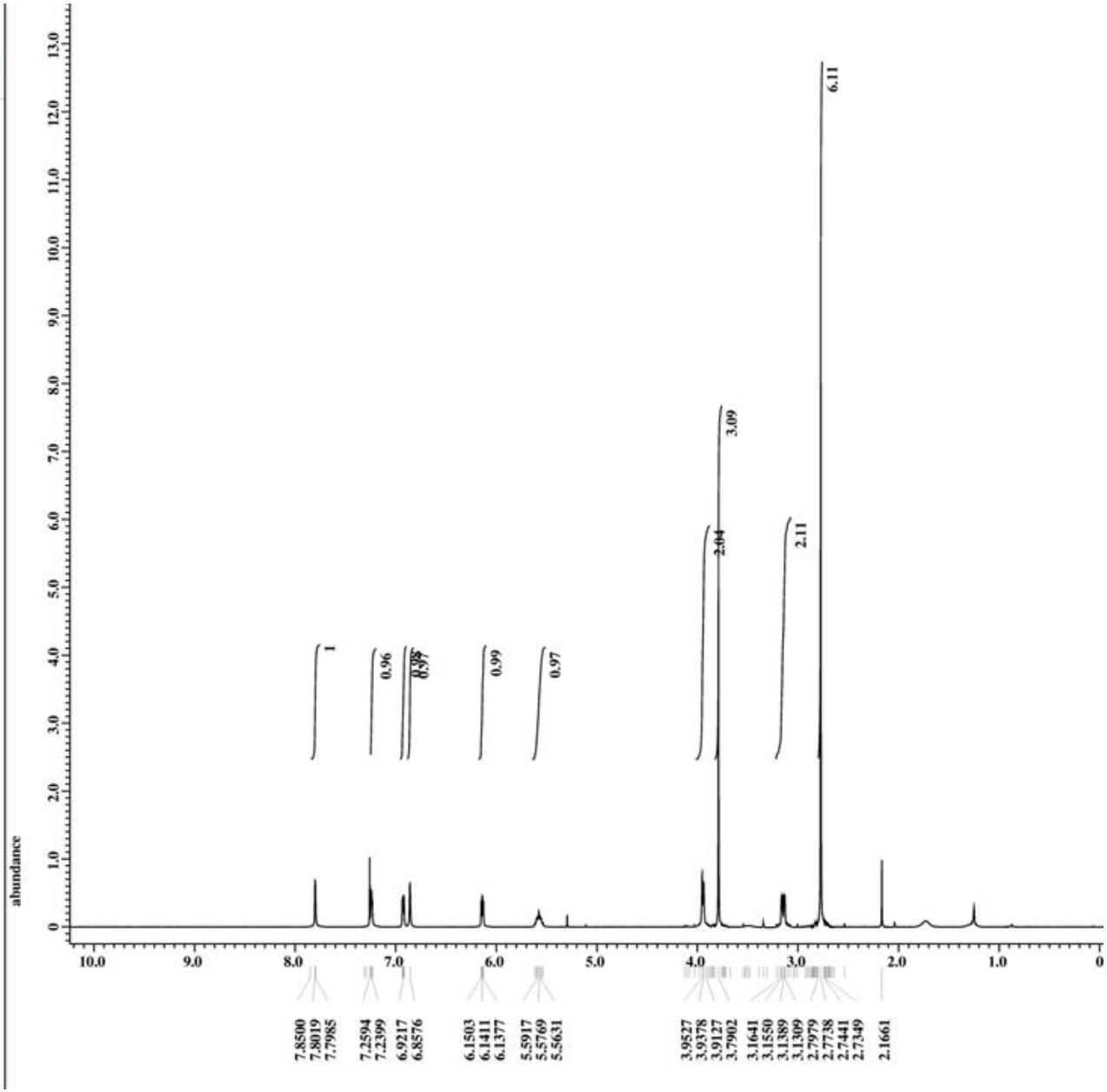




APPENDIX 22
^{1}H AND ^{13}C NMR SPECTRUM OF
(*S*)-methyl 1-(1-(1-(N,N-dimethylsulfamoyl)-1H-imidazol-4-yl)-3-hydroxypropan-2-yl)-1H-pyrrole-2-carboxylate (89)

```
ilename          = sm_V_106_pure-4.jdf
uthor            = delta
xperiment        = single_pulse.ex2
ample_id         = S#503627
olvent           = CHLOROFORM-D
reation_time     = 26-MAR-2009 13:21:57
evision_time     = 28-MAR-2010 11:11:40
urrent_time      = 28-MAR-2010 11:12:13

omment           = single_pulse
ata_format       = 1D REAL
im_size          = 13107
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.90717696[s]
_domain          = 1H
_freq            = 300.52965592[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.34397631[Hz]
_sweep           = 5.63570784[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
ri_domain        = 1H
ri_freq          = 300.52965592[MHz]
ri_offset        = 5[ppm]
lipped           = FALSE
od_return        = 1
cans             = 24
otal_scans       = 24

_90_width        = 13.01[us]
_acq_time        = 2.90717696[s]
_angle           = 45[deg]
_atn             = 4[dB]
_pulse           = 6.505[us]
rr_mode          = Off
ri_mode          = Off
ante_presat      = FALSE
nitial_wait      = 1[s]
ecvr_gain        = 46
elaxation_delay  = 5[s]
epetition_time   = 7.90717696[s]
emp_get          = 23.1[dC]
```

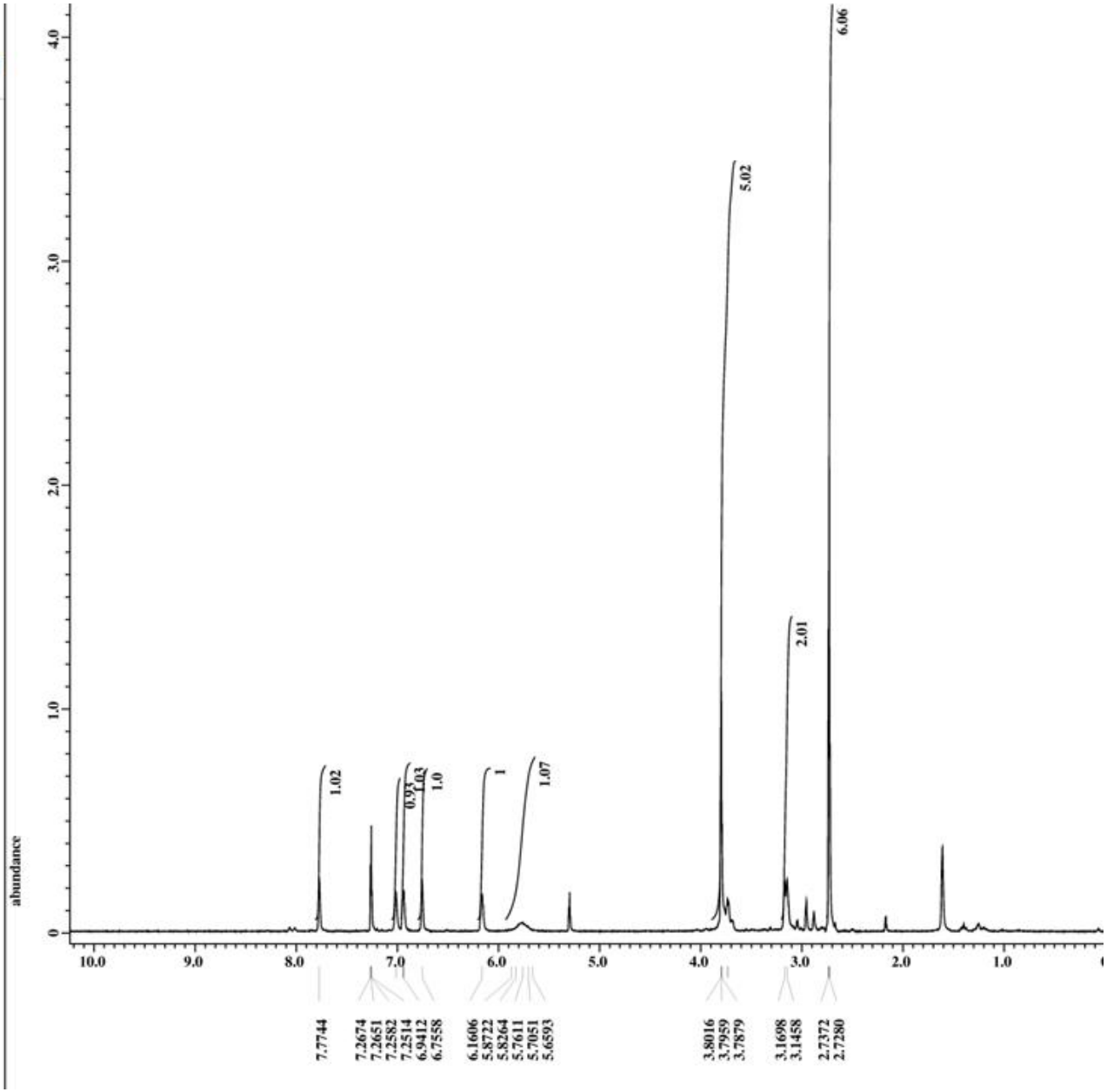




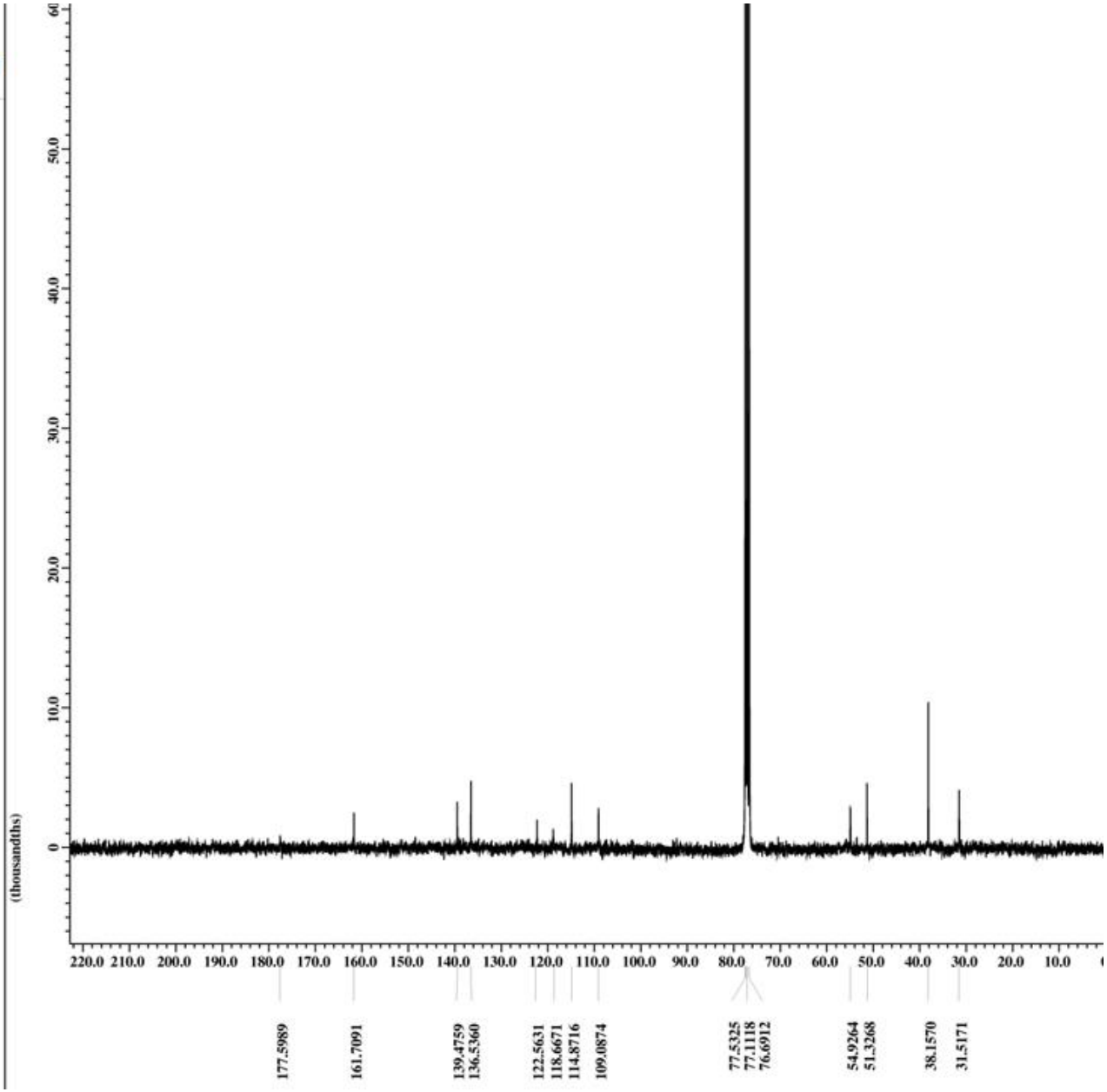
JEOL
ilename = sm_V_106_pure-2.jdf
uthor = delta
xperiment = single_pulse_dec
ample_id = S#516083
olvent = CHLOROFORM-D
reation_time = 27-MAR-2009 15:15:46
evision_time = 27-MAR-2009 15:59:36
urrent_time = 28-MAR-2010 11:16:33
omment = single pulse decouple
ata_format = 1D COMPLEX
im_size = 52428
im_title = 13C
im_units = [ppm]
imensions = X
ite = ECX 300
pectrometer = DELTA2_NMR
ield_strength = 7.0586013[T] (300[MHz
_acq_duration = 2.76824064[s]
_domain = 13C
_freq = 75.56823426[MHz]
_offset = 100[ppm]
_points = 65536
_prescans = 4
_resolution = 0.36124027[Hz]
_sweep = 23.67424242[kHz]
rr_domain = 1H
rr_freq = 300.52965592[MHz]
rr_offset = 5[ppm]
lipped = FALSE
od_return = 10
cans = 1000
otal_scans = 1000
_90_width = 9.75[us]
_acq_time = 2.76824064[s]
_angle = 30[deg]
_atn = 8[dB]
_pulse = 3.25[us]
rr_atn_dec = 25[dB]
rr_atn_noe = 25[dB]
rr_noise = WALTZ
ecoupling = TRUE
nitial_wait = 1[s]
oe = TRUE
oe_time = 3[s]
ecvr_gain = 50
elaxation_delay = 3[s]
epetition_time = 5.76824064[s]
emp_get = 23.3[dC]
abundance
162.0103
139.8918
136.4308
126.2822
122.0660
118.2895
114.9672
108.8101
77.5421
77.1166
76.6959
64.8503
57.8471
51.2503
38.2096
31.1252
OH
OMe

APPENDIX 23
^{1}H AND ^{13}C NMR SPECTRUM OF
(*S*)-methyl 1-(1-azido-3-(1-(N,N-dimethylsulfamoyl)-1H-imidazol-4-yl)propan-2-yl)-1H-pyrrole-2-carboxylate (91)

```
ilename          = sm_VI_39_pure-3.jdf
uthor            = delta
xperiment        = single_pulse.ex2
mple_id          = S#638625
olvent           = CHLOROFORM-D
reation_time     = 26-NOV-2009 17:53:41
evision_time     = 28-MAR-2010 11:21:55
urrent_time      = 28-MAR-2010 11:22:12

omment           = single_pulse
ata_format       = 1D COMPLEX
im_size          = 13107
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.90717696[s]
_domain          = 1H
_freq            = 300.52965592[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.34397631[Hz]
_sweep           = 5.63570784[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
ri_domain        = 1H
ri_freq          = 300.52965592[MHz]
ri_offset        = 5[ppm]
lipped           = FALSE
od_return        = 1
cans             = 23
otal_scans       = 23

_90_width        = 13.01[us]
_acq_time        = 2.90717696[s]
_angle           = 45[deg]
_atn             = 4[dB]
_pulse           = 6.505[us]
rr_mode          = Off
ri_mode          = Off
ante_presat      = FALSE
nitial_wait      = 1[s]
ecvr_gain        = 46
elaxation_delay  = 5[s]
epetition_time   = 7.90717696[s]
emp_get          = 23.4[dC]
```

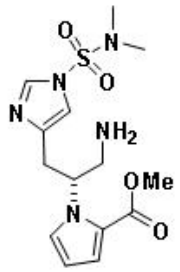


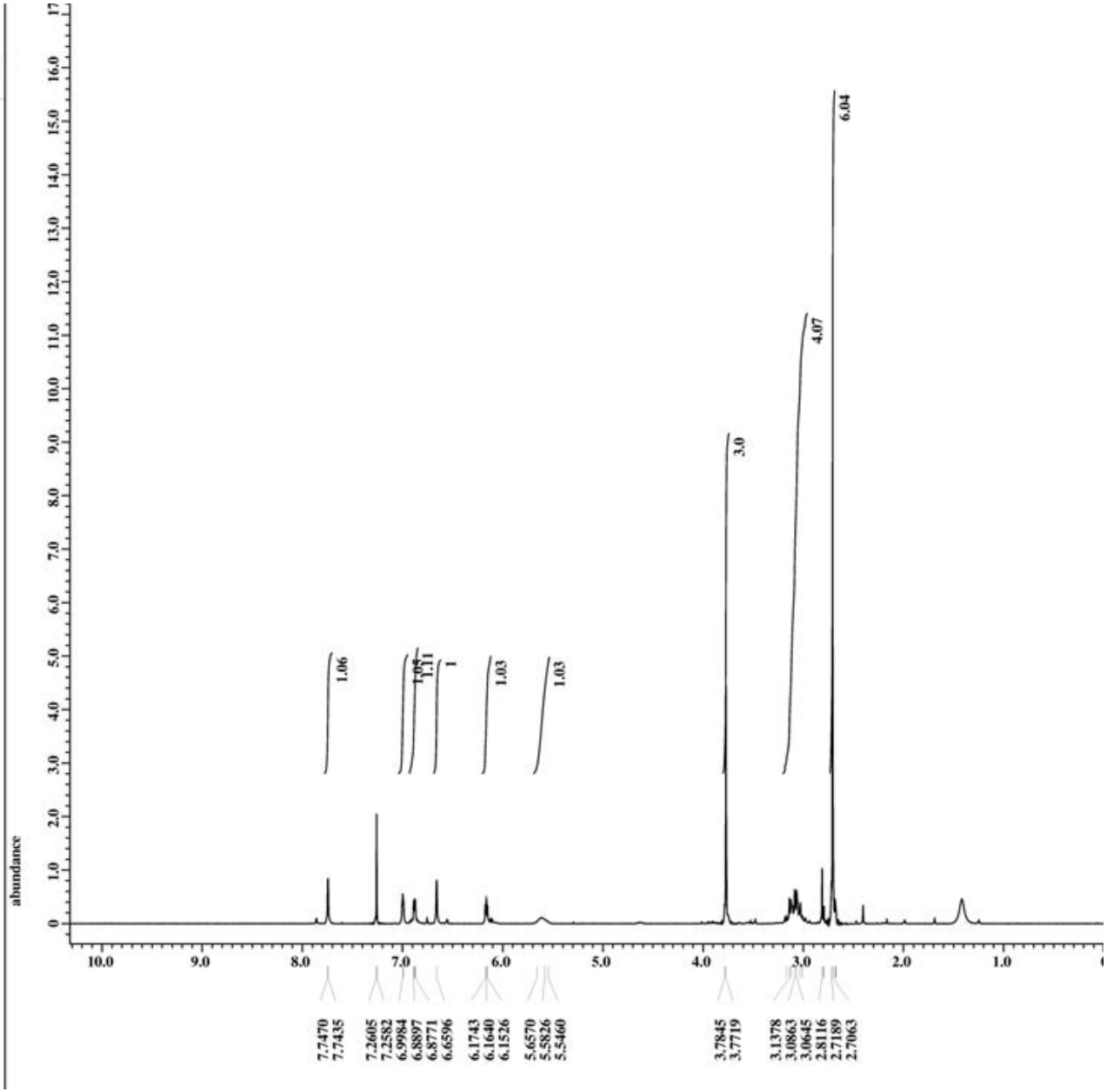
```
ilename          = sm_VI_39_pure-2.jdf
uthor            = delta
xperiment        = single_pulse_dec
mple_id          = S#641182
olvent           = CHLOROFORM-D
reation_time     = 27-NOV-2009 00:19:11
evision_time     = 27-NOV-2009 17:46:00
urrent_time      = 28-MAR-2010 11:30:13

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 52428
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.76824064[s]
_domain          = 13C
_freq            = 75.56823426[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.36124027[Hz]
_sweep           = 23.67424242[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
lipped           = FALSE
od_return        = 10
cans             = 4000
otal_scans       = 4000

_90_width        = 9.75[us]
_acq_time        = 2.76824064[s]
_angle           = 30[deg]
_atn             = 8[dB]
_pulse           = 3.25[us]
rr_atn_dec       = 25[dB]
rr_atn_noe       = 25[dB]
rr_noise         = WALTZ
ecoupling        = TRUE
nitial_wait      = 1[s]
oe               = TRUE
oe_time          = 3[s]
ecvr_gain        = 50
elaxation_delay  = 3[s]
epetition_time   = 5.76824064[s]
emp_get          = 22.9[dC]
```



APPENDIX 24
^{1}H AND ^{13}C NMR SPECTRUM OF
(*S*)-methyl 1-(1-amino-3-(1-(N,N-dimethylsulfamoyl)-1H-imidazol-4-yl)propan-2-yl)-1H-pyrrole-2-carboxylate (92)

```
ilename          = sm_V_181-4.jdf
uthor            = delta
xperiment        = single_pulse.ex2
ample_id         = S#664788
olvent           = CHLOROFORM-D
reation_time     =  3-AUG-2009 18:24:07
evision_time     = 28-MAR-2010 11:34:56
urrent_time      = 28-MAR-2010 11:35:12

omment           = single_pulse
ata_format       = 1D REAL
im_size          = 13107
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.90717696[s]
_domain          = 1H
_freq            = 300.52965592[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.34397631[Hz]
_sweep           = 5.63570784[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
ri_domain        = 1H
ri_freq          = 300.52965592[MHz]
ri_offset        = 5[ppm]
lipped           = FALSE
od_return        = 1
cans             = 24
otal_scans       = 24

_90_width        = 13.01[us]
_acq_time        = 2.90717696[s]
_angle           = 45[deg]
_atn             = 4[dB]
_pulse           = 6.505[us]
rr_mode          = Off
ri_mode          = Off
ante_presat      = FALSE
nitial_wait      = 1[s]
ecvr_gain        = 50
elaxation_delay  = 5[s]
epetition_time   = 7.90717696[s]
emp_get          = 23.2[dC]
```



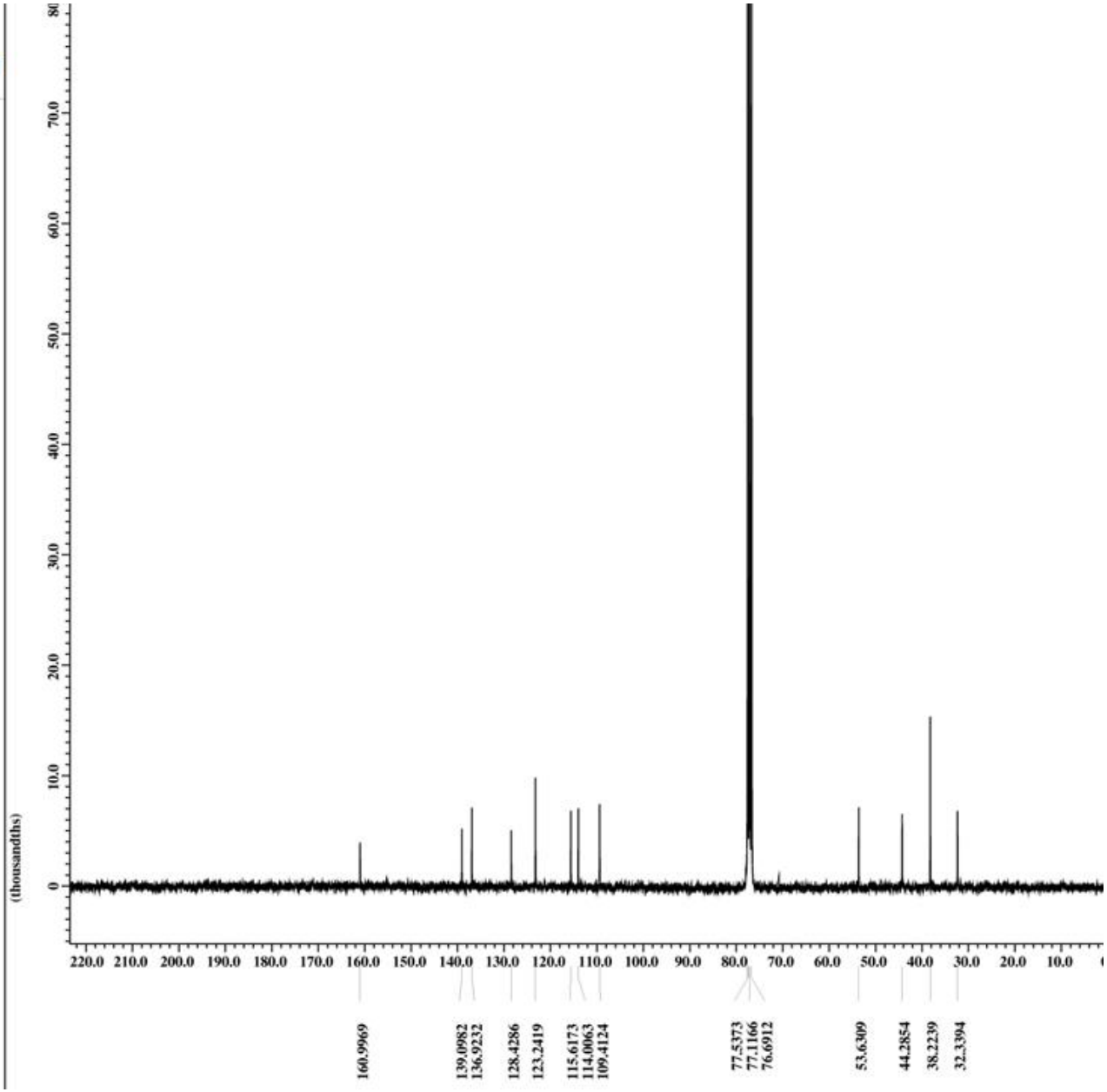


JEOL
ilename = sm_V_181-2.jdf
uthor = delta
xperiment = single_pulse_dec
ample_id = S#666919
olvent = CHLOROFORM-D
reation_time = 3-AUG-2009 20:02:03
evision_time = 3-AUG-2009 22:31:12
urrent_time = 28-MAR-2010 11:39:24
omment = single pulse decouple
ata_format = 1D COMPLEX
im_size = 52428
im_title = 13C
im_units = [ppm]
imensions = X
ite = ECX_300
pectrometer = DELTA2_NMR
ield_strength = 7.0586013[T] (300[MHz
_acq_duration = 2.76824064[s]
_domain = 13C
_freq = 75.56823426[MHz]
_offset = 100[ppm]
_points = 65536
_prescans = 4
_resolution = 0.36124027[Hz]
_sweep = 23.67424242[kHz]
rr_domain = 1H
rr_freq = 300.52965592[MHz]
rr_offset = 5[ppm]
lipped = FALSE
od_return = 10
cans = 1000
otal_scans = 1000
_90_width = 9.75[us]
_acq_time = 2.76824064[s]
_angle = 30[deg]
_atn = 8[dB]
_pulse = 3.25[us]
rr_atn_dec = 25[dB]
rr_atn_noe = 25[dB]
rr_noise = WALTZ
ecoupling = TRUE
nitial_wait = 1[s]
oe = TRUE
oe_time = 3[s]
ecvr_gain = 50
elaxation_delay = 3[s]
epetition_time = 5.76824064[s]
emp_get = 23.3[dC]
(thousandths)
162.0151
140.1451
136.2874
123.0555
118.2799
114.2358
109.0922
103.7621
77.3078
51.2025
46.7950
37.9754
32.2772
NH2
OMe

APPENDIX 25
^{1}H AND ^{13}C NMR SPECTRUM OF
(*S*)-N,N-dimethyl-4-((1-oxo-1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazin-4-yl)methyl)-1H-imidazole-1-sulfonamide (55)

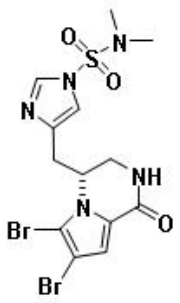

ilename = sm_V_189_CRUDE-4.jdf
uthor = delta
xperiment = single_pulse.ex2
mple_id = S#483444
olvent = CHLOROFORM-D
reation_time = 14-AUG-2009 13:23:17
evision_time = 28-MAR-2010 11:42:50
urrent_time = 28-MAR-2010 11:43:37
omment = single_pulse
ata_format = 1D REAL
im_size = 13107
im_title = 1H
im_units = [ppm]
imensions = X
ite = ECX 300
pectrometer = DELTA2_NMR
ield_strength = 7.0586013[T] (300[MHz
_acq_duration = 2.90717696[s]
_domain = 1H
_freq = 300.52965592[MHz]
_offset = 5[ppm]
_points = 16384
_prescans = 0
_resolution = 0.34397631[Hz]
_sweep = 5.63570784[kHz]
rr_domain = 1H
rr_freq = 300.52965592[MHz]
rr_offset = 5[ppm]
ri_domain = 1H
ri_freq = 300.52965592[MHz]
ri_offset = 5[ppm]
lipped = FALSE
od_return = 1
cans = 24
otal_scans = 24
_90_width = 13.01[us]
_acq_time = 2.90717696[s]
_angle = 45[deg]
_atn = 4[dB]
_pulse = 6.505[us]
rr_mode = Off
ri_mode = Off
ante_presat = FALSE
nitial_wait = 1[s]
ecvr_gain = 46
elaxation_delay = 5[s]
epetition_time = 7.90717696[s]
emp_get = 22.8[dC]
O
S
N
O
N
N
NH
N
O
abundance
1
1.03
0.99
1.03
1.0
1.0
1.0
1.01
2.01
6.09
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
7.8649
7.8603
7.2594
6.9034
6.7638
6.5509
6.5486
6.1205
6.1125
6.1079
5.2942
4.6440
4.6303
4.6211
3.9058
3.8921
3.5487
3.5407
3.0920
3.0668
3.0497
3.0279
2.8116

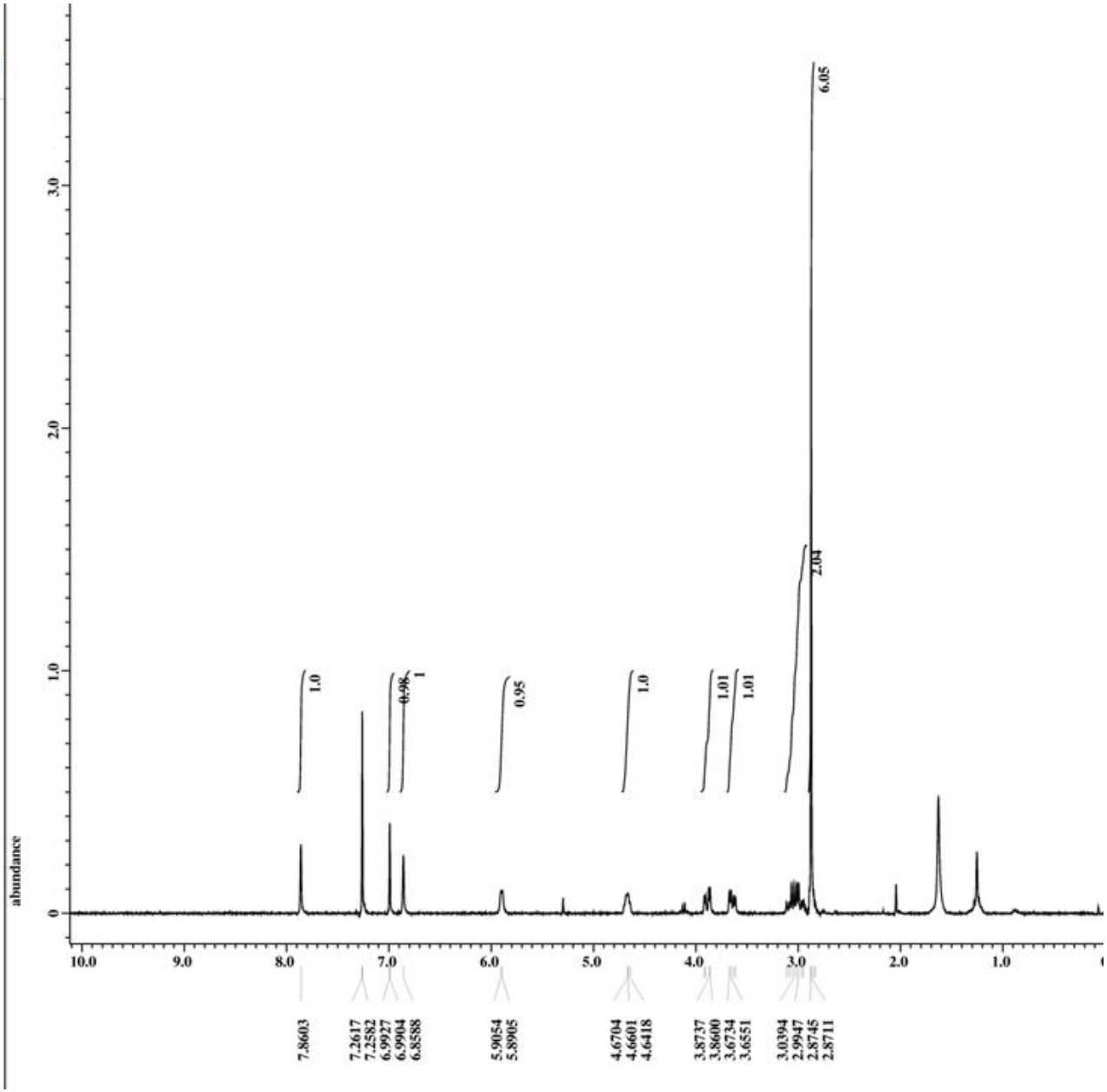
```
ilename          = sm_V_189_pure-2.jdf
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#806600
olvent           = CHLOROFORM-D
reation_time     = 15-AUG-2009 07:55:35
evision_time     = 15-AUG-2009 11:46:50
urrent_time      = 28-MAR-2010 11:46:47

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 52428
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.76824064[s]
_domain          = 13C
_freq            = 75.56823426[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.36124027[Hz]
_sweep           = 23.67424242[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
lipped           = FALSE
od_return        = 10
cans             = 6000
otal_scans       = 6000

_90_width        = 9.75[us]
_acq_time        = 2.76824064[s]
_angle           = 30[deg]
_atn             = 8[dB]
_pulse           = 3.25[us]
rr_atn_dec       = 25[dB]
rr_atn_noe       = 25[dB]
rr_noise         = WALTZ
ecoupling        = TRUE
nitial_wait      = 1[s]
oe               = TRUE
oe_time          = 3[s]
ecvr_gain        = 50
elaxation_delay  = 3[s]
epetition_time   = 5.76824064[s]
emp_get          = 23.7[dC]
```

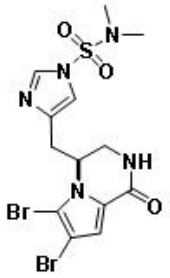
APPENDIX 26
^{1}H AND ^{13}C NMR SPECTRUM OF
(*S*)-4-((6,7-dibromo-1-oxo-1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazin-4-yl)methyl)-N,N-dimethyl-1H-imidazole-1-sulfonamide (93)

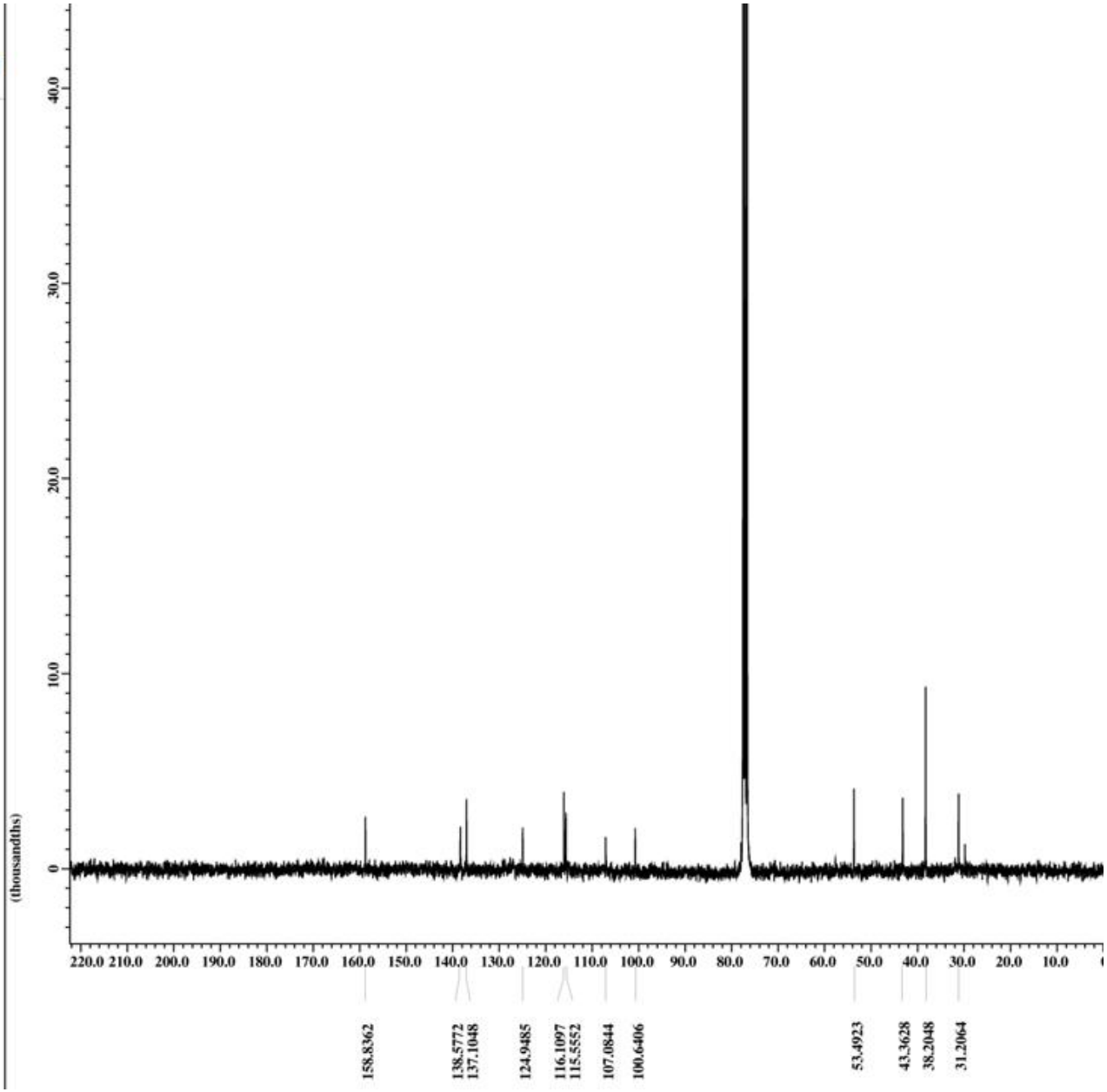
```
ilename          = sm_VI_7B_pure-3.jdf
uthor            = delta
xperiment        = single_pulse.ex2
ample_id         = S#665729
olvent           = CHLOROFORM-D
reation_time     = 20-OCT-2009 18:33:57
evision_time     = 20-OCT-2009 18:35:46
urrent_time      = 28-MAR-2010 11:54:59

omment           = single_pulse
ata_format       = 1D REAL
im_size          = 13107
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.90717696[s]
_domain          = 1H
_freq            = 300.52965592[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.34397631[Hz]
_sweep           = 5.63570784[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
ri_domain        = 1H
ri_freq          = 300.52965592[MHz]
ri_offset        = 5[ppm]
lipped           = FALSE
od_return        = 1
cans             = 16
otal_scans       = 16

_90_width        = 13.01[us]
_acq_time        = 2.90717696[s]
_angle           = 45[deg]
_atn             = 4[dB]
_pulse           = 6.505[us]
rr_mode          = Off
ri_mode          = Off
ante_presat      = FALSE
nitial_wait      = 1[s]
ecvr_gain        = 48
elaxation_delay  = 5[s]
epetition_time   = 7.90717696[s]
emp_get          = 23.5[dC]
```



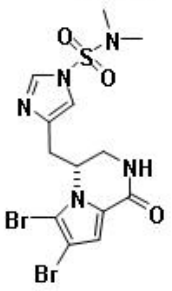


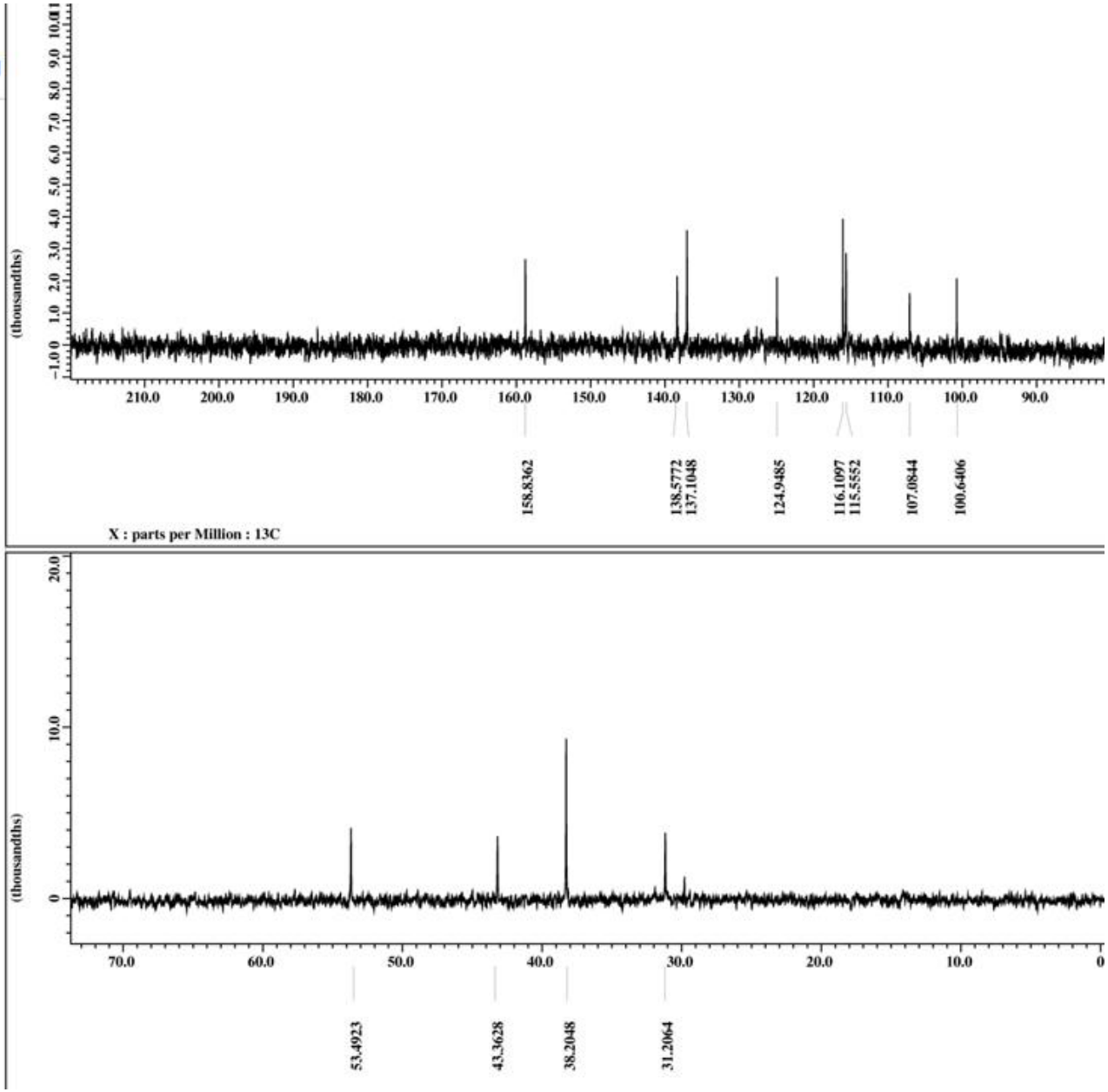
```
ilename          = sm_VI_7B_ii_pure-2.jd
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#5710
olvent           = CHLOROFORM-D
reation_time     = 21-OCT-2009 09:48:21
evision_time     = 21-OCT-2009 09:50:27
urrent_time      = 28-MAR-2010 11:57:45

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 52428
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.76824064[s]
_domain          = 13C
_freq            = 75.56823426[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.36124027[Hz]
_sweep           = 23.67424242[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
lipped           = FALSE
od_return        = 10
cans             = 6000
otal_scans       = 6000

_90_width        = 9.75[us]
_acq_time        = 2.76824064[s]
_angle           = 30[deg]
_atn             = 8[dB]
_pulse           = 3.25[us]
rr_atn_dec       = 25[dB]
rr_atn_noe       = 25[dB]
rr_noise         = WALTZ
ecoupling        = TRUE
nitial_wait      = 1[s]
oe               = TRUE
oe_time          = 3[s]
ecvr_gain        = 50
elaxation_delay  = 3[s]
epetition_time   = 5.76824064[s]
emp_get          = 23.7[dC]
```



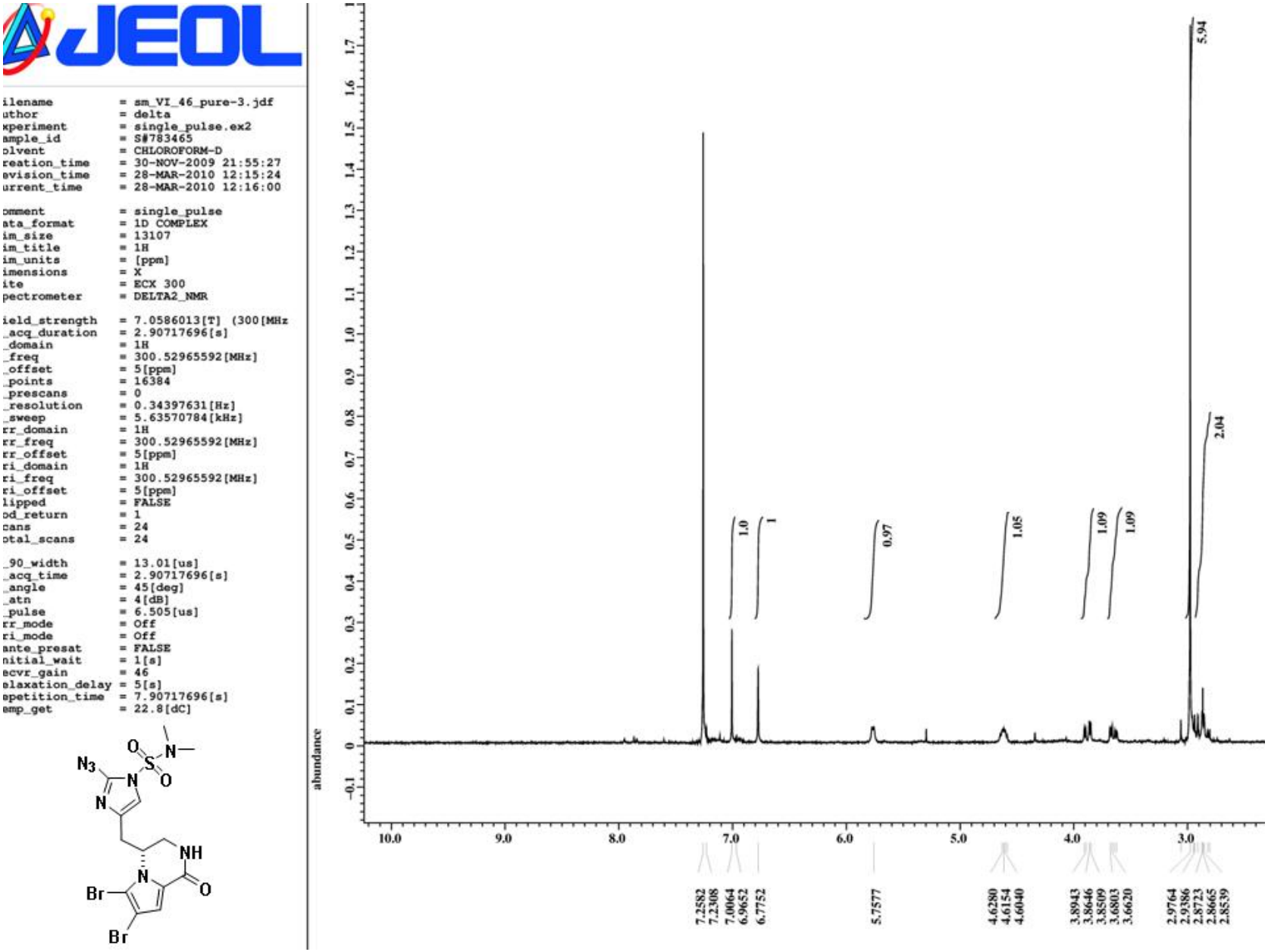


```
ilename          = sm_VI_7B_ii_pure-2.jd
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#5710
olvent           = CHLOROFORM-D
reation_time     = 21-OCT-2009 09:48:21
evision_time     = 21-OCT-2009 09:50:27
urrent_time      = 28-MAR-2010 11:59:46

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 52428
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.76824064[s]
_domain          = 13C
_freq            = 75.56823426[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.36124027[Hz]
_sweep           = 23.67424242[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
lipped           = FALSE
od_return        = 10
cans             = 6000
otal_scans       = 6000

_90_width        = 9.75[us]
_acq_time        = 2.76824064[s]
_angle           = 30[deg]
_atn             = 8[dB]
_pulse           = 3.25[us]
rr_atn_dec       = 25[dB]
rr_atn_noe       = 25[dB]
rr_noise         = WALTZ
ecoupling        = TRUE
nitial_wait      = 1[s]
oe               = TRUE
oe_time          = 3[s]
ecvr_gain        = 50
elaxation_delay  = 3[s]
epetition_time   = 5.76824064[s]
emp_get          = 23.7[dC]
```





APPENDIX 27
^{1}H AND ^{13}C NMR SPECTRUM OF
(*S*)-2-azido-4-((6,7-dibromo-1-oxo-1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazin-4-yl)methyl)-N,N-dimethyl-1H-imidazole- 1-sulfonamide (94)

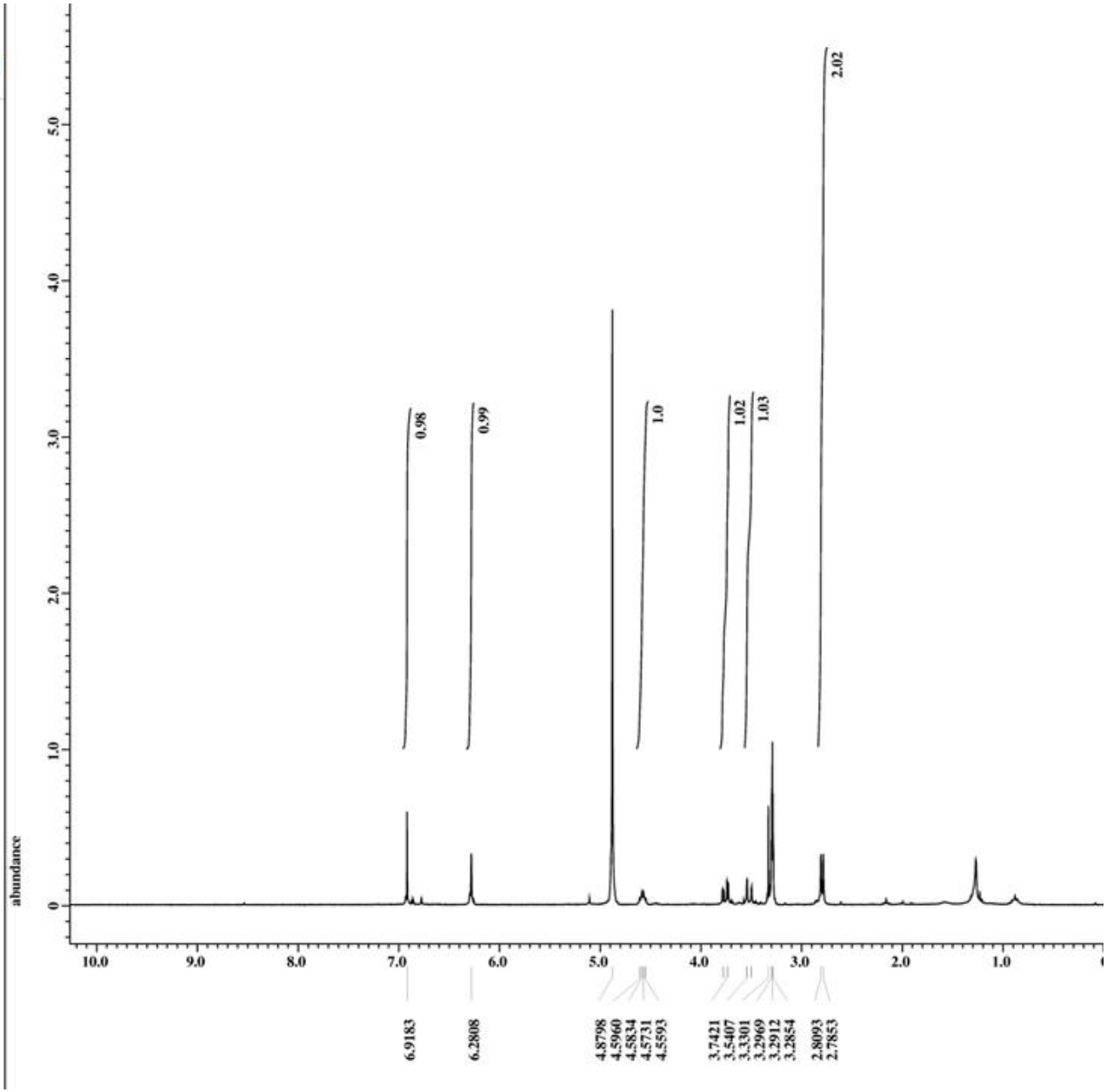


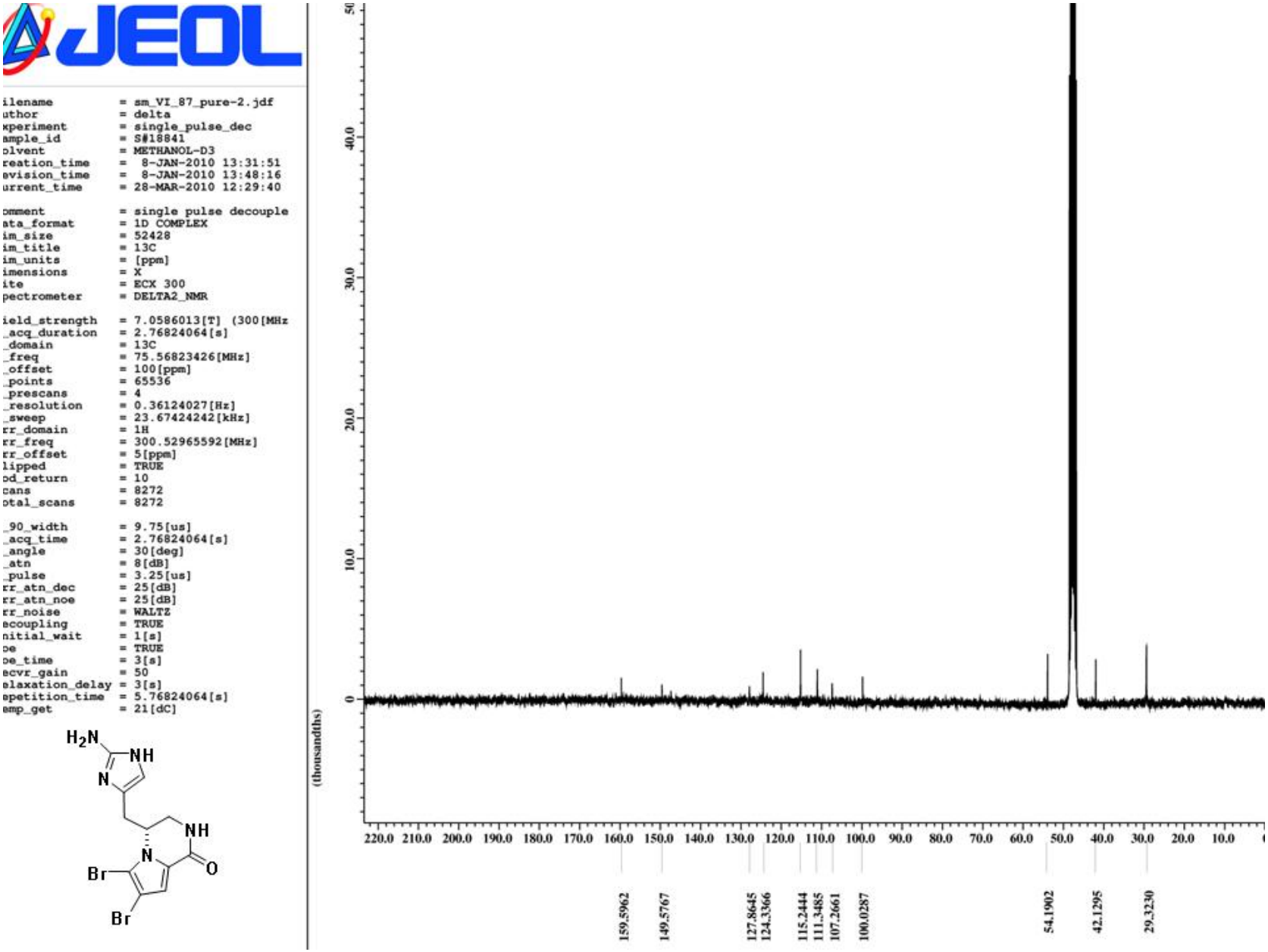
```
ilename          = sm_VI_46_pure-3.jdf
uthor            = delta
xperiment        = single_pulse.ex2
ample_id         = S#783465
olvent           = CHLOROFORM-D
reation_time     = 30-NOV-2009 21:55:27
evision_time     = 28-MAR-2010 12:15:24
urrent_time      = 28-MAR-2010 12:16:00

omment           = single_pulse
ata_format       = 1D COMPLEX
im_size          = 13107
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.90717696[s]
_domain          = 1H
_freq            = 300.52965592[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.34397631[Hz]
_sweep           = 5.63570784[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
ri_domain        = 1H
ri_freq          = 300.52965592[MHz]
ri_offset        = 5[ppm]
lipped           = FALSE
od_return        = 1
cans             = 24
otal_scans       = 24

_90_width        = 13.01[us]
_acq_time        = 2.90717696[s]
_angle           = 45[deg]
_atn             = 4[dB]
_pulse           = 6.505[us]
rr_mode          = Off
ri_mode          = Off
ante_presat      = FALSE
nitial_wait      = 1[s]
ecvr_gain        = 46
elaxation_delay  = 5[s]
epetition_time   = 7.90717696[s]
emp_get          = 22.8[dC]
```

JEOL
ilename = sm_VI_46_pure-2.jdf
uthor = delta
xperiment = single_pulse_dec
ample_id = S#788174
olvent = CHLOROFORM-D
reation_time = 1-DEC-2009 10:13:11
evision_time = 1-DEC-2009 10:07:54
urrent_time = 28-MAR-2010 12:21:26
omment = single pulse decouple
ata_format = 1D COMPLEX
im_size = 52428
im_title = 13C
im_units = [ppm]
imensions = X
ite = ECX 300
pectrometer = DELTA2_NMR
ield_strength = 7.0586013[T] (300[MHz
_acq_duration = 2.76824064[s]
_domain = 13C
_freq = 75.56823426[MHz]
_offset = 100[ppm]
_points = 65536
_prescans = 4
_resolution = 0.36124027[Hz]
_sweep = 23.67424242[kHz]
rr_domain = 1H
rr_freq = 300.52965592[MHz]
rr_offset = 5[ppm]
lipped = FALSE
od_return = 10
cans = 7625
otal_scans = 7625
_90_width = 9.75[us]
_acq_time = 2.76824064[s]
_angle = 30[deg]
_atn = 8[dB]
_pulse = 3.25[us]
rr_atn_dec = 25[dB]
rr_atn_noe = 25[dB]
rr_noise = WALTZ
ecoupling = TRUE
nitial_wait = 1[s]
oe = TRUE
oe_time = 3[s]
ecvr_gain = 50
elaxation_delay = 3[s]
epetition_time = 5.76824064[s]
emp_get = 23.3[dC]
(thousandths)
158.4968
140.6757
134.4279
124.5039
117.1566
115.8707
107.4191
100.6167
53.7648
42.7413
37.9658
30.6137

APPENDIX 28
^{1}H AND ^{13}C NMR SPECTRUM OF
(*ent*)-Cyclooroidin (3)

```
ilename          = sm_VI_87_pure-2.jdf
uthor            = delta
xperiment        = single_pulse.ex2
ample_id         = S#15125
olvent           = METHANOL-D3
reation_time     =  8-JAN-2010 00:15:58
evision_time     =  8-JAN-2010 00:34:38
urrent_time      = 28-MAR-2010 12:25:51

omment           = single_pulse
ata_format       = 1D COMPLEX
im_size          = 13107
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.90717696[s]
_domain          = 1H
_freq            = 300.52965592[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.34397631[Hz]
_sweep           = 5.63570784[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
ri_domain        = 1H
ri_freq          = 300.52965592[MHz]
ri_offset        = 5[ppm]
lipped           = FALSE
od_return        = 1
cans             = 40
otal_scans       = 40

_90_width        = 13.01[us]
_acq_time        = 2.90717696[s]
_angle           = 45[deg]
_atn             = 4[dB]
_pulse           = 6.505[us]
rr_mode          = Off
ri_mode          = Off
ante_presat      = FALSE
nitial_wait      = 1[s]
ecvr_gain        = 46
elaxation_delay  = 5[s]
epetition_time   = 7.90717696[s]
emp_get          = 20.8[dC]
```

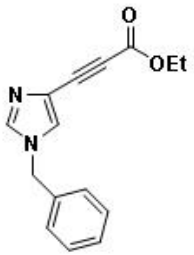



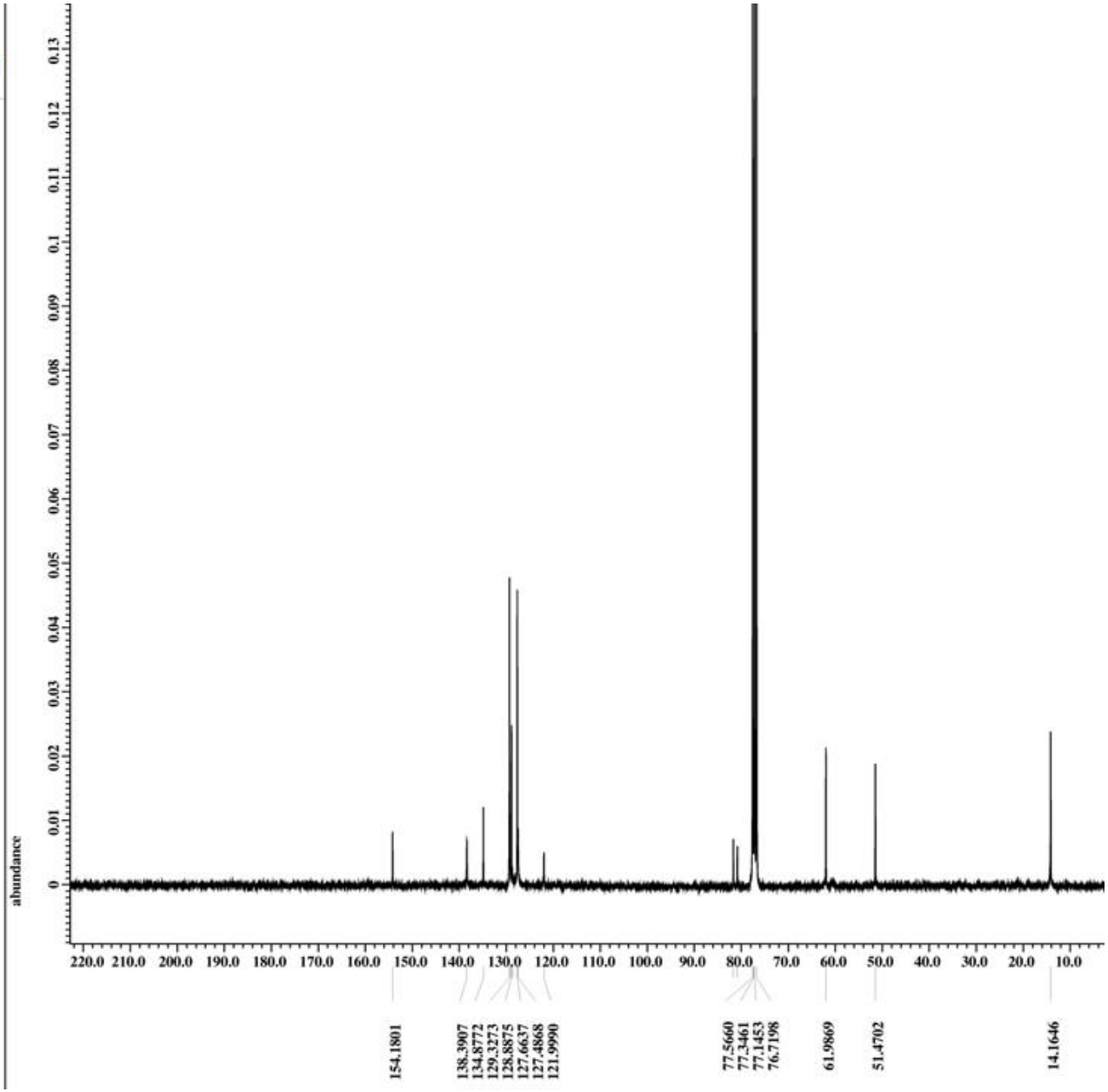

ilename = sm_VI_87_pure-2.jdf
uthor = delta
xperiment = single_pulse_dec
ample_id = S#18841
olvent = METHANOL-D3
reation_time = 8-JAN-2010 13:31:51
evision_time = 8-JAN-2010 13:48:16
urrent_time = 28-MAR-2010 12:29:40
omment = single pulse decouple
ata_format = 1D COMPLEX
im_size = 52428
im_title = 13C
im_units = [ppm]
imensions = X
ite = ECX 300
pectrometer = DELTA2_NMR
ield_strength = 7.0586013[T] (300[MHz
_acq_duration = 2.76824064[s]
_domain = 13C
_freq = 75.56823426[MHz]
_offset = 100[ppm]
_points = 65536
_prescans = 4
_resolution = 0.36124027[Hz]
_sweep = 23.67424242[kHz]
rr_domain = 1H
rr_freq = 300.52965592[MHz]
rr_offset = 5[ppm]
lipped = TRUE
od_return = 10
cans = 8272
otal_scans = 8272
_90_width = 9.75[us]
_acq_time = 2.76824064[s]
_angle = 30[deg]
_atn = 8[dB]
_pulse = 3.25[us]
rr_atn_dec = 25[dB]
rr_atn_noe = 25[dB]
rr_noise = WALTZ
ecoupling = TRUE
nitial_wait = 1[s]
oe = TRUE
oe_time = 3[s]
ecvr_gain = 50
elaxation_delay = 3[s]
epetition_time = 5.76824064[s]
emp_get = 21[dC]
H2N
NH
N
NH
N
Br
O
Br
(thousandths)
50
40.0
30.0
20.0
10.0
0
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0
159.5962
149.5767
127.8645
124.3366
115.2444
111.3485
107.2661
100.0287
54.1902
42.1295
29.3230

APPENDIX 29
^{1}H AND ^{13}C NMR SPECTRUM OF
Ethyl 3-(1-benzyl-1H-imidazol-4-yl)propiolate (224)

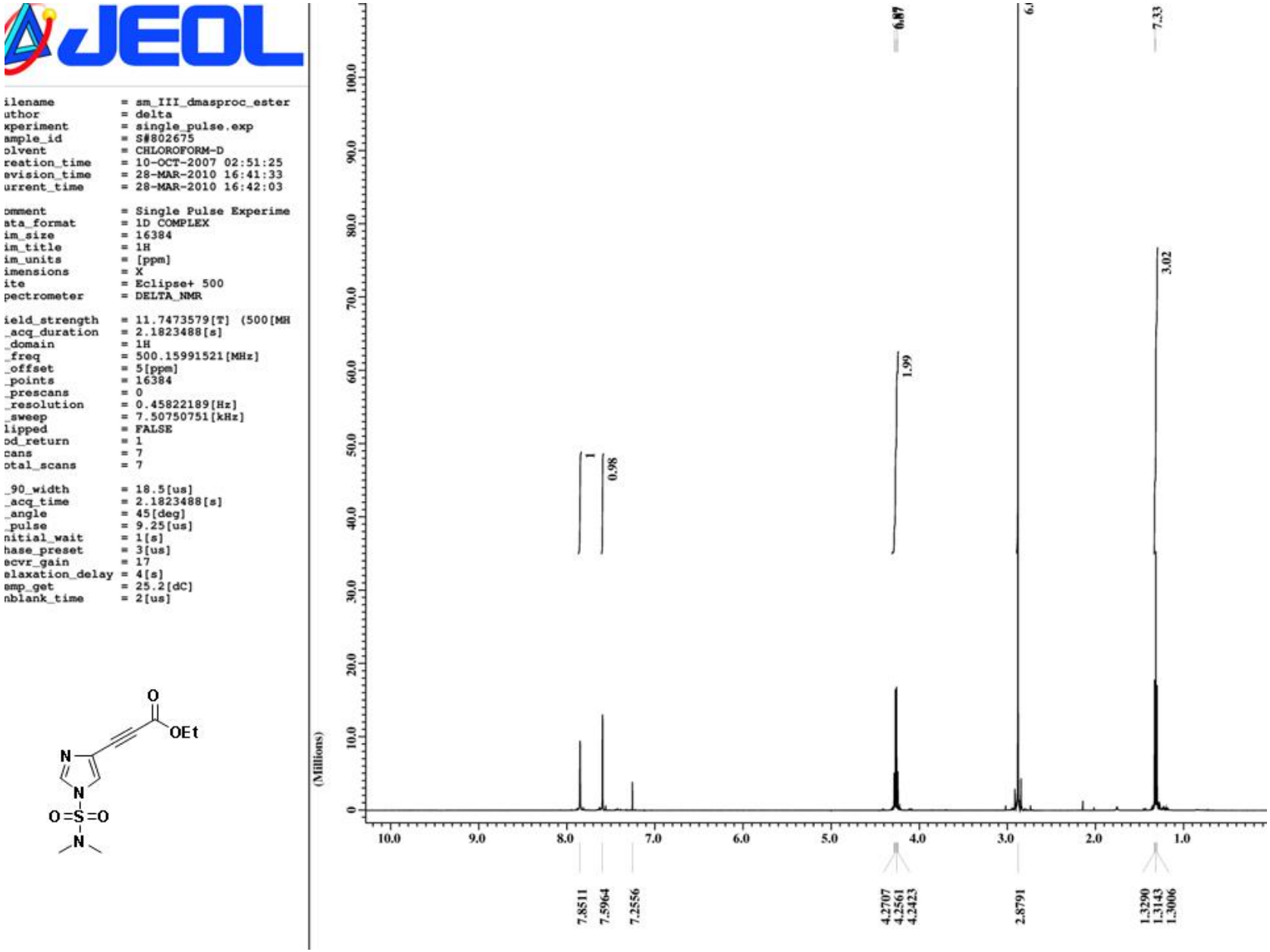
JEOL
filename = sm_III_88_PURE_300-4.
author = delta
experiment = single_pulse.ex2
sample_id = S#576335
solvent = CHLOROFORM-D
creation_time = 12-OCT-2007 16:24:59
revision_time = 28-MAR-2010 12:39:32
current_time = 28-MAR-2010 12:40:42
comment = single_pulse
data_format = 1D COMPLEX
dim_size = 13107
dim_title = 1H
dim_units = [ppm]
dimensions = X
site = ECX 300
spectrometer = DELTA2_NMR
field_strength = 7.0586013[T] (300[MHz
acq_duration = 2.90717696[s]
domain = 1H
freq = 300.52965592[MHz]
offset = 5[ppm]
points = 16384
prescans = 0
resolution = 0.34397631[Hz]
sweep = 5.63570784[kHz]
xr_domain = 1H
xr_freq = 300.52965592[MHz]
xr_offset = 5[ppm]
xi_domain = 1H
xi_freq = 300.52965592[MHz]
xi_offset = 5[ppm]
zipped = FALSE
acqd_return = 1
scans = 24
total_scans = 24
x_90_width = 13.01[us]
x_acq_time = 2.90717696[s]
x_angle = 45[deg]
x_atn = 4[dB]
x_pulse = 6.505[us]
xr_mode = Off
xi_mode = Off
gamma_preamp = FALSE
initial_wait = 1[s]
recvr_gain = 46
relaxation_delay = 5[s]
repetition_time = 7.90717696[s]
temp_get = 23[dC]
abundance
4.06
3.0
2.03
2
3.07
7.57
7.52
7.3853
7.3693
7.3658
7.2559
7.1701
5.1145
4.2686
4.2446
4.2217
1.3408
1.3156
1.2927
O
OEt
N
N

```
ilename          = sm_III_88-3.jdf
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#836837
olvent           = CHLOROFORM-D
reation_time     = 11-APR-2009 06:36:41
evision_time     = 28-MAR-2010 12:46:18
urrent_time      = 28-MAR-2010 12:50:11

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 52428
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.76824064[s]
_domain          = 13C
_freq            = 75.56823426[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.36124027[Hz]
_sweep           = 23.67424242[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
lipped           = TRUE
od_return        = 10
cans             = 5000
otal_scans       = 5000

_90_width        = 9.75[us]
_acq_time        = 2.76824064[s]
_angle           = 30[deg]
_atn             = 8[dB]
_pulse           = 3.25[us]
rr_atn_dec       = 25[dB]
rr_atn_noe       = 25[dB]
rr_noise         = WALTZ
ecoupling        = TRUE
nitial_wait      = 1[s]
oe               = TRUE
oe_time          = 3[s]
ecvr_gain        = 50
elaxation_delay  = 3[s]
epetition_time   = 5.76824064[s]
emp_get          = 23.3[dC]
```

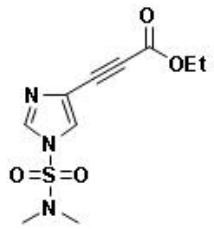


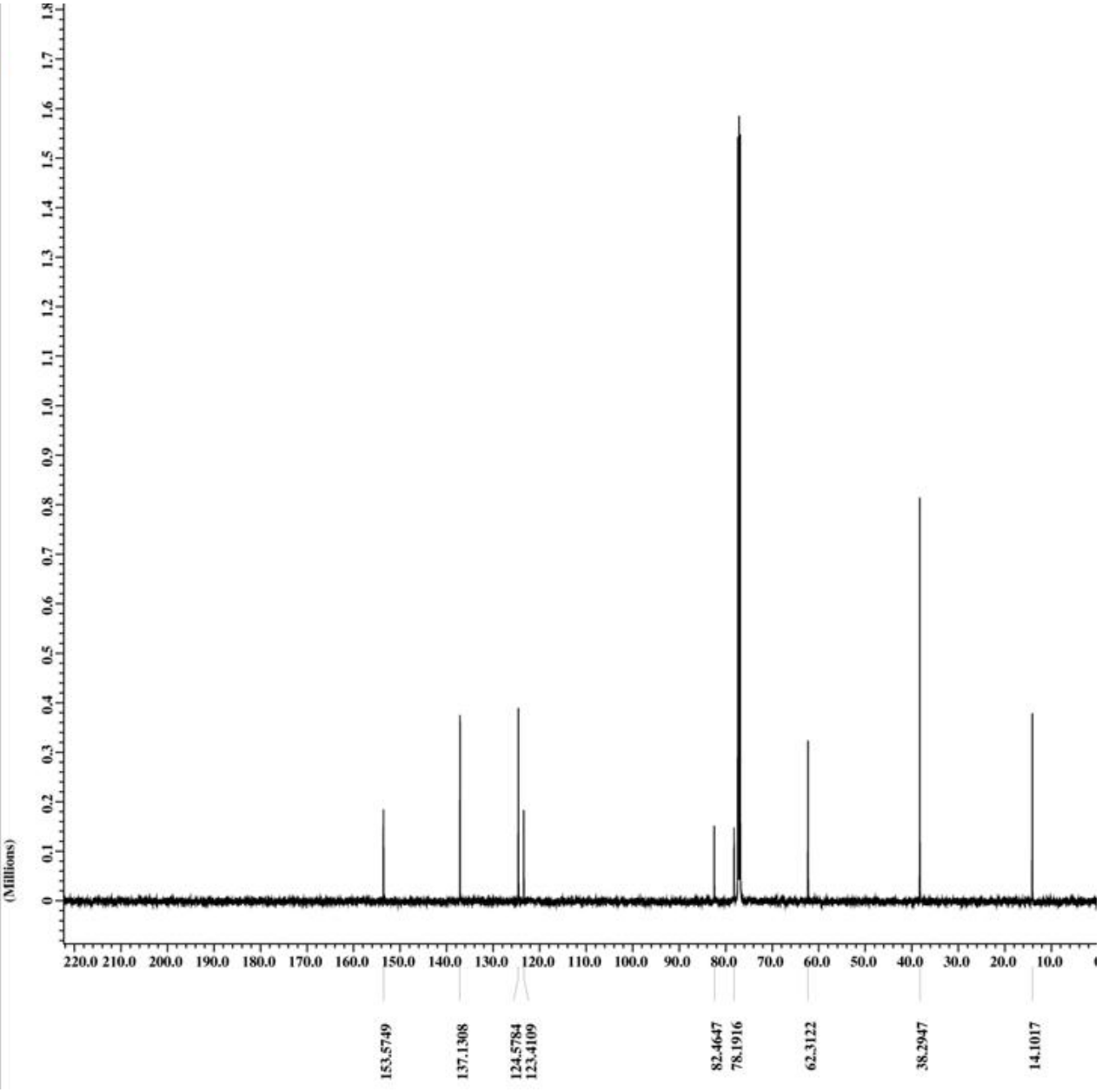


APPENDIX 30
^{1}H AND ^{13}C NMR SPECTRUM OF
Ethyl 3-(1-(N,N-dimethylsulfamoyl)-1H-imidazol-4-yl)propiolate (223)


ilename = sm_III_dmasproc_ester
uthor = delta
xperiment = single_pulse.exp
ample_id = S#802675
olvent = CHLOROFORM-D
reation_time = 10-OCT-2007 02:51:25
evision_time = 28-MAR-2010 16:41:33
urrent_time = 28-MAR-2010 16:42:03
omment = Single Pulse Experime
ata_format = 1D COMPLEX
im_size = 16384
im_title = 1H
im_units = [ppm]
imensions = X
ite = Eclipse+ 500
pectrometer = DELTA_NMR
ield_strength = 11.7473579[T] (500[MH
_acq_duration = 2.1823488[s]
_domain = 1H
_freq = 500.15991521[MHz]
_offset = 5[ppm]
_points = 16384
_prescans = 0
_resolution = 0.45822189[Hz]
_sweep = 7.50750751[kHz]
lipped = FALSE
od_return = 1
cans = 7
otal_scans = 7
_90_width = 18.5[us]
_acq_time = 2.1823488[s]
_angle = 45[deg]
_pulse = 9.25[us]
nitial_wait = 1[s]
hase_preset = 3[us]
ecvr_gain = 17
elaxation_delay = 4[s]
mp_get = 25.2[dC]
nblank_time = 2[us]
O
OEt
N
N
O=S=O
N
(Millions)
6.87
7.33
3.02
1.99
1
0.98
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
7.8511
7.5964
7.2556
4.2707
4.2561
4.2423
2.8791
1.3290
1.3143
1.3006

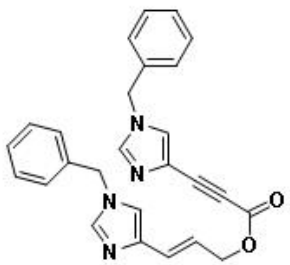
```
ilename          = sm_III_dmasproc_ester
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#804229
olvent           = CHLOROFORM-D
reation_time     = 10-OCT-2007 04:18:23
evision_time     = 10-OCT-2007 00:04:53
urrent_time      = 28-MAR-2010 16:45:21

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 65536
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7473579[T] (500[MH
_acq_duration    = 2.0840448[s]
_domain          = 13C
_freq            = 125.76529768[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.47983613[Hz]
_sweep           = 31.44654088[kHz]
rr_domain        = 1H
rr_freq          = 500.15991521[MHz]
rr_offset        = 5[ppm]
lipped           = TRUE
od_return        = 10
cans             = 1000
otal_scans       = 1000

_90_width        = 14.2[us]
_acq_time        = 2.0840448[s]
_angle           = 30[deg]
_pulse           = 4.73333333[us]
nitial_wait      = 1[s]
pe_time          = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 27
elaxation_delay  = 2[s]
emp_get          = 27[dC]
nblank_time      = 2[us]
```

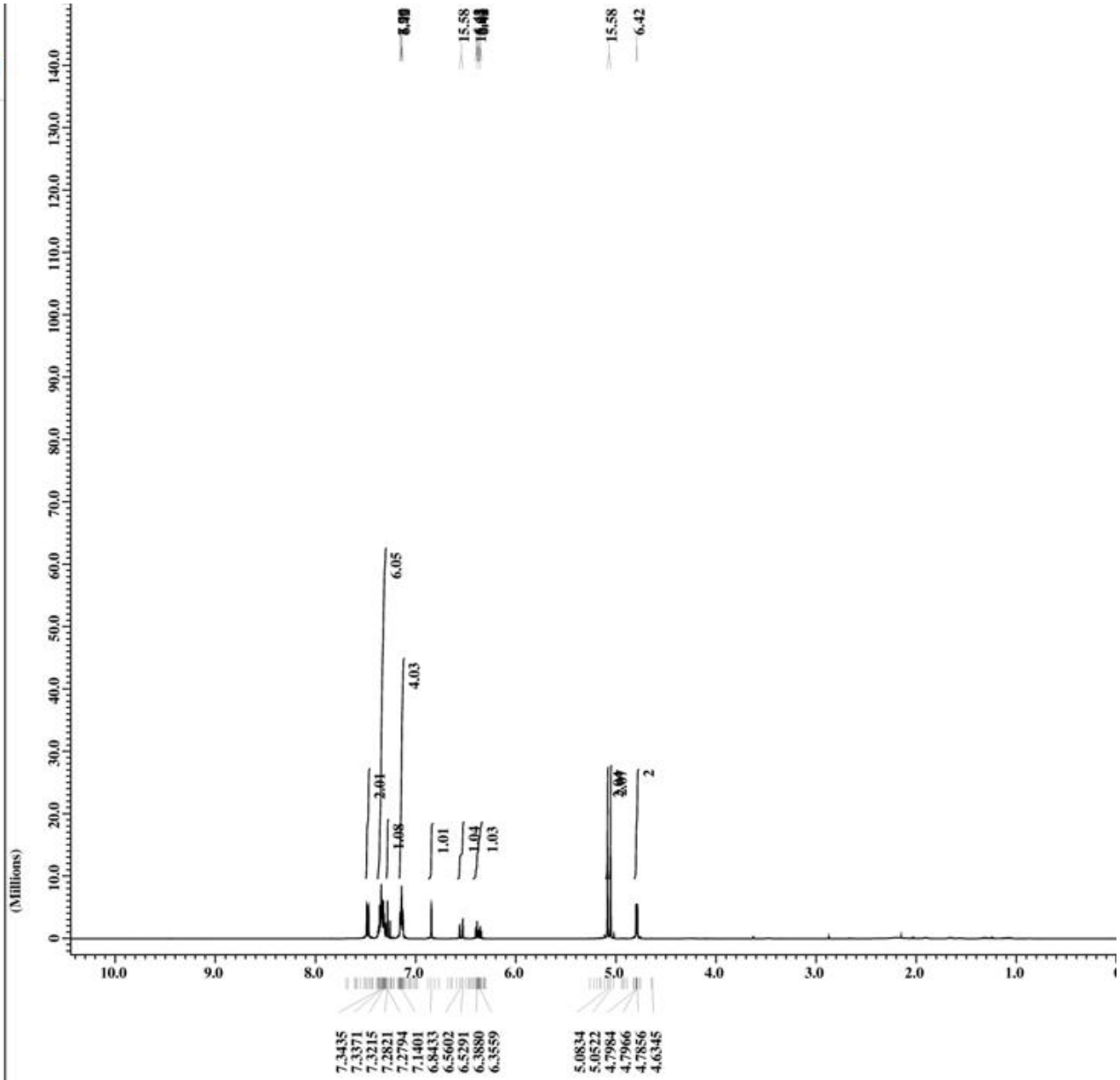




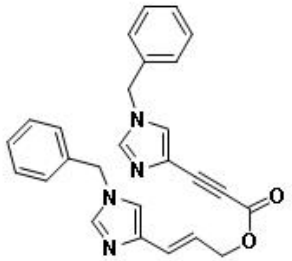
APPENDIX 31
^{1}H AND ^{13}C NMR SPECTRUM OF
(*E*)-3-(1-benzyl-1H-imidazol-4-yl)allyl 3-(1-benzyl-1H-imidazol-4-yl)propiolate
(228)

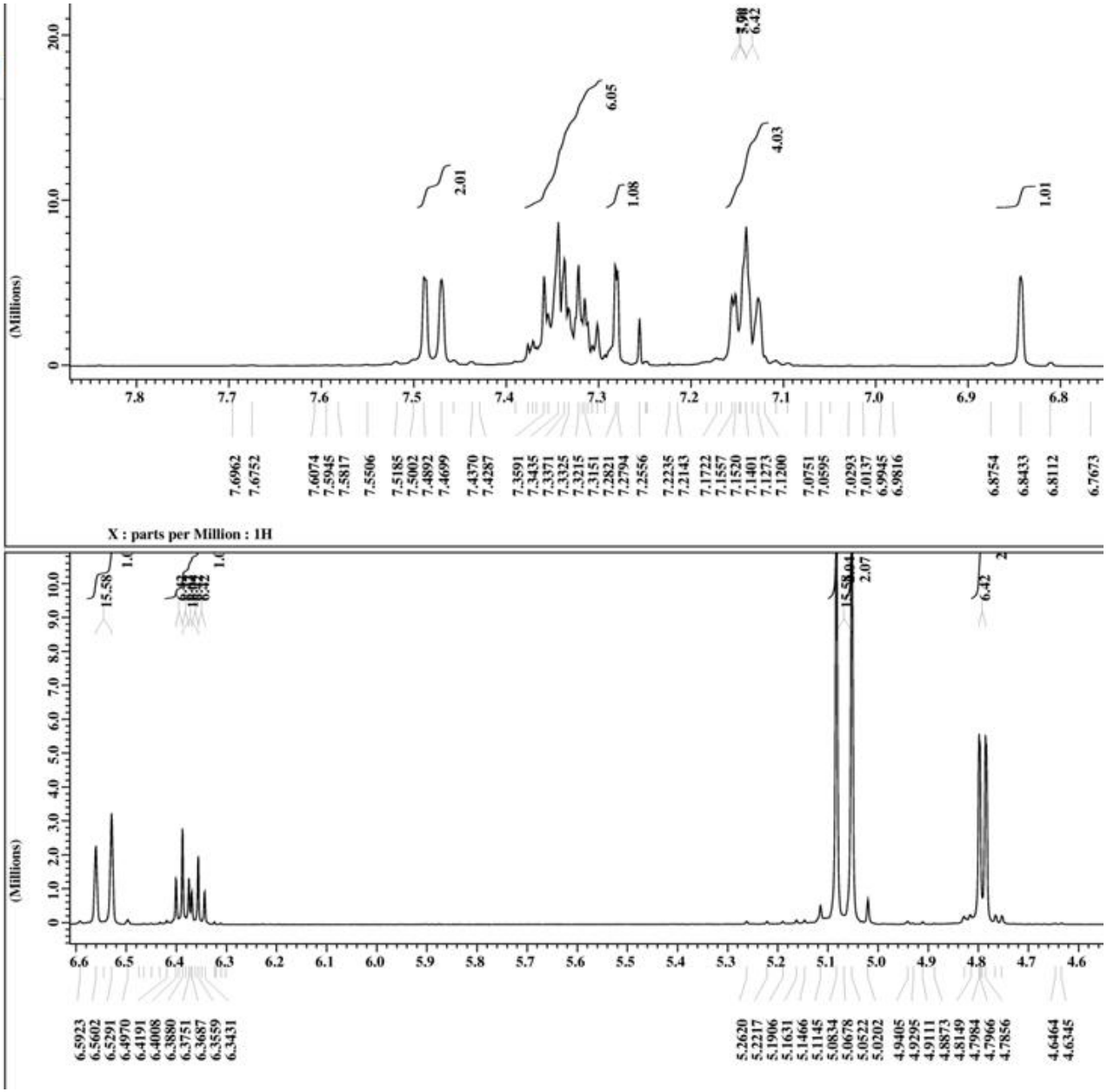
```
ilename          = sm_III_99_pure_500_2-
uthor            = delta
xperiment        = single_pulse.exp
ample_id         = S#448020
olvent           = CHLOROFORM-D
reation_time     = 17-OCT-2007 17:05:04
evision_time     = 28-MAR-2010 16:52:37
urrent_time      = 28-MAR-2010 16:54:15

omment           = Single Pulse Experime
ata_format       = 1D COMPLEX
im_size          = 16384
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7473579[T] (500[MH
_acq_duration    = 2.1823488[s]
_domain          = 1H
_freq            = 500.15991521[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.45822189[Hz]
_sweep           = 7.50750751[kHz]
lipped           = FALSE
od_return        = 1
cans             = 8
otal_scans       = 8

_90_width        = 18.5[us]
_acq_time        = 2.1823488[s]
_angle           = 45[deg]
_pulse           = 9.25[us]
nitial_wait      = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 18
elaxation_delay  = 4[s]
mp_get           = 25.2[dC]
nblank_time      = 2[us]
```



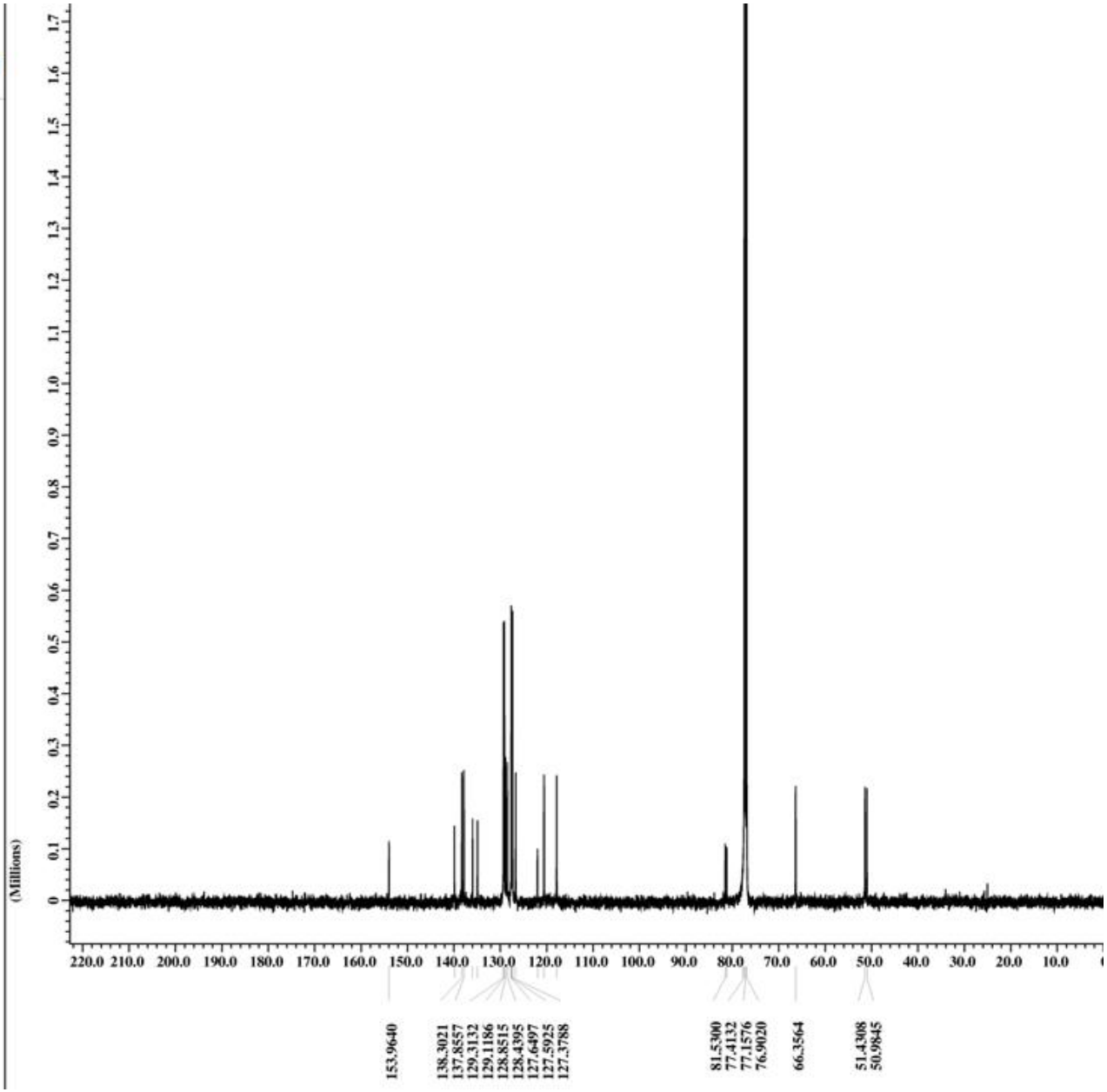


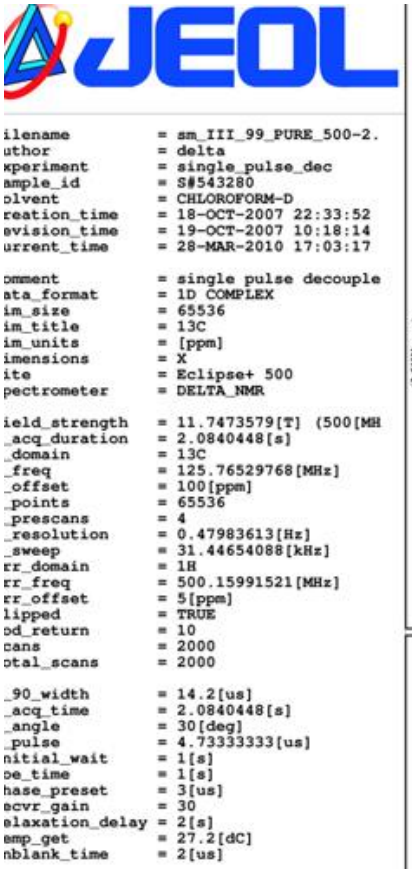
ilename	= sm_III_99_pure_500_2-
uthor	= delta
xperiment	= single_pulse.exp
ample_id	= S#448020
olvent	= CHLOROFORM-D
reation_time	= 17-OCT-2007 17:05:04
evision_time	= 28-MAR-2010 16:52:37
urrent_time	= 28-MAR-2010 16:58:03
omment	= Single Pulse Experime
ata_format	= 1D COMPLEX
im_size	= 16384
im_title	= 1H
im_units	= [ppm]
imensions	= X
ite	= Eclipse+ 500
pectrometer	= DELTA_NMR
ield_strength	= 11.7473579[T] (500[MH
_acq_duration	= 2.1823488[s]
_domain	= 1H
_freq	= 500.15991521[MHz]
_offset	= 5[ppm]
_points	= 16384
_prescans	= 0
_resolution	= 0.45822189[Hz]
_sweep	= 7.50750751[kHz]
lipped	= FALSE
od_return	= 1
cans	= 8
otal_scans	= 8
_90_width	= 18.5[us]
_acq_time	= 2.1823488[s]
_angle	= 45[deg]
_pulse	= 9.25[us]
nitial_wait	= 1[s]
hase_preset	= 3[us]
ecvr_gain	= 18
elaxation_delay	= 4[s]
mp_get	= 25.2[dC]
nblank_time	= 2[us]



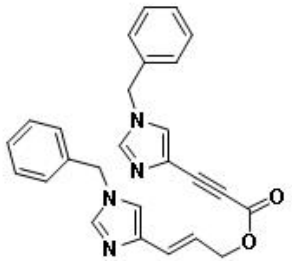


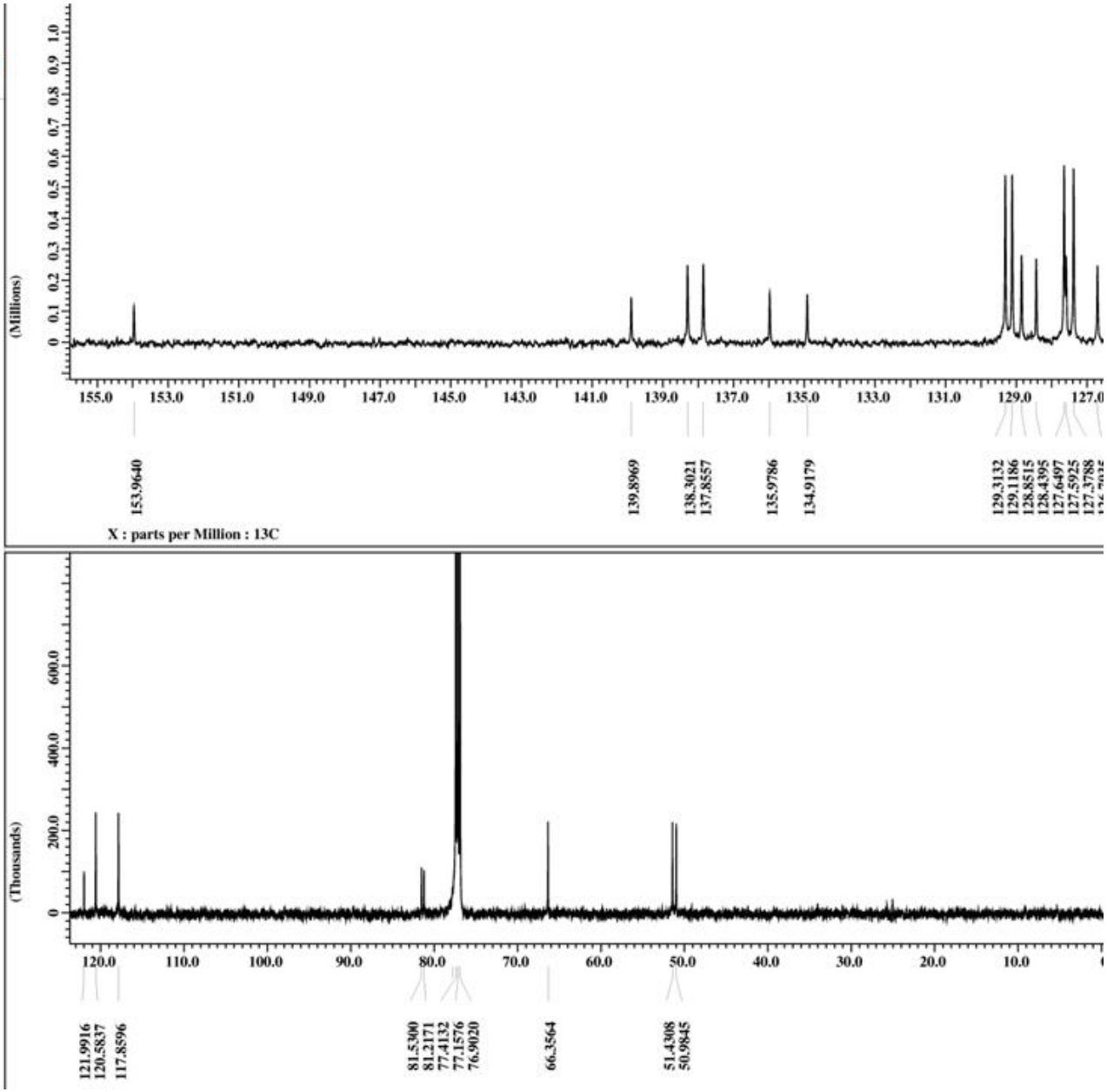
```
ilename          = sm_III_99_PURE_500-2.
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#543280
olvent           = CHLOROFORM-D
reation_time     = 18-OCT-2007 22:33:52
evision_time     = 19-OCT-2007 10:18:14
urrent_time      = 28-MAR-2010 17:01:01

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 65536
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7473579[T] (500[MH
_acq_duration    = 2.0840448[s]
_domain          = 13C
_freq            = 125.76529768[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.47983613[Hz]
_sweep           = 31.44654088[kHz]
rr_domain        = 1H
rr_freq          = 500.15991521[MHz]
rr_offset        = 5[ppm]
lipped           = TRUE
od_return        = 10
cans             = 2000
otal_scans       = 2000

_90_width        = 14.2[us]
_acq_time        = 2.0840448[s]
_angle           = 30[deg]
_pulse           = 4.73333333[us]
nitial_wait      = 1[s]
oe_time          = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 30
elaxation_delay  = 2[s]
emp_get          = 27.2[dC]
nblank_time      = 2[us]
```



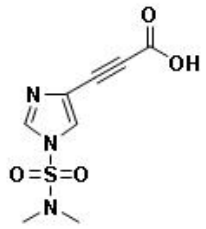
```
ilename          = sm_III_99_PURE_500-2.
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#543280
olvent           = CHLOROFORM-D
reation_time     = 18-OCT-2007 22:33:52
evision_time     = 19-OCT-2007 10:18:14
urrent_time      = 28-MAR-2010 17:03:17

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 65536
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7473579[T] (500[MH
_acq_duration    = 2.0840448[s]
_domain          = 13C
_freq            = 125.76529768[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.47983613[Hz]
_sweep           = 31.44654088[kHz]
rr_domain        = 1H
rr_freq          = 500.15991521[MHz]
rr_offset        = 5[ppm]
lipped           = TRUE
od_return        = 10
cans             = 2000
otal_scans       = 2000

_90_width        = 14.2[us]
_acq_time        = 2.0840448[s]
_angle           = 30[deg]
_pulse           = 4.73333333[us]
nitial_wait      = 1[s]
oe_time          = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 30
elaxation_delay  = 2[s]
emp_get          = 27.2[dC]
nblank_time      = 2[us]
```

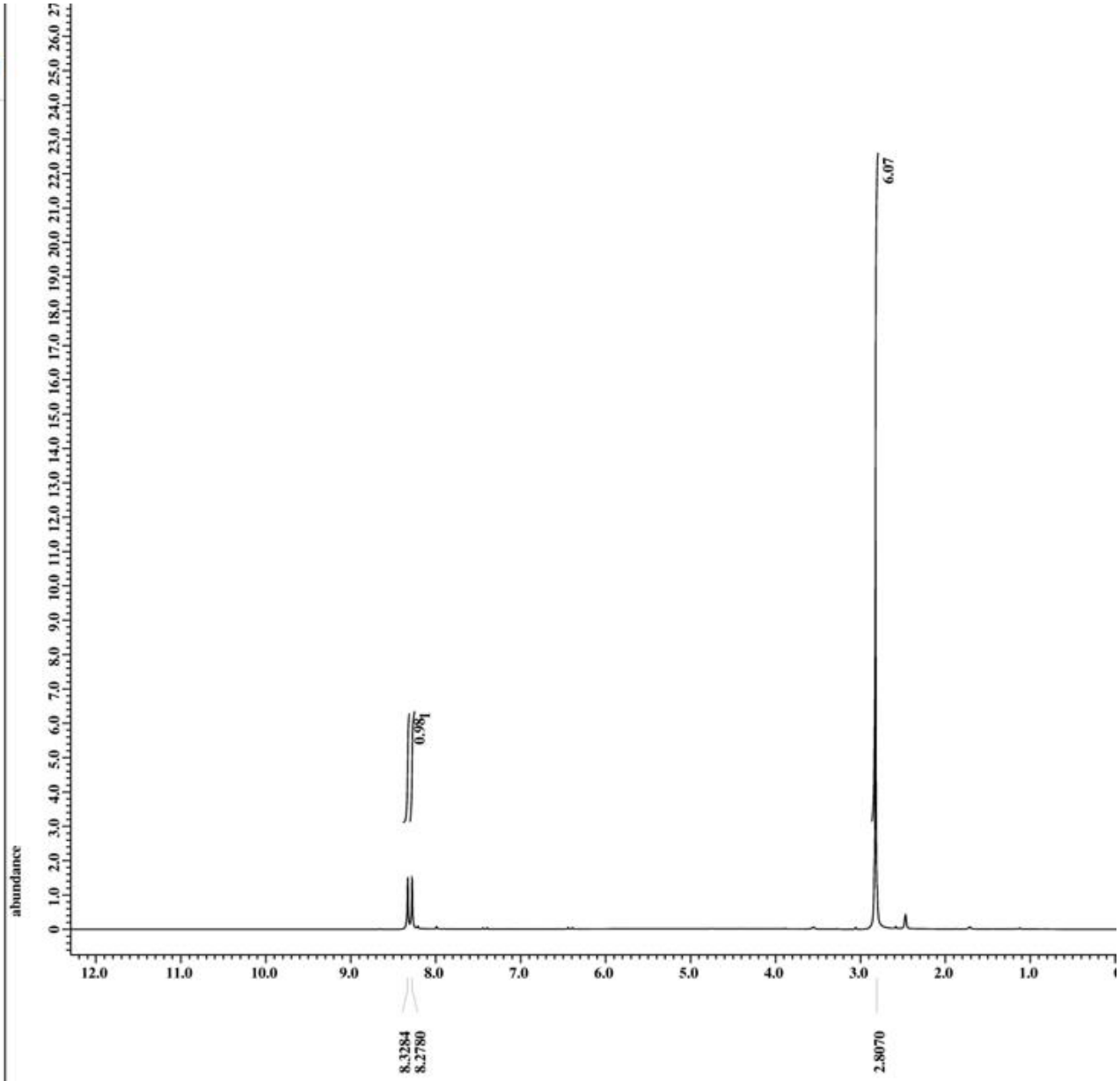




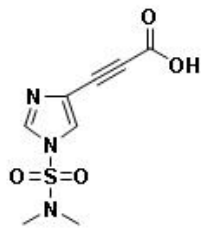
APPENDIX 32
^{1}H AND ^{13}C NMR SPECTRUM OF
3-(1-(N,N-dimethylsulfamoyl)-1H-imidazol-4-yl)propiolic acid (225)

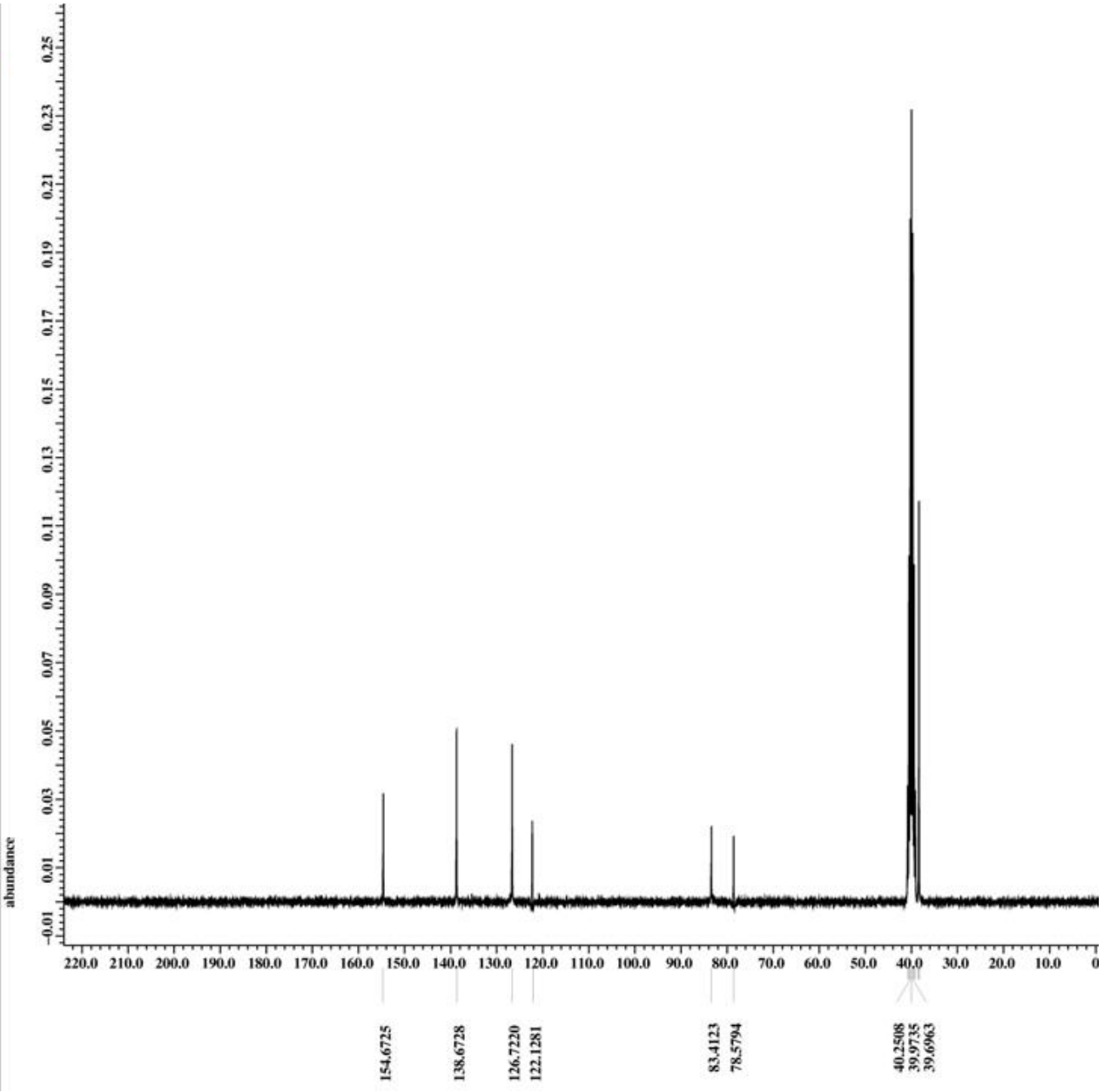
```
ilename          = sm_V_dmas_acid-4.jdf
uthor            = delta
xperiment        = single_pulse.ex2
ample_id         = S#679031
olvent           = DMSO-D6
reation_time     =  7-APR-2009 18:15:54
evision_time     = 28-MAR-2010 17:14:27
urrent_time      = 28-MAR-2010 17:22:01

omment           = single_pulse
ata_format       = 1D COMPLEX
im_size          = 13107
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.90717696[s]
_domain          = 1H
_freq            = 300.52965592[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.34397631[Hz]
_sweep           = 5.63570784[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
ri_domain        = 1H
ri_freq          = 300.52965592[MHz]
ri_offset        = 5[ppm]
lipped           = FALSE
od_return        = 1
cans             = 23
otal_scans       = 23

_90_width        = 13.01[us]
_acq_time        = 2.90717696[s]
_angle           = 45[deg]
_atn             = 4[dB]
_pulse           = 6.505[us]
rr_mode          = Off
ri_mode          = Off
ante_presat      = FALSE
nitial_wait      = 1[s]
ecvr_gain        = 38
elaxation_delay  = 5[s]
epetition_time   = 7.90717696[s]
emp_get          = 23.2[dC]
```





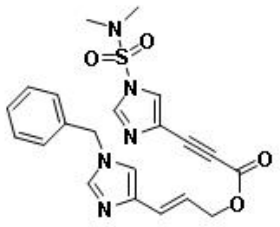
```
ilename          = sm_V_dmas_acid-3.jdf
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#681372
olvent           = DMSO-D6
reation_time     =  7-APR-2009 19:52:38
evision_time     =  8-APR-2009 11:41:20
urrent_time      = 28-MAR-2010 17:26:19

omment           = single pulse decouple
ata_format       = 1D REAL
im_size          = 52428
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.76824064[s]
_domain          = 13C
_freq            = 75.56823426[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.36124027[Hz]
_sweep           = 23.67424242[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
lipped           = FALSE
od_return        = 10
cans             = 1000
otal_scans       = 1000

_90_width        = 9.75[us]
_acq_time        = 2.76824064[s]
_angle           = 30[deg]
_atn             = 8[dB]
_pulse           = 3.25[us]
rr_atn_dec       = 25[dB]
rr_atn_noe       = 25[dB]
rr_noise         = WALTZ
ecoupling        = TRUE
nitial_wait      = 1[s]
oe               = TRUE
oe_time          = 3[s]
ecvr_gain        = 50
elaxation_delay  = 3[s]
epetition_time   = 5.76824064[s]
emp_get          = 23.2[dC]
```

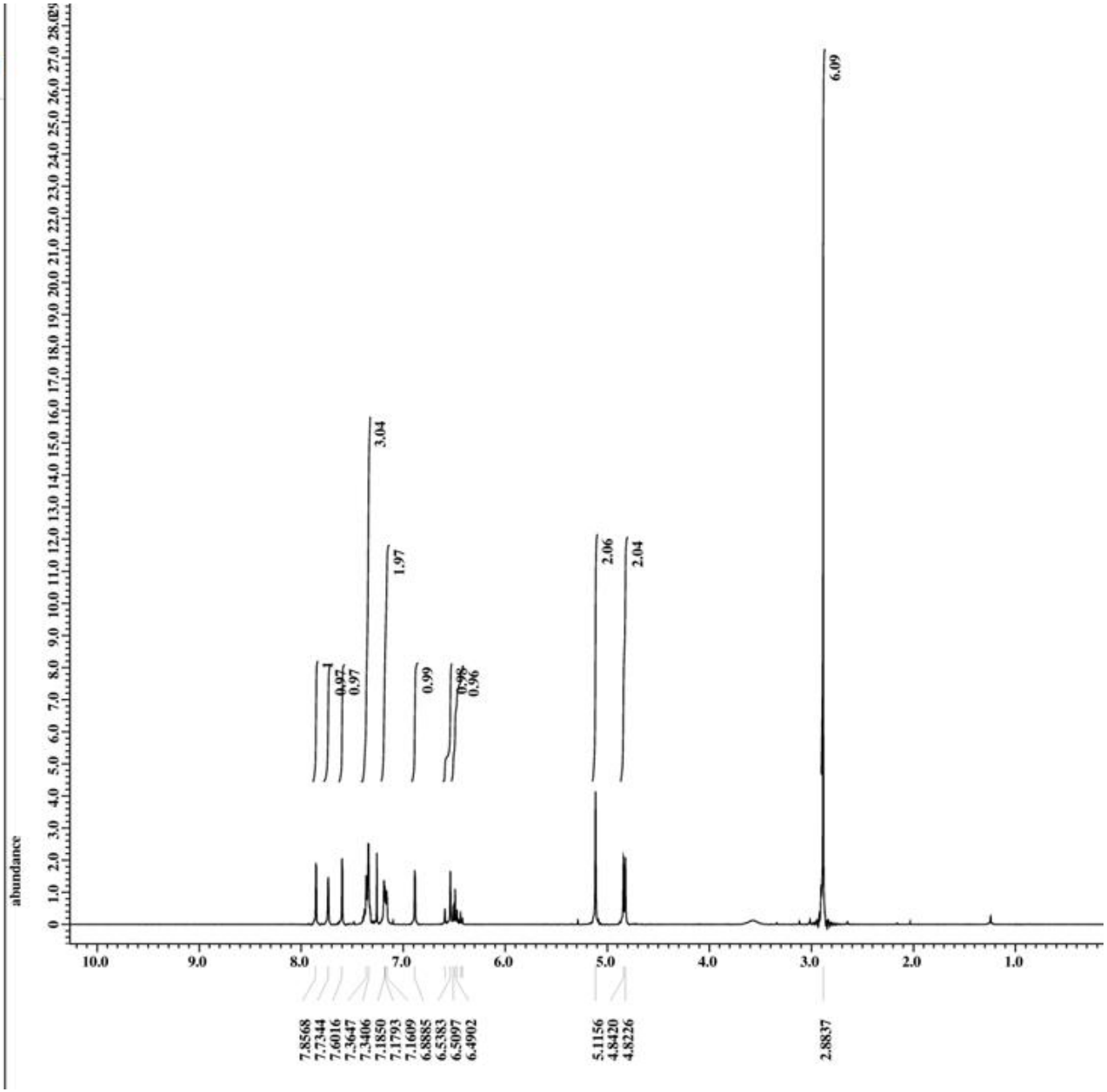


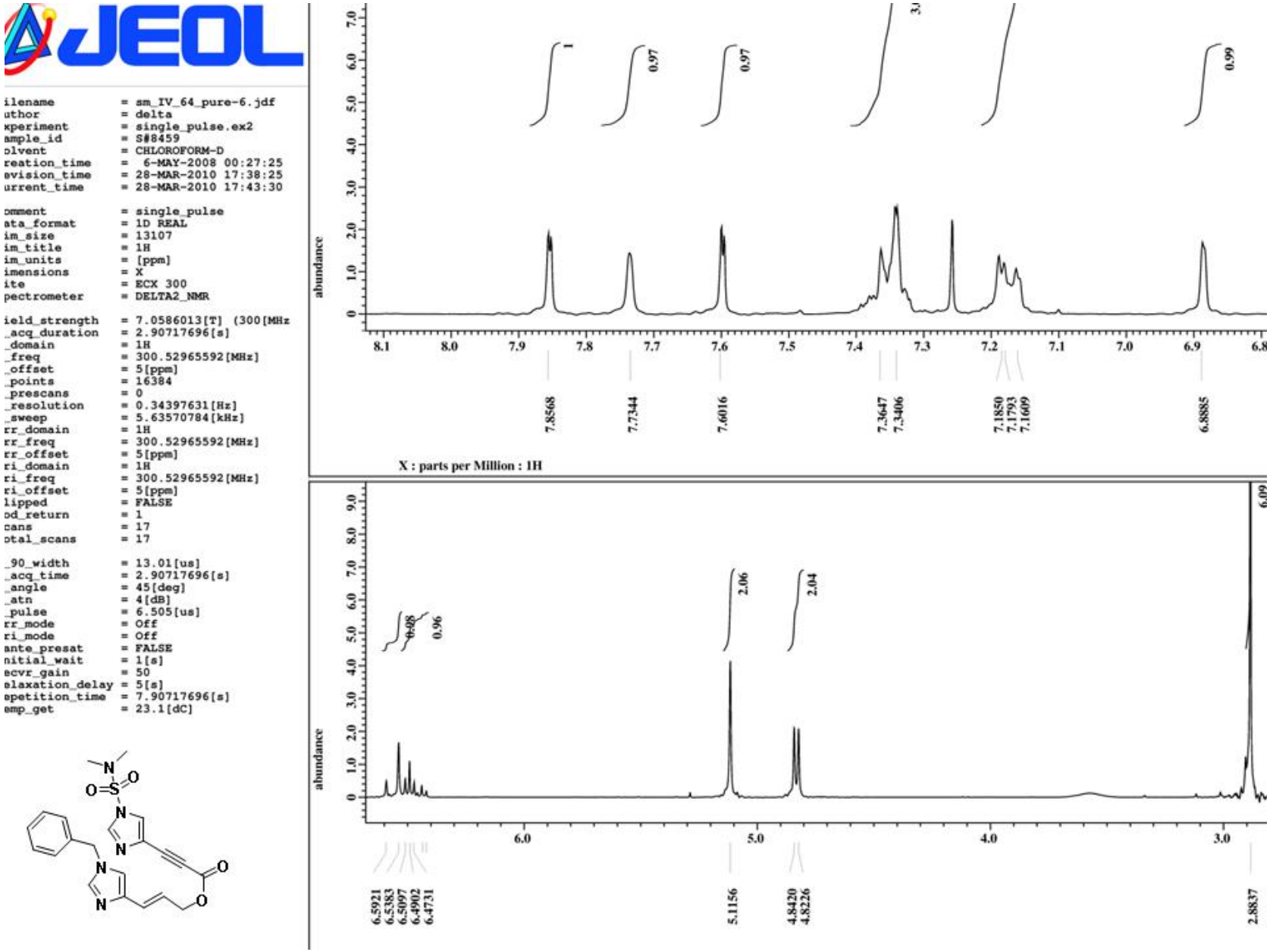


APPENDIX 33
^{1}H AND ^{13}C NMR SPECTRUM OF
(*E*)-3-(1-benzyl-1H-imidazol-4-yl)allyl-3-(1-(N,N-dimethylsulfamoyl)-1H-imidazol-4-yl)propiolate (227)

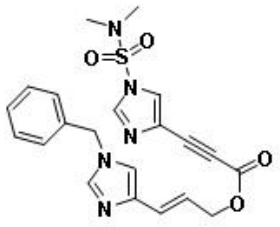
```
ilename          = sm_IV_64_pure-6.jdf
uthor            = delta
xperiment        = single_pulse.ex2
ample_id         = S#8459
olvent           = CHLOROFORM-D
reation_time     =  6-MAY-2008 00:27:25
evision_time     = 28-MAR-2010 17:38:25
urrent_time      = 28-MAR-2010 17:39:10

omment           = single_pulse
ata_format       = 1D REAL
im_size          = 13107
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.90717696[s]
_domain          = 1H
_freq            = 300.52965592[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.34397631[Hz]
_sweep           = 5.63570784[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
ri_domain        = 1H
ri_freq          = 300.52965592[MHz]
ri_offset        = 5[ppm]
lipped           = FALSE
od_return        = 1
cans             = 17
otal_scans       = 17

_90_width        = 13.01[us]
_acq_time        = 2.90717696[s]
_angle           = 45[deg]
_atn             = 4[dB]
_pulse           = 6.505[us]
rr_mode          = Off
ri_mode          = Off
ante_presat      = FALSE
nitial_wait      = 1[s]
ecvr_gain        = 50
elaxation_delay  = 5[s]
epetition_time   = 7.90717696[s]
emp_get          = 23.1[dC]
```

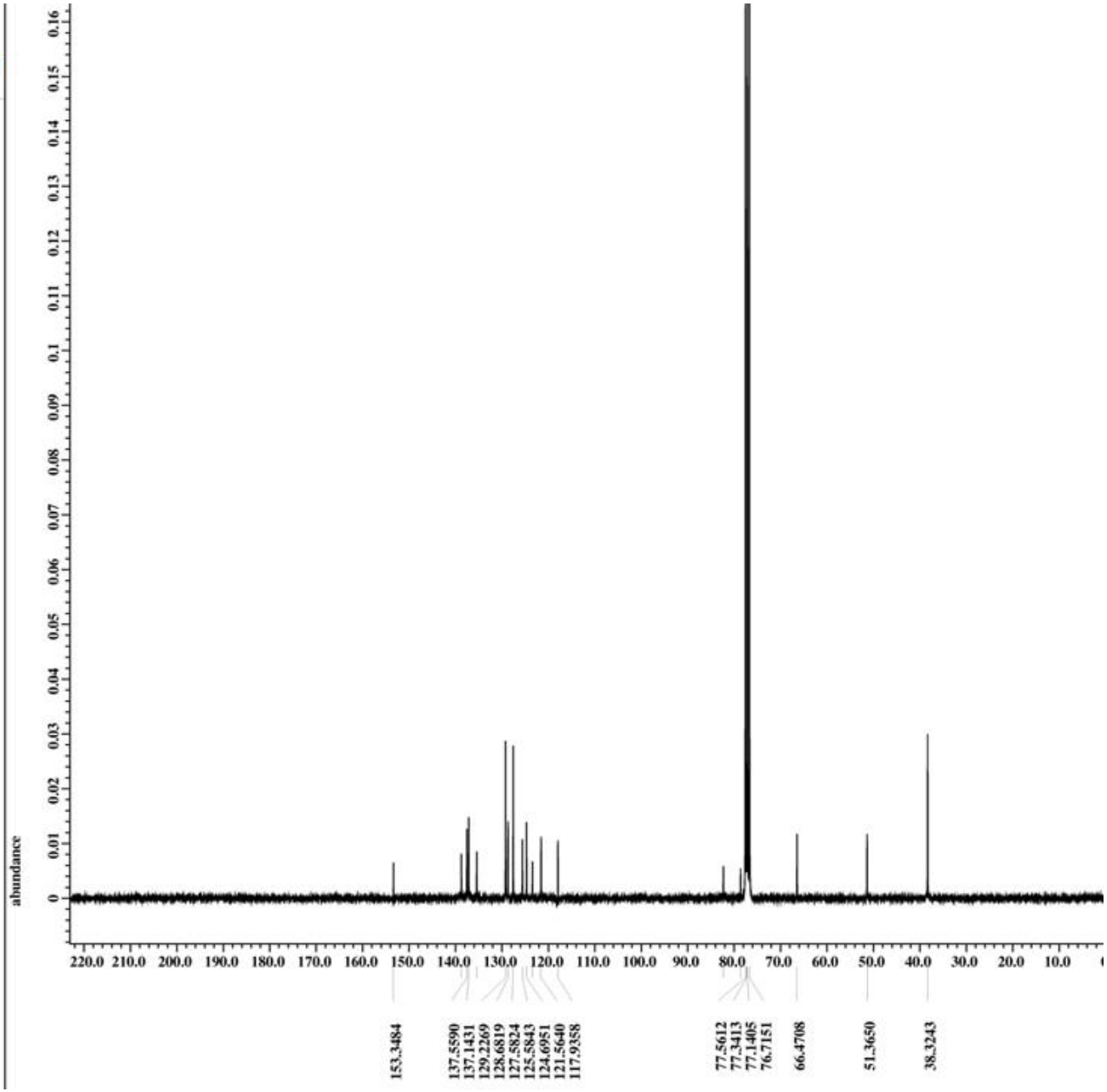




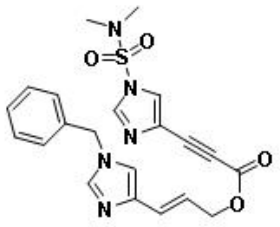

ilename = sm_IV_64_pure-6.jdf
uthor = delta
xperiment = single_pulse.ex2
ample_id = S#8459
olvent = CHLOROFORM-D
reation_time = 6-MAY-2008 00:27:25
evision_time = 28-MAR-2010 17:38:25
urrent_time = 28-MAR-2010 17:43:30
omment = single_pulse
ata_format = 1D REAL
im_size = 13107
im_title = 1H
im_units = [ppm]
imensions = X
ite = ECX 300
pectrometer = DELTA2_NMR
ield_strength = 7.0586013[T] (300[MHz
_acq_duration = 2.90717696[s]
_domain = 1H
_freq = 300.52965592[MHz]
_offset = 5[ppm]
_points = 16384
_prescans = 0
_resolution = 0.34397631[Hz]
_sweep = 5.63570784[kHz]
rr_domain = 1H
rr_freq = 300.52965592[MHz]
rr_offset = 5[ppm]
ri_domain = 1H
ri_freq = 300.52965592[MHz]
ri_offset = 5[ppm]
lipped = FALSE
od_return = 1
cans = 17
otal_scans = 17
_90_width = 13.01[us]
_acq_time = 2.90717696[s]
_angle = 45[deg]
_atn = 4[dB]
_pulse = 6.505[us]
rr_mode = Off
ri_mode = Off
ante_presat = FALSE
nitial_wait = 1[s]
ecvr_gain = 50
elaxation_delay = 5[s]
epetition_time = 7.90717696[s]
emp_get = 23.1[dC]
abundance
1
0.97
0.97
0.99
7.8568
7.7344
7.6016
7.3647
7.3406
7.1850
7.1793
7.1609
6.8885
X : parts per Million : 1H
abundance
0.98
0.96
2.06
2.04
6.5921
6.5383
6.5097
6.4902
6.4731
5.1156
4.8420
4.8226
2.8837

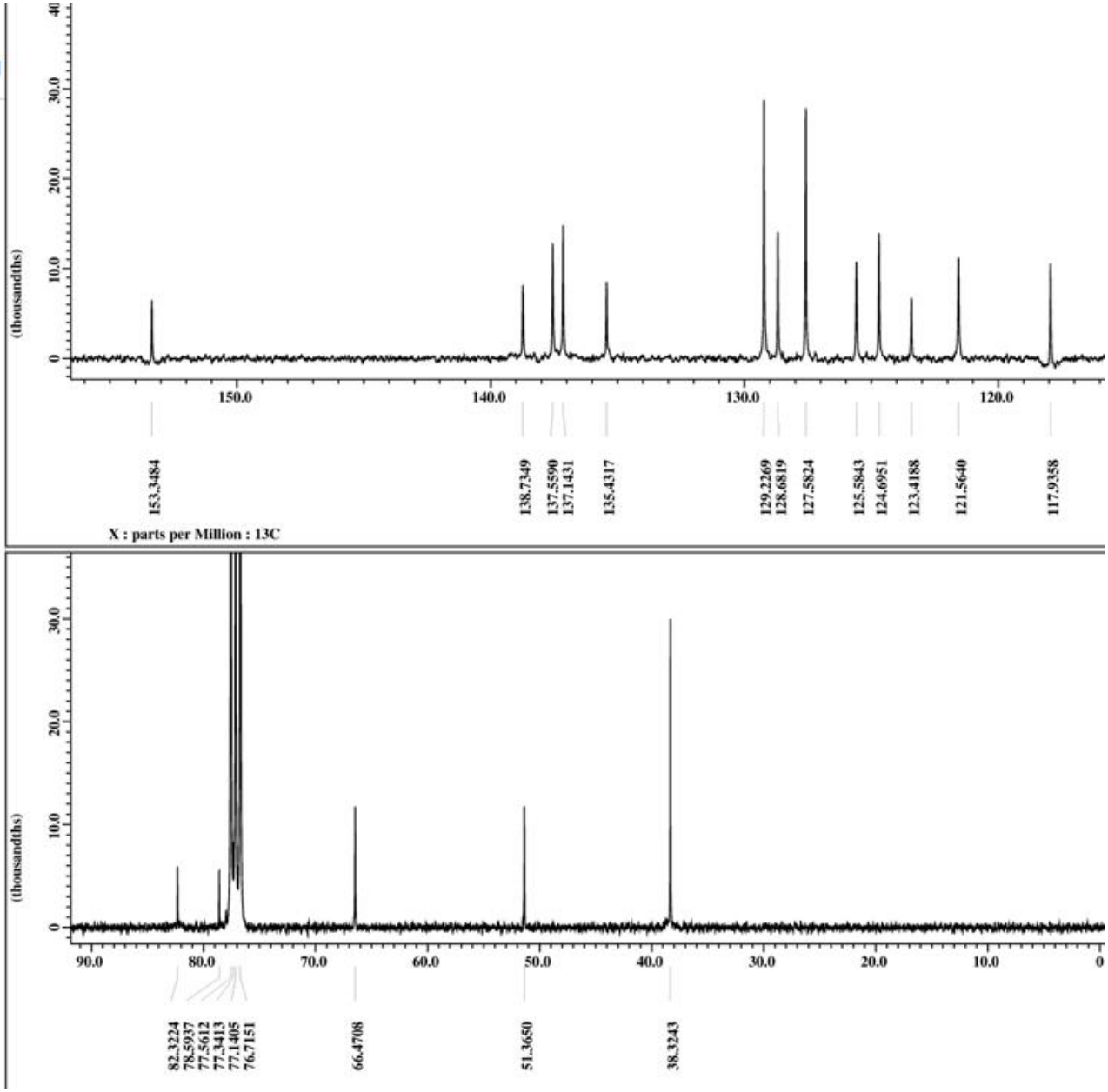
```
ilename          = sm_IV_64_pure-3.jdf
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#10441
olvent           = CHLOROFORM-D
reation_time     =  6-MAY-2008 08:29:25
evision_time     =  6-MAY-2008 11:49:19
urrent_time      = 28-MAR-2010 17:49:18

omment           = single pulse decouple
ata_format       = 1D REAL
im_size          = 52428
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.76824064[s]
_domain          = 13C
_freq            = 75.56823426[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.36124027[Hz]
_sweep           = 23.67424242[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
lipped           = TRUE
od_return        = 10
cans             = 5000
otal_scans       = 5000

_90_width        = 9.75[us]
_acq_time        = 2.76824064[s]
_angle           = 30[deg]
_atn             = 8[dB]
_pulse           = 3.25[us]
rr_atn_dec       = 25[dB]
rr_atn_noe       = 25[dB]
rr_noise         = WALTZ
ecoupling        = TRUE
nitial_wait      = 1[s]
oe               = TRUE
oe_time          = 3[s]
ecvr_gain        = 50
elaxation_delay  = 3[s]
epetition_time   = 5.76824064[s]
emp_get          = 23.3[dC]
```





```
ilename          = sm_IV_64_pure-3.jdf
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#10441
olvent           = CHLOROFORM-D
reation_time     =  6-MAY-2008 08:29:25
evision_time     =  6-MAY-2008 11:49:19
urrent_time      = 28-MAR-2010 17:52:01

omment           = single pulse decouple
ata_format       = 1D REAL
im_size          = 52428
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.76824064[s]
_domain          = 13C
_freq            = 75.56823426[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.36124027[Hz]
_sweep           = 23.67424242[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
lipped           = TRUE
od_return        = 10
cans             = 5000
otal_scans       = 5000

_90_width        = 9.75[us]
_acq_time        = 2.76824064[s]
_angle           = 30[deg]
_atn             = 8[dB]
_pulse           = 3.25[us]
rr_atn_dec       = 25[dB]
rr_atn_noe       = 25[dB]
rr_noise         = WALTZ
ecoupling        = TRUE
nitial_wait      = 1[s]
oe               = TRUE
oe_time          = 3[s]
ecvr_gain        = 50
elaxation_delay  = 3[s]
epetition_time   = 5.76824064[s]
emp_get          = 23.3[dC]
```

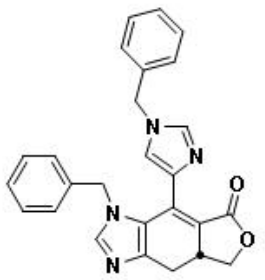


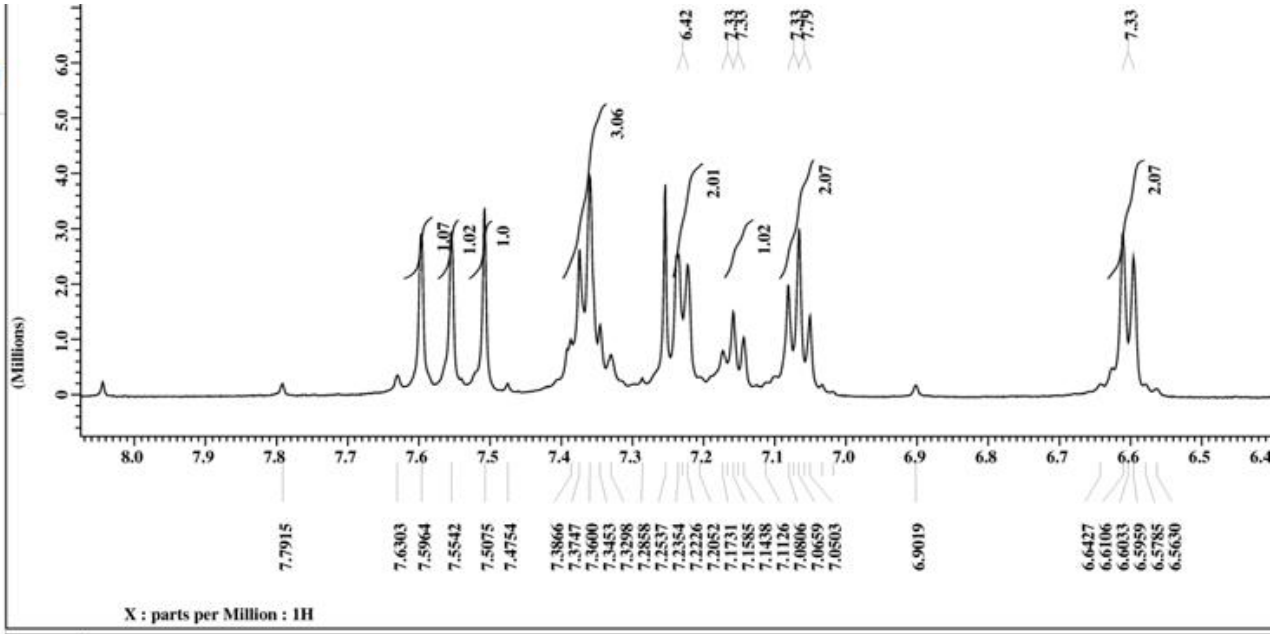


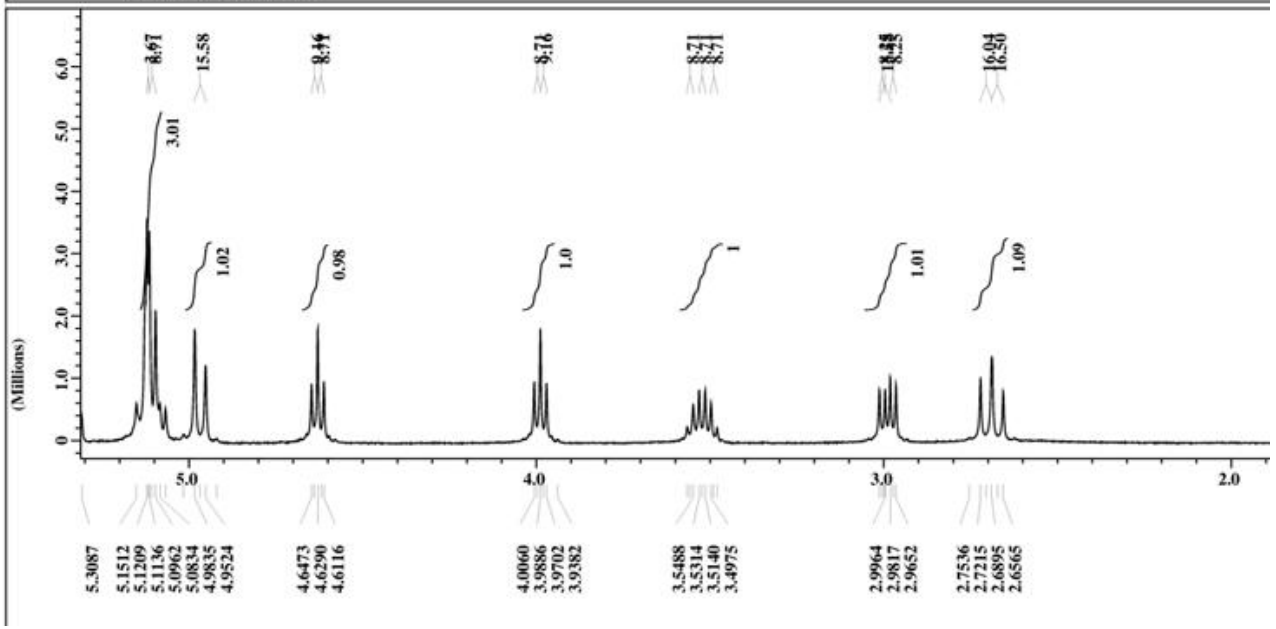
APPENDIX 34
^{1}H AND ^{13}C NMR SPECTRUM OF
(*R)-1-benzyl-8-(1-benzyl-1H-imidazol-4-yl)-4a,5-dihydro-1H-isobenzofuro[5,6-d]imidazol-7(4H)-one (230)**

JEOL
ilename = sm_III_100_pure_2~4.j
uthor = delta
xperiment = single_pulse.exp
ample_id = S#10791
olvent = CHLOROFORM-D
reation_time = 20-JAN-2008 05:45:53
evision_time = 28-MAR-2010 18:01:02
urrent_time = 28-MAR-2010 18:01:32
omment = Single Pulse Experime
ata_format = 1D COMPLEX
im_size = 16384
im_title = 1H
im_units = [ppm]
imensions = X
ite = Eclipse+ 500
pectrometer = DELTA_NMR
ield_strength = 11.7473579[T] (500[MH
_acq_duration = 2.1823488[s]
_domain = 1H
_freq = 500.15991521[MHz]
_offset = 5[ppm]
_points = 16384
_prescans = 0
_resolution = 0.45822189[Hz]
_sweep = 7.50750751[kHz]
lipped = FALSE
od_return = 1
cans = 7
otal_scans = 7
_90_width = 18.5[us]
_acq_time = 2.1823488[s]
_angle = 45[deg]
_pulse = 9.25[us]
nitial_wait = 1[s]
hase_preset = 3[us]
ecvr_gain = 20
elaxation_delay = 4[s]
emp_get = 25[dC]
nblank_time = 2[us]
(Millions)
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
40.0
30.0
20.0
10.0
0
16.84
8.74
8.71
6.74
8.74
15.58
8.67
7.33
7.39
7.42
3.01
3.06
2.07
2.07
2.01
1.02
1.02
0.98
1.0
1
1.01
1.09
7.7915
7.5964
7.5542
7.5075
7.3600
7.2537
7.0659
6.6106
6.5959
5.4452
5.1209
5.1136
4.6290
4.6116
4.0060
3.9886
3.9702
3.5314
3.5140
3.4975
2.9817
2.9652
2.7215
2.6895

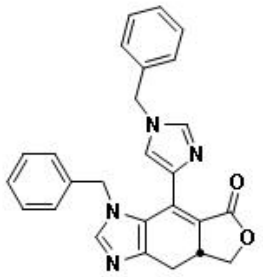
```
ilename          = sm_III_100_pure_2-4.j
uthor            = delta
xperiment        = single_pulse.exp
ample_id         = S#10791
olvent           = CHLOROFORM-D
reation_time     = 20-JAN-2008 05:45:53
evision_time     = 28-MAR-2010 18:01:02
urrent_time      = 28-MAR-2010 18:06:44

omment           = Single Pulse Experime
ata_format       = 1D COMPLEX
im_size          = 16384
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7473579[T] (500[MH
_acq_duration    = 2.1823488[s]
_domain          = 1H
_freq            = 500.15991521[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.45822189[Hz]
_sweep           = 7.50750751[kHz]
lipped           = FALSE
od_return        = 1
cans             = 7
otal_scans       = 7

_90_width        = 18.5[us]
_acq_time        = 2.1823488[s]
_angle           = 45[deg]
_pulse           = 9.25[us]
nitial_wait      = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 20
elaxation_delay  = 4[s]
emp_get          = 25[dC]
nblank_time      = 2[us]
```

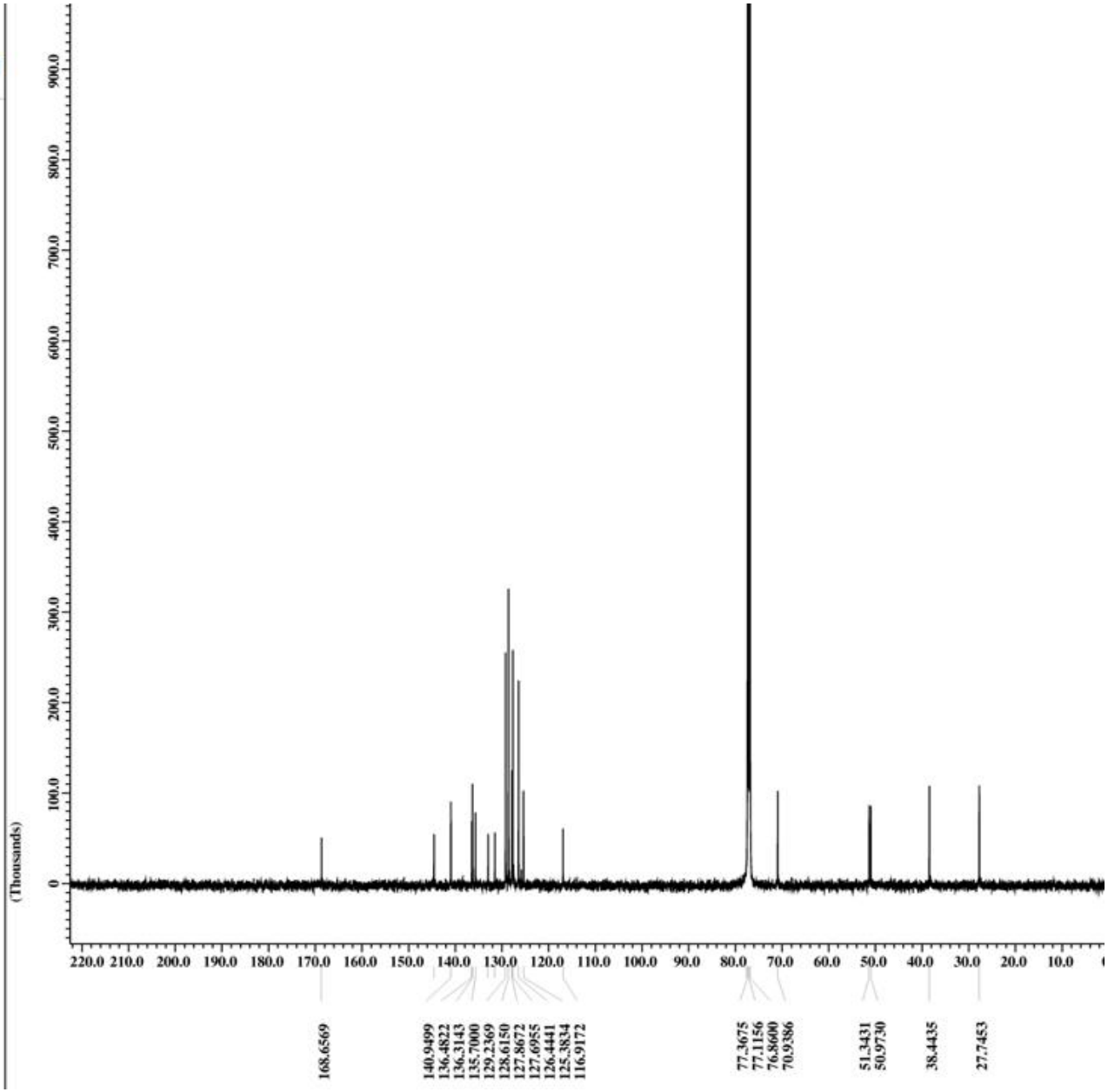




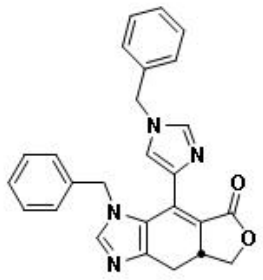


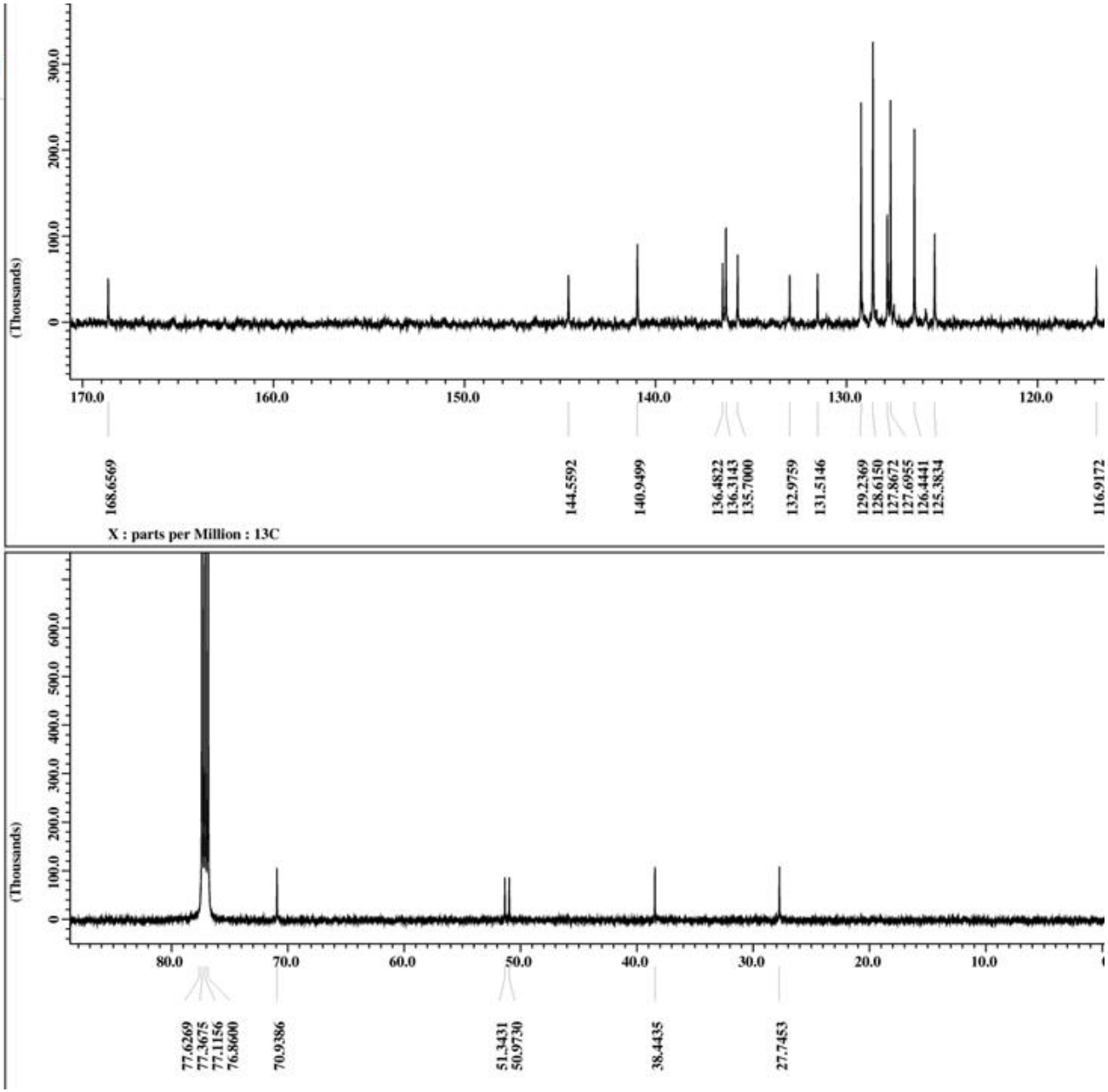
```
ilename          = sm_III_100_pure_2-2.j
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#12042
olvent           = CHLOROFORM-D
reation_time     = 20-JAN-2008 14:17:55
evision_time     = 20-JAN-2008 13:52:06
urrent_time      = 28-MAR-2010 18:09:27

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 65536
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7473579[T] (500[MH
_acq_duration    = 2.0840448[s]
_domain          = 13C
_freq            = 125.76529768[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.47983613[Hz]
_sweep           = 31.44654088[kHz]
rr_domain        = 1H
rr_freq          = 500.15991521[MHz]
rr_offset        = 5[ppm]
lipped           = FALSE
od_return        = 10
cans             = 6000
otal_scans       = 6000

_90_width        = 14.2[us]
_acq_time        = 2.0840448[s]
_angle           = 30[deg]
_pulse           = 4.73333333[us]
nitial_wait      = 1[s]
oe_time          = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 29
elaxation_delay  = 2[s]
amp_get          = 26.9[dC]
nblank_time      = 2[us]
```





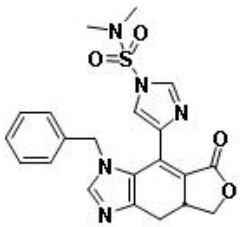
```
ilename          = sm_III_100_pure_2-2.j
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#12042
olvent           = CHLOROFORM-D
reation_time     = 20-JAN-2008 14:17:55
evision_time     = 20-JAN-2008 13:52:06
urrent_time      = 28-MAR-2010 18:12:13

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 65536
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7473579[T] (500[MH
_acq_duration    = 2.0840448[s]
_domain          = 13C
_freq            = 125.76529768[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.47983613[Hz]
_sweep           = 31.44654088[kHz]
rr_domain        = 1H
rr_freq          = 500.15991521[MHz]
rr_offset        = 5[ppm]
lipped           = FALSE
od_return        = 10
cans             = 6000
otal_scans       = 6000

_90_width        = 14.2[us]
_acq_time        = 2.0840448[s]
_angle           = 30[deg]
_pulse           = 4.73333333[us]
nitial_wait      = 1[s]
oe_time          = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 29
elaxation_delay  = 2[s]
amp_get          = 26.9[dC]
nblank_time      = 2[us]
```

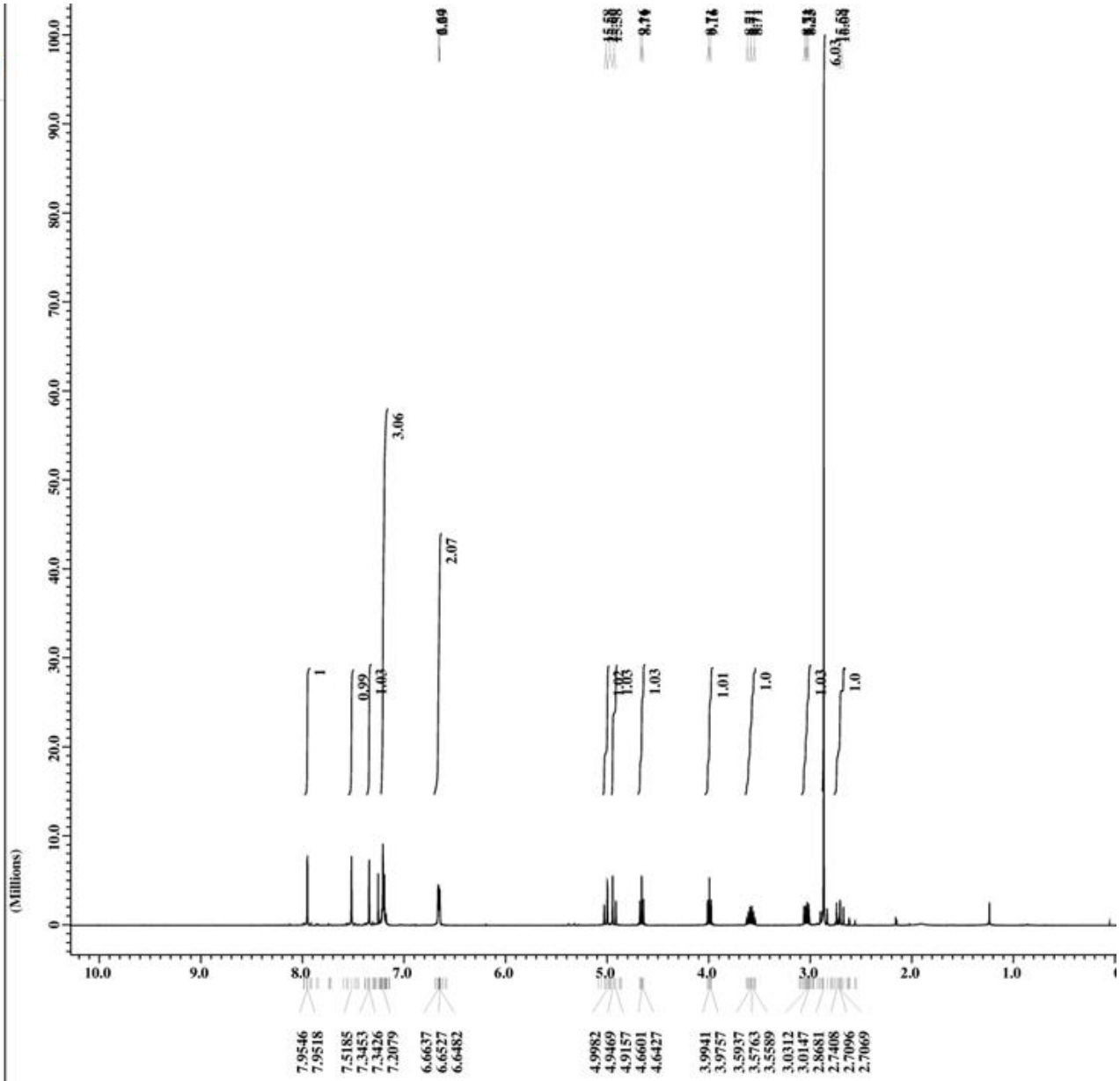




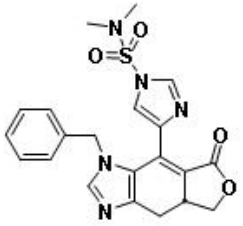
APPENDIX 35
^{1}H AND ^{13}C NMR SPECTRUM OF
(*R)-4-(1-benzyl-7-oxo-4,4a,5,7-tetrahydro-1H-isobenzofuro[5,6-d]imidazol-8-yl)-N,N-dimethyl-1H-imidazole-1-sulfonamide (229)**

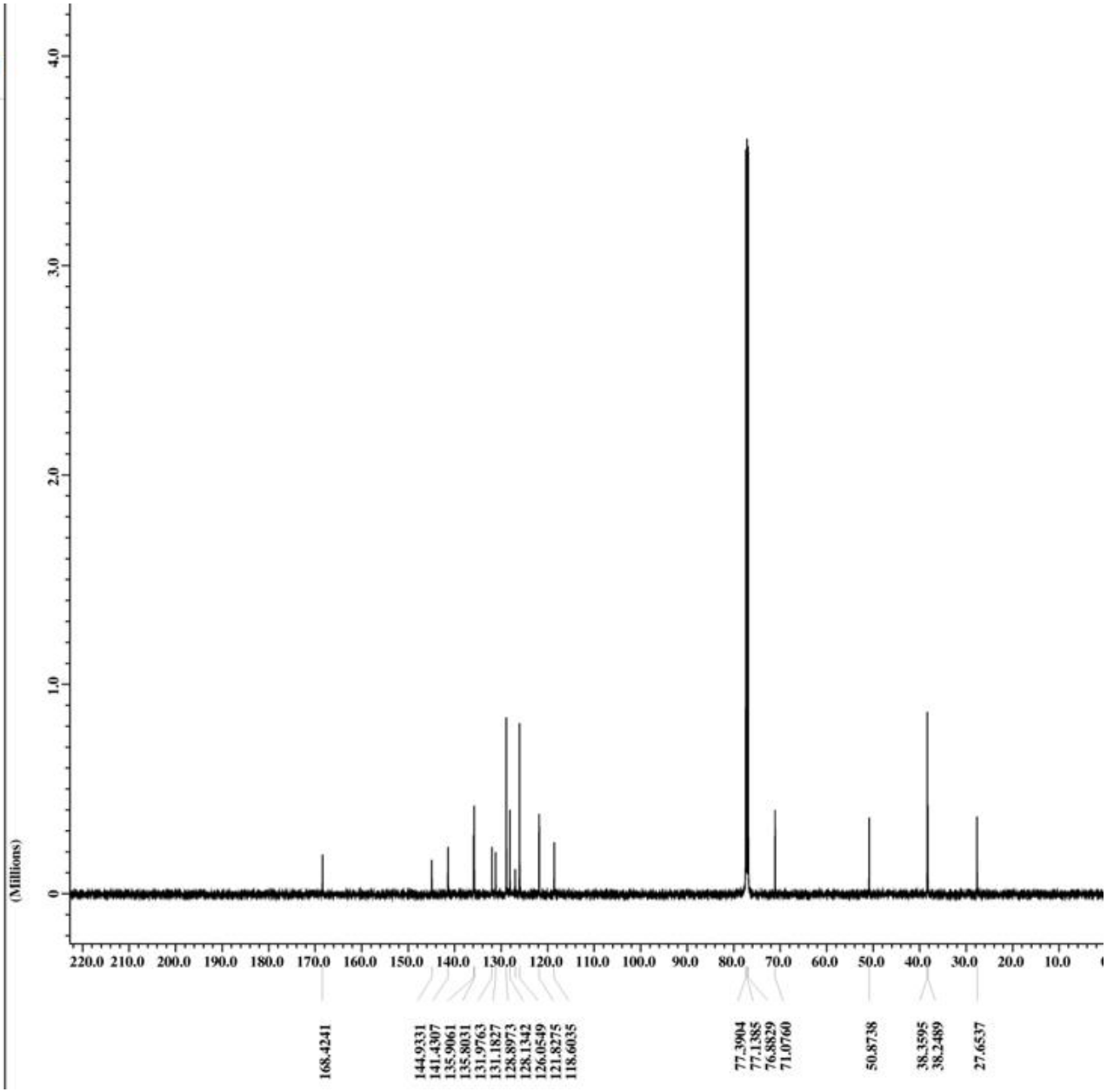
```
ilename          = sm_III_61_pure_500-6.
uthor            = delta
xperiment        = single_pulse.exp
ample_id         = S#822134
olvent           = CHLOROFORM-D
reation_time     =  4-SEP-2007 03:12:00
evision_time     = 28-MAR-2010 18:18:39
urrent_time      = 28-MAR-2010 18:19:05

omment           = Single Pulse Experime
ata_format       = 1D COMPLEX
im_size          = 16384
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7473579[T] (500[MH
_acq_duration    = 2.1823488[s]
_domain          = 1H
_freq            = 500.15991521[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.45822189[Hz]
_sweep           = 7.50750751[kHz]
lipped           = FALSE
od_return        = 1
cans             = 8
otal_scans       = 8

_90_width        = 18.5[us]
_acq_time        = 2.1823488[s]
_angle           = 45[deg]
_pulse           = 9.25[us]
nitial_wait      = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 18
elaxation_delay  = 4[s]
mp_get           = 25.1[dC]
nblank_time      = 2[us]
```



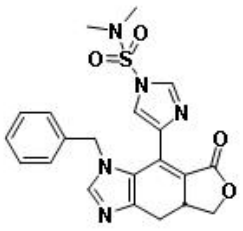


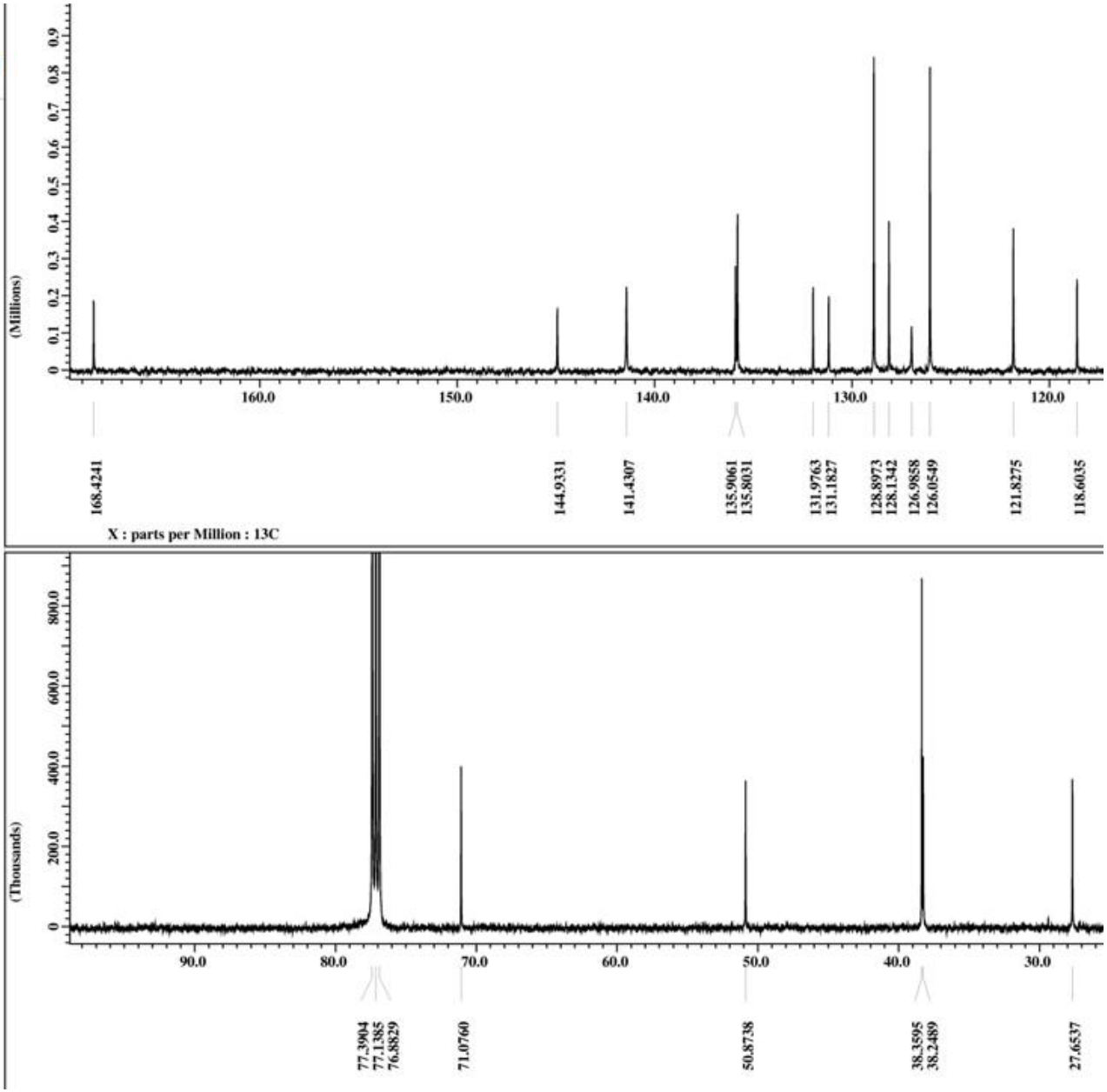
```
ilename          = sm_III_61_pure_500-2.
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#827058
olvent           = CHLOROFORM-D
reation_time     =  4-SEP-2007 10:23:45
evision_time     =  4-SEP-2007 09:55:03
urrent_time      = 28-MAR-2010 18:22:48

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 65536
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7473579[T] (500[MH
_acq_duration    = 2.0840448[s]
_domain          = 13C
_freq            = 125.76529768[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.47983613[Hz]
_sweep           = 31.44654088[kHz]
rr_domain        = 1H
rr_freq          = 500.15991521[MHz]
rr_offset        = 5[ppm]
lipped           = FALSE
od_return        = 10
cans             = 5000
otal_scans       = 5000

_90_width        = 14.2[us]
_acq_time        = 2.0840448[s]
_angle           = 30[deg]
_pulse           = 4.73333333[us]
nitial_wait      = 1[s]
pe_time          = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 30
elaxation_delay  = 2[s]
emp_get          = 25.7[dC]
nblank_time      = 2[us]
```





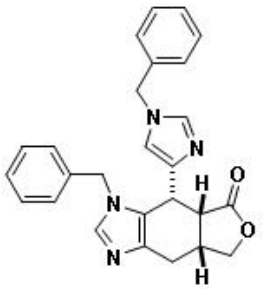
```
ilename          = sm_III_61_pure_500-2.
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#827058
olvent           = CHLOROFORM-D
reation_time     =  4-SEP-2007 10:23:45
evision_time     =  4-SEP-2007 09:55:03
urrent_time      = 28-MAR-2010 18:24:53

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 65536
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7473579[T] (500[MH
_acq_duration    = 2.0840448[s]
_domain          = 13C
_freq            = 125.76529768[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.47983613[Hz]
_sweep           = 31.44654088[kHz]
rr_domain        = 1H
rr_freq          = 500.15991521[MHz]
rr_offset        = 5[ppm]
lipped           = FALSE
od_return        = 10
cans             = 5000
otal_scans       = 5000

_90_width        = 14.2[us]
_acq_time        = 2.0840448[s]
_angle           = 30[deg]
_pulse           = 4.73333333[us]
nitial_wait      = 1[s]
pe_time          = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 30
elaxation_delay  = 2[s]
emp_get          = 25.7[dC]
nblank_time      = 2[us]
```

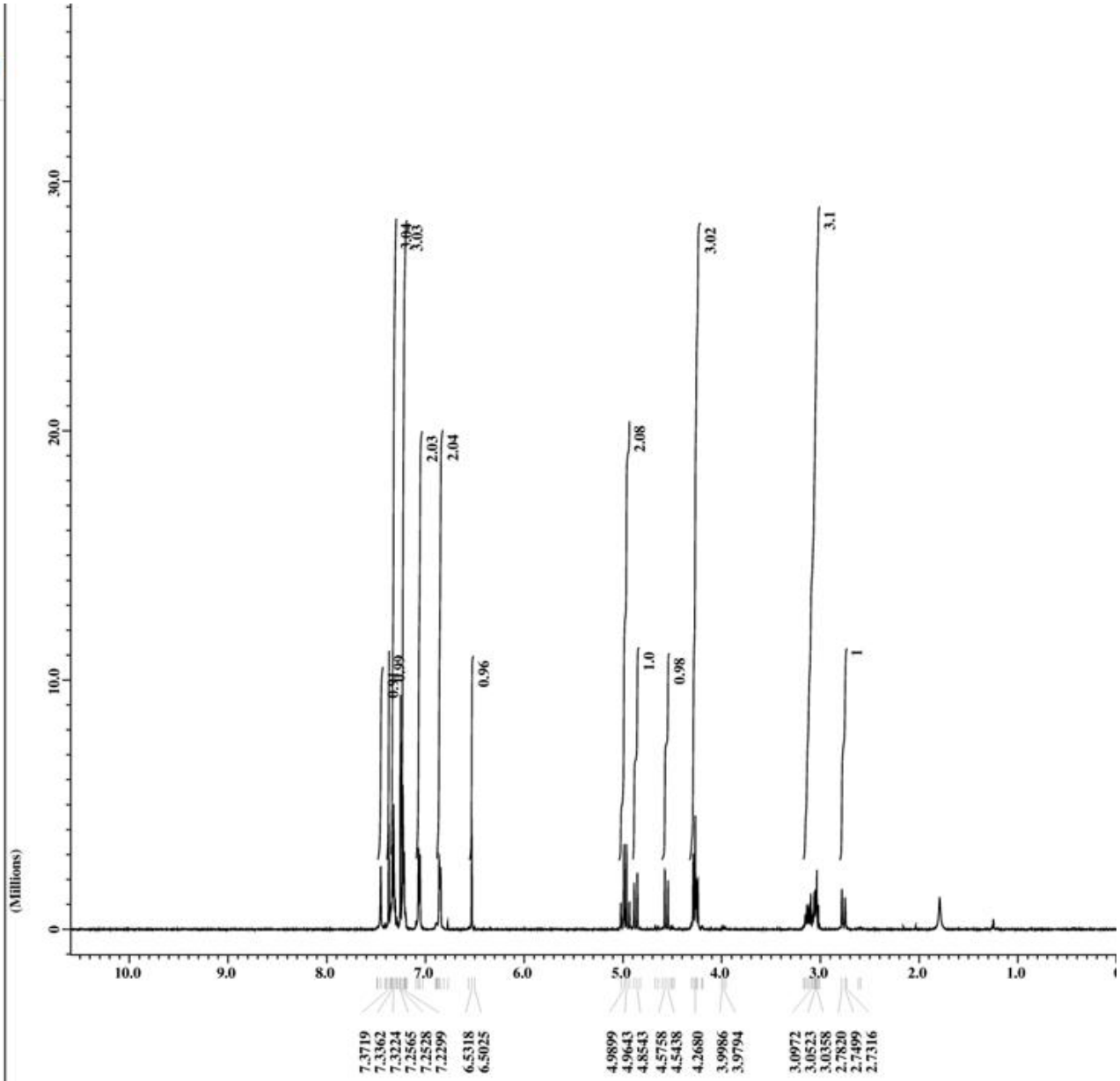




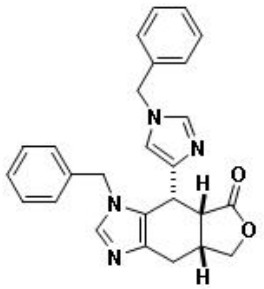
APPENDIX 36
^{1}H AND ^{13}C NMR SPECTRUM OF
(4a*R,7a*S**,8*R**)-1-benzyl-8-(1-benzyl-1H-imidazol-4-yl)-4a,5,7a,8-tetrahydro-1H-isobenzofuro[5,6-d]imidazol- 7(4H)-one (232)**

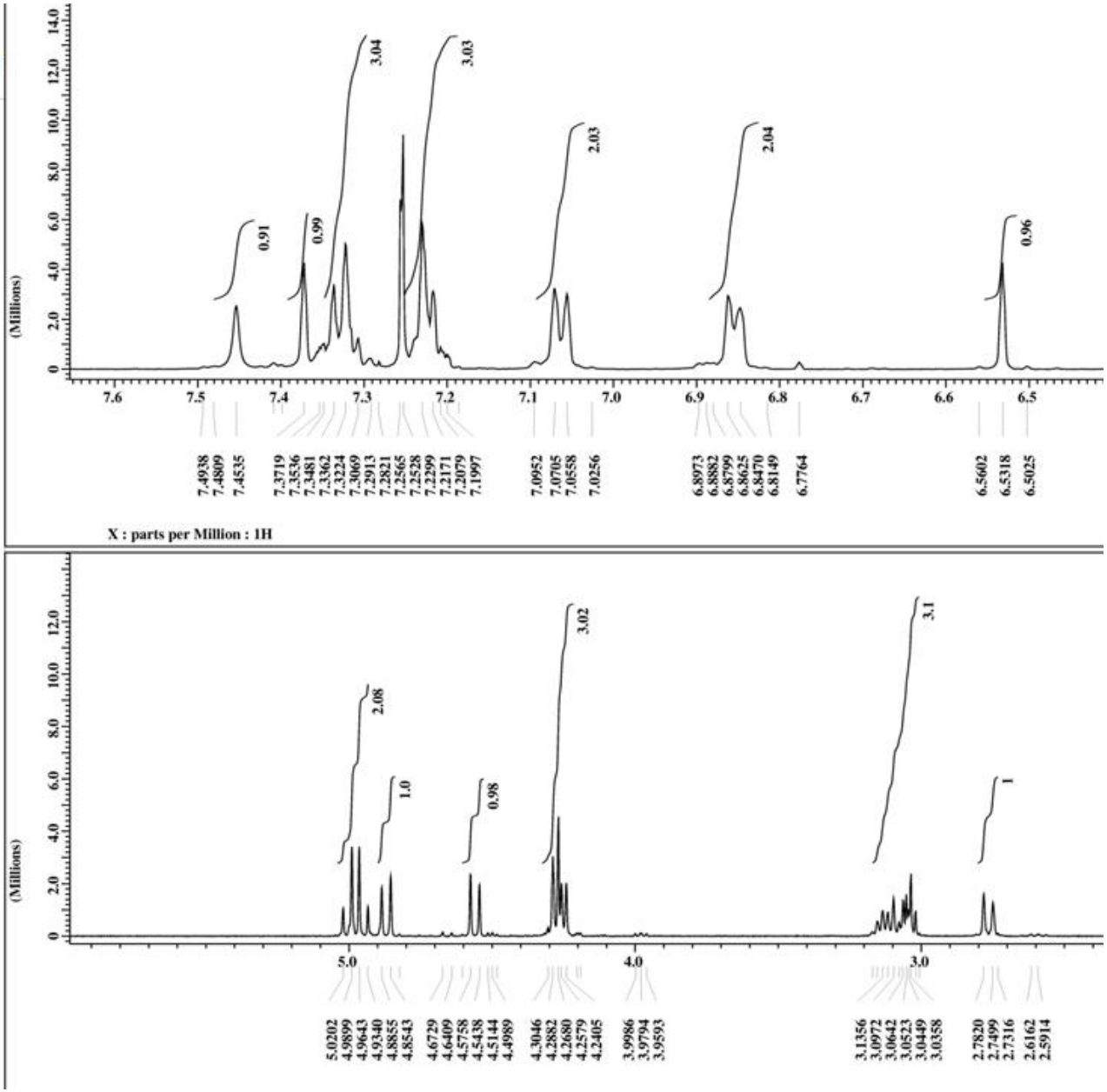
```
ilename          = sm_V_Bn-Bn_Hy_pure-4.
uthor            = delta
xperiment        = single_pulse.exp
ample_id         = S#518212
olvent           = CHLOROFORM-D
reation_time     = 15-JAN-2009 22:46:52
evision_time     = 28-MAR-2010 20:03:50
urrent_time      = 28-MAR-2010 20:04:20

omment           = Single Pulse Experime
ata_format       = 1D REAL
im_size          = 16384
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7473579[T] (500[MH
_acq_duration    = 2.1823488[s]
_domain          = 1H
_freq            = 500.15991521[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.45822189[Hz]
_sweep           = 7.50750751[kHz]
lipped           = FALSE
od_return        = 1
cans             = 12
otal_scans       = 12

_90_width        = 18.5[us]
_acq_time        = 2.1823488[s]
_angle           = 45[deg]
_pulse           = 9.25[us]
nitial_wait      = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 22
elaxation_delay  = 4[s]
mp_get           = 26.1[dC]
nblank_time      = 2[us]
```



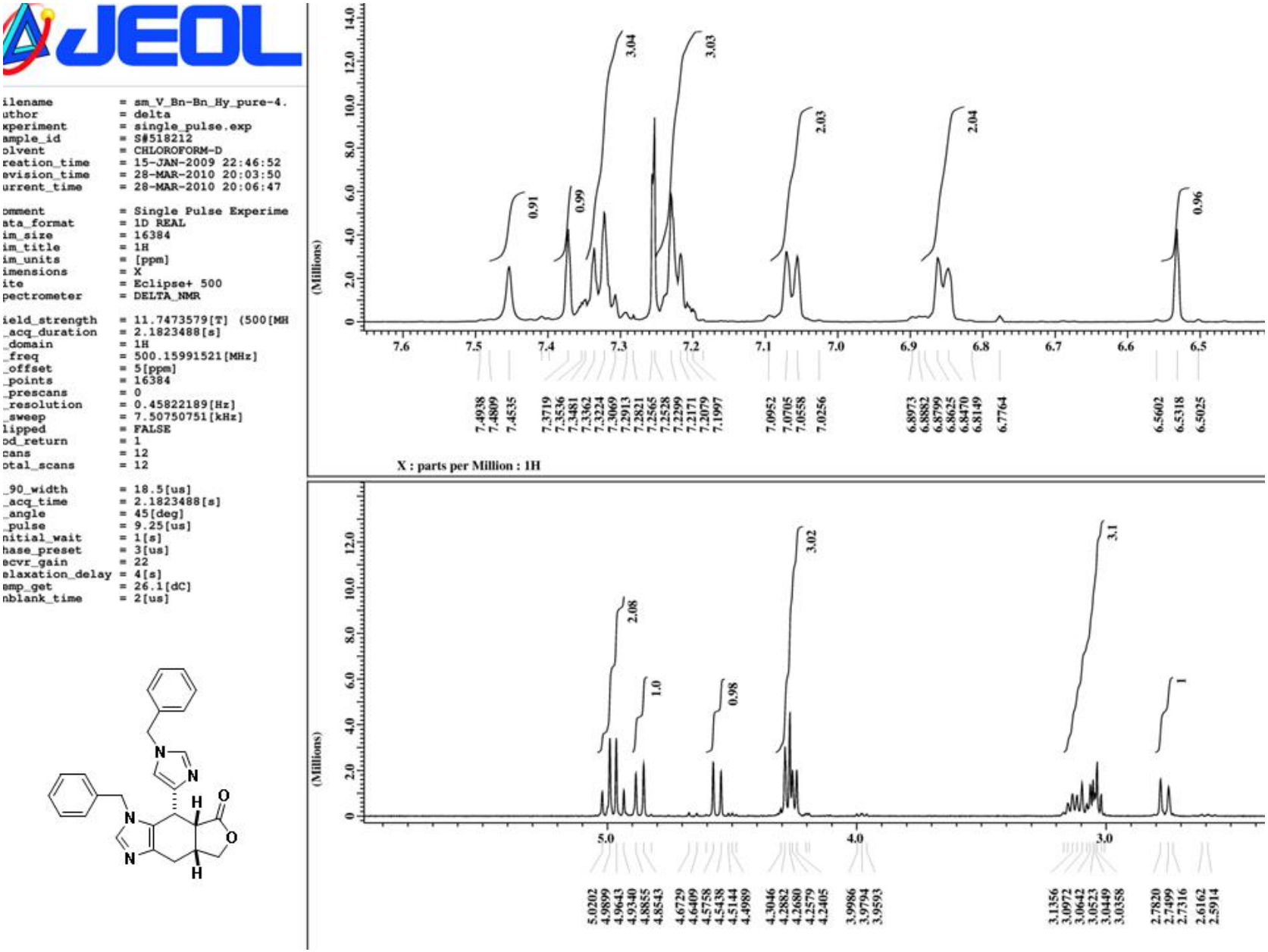


```
ilename          = sm_V_Bn-Bn_Hy_pure-4.
uthor            = delta
xperiment        = single_pulse.exp
ample_id         = S#518212
olvent           = CHLOROFORM-D
reation_time     = 15-JAN-2009 22:46:52
evision_time     = 28-MAR-2010 20:03:50
urrent_time      = 28-MAR-2010 20:06:47

omment           = Single Pulse Experime
ata_format       = 1D REAL
im_size          = 16384
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7473579[T] (500[MH
_acq_duration    = 2.1823488[s]
_domain          = 1H
_freq            = 500.15991521[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.45822189[Hz]
_sweep           = 7.50750751[kHz]
lipped           = FALSE
od_return        = 1
cans             = 12
otal_scans       = 12

_90_width        = 18.5[us]
_acq_time        = 2.1823488[s]
_angle           = 45[deg]
_pulse           = 9.25[us]
nitial_wait      = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 22
elaxation_delay  = 4[s]
mp_get           = 26.1[dC]
nblank_time      = 2[us]
```



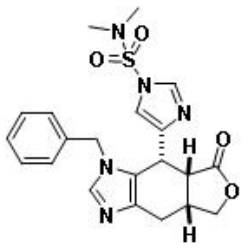


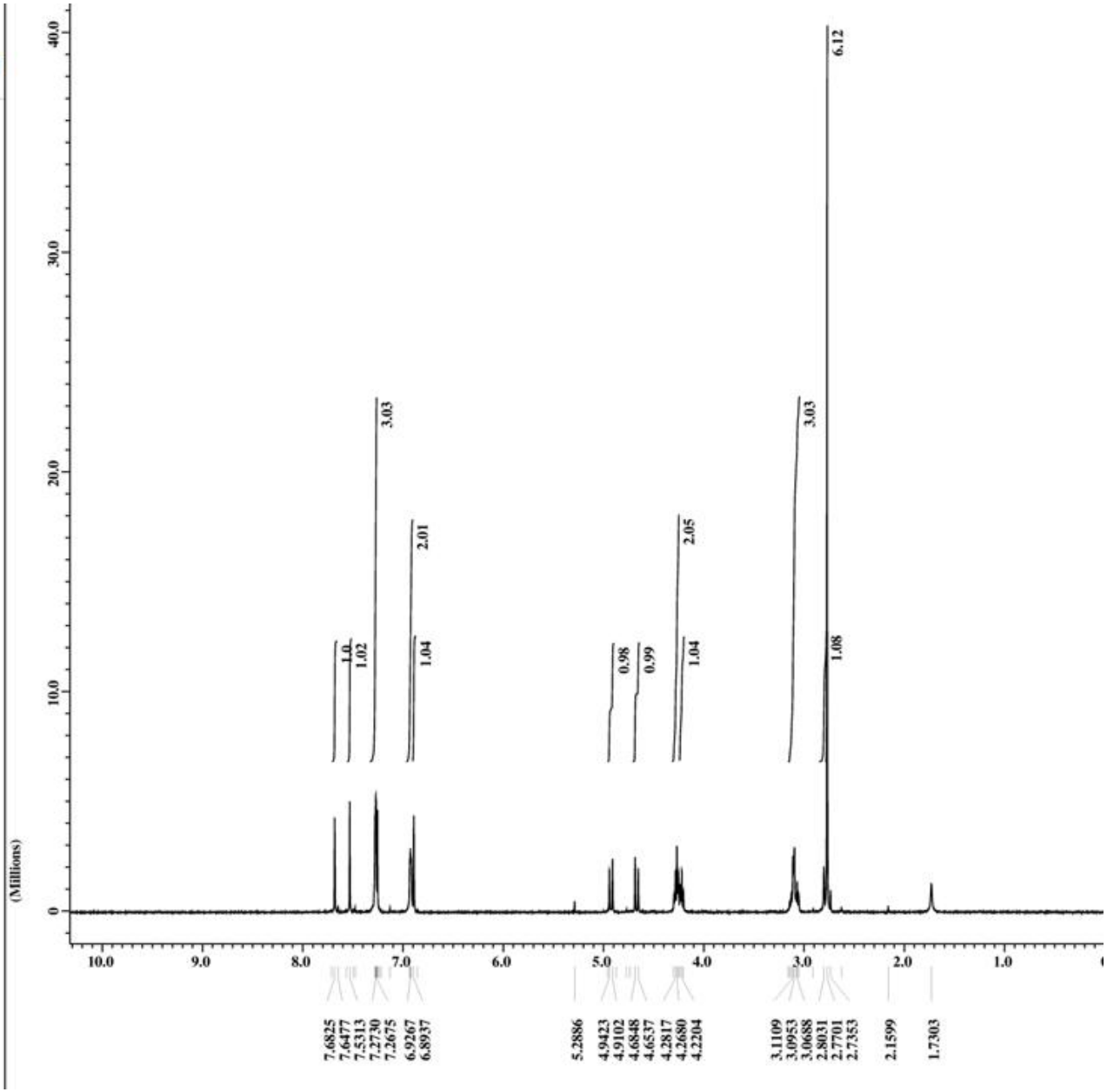
sm_V_Bn-Bn_Hy_pure-3.
delta
single_pulse_dec
S#835108
CHLOROFORM-D
15-JAN-2009 07:31:35
15-JAN-2009 11:11:15
28-MAR-2010 20:08:52
single pulse decouple
1D REAL
52428
13C
[ppm]
X
ECX 300
DELTA2_NMR
7.05860013[T] (300[MHz
2.76824064[s]
13C
75.56823426[MHz]
100[ppm]
65536
4
0.36124027[Hz]
23.67424242[kHz]
1H
300.52965592[MHz]
5[ppm]
FALSE
10
5000
5000
9.75[us]
2.76824064[s]
30[deg]
8[dB]
3.25[us]
25[dB]
25[dB]
WALTZ
TRUE
1[s]
TRUE
3[s]
50
3[s]
5.76824064[s]
23.3[dC]
(thousandths)
177.3121
137.3869
136.0532
129.1074
128.8875
128.3999
128.0652
127.1809
126.8797
118.4377
77.5564
77.1357
76.7103
72.5323
50.9013
48.7263
44.3858
34.9542
30.7810
22.3820


ilename = sm_V_Bn-Bn_Hy_pure-4.
uthor = delta
xperiment = single_pulse.exp
ample_id = S#518212
olvent = CHLOROFORM-D
reation_time = 15-JAN-2009 22:46:52
evision_time = 28-MAR-2010 20:03:50
urrent_time = 28-MAR-2010 20:06:47
omment = Single Pulse Experime
ata_format = 1D REAL
im_size = 16384
im_title = 1H
im_units = [ppm]
imensions = X
ite = Eclipse+ 500
pectrometer = DELTA_NMR
ield_strength = 11.7473579[T] (500[MH
_acq_duration = 2.1823488[s]
_domain = 1H
_freq = 500.15991521[MHz]
_offset = 5[ppm]
_points = 16384
_prescans = 0
_resolution = 0.45822189[Hz]
_sweep = 7.50750751[kHz]
lipped = FALSE
od_return = 1
cans = 12
otal_scans = 12
_90_width = 18.5[us]
_acq_time = 2.1823488[s]
_angle = 45[deg]
_pulse = 9.25[us]
nitial_wait = 1[s]
hase_preset = 3[us]
ecvr_gain = 22
elaxation_delay = 4[s]
mp_get = 26.1[dC]
nblank_time = 2[us]
(Millions)
0.91
0.99
3.04
3.03
2.03
2.04
0.96
7.4938
7.4809
7.4535
7.3719
7.3536
7.3481
7.3362
7.3224
7.3069
7.2913
7.2821
7.2565
7.2528
7.2299
7.2171
7.2079
7.1997
7.0952
7.0705
7.0558
7.0256
6.8973
6.8882
6.8799
6.8625
6.8470
6.8149
6.7764
6.5602
6.5318
6.5025
X : parts per Million : 1H
(Millions)
2.08
1.0
0.98
3.02
3.1
1
5.0202
4.9899
4.9643
4.9340
4.8855
4.8543
4.6729
4.6409
4.5758
4.5438
4.5144
4.4989
4.3046
4.2882
4.2680
4.2579
4.2405
3.9986
3.9794
3.9593
3.1356
3.0972
3.0642
3.0523
3.0449
3.0358
2.7820
2.7499
2.7316
2.6162
2.5914
O
O
H
H
N
N
N
N

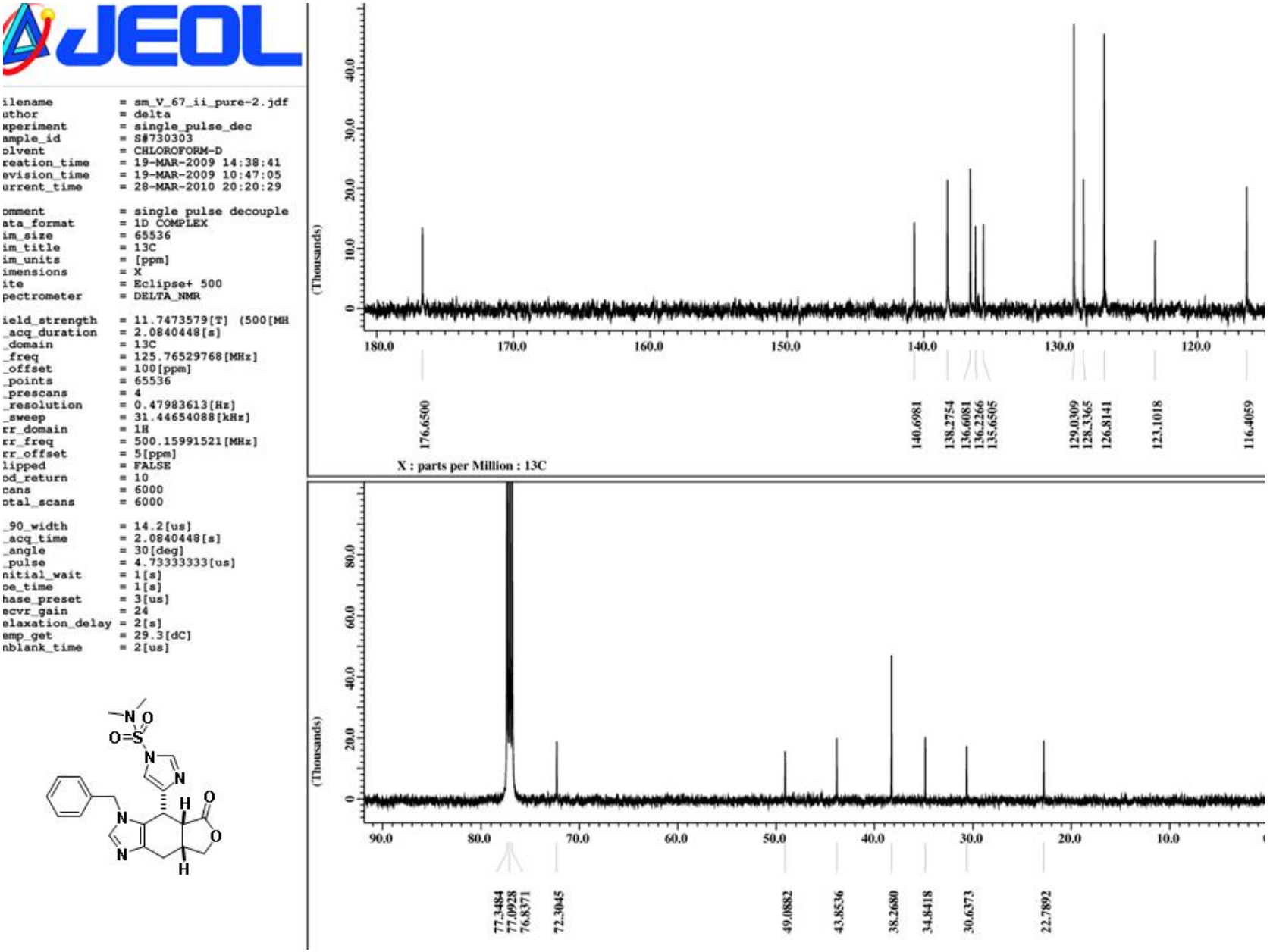
APPENDIX 37
^{1}H AND ^{13}C NMR SPECTRUM OF
4-((4a*R,7a*S**,8*R**)-1-benzyl-7-oxo-4,4a,5,7,7a,8-hexahydro-1H-isobenzofuro[5,6-d]imidazol-8-yl)-N,N-dimethyl-1H-imidazole-1-sulfonamide (231)**

```
ilename          = sm_V_102_pure-3.jdf
uthor            = delta
xperiment        = single_pulse.exp
ample_id         = S#389287
olvent           = CHLOROFORM-D
reation_time     = 18-MAR-2009 20:38:58
evision_time     = 28-MAR-2010 20:15:37
urrent_time      = 28-MAR-2010 20:16:08

omment           = Single Pulse Experime
ata_format       = 1D COMPLEX
im_size          = 16384
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7473579[T] (500[MH
_acq_duration    = 2.1823488[s]
_domain          = 1H
_freq            = 500.15991521[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.45822189[Hz]
_sweep           = 7.50750751[kHz]
lipped           = FALSE
od_return        = 1
cans             = 8
otal_scans       = 8

_90_width        = 18.5[us]
_acq_time        = 2.1823488[s]
_angle           = 45[deg]
_pulse           = 9.25[us]
nitial_wait      = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 23
elaxation_delay  = 4[s]
mp_get           = 26[dC]
nblank_time      = 2[us]
```



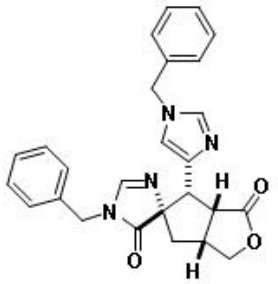


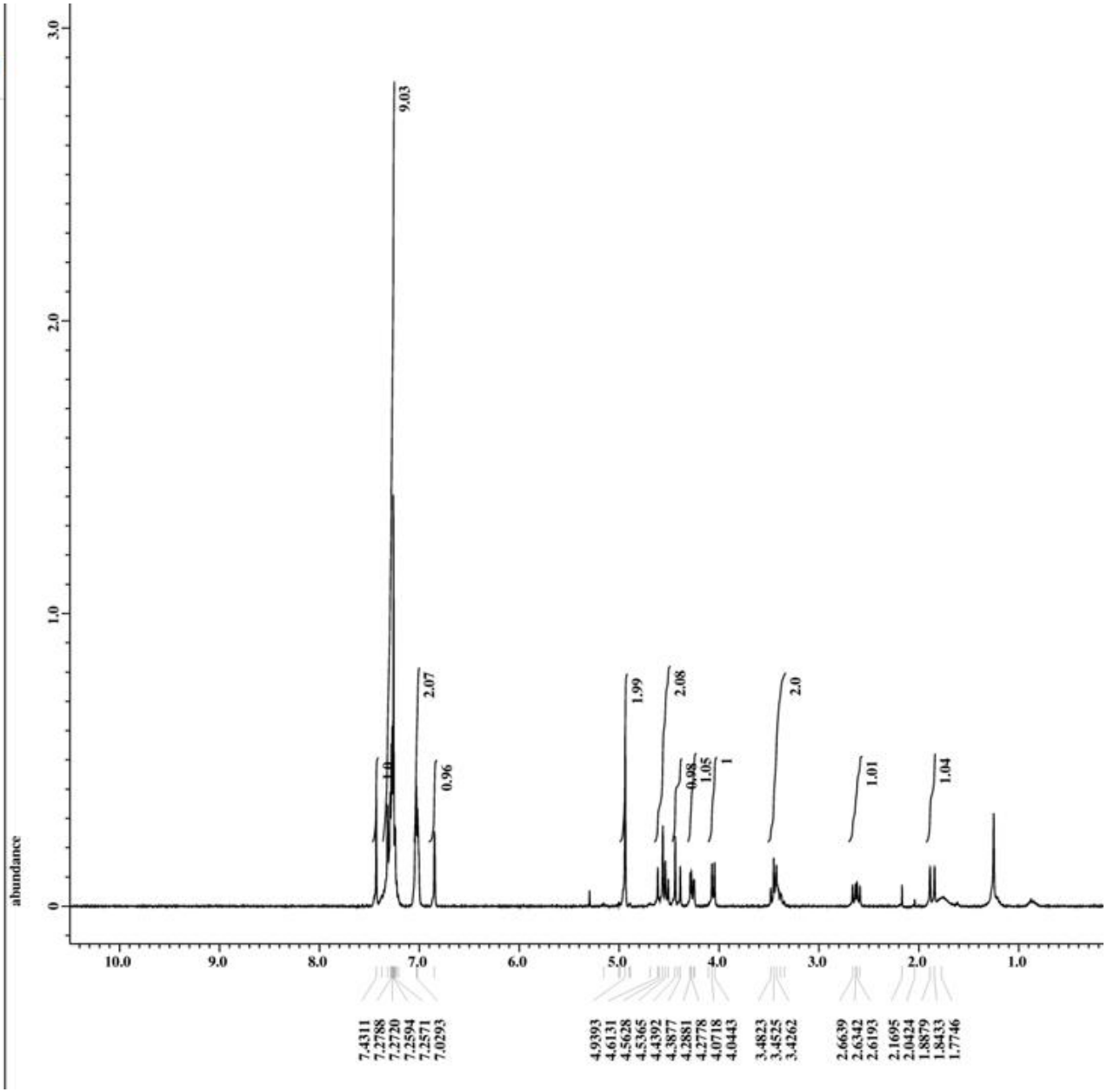
JEOL
ilename = sm_V_67_ii_pure-2.jdf
uthor = delta
xperiment = single_pulse_dec
ample_id = S#7303030
olvent = CHLOROFORM-D
reation_time = 19-MAR-2009 14:38:41
evision_time = 19-MAR-2009 10:47:05
urrent_time = 28-MAR-2010 20:18:50
omment = single pulse decouple
ata_format = 1D COMPLEX
im_size = 65536
im_title = 13C
im_units = [ppm]
imensions = X
ite = Eclipse+ 500
pectrometer = DELTA_NMR
ield_strength = 11.74735791[T] (500[MH
_acq_duration = 2.0840448[s]
_domain = 13C
_freq = 125.76529768[MHz]
_offset = 100[ppm]
_points = 65536
_prescans = 4
_resolution = 0.47983613[Hz]
_sweep = 31.44654088[kHz]
rr_domain = 1H
rr_freq = 500.15991521[MHz]
rr_offset = 5[ppm]
lipped = FALSE
od_return = 10
cans = 6000
otal_scans = 6000
_90_width = 14.2[us]
_acq_time = 2.0840448[s]
_angle = 30[deg]
_pulse = 4.73333333[us]
nitial_wait = 1[s]
pe_time = 1[s]
hase_preset = 3[us]
ecvr_gain = 24
elaxation_delay = 2[s]
emp_get = 29.3[dC]
nblank_time = 2[us]
(Thousands)
176.6500
140.6981
138.2754
136.6081
136.2266
135.6505
129.0309
128.3365
126.8141
123.1018
116.4059
77.3484
77.0928
76.8371
72.3045
49.0882
43.8536
38.2680
34.8418
30.6373
22.7892

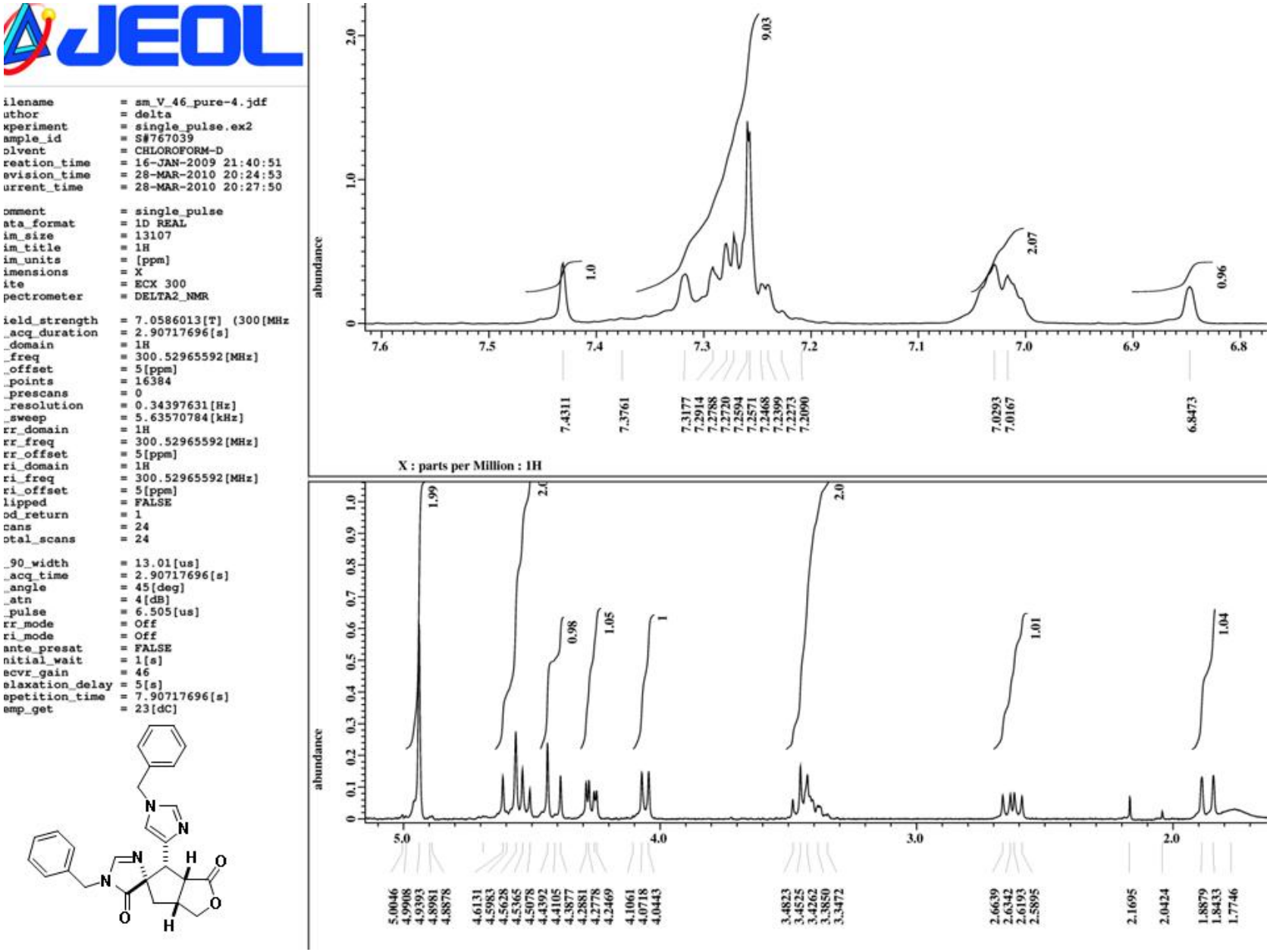

ilename = sm_V_67_ii_pure-2.jdf
uthor = delta
xperiment = single_pulse_dec
ample_id = S#730303
olvent = CHLOROFORM-D
reation_time = 19-MAR-2009 14:38:41
evision_time = 19-MAR-2009 10:47:05
urrent_time = 28-MAR-2010 20:20:29
omment = single pulse decouple
ata_format = 1D COMPLEX
im_size = 65536
im_title = 13C
im_units = [ppm]
imensions = X
ite = Eclipse+ 500
pectrometer = DELTA_NMR
ield_strength = 11.7473579[T] (500[MH
_acq_duration = 2.0840448[s]
_domain = 13C
_freq = 125.76529768[MHz]
_offset = 100[ppm]
_points = 65536
_prescans = 4
_resolution = 0.47983613[Hz]
_sweep = 31.44654088[kHz]
rr_domain = 1H
rr_freq = 500.15991521[MHz]
rr_offset = 5[ppm]
lipped = FALSE
od_return = 10
cans = 6000
otal_scans = 6000
_90_width = 14.2[us]
_acq_time = 2.0840448[s]
_angle = 30[deg]
_pulse = 4.73333333[us]
nitial_wait = 1[s]
oe_time = 1[s]
hase_preset = 3[us]
ecvr_gain = 24
elaxation_delay = 2[s]
emp_get = 29.3[dC]
nblank_time = 2[us]
(Thousands)
176.6500
140.6981
138.2754
136.6081
136.2266
135.6505
129.0309
128.3365
126.8141
123.1018
116.4059
X : parts per Million : 13C
(Thousands)
77.3484
77.0928
76.8371
72.3045
49.0882
43.8536
38.2680
34.8418
30.6373
22.7892

APPENDIX 38
^{1}H AND ^{13}C NMR SPECTRUM OF
(3a*R,4'*S**,6*R**,6a*S**)-1'-benzyl-6-(1-benzyl-1H-imidazol-4-yl)-3a,4,6,6a-tetrahydrospiro[cyclopenta[c]furan-5,4'-imidazole]-1,5'(1'H,3H)-dione (234)**

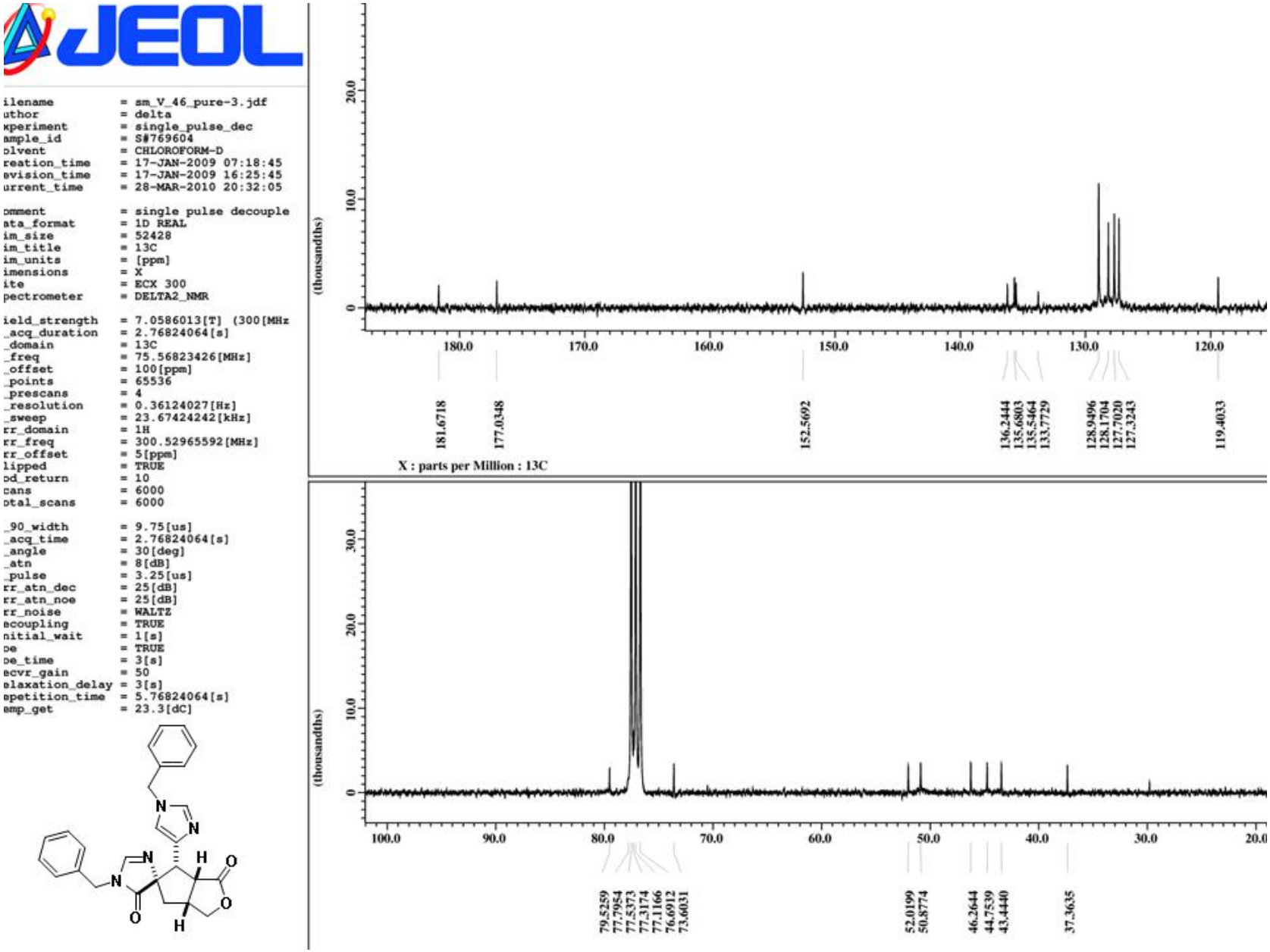
```
ilename          = sm_V_46_pure-4.jdf
uthor            = delta
xperiment        = single_pulse.ex2
ample_id         = S#767039
olvent           = CHLOROFORM-D
reation_time     = 16-JAN-2009 21:40:51
evision_time     = 28-MAR-2010 20:24:53
urrent_time      = 28-MAR-2010 20:25:38

omment           = single_pulse
ata_format       = 1D REAL
im_size          = 13107
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.90717696[s]
_domain          = 1H
_freq            = 300.52965592[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.34397631[Hz]
_sweep           = 5.63570784[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
ri_domain        = 1H
ri_freq          = 300.52965592[MHz]
ri_offset        = 5[ppm]
lipped           = FALSE
od_return        = 1
cans             = 24
otal_scans       = 24

_90_width        = 13.01[us]
_acq_time        = 2.90717696[s]
_angle           = 45[deg]
_atn             = 4[dB]
_pulse           = 6.505[us]
rr_mode          = Off
ri_mode          = Off
ante_presat      = FALSE
nitial_wait      = 1[s]
ecvr_gain        = 46
elaxation_delay  = 5[s]
epetition_time   = 7.90717696[s]
emp_get          = 23[dC]
```





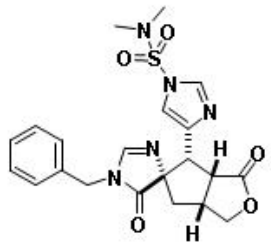

ilename = sm_V_46_pure-4.jdf
uthor = delta
xperiment = single_pulse.ex2
ample_id = S#767039
olvent = CHLOROFORM-D
reation_time = 16-JAN-2009 21:40:51
evision_time = 28-MAR-2010 20:24:53
urrent_time = 28-MAR-2010 20:27:50
omment = single_pulse
ata_format = 1D REAL
im_size = 13107
im_title = 1H
im_units = [ppm]
imensions = X
ite = ECX 300
pectrometer = DELTA2_NMR
ield_strength = 7.0586013[T] (300[MHz
_acq_duration = 2.90717696[s]
_domain = 1H
_freq = 300.52965592[MHz]
_offset = 5[ppm]
_points = 16384
_prescans = 0
_resolution = 0.34397631[Hz]
_sweep = 5.63570784[kHz]
rr_domain = 1H
rr_freq = 300.52965592[MHz]
rr_offset = 5[ppm]
ri_domain = 1H
ri_freq = 300.52965592[MHz]
ri_offset = 5[ppm]
lipped = FALSE
od_return = 1
cans = 24
otal_scans = 24
_90_width = 13.01[us]
_acq_time = 2.90717696[s]
_angle = 45[deg]
_atn = 4[dB]
_pulse = 6.505[us]
rr_mode = Off
ri_mode = Off
ante_presat = FALSE
nitial_wait = 1[s]
ecvr_gain = 46
elaxation_delay = 5[s]
epetition_time = 7.90717696[s]
emp_get = 23[dC]
abundance
9.03
1.0
2.07
0.96
7.4311
7.3761
7.3177
7.2914
7.2788
7.2720
7.2594
7.2571
7.2468
7.2399
7.2273
7.2090
7.0293
7.0167
6.8473
X : parts per Million : 1H
abundance
1.99
0.98
1.05
1
2.0
1.01
1.04
5.0046
4.9908
4.9393
4.8981
4.8878
4.6131
4.5983
4.5628
4.5365
4.5078
4.4392
4.4105
4.3877
4.2881
4.2778
4.2469
4.1061
4.0718
4.0443
3.4823
3.4525
3.4262
3.3850
3.3472
2.6639
2.6342
2.6193
2.5895
2.1695
2.0424
1.8879
1.8433
1.7746

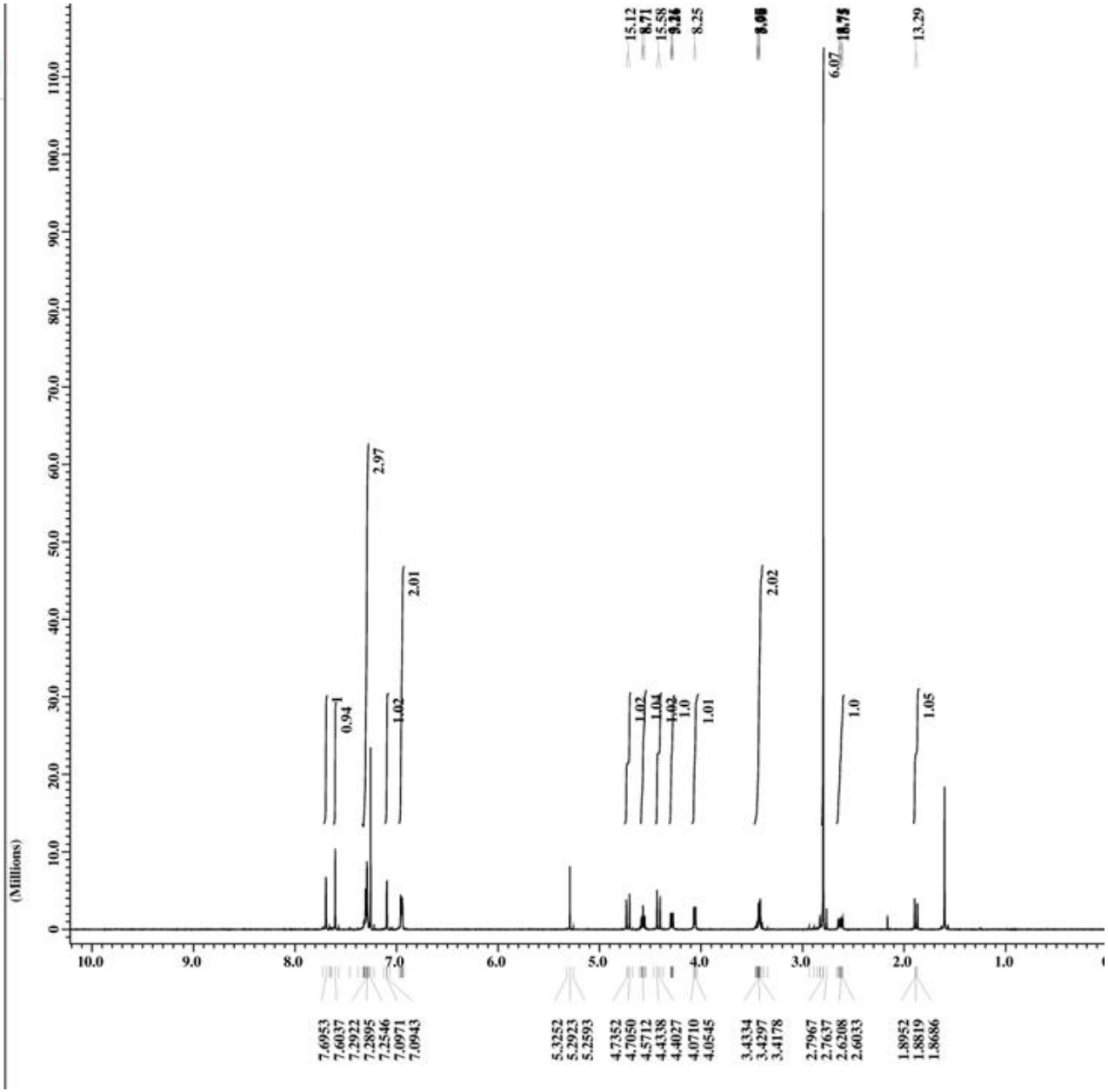
JEOL
ilename = sm_V_46_pure-3.jdf
uthor = delta
xperiment = single_pulse_dec
ample_id = S#769604
olvent = CHLOROFORM-D
reation_time = 17-JAN-2009 07:18:45
evision_time = 17-JAN-2009 16:25:45
urrent_time = 28-MAR-2010 20:30:27
omment = single pulse decouple
ata_format = 1D REAL
im_size = 52428
im_title = 13C
im_units = [ppm]
imensions = X
ite = ECX 300
pectrometer = DELTA2_NMR
ield_strength = 7.0586013[T] (300[MHz
acq_duration = 2.76824064[s]
domain = 13C
freq = 75.56823426[MHz]
offset = 100[ppm]
points = 65536
prescans = 4
resolution = 0.36124027[Hz]
sweep = 23.67442242[kHz]
rr_domain = 1H
rr_freq = 300.52965592[MHz]
rr_offset = 5[ppm]
lipped = TRUE
od_return = 10
cans = 6000
otal_scans = 6000
90_width = 9.75[us]
acq_time = 2.76824064[s]
angle = 30[deg]
atn = 8[dB]
pulse = 3.25[us]
rr_atn_dec = 25[dB]
rr_atn_noe = 25[dB]
rr_noise = WALTZ
ecoupling = TRUE
nitial_wait = 1[s]
oe = TRUE
oe_time = 3[s]
ecvr_gain = 50
elaxation_delay = 3[s]
epetition_time = 5.76824064[s]
emp_get = 23.3[dC]
(thousandths)
181.6718
177.0348
152.5692
136.2444
136.0803
135.5464
128.9496
128.1704
127.7020
127.3243
119.4033
77.5373
77.3174
77.1166
76.6912
52.0199
50.8774
46.2644
44.7539
43.4440
37.3635


ilename = sm_V_46_pure-3.jdf
uthor = delta
xperiment = single_pulse_dec
ample_id = S#769604
olvent = CHLOROFORM-D
reation_time = 17-JAN-2009 07:18:45
evision_time = 17-JAN-2009 16:25:45
urrent_time = 28-MAR-2010 20:32:05
omment = single pulse decouple
ata_format = 1D REAL
im_size = 52428
im_title = 13C
im_units = [ppm]
imensions = X
ite = ECX 300
pectrometer = DELTA2_NMR
ield_strength = 7.0586013[T] (300[MHz
_acq_duration = 2.76824064[s]
_domain = 13C
_freq = 75.56823426[MHz]
_offset = 100[ppm]
_points = 65536
_prescans = 4
_resolution = 0.36124027[Hz]
_sweep = 23.67424242[kHz]
rr_domain = 1H
rr_freq = 300.52965592[MHz]
rr_offset = 5[ppm]
lipped = TRUE
od_return = 10
cans = 6000
otal_scans = 6000
_90_width = 9.75[us]
_acq_time = 2.76824064[s]
_angle = 30[deg]
_atn = 8[dB]
_pulse = 3.25[us]
rr_atn_dec = 25[dB]
rr_atn_noe = 25[dB]
rr_noise = WALTZ
ecoupling = TRUE
nitial_wait = 1[s]
oe = TRUE
oe_time = 3[s]
ecvr_gain = 50
elaxation_delay = 3[s]
epetition_time = 5.76824064[s]
emp_get = 23.3[dC]
(thousandths)
181.6718
177.0348
152.5692
136.2444
135.6803
135.5464
133.7729
128.9496
128.1704
127.7020
127.3343
119.4033
X : parts per Million : 13C
79.5259
77.7954
77.5373
77.3174
77.1166
76.6912
73.6031
52.0199
50.8774
46.2644
44.7539
43.4440
37.3635

APPENDIX 39
^{1}H AND ^{13}C NMR SPECTRUM OF
4-((3a*R,4'*S**,6R*,6a*S**)-1'-benzyl-1,5'-dioxo-1,1',3,3a,4,5',6,6a-octahydrospiro[cyclopenta[c]furan-5,4'-imidazole]-6-yl)-N,N-dimethyl-1H-imidazole-1-sulfonamide (233)**

```
ilename          = sm_V_spiro_Bn_Dmas_pu
uthor            = delta
xperiment        = single_pulse.exp
ample_id         = S#714680
olvent           = CHLOROFORM-D
reation_time     = 22-MAR-2009 05:49:02
evision_time     = 28-MAR-2010 20:35:38
urrent_time      = 28-MAR-2010 20:36:11

omment           = Single Pulse Experime
ata_format       = 1D REAL
im_size          = 16384
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7473579[T] (500[MH
_acq_duration    = 2.1823488[s]
_domain          = 1H
_freq            = 500.15991521[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.45822189[Hz]
_sweep           = 7.50750751[kHz]
lipped           = FALSE
od_return        = 1
cans             = 18
otal_scans       = 18

_90_width        = 18.5[us]
_acq_time        = 2.1823488[s]
_angle           = 45[deg]
_pulse           = 9.25[us]
nitial_wait      = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 24
elaxation_delay  = 4[s]
emp_get          = 26.1[dC]
nblank_time      = 2[us]
```

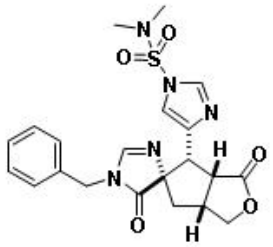


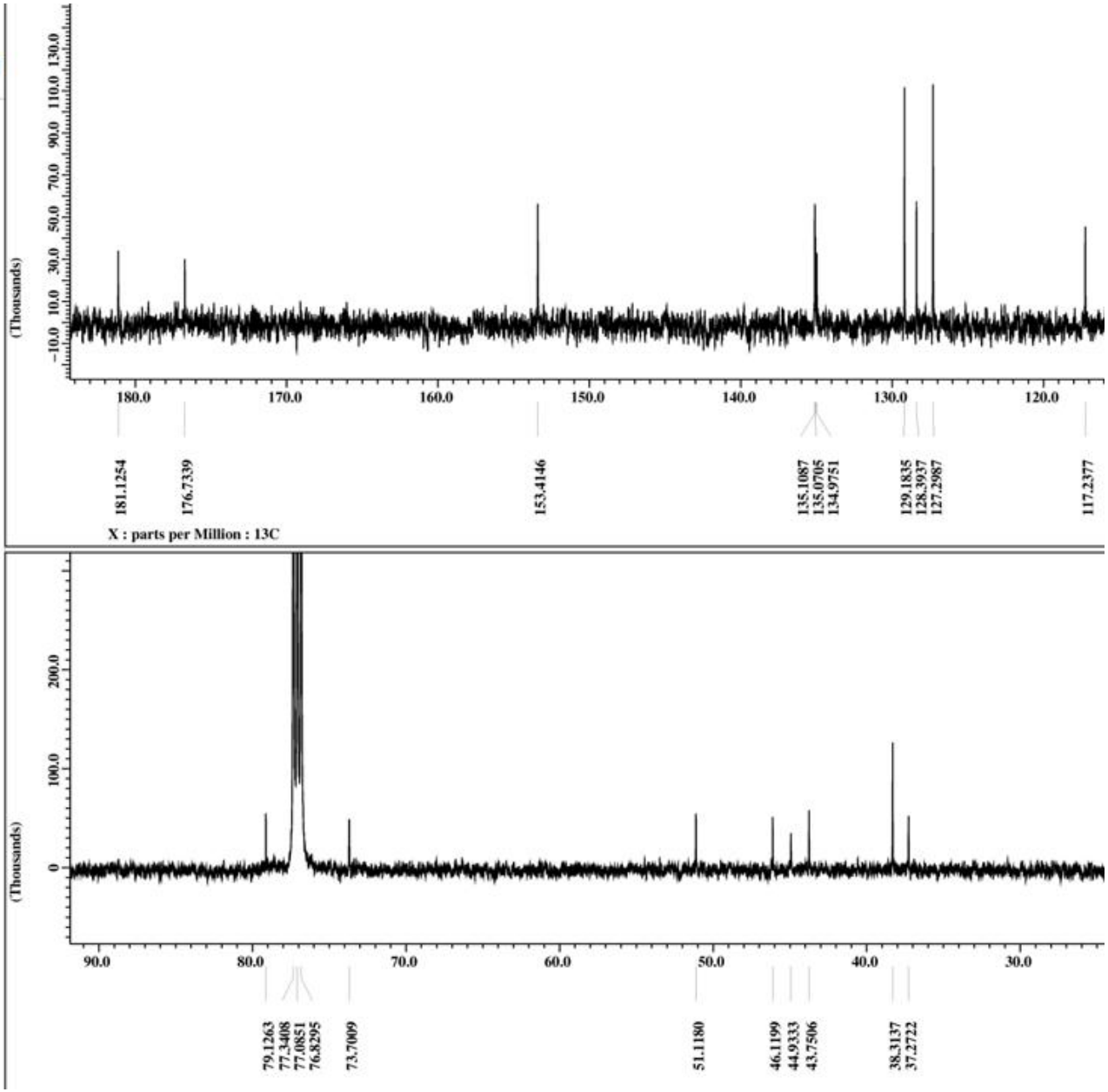


JEOL
ilename = sm_V_spiro_pure-2.jdf
uthor = delta
xperiment = single_pulse_dec
ample_id = SM717231
olvent = CHLOROFORM-D
reation_time = 22-MAR-2009 12:55:48
evision_time = 28-MAR-2010 20:38:42
urrent_time = 28-MAR-2010 20:39:11
omment = single_pulse decouple
ata_format = 1D COMPLEX
im_size = 65536
im_title = 13C
im_units = [ppm]
imensions = X
ite = Eclipse+ 500
pectrometer = DELTA_NMR
ield_strength = 11.7473579[T] (500[MH
_acq_duration = 2.0840448[s]
_domain = 13C
_freq = 125.76529768[MHz]
_offset = 100[ppm]
_points = 65536
_prescans = 4
_resolution = 0.47983613[Hz]
_sweep = 31.44654088[kHz]
rr_domain = 1H
rr_freq = 500.15991521[MHz]
rr_offset = 5[ppm]
lipped = TRUE
od_return = 10
cans = 5000
otal_scans = 5000
_90_width = 14.2[us]
_acq_time = 2.0840448[s]
_angle = 30[deg]
_pulse = 4.73333333[us]
nitial_wait = 1[s]
pe_time = 1[s]
hase_preset = 3[us]
ecvr_gain = 30
elaxation_delay = 2[s]
emp_get = 29.2[dC]
nblank_time = 2[us]
(Thousands)
181.1254
176.7339
153.4146
135.1087
135.0705
134.9751
129.1835
128.3937
127.2987
117.2377
79.1263
77.3408
77.0851
76.8295
51.1180
46.1199
44.9333
43.7506
38.3137
37.2722

JEOL

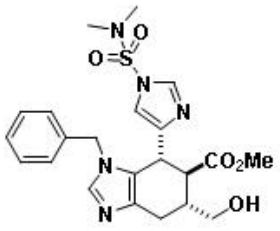
ilename	= sm_V_spiro_pure-2.jdf
uthor	= delta
xperiment	= single_pulse_dec
ample_id	= S#717231
olvent	= CHLOROFORM-D
reation_time	= 22-MAR-2009 12:55:48
evision_time	= 28-MAR-2010 20:38:42
urrent_time	= 28-MAR-2010 20:40:42
omment	= single pulse decouple
ata_format	= 1D COMPLEX
im_size	= 65536
im_title	= 13C
im_units	= [ppm]
imensions	= X
ite	= Eclipse+ 500
pectrometer	= DELTA_NMR
ield_strength	= 11.7473579[T] (500[MH
_acq_duration	= 2.0840448[s]
_domain	= 13C
_freq	= 125.76529768[MHz]
_offset	= 100[ppm]
_points	= 65536
_prescans	= 4
_resolution	= 0.47983613[Hz]
_sweep	= 31.44654088[kHz]
rr_domain	= 1H
rr_freq	= 500.15991521[MHz]
rr_offset	= 5[ppm]
lipped	= TRUE
od_return	= 10
cans	= 5000
otal_scans	= 5000
_90_width	= 14.2[us]
_acq_time	= 2.0840448[s]
_angle	= 30[deg]
_pulse	= 4.73333333[us]
nitial_wait	= 1[s]
oe_time	= 1[s]
hase_preset	= 3[us]
ecvr_gain	= 30
elaxation_delay	= 2[s]
amp_get	= 29.2[dC]
nblank_time	= 2[us]

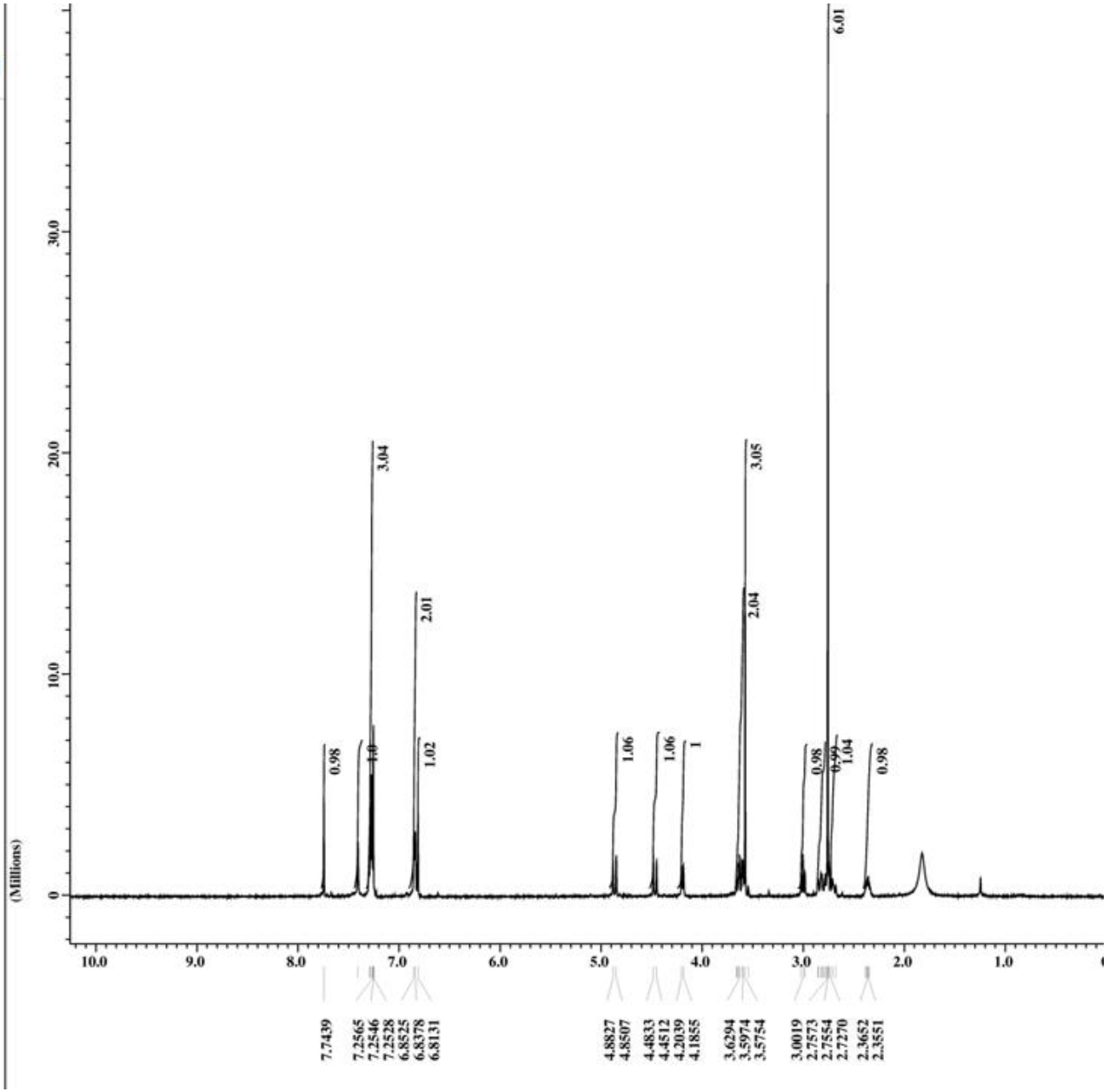




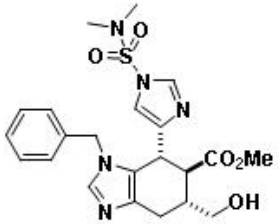
APPENDIX 40
^{1}H AND ^{13}C NMR SPECTRUM OF (5*R,6*R**,7*R**)-methyl-1-benzyl-7-(1-(N,N-dimethylsulfamoyl)-1H-imidazol-4-yl)-5-(hydroxymethyl)-4,5,6,7-tetrahydro-1H-benzo[d]imidazole-6-carboxylate (235)**

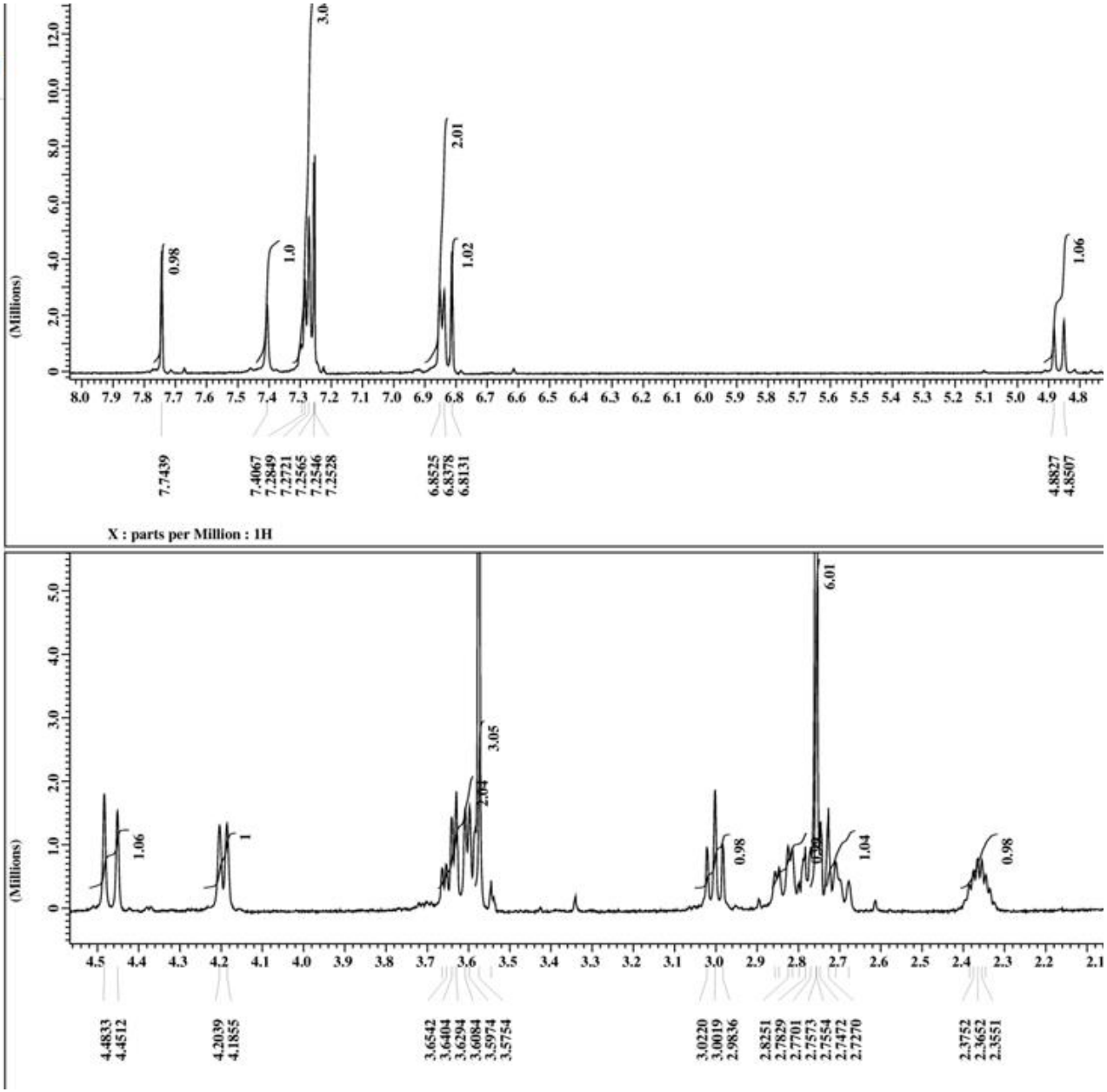
```
ilename          = sm_V_105_pure-2.jdf
uthor            = delta
xperiment        = single_pulse.exp
ample_id         = S#763077
olvent           = CHLOROFORM-D
reation_time     = 23-MAR-2009 07:11:33
evision_time     = 28-MAR-2010 20:46:28
urrent_time      = 28-MAR-2010 20:46:53

omment           = Single Pulse Experime
ata_format       = 1D COMPLEX
im_size          = 16384
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7473579[T] (500[MH
_acq_duration    = 2.1823488[s]
_domain          = 1H
_freq            = 500.15991521[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.45822189[Hz]
_sweep           = 7.50750751[kHz]
lipped           = FALSE
od_return        = 1
cans             = 16
otal_scans       = 16

_90_width        = 18.5[us]
_acq_time        = 2.1823488[s]
_angle           = 45[deg]
_pulse           = 9.25[us]
nitial_wait      = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 24
elaxation_delay  = 4[s]
emp_get          = 26[dC]
nblank_time      = 2[us]
```





ilename	= sm_V_105_pure-2.jdf
uthor	= delta
xperiment	= single_pulse.exp
ample_id	= S#763077
olvent	= CHLOROFORM-D
reation_time	= 23-MAR-2009 07:11:33
evision_time	= 28-MAR-2010 20:46:28
urrent_time	= 28-MAR-2010 20:48:59
omment	= Single Pulse Experime
ata_format	= 1D COMPLEX
im_size	= 16384
im_title	= 1H
im_units	= [ppm]
imensions	= X
ite	= Eclipse+ 500
pectrometer	= DELTA_NMR
ield_strength	= 11.7473579[T] (500[MH
_acq_duration	= 2.1823488[s]
_domain	= 1H
_freq	= 500.15991521[MHz]
_offset	= 5[ppm]
_points	= 16384
_prescans	= 0
_resolution	= 0.45822189[Hz]
_sweep	= 7.50750751[kHz]
lipped	= FALSE
od_return	= 1
cans	= 16
otal_scans	= 16
_90_width	= 18.5[us]
_acq_time	= 2.1823488[s]
_angle	= 45[deg]
_pulse	= 9.25[us]
nitial_wait	= 1[s]
hase_preset	= 3[us]
ecvr_gain	= 24
elaxation_delay	= 4[s]
mp_get	= 26[dC]
nblank_time	= 2[us]

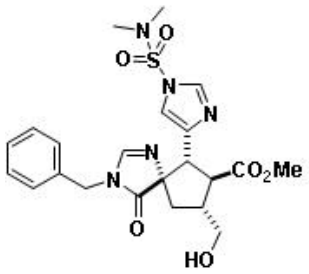


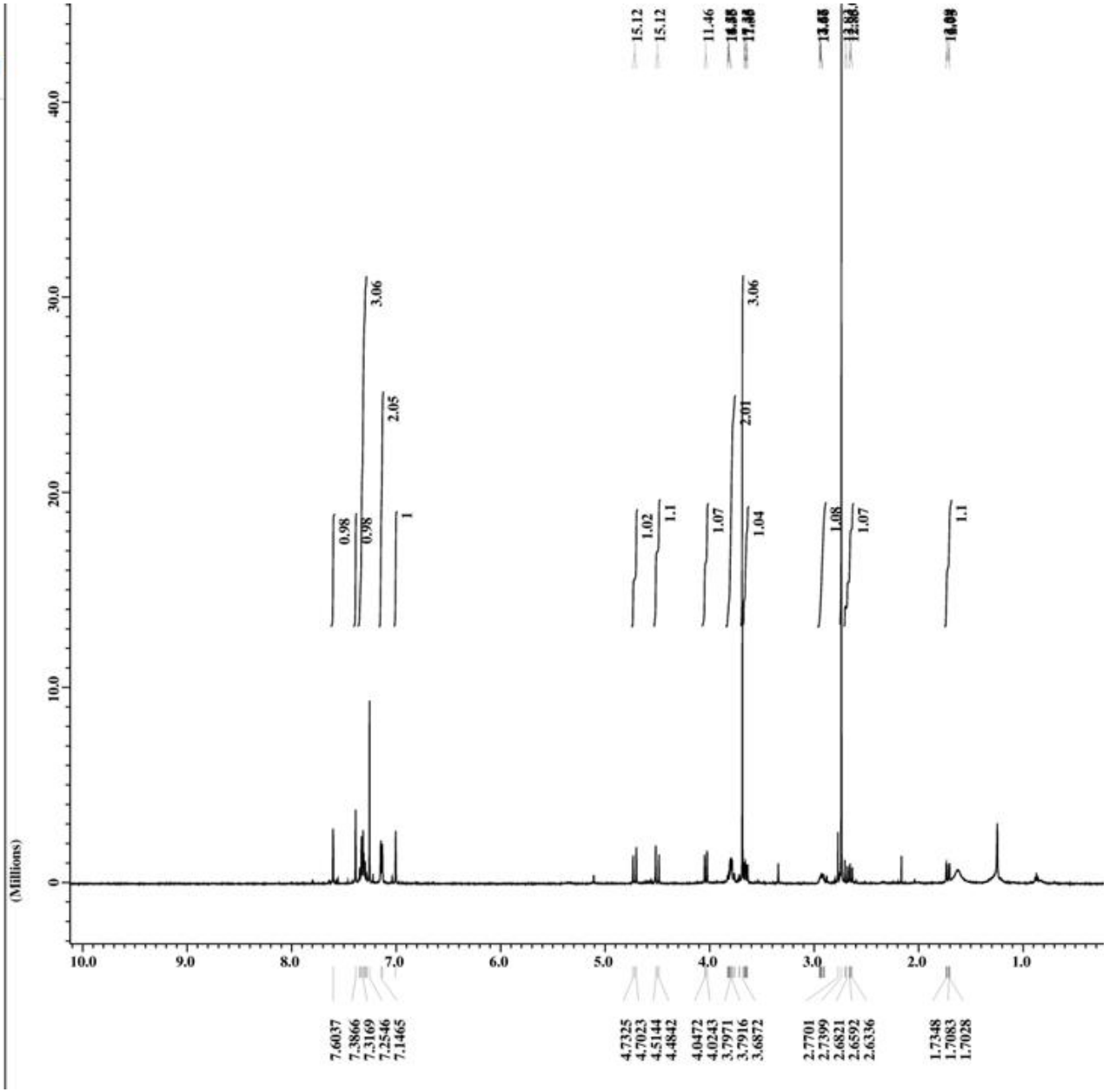


JEOL
ilename = sm_V_105_pure-2.jdf
uthor = delta
xperiment = single_pulse_dec
ample_id = S#765343
olvent = CHLOROFORM-D
reation_time = 23-MAR-2009 14:19:47
evision_time = 23-MAR-2009 08:30:23
urrent_time = 28-MAR-2010 20:51:12
omment = single pulse decouple
ata_format = 1D COMPLEX
im_size = 65536
im_title = 13C
im_units = [ppm]
imensions = X
ite = Eclipse+ 500
pectrometer = DELTA_NMR
ield_strength = 11.74735791[T] (500[MH
_acq_duration = 2.0840448[s]
_domain = 13C
_freq = 125.76529768[MHz]
_offset = 100[ppm]
_points = 65536
_prescans = 4
_resolution = 0.47983613[Hz]
_sweep = 31.44654088[kHz]
rr_domain = 1H
rr_freq = 500.15991521[MHz]
rr_offset = 5[ppm]
lipped = TRUE
od_return = 10
cans = 5000
otal_scans = 5000
_90_width = 14.2[us]
_acq_time = 2.0840448[s]
_angle = 30[deg]
_pulse = 4.73333333[us]
nitial_wait = 1[s]
pe_time = 1[s]
hase_preset = 3[us]
ecvr_gain = 30
elaxation_delay = 2[s]
emp_get = 29.3[dC]
nblank_time = 2[us]
(Thousands)
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
100.0
200.0
300.0
400.0
500.0
600.0
700.0
174.5592
142.6707
137.9473
137.1804
136.1159
129.0309
127.9702
126.2571
115.3910
65.0821
51.9726
51.6178
49.1989
40.6182
38.1382
35.8376
26.8029
N
O
O
S
N
N
N
N
CO2Me
OH

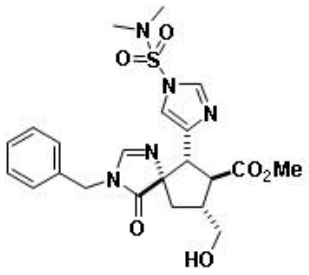
APPENDIX 41
^{1}H AND ^{13}C NMR SPECTRUM OF (5*S,6*R**,7*R**,8*R**)-methyl-3-benzyl-6-(1-(N,N-dimethylsulfamoyl)-1H-imidazol-4-yl)-8-(hydroxymethyl)-4-oxo-1,3-diazaspiro[4.4]non-1-ene-7-carboxylate (236)**

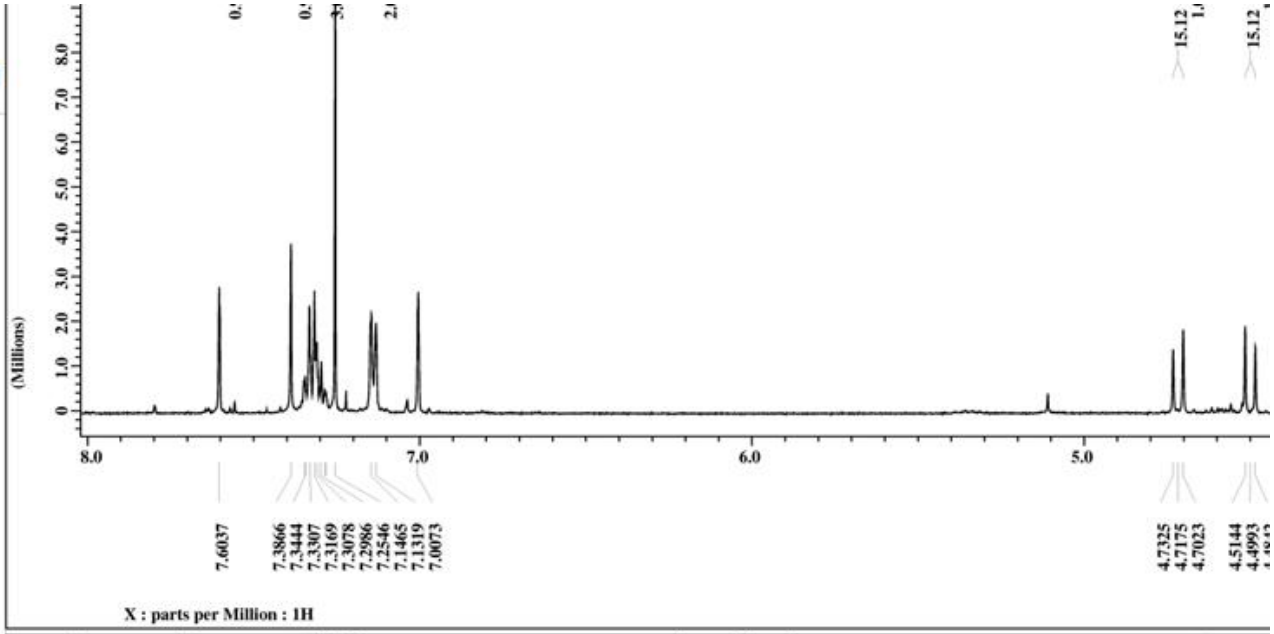
```
ilename          = sm_V_104_PURE-4.jdf
uthor            = delta
xperiment        = single_pulse.exp
ample_id         = S#598701
olvent           = CHLOROFORM-D
reation_time     =  4-APR-2009 03:00:34
evision_time     = 28-MAR-2010 20:56:54
urrent_time      = 28-MAR-2010 20:57:24

omment           = Single Pulse Experime
ata_format       = 1D COMPLEX
im_size          = 16384
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7473579[T] (500[MH
_acq_duration    = 2.1823488[s]
_domain          = 1H
_freq            = 500.15991521[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.45822189[Hz]
_sweep           = 7.50750751[kHz]
lipped           = FALSE
od_return        = 1
cans             = 16
otal_scans       = 16

_90_width        = 18.5[us]
_acq_time        = 2.1823488[s]
_angle           = 45[deg]
_pulse           = 9.25[us]
nitial_wait      = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 23
elaxation_delay  = 4[s]
emp_get          = 24.9[dC]
nblank_time      = 2[us]
```

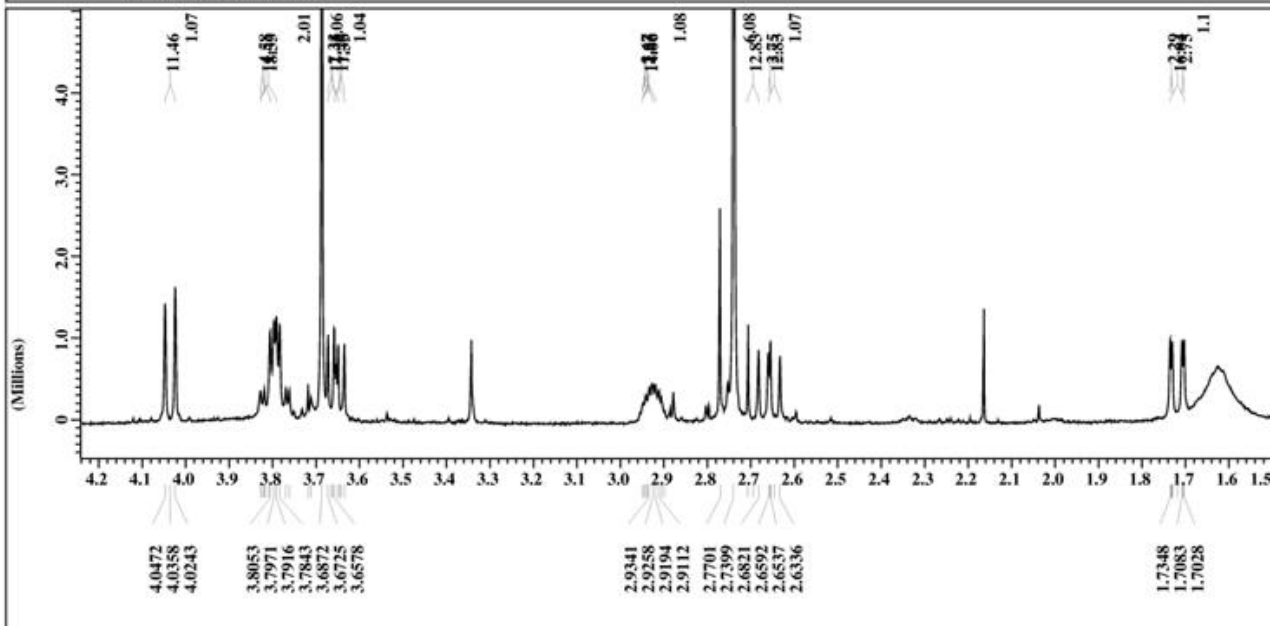




```
ilename          = sm_V_104_PURE-4.jdf
uthor            = delta
xperiment        = single_pulse.exp
ample_id         = S#598701
olvent           = CHLOROFORM-D
reation_time     =  4-APR-2009 03:00:34
evision_time     = 28-MAR-2010 20:56:54
urrent_time      = 28-MAR-2010 20:59:24

omment           = Single Pulse Experime
ata_format       = 1D COMPLEX
im_size          = 16384
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7473579[T] (500[MH
_acq_duration    = 2.1823488[s]
_domain          = 1H
_freq            = 500.15991521[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.45822189[Hz]
_sweep           = 7.50750751[kHz]
lipped           = FALSE
od_return        = 1
cans             = 16
otal_scans       = 16

_90_width        = 18.5[us]
_acq_time        = 2.1823488[s]
_angle           = 45[deg]
_pulse           = 9.25[us]
nitial_wait      = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 23
elaxation_delay  = 4[s]
mp_get           = 24.9[dC]
nblank_time      = 2[us]
```

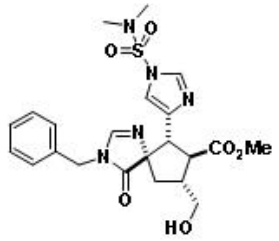


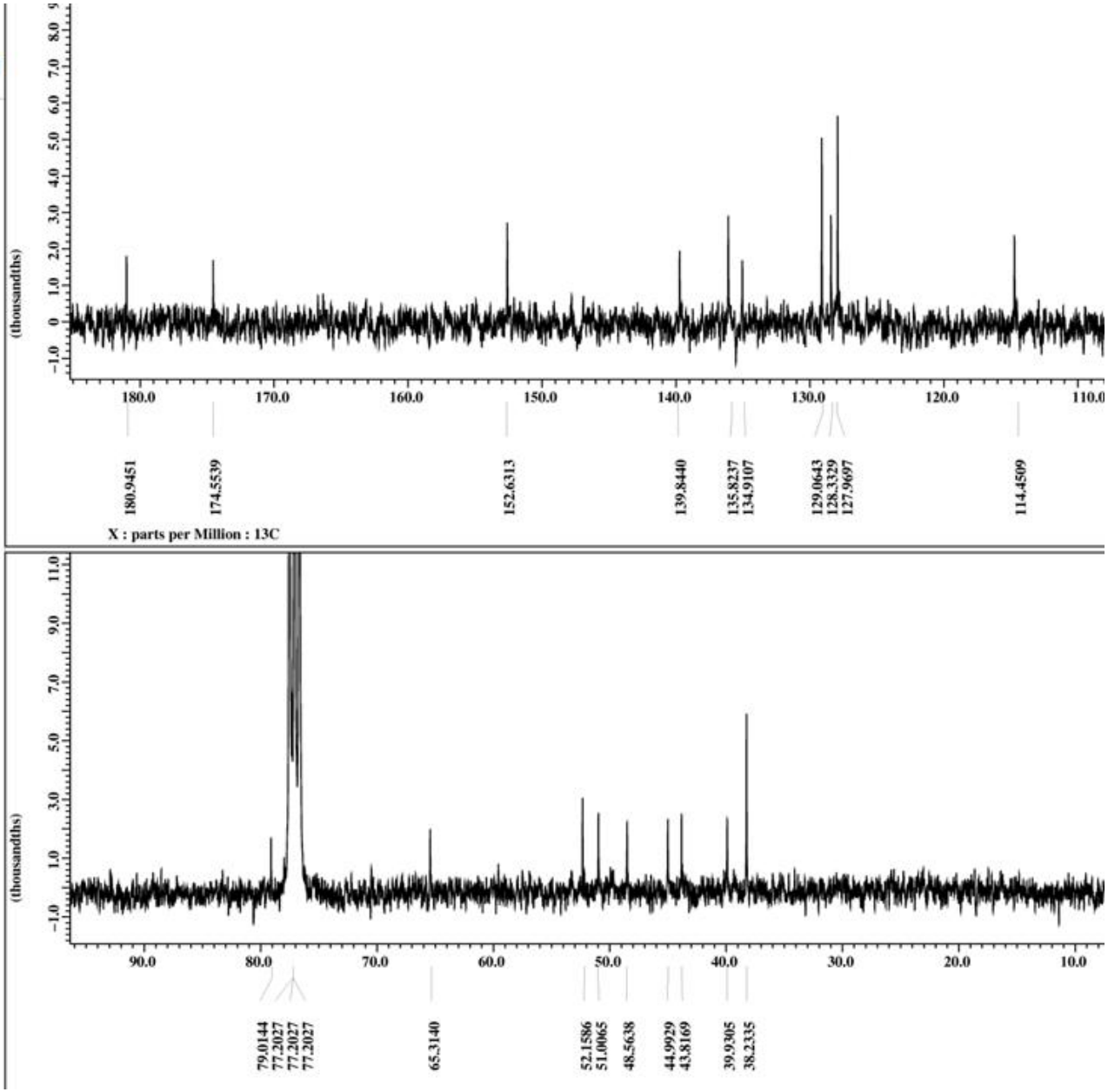




JEOL
ilename = sm_V_104_pure_ii-2.jd
uthor = delta
xperiment = single_pulse_dec
ample_id = SM400830
olvent = CHLOROFORM-D
reation_time = 21-MAR-2009 16:06:14
evision_time = 21-MAR-2009 15:45:31
urrent_time = 28-MAR-2010 21:01:33
omment = single_pulse decouple
ata_format = 1D COMPLEX
im_size = 52428
im_title = 13C
im_units = [ppm]
imensions = X
ite = ECX 300
pectrometer = DELTA2_NMR
ield_strength = 7.0586013[T] (300[MHz
_acq_duration = 2.76824064[s]
_domain = 13C
_freq = 75.56823426[MHz]
_offset = 100[ppm]
_points = 65536
_prescans = 4
_resolution = 0.36124027[Hz]
_sweep = 23.67424242[kHz]
rr_domain = 1H
rr_freq = 300.52965592[MHz]
rr_offset = 5[ppm]
lipped = FALSE
od_return = 10
cans = 2859
otal_scans = 2859
_90_width = 9.75[us]
_acq_time = 2.76824064[s]
_angle = 30[deg]
_atn = 8[dB]
_pulse = 3.25[us]
rr_atn_dec = 25[dB]
rr_atn_noe = 25[dB]
rr_noise = WALTZ
ecoupling = TRUE
nitial_wait = 1[s]
oe = TRUE
oe_time = 3[s]
ecvr_gain = 50
elaxation_delay = 3[s]
epetition_time = 5.76824064[s]
emp_get = 23.1[dC]
(thousandths)
40.0
30.0
20.0
10.0
0
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0
180.9451
174.5539
152.6313
139.8440
135.8237
134.9107
129.0643
128.3329
127.9697
114.4509
77.2027
77.2027
77.2027
65.3140
52.1586
51.0065
48.5638
44.9929
43.8169
39.9305
38.2335
O=S
N
N
N
N
O
CO2Me
HO

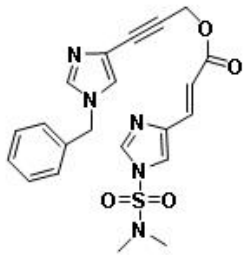
```
ilename          = sm_V_104_pure_ii-2.jd
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#400830
olvent           = CHLOROFORM-D
reation_time     = 21-MAR-2009 16:06:14
evision_time     = 21-MAR-2009 15:45:31
urrent_time      = 28-MAR-2010 21:03:00

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 52428
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.76824064[s]
_domain          = 13C
_freq            = 75.56823426[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.36124027[Hz]
_sweep           = 23.67424242[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
lipped           = FALSE
od_return        = 10
cans             = 2859
otal_scans       = 2859

_90_width        = 9.75[us]
_acq_time        = 2.76824064[s]
_angle           = 30[deg]
_atn             = 8[dB]
_pulse           = 3.25[us]
rr_atn_dec       = 25[dB]
rr_atn_noe       = 25[dB]
rr_noise         = WALTZ
ecoupling        = TRUE
nitial_wait      = 1[s]
oe               = TRUE
oe_time          = 3[s]
ecvr_gain        = 50
elaxation_delay  = 3[s]
epetition_time   = 5.76824064[s]
emp_get          = 23.1[dC]
```

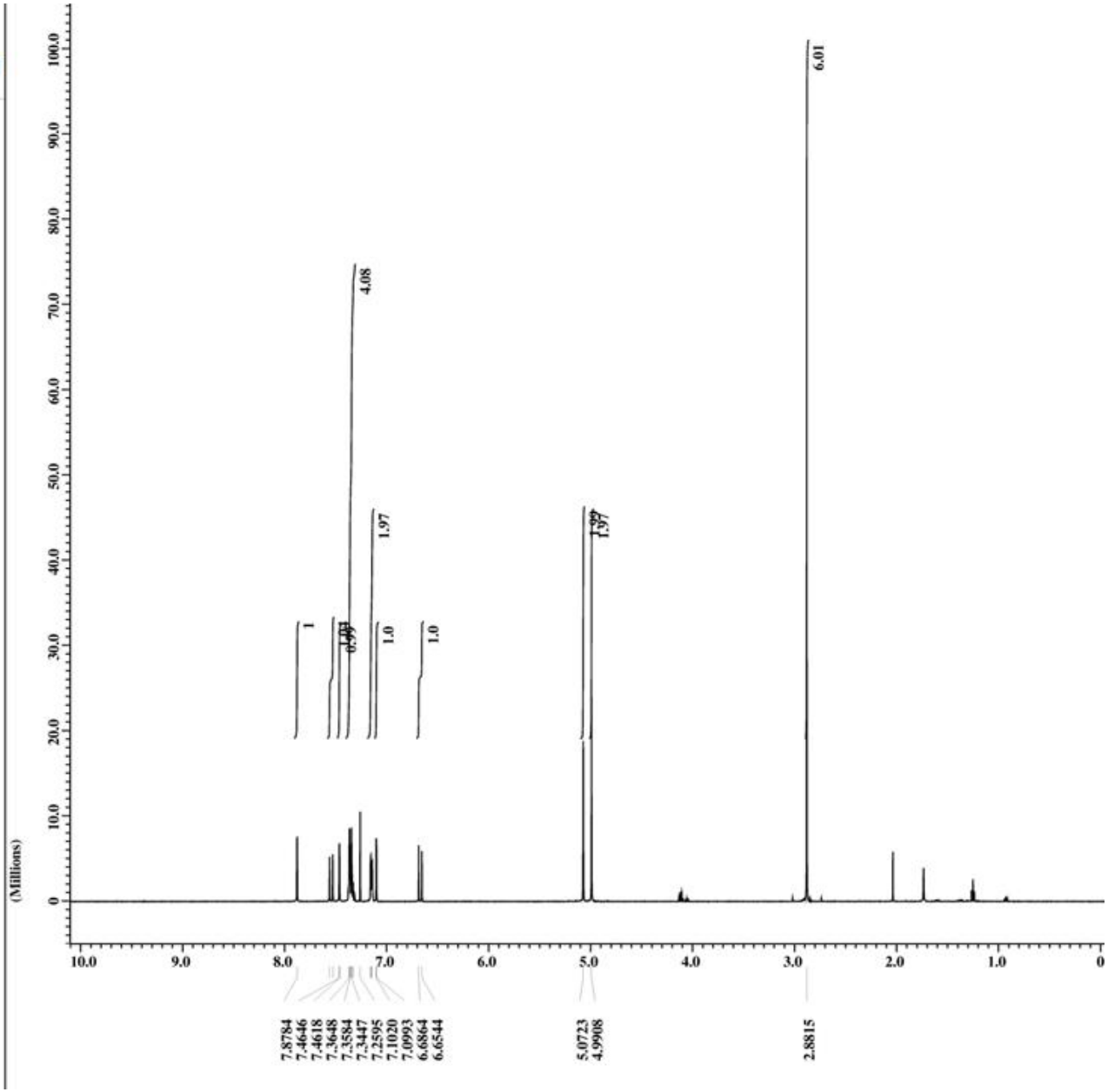




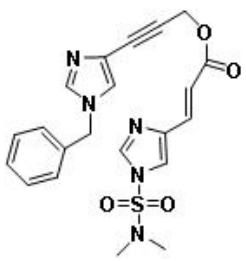
APPENDIX 42
^{1}H AND ^{13}C NMR SPECTRUM OF
(*E*)-3-(1-benzyl-1H-imidazol-4-yl)prop-2-ynyl-3-(1-(N,N-dimethylsulfamoyl)-1H-imidazol-4-yl)acrylate (239)

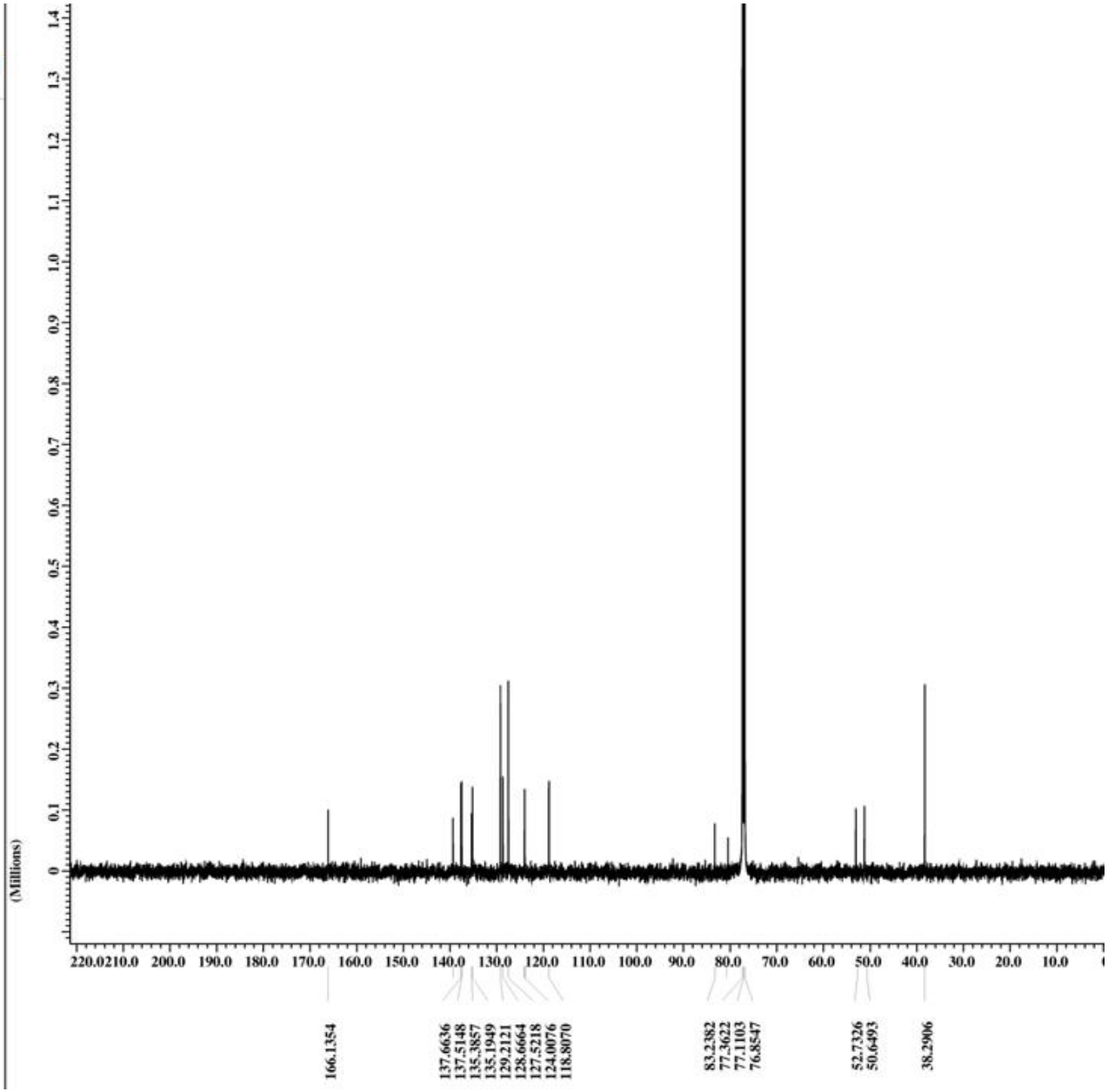
```
ilename          = sm_VI_78_pure-3.jdf
uthor            = delta
xperiment        = single_pulse.exp
ample_id         = S#587591
olvent           = CHLOROFORM-D
reation_time     = 26-DEC-2009 08:01:09
evision_time     = 28-MAR-2010 21:16:38
urrent_time      = 28-MAR-2010 21:17:02

omment           = Single Pulse Experime
ata_format       = 1D COMPLEX
im_size          = 16384
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7465928[T] (500[MH
_acq_duration    = 2.1839872[s]
_domain          = 1H
_freq            = 500.12734003[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.45787814[Hz]
_sweep           = 7.50187547[kHz]
lipped           = FALSE
od_return        = 1
cans             = 8
otal_scans       = 8

_90_width        = 18.5[us]
_acq_time        = 2.1839872[s]
_angle           = 45[deg]
_pulse           = 9.25[us]
nitial_wait      = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 23
elaxation_delay  = 4[s]
emp_get          = 25.8[dC]
nblank_time      = 2[us]
```



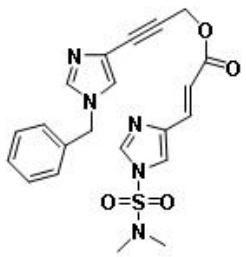


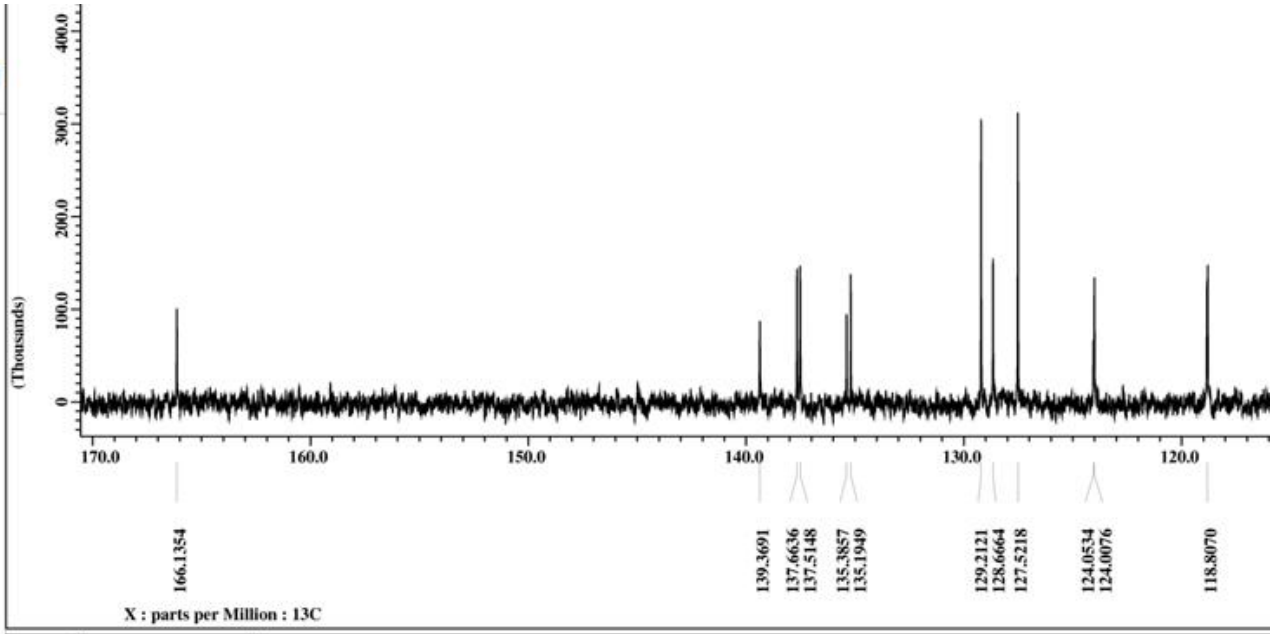
```
ilename          = sm_VI_78_pure-2.jdf
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#588949
olvent           = CHLOROFORM-D
reation_time     = 26-DEC-2009 10:11:45
evision_time     = 26-DEC-2009 16:23:16
urrent_time      = 28-MAR-2010 21:19:48

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 65536
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7465928[T] (500[MH
_acq_duration    = 2.0840448[s]
_domain          = 13C
_freq            = 125.75710665[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.47983613[Hz]
_sweep           = 31.44654088[kHz]
rr_domain        = 1H
rr_freq          = 500.12734003[MHz]
rr_offset        = 5[ppm]
lipped           = TRUE
od_return        = 10
cans             = 1500
otal_scans       = 1500

_90_width        = 14.2[us]
_acq_time        = 2.0840448[s]
_angle           = 30[deg]
_pulse           = 4.73333333[us]
nitial_wait      = 1[s]
oe_time          = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 30
elaxation_delay  = 2[s]
amp_get          = 28.5[dC]
nblank_time      = 2[us]
```

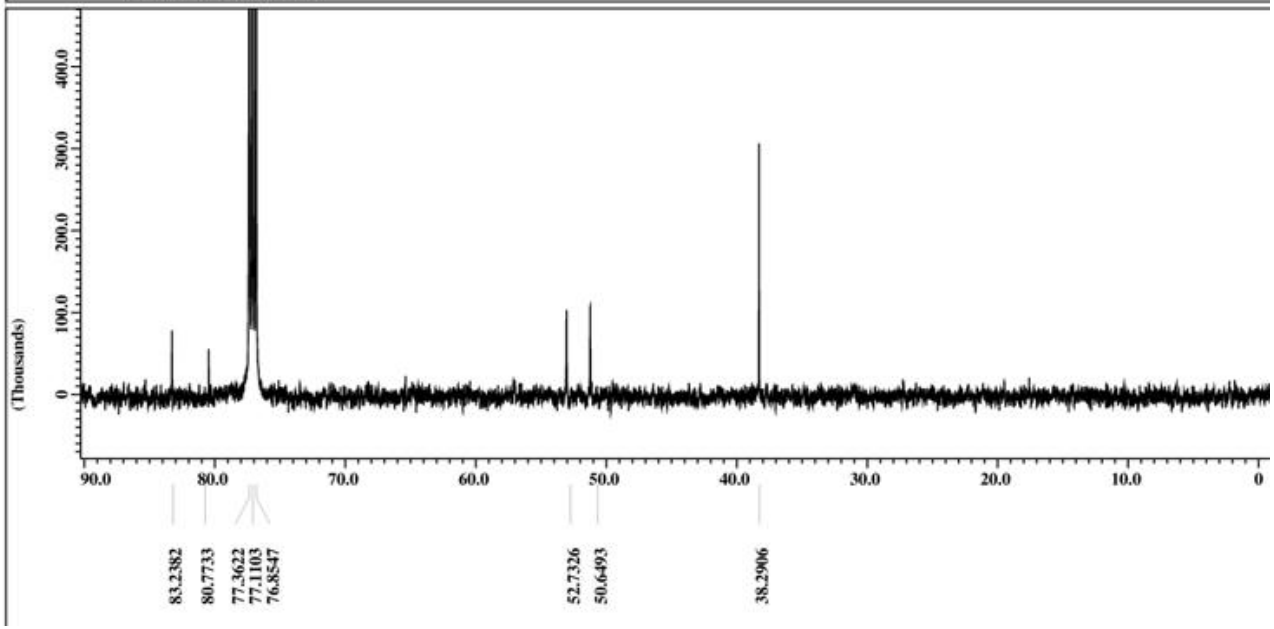




```
ilename          = sm_VI_78_pure-2.jdf
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#588949
olvent           = CHLOROFORM-D
reation_time     = 26-DEC-2009 10:11:45
evision_time     = 26-DEC-2009 16:23:16
urrent_time      = 28-MAR-2010 21:21:28

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 65536
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7465928[T] (500[MH
_acq_duration    = 2.0840448[s]
_domain          = 13C
_freq            = 125.75710665[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.47983613[Hz]
_sweep           = 31.44654088[kHz]
rr_domain        = 1H
rr_freq          = 500.12734003[MHz]
rr_offset        = 5[ppm]
lipped           = TRUE
od_return        = 10
cans             = 1500
otal_scans       = 1500

_90_width        = 14.2[us]
_acq_time        = 2.0840448[s]
_angle           = 30[deg]
_pulse           = 4.73333333[us]
nitial_wait      = 1[s]
oe_time          = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 30
elaxation_delay  = 2[s]
amp_get          = 28.5[dC]
nblank_time      = 2[us]
```





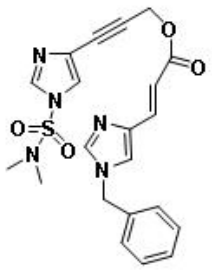


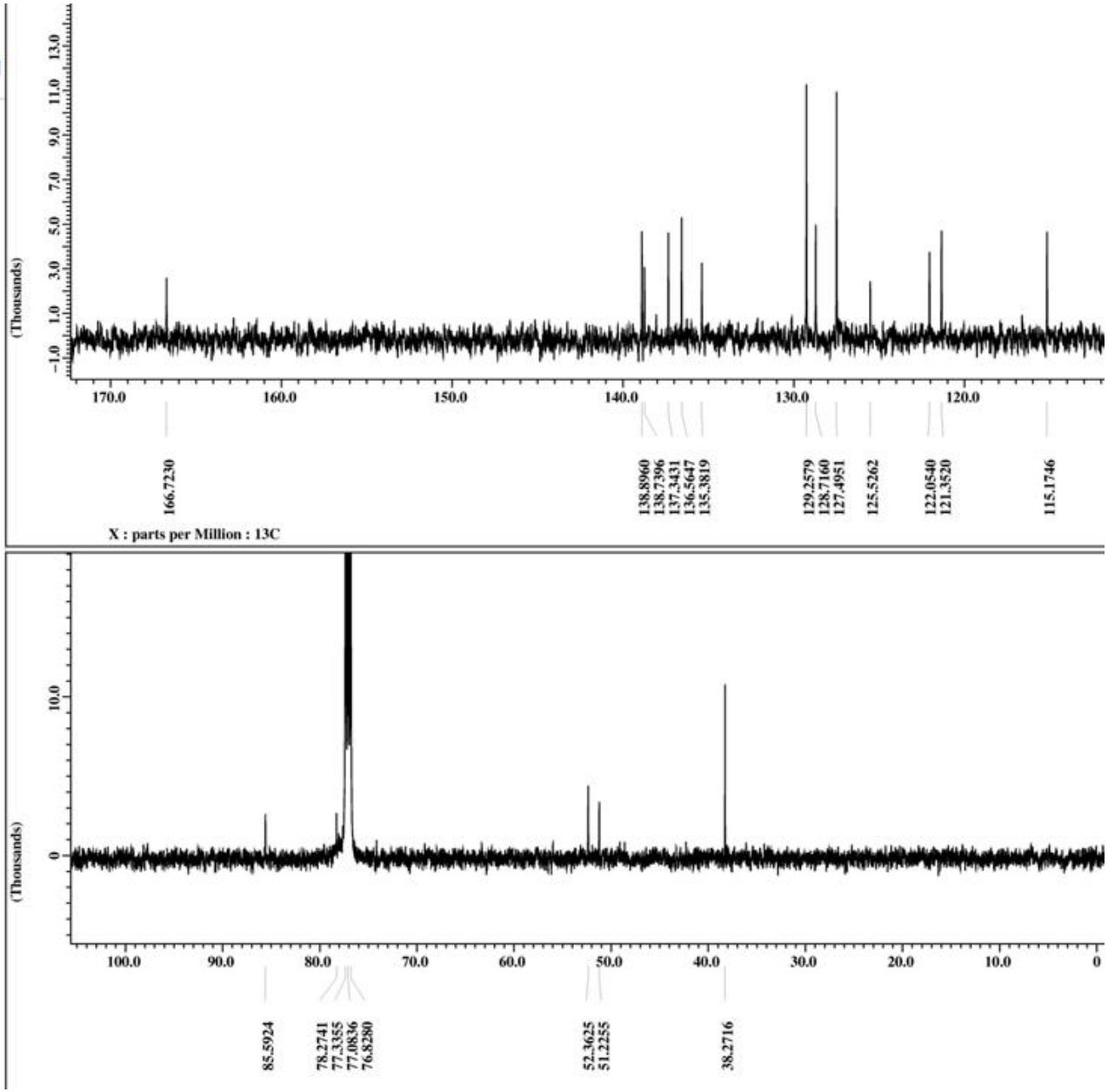
APPENDIX 43
^{1}H AND ^{13}C NMR SPECTRUM OF
(*E*)-3-(1-(N,N-dimethylsulfamoyl)-1H-imidazol-4-yl)prop-2-ynyl-3-(1-benzyl-1H-imidazol-4-yl)acrylate (242)

JEOL
ilename = sm_VI_80_pure-4.jdf
uthor = delta
xperiment = single_pulse.exp
ample_id = S#505736
olvent = CHLOROFORM-D
reation_time = 30-DEC-2009 05:46:49
evision_time = 28-MAR-2010 21:26:19
urrent_time = 28-MAR-2010 21:26:52
omment = Single Pulse Experime
ata_format = 1D COMPLEX
im_size = 16384
im_title = 1H
im_units = [ppm]
imensions = X
ite = Eclipse+ 500
pectrometer = DELTA_NMR
ield_strength = 11.7465928[T] (500[MH
_acq_duration = 2.1839872[s]
_domain = 1H
_freq = 500.12734003[MHz]
_offset = 5[ppm]
_points = 16384
_prescans = 0
_resolution = 0.45787814[Hz]
_sweep = 7.50187547[kHz]
lipped = FALSE
od_return = 1
cans = 8
otal_scans = 8
_90_width = 18.5[us]
_acq_time = 2.1839872[s]
_angle = 45[deg]
_pulse = 9.25[us]
nitial_wait = 1[s]
hase_preset = 3[us]
ecvr_gain = 25
elaxation_delay = 4[s]
emp_get = 29.8[dC]
nblank_time = 2[us]
(Millions)
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
6.01
4.01
2.16
2.11
2.08
1.06
1.0
0.99
1.6272
2.1637
2.8650
4.9835
5.1044
5.2939
6.5509
6.5820
7.0938
7.2586
7.3611
7.3968
7.3996
7.5516
7.8171
O
O
N
N
N
N
S
O
O

JEOL
ilename = sm_VI_80_pure-2.jdf
uthor = delta
xperiment = single_pulse_dec
ample_id = S#7522
olvent = CHLOROFORM-D
reation_time = 28-DEC-2009 22:58:07
evision_time = 28-DEC-2009 14:09:09
urrent_time = 28-MAR-2010 21:29:38
comment = single pulse decouple
ata_format = 1D COMPLEX
im_size = 65536
im_title = 13C
im_units = [ppm]
imensions = X
ite = Eclipse+ 500
pectrometer = DELTA_NMR
ield_strength = 11.7465928[T] (500[MH
acq_duration = 2.0840448[s]
domain = 13C
freq = 125.75710665[MHz]
offset = 100[ppm]
points = 65536
prescans = 4
resolution = 0.47983613[Hz]
sweep = 31.44654088[kHz]
rr_domain = 1H
rr_freq = 500.12734003[MHz]
rr_offset = 5[ppm]
lipped = FALSE
od_return = 10
cans = 5000
otal_scans = 5000
90_width = 14.2[us]
acq_time = 2.0840448[s]
angle = 30[deg]
pulse = 4.73333333[us]
nitial_wait = 1[s]
pe_time = 1[s]
hase_preset = 3[us]
ecvr_gain = 22
elaxation_delay = 2[s]
emp_get = 32.1[dC]
nblank_time = 2[us]
(Thousands)
166.7230
138.8960
137.3431
136.5647
135.3819
129.2579
128.7160
127.4951
122.0540
121.3520
115.1746
85.5924
78.2741
77.3355
77.0836
76.8280
52.3625
51.2255
38.2716

```
ilename          = sm_VI_80_pure-2.jdf
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#7522
olvent           = CHLOROFORM-D
reation_time     = 28-DEC-2009 22:58:07
evision_time     = 28-DEC-2009 14:09:09
urrent_time      = 28-MAR-2010 21:31:55

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 65536
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7465928[T] (500[MH
_acq_duration    = 2.0840448[s]
_domain          = 13C
_freq            = 125.75710665[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.47983613[Hz]
_sweep           = 31.44654088[kHz]
rr_domain        = 1H
rr_freq          = 500.12734003[MHz]
rr_offset        = 5[ppm]
lipped           = FALSE
od_return        = 10
cans             = 5000
otal_scans       = 5000

_90_width        = 14.2[us]
_acq_time        = 2.0840448[s]
_angle           = 30[deg]
_pulse           = 4.73333333[us]
nitial_wait      = 1[s]
pe_time          = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 22
elaxation_delay  = 2[s]
emp_get          = 32.1[dC]
nblank_time      = 2[us]
```





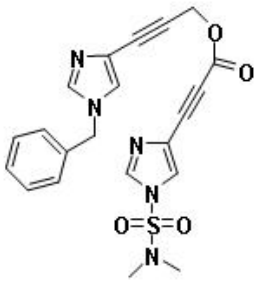
APPENDIX 44
^{1}H AND ^{13}C NMR SPECTRUM OF
(*Z*)-3-(1-benzyl-1H-imidazol-4-yl)-3-iodoallyl-3-(1-(N,N-dimethylsulfamoyl)-1H-imidazol-4-yl)propiolate (250)

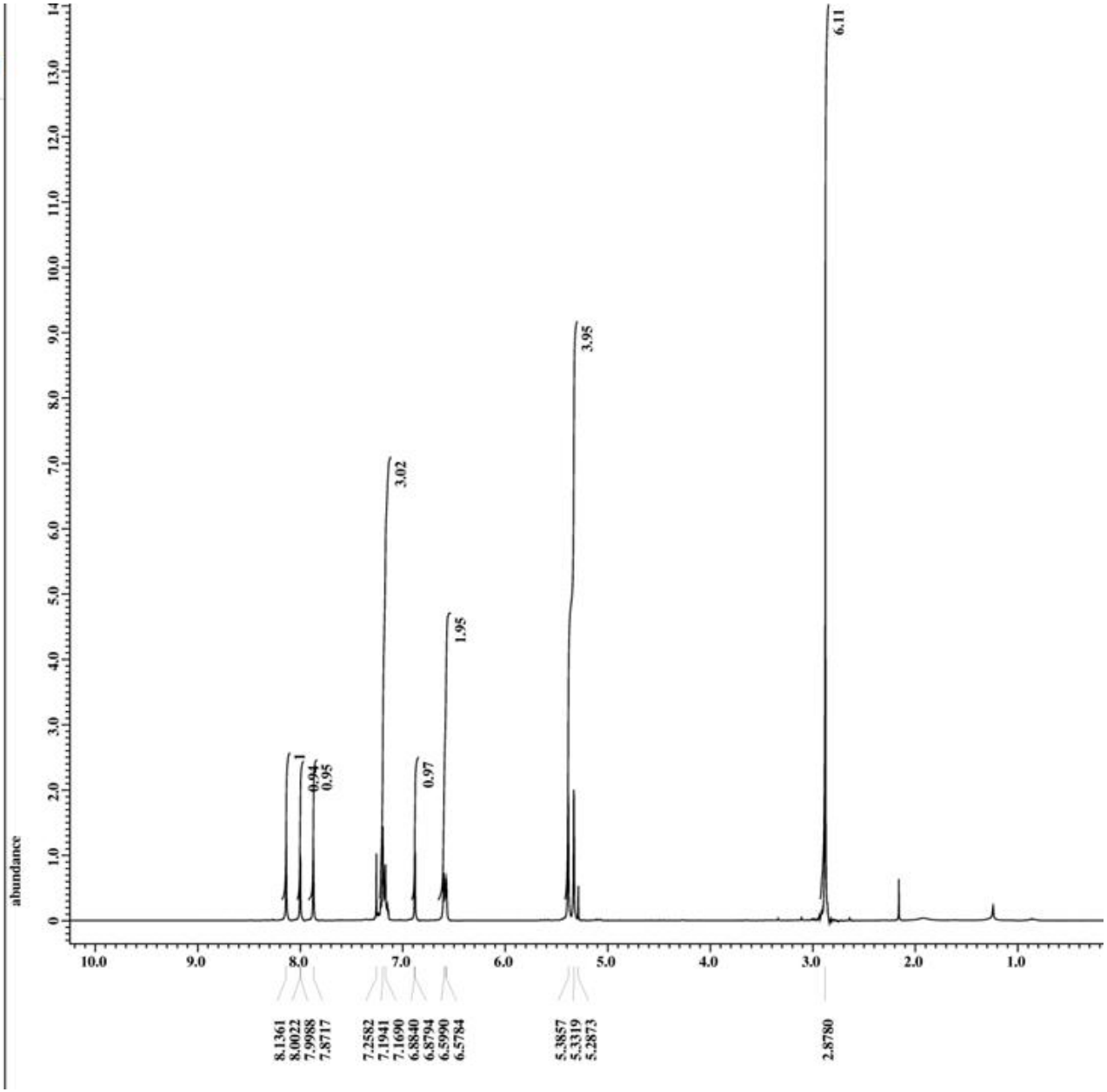
JEOL
Filename = sm_V_193_crude-4.jdf
Author = delta
Experiment = single_pulse.ex2
Sample_id = S#732653
Solvent = CHLOROFORM-D
Creation_time = 1-SEP-2009 20:20:29
Revision_time = 28-MAR-2010 21:36:43
Current_time = 28-MAR-2010 21:37:24
Comment = single_pulse
Data_format = 1D REAL
Dim_size = 13107
Dim_title = 1H
Dim_units = [ppm]
Dimensions = X
Site = ECX 300
Spectrometer = DELTA2_NMR
Field_strength = 7.05860137[T] (300[MHz
Acq_duration = 2.90717696[s]
X_domain = 1H
X_freq = 300.52965592[MHz]
X_offset = 5[ppm]
X_points = 16384
X_prescans = 0
X_resolution = 0.34397631[Hz]
X_sweep = 5.63570784[kHz]
Xr_domain = 1H
Xr_freq = 300.52965592[MHz]
Xr_offset = 5[ppm]
Xi_domain = 1H
Xi_freq = 300.52965592[MHz]
Xi_offset = 5[ppm]
Clipped = FALSE
Mod_return = 1
Scans = 23
Total_scans = 23
X_90_width = 13.01[us]
X_acq_time = 2.90717696[s]
X_angle = 45[deg]
X_atn = 4[dB]
X_pulse = 6.505[us]
Xr_mode = Off
Xi_mode = Off
Sante_presat = FALSE
Initial_wait = 1[s]
Recvr_gain = 46
Relaxation_delay = 5[s]
Repetition_time = 7.90717696[s]
Temp_get = 23.3[dC]
Me
Me-N
O=S=O
N
N
N
N
O
O
O
I
abundance
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
6.05
2.07
3.05
2.01
2.0
1.0
1.0
1.0
7.8649
7.6085
7.6062
7.6039
7.6016
7.5627
7.3841
7.3601
7.2605
7.2582
7.1094
5.0836
4.9805
4.9599
2.9089
2.8963
2.8940

JEOL
ilename = sm_VI_iodo_DCC_coupli
uthor = delta
xperiment = single_pulse_dec
ample_id = S#793596
olvent = CHLOROFORM-D
reation_time = 20-JAN-2010 01:50:29
evision_time = 19-APR-2010 19:25:03
urrent_time = 19-APR-2010 19:26:04
comment = single pulse decouple
ata_format = 1D COMPLEX
im_size = 52428
im_title = 13C
im_units = [ppm]
imensions = X
ite = ECX 300
pectrometer = DELTA2_NMR
ield_strength = 7.0586013[T] (300[MHz
_acq_duration = 2.76824064[s]
_domain = 13C
_freq = 75.56823426[MHz]
_offset = 100[ppm]
_points = 65536
_prescans = 4
_resolution = 0.36124027[Hz]
_sweep = 23.67424242[kHz]
rr_domain = 1H
rr_freq = 300.52965592[MHz]
rr_offset = 5[ppm]
lipped = FALSE
od_return = 10
cans = 2500
otal_scans = 2500
_90_width = 9.75[us]
_acq_time = 2.76824064[s]
_angle = 30[deg]
_atn = 8[dB]
_pulse = 3.25[us]
rr_atn_dec = 25[dB]
rr_atn_noe = 25[dB]
rr_noise = WALTZ
ecoupling = TRUE
nitial_wait = 1[s]
oe = TRUE
oe_time = 3[s]
ecvr_gain = 50
elaxation_delay = 3[s]
epetition_time = 5.76824064[s]
emp_get = 21.3[dC]
(thousandths)
153.3484
137.5781
137.2817
129.5424
129.1839
127.9983
124.9485
122.1424
82.1933
79.2582
70.1612
52.1538
38.4582
Me
Me
N
O
S
O
O
N
N
N
N
O
O
I

APPENDIX 45
^{1}H AND ^{13}C NMR SPECTRUM OF
3-(1-benzyl-1H-imidazol-4-yl)prop-2-ynyl-3-(1-(N,N-dimethylsulfamoyl)-1H-imidazol-4-yl)propiolate (251)

```
ilename          = sm_VI_yne_yne_pure-2.
uthor            = delta
xperiment        = single_pulse.ex2
ample_id         = S#658718
olvent           = CHLOROFORM-D
reation_time     =  2-FEB-2010 18:09:37
evision_time     =  2-FEB-2010 18:23:03
urrent_time      = 19-APR-2010 19:31:36

omment           = single_pulse
ata_format       = 1D COMPLEX
im_size          = 13107
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.90717696[s]
_domain          = 1H
_freq            = 300.52965592[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.34397631[Hz]
_sweep           = 5.63570784[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
ri_domain        = 1H
ri_freq          = 300.52965592[MHz]
ri_offset        = 5[ppm]
lipped           = FALSE
od_return        = 1
cans             = 19
otal_scans       = 19

_90_width        = 13.01[us]
_acq_time        = 2.90717696[s]
_angle           = 45[deg]
_atn             = 4[dB]
_pulse           = 6.505[us]
rr_mode          = Off
ri_mode          = Off
ante_presat      = FALSE
nitial_wait      = 1[s]
ecvr_gain        = 42
elaxation_delay  = 5[s]
epetition_time   = 7.90717696[s]
emp_get          = 19.8[dC]
```

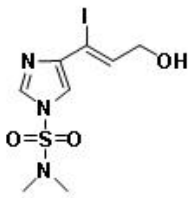


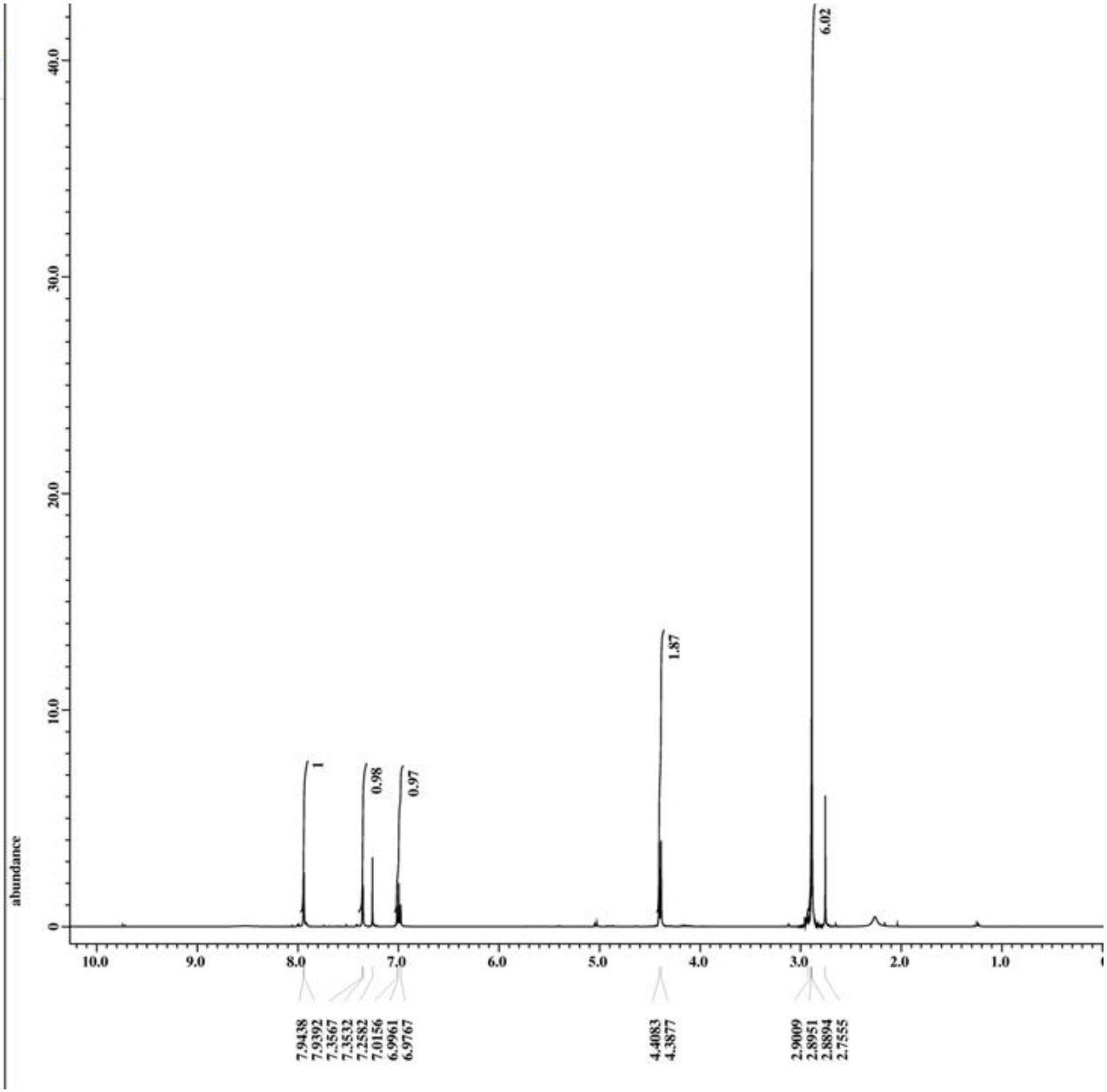


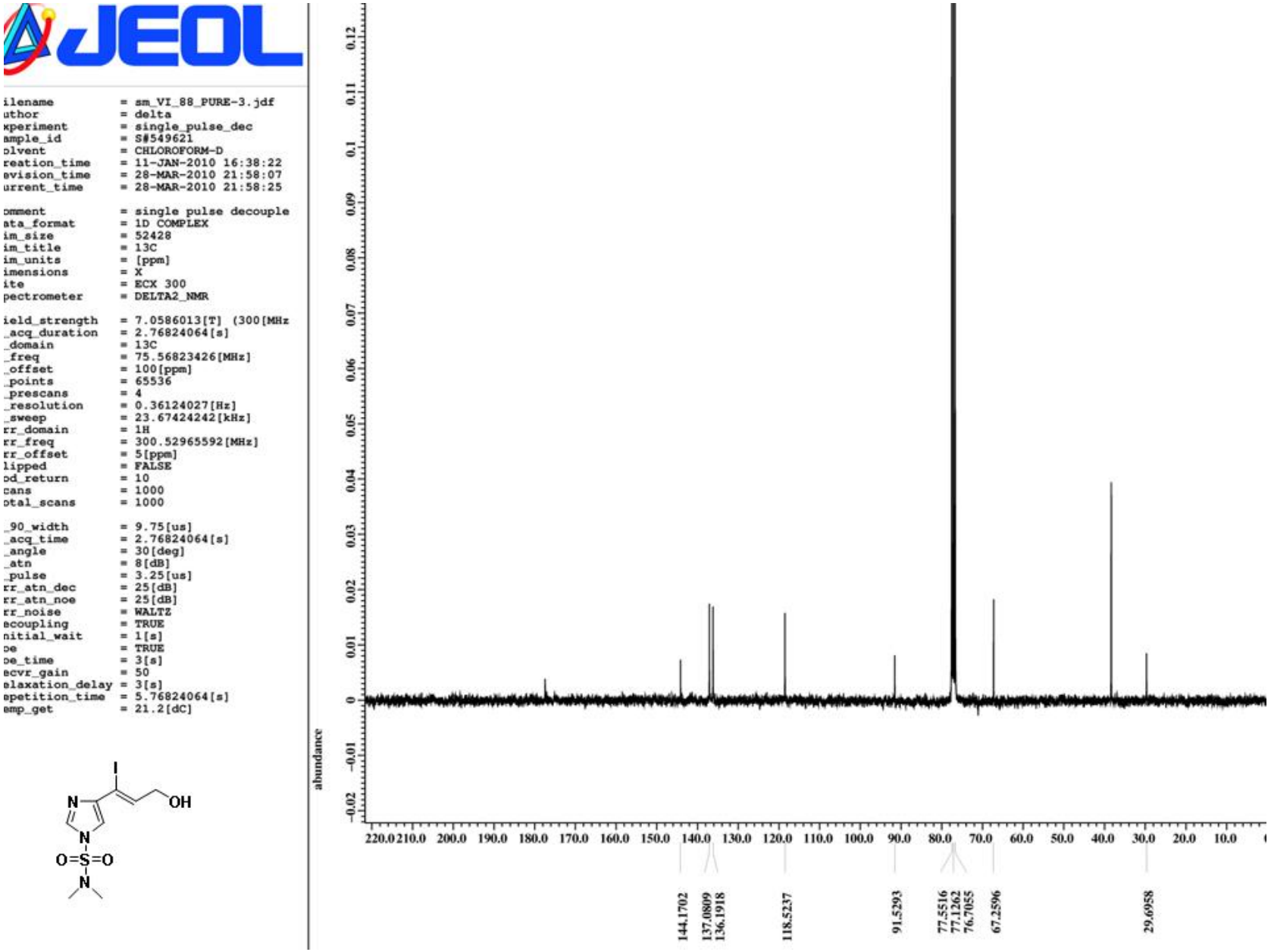
JEOL
ilename = sm_VI_yne_yne_pure-2.
uthor = delta
xperiment = single_pulse_dec
ample_id = S#660727
olvent = CHLOROFORM-D
reation_time = 2-FEB-2010 20:35:31
evision_time = 2-FEB-2010 23:41:18
urrent_time = 19-APR-2010 19:34:35
omment = single pulse decouple
ata_format = 1D COMPLEX
im_size = 52428
im_title = 13C
im_units = [ppm]
imensions = X
ite = ECX 300
pectrometer = DELTA2_NMR
ield_strength = 7.0586013[T] (300[MHz
_acq_duration = 2.76824064[s]
_domain = 13C
_freq = 75.56823426[MHz]
_offset = 100[ppm]
_points = 65536
_prescans = 4
_resolution = 0.36124027[Hz]
_sweep = 23.67424242[kHz]
rr_domain = 1H
rr_freq = 300.52965592[MHz]
rr_offset = 5[ppm]
lipped = FALSE
od_return = 10
cans = 1500
otal_scans = 1500
_90_width = 9.75[us]
_acq_time = 2.76824064[s]
_angle = 30[deg]
_atn = 8[dB]
_pulse = 3.25[us]
rr_atn_dec = 25[dB]
rr_atn_noe = 25[dB]
rr_noise = WALTZ
ecoupling = TRUE
nitial_wait = 1[s]
oe = TRUE
oe_time = 3[s]
ecvr_gain = 50
elaxation_delay = 3[s]
epetition_time = 5.76824064[s]
emp_get = 19.8[dC]
abundance
170.1990
150.0165
149.2038
140.4702
135.7759
135.5417
133.3666
132.2002
128.9353
128.1274
125.3500
119.5467
118.5237
118.3994
113.6717
77.5707
77.1453
76.7246
68.0483
50.7101
38.3530
O
O
O
N
N
N
O=S=O
N

APPENDIX 46
^{1}H AND ^{13}C NMR SPECTRUM OF
(*Z*)-4-(3-hydroxy-1-iodoprop-1-enyl)-N,N-dimethyl-1H-imidazole-1-sulfonamide (244)

```
ilename          = sm_VI_88_pure-4.jdf
uthor            = delta
xperiment        = single_pulse.ex2
mple_id          = S#543823
olvent           = CHLOROFORM-D
reation_time     = 11-JAN-2010 14:55:29
evision_time     = 28-MAR-2010 21:54:44
urrent_time      = 28-MAR-2010 21:55:17

omment           = single_pulse
ata_format       = 1D COMPLEX
im_size          = 13107
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.90717696[s]
_domain          = 1H
_freq            = 300.52965592[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.34397631[Hz]
_sweep           = 5.63570784[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
ri_domain        = 1H
ri_freq          = 300.52965592[MHz]
ri_offset        = 5[ppm]
lipped           = FALSE
od_return        = 1
cans             = 24
otal_scans       = 24

_90_width        = 13.01[us]
_acq_time        = 2.90717696[s]
_angle           = 45[deg]
_atn             = 4[dB]
_pulse           = 6.505[us]
rr_mode          = Off
ri_mode          = Off
ante_presat      = FALSE
nitial_wait      = 1[s]
ecvr_gain        = 50
elaxation_delay  = 5[s]
epetition_time   = 7.90717696[s]
emp_get          = 21[dC]
```



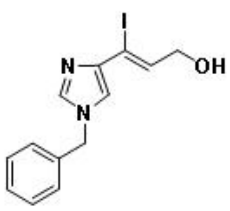


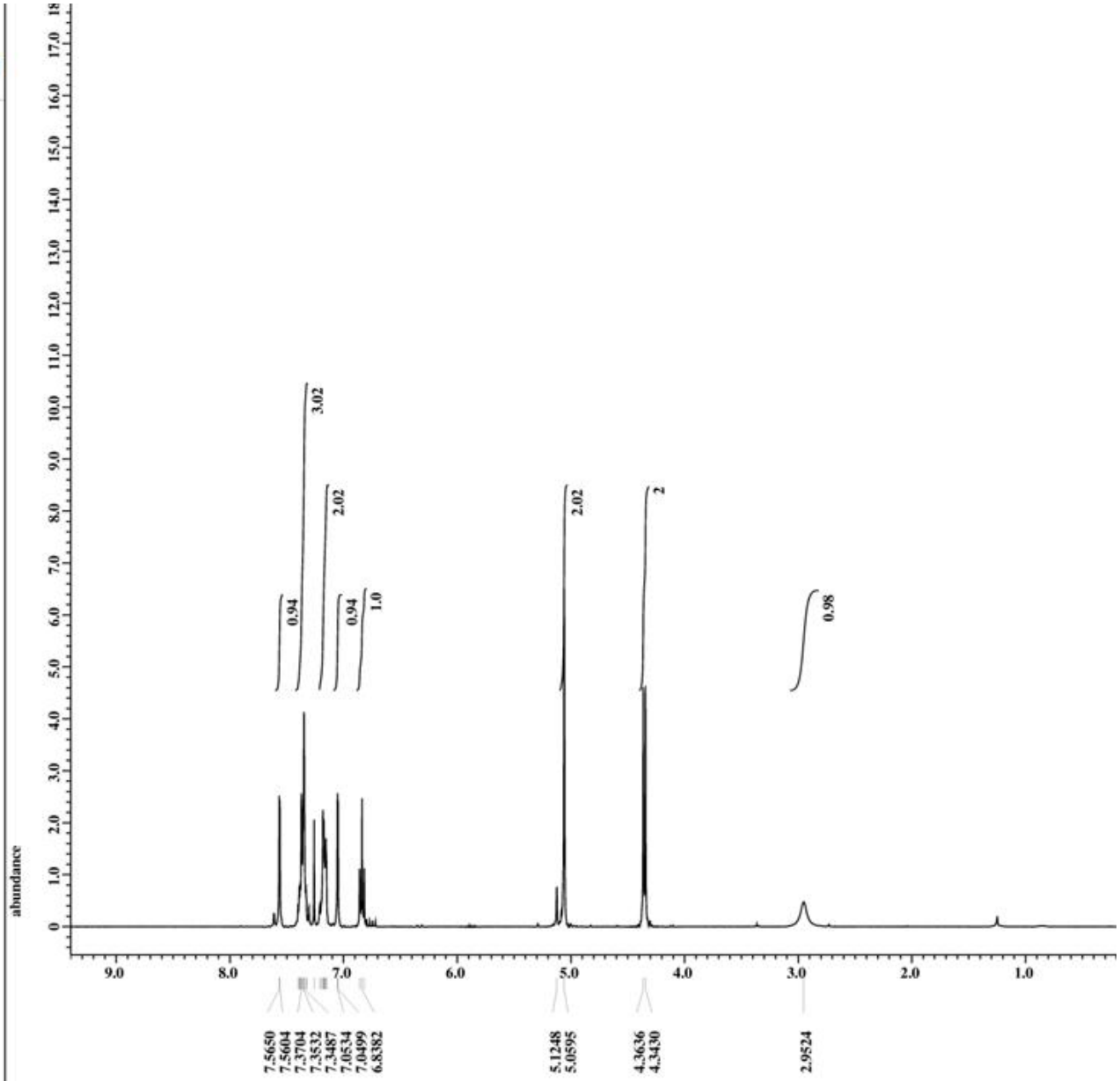


```
ilename          = sm_VI_88_PURE-3.jdf
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#549621
olvent           = CHLOROFORM-D
reation_time     = 11-JAN-2010 16:38:22
evision_time     = 28-MAR-2010 21:58:07
urrent_time      = 28-MAR-2010 21:58:25

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 52428
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.76824064[s]
_domain          = 13C
_freq            = 75.56823426[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.36124027[Hz]
_sweep           = 23.67424242[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
lipped           = FALSE
od_return        = 10
cans             = 1000
otal_scans       = 1000

_90_width        = 9.75[us]
_acq_time        = 2.76824064[s]
_angle           = 30[deg]
_atn             = 8[dB]
_pulse           = 3.25[us]
rr_atn_dec       = 25[dB]
rr_atn_noe       = 25[dB]
rr_noise         = WALTZ
ecoupling        = TRUE
nitial_wait      = 1[s]
oe               = TRUE
oe_time          = 3[s]
ecvr_gain        = 50
elaxation_delay  = 3[s]
epetition_time   = 5.76824064[s]
emp_get          = 21.2[dC]
```

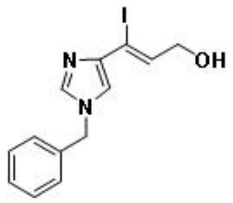
APPENDIX 47
^{1}H AND ^{13}C NMR SPECTRUM OF
(*Z*)-3-(1-benzyl-1H-imidazol-4-yl)-3-iodoprop-2-en-1-ol (245)

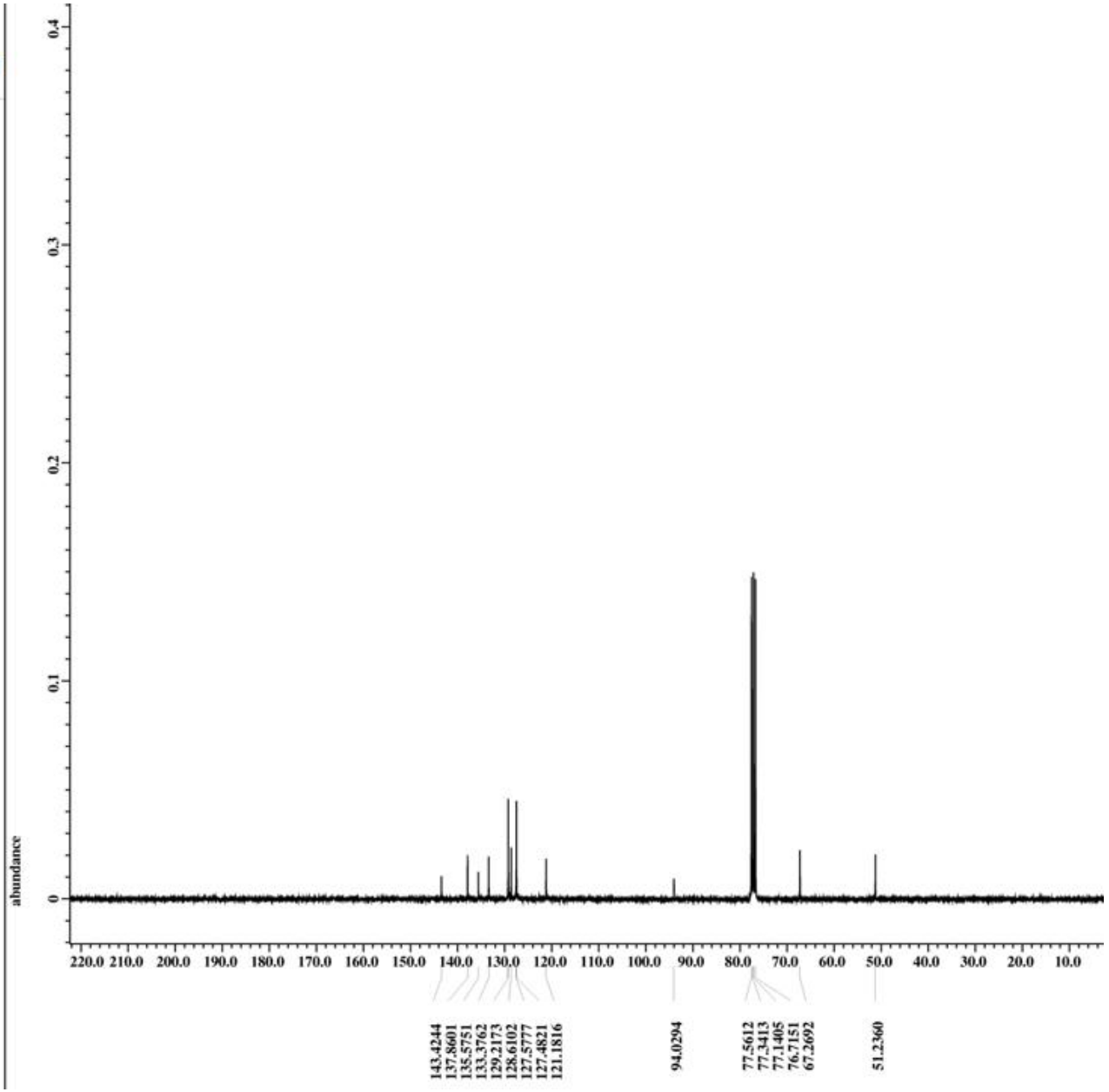
```
ilename          = sm_V_180_pure-7.jdf
uthor            = delta
xperiment        = single_pulse.ex2
mple_id          = S#811089
olvent           = CHLOROFORM-D
reation_time     =  3-AUG-2009 22:27:59
evision_time     = 28-MAR-2010 22:03:00
urrent_time      = 28-MAR-2010 22:03:34

omment           = single_pulse
ata_format       = 1D REAL
im_size          = 13107
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.90717696[s]
_domain          = 1H
_freq            = 300.52965592[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.34397631[Hz]
_sweep           = 5.63570784[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
ri_domain        = 1H
ri_freq          = 300.52965592[MHz]
ri_offset        = 5[ppm]
lipped           = FALSE
od_return        = 1
cans             = 24
otal_scans       = 24

_90_width        = 13.01[us]
_acq_time        = 2.90717696[s]
_angle           = 45[deg]
_atn             = 4[dB]
_pulse           = 6.505[us]
rr_mode          = Off
ri_mode          = Off
ante_presat      = FALSE
nitial_wait      = 1[s]
ecvr_gain        = 50
elaxation_delay  = 5[s]
epetition_time   = 7.90717696[s]
emp_get          = 23.2[dC]
```





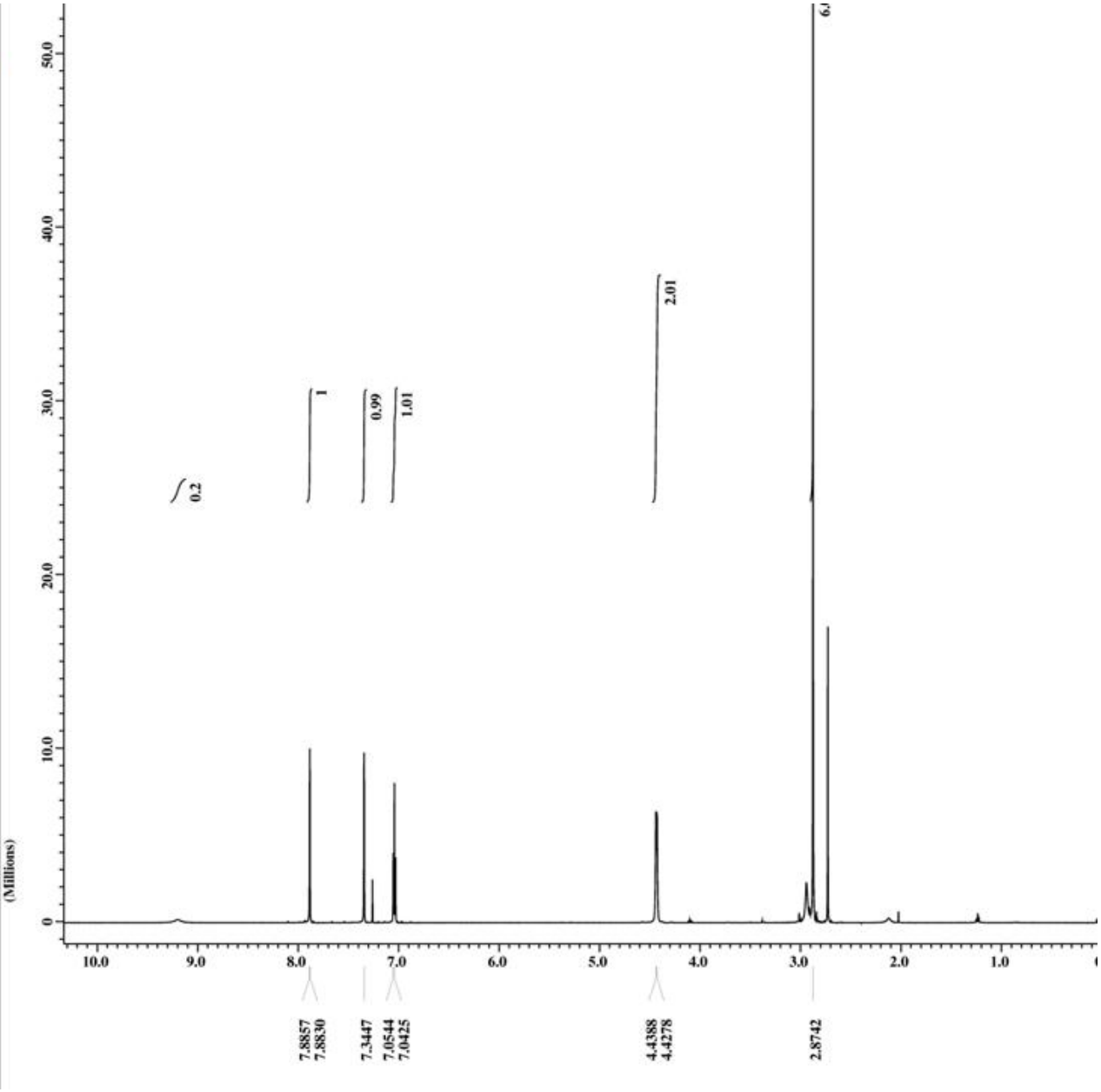
```
ilename          = sm_V_180_pure-2.jdf
uthor            = delta
xperiment        = single_pulse_dec
mple_id          = S#813546
olvent           = CHLOROFORM-D
reation_time     =  4-AUG-2009 03:17:32
evision_time     =  4-AUG-2009 12:18:54
urrent_time      = 28-MAR-2010 22:05:58

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 52428
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.76824064[s]
_domain          = 13C
_freq            = 75.56823426[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.36124027[Hz]
_sweep           = 23.67424242[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
lipped           = FALSE
od_return        = 10
cans             = 3000
otal_scans       = 3000

_90_width        = 9.75[us]
_acq_time        = 2.76824064[s]
_angle           = 30[deg]
_atn             = 8[dB]
_pulse           = 3.25[us]
rr_atn_dec       = 25[dB]
rr_atn_noe       = 25[dB]
rr_noise         = WALTZ
ecoupling        = TRUE
nitial_wait      = 1[s]
oe               = TRUE
oe_time          = 3[s]
ecvr_gain        = 50
elaxation_delay  = 3[s]
epetition_time   = 5.76824064[s]
emp_get          = 23.2[dC]
```



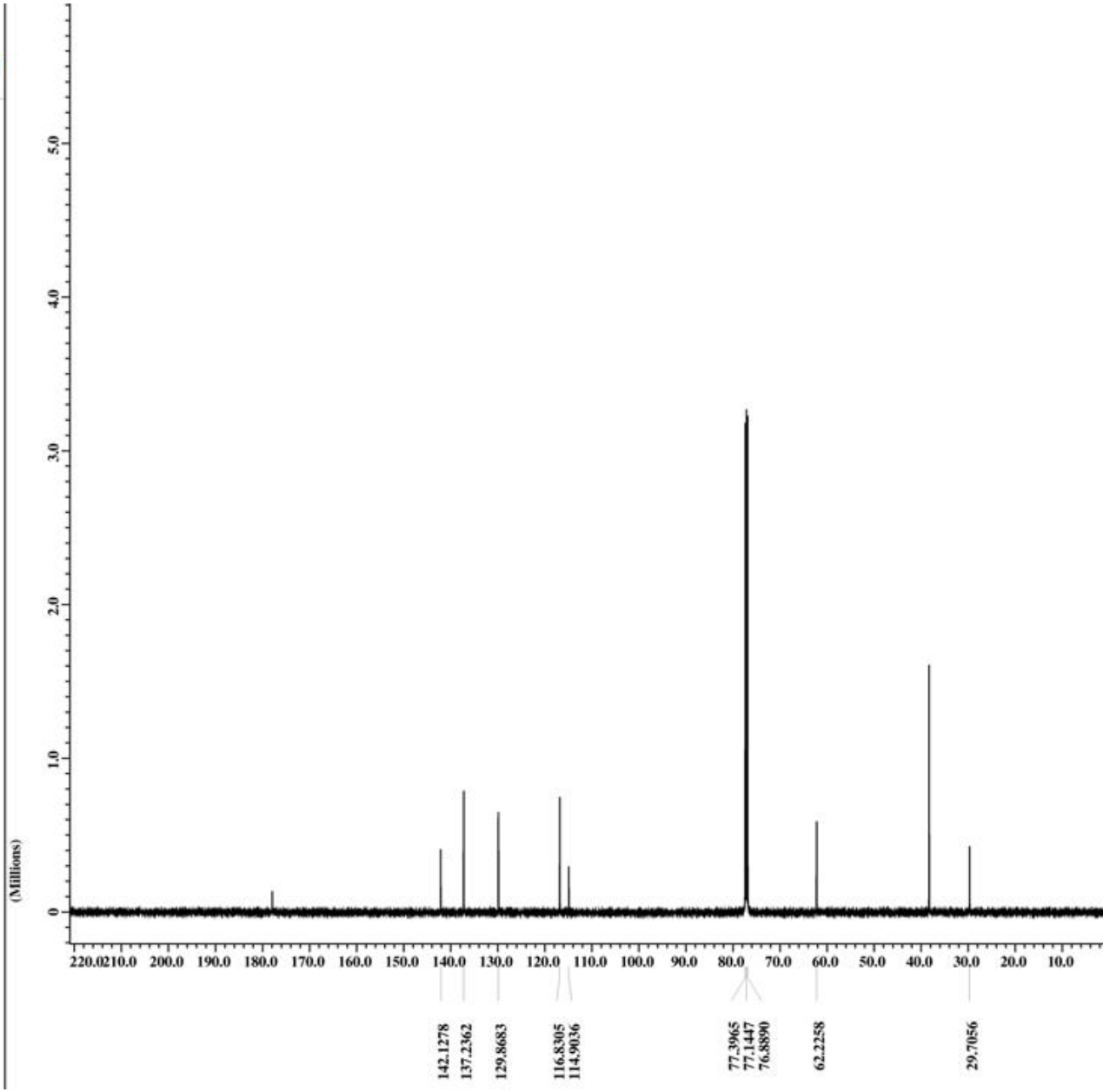


APPENDIX 48
^{1}H AND ^{13}C NMR SPECTRUM OF
(*Z*)-4-(1-bromo-3-hydroxyprop-1-enyl)-N,N-dimethyl-1H-imidazole-1-sulfonamide (259)

```
ilename          = sm_VI_74_pure-3.jdf
uthor            = delta
xperiment        = single_pulse.exp
ample_id         = S#862202
olvent           = CHLOROFORM-D
reation_time     = 22-DEC-2009 15:36:16
evision_time     = 28-MAR-2010 22:10:17
urrent_time      = 28-MAR-2010 22:10:54

omment           = Single Pulse Experime
ata_format       = 1D COMPLEX
im_size          = 16384
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7465928[T] (500[MH
_acq_duration    = 2.1839872[s]
_domain          = 1H
_freq            = 500.12734003[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.45787814[Hz]
_sweep           = 7.50187547[kHz]
lipped           = FALSE
od_return        = 1
cans             = 8
otal_scans       = 8

_90_width        = 18.5[us]
_acq_time        = 2.1839872[s]
_angle           = 45[deg]
_pulse           = 9.25[us]
nitial_wait      = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 17
elaxation_delay  = 4[s]
mp_get           = 25.5[dC]
nblank_time      = 2[us]
```

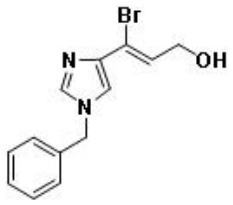


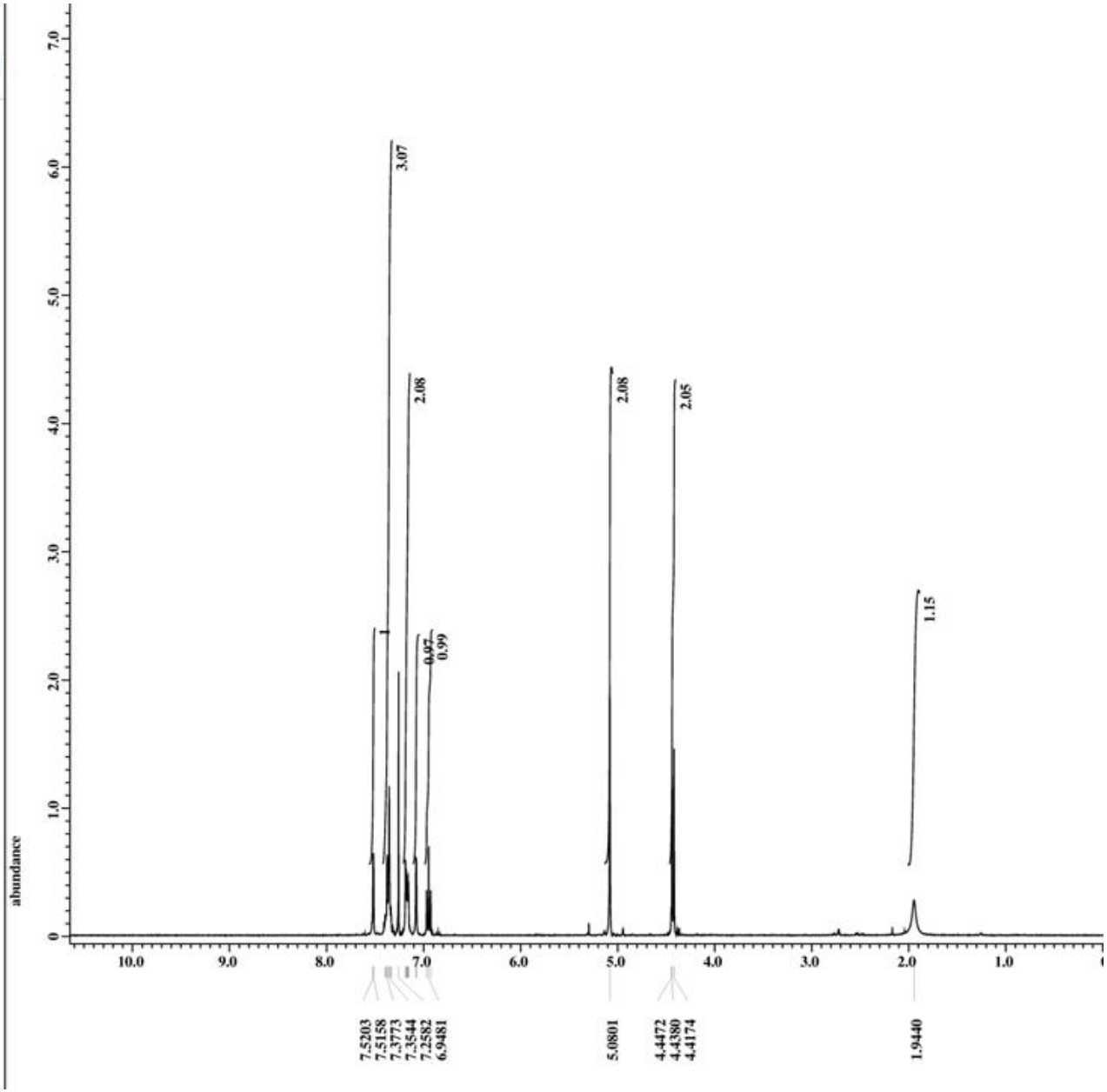
```
ilename          = sm_VI_74_pure-3.jdf
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#863468
olvent           = CHLOROFORM-D
reation_time     = 22-DEC-2009 22:42:01
evision_time     = 28-MAR-2010 22:13:15
urrent_time      = 28-MAR-2010 22:13:28

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 65536
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7465928[T] (500[MH
_acq_duration    = 2.0840448[s]
_domain          = 13C
_freq            = 125.75710665[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.47983613[Hz]
_sweep           = 31.44654088[kHz]
rr_domain        = 1H
rr_freq          = 500.12734003[MHz]
rr_offset        = 5[ppm]
lipped           = TRUE
od_return        = 10
cans             = 5000
otal_scans       = 5000

_90_width        = 14.2[us]
_acq_time        = 2.0840448[s]
_angle           = 30[deg]
_pulse           = 4.73333333[us]
nitial_wait      = 1[s]
pe_time          = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 30
elaxation_delay  = 2[s]
emp_get          = 28.5[dC]
nblank_time      = 2[us]
```

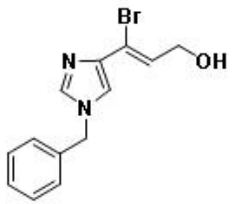
APPENDIX 49
^{1}H AND ^{13}C NMR SPECTRUM OF
(*Z*)-3-(1-benzyl-1H-imidazol-4-yl)-3-bromoprop-2-en-1-ol (260)

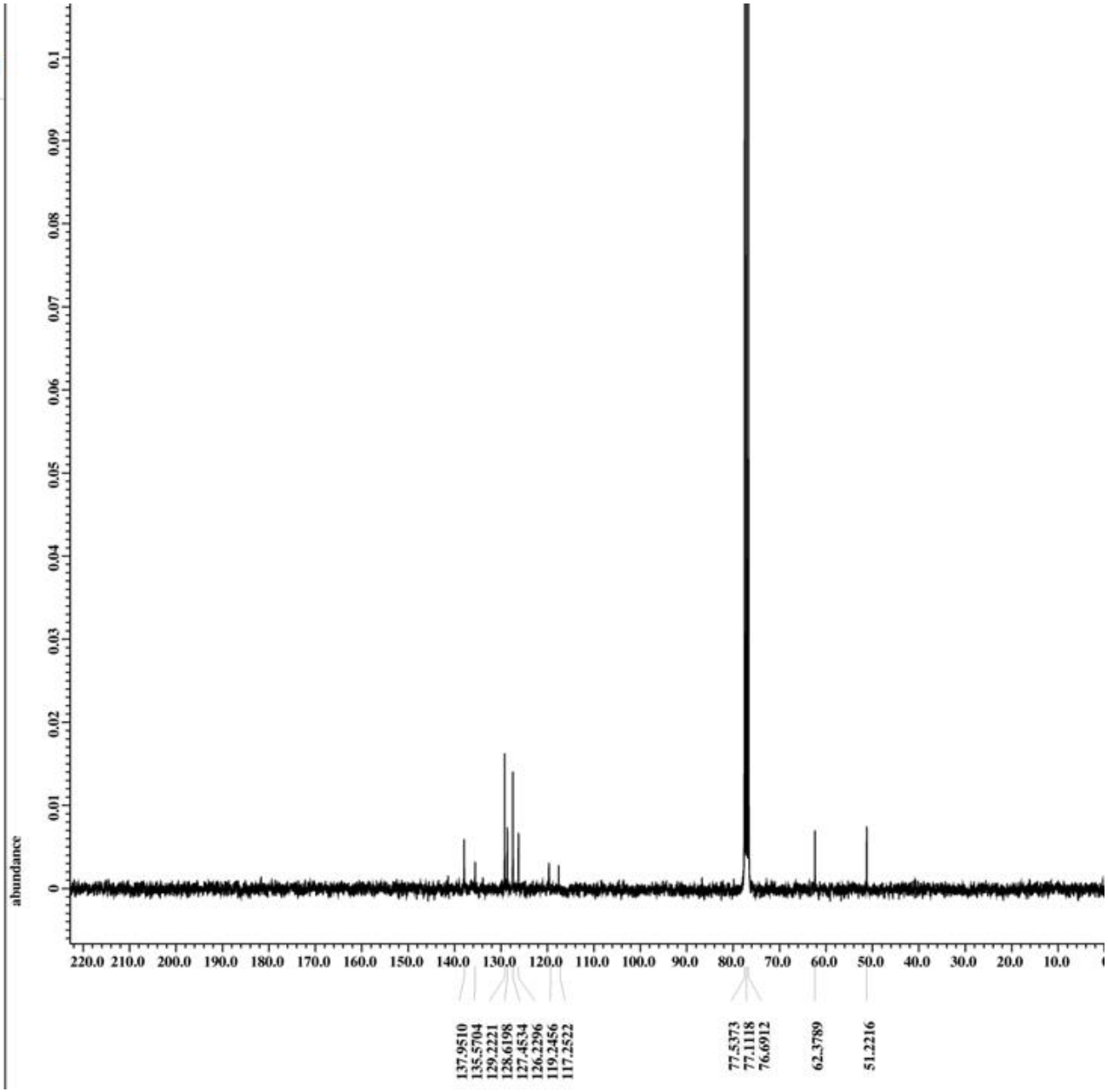
```
ilename          = sm_VI_67_pure-3.jdf
uthor            = delta
xperiment        = single_pulse.ex2
ample_id         = S#610342
olvent           = CHLOROFORM-D
reation_time     = 15-DEC-2009 17:08:45
evision_time     = 28-MAR-2010 22:16:54
urrent_time      = 28-MAR-2010 22:17:17

omment           = single_pulse
ata_format       = 1D COMPLEX
im_size          = 13107
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.90717696[s]
_domain          = 1H
_freq            = 300.52965592[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.34397631[Hz]
_sweep           = 5.63570784[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
ri_domain        = 1H
ri_freq          = 300.52965592[MHz]
ri_offset        = 5[ppm]
lipped           = FALSE
od_return        = 1
cans             = 24
otal_scans       = 24

_90_width        = 13.01[us]
_acq_time        = 2.90717696[s]
_angle           = 45[deg]
_atn             = 4[dB]
_pulse           = 6.505[us]
rr_mode          = Off
ri_mode          = Off
ante_presat      = FALSE
nitial_wait      = 1[s]
ecvr_gain        = 48
elaxation_delay  = 5[s]
epetition_time   = 7.90717696[s]
emp_get          = 23.1[dC]
```





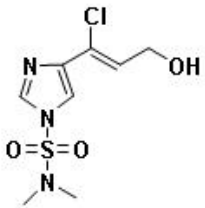
```
ilename          = sm_VI_67_pure-2.jdf
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#612850
olvent           = CHLOROFORM-D
reation_time     = 15-DEC-2009 19:06:01
evision_time     = 15-DEC-2009 21:41:28
urrent_time      = 28-MAR-2010 22:19:39

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 52428
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.76824064[s]
_domain          = 13C
_freq            = 75.56823426[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.36124027[Hz]
_sweep           = 23.67424242[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
lipped           = FALSE
od_return        = 10
cans             = 1200
otal_scans       = 1200

_90_width        = 9.75[us]
_acq_time        = 2.76824064[s]
_angle           = 30[deg]
_atn             = 8[dB]
_pulse           = 3.25[us]
rr_atn_dec       = 25[dB]
rr_atn_noe       = 25[dB]
rr_noise         = WALTZ
ecoupling        = TRUE
nitial_wait      = 1[s]
oe               = TRUE
oe_time          = 3[s]
ecvr_gain        = 50
elaxation_delay  = 3[s]
epetition_time   = 5.76824064[s]
emp_get          = 23.4[dC]
```

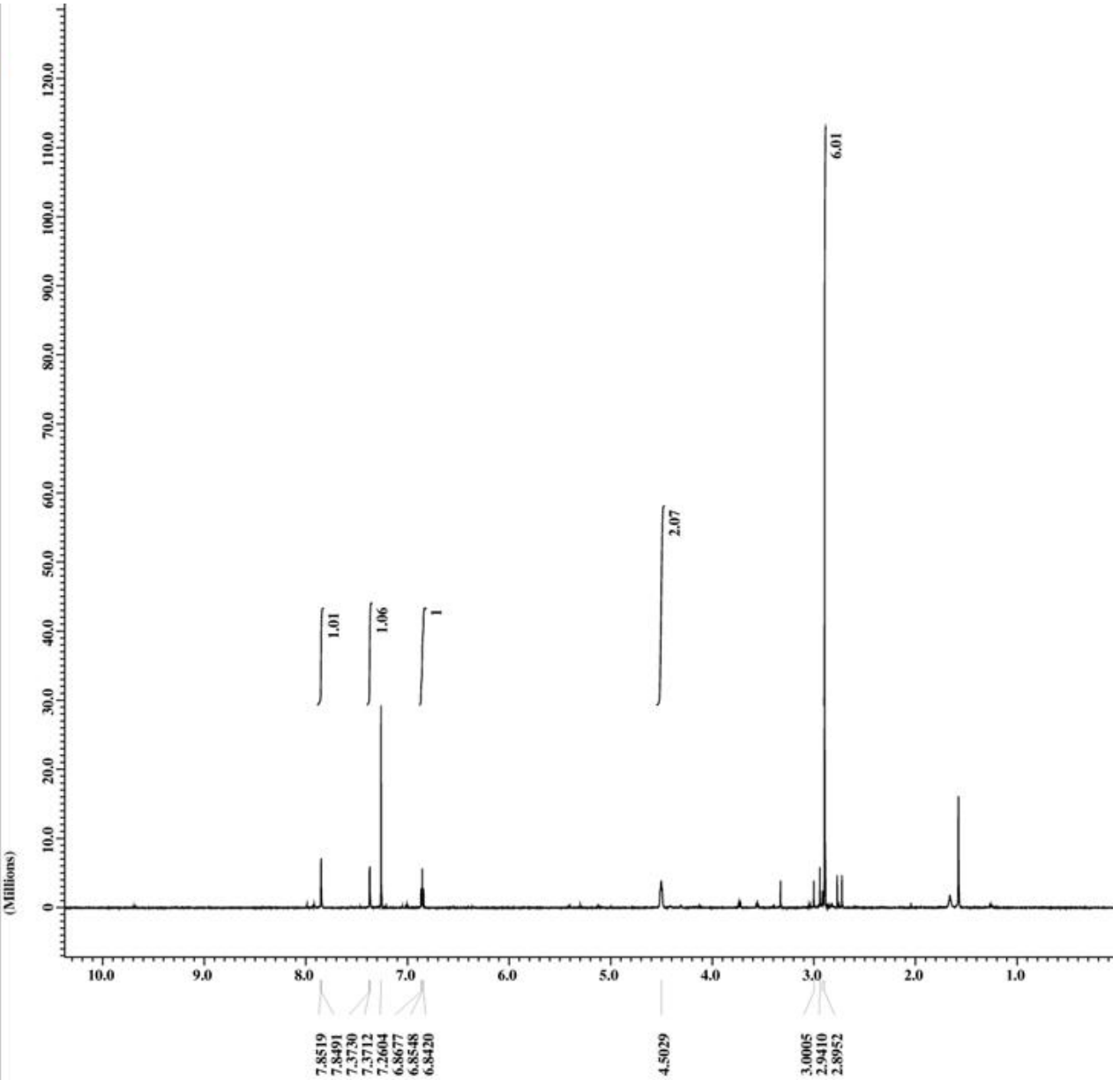




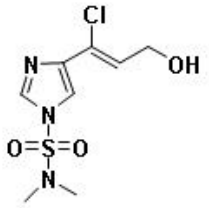
APPENDIX 50
^{1}H AND ^{13}C NMR SPECTRUM OF
(*Z*)-4-(1-chloro-3-hydroxyprop-1-enyl)-N,N-dimethyl-1H-imidazole-1-sulfonamide (263)

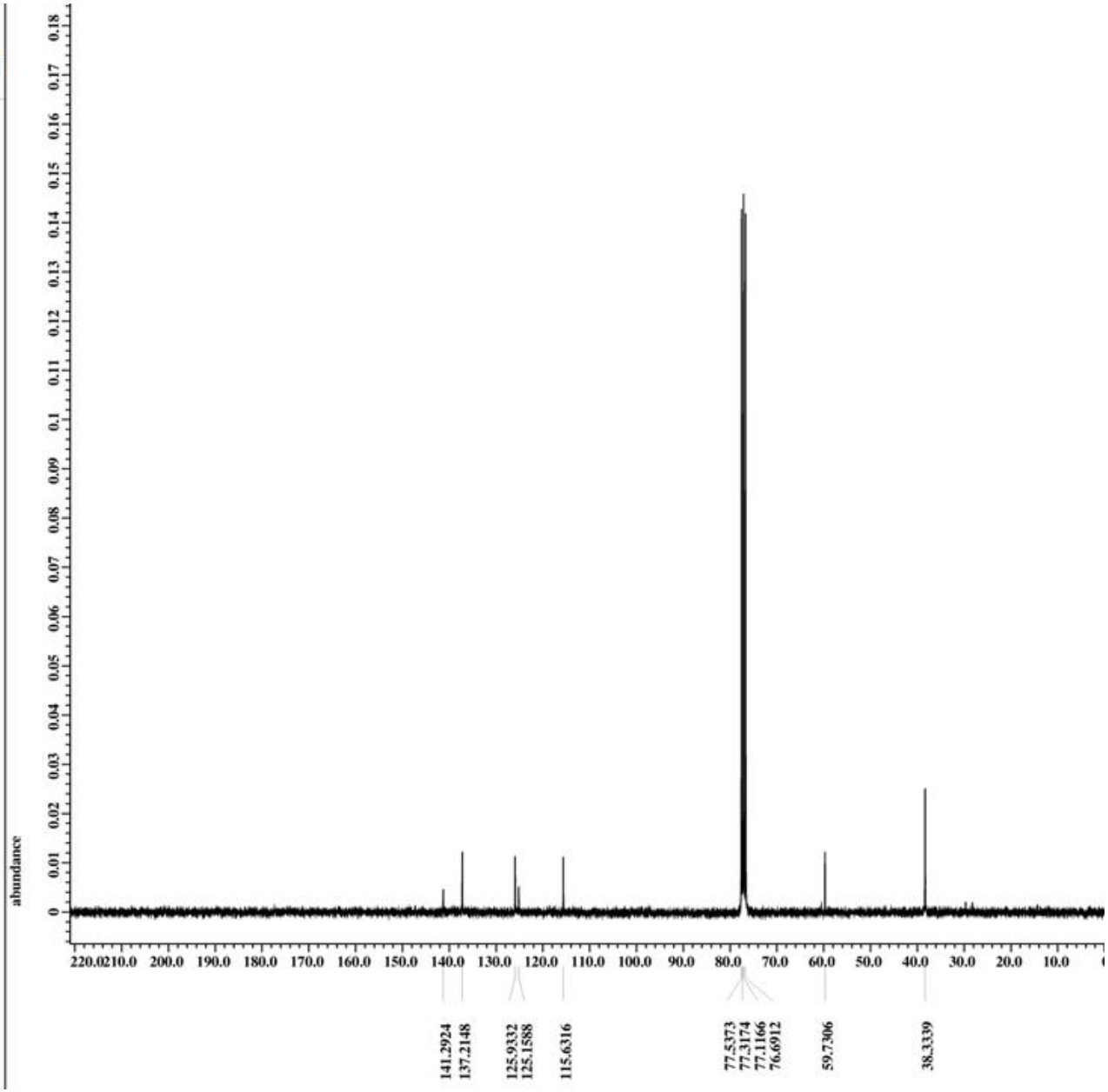
```
ilename          = sm_VI_RED_AL_Chloro_c
uthor            = delta
xperiment        = single_pulse.exp
ample_id         = S#545276
olvent           = CHLOROFORM-D
reation_time     = 15-DEC-2009 06:43:31
evision_time     = 28-MAR-2010 22:22:59
urrent_time      = 28-MAR-2010 22:23:30

omment           = Single Pulse Experime
ata_format       = 1D COMPLEX
im_size          = 16384
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7465928[T] (500[MH
_acq_duration    = 2.1839872[s]
_domain          = 1H
_freq            = 500.12734003[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.45787814[Hz]
_sweep           = 7.50187547[kHz]
lipped           = FALSE
od_return        = 1
cans             = 8
otal_scans       = 8

_90_width        = 18.5[us]
_acq_time        = 2.1839872[s]
_angle           = 45[deg]
_pulse           = 9.25[us]
nitial_wait      = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 25
elaxation_delay  = 4[s]
mp_get           = 25.7[dC]
nblank_time      = 2[us]
```





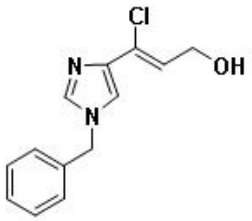
```
ilename          = sm_VI_64_pure-2.jdf
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#808732
olvent           = CHLOROFORM-D
reation_time     = 15-DEC-2009 06:36:33
evision_time     = 28-MAR-2010 22:26:29
urrent_time      = 28-MAR-2010 22:26:51

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 52428
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.76824064[s]
_domain          = 13C
_freq            = 75.56823426[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.36124027[Hz]
_sweep           = 23.67424242[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
lipped           = FALSE
od_return        = 10
cans             = 5000
otal_scans       = 5000

_90_width        = 9.75[us]
_acq_time        = 2.76824064[s]
_angle           = 30[deg]
_atn             = 8[dB]
_pulse           = 3.25[us]
rr_atn_dec       = 25[dB]
rr_atn_noe       = 25[dB]
rr_noise         = WALTZ
ecoupling        = TRUE
nitial_wait      = 1[s]
oe               = TRUE
oe_time          = 3[s]
ecvr_gain        = 50
elaxation_delay  = 3[s]
epetition_time   = 5.76824064[s]
emp_get          = 23.1[dC]
```

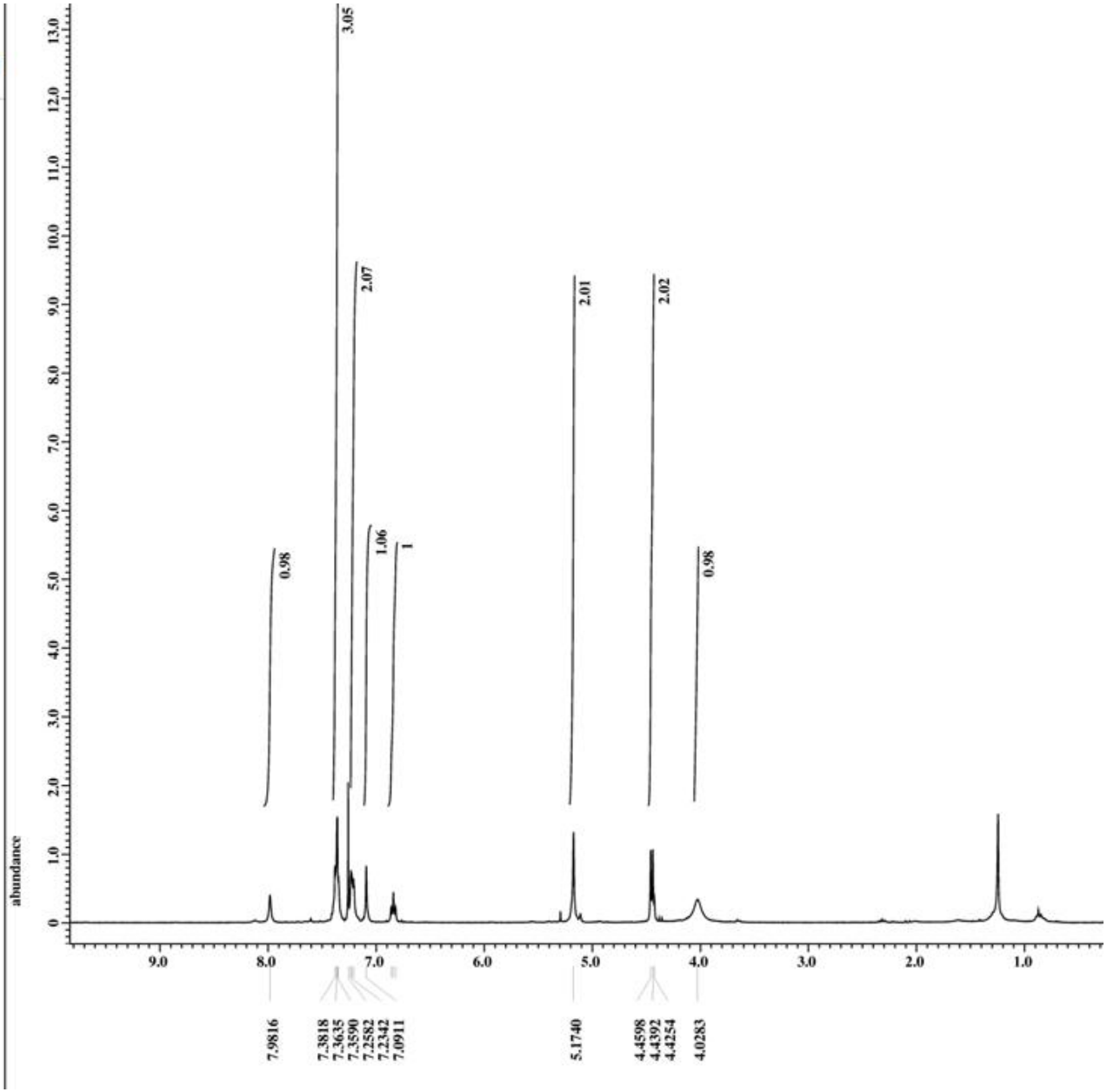




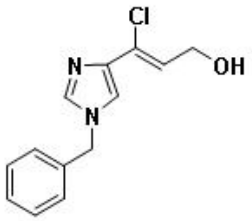
APPENDIX 51
^{1}H AND ^{13}C NMR SPECTRUM OF
(*Z*)-3-(1-benzyl-1H-imidazol-4-yl)-3-chloroprop-2-en-1-ol (264)

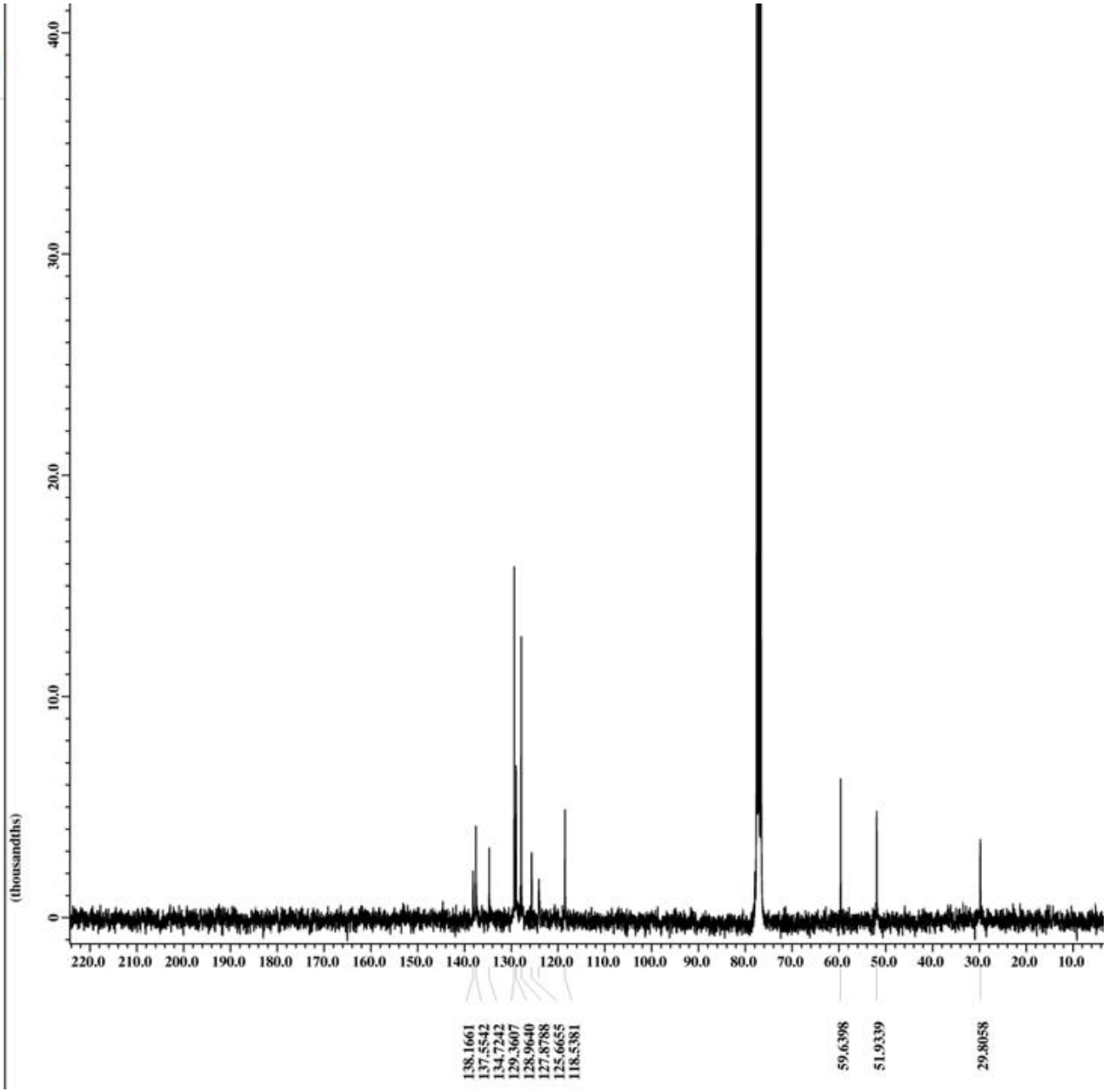
```
ilename          = sm_VI_Bn_Chloro_alcoh
uthor            = delta
xperiment        = single_pulse.ex2
ample_id         = S#652470
olvent           = CHLOROFORM-D
reation_time     =  2-FEB-2010 17:59:21
evision_time     = 19-APR-2010 19:08:12
urrent_time      = 19-APR-2010 19:11:47

omment           = single_pulse
ata_format       = 1D COMPLEX
im_size          = 13107
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.90717696[s]
_domain          = 1H
_freq            = 300.52965592[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.34397631[Hz]
_sweep           = 5.63570784[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
ri_domain        = 1H
ri_freq          = 300.52965592[MHz]
ri_offset        = 5[ppm]
lipped           = FALSE
od_return        = 1
cans             = 24
otal_scans       = 24

_90_width        = 13.01[us]
_acq_time        = 2.90717696[s]
_angle           = 45[deg]
_atn             = 4[dB]
_pulse           = 6.505[us]
rr_mode          = Off
ri_mode          = Off
ante_presat      = FALSE
nitial_wait      = 1[s]
ecvr_gain        = 50
elaxation_delay  = 5[s]
epetition_time   = 7.90717696[s]
emp_get          = 19.8[dC]
```





```
ilename          = sm_VI_Bn_Chloro_alcoh
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#854224
olvent           = CHLOROFORM-D
reation_time     =  3-FEB-2010 05:09:11
evision_time     = 19-APR-2010 19:19:07
urrent_time      = 19-APR-2010 19:20:08

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 52428
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.76824064[s]
_domain          = 13C
_freq            = 75.56823426[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.36124027[Hz]
_sweep           = 23.67424242[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
lipped           = FALSE
od_return        = 10
cans             = 3500
otal_scans       = 3500

_90_width        = 9.75[us]
_acq_time        = 2.76824064[s]
_angle           = 30[deg]
_atn             = 8[dB]
_pulse           = 3.25[us]
rr_atn_dec       = 25[dB]
rr_atn_noe       = 25[dB]
rr_noise         = WALTZ
ecoupling        = TRUE
nitial_wait      = 1[s]
oe               = TRUE
oe_time          = 3[s]
ecvr_gain        = 50
elaxation_delay  = 3[s]
epetition_time   = 5.76824064[s]
emp_get          = 19.5[dC]
```

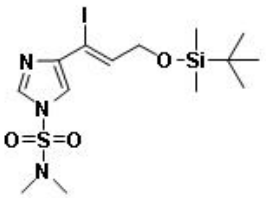


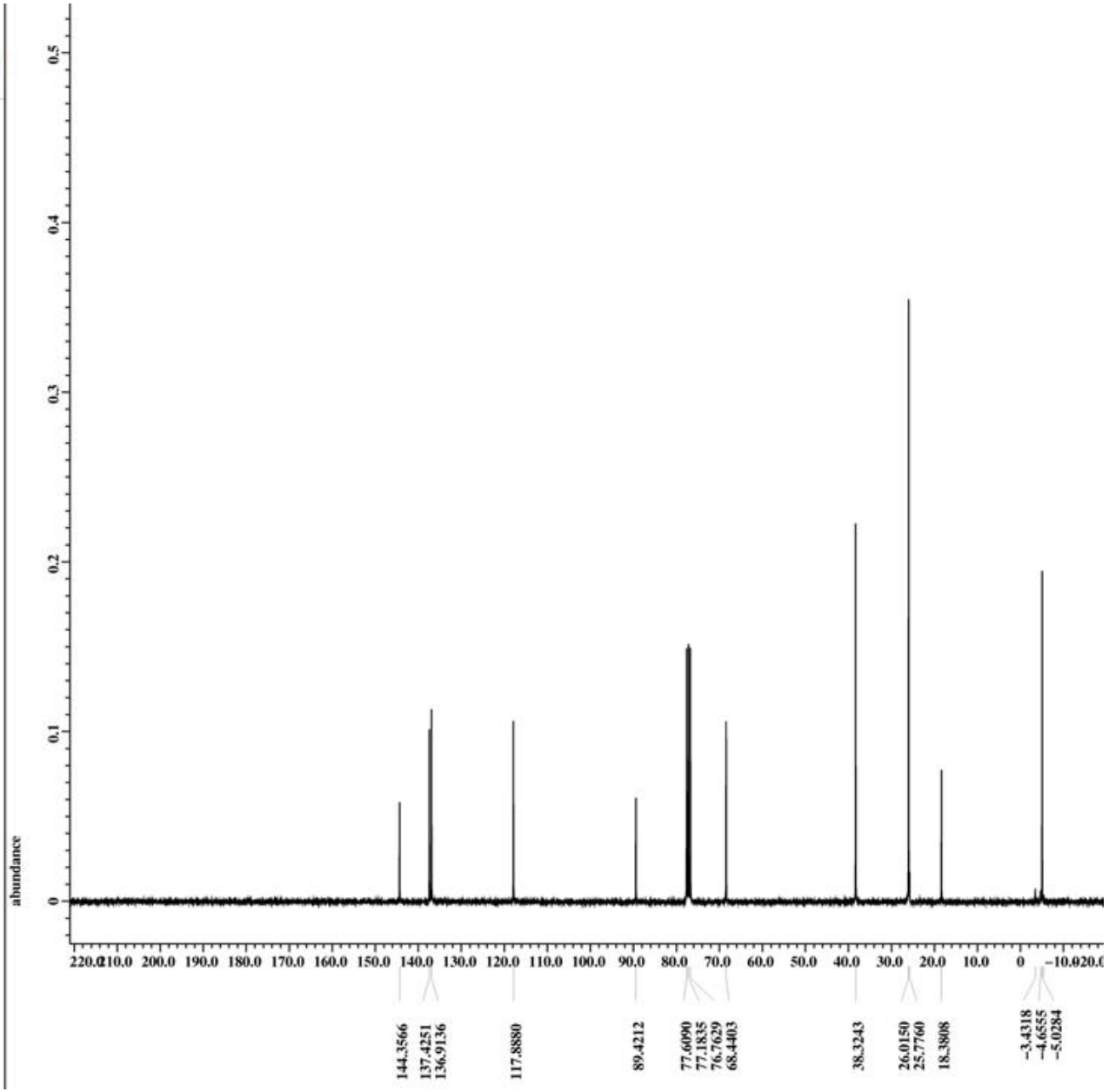


APPENDIX 52
^{1}H AND ^{13}C NMR SPECTRUM OF
(*Z*)-4-(3-(tert-butyldimethylsilyloxy)-1-iodoprop-1-enyl)-N,N-dimethyl-1H-imidazole-1-sulfonamide (255)

JEOL
ilename = sm_VI_65_pure-2.jdf
uthor = delta
xperiment = single_pulse.ex2
ample_id = S#834849
olvent = CHLOROFORM-D
reation_time = 15-DEC-2009 23:22:18
evision_time = 28-MAR-2010 22:33:10
urrent_time = 28-MAR-2010 22:33:37
omment = single_pulse
ata_format = 1D COMPLEX
im_size = 13107
im_title = 1H
im_units = [ppm]
imensions = X
ite = ECX 300
pectrometer = DELTA2_NMR
ield_strength = 7.0586013[T] (300[MHz
_acq_duration = 2.90717696[s]
_domain = 1H
_freq = 300.52965592[MHz]
_offset = 5[ppm]
_points = 16384
_prescans = 0
_resolution = 0.34397631[Hz]
_sweep = 5.63570784[kHz]
rr_domain = 1H
rr_freq = 300.52965592[MHz]
rr_offset = 5[ppm]
ri_domain = 1H
ri_freq = 300.52965592[MHz]
ri_offset = 5[ppm]
lipped = FALSE
od_return = 1
cans = 20
otal_scans = 20
_90_width = 13.01[us]
_acq_time = 2.90717696[s]
_angle = 45[deg]
_atn = 4[dB]
_pulse = 6.505[us]
rr_mode = Off
ri_mode = Off
ample_preset = FALSE
nitial_wait = 1[s]
ecvr_gain = 30
elaxation_delay = 5[s]
epetition_time = 7.90717696[s]
emp_get = 23.1[dC]
abundance
9.11
6.09
6.03
2.01
0.94
0.93
1
7.8877
7.8843
7.3109
7.3074
6.9091
6.8908
6.8725
4.3968
4.3796
2.8562
0.8910
0.8807
0.0932
0.0841
0.0612
O
Si
I
N
N
O
S
O
N

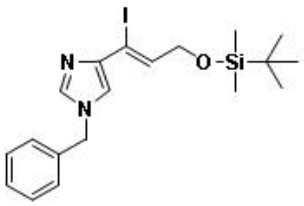
```
ilename          = sm_VI_65_pure-2.jdf
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#836865
olvent           = CHLOROFORM-D
reation_time     = 16-DEC-2009 02:38:36
evision_time     = 16-DEC-2009 13:10:09
urrent_time      = 28-MAR-2010 22:36:13

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 52428
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.76824064[s]
_domain          = 13C
_freq            = 75.56823426[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 40
_resolution      = 0.36124027[Hz]
_sweep           = 23.67424242[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
lipped           = TRUE
od_return        = 10
cans             = 2000
otal_scans       = 2000

_90_width        = 9.75[us]
_acq_time        = 2.76824064[s]
_angle           = 30[deg]
_atn             = 8[dB]
_pulse           = 3.25[us]
rr_atn_dec       = 25[dB]
rr_atn_noe       = 25[dB]
rr_noise         = WALTZ
ecoupling        = TRUE
nitial_wait      = 1[s]
oe               = TRUE
oe_time          = 3[s]
ecvr_gain        = 50
elaxation_delay  = 3[s]
epetition_time   = 5.76824064[s]
emp_get          = 24.4[dC]
```

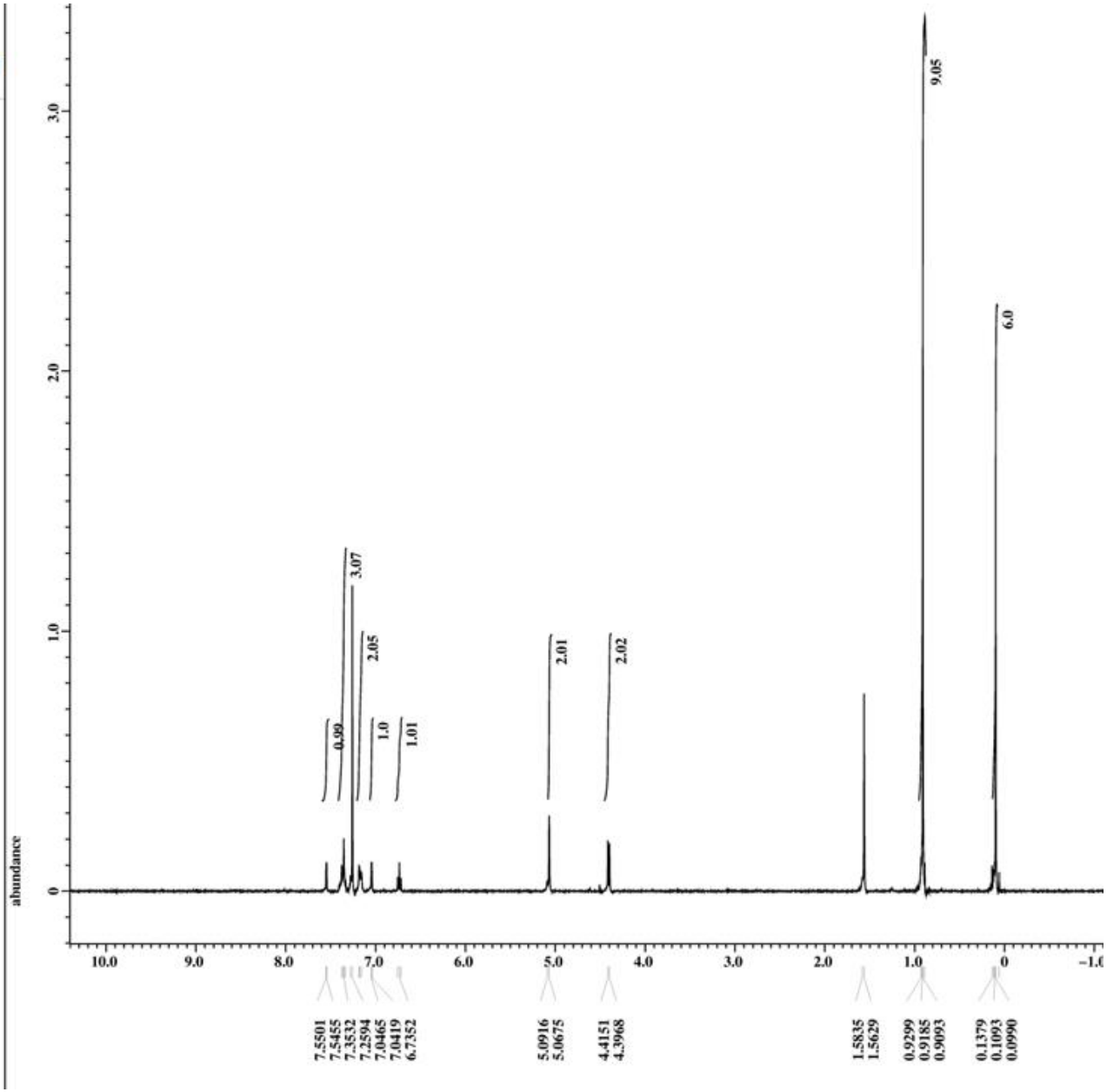




APPENDIX 53
^{1}H AND ^{13}C NMR SPECTRUM OF
(*Z*)-1-benzyl-4-(3-(tert-butyldimethylsilyloxy)-1-iodoprop-1-enyl)-1H-imidazole (253)

```
ilename          = sm_VI_15_pure-4.jdf
uthor            = delta
xperiment        = single_pulse.ex2
ample_id         = S#799735
olvent           = CHLOROFORM-D
reation_time     = 14-OCT-2009 22:16:13
evision_time     = 28-MAR-2010 22:39:23
urrent_time      = 28-MAR-2010 22:39:45

omment           = single_pulse
ata_format       = 1D REAL
im_size          = 13107
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.90717696[s]
_domain          = 1H
_freq            = 300.52965592[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.34397631[Hz]
_sweep           = 5.63570784[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
ri_domain        = 1H
ri_freq          = 300.52965592[MHz]
ri_offset        = 5[ppm]
lipped           = FALSE
od_return        = 1
cans             = 16
otal_scans       = 16

_90_width        = 13.01[us]
_acq_time        = 2.90717696[s]
_angle           = 45[deg]
_atn             = 4[dB]
_pulse           = 6.505[us]
rr_mode          = Off
ri_mode          = Off
ante_presat      = FALSE
nitial_wait      = 1[s]
ecvr_gain        = 46
elaxation_delay  = 5[s]
epetition_time   = 7.90717696[s]
emp_get          = 23.1[dC]
```

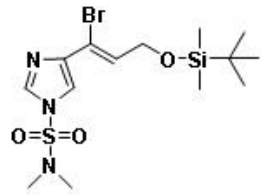


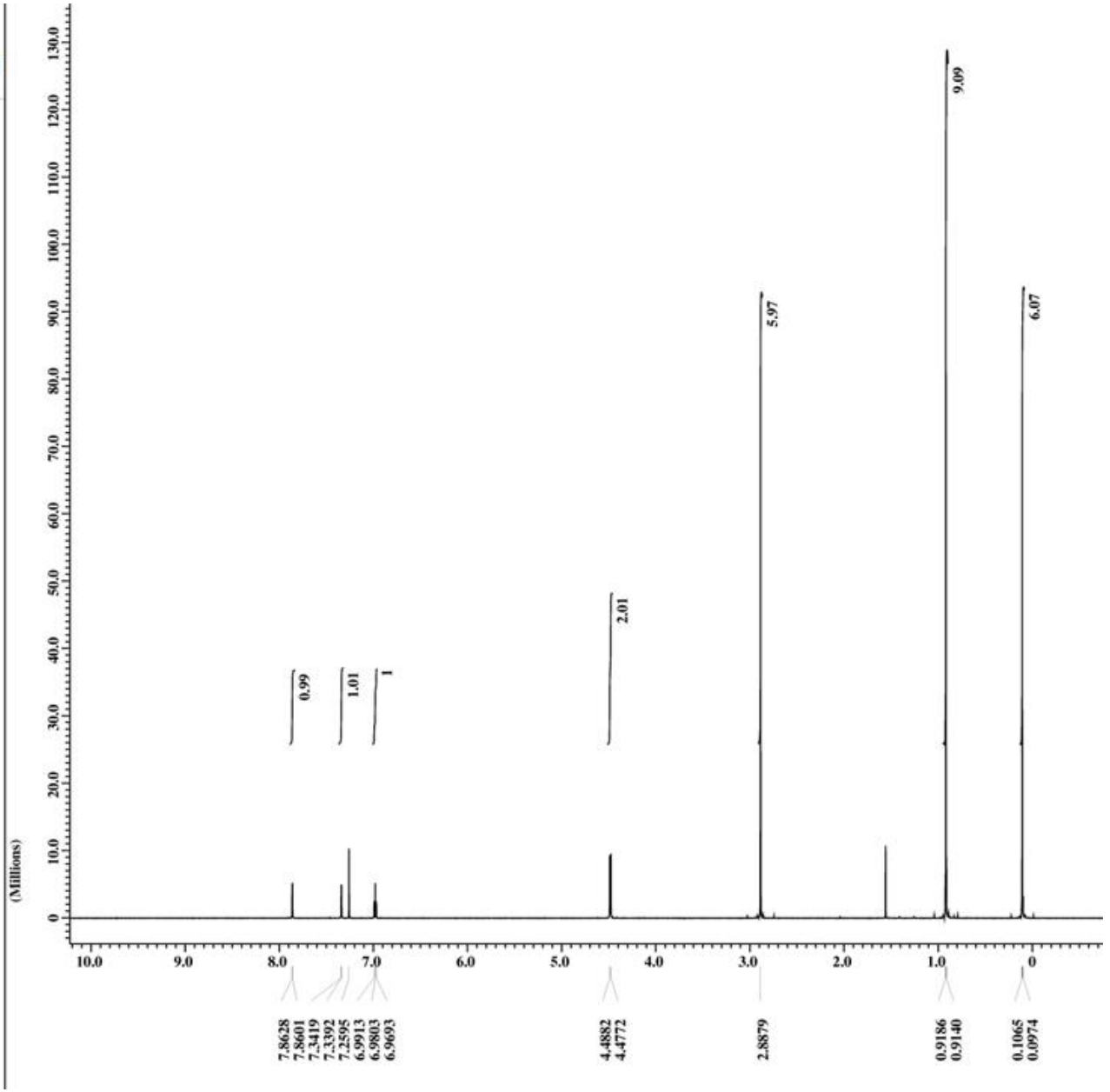


JEOL
ilename = sm_VI_15_pure-3.jdf
uthor = delta
xperiment = single_pulse_dec
ample_id = S#801383
olvent = CHLOROFORM-D
reation_time = 15-OCT-2009 03:05:14
evision_time = 28-MAR-2010 22:43:04
urrent_time = 28-MAR-2010 22:43:39
omment = single pulse decouple
ata_format = 1D COMPLEX
im_size = 52428
im_title = 13C
im_units = [ppm]
imensions = X
ite = ECX 300
pectrometer = DELTA2_NMR
ield_strength = 7.0586013[T] (300[MHz
_acq_duration = 2.76824064[s]
_domain = 13C
_freq = 75.56823426[MHz]
_offset = 100[ppm]
_points = 65536
_prescans = 4
_resolution = 0.36124027[Hz]
_sweep = 23.67424242[kHz]
rr_domain = 1H
rr_freq = 300.52965592[MHz]
rr_offset = 5[ppm]
lipped = FALSE
od_return = 10
cans = 3000
otal_scans = 3000
_90_width = 9.75[us]
_acq_time = 2.76824064[s]
_angle = 30[deg]
_atn = 8[dB]
_pulse = 3.25[us]
rr_atn_dec = 25[dB]
rr_atn_noe = 25[dB]
rr_noise = WALTZ
ecoupling = TRUE
nitial_wait = 1[s]
oe = TRUE
oe_time = 3[s]
ecvr_gain = 50
elaxation_delay = 3[s]
epetition_time = 5.76824064[s]
emp_get = 23.2[dC]
(thousandths)
20.0
10.0
0
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 -10.0
143.5535
137.1909
134.0072
129.1839
128.4955
127.4008
120.2207
92.2224
78.2256
77.5277
77.3126
77.1071
76.6864
50.6528
26.0437
17.9888
-5.1336
Si
O
I
N
N

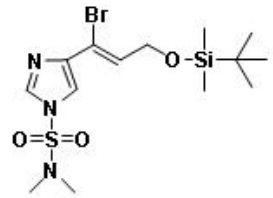
APPENDIX 54
^{1}H AND ^{13}C NMR SPECTRUM OF
(*Z*)-4-(1-bromo-3-(tert-butyldimethylsilyloxy)prop-1-enyl)-N,N-dimethyl-1H-imidazole-1-sulfonamide (261)

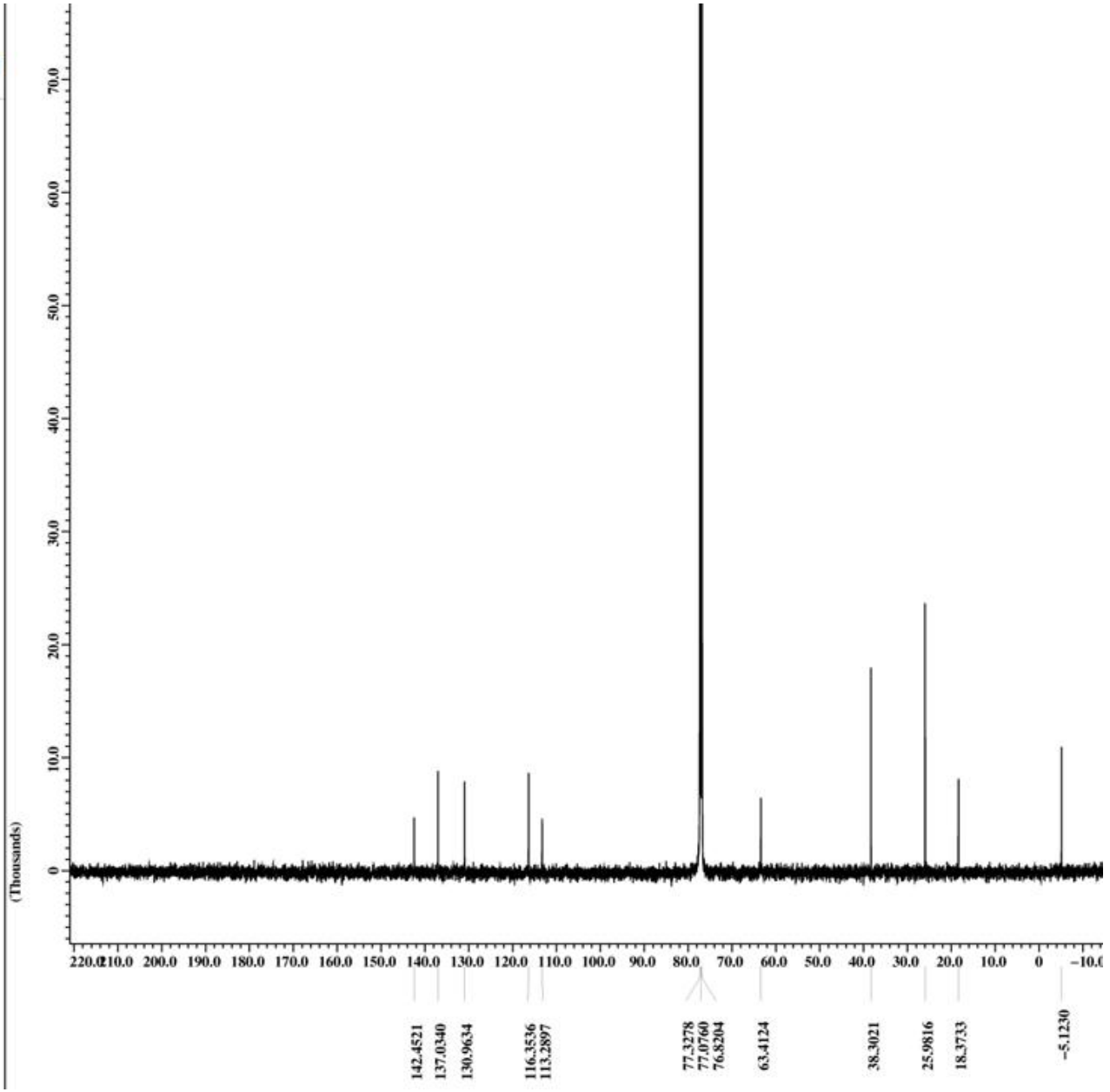
```
ilename          = sm_VI_76_pure-3.jdf
uthor            = delta
xperiment        = single_pulse.exp
ample_id         = S#7037
olvent           = CHLOROFORM-D
reation_time     = 29-DEC-2009 15:55:28
evision_time     = 28-MAR-2010 22:46:51
urrent_time      = 28-MAR-2010 22:47:13

omment           = Single Pulse Experime
ata_format       = 1D COMPLEX
im_size          = 16384
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7465928[T] (500[MH
_acq_duration    = 2.1839872[s]
_domain          = 1H
_freq            = 500.12734003[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.45787814[Hz]
_sweep           = 7.50187547[kHz]
lipped           = FALSE
od_return        = 1
cans             = 8
otal_scans       = 8

_90_width        = 18.5[us]
_acq_time        = 2.1839872[s]
_angle           = 45[deg]
_pulse           = 9.25[us]
nitial_wait      = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 22
elaxation_delay  = 4[s]
mp_get           = 29.6[dC]
nblank_time      = 2[us]
```





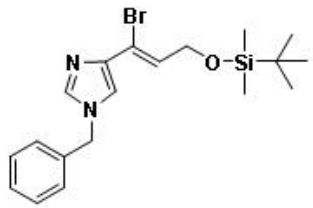
```
ilename          = sm_VI_76_pure-2.jdf
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#8266
olvent           = CHLOROFORM-D
reation_time     = 29-DEC-2009 23:00:01
evision_time     = 29-DEC-2009 13:52:02
urrent_time      = 28-MAR-2010 22:49:53

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 65536
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7465928[T] (500[MH
_acq_duration    = 2.0840448[s]
_domain          = 13C
_freq            = 125.75710665[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.47983613[Hz]
_sweep           = 31.44654088[kHz]
rr_domain        = 1H
rr_freq          = 500.12734003[MHz]
rr_offset        = 5[ppm]
lipped           = FALSE
od_return        = 10
cans             = 5000
otal_scans       = 5000

_90_width        = 14.2[us]
_acq_time        = 2.0840448[s]
_angle           = 30[deg]
_pulse           = 4.73333333[us]
nitial_wait      = 1[s]
pe_time          = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 22
elaxation_delay  = 2[s]
emp_get          = 32.5[dC]
nblank_time      = 2[us]
```

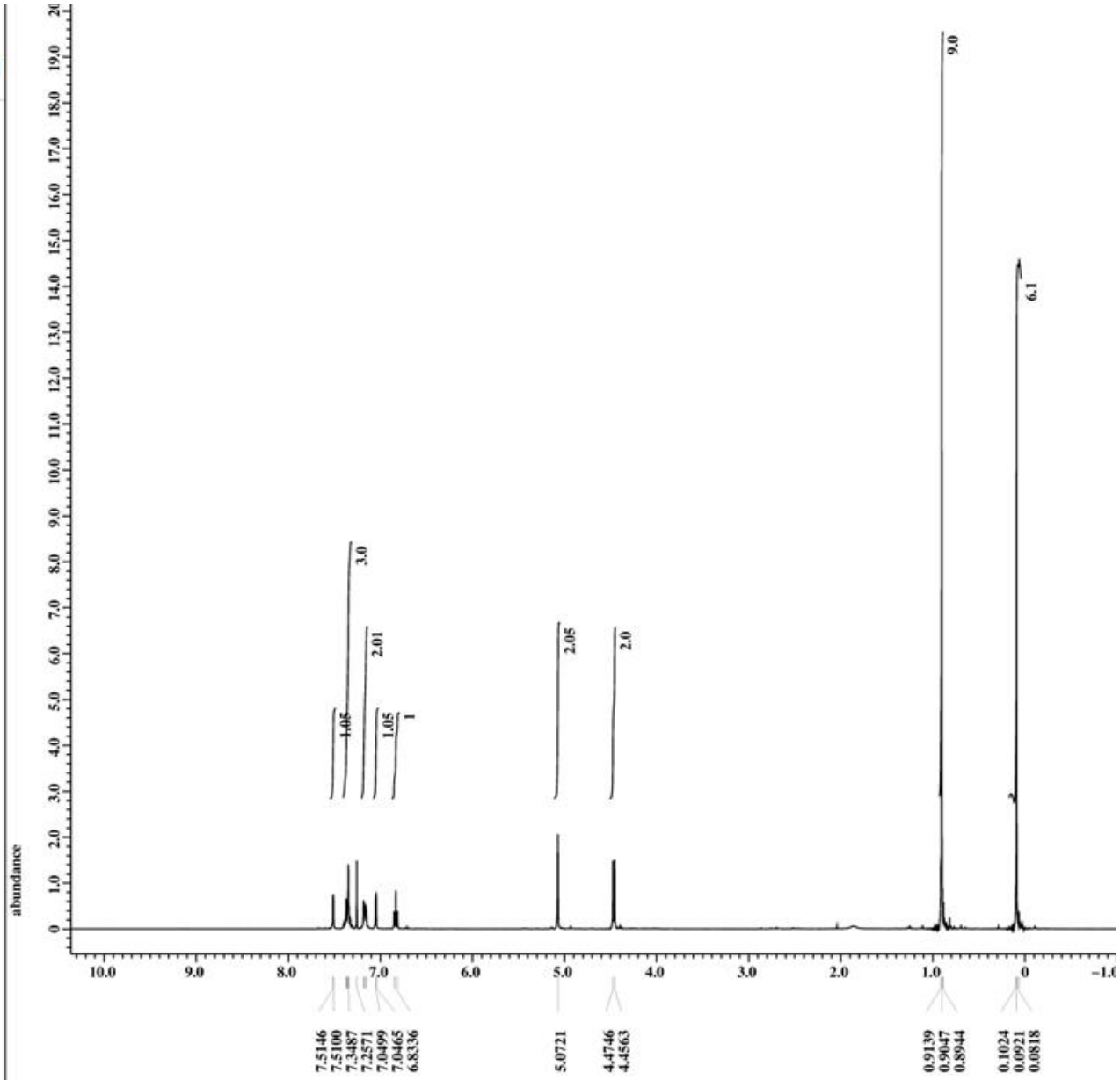




APPENDIX 55
^{1}H AND ^{13}C NMR SPECTRUM OF
(*Z*)-1-benzyl-4-(1-bromo-3-(tert-butyldimethylsilyloxy)prop-1-enyl)-1H-imidazole (262)

```
ilename          = sm_VI_70_pure-3.jdf
uthor            = delta
xperiment        = single_pulse.ex2
ample_id         = S#807529
olvent           = CHLOROFORM-D
reation_time     = 17-DEC-2009 22:37:15
evision_time     = 28-MAR-2010 22:53:12
urrent_time      = 28-MAR-2010 22:53:32

omment           = single_pulse
ata_format       = 1D COMPLEX
im_size          = 13107
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.90717696[s]
_domain          = 1H
_freq            = 300.52965592[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.34397631[Hz]
_sweep           = 5.63570784[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
ri_domain        = 1H
ri_freq          = 300.52965592[MHz]
ri_offset        = 5[ppm]
lipped           = FALSE
od_return        = 1
cans             = 21
otal_scans       = 21

_90_width        = 13.01[us]
_acq_time        = 2.90717696[s]
_angle           = 45[deg]
_atn             = 4[dB]
_pulse           = 6.505[us]
rr_mode          = Off
ri_mode          = Off
ante_presat      = FALSE
nitial_wait      = 1[s]
ecvr_gain        = 44
elaxation_delay  = 5[s]
epetition_time   = 7.90717696[s]
emp_get          = 23.2[dC]
```





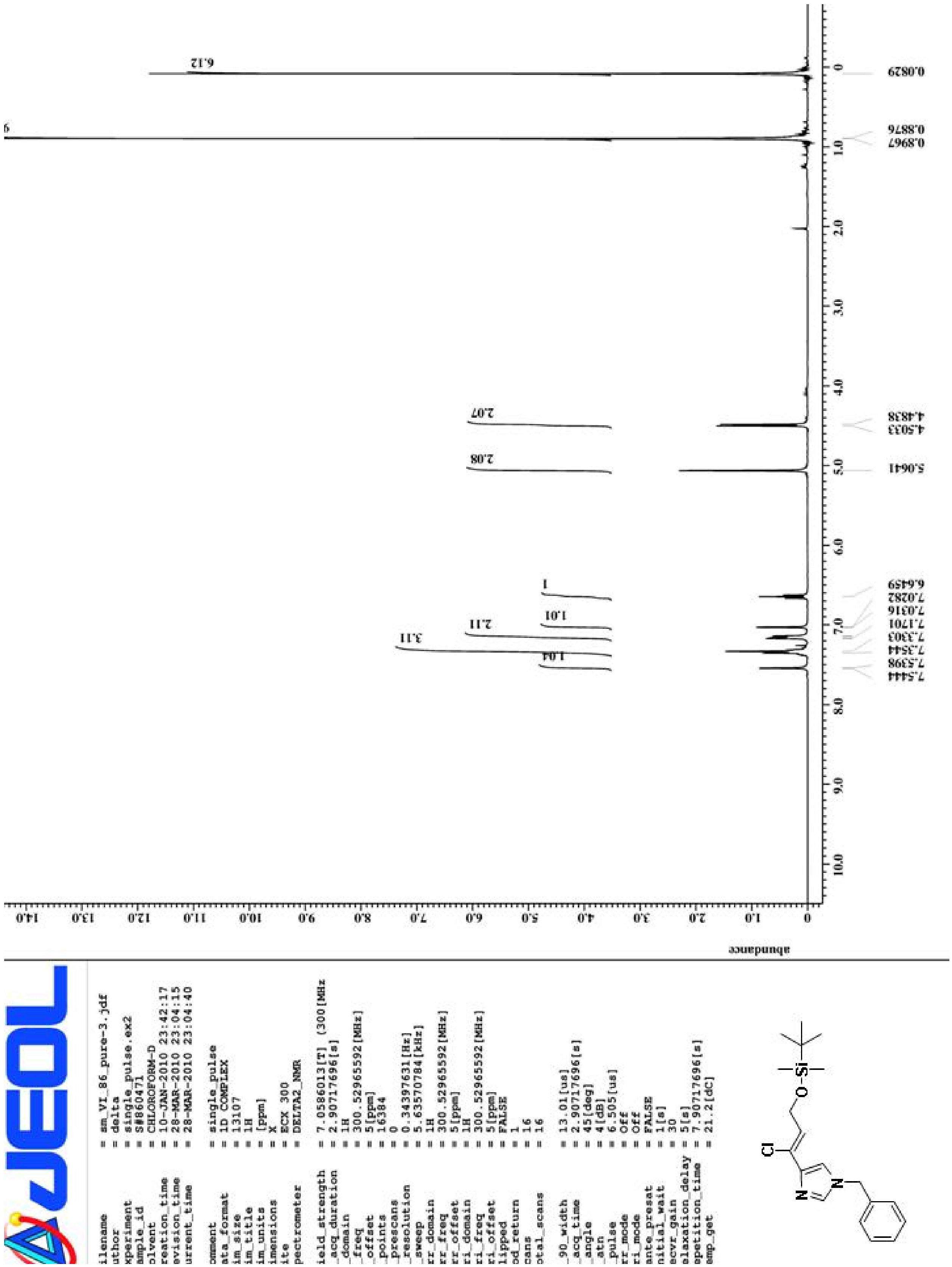
JEOL
ilename = sm_VI_70_pure-2.jdf
uthor = delta
xperiment = single_pulse_dec
ample_id = S#809631
olvent = CHLOROFORM-D
reation_time = 18-DEC-2009 06:38:27
evision_time = 18-DEC-2009 13:11:57
urrent_time = 28-MAR-2010 22:56:31
omment = single pulse decouple
ata_format = 1D COMPLEX
im_size = 52428
im_title = 13C
im_units = [ppm]
imensions = X
ite = ECX 300
pectrometer = DELTA2_NMR
ield_strength = 7.0586013[T] (300[MHz
_acq_duration = 2.76824064[s]
_domain = 13C
_freq = 75.56823426[MHz]
_offset = 100[ppm]
_points = 65536
_prescans = 4
_resolution = 0.36124027[Hz]
_sweep = 23.67424242[kHz]
rr_domain = 1H
rr_freq = 300.52965592[MHz]
rr_offset = 5[ppm]
lipped = FALSE
od_return = 10
cans = 5000
otal_scans = 5000
_90_width = 9.75[us]
_acq_time = 2.76824064[s]
_angle = 30[deg]
_atn = 8[dB]
_pulse = 3.25[us]
rr_atn_dec = 25[dB]
rr_atn_noe = 25[dB]
rr_noise = WALTZ
ecoupling = TRUE
nitial_wait = 1[s]
oe = TRUE
oe_time = 3[s]
ecvr_gain = 50
elaxation_delay = 3[s]
epetition_time = 5.76824064[s]
emp_get = 23.2[dC]
(thousandths)
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 -10.0
-5.0666
18.4047
26.0246
51.1690
63.5596
77.5373
77.1166
76.6912
141.5553
137.8267
135.6994
129.1934
128.5624
127.6350
127.4295
119.1452
115.2922
Br
O-Si
N
N

APPENDIX 56
^{1}H AND ^{13}C NMR SPECTRUM OF
(*Z*)-4-(3-(tert-butyldimethylsilyloxy)-1-chloroprop-1-enyl)-N,N-dimethyl-1H-imidazole-1-sulfonamide (265)

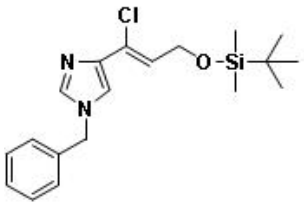
JEOL
sm_VI_77_pure-3.jdf
delta
single_pulse.exp
S#529045
CHLOROFORM-D
28-DEC-2009 06:24:34
28-MAR-2010 22:58:44
28-MAR-2010 22:59:05
Single Pulse Experime
1D COMPLEX
16384
1H
[ppm]
X
Eclipse+ 500
DELTA_NMR
11.7465928[T] (500[MH
2.1839872[s]
1H
500.12734003[MHz]
5[ppm]
16384
0
0.45787814[Hz]
7.50187547[kHz]
FALSE
1
8
8
18.5[us]
2.1839872[s]
45[deg]
9.25[us]
1[s]
3[us]
22
4[s]
29[dC]
2[us]
(Millions)
6.0
9.01
6.18
2.13
1
1.02
1.03
6.7596
7.3364
7.2586
7.8363
7.8335
0.0974
0.1038
0.1102
0.9159
2.8861
4.5148
4.5267
Cl
O-Si
N
O=S=O
N

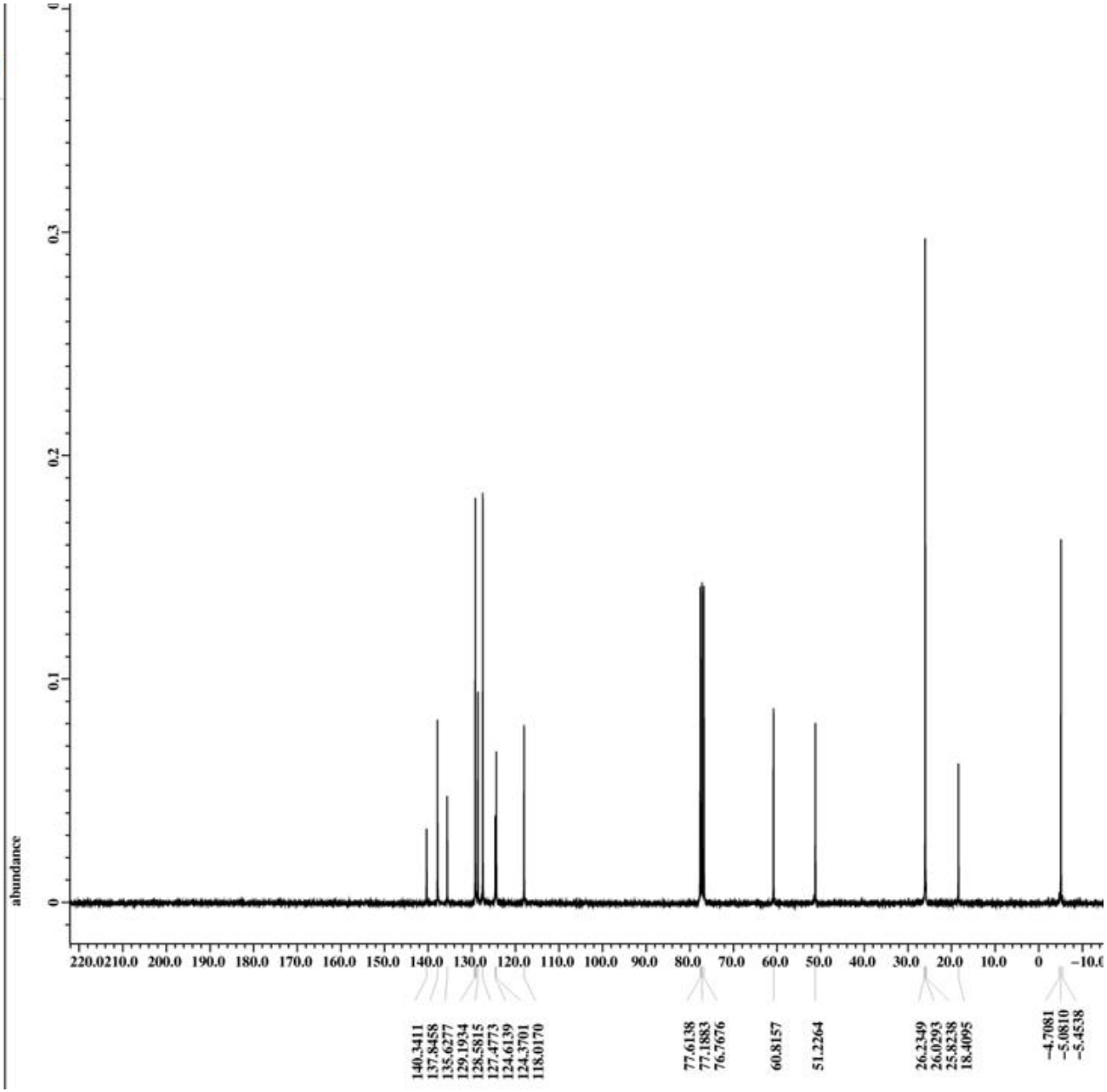
JEOL
ilename = sm_VI_77_pure-2.jdf
uthor = delta
xperiment = single_pulse_dec
ample_id = S#530285
olvent = CHLOROFORM-D
reation_time = 28-DEC-2009 08:33:31
evision_time = 28-DEC-2009 00:06:42
urrent_time = 28-MAR-2010 23:01:53
comment = single pulse decouple
ata_format = 1D COMPLEX
im_size = 65536
im_title = 13C
im_units = [ppm]
imensions = X
ite = Eclipse+ 500
pectrometer = DELTA_NMR
ield_strength = 11.7465928[T] (500[MH
_acq_duration = 2.0840448[s]
_domain = 13C
_freq = 125.75710665[MHz]
_offset = 100[ppm]
_points = 65536
_prescans = 4
_resolution = 0.47983613[Hz]
_sweep = 31.44654088[kHz]
rr_domain = 1H
rr_freq = 500.12734003[MHz]
rr_offset = 5[ppm]
lipped = TRUE
od_return = 10
cans = 1500
otal_scans = 1500
_90_width = 14.2[us]
_acq_time = 2.0840448[s]
_angle = 30[deg]
_pulse = 4.73333333[us]
nitial_wait = 1[s]
pe_time = 1[s]
hase_preset = 3[us]
ecvr_gain = 29
elaxation_delay = 2[s]
emp_get = 31.9[dC]
nblank_time = 2[us]
(Thousands)
-5.1421
18.3810
25.9778
38.2983
60.7186
76.8242
77.0798
77.3316
115.1707
123.2216
127.4569
137.0836
141.5707
Cl
O
Si
N
N
O=S=O
N

APPENDIX 57
^{1}H AND ^{13}C NMR SPECTRUM OF
(*Z*)-1-benzyl-4-(3-(tert-butyldimethylsilyloxy)-1-chloroprop-1-enyl)-1H-imidazole (266)



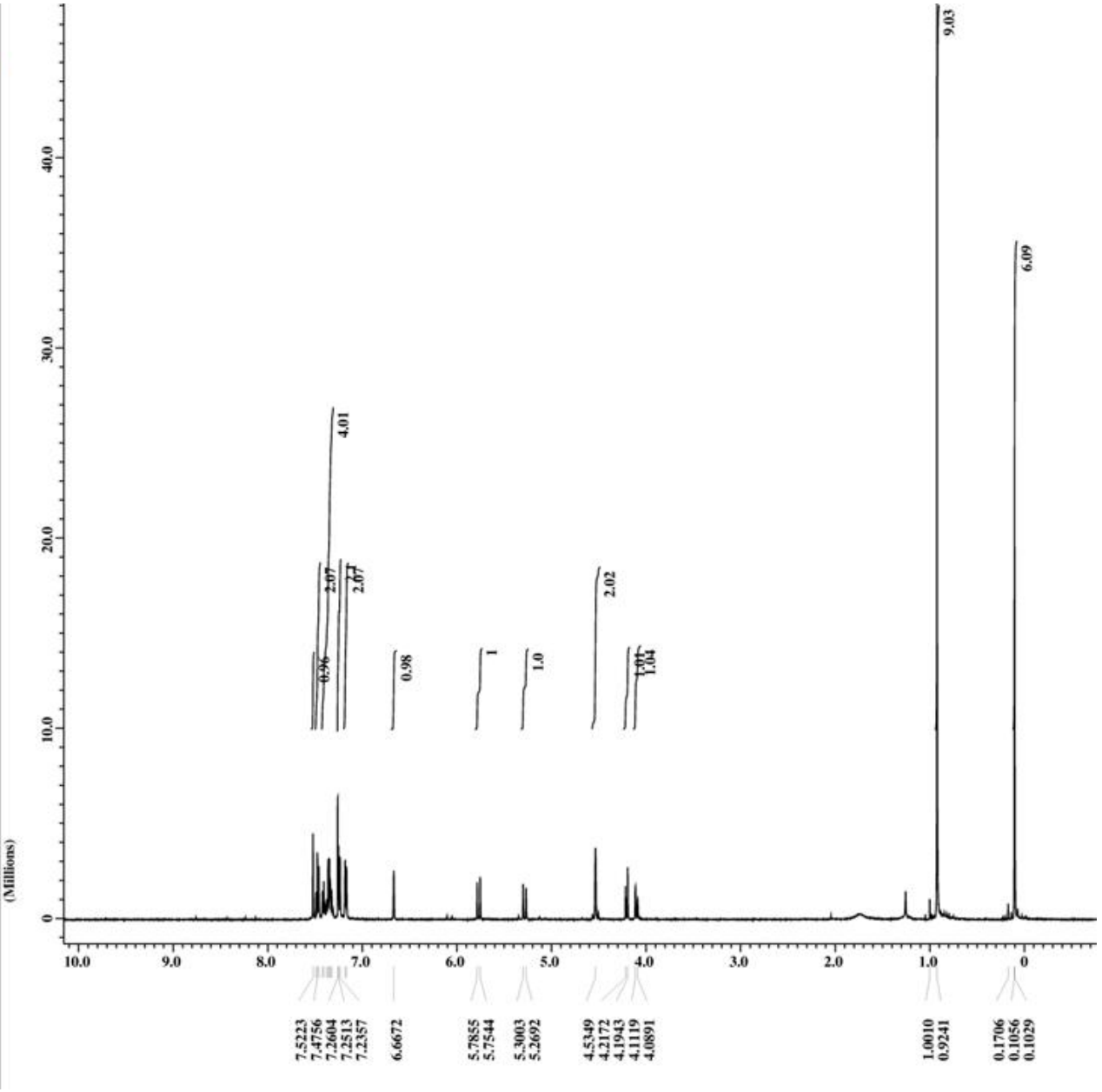
```
ilename          = sm_VI_86-pure-2.jdf
uthor            = delta
xperiment        = single_pulse_dec
ample_id         = S#862122
olvent           = CHLOROFORM-D
reation_time     = 11-JAN-2010 05:20:31
evision_time     = 28-MAR-2010 23:06:56
urrent_time      = 28-MAR-2010 23:07:05

omment           = single pulse decouple
ata_format       = 1D COMPLEX
im_size          = 52428
im_title         = 13C
im_units         = [ppm]
imensions        = X
ite              = ECX 300
pectrometer      = DELTA2_NMR

ield_strength    = 7.0586013[T] (300[MHz
_acq_duration    = 2.76824064[s]
_domain          = 13C
_freq            = 75.56823426[MHz]
_offset          = 100[ppm]
_points          = 65536
_prescans        = 4
_resolution      = 0.36124027[Hz]
_sweep           = 23.67424242[kHz]
rr_domain        = 1H
rr_freq          = 300.52965592[MHz]
rr_offset        = 5[ppm]
lipped           = FALSE
od_return        = 10
cans             = 3500
otal_scans       = 3500

_90_width        = 9.75[us]
_acq_time        = 2.76824064[s]
_angle           = 30[deg]
_atn             = 8[dB]
_pulse           = 3.25[us]
rr_atn_dec       = 25[dB]
rr_atn_noe       = 25[dB]
rr_noise         = WALTZ
ecoupling        = TRUE
nitial_wait      = 1[s]
oe               = TRUE
oe_time          = 3[s]
ecvr_gain        = 50
elaxation_delay  = 3[s]
epetition_time   = 5.76824064[s]
emp_get          = 21[dC]
```



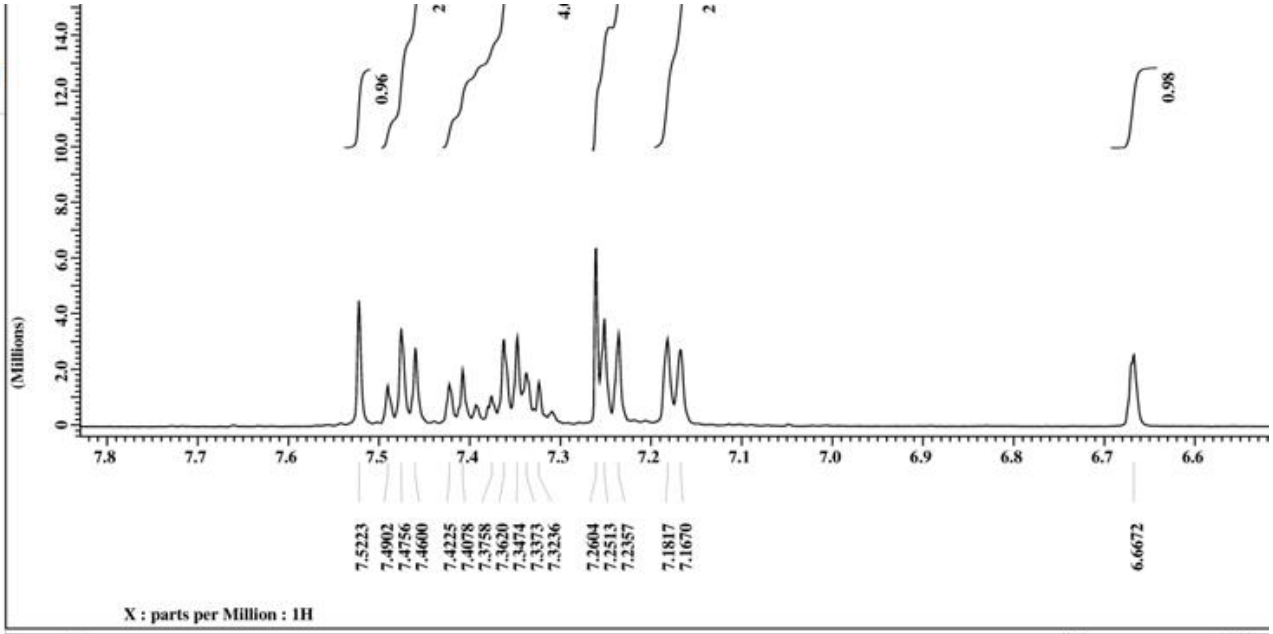


APPENDIX 58
^{1}H AND ^{13}C NMR SPECTRUM OF
(5a*R,8a*S**)-1-benzyl-5-((tert-butyldimethylsilyloxy)methyl)-7-phenyl-7,8a-dihydroimidazo[4,5-e]isoindole-6,8(1H,5aH)-dione (257)**

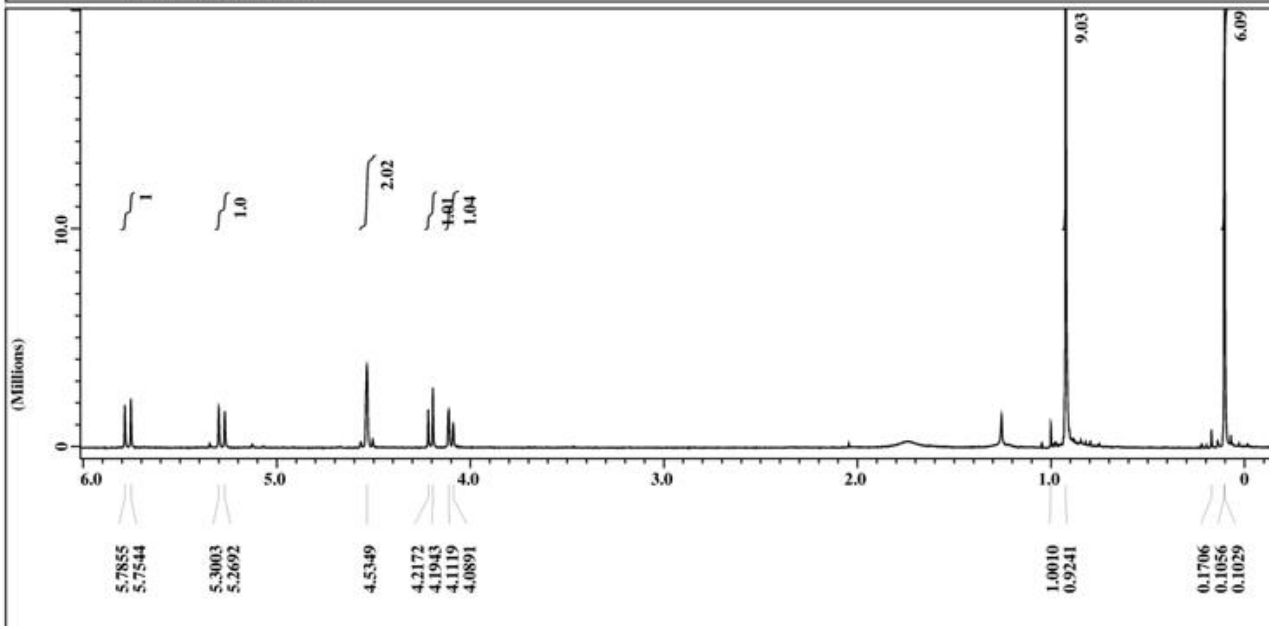
```
ilename          = sm_VI_44_pure_ii-3.jd
uthor            = delta
xperiment        = single_pulse.exp
ample_id         = S#696981
olvent           = CHLOROFORM-D
reation_time     = 29-NOV-2009 10:46:29
evision_time     = 28-MAR-2010 23:11:33
urrent_time      = 28-MAR-2010 23:11:51

omment           = Single Pulse Experime
ata_format       = 1D COMPLEX
im_size          = 16384
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7465928[T] (500[MH
_acq_duration    = 2.1839872[s]
_domain          = 1H
_freq            = 500.12734003[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.45787814[Hz]
_sweep           = 7.50187547[kHz]
lipped           = FALSE
od_return        = 1
cans             = 8
otal_scans       = 8

_90_width        = 18.5[us]
_acq_time        = 2.1839872[s]
_angle           = 45[deg]
_pulse           = 9.25[us]
nitial_wait      = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 22
elaxation_delay  = 4[s]
mp_get           = 25.9[dC]
nblank_time      = 2[us]
```



```
ilename          = sm_VI_44_pure_ii-3.jd
uthor            = delta
xperiment        = single_pulse.exp
ample_id         = S#696981
olvent           = CHLOROFORM-D
reation_time     = 29-NOV-2009 10:46:29
evision_time     = 28-MAR-2010 23:11:33
urrent_time      = 28-MAR-2010 23:13:45

omment           = Single Pulse Experime
ata_format       = 1D COMPLEX
im_size          = 16384
im_title         = 1H
im_units         = [ppm]
imensions        = X
ite              = Eclipse+ 500
pectrometer      = DELTA_NMR

ield_strength    = 11.7465928[T] (500[MH
_acq_duration    = 2.1839872[s]
_domain          = 1H
_freq            = 500.12734003[MHz]
_offset          = 5[ppm]
_points          = 16384
_prescans        = 0
_resolution      = 0.45787814[Hz]
_sweep           = 7.50187547[kHz]
lipped           = FALSE
od_return        = 1
cans             = 8
otal_scans       = 8

_90_width        = 18.5[us]
_acq_time        = 2.1839872[s]
_angle           = 45[deg]
_pulse           = 9.25[us]
nitial_wait      = 1[s]
hase_preset      = 3[us]
ecvr_gain        = 22
elaxation_delay  = 4[s]
mp_get           = 25.9[dC]
nblank_time      = 2[us]
```



X : parts per Million : 1H



JEOL
ilename = sm_VI_44_pure_ii-2.jd
uthor = delta
xperiment = single_pulse_dec
ample_id = S#698993
olvent = CHLOROFORM-D
reation_time = 29-NOV-2009 16:28:27
evision_time = 30-NOV-2009 00:33:02
urrent_time = 28-MAR-2010 23:15:26
omment = single pulse decouple
ata_format = 1D COMPLEX
im_size = 65536
im_title = 13C
im_units = [ppm]
imensions = X
ite = Eclipse+ 500
pectrometer = DELTA_NMR
ield_strength = 11.7465928[T] (500[MH
_acq_duration = 2.0840448[s]
_domain = 13C
_freq = 125.75710665[MHz]
_offset = 100[ppm]
_points = 65536
_prescans = 4
_resolution = 0.47983613[Hz]
_sweep = 31.44654088[kHz]
rr_domain = 1H
rr_freq = 500.12734003[MHz]
rr_offset = 5[ppm]
lipped = TRUE
od_return = 10
cans = 4000
otal_scans = 4000
_90_width = 14.2[us]
_acq_time = 2.0840448[s]
_angle = 30[deg]
_pulse = 4.73333333[us]
nitial_wait = 1[s]
pe_time = 1[s]
hase_preset = 3[us]
ecvr_gain = 28
elaxation_delay = 2[s]
emp_get = 28.6[dC]
nblank_time = 2[us]
(Thousands)
500.0
400.0
300.0
200.0
100.0
0
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 -10.0
-5.2527
18.5031
26.0617
39.8054
43.4226
50.0007
64.6410
76.8433
77.0989
77.3507
119.1046
126.5564
127.5370
128.3536
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129.1701
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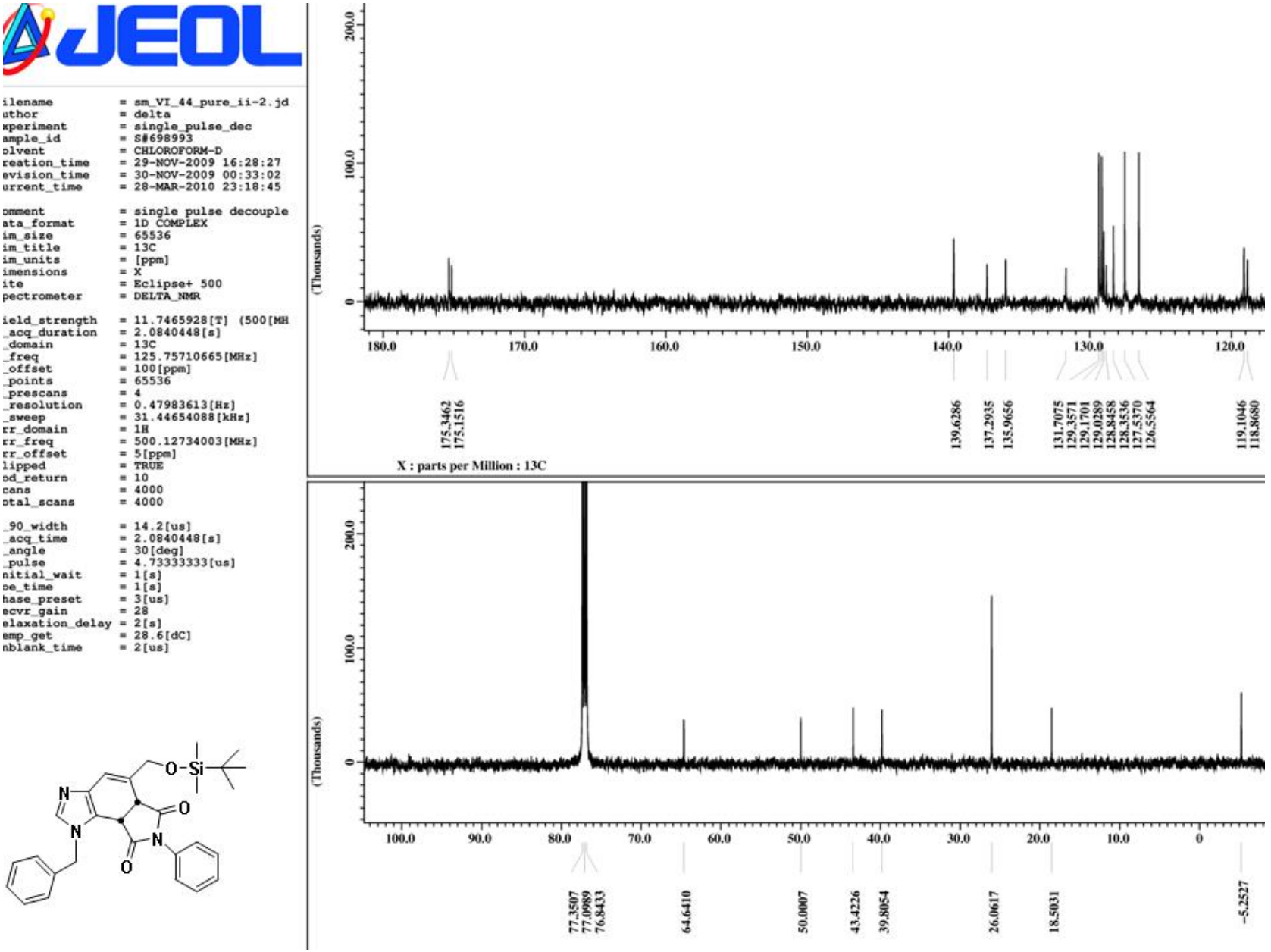
139.6286
175.1516
175.3462
O-Si
O
O
N
N
N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uthor = delta
xperiment = single_pulse_dec
ample_id = S#698993
olvent = CHLOROFORM-D
reation_time = 29-NOV-2009 16:28:27
evision_time = 30-NOV-2009 00:33:02
urrent_time = 28-MAR-2010 23:18:45
omment = single pulse decouple
ata_format = 1D COMPLEX
im_size = 65536
im_title = 13C
im_units = [ppm]
imensions = X
ite = Eclipse+ 500
pectrometer = DELTA_NMR
ield_strength = 11.7465928[T] (500[MH
_acq_duration = 2.0840448[s]
_domain = 13C
_freq = 125.75710665[MHz]
_offset = 100[ppm]
_points = 65536
_prescans = 4
_resolution = 0.47983613[Hz]
_sweep = 31.44654088[kHz]
rr_domain = 1H
rr_freq = 500.12734003[MHz]
rr_offset = 5[ppm]
lipped = TRUE
od_return = 10
cans = 4000
otal_scans = 4000
_90_width = 14.2[us]
_acq_time = 2.0840448[s]
_angle = 30[deg]
_pulse = 4.73333333[us]
nitial_wait = 1[s]
oe_time = 1[s]
hase_preset = 3[us]
ecvr_gain = 28
elaxation_delay = 2[s]
emp_get = 28.6[dC]
nblank_time = 2[us]
(Thousands)
200.0
100.0
0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
175.3462
175.1516
139.6286
137.2935
135.9656
131.7075
129.3571
129.1701
129.0289
128.8458
128.3536
127.5370
126.5564
119.1046
118.8680
X : parts per Million : 13C
(Thousands)
200.0
100.0
0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
77.3507
77.0989
76.8433
64.6410
50.0007
43.4226
39.8054
26.0617
18.5031
-5.3527
O-Si
N
N
O
N
O

REFERENCES

1. Garcia, E. E.; Benjamin, L. E.; Fryer, R. I. *J. Chem. Soc., Chem. Commun*. **1973**, 78-81.
2. Forenza, S.; Minale, L.; Riccio, R.; Fattorusso, E. *J. Chem. Soc., Chem. Commun*. **1971**, 1129-1132.
3. Mourabit, A. Al.; Potier, P.; *Eur. J. Org. Chem.* **2001**, 237-243.
4. (a) Hoffmann, H.; Lindel, T. *Synthesis* **2003**, 1753. (b) Forte, B.; Malgesini, B.; Piutti, C.; Scolaro, F.; Papeo, G. *Mar. Drugs* **2009**, *7*, 705-753.
5. Du, H. *Synthetic Studies Towards the Total Synthesis of Palau'amine*, Ph.D. Dissertation, 2004, The University of Texas at Arlington.
6. (a) Lovely, C. J.; Du, H.; Dias, H. V. R*. Org. Lett.* **2001**, *3*, 1319-1322. (b) Lovely, C. J.; Du, H.; Dias, H. V. R*. Heterocycles* **2003**, *60*, 1-7.
7. He, Y.; Lovely, C. J. ACS 57th Southwest Regional Meeting, San Antonio, TX, Oct. 17-20, 2001.
8. Chen, Y.; Dias, H. V. R.; Lovely, C. J*. Tetrahedron Lett*. **2003**, *44*, 1379-1382.
9. Chen, Y.; *Synthetic Approaches to the Total Synthesis of Agelastatin A and Intramolecular Diels-Alder Reactions of 4-Vinylimidazoles Derivatives, II*, Ph.D. Dissertation, 2002, The University of Texas at Arlington.
10. (a) He, Y.; Chen, Y.; Wu, H.; Lovely, C. J. *Org. Lett*. **2003**, *5*, 3623-3626. (b) Lovely, C. J.; Du, H.; He, Y.; Dias, H. V. R. *Org. Lett*. **2004**, *6*, 735-738.

11. Kock, M.; Grube, A.; Seiple, I. B.; Baran, P. S. *Angew. Chem. Int. Ed.* **2007**, 119, 6706-6714.

12. Andrade, P.; Willoughby, R.; Pomponi, S. A.; Kerr, R. G. *Tetrahedron Lett.* **1999**, *40*, 4775-4778.

13. Papeo, G.; Gomez, Z.; Maria, A.; Borghi, D.; Varasi, M. *Tetrahedron Lett*. **2005**, *46*, 8635-8638.

14. Fattorusso, E.; Taglialatela-Scafati, O. *Tetrahedron Lett.* **2000**, *41*, 9971-9922.

15. Endo, T.; Tsuda, M.; Okada, T.; Mitsuhashi, S.; Shima, H.; Kikuchi, K.; Mikami, Y.; Fromont, J.; Kobayashi, *J. Nat. Prod.* **2004**, *67*, 1262-1267.

16. Tsuda, M., Yasuda, T.; Fukushi, E.; Kawabata, J.; Sekiguchi, M.; Fromont, J.; Kobayashi, J. *Org. Lett*. **2006**, *8*, 4235-4238.

17. Grube, A.; Köck, M. *J. Nat. Prod*. **2006**, *69*, 1212-1214.

18. Banwell, M. G.; Bray, A. M.; Willis, A. C.; Wong, D. *J. New J. Chem*. **1999**, *23*, 687-690.

19. Wolff, L.; Greulich, R. *Ber. Dtsch. Chem. Ges*. **1912**, *45*, 23-26.

20. Bailey, D. M.; Johnson, R. E. *J. Med. Chem*. **1973**, *16*, 1300-1302.

21. (a) Marchais, S.; Al Mourabit, A.; Ahond, A.; Poupat, C.; Potier, P. *Tetrahedron Lett*. **1999**, *40*, 5519-5522; (b) Barrios Sosa, A. C.; Yakushijin, K.; Horne, D. A. *Tetrahedron Lett*. **2000**, *41*, 4295-4299.

22. Ye, T.; McKervey, M. A. *Chem. Rev*. **1994**, *94*, 1091-1160.

23. Aoyama, T.; Shioiri, T. *Chem. Pharm. Bull*. **1981**, *29*, 3249-3255.

24. (a) Little, T. L.; Weber, S. E. *J. Org. Chem.* **1994**, *59*, 7299-7305; (b) Birman,

V. B.; Jiang, X.-T. *Org. Lett*. **2004**, *6*, 2369-2371.

25. (a) Zapf, C. W.; Creighton, C. J.; Tomioka, M.; Goodman, M. *Org. Lett*. **2001**, *3*, 1133-1136; (b) Abou-Jneid, R.; Ghoulami, S.; Martin, M.-T.; Tran Huu Dau, E.; Travert, N.; Al Mourabit, A. *Org. Lett*. **2004**, *6*, 3933-3936.
26. Poverlein, C.; Breckle, G.; Lindel, T. *Org. Lett*. **2006**, *8*, 819-821.
27. Olofson, A.; Yakushijin, K.; Horne, D. A. *J. Org. Chem.* **1997**, *62*, 7918-7919.
28. Fringuelli, F.; Piermatti, O.; Pizzo, F.; Vaccaro, L. *Eur. J. Org. Chem.* **2001**, 439-455.
29. Mukherjee, S.; Rasapalli, S.; Yousufuddin, M.; Lovely, C. J. *Synlett* **2010** DOI: 10.1055/s-0029-1219351.
30. Patel, J.; Pelloux-Léon, N.; Minassian, F.; Vallée, Y. *J. Org. Chem*. **2005**, *70*, 9081-9084.
31. (a) Ullman, B. R.; Aja, T.; Chen, N.; Diaz, J. L.; Gu, X.; Herrmann, J.; Kalish, V. J.; Karanewsky, D. S.; Kodandapani, L.; Krebs, J. J.; Linton, S. D.; Meduna, S. P.; Nalley, K.; Robinson, E. D.; Roggo, S. P.; Sayers, R. O.; Schmitz, A.; Ternansky, R. J.; Tomaselli, K. J.; Wu, J. C. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 3632-3636;
32. Patel, J.; Pelloux- Léon, N.; Minassian, F.; Vallée, Y. *Tetrahedron Lett*. **2006**, *47*, 5561-5563.
33. Trost, B. M.; Dong, G. *Org. Lett*. **2007**, *9*, 2357-2359.
34 Trost, B. M.; Fandrick, D. *Org. Lett*. **2005**, *7*, 823-826.
35. Trost, B. M.; Fandrick, D. *J. Am. Chem. Soc.* **2003**, *125*, 11836-11837.
36. Hunsen, M. *Synthesis* **2005**, 2487-2490.

37. De Mico, A.; Margarita, R.; Parlanti, L.; Vescovi, A.; Piancatelli, G. *J. Org. Chem.* **1997**, *62*, 6974-6977.

38. Edlbacher, S.; Von Bidder, *Z. Physiol. Chem*. **1942**, *276*, 126-129.

39. (a) Valeev, F. A.; Salikhov, S. M.; Krasnoslobodtseva, O. Y.; Sharipov, B. T.; Spirikhin, L. V.; Tolstikov, G. A. *Chem. Nat. Comp.,* **2007**, *43*, 143-148. (b) Griffith, R. K.; DiPietro, R. A. *Synth. Commun.,* **1986**, *16*, 1761-1764. (c) Daninos, Z. S.; Mourabit, A. Al.; Ahond, A.; Poupat, C.; Potier, P. *Tetrahedron,* **1997**, *53*, 7605-7614. (d) Nanteuil, G. De.; Ahond, A.; Poupat, C.; Thoison, O.; Potier, P. *Bull. Soc. Chim. Fr.,* **1986**, 813-816. (e) Wolin, R.; Connolly, M.; Afonso, A.; Hey, J. A.; She, H.; Rivelli, M. A.; Willams, S. M.; West, Jr, R. E. *Bioorg. Med. Chem. Lett*., **1998**, *8*, 2157-2162. (f) Commercon, A.; Ponsinet, G. *Tetrahedron Lett.,* **1990**, *31*, 3871-3874. (g) Kantchev, E. A. B.; Peh, G.-R.; Zhang, C.; Ying, J. Y. *Org. Lett.,* **2008**, *10*, 3949-3952. (h) Sakamoto, T.; Nagata, H.; Kondo, Y.; Shiraiwa, M.; Yamanaka, H. *Chem. Pharm. Bull.,* **1987**, *35*, 823-827. (i) Benhida, R.; Lezama, R.; Fourrey, J.-L. *Tetrahedron Lett.,* **1998**, *39*, 5963-5964. (j) Yamashita, M.; Oda, M.; Hayashi, K.; Kawasaki, I.; Ohta, S. *Heterocycles,* **1998**, *48*, 2543-2550.

40. Beyerman, H. C.; Van Weelderman, A. W.; Maat, L.; Noordam, A. *Recl. Trav. Chim. Pays-Bas.* **1977**, *96*, 191-193.

41. (a) Otte, R. D.; Sakata, T.; Guzei, I. A.; Lee, D. *Org. Lett.* **2005**, *7*, 495-498. (b) Lepore, S. D.; He, Y. *J. Org. Chem.* **2003**, *68*, 8261-8263. (c) Mitsunobu, O.; *Synthesis* **1981**, 1-28.

42. Papadopoulos, E. P. *J. Org. Chem.* **1972**, *37*, 351-355.

43. (a) Sosa, A. C. B.; Yakushijin, K.; Horne, D. A. *Org. Lett.* **2000,** *2*, 3443-3444. (b) Appenzeller, J.; Tilvi, S.; Martin, M. T.; Gallard, J. F.; El-bitar, H.; Dau, E. T. H.; Debitus, C.; Laurent, D.; Moriou, C.; Mourabit, A. Al. *Org. Lett.* **2009**, *11*, 4874-4877.

44. Araki, A.; Kubota, T.; Aoyama, K.; Mikami, Y.; Fromont, J.; Kobayashi, J. *Org. Lett.* **2009**, *11*, 1785-1788.

45. Meketa, M. L.; Weinreb, S. M. *Tetrahedron Lett.* **2007**, *63*, 9112-9119.

46. Poverlein, C.; Jacobi, N.; Mayer, P.; Lindel, T. *Synthesis* **2007**, *23*, 3620-3626.

47. Bhandari, M.; Sivappa, R.; Lovely, C. *Org. Lett*. **2009**, *11*, 1535-1538.

48. Spoering, R. M. *Dissertation*; Harvard University: USA, **2005**.

49. Mancini, M.; Honek, J. *Tetrahedron Lett*. **1982**, *23*, 3249-3250.

50. Sunazuka, T.; Hirose, T.; Harigaya, Y.; Takamatsu, S.; Hayashi, M.; Komiyama, K.; Mura, S.; Sprengeler, P. A.; Smith, A. B. *J. Am. Chem. Soc.* **1997**, *119*, 10247-10248.

51. Colacino, E.; André, C.; Martinez, J.; Lamaty, F. *Tetrahedron Lett*. **2008**, *49*, 4953-4955.

52. Garg, N. K.; Caspi, D. D.; Stoltz, B. M. *Synlett*, **2006**, *18*, 3081-3087.

53. Zancanella, M. A.; Romo, D. *Org. Lett*. **2008**, *10*, 3685-3688.

54. Thompson, A. S.; Humphrey, G. R.; DeMarco, A. M.; Mathre, D. J.; Grabowski, E. J. J. *J. Org. Chem*. **1993**, *58*, 5886-5888.

55. Monguchi, Y.; Fujita, Y.; Endo, K.; Takao, S.; Yoshimura, M.; Takagi, Y.;

Maegawa, T.; Sajiki, H. *Eur. J. Org. Chem.* **2009**, *15*, 834-837.

56. (a) Berglund, S.; Egner, B. J.; Graden, H.; Graden, J.; Morgan, D. G. A.;Inghardt, T.; Giordanetto, F. *Bioorg. & Med. Chem. Lett*. **2009**, *19*, 4268-4273. (b) Arndt, H.-D.; Koert, U. in Organic Synthesis Highlights 4 Wiley-VCH, Weinheim, **2000**, pp. 241-250.
57. Du, H.; He, Y.; Rassapali, S.; Lovely, C. J. *Synlett* **2006**, 965-992.
58. Weinreb, S. M. *Nat. Prod. Rep.* **2007**, *24*, 931-948.
59. Arndt, H. D.; Riedrich, M*. Angew. Chem. Int. Ed*. **2008**, *47*, 4785-4788.
60. Heasley, B. *Eur. J. Org. Chem*. **2009**, 1477-1489.
61. Forenza, S.; Minale, L.; Riccio, R.; Fattorusso, E. *J. Chem. Soc. D* **1971**, 1129-1130.
62. Kinnel, R. ; Gehrken, H.-P.; Swali, R.; Skoporowski, G.;. Scheurer, P. J *J. Org. Chem.* **1998**, *63*, 3281-3286.
63. Hernandez, H. G.; Nakadai, M.; Vimolratana, M.; Li, Q.; Doundolakis, T.; Harran, P. G. *Angew. Chem.* **2005**, *117*, 775-779.
64. Kinnel, R. B.; Gehrken, H.-P.; Scheurer, P. J. *J. Am. Chem. Soc.* **1993**, *115*, 3376-3377.
65. Grube, A.; Kock, M.; *Angew. Chem.* **2007**, *119*, 2372-2376.
66. Katz, J. D.; Overman, L. E. *Tetrahedron* **2004**, *60*, 9559-9586.
67. Lanman, B. A.; Overman, L. E.; Paulini, R.; White, N. S. *J. Am. Chem. Soc.* **2007**, *129*, 12896-12900.
68. Hudson, J.; Cernak, T.; Ashenhurst, J.; Gleason, J. *Angew. Chem. Int. Ed*. **2008**, *47*, 8885-8888.

69. Cernak, T.; Gleason, J. *J. Org. Chem*. **2008**, *73*, 102-110.

70. I. Kawasaki, N.; Sakaguchi, N.; Fukushima, N.; Fujioka, F.; Nikaido, M.; Yamashita, S. Ohta *Tetrahedron Lett*. **2002**, *43*, 4377-4380.

71. Tan, X.; Chen, C. *Angew. Chem*. **2006**, *118*, 4451-4454.

72. Baran, P. S.; O'Malley, D. P.; Zografos, A. L. *Angew. Chem*. **2004**, *116*, 2728-2731.

73. Northrop, B. H.; O'Malley, D. P.; Zografos, A. L.; Baran, P. S.; Houk, K. N. *Angew. Chem.* **2006**, *118*, 4232-4236.

74. Baran, P. S.; Zografos, A. L.; O'Malley, D. P. *J. Am. Chem. Soc*. **2004**, *126*, 3726-3727.

75. O'Malley, D. P.; Li, K.; Maue, M.; Zografos, A. L.; Baran, P. S. *J. Am. Chem. Soc.* **2007**, *129*, 4762-4775.

76. Dilley, A. S.; Romo, D. *Org. Lett*. **2001**, *3*, 1535-1538.

77. Starr, J. T.; Koch, G.; Carreira, E. M. *J. Am. Chem. Soc.* **2000**, *122*, 8793-8794.

78. O'Malley, D. P.; Yamaguchi, J.; Young, I. S.; Seiple, I. B.; Baran, P. S. *Angew. Chem.* **2008,** *120*, 3637-3639.

79. Yamaguchi, J.; Seiple, I. B.; Young, I. S.; O'Malley, D. P.; Maue, M.; Baran, P. S. *Angew. Chem*. **2008**, *120*, 3634-3636.

80. Assmann, M.; Kock, M.; *Z. Naturforsch. C* **2002**, *57c*, 157-160.

81. Assmann, M.; Lichte, E.; Kock, M.; *Bull. Mus. Ist. Biol. Univ. Genova* **2004**, *68*, 189-193.

82. Namyslo, J. C.; Kaufmann, D. E. *Chem. Rev*. **2003**, *103*, 1485-1537.

83. Morisaki, N.; Furukawa, J.; Kobayashi, H.; Iwasaki, S.; Nozoe, S.; Okuda, S. *Chem. Pharm. Bull*. **1987**, *35*, 2678-2685.

84. Breder, A.; Chinigo, G.; Waltman, A.; Carreira, E. M. *Angew. Chem. Int. Ed.* **2008**, *47*, 8514-8517.

85. Massadine isolation and structure elucidation: Nishimura, S.; Matsunaga, S.; Shibazaki, M.; Suzuki, K.; Furihata, K.; Soest, R. van; Fusetani, N. *Org. Lett.* **2003**, *5*, 2255-2257.

86. Denney, D. B.; Sherman, N. *J. Org. Chem.* **1965**, *30*, 3760-3761.

87. Bultman, M.; Ma, J.; Gin, D. Y. *Angew. Chem. Int. Ed.* **2008**, *47*, 6821-6824.

88. Woodward, R. B.; Katz, T. J. *Tetrahedron* **1959**, *5*, 70-89.

89. Lanman, B.; Overman, L. E.; Paulini, R.; White, N. *J. Am. Chem. Soc.* **2007**, *129*, 12896-12900.

90. M. Buchanan, A. Carroll, R. J. Quinn, *Tetrahedron Lett.* **2007**, *48*, 4573-4574.

91. Corey, E. J.; Kang, M.-C. *J. Am. Chem. Soc.* **1984**, *106*, 5384-5385.

92. Yang, D.; Ye, X.-Y.; Xu, M.; Pang, K.-W.; Cheung, K.-K. *J. Am. Chem. Soc.* **2000**,*122*, 1658-1663.

93. Dransfield, P.; Dilley, A.; Wang, S.; Romo, D. *Tetrahedron* **2006**, *62*, 5223-5247.

94. Sivappa, R.; Hernandez, N.; He, Y.; Lovely, C. J. *Org. Lett.* **2007**, *9*, 3861-3864.

95. He, Y.; Chen, Y.; Du, H.; Schmid, L. A.; Lovely, C. J. *Tetrahedron Lett.*, **2004**, 45, 5529-5532.

96. Sivappa,R.; Koswatta, P.; Lovely, C. J. *Tetrahedron Lett.*, **2007**, *48*, 577-581.

97. Naidu, M.S.R.; Bensusan,H.B. *J. Org. Che*m. **1968**, *33*, 1307-1309.

98. (a) Gassman, P. G; Chavan, S. P *J. Am. Chem. Soc* **1988**, *53*, 2394-2396.

(b)Sakamoto, T.; Shiga, F.; Yasuhara, A.; Uchiyama, D.; Kondo, Y.; Yamanaka, Y. H. *Synthesis*, 1992, 746-770.

99. Chinchilla, R.; Najera, C. *Chem. Rev*. **2007**, *107*, 874-922.

100. Davis, F. A.; Sheppard, A. C. *Tetrahedron*, **1989**, *45*, 5703-5707.

101. Denmark, S. E.; Jones, T. K. *J. Org. Chem*. **1982**, *47*, 4595-4597.

102. Lovely, C. J.; Du, H.; Sivappa, R.; Bhandari, M. K.; He, Y.; Dias, H. V. R. *J. Org. Chem.* **2007**, *72*, 3741-3747.

103. Fringuelli, F.; Piermatti, O.; Pizzo, F.; Vaccaro, L. *Eur. J. Org. Chem.* **2001**, 439-455.

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