APPLICATION OF Pd-CATALYZED REACTIONS IN THE TOTAL SYNTHESIS OF OROIDIN-DERIVED ALKALOIDS

by

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ABSTRACT

APPLICATION OF Pd-CATALYZED REACTIONS IN THE TOTAL SYNTHESIS OF OROIDIN-DERIVED ALKALOIDS

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The oroidin family of marine natural products is a growing group of sponge-derived alkaloids which contain 2-aminoimidazole and pyrrolecarboxamide fragments as their signature features. Due to their structural diversity and biological activity, many groups are interested in the total synthesis of these natural products. It has been proposed that many of the alkaloids in this family are produced in nature simply by dimerization and/or cyclization of the simplest member, oroidin. In this dissertation we have attempted to explore these biosynthetic relationships to complete the total synthesis of several oridin-derived natural products. This dissertation consists of two parts. The first part describes the total synthesis of the nominal structure of nagelamide D and the development

of approaches towards total synthesis of other congeners with the nagelamide family. The second part of this dissertation describes studies of intramolecular cyclization reactions of imidazolylpropargyl amides as linchpin synthons for the assembly of imidazole-containing natural products.

In the first part, a Pd-catalyzed Stille reaction was used as a transformation to construct divinyl imidazole derivatives in convergent fashion. A divergent approach was used to further functionalize intermediates obtained from Stille reaction towards the total synthesis of several nagelamides. The total synthesis of nagelamide D was accomplished by using a double Mitsunobu reaction to install pyrrolecarboxamides. Selective hydrogenation of a trisubstituted olefin or electrocyclization reactions of divinyl intermediates obtained from the Stille reaction provided key frameworks required for the total synthesis of nagelamide A, nagelamide E and ageliferin respectively. Construction of the stereoisomeric Z-vinyl stannane provided access to the divinyl imidazole fragment required for the total synthesis of nagelamide C.

In the second part, Pd-catalyzed and/or base promoted intramolecular cyclization reactions of imidazolylpropargyl amides were screened as a part of diversity oriented strategy for the assembly of natural product-like frameworks. Several novel heterocycles including morpholine, pyrazinone, oxazole, pyridinone and azepin derivatives were prepared using intramolecular cyclization. Many of these heterocyclic compounds have potential to serve as intermediates en route to the

total synthesis of oroidin-derived alkaloids including stevensine, nagelamide R, nagelamide T, oxocyclostylidol, agelastatin A. The potential of this approach was demonstrated in a formal total synthesis of cyclooroidin

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PART I

APPROACHES TOWARDS THE TOTAL SYNTHESIS OF NAGELAMIDES

CHAPTER 1

INTRODUCTION

1.1 Oroidin alkaloids

Intellectually at least, 50% of the clinically used drugs are derived from bioactive natural products, including from marine sources.[1,2] As a result marine natural products have attracted scientists from different areas such as chemists, biochemists, biologists, pharmacologists and ecologists. All forms of life engage in severe competition for resources to enable existence; it is probably due to this phenomenon that organisms which live in marine environments produce secondary metabolites with a wide range of biological activities to provide a competitive advantage. Many times however, the limited availability of these natural products makes it difficult to explore their complete biological profile and thus opportunities are potentially missed for discoveries in therapeutic areas outside the mainstream (e.g. antibiotics, anti-cancer) in the search for biological probes. Because of their biological activity and the demanding structural complexity, many chemists over the world are interested in the total synthesis of natural products.[3-5]

Among the various marine natural product families, the pyrrole-imidazole alkaloids, the so-called oroidin natural products are a growing family of

secondary metabolites (over 150 members) isolated from marine sponges mainly in the *Agelasidae, Axinellidae* and *Halichondridae* families.[6-8] The simplest member of this group, oroidin (**1**), which is considered to be the parent compound of this family, was isolated from the marine sponge *Agelas oroides* in 1971.[7,9] A series of purely hypothetical biogenetic pathways have been proposed suggesting oroidin (**1**), hymenidin (**2**)[10] and clathrodin (**3**)[11] undergo various modes of dimerization and/or cyclization[8] to give other complex natural products belonging to this family containing one e.g., **4**,[12-14] two e.g., **5-8**[15-26] or even up to four molecules e.g., **9**[27,28] of **1**, **2** and/or **3** (Figure 1-1).[29,30] Though many monomeric natural products (for example: oroidin (**1**), phakellin (**4**), dispacamide A/B, slagenins, dibromophakellastatin, agelastatins)[30-37] of this family have been successfully synthesized (total synthesis), it is only very recently some dimers have yielded to total synthesis, for example: ageliferin (**5**),[38,39] axinellamine A (**7**),[40] massadine (**8**)[41] and most recently palau'amine (**6**).[42] The nagelamides are a growing subgroup of oroidin dimers and these natural products are the focus of the first section of this dissertation.

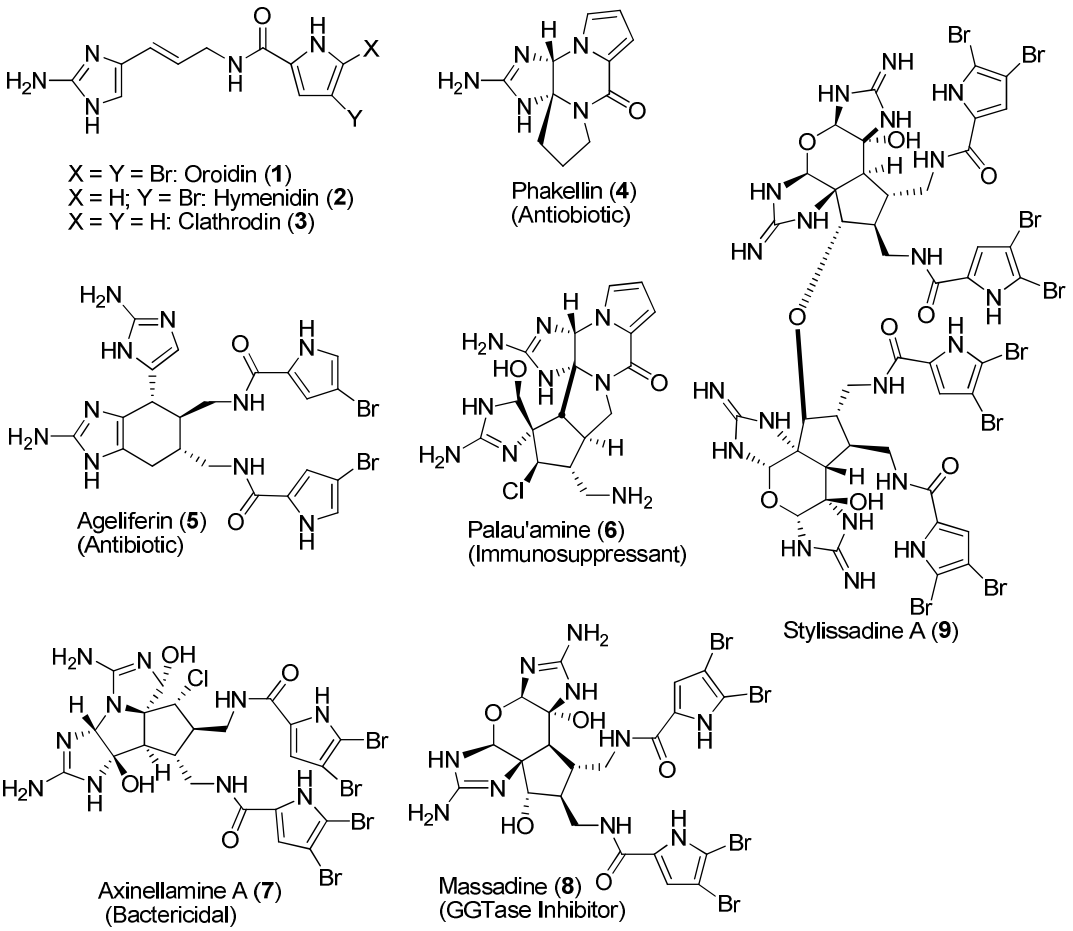


Figure 1-1 Oroidin alkaloids

1.2 The Nagelamides

In 2004, the Kobayashi lab reported the isolation of the first group of eight nagelamides, nagelamide A-H (**10**-**17**) from an Okinawan marine sponge *Agelas sp* (Figure 1-2).[24] All of these nagelamides have shown modest antimicrobial activity against Gram-positive bacteria *Micrococcus luteus* and *Bacillus subtilis* and the Gram-negative bacterium *E. Coli*.

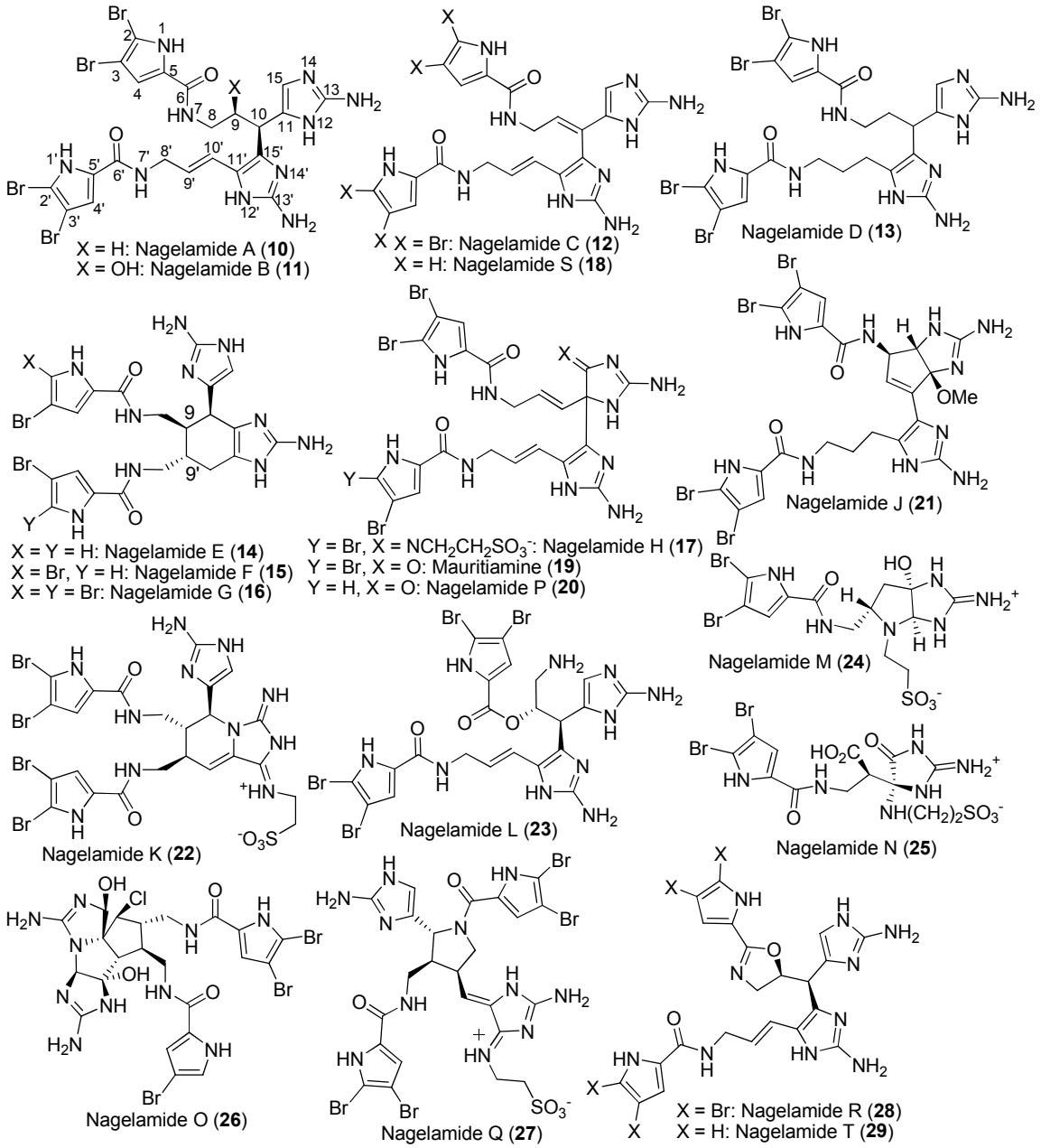


Figure 1-2 Nagelamides

The best activity was shown against *M. luteus* with MIC (minimum inhibitory concentration) values of 2.1-4.2 μM. Additionally, nagelamides A, G and H have shown inhibitory activity against protein phosphatase type 2A with IC50 values of 48, 13 and 46 μM respectively. Since then, over a period of six years, an

additional 11 or so other members of this family were isolated, predominantly from Japanese marine sponges, by the same group (Figure 1-2). Nagelamide J (**21**),[43] nagelamide Q (**27**),[44] nagelamide R (**28**)[44] and nagelamide T (**29**)[45] are some recently isolated examples of this family. Structurally, these examples are very interesting and unique. Nagelamide J (**21**)[43] is the first bromopyrrole alkaloid possessing a cyclopentane ring fused to 2-aminoimidazole ring. Nagelamide L (**23**)[46] is a unique dimeric alkaloid containing an ester linkage. Nagelamide M (**24**) possesses a 2-amino-octahydropyrroloimidazole ring with a taurine unit, while nagelamide N (**25**) contains a 2-aminotetrahydroimidazolone with a taurine unit.[47] Nagelamide K (**22**)[46] and nagelamide Q (**27**)[44] are rare dimeric bromopyrrole alkaloids possessing a piperidinoiminoimidazolone ring and pyrrolidine ring respectively, while nagelamide R (**28**)[44] and nagelamide T (**29**)[45] are the only examples in the oroidin family which contain oxazoline moieties. Nagelamide O (**26**) and nagelamide P (**20**)[48] are 2'-debrominated version of axinellamine A (**7**) and mauritiamine (**19**) respectively. Most of these molecules exhibit modest antibacterial activity however, apart from this activity, these molecules are rarely screened for other types of biological activities. Since many related natural products in the oroidin family have shown broad range of biological activities, it is very likely that the nagelamides (and conceivably intermediates en route to their total syntheses) are also going to possess a variety of activity.

1.3 Biosynthetic considerations

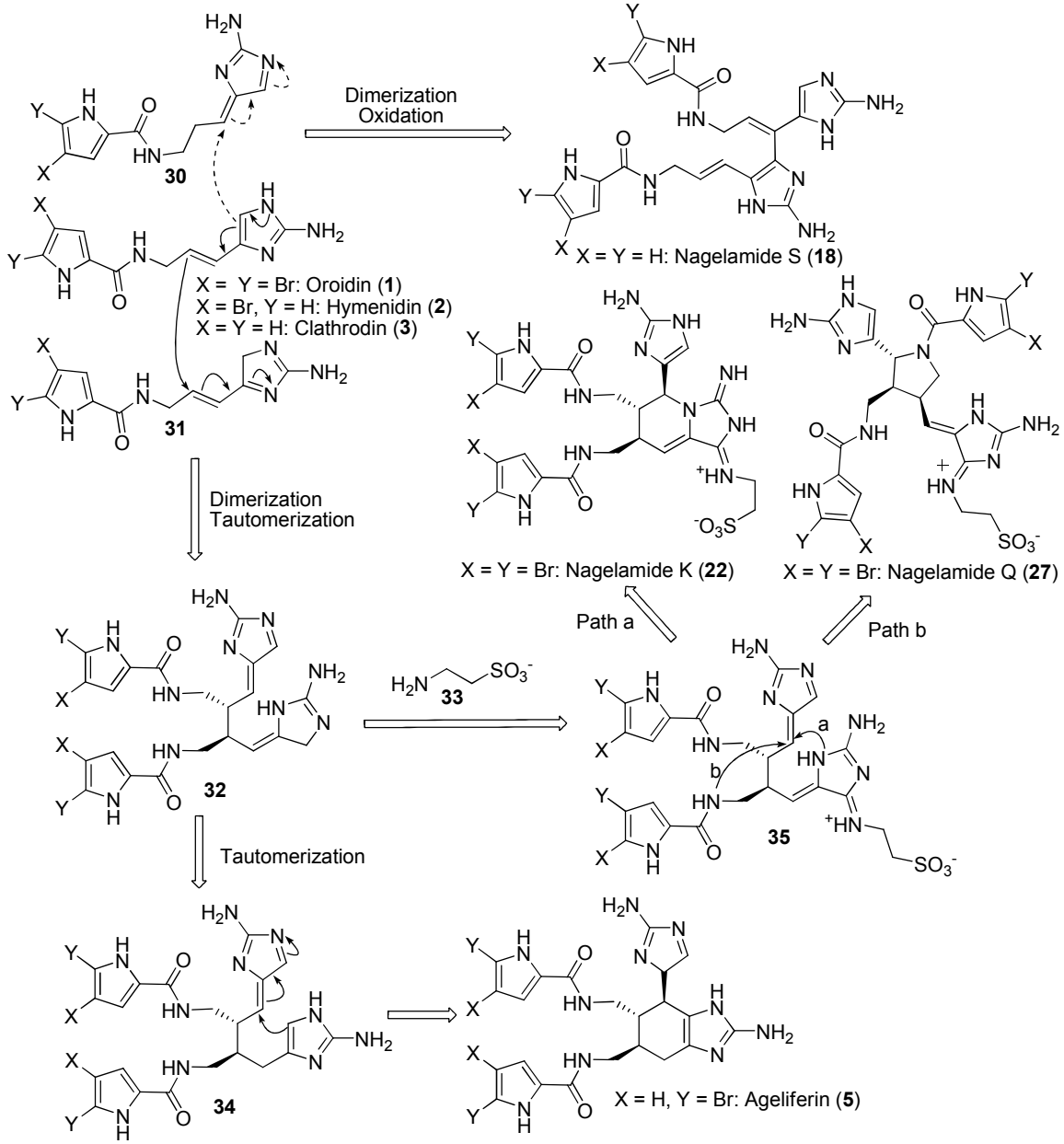


Figure 1-3 Proposed biosynthetic pathways

Although several ideas have been hypothesized regarding the biosynthesis (Figure 1-3) both in a general sense for the oroidin alkaloids and for the nagelamides specifically, essentially nothing is known from an experimental

perspective.[49,50] For example, oroidin (**1**) can undergo dimerization with its tautomer **31** to give intermediate **32**, which upon further tautomerization and cyclization should give ageliferin (**5**) via **34**.[8] A similar pathway, but with a different with stereochemical outcome rationalizes the formation of nagelamide E (**14**). Biosynthetically nagelamide S (**18**) can be envisioned to arise from dimerization of clathrodin (**3**) followed by oxidation.[45] Similarly, oroidin (**1**) might undergo dimerization followed by adjustments of oxidation or hydration state and thus providing access to nagelamide A-D (**10-14**). Biogenetically nagelamide J (**21**) can be derived from nagelamide A or related nagelamides by bond formation between C-8 and C-15.[43] Intermediate **32** may react with taurine (**33**), resulting in the formation of intermediate **35**. Nagelamide K (**22**) and nagelamide Q (**27**) would then form by intramolecular cyclization of intermediate **35** via alternate nitrogen atoms as nucleophiles (path a or path b).[44] Nagelamide R (**28**) when hydrolyzed with TFA generated nagelamide L (**23**) which suggests nagelamide L (**23**) might be derived from nagelamide R (**28**) by enzymatic or spontaneous hydrolysis in the host organism.[44] In another plausible biosynthetic approach for the monomeric congeners as illustrated in Figure 1-4, cyclization followed by oxidation of taurodispacamide A (**36**) should provide nagelamide M (**24**).[47] Alternatively, Baeyer-Villiger oxidation of taurodispacamide A (**36**) should give intermediate **38** which on further oxidation followed by hydrolysis should provide access to nagelamide N (**25**).[47] At this moment, these are only

hypotheses with little experimental evidence for any of these putative transformations.

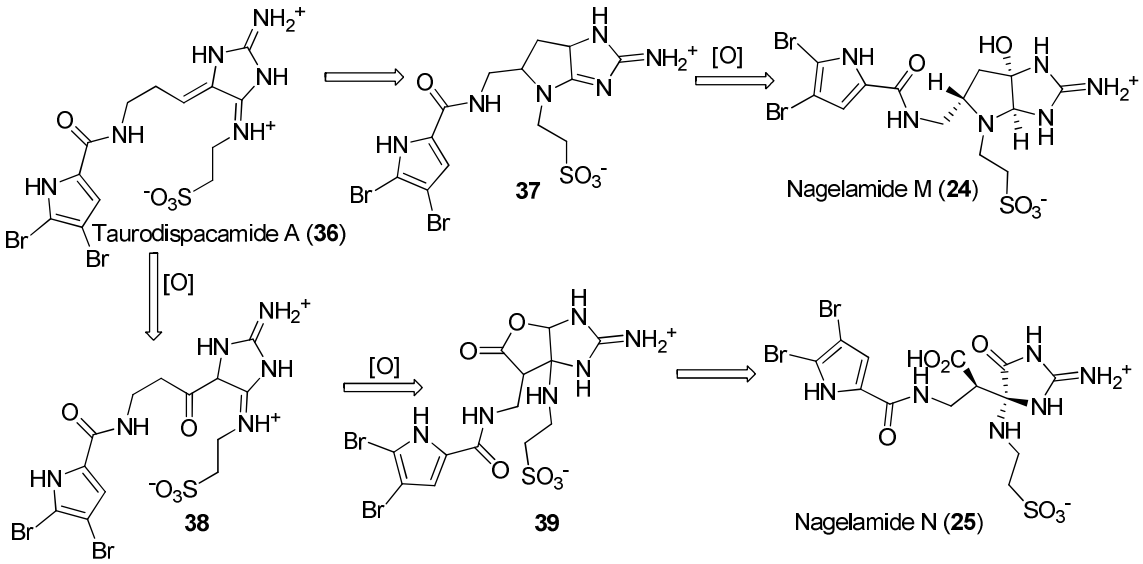


Figure 1-4 Proposed biosynthetic pathways for nagelamide M and N

1.4 Previous approach

To date, the nagelamides have attracted very little attention from the synthetic community. In the literature there are only two reports of the total synthesis of these molecules. The Baran lab has reported total synthesis of nagelamide E (**14**) as a byproduct in the total synthesis of ageliferin,[38,39,51] while the Horne lab has accomplished total synthesis of nagelamide D (**10**) and nagelamide A (**11**).[52] Quite recently, the Lindel lab has reported preliminary experiments in model systems towards some members of the nagelamides.[53] Most of the other nagelamides still remain unsynthesized.

1.4.1 Nagelamide E by Baran

During their approach towards ageliferin (**5**), when sceptrin (**40**) was heated under microwave radiation, the Baran group isolated ageliferin (**5**) in addition to nagelamide E (**14**) as a byproduct in 2:1 ratio (Figure 1-5). Interestingly when pure ageliferin (**5**) or nagelamide E (**14**) were subjected under the same reaction conditions, pure samples returned to the same 2:1 ratio in favor of ageliferin (**5**) suggesting it is the thermodynamically more stable product.[38,39,51]

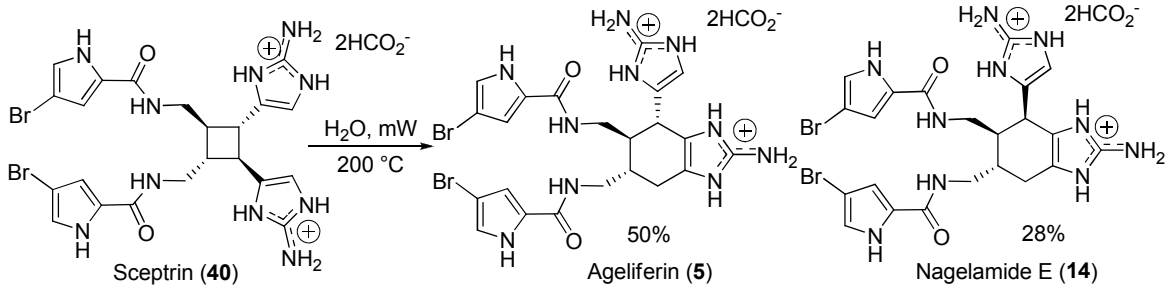


Figure 1-5 Synthesis of ageliferin

1.4.2 Nagelamide D and A by Horne

Tonsiengsom from Horne's lab reported in her dissertation[52] that when diamines **41** and **43** were subjected to oxidative homodimerization using 0.5 eq of NCS, tetraamine **42** and **44** were obtained. Each diamine undergoes acylation at the primary alkyl amines with dibromopyrrole derivative **45** to complete the total synthesis of nagelamide D (**13**) and A (**10**) respectively (Figure 1-6). Although this route looks attractive, especially in terms of the step count, it is difficult to

envision the completion of the total synthesis of other nagelamides using this methodology without substantial modification.

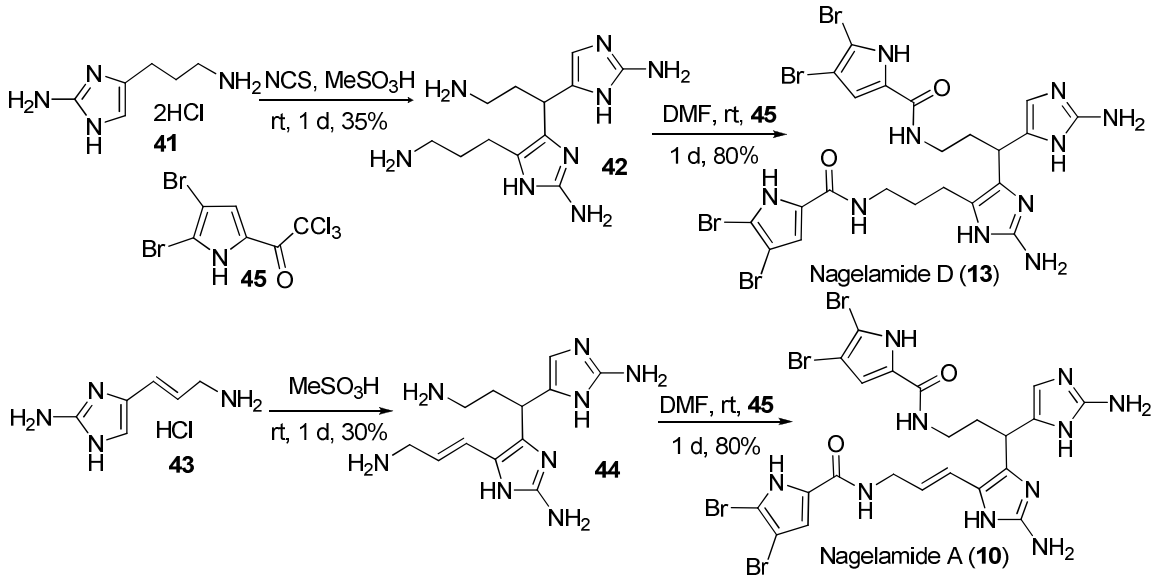


Figure 1-6 Synthesis of nagelamide A and D

1.4.3 Lindel's approach

Very recently Lindel reported another dimerization strategy using Grignard chemistry.[53] In this approach, monoiodoimidazole **46** was converted to the Grignard reagent and subjected to double addition to the saturated esters **47** to provide alcohol **48**, followed by dehydration leading to the bisimidazolylpropenes **49**.

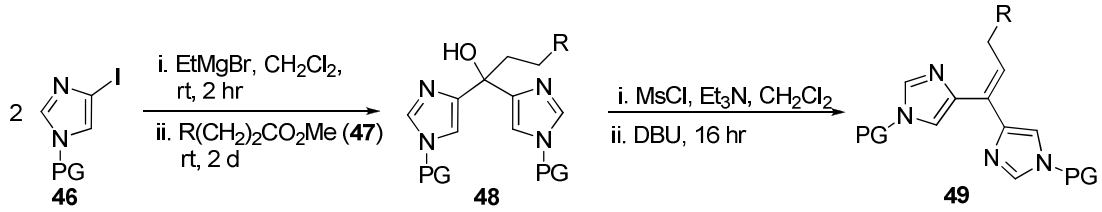


Figure 1-7 Synthesis of bisimidazolylpropenes

Table 1-1 Synthesis of bisimidazolylpropenes

Entry	PG	R	Yield of **48** (%)	Yield of **49** (%)
1	DMAS	H	64	99
2	DMAS	OMe	71	98
3	Tr	NHBoc	61	76

Some of the chemistry developed and reported by our lab (and described in this dissertation) was used to further functionalize intermediate **49**. The Lindel group did not comment on how they are planning to convert intermediate **49** into the nagelamides, as the additional propenyl fragment is still missing on one of the imidazole rings.

Thus because of the structure challenge, the lack of general synthetic approaches, insufficient knowledge of the biosynthesis and biological activity have led us to undertake this project of developing the total synthesis of nagelamides. Also, the possibility of interconverting some of these simple nagelamides into more complex derivatives of the oroidin family makes their synthesis more attractive.

1.5 Our approach

Our approach to this family of molecules is based on a **divergent** strategy where we can potentially access many of these nagelamides using a common intermediate. Since many of these natural products are present together in nature we thought there might be a common intermediate or a common pathway

which might be responsible for formation of these molecules. Specifically nagelamide C (**12**) (or related late stage intermediate **50** in a synthetic context) could serve as divergence point for many of the other nagelamides (Figure 1-8). In principle the total synthesis of nagelamide C (**12**) can be accomplished from intermediate **50** by further manipulating the diol and introducing amino groups at the C2 positions of each imidazole moiety. Nagelamide D (**13**) and nagelamide A (**11**) can be approached from the same intermediate **50** simply by changing the oxidation state of olefins.

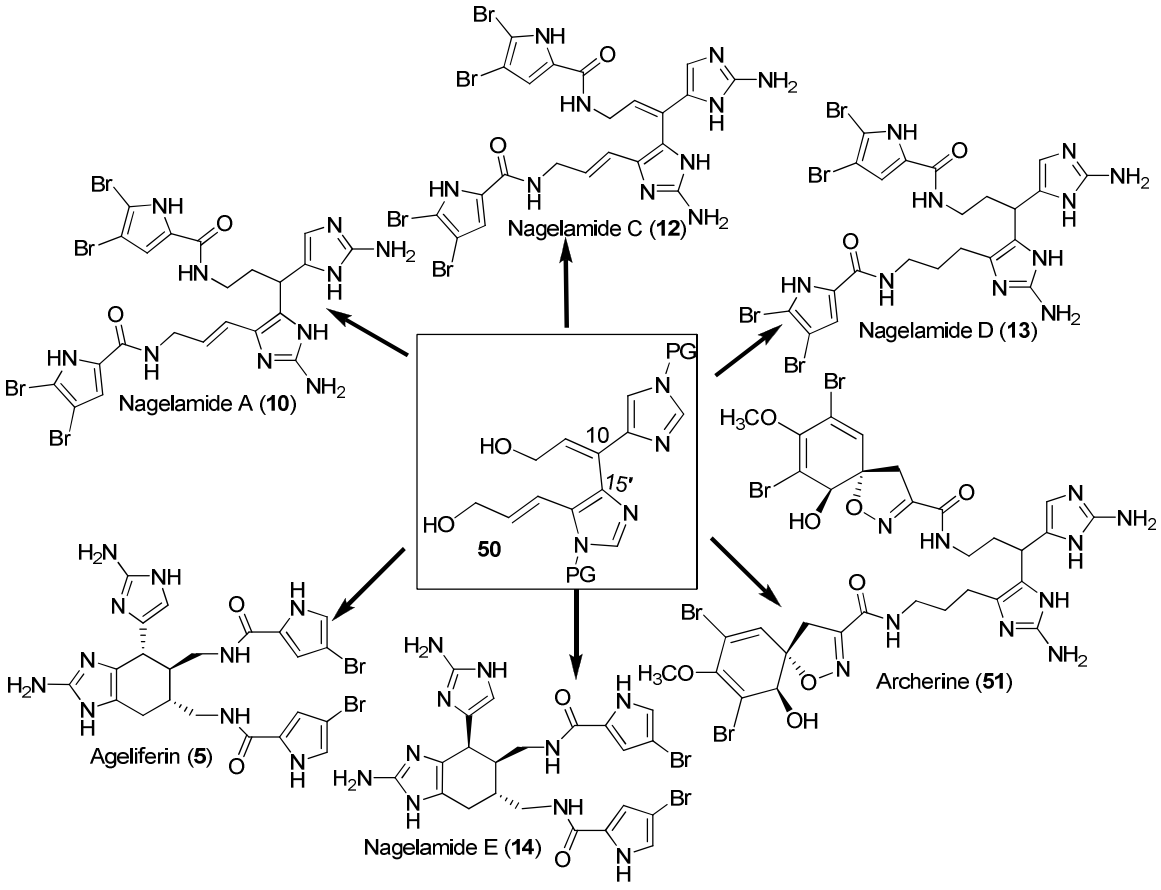


Figure 1-8 Divergent approach towards nagelamides

Archerine (**51**) which was reported in 2001, was isolated from the Caribbean sponge *Aplysina archeri* in 2001 shares the eastern fragment with nagelamide D (**13**).[54] The western fragment just requires diol functionalization with appropriate reagents in the latter stages of the synthesis. In the cases of ageliferin (**5**), nagelamide E (**14**) and other related tetrahydrobenzimidazoles, additional C9-C9' connectivity is required. This can be easily traced back to 6π-electrocyclization of triene **50** and further manipulation of the oxidation state.

The C10-C15' connectivity in common intermediate **50**, which is also common in most of the nagelamides shown in Figure 1-9, can be constructed through a Pd-catalyzed cross coupling between a vinyl stannane and an aryl iodide.[55]

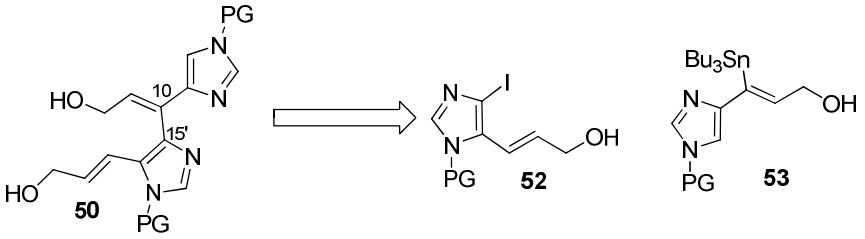


Figure 1-9 Retrosynthetic analysis of divinylimidazole

Preparation of the coupling partners **52** and **53** was envisioned to be feasible through functionalization of 4,5-diiodoimidazole and a 4-iodoimidazole derivative respectively, rather than the de novo synthesis of the heterocycle. We and others have demonstrated that these derivatives undergo position specific functionalization with strong bases, Grignard reagents, and Pd-catalyzed reactions.[56-62] In our group, we have been able to convert simple imidazole derivatives into complex molecules using a variety of synthetic approaches such

as the inter and intramolecular Diels-Alder reactions,[63,64] oxidative additions and rearrangements[65-68] and ring-closing metathesis reactions of imidazoles.[69,70] This chemistry was successfully used to complete total synthesis of several *Leucetta* alkaloids and oroidin alkaloids.[71-75]

CHAPTER 2

RESULTS AND DISCUSSION

2.1 Total synthesis of nagelamide D

Our initial choice of target was nagelamide C as we envisioned intermediates en route to this natural product would serve as a divergence point towards a number of other potential targets, specifically nagelamides A and D which are more highly reduced congeners. All of the nagelamides depicted in Figure 1-2 are dimeric in nature, and thus we decided to use a convergent strategy where two imidazole fragments, vinyl stannane **55** and imidazol-5-yl iodide **54** would be coupled using a Pd-catalyzed Stille reaction[55] as shown in Figure 2-1. In our lab we have used Stille reactions to prepare simple vinyl imidazoles and so our strategy was an extension of our past efforts,[64] but this time it was anticipated that the cross-coupling would be much more difficult because of the steric congestion around the vinylstannane. Our initial efforts to synthesize *Z*-vinylstannane **55** were unsuccessful; so we quickly moved to a backup plan, where we decided to attempt the Stille reaction with the isomeric *E*-vinylstannane **57** which would lead to bisvinylimidazole **58**.

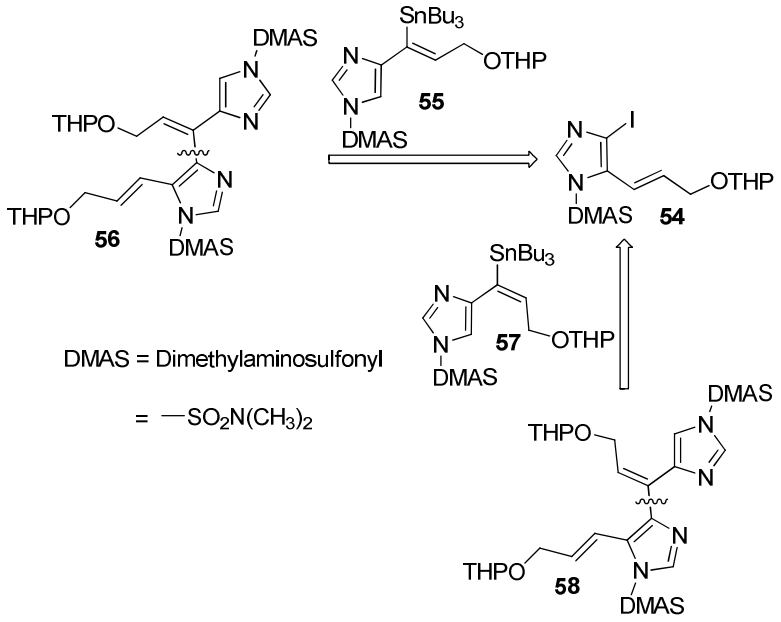


Figure 2-1 Retrosynthetic analysis of divinylimidazole

Of course, this change in strategy had some consequences, specifically with proposed intermediate **58**, it will be possible to attempt total synthesis of all nagelamides shown in Figure 2-2 with the exception of nagelamide C (**12**). In concert with these efforts, attempts were made to synthesize *Z*-vinylstannane **55** in order to explore an approach the total synthesis of nagelamide C (**12**).

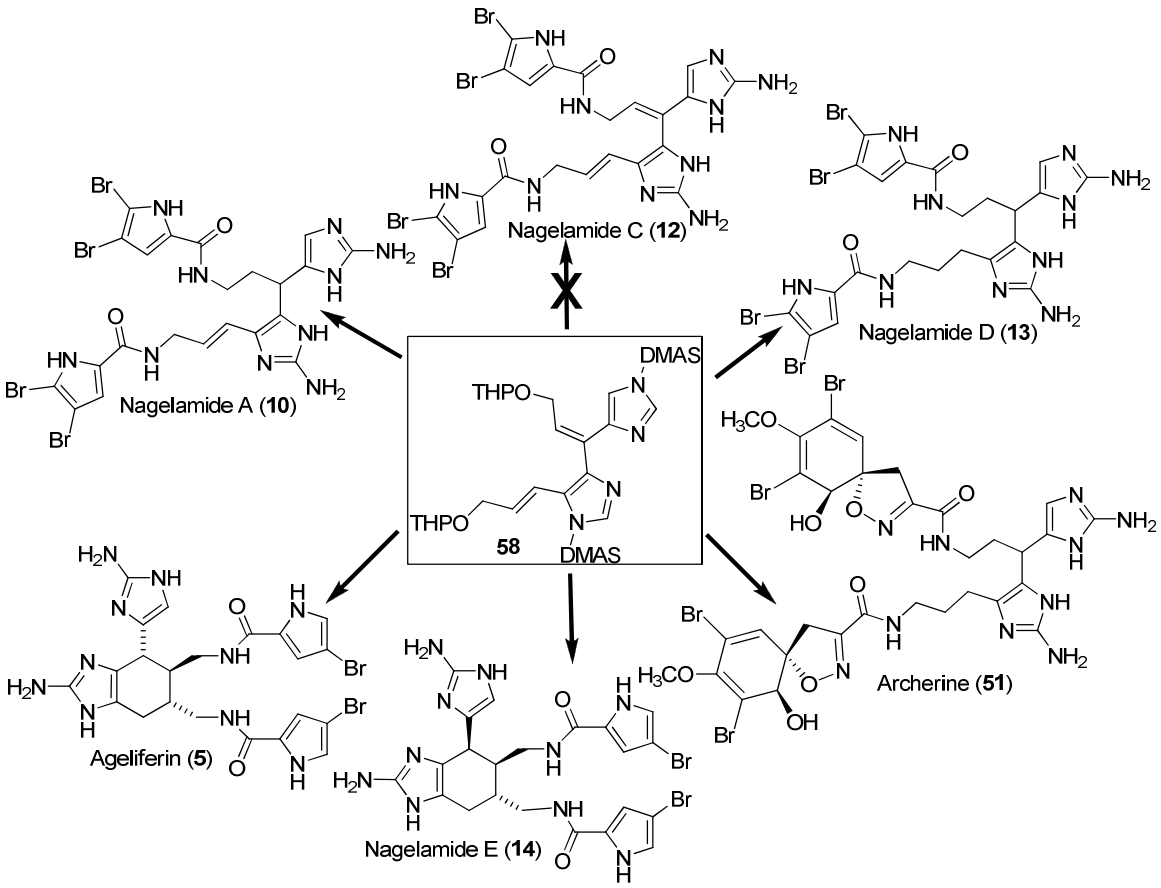
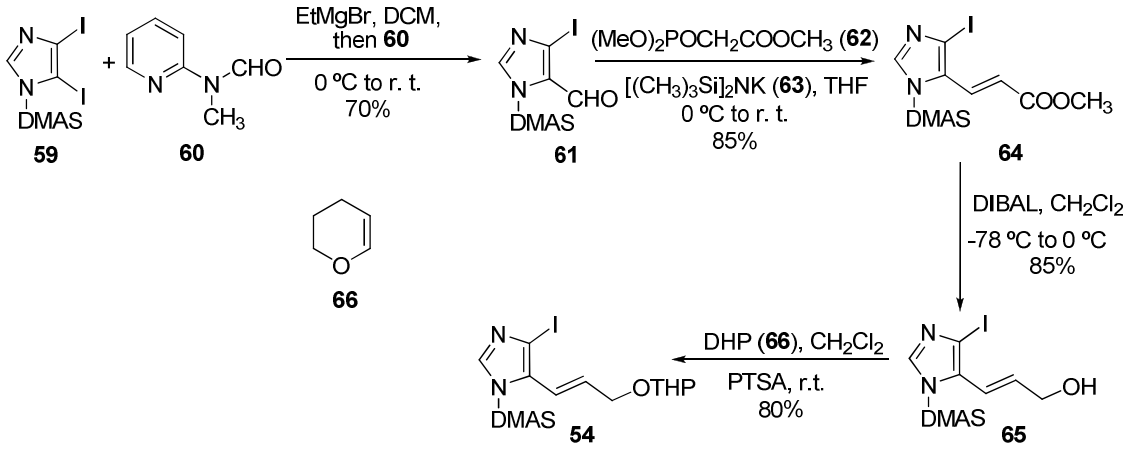


Figure 2-2 Divergent approach towards nagelamides

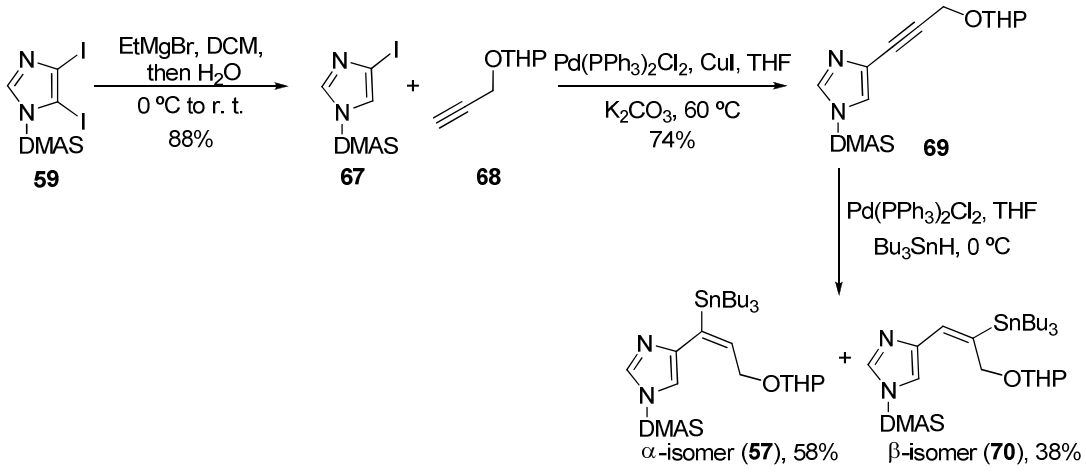
To prepare the required coupling fragments **54** and **57**, DMAS-protected (*N*,*N*-dimethylaminosulfonyl)-4,5-diiodoimidazole **59** was used as a building block. The diiodoimidazole **59** was first metallated at C5 with EtMgBr and then formylated using *N*-methyl-*N*-(2-pyridyl)formamide (**60**) to obtain aldehyde **61**[69,70] in good yield (Scheme 2-1). The resulting aldehyde was then subjected to a Horner-Wadsworth-Emmons reaction, providing acrylate derivative **61**. The ester **61** was then reduced with DIBAL to produce alcohol **64** which was subsequently protected with a THP protecting group. During reduction of ester to the alcohol,

the reaction temperature needs to be carefully controlled; otherwise concomitant reduction of iodo substituent was observed.



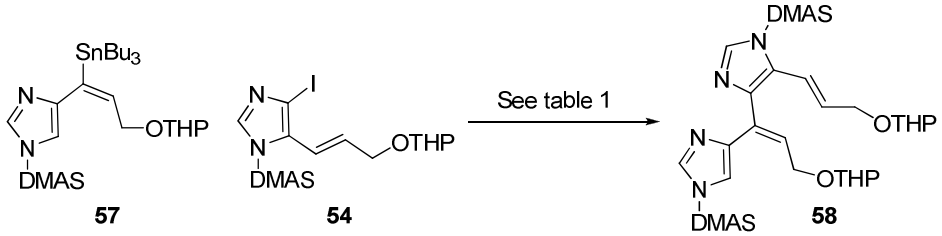
Scheme 2-1

For construction of second fragment, the known 4-iodoimidazole **67** (prepared from **59**) was subjected to a Sonogashira reaction with a THP-protected propargyl alcohol **68** to give the corresponding alkynyl imidazole **69** (Scheme 2-2)**.** Subsequent hydrostannylation of **69** using a Pd(II)-catalyst gave the required organostannane **57**.[76] Since an internal alkyne was used, as expected, two regioisomers (α and β) with *E*-stereochemistry were obtained. The stereochemistry of hydrostannylation product was confirmed by comparing ^{3}J Sn-H coupling constants (^{3}J Sn-H = 63.9 Hz for **57** vs ^{3}J Sn-H = 114.5 Hz for **110**).[77] Attempts to improve the ratio of α:β isomers in favor of α-isomer (**57**) by changing protecting group at alcoholic position (MOM, TBDMS, TBPDS) or by changing the Pd-catalyst source ($Pd_2[dba]_3$, $PdCl_2$) were unsuccessful. While the regiochemical outcome of this reaction was suboptimal, sufficient material could be obtained to advance the synthesis.



Scheme 2-2

Initial attempts to subject some related derivatives of vinyl stannane **57** and imidazolyl iodide **54** to the Stille reaction were unsuccessful under standard reaction conditions (Pd[0], various ligands, solvent). However, at this time we came across a report by the Baldwin lab describing that a combination of CuI and CsF increases the rate of the Stille reaction dramatically,[78] which thus permitted cross coupling of electronically and sterically unfavorable partners. When we subjected vinyl stannane **57** and aryl iodide **54** under these reaction conditions, we were delighted to observe the formation of the required divinylimidazole **58** (see **Table 2-1**).

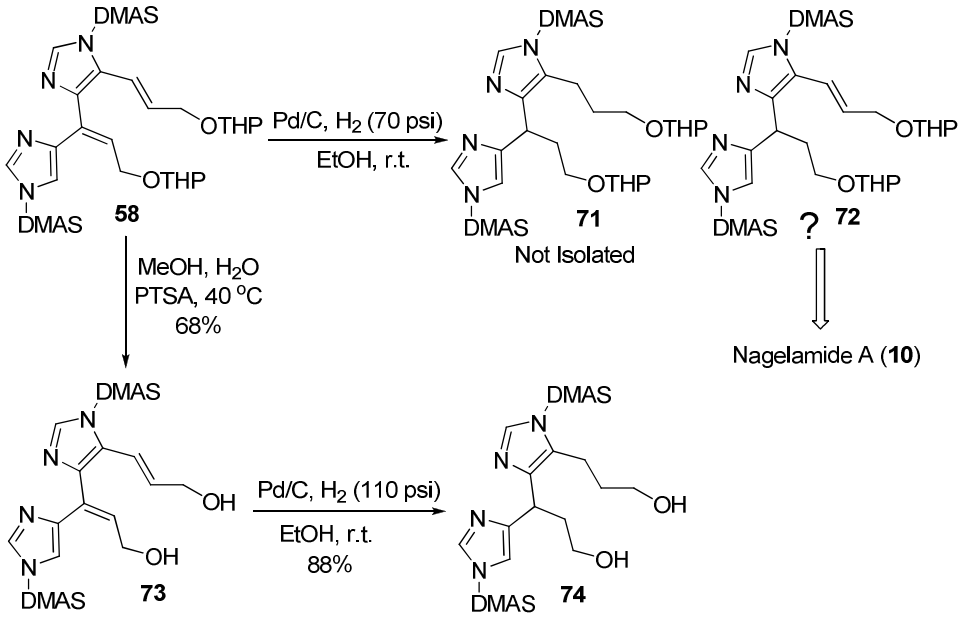


Scheme 2-3

Table 2-1 Stille reaction

Entry	Reaction Conditions	Yield(%)
1	$Pd_2(dba)_3$, CuI, PPh_3, THF, TBAF (dropwise addition), reflux, 1 h	60-70
2	$Pd_2(dba)_3$, CuI, PPh_3, DMF, CsF, 60 ºC, 30min	75

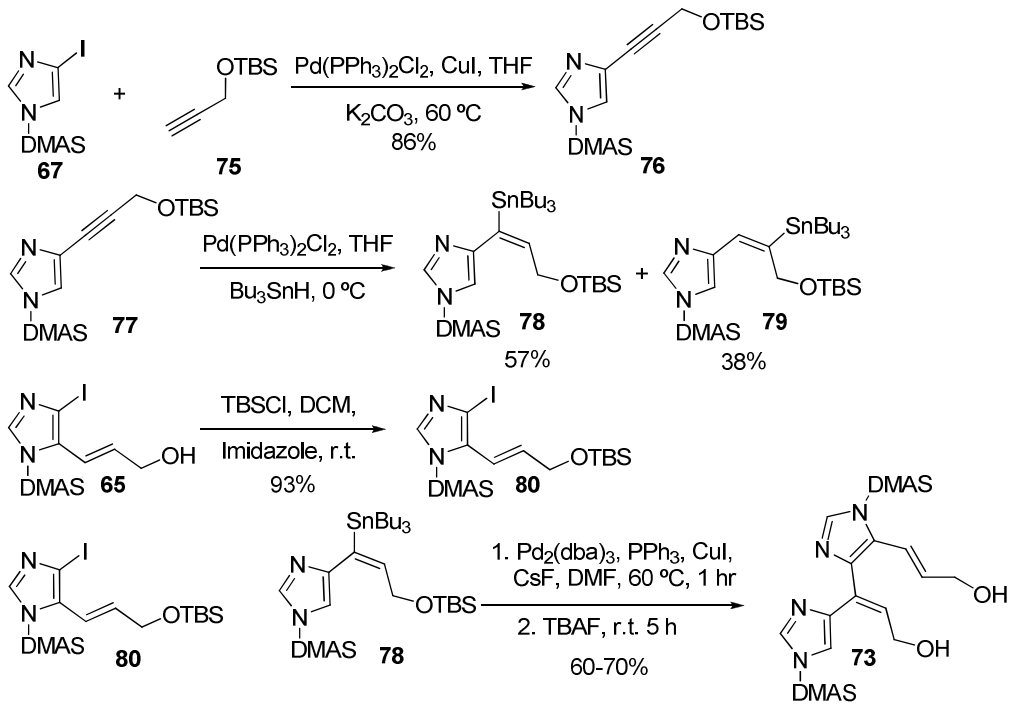
As shown in entry 1, the Stille reaction of these partners proceeded well using TBAF as a fluoride source, but during scale-up of this reaction, the yields were not consistent and tended to be on the lower side of the indicated range. However, by changing the fluoride source from TBAF to CsF, a 75% yield could be obtained on a consistent basis. This observation could be due to water present in TBAF but this was not pursued through the preparation and evaluation of anhydrous TBAF. The divinylimidazole **58** was subjected to hydrogenation using Pd/C under hydrogen pressure of 70 psi (Scheme 2-2). Surprisingly, rather than the completely saturated intermediate **71**, monoolefin **72** was isolated in our initial reductions and attempts to further reduce this compound were not successful. Although we were not able to obtain **71**, compound **72** may serve as an important precursor towards the synthesis of nagelamide A (**10**) (see Section 2.2).



Scheme 2-2

Because of the failure to completely saturate the protected alcohol **58**, we reasoned that removal of the THP groups may facilitate reduction through coordination of the alcohols to the catalyst surface. Therefore a chance was taken to deprotect the alcohol, and then subject it to hydrogenation. The THP groups were removed using a catalytic amount of PTSA in methanol to provide the diol **73** (Scheme 2-2). Gratifyingly the hydrogenation reaction gave the desired diol **74** in good yield. Unfortunately upon scale-up, the yield for THP deprotection reaction was modest (68%) and there were reproducibility problems. This could be due to either competitive DMAS deprotection of imidazole in same pot or some unknown acid catalyzed reactions of deprotected diol **73**. This issue was exacerbated as a result of the formation of diastereomeric products in the cross coupling (and later intermediates) due to the presence of a chiral center in the THP groups which complicated characterization. To address these problems,

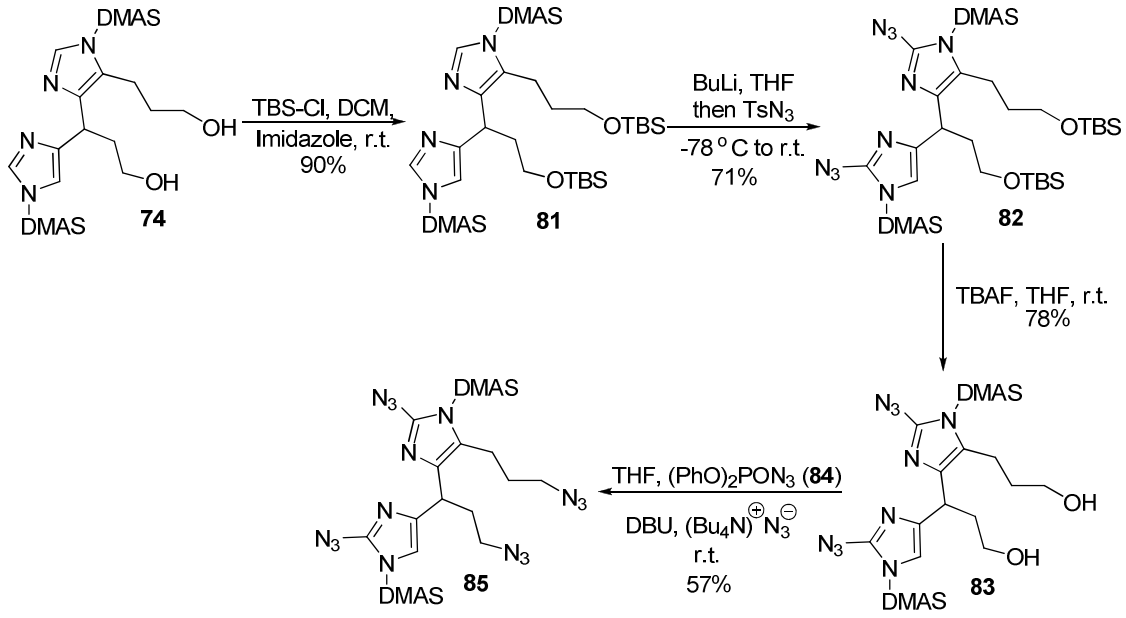
it was decided to use TBS-protected coupling partners **80** and **78**. The advantage of using TBS-protecting group was it can be deprotected in one pot during the Stille reaction under mild, non-acidic conditions due to the presence of fluoride ion. To achieve this, the required coupling partners were prepared in an analogous fashion to **54** and **57** as shown in Scheme 2-3. The aryl iodide **80** and stannane **78** underwent Stille reaction, smoothly providing the allylic diol **73** in good yield after adding TBAF to complete desilylation of silyl ethers. The allylic diol **73** was then reduced to diol **74** as shown in Scheme 2-2.



Scheme 2-3

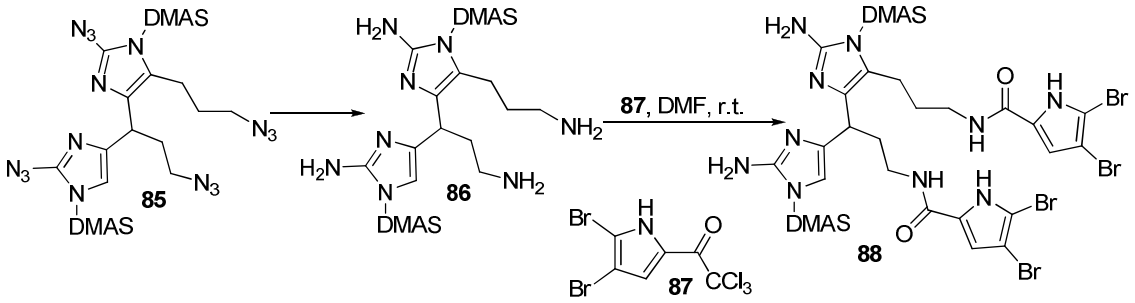
The diol **74** was protected as the bis silyl ether **81**, followed by azidation (n-BuLi then TsN_3) and deprotection of silyl groups to give the diazide **83** (Scheme 2-4).[79] Conversion to the tetraazide **85** was accomplished using diphenylphosphoryl

azide (**84**) and DBU as base in the presence of tetrabutylammonium azide as an external azide source.[80]



Scheme 2-4

At this point the plan was to reduce tetraazide **85** to tetraamine **86** followed by bisacylation with dibromopyrrole trichloroketone (**87**) to give DMAS-protected nagelamide D (**88**) (Scheme 2-7). Removal of the imidazole protecting groups would then provide nagelamide D (**13**).



Scheme 2-5

Several attempts were made to convert this tetraazide **85** to tetraamine **86**, but as shown in Table 2-2, with $NaBH_4$ only the C2 azides were reduced leaving behind primary azide intact. Under Pd-catalyzed hydrogenation conditions or Staudinger reaction conditions, we could not isolate or characterize the required tetraamine **86**.

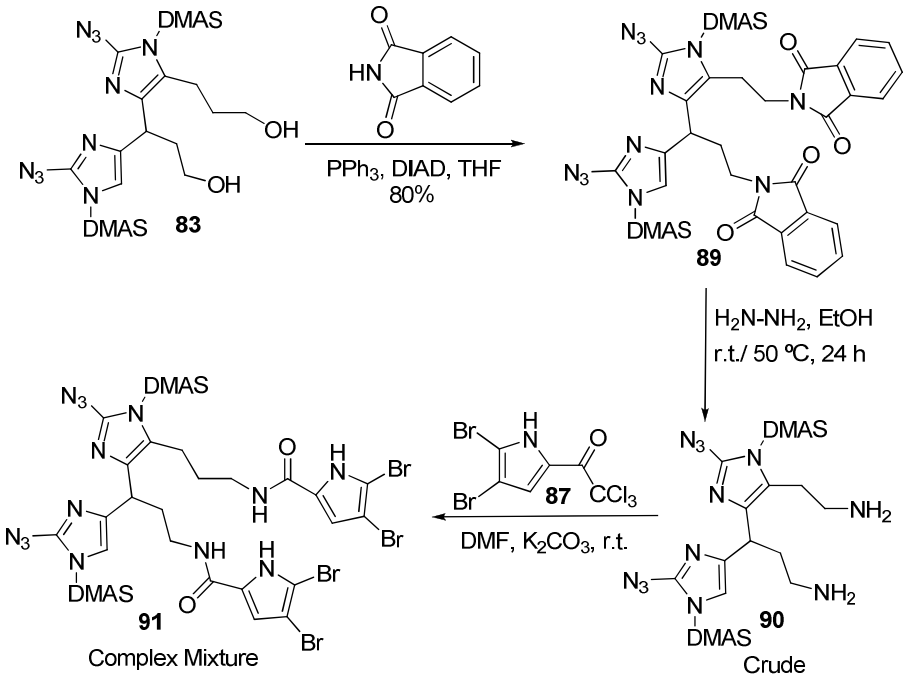
Table 2-2 Reduction of primary azides

Entry	Reaction Conditions	Conclusion
1	$NaBH_4$, MeOH	Only C-2 azides were reduced.
2	Pd/C, EtOH, r.t., H_2 balloon pressure	Unable to isolate or characterize product.
3	(i) PPh_3, THF, water, r.t. (ii) DMF, **87**, 40 ºC	Unable to isolate or characterize product.
4	(i) Pd/C, EtOH, 40 ºC, H_2 70 PSI (ii) DMF, **87**, 40 ºC	Though ^{1}H NMR spectrum was not clean, ESI-MS showed desired analyte peak.

It was hypothesized that tetraamine **86** might not be stable, so to assess this problem, the crude product from the hydrogenation reaction was subjected

directly to acylation with the dibromopyrrole derivative **87**. As shown in entry 4, we could see the required analyte (**88**) peak by ESI-MS. But attempts to further purify or scale up the reaction to isolate product in sufficient quantity were unsuccessful. While this experiment does not prove our hypotheses regarding the instability of **86**, we chose to avoid the preparation of the tetraamine.

At this point a new strategy was explored to introduce primary amines, by using a phthalimide as a masked ammonia equivalent to introduce a primary amine rather than azide.[81] One advantage of this revised strategy was to avoid handling the polar and potentially sensitive tetraamine. To achieve this objective, diol **83** was subjected to a Mitsunobu reaction with phthalimide. By choosing the appropriate sequence of addition, i.e., no free triphenylphosphine in the presence of azide, we could maintain the azides intact i.e., preventing a Staudinger reaction (Scheme 2-6).[82] The resulting imide **89** was then converted to amine **90** by treatment with hydrazine[81] and then the crude reaction mixture was subjected to an acylation reaction with dibromopyrrole derivative **87** to provide diamide **91**. But once again we obtained complex products from this reaction and we could not isolate required product.



Scheme 2-6

Up until this point, we were attempting to install the required amido-pyrrole moiety stepwise i.e., first introducing the amine and then subjecting it to an acylation reaction (Figure 2-3). After revisiting the strategy it was decided to employ a modified imide and to introduce both the amine and the pyrrole carboxamide simultaneously, and thus the dibromohydantoin **94**[83] was used as a nucleophile in a Mitsunobu reaction. There were two main advantages of following this strategy: (1) The polar primary amines will never be prepared in the course of this route. (2) This transformation reduces the overall step count.

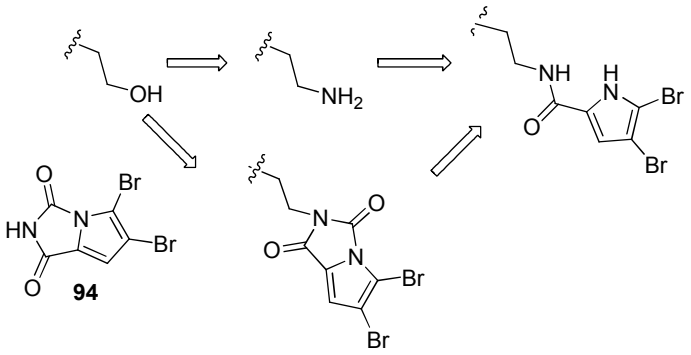
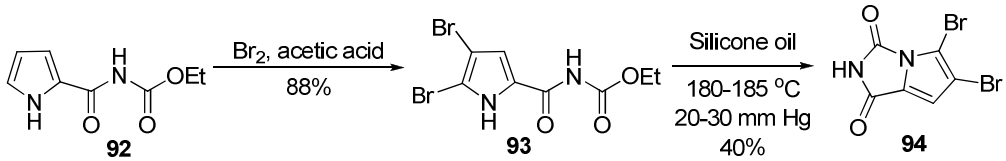


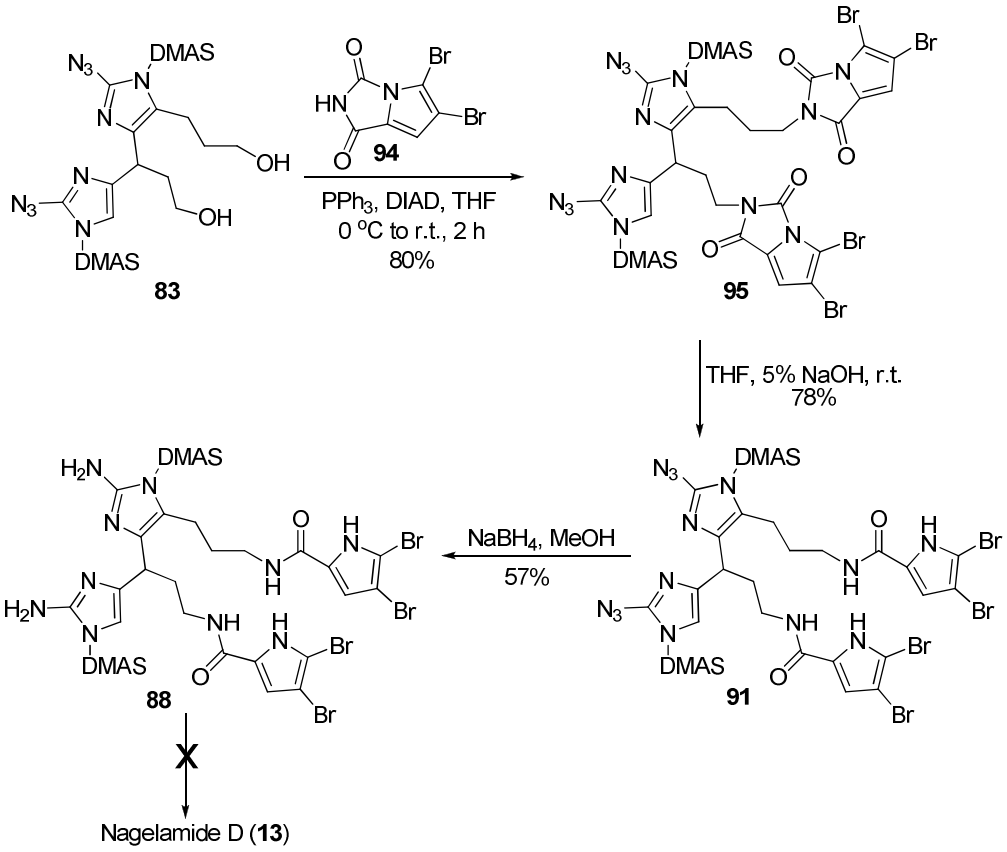
Figure 2-3 Strategy towards installation of pyrrolecarboxamides

Using a known protocol from Prof. Shair's lab,[83] the required nucleophile **94** was prepared from the known imide **92** by first subjecting it to dibromination followed by pyrolysis at 185 ℃ in silicone oil to give required product which was further recrystallized to isolate pure dibromohydantoin **94** as a pale yellow solid (Scheme 2-7).



Scheme 2-7

With the required nucleophile in hand, diol **83** was then subjected to the Mitsunobu reaction with dibromohydantoin **94** to give bis hydantoin **95** in 80% yield, which upon base hydrolysis provided the pyrrolecarboxamides **91** in good yield. Reduction of the C2 azides to the amine with $NaBH_4$ proceeded uneventfully yielding DMAS-protected nagelamide D **88** in moderate yield (Scheme 2-8).



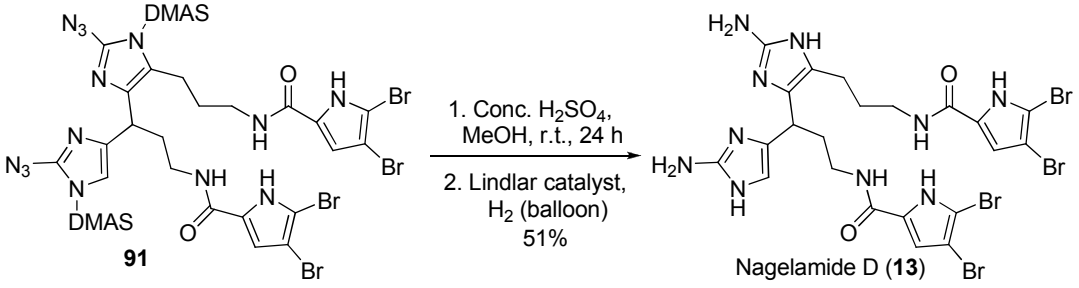
Scheme 2-8

Disappointingly however, attempts to deprotect the DMAS groups under acidic conditions and thus complete the total synthesis of nagelamide D (**13**) were unsuccessful. Under some of the reported reaction conditions[84-86] (entry 1 and 2) for DMAS deprotection of imidazole (Table 2-3), the starting material was recovered intact. Use of harsher condition (entry 3) resulted in degradation of the starting material. Recently, similar observations have been reported by the Lindel group on attempted deprotection of related systems.[53]

Table 2-3 Removal of DMAS group

Entry	Reaction Conditions	Remarks
1	6M HCl, EtOH, reflux, 24 h	No reaction
2	HCl gas, MeOH, r.t., 3 days	No reaction
3	HBr, EtOH, reflux, 24 h	Complex mixture

Since the deprotection of **88** was not working at the last step, an obvious option was to attempt the deprotection at an earlier stage in the sequence and so we decided to try deprotection at the diazide stage. Gratifyingly the diazide **91** was successfully deprotected under very mild conditions and subsequently the azide was reduced with Lindlar catalyst[79] and hydrogen to obtain nagelamide D (**13**) (Scheme 2-9).



Scheme 2-9

Somewhat to our surprise, we found on comparison of the spectroscopic data for the synthetic and naturally-occurring material that they were not completely identical.[24]

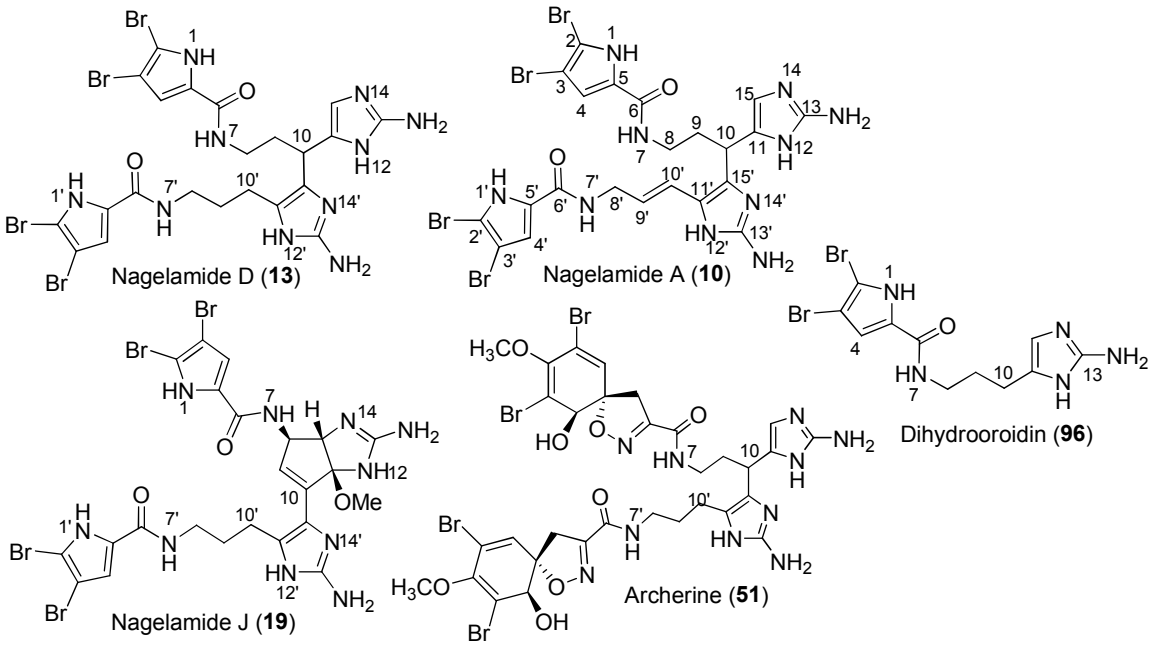


Figure 2-4 Nagelamide D and model compounds

In particular in the ^{1}H NMR spectra, there were several notable discrepancies in the signals due to the aliphatic protons, and to a lesser extent in the ^{13}C NMR spectrum for the corresponding carbon atoms. Notably, two of the reported shifts δ_H 2.14/2.72 (nat.) vs 1.68 (syn.) for H9' and δ_H 3.20-3.30 (nat.) vs 2.40 for H10' (syn.) were substantially different, whereas our data was very similar to that obtained for the parent monomeric unit dihydrooroidin (**96**).[87] A full comparison of the spectroscopic data for nagelamide D (**13**), natural and synthetic, in addition to the corresponding data for nagelamide A (**10**),[24] nagelamide J (**19**),[43] archerine (**51**)[54] and dihydrooroidin (**96**)[72] are provided in Table 2-4 (major discrepancies are highlighted).

Table 2-4 Comparison of ^{1}H NMR data for nagelamide D and model compounds

Proton #	Nagelamide D (**13**) natural	Nagelamide D (**13**) synthetic	Nagelamide A (**10**)	Nagelamide J (**19**)	Dihydro-oroidin (**96**)[87]	Arche-rine (**51**)
1	12.65	12.66 d, 2.7	12.72	12.75	12.76	
1’		12.64 d, 2.2	12.70	12.65		
4	6.95	6.88 d, 2.7	6.92	7.02	6.95 d, 2.7	
4’	6.96	6.92 d, 2.7	6.96	6.89		
7	8.13 t	8.15 t	8.41	8.68 d, 7.0	8.35 t, 5.7	
7’	8.21 t	8.17 t	8.25	8.20 t, 5.6		
8	2.90, 3.20-3.30	3.10, 3.20	3.09-3.19	4.82		3.28
8’	3.20-3.30	3.15	3.90	3.21	3.21 q, 5.9	3.29
9	2.20	1.95, 2.25	1.98, 2.20	6.08 d, 2.2		2.07, 2.29
9’	2.14, 2.72	1.68	6.02	1.73	1.74	1.81
10	4.18	3.99 t, 7.7	4.17 t, 7.8			3.96 t, 7.4
10’	3.20-3.30	2.40	6.42	2.58	2.44 t, 7.3	2.48 t, 6.8
12		12.24	12.77	9.71	11.60	
12’	12.36	12.17	12.63	11.50		
13	7.50	7.40	7.74	7.43	7.33	
13’		7.50	7.50			
14	12.15	12.14	12.33	9.18	12.07	
14’	12.05	12.06	12.18	12.62		
15	6.75	6.72	6.75	4.31	6.61	

It should be noted that archerine contains the complete bis imidazole skeleton of nagelamide D (**13**), whereas nagelamide A (**10**) and nagelamide J (**19**) contain (N1-C15 and N1'-C15' respectively) to the proposed structure of nagelamide D (**13**). The chemical shifts of H9' and H10' (1.68 and 2.40) in synthesized nagelamide D (**13**) were in good agreement with nagelamide J (1.73 and 2.58), dihydrooroidin (1.74 and 2.44) and archerine (1.81 and 2.48). An obvious possible cause of the spectroscopic discrepancy may be a consequence of the concentration differences between the samples used, as Kobayashi and coworkers report isolation of ~ 2 mg of nagelamide D (**13**). However, we found essentially no differences in the ^{1}H NMR spectra on serial dilutions down to approximately the same estimated concentration used by Kobayashi. Addition of a couple of drops of TFA to the final dilution sample exhibited no substantial differences in the chemical shift in the ^{1}H NMR spectrum. Prior to conversion of synthetic **13** to the TFA salt, we checked the ^{1}H NMR spectrum of the free base in MeOH-d_4, which exhibited essentially identical chemical shifts to the salt in DMSO-d_6. Thus, it appears that neither solvent concentration nor pH make a major difference in the appearance of the ^{1}H NMR spectra. Similarly, there were discrepancies in the ^{13}C NMR spectra between synthetic and natural nagelamide D (**13**), in particular a CH_2 signal is reported at δ_c 16.6 (t), whereas for synthetic material the highest field signal is observed at δ_c 21.1 (Table 2-5). Based on the same set of comparative molecules, our data appears to be completely consistent with the assigned structure of nagelamide D.

Table 2-5 Comparison of ^{13}C NMR data for nagelamide D and model compounds

Carbon #	Nagelamide D(**13**) natural	Nagelamide D(**13**) Synthetic	Nagelamide A (**10**)	Nagelamide J (**19**)	Dihydro-oroidin (**96**)	Archer-ine (**51**)
2	104.51	105.1	104.7	105.3		
2’	104.52	105.2	104.6	104.5		
3	97.8	98.4	97.90	98.0	99.8	
3’	97.2	98.4	97.85	97.8		
4	112.6	113.1	112.8	113.6	114.3	
4’	112.7	113.1	112.7	112.5		
5	127.9	128.6	128.1	127.4	127.7	
5’	127.9	128.5	128.0	128.1		
6	159.0	159.5	158.2	158.6	162.0	
6’	159.0	159.5	158.7	158.9		
8	36.5	37.1	34.5	60.3		39.1
8’	41.2	38.6	40.6	38.9	39.5	40.0
9	31.1	31.9	31.3	130.9		33.9
9’	22.0	29.4	126.4	28.8	27.9	30.1
10	28.8	29.2	28.7	137.4		33.5
10’	16.6	21.1	116.1	21.9	22.5	23.1
11	124.5	127.2	126.2	103.5	127.3	
11’	121.4	123.5	122.2	126.7		
13	147.3	147.8	148.3	157.2	147.2	
13’	147.4	147.8	147.4	146.9		
15	111.5	110.3	110.0	66.8	109.5	
15’	120.3	120.3	121.4	113.9		

Unfortunately, we have been unable to obtain a sample nor copies of the original NMR data of the genuine natural product from the Kobayashi lab to compare directly the chromatographic and spectroscopic properties of the synthetic and natural material, and therefore we could not establish the source of this inconsistency at this time. While our own work was in progress, we became aware of a biomimetic total synthesis of nagelamide D (**13**) by the Horne lab (Section 1.4.2).[52] It was significant that both the ^{1}H and ^{13}C NMR data reported in this work matched very well with that obtained by us, **in spite of there being no common intermediates in either of the two routes until the final compound**, indicating that the structural identity of the synthetic material is secure. Our structural assignment was further supported through a X-ray structure determinations on a rearrangement product obtained from diol **73** and a partial reduction product derived **73**. The details of this chemistry and assignment are discussed in section 2.3. Therefore, pending additional information we were required to conclude that either the assigned structure or the reported NMR data were in error, unraveling this structural mystery may require re-isolation and re-characterization of the natural material.

2.2 Approach towards the total synthesis of nagelamide A

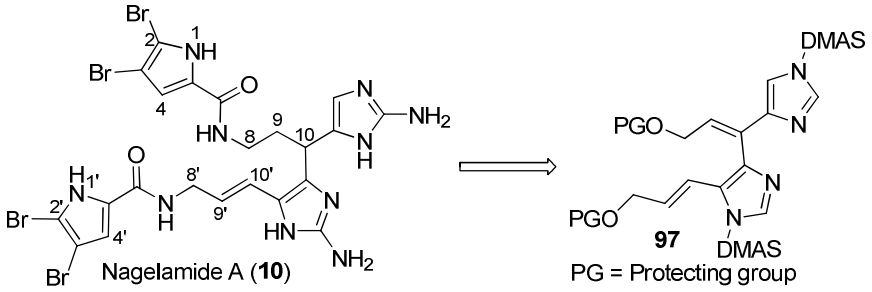
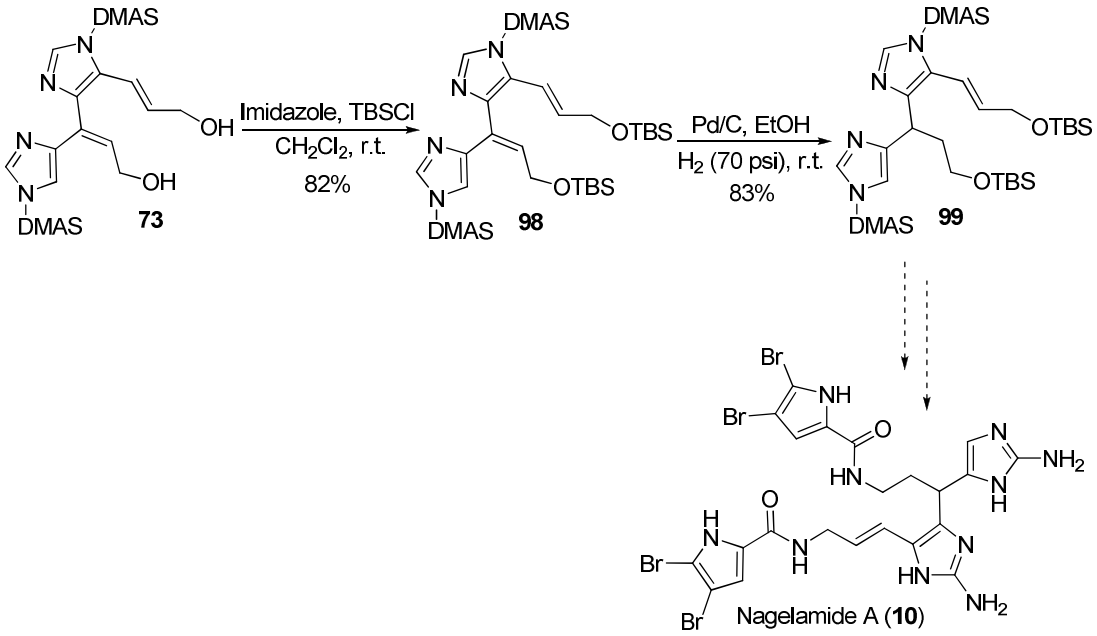


Figure 2-5 Nagelamide A

Nagelamide A (**10**) was identified during the isolation of the first group of this family of alkaloids by Kobayashi and co-workers.[24] The only difference between nagelamide A (**10**) and nagelamide D (**13**) is the oxidation state of one of the three carbon linking moieties, specifically the bond between C9'-C10' is unsaturated (olefin) in the case of nagelamide A (**10**). So in the forward synthetic sense, the trisubstituted olefin in the divinyl intermediate **97**, obtained by the Stille cross-coupling, will be required to undergo chemoselective reduction in the presence of the disubstituted olefin. During the total synthesis of the nagelamide D, as shown in Scheme 2-2, our initial attempts to completely reduce THP-protected bisvinyl imidazole **58** to **71** were unsuccessful. The ^{1}H NMR spectrum of the reduced product was not easy to analyze in the first instance; the suspected product of this reaction was thought to be partially reduced olefin **72** due to the absence of one set of olefinic protons. The complex ^{1}H NMR spectrum was most likely due to the formation of a new chiral center (C10) during the reduction, which in addition to the two intrinsic chiral centers already present in the substrate within the THP groups, results in the possibility of a total of four

possible diastereomers. This is exacerbated due to the presence of three methylene groups in which the germinal protons are diastereotopic and further complicate the spectra. To avoid this problem, the TBS-protected divinyl intermediate **98** was prepared from the diol **73** and subjected to hydrogenation, leading to the required partially reduced olefin **99**. This time ^{1}H NMR spectrum was clean and conclusive in favor of the formation of the intermediate **99** (Scheme 2-10).



Scheme 2-10

To the best of our knowledge this is the first example of hydrogenation reaction in which the trisubstituted olefin is selectively reduced in the presence of disubstituted olefin. Probably the result can be explained in terms of more substituted double bond being more nucleophilic. The precise details behind this observation notwithstanding, in principle nagelamide A (**10**) can be obtained from

the intermediate **99** by relying on the same types of the transformations used in the total synthesis of nagelamide D (**13**).[71]

2.3 Approach towards total synthesis of nagelamide E and Ageliferin

Electrocyclization has a rich history in total synthesis,[88] but there are to date only limited examples in the literature of imidazole derivatives participating in this reaction.[89-95] Perhaps the most pertinent results are those obtained by van Leusen and co-workers[96] who utilized this strategy to prepare benzimidazoles after oxidation of the initial adduct. The divinyl intermediates obtained during the total synthesis of nagelamide D (**13**) or nagelamide C (**12**) with various levels of functionalization and stereochemistry should provide interesting substrates to investigate the hypothesis that the polysubstituted tetrahydrobenzimidazole-type of skeleton found in ageliferin (**5**) and nagelamides E-G (**14**-**16**) can be accessed via a 6π-electrocyclization reaction (Figure 2-6). Subsequent functionalization, either reduction or oxidation would provide access to either the ageliferin/*epi*-ageliferin (nagelamide E-G) system or potential precursors to palau'amine. Whether or not this is the biosynthetic pathway remains to be seen, but it does provide a potentially expedient approach to this framework from a synthetic viewpoint.

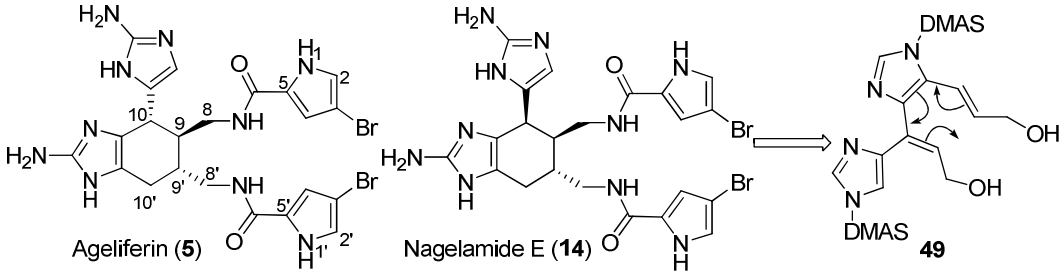
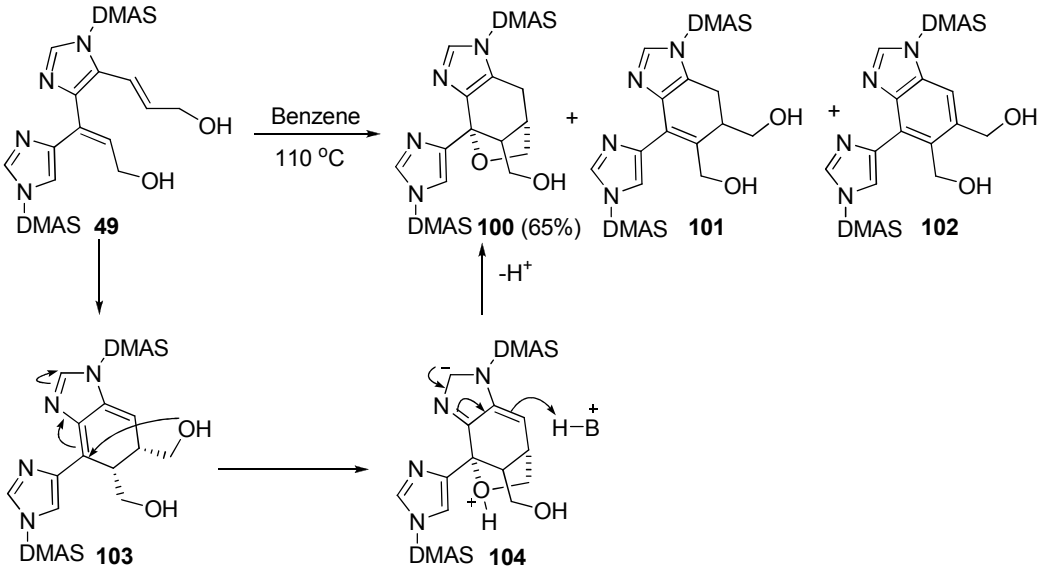


Figure 2-6 Ageliferin and nagelamide E

Specifically the diol **49** obtained during the total synthesis of nagelamide D (**13**) was thought to be a good substrate for initial screening of the electrocyclization reaction. Surprisingly, the divinylimidazole **49** upon heating in toluene at 110 ℃ gave cyclic ether **100**, the structure of which was confirmed by X-ray crystallography (Figure 2-7), as the major product. The product formation can be explained by the attack of an alcohol on tetrasubstituted double bond of the cyclohexadiene **103**, formed by electrocyclization reaction, providing the oxonium intermediate **104**. Proton transfer results in the formation of the ether **100**. In addition to the cyclic ether **100**, other products consistent with expected hexadiene **101** (15%) and benzimidazole **102** (10%) were isolated as impure minor products (Scheme 2-11). In passing, it is worthwhile pointing out that the crystal structure determination provided confirmation of the C10-C15' connectivity of the two vinylimidazole units resulting from the cross-coupling chemistry.



Scheme 2-11

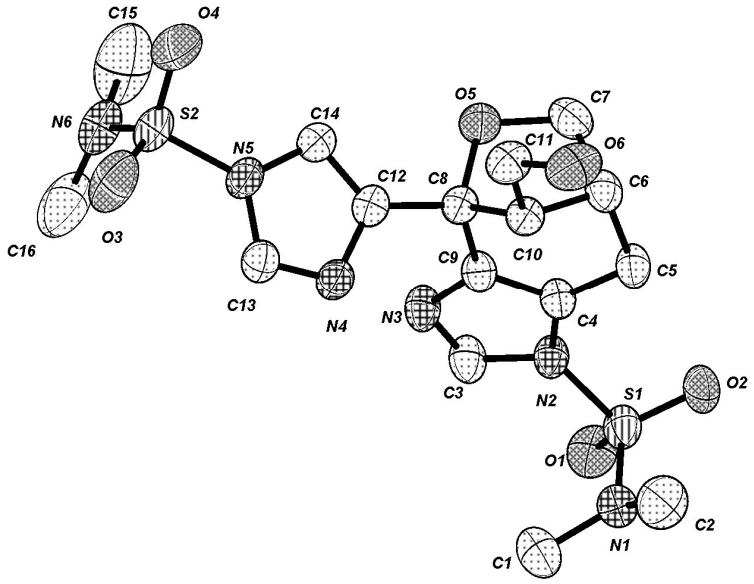
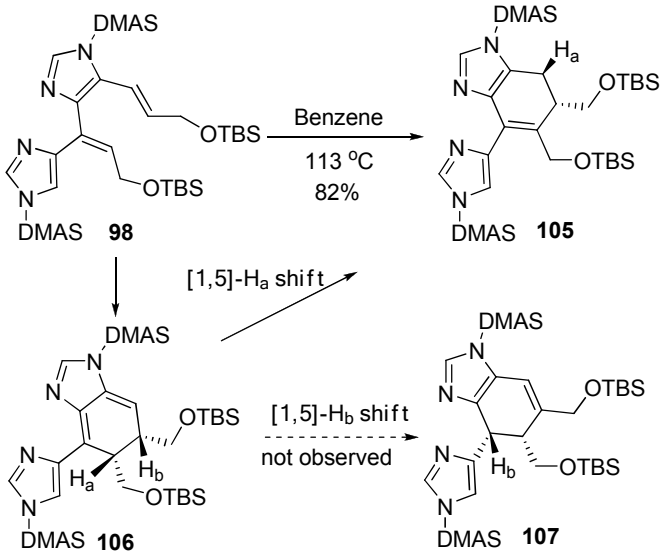


Figure 2-7 X-ray crystal structure of 100

Though the secondary reorganization to form the cyclic ether was disappointing, we were delighted to see initial electrocyclization reaction of divinyl intermediate **49** providing hexadiene **101** which further undergo secondary rearrangement. Since an unexpected post rearrangement reaction occurred due to the presence of the free alcohol, the corresponding TBS-protected divinyl imidazole **98** was

subjected to the electrocyclization reaction. Gratifyingly, we were able to isolate cyclohexene **105** in very good yield (Scheme 2-12).

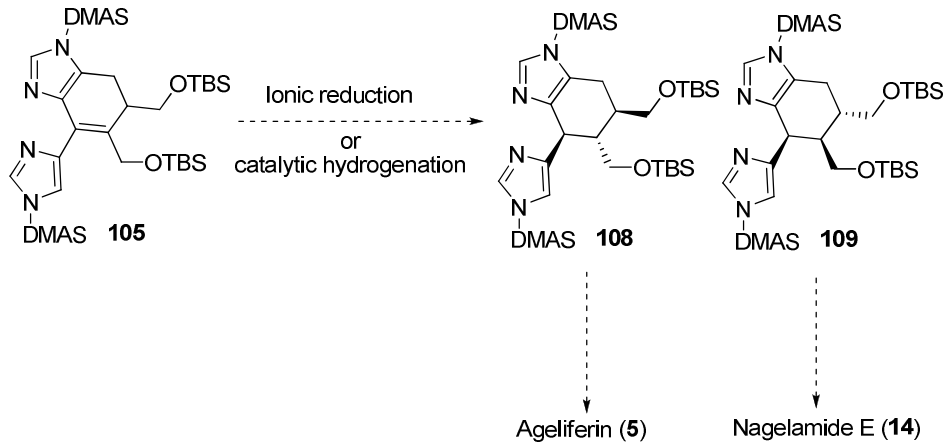
The initial electrocyclization proceeds in a disrotatory fashion providing hexadiene **106**. At this point the initial adduct **106** is relatively unstable, presumably due to the loss of aromaticity in one of the imidazole rings, undergoes a second pericyclic reaction, a suprafacial [1,5]-H shift, to give vinylimidazole **105**. In principle either H_a or H_b can undergo the [1,5]-H shift, but in our case we observed selective H_a shift. The result can be rationalized in favor of migration of H_a as a result of the product containing the more substituted double bond and the most highly conjugated double bond.



Scheme 2-12

The stereoselective reduction of the vinyl intermediate **105** should give the required skeletons for the total synthesis of the nagelamide E (**14**) and ageliferin (**5**). Though either catalytic hydrogenation or ionic reduction (acid and silane

derivatives)[97] can be employed to achieve this purpose, ionic reduction will be explored as the preferred initial choice since the reaction will be conducted under thermodynamic conditions. From a stereoselectivity perspective, the Baran lab has demonstrated that sceptrin (**40**) can be converted into a separable mixture of ageliferin (**5**) and nagelamide E (**14**) under microwave irradiation (Figure 1-5) to provide a 2:1 mixture of **5** and **14**.[38,39,51] Independent submission of either **5** or **14** to the same reaction conditions returned to a 2:1 mixture of the two diastereomers. The latter observation suggests that ageliferin (**5**) is thermodynamically more stable than nagelamide E (**14**), which is no surprise given that in the former derivative all substituents will be disposed pseudoequatorially. Using same argument, the use of ionic reduction involving the use of an acid and silane derivative should give tetrahydrobenzimidazoles **108** and **109**.



Scheme 2-13

Though the formation of intermediate **108** is conceivable under thermodynamic conditions, formation of intermediate **109** is less secure. In that case, catalytic

hydrogenation could be the attractive option. Also it should be noted that this selectivity may be controllable to some extent based on the choice of reducing agent used as Doyle has reported that bulky silanes,[97] e.g., *t*-Bu_3SiH, provide very high levels of cis-decahydronaphthalene in the reduction $\Delta^{9(10)}$–octalin compared to smaller silanes.

Presumably, the end game chemistry developed during the total synthesis of the nagelamide D (**13**)[71] can be applied to complete total synthesis of ageliferin (**5**) and nagelamide E (**14**) starting from the tetrahydrobenzimidazoles **108** and **109** respectively. Ohta and coworkers have taken an intermediate related to **108** (imidazole “protecting groups” were methyls) and converted it into an ageliferin-type of derivative,[98,99] including the installation of the remaining nitrogen through Mitsunobu chemistry (aminomethyls via phthalimides) and lithiation-azidation (2-amino groups); this precedent suggests that we should be able to apply our related methods to complete the total syntheses of ageliferin (**5**) and/or nagelamide E (**14**).

2.4 Approach towards total synthesis of nagelamide C

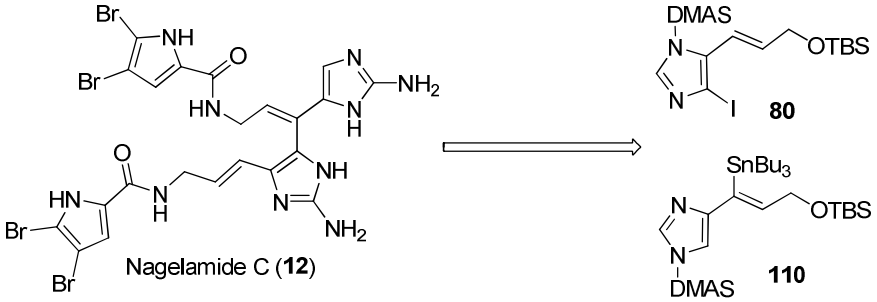
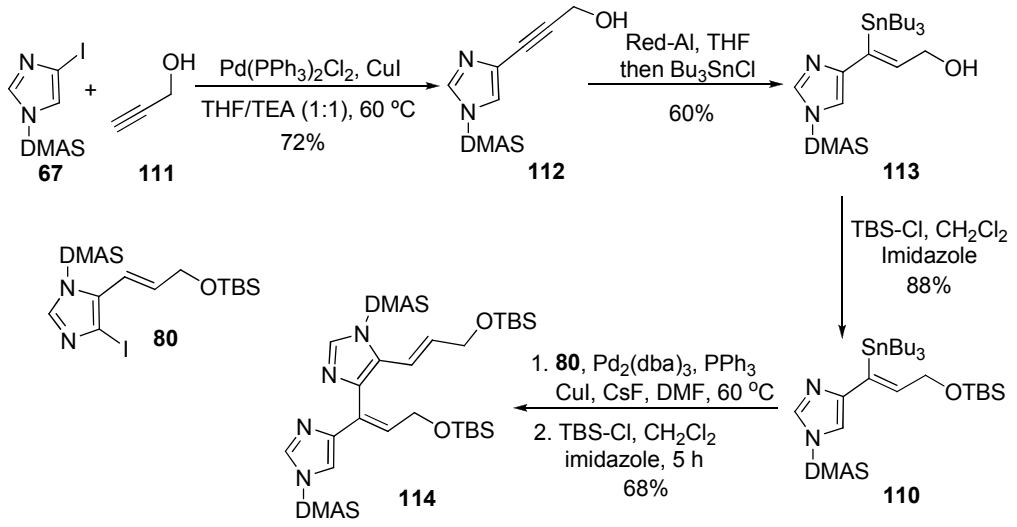


Figure 2-8 Nagelamide C

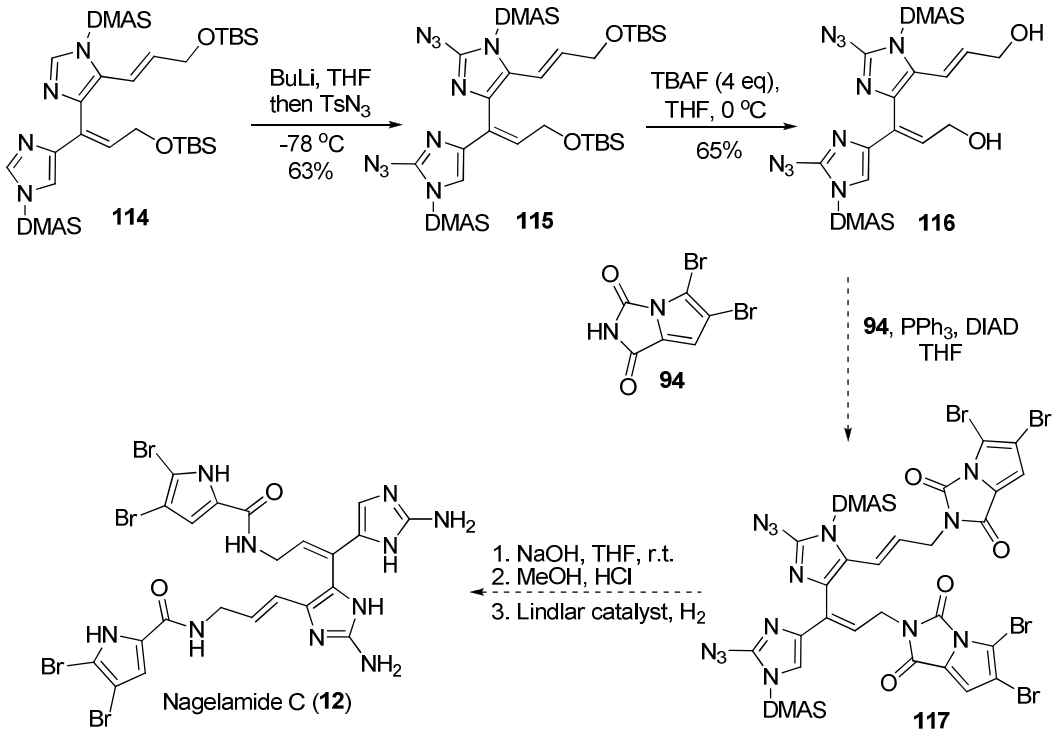
In order to advance the synthesis of nagelamide C (**12**), access to the isomeric *Z*-vinylstannane **110** (Figure 2-8) was required rather than the *E*-isomer **78** that we had already used en route to nagelamide D (**13**), nagelamide A (**10**) and the tetrahydrobenzimidazole family. We eventually discovered that this vinylstannane could be procured via hydroalumination of alkyne **112** with Red-Al, followed by treatment of the vinylalane with Bu_3SnCl in 60% yield (Scheme 2-14).[100,101] Silylation with TBSCl provides the protected vinylstannane **110** ready for Stille cross-coupling with the 4-iodoimidazole **80**. As before, this reaction was conducted under the Baldwin reaction conditions providing the divinylimidazole **114** after treatment with TBSCl to resilylate the partially deprotected diol. While this resilylation is a bit of a nuisance, other protecting groups (THP, MOM) that we have explored are not without flaws (see section 2-1) and so we have continued on with the TBS protecting group.



Scheme 2-14

Accordingly, metalation of **114** at C2 with n-BuLi and treatment with TsN_3 provides the bis azide **115** in modest yield (Scheme 2-15). Initial attempts to deprotect the TBS groups using TBAF (2.5 eq) at room temperature resulted in the formation of some type of rearranged product that we have not identified. Eventually, deprotection of the two silyl ethers was accomplished by treatment with TBAF (4 eq) at 0 °C providing the bis allylic alcohol **116** and this is where our synthesis currently stands. Our plan to complete the synthesis will rely on application of our Mitsunobu chemistry for introduction of the pyrrolecarboxamides (via **117**). Initial attempts to subject diol **116** to a double Mitsunobu reaction with dibromohydantoin **94** were unsuccessful providing product mixtures. The ^{1}H NMR spectra of these materials suggest that S_N2' reactions may be occurring. So reaction conditions will need to be optimized for the formation of the required product **117**. Deprotection of the DMAS-groups and

then reduction with H_2 in the presence of the Lindlar catalyst should provide nagelamide C (**12**).



Scheme 2-15

Thus in summary, by using a dimerization-like approach, we were able to couple two imidazole fragments using a Stille cross-coupling reaction, providing divinyl imidazole intermediate **50** in a convergent fashion. A divergent approach was successfully employed using the divinyl imidazole **50** or related systems for the total synthesis of various nagelamides. Towards this end, the total synthesis of the nominal structure of nagelamide D (**13**) was accomplished and the key structural frameworks of nagelamide A (**10**), C (**12**), E (**14**) and ageliferin (**5**) were also constructed.

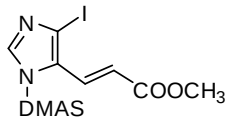
CHAPTER 3

EXPERIMENTAL

3.1 General Considerations

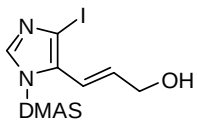
All reagents were purchased from commercial suppliers and were used as received unless otherwise noted. All reactions involving air- or water-sensitive compounds were conducted in oven-dried glassware under an atmosphere of dry argon or nitrogen. A Pure-Solv 400 solvent purification system from Innovative Technology Inc. was also used to obtain THF, CH_2Cl_2 CH_3CN and benzene. Flash chromatography was performed using standard grade silica gel (230-400 mesh) from Sorbent technologies. Melting points were uncorrected. ^{1}H and ^{13}C NMR (δ in ppm) spectra were recorded in $CDCl_3$ (unless otherwise noted) at 500 and 125 MHz, respectively; using a JEOL Eclipse+ 500 spectrometer unless otherwise noted using residual $CHCl_3$ as reference ^{1}H NMR spectra (δ = 7.26 ppm) and the central carbon absorption of $CDCl_3$ (δ = 77.0 ppm) for ^{13}C NMR spectra. Infrared spectra were recorded either as KBr pressed pellets for solids or neat films on NaCl plate for liquids using a Bruker Vector 22 spectrometer or films or solids using Bruker Alpha spectrometer (ATR spectroscopy). High resolution mass spectra (HR-MS) were obtained by Dr. Powell through the mass spectrometry service at the University of Florida, Gainesville, Florida.

(*E*)-Methyl 3-(4-iodo-1-dimethylsulfamoylimidazol-5-yl)-2-propenoate (64):



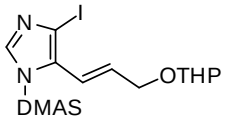
KHDMS (5.73 g, 27.3 mmol) was added portionwise to a solution of trimethyl phosphonate (5.07 g, 27.3 mmol) in dry THF (100 mL), under N_2. The resulting mixture was stirred at r.t. for 1 h followed by dropwise addition of aldehyde **61**[69] (4.50 g, 13.7 mmol) in THF (80 mL). The resulting solution was stirred at r.t. for 2 h and quenched with NH_4Cl (40 mL) solution. The aqueous layer was repeatedly extracted with EtOAc. The combined organic solutions were washed with brine, dried (Na_2SO_4) and concentrated to give crude product which was purified by column chromatography (hexane/EtOAc, 50:50) to give **64** (4.47 g, 85%) as a colorless solid; m.p. 128-131 ℃; ^{1}H NMR (300 MHz): δ = 7.94 (s, 1H), 7.83 (d, *J* = 16.2 Hz, 1H), 6.94 (d, *J* = 16.2 Hz, 1H), 3.79 (s, 3H), 2.89 (s, 6H); ^{13}C NMR (75 MHz): δ = 166.6, 141.4, 129.1, 127.9, 122.1, 90.8, 52.2, 38.2; IR (KBr, cm^{-1}): 3119, 2955, 1717, 1636, 1501, 1443, 1396, 1342, 1253, 1152, 975, 729; HR-ESIMS (m/z): Calcd. for $C_9H_{12}IN_3O_4S$ $[M+H]^+$ 385.9666, found 385.9657.

(*E*)-3-(4-Iodo-1-dimethylsulfamoylimidazol-5-yl)-2-propen-1-ol (65): A solution of DIBAL (1.0 M in hexanes, 28.2 mL, 28.2 mmol) was added dropwise to a solution of ester **64** (4.94 g, 12.8 mmol) in dry CH_2Cl_2 (250 mL) at -78 ℃. The reaction mixture was allowed to warm at 0 ℃ and stirred at same temperature for a further 30 min. The solution was cooled to -78 ℃ before quenching with methanol (14 mL) followe d by water (14 mL). Then



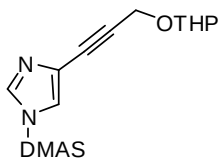
the reaction mixture was warmed to r.t. and stirred for additional 3-5 h. The resulting mixture was filtered through a pad of Celite and the filtrate was concentrated to give the crude product as a solid. The crude material was purified by column chromatography (hexane/EtOAc, 30:70) to give the alcohol as a white solid of **65** (4.26 g, 93%); m.p. 108-110 ℃; ^{1}H NMR (300 MHz): δ = 7.88 (s, 1H), 6.73-6.72 (m, 2H), 4.39 (d, *J* = 2.7 Hz, 2H), 2.88 (s, 6H), 1.89 (brs, 1H); ^{13}C NMR (75 MHz): δ = 139.6, 137.4, 129.9, 115.4, 86.2, 62.7, 38.4; IR (KBr, cm^{-1}): 3459, 3284, 3130, 2853, 1657, 1521, 1459, 1391, 1271, 1149, 1083, 967, 729; HR-ESIMS (m/z): Calcd. for $C_8H_{13}IN_3O_3S$ $[M+H]^+$ 357.9717, found 357.9728.

(*E*)-3-(4-Iodo-1-dimethylsulfamoylimidazol-5-yl)-1-(tetrahydro-2*H*-pyran-2-yloxy)-2-propene (54): Alcohol **65** (2.00 g, 5.6 mmol) and dihydropyran (1.01 mL, 11.2 mmol) were dissolved in dry THF (20 mL). The solution was cooled to 0 ℃ and then *p*-toluenesulfonic acid (0.04 g, 0.2 mmol) was added and stirred at r.t. for 24 h. The reaction mixture was neutralized with half saturated solution of $NaHCO_3$ (20 mL) and aqueous layer was extracted with EtOAc, and the combined organic layers were washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by chromatography (hexane/EtOAc, 50:50) to give **54** (1.97 g, 80%) as an oil; ^{1}H NMR (300 MHz): δ = 7.86 (s, 1H), 6.76 (dt, *J* = 1.3, 15.4 Hz, 1H), 6.66 (dt, *J* = 4.5, 15.4 Hz, 1H), 4.69 (t, *J* = 3.1 Hz, 1H), 4.43 (ddd, *J* = 1.3, 4.5, 15.4



Hz, 1H), 4.19 (ddd, *J* = 1.3, 4.5, 15.4 Hz, 1H), 3.90-3.82 (m, 1H), 3.56-3.49 (m, 1H), 2.87 (s, 6H), 1.85-1.52 (m, 6H); ^{13}C NMR (75 MHz): δ = 139.5, 134.6, 129.9, 116.4, 98.1, 86.3, 66.6, 62.3, 38.3, 30.6, 25.5, 19.4; IR (neat, cm^{-1}): 3125, 2940, 2851, 1453, 1389, 1282, 1178, 1022, 972, 902, 813, 768, 724; HR-ESIMS (m/z): Calcd. for $C_{13}H_{21}IN_3O_4S$ $[M+H]^+$ 442.0292, found 442.0306.

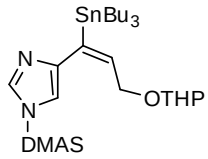
1-(Tetrahydro-2*H*-pyran-2-yloxy)-3-(1-dimethylsulfamoylimidazol-4-yl)-2-propyne (69): 4-Iodoimidazole **67** (5.00 g, 16.6 mmol), THP-protected propargyl alcohol **68** (3.36 g, 24.0 mmol), K_2CO_3 (6.87 g, 49.8 mmol), CuI (158 mg, 0.83 mmol) and $Pd(PPh_3)_2Cl_2$ (291 mg, 0.42 mmol) were placed in a reaction flask. To the above reaction mixture dry THF (100 mL) was added and N_2 was bubbled through it for 3-5 min. The heterogeneous mixture was stirred at 55 ℃ overnight. The reaction mixture was cooled to r.t. and water (40 mL) was added. The layers were separated and the aqueous layer was extracted with EtOAc. The combined organic extracts were dried (Na_2SO_4) and concentrated to give thick brown oil. The crude product was purified by flash chromatography (hexane/EtOAc, 70:30) to give product **19** (3.85 g, 74%) as a pale yellow solid; m.p 91-92 ℃; ^{1}H NMR (300 MHz): δ = 7.78 (d, *J* = 1.4 Hz, 1H), 7.34 (d, *J* = 1.4 Hz, 1H), 4.83 (t, *J* = 3.3 Hz, 1H), 4.43 (ABq, *J* = 5.2 Hz, Δv = 13.8 Hz, 2H), 3.86-3.78 (m, 1H), 3.54-3.47 (m, 1H), 2.83 (s, 6H), 1.81-1.66 (m, 2H), 1.62-1.48 (m, 4H); ^{13}C NMR (75 MHz): δ = 136.5, 125.7,



121.0, 96.9, 87.3, 77.8, 62.1, 54.6, 38.3, 30.3, 25.4, 19.1; IR (neat, cm^{-1}): 3113, 3058, 2957, 2855, 1466, 1391, 1262, 1173, 1023, 956, 820, 727; HR-ESIMS (m/z): Calcd. for $C_{13}H_{20}N_3O_4S$ $[M+H]^+$ 314.1169, found 314.1170; Calcd. for $C_{13}H_{19}N_3O_4SNa$ $[M+Na]^+$ 336.0988, found 336.0993.

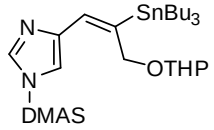
(*E*)-1-(Tetrahydro-2*H*-pyran-2-yloxy)-3-tributylstannyl-3-(1-dimethylsulfamoylimidazol-4-yl)-2-propene (57) and (*E*)-1-(Tetrahydro-2*H*-pyran-2-yloxy)-2-tributylstannyl-3-(1-dimethylsulfamoylimidazol-4-yl)-2-propene (70): A solution of alkyne **69** (1.60 g, 5.1 mmol) and $Pd(PPh_3)_2Cl_2$ (36 mg, 0.05 mmol) in dry THF (40 mL) was ice-cooled and Bu_3SnH (97%, 1.53 mL, 5.6 mmol) was added dropwise. After 45 min (monitored by TLC), the mixture was concentrated and subjected to column chromatography (hexane→hexane/EtOAc, 90:10) providing the two regioisomeric vinylstannanes.

α-isomer 57 (1.79 g, 58%, colorless oil): ^{1}H NMR (300 MHz): δ = 7.80 (d, *J* = 1.0 Hz, 1H), 7.04 (d, *J* = 1.0 Hz, 1H), 6.02 (t, *J* = 5.6 Hz, $^3J_{Sn-H}$ = 63.9 Hz, 1H), 4.64-4.62 (m, 1H), 4.43 (dd, *J* = 5.6, 13.1 Hz, 1H), 4.28 (dd, *J* = 5.6, 13.1 Hz, 1H), 3.90-3.84 (m, 1H), 3.51-3.44 (m, 1H), 2.83 (s, 6H), 1.86-1.69 (m, 2H), 1.61-1.39 (m, 10H), 1.39-1.21 (m, 6H), 1.01-0.93 (m, 6H), 0.88-0.82 (m, 9H); ^{13}C NMR (75 MHz): δ = 144.7, 138.7, 135.7, 113.6, 98.5, 65.8, 62.7, 38.3, 30.9, 29.1, 27.4, 25.5, 19.8, 13.8, 10.6; IR (neat, cm^{-1}): 3125, 2952, 2869, 1460, 1391, 1268, 1174, 1032, 961, 868, 724; HR-ESIMS



(m/z): Calcd. for $C_{25}H_{48}N_3O_4SSn$ $[M+H]^+$ 606.2382, found 606.2382; Calcd. for $C_{25}H_{47}N_3O_4SSnNa$ $[M+Na]^+$ 628.2201, found 628.2197.

.**β-isomer 70** (1.17 g, 38%, white solid): m.p 69-72 ℃; ^{1}H NMR (300 MHz): δ =



7.84 (s, 1H), 7.03 (s, 1H), 6.44 (t, *J* = 2.4 Hz, $^3J_{Sn-H}$ = 63.9 Hz, 1H), 4.85 (dd, *J* = 2.4, 14.5 Hz, 1H), 4.73 (t, *J* = 3.1 Hz, 1H), 4.33 (dd, *J* = 2.4, 14.5 Hz, 1H), 3.87-3.80 (m, 1H), 3.55-3.49 (m, 1H), 2.85 (s, 6H), 1.83-1.68 (m, 2H), 1.66-1.43 (m, 10H), 1.31 (sextet, *J* = 7.2 Hz, 6H), 1.02-0.91 (m, 6H), 0.89-0.85 (m, 9H); ^{13}C NMR (75 MHz): δ = 151.0,141.6, 136.1, 126.4, 115.2, 98.7, 71.7, 61.8, 38.3, 30.6, 29.3, 27.5, 25.5, 19.3, 13.8, 10.7; IR (neat, cm^{-1}): 3100, 2949, 2869, 1465, 1388, 1267, 1173, 1074, 1023, 962, 866, 725; HR-ESIMS (m/z): Calcd. for $C_{25}H_{48}N_3O_4SSn$ $[M+H]^+$ 606.2382, found 606.2382; Calcd. for $C_{25}H_{47}N_3O_4SSnNa$ $[M+Na]^+$ 628.2201, found 628.2203.

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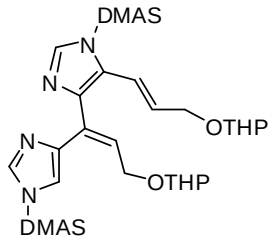
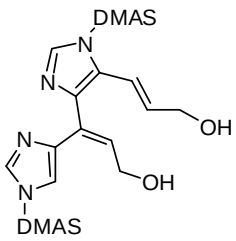
4-((*E*)-1-Dimethylsulfamoyl-4-(3-(tetrahydro-2*H*-pyran-2-yloxy)-2-propenyl)imidazol-4-yl)-1-dimethylsulfamoyl-5-((*E*)-3-(tetrahydro-2*H*-pyran-2-yloxy)-2-propenyl)imidazole (58): N_2 was bubbled through solution of **54**



(3.70 g, 8.39 mmol) and stannane **57** (7.58 g, 12.58 mmol) in dry DMF (150 mL). PPh_3 (440 mg, 1.68 mmol), CuI (319 mg, 1.68 mmol) and $Pd_2(dba)_3$ (383 mg, 0.42 mmol) were added and bubbling of N_2 was continued for additional 2 min. The reaction mixture was heated at 55 ℃ for 3 m in. followed by addition of

CsF (2.55 g, 16.8 mmol) and heating was continued for additional 1 h. Then the DMF was removed by distillation under vaccum. Water (50 mL) and EtOAc (100 mL) were added to the residue, which was stirred vigorously and then the mixture was filtered through bed of Celite. The filtrate was partitioned and the aqueous layer was extracted with EtOAc. The organic extracts were combined, dried (Na_2SO_4), concentrated and the residue was purified by flash chromatography (EtOAc→EtOAc/MeOH, 95:5) to give product **58** (3.95 g, 75%) as a yellowish semi-solid; ^{1}H NMR (300 MHz): δ = 7.91 (s, 1H), 7.84 (d, *J* = 1.4 Hz, 1H), 7.10 (d, *J* = 1.4 Hz, 1H), 6.67 (dt, *J* = 1.9, 16.2 Hz, 1H), 6.25 (t, *J* = 6.2 Hz, 1H), 6.01 (dt, *J* = 5.1, 16.2 Hz, 1H), 4.77-4.69 (m, 2H), 4.61 (dd, *J* = 6.5, 14.5 Hz, 1H), 4.53 (t, *J* = 3.3 Hz, 1H), 4.16 (ddd, *J* = 1.4, 4.8, 14.5 Hz, 1H), 3.94-3.83 (m, 2H), 3.80-3.73 (m, 1H), 3.52-3.43 (m, 2H), 2.87 (s, 6H), 2.84 (s, 6H), 1.84-1.65 (m, 5H), 1.61-1.49 (m, 7H); ^{13}C NMR (75 MHz): δ = 140.7, 140.4, 137.6, 136.1, 134.0, 133.4, 126.5, 126.0, 117.1, 116.5, 98.4, 98.2, 66.8, 65.1, 62.3, 62.2, 38.3, 38.2, 30.8, 30.5, 25.5, 25.4, 19.6, 19.4; IR (neat, cm^{-1}): 3124, 2940, 2867, 1459, 1388, 1265, 1174, 1073, 958, 867, 722; HR-ESIMS (m/z): Calcd. for $C_{26}H_{41}N_6O_8S_2$ $[M+H]^+$ 629.2421, found 629.2411; Calcd. for $C_{26}H_{40}N_6O_8S_2Na$ $[M+Na]^+$ 651.2241, found 651.2234.

4-((*E*)-1-Dimethylsulfamoyl-4-(3-hydroxy-2-propenyl)imidazol-4-yl)-1-dimethylsulfamoyl-5-((*E*)-3-hydroxy-2-propenyl)imidazole (73): The



intermediate **58** (3.80 g, 6.1 mmol) and PTSA•H_2O (2.30 g, 12.1 mmol) were dissolved in MeOH (75 mL) and H_2O (3 mL) and heated to 40 ℃ for 25 minutes. To the above mixture K_2CO_3 (1.67 g, 12.1 mmol) was added and concentrated under vaccum. Water (20 mL) was added to the residue and aqueous layer was repeatedly extracted with EtOAc and combined organic layer was washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by chromatography (EtOAc/MeOH, 85:15) to give **73** (1.91 g, 68%) as a yellowish solid; m.p. 135-139 ℃; ^{1}H NMR (300 MHz): δ = 7.90 (s, 1H), 7.89 (d, *J* = 1.4 Hz 1H), 7.04 (d, *J* = 1.4 Hz 1H), 6.60 (dt, *J* = 1.7, 16.1 Hz, 1H), 6.31 (t, *J* = 6.9 Hz, 1H), 6.02 (dt, *J* = 5.1, 16.1 Hz, 1H), 4.32 (d, *J* = 6.9 Hz, 2H), 4.05 (dd, *J* = 1.7, 5.1 Hz, 2H), 2.91-2.79 (m, 2H), 2.87 (s, 6H), 2.85 (s, 6H); ^{13}C NMR (75 MHz): δ = 140.6, 140.1, 137.6, 137.4, 136.2, 134.8, 128.4, 126.1, 117.2, 115.5, 62.6, 58.4, 38.4, 38.3; IR (KBr, cm^{-1}): 3360, 3136, 2868, 1476, 1420, 1386, 1276, 1180, 1099, 971, 730; HR-ESIMS (m/z): Calcd. for $C_{16}H_{25}N_6O_6S_2$ $[M+H]^+$ 461.1271, found 461.1277; Calcd. for $C_{16}H_{24}N_6O_6S_2Na$ $[M+Na]^+$ 483.1090, found 483.1098.

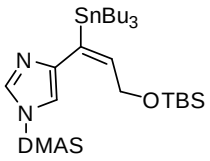
(*E*)-3-(4-Iodo-1-dimethylsulfamoylimidazol-5-yl)-1-(*t*-butyldimethylsilyloxy)-2-propene (80): Alcohol **65** (6.20 g, 17.4 mmol) and imidazole (2.36 g, 34.7 mmol) were dissolved in dry CH_2Cl_2 (100 mL). The solution was cooled to 0 ℃ and then TBSCl (3.41 g, 22.6 mmol) was added and stirred at r.t. for overnight. The reaction mixture was partitioned with water (45 mL), and organic layer was washed with brine, dried (Na_2SO_4) and concentrated. The residue was purified by chromatography (hexane/EtOAc, 70:30) to give **80** (7.61 g, 93%) as a white solid; m.p 58-61 ℃; ^{1}H NMR: δ = 7.86 (s, 1H), 6.76 (dt, *J* = 2.1, 16.0 Hz, 1H), 6.66 (dt, *J* = 3.9, 16.0 Hz, 1H), 4.36 (dd, *J* = 2.1, 3.9 Hz, 2H), 2.86 (s, 6H), 0.93 (s, 9H), 0.09 (s, 6H); ^{13}C NMR: δ = 139.5, 137.3, 130.2, 114.4, 85.9, 62.6, 38.4, 25.9, 18.4, -5.3; IR (KBr, cm^{-1}): 3127, 2951, 2854, 1664, 1462, 1388, 1260, 1181, 1055, 965, 839, 727; HR-ESIMS (m/z): Calcd. for $C_{14}H_{27}IN_3O_3SSi$ $[M+H]^+$ 472.0582, found 472.0592.

1-*t*-Butyldimethylsilyloxy-3-(1-dimethylsulfamoylimidazol-4-yl)-2-propyne (76): 4-Iodoimidazole **67** (5.00 g, 16.6 mmol), TBS-protected propargyl alcohol **75** (4.24 g, 24.9 mmol), K_2CO_3 (4.58 g, 33.2 mmol), CuI (789 mg, 0.42 mmol) and $Pd(PPh_3)_2Cl_2$ (583 mg, 0.83 mmol) were placed in a reaction flask. To the above reaction mixture dry THF (100 mL) was added and N_2 was bubbled through it for 3-5 min. The

heterogeneous mixture was stirred at 55 ℃ overnight. The reaction mixture was cooled to r.t. and water (40 mL) was added, layers were separated. The aqueous layer was extracted with EtOAc. The combined organic extracts were dried (Na_2SO_4) and concentrated to give thick brown oil. The crude product was purified by flash chromatography (hexane/EtOAc, 70:30) to give product **76** (5.69 g, 86%) as a white solid; m.p. 60-63 ℃; ^{1}H NMR: δ = 7.79 (d, *J* = 1.1 Hz, 1H), 7.32 (d, *J* = 1.1 Hz, 1H), 4.49 (s, 2H), 2.84 (s, 6H), 0.89 (s, 9H), 0.12 (s, 6H); ^{13}C NMR (125 MHz): δ = 136.5, 125.9, 120.7, 89.8, 52.1, 38.3, 25.9, 18.4, -5.0; IR (KBr, cm^{-1}): 3137, 2954, 2857, 2239, 1541, 1473, 1380, 1260, 1168, 1065, 979, 842, 745; HR-ESIMS (m/z): Calcd. for $C_{14}H_{26}N_3O_3SSi$ $[M+H]^+$ 344.1458, found 344.1472; Calcd. for $C_{14}H_{25}N_3O_3SSiNa$ $[M+Na]^+$ 366.1278, found 366.1290.

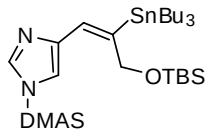
(*E*)-1-*t*-Butyldimethylsilyloxy-3-tributylstannyl-3-(1-dimethylsulfamoylimidazol-4-yl)-2-propene (78) and (*E*)-1-*t*-butyldimethylsilyloxy-2-tributylstannyl-3-(1-dimethylsulfamoylimidazol-4-yl)-2-propene (79): A solution of alkyne **77** (6.00 g, 17.5 mmol) and $Pd(PPh_3)_2Cl_2$ (122 mg, 0.17 mmol) in dry THF (200 mL) was ice-cooled and Bu_3SnH (97%, 5.00 mL, 18.3 mmol) was added dropwise. After 30 min (monitored by TLC), the mixture was concentrated and subjected to column chromatography (hexane→hexane/EtOAc, 90:10) providing the two regioisomeric vinylstannanes.

α-isomer 78 (6.32 g, 57%, colorless oil): ^{1}H NMR: δ = 7.81 (d, *J* = 1.1 Hz, 1H),



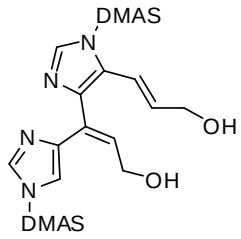
6.95 (d, *J* = 1.1 Hz, 1H), 5.99 (t, *J* = 5.5 Hz, $^{3}J_{Sn-H}$ = 65.5 Hz, 1H), 4.41 (d, *J* = 5.5 Hz, 2H), 2.84 (s, 6H), 1.50-1.43 (m, 6H), 1.29 (sextet, *J* = 7.3 Hz, 6H), 1.01-0.90 (m, 6H), 0.89 (s, 9H), 0.85 (t, *J* = 7.3 Hz, 9H), 0.06 (s, 6H); ^{13}C NMR δ = 144.9, 142.8, 135.8, 135.7, 113.7, 62.2, 38.3, 29.1, 27.4, 25.9, 18.3, 13.8, 10.5, -4.9; IR (neat, cm^{-1}): 2955, 2855, 1465, 1420, 1393, 1255, 1177, 1078, 963, 834, 725; HR-ESIMS (m/z): Calcd. for $C_{26}H_{54}N_3O_3SSiSn$ $[M+H]^+$ 636.2675, found 636.2685.

β-isomer 79 (4.21 g, 38%, pale yellow oil): ^{1}H NMR: δ = 7.84 (d, *J* = 1.1 Hz, 1H),



6.95 (d, *J* = 1.1 Hz, 1H), 6.38 (t, *J* = 2.3 Hz, $^{3}J_{Sn-H}$ = 68.5 Hz, 1H), 4.69 (d, *J* = 2.3 Hz, 2H), 2.86 (s, 6H), 1.55-1.45 (m, 6H), 1.31 (sextet, *J* = 7.3 Hz, 6H), 0.99-0.90 (m, 15H), 0.88 (t, *J* = 7.3 Hz, 9H), 0.09 (s, 6H); ^{13}C NMR δ = 155.6, 141.8, 136.0, 125.1, 115.1, 67.2, 38.3, 29.3, 27.5, 26.3, 18.7, 13.8, 10.7, -5.1; IR (neat, cm^{-1}): 2955, 2855, 1463, 1420, 1394, 1258, 1175, 1075, 964, 855, 726; HR-ESIMS (m/z): Calcd. for $C_{26}H_{54}N_3O_3SSiSn$ $[M+H]^+$ 636.2675, found 636.2641.

4-((*E*)-1-Dimethylsulfamoyl-4-(3-hydroxy-2-propenyl)imidazol-4-yl)-1-dimethylsulfamoyl-5-((*E*)-3-hydroxy-2-propenyl)imidazole (73): N_2 was



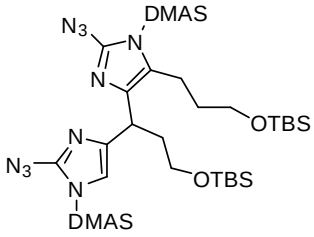
bubbled through solution of **80** (2.43 g, 5.15 mmol) and stannane **78** (4.90 g, 7.73 mmol) in dry DMF (100 mL). PPh_3 (270 mg, 1.03 mmol), CuI (196 mg, 1.03 mmol) and $Pd_2(dba)_3$ (236 mg, 0.26 mmol) were added and bubbling of N_2 was continued for additional 2 min. The reaction mixture was heated at 55 ℃ for 3 min. followed by addition of CsF (1.96 g, 12.9 mmol) and heating was continued for additional 1 h. The reaction mixture was cooled to r.t and a solution of TBAF (1M in THF, 12.87 mL, 12.87 mmol) was added. The reaction was stirred at r.t. for 5 h. Then the DMF was removed by distillation under vaccum. Water (50 mL) and EtOAc (100mL) were added to the residue, which was stirred vigorously and then the mixture was filtered through bed of Celite. The filtrate was partitioned and the aqueous layer was extracted with EtOAc. The organic extracts were combined, dried (Na_2SO_4), concentrated and the residue was purified by flash chromatography (EtOAc→EtOAc/MeOH, 85:15) to give product **73** (1.89 g, 80%) as a yellowish solid.

4-(1-Dimethylsulfamoyl-4-(3-hydroxypropyl)imidazol-4-yl)-1-dimethylsulfamoyl-5-(3-hydroxypropyl)imidazole (74): Diol **73** (1.00 g, 2.17 mmol) and Pd/C (10%, 0.80 g, 0.75 mmol) were taken up in absolute ethanol (100 mL). The mixture was stirred under a hydrogen atmosphere (110 psi) at 34 ℃ for 18 h. Then the reaction mixture was filtered through a pad of Celite, the filtrate was concentrated and the residue was purified by column chromatography (EtOAc/MeOH, 80:20) to give saturated diol **74** (0.89 g, 88%) as a white semi-solid; ^{1}H NMR: δ = 7.87 (s, 1H), 7.80 (s, 1H), 7.15(s, 1H), 4.32 (t, *J* = 7.3 Hz, 1H), 3.67-3.40 (m, 6H), 3.07-2.95 (m, 1H); 2.93-2.78 (m, 1H), 2.88 (s, 6H), 2.84 (s, 6H), 2.29-2.19 (m, 2H), 1.90-1.78 (m, 2H); ^{13}C NMR δ = 145.8, 141.0, 137.8, 135.9, 127.8, 114.5, 59.9, 59.7, 38.3, 38.2, 36.9, 33.1, 32.1, 19.7; IR (neat, cm^{-1}): 3334, 2927, 1477, 1389, 1175, 1087, 965, 729; HR-ESIMS (m/z): Calcd. for $C_{16}H_{29}N_6O_6S_2$ $[M+H]^+$ 465.1585, found 465.1585.

4-(1-Dimethylsulfamoyl-4-(3-*t*-butyldimethylsilyloxypropyl)imidazol-4-yl)-1-dimethylsulfamoyl-5-(3-*t*-butyldimethylsilyloxypropyl)imidazole (81): Diol **74** (860 mg, 1.85 mmol) and imidazole (503 mg, 7.40 mmol) were dissolved in dry CH_2Cl_2 (60 mL). The solution was cooled to 0 ℃ and TBSCl (754 mg, 4.99 mmol) was added to it. The mixture was stirred at r.t. overnight. The reaction mixture was partitioned with water (45 mL), and the organic layer was washed

with brine, dried (Na_2SO_4) and concentrated. The residue was purified by chromatography (hexane/EtOAc, 20:80) to give **81** (1.15 g, 90%) as a thick colorless oil; ^{1}H NMR: δ = 7.86 (s, 1H), 7.78 (s, 1H), 7.00 (s, 1H), 4.14 (dd, *J* = 5.5, 9.1 Hz, 1H), 3.66-3.54 (m, 3H), 3.46-3.37 (m, 1H), 2.90-2.77 (m, 2H), 2.87 (s, 6H), 2.81 (s, 6H), 2.34-2.27 (m, 1H), 2.24-2.17 (m, 1H), 1.84-1.75 (m, 1H), 1.74-1.64 (m, 1H), 0.87 (s, 9H), 0.86 (s, 9H), 0.02 (s, 3H), 0.02 (s, 3H), -0.01 (s, 3H), -0.02(s, 3H); ^{13}C NMR δ = 146.4, 140.5, 137.4, 1361, 128.4, 114.0, 62.6, 60.7, 38.2, 38.1, 37.0, 33.5, 32.7, 26.1, 26.0, 20.6, 18.4, 18.3, -5.2, -5.3; IR (neat, cm^{-1}): 2931, 2855, 1472, 1391, 1255, 1175, 1091, 964, 835, 726; HR-ESIMS (m/z): Calcd. for $C_{28}H_{57}N_6O_6S_2Si_2$ $[M+H]^+$ 693.3314, found 693.3303.

2-Azido-4-(2-azido-1-dimethylsulfamoyl-4-(3-*t*-butyldimethylsilyloxypropyl)imidazol-4-yl)-1-dimethylsulfamoyl-5-(3-*t*-butyldimethylsilyloxypropyl)imidazole (82): n-Butyllithium (2.5 M in hexanes, 2.73 mL, 6.82 mmol) was added to a solution of **81** (1.35 g, 1.95 mmol) in dry THF (150 mL) at -78 ℃. The reaction mixture stirred at same temperature for 1 h before addition of the tosyl azide (1.42 g, 7.22 mmol). The reaction was allowed to warm to r.t. and stirred for an additional 2 h. Finally the reaction was quenched by the addition of sat. NH_4Cl (20 mL). To the above mixture water (10 mL) was added and the aqueous layer was repeatedly extracted with EtOAc. The organic extracts were combined, dried (Na_2SO_4),



concentrated and purified on silica gel (hexane/EtOAc, 75:25) to give diazide **82** (1.07 g, 71%) as a thick reddish oil; ^{1}H NMR: δ = 6.83 (d, *J* = 0.9 Hz, 1H), 3.94 (dd, *J* = 5.5, 9.2 Hz, 1H), 3.62-3.57 (m, 3H), 3.50-3.45 (m, 1H), 2.99 (s, 6H), 2.94 (s, 6H), 2.85-2.73 (m, 2H), 2.23-2.09 (m, 2H), 1.81-1.68 (m, 2H), 0.88 (s, 18H), 0.03 (s, 6H), 0.02 (s, 3H), 0.01 (s, 3H); ^{13}C NMR δ = 142.1, 139.5, 139.2, 136.3, 130.0, 115.5, 62.6, 60.9, 38.5, 38.4, 36.2, 33.7, 32.9, 26.1, 26.0, 21.4, 18.4, 18.3, -5.2, -5.3; IR (neat, cm^{-1}): 2931, 2863, 2145, 1515, 1470, 1393, 1252, 1181, 1098, 973, 836, 726; HR-ESIMS (m/z): Calcd. for $C_{28}H_{55}N_{12}O_6S_2Si_2$ $[M+H]^+$ 775.3342, found 775.3351.

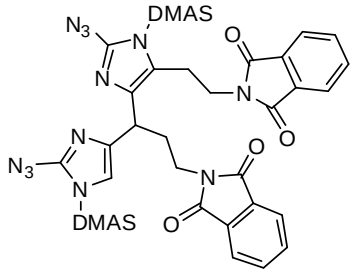
2-Azido-4-(2-azido-1-dimethylsulfamoyl-4-(3-hydroxypropyl)imidazol-4-yl)-1-dimethylsulfamoyl-5-(3-hydroxypropyl)imidazole (83): TBAF (1 M in THF, 3.26 mL, 3.26 mmol) was added dropwise to ice cooled solution of diazide **82** (1.20 g, 1.55 mmol) in dry THF (80 mL). Then the solution was stirred at r.t. for 4-6 h until the reaction goes to completion. Then the solvent was removed under vacuum and the resulting residue was purified by the column chromatography (EtOAc/MeOH, 98:2) to give diol **83** (660 mg, 78%) as a brown semi-solid; ^{1}H NMR: δ = 6.92 (s, 1H), 4.11 (t, *J* = 7.3 Hz, 1H), 3.65-3.61 (m, 1H), 3.58-3.45 (m, 3H), 3.01-2.86 (m, 4H), 2.98 (s, 6H), 2.95 (s, 6H), 2.18-2.11 (m, 2H), 1.86-1.78 (m, 2H); ^{13}C NMR δ = 141.4, 140.1, 139.5, 136.9, 129.2, 115.8, 60.0, 59.8, 38.5, 35.8, 32.9, 32.1, 20.6; IR (KBr, cm^{-1}): 3400, 2856, 2146, 1509,

1392, 1178, 990, 727; HR-ESIMS (*m/z*): Calcd. for $C_{16}H_{27}N_{12}O_6S_2$ $[M+H]^+$ 547.1612, found 547.1620; Calcd. for $C_{16}H_{26}N_{12}O_6S_2Na$ $[M+Na]^+$ 569.1432, found 569.1436.

2-Azido-4-(2-azido-1-dimethylsulfamoyl-4-(3-azidopropyl)imidazol-4-yl)-1-dimethylsulfamoyl-5-(3-azidopropyl)imidazole (85): The alcohol **83** (144 mg, 0.26 mmol) was dissolved in dry THF (8 mL) and cooled to 0 ℃. To above solution, diphenyl phosphoryl azide (97%, 0.13 mL, 0.59 mmol) followed by DBU (98%, 0.09 mL, 0.59 mmol) was added dropwise. The solution was then warmed to room temperature and stirred for 2 h. Tetrabutylammonium azide solution (148 mg, 0.52 mmol) in THF (1 mL) was added to the above solution and the resulting mixture was heated at 50 ℃ for 12 h. The solution was quenched with NH_4Cl at room temperature and the aqueous solution was repeatedly extracted with EtOAc. The organic extracts were combined, dried (Na_2SO_4), concentrated and purified on silica gel (hexane/EtOAc, 70:30) to give tetraazide **85** (88 mg, 57%) as a reddish oil; ^{1}H NMR: δ = 6.85 (s, 1H), 3.89 (dd, *J* = 6.3, 8.7 Hz, 1H), 3.36-3.29 (m, 3H), 3.21-3.15 (m, 1H), 3.01 (s, 6H), 2.95 (s, 6H), 2.91-2.84 (m, 1H), 2.81-2.75 (m, 1H), 2.26-2.21 (m, 2H), 1.87-1.82 (m, 2H); ^{13}C NMR δ = 141.0, 140.2, 139.6, 136.0, 128.9, 115.6, 50.7, 49.5, 38.6, 38.5, 34.0, 32.2, 29.4, 21.9; IR (neat, cm^{-1}): 2935, 2871, 2141, 2092, 1511, 1387, 1260, 1174, 1076, 971,

725; HR-ESIMS (*m/z*): Calcd. for $C_{16}H_{25}N_{18}O_4S_2$ $[M+H]^+$ 594.1742, found 594.1727; Calcd. for $C_{16}H_{24}N_{18}O_4S_2Na$ $[M+Na]^+$ 619.1562, found 619.1546.

2-Azido-4-(2-azido-1-dimethylsulfamoyl-4-(3-phthalimidoylpropyl)imidazol-4-yl)-1-dimethylsulfamoyl-5-(3-phthalimidoylpropyl)imidazole (89): In a



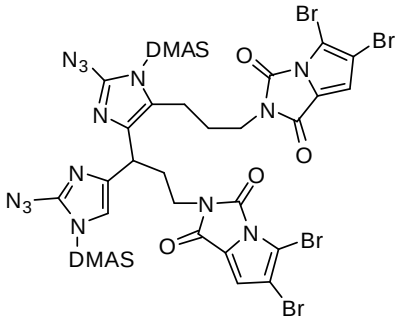
round bottom flask containing phthalimide (100 mg, 0.686 mmol), triphenylphosphine (180 mg, 0.686 mmol), were dissolved in dry THF (4 mL) under an N_2 atmosphere. The reaction mixture was cooled to 0 ºC and DIAD (0.140 mL, 0.686 mmol) was added dropwise. After 20 min, diol **83** (75.0 mg, 0.137 mmol) dissolved in THF (1 mL) was added to the reaction mixture dropwise. The reaction mixture was stirred for overnight and then concentrated. The crude product was purified by chromatography (hexane/EtOAc, 40:60) to provide **89** (88 mg, 80%) as a yellow semi-solid; ^{1}H NMR: δ = 7.81-7.79 (m, 4H), 7.69-7.67 (m, 4H), 6.82 (s, 1H), 3.76 (t, *J* = 7.4 Hz, 1H), 3.71-3.66 (m, 4H), 2.96 (s, 6H), 2.94 (s, 6H), 2.88-2.82 (m, 1H), 2.74-2.68 (m, 1H), 2.41-2.37 (m, 2H), 1.95-1.89 (m, 2H); ^{13}C NMR δ = 168.4, 168.1, 141.2, 139.9, 139.4, 135.9, 133.9, 133.8, 132.2, 132.1, 129.1, 123.2, 123.1, 115.5, 38.5, 37.7, 36.4, 35.0, 31.5, 29.3, 22.5; IR (KBr, cm^{-1}): 2978, 2936, 2142, 1770, 1705, 1510, 1391, 1172, 1078, 968, 866, 718.

4,5-Dibromopyrrole-*N*-ethoxycarbonyl-2-carboxamide (93): This and the following procedure are taken from the Ph.D. dissertation of R.M. Spoering.[83] Bromine (3.0 mL, 59 mmol) in acetic acid (25 mL) was added dropwise to a solution of pyrrole-*N*-ethoxycarbonyl-2-carboxamide **92** (5.00 g, 27.4 mmol) in acetic acid (100 mL) over a 10 min period and then stirred for an additional 2 h. The resulting mixture was filtered and washed with cold CH_2Cl_2 to give product **93** (6.4 g, 69%) as gray solids which were used directly in the next step. ^{1}H NMR (300 MHz, DMSO-d_6): δ = 10.57 (s, 1H), 7.27 (s, 1H), 4.12 (q, *J* = 7.1 Hz, 2H), 1.22 (t, *J* = 7.1 Hz, 2H); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 157.1, 151.7, 127.1, 116.6, 108.8, 99.1, 61.5, 14.7; ESIMS (m/z, -ve mode): Calcd. for $C_8H_7Br_2N_2O_3$ $[M-H]^-$ 338.88, found 338.80.

4,5-Dibromopyrrole-1,2-dicarboximide (94): Dibromopyrrole **93** (4.0 g, 11.76 mmol) was mixed with silicone oil (4.0 mL) and heated in an oil bath to 180-185 ℃ at 30-40 mmHg. After 3 h, the re sidue was cooled, hexanes were added and solids were filtered and repeatedly washed with hexanes to give gray colored solids (3.5 g). The above procedure was repeated with resulting solids in silicone oil (3.5 mL) to give 3.0 g of crude product. The crude product was taken into 300 mL of diethyl ether and heated to reflux for 30 h. Then the mixture was filtered. The filtrate was concentrated until ~25% of the solvent was removed and the resulting mixture was filtered to give pale yellowish

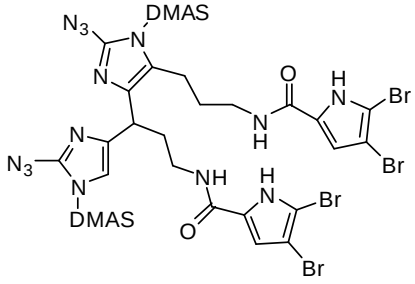
solid as a product (1.38 g, 40%). ^{1}H NMR (500 MHz, DMSO-d_6): δ = 11.73 (s, 1H), 7.15 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ = 157.5, 147.1, 127.1, 113.4, 107.4, 102.9; ESIMS (m/z, -ve mode): Calcd. for $C_6HBr_2N_2O_2$ $[M-H]^-$ 292.84, found 292.93.

2-Azido-4-(2-azido-1-dimethylsulfamoyl-4-(3-(5,6-dibromo-1,3-dioxo-1H-pyrrolo[1,2-c]imidazol-2(3H)-yl)propyl)imidazol-4-yl)-1-dimethylsulfamoyl-5-(3-(5,6-dibromo-1,3-dioxo-1H-pyrrolo[1,2-c]imidazol-2(3H)-yl)propyl)imidazole (95): Diisopropyl diazodicarboxylate (0.42 mL, 2.04 mmol) was added dropwise to the solution of PPh_3 (534 mg, 2.04 mmol) and dibromohydantoin **94** (599 mg, 2.04 mmol) in dry THF (25 mL) at 0 ℃ and stirred for 15 min. The solution of diol **83** (370 mg, 0.68 mmol) in dry THF (5 mL) was added dropwise. Then the mixture was warmed to r.t. and stirred for 3 h, concentrated and purified by flash chromatography (hexane/EtOAc, 60:40) to give product **95** (600 mg, 80%) as a brown solid; ^{1}H NMR: δ = 6.82-6.75 (m, 3H), 3.79 (dd, *J* = 5.9, 9.2 Hz, 1H), 3.68-3.59 (m, 4H), 2.98 (s, 6H), 2.95 (s, 6H), 2.85-2.65 (m, 2H), 2.48-2.33 (m, 2H), 1.95-1.88 (m, 2H); ^{13}C NMR: δ = 156.6, 156.3, 147.2, 146.9, 140.9, 140.0, 139.6, 135.7, 128.8, 126.0, 125.8, 115.6, 1125.3, 115.2, 108.9, 108.8, 104.4, 104.3, 39.0, 38.6, 38.5, 37.8, 34.9, 31.0, 29.8, 28.9, 22.3; IR (KBr, cm^{-1}): 3136, 2941, 2146, 1803, 1738, 1514, 1425, 1390, 1266, 1177, 974, 727; HR-

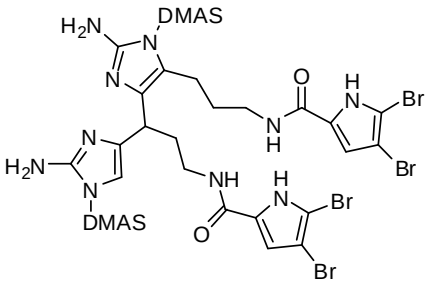


ESIMS (m/z): Calcd. for $C_{28}H_{27}Br_4N_{16}O_8S_2$ $[M+H]^+$ 1098.8329, found 1098.8327; Calcd. for $C_{28}H_{26}Br_4N_{16}O_8S_2Na$ $[M+Na]^+$ 1120.8148, found 1120.8157.

2-Azido-4-(2-azido-1-dimethylsulfamoyl-4-(3-(4,5-dibromo-1H-pyrrole-2-carboxamido)propyl)imidazol-4-yl)-1-dimethylsulfamoyl-5-(3-(4,5-dibromo-1H-pyrrole-2-carboxamido)propyl)imidazole (91): 2% NaOH (6.5 mL, 3.3 mmol) solution was added to the solution bis hydantoin **95** (600 mg, 0.55 mmol) in THF (20 mL) and mixture was stirred at r.t. until reaction goes to completion (3-5 h). Then the mixture was neutralized with 10% citric acid and the aqueous layer was extracted with EtOAc. The organic layers were concentrated, dried (Na_2SO_4) and purified by column chromatography (hexane/EtOAc, 20:80) to give product **91** (449 mg, 78%) as a brown solid; ^{1}H NMR: δ = 11.59 (brs, 1H), 11.41 (brs, 1H), 6.87 (s, 1H), 6.77 (brt, *J* = 4.6 Hz, 1H), 6.59-6.49 (m, 3H), 3.87 (dd, *J* = 5.9, 8.2 Hz, 1H), 3.49-3.33 (m, 4H), 2.96 (s, 6H), 2.95 (s, 6H), 2.81-2.75 (m, 2H), 2.37-2.20 (m, 2H), 1.92-1.83 (m, 2H); ^{13}C NMR δ = 160.1, 160.0, 141.1, 140.1, 139.7, 136.3, 129.3, 127.1, 127.0, 115.8, 112.4, 106.1, 105.9, 99.5, 99.4, 39.1, 38.6, 38.5, 38.2, 34.9, 32.5, 29.2, 22.1; IR (KBr, cm^{-1}): 3419, 3154, 2938, 2145, 1636, 1563, 1517, 1392, 1179, 976, 728; HR-ESIMS (m/z): Calcd. for $C_{26}H_{31}Br_4N_{16}O_6S_2$ $[M+H]^+$ 1046.8743, found 1046.8713; Calcd. for $C_{26}H_{30}Br_4N_{16}O_6S_2Na$ $[M+Na]^+$ 1068.8562, found 1068.8529.

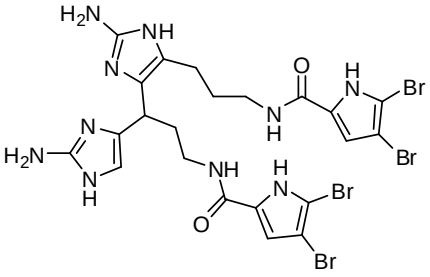


2-Amino-4-(2-amino-1-dimethylsulfamoyl-4-(3-(4,5-dibromo-1H-pyrrole-2-carboxamido)propyl)imidazol-4-yl)-1-dimethylsulfamoyl-5-(3-(4,5-dibromo-1H-pyrrole-2-carboxamido)propyl)imidazole (88): A solution of diazide **91**



(70.0 mg, 0.07 mmol) in dry MeOH (2.5 mL) was cooled to 0 ℃ and added $NaBH_4$ (50.8 mg, 1.34 mmol) in portions. Then reaction mixture was warmed to r.t. and stirred for 6 h. The reaction mixture was quenched with H_2O (0.5 mL) and crude product was preabsorbed on silica gel. The product was purified by chromatography (EtOAc→EtOAc/MeOH/NH_3, 90:9:1) providing diamine derivative **88** (40 mg, 57%) as a yellow solid; m.p degradation at 169-174 ℃; ^{1}H NMR (MeOH-d_4): δ = 6.77 (s, 1H), 6.70 (s, 1H), 6.55 (s, 1H), 3.68 (dd, *J* = 5.7, 9.1 Hz, 1H), 3.26-3.15 (m, 4H), 2.84 (s, 12H), 2.74-2.62 (m, 2H), 2.24-2.17 (m, 1H), 2.12-2.05 (m, 1H), 1.77-1.72 (m, 2H); ^{13}C NMR (MeOH-d_4): δ = 160.3, 160.2, 150.3, 149.0, 139.8, 134.5, 127.7, 127.6, 122.5, 112.8, 112.7, 108.9, 104.6, 104.5, 98.6, 98.5, 48.5, 38.5, 37.6, 37.3, 33.8, 31.8, 29.9, 21.9; IR (neat, cm^{-1}): 3371, 3256, 3115, 2926, 1613, 1558, 1413, 1236, 1169, 1051, 963, 722; HR-ESIMS (m/z): Calcd. for $C_{26}H_{35}Br_4N_{12}O_6S_2$ $[M+H]^+$ 990.8971, found 990.8974; Calcd. for $C_{26}H_{34}Br_4N_{12}O_6S_2Na$ $[M+Na]^+$ 1012.8791, found 1012.8792.

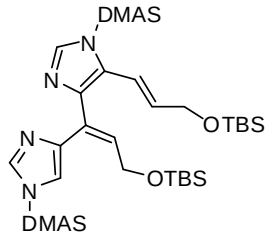
Nagelamide D (13): Conc. HCl (0.02 mL) was added to the solution of diazide **91**



(90 mg, 0.086 mmol) in methanol (2.5 mL) and stirred at 33 ℃ for 25 h. Then the mixture was concentrated under vacuum and the residue was neutralized with $NaHCO_3$ solution and extracted with EtOAc. The organic layers were combined, concentrate and purified by column chromatography (EtOAc/methanol/NH_3, 94:5:1) to give the DMAS-deprotected product (48 mg, 67%) as a brown solid. This material was subjected to azide reduction by dissolving it in methanol (2.5 mL) in presence of Lindlar catalyst (25 mg) and stirring it at r.t. under 1 atm H_2 (balloon) overnight. The reaction mixture was filtered through a pad of Celite and the filtrate was concentrated. The residue was purified on silica gel (CH_2Cl_2/MeOH/NH_3, 80:19:1 → CH_2Cl_2/MeOH/NH_3, 60:38:2) by preabsorbing it on silica to give nagelamide D (**13**) (23 mg, 51%) as a brown solid. Finally the free base was converted to its TFA salt by dissolving it in methanol, adding few drops of trifluoroacetic acid and concentrating under vacuum to give **13**•2TFA (28 mg); ^{1}H NMR (DMSO-d_6): δ = 12.66 (d, *J* = 2.7 Hz, 1H), 12.65 (d, *J* = 2.2 Hz, 1H), 12.24 (s, 1H), 12.17 (s, 1H), 12.14 (s, 1H), 12.06 (s, 1H), 8.19-8.14 (m, 2H), 7.47 (s, 2H), 7.41 (s, 2H), 6.92 (d, *J* = 2.7 Hz, 1H), 6.89 (d, *J* = 2.7 Hz, 1H), 6.75 (s, 1H), 3.99 (t, *J* = 7.7 Hz, 1H), 3.24-3.05 (m, 4H), 2.47-2.38 (m, 2H), 2.19-2.12 (m, 1H), 1.98-1.91 (m, 1H), 1.73-1.63 (m, 2H); ^{13}C NMR (DMSO-d_6, 75 MHz): δ = 159.5 (2C), 147.8, 147.4, 128.6, 128.5, 127.2, 123.5, 120.3, 113.1 (2C), 110.3,

105.2, 105.1, 98.4 (2C), 38.6, 37.1, 31.9, 29.4, 29.2, 21.1; IR (KBr, cm^{-1}): 3305, 3171, 1687, 1628, 1567, 1526, 1428, 1325, 1202, 1138, 978; HR-ESIMS (m/z): Calcd. for $C_{22}H_{25}Br_4N_{10}O_2^+$ 776.8890, found 776.8873.

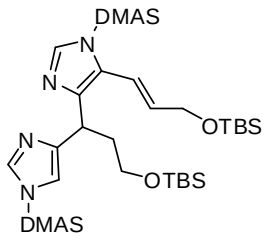
4-((*E*)-1-Dimethylsulfamoyl-4-(3-(*t*-butyldimethylsilyloxy)-2-propenyl)imidazol-4-yl)-1-dimethylsulfamoyl-5-((*E*)-3-(*t*-butyldimethylsilyloxy)-2-propenyl)imidazole (98): In a round bottom flask



compound **73** (1.65 g, 3.58 mmol) was dissolved in CH_2Cl_2 (50 mL) under a nitrogen atmosphere. The solution was cooled to 0 ºC and then to the reaction mixture imidazole (973 mg, 14.3 mmol) and TBSCl (1.35 g, 8.95 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 CH_2Cl_2, then the combined organic solutions were dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by chromatography providing **98** (2.02 g, 82%) as a white solid; m.p 84-87 ℃; ^{1}H NMR: δ = 7.89 (s, 1H), 7.82 (d, *J* = 1.1 Hz 1H), 7.03 (d, *J* = 1.1 Hz 1H), 6.68 (dt, *J* = 2.3, 15.7 Hz, 1H), 6.13 (t, *J* = 6.0 Hz, 1H), 6.02 (dt, *J* = 3.8, 15.7 Hz, 1H), 4.72 (d, *J* = 6.0 Hz, 2H), 4.05 (dd, *J* = 2.3, 3.8 Hz, 2H), 2.86 (s, 6H), 2.81 (s, 6H), 0.88 (s, 9H), 0.86 (s, 9H), 0.05 (s, 6H), 0.00 (6H); ^{13}C NMR: δ = 140.9, 140.3, 137.4, 136.7, 136.5, 135.9, 126.3, 124.8, 116.9, 114.3, 62.8, 61.3, 38.3, 38.2, 26.0, 25.9, 18.4, 18.3, -4.9, -5.4; IR (neat, cm^{-1}): 3124, 2928, 2856, 471, 1384, 1252, 1176, 1074, 955,

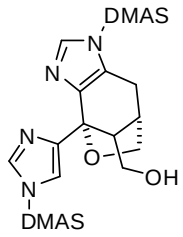
834, 775, 725; HR-ESIMS (m/z): Calcd. for $C_{28}H_{53}N_6O_6S_2Si_2$ $[M+H]^+$ 689.3001, found 689.3014; Calcd. for $C_{28}H_{52}N_6O_6S_2Si_2Na$ $[M+Na]^+$ 711.2820, found 711.2837.

4-(1-Dimethylsulfamoyl-4-(3-(*t*-butyldimethylsilyloxy)propyl)imidazol-4-yl)-1-dimethylsulfamoyl-5-((*E*)-3-(*t*-butyldimethylsilyloxy)-2-propenyl)imidazole (99): A divinyl intermediate **98** (1.00 g, 1.45 mmol) and Pd/C (10%, 0.30 g, 0.28 mmol) were taken up in absolute ethanol (40 mL). The mixture was stirred under a hydrogen atmosphere (70 psi) at r.t. for overnight. Then the reaction mixture was filtered through a pad of Celite, the filtrate was concentrated and the residue was purified by column chromatography (EtOAc/MeOH, 95:5) to give vinyl intermediate **99** (832 mg, 83%) as a white solid; m.p 78-81 ℃; ^{1}H NMR: δ = 7.86 (s, 1H), 7.77 (d, *J* = 1.7 Hz 1H), 6.98 (s, 1H), 6.77 (dt, *J* = 2.3, 16.0 Hz, 1H), 6.28 (dt, *J* = 4.0, 16.0 Hz, 1H), 4.31-4.28 (m, 3H), 3.59-3.55 (m, 1H), 3.45-3.40 (m, 1H), 2.83 (s, 6H), 2.81 (s, 6H), 2.29-2.25 (m, 2H), 0.90 (s, 9H), 0.84 (s, 9H), 0.07 (s, 6H), -0.03 (s, 3H), -0.04 (s, 3H); ^{13}C NMR: δ = 146.7, 141.3, 137.8, 136.0, 135.8, 126.4, 115.3, 114.1, 62.9, 60.6, 38.3, 37.3, 33.3, 26.0, 25.9, 18.4, 18.3, -5.2, -5.3; IR (neat, cm^{-1}): 3119, 298, 2857, 1471, 1381, 1248, 1173, 1049, 962, 830, 723; HR-ESIMS (m/z): Calcd. for $C_{28}H_{55}N_6O_6S_2Si_2$ $[M+H]^+$ 691.3158,

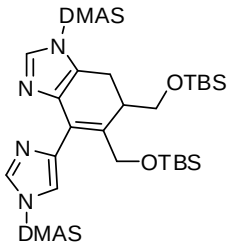


found 691.3166; Calcd. for $C_{28}H_{54}N_6O_6S_2Si_2Na$ $[M+Na]^+$ 713.2977, found 713.2992.

5-Dimethylsulfamoyl-1-(1-dimethylulfamoylimidazol-4-yl)-11-hydroxymethyl-10-oxa-3,5-diazatricyclo[6.2.1.02,6]undeca-2(6),3-diene (100): N_2 was bubbled through solution of a divinyl imidazole **49** (100 mg, 0.22 mmol) in dry benzene (10 mL) for 3-4 min. Then the reaction mixture was stirred at 110 ºC for 1.5 h. The solution was allowed to cool to r.t. The precipitated solids were filtered and washed with ether providing ether **100** (65 mg, 65%) as white solid. The filtrate contained byproducts **101** and **102**, which turned out to be difficult to purify by chromatography; m.p 203-205 ℃ ^{1}H NMR: δ = 7.95 (d, *J* = 1.1 Hz, 1H), 7.72 (s, 1H), 7.70 (d, *J* = 1.1 Hz, 1H), 4.30 (t, *J* = 6.8 Hz, 1H), 3.65-3.61 (m, 2H), 3.51-3.46 (m, 1H), 3.17-3.13 (m, 1H), 2.98-2.94 (m, 2H), 2.92-2.85 (m, 1H), 2.90 (s, 6H), 2.89 (s, 6H), 2.63 (t, *J* = 5.4 Hz, 1H); ^{13}C NMR: δ = 143.6, 139.9, 136.7, 136.4, 125.9, 117.6, 80.8, 71.9, 62.5, 53.6, 39.2, 384, 38.2, 31.7; IR (neat, cm^{-1}): 3298, 2962, 2845, 1470, 1388, 1271, 1173, 1140, 1047, 958, 876, 721; HR-ESIMS (m/z): Calcd. for $C_{16}H_{25}N_6O_6S_2$ $[M+H]^+$ 461.1272, found 461.1268; Calcd. for $C_{16}H_{24}N_6O_6S_2Na$ $[M+Na]^+$ 483.1091, found 483.1104.

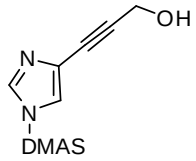


5,6-Bis((*t*-butyldimethylsilyloxy)methyl)-4-(1-dimethylsulfamoyl-1H-imidazol-4-yl)-1-dimethylsulfamoyl-6,7-dihydro-1H-benz[d]imidazole (105):



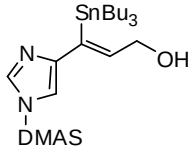
N_2 was bubbled through solution of a divinyl imidazole **98** (100 mg, 0.15 mmol) in dry benzene (10 mL) for 3-4 min. Then the reaction mixture was stirred at 110 ºC for overnight. The solution was concentrated and the residue was purified by column chromatography (EtOAc) to obtain compound **105** (82 mg, 82%) as a colorless liquid; ^{1}H NMR: δ = 7.92 (d, *J* = 1.3 Hz, 1H), 7.76 (s, 1H); 7.69 (d, *J* = 1.3 Hz, 1H), 4.78 (d, *J* = 12.8 Hz, 1H), 4.40 (d, *J* = 12.8 Hz, 1H), 3.68 (dd, *J* = 4.3, 10.1 Hz, 1H), 3.55 (d, *J* = 17.1 Hz, 1H), 3.35 (t, *J* = 10.1 Hz, 1H), 3.12-3.07 (m, 1H), 2.92-2.83 (m, 1H), 2.89 (s, 6H), 2.88 (s, 6H), 0.88 (s, 9H), 0.85 (s, 9H), 0.03 (s, 3H), 0.02 (s, 3H), 0.01 (s, 3H), -0.01 (s, 3H); ^{13}C NMR: δ = 137.8, 137.6, 136.3, 135.6, 134.7, 124.7, 122.8, 118.1, 62.3, 61.4, 39.7, 38.4, 38.2, 26.0, 25.9, 21.2, 18.3, -5.0, -5.1, -5.2, -5.3; IR (neat, cm^{-1}): 3130, 2953, 2855, 1462, 1390, 1252, 1174, 1079, 963, 832, 722; HR-ESIMS (m/z): Calcd. for $C_{28}H_{53}N_6O_6S_2Si_2$ $[M+H]^+$ 689.3001, found 689.2994; Calcd. for $C_{28}H_{52}N_6O_6S_2Si_2Na$ $[M+Na]^+$ 711.2820, found 711.2841.

3-(1-dimethylsulfamoylimidazole-4-yl)-1-hydroxy-2-propyne (112):



N_2 was bubbled through solution of 4-iodoimidazole **67** (8.00 g, 26.4 mmol), distilled propargyl alcohol (2.22 g, 39.6 mmol), $Pd(PPh_3)_2Cl_2$ (463 mg, 0.66 mmol), CuI (251 mg, 1.32 mmol) in THF/TEA (120 mL/120 mL). The reaction mixture was heated at 60 ºC overnight. The reaction mixture was concentrated and the resulting residue was preabsorbed on silica gel by dissolving it in methanol and then purified by chromatography (EtOAc→EtOAc/MeOH, 98:2) providing **112** (4.37 g, 72%) as a white solid; m.p. 129-131 ℃; ^{1}H NMR (300 MHz): δ = 7.84 (s, 1H), 7.37 (s, 1H), 4.48 (d, *J* = 6.2 Hz, 2H), 2.86 (s, 6H), 2.79 (t, *J* = 6.2 Hz, 1H); ^{13}C NMR (75 MHz): δ = 136.6, 125.6, 120.9, 89.8, 77.3, 51.3, 38.3; IR (neat, cm^{-1}): 3242, 3150, 3122, 2927, 2222, 1685, 1548, 1386, 1266, 1170, 1087, 1030, 958, 843, 722; HR-ESIMS (m/z): Calcd. for $C_8H_{12}N_3O_3S$ $[M+H]^+$ 230.0593, found 230.0591; Calcd. for $C_8H_{11}N_3O_3SNa$ $[M+Na]^+$ 252.0413, found 252.0407.

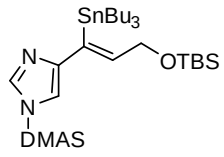
(*Z*)-1-hydroxy-3-tributylstannyl-3-(1-dimethylsulfamoylimidazole-4-yl)-2-propene (113): In a round bottom flask compound **112** (5.00 g, 21.8 mmol) was



dissolved under N_2 atmosphere in anhydrous THF (150 mL). The reaction mixture was cooled to 0 ºC and then to it Red-Al (65 wt.% in toluene, 7.90 mL, 26.2 mmol) was added dropwise. After stirring the reaction mixture for 30 min, Bu_3SnCl (8.80 mL, 32.7 mmol) was

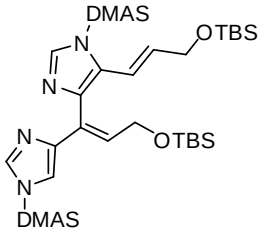
added. Then the reaction mixture was stirred overnight at r.t. Finally the reaction was quenched with NH_4Cl (50 mL) then the organic layer was separated. The aqueous layer was extracted with EtOAC, then the combined organic solutions were dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by chromatography (hexane/EtOAc, 60:40) providing **113** (6.80 g, 60%) as a pale yellow oil; ^{1}H NMR: δ = 7.79 (d, *J* = 1.1 Hz, 1H), 7.02 (d, *J* = 1.1 Hz, 1H), 6.87 (t, *J* = 6.4 Hz, $^3J_{Sn\text{-}H}$ = 110.4 Hz, 1H), 4.23 (t, *J* = 6.0 Hz, 2H), 2.84 (s, 6H), 1.61 (t, *J* = 5.8 Hz, 1H), 1.51-1.41 (m, 6H), 1.28 (sextet, *J* = 7.3 Hz, 6H), 1.05-0.95 (m, 6H), 0.86 (t, *J* = 7.3 Hz, 9H); ^{13}C NMR: δ = 148.5, 141.7, 138.3, 135.9, 111.7, 64.5, 38.2, 29.1, 27.3, 13.7, 11.7; IR (neat, cm^{-1}): 3323, 2954, 2870, 1459, 1391, 1269, 1173, 1080, 961, 829, 725; HR-ESIMS (m/z): Calcd. for $C_{20}H_{39}N_3O_3SSnNa$ $[M+Na]^+$ 544.1629, found 544.1642.

(*Z*)-1-*t*-Butyldimethylsilyloxy-3-tributylstannyl-3-(1-dimethylsulfamoylimidazole-4-yl)-2-propene (110): Alcohol **113** (4.00 g, 7.69 mmol) and imidazole (1.04 g, 15.38 mmol) were dissolved in dry CH_2Cl_2 (150 mL). The solution was cooled to 0 ℃ and TBSCl (1.51 g, 9.99 mmol) was added to it. The mixture was stirred at r.t. overnight. The reaction mixture was partitioned with water (45 mL), and the organic layer was washed with brine, dried (Na_2SO_4) and concentrated.



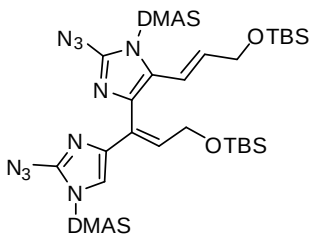
The residue was purified by chromatography (hexane/EtOAc, 75:25) to give **110** (4.29 g, 88%) as a thick colorless oil; ^{1}H NMR: δ = 7.77 (d, *J* = 1.1 Hz, 1H), 7.01 (d, *J* = 1.1 Hz, 1H), 6.76 (t, *J* = 6.4 Hz, $^{3}J_{Sn-H}$ = 114.5 Hz, 1H), 4.25 (d, *J* = 6.4 Hz, 2H), 2.83 (s, 6H), 1.51-1.42 (m, 6H), 1.29 (sextet, *J* = 7.3 Hz, 6H), 1.06-0.96 (m, 6H), 0.90 (s, 9H), 0.86 (t, *J* = 7.3 Hz, 9H), 0.09 (s, 6H); ^{13}C NMR: δ = 148.8, 143.1, 135.8, 135.7, 111.3, 65.2, 38.2, 29.1, 27.4, 26.0, 18.5, 13.7, 11.6, -5.0; IR (neat, cm^{-1}): 2953, 2925, 2854, 1461, 1391, 1250, 1174, 1066, 961, 833, 724; HR-ESIMS (m/z): Calcd. for $C_{26}H_{53}N_3O_3SSiSnNa$ $[M+Na]^+$ 658.2494, found 658.2488.

4-((*Z*)-1-Dimethylsulfamoyl-4-(3-(*t*-butyldimethylsilyloxy)-2-propenyl)imidazol-4-yl)-1-dimethylsulfamoyl-5-((*E*)-3-(*t*-butyldimethylsilyloxy)-2-propenyl)imidazole (114): N_2 was bubbled through solution of **80** (1.25 g, 2.65 mmol) and stannane **110** (2.52 g, 3.97 mmol) in dry DMF (40 mL). PPh_3 (138 mg, 0.53 mmol), CuI (101 mg, 0.53 mmol) and $Pd_2(dba)_3$ (121 mg, 0.13 mmol) were added and bubbling of N_2 was continued for additional 2 min. The reaction mixture was heated at 55 ℃ for 3 min. followed by addition of CsF (1.81 g, 11.9 mmol) and heating was continued for additional 2.5 h. Then the DMF was removed by distillation under vaccum. Water (50 mL) and EtOAc



(100mL) were added to the residue, which was stirred vigorously and then the mixture was filtered through bed of Celite. The filtrate was partitioned and the aqueous layer was extracted with EtOAc. The organic extracts were combined, dried (Na_2SO_4), and concentrated under vaccum. The residue was dissolved in dry DCM (60 mL). To above solution imidazole (720 mg, 10.6 mmol) and TBSCl (1.00 g, 6.62 mmol) were added at 0 ℃ and then stir red at r.t. for 5 h. NH_4Cl (30 mL) was added to the reaction mixture and layers were separated. The organic layer was dried (Na_2SO_4), concentrated and the residue was purified by flash chromatography (hexane/EtOAc, 60:40 →hexane/EtOAc, 10:90) to give product **114** (1.24 g, 68%) as a yellowish semi-solid; ^{1}H NMR: δ = 7.94 (s, 1H), 7.82 (d, *J* = 1.3 Hz, 1H), 6.81-6.74 (m, 3H), 6.11 (dt, *J* = 3.7, 16.0 Hz, 1H), 4.19 (d, *J* = 6.4 Hz, 2H), 4.12 (dd, *J* = 2.3, 3.7 Hz, 2H), 2.87 (s, 6H), 2.79 (s, 6H), 0.86 (s, 9H), 0.83 (s, 9H), 0.00 (s, 6H), -0.01 (s, 6H); ^{13}C NMR: δ = 142.3, 137.8, 136.7, 136.0, 135.9, 132.5, 127.2, 125.4, 114.7, 113.8, 62.7, 61.1, 38.3, 38.2, 25.9, 25.8, 18.4, 18.3, -5.1, -5.4; IR (neat, cm^{-1}): 3129, 2953, 2856, 1471, 1389, 1252, 1175, 1071, 962, 833, 723; HR-ESIMS (m/z): Calcd. for $C_{28}H_{53}N_6O_6S_2Si_2$ $[M+H]^+$ 689.3001, found 689.2988; Calcd. for $C_{28}H_{52}N_6O_6S_2Si_2Na$ $[M+Na]^+$ 711.2820, found 711.2813.

2-Azido-4-((*Z*)-2-azido-1-Dimethylsulfamoyl-4-(3-(*t*-butyldimethylsilyloxy)-2-propenyl)imidazol-4-yl)-1-dimethylsulfamoyl-5-((*E*)-3-(*t*-butyldimethylsilyloxy)-2-propenyl)imidazole (115): Divinyl intermediate **114**



(380 mg, 0.55 mmol) was dissolved in anhydrous THF (10 mL) and the reaction mixture was cooled to -78 ºC and BuLi (2.5M, 0.77 mL, 1.92 mmol) was added dropwise to the reaction mixture and stirred for 1 h and then tosyl azide (433 mg, 2.20 mmol) was added. The reaction mixture was allowed to come to r.t. and then stirred for an additional 30 min, followed by addition of aqueous NH_4Cl (5 mL) to quench the reaction mixture. The organic layer was separated and the aqueous layer was extracted with EtOAc. The organic solutions were combined, dried with anhydrous Na_2SO_4 and concentrated. The crude product was purified by chromatography (hexane/EtOAc, 75:25) giving **115** (267 mg, 63%) as a yellow thick oil; ^{1}H NMR: δ = 6.69-6.63 (m, 3H), 5.94 (dt, *J* = 4.0, 15.6 Hz, 1H), 4.17 (d, *J* = 6.4 Hz, 2H), 4.13-4.12 (m, 2H), 2.97 (s, 6H), 2.92 (s, 6H), 0.86 (s, 9H), 0.84 (s, 9H), 0.00 (s, 12H); ^{13}C NMR: δ = 140.7, 140.3, 137.7, 134.9, 132.2, 131.7, 128.6, 124.8, 116.4, 115.3, 63.0, 61.1, 38.5, 38.4, 26.0, 25.8, 18.4, 18.3, -5.1, -5.4; IR (neat, cm^{-1}): 2953, 2856, 2142, 1513, 1461, 1393, 1250, 1172, 1072, 966, 832, 722; HR-ESIMS (m/z): Calcd. for $C_{28}H_{50}N_{12}O_6S_2Si_2Na$ $[M+Na]^+$ 793.2848, found 793.2865.

PART II

DIVERSITY ORIENTED SYNTHESIS WITH IMIDAZOLYLPROPARGYL AMIDES

CHAPTER 4

INTRODUCTION

In the synthetic and biosynthetic communities, hypothetical pathways involving oligomerization and cyclization of oroidin (**1**) or its monobromo (**2**) or desbromo (**3**) congeners,[8] leading to oroidin-derived alkaloids have been proposed and are generally well accepted, at least in terms of establishing skeletal connectivities. No in depth biosynthetic studies have been performed to provide experimental support for these hypothetical pathways. This lack of evidence notwithstanding, it is not clear whether employing such a biomimetic approach will provide general experimental solutions to accessing a variety of different frameworks from such building blocks. Further, it is not immediately evident that this type of approach will permit evaluation of structure-activity relationship with deletion analogs (wherein key activating groups are missing) or substitution analogs (changing chemical reactivity). So bearing these considerations in mind, we decided to employ an approach which exploits a biomimetically inspired approach but relies on synthetically accessible reactions.

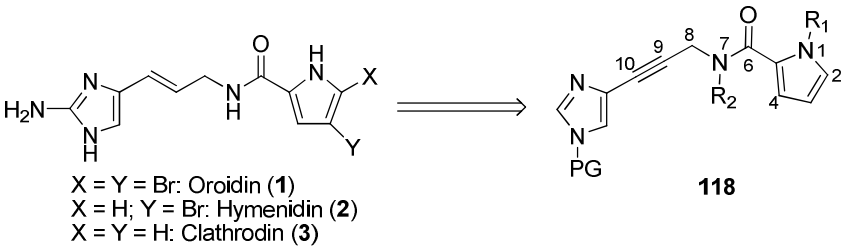


Figure 4-1 Oroidin and model compound

It was envisioned that instead of subjecting oroidin (**1**) to a variety of intramolecular cyclizations, a surrogate, the propargylic imidazole derivative **118** (Figure 4-1) could undergo related transformations in a much more efficient and controlled manner. Transition metal-catalyzed carbon-carbon and carbon-heteroatom bond formation reactions are well known in the literature,[102-104] however, examples of their use in the elaboration of simple imidazole derivatives are quite limited.[105,106] It was hypothesized that these imidazolylpropargyl amides (**118**) could be used as lynchpin synthons for the assembly of a variety of imidazole-containing natural products by using transition metal catalyzed intramolecular cyclization reactions. This strategy can be viewed as an attempt to mimic Nature's approach to complex molecule synthesis, wherein the latent reactivity within a common building block is harnessed to access a wide variety of structural different frameworks through enzymatic reactions. The heterocycles obtained from these reactions may then serve as key intermediates en route to the total synthesis of a number of oroidin-derived alkaloids, including for example cyclooroidin (**120**),[107] oxocyclostylidol (**121**),[108] stevensine (**122**),[109] agelastatin A (**124**),[110-113] and nagelamide R (**28**)[44] as well as for the synthesis of non-natural analogs (Figure 4-2).

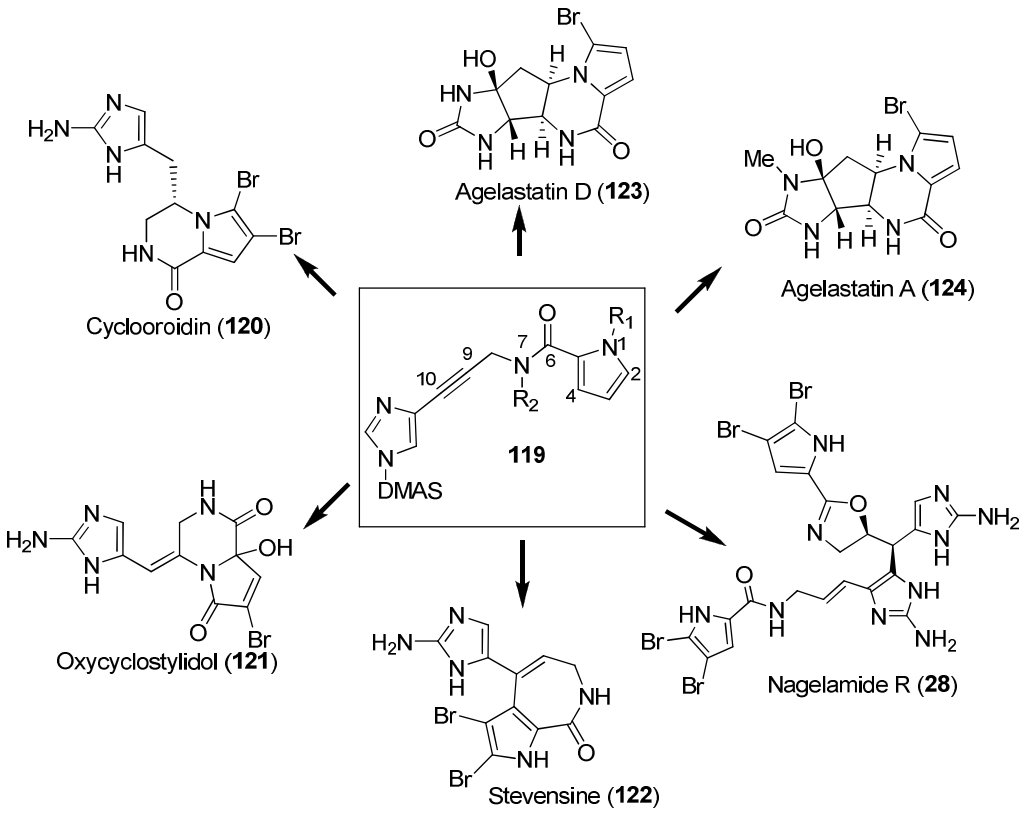


Figure 4-2 Divergent synthesis of oroidin alkaloids

The imidazolylpropargyl amide (**119**) contains an acetylenic bond which in principle can undergo a variety of addition reactions at either of two sites (C9 or C10). The pyrrole moiety has at least two nucleophilic sites at N1 and C4[114] (note: the numbering of the atoms within **119** follows the original assignment system used for the isolated natural products and is not consistent with IUPAC numbering). In addition, the amide oxygen can also serve as a nucleophile under appropriate conditions. We decided to exploit all these considerations and arrived at the divergent strategy as depicted in Figure 4-3.

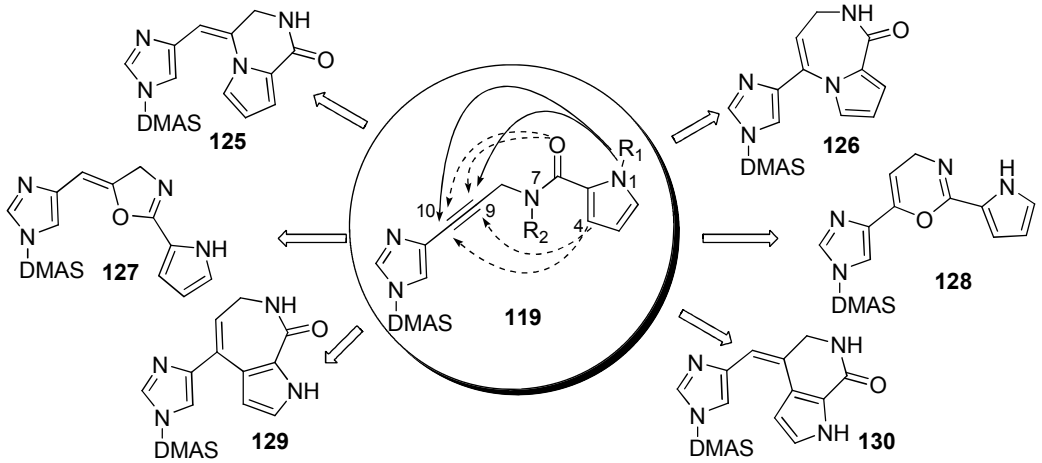


Figure 4-3 Diversity oriented synthesis

This type of strategy would produce a library of novel heterocycles which can ultimately be used in a structure-activity investigation. Specifically, intermediates **125**, **127**, and **129** should be useful in the context of the total synthesis of cyclooroidin (**120**), nagelamide R and T (**28** and **29**), and stevensine (**122**) respectively. In addition, this strategy may allow access to molecules resulting from alternative modes of reactivity and ultimately permit exploration of their biological potential. For example, there are several examples of oroidin alkaloids with essentially identical frameworks which differ only in how the pyrrole moiety is connected to the rest of the structure, either through N1 or C4. It is conceivable that this duality is widespread in the oroidin family, and it is simply a matter of time before these unknown regioisomers are isolated from natural sources. For example, cyclooroidin (**120**) has been described, but the isomeric "isocyclooroidin" (**131**) has not been reported in the literature (Figure 4-4), but based on the methods outline below it may be possible to prepare it synthetically and subsequently evaluate its biological activity. Similarly, stevensine (**122**) the

C4-pyrrole substituted derivative is known, but does the corresponding N1-substituted derivative “isostevensine” (**132**) exist in nature? It is relevant to note that Lindel, in a 2003 review of the chemistry of the oroidin alkaloids,[29] speculated that only a fraction of the possible structural frameworks had been observed in isolated natural products as there are many other conceivable pathways for cyclization. The chemistry described in the following chapter will demonstrate that many of these frameworks are indeed accessible synthetically, as well as the discovery of a few unexpected outcomes.

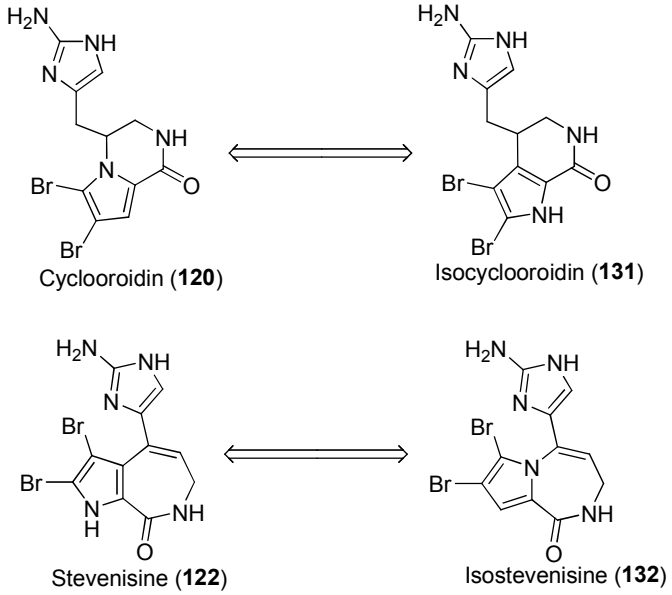


Figure 4-4 Proposed non natural analog of oroidin alkaloids

CHAPTER 5

RESULTS AND DISCUSSION

5.1 Formal total synthesis of cyclooroidin

In 2000,[107] Fattorusso et al. reported the isolation of (-)-cyclooroidin (**120**) from the Mediterranean sponge *Agelas oroides.* After comparing its CD spectrum with one reported for dibromophakellin (**180**), the absolute stereochemistry of **120** was assigned to be *S*. Recently two more related natural products were isolated as depicted in Figure 5-1. Agesamide A (**133**) and B (**134**) were obtained from the Okinawan marine sponge *Agelas sp*.[115]

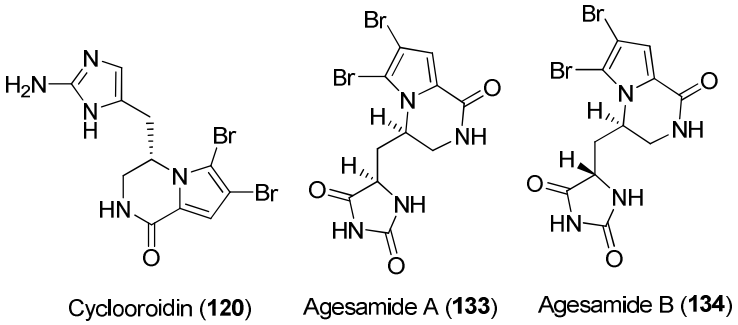


Figure 5-1 Cyclooroidin and related alkaloids

To date, there are five reported total syntheses (two racemic and three enantioselective) of the cyclooroidin (**120**),[116-119] including one recently published approach from our lab.[75] Most of these approaches are characterized by strategies in which the imidazole ring was constructed at a late stage of the synthesis. In our approach it was decided to disconnect the N1-C9 bond of the

pyrazinone **125** to obtain the alkyne **135** or **137**, with imidazole ring already present (Figure 5-2).[114]

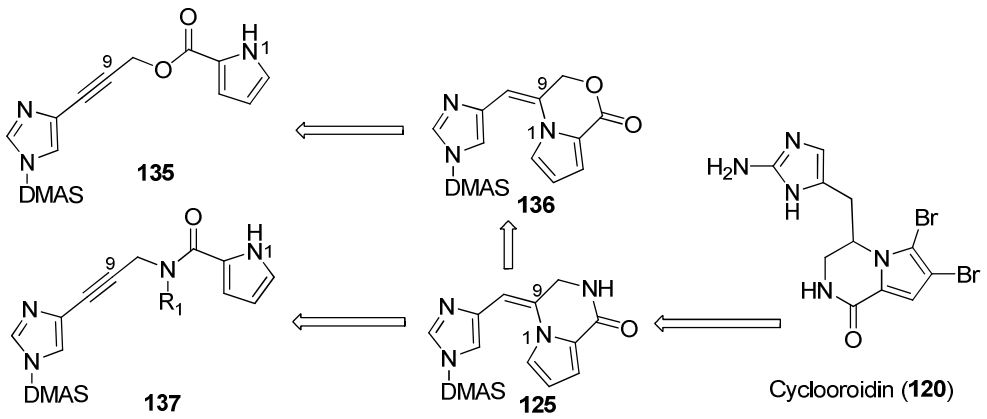
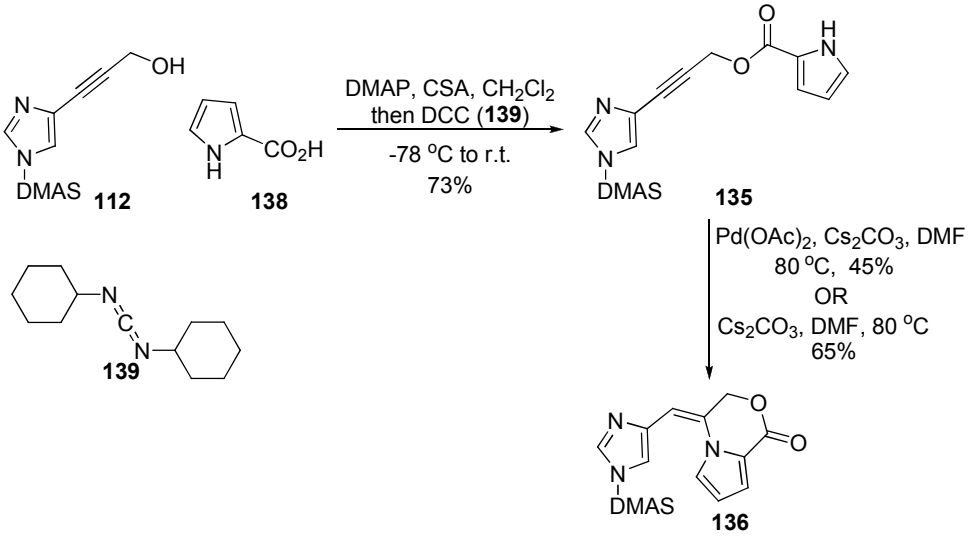


Figure 5-2 Retrosynthetic analysis of cyclooroidin

As proposed in Figure 5-2, either ester **135** or protected amide **137** can be subjected to an intramolecular cyclization reaction to obtain morpholine **136** or pyrazinone **125**. The morpholine **136** can be subsequently converted to pyrazinone **125** by first ring opening of lactone, followed by conversion of the resulting alcohol to corresponding amine and finally ring closure. A similar strategy was used to complete the total synthesis of cyclooroidin (**120**) in the recently published approach from our lab.[75]

During our initial studies, to establish the general feasibility of intramolecular cyclization reaction between pyrrole nitrogen (N1) and alkyne (C9) it was decided use the easily available ester **135**. The ester **135** can be synthesized in one step from alcohol **112** and pyrrole carboxylic acid **138** in presence of DCC (**139**) as a coupling reagent (Scheme 5-1). The cyclization of the ester **135** proceeded in presence of $Pd(OAc)_2$ and base to obtain morpholine derivative **136** in moderate

yield, which was confirmed by X-ray crystal structure (Figure 5-3). As a control reaction we conducted the reaction in absence of the Pd(II) catalyst and we were surprised to observe that the intramolecular cyclization of alkyne **135** proceeded smoothly providing **136** in an improved 65% yield.[104]



Scheme 5-1

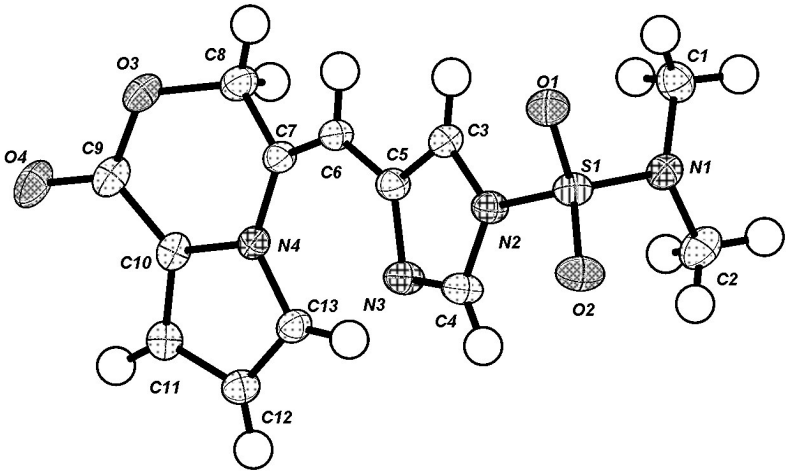
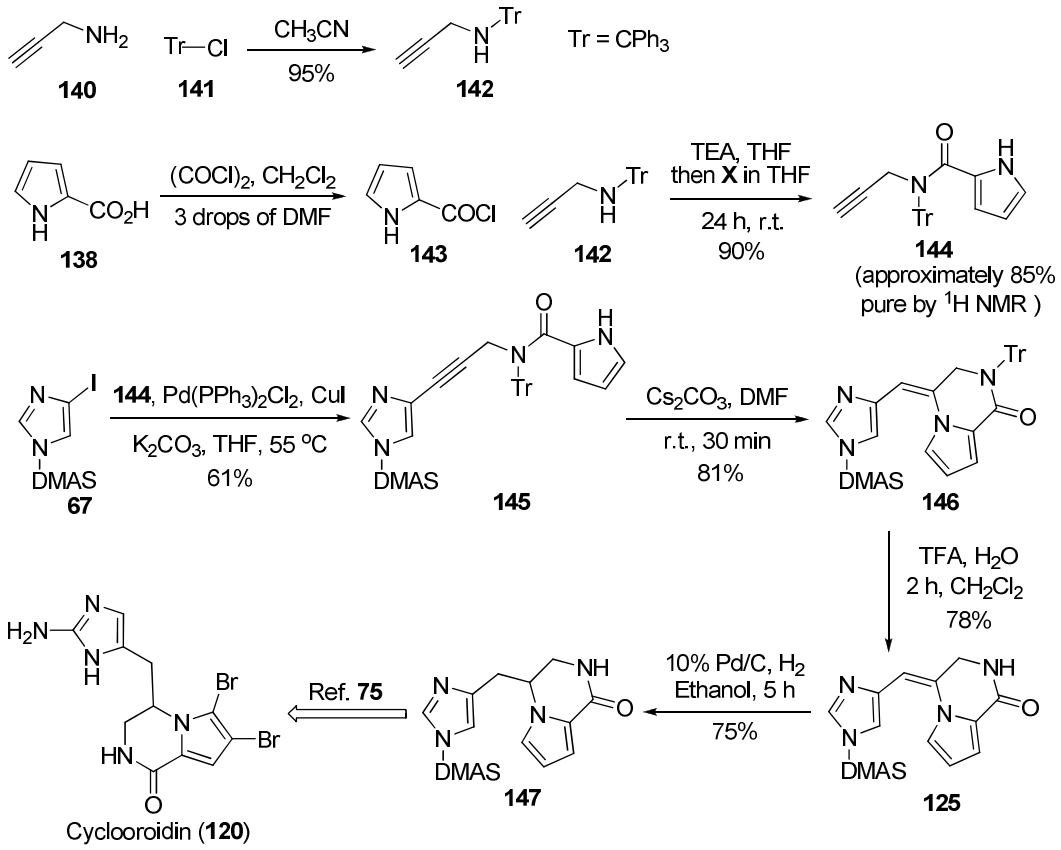


Figure 5-3: X-ray crystal structure of 136

Though it is possible to convert morpholine **136** into pyrazinone **125** via alkene reduction and conversion of lactone to the lactam,[75] to reduce step count on the cyclized intermediate and to make synthesis more efficient, it was decided to explore intramolecular cyclization of the corresponding protected amide **137**.

To accomplish this, it was decided to examine a substrate in which the amide nitrogen was protected with trityl group (**145**). The choice of the trityl protecting group was driven by two considerations. First, it is readily removable under mildly acidic conditions and second, it provides a bulky nitrogen substituent which potentially will facilitate cyclization reactions.[120,121] The syntheses started with protection of propargyl amine (**140**) with trityl chloride to obtain trityl-protected propargylamine **142** in very good yield (Scheme 5-2). At this point the amine **142** was acylated with pyrrole acid chloride **143** in presence of triethylamine as a base providing terminal alkyne **144**. Subsequent subjection of **144** to a Sonogashira reaction with **67** led to the formation of alkyne **145** in good yield. We were delighted to see intramolecular cyclization mediated by Cs_2CO_3 of alkyne **145** proceeded at room temperature in 30 minutes compared to 1.5 hr for ester **135** (Scheme 5-1) at 80 ℃. This result could be easily e xplained by increased proximity of pyrrole nitrogen and alkyne due to steric buttressing of the trityl protecting group. We would note that related reactions have been reported by Llauger et al. with phenyl propargylic derivatives,[122] in the presence of DBU as a base. But in addition to expected pyrazinone with *Z*-exocyclic olefin (net anti-

addition), they isolated *E*-isomer and an other byproduct where the exocyclic double migrated into the pyrazinone ring (c.f. **125** →**182**, Scheme 5-10).



Scheme 5-2

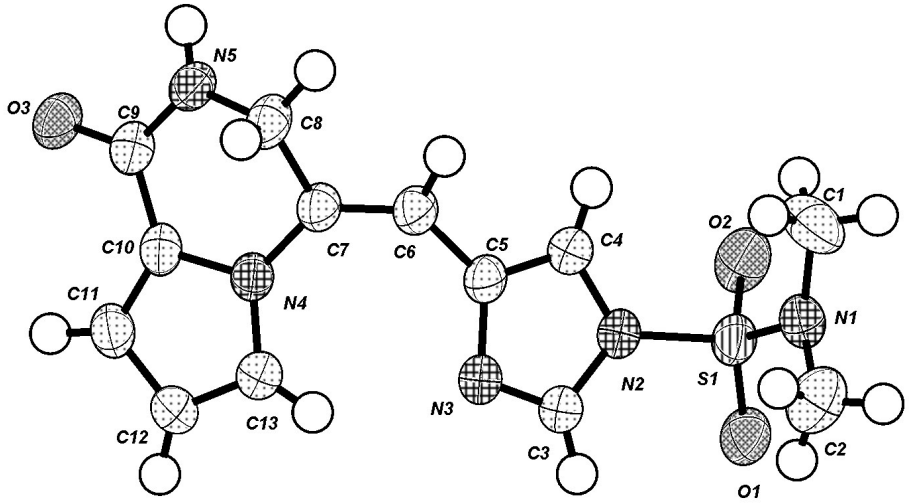


Figure 5-4: X-ray crystal structure of 125

Deprotection of the trityl group by addition of trifluoroacetic acid provided **125**, the structure of which was confirmed by X-ray crystallography (Figure 5-4) clearly illustrating that the olefinic bond is exocyclic and possesses *Z*-geometry. Reduction of the enamine-like C=C by catalytic hydrogenation gave the racemic pyrazinone **147**, which has served as an intermediate in the total synthesis of cyclooroidin (**120**) in our lab,[75] and thus the chemistry depicted in Scheme 5-2 represents a formal total synthesis of this natural product.

5.2 Approach towards total synthesis of nagelamide R and T

In 2009, the isolation of nagelamide R (**28**) from an Okinawan marine sponge of the genus *Agelas* was reported by Kobayashi and co-workers,[44] while nagelamide T (**29**) was extracted more recently from the Pacific marine sponges *Agelas cf. mauritiana* and *Phakellia sp.* by Al-Mourabit and co-workers.[45]

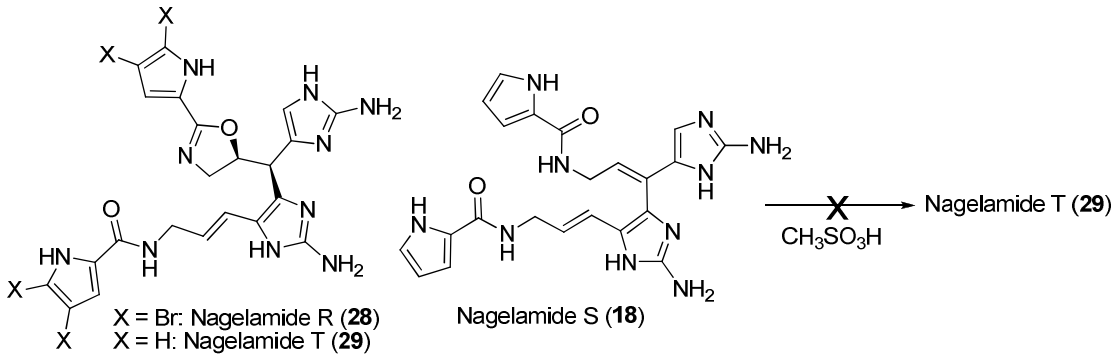


Figure 5-5 Nagelamide R and T

Even though the nagelamide R and T (**28** and **29**) are the only examples of oroidin family which contain an oxazoline moiety, oxazoline formation has been noted before in oroidin derivatives through acid-catalyzed cyclization or oxidative cyclization.[35,45,123] Al-Mourabit and co-workers attempted to apply these literature precedents to convert nagelamide S (**18**) into nagelamide T (**29**) under acidic conditions but with no success (Figure 5-5).[45] There are no reports in literature towards the total synthesis of nagelamide R and T except one which was published recently by our lab which is based on an intramolecular S_N2 reaction.[124]

In principle, synthon **148** can be used to form oxazoline moiety via nucleophilic attack of the amide oxygen on the alkyne as shown Figure 5-6, leading to formation of the northern fragments of nagelamide R and T. With the southern fragment **80** already in hand, the development of appropriate reaction conditions to join both of these fragment should permit completion of the total synthesis of these molecules.

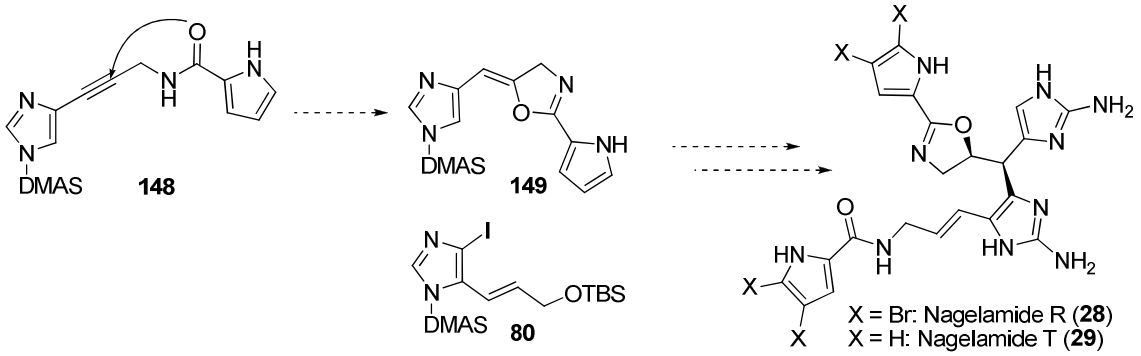
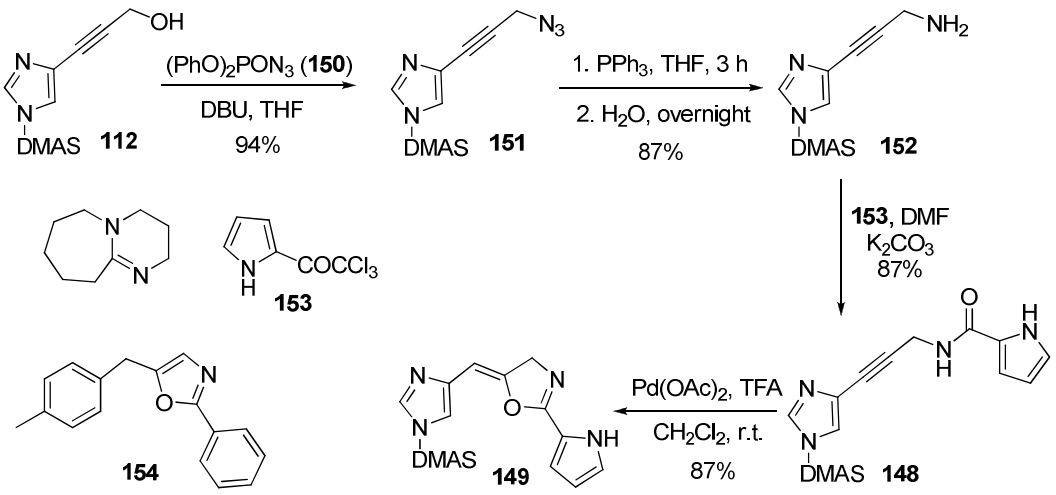


Figure 5-6 Proposed synthesis of nagelamide R and T

The preparation of alkyne intermediate **148** began from the previously prepared alcohol **112**. The alcohol **112** was first converted into azide **152** using diphenyl phosphoryl azide **150** and DBU as a base (Scheme 5-3).[80] Using Staudinger reaction conditions, the azide **152** was transformed into the corresponding amine **153** which was then subsequently acylated with trichloroacetyl pyrrole derivative **154** to obtain the alkyne synthon **148**. Gratifyingly the alkyne **148** underwent intramolecular cyclization in the presence of trifluoroacetic acid and $Pd(OAc)_2$[125] providing the required oxazoline fragment **149** in excellent yield. In the absence of $Pd(OAc)_2$, the reaction was very sluggish and did not go to completion even after 24 h.



Scheme 5-3

Assignment of the formation of an exocyclic double bond was made by comparing the olefinic proton shift and splitting pattern in the ^1H NMR spectrum with the endocyclic double bond of related phenyl derivatives (i.e., the oxazole

e.g. **154**)[126-128] where a singlet is observed in the range δ = 6.5-7.0 compared to a triplet (δ = 5.73, *J* = 2.2 Hz, long range coupling) in our exocyclic system.

In principle, it is conceivable that the two fragments, the northern fragment **149** and the southern fragment **80** could be coupled to obtain the required advanced intermediate **156** (Figure 5-7), but practically we thought it might be a difficult goal to achieve. Instead, an appropriate functional handle on the oxazoline fragment **149** should make cross-coupling a much more achievable goal. Hence we decided to examine syntheses of the bromooxazoline fragment **155**.

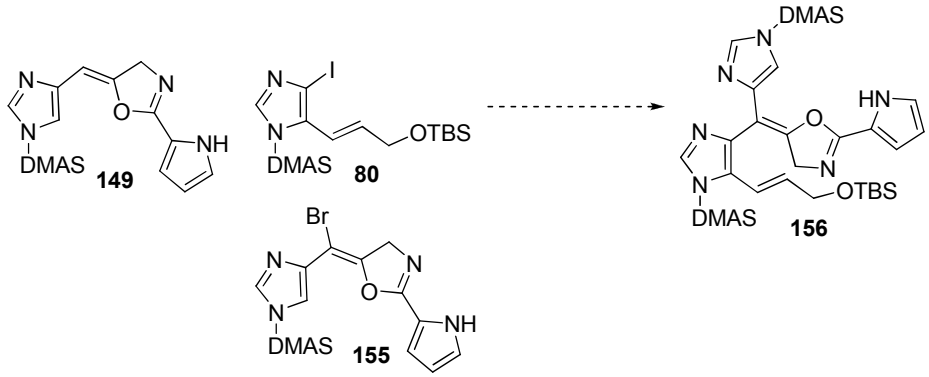
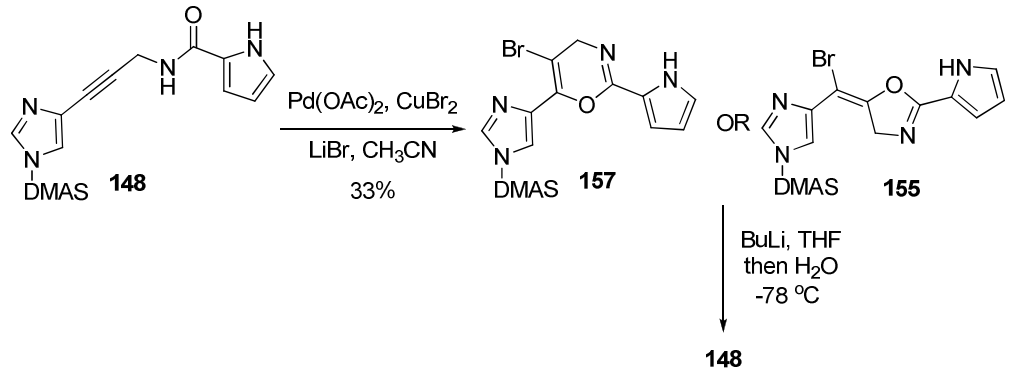


Figure 5-7 Coupling of two fragments

We decided to use reaction conditions known for other systems in literature,[129] to prepare the bromooxazoline derivative **155**. As shown in Scheme 5-4, in the presence of $Pd(OAc)_2$ and $CuBr_2$ as a bromide ion source, either bromooxazoline **155** or bromooxazine **157** was isolated.

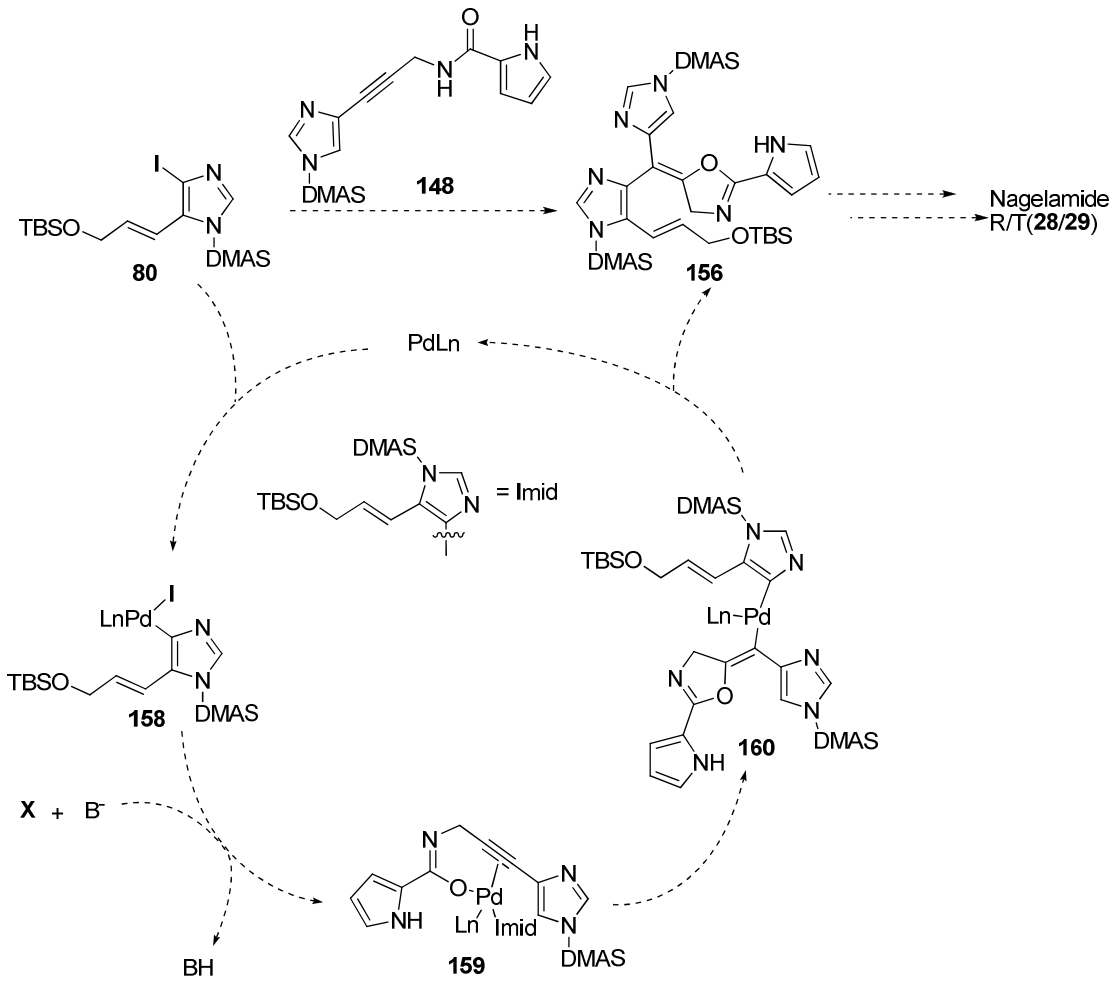


Scheme 5-4

At this point we could not confirm the identity of the product unambiguously since it is difficult to think of any spectroscopic method which will be useful for differentiation between the two products. The identification was further complicated because attempts to prepare the desbromo derivative (via metallation) failed due to formation of the alkyne **148** via β-elimination. In reality both the compound **155** and **157** are useful. Specifically bromooxazoline **155** will be useful in the context of the total synthesis of nagelamide R and T (**28** and **29**), while the formation of bromooxazine **157** will expand the scope of this strategy in which the lynchpin synthon **148** can undergo several modes of intramolecular cyclization leading to novel heterocycles, especially in the context of investigation of structure-activity relationships.

At this point we thought since all of these Pd-catalyzed processes proceed through oxidation state changes (either 0 to II or in one case possibly II to IV), in principle, it may be possible to achieve a tandem cross-coupling/oxazoline formation in same reaction pot (Scheme 5-5).[126,130] Specifically Pd(0) should insert in imidazol-5-yl iodide **80** to give Pd(II) intermediate **158** which should

serve as a catalytically viable species to facilitate intramolecular cyclization of the amide oxygen to form oxazoline intermediate **160**. Finally reductive elimination should give cross-coupled product **156**.



Scheme 5-5

Unfortunately, preliminary scouting studies towards this end have been unsuccessful to date. This is perhaps not unexpected as in many cases, the development of tandem processes requires significant trial and error to establish appropriate reaction conditions. So more experimentation is required in this direction, before this work reaches a conclusion. The completion of total

synthesis of nagelamide R and T can be envisioned from cross-coupled intermediate **156** by using analogous transformations to those used in the total synthesis of nagelamide D (**13**).

5.3 Approach towards total synthesis of stevensine

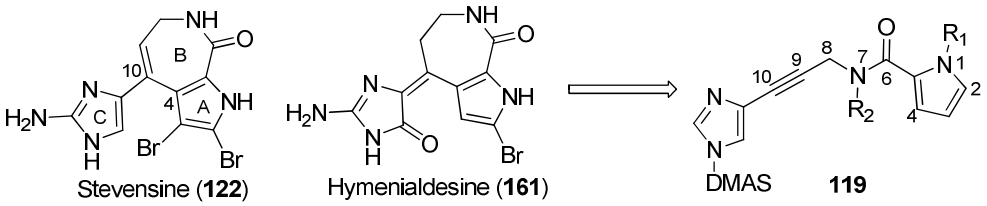
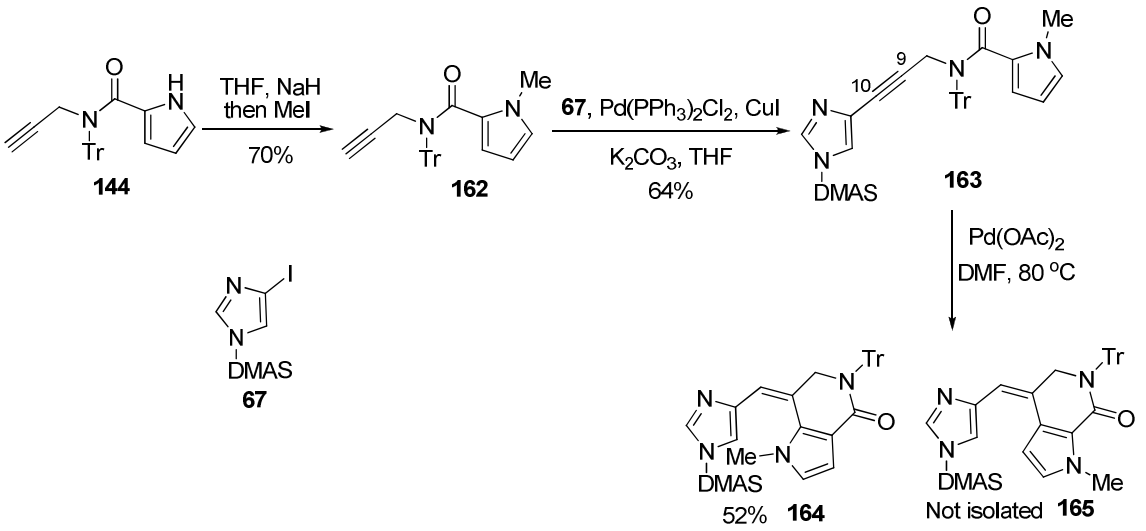


Figure 5-8 Stevensine

Stevensine was isolated from an unidentified Micronesian sponge by Faulkner in 1985.[109] Only one total synthesis of this molecule has been reported by the Horne group,[131,132] although there are several reported approaches to the related and cytotoxic hymenialdisine (**161**).[133] All of these syntheses follow a common strategy in which the pyrroloazepine fragment (AB-ring) is assembled first and the 2-aminoimidazole (or related fragment) is introduced toward the end of the synthesis.[134-136] In our approach, it was decided to break bond between C10 and C4 to give back our lynchpin synthon **119**. In a forward sense regioselective intramolecular C-H insertion reaction of pyrrole across an acetylenic bond is required to form bond between C4-C10.

To avoid potentially competing reactions, both the amide nitrogen and pyrrole nitrogen of common intermediate **119** were protected. The pyrrole nitrogen of trityl protected amide derivative **144** was protected with a methyl group using methyl iodide (Scheme 5-6). Interestingly, if DMF was used as solvent for this

reaction instead of THF, intramolecular cyclization of pyrrole nitrogen with alkyne was observed.



Scheme 5-6

The alkyne **162** and monoiodo imidazole **67** underwent a Sonogashira reaction, providing the required synthon **163**. When a Pd(II) salt was used for catalysis, as expected an intramolecular cyclization reaction occurred through C9 of the alkyne instead of C10. But surprisingly, only dihydropyridinone **164** was isolated, the structure of which was confirmed by X-ray crystallography (Figure 5-9).

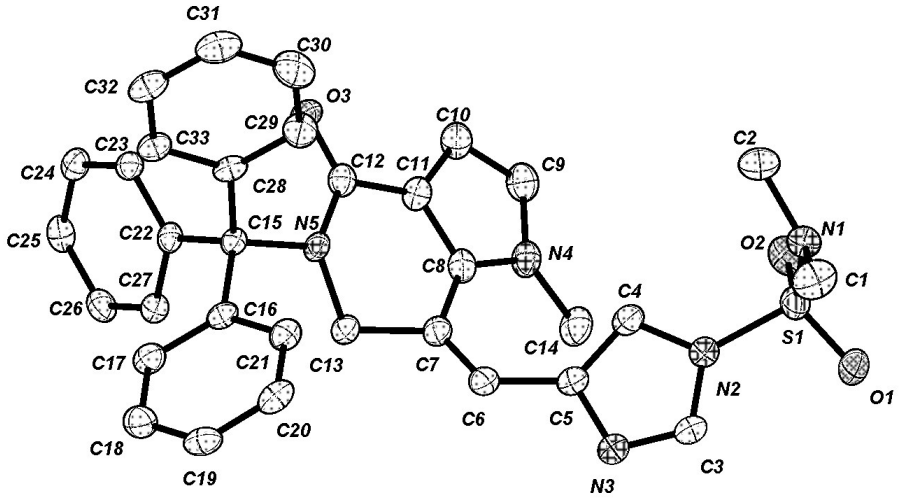
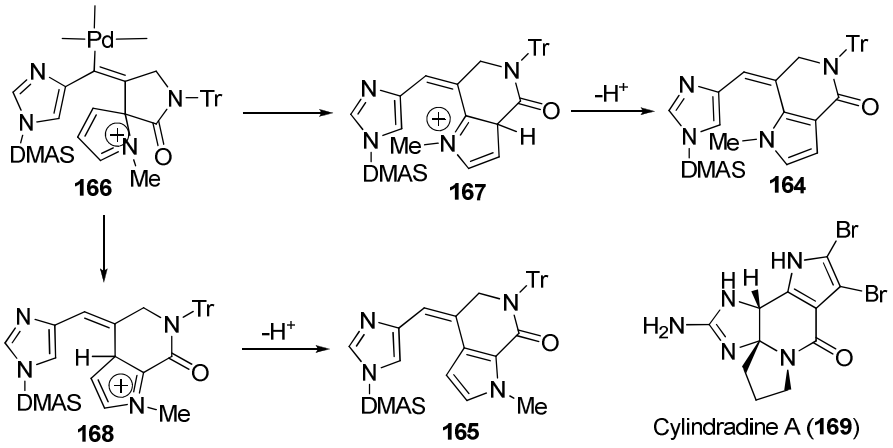


Figure 5-9 X-ray crystal structure of 164

The observed result requires that there is net migration of acyl group of the pyrrolecarboxamides moiety.[114] Similar rearrangements have been observed recently by the Beller lab with aryl propargylamides related to **163** using Pt-catalysis.[137] From a mechanistic perspective, we assume that the cyclization proceeds via ipso addition to the pyrrole moiety and the formation of the spiro adduct **166** (Scheme 5-7), which then rearranges to provide **167** which upon deprotonation then forms **164**. This observation can be explained in terms of intermediate **167** is more stable compared to the intermediate **168** in which the pyrrole carbon next to the carbonyl group bears partial positive charge making it relatively unstable.

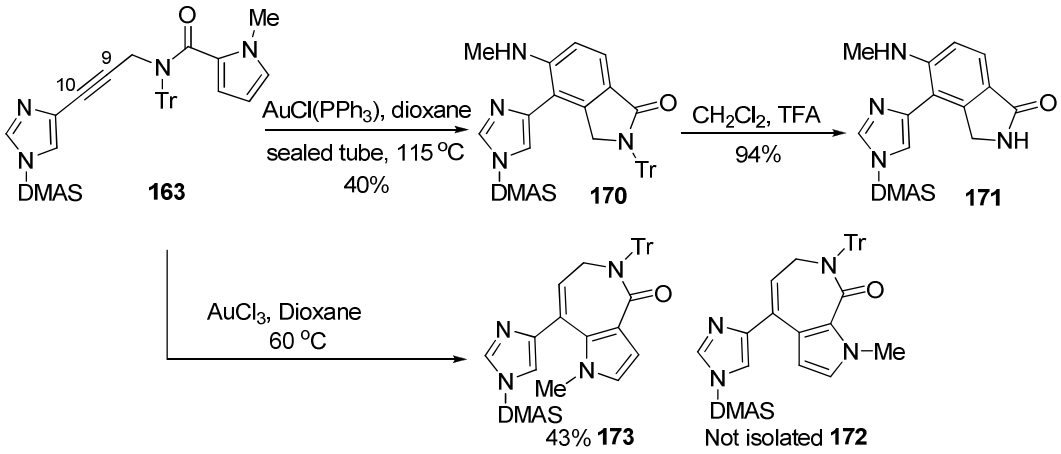


Scheme 5-7

While on the one hand the formation of these rearranged adducts was disappointing, a rearranged pyrrole fragment has been observed in two examples of the oroidin alkaloids (e.g., cylindradine A (**169**))[138] and thus we speculate that this may be a more common arrangement in this family that has simply not been observed in molecules isolated to date. Since this intermediate was not useful from a total synthesis perspective, at this stage the reaction was not further optimized for yield or regioisomer selectivity.

It is known in the literature that in presence of gold catalysts, related systems undergo intramolecular cyclization selectively in endo fashion (C10 of the alkyne) giving larger ring size product.[137,139] So the propargylamide **163** was evaluated with an Au(I) catalyst and found to undergo a cyclization to form **170** (Scheme 5-8), followed by trityl deprotection under acidic conditions, to provide the methylaniline derivative **171** (confirmed by X-ray crystallography, Figure 5-10). Since product formation was observed in absence of the gold catalyst, presumably the reaction proceeds via Diels-Alder reaction between pyrrole diene

and alkyne as a dieneophile. As best we can tell, the conversion of **163→171** represents the first example of such a reaction, and thus may have utility in the preparation of anilines with substitution patterns that might otherwise difficult to access in a general sense.



Scheme 5-8

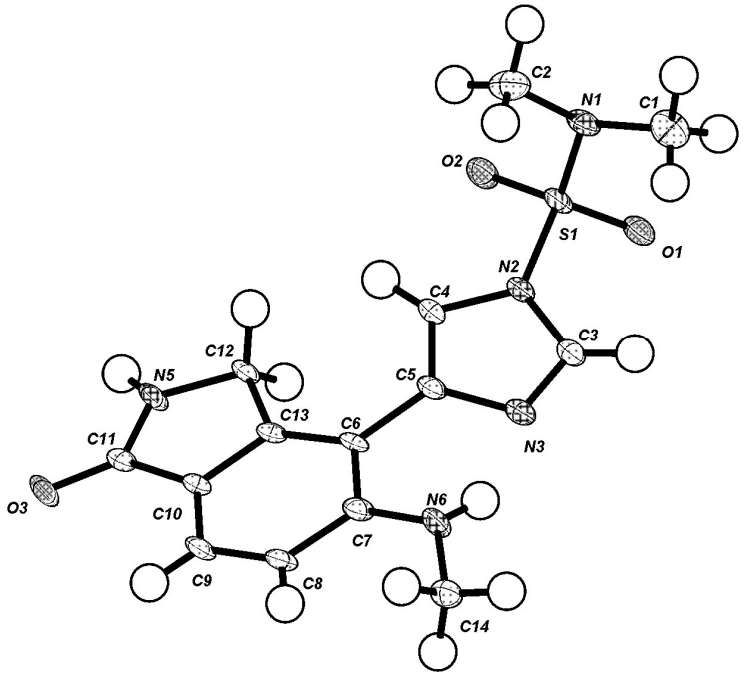


Figure 5-10 X-ray crystal structure of 171

At this point, instead of Au(I) catalyst, $AuCl_3$ was evaluated in the intramolecular cyclization.[137] Although the reaction proceeded via cyclization at C10, to our disappointment, once again the acyl rearranged azepinone **173** (X-ray crystal structure, Figure 5-11) was formed in 43%. We would like to note that byproducts were isolated that showed the absence of the trityl protecting group combined with some type of intramolecular cyclization, but we were unable to fully characterize these products due to the presence of inseparable impurities. Since all of the starting material was consumed and isolated yield was only 43%, we cannot rule out the possibility of the formation of the expected non-rearranged azepinone **172**, however it is not a major product

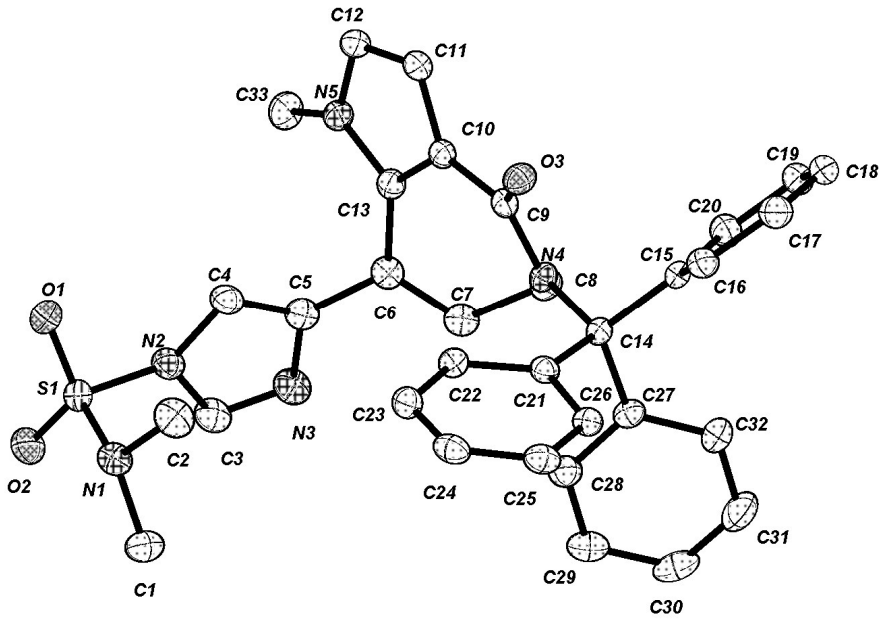
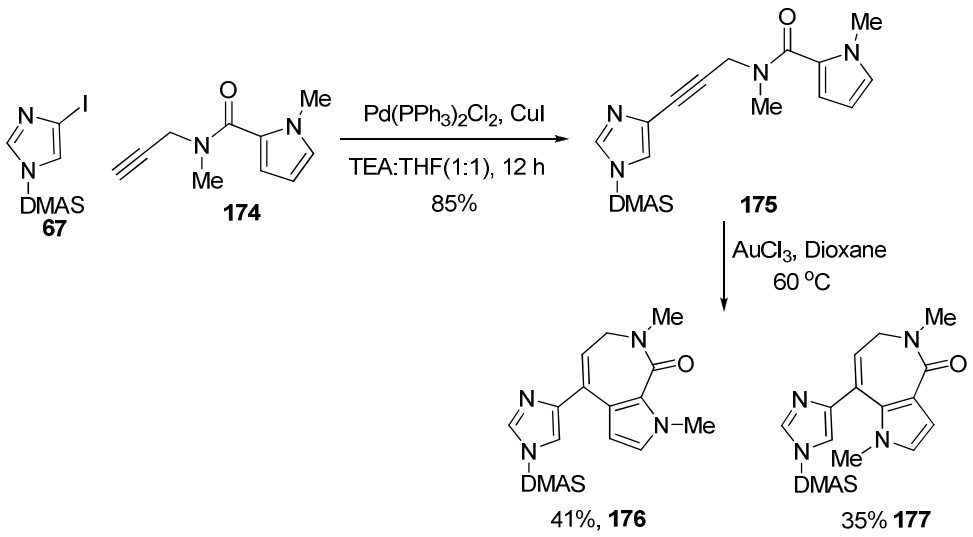


Figure 5-11 X-ray crystal structure of 173

Since the trityl group was somewhat labile under the reaction conditions and related systems were studied possessing methyl substitution,[137] both the pyrrole

nitrogen and amide nitrogen were protected with methyl groups in order to compare results. The terminal alkyne **174**, prepared using the known protocol described by Beller and co-workers,[137] underwent Sonogashira reaction with monoiodo imidazole **67** to obtain the required alkyne **175** in good yield (Scheme 5-9). Fortunately we were able to isolate both the rearranged and non-rearranged azepinone derivatives **177** and **176** when subjected to intramolecular cyclization with $AuCl_3$. Once again we confirmed the structure of non-rearranged intermediate **176** using X-ray crystal structure analysis (Figure 5-12) and by comparison of ^1H NMR data of related systems. For example, the reported pyrrole proton shifts (non-rearranged azepin: δ = 6.71, 5.94; rearranged azepin: δ = 6.73, 6.61) for one of the phenyl derivative described by Beller and co-workers[137] were well in agreement with our imidazole derivatives (non-rearranged azepin: δ = 6.77, 6.30; rearranged azepin: δ = 6.74, 6.69).



Scheme 5-9

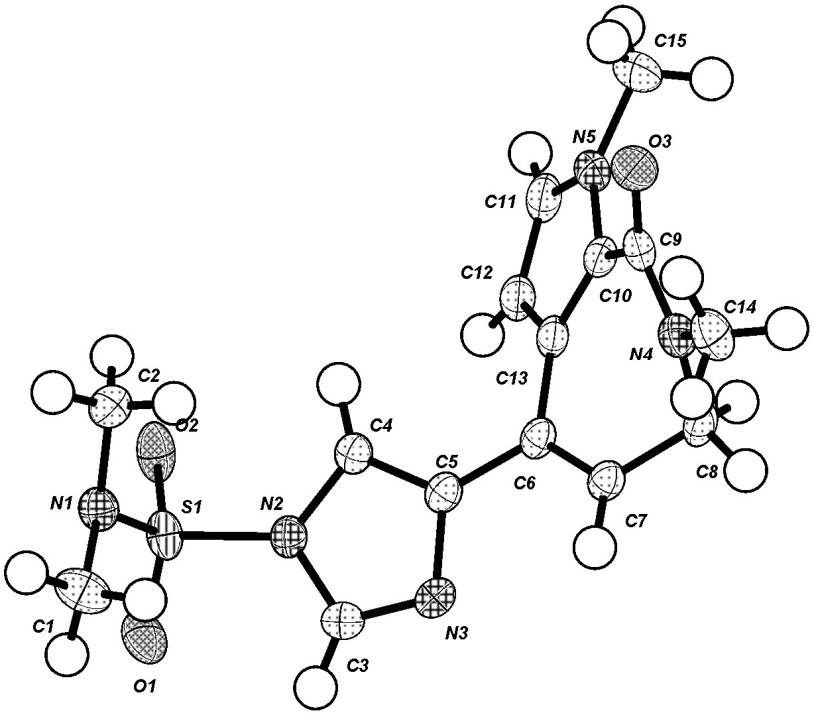


Figure 5-12 X-ray crystal structure of 176

This result clearly suggests that outcome of cyclization depends on the nature of protecting group. Compound **176** contains the complete framework found in stevensine, and so suitably functionalized precursors may permit convenient access to this natural product. The major issue with the intermediate **176** is removal of the methyl groups, which is likely to be difficult. In this direction, we tried to employ protecting groups such as diphenylmethyl, 2,4-dimethoxybenzyl, and methoxymethyl (MOM) group. In preliminary scouting experiments, we either could not obtain the required non-rearranged isomer, or in other cases we could not prepare propargylamide **119** with MOM protection of both pyrrole and amide nitrogen. Hence additional work needs to be done to find suitable protecting group which would lead to the formation of the non-rearranged azepinone derivative and also should be easy to deprotect. Once these issues are resolved,

completion of the total synthesis would rely on well established chemistry already developed in our group.

5.4 Approach towards the total synthesis of oxocyclostylidol

Oxocyclostylidol (**121**) was isolated from the Caribbean derived sponge *Stylissa caribica* by Kőck and co-workers in 2006.[108] This is first example in the oroidin family which contains an oxidized pyrrole moiety, although oxocyclostylidol and cyclooroidin (**120**) contain the same carbon-nitrogen skeleton. Oxocyclostylidol has not been extensively investigated with respect to its medicinal potential, only exhibiting some modest activity against several pathogenic bacteria.[95]

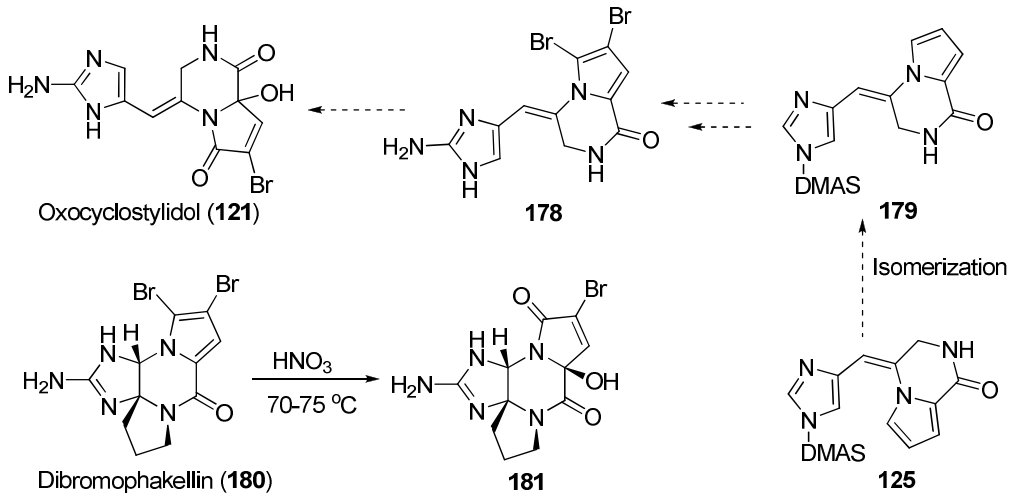
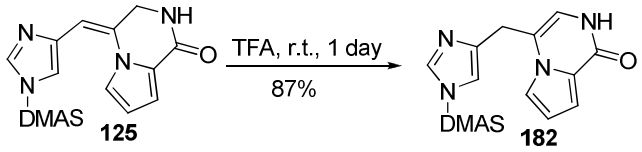


Figure 5-13 Retrosynthetic analysis of oxocyclostylidol

Magdoff-Fairchild and co-workers[140] have reported that the pyrrole moiety of dibromophakellin (**180**) undergoes oxidation with nitric acid to give intermediate **181** (Figure 5-13). Based on this precedent, it was thought that intermediate **178**

on treatment with nitric acid should give rise to oxocyclostylidol (**121**). Pyrazinone **179** should afford the required intermediate **178** on appropriate functionalization, including dibromination, azidation and DMAS deprotection. We anticipated that pyrazinone **179** may be accessible by olefin isomerization of the pyrazinone **125**, the intermediate already synthesized in the course of the formal total synthesis of cyclooroidin (**120**).

Unfortunately, when the *Z*-pyrazinone **125** was subjected to attempted isomerization to obtain the *E*-derivative, intermediate **182** was isolated instead of the required pyrazinone **179** (Scheme 5-10). Rather than formation of the geometric double bond had migrated inside the pyrazinone ring. The location of the double bond was confirmed through X-ray crystallography of the product (Figure 5-14).



Scheme 5-10

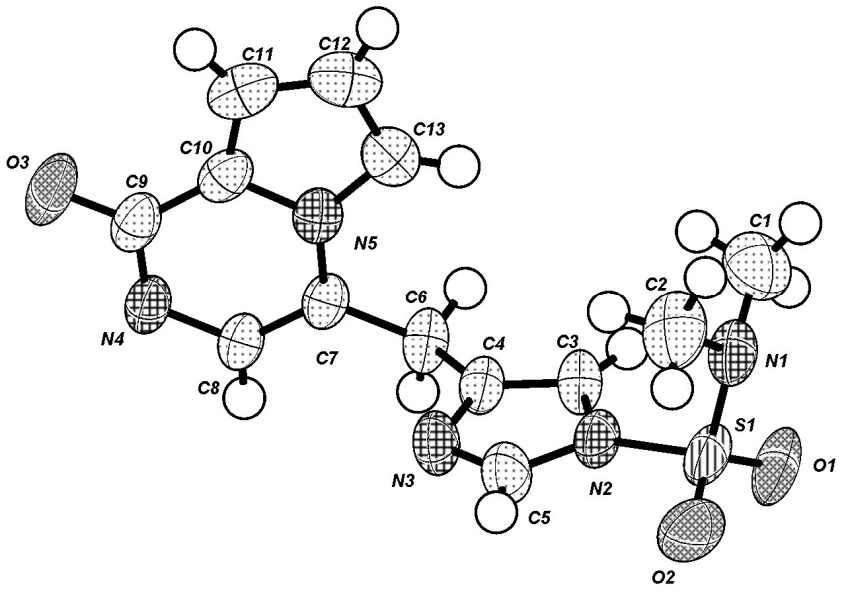
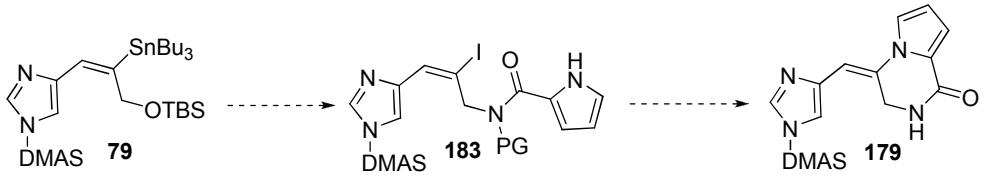


Figure 5-14 X-ray crystal structure of 182

Potentially, this problem can be solved either by trying other reaction conditions for isomerization or redesigning strategy in which the required *E*-double bond geometry is already in place. Specifically the *E*-vinyl stannane **79** obtained as a byproduct of the hydrostannylation reaction during the nagelamide D (**13**) synthesis could serve this purpose (Scheme 5-11). The *E*-vinyl stannane **79** should provide *E*-vinyl iodide **183** in few common synthetic transformations. The Pd-catalyzed C-N insertion reaction of vinyl iodide **183** should allow the formation the required pyrazinone **179**, which then can be further studied for its transformation into oxocyclostylidol (**121**).



Scheme 5-11

5.5 Approach towards total synthesis of agelastatin A

Agelastatin A (**124**) was reported in 1993 by Pietra and co-workers from *Agelas dendromorpha*, and it was shown to exhibit potent cytotoxicity against a variety of cell lines.[110-112] Over the years, other agelastatin congeners have been isolated which differ primarily in the oxidation state of the D-ring and in the level of the bromination of the A-ring.[113]

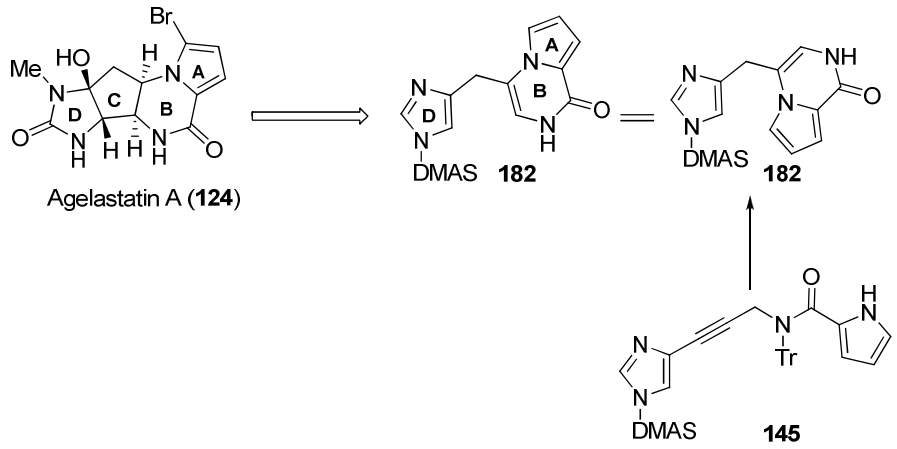
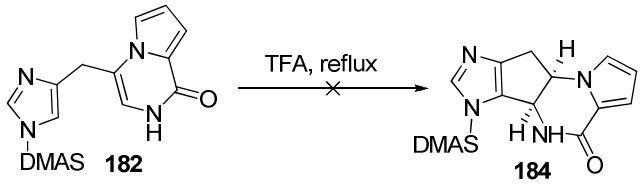


Figure 5-15 Retrosynthetic analysis of agelastatin A

Over ten syntheses of agelastatin A (**124**) have been reported in literature which, with the exception of Movassaghi's recently described approach,[141] have involved construction and elaboration of the cyclopentyl C-ring in a C→ABCD strategy; these have recently been reviewed.[37] We have chosen to pursue a biomimetically-guided strategy which takes a linear precursor **145** containing the entire carbon and nitrogen complement and subject it to two sequential cyclization reactions (Figure 5-15). Specifically pyrazinone **182** obtained in earlier studies is suitably functionalized to form the C-ring, with the ABD rings already in place. The Horne lab has attempted to execute a strategy related to

ours,[52] but this chemistry has only been described in a dissertation and appears to be stalled at this point.

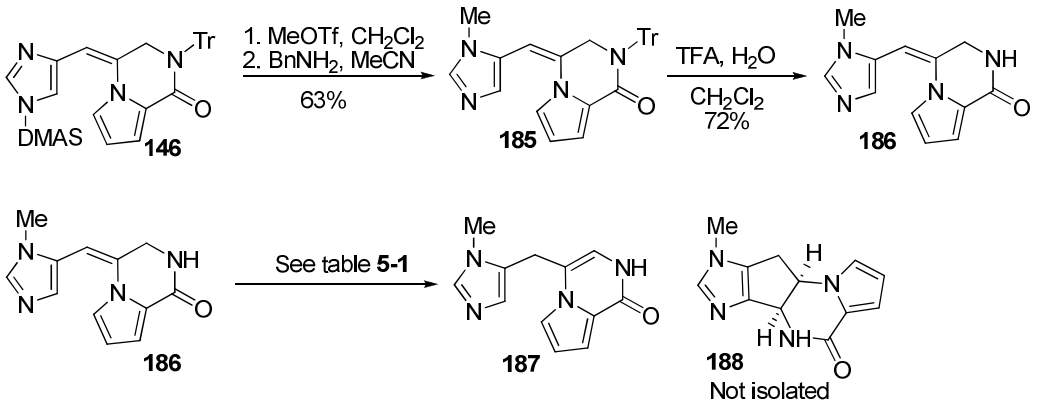
Unfortunately attempts to convert the pyrazinone **182** into the tetracyclic intermediate **184** under acidic conditions were unsuccessful. We were not overly surprised at this outcome as the imidazole moiety is relatively electron deficient and thus may not be sufficiently nucleophilic to engage in the Friedel-Crafts-like reaction.



Scheme 5-12

Since agelastatin A (**124**) is N-methylated, we decided to prepare and evaluate the N-methyl imidazole derivative **186** (Scheme 5-13). Based on the location of the methyl group in the target molecule, we would need to prepare the isomeric propargylic amide, which while this is feasible, we have previously used the convenient method of Delest[142] for exchanging a DMAS-group for a methyl group in a position specific manner via the corresponding imidazolium salt. Gratifyingly this chemistry proceeded uneventfully to provide **185**, subsequent trityl group removal provided the putative cyclization precursor **186**. Unfortunately, we have not been able to coax this substrate to cyclize under a variety of acidic conditions. As shown in Table 5-1 under mild acidic conditions the starting

material remained intact, while utilization of relatively harsh conditions resulted only in migration of the double bond inside the ring leading to intermediate **187**.



Scheme 5-13

Table 5-1 Attempts towards C-ring formation of agelastatin A

Entry	Condition	Remarks
1	TFA (0.15 eq), DCM, sealed tube	No reaction
2	TFA (0.5 eq), DCM, sealed tube	No reaction
3	HCl (0.2 eq), Acetone, sealed tube 80 ^{0}C	No reaction
4	Excess HCl, heat	Double bond migrated in ring

C-ring formation was also attempted with the C2-thioether derivative of **186**, but without any success. At this point, it seems reluctance of these substrates to participate in the cyclization chemistry is due to low nucleophilicity of imidazole ring. So it might be worthwhile to convert imidazole ring into imidazolone intermediate **189** before subjecting it to the cyclization reaction (Figure 5-16).

The reduction of aromaticity in the imidazole ring might render the resulting olefin more nucleophilic and thus facilitating cyclization. It should be noted that the natural product contains an imidazolone rather than an imidazole and so such an oxidative modification is necessary at some stage in this synthetic approach.

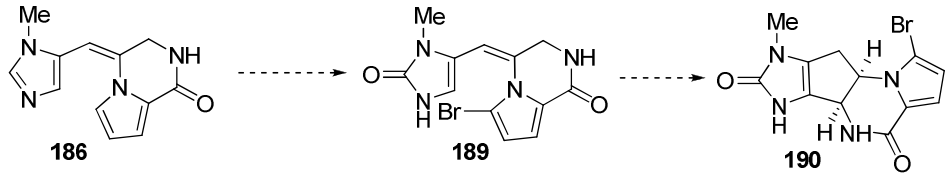
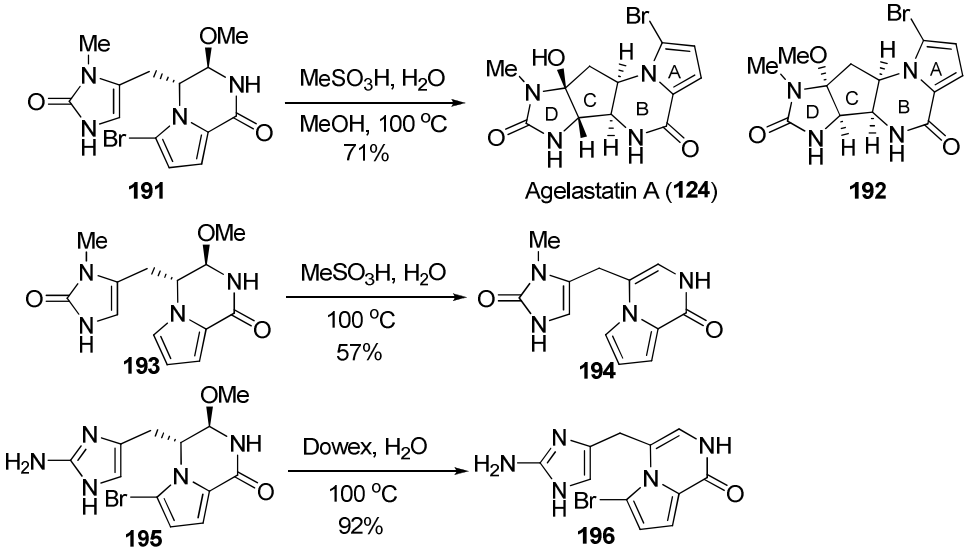


Figure 5-16 Proposed synthesis of agelastatin A

Our hypothesis was further supported by recent publication from Movassaghi's laboratory.[141] In this work, they were able to form C-ring from intermediate **191** under acidic conditions to complete total synthesis of agelastatin A (**124**) along with O-methoxy *epi*-agelastatin A **192** in a 2:1 ratio (Scheme 5-14).



Scheme 5-14

More importantly, C-ring formation was not observed with desbromo intermediate **193** or 2-aminoimidazole intermediate **195**, leading only to elimination products

194 or **196** respectively (c.f. **187**). This clearly suggests that not only is an imidazolone ring required, but also bromine on the pyrrole moiety is necessary to accomplish the C-ring formation. Once the required cyclization is achieved to form the C-ring, one additional transformation would allow the realization of a total synthesis of agelastatin A from the tetracycle **190**.

In summary, the propargylic imidazole derivative **119** was successfully utilized as a linchpin intermediate to access various frameworks prevalent in oroidin alkaloids. Various modes of intramolecular cyclizations were studied to obtain novel heterocycles which could be also useful for the total synthesis of oroidin alkaloids. Specifically, using this divergent methodology, formal total synthesis of cyclooroidin (**120**) was completed. Also key frameworks of stevensine (**122**) and nagelamide R and T (**28** and **29**) were prepared. Importantly, heterocycles prepared in the course of study will be offered for acceptance into the NCI Developmental Therapeutics Program (NCI-DTP) and Molecular Libraries Screening Centers Network (MLSCN) and thus evaluating in a comprehensive manner their biological potential.

CHAPTER 6

EXPERIMENTAL

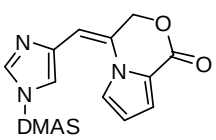
6.1 General Considerations

Same as in Part I, Chapter 3

3-(1-(*N*,*N*-Dimethylsulfamoyl)-1H-imidazol-4-yl)prop-2-ynyl-1H-pyrrole-2-carboxylate (135): To a mixture of alcohol **112** (1.20 g, 5.24 mmol), pyrrole carboxylic acid **138** (640 mg, 5.76 mmol), DMAP (64 mg, 0.52 mmol) and CSA (73 mg, 0.31 mmol) in dry CH_2Cl_2 (120 mL), a solution of DCC (1.62 g, 7.86 mmol) in dry CH_2Cl_2 (10 mL) was added dropwise at -78 ℃. The solution was then stirred at r.t. for 24 h. The mixture was filtered, the filtrate was concentrated and purified by column chromatography (hexane/EtOAc, 40:60) to obtain ester **135** (1.23 g, 73%) as a white solid; m.p 156-158 ℃; ^{1}H NMR (300 MHz): δ = 9.32 (brs, 1H), 7.83 (d, *J* = 1.4 Hz, 1H), 7.40 (d, *J* = 1.4 Hz, 1H), 7.00-6.98 (m, 2H), 6.28-6.26 (m, 1H), 5.07 (s, 2H), 2.86 (s, 6H); ^{13}C NMR (75 MHz): δ = 160.2, 136.6, 125.3, 123.6, 121.9, 121.5, 116.3, 110.8, 85.4, 78.6, 52.4, 38.3; IR (neat,

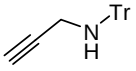
cm^{-1}): 3321, 3132, 3070, 2969, 2244, 1713, 1392, 1317, 1266, 1163, 1080, 960, 857, 748, 724; HR-ESIMS (m/z): Calcd. for $C_{13}H_{15}N_4O_4S$ $[M+H]^+$ 323.0809, found 323.0805; Calcd. for $C_{13}H_{14}N_4O_4SNa$ $[M+Na]^+$ 345.0628, found 345.0646.

(*Z*)-*N*,*N*-Dimethyl-4-((1-oxo-1H-pyrrolo[2,1-c][1,4]oxazin-4(3H)-ylidene)methyl)-1H-imidazole-1-sulfonamide (136): The mixture of ester **135**



(100 mg, 0.31 mmol) and Cs_2CO_3 (131 mg, 0.40 mmol) in dry DMF (2.5 mL) was heated at 80 ℃ for 1.5 h. Then the reaction mixture was neutralized with 1N HCl at 0 ℃ and the resulting aqueous layer was repeatedly extracted with EtOAc. The organic layers were combined, washed with the brine solution, dried with Na_2SO_4 and purified on column (hexane/EtOAc, 30:70) to give morpholine **136** (65 mg, 65%) as a pale yellowish powder; m.p 156-157 ℃; ^{1}H NMR: δ = 8.04-8.03 (m, 1H), 7.90 (s, 1H), 7.30 (s, 1H), 7.18-7.17 (m, 1H), 6.38 (t, *J* = 3.4 Hz, 1H), 6.13 (s, 1H), 4.92 (s, 2H), 2.88 (s, 6H); ^{13}C NMR (75 MHz): δ = 158.7, 136.7, 136.6, 126.7, 126.6, 119.7, 118.9, 118.1, 111.6, 107.5, 71.7, 38.3; IR (neat, cm^{-1}): 3142, 3127, 2927, 1700, 1519, 1462, 1391, 1291, 1241, 1173, 1078, 1016, 884, 755, 718; HR-ESIMS (m/z): Calcd. for $C_{13}H_{15}N_4O_4S$ $[M+H]^+$ 323.0809, found 323.0801; Calcd. for $C_{13}H_{14}N_4O_4SNa$ $[M+Na]^+$ 345.0628, found 345.0634.

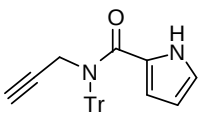
***N*-Tritylprop-2-yn-1-amine (142):** To a solution of propargyl amine (**140**) (14.78



g, 0.269 mol) in dry CH_2Cl_2 (100 mL), the solution of trityl chloride (35.80 g, 0.128 mol) in CH_2Cl_2 (75 mL) was added dropwise at 0 ℃.

the solution was stirred at r.t. overnight. The reaction mixture was partitioned with water (50 mL), and the organic layer was washed with brine, dried (Na_2SO_4) and concentrated. The residue was crystallized from hexane to give **142** (34.65 g, 91%) as a white solid; m.p 73-75 ℃; ^{1}H NMR: δ = 7.52-7.50 (m, 6H), 7.32-7.29 (m, 6H), 7.23-7.21 (m, 3H), 2.97 (s, 2H), 2.20 (t, *J* = 2.5 Hz, 1H), 2.02 (brs, 1H); ^{13}C NMR: δ = 145.3, 128.7, 128.1, 126.7, 82.8, 71.1, 70.8, 33.7; IR (neat, cm^{-1}): 3326, 3289, 3278, 3054, 2840, 2125, 1594, 1487, 1447, 1209, 1097, 1029, 899, 768, 744, 694; HR-ESIMS (m/z): Calcd. for $C_{22}H_{19}NNa$ $[M+Na]^+$ 320.1410, found 320.1412; Calcd. for $C_{22}H_{19}NK$ $[M+K]^+$ 336.1149, found 336.1153.

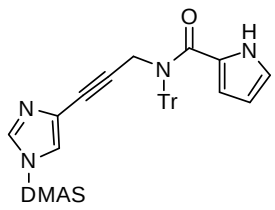
***N*-(Prop-2-ynyl)-*N*-trityl-1H-pyrrole-2-carboxamide (144):** To the mixture of



pyrrole carboxylic acid **138** (10.00 g, 90.09 mmol) in dry CH_2Cl_2 (125 mL), oxalyl chloride (19.65 mL, 225.2 mmol) was added followed by two drops of DMF. The solution was stirred for 3-4 h and then concentrated to obtain crude acid chloride **143**. The amine **142** (10.72 g, 36.04 mmol) and triethylamine (17.54 mL, 126.1mmol) were dissolved in dry THF (150 mL) and cooled to 0 ℃. The solution of crude acid chlor ide in dry THF (100 mL) was added to above solution over a period of 20-30 min. The solution was warmed to r.t. and stirred overnight. The reaction mixture was worked up by adding NH_4Cl and repeatedly extracting with EtOAc. The combined organic extracts were washed with $NaHCO_3$ solution, followed by the brine solution, dried (Na_2SO_4) and concentrated. The residue was purified by column chromatography

(hexane/EtOAc, 80:20) to obtain product **144** (12.65 g, 90%) with an estimated 85% purity. This product was used in excess for next reaction. For characterization purpose amide **144** was purified by repeated recrystallization from CH_2Cl_2; m.p 198-202 ℃; ^{1}H NMR: δ = 9.48 (brs, 1H), 7.38-7.37 (m, 6H), 7.28-7.19 (m, 10H), 6.76-6.75 (m, 1H), 6.27-6.25 (m, 1H), 4.62 (d, *J* = 2.3 Hz, 2H), 2.17 (t, *J* = 2.3 Hz, 1H); ^{13}C NMR: δ = 163.5, 143.1, 130.3, 127.5, 126.8, 126.2, 121.8, 112.8, 109.9, 80.9, 78.2, 72.9, 40.1; IR (neat, cm^{-1}): 3288, 3244, 3058, 3032, 2120, 1604, 1490, 1403, 1342, 1131, 917, 840, 724, 698; HR-ESIMS (m/z): Calcd. for $C_{27}H_{22}N_2ONa$ $[M+Na]^+$ 413.1624, found 413.1638; Calcd. for $C_{27}H_{22}N_2OK$ $[M+K]^+$ 429.1364, found 429.1360.

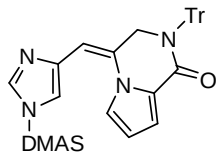
***N*-(3-(1-(*N*,*N*-Dimethylsulfamoyl)-1H-imidazol-4-yl)prop-2-ynyl)-*N*-trityl-1H-pyrrole-2-carboxamide (145):** 4-Iodoimidazole **67** (1.28 g, 4.25 mmol), alkyne



144 (2.48 g, 6.37 mmol), K_2CO_3 (1.17 g, 8.52 mmol), CuI (40 mg, 0.21 mmol) and $Pd(PPh_3)_2Cl_2$ (74 mg, 0.11 mmol) were placed in a reaction flask. To the above reaction mixture dry THF (40 mL) was added and N_2 was bubbled through it for 3-5 min. The heterogeneous mixture was stirred at 55 ℃ overnig ht. The reaction mixture was cooled to r.t. and water (15 mL) was added and the layers were separated. The aqueous layer was extracted with EtOAc. The combined organic extracts were dried (Na_2SO_4) and concentrated to provide brown solids. The crude

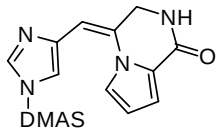
product was purified by chromatography (CH_2Cl_2→hexane/EtOAc, 45:55) to give product **145** (1.46 g, 61%) as a pale yellowish solid; m.p 170-173 ℃; ^{1}H NMR: δ = 9.43 (brs, 1H), 7.78 (d, *J* = 1.3 Hz, 1H), 7.41-7.39 (m, 6H), 7.29-7.25 (m, 6H), 7.23-7.20 (m, 4H), 7.19-7.18 (m, 1H), 6.80-6.78 (m, 1H), 6.28-6.26 (m, 1H), 4.82 (s, 2H), 2.88 (s, 6H); ^{13}C NMR: δ = 163.7, 143.0, 136.4, 130.3, 127.5, 126.8, 126.2, 125.7, 121.8, 121.1, 112.9, 110.2, 88.2, 78.0, 76.4, 40.9, 38.3; IR (neat, cm^{-1}): 3248, 3140, 3055, 1595, 1396, 1344, 1259, 1177, 1132, 1083, 958, 836, 745, 721; HR-ESIMS (m/z): Calcd. for $C_{32}H_{29}N_5O_3SNa$ $[M+Na]^+$ 586.1883, found 586.1899; Calcd. for $C_{32}H_{29}N_5O_3SK$ $[M+K]^+$ 602.1623, found 602.1610.

(*Z*)-*N*,*N*-Dimethyl-4-((1-oxo-2-trityl-2,3-dihydropyrrolo[1,2-a]pyrazin-4(1H)-ylidene)methyl)-1H-imidazole-1-sulfonamide (146): The alkyne **145** (2.68 g, 4.75 mmol) and Cs_2CO_3 (2.32 g, 7.12 mmol) were dissolved in dry DMF (30 mL) and stirred at r.t. for 30 min. The reaction mixture was quenched with NH_4Cl solution and extracted with EtOAc. The combined organic extracts were washed with brine solution, dried (Na_2SO_4), concentrated, and purified by column chromatography (hexane/EtOAc, 45:55) to give pyrazine **146** (2.17 g, 81%) as a pale yellow solid; m.p 181-184 ℃ ; ^{1}H NMR: δ = 7.93 (s, 1H), 7.63-7.62 (m, 1H), 7.55-7.54 (m, 6H), 7.34 (s, 1H), 7.29-7.25 (m, 6H), 7.18-7.15 (m, 3H), 6.90-6.89 (m, 1H), 6.22-6.21 (m, 1H), 5.94 (s, 1H), 4.06 (s, 2H), 2.91 (s, 6H); ^{13}C NMR: δ = 161.1, 142.9, 137.4, 136.6, 130.3, 128.9, 127.9, 126.7, 126.5, 123.2, 116.9, 115.8, 111.0, 104.8, 76.0, 52.7,



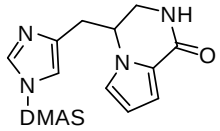
38.4; IR (neat, cm^{-1}): 3148, 3116, 1698, 1663, 1640, 1463, 1382, 1169, 1078, 963, 777, 748, 706; HR-ESIMS (m/z): Calcd. for $C_{32}H_{29}N_5O_3SNa$ $[M+Na]^+$ 586.1883, found 586.1899; Calcd. for $C_{32}H_{29}N_5O_3SK$ $[M+K]^+$ 602.1623, found 602.1611.

(*Z*)-*N*,*N*-Dimethyl-4-((1-oxo-2,3-dihydropyrrolo[1,2-a]pyrazin-4(1H)-ylidene)methyl)-1H-imidazole-1-sulfonamide (125): The pyrazine derivative



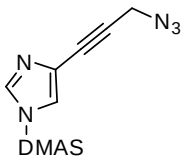
146 (800 mg, 1.42 mmol) was dissolved in mixture of CH_2Cl_2 (5 mL), TFA (7 mL) and H_2O (2.5 mL) and stirred for 1.5 h and then it was concentrated. The residue was dissolved in CH_2Cl_2 and neutralized with $NaHCO_3$ solution. The organic layer was washed with brine solution, dried (Na_2SO_4) and purified on column (EtOAc→EtOAc/MeOH, 90:10) to give amide **125** (355 mg, 78%) as a white solid; m.p 172-175 ℃; ^{1}H NMR: δ = 7.87 (s, 1H), 7.59 (s, 1H), 7.47-7.46 (m, 1H), 7.18 (s, 1H), 6.97-6.96 (m, 1H), 6.26 (t, *J* = 3.2 Hz, 1H), 5.99 (s, 1H), 4.19 (s, 2H), 2.84 (s, 6H); ^{13}C NMR: δ = 161.3, 137.2, 136.5, 129.4, 124.6, 124.1, 116.6, 114.6, 110.8, 106.3, 47.6, 38.3; IR (neat, cm^{-1}): 3294, 3191, 3127, 3059, 2928, 1659, 1556, 1431, 1387, 1230, 1173, 1081, 999, 843, 725, 668; HR-ESIMS (m/z): Calcd. for $C_{13}H_{16}N_5O_3S$ $[M+H]^+$ 322.0968, found 322.0963; Calcd. for $C_{13}H_{15}N_5O_3SNa$ $[M+Na]^+$ 344.0788, found 344.0794.

***N*,*N*-Dimethyl-4-((1-oxo-1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazin-4-yl)methyl)-1H-imidazole-1-sulfonamide (147):**[75] The olefin **125** (100 mg, 0.31 mmol) was



subjected to reduction by dissolving it in ethanol (4 mL) in presence of 10% Pd/C (30 mg, 0.03 mmol) with stirring at r.t. under 1 atm H_2 (balloon) for 5 h. The reaction mixture was filtered through a pad of Celite and the filtrate was concentrated. The residue was purified on silica gel (EtOAc/MeOH, 90:10) to provide pyrazine derivative **147** (75 mg, 75%) as a white powder; ^{1}H NMR: δ = 7.86 (s, 1H), 6.91 (dd, *J* = 4.0, 1.4 Hz, 1H), 6.76 (s 1H), 6.55-6.54 (m, 1H), 6.11-6.10 (s, 1H), 5.84 (brs, 1H), 4.64-4.62 (m, 1H), 3.92 (dd, *J* = 12.6, 4.6 Hz, 1H), 3.53-3.50 (m, 1H), 3.11-3.07 (m, 1H), 3.04-3.00 (m, 1H), 2.81 (s, 6H); ^{13}C NMR: δ = 161.2, 139.1, 136.9, 123.3, 123.2, 115.6, 113.9, 109.4, 53.6, 44.2, 38.2, 32.3.

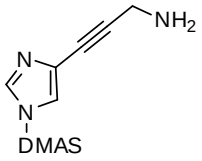
4-(3-Azidoprop-1-ynyl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide (151): To



an ice-cooled solution of the alcohol **112** (1.50 g, 6.55 mmol) in dry THF (50 mL), diphenyl phosphoryl azide (1.70 mL, 7.86 mmol) followed by DBU (1.17 mL, 7.86 mmol) was added dropwise. The solution was allowed to warm to r.t. and stirred overnight. The reaction mixture was partitioned between NH_4Cl solution and extracted with EtOAc. The organic layer was washed with brine solution, dried (Na_2SO_4), and concentrated to give brown solids. These solids were purified by flash chromatography providing azide **151** (1.56 g, 94%) as a brown solid; m.p 75-76

℃; ^{1}H NMR (300 MHz): δ = 7.81 (s, 1H), 7.40 (s, 1H), 4.11 (s, 2H), 2.86 (s, 6H); ^{13}C (75 MHz) NMR: δ = 136.7, 125.0, 121.5, 83.4, 79.2, 40.5, 38.3; IR (neat, cm^{-1}): 3132, 3114, 2920, 2114, 2070, 1466, 1392, 1268, 1181, 1088, 963, 854, 719; HR-ESIMS (m/z): Calcd. for $C_8H_{11}N_6O_2S$ $[M+H]^+$ 255.0659, found 255.0661; Calcd. for $C_8H_{10}N_6O_2SNa$ $[M+Na]^+$ 277.0478, found 277.0490.

4-(3-Aminoprop-1-ynyl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide(152):



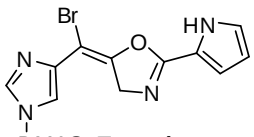
PPh_3 (1.62 g, 6.19 mmol) was added to the solution of azide **151** (1.05 g, 4.13 mmol) in dry THF (40 mL) and stirred for 4 h. H_2O (3 mL) was added to above solution and stirred overnight. The reaction mixture was concentrated purified on silica gel (EtOAc→EtOAc/MeOH/Et_3N, 70:25:5) to obtain amine **152** (819 mg, 87%) as a thick oil. ^{1}H NMR (300 MHz): δ = 7.79 (d, *J* = 1.1 Hz, 1H), 7.30 (d, *J* = 1.1 Hz, 1H), 3.61 (s, 2H), 2.84 (s, 6H), 1.56 (brs, 2H); ^{13}C NMR (75 MHz): δ = 136.5, 126.1, 120.2, 92.3, 74.5, 38.3, 32.2; IR (neat, cm^{-1}): 3369, 3303, 3126, 2923, 2233, 1671, 1602, 1541, 1387, 1325, 1170, 1085, 960, 723; HR-ESIMS (m/z): Calcd. for $C_8H_{13}N_4O_2S$ $[M+H]^+$ 229.0754, found 229.0747; Calcd. for $C_8H_{12}N_4O_2SNa$ $[M+Na]^+$ 251.0573, found 251.0566.

***N*-(3-(1-(*N*,*N*-Dimethylsulfamoyl)-1H-imidazol-4-yl)prop-2-ynyl)-1H-pyrrole-2-carboxamide (148):** A mixture of amine **152** (750 mg, 3.28 mmol), trichloroacetyl pyrrole **153** (905 mg, 4.26 mmol) and K_2CO_3 (587 mg, 4.26 mmol) in dry DMF (12 mL) was stirred at r.t. overnight. To the resulting mixture was added half saturated NH_4Cl solution and the aqueous layer was repeatedly extracted with EtOAc. The organic extracts were combined, washed with brine solution, dried (Na_2SO_4), concentrated and purified on silica gel (CH_2Cl_2→hexane/EtOAc, 20:80) to give amide **148** (916 mg, 87%) as a white solid; m.p 179-182 ℃; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 11.49 (s, 1H), 8.50 (t, *J* = 5.6 Hz, 1H), 8.16 (d, *J* = 1.4 Hz, 1H), 7.91 (d, *J* = 1.4 Hz, 1H), 6.86-6.83 (m, 1H), 6.79-6.76 (m, 1H), 6.07-6.04 (m, 1H), 4.22 (d, *J* = 5.6 Hz, 2H), 2.78 (s, 6H); ^{13}C NMR (75 MHz): δ = 160.9, 137.8, 126.2, 125.1, 122.3, 122.2, 110.9, 109.2, 89.1, 74.9, 38.3, 28.9; IR (neat, cm^{-1}): 3236, 3140, 3049, 1620, 1563, 1421, 1390, 1261, 1178, 1088, 1037, 964, 837, 769, 725; HR-ESIMS (m/z): Calcd. for $C_{13}H_{16}N_5O_3S$ $[M+H]^+$ 322.0968, found 322.0969; Calcd. for $C_{13}H_{15}N_5O_3SNa$ $[M+Na]^+$ 344.0788, found 344.0804.

(*Z*)-4-((2-(1H-Pyrrol-2-yl)oxazol-5(4H)-ylidene)methyl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide (149): $Pd(OAc)_2$ (1.98 mg, 0.02 mmol) was added to the solution of amide **148** (100 mg, 0.31 mmol) in CH_2Cl_2/TFA (1.5 mL/1 mL) and stirred for 1 h. After the starting material was consumed, the reaction mixture was concentrated and partitioned between

half saturated $NaHCO_3$ solution and EtOAc. The organic layer was dried (Na_2SO_4), concentrated and purified by column chromatography (hexane/EtOAc, 20:80) providing oxazole **149** (87 mg, 87%) as a yellowish powder; m.p 193-195 ℃; ^{1}H NMR (300 MHz, DMSO-d_6): δ = 11.98 (s, 1H), 8.12 (d, *J* = 1.0 Hz, 1H), 7.59 (s, 1H), 7.05-7.02 (m, 1H), 6.71-6.69 (m, 1H), 6.22-6.19 (m, 1H), 5.73 (t, *J* = 2.2 Hz, 1H), 4.73 (d, *J* = 2.2 Hz, 2H), 2.82 (s, 6H); ^{13}C NMR (75 MHz): δ = 156.9, 153.0, 137.1, 137.0, 124.2, 118.7, 114.9, 113.4, 109.9, 93.0, 58.2, 38.4; IR (neat, cm^{-1}): 3168, 3143, 2972, 1714, 1667, 1430, 1393, 1153, 1091, 991, 946, 803, 729; HR-ESIMS (m/z): Calcd. for $C_{13}H_{16}N_5O_3S$ $[M+H]^+$ 322.0968, found 322.0967; Calcd. for $C_{13}H_{15}N_5O_3SNa$ $[M+Na]^+$ 344.0788, found 344.0794.

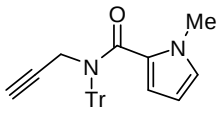
(*Z*)-4-((2-(1H-Pyrrol-2-yl)oxazol-5(4H)-ylidene)bromomethyl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide (151): Amide **148** (150 mg, 0.46 mmol) was dissolved in dry THF (5 mL). To this mixture, $Pd(OAc)_2$ (15 mg, 0.02 mmol), $CuBr_2$ (205 mg, 0.92 mmol) and LiBr (40 mg, 0.46 mmol) were added and stirred at r.t. for 30 min. The resulting mixture was cooled to 0℃ followed by additi on of EtOAc and $NaHCO_3$ solution. The layers were separated and aqueous layer was repeatedly extracted with EtOAc. The combined organic extracts was dried (Na_2SO_4), concentrated and purified by flash chromatography (hexane/EtOAc, 50:50) to give bromooxazole **151** (60 mg, 33%) as a white solid; m.p <240 ℃; ^{1}H NMR (DMSO-



Tentative

d_6): δ = 11.99 (s, 1H), 8.22 (s, 1H), 7.72 (s, 1H), 7.05 (s, 1H), 6.64 (s, 1H), 6.20 (d, *J* = 1.7 Hz, 1H), 4.78 (s, 2H), 4.73 (d, *J* = 2.2 Hz, 2H), 2.84 (s, 6H); ^{13}C NMR: δ = 157.2, 151.7, 136.9, 136.8, 124.6, 118.3, 115.9, 113.7, 110.0, 90.2, 61.2, 38.4; IR (neat, cm^{-1}): 3165, 3083, 2922, 1698, 1655, 1458, 1384, 1275, 1170, 1125, 1070, 957, 833, 727; HR-ESIMS (m/z): Calcd. for $C_{13}H_{15}BrN_5O_3S$ $[M+H]^+$ 400.0073, found 400.0066; Calcd. for $C_{13}H_{14}BrN_5O_3SNa$ $[M+Na]^+$ 421.9893, found 421.9893.

1-Methyl-*N*-(prop-2-ynyl)-*N*-trityl-1H-pyrrole-2-carboxamide (162): To an ice-



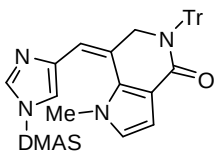
cold solution of a pyrrole derivative **144** (≈85%, 1.10 g, 2.81 mmol) in dry THF (25 mL), NaH (60%, 146 mg, 3.65 mmol) was added and the solution was allowed to warm to 20 ℃ o ver a period of 10-15 min. The solution was cooled back to 0 ℃ and MeI (0.88 mL, 1 4.1 mmol) was added dropwise and stirring was continued for 1 h at r.t. The resulting mixture was quenched with NH_4Cl solution and extracted repeatedly with EtOAc. The organic extracts were combined, washed with brine solution, dried (Na_2SO_4) and concentrated to give a brown solid. The crude material was purified on silica gel (hexane/EtOAc, 70:30) to obtain methyl protected derivative **162** (795 mg, 70%) as a white solid; m.p 200-202 ℃; ^{1}H NMR: δ = 7.51-7.49 (m, 6H), 7.29-7.25 (m, 6H), 7.22-7.19 (m, 3H), 6.98 (dd, *J* = 4.0, 2.2 Hz, 1H), 6.68 (t, *J* = 2.1 Hz, 1H), 6.14 (dd, *J* = 4.0, 2.5 Hz, 1H), 4.47 (d, *J* = 2.3 Hz, 2H), 3.58 (s, 3H), 1.76 (t, *J* =

2.3 Hz, 1H); ^{13}C NMR: δ = 166.5, 143.3, 129.7, 127.9, 127.7, 127.0, 126.6, 112.7, 107.1, 80.7, 76.8, 70.6, 41.5, 35.8; IR (neat, cm^{-1}): 3311, 3128, 3056, 1620, 1414, 1337, 1249, 1116, 967, 904, 742, 697; HR-ESIMS (m/z): Calcd. for $C_{28}H_{24}N_2ONa$ $[M+Na]^+$ 427.1718, found 427.1798; Calcd. for $C_{28}H_{24}N_2OK$ $[M+K]^+$ 443.1520, found 443.1520.

***N*-(3-(1-(*N*,*N*-Dimethylsulfamoyl)-1H-imidazol-4-yl)prop-2-ynyl)-1-methyl-*N*-trityl-1H-pyrrole-2-carboxamide (163):** 4-Iodoimidazole **67** (462 mg, 1.53 mmol), alkyne **162** (926 mg, 2.29 mmol), K_2CO_3 (422 mg, 3.06 mmol), CuI (15 mg, 0.08 mmol) and $Pd(PPh_3)_2Cl_2$ (27 mg, 0.04 mmol) were placed in a reaction flask. To the above reaction mixture dry THF (25 mL) was added and N_2 was bubbled through it for 3-5 min. The heterogeneous mixture was stirred at 55 ℃ overnight. The reaction mixture was cooled to r.t. and water (15 mL) was added and the layers separated. The aqueous layer was extracted with EtOAc. The combined organic extracts were dried (Na_2SO_4) and concentrated to brown solids. The crude product was purified by flash chromatography (CH_2Cl_2→hexane/EtOAc, 50:50) to give product **163** (566 mg, 64%) as a yellowish solid; m.p 189-191 ℃; ^{1}H NMR: δ = 7.70 (d, *J* = 1.1 Hz, 1H), 7.54-7.52 (m, 6H), 7.29-7.26 (m, 6H), 7.20-7.18 (m, 3H), 6.99-6.98 (m, 2H), 6.67 (t, *J* = 2.1 Hz, 1H), 6.14 (dd, *J* = 4.0, 2.5 Hz, 1H), 4.67 (s, 2H), 3.58 (s, 3H), 2.85 (s, 6H); ^{13}C NMR: δ = 166.8, 143.3, 136.2, 129.7, 127.9, 127.7, 127.3, 126.6, 125.6, 121.1, 113.0, 107.3, 88.2, 76.6, 74.6, 42.3,

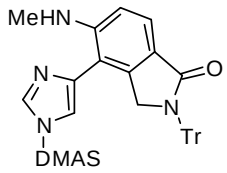
38.3, 35.7; IR (neat, cm^{-1}): 3148, 3085, 2980, 2239, 1736, 1659, 1437, 1392, 1175, 1087, 960, 828, 777, 704; HR-ESIMS (m/z): Calcd. for $C_{33}H_{31}N_5O_3SNa$ $[M+Na]^+$ 600.2040, found 600.2057; Calcd. for $C_{33}H_{31}N_5O_3SK$ $[M+K]^+$ 616.1779, found 616.1775.

(*Z*)-*N*,*N*-Dimethyl-4-((1-methyl-4-oxo-5-trityl-5,6-dihydro-1H-pyrrolo[3,2-c]pyridin-7(4H)-ylidene)methyl)-1H-imidazole-1-sulfonamide (164): The

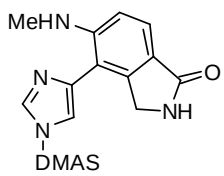


alkyne **163** (150 mg, 0.26 mmol) and $Pd(OAc)_2$ (9.0 mg, 0.013 mmol) were dissolved in dry DMF (3 mL) and stirred at 80 ℃ for 24 h. The reaction mixture was partitioned between H_2O and EtOAc. The organic extract was washed with brine solution, dried (Na_2SO_4), concentrated, and purified by column chromatography (hexane/EtOAc, 40:60) to give pyridine derivative **164** (79 mg, 52%) as a pale yellow solid; m.p 172-176 ℃; ^{1}H NMR: δ = 7.92 (d, *J* = 1.1 Hz, 1H), 7.55 (d, *J* = 7.5 Hz, 6H), 7.23 (t, *J* = 7.6Hz, 6H), 7.18 (s, 1H), 7.14-7.12 (m, 3H), 6.56 (d, *J* = 2.9 Hz, 6H), 6.52 (d, *J* = 2.9 Hz, 1H), 6.40 (s, 1H), 4.05 (s, 2H), 3.15 (s, 3H), 2.93 (s, 6H); ^{13}C NMR: δ = 165.9, 143.8, 140.2, 136.9, 134.2, 129.0, 127.6, 126.6, 126.1, 126.0, 120.0, 116.4, 116.3, 109.0, 76.0, 57.1, 38.4, 36.4; IR (neat, cm^{-1}): 3111, 3022, 2921, 1650, 1595, 1448, 1389, 1262, 1170, 1074, 961, 800, 721; HR-ESIMS (m/z): Calcd. for $C_{33}H_{32}N_5O_3S$ $[M+H]^+$ 578.2220, found 578.2199; Calcd. for $C_{33}H_{31}N_5O_3SNa$ $[M+Na]^+$ 600.2040, found 600.2051.

***N*,*N*-Dimethyl-4-(5-(methylamino)-3-oxo-2-tritylisoindolin-4-yl)-1H-imidazole-1-sulfonamide (170):** N_2 was bubbled through solution of the alkyne **163** (150 mg, 0.259 mmol), $AuCl(PPh_3)$ (13 mg, 0.025 mmol) in dry dioxane (15 mL) for 2-3 min and then the solution was heated to 115 ℃ in sealed tube for 24 h. The reaction mixtu re was concentrated and purified by column chromatography (hexane/EtOAc, 30:70) providing pale yellowish solid of aniline derivative **170** (60 mg, 40%); ^{1}H NMR: δ = 7.94-7.92 (m, 2H), 7.66 (d, *J* = 8.6 Hz, 1H), 7.30-7.25 (m, 15H), 6.84 (s, 1H), 6.76 (d, *J* = 8.6 Hz, 1H), 4.27 (s, 2H), 2.96 (d, *J* = 4.6 Hz, 3H), 2.72 (s, 6H); ^{13}C NMR: δ = 169.7, 151.2, 143.4, 140.4, 140.2, 134.9, 130.1, 127.7, 127.1, 125.5, 121.2, 114.1, 110.8, 108.4, 73.8, 54.9, 38.4, 30.4; IR (neat, cm^{-1}): 3307, 3254, 3126, 2923, 2234, 1673, 1601, 1444, 1372, 1278, 1170, 1084, 961, 907, 751, 723; HR-ESIMS (m/z): Calcd. for $C_{33}H_{32}N_5O_3S$ $[M+H]^+$ 578.2220, found 578.2215; Calcd. for $C_{33}H_{31}N_5O_3SNa$ $[M+Na]^+$ 600.2040, found 600.2055.

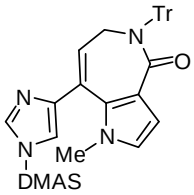


***N*,*N*-Dimethyl-4-(5-(methylamino)-3-oxoisoindolin-4-yl)-1H-imidazole-1-sulfonamide (171):** A solution of aniline derivative **170** (55.0 mg, 0.095 mmol) in TFA/CH_2Cl_2 (1 mL/2 mL) was stirred at r.t. for 3 h. Then the reaction mixture was concentrated, dissolved in EtOAc and partitioned with half saturated solution of $NaHCO_3$. The organic layer was dried (Na_2SO_4), concentrated and purified on silica gel (EtOAc/MeOH,



98:2) obtaining amide **171** (30 mg, 94%) as a white solid; m.p 226-227 ℃; ^{1}H NMR: δ = 7.96 (s, 1H), 7.64 (d, *J* = 8.6 Hz, 1H), 7.27 (s, 1H), 6.73 (d, *J* = 8.6 Hz, 1H), 4.35 (s, 2H), 2.90 (s, 3H), 2.87 (s, 6H); ^{13}C NMR: δ = 151.3, 143.1, 139.7, 135.4, 125.1, 119.4, 114.7, 110.8, 109.6, 46.6, 38.3, 30.3, 29.7; IR (neat, cm^{-1}): 3305, 3175, 3066, 2920, 2439, 2320, 1668, 1597, 1487, 1383, 1279, 1164, 966, 822, 730; HR-ESIMS (m/z): Calcd. for $C_{14}H_{18}N_5O_3S$ $[M+H]^+$ 336.1125, found 336.1118; Calcd. for $C_{14}H_{17}N_5O_3SNa$ $[M+Na]^+$ 358.0944, found 358.0948.

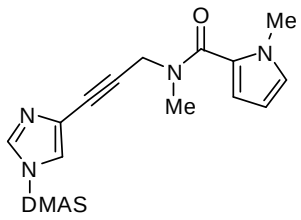
***N*,*N*-Dimethyl-4-(1-methyl-4-oxo-5-trityl-1,4,5,6-tetrahydropyrrolo[3,2-c]azepin-8-yl)-1H-imidazole-1-sulfonamide (173):** A solution of alkyne **163**



(100 mg, 0.173 mmol) and $AuCl_3$ (5.24 mg, 0.017mmol) in dry dioxane (10 mL) was heated to 60 ℃ in sealed tube for overnight. The reaction mixture was concentrated purified by flash chromatography (hexane/EtOAc, 25:75) providing azepin **173** in 43% yield; m.p 225-228 ℃; ^{1}H NMR: δ = 7.97 (s, 1H), 7.39-7.38 (m, 6H), 7.25-7.21 (m, 6H), 7.17-7.13 (m, 4H), 6.61 (s, 2H), 6.52 (t, *J* = 7.5 Hz, 1H), 4.07-4.04 (m, 1H), 3.71-3.66 (m, 1H), 3.32 (s, 3H), 2.97 (s, 6H); ^{13}C NMR: δ = 166.4, 144.2, 141.7, 136.9, 130.2, 129.5, 128.5, 127.6, 127.5, 126.3, 125.1, 124.8, 115.2, 111.4, 77.6, 45.6, 38.4, 36.9; IR (neat, cm^{-1}): 3133, 3122, 2915, 1637, 1593, 1492, 1454, 1393, 1260, 1171, 1081, 955, 914, 837, 729; HR-ESIMS (m/z): Calcd. for

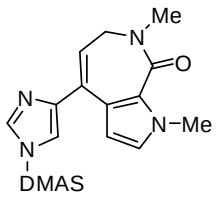
$C_{33}H_{32}N_5O_3S$ $[M+H]^+$ 578.2220, found 578.2207; Calcd. for $C_{33}H_{31}N_5O_3SNa$ $[M+Na]^+$ 600.2040, found 600.2058.

***N*-(3-(1-(*N*,*N*-Dimethylsulfamoyl)-1H-imidazol-4-yl)prop-2-ynyl)-*N*-1-dimethyl-1H-pyrrole-2-carboxamide (175):** 4-Iodoimidazole **67** (343 mg, 1.14 mmol), alkyne **174** (260 mg, 1.48 mmol),[137] CuI (10.7 mg, 0.057 mmol) and $Pd(PPh_3)_2Cl_2$ (20.0 mg, 0.028 mmol) were placed in a reaction flask. To the above reaction mixture 1:1 mixture of dry THF (5 mL) and triethyl amine (5 mL) was added and N_2 was bubbled through it for 3-5 min. The solution was stirred at 60 ℃ for 15 h. The reaction mixture was concentrated and purified by flash chromatography (hexane/EtOAc, 30:70→EtOAc) to give product **175** (338 mg, 85%) as a pale yellowish solid; m.p 135-137 ℃; ^{1}H NMR: δ = 7.83 (s, 1H), 7.34 (s, 1H), 6.70 (s, 1H), 6.57(s, 1H), 6.08 (t, *J* = 3.1 Hz, 1H), 4.54 (s, 2H), 3.79 (s, 3H), 3.23 (s, 3H), 2.87 (s, 6H); ^{13}C NMR (75 MHz): δ = 163.8, 136.6, 126.9, 125.7, 124.5, 121.0, 113.8, 107.1, 86.5, 38.3, 36.0; IR (neat, cm^{-1}): 3132, 3117, 2961, 1618, 1532, 1456, 1380, 1324, 1243, 1171, 1085, 958, 841, 722; HR-ESIMS (m/z): Calcd. for $C_{15}H_{20}N_5O_3S$ $[M+H]^+$ 350.1281, found 350.1283; Calcd. for $C_{15}H_{19}N_5O_3SNa$ $[M+Na]^+$ 372.1101, found 372.1119.



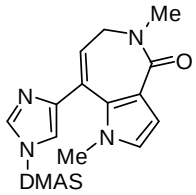
4-(1,7-Dimethyl-8-oxo-1,6,7,8-tetrahydropyrrolo[2,3-c]azepin-4-yl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide (176) and 4-(1,5-Dimethyl-4-oxo-1,4,5,6-tetrahydropyrrolo[3,2-c]azepin-8-yl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide (177): A solution of alkyne **175** (200 mg, 0.57 mmol) and $AuCl_3$ (17.3 mg, 0.057mmol) in dry dioxane (15 mL) was heated to 65 ℃ in sealed tube for overnight. The reaction mixture was concentrated purified by flash chromatography (hexane/EtOAc, 30:70→ EtOAc) providing two azepin **176** and **177**.

Azepine 176 (82 mg, 41%, pale yellowish solid): m.p 212-215 ℃; ^{1}H NMR: δ =



7.89 (d, *J* = 1.3 Hz, 1H), 7.25 (s, 1H), 6.77 (d, *J* = 2.9 Hz, 1H), 6.70 (t, *J* = 7.0 Hz, 1H), 6.31(d, *J* = 2.9 Hz, 1H), 3.97 (s, 3H), 3.78 (d, *J* = 7.0 Hz, 1H), 3.15 (s, 3H), 2.84 (s, 6H); ^{13}C NMR: δ = 162.2, 142.1, 136.7, 132.7, 127.3, 127.1, 124.5, 120.1, 115.3, 106.7, 47.3, 38.3, 36.7, 34.7; IR (neat, cm^{-1}): 3137, 3041, 2924, 1727, 1619, 1481, 1386, 1262, 1174, 1099, 959, 821, 721; HR-ESIMS (m/z): Calcd. for $C_{15}H_{20}N_5O_3S$ $[M+H]^+$ 350.1281, found 350.1286; Calcd. for $C_{15}H_{19}N_5O_3SNa$ $[M+Na]^+$ 372.1101, found 372.1118.

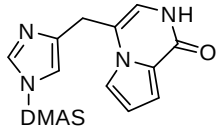
Azepine 177 (70 mg, 35%, pale yellowish solid): m.p 229-232 ℃; ^{1}H NMR: δ =



7.89 (s, 1H), 7.00 (s, 1H), 6.74 (d, *J* = 2.9 Hz, 1H), 6.69 (d, *J* = 2.9 Hz, 1H), 6.58 (t, *J* = 7.6 Hz, 1H), 3.74 (d, *J* = 7.6 Hz, 1H), 3.35 (s, 3H), 3.16 (s, 3H), 2.85 (s, 6H); ^{13}C NMR: δ = 166.0, 141.3, 136.8,

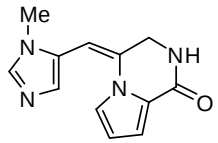
130.6, 128.6, 125.3, 125.2, 123.8, 115.1, 109.9, 47.3, 38.3, 36.7, 35.4; IR (neat, cm^{-1}): 3131, 3088, 2955, 1603, 1556, 1496, 1379, 1262, 1169, 1087, 959, 861, 727; HR-ESIMS (m/z): Calcd. for $C_{15}H_{20}N_5O_3S$ $[M+H]^+$ 350.1281, found 350.1283; Calcd. for $C_{15}H_{19}N_5O_3SNa$ $[M+Na]^+$ 372.1101, found 372.1115.

***N*,*N*-Dimethyl-4-((1-oxo-1,2-dihydropyrrolo[1,2-a]pyrazin-4-yl)methyl)-1H-imidazole-1-sulfonamide (182):** A solution of pyrazinone **125** (100 mg, 0.31 mmol) in TFA (3 mL) was stirred at r.t. for 20 h. Then reaction mixture was concentrated and dissolved in EtOAc. The organic layer was washed with aq. $NaHCO_3$ solution, dried (Na_2SO_4) and purified by column chromatography to obtain isomeric pyrazinone **182** (87 mg, 87%) as a white solid; m.p 202-203 ℃; ^{1}H NMR: δ = 10.10 (brs, 1H), 7.86 (d, *J* = 1.1 Hz, 1H), 7.19-7.18 (m, 2H), 7.01 (s, 1H), 6.59 (dd, *J* = 3.6, 2.7 Hz, 1H), 6.39 (d, *J* = 5.1 Hz, 1H), 3.96 (s, 2H), 2.81 (s, 6H); ^{13}C NMR: δ = 157.6, 139.0, 136.8, 124.1, 117.3, 115.2, 112.7, 112.1, 111.1, 38.3, 28.6; IR (neat, cm^{-1}): 3293, 3159, 3121, 3008, 2894, 1680, 1633, 1473, 1380, 1275, 1168, 1083, 963, 841, 725; HR-ESIMS (m/z): Calcd. for $C_{13}H_{16}N_5O_3S$ $[M+H]^+$ 322.0968, found 322.0969; Calcd. for $C_{13}H_{15}N_5O_3SNa$ $[M+Na]^+$ 344.0788, found 344.0803.



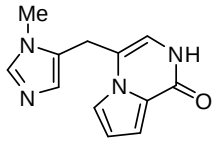
(*Z*)-4-((1-Methyl-1H-imidazol-5-yl)methylene)-2-trityl-3,4-dihydropyrrolo[1,2-a]pyrazin-1(2H)-one (185): To a ice-cold solution of pyrazinone **146** (1.00 g, 1.83 mmol) in dry CH_2Cl_2 (15 mL), MeOTf (0.24 mL, 2.19 mmol) was added dropwise and the resulting solution was stirred at r.t. for overnight. The reaction mixture was concentrated and dissolved in dry CH_3CN (15 mL). The reaction mixture was heated to reflux after adding benzylamine (0.42 mL, 3.84 mmol) for 7 h. H_2O (5 mL) was added to a reaction mixture and repeatedly extracted with EtOAc, dried (Na_2SO_4), concentrated and purified by chromatography (EtOAc→EtOAc/MeOH, 90:10) to obtain pale yellowish solid of a methyl protected imidazole derivative **185** (542 mg, 63%); m.p 230-233 ℃; ^{1}H NMR: δ = 7.54-7.53 (m, 7H), 7.29-7.26 (m, 6H), 7.20-7.16 (m, 4H), 6.87-6.86 (m, 1H), 6.76-6.75 (m, 1H), 6.16-6.15 (m, 1H), 5.83 (s, 1H), 4.09 (s, 2H), 3.47 (s, 3H); ^{13}C NMR: δ = 160.9, 142.8, 138.7, 132.8, 129.6, 128.8, 127.9, 126.7, 125.5, 120.7, 115.8, 112.3, 100.0, 76.2, 51.7, 31.7; IR (neat, cm^{-1}): 3174, 3000, 1666, 1552, 1448, 1391, 1297, 1202, 1098, 919, 737; HR-ESIMS (m/z): Calcd. for $C_{31}H_{27}N_4O$ $[M+H]^+$ 471.2179, found 471.2178; Calcd. for $C_{31}H_{26}N_4ONa$ $[M+Na]^+$ 493.1999, found 493.2007.

(*Z*)-4-((1-Methyl-1H-imidazol-5-yl)methylene)-3,4-dihydropyrrolo[1,2-a]pyrazin-1(2H)-one (186): A solution methyl protected imidazole derivative **185**



(200 mg, 0.42 mmol) in CH_2Cl_2/TFA (3 mL/2mL) was stirred at r.t. for 3 h. The reaction mixture was concentrated and residue was dissolved in EtOAc, washed with $NaHCO_3$ solution, dried (Na_2SO_4) and purified on silica gel (EtOAc→EtOAc/MeOH/NH_3, 80:18:2) to obtain trityl deprotected derivative **186** (70.3 mg, 72%) as yellowish film; ^{1}H NMR (MeOH-d_4): δ = 7.64 (s, 1H), 6.89-6.88 (m, 2H), 6.74-6.73 (m, 1H), 6.25 (t, *J* = 3.1 Hz, 1H), 6.15 (s, 1H), 4.25 (s, 2H), 3.40 (s, 3H); ^{13}C NMR (MeOH-d_4): δ = 161.0, 138.6, 132.0, 127.3, 126.2, 124.3, 122.1, 114.1, 111.4, 101.1, 45.8, 30.5; IR (neat, cm^{-1}): 3200, 3107, 2916, 1640, 1560, 1450, 1312, 1199, 1054, 930, 744; HR-ESIMS (m/z): Calcd. for $C_{12}H_{13}N_4O$ $[M+H]^+$ 229.1084, found 229.1083; Calcd. for $C_{12}H_{12}N_4ONa$ $[M+Na]^+$ 251.0903, found 251.0906.

4-((1-Methyl-1H-imidazol-5-yl)methyl)pyrrolo[1,2-a]pyrazin-1(2H)-one (187):

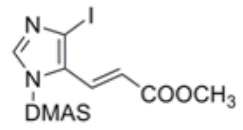


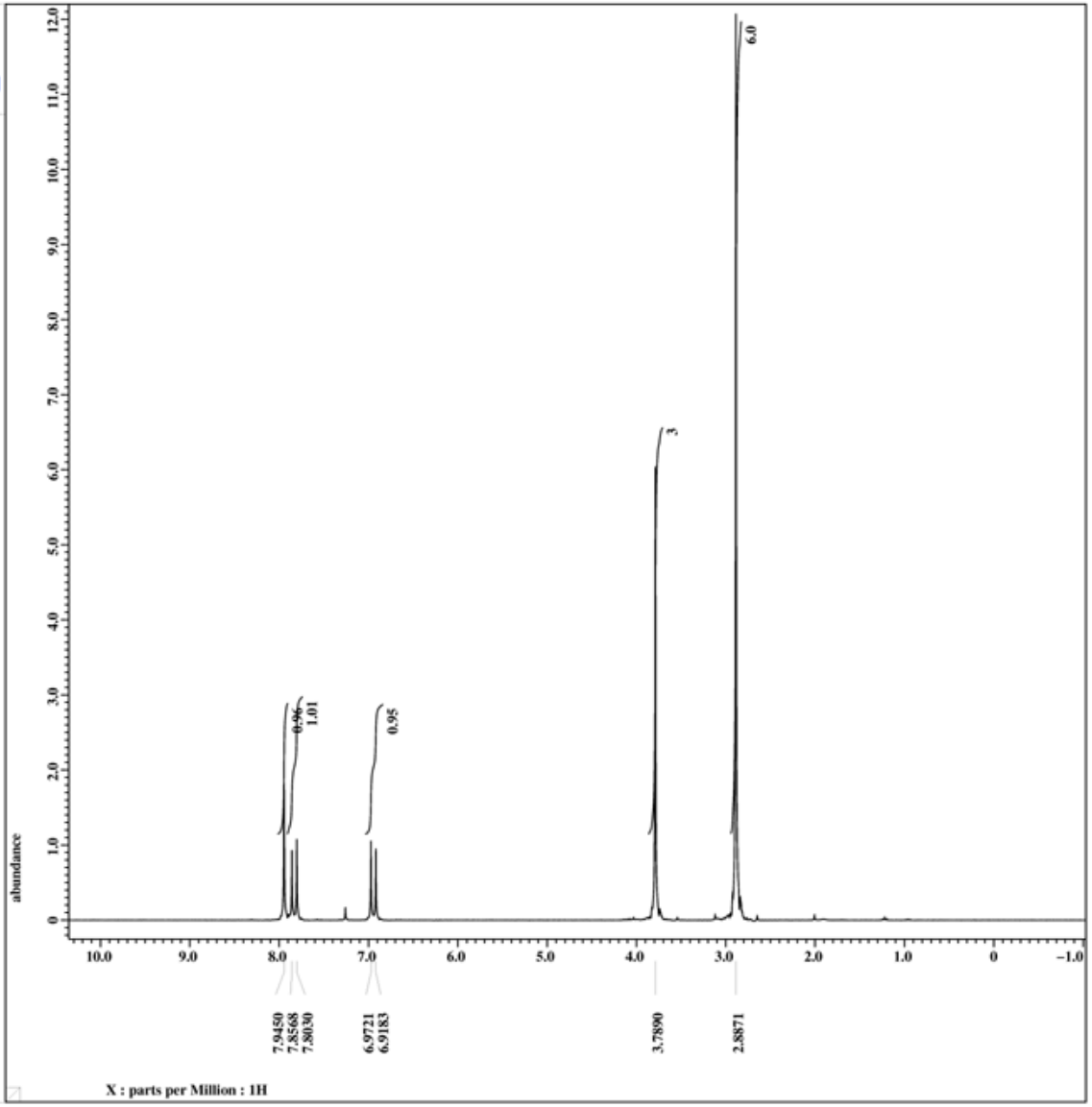
A pyrazinone **186** (60 mg, 0.26 mmol) was dissolved in TFA/H_2O (2 mL/1mL) and heated to reflux for overnight. The reaction mixture was concentrated and residue was dissolved in MeOH, neutralized with aq. NH_3, and preabsorbed on silica gel. The product was purified by chromatography (EtOAc/MeOH/NH_3, 80:18:2) to obtain isomerized derivative **187** (38 mg, 63%) as a yellowish film; ^{1}H NMR (MeOH-d_4): δ = 7.67 (s, 1H), 7.42

(s, 1H), 7.13-7.12 (m, 1H), 6.82 (s, 1H), 6.63 (t, *J* = 3.1 Hz, 1H), 6.20 (s, 1H), 4.10 (s, 2H), 3.65 (s, 3H); ^{13}C NMR (MeOH-d_4): δ = 157.2, 138.5, 126.8, 126.6, 123.7, 117.5, 117.0, 112.3, 111.7, 110.5, 30.6, 23.1; IR (neat, cm^{-1}): 3170, 3060, 2908, 1633, 1507, 1468, 1402, 1342, 1200, 1104, 798, 718; HR-ESIMS (m/z): Calcd. for $C_{12}H_{13}N_4O$ $[M+H]^+$ 229.1084, found 229.1089; Calcd. for $C_{12}H_{12}N_4ONa$ $[M+Na]^+$ 251.0903, found 251.0914.

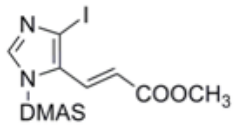
APPENDIX 1
^{1}H AND ^{13}C NMR SPECTRA OF
(E)-Methyl 3-(4-iodo-1-dimethylsulfamoylimidazol-5-yl)-2-propenoate (64)

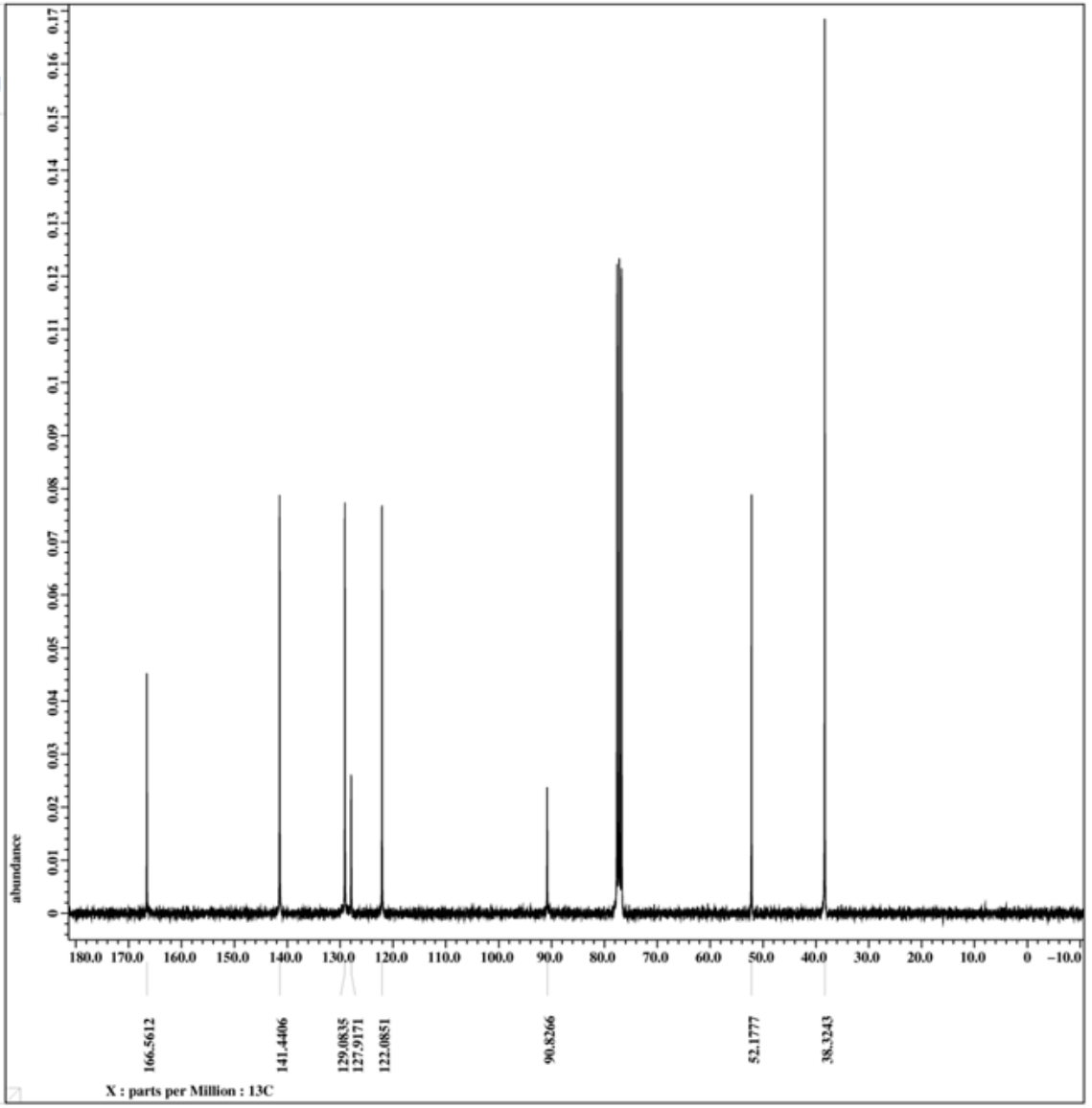
```
Filename          = MRB_II_246_wittig_pro
Author            = delta
Experiment        = single_pulse.ex2
Sample_id         = S#470067
Solvent           = CHLOROFORM-D
Creation_time     = 11-FEB-2008 13:33:15
Revision_time     = 28-OCT-2010 01:35:05
Current_time      =  5-NOV-2010 00:42:27

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    = 7.0586013[T] (300[MHz
X_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]
Irr_domain        = 1H
Irr_freq          = 300.52965592[MHz]
Irr_offset        = 5[ppm]
Tri_domain        = 1H
Tri_freq          = 300.52965592[MHz]
Tri_offset        = 5[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 16
Total_scans       = 16

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]
Irr_mode          = Off
Tri_mode          = Off
Dante_presat      = FALSE
Initial_wait      = 1[s]
Recvr_gain        = 36
Relaxation_delay  = 5[s]
Repetition_time   = 7.90717696[s]
Temp_get          = 23.4[dC]
```





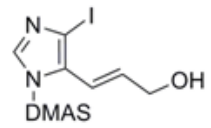
```
Filename          = MRB_II_246_wittig_car
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#470131
Solvent           = CHLOROFORM-D
Creation_time     = 11-FEB-2008 14:34:47
Revision_time     = 28-OCT-2010 01:38:22
Current_time      =  5-NOV-2010 00:45:18

Comment           = single pulse decouple
Data_format       = 1D REAL
Dim_size          = 52428
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = ECX 300
Spectrometer      = DELTA2_NMR

Field_strength    = 7.0586013[T] (300[MHz
X_acq_duration    = 2.76824064[s]
X_domain          = 13C
X_freq            = 75.56823426[MHz]
X_offset          = 100[ppm]
X_points          = 65536
X_prescans        = 4
X_resolution      = 0.36124027[Hz]
X_sweep           = 23.67424242[kHz]
Irr_domain        = 1H
Irr_freq          = 300.52965592[MHz]
Irr_offset        = 5[ppm]
Clipped           = FALSE
Mod_return        = 10
Scans             = 768
Total_scans       = 768

X_90_width        = 9.75[us]
X_acq_time        = 2.76824064[s]
X_angle           = 30[deg]
X_atn             = 8[dB]
X_pulse           = 3.25[us]
Irr_atn_dec       = 25[dB]
Irr_atn_noe       = 25[dB]
Irr_noise         = WALTZ
Decoupling        = TRUE
Initial_wait      = 1[s]
Noe               = TRUE
Noe_time          = 2[s]
Recvr_gain        = 50
Relaxation_delay  = 2[s]
Repetition_time   = 4.76824064[s]
Temp_get          = 23.3[dC]
```

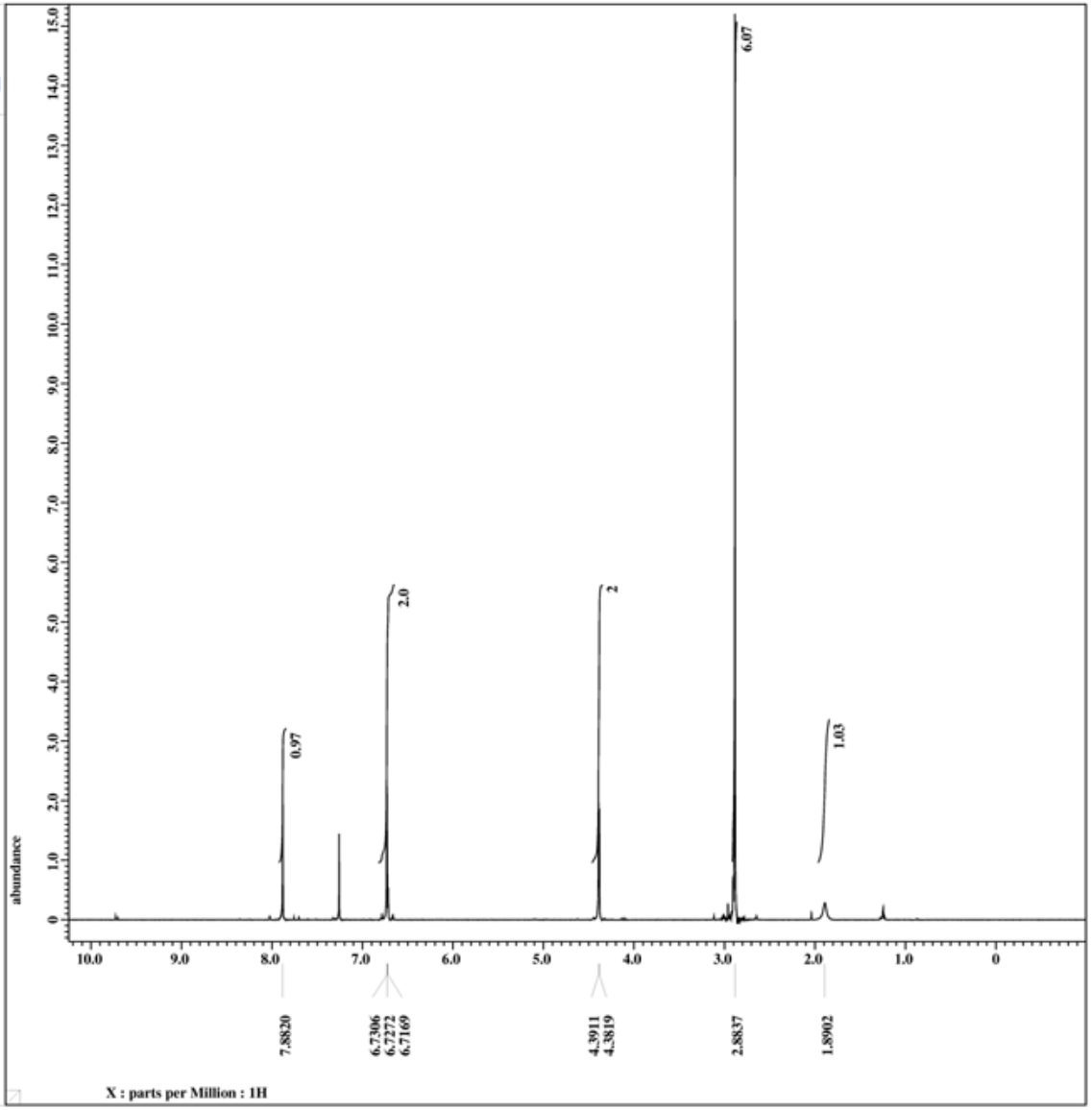




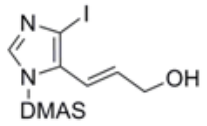
APPENDIX 2
^{1}H AND ^{13}C NMR SPECTRA OF
(*E*)-3-(4-Iodo-1-dimethylsulfamoylimidazol-5-yl)-2-propen-1-ol (65)

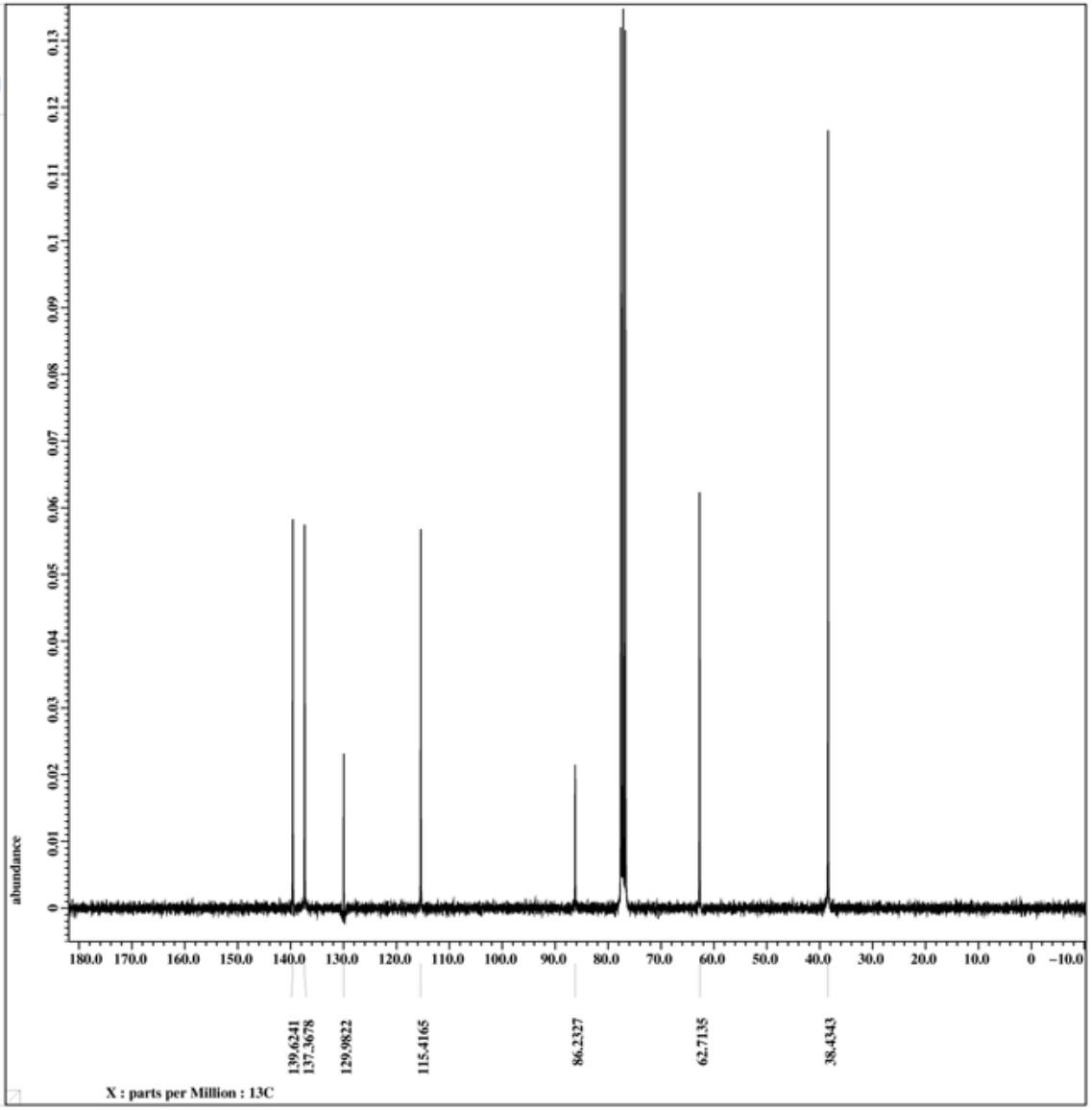
Filename	= MRB_II_261_proton-5.j
Author	= delta
Experiment	= single_pulse.ex2
Sample_id	= S#477259
Solvent	= CHLOROFORM-D
Creation_time	= 21-FEB-2008 13:29:20
Revision_time	= 5-NOV-2010 00:51:38
Current_time	= 5-NOV-2010 00:52:27
Comment	= single_pulse
Data_format	= 1D REAL
Dim_size	= 13107
Dim_title	= 1H
Dim_units	= [ppm]
Dimensions	= X
Site	= ECX 300
Spectrometer	= DELTA2_NMR
Field_strength	= 7.0586013[T] (300[MHz
X_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]
Irr_domain	= 1H
Irr_freq	= 300.52965592[MHz]
Irr_offset	= 5[ppm]
Tri_domain	= 1H
Tri_freq	= 300.52965592[MHz]
Tri_offset	= 5[ppm]
Clipped	= FALSE
Mod_return	= 1
Scans	= 16
Total_scans	= 16
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]
Irr_mode	= Off
Tri_mode	= Off
Dante_presat	= FALSE
Initial_wait	= 1[s]
Recvr_gain	= 46
Relaxation_delay	= 5[s]
Repetition_time	= 7.90717696[s]
Temp_get	= 23.2[dC]



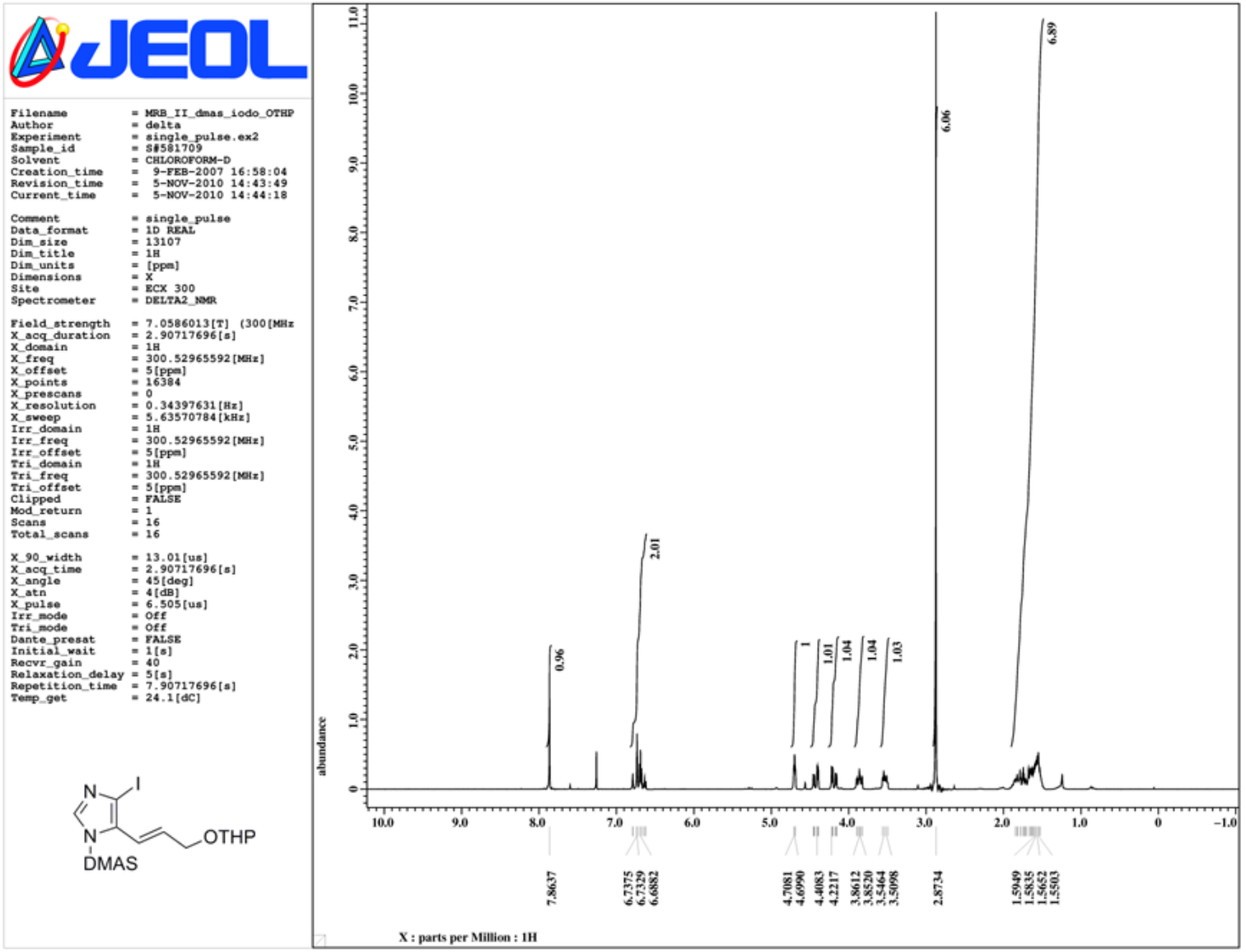


```
Filename          = MRB_II_261_carbon-3.j
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#619859
Solvent           = CHLOROFORM-D
Creation_time     = 20-FEB-2008 19:02:25
Revision_time     =  8-DEC-2008 20:09:53
Current_time      =  5-NOV-2010 00:56:05

Comment           = single pulse decouple
Data_format       = 1D REAL
Dim_size          = 52428
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = ECX 300
Spectrometer      = DELTA2_NMR

Field_strength    = 7.0586013[T] (300[MHz
X_acq_duration    = 2.76824064[s]
X_domain          = 13C
X_freq            = 75.56823426[MHz]
X_offset          = 100[ppm]
X_points          = 65536
X_prescans        = 4
X_resolution      = 0.36124027[Hz]
X_sweep           = 23.67424242[kHz]
Irr_domain        = 1H
Irr_freq          = 300.52965592[MHz]
Irr_offset        = 5[ppm]
Clipped           = FALSE
Mod_return        = 10
Scans             = 1000
Total_scans       = 1000

X_90_width        = 9.75[us]
X_acq_time        = 2.76824064[s]
X_angle           = 30[deg]
X_atn             = 8[dB]
X_pulse           = 3.25[us]
Irr_atn_dec       = 25[dB]
Irr_atn_noe       = 25[dB]
Irr_noise         = WALTZ
Decoupling        = TRUE
Initial_wait      = 1[s]
Noe               = TRUE
Noe_time          = 2[s]
Recvr_gain        = 50
Relaxation_delay  = 2[s]
Repetition_time   = 4.76824064[s]
Temp_get          = 23.9[dC]
```



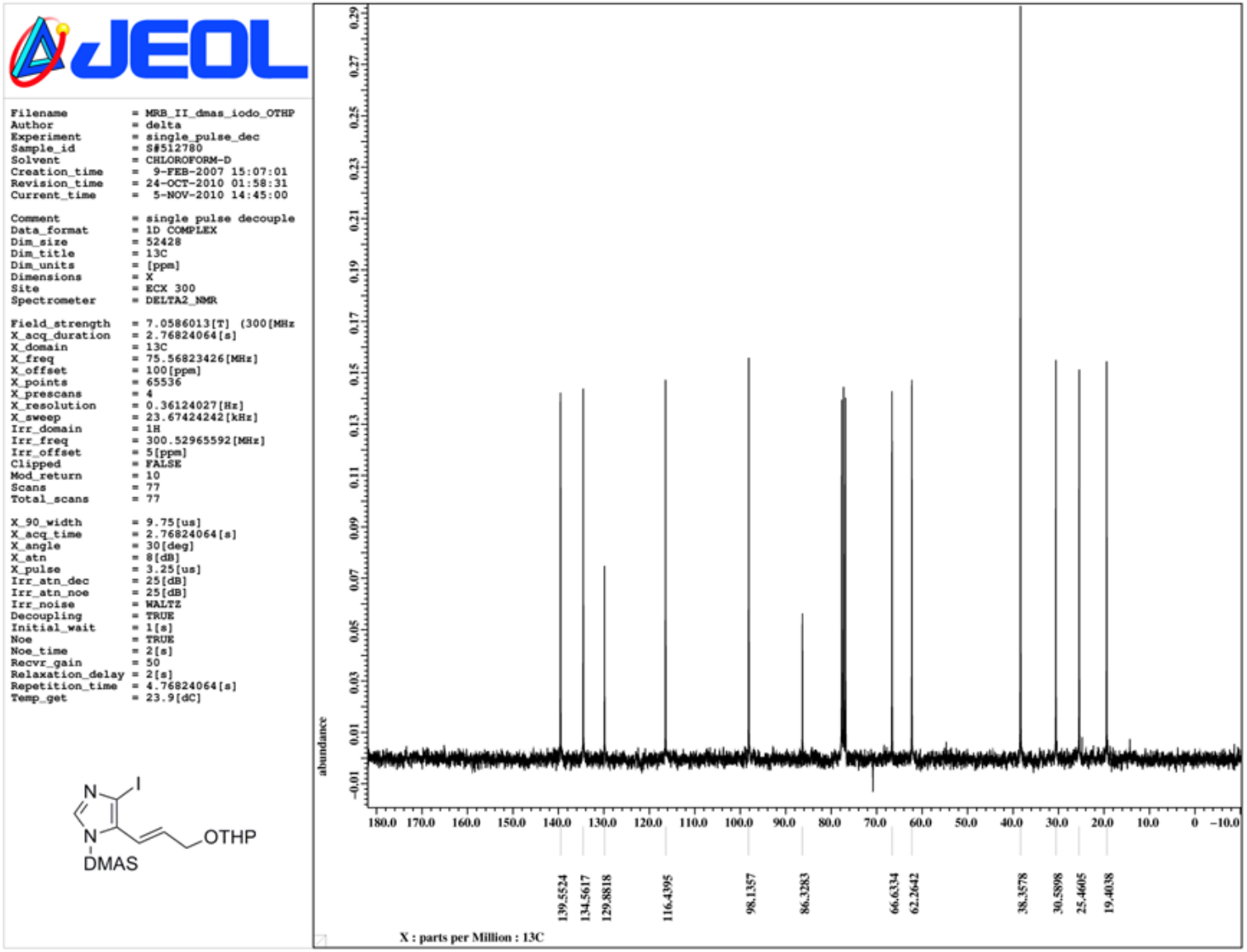


APPENDIX 3
^{1}H AND ^{13}C NMR SPECTRA OF
(*E*)-3-(4-Iodo-1-dimethylsulfamoylimidazol-5-yl)-1-(tetrahydro-2*H*-pyran-2-yloxy)-2-propene (54)



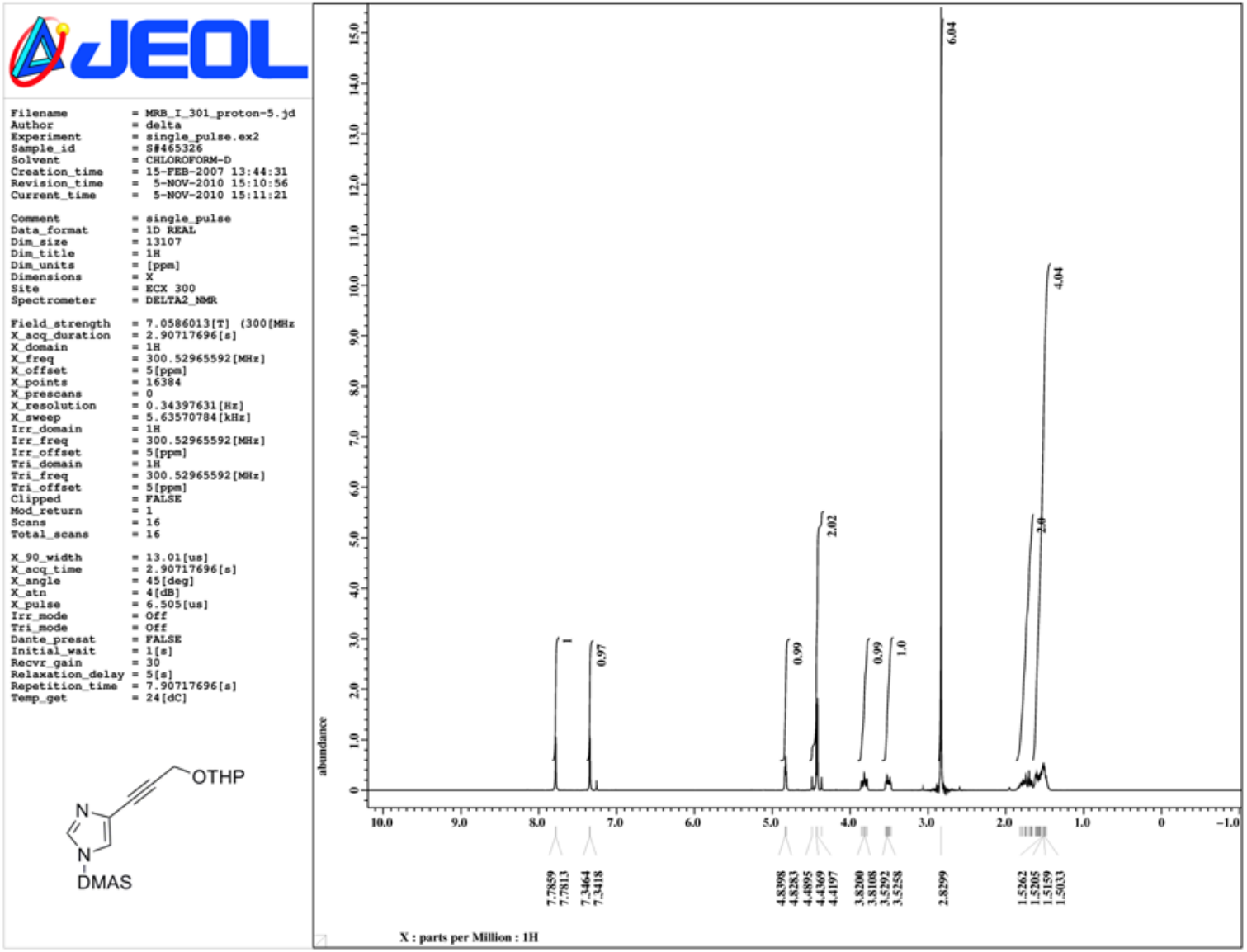
JEOL

```
Filename          = MRB_II_dmas_iodo_OTHP
Author            = delta
Experiment        = single_pulse.ex2
Sample_id         = S#581709
Solvent           = CHLOROFORM-D
Creation_time     =  9-FEB-2007 16:58:04
Revision_time     =  5-NOV-2010 14:43:49
Current_time      =  5-NOV-2010 14:44:18

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    = 7.0586013[T] (300[MHz
X_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]
Irr_domain        = 1H
Irr_freq          = 300.52965592[MHz]
Irr_offset        = 5[ppm]
Tri_domain        = 1H
Tri_freq          = 300.52965592[MHz]
Tri_offset        = 5[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 16
Total_scans       = 16

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]
Irr_mode          = Off
Tri_mode          = Off
Dante_presat      = FALSE
Initial_wait      = 1[s]
Recvr_gain        = 40
Relaxation_delay  = 5[s]
Repetition_time   = 7.90717696[s]
Temp_get          = 24.1[dC]
```

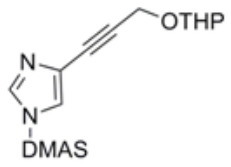


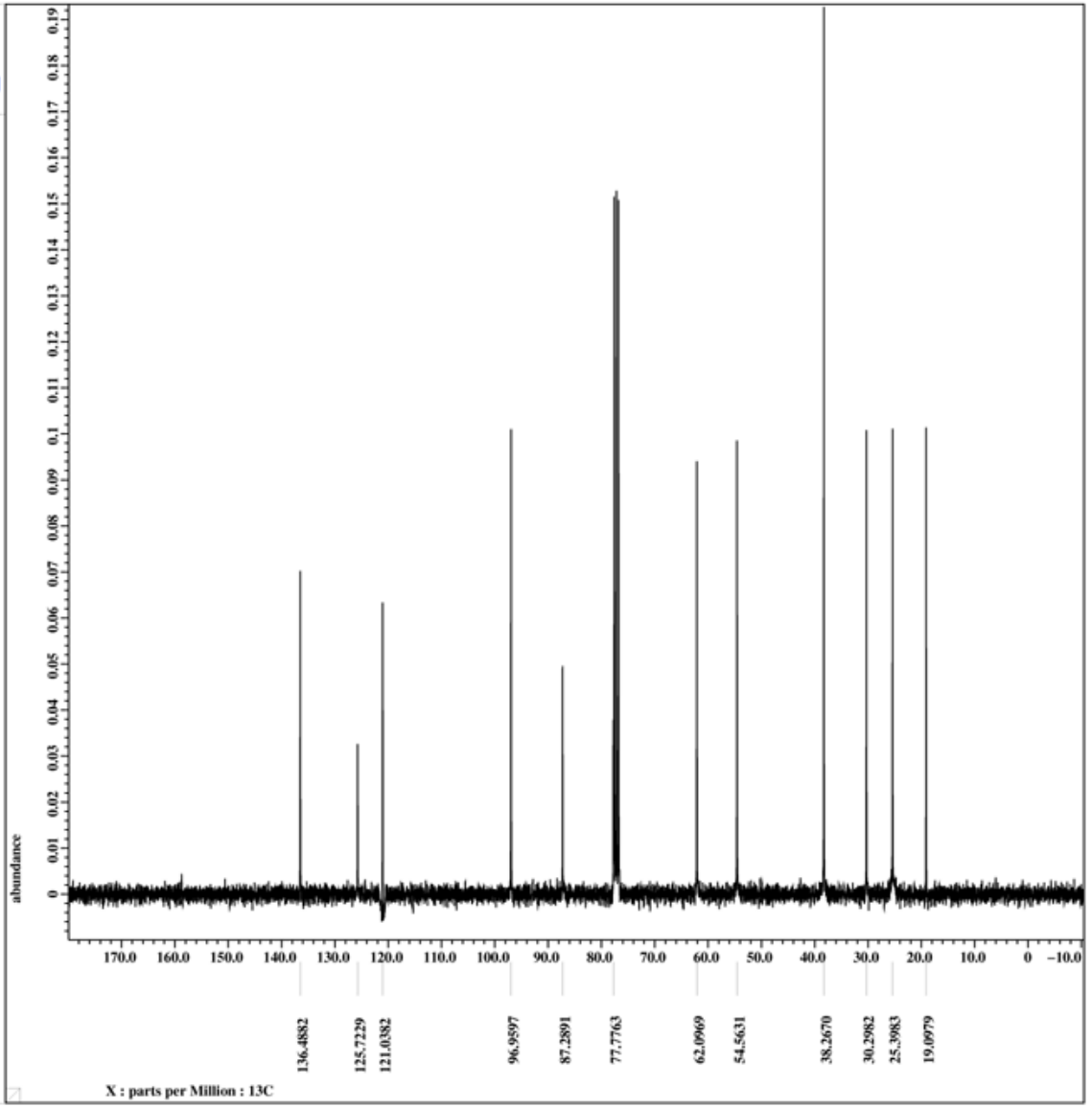
```
Filename          = MRB_II_dmas_iodo_OTHP
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#512780
Solvent           = CHLOROFORM-D
Creation_time     =  9-FEB-2007 15:07:01
Revision_time     = 24-OCT-2010 01:58:31
Current_time      =  5-NOV-2010 14:45:00

Comment           = single pulse decouple
Data_format       = 1D COMPLEX
Dim_size          = 52428
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = ECX 300
Spectrometer      = DELTA2_NMR

Field_strength    = 7.0586013[T] (300[MHz
X_acq_duration    = 2.76824064[s]
X_domain          = 13C
X_freq            = 75.56823426[MHz]
X_offset          = 100[ppm]
X_points          = 65536
X_prescans        = 4
X_resolution      = 0.36124027[Hz]
X_sweep           = 23.67424242[kHz]
Irr_domain        = 1H
Irr_freq          = 300.52965592[MHz]
Irr_offset        = 5[ppm]
Clipped           = FALSE
Mod_return        = 10
Scans             = 77
Total_scans       = 77

X_90_width        = 9.75[us]
X_acq_time        = 2.76824064[s]
X_angle           = 30[deg]
X_atn             = 8[dB]
X_pulse           = 3.25[us]
Irr_atn_dec       = 25[dB]
Irr_atn_noe       = 25[dB]
Irr_noise         = WALTZ
Decoupling        = TRUE
Initial_wait      = 1[s]
Noe               = TRUE
Noe_time          = 2[s]
Recvr_gain        = 50
Relaxation_delay  = 2[s]
Repetition_time   = 4.76824064[s]
Temp_get          = 23.9[dC]
```

APPENDIX 4
^{1}H AND ^{13}C NMR SPECTRA OF
1-(Tetrahydro-2*H*-pyran-2-yloxy)-3-(1-dimethylsulfamoylimidazol-4-yl)-2-propyne (69)

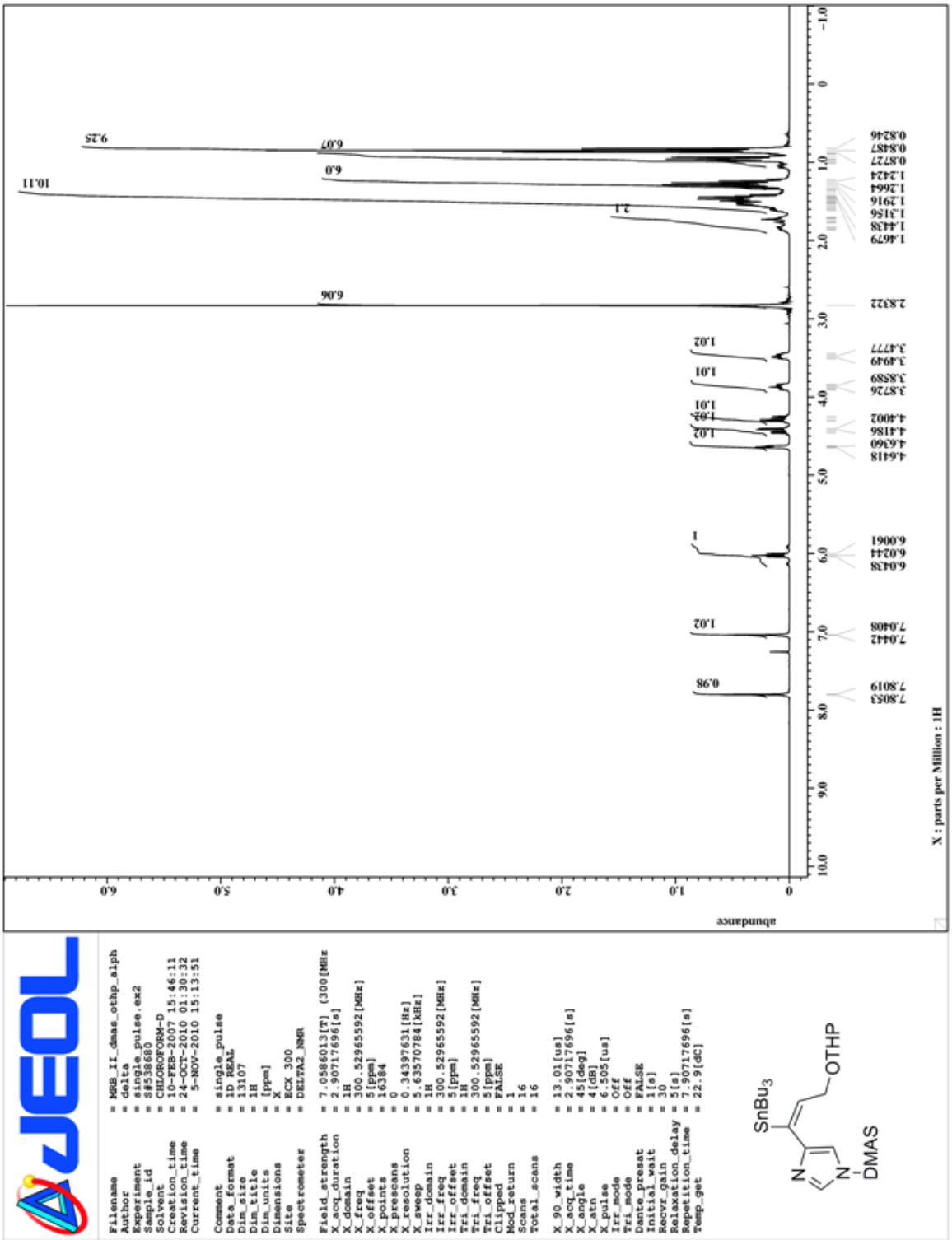

Filename = MRB_I_301_proton-5.jd
Author = delta
Experiment = single_pulse.ex2
Sample_id = S#465326
Solvent = CHLOROFORM-D
Creation_time = 15-FEB-2007 13:44:31
Revision_time = 5-NOV-2010 15:10:56
Current_time = 5-NOV-2010 15:11:21
Comment = single_pulse
Data_format = 1D REAL
Dim_size = 13107
Dim_title = 1H
Dim_units = [ppm]
Dimensions = X
Site = ECX 300
Spectrometer = DELTA2_NMR
Field_strength = 7.0586013[T] (300[MHz
X_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]
Irr_domain = 1H
Irr_freq = 300.52965592[MHz]
Irr_offset = 5[ppm]
Tri_domain = 1H
Tri_freq = 300.52965592[MHz]
Tri_offset = 5[ppm]
Clipped = FALSE
Mod_return = 1
Scans = 16
Total_scans = 16
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]
Irr_mode = Off
Tri_mode = Off
Dante_presat = FALSE
Initial_wait = 1[s]
Recvr_gain = 30
Relaxation_delay = 5[s]
Repetition_time = 7.90717696[s]
Temp_get = 24[dC]
OTHP
N
N
DMAS
abundance
6.04
4.04
2.02
2.0
1
0.97
0.99
0.99
1.0
7.7859
7.7813
7.3464
7.3418
4.8398
4.8283
4.4895
4.4369
4.4197
3.8200
3.8108
3.5292
3.5258
2.8299
1.5262
1.5205
1.5159
1.5033
X : parts per Million : 1H

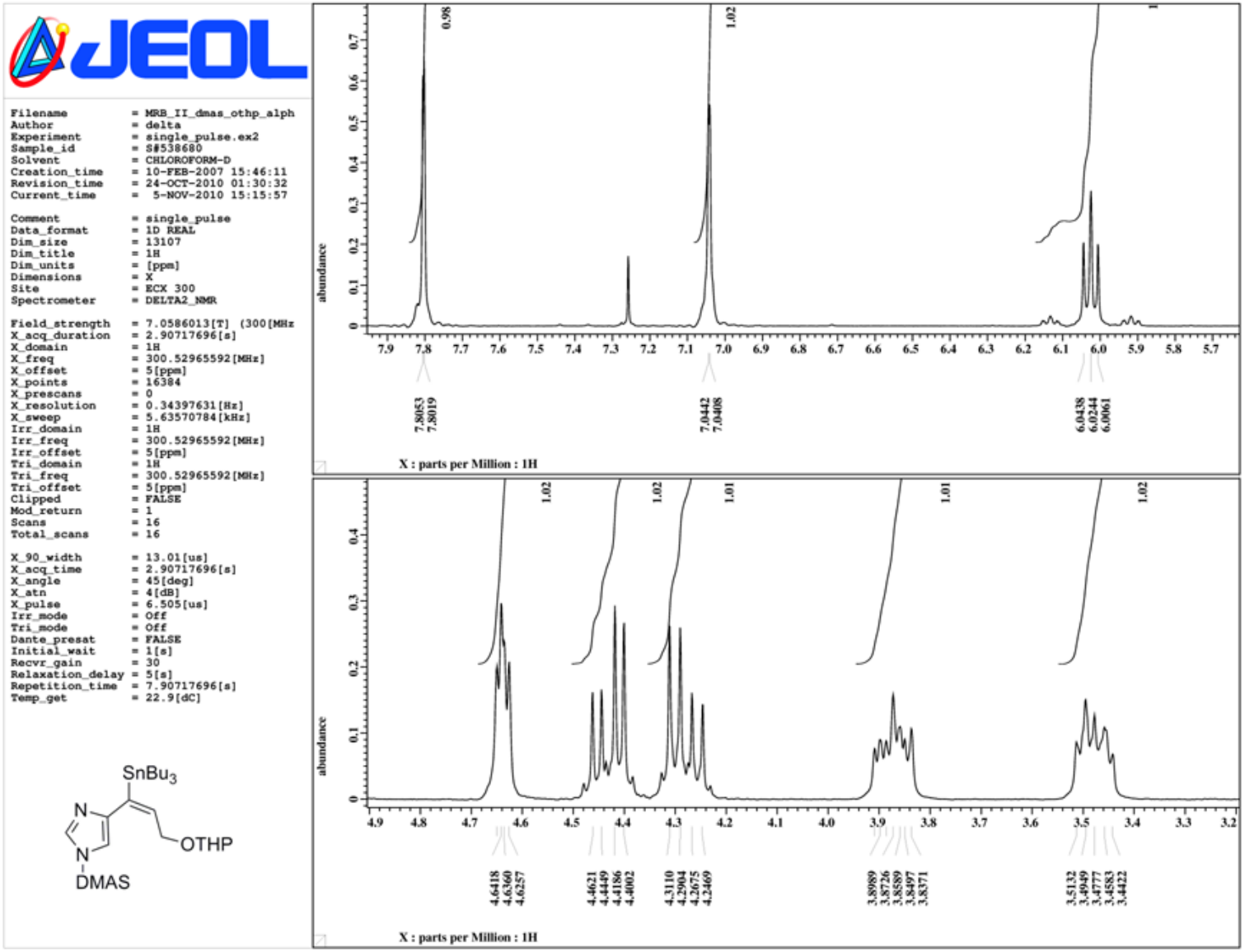
```
Filename          = MRB_I_301_carbon-3.jd
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#466800
Solvent           = CHLOROFORM-D
Creation_time     = 15-FEB-2007 13:58:08
Revision_time     = 24-OCT-2010 01:13:13
Current_time      =  5-NOV-2010 15:12:15

Comment           = single pulse decouple
Data_format       = 1D REAL
Dim_size          = 52428
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = ECX 300
Spectrometer      = DELTA2_NMR

Field_strength    = 7.0586013[T] (300[MHz
X_acq_duration    = 2.76824064[s]
X_domain          = 13C
X_freq            = 75.56823426[MHz]
X_offset          = 100[ppm]
X_points          = 65536
X_prescans        = 4
X_resolution      = 0.36124027[Hz]
X_sweep           = 23.67424242[kHz]
Irr_domain        = 1H
Irr_freq          = 300.52965592[MHz]
Irr_offset        = 5[ppm]
Clipped           = FALSE
Mod_return        = 10
Scans             = 152
Total_scans       = 152

X_90_width        = 9.75[us]
X_acq_time        = 2.76824064[s]
X_angle           = 30[deg]
X_atn             = 8[dB]
X_pulse           = 3.25[us]
Irr_atn_dec       = 25[dB]
Irr_atn_noe       = 25[dB]
Irr_noise         = WALTZ
Decoupling        = TRUE
Initial_wait      = 1[s]
Noe               = TRUE
Noe_time          = 2[s]
Recvr_gain        = 50
Relaxation_delay  = 2[s]
Repetition_time   = 4.76824064[s]
Temp_get          = 23.9[dC]
```





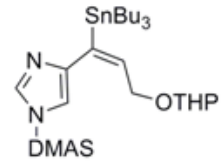
APPENDIX 5
^{1}H AND ^{13}C NMR SPECTRA OF
(*E*)-1-(Tetrahydro-2*H*-pyran-2-yloxy)-3-tributylstannyl-3-(1-dimethylsulfamoylimidazol-4-yl)-2-propene (57)

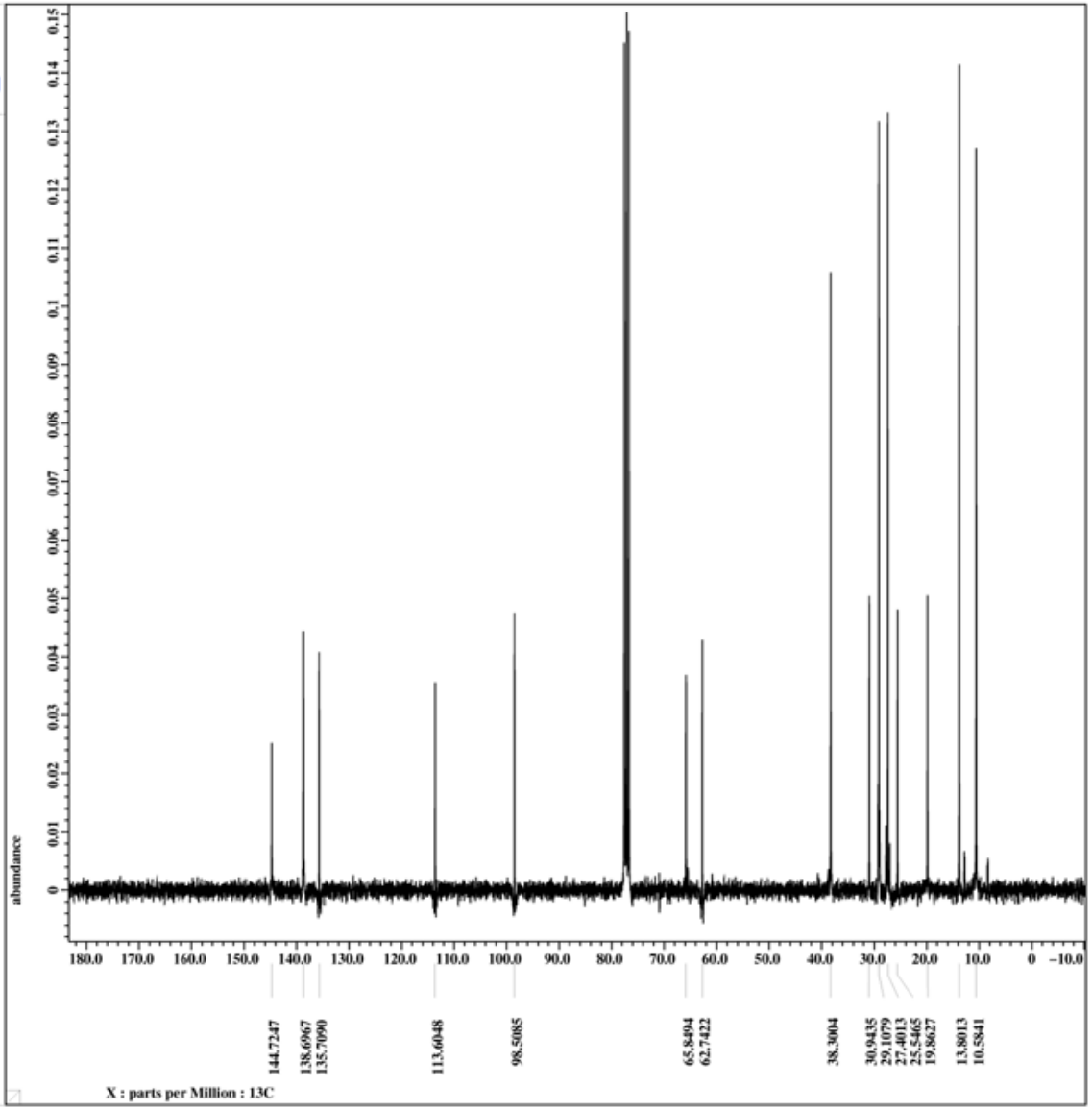

JEOL
Filename = MRB_II_dmas_othp_alph
Author = delta
Experiment = single_pulse.ex2
Sample_id = s#5380680
Solvent = CHLOROFORM-D
Creation_time = 10-FEB-2007 15:46:11
Revision_time = 24-OCT-2010 01:30:32
Current_time = 5-NOV-2010 15:13:51
Comment = single_pulse
Data_format = 1D REAL
Dim_size = 13107
Dim_title = 1H
Dim_units = [ppm]
Dimensions = X
Site = ECX 300
Spectrometer = DELTA2_NMR
Field_strength = 7.0586013[T] (300[MHz
X_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]
Irr_domain = 1H
Irr_freq = 300.52965592[MHz]
Irr_offset = 5[ppm]
Tri_domain = 1H
Tri_freq = 300.52965592[MHz]
Tri_offset = 5[ppm]
Clipped = FALSE
Mod_return = 1
Scans = 16
Total_scans = 16
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]
Irr_mode = Off
Tri_mode = Off
Dante_presat = FALSE
Initial_wait = 1[s]
Recvr_gain = 30
Relaxation_delay = 5[s]
Repetition_time = 7.90717696[s]
Temp_get = 22.9[dC]
SnBu3
OTHP
N
N
DMAS
abundance
X : parts per Million : 1H
9.25
10.11
6.07
6.0
6.06
2.1
1.02
1.01
1.02
1.01
1.02
1.02
1
1.02
0.98
7.8053
7.8019
7.0442
7.0408
6.0438
6.0244
6.0061
4.6418
4.6360
4.4186
4.4002
3.8726
3.8589
3.4949
3.4777
2.8322
1.4679
1.4438
1.3156
1.2916
1.2664
1.2424
0.8727
0.8487
0.8246



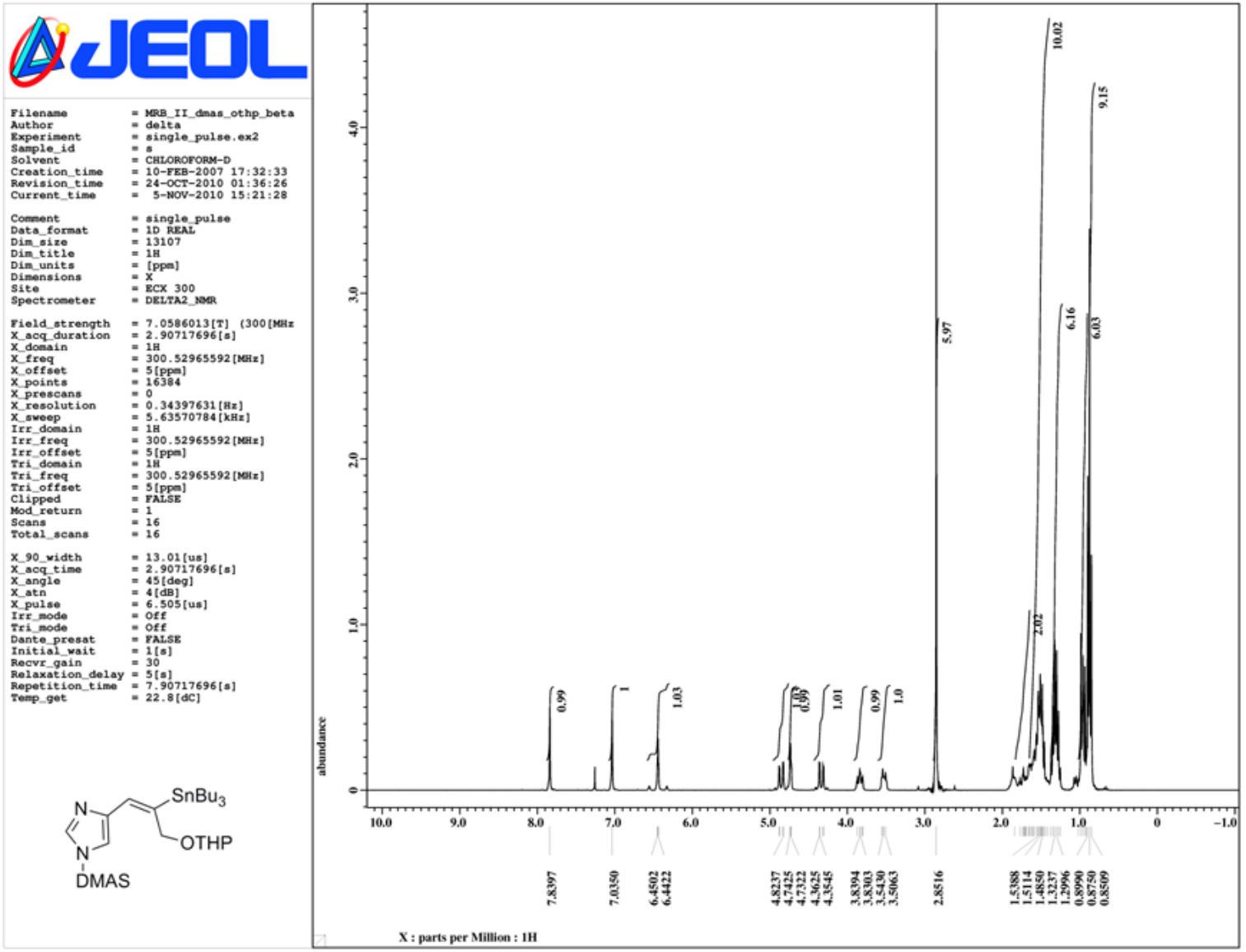
```
Filename          = MRB_II_dmas_othp_alph
Author            = delta
Experiment        = single_pulse.ex2
Sample_id         = S#538680
Solvent           = CHLOROFORM-D
Creation_time     = 10-FEB-2007 15:46:11
Revision_time     = 24-OCT-2010 01:30:32
Current_time      =  5-NOV-2010 15:15:57

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    = 7.0586013[T] (300[MHz
X_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]
Irr_domain        = 1H
Irr_freq          = 300.52965592[MHz]
Irr_offset        = 5[ppm]
Tri_domain        = 1H
Tri_freq          = 300.52965592[MHz]
Tri_offset        = 5[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 16
Total_scans       = 16

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]
Irr_mode          = Off
Tri_mode          = Off
Dante_presat      = FALSE
Initial_wait      = 1[s]
Recvr_gain        = 30
Relaxation_delay  = 5[s]
Repetition_time   = 7.90717696[s]
Temp_get          = 22.9[dC]
```

```
Filename          = MRB_II_dmas_othp_alph
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#539962
Solvent           = CHLOROFORM-D
Creation_time     = 10-FEB-2007 16:09:16
Revision_time     = 24-OCT-2010 01:54:26
Current_time      =  5-NOV-2010 15:16:28

Comment           = single pulse decouple
Data_format       = 1D REAL
Dim_size          = 52428
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = ECX 300
Spectrometer      = DELTA2_NMR

Field_strength    = 7.0586013[T] (300[MHz
X_acq_duration    = 2.76824064[s]
X_domain          = 13C
X_freq            = 75.56823426[MHz]
X_offset          = 100[ppm]
X_points          = 65536
X_prescans        = 4
X_resolution      = 0.36124027[Hz]
X_sweep           = 23.67424242[kHz]
Irr_domain        = 1H
Irr_freq          = 300.52965592[MHz]
Irr_offset        = 5[ppm]
Clipped           = FALSE
Mod_return        = 10
Scans             = 284
Total_scans       = 284

X_90_width        = 9.75[us]
X_acq_time        = 2.76824064[s]
X_angle           = 30[deg]
X_atn             = 8[dB]
X_pulse           = 3.25[us]
Irr_atn_dec       = 25[dB]
Irr_atn_noe       = 25[dB]
Irr_noise         = WALTZ
Decoupling        = TRUE
Initial_wait      = 1[s]
Noe               = TRUE
Noe_time          = 2[s]
Recvr_gain        = 50
Relaxation_delay  = 2[s]
Repetition_time   = 4.76824064[s]
Temp_get          = 24[dC]
```

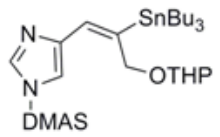


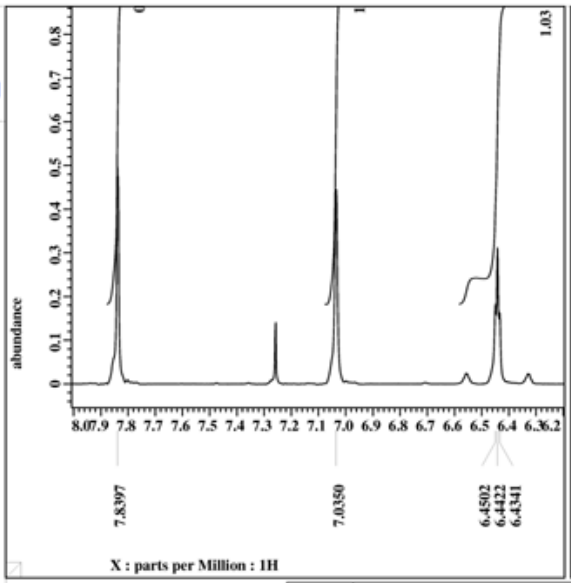


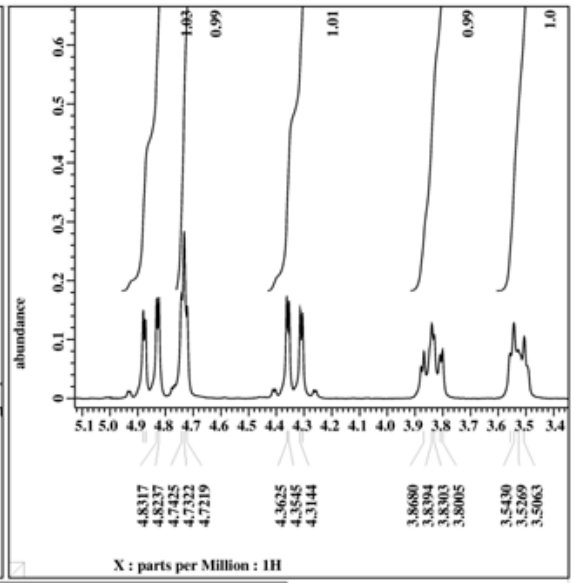
APPENDIX 6
^{1}H AND ^{13}C NMR SPECTRA OF
(*E*)-1-(Tetrahydro-2*H*-pyran-2-yloxy)-2-tributylstannyl-3-(1-dimethylsulfamoylimidazol-4-yl)-2-propene (70)

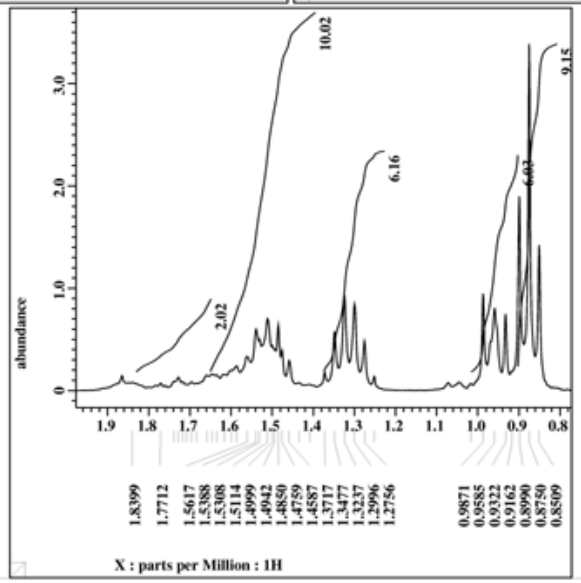

Filename = MRB_II_dmas_othp_beta
Author = delta
Experiment = single_pulse.ex2
Sample_id = s
Solvent = CHLOROFORM-D
Creation_time = 10-FEB-2007 17:32:33
Revision_time = 24-OCT-2010 01:36:26
Current_time = 5-NOV-2010 15:21:28
Comment = single_pulse
Data_format = 1D REAL
Dim_size = 13107
Dim_title = 1H
Dim_units = [ppm]
Dimensions = X
Site = ECX 300
Spectrometer = DELTA2_NMR
Field_strength = 7.0586013[T] (300[MHz
X_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]
Irr_domain = 1H
Irr_freq = 300.52965592[MHz]
Irr_offset = 5[ppm]
Tri_domain = 1H
Tri_freq = 300.52965592[MHz]
Tri_offset = 5[ppm]
Clipped = FALSE
Mod_return = 1
Scans = 16
Total_scans = 16
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]
Irr_mode = Off
Tri_mode = Off
Dante_presat = FALSE
Initial_wait = 1[s]
Recvr_gain = 30
Relaxation_delay = 5[s]
Repetition_time = 7.90717696[s]
Temp_get = 22.8[dC]
SnBu3
OTHP
N
N
DMAS
abundance
0
1.0
2.0
3.0
4.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
−1.0
0.99
1
1.03
1.03
0.99
1.01
0.99
1.0
5.97
2.02
10.02
6.16
6.03
9.15
7.8397
7.0350
6.4502
6.4422
4.8237
4.7425
4.7322
4.3625
4.3545
3.8394
3.8303
3.5430
3.5063
2.8516
1.5388
1.5114
1.4850
1.3237
1.2996
0.8990
0.8750
0.8509
X : parts per Million : 1H

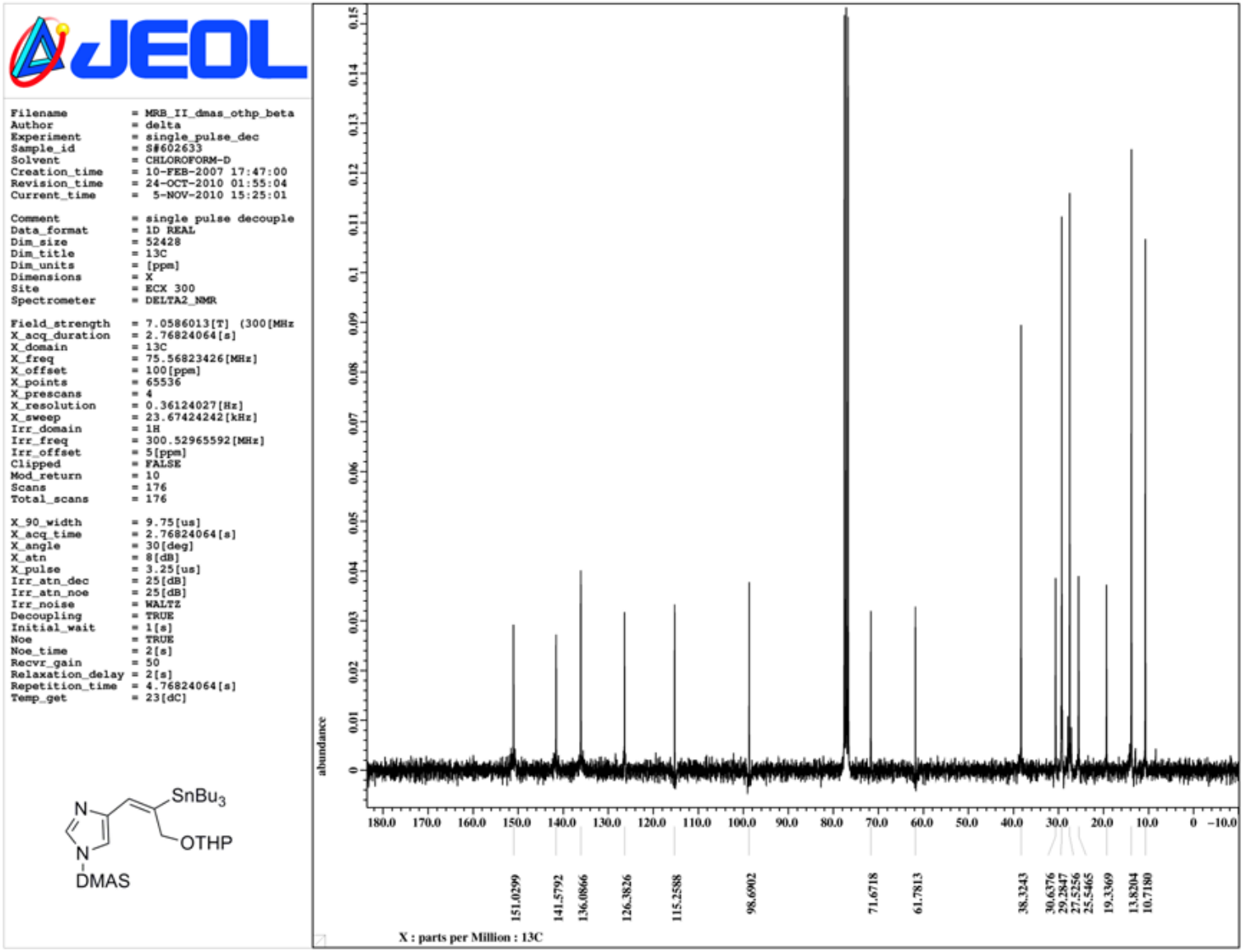
```
Filename          = MRB_II_dmas_othp_beta
Author            = delta
Experiment        = single_pulse.ex2
Sample_id         = s
Solvent           = CHLOROFORM-D
Creation_time     = 10-FEB-2007 17:32:33
Revision_time     = 24-OCT-2010 01:36:26
Current_time      =  5-NOV-2010 15:23:42

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    = 7.0586013[T] (300[MHz
X_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]
Irr_domain        = 1H
Irr_freq          = 300.52965592[MHz]
Irr_offset        = 5[ppm]
Tri_domain        = 1H
Tri_freq          = 300.52965592[MHz]
Tri_offset        = 5[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 16
Total_scans       = 16

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]
Irr_mode          = Off
Tri_mode          = Off
Dante_presat      = FALSE
Initial_wait      = 1[s]
Recvr_gain        = 30
Relaxation_delay  = 5[s]
Repetition_time   = 7.90717696[s]
Temp_get          = 22.8[dC]
```



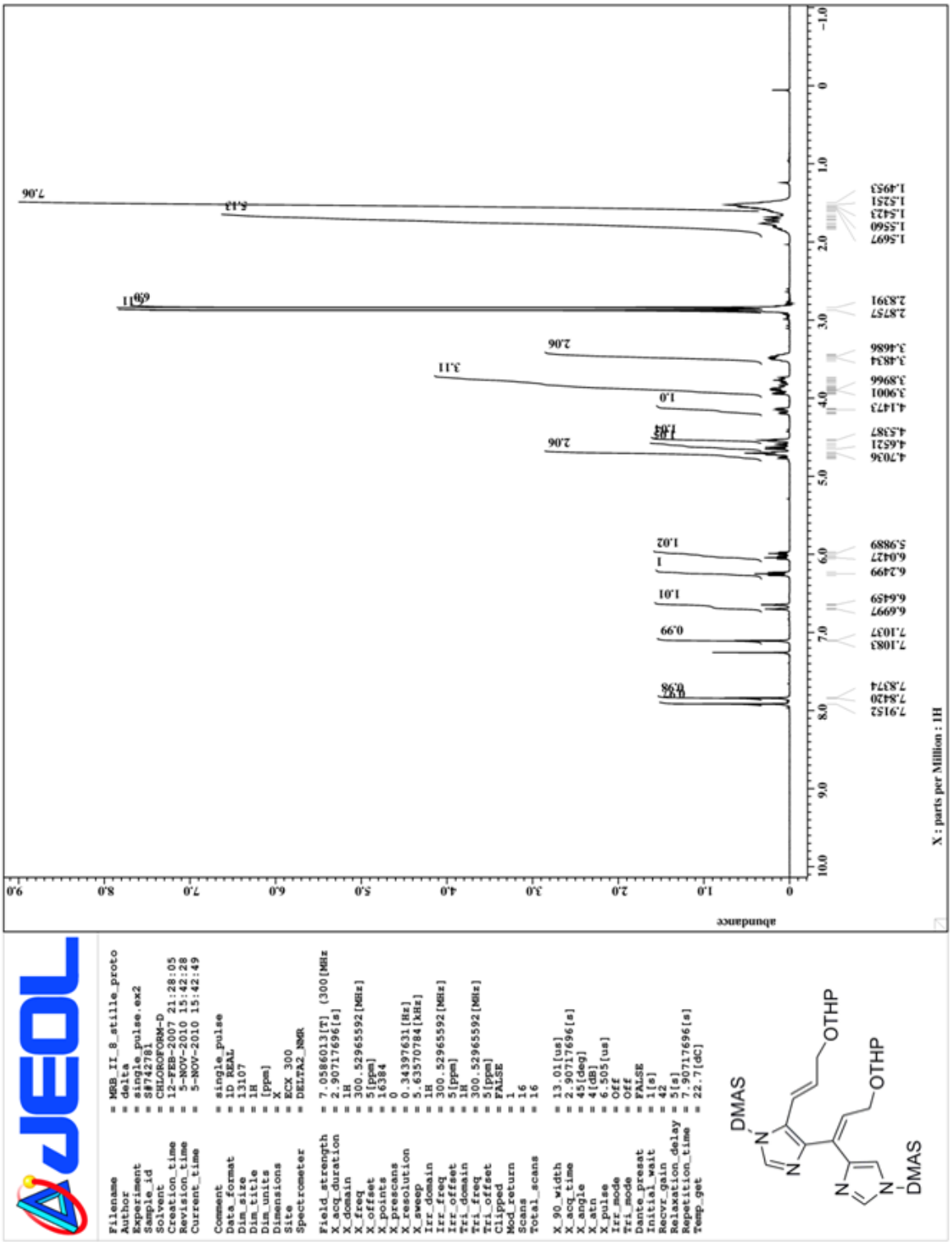


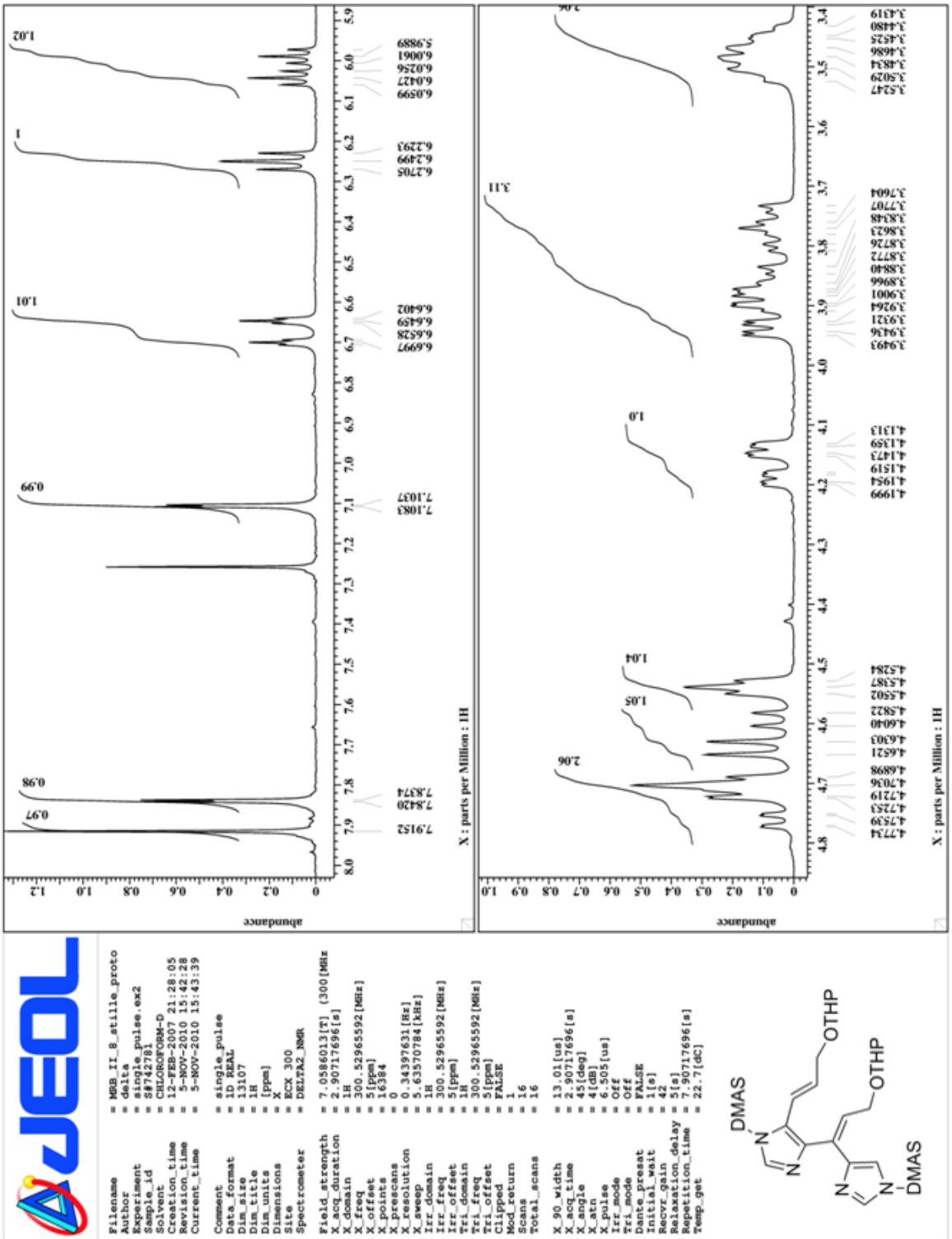


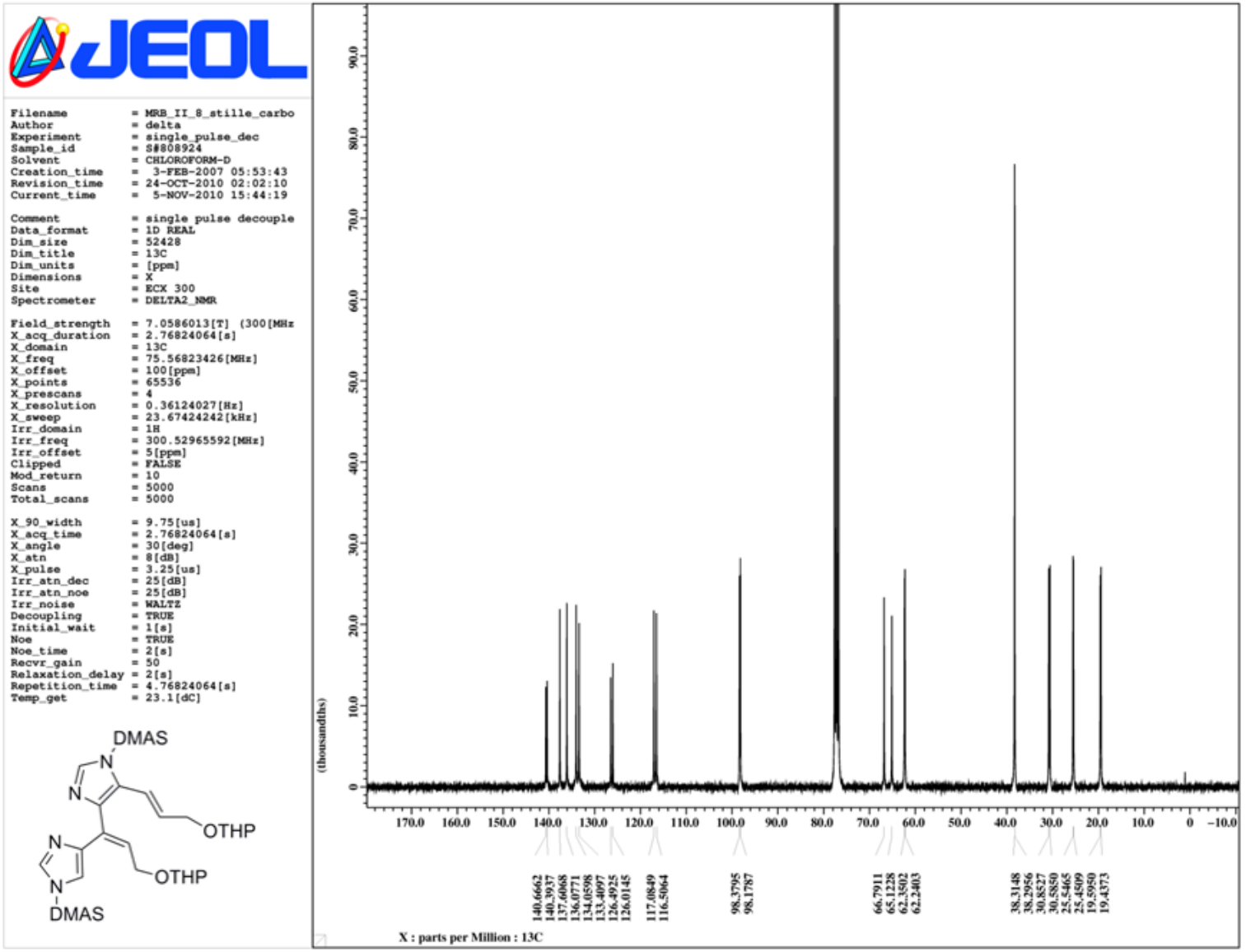



Filename = MRB_II_dmas_othp_beta
Author = delta
Experiment = single_pulse_dec
Sample_id = S#602633
Solvent = CHLOROFORM-D
Creation_time = 10-FEB-2007 17:47:00
Revision_time = 24-OCT-2010 01:55:04
Current_time = 5-NOV-2010 15:25:01
Comment = single pulse decouple
Data_format = 1D REAL
Dim_size = 52428
Dim_title = 13C
Dim_units = [ppm]
Dimensions = X
Site = ECX 300
Spectrometer = DELTA2_NMR
Field_strength = 7.0586013[T] (300[MHz
X_acq_duration = 2.76824064[s]
X_domain = 13C
X_freq = 75.56823426[MHz]
X_offset = 100[ppm]
X_points = 65536
X_prescans = 4
X_resolution = 0.36124027[Hz]
X_sweep = 23.67424242[kHz]
Irr_domain = 1H
Irr_freq = 300.52965592[MHz]
Irr_offset = 5[ppm]
Clipped = FALSE
Mod_return = 10
Scans = 176
Total_scans = 176
X_90_width = 9.75[us]
X_acq_time = 2.76824064[s]
X_angle = 30[deg]
X_atn = 8[dB]
X_pulse = 3.25[us]
Irr_atn_dec = 25[dB]
Irr_atn_noe = 25[dB]
Irr_noise = WALTZ
Decoupling = TRUE
Initial_wait = 1[s]
Noe = TRUE
Noe_time = 2[s]
Recvr_gain = 50
Relaxation_delay = 2[s]
Repetition_time = 4.76824064[s]
Temp_get = 23[dC]
SnBu3
OTHP
N
N
DMAS
abundance
0
0.01
0.02
0.03
0.04
0.05
0.06
0.07
0.08
0.09
0.1
0.11
0.12
0.13
0.14
0.15
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
151.0299
141.5792
136.0866
126.3826
115.2588
98.6902
71.6718
61.7813
38.3243
30.6376
29.2847
27.5256
25.5465
19.3369
13.8204
10.7180
X : parts per Million : 13C

APPENDIX 7
^{1}H AND ^{13}C NMR SPECTRA OF
4-((*E*)-1-Dimethylsulfamoyl-4-(3-(tetrahydro-2*H*-pyran-2-yloxy)-2-propenyl)imidazol-4-yl)-1-dimethylsulfamoyl-5-((*E*)-3-(tetrahydro-2*H*-pyran-2-yloxy)-2-propenyl)imidazole (58)

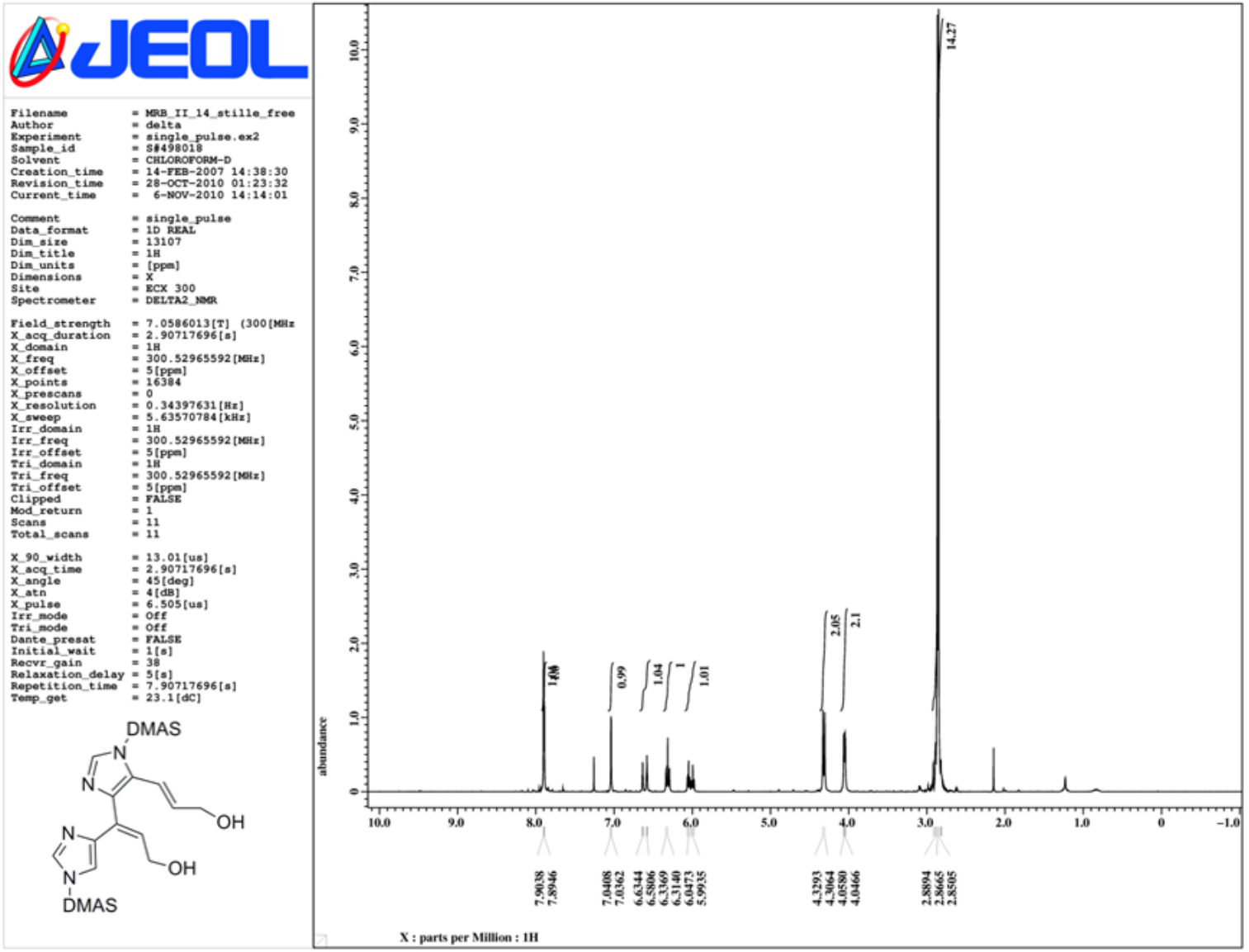

JEOL
Filename = MRB_II_8_stille_proto
Author = delta
Experiment = single_pulse.ex2
Sample_id = s#742781
Solvent = CHLOROFORM-D
Creation_time = 12-FEB-2007 21:28:05
Revision_time = 5-NOV-2010 15:42:28
Current_time = 5-NOV-2010 15:42:49
Comment = single_pulse
Data_format = 1D REAL
Dim_size = 13107
Dim_title = 1H
Dim_units = [ppm]
Dimensions = X
Site = ECX 300
Spectrometer = DELTA2_NMR
Field_strength = 7.05860131[T] (300[MHz
X_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]
Irr_domain = 1H
Irr_freq = 300.52965592[MHz]
Irr_offset = 5[ppm]
Tri_domain = 1H
Tri_freq = 300.52965592[MHz]
Tri_offset = 5[ppm]
Clipped = FALSE
Mod_return = 1
Scans = 16
Total_scans = 16
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]
Irr_mode = Off
Tri_mode = Off
Dante_presat = FALSE
Initial_wait = 1[s]
Recvr_gain = 42
Relaxation_delay = 5[s]
Repetition_time = 7.90717696[s]
Temp_get = 22.7[dC]
DMAS
OTHP
OTHP
DMAS
abundance
X : parts per Million : 1H
7.06
6.13
6.11
2.06
3.11
2.06
2.06
1.0
1.02
1.01
0.99
0.98
0.98
7.9152
7.8420
7.8374
7.1083
7.1037
6.6997
6.6459
6.2499
6.0427
5.9889
4.7036
4.6521
4.5387
4.1473
3.9001
3.8966
3.4834
3.4686
2.8757
2.8391
1.5697
1.5560
1.5423
1.5251
1.4953

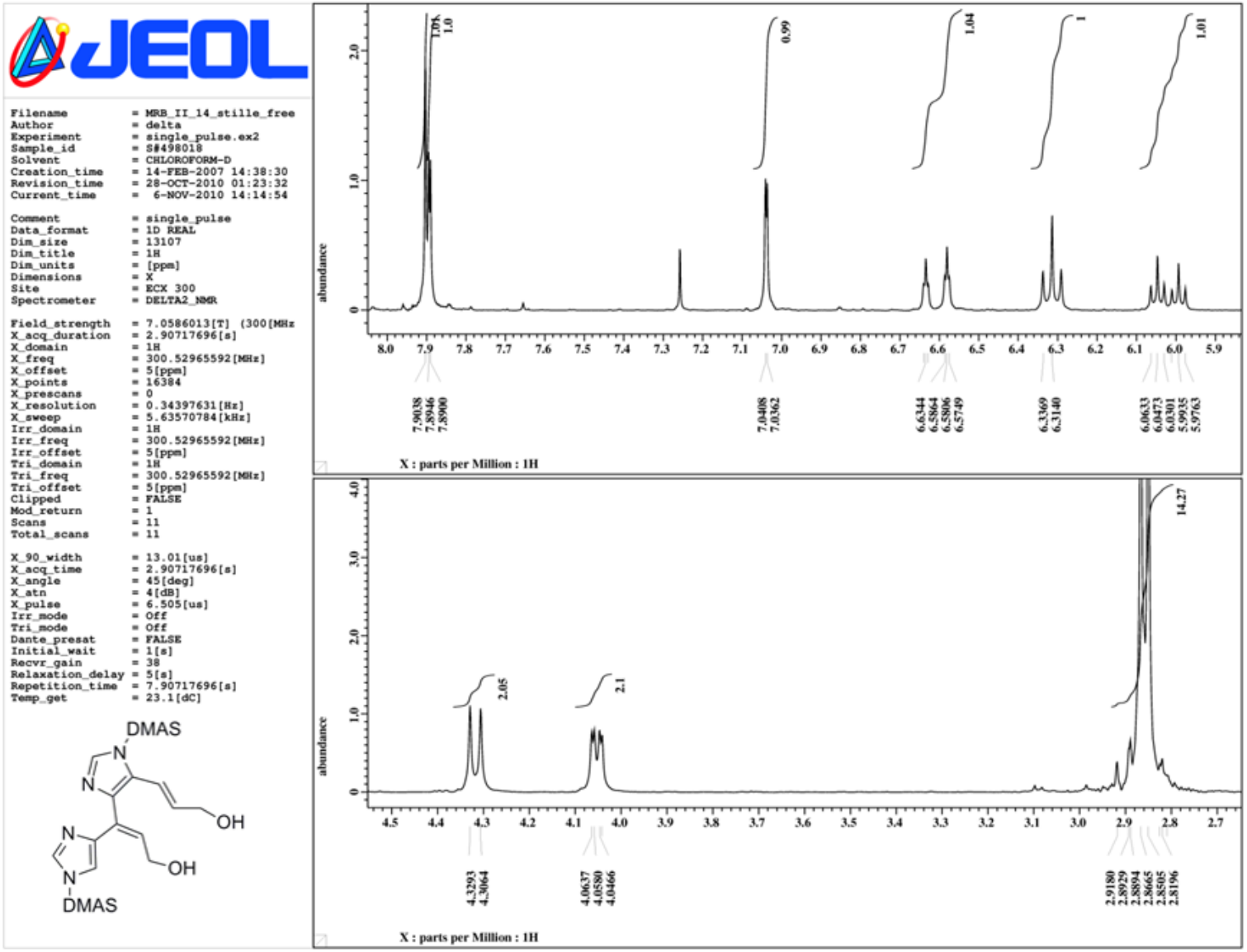

JEOL
Filename = MRB_II_8_stille_proto
Author = delta
Experiment = single_pulse.ex2
Sample_id = s#742781
Solvent = CHLOROFORM-D
Creation_time = 12-FEB-2007 21:28:05
Revision_time = 5-NOV-2010 15:42:28
Current_time = 5-NOV-2010 15:43:39
Comment = single_pulse
Data_format = 1D REAL
Dim_size = 13107
Dim_title = 1H
Dim_units = [ppm]
Dimensions = X
Site = ECX 300
Spectrometer = DELTA2_NMR
Field_strength = 7.05860131[T] (300[MHz
X_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]
Irr_domain = 1H
Irr_freq = 300.52965592[MHz]
Irr_offset = 5[ppm]
Tri_domain = 1H
Tri_freq = 300.52965592[MHz]
Tri_offset = 5[ppm]
Clipped = FALSE
Mod_return = 1
Scans = 16
Total_scans = 16
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]
Irr_mode = Off
Tri_mode = Off
Dante_presat = FALSE
Initial_wait = 1[s]
Recvr_gain = 42
Relaxation_delay = 5[s]
Repetition_time = 7.90717696[s]
Temp_get = 22.7[dC]
DMAS
OTHP
OTHP
DMAS
abundance
X : parts per Million : 1H
0.97
0.98
0.99
1.01
1.02
1
7.9152
7.8420
7.8374
7.1083
7.1037
6.6997
6.6528
6.6459
6.6402
6.2705
6.2499
6.2293
6.0599
6.0427
6.0256
6.0061
5.9889
2.06
1.04
1.05
1.0
3.11
1.0
4.7734
4.7539
4.7253
4.7219
4.7036
4.6898
4.6521
4.6303
4.6040
4.5822
4.5502
4.5387
4.5284
4.1999
4.1954
4.1519
4.1473
4.1359
4.1313
3.9493
3.9436
3.9321
3.9264
3.9001
3.8966
3.8840
3.8772
3.8726
3.8623
3.8348
3.7707
3.7604
3.5247
3.5029
3.4834
3.4686
3.4525
3.4480
3.4319



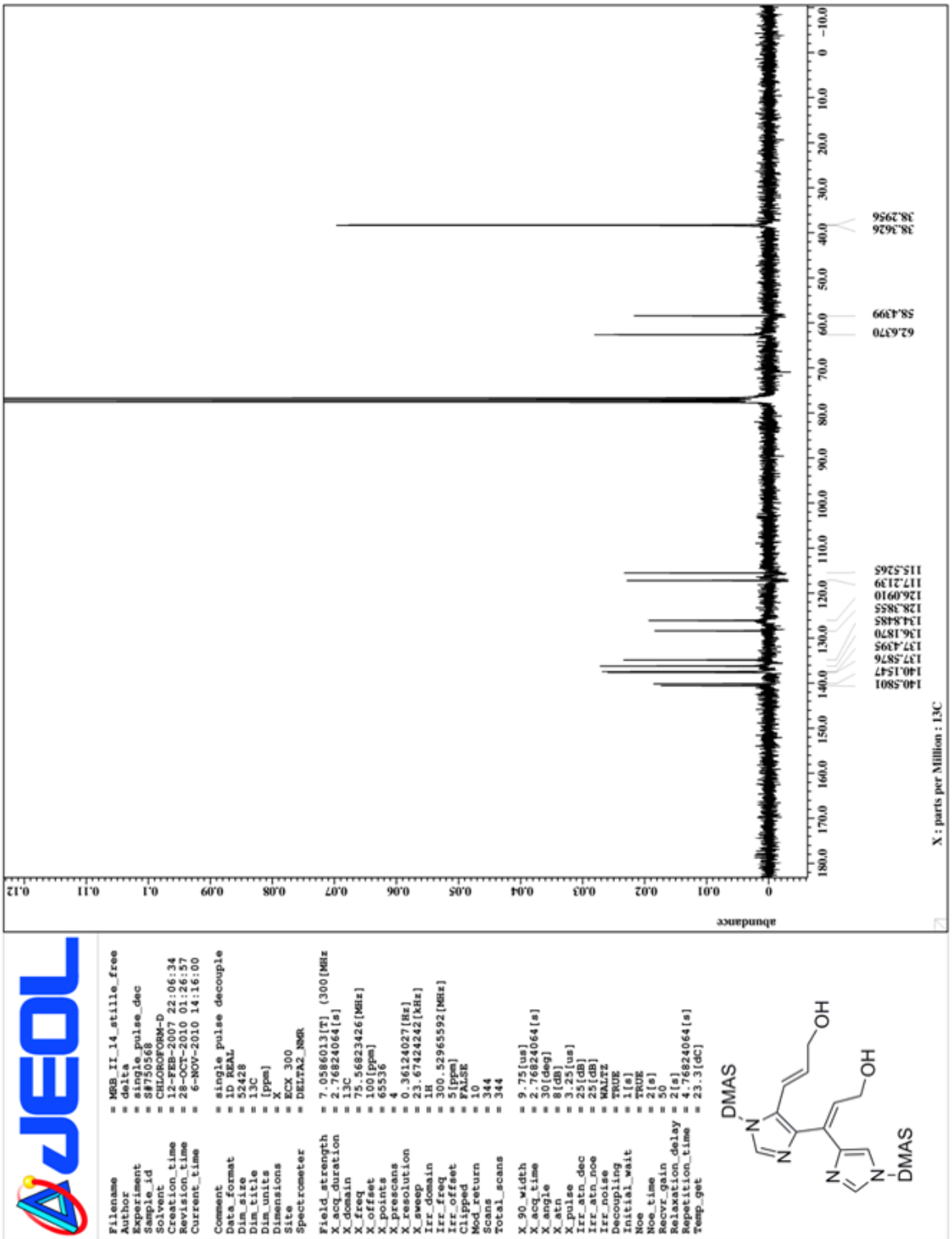
```
Filename          = MRB_II_8_stille_carbo
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#808924
Solvent           = CHLOROFORM-D
Creation_time     =  3-FEB-2007 05:53:43
Revision_time     = 24-OCT-2010 02:02:10
Current_time      =  5-NOV-2010 15:44:19

Comment           = single pulse decouple
Data_format       = 1D REAL
Dim_size          = 52428
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = ECX 300
Spectrometer      = DELTA2_NMR

Field_strength    = 7.0586013[T] (300[MHz
X_acq_duration    = 2.76824064[s]
X_domain          = 13C
X_freq            = 75.56823426[MHz]
X_offset          = 100[ppm]
X_points          = 65536
X_prescans        = 4
X_resolution      = 0.36124027[Hz]
X_sweep           = 23.67424242[kHz]
Irr_domain        = 1H
Irr_freq          = 300.52965592[MHz]
Irr_offset        = 5[ppm]
Clipped           = FALSE
Mod_return        = 10
Scans             = 5000
Total_scans       = 5000

X_90_width        = 9.75[us]
X_acq_time        = 2.76824064[s]
X_angle           = 30[deg]
X_atn             = 8[dB]
X_pulse           = 3.25[us]
Irr_atn_dec       = 25[dB]
Irr_atn_noe       = 25[dB]
Irr_noise         = WALTZ
Decoupling        = TRUE
Initial_wait      = 1[s]
Noe               = TRUE
Noe_time          = 2[s]
Recvr_gain        = 50
Relaxation_delay  = 2[s]
Repetition_time   = 4.76824064[s]
Temp_get          = 23.1[dC]
```

APPENDIX 8
^{1}H AND ^{13}C NMR SPECTRA OF
4-((*E*)-1-Dimethylsulfamoyl-4-(3-hydroxy-2-propenyl)imidazol-4-yl)-1-dimethylsulfamoyl-5-((*E*)-3-hydroxy-2-propenyl)imidazole (73)

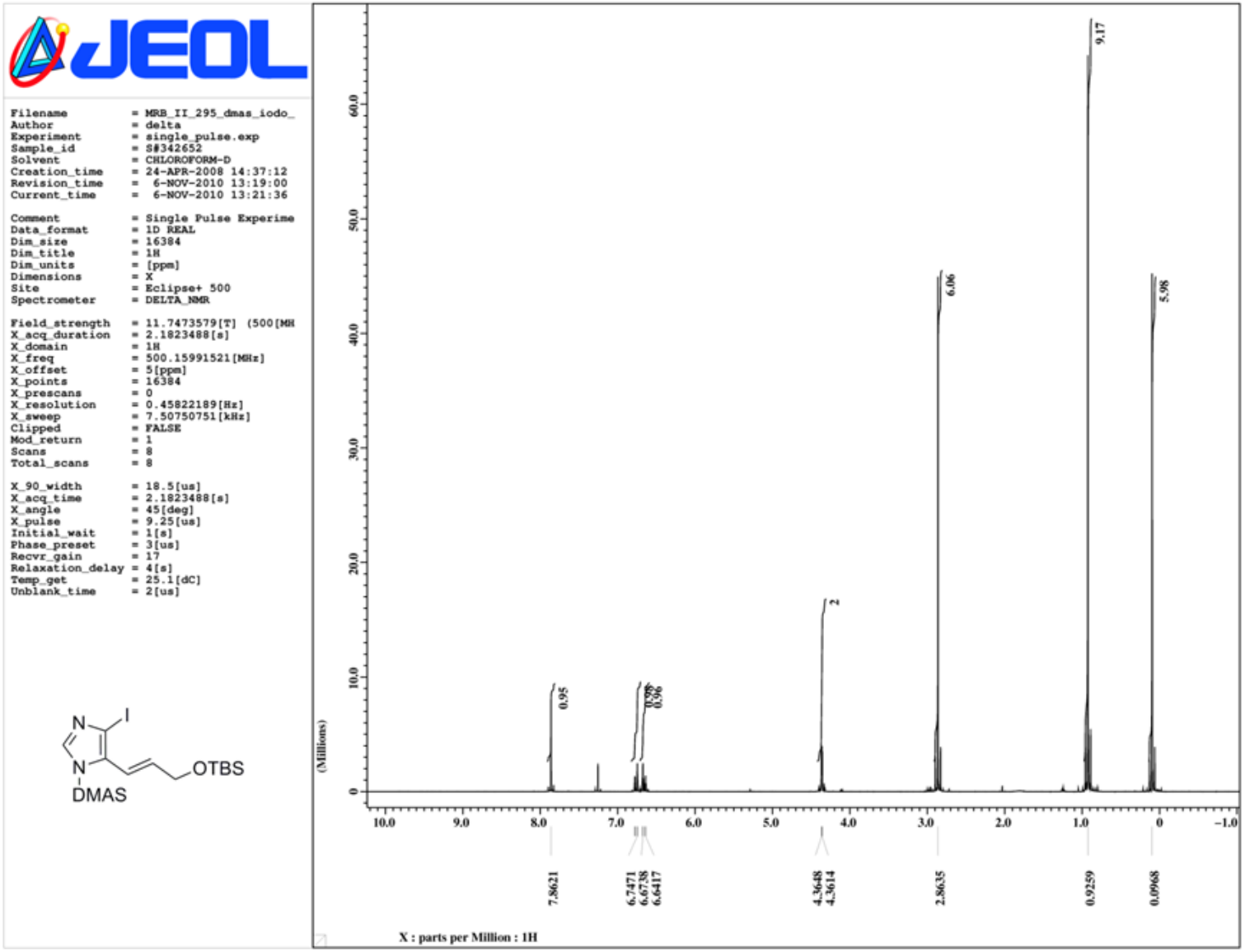

Filename = MRB_II_14_stille_free
Author = delta
Experiment = single_pulse.ex2
Sample_id = S#498018
Solvent = CHLOROFORM-D
Creation_time = 14-FEB-2007 14:38:30
Revision_time = 28-OCT-2010 01:23:32
Current_time = 6-NOV-2010 14:14:01
Comment = single_pulse
Data_format = 1D REAL
Dim_size = 13107
Dim_title = 1H
Dim_units = [ppm]
Dimensions = X
Site = ECX 300
Spectrometer = DELTA2_NMR
Field_strength = 7.0586013[T] (300[MHz
X_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]
Irr_domain = 1H
Irr_freq = 300.52965592[MHz]
Irr_offset = 5[ppm]
Tri_domain = 1H
Tri_freq = 300.52965592[MHz]
Tri_offset = 5[ppm]
Clipped = FALSE
Mod_return = 1
Scans = 11
Total_scans = 11
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]
Irr_mode = Off
Tri_mode = Off
Dante_presat = FALSE
Initial_wait = 1[s]
Recvr_gain = 38
Relaxation_delay = 5[s]
Repetition_time = 7.90717696[s]
Temp_get = 23.1[dC]
DMAS
OH
OH
DMAS
abundance
14.27
2.05
2.1
0.99
1.04
1
1.01
7.9038
7.8946
7.0408
7.0362
6.6344
6.5806
6.3369
6.3140
6.0473
5.9935
4.3293
4.3064
4.0580
4.0466
2.8894
2.8665
2.8505
X : parts per Million : 1H



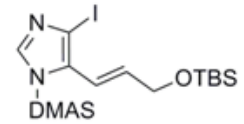
```
Filename          = MRB_II_14_stille_free
Author            = delta
Experiment        = single_pulse.ex2
Sample_id         = S#498018
Solvent           = CHLOROFORM-D
Creation_time     = 14-FEB-2007 14:38:30
Revision_time     = 28-OCT-2010 01:23:32
Current_time      =  6-NOV-2010 14:14:54

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    = 7.0586013[T] (300[MHz
X_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]
Irr_domain        = 1H
Irr_freq          = 300.52965592[MHz]
Irr_offset        = 5[ppm]
Tri_domain        = 1H
Tri_freq          = 300.52965592[MHz]
Tri_offset        = 5[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 11
Total_scans       = 11

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]
Irr_mode          = Off
Tri_mode          = Off
Dante_presat      = FALSE
Initial_wait      = 1[s]
Recvr_gain        = 38
Relaxation_delay  = 5[s]
Repetition_time   = 7.90717696[s]
Temp_get          = 23.1[dC]
```

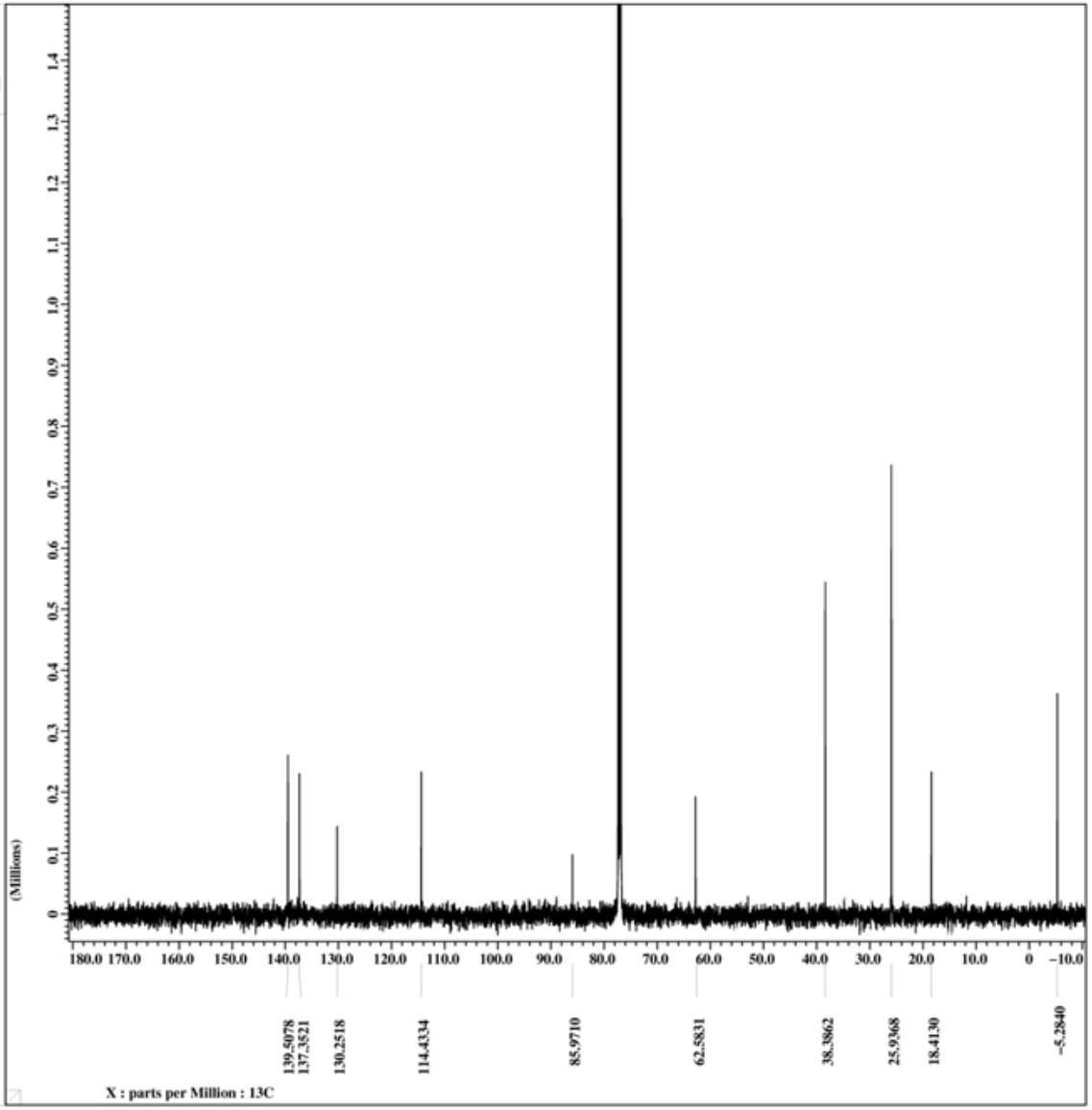

JEOL
Filename = MRB_II_14_stille_free
Author = delta
Experiment = single_pulse_dec
Sample_id = s#750560
Solvent = CHLOROFORM-D
Creation_time = 12-FEB-2007 22:06:34
Revision_time = 28-OCT-2010 01:26:57
Current_time = 6-NOV-2010 14:16:00
Comment = single pulse decouple
Data_format = 1D REAL
Dim_size = 52428
Dim_title = 13C
Dim_units = [ppm]
Dimensions = X
Site = ECX 300
Spectrometer = DELTA2_NMR
Field_strength = 7.0586013[T] (300[MHz
X_acq_duration = 2.76824064[s]
X_domain = 13C
X_freq = 75.56823426[MHz]
X_offset = 100[ppm]
X_points = 65536
X_prescans = 4
X_resolution = 0.36124027[Hz]
X_sweep = 23.67424242[kHz]
Irr_domain = 1H
Irr_freq = 300.52965592[MHz]
Irr_offset = 5[ppm]
Clipped = FALSE
Mod_return = 10
Scans = 344
Total_scans = 344
X_90_width = 9.75[us]
X_acq_time = 2.76824064[s]
X_angle = 30[deg]
X_atn = 8[dB]
X_pulse = 3.25[us]
Irr_atn_dec = 25[dB]
Irr_atn_noe = 25[dB]
Irr_noise = WALTZ
Decoupling = TRUE
Initial_wait = 1[s]
Noe = TRUE
Noe_time = 2[s]
Recvr_gain = 50
Relaxation_delay = 2[s]
Repetition_time = 4.76824064[s]
Temp_get = 23.3[dC]
DMAS
DMAS
OH
OH
abundance
X : parts per Million : 13C
140.5801
140.1547
137.5876
137.4395
136.1870
134.8485
128.3855
126.0910
117.2139
115.5265
62.6370
58.4399
38.3626
38.2956

APPENDIX 9
^{1}H AND ^{13}C NMR SPECTRA OF
(*E*)-3-(4-Iodo-1-dimethylsulfamoylimidazol-5-yl)-1-(*t*-butyldimethylsilyloxy)-2-propene (80)

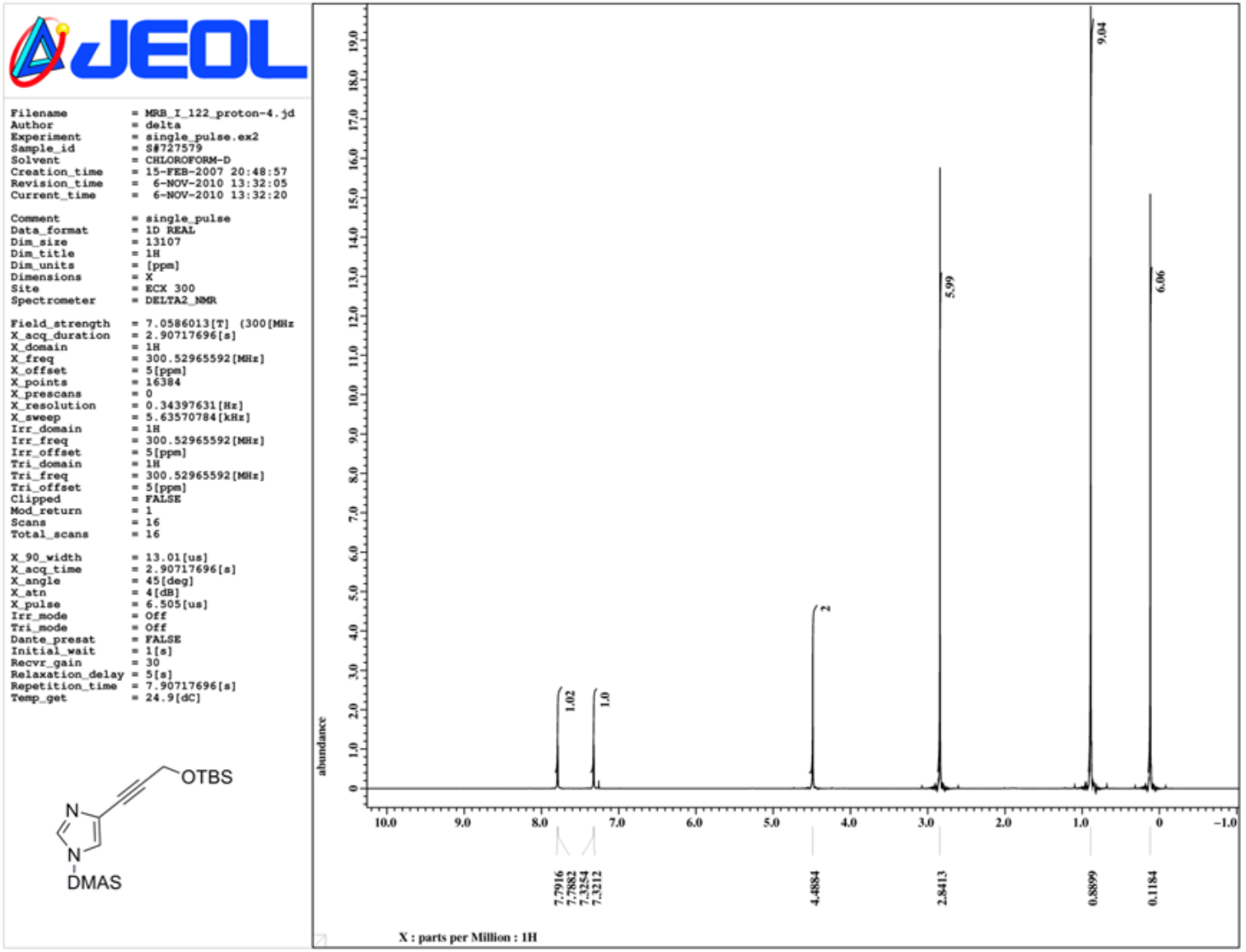

Filename = MRB_II_295_dmas_iodo_
Author = delta
Experiment = single_pulse.exp
Sample_id = S#342652
Solvent = CHLOROFORM-D
Creation_time = 24-APR-2008 14:37:12
Revision_time = 6-NOV-2010 13:19:00
Current_time = 6-NOV-2010 13:21:36
Comment = Single Pulse Experime
Data_format = 1D REAL
Dim_size = 16384
Dim_title = 1H
Dim_units = [ppm]
Dimensions = X
Site = Eclipse+ 500
Spectrometer = DELTA_NMR
Field_strength = 11.7473579[T] (500[MH
X_acq_duration = 2.1823488[s]
X_domain = 1H
X_freq = 500.15991521[MHz]
X_offset = 5[ppm]
X_points = 16384
X_prescans = 0
X_resolution = 0.45822189[Hz]
X_sweep = 7.50750751[kHz]
Clipped = FALSE
Mod_return = 1
Scans = 8
Total_scans = 8
X_90_width = 18.5[us]
X_acq_time = 2.1823488[s]
X_angle = 45[deg]
X_pulse = 9.25[us]
Initial_wait = 1[s]
Phase_preset = 3[us]
Recvr_gain = 17
Relaxation_delay = 4[s]
Temp_get = 25.1[dC]
Unblank_time = 2[us]
N
I
N
OTBS
DMAS
(Millions)
60.0
50.0
40.0
30.0
20.0
10.0
0
9.17
6.06
5.98
2
0.95
0.98
0.98
0.96
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
−1.0
7.8621
6.7471
6.6738
6.6417
4.3648
4.3614
2.8635
0.9259
0.0968
X : parts per Million : 1H

```
Filename          = MRB_II_295_dmas_iodo_
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#342701
Solvent           = CHLOROFORM-D
Creation_time     = 24-APR-2008 16:00:30
Revision_time     =  6-NOV-2010 13:22:42
Current_time      =  6-NOV-2010 13:27:58

Comment           = single pulse decouple
Data_format       = 1D COMPLEX
Dim_size          = 65536
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = Eclipse+ 500
Spectrometer      = DELTA_NMR

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 2.0840448[s]
X_domain          = 13C
X_freq            = 125.76529768[MHz]
X_offset          = 100[ppm]
X_points          = 65536
X_prescans        = 4
X_resolution      = 0.47983613[Hz]
X_sweep           = 31.44654088[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 800
Total_scans       = 800

X_90_width        = 14.2[us]
X_acq_time        = 2.0840448[s]
X_angle           = 30[deg]
X_pulse           = 4.73333333[us]
Initial_wait      = 1[s]
Noe_time          = 1[s]
Phase_preset      = 3[us]
Recvr_gain        = 30
Relaxation_delay  = 3[s]
Temp_get          = 26.7[dC]
Unblank_time      = 2[us]
```

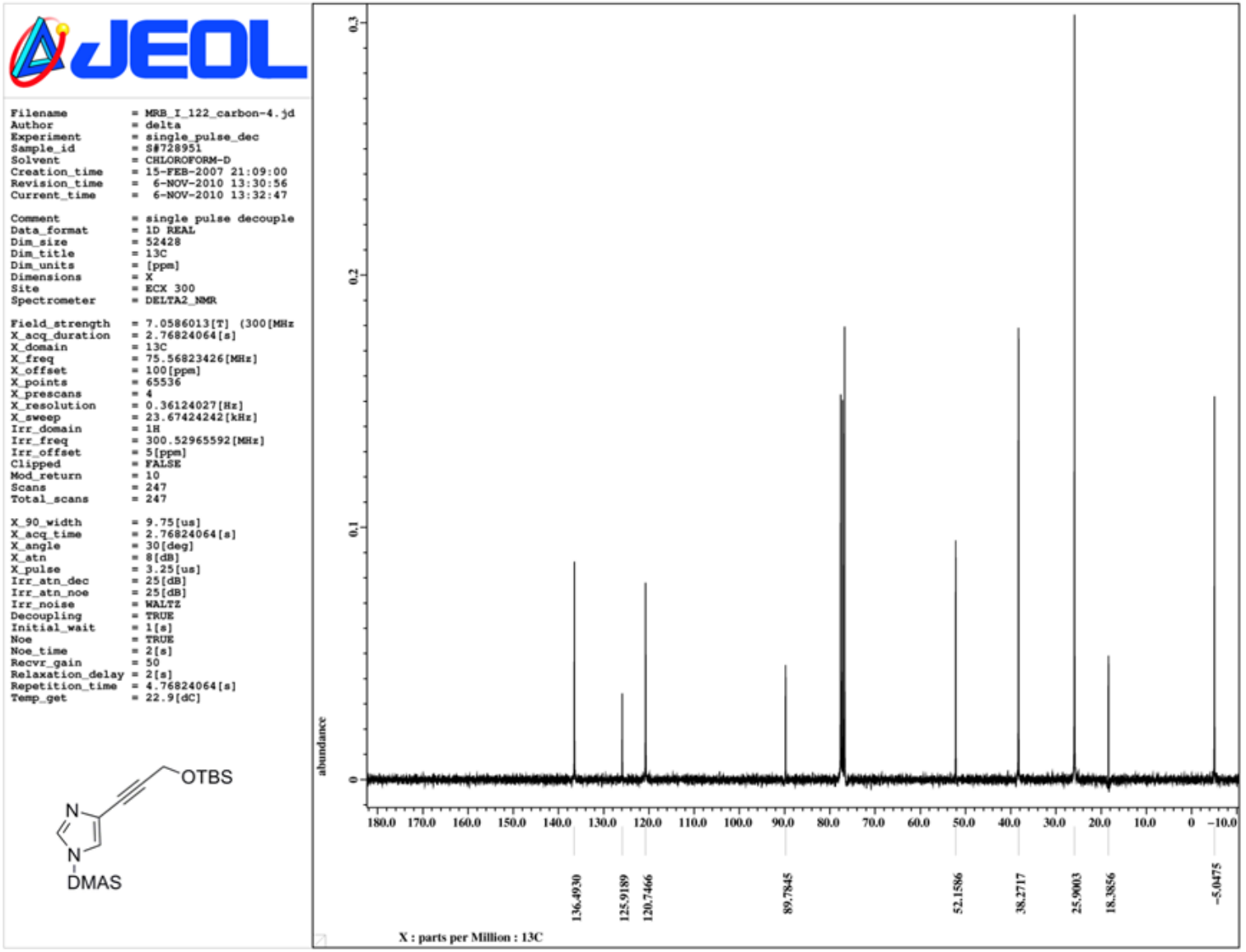




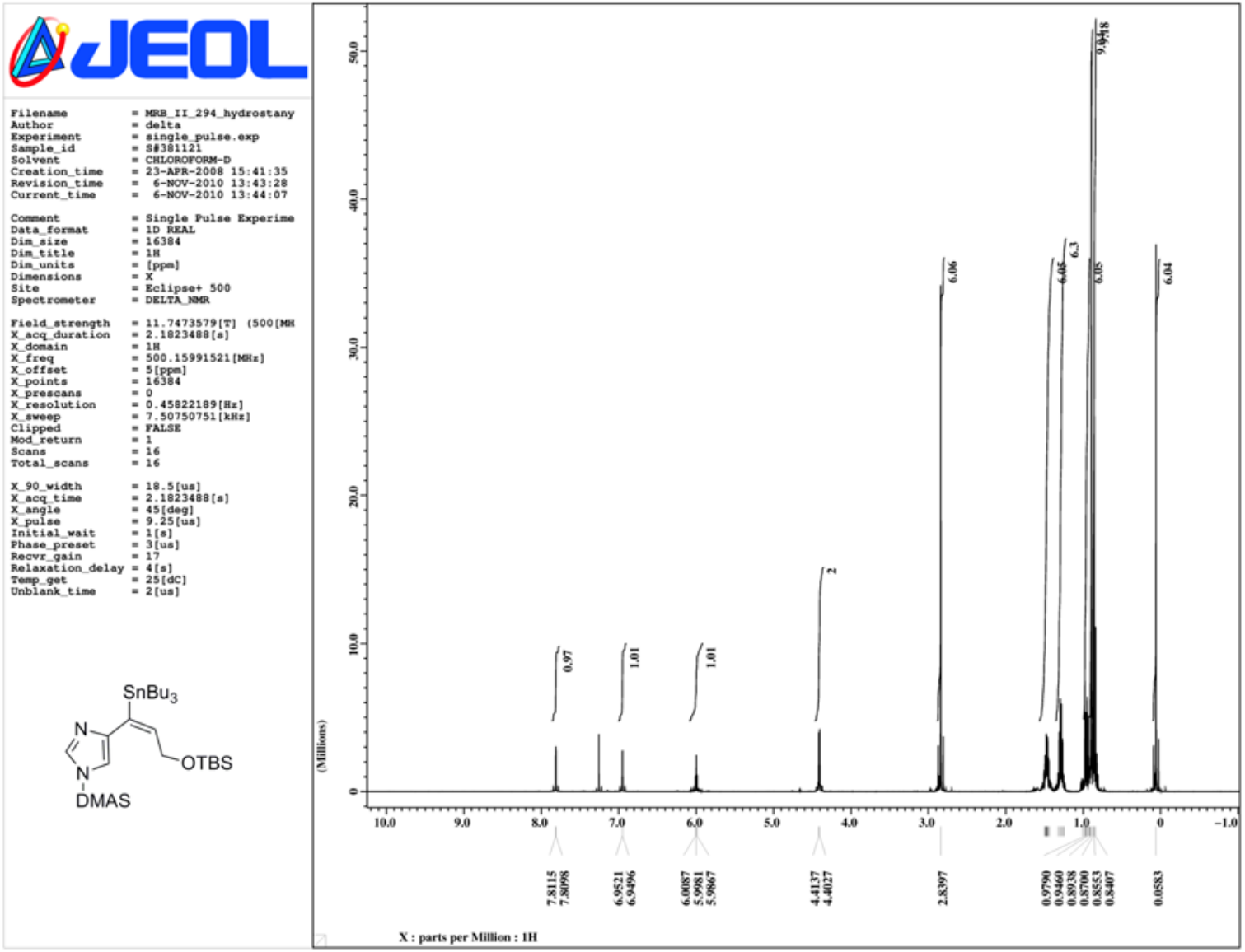
APPENDIX 10
^{1}H AND ^{13}C NMR SPECTRA OF
1-*t*-Butyldimethylsilyloxy-3-(1-dimethylsulfamoylimidazol-4-yl)-2-propyne
(76)



```
Filename          = MRB_I_122_proton-4.jd
Author            = delta
Experiment        = single_pulse.ex2
Sample_id         = S#727579
Solvent           = CHLOROFORM-D
Creation_time     = 15-FEB-2007 20:48:57
Revision_time     =  6-NOV-2010 13:32:05
Current_time      =  6-NOV-2010 13:32:20

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    = 7.0586013[T] (300[MHz
X_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]
Irr_domain        = 1H
Irr_freq          = 300.52965592[MHz]
Irr_offset        = 5[ppm]
Tri_domain        = 1H
Tri_freq          = 300.52965592[MHz]
Tri_offset        = 5[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 16
Total_scans       = 16

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]
Irr_mode          = Off
Tri_mode          = Off
Dante_presat      = FALSE
Initial_wait      = 1[s]
Recvr_gain        = 30
Relaxation_delay  = 5[s]
Repetition_time   = 7.90717696[s]
Temp_get          = 24.9[dC]
```

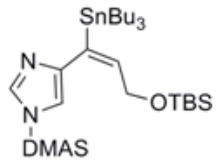

Filename = MRB_I_122_carbon-4.jd
Author = delta
Experiment = single_pulse_dec
Sample_id = S#728951
Solvent = CHLOROFORM-D
Creation_time = 15-FEB-2007 21:09:00
Revision_time = 6-NOV-2010 13:30:56
Current_time = 6-NOV-2010 13:32:47
Comment = single pulse decouple
Data_format = 1D REAL
Dim_size = 52428
Dim_title = 13C
Dim_units = [ppm]
Dimensions = X
Site = ECX 300
Spectrometer = DELTA2_NMR
Field_strength = 7.0586013[T] (300[MHz
X_acq_duration = 2.76824064[s]
X_domain = 13C
X_freq = 75.56823426[MHz]
X_offset = 100[ppm]
X_points = 65536
X_prescans = 4
X_resolution = 0.36124027[Hz]
X_sweep = 23.67424242[kHz]
Irr_domain = 1H
Irr_freq = 300.52965592[MHz]
Irr_offset = 5[ppm]
Clipped = FALSE
Mod_return = 10
Scans = 247
Total_scans = 247
X_90_width = 9.75[us]
X_acq_time = 2.76824064[s]
X_angle = 30[deg]
X_atn = 8[dB]
X_pulse = 3.25[us]
Irr_atn_dec = 25[dB]
Irr_atn_noe = 25[dB]
Irr_noise = WALTZ
Decoupling = TRUE
Initial_wait = 1[s]
Noe = TRUE
Noe_time = 2[s]
Recvr_gain = 50
Relaxation_delay = 2[s]
Repetition_time = 4.76824064[s]
Temp_get = 22.9[dC]
OTBS
N
N
DMAS
abundance
0.3
0.2
0.1
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
136.4930
125.9189
120.7466
89.7845
52.1586
38.2717
25.9003
18.3856
−5.0475
X : parts per Million : 13C

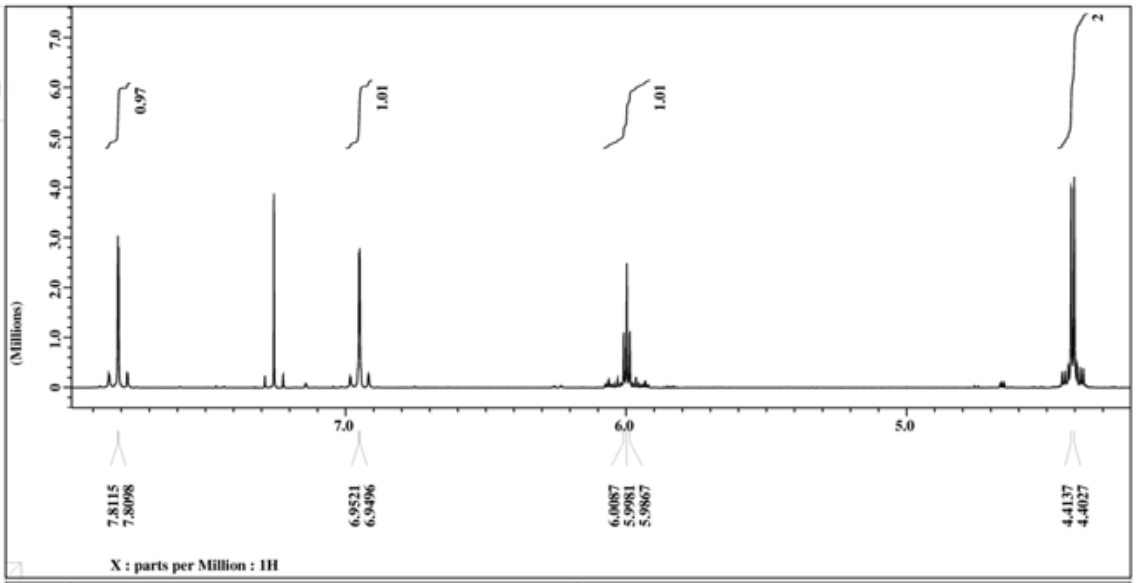
APPENDIX 11
^{1}H AND ^{13}C NMR SPECTRA OF
(*E*)-1-*t*-Butyldimethylsilyloxy-3-tributylstannyl-3-(1-dimethylsulfamoylimidazol-4-yl)-2-propene (78)

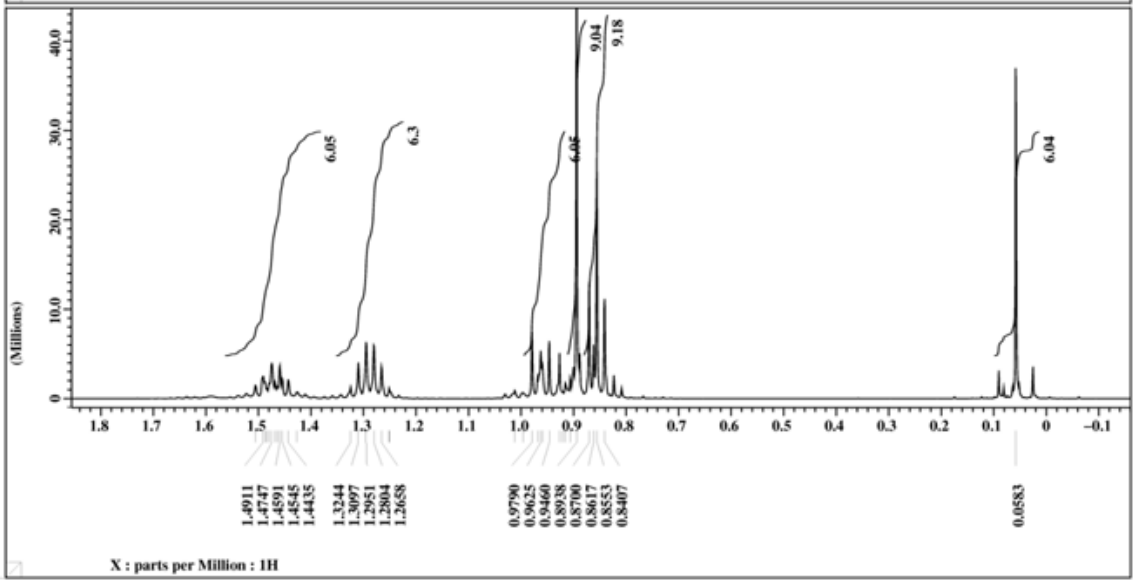


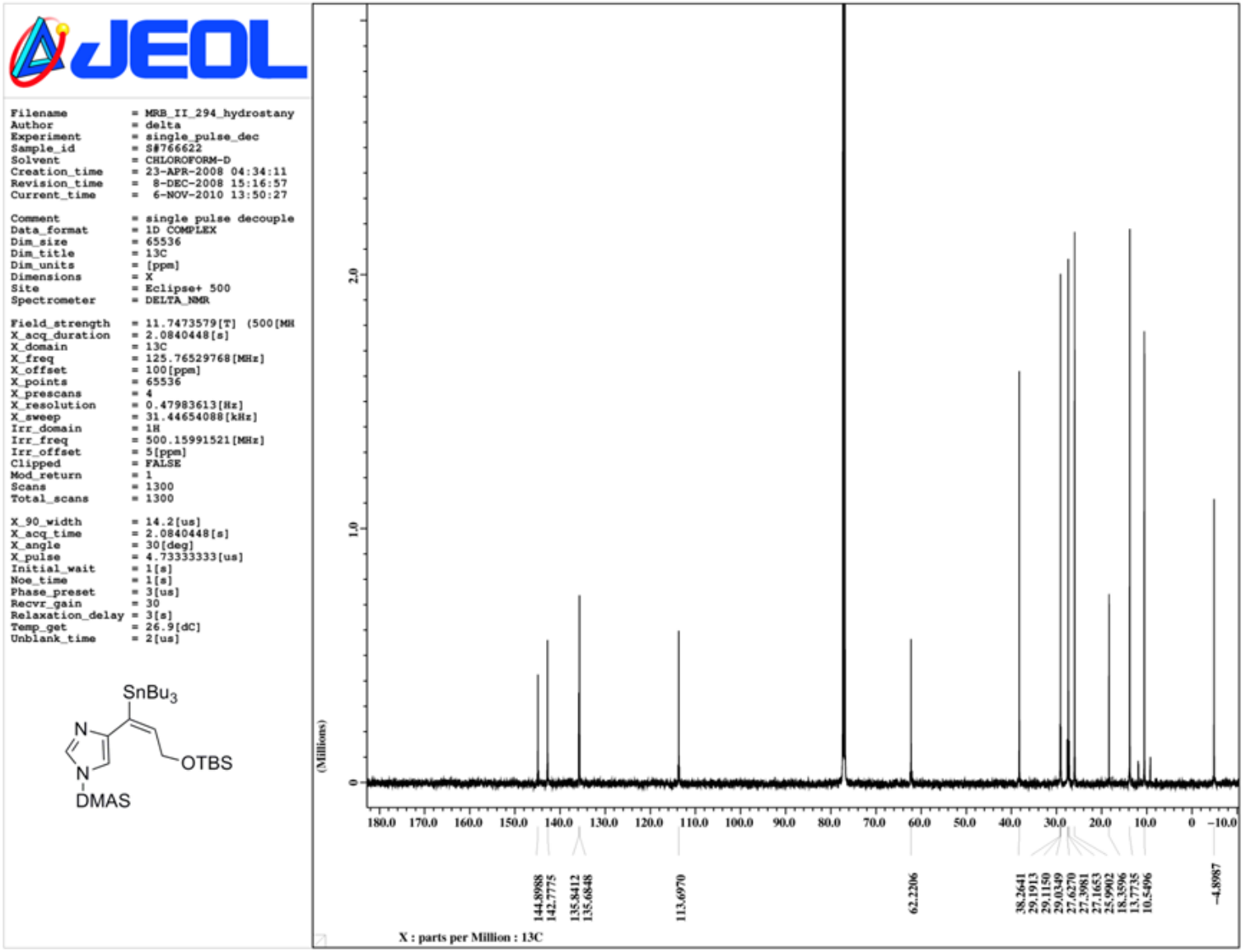
```
Filename          = MRB_II_294_hydrostany
Author            = delta
Experiment        = single_pulse.exp
Sample_id         = S#381121
Solvent           = CHLOROFORM-D
Creation_time     = 23-APR-2008 15:41:35
Revision_time     =  6-NOV-2010 13:43:28
Current_time      =  6-NOV-2010 13:44:07

Comment           = Single Pulse Experime
Data_format       = 1D REAL
Dim_size          = 16384
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = Eclipse+ 500
Spectrometer      = DELTA_NMR

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 2.1823488[s]
X_domain          = 1H
X_freq            = 500.15991521[MHz]
X_offset          = 5[ppm]
X_points          = 16384
X_prescans        = 0
X_resolution      = 0.45822189[Hz]
X_sweep           = 7.50750751[kHz]
Clipped           = FALSE
Mod_return        = 1
Scans             = 16
Total_scans       = 16

X_90_width        = 18.5[us]
X_acq_time        = 2.1823488[s]
X_angle           = 45[deg]
X_pulse           = 9.25[us]
Initial_wait      = 1[s]
Phase_preset      = 3[us]
Recvr_gain        = 17
Relaxation_delay  = 4[s]
Temp_get          = 25[dC]
Unblank_time      = 2[us]
```

```
Filename          = MRB_II_294_hydrostany
Author            = delta
Experiment        = single_pulse.exp
Sample_id         = S#381121
Solvent           = CHLOROFORM-D
Creation_time     = 23-APR-2008 15:41:35
Revision_time     =  6-NOV-2010 13:43:28
Current_time      =  6-NOV-2010 13:49:37

Comment           = Single Pulse Experime
Data_format       = 1D REAL
Dim_size          = 16384
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = Eclipse+ 500
Spectrometer      = DELTA_NMR

Field_strength    = 11.7473579[T]  (500[MH
X_acq_duration    = 2.1823488[s]
X_domain          = 1H
X_freq            = 500.15991521[MHz]
X_offset          = 5[ppm]
X_points          = 16384
X_prescans        = 0
X_resolution      = 0.45822189[Hz]
X_sweep           = 7.50750751[kHz]
Clipped           = FALSE
Mod_return        = 1
Scans             = 16
Total_scans       = 16

X_90_width        = 18.5[us]
X_acq_time        = 2.1823488[s]
X_angle           = 45[deg]
X_pulse           = 9.25[us]
Initial_wait      = 1[s]
Phase_preset      = 3[us]
Recvr_gain        = 17
Relaxation_delay  = 4[s]
Temp_get          = 25[dC]
Unblank_time      = 2[us]
```

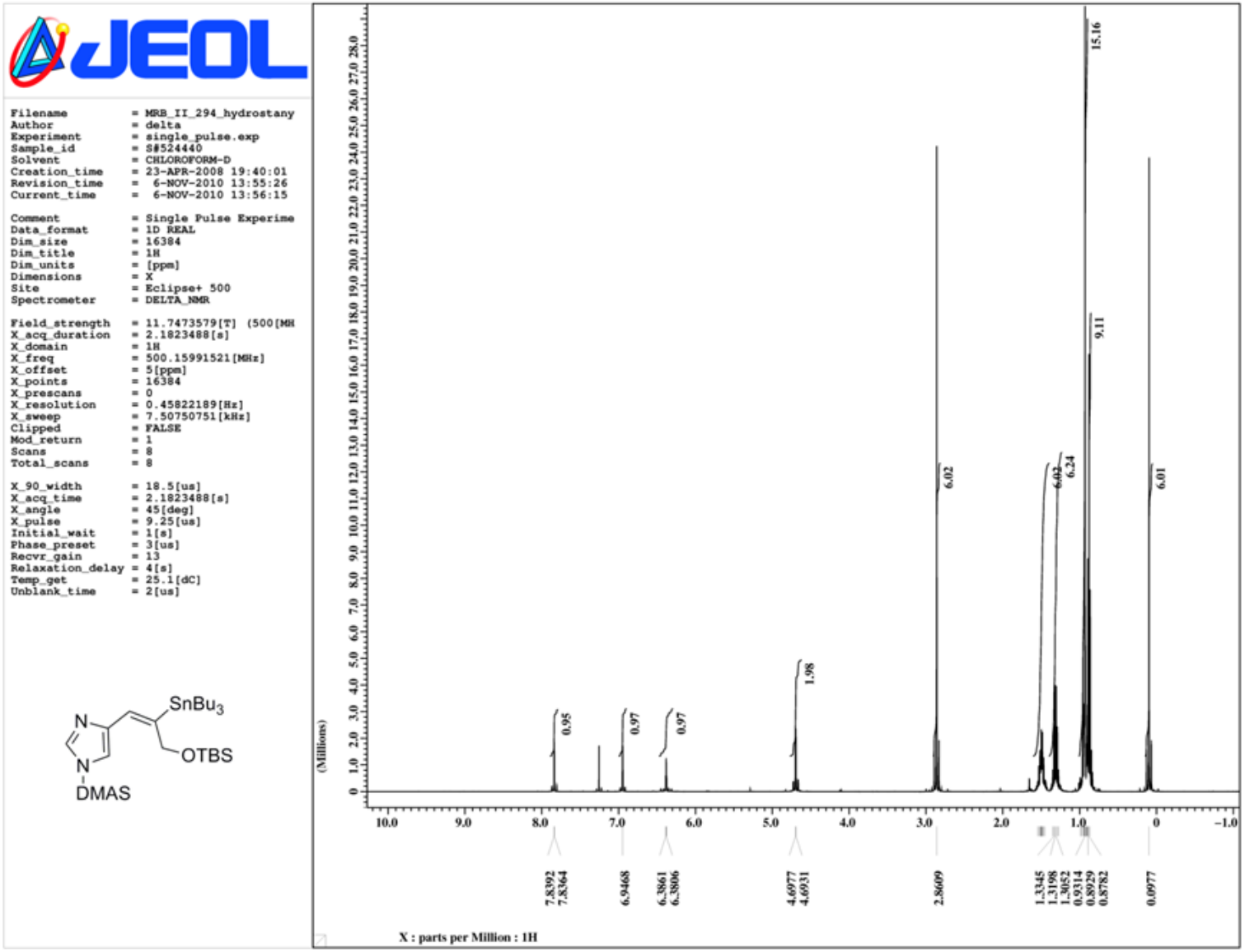






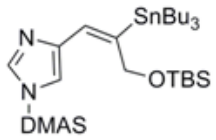

Filename = MRB_II_294_hydrostany
Author = delta
Experiment = single_pulse_dec
Sample_id = S#766622
Solvent = CHLOROFORM-D
Creation_time = 23-APR-2008 04:34:11
Revision_time = 8-DEC-2008 15:16:57
Current_time = 6-NOV-2010 13:50:27
Comment = single pulse decouple
Data_format = 1D COMPLEX
Dim_size = 65536
Dim_title = 13C
Dim_units = [ppm]
Dimensions = X
Site = Eclipse+ 500
Spectrometer = DELTA_NMR
Field_strength = 11.7473579[T] (500[MH
X_acq_duration = 2.0840448[s]
X_domain = 13C
X_freq = 125.76529768[MHz]
X_offset = 100[ppm]
X_points = 65536
X_prescans = 4
X_resolution = 0.47983613[Hz]
X_sweep = 31.44654088[kHz]
Irr_domain = 1H
Irr_freq = 500.15991521[MHz]
Irr_offset = 5[ppm]
Clipped = FALSE
Mod_return = 1
Scans = 1300
Total_scans = 1300
X_90_width = 14.2[us]
X_acq_time = 2.0840448[s]
X_angle = 30[deg]
X_pulse = 4.73333333[us]
Initial_wait = 1[s]
Noe_time = 1[s]
Phase_preset = 3[us]
Recvr_gain = 30
Relaxation_delay = 3[s]
Temp_get = 26.9[dC]
Unblank_time = 2[us]
SnBu3
N
N
OTBS
DMAS
(Millions)
2.0
1.0
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
144.8988
142.7775
135.8412
135.6848
113.6970
62.2206
38.2641
29.1913
29.1150
29.0349
27.6270
27.3981
27.1653
25.9902
18.3596
13.7735
10.5496
−4.8987
X : parts per Million : 13C

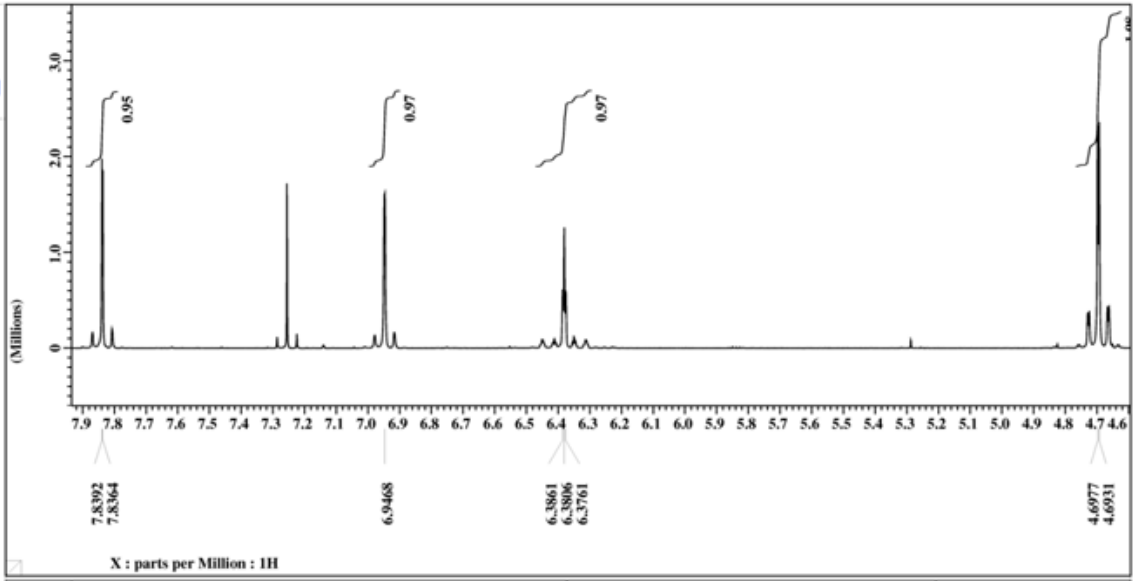
APPENDIX 12
^{1}H AND ^{13}C NMR SPECTRA OF
(*E*)-1-*t*-butyldimethylsilyloxy-2-tributylstannyl-3-(1-dimethylsulfamoylimidazol-4-yl)-2-propene (79)

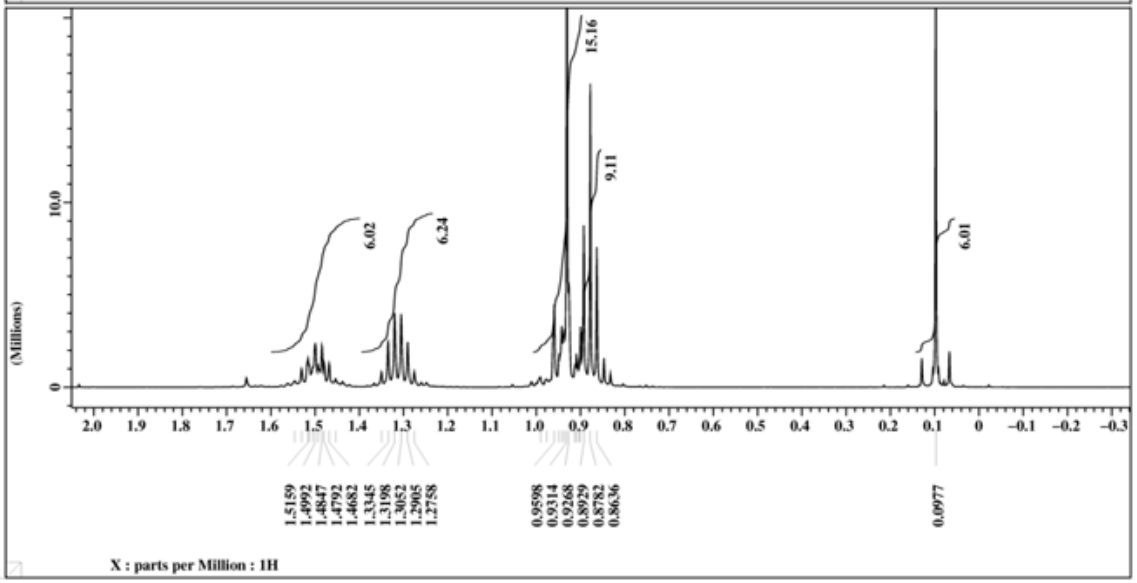


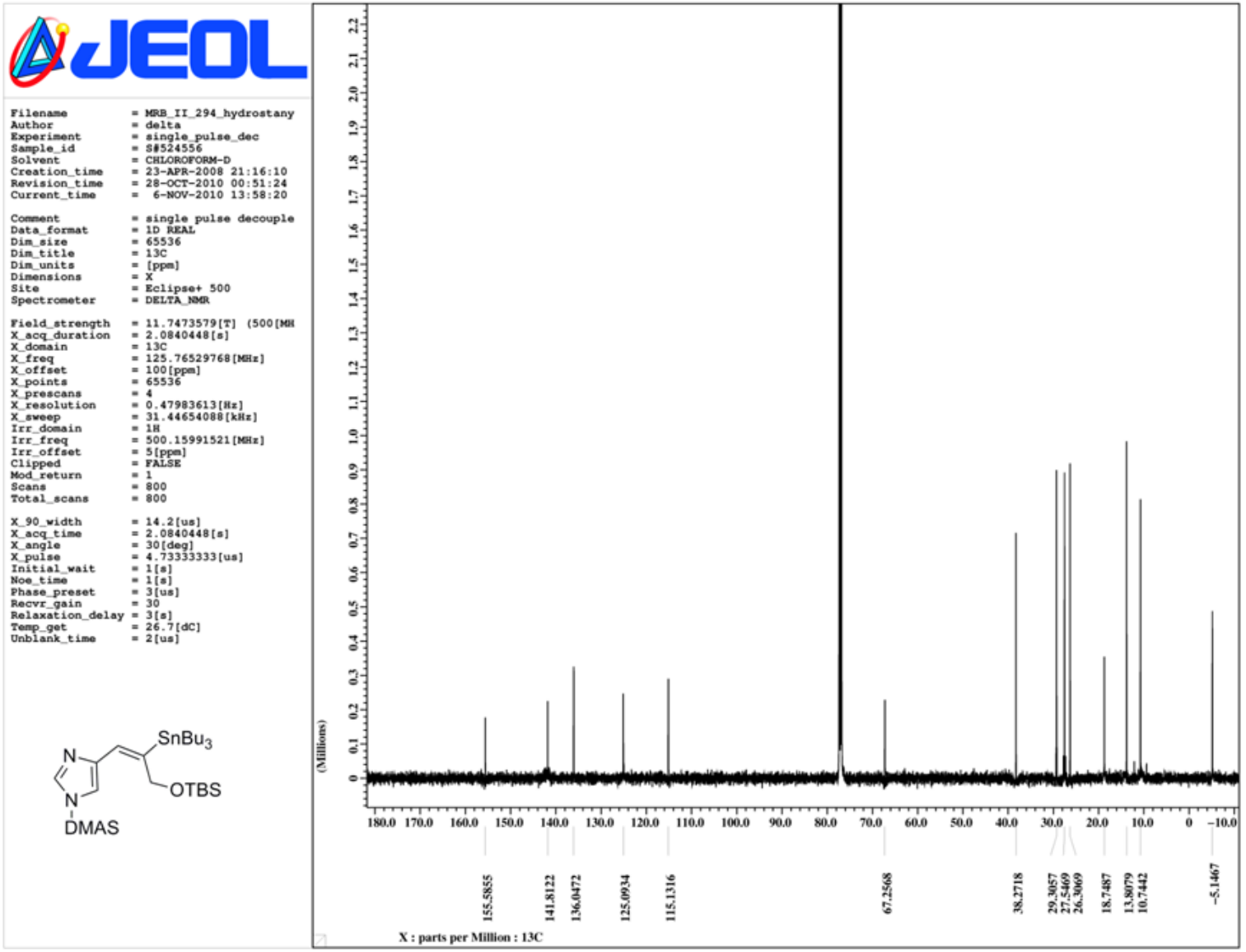
```
Filename          = MRB_II_294_hydrostany
Author            = delta
Experiment        = single_pulse.exp
Sample_id         = S#524440
Solvent           = CHLOROFORM-D
Creation_time     = 23-APR-2008 19:40:01
Revision_time     =  6-NOV-2010 13:55:26
Current_time      =  6-NOV-2010 13:56:15

Comment           = Single Pulse Experime
Data_format       = 1D REAL
Dim_size          = 16384
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = Eclipse+ 500
Spectrometer      = DELTA_NMR

Field_strength    = 11.7473579[T]  (500[MH
X_acq_duration    = 2.1823488[s]
X_domain          = 1H
X_freq            = 500.15991521[MHz]
X_offset          = 5[ppm]
X_points          = 16384
X_prescans        = 0
X_resolution      = 0.45822189[Hz]
X_sweep           = 7.50750751[kHz]
Clipped           = FALSE
Mod_return        = 1
Scans             = 8
Total_scans       = 8

X_90_width        = 18.5[us]
X_acq_time        = 2.1823488[s]
X_angle           = 45[deg]
X_pulse           = 9.25[us]
Initial_wait      = 1[s]
Phase_preset      = 3[us]
Recvr_gain        = 13
Relaxation_delay  = 4[s]
Temp_get          = 25.1[dC]
Unblank_time      = 2[us]
```

```
Filename          = MRB_II_294_hydrostany
Author            = delta
Experiment        = single_pulse.exp
Sample_id         = S#524440
Solvent           = CHLOROFORM-D
Creation_time     = 23-APR-2008 19:40:01
Revision_time     =  6-NOV-2010 13:56:24
Current_time      =  6-NOV-2010 13:57:42

Comment           = Single Pulse Experime
Data_format       = 1D REAL
Dim_size          = 16384
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = Eclipse+ 500
Spectrometer      = DELTA_NMR

Field_strength    = 11.7473579[T]  (500[MH
X_acq_duration    = 2.1823488[s]
X_domain          = 1H
X_freq            = 500.15991521[MHz]
X_offset          = 5[ppm]
X_points          = 16384
X_prescans        = 0
X_resolution      = 0.45822189[Hz]
X_sweep           = 7.50750751[kHz]
Clipped           = FALSE
Mod_return        = 1
Scans             = 8
Total_scans       = 8

X_90_width        = 18.5[us]
X_acq_time        = 2.1823488[s]
X_angle           = 45[deg]
X_pulse           = 9.25[us]
Initial_wait      = 1[s]
Phase_preset      = 3[us]
Recvr_gain        = 13
Relaxation_delay  = 4[s]
Temp_get          = 25.1[dC]
Unblank_time      = 2[us]
```





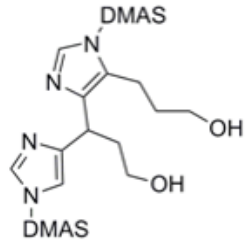


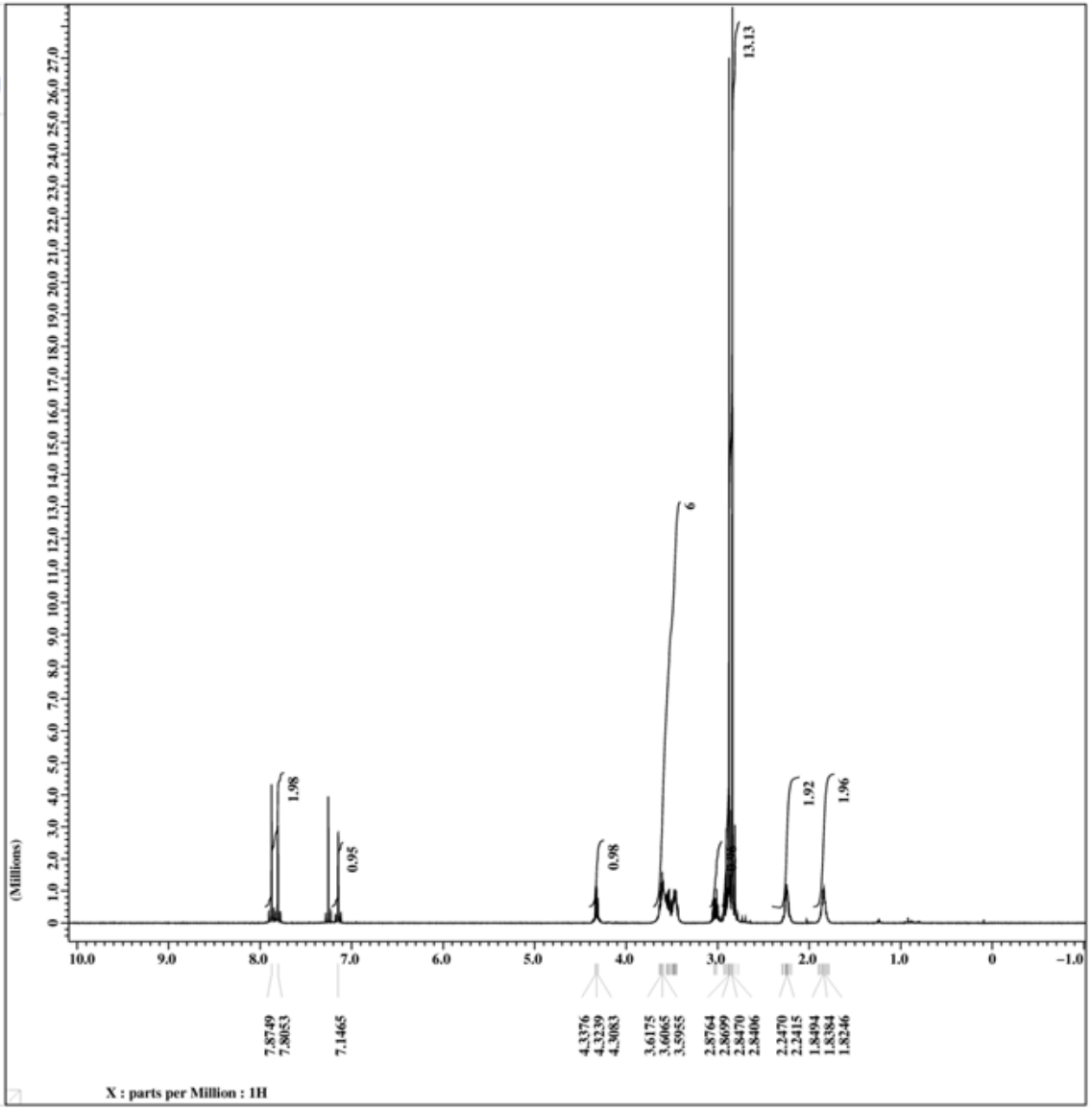


```
Filename          = MRB_II_294_hydrostany
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#524556
Solvent           = CHLOROFORM-D
Creation_time     = 23-APR-2008 21:16:10
Revision_time     = 28-OCT-2010 00:51:24
Current_time      =  6-NOV-2010 13:58:20

Comment           = single pulse decouple
Data_format       = 1D REAL
Dim_size          = 65536
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = Eclipse+ 500
Spectrometer      = DELTA_NMR

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 2.0840448[s]
X_domain          = 13C
X_freq            = 125.76529768[MHz]
X_offset          = 100[ppm]
X_points          = 65536
X_prescans        = 4
X_resolution      = 0.47983613[Hz]
X_sweep           = 31.44654088[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 800
Total_scans       = 800

X_90_width        = 14.2[us]
X_acq_time        = 2.0840448[s]
X_angle           = 30[deg]
X_pulse           = 4.73333333[us]
Initial_wait      = 1[s]
Noe_time          = 1[s]
Phase_preset      = 3[us]
Recvr_gain        = 30
Relaxation_delay  = 3[s]
Temp_get          = 26.7[dC]
Unblank_time      = 2[us]
```

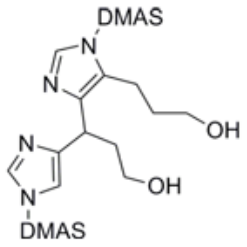
APPENDIX 13
^{1}H AND ^{13}C NMR SPECTRA OF
4-(1-Dimethylsulfamoyl-4-(3-hydroxypropyl)imidazol-4-yl)-1-dimethylsulfamoyl-5-(3-hydroxypropyl)imidazole (74)

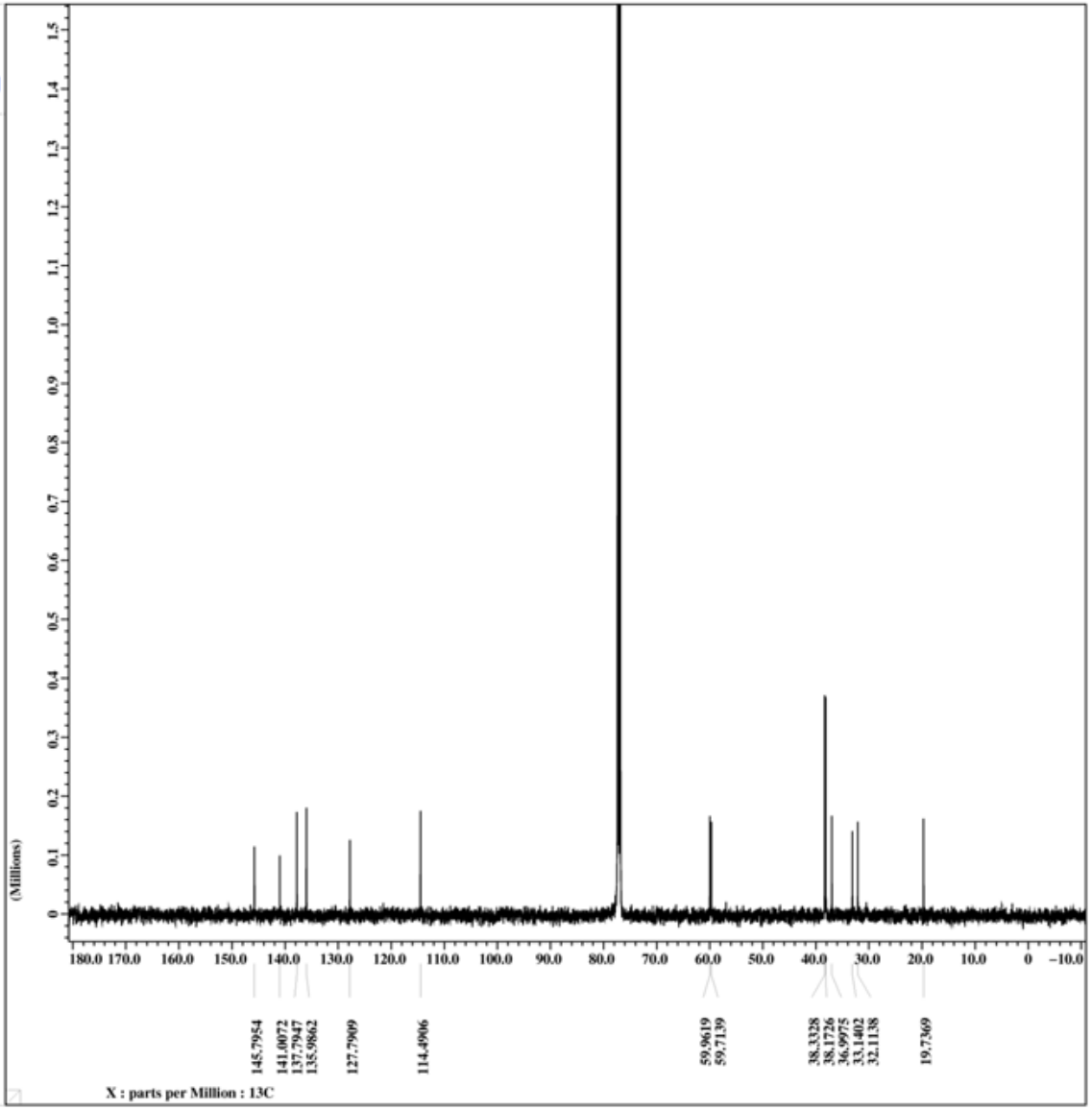
```
Filename          = MRB_II_297_hydrogenat
Author            = delta
Experiment        = single_pulse.exp
Sample_id         = S#576331
Solvent           = CHLOROFORM-D
Creation_time     = 27-APR-2008 22:09:51
Revision_time     =  6-NOV-2010 15:20:43
Current_time      =  6-NOV-2010 15:24:03

Comment           = Single Pulse Experime
Data_format       = 1D REAL
Dim_size          = 16384
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = Eclipse+ 500
Spectrometer      = DELTA_NMR

Field_strength    = 11.7473579[T]  (500[MH
X_acq_duration    = 2.1823488[s]
X_domain          = 1H
X_freq            = 500.15991521[MHz]
X_offset          = 5[ppm]
X_points          = 16384
X_prescans        = 0
X_resolution      = 0.45822189[Hz]
X_sweep           = 7.50750751[kHz]
Clipped           = FALSE
Mod_return        = 1
Scans             = 16
Total_scans       = 16

X_90_width        = 18.5[us]
X_acq_time        = 2.1823488[s]
X_angle           = 45[deg]
X_pulse           = 9.25[us]
Initial_wait      = 1[s]
Phase_preset      = 3[us]
Recvr_gain        = 19
Relaxation_delay  = 4[s]
Temp_get          = 25.1[dC]
Unblank_time      = 2[us]
```



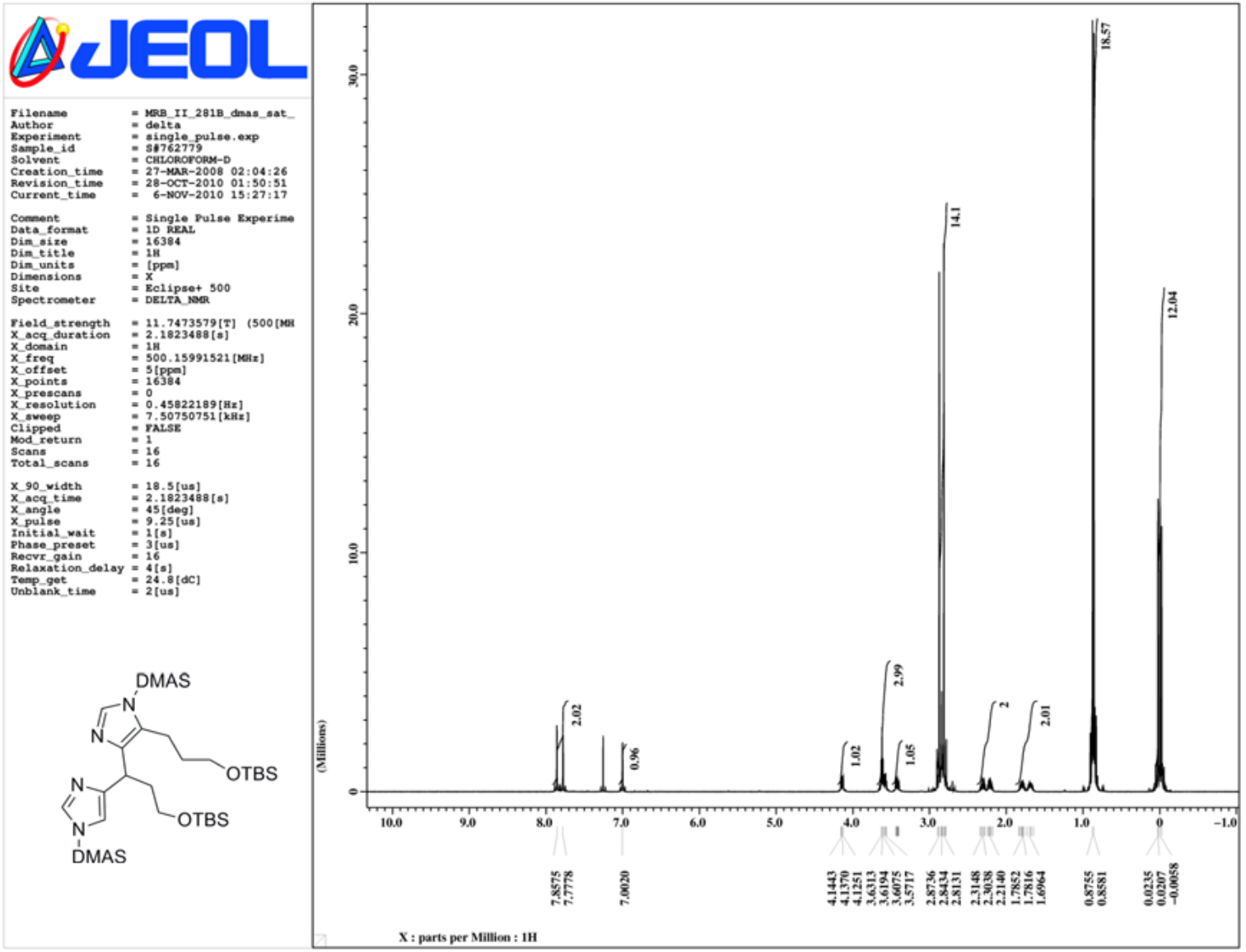


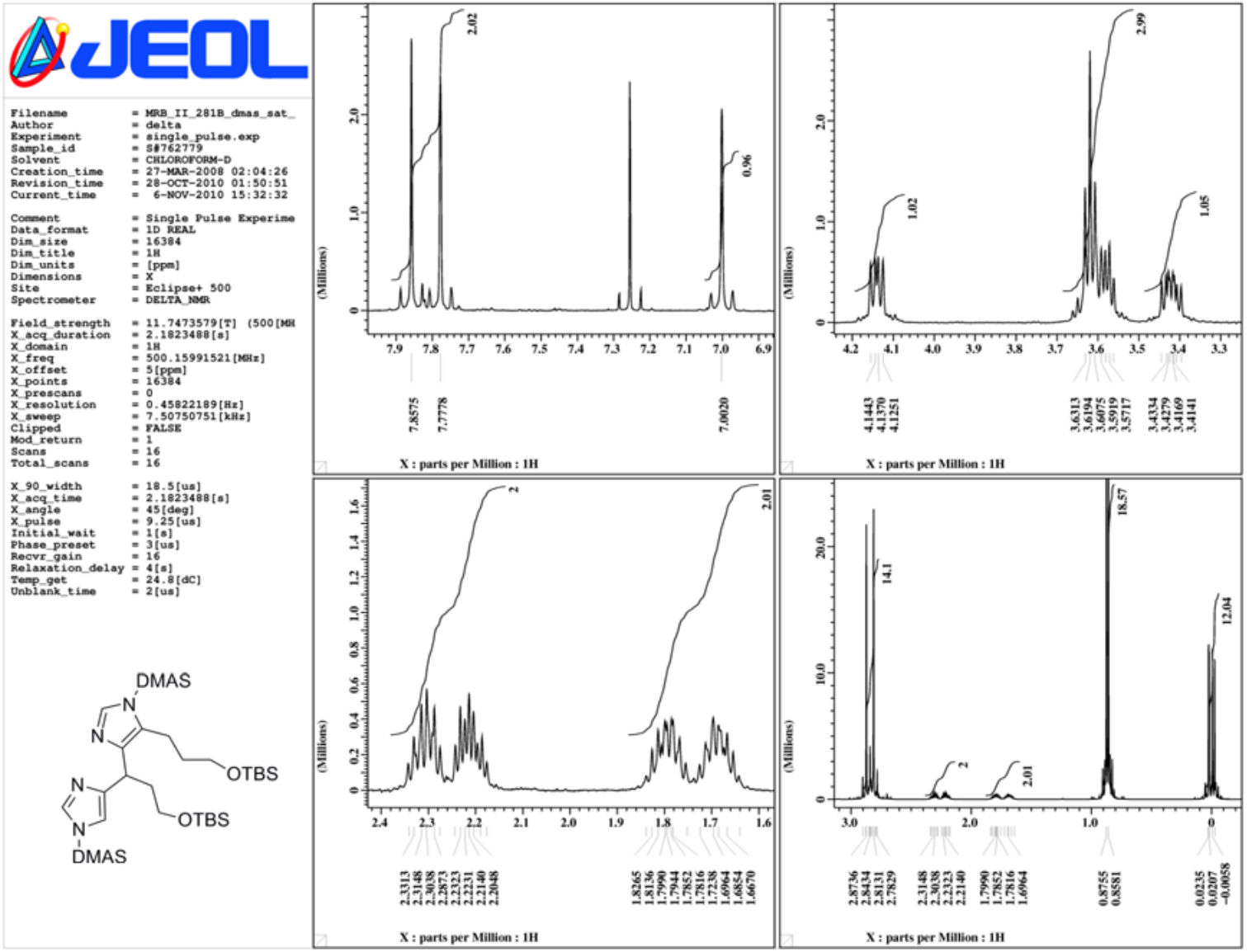
```
Filename          = MRB_II_297_hydrogenat
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#577883
Solvent           = CHLOROFORM-D
Creation_time     = 28-APR-2008 01:06:45
Revision_time     = 27-APR-2008 20:15:01
Current_time      =  6-NOV-2010 15:24:56

Comment           = single pulse decouple
Data_format       = 1D COMPLEX
Dim_size          = 65536
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = Eclipse+ 500
Spectrometer      = DELTA_NMR

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 2.0840448[s]
X_domain          = 13C
X_freq            = 125.76529768[MHz]
X_offset          = 100[ppm]
X_points          = 65536
X_prescans        = 4
X_resolution      = 0.47983613[Hz]
X_sweep           = 31.44654088[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 1700
Total_scans       = 1700

X_90_width        = 14.2[us]
X_acq_time        = 2.0840448[s]
X_angle           = 30[deg]
X_pulse           = 4.73333333[us]
Initial_wait      = 1[s]
Noe_time          = 1[s]
Phase_preset      = 3[us]
Recvr_gain        = 30
Relaxation_delay  = 3[s]
Temp_get          = 26.9[dC]
Unblank_time      = 2[us]
```



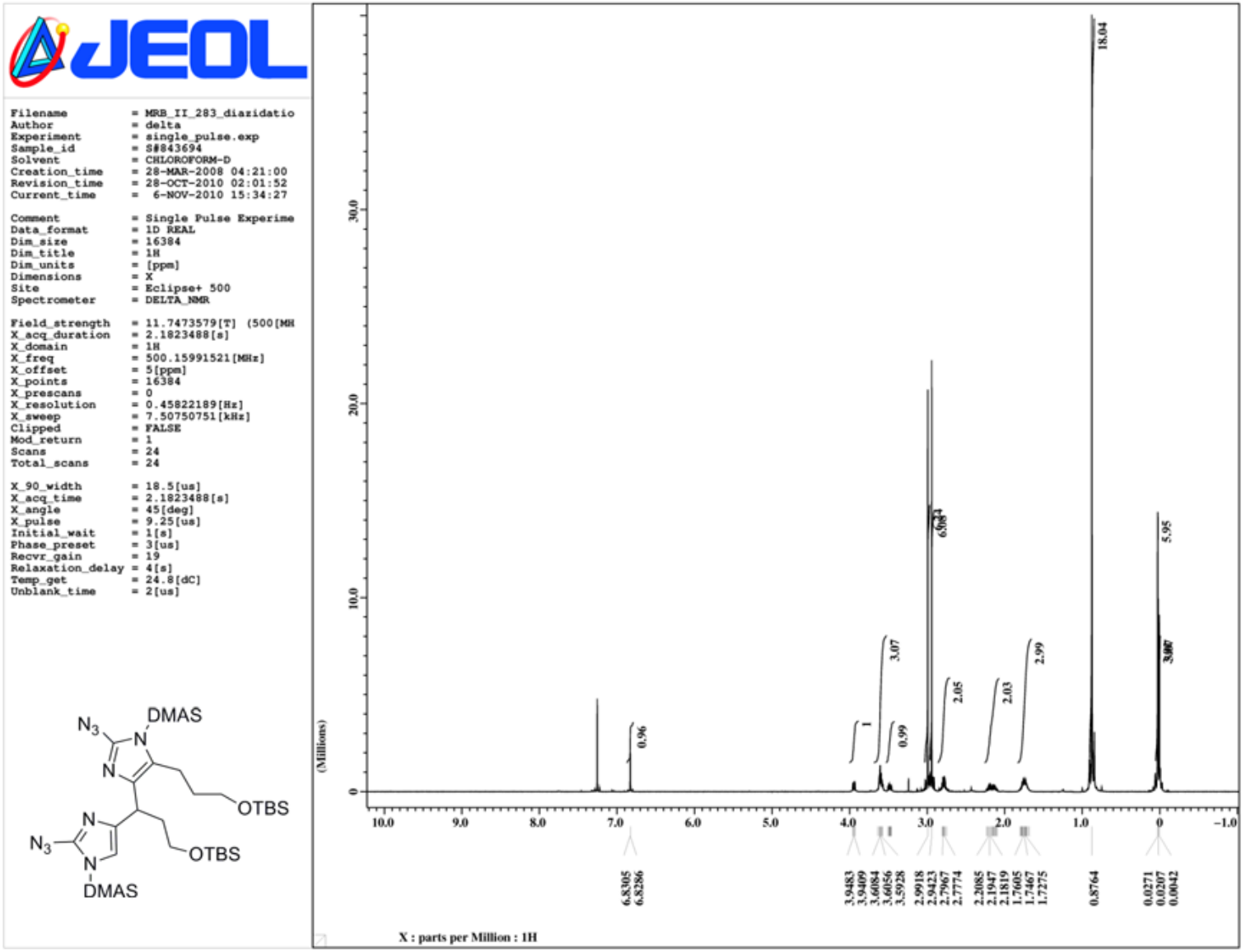


APPENDIX 14
^{1}H AND ^{13}C NMR SPECTRA OF
4-(1-Dimethylsulfamoyl-4-(3-*t*-butyldimethylsilyloxypropyl)imidazol-4-yl)-1-dimethylsulfamoyl-5-(3-*t*-butyldimethylsilyloxypropyl)imidazole (81)


Filename = MRB_II_281B_dmas_sat_
Author = delta
Experiment = single_pulse.exp
Sample_id = S#762779
Solvent = CHLOROFORM-D
Creation_time = 27-MAR-2008 02:04:26
Revision_time = 28-OCT-2010 01:50:51
Current_time = 6-NOV-2010 15:27:17
Comment = Single Pulse Experime
Data_format = 1D REAL
Dim_size = 16384
Dim_title = 1H
Dim_units = [ppm]
Dimensions = X
Site = Eclipse+ 500
Spectrometer = DELTA_NMR
Field_strength = 11.7473579[T] (500[MH
X_acq_duration = 2.1823488[s]
X_domain = 1H
X_freq = 500.15991521[MHz]
X_offset = 5[ppm]
X_points = 16384
X_prescans = 0
X_resolution = 0.45822189[Hz]
X_sweep = 7.50750751[kHz]
Clipped = FALSE
Mod_return = 1
Scans = 16
Total_scans = 16
X_90_width = 18.5[us]
X_acq_time = 2.1823488[s]
X_angle = 45[deg]
X_pulse = 9.25[us]
Initial_wait = 1[s]
Phase_preset = 3[us]
Recvr_gain = 16
Relaxation_delay = 4[s]
Temp_get = 24.8[dC]
Unblank_time = 2[us]
DMAS
OTBS
OTBS
DMAS
(Millions)
30.0
20.0
10.0
0
18.57
14.1
12.04
2.99
2.02
2
2.01
1.05
1.02
0.96
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
−1.0
7.8575
7.7778
7.0020
4.1443
4.1370
4.1251
3.6313
3.6194
3.6075
3.5717
2.8736
2.8434
2.8131
2.3148
2.3038
2.2140
1.7852
1.7816
1.6964
0.8755
0.8581
0.0235
0.0207
−0.0058
X : parts per Million : 1H

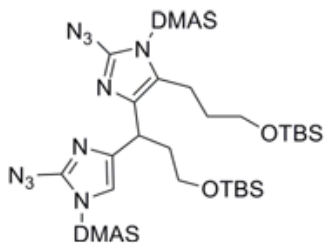

Filename = MRB_II_281B_dmas_sat_
Author = delta
Experiment = single_pulse.exp
Sample_id = S#762779
Solvent = CHLOROFORM-D
Creation_time = 27-MAR-2008 02:04:26
Revision_time = 28-OCT-2010 01:50:51
Current_time = 6-NOV-2010 15:32:32
Comment = Single Pulse Experime
Data_format = 1D REAL
Dim_size = 16384
Dim_title = 1H
Dim_units = [ppm]
Dimensions = X
Site = Eclipse+ 500
Spectrometer = DELTA_NMR
Field_strength = 11.7473579[T] (500[MH
X_acq_duration = 2.1823488[s]
X_domain = 1H
X_freq = 500.15991521[MHz]
X_offset = 5[ppm]
X_points = 16384
X_prescans = 0
X_resolution = 0.45822189[Hz]
X_sweep = 7.50750751[kHz]
Clipped = FALSE
Mod_return = 1
Scans = 16
Total_scans = 16
X_90_width = 18.5[us]
X_acq_time = 2.1823488[s]
X_angle = 45[deg]
X_pulse = 9.25[us]
Initial_wait = 1[s]
Phase_preset = 3[us]
Recvr_gain = 16
Relaxation_delay = 4[s]
Temp_get = 24.8[dC]
Unblank_time = 2[us]
DMAS
OTBS
OTBS
DMAS
(Millions)
X : parts per Million : 1H

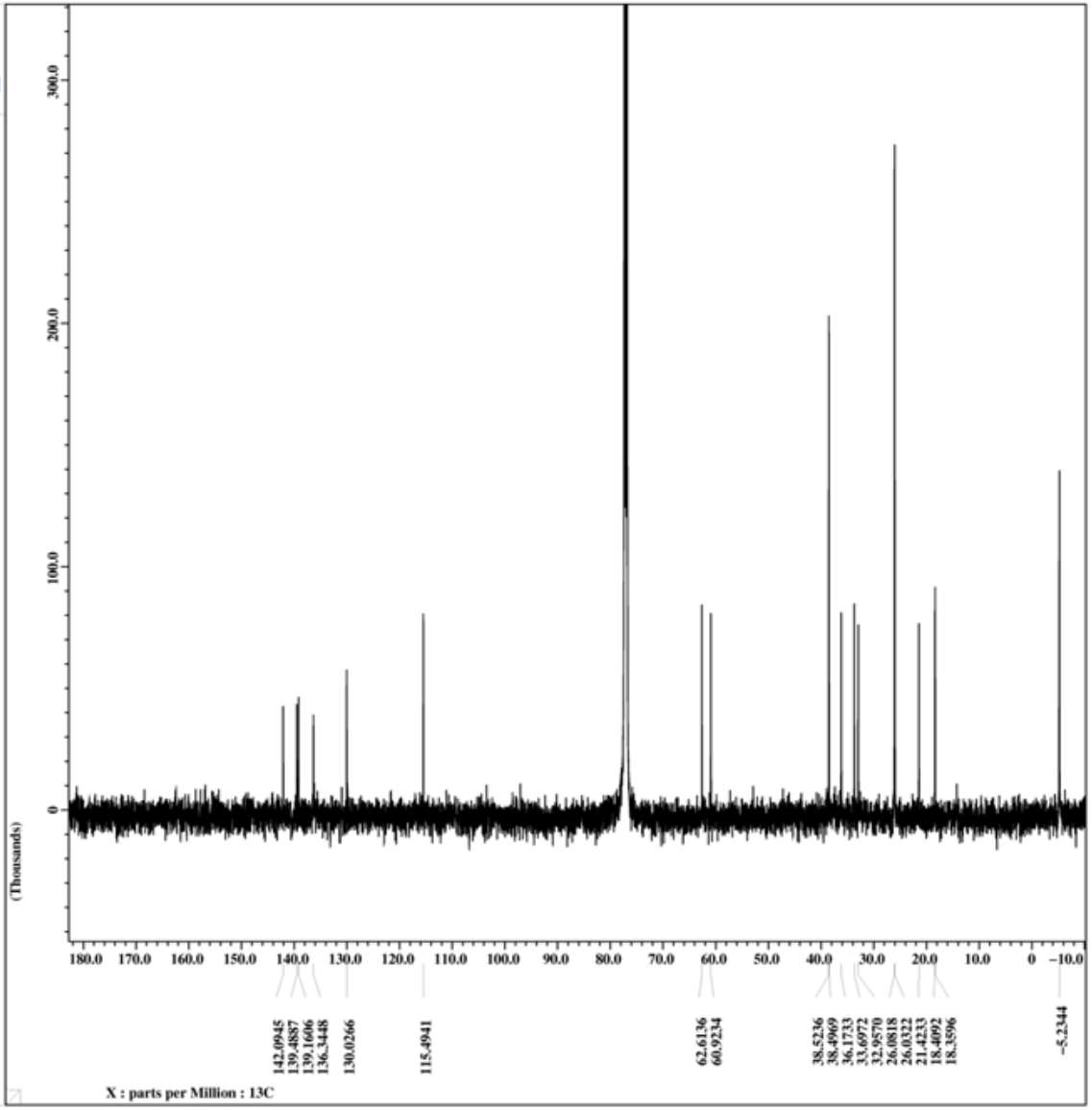
APPENDIX 15
^{1}H AND ^{13}C NMR SPECTRA OF
2-Azido-4-(2-azido-1-dimethylsulfamoyl-4-(3-*t*-butyldimethylsilyloxypropyl)imidazol-4-yl)-1-dimethylsulfamoyl-5-(3-*t*-butyldimethylsilyloxypropyl)imidazole (82)



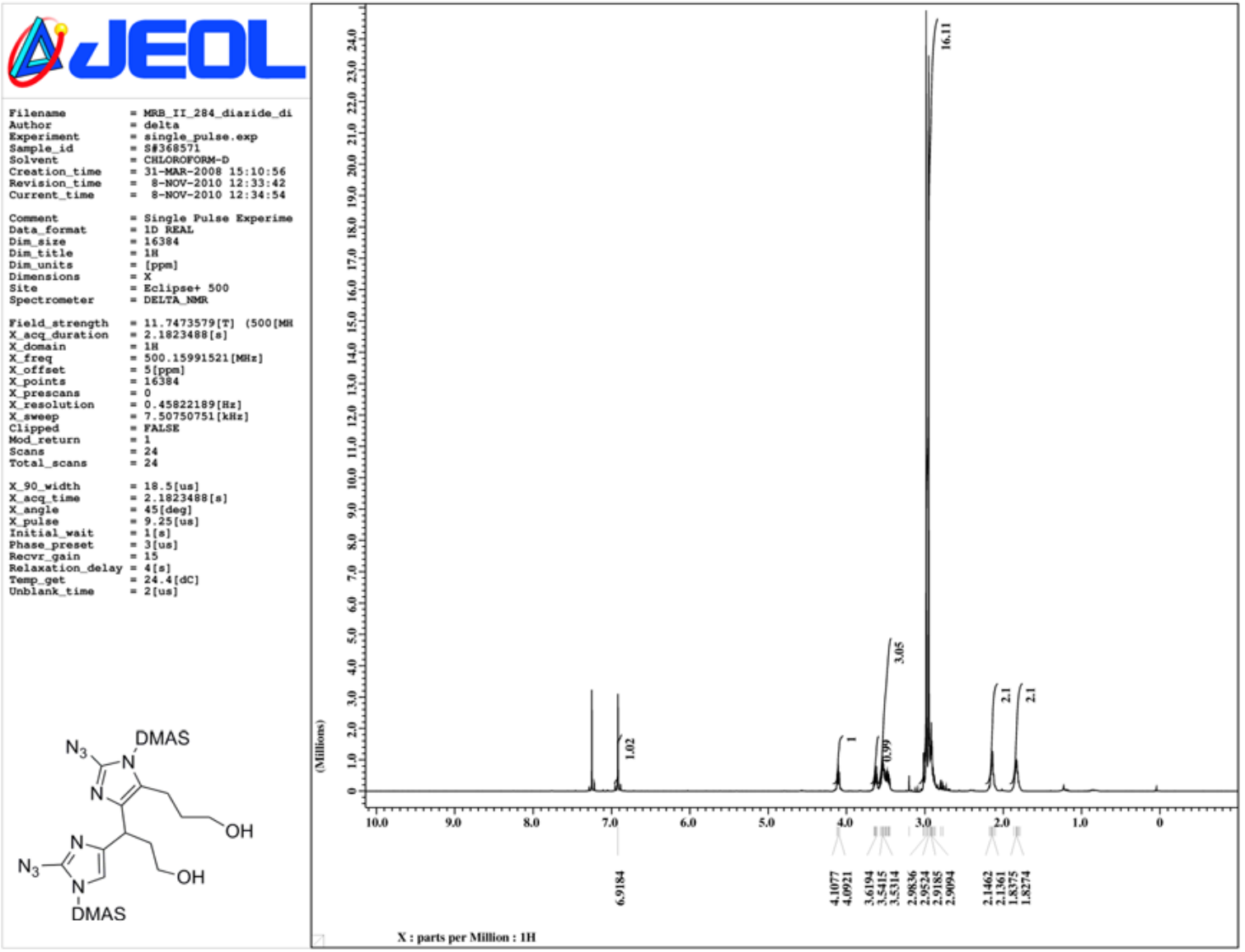
```
Filename          = MRB_II_283_diazidatio
Author            = delta
Experiment        = single_pulse.exp
Sample_id         = S#843694
Solvent           = CHLOROFORM-D
Creation_time     = 28-MAR-2008 04:21:00
Revision_time     = 28-OCT-2010 02:01:52
Current_time      =  6-NOV-2010 15:34:27

Comment           = Single Pulse Experime
Data_format       = 1D REAL
Dim_size          = 16384
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = Eclipse+ 500
Spectrometer      = DELTA_NMR

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 2.1823488[s]
X_domain          = 1H
X_freq            = 500.15991521[MHz]
X_offset          = 5[ppm]
X_points          = 16384
X_prescans        = 0
X_resolution      = 0.45822189[Hz]
X_sweep           = 7.50750751[kHz]
Clipped           = FALSE
Mod_return        = 1
Scans             = 24
Total_scans       = 24

X_90_width        = 18.5[us]
X_acq_time        = 2.1823488[s]
X_angle           = 45[deg]
X_pulse           = 9.25[us]
Initial_wait      = 1[s]
Phase_preset      = 3[us]
Recvr_gain        = 19
Relaxation_delay  = 4[s]
Temp_get          = 24.8[dC]
Unblank_time      = 2[us]
```

```
Filename          = MRB_II_283_diazidatio
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#845222
Solvent           = CHLOROFORM-D
Creation_time     = 28-MAR-2008 12:50:18
Revision_time     = 28-OCT-2010 01:55:03
Current_time      =  6-NOV-2010 15:35:25

Comment           = single pulse decouple
Data_format       = 1D COMPLEX
Dim_size          = 65536
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = Eclipse+ 500
Spectrometer      = DELTA_NMR

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 2.0840448[s]
X_domain          = 13C
X_freq            = 125.76529768[MHz]
X_offset          = 100[ppm]
X_points          = 65536
X_prescans        = 4
X_resolution      = 0.47983613[Hz]
X_sweep           = 31.44654088[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 5000
Total_scans       = 5000

X_90_width        = 14.2[us]
X_acq_time        = 2.0840448[s]
X_angle           = 30[deg]
X_pulse           = 4.73333333[us]
Initial_wait      = 1[s]
Noe_time          = 1[s]
Phase_preset      = 3[us]
Recvr_gain        = 30
Relaxation_delay  = 3[s]
Temp_get          = 27.1[dC]
Unblank_time      = 2[us]
```

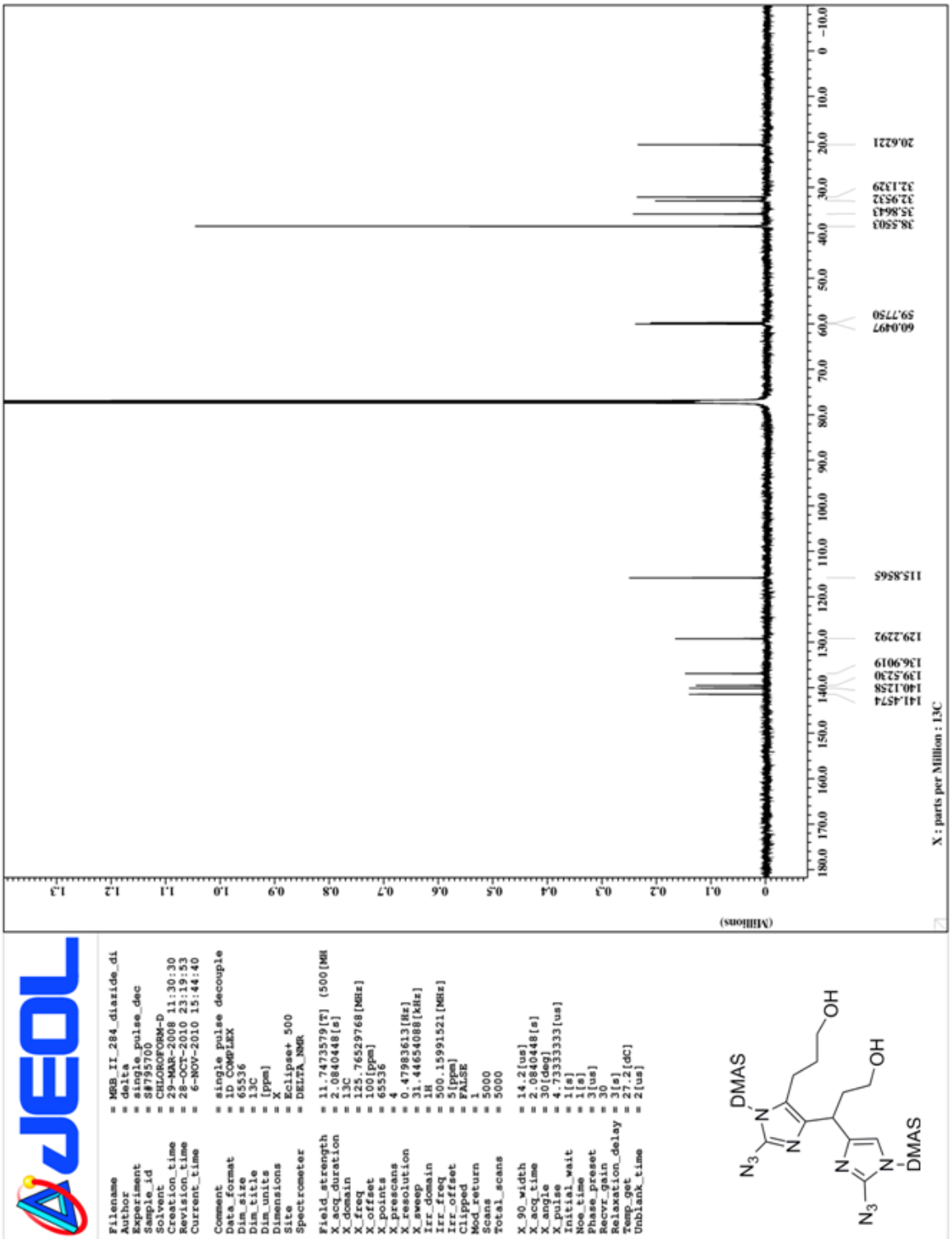




APPENDIX 16
^{1}H AND ^{13}C NMR SPECTRA OF
2-Azido-4-(2-azido-1-dimethylsulfamoyl-4-(3-hydroxypropyl)imidazol-4-yl)-1-dimethylsulfamoyl-5-(3-hydroxypropyl)imidazole (83)



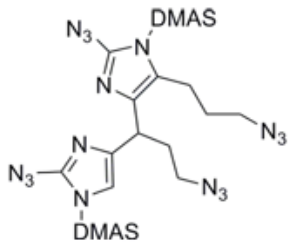
```
Filename          = MRB_II_284_diazide_di
Author            = delta
Experiment        = single_pulse.exp
Sample_id         = S#368571
Solvent           = CHLOROFORM-D
Creation_time     = 31-MAR-2008 15:10:56
Revision_time     =  8-NOV-2010 12:33:42
Current_time      =  8-NOV-2010 12:34:54

Comment           = Single Pulse Experime
Data_format       = 1D REAL
Dim_size          = 16384
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = Eclipse+ 500
Spectrometer      = DELTA_NMR

Field_strength    = 11.7473579[T]  (500[MH
X_acq_duration    = 2.1823488[s]
X_domain          = 1H
X_freq            = 500.15991521[MHz]
X_offset          = 5[ppm]
X_points          = 16384
X_prescans        = 0
X_resolution      = 0.45822189[Hz]
X_sweep           = 7.50750751[kHz]
Clipped           = FALSE
Mod_return        = 1
Scans             = 24
Total_scans       = 24

X_90_width        = 18.5[us]
X_acq_time        = 2.1823488[s]
X_angle           = 45[deg]
X_pulse           = 9.25[us]
Initial_wait      = 1[s]
Phase_preset      = 3[us]
Recvr_gain        = 15
Relaxation_delay  = 4[s]
Temp_get          = 24.4[dC]
Unblank_time      = 2[us]
```

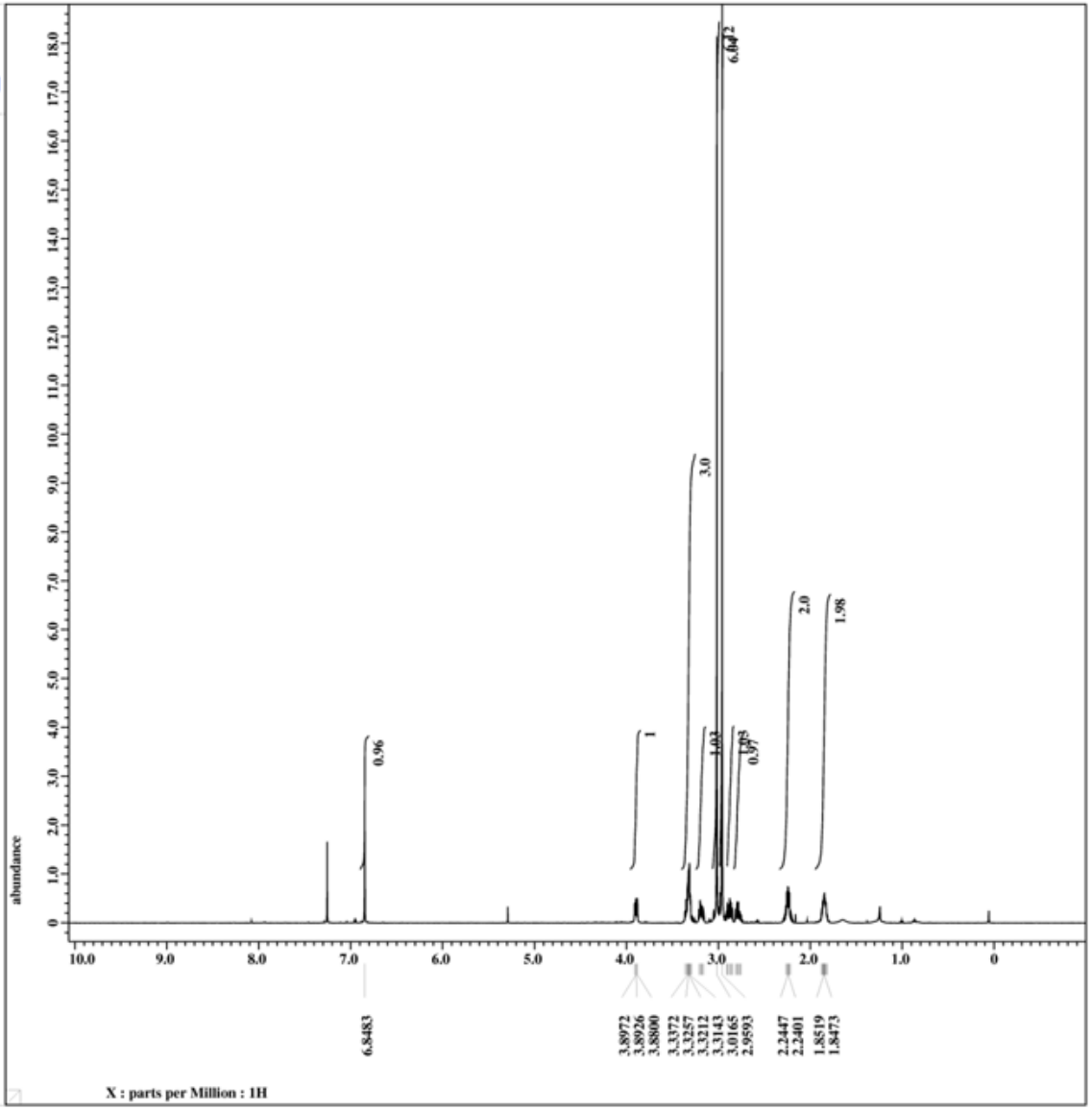

JEOL
Filename = MRB_II_284_diazide_di
Author = delta
Experiment = single_pulse_dec
Sample_id = s#795700
Solvent = CHLOROFORM-D
Creation_time = 29-MAR-2008 11:30:30
Revision_time = 28-OCT-2010 23:19:53
Current_time = 6-NOV-2010 15:44:40
Comment = single pulse decouple
Data_format = 1D COMPLEX
Dim_size = 65536
Dim_title = 13C
Dim_units = [ppm]
Dimensions = X
Site = Eclipse+ 500
Spectrometer = DELTA_NMR
Field_strength = 11.7473579[T] (500[MH
X_acq_duration = 2.0840448[s]
X_domain = 13C
X_freq = 125.765297681MHz]
X_offset = 100[ppm]
X_points = 65536
X_prescans = 4
X_resolution = 0.47983613[Hz]
X_sweep = 31.44654088[kHz]
Irr_domain = 1H
Irr_freq = 500.15991521[MHz]
Irr_offset = 5[ppm]
Clipped = FALSE
Mod_return = 1
Scans = 5000
Total_scans = 5000
X_90_width = 14.2[us]
X_acq_time = 2.0840448[s]
X_angle = 30[deg]
X_pulse = 4.733333333[us]
Initial_wait = 1[s]
Noe_time = 1[s]
Phase_preset = 3[us]
Recvr_gain = 30
Relaxation_delay = 3[s]
Temp_get = 27.2[dC]
Unblank_time = 2[us]
(Millions)
X : parts per Million : 13C
141.4574
140.1258
139.5230
136.9019
129.2292
115.8565
60.0497
59.7750
38.5503
35.8643
32.9532
32.1329
20.6221
DMAS
OH
OH
DMAS

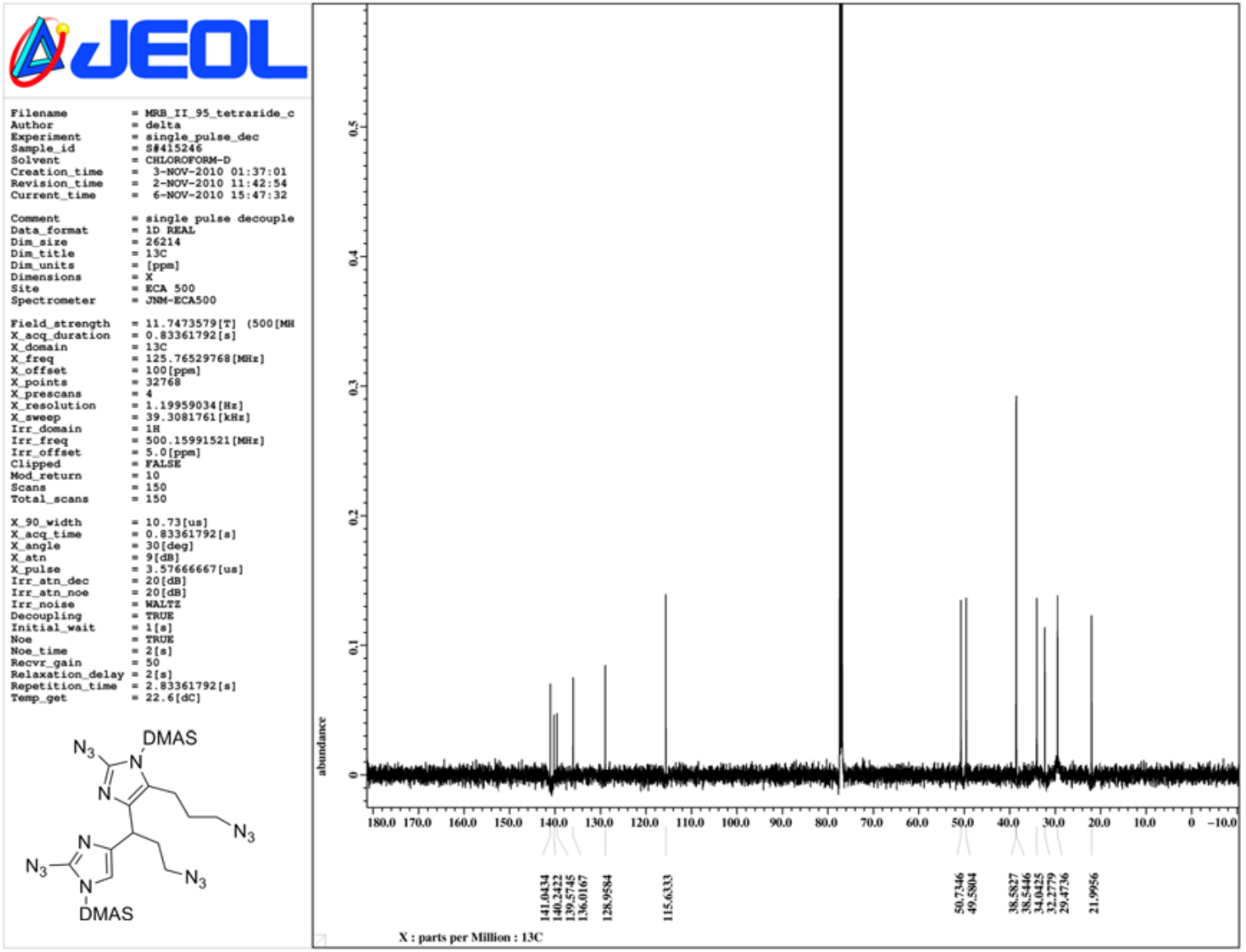
APPENDIX 17
^{1}H AND ^{13}C NMR SPECTRA OF
2-Azido-4-(2-azido-1-dimethylsulfamoyl-4-(3-azidopropyl)imidazol-4-yl)-1-dimethylsulfamoyl-5-(3-azidopropyl)imidazole (85)

JEOL

Filename	= MRB_II_95_tetraazide_
Author	= delta
Experiment	= single_pulse.ex2
Sample_id	= S#414575
Solvent	= CHLOROFORM-D
Creation_time	= 3-NOV-2010 01:29:42
Revision_time	= 6-NOV-2010 15:45:59
Current_time	= 6-NOV-2010 15:46:28
Comment	= single_pulse
Data_format	= 1D REAL
Dim_size	= 13107
Dim_title	= 1H
Dim_units	= [ppm]
Dimensions	= X
Site	= ECA 500
Spectrometer	= JNM-ECA500
Field_strength	= 11.7473579[T] (500[MH
X_acq_duration	= 1.74587904[s]
X_domain	= 1H
X_freq	= 500.15991521[MHz]
X_offset	= 5.0[ppm]
X_points	= 16384
X_prescans	= 0
X_resolution	= 0.57277737[Hz]
X_sweep	= 9.38438438[kHz]
Irr_domain	= 1H
Irr_freq	= 500.15991521[MHz]
Irr_offset	= 5.0[ppm]
Tri_domain	= 1H
Tri_freq	= 500.15991521[MHz]
Tri_offset	= 5.0[ppm]
Clipped	= FALSE
Mod_return	= 1
Scans	= 16
Total_scans	= 16
X_90_width	= 12.54[us]
X_acq_time	= 1.74587904[s]
X_angle	= 45[deg]
X_atn	= 4[dB]
X_pulse	= 6.27[us]
Irr_mode	= Off
Tri_mode	= Off
Dante_presat	= FALSE
Initial_wait	= 1[s]
Recvr_gain	= 42
Relaxation_delay	= 5[s]
Repetition_time	= 6.74587904[s]
Temp_get	= 22[dC]

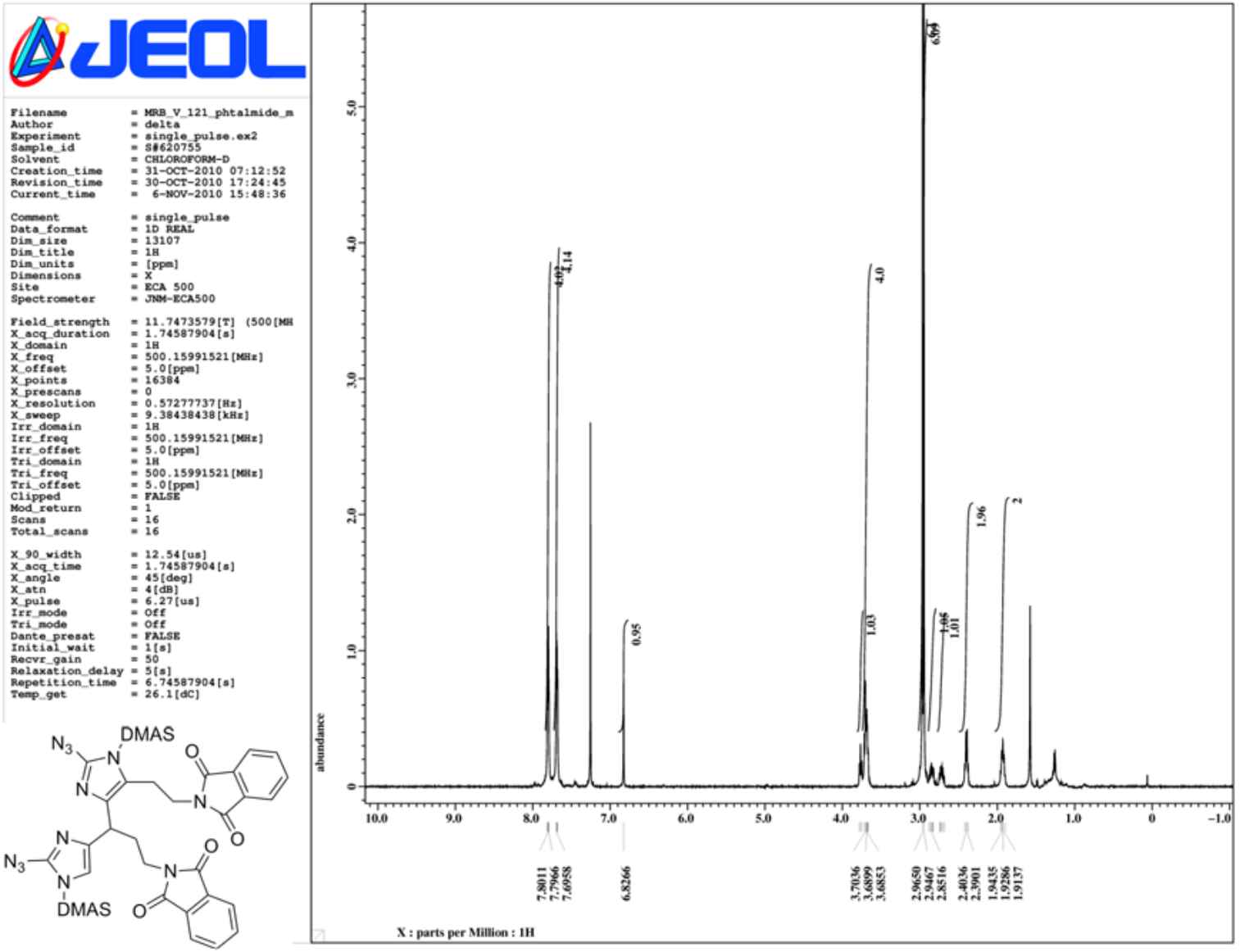






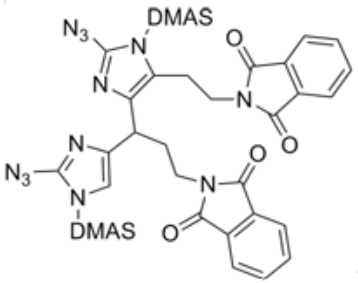
```
Filename          = MRB_II_95_tetraziide_c
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#415246
Solvent           = CHLOROFORM-D
Creation_time     =  3-NOV-2010 01:37:01
Revision_time     =  2-NOV-2010 11:42:54
Current_time      =  6-NOV-2010 15:47:32

Comment           = single pulse decouple
Data_format       = 1D REAL
Dim_size          = 26214
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 0.83361792[s]
X_domain          = 13C
X_freq            = 125.76529768[MHz]
X_offset          = 100[ppm]
X_points          = 32768
X_prescans        = 4
X_resolution      = 1.19959034[Hz]
X_sweep           = 39.3081761[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 10
Scans             = 150
Total_scans       = 150

X_90_width        = 10.73[us]
X_acq_time        = 0.83361792[s]
X_angle           = 30[deg]
X_atn             = 9[dB]
X_pulse           = 3.57666667[us]
Irr_atn_dec       = 20[dB]
Irr_atn_noe       = 20[dB]
Irr_noise         = WALTZ
Decoupling        = TRUE
Initial_wait      = 1[s]
Noe               = TRUE
Noe_time          = 2[s]
Recvr_gain        = 50
Relaxation_delay  = 2[s]
Repetition_time   = 2.83361792[s]
Temp_get          = 22.6[dC]
```

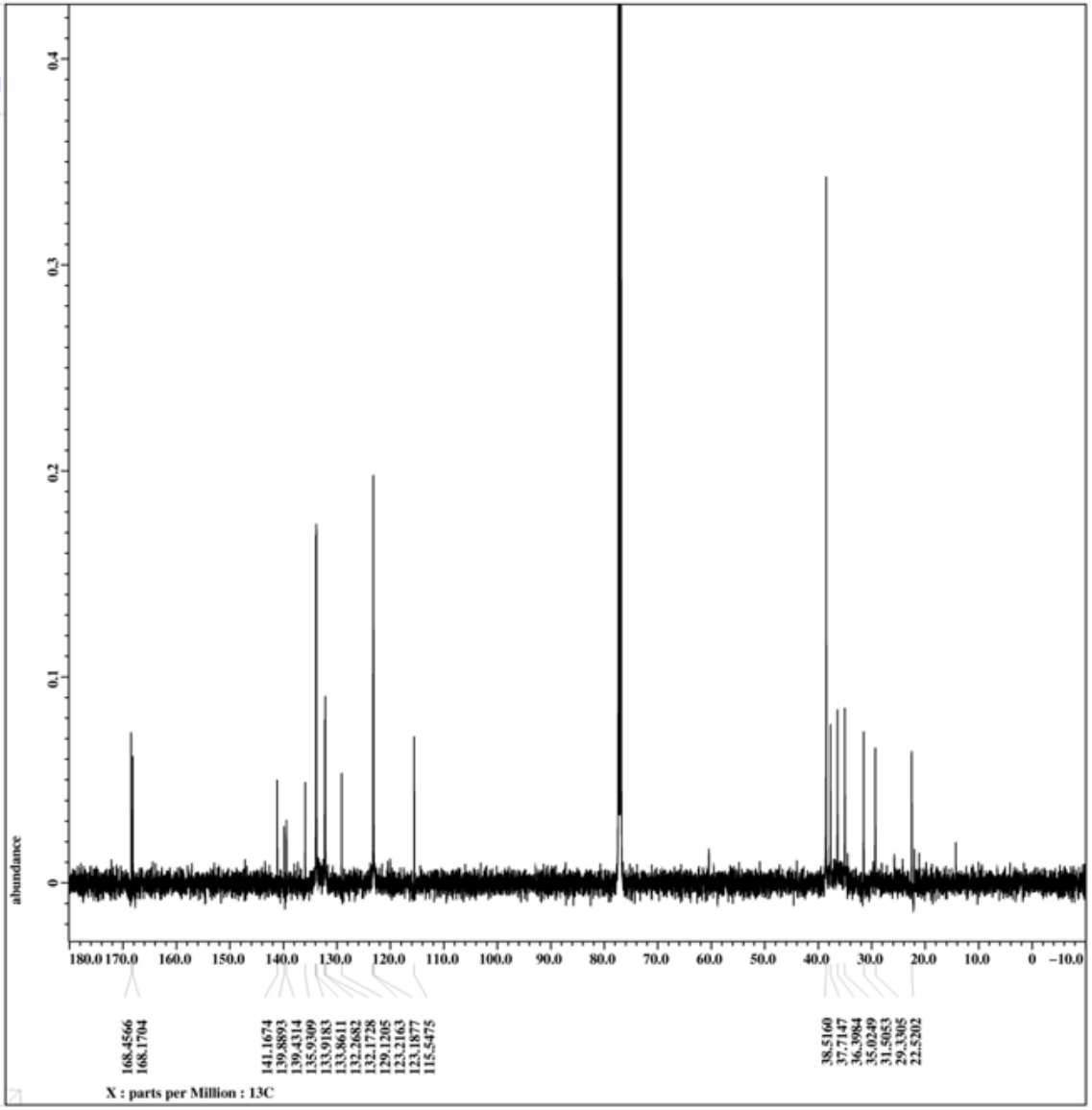
APPENDIX 18
^{1}H AND ^{13}C NMR SPECTRA OF
2-Azido-4-(2-azido-1-dimethylsulfamoyl-4-(3-phthalimidoylpropyl)imidazol-4-yl)-1-dimethylsulfamoyl-5-(3-phthalimidoylpropyl)imidazole (89)



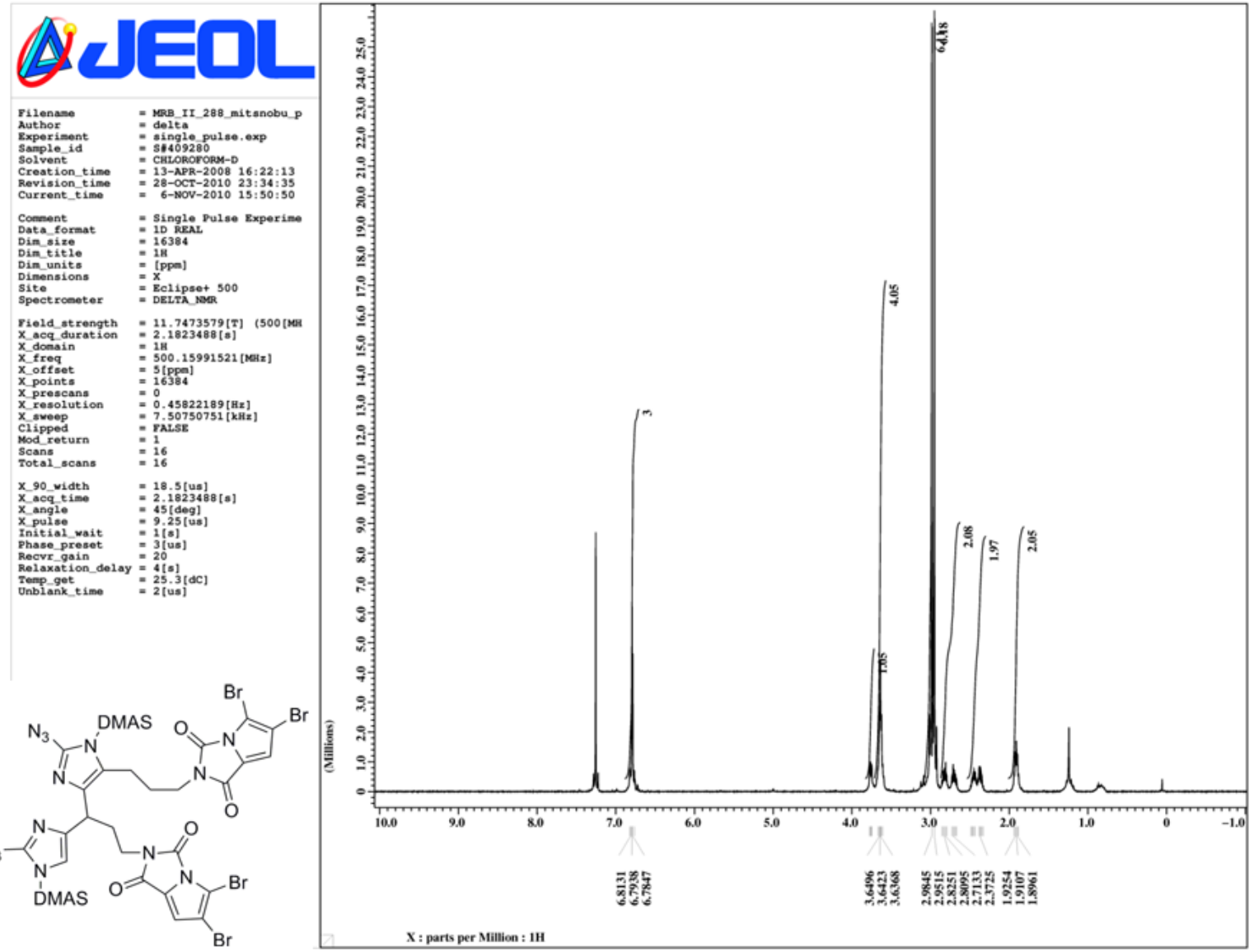
```
Filename          = MRB_V_121_phtalmide_m
Author            = delta
Experiment        = single_pulse.ex2
Sample_id         = S#620755
Solvent           = CHLOROFORM-D
Creation_time     = 31-OCT-2010 07:12:52
Revision_time     = 30-OCT-2010 17:24:45
Current_time      =  6-NOV-2010 15:48:36

Comment           = single_pulse
Data_format       = 1D REAL
Dim_size          = 13107
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 1.74587904[s]
X_domain          = 1H
X_freq            = 500.15991521[MHz]
X_offset          = 5.0[ppm]
X_points          = 16384
X_prescans        = 0
X_resolution      = 0.57277737[Hz]
X_sweep           = 9.38438438[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Tri_domain        = 1H
Tri_freq          = 500.15991521[MHz]
Tri_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 16
Total_scans       = 16

X_90_width        = 12.54[us]
X_acq_time        = 1.74587904[s]
X_angle           = 45[deg]
X_atn             = 4[dB]
X_pulse           = 6.27[us]
Irr_mode          = Off
Tri_mode          = Off
Dante_presat      = FALSE
Initial_wait      = 1[s]
Recvr_gain        = 50
Relaxation_delay  = 5[s]
Repetition_time   = 6.74587904[s]
Temp_get          = 26.1[dC]
```

```
Filename          = MRB_V_121_phtalimide_
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#761732
Solvent           = CHLOROFORM-D
Creation_time     = 30-OCT-2010 11:15:09
Revision_time     = 29-OCT-2010 21:19:25
Current_time      =  6-NOV-2010 15:49:11

Comment           = single pulse decouple
Data_format       = 1D REAL
Dim_size          = 26214
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 0.83361792[s]
X_domain          = 13C
X_freq            = 125.76529768[MHz]
X_offset          = 100[ppm]
X_points          = 32768
X_prescans        = 4
X_resolution      = 1.19959034[Hz]
X_sweep           = 39.3081761[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 10
Scans             = 190
Total_scans       = 190

X_90_width        = 10.73[us]
X_acq_time        = 0.83361792[s]
X_angle           = 30[deg]
X_atn             = 9[dB]
X_pulse           = 3.57666667[us]
Irr_atn_dec       = 20[dB]
Irr_atn_noe       = 20[dB]
Irr_noise         = WALTZ
Decoupling        = TRUE
Initial_wait      = 1[s]
Noe               = TRUE
Noe_time          = 2[s]
Recvr_gain        = 50
Relaxation_delay  = 2[s]
Repetition_time   = 2.83361792[s]
Temp_get          = 26.2[dC]
```

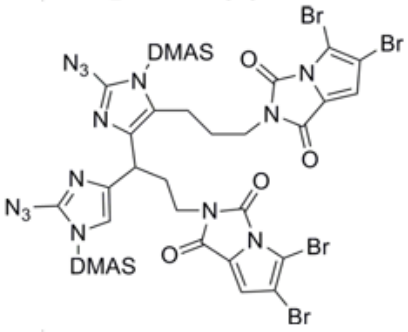


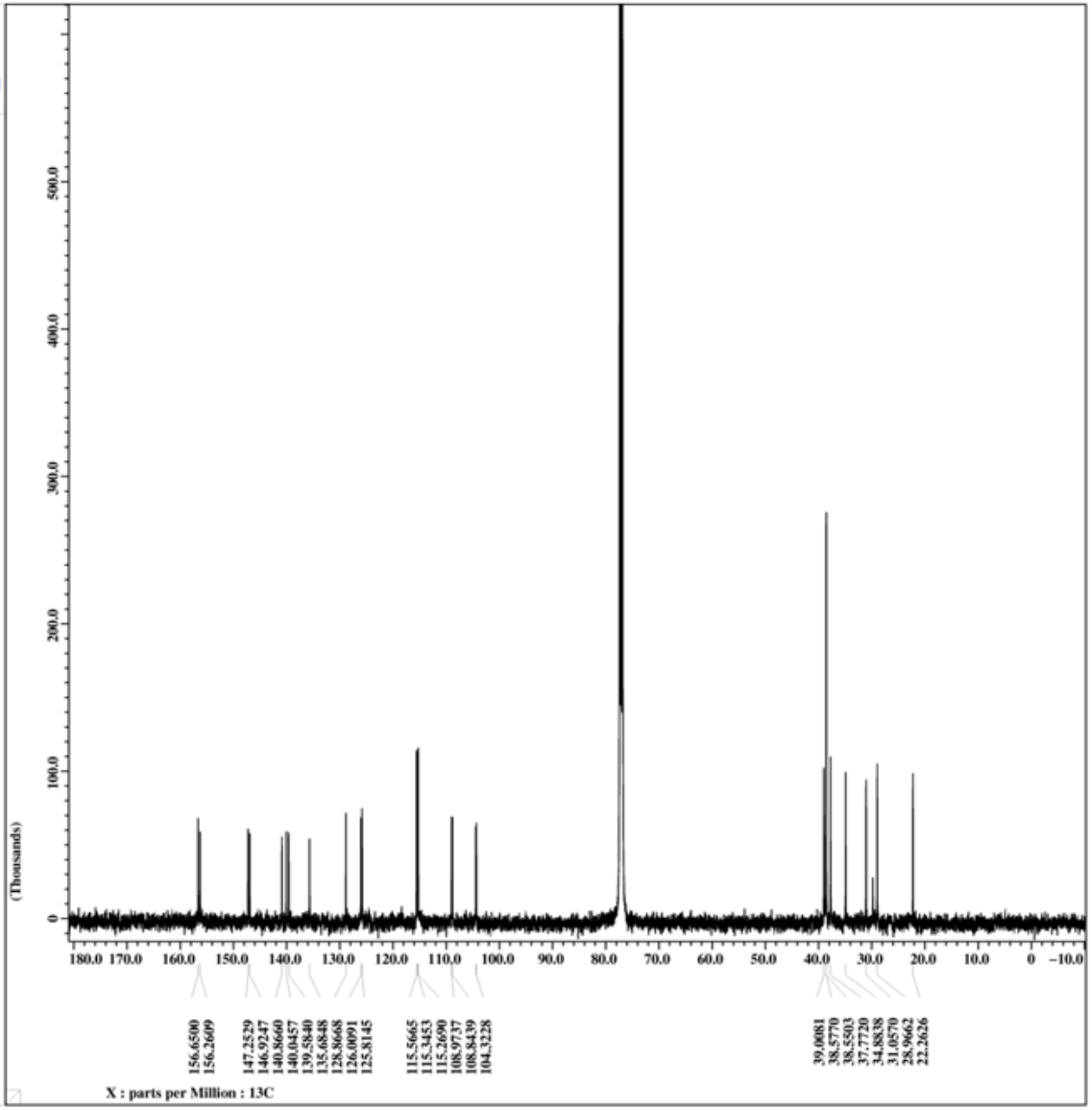


APPENDIX 19
^{1}H AND ^{13}C NMR SPECTRA OF
2-Azido-4-(2-azido-1-dimethylsulfamoyl-4-(3-(5,6-dibromo-1,3-dioxo-1H-pyrrolo[1,2-c]imidazol-2(3H)-yl)propyl)imidazol-4-yl)-1-dimethylsulfamoyl-5-(3-(5,6-dibromo-1,3-dioxo-1H-pyrrolo[1,2-c]imidazol-2(3H)-yl)propyl)imidazole (95)

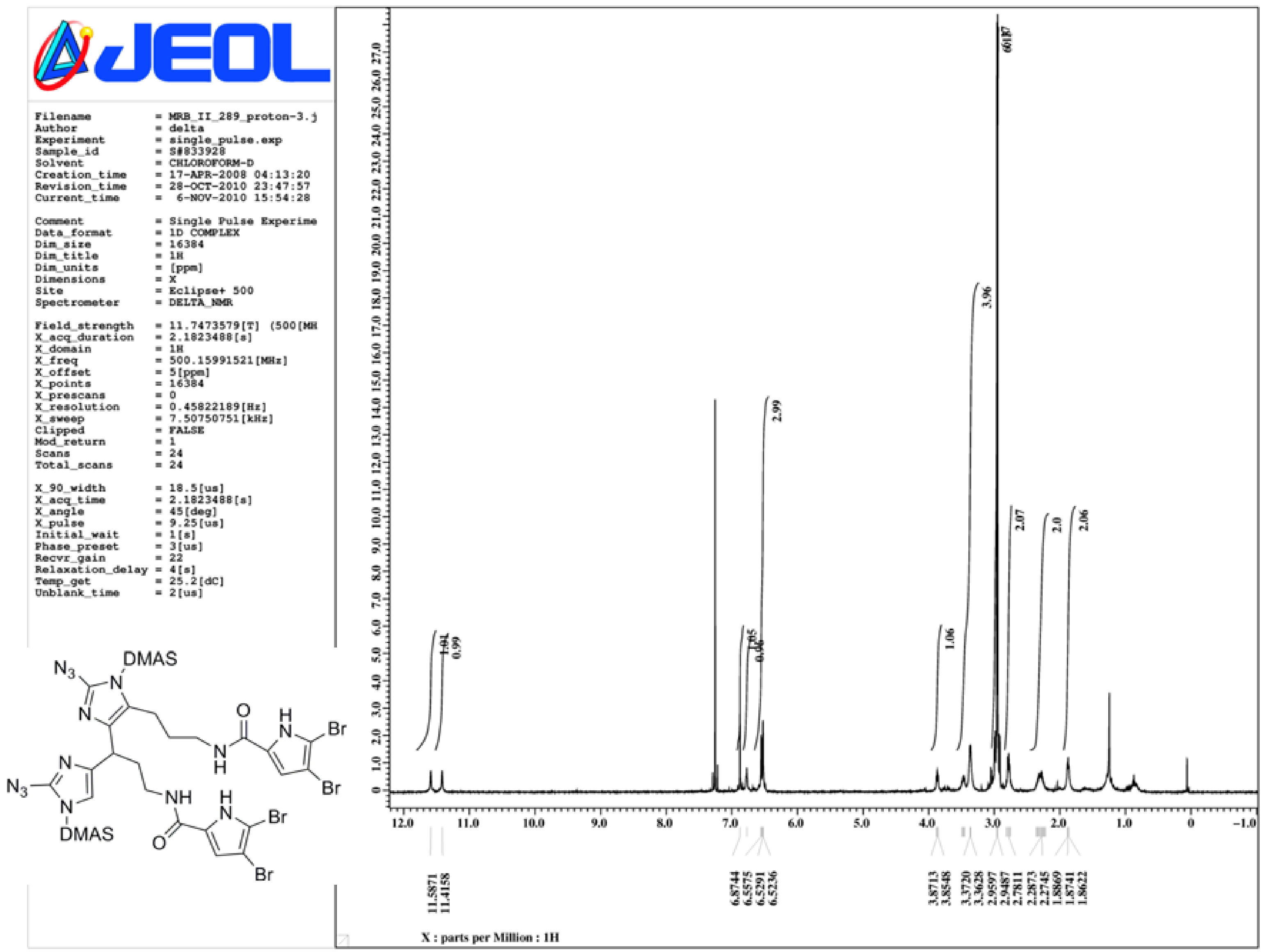

JEOL
Filename = MRB_II_288_mitsnobu_p
Author = delta
Experiment = single_pulse.exp
Sample_id = S#409280
Solvent = CHLOROFORM-D
Creation_time = 13-APR-2008 16:22:13
Revision_time = 28-OCT-2010 23:34:35
Current_time = 6-NOV-2010 15:50:50
Comment = Single Pulse Experime
Data_format = 1D REAL
Dim_size = 16384
Dim_title = 1H
Dim_units = [ppm]
Dimensions = X
Site = Eclipse+ 500
Spectrometer = DELTA_NMR
Field_strength = 11.7473579[T] (500[MH
X_acq_duration = 2.1823488[s]
X_domain = 1H
X_freq = 500.15991521[MHz]
X_offset = 5[ppm]
X_points = 16384
X_prescans = 0
X_resolution = 0.45822189[Hz]
X_sweep = 7.50750751[kHz]
Clipped = FALSE
Mod_return = 1
Scans = 16
Total_scans = 16
X_90_width = 18.5[us]
X_acq_time = 2.1823488[s]
X_angle = 45[deg]
X_pulse = 9.25[us]
Initial_wait = 1[s]
Phase_preset = 3[us]
Recvr_gain = 20
Relaxation_delay = 4[s]
Temp_get = 25.3[dC]
Unblank_time = 2[us]
DMAS
DMAS
Br
Br
Br
Br
(Millions)
3
4.05
64.18
2.08
1.97
2.05
1.05
6.8131
6.7938
6.7847
3.6496
3.6423
3.6368
2.9845
2.9515
2.8251
2.8095
2.7133
2.3725
1.9254
1.9107
1.8961
X : parts per Million : 1H

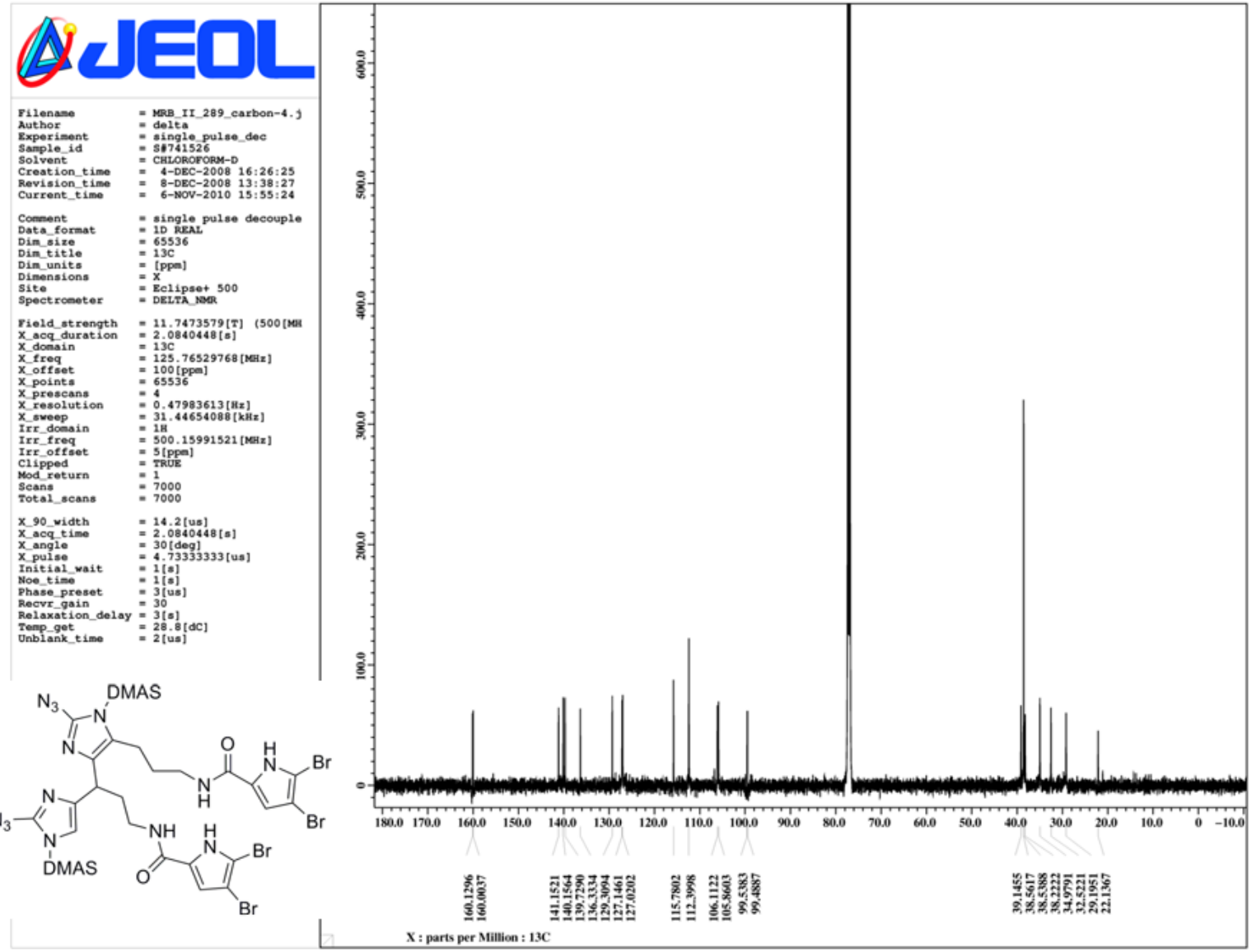
```
Filename          = MRB_II_288_mitsnobu_c
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#717266
Solvent           = CHLOROFORM-D
Creation_time     = 13-APR-2008 14:26:40
Revision_time     =  8-DEC-2008 20:30:09
Current_time      =  6-NOV-2010 15:53:03

Comment           = single pulse decouple
Data_format       = 1D COMPLEX
Dim_size          = 65536
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = Eclipse+ 500
Spectrometer      = DELTA_NMR

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 2.0840448[s]
X_domain          = 13C
X_freq            = 125.76529768[MHz]
X_offset          = 100[ppm]
X_points          = 65536
X_prescans        = 4
X_resolution      = 0.47983613[Hz]
X_sweep           = 31.44654088[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 8000
Total_scans       = 8000

X_90_width        = 14.2[us]
X_acq_time        = 2.0840448[s]
X_angle           = 30[deg]
X_pulse           = 4.73333333[us]
Initial_wait      = 1[s]
Noe_time          = 1[s]
Phase_preset      = 3[us]
Recvr_gain        = 30
Relaxation_delay  = 3[s]
Temp_get          = 27[dC]
Unblank_time      = 2[us]
```



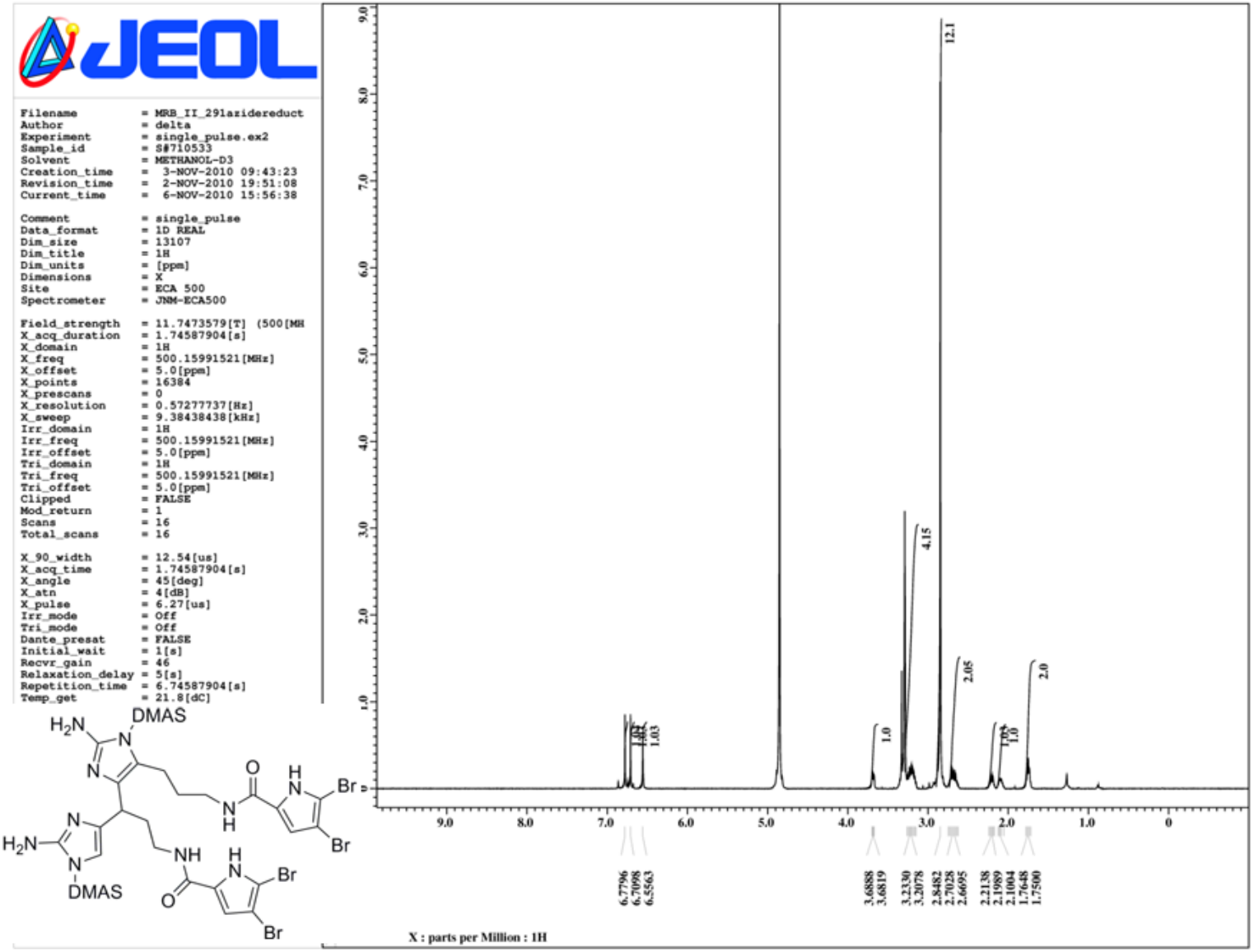


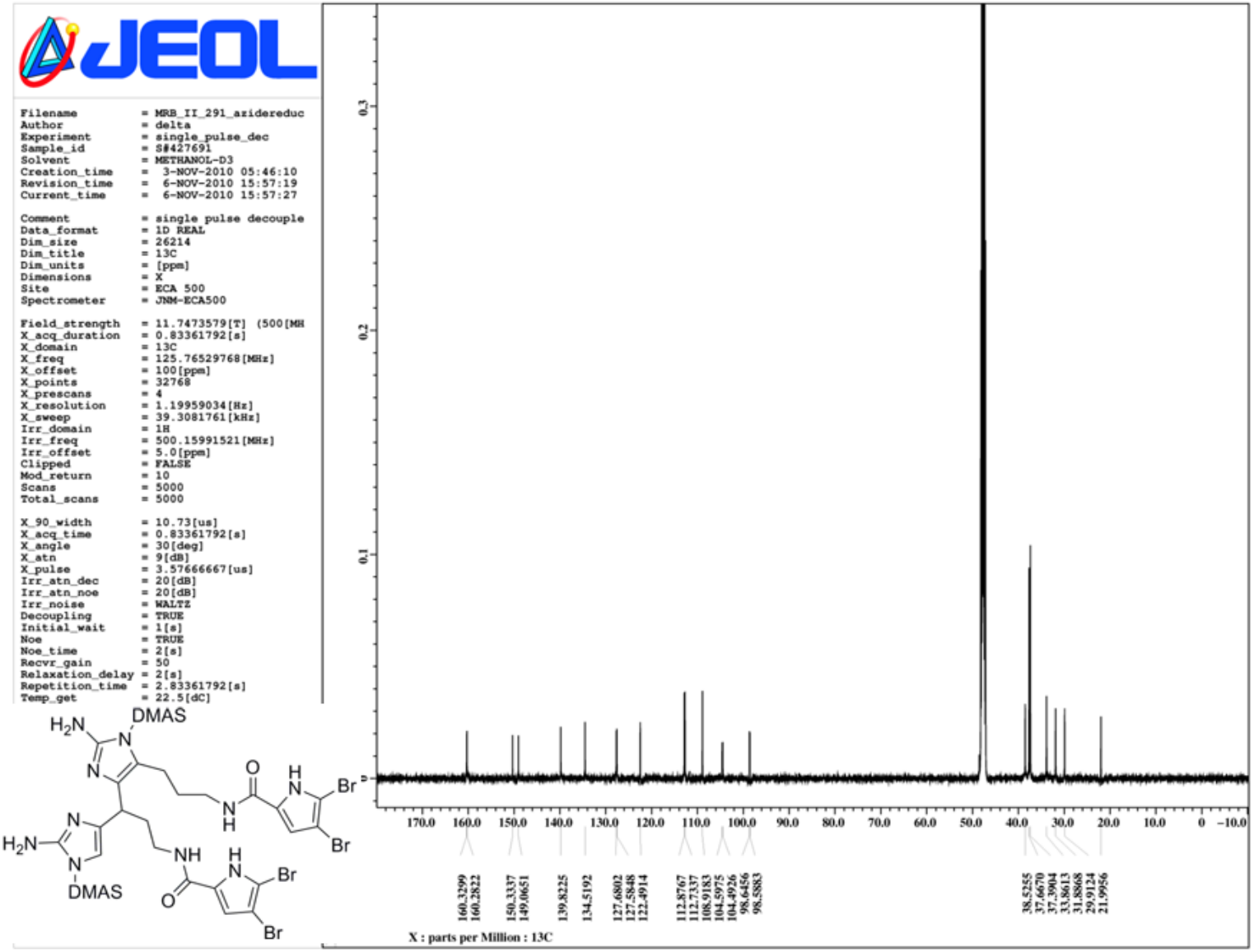
APPENDIX 20
^{1}H AND ^{13}C NMR SPECTRA OF
2-Azido-4-(2-azido-1-dimethylsulfamoyl-4-(3-(4,5-dibromo-1H-pyrrole-2-carboxamido)propyl)imidazol-4-yl)-1-dimethylsulfamoyl-5-(3-(4,5-dibromo-1H-pyrrole-2-carboxamido)propyl)imidazole (91)


JEOL
Filename = MRB_II_289_proton-3.j
Author = delta
Experiment = single_pulse.exp
Sample_id = S#833928
Solvent = CHLOROFORM-D
Creation_time = 17-APR-2008 04:13:20
Revision_time = 28-OCT-2010 23:47:57
Current_time = 6-NOV-2010 15:54:28
Comment = Single Pulse Experime
Data_format = 1D COMPLEX
Dim_size = 16384
Dim_title = 1H
Dim_units = [ppm]
Dimensions = X
Site = Eclipse+ 500
Spectrometer = DELTA_NMR
Field_strength = 11.7473579[T] (500[MH
X_acq_duration = 2.1823488[s]
X_domain = 1H
X_freq = 500.15991521[MHz]
X_offset = 5[ppm]
X_points = 16384
X_prescans = 0
X_resolution = 0.45822189[Hz]
X_sweep = 7.50750751[kHz]
Clipped = FALSE
Mod_return = 1
Scans = 24
Total_scans = 24
X_90_width = 18.5[us]
X_acq_time = 2.1823488[s]
X_angle = 45[deg]
X_pulse = 9.25[us]
Initial_wait = 1[s]
Phase_preset = 3[us]
Recvr_gain = 22
Relaxation_delay = 4[s]
Temp_get = 25.2[dC]
Unblank_time = 2[us]
DMAS
N_3
N
NH
O
H
Br
11.5871
11.4158
6.8744
6.5575
6.5291
6.5236
3.8713
3.8548
3.3720
3.3628
2.9597
2.9487
2.7811
2.2873
2.2745
1.8869
1.8741
1.8622
1.01
0.99
1.05
0.96
2.99
1.06
3.96
2.07
2.0
2.06
X : parts per Million : 1H

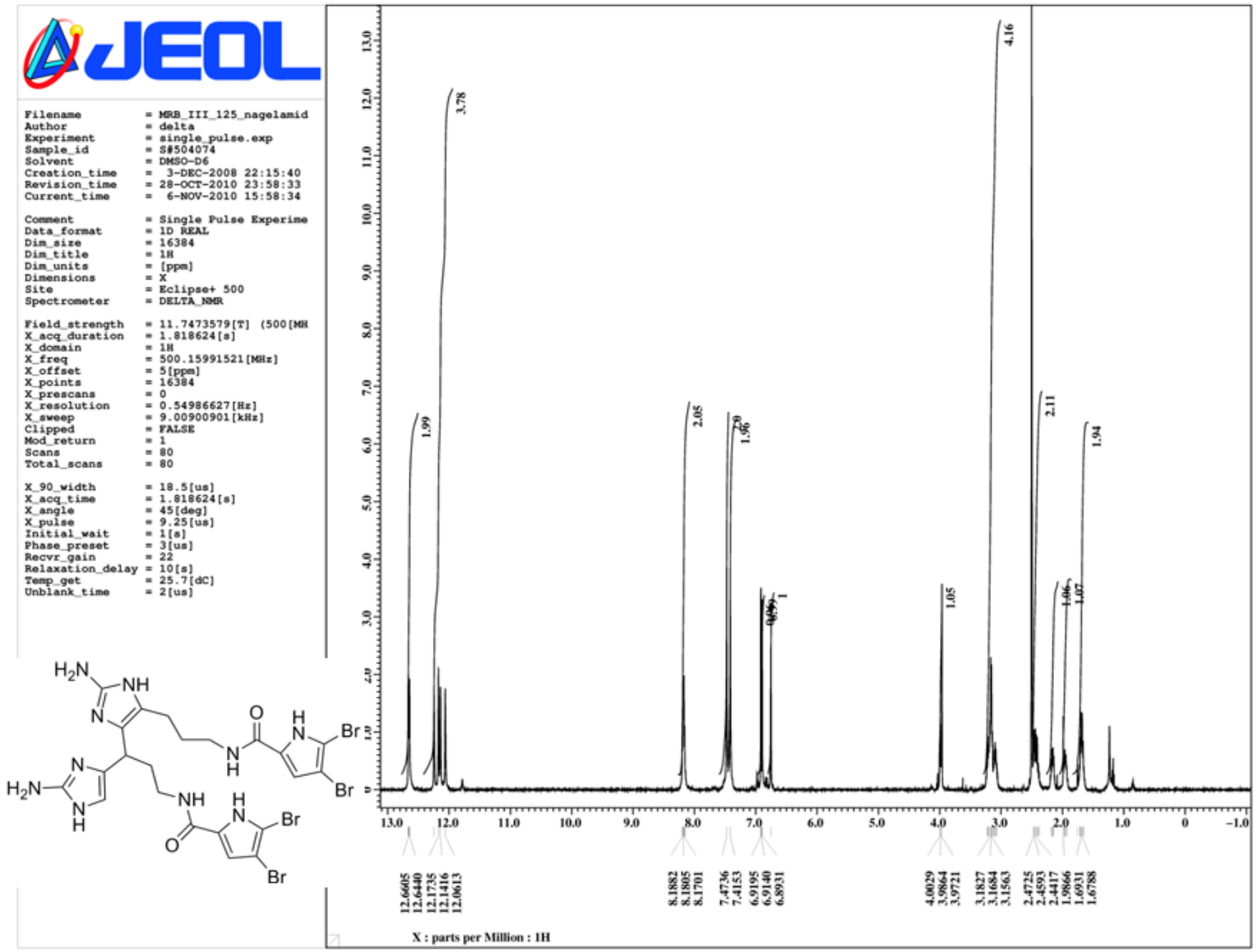

JEOL
Filename = MRB_II_289_carbon-4.j
Author = delta
Experiment = single_pulse_dec
Sample_id = S#741526
Solvent = CHLOROFORM-D
Creation_time = 4-DEC-2008 16:26:25
Revision_time = 8-DEC-2008 13:38:27
Current_time = 6-NOV-2010 15:55:24
Comment = single pulse decouple
Data_format = 1D REAL
Dim_size = 65536
Dim_title = 13C
Dim_units = [ppm]
Dimensions = X
Site = Eclipse+ 500
Spectrometer = DELTA_NMR
Field_strength = 11.7473579[T] (500[MH
X_acq_duration = 2.0840448[s]
X_domain = 13C
X_freq = 125.76529768[MHz]
X_offset = 100[ppm]
X_points = 65536
X_prescans = 4
X_resolution = 0.47983613[Hz]
X_sweep = 31.44654088[kHz]
Irr_domain = 1H
Irr_freq = 500.15991521[MHz]
Irr_offset = 5[ppm]
Clipped = TRUE
Mod_return = 1
Scans = 7000
Total_scans = 7000
X_90_width = 14.2[us]
X_acq_time = 2.0840448[s]
X_angle = 30[deg]
X_pulse = 4.73333333[us]
Initial_wait = 1[s]
Noe_time = 1[s]
Phase_preset = 3[us]
Recvr_gain = 30
Relaxation_delay = 3[s]
Temp_get = 28.8[dC]
Unblank_time = 2[us]
DMAS
DMAS
Br
Br
Br
Br
600.0
500.0
400.0
300.0
200.0
100.0
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
160.1296
160.0037
141.1521
140.1564
139.7290
136.3334
129.3094
127.1461
127.0202
115.7802
112.3998
106.1122
105.8603
99.5383
99.4887
39.1455
38.5617
38.5388
38.2222
34.9791
32.5221
29.1951
22.1367
X : parts per Million : 13C

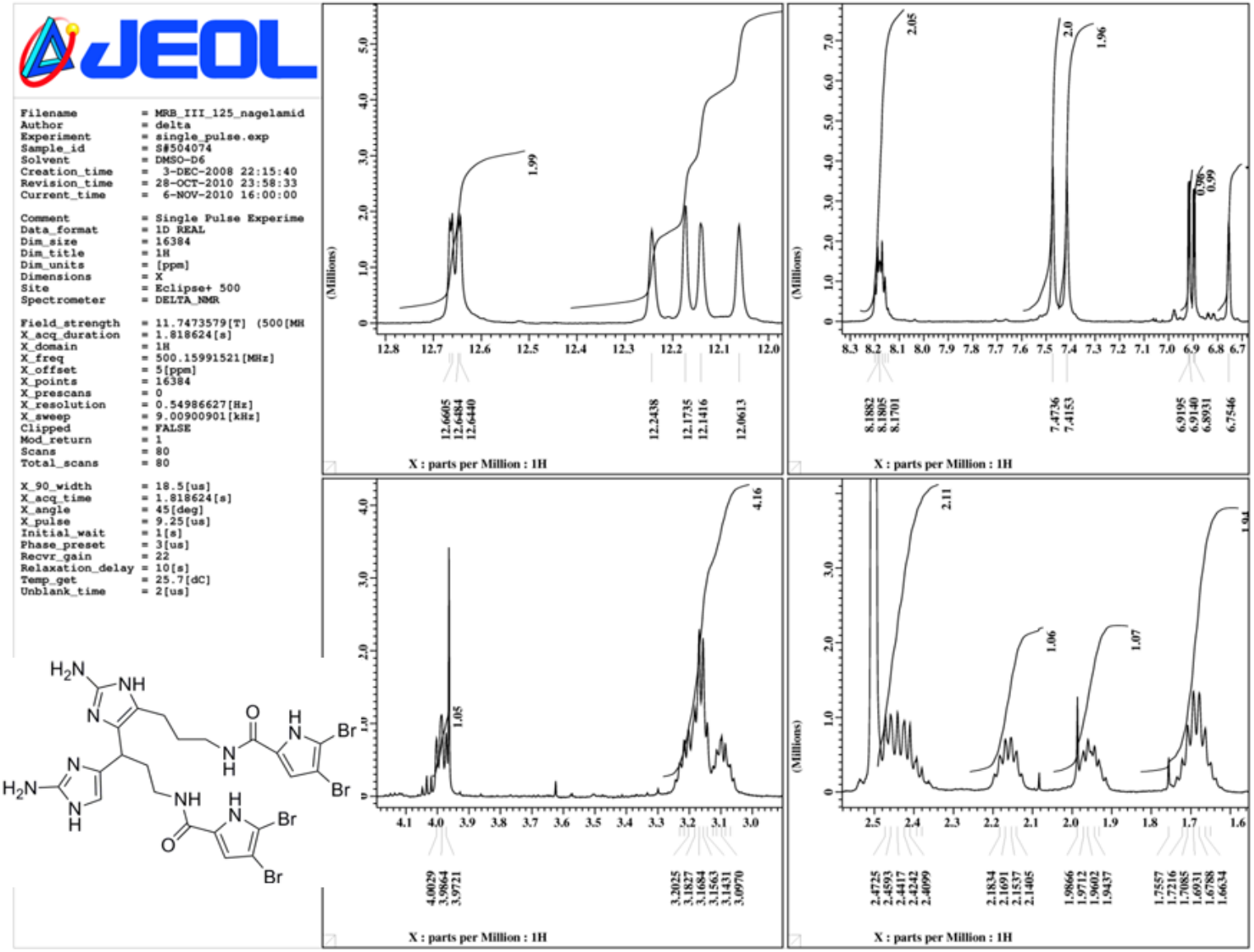
APPENDIX 21
^{1}H AND ^{13}C NMR SPECTRA OF
2-Amino-4-(2-amino-1-dimethylsulfamoyl-4-(3-(4,5-dibromo-1H-pyrrole-2-carboxamido)propyl)imidazol-4-yl)-1-dimethylsulfamoyl-5-(3-(4,5-dibromo-1H-pyrrole-2-carboxamido)propyl)imidazole (88)

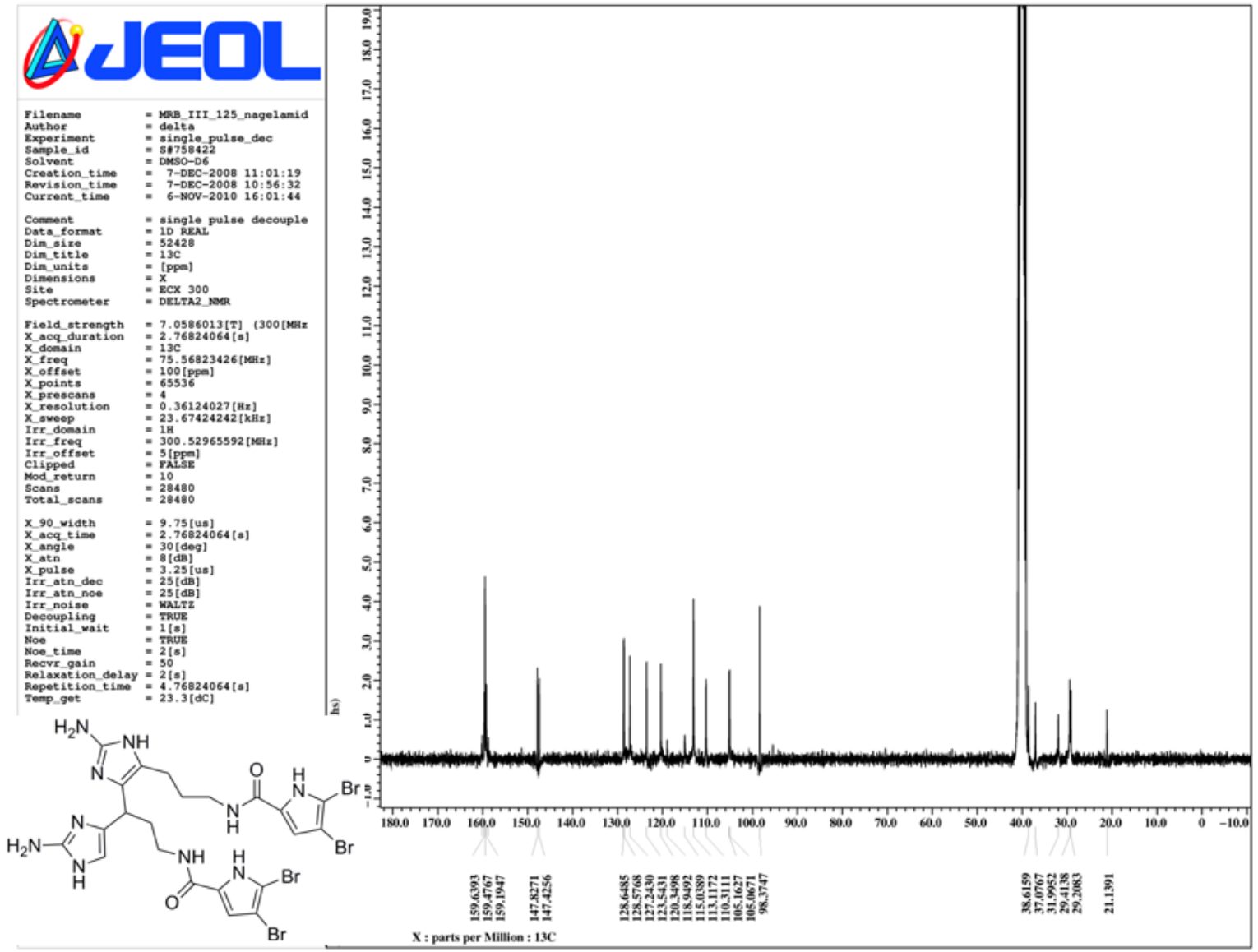

JEOL
Filename = MRB_II_291azidereduct
Author = delta
Experiment = single_pulse.ex2
Sample_id = S#710533
Solvent = METHANOL-D3
Creation_time = 3-NOV-2010 09:43:23
Revision_time = 2-NOV-2010 19:51:08
Current_time = 6-NOV-2010 15:56:38
Comment = single_pulse
Data_format = 1D REAL
Dim_size = 13107
Dim_title = 1H
Dim_units = [ppm]
Dimensions = X
Site = ECA 500
Spectrometer = JNM-ECA500
Field_strength = 11.7473579[T] (500[MH
X_acq_duration = 1.74587904[s]
X_domain = 1H
X_freq = 500.15991521[MHz]
X_offset = 5.0[ppm]
X_points = 16384
X_prescans = 0
X_resolution = 0.57277737[Hz]
X_sweep = 9.38438438[kHz]
Irr_domain = 1H
Irr_freq = 500.15991521[MHz]
Irr_offset = 5.0[ppm]
Tri_domain = 1H
Tri_freq = 500.15991521[MHz]
Tri_offset = 5.0[ppm]
Clipped = FALSE
Mod_return = 1
Scans = 16
Total_scans = 16
X_90_width = 12.54[us]
X_acq_time = 1.74587904[s]
X_angle = 45[deg]
X_atn = 4[dB]
X_pulse = 6.27[us]
Irr_mode = Off
Tri_mode = Off
Dante_presat = FALSE
Initial_wait = 1[s]
Recvr_gain = 46
Relaxation_delay = 5[s]
Repetition_time = 6.74587904[s]
Temp_get = 21.8[dC]
DMAS
DMAS
12.1
4.15
2.05
2.0
1.0
1.03
6.7796
6.7098
6.5563
3.6888
3.6819
3.2330
3.2078
2.8482
2.7028
2.6695
2.2138
2.1989
2.1004
1.7648
1.7500
X : parts per Million : 1H


JEOL
Filename = MRB_II_291_azidereduc
Author = delta
Experiment = single_pulse_dec
Sample_id = S#427691
Solvent = METHANOL-D3
Creation_time = 3-NOV-2010 05:46:10
Revision_time = 6-NOV-2010 15:57:19
Current_time = 6-NOV-2010 15:57:27
Comment = single pulse decouple
Data_format = 1D REAL
Dim_size = 26214
Dim_title = 13C
Dim_units = [ppm]
Dimensions = X
Site = ECA 500
Spectrometer = JNM-ECA500
Field_strength = 11.7473579[T] (500[MH
X_acq_duration = 0.83361792[s]
X_domain = 13C
X_freq = 125.76529768[MHz]
X_offset = 100[ppm]
X_points = 32768
X_prescans = 4
X_resolution = 1.19959034[Hz]
X_sweep = 39.3081761[kHz]
Irr_domain = 1H
Irr_freq = 500.15991521[MHz]
Irr_offset = 5.0[ppm]
Clipped = FALSE
Mod_return = 10
Scans = 5000
Total_scans = 5000
X_90_width = 10.73[us]
X_acq_time = 0.83361792[s]
X_angle = 30[deg]
X_atn = 9[dB]
X_pulse = 3.57666667[us]
Irr_atn_dec = 20[dB]
Irr_atn_noe = 20[dB]
Irr_noise = WALTZ
Decoupling = TRUE
Initial_wait = 1[s]
Noe = TRUE
Noe_time = 2[s]
Recvr_gain = 50
Relaxation_delay = 2[s]
Repetition_time = 2.83361792[s]
Temp_get = 22.5[dC]
DMAS
DMAS
0.3
0.2
0.1
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
160.3399
160.2822
150.3337
149.0651
139.8225
134.5192
127.6802
127.5848
122.4914
112.8767
112.7337
108.9183
104.5975
104.4926
98.6456
98.5883
38.5255
37.6670
37.3904
33.8613
31.8868
29.9124
21.9956
X : parts per Million : 13C

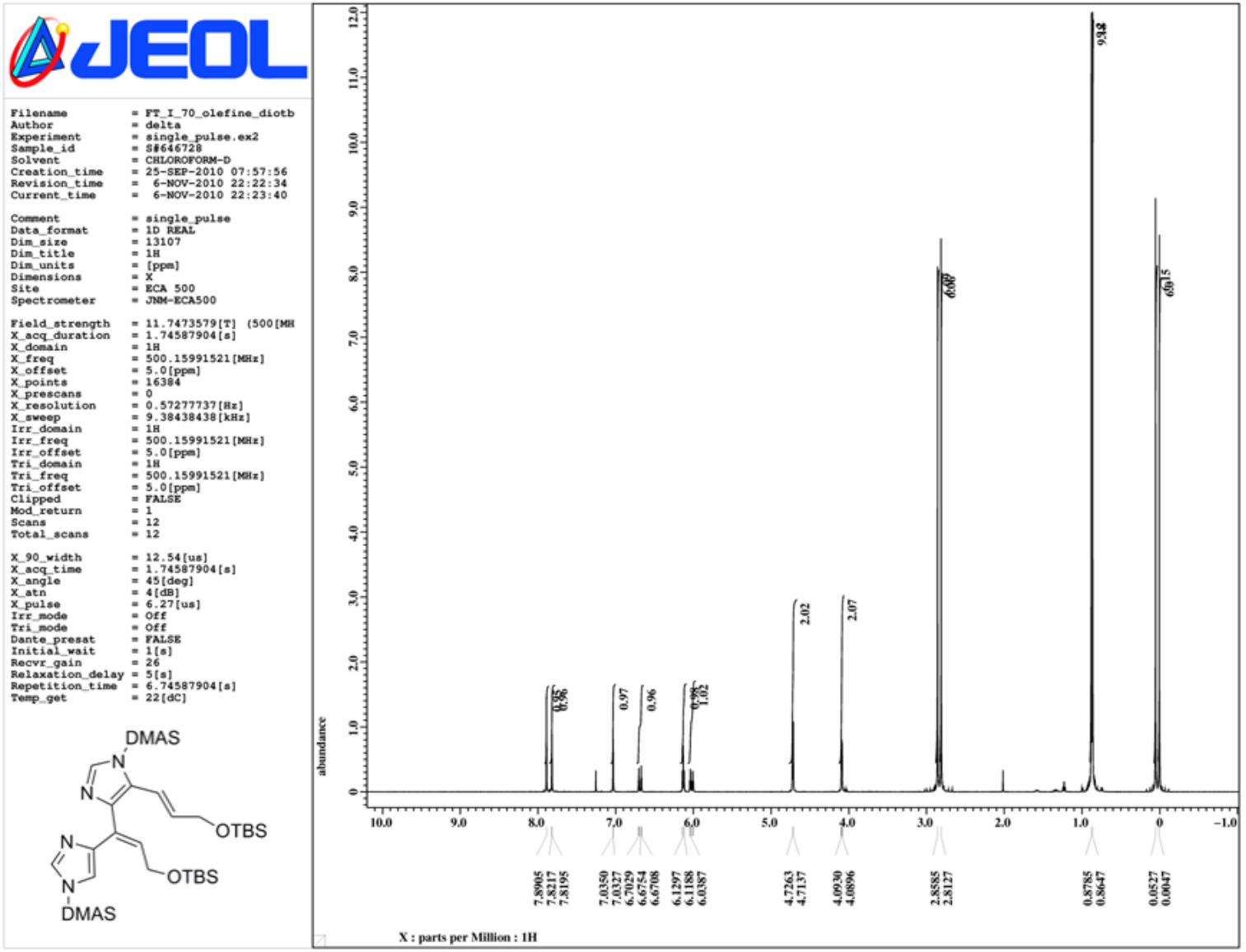
APPENDIX 22
^{1}H AND ^{13}C NMR SPECTRA OF
Nagelamide D (13)

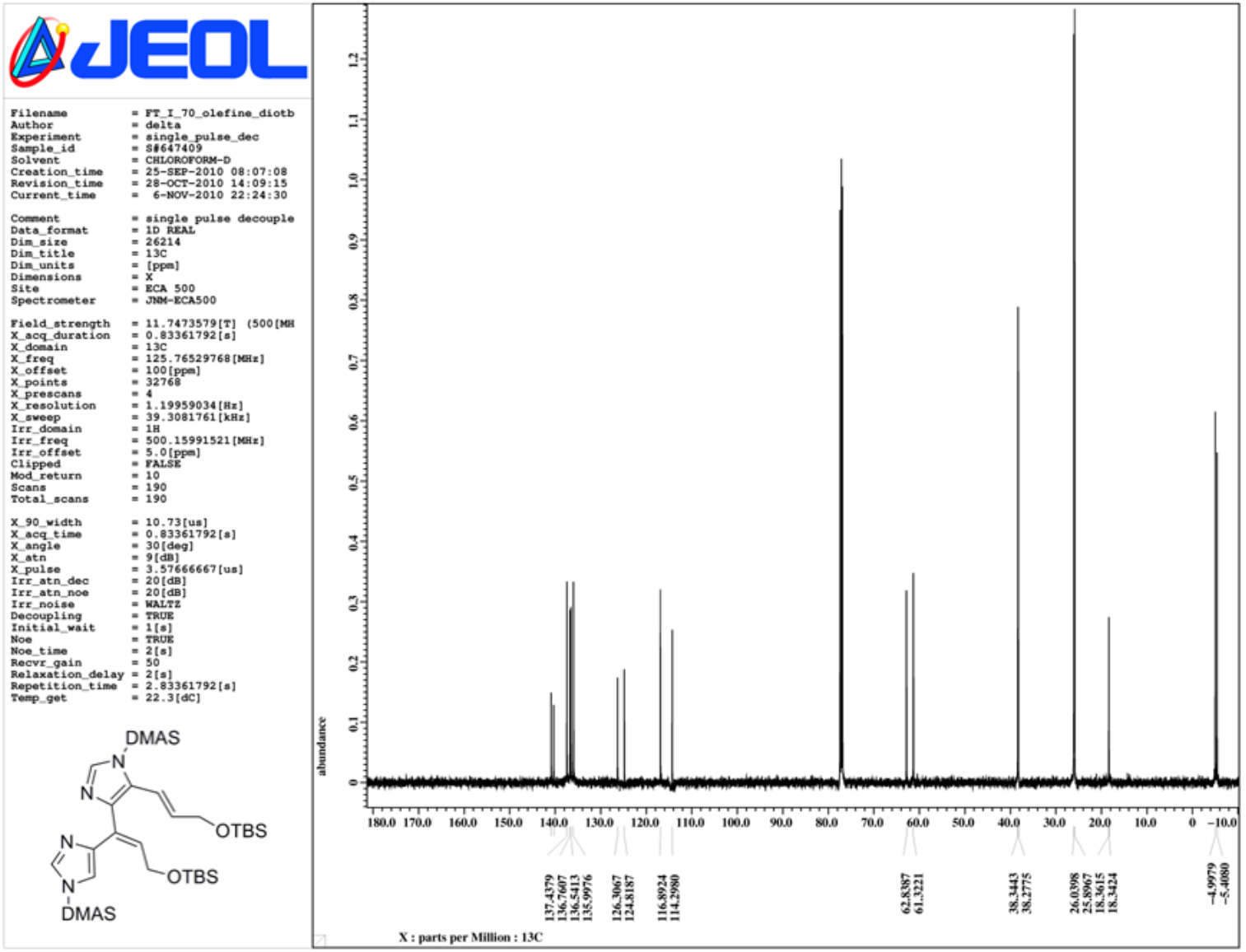

Filename = MRB_III_125_nagelamid
Author = delta
Experiment = single_pulse.exp
Sample_id = S#504074
Solvent = DMSO-D6
Creation_time = 3-DEC-2008 22:15:40
Revision_time = 28-OCT-2010 23:58:33
Current_time = 6-NOV-2010 15:58:34
Comment = Single Pulse Experime
Data_format = 1D REAL
Dim_size = 16384
Dim_title = 1H
Dim_units = [ppm]
Dimensions = X
Site = Eclipse+ 500
Spectrometer = DELTA_NMR
Field_strength = 11.7473579[T] (500[MH
X_acq_duration = 1.818624[s]
X_domain = 1H
X_freq = 500.15991521[MHz]
X_offset = 5[ppm]
X_points = 16384
X_prescans = 0
X_resolution = 0.54986627[Hz]
X_sweep = 9.00900901[kHz]
Clipped = FALSE
Mod_return = 1
Scans = 80
Total_scans = 80
X_90_width = 18.5[us]
X_acq_time = 1.818624[s]
X_angle = 45[deg]
X_pulse = 9.25[us]
Initial_wait = 1[s]
Phase_preset = 3[us]
Recvr_gain = 22
Relaxation_delay = 10[s]
Temp_get = 25.7[dC]
Unblank_time = 2[us]
H2N
NH
N
O
H
N
Br
Br
NH
O
Br
4.16
3.78
2.11
2.05
1.99
1.96
1.94
1.05
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
−1.0
12.6605
12.6440
12.1735
12.1416
12.0613
8.1882
8.1805
8.1701
7.4736
7.4153
6.9195
6.9140
6.8931
4.0029
3.9864
3.9721
3.1827
3.1684
3.1563
2.4725
2.4593
2.4417
1.9866
1.6931
1.6788
X : parts per Million : 1H


Filename = MRB_III_125_nagelamid
Author = delta
Experiment = single_pulse.exp
Sample_id = S#504074
Solvent = DMSO-D6
Creation_time = 3-DEC-2008 22:15:40
Revision_time = 28-OCT-2010 23:58:33
Current_time = 6-NOV-2010 16:00:00
Comment = Single Pulse Experime
Data_format = 1D REAL
Dim_size = 16384
Dim_title = 1H
Dim_units = [ppm]
Dimensions = X
Site = Eclipse+ 500
Spectrometer = DELTA_NMR
Field_strength = 11.7473579[T] (500[MH
X_acq_duration = 1.818624[s]
X_domain = 1H
X_freq = 500.15991521[MHz]
X_offset = 5[ppm]
X_points = 16384
X_prescans = 0
X_resolution = 0.54986627[Hz]
X_sweep = 9.00900901[kHz]
Clipped = FALSE
Mod_return = 1
Scans = 80
Total_scans = 80
X_90_width = 18.5[us]
X_acq_time = 1.818624[s]
X_angle = 45[deg]
X_pulse = 9.25[us]
Initial_wait = 1[s]
Phase_preset = 3[us]
Recvr_gain = 22
Relaxation_delay = 10[s]
Temp_get = 25.7[dC]
Unblank_time = 2[us]
(Millions)
X : parts per Million : 1H
X : parts per Million : 1H
X : parts per Million : 1H
X : parts per Million : 1H


Filename = MRB_III_125_nagelamid
Author = delta
Experiment = single_pulse_dec
Sample_id = S#758422
Solvent = DMSO-D6
Creation_time = 7-DEC-2008 11:01:19
Revision_time = 7-DEC-2008 10:56:32
Current_time = 6-NOV-2010 16:01:44
Comment = single pulse decouple
Data_format = 1D REAL
Dim_size = 52428
Dim_title = 13C
Dim_units = [ppm]
Dimensions = X
Site = ECX 300
Spectrometer = DELTA2_NMR
Field_strength = 7.0586013[T] (300[MHz
X_acq_duration = 2.76824064[s]
X_domain = 13C
X_freq = 75.56823426[MHz]
X_offset = 100[ppm]
X_points = 65536
X_prescans = 4
X_resolution = 0.36124027[Hz]
X_sweep = 23.67424242[kHz]
Irr_domain = 1H
Irr_freq = 300.52965592[MHz]
Irr_offset = 5[ppm]
Clipped = FALSE
Mod_return = 10
Scans = 28480
Total_scans = 28480
X_90_width = 9.75[us]
X_acq_time = 2.76824064[s]
X_angle = 30[deg]
X_atn = 8[dB]
X_pulse = 3.25[us]
Irr_atn_dec = 25[dB]
Irr_atn_noe = 25[dB]
Irr_noise = WALTZ
Decoupling = TRUE
Initial_wait = 1[s]
Noe = TRUE
Noe_time = 2[s]
Recvr_gain = 50
Relaxation_delay = 2[s]
Repetition_time = 4.76824064[s]
Temp_get = 23.3[dC]
159.6393
159.4767
159.1947
147.8271
147.4256
128.6485
128.5768
127.2430
123.5431
120.3498
118.9492
115.0389
113.1172
110.3111
105.1627
105.0671
98.3747
38.6159
37.0767
31.9952
29.4138
29.2083
21.1391
X : parts per Million : 13C

APPENDIX 23
^{1}H AND ^{13}C NMR SPECTRA OF
4-((*E*)-1-Dimethylsulfamoyl-4-(3-(*t*-butyldimethylsilyloxy)-2-propenyl)imidazol-4-yl)-1-dimethylsulfamoyl-5-((*E*)-3-(*t*-butyldimethylsilyloxy)-2-propenyl)imidazole (98)

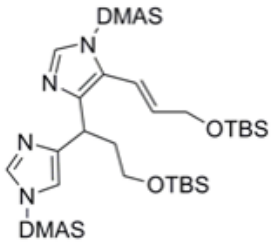

Filename = FT_I_70_olefine_diotb
Author = delta
Experiment = single_pulse.ex2
Sample_id = S#646728
Solvent = CHLOROFORM-D
Creation_time = 25-SEP-2010 07:57:56
Revision_time = 6-NOV-2010 22:22:34
Current_time = 6-NOV-2010 22:23:40
Comment = single_pulse
Data_format = 1D REAL
Dim_size = 13107
Dim_title = 1H
Dim_units = [ppm]
Dimensions = X
Site = ECA 500
Spectrometer = JNM-ECA500
Field_strength = 11.7473579[T] (500[MH
X_acq_duration = 1.74587904[s]
X_domain = 1H
X_freq = 500.15991521[MHz]
X_offset = 5.0[ppm]
X_points = 16384
X_prescans = 0
X_resolution = 0.57277737[Hz]
X_sweep = 9.38438438[kHz]
Irr_domain = 1H
Irr_freq = 500.15991521[MHz]
Irr_offset = 5.0[ppm]
Tri_domain = 1H
Tri_freq = 500.15991521[MHz]
Tri_offset = 5.0[ppm]
Clipped = FALSE
Mod_return = 1
Scans = 12
Total_scans = 12
X_90_width = 12.54[us]
X_acq_time = 1.74587904[s]
X_angle = 45[deg]
X_atn = 4[dB]
X_pulse = 6.27[us]
Irr_mode = Off
Tri_mode = Off
Dante_presat = FALSE
Initial_wait = 1[s]
Recvr_gain = 26
Relaxation_delay = 5[s]
Repetition_time = 6.74587904[s]
Temp_get = 22[dC]
DMAS
OTBS
OTBS
DMAS
abundance
9.38
6.07
6.15
2.02
2.07
0.97
0.96
1.02
7.8905
7.8217
7.8195
7.0350
7.0327
6.7029
6.6754
6.6708
6.1297
6.1188
6.0387
4.7263
4.7137
4.0930
4.0896
2.8585
2.8127
0.8785
0.8647
0.0527
0.0047
X : parts per Million : 1H

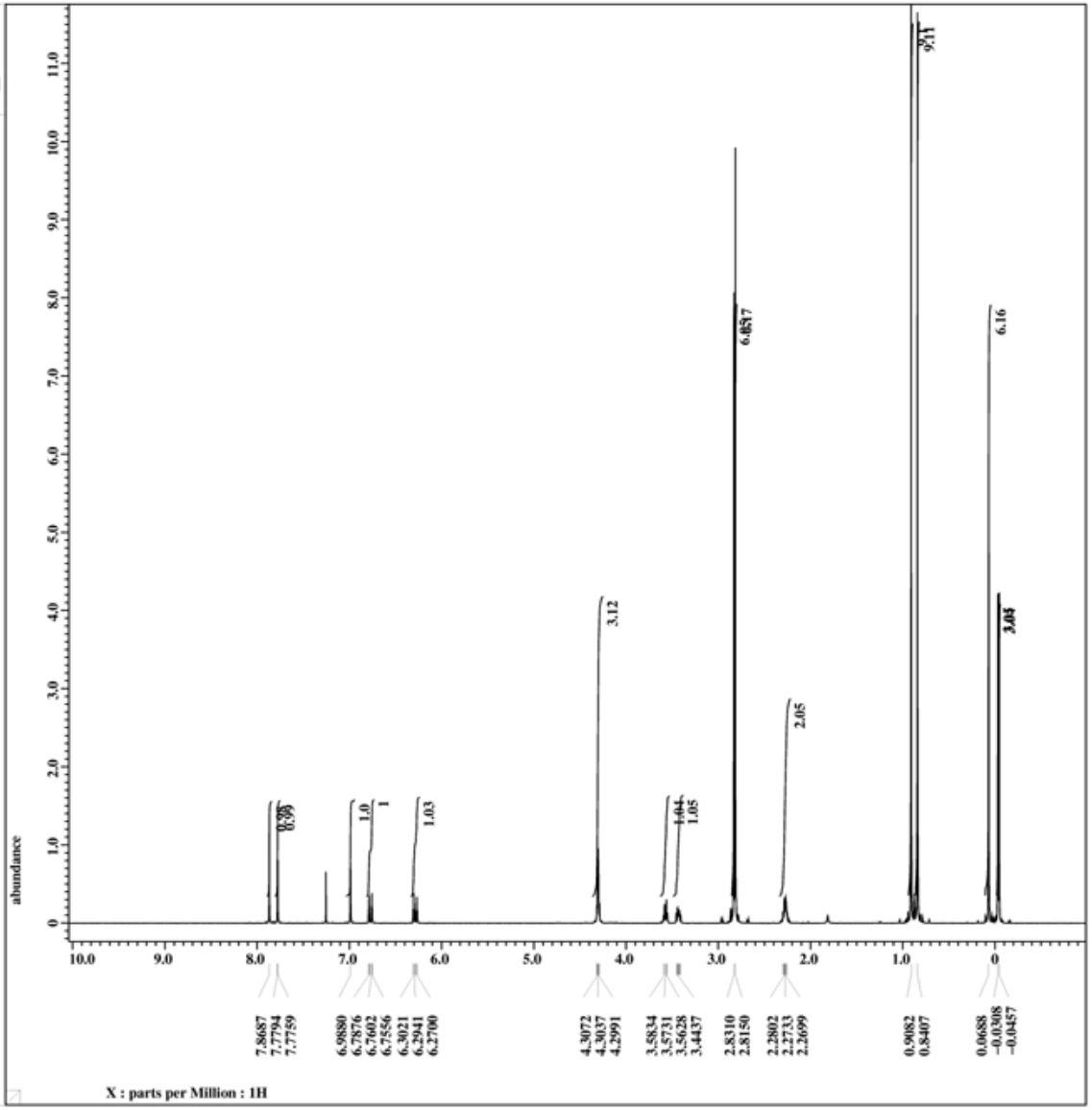

JEOL
Filename = FT_I_70_olefine_diotb
Author = delta
Experiment = single_pulse_dec
Sample_id = S#647409
Solvent = CHLOROFORM-D
Creation_time = 25-SEP-2010 08:07:08
Revision_time = 28-OCT-2010 14:09:15
Current_time = 6-NOV-2010 22:24:30
Comment = single pulse decouple
Data_format = 1D REAL
Dim_size = 26214
Dim_title = 13C
Dim_units = [ppm]
Dimensions = X
Site = ECA 500
Spectrometer = JNM-ECA500
Field_strength = 11.7473579[T] (500[MH
X_acq_duration = 0.83361792[s]
X_domain = 13C
X_freq = 125.76529768[MHz]
X_offset = 100[ppm]
X_points = 32768
X_prescans = 4
X_resolution = 1.19959034[Hz]
X_sweep = 39.3081761[kHz]
Irr_domain = 1H
Irr_freq = 500.15991521[MHz]
Irr_offset = 5.0[ppm]
Clipped = FALSE
Mod_return = 10
Scans = 190
Total_scans = 190
X_90_width = 10.73[us]
X_acq_time = 0.83361792[s]
X_angle = 30[deg]
X_atn = 9[dB]
X_pulse = 3.57666667[us]
Irr_atn_dec = 20[dB]
Irr_atn_noe = 20[dB]
Irr_noise = WALTZ
Decoupling = TRUE
Initial_wait = 1[s]
Noe = TRUE
Noe_time = 2[s]
Recvr_gain = 50
Relaxation_delay = 2[s]
Repetition_time = 2.83361792[s]
Temp_get = 22.3[dC]
DMAS
OTBS
OTBS
DMAS
abundance
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
137.4379
136.7607
136.5413
135.9976
126.3067
124.8187
116.8924
114.2980
62.8387
61.3221
38.3443
38.2775
26.0398
25.8967
18.3615
18.3424
−4.9979
−5.4080
X : parts per Million : 13C

APPENDIX 24
^{1}H AND ^{13}C NMR SPECTRA OF
4-(1-Dimethylsulfamoyl-4-(3-(*t*-butyldimethylsilyloxy)propyl)imidazol-4-yl)-1-dimethylsulfamoyl-5-((*E*)-3-(*t*-butyldimethylsilyloxy)-2-propenyl)imidazole (99)

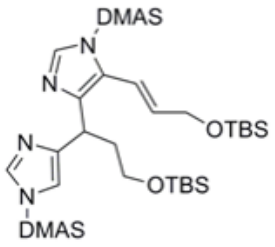
JEOL

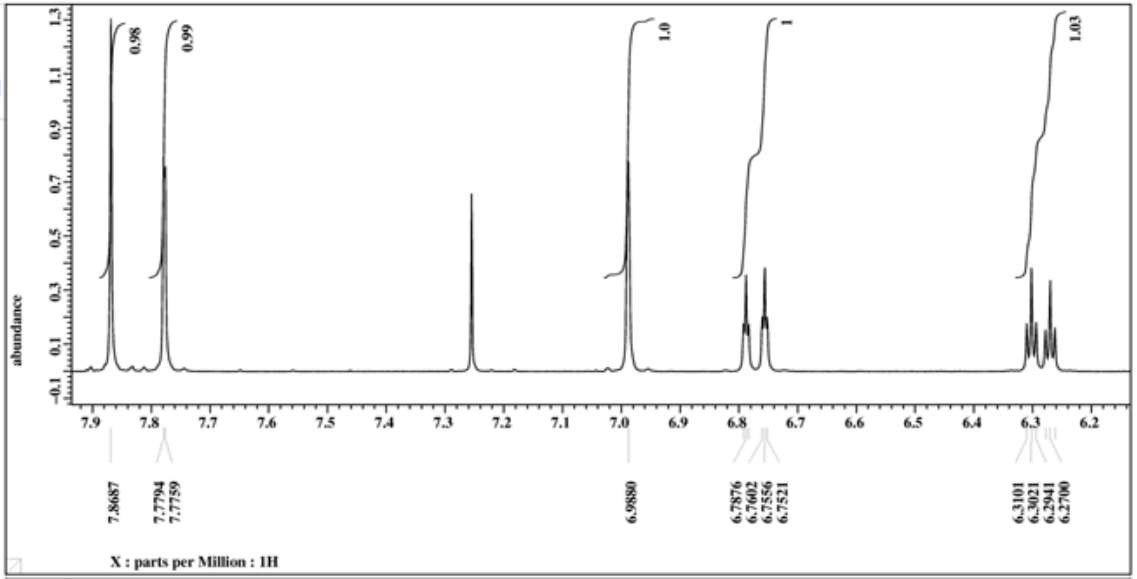
Filename	= FT_I_71_hydrogenation
Author	= delta
Experiment	= single_pulse.ex2
Sample_id	= S#624603
Solvent	= CHLOROFORM-D
Creation_time	= 31-OCT-2010 07:19:45
Revision_time	= 30-OCT-2010 17:32:09
Current_time	= 6-NOV-2010 22:25:10
Comment	= single_pulse
Data_format	= 1D REAL
Dim_size	= 13107
Dim_title	= 1H
Dim_units	= [ppm]
Dimensions	= X
Site	= ECA 500
Spectrometer	= JNM-ECA500
Field_strength	= 11.7473579[T] (500[MH
X_acq_duration	= 1.74587904[s]
X_domain	= 1H
X_freq	= 500.15991521[MHz]
X_offset	= 5.0[ppm]
X_points	= 16384
X_prescans	= 0
X_resolution	= 0.57277737[Hz]
X_sweep	= 9.38438438[kHz]
Irr_domain	= 1H
Irr_freq	= 500.15991521[MHz]
Irr_offset	= 5.0[ppm]
Tri_domain	= 1H
Tri_freq	= 500.15991521[MHz]
Tri_offset	= 5.0[ppm]
Clipped	= FALSE
Mod_return	= 1
Scans	= 16
Total_scans	= 16
X_90_width	= 12.54[us]
X_acq_time	= 1.74587904[s]
X_angle	= 45[deg]
X_atn	= 4[dB]
X_pulse	= 6.27[us]
Irr_mode	= Off
Tri_mode	= Off
Dante_presat	= FALSE
Initial_wait	= 1[s]
Recvr_gain	= 32
Relaxation_delay	= 5[s]
Repetition_time	= 6.74587904[s]
Temp_get	= 26.1[dC]

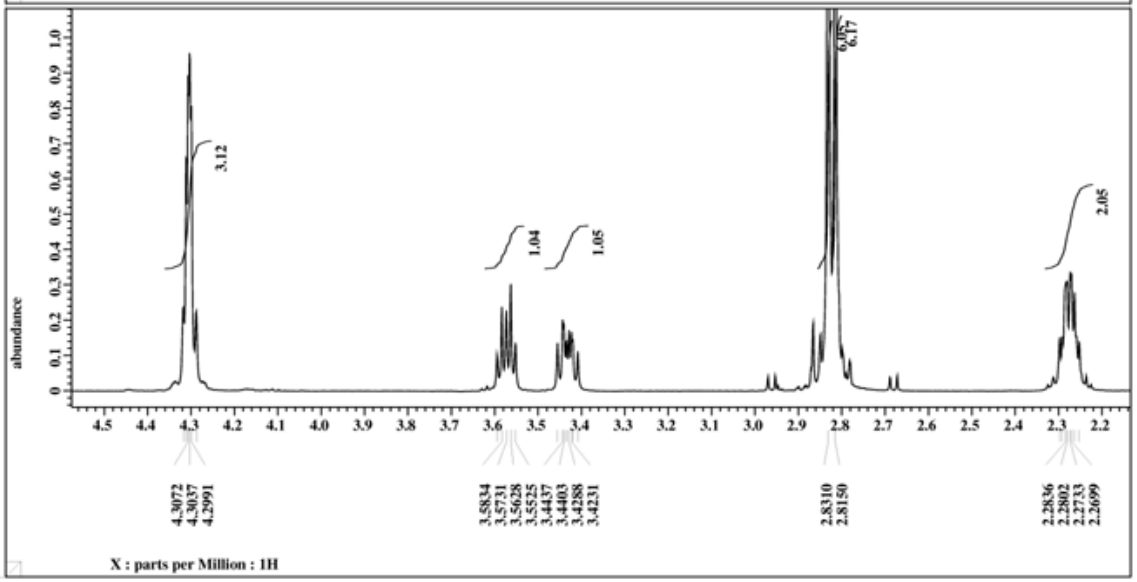


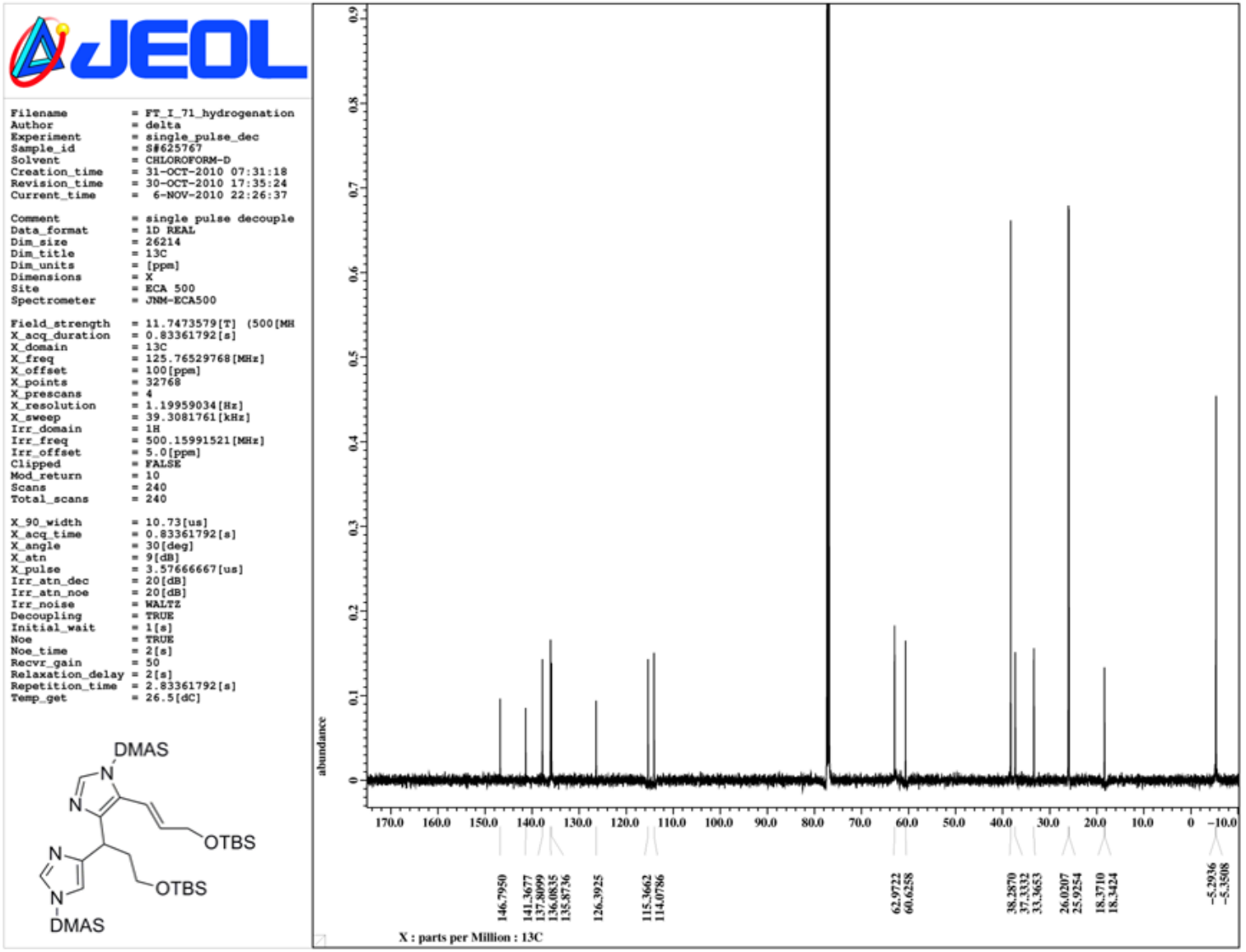


```
Filename          = FT_I_71_hydrogenation
Author            = delta
Experiment        = single_pulse.ex2
Sample_id         = S#624603
Solvent           = CHLOROFORM-D
Creation_time     = 31-OCT-2010 07:19:45
Revision_time     = 30-OCT-2010 17:32:09
Current_time      =  6-NOV-2010 22:26:05

Comment           = single_pulse
Data_format       = 1D REAL
Dim_size          = 13107
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 1.74587904[s]
X_domain          = 1H
X_freq            = 500.15991521[MHz]
X_offset          = 5.0[ppm]
X_points          = 16384
X_prescans        = 0
X_resolution      = 0.57277737[Hz]
X_sweep           = 9.38438438[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Tri_domain        = 1H
Tri_freq          = 500.15991521[MHz]
Tri_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 16
Total_scans       = 16

X_90_width        = 12.54[us]
X_acq_time        = 1.74587904[s]
X_angle           = 45[deg]
X_atn             = 4[dB]
X_pulse           = 6.27[us]
Irr_mode          = Off
Tri_mode          = Off
Dante_presat      = FALSE
Initial_wait      = 1[s]
Recvr_gain        = 32
Relaxation_delay  = 5[s]
Repetition_time   = 6.74587904[s]
Temp_get          = 26.1[dC]
```





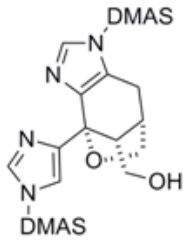


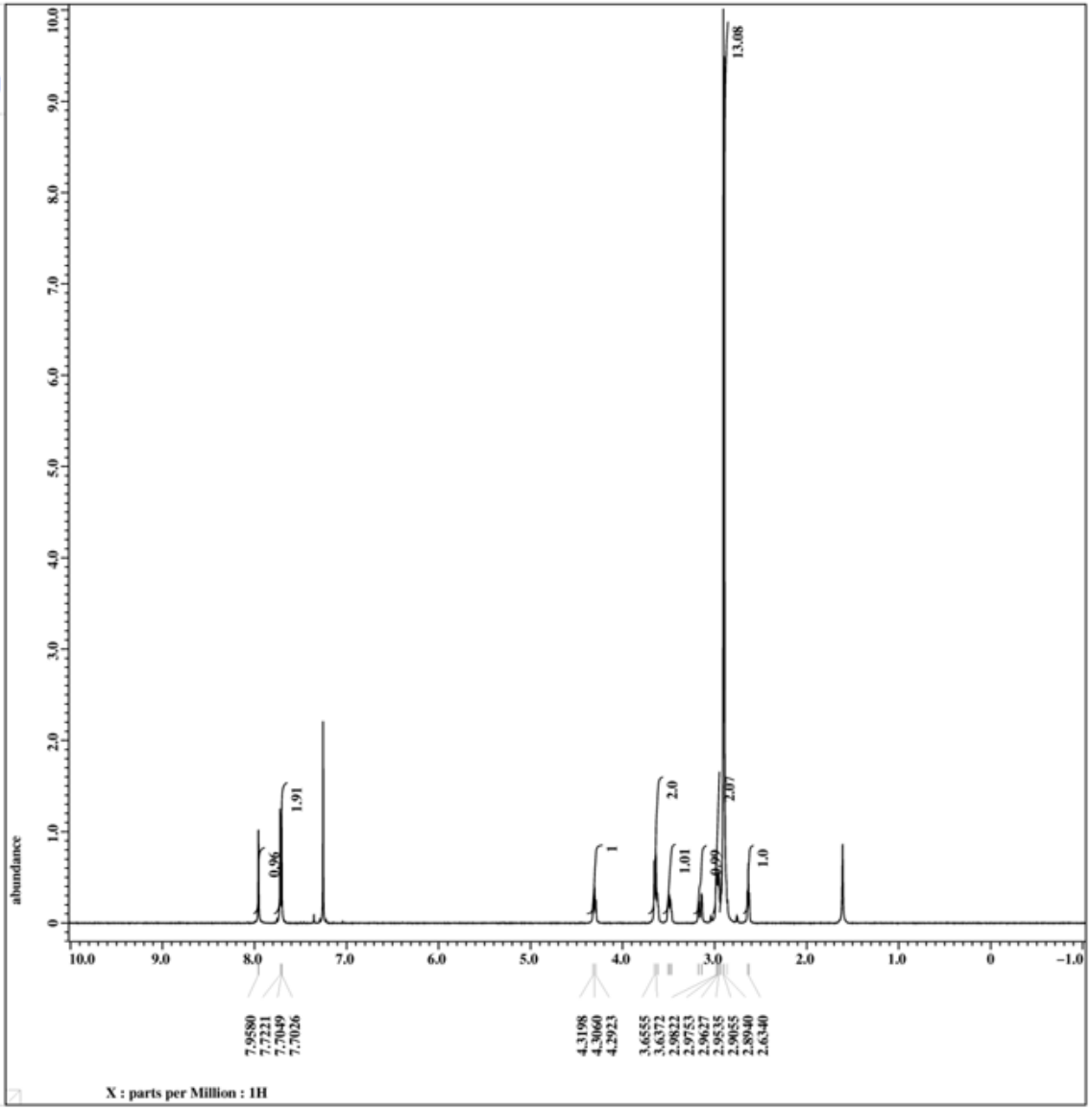


```
Filename          = FT_I_71_hydrogenation
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#625767
Solvent           = CHLOROFORM-D
Creation_time     = 31-OCT-2010 07:31:18
Revision_time     = 30-OCT-2010 17:35:24
Current_time      =  6-NOV-2010 22:26:37

Comment           = single pulse decouple
Data_format       = 1D REAL
Dim_size          = 26214
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 0.83361792[s]
X_domain          = 13C
X_freq            = 125.76529768[MHz]
X_offset          = 100[ppm]
X_points          = 32768
X_prescans        = 4
X_resolution      = 1.19959034[Hz]
X_sweep           = 39.3081761[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 10
Scans             = 240
Total_scans       = 240

X_90_width        = 10.73[us]
X_acq_time        = 0.83361792[s]
X_angle           = 30[deg]
X_atn             = 9[dB]
X_pulse           = 3.57666667[us]
Irr_atn_dec       = 20[dB]
Irr_atn_noe       = 20[dB]
Irr_noise         = WALTZ
Decoupling        = TRUE
Initial_wait      = 1[s]
Noe               = TRUE
Noe_time          = 2[s]
Recvr_gain        = 50
Relaxation_delay  = 2[s]
Repetition_time   = 2.83361792[s]
Temp_get          = 26.5[dC]
```

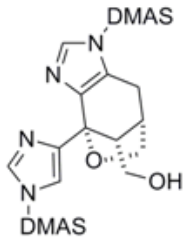
APPENDIX 25
^{1}H AND ^{13}C NMR SPECTRA OF
5-Dimethylsulfamoyl-1-(1-dimethylulfamoylimidazol-4-yl)-11-hydroxymethyl-10-oxa-3,5-diazatricyclo[6.2.1.02,6]undeca-2(6),3-dien (100)

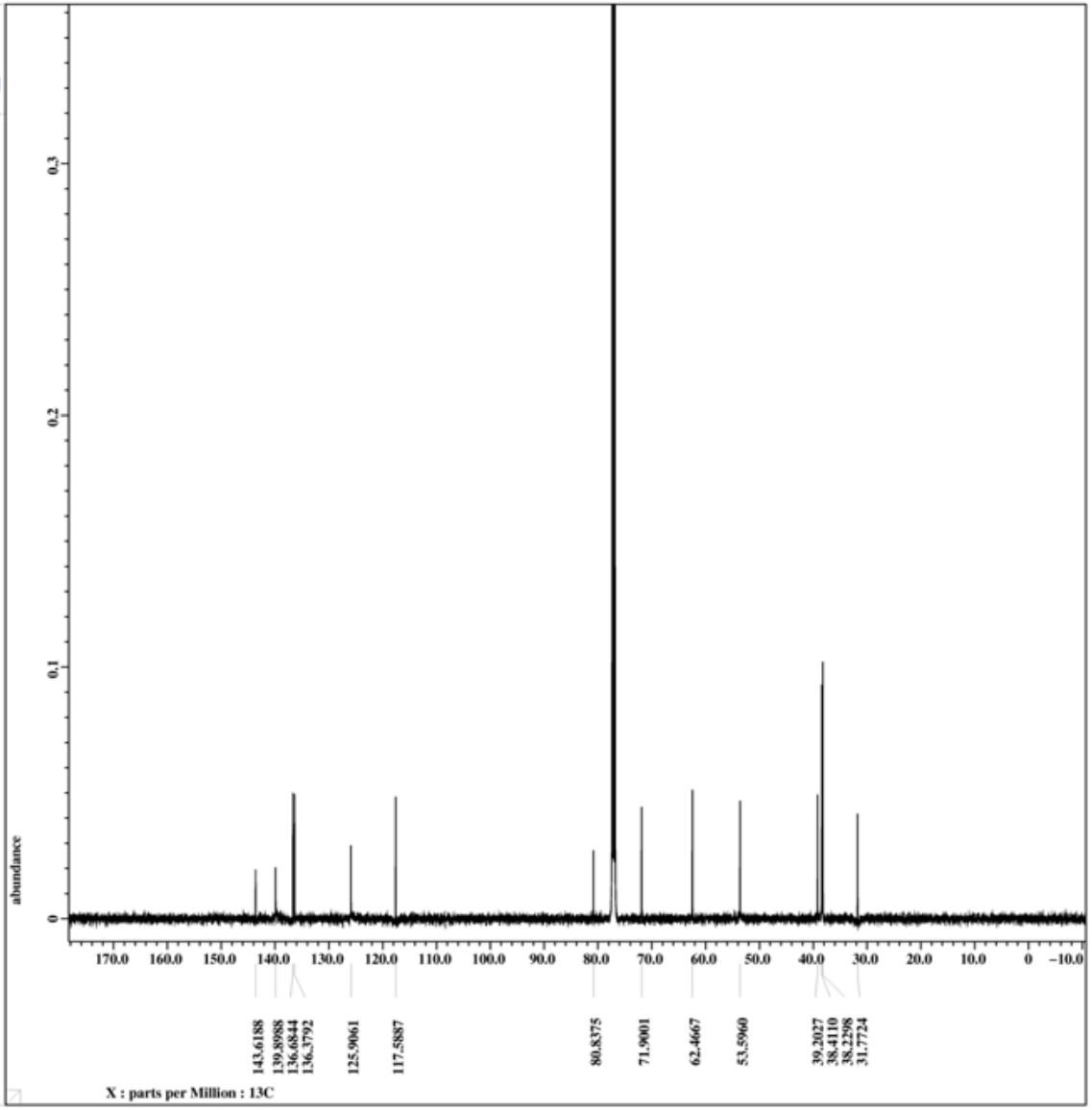
```
Filename          = MRB_V_122_alchol_elec
Author            = delta
Experiment        = single_pulse.ex2
Sample_id         = S#612259
Solvent           = CHLOROFORM-D
Creation_time     =  4-NOV-2010 06:59:42
Revision_time     =  3-NOV-2010 17:07:09
Current_time      =  6-NOV-2010 22:27:55

Comment           = single_pulse
Data_format       = 1D REAL
Dim_size          = 13107
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 1.74587904[s]
X_domain          = 1H
X_freq            = 500.15991521[MHz]
X_offset          = 5.0[ppm]
X_points          = 16384
X_prescans        = 0
X_resolution      = 0.57277737[Hz]
X_sweep           = 9.38438438[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Tri_domain        = 1H
Tri_freq          = 500.15991521[MHz]
Tri_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 16
Total_scans       = 16

X_90_width        = 12.54[us]
X_acq_time        = 1.74587904[s]
X_angle           = 45[deg]
X_atn             = 4[dB]
X_pulse           = 6.27[us]
Irr_mode          = Off
Tri_mode          = Off
Dante_presat      = FALSE
Initial_wait      = 1[s]
Recvr_gain        = 48
Relaxation_delay  = 5[s]
Repetition_time   = 6.74587904[s]
Temp_get          = 21.8[dC]
```



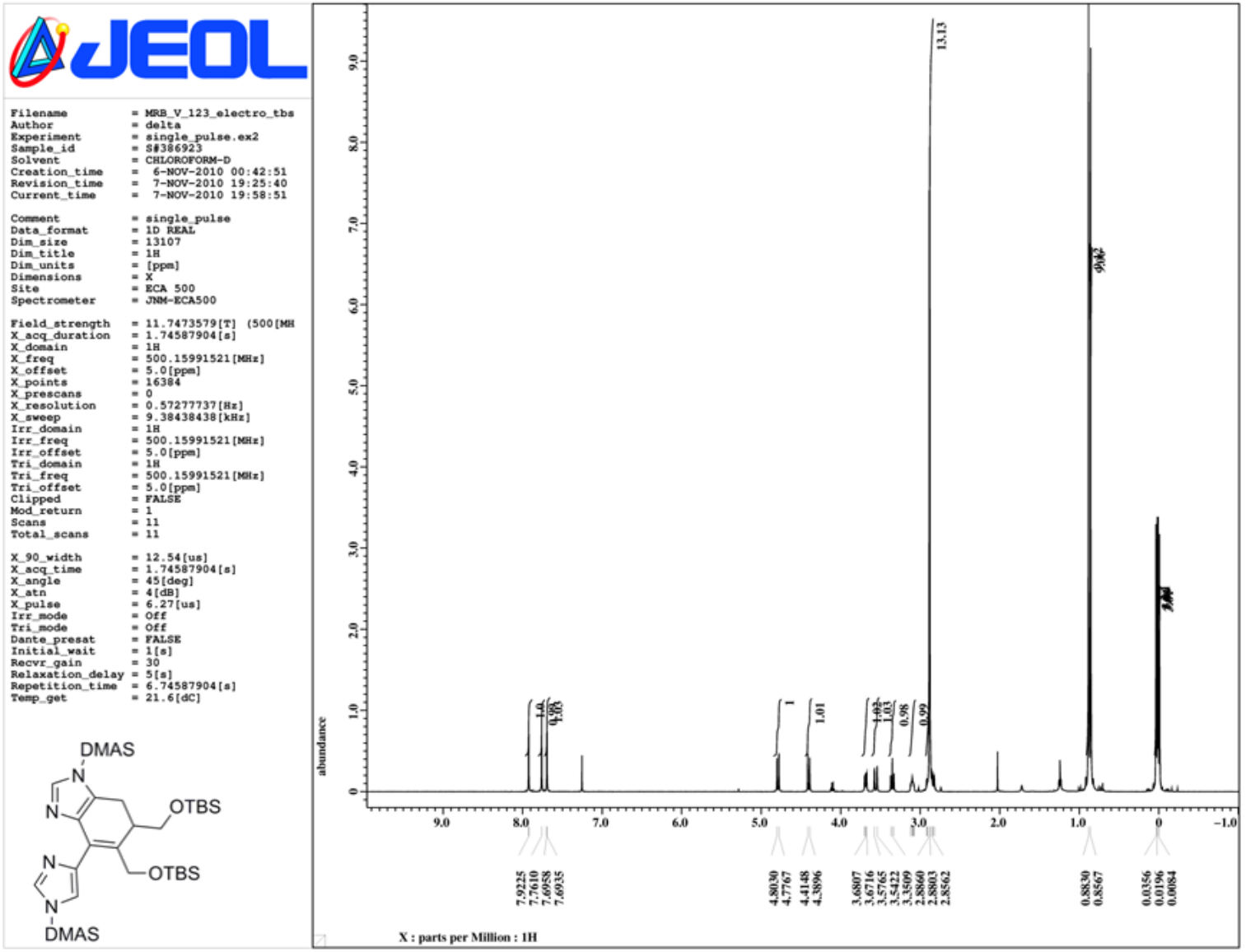


```
Filename          = MRB_V_122_alcohol_ele
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#612327
Solvent           = CHLOROFORM-D
Creation_time     =  4-NOV-2010 09:28:42
Revision_time     =  3-NOV-2010 19:34:26
Current_time      =  6-NOV-2010 22:28:32

Comment           = single pulse decouple
Data_format       = 1D REAL
Dim_size          = 26214
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 0.83361792[s]
X_domain          = 13C
X_freq            = 125.76529768[MHz]
X_offset          = 100[ppm]
X_points          = 32768
X_prescans        = 4
X_resolution      = 1.19959034[Hz]
X_sweep           = 39.3081761[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 10
Scans             = 3150
Total_scans       = 3150

X_90_width        = 10.73[us]
X_acq_time        = 0.83361792[s]
X_angle           = 30[deg]
X_atn             = 9[dB]
X_pulse           = 3.57666667[us]
Irr_atn_dec       = 20[dB]
Irr_atn_noe       = 20[dB]
Irr_noise         = WALTZ
Decoupling        = TRUE
Initial_wait      = 1[s]
Noe               = TRUE
Noe_time          = 2[s]
Recvr_gain        = 50
Relaxation_delay  = 2[s]
Repetition_time   = 2.83361792[s]
Temp_get          = 22.5[dC]
```

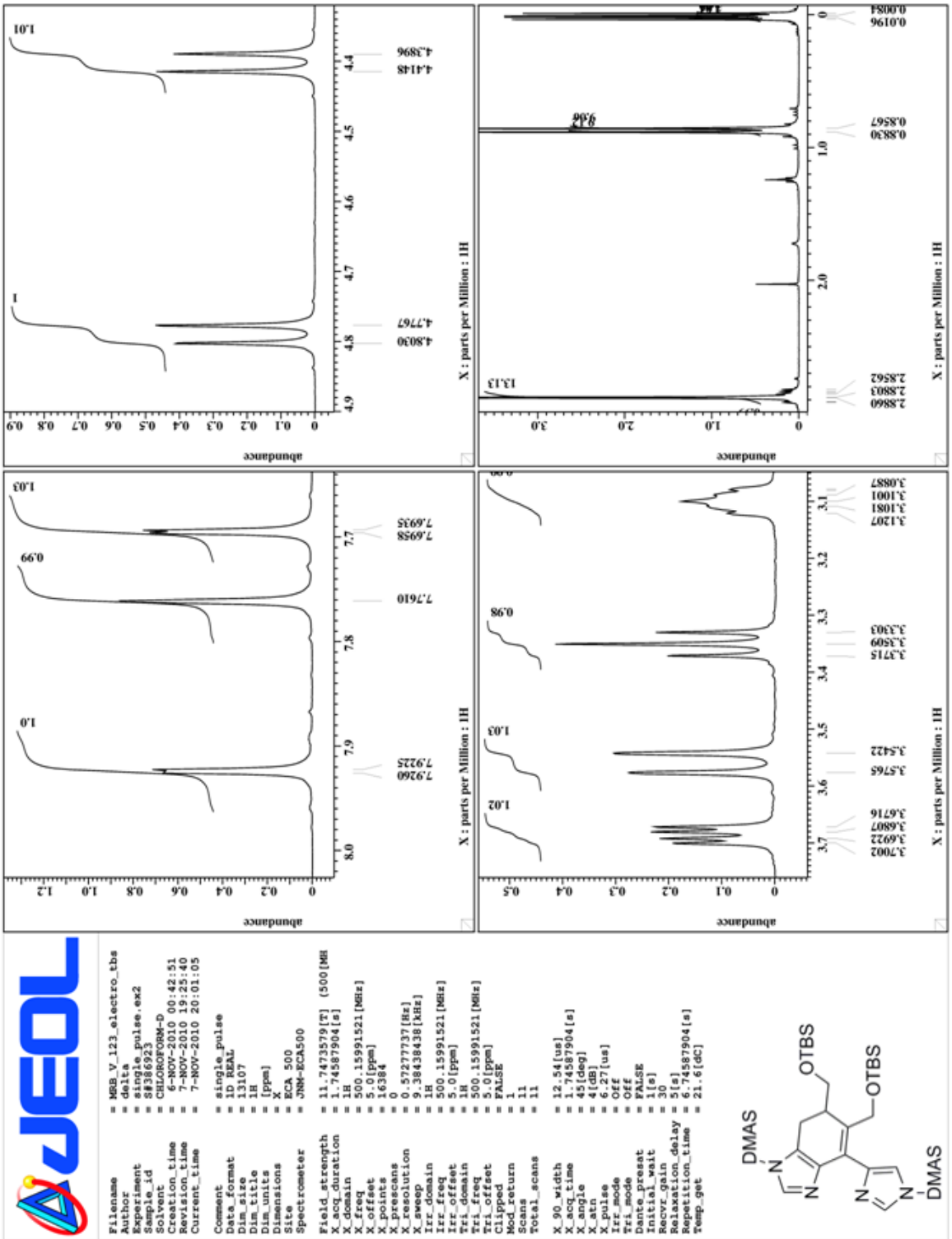


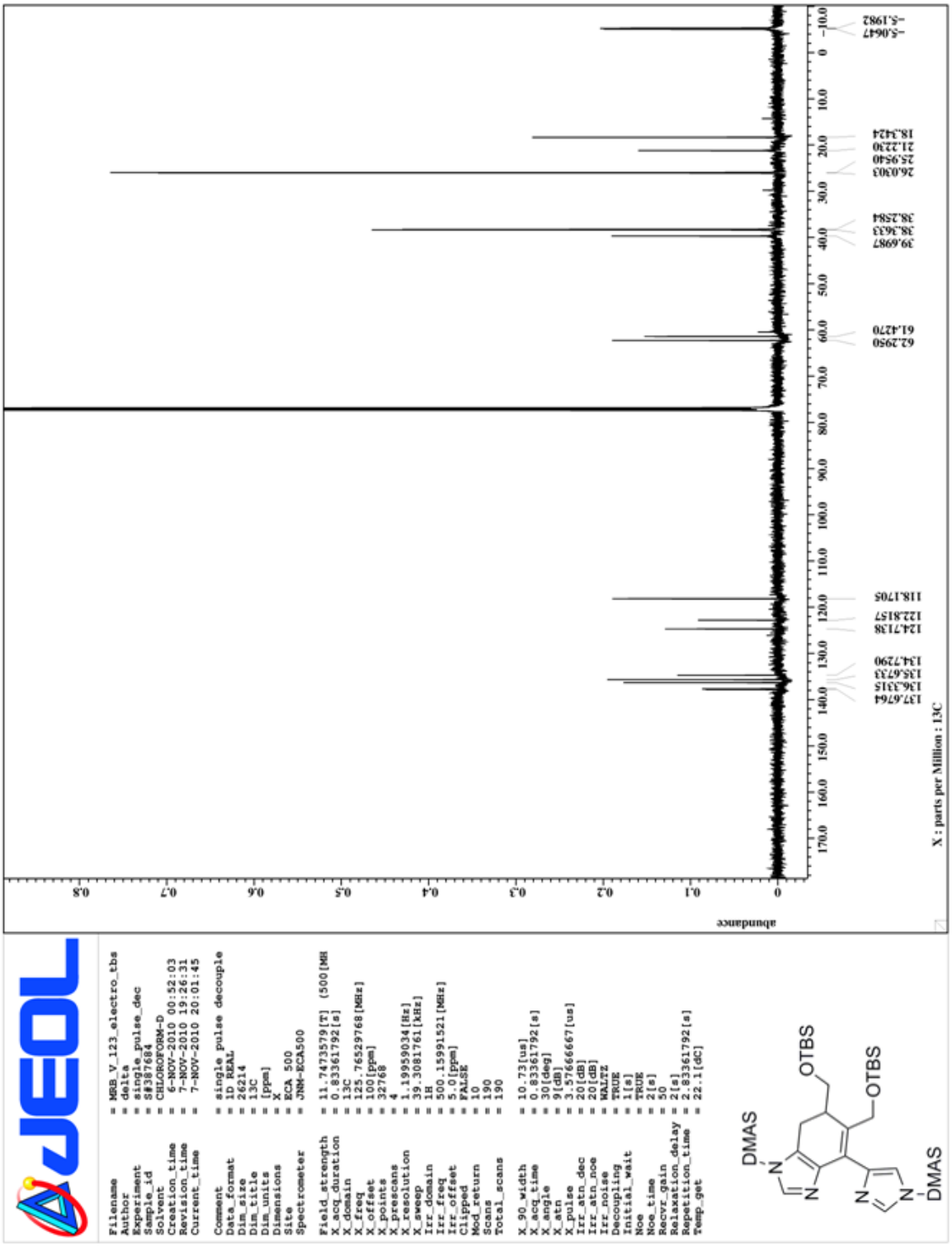


APPENDIX 26
^{1}H AND ^{13}C NMR SPECTRA OF
5,6-Bis((*t*-butyldimethylsilyloxy)methyl)-4-(1-dimethylsulfamoyl-1H-imidazol-4-yl)-1-dimethylsulfamoyl-6,7-dihydro-1H-benz[d]imidazole (105)

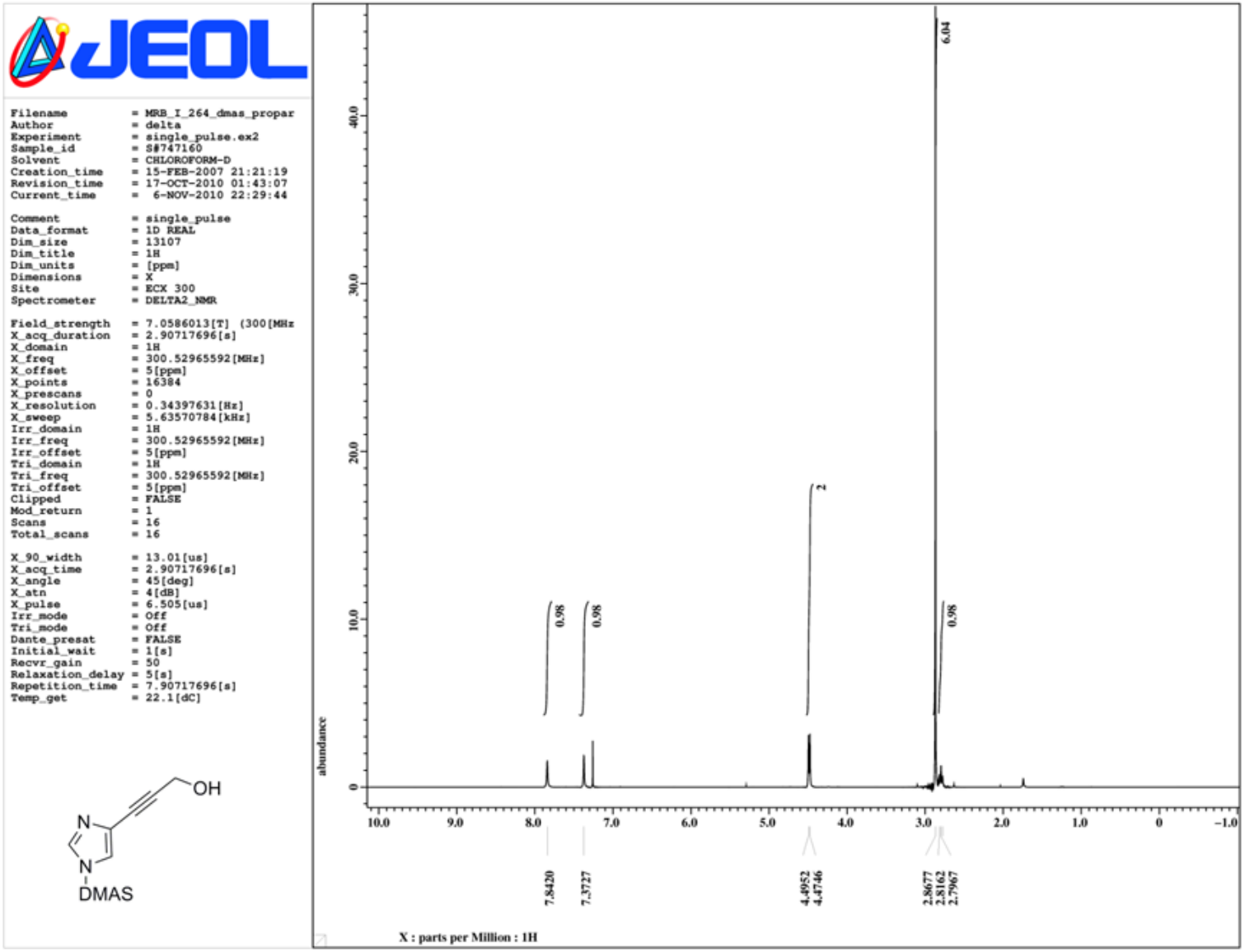


```
Filename          = MRB_V_123_electro_tbs
Author            = delta
Experiment        = single_pulse.ex2
Sample_id         = S#386923
Solvent           = CHLOROFORM-D
Creation_time     =  6-NOV-2010 00:42:51
Revision_time     =  7-NOV-2010 19:25:40
Current_time      =  7-NOV-2010 19:58:51

Comment           = single_pulse
Data_format       = 1D REAL
Dim_size          = 13107
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 1.74587904[s]
X_domain          = 1H
X_freq            = 500.15991521[MHz]
X_offset          = 5.0[ppm]
X_points          = 16384
X_prescans        = 0
X_resolution      = 0.57277737[Hz]
X_sweep           = 9.38438438[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Tri_domain        = 1H
Tri_freq          = 500.15991521[MHz]
Tri_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 11
Total_scans       = 11

X_90_width        = 12.54[us]
X_acq_time        = 1.74587904[s]
X_angle           = 45[deg]
X_atn             = 4[dB]
X_pulse           = 6.27[us]
Irr_mode          = Off
Tri_mode          = Off
Dante_presat      = FALSE
Initial_wait      = 1[s]
Recvr_gain        = 30
Relaxation_delay  = 5[s]
Repetition_time   = 6.74587904[s]
Temp_get          = 21.6[dC]
```

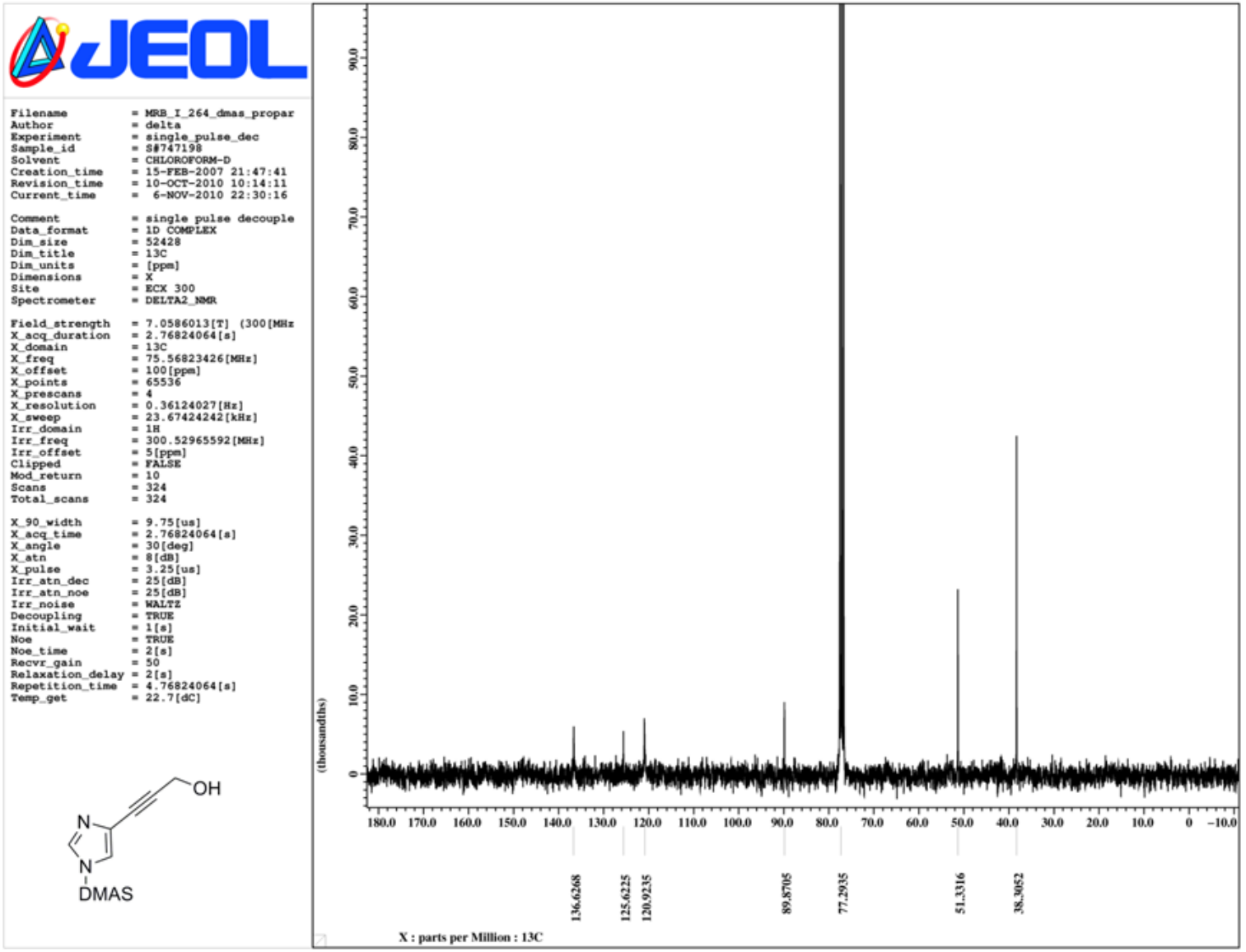

JEOL
Filename = MRB_V_123_electro_tbs
Author = delta
Experiment = single_pulse.ex2
Sample_id = s#386923
Solvent = CHLOROFORM-D
Creation_time = 6-NOV-2010 00:42:51
Revision_time = 7-NOV-2010 19:25:40
Current_time = 7-NOV-2010 20:01:05
Comment = single_pulse
Data_format = 1D REAL
Dim_size = 13107
Dim_title = 1H
Dim_units = [ppm]
Dimensions = X
Site = ECA 500
Spectrometer = JNM-ECA500
Field_strength = 11.7473579[T] (500[MH
X_acq_duration = 1.74587904[s]
X_domain = 1H
X_freq = 500.15991521[MHz]
X_offset = 5.0[ppm]
X_points = 16384
X_prescans = 0
X_resolution = 0.57277337[Hz]
X_sweep = 9.38438438[kHz]
Irr_domain = 1H
Irr_freq = 500.15991521[MHz]
Irr_offset = 5.0[ppm]
Tri_domain = 1H
Tri_freq = 500.15991521[MHz]
Tri_offset = 5.0[ppm]
Clipped = FALSE
Mod_return = 1
Scans = 11
Total_scans = 11
X_90_width = 12.54[us]
X_acq_time = 1.74587904[s]
X_angle = 45[deg]
X_atn = 4[dB]
X_pulse = 6.27[us]
Irr_mode = Off
Tri_mode = Off
Dante_presat = FALSE
Initial_wait = 1[s]
Recvr_gain = 30
Relaxation_delay = 5[s]
Repetition_time = 6.74587904[s]
Temp_get = 21.6[dC]
abundance
X : parts per Million : 1H
DMAS
OTBS
OTBS
DMAS


JEOL
Filename = MRB_V_123_electro_tbs
Author = delta
Experiment = single_pulse_dec
Sample_id = s#387684
Solvent = CHLOROFORM-D
Creation_time = 6-NOV-2010 00:52:03
Revision_time = 7-NOV-2010 19:26:31
Current_time = 7-NOV-2010 20:01:45
Comment = single pulse decouple
Data_format = 1D REAL
Dim_size = 26214
Dim_title = 13C
Dim_units = [ppm]
Dimensions = X
Site = ECA 500
Spectrometer = JNM-ECA500
Field_strength = 11.7473579[T] (500[MH
X_acq_duration = 0.83361792[s]
X_domain = 13C
X_freq = 125.765297668[MHz]
X_offset = 100[ppm]
X_points = 32768
X_prescans = 4
X_resolution = 1.19950034[Hz]
X_sweep = 39.3081761[kHz]
Irr_domain = H
Irr_freq = 500.159991521[MHz]
Irr_offset = 5.0[ppm]
Clipped = FALSE
Mod_return = 10
Scans = 190
Total_scans = 190
X_90_width = 10.73[us]
X_acq_time = 0.83361792[s]
X_angle = 30[deg]
X_atn = 9[dB]
X_pulse = 3.57666667[us]
Irr_atn_dec = 20[dB]
Irr_atn_noe = 20[dB]
Irr_noise = WALTZ
Decoupling = TRUE
Initial_wait = 1[s]
Noe = TRUE
Noe_time = 2[s]
Recvr_gain = 50
Relaxation_delay = 2[s]
Repetition_time = 2.83361792[s]
Temp_get = 22.1[dC]
DMAS
OTBS
OTBS
DMAS
abundance
X : parts per Million : 13C
137.6764
136.3315
135.6733
134.7290
124.7138
122.8157
118.1705
62.2950
61.4270
39.6987
38.3633
38.2584
26.0303
25.9540
21.2230
18.3424
-5.0647
-5.1982

APPENDIX 27
^{1}H AND ^{13}C NMR SPECTRA OF
3-(1-dimethylsulfamoylimidazole-4-yl)-1-hydroxy-2-propyne (112)



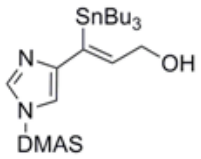
```
Filename          = MRB_I_264_dmas_propar
Author            = delta
Experiment        = single_pulse.ex2
Sample_id         = S#747160
Solvent           = CHLOROFORM-D
Creation_time     = 15-FEB-2007 21:21:19
Revision_time     = 17-OCT-2010 01:43:07
Current_time      =  6-NOV-2010 22:29:44

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    = 7.0586013[T] (300[MHz
X_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]
Irr_domain        = 1H
Irr_freq          = 300.52965592[MHz]
Irr_offset        = 5[ppm]
Tri_domain        = 1H
Tri_freq          = 300.52965592[MHz]
Tri_offset        = 5[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 16
Total_scans       = 16

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]
Irr_mode          = Off
Tri_mode          = Off
Dante_presat      = FALSE
Initial_wait      = 1[s]
Recvr_gain        = 50
Relaxation_delay  = 5[s]
Repetition_time   = 7.90717696[s]
Temp_get          = 22.1[dC]
```

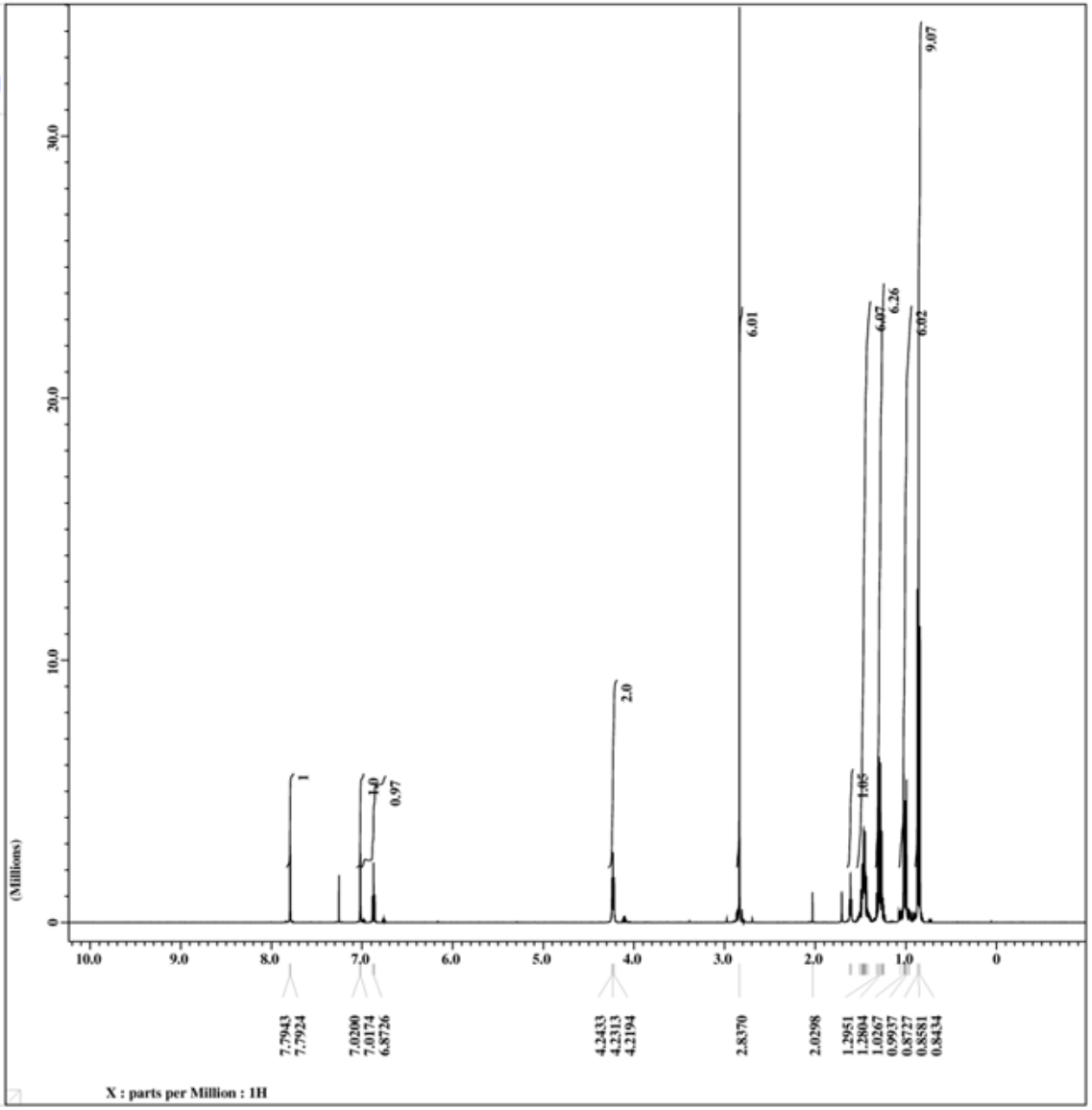


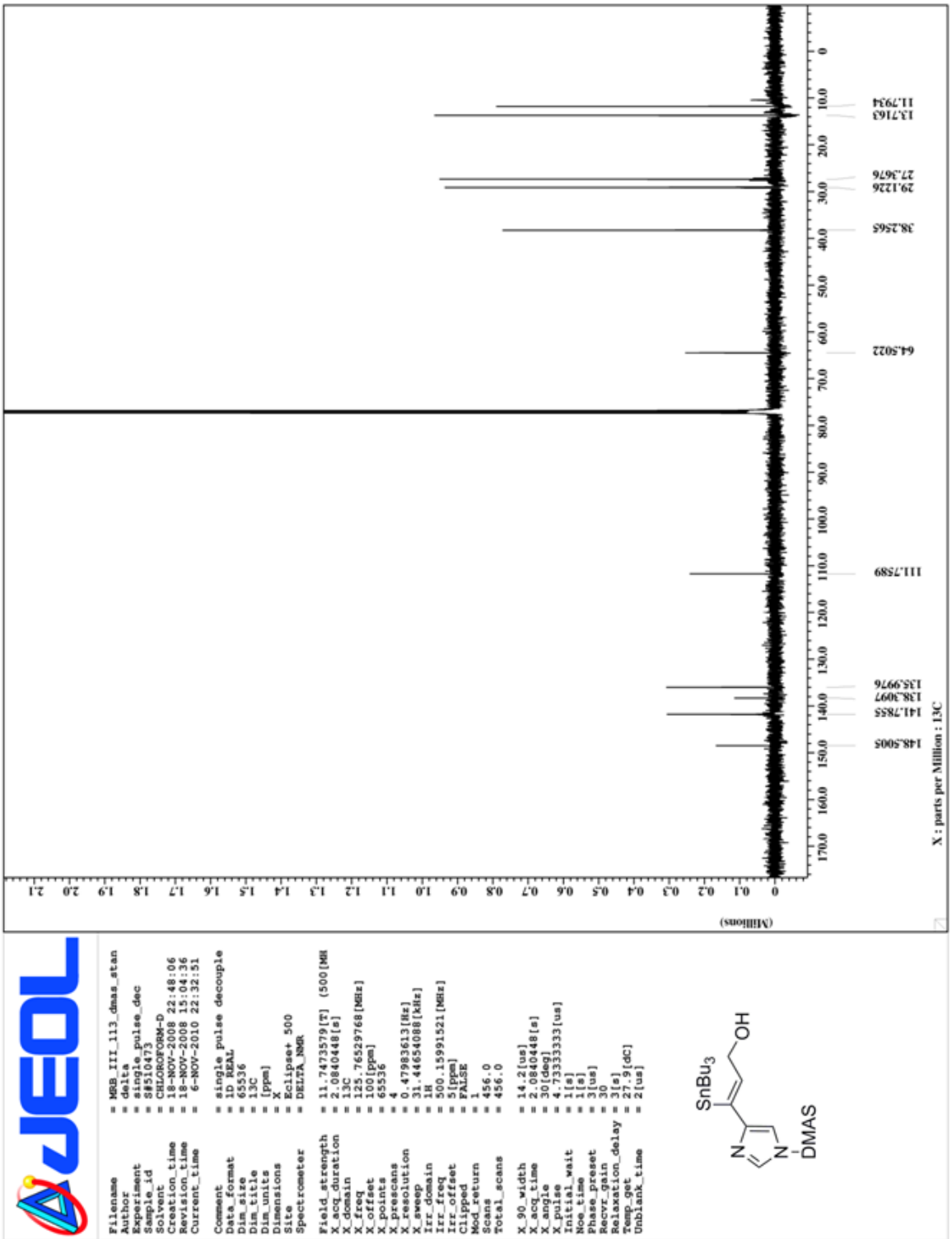
```
Filename          = MRB_I_264_dmas_propar
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#747198
Solvent           = CHLOROFORM-D
Creation_time     = 15-FEB-2007 21:47:41
Revision_time     = 10-OCT-2010 10:14:11
Current_time      =  6-NOV-2010 22:30:16

Comment           = single pulse decouple
Data_format       = 1D COMPLEX
Dim_size          = 52428
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = ECX 300
Spectrometer      = DELTA2_NMR

Field_strength    = 7.0586013[T] (300[MHz
X_acq_duration    = 2.76824064[s]
X_domain          = 13C
X_freq            = 75.56823426[MHz]
X_offset          = 100[ppm]
X_points          = 65536
X_prescans        = 4
X_resolution      = 0.36124027[Hz]
X_sweep           = 23.67424242[kHz]
Irr_domain        = 1H
Irr_freq          = 300.52965592[MHz]
Irr_offset        = 5[ppm]
Clipped           = FALSE
Mod_return        = 10
Scans             = 324
Total_scans       = 324

X_90_width        = 9.75[us]
X_acq_time        = 2.76824064[s]
X_angle           = 30[deg]
X_atn             = 8[dB]
X_pulse           = 3.25[us]
Irr_atn_dec       = 25[dB]
Irr_atn_noe       = 25[dB]
Irr_noise         = WALTZ
Decoupling        = TRUE
Initial_wait      = 1[s]
Noe               = TRUE
Noe_time          = 2[s]
Recvr_gain        = 50
Relaxation_delay  = 2[s]
Repetition_time   = 4.76824064[s]
Temp_get          = 22.7[dC]
```

APPENDIX 28
^{1}H AND ^{13}C NMR SPECTRA OF
(*Z*)-1-hydroxy-3-tributylstannyl-3-(1-dimethylsulfamoylimidazole-4-yl)-2-propene (113)

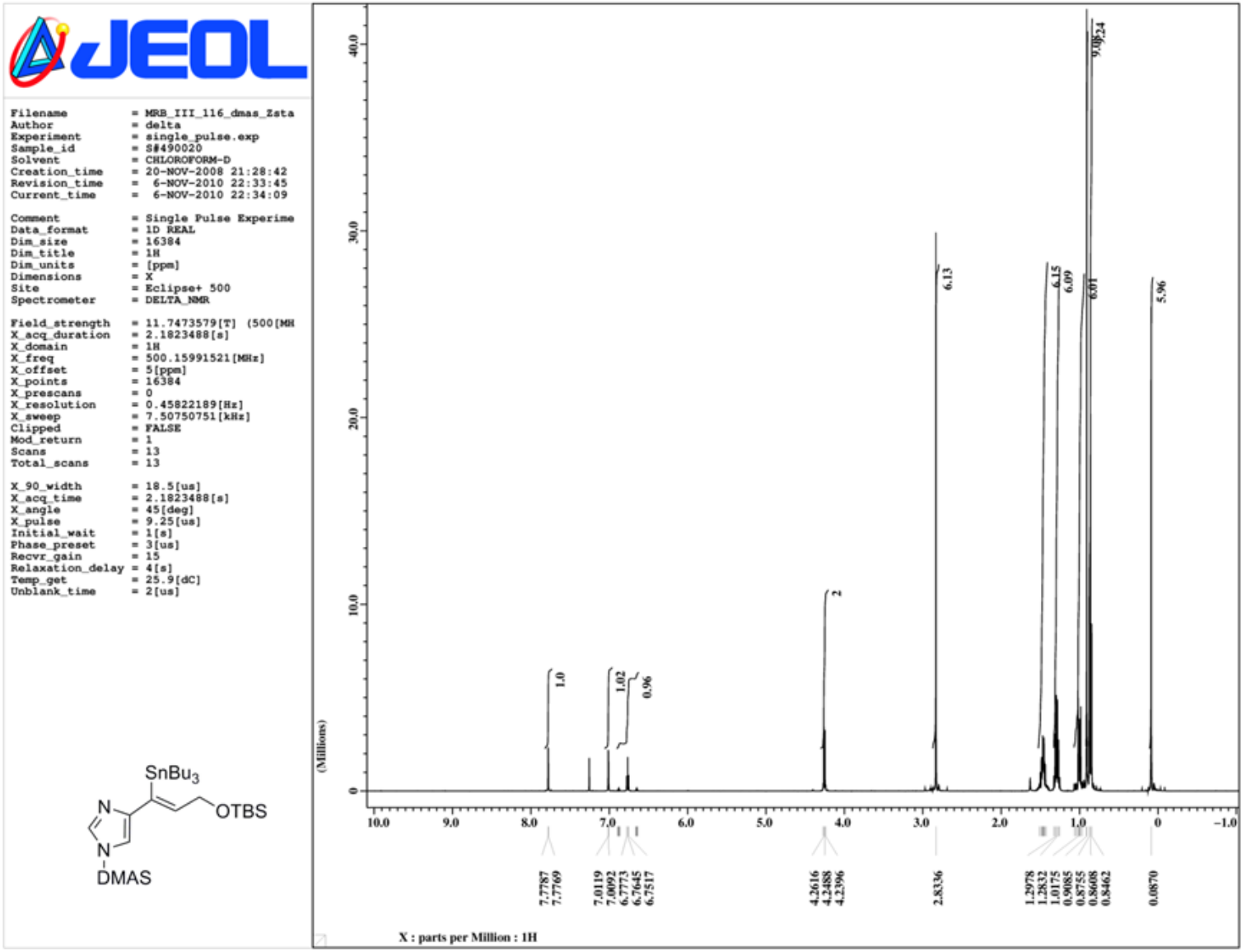
```
Filename          = MRB_III_113_dmas_stan
Author            = delta
Experiment        = single_pulse.exp
Sample_id         = S#508960
Solvent           = CHLOROFORM-D
Creation_time     = 18-NOV-2008 21:59:43
Revision_time     =  6-NOV-2010 22:31:30
Current_time      =  6-NOV-2010 22:31:57

Comment           = Single Pulse Experime
Data_format       = 1D REAL
Dim_size          = 16384
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = Eclipse+ 500
Spectrometer      = DELTA_NMR

Field_strength    = 11.7473579[T]  (500[MH
X_acq_duration    = 2.1823488[s]
X_domain          = 1H
X_freq            = 500.15991521[MHz]
X_offset          = 5[ppm]
X_points          = 16384
X_prescans        = 0
X_resolution      = 0.45822189[Hz]
X_sweep           = 7.50750751[kHz]
Clipped           = FALSE
Mod_return        = 1
Scans             = 16
Total_scans       = 16

X_90_width        = 18.5[us]
X_acq_time        = 2.1823488[s]
X_angle           = 45[deg]
X_pulse           = 9.25[us]
Initial_wait      = 1[s]
Phase_preset      = 3[us]
Recvr_gain        = 15
Relaxation_delay  = 4[s]
Temp_get          = 25.9[dC]
Unblank_time      = 2[us]
```



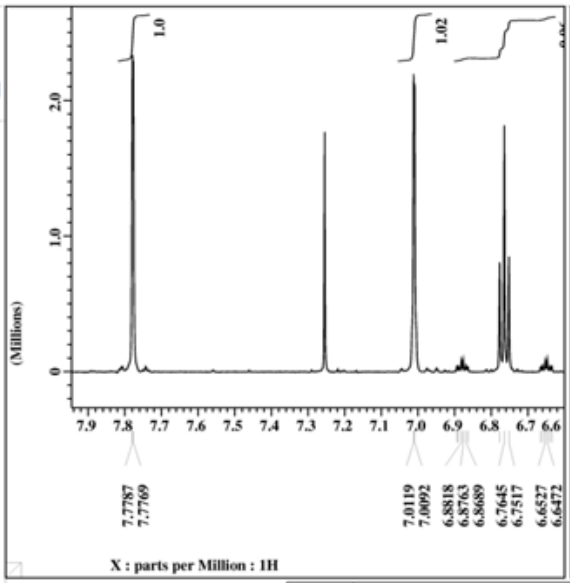


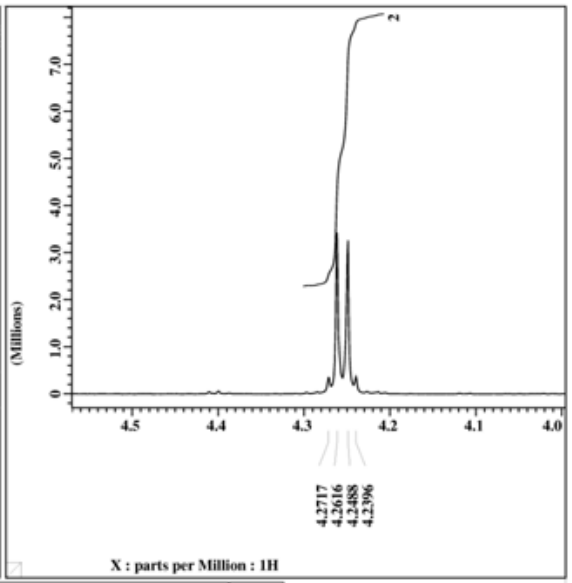

JEOL
Filename = MRB_III_113_dmas_stan
Author = delta
Experiment = single_pulse_dec
Sample_id = s#510473
Solvent = CHLOROFORM-D
Creation_time = 18-NOV-2008 22:48:06
Revision_time = 18-NOV-2008 15:04:36
Current_time = 6-NOV-2010 22:32:51
Comment = single pulse decouple
Data_format = 1D REAL
Dim_size = 65536
Dim_title = 13C
Dim_units = [ppm]
Dimensions = X
Site = Eclipse+ 500
Spectrometer = DELTA_NMR
Field_strength = 11.7473579[T] (500[MH
X_acq_duration = 2.0840448[s]
X_domain = 13C
X_freq = 125.765297681MHz]
X_offset = 100[ppm]
X_points = 65536
X_prescans = 4
X_resolution = 0.47983613[Hz]
X_sweep = 31.44654088[kHz]
Irr_domain = 1H
Irr_freq = 500.15991521[MHz]
Irr_offset = 5[ppm]
Clipped = FALSE
Mod_return = 1
Scans = 456.0
Total_scans = 456.0
X_90_width = 14.2[us]
X_acq_time = 2.0840448[s]
X_angle = 30[deg]
X_pulse = 4.733333333[us]
Initial_wait = 1[s]
Noe_time = 1[s]
Phase_preset = 3[us]
Recvr_gain = 30
Relaxation_delay = 3[s]
Temp_get = 27.9[dC]
Unblank_time = 2[us]
SnBu3
OH
N
N
DMAS
(Millions)
X : parts per Million : 13C
148.5005
141.7855
138.3097
135.9976
111.7589
64.5022
38.2565
29.1226
27.3676
13.7163
11.7934

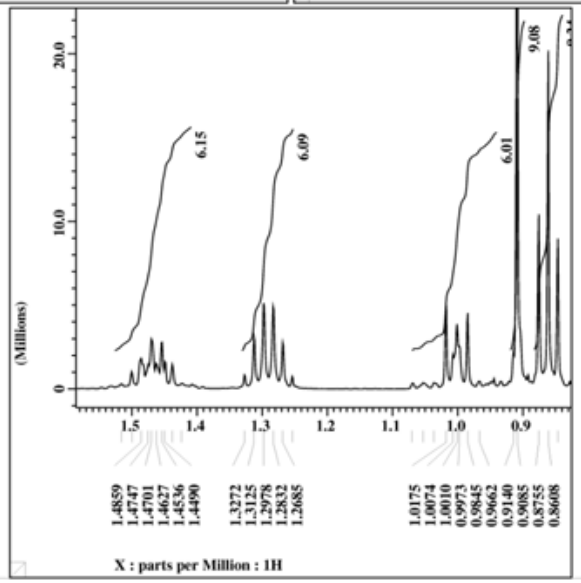
APPENDIX 29
^{1}H AND ^{13}C NMR SPECTRA OF
(*Z*)-1-*t*-Butyldimethylsilyloxy-3-tributylstannyl-3-(1-dimethylsulfamoylimidazole-4-yl)-2-propene (110)

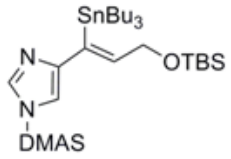

Filename = MRB_III_116_dmas_Zsta
Author = delta
Experiment = single_pulse.exp
Sample_id = S#490020
Solvent = CHLOROFORM-D
Creation_time = 20-NOV-2008 21:28:42
Revision_time = 6-NOV-2010 22:33:45
Current_time = 6-NOV-2010 22:34:09
Comment = Single Pulse Experime
Data_format = 1D REAL
Dim_size = 16384
Dim_title = 1H
Dim_units = [ppm]
Dimensions = X
Site = Eclipse+ 500
Spectrometer = DELTA_NMR
Field_strength = 11.7473579[T] (500[MH
X_acq_duration = 2.1823488[s]
X_domain = 1H
X_freq = 500.15991521[MHz]
X_offset = 5[ppm]
X_points = 16384
X_prescans = 0
X_resolution = 0.45822189[Hz]
X_sweep = 7.50750751[kHz]
Clipped = FALSE
Mod_return = 1
Scans = 13
Total_scans = 13
X_90_width = 18.5[us]
X_acq_time = 2.1823488[s]
X_angle = 45[deg]
X_pulse = 9.25[us]
Initial_wait = 1[s]
Phase_preset = 3[us]
Recvr_gain = 15
Relaxation_delay = 4[s]
Temp_get = 25.9[dC]
Unblank_time = 2[us]
SnBu3
OTBS
N
N
DMAS
(Millions)
40.0
30.0
20.0
10.0
0
1.0
1.02
0.96
2
6.13
6.15
6.09
6.01
9.08
5.96
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
−1.0
7.7787
7.7769
7.0119
7.0092
6.7773
6.7645
6.7517
4.2616
4.2488
4.2396
2.8336
1.2978
1.2832
1.0175
0.9085
0.8755
0.8608
0.8462
0.0870
X : parts per Million : 1H

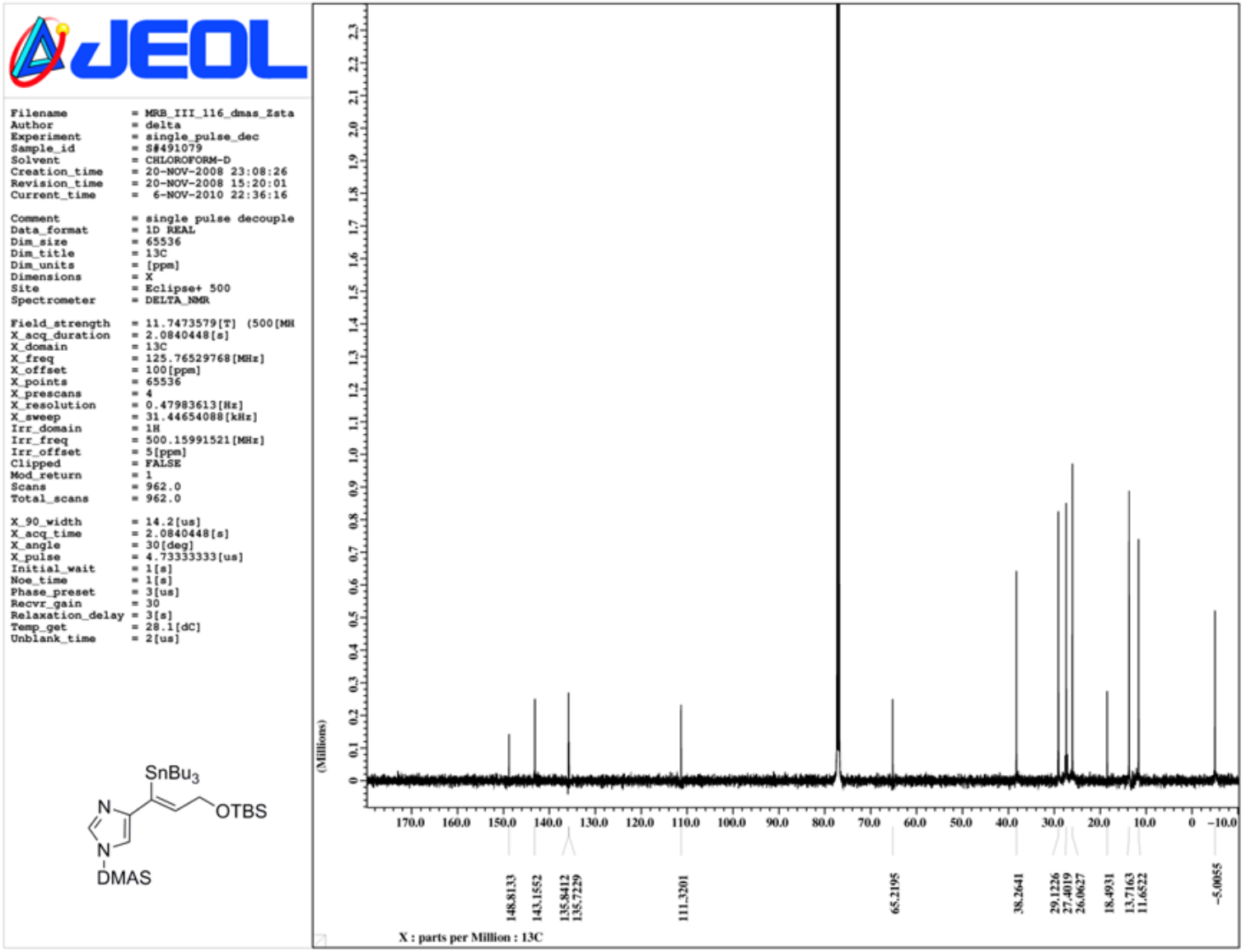
```
Filename          = MRB_III_116_dmas_Zsta
Author            = delta
Experiment        = single_pulse.exp
Sample_id         = S#490020
Solvent           = CHLOROFORM-D
Creation_time     = 20-NOV-2008 21:28:42
Revision_time     =  6-NOV-2010 22:33:45
Current_time      =  6-NOV-2010 22:35:48

Comment           = Single Pulse Experime
Data_format       = 1D REAL
Dim_size          = 16384
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = Eclipse+ 500
Spectrometer      = DELTA_NMR

Field_strength    = 11.7473579[T]  (500[MH
X_acq_duration    = 2.1823488[s]
X_domain          = 1H
X_freq            = 500.15991521[MHz]
X_offset          = 5[ppm]
X_points          = 16384
X_prescans        = 0
X_resolution      = 0.45822189[Hz]
X_sweep           = 7.50750751[kHz]
Clipped           = FALSE
Mod_return        = 1
Scans             = 13
Total_scans       = 13

X_90_width        = 18.5[us]
X_acq_time        = 2.1823488[s]
X_angle           = 45[deg]
X_pulse           = 9.25[us]
Initial_wait      = 1[s]
Phase_preset      = 3[us]
Recvr_gain        = 15
Relaxation_delay  = 4[s]
Temp_get          = 25.9[dC]
Unblank_time      = 2[us]
```





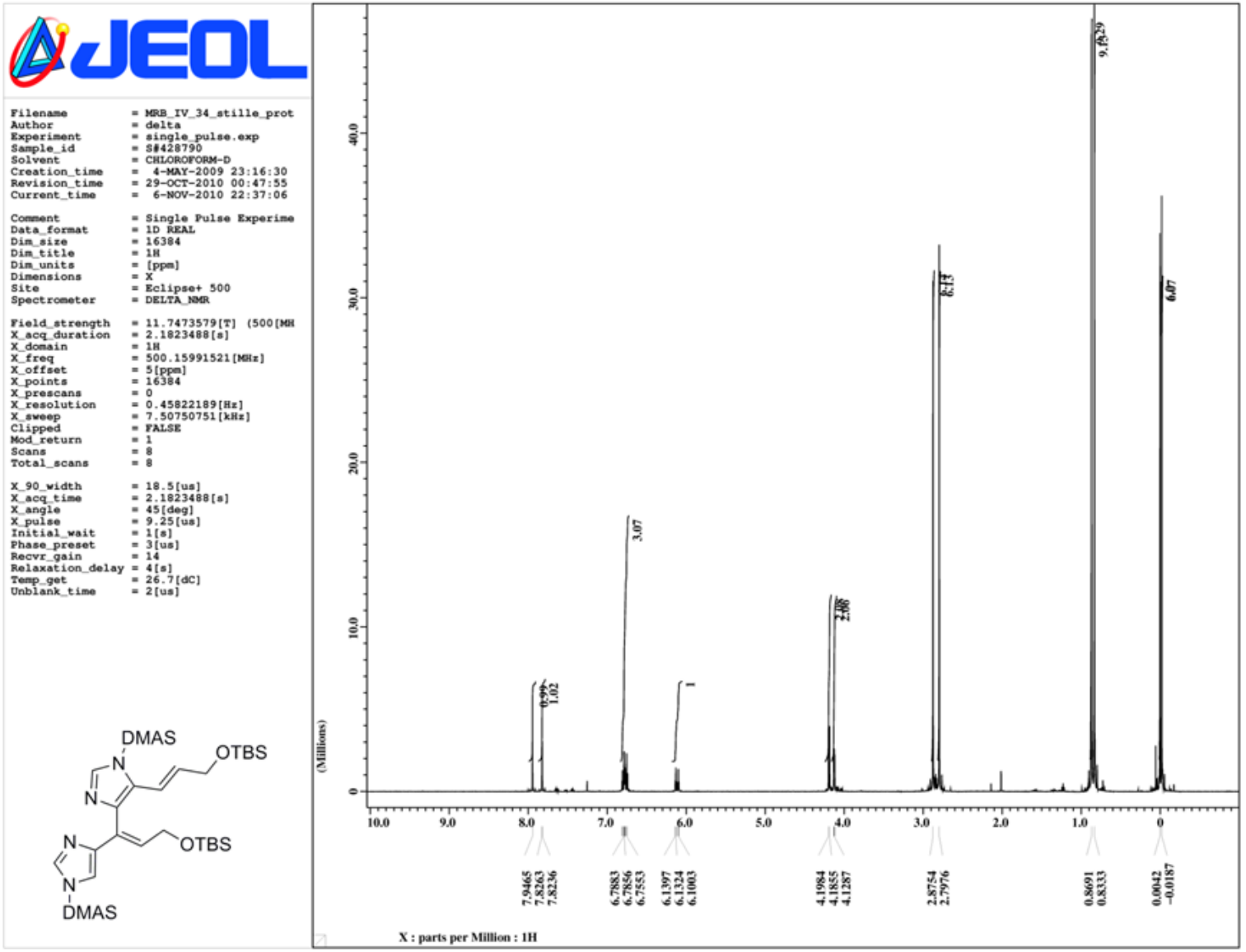




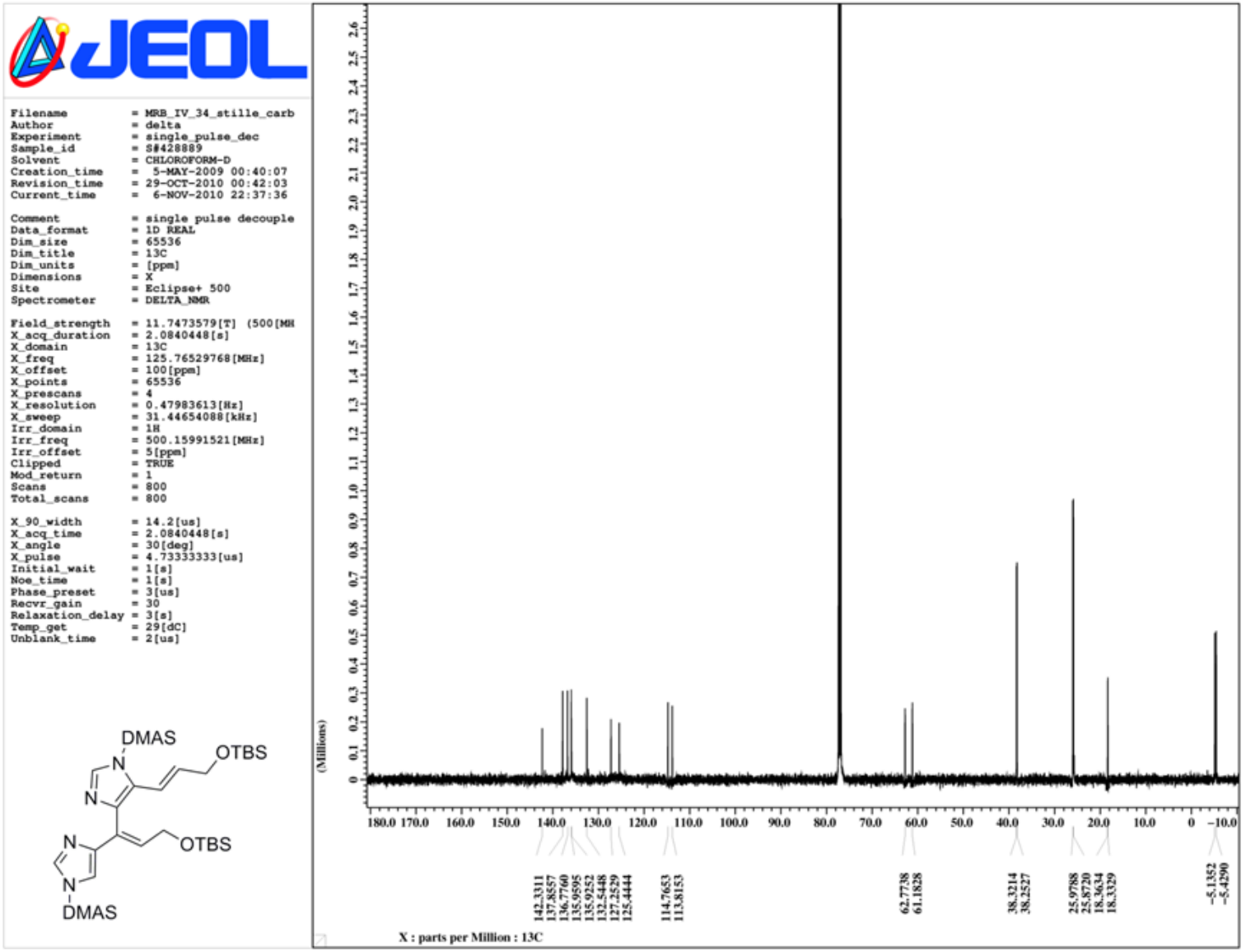


```
Filename          = MRB_III_116_dmas_Zsta
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#491079
Solvent           = CHLOROFORM-D
Creation_time     = 20-NOV-2008 23:08:26
Revision_time     = 20-NOV-2008 15:20:01
Current_time      =  6-NOV-2010 22:36:16

Comment           = single pulse decouple
Data_format       = 1D REAL
Dim_size          = 65536
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = Eclipse+ 500
Spectrometer      = DELTA_NMR

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 2.0840448[s]
X_domain          = 13C
X_freq            = 125.76529768[MHz]
X_offset          = 100[ppm]
X_points          = 65536
X_prescans        = 4
X_resolution      = 0.47983613[Hz]
X_sweep           = 31.44654088[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 962.0
Total_scans       = 962.0

X_90_width        = 14.2[us]
X_acq_time        = 2.0840448[s]
X_angle           = 30[deg]
X_pulse           = 4.73333333[us]
Initial_wait      = 1[s]
Noe_time          = 1[s]
Phase_preset      = 3[us]
Recvr_gain        = 30
Relaxation_delay  = 3[s]
Temp_get          = 28.1[dC]
Unblank_time      = 2[us]
```

APPENDIX 30
^{1}H AND ^{13}C NMR SPECTRA OF
4-((*Z*)-1-Dimethylsulfamoyl-4-(3-(*t*-butyldimethylsilyloxy)-2-propenyl)imidazol-4-yl)-1-dimethylsulfamoyl-5-((*E*)-3-(*t*-butyldimethylsilyloxy)-2-propenyl)imidazole (114)

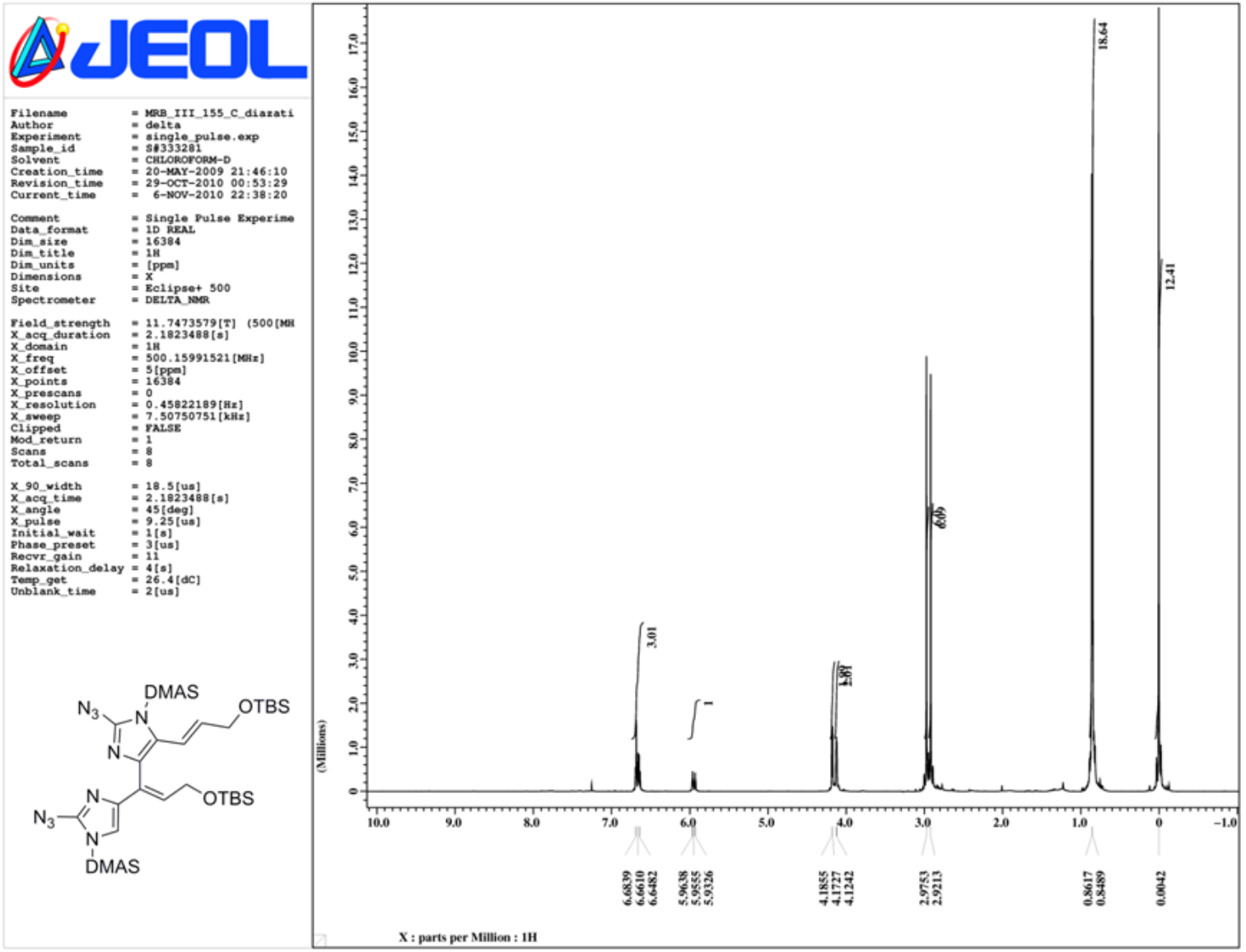


```
Filename          = MRB_IV_34_stille_prot
Author            = delta
Experiment        = single_pulse.exp
Sample_id         = S#428790
Solvent           = CHLOROFORM-D
Creation_time     =  4-MAY-2009 23:16:30
Revision_time     = 29-OCT-2010 00:47:55
Current_time      =  6-NOV-2010 22:37:06

Comment           = Single Pulse Experime
Data_format       = 1D REAL
Dim_size          = 16384
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = Eclipse+ 500
Spectrometer      = DELTA_NMR

Field_strength    = 11.7473579[T]  (500[MH
X_acq_duration    = 2.1823488[s]
X_domain          = 1H
X_freq            = 500.15991521[MHz]
X_offset          = 5[ppm]
X_points          = 16384
X_prescans        = 0
X_resolution      = 0.45822189[Hz]
X_sweep           = 7.50750751[kHz]
Clipped           = FALSE
Mod_return        = 1
Scans             = 8
Total_scans       = 8

X_90_width        = 18.5[us]
X_acq_time        = 2.1823488[s]
X_angle           = 45[deg]
X_pulse           = 9.25[us]
Initial_wait      = 1[s]
Phase_preset      = 3[us]
Recvr_gain        = 14
Relaxation_delay  = 4[s]
Temp_get          = 26.7[dC]
Unblank_time      = 2[us]
```

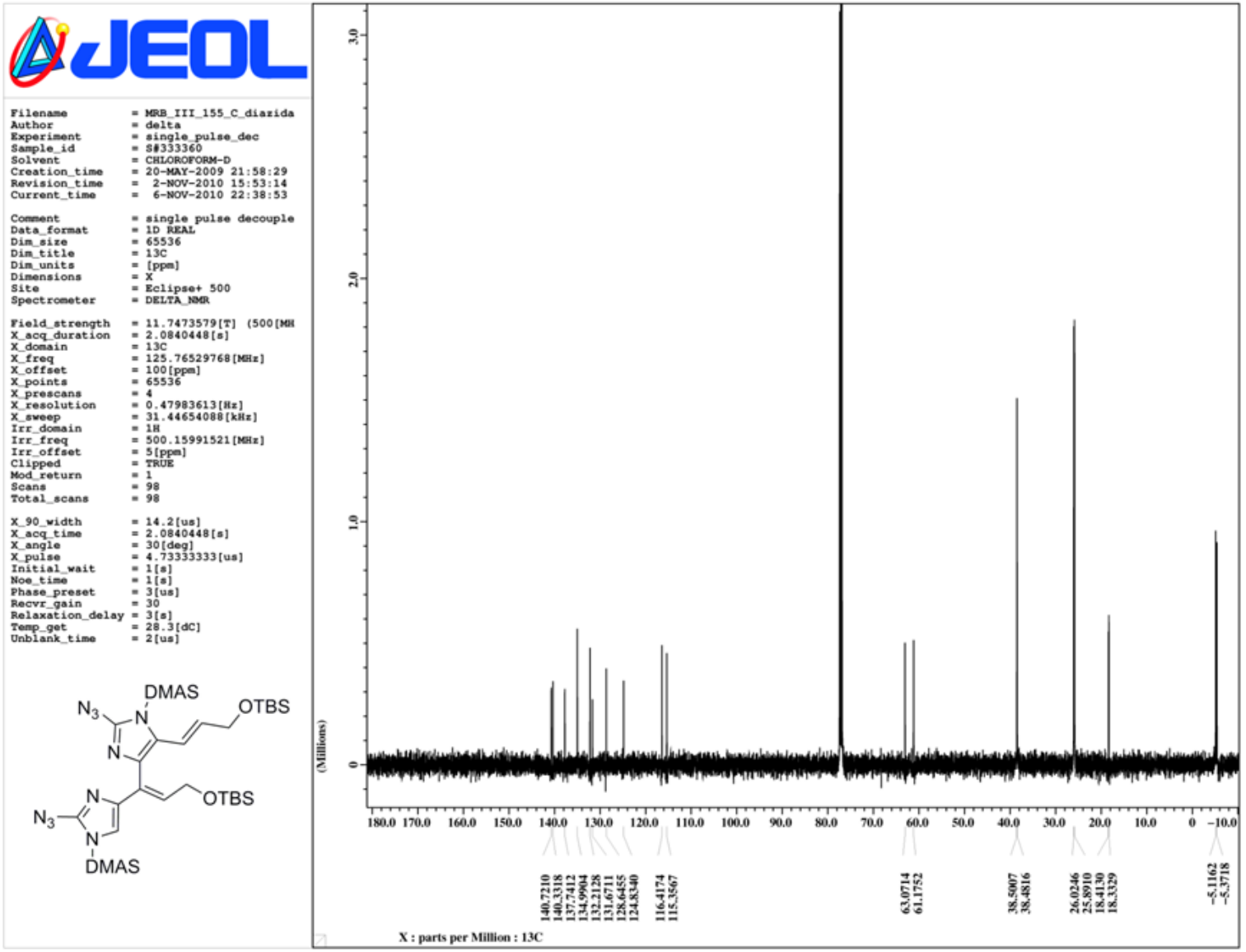


```
Filename          = MRB_IV_34_stille_carb
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#428889
Solvent           = CHLOROFORM-D
Creation_time     =  5-MAY-2009 00:40:07
Revision_time     = 29-OCT-2010 00:42:03
Current_time      =  6-NOV-2010 22:37:36

Comment           = single pulse decouple
Data_format       = 1D REAL
Dim_size          = 65536
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = Eclipse+ 500
Spectrometer      = DELTA_NMR

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 2.0840448[s]
X_domain          = 13C
X_freq            = 125.76529768[MHz]
X_offset          = 100[ppm]
X_points          = 65536
X_prescans        = 4
X_resolution      = 0.47983613[Hz]
X_sweep           = 31.44654088[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5[ppm]
Clipped           = TRUE
Mod_return        = 1
Scans             = 800
Total_scans       = 800

X_90_width        = 14.2[us]
X_acq_time        = 2.0840448[s]
X_angle           = 30[deg]
X_pulse           = 4.73333333[us]
Initial_wait      = 1[s]
Noe_time          = 1[s]
Phase_preset      = 3[us]
Recvr_gain        = 30
Relaxation_delay  = 3[s]
Temp_get          = 29[dC]
Unblank_time      = 2[us]
```

APPENDIX 31
^{1}H AND ^{13}C NMR SPECTRA OF
2-Azido-4-((*Z*)-2-azido-1-Dimethylsulfamoyl-4-(3-(*t*-butyldimethylsilyloxy)-2-propenyl)imidazol-4-yl)-1-dimethylsulfamoyl-5-((*E*)-3-(*t*-butyldimethylsilyloxy)-2-propenyl)imidazole (115)

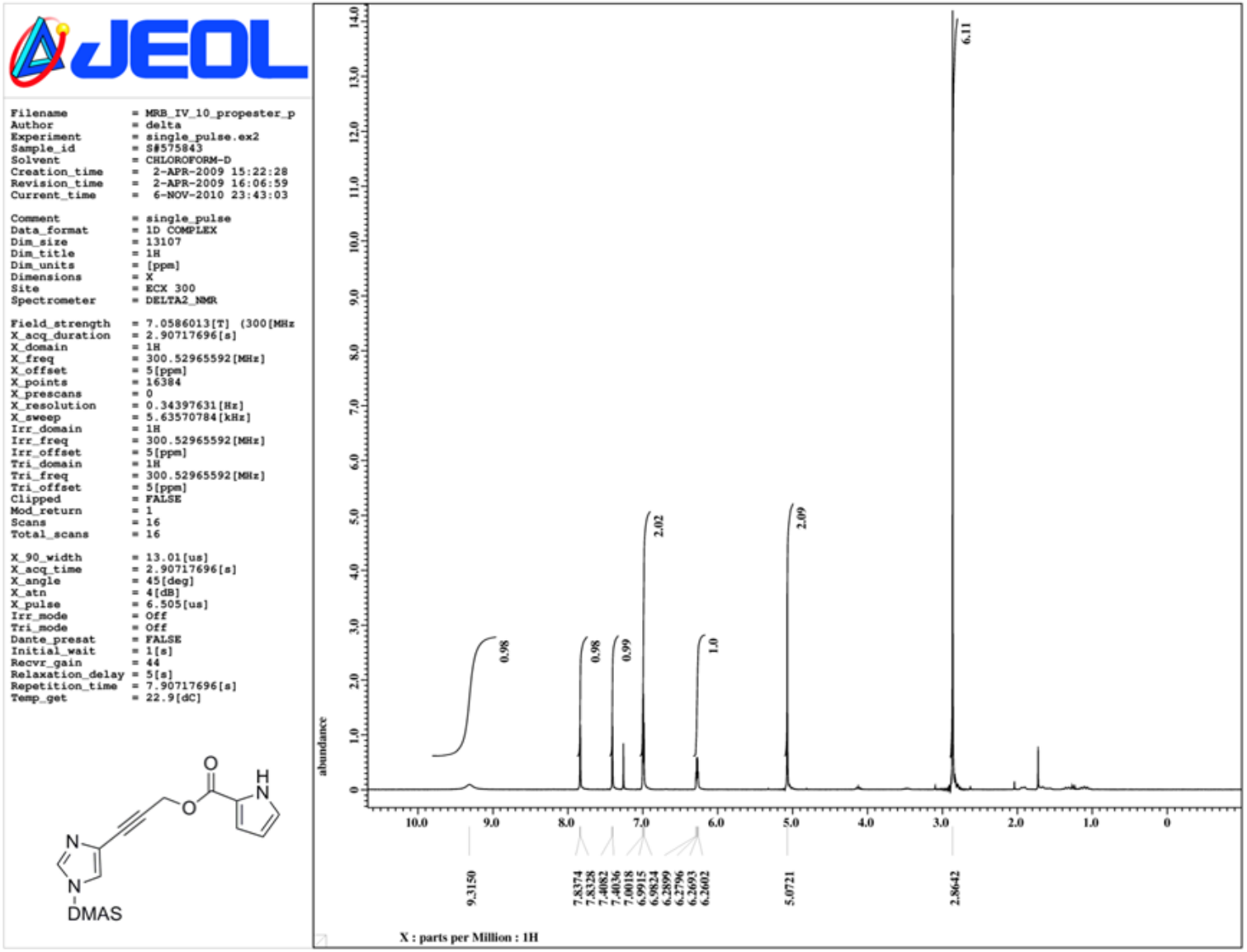


```
Filename          = MRB_III_155_C_diazati
Author            = delta
Experiment        = single_pulse.exp
Sample_id         = S#333281
Solvent           = CHLOROFORM-D
Creation_time     = 20-MAY-2009 21:46:10
Revision_time     = 29-OCT-2010 00:53:29
Current_time      =  6-NOV-2010 22:38:20

Comment           = Single Pulse Experime
Data_format       = 1D REAL
Dim_size          = 16384
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = Eclipse+ 500
Spectrometer      = DELTA_NMR

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 2.1823488[s]
X_domain          = 1H
X_freq            = 500.15991521[MHz]
X_offset          = 5[ppm]
X_points          = 16384
X_prescans        = 0
X_resolution      = 0.45822189[Hz]
X_sweep           = 7.50750751[kHz]
Clipped           = FALSE
Mod_return        = 1
Scans             = 8
Total_scans       = 8

X_90_width        = 18.5[us]
X_acq_time        = 2.1823488[s]
X_angle           = 45[deg]
X_pulse           = 9.25[us]
Initial_wait      = 1[s]
Phase_preset      = 3[us]
Recvr_gain        = 11
Relaxation_delay  = 4[s]
Temp_get          = 26.4[dC]
Unblank_time      = 2[us]
```

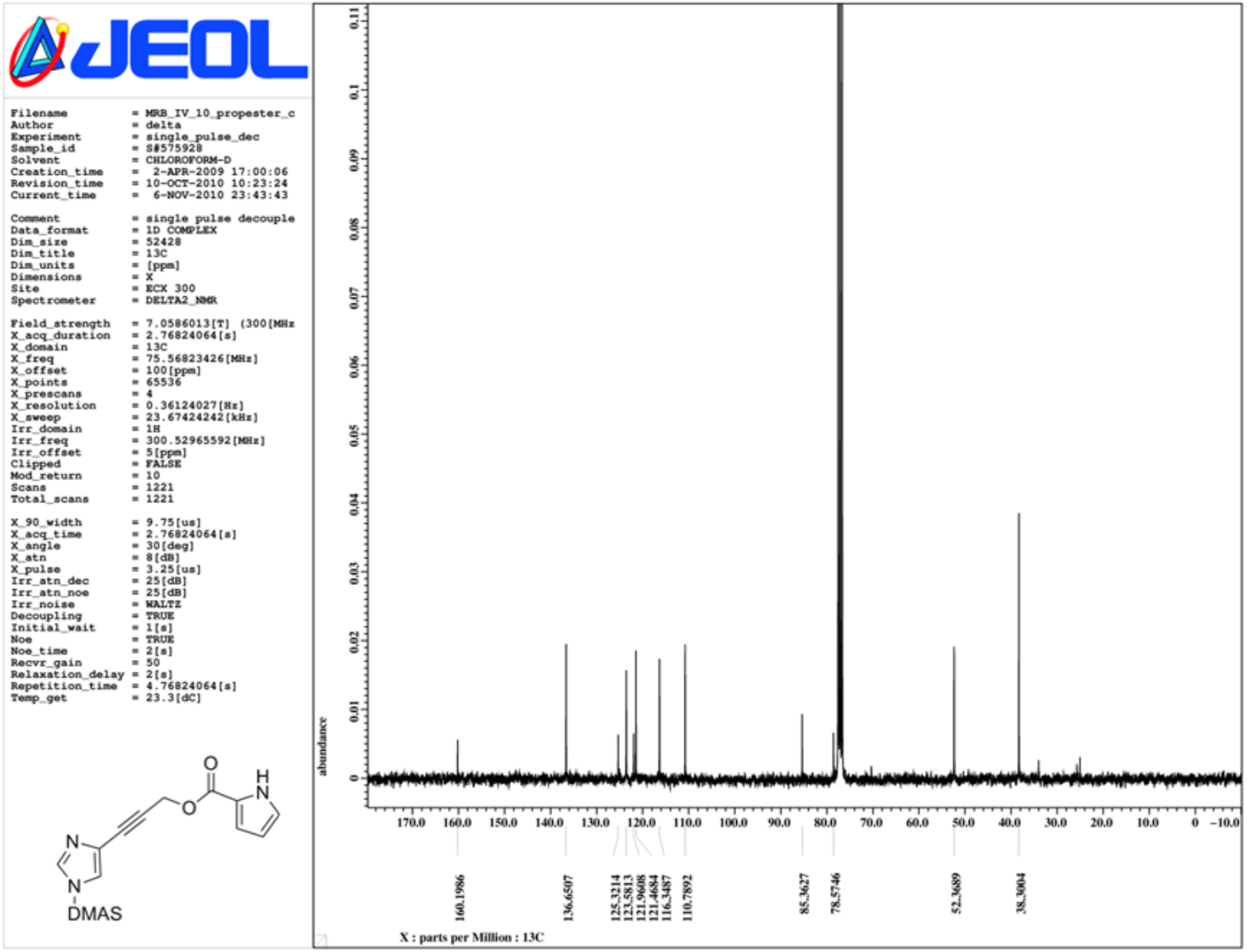


```
Filename          = MRB_III_155_C_diazida
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#333360
Solvent           = CHLOROFORM-D
Creation_time     = 20-MAY-2009 21:58:29
Revision_time     =  2-NOV-2010 15:53:14
Current_time      =  6-NOV-2010 22:38:53

Comment           = single pulse decouple
Data_format       = 1D REAL
Dim_size          = 65536
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = Eclipse+ 500
Spectrometer      = DELTA_NMR

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 2.0840448[s]
X_domain          = 13C
X_freq            = 125.76529768[MHz]
X_offset          = 100[ppm]
X_points          = 65536
X_prescans        = 4
X_resolution      = 0.47983613[Hz]
X_sweep           = 31.44654088[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5[ppm]
Clipped           = TRUE
Mod_return        = 1
Scans             = 98
Total_scans       = 98

X_90_width        = 14.2[us]
X_acq_time        = 2.0840448[s]
X_angle           = 30[deg]
X_pulse           = 4.73333333[us]
Initial_wait      = 1[s]
Noe_time          = 1[s]
Phase_preset      = 3[us]
Recvr_gain        = 30
Relaxation_delay  = 3[s]
Temp_get          = 28.3[dC]
Unblank_time      = 2[us]
```

APPENDIX 32
^{1}H AND ^{13}C NMR SPECTRA OF
3-(1-(*N*,*N*-Dimethylsulfamoyl)-1H-imidazol-4-yl)prop-2-ynyl-1H-pyrrole-2-carboxylate (135)

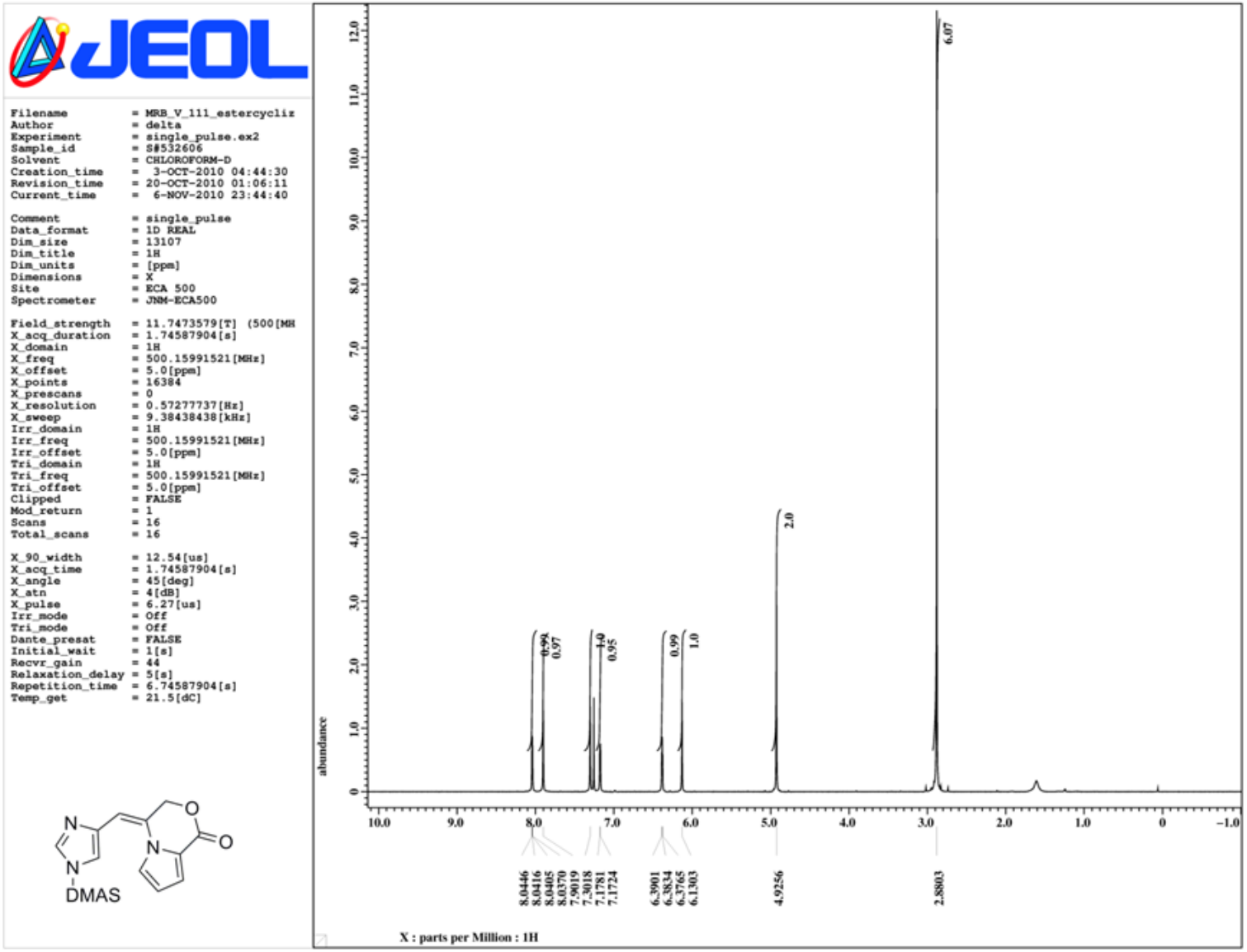


```
Filename          = MRB_IV_10_propester_p
Author            = delta
Experiment        = single_pulse.ex2
Sample_id         = S#575843
Solvent           = CHLOROFORM-D
Creation_time     =  2-APR-2009 15:22:28
Revision_time     =  2-APR-2009 16:06:59
Current_time      =  6-NOV-2010 23:43:03

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
X_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]
Irr_domain        = 1H
Irr_freq          = 300.52965592[MHz]
Irr_offset        = 5[ppm]
Tri_domain        = 1H
Tri_freq          = 300.52965592[MHz]
Tri_offset        = 5[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 16
Total_scans       = 16

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]
Irr_mode          = Off
Tri_mode          = Off
Dante_presat      = FALSE
Initial_wait      = 1[s]
Recvr_gain        = 44
Relaxation_delay  = 5[s]
Repetition_time   = 7.90717696[s]
Temp_get          = 22.9[dC]
```

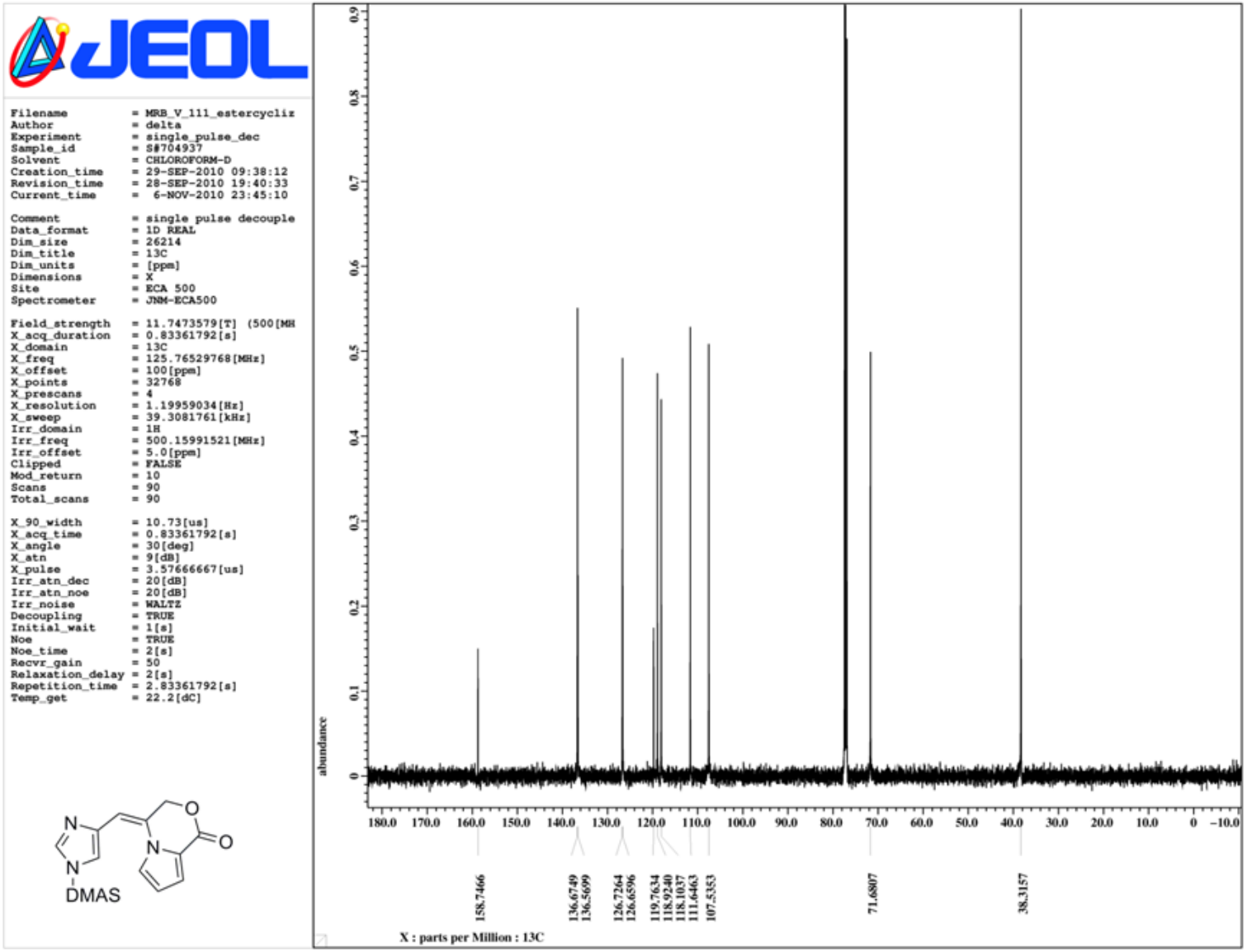


```
Filename          = MRB_IV_10_propester_c
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#575928
Solvent           = CHLOROFORM-D
Creation_time     =  2-APR-2009 17:00:06
Revision_time     = 10-OCT-2010 10:23:24
Current_time      =  6-NOV-2010 23:43:43

Comment           = single pulse decouple
Data_format       = 1D COMPLEX
Dim_size          = 52428
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = ECX 300
Spectrometer      = DELTA2_NMR

Field_strength    = 7.0586013[T] (300[MHz
X_acq_duration    = 2.76824064[s]
X_domain          = 13C
X_freq            = 75.56823426[MHz]
X_offset          = 100[ppm]
X_points          = 65536
X_prescans        = 4
X_resolution      = 0.36124027[Hz]
X_sweep           = 23.67424242[kHz]
Irr_domain        = 1H
Irr_freq          = 300.52965592[MHz]
Irr_offset        = 5[ppm]
Clipped           = FALSE
Mod_return        = 10
Scans             = 1221
Total_scans       = 1221

X_90_width        = 9.75[us]
X_acq_time        = 2.76824064[s]
X_angle           = 30[deg]
X_atn             = 8[dB]
X_pulse           = 3.25[us]
Irr_atn_dec       = 25[dB]
Irr_atn_noe       = 25[dB]
Irr_noise         = WALTZ
Decoupling        = TRUE
Initial_wait      = 1[s]
Noe               = TRUE
Noe_time          = 2[s]
Recvr_gain        = 50
Relaxation_delay  = 2[s]
Repetition_time   = 4.76824064[s]
Temp_get          = 23.3[dC]
```

APPENDIX 33
^{1}H AND ^{13}C NMR SPECTRA OF
(*Z*)-*N*,*N*-Dimethyl-4-((1-oxo-1H-pyrrolo[2,1-c][1,4]oxazin-4(3H)-ylidene)methyl)-1H-imidazole-1-sulfonamide (136)

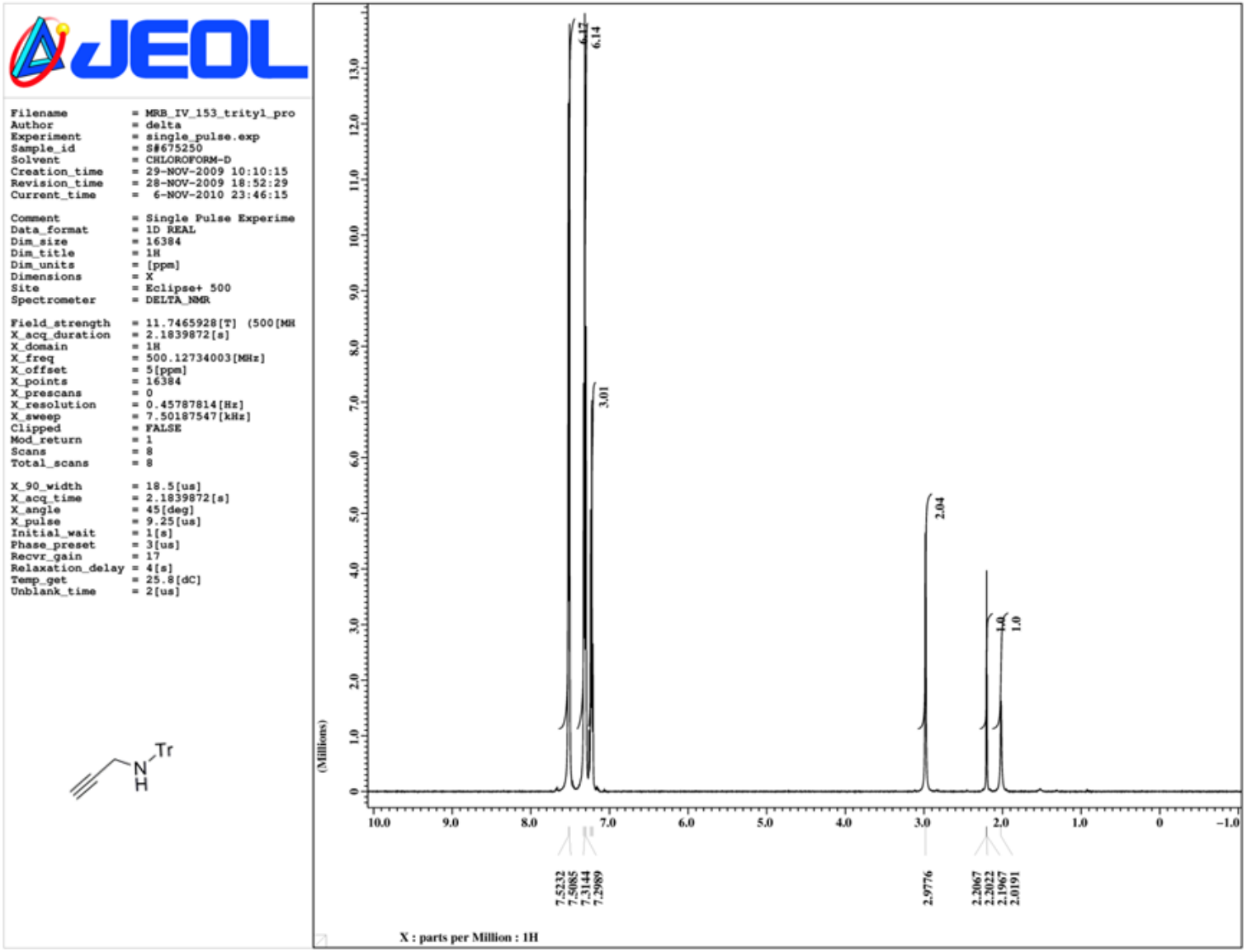


```
Filename          = MRB_V_111_estercycliz
Author            = delta
Experiment        = single_pulse.ex2
Sample_id         = S#532606
Solvent           = CHLOROFORM-D
Creation_time     =  3-OCT-2010 04:44:30
Revision_time     = 20-OCT-2010 01:06:11
Current_time      =  6-NOV-2010 23:44:40

Comment           = single_pulse
Data_format       = 1D REAL
Dim_size          = 13107
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 1.74587904[s]
X_domain          = 1H
X_freq            = 500.15991521[MHz]
X_offset          = 5.0[ppm]
X_points          = 16384
X_prescans        = 0
X_resolution      = 0.57277737[Hz]
X_sweep           = 9.38438438[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Tri_domain        = 1H
Tri_freq          = 500.15991521[MHz]
Tri_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 16
Total_scans       = 16

X_90_width        = 12.54[us]
X_acq_time        = 1.74587904[s]
X_angle           = 45[deg]
X_atn             = 4[dB]
X_pulse           = 6.27[us]
Irr_mode          = Off
Tri_mode          = Off
Dante_presat      = FALSE
Initial_wait      = 1[s]
Recvr_gain        = 44
Relaxation_delay  = 5[s]
Repetition_time   = 6.74587904[s]
Temp_get          = 21.5[dC]
```



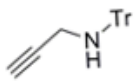
```
Filename          = MRB_V_111_estercycliz
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#704937
Solvent           = CHLOROFORM-D
Creation_time     = 29-SEP-2010 09:38:12
Revision_time     = 28-SEP-2010 19:40:33
Current_time      =  6-NOV-2010 23:45:10

Comment           = single pulse decouple
Data_format       = 1D REAL
Dim_size          = 26214
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 0.83361792[s]
X_domain          = 13C
X_freq            = 125.76529768[MHz]
X_offset          = 100[ppm]
X_points          = 32768
X_prescans        = 4
X_resolution      = 1.19959034[Hz]
X_sweep           = 39.3081761[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 10
Scans             = 90
Total_scans       = 90

X_90_width        = 10.73[us]
X_acq_time        = 0.83361792[s]
X_angle           = 30[deg]
X_atn             = 9[dB]
X_pulse           = 3.57666667[us]
Irr_atn_dec       = 20[dB]
Irr_atn_noe       = 20[dB]
Irr_noise         = WALTZ
Decoupling        = TRUE
Initial_wait      = 1[s]
Noe               = TRUE
Noe_time          = 2[s]
Recvr_gain        = 50
Relaxation_delay  = 2[s]
Repetition_time   = 2.83361792[s]
Temp_get          = 22.2[dC]
```

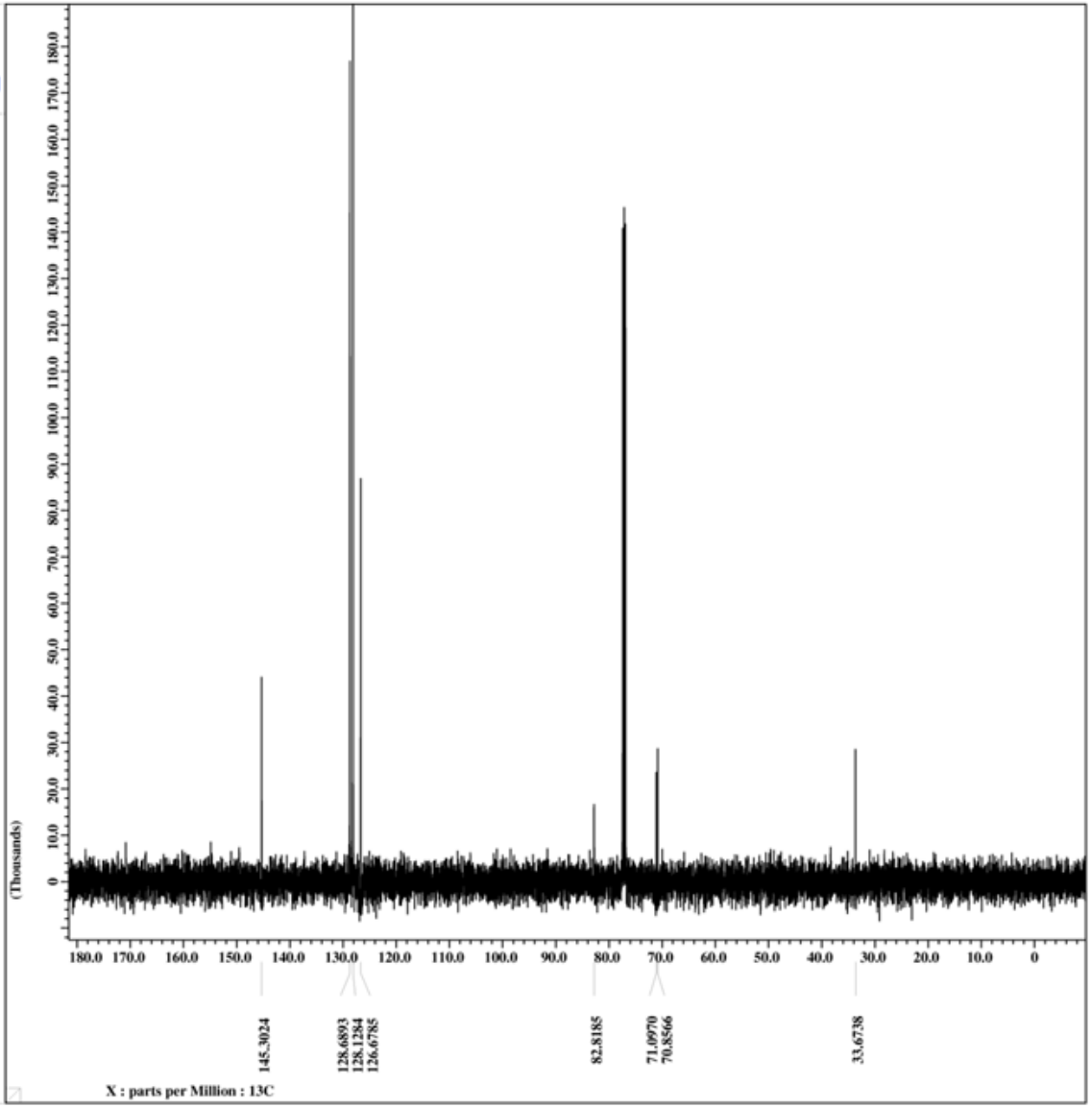
APPENDIX 34
^{1}H AND ^{13}C NMR SPECTRA OF
***N*-Tritylprop-2-yn-1-amine (142)**



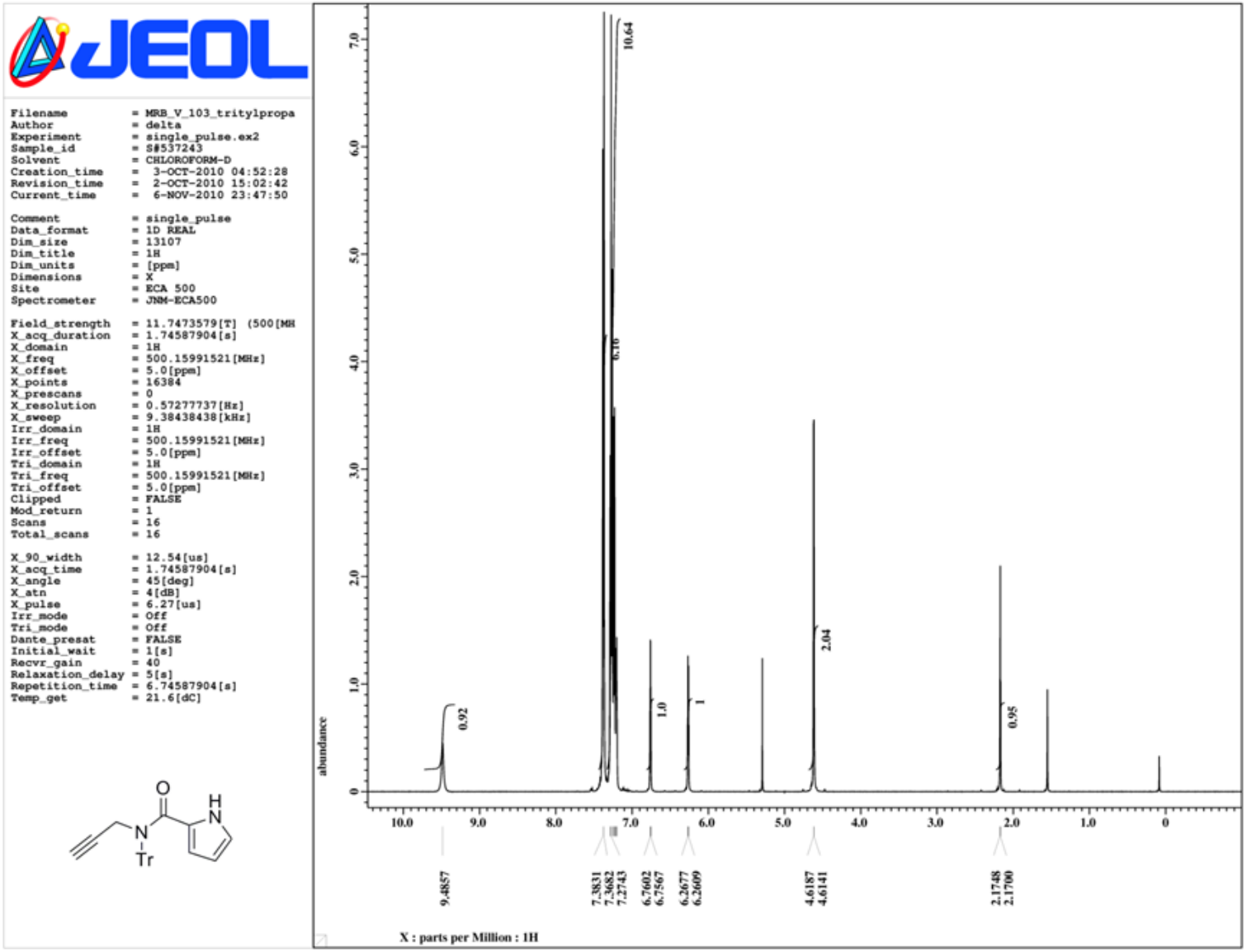
```
Filename          = MRB_IV_153_trityl_pro
Author            = delta
Experiment        = single_pulse.exp
Sample_id         = S#675250
Solvent           = CHLOROFORM-D
Creation_time     = 29-NOV-2009 10:10:15
Revision_time     = 28-NOV-2009 18:52:29
Current_time      =  6-NOV-2010 23:46:15

Comment           = Single Pulse Experime
Data_format       = 1D REAL
Dim_size          = 16384
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = Eclipse+ 500
Spectrometer      = DELTA_NMR

Field_strength    = 11.7465928[T] (500[MH
X_acq_duration    = 2.1839872[s]
X_domain          = 1H
X_freq            = 500.12734003[MHz]
X_offset          = 5[ppm]
X_points          = 16384
X_prescans        = 0
X_resolution      = 0.45787814[Hz]
X_sweep           = 7.50187547[kHz]
Clipped           = FALSE
Mod_return        = 1
Scans             = 8
Total_scans       = 8

X_90_width        = 18.5[us]
X_acq_time        = 2.1839872[s]
X_angle           = 45[deg]
X_pulse           = 9.25[us]
Initial_wait      = 1[s]
Phase_preset      = 3[us]
Recvr_gain        = 17
Relaxation_delay  = 4[s]
Temp_get          = 25.8[dC]
Unblank_time      = 2[us]
```

```
Filename          = MRB_IV_153_trityl_pro
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#676648
Solvent           = CHLOROFORM-D
Creation_time     = 29-NOV-2009 10:24:48
Revision_time     = 28-NOV-2009 19:03:18
Current_time      =  6-NOV-2010 23:47:02

Comment           = single pulse decouple
Data_format       = 1D REAL
Dim_size          = 65536
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = Eclipse+ 500
Spectrometer      = DELTA_NMR

Field_strength    = 11.7465928[T] (500[MH
X_acq_duration    = 2.0840448[s]
X_domain          = 13C
X_freq            = 125.75710665[MHz]
X_offset          = 100[ppm]
X_points          = 65536
X_prescans        = 4
X_resolution      = 0.47983613[Hz]
X_sweep           = 31.44654088[kHz]
Irr_domain        = 1H
Irr_freq          = 500.12734003[MHz]
Irr_offset        = 5[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 102
Total_scans       = 102

X_90_width        = 14.2[us]
X_acq_time        = 2.0840448[s]
X_angle           = 30[deg]
X_pulse           = 4.73333333[us]
Initial_wait      = 1[s]
Noe_time          = 1[s]
Phase_preset      = 3[us]
Recvr_gain        = 23
Relaxation_delay  = 3[s]
Temp_get          = 27.4[dC]
Unblank_time      = 2[us]
```

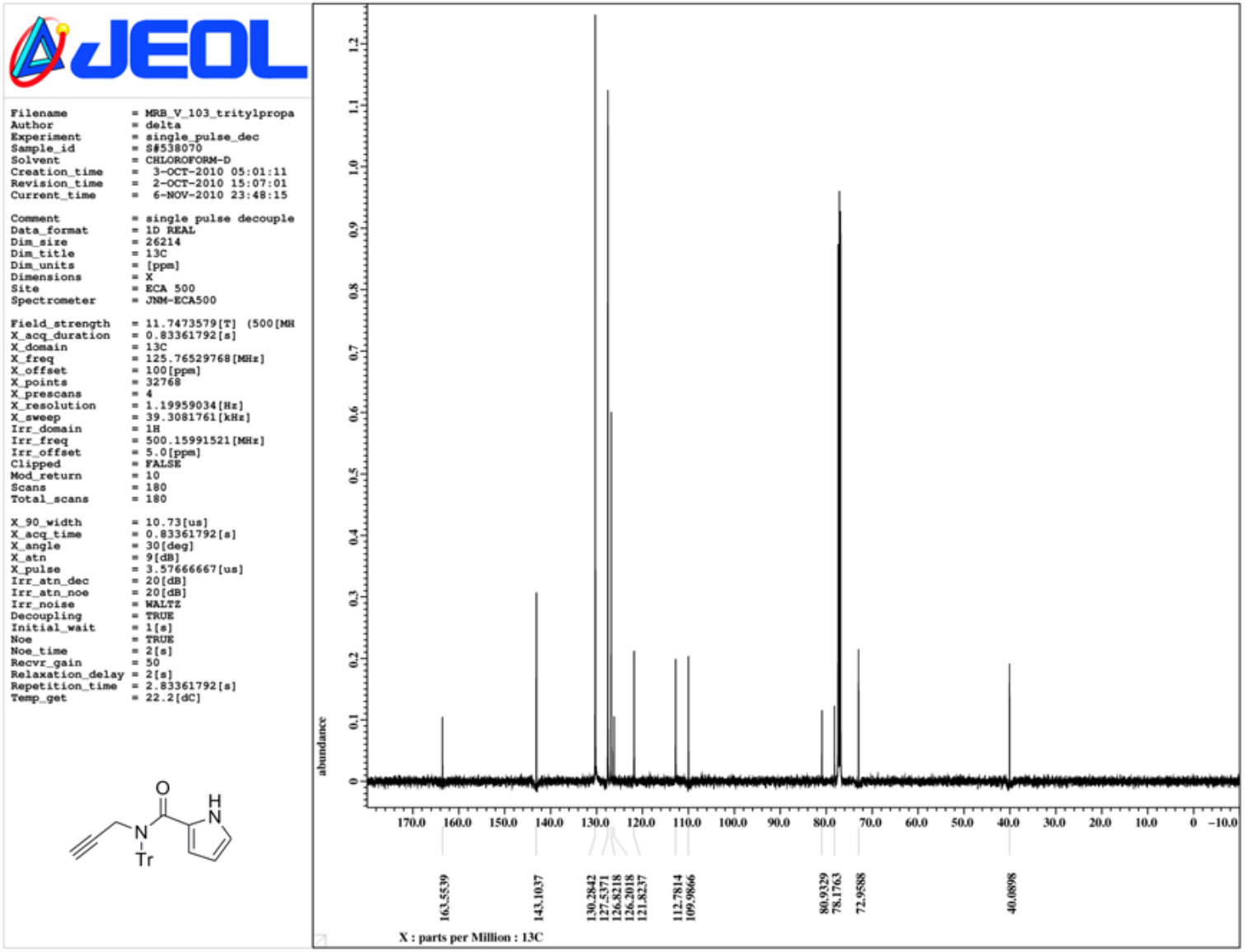




APPENDIX 35
^{1}H AND ^{13}C NMR SPECTRA OF
***N*-(Prop-2-ynyl)-*N*-trityl-1H-pyrrole-2-carboxamide (144)**

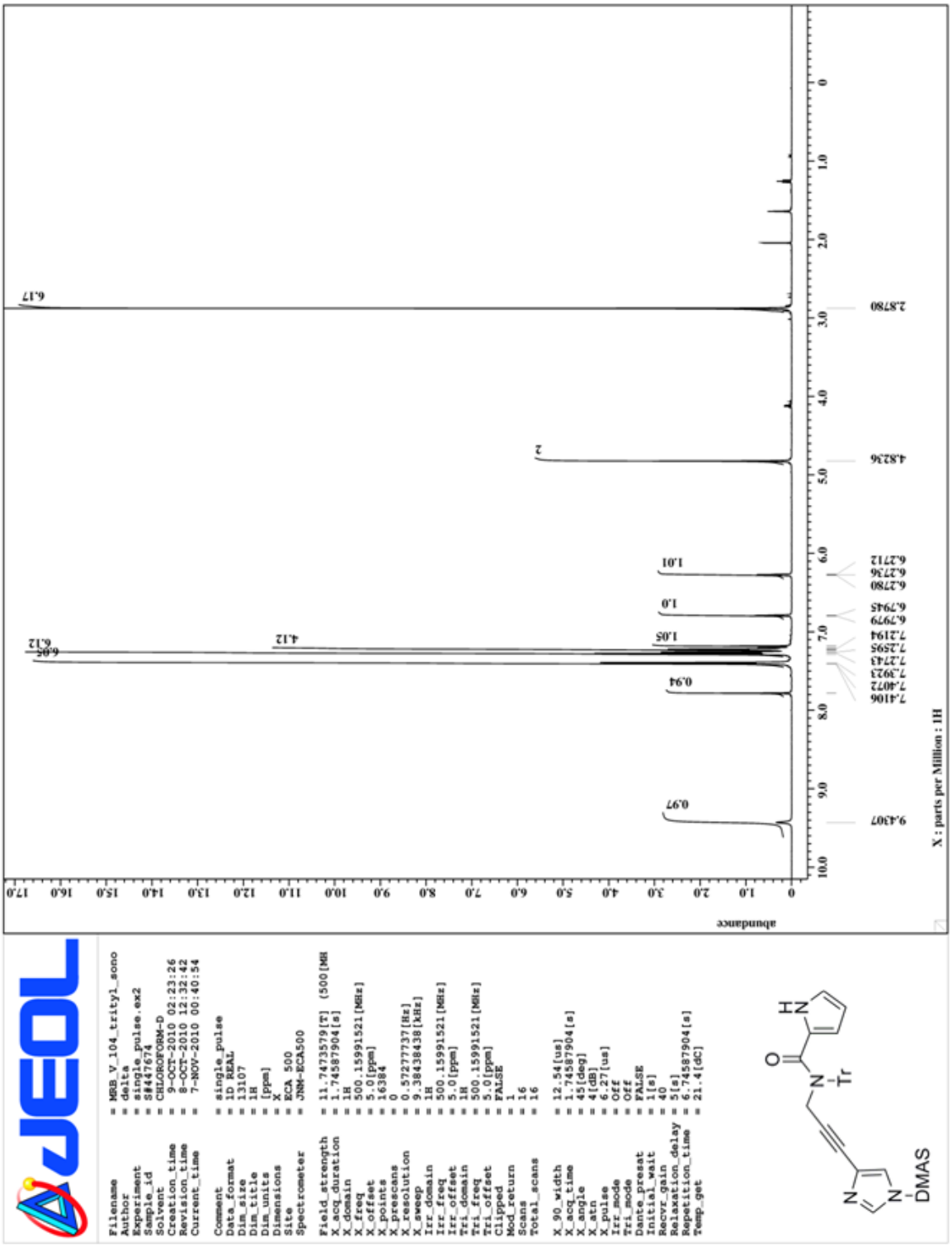


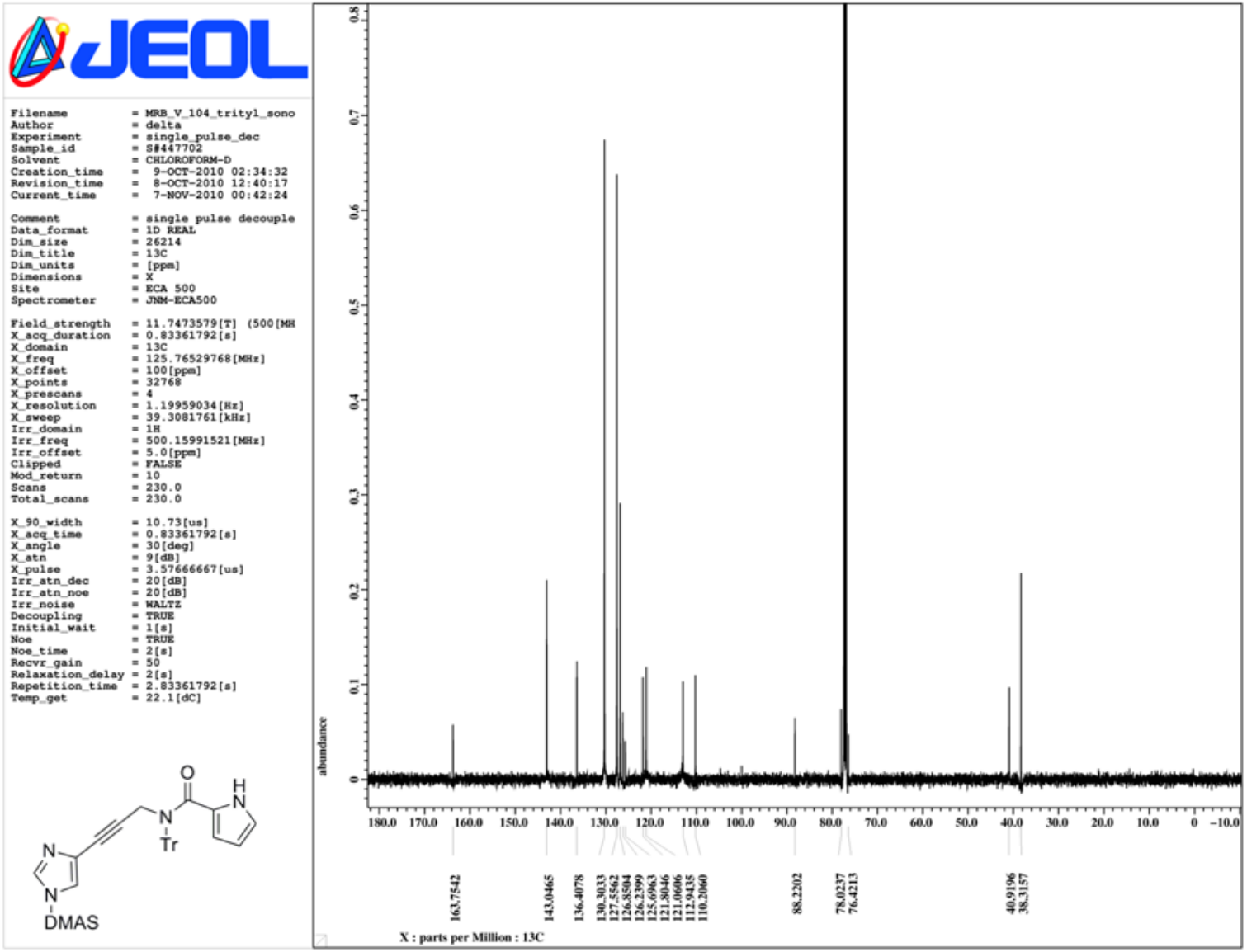
```
Filename          = MRB_V_103_tritylpropa
Author            = delta
Experiment        = single_pulse.ex2
Sample_id         = S#537243
Solvent           = CHLOROFORM-D
Creation_time     =  3-OCT-2010 04:52:28
Revision_time     =  2-OCT-2010 15:02:42
Current_time      =  6-NOV-2010 23:47:50

Comment           = single_pulse
Data_format       = 1D REAL
Dim_size          = 13107
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 1.74587904[s]
X_domain          = 1H
X_freq            = 500.15991521[MHz]
X_offset          = 5.0[ppm]
X_points          = 16384
X_prescans        = 0
X_resolution      = 0.57277737[Hz]
X_sweep           = 9.38438438[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Tri_domain        = 1H
Tri_freq          = 500.15991521[MHz]
Tri_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 16
Total_scans       = 16

X_90_width        = 12.54[us]
X_acq_time        = 1.74587904[s]
X_angle           = 45[deg]
X_atn             = 4[dB]
X_pulse           = 6.27[us]
Irr_mode          = Off
Tri_mode          = Off
Dante_presat      = FALSE
Initial_wait      = 1[s]
Recvr_gain        = 40
Relaxation_delay  = 5[s]
Repetition_time   = 6.74587904[s]
Temp_get          = 21.6[dC]
```



```
Filename          = MRB_V_103_tritylpropa
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#538070
Solvent           = CHLOROFORM-D
Creation_time     =  3-OCT-2010 05:01:11
Revision_time     =  2-OCT-2010 15:07:01
Current_time      =  6-NOV-2010 23:48:15

Comment           = single pulse decouple
Data_format       = 1D REAL
Dim_size          = 26214
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 0.83361792[s]
X_domain          = 13C
X_freq            = 125.76529768[MHz]
X_offset          = 100[ppm]
X_points          = 32768
X_prescans        = 4
X_resolution      = 1.19959034[Hz]
X_sweep           = 39.3081761[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 10
Scans             = 180
Total_scans       = 180

X_90_width        = 10.73[us]
X_acq_time        = 0.83361792[s]
X_angle           = 30[deg]
X_atn             = 9[dB]
X_pulse           = 3.57666667[us]
Irr_atn_dec       = 20[dB]
Irr_atn_noe       = 20[dB]
Irr_noise         = WALTZ
Decoupling        = TRUE
Initial_wait      = 1[s]
Noe               = TRUE
Noe_time          = 2[s]
Recvr_gain        = 50
Relaxation_delay  = 2[s]
Repetition_time   = 2.83361792[s]
Temp_get          = 22.2[dC]
```

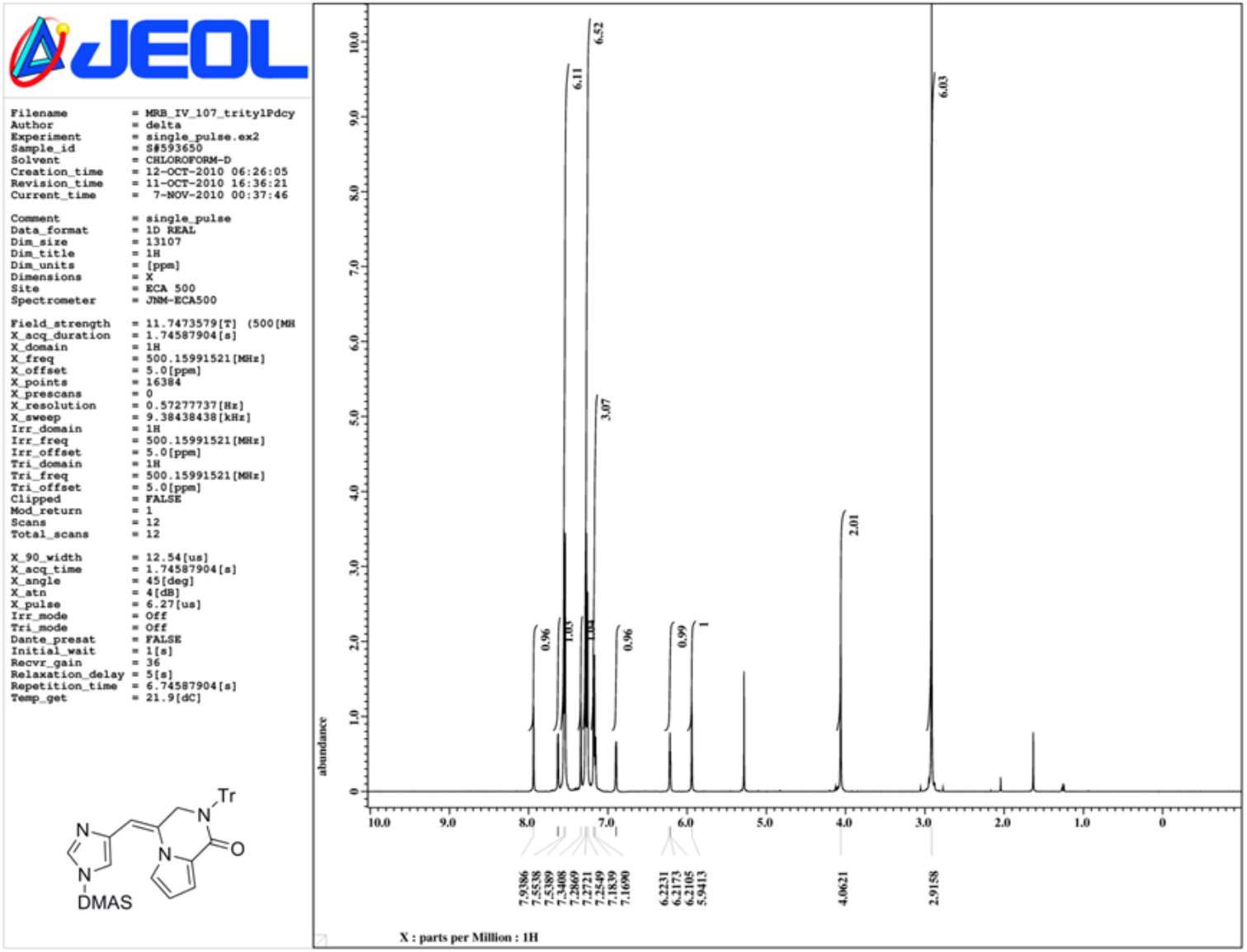
APPENDIX 36
^{1}H AND ^{13}C NMR SPECTRA OF
***N*-(3-(1-(*N*,*N*-Dimethylsulfamoyl)-1H-imidazol-4-yl)prop-2-ynyl)-*N*-trityl-1H-pyrrole-2-carboxamide (145)**


JEOL
Filename = MRB_V_104_trityl_sono
Author = delta
Experiment = single_pulse.ex2
Sample_id = S#447674
Solvent = CHLOROFORM-D
Creation_time = 9-OCT-2010 02:23:26
Revision_time = 8-OCT-2010 12:32:42
Current_time = 7-NOV-2010 00:40:54
Comment = single_pulse
Data_format = 1D REAL
Dim_size = 13107
Dim_title = 1H
Dim_units = [ppm]
Dimensions = X
Site = ECA 500
Spectrometer = JNM-ECA500
Field_strength = 11.7473579[T] (500[MH
X_acq_duration = 1.74587904[s]
X_domain = 1H
X_freq = 500.15991521[MHz]
X_offset = 5.0[ppm]
X_points = 16384
X_prescans = 0
X_resolution = 0.57277737[Hz]
X_sweep = 9.38438438[kHz]
Irr_domain = 1H
Irr_freq = 500.15991521[MHz]
Irr_offset = 5.0[ppm]
Tri_domain = 1H
Tri_freq = 500.15991521[MHz]
Tri_offset = 5.0[ppm]
Clipped = FALSE
Mod_return = 1
Scans = 16
Total_scans = 16
X_90_width = 12.54[us]
X_acq_time = 1.74587904[s]
X_angle = 45[deg]
X_atn = 4[dB]
X_pulse = 6.27[us]
Irr_mode = Off
Tri_mode = Off
Dante_presat = FALSE
Initial_wait = 1[s]
Recvr_gain = 40
Relaxation_delay = 5[s]
Repetition_time = 6.74587904[s]
Temp_get = 21.4[dC]
abundance
X : parts per Million : 1H
6.17
6.05
6.12
4.12
2
1.01
1.0
1.05
0.94
0.97
9.4307
4.8236
2.8780
7.4106
7.4072
7.3923
7.2743
7.2595
7.2194
6.7979
6.7945
6.2780
6.2736
6.2712
DMAS



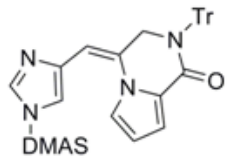
```
Filename          = MRB_V_104_trityl_sono
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#447702
Solvent           = CHLOROFORM-D
Creation_time     =  9-OCT-2010 02:34:32
Revision_time     =  8-OCT-2010 12:40:17
Current_time      =  7-NOV-2010 00:42:24

Comment           = single pulse decouple
Data_format       = 1D REAL
Dim_size          = 26214
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 0.83361792[s]
X_domain          = 13C
X_freq            = 125.76529768[MHz]
X_offset          = 100[ppm]
X_points          = 32768
X_prescans        = 4
X_resolution      = 1.19959034[Hz]
X_sweep           = 39.3081761[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 10
Scans             = 230.0
Total_scans       = 230.0

X_90_width        = 10.73[us]
X_acq_time        = 0.83361792[s]
X_angle           = 30[deg]
X_atn             = 9[dB]
X_pulse           = 3.57666667[us]
Irr_atn_dec       = 20[dB]
Irr_atn_noe       = 20[dB]
Irr_noise         = WALTZ
Decoupling        = TRUE
Initial_wait      = 1[s]
Noe               = TRUE
Noe_time          = 2[s]
Recvr_gain        = 50
Relaxation_delay  = 2[s]
Repetition_time   = 2.83361792[s]
Temp_get          = 22.1[dC]
```

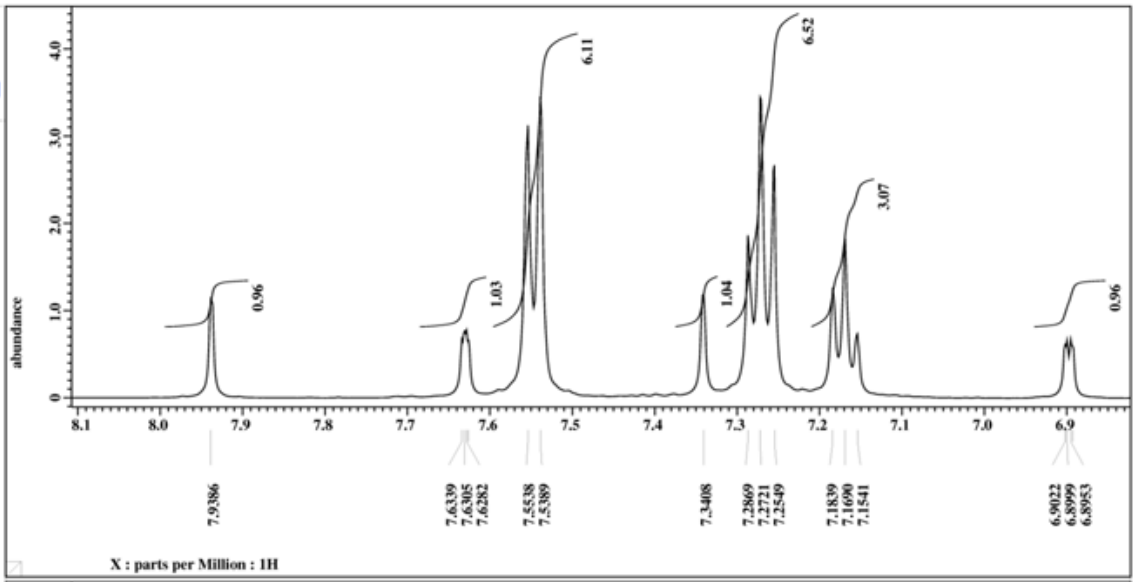
APPENDIX 37
^{1}H AND ^{13}C NMR SPECTRA OF
(*Z*)-*N*,*N*-Dimethyl-4-((1-oxo-2-trityl-2,3-dihydropyrrolo[1,2-a]pyrazin-4(1H)-ylidene)methyl)-1H-imidazole-1-sulfonamide (146)

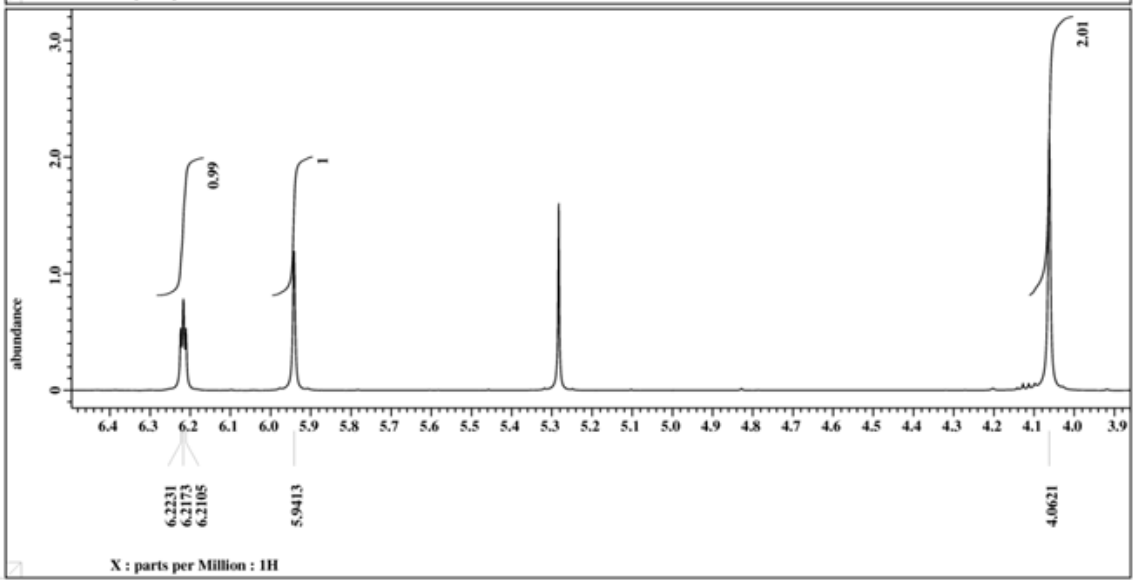


```
Filename          = MRB_IV_107_tritylPdcy
Author            = delta
Experiment        = single_pulse.ex2
Sample_id         = S#593650
Solvent           = CHLOROFORM-D
Creation_time     = 12-OCT-2010 06:26:05
Revision_time     = 11-OCT-2010 16:36:21
Current_time      =  7-NOV-2010 00:37:46

Comment           = single_pulse
Data_format       = 1D REAL
Dim_size          = 13107
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 1.74587904[s]
X_domain          = 1H
X_freq            = 500.15991521[MHz]
X_offset          = 5.0[ppm]
X_points          = 16384
X_prescans        = 0
X_resolution      = 0.57277737[Hz]
X_sweep           = 9.38438438[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Tri_domain        = 1H
Tri_freq          = 500.15991521[MHz]
Tri_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 12
Total_scans       = 12

X_90_width        = 12.54[us]
X_acq_time        = 1.74587904[s]
X_angle           = 45[deg]
X_atn             = 4[dB]
X_pulse           = 6.27[us]
Irr_mode          = Off
Tri_mode          = Off
Dante_presat      = FALSE
Initial_wait      = 1[s]
Recvr_gain        = 36
Relaxation_delay  = 5[s]
Repetition_time   = 6.74587904[s]
Temp_get          = 21.9[dC]
```

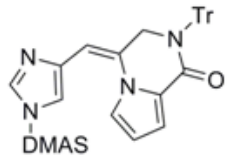
```
Filename          = MRB_IV_107_tritylPdcy
Author            = delta
Experiment        = single_pulse.ex2
Sample_id         = S#593650
Solvent           = CHLOROFORM-D
Creation_time     = 12-OCT-2010 06:26:05
Revision_time     = 11-OCT-2010 16:36:21
Current_time      =  6-NOV-2010 23:52:41

Comment           = single_pulse
Data_format       = 1D REAL
Dim_size          = 13107
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 1.74587904[s]
X_domain          = 1H
X_freq            = 500.15991521[MHz]
X_offset          = 5.0[ppm]
X_points          = 16384
X_prescans        = 0
X_resolution      = 0.57277737[Hz]
X_sweep           = 9.38438438[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Tri_domain        = 1H
Tri_freq          = 500.15991521[MHz]
Tri_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 12
Total_scans       = 12

X_90_width        = 12.54[us]
X_acq_time        = 1.74587904[s]
X_angle           = 45[deg]
X_atn             = 4[dB]
X_pulse           = 6.27[us]
Irr_mode          = Off
Tri_mode          = Off
Dante_presat      = FALSE
Initial_wait      = 1[s]
Recvr_gain        = 36
Relaxation_delay  = 5[s]
Repetition_time   = 6.74587904[s]
Temp_get          = 21.9[dC]
```

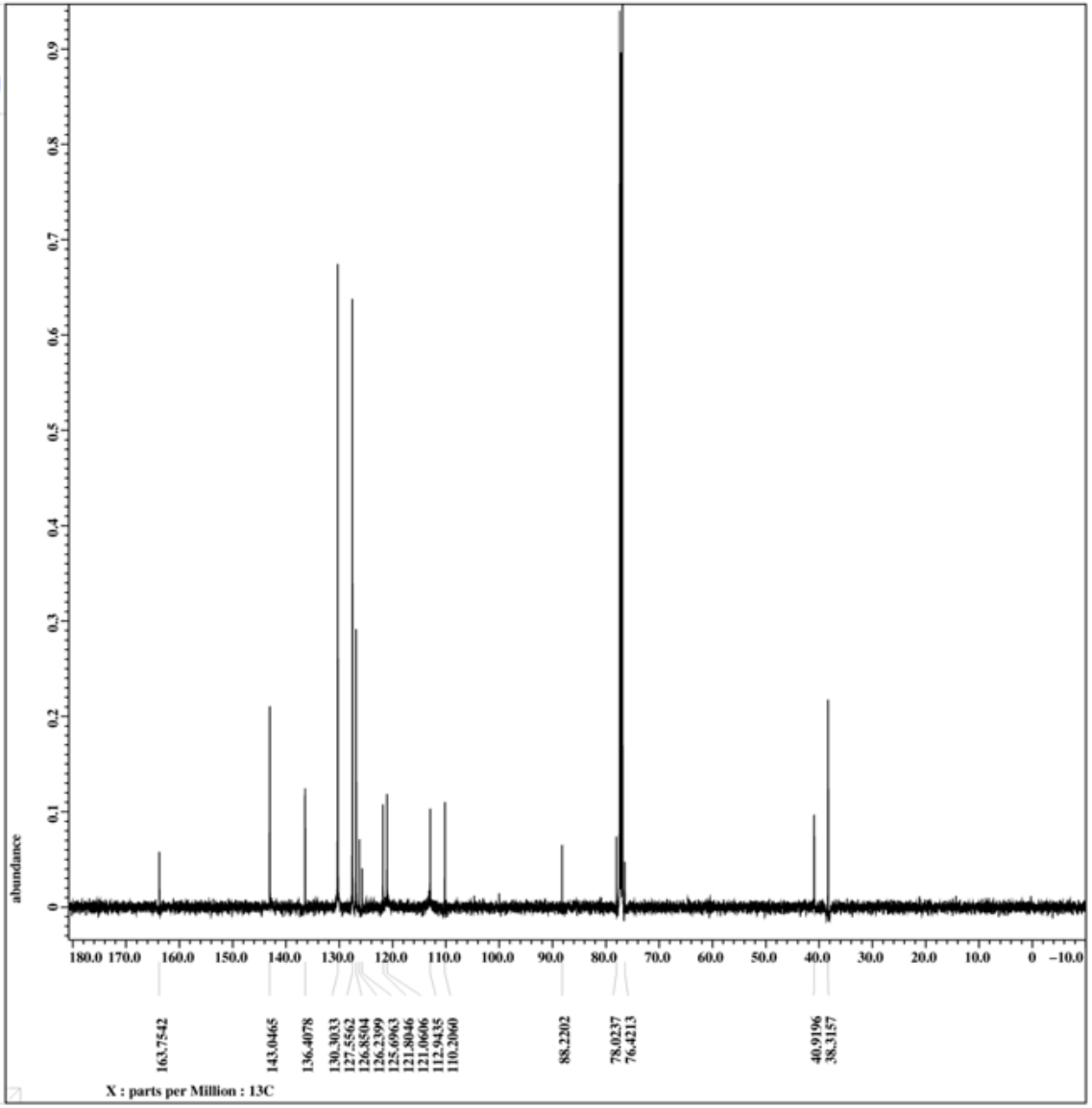






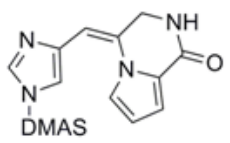
Filename	= MRB_V_104_trityl_sono
Author	= delta
Experiment	= single_pulse_dec
Sample_id	= S#447702
Solvent	= CHLOROFORM-D
Creation_time	= 9-OCT-2010 02:34:32
Revision_time	= 8-OCT-2010 12:40:17
Current_time	= 7-NOV-2010 00:41:20
Comment	= single pulse decouple
Data_format	= 1D REAL
Dim_size	= 26214
Dim_title	= 13C
Dim_units	= [ppm]
Dimensions	= X
Site	= ECA 500
Spectrometer	= JNM-ECA500
Field_strength	= 11.7473579[T] (500[MH
X_acq_duration	= 0.83361792[s]
X_domain	= 13C
X_freq	= 125.76529768[MHz]
X_offset	= 100[ppm]
X_points	= 32768
X_prescans	= 4
X_resolution	= 1.19959034[Hz]
X_sweep	= 39.3081761[kHz]
Irr_domain	= 1H
Irr_freq	= 500.15991521[MHz]
Irr_offset	= 5.0[ppm]
Clipped	= FALSE
Mod_return	= 10
Scans	= 230.0
Total_scans	= 230.0
X_90_width	= 10.73[us]
X_acq_time	= 0.83361792[s]
X_angle	= 30[deg]
X_atn	= 9[dB]
X_pulse	= 3.57666667[us]
Irr_atn_dec	= 20[dB]
Irr_atn_noe	= 20[dB]
Irr_noise	= WALTZ
Decoupling	= TRUE
Initial_wait	= 1[s]
Noe	= TRUE
Noe_time	= 2[s]
Recvr_gain	= 50
Relaxation_delay	= 2[s]
Repetition_time	= 2.83361792[s]
Temp_get	= 22.1[dC]

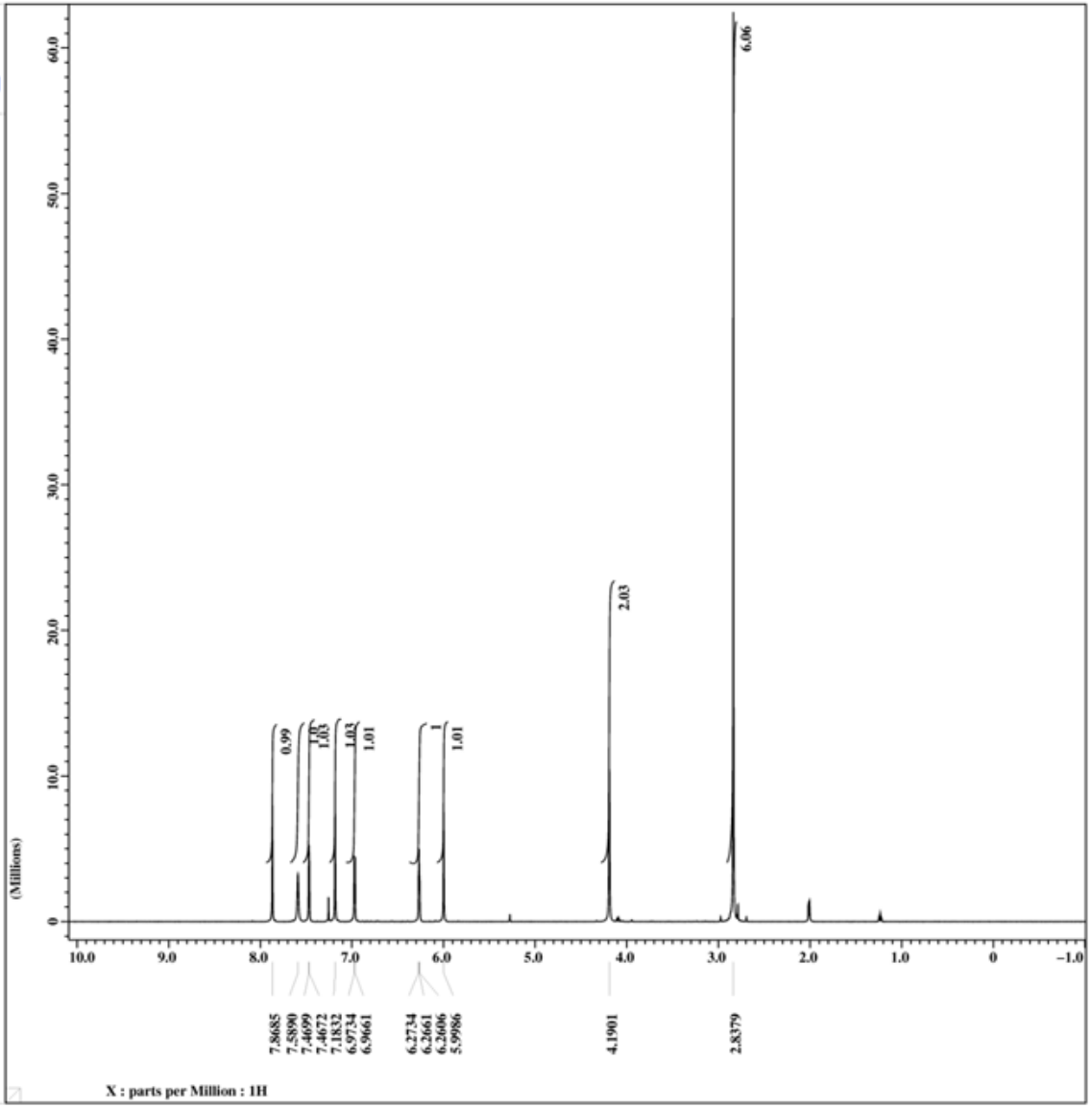


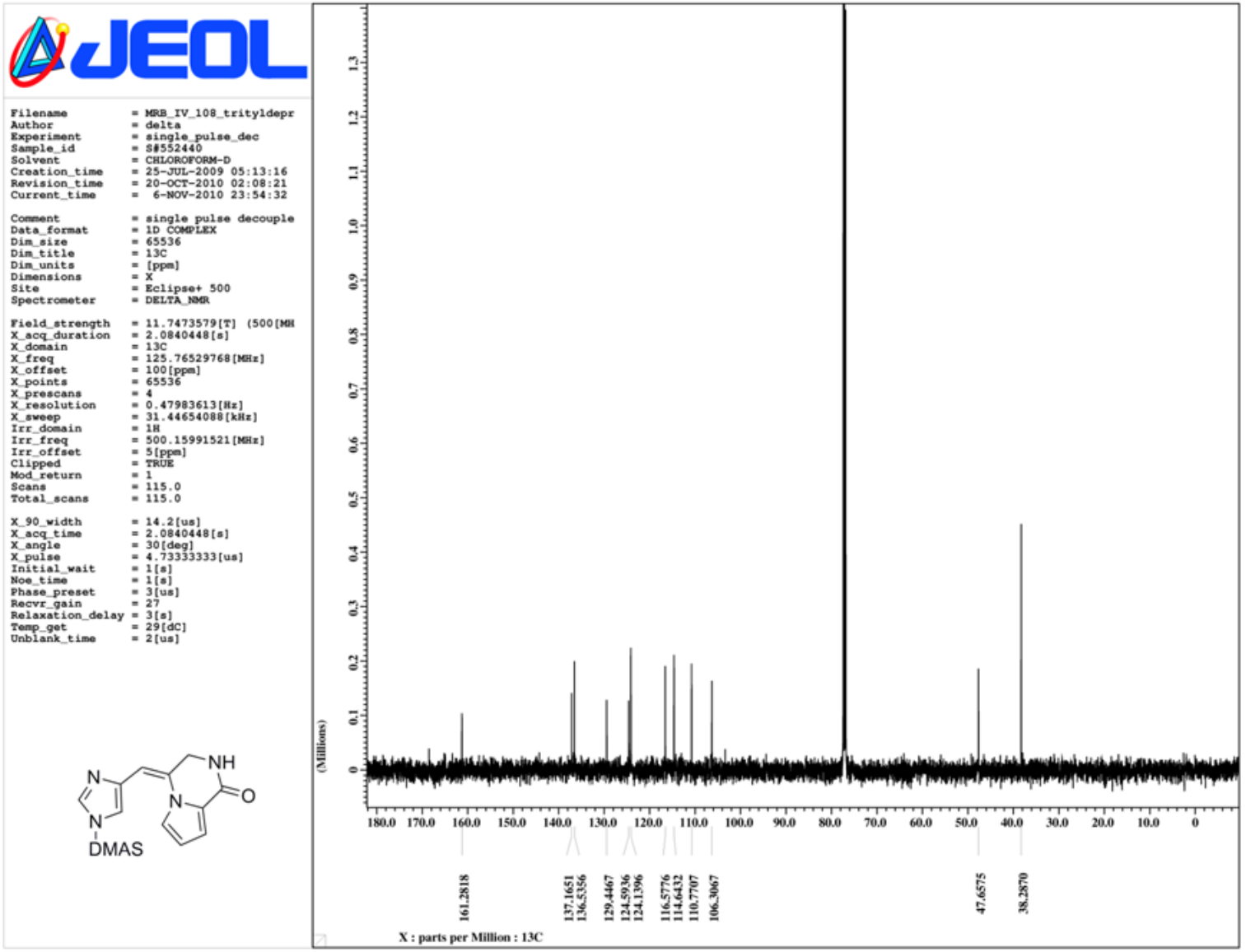


APPENDIX 38
^{1}H AND ^{13}C NMR SPECTRA OF
(*Z*)-*N*,*N*-Dimethyl-4-((1-oxo-2,3-dihydropyrrolo[1,2-a]pyrazin-4(1H)-ylidene)methyl)-1H-imidazole-1-sulfonamide (125)

```
Filename          = MRB_IV_108_trityldepr
Author            = delta
Experiment        = single_pulse.exp
Sample_id         = S#552389
Solvent           = CHLOROFORM-D
Creation_time     = 25-JUL-2009 04:59:45
Revision_time     = 24-JUL-2009 15:26:16
Current_time      =  6-NOV-2010 23:54:01

Comment           = Single Pulse Experime
Data_format       = 1D REAL
Dim_size          = 16384
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = Eclipse+ 500
Spectrometer      = DELTA_NMR

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 2.1823488[s]
X_domain          = 1H
X_freq            = 500.15991521[MHz]
X_offset          = 5[ppm]
X_points          = 16384
X_prescans        = 0
X_resolution      = 0.45822189[Hz]
X_sweep           = 7.50750751[kHz]
Clipped           = FALSE
Mod_return        = 1
Scans             = 8
Total_scans       = 8

X_90_width        = 18.5[us]
X_acq_time        = 2.1823488[s]
X_angle           = 45[deg]
X_pulse           = 9.25[us]
Initial_wait      = 1[s]
Phase_preset      = 3[us]
Recvr_gain        = 18
Relaxation_delay  = 4[s]
Temp_get          = 27.4[dC]
Unblank_time      = 2[us]
```

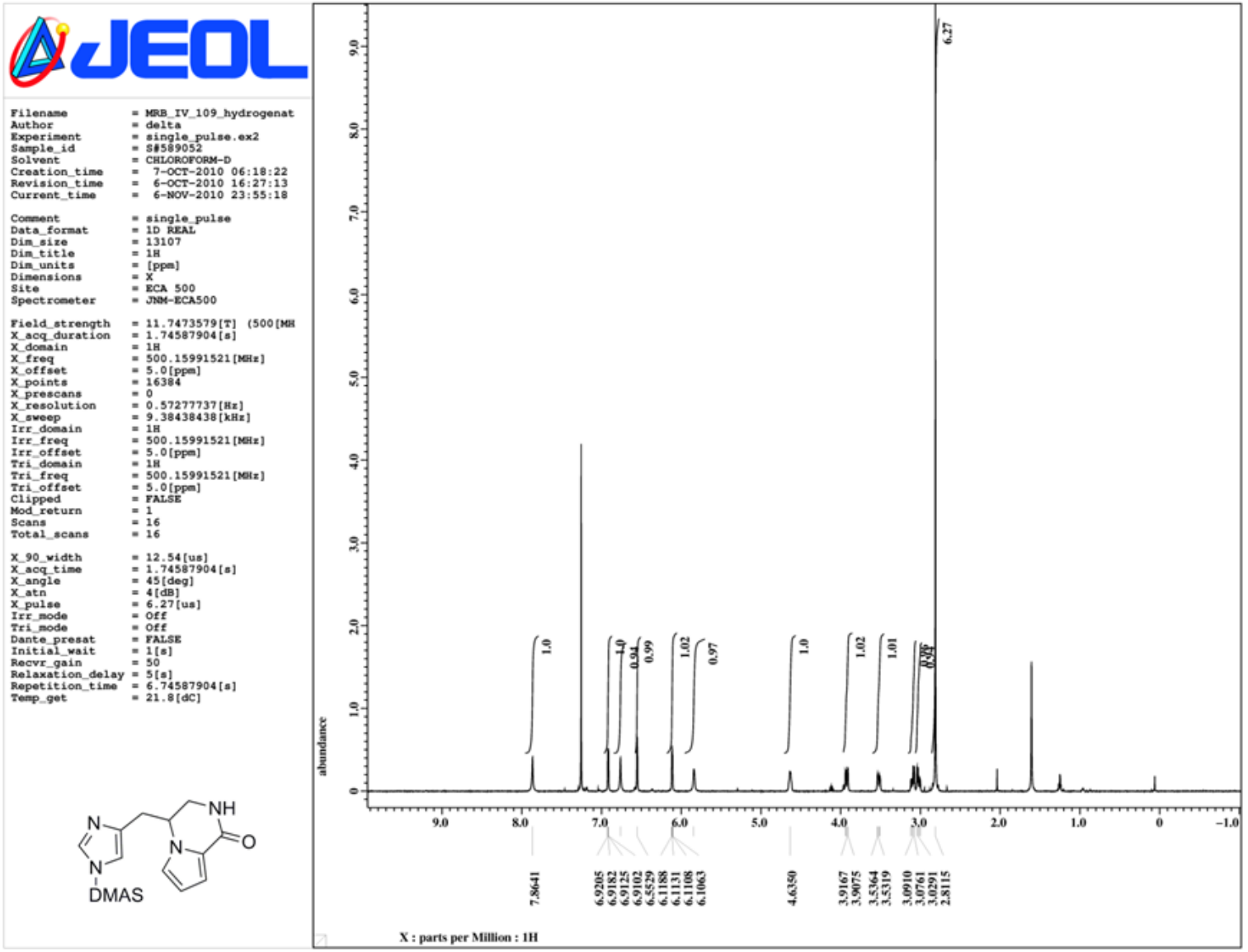






```
Filename          = MRB_IV_108_trityldepr
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#552440
Solvent           = CHLOROFORM-D
Creation_time     = 25-JUL-2009 05:13:16
Revision_time     = 20-OCT-2010 02:08:21
Current_time      =  6-NOV-2010 23:54:32

Comment           = single pulse decouple
Data_format       = 1D COMPLEX
Dim_size          = 65536
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = Eclipse+ 500
Spectrometer      = DELTA_NMR

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 2.0840448[s]
X_domain          = 13C
X_freq            = 125.76529768[MHz]
X_offset          = 100[ppm]
X_points          = 65536
X_prescans        = 4
X_resolution      = 0.47983613[Hz]
X_sweep           = 31.44654088[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5[ppm]
Clipped           = TRUE
Mod_return        = 1
Scans             = 115.0
Total_scans       = 115.0

X_90_width        = 14.2[us]
X_acq_time        = 2.0840448[s]
X_angle           = 30[deg]
X_pulse           = 4.73333333[us]
Initial_wait      = 1[s]
Noe_time          = 1[s]
Phase_preset      = 3[us]
Recvr_gain        = 27
Relaxation_delay  = 3[s]
Temp_get          = 29[dC]
Unblank_time      = 2[us]
```

APPENDIX 39
^{1}H AND ^{13}C NMR SPECTRA OF
***N*,*N*-Dimethyl-4-((1-oxo-1,2,3,4-tetrahydropyrrolo[1,2-a]pyrazin-4-yl)methyl)-1H-imidazole-1-sulfonamide (147)**

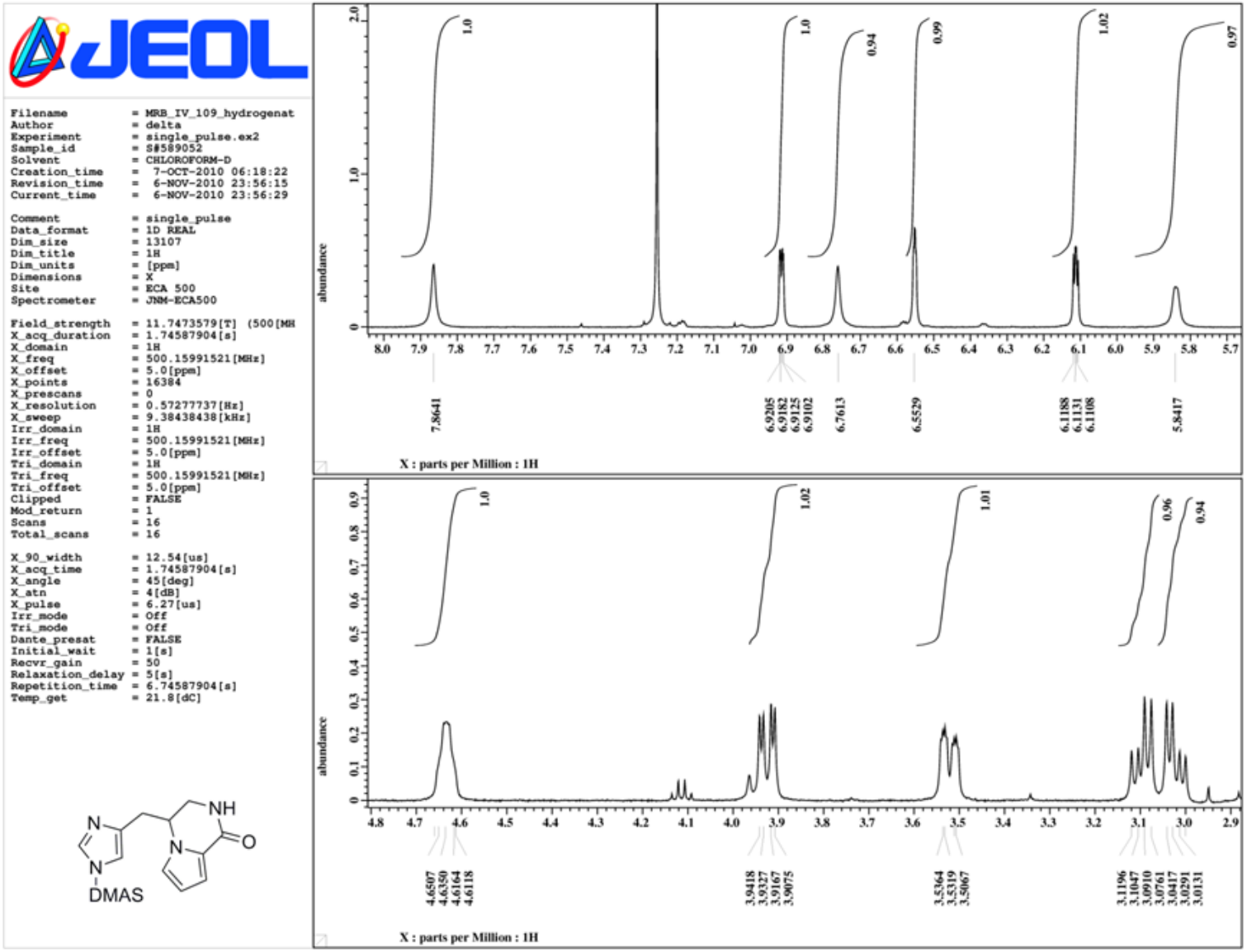


Filename = MRB_IV_109_hydrogenat
Author = delta
Experiment = single_pulse.ex2
Sample_id = S#589052
Solvent = CHLOROFORM-D
Creation_time = 7-OCT-2010 06:18:22
Revision_time = 6-OCT-2010 16:27:13
Current_time = 6-NOV-2010 23:55:18

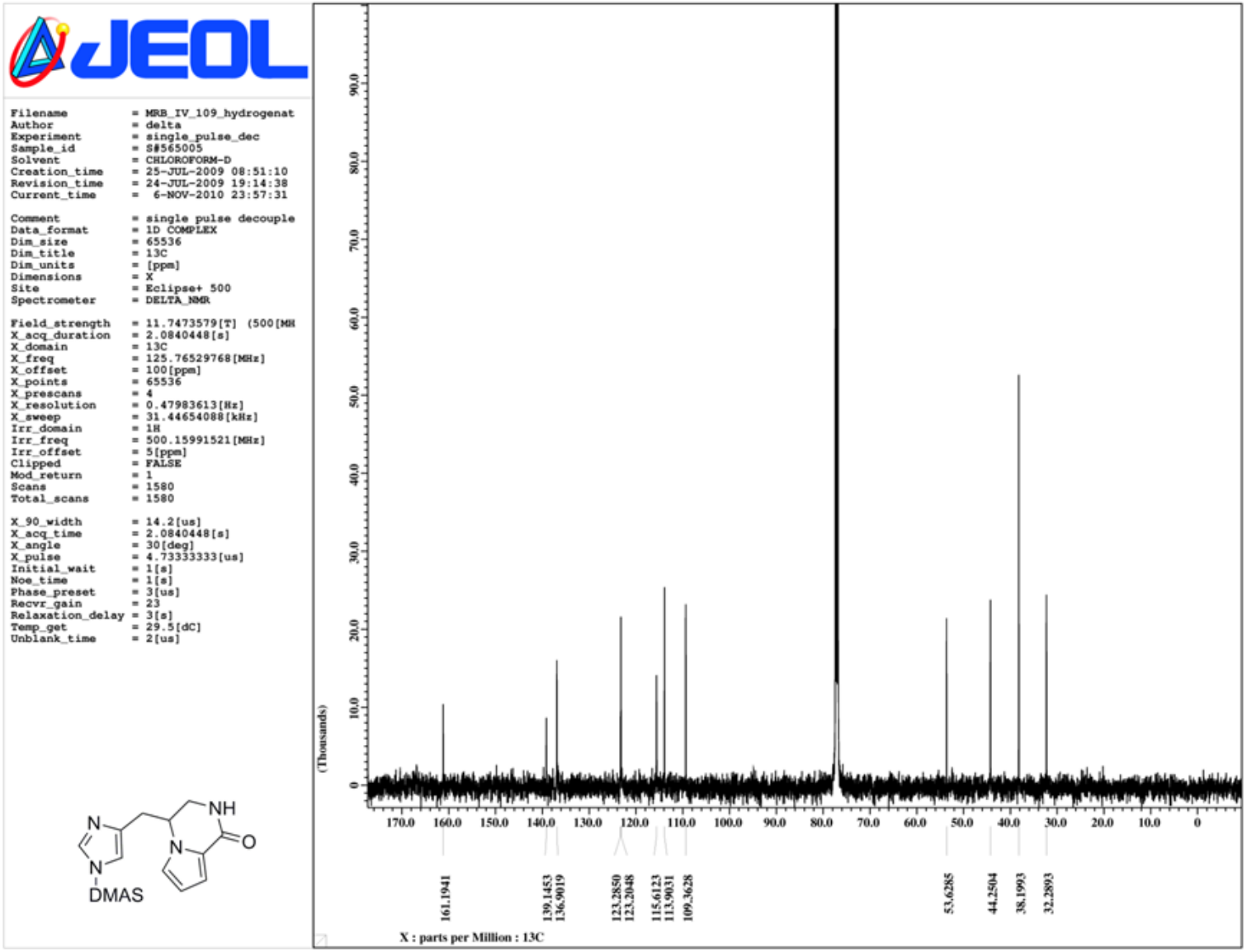
Comment = single_pulse
Data_format = 1D REAL
Dim_size = 13107
Dim_title = 1H
Dim_units = [ppm]
Dimensions = X
Site = ECA 500
Spectrometer = JNM-ECA500

Field_strength = 11.7473579[T] (500[MH
X_acq_duration = 1.74587904[s]
X_domain = 1H
X_freq = 500.15991521[MHz]
X_offset = 5.0[ppm]
X_points = 16384
X_prescans = 0
X_resolution = 0.57277737[Hz]
X_sweep = 9.38438438[kHz]
Irr_domain = 1H
Irr_freq = 500.15991521[MHz]
Irr_offset = 5.0[ppm]
Tri_domain = 1H
Tri_freq = 500.15991521[MHz]
Tri_offset = 5.0[ppm]
Clipped = FALSE
Mod_return = 1
Scans = 16
Total_scans = 16

X_90_width = 12.54[us]
X_acq_time = 1.74587904[s]
X_angle = 45[deg]
X_atn = 4[dB]
X_pulse = 6.27[us]
Irr_mode = Off
Tri_mode = Off
Dante_presat = FALSE
Initial_wait = 1[s]
Recvr_gain = 50
Relaxation_delay = 5[s]
Repetition_time = 6.74587904[s]
Temp_get = 21.8[dC]

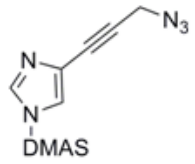


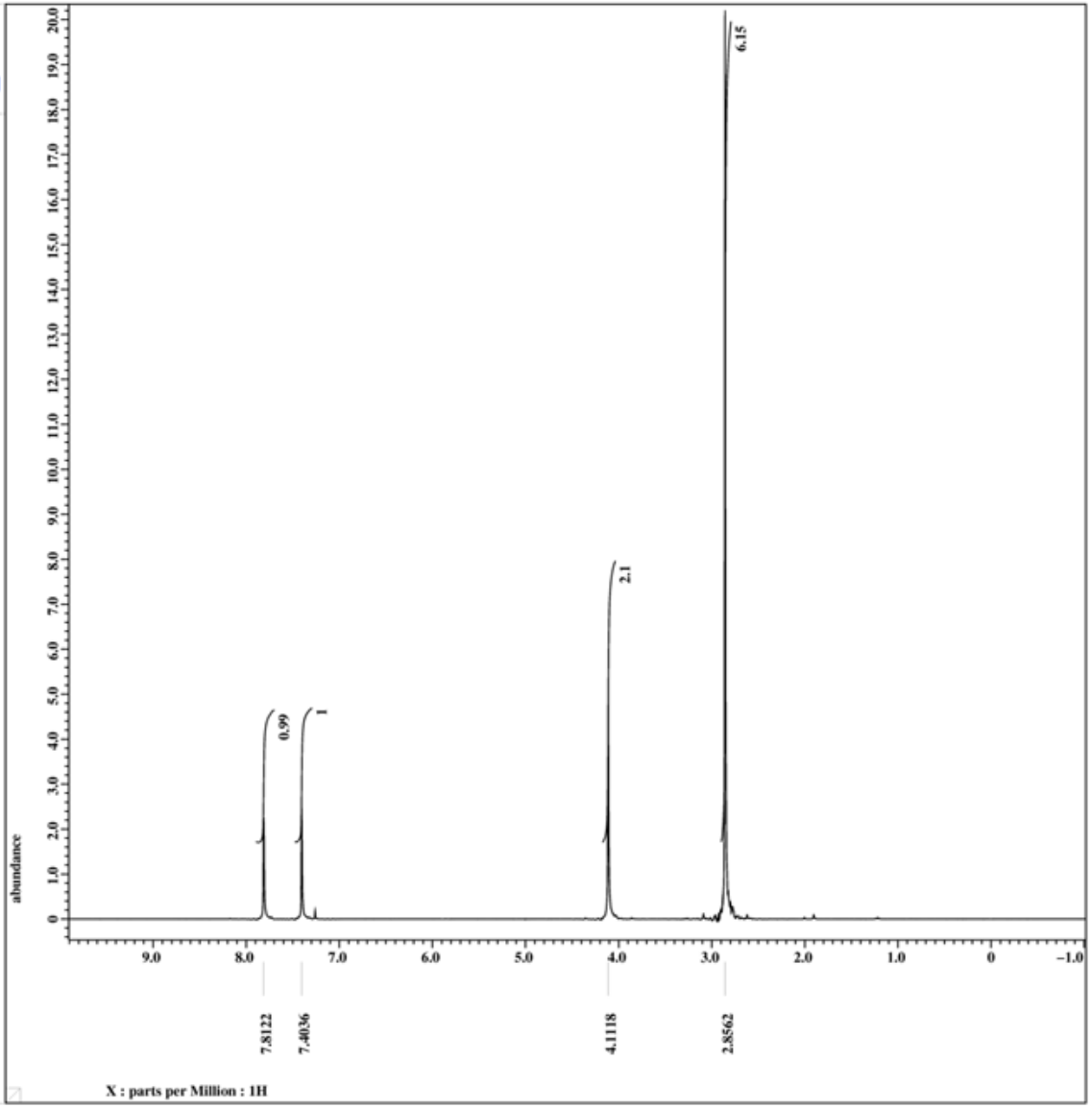
```
Filename          = MRB_IV_109_hydrogenat
Author            = delta
Experiment        = single_pulse.ex2
Sample_id         = S#589052
Solvent           = CHLOROFORM-D
Creation_time     =  7-OCT-2010 06:18:22
Revision_time     =  6-NOV-2010 23:56:15
Current_time      =  6-NOV-2010 23:56:29

Comment           = single_pulse
Data_format       = 1D REAL
Dim_size          = 13107
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T]  (500[MH
X_acq_duration    = 1.74587904[s]
X_domain          = 1H
X_freq            = 500.15991521[MHz]
X_offset          = 5.0[ppm]
X_points          = 16384
X_prescans        = 0
X_resolution      = 0.57277737[Hz]
X_sweep           = 9.38438438[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Tri_domain        = 1H
Tri_freq          = 500.15991521[MHz]
Tri_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 16
Total_scans       = 16

X_90_width        = 12.54[us]
X_acq_time        = 1.74587904[s]
X_angle           = 45[deg]
X_atn             = 4[dB]
X_pulse           = 6.27[us]
Irr_mode          = Off
Tri_mode          = Off
Dante_presat      = FALSE
Initial_wait      = 1[s]
Recvr_gain        = 50
Relaxation_delay  = 5[s]
Repetition_time   = 6.74587904[s]
Temp_get          = 21.8[dC]
```


Filename = MRB_IV_109_hydrogenat
Author = delta
Experiment = single_pulse_dec
Sample_id = S#565005
Solvent = CHLOROFORM-D
Creation_time = 25-JUL-2009 08:51:10
Revision_time = 24-JUL-2009 19:14:38
Current_time = 6-NOV-2010 23:57:31
Comment = single pulse decouple
Data_format = 1D COMPLEX
Dim_size = 65536
Dim_title = 13C
Dim_units = [ppm]
Dimensions = X
Site = Eclipse+ 500
Spectrometer = DELTA_NMR
Field_strength = 11.7473579[T] (500[MH
X_acq_duration = 2.0840448[s]
X_domain = 13C
X_freq = 125.76529768[MHz]
X_offset = 100[ppm]
X_points = 65536
X_prescans = 4
X_resolution = 0.47983613[Hz]
X_sweep = 31.44654088[kHz]
Irr_domain = 1H
Irr_freq = 500.15991521[MHz]
Irr_offset = 5[ppm]
Clipped = FALSE
Mod_return = 1
Scans = 1580
Total_scans = 1580
X_90_width = 14.2[us]
X_acq_time = 2.0840448[s]
X_angle = 30[deg]
X_pulse = 4.73333333[us]
Initial_wait = 1[s]
Noe_time = 1[s]
Phase_preset = 3[us]
Recvr_gain = 23
Relaxation_delay = 3[s]
Temp_get = 29.5[dC]
Unblank_time = 2[us]
N
NH
N
O
N
DMAS
(Thousands)
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
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
161.1941
139.1453
136.9019
123.2850
123.2048
115.6123
113.9031
109.3628
53.6285
44.2504
38.1993
32.2893
X : parts per Million : 13C

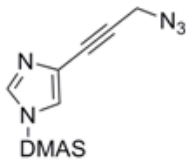
APPENDIX 40
^{1}H AND ^{13}C NMR SPECTRA OF
4-(3-Azidoprop-1-ynyl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide (151)

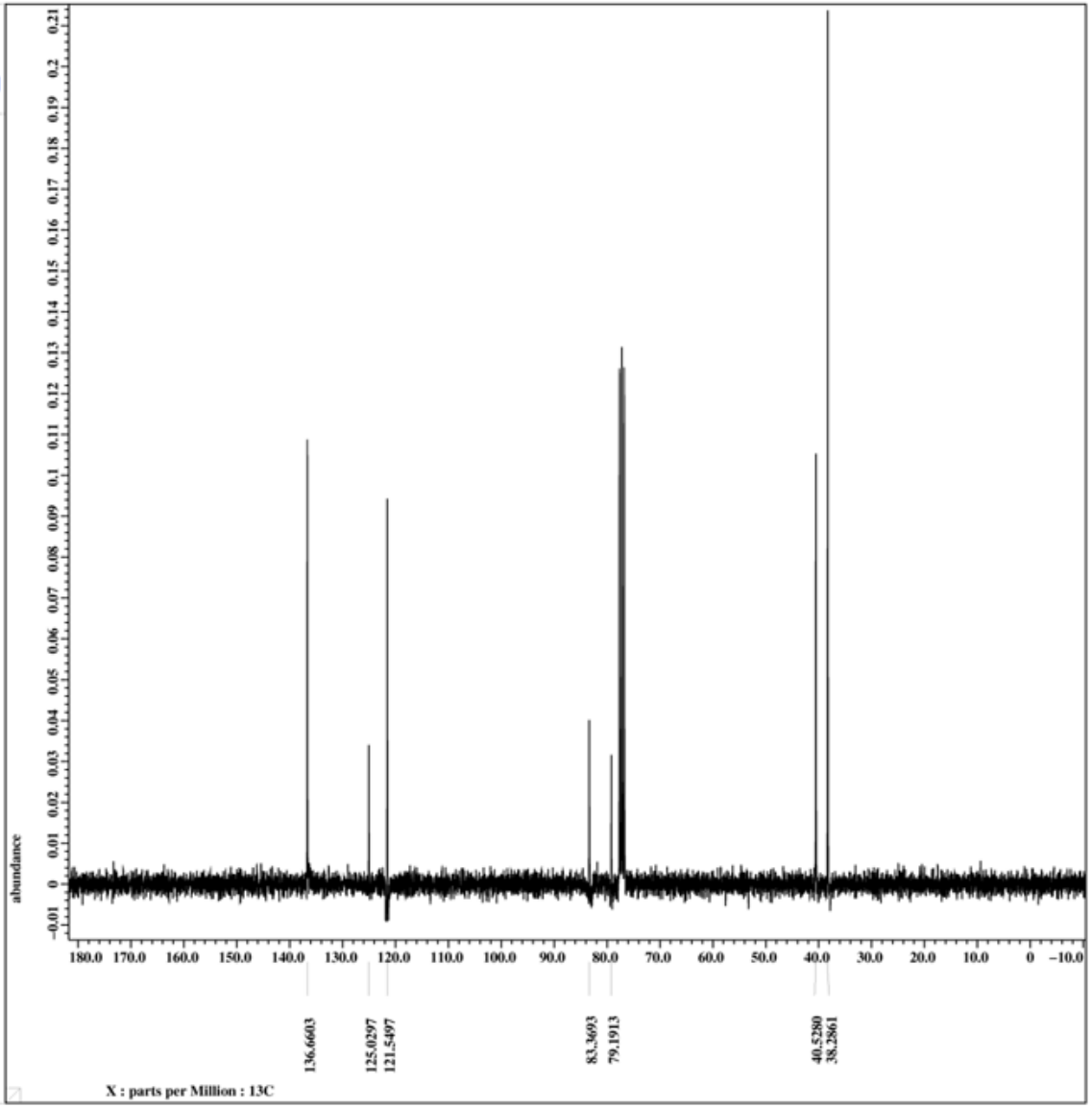
Filename	= MRB_IV_3_dmas_propazi
Author	= delta
Experiment	= single_pulse.ex2
Sample_id	= S#598346
Solvent	= CHLOROFORM-D
Creation_time	= 27-MAR-2009 15:57:49
Revision_time	= 27-MAR-2009 16:42:05
Current_time	= 6-NOV-2010 23:58:13
Comment	= single_pulse
Data_format	= 1D REAL
Dim_size	= 13107
Dim_title	= 1H
Dim_units	= [ppm]
Dimensions	= X
Site	= ECX 300
Spectrometer	= DELTA2_NMR
Field_strength	= 7.0586013[T] (300[MHz
X_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]
Irr_domain	= 1H
Irr_freq	= 300.52965592[MHz]
Irr_offset	= 5[ppm]
Tri_domain	= 1H
Tri_freq	= 300.52965592[MHz]
Tri_offset	= 5[ppm]
Clipped	= FALSE
Mod_return	= 1
Scans	= 6
Total_scans	= 6
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]
Irr_mode	= Off
Tri_mode	= Off
Dante_presat	= FALSE
Initial_wait	= 1[s]
Recvr_gain	= 38
Relaxation_delay	= 5[s]
Repetition_time	= 7.90717696[s]
Temp_get	= 22.9[dC]





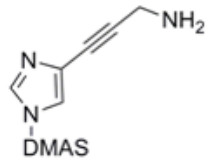
```
Filename          = MRB_IV_3_dmas_propazi
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#598918
Solvent           = CHLOROFORM-D
Creation_time     = 27-MAR-2009 16:03:41
Revision_time     = 27-MAR-2009 16:45:05
Current_time      =  6-NOV-2010 23:58:38

Comment           = single pulse decouple
Data_format       = 1D REAL
Dim_size          = 52428
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = ECX 300
Spectrometer      = DELTA2_NMR

Field_strength    = 7.0586013[T] (300[MHz
X_acq_duration    = 2.76824064[s]
X_domain          = 13C
X_freq            = 75.56823426[MHz]
X_offset          = 100[ppm]
X_points          = 65536
X_prescans        = 4
X_resolution      = 0.36124027[Hz]
X_sweep           = 23.67424242[kHz]
Irr_domain        = 1H
Irr_freq          = 300.52965592[MHz]
Irr_offset        = 5[ppm]
Clipped           = FALSE
Mod_return        = 10
Scans             = 68
Total_scans       = 68

X_90_width        = 9.75[us]
X_acq_time        = 2.76824064[s]
X_angle           = 30[deg]
X_atn             = 8[dB]
X_pulse           = 3.25[us]
Irr_atn_dec       = 25[dB]
Irr_atn_noe       = 25[dB]
Irr_noise         = WALTZ
Decoupling        = TRUE
Initial_wait      = 1[s]
Noe               = TRUE
Noe_time          = 2[s]
Recvr_gain        = 50
Relaxation_delay  = 2[s]
Repetition_time   = 4.76824064[s]
Temp_get          = 22.8[dC]
```

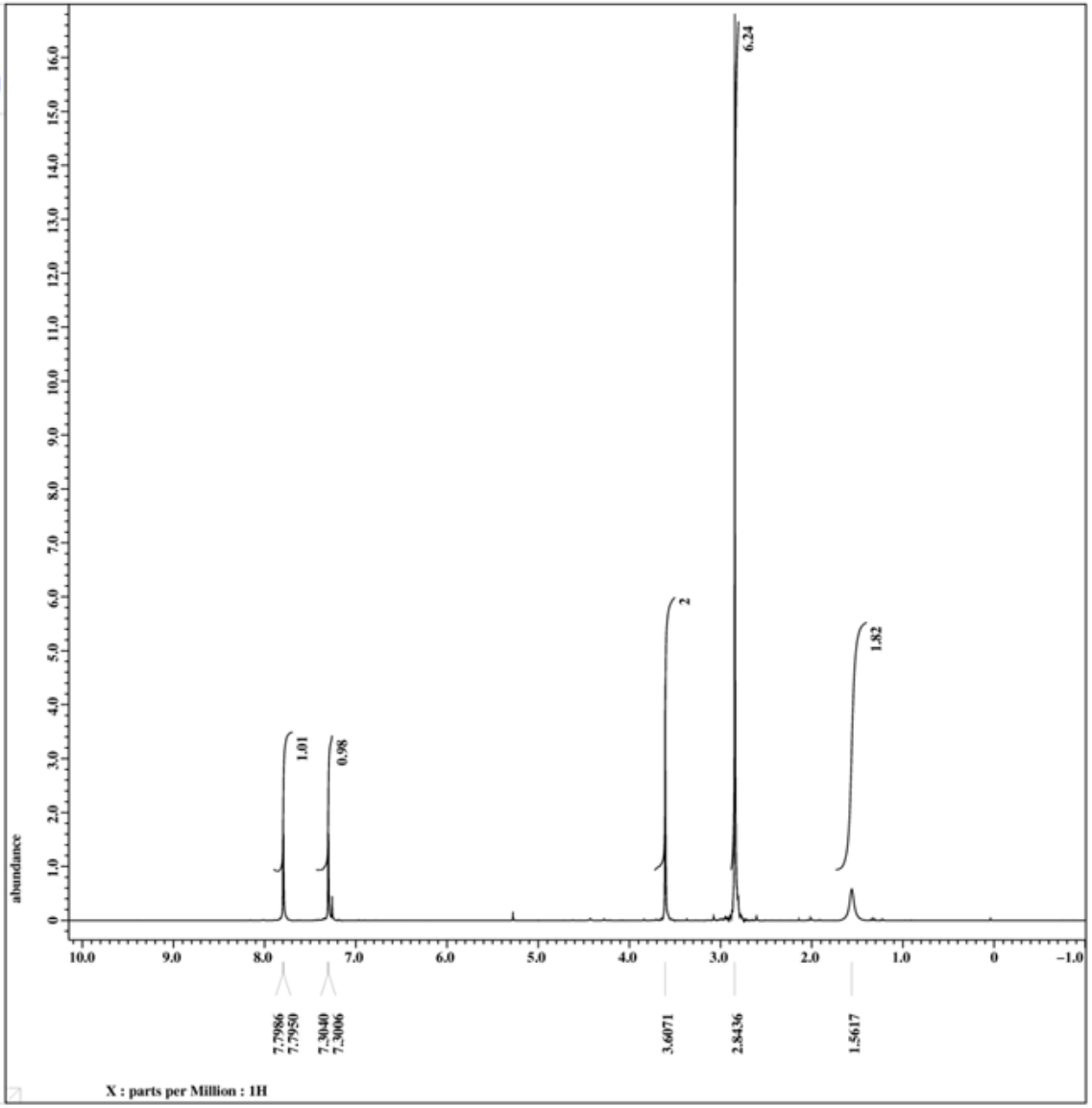




APPENDIX 41
^{1}H AND ^{13}C NMR SPECTRA OF
4-(3-Aminoprop-1-ynyl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide(152)

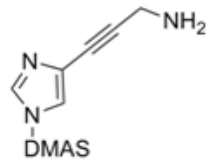
```
Filename          = MRB_IV_6_dmas_propami
Author            = delta
Experiment        = single_pulse.ex2
Sample_id         = S#343419
Solvent           = CHLOROFORM-D
Creation_time     = 30-MAR-2009 08:54:10
Revision_time     = 30-MAR-2009 09:40:01
Current_time      =  6-NOV-2010 23:59:36

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    = 7.0586013[T] (300[MHz
X_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]
Irr_domain        = 1H
Irr_freq          = 300.52965592[MHz]
Irr_offset        = 5[ppm]
Tri_domain        = 1H
Tri_freq          = 300.52965592[MHz]
Tri_offset        = 5[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 13
Total_scans       = 13

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]
Irr_mode          = Off
Tri_mode          = Off
Dante_presat      = FALSE
Initial_wait      = 1[s]
Recvr_gain        = 40
Relaxation_delay  = 5[s]
Repetition_time   = 7.90717696[s]
Temp_get          = 23.2[dC]
```

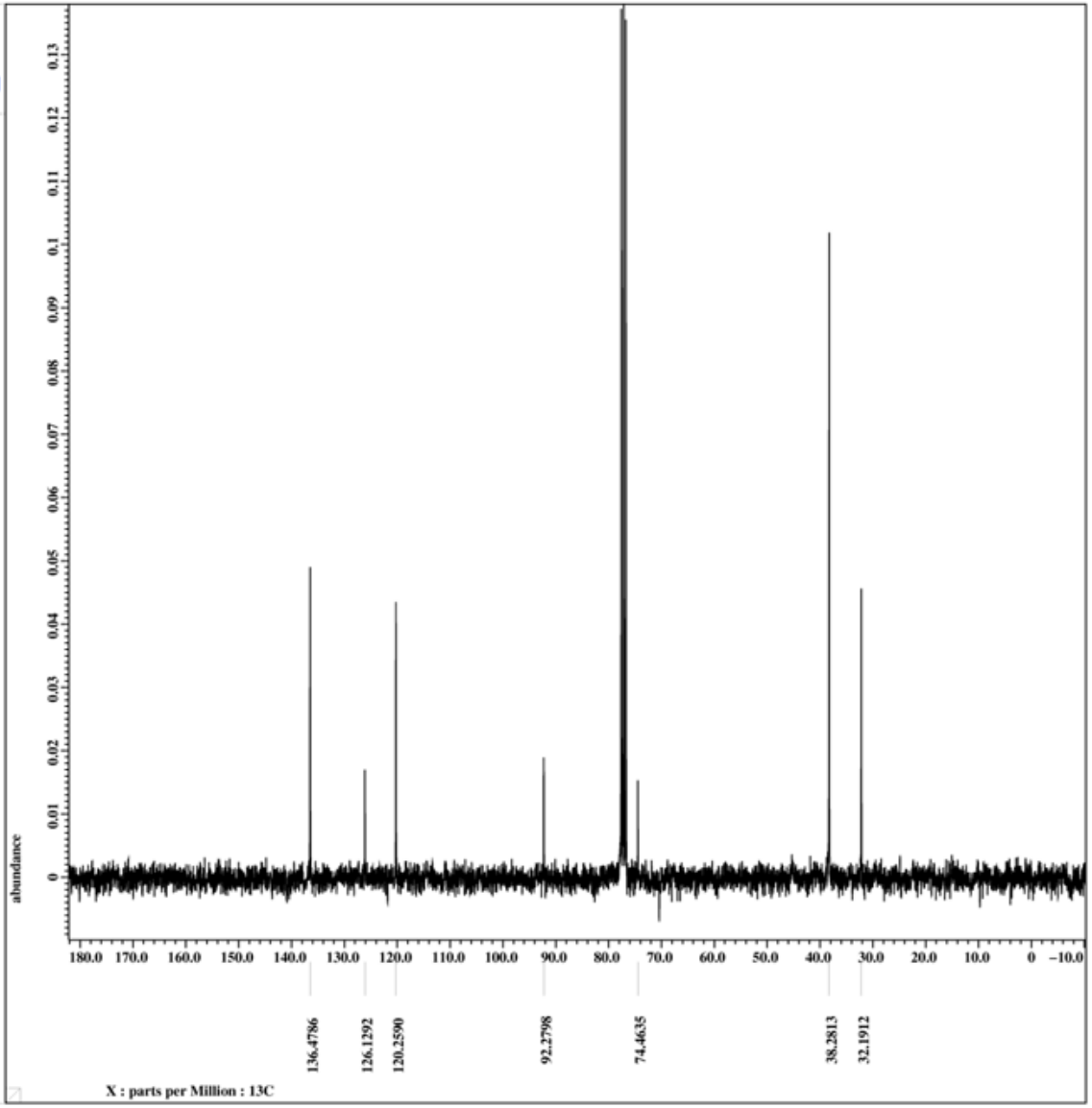




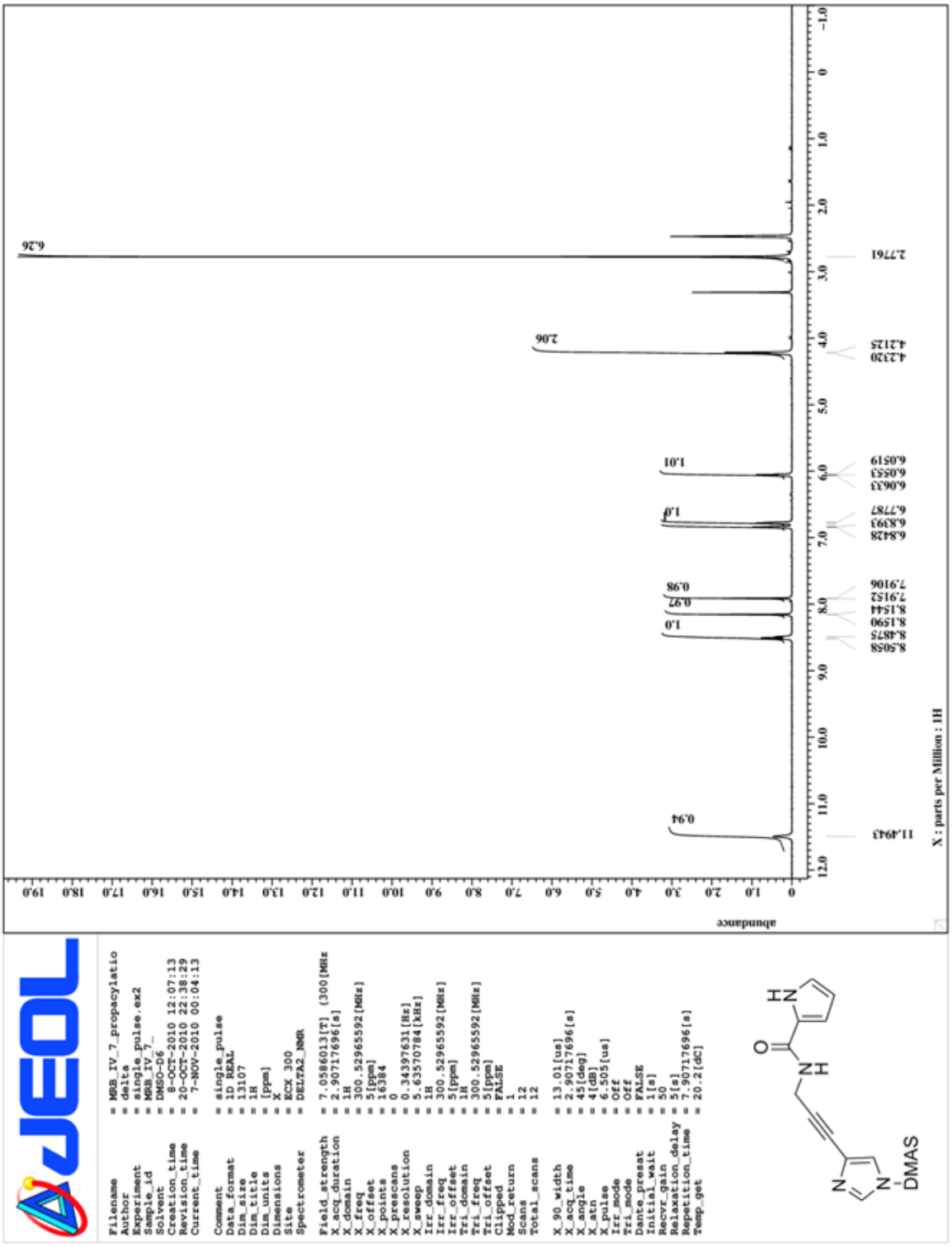
JEOL

Filename	= MRB_IV_6_dmas_propami
Author	= delta
Experiment	= single_pulse_dec
Sample_id	= S#344587
Solvent	= CHLOROFORM-D
Creation_time	= 30-MAR-2009 09:06:29
Revision_time	= 10-OCT-2010 10:06:25
Current_time	= 7-NOV-2010 00:00:01
Comment	= single pulse decouple
Data_format	= 1D COMPLEX
Dim_size	= 52428
Dim_title	= 13C
Dim_units	= [ppm]
Dimensions	= X
Site	= ECX 300
Spectrometer	= DELTA2_NMR
Field_strength	= 7.0586013[T] (300[MHz
X_acq_duration	= 2.76824064[s]
X_domain	= 13C
X_freq	= 75.56823426[MHz]
X_offset	= 100[ppm]
X_points	= 65536
X_prescans	= 4
X_resolution	= 0.36124027[Hz]
X_sweep	= 23.67424242[kHz]
Irr_domain	= 1H
Irr_freq	= 300.52965592[MHz]
Irr_offset	= 5[ppm]
Clipped	= FALSE
Mod_return	= 10
Scans	= 150
Total_scans	= 150
X_90_width	= 9.75[us]
X_acq_time	= 2.76824064[s]
X_angle	= 30[deg]
X_atn	= 8[dB]
X_pulse	= 3.25[us]
Irr_atn_dec	= 25[dB]
Irr_atn_noe	= 25[dB]
Irr_noise	= WALTZ
Decoupling	= TRUE
Initial_wait	= 1[s]
Noe	= TRUE
Noe_time	= 2[s]
Recvr_gain	= 50
Relaxation_delay	= 2[s]
Repetition_time	= 4.76824064[s]
Temp_get	= 23.4[dC]

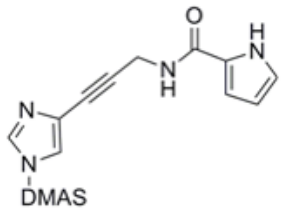


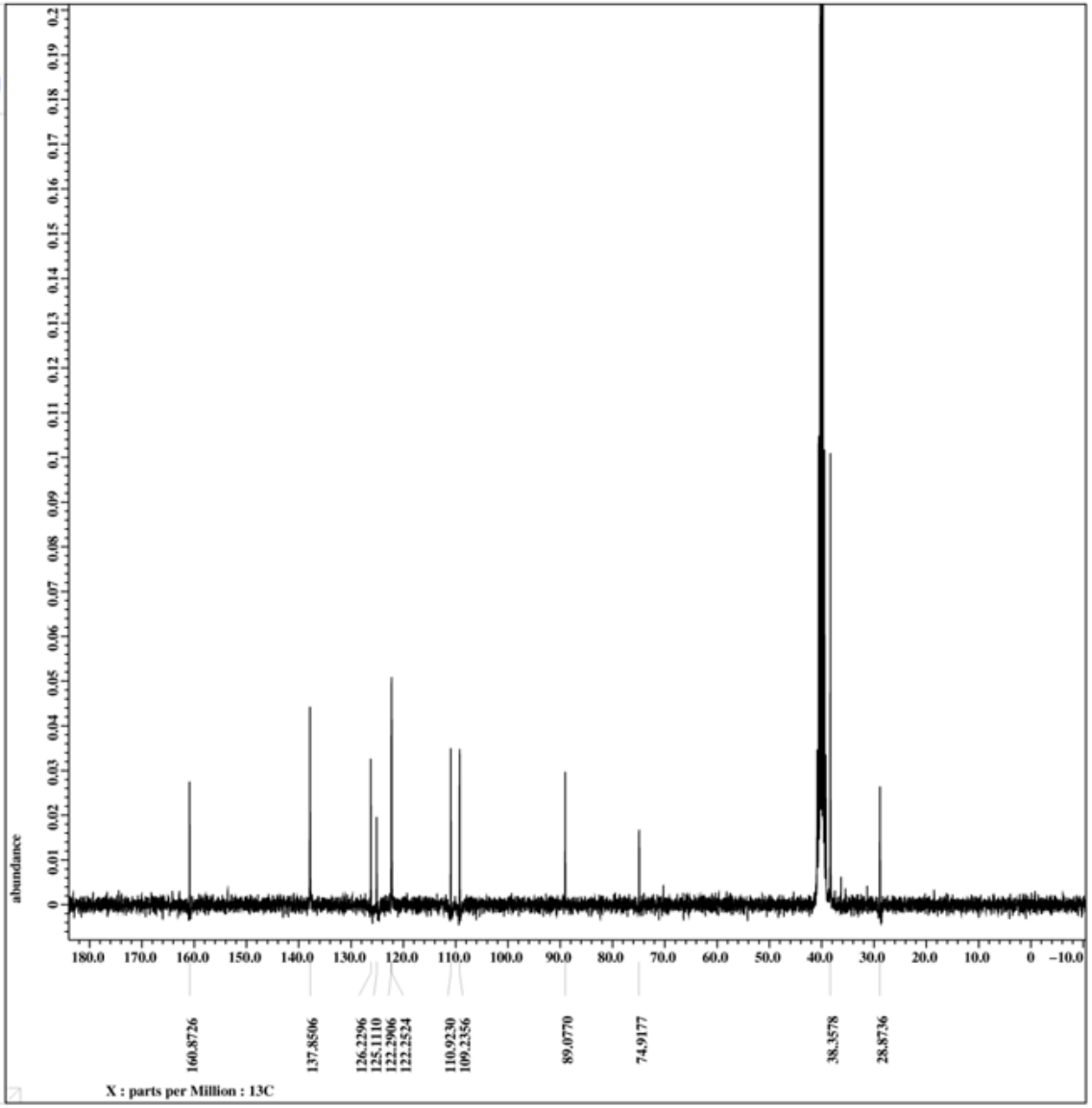


APPENDIX 42
^{1}H AND ^{13}C NMR SPECTRA OF
***N*-(3-(1-(*N*,*N*-Dimethylsulfamoyl)-1H-imidazol-4-yl)prop-2-ynyl)-1H-pyrrole-2-carboxamide (148)**

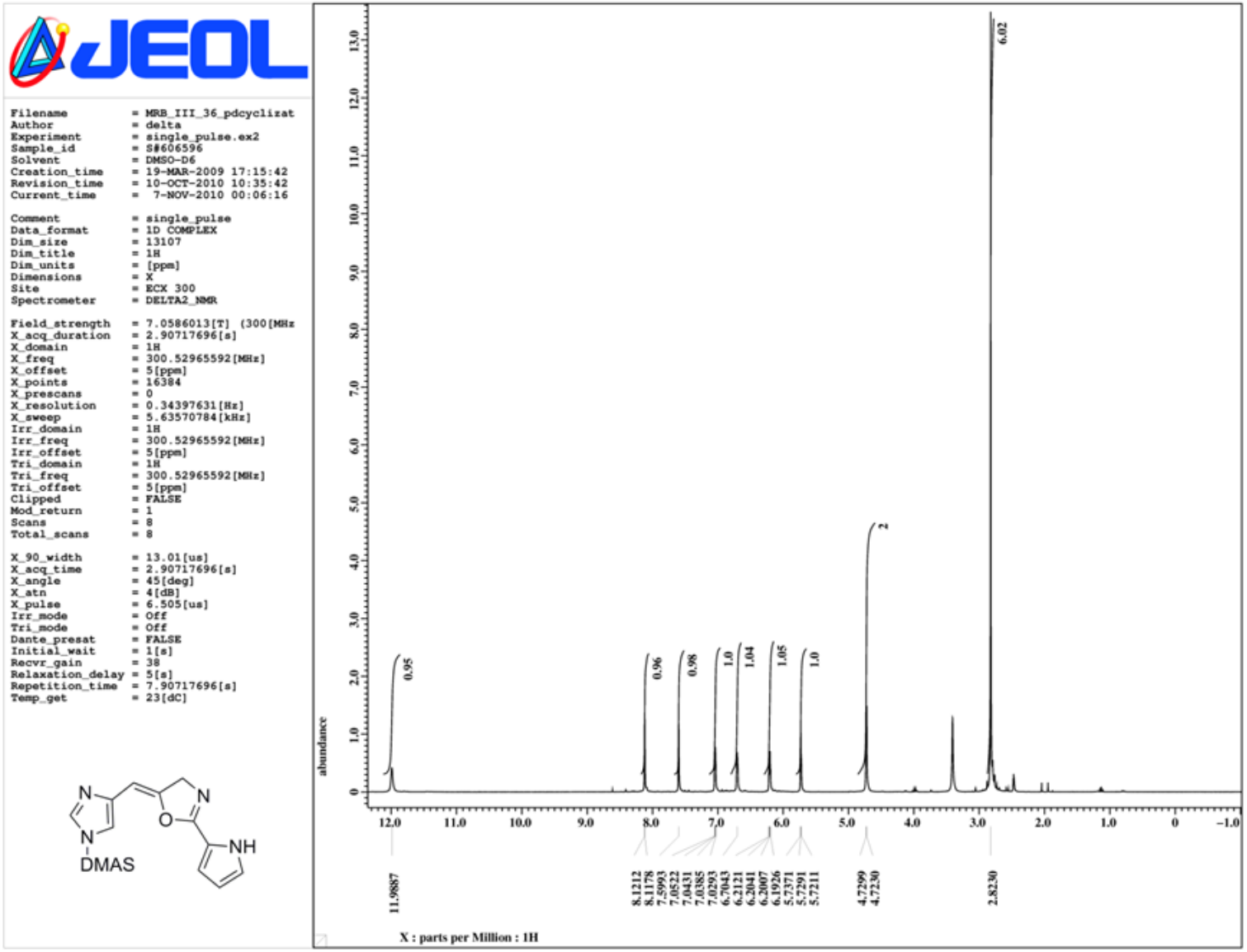

JEOL
Filename = MRB_IV_7_propacylatio
Author = delta
Experiment = single_pulse.ex2
Sample_id = MRB_IV_7_
Solvent = DMSO-D6
Creation_time = 8-OCT-2010 12:07:13
Revision_time = 20-OCT-2010 22:38:29
Current_time = 7-NOV-2010 00:04:13
Comment = single_pulse
Data_format = 1D REAL
Dim_size = 13107
Dim_title = 1H
Dim_units = [ppm]
Dimensions = X
Site = ECX 300
Spectrometer = DELTA2_NMR
Field_strength = 7.0586013[T] (300[MHz
X_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]
Irr_domain = 1H
Irr_freq = 300.52965592[MHz]
Irr_offset = 5[ppm]
Tri_domain = 1H
Tri_freq = 300.52965592[MHz]
Tri_offset = 5[ppm]
Clipped = FALSE
Mod_return = 1
Scans = 12
Total_scans = 12
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]
Irr_mode = Off
Tri_mode = Off
Dante_presat = FALSE
Initial_wait = 1[s]
Recvr_gain = 50
Relaxation_delay = 5[s]
Repetition_time = 7.90717696[s]
Temp_get = 20.2[dC]
DMAS
abundance
X : parts per Million : 1H
6.26
2.06
1.01
1.0
1.0
0.97
0.98
0.94
11.4943
8.5058
8.4875
8.1590
8.1544
7.9152
7.9106
6.8428
6.8393
6.7787
6.0633
6.0553
6.0519
4.2320
4.2125
2.7761

```
Filename          = MRB_IV_7_propacylatio
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#525712
Solvent           = DMSO-D6
Creation_time     =  1-APR-2009 14:11:21
Revision_time     =  1-APR-2009 14:52:01
Current_time      =  7-NOV-2010 00:05:02

Comment           = single pulse decouple
Data_format       = 1D REAL
Dim_size          = 52428
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = ECX 300
Spectrometer      = DELTA2_NMR

Field_strength    = 7.0586013[T] (300[MHz
X_acq_duration    = 2.76824064[s]
X_domain          = 13C
X_freq            = 75.56823426[MHz]
X_offset          = 100[ppm]
X_points          = 65536
X_prescans        = 4
X_resolution      = 0.36124027[Hz]
X_sweep           = 23.67424242[kHz]
Irr_domain        = 1H
Irr_freq          = 300.52965592[MHz]
Irr_offset        = 5[ppm]
Clipped           = FALSE
Mod_return        = 10
Scans             = 170
Total_scans       = 170

X_90_width        = 9.75[us]
X_acq_time        = 2.76824064[s]
X_angle           = 30[deg]
X_atn             = 8[dB]
X_pulse           = 3.25[us]
Irr_atn_dec       = 25[dB]
Irr_atn_noe       = 25[dB]
Irr_noise         = WALTZ
Decoupling        = TRUE
Initial_wait      = 1[s]
Noe               = TRUE
Noe_time          = 2[s]
Recvr_gain        = 50
Relaxation_delay  = 2[s]
Repetition_time   = 4.76824064[s]
Temp_get          = 23.3[dC]
```

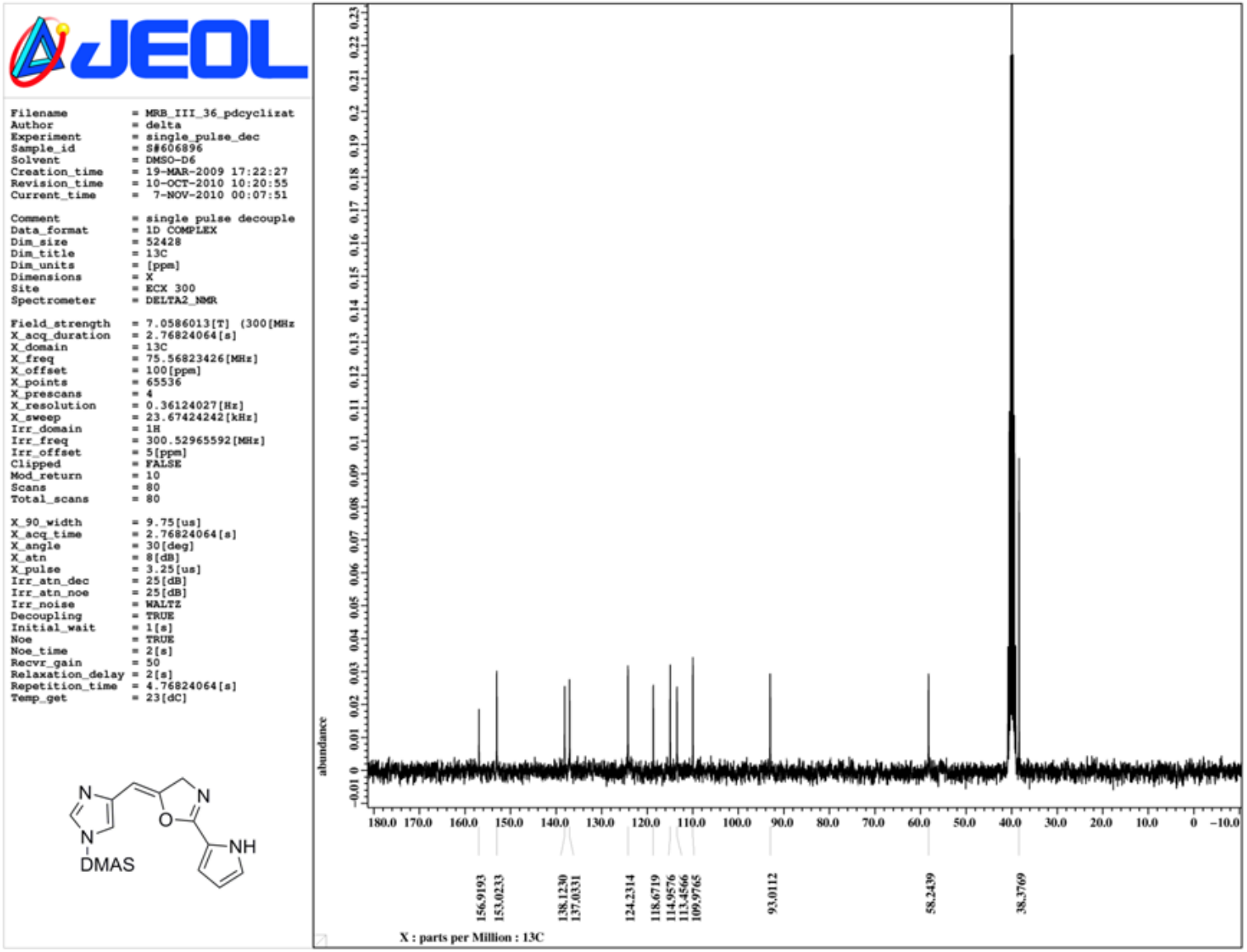




APPENDIX 43
^{1}H AND ^{13}C NMR SPECTRA OF
(*Z*)-4-((2-(1H-Pyrrol-2-yl)oxazol-5(4H)-ylidene)methyl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide (149)



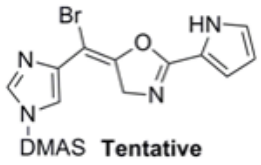
```
Filename          = MRB_III_36_pdcyclizat
Author            = delta
Experiment        = single_pulse.ex2
Sample_id         = S#606596
Solvent           = DMSO-D6
Creation_time     = 19-MAR-2009 17:15:42
Revision_time     = 10-OCT-2010 10:35:42
Current_time      =  7-NOV-2010 00:06:16

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
X_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]
Irr_domain        = 1H
Irr_freq          = 300.52965592[MHz]
Irr_offset        = 5[ppm]
Tri_domain        = 1H
Tri_freq          = 300.52965592[MHz]
Tri_offset        = 5[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 8
Total_scans       = 8

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]
Irr_mode          = Off
Tri_mode          = Off
Dante_presat      = FALSE
Initial_wait      = 1[s]
Recvr_gain        = 38
Relaxation_delay  = 5[s]
Repetition_time   = 7.90717696[s]
Temp_get          = 23[dC]
```



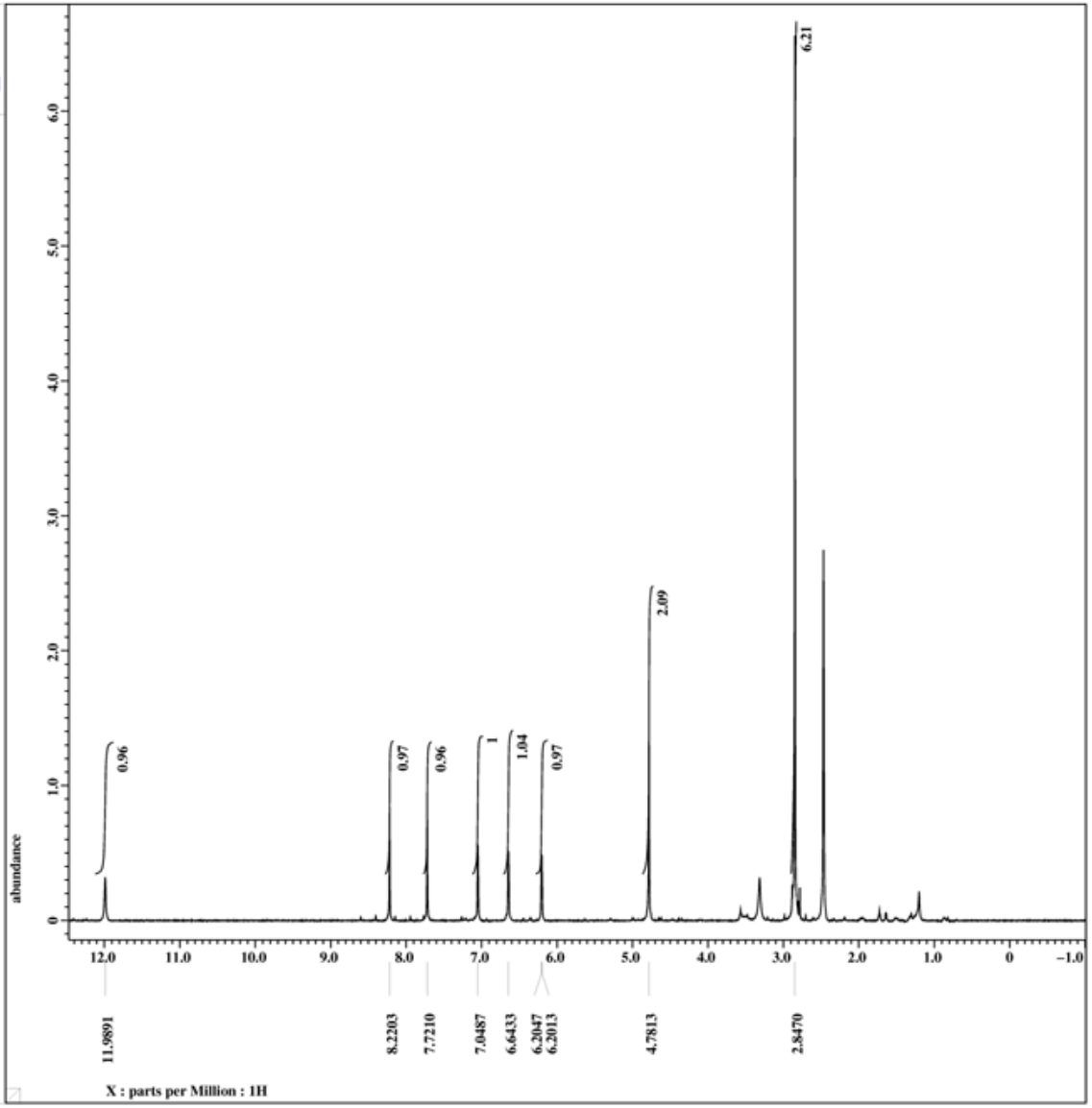
```
Filename          = MRB_III_36_pdcyclizat
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#606896
Solvent           = DMSO-D6
Creation_time     = 19-MAR-2009 17:22:27
Revision_time     = 10-OCT-2010 10:20:55
Current_time      =  7-NOV-2010 00:07:51

Comment           = single pulse decouple
Data_format       = 1D COMPLEX
Dim_size          = 52428
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = ECX 300
Spectrometer      = DELTA2_NMR

Field_strength    = 7.0586013[T] (300[MHz
X_acq_duration    = 2.76824064[s]
X_domain          = 13C
X_freq            = 75.56823426[MHz]
X_offset          = 100[ppm]
X_points          = 65536
X_prescans        = 4
X_resolution      = 0.36124027[Hz]
X_sweep           = 23.67424242[kHz]
Irr_domain        = 1H
Irr_freq          = 300.52965592[MHz]
Irr_offset        = 5[ppm]
Clipped           = FALSE
Mod_return        = 10
Scans             = 80
Total_scans       = 80

X_90_width        = 9.75[us]
X_acq_time        = 2.76824064[s]
X_angle           = 30[deg]
X_atn             = 8[dB]
X_pulse           = 3.25[us]
Irr_atn_dec       = 25[dB]
Irr_atn_noe       = 25[dB]
Irr_noise         = WALTZ
Decoupling        = TRUE
Initial_wait      = 1[s]
Noe               = TRUE
Noe_time          = 2[s]
Recvr_gain        = 50
Relaxation_delay  = 2[s]
Repetition_time   = 4.76824064[s]
Temp_get          = 23[dC]
```

APPENDIX 44
^{1}H AND ^{13}C NMR SPECTRA OF
(*Z*)-4-((2-(1H-Pyrrol-2-yl)oxazol-5(4H)-ylidene)bromomethyl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide (151)

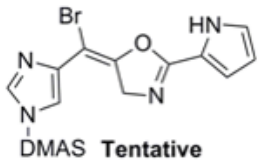
```
Filename          = MRB_V_116_bromooxazol
Author            = delta
Experiment        = single_pulse.ex2
Sample_id         = S#459306
Solvent           = DMSO-D6
Creation_time     = 31-OCT-2010 02:44:00
Revision_time     =  8-NOV-2010 12:45:03
Current_time      =  8-NOV-2010 12:46:08

Comment           = single_pulse
Data_format       = 1D REAL
Dim_size          = 13107
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 1.74587904[s]
X_domain          = 1H
X_freq            = 500.15991521[MHz]
X_offset          = 5.0[ppm]
X_points          = 16384
X_prescans        = 0
X_resolution      = 0.57277737[Hz]
X_sweep           = 9.38438438[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Tri_domain        = 1H
Tri_freq          = 500.15991521[MHz]
Tri_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 16
Total_scans       = 16

X_90_width        = 12.54[us]
X_acq_time        = 1.74587904[s]
X_angle           = 45[deg]
X_atn             = 4[dB]
X_pulse           = 6.27[us]
Irr_mode          = Off
Tri_mode          = Off
Dante_presat      = FALSE
Initial_wait      = 1[s]
Recvr_gain        = 46
Relaxation_delay  = 5[s]
Repetition_time   = 6.74587904[s]
Temp_get          = 26[dC]
```



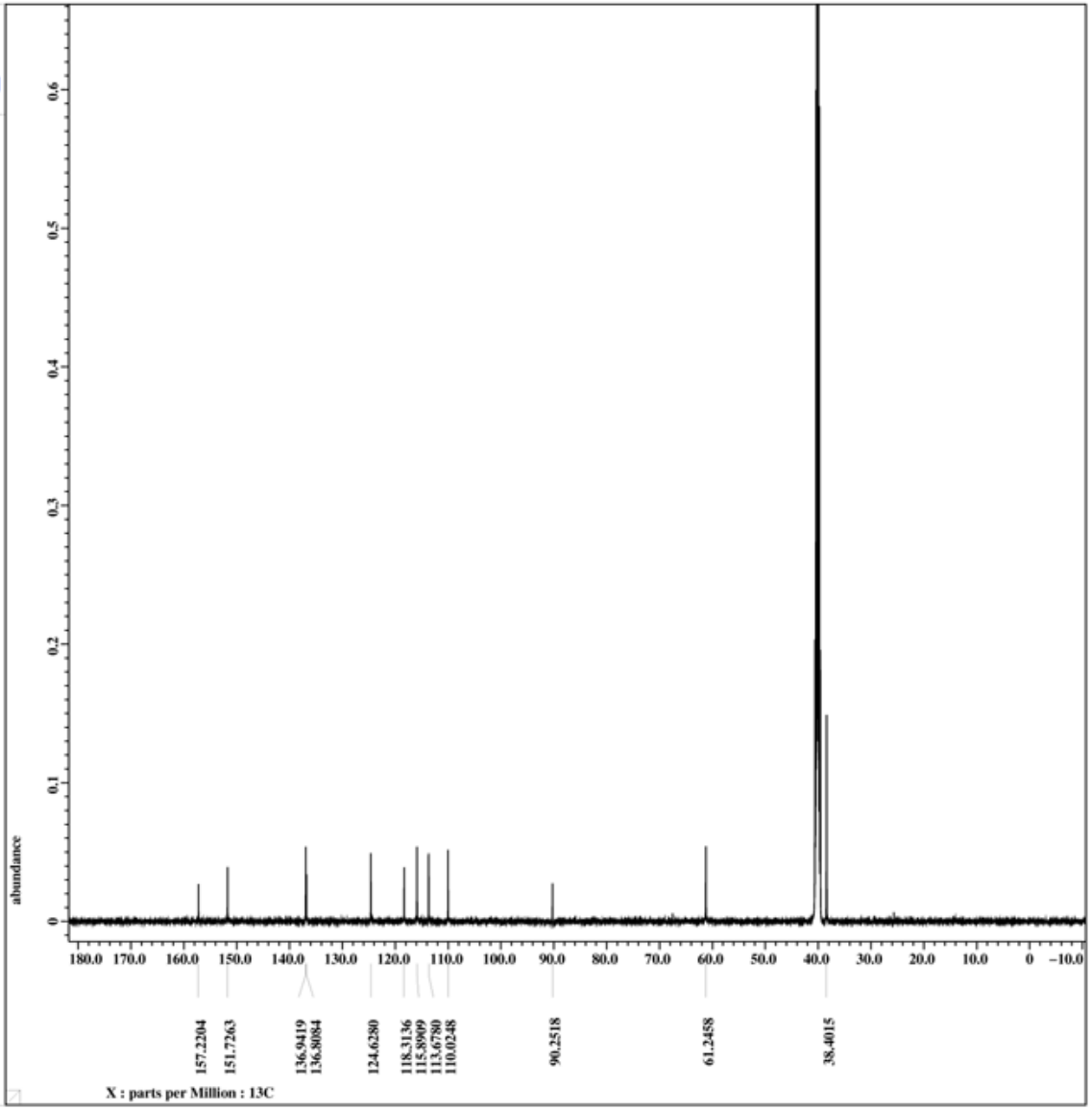
Tentative



```
Filename          = MRB_V_116_bromooxazol
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#739343
Solvent           = DMSO-D6
Creation_time     = 29-OCT-2010 22:17:34
Revision_time     = 29-OCT-2010 11:49:58
Current_time      =  8-NOV-2010 12:46:44

Comment           = single pulse decouple
Data_format       = 1D REAL
Dim_size          = 26214
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 0.83361792[s]
X_domain          = 13C
X_freq            = 125.76529768[MHz]
X_offset          = 100[ppm]
X_points          = 32768
X_prescans        = 4
X_resolution      = 1.19959034[Hz]
X_sweep           = 39.3081761[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 10
Scans             = 15000
Total_scans       = 15000

X_90_width        = 10.73[us]
X_acq_time        = 0.83361792[s]
X_angle           = 30[deg]
X_atn             = 9[dB]
X_pulse           = 3.57666667[us]
Irr_atn_dec       = 20[dB]
Irr_atn_noe       = 20[dB]
Irr_noise         = WALTZ
Decoupling        = TRUE
Initial_wait      = 1[s]
Noe               = TRUE
Noe_time          = 2[s]
Recvr_gain        = 50
Relaxation_delay  = 2[s]
Repetition_time   = 2.83361792[s]
Temp_get          = 26.2[dC]
```



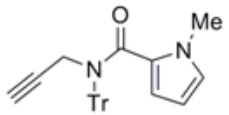
DMAS **Tentative**

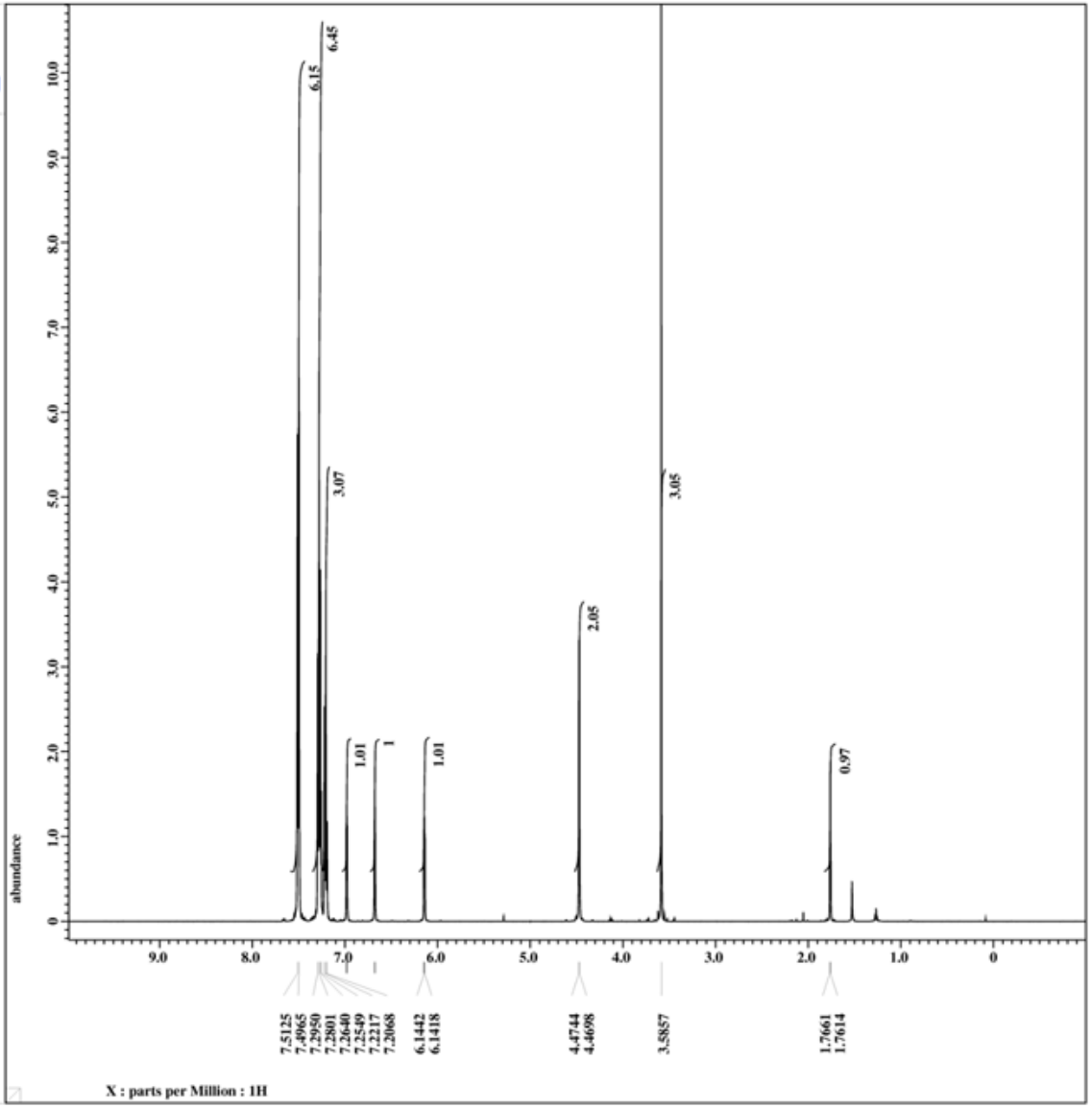


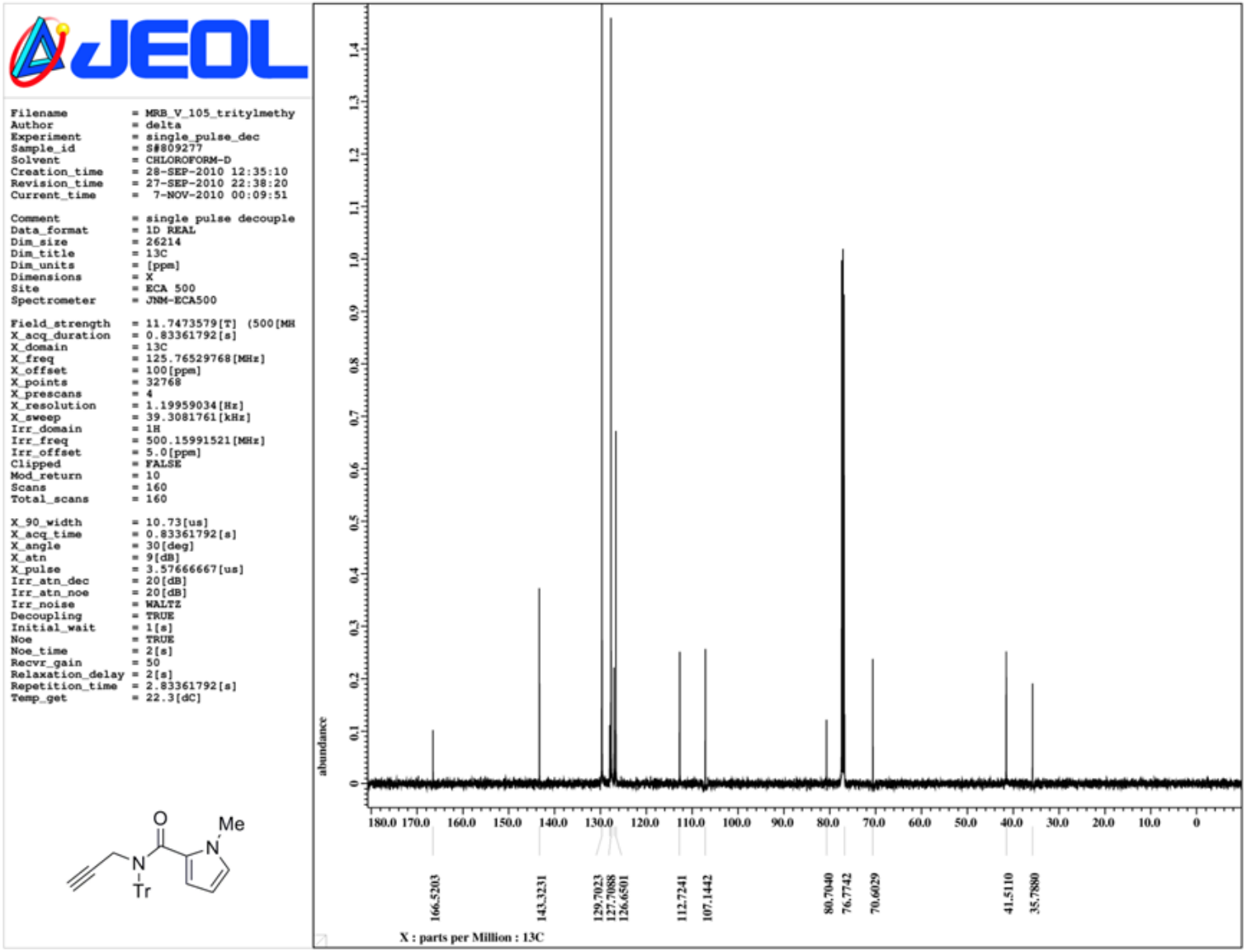
APPENDIX 45
^{1}H AND ^{13}C NMR SPECTRA OF
1-Methyl-*N*-(prop-2-ynyl)-*N*-trityl-1H-pyrrole-2-carboxamide (162)

JEOL

Filename	= MRB_V_105_tritylmethy
Author	= delta
Experiment	= single_pulse.ex2
Sample_id	= S#808453
Solvent	= CHLOROFORM-D
Creation_time	= 28-SEP-2010 12:27:23
Revision_time	= 27-SEP-2010 22:34:58
Current_time	= 7-NOV-2010 00:09:23
Comment	= single_pulse
Data_format	= 1D REAL
Dim_size	= 13107
Dim_title	= 1H
Dim_units	= [ppm]
Dimensions	= X
Site	= ECA 500
Spectrometer	= JNM-ECA500
Field_strength	= 11.7473579[T] (500[MH
X_acq_duration	= 1.74587904[s]
X_domain	= 1H
X_freq	= 500.15991521[MHz]
X_offset	= 5.0[ppm]
X_points	= 16384
X_prescans	= 0
X_resolution	= 0.57277737[Hz]
X_sweep	= 9.38438438[kHz]
Irr_domain	= 1H
Irr_freq	= 500.15991521[MHz]
Irr_offset	= 5.0[ppm]
Tri_domain	= 1H
Tri_freq	= 500.15991521[MHz]
Tri_offset	= 5.0[ppm]
Clipped	= FALSE
Mod_return	= 1
Scans	= 11
Total_scans	= 11
X_90_width	= 12.54[us]
X_acq_time	= 1.74587904[s]
X_angle	= 45[deg]
X_atn	= 4[dB]
X_pulse	= 6.27[us]
Irr_mode	= Off
Tri_mode	= Off
Dante_presat	= FALSE
Initial_wait	= 1[s]
Recvr_gain	= 38
Relaxation_delay	= 5[s]
Repetition_time	= 6.74587904[s]
Temp_get	= 21.6[dC]





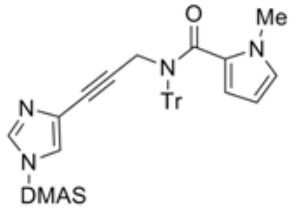


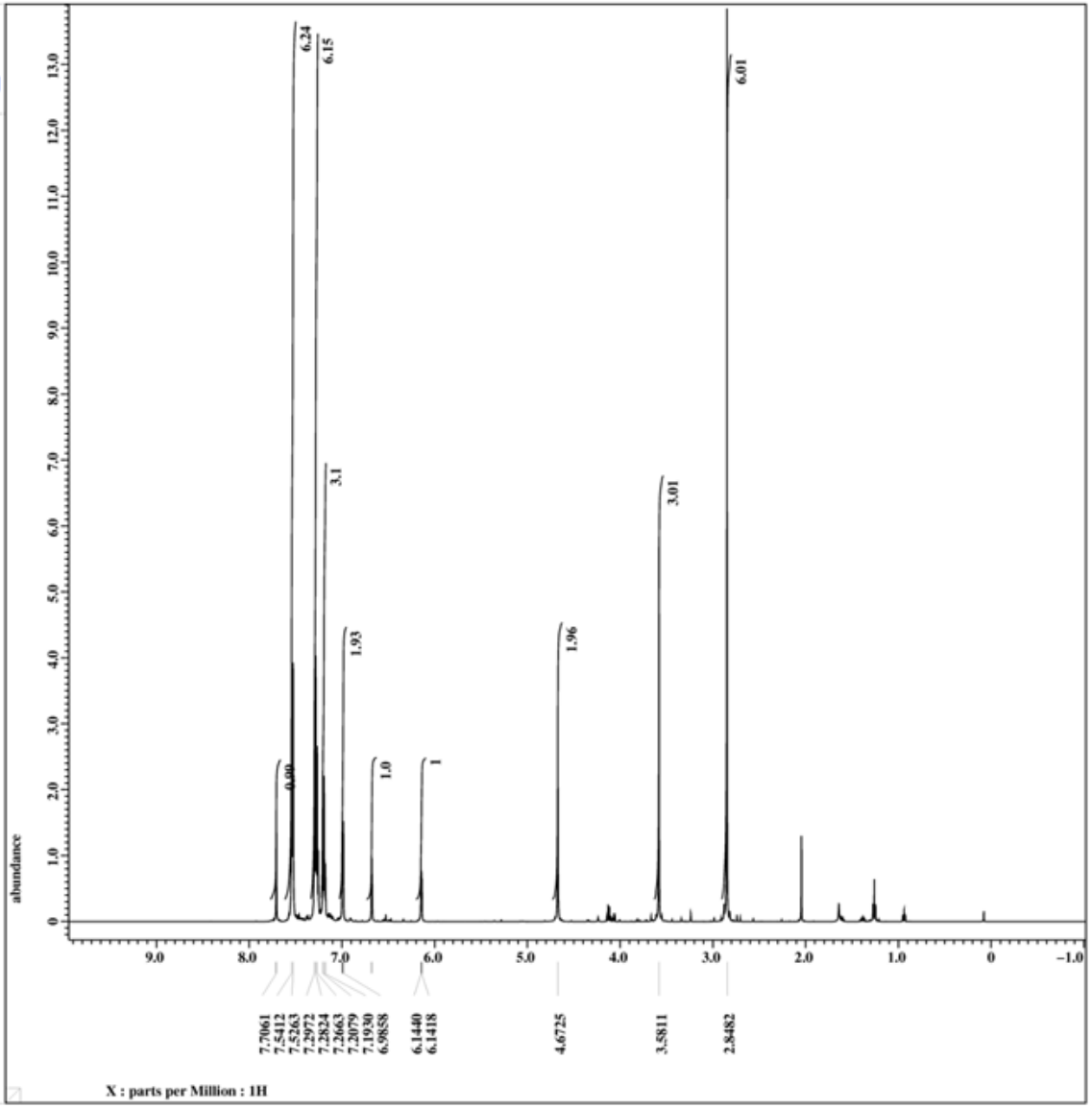
```
Filename          = MRB_V_105_tritylmethy
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#809277
Solvent           = CHLOROFORM-D
Creation_time     = 28-SEP-2010 12:35:10
Revision_time     = 27-SEP-2010 22:38:20
Current_time      =  7-NOV-2010 00:09:51

Comment           = single pulse decouple
Data_format       = 1D REAL
Dim_size          = 26214
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 0.83361792[s]
X_domain          = 13C
X_freq            = 125.76529768[MHz]
X_offset          = 100[ppm]
X_points          = 32768
X_prescans        = 4
X_resolution      = 1.19959034[Hz]
X_sweep           = 39.3081761[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 10
Scans             = 160
Total_scans       = 160

X_90_width        = 10.73[us]
X_acq_time        = 0.83361792[s]
X_angle           = 30[deg]
X_atn             = 9[dB]
X_pulse           = 3.57666667[us]
Irr_atn_dec       = 20[dB]
Irr_atn_noe       = 20[dB]
Irr_noise         = WALTZ
Decoupling        = TRUE
Initial_wait      = 1[s]
Noe               = TRUE
Noe_time          = 2[s]
Recvr_gain        = 50
Relaxation_delay  = 2[s]
Repetition_time   = 2.83361792[s]
Temp_get          = 22.3[dC]
```

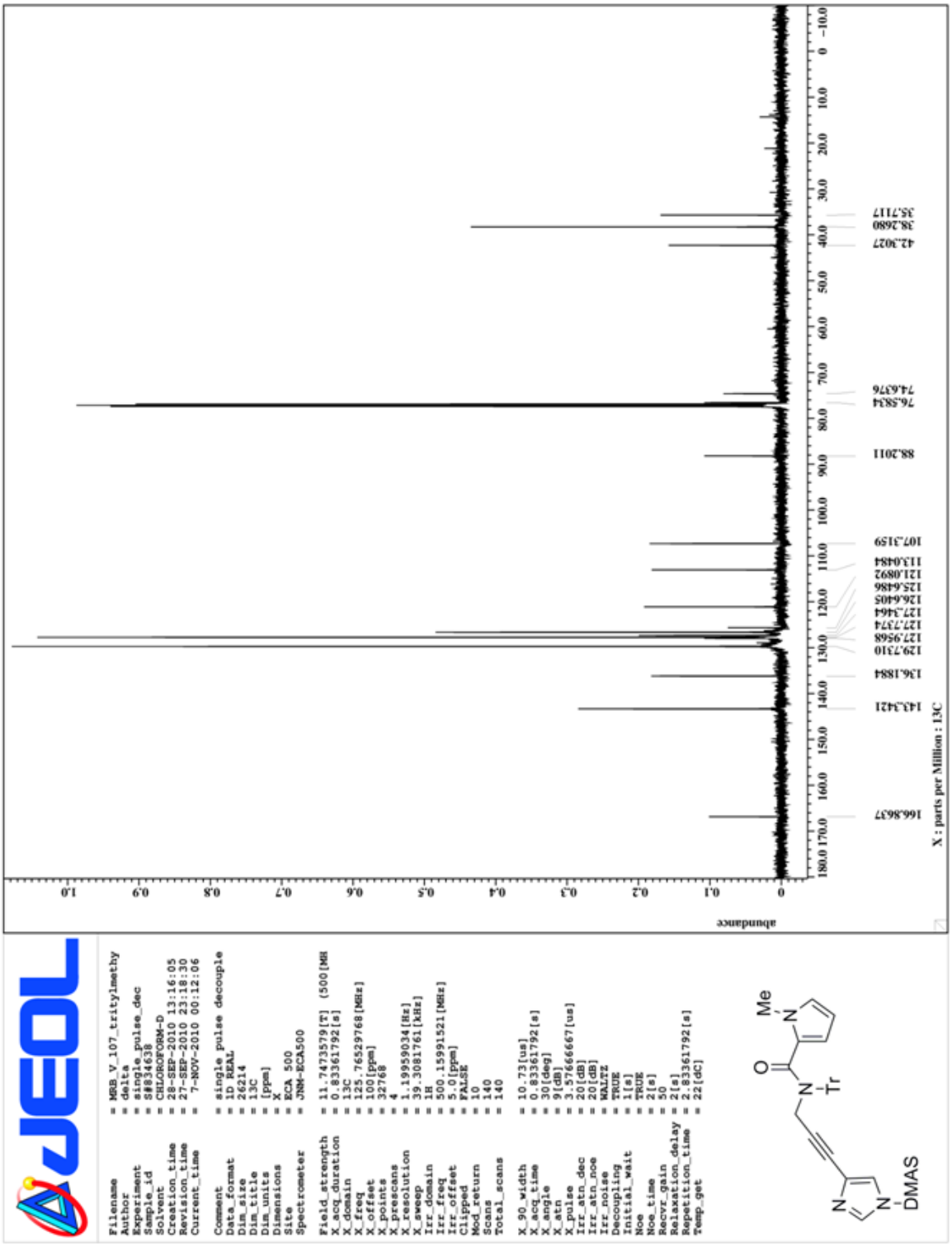
APPENDIX 46
^{1}H AND ^{13}C NMR SPECTRA OF
***N*-(3-(1-(*N*,*N*-Dimethylsulfamoyl)-1H-imidazol-4-yl)prop-2-ynyl)-1-methyl-*N*-trityl-1H-pyrrole-2-carboxamide (163)**

JEOL

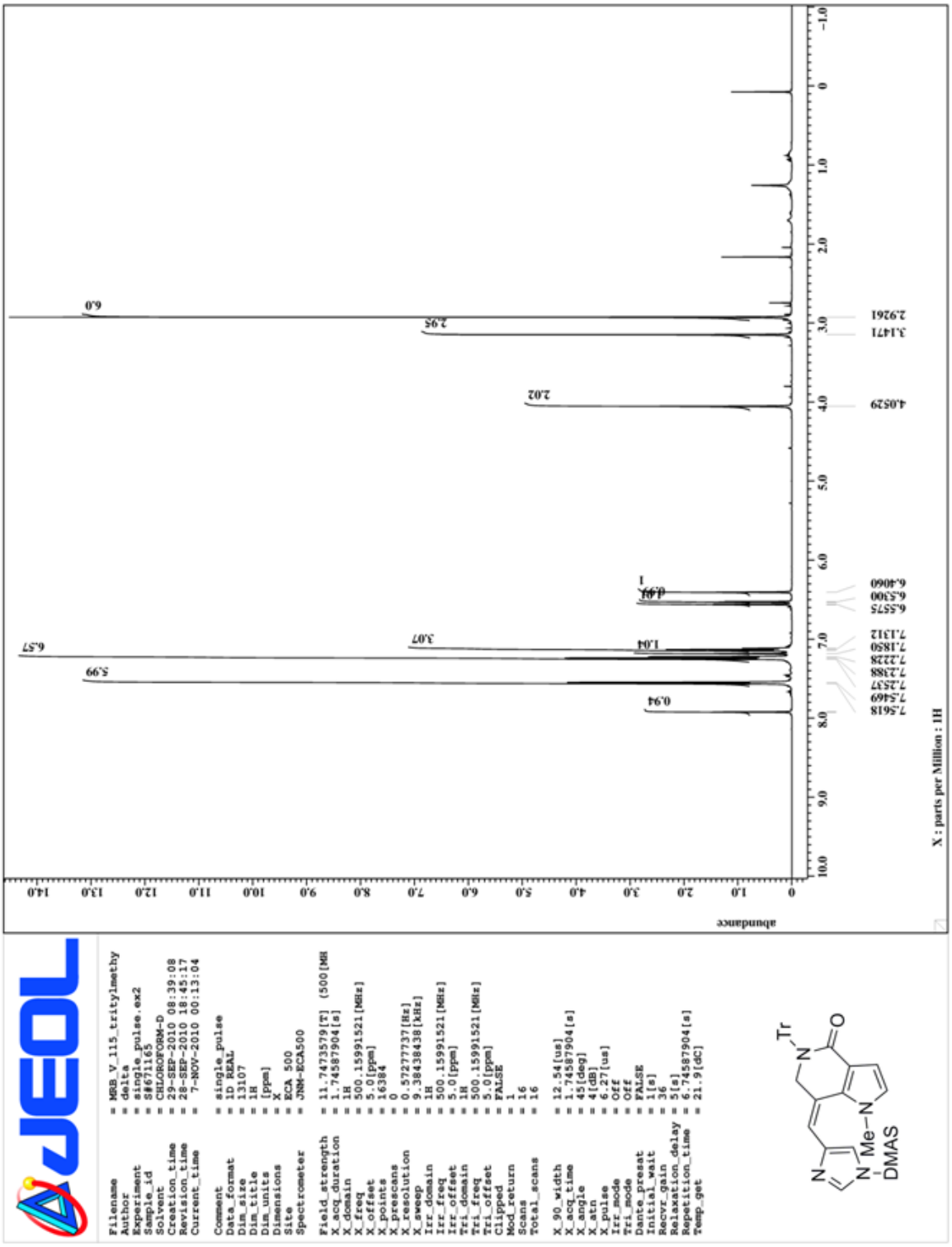
Filename	= MRB_V_107_tritylmethy
Author	= delta
Experiment	= single_pulse.ex2
Sample_id	= S#835924
Solvent	= CHLOROFORM-D
Creation_time	= 28-SEP-2010 13:18:31
Revision_time	= 27-SEP-2010 23:22:55
Current_time	= 7-NOV-2010 00:11:36
Comment	= single_pulse
Data_format	= 1D REAL
Dim_size	= 13107
Dim_title	= 1H
Dim_units	= [ppm]
Dimensions	= X
Site	= ECA 500
Spectrometer	= JNM-ECA500
Field_strength	= 11.7473579[T] (500[MH
X_acq_duration	= 1.74587904[s]
X_domain	= 1H
X_freq	= 500.15991521[MHz]
X_offset	= 5.0[ppm]
X_points	= 16384
X_prescans	= 0
X_resolution	= 0.57277737[Hz]
X_sweep	= 9.38438438[kHz]
Irr_domain	= 1H
Irr_freq	= 500.15991521[MHz]
Irr_offset	= 5.0[ppm]
Tri_domain	= 1H
Tri_freq	= 500.15991521[MHz]
Tri_offset	= 5.0[ppm]
Clipped	= FALSE
Mod_return	= 1
Scans	= 16
Total_scans	= 16
X_90_width	= 12.54[us]
X_acq_time	= 1.74587904[s]
X_angle	= 45[deg]
X_atn	= 4[dB]
X_pulse	= 6.27[us]
Irr_mode	= Off
Tri_mode	= Off
Dante_presat	= FALSE
Initial_wait	= 1[s]
Recvr_gain	= 36
Relaxation_delay	= 5[s]
Repetition_time	= 6.74587904[s]
Temp_get	= 21.7[dC]

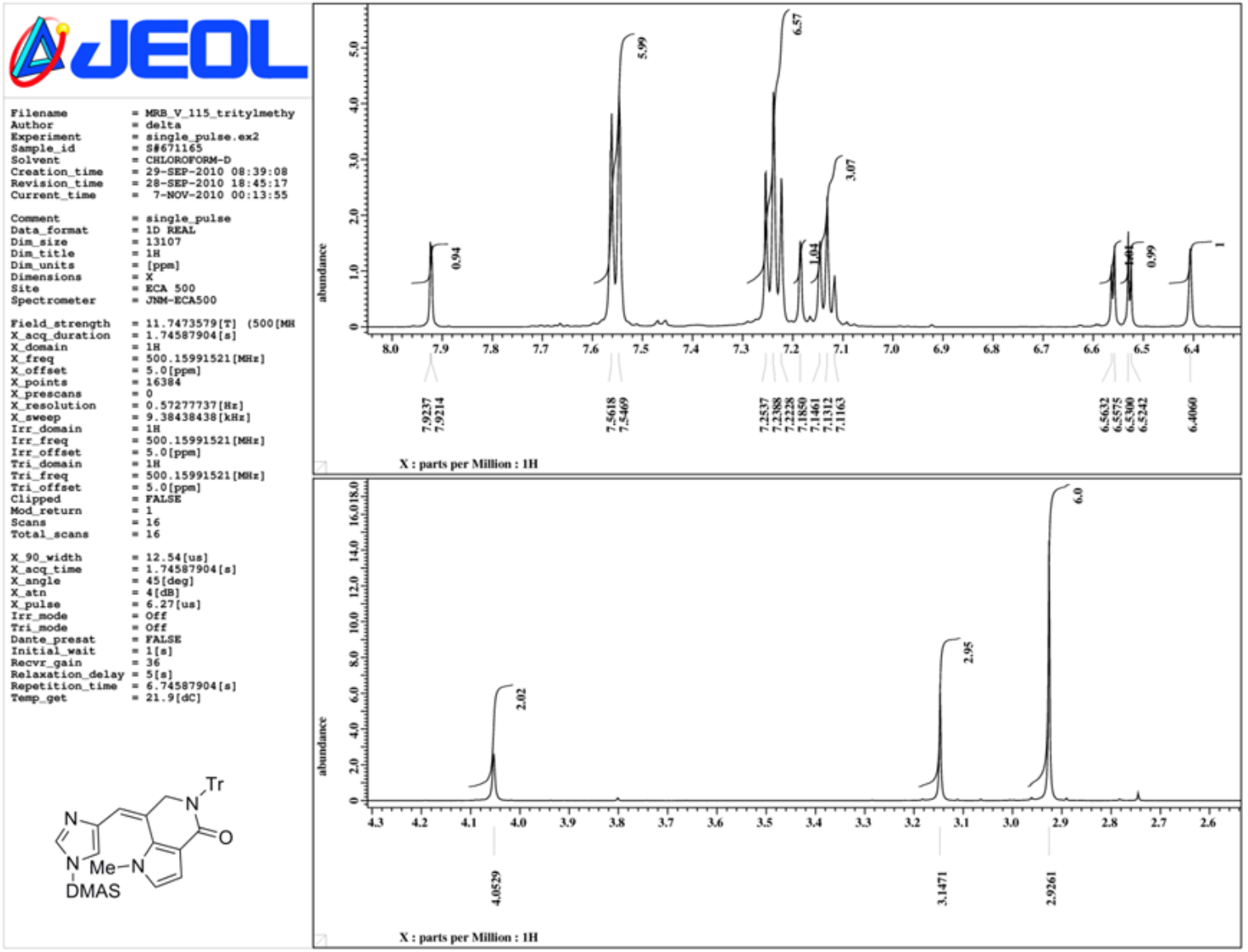





JEOL
Filename = MRB_V_107_tritylmethy
Author = delta
Experiment = single_pulse_dec
Sample_id = s#834638
Solvent = CHLOROFORM-D
Creation_time = 28-SEP-2010 13:16:05
Revision_time = 27-SEP-2010 23:18:30
Current_time = 7-NOV-2010 00:12:06
Comment = single pulse decouple
Data_format = 1D REAL
Dim_size = 26214
Dim_title = 13C
Dim_units = [ppm]
Dimensions = X
Site = ECA 500
Spectrometer = JNM-ECA500
Field_strength = 11.7473579[T] (500[MH
X_acq_duration = 0.83361792[s]
X_domain = 13C
X_freq = 125.765297681MHz]
X_offset = 100[ppm]
X_points = 32768
X_prescans = 4
X_resolution = 1.19959034[Hz]
X_sweep = 39.3081761[kHz]
Irr_domain = H
Irr_freq = 500.159915211MHz]
Irr_offset = 5.0[ppm]
Clipped = FALSE
Mod_return = 10
Scans = 140
Total_scans = 140
X_90_width = 10.73[us]
X_acq_time = 0.83361792[s]
X_angle = 30[deg]
X_atn = 9[dB]
X_pulse = 3.57666667[us]
Irr_atn_dec = 20[dB]
Irr_atn_noe = 20[dB]
Irr_noise = WALTZ
Decoupling = TRUE
Initial_wait = 1[s]
Noe = TRUE
Noe_time = 2[s]
Recyc_gain = 50
Relaxation_delay = 2[s]
Repetition_time = 2.83361792[s]
Temp_get = 22[dC]
abundance
X : parts per Million : 13C
166.8637
143.3421
136.1884
129.7310
127.9568
127.7374
127.3464
126.6405
125.6486
121.0892
113.0884
107.3159
88.2011
76.5834
74.6376
42.3027
38.2680
35.7117
Me
O
N
N
Tr
N
N
DMAS

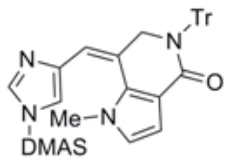
APPENDIX 47
^{1}H AND ^{13}C NMR SPECTRA OF
(*Z*)-*N*,*N*-Dimethyl-4-((1-methyl-4-oxo-5-trityl-5,6-dihydro-1H-pyrrolo[3,2-c]pyridin-7(4H)-ylidene)methyl)-1H-imidazole-1-sulfonamide (164)

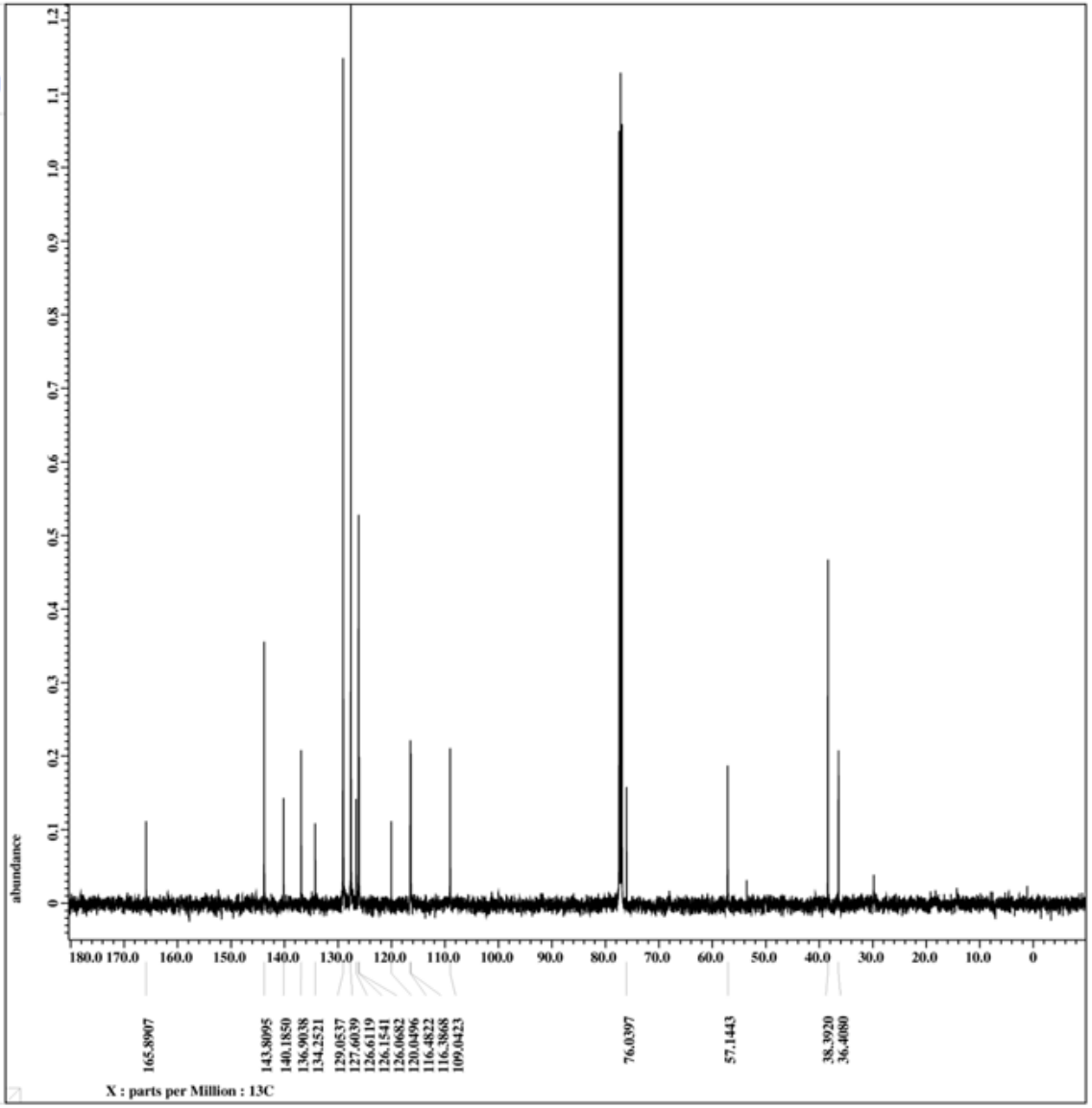

JEOL
Filename = MRB_V_115_tritylmethy
Author = delta
Experiment = single_pulse.ex2
Sample_id = S#671165
Solvent = CHLOROFORM-D
Creation_time = 29-SEP-2010 08:39:08
Revision_time = 28-SEP-2010 18:45:17
Current_time = 7-NOV-2010 00:13:04
Comment = single_pulse
Data_format = 1D REAL
Dim_size = 13107
Dim_title = 1H
Dim_units = [ppm]
Dimensions = X
Site = ECA 500
Spectrometer = JNM-ECA500
Field_strength = 11.7473579[T] (500[MH
X_acq_duration = 1.74587904[s]
X_domain = 1H
X_freq = 500.15991521[MHz]
X_offset = 5.0[ppm]
X_points = 16384
X_prescans = 0
X_resolution = 0.57277737[Hz]
X_sweep = 9.38438438[kHz]
Irr_domain = 1H
Irr_freq = 500.15991521[MHz]
Irr_offset = 5.0[ppm]
Tri_domain = 1H
Tri_freq = 500.15991521[MHz]
Tri_offset = 5.0[ppm]
Clipped = FALSE
Mod_return = 1
Scans = 16
Total_scans = 16
X_90_width = 12.54[us]
X_acq_time = 1.74587904[s]
X_angle = 45[deg]
X_atn = 4[dB]
X_pulse = 6.27[us]
Irr_mode = Off
Tri_mode = Off
Dante_presat = FALSE
Initial_wait = 1[s]
Recvr_gain = 36
Relaxation_delay = 5[s]
Repetition_time = 6.74587904[s]
Temp_get = 21.9[dC]
Tr
N
O
N
N
Me
N
DMAS
abundance
X : parts per Million : 1H
6.0
2.95
2.02
1.04
3.07
5.99
6.57
0.94
1
0.94
7.5618
7.5469
7.2537
7.2388
7.2228
7.1850
7.1312
6.5575
6.5300
6.4060
4.0529
3.1471
2.9261



```
Filename          = MRB_V_115_tritylmethy
Author            = delta
Experiment        = single_pulse.ex2
Sample_id         = S#671165
Solvent           = CHLOROFORM-D
Creation_time     = 29-SEP-2010 08:39:08
Revision_time     = 28-SEP-2010 18:45:17
Current_time      =  7-NOV-2010 00:13:55

Comment           = single_pulse
Data_format       = 1D REAL
Dim_size          = 13107
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 1.74587904[s]
X_domain          = 1H
X_freq            = 500.15991521[MHz]
X_offset          = 5.0[ppm]
X_points          = 16384
X_prescans        = 0
X_resolution      = 0.57277737[Hz]
X_sweep           = 9.38438438[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Tri_domain        = 1H
Tri_freq          = 500.15991521[MHz]
Tri_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 16
Total_scans       = 16

X_90_width        = 12.54[us]
X_acq_time        = 1.74587904[s]
X_angle           = 45[deg]
X_atn             = 4[dB]
X_pulse           = 6.27[us]
Irr_mode          = Off
Tri_mode          = Off
Dante_presat      = FALSE
Initial_wait      = 1[s]
Recvr_gain        = 36
Relaxation_delay  = 5[s]
Repetition_time   = 6.74587904[s]
Temp_get          = 21.9[dC]
```

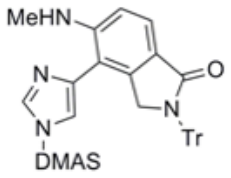
```
Filename          = MRB_V_115_tritylmethy
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#828526
Solvent           = CHLOROFORM-D
Creation_time     = 28-SEP-2010 13:02:59
Revision_time     = 10-OCT-2010 23:21:41
Current_time      =  7-NOV-2010 00:14:37

Comment           = single pulse decouple
Data_format       = 1D COMPLEX
Dim_size          = 26214
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 0.83361792[s]
X_domain          = 13C
X_freq            = 125.76529768[MHz]
X_offset          = 100[ppm]
X_points          = 32768
X_prescans        = 4
X_resolution      = 1.19959034[Hz]
X_sweep           = 39.3081761[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 10
Scans             = 80
Total_scans       = 80

X_90_width        = 10.73[us]
X_acq_time        = 0.83361792[s]
X_angle           = 30[deg]
X_atn             = 9[dB]
X_pulse           = 3.57666667[us]
Irr_atn_dec       = 20[dB]
Irr_atn_noe       = 20[dB]
Irr_noise         = WALTZ
Decoupling        = TRUE
Initial_wait      = 1[s]
Noe               = TRUE
Noe_time          = 2[s]
Recvr_gain        = 50
Relaxation_delay  = 2[s]
Repetition_time   = 2.83361792[s]
Temp_get          = 22.3[dC]
```

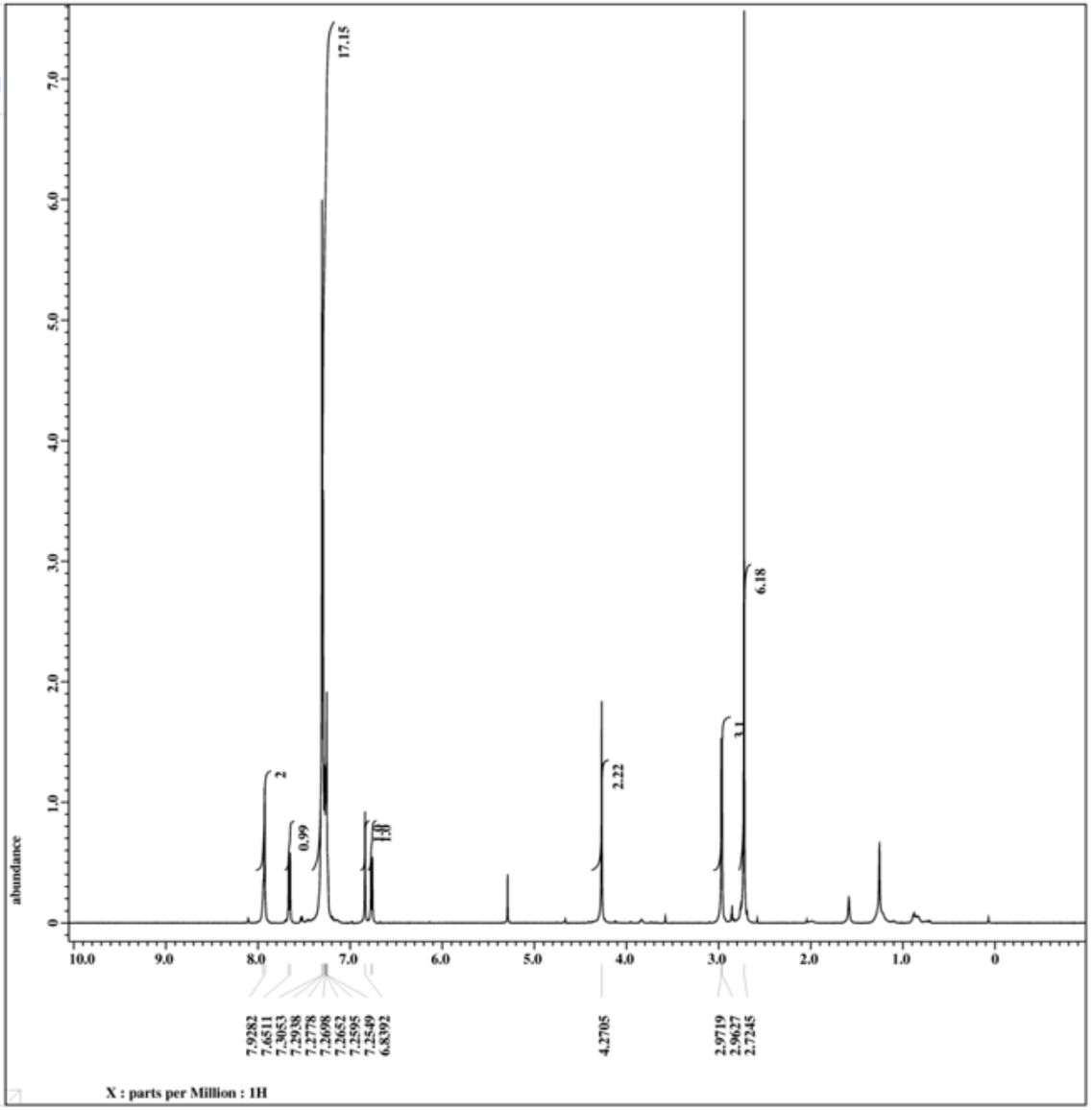


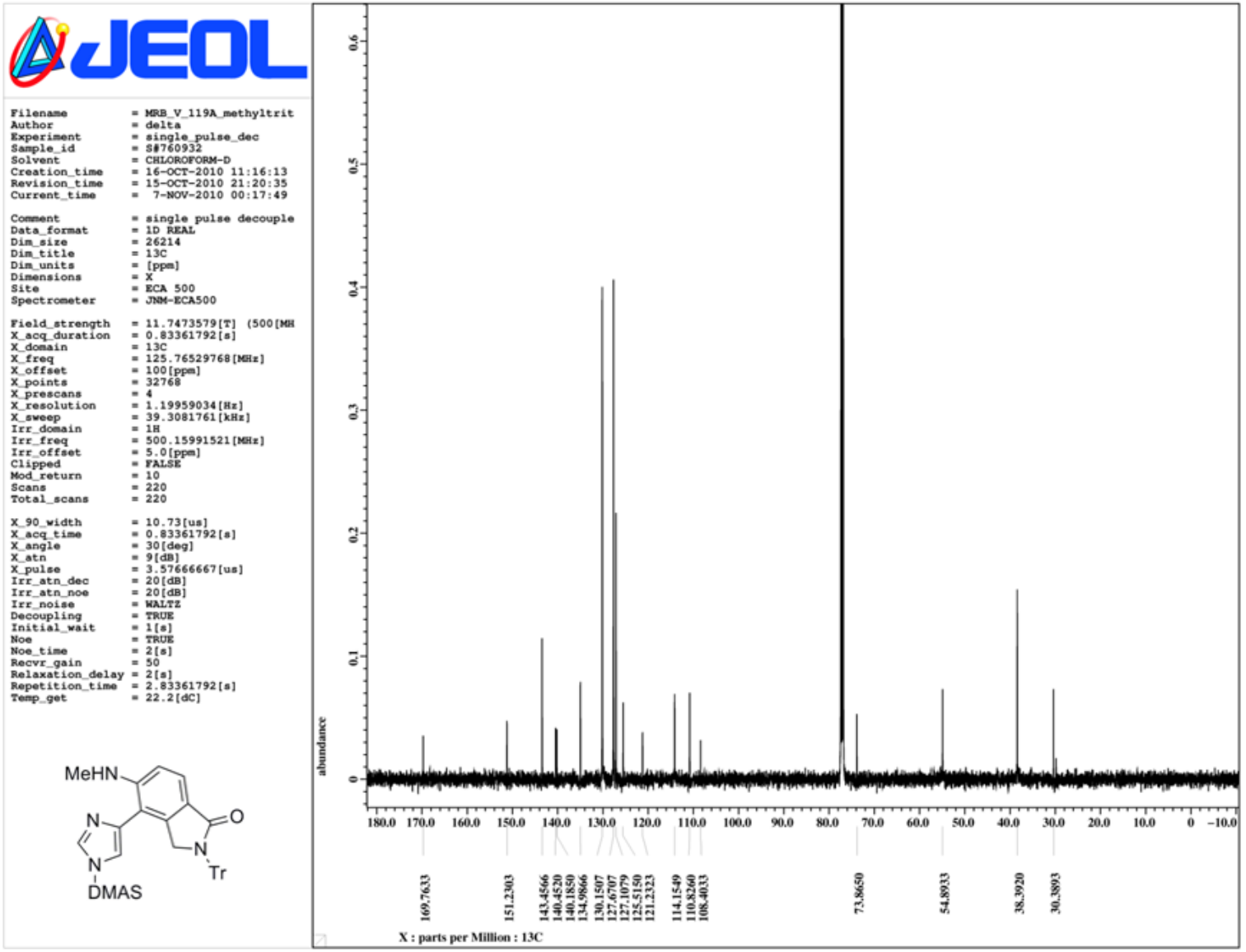


APPENDIX 48
^{1}H AND ^{13}C NMR SPECTRA OF
***N*,*N*-Dimethyl-4-(5-(methylamino)-3-oxo-2-tritylisoindolin-4-yl)-1H-imidazole-1-sulfonamide (170)**

Filename	= MRB_V_119A_methyltrit
Author	= delta
Experiment	= single_pulse.ex2
Sample_id	= S#759695
Solvent	= CHLOROFORM-D
Creation_time	= 16-OCT-2010 11:04:48
Revision_time	= 7-NOV-2010 00:16:33
Current_time	= 7-NOV-2010 00:17:15
Comment	= single_pulse
Data_format	= 1D REAL
Dim_size	= 13107
Dim_title	= 1H
Dim_units	= [ppm]
Dimensions	= X
Site	= ECA 500
Spectrometer	= JNM-ECA500
Field_strength	= 11.7473579[T] (500[MH
X_acq_duration	= 1.74587904[s]
X_domain	= 1H
X_freq	= 500.15991521[MHz]
X_offset	= 5.0[ppm]
X_points	= 16384
X_prescans	= 0
X_resolution	= 0.57277737[Hz]
X_sweep	= 9.38438438[kHz]
Irr_domain	= 1H
Irr_freq	= 500.15991521[MHz]
Irr_offset	= 5.0[ppm]
Tri_domain	= 1H
Tri_freq	= 500.15991521[MHz]
Tri_offset	= 5.0[ppm]
Clipped	= FALSE
Mod_return	= 1
Scans	= 16
Total_scans	= 16
X_90_width	= 12.54[us]
X_acq_time	= 1.74587904[s]
X_angle	= 45[deg]
X_atn	= 4[dB]
X_pulse	= 6.27[us]
Irr_mode	= Off
Tri_mode	= Off
Dante_presat	= FALSE
Initial_wait	= 1[s]
Recvr_gain	= 42
Relaxation_delay	= 5[s]
Repetition_time	= 6.74587904[s]
Temp_get	= 21.8[dC]





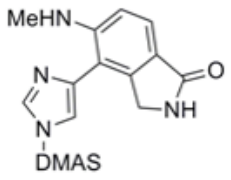


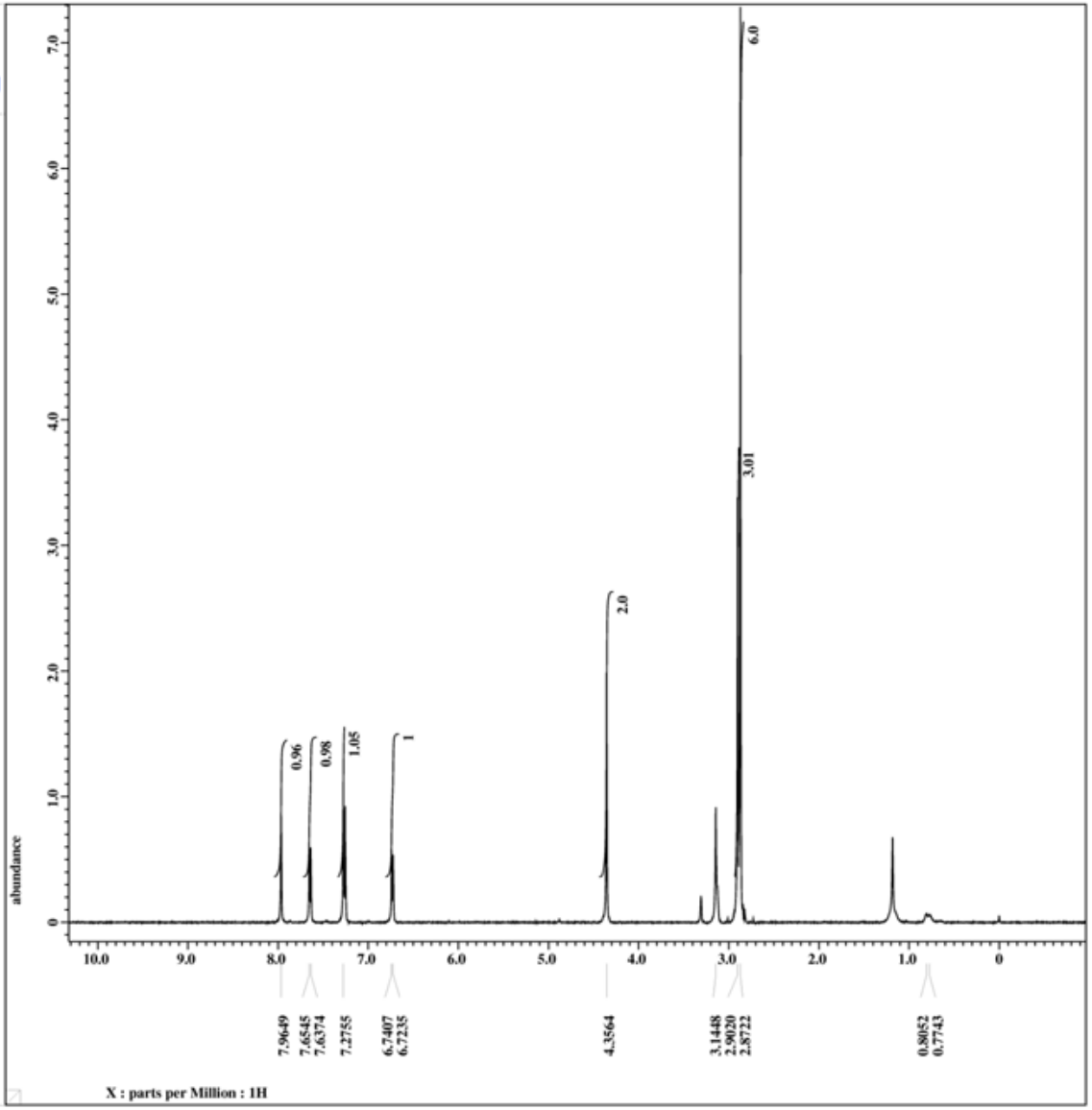
```
Filename          = MRB_V_119A_methyltrit
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#760932
Solvent           = CHLOROFORM-D
Creation_time     = 16-OCT-2010 11:16:13
Revision_time     = 15-OCT-2010 21:20:35
Current_time      =  7-NOV-2010 00:17:49

Comment           = single pulse decouple
Data_format       = 1D REAL
Dim_size          = 26214
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 0.83361792[s]
X_domain          = 13C
X_freq            = 125.76529768[MHz]
X_offset          = 100[ppm]
X_points          = 32768
X_prescans        = 4
X_resolution      = 1.19959034[Hz]
X_sweep           = 39.3081761[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 10
Scans             = 220
Total_scans       = 220

X_90_width        = 10.73[us]
X_acq_time        = 0.83361792[s]
X_angle           = 30[deg]
X_atn             = 9[dB]
X_pulse           = 3.57666667[us]
Irr_atn_dec       = 20[dB]
Irr_atn_noe       = 20[dB]
Irr_noise         = WALTZ
Decoupling        = TRUE
Initial_wait      = 1[s]
Noe               = TRUE
Noe_time          = 2[s]
Recvr_gain        = 50
Relaxation_delay  = 2[s]
Repetition_time   = 2.83361792[s]
Temp_get          = 22.2[dC]
```

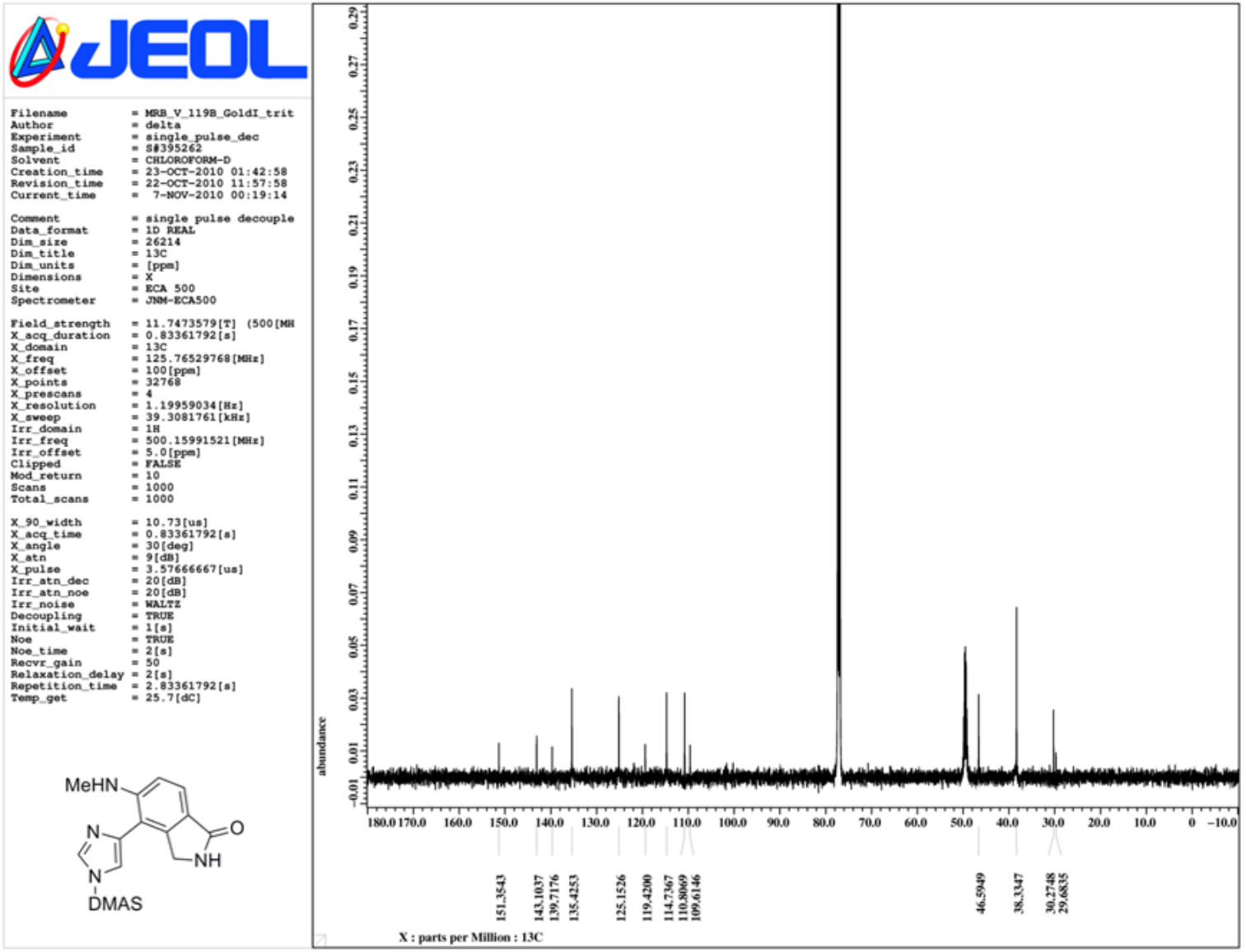
APPENDIX 49
^{1}H AND ^{13}C NMR SPECTRA OF *N*,*N*-Dimethyl-4-(5-(methylamino)-3-oxoisoindolin-4-yl)-1H-imidazole-1-sulfonamide (171)

JEOL

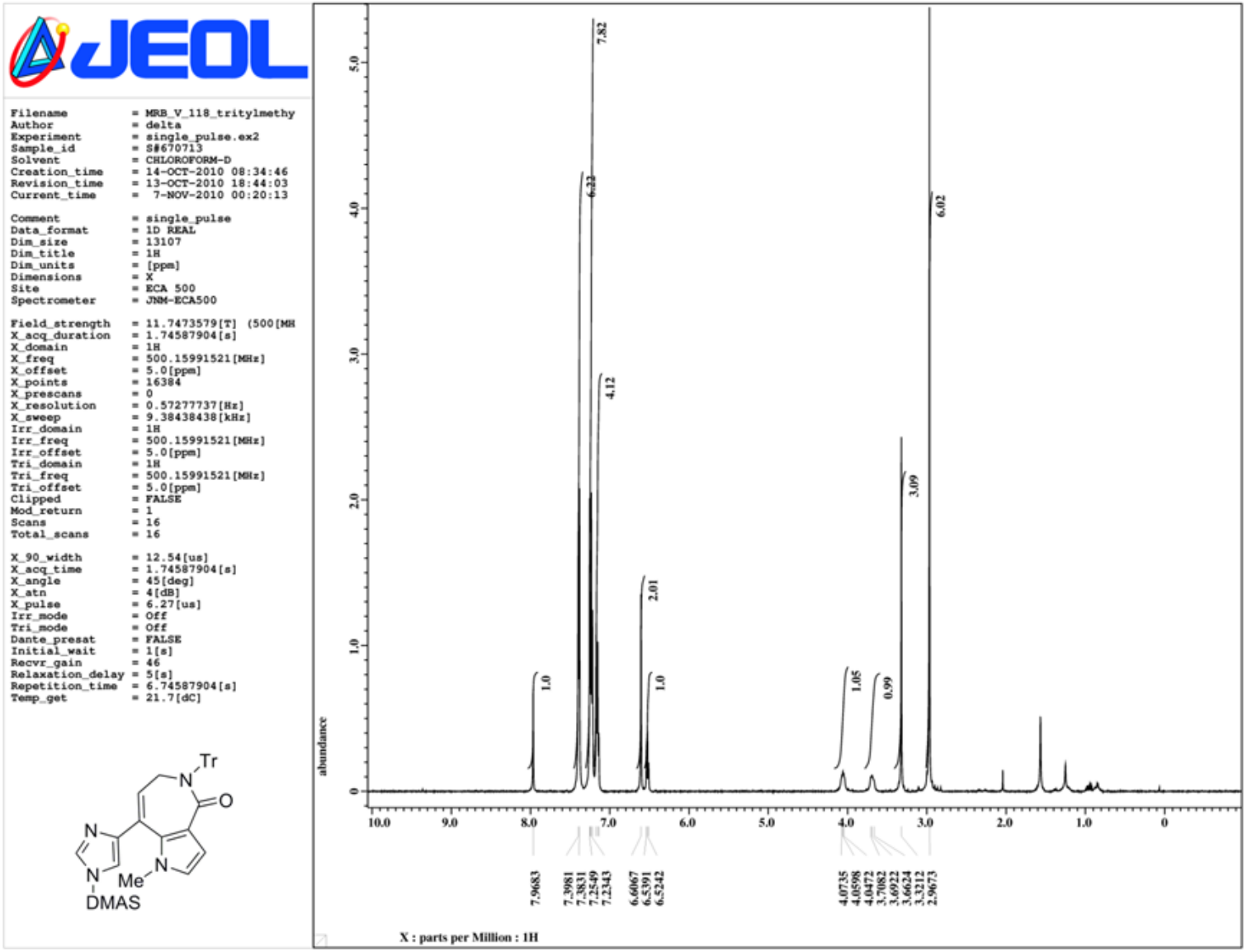
```
Filename          = MRB_V_119B_GoldI_trit
Author            = delta
Experiment        = single_pulse.ex2
Sample_id         = S#774232
Solvent           = CHLOROFORM-D
Creation_time     = 23-OCT-2010 11:28:04
Revision_time     = 22-OCT-2010 21:36:31
Current_time      =  7-NOV-2010 00:18:34

Comment           = single_pulse
Data_format       = 1D REAL
Dim_size          = 13107
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 1.74587904[s]
X_domain          = 1H
X_freq            = 500.15991521[MHz]
X_offset          = 5.0[ppm]
X_points          = 16384
X_prescans        = 0
X_resolution      = 0.57277737[Hz]
X_sweep           = 9.38438438[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Tri_domain        = 1H
Tri_freq          = 500.15991521[MHz]
Tri_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 9
Total_scans       = 9

X_90_width        = 12.54[us]
X_acq_time        = 1.74587904[s]
X_angle           = 45[deg]
X_atn             = 4[dB]
X_pulse           = 6.27[us]
Irr_mode          = Off
Tri_mode          = Off
Dante_presat      = FALSE
Initial_wait      = 1[s]
Recvr_gain        = 46
Relaxation_delay  = 5[s]
Repetition_time   = 6.74587904[s]
Temp_get          = 25.2[dC]
```



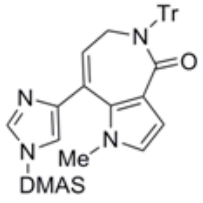


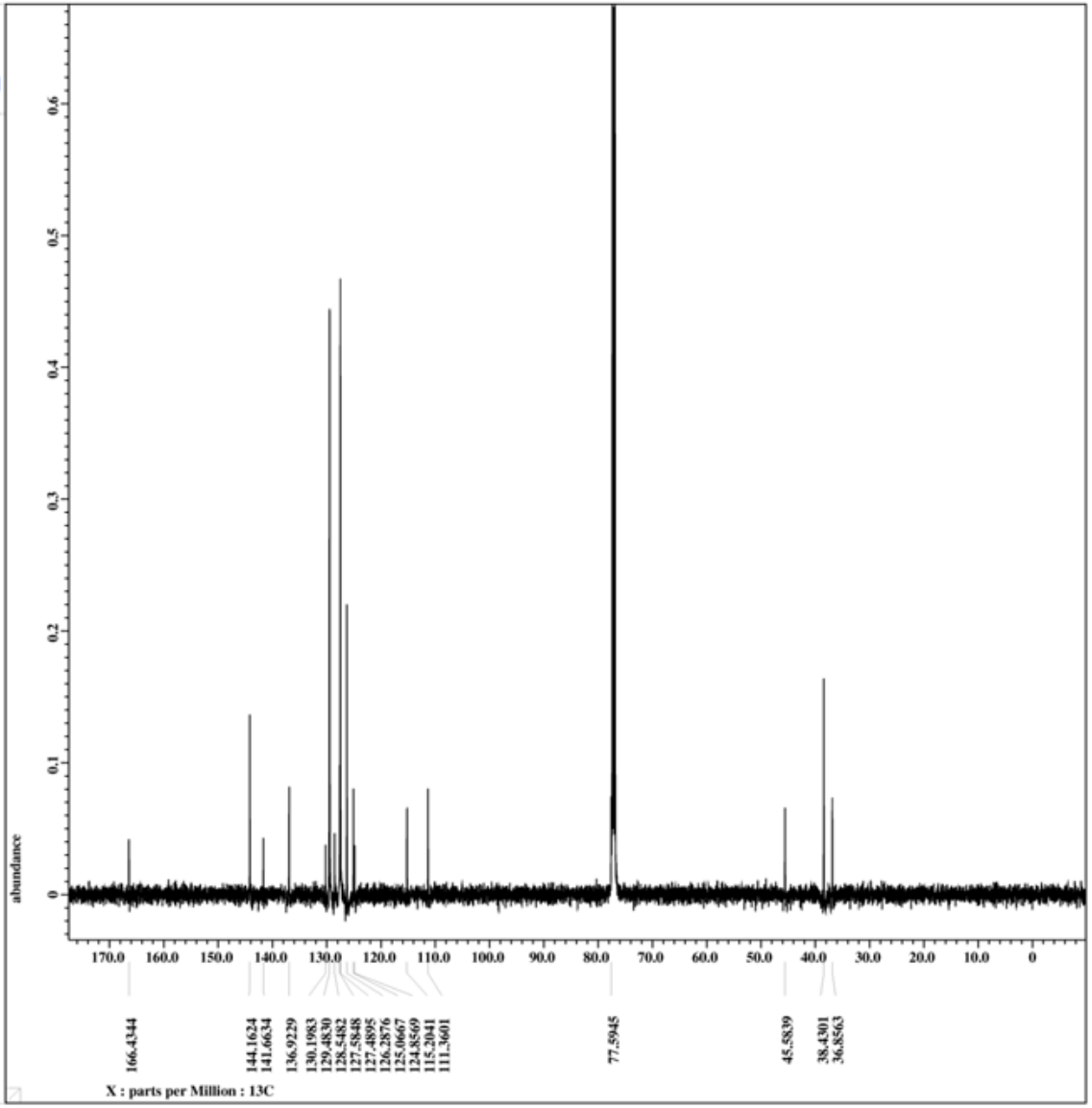

Filename = MRB_V_119B_GoldI_trit
Author = delta
Experiment = single_pulse_dec
Sample_id = S#395262
Solvent = CHLOROFORM-D
Creation_time = 23-OCT-2010 01:42:58
Revision_time = 22-OCT-2010 11:57:58
Current_time = 7-NOV-2010 00:19:14
Comment = single pulse decouple
Data_format = 1D REAL
Dim_size = 26214
Dim_title = 13C
Dim_units = [ppm]
Dimensions = X
Site = ECA 500
Spectrometer = JNM-ECA500
Field_strength = 11.7473579[T] (500[MH
X_acq_duration = 0.83361792[s]
X_domain = 13C
X_freq = 125.76529768[MHz]
X_offset = 100[ppm]
X_points = 32768
X_prescans = 4
X_resolution = 1.19959034[Hz]
X_sweep = 39.3081761[kHz]
Irr_domain = 1H
Irr_freq = 500.15991521[MHz]
Irr_offset = 5.0[ppm]
Clipped = FALSE
Mod_return = 10
Scans = 1000
Total_scans = 1000
X_90_width = 10.73[us]
X_acq_time = 0.83361792[s]
X_angle = 30[deg]
X_atn = 9[dB]
X_pulse = 3.57666667[us]
Irr_atn_dec = 20[dB]
Irr_atn_noe = 20[dB]
Irr_noise = WALTZ
Decoupling = TRUE
Initial_wait = 1[s]
Noe = TRUE
Noe_time = 2[s]
Recvr_gain = 50
Relaxation_delay = 2[s]
Repetition_time = 2.83361792[s]
Temp_get = 25.7[dC]
MeHN
N
N
DMAS
O
NH
abundance
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
151.3543
143.1037
139.7176
135.4253
125.1526
119.4200
114.7367
110.8069
109.6146
46.5949
38.3347
30.2748
29.6835
X : parts per Million : 13C

APPENDIX 50
^{1}H AND ^{13}C NMR SPECTRA OF
***N*,*N*-Dimethyl-4-(1-methyl-4-oxo-5-trityl-1,4,5,6-tetrahydropyrrolo[3,2-c]azepin-8-yl)-1H-imidazole-1-sulfonamide (173)**


JEOL
Filename = MRB_V_118_tritylmethy
Author = delta
Experiment = single_pulse.ex2
Sample_id = S#670713
Solvent = CHLOROFORM-D
Creation_time = 14-OCT-2010 08:34:46
Revision_time = 13-OCT-2010 18:44:03
Current_time = 7-NOV-2010 00:20:13
Comment = single_pulse
Data_format = 1D REAL
Dim_size = 13107
Dim_title = 1H
Dim_units = [ppm]
Dimensions = X
Site = ECA 500
Spectrometer = JNM-ECA500
Field_strength = 11.7473579[T] (500[MH
X_acq_duration = 1.74587904[s]
X_domain = 1H
X_freq = 500.15991521[MHz]
X_offset = 5.0[ppm]
X_points = 16384
X_prescans = 0
X_resolution = 0.57277737[Hz]
X_sweep = 9.38438438[kHz]
Irr_domain = 1H
Irr_freq = 500.15991521[MHz]
Irr_offset = 5.0[ppm]
Tri_domain = 1H
Tri_freq = 500.15991521[MHz]
Tri_offset = 5.0[ppm]
Clipped = FALSE
Mod_return = 1
Scans = 16
Total_scans = 16
X_90_width = 12.54[us]
X_acq_time = 1.74587904[s]
X_angle = 45[deg]
X_atn = 4[dB]
X_pulse = 6.27[us]
Irr_mode = Off
Tri_mode = Off
Dante_presat = FALSE
Initial_wait = 1[s]
Recvr_gain = 46
Relaxation_delay = 5[s]
Repetition_time = 6.74587904[s]
Temp_get = 21.7[dC]
Tr
N
O
N
N
N
Me
DMAS
abundance
7.82
6.33
4.12
6.02
3.09
2.01
1.0
1.0
1.05
0.99
1.0
7.9683
7.3981
7.3831
7.2549
7.2343
6.6067
6.5391
6.5242
4.0735
4.0598
4.0472
3.7082
3.6922
3.6624
3.3212
2.9673
X : parts per Million : 1H

```
Filename          = MRB_V_118_tritylmethy
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#653707
Solvent           = CHLOROFORM-D
Creation_time     = 14-OCT-2010 08:12:30
Revision_time     = 13-OCT-2010 18:19:07
Current_time      =  7-NOV-2010 00:20:38

Comment           = single pulse decouple
Data_format       = 1D REAL
Dim_size          = 26214
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 0.83361792[s]
X_domain          = 13C
X_freq            = 125.76529768[MHz]
X_offset          = 100[ppm]
X_points          = 32768
X_prescans        = 4
X_resolution      = 1.19959034[Hz]
X_sweep           = 39.3081761[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 10
Scans             = 160
Total_scans       = 160

X_90_width        = 10.73[us]
X_acq_time        = 0.83361792[s]
X_angle           = 30[deg]
X_atn             = 9[dB]
X_pulse           = 3.57666667[us]
Irr_atn_dec       = 20[dB]
Irr_atn_noe       = 20[dB]
Irr_noise         = WALTZ
Decoupling        = TRUE
Initial_wait      = 1[s]
Noe               = TRUE
Noe_time          = 2[s]
Recvr_gain        = 50
Relaxation_delay  = 2[s]
Repetition_time   = 2.83361792[s]
Temp_get          = 22.1[dC]
```

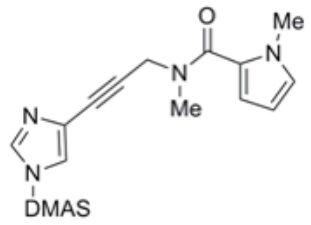


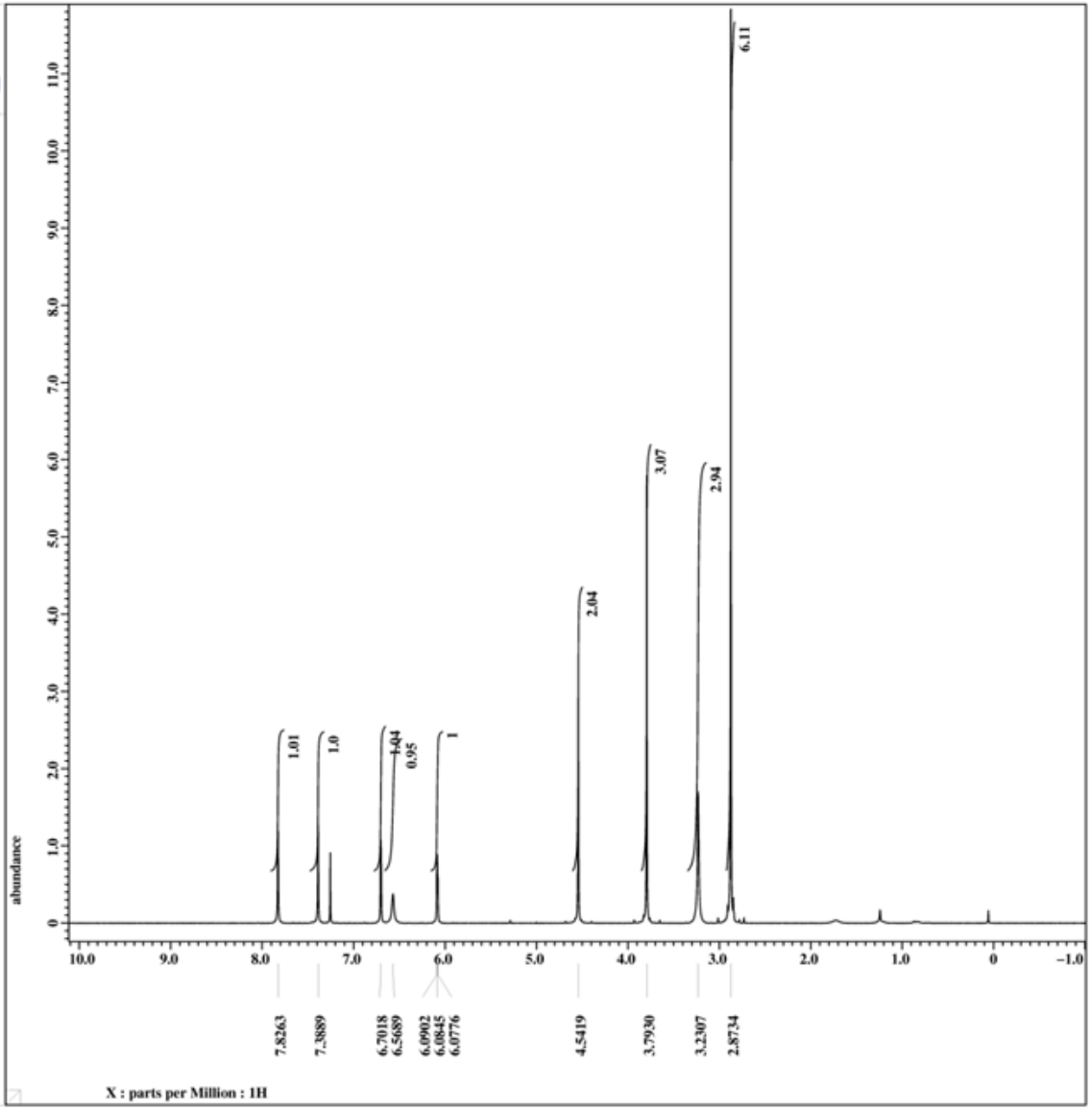


APPENDIX 51
^{1}H AND ^{13}C NMR SPECTRA OF
***N*-(3-(1-(*N*,*N*-Dimethylsulfamoyl)-1H-imidazol-4-yl)prop-2-ynyl)-*N*-1-dimethyl-1H-pyrrole-2-carboxamide (175)**

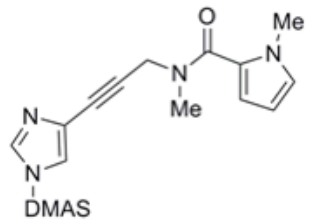
JEOL

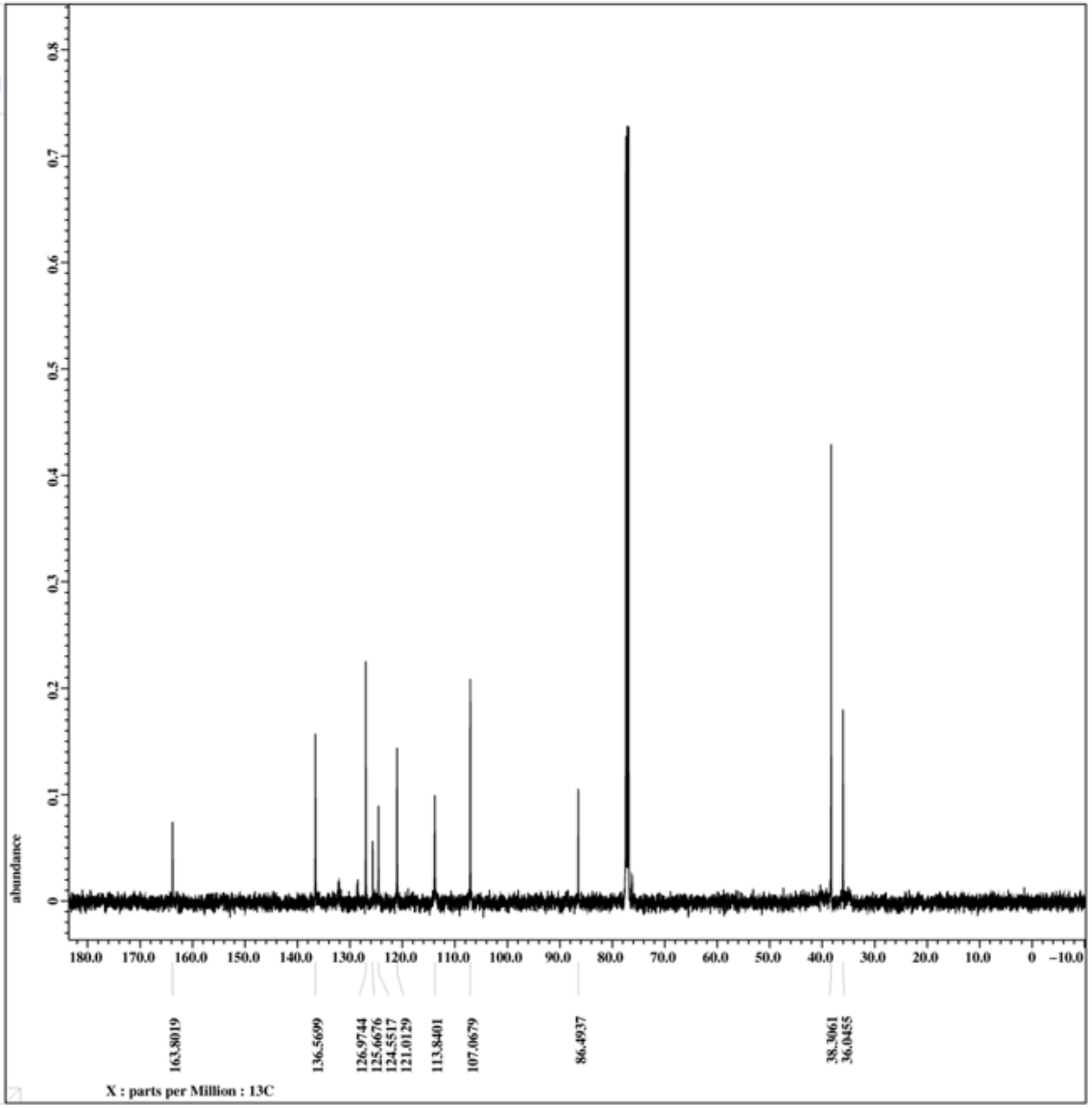
```
Filename          = MRB_V_7_methtlmethyl_
Author            = delta
Experiment        = single_pulse.ex2
Sample_id         = S#680671
Solvent           = CHLOROFORM-D
Creation_time     = 29-SEP-2010 08:54:45
Revision_time     = 28-SEP-2010 18:59:36
Current_time      =  7-NOV-2010 00:21:28

Comment           = single_pulse
Data_format       = 1D REAL
Dim_size          = 13107
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 1.74587904[s]
X_domain          = 1H
X_freq            = 500.15991521[MHz]
X_offset          = 5.0[ppm]
X_points          = 16384
X_prescans        = 0
X_resolution      = 0.57277737[Hz]
X_sweep           = 9.38438438[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Tri_domain        = 1H
Tri_freq          = 500.15991521[MHz]
Tri_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 12
Total_scans       = 12

X_90_width        = 12.54[us]
X_acq_time        = 1.74587904[s]
X_angle           = 45[deg]
X_atn             = 4[dB]
X_pulse           = 6.27[us]
Irr_mode          = Off
Tri_mode          = Off
Dante_presat      = FALSE
Initial_wait      = 1[s]
Recvr_gain        = 40
Relaxation_delay  = 5[s]
Repetition_time   = 6.74587904[s]
Temp_get          = 21.8[dC]
```





Filename	= MRB_V_7_methylmethyl_
Author	= delta
Experiment	= single_pulse_dec
Sample_id	= S#818369
Solvent	= CHLOROFORM-D
Creation_time	= 28-SEP-2010 12:51:02
Revision_time	= 10-OCT-2010 23:27:25
Current_time	= 7-NOV-2010 00:22:08
Comment	= single pulse decouple
Data_format	= 1D COMPLEX
Dim_size	= 26214
Dim_title	= 13C
Dim_units	= [ppm]
Dimensions	= X
Site	= ECA 500
Spectrometer	= JNM-ECA500
Field_strength	= 11.7473579[T] (500[MH
X_acq_duration	= 0.83361792[s]
X_domain	= 13C
X_freq	= 125.76529768[MHz]
X_offset	= 100[ppm]
X_points	= 32768
X_prescans	= 4
X_resolution	= 1.19959034[Hz]
X_sweep	= 39.3081761[kHz]
Irr_domain	= 1H
Irr_freq	= 500.15991521[MHz]
Irr_offset	= 5.0[ppm]
Clipped	= FALSE
Mod_return	= 10
Scans	= 160
Total_scans	= 160
X_90_width	= 10.73[us]
X_acq_time	= 0.83361792[s]
X_angle	= 30[deg]
X_atn	= 9[dB]
X_pulse	= 3.57666667[us]
Irr_atn_dec	= 20[dB]
Irr_atn_noe	= 20[dB]
Irr_noise	= WALTZ
Decoupling	= TRUE
Initial_wait	= 1[s]
Noe	= TRUE
Noe_time	= 2[s]
Recvr_gain	= 50
Relaxation_delay	= 2[s]
Repetition_time	= 2.83361792[s]
Temp_get	= 22.5[dC]

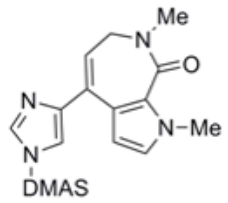


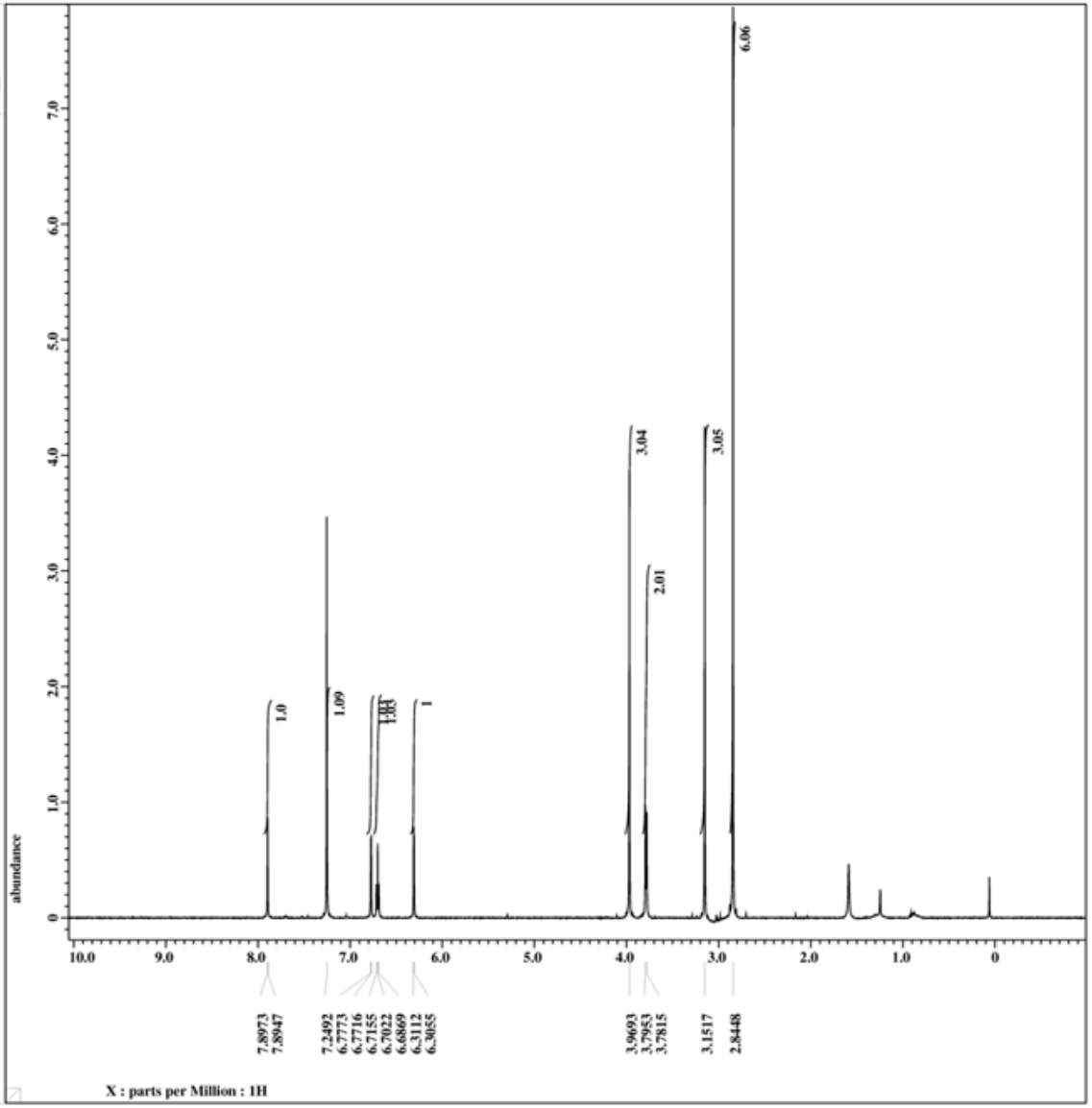


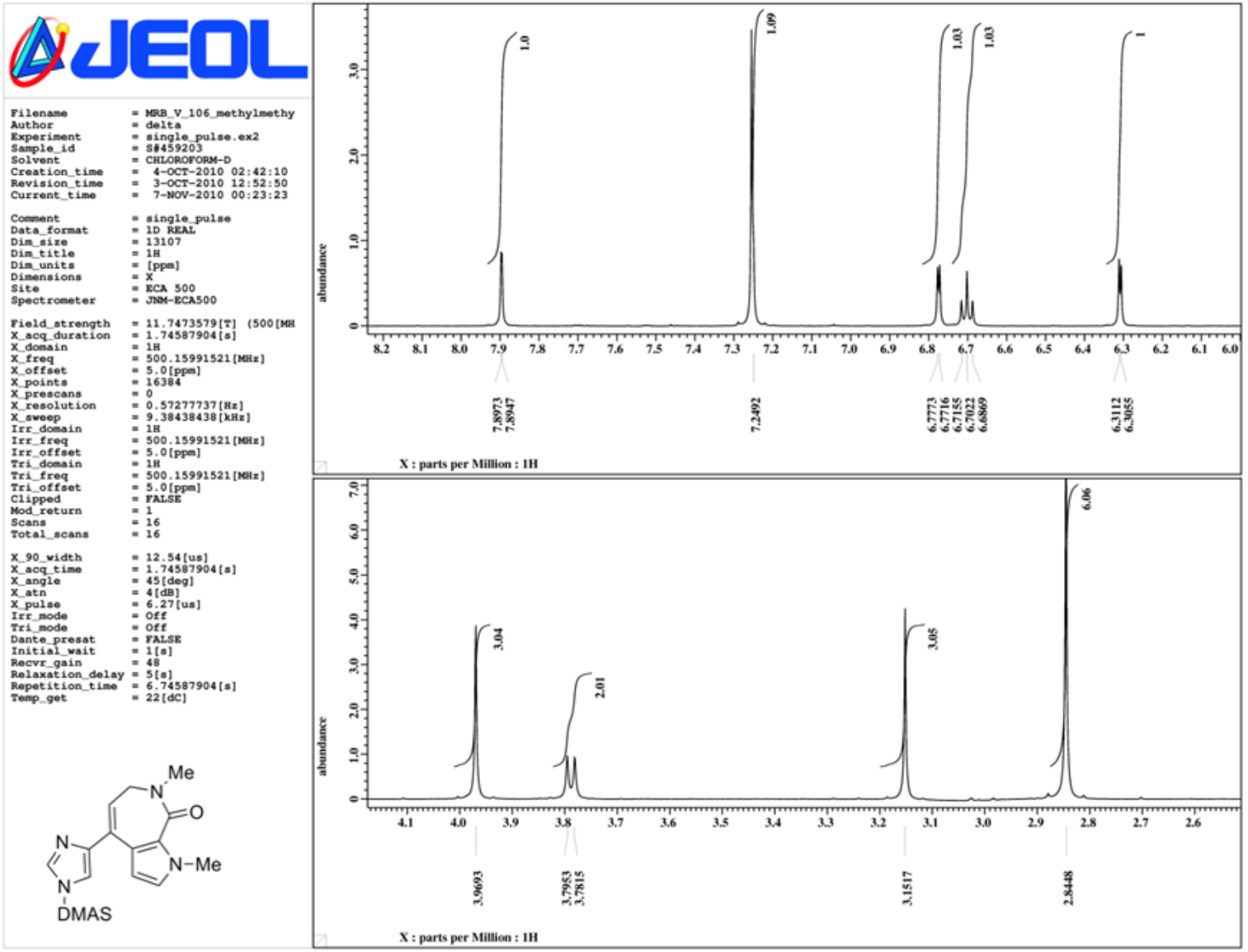
APPENDIX 52
^{1}H AND ^{13}C NMR SPECTRA OF
4-(1,7-Dimethyl-8-oxo-1,6,7,8-tetrahydropyrrolo[2,3-c]azepin-4-yl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide (176)

JEOL

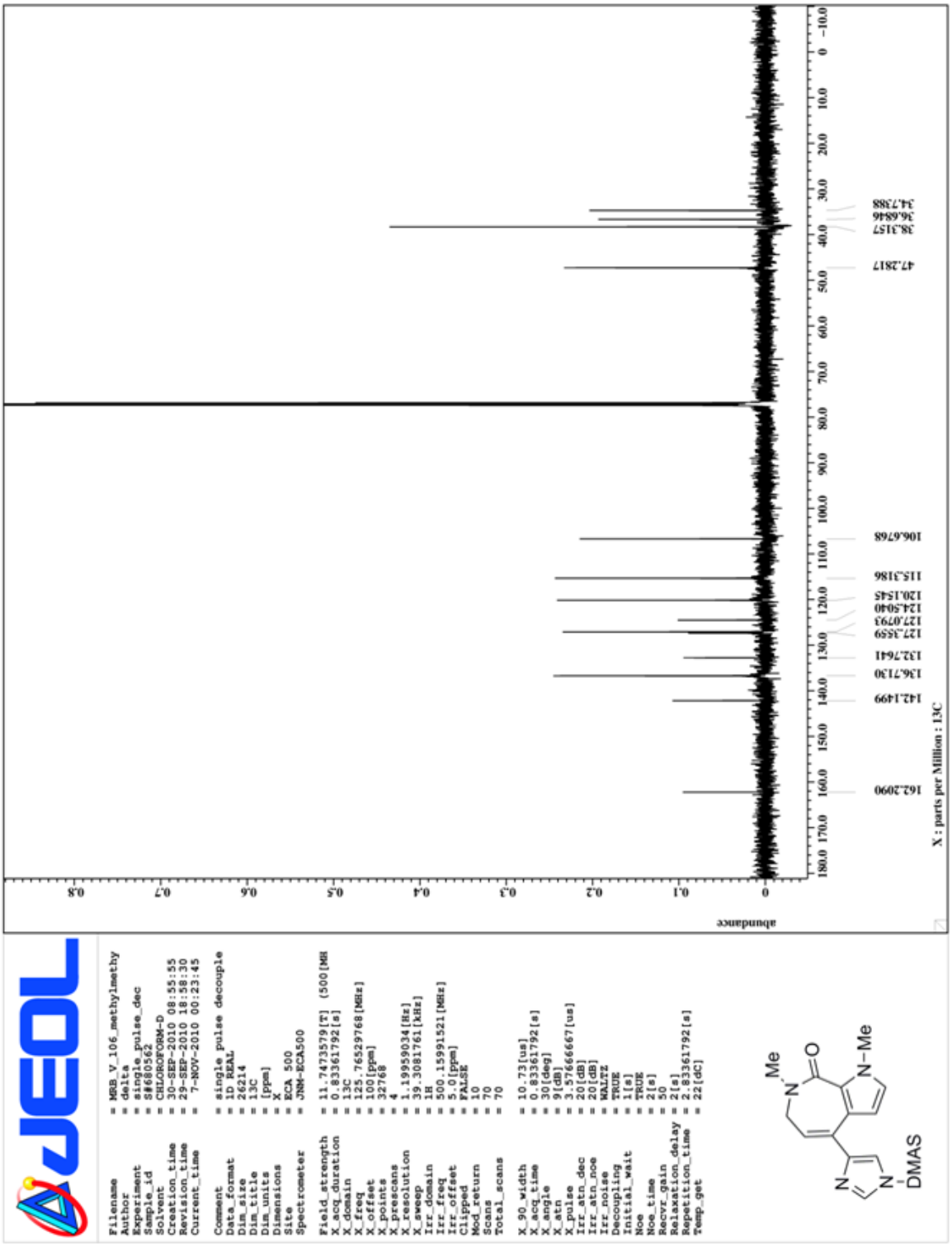
Filename	= MRB_V_106_methylmethy
Author	= delta
Experiment	= single_pulse.ex2
Sample_id	= S#459203
Solvent	= CHLOROFORM-D
Creation_time	= 4-OCT-2010 02:42:10
Revision_time	= 3-OCT-2010 12:52:50
Current_time	= 7-NOV-2010 00:22:55
Comment	= single_pulse
Data_format	= 1D REAL
Dim_size	= 13107
Dim_title	= 1H
Dim_units	= [ppm]
Dimensions	= X
Site	= ECA 500
Spectrometer	= JNM-ECA500
Field_strength	= 11.7473579[T] (500[MH
X_acq_duration	= 1.74587904[s]
X_domain	= 1H
X_freq	= 500.15991521[MHz]
X_offset	= 5.0[ppm]
X_points	= 16384
X_prescans	= 0
X_resolution	= 0.57277737[Hz]
X_sweep	= 9.38438438[kHz]
Irr_domain	= 1H
Irr_freq	= 500.15991521[MHz]
Irr_offset	= 5.0[ppm]
Tri_domain	= 1H
Tri_freq	= 500.15991521[MHz]
Tri_offset	= 5.0[ppm]
Clipped	= FALSE
Mod_return	= 1
Scans	= 16
Total_scans	= 16
X_90_width	= 12.54[us]
X_acq_time	= 1.74587904[s]
X_angle	= 45[deg]
X_atn	= 4[dB]
X_pulse	= 6.27[us]
Irr_mode	= Off
Tri_mode	= Off
Dante_presat	= FALSE
Initial_wait	= 1[s]
Recvr_gain	= 48
Relaxation_delay	= 5[s]
Repetition_time	= 6.74587904[s]
Temp_get	= 22[dC]





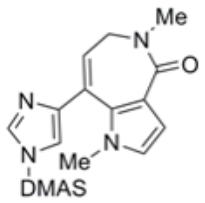


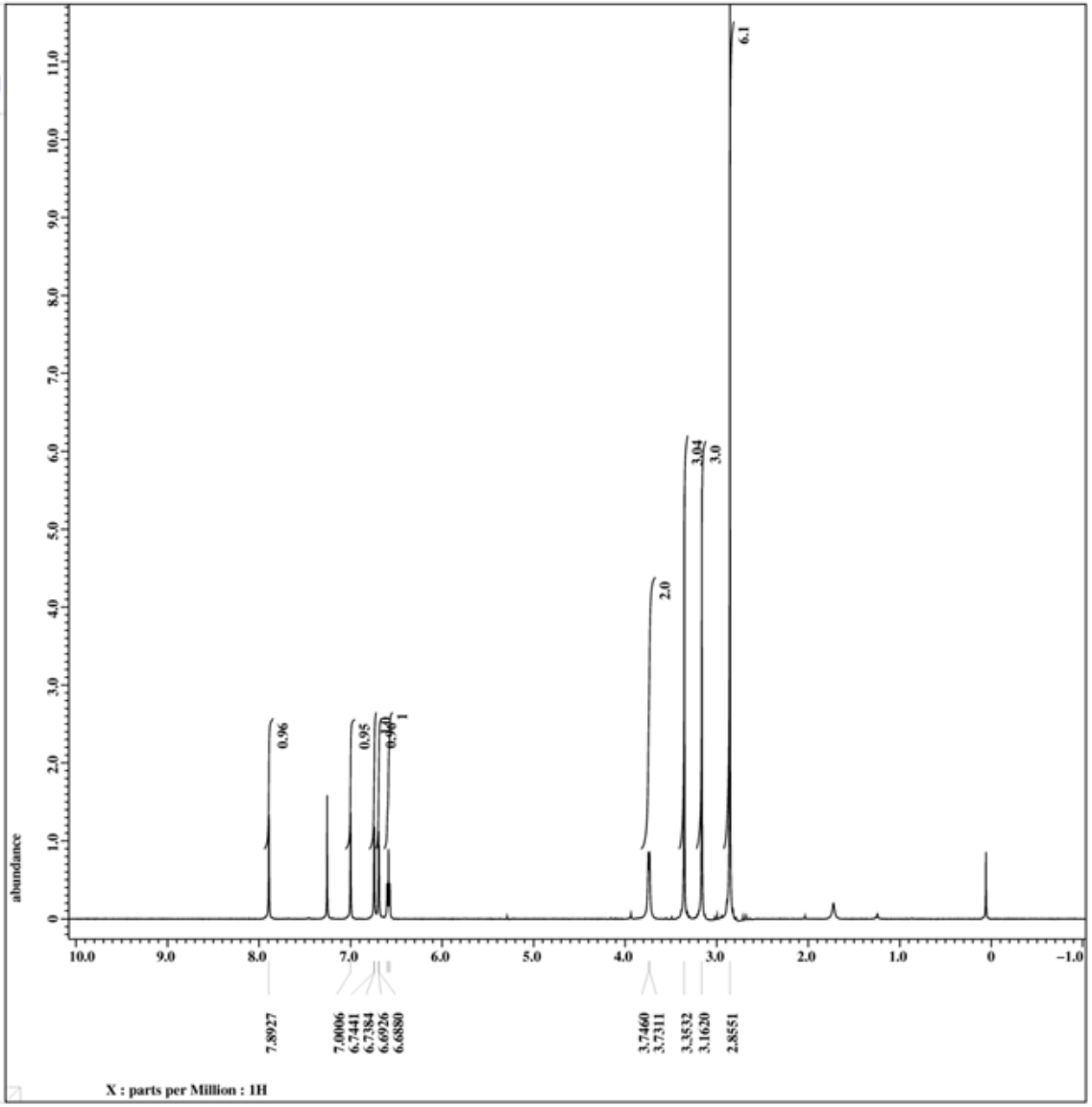
```
Filename          = MRB_V_106_methylmethy
Author            = delta
Experiment        = single_pulse.ex2
Sample_id         = S#459203
Solvent           = CHLOROFORM-D
Creation_time     =  4-OCT-2010 02:42:10
Revision_time     =  3-OCT-2010 12:52:50
Current_time      =  7-NOV-2010 00:23:23

Comment           = single_pulse
Data_format       = 1D REAL
Dim_size          = 13107
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T]  (500[MH
X_acq_duration    = 1.74587904[s]
X_domain          = 1H
X_freq            = 500.15991521[MHz]
X_offset          = 5.0[ppm]
X_points          = 16384
X_prescans        = 0
X_resolution      = 0.57277737[Hz]
X_sweep           = 9.38438438[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Tri_domain        = 1H
Tri_freq          = 500.15991521[MHz]
Tri_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 16
Total_scans       = 16

X_90_width        = 12.54[us]
X_acq_time        = 1.74587904[s]
X_angle           = 45[deg]
X_atn             = 4[dB]
X_pulse           = 6.27[us]
Irr_mode          = Off
Tri_mode          = Off
Dante_presat      = FALSE
Initial_wait      = 1[s]
Recvr_gain        = 48
Relaxation_delay  = 5[s]
Repetition_time   = 6.74587904[s]
Temp_get          = 22[dC]
```

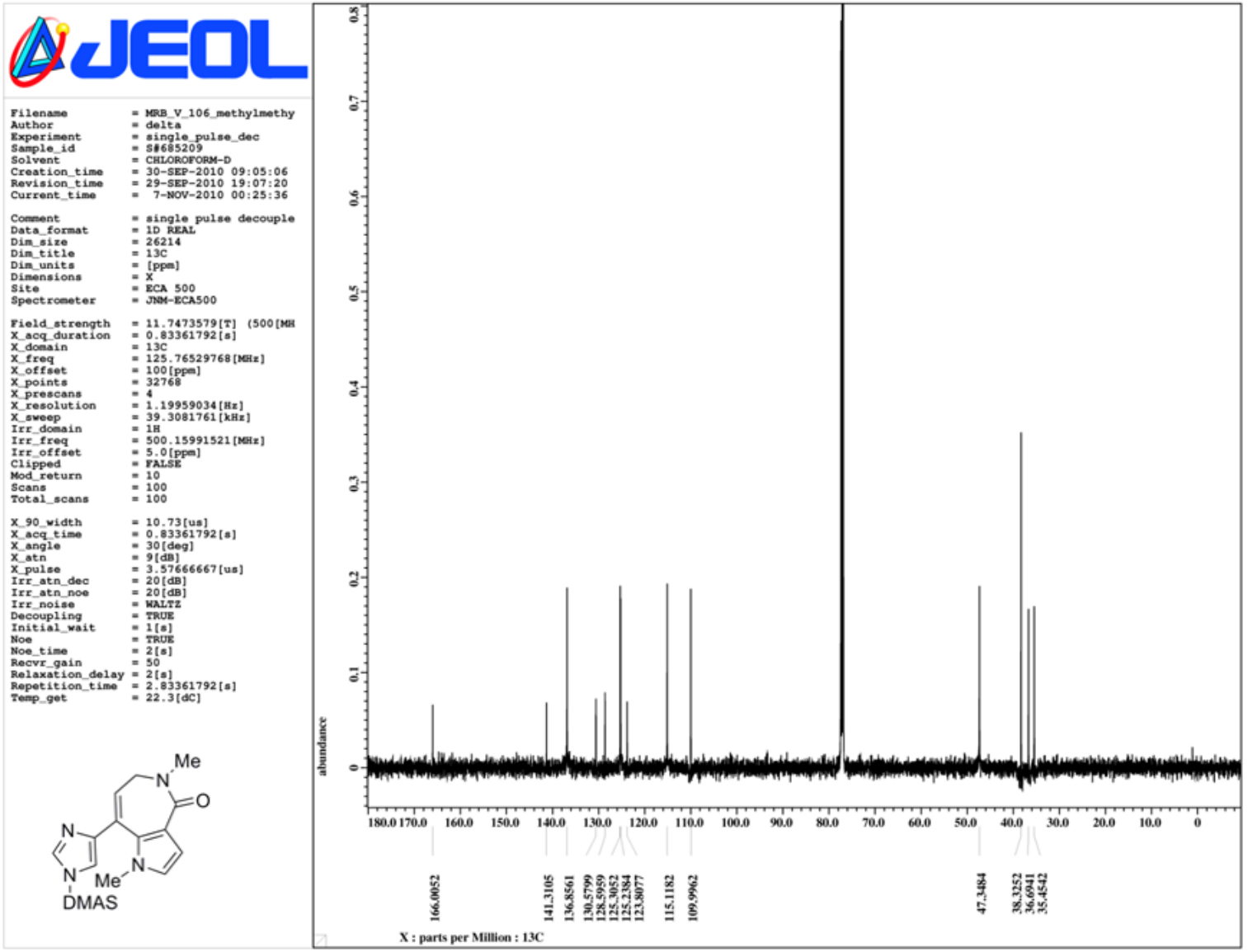

JEOL
Filename = MRB_V_106_methylmethy
Author = delta
Experiment = single_pulse_dec
Sample_id = S#680562
Solvent = CHLOROFORM-D
Creation_time = 30-SEP-2010 08:55:55
Revision_time = 29-SEP-2010 18:58:30
Current_time = 7-NOV-2010 00:23:45
Comment = single pulse decouple
Data_format = 1D REAL
Dim_size = 26214
Dim_title = 13C
Dim_units = [ppm]
Dimensions = X
Site = ECA 500
Spectrometer = JNM-ECA500
Field_strength = 11.7473579[T] (500[MH
X_acq_duration = 0.83361792[s]
X_domain = 13C
X_freq = 125.765297768[MHz]
X_offset = 100[ppm]
X_points = 32768
X_prescans = 4
X_resolution = 1.19959034[Hz]
X_sweep = 39.3081761[kHz]
Irr_domain = H
Irr_freq = 500.159991521[MHz]
Irr_offset = 5.0[ppm]
Clipped = FALSE
Mod_return = 10
Scans = 70
Total_scans = 70
X_90_width = 10.73[us]
X_acq_time = 0.83361792[s]
X_angle = 30[deg]
X_atn = 9[dB]
X_pulse = 3.57666667[us]
Irr_atn_dec = 20[dB]
Irr_atn_noe = 20[dB]
Irr_noise = WALTZ
Decoupling = TRUE
Initial_wait = 1[s]
Noe = TRUE
Noe_time = 2[s]
Recvr_gain = 50
Relaxation_delay = 2[s]
Repetition_time = 2.83361792[s]
Temp_get = 22[dC]
Me
N
O
N-Me
N
N
DMAS
abundance
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
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
X : parts per Million : 13C
162.2090
142.1499
136.7130
132.7641
127.3559
127.0793
124.5040
120.1545
115.3186
106.6768
47.2817
38.3157
36.6846
34.7388

APPENDIX 53
^{1}H AND ^{13}C NMR SPECTRA OF
4-(1,5-Dimethyl-4-oxo-1,4,5,6-tetrahydropyrrolo[3,2-c]azepin-8-yl)-*N*,*N*-dimethyl-1H-imidazole-1-sulfonamide (177)

```
Filename          = MRB_V_106_methylmethy
Author            = delta
Experiment        = single_pulse.ex2
Sample_id         = S#473281
Solvent           = CHLOROFORM-D
Creation_time     =  4-OCT-2010 03:05:52
Revision_time     =  3-OCT-2010 13:15:50
Current_time      =  7-NOV-2010 00:24:59

Comment           = single_pulse
Data_format       = 1D REAL
Dim_size          = 13107
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 1.74587904[s]
X_domain          = 1H
X_freq            = 500.15991521[MHz]
X_offset          = 5.0[ppm]
X_points          = 16384
X_prescans        = 0
X_resolution      = 0.57277737[Hz]
X_sweep           = 9.38438438[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Tri_domain        = 1H
Tri_freq          = 500.15991521[MHz]
Tri_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 16
Total_scans       = 16

X_90_width        = 12.54[us]
X_acq_time        = 1.74587904[s]
X_angle           = 45[deg]
X_atn             = 4[dB]
X_pulse           = 6.27[us]
Irr_mode          = Off
Tri_mode          = Off
Dante_presat      = FALSE
Initial_wait      = 1[s]
Recvr_gain        = 46
Relaxation_delay  = 5[s]
Repetition_time   = 6.74587904[s]
Temp_get          = 21.8[dC]
```

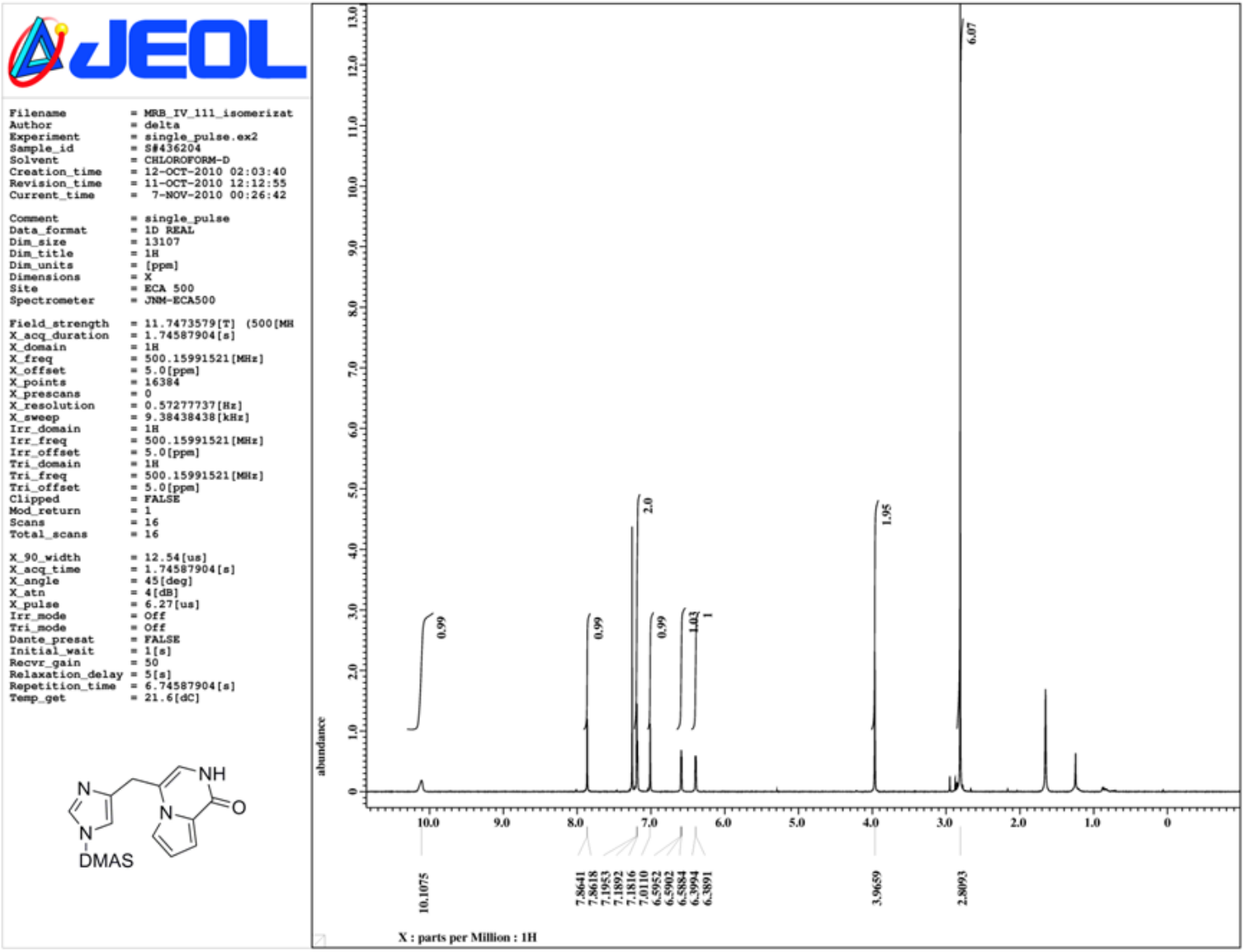






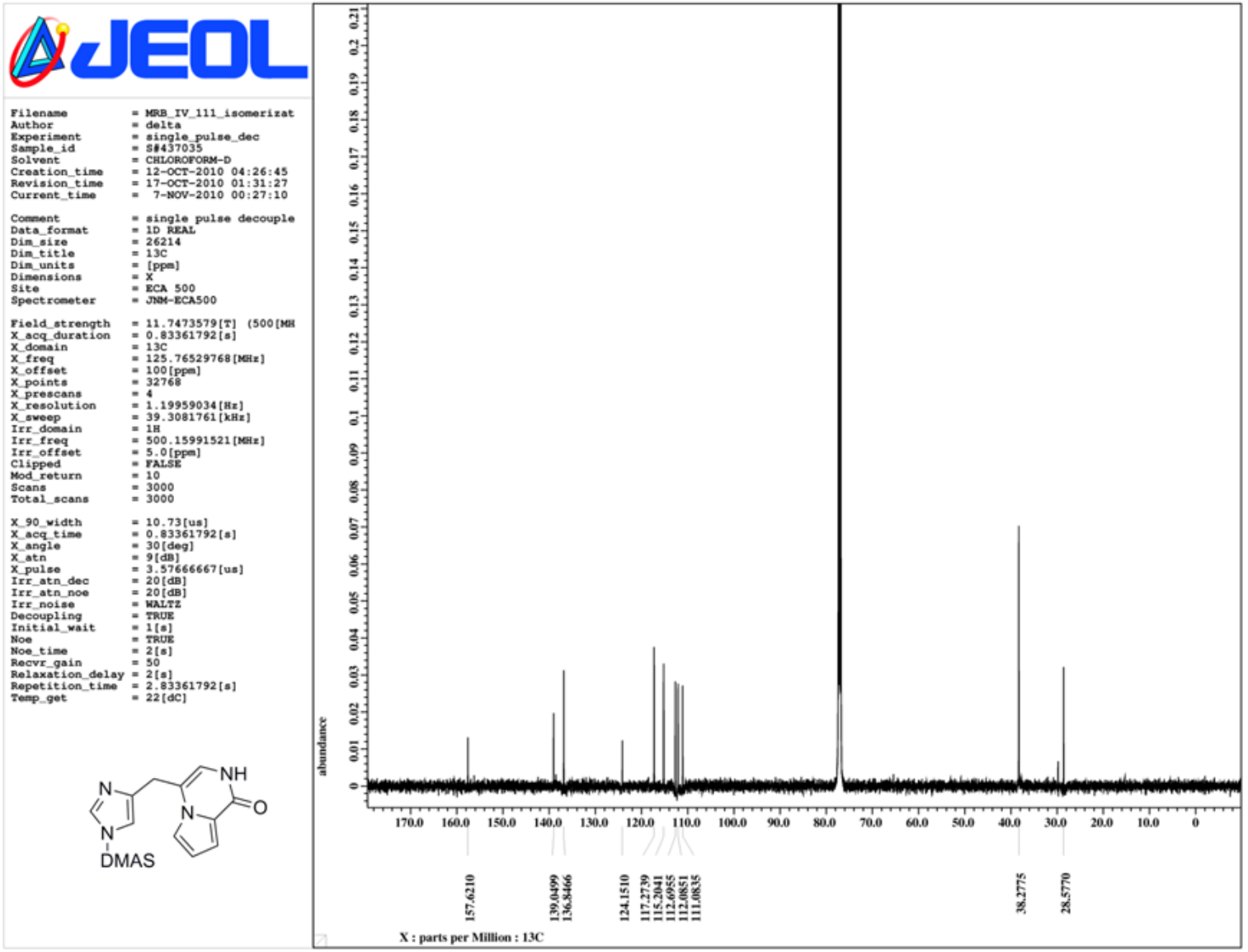
```
Filename          = MRB_V_106_methylmethy
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#685209
Solvent           = CHLOROFORM-D
Creation_time     = 30-SEP-2010 09:05:06
Revision_time     = 29-SEP-2010 19:07:20
Current_time      =  7-NOV-2010 00:25:36

Comment           = single pulse decouple
Data_format       = 1D REAL
Dim_size          = 26214
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 0.83361792[s]
X_domain          = 13C
X_freq            = 125.76529768[MHz]
X_offset          = 100[ppm]
X_points          = 32768
X_prescans        = 4
X_resolution      = 1.19959034[Hz]
X_sweep           = 39.3081761[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 10
Scans             = 100
Total_scans       = 100

X_90_width        = 10.73[us]
X_acq_time        = 0.83361792[s]
X_angle           = 30[deg]
X_atn             = 9[dB]
X_pulse           = 3.57666667[us]
Irr_atn_dec       = 20[dB]
Irr_atn_noe       = 20[dB]
Irr_noise         = WALTZ
Decoupling        = TRUE
Initial_wait      = 1[s]
Noe               = TRUE
Noe_time          = 2[s]
Recvr_gain        = 50
Relaxation_delay  = 2[s]
Repetition_time   = 2.83361792[s]
Temp_get          = 22.3[dC]
```

APPENDIX 54
^{1}H AND ^{13}C NMR SPECTRA OF
***N*,*N*-Dimethyl-4-((1-oxo-1,2-dihydropyrrolo[1,2-a]pyrazin-4-yl)methyl)-1H-imidazole-1-sulfonamide (182)**



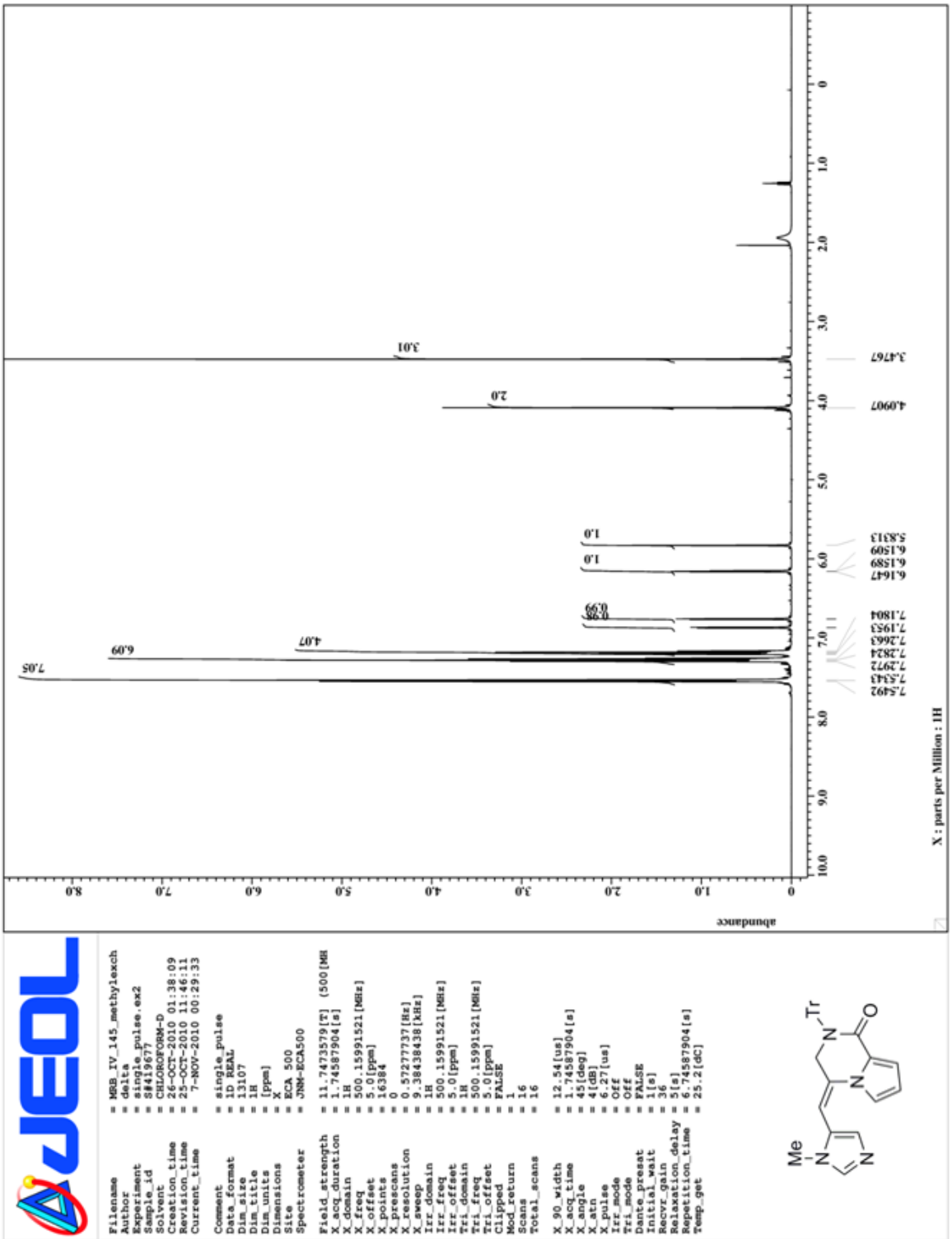
JEOL

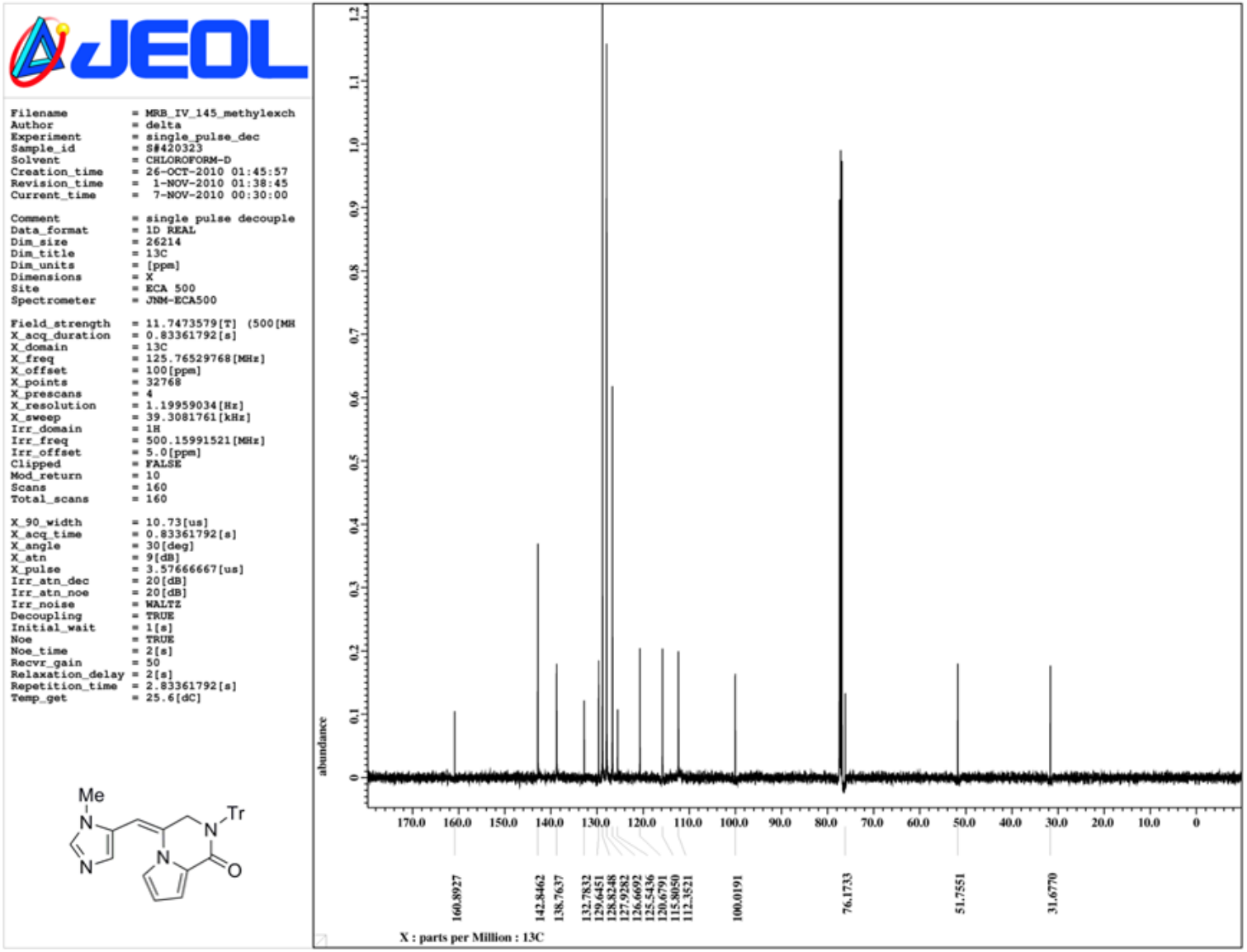
```
Filename          = MRB_IV_111_isomerizat
Author            = delta
Experiment        = single_pulse.ex2
Sample_id         = S#436204
Solvent           = CHLOROFORM-D
Creation_time     = 12-OCT-2010 02:03:40
Revision_time     = 11-OCT-2010 12:12:55
Current_time      =  7-NOV-2010 00:26:42

Comment           = single_pulse
Data_format       = 1D REAL
Dim_size          = 13107
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 1.74587904[s]
X_domain          = 1H
X_freq            = 500.15991521[MHz]
X_offset          = 5.0[ppm]
X_points          = 16384
X_prescans        = 0
X_resolution      = 0.57277737[Hz]
X_sweep           = 9.38438438[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Tri_domain        = 1H
Tri_freq          = 500.15991521[MHz]
Tri_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 16
Total_scans       = 16

X_90_width        = 12.54[us]
X_acq_time        = 1.74587904[s]
X_angle           = 45[deg]
X_atn             = 4[dB]
X_pulse           = 6.27[us]
Irr_mode          = Off
Tri_mode          = Off
Dante_presat      = FALSE
Initial_wait      = 1[s]
Recvr_gain        = 50
Relaxation_delay  = 5[s]
Repetition_time   = 6.74587904[s]
Temp_get          = 21.6[dC]
```



```
Filename          = MRB_IV_111_isomerizat
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#437035
Solvent           = CHLOROFORM-D
Creation_time     = 12-OCT-2010 04:26:45
Revision_time     = 17-OCT-2010 01:31:27
Current_time      =  7-NOV-2010 00:27:10

Comment           = single pulse decouple
Data_format       = 1D REAL
Dim_size          = 26214
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 0.83361792[s]
X_domain          = 13C
X_freq            = 125.76529768[MHz]
X_offset          = 100[ppm]
X_points          = 32768
X_prescans        = 4
X_resolution      = 1.19959034[Hz]
X_sweep           = 39.3081761[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 10
Scans             = 3000
Total_scans       = 3000

X_90_width        = 10.73[us]
X_acq_time        = 0.83361792[s]
X_angle           = 30[deg]
X_atn             = 9[dB]
X_pulse           = 3.57666667[us]
Irr_atn_dec       = 20[dB]
Irr_atn_noe       = 20[dB]
Irr_noise         = WALTZ
Decoupling        = TRUE
Initial_wait      = 1[s]
Noe               = TRUE
Noe_time          = 2[s]
Recvr_gain        = 50
Relaxation_delay  = 2[s]
Repetition_time   = 2.83361792[s]
Temp_get          = 22[dC]
```

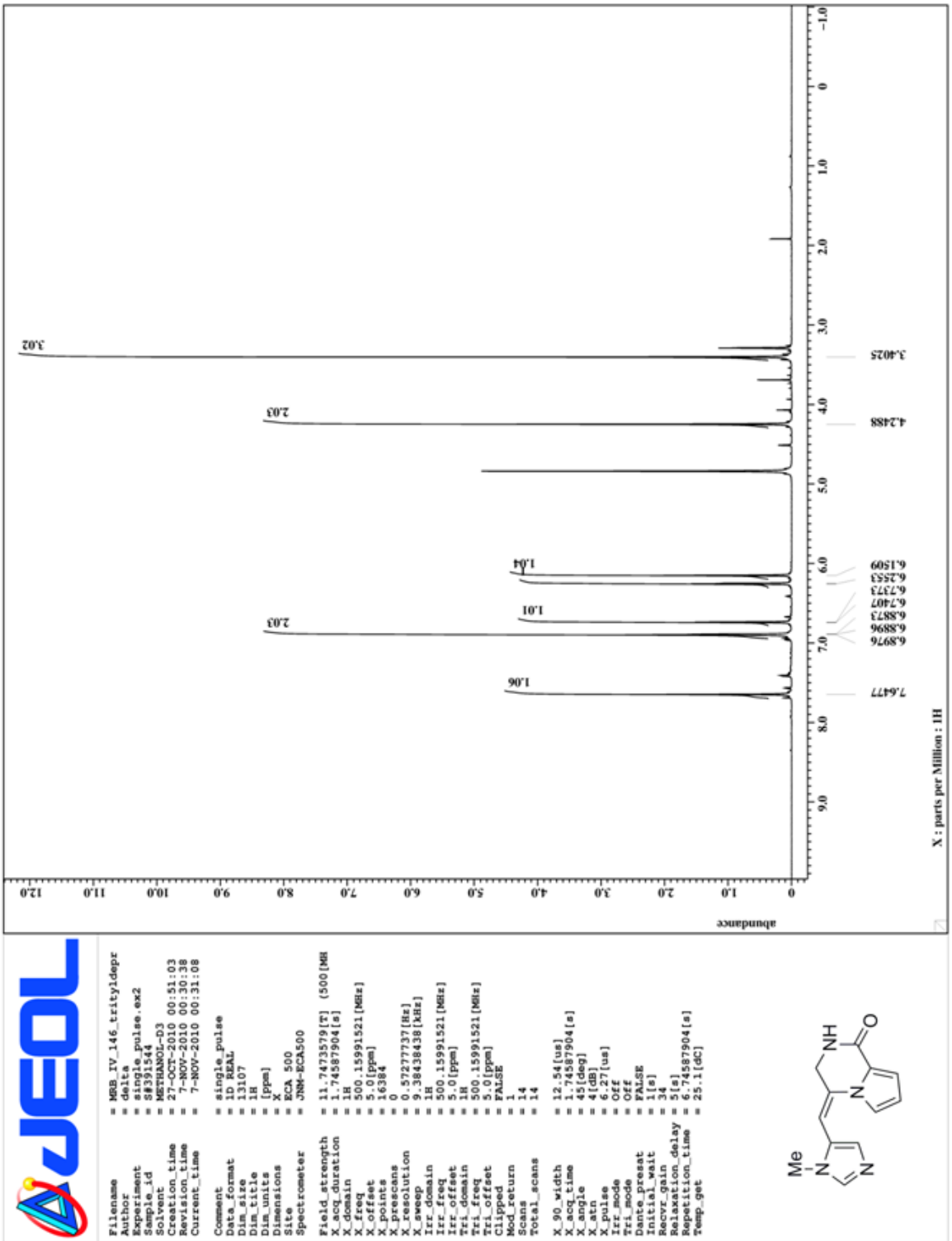
APPENDIX 55
^{1}H AND ^{13}C NMR SPECTRA OF
(*Z*)-4-((1-Methyl-1H-imidazol-5-yl)methylene)-2-trityl-3,4-dihydropyrrolo[1,2-a]pyrazin-1(2H)-one (185)

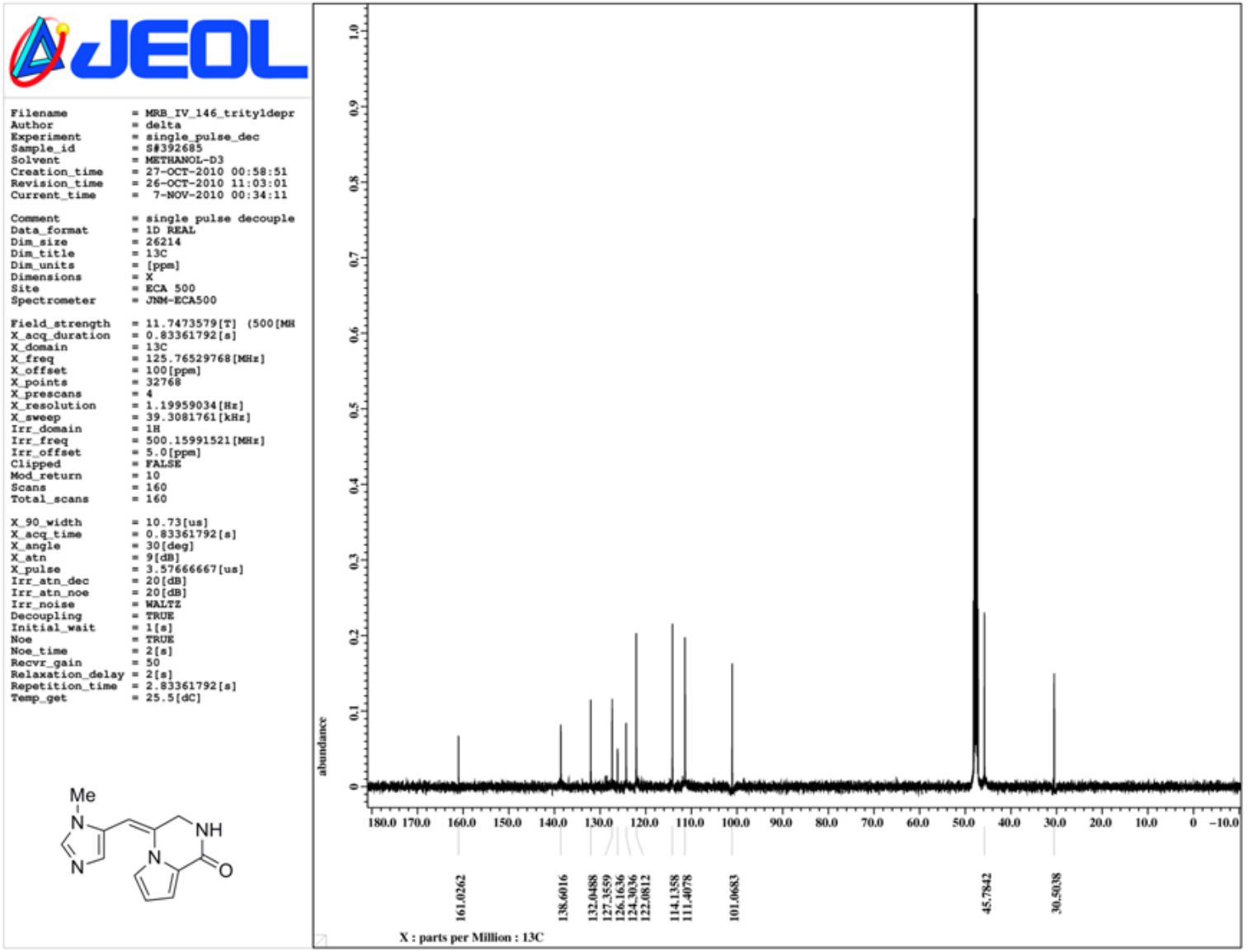

JEOL
Filename = MRB_IV_145_methylexch
Author = delta
Experiment = single_pulse.ex2
Sample_id = S#419677
Solvent = CHLOROFORM-D
Creation_time = 26-OCT-2010 01:38:09
Revision_time = 25-OCT-2010 11:46:11
Current_time = 7-NOV-2010 00:29:33
Comment = single_pulse
Data_format = 1D REAL
Dim_size = 13107
Dim_title = 1H
Dim_units = [ppm]
Dimensions = X
Site = ECA 500
Spectrometer = JNM-ECA500
Field_strength = 11.7473579[T] (500[MH
X_acq_duration = 1.74587904[s]
X_domain = 1H
X_freq = 500.15991521[MHz]
X_offset = 5.0[ppm]
X_points = 16384
X_prescans = 0
X_resolution = 0.57277337[Hz]
X_sweep = 9.38438438[kHz]
Irr_domain = 1H
Irr_freq = 500.15991521[MHz]
Irr_offset = 5.0[ppm]
Tri_domain = 1H
Tri_freq = 500.15991521[MHz]
Tri_offset = 5.0[ppm]
Clipped = FALSE
Mod_return = 1
Scans = 16
Total_scans = 16
X_90_width = 12.54[us]
X_acq_time = 1.74587904[s]
X_angle = 45[deg]
X_atn = 4[dB]
X_pulse = 6.27[us]
Irr_mode = Off
Tri_mode = Off
Dante_presat = FALSE
Initial_wait = 1[s]
Recvr_gain = 36
Relaxation_delay = 5[s]
Repetition_time = 6.74587904[s]
Temp_get = 25.2[dC]
abundance
X : parts per Million : 1H
7.7.5492
7.5343
7.2972
7.2824
7.2663
7.1953
7.1804
6.1647
6.1589
6.1509
5.8313
4.0907
3.4767
7.05
6.09
4.07
3.01
2.0
1.0
1.0
0.99
0.98
Me
Tr
N
N
N
O



```
Filename          = MRB_IV_145_methylexch
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#420323
Solvent           = CHLOROFORM-D
Creation_time     = 26-OCT-2010 01:45:57
Revision_time     =  1-NOV-2010 01:38:45
Current_time      =  7-NOV-2010 00:30:00

Comment           = single pulse decouple
Data_format       = 1D REAL
Dim_size          = 26214
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 0.83361792[s]
X_domain          = 13C
X_freq            = 125.76529768[MHz]
X_offset          = 100[ppm]
X_points          = 32768
X_prescans        = 4
X_resolution      = 1.19959034[Hz]
X_sweep           = 39.3081761[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 10
Scans             = 160
Total_scans       = 160

X_90_width        = 10.73[us]
X_acq_time        = 0.83361792[s]
X_angle           = 30[deg]
X_atn             = 9[dB]
X_pulse           = 3.57666667[us]
Irr_atn_dec       = 20[dB]
Irr_atn_noe       = 20[dB]
Irr_noise         = WALTZ
Decoupling        = TRUE
Initial_wait      = 1[s]
Noe               = TRUE
Noe_time          = 2[s]
Recvr_gain        = 50
Relaxation_delay  = 2[s]
Repetition_time   = 2.83361792[s]
Temp_get          = 25.6[dC]
```

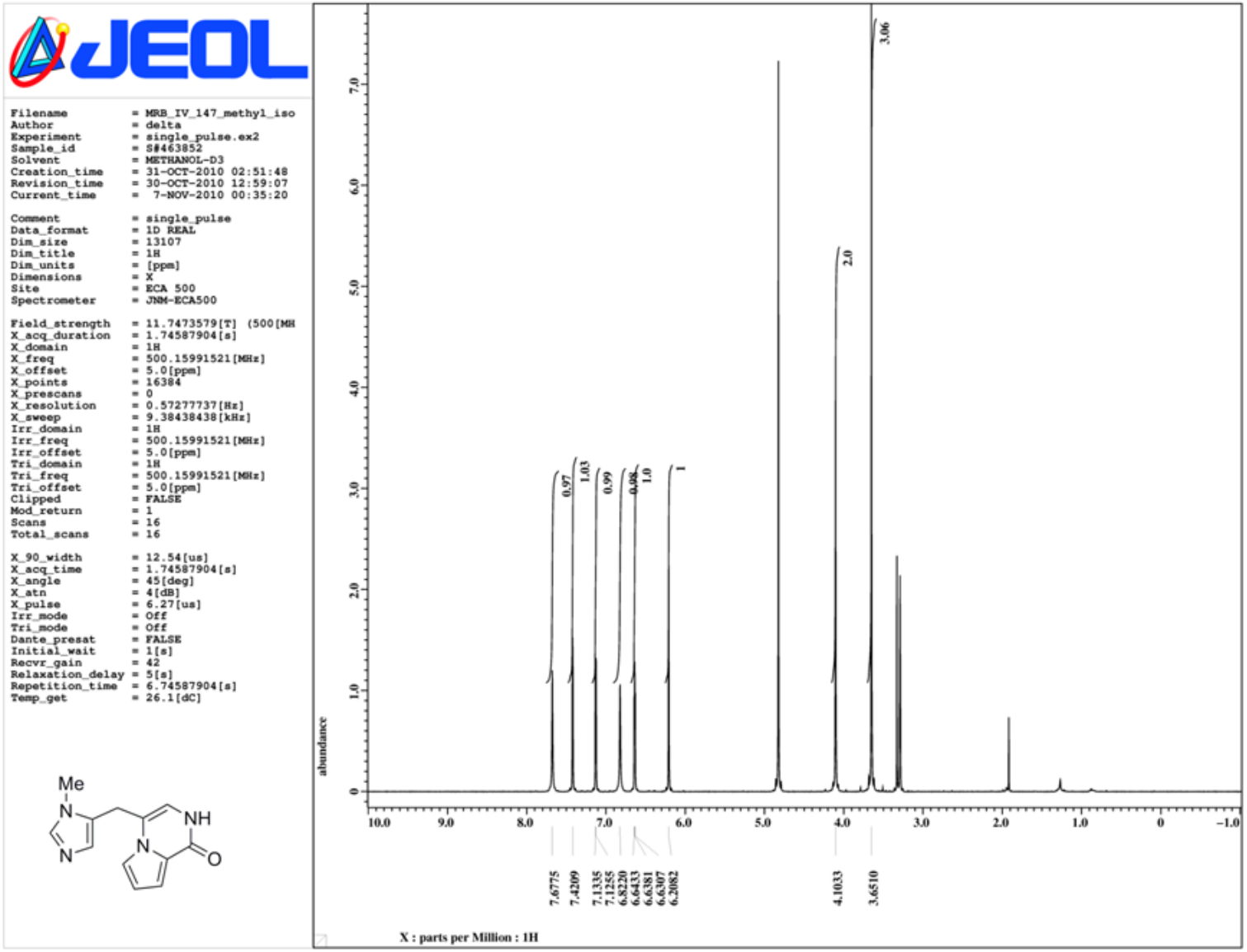
APPENDIX 56
^{1}H AND ^{13}C NMR SPECTRA OF
(*Z*)-4-((1-Methyl-1H-imidazol-5-yl)methylene)-3,4-dihydropyrrolo[1,2-a]pyrazin-1(2H)-one (186)


JEOL
Filename = MRB_IV_146_trityldepr
Author = delta
Experiment = single_pulse.ex2
Sample_id = s#391544
Solvent = METHANOL-d3
Creation_time = 27-OCT-2010 00:51:03
Revision_time = 7-NOV-2010 00:30:38
Current_time = 7-NOV-2010 00:31:08
Comment = single_pulse
Data_format = 1D REAL
Dim_size = 13107
Dim_title = 1H
Dim_units = [ppm]
Dimensions = X
Site = ECA 500
Spectrometer = JNM-ECA500
Field_strength = 11.7473579[T] (500[MH
X_acq_duration = 1.74587904[s]
X_domain = 1H
X_freq = 500.15991521[MHz]
X_offset = 5.0[ppm]
X_points = 16384
X_prescans = 0
X_resolution = 0.57277737[Hz]
X_sweep = 9.38438438[kHz]
Irr_domain = 1H
Irr_freq = 500.15991521[MHz]
Irr_offset = 5.0[ppm]
Tri_domain = 1H
Tri_freq = 500.15991521[MHz]
Tri_offset = 5.0[ppm]
Clipped = FALSE
Mod_return = 1
Scans = 14
Total_scans = 14
X_90_width = 12.54[us]
X_acq_time = 1.74587904[s]
X_angle = 45[deg]
X_atn = 4[dB]
X_pulse = 6.27[us]
Irr_mode = Off
Tri_mode = Off
Dante_presat = FALSE
Initial_wait = 1[s]
Recvr_gain = 34
Relaxation_delay = 5[s]
Repetition_time = 6.74587904[s]
Temp_get = 25.1[dC]
abundance
X : parts per Million : 1H
3.02
2.03
2.03
1.04
1.01
1.06
7.6477
6.8976
6.8896
6.8873
6.7407
6.7373
6.2553
6.1509
4.2488
3.4025
Me
N
N
NH
O

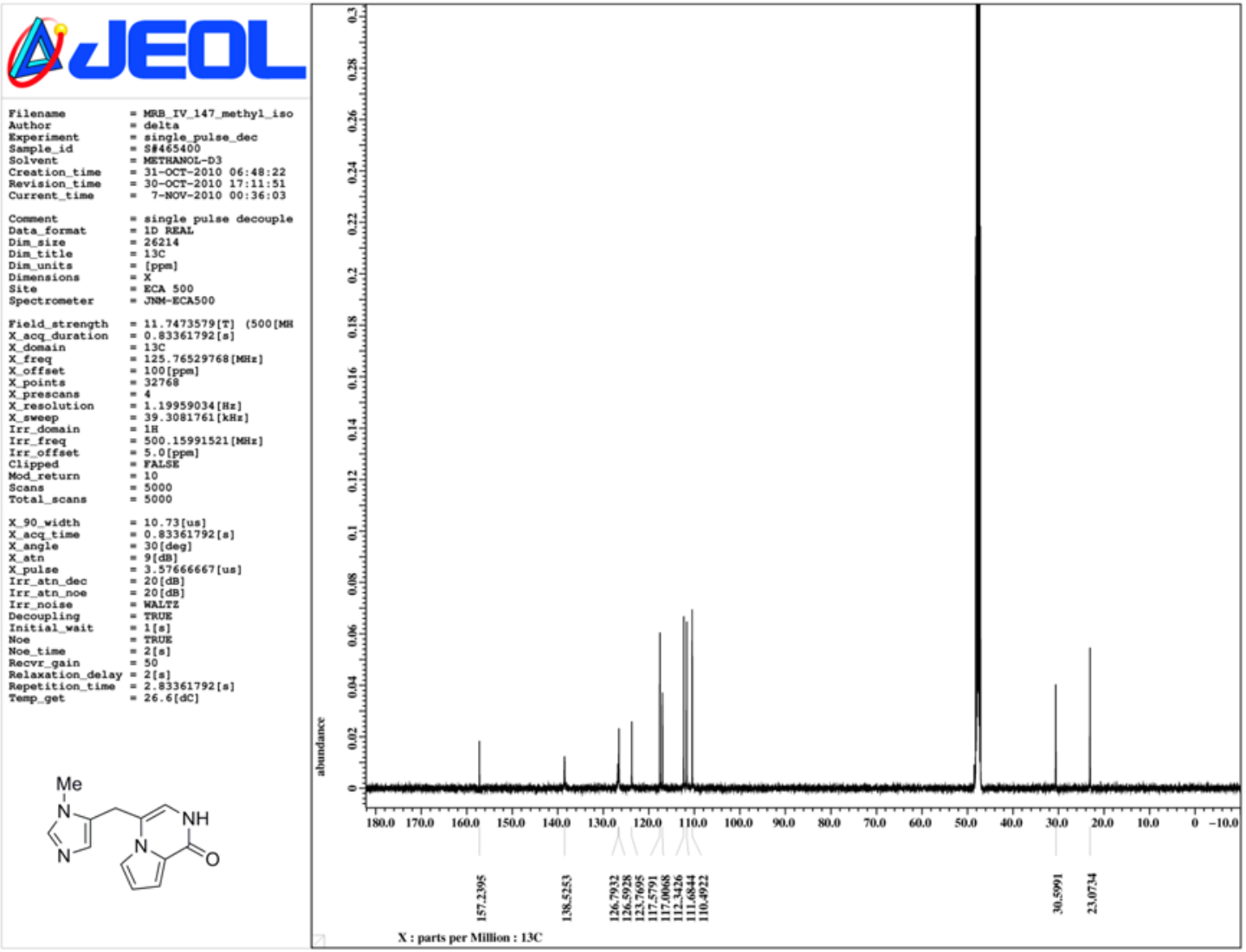


```
Filename          = MRB_IV_146_trityldepr
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#392685
Solvent           = METHANOL-D3
Creation_time     = 27-OCT-2010 00:58:51
Revision_time     = 26-OCT-2010 11:03:01
Current_time      =  7-NOV-2010 00:34:11

Comment           = single pulse decouple
Data_format       = 1D REAL
Dim_size          = 26214
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 0.83361792[s]
X_domain          = 13C
X_freq            = 125.76529768[MHz]
X_offset          = 100[ppm]
X_points          = 32768
X_prescans        = 4
X_resolution      = 1.19959034[Hz]
X_sweep           = 39.3081761[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 10
Scans             = 160
Total_scans       = 160

X_90_width        = 10.73[us]
X_acq_time        = 0.83361792[s]
X_angle           = 30[deg]
X_atn             = 9[dB]
X_pulse           = 3.57666667[us]
Irr_atn_dec       = 20[dB]
Irr_atn_noe       = 20[dB]
Irr_noise         = WALTZ
Decoupling        = TRUE
Initial_wait      = 1[s]
Noe               = TRUE
Noe_time          = 2[s]
Recvr_gain        = 50
Relaxation_delay  = 2[s]
Repetition_time   = 2.83361792[s]
Temp_get          = 25.5[dC]
```

APPENDIX 57
^{1}H AND ^{13}C NMR SPECTRA OF
4-((1-Methyl-1H-imidazol-5-yl)methyl)pyrrolo[1,2-a]pyrazin-1(2H)-one (187)



```
Filename          = MRB_IV_147_methyl_iso
Author            = delta
Experiment        = single_pulse.ex2
Sample_id         = S#463852
Solvent           = METHANOL-D3
Creation_time     = 31-OCT-2010 02:51:48
Revision_time     = 30-OCT-2010 12:59:07
Current_time      =  7-NOV-2010 00:35:20

Comment           = single_pulse
Data_format       = 1D REAL
Dim_size          = 13107
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 1.74587904[s]
X_domain          = 1H
X_freq            = 500.15991521[MHz]
X_offset          = 5.0[ppm]
X_points          = 16384
X_prescans        = 0
X_resolution      = 0.57277737[Hz]
X_sweep           = 9.38438438[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Tri_domain        = 1H
Tri_freq          = 500.15991521[MHz]
Tri_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 1
Scans             = 16
Total_scans       = 16

X_90_width        = 12.54[us]
X_acq_time        = 1.74587904[s]
X_angle           = 45[deg]
X_atn             = 4[dB]
X_pulse           = 6.27[us]
Irr_mode          = Off
Tri_mode          = Off
Dante_presat      = FALSE
Initial_wait      = 1[s]
Recvr_gain        = 42
Relaxation_delay  = 5[s]
Repetition_time   = 6.74587904[s]
Temp_get          = 26.1[dC]
```



```
Filename          = MRB_IV_147_methyl_iso
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#465400
Solvent           = METHANOL-D3
Creation_time     = 31-OCT-2010 06:48:22
Revision_time     = 30-OCT-2010 17:11:51
Current_time      =  7-NOV-2010 00:36:03

Comment           = single pulse decouple
Data_format       = 1D REAL
Dim_size          = 26214
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = ECA 500
Spectrometer      = JNM-ECA500

Field_strength    = 11.7473579[T]  (500[MH
X_acq_duration    = 0.83361792[s]
X_domain          = 13C
X_freq            = 125.76529768[MHz]
X_offset          = 100[ppm]
X_points          = 32768
X_prescans        = 4
X_resolution      = 1.19959034[Hz]
X_sweep           = 39.3081761[kHz]
Irr_domain        = 1H
Irr_freq          = 500.15991521[MHz]
Irr_offset        = 5.0[ppm]
Clipped           = FALSE
Mod_return        = 10
Scans             = 5000
Total_scans       = 5000

X_90_width        = 10.73[us]
X_acq_time        = 0.83361792[s]
X_angle           = 30[deg]
X_atn             = 9[dB]
X_pulse           = 3.57666667[us]
Irr_atn_dec       = 20[dB]
Irr_atn_noe       = 20[dB]
Irr_noise         = WALTZ
Decoupling        = TRUE
Initial_wait      = 1[s]
Noe               = TRUE
Noe_time          = 2[s]
Recvr_gain        = 50
Relaxation_delay  = 2[s]
Repetition_time   = 2.83361792[s]
Temp_get          = 26.6[dC]
```

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