STUDIES TOWARDS BIOACTIVE IMIDAZOLES

by

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ABSTRACT

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The work presented in this thesis focuses on the development of an enantioselective and practical route for the total synthesis of villagorgin via haploscleridamine. These marine sponge derived alkaloids contain both a *β*-carboline and an imidazole moiety. Our approach employed the well-known Pictet-Spengler and Fischer indole reactions. Two different strategies were investigated in order to synthesize these molecules

The first approach focused on using a Dieckmann condensation to construct the key piperidinone, requiring the preparation of the corresponding diester. Initial attempts to prepare this substrate directly from histidine were unsuccessful, however after conversion to the *N*-benzylamine and reductive amination with ester provided the key diester. Unfortunately, attempts to effect the Dieckmann reaction were not

successful. In addition we became concerned about the possibility of racemization nder the basic conditions utilized for this transformation and therefore pursued an alternative route.

In the second approach, which relied on ring closing metathesis (RCM), the key intermediate piperidinone was assembled from a protected histidine derivative. The RCM precursor was obtained by *N*-allylation and Grignard chemistry. Reduction followed by the installation of the indole moiety, which would complete the core framework. Deprotection would then give the halopscleridamine and a subsequent Pictet-Spengler reaction would then give villagorgin A.

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CHAPTER 1

INTRODUCTION

1.1 Natural Products

Traditionally plants and terrestrial microorganisms have been the primary focus in the search for new drug candidates from nature. In recent years, however, marine organisms such as sponges, tunicates, shell-less molluscs and others are increasingly attracting attention due to their production of structurally unique and pharmacologically active compounds (figure 1.1).

The chemistry and biology of indole, annulated indole and carbazole alkaloids with imidazole ring of marine origin is a steadily growing and very promising field for the development of pharmacologically active compounds for use as medicinal agents. Indole alkaloids have been extensively investigated for a wide variety of parmacological effects, including anti-tumor, anti-inflammatory, anti-malarial, anti-HIV, contraceptive and bactericidal activities, as well as a stimulatory action on the central nervous system. Up to date, more than 2000 different compounds of this class have been isolated and are one of the most studied classes of alkaloids due to their CNS- related activity, their anti-cancer activity and their potential use as anti-addiction agents.[1a- c]

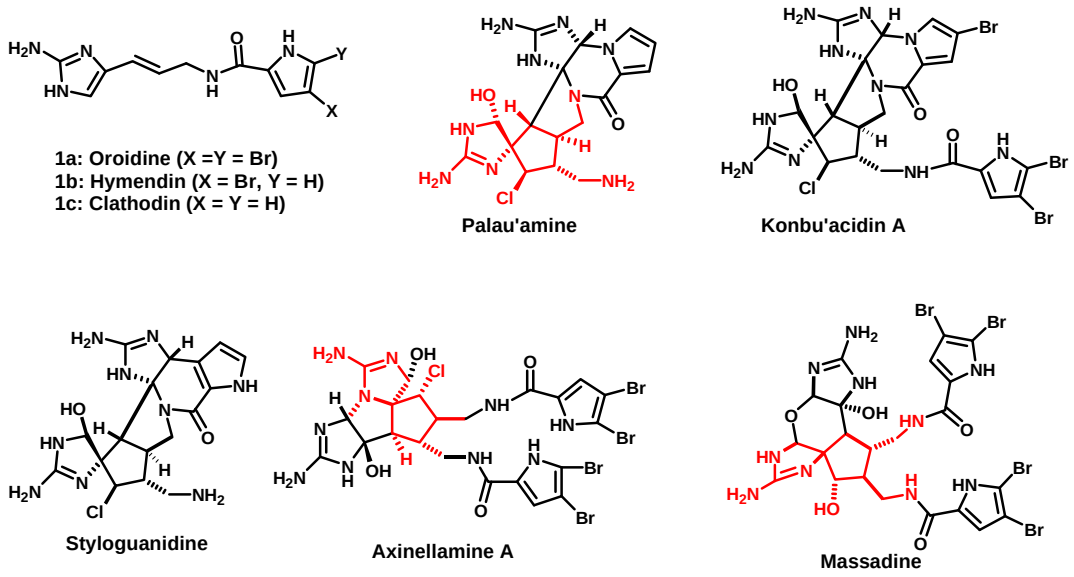


Fig 1.1 Some Marine Natural Products.

1.2 Importance of Natural Products as Drugs

In earlier times, all drugs and medicinal agents were derived from natural substances, and most of these remedies were obtained from higher plants. Today, many new chemotherapeutic agents are synthetically derived, based on "rational" drug design. The study of natural products has advantages over *de novo* drug design is that it often leads to materials having new structural features with novel biological active. Nature continues to be one of the most important sources of pharmacologically active compounds in the quest for drugs against life-threatening diseases such as microbial infections, diseases of the heart and the circulatory system, cancer and others. Almost 40% of the top selling pharmaceutical drugs are natural products or natural product derivatives even though compounds from nature constitute less than 1% of the molecules structurally known today.[2]

Today, natural products (their derivatives and analogs) still represent over 50% of all drugs in clinical use, with higher plant-derived natural products representing *ca*. 25% of the total.[2] The World Health Organization estimates that 80% of people in developing countries of the world rely on traditional medicine for their primary health care, and about 85% of traditional medicine involves the use of plant extracts. This means that about 3.5 to 4 billion people in the world rely on plants as sources of drugs.[3]

In the United States plant-derived drugs represent about 25% of the prescription drug market, and in 1991 this equated to a retail value of approximately $15.5 billion.[4] From 1983 to 1994 39% of the New Approved Drugs (NAD) were of natural origin, including original natural products, products derived semisynthetically from natural products, and synthetic products based on natural product models.[5] Further evidence of the importance of natural products is provided by the fact that almost half of the world's 25 best selling pharmaceuticals in 1991 were either natural products or their derivatives.[6]

Conservative estimates suggest that there are more than 250,000 species of higher plants existing on this planet, and only a very small percentage of plants have been exhaustively studied for their potential value as a source of drugs. Obviously natural products will continue to be extremely important as sources of medicinal agents. In addition to the natural products which have found direct medicinal application as drug entities, many others can serve as chemical models or templates for the design, synthesis, and semisynthesis of novel substances for treating humankind's diseases. Although there are some new approaches to drug discovery, such as combinatorial

chemistry and computer-based molecular modeling design, it is likely that none of them can replace the important role of natural products in drug discovery and development.[7, 8]

Alkaloids are (in a chemical sense) basic natural products occurring primarily in plants that in most cases, are nitrogen-containing heterocyclic which exhibit pronounced physiological activities.[9,10] As of 1990, over 5,000 alkaloids of various structural types have been isolated.[11] The biogenesis of alkaloids involves the derivatization of amino acids especially ornithine, lysine, phenylalanine, tyrosine and tryptophan. Akin to other natural products, the micro-scale occurrence of alkaloids in nature makes their isolation and their broadscale pharmacological evaluation difficult. Furthermore, preparing derivatives of natural products which aid in the identification of pharmacophore (i.e., the minimal active moiety), becomes a tedious task with a limited amount of material. The total synthesis of natural products can provide sufficient material to enable a complete pharmacological evaluation. An additional benefit is that total synthesis can allow the preparation of a number of structural analogs, which may play a crucial role in identifying the active pharmacophore. Once the active parts of the natural products are determined, the structure-activity relationship can be established, and possibly a mechanism of action, which in turn can provide an opportunity to develop a novel therapeutic agent.

1.3 *β*-Carboline Imidazole Alkaloids

A large number of alkaloids containing imidazole rings have been isolated from natural sources which are different in structure and origin (Fig 1.2).[12] These compounds have been found in plants (e.g., *Cactaeae, Euphorbiaceae and Orchidacea*), in bacteria (e.g., *Aspergillus* species), in fungi (e.g., *Streptomyces* and *Penicillium* species), and in animal sources (mainly marine sponges).[12-15]

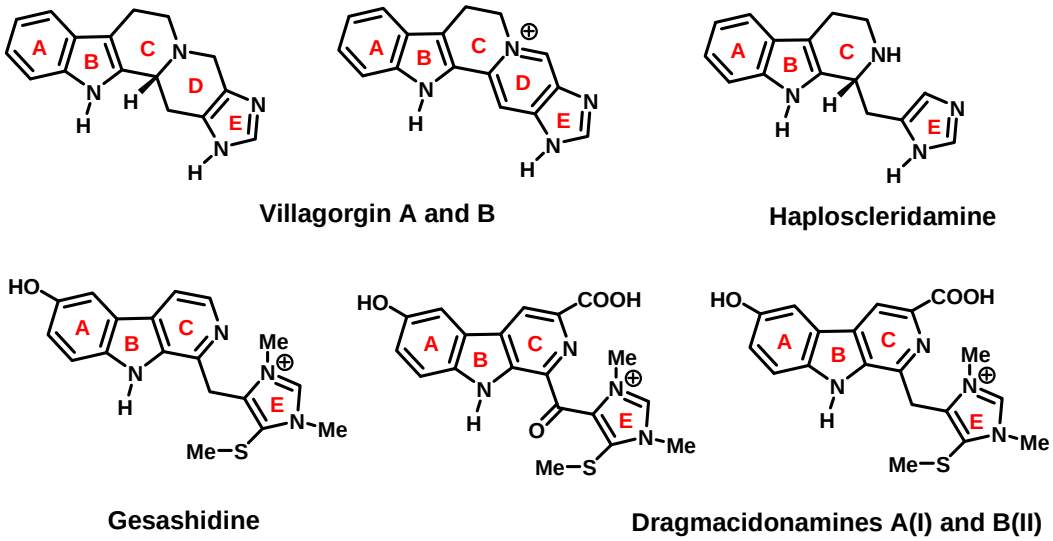


Fig 1.2 *β*-Carboline Imidazole Alkaloids

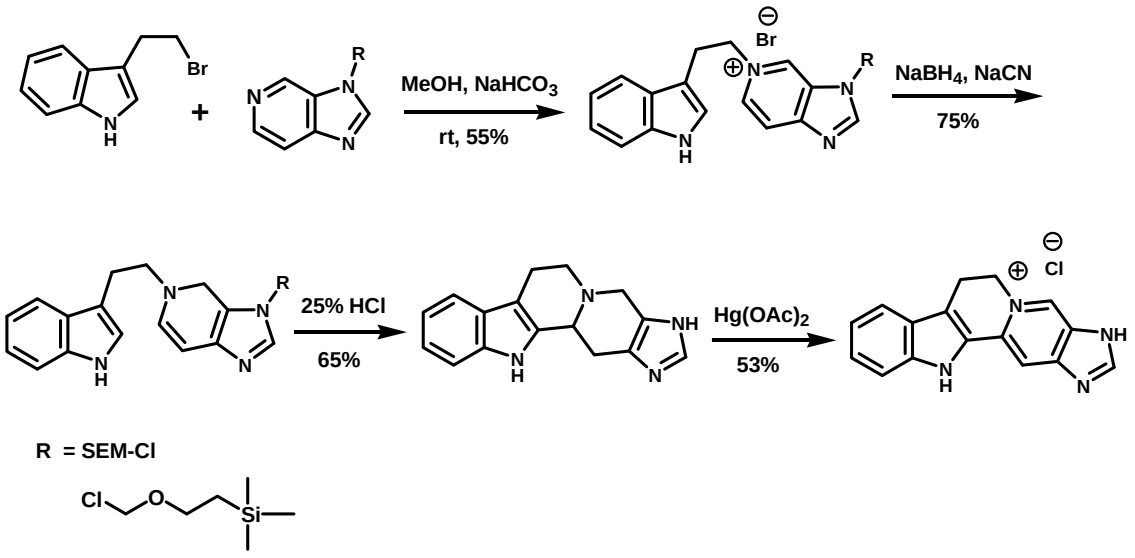
Many of these systems are found to exhibit pronounced biological activity, including antimicrobial, antitumor and antiviral activities.[16] Some of these marine derived *β*-carboline imidazole alkaloids are relatively rare, several of which are shown in Figure 1.2. Villagorgin A and villagorgin B were isolated from the gorgonian *Villagorgia rubra* found in New Caledonia.[17] Ricardo and coworkers focused their attention on the gorgonian *Villagorgia rubra*, which selected for the study because the methanol extracts were very active in the guinea-pig ileum contraction test. *V. rubra* is a rich source of nitrogenous metablolites that were isolated from the butanolic fraction and identified as caffeine, the simple indoles, tryptamine, 1,2,3,4-tetrahydro-*β*-carboline and two new complex indole alkaloids named villagorgin A and villagorgin B. The structure and absolute configuration of the villagorgins were deduced by extensive use of 2D-NMR, FABMS and HREIMS, and CD data. It was further determined that villagorgin A has a calmodulin-related antagonist activity. Calmodulin is a calcium–binding protein that is involved in the regulation of various cellular functions including inflammation, metabolism, muscle contraction, intracellular movement, short-term and long-term memory, nerve growth and the immune response.[18]

The next interesting alkaloid is haploscleridamine, a novel tryptamine derived alkaloid from a sponge of the order *Haplosclerida*.[19, 20] This alkaloid inhibits cathepsin K, a cysteine protease enzyme, which is involved in the catabolism of elastin, collagen, and gelatin allowing the break down of bone and cartilage. Cathepsin K "blockers" show great potential in the treatment of osteoporosis.[19]

1.4 Reported Synthesis on Villagorgin

Villagorgin A and villagorgin B alkaloids are attractive synthetic targets due to their biological properties and their novel structure. However, since their isolation in 1993, villagorgin A and villagorgin B have not attracted substantial synthetic attention. Kuehne and coworkers have been the only group so far to publish a synthetic approach to these two natural products, leading to racemic material. Their synthetic route involved a reduction and a Pictet-Spengler-like cyclization of an indolylethylimidazopyridium salt. Subsequent oxidation of villagorgin A with mercuric acetate gave villagorgin B (Scheme 1.1).[21]

Scheme 1.1 Synthesis of Racemic Villagorgin



Our group had begun working on a non-racemic approach toward the total synthesis of these alkaloids. Details of the synthesis will be discussed in the subsequent chapter of this thesis.

1.5 Our Retrosynthetic Analysis of Villagorgin

The research outlined herein is focused on the development of stereoselective and practical route for the synthesis of villagorgin A. Our planned synthesis towards these imidazole derivatives employs the well-known Pictet-Spengler [23-25] and Fischer indole[24] reactions, although these have not been extensively used with imidazole containing substrate and in particular in total synthesis endeavors. A potentially versatile and attractive route for the synthesis of imidazolyl β-carboline ring systems using the amino acid L-histidine as starting material has been designed (Scheme 1.3)

In the course of a literature search we came across additional alkaloids hapaloscleridamine and lissoclin C that are related to villagorgin A, only lacking the D-ring.

These molecules by nature are chiral but appear to have lost their optical activity during isolation and purification (figure 1.3).[26]

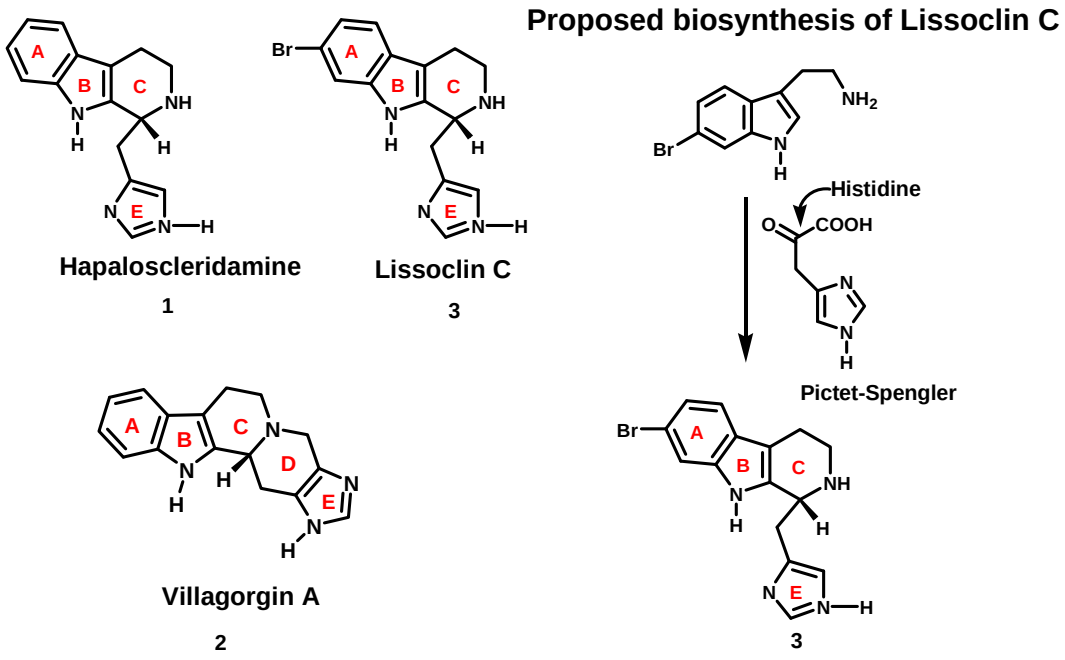


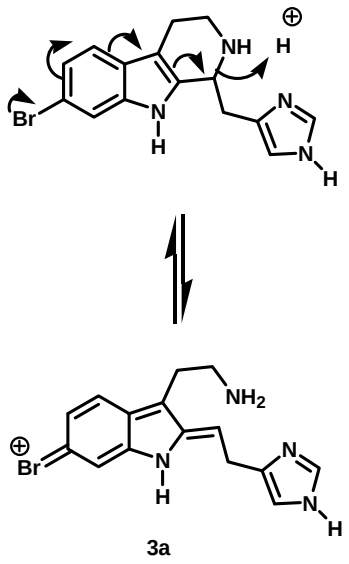
Figure 1.3 Proposed Biosynthesis of *β*-Carboline Alkaloids

From a biosynthetic perspective, **3** is formally obtained from condensation of 6-bromotryptamine with C2 rather than C1 of 4-imidazolypyruvic acid, probably derived by transamination from histidine, followed by the loss of C1.

Compound **3** is chiral, but the optical activity of the isolated natural product was almost zero. Both the specific rotation and circular dichroism spectrum (CD) of the TFA salt of **3** were neglible; thus indicating the compound was nearly racemic. Brossi

and Cook have pointed out that C1-substituted tetrahydro-*β*-carbolines readily racemize in acidic solution, a property that is enhanced with substitution of C6 (indole numbering) with electron-donating groups. Although the mechanism of racemization is not clear, a possible explanation for loss of optical activity **3** would involve protonation of the piperidine ring followed by reversible ring opening to the achiral intermediate **3a**, stabilized by electron donating from 7-bromo substituent (Scheme 1.2).[26]

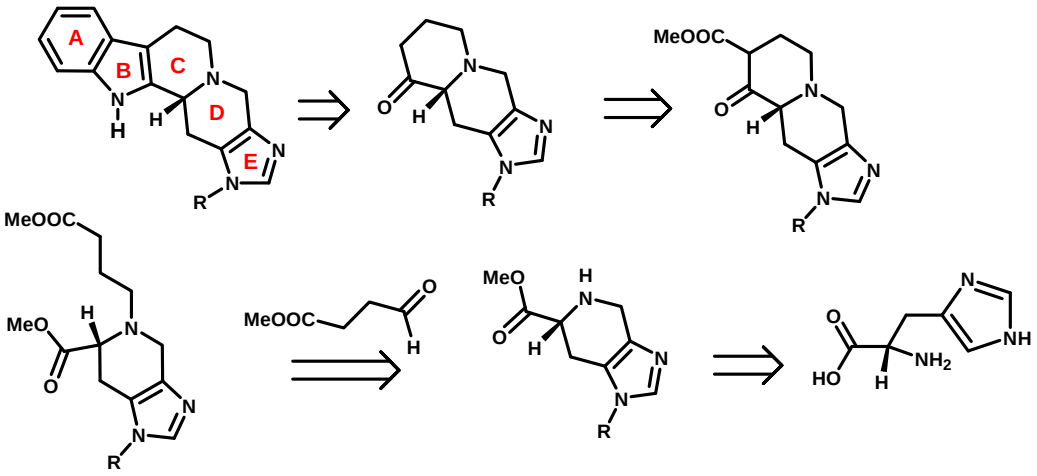
Scheme 1.2 Mechanism for Loss of Optical Activity



3a

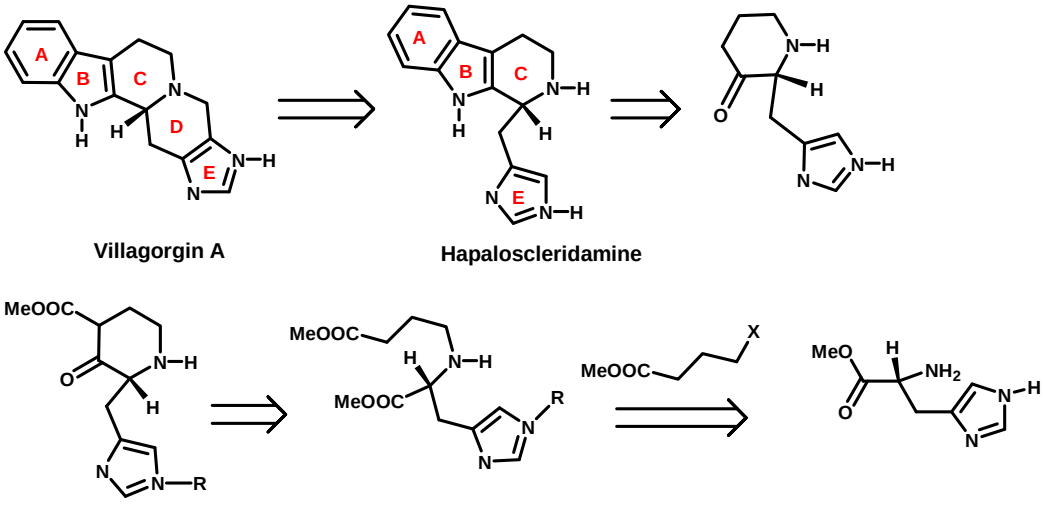
All together three different routes to access villagorgin were explored. It was planned to assemble the key intermediate either from a Dieckmann cyclization [27, 28] of diester or through ring-closing metathesis of the appropriate diene (Scheme 1.3, 1.4 and 1.5).

Scheme 1.3 Retrosynthetic Analysis (Route I) for Villagorgin A



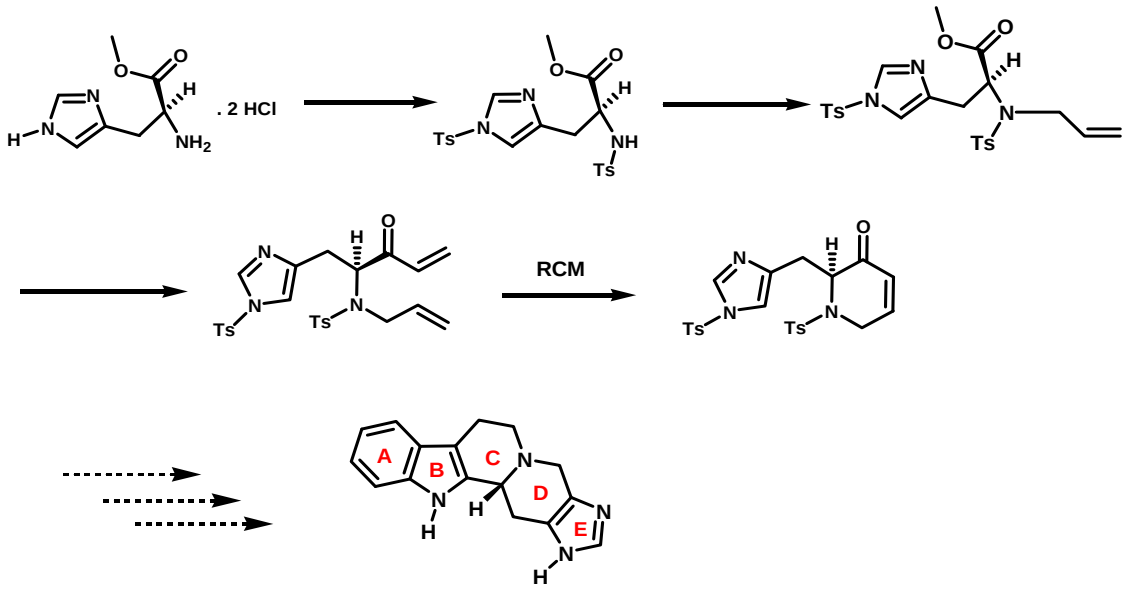
Two different retrosynthetic routes, involving the Dieckmann condensation were proposed (Scheme1.3 and 1.4). In route I, the retrosynthetic approach employs a Pictet-Spengler reaction early in the sequence followed by Fischer indole synthesis, whereas in route II, the Pictet-Spengler [28] reaction will be employed in the later stages of the synthesis. Route II, is also synthetically appealing because it potentially gives access to haploscleridamine which is structurally related to villagorgin A, expect it is devoid of the D-ring. This sequence of disconnections will allow the synthesis of non-racemic villagorgin via haploscleridamine. In addition, if the Fischer indole synthesis is carried out under non-acidic conditions, it should be possible to obtain both antipodes of hapaloscleridamine starting from either enantiomer of histidine.

Scheme 1.4 Retrosynthetic Analysis (Route II) for Villagorgin A



However, the Dieckmann condensation is a potentially risky step in these two approaches, due to the presence of acidic protons in the substrate which means that it can undergo racemization. In order to avoid racemization we investigated another approach towards villagorgin, a second generation approach involving – ring closing metathesis (RCM) (Scheme 1.5).

Scheme 1.5 Second Generation Approach - RCM

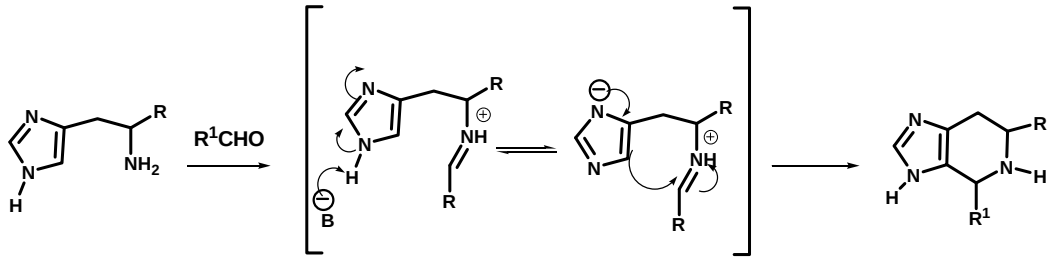


1.6 Various Key Reactions for Complete Construction of Tetrahydro *β*-Carboline Ring.

1.6.1 Pictet-Spengler Reaction

Historically, the reaction of L-histidine and formaldehyde to give spinacine (*S*)-4,5,6,7-tetrahydro-1*H*-imidazole[4,5-*c*]pyridine carboxylic acid) first reported by Wellish in 1913.[25] The reaction mechanism of the Pictet-Spengler reaction occurs by initial formation of an iminium ion followed by electrophilic substitution at the 2-position. After deprotonation, the desired product is formed. While iminium ions are powerful electrophiles, the Pictet-Spengler reaction only succeeds within an intramolecular sense (Scheme 1.6).[29-30a, b]

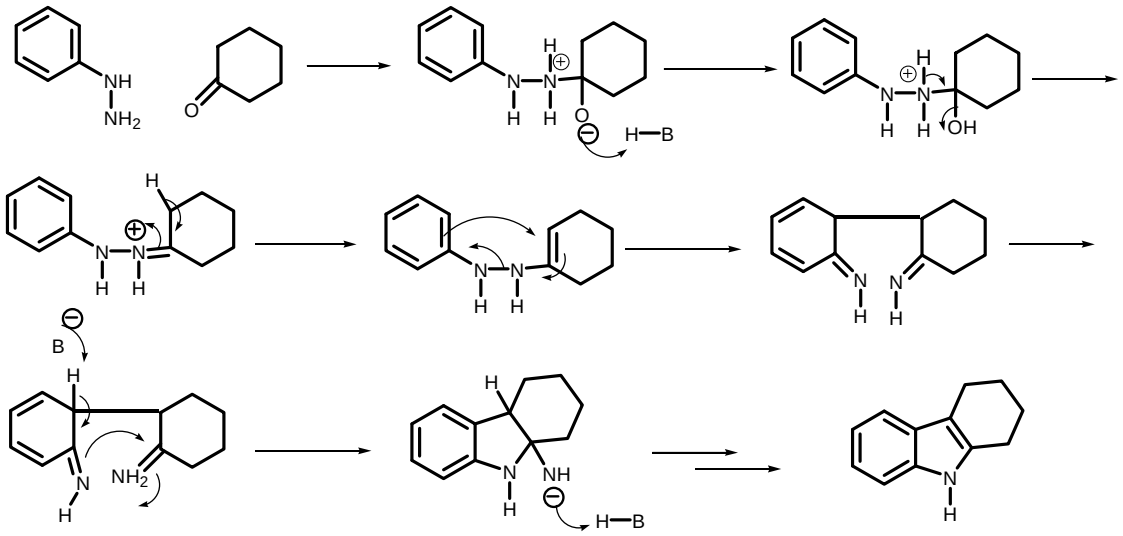
Scheme 1.6 Pictet-Spengler Mechanism



1.6.2 Fischer Indole Synthesis

The cyclization of aryl hydrazones to form indoles, known as the Fischer indole synthesis, is based the discovery of the reaction a century ago by Emil Fischer.[31] This reaction become one of the most versatile and widely studied reactions in organic chemistry. The reaction of a (substituted) phenyl hydrazine with an aldehyde or ketone initially forms a phenyl hydrazone which isomerizes to the corresponding enamine (ene-hydrazine). After protonation, a [3,3]-sigmatropic rearrangement occurs producing an imine. The resulting imine forms a cyclic aminoacetal (or aminal), which under acid catalysis eliminates NH_3, resulting in the energetically favorable aromatic indole (Scheme 1.7).

Scheme 1.7 Fischer Indole Synthesis



Two major drawbacks of the traditional Fischer indole reaction are that the yields are often low with numerous byproducts being formed, and reactions involving unsymmetrical hydrazines or ketones often give products of mixed regiochemistry. As a result several other methods have been developed for construction of indoles. [32-38]

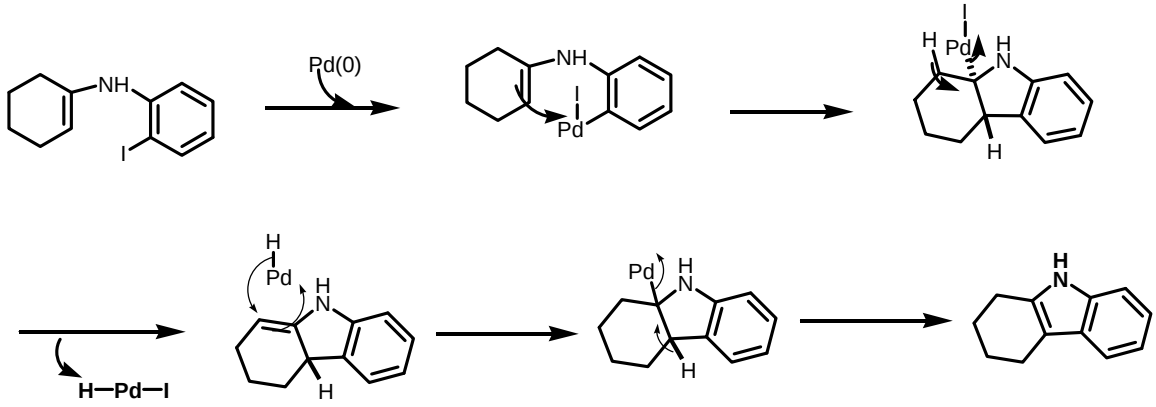
1.6.3 Heck- type Reaction

An alternative approach to indole formation involves an intramolecular Heck reaction of aryl enamines.[39]

The catalytic cycle for Heck reaction involves a series of transformations around the palladium catalyst. The palladium(0) species required in the cycle is generally prepared in situ from a palladium(II) precursor. For instance, palladium(II) acetate is reduced to palladium(0). An oxidative addition occurs in which palladium inserts into the aryl

bromide bond. The palladium forms a π-complex with the alkene and the alkene inserts into the palladium-carbon bond via a *syn* addition. *Syn* beta-hydride elimination leads to the formation of a new palladium-alkene π-complex. Readdition of Pd-H in the alternative orientation and second *β*-hydride elimination provides the indole. This palladium(0) compound is regenerated by reductive elimination of the palladium(II) compound by base (Scheme 1.8).

Scheme 1.8 Heck - type Reaction

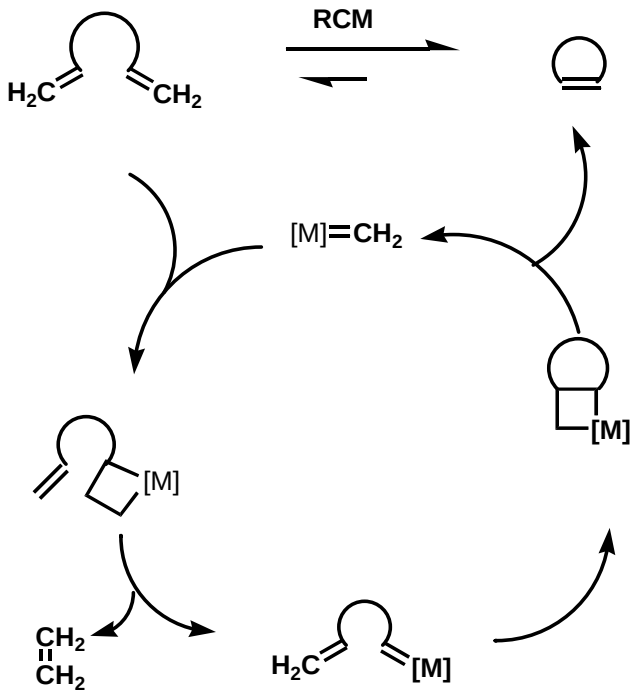


1.6.4 Olefin Ring-Closing Metathesis Reactions

Ring-closing metathesis (RCM) is an extremely powerful method for the formation of carbon-carbon bonds in the construction of unsaturated cyclic systems from acyclic dienes. According to the generally accepted mechanism, the reaction proceeds via a sequence of [2+2] cycloaddition/cycloreversion reactions and is mainly

driven by entropy gained by release of ethylene or other volatile side products (Scheme1.9).[40-44]

Scheme 1.9 Ring Closing Metathesis



CHAPTER 2

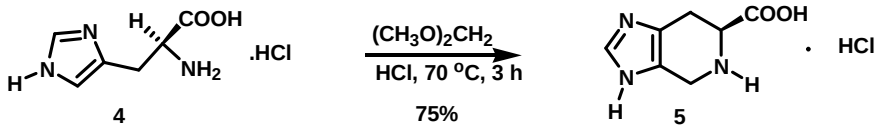
RESULTS AND DISCUSSION

2.1 First Generation Approach

2.1.1 Spinacine

According to our retrosynthetic analysis for approaches to the total synthesis of villagorgin (Scheme 1.7), the first step was to synthesize spinacine. Spinacine preparation involves direct cyclization of L-histidine hydrochloride **4** with methylal (formaldehyde dimethyl acetal) and hydrochloric acid (Pictet-Spengler reaction) providing **5** in good yield 75% (Scheme 2.1).[25]

Scheme 2.1



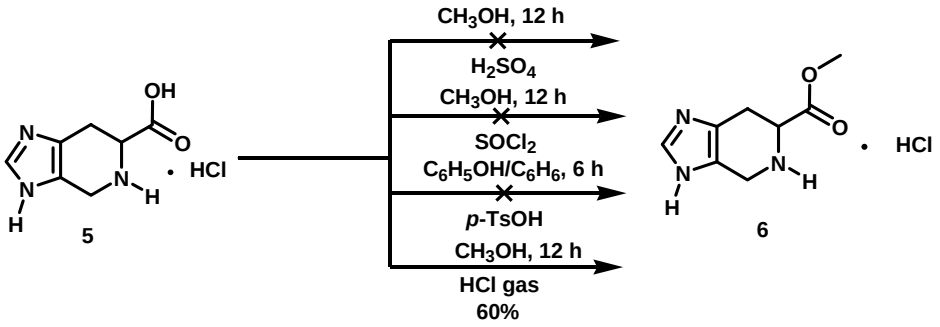
4 5

2.1.2 Spinacine Methyl Ester

Several attempts were made to prepare the methyl ester **6**, from spinacine **5** via various methods shown in Scheme 2.2. By TLC analysis, it appeared that the reaction was occurring but attempts to isolate the product were unsuccessful. Ultimately, the hydrochloride salt **6** was obtained via the reaction of **5** with MeOH and HCl gas in 60%

yield, although we anticipate that this can be improved through optimization (Scheme 2.2).[25]

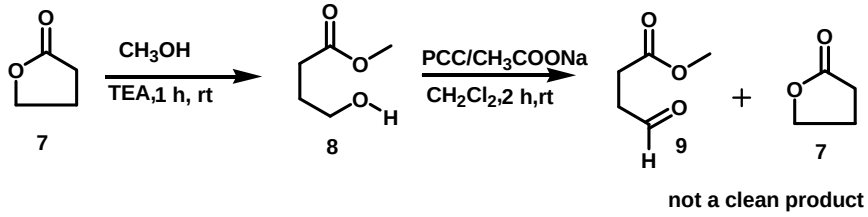
Scheme 2.2



2.1.3 4-Oxobutanoic Acid

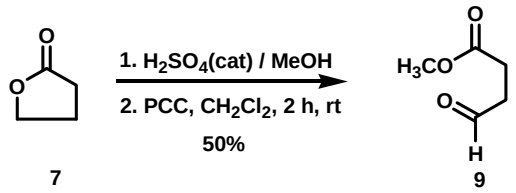
With one of the required fragments, spinacine ester **6**, in hand, we focused on obtaining the second fragment, 4-oxobutanoic acid methyl ester **6** (Scheme 2.3).[45] This involved the opening of butyrolactone (**7)** with MeOH in the presence of triethylamine at rt., followed by PCC oxidation. The expected aldehyde **9** was obtained along with some unreacted alcohol **8** and butyrolactone **7**. Unfortunately however, attempted purification did not provide pure aldehyde **9** (Scheme 2.3).

Scheme 2.3



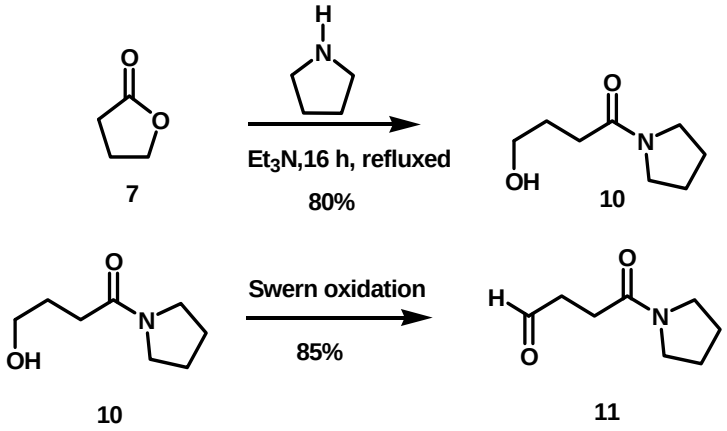
Alternatively, butyrolactone (**7)** was opened with methanol in the presence of H_2SO_4 (cat) followed by PCC oxidation of the alcohol (Scheme 2.4) which gave relatively pure aldehyde **9** (Scheme 2.4). [45a]

Scheme 2.4



The other aldehyde **11** was also synthesized from butyrolactone **(7)** using pyrrolidine in the presence of Et_3N to form corresponding alcohol **10** and then the alcohol was oxidized to aldehyde using Swern oxidation conditions, oxalyl chloride in DMSO to **11** in 85% overall yield (Scheme 2.5). [45b]

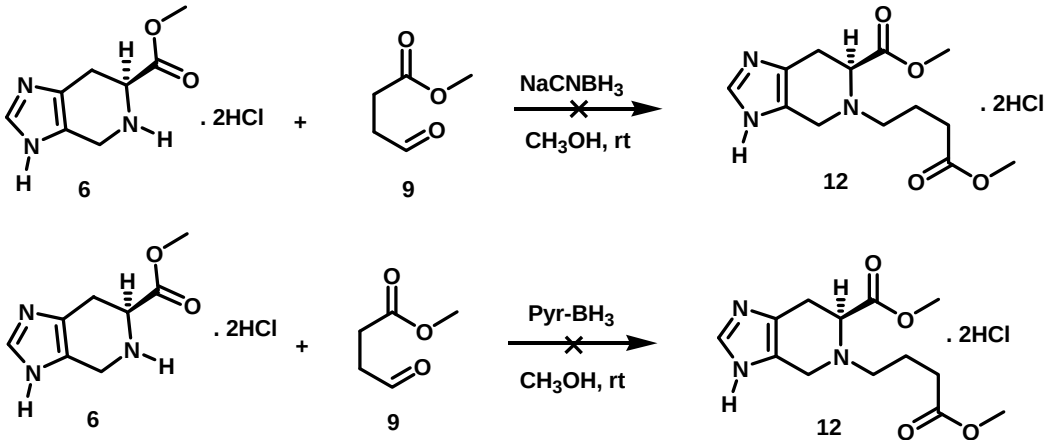
Scheme 2.5



2.1.4 Reductive Amination

Aldehyde **9** was subjected to reductive amination with spinacine methyl ester **6** using $NaCNBH_3$ [46-48a] or Pyr-BH_3 [48b] as reducing agents and methanol as a solvent to prepare diester compound **12,** but unfortunately neither reagent gave the required precursor **12** for Dieckmann condensation. The possible reason for the failure of this reaction is that spinacine methyl ester is in the form of hydrochloride salt and therefore there is insufficient free base for imine formation (Scheme 2.5). Also by this time we recognized that if the Pictet-Spengler reaction were conducted later, then haplocleridamine would serve as a precursor to villagorgin A, therefore this approach was not pursued any further.

Scheme 2.5

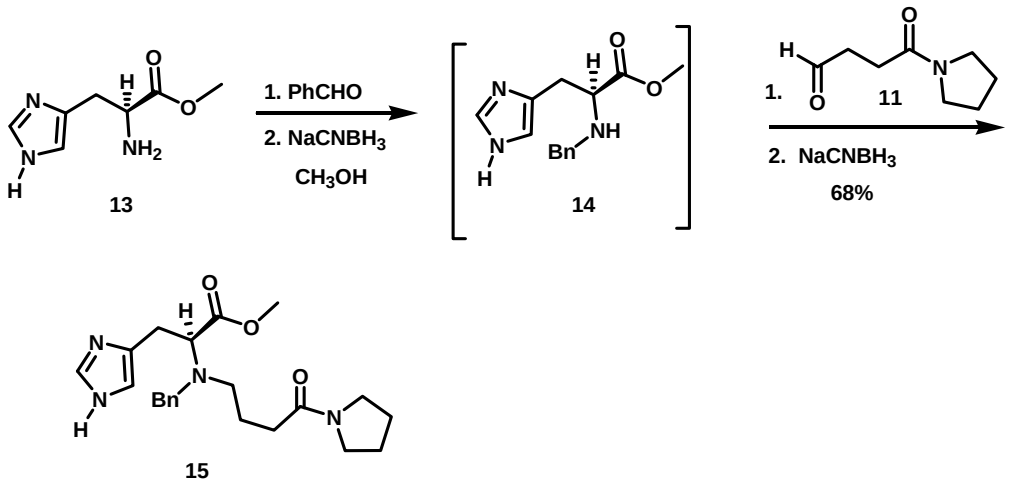


2.1.5 Reductive Amination with the Free Base

The free base of histidine methyl ester **13** was prepared by treatment of the corresponding hydrochloride salt with sodium methoxide in absolute methanol.[49] The reductive amination procedure is performed without resorting to side-chain protection for the imidazole ring via consecutive reductive amination reactions, first with benzaldehyde, to form benzylamine **15** and then with pyrrolidine substituted aldehyde **11**. Both sequences of imine (iminium) formation/reduction are performed in the same flask without isolation of amine **14**.

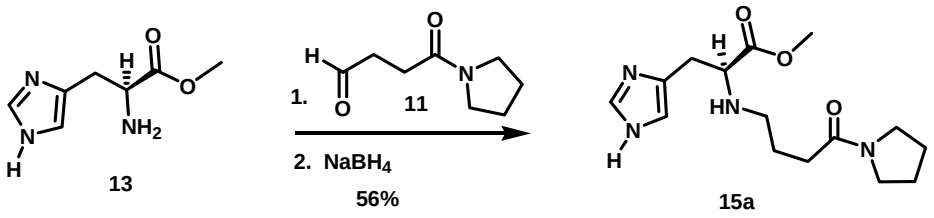
As shown in Scheme 2.6, our method involves treatment of the amino acid ester, in methanol, first with benzaldehyde for 1 h, followed by overnight reduction with sodium cyanoborohydride. The benzylamine **14** formed in situ is treated with pyrrolidine substituted aldehyde **11**. Then another equivalent of sodium cyanoborohydride is added and again the mixture was allowed to react overnight to furnish the required pyrrolidine substituted ester **15** in 68% overall yield (Scheme 2.6).[50-51]

Scheme 2.6



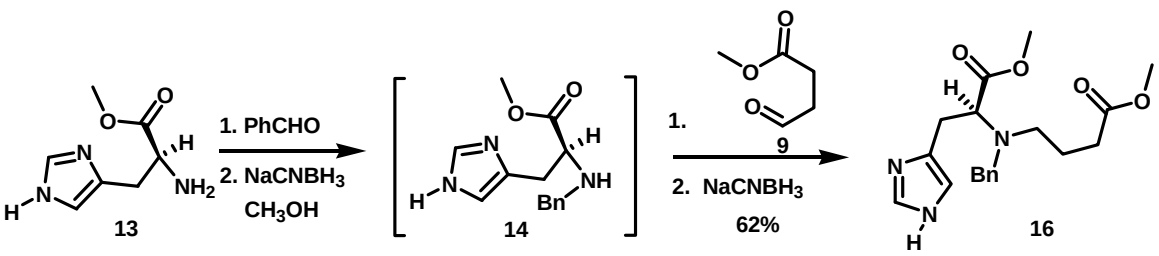
The reductive amination was also successful without amine protection using $NaBH_4$ as reducing agent. This time reductive amination was performed using free base **13** and aldehyde **11** with $NaBH_4$ as reducing agent to obtain **15a** in 56% yield (Scheme 2.6.1).

Scheme 2.6.1



This sequence of two reductive aminations was repeated with 4-oxobutanoic acid methyl ester **9**, and the reaction also worked, providing diester **16** which is obtained 62% yield (Scheme 2.7).

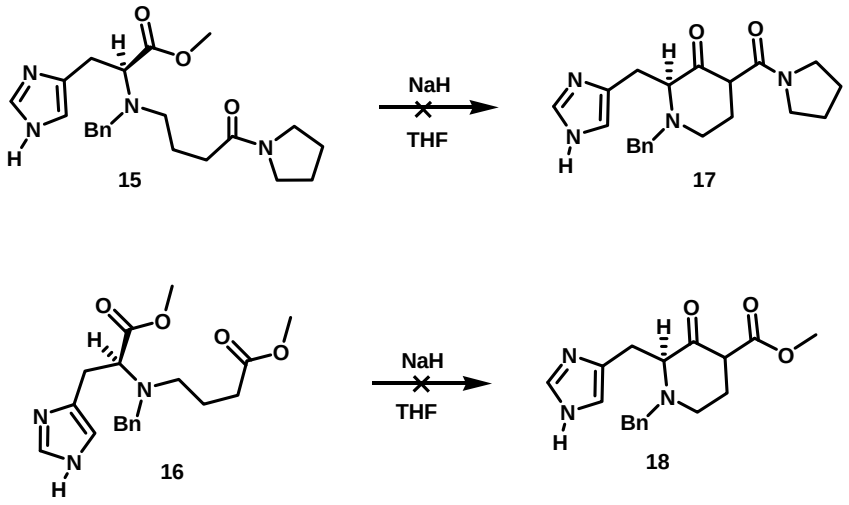
Scheme 2.7



2.1.6 Attempted Dieckman Condensation

The pyrrolidine substituted ester **15** was subjected to the Dieckmann reaction by treatment of the reactant with 1.5 equivalents of sodium hydride as a base in THF to obtain the six-membered cyclic product **17.** Unfortunately, none of the desired *β*-ketoamide **17** was obtained from the reaction. A similar procedure was used to cyclize the diester substrate **16** to a six-membered ring containing product, but again this substrate gave none of the required cyclic ring product **18**. Instead, in both cases, we obtained a complex product mixture along with unreacted starting material which rendered the purification difficult (Scheme 2.8).

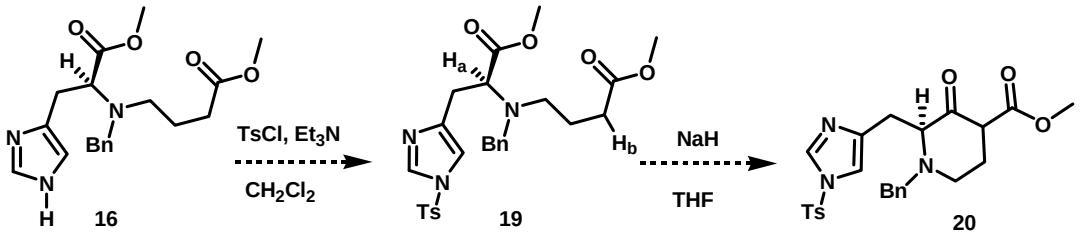
Scheme 2.8



2.1.7 Conclusion for Dieckmann Condensation

After encountering difficulties with these initial Dieckmann cyclizations, we considered protecting the imidazole proton to obtain for example **19,** progressing to the cyclization to afford **20**. However, we anticipated that there might be a problem with this approach due to the acidic α-protons. Due to two acidic protons H_a and H_b the substrate has the potential to undergo cyclization via two different pathways, presenting a chemoselectivity issue. In addition should the cyclization be slow relative to reprotonation of the enolate, racemization may occur. Further, it is also possible that racemization of the adduct may occur on post-cyclization, even if the first two concerns proved not to be an issue (Scheme 2.9).[52] Based on this analysis, we decided to pursue an alternative approach.

Scheme 2.9



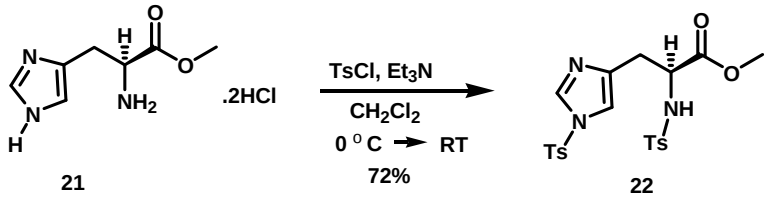
2.2 Second Generation Approach – Ring Closing Metathesis

After considering the racemization may be problem, it was decided to switch to pathway III which would provide a potentional solution to avoid the racemization issue.

2.2.1 Protection of Histidine Methyl Ester

Installing a blocking group which protects the *N* (π)-position of imidazole moiety against racemization of the histidine at the α-carbon center, an electon-withdrawing group was used to protect N1 in the imidazole to decrease the basicity of N3.[53-56] Treatment of histidine methyl ester **21** with four equivalents of triethylamine in dichloromethane and two equivalents of tosyl chloride provided the histidine ditosylate **22** in 72% yield (Scheme 2.10). [57] NMR spectral studies show no indication of the formation of mixtures of isomers (i.e., both N-1 and N-3 derivatives). Our ^{1}H NMR, ^{13}C NMR and NOESY spectra are consistent with the literature data, although it should be noted that the position of substitution was not unambiguously assigned in this report.[58]

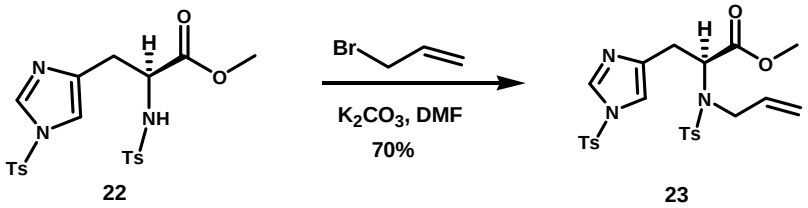
Scheme 2.10



2.2.2 Allylation

Reaction of tosylated product **22** with allyl bromide in the presence of K_2CO_3 at room temperature yielded the *N*-allylated ester **23** in 70% yield.[59] The identity of the product was confirmed through ^1H and ^{13}C NMR spectroscopy, NOESY and by deuterium exchange, which gives an indication that the allylation has occurred at the amine nitrogen and not at the imidazole nitrogen (Scheme 2.11).

Scheme 2.11

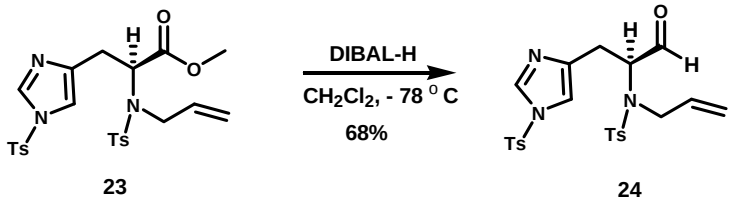


2.2.3 Selective Reduction

With the allylated product **23** in hand, the next step was selective reduction of the ester group. The ester group was reduced selectively to the aldehyde using DIBAL-H at -78 ^oC and dichloromethane as a solvent. The identity of the product obtained **24** was confirmed through ^1H NMR spectroscopy analysis as distinct aldehyde peak at δ

9.65 was observed along with the disappearance of the ester peak at δ 3.5 (Scheme 2.12).[60a]

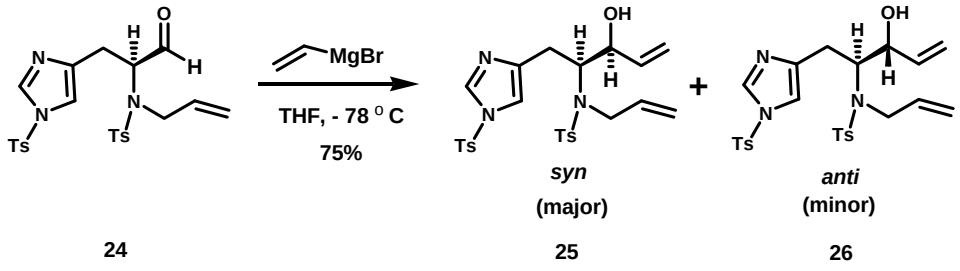
Scheme 2.12



2.2.4 Conversation of Aldehyde to Alcohol using Grignard Chemistry

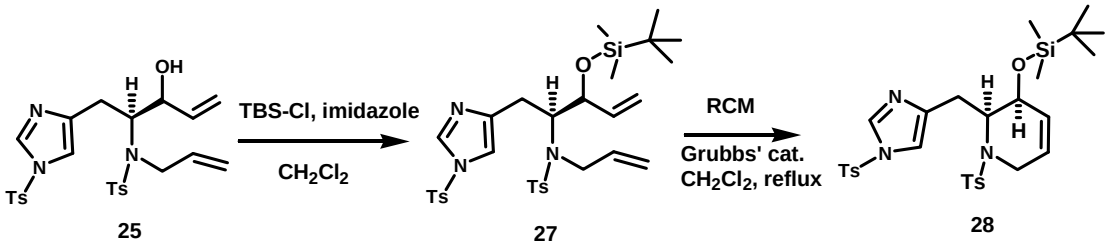
Aldehyde **24,** on treatment with vinyl magnesium bromide, afforded allylic alcohol **25** with an overall yield of 75%. The experiment was conducted at -78 ^{o}C in THF and the vinyl magnesium bromide was prepared by treating magnesium turnings with vinyl bromide. As per the literature, Grignard reagents generally react with chiral aldehydes to give diastereomeric mixtures (**25** and **26)**. In our case, we observe only one isomer which we assume to be *syn* **25** (Scheme 2.13) [61- 62] based on application of 'Crams' rule'.

Scheme 2.13



We confirmed the stereochemistry of this isomer by treatment of allylic alcohol **25** with *t*-butyldimethylsilyl chloride in CH_2Cl_2 to obtain silyl protected allylic alcohol **27.** Then **27** was subjected to RCM with 10 mol% of Grubbs' second generation catalyst to obtain the cyclic product **28**. ^1H NMR spectral studies indicate that the coupling constant between two protons in **27** is 6 Hz, and is consistent with the *syn* isomer **25** (Scheme 2.14).

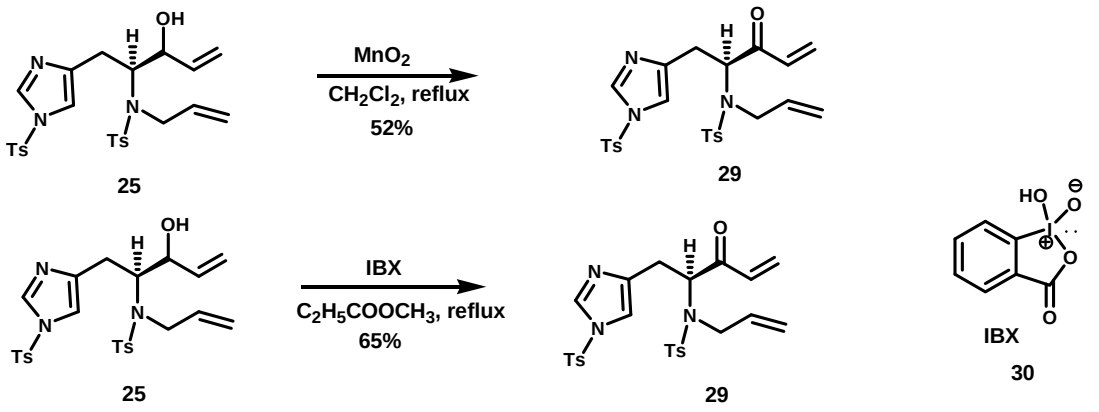
Scheme 2.14



2.2.5 Oxidation of Allylic Alcohol to Ketone

Oxidation of allylic alcohol **25** with MnO_2 afforded the ketone **29** in 56% yields. Further attempts to improve the yield of this reaction treatment of allylic alcohol **25** with iodoxybenzoic acid (IBX)[65] **30** as oxidizing agent to gave **29** in 65% yield (Scheme 2.15). [63- 64]

Scheme 2.15



2.2.6 Ring-Closing Metathesis

At this point, it was decided for completeness that the diene substrates **29** should be evaluated in the RCM reaction. The first attempts to perform this reaction were done using the first generation Grubbs' catalyst. When this reaction was performed for the first time, the starting material was dissolved in CH_2Cl_2 to prepare a 0.1 M solution with 1.1 equivalents of *p*-TsOH. The reaction occurred to give the cyclic product **31** in 20% yield. Motivated by this promising result, the reaction was attempted, using the 0.1 M solution of the starting material but was initially heated at reflux with 1.1 equivalents of *p*-TsOH in CH_2Cl_2 for 30 minutes and then second generation Grubbs' catalyst **32** was added instead of first generation Grubbs' catalyst. The mixture was refluxed for another 3 h, and then allowed to cool down to room temperature and stirred overnight. After work up with aqueous $NaHCO_3$ and extracting with CH_2Cl_2 the ^1H NMR spectrum of the crude product showed the RCM product along with the starting

material. Purification of the crude material by column chromatography provided the pure enone in 40% yield (Scheme 2.16).[66-68]

Scheme 2.16

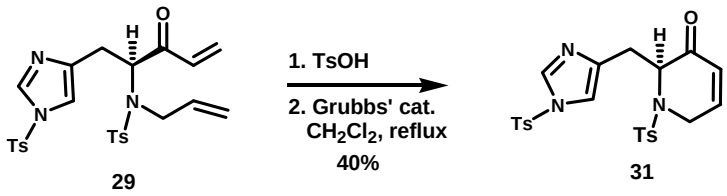
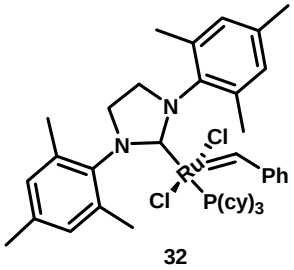


Table 1.1 Reaction Condition for RCM

entry	catalyst	Solvent	T(^{o}C)	Time	yield
1	5	CH_2Cl_2	reflux	3h	15
2	10	CH_2Cl_2	reflux	3h	40
3	10	CH_2Cl_2	reflux	24h	40
4	5+5	CH_2Cl_2	reflux	24h	40
5.	10	C_6H_6	reflux	24h	No rxn
6.	10	$C_6H_5CH_3$	reflux	24h	No rxn
7.	10	1,2-Dichloro Ethane	reflux	24h	No rxn

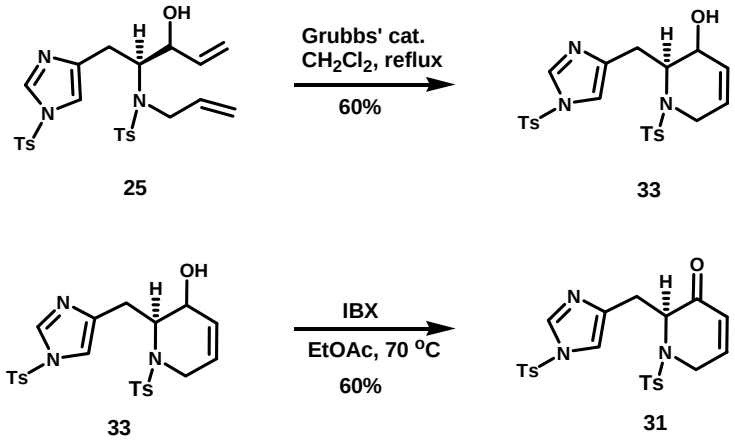
Grubbs' 2nd generation catalyst



Further attempts were made to optimize the yield by studying the reaction in other solvents and changing the reaction conditions, (Table 1.1) but there was no

significant improvement in the yield. Therefore we evaluated the allylic alcohol **25** rather than the allylic ketone in the RCM reaction using same reaction condition in the absence of *p*-TsOH to get RCM product **33**. We were delighted to find that the yield improved to 60% (Scheme2.17).[69] Once again taking advantage of IBX, enol **33** was oxidized to enone in ethyl acetate as solvent to obtain **31** in 60% yield.

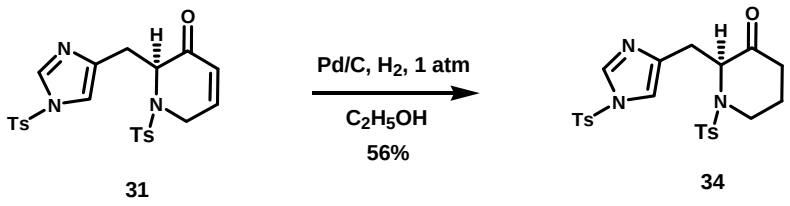
Scheme 2.17



2.2.7 Hydrogenation

Hydrogenation of **31** with Pd/C in ethanol gave compound **34** in 56% yield (Scheme 2.18).[70] The structure was confirmed by IR, ^{1}H and ^{13}C NMR spectroscopy.

Scheme 2.18

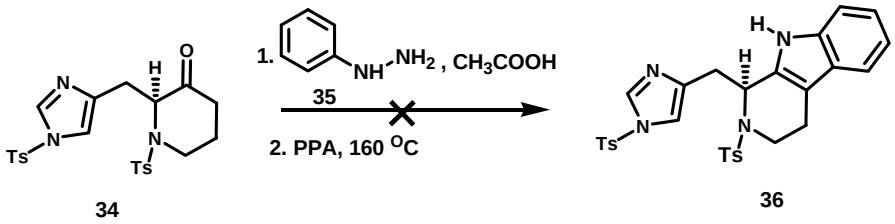


2.3 Progress towards Completion of Villagorgin

2.3.1 Indole Moiety Insertion: Fischer Indole Synthesis

After successful synthesis of the key intermediate **34,** the piperidone ring was subjected to the Fischer indole synthesis using phenylhydrazine **35** in absolute ethanol with few drops of acetic acid. After refluxing for 1 h, the formation of hydrazone was confirmed through TLC, by the complete disappearance of starting material, and formation of a new spot more polar than the starting material. The solvent was removed and the crude phenylhydrazone was treated with PPA and heated to 160 ^{o}C for 45 minutes. But further cyclization of the hydrazone to the indole **36** ring did not appear to take place (Scheme 2.19).[33-34] Other catalysts such as HCl/EtOH, $ZnCl_2$/AcOH and AcOH/HCl gave poor result for the formation of hydrazone.[71]

Scheme 2.19

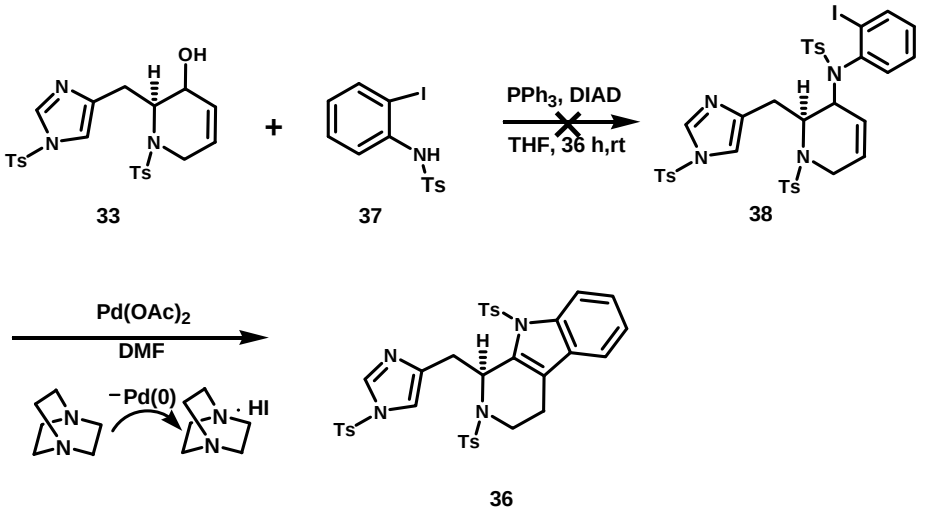


2.3.2 Mitsunobu-Heck Reaction to Construct the Indole Ring

Synthesis of **36** was attempted making use of Mitsunobu reaction between allylic alchol **33** and tosyl protected iodoaniline **37** (Scheme 2.20)[72]. By employing of 1.3 equivalents each of PPh_3 and diisopropyl azodicarboxylate (DIAD) in THF we

anticipated that **38** would be obtained. However, no evidence of carbon-nitrogen bond formation was obtained.

Scheme 2.20

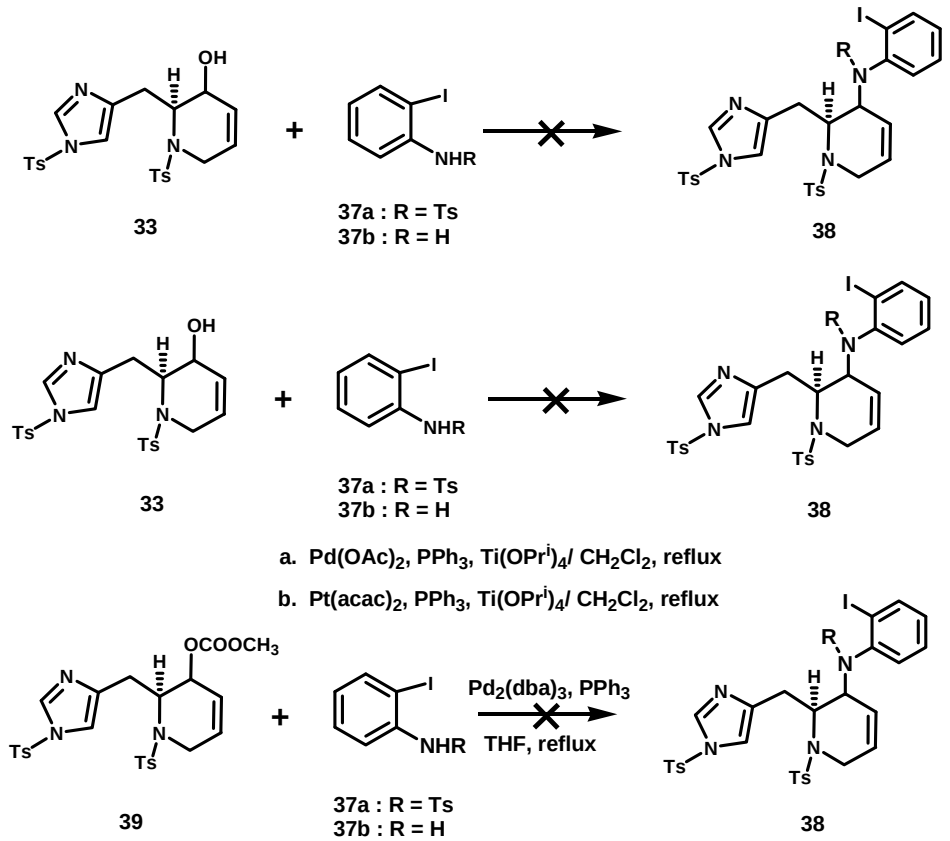


2.3.3 Palladium-Catalyzed Allylation using Allylic Alcohol to Construct the Indole Ring

After the unsuccessful results obtained from the Mitsunobu reaction we attempted palladium-catalyzed allylation with an allylic alcohol substrate. The palladium-catalyzed allylation is an established, efficient, and highly stereo- and chemoselective method for C–C, C–N, and C–O bond formation. This process proceeds by attack of nucleophiles on a intermediate η^3-allylpalladium(II) complexes generated by oxidative addition of allylic compounds including alcohols, halides, esters, carbonates, carbamates, phosphates.[73-75] Allylic alcohol **33** mixed with tosyl- protected amine *o*-iodoaniline, **37a,** also with free amine **37b** was subjected to palladium-catalyzed allylation in the presence of palladium(II) catalyst. A Similar reaction was

attempted with **39**, once again we were unsuccessful with the C-N bond formation to obtain **38** (Scheme: 2.21).[76- 77]

Scheme: 2.21

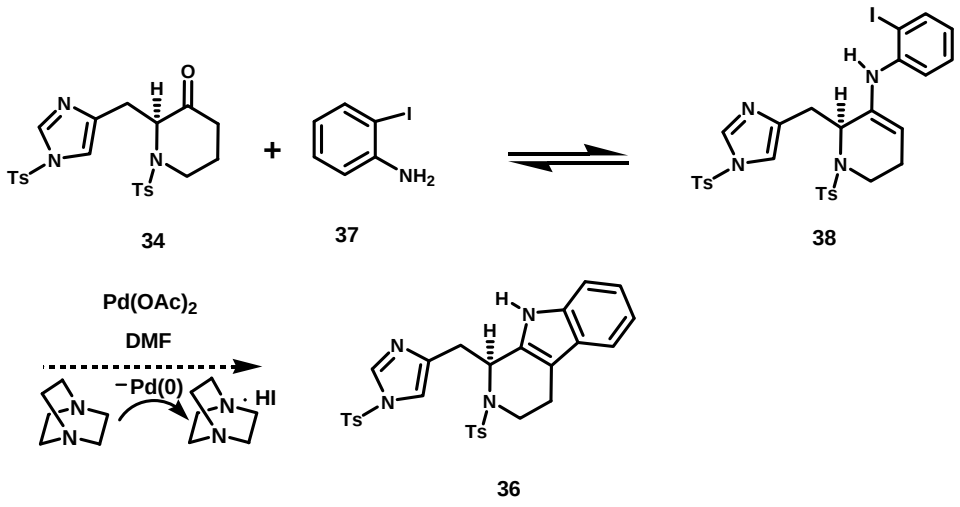


2.3.4 Heck-type Reaction to Construct Angular Indole Ring

The traditional approach for preparing the indole nucleus is the Fischer indole reaction. After several attempts to install the indole group by traditional approaches had failed, we tried to use palladium-catalyzed coupling of *o*-haloanilines **37** with the piperidone ring **34** as an alternative approach. A combination of such palladium-catalyzed reaction with ketones and aldehyde would be a tremendously straightforward

approach which could be an efficient method for indole synthesis using palladium-catalyzed annulation between *o*-iodoanilines **37** and ketones **34** (Scheme 2.22).[78] The reaction would proceed by enamine **38** formation followed by an intramolecular Heck reaction may give the required compound **36** with angular indole ring substitution. Unfortunately, the Heck type reaction did not work with the substrate **34**.

Scheme 2.22

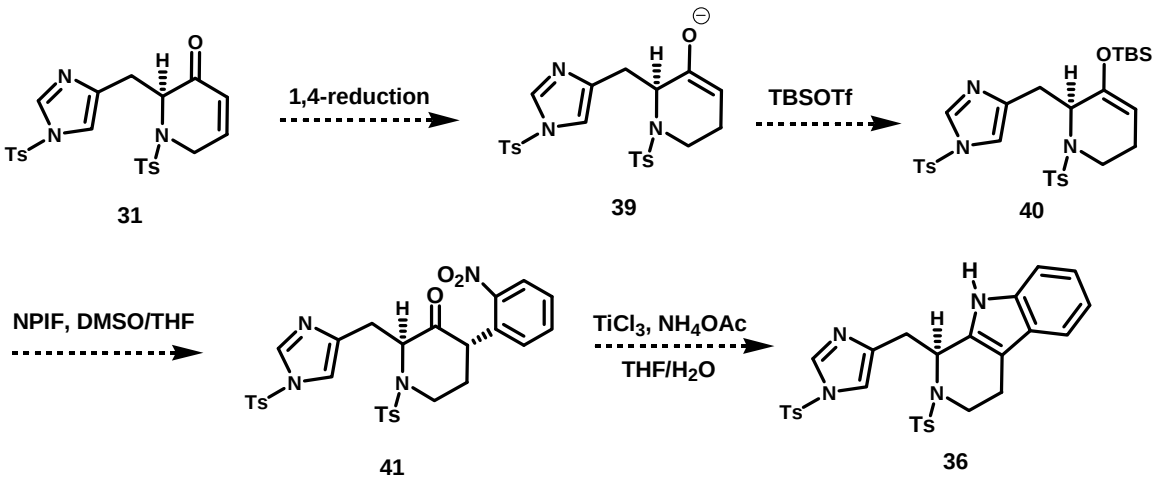


2.3.5 Alternative Synthesis for Indole Ring Substitution

(o- Nitrophenyl)phenyliodonium Fluoride (NPIF reagent)

The enone **31** can be subjected to a 1, 4-reduction to form enolate **39** and the enolate can be trapped with TBSOTf to give **40**. Further, subjecting **40** to NPIF reagent, *o*-nitophenylation of the silyl ether (Scheme 2.23)[79-80] to obtain the nitroaryl group substituted product **41**. Subsequent reduction of the nitro group on aryl ketone **41** followed by spontaneous cyclization should afford the indole product **34**.

Scheme 2.23


1,4-reduction
TBSOTf
NPIF, DMSO/THF
TiCl3, NH4OAc
THF/H2O
31
39
40
41
36

CHAPTER 3

EXPERIMENTAL DETAILS

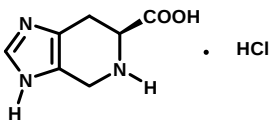
3.1 Instrumental Information

All chemicals and solvents were purchased from commercial vendors and were used as received unless indicated otherwise. All reactions involving air- or water-sensitive compounds were conducted in oven-dried (overnight) glassware under an atmosphere of dry argon or nitrogen. Tetrahydrofuran (THF) and ether were distilled from sodium/benzophenone ketyl and dichloromethane from calcium hydride (CaH_2) under a nitrogen atmosphere. A pure-Solv 400 solvent purification system from Innovative Technology Inc. was also used to obtain anhydrous solvents CH_3CN, THF, CH_2Cl_2 benzene and toluene. ^1H NMR spectra of 1.0-1.5% solutions in a deuterated solvent were recorded at spectrometer frequencies of 500.16 and 300.13 MHz on JEOL Eclipse+ 500 and 300 spectrometers, respectively. The ^{13}C NMR spectra of 1.5-4.0% solutions in the appropriate deuterated solvent were measured at 125.79 and 75.47 MHZ on JEOL Eclipse 500 and 300 spectrometers, respectively using $^{13}CDCl_3$ ($\delta = 77.0$) as internal reference. Infrared (IR) spectra were obtained on a Bruker Vector 22 FT-IR spectromenter, using KBr pressed pellets for solids or neat films on NaCl plate for liquids and oils, and are reported in cm^{-1}. High resolution spectra (HR-MS) were obtained from Dr. Powell's laboratory at the University of Florida, Gainesville, Florida. Melting points were recorded on a Thomas Hoover Scientific capillary tube melting

point apparatus and were uncorrected. Analytical thin layer chromatography (TLC) was performed on silica gel 60_{F254} aluminium backed precoated plates (layer thickness: 200 μm). Preparative thin layer chromatography (PTLC) was performed on silica gel 150 Å. All liquid chromatography (LSC) separations were performed using silica gel (200-400 mesh) employing the flash technique.

3.2 Synthesis Information

4,5,6,7-Tetrahydro-3*H*-imidazo[4,5-*c*]pyridine-6-carboxylic acid hydrochloride



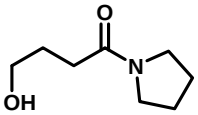
(5): A mixture of L-histidine (41.5 g, 0.20 mol), 12 N hydrochloric acid (400 mL) and methylal (60 mL) was added and the mixture was stirred at room temperature, overnight. An additional portion of methylal (60 mL) was added and stirred for three hour under reflux. The resulting solution was concentrated to half the volume at reduced pressure and adjusted to pH 8 using ammonia, crystals separated upon standing. The resulting solid filtered and air-dried to afford the pure product **2** (42.0 g, 93%) as colorless crystals. mp: 283-284 ^{o}C [lit. mp[25]: 279-280 ^{o}C] ^{1}H NMR (300 MHz, D_2O): δ = 7.70 (s, 1H), 4.21 (dd, 2H, J = 14.8, 25.1), 4.0 (dd, 1H, J = 5.5, 11.0 Hz), 3.20 (dd, 1H, J = 5.9, 17.2 Hz), 2.90 (dd, 1H, J = 11.7, 16.5 Hz). ^{13}C NMR: δ = 171.8, 134.8, 124.7, 120.4, 55.8, 38.6, 21.8.

4,5,6,7-Tetrahydro-3*H*-imidazo[4,5-*c*]pyridine-6-carboxylic acid Hydrochloride methyl ester (6): Spinacine **5** (22.0 g, 0.13 moles) and methanol (150 mL) saturated with gaseous hydrochloric acid was heated to reflux overnight. The resulting solution was again treated with a stream of hydrogen chloride and refluxed for an additional 1 h to complete the reaction. The solution was concentrated to half its volume and ether was added, the precipitated solid was filtered to obtain the dihydrochloride salt **3** (16.1 g, 65%) as pale yellow solid. mp: 90-92 ^{o}C [lit. mp[25]: 89-90 ^{o}C]

Methyl 4-oxobutanoate (9):

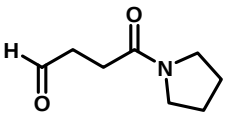
A catalytic amount of conc. H_2SO_4 (1 mL) was added to a solution of butyrolactone **(7)** (10.0 g, 0.117 mol) in methanol (30 mL). The mixture was refluxed for 12 h, and then cooled to room temperature. Imidazole was added and the mixture was stirred for 5 min. The solvent was evaporated and the residue was dissolved in dry CH_2Cl_2 (200 mL). PCC (29.31 g, 0.14 mol) was added and stirring was continued for 5 h. The mixture was filtered through Celite, and the residue was washed with CH_2Cl_2. Evaporation of the solvent and flash chromatography of the residue over silica gel using 1:4 EtOAc-hexane gave methyl 4-oxobutanoate acid **9** (6.80 g, 50%) as yellow oil.[45] ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.78 (s, 1H), 3.80 (s, 3H), 2.80 (t, 2H, *J* = 6.4 Hz), 2.60 (t, 2H, *J* = 6.4 Hz); ^{13}C NMR: δ =177.8, 174.5, 68.60, 51.80, 30.40; FT-IR (CCl_4 cm^{-1}): 2950, 2871, 2713, 1738, 1200.

1-(4-Hydroxy-1-oxobutyl) pyrrolidine (10):



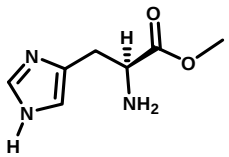
Butyrolactone **(7)** (4.0 mL, 0.046 mol) in pyrrolidine (5.7 m L, 0.093 mol) and Et_3N (13.67 mL, 0.186 mol) was refluxed for 2 days. The resulting mixture was concentrated to provide the title compound **10** (5.9 g, 80%) was obtained in the form of viscous yellow oil.[45b] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.67 (t, 2H, *J* = 5.9 Hz), 3.45 (t, 2H, *J* = 6.9 Hz), 3.40 (t, 2H, *J* = 5.9 Hz), 2.45 (t, 2H, *J* = 6.6 Hz), 2.14 (d, 1H, *J* = 1.3 Hz), 1.8 - 2.0 (m, 4H).

4-Oxo-4-pyrrolidin-1-yl-butyraldehyde (11):

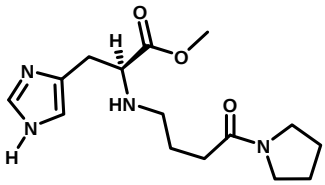


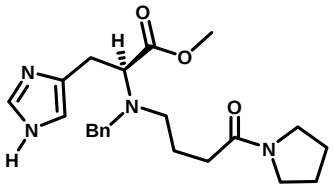
DMSO (5.65 m L, 0.66 mol) in 13mL CH_2Cl_2 were added to a cold (-70 ^{o}C) solution of oxalyl chloride (6 mL, 0.034 mol) in (50 mL) dry CH_2Cl_2 over a period of 15-20 minute and the resulting mixture were stirred for 15 min at -70 ^{o}C. Then **10** (5.0 g, 0.31 mol) in10mL CH_2Cl_2 was added. After 1 h stirring at -70 ^{o}C, Et_3N (11.2 mL) was added and the reaction mixture was allowed to warm-up to room temperature. The reaction mixture was quenched with 100 mL of water. The separated organic layer was dried over Na_2SO_4, filtered and concentrated to obtain the crude product which was purified using flash chromatography over silica gel (EtOAc/hexanes: 40/60)to give **11** as viscous yellow oil (4.2 g, 85%).[45b] ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.9 (s, 1H), 3.44 (t, 2H, *J* = 6.9 Hz), 2.82 (t, 2H, *J* = 6.5 Hz), 2.58 (t, 2H, *J* = 6.9 Hz), 1.96 (q, 2H, *J* = 6.5 Hz), 1.85 (q, 2H, *J* = 6.9 Hz) ; ^{13}C NMR: δ = 201.4, 169.5, 46.5, 45.7, 38.5, 27.1, 24.4, 21.0.

2-Amino-3(1*H*-imidazo-4-yl)propionic acid methyl ester (13):

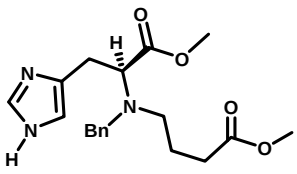


(29.0 g, 0.12 mol) of finely powered histidine methyl ester dihydrochloride was dissolved in absolute methanol (300 mL) by heating and stirring for 1 h. When all the material was dissolved, the flask was placed into an ice-salt bath and rapidly cooled to 0-10 ^{o}C. Before crystallization began a cold solution of NaOMe (prepared from sodium 5.52 g, 0.24 mol) in absolute methanol (150 mL) was added and the mixture was thoroughly swirled. Sodium chloride started to precipitate almost immediately. To complete the removal of the salt, ether (200 mL) was added; the mixture was again thoroughly mixed and kept in the cold bath for 15-20 minutes. The sodium chloride precipitate was finely divided and is difficult to remove. The filtration is best performed by gravity filtration using fluted filter paper. The filtrate was collected and concentrated under reduced pressure to provide thick syrup. Chloroform (25 mL) was added, and the solution was again concentrated. This was repeated twice more to remove the last traces of methanol. The residue was then extracted with (4x50 mL) of chloroform. The chloroform extracts are combined, dried over Na_2SO_4, and concentrated with a bath temperature of 20-40 ^{o}C to approximately (100 mL). This solution of the histidine free ester was protected from moisture by a calcium chloride tube at 0 ^{o}C or below. The title compound **13** (10.0 g, 50%) was obtained in the form of viscous clear oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.56 (s, 1H), 6.85 (s, 1H), 3.77 (dd, 2H, J = 8.0, 12.0 Hz), 3.70 (s, 3H), 3.0 (dd, 1H, J = 4.1, 14.8 Hz), 2.81 (dd, 2H, J = 8.3, 14.8 Hz). FT-IR (neat solvent, cm^{-1}): 3523, 3496, 3460, 3420, 2291, 2341, 1375, 1174, 960, 770. 520.

3-(1*H*-Imidazol-4-yl)-2-94-oxo-4-pyrrolidin-1-yl-butylamino-propionic acid methyl ester (15a):  Histidine free base **11** (1.7 g, 0.01 mol) was dissolved in methanol (10 mL) containing molecular sieves 4 Å (1 g). To this solution was added 4- oxo pyrrolidine (1.55 g, 0.01 mol) added and stirred at room temperature for 5 h. Then, 5 equivalents of $NaBH_4$ (1.85 g, 0.05 mol) added, cooling at 0 ^oC, stirred for 5 h at this temperature. The reaction mixture was worked up by ethyl acetate and water (1:1) extraction and then concentrated to obtain the crude compound. The crude product was purified by chromatography (EtOAc/hexanes: 60/40) to give the title compound **15a** as a viscous oil (1.74 g, 56%). ^1H NMR (300 MHz, $CDCl_3$): δ = 7.50 (d, 1H, *J* = 4.8 Hz), 6.84 (d, 1H, *J* = 4.8 Hz), 4.43 (dd, 1H, *J* = 1.4, 5.5 Hz), 3.72 (d, 2H, *J* = 1.4 Hz) 3.50 (t, 2H, *J* = 6.5 Hz), 3.4 (t, 2H, *J* = 6.9 Hz), 3.3 (d, 3H, *J* = 1.7 Hz), 3.03 – 3.12 (m, 1H), 2.84 – 2.92 (m, 1H) , 2.62 - 2.69 (m, 1H), 2.34 (t, 1.5H, *J* = 6.9Hz), 2.30 (t, 1.5H, *J* = 7.2 Hz), 1.92 (q, 2H, *J* = 7.2 Hz), 1.76 (q, 2H, *J* = 7.2 Hz); ^{13}C NMR: δ = 174.8, 171.6, 135.1, 131.6, 120.0, 61.4, 52.0, 47.4, 46.7, 45.8, 32.3, 29.8, 26.1, 25.1, 24.2. EI-MS (*m/z*): calcd. for $[M+H]^+$ $C_{15}H_{24}N_4O$ 309.3761, found 309.3321. Anal. Calcd. : C 58.42; H, 7.84; N, 18.17; O, 15.56.

2-[Benzyl-(4-oxo-4-pyrrolidin-1-yl-butyl)amino]-3-(1*H*-imidazol-4-yl)propionic acid methyl ester (15):  The free base **13** (0.50 g, 2.9 mmol) was dissolved in methanol (100 mL). To this solution benzaldehyde (0.20 g, 3.0 mmol) was added in one portion. The Reaction mixture was stirred at room temperature for 1 h. Then, 1.05 equivalents of $NaBH_3CN$ (0.2 g, 3.0 mmol) was added and the reaction was allowed to stir at room temperature for 18 h, after which 1.0 equivalent of aldehyde **13** (0.47 g, 3.0 mmol) was added. An additional 1.05 equivalent $NaBH_3CN$ was added and the reaction was allowed to stir at room temperature for 18 h. After this period the reaction mixture was concentrated in vacuo, taken up in CH_2Cl_2 (10 mL) and washed twice with de-ionized water (2x5 mL). The organic layer was dried with anhydrous $MgSO_4$ and concentrated in vacuo, to give the final product as a sticky oily compound. The crude product was purified by chromatography (EtOAc/hexanes: 60/40) to give the title compound **15** as a viscous oil (0.66 g, 68%). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.50 (d, 1H, *J* = 6.9), 7.34 (d, 2H, *J* = 5.5), 7.28 (d, 1H, *J* = 5.5), 7.21 (d, 1H, *J* = 7.2 Hz), 7.10 (d, 2H, *J* = 7.2 Hz), 6.65 (d, 2H, *J* = 6.9 Hz), 3.90 (dd, 2H, *J* = 3.8, 13.8Hz), 3.70 (s, 3H), 3.43 (t, 2H, *J* = 6.9 Hz), 3.40 (t, 2H, *J* = 6.9 Hz), 3.30 (d, 1H, *J* = 6.9 Hz), 2.80 – 3.10 (m, 2H), 2.50 – 2.71 (m, 2H), 2.06 - 2.25 (m, 2H), 1.94 (q, 2H, *J* = 7.6 Hz), 1.86 (q, 2H, *J* = 7.6 Hz); ^{13}C NMR: δ = 172.9, 171.8, 139.6, 134.7, 128.7, 128.6, 128.3, 127.0, 77.3, 70.8, 62.5, 55.5, 51.3, 49.5, 46.7, 46.0, 31.6, 26.1, 24.5, 23.0. FT-IR (neat solvent, cm^{-1}): 3769, 3131, 2891, 1734, 1620,

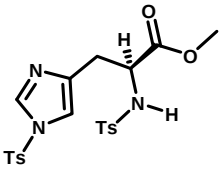
1456, 1357, 1193, 1027, 477. HR-MS (*m/z*): calcd. for $[M+H]^+$ $C_{22}H_{30}N_4O_3$ 399.2318, found 399.2391.

4-{Benzyl-[2-(1H-imidazol-4-yl)-1-methoxycarbonylethyl]amino}butyric acid methyl ester (16): 

The free base **13** (0.25 g, 1.5 mmol) was dissolved in methanol (100 mL). To this solution benzaldehyde (0.19g, 1.6 mmol) was added in one portion. The reaction was stirred at room temperature for 1 h. Then, 1.05 equivalents of $NaBH_3CN$ (0.2 g, 3.0 mmol) was added and the reaction was allowed to stir at room temperature for 18 h, after which1.0 equivalent of aldehyde **9** (0.17 g, 1.5 mmol) was added. An additional 1.05 equivalents of $NaBH_3CN$ was added and the reaction was allowed to stir at room temperature for 18h. After this period the reaction mixture was concentrated in vacuo, taken up in CH_2Cl_2 (10 mL) and washed twice with de-ionized water (5 mL). The organic solution was dried with anhydrous $MgSO_4$ and concentrated in vacuo, to give the final product as a sticky oily compound. The crude product was purified by chromatography (silica gel, EtOAc/hexanes: 60/40) to give the title compound **16** as a viscous oil (0.33 g, 62%).^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.55 (d, 2H, *J* = 6.2 Hz), 7.49 (s, 1H), 7.39 (d, 2H, *J* = 4.9 Hz), 7.23 (d, 2H, *J* = 4.9 Hz), 7.21 (d, 2H, *J* = 7.91 Hz), 6.74 (s, 1H), 3.90 (d, 1H, *J* = 13.8 Hz), 3.72 (s, 3H), 3.64 (s, 3H, *J* =), 3.55 (d, 1H, *J* = 13.8 Hz), 3.10 (dd, 2H, *J* = 4.8, 12.0 Hz), 2.84 – 3.00 (m, 2H), 2.52 - 2.72 (m, 4H), 1.76 (t, 2H, *J* = 7.6 Hz); ^{13}C NMR: δ = 174.7, 174.4, 139.4, 134.7, 129.1, 128.8, 128.7, 127.7, 127.4, 127.2, 62.6, 60.7, 55.5, 52.2, 51.7, 49.8, 31.3, 29.5; FT-IR

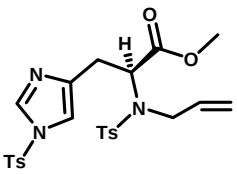
(neat solvent, cm^{-1}): 3654, 2840, 1894, 1754, 1433, 1181. HR-MS (*m/z*): calcd. for $[M+H]^+$ $C_{19}H_{25}N_3O_4$ 360.1819, found 360.1883.

2-(Toluene-4-sulfonylamino)-3-[1-(toluene-4-sulfonyl)-1*H*-imidazol-4-ylpropionic

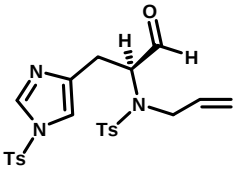


acid methyl ester (22): Histidine methyl ester hydrochloride (0.25g, 1.47 mmol), was dissolved in dichloromethane (5 mL), triethylamine (1 mL) and tosyl chloride (0.563 g, 2.95 mmol) were slowly added with vigorous stirring and cooled in an ice bath. The reaction mixture was stirred at ^oC for 30 min and then room temperature for 2 h, additional dichloromethane1(10 mL) was added to the reaction mixture and the solution was washed with water and brine (3 x 2.5 mL) and dried with Na_2SO_4. The extract was concentrated under reduced pressure. The residue was purified by flash chromatography (silica gel, 50/50 EtOAc/hexane) to furnish solid **22** (0.50 g, 73%) as colorless crystalline solid: mp: 185-187 ^oC, [lit. mp[58]: 89-90 ^oC], $[\alpha] = +10.27$ (c = 0.01, CH_2Cl_2). ^1H NMR (500 MHz, $CDCl_3$): δ = 7.84 (s, 1H), 7.77 (d, 2H, *J* = 8.3 Hz), 7.66 (d, 2H, *J* = 8.7 Hz), 7.35 (d, 2H, *J* = 8.3 Hz), 7.24 (d, 2H, *J* = 8.3 Hz), 7.00 (s, 1H), 5.65 (d, 2H, *J* = 8.7 Hz), 4.19 (dt, 1H, *J* = 5.0, 9.2 Hz), 3.47 (s, 3H), 2.91 (dd, 2H, *J* = 3.2, 5.0 Hz), 2.42 (s, 3H), 2.41 (s, 3H); ^{13}C NMR: δ =174.8, 146.3, 141.4, 139.1, 136.3, 135.0, 130.5, 128.4, 128.3, 127.4, 127.1, 114.6, 60.0, 52.0, 51.8, 32.0, 21.8; FT-IR (KBr cm^{-1}): 3479, 3111, 2588, 2315, 2180, 2091, 1923, 1806, 1747, 1632, 1594, 1458, 969, 913, 845, 813, 781, 667, 570, 497.

2-[Allyl-(toluene-4-sulfonyl)-amino]-3-[1-(toluene-4-sulfonyl)-1*H*-imidazol-4-yl]-propionic acid methyl ester (23): Tosyl protected histidine **21** (0.15 g, 3.23 mmol) was

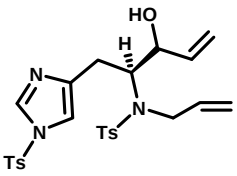


dissolved in DMF (10 mL) and K_2CO_3 (0.05 g, 4.85 mmol) was added and stirred for 1h. Then allyl bromide (0.05mL, 3.23 mmol) was added and the reaction miture was stirred at room temperature for 34 h. After this period the mixture was diluted with equal amount of water and extracted with CH_2Cl_2. The organic extracts were combined and washed thoroughly with brine. The organic extracts were dried over Na_2SO_4, filtered and concentrated to provide the crude product. The crude compound was purified through flash chromatography (silica gel, EtOAc/hexane 40/60) to afford **22** (0.33 g, 79%) as white solid: mp: 118-120 ^oC, [α] = - 47.4 (c = 0.01, CH_2Cl_2). ^1H NMR (500 MHz, $CDCl_3$): δ = 7.80 (s, 1H), 7.78 (d, 2H, *J* = 8.3 Hz), 7.62 (d, 2H, *J* = 8.3 Hz), 7.35 (d, 2H, *J* = 8.3 Hz), 7.23 (d, 2H, *J* = 8.3 Hz), 7.04 (s, 1H, *J* = 8.3 Hz), 5.58 (ddt, 1H, *J* = 6.4, 10.6, 17.0 Hz), 5.07 (d, 1H, *J* = 17.4 Hz), 4.98 (d, 1H, *J* = 10.1), 4.8 (dd, 1H, *J* = 6.0, 8.7 Hz), 3.86 (dd, 1H, *J* = 6.4, 16.5 Hz), 3.69 (dd, 1H , *J* = 6.4, 16.0 Hz), 3.52 (s, 3H), 3.19 (dd, 1H, *J* = 6.0, 15.1 Hz), 2.93 (dd, 2H , *J* = 9.2, 15.1 Hz), 2.40 (s, 6H); ^{13}C NMR: δ = 171.0, 146.2, 143.5, 140.4, 137.3, 136.2, 135.1, 134.3, 130.4, 129.5, 127.5, 127.4, 118.1, 115.3, 59.0, 52.2, 49.0, 29.3, 21.8, 21.6; FT-IR (KBr, cm^{-1}): 3131, 3121, 2956, 1753, 1641, 1607, 1595, 1480, 1430, 1332, 1294, 1252, 1221, 1161, 1081, 995, 878, 798, 761, 734, 677, 590, 551, 501. HR-MS (*m/z*): calcd. for $[M+H]^+$ $C_{24}H_{28}N_3O_5S_2$ 518.1420, found 518.1414.

***N*-Allyl-*N*-{1-formyl-2-[1-(toluene-4-sulfonyl)-1*H*-imidazol-4-yl]-ethyl}-4-methyl-benzenesulfonamide (24):** 

The ester **22** (4.47 g, 8.6 mmol) was dissolved in dry CH_2Cl_2 (50 mL) and cooled to -78 ^oC. A precooled (-78 ^{o} C) solution of DIBAL-H (22.8 mL) was slowly added to the reaction mixture. After stirring for 2h at this temperature the reaction was quenched with methanol (50 mL), warmed to room temperature and the resulting mixture was stirred for 1 h with saturated K-Na-tartrate solution, then extracted with CH_2Cl_2. The collected organic layers were washed with brine and dried over Na_2SO_4. The concentrated residue as purified by flash chromatography (silica gel, EtOAc/hexane 40/60) to furnish the product **24** as a colorless solid: mp: 108-110 ^oC, [α] = + 0.42 (c = 0.014, CH_2Cl_2). ^1H NMR (500 MHz, $CDCl_3$): δ = 9.65 (s, 1H), 7.75 (d, 1H, *J* = 8.7 Hz), 7.73 (d, 2H, *J* = 8.7 Hz), 7.60 (d, 2H, *J* = 8.3 Hz), 7.34 (d, 2H, *J* = 8.3 Hz), 7.26 (d, 2H, *J* = 8.3 Hz), 6.70 (s, 1H), 5.68 (ddt, 1H, *J* = 6.4, 10.5, 17.0 Hz), 5.14 (dt, 2H, *J* = 1.4, 8.3 Hz), 4.47 (dd, 1H, *J* = 9.2, 5.0 Hz), 3.86 (dd, 1H, *J* = 15.6, 6.9), 3.64 (dd, 1H, *J* = 6.4, 15.6 Hz), 3.20 (dd, 1H , *J* = 16.0, 5.0 Hz), 2.93 (dd, 2H , *J* = 15.1, 9.2 Hz), 2.45 (s, 3H), 2.42 (s, 3H); ^{13}C NMR: δ = 198.8, 146.4, 144.0, 140.4, 137.5, 136.2, 135.0, 133.3, 130.5, 129.9, 127.3, 127.2, 120.4, 114.9, 65.6, 49.9, 25.9, 21.8, 21.6; FT-IR (KBr, cm^{-1}): 3157, 3126, 2924, 2863, 1909, 1731, 1596, 1478, 1256, 1217, 1154, 940, 793, 625, 520. HR-MS (*m/z*): calcd. for $[M+H]^+C_{23}H_{26}N_3O_5S_2$ 488.1314, found 488.1308.

***N*-Allyl-*N*-{2-hydroxy-1-[1-(toluene-4-sulfonyl)-1*H*-imidazol-4-yl-methyl]-but-3-enyl}-4-methyl-benzenesulfonamide (25):** A solution of **24** (0.20 g, 4.1 mmol) in



THF (5.0 mL) was added to a solution of vinylmagnesium bromide (1.3 M in THF, 5.3 mL) at -78 ^{o}C, and the mixture was stirred for 2 h. After stirring for an additional 1 h at 25 ^{o}C, a saturated solution of NH_4Cl (25 ml) was added to the mixture which was then extracted with EtOAc. The organic phase was washed with brine, dried (Na_2SO_4), and then evaporated to give an oil. The crude product was purified by flash chromatography (silica gel, EtOAc/hexane 50/50), to give the desired alcohol **25** (0.33 g, 75%): [α] = + 1.59 (c = 0.014, CH_2Cl_2). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.76 (d, 2H, *J* = 8.3 Hz), 7.72 (s, 1H), 7.56 (d, 2H, *J* = 8.3 Hz), 7.55 (d, 2H, *J* = 8.3 Hz), 7.34 (d, 2H, *J* = 8.3 Hz), 7.21 (d, 2H, *J* = 7.8 Hz), 6.82 (s, 1H), 5.72-5.82 (m, 2H), 5.01-5.21 (m, 4H), 4.3 (br, t 1H), 4.03-4.09 (m, 1H), 3.88 (dd, 1H, *J* = 6.4, 16.5 Hz), 3.82 (dd, 1H, *J* = 6.0, 16.0 Hz), 2.81 (dd, 1H, *J* = 5.6, 15.6 Hz), 2.74 (dd, 1H , *J* = 8.3, 15.1 Hz), 2.45 (s, 3H), 2.42 (s, 3H); ^{13}C NMR: δ =146.4, 143.5, 141.4, 138.2, 137.8, 136.1, 135.9, 135.05, 130.5, 129.7, 127.3, 127.2, 117.7, 115.9, 114.8, 74.9, 62.6, 48.5, 26.6, 21.8, 21.6; FT-IR (KBr, cm^{-1}):3112, 1749, 1641, 1515, 1240, 1174, 1090, 994, 925, 824, 771, 674, 592, 478, 455, 417. HR-MS (*m/z*): calcd. for $[M+H]^+$ $C_{25}H_{30}N_3O_5S_2$ 516.1627, found 516.1621.

Oxidation of Allylic Alcohol:

General Procedure for MnO_2 Oxidation:

The alcohol (200 mg, 0.39 mmol) was dissolved in CH_2Cl_2 (20 mL), then MnO_2 (33.0 mg, 75% Aldrich, 3.87 mmol) was added and the resulting mixture was stirred at room temperature for 3 days. The reaction mixture was filtered and washed thoroughly with EtOAc. The combined filtrates were concentrated. The residue was purified through a short pad of silica gel (hexanes/EtOAc: 40/60) to give the title compound as a yellow solid compound (100 mg, 52%): mp: 107-109 ^{o}C.

General Procedure for IBX oxidation: Alcohol (550 mg, 0.10 mmol, 1 eq) was dissolved in EtOAc (4 mL) and the IBX (740 mg, 0.26 mmol, 2.5 eq) was added and the reaction mixture was refluxed for 16 h. The mixture was filtered and washed thoroughly with EtOAC. The combined filtrated were concentrated. The residue was purified through a short pad of silica gel (EtOAc:hexnes 60/40) to give the title compound as yellow solid (300 mg, 62%).

***N*-Allyl-4-methyl-*N*-{2-oxo-1-[1-(toluene-4-sulfonyl)-1*H*-imidazol-4-yl-methyl]but-3-enyl}benzenesulfonamide (29):** The allylic alcohol **25** (0.55 g, 0.10 mmol, 1eq), IBX (0.74 g, 0.26 mmol, 2.5 eq) in (EtOAc 50 mL) was refluxed at 80 ^{o}C for 16 h. The slurry was filtered through Celite with EtOAc washing. The solvent was removed by rotary evaporation to get the crude product. The crude product was purified by flash chromatography (silica gel,

EtOAc/hexane 50/50), giving the desired ketone **29** as a yellow solid (0.35 g, 65%): mp:107-109 ^{o}C. ^{1}H NMR (500 MHz, $CDCl_3$): 7.80 (s, 1H), 7.75 (d, 2H, *J* = 8.3 Hz), 7.64 (d, 2H, *J* = 8.3 Hz), 7.33 (d, 2H, *J* = 8.3 Hz), 7.26 (d, 2H, *J* = 8.3 Hz), 6.83 (s, 1H), 6.74 (dd, 1H, *J* = 10.5, 17.4 Hz), 6.35 (dd, 1H, *J* = 1.8, 17.4 Hz), 5.75 (dd, 1H, *J* = 1.4, 10.5 Hz), 5.64 (ddt, 1H, *J* = 6.4, 10.0, 16.5 Hz), 5.11 (dd, 1H, *J* = 1.4, 17.4 Hz), 5.04 (dd, 1H, *J* = 1.0, 10.0 Hz), 4.98 (t, 2H, *J* = 6.9 Hz), 3.80 (dd, 1H, *J* = 6.9, 15.6 Hz), 3.73 (dd, 1H, *J* = 6.4, 15.6 Hz), 3.15 (dd, 1H, *J* = 7.3, 14.7 Hz), 2.48 (dd, 2H , *J* = 6.4, 15.1 Hz), 2.45 (s, 3H), 2.42 (s, 3H); ^{13}C NMR: δ = 195.8, 146.4, 144.0, 140.9, 137.4, 136.3, 135.2, 133.8, 133.3, 130.6, 130.0, 129.9, 127.5, 127.4, 119.4, 115.0, 63.0, 48.8, 26.5, 21.9, 21.8; FT-IR (KBr, cm^{-1}): 3121, 2923, 2850, 1726, 1656, 1595, 1487, 1426, 1335, 1265, 1195, 1130, 1158, 1034, 1094, 1010, 816, 756. HR-MS (*m/z*): calcd. for $[M+H]^{+}C_{25}H_{28}N_3O_5S_2$ 514.1470, found 514.1465.

Ring Closing Metathesis:

General procedure for the RCM reactions with the first or second generation Grubbs' catalyst:

The metathesis substrate was dissolved in CH_2Cl_2 to prepare about 0.004-0.01 M solution under N_2 protection. The first or second generation Grubbs' catalyst (5-20 mol %) which was dissolved in CH_2Cl_2 was added dropwise and the mixture was heated at reflux for the indicated time. TLC and ^{1}H NMR spectroscopy of the crude reaction mixtures were used to monitor the reactions.

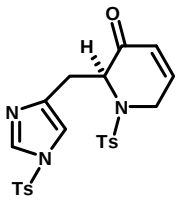
General procedure for the RCM reactions with the first generation Grubbs' catalyst and *p*-TsOH:

The metathesis substrate was dissolved in CH_2Cl_2 to prepare about 0.004-0.01 M solution under N_2 protection, then 1.1 equivalent of *p*-TsOH or freshly $Ti(O_iPr)_4$ was added. The mixture was stirred at RT or refluxed for 1 hour. The first generation Grubbs' catalyst (5-40 mol %) which was dissolved in CH_2Cl_2 was added and the mixture was heated at reflux for the indicated time. TLC and ^1H NMR spectroscopy of the crude reaction mixtures were used to monitor the reactions.

General procedure for the RCM reactions with *p*-TsOH using second generation Grubbs' catalyst.

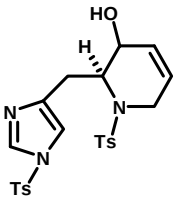
The metathesis substrate (1 equivalent) and *p*-TsOH (1.1 equivalent) were dissolved in CH_2Cl_2 to prepare a 0.1 M solution under N_2 protection. The mixture was heated at reflux for 30 minutes. Then the second generation Grubbs'catalyst (5 mol %) was added to the reaction mixture in solid form. The mixture was refluxed for 20 minutes, then either refluxed for an additional period or stirred at room temperature for an additional period until reaction finished as indicated by TLC and NMR of the crude reaction mixture. After the reaction was finished, the solvent was concentrated and $NaHCO_3$ solution was added to the residue, some K_2CO_3 solid was also added until the solution was basic. The solution was extracted with CH_2Cl_2 several times and the combined organic phase was dried over $MgSO_4$ and concentrated. Flash chromatography afforded the pure product.

1-(Toluene-4-sulfonyl)-3-[1-(toluene-4-sulfonyl)-1*H*-imidazol-4-yl-methyl]-2,3-dihydro-1*H*-pyridin-4-one (31):



The allylic ketone **29** (200 mg, 0.38 mmol), and *p*- TsOH (73 mg, 0.43 mmol) was mixed in dry CH_2Cl_2 (5 mL). The mixture were heated under reflux for 30 mintues, then the reaction mixture was taken to room temperature and Grubbs' second generation catalyst 10 mol% was added and it was heated at reflux for 3 h. The mixture was stirred at room temperature for further 3 h, at which time TLC analysis indicated the completion of the reaction. The solvent was concentrated and $NaHCO_3$ solution was added to the residue, some solid K_2CO_3 was also added until the solution was basic. The solution was extracted with CH_2Cl_2 several times and the combined organic phase was dried over $MgSO_4$ and concentrated. The crude product was purified by chromatography (silica gel, CH_2Cl_2/ EtOAc: 75/25) to give the title compound solid **31**: mp: 103-105 ^oC (56 mg, 30 %). ^1H NMR (500 MHz, $CDCl_3$): δ = 7.83 (s, 1H), 7.79 (d, 2H, *J* = 8.3 Hz), 7.52 (d, 2H, *J* = 8.3 Hz), 7.34 (d, 2H, *J* = 8.3 Hz), 7.23 (d, 2H, *J* = 8.3 Hz), 7.20 (s, 1H), 6.68 (ddd, 1H, 2.0, 4.8, 10.6Hz), 5.77 (d, 1H, *J* = 10.3 Hz), 4.64 (t, 1H, *J* = 7.6 Hz), 4.44 (ddd, 1H, *J* = 1.0, 4.5, 22.0 Hz), 4.02 (dt, 1H, *J* = 2.4, 21.7 Hz), 2.89 (d, 2H, *J* = 7.6 Hz), 2.42 (s, 3H), 2.39 (s, 3H); ^{13}C NMR: δ =193.4, 146.2, 144.2, 144.0, 139.5, 136.3, 136.2, 135.0, 130.5, 130.0, 127.4, 127.0, 126.7, 115.3, 61.1, 41.2, 29.3, 21.8, 21.6; FT-IR (KBr, cm^{-1}): 3427, 3129, 2940, 1686, 1490, 1464, 1387, 1163, 1154, 1100, 757, 698, 550, 520. HR-MS (*m/z*): calcd. for $[M+H]^+$ $C_{23}H_{24}N_3O_5S_2$ 486.1157, found 486.1152.

1-(Toluene-4-sulfonyl)-3-[1-(toluene-4-sulfonyl)-1H-imidazol-4-yl-methyl]-1,2,3,4-tetrahydropyridin-4-ol (33):



The allylic alcohol **25** (200 mg, 0.38 mmol), was taken up in dry CH_2Cl_2 (5 m L). The Grubbs' second generation catalyst, 10 mol%, was added and continued the mixture was stirred at room temperater for 6 h, at which time TLC analysis indicated the completion of the reaction. The solvent was concentrated. The crude product was purified by chromatography (silica gel, CH_2Cl_2/ EtOAc: 75/25) to give the title compound **33** as a colorless solid (56 mg, 60%): mp: 147-149 ^oC, [α] = - 4.14 (c = 0.014, CH_2Cl_2). ^1H NMR (500 MHz, $CDCl_3$): δ = 7.81 (s, 1H), 7.80 (d, 2H, *J* = 8.7 Hz), 7.64 (d, 2H, *J* = 8.7 Hz), 7.30 (d, 2H, *J* = 8.3 Hz), 7.23 (d, 2H, *J* = 8.3 Hz), 7.01 (s, 1H), 5.87-5.93 (m, 1H), 4.35 (dd, 1H, *J* = 7.3, 8.3 Hz), 4.12 (dt1H, *J* = 2.3, 18.3 Hz), 3.58 (dt, 1.4H, *J* = 19.7 Hz), 2.52 (dd, 1H, *J* = 8.3, 14.7 Hz), 2.46 (dd, 1H, *J* = 8.3, 14.7 Hz), 2.42 (s, 3H), 2.40 (s, 3H); ^{13}C NMR: δ = 146.4, 143.7, 140.1, 136.8, 136.2, 135.0, 130.6, 129.8, 127.4, 127.3, 127.1, 125.8, 114.4, 65.0, 58.6, 40.6, 27.8, 21.8, 21.6; FT-IR (KBr, cm^{-1}): 3747, 3115, 1796, 1592, 1388, 1173, 1080, 930, 840, 770, 550. HR-MS (*m/z*): calcd. for $[M+H]^+C_{23}H_{26}N_3O_5S_2$ 488.1314, found 488.1308.

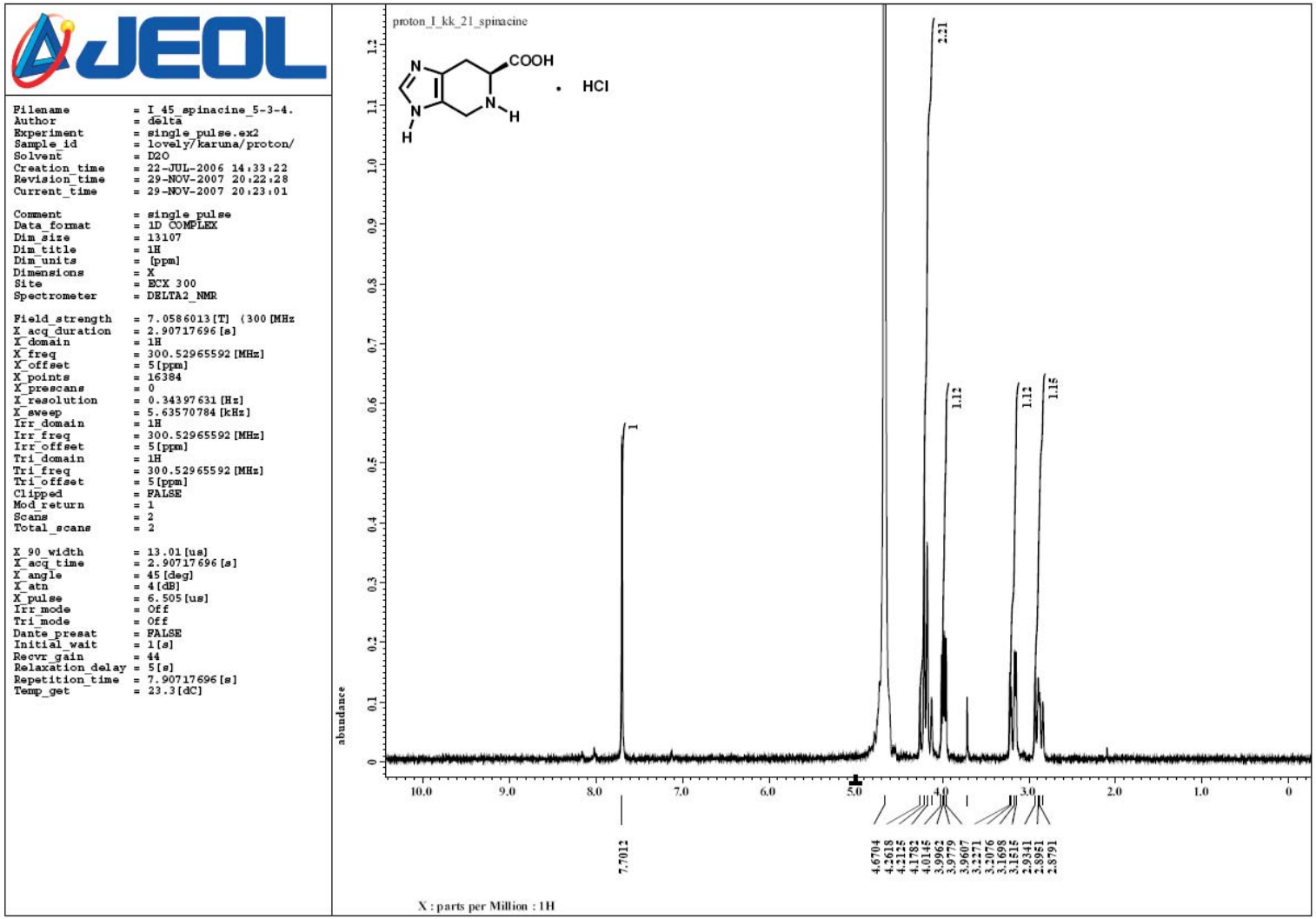
1-(Toluene-4-sulfonyl)-3-[1-(toluene-4-sulfonyl)-1*H*-imidazol-4-ylmethyl]-piperidin-4-one (34): The enone **31** (33 mg, 0.67 mmol) was mixed with a 1:3 mixture of ethyl acetate and ethanol (4 mL) and 10% Pd/C (10 mg, 0.67 mmol, 10 mol %) under a H_2 balloon at rt for 1 day. Then, the catalyst was filtered and rinsed with ethyl acetate and the filtrate was completely concentrated. The crude product was purified by flash chromatography(EtOAc/hexanes: 50/50) and dried to provide the pure title compound **34** (170 mg, 51%) as a yellow solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.76 (s, 1H), 7.74 (d, 2H, *J* = 8.3 Hz), 7.53 (d, 2H, *J* = 8.3 Hz), 7.30 (d, 2H,), 7.2 (d, 2H, *J* = 8.3 Hz), 7.03 (s, 1H), 4.49 (t, 1H, *J* = 7.33 Hz), 3.73 (ddd, 1H, *J* = 4.6, 9.6, 19.3 Hz), 3.20 (ddd, 1H, *J* = 5.0, 9.6, 19.3 Hz), 2.95 (d, 2H, *J* = 7.3 Hz), 2.42 (dd, 2H, *J* = 6.9, 14.7 Hz), 2.43 (s, 6H), 2.20 (ddd, 1H , *J* = 5.5, 11.0, 21.5 Hz), 1.64-1.74 (m, 2H); ^{13}C NMR: δ = 206.2, 146.3, 143.9, 139.5, 137.2, 136.2, 135.0, 130.5, 130.0, 127.3, 127.0, 115.5, 63.7, 40.3, 36.5, 30.1, 23.2, 21.8, 21.6; FT-IR (KBr, cm^{-1}): 3422, 3119, 2930, 1738, 1620, 1510, 1360, 1260, 1210, 1100, 1010, 720, 680, 550, 530, 510. HR-MS (*m/z*): calcd. for $[M+H]^+$ $C_{23}H_{26}N_3O_5S_2$ 488.1314, found 488.1308.

Carbonic acid methyl ester1-(toluene-4-sulfonyl)-2-[1-{toluene-4-sulfonyl)-1*H*-imidazol-4-ylmethyl]-1,2,3,6-tetrahydro-pyridin-3-ylester(39):Methyl chloroformate (0.05 m L, 0.65mmol) was added dropwise to the solution of alcohol **33** (200 mg, 0.040 mmol) and pyridine (0.5 m L) in CH_2Cl_2 at 0^{o}C. The reaction mixture was stirred for 15 h at room temperature. The

reaction mixture was worked up by addition of CH_2Cl_2, washed with HCl (1N), sat. $NaHCO_3$ and then final wash with brine. The organic phases were dried over Na_2SO_4, filtered and concentrated to get crude product. The crude product was purified by flash chromatography (silica gel, EtOAc/hexanes: 50/50) and dried to provide the pure title compound **39** (160 mg, 72%). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.88 (s, 1H), 7.82 (d, 2H, *J* = 8.3 Hz), 7.53 (d, 2H, *J* = 8.3 Hz), 7.35 (d, 2H, *J* = 8.3 Hz), 7.23 (d, 3H, *J* = 7.3 Hz), 5.95-6.05 (m, 1H), 5.80-5.91 (m, 1H), 4.93 (d, 1H, *J* = 4.6 Hz), 4.6(d, 1H, *J* = 8.3Hz), 3.97 (d, 1H, *J* = 21.1 Hz), 3.7 (s, 3H), 2.71 (d, 1H , *J* = 7.6 Hz), 2.46 (s, 3H), 2.4 (s, 3H), 2.44 (s, 3H); ^{13}C NMR: δ = 155.0, 146.1, 143.3, 140.3, 137.2 136.2, 130.5, 130.4, 130.3, 129.6, 127.5, 127.4, 120.8, 115.0, 70.2, 55.1, 54.9, 40.5, 28.9, 21.8, 21.6.

APPENDIX 1

^{1}HNMR AND ^{13}C NMR SPECTRA OF **4,5,6,7-TETRAHYDRO-3*H*-IMIDAZO[4,5-*C*]PYRIDINE-6-CARBOXYLIC ACID HYDROCHLORIDE (5)** MEASURED ON A JEOL ECLIPSE 300+ SPECTROMETER IN D_2O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Author = delta
Experiment = single_pulse.ex2
Sample_id = lovely7/karuna/proton/
Solvent = D2O
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Revision_time = 29-NOV-2007 20:22:28
Current_time = 29-NOV-2007 20:23:01
Comment = single_pulse
Data_format = 1D COMPLEX
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Dim_title = 1H
Dim_units = [ppm]
Dimensions = X
Site = ECX 300
Spectrometer = DELTA2_NMR
Field_strength = 7.0586013[T] (300[MHz
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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 = 2
Total_scans = 2
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 = 23.3[dC]
proton_I_kk_21_spinacine
COOH
HCl
N
N
H
H
abundance
1
2.21
1.12
1.12
1.15
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.7012
4.6704
4.2618
4.2125
4.1782
4.0145
3.9962
3.9779
3.9607
3.2271
3.2076
3.1698
3.1515
2.9341
2.8961
2.8791
X : parts per Million : 1H

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Author            = delta
Experiment        = single_pulse.ex2
Sample_id         = lovely/karuna/proton/
Solvent           = D2O
Creation_time     = 22-JUL-2006 14:33:22
Revision_time     = 29-NOV-2007 20:25:27
Current_time      = 29-NOV-2007 20:25:52

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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             = 2
Total_scans       = 2

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          = 23.3[dC]
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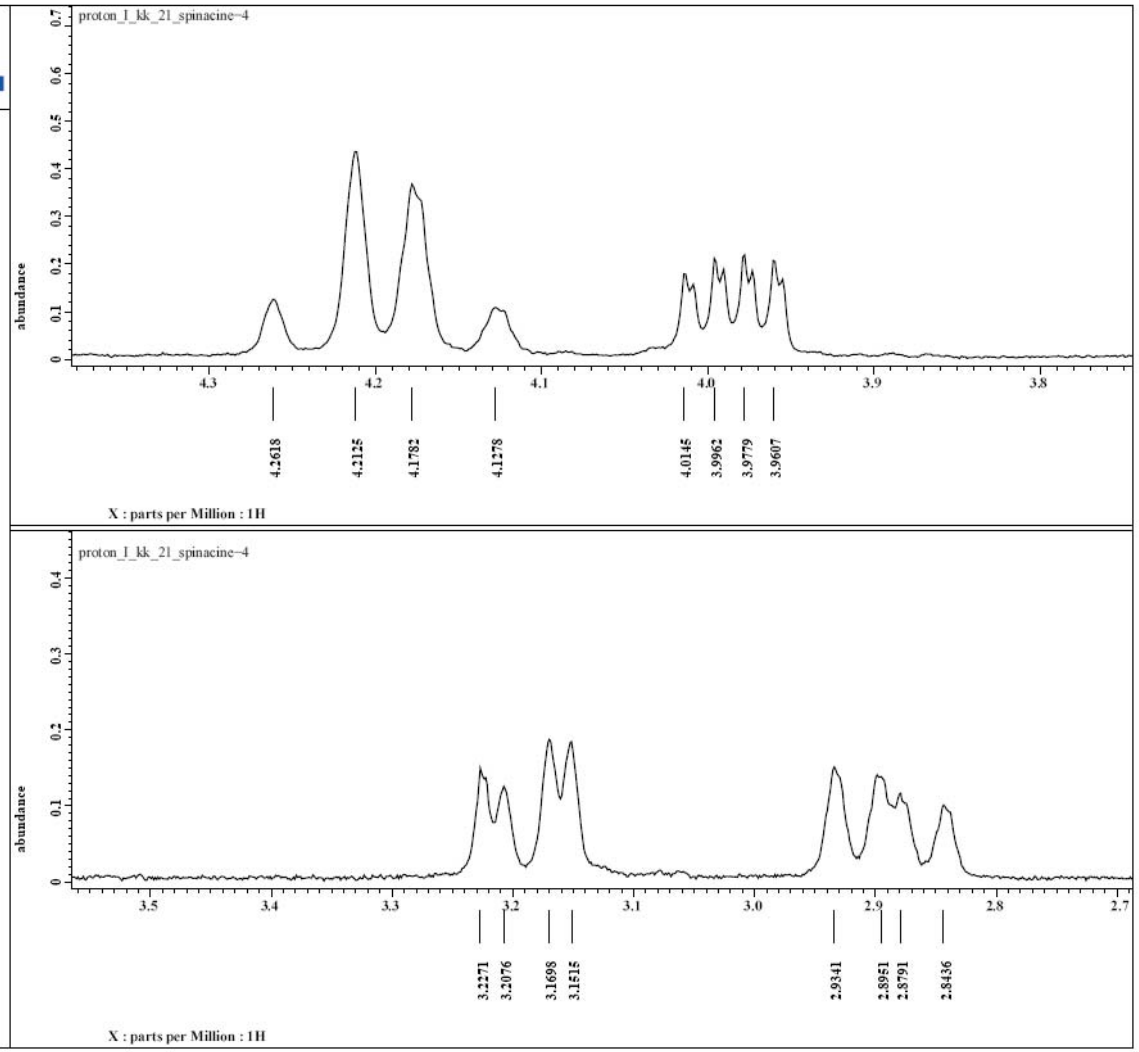

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Filename	= I_kk_spinacine-3.jdf
Author	= delta
Experiment	= single_pulse_dec
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Solvent	= D2O
Creation_time	= 12-OCT-2006 22:03:09
Revision_time	= 1-DEC-2007 11:39:20
Current_time	= 1-DEC-2007 11:39:36
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Spectrometer	= DELTA2_NMR
Field_strength	= 7.0586013[T] (300[MHz
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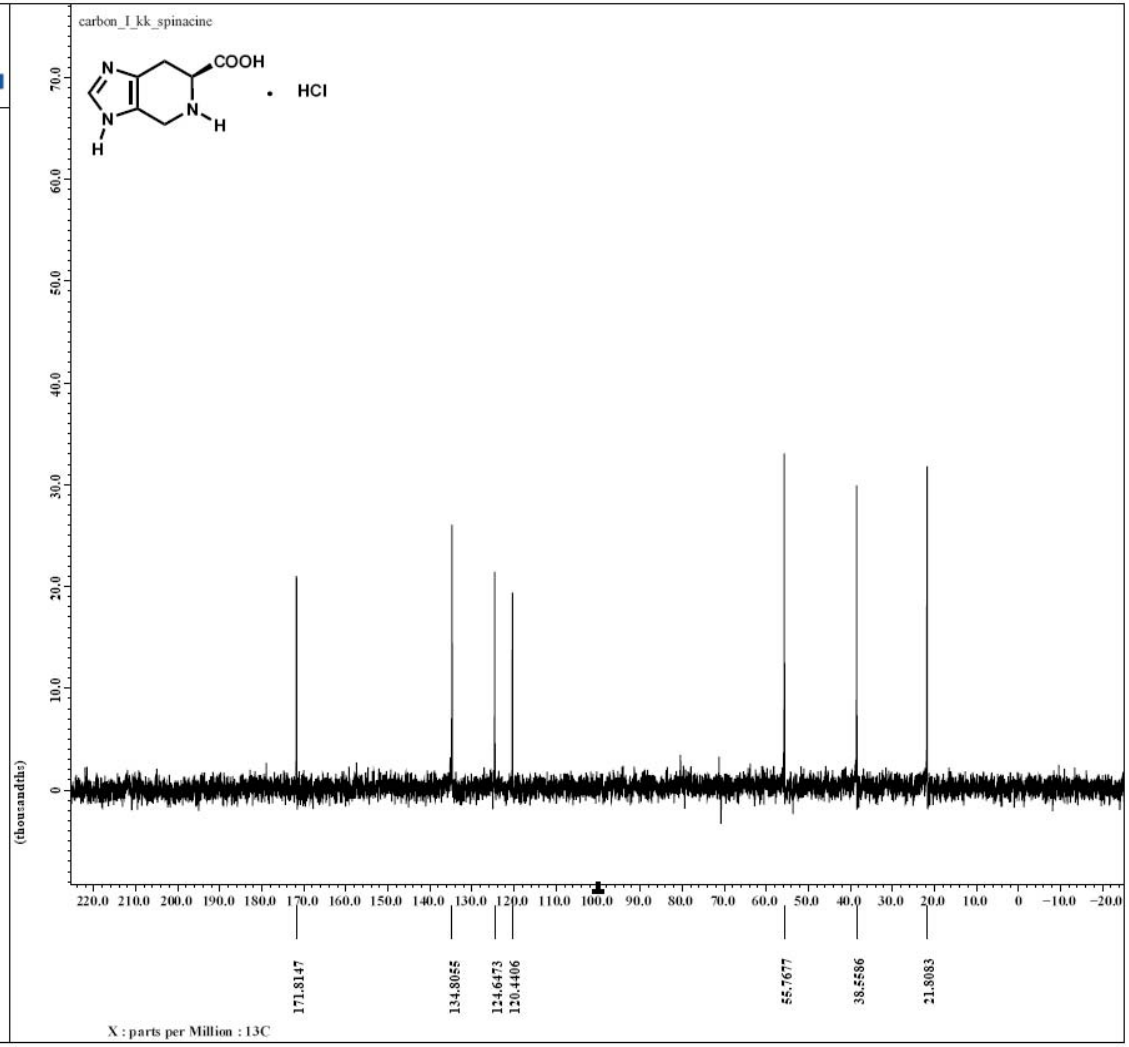
X_domain	= 13C
X_freq	= 75.56823426[MHz]
X_offset	= 100[ppm]
X_points	= 65536
X_prescans	= 4
X_resolution	= 0.36124027[Hz]
X_sweep	= 23.67424242[kHz]
Irr_domain	= 1H
Irr_freq	= 300.52965592[MHz]
Irr_offset	= 5[ppm]
Clipped	= FALSE
Mod_return	= 10
Scans	= 430
Total_scans	= 430
X_90_width	= 9.75[us]
X_acq_time	= 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	= 4[s]
Recvr_gain	= 50
Relaxation_delay	= 4[s]
Repetition_time	= 6.76824064[s]
Temp_get	= 23.6[dC]



APPENDIX 2

^{1}HNMR AND ^{13}C NMR SPECTRA OF **METHYL 4-OXOBUTANOIC ACID (9)**
MEASURED ON A JEOL ECLIPSE 300+ SPECTROMETER IN $CDCl_3$

```
Filename          = I_kk_155-6.jdf
Author            = delta
Experiment        = single_pulse.exp
Sample_id         = S#458632
Solvent           = CHLOROFORM-D
Creation_time     = 14-AUG-2007 16:54:19
Revision_time     = 28-NOV-2007 14:22:40
Current_time      = 28-NOV-2007 14:22:58

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             = 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        = 16
Relaxation_delay  = 4[s]
Temp_get          = 24.3[dC]
Unblank_time      = 2[us]
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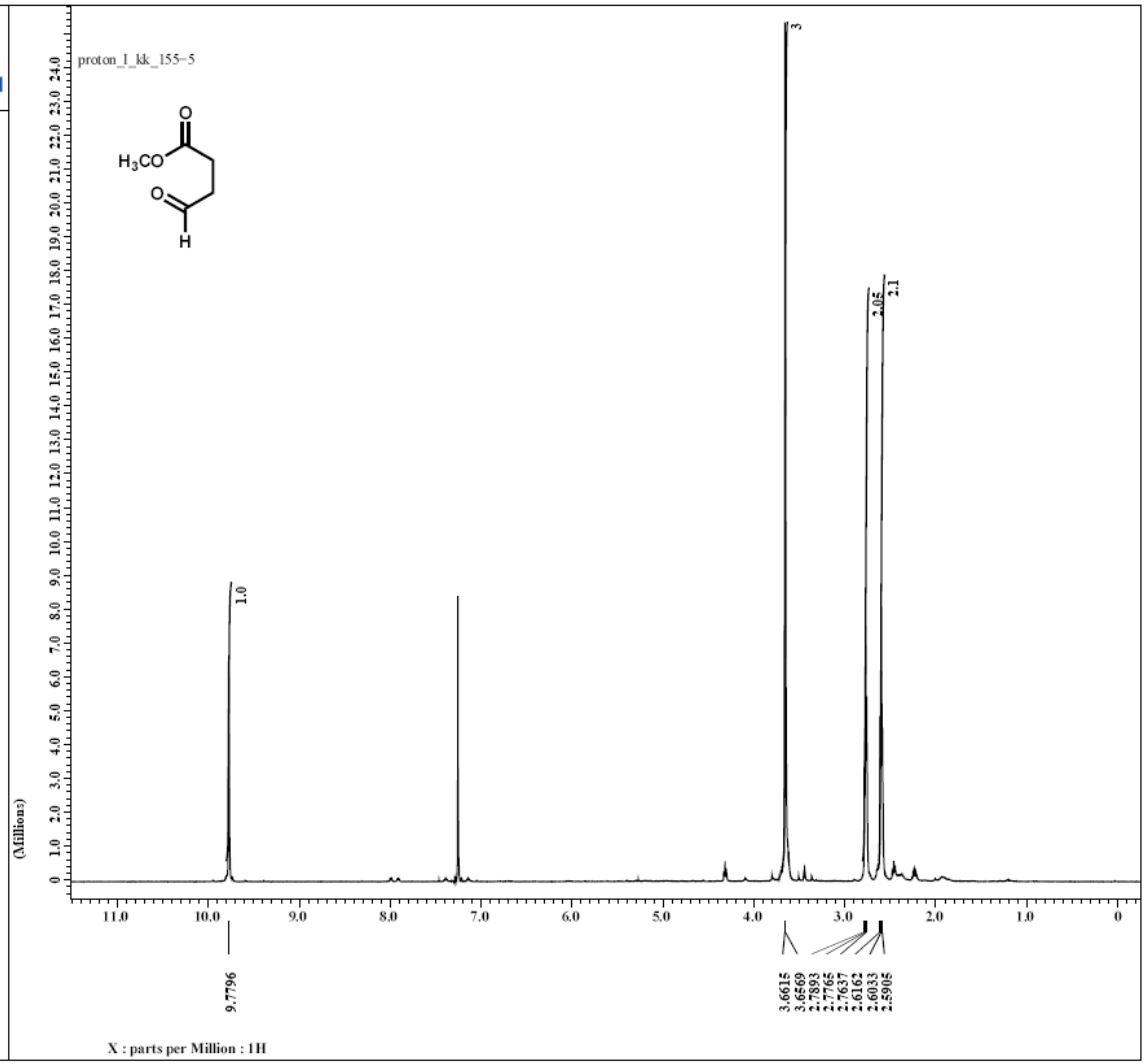

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Site              = Eclipse+ 500
Spectrometer      = DELTA_NMR

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X_acq_duration    = 2.1823488[s]
X_domain          = 1H
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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        = 16
Relaxation_delay  = 4[s]
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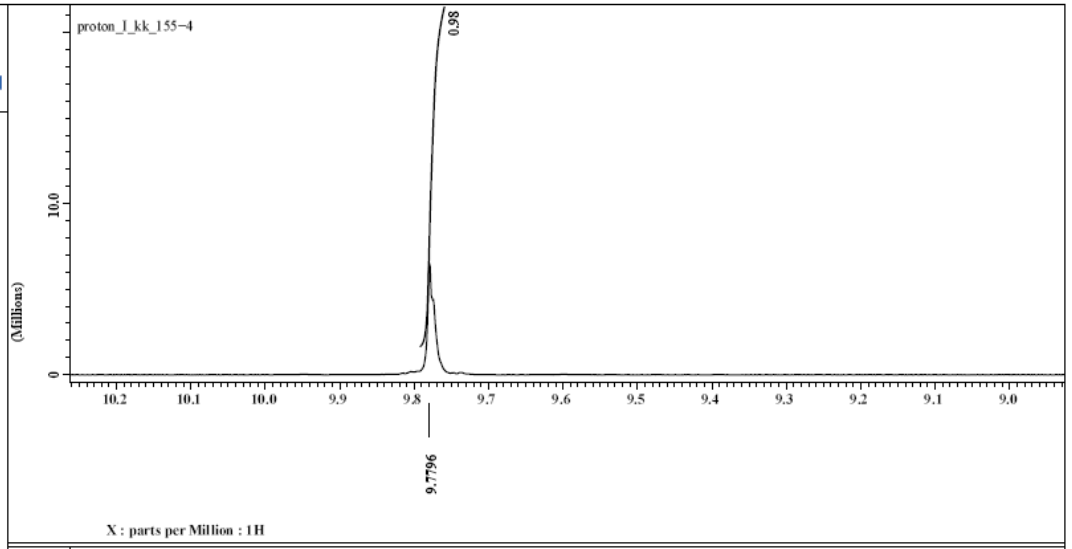

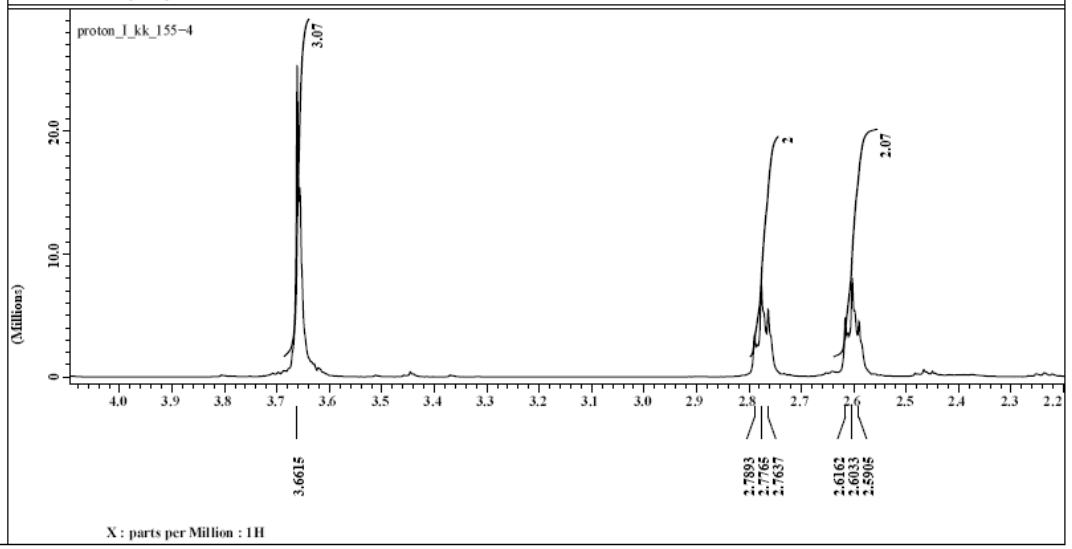

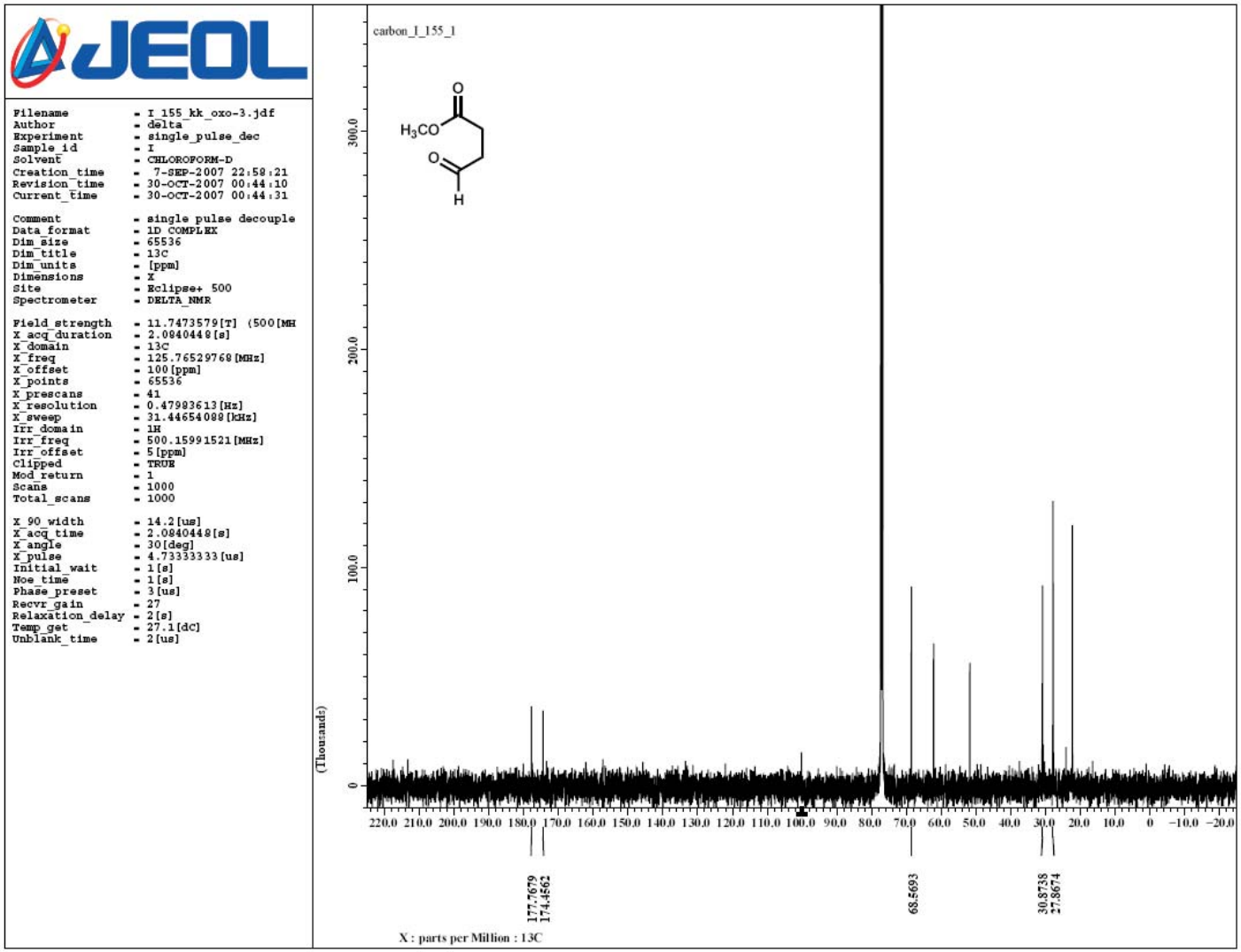
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X_freq = 125.76529768[MHz]
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Mod_return = 1
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X_angle = 30[deg]
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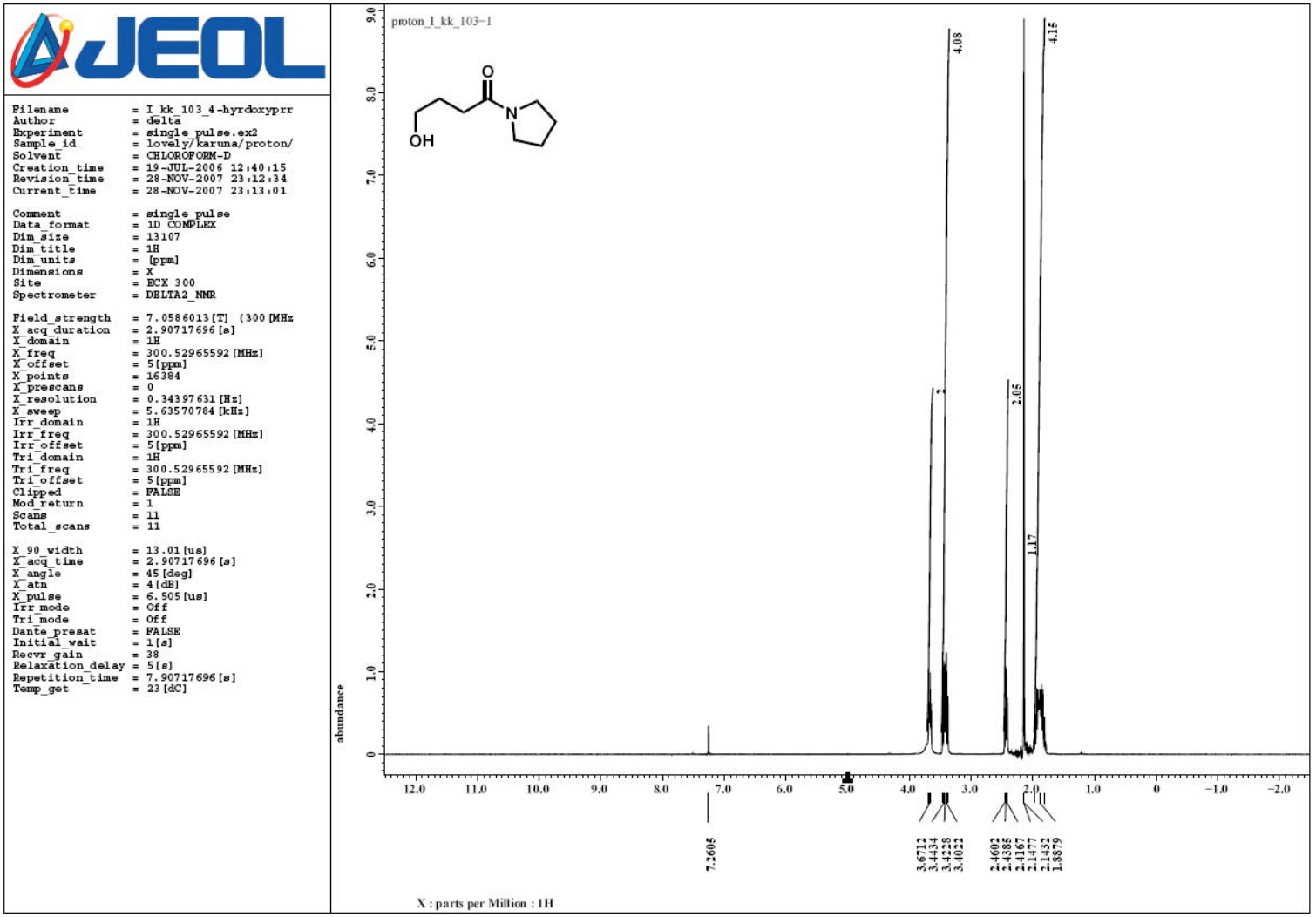
Noe_time = 1[s]
Phase_preset = 3[us]
Recvr_gain = 27
Relaxation_delay = 2[s]
Temp_get = 27.1[dC]
Unblank_time = 2[us]
carbon_1_155_1
O
H3CO
O
H
300.0
200.0
100.0
0
(Thousands)
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 −10.0 −20.0
177.7679
174.4562
68.5693
30.8738
27.3674
X : parts per Million : 13C

APPENDIX 3

^{1}HNMR SPECTRA OF**1-(4-HYDROXY-1-OXOBUTYL) PYRROLIDINE (10)**
MEASURED ON A JEOL ECLIPSE 300+ SPECTROMETER IN $CDCl_3$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Dim_units = [ppm]
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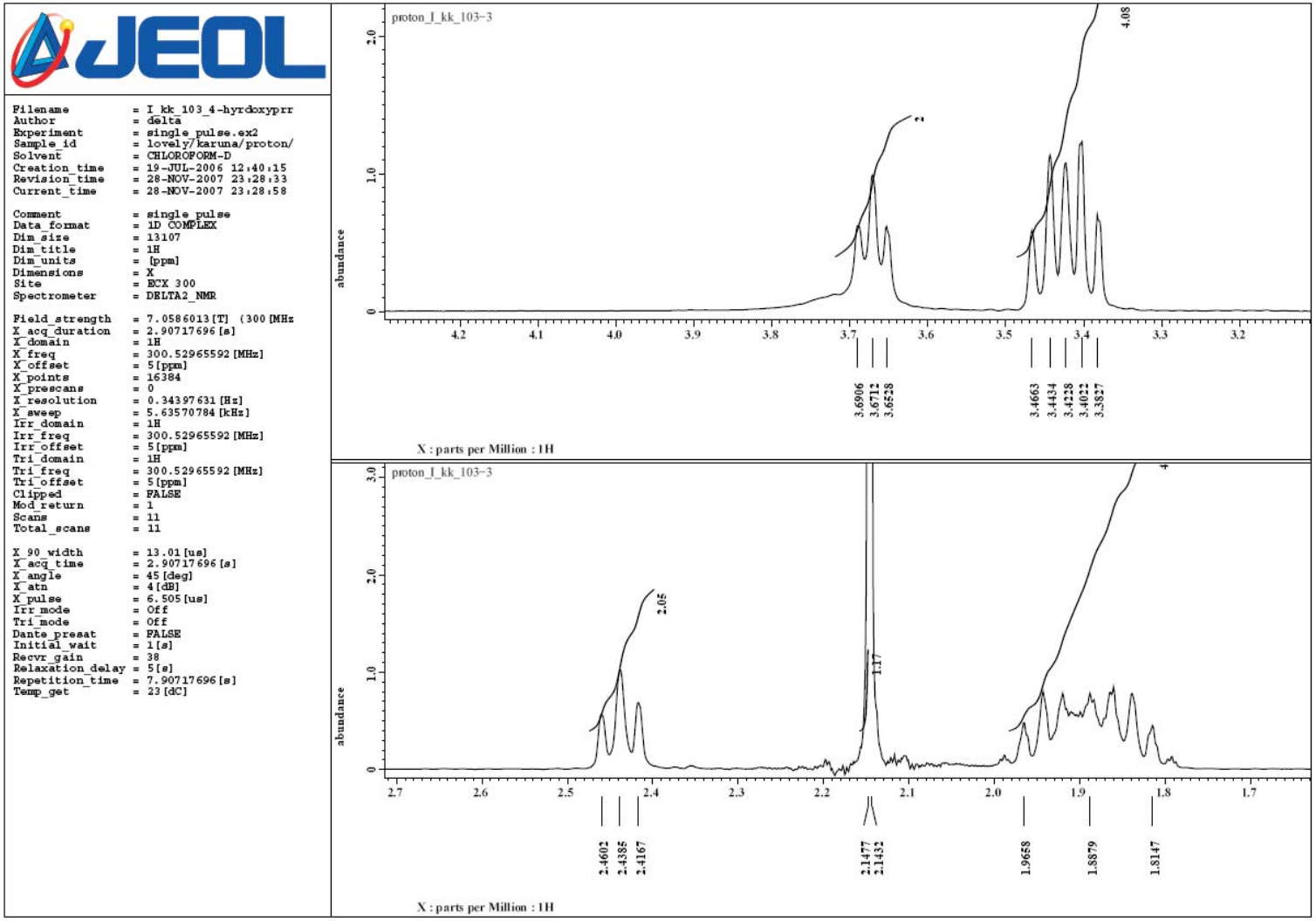
X_domain = 1H
X_freq = 300.52965592[MHz]
X_offset = 5[ppm]
X_points = 16384
X_prescans = 0
X_resolution = 0.34397631[Hz]
X_sweep = 5.63570784[kHz]
Irr_domain = 1H
Irr_freq = 300.52965592[MHz]
Irr_offset = 5[ppm]
Tri_domain = 1H
Tri_freq = 300.52965592[MHz]
Tri_offset = 5[ppm]
Clipped = FALSE
Mod_return = 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[dC]
proton_I_kk_103-1
O
N
OH
4.08
4.15
2.05
1.17
abundance
7.2605
3.6712
3.4434
3.4228
3.4022
2.4602
2.4385
2.4167
2.1477
2.1432
1.8879
X : parts per Million : 1H



```
Filename          = I_kk_103_4-hyrdoxyprr
Author            = delta
Experiment        = single_pulse.ex2
Sample_id         = lovely/karuna/proton/
Solvent           = CHLOROFORM-D
Creation_time     = 19-JUL-2006 12:40:15
Revision_time     = 28-NOV-2007 23:28:33
Current_time      = 28-NOV-2007 23:28:58

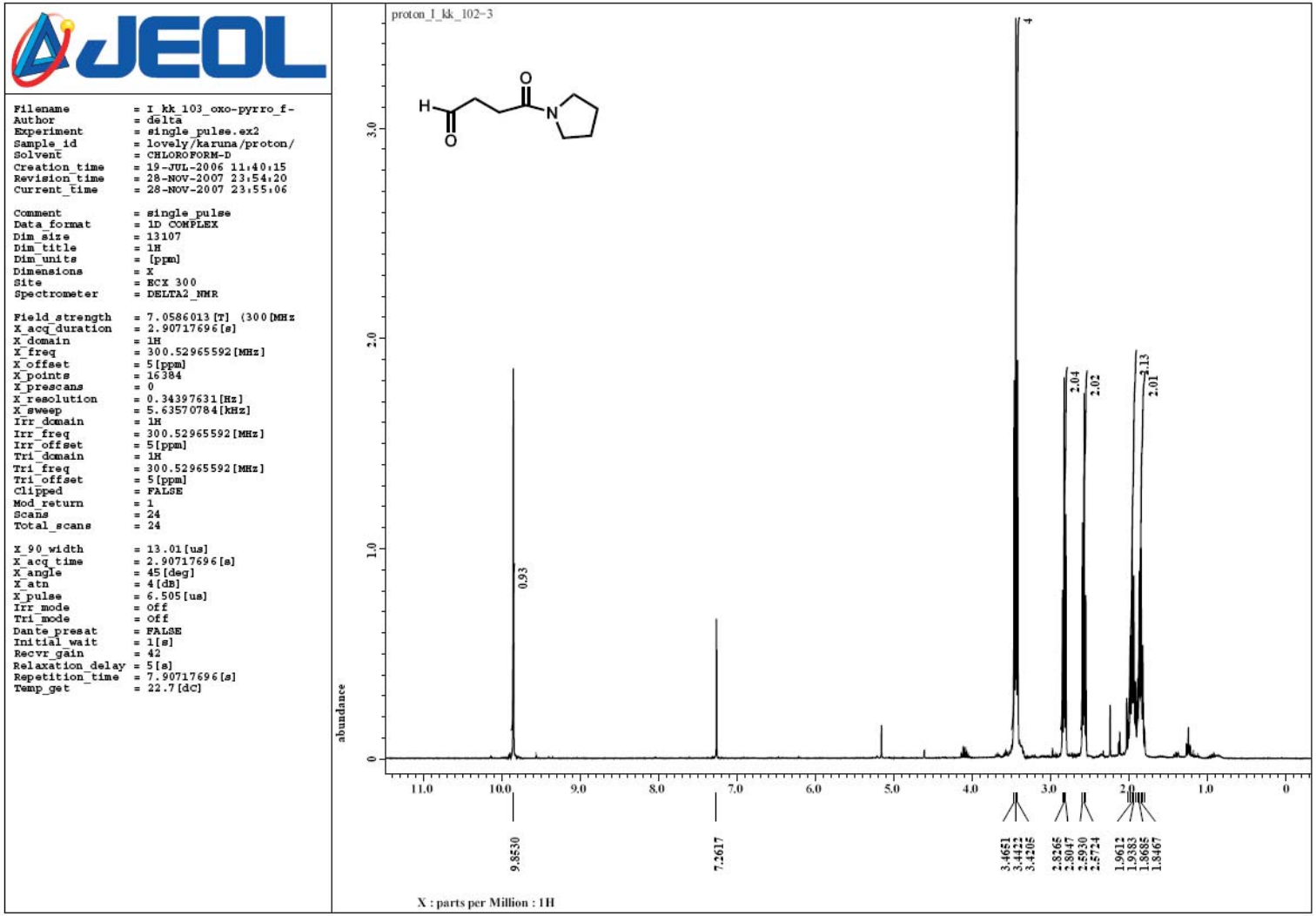
Comment           = single pulse
Data_format       = 1D COMPLEX
Dim_size          = 13107
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = ECX 300
Spectrometer      = DELTA2_NMR

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             = 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[dC]
```

APPENDIX 4

^{1}HNMR AND ^{13}C NMR SPECTRA OF **4-OXO-4-PYRROLIDIN-1-YL-BUTYRALDEHYDE (11)** MEASURED ON A JEOL ECLIPSE 300+ SPECTROMETER IN $CDCl_3$

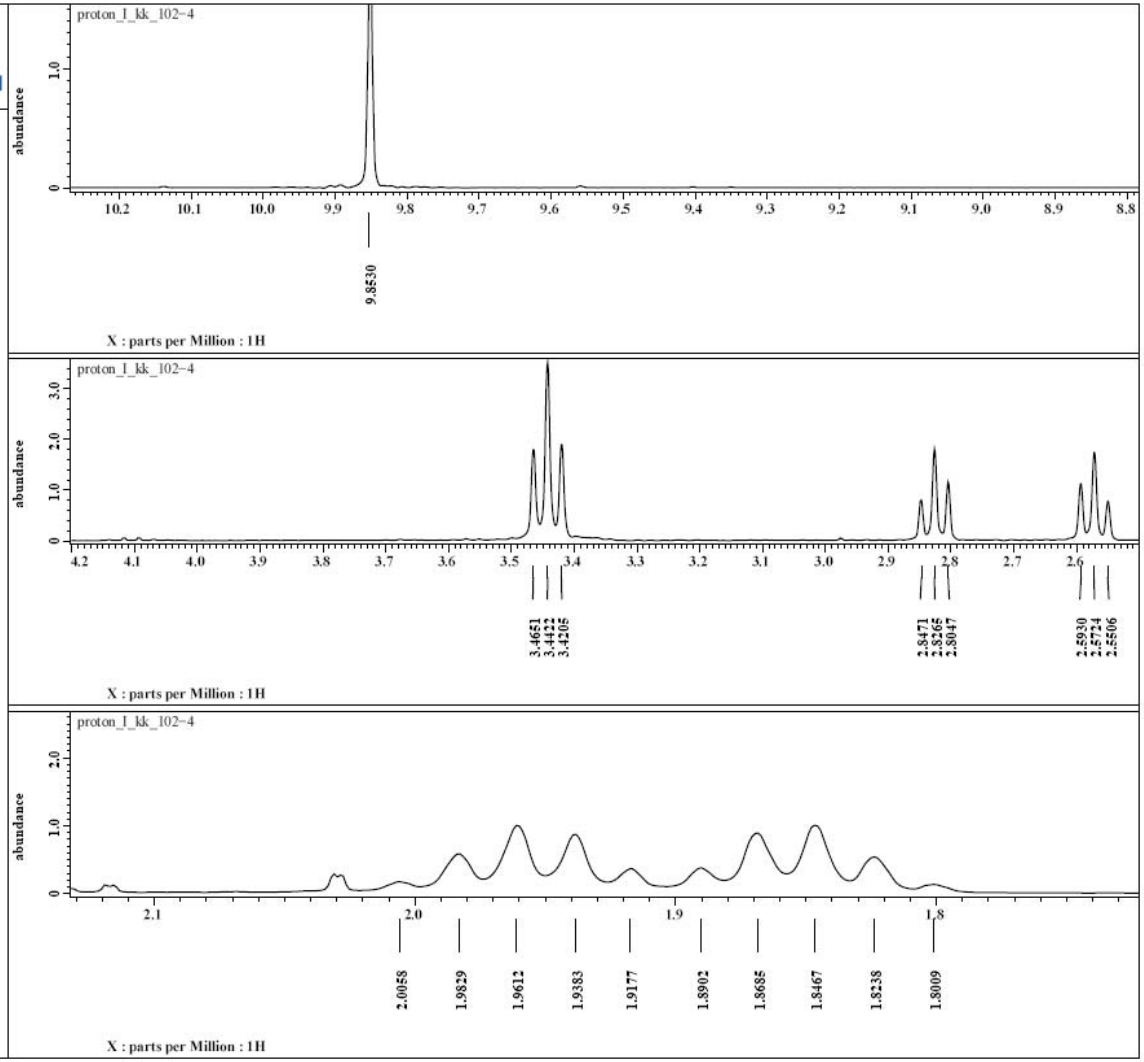

JEOL
Filename = I_kk_103_oxo-pyrro_f-
Author = delta
Experiment = single_pulse.ex2
Sample_id = lovely/karuna/proton/
Solvent = CHLOROFORM-D
Creation_time = 19-JUL-2006 11:40:15
Revision_time = 28-NOV-2007 23:54:20
Current_time = 28-NOV-2007 23:55:06
Comment = single_pulse
Data_format = 1D COMPLEX
Dim_size = 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 = 24
Total_scans = 24
X_90_width = 13.01[us]
X_acq_time = 2.90717696[s]
X_angle = 45[deg]
X_atn = 4[dB]
X_pulse = 6.505[us]
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]
proton_1_kk_102-3
O
H
O
N
4
0.93
2.04
2.02
2.13
2.01
abundance
0
1.0
2.0
3.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
9.8530
7.2617
3.4661
3.4422
3.4205
2.8265
2.8047
2.5930
2.5724
1.9612
1.9383
1.8685
1.8467
X : parts per Million : 1H

```
Filename          = I_kk_103_oxo-pyrro_f-
Author            = delta
Experiment        = single_pulse.ex2
Sample_id         = lovely/karuna/proton/
Solvent           = CHLOROFORM-D
Creation_time     = 19-JUL-2006 11:40:15
Revision_time     = 28-NOV-2007 23:58:54
Current_time      = 28-NOV-2007 23:59:22

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             = 24
Total_scans       = 24

X_90_width        = 13.01[us]
X_acq_time        = 2.90717696[s]
X_angle           = 45[deg]
X_atn             = 4[dB]
X_pulse           = 6.505[us]
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]
```

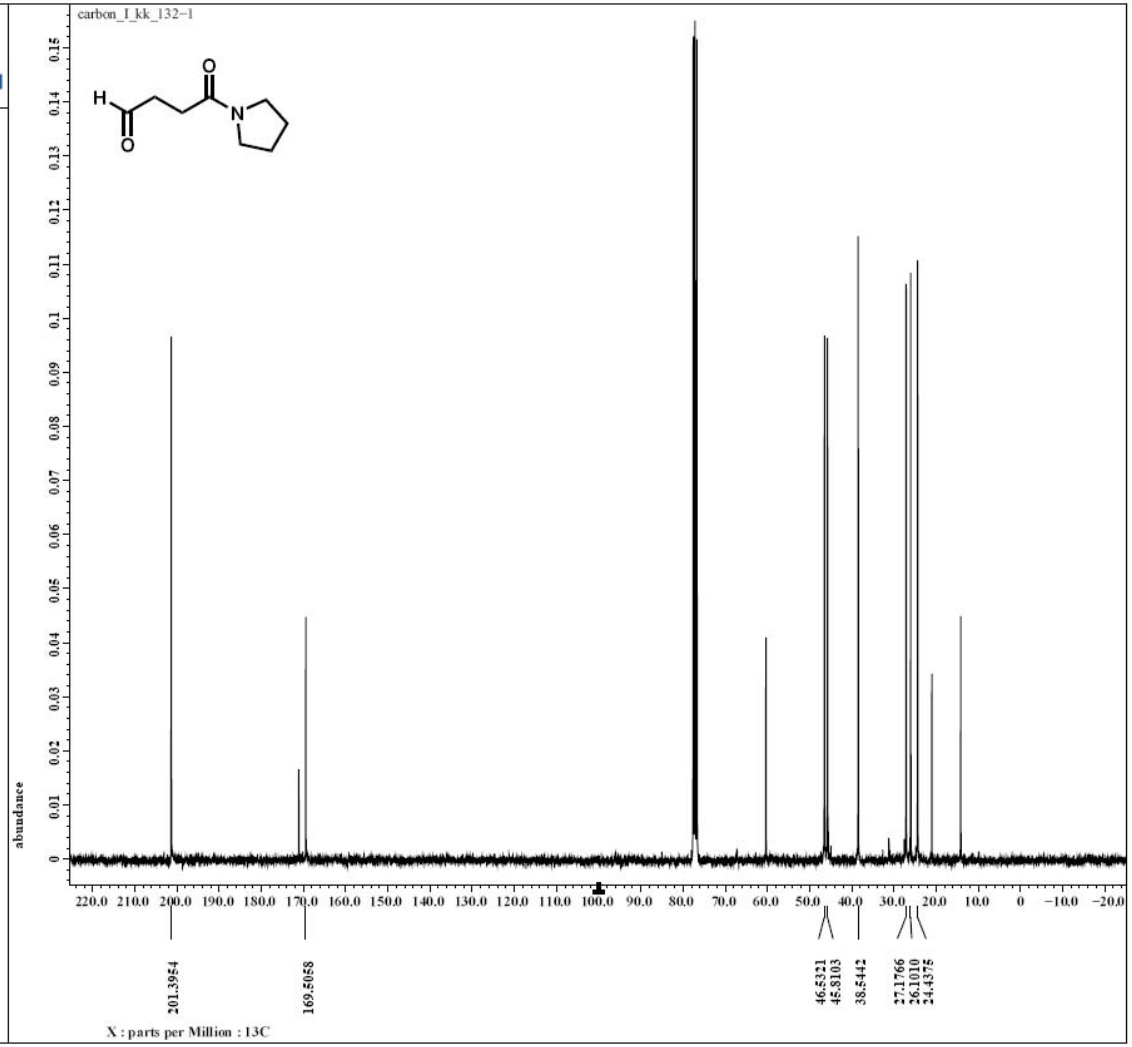


```
Filename          = I_KK_136_ALD-3.jdf
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#515478
Solvent           = CHLOROFORM-D
Creation_time     = 16-SEP-2006 18:08:35
Revision_time     = 30-NOV-2007 01:10:29
Current_time      = 30-NOV-2007 01:10:45

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             = 1663
Total_scans       = 1663

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          = 4[s]
Recvr_gain        = 50
Relaxation_delay  = 4[s]
Repetition_time   = 6.76824064[s]
Temp_get          = 23.1[dC]
```



APPENDIX 5

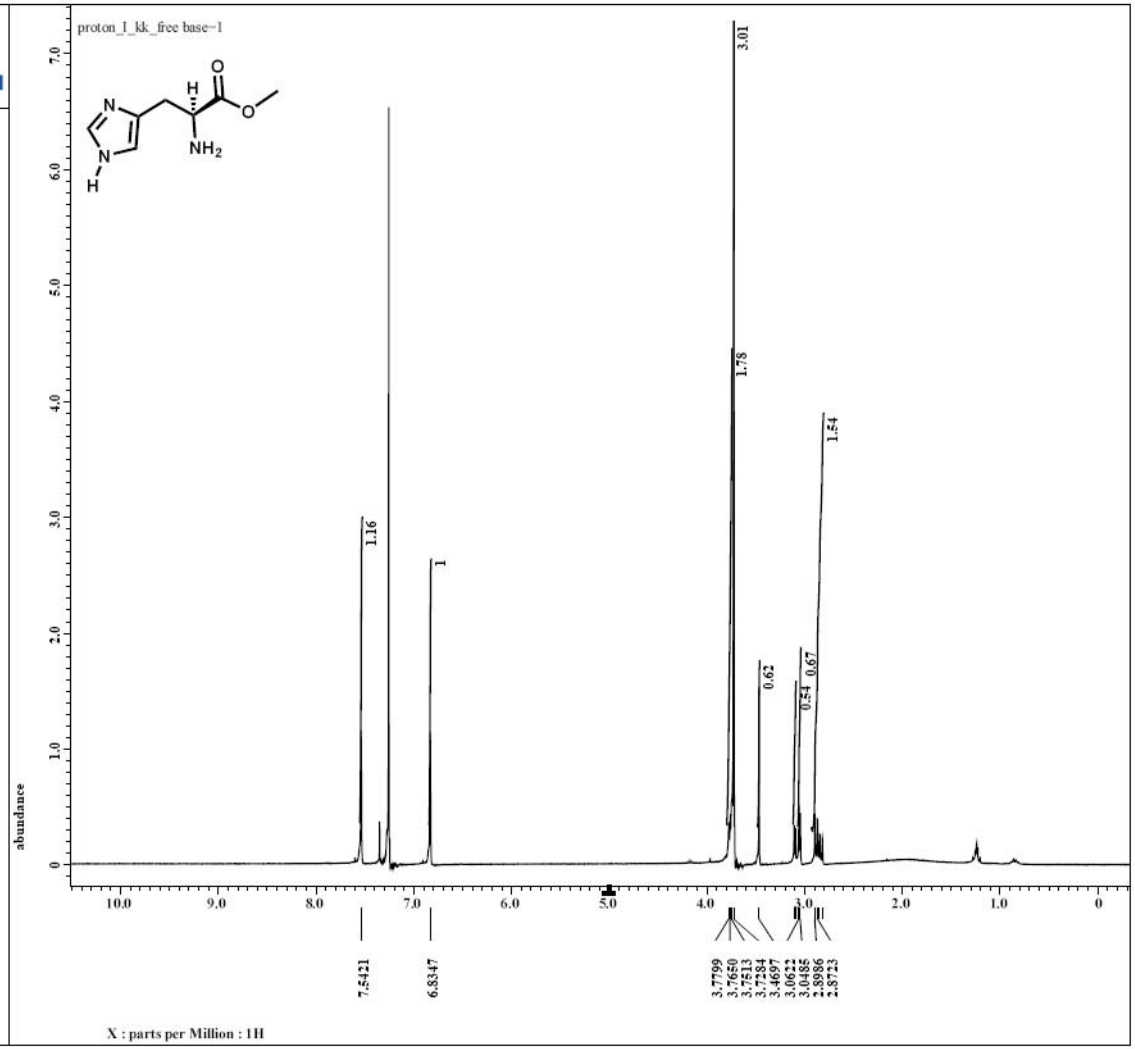
^{1}HNMR SPECTRA OF **2-AMINO-3(1*H*-IMIDAZO-4-YL) PROPIONIC ACID METHYL ESTER (13)** MEASURED ON A JEOL ECLIPSE 300+ SPECTROMETER IN $CDCl_3$

```
Filename          = I_kk_free base-3.jdf
Author            = delta
Experiment        = single_pulse.ex2
Sample_id         = lovely/karuna/proton/
Solvent           = CHLOROFORM-D
Creation_time     = 27-SEP-2006 10:45:06
Revision_time     = 28-NOV-2007 17:06:20
Current_time      = 28-NOV-2007 17:06:39

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             = 24
Total_scans       = 24

X_90_width        = 13.01[us]
X_acq_time        = 2.90717696[s]
X_angle           = 45[deg]
X_atn             = 4[dB]
X_pulse           = 6.505[us]
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          = 22.7[dC]
```

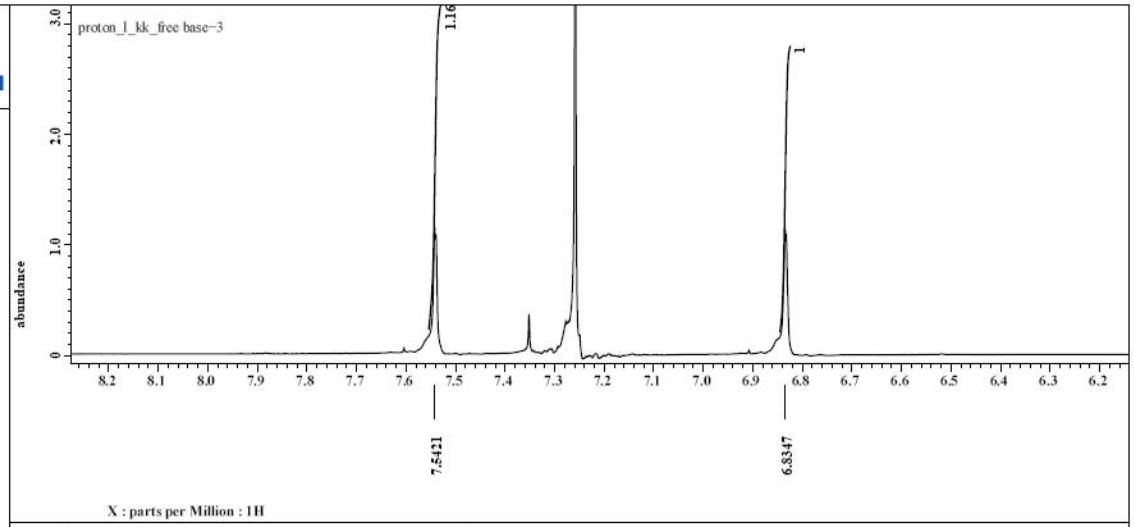


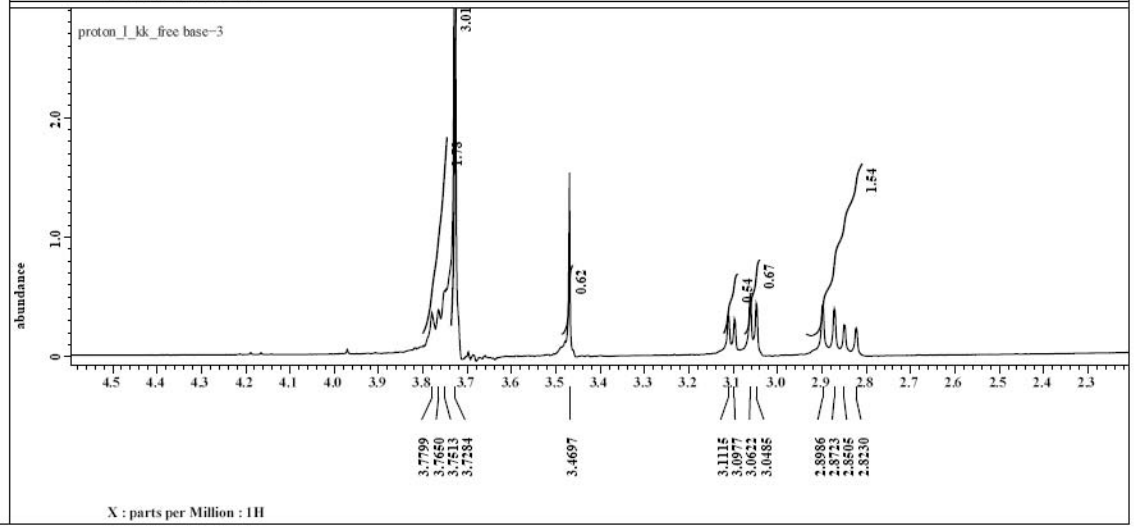
```
Filename          = I_kk_free base-3.jdf
Author            = delta
Experiment        = single_pulse.ex2
Sample_id         = lovely/karuna/proton/
Solvent           = CHLOROFORM-D
Creation_time     = 27-SEP-2006 10:45:06
Revision_time     = 28-NOV-2007 17:08:27
Current_time      = 28-NOV-2007 17:08:49

Comment           = single_pulse
Data_format       = 1D COMPLEX
Dim_size          = 13107
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = BCX 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             = 24
Total_scans       = 24

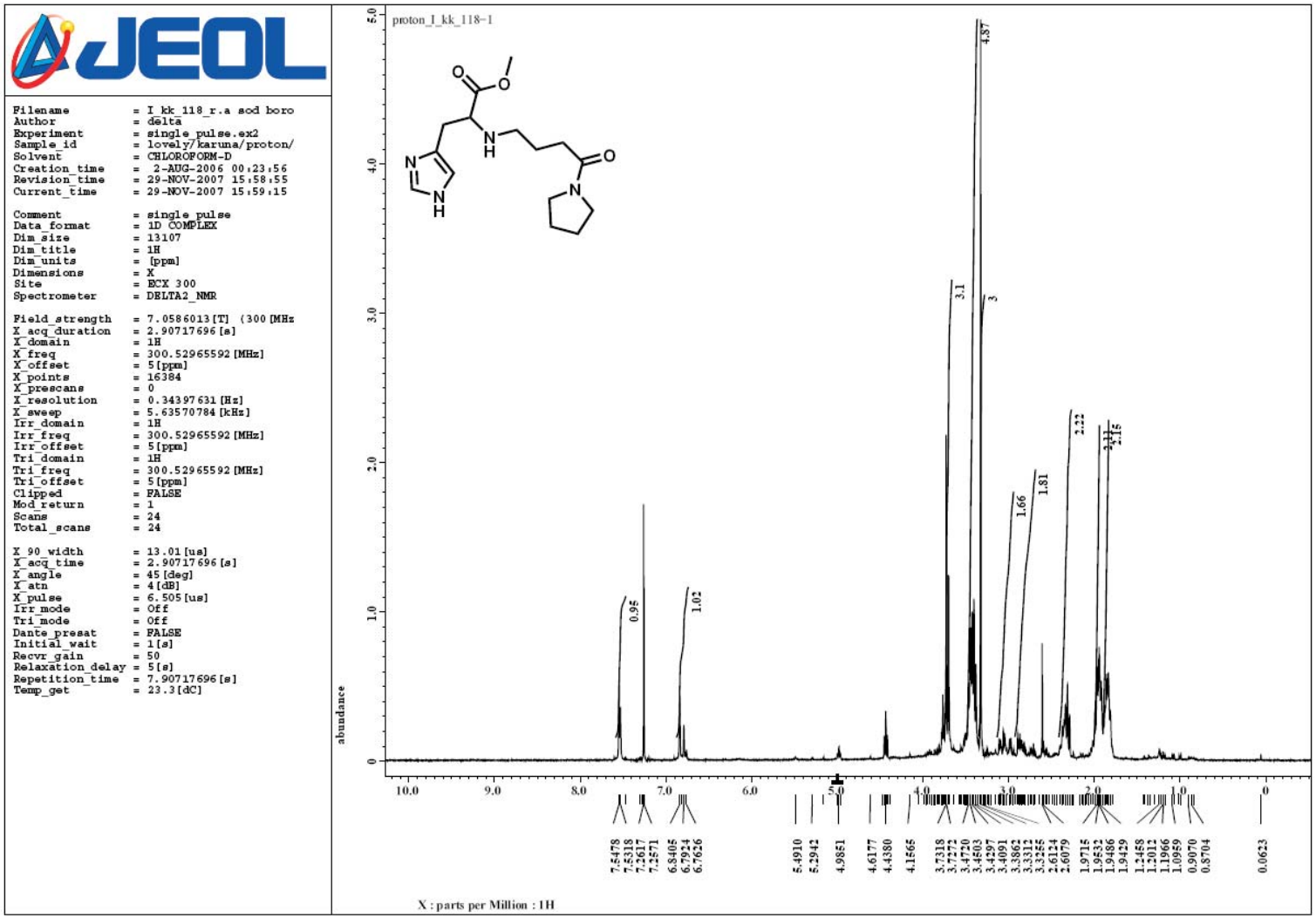
X_90_width        = 13.01[us]
X_acq_time        = 2.90717696[s]
X_angle           = 45[deg]
X_atn             = 4[dB]
X_pulse           = 6.505[us]
Irr_mode          = off
Tri_mode          = off
Dante_presat      = FALSE
Initial_wait      = 1[s]
Recvr_gain        = 46
Relaxation_delay  = 5[s]
Repetition_time   = 7.90717696[s]
Temp_get          = 22.7[dC]
```

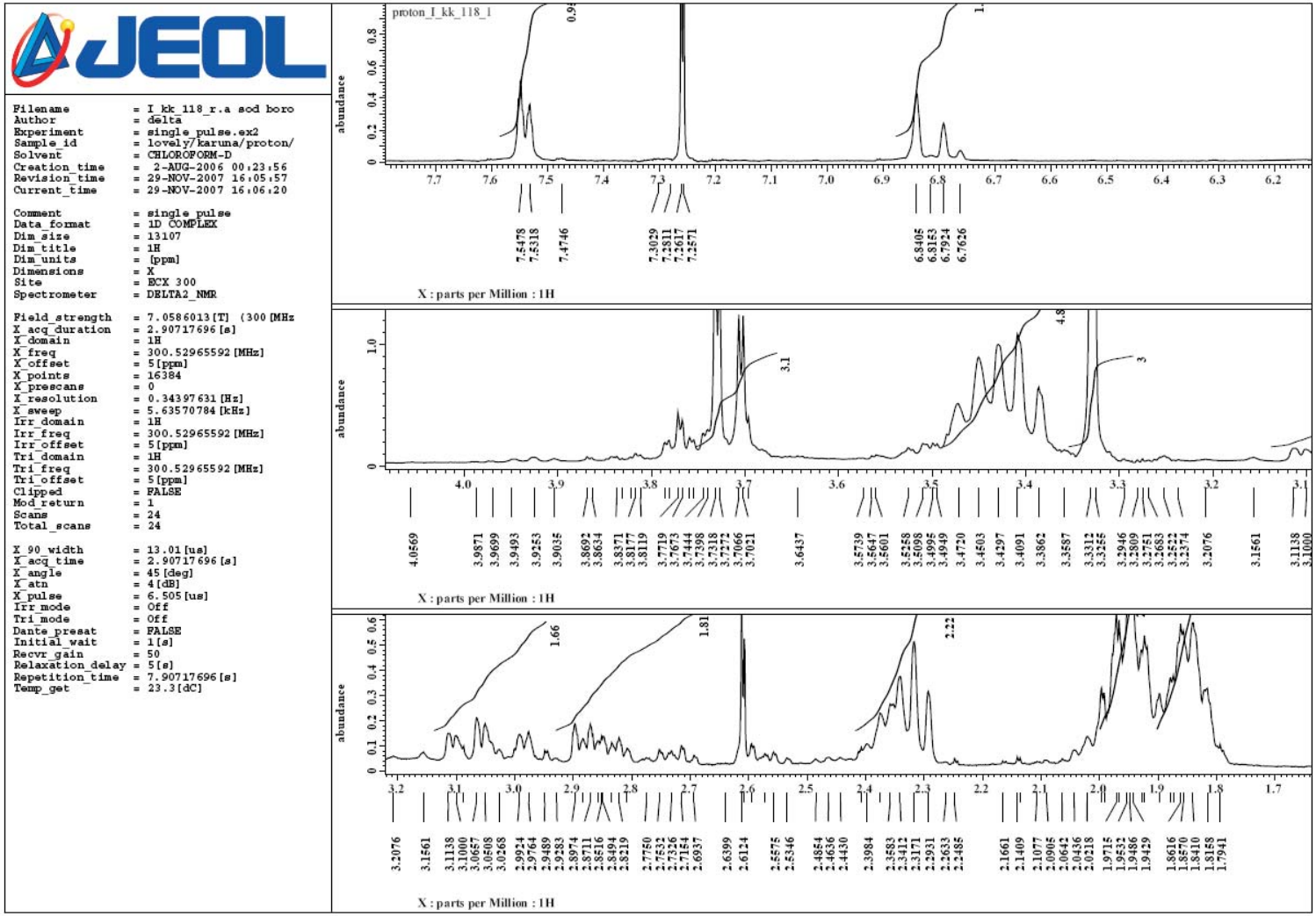




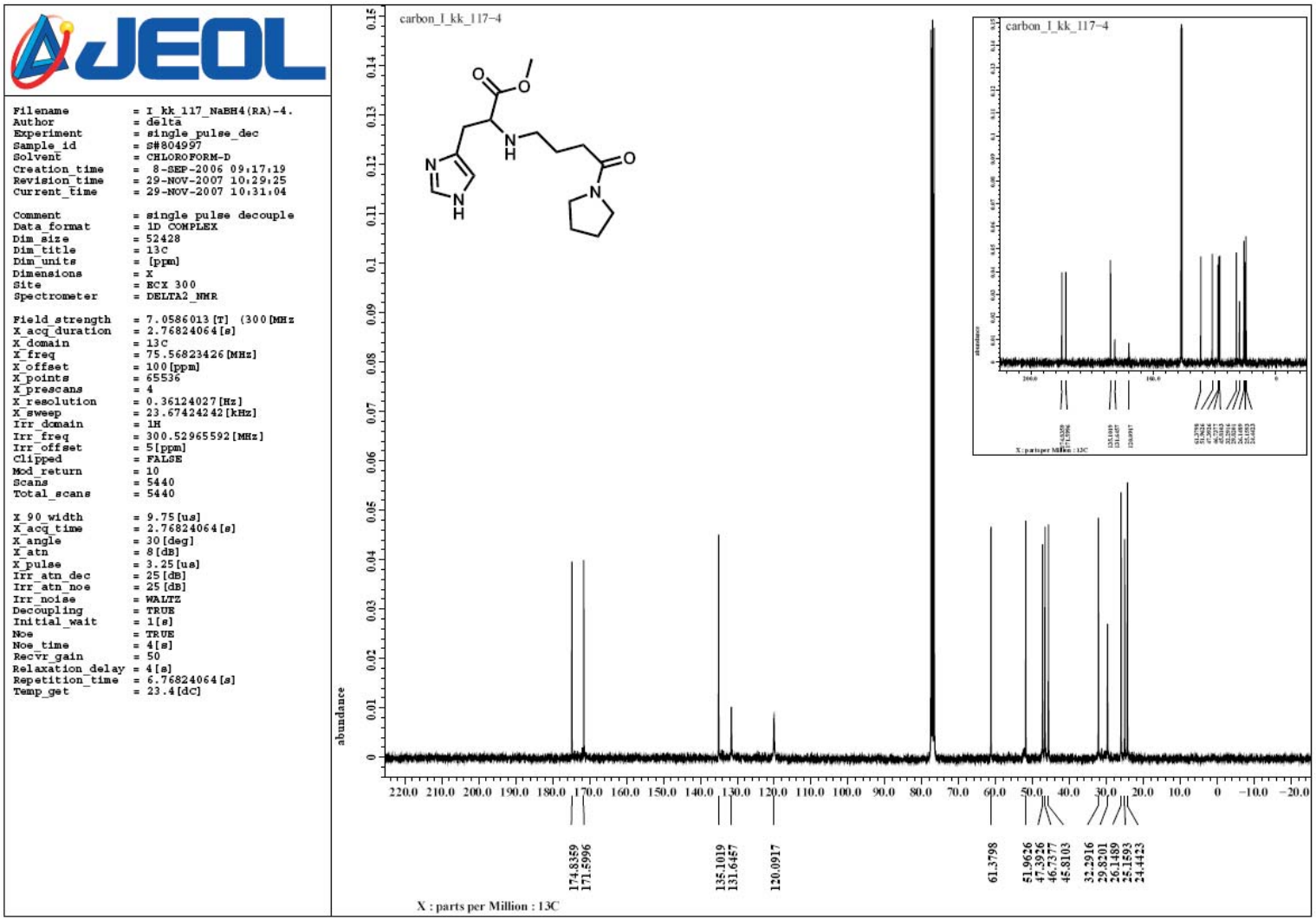
APPENDIX 6

^{1}HNMR AND ^{13}C NMR SPECTRA OF **3-(1*H*-IMIDAZOL-4-YL)-2-94-OXO-4-PYRROLIDIN-1-YL-BUTYLAMINO-PROPIONIC ACID METHYL ESTER (15A)** MEASURED ON A JEOL ECLIPSE 300+ SPECTROMETER IN $CDCl_3$


JEOL
Filename = I_kk_118_r.a sod boro
Author = delta
Experiment = single_pulse.ex2
Sample_id = lovely/karuna/proton/
Solvent = CHLOROFORM-D
Creation_time = 2-AUG-2006 00:23:56
Revision_time = 29-NOV-2007 15:58:55
Current_time = 29-NOV-2007 15:59:15
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 = 24
Total_scans = 24
X_90_width = 13.01[us]
X_acq_time = 2.90717696[s]
X_angle = 45[deg]
X_atn = 4[dB]
X_pulse = 6.505[us]
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 = 23.3[dC]
proton_I_kk_118-1
abundance
4.87
3.1
3
2.22
2.15
1.81
1.66
1.02
0.95
7.5478
7.5318
7.2617
7.2571
6.8405
6.7924
6.7626
5.4910
5.2942
4.9851
4.6177
4.4380
4.1565
3.7318
3.7272
3.4720
3.4503
3.4297
3.4091
3.3862
3.3312
3.3255
2.6124
2.6079
1.9715
1.9532
1.9486
1.9429
1.2458
1.2012
1.1966
1.1059
0.9070
0.8704
0.0623
X : parts per Million : 1H

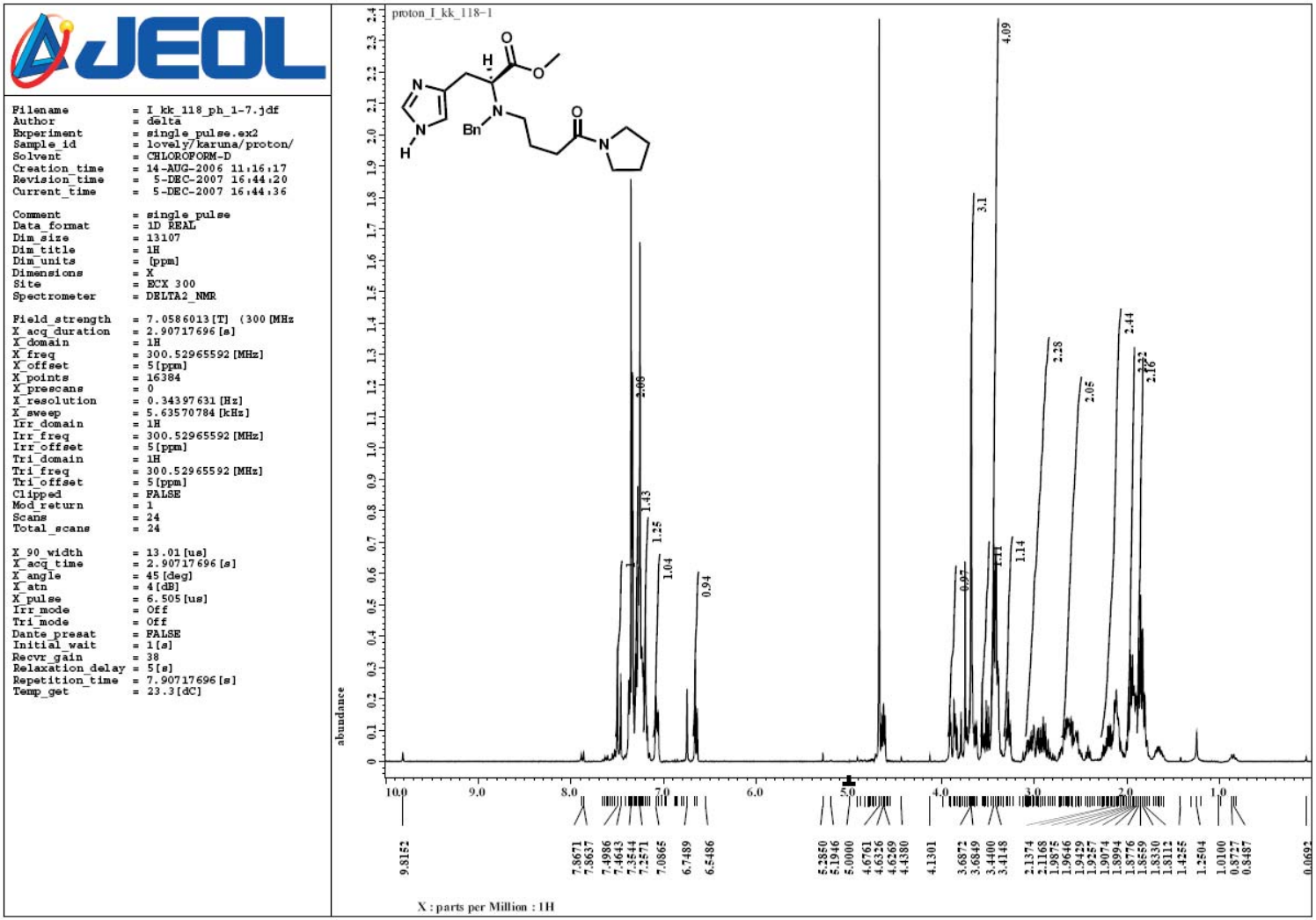


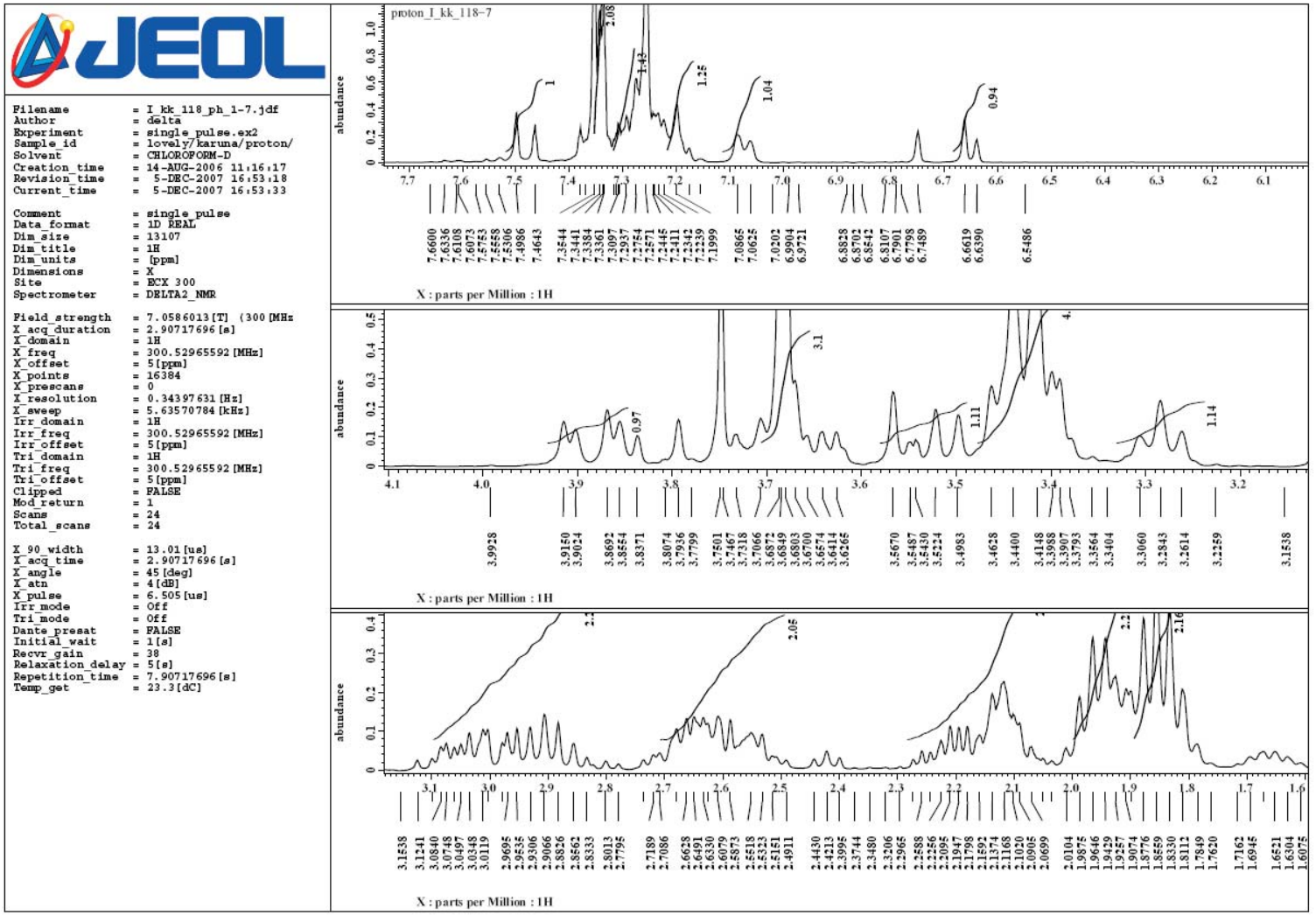
Filename	= I_kk_118_r.a sod boro
Author	= delta
Experiment	= single_pulse.ex2
Sample_id	= lovely/karuna/proton/
Solvent	= CHLOROFORM-D
Creation_time	= 2-AUG-2006 00:23:56
Revision_time	= 29-NOV-2007 16:05:57
Current_time	= 29-NOV-2007 16:06:20
Comment	= single_pulse
Data_format	= 1D COMPLEX
Dim_size	= 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	= 24
Total_scans	= 24
X_90_width	= 13.01[us]
X_acq_time	= 2.90717696[s]
X_angle	= 45[deg]
X_atn	= 4[dB]
X_pulse	= 6.505[us]
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	= 23.3[dC]


JEOL
Filename = I_kk_117_NaBH4(RA)-4.
Author = delta
Experiment = single_pulse_dec
Sample_id = S#804997
Solvent = CHLOROFORM-D
Creation_time = 8-SEP-2006 09:17:19
Revision_time = 29-NOV-2007 10:29:25
Current_time = 29-NOV-2007 10:31:04
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 = 5440
Total_scans = 5440
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 = 4[s]
Recvr_gain = 50
Relaxation_delay = 4[s]
Repetition_time = 6.76824064[s]
Temp_get = 23.4[dC]
carbon_I_kk_117-4
carbon_I_kk_117-4
abundance
X : parts per Million : 13C
174.8359
171.5996
135.1019
131.6457
120.0917
61.3798
51.9626
47.3926
46.7377
45.8103
32.2916
29.8201
26.1489
25.1593
24.4423

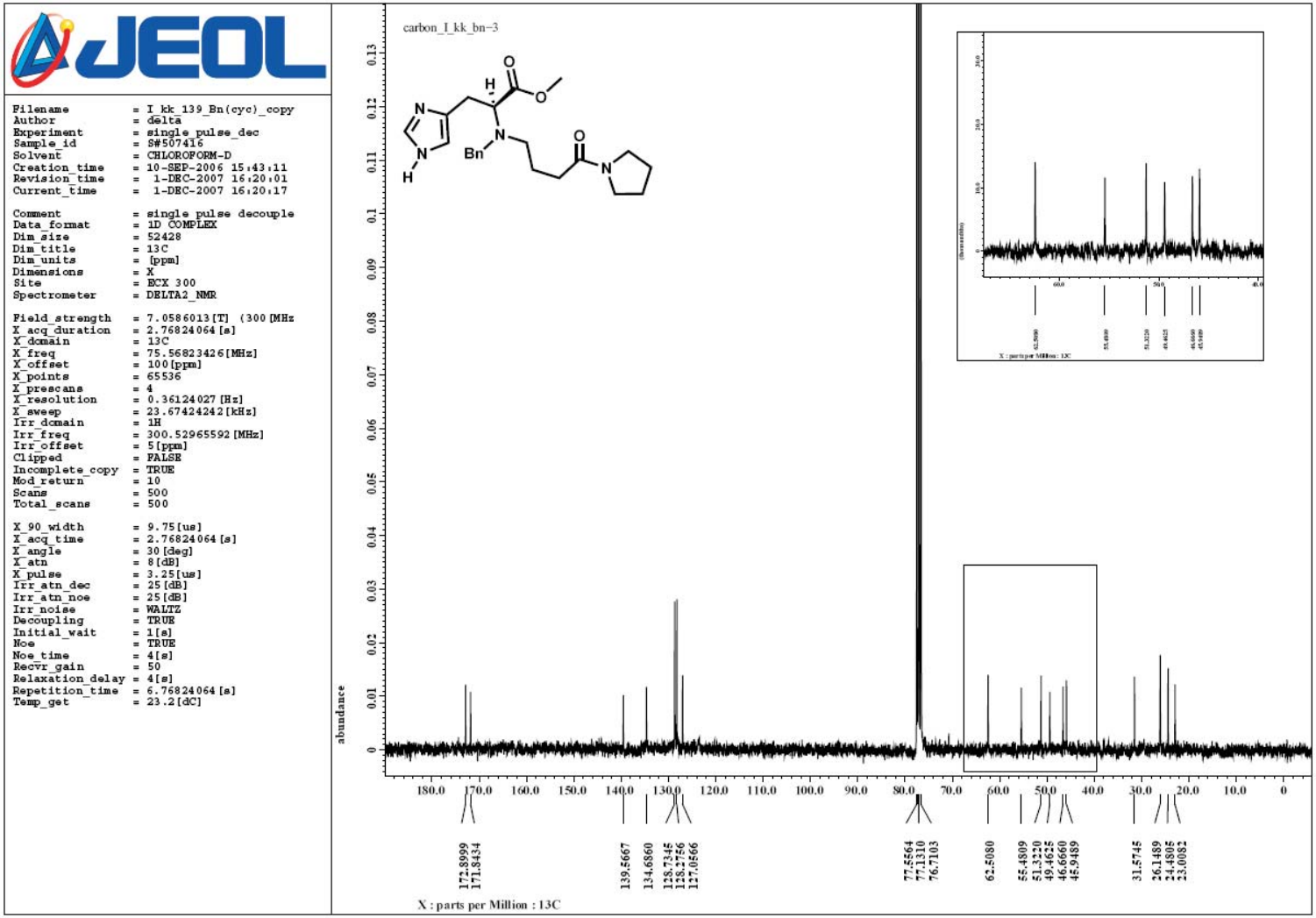
APPENDIX 7

^{1}HNMR AND ^{13}C NMR SPECTRA OF **2-[BENZYL-(4-OXO-4-PYRROLIDIN-1-YL-BUTYL) AMINO]-3-(1*H*-IMIDAZOL-4-YL) PROPIONIC ACID METHYL ESTER (15)** MEASURED ON A JEOL ECLIPSE 300+ SPECTROMETER IN $CDCl_3$


JEOL
Filename = I_kk_118_ph_1-7.jdf
Author = delta
Experiment = single_pulse.ex2
Sample_id = lovely/karuna/proton/
Solvent = CHLOROFORM-D
Creation_time = 14-AUG-2006 11:16:17
Revision_time = 5-DEC-2007 16:44:20
Current_time = 5-DEC-2007 16:44:36
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 = 24
Total_scans = 24
X_90_width = 13.01[us]
X_acq_time = 2.90717696[s]
X_angle = 45[deg]
X_atn = 4[dB]
X_pulse = 6.505[us]
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 = 23.3[dC]
proton_I_kk_118-1
abundance
X : parts per Million : 1H



Filename	= I_kk_118_ph_1-7.jdf
Author	= delta
Experiment	= single_pulse.ex2
Sample_id	= lovely7/karuna/proton/
Solvent	= CHLOROFORM-D
Creation_time	= 14-AUG-2006 11:16:17
Revision_time	= 5-DEC-2007 16:53:18
Current_time	= 5-DEC-2007 16:53:33
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	= 24
Total_scans	= 24
X_90_width	= 13.01[us]
X_acq_time	= 2.90717696[s]
X_angle	= 45[deg]
X_atn	= 4[dB]
X_pulse	= 6.505[us]
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	= 23.3[dC]



```
Filename          = I_kk_139_Bn(cyc)_copy
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#507416
Solvent           = CHLOROFORM-D
Creation_time     = 10-SEP-2006 15:43:11
Revision_time     =  1-DEC-2007 16:20:01
Current_time      =  1-DEC-2007 16:20:17

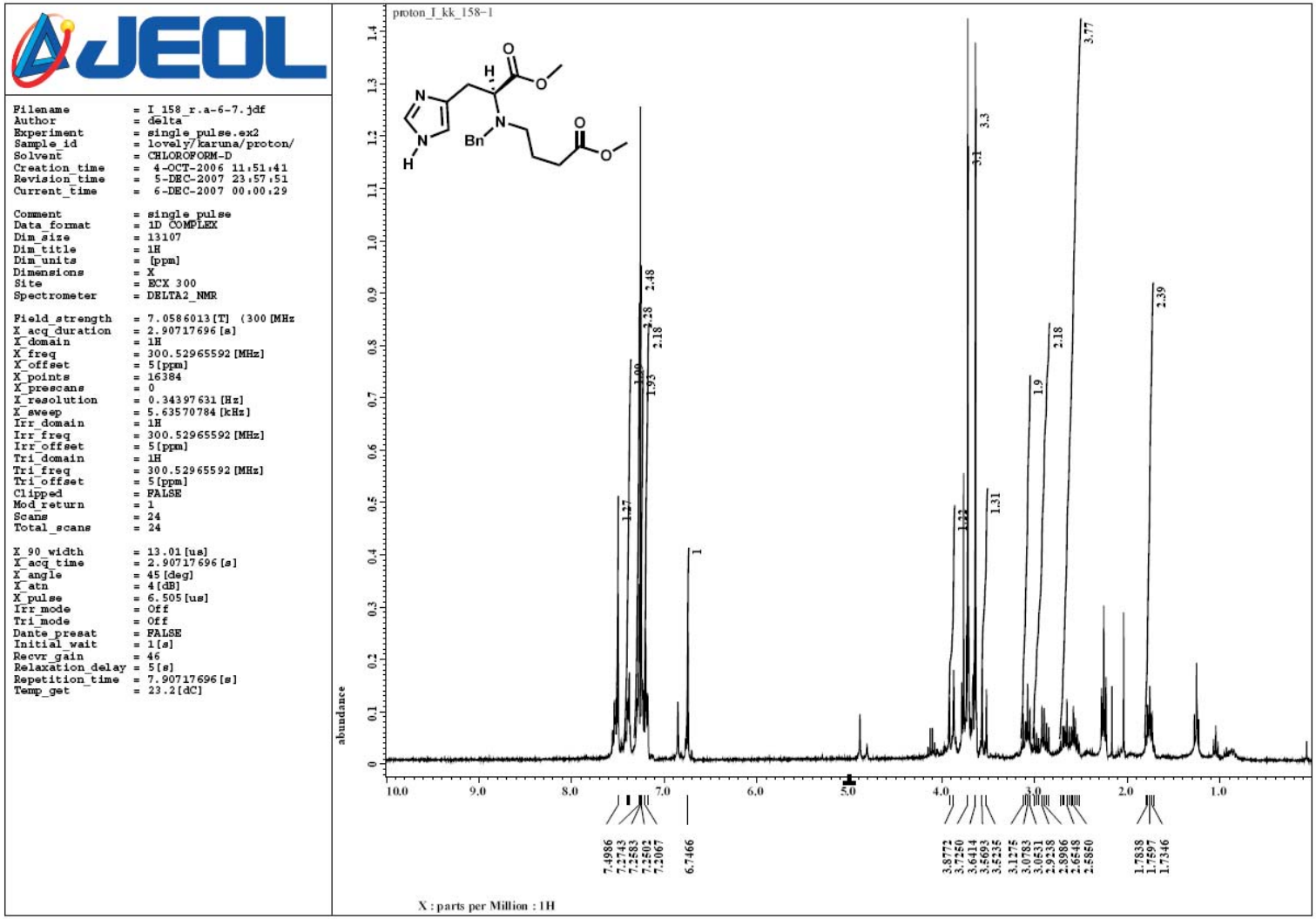
Comment           = single pulse decouple
Data_format       = 1D COMPLEX
Dim_size          = 52428
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = ECX 300
Spectrometer      = DELTA2_NMR

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
Incomplete_copy   = TRUE
Mod_return        = 10
Scans             = 500
Total_scans       = 500

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          = 4[s]
Recvr_gain        = 50
Relaxation_delay  = 4[s]
Repetition_time   = 6.76824064[s]
Temp_get          = 23.2[dC]
```

APPENDIX 8

^{1}HNMR AND ^{13}C NMR SPECTRA OF **4-{BENZYL-[2-(1H-IMIDAZOL-4-YL)-1-METHOXYCARBONYLETHYL] AMINO} BUTYRIC ACID METHYL ESTER (16)** MEASURED ON A JEOL ECLIPSE 500+ SPECTROMETER IN $CDCl_3$

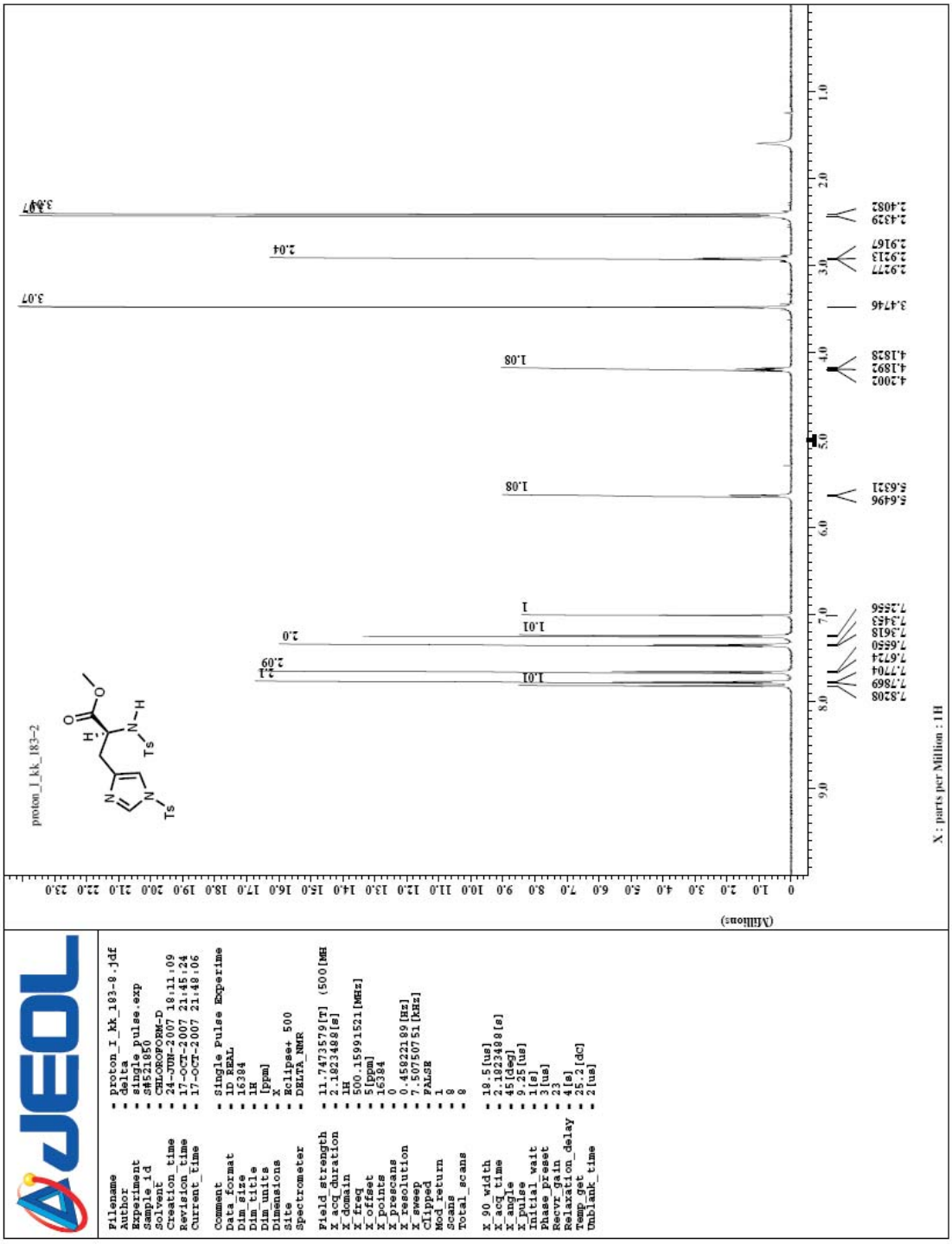

JEOL
Filename = I_158_r.a-6-7.jdf
Author = delta
Experiment = single_pulse.ex2
Sample_id = lovely7/karuna/proton/
Solvent = CHLOROFORM-D
Creation_time = 4-OCT-2006 11:51:41
Revision_time = 5-DEC-2007 23:57:51
Current_time = 6-DEC-2007 00:00:29
Comment = single_pulse
Data_format = 1D COMPLEX
Dim_size = 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 = 24
Total_scans = 24
X_90_width = 13.01[us]
X_acq_time = 2.90717696[s]
X_angle = 45[deg]
X_atn = 4[dB]
X_pulse = 6.505[us]
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]
proton_I_kk_158-1
abundance
X : parts per Million : 1H
7.4986
7.2743
7.2583
7.2502
7.2067
6.7466
3.8772
3.7250
3.6414
3.5693
3.5235
3.1275
3.0783
3.0531
2.9238
2.8986
2.6648
2.5850
1.7838
1.7597
1.7346

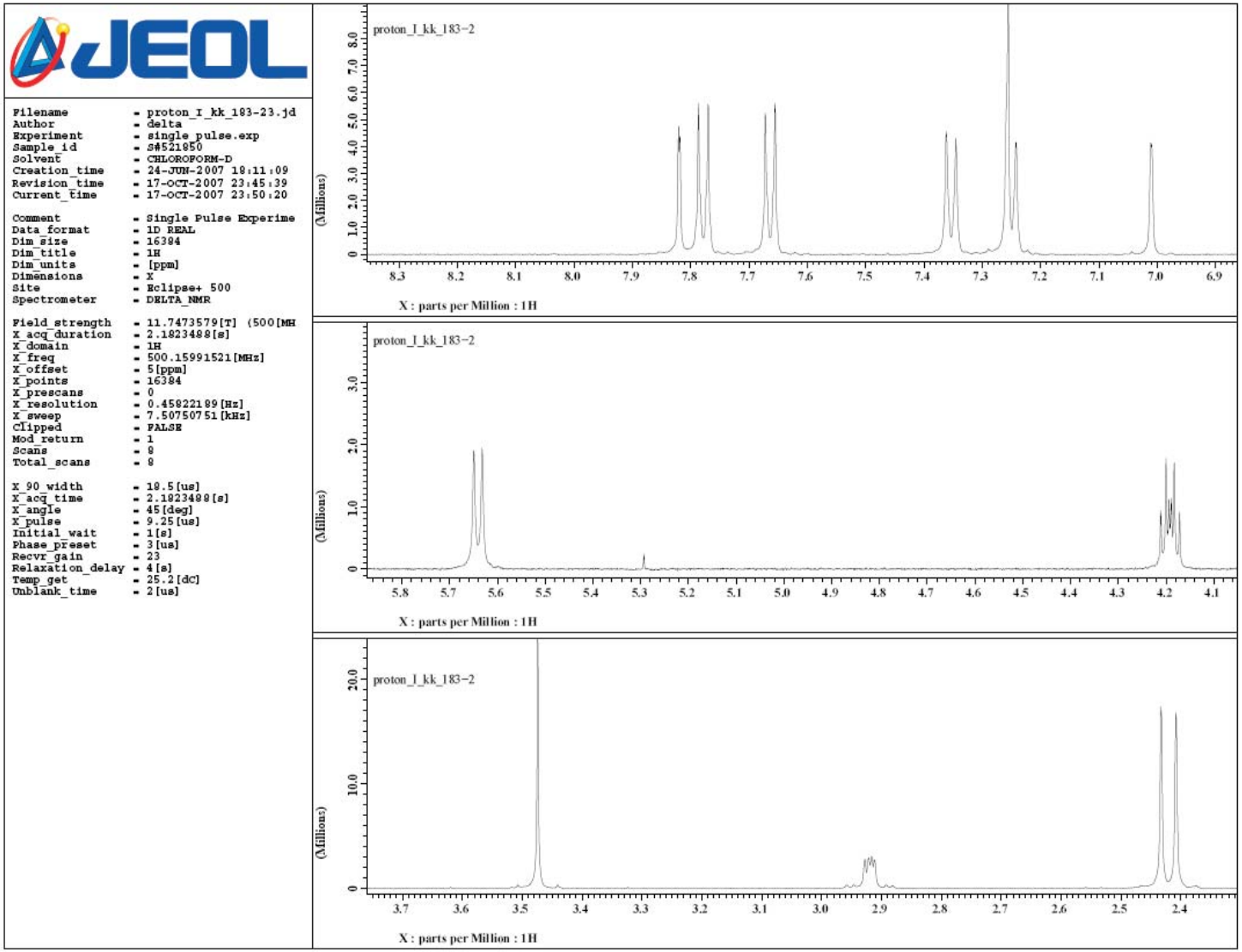
JEOL
Filename = I_158_r.a-6-7.jdf
Author = delta
Experiment = single_pulse.ex2
Sample_id = lovely/karuna/proton/
Solvent = CHLOROFORM-D
Creation_time = 4-OCT-2006 11:51:41
Revision_time = 6-DEC-2007 00:07:16
Current_time = 6-DEC-2007 00:07:31
Comment = single pulse
Data_format = 1D COMPLEX
Dim_size = 13107
Dim_title = 1H
Dim_units = [ppm]
Dimensions = X
Site = EOX 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 = 24
Total_scans = 24
X_90_width = 13.01[us]
X_acq_time = 2.90717696[s]
X_angle = 45[deg]
X_atn = 4[dB]
X_pulse = 6.505[us]
Irr_mode = Off
Tri_mode = Off
Dante_preset = FALSE
Initial_wait = 1[s]
Recvr_gain = 46
Relaxation_delay = 5[s]
Repetition_time = 7.90717696[s]
Temp_get = 23.2[dC]
proton_I_kk_158-7
abundance
X : parts per Million : 1H
7.4986
7.4013
7.3932
7.3841
7.3773
7.2743
7.2583
7.2502
7.2067
7.1804
6.7466
3.9230
3.8772
3.7250
3.6414
3.5693
3.5236
3.1275
3.1035
3.0783
3.0531
3.0073
2.9810
2.9692
2.9238
2.8986
2.8734
2.8494
2.7236
2.6983
2.6648
2.6296
2.6056
2.5850
2.5632
2.5415
2.5209
1.8021
1.7838
1.7697
1.7346
1.7094

JEOL
Filename = I_kk_125_hnprotester-dGlta
Author = single_pulse_dec
Experiment = S#633482
Sample_id = CHLOROFORM-D
Solvent = 30-NOV-2007 02:12:51
Creation_time = 3-DEC-2007 11:20:41
Revision_time = 3-DEC-2007 11:21:22
Current_time = single_pulse decouple
Comment = 1D COMPLEX
Data_format = 65536
Dim_size = 13C
Dim_title = [ppm]
Dim_units = X
Dimensions = Eclipse+ 500
Site = DELTA_NMR
Spectrometer = 11.7473579[T] (500[MH
Field_strength = 2.08440448[s]
X_acq_duration = 13C
X_domain = 125.765297681MHz]
X_freq = 65536
X_offset = 100[ppm]
X_points = 4
X_prescans = 0.47983613[Hz]
X_resolution = 31.44654088[kHz]
X_sweep = 1H
Irr_domain = 500.15991521[MHz]
Irr_freq = 5[ppm]
Irr_offset = FALSE
Clipped = 2500
Mod_return = 2500
Scans = 2500
Total_scans = 14.2[us]
X_90_width = 2.08440448[s]
X_acq_time = 30[deg]
X_angle = 4.73333333[us]
X_pulse = 1[s]
Initial_wait = 1[s]
Noe_time = 3[us]
Phase_preset = 29
Recvr_gain = 2[s]
Relaxation_delay = 26.8[dC]
Temp_get = 2[us]
Unblank_time
carbon_1_kk_129-1
Bn
(Thousands)
X : parts per Million : 13C
174.6584
174.3989
173.0216
134.7004
134.4906
128.7906
128.6493
128.3976
128.3632
127.4093
77.3636
77.1080
76.8562
62.5449
60.6449
52.1473
52.1329
51.6865
51.4690
49.7483
31.3050
29.4774
26.5473
23.3167

APPENDIX 9

^{1}HNMR AND ^{13}C NMR SPECTRA OF **2-(TOLUENE-4 SULFONYLAMINO)-3-[1-(TOLUENE-4-SULFONYL)-1*H*-IMIDAZOL-4-YLPROPIONIC ACID METHYL ESTER (22)** MEASURED ON A JEOL ECLIPSE 500+ SPECTROMETER IN $CDCl_3$


JEOL
Filename = proton_I_kk_183-8.jdf
Author = delta
Experiment = single_pulse.exp
Sample_id = SM521850
Solvent = CHLOROFORM-D
Creation_time = 24-JUN-2007 18:11:09
Revision_time = 17-OCT-2007 21:45:24
Current_time = 17-OCT-2007 21:48:06
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 = 2.18234888[s]
X_domain = H1
X_freq = 500.15991521[MHz]
X_offset = 5[ppm]
X_points = 16384
X_prescans = 0
X_resolution = 0.458221189[Hz]
X_sweep = 7.50750751[kHz]
Clipped = FALSE
Mod_return = 1
Scans = 8
Total_scans = 8
X_90_width = 10.5[us]
X_acq_time = 2.18234888[s]
X_angle = 45[deg]
X_pulse = 9.25[us]
Initial_wait = 1[s]
Phase_preset = 3[us]
Recvr_gain = 23
Relaxation_delay = 4[s]
Temp_get = 25.2[dC]
Unblank_time = 2[us]
proton_I_kk_183-2
(Million)
X : parts per Million : 1H
3.07
2.04
1.08
1.08
1.01
2.0
2.09
2.1
1.01
1
1.01
2.0
1.08
1.08
3.07
7.8208
7.7869
7.7704
7.6724
7.6550
7.3618
7.3463
7.2556
5.6496
5.6321
4.2002
4.1892
4.1828
3.4746
2.9277
2.9213
2.9167
2.4329
2.4082



```
Filename          = proton_1_kk_183-23.jd
Author            = delta
Experiment        = single_pulse.exp
Sample_id         = S#521850
Solvent           = CHLOROFORM-D
Creation_time     = 24-JUN-2007 18:11:09
Revision_time     = 17-OCT-2007 23:45:39
Current_time      = 17-OCT-2007 23:50:20

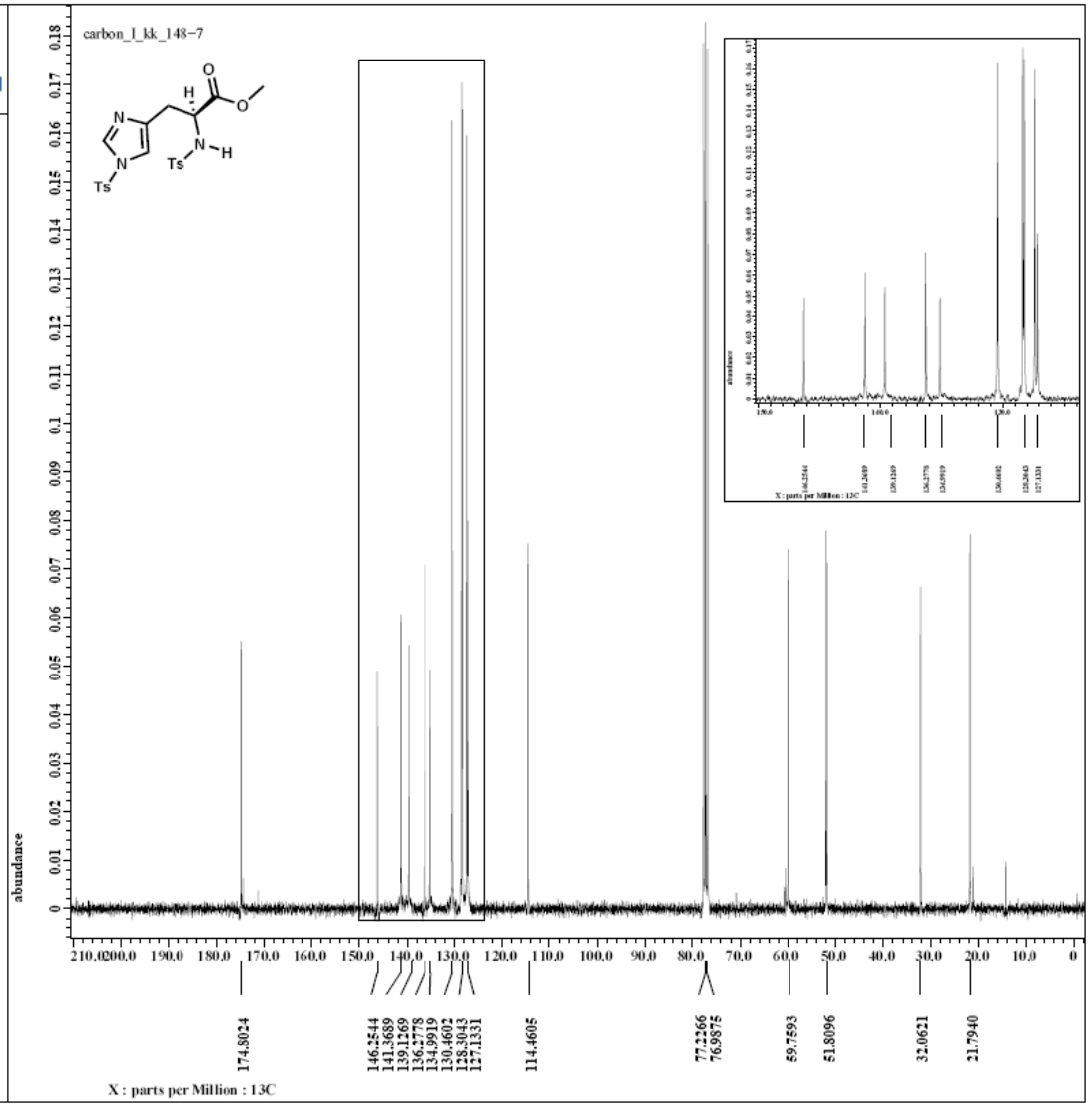
Comment           = Single Pulse Experime
Data_format       = 1D REAL
Dim_size          = 16384
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = Eclipse+ 500
Spectrometer      = DELTA_NMR

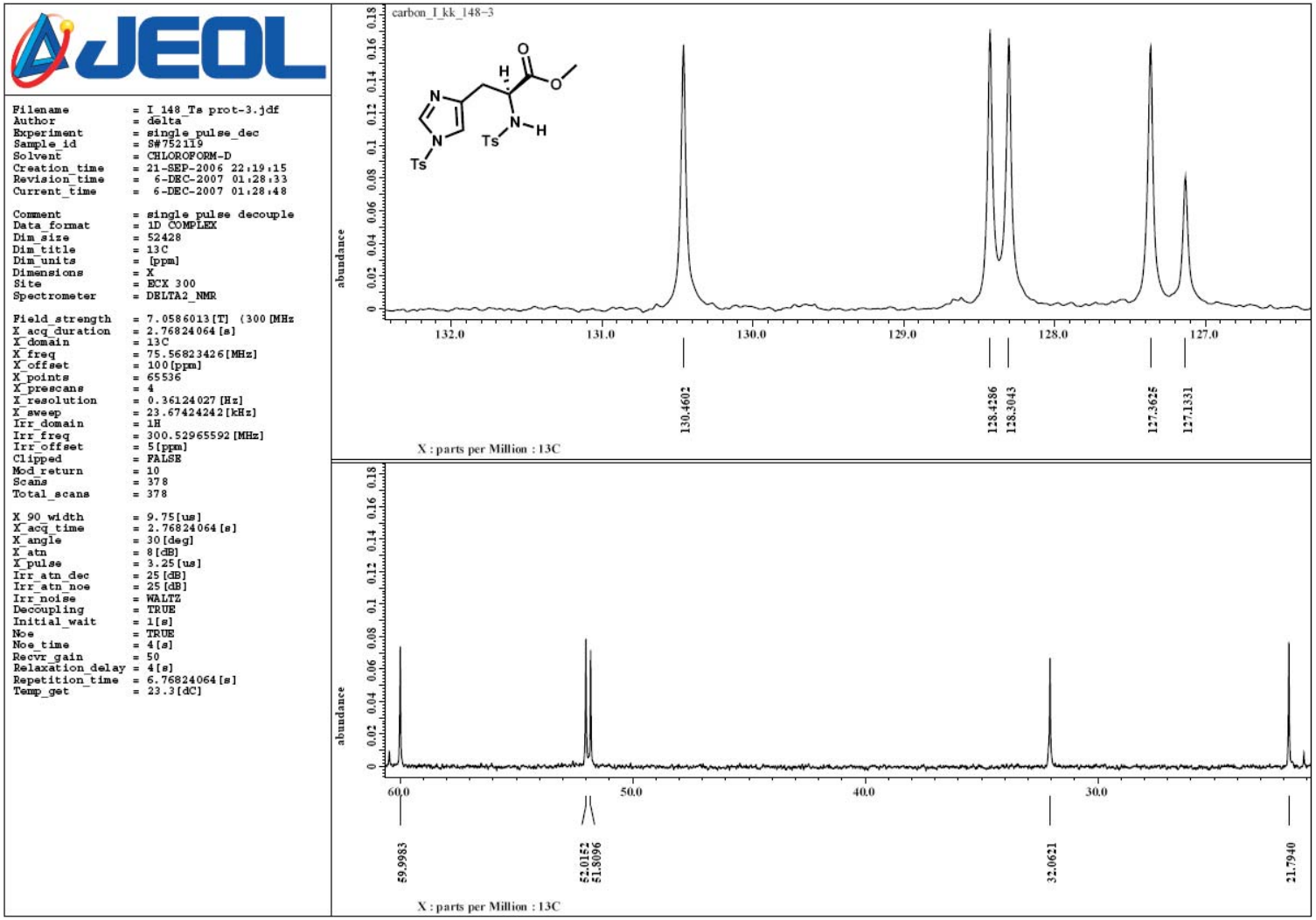
Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 2.1823488[s]
X_domain          = 1H
X_freq            = 500.15991521[MHz]
X_offset          = 5[ppm]
X_points          = 16384
X_prescans        = 0
X_resolution      = 0.45822189[Hz]
X_sweep           = 7.50750751[kHz]
Clipped           =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

X_90_width        = 10.5[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        = 23
Relaxation_delay  = 4[s]
Temp_get          = 25.2[dC]
Unblank_time      = 2[us]
```

JEOL

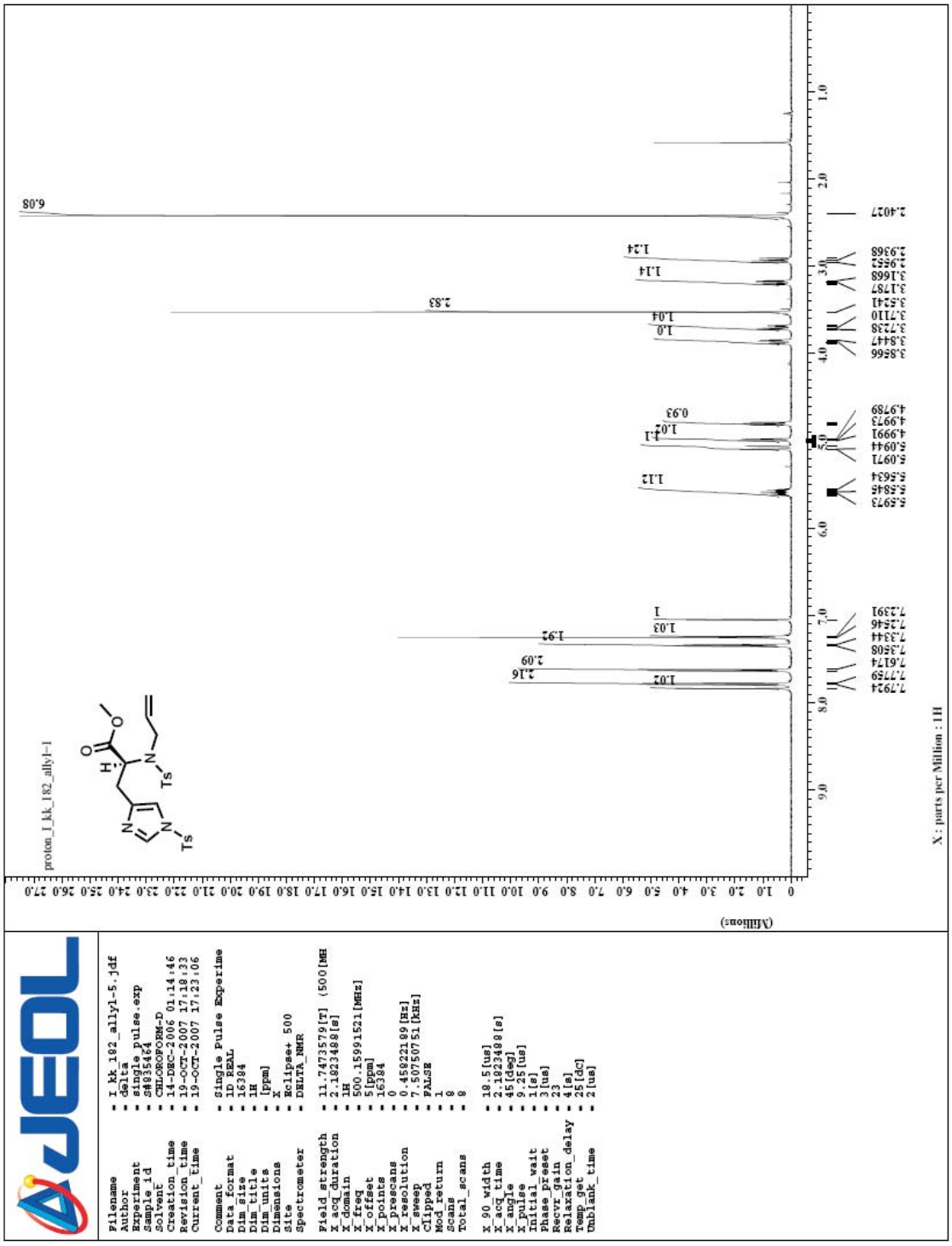
Filename	= I_148_Ts prot-7.jdf
Author	= delta
Experiment	= single_pulse_dec
Sample_id	= S#752119
Solvent	= CHLOROFORM-D
Creation_time	= 21-SEP-2006 22:19:15
Revision_time	= 18-OCT-2007 00:57:20
Current_time	= 18-OCT-2007 00:58:28
Comment	= single pulse decouple
Data_format	= 1D REAL
Dim_size	= 52428
Dim_title	= 13C
Dim_units	= [ppm]
Dimensions	= X
Site	= RCX 300
Spectrometer	= DELTA2_NMR
Field_strength	= 7.0586013[T] (300[MHz
X_acq_duration	= 2.76824064[s]
X_domain	= 13C
X_freq	= 75.56023426[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	= 378
Total_scans	= 378
X_90_width	= 9.75[us]
X_acq_time	= 2.76824064[s]
X_angle	= 30[deg]
X_atn	= 9[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	= 4[s]
Recvr_gain	= 50
Relaxation_delay	= 4[s]
Repetition_time	= 6.76824064[s]
Temp_get	= 23.3[dC]




Filename = I_148_Ts prot-3.jdf
Author = delta
Experiment = single_pulse_dec
Sample_id = S#752119
Solvent = CHLOROFORM-D
Creation_time = 21-SEP-2006 22:19:15
Revision_time = 6-DEC-2007 01:28:33
Current_time = 6-DEC-2007 01:28:48
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 = 378
Total_scans = 378
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 = 4[s]
Recvr_gain = 50
Relaxation_delay = 4[s]
Repetition_time = 6.76824064[s]
Temp_get = 23.3[dC]
carbon_I_kk_148-3
abundance
130.4602
128.4286
128.3043
127.3625
127.1331
X : parts per Million : 13C
abundance
59.9983
52.0152
51.8096
32.0621
21.7940
X : parts per Million : 13C

APPENDIX 10

^{1}HNMR AND ^{13}C NMR SPECTRA OF **2-[ALLYL-(TOLUENE-4-SULFONYL)-AMINO]-3-[1-(TOLUENE-4-SULFONYL)-1*H*-IMIDAZOL-4-YL]-PROPIONIC ACID METHYL ESTER (23)** MEASURED ON A JEOL ECLIPSE 500+ SPECTROMETER IN $CDCl_3$

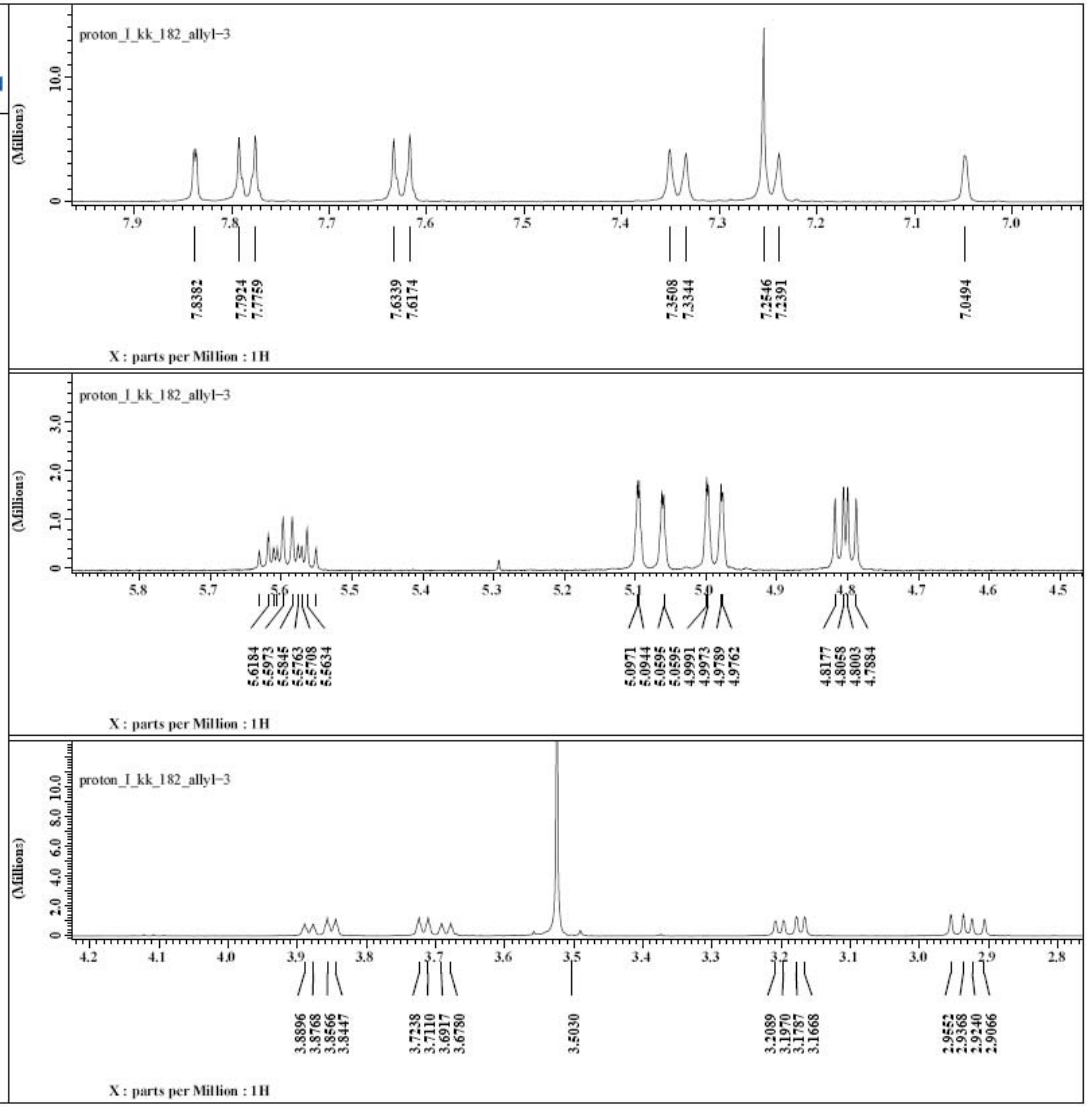

JEOL
Filename = I_kk_182_allyl-5.jdf
Author = delta
Experiment = single_pulse.exp
Sample_id = CHCl3+TMS+BM-D
Solvent = CHCl3
Creation_time = 14-DEC-2006 01:14:46
Revision_time = 19-OCT-2007 17:18:33
Current_time = 19-OCT-2007 17:23:06
Comment = Single Pulse Experime
Data_format = 1D REAL
Dim_size = 16384
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 = 23
Relaxation_delay = 4[s]
Temp_get = 25[dc]
Unblank_time = 2[us]
proton_I_kk_182_allyl-1
(Millions)
X : parts per Million : 1H
6.08
2.83
2.09
2.16
1.92
1.24
1.14
1.12
1.04
1.03
1.02
1.02
1.0
1.0
0.93
2.4027
3.8566
3.8447
3.7238
3.7110
3.5241
3.1787
3.1668
2.9652
2.9368
4.9789
4.9973
4.9991
5.0944
5.0971
5.5634
5.5846
5.5973
7.2391
7.2546
7.3344
7.3508
7.6174
7.7759
7.7924

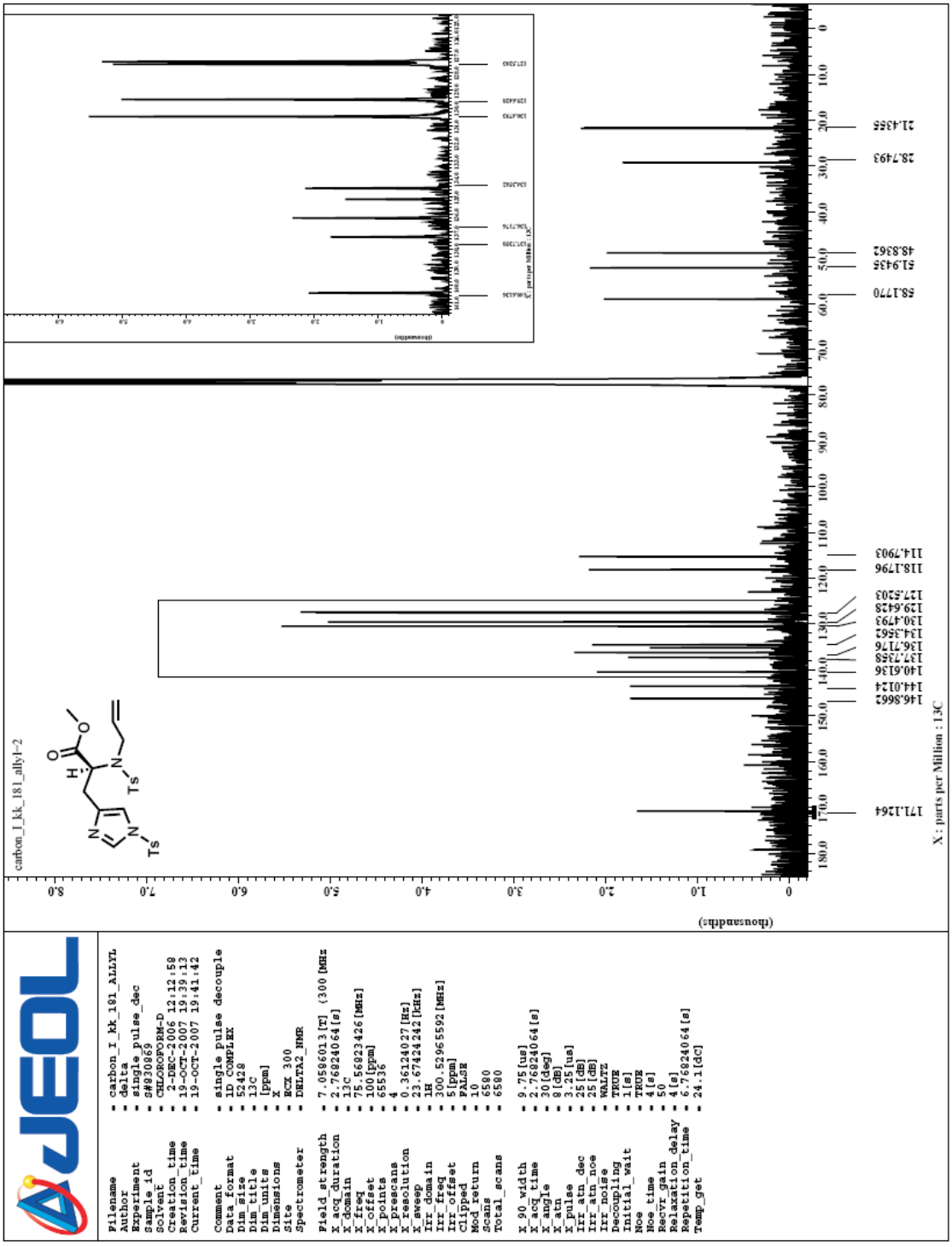
```
Filename          = proton_1_kk_182_allyl
Author            = delta
Experiment        = single_pulse.exp
Sample_id         = S#035464
Solvent           = CHLOROFORM-D
Creation_time     = 14-DEC-2006 01:14:46
Revision_time     = 19-OCT-2007 21:24:18
Current_time      = 19-OCT-2007 21:25:01

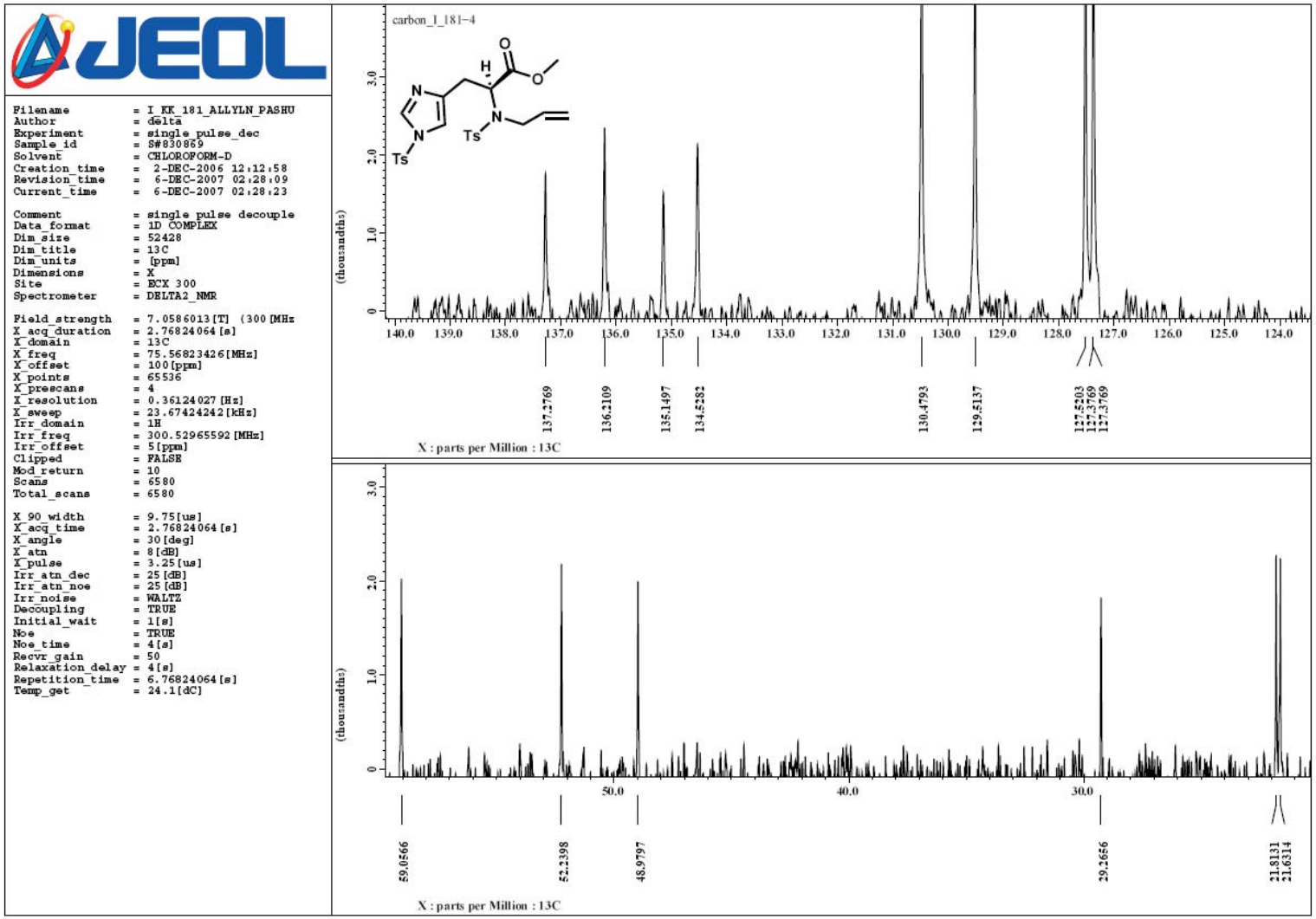
Comment           = Single Pulse Experime
Data_format       = 1D COMPLEX
Dim_size          = 16384
Dim_title         = 1H
Dim_units         = [ppm]
Dimensions        = X
Site              = Eclipse+ 500
Spectrometer      = DELTA_NMR

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             = 8
Total_scans       = 8

X_90_width        = 19.5[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        = 23
Relaxation_delay  = 4[s]
Temp_get          = 25[dC]
Unblank_time      = 2[us]
```




carbon_1_kk_181_allyl-2
Filename - carbon_1_kk_181_ALLYL
Author - delta
Experiment - single_pulse_dec
Sample_id - S#830869
Solvent - CHLOROFORM-D
Creation_time - 2-DEC-2006 12:12:58
Revision_time - 19-OCT-2007 19:39:13
Current_time - 19-OCT-2007 19:41:42
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 - 7.0596013[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]
X_window - EM
Irr_domain - 1H
Irr_freq - 300.52965592[MHz]
Irr_offset - 5[ppm]
Clipped - FALSE
Mod_return - 10
Scans - 6580
Total_scans - 6580
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 - 4[s]
Recvr_gain - 50
Relaxation_delay - 4[s]
Repetition_time - 6.76824064[s]
Temp_get - 24.1[dC]
Ts
Ts
Ts
(thousandths)
171.1264
146.8662
144.0124
140.6136
137.7358
136.7176
134.3562
130.4793
129.6428
127.5203
118.1796
114.7903
58.1770
51.9435
48.8362
28.7493
21.4356
X : parts per Million : 13C




```
Filename          = I_KK_181_ALLYLN_PASHU
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#830869
Solvent           = CHLOROFORM-D
Creation_time     =  2-DEC-2006 12:12:58
Revision_time     =  6-DEC-2007 02:28:09
Current_time      =  6-DEC-2007 02:28:23

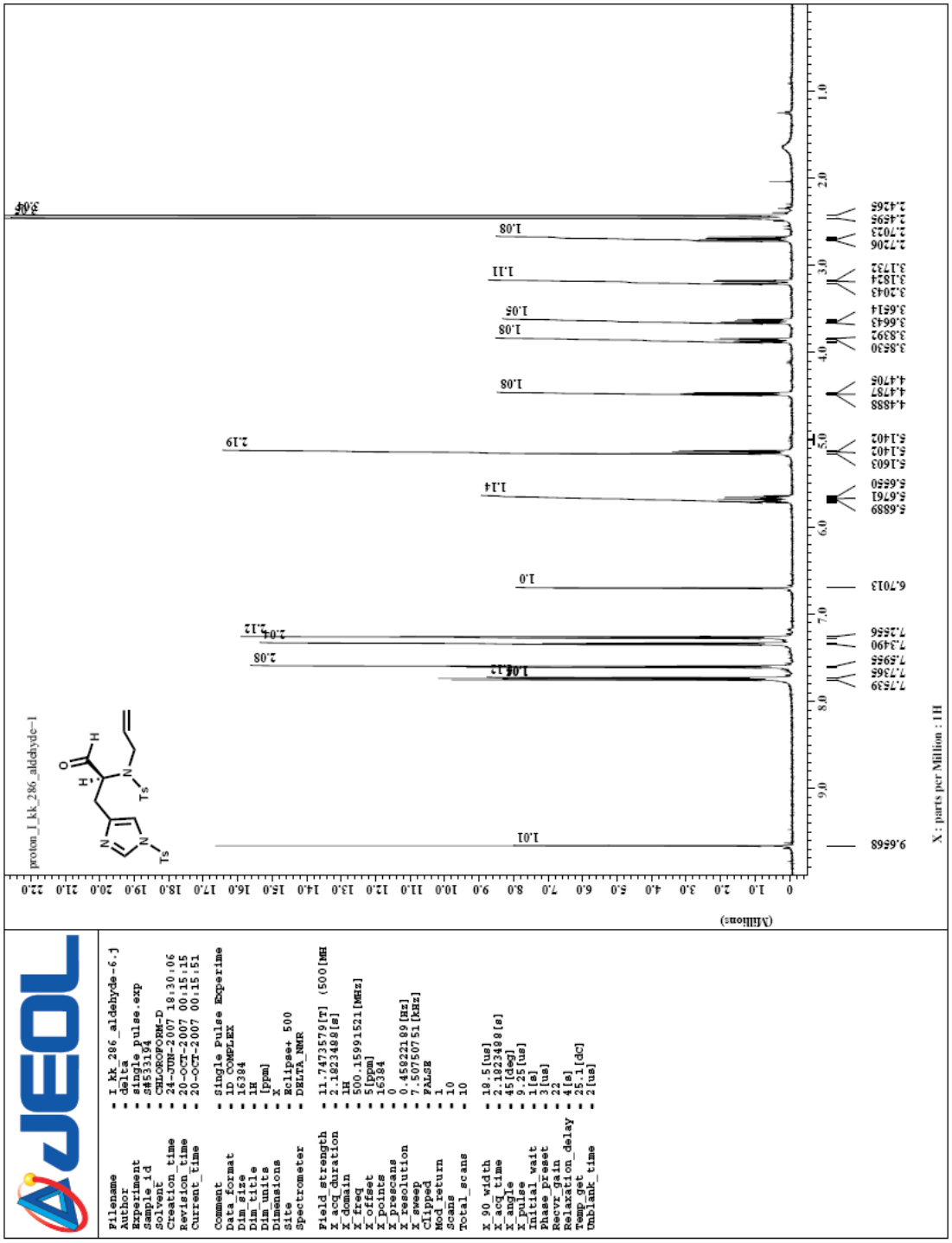
Comment           = single pulse decouple
Data_format       = 1D COMPLEX
Dim_size          = 52428
Dim_title         = 13C
Dim_units         = [ppm]
Dimensions        = X
Site              = ECX 300
Spectrometer      = DELTA2_NMR

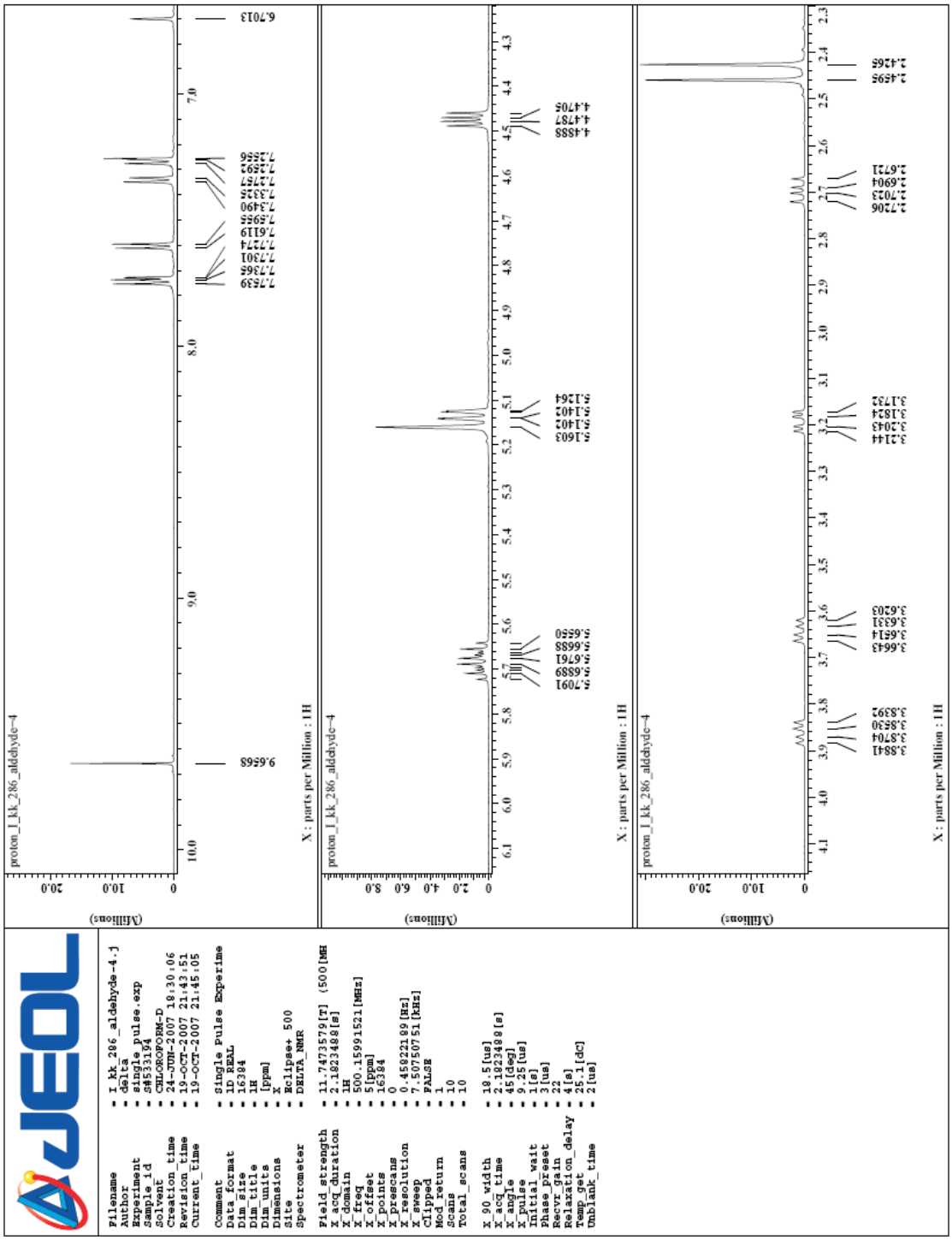
Field_strength    = 7.0586013[T] (300[MHz
X_acq_duration    = 2.76824064[s]
X_domain          = 13C
X_freq            = 75.56823426[MHz]
X_offset          = 100[ppm]
X_points          = 65536
X_prescans        = 4
X_resolution      = 0.36124027[Hz]
X_sweep           = 23.67424242[kHz]
Irr_domain        = 1H
Irr_freq          = 300.52965592[MHz]
Irr_offset        = 5[ppm]
Clipped           = FALSE
Mod_return        = 10
Scans             = 6580
Total_scans       = 6580

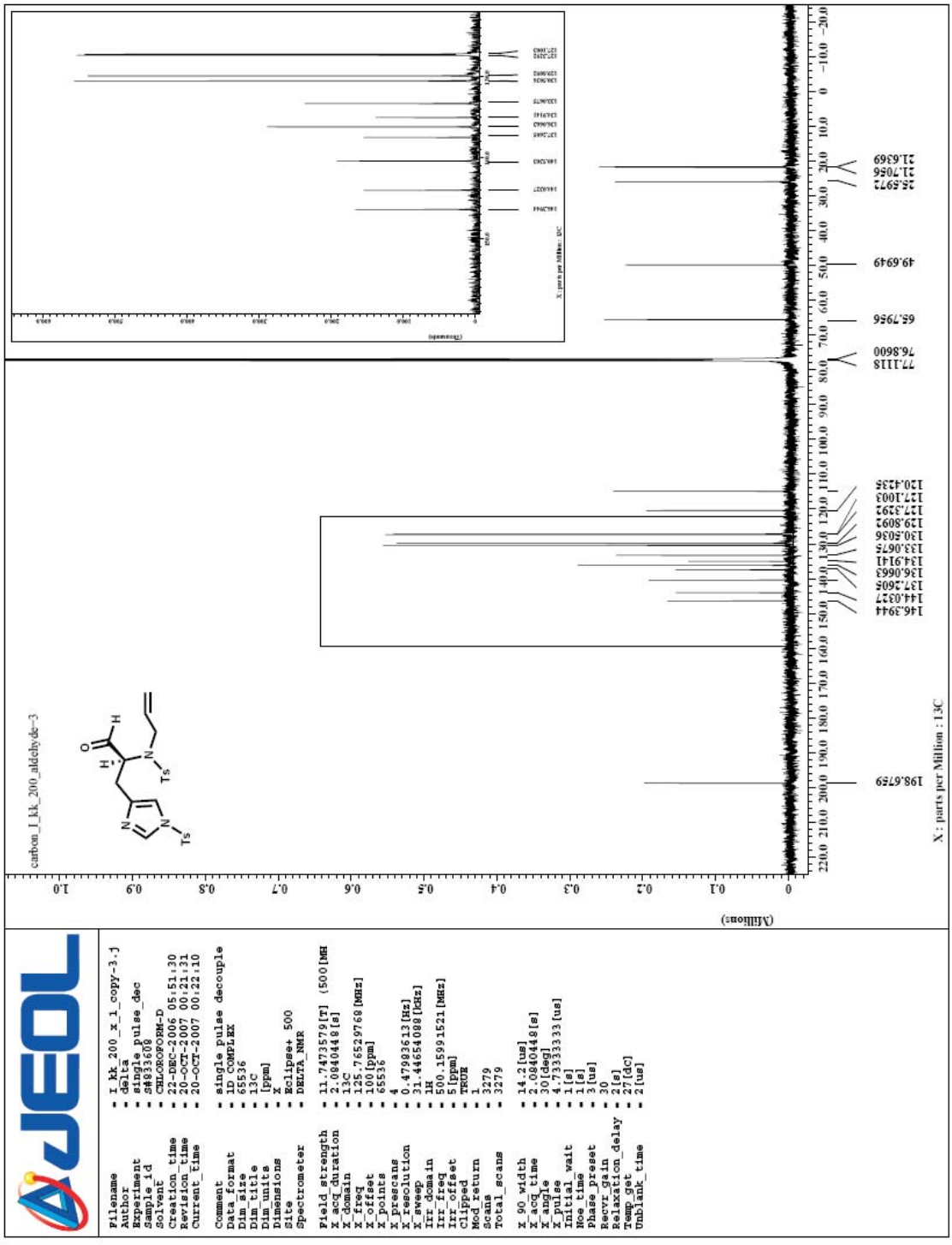
X_90_width        = 9.75[us]
X_acq_time        = 2.76824064[s]
X_angle           = 30[deg]
X_atn             = 8[dB]
X_pulse           = 3.25[us]
Irr_atn_dec       = 25[dB]
Irr_atn_noe       = 25[dB]
Irr_noise         = WALTZ
Decoupling        = TRUE
Initial_wait      = 1[s]
Noe               = TRUE
Noe_time          = 4[s]
Recvr_gain        = 50
Relaxation_delay  = 4[s]
Repetition_time   = 6.76824064[s]
Temp_get          = 24.1[dC]
```

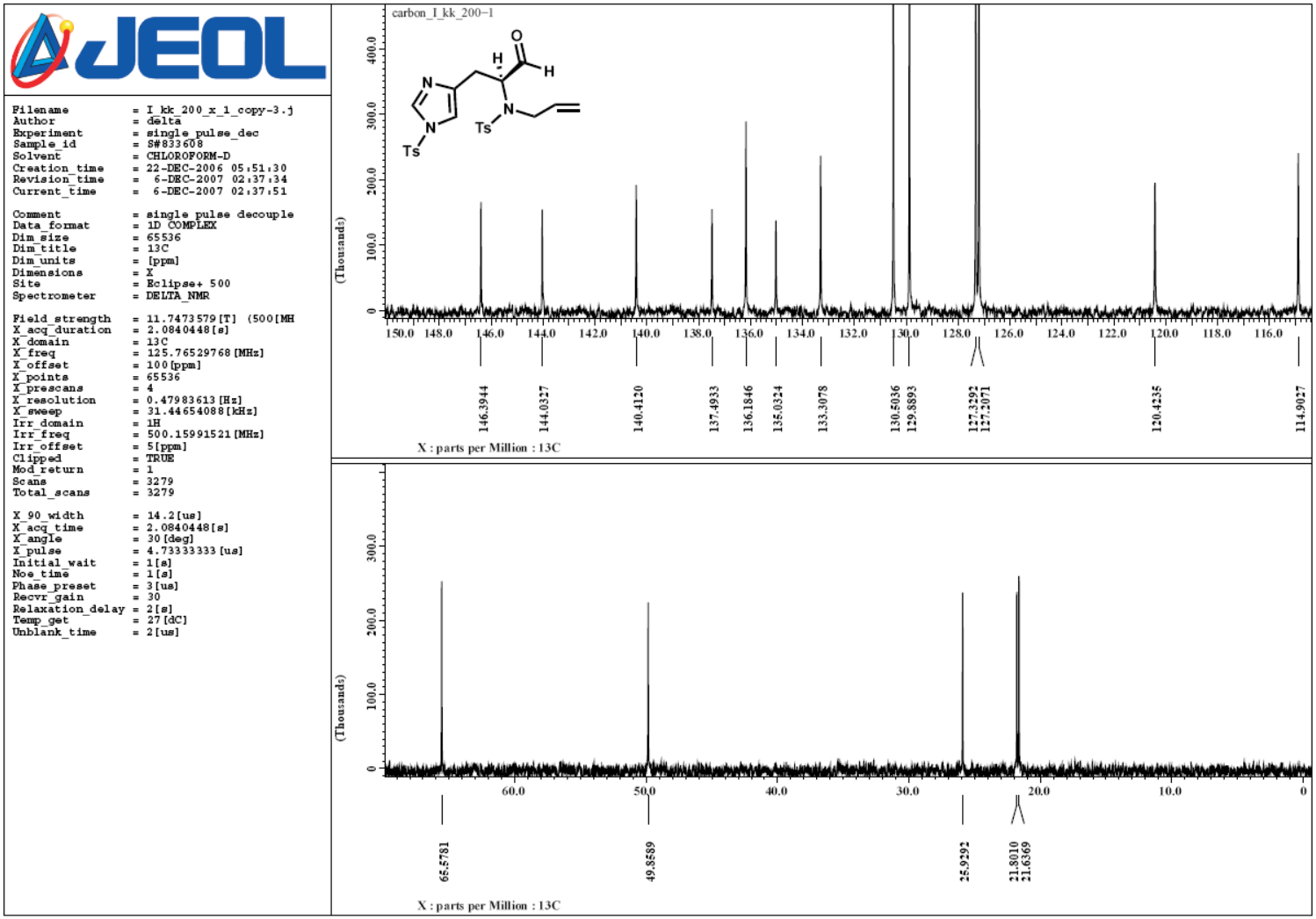
APPENDIX 11

^{1}HNMR AND ^{13}C NMR SPECTRA OF ***N*-ALLYL-*N*-{1-FORMYL-2-[1-(TOLUENE-4-SULFONYL)-1*H*-IMIDAZOL-4-YL]-ETHYL}-4-METHYL-BENZENESULFONAMIDE (24)** MEASURED ON A JEOL ECLIPSE 500+ SPECTROMETER IN $CDCl_3$


JEOL
Filename = 1_kk_286_aldehyde-6.j
Author = delta
Experiment = single_pulse.exp
Sample_id = SM533194
Solvent = CHLOROFORM-D
Creation_time = 24-JUN-2007 18:30:06
Revision_time = 20-OCT-2007 00:15:15
Current_time = 20-OCT-2007 00:15:51
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 = 11.7473570[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 = 10
Total_scans = 10
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 = 25.1[dc]
Unblank_time = 2[us]
proton_1_kk_286_aldehyde-1
(Millions)
X : parts per Million : 1H
9.6568
7.7539
7.7366
7.5956
7.3490
7.3666
6.7013
5.6889
5.6761
5.6650
5.1603
5.1402
5.1402
4.4888
4.4787
4.4706
3.8530
3.8392
3.6643
3.6514
3.3043
3.1824
3.1732
2.7206
2.7023
2.4696
2.4265
1.01
2.19
1.14
1.0
2.12
2.08
1.08
1.11
1.08
1.05
1.08
1.08
3.05


JEOL
Filename = 1_kk_286_aldehyde-4.1
Author = delta
Experiment = single pulse.exp
Sample_id = CHLOROFORM-D
Solvent = CHLOROFORM-D
Creation_time = 24-JUN-2007 19:30:06
Revision_time = 19-OCT-2007 21:43:51
Current_time = 19-OCT-2007 21:45:05
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 = 11.74735579[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 = 10
Total_scans = 10
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 = 25.1[dC]
Unblank_time = 2[us]
proton_1_kk_286_aldehyde-4
(Millions)
9.6568
7.7539
7.7365
7.7301
7.7274
7.6119
7.6955
7.3490
7.3325
7.1757
7.1592
7.1566
6.7013
X : parts per Million : 1H
5.7091
5.6889
5.6761
5.6688
5.6550
5.1603
5.1402
5.1402
5.1264
4.4888
4.4787
4.4705
3.8841
3.8704
3.8530
3.8392
3.6643
3.6514
3.6331
3.6203
3.2144
3.2043
3.1834
3.1732
2.7206
2.7023
2.6904
2.6721
2.4595
2.4268


carbon_1_kk_200_aldehyde-3
X : parts per Million : 13C
198.6759
146.3944
144.0327
137.7605
136.0663
134.9141
133.0675
130.5036
129.8092
127.3292
127.1003
120.4235
77.1118
76.8600
65.7956
49.6949
25.6972
21.7056
21.6369



Filename = I_kk_200_x_1_copy-3.j
Author = delta
Experiment = single_pulse_dec
Sample_id = S#833608
Solvent = CHLOROFORM-D
Creation_time = 22-DEC-2006 05:51:30
Revision_time = 6-DEC-2007 02:37:34
Current_time = 6-DEC-2007 02:37:51

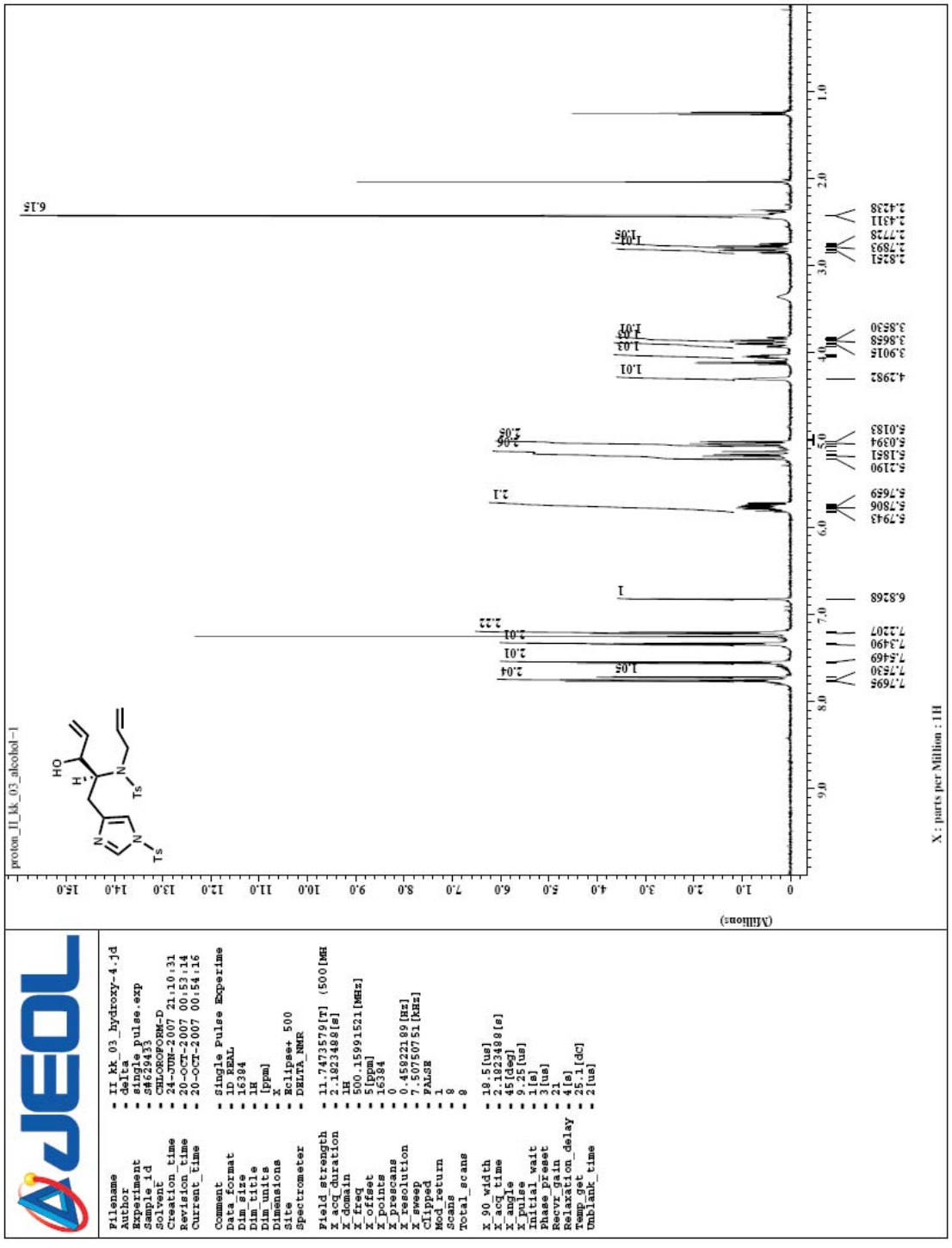
Comment = single pulse decouple
Data_format = 1D COMPLEX
Dim_size = 65536
Dim_title = 13C
Dim_units = [ppm]
Dimensions = X
Site = Eclipse+ 500
Spectrometer = DELTA_NMR

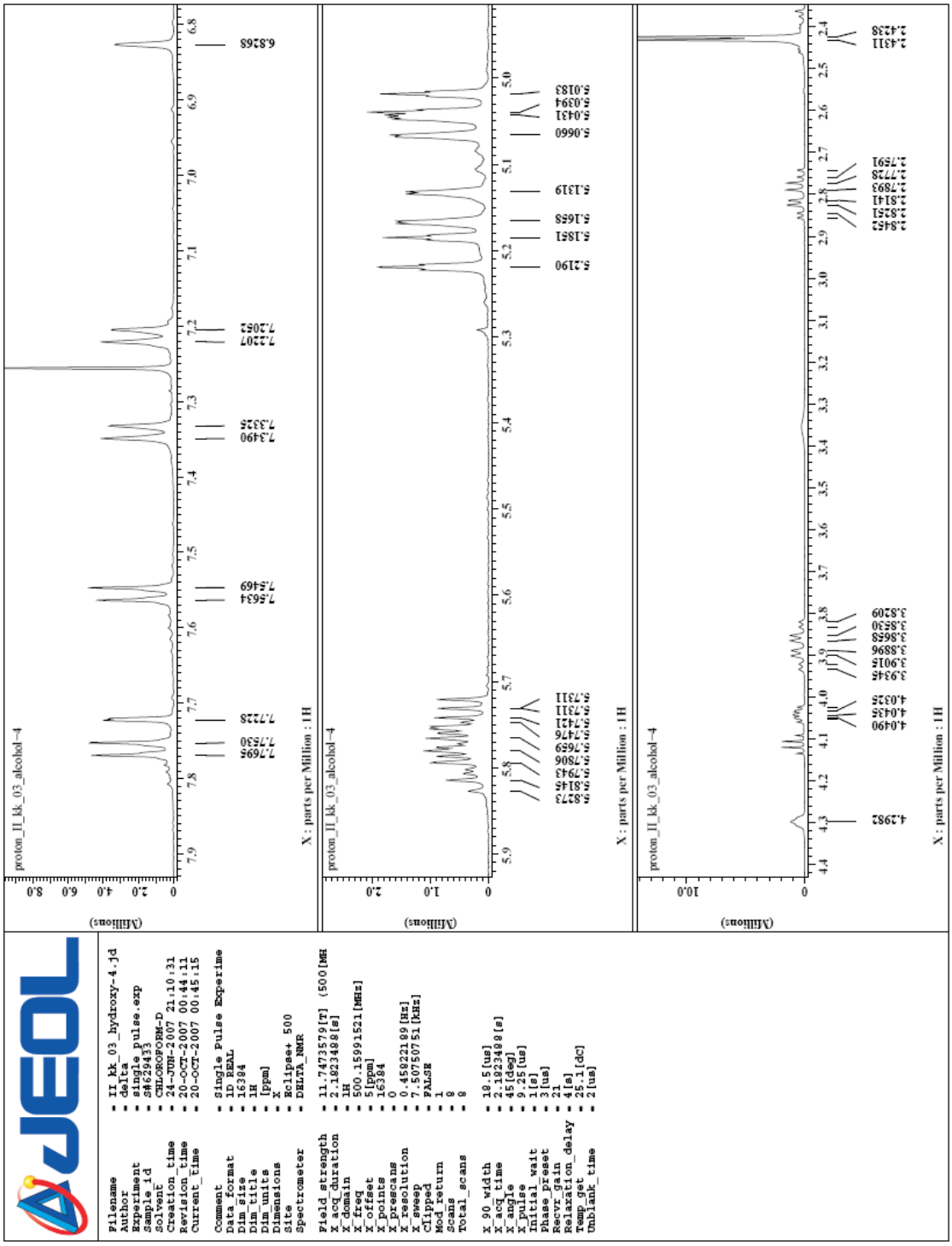
Field_strength = 11.7473579[T] (500[MH
X_acq_duration = 2.0840448[s]
X_domain = 13C
X_freq = 125.76529768[MHz]
X_offset = 100[ppm]
X_points = 65536
X_prescans = 4
X_resolution = 0.47983613[Hz]
X_sweep = 31.44654088[kHz]
Irr_domain = 1H
Irr_freq = 500.15991521[MHz]
Irr_offset = 5[ppm]
Clipped = TRUE
Mod_return = 1
Scans = 3279
Total_scans = 3279

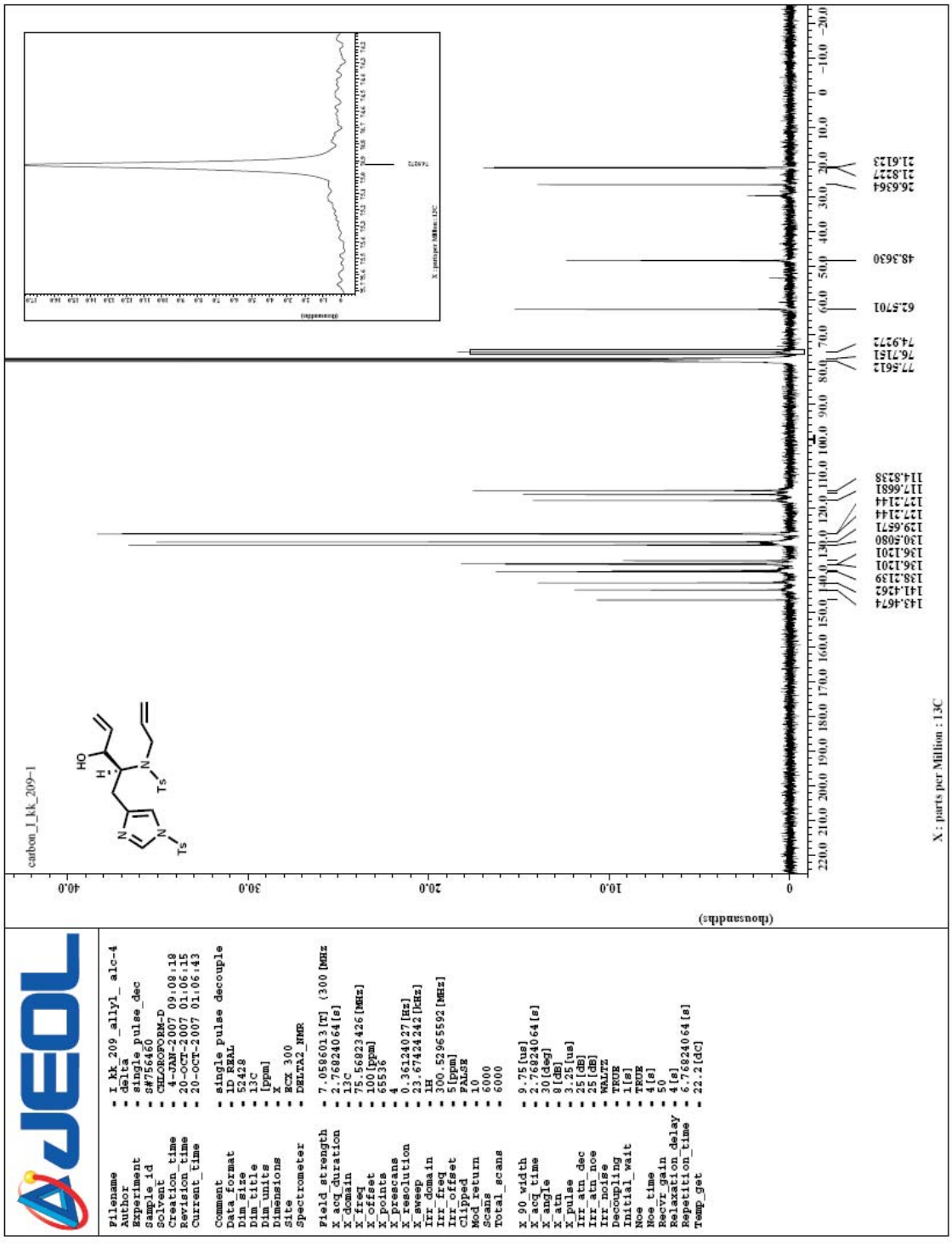
X_90_width = 14.2[us]
X_acq_time = 2.0840448[s]
X_angle = 30[deg]
X_pulse = 4.73333333[us]
Initial_wait = 1[s]
Noe_time = 1[s]
Phase_preset = 3[us]
Recvr_gain = 30
Relaxation_delay = 2[s]
Temp_get = 27[dC]
Unblank_time = 2[us]

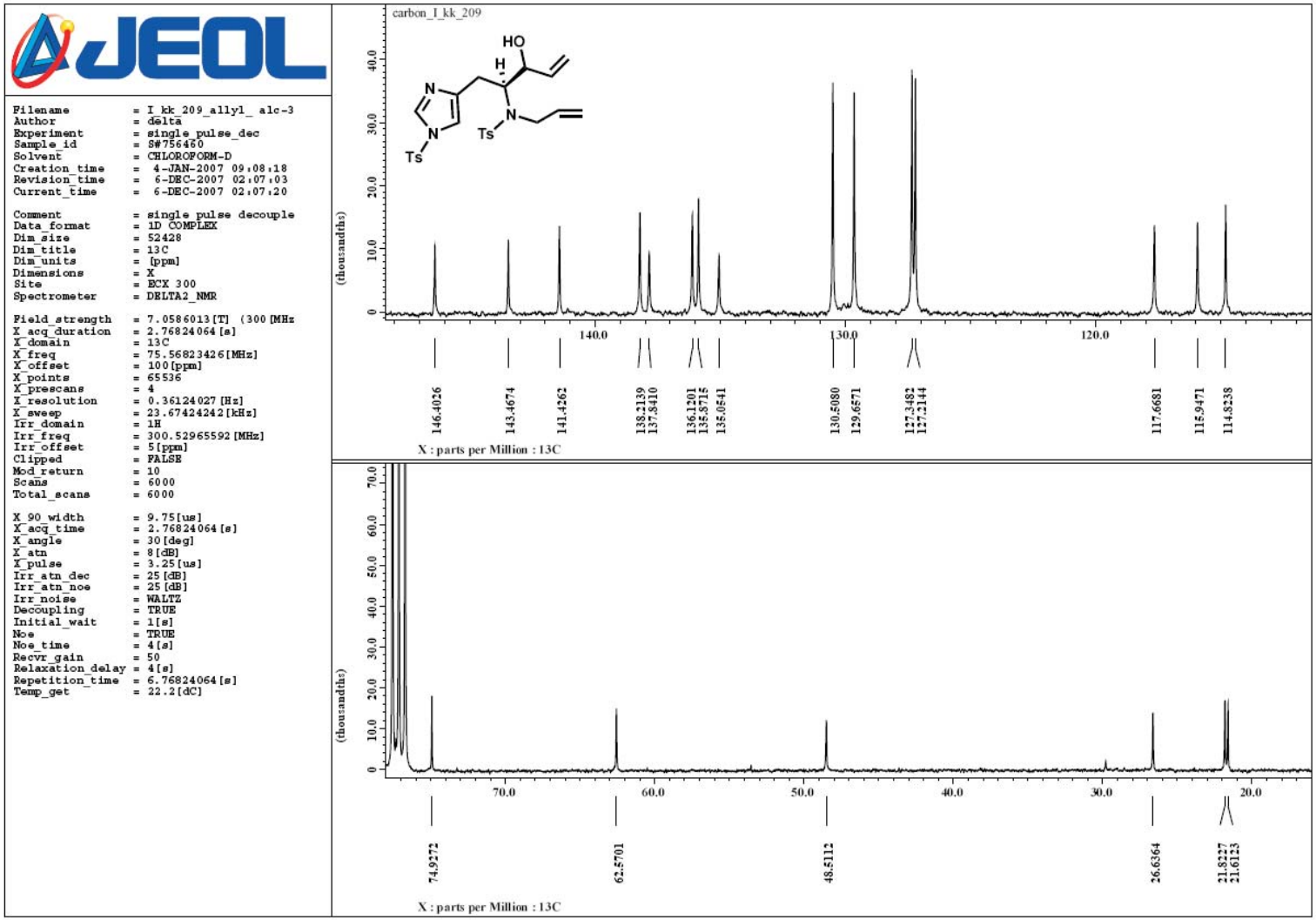
APPENDIX 12

^{1}HNMR AND ^{13}C NMR SPECTRA OF ***N*-ALLYL-*N*-{2-HYDROXY-1-[1-(TOLUENE-4-SULFONYL)-1*H*-IMIDAZOL-4-YLMETHYL]-BUT-3-ENYL}-4-METHYL-BENZENESULFONAMIDE (25)** MEASURED ON A JEOL ECLIPSE 300+ SPECTROMETER IN $CDCl_3$


proton_II_kk_03_alcohol-1
X : parts per Million : 1H
(Millions)
Filename - II_kk_03_hydroxy-4.jd
Author - delta
Experiment - single_pulse.exp
Sample_id - SM629433
Solvent - CHLOROFORM-D
Creation_time - 24-JUN-2007 21:10:31
Revision_time - 20-OCT-2007 00:53:14
Current_time - 20-OCT-2007 00:54:16
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 - 11.74723579[T] (500[MH
X_acq_duration - 2.1823480[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 - 10.5[us]
X_acq_time - 2.1823480[s]
X_angle - 45[deg]
X_pulse - 9.25[us]
Initial_wait - 1[s]
Phase_preset - 3[us]
Recvr_gain - 21
Relaxation_delay - 4[s]
Temp_get - 25.1[dc]
Umblank_time - 2[us]
6.15
2.22
2.04
2.01
1.05
1
2.1
2.05
2.05
1.01
1.03
1.05
1.01
1.05
7.7695
7.7530
7.5469
7.3490
7.2207
6.8268
5.7943
5.7806
5.7659
5.3190
5.1851
5.0394
5.0183
4.7982
3.9015
3.8658
3.8530
2.8251
2.7893
2.7738
2.4311
2.4238

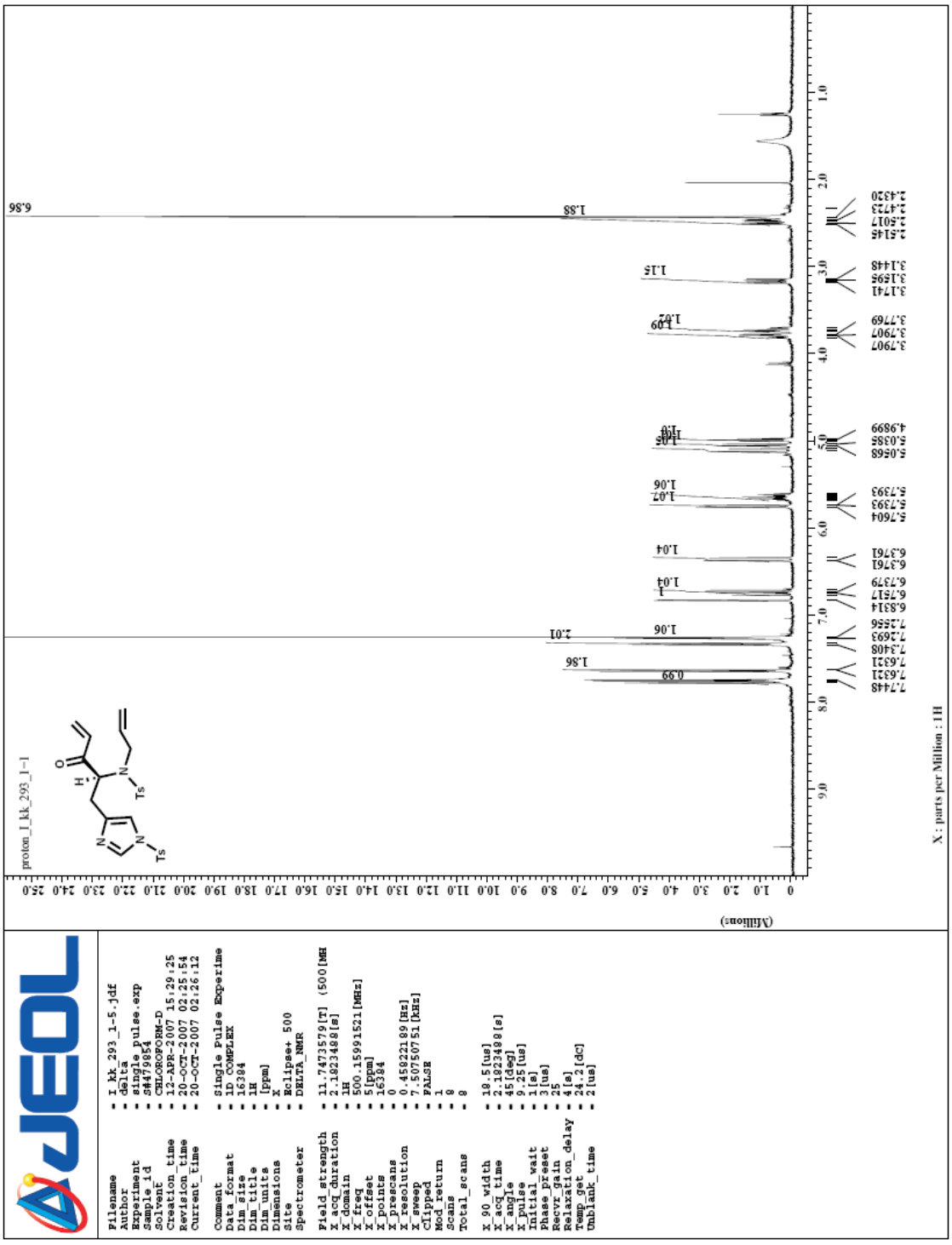

JEOL
Filename - II_kk_03_hydroxy-4.jd
Author - delta
Experiment - single_Pulse.exp
Sample_id - SM629433
Solvent - CHLOROFORM-D
Creation_time - 24-JUN-2007 21:10:31
Revision_time - 20-OCT-2007 00:44:11
Current_time - 20-OCT-2007 00:45:15
Comment - Single Pulse Experime
Data_format - 1D REAL
Dim_size - 16384
Dim_title - H
Dim_units - [ppm]
Dimensions - X
Site - Eclipse+ 500
Spectrometer - DELTA_NMR
Field_strength - 11.7473579[T] (500[MH
X_acq_duration - 2.1023488[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 - 10.5[us]
X_acq_time - 2.1023488[s]
X_angle - 45[deg]
X_pulse - 9.25[us]
Initial_wait - 1[s]
Phase_preset - 3[us]
Recvr_gain - 21
Relaxation_delay - 4[s]
Temp_get - 25.1[dC]
Unblank_time - 2[us]
proton_II_kk_03_alcohol-4
(Millions)
X : parts per Million : 1H
7.7694
7.7530
7.7228
7.5634
7.5469
7.3490
7.3325
7.2207
7.2062
6.8268
proton_II_kk_03_alcohol-4
(Millions)
X : parts per Million : 1H
5.3111
5.2190
5.1851
5.1658
5.1319
5.0660
5.0431
5.0394
5.0183
proton_II_kk_03_alcohol-4
(Millions)
X : parts per Million : 1H
4.2982
4.0490
4.0435
4.0325
3.9345
3.9015
3.8896
3.8658
3.8530
3.8209
2.8462
2.8251
2.8141
2.7893
2.7728
2.7591
2.4311
2.4238

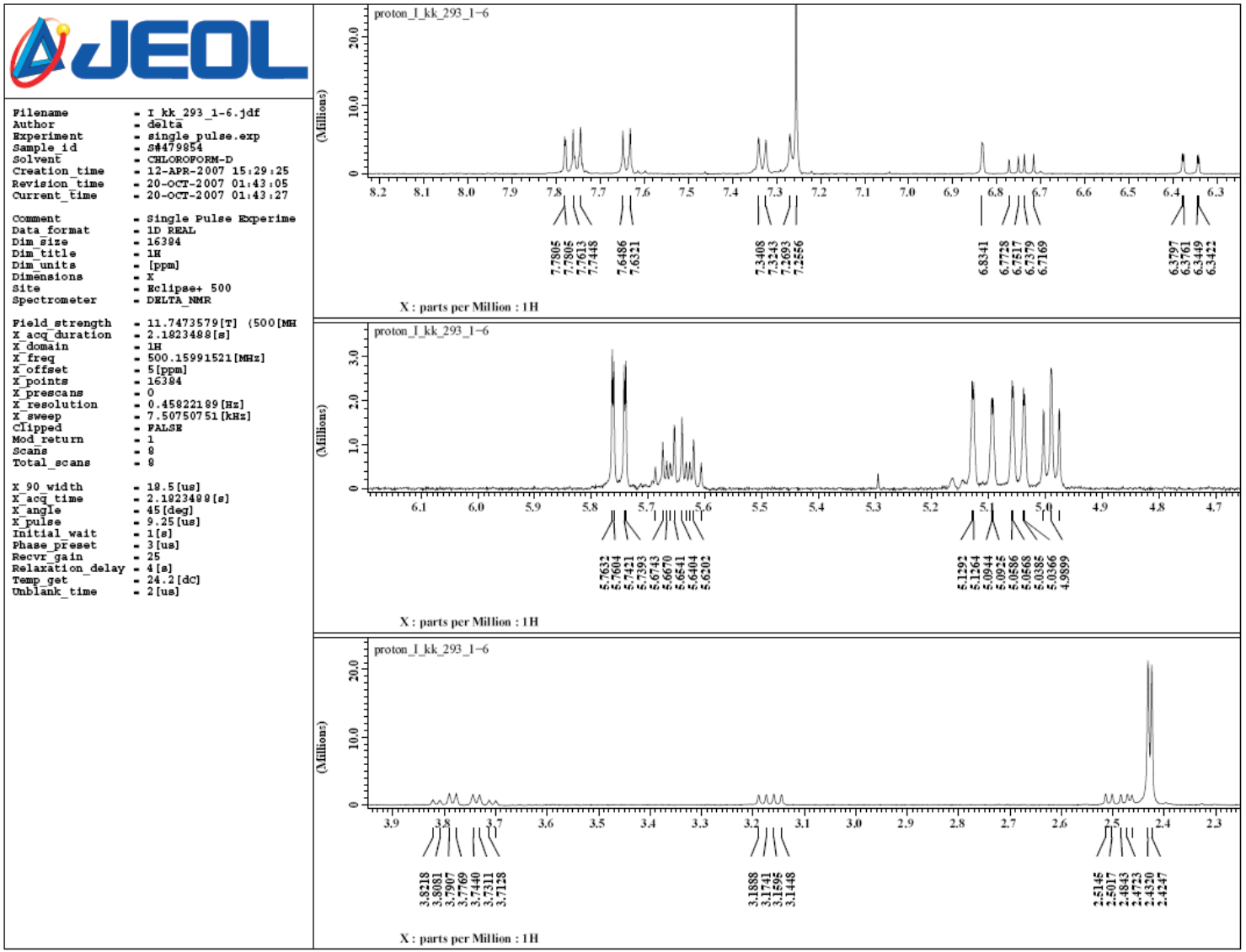

carbon_1_kk_209-1
(thousandths)
X : parts per Million : 13C
143.4674
141.4262
138.2139
136.1201
136.1201
130.5080
129.6571
127.3144
127.3144
117.6681
114.8238
77.5612
76.7151
74.9272
62.5701
48.3630
26.6364
21.8227
21.6123


JEOL
Filename = I_kk_209_allyl_ alc-3
Author = delta
Experiment = single_pulse_dec
Sample_id = S#756460
Solvent = CHLOROFORM-D
Creation_time = 4-JAN-2007 09:08:18
Revision_time = 6-DEC-2007 02:07:03
Current_time = 6-DEC-2007 02:07:20
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 = 6000
Total_scans = 6000
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 = 4[s]
Recvr_gain = 50
Relaxation_delay = 4[s]
Repetition_time = 6.76824064[s]
Temp_get = 22.2[dC]
carbon_I_kk_209
HO
H
N
N
Ts
N
Ts
(thousandths)
140.0
130.0
120.0
146.4026
143.4674
141.4262
138.2139
137.8410
136.1201
135.8715
135.0541
130.5080
129.6571
127.3482
127.2144
117.6681
115.9471
114.8238
X : parts per Million : 13C
70.0
60.0
50.0
40.0
30.0
20.0
74.9272
62.5701
48.5112
26.6364
21.8227
21.6123
X : parts per Million : 13C

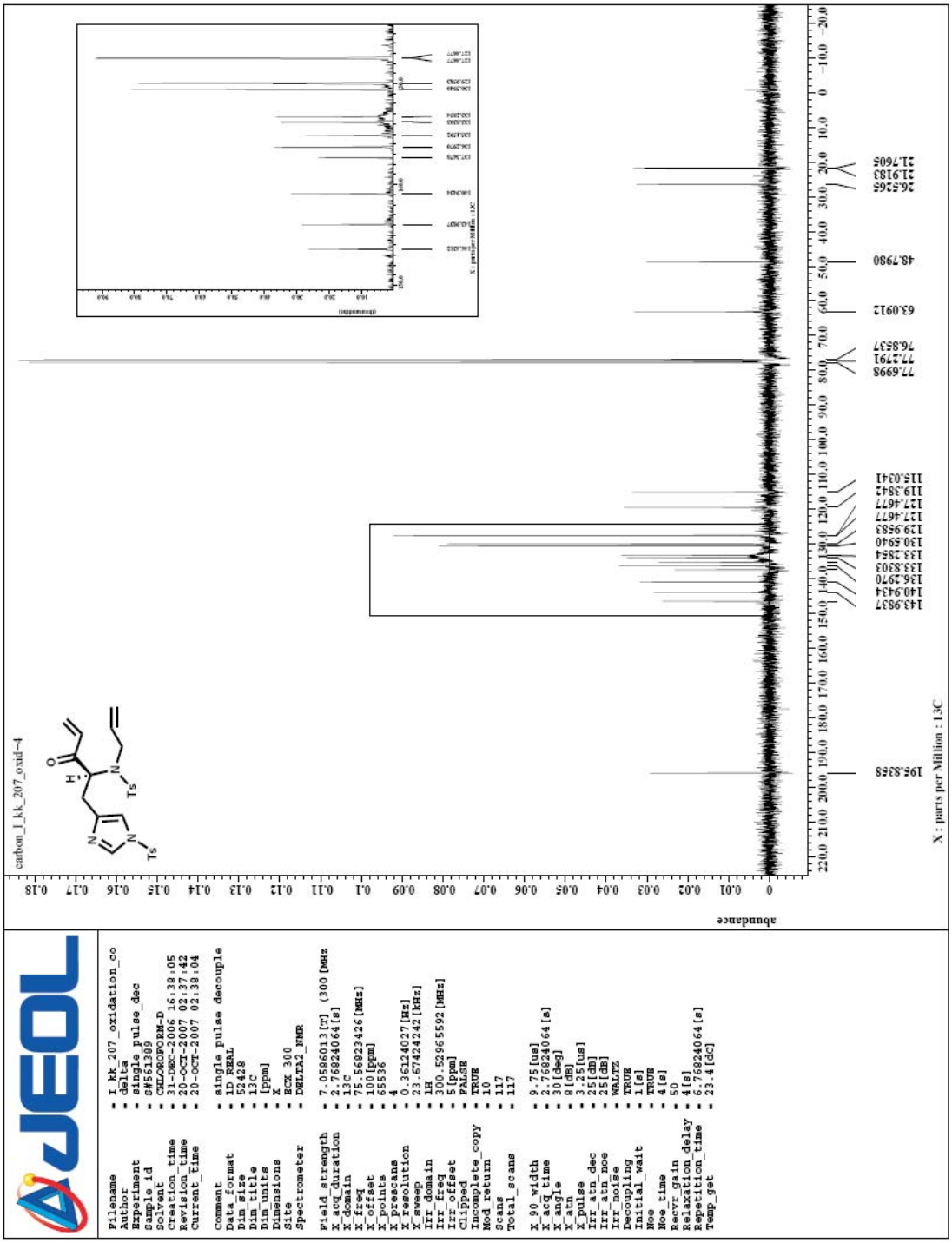
APPENDIX 13

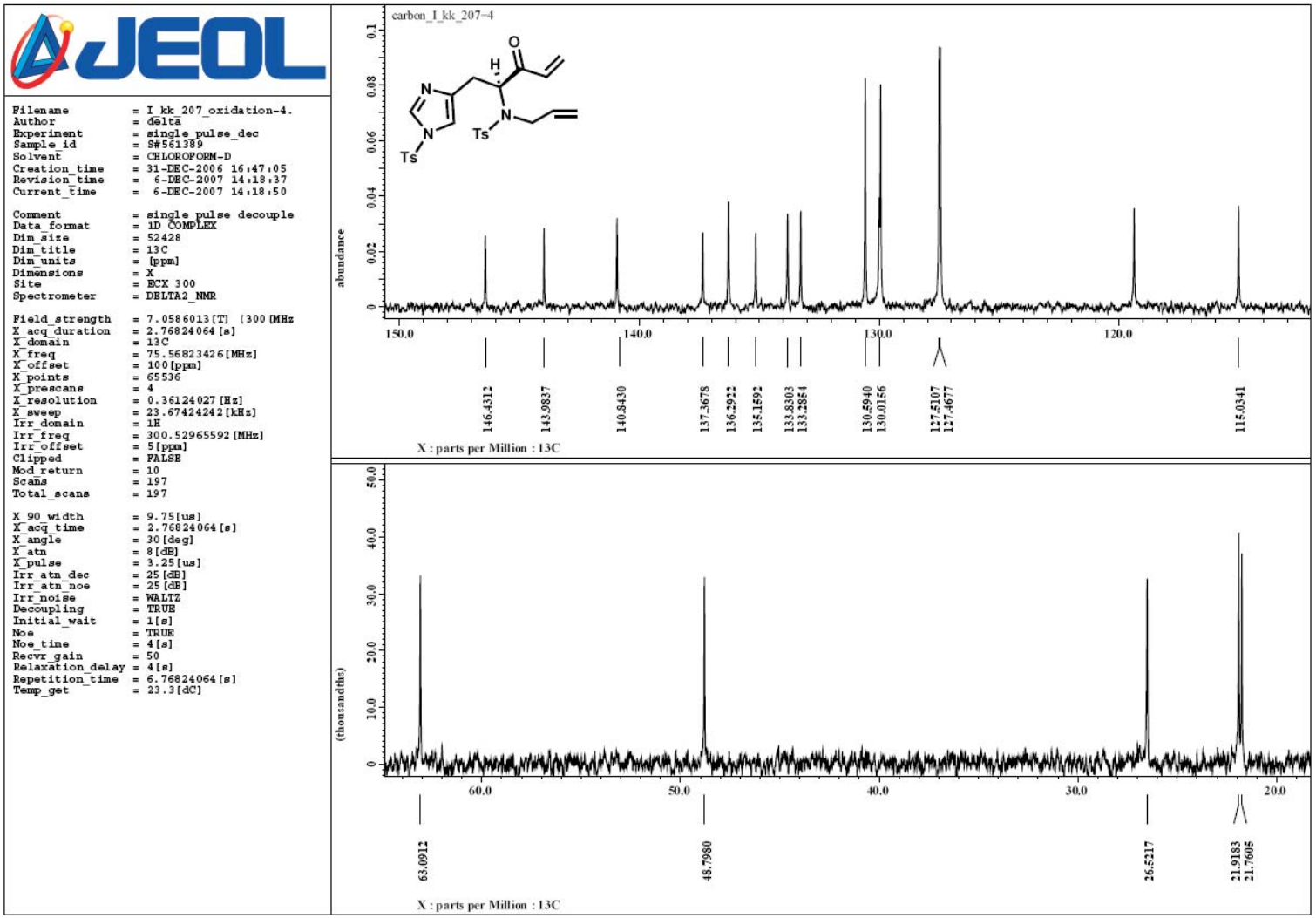
^{1}HNMR AND ^{13}C NMR SPECTRA OF ***N*-ALLYL-4-METHYL-*N*-{2-OXO-1-[1-(TOLUENE-4-SULFONYL)-1*H*-IMIDAZOL-4-YLMETHYL] BUT-3-ENYL} BENZENESULFONAMIDE (29)** MEASURED ON A JEOL ECLIPSE 300+ SPECTROMETER IN $CDCl_3$


JEOL
Filename = 1 kk 293 1-5.jdf
Author = delta
Experiment = single_pulse.exp
Sample_id = S#479954
Solvent = CHLOROFORM-D
Creation_time = 12-APR-2007 15:29:25
Revision_time = 20-OCT-2007 02:25:54
Current_time = 20-OCT-2007 02:26:12
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 = 500.1599152l[MHz]
X_offset = 5[ppm]
X_points = 16384
X_prescans = 0
X_resolution = 0.4582219 9[Hz]
X_sweep = 7.5075075l[kHz]
Clipped = FALSE
Mod_return = 1
Scans = 8
Total_scans = 8
X_90_width = 10.5[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 = 25
Relaxation_delay = 4[s]
Temp_get = 24.2[dc]
Unblank_time = 2[us]
proton_1 kk_293_1-1
(Millions)
X : parts per Million : 1H
6.86
1.88
2.01
1.86
0.99
1.06
1.04
1
1.04
1.06
1.07
1.09
1.15
1.02
1.09
7.7448
7.6321
7.6321
7.3408
7.2693
7.2556
6.8314
6.7517
6.7379
6.3761
6.3761
5.7604
5.7393
5.7393
5.0568
5.0386
4.9899
3.7907
3.7907
3.7769
3.1741
3.1595
3.1448
2.5146
2.5017
2.4723
2.4320



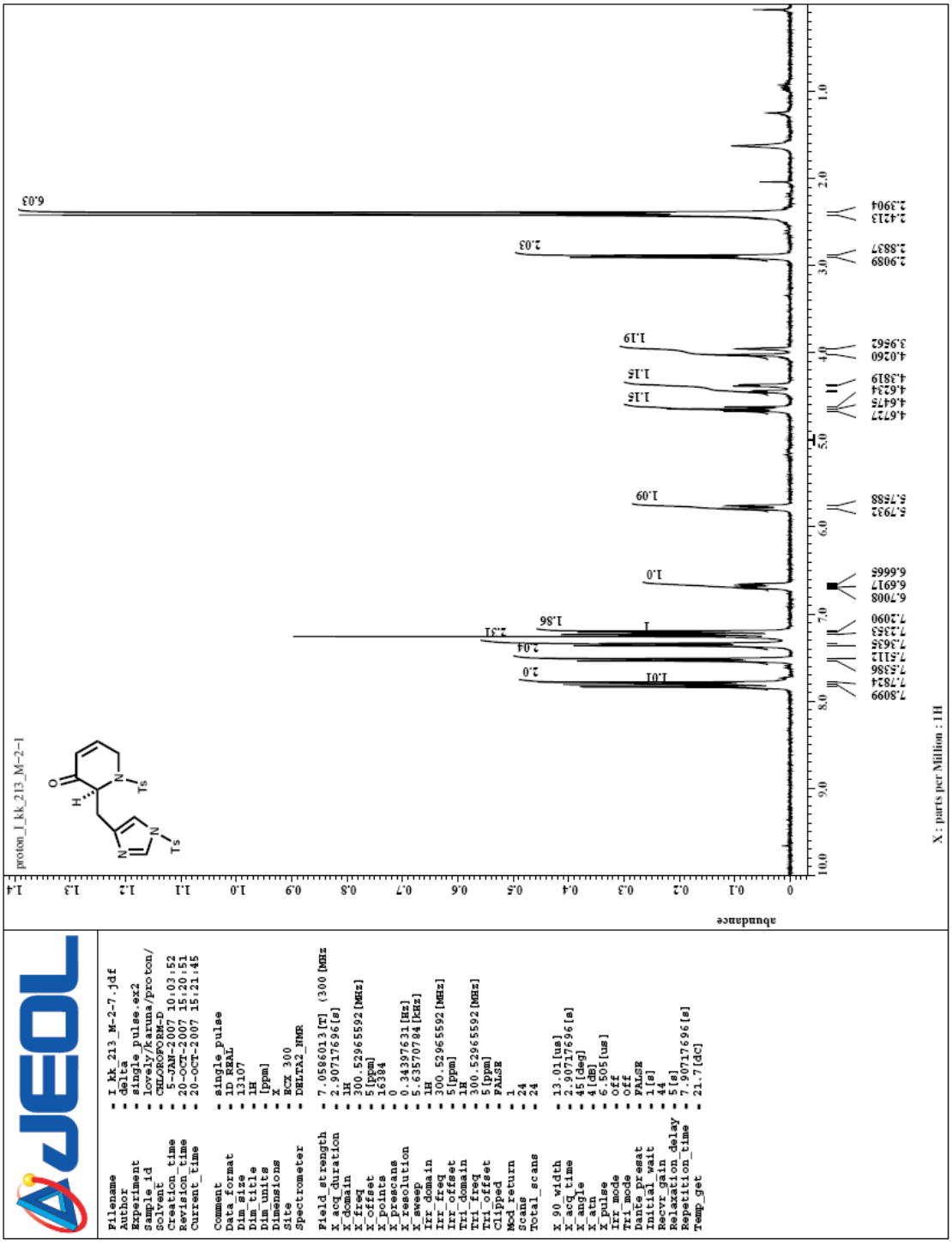
Filename	= I_kk_293_1-6.jdf
Author	= delta
Experiment	= single_pulse.exp
Sample_id	= s#479854
Solvent	= CHLOROFORM-D
Creation_time	= 12-APR-2007 15:29:25
Revision_time	= 20-OCT-2007 01:43:05
Current_time	= 20-OCT-2007 01:43:27
Comment	= Single Pulse Experime
Data_format	= 1D REAL
Dim_size	= 16384
Dim_title	= 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	= 8
Total_scans	= 8
X_90_width	= 19.5[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	= 25
Relaxation_delay	= 4[s]
Temp_get	= 24.2[dc]
Unblank_time	= 2[us]

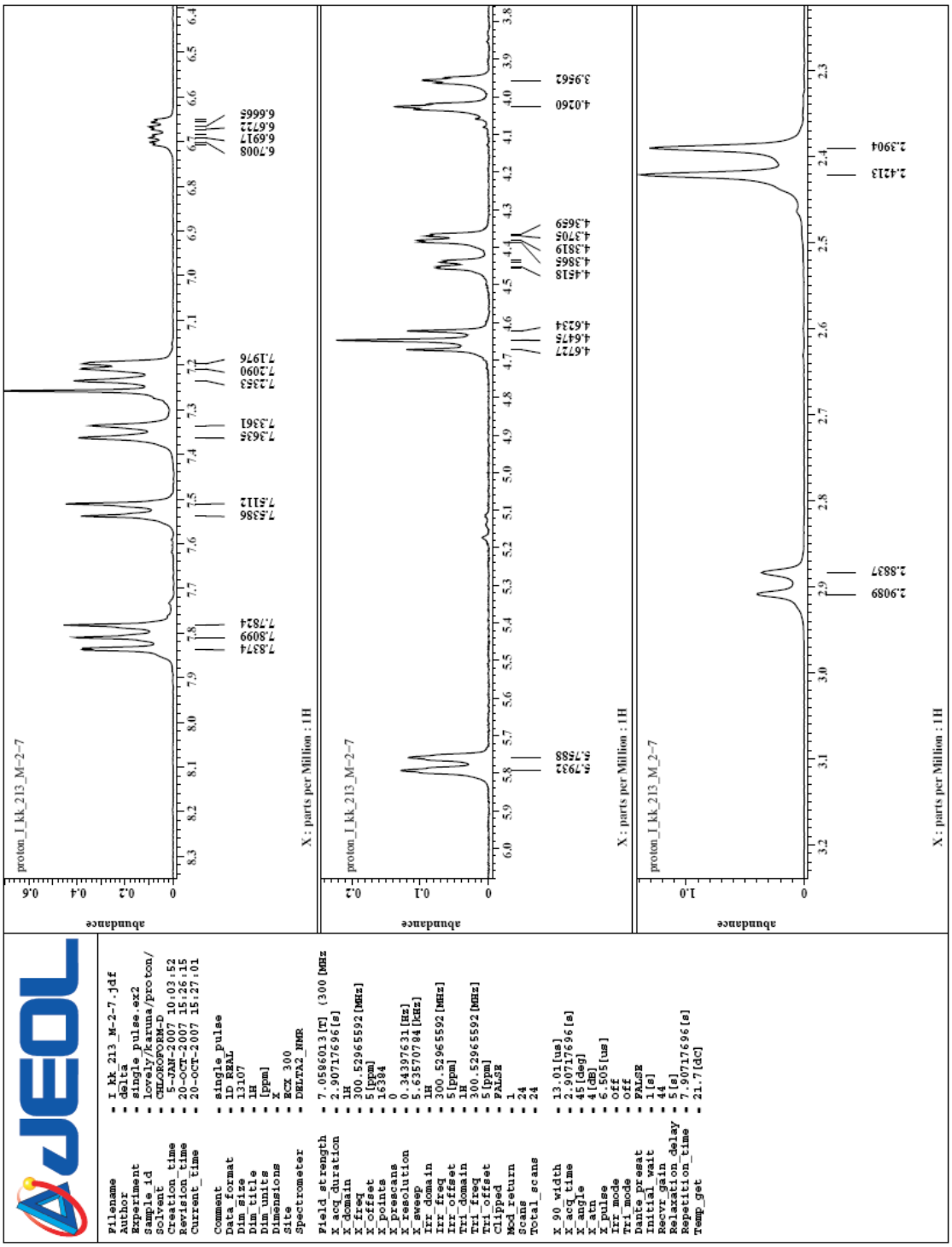

carbon_1_kk_207_oxid-4
Filename = 1_kk_207_oxidation_co
Author = delta
Experiment = single_pulse_dec
Sample_id = s#561389
Solvent = CHLOROFORM-D
Creation_time = 31-DEC-2006 16:38:05
Revision_time = 20-OCT-2007 02:37:42
Current_time = 20-OCT-2007 02:38:04
Comment = single pulse decouple
Data_format = 1D REAL
Dim_size = 52428
Dim_title = 13C
Dim_units = [ppm]
Dimensions = X
Site = BCX 300
Spectrometer = DELTA2_NMR
Field_strength = 7.0586013[T] (300 [MHz
X_acq_duration = 2.76824064[s]
X_domain = 13C
X_freq = 75.56923426[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
Incomplete_copy = TRUE
Mod_return = 10
Scans = 117
Total_scans = 117
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 = 4[s]
Recvr_gain = 50
Relaxation_delay = 4[s]
Repetition_time = 6.76824064[s]
Temp_get = 23.4[dC]
abundance
X : parts per Million : 13C
195.8358
143.9837
140.9434
136.7970
133.8303
133.3854
130.5940
129.9583
127.4677
127.4677
119.3842
115.0341
77.6998
77.2791
76.8537
63.0912
48.7980
26.5365
21.9183
21.7605

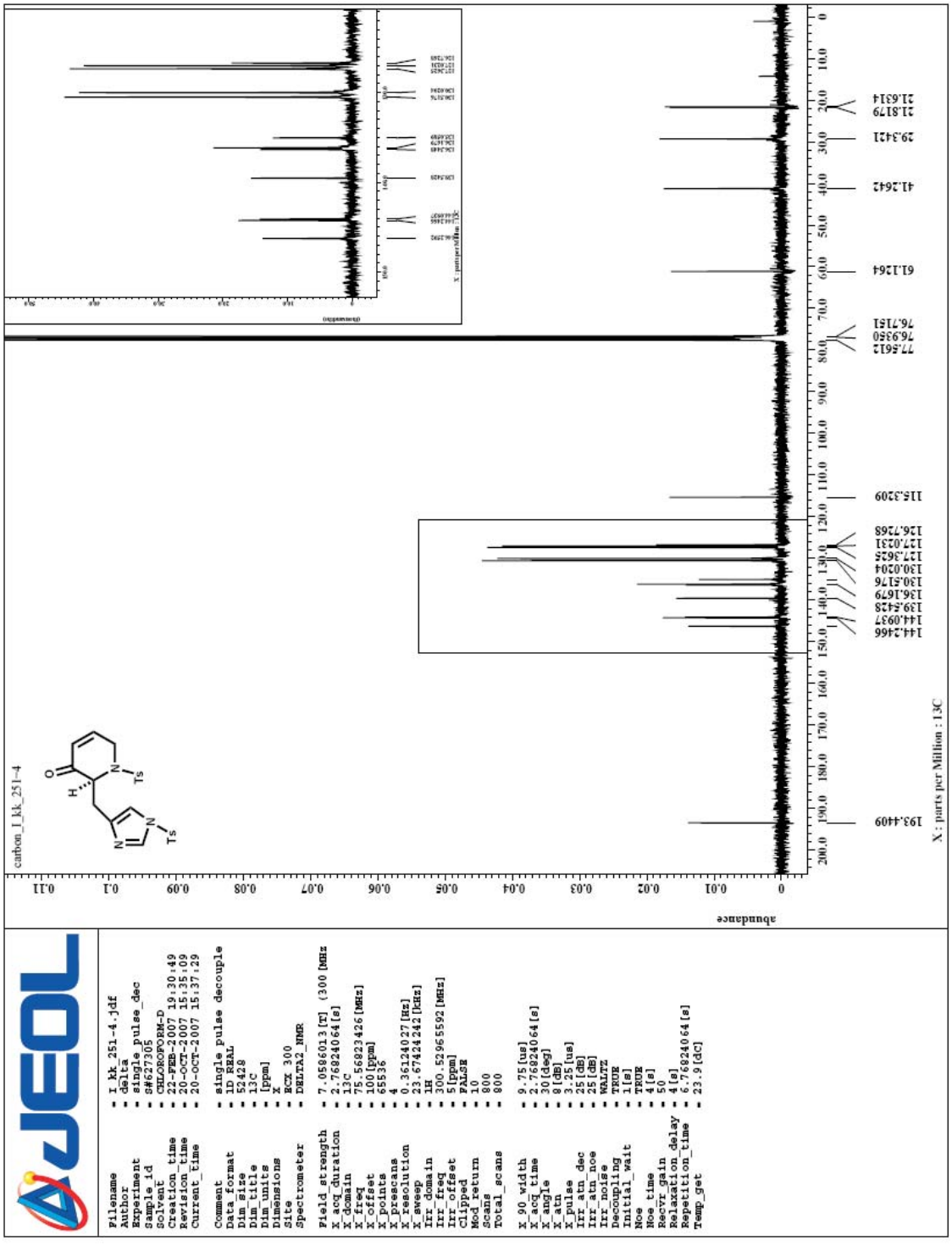

JEOL
Filename = I_kk_207_oxidation-4.
Author = delta
Experiment = single_pulse_dec
Sample_id = S#561389
Solvent = CHLOROFORM-D
Creation_time = 31-DEC-2006 16:47:05
Revision_time = 6-DEC-2007 14:18:37
Current_time = 6-DEC-2007 14:18:50
Comment = single pulse decouple
Data_format = 1D COMPLEX
Dim_size = 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 = 197
Total_scans = 197
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 = 4[s]
Recvr_gain = 50
Relaxation_delay = 4[s]
Repetition_time = 6.76824064[s]
Temp_get = 23.3[dC]
carbon_I_kk_207-4
abundance
146.4312
143.9837
140.8430
137.3678
136.2922
135.1592
133.8303
133.2854
130.5940
130.0156
127.5107
127.4677
115.0341
X : parts per Million : 13C
(thousandths)
63.0912
48.7980
26.5217
21.9183
21.7605
X : parts per Million : 13C

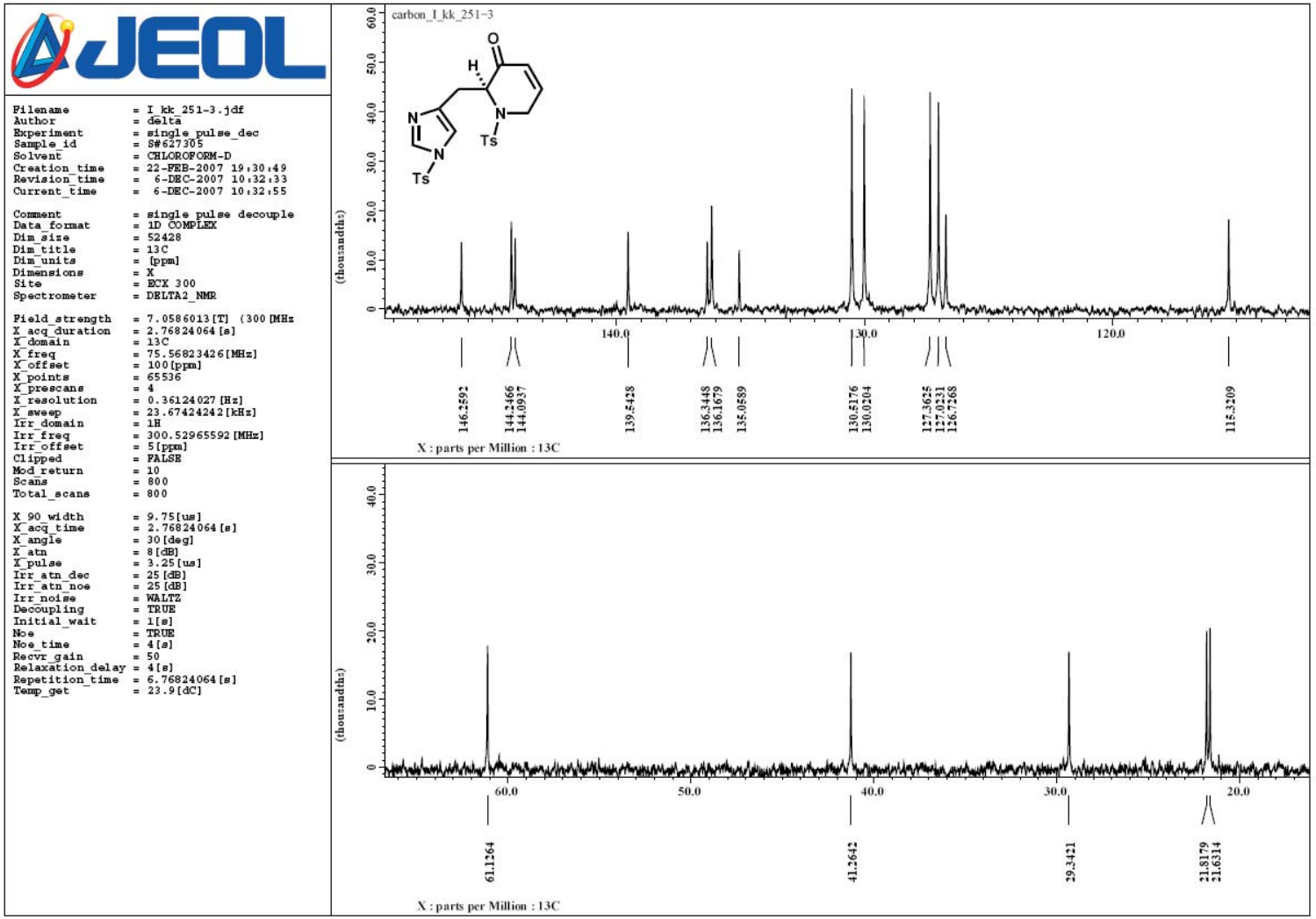
APPENDIX 14

^{1}HNMR AND ^{13}C NMR SPECTRA OF **1-(TOLUENE-4-SULFONYL)-3-[1-(TOLUENE-4-SULFONYL)-1*H*-IMIDAZOL-4-YLMETHYL]-2,3-DIHYDRO-1*H*-PYRIDIN-4-ONE (31)**MEASURED ON A JEOL ECLIPSE 300+ SPECTROMETER IN $CDCl_3$


JEOL
Filename = 1_kk_213_M-2-7.jdf
Author = delta
Experiment = single_pulse_ex2
Sample_id = lovely/karuna/proton/
Solvent = CHLOROFORM-D
Creation_time = 5-JAN-2007 10:03:52
Revision_time = 20-OCT-2007 15:20:51
Current_time = 20-OCT-2007 15:21:45
Comment = single_pulse
Data_format = 1D REAL
Dim_size = 13107
Dim_title = 1H
Dim_units = [ppm]
Dimensions = X
Site = BCX 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 = 24
Total_scans = 24
X_90_width = 13.01[us]
X_acq_time = 2.90717696[s]
X_angle = 45[deg]
X_atn = 4[dB]
X_pulse = 6.505[us]
Irr_mode = Off
Tri_mode = Off
Decpl_presat = FALSE
Initial_wait = 1[s]
Recvr_gain = 44
Relaxation_delay = 5[s]
Repetition_time = 7.90717696[s]
Temp_get = 21.7[dC]
proton_1_kk_213_M-2-1
O
H
N
Ts
N
N
Ts
abundance
6.03
2.03
1.19
1.15
1.15
1.09
1.0
1.86
2.31
2.04
2.0
1.01
1
7.8099
7.7824
7.5386
7.5112
7.3635
7.3353
7.2090
6.7008
6.6917
6.6665
5.7932
5.7588
4.6727
4.6475
4.6234
4.3819
4.0260
3.9562
2.9089
2.8837
2.4213
2.3904
X : parts per Million : 1H

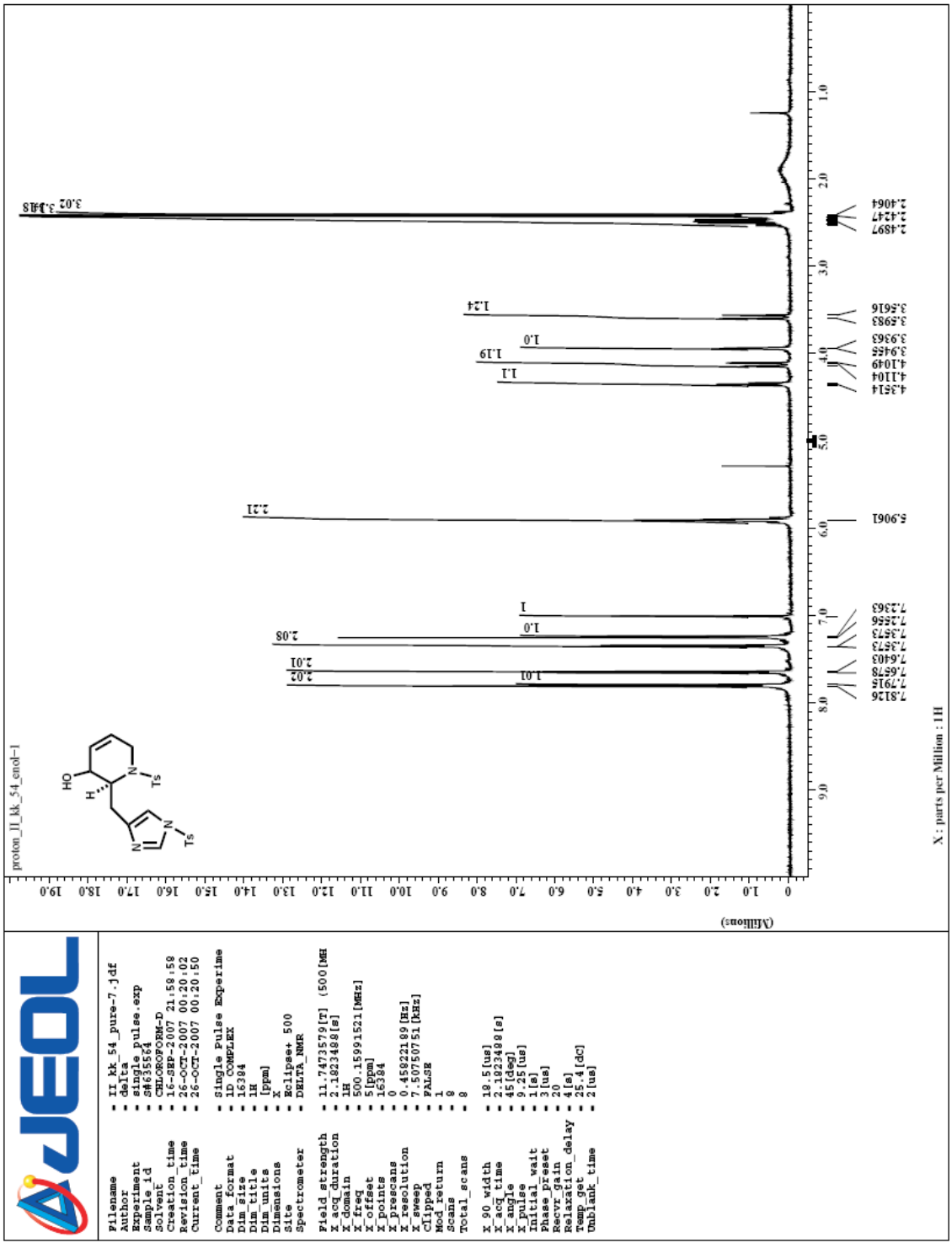

JEOL
Filename = I_kk_213_M-2-7.jdf
Author = delta
Experiment = single_pulse.ex2
Sample_id = lovely/Karuna/proton/
Solvent = CHLOROFORM-D
Creation_time = 5-JAN-2007 10:03:52
Revision_time = 20-OCT-2007 15:26:15
Current_time = 20-OCT-2007 15:27:01
Comment = single_pulse
Data_format = 1D REAL
Dim_size = 13107
Dim_title = 1H
Dim_units = [ppm]
Dimensions = X
Site = RCX 300
Spectrometer = DELTA2_NMR
Field_strength = 7.05860137[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 = 24
Total_scans = 24
X_90_width = 13.01[us]
X_acq_time = 2.90717696[s]
X_angle = 45[deg]
X_atn = 4[dB]
X_pulse = 6.505[us]
Irr_mode = off
Tri_mode = off
Dante_presat = FALSE
Dantel_wait = 44[s]
Relaxation_delay = 5[s]
Repetition_time = 7.90717696[s]
Temp_get = 21.7[dC]
proton_I_kk_213_M-2-7
abundance
X : parts per Million : 1H
7.8374
7.8099
7.7824
7.5386
7.5112
7.3635
7.3361
7.3353
7.3090
7.1976
6.7008
6.6917
6.6722
6.6665
proton_I_kk_213_M-2-7
abundance
X : parts per Million : 1H
5.7588
5.7932
4.6727
4.6475
4.6234
4.4518
4.3866
4.3819
4.3705
4.3659
4.0260
3.9562
proton_I_kk_213_M_2-7
abundance
X : parts per Million : 1H
2.9089
2.8837
2.4213
2.3904

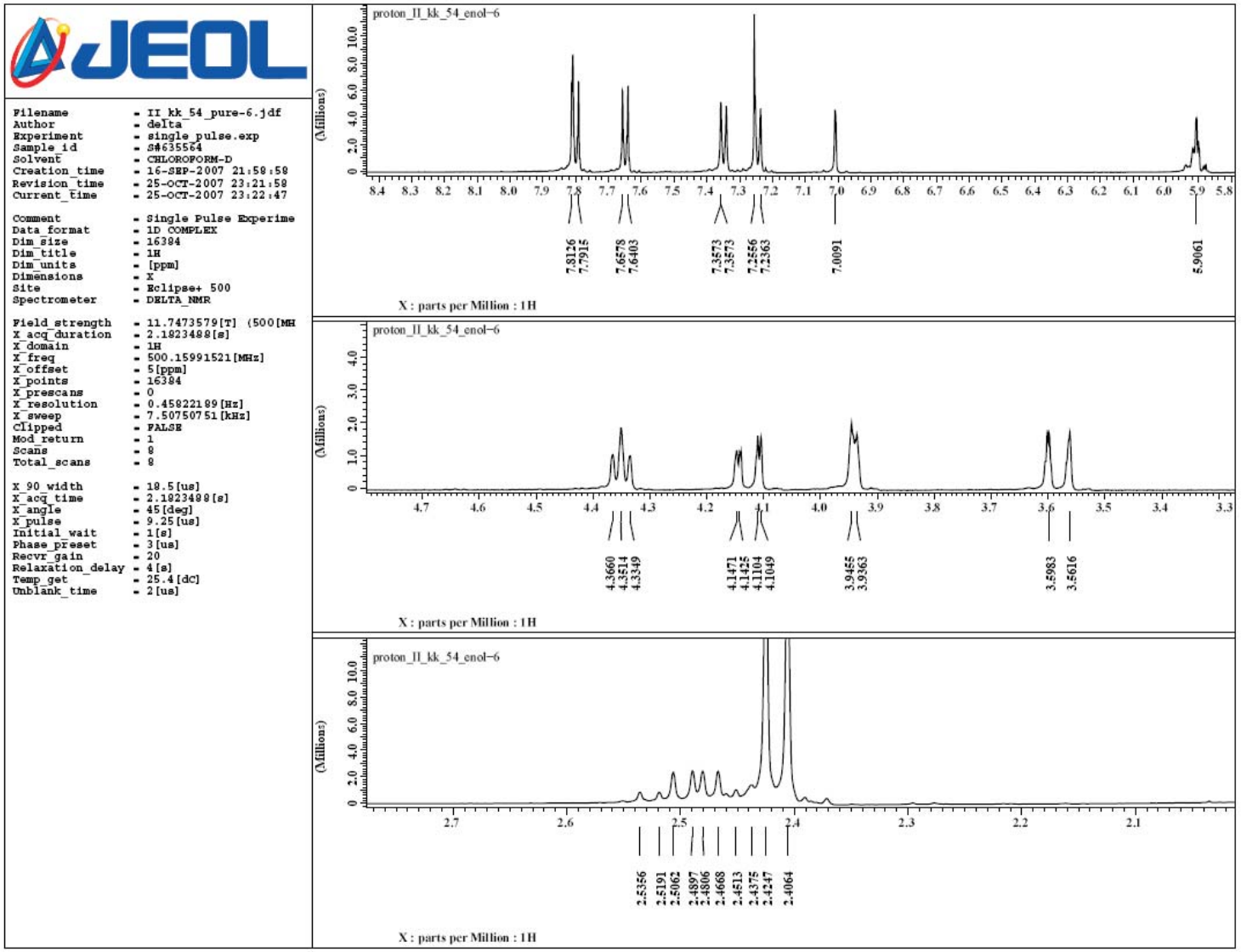

carbon_I_kk_251-4
Filename = I_kk_251-4.jdf
Author = delta
Experiment = single_pulse_dec
Sample_id = @#627305
Solvent = CHLOROFORM-D
Creation_time = 22-FEB-2007 19:30:49
Revision_time = 20-OCT-2007 15:35:09
Current_time = 20-OCT-2007 15:37:29
Comment = single pulse decouple
Data_format = 1D REAL
Dim_size = 52428
Dim_title = 13C
Dim_units = [ppm]
Dimensions = X
Site = BCX 300
Spectrometer = DELTA2_NMR
Field_strength = 7.05860137[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]
X_domain = 1H
Irr_freq = 300.52965592[MHz]
Irr_offset = 5[ppm]
Clipped = FALSE
Mod_return = 10
Scans = 800
Total_scans = 800
X_90_width = 9.75[us]
X_acq_time = 2.76824064[s]
X_angle = 30[deg]
X_atn = 0[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 = 4[s]
Recvr_gain = 50
Relaxation_delay = 4[s]
Repetition_time = 6.76824064[s]
Temp_get = 23.9[dC]
abundance
X : parts per Million : 13C
193.4409
144.2466
144.0937
139.5428
136.1679
130.5176
130.0204
127.3625
127.0231
126.7268
115.3209
77.5612
76.9380
76.7151
61.1264
41.2642
29.3421
21.8179
21.6314
Ts
Ts
O
H

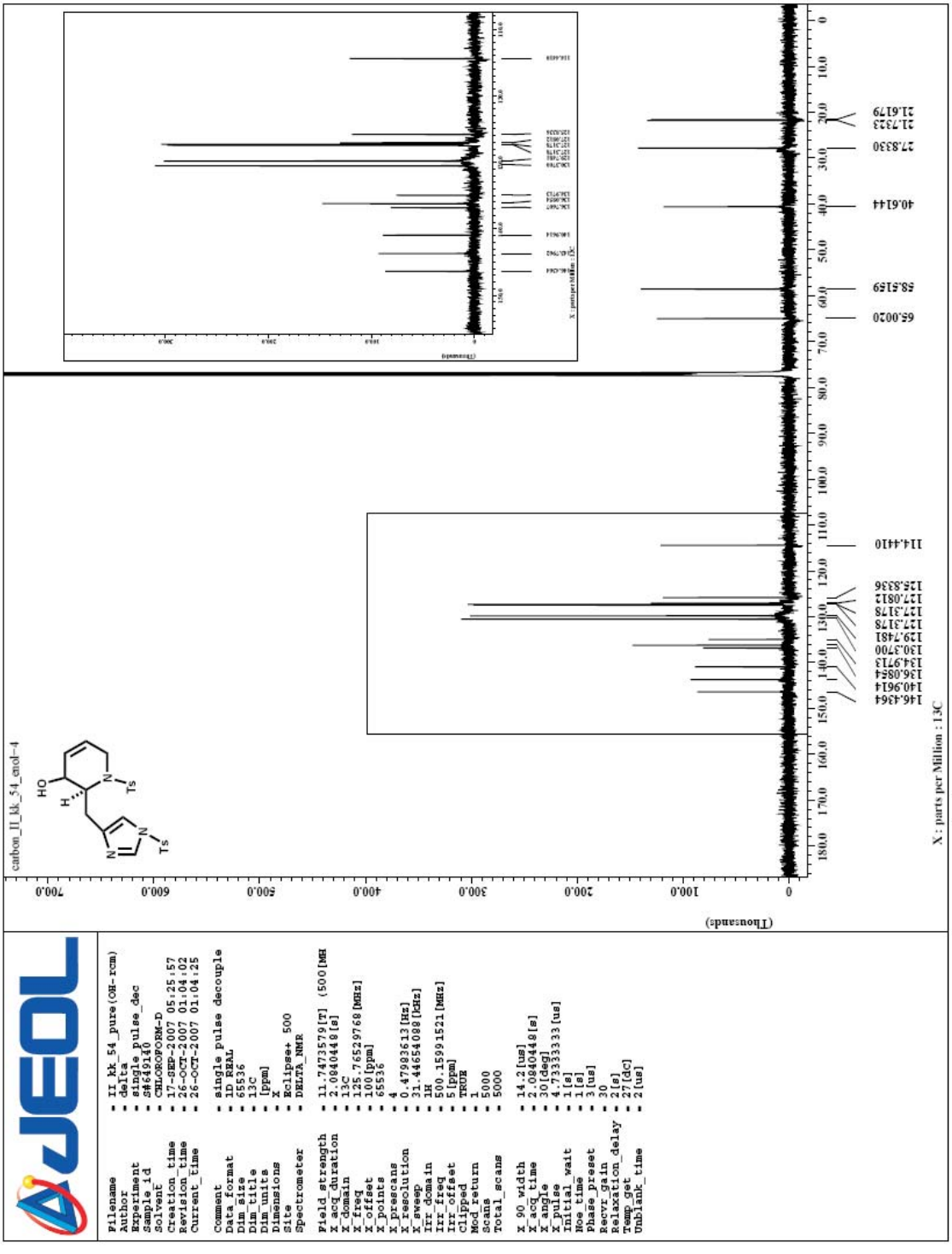

carbon_I_kk_251-3
Filename = I_kk_251-3.jdf
Author = delta
Experiment = single_pulse_dec
Sample_id = S#627305
Solvent = CHLOROFORM-D
Creation_time = 22-FEB-2007 19:30:49
Revision_time = 6-DEC-2007 10:32:33
Current_time = 6-DEC-2007 10:32:55
Comment = single pulse decouple
Data_format = 1D COMPLEX
Dim_size = 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 = 800
Total_scans = 800
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 = 4[s]
Recvr_gain = 50
Relaxation_delay = 4[s]
Repetition_time = 6.76824064[s]
Temp_get = 23.9[dC]
O
H
N
N
Ts
N
Ts
(thousandths)
140.0
130.0
120.0
146.2592
144.2466
144.0937
139.5428
136.3448
136.1679
135.0589
130.5176
130.0204
127.3625
127.0231
126.7268
115.3209
X : parts per Million : 13C
(thousandths)
60.0
50.0
40.0
30.0
20.0
61.1264
41.2642
29.3421
21.8179
21.6314
X : parts per Million : 13C

APPENDIX 15

^{1}HNMR AND ^{13}C NMR SPECTRA OF **1-(TOLUENE-4-SULFONYL)-3-[1-(TOLUENE-4-SULFONYL)-1H-IMIDAZOL-4-YLMETHYL]-1,2,3,4-TETRAHYDROPYRIDIN-4-OL (33)**MEASURED ON A JEOL ECLIPSE 300+ SPECTROMETER IN $CDCl_3$


JEOL
Filename = II_kk_54_pure-7.jdf
Author = delta
Experiment = single_pulse.exp
Sample_id = S#635564
Solvent = CHLOROFORM-D
Creation_time = 16-SEP-2007 21:58:58
Revision_time = 26-OCT-2007 00:20:02
Current_time = 26-OCT-2007 00:20:50
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 = 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 = 30[us]
Receiver_gain = 4[s]
Relaxation_delay = 25.4[dc]
Temp_get_time = 2[us]
Unblank_time
proton_II_kk_54_enol-1
(Millions)
X : parts per Million : 1H
3.02
2.21
2.08
2.01
2.02
1.24
1.19
1.1
1.0
1.01
1
5.9061
7.8136
7.7919
7.6578
7.6403
7.3573
7.3573
7.3556
7.2363
4.3514
4.1104
4.1049
3.9456
3.9363
3.5983
3.5616
2.4897
2.4247
2.4064


Filename = II_kk_54_pure-6.jdf
Author = delta
Experiment = single_pulse.exp
Sample_id = S#635564
Solvent = CHLOROFORM-D
Creation_time = 16-SEP-2007 21:58:58
Revision_time = 25-OCT-2007 23:21:58
Current_time = 25-OCT-2007 23:22:47
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 = 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 = 20
Relaxation_delay = 4[s]
Temp_get = 25.4[dC]
Unblank_time = 2[us]
proton_II_kk_54_enol-6
(Millions)
7.8126
7.7915
7.6578
7.6403
7.3573
7.3573
7.2556
7.2363
7.0091
5.9061
X : parts per Million : 1H
proton_II_kk_54_enol-6
(Millions)
4.3660
4.3514
4.3349
4.1471
4.1425
4.1104
4.1049
3.9455
3.9363
3.5983
3.5616
X : parts per Million : 1H
proton_II_kk_54_enol-6
(Millions)
2.5356
2.5191
2.5062
2.4897
2.4806
2.4668
2.4513
2.4375
2.4247
2.4064
X : parts per Million : 1H

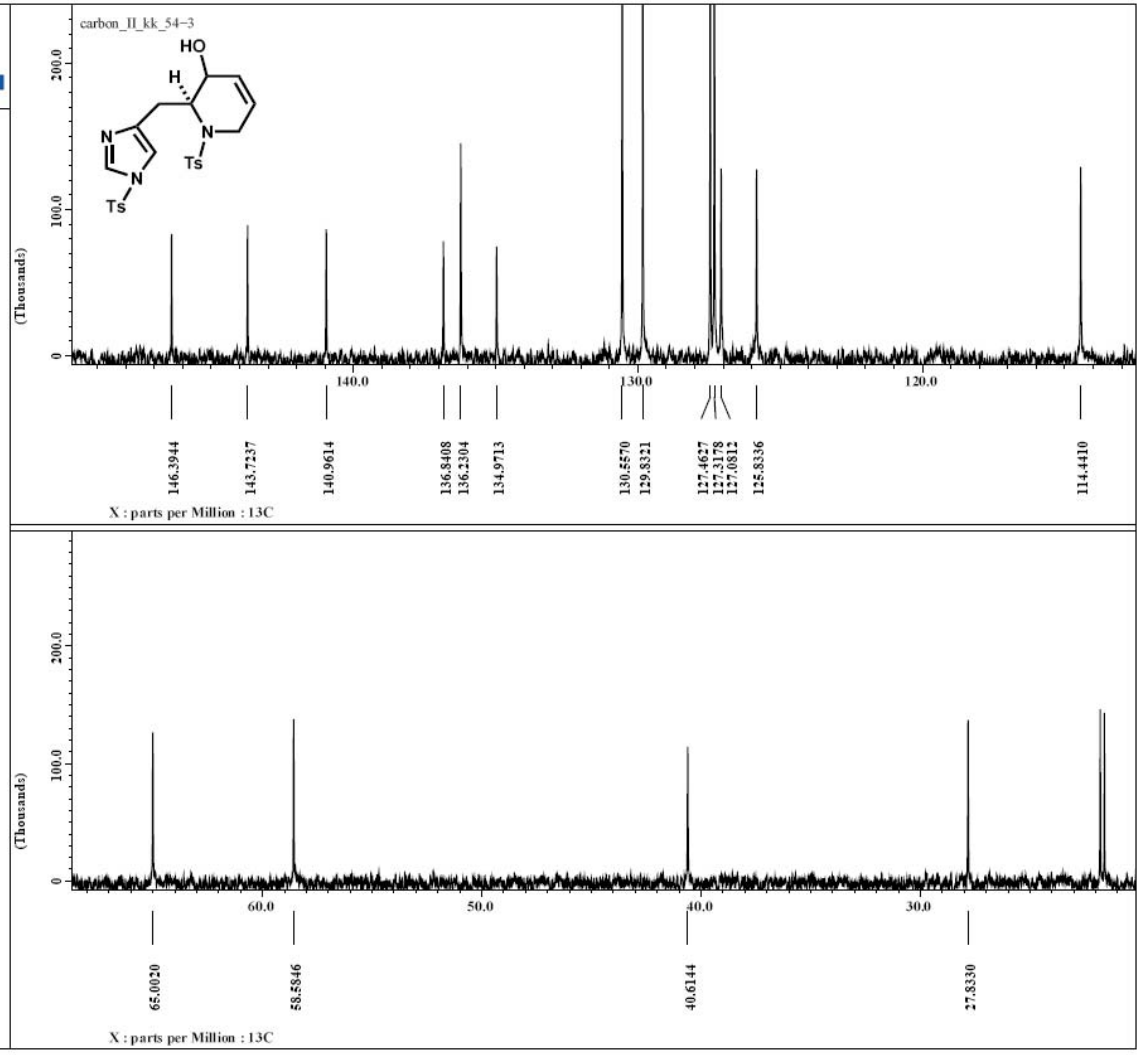

carbon_II_kk_54_enol-4
HO
H
N
Ts
N
N
Ts
(Thousands)
X : parts per Million : 13C
114.4410
125.8336
127.0812
127.3178
127.3178
129.7481
130.3700
134.9713
136.0854
140.9614
146.4364
65.0020
58.5159
40.6144
27.8330
21.7323
21.6179

```
Filename          = II_kk_54_pure(OH-rcm)
Author            = delta
Experiment        = single_pulse_dec
Sample_id         = S#649140
Solvent           = CHLOROFORM-D
Creation_time     = 17-SEP-2007 05:25:57
Revision_time     =  6-DEC-2007 11:02:46
Current_time      =  6-DEC-2007 11:03:01

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

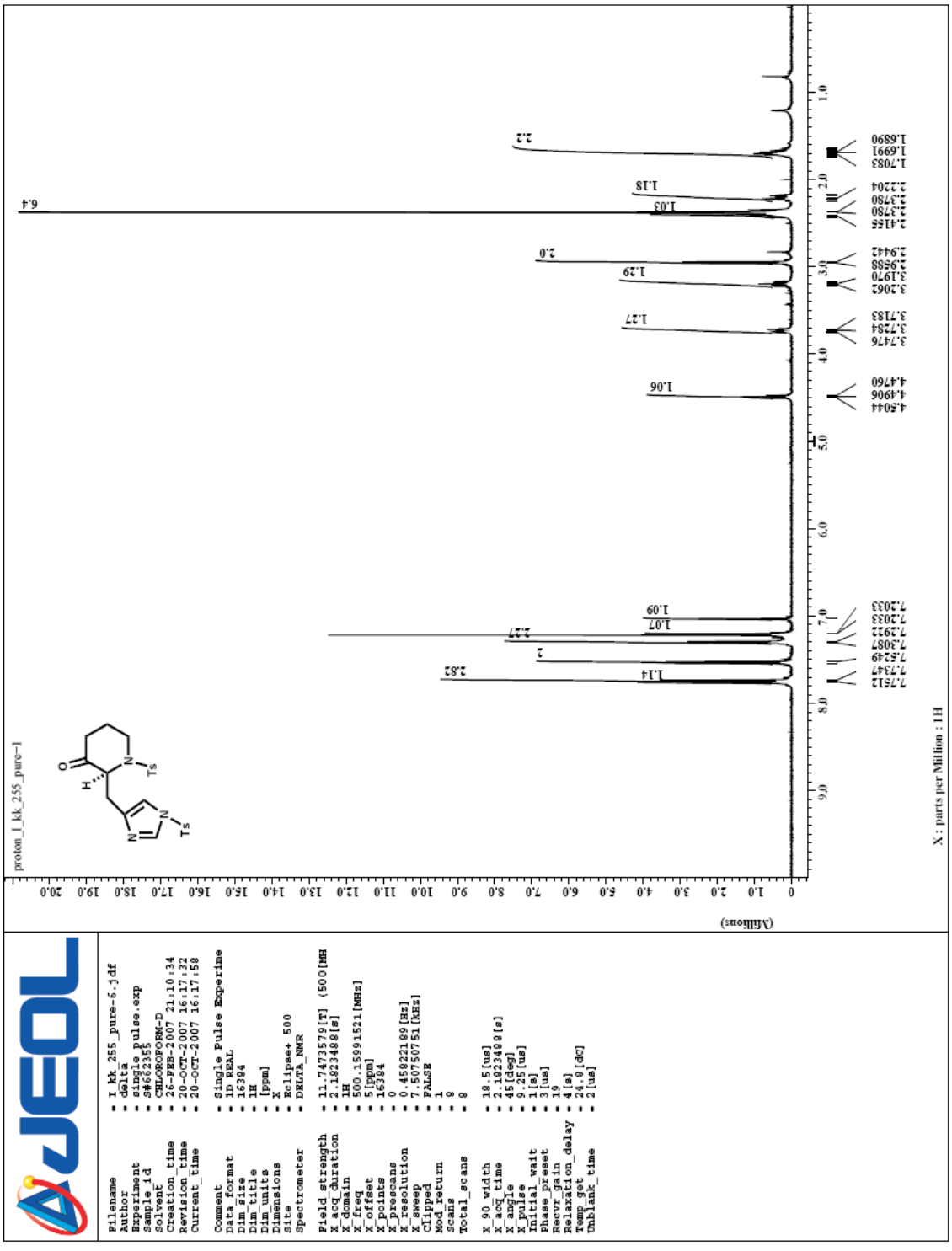
Field_strength    = 11.7473579[T] (500[MH
X_acq_duration    = 2.0840448[s]
X_domain          = 13C
X_freq            = 125.76529768[MHz]
X_offset          = 100[ppm]
X_points          = 65536
X_prescans        = 4
X_resolution      = 0.47983613[Hz]
X_sweep           = 31.44654088[kHz]
Irr_domain    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

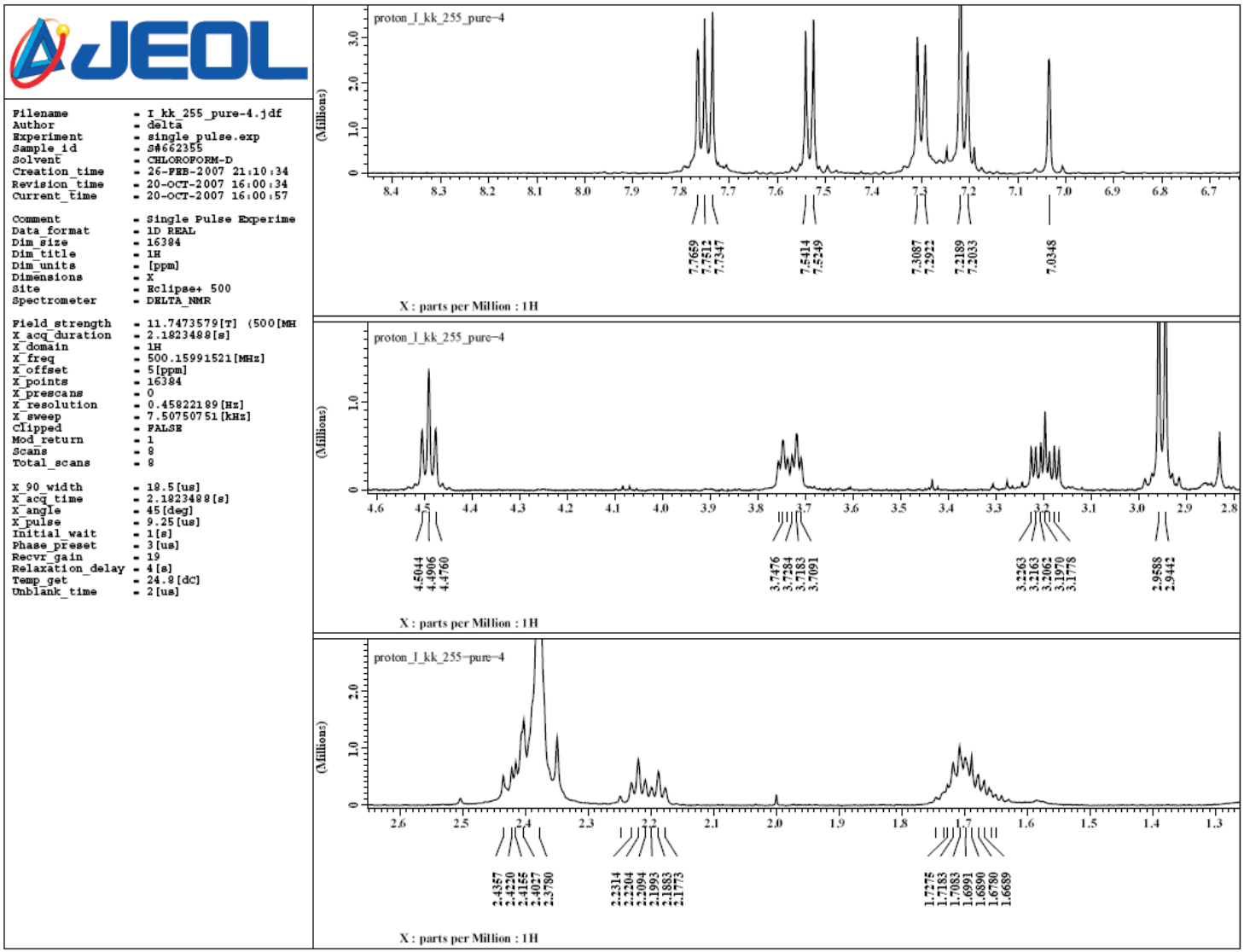
X_90_width        = 14.2[us]
X_acq_time        = 2.0840448[s]
X_angle           = 30[deg]
X_pulse           = 4.73333333[us]
Initial_wait      = 1[s]
Noe_time          = 1[s]
Phase_preset      = 3[us]
Recvr_gain        = 30
Relaxation_delay  = 2[s]
Temp_get          = 27[dC]
Unblank_time      = 2[us]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

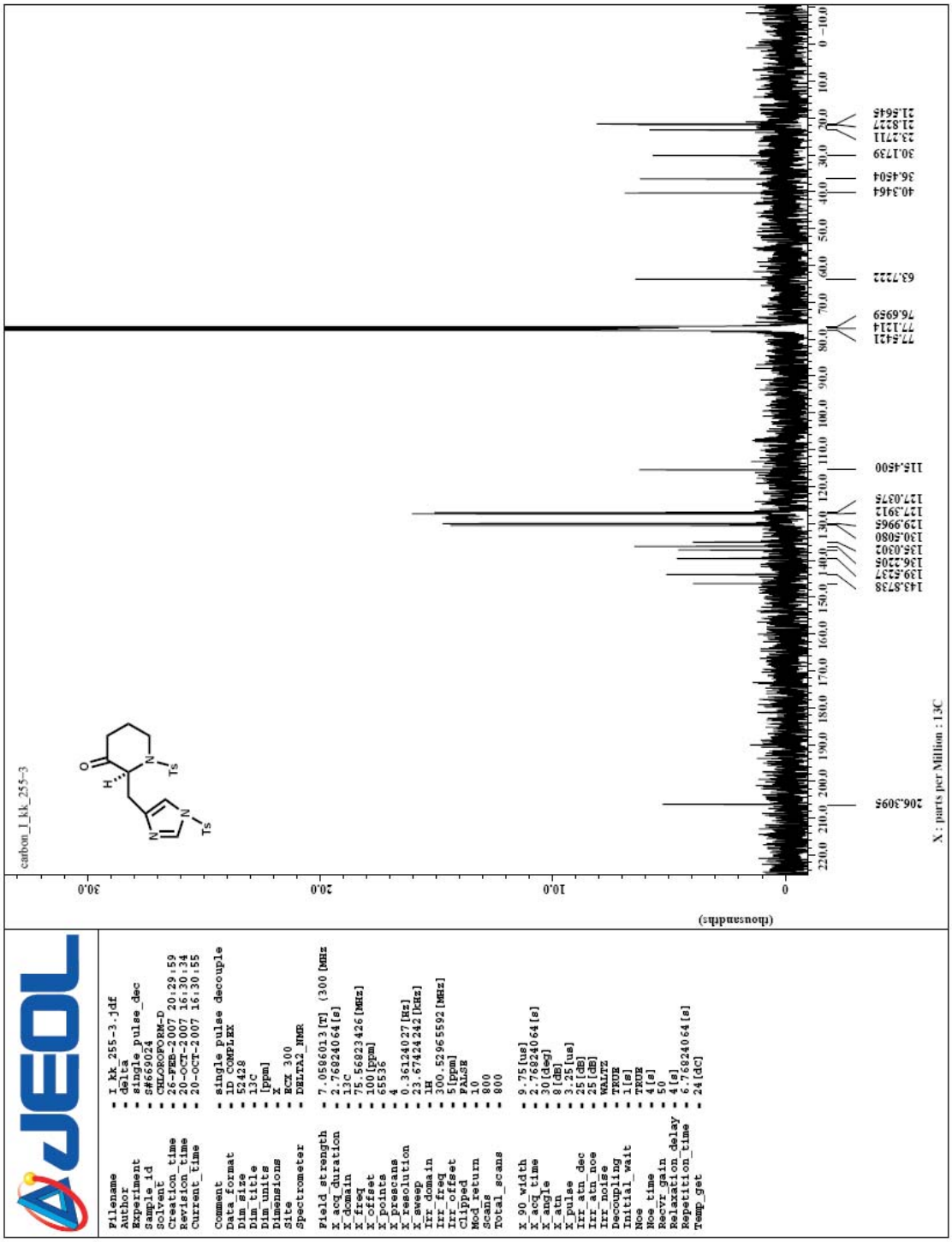


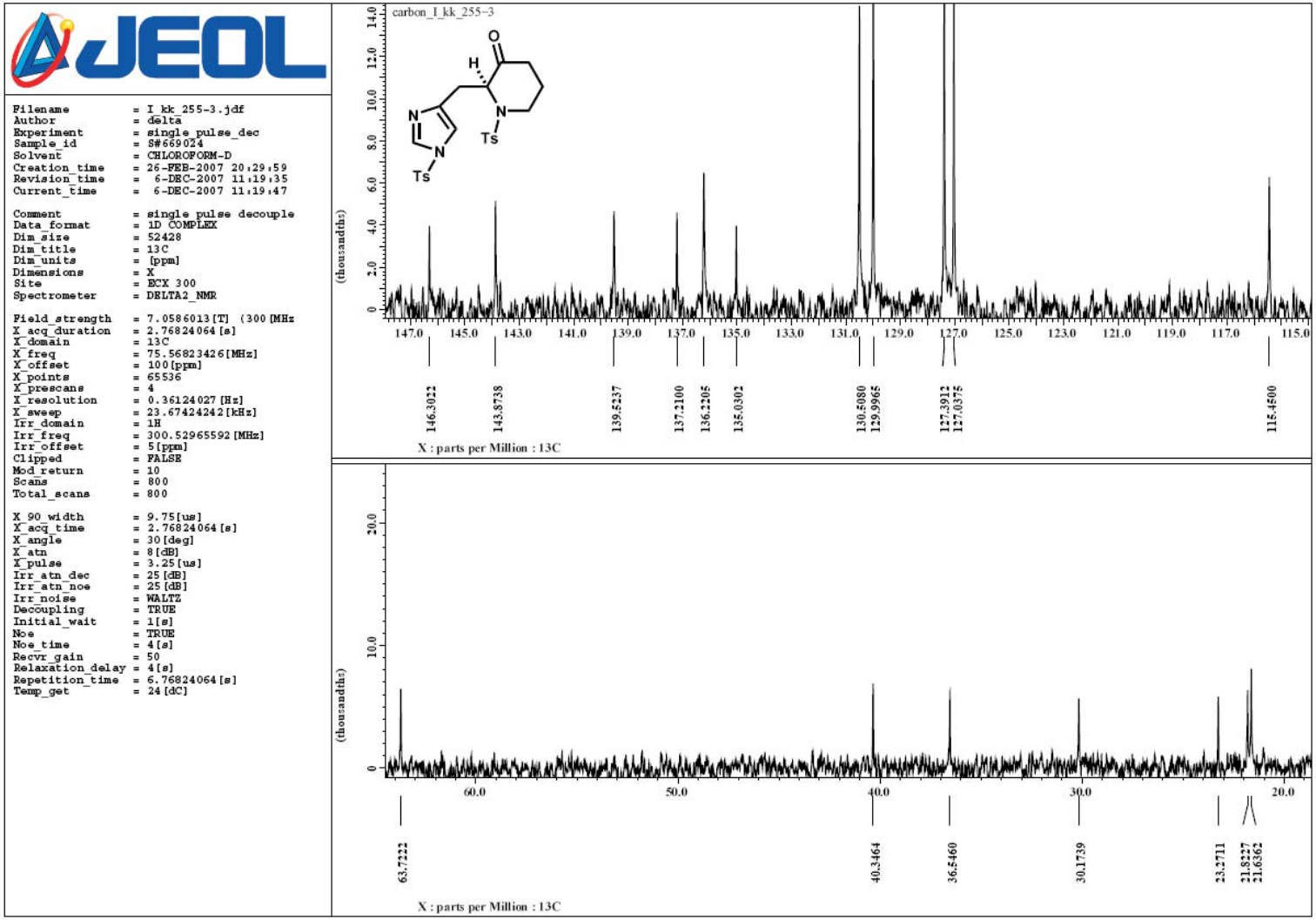
APPENDIX 16

^{1}HNMR AND ^{13}C NMR SPECTRA OF **1-(TOLUENE-4-SULFONYL)-3-[1-(TOLUENE-4-SULFONYL)-1*H*-IMIDAZOL-4-YLMETHYL]-PIPERIDIN-4-ONE (34)** MEASURED ON A JEOL ECLIPSE 300+ SPECTROMETER IN $CDCl_3$


proton_1_kk_255_pure-1
(Million)
X : parts per Million : 1H
6.4
2.2
1.18
1.03
2.0
1.29
1.27
1.06
2.27
2
1.14
2.82
1.09
1.07
7.7512
7.7347
7.5249
7.3087
7.2922
7.2033
7.2033
4.5044
4.4906
4.4760
3.7476
3.7254
3.7183
3.2062
3.1970
2.9588
2.9442
2.4155
2.3780
2.3780
2.2204
1.7083
1.6991
1.6890

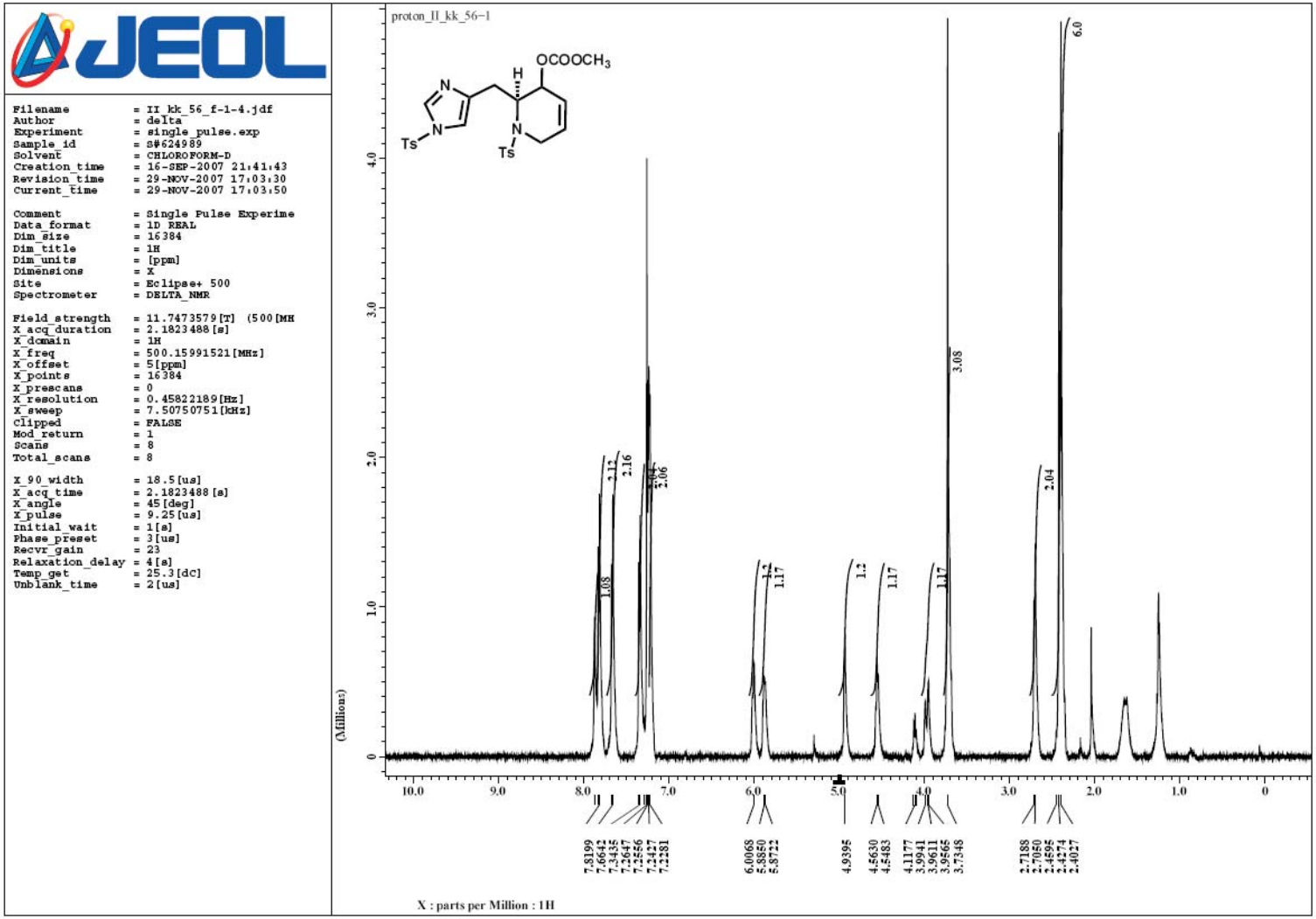

Filename = I_kk_255_pure-4.jdf
Author = delta
Experiment = single_pulse.exp
Sample_id = S#662355
Solvent = CHLOROFORM-D
Creation_time = 26-FEB-2007 21:10:34
Revision_time = 20-OCT-2007 16:00:34
Current_time = 20-OCT-2007 16:00:57
Comment = Single Pulse Experime
Data_format = 1D REAL
Dim_size = 16384
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 = 8
Total_scans = 8
X_90_width = 10.5[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]
proton_1_kk_255_pure-4
(Millions)
7.7659
7.7512
7.7347
7.5414
7.5249
7.3087
7.2922
7.2189
7.2033
7.0348
X : parts per Million : 1H
proton_1_kk_255_pure-4
(Millions)
4.5044
4.4906
4.4760
3.7476
3.7284
3.7183
3.7091
3.2263
3.2163
3.2062
3.1970
3.1778
2.9588
2.9442
X : parts per Million : 1H
proton_1_kk_255_pure-4
(Millions)
2.4357
2.4220
2.4155
2.4027
2.3780
2.2314
2.2204
2.2094
2.1993
2.1883
2.1773
1.7275
1.7183
1.7083
1.6991
1.6890
1.6780
1.6689
X : parts per Million : 1H

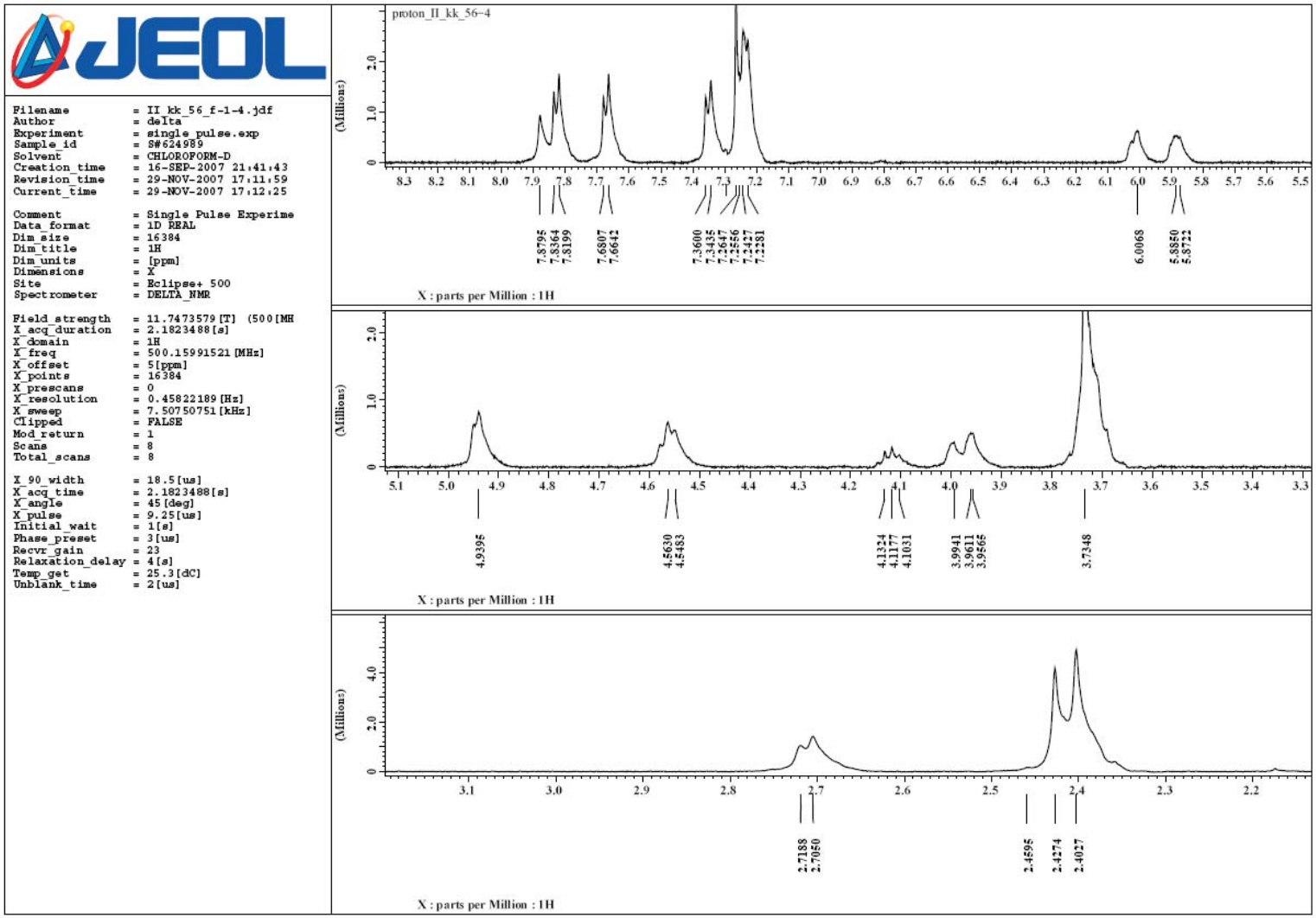

carbon_1_kk_255-3
(thousandths)
X : parts per Million : 13C
206.3095
143.8738
139.5137
136.2206
135.0302
130.5080
129.9965
127.3912
127.0375
115.4500
77.5421
77.1214
76.6959
63.7222
40.3464
36.4504
30.1739
23.2711
21.8217
21.5645

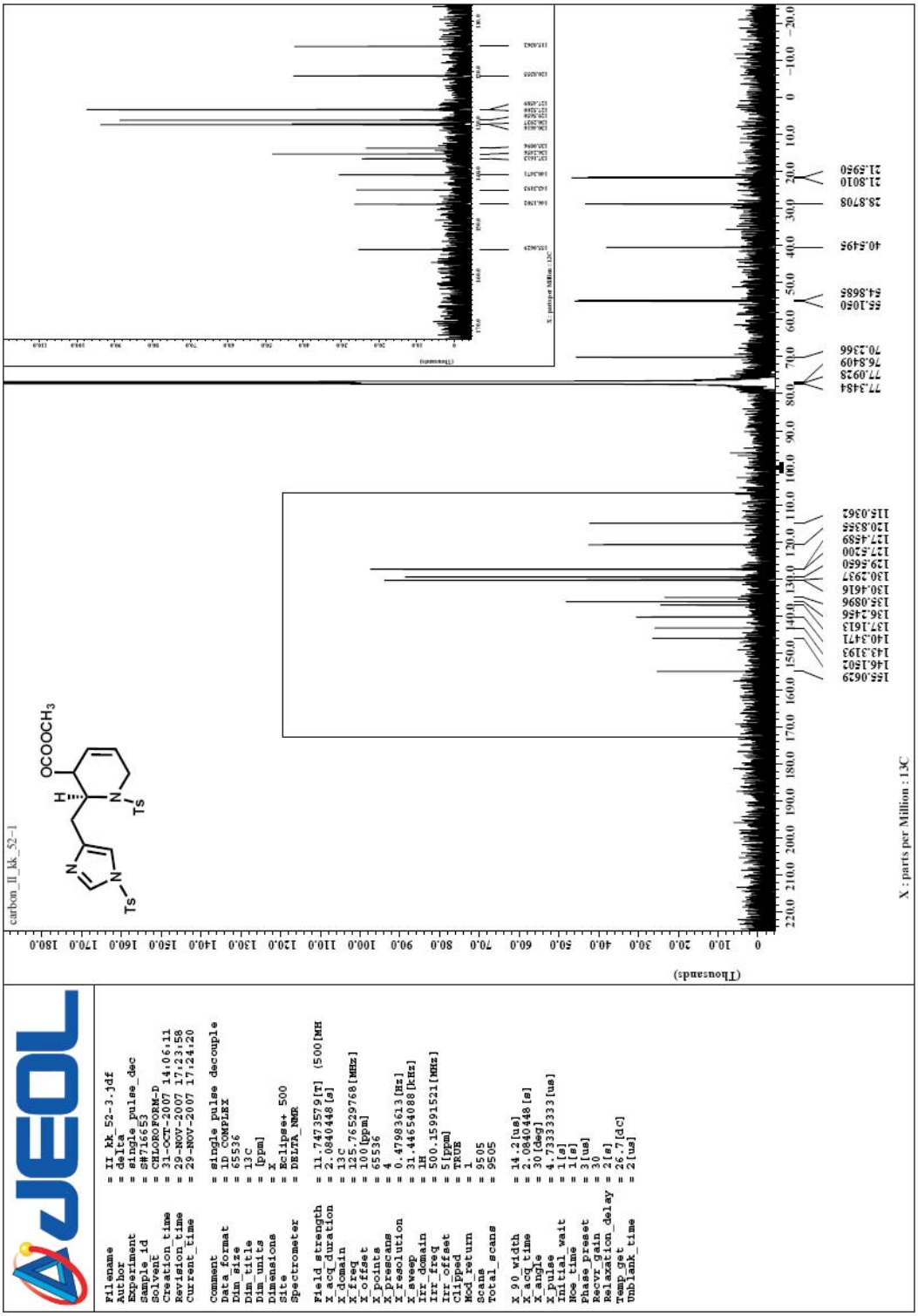

JEOL
Filename = I_kk_255-3.jdf
Author = delta
Experiment = single_pulse_dec
Sample_id = S#669024
Solvent = CHLOROFORM-D
Creation_time = 26-FEB-2007 20:29:59
Revision_time = 6-DEC-2007 11:19:35
Current_time = 6-DEC-2007 11:19:47
Comment = single pulse decouple
Data_format = 1D COMPLEX
Dim_size = 52428
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 = 800
Total_scans = 800
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 = 4[s]
Recvr_gain = 50
Relaxation_delay = 4[s]
Repetition_time = 6.76824064[s]
Temp_get = 24[dC]
carbon_I_kk_255-3
O
H
N
N
Ts
N
Ts
(thousandths)
146.3022
143.8738
139.5237
137.2100
136.2205
135.0302
130.5080
129.9965
127.3912
127.0375
115.4500
X : parts per Million : 13C
(thousandths)
63.7222
40.3464
36.5460
30.1739
23.2711
21.8227
21.6362
X : parts per Million : 13C

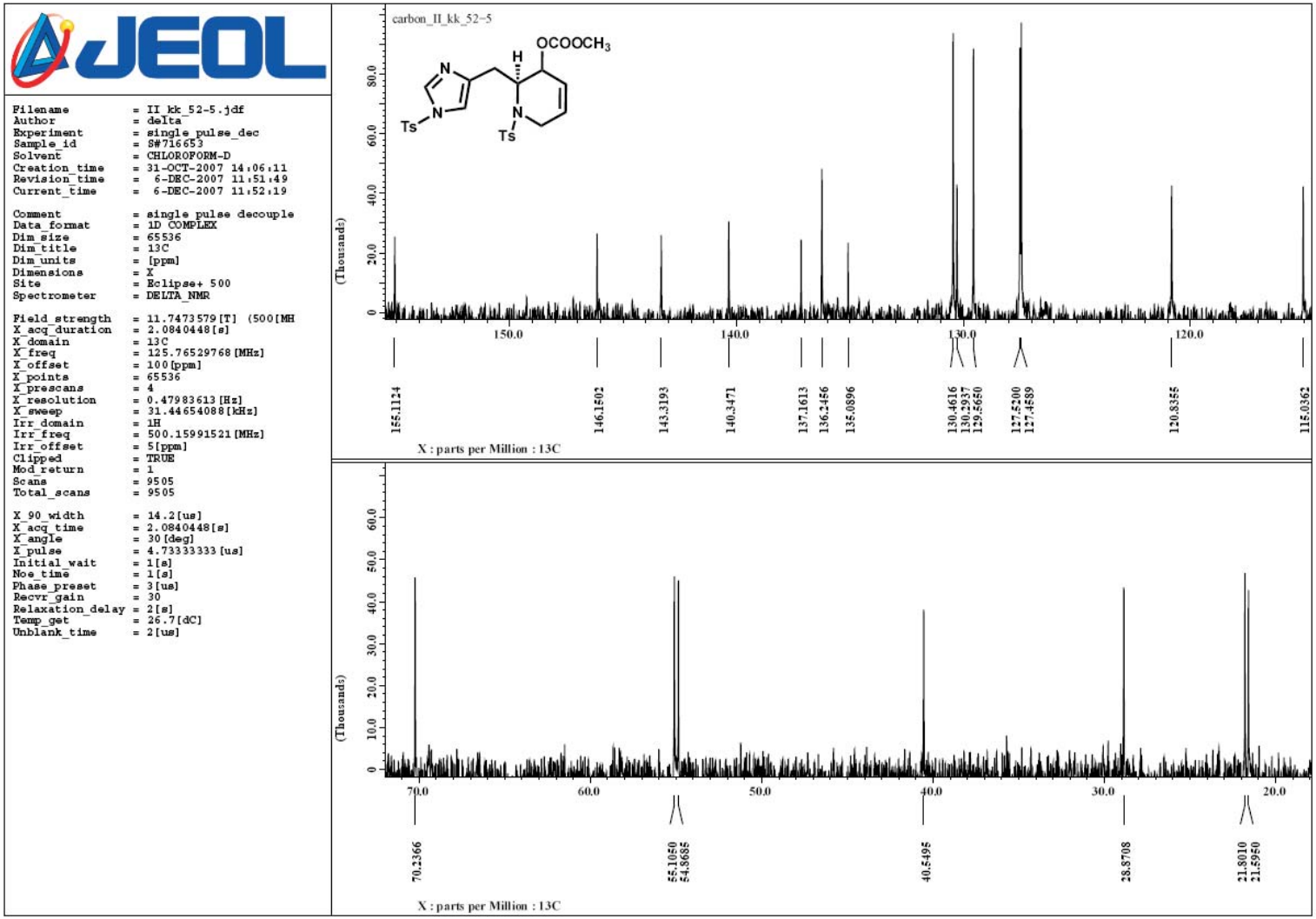
APPENDIX 17

^{1}HNMR AND ^{13}C NMR SPECTRA OF **CARBONIC ACID METHYL ESTER1-(TOLUENE-4-SULFONYL)-2-[1-{TOLUENE-4-SULFONYL)-1*H*-IMIDAZOL-4-YLMETHYL]-1,2,3,6-TETRAHYDRO-PYRIDIN-3-YLESTER (39)** MEASURED ON A JEOL ECLIPSE 300+ SPECTROMETER IN $CDCl_3$


JEOL
Filename = II_kk_56_f-1-4.jdf
Author = delta
Experiment = single_pulse.exp
Sample_id = S#624989
Solvent = CHLOROFORM-D
Creation_time = 16-SEP-2007 21:41:43
Revision_time = 29-NOV-2007 17:03:30
Current_time = 29-NOV-2007 17:03:50
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 = 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 = 23
Relaxation_delay = 4[s]
Temp_get = 25.3[dC]
Unblank_time = 2[us]
proton_II_kk_56-1
OCOOCH3
H
N
N
Ts
N
Ts
6.0
3.08
2.16
2.12
2.06
2.04
1.08
1.17
1.2
(Millions)
7.8199
7.6642
7.3435
7.2647
7.2566
7.2427
7.2281
6.0068
5.8850
5.8722
4.9395
4.5630
4.5483
4.1177
3.9941
3.9611
3.9565
3.7348
2.7188
2.7050
2.4595
2.4274
2.4027
X : parts per Million : 1H


Filename = II_kk_56_f-1-4.jdf
Author = delta
Experiment = single_pulse.exp
Sample_id = S#624989
Solvent = CHLOROFORM-D
Creation_time = 16-SEP-2007 21:41:43
Revision_time = 29-NOV-2007 17:11:59
Current_time = 29-NOV-2007 17:12:25
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 = 23
Relaxation_delay = 4[s]
Temp_get = 25.3[dC]
Unblank_time = 2[us]
proton_II_kk_56-4
(Millions)
7.8795
7.8364
7.8199
7.6807
7.6642
7.3600
7.3435
7.2647
7.2556
7.2427
7.2281
6.0068
5.8850
5.8722
X : parts per Million : 1H
4.9395
4.5630
4.5483
4.1324
4.1177
4.1031
3.9941
3.9611
3.9565
3.7348
2.7188
2.7050
2.4595
2.4274
2.4027


carbon_II_kk_52-1
OCOOCH3
H
N
Ts
N
N
Ts
(Thousands)
X : parts per Million : 13C
155.0629
146.1502
143.3193
140.3471
137.1613
136.2456
135.0896
130.4616
130.2937
129.5650
127.5200
127.4589
120.8355
115.0362
77.3484
77.0928
76.8409
70.2366
55.1050
54.8685
40.5495
28.8708
21.8010
21.5950


Filename = II_kk_52-5.jdf
Author = delta
Experiment = single_pulse_dec
Sample_id = SW716653
Solvent = CHLOROFORM-D
Creation_time = 31-OCT-2007 14:06:11
Revision_time = 6-DEC-2007 11:51:49
Current_time = 6-DEC-2007 11:52:19
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 = 9505
Total_scans = 9505
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 = 2[s]
Temp_get = 26.7[dC]
Unblank_time = 2[us]
carbon_II_kk_52-5
OCOOCH3
H
N
N
Ts
N
Ts
(Thousands)
150.0
140.0
130.0
120.0
155.1124
146.1502
143.3193
140.3471
137.1613
136.2456
135.0896
130.4616
130.2937
129.5650
127.5200
127.4589
120.8355
115.0362
X : parts per Million : 13C
(Thousands)
70.0
60.0
50.0
40.0
30.0
20.0
70.2366
55.1050
54.8685
40.5495
28.8708
21.8010
21.5950
X : parts per Million : 13C

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BIOGRAPHICAL INFORMATION

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