2001

Lewis Acid Catalyzed Reactions of Aziridino-Olefins

Steven Tymonko '01
Illinois Wesleyan University

Lewis Acid Catalyzed Reactions of Aziridino-Olefins

Steven Tymonko

Advisor: Dr. Ram S. Mohan
Reseach Honors Senior Thesis
Illinois Wesleyan University
Spring 2001

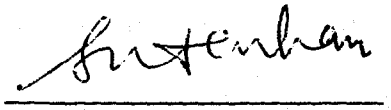
Approval Page

Lewis Acid Catalyzed Reactions of Aziridino-Olefins

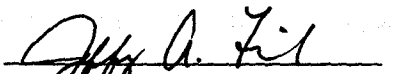
Steven Tymonko

A PAPER SUBMITTED AS PART OF THE REQUIREMENTS FOR CHEMISTRY 499 AND RESEARCH HONORS IN CHEMISTRY

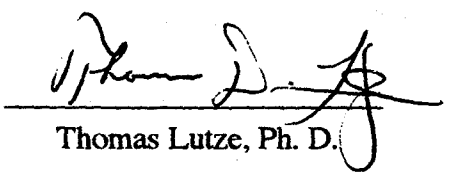
Approved:



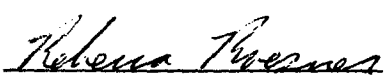
Ram S. Mohan, Ph. D., Research Advisor



Jeffrey A. Frick, Ph. D.



Thomas Lutze, Ph. D.



Rebecca Roesner, Ph. D.

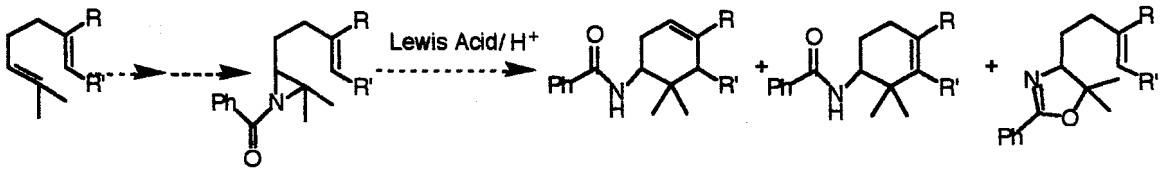
Illinois Wesleyan University, 2000-2001

Acknowledgements

I would like to thank Dr. Ram Mohan for the countless hours he has spent teaching and challenging me to better understand my work and chemistry in general. His support over the past few years has been key in my growth as a chemist and preparation for graduate study. I would also like to thank Dr. Coates for all his help as well as the opportunity to work on this project which was started in his group at the University of Illinois. A special thanks goes to all the members of the research group that I have been fortunate to work with over the past two and a half years: Kostas Gavardinas for taking the time to teach me how to get around the lab when I began as a sophomore; Keith Monk, Andy Anderson, Rebecca Centko, Adam Tuite, Jesse Blazek, Mike Pulia, Dusan Sarapa, Bryce Nattier, Laura Wieland, Nick Leonard, Kyle Eash, Herb Zerth, Kaushik Bhatia, and Derek Freiberg for helping to make my research experience an enjoyable one. I would also like to thank Cindy Honegger for her help on the hundreds of occasions when I have found myself lost in the stockroom looking for an elusive chemical or piece of glassware.

Abstract

Electrophilic reactions resulting in the formation of new carbon-carbon bonds are important tools in organic synthesis. For example, the acid catalyzed cyclization of epoxy olefins has been well documented, while similar cyclizations with aziridines have been largely unexplored. The aim of this project is to develop and demonstrate the formation of a carbocyclic compound from aziridino-olefins utilizing a Lewis acid to catalyze the cyclization. In working toward this goal, a number of aziridino-olefins were synthesized from isoprenoid start materials. These aziridino-olefins were then reacted with both Lewis and protic acids in an attempt to induce cyclization. As a result, we have demonstrated the formation of both the desired cabocyclic products as well as competing cyclizations to oxazoline products.



Contents

I. Introduction

A. Background 1

B. Olefin-Epoxide Cyclization 4

C. Ring opening reactions of aziridines 10

D. Research Goals 16

II. Discussion

A. Preparation of aziridines derived from geranyl and neryl acetate 17

B. Studies with geranyl and neryl benzoyl aziridines 21

C. Preparation of geraniolene derived aziridines 24

D. Studies with geraniolene derived aziridines 27

E. Future work 29

III. Experimental 31

IV. References 47

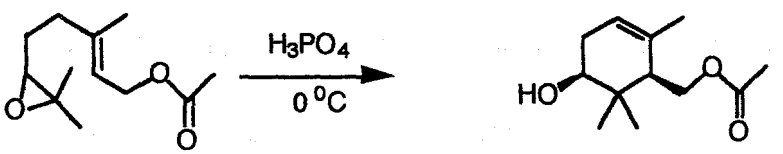
V. Appendix: Spectral Data 48

I. Introduction

A. Background

Electrophilic reactions resulting in the formation of new carbon-carbon bonds are important tools in organic synthesis.[1] These reactions allow for the backbone of a structure to be altered in preparation of a target molecule. For example, epoxy-olefins such as **1** cyclize to produce the carbocyclic product **2**.[2] (scheme1.1) These reactions are particularly useful since they generate new carbon-carbon bonds in a stereoselective manner.

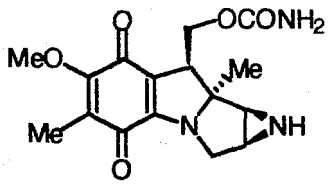
Scheme 1.1



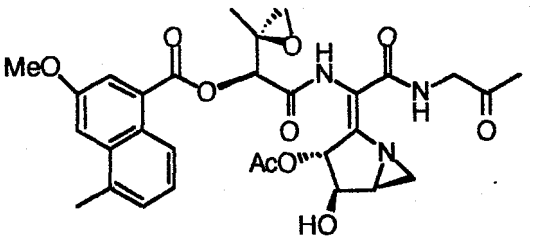
1 **2**

Aziridines, the nitrogen analogs of epoxides, are found in a number of naturally occuring compounds. For example, the antibacterial agents mitomycin **3** and azinomycin **4** (figure 1.1), which have been isolated from bacteria, contain an aziridine ring[3].

Figure 1.1



mitomycin A
3



azinomycin A
4

The similarity between aziridines **5** and epoxides **6** makes aziridines attractive candidates for development of new electrophilic cyclization reactions. The structural similarity between the two three-membered heterocycles results in comparable ring strains, specifically 27 kJ/mol for epoxides and 26 kJ/mol for aziridines (figure 1.2).[4] High ring strain arises from the fact that the bond angle of 60^0 in aziridines and epoxides is considerably smaller than the normal value for a sp^3 hybridized carbon (109.5^0). The high strain inherent in three-membered rings makes both aziridines and epoxides prone to ring-opening reactions.

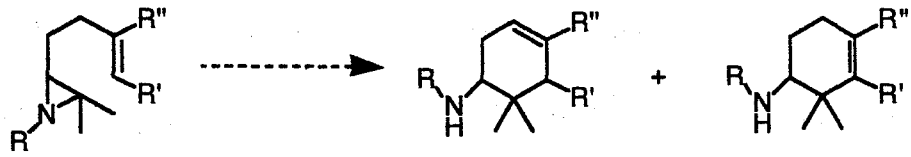
Figure 1.2

5 **6**

Development of procedures by which aziridino-olefins can be converted to carbocyclic compounds would be synthetically very useful since these reactions

would allow for synthesis of useful nitrogen containing functional groups, such as amides.

Scheme1.2

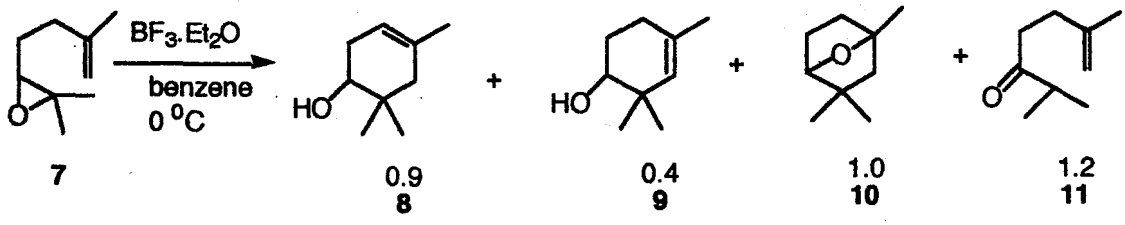


The result of ring opening of an acyl aziridine would be an amide. This is advantageous because the resulting amide could be converted to the corresponding amine by reduction.

B. Olefin-Epoxide Cyclizations

The initial demonstration of epoxy-olefin cyclization was carried out by Goldsmith nearly forty years ago.[5] Goldsmith demonstrated that epoxide **7** underwent cyclization in the presence of boron trifluoride etherate to give six-membered carbocyclic compounds and other products.

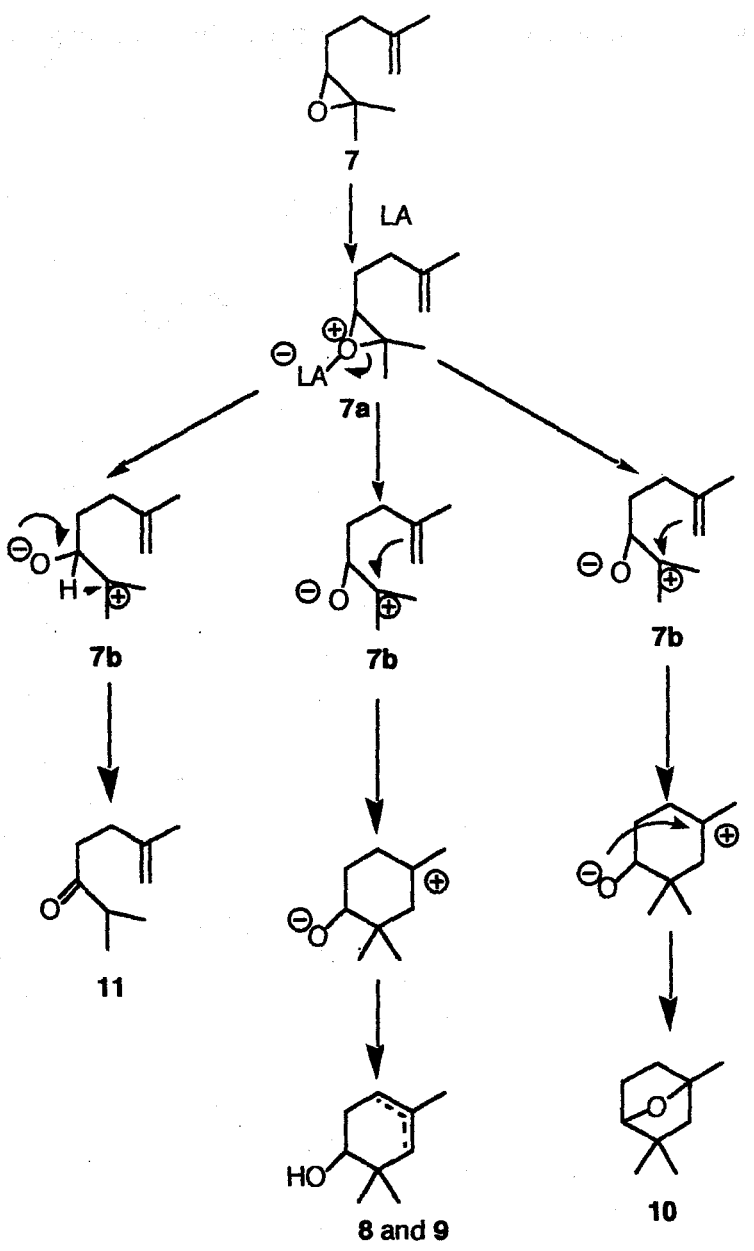
Scheme 1.3



7 → 0.9 **8** + 0.4 **9** + 1.0 **10** + 1.2 **11**

The products obtained from this reaction included both cyclohexenols **8** and **9** as well as the bicyclic ether **10** and ketone **11** shown above (scheme 1.3). Goldsmith provided a mechanistic explanation for the observed results (scheme 1.4). This mechanism involves the formation of a common carbocation intermediate **7b** which can then rearrange to the observed products. In subsequent work, Goldsmith utilized similar cyclizations in the preparation of other cyclohexenols from epoxy-olefins utilizing boron trifluoride etherate.[6]

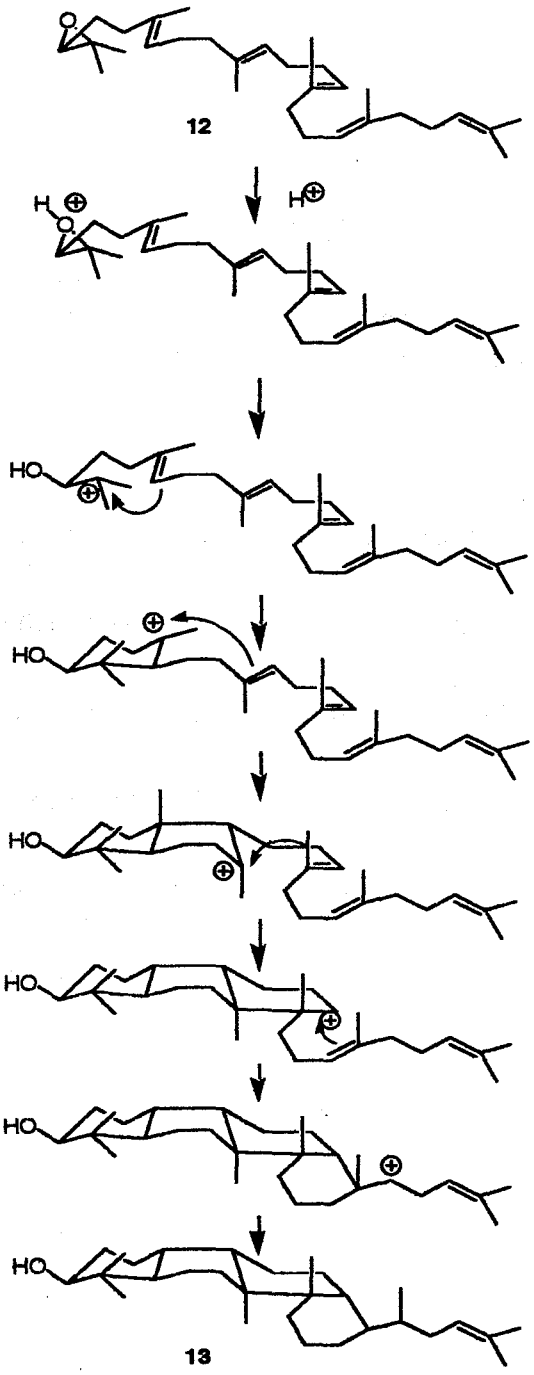
Scheme 1.4



Van Tamelen[2,7] demonstrated the stereospecific nature of the cyclization, utilized a variety of acid catalysts, and demonstrated cyclizations to form multicyclic systems in a single step (scheme 1.5). In van Tamelen's study, a series of epoxides was prepared from the terpenoids methyl farnesate **14**,

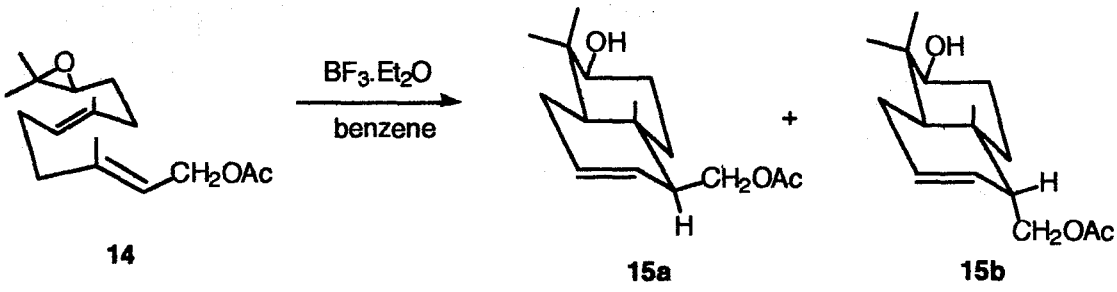
geranylgeraniol **16**, and squalene **12**. Van Tamelen utilized these terpenoids as models for studying the biosynthesis of lanosterol **13** from squalene oxide **12**.(scheme 1.5)

Scheme 1.5



Treatment of the epoxide **14**, derived from *trans-trans*--farnesyl acetate, with boron trifluoride etherate gave a 10% yield of the bicyclic products **15a** and **15b** in a ratio of 85:15. The same reaction carried out with cold H_3PO_4 in place of $BF_3.Et_2O$ gave similar yields with opposite diastereoselectivity (85:15 **15b: 15a**) (scheme 1.6).

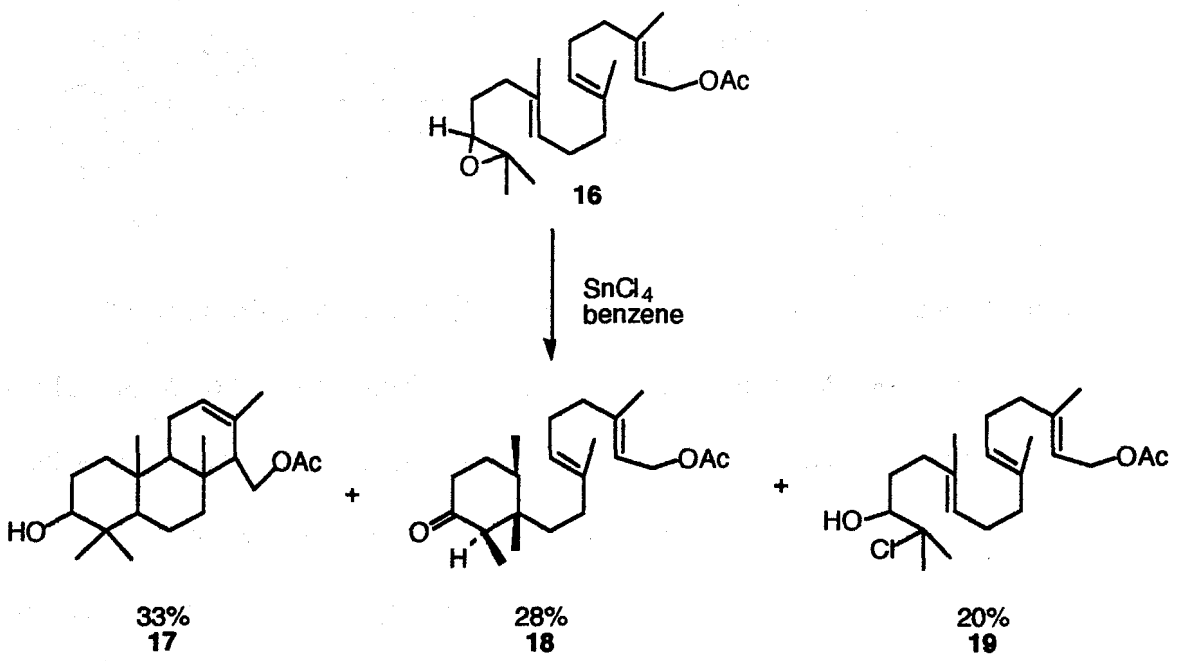
Scheme 1.6



14 **15a** **15b**

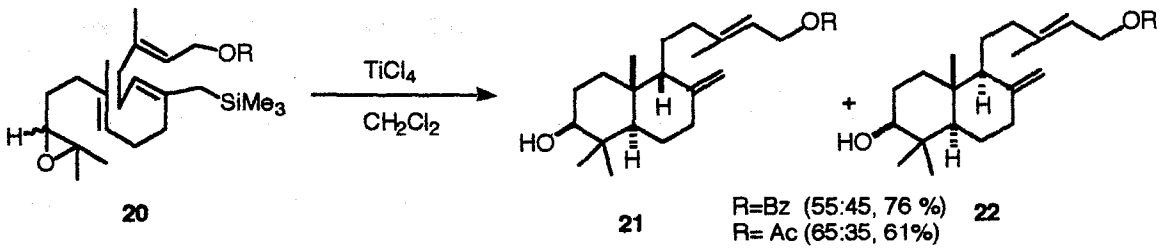
Treatment of the epoxide derived from *trans-trans-cis*- ethyl geranylgeranate **16** with stannic chloride generated a mixture of products primarily composed of the corresponding hydroxyacetate **17**, monocyclic ketone **18**, and chlorohydrin **19** (scheme 1.7). Like the previous examples, the reaction involving stannic chloride is stereospecific resulting in the formation of compounds **17** and **18** as single diastereomers.

Scheme 1.7



During the course of the total synthesis of Copalol, Coates further explored epoxy cyclizations.[8] The results of this investigation showed that the presence of a silyl group as in **20** greatly enhanced the ratio of bicyclic to monocyclic products from 0.5 to as high as 7. Coates attributed the improved ratio to enhanced nucleophilicity of the allylsilane double bond as well as greater stability of the β-silyl carbocation. The other trend accompanying the increased yields was decreased selectivity between the syn and anti products, **21** and **22** respectively. Coates observed comparable amounts of both syn and anti bicyclic products when a silyl terminator was present (scheme 1.8).

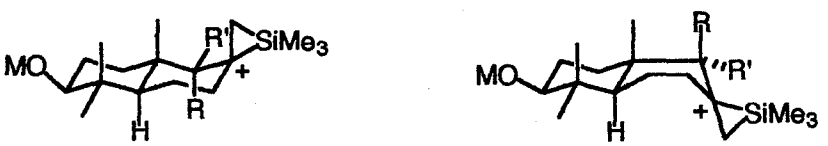
Scheme 1.8



20 **21** **22**

This is attributed to a shift in transition states from favoring a chair-chair conformation **23** to nearly equal energies for the chair-chair and chair-boat conformations **24** (scheme 1.9). The shift was attributed to silicon bridging. The resulting chair-chair conformation would be destabilized by 1,3-diaxial interactions to a greater extent than the chair-boat conformation.

Scheme 1.9



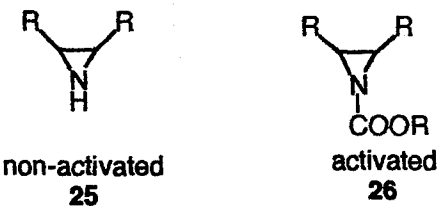
chair-chair intermediate
23

chair-boat intermediate
24

C. Ring opening reactions of aziridines

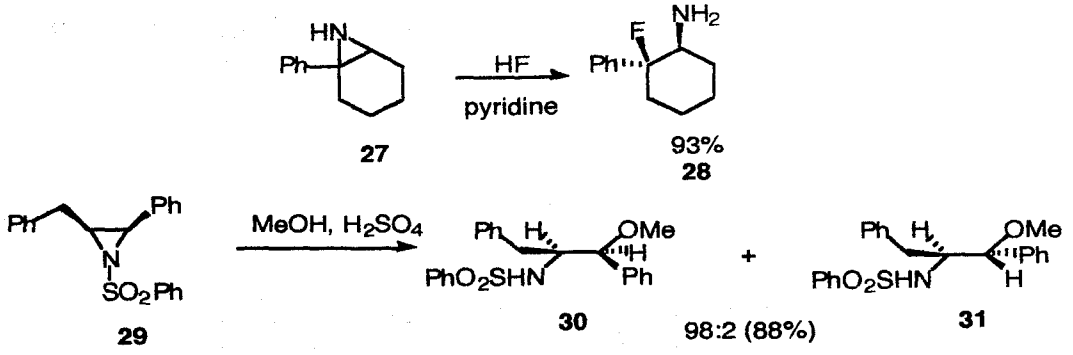
Due to the high levels of strain inherent in three-membered rings, ring-opening reactions are the dominant feature of aziridine chemistry. When dealing with ring-opening reactions it is useful to divide aziridines into two classes. These are nonactivated aziridines **25**, in which the nitrogen is bound to a proton or alkyl group, and activated aziridines **26** (scheme 1.10) where the electron withdrawing substituent conjugatively stabilizes the negative charge on the nitrogen in the transition state in nucleophilic ring-opening.

Scheme 1.10



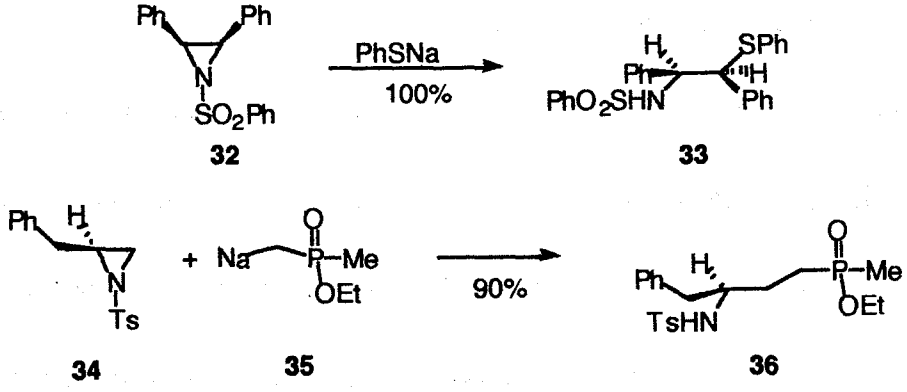
Under acidic conditions, both nonactivated and activated aziridines, **27** and **29** respectively, are observed to undergo ring opening[3]. (scheme 1.11)

Scheme 1.11



Activated aziridines **32** and **34** are known to undergo nucleophilic ring opening reactions. These reactions proceed by a S_N2 mechanism resulting in complete inversion[3]. (scheme 1.12)

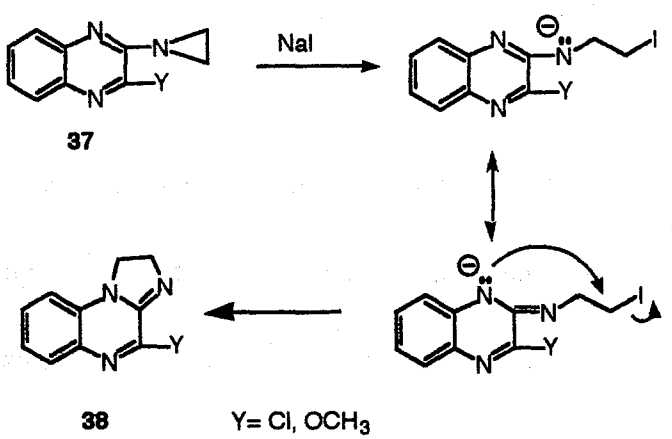
Scheme 1.12



Several examples of aziridine ring opening to form new heterocycles have been reported in the literature. Heine showed that aziridines **37** can be converted by nucleophiles into effective alkylating agents for a neighboring nitrogen.[10,11] The proposed mechanism for this reaction involves the opening of the aziridine by

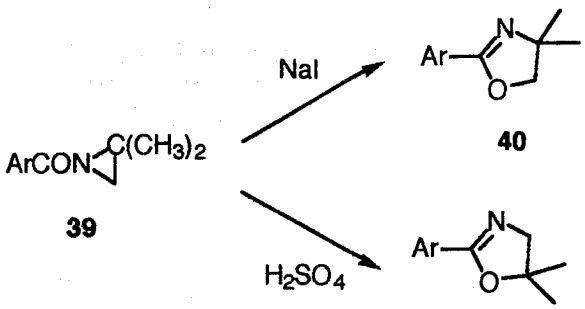
iodide ion followed by ring closure and departure of iodide to give the corresponding products **38** (scheme 1.13)

Scheme 1.13



In a similar manner, N-acyl aziridines **39** undergo rearrangement in the presence of sodium iodide or sulfuric acid to give the corresponding oxazolines **40**, **41**(scheme 1.14).[12, 13] In this reaction, when an unsymmetrical aziridine is used, treatment with sodium iodide gives the oxazoline derived from nitrogen-primary carbon fission **40** in a S_N2-like reaction while sulfuric acid gives the oxazoline resulting from nitrogen-tertiary carbon fission **41** in a S_N1-like reaction.

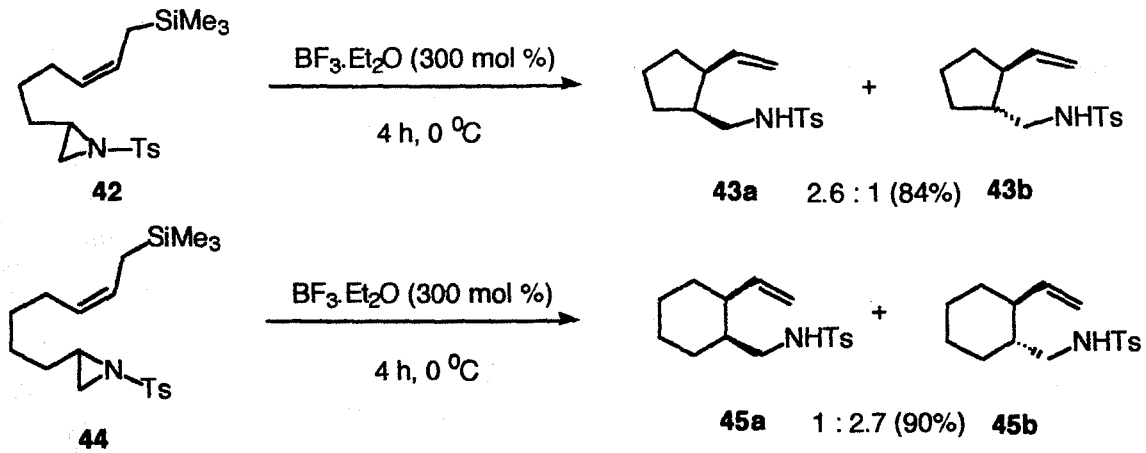
Scheme 1.14



Similar results are observed with benzoyl aziridines using a variety of catalysts including Lewis acids, protic acids, and nucleophiles such as in the sodium iodide example already discussed. In each case it is reported that the oxazolines are formed in excellent yields.[4]

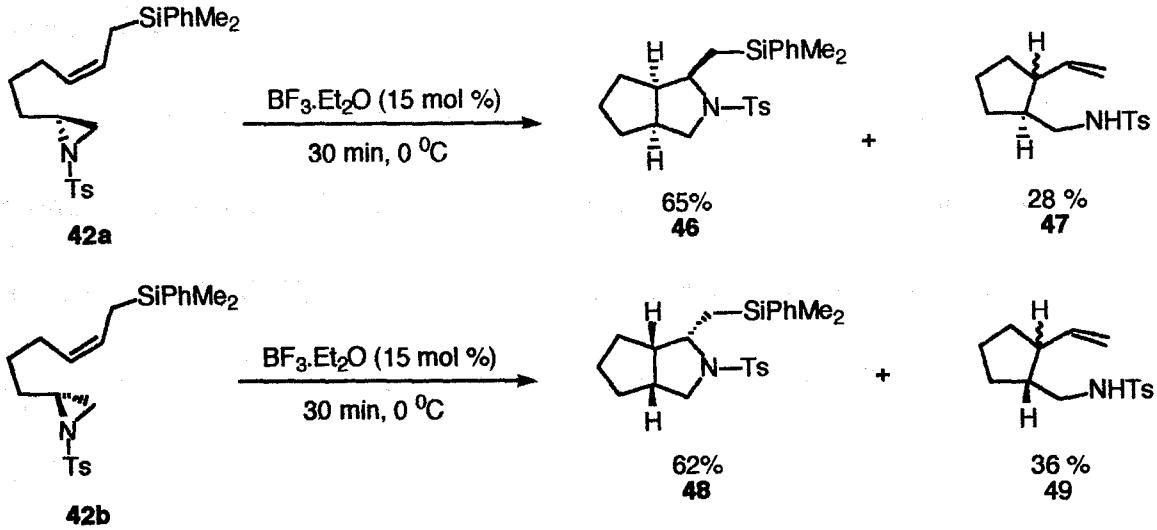
Bergmeier has demonstrated in a series of studies the formation of both heterocyclic and carbocyclic compounds through the treatment of aziridines with Lewis acids. Bergmeier utilized boron trifluoride etherate as a catalyst for intramolecular cyclization of allylsilanes with aziridines **42** and **44** to produce both five-membered **43a**, and **43b** and six-membered **45a** and **45b** carbocyclic compounds (scheme 1.15).[14] One interesting result of this study for which Bergmeier did not offer an explain is the preferential formation of the cis product **43a** from aziridine **42** and of the trans product **45b** from aziridine **44**.

Scheme 1.15



In another study, Bergmeier reported the formation of both 5-5 and 6-5 fused ring systems containing a nitrogen.[16] These products arise from a formal [3 + 2] intramolecular aziridine-allylsilane cycloaddition. The authors chose a silane that could be readily converted to other functionalities. The dimethylphenyl group was chosen since it can be easily oxidized to a hydroxyl group[17] and the silyl chloride required for its synthesis is commercially available. The amount of catalyst used was reduced from 300 mol % to 15 mol % and reaction times shortened from 4 hours to 30 minutes. The result is the preferential formation of a nitrogen containing heterocycle **46** and **48** over the carbocyclic product **47** and **49**. (scheme 1.16)

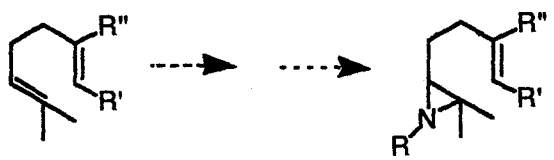
Scheme 1.16


SiPhMe2
BF3.Et2O (15 mol %)
30 min, 0 °C
Ts
42a
65%
46
28 %
47
NHTs
42b
62%
48
36 %
49

D. Research Goals

This project was undertaken with the primary goal of demonstrating the formation of a carbocyclic compound through aziridino-olefin cyclization. This project can be divided into two parts. The first project involved the synthesis of appropriate activated aziridines **51** from corresponding precursors **50** (scheme 1.17).

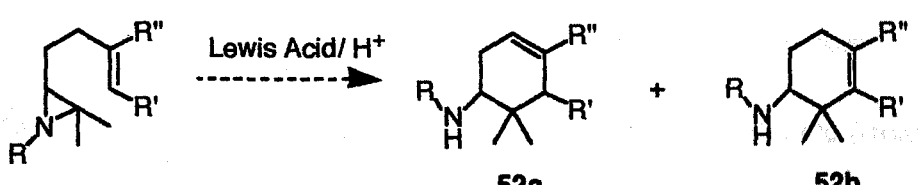
Scheme 1.17



50 **51**

The second part of the study was to explore the reactions of the activated aziridino-olefins with Lewis acids as well as protic acids. Variations in the acid catalyst as well as the structure of the chosen aziridino-olefin were explored to determine if cyclization of the aziridino-olefin to carbocyclic compounds **52a** and/or **52b** could be carried out (scheme 1.18).

Scheme 1.18

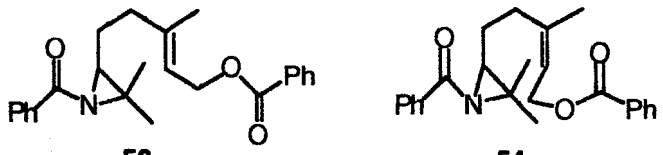


51 **52a** **52b**

II. Discussion

A. Preparation of aziridines derived from geranyl and neryl acetate

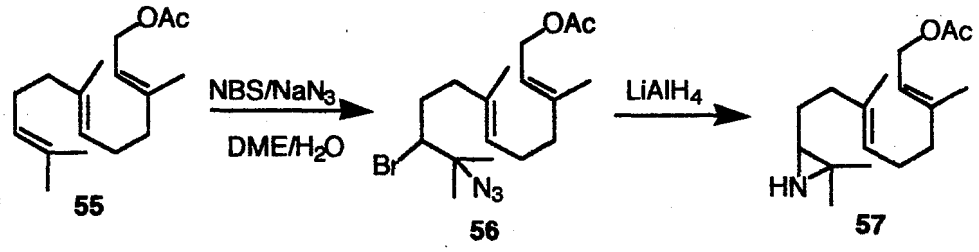
Figure 2.1



53 **54**

The synthesis of the aziridine rings in the substrates **53** and **54** were based on a general method developed by Krief for aziridine synthesis.[18] In this procedure, a trisubstituted olefin **55** is treated with *N*-bromosuccinimide and sodium azide to form a bromoazide intermediate **56** which is then reduced with lithium aluminum hydride to form the aziridine **57** in 48% total yield. When multiple double bonds are present, the reaction is found to be highly selective for the terminal olefin.

Scheme 2.2

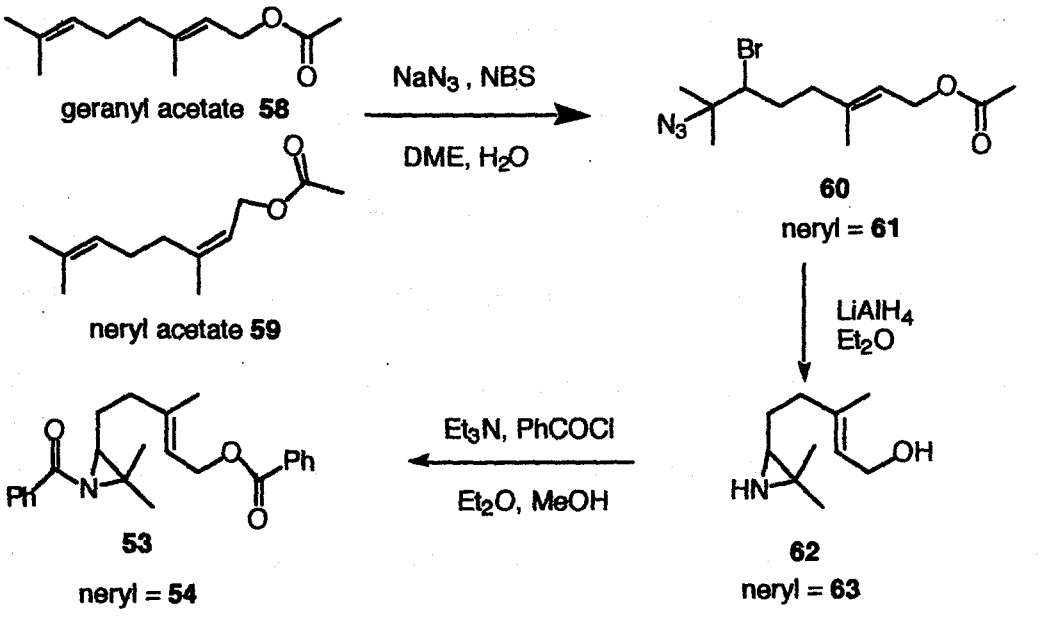


55 **56** **57**

In the case of both geranyl acetate **58** and neryl acetate **59** the reaction proceeded smoothly to give the bromoazide **60** or **61,** respectively which were then reduced without purification to give the aziridino-alcohol **62** or **63** in 59% overall yield (from geranyl acetate) after purification by flash chromatography (scheme 2.3). The

reduction of the bromoazide **60** or **61** requires three equivalents of hydride, one equivalent to reduce the acetate to alcohol, one equivalent to reduce the acetaldehyde by-product and one equivalent to form the aziridine from the bromoazide.

Scheme 2.3



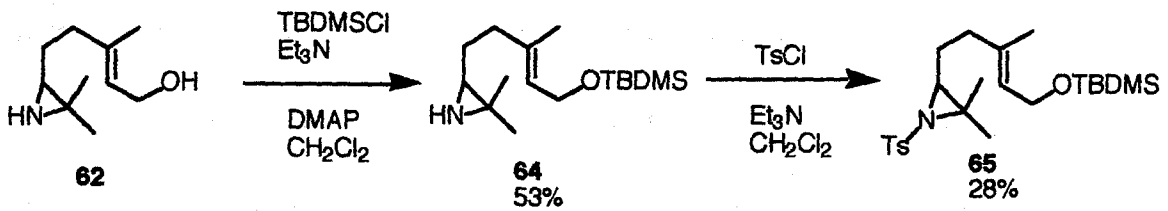
Stanchina[19] reports benzoylation of aziridine **62** or **63** to benzoyl aziridine **53** in 64% yield by treatment of **58** with two equivalents of benzoyl chloride and three equivalents of triethylamine for 2 hours at room temperature. However, repetition of this experiment gave lower than reported yields. In an attempt to optimize this reaction, the benzoylation was attempted at different temperatures and by varying the equivalents of both benzoyl chloride and triethylamine. It was found that the reaction gave the best yields when benzoyl chloride was added at 0 ^{0}C and the mixture was

then allowed to warm to room temperature. The use of three equivalents of benzoyl chloride and four equivalents of triethylamine was found to give the best yields. Since the aziridine product is acid sensitive, care was taken to avoid generation of acid in the reaction mixture during work-up. Since an aqueous work-up would have generated hydrochloric acid and benzoic acid from the hydrolysis of excess benzoyl chloride, the reaction was quenched with methanol. The resulting product methyl benzoate was separated from the desired aziridine through flash chromatography on silica gel using 1:9 Et_3N/ hexanes. The presence of triethylamine in the eluent was necessary since the benzoyl aziridine **53** is sensitive to the silica gel and undergoes decomposition unless the eluent is basic. Chromatographic purification gave a colorless oil in 72% yield for the geranyl isomer **53** and 69% yield for the neryl isomer **54**.

In addition to the benzoyl aziridines **53** and **54**, several other aziridines were also prepared. Addition of tosyl chloride to aziridino- alcohol **62** gave a complex mixture of unidentifiable products but not the desired tosyl aziridine. Since the allylic tosylate would be expected to be highly reactive, it is possible that the desired product formed but under the reaction conditions underwent further reactions. It was then decided to first protect the alcohol **62** before attempting tosylation of the aziridine. It was imporant to select a protecting group that would survive in the presence of Lewis acids. In a study devoted to developing Lewis acid promoted deprotections of trityl

groups, Jones[20] has shown that *t*-butyldimethylsilyl (TBDMS) ethers survive both BBr_3 and BCl_3. Therefore, it was thought that the TBDMS ether **65** would be unaffected by Lewis acids such as $BF_3{\cdot}Et_2O$ during the rearrangement. Compound **65** was successfully synthesized but unfortunately in the presence of $BF_3{\cdot}Et_2O$, **65** gave a complex unidentifiable mixture of products which did not contain the TBDMS group.

Scheme2.4

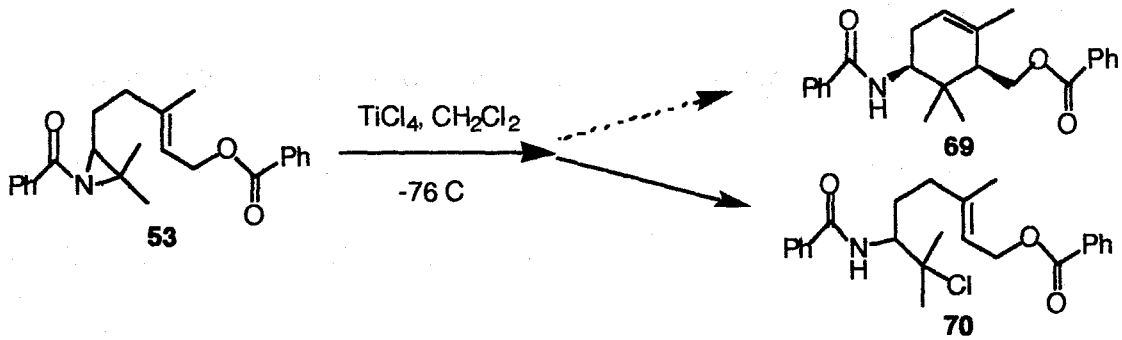


62 **64** 53% **65** 28%

B. Studies with geranyl and neryl benzoyl aziridines

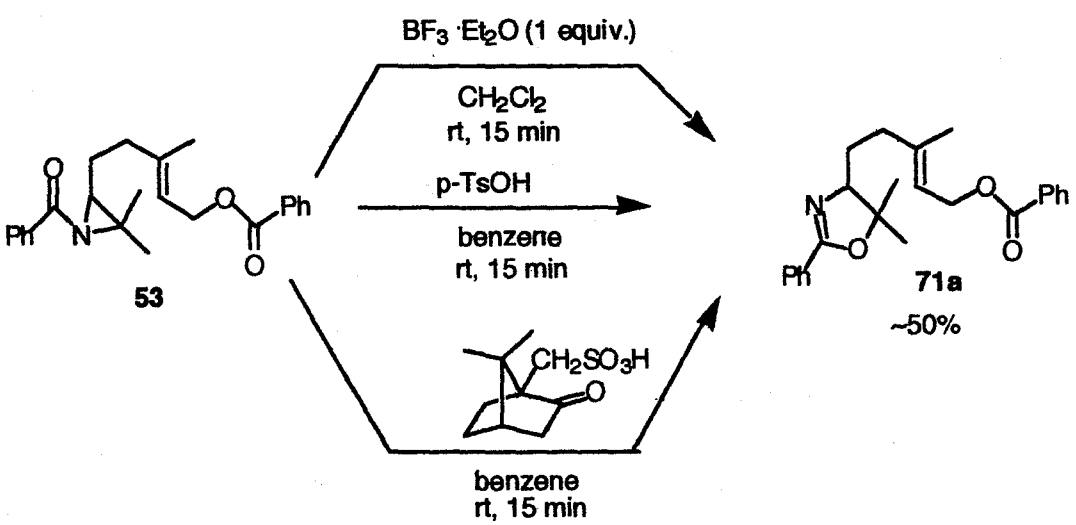
The initial rearrangement of aziridino-olefins was carried out as performed by Stanchina[17]. This involved the addition of 1 equivalent of $TiCl_4$ to benzoyl aziridine **53** in CH_2Cl_2 at –78 °C. When the reaction was quenched after 3 minutes and worked-up, a white crystalline solid was obtained in 49% yield. Stanchina initially assigned structure **69** to this product. However, the product failed elemental analysis for structure **69**. Repetitions of this reaction gave the same product based on NMR spectoscopy but it consistently failed elemental analysis. Due to the repeatability of the experiment and reproducibility of elemental analysis results, alternate structures were considered for the product of the $TiCl_4$ reaction. When the reaction product was treated with alcoholic silver nitrate, a white precipitate was obtained, suggesting the presence of chlorine. The results of both FAB spectroscopy (MW= 414.1) and elemental analysis are consistent with strucure **70.** Repetition of the $TiCl_4$ rearrangement with the neryl dibenzoate **54** gave similar results. Thus it was concluded that the $TiCl_4$ reaction resulted in adition of HCl to **53**. Since the product **70** was obtained even when $TiCl_4$ was freshly distilled (to eliminate presence of HCl), the product observed must arise by transfer of a chlorine from $TiCl_4$.

Scheme 2.5



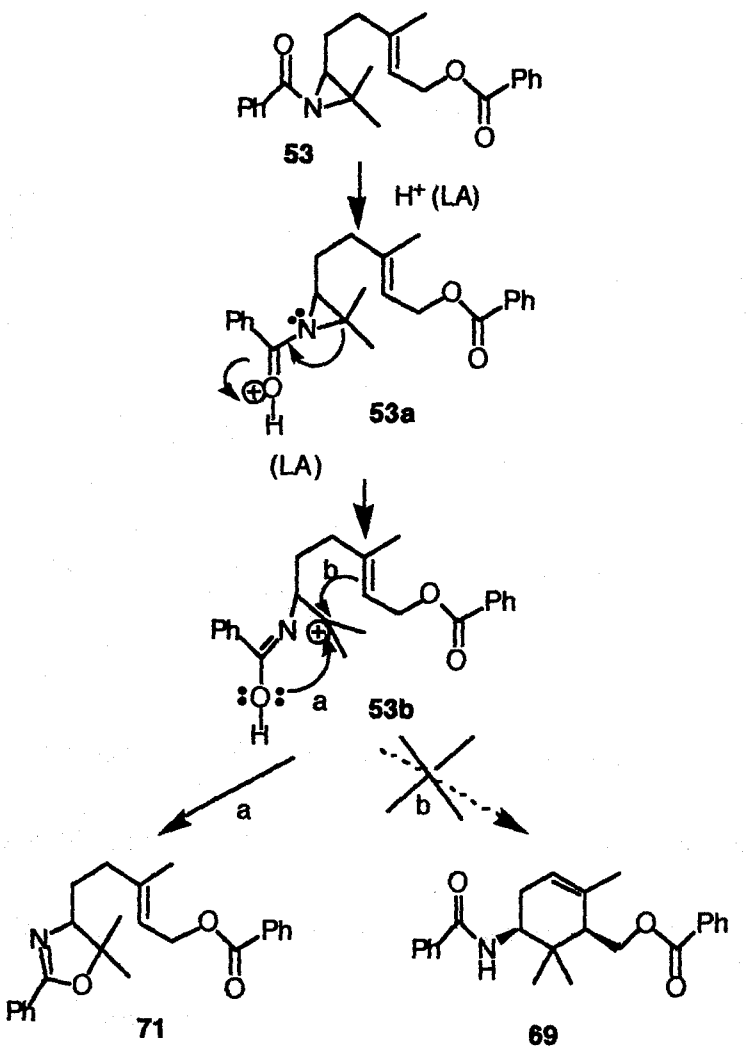
Since $TiCl_4$ failed to effect cyclization, it was decided to repeat the attempt at ring closure using other Lewis acids as well as protic acids. It was found that treatment of either the geranyl aziridine **53** or neryl aziridine **54** with boron trifluoride etherate gave the corresponding oxazoline product **71a** and **71b** in approximately 50% yield. Similar results were obtained upon treatment with camphor sulfonic acid as well as *p*-toluenesulfonic acid.

Scheme 2.6



One possible mechanistic explanation for the observed results is shown in scheme 2.7. It is proposed that the closure of **53b** to oxazoline **71** by path *a* is faster than ring closure via path *b* to give **69**. The formation of oxazolines from acyl aziridines has ample literature precedent (scheme 1.14, page 11).

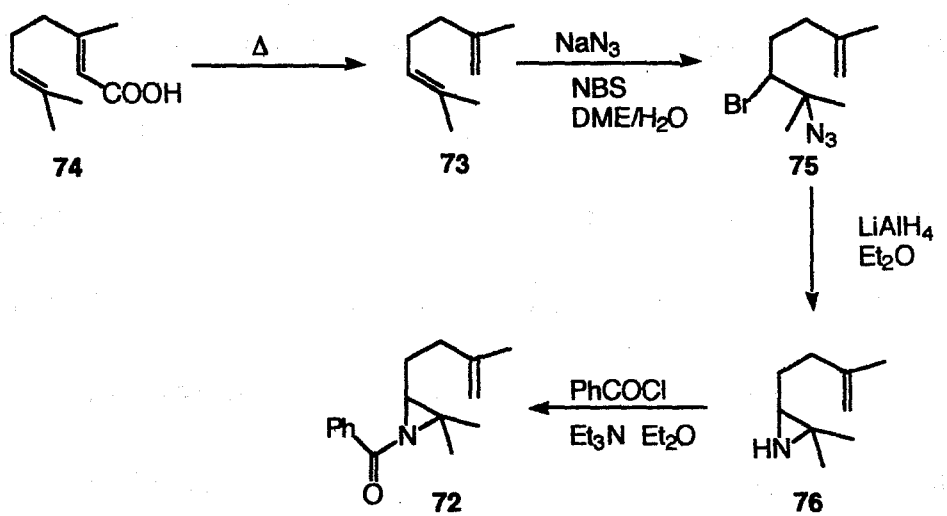
Scheme 2.7



C. Preparation of geraniolene derived aziridines

The failure of **53** and **54** to undergo the expected cyclization to the carbocyclic product suggested that the carbon-carbon double bond in these compounds is not sufficiently nucleophilic. Hence it was decided to prepare the benzoyl aziridine **72** derived from gerniolene **73** and attempt cyclization with this substrate.

Scheme 2.8



74 **73** **75** **76** **72**

Since the geraniolene derived aziridine **72** does not have a deactivating group, it was thought that this carbon-carbon double bond would be more nucleophilic and hence cyclization to give a six-membered ring would be expected to compete favorably with oxazoline formation.

Aziridine **72** was prepared by a route similar to that used for preparation of benzoyl aziridines developed by Stanchina. Geraniolene **73** was easily prepared by distillation of geranic acid **74**. Formation of the bromoazide was carried out as earlier discussed with a number of modifications. It was found that in order to attain good yields, ten equivalents of sodium azide were needed. Also, the sodium azide was dissolved in a minimal amount of DME and the NBS in a minimal amount of water prior to addition rather than adding the solids to the reaction mixture. The crude bromoazide **75** was purified through flash chromatography to give a clear liquid in 40% yield. Purification was found to be necessary since the crude bromoazide was found to be unstable over long periods of time, even at –20 °C.

The bromoazide **75** was reduced with $LiAlH_4$ to give aziridine **76** as a clear liquid in 73% yield. In this case, the reaction was less vigorous than was observed with bromoazides **60** and **61** (scheme 2.3, page 17). The reduction of this bromoazide **75** also took longer than the reductions of bromoazides **60** and **61**. The crude aziridine was not stable to silica and attempted purification did not yield any product.

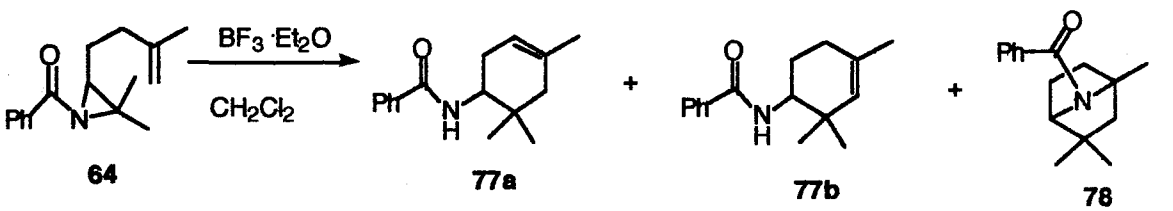
Benzoylation of **76** was performed with 1.5 equivalents of benzoyl chloride in triethylamine to give the benzoyl aziridine **72** in 69% yield after purification by flash chromatography. In this case the reaction was quenched with water instead of the methanol used in previous experiments due to similar polarity of the product **72** and methyl benzoate. This similarity made separation of the products by column

chromatography difficult. The reaction mixture contained 1.5 more equivalents of triethylamine mixture to prevent decomposition of the aziridine due to the liberated hydrochloric acid and benzoic acid. Like in earlier experiments, flash chromatography was performed in the presence of triethylamine to prevent decomposition.

D. Studies with geraniolene derived aziridines

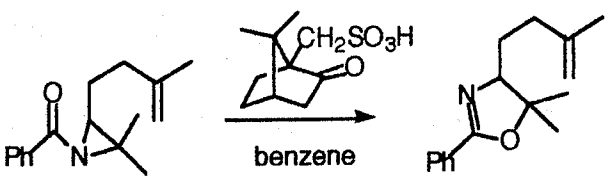
In the presence of one equivalent of $BF_3{\cdot}Et_2O$, aziridine **64** gave a mixture of products. Two fractions were isolated by column chromatography. The first fraction gave a crystalline solid which was determined to be a mixture of **77a** and **77b**. The second fraction gave a solid whose structure is not yet determined. One structure consistent with observed spectra is **78.**

Scheme 2.9



When aziridine **64** is treated with camphor sulfonic acid, a different product is observed. Thin layer chromatography shows formation of a single product which was identified as oxazoline **79**. This result is surprising based upon earlier results with aziridines **53** and **54** which gave the same product from reactions with boron trifluoride as well as camphorsulfonic acid. The results from these studies show that attack on the cation by the olefin to give **77a** and **77b** is faster with Lewis acids and attack by the carbonyl group to give **79** is faster with protic acids. However the reason for this observed trend is unclear at this time.

Scheme 2.10

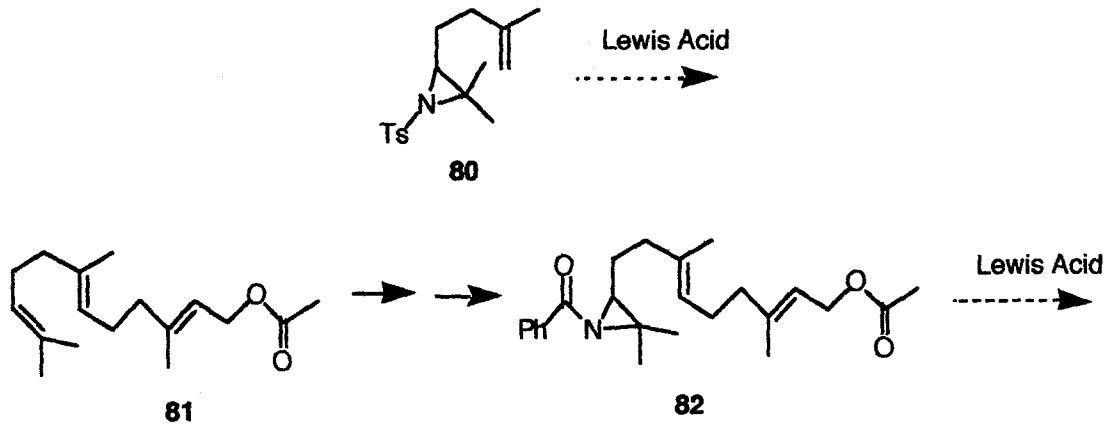


64 **79**

E. Future work

The results obtained in this study suggest two main possibilities for future study. First is the preparation and exploration of the tosyl aziridine **80** derived from geraniolene **73**.

Scheme 2.11



This aziridine is attractive for exploration for a number of reasons. As another derivative of geraniolene, it is similar in structure to the benzoyl aziridine **64** for which a cyclization has been demonstrated. In addition, the sulfur-oxygen double bond in the tosyl group is less basic than the carbonyl group in the benzoyl aziridine, which is likely to reduce the extent of attack by the sulfonyl oxygen.

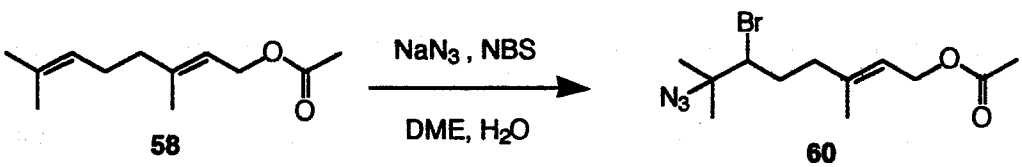
The other compound of interest for continuation of this study is farnesyl acetate **81**, which is another member of the isopreniod family. However, the central double bond in **82** is not deactivated, so it would be expected to be more nucleophilic then

the double bond in geranyl and neryl benzoates. In much the same manner as geranyl and neryl acetate, the benzoyl aziridine **82** can be prepared from farnesyl acetate. This synthesis has already been demonstrated by Krief.[18] The resulting aziridine can then be subjected to the same experiments already carried out in this study.

III. Experimental

General. All reagents were purchased from Aldrich Chemical Company, Fisher, or Baker. ^{1}H NMR spectra were recorded in $CDCl_3$ at 270 MHz (67.5 MHz for ^{13}C) on a JEOL Eclipse NMR spectrometer. Chemical shifts (δ) are reported in parts per million. Coupling constants (*J*) are reported in Hz. Abbreviations used in description of ^{1}H NMR spectra are s (singlet), d (doublet), t (triplet), and m (multiplet). Reactions were performed in flame-dried glassware under N_2 where appropriate. Reactions were followed by TLC on silica gel plates using phosphomolybdic acid (PMA) and/or UV light for visualization. All products were purified by flash chromatography on silca gel[20]. FAB and elemental analysis were performed at the University of Illinois.

SATI/111

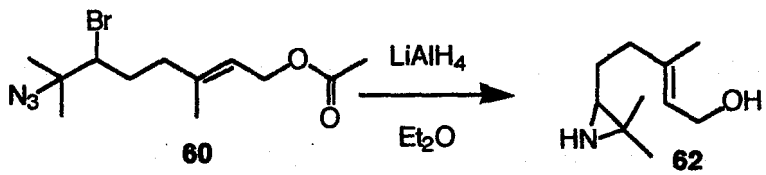


58 **60**

A biphasic mixture of NaN_3 (1.66 g, 25.4 mmol), DME (34 mL), water (9 mL), and geranyl acetate (1.0 g, 5.1 mmol) was stirred and cooled to –5 °C. NBS (1.27 g, 7.1 mmol) was added slowly over 15 minutes and the mixture stirred under nitrogen at –5 °C for 2.5 hours. Water (50 mL) was added and the aqueous layers were extracted with hexanes (4x25 mL). The organic extracts were combined, dried with Na_2SO_4, and concentrated to give 1.46 g of a clear liquid. One gram of the crude product was purified

by flash chromatography on 30 g silica gel using 3:7 EtOAc/hexanes to yield 0.21 g (19 %) of a yellow liquid. ^{1}H NMR ($CDCl_3$) **(SATI/111) (spectrum 1)** δ 1.30 (d, 6H, *J*=19 Hz) 1.67 (s, 4 H) 2.02 (s, 6H) 2.37 (m, 1H) 3.91 (d, 1H, *J*= 13.5, 1.35) 4.55 (d, 2H, *J*=8.1 Hz) 5.37 (t, 1H, *J*=8.1, 2.7 Hz) **^{13}CNMR (SATI/111) (spectrum 2)** δ 16.49, 21.11, 26.13, 26.58, 31.77, 38.15, 61.30, 70.16, 72.54, 119.69, 140.45, 171.21.

SATII/007

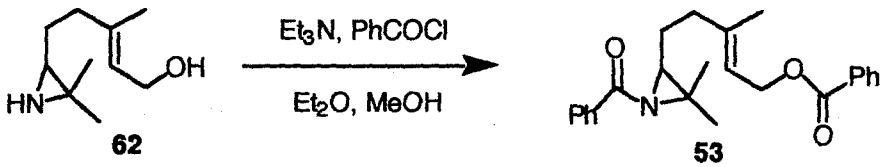


60 **62**

A solution of the bromoazide **60** (32.31 g, 81.5 mmol) in anhydrous diethyl ether (20 mL) was added dropwise over 45 minutes to a suspension of $LiAlH_4$ (9.30g, 0.245 mol) in 275 mL diethyl ether at 0 °C. The mixture was stirred for one hour and $LiAlH_4$ was quenched by slow sequential addition of water (12 mL), 3 M NaOH (12 mL), and water (32 mL).[17] The mixture was decanted and the salts washed with diethyl ether (3x100 mL). The filtrates were combined, dried (Na_2SO_4), and concentrated on a rotary evaporator to give 13.26 g of a yellow liquid. The crude product was purified by flash chromatography on 300 g silica using 7:2 EtOAc/MeOH to yield 7.00 g of a yellow oil (51% from geranyl acetate). ^{1}H NMR ($CDCl_3$) **(SATII/007)** (**spectrum 3**) δ 1.13 (s, 3H), 1.22 (s, 3H), 1.52 (m, *J*=8 Hz, 2H), 1.64 (s, 3H), 1.75 (t, *J*= 6 Hz, 1H), 2.10 (m, *J*=8 Hz,

2H), 4.10 (d, *J*=7 Hz, 2H), 5.39 (t, *J*=8 Hz, 1H). ^{13}C NMR ($CDCl_3$) **(SATII/007)** **(spectrum 4)** δ 16.3, 19.5, 22.2, 22.7, 36.2, 37.6, 43.4, 58.7, 124.6, 137.8.

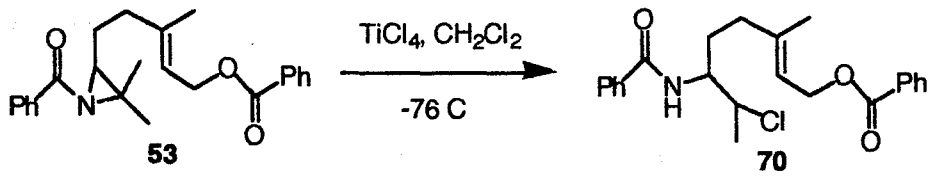
SATII/011



62 **53**

A solution of aziridino alcohol (**62**, 5.34 g, 31.7 mmol) in diethyl ether (150 mL) and triethylamine (12.87 g, 0.127 mol) was stirred and cooled to 0 ^{0}C as benzoyl chloride (13.38 g, 95.2 mmol) was added. After 1 1/2 hours at room temperature, methanol (20 mL) was added and the resulting suspension was stirred for an additional 30 min. Water (75 mL) was added and the aqueous layer was extracted with diethyl ether (4x60 mL). The organic layers were combined, washed with saturated $NaHCO_3$ (50mL), dried (Na_2SO_4), and concentrated to give 14.18 g of an oil that was purified through flash chromatography on 450 g silica gel using 1:9 Et_3N/hexanes to give 8.68 g (72%) yellow oil. ^{1}H NMR ($CDCl_3$) **(SATII/011)** **(spectrum 5)** δ 1.00 (s, 3H), 1.40 (s, 3H), 1.82 (s, 3H) 2.30 (t, *J*=8 Hz, 2H), 2.47 (m, 3H), 4.86 (d, *J*=7 Hz, 2H), 5.61 (t, *J*=7 Hz, 1H), 7.45 (m, 4H) 7.55 (m, 2H), 7.91 (d, *J*=8 Hz, 2H), 8.04 (dd, *J*=2,8 Hz, 2H) ^{13}C NMR ($CDCl_3$) **(SATII/011)** **(spectrum 6)** δ 16.80, 20.05, 23.30, 26.97, 37.38, 46.14, 46.28, 61.88, 118.98, 126.90, 128.37, 128.68, 128.80, 129.66, 130.52, 132.46, 132.88, 135.13, 141.64, 166.72.

SATI/191

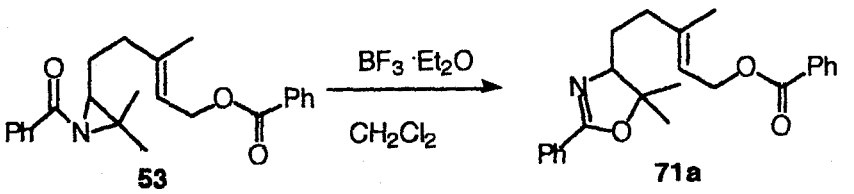


A solution of benzoyl aziridine **53** (0.4601g, 1.21 mmol) in CH_2Cl_2 (25 mL) was stirred and cooled to –65 ^{0}C as $TiCl_4$ (1.21 mL 1 M in CH_2Cl_2, 1.21 mmol) was added. The solution was stirred under nitrogen for 3 minutes and then quenched with a solution of triethylamine (1.21 g, 12 mmol) in methanol (10 mL). The resulting solution was allowed to warm to room temperature. Water (30 mL) was added and the aqueous layer was extracted with diethyl ether (3x 30 mL). The organic extracts were combined, dried with Na_2SO_4, and concentrated on a rotary evaporator. The residue was placed under vacuum (<1 mm Hg) for 2 hours to give 0.4099 g of a yellow oil. The crude product was purified by flash chromatography using 3:7 EtOAc/ hexanes to give 0.2245 g of a white solid. (49%) mp 114-118 ^{0}C ^{1}H NMR ($CDCl_3$) **(SATI/191) (spectrum 7)** δ 1.60 (s, 3H), 1.68 (s, 3H), 1.77 (s, 3H), 2.04 (s, 1H), 2.16 (t, *J*= 11 Hz, 2H), 4.25 (td, *J*=3, 13 Hz, 1H), 4.80 (d, *J*=7 Hz, 2H), 5.48 (td, *J*=1,7 Hz, 1H), 6.23 (d, *J*=10 Hz, 1H), 7.43 (m, 3H), 7.50 (m, 3H), 7.79 (dd, *J*=2, 8 Hz, 2H), 8.02 (dd, *J*=2, 8 Hz, 2H) ^{13}CNMR **(SATI/191) (spectrum 8)** δ 16.9, 29.0, 30.4, 31.2, 36.0, 57.6, 61.2, 74.9, 119.0, 127.0, 128.4, 128.8, 129.6, 130.5, 131.8, 132.9, 134.2, 141.5, 166.7, 167.4. **Elemental Analysis** calcd C 69.64

%, H 6.87 %, N 3.38 %, Cl 8.56 % obsd C 69.64 %, H 6.77 %, N 3.17 %, Cl 7.95 %

FAB calcd 413.98 obsd 414.18

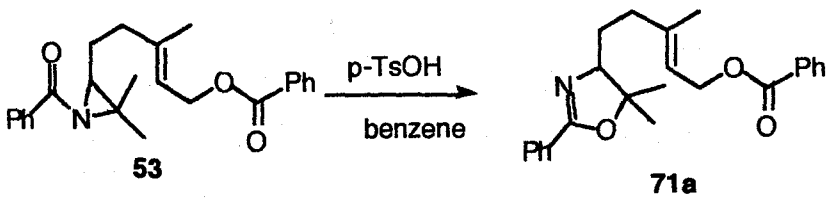
RAM2/027



53 **71a**

A solution of benzoyl aziridine **53** (110 mg, 0.291 mmol) in CH_2Cl_2 was stirred as $BF_3.Et_2O$ (41.4 mg, 0.32 mmol) was added. After 15 minutes, water (4 mL) was added followed by CH_2Cl_2 (15 mL) The aqueous layer was extracted with CH_2Cl_2 (10 mL). The organic extracts were combined, washed with NaCl (10 mL), dried (Na_2SO_4) and concentrated on a rotary evaporator to give 76 mg oil. The crude product was purified on 6 g silica using 1:4 EtOAc: hexanes to give 6.2 mg (6 %) white solid. (RAM2/027a) (this experiment was carried out by Dr. Ram Mohan) ^{1}H NMR ($CDCl_3$) **(RAM2/027a)** **(spectrum 9)** δ 1.38 (s, 3H), 1.51 (s, 3H), 1.81 (s, 3H), 2.24 (m, 1H), 2.50 (m, 1H), 3.81, (dd, *J*= 6.7, 8.1 Hz, 1H), 4.87 (d, *J*=8 Hz, 2H), 5.54 (t, *J*= 8 Hz, 1H), 7.42 (t, 4H), 7.49 (m, 4H), 8.02 (d, 4H) ^{13}C NMR ($CDCl_3$) **(RAM2/027)** **(spectrum 10)** δ 16.36, 21.56, 28.21, 29.35, 36.98, 61.66, 73.75, 86.09, 118.38, 128.02, 128.07, 128.12, 128.15, 129.41, 130.30, 130.90, 132.70, 142.02, 162.14, 166.44.

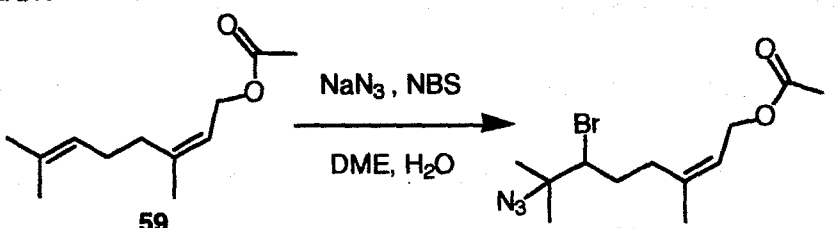
RAM2/023



53 **71a**

To a solution of benzoyl aziridine **53** (155 mg, 0.41 mmol) in benzene (1 mL) was added *p*-TsOH (78 mg, 0.41 mmol). The resulting solution was stirred at room temperature for one hour. The solution was diluted with Et_2O (15 mL), washed with $NaHCO_3$ (10 mL), NaCl (10 mL) dried (Na_2SO_4) and concentrated to give 77.6 mg oil. .(RAM2/0233) (this experiment was carried out by Dr. Ram Mohan) ^1H NMR ($CDCl_3$) spectrum of this product matches the spectrum RAM2/027a.

SATI/179

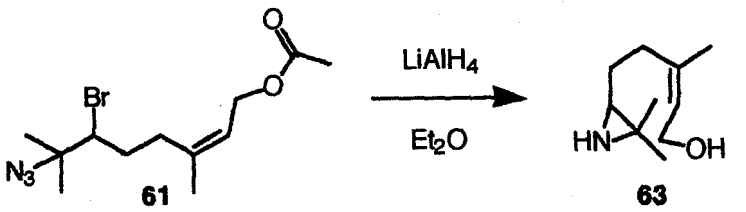


59 **61**

A mixture of NaN_3 (13.26 g, 0.204 mol), DME (270 mL), water (68 mL), and neryl acetate (8.0 g, 0.0408 mol) was stirred and cooled to –5 °C. NBS (13.26 g, 0.204 mol) was added slowly over 10 minutes and the mixture stirred under N_2 at –5 °C for 2 h.

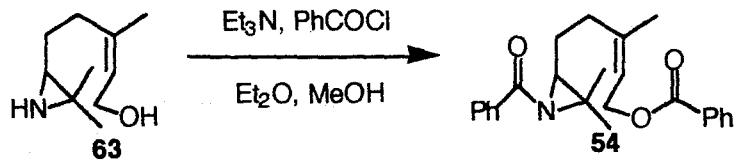
Water (200 mL) was added and the aqueous layer extracted with hexanes (5x100 mL). The organic extracts were combined, dried with Na_2SO_4, and concentrated to give 15.44 g of a clear liquid (product was not purified).

SATI/181



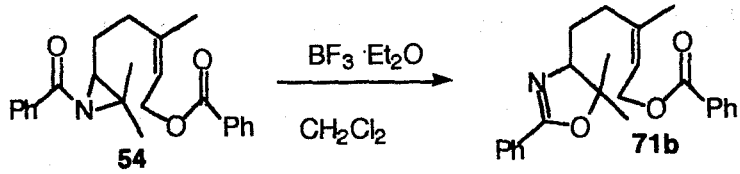
A solution of the bromoazide **61** (14.63 g) in diethyl ether (20 mL) was added dropwise over 45 minutes to a suspension of $LiAlH_4$ (4.42 g, 0.116 mol) in diethyl ether (275 mL) at 0 °C. The mixture was mechanically stirred for one hour, and excess $LiAlH_4$ was quenched by slow sequential addition of water (8 mL), 3M NaOH (8 mL), and water (20 mL). The mixture was decanted and the salts washed with diethyl ether (2x100 mL). The filtrates were combined, dried (Na_2SO_4), and concentrated to give 7.16 g of a yellow liquid. The crude product was purified by flash chromatography on 200 g silica using 7:2 EtOAc/MeOH to yield 4.39 g yellow oil (67.3% from neryl acetate). ^{1}H NMR ($CDCl_3$) **(SATI/181)** **(spectrum 11)** δ 1.08 (s, 3H), 1.17 (s, 3H), 1.36 (m, 1H), 1.54 (m, 1H), 1.66 (s), 1.95 (s, 3H), 2.11 (m, 2H), 4.04 (t, *J*= 5 Hz, 2H), 5.38 (t, *J*= 5 Hz, 1H). ^{13}C NMR ($CDCl_3$) **(SATI/181)** **(spectrum 12)** δ 19.60, 23.51, 27.21, 27.95, 29.98, 36.13, 43.31, 58.24, 125.42, 138.38.

SATII/013



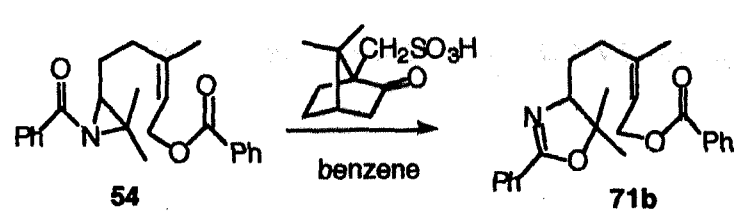
A solution of aziridine **63** (4.56 g, 27 mmol) in triethylamine (10.93 g, 0.108 mol) and diethyl ether (150 mL) was stirred and cooled to 0 °C as benzoyl chloride (11.38 g, 81 mmol) was added. The mixture was stirred overnight and then methanol (20 mL) was added. The resulting suspension was stirred for an additional 30 min. Water (75 mL) was added and the aqueous layer was extracted with diethyl ether (4x60 mL). The organic layers were combined, washed with saturated $NaHCO_3$ (50 mL), dried (Na_2SO_4), and concentrated to give 11.79 g of a yellow oil. The crude product was purified by flash chromatography on 260 g silica gel using 1:9 Et_3N/ hexanes to give 7.07 g (69%) of a yellow oil. ^1H NMR ($CDCl_3$) **(SATII/013) (spectrum 13)** δ 1.01 (s, 3H), 1.43 (s, 3H), 1.70 (m, 1H), 1.81 (s, 3H), 2.39 (t, *J*=10 Hz, 2H), 2.48 (t, *J*=10 Hz, 1H, =N**H**), 4.84 (d, J=8 Hz, 2H), 5.53 (t, *J*=5 Hz, 1H), 7.42 (m, 4H), 7.53 (m, 2H), 7.90 (d, *J*=8 Hz, 2H), 8.03 (d, *J*=8 Hz, 2H) ^{13}C NMR ($CDCl_3$) **(SATII/013) (spectrum 14)** δ 19.67, 23.24, 23.48, 27.42, 29.99, 45.89, 46.06, 61.38, 119.76, 128.20, 128.26, 128.65, 129.50, 130.32, 132.32, 132.72, 134.92, 141.79, 166.49, 178.71.

RAM2/029



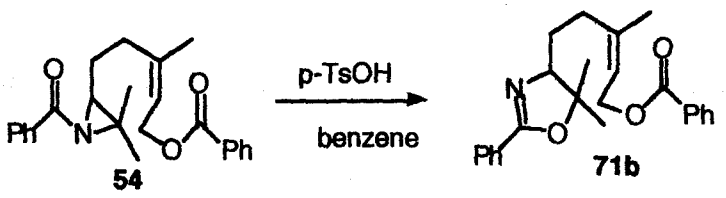
A solution of benzoyl aziridine **54** (200 mg, 0.53 mmol) in CH_2Cl_2 (2 mL)was stirred as $BF_3.Et_2O$ (82.7 mg, 0.58 mmol) was added. After 15 minutes, water (4 mL) was added followed by CH_2Cl_2 (15 mL) The aqueous layer was extracted with CH_2Cl_2 (10 mL). The organic extracts were combined, washed with saturated NaCl (10 mL), dried (Na_2SO_4) and concentrated to give 174 mg oil. The crude product was purified on 10 g silica using 1:4 EtOAc: hexanes to give 58 mg (29 %) white solid. (RAM2/029) (this experiment was carried out by Dr. Ram Mohan) ^{1}H NMR ($CDCl_3$) **(RAM2/029) (spectrum 15)** δ 1.35 (s, 3H), 1.48 (s, 3H),1.63 (m, 2H), 1.83 (s, 3H), 2.47 (m, 2H), 3.76, (dd, *J*= 6, 7 Hz, 1H), 4.90 (d, *J*=8 Hz, 2H), 5.54 (t, *J*= 8Hz, 1H), 7.42 (t, 4H), 7.49 (m, 4H), 8.02 (d, 4H). ^{13}C NMR ($CDCl_3$) **(RAM2/029) (spectrum 16)** δ 21.74, 23.60, 28.44, 30.07, 61.64, 73.76, 86.47, 119.81, 128.34, 129.64, 130.55, 131.43, 132.83, 142.79, 162.54, 166.68.

RAM2/075



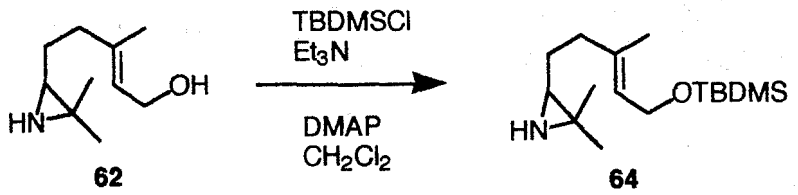
A solution of benzoyl aziridine **54** (0.5 g, 1.32 mmol) in benzene (5 mL)was stirred as camphor sulfonic acid (0.308 g, 1.32 mmol) was added. After 15 minutes, water (15 mL) was added and the mixture diluted with Et_2O (40 mL) The organic layer was separated, washed with sat. $NaHCO_3$ washed with NaCl, dried (Na_2SO_4) and concentrated to give 0.51 g colorless oil. The crude product was purified on 25 g silica using 3:7 EtOAc: hexanes. (RAM2/075) (this experiment was carried out by Dr. Ram Mohan) ^1H NMR spectrum ($CDCl_3$) of this product matches RAM2/029.

RAM2/027



A solution of benzoyl aziridine **54** (1.07 g, 2.84 mmol) in benzene (10 mL) was stirred as *p*- TsOH (0.541 g, 2.84 mmol) was added. After 55 minutes, water (10 mL) was added, followed by Et_2O (15 mL). The aqueous layer was extracted with Et_2O (15 mL). The combined organic extracts were washed with sat. $NaHCO_3$ (15 mL), NaCl (15 mL), dried (Na_2SO_4) and concentrated to give 0.84 g of a colorless oil. The crude product was purified on 30 g silica using 1:4 EtOAc: hexanes to give 0.29 g. (RAM2/035) (this experiment was carried out by Dr. Ram Mohan) ^1H and ^{13}C NMR match RAM2/027.

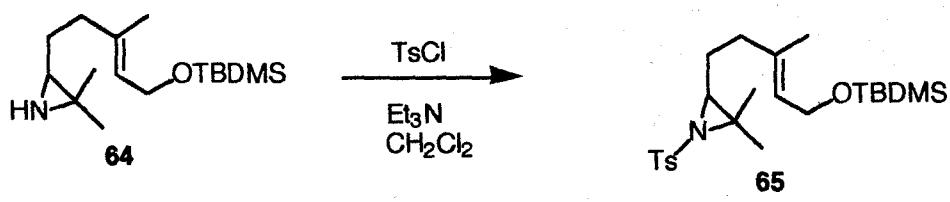
SAT2/029



62 **64**

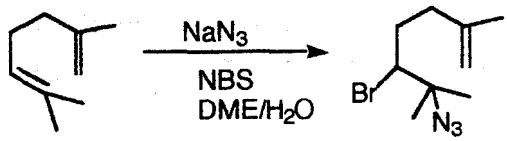
A solution of aziridine **62** (1.00g, 5.9 mmol) in anhydrous CH_2Cl_2 (10 mL) was stirred at room temperature under nitrogen as Et_3N (0.99 mL, 7.10 mL), DMAP (0.36 g, 2.96 mmol), and TBDMSCl (1.07 g, 7.1 mmol) were added. After 20 minutes the solution was diluted with CH_2Cl_2 (25 mL). The organic layer was washed with water (4x 20 mL) and saturated NaCl (20 mL) and then dried (Na_2SO_4). The solvent was removed to give 1.57 g clear liquid. The crude product was purified twice on silica gel using 75 and 115 g of silica gel with 1:2 MeOH/EtOAc to give 0.8997 g of a clear oil. (53 %) ^{1}H NMR ($CDCl_3$) (**SATII/029**) (**spectrum 17**) δ 0.05 (s, 6H), 0.88 (s, 9H), 1.187 (s, 3H), 1.26 (s, 3H), 1.62 (s, 3H), 1.82 (t, *J*= 7 Hz, 2H), 2.12 (q, *J*= 7 Hz, 2H), 3.44 (s, <1H, impurity), 4.17 (d, *J*= 6Hz, 2H), 5.31 (t, *J*= 6 Hz, 2H) ^{13}C NMR ($CDCl_3$) (**SATII/029**) (**spectrum 18**) δ -5.0, 16.43, 18.48, 19.69, 26.07, 27.53, 28.16, 35.88, 37.74, 43.23, 60.31, 124.80, 136.46.

SATII/033



A solution of **64** (0.50 g, 1.77 mmol) and Et_3N (0.54 mL, 3.9 mmol) in anhydrous CH_2Cl_2 (10 mL) was stirred at 0 °C as TsCl (0.37 g, 1.95 mmol) was added. After 1.5 hours, the solution was diluted with CH_2Cl_2 (40 mL) and washed with water (3 x 30 mL) and saturated NaCl (30 mL). The organic layer was dried (Na_2SO_4) and concentrated on a rotovap to give 0.78 g of a yellow oil. (101 %) The crude product was purified on 50 g silica gel using 1:4 EtOAc/ hexanes to give 0.22 g clear liquid (28%) ^1H NMR ($CDCl_3$) **(SATII/033) (spectrum 19)** δ 0.00 (s, 6H), 0.85 (s, 9H), 1.21 (s, 3H), 1.46 (s, 3H), 1.65 (s, 3H), 1.97 (s, <1H), 2.35 (s, 3H), 2.76 (t, *J*= 1.7 Hz 1H,), 4.08 (d, 2H, *J*= 6Hz), 5.13 (t, 1H, *J*= 5Hz), 7.24 (d, 2H, *J*= 7.9Hz), 7.76 (d, 2H, *J*= 8.1Hz) ^{13}C NMR ($CDCl_3$) **(SATII/033) (spectrum 20)** δ -5.05, 14.19, 16.33, 18.43, 21.25, 21.34, 21.59, 22.69, 26.04, 26.23, 31.63, 36.96, 51.90, 52.44, 60.13, 60.36, 125.03, 127.41, 129.40, 135.55, 138.45, 143.58

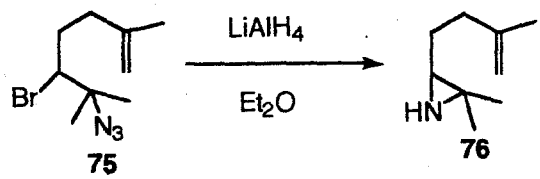
SATII/067



73 **75**

To a solution of geraniolene **73** (7.50 g, 0.060 mol) in DME (50 mL) was added NaN_3 (39.00 g, 0.60 mol) in minimal water (~150 mL). The clear solution was cooled to 0 ^{0}C and NBS (16.11 g, 0.090 mol) in minimal DME (~300 mL) was added over 10 minutes. The reaction was stirred for 3 hours and then water (150 mL) was added. The aqueous layer was extracted with hexanes (4 x 200 mL) and the combined organic extracts were dried (Na_2SO_4) and concentrated on a rotary evaporator to give 14.37 g of a clear yellow liquid. The crude product was purified in two portions using 300 g silica each time with 1:19 EtOAc/ Hexanes as eluent to give a combined yield of 5.61 g (40%) of a clear liquid. ^{1}H NMR ($CDCl_3$) **(SATII/067) (spectrum 23)** δ 1.41 (s, 3H), 1.47 (s, 3H), 1.73 (s, 3H), 2.12 (m, 2H), 2.31 (m, 2H), 3.80 (dd, 1H, *J*= 11.3, <2 Hz), 4.75 (d, 2H, *J*=9 Hz) ^{13}C NMR ($CDCl_3$) **(SATII/067) (spectrum 24)** δ 22.36, 23.01, 25.31, 31.42, 36.05, 63.86, 64.22, 111.47, 143.88.

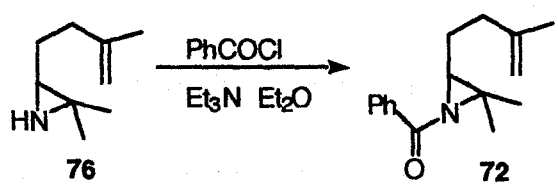
SAT2/069



75 **76**

To a mechanically stirred suspension of $LiAlH_4$ (2.70 g, 0.711 mol) in Et_2O (50 mL) at 0°C was added compound **75** (5.50 g, 0.0237 mol) in Et_2O (10 mL) dropwise over 10 min. The resulting mixture was stirred under N_2 for 2 hours at 0 °C. Water (12 mL), 3M NaOH (8 mL) and additional water (8 mL) were added dropwise over 25 min. The salts were collected by suction filtration and washed with Et_2O (75 mL). The filtrates were dried (Na_2SO_4) and concentrated on a rotovap at low temperature under house vacuum to give 2.57 g (73%) of a clear liquid. ^1H NMR ($CDCl_3$) **(SATII/069) (spectrum 25)** δ 0.5 (s, 1H), 1.06 (s, 3H), 1.15 (s, 3H), 1.46 (m, 2H), 1.65 (s, 3H), 2.04 (q, 2H, *J*=7.6 Hz), 4.61 (s, 2H) ^{13}C NMR ($CDCl_3$) **(SATII/069) (spectrum 26)** δ 19.69, 22.45, 27.55, 28.15, 35.53, 36.02, 43.04, 110.06, 145.34.

SATII/075

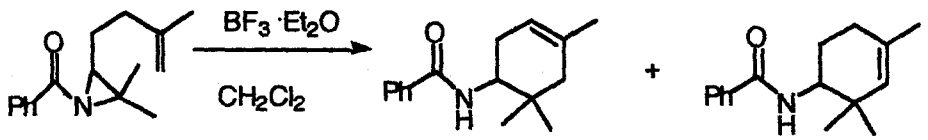


76 **72**

To a solution of compound **76** (1.00 g, 7.18 mmol) in Et_3N (3.00 mL, 21.5 mmol) and Et_2O (15 mL) at 0°C was added benzoyl chloride (1.25 mL, 10.7 mmol). The resulting mixture was stirred under N_2 overnight. Water (20 mL) was added and the

aqueous layer was extracted with ether (4x 30 mL). The organic extracts were combined, washed with saturated $NaHCO_3$ (15 mL), dried (Na_2SO_4), and concentrated on a rotary evaporator to give 2.13 g of a yellow liquid. The crude product was purified on 60 g silica using 1:9 Et_3N: hexanes. To the resulting product was added pentane (~ 30 mL). The solution was washed with water (2 x 10 mL), dried (Na_2SO_4) and concentrated to give 1.19 g (69%) of a clear liquid. ^1H NMR ($CDCl_3$) **(SATII/075) (spectrum 27)** δ 1.00 (s, 3H, =C**H**$_3$), 1.42 (s, 3H, =C**H**$_3$), 1.80 (s, m, 5H, =C**H**$_3$, C**H**$_2$), 2.22, (t, 2H, *J*=7.2 Hz, =C**H**$_2$), 2.47 (t, 1H, *J*= 6.8 Hz, =NC$_2$C**H**), 4.73 (s, 2H, =C=C**H**$_2$), 7.42 (m, 2H), 7.52 (m 1H), 7.90 (dd, 2H) ^{13}C NMR ($CDCl_3$) **(SATII/075) (spectrum 28)** δ 20.01, 22.67, 23.47, 27.00, 35.66, 46.24, 110.35, 128.40, 128.80, 132.44, 135.17, 145.18, 178.97.

SATII/091

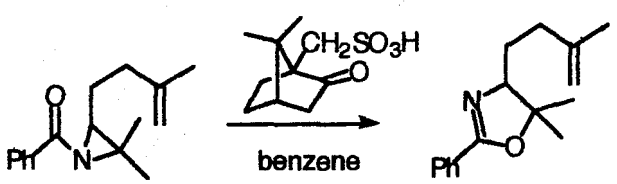


64 **77a** **77b**

To a solution of compound **64** (0.1827 g, 0.75 mmol) in CH_2Cl_2 (5 mL) was added $BF_3.Et_2O$ (0.085 g, 0.75 mmol). The solution was stirred at 0 °C for 10 min then quenched with water (5 mL). The aqueous layer was extracted with ether (3x 15 mL). The organic extracts were combined, dried (Na_2SO_4) and concentrated on a rotovap to give 0.1582 g of a white solid. The crude product was purified on 6 g silica using 1:9 EtOAc/ Hexanes to give 0.064 g of a white solid. (35%) ^1H NMR ($CDCl_3$) **(SATII/091)**

(**spectrum 29**) δ 0.93 (s), 0.98 (s), 1.01 (s), 1.06 (s), 1.67 (s), 1.87 (s), 2.40 (broad s), 2.48 (broad s), 4.12 (m), 5.14 (s), 5.30 (s), 6.01 (m), 7.44 (m), 7.73 (m). ^{13}CNMR ($CDCl_3$) (**SATII/091**) (**spectrum 30**) δ 23.74, 23.90, 26.97, 30.04, 33.37, 42.57, 51.57, 117.67, 126.87, 128.63, 131.34, 133.25, 135.30, 167.29 minor peaks δ 23.6, 24.1, 25.4, 28.4, 29.0, 35.6, 53.0, 130.8, 131.9, 167.2.

SATII/081



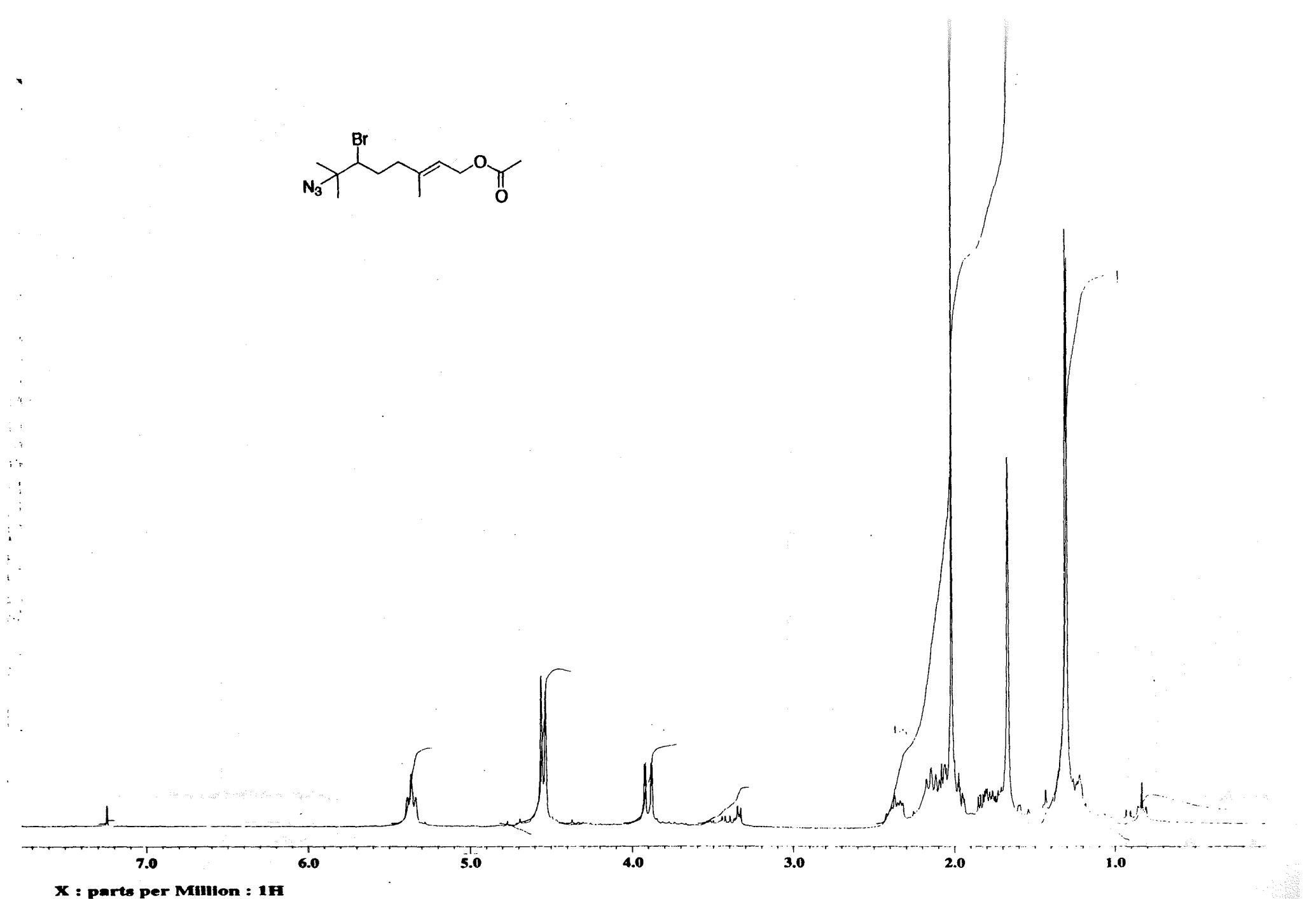
64 **79**

To a solution of compound **64** (0.0432 g, 0.18 mmol) in benzene (1 mL) at 10 °C was added camphorsulfonic acid (0.041 g, 0.18 mmol). The solution was stirred at 10 °C for 15 min and then quenched with water (3 mL). The aqueous layer was extracted with ether (3x 5 mL). The organic extracts were combined, dried (Na_2SO_4) and concentrated on a rotovap to give 0.1466 g of a yellow liquid. The crude product was purified on 1 g silica using 1:9 EtOAc/ Hexanes to give 74mg of a white solid. (17%) %) ^{1}H NMR ($CDCl_3$) (**SATII/081**) (**spectrum 31**) δ 1.37 (s, 3H, =C**H**$_3$), 1.51 (s, 3H, =C**H**$_3$), 1.76 (s, 3H, =C**H**$_3$), 2.18 (m, 2H, =C**H**$_2$), 2.42 (m, 2H, =C**H**$_2$), 3.84 (t, *J*= 5 Hz, 1H, , =NC$_2$C**H**) 4.75 (broad s, 2H, =C=C**H**$_2$), 7.40 (m, 3H, =Ar**H**), 8.05 (m, 2H, =Ar**H**)

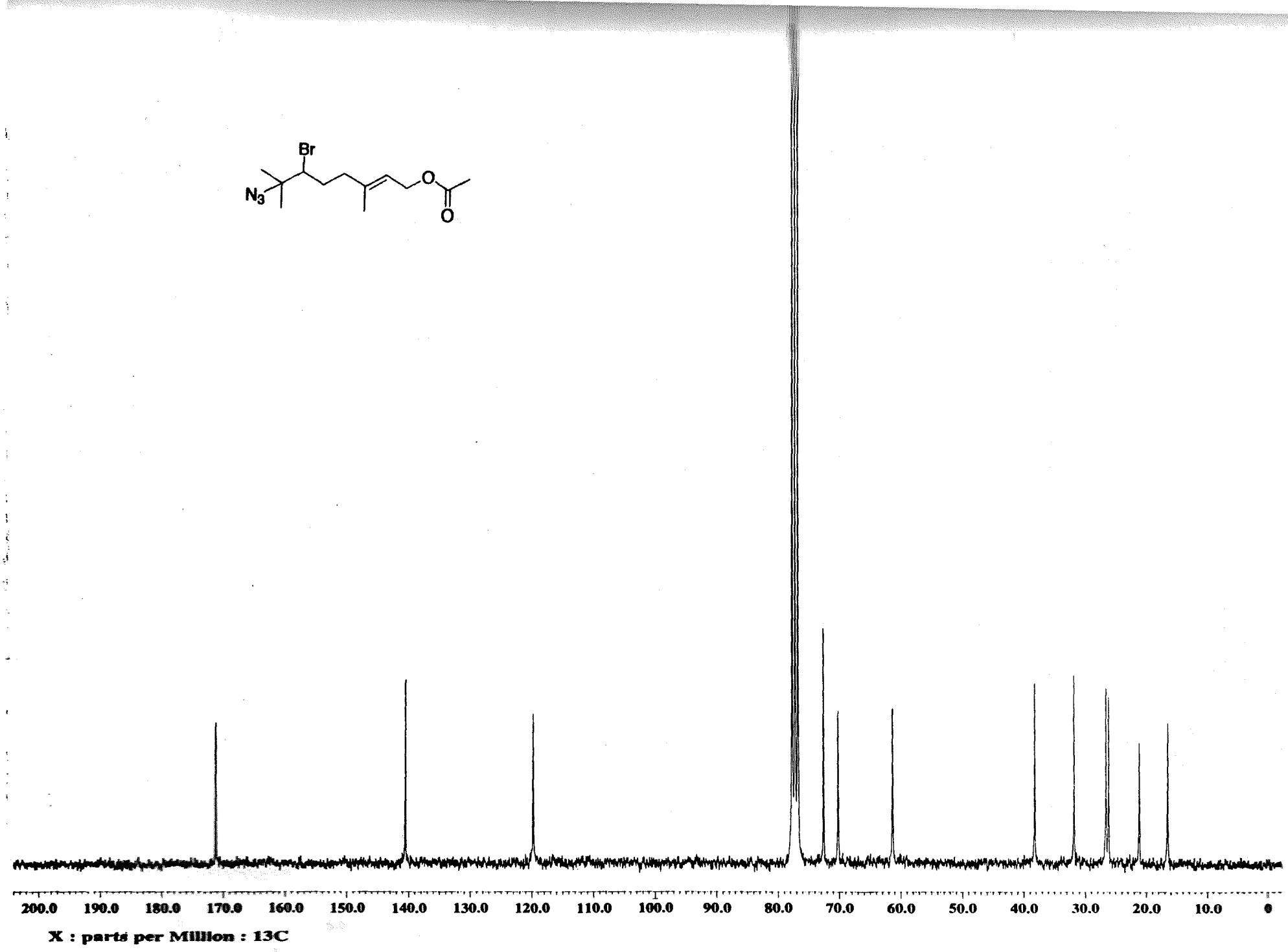
IV. References

1. Morrison, James. Asymmetric Synthesis. Vol. 3, Academic Press, Orlando 1984.
2. Hesler, E.J.; Schwartz, M.A.; Storni,A.; van Tamelen, E.E. *Bioorg. Chem.* **1982,** *11*, 133.
3. Tanner, D. *Angew. Chem. Int. Ed. Engl.* **1994,** *33*, 599.
4. Van Der Plas, H. Ring Transformations of Heterocycles. Vol 1, Academic Press, New York 1973.
5. Goldsmith, D. *J. Am. Chem. Soc.* **1962,** 3913.
6. Goldsmith, D. *Tet. Let.* **1966**, *13*, 1215.
7. Van Tamelen, E. E.; Nadeau, R.G. *Bioorganic Chemistry.* **1982,** *11*, 197.
8. Coates, R.; Yee, N. *J. Org. Chem.* **1992,** *57*. 4598.
9. Seebach, D. *Chem. Lett.* **1987,** *49*.
10. Heine, H.; Kenyon, W.; Johnson, E. *J. Am. Chem. Soc.* **1961,** *83*, 2570.
11. Heine, H.; Brooker, A. *J. Org. Chem.* **1962,** *27*. 2943.
12. Weissberger, Arnold. Heterocyclic Compounds with Three- and Four-Membered Rings. Interscience Publishers, New York, 1964.
13. Heine H. *J. Org. Chem* **1958**, *23*, 1554.
14. Bergmeier, S.; Seth, P. *Tet. Let.* **1995**,*36*, 2793.
15. Bergmeier, S.; Fundy, S.; Seth, P. *Tet. Let.* **1999**,*55*, 8025.
16. Bergmeier, S.; Seth, P. *J. Org. Chem.*. **1999**,*64*, 3237.
17. Jones, G.; Landais, Y. *Tetrahedron.* **1996**, *52*, 7599.
18. Krief, A.; Van Ende, D. *Angew. Chem. Int.* **1974**, *13*, 279.
19. Stanchina, C. Masters thesis, University of Illinois, 1998.
20. Jones, G.; Hynd, G.; Wright, J.; Sharma, A. *J. Org. Chem* **2000**, *65*, 263.
21. Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

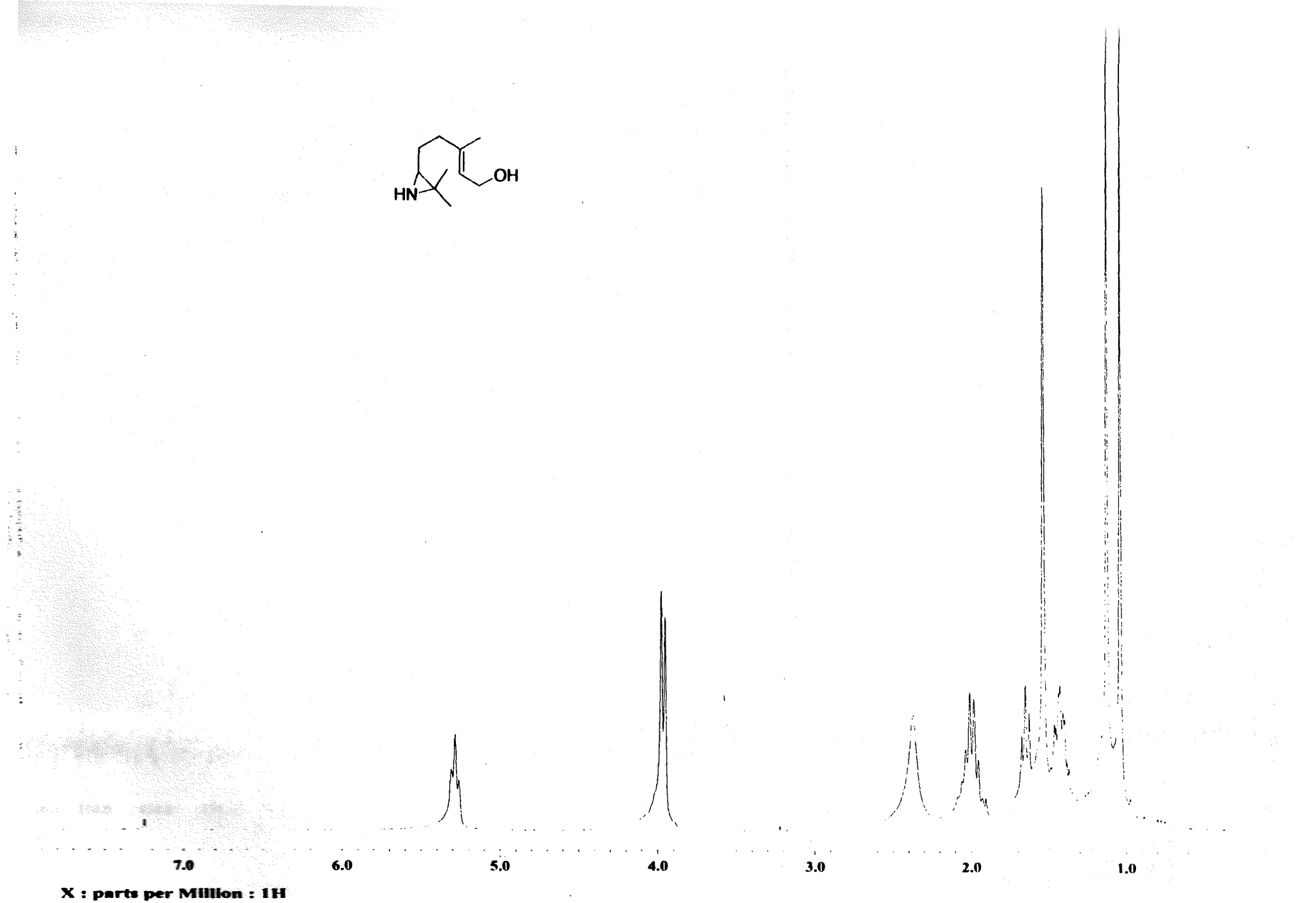
V. Appendix: Spectral Data



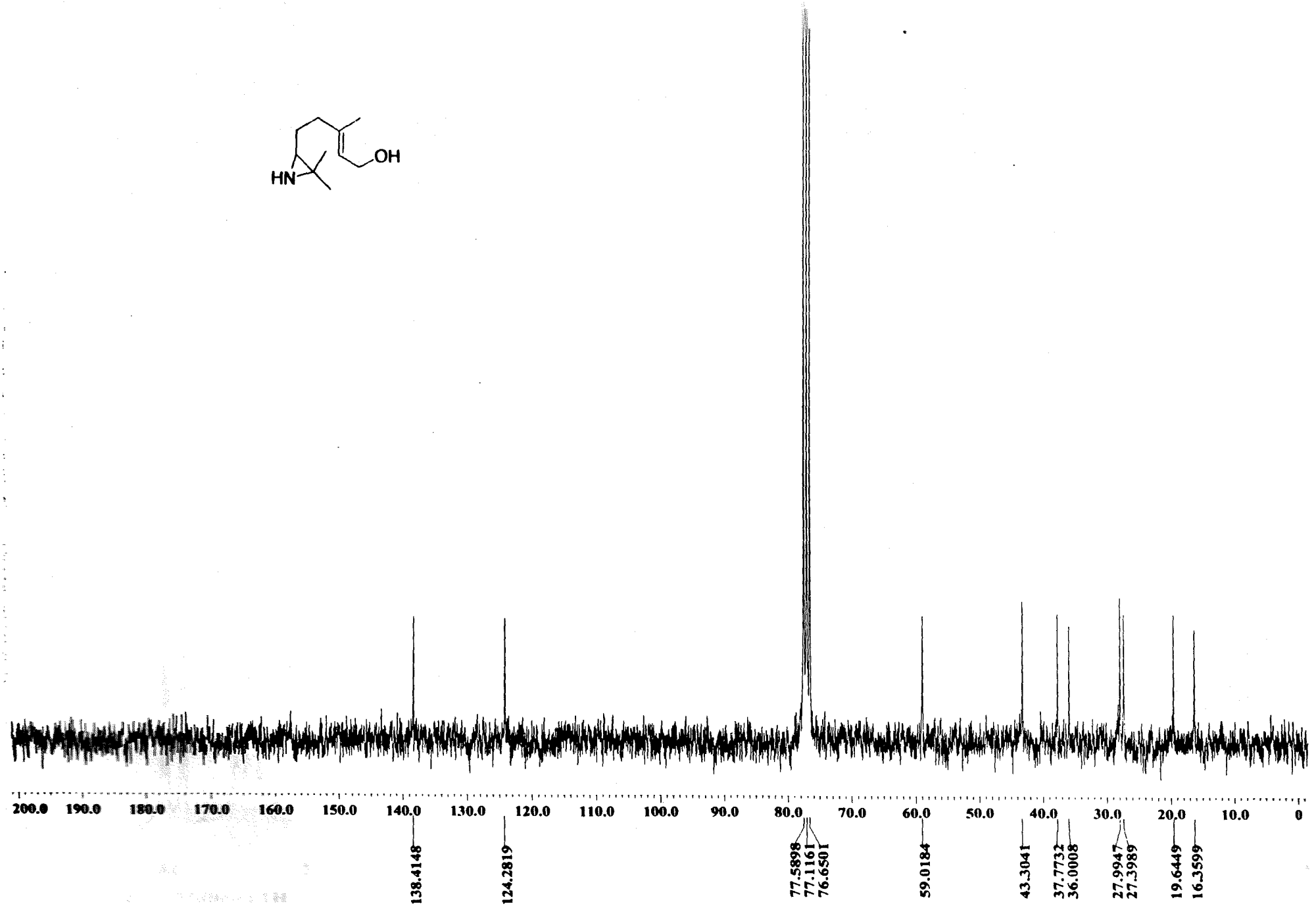
Spectrum 1 ^{1}H NMR of compound **60** (SATI/111)



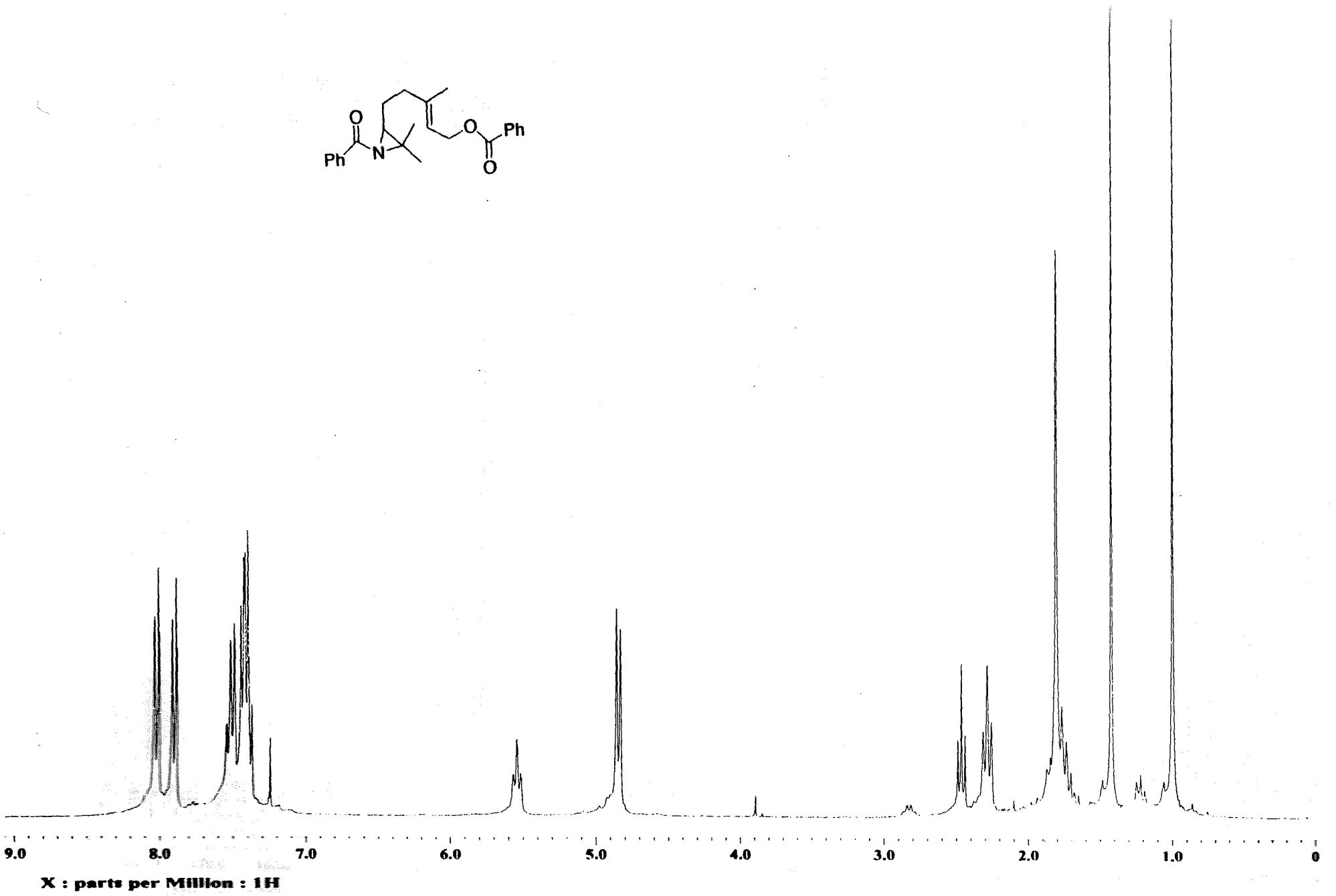
Spectrum 2 ^{13}C NMR of compound **60** (SATI/111)



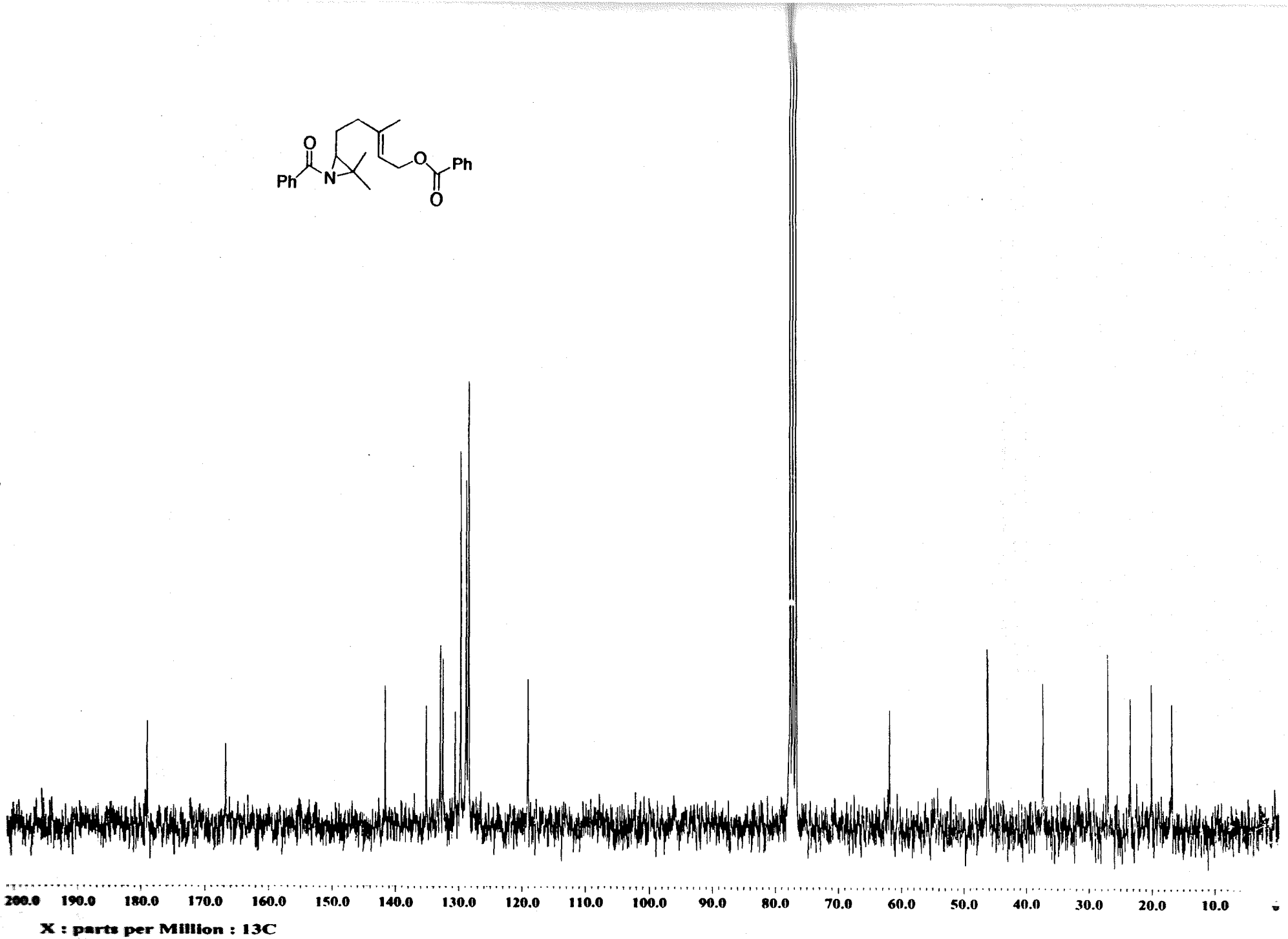
Spectrum 3 ^{1}H NMR of compound **62** (SATII/007)



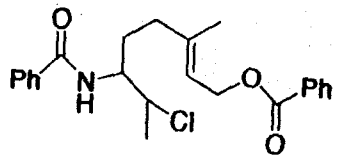
Spectrum 4 ^{13}C NMR of compound **62** (SATII/007)



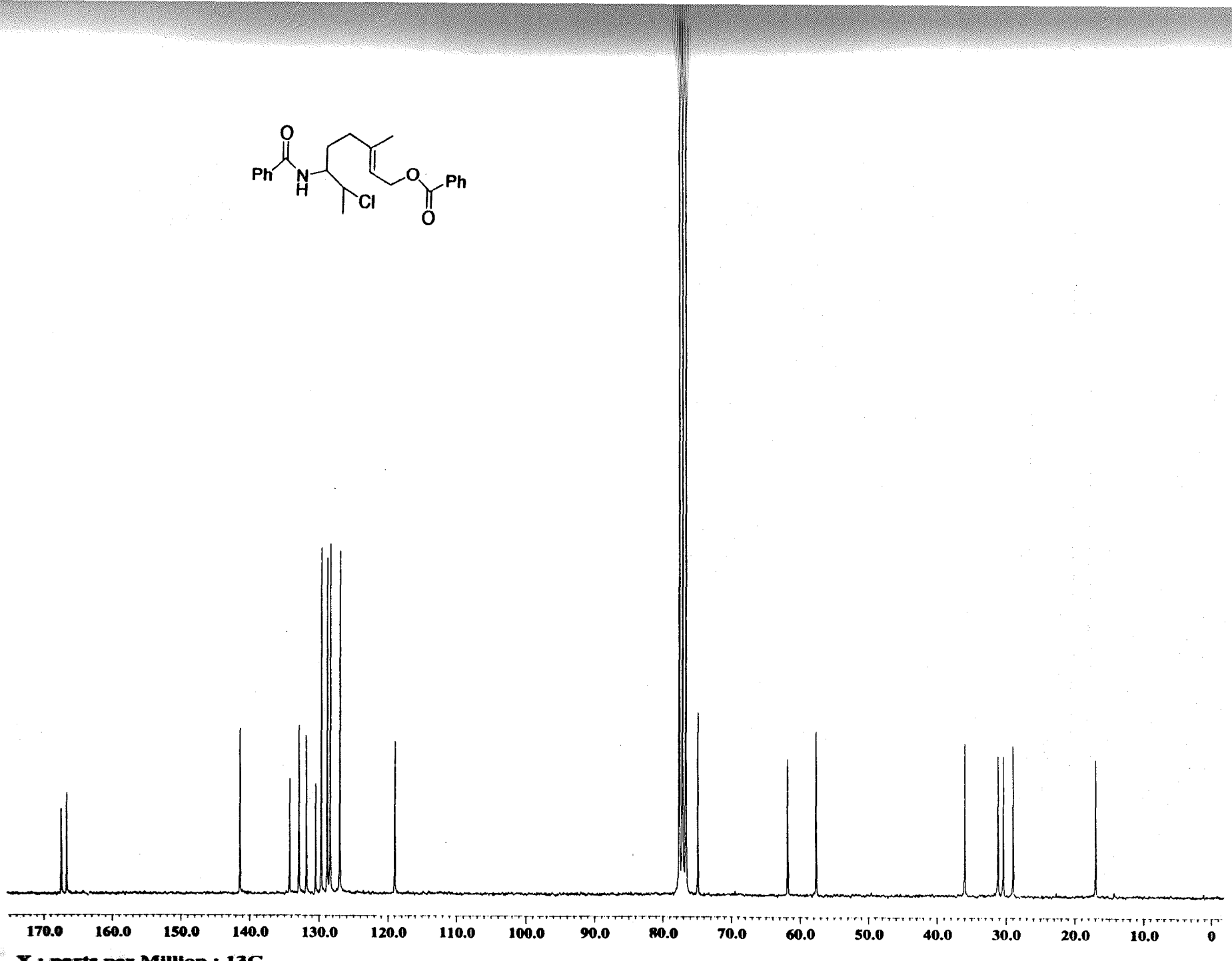
Spectrum 5 ^{1}H NMR of compound **53** (SATII/011)



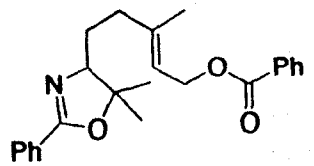
Spectrum 6 ^{13}C NMR of compound **53** (SATII/011)



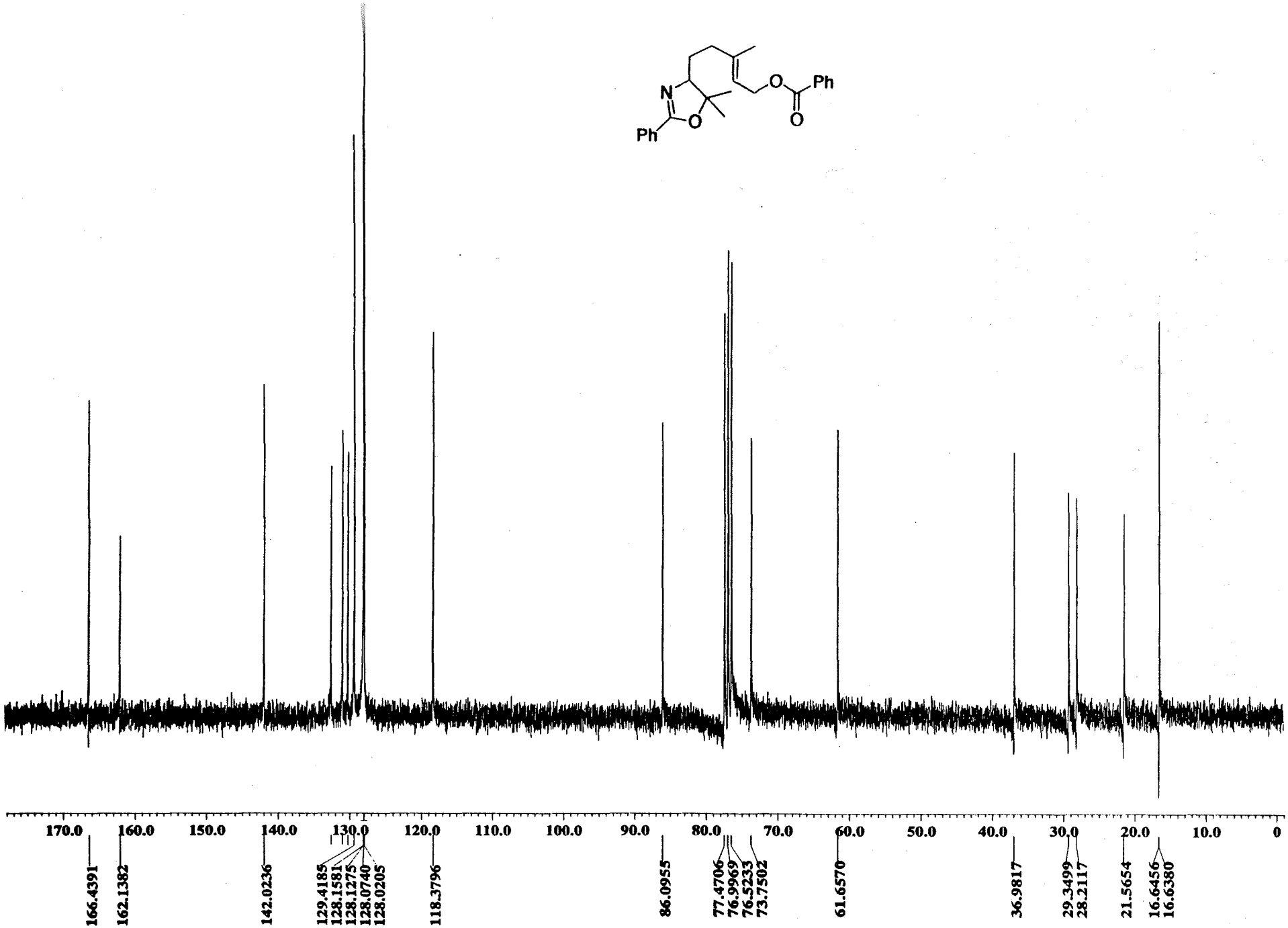
Spectrum 7 ^{1}H NMR of compound **70** (SATI/191)



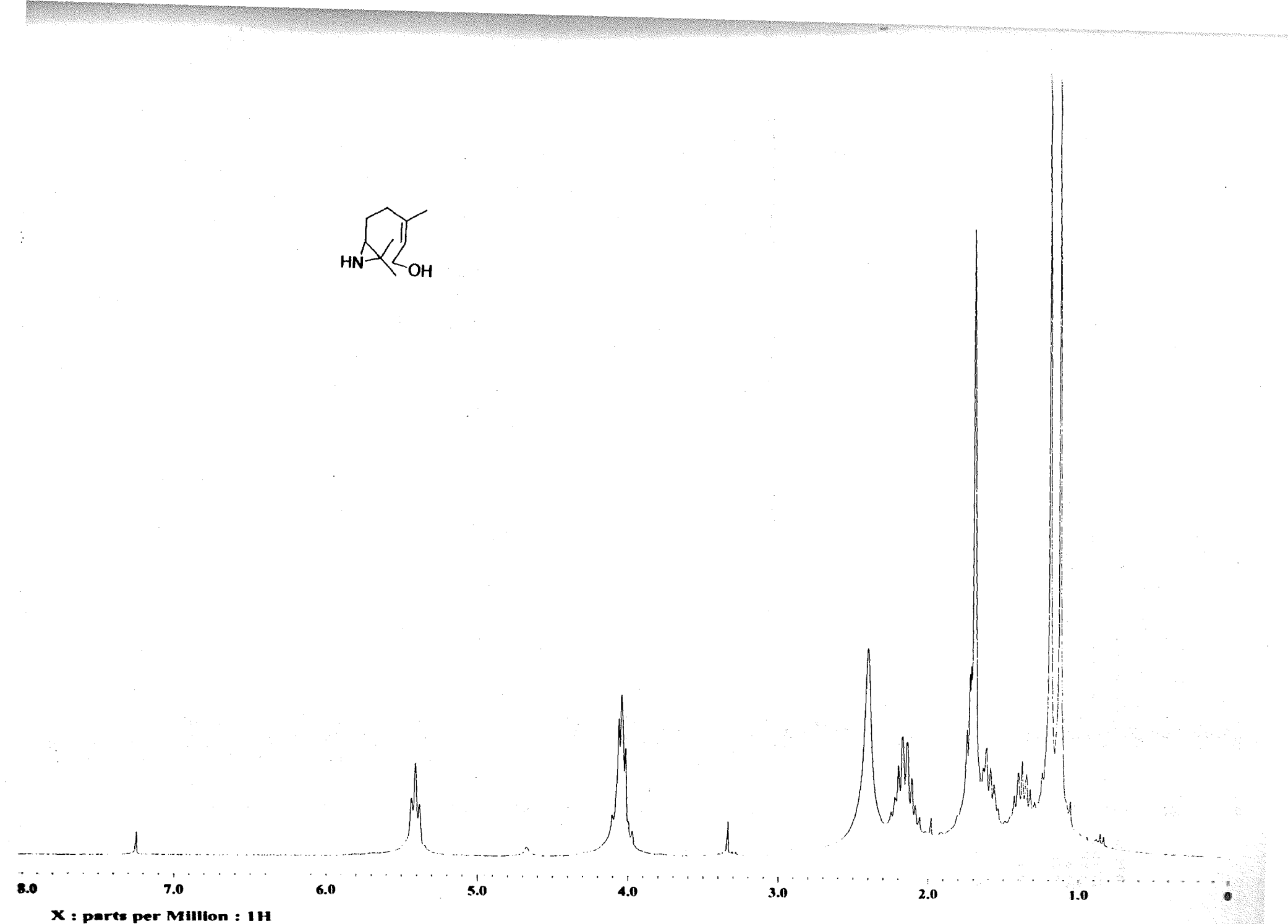
Spectrum 8 ^{13}C NMR of compound **70** (SATI/191)



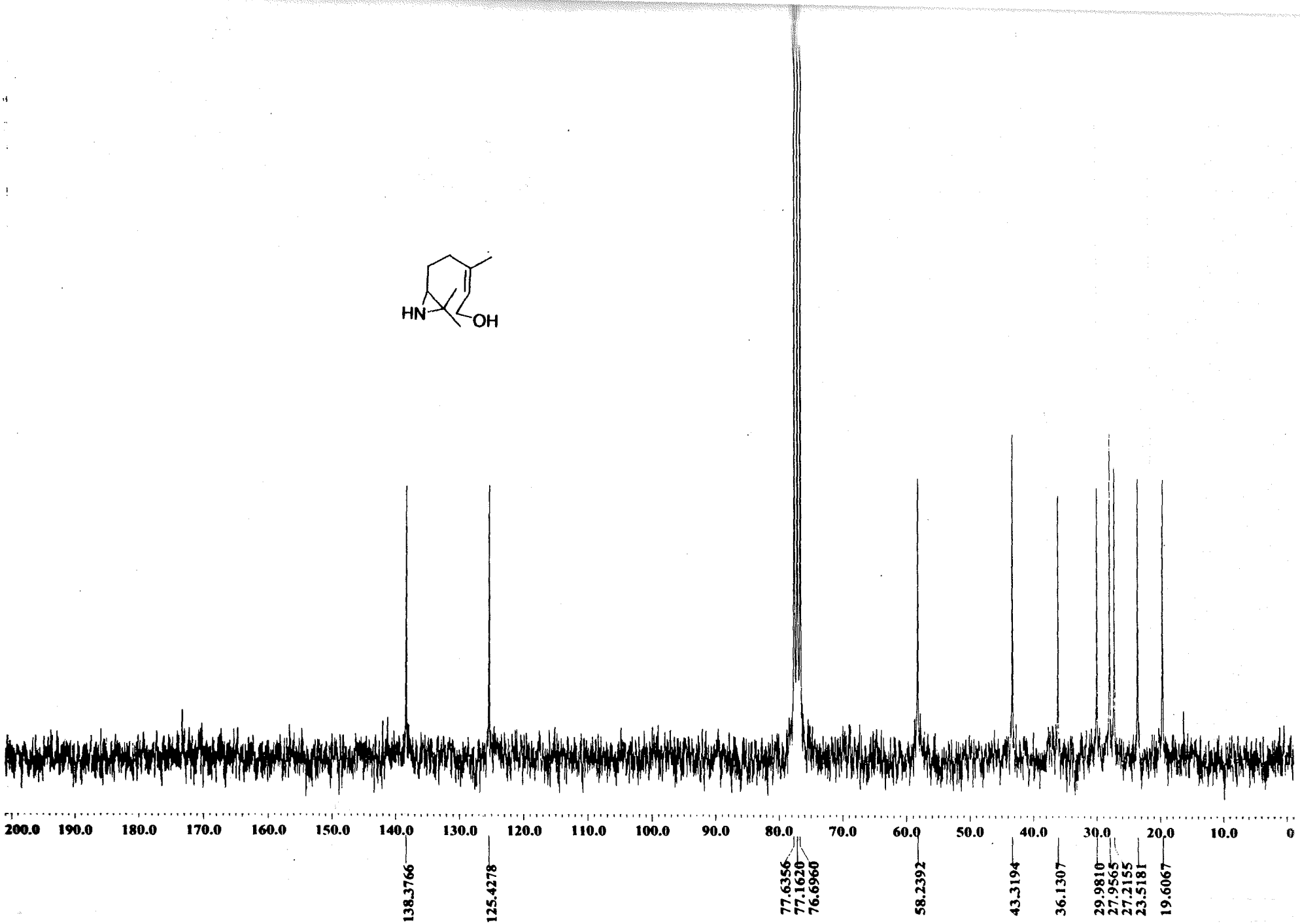
Spectrum 9 ^{1}H NMR of compound **71a** (RAM2/027a)



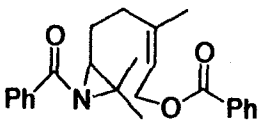
Spectrum 10 ^{13}C NMR of compound **71a** (RAM2/027a)



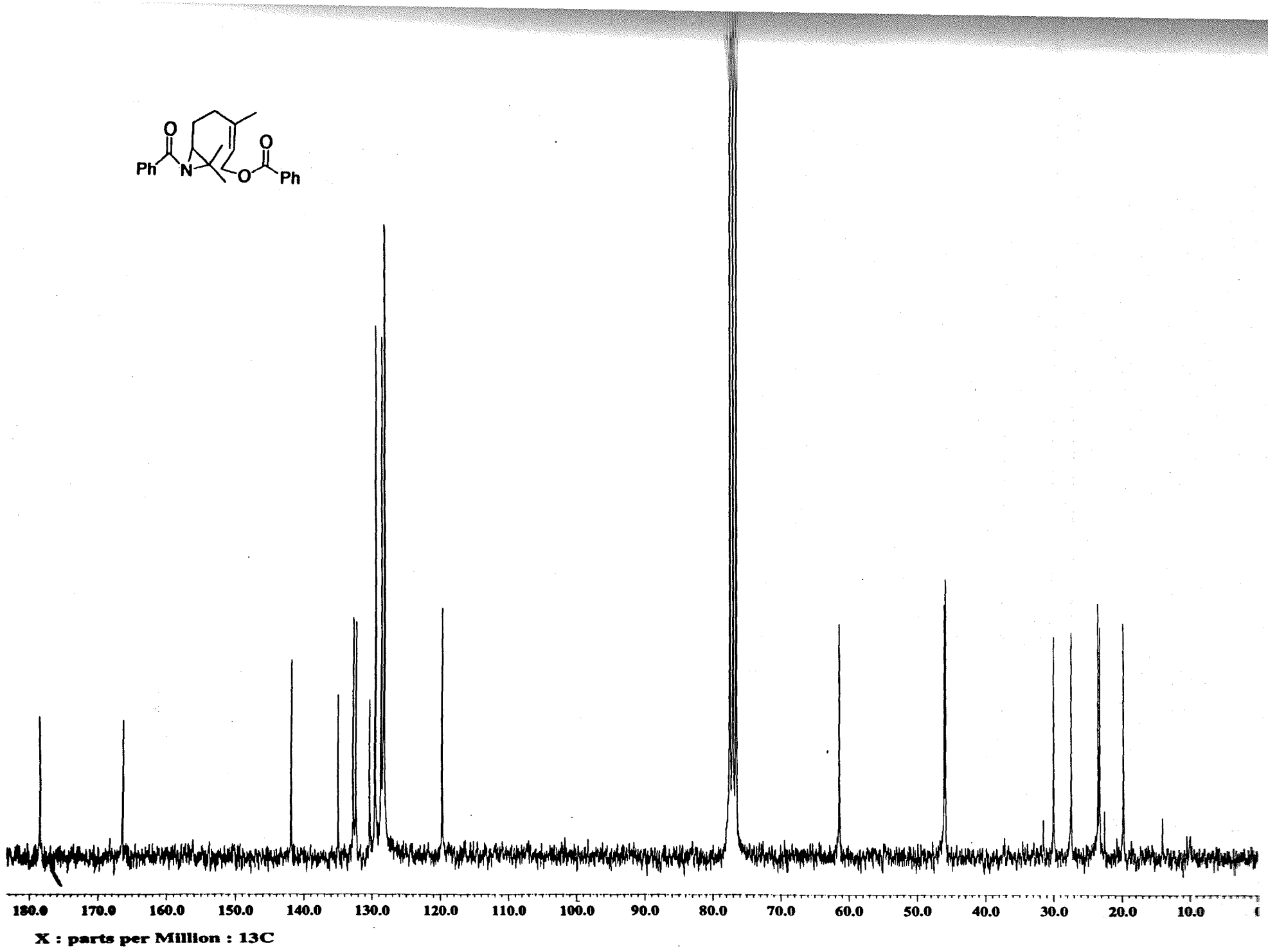
Spectrum 11 ^{1}H NMR of compound **63** (SATI/181)



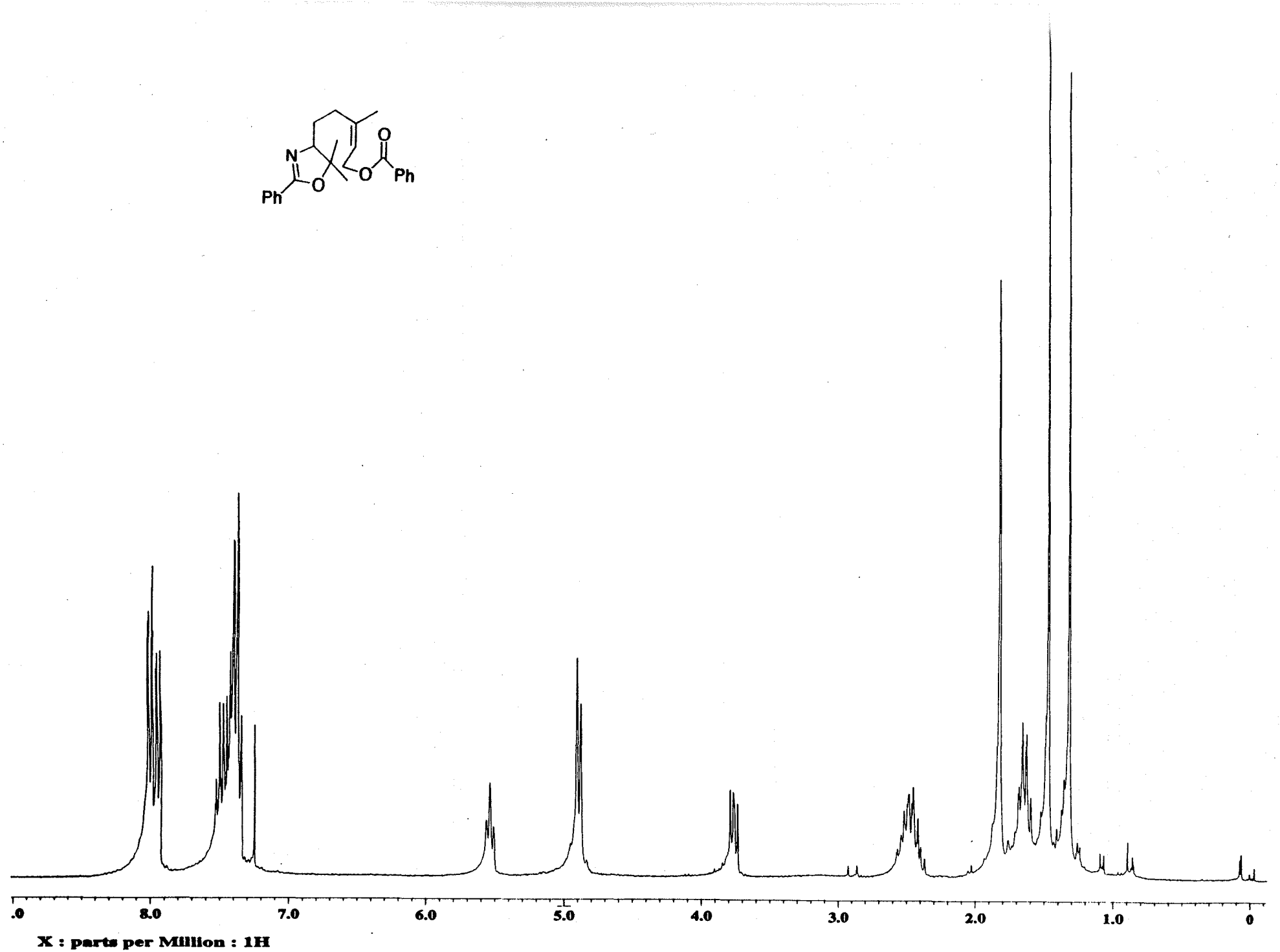
Spectrum 12 ^{13}C NMR of compound **63** (SATI/181)



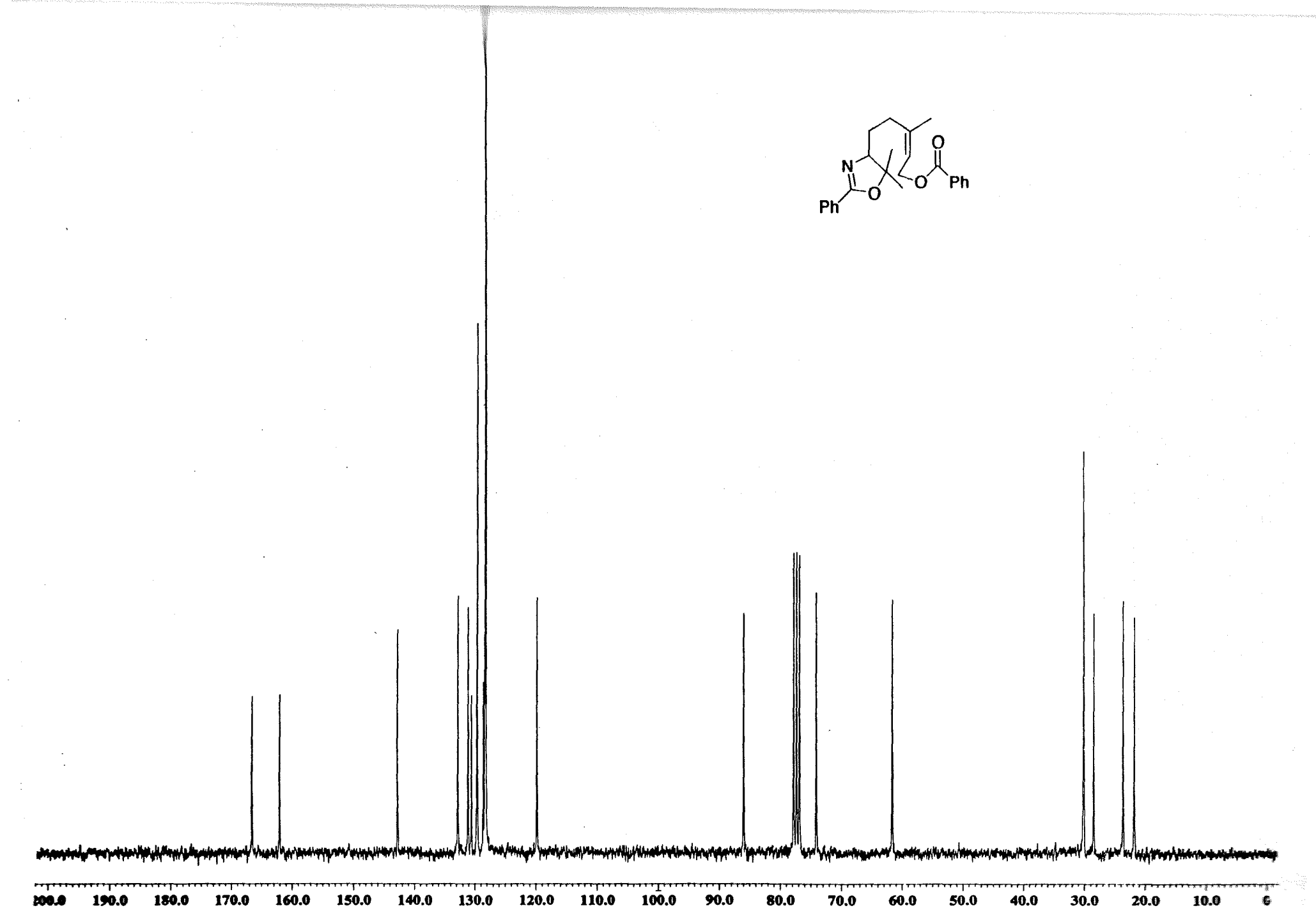
Spectrum 13 ^{1}H NMR of compound **54** (SATII/013)



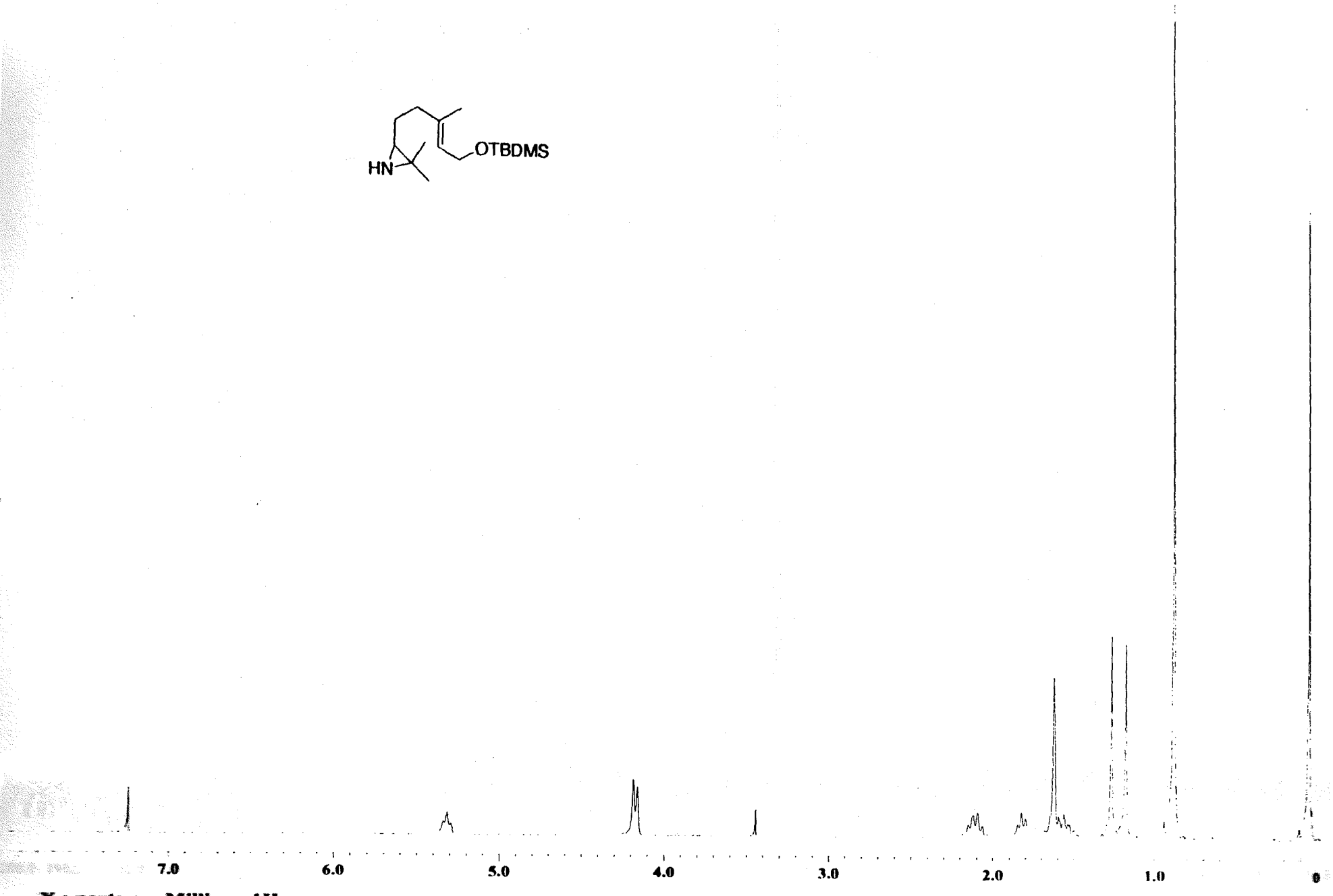
Spectrum 14 ^{13}C NMR of compound **54** (SATII/013)



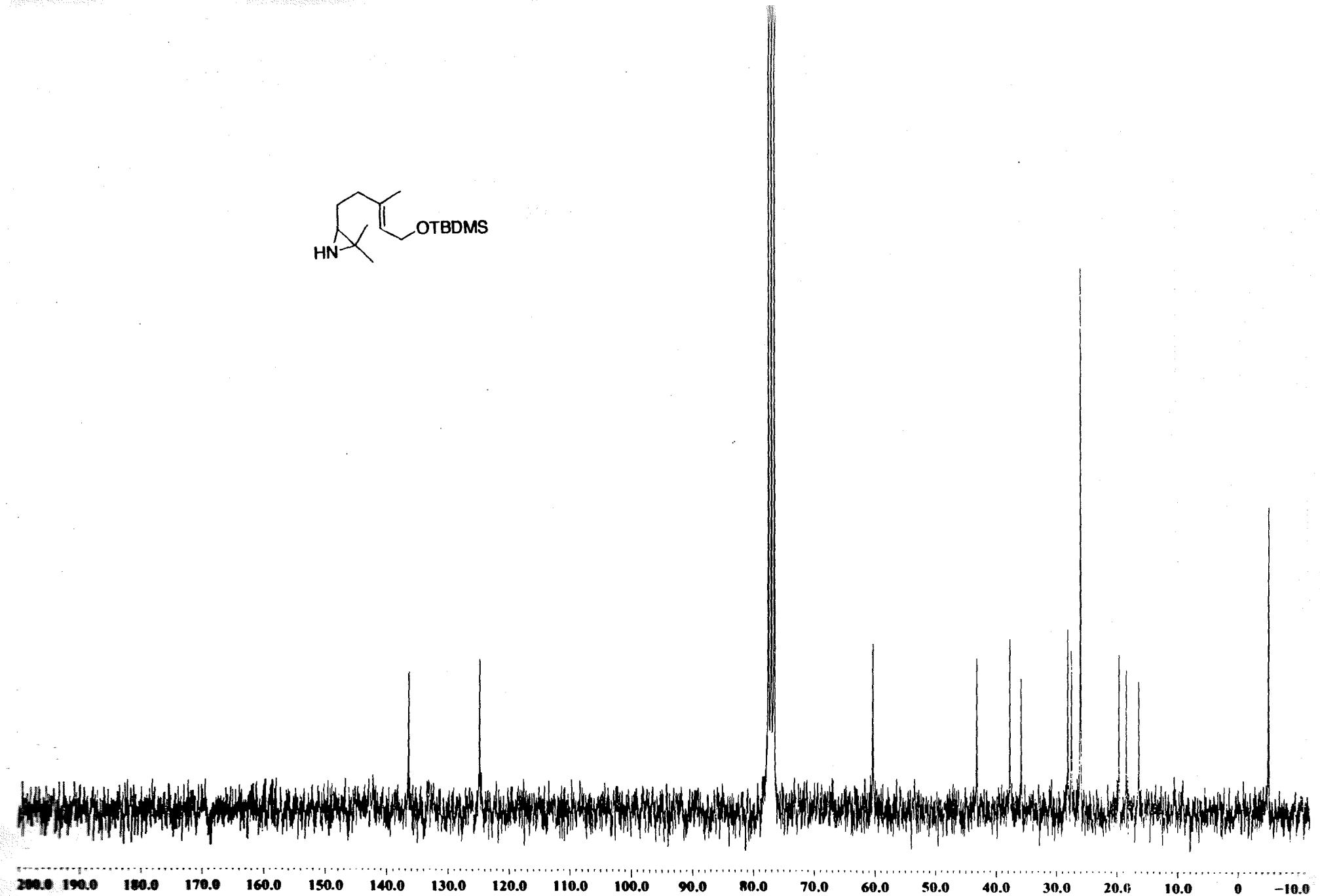
Spectrum 15 ^{1}H NMR of compound **71b** (RAM2/029)



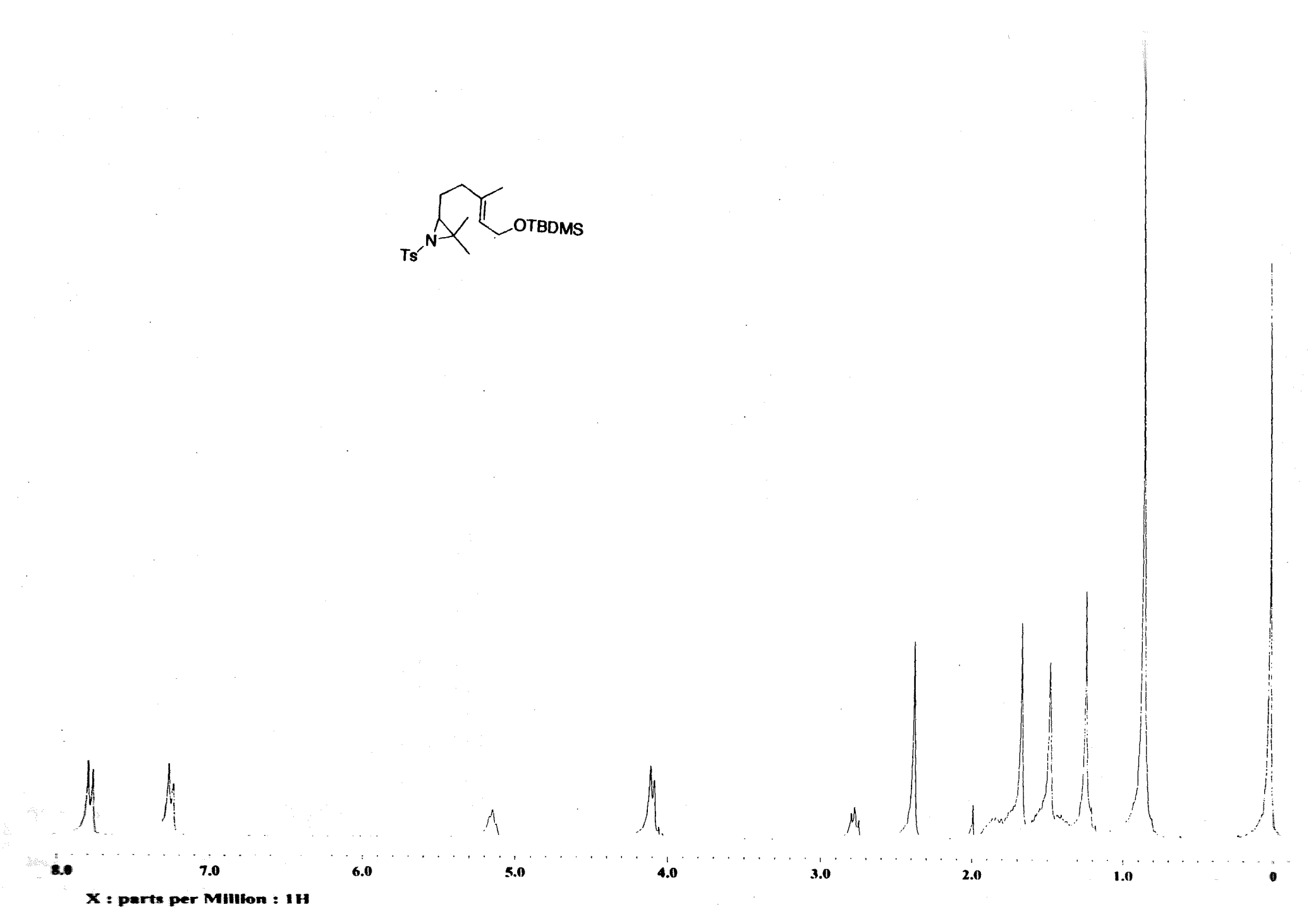
Spectrum 16 ^{13}C NMR of compound **71b** (RAM2/029)



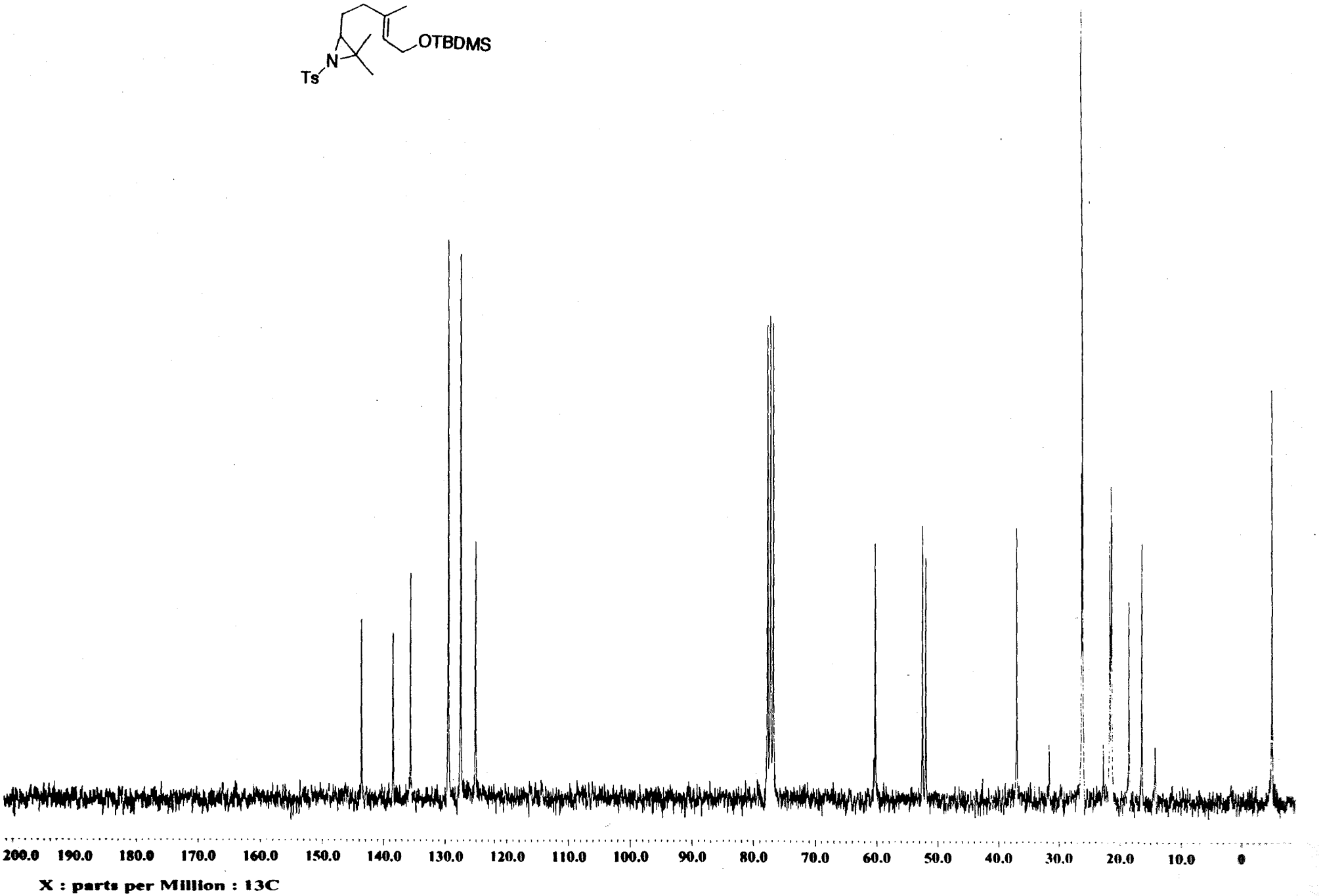
Spectrum 17 ^{1}H NMR of compound **64** (SATII/029)



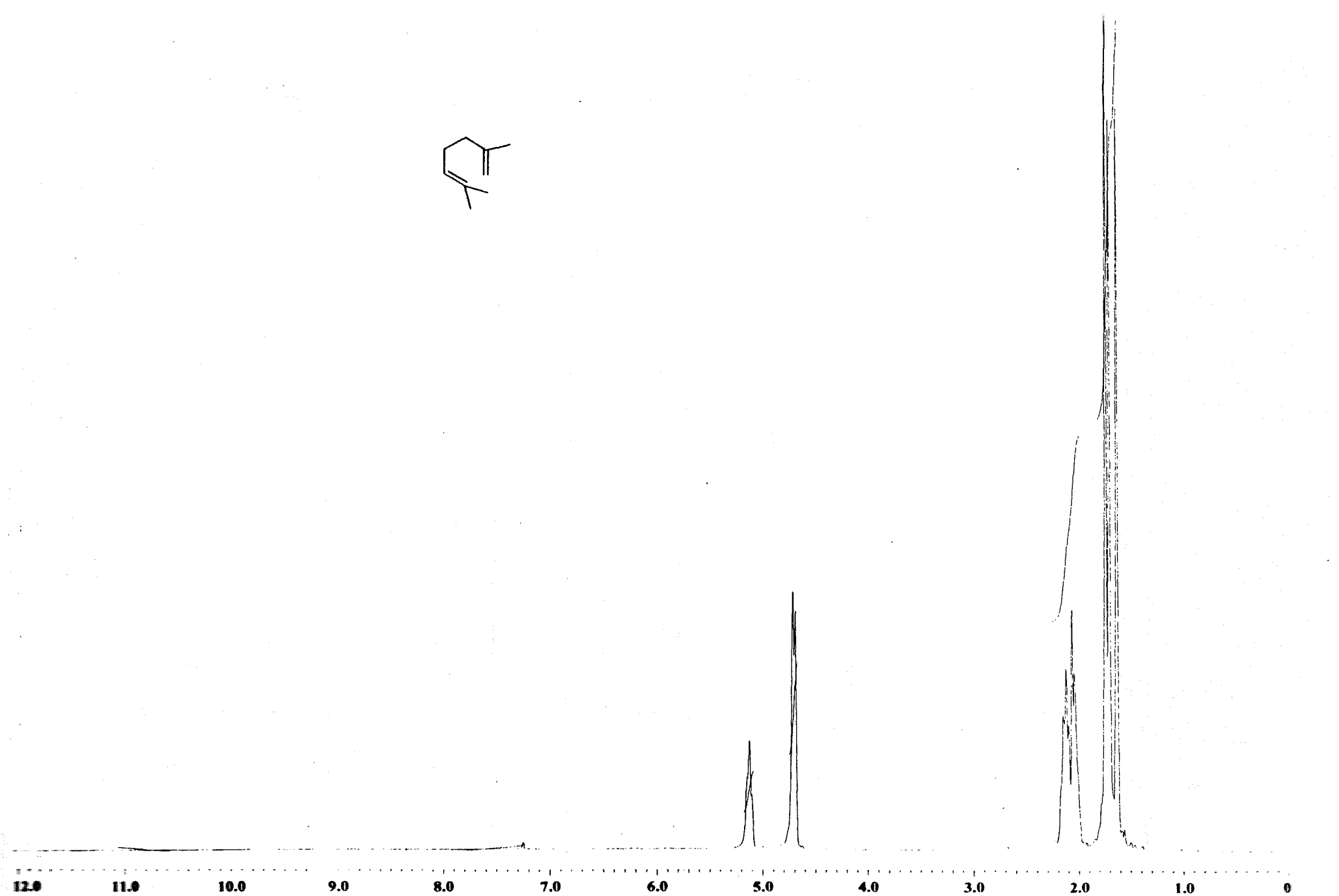
Spectrum 18 ^{13}C NMR of compound **64** (SATII/029)



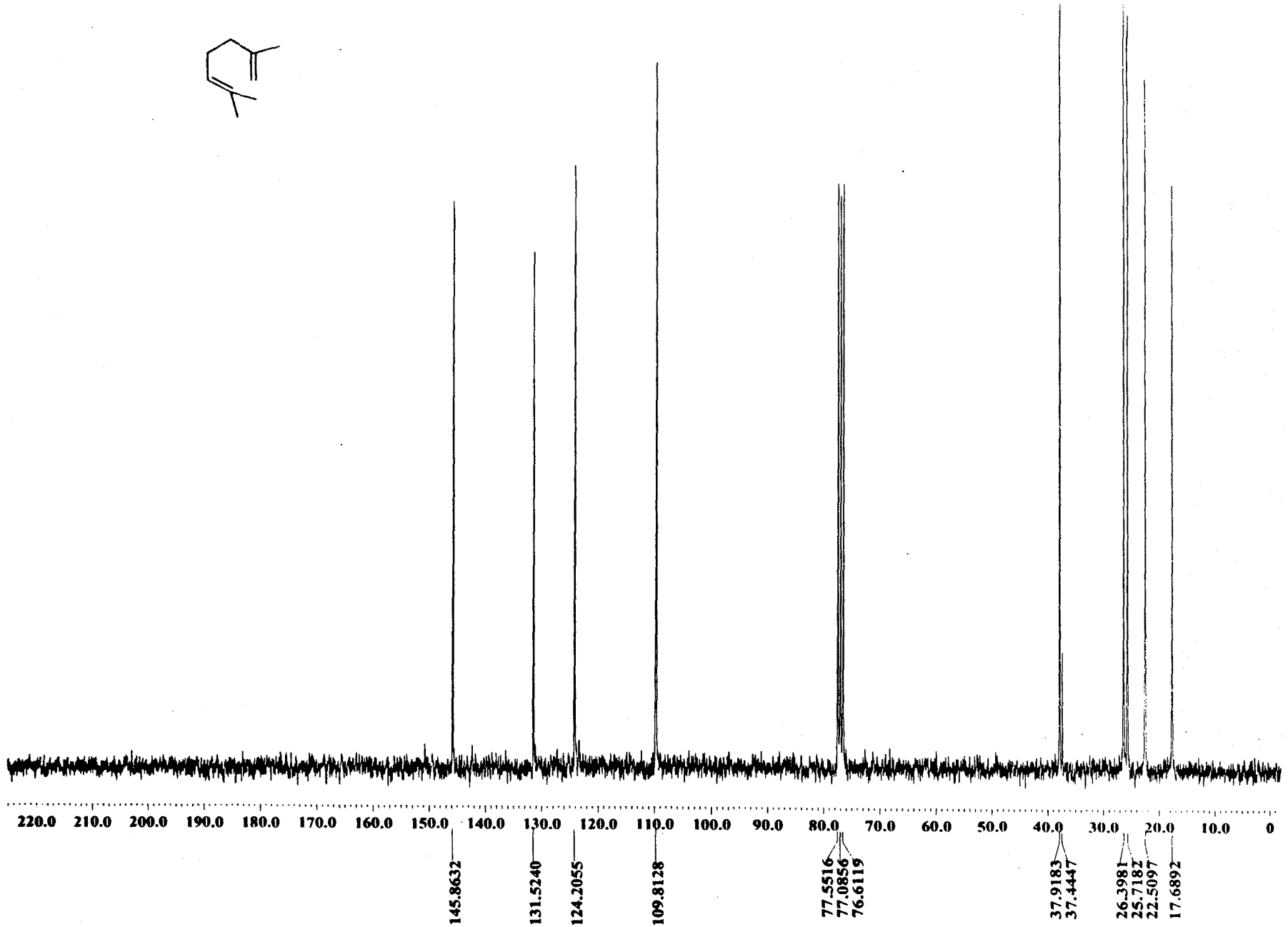
Spectrum 19 ^{1}H NMR of compound **65** (SATII/033)



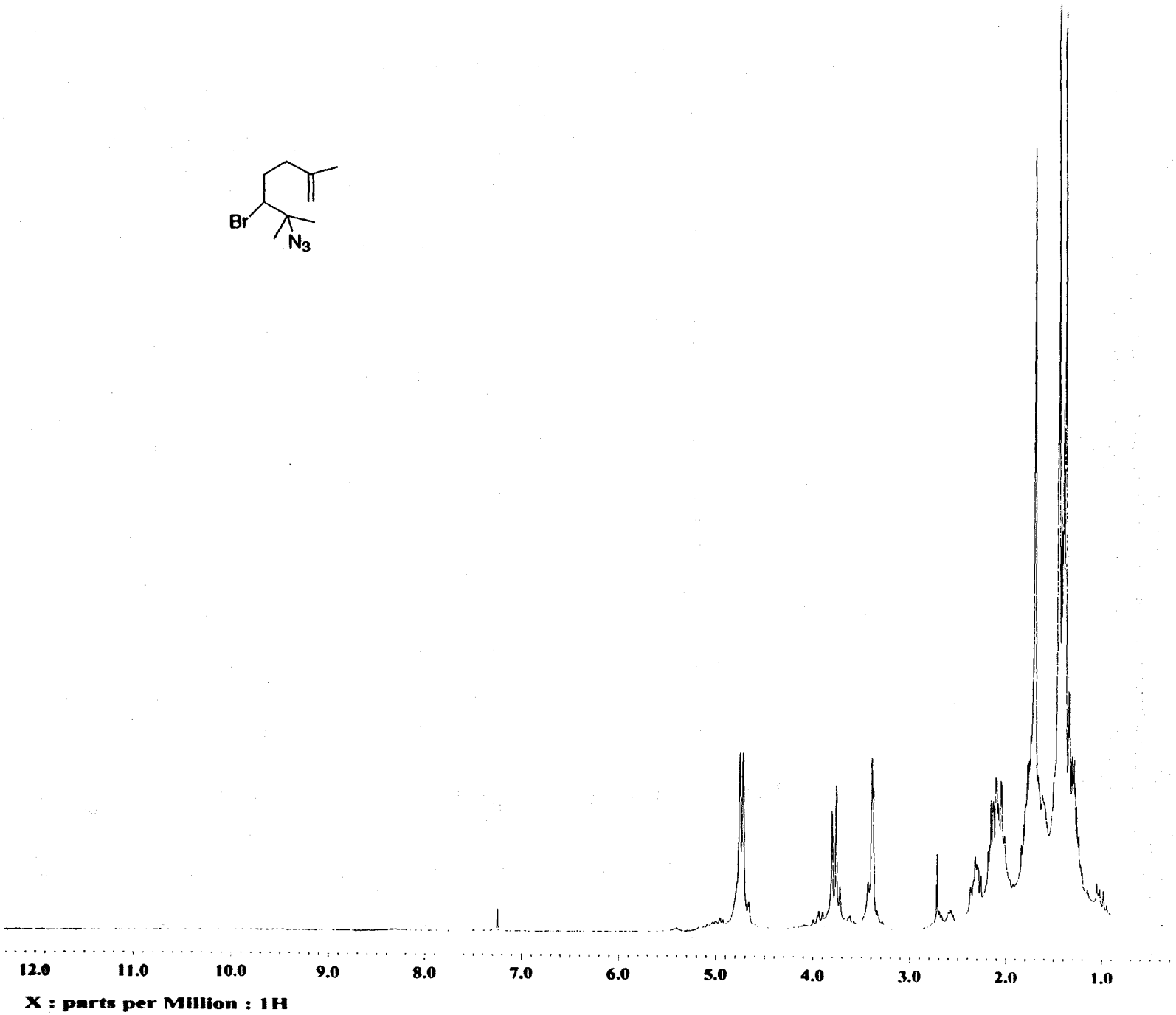
Spectrum 20 ^{13}C NMR of compound **65** (SATII/033)



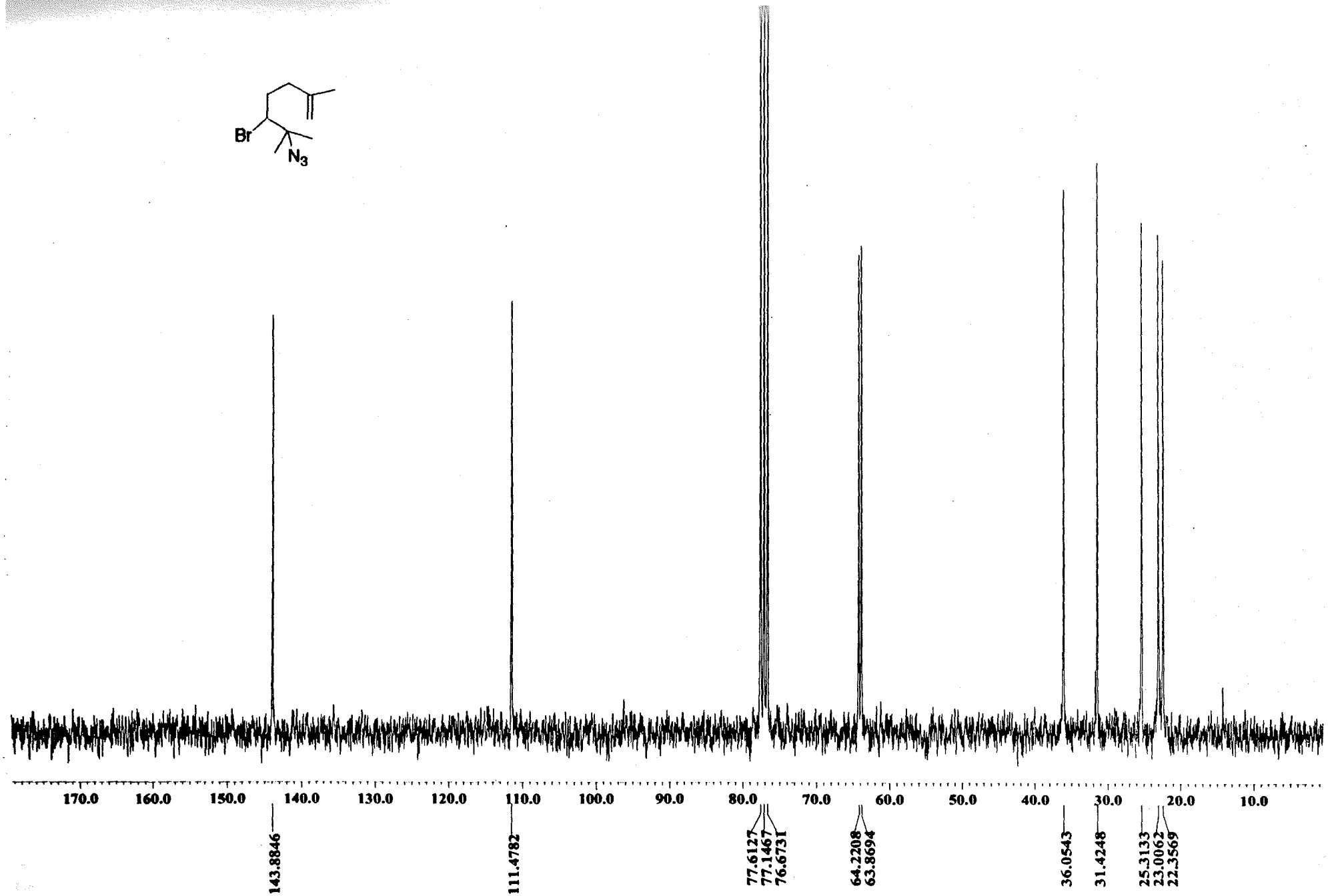
Spectrum 21 ^{1}H NMR of compound **73** geraniolene



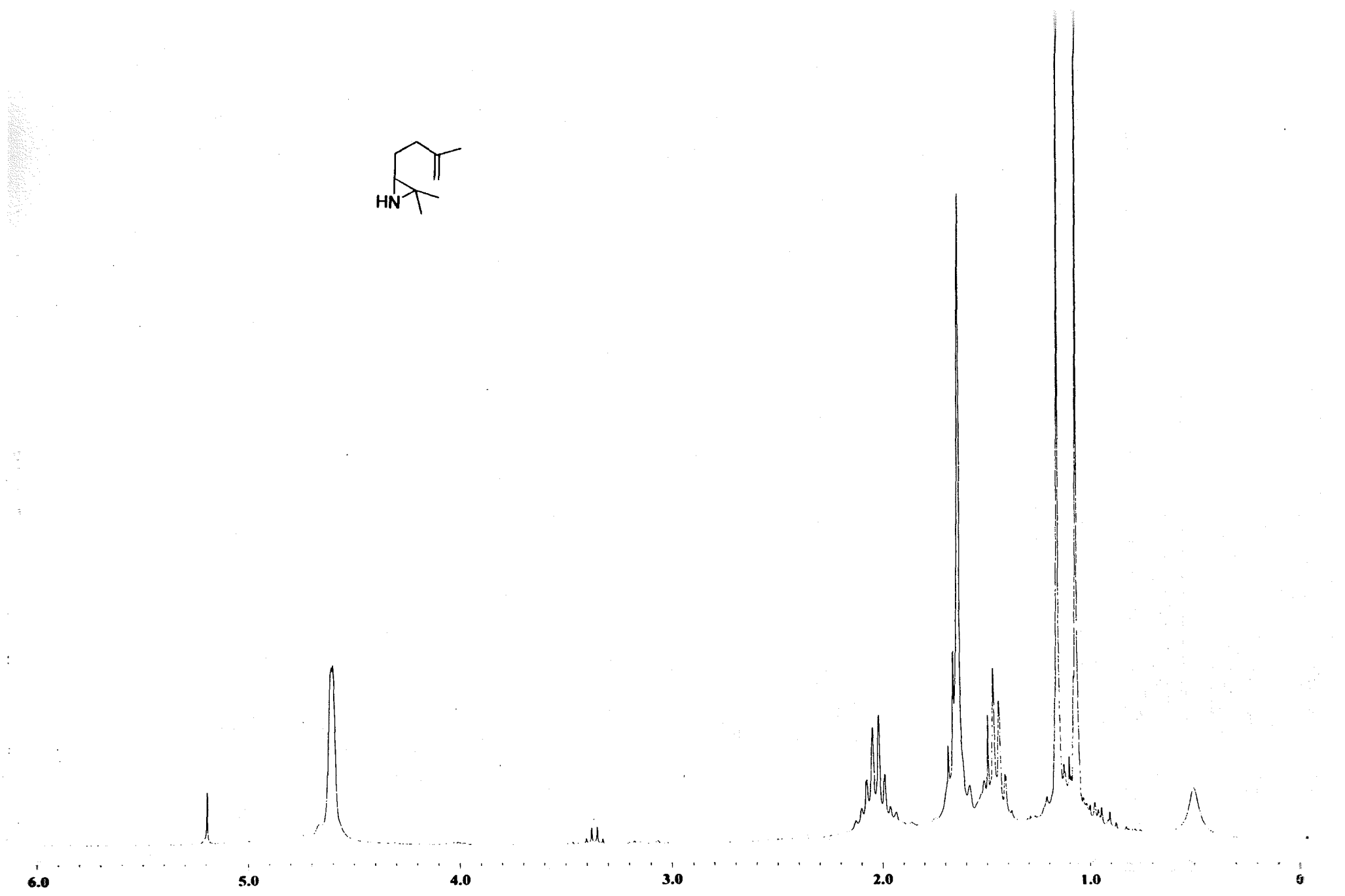
Spectrum 22 ^{13}C NMR of compound **73** geraniolene



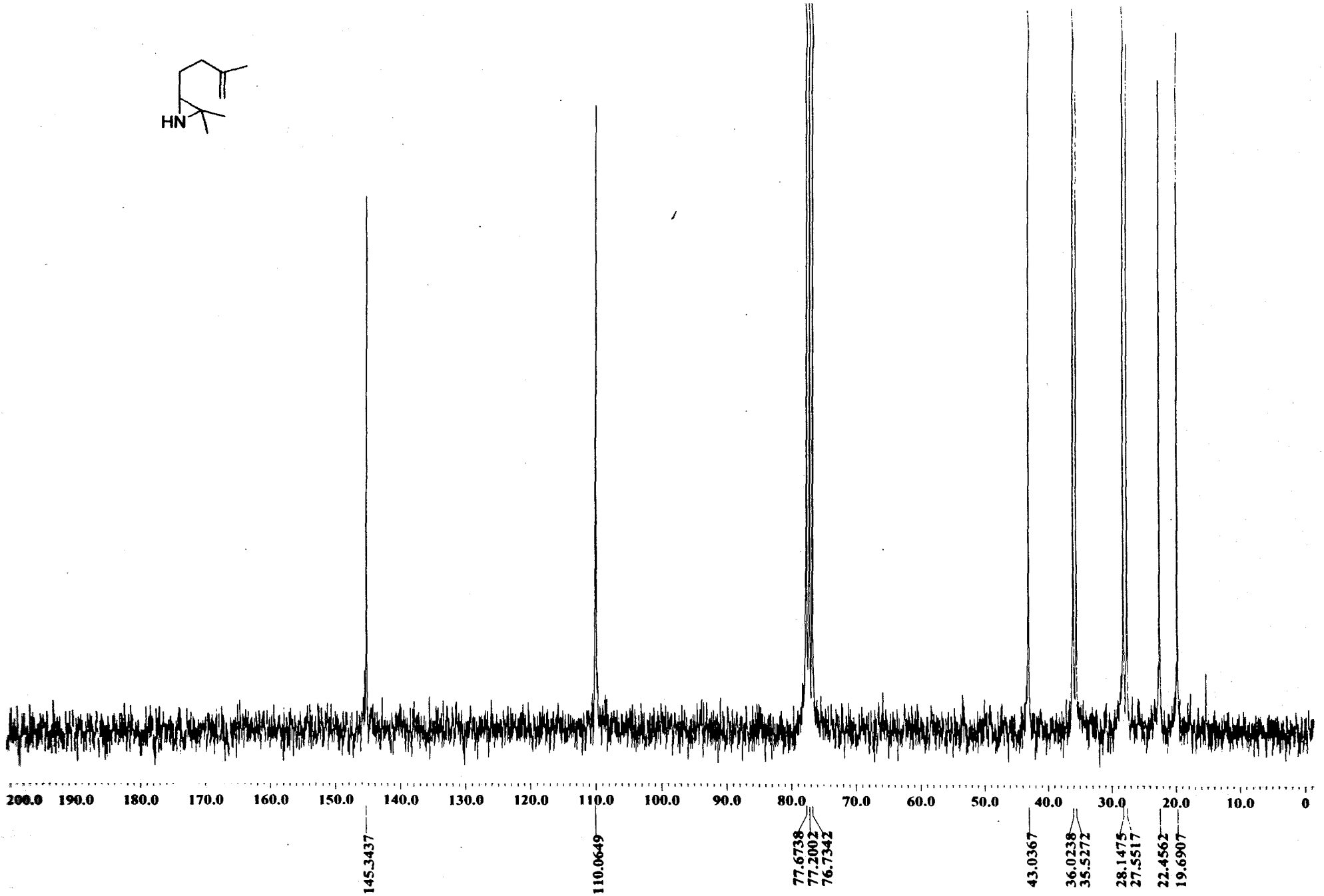
Spectrum 23 ^{1}H NMR of compound **75** (SATII/067)



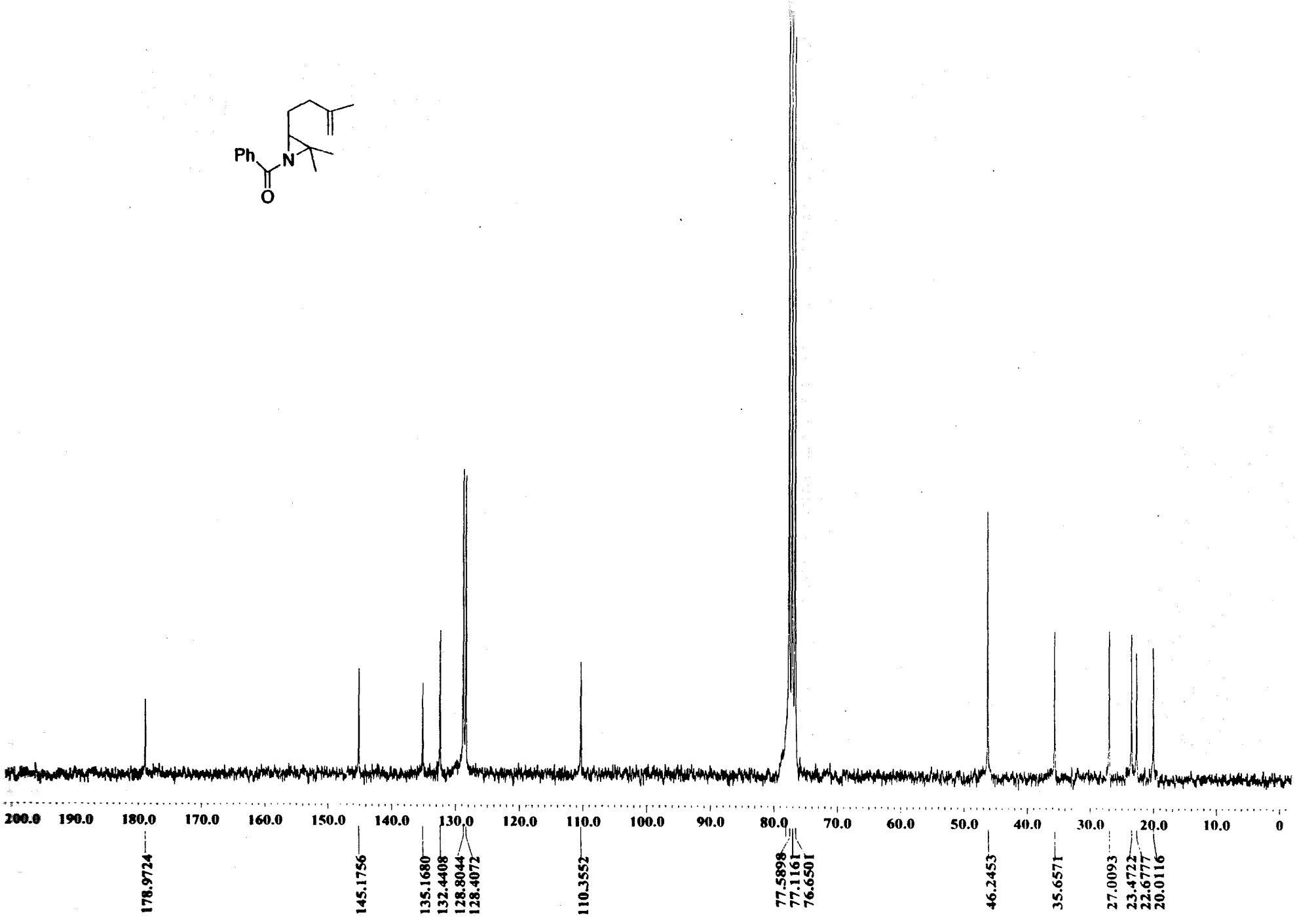
Spectrum 24 ^{13}C NMR of compound **75** (SATII/067)



Spectrum 25 ^{1}H NMR of compound **76** (SATII/069)

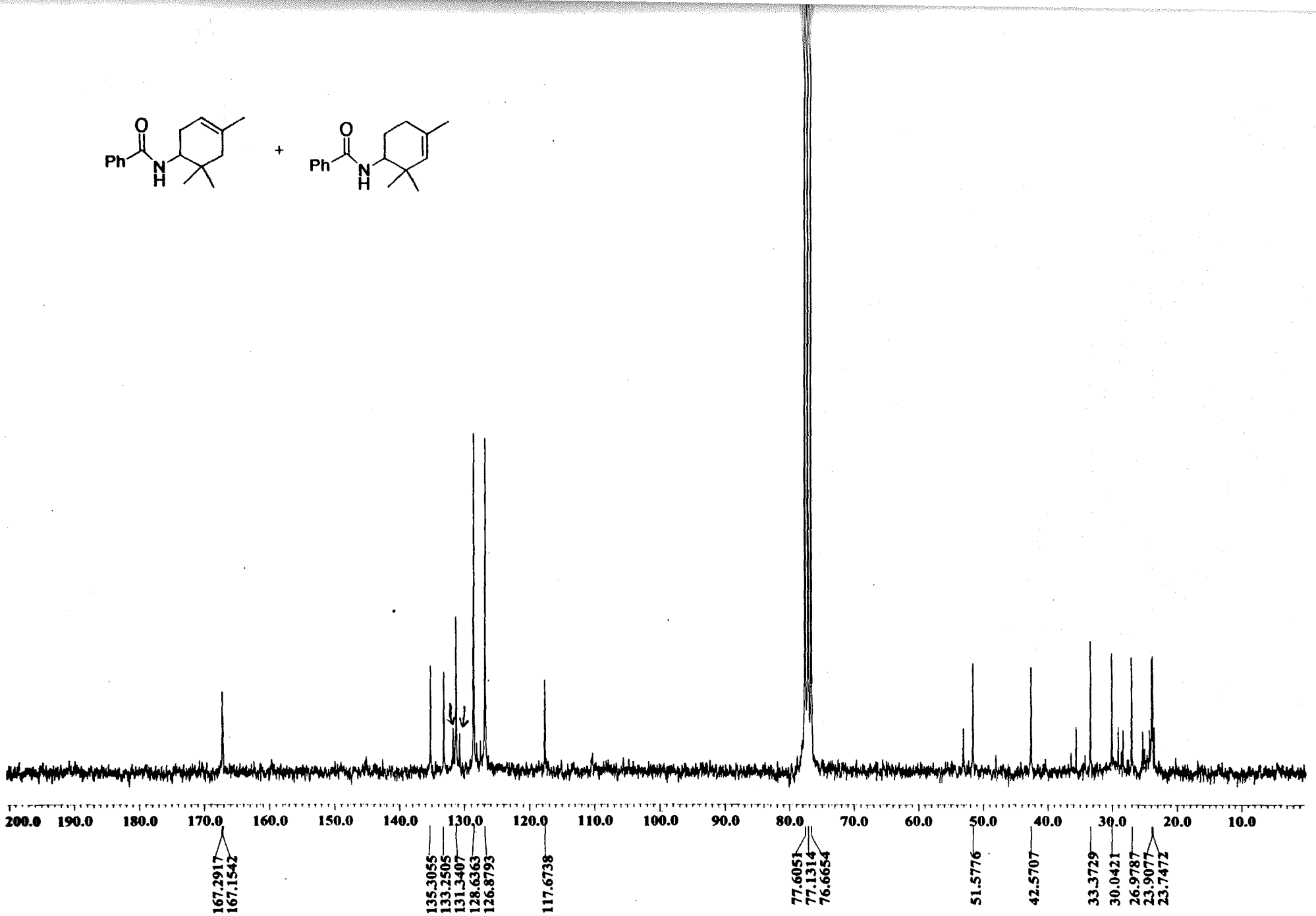


Spectrum 26 ^{13}C NMR of compound **76** (SATII/069)

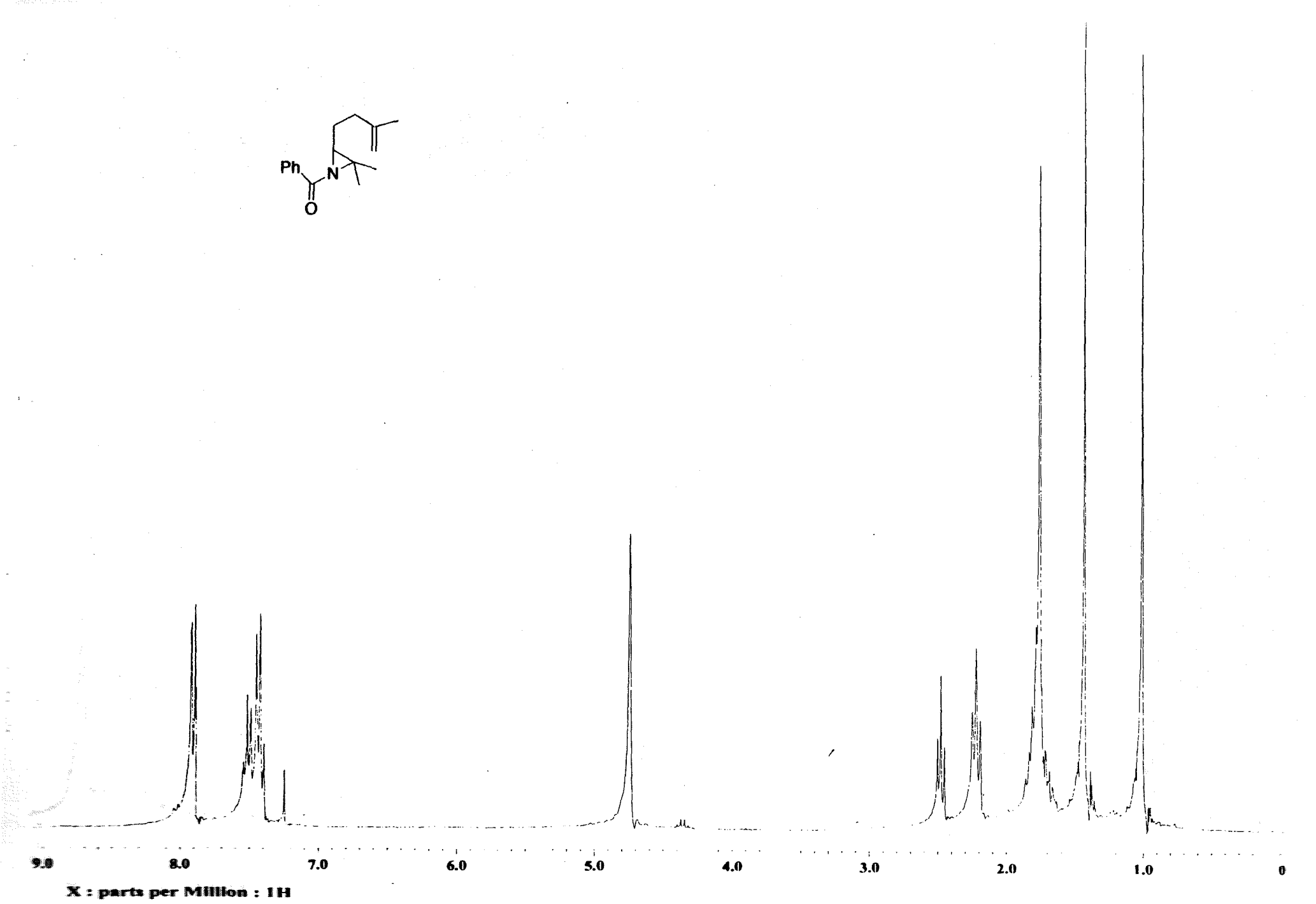


X : parts per Million : 13C

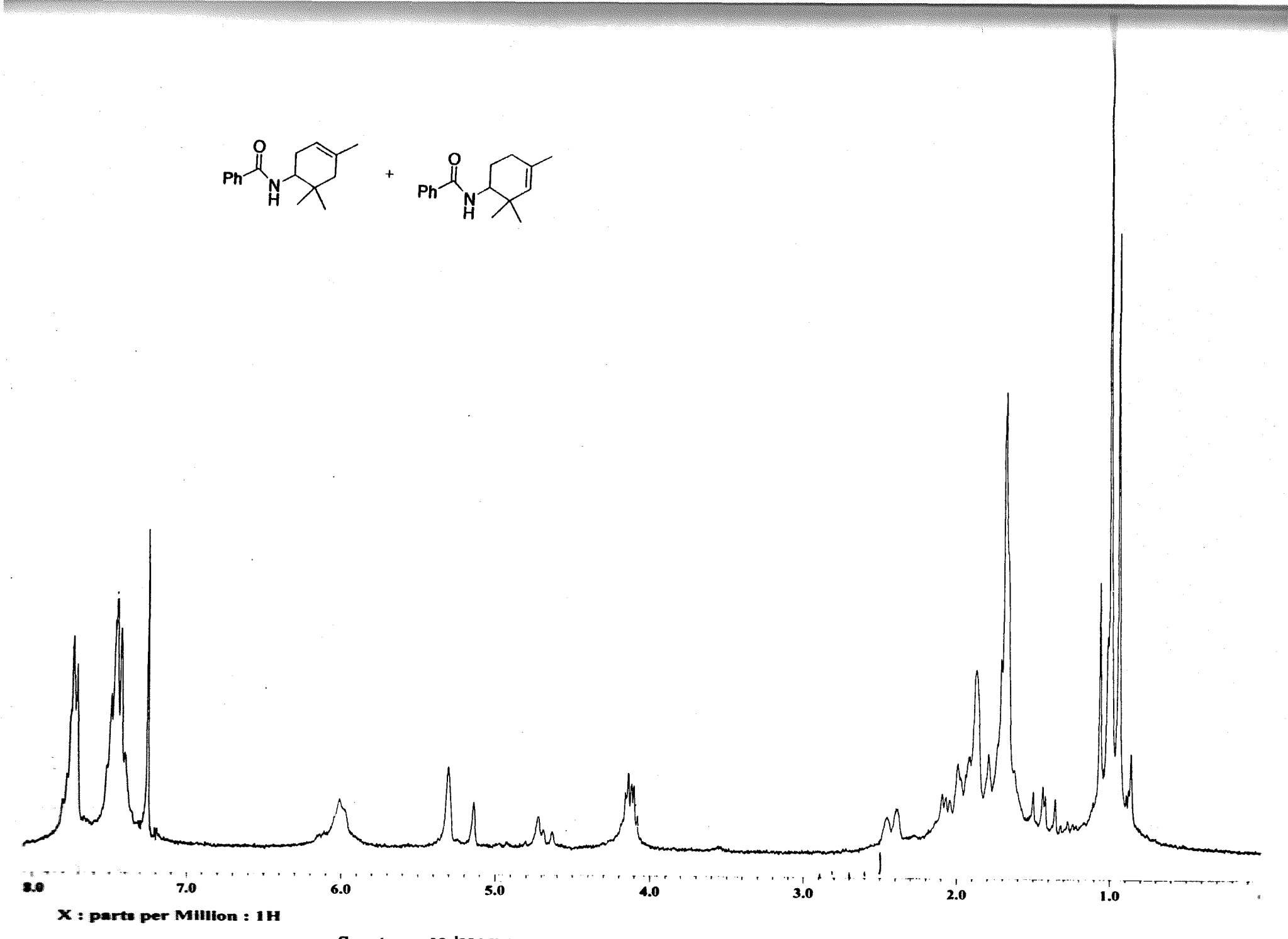
Spectrum 28 ^{13}C NMR of compound **72** (SATII/075)



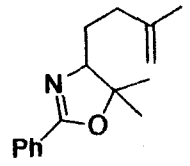
Spectrum 30 ^{13}C NMR of compound **77a** and **77b** (SATII/091)

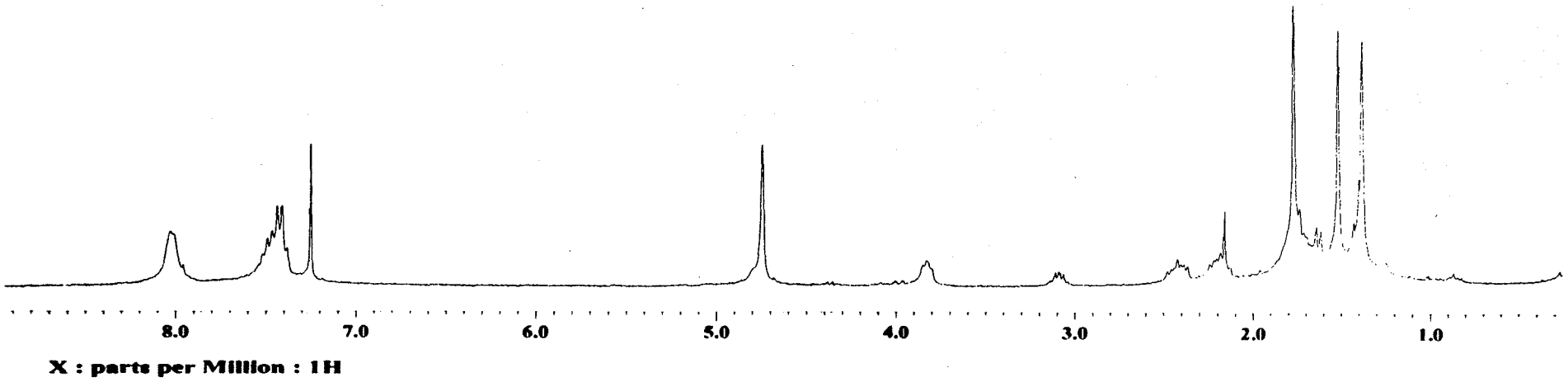


Spectrum 27 ^{1}H NMR of compound **72** (SATII/075)



Spectrum 29 ^{1}H NMR of compounds **77a** and **77b** (SATII/091)





Spectrum 31 ^{1}H NMR of compound **79** (SATII/081)