NOTE TO USERS

uOttawa

L'Université canadienne
Canada's university

FACULTÉ DES ÉTUDES SUPÉRIEURES ET POSTOCTORALES

uOttawa

L'Université canadienne
Canada's university

FACULTY OF GRADUATE AND POSDOCTORAL STUDIES

Natalie Nguyen

AUTEUR DE LA THÈSE / AUTHOR OF THESIS

M.Sc. (Chemistry)

GRADE / DEGREE

Department of Chemistry

FACULTÉ, ÉCOLE, DÉPARTEMENT / FACULTY, SCHOOL, DEPARTMENT

Intramolecular Diels Alder – ROM – RCM Approach Towards the Synthesis of Triquinanes and Magnesium Mediated Carbometallation-Annulation for the Synthesis of Fused Rings

TITRE DE LA THÈSE / TITLE OF THESIS

A. Fallis

DIRECTEUR (DIRECTRICE) DE LA THÈSE / THESIS SUPERVISOR

CO-DIRECTEUR (CO-DIRECTRICE) DE LA THÈSE / THESIS CO-SUPERVISOR

EXAMINATEURS (EXAMINATRICES) DE LA THÈSE / THESIS EXAMINERS

L. Barrault

R. Ben

Gary W. Slater

LE DOYEN DE LA FACULTÉ DES ÉTUDES SUPÉRIEURES ET POSTDOCTORALES /
DEAN OF THE FACULTY OF GRADUATE AND POSTDOCORAL STUDIES

INTRAMOLECULAR DIELS ALDER – ROM – RCM APPROACH TOWARDS THE SYNTHESIS OF TRIQUINANES AND MAGNESIUM MEDIATED CARBOMETALLATION-ANNULATION FOR THE SYNTHESIS OF FUSED RINGS

NATALIE N. M. NGUYEN

Thesis submitted to the
School of Graduate Studies and Research
University of Ottawa
In partial fulfillment of the requirements for
the degree of Master of Science

Ottawa-Carleton Chemistry Institute

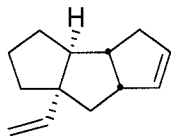
June 2005

Candidate	Supervisor
Natalie N. M. Nguyen	Professor A. G. Fallis

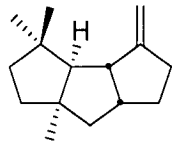
Your file Votre référence
ISBN: 0-494-11363-4
Our file Notre référence
ISBN: 0-494-11363-4

Abstract

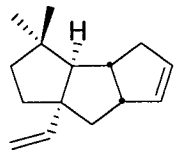
In recent years, there has been a shift in focus in organic synthetic chemistry, steering away from multistep synthesis, leaning towards tandem and one pot reactions. Described herein is a unique, one pot method for the synthesis of linear triquinanes. The strategy involved a one pot intramolecular Diels-Alder – ring opening metathesis – ring closing metathesis sequence to form triquinane **85**. Application of the new methodology towards the synthesis of antibiotic $\Delta^{(9,12)}$- capnellene (**13**) was performed. During our endeavors, the core ring structure **86** was synthesized.



85

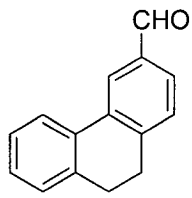


13
(±) -Capnellene

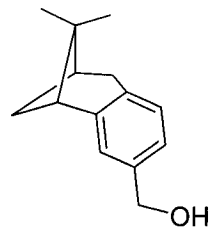


86

Also described is a second project which involved the synthesis of bicyclic compounds through a new carbometallation-annulation reaction. The reaction was used for the synthesis of dihydrophenanthrene **129** and chiral tricycle **137**. Insight into the application to the synthesis of indoles was also investigated.



129



137

Acknowledgements

I have had the most incredible and memorable experience in Ottawa. I came here from a little place called Surrey, not knowing anyone and now I'm leaving with an amazing family.

First and foremost, I need to thank Dr. Alex Fallis for letting me join his lab group. His infectious enthusiasm for chemistry and life and his compassionate nature is what I will remember the most. His door was always open for asking questions and advice; I do not think I could have found a nicer supervisor.

I had the great pleasure of working with some wonderful people. Matt Clay, I owe all my chemistry knowledge to you. Our Classics sessions were invaluable and your help with my seminar was amazing. All your kindness was appreciated and did not go unnoticed. Thanks to Kelly VanCrey for sharing this experience with me and for all our lunchtime drinks. I am forever grateful for you editing my thesis and lending me your keys! Thanks to Matt Heuft for being a great friend in and out of the lab. Thanks to Dr. Nancy Lamb for being so patient and an amazing teacher in the lab. You are a very strong woman and I hope in the future I can have a fraction of the strength that you have. Dr. Sara Palmier and Dr. Christophe Bernard, my favourite french post docs, thanks for all the wonderful talks and all the french lessons. Thanks to Nicole Stogaitis for helping me with my project and thanks to everyone else who has passed through the Fallis lab and making my time here so enjoyable.

Thanks to Cheryl McDonald and Glen Facey for all their help with NMR experiments. Thanks to Jay Conrad for giving me his catalysts.

I have made so many life long friendships at this school. Pat Bazinet, we need a plan, we have to set goals! Jenny Scott, thanks for all the baking adventures, the hockey, the rubber regatta, the Mangoes, the NAC and the list just keeps going. Your zest for life is truly remarkable. Joe Jebreen, I followed you to Beausoleil, then to Lees and now to Montreal. Where to next?!!!! Marc Lafrance: my loyal, but dumba** friend, "It's all goodsssss." Pat Crewdson, vodka looks like water……gulp, gulp!

Other people who have helped me along the way: Livia Aumand, Joe 2.0, Gan Ong, Ami Chin, Josee Cloutier and my non-chemistry friends, Bryce Crossman and Carol

Wai. I also cannot forget my friends from Surrey, Kim Pham, Tracy Sato and Karen Tabata. Each and every single one of you have touched and enhanced my life in some way. I will cherish all the wonderful memories we had together. A special thanks to the floor hockey team for introducing me to Mangos!

I have to thank my best friend, Matt Lemay. You have supported me through thick and thin and through the smiles and tears (and there were lots of tears). What am I going to do without our daily coffees? Who am I going to go visit when I feel like chatting? We have grown as chemists and as friends. Grad school would not have been the same without you. You are such an important part of my life, thank you for you never wavering support.

Above all, I need to thank my family. My parents came to Canada searching for a better life for their children. All they wanted was a nice quiet daughter who would lead a nice quiet life in Surrey. Sorry! Although I have chosen a path that is relatively odd, you still were 100% supportive of all my decisions. I would not have come to Ottawa and completed my degree without your support. Thank you for your unconditional love. And thanks to my brother Lewis for breaking all the rules before me and being a fantastic role model.

Table of Contents

List of Figures

List of Schemes

List of Tables

List Abbreviations

Ac	acetyl
ADMP	acyclic diene metathesis polmerization
aq	aqueous
bp	boiling point
calcd	ccatalytic
CM	cross metathesis
d	doublet
dd	doublet of doublet
dt	doublet of triplets
DMAP	*N,N'*-dimethyl-4-aminopyridine
Et_2O	diethyl ether
EtOAc	ethyl acetate
eq.	equivalent
HRMS	high resolution mass spectroscopy
IR	infrared
J	coupling constant
LDA	lithium diisopropylamide
M^+	molecular ion
MeOH	methanol
mp	melting point
MS (EI)	mass spectrum by chemical ionization
NMR	nuclear magnetic resonance
Pet ether	petroleum ether
ppm	parts per million
py	pyridine
PDC	pyridinium dichromate
$PhN(Tf)_2$	*N*-phenyltrifluoromethanesulfonimide
q	quartet
R	alkyl

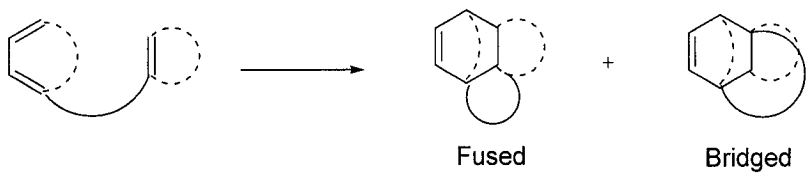
RCM	ring closing metathesis
ROM	ring opening metathesis
ROMP	ring opening metathesis polymerization
rt	room temperature
s	singlet
t	triplet
THF	tetrahydrofuran
TLC	thin layer chromatography
Ts	tosyl (toluenesulfonyl)

1 Introduction – Synthesis of Linear Triquinanes

1.1 Intramolecular Diels-Alder Reaction

The Diels-Alder reaction is undoubtedly one of the most powerful and useful transformations in organic chemistry. Discovered in 1928 by Otto Diels and Kurt Alder,[1] the pericyclic reaction is able to create high molecular complexity from relatively simple precursors. It generates a cyclohexene ring with up to four stereogenic centers and many elegant applications have been reported for the total synthesis of complex natural products.[2] Due to the supra-suprafacial reaction, polarity controlled orientation, and endo/exo selectivity of the diene and dienophile, usually one pair of enantiomers is obtained out of a maximum thirty-two possible isomers.[3] Furthermore, enantioselective [4+2] cycloaddtions can be achieved with the use of chiral catalysts, such as Lewis acids[4] and organocatalysts.[5]

The intramolecular version has provided access to diverse polycyclic ring systems which are otherwise difficult to prepare.[6] One can imagine that when both the diene and the dienophile are cyclic, stereoselective preparation of a variety of tricyclic sesquiterpenoids can be achieved (Scheme 1). Depending on the approach of the dienophile to the diene, two compounds can be produced, either the fused or the bridged product. Due to steric constraints the fused ring system is produced more readily. For longer tether lengths, the bridged compound can be formed.



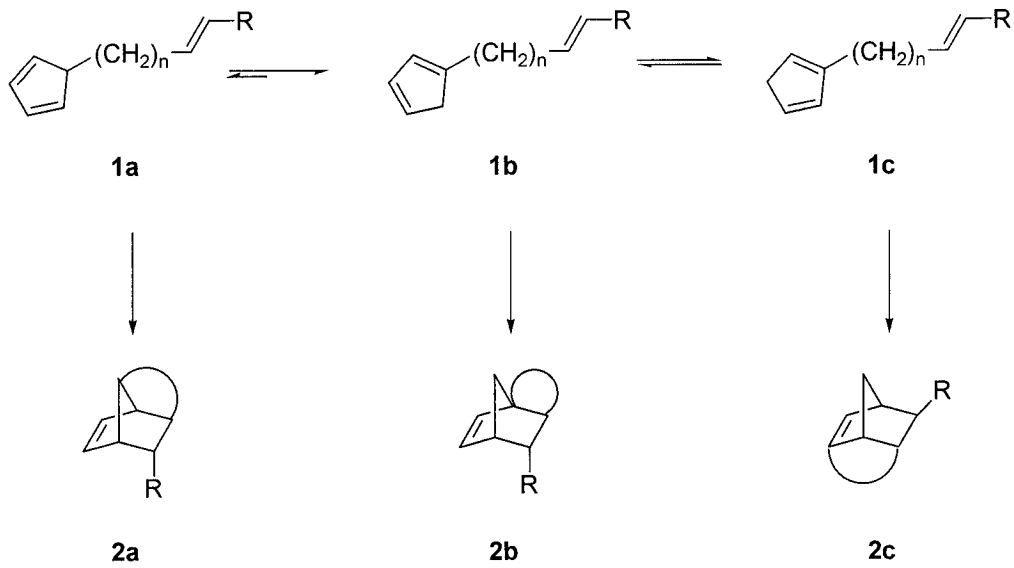
Scheme 1: Ring systems from the intramolecular Diels-Alder reaction

---

[1] Diels, O.; Alder, K. *Justus Liebigs Ann. Chem.* **1928,** *460,* 98.
[2] For a review see: Nicolaou, K. C.; Snyder, S. A.; Montagnon, T.; Vassilikogiannakis, G. *Angew. Chem. Int. Ed.* **2002,** *41,* 1668.
[3] Schmidt, R. R. *Acc. Chem, Res.* **1986,** *19,* 250.
[4] For a review see: Corey, E. J. *Angew. Chem. Int. Ed.* **2002,** *41,* 1650.
[5] For a review see (a) Notz, W.; Tanaka, F.; Barbas, C. F., III *Acc. Chem. Res.***2004,** *37,* 580; (b) Ahrendt, K. A.; Borths, C. J.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2000,** *122,* 4243.
[6] For a review see: Brieger, G.; Bennet, J. N. *Chem. Rev.* **1980,** *80,* 63.

1.2 Cycloaddition of Substituted Cyclopentadiene

The Diels-Alder reaction of cyclopentadiene with a dienophile has been widely used for the formation of bicyclo[2.2.1]heptene compounds. The intramolecular Diels-Alder (IMDA) can therefore incorporate a fused ring on the norbornene skeleton and the type of ring structure depends on the location of the side chain on cyclopentadiene (Scheme 2).[7,8] It is a well known fact that substituted cyclopentadienes undergo 1,5-sigmatropic hydrogen shifts to give a mixture of three isomers, **1a-1c**, and the cycloaddition of each isomer therefore provides a possibility of three products. The initial product from the alkylation of a cyclopentadienyl anion **1a** quickly isomerizes to the more stable 1**b**, and if left for a few days, **1c** is also produced to give a mixture of **1b** and **1c**. It is unlikely that **2c** would form since the structure violates Bredt's rule. If **1a** is in sufficient concentration, it has all the electronic and steric requirements to cyclize to form **1a**. However this is unlikely since the isomerization of **1a** to **1b** is faster than the IMDA of **2a**. Thus, from a possibility of three products, **2b** is the sole product, depending on the tether length of selected.



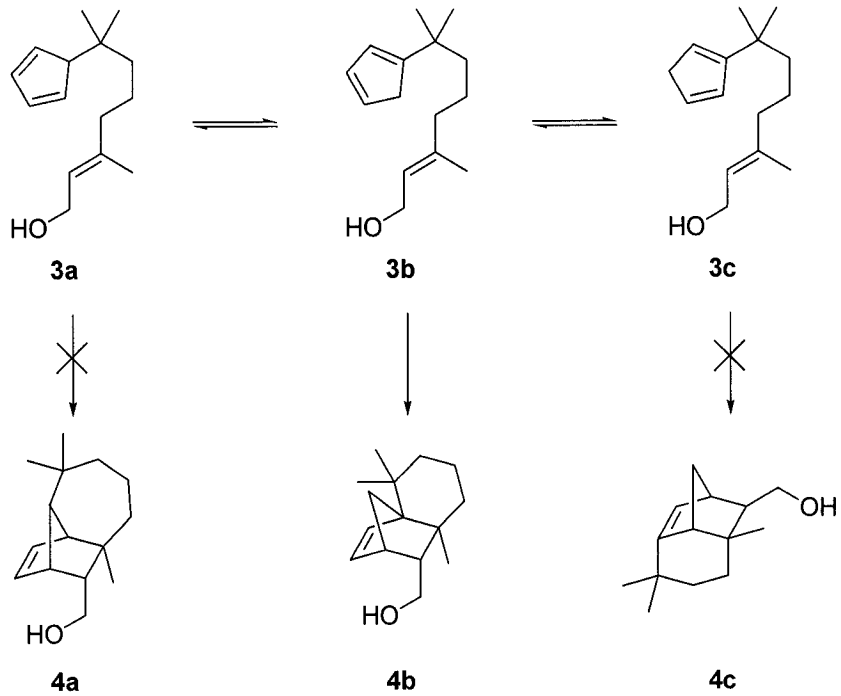
Scheme 2: Intramolecular Diels-Alder reaction of substituted cyclopentadienes

[7] Stille, J. R.; Grubbs, R. H. *J. Org. Chem.* **1989,** *54,* 434.
[8] (a) Corey, E. J.; Glass, R. S. *J. Am. Chem. Soc.* **1967,** *8,*. 2600; (b) Brieger, G.; Anderson, D. R. *J. Org. Chem.* **1971,** *36,* 243; (c) Snowden, R. L. *Tetrahedron Lett.* **1981,** *22,* 97; (d) Snowden, R. L. *Tetrahedron Lett.* **1986,** *42,* 3277;

1.2.1 Brieger's Attempted Synthesis of Longifolene

One of the first examples of the IMDA reaction involved a substituted cyclopentadiene, which was performed by Brieger in 1963 while he unsuccessfully attempted the synthesis of longifolene.[9] Brieger envisaged the longifolene skeleton coming from the cycloaddition of **3a** (Scheme 3). It was hoped that upon heating the mixture of isomers **3a-3c**, thermal equilibration would shift towards isomer **3a**, which would then cyclize to **4a**. Unfortunately, the only product obtained was cycloadduct **4b**, which came from isomer **3b**.

Based on his results, it was concluded that substituted cyclopentadienes underwent a facile 1,5-sigmatropic hydrogen shift at room temperature, and that isomers **3b** and **3c** are thermodynamically more stable than **3a**.

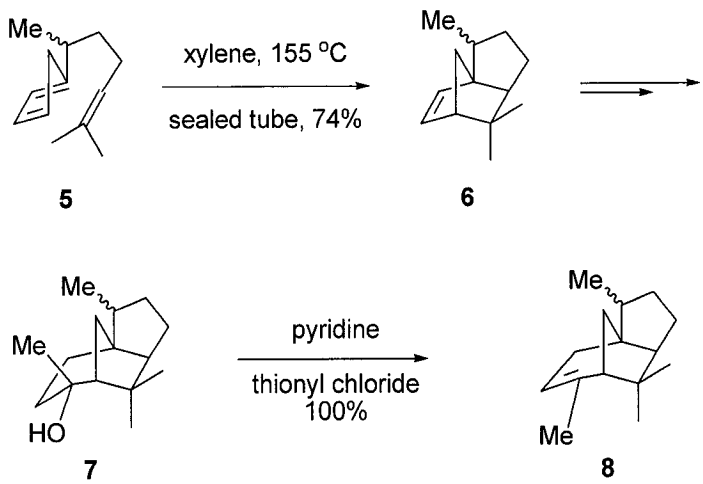


Scheme 3: Brieger's attempt at the longifolene ring structure

[9] Brieger, G. *J. Am. Chem. Soc.* **1963,** *85,* 3783.

1.2.2 Fallis' Synthesis of (±)-Cedrene and (±)-Cedrol

With this knowledge in hand, intermediate of type **3b** has been used in a variety of natural product syntheses including Fallis' total synthesis of (±)-cedrene and (±)-cedrol (Scheme 4).[10] Alkenylcyclopentadiene **5**, which was prepared from alkylation of the corresponding tosylate and sodium cyclopentadiene, was heated in a sealed tube in xylene at 155 °C. The cycloaddition proceeded *via* a regioselective *exo* addition to give product **6** in 74% yield. Subsequent ring expansion and stereoselective methylation of the resulting ketone afforded the racemic synthesis of cedrol (**7**) and dehydration of **7** gave the racemic product cedrene (**8**).



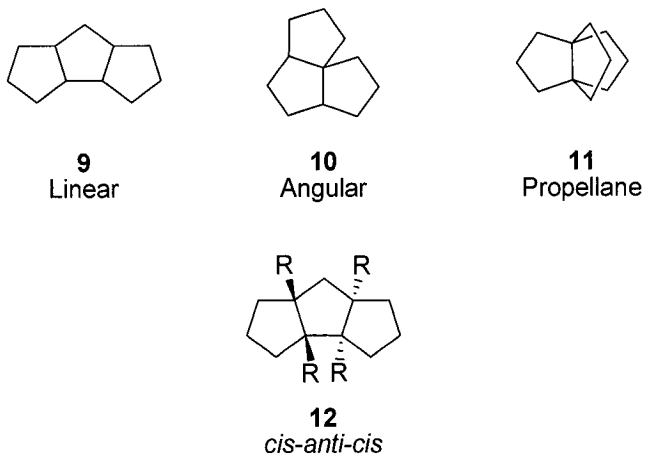
Scheme 4: Fallis' approach to (±)-cedrol and (±)-cedrene

Other examples involving the IMDA reaction as the key step include the synthesis of triquinanes hirsutene[11] and capnellene.[12] Through the cleavage of the strained olefin to give the diquinane, further transformations converted the key intermediate to the triquinane.

[10] Breitholle, E. G.; Fallis, A. G. *J. Org. Chem.* **1978,** *43,* 1964.
[11] Sternbach, D. D.; Ensinger, C. L. *J. Org. Chem.***1990,** *55,* 2725
[12] Grubbs, R. H.; Stille, J. R. *J. Am. Chem. Soc.* **1986,** *108,* 855.

1.3 Polyquinanes and $\Delta^{(9,12)}$- Capnellene

The growth in research devoted to polyquinane chemistry has steadily increased since the discovery of the first polyquinane, hirsutic acid in 1966.[13] The attention they have garnered in the past four decades is in large part due to their potential biological activity and more significantly, their structural complexity; the main attraction being the challenge that comes in synthesizing the complicated, multicyclic cyclopentanoid ring structure. Triquinanes (**9-11**) are the most abundant members of the polyquinane family, where linear triquinane **9** has acquired the most attention (Figure 1).[13b] The key synthetic difficulty associated with linear triquinanes is the rapid construction of the *cis-anti-cis*-tricyclo[6.3.0.$0^{2,6}$]undecane skeletal framework (**12**) and thus has triggered significant efforts in overcoming this synthetic dilemma. Similar to the history of steroids, triquinanes serve as target molecules to test experimental procedures and develop methodologies. The investigation for an efficient and attractive route to the polyquinane core is a continuing process.



9 Linear

10 Angular

11 Propellane

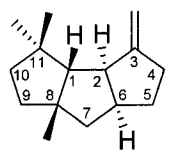
12 *cis-anti-cis*

Figure 1: Triquinane skeletons

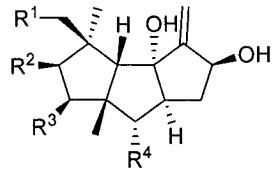
One of the more prominent triquinane natural products that has attracted the attention of synthetic organic chemists is $\Delta^{(9,12)}$- capnellene (**13,** Figure 2). Natural

[13] For reviews see: (a) Paquette, L. A. *Curr. Org. Chem.* **2002,** *6,* 1045; (b) Singh, V.; Thomas, B. *Tetrahedron* **1998,** *54,* 3647; (c) Mehta, G.; Srikrishna, A. *Chem. Rev.* **1997,** *97,* 671; (d) Paquette, L. A.; Doherty, A. M. *Polyquinane Chemistry;* Springer-Verlag: New York, **1987.**

occurring (-)-**13** was isolated from the soft coral *Capnella imbricata,*[14] and is believed to be the biogenetic precursor to the more oxygenated members of the capnellane family (**14a-14f**). These compounds exhibit antibacterial and antitumor activity, similar properties to that of the hirsutane family. Capnellanes are thought to be a chemical defense agent for larvae deposition[15] and microbial growth[16] on coral. The popularity of **13** has lead to an impressive number of total and formal syntheses.[17]



13



14a $R^1 = R^2 = R^3 = H$, $R^4 = OH$
14b $R^1 = R^3 = H$, $R^2 = R^4 = OH$
14c $R^1 = R^2 = R^3 = R^4 = H$
14d $R^1 = R^2 = R^4 = H$, $R^3 = OH$
14e $R^1 = R^3 = R^4 = H$, $R^2 = OH$
14f $R^2 = R^4 = H$, $R^1 = R^3 = OH$

Figure 2: Capnellane Family

1.4 Methods Leading to Linear Triquinanes via Diquinanes

There has been an explosion of research and development devoted to the formation of linear triquinanes. Research groups strive to assemble the ring structure with high

---

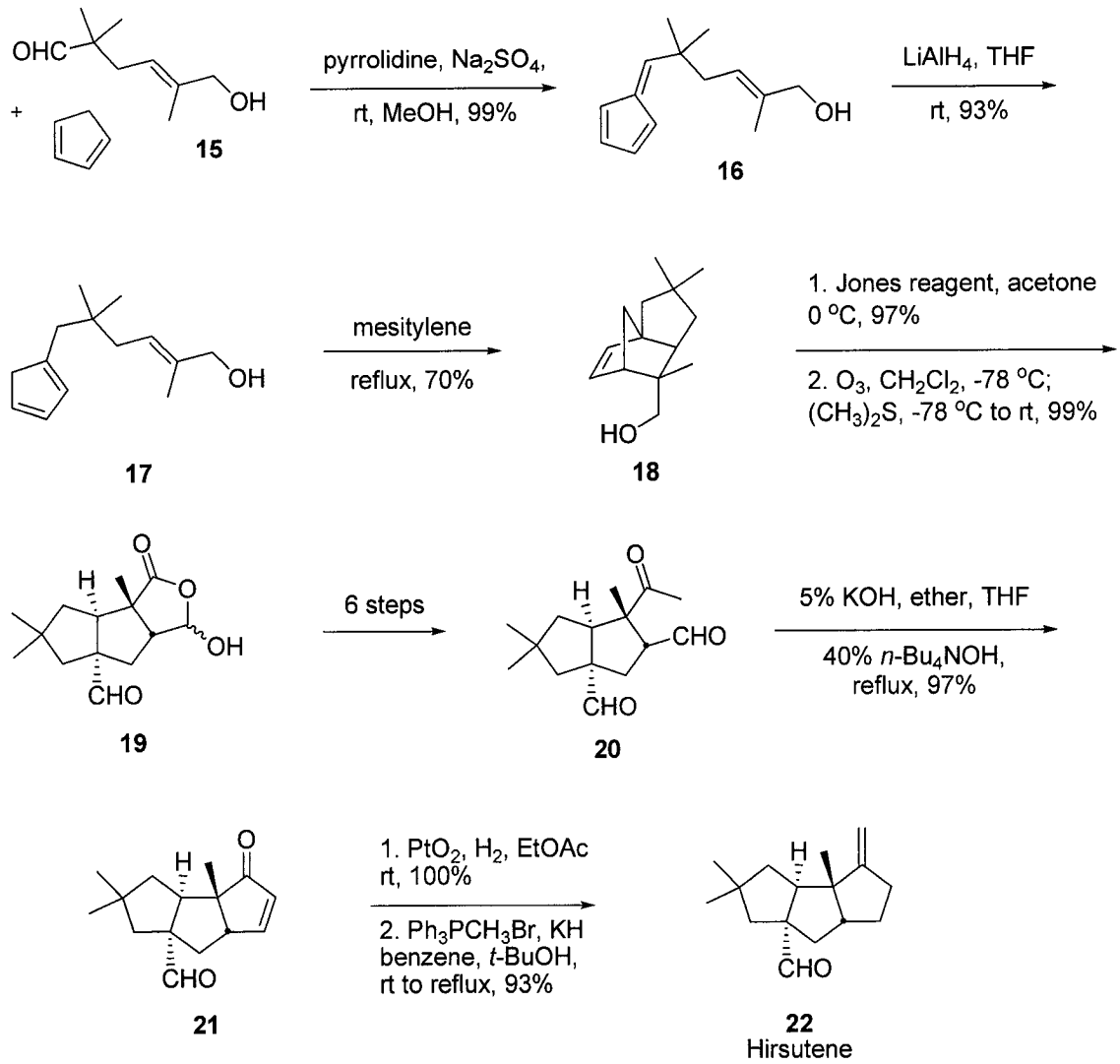
[14] Ayanoglu, E.; Gebreyesus, T.; Beechan, C. M.; Djerassi, C.; Kaisin, M. *Tetrahedron Lett.* **1978,** 1671.
[15] Cierzsko, L. S.; Karns, T. K. B. *Biology and Geology of Coral Reefs;* Jones, O. A., Endean, R., Eds.; Academic Press: New York, 1972; Vol. 2, Chapter 6.
[16] (a) Burkolder, P. R.; Burkolder, L. M. *Science* **1958,** *127,* 1174; (b) Cierzsko, L. S. *Trans. N.Y. Acad. Sci.* **1962,** *24,* 502.
[17] (a) Singh, V.; Porinchu, M.; Prathap, S. *J. Org. Chem.* **1998,** *63,* 4011; (b) Singh, V.; Prathap, S.; Porinchu, M. *Tetrahedron Lett.* **1997,** *38,* 2911; (c) Ohshima, T.; Kagechika, K.; Adachi, M.; Sodeoka, M.; Shibasaki, M.; *J. Am. Chem. Soc.* **1996,** *118,* 7108; (d) Ihara, M.; Suzuki, T.; Katogi, M.; Taniguchi, N.; Fukumoto, K. *J. Chem. Soc., Chem. Comm.* **1991,** 646; (e) Wang, Y.; Mukherjee, D.; Birney, D.; Houk, K. N. *J. Org. Chem.* **1990,** *55,* 4504; (f) Meyers, A. I.; Bienz, S. *J. Org. Chem.* **1990,** *55,* 3966; (g) Uyehara, T.; Furuta, T.; Akamatsu, M.; Kato, T.; Yamamoto, Y. *J. Org. Chem.* **1989,** *54,* 5411; (h) Iyoda, M.; (i) Kushida, T.; Kitami, S; Oda, M. *J. Chem. Soc., Chem. Comm.* **1987,** 1607; (j) Mehta, G.; Murthy, A. N.; Reddy, D. S.; Reddy, A. V. *J. Am. Chem. Soc.* **1986,** *108,* 3443; (k) Stille, J. R.; Grubbs, R. H. *J. Am. Chem. Soc.* **1986,** *108,* 855; (l) Curran, D. P.; Chen, M. H. *Tetrahedron Lett.* **1985,** *26,* 4991; (m) Crisp, G. T.; Scott, W. T.; Stille, J. K. *J. Am. Chem. Soc.* **1984,** *106,* 7500; (n) Stevens, K. E.; Paquette, L. A. *Can. J. Chem.* **1984,** *62,* 2415; (o) Piers, E.; Karunaratne, V. *Can. J. Chem.* **1984,** *62,* 629; (p) Little, R. D.; Carroll, G. L.; Petersen, J. L. *J. Am. Chem. Soc.* **1983,** *105,* 928; (q) Mehta, G.; Reddy, D. S.; Murty, S. *J. Chem. Soc., Chem. Comm.* **1983,** 824; (r) Oppolzer, W.; Bätig, K. *Tetrahedron Lett.* **1982,** *23,* 4669; (s) Fujita, T.; Ohtsuka, T.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* **1982,** *23,* 4091; (t) Birch, A. M.; Pattenden, G. *Tetrahedron Lett.* **1982,** *23,* 991; (u) Stevens, K. E.; Paquette, L. A. *Tetrahedron Lett.* **1981,** *22,* 4393; (v) Little, R. D.; Caroll, G. L. *Tetrahedron Lett.* **1981,** *22,* 4389;

regio- and stereo-selectivity in the shortest number of steps and attempts to be general enough to apply the methodology to other polyquinane natural products. There are two different views on approaching the triquinane core, the first, starting from a diquinane intermediate that contains appropriate side chains for further annulation to install the third ring. The second view involves generating the tricyclopentanoid framework in a single step. As mentioned above, $\Delta^{(9,12)}$- capnellene (**13**) has served as an attractive target to test different methodologies.

1.4.1 Sternbach's Approach

Sternbach and coworkers' strategy towards (±)-hirsutene (**22**)[11] involves the generation of the diquinane intermediate *via* the IMDA reaction of a substituted cyclopentadiene.[18] The Diels-Alder precursor was prepared, first through condensation of aldehyde **15** and cyclopentadiene to yield fulvene **16** (Scheme 5). The exocyclic double bond, which has Michael accepting character, was easily reduced using lithium aluminum hydride in 93% yield. The crucial IMDA reaction was conducted at 160 °C in refluxing mesitylene to provide tricyclic product **18** in 70% yield. Followed by Jones oxidation of the primary alcohol and ozonolysis of the olefin afforded the key diquinane intermediate **19**. Five steps were required to obtain dicarbonyl **20**, which then underwent an aldol condensation to form the third ring in triquinane **21**. Completion of the synthesis involved hydrogenation of enone **21** over PtO_2 and finally a Wittig reaction with methylene ylide to provide (±)-**22** in 93% yield.

[18] (a) Sternbach, D. D.; Hughes, J. W.; Burdi, D. F. *J. Org. Chem.* **1984,** *49,* 201; (b) Sternbach, D. D.; Hughes, J. W.; Burdi, D. F.; Banks, B. A. *J. Am. Chem. Soc.* **1985,** *107,* 2149.



Scheme 5: Sternbach's general approach to linear triquinanes via an intramolecular Diels-Alder reaction

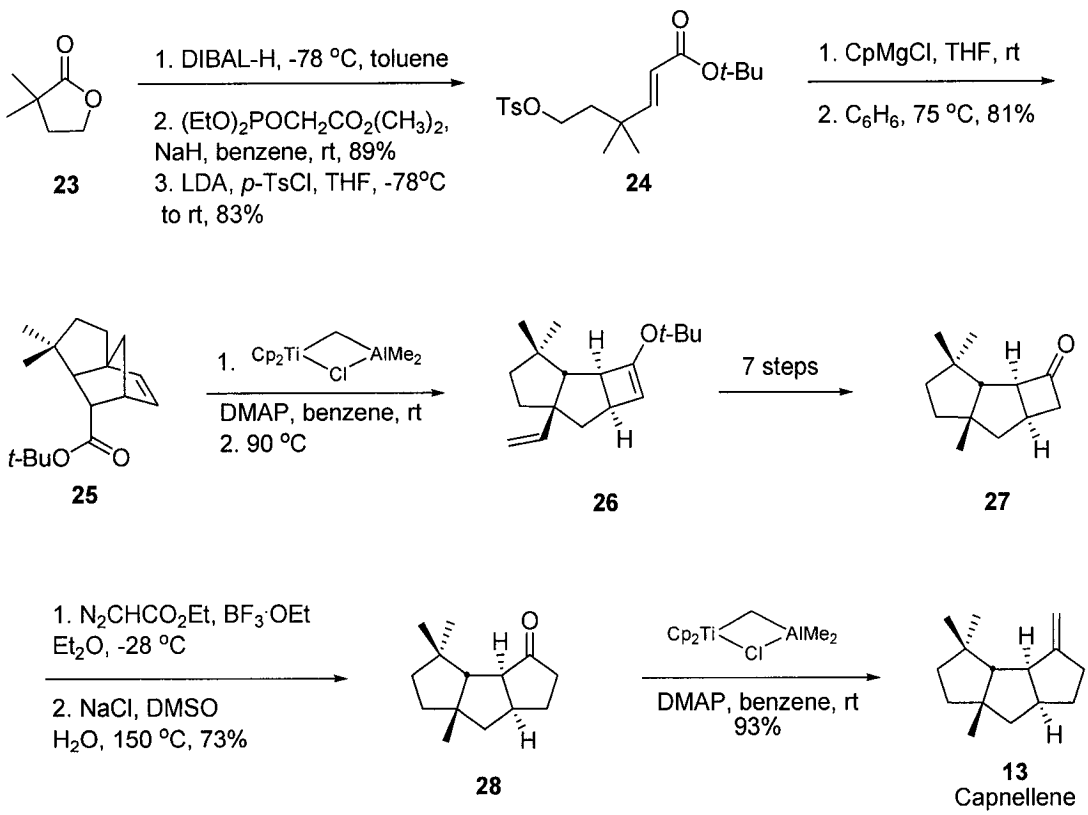
This methodology was also applied to the synthesis of angular triquinane sliphinene.[18b]

1.4.2 Grubbs Approach

Grubbs and Stille also use the IMDA reaction as a key step for their synthesis of capnellene (**13**, Scheme 6).[12] To make this synthetic route even more interesting, they employ a unique ring opening of the Diels-Alder adduct using Tebbe reagent, a titanium based reagent normally used for olefination of carbonyls.[19] This reaction sequence started

[19] Tebbe, F. N.; Parshall, G. W.; Reddy, G. S. *J. Am. Chem. Soc.* **1978,** *100,* 3611.

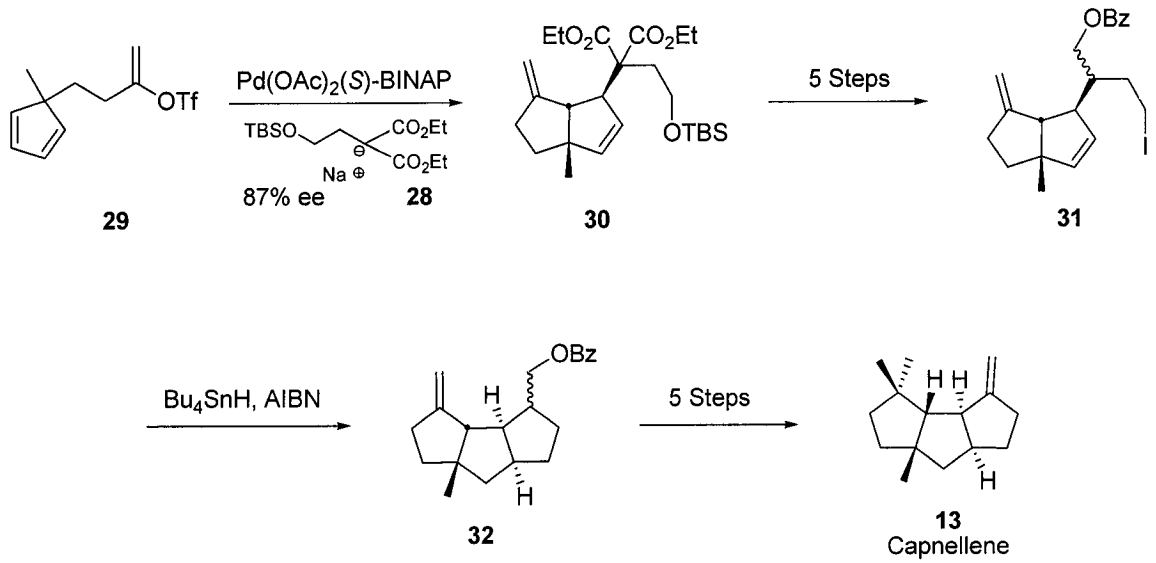
with lactone **23** and reduction with DIBAL-H to the corresponding lactol. Horner-Emmons-Wadsworth olefination converted the aldehyde to the α-β unsaturated ketone, however conjugate addition of the alcohol onto enone resulted. It was therefore necessary to treat the compound with LDA and trap the alcohol with *p*-TsCl to give tosylate **24**. Treatment of the tosylate with cyclopentadienyl magnesium chloride provided the substituted cyclopentadiene and heating in benzene, the IMDA reaction gave adduct **25**. Tebbe reagent was used to ring open the norbornene compound, resulting in diquinane moiety **26**. It then required 7 steps to reduce the vinyl group to the methyl substituent and to convert the enol ether to ketone **27**. Ethyldiazoacetate ring expanded the cyclobutane ring to the third cyclopentane ring and decarboxylation with wet DMSO and sodium chloride gave triquinane **28**. Lastly, conversion of the carbonyl to the exocyclic olefin using Tebbe reagent completed the racemic synthesis of capnellene (**13**).



Scheme 6: Grubbs' synthesis of capnellene via an intramolecular Diels-Alder reaction

1.4.3 Shibasaki's Approach

Another strategy worth mentioning is Shibasaki's asymmetric Heck reaction.[20] This was the first catalytic asymmetric synthesis of naturally occurring (-)-**13**. The reaction sequence started with an intramolecular asymmetric Heck reaction of compound **29** (Scheme 7), between the vinyl triflate and the olefin of cyclopentadiene. Using $Pd(OAc)_2$, (*S*)-BINAP ligand, and quenching of the reaction with nucleophile **28** provided diquinane **30** in 87% ee. Five steps were then required to obtain iodide **31**, which then underwent radical cyclization to form the third cyclopentane ring. Another five reaction steps were required to complete the enantioselective synthesis of (-)-**13**. Shibasaki and coworkers have also successfully synthesized $\Delta^{(9,12)}$- capnellene-3β,8β,10α-triol and $\Delta^{(9,12)}$- capnellene-3β,8β,10α,14-tetraol using the synthetic route.[21]



Scheme 7: Shibasaki's asymmetric synthesis of (-)-capnellene via an asymmetric Heck reaction

As shown, one can approach the synthesis of linear triquinanes through a diquinane intermediate. Although the key steps that lead towards the diquinane are highly creative, each approach requires a large number of additional reaction steps to achieve the triquinane and this can be quite time consuming and inefficient. To circumvent this

[20] Ohshima, T.; Kagechika, K.; Adachi, M.; Sodeoka, M.; Shibasaki M. *J. Am. Chem. Soc.* **1996,** *118,* 7108.
[21] Kagechika, K.; Shibasaki, S. *J. Org. Chem.* **1991,** *56,* 4093.

problem, a variety of methods have been developed which furnishes the triquinane core in one step from the appropriate starting material.

1.5 Methods Leading to Linear Triquinanes in a Single Step

In recent years, there has been a shift in focus in organic synthetic chemistry, steering away from multistep synthesis, leaning towards tandem and one pot reactions.[22] Tandem reactions are a series of conversions, combined into one synthetic procedure where the product from the initial reaction is perfectly set up to perform the next reaction. Sequential reactions or one pot procedures involve several transformations that work independently of each other that may require additional reagents, but occur in one reaction vessel. The goal here for both types of procedure is to obtain the highest degree of molecular complexity from relatively simple precursors in just one reaction step.

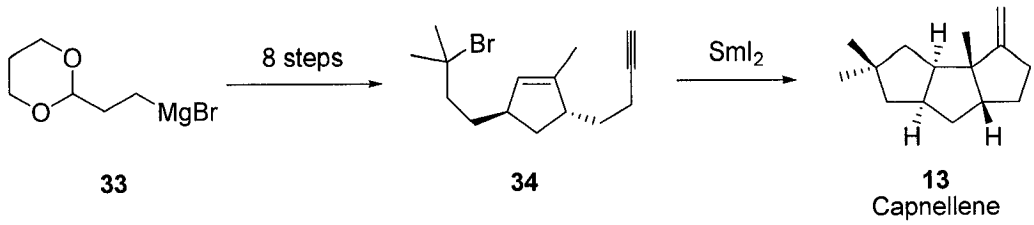
1.5.1 Curran's Approach

Curran and co-workers have developed a novel synthetic approach that uses a samarium iodide promoted radical cyclization.[23] They have impressively shown that radical cyclization can construct five membered rings in a controlled fashion, synthesizing linear triquinanes hirsutene (**20**),[23a] hypnophilin,[23e] and angular triquinane silphiperfolene.[23d] The general view can be seen in their synthesis of capnellene (**13**, Scheme 8).[23a] Key substrate **34** was prepared in eight steps from acetal protected Grignard reagent **33**. The radical produced on the tertiary carbon of compound **34**, using samarium iodide, reacted with the cyclopentene ring to form the initial diquinane, but the resulting radical quickly underwent a five-exo dig cyclization with the alkyne to furnish **13**.

---

[22] Wasilke, J. C.; Obrey, S. J.; Baker, R. T; Bazan, G. C. *Chem. Rev.* **2005,** *105,* 1001

[23] (a) Curran, D. P.; Chen, M. –H. *Tetrahedron Lett.***1985,** *26,* 4991; (b) Curran, D. P; Rakiewicz, D. M. *Tetrahedron Lett..* **1985,** *41,* 3943; (c) Curran, D. P; Rakiewicz, D. M. *J. Am. Chem. Soc.* **1985,** *107,* 1448; (d) Curran, D. P.; Kuo, S. –C. *J. Am. Chem. Soc,* **1986,** *108,* 1106; (e) Fevig, T. L.; Elliot, R. L.; Curran, D. P. *J. Am. Chem. Soc.* **1988,** *110,* 5064.

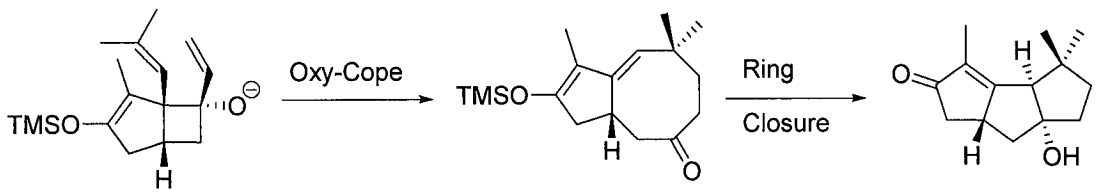


33 34 13 Capnellene

Scheme 8: Curran's SmI_2 promoted tandem radical cyclization

1.5.2 Moore's Approach

Another inventive approach was conceived by Moore and coworkers where they utilize the well known oxy-cope rearrangement to incorporate complexity in the molecules.[24] Their work was based on additions of vinyl anions to squarate esters, research that was pioneered by Paquette and coworkers.[25] The corresponding bicycle[6.3.0]heptenone was treated with vinyl lithium to give anion **35** (Scheme 9). The resulting 1,5-diene and undewent the charge accelerated oxy-cope rearrangement to obtain 5-8 fused ring structure **36**. Hydrolysis of the silyl enol ether during workup initiated a transannular ring closure to provide substituted linear triquinane **37** in one step. Adding functionality to the ring was achieved by altering the substituents on the vinyl piece located at the ring junction of the 5-4 fused ring system as well as changing the substitution pattern on the vinyl lithium that was added to the carbonyl.



35 36 37

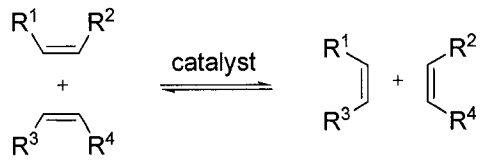
Scheme 9: Moore's tandem oxy-cope – transannular ring closure approach to linear triquinanes

[24] (a) Santora, V. J.; Moore, H. W. *J. Am. Chem. Soc.* **1995,** *117,* 8486; (b) MacDougall, J. M.; Santora, V. J.; Verma, S. K.; Turnball, P,; Hernandez, C. R.; Moore, H. W. *J. Org. Chem.* **1998,** *63,* 6905.

[25] (a) Negri, J. T.; Morwick, T.; Doyon, J.; Wilson, P. D.; Hickey, E. R; Paquette, L. A. *J. Am. Chem. Soc.* **1993,** *115,* 12189; (b) Paquette, L. A.; Morwick, T. *J. Am. Chem. Soc.* **1995,** *117,* 1451; (c) Geng, F.; Liu, J.; Paquette, L. A. *Org. Lett.* **2002,** *4,* 71.

1.6 Olefin Metathesis

Carbon-carbon bond forming reactions remain one of the most important transformations in the synthesis of organic compounds. Recently olefin metathesis has become part of the organic chemistry arsenal to do such transformations.[26] Olefin metathesis is essentially the cleavage and the formation of double bonds (Scheme 10).



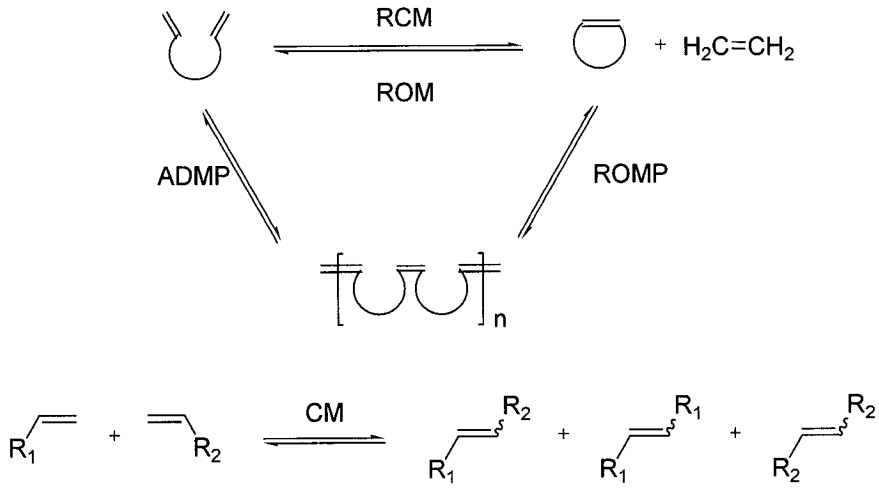
Scheme 10: Olefin metathesis

Synthetically useful, high-yielding procedures include ring closing metathesis (RCM) between terminal alkenes of an acyclic diene, cross metathesis (CM), the intermolecular reaction of terminal vinyl groups, and ring opening metathesis (ROM) of strained cyclic alkenes (Scheme 11). Furthermore, traditional methods for synthesizing polymers are acyclic diene metathesis polymerization (ADMP) and ring opening metathesis polymerization (ROMP). Given that the starting material for the RCM and ADMP are the same, the outcome of the reaction can be controlled to some extent by adjusting the dilution of the reaction mixture and product formation is strongly influenced by preexisting conformational constraints in the substrate. This is also the same for preventing or permitting the polymerization step after ROM.

Olefin metathesis is a completely reversible reaction, hence there must be a driving force to push the equilibrium in the appropriate direction. In the case of RCM, CM and the polymerization reactions the equilibrium can be driven by the removal of byproduct ethylene from the reaction mixture. Thus, these reactions are entropically favoured. On the other hand, ROM is energetically favoured and the loss of ring strain pushes the reaction forward.

---

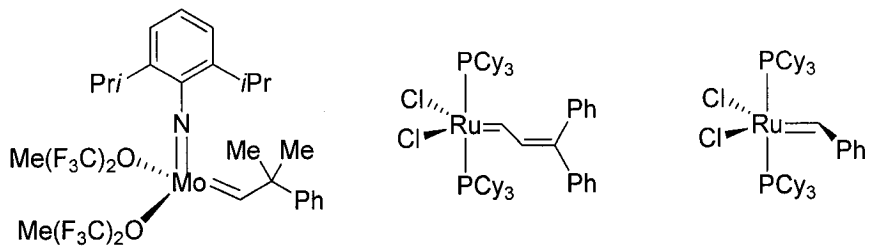
[26] For reviews see: (a) Furstner, A. *Angew. Chem. Int. Ed.* **2000,** *39,* 3012; (b) Hoveyda, A. H.; Schrock, R. R. *Chem. Eur. J.* **2001,** *7,* 945; (c) Blechert, S.; Connon, S. J. *Angew. Chem. Int. Ed.* **2003,** *42,* 1900; (d) Grubbs, R. H.; Miller, S. J.; Fu, G. C. *Acc. Chem. Res.* **1995,** *28,* 446.



Scheme 11: Important types of olefin metathesis

1.6.1 Alkylidene Based Olefin Metathesis Catalysts

Part of the reason for its belated application is due to the fact that initial catalysts possessed strong Lewis-acidic character and therefore showed poor activity in the presence of polar functional groups. As a result, applications of olefin metathesis were restricted to the production of nonfunctionalized polymers. Another drawback was its instability in air and water. The popularity of this reaction arose during the development of molybdenum (**38**) and ruthenium (**39**, **40**) alkylidene based catalysts (Figure 3).



38 **39** **40**

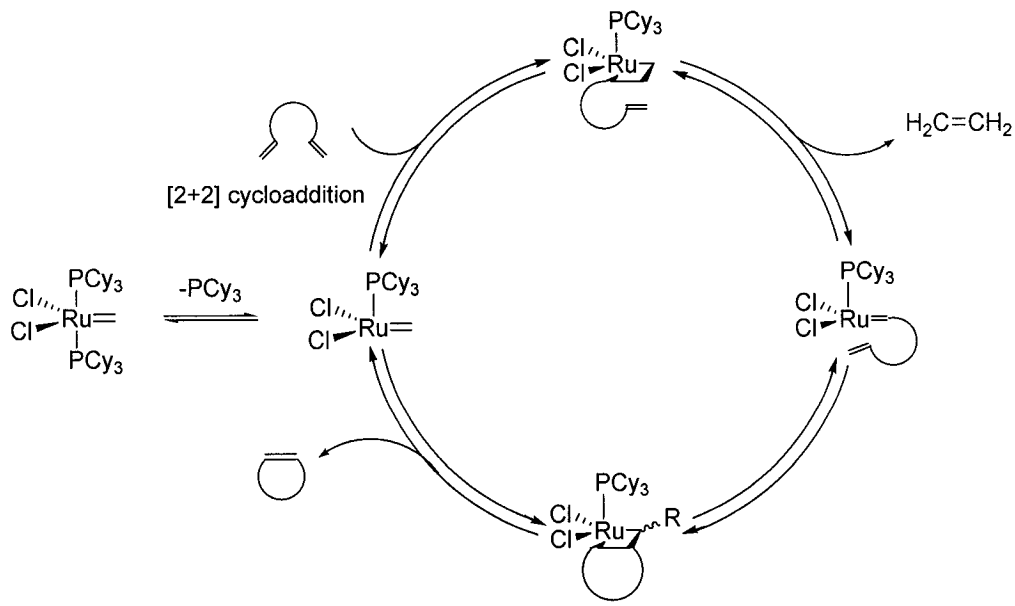
Figure 3: First generation Schrock and Grubb catalysts

Schrock's molybdenum catalyst **38** was one of the first catalysts to be widely used. The most impressive feature of **38** is its high activity, which allows it to react with both terminal and internal olefins and to ROMP low strain monomers. It also has the

ability to ring close sterically demanding and electron poor substrates. Despite its remarkable utility and potential applications, synthetic organic chemists did not embrace it immediately. Unfortunately, molybdenum catalysts are extremely sensitive to oxygen and water, therefore difficult to handle and an inconvenience to use. As well, they have poor functional group tolerability, unable to react in the presence of common substituents such as aldehydes and alcohols.

Grubbs ruthenium based catalyst, **39** and **40** were a real breakthrough. Although it doesn't have the high activity of the molybdenum catalyst, the tolerance toward an array of functional groups and the ease of handling due to reasonable stability against oxygen, water and minor impurities in the solvents makes them extremely practical tools and explains their unrivaled popularity.

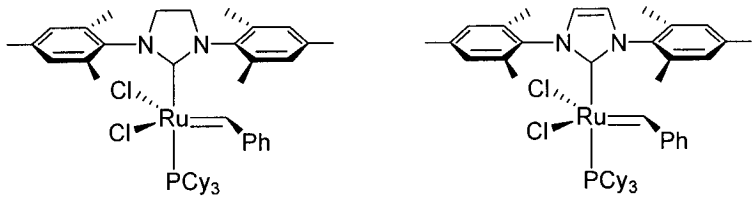
The general accepted mechanism of metathesis reactions, the Chauvin mechanism, involves the interconversion of an olefin and a metal alkylidene, as seen in Scheme 12, the general RCM reaction after one catalytic cycle. The first step in the mechanism is a dissociative pathway, starting with a loss of phosphine to go from a $16e^-$ species to the reactive $14e^-$ intermediate. The process generates a metallacyclobutane which then undergoes a series of [2+2] cycloadditions and cycloreversions, while generating ethylene during the cycle.



Scheme 12: Proposed mechanism of ring closing metathesis

1.6.2 Second Generation Olefin Metathesis Catalysts

Continuing research in this area has seen more improvement in catalyst activity and stability. A second generation of ruthenium catalysts has been developed which contains the stable Fischer carbene, the *N*-hetercyclic carbene (Figure 4). With its increased basicity and increase steric environment as compared to phosphine ligand PCy_3, these catalysts have a greater lifetime and reactivity.

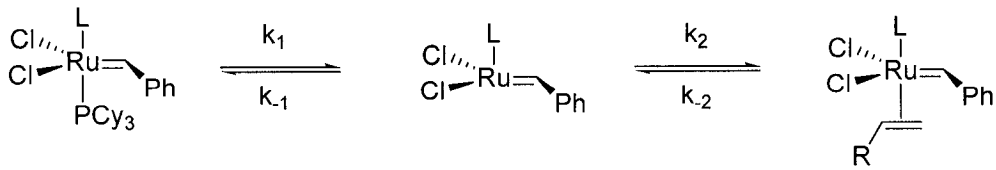


41 **42**

Figure 4: Grubbs 2nd generation catalysts

Now, these ruthenium based complexes such as **41** and **42** have similar activity to the molybdenum complexes while still maintaining the high functional group tolerance and air and moisture stability of **40**. Grubbs 2nd generation catalysts are able to react with electron deficient and sterically hindered olefins.

It was originally thought that increased reactivity of the 2nd generation was due to increased rate of the phosphine dissociation, however after extensive kinetic studies,[27] it was discovered that this is not the case and that 1st generation Grubbs catalyst **40** dissociates at a faster rate than **41**. This also means that the backwards reaction, phosphine association (k_{-1}), is also faster. For **41**, the coordination of the olefin (k_2) is so much faster than k_{-1}, this accounts for the increased activity (Scheme 13).



Scheme 13: Dissociative mechanism

[27] Sanford, M. S.; Ulman, M.; Grubbs, R. H. *J. Am. Chem. Soc.* **2001,** *123,* 749.

The development of Grubbs 2nd generation has exploded and has led to an extreme number of applications. It still has some limitations mainly CM of directly functionlized olefins, such as acrylonitrile.[28] Despite this restriction it has been involved in key steps for the synthesis of medium rings and macrocyclic molecules. There are also examples of enantioselective RCM, where chirality is induced from a chiral *N*-heterocyclic carbene ligand.[29]

1.6.3 Third Generation Olefin Metathesis Catalysts

Very recently, a group of 3rd generation ruthenium based catalysts has been developed that are all phosphine free (Figure 5). Complex **43a** developed by Hoveyda and coworkers utilize an *i*-propoxy group on the phenylcarbene unit which stabilizes the complex during its resting state.[30] It readily opens up a coordination site in the presence of the substrate. Grela and coworkers synthesized the bromo (**43b**) and the nitro (**43c**) analogues.[31] Although complex **43b** was in general less reactive than **43a**, nitro derivative **43c** showed great promise in that it was able to undergo CM of directly functionlized olefins including acrylonitrile. Blechert and Wakamatsu have shown that binol- or biphenyl based styrene ligands on their complexes (**44** and **45**) were more reactive than **43a** and Grubbs 2nd generation catalyst (**41**). Grubbs developed the bispyridine ruthenium catalyst **46**,[28] and Chang and co-workers have applied this catalyst for CM of conjugated enynes.[32]

---

[28] Love, J. A.; Morgan, J. P.; Trnka, T. A.; Grubbs, R. H. *Angew. Chem. Int. Ed.* **2002,** *41,* 4035.
[29] Seiders, T. J.; Ward, D. W.; Grubbs, R. H. *Org. Lett.* **2001,** *3,* 3225.
[30] Garber, S. B.; Kingsbury, J. S.; Gray, B. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000,** *122,* 8168.
[31] Grela, K.; Harutyunyan, S.; Michrowska, A. *Angew. Chem. Int. Ed.* **2002,** *41,* 4038.
[32] Kang, B.; Kim, D- H.; Do, Y.; Chang, S. *Org. Lett.* **2003,** *5,* 3041.

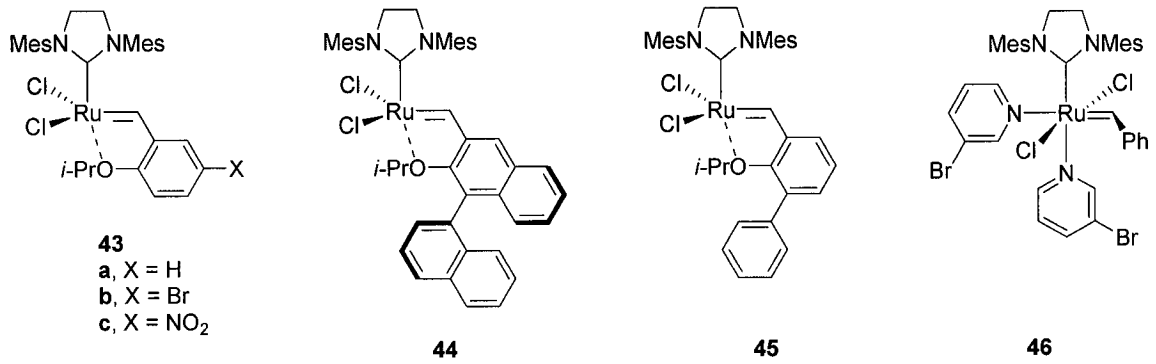
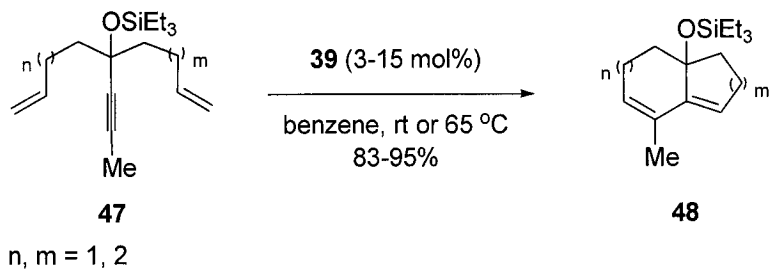


Figure 5: 3rd Generation Catalyst

1.6.4 Tandem Olefin Metathesis

Tandem reactions are very attractive in the sense that it can build high molecular complexity rapidly from relatively simple starting substrates. One of the first examples of tandem olefin metathesis was reported by Grubbs and co-workers where they synthesized fused bicyclo[*n, m,* 0] ring systems through a RCM/RCM of dienynes (Scheme 14).[33] The acetylene (**47**) positioned between the two olefins, acts as an olefin metathesis relay and generates five, six and seven membered rings (**48**).



Scheme 14: RCM/RCM of dienynes

It has also shown that combining the energetically favoured ROM and the entropically favoured RCM can be a very useful method for the construction of complex ring systems.[34] The ROM-CM combination[35] has also been reported and even the ROM-RCM-CM sequence is feasible.[36]

---

[33] (a) Kim, S-. H.; Bowden, N.; Grubbs, R. H. *J. Am. Chem. Soc.* **1994,** *116,* 10801; (b) Kim, S-, H.; Zuercher, W. J.; Bowden, N.; Grubbs, R. H. *J. Org. Chem.* **1996, *61,*** 1073.

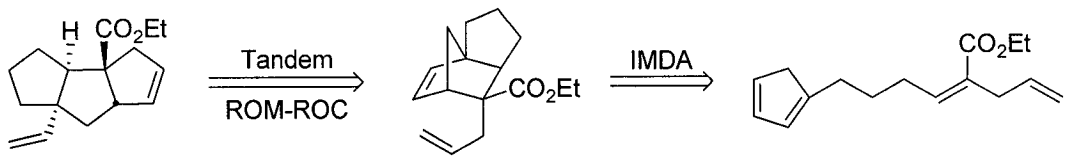
[34] (a) Zuercher, W. J.; Hashimoto, M.; Grubbs, R. H. *J. Am. Chem. Soc.* **1996,** *118,* 6634; (b) Hagiwara, H.; Katsumi, T.; Endou, S.; Hoshi, T.; Suzuki, T. *Tetrahedron* **2002,** *58,* 6651; (c) Minger, T. L.; Phillips, A. J.

1.7 Research Objectives

The main objective for the project is to develop a one pot procedure towards the linear triquinane core.

1.7.1 Retrosynthesis

Inspired by the work of Grubbs and Stille, and of Fallis[37], our synthetic strategy involves an IMDA reaction of cyclopentadiene and the dienophile tethered by a three-carbon chain (**51**, Scheme 15). Our desired precursor would contain an activated dienophile, making the Diels-Alder reaction more facile. As well, the dienophile would be part of a 1,4-diene moiety. Ideally, once the cycloaddition occurs to give adduct **50** the allyl group would be in the endo position, necessary for the tandem ROM-RCM sequence. The overall plan would furnish the tricyclo(6.3.0.$0^{2,6}$)undecane skeleton (**49**).



49 **50** **51**

Scheme 15: Retrosynthetic plan for the synthesis of the linear triquinane skeleton

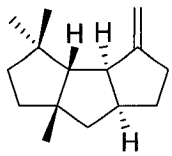
Our approach is a one pot procedure (IMDA – ROM – RCM) that assembles the triquinane core from readily accessible precursors, the requisite *cis-anti-cis* ring junction is set in the Diels-Alder reaction and the final product contains double bonds which can be easily derivatized for further functionalization. Once our synthetic strategy is validated, we would apply the methodology towards the total synthesis of $\Delta^{(9,12)}$-capnellene (**13**).

Tetrahedron Lett. **2002,** *43,* 5357; (d) Weatherhead, G. S.; Ford, J. G.; Alexanian. E. J.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2000,** *122,* 1828; (e) Holtsclaw, J.; Koreeda, M. *Org. Lett.* **2004,** *6,* 3719.

[35] (a) Tallarico, J. A.; Bonitatebus, P. J.; Snapper, M. L. *J. Am. Chem. Soc.* **1997,** *119,* 7157; (b) Liu, Z.; Rainier, J. D. *Org. Lett.* **2005,** *7,* 131; (c) Weeresakare, G. M.; Liu, Z.; Rainier, J. D. *Org. Chem.* **2004,** *6,* 1625; (d) La, D. S.; Ford, J. G.; Sattely, E. S.; Bonitatebus, P. J.; Schrock, R. R.; Hoveyda, A. H. *J. Am. Chem. Soc.* **1999,** *121,* 11603.

[36] Arjona, O.; Csákÿ, A. G.; Murcia, M. C.; Plumet, J. *Tetrahedron Lett.* **2000,** *41,* 9777.

[37] IMDA model studies for the total synthesis of capnellene (a) Hellou, J.; Berube, G.; Newlands, M. J.; Fallis, A. G.; Gabe, E. J. *Can. J. Chem.* **1988,** *66,* 439; Total synthesis of Longifolene *via* IMDA (b) Lei, B.; Fallis, A. G. *J. Am. Chem. Soc.* **1990,** *112,* 4609.

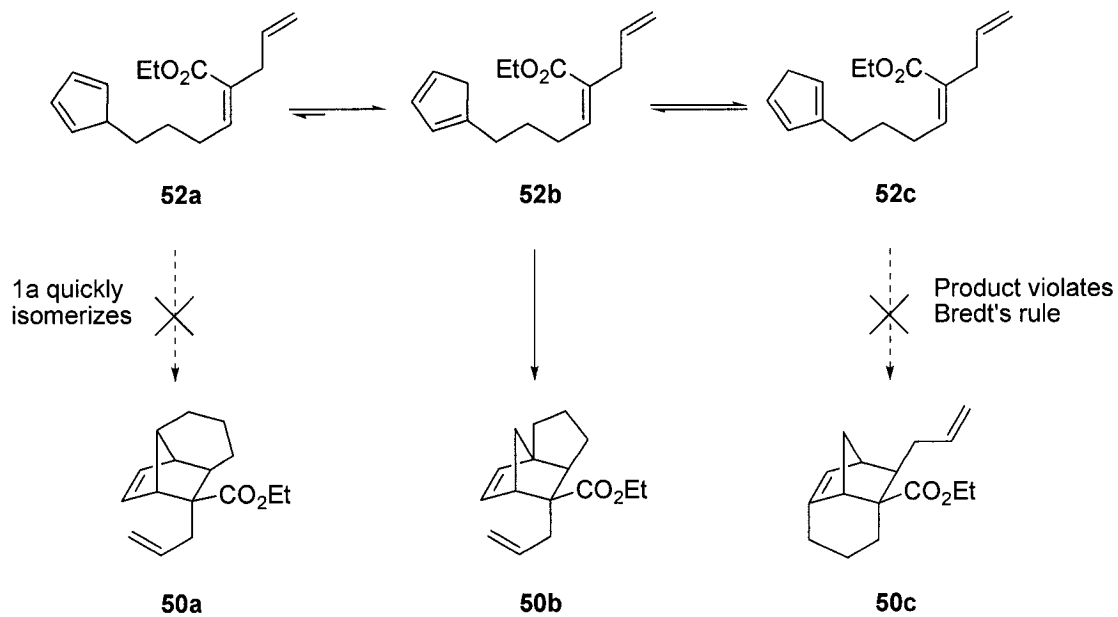


13
Capnellene

Figure 6: Synthetic target

1.7.2 Intramolecular Diels-Alder

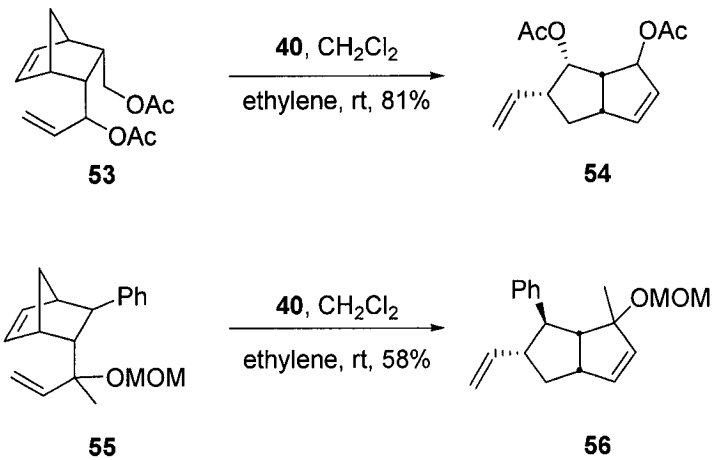
The rational behind our approach begins with the selectivity in the IMDA reaction, where literature precedence predicts the selective formation of tricycle **50b** (Scheme 16). Due to 1,5-sigmatropic hydrogen shift, alkyaltion of cyclopentadienyl anion will a yield a mixture of three isomers **52a-52c**,where only **52b** will cyclize to yield the desired product. The cycloaddition of **52c** is unlikely as the product formed from this reaction violates Bredt's rule. If **52a** is in sufficient concentration, it has all the electronic and steric requirements to cyclize to form **50a**, but this is unlikely since in order for this to occur the Diels-Alder reaction of **50a** must be faster than the isomerization to **52b**, which is not known to occur. Thus, from a possibility of three products, only one is formed, **50b**.



Scheme 16: Predicted outcome of intramolecular Diels-Alder

1.7.3 Tandem Ring Opening Metathesis – Ring Closing Metathesis

The rational for the next part of our strategy, the tandem ROM-RCM reaction, is based on numerous examples of diquinane formation through this protocol. Norbornene compounds are common substrates for ROM because of the strained olefin it contains and has been employed in tandem ROM-RCM sequences. Hagiwara and co-workers have shown that with an allyl group on norbornene structure can produce diquinanes very effectively (Scheme 17).[34b] Starting materials **53** and **55** were prepared by Diels-Alder reactions of cyclopentadiene with the corresponding α,β-unsaturated carbonyls, followed by addition of vinylmagnesium bromide. Treatment with 1st generation Grubbs catalyst (**40**), in an atmosphere of ethylene at room temperature, effectively performs the tandem reaction giving diquinanes **54** and **56**. Reaction yields ranged from 50-81%.



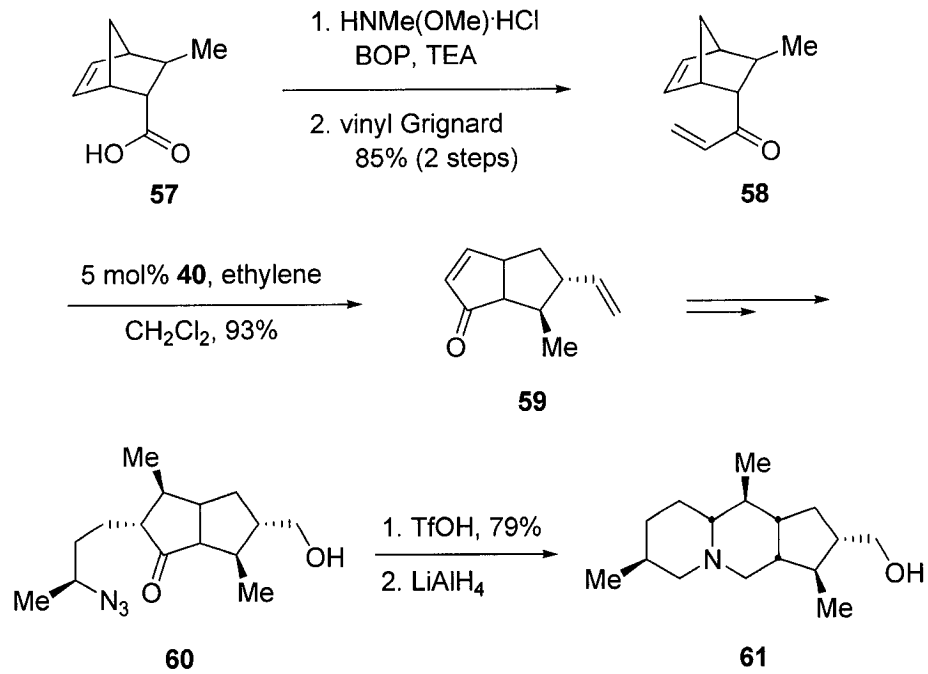
53 **54**

55 **56**

Scheme 17: Synthesis of diquinanes via tandem ROM-RCM

To further validate our strategy, Aubé and co-workers used the tandem sequence to synthesize their Schmidt rearrangement precursor which was the key step for the total synthesis of 251F (**61**, Scheme 18).[38] Treatment of **58** with catalyst **40** in methylene chloride saturated with ethylene afforded the bicyclic enone **59** in 93% yield. Further functional group manipulations, including the intramolecular Schmidt rearrangement of **60**, completed the synthesis of **61**.

[38] Wrobleski, A.; Sahasrabudhe, K.; Aubé, J. *J. Am. Chem. Soc.* **2002,** *124,* 9974.



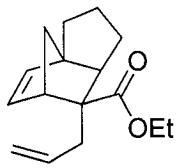
Scheme 18: Aubé synthesis of diquinane intermediate **59** via tandem ROM-RCM

With this theory and background, our attempt to the linear triquinane core was pursued. The next section discusses the results obtained from our approach.

2 Results and Discussion – One Pot Intramolecular Diels-Alder – Ring Opening Metathesis – Ring Closing Metathesis Approach to Linear Triquinanes

2.1 Attempts at the synthesis of a cyclopentadiene with an activated dienophile

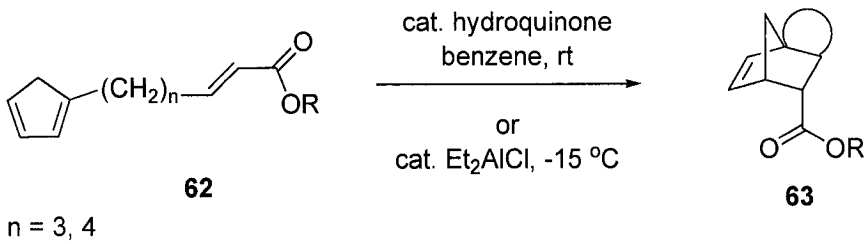
With a plan in place, our first synthetic target was compound **50**.



50

Figure 7: Precursor required for the tandem ROM-RCM

Grubbs and Stille investigated extensively on cyclopentadiene compounds tethered to an α,β-unsaturated ester dienophile as Diels-Alder precursors.[7] When the tether length was either three or four carbon units long, the major product obtained was adduct **63** (Scheme 19). This reaction occurred smoothly under very mild conditions, either at room temperature in benzene in the presence of catalytic hydroquinone, or Lewis acid catalyzed with diethyl aluminum chloride at -15 °C.



62

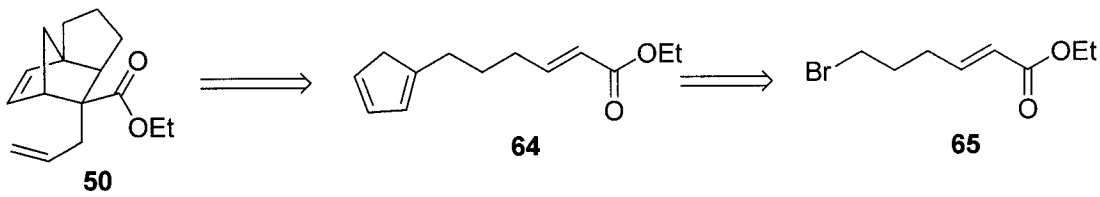
n = 3, 4

63

Scheme 19: IMDA of α,β-unsaturated ester

Our plan to synthesize **50**, described in Scheme 20, required the substituted cyclopentadiene **64** which could be prepared from the addition of a cyclopentadienyl anion to alkyl bromide **65**. The addition of the necessary allyl group would be installed after the cycloaddition reaction. It is necessary for the tandem olefin metathesis sequence.

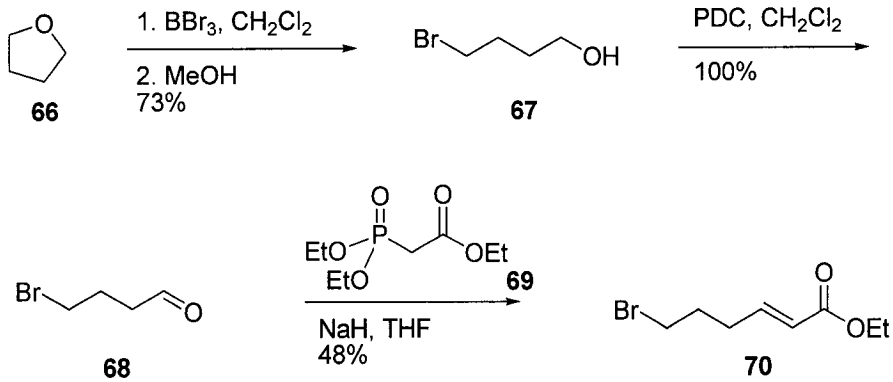
Although this was not the one pot IMDA-ROM-RCM we were envisioning, it was good starting point and a good model study for the investigations of this approach.



Scheme 20: Retrosynthetic plan for the synthesis of **50**

The synthesis of the required side chain started with ring opening of tetrahydrofuran (**66**) using boron tribromide and quenching with MeOH giving bromo alcohol **67** in 73% yield.[39] Oxidation of the primary alcohol to aldehyde **68** occurred smoothly with pyridinum dichromate (PDC) in quantitative yield. Kulkarni and coworkers reported a one pot procedure where PDC was added immediately after **67** was formed. However, it was found that better yields were observed when each reaction was performed separately.

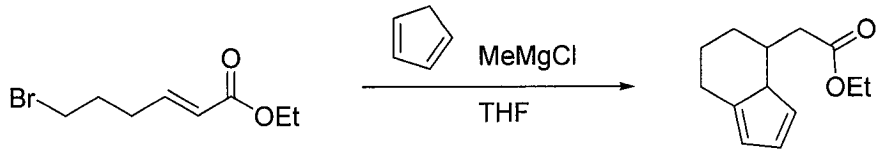
Generation of the desired alkyl bromide was accomplished using the Horner-Wadsworth-Emmons reaction. Phosphonate **69** and sodium hydride converted the aldehyde to enone **70** in 48% yield. [40]



Scheme 21: Synthesis of α-β unsaturated ester

[39] (a) Kulkarni, S. U.; Patil, V. D. *Heterocycles* **1982,** *18,* 163; (b) Guindon, Y.; Therien, M.; Girard, Y.; Yoakim, C. *J. Org. Chem.* **1987,** *52,* 1680.
[40] Vedejs, E.; Arnost, M. J.; Hagen, J. P. *J. Org. Chem.* **1979**, *44,* 3230.

With the necessary α-β unsaturated ester in hand, the next task was to alkylate cyclopentadiene using reaction conditions employed by Grubbs and Stille.[7] Following literature procedure, cyclopentadiene was treated with methyl magnesium chloride and to this solution was added alkyl bromide **70**. Monitoring the reaction by TLC, starting material was still present after two days of stirring at room temperature. Addition of excess cyclopentadiene and base pushed the reaction to completion and upon purification of the reaction mixture an unknown product was formed in 80% yield. ^{1}H and ^{13}C NMR data suggested that the product formed was bicyclic compound **72** (Scheme 22).

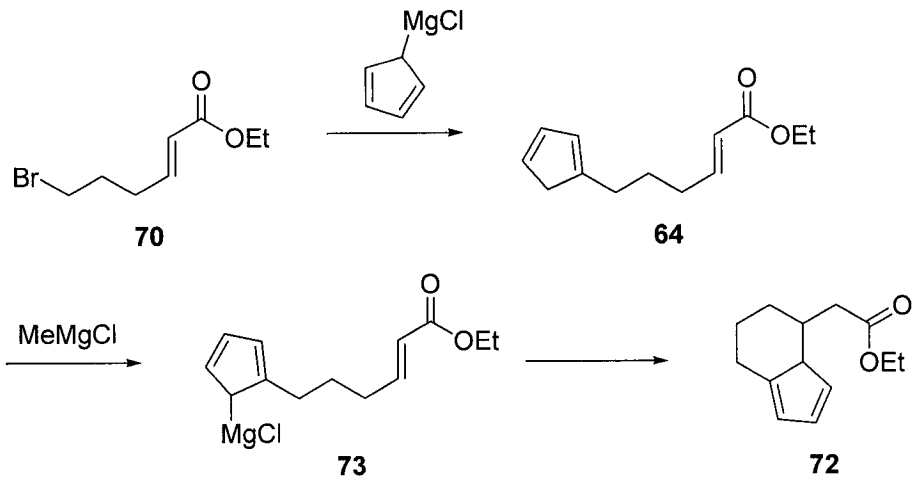


70 **72** 80%

Scheme 22: Alkyation of cyclopentadiene

Grubbs and Stille as well as Sternbach[41] observed this type of product during their initial investigations. The proposed formation of bicyclic product **72** involves the S_n2 displacement of the bromide with cyclopentadienyl magnesium chloride to give desired substituted cyclopentadiene **64** as an intermediate (Scheme 23). However, in the presence of base, the cyclopentadiene moiety gets deprotonated again and the substrate undergoes a 1,4-conjugate addition to yield the observed product. They suggested that cyclopentadienyl sodium and lithium favored the intramolecular Michael reaction and that using cyclopentadienyl magnesium chloride or bromide circumvented this issue. However, this was not the case for us.

[41] Sternbach, D. D.; Hughes, J. W.; Burdi, D. F. *J. Org. Chem.* **1984**, *49*, 201-202.

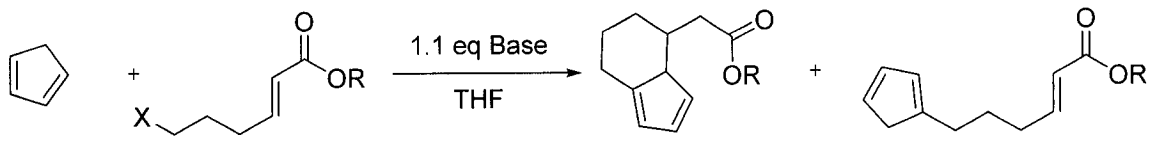


Scheme 23: Proposed reaction sequence for the formation of bicycle **12**

Based on the proposed mechanism, we knew the desired product was forming as an intermediate. The reaction was repeated with MeMgCl, this time using 1.1 equivalence. With this, 35% of **72** was obtained (Entry 1), while the remaining mass balance was starting material (45%).

As outlined in Table 1, our investigations began at varying the base and changing the nature of the metal counterion. It was thought by using a harder counterion, as lithium or sodium, the cyclopentadienyl anion would in turn become a harder nucleophile and thus slow the rate of the 1,4-conjugate addition. Grubbs and Stille stated that sodium and lithium counterions favoured the intramolecular Michael reaction, yet we decided to try butyl lithium (Entry 2) and sodium hydride (Entry 3). As reported, these bases afforded bicycle **72** in 45% and 47% yield respectively. No trace of the desired product was observed.

Table 1 : Conditions tested the attempted formation of substituted cyclopentadiene

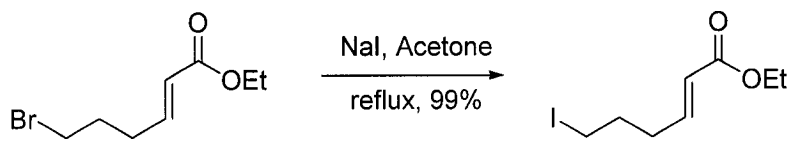


70 **72** **64**

Entry	R	X	Base	pKa	Temp	Yield* 72 (%)	Yield 64 (%)
1	Et	Br	MeMgCl	48	rt	35	0
2	Et	Br	BuLi	55	rt	45	0
3	Et	Br	NaH	35	rt	47	0
4	Et	I	EtMgCl	50	rt	40	0
5	*t*-Bu	Br	EtMgCl	50	rt	40	0
6	Et	Br	EtMgCl	50	0 °C	38	0

*Starting material was recovered in all cases

It was considered that using a better leaving group would increase the tendency for the leaving group to undergo displacement. Therefore, the bromide was converted to the iodide. Alkyl iodide **70a** was easily prepared from bromide **70**, using sodium iodide in refluxing acetone giving the desired alkyl chain in quantitative yields (Scheme 24).[42] Testing the iodide and using ethylmagnesium chloride as base unfortunately had no effect on the reaction, giving the bicyclic product **72** in 40% yield (Entry 4).



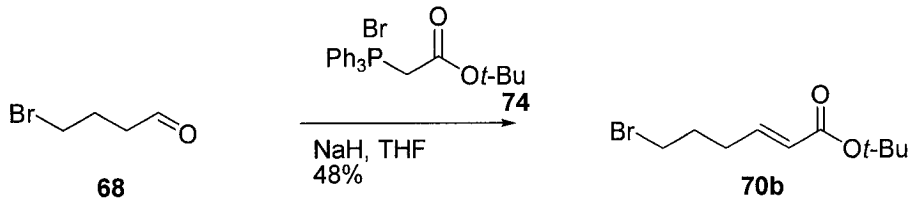
70 **70a**

Scheme 24: Synthesis of alkyl iodide **14**

Another attempt at synthesizing the substituted cyclopentadiene containing an activated dienophile involved increasing the steric bulk around the alkene by employing a

[42] Bunce, R. A.; Peeples, C. J.; Jones, P. B. *J. Org. Chem.* **1992,** *57,* 1727.

t-butyl ester functionality. The α-β-unsaturated *t*-butyl ester **75** was synthesized from aldehyde **68** and treating it with phophonium **74** and sodium hydride in 48% yield (Scheme 25). Again, this substrate had no effect on the reaction. With ethylmagnesium chloride as base, product **72a** was formed in 40% yield (Entry 5).

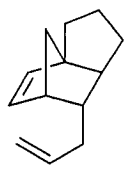


Scheme 25: Synthesis of α-β unsaturated *t*-butyl ester alkyl bromide

Perhaps the temperature of the reaction was too high, thus making the Michael reaction feasible. However, performing the reaction at 0 °C provided only the bicyclic compound as well (Entry 6).

2.2 The synthesis of a cyclopentadiene with an unactivated dienophile

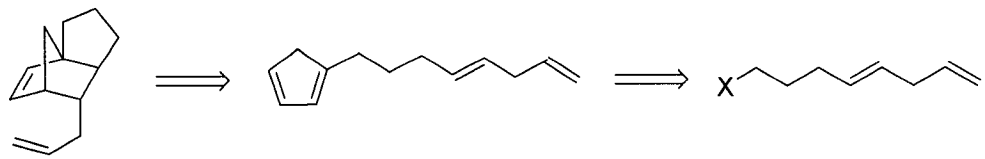
Disappointed by our initial results, we decided to abandon this route and concentrate on the synthesis of compound **75**.



75

Scheme 26: Precursor required for the tandem ROM-RCM

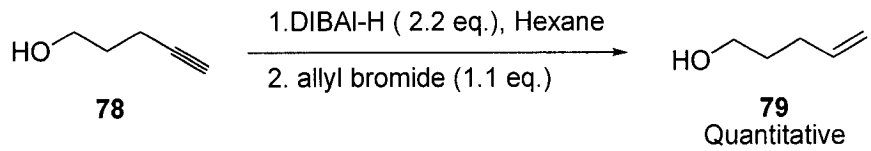
Described in Scheme 27 is our retrosynthetic plan to tricyclic compound **75**. It would be prepared from a thermal [4+2] cycloaddition of substituted cyclopentadiene **76**. Side chain **77** would contain a 1,4-diene where upon cycloaddition, the allyl group would directly be incorporated in the endo position for the tandem olefin metathesis sequence. Substituted cyclopentadiene **76** would be prepared by alkylation of the appropriate side chain with cyclopentadiene.



75 **76** **77**

Scheme 27: Retrosynthetic plan for the synthesis of olefin metathesis precursor 75

We initially tried to prepare the desired alkyl chain *via* carbometallation of an alkyne with DIBAl-H (Scheme 28).[43] Hydroalumination of 4-pentyn-1-ol (**78**) with DIBAl-H and quenching of the aluminum intermediate with allyl bromide did not provide the desired 1,4-diene. Instead, the intermediate quenched by a proton was recovered in quantitative yields (**79**).



78 **79** Quantitative

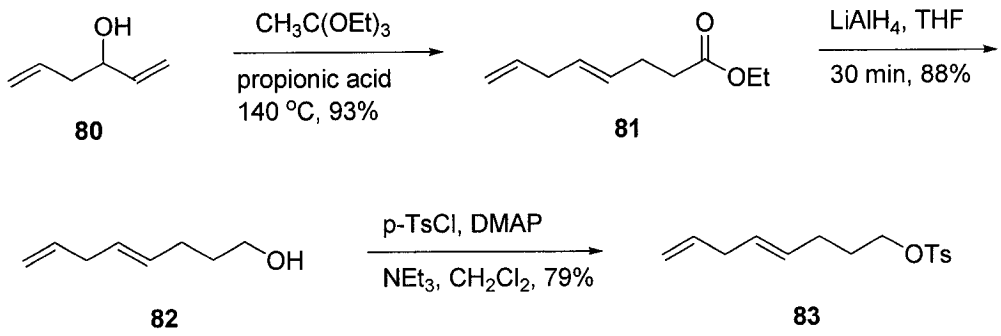
Scheme 28: Hydroalumination of 4-pentyn-1-ol

A thorough scan of reaction conditions would have probably led to the desired product, but and a literature procedure was found where a Claisen rearrangement was employed.[44] Using the protocol, the synthesis of 1,4-diene **79** was easily prepared by a Johnson orthoester Claisen rearrangement of commercially available 1,5-hexadien-3-ol (**78**) with catalytic propionic acid in reluxing triethylorthocacetate in 93% yield (Scheme 29). The ester functionality was cleanly reduced to the corresponding alcohol **80** with lithium aluminum hydride ($LiAlH_4$) and subsequent tosylation with *p*-toluenesulfonyl chloride afforded desired side chain **81** in 79% yield.

---

[43] (a) Zweifel, G.; Steele, R. B. *J. Am. Chem. Soc.* **1967,** *89,* 5085; (b) Baba, S.; Van Horn, D. E.; Negishi, E. -I. *Tetrahedron Lett.* **1976,** *23,* 1927; (c) Sonengam, B. L.; Charles, G.; Akam, T. M. *Tetrahedron Lett.* **1980,** *21,* 1069; (d) Matsushita, H.; Negishi, E. –I, *J. Am. Chem. Soc.* **1981,** *103,* 2882.

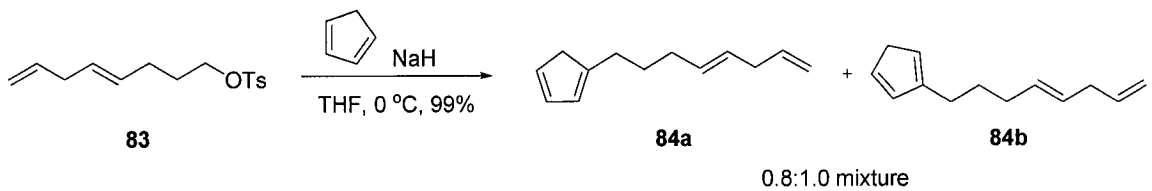
[44] (a) Chattopadhyay, A.; Mamdapur, V.R. *Indian J. Chem.* **1988,** *27,* 169; (b) Nonoshita, K.; Banno, H.; Maruoka, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1990,** *112,* 316.



Scheme 29: Synthesis of unactivated dienophile

With the 1,4-diene in hand, the next task was the alkylation of cyclopentadiene. As predicted, the addition occurred smoothly. Treating cyclopentadiene with sodium hydride, the addition of the alkyl chain to give **84** occurred in quantitative yield (Scheme 30). At equilibrium, the mixture of **84a** and **84b** was found to be in approximately a 0.8:1.0 ratio.

Ethylmagnesium bromide can also be used as base to deprotonate cyclopentadiene. Refluxing a solution of ethylmagnesium bromide and cyclopentadiene to form the nucleophile, then adding tosylate **83** provided **84**, albeit in lower yields (60-70%). Though, cleaner material is obtained with this approach.



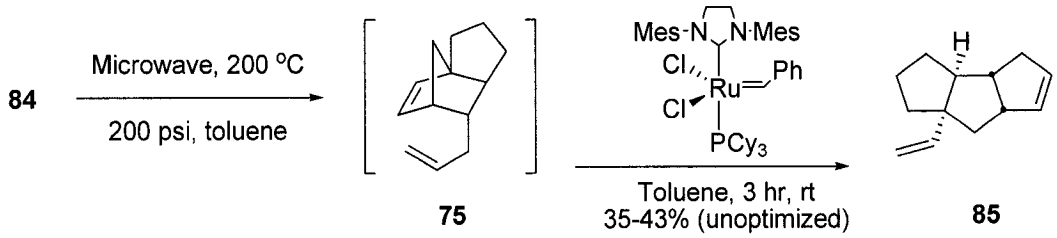
Scheme 30: Alkylation of cyclopentadiene

We were now able to attempt the one pot IMDA-ROM-RCM reaction sequence. Based on previous experience, we felt the most efficient way to conduct the Diels-Alder was to use the microwave.[45]

The key step was carried out in toluene at 200 °C at 200 psi for three hours (Scheme 31). Upon completion of the reaction, the vessel was removed from the microwave, purged with argon and Grubbs 2nd generation catalyst (5 mol% based on

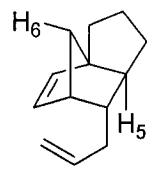
[45] For a recent review of Microwaves in Organic Synthesis: Kappe, C. O. *Angew. Chem. Int. Ed.* **2004,** *43,* 6250.

starting material) was added to the vessel. The reaction stirred under an atmosphere of argon for 3 hours. Monitoring the reaction by TLC was difficult since the R_f value of the starting material and product were the same. However, the reaction was allowed to stir for 3 hours and after purification, the desired triquinane core **85** was synthesized. The highest yield obtained for the reaction was 43% yield. ^1H NMR showed no trace of starting material.



Scheme 31: Synthesis of triquinane core

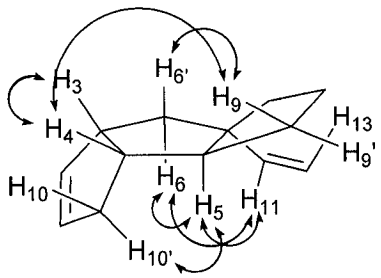
Structure **75** was isolated to elucidate the structure by NMR spectroscopy. COSY and HMQC experiments confirmed the regiochemistry of the cycloaddition. The COSY experiment exhibited long range coupling between H_6 and H_5 that is attributed to the W conformation between these two protons (Figure 8). The W coupling proposes that the cycloaddition proceeded *via* a regioselective *exo* addition.



75

Figure 8: Long range W coupling

COSY and HMQC experiments were also performed on the triquinane **85**. NMR spectra further confirmed the regiochemistry of the tandem olefin metathesis sequence and NOESY experiments confirmed the *cis-anti-cis* ring junction (Figure 9). From the spectrum, it was seen that H_5 correlates with H_1, H_6, $H_{10'}$ and H_4 correlates with $H_{6'}$, H_9. We also that H_1 correlates with H_6, H_5 and H_3 sees H_9.



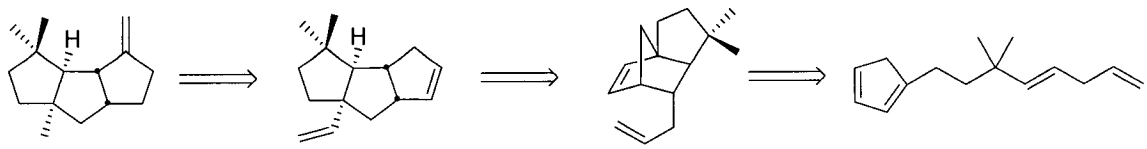
Proton	Correlation
H_2	H_1, H_6
H_3	$H_9, H_{6'}, H_4$
H_4	$H_{6'}, H_9, H_{10}, H_3$
H_5	$H_{11}, H_6, H_{10'}$
H_6	$H_5, H_{11}, H_{13}, H_{6'}$
$H_{6'}$	H_3, H_6, H_4, H_7
H_9	$H_{6'}, H_4$
H_{11}	$H_{6'}, H_5, H_{12}$

Figure 9: Important NOESY correlations of **85**

Although the one pot reaction has yet to be optimized, we felt it was appropriate to apply the methodology to the total synthesis of capnellene.

2.3 Towards the synthesis of (±)-Capnellene

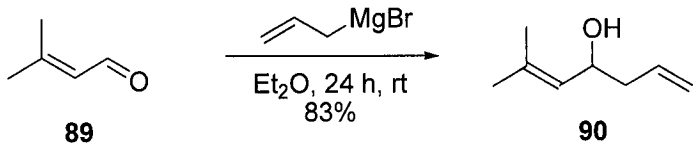
Our synthesis of capnellene (**13**) was slightly modified from our original route in that we wanted to incorporate the gem-dimethyl groups directly on the triquinane core. Our retrosynthetic plan is outlined in Scheme 32, where we started from the corresponding substituted cyclopentadiene. The alkyl substitutent would contain the gem-dimethyl group in the 3 position and the one pot IMDA-ROM-RCM would yield the capnellene core **86**. Subsequent functional group manipulations, mainly the reduction of the vinyl group to the methyl group, would provide the total synthesis of **13**.



13 (±)-Capnellene **86** **87** **88**

Scheme 32: Retrosynthetic plan to capnellene

Our original synthesis commenced with the Claisen rearrangement, however we wanted to incorporate the gem-dimethyl groups at this step. The required allylic alcohol was not commercially available, therefore the preparation involved the addition of allyl magnesium bromide to 3-methyl-2-butenal (**89**) to give 6-methyl-1,5-hexadien-4-ol (**90**) in 83% yield (Scheme 33).[46]

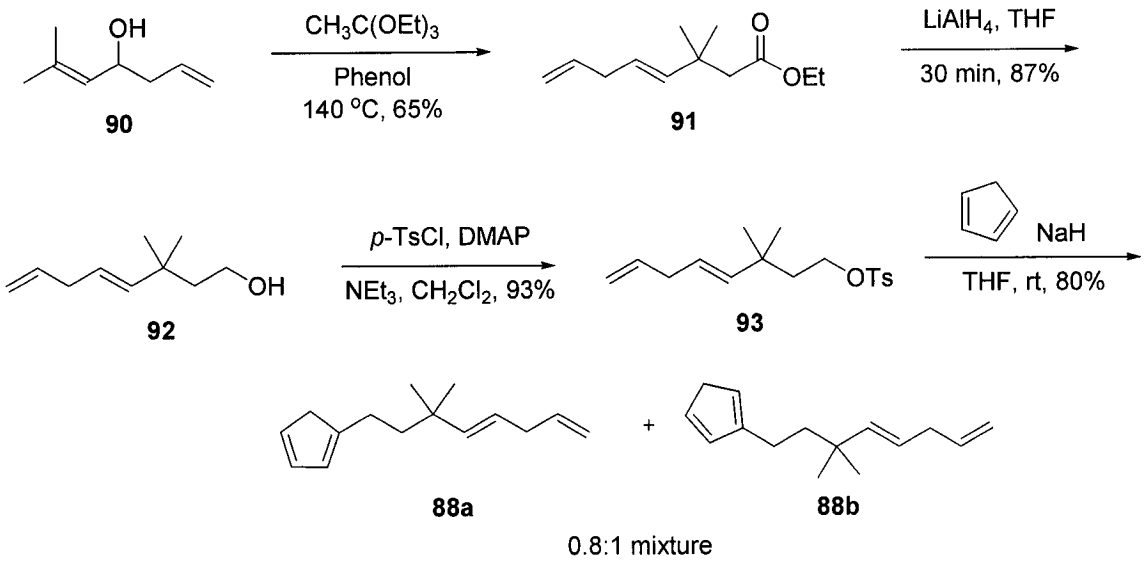


89 **90**

Scheme 33: Synthesis of Claisen rearrangement precursor

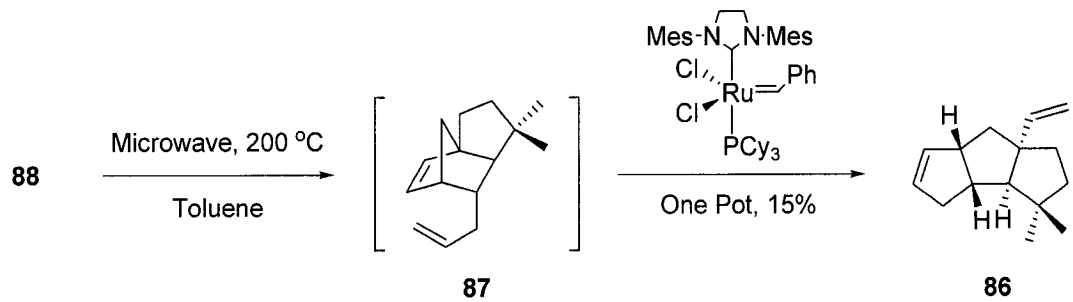
Heating of alcohol **90** in refluxing triethyl orthoacetate in the presence of catalytic phenol overnight afforded the γ,δ-unsaturated ester in 65% yield (Scheme 34).[47] We found that a weaker acid was necessary to achieve the highest yield. Normally propionic acid is used for this variant of the Claisen rearrangement, but we only obtained poor yields with the protocol. Reduction of ester **91** with $LiAlH_4$ to primary alcohol **92** was accomplished in 87% yield and subsequent treatment with *p*-toluenesulfonyl chloride gave tosylate **93** in 93% yield. Treating cyclopentadiene with sodium hydride, the addition of the alkyl chain supplied **88** in 80% yield and at equilibrium, the mixture of **84a** and **84b** was found to be in approximately a 0.8:1.0 ratio.

[46] Antonsson, T.; Moberg, C.; Tottie, L. *J. Org. Chem.* **1989,** *54,* 4914
[47] Kondo, K.; Matsui, K.; Takahatake, Y. *Tetrahedron Lett.* **1976,** *48,* 4359.



Scheme 34: Synthesis of substituted cyclopentadiene

With the substituted cyclopentadiene in hand, we were now ready to perform the one pot IMDA-ROM-RCM strategy (Scheme 35). The Diels-Alder reaction was performed in the microwave, at 200 °C in toluene and upon completion Grubb's 2nd Generation catalyst was added to the reaction vessel. Stirring at room temperature for three hours we did obtain the desired triquinane core however in a very low 15% yield.



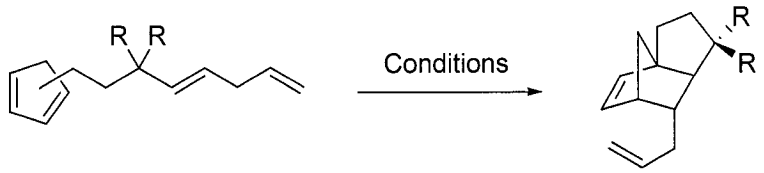
Scheme 35: Synthesis of capnellene triquinane core

In order to try and figure out what was going wrong, we decided to look at each step individually to determine which part of the sequence was causing problems.[48] Examining the IMDA reaction first, we varied the temperature of the reaction (Table 2). Repeating the microwave conditions, 200 °C at 200 psi afforded the tricyclic structure in 31% yield (Entry 1). Refluxing the reaction in toluene provide us with no reaction even

[48] A portion of the work was performed by summer student Nicole Stogaitis

after three days (Entry 2). The sealed tube reaction, at 200 °C in toluene, provided the cycloaddition adduct in a low 20% yield after three days. Starting material was recovered in 10% and rest was decomposition (Entry 3). Returning to microwave conditions, we increased the reaction pressure to 300 psi and switched the solvent to benzene, and after four hours the desired product was made in 35% yield (Entry 4). Increasing the temperature and pressure to 260 °C and 400 psi had a negative effect on the reaction as was performing the reaction in toluene (Entry 5 and 6). Higher temperature seems to promote decomposition of the starting material or product. Heating in benzene at 210 °C and 310 psi gave an improved yield of 45% (Entry 7). We repeated the reaction with the unsubstituted version (R = H), and similar yields were obtained (Entry 8).

Table 2: Intramolecular Diels-Alder reaction conditions

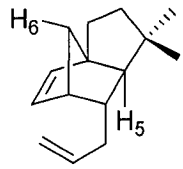


Entry	R	Solvent	Conditions	Temp (°C)	psi	Time	Yield
1	Me	Toluene	μv	200	200	3 h	31%
2	Me	Toluene	Reflux	110	-	3 d	0%
3	Me	Toluene	Sealed tube	200	-	3 d	20%
4	Me	Benzene	μv	200	300	4 h	35%
5	Me	Benzene	μv	260	400	2.5 h	25%
6	H	Toluene	μv	210	310	2 h	20%
7	Me	Benzene	μv	210	310	1.5 h	45%
8	H	Benzene	μv	210	310	1.5 h	46%
9	H	DCE	μv	210	310	1.5 h	44%
10	H	DMF	μv	210	310	1.5 h	49%
11	H	Chlorobenzene	μv	210	310	1.5 h	80%

More polar solvents to increase the microwave absorption were then investigated. Dichloroethane and DMF provided similar yields to that of benzene, 44% and 49%

respectively (Entry 9 and 10). Lastly, chlorobenzene was used which offered the highest yields (80%, Entry 11).

COSY and HMQC experiments of compound **87** confirmed the regiochemistry of the cycloaddition. As in the unsubstituted analogue, the COSY experiment exhibited long range coupling between H_6 and H_5 that is attributed to the W conformation between these two protons (Figure 10).



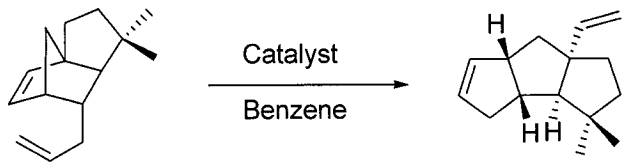
87

Figure 10 : Long range W coupling of **87**

Turning our attention to the olefin metathesis portion of the reaction sequence, both 1st generation Grubbs catalyst and 2nd generation Grubbs catalyst was examined. Performing the tandem ROM-RCM of **87** to **86** in an atmosphere of argon,[49] 1st generation catalyst clearly showed to be superior, increasing the yield from 70% for 2nd generation (Entry 3) to 82% (Entry 1). It was then thought to perform the tandem olefin metathesis reaction in an ethylene atmosphere.[34] Ethylene helps initiate the ROM step and is known to breakdown any intermediates that are stuck in the catalytic cycle. Repeating the same reactions, this time in benzene saturated with ethylene, reactions with both catalysts showed an improvement (Entry 2 and 4). Employing 1st generation Grubbs catalyst converted **87** to triquinane **86** in quantitative yields (Entry 2).

[49] For Tandem ROM-RCM procedures under argon atmosphere: (a) Kim, H. K.; Bowden, N.; Grubbs, R. H. *J. Am. Chem. Soc.* **1994,** *116,* 10801; (b) Hotsclaw, J.; Koreeda, M. *Org. Lett.* **2004,** *6,* 3719.

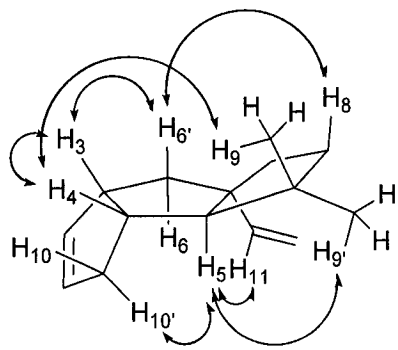
Table 3: Conditions for tandem ROM-RCM



87 **86**

Entry	Catalyst	Conditions	Time	Yield (%)
1	1st Generation	Argon	3 h	82
2	1st Generation	Ethylene	1 h	99
3	2nd Generation	Argon	3 h	70
4	2nd Generation	Ethylene	1.5 h	75-92

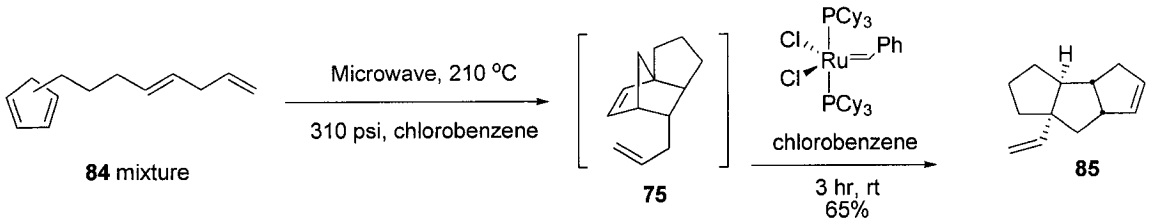
COSY and HMQC experiments were also performed on triquinane **86**. The *cis-anti-cis* ring junction was confirmed from the NOESY spectrum (Figure 11).



Proton	Correlation
H_3	H_4, $H_{6'}$, H_1
H4,	H_3, H_9, H_8, H_{10}
H_{10}	$H_{10'}$, H_4, H_9
$H_{10'}$	H_5, H_{10}, H_4
H_8	$H_{6'}$
H_6	H_3, H_6, H_{13},
H_5	$H_{9'}$, $H_{10'}$, H_{11}

Figure 11: Important NOESY correlations of **86**

With the optimized conditions the one pot IMDA-ROM-RCM was repeated for the unsubstituted version and the triquinane core was achieved in an improved 65% yield (Scheme 36).



84 mixture

75

85

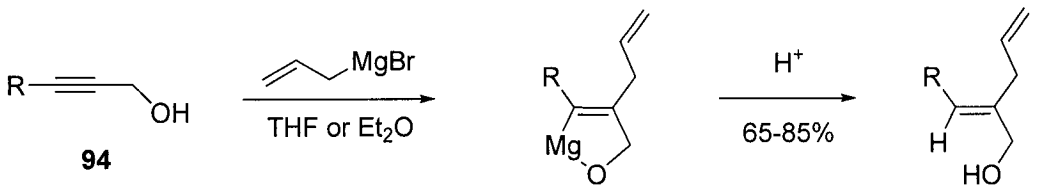
Scheme 36: One pot IMDA-ROM-RCM with optimized conditions

3 Introduction – Magnesium-Mediated Carbometallation of Propargyl Alcohols

3.1 Carbometallation

The carbometallation reaction has been of great interest since the first reported example by Bähr and Ziegler in 1967.[50] It was not until the last decade has research been largely devoted to this area. Carbometallation involves adding an organometallic reagent across an unsaturated carbon-carbon bond to form a new organometallic species. This can in turn react with a variety of electrophiles to give the desired product. A wide range of metals have been examined including zinc, aluminum, boron, tin, and reactions with an array of unsaturated acceptors have been reported and reviewed.[51] Alkynes containing a propargyl or homopropargyl oxygen are the most widely studied where the oxygen is usually a free hydroxyl group or protected as an ether.

Organomagnesium compounds are versatile reagents for carbon-carbon bond formation. While they do not generally add across non-functionalized triple bonds, allyl magnesium halides have been reported to react easily with propargyl alcohols (Scheme 37).[52]



Scheme 37: Magnesium medatiated carbometallation of propargyl alcohols

---

Note: Portions of the section are taken from the following theses: Forgione, P. *PhD (Chemistry)* **2001**; Penwell, A. J. *M.Sc. (Chemistry)* **2003**; Tessier, P. *M.Sc. (Chemistry)* **2003**.

[50] Ziegler, K.; Bahr, K. *Chem. Ber.* **1928,** 253.

[51] For reviews see: (a) Normant, J. F.; Alexakis, A. *Synthesis.* **1981,** 841; (b) Negishi, E. *Pure Appl. Chem.* **1981,** *53,* 2333; (c) Oppolzer, W. *Angew. Chem. Int. Ed. Engl.* **1989,** *28,* 38; (d) Knochel, P. in Comprehensive Organometallic Chemistry II; Able, E. W.; Stone, F. G. A.; Wilkinson, G. Eds.; Pergamon Press: Oxford, 1995; Vol. 11, p. 159; (e) Knochel, P. in Comprehensive Organic Synthesis; Trost, B. M.; Fleming, I.; Eds; Pergamon Press: Oxford, 1991; Vol. 4, p. 865; (f) Negishi, E.; Kondakov, D. Y. *Chem. Rev.* **1996,** *96,* 417; (g) Marek, I. *J. Chem. Soc., Perkin Trans. I.* **1999,** 535; (h) Fallis, A. G.; Forgione, P. *Tetrahedron* **2001,** *57,* 5899.

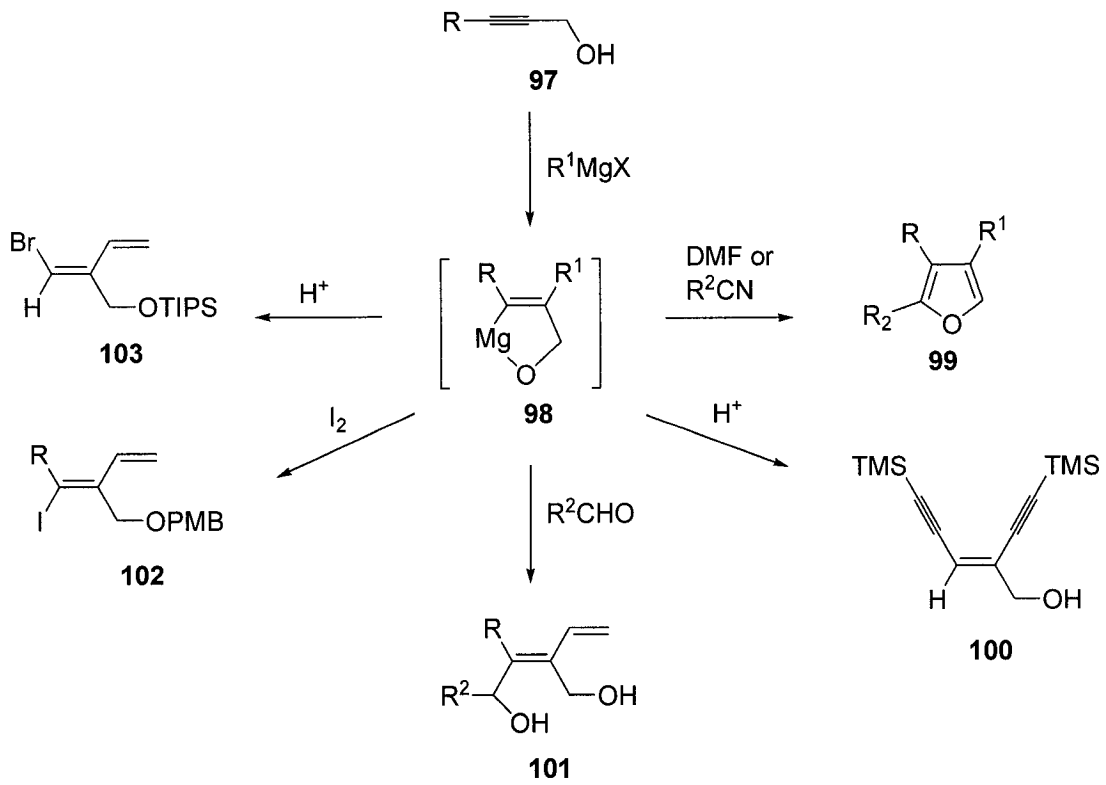
[52] (a) Eisch, J. J.; Merkley, J. H. *J. Organomet. Chem.* **1969,** *20,* 27 (b) Eisch, J. J.; Merkley, J. H.; Galle, J. E. *J. Org. Chem.* **1979,** *44,* 587; (c) Richey, H. G.; von Rein, F. W. *Tetrahedron Lett.* **1971,** *41,* 3777.

The addition of organomagnesium compounds to the propargyl alcohol is a regiocontrolled *anti*-carbometallation and the reaction is thought to precede *via* magnesium chelate intermediate **95** (or a closely related species). The use of other Grignard reagents were attempted with little success resulting in low yields. It was found that an addition of copper iodide circumvented this problem and the improvement is thought to be due to transmetallation with the magnesium to form a softer nucleophile.

3.2 Magnesium-Mediated Carbometallation in Synthesis

Motivated by their interest in the synthesis of taxoids and the development of tether controlled intramolecular reactions, the Fallis research group has developed several procedures for the magnesium mediated carbometallation of propargyl alcohols (Scheme 38). Chelate intermediate **98** has reacted with a variety of electrophiles to generate a large library of diverse compounds. The reaction has been used to prepare substituted furans (**99**)[53] and stereodefined enediynes (**100**).[54] Vinyl magnesium chloride as the Grignard reagent dienediols (**101**), and halodienes (**102**, **103**) can easily be obtained.[55]

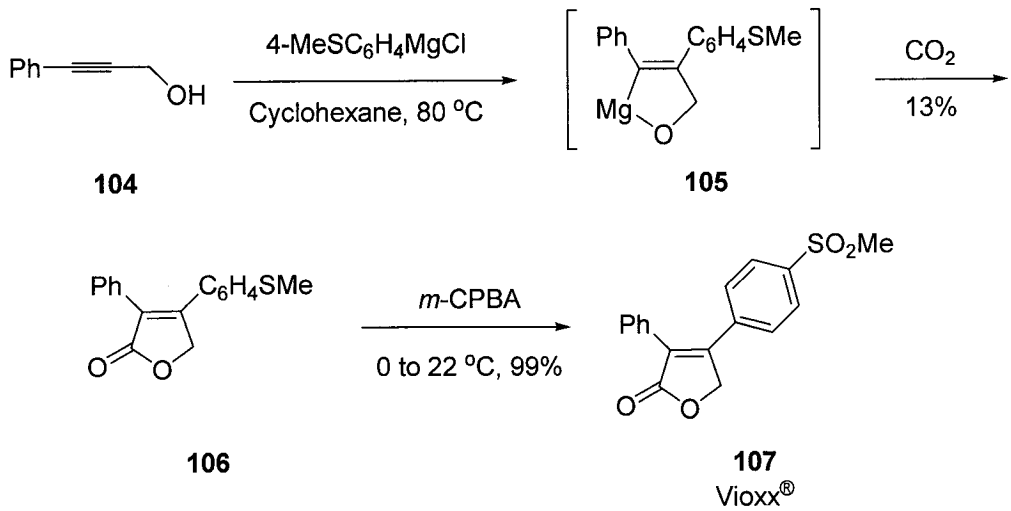
[53] Forgione, P.; Wilson, P. D.; Fallis, A. G. *Tetrahedron Lett.* **2000,** *41,* 17.
[54] Wong, T.; Tjepkema, M. W.; Audrain, H.; Wilson, P. D.; Fallis, A. G. *Tetrahedron Lett.* **1996,** *37,* 755.
[55] Forgione, P.; Fallis, A. G. *Tetrahedron Lett.* **2000,** *41,* 11.



Scheme 38: Magnesium-mediated carbometallation of propargyl alcohols

A desirable aspect of this reaction is that switching the substituents on the propargyl alcohol and the Grignard reagent can change the substitution pattern.

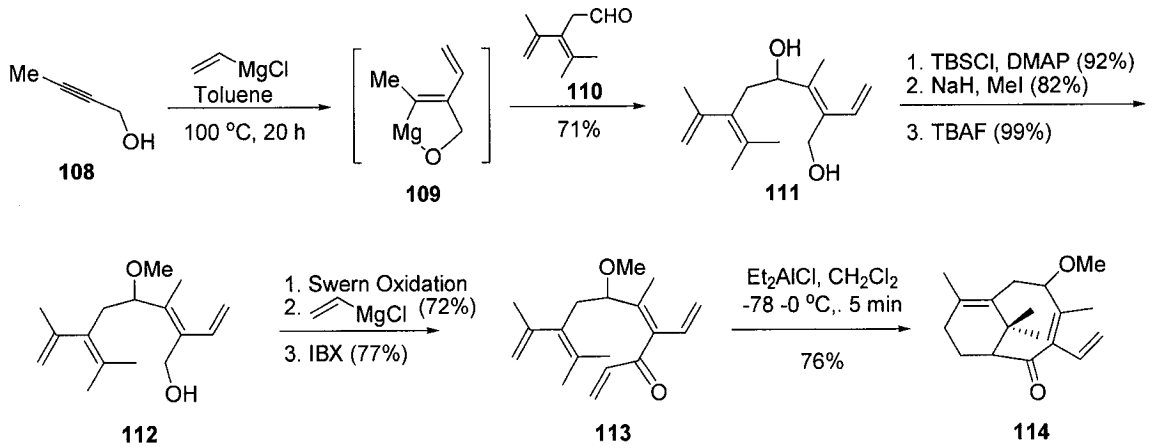
The versatility of this procedure has been shown in the synthesis of complex compounds. Along with the examples presented above, one can synthesize substituted furanones,[53] such as in the short synthesis of the Merck anti-inflammatory drug Vioxx® (**107**, Scheme 39). Carbometallation of phenylpropargyl alcohol (**104**) with 4-thioanisylmagnesium chloride and quenching chelate **105** with carbon dioxide provided furanone **106**. Oxidation of the thiol to the sulfoxide with *m*-CPBA gave **107**, in a total of two steps.



Scheme 39: Synthesis of Vioxx® via magnesium-mediated carbometallation

A dienediol of type **101** was used as the key intermediate towards the synthesis of the taxane AB ring system.[56] The key steps in the synthesis are carbometallation to prepare the dienediol and a diastereoselective, Lewis acid catalyzed Diels-Alder reaction to form the 6-8 fused ring system (Scheme 40). Addition of vinyl magnesium chloride to methyl propargyl alcohol (**108**) and quenching the reaction with aldehyde **110** afforded diol **111** in 71% yield. A protection/deprotection sequence, then a series of oxidation procedures furnished Diels-Alder precursor **113** in high yields. In the presence of diethylaluminum chloride, the diastereoselective, Lewis acid catalyzed Diels-Alder reaction completed the taxane AB ring system (**114**) in a total of eight steps and 22% overall yield.

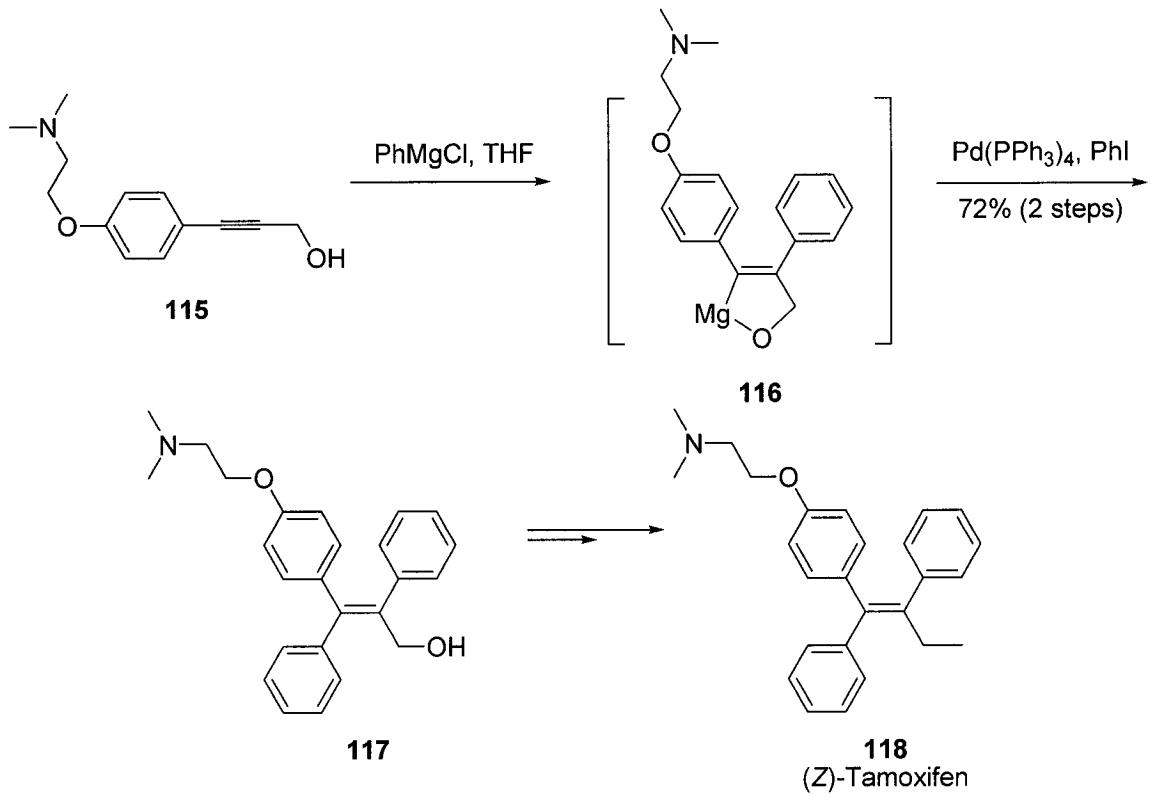
[56] Forgione, P.; Wilson, P. D.; Yap, G.; Fallis, A. G *Synthesis* **2000,** *7,* 921.



Scheme 40: Synthesis of taxane AB ring system *via* magnesium-mediated carbometallation

Recently, it was shown that formation of the magnesium chelate intermediate followed by a palladium cross coupling with an aryl iodide provided a facile route to new tetrasubstituted alkene analogues. This new method was applied to the total synthesis of (*Z*)-tamoxifen, a selective estrogen receptor modulator (Scheme 41).[57] Alkynol **115** was easily prepared through Sonogashira coupling of propargyl alcohol and the corresponding aryl iodide. Carbometallation of phenylmagnesium chloride, transmetallation of magnesium chelate **116** with palladium (0), followed by palladium catalyzed cross coupling reaction with iodobenzene produced the desired analogue **117**. Conversion of the primary alcohol to the ethyl substituents afforded the stereoselective synthesis of (*Z*)-tamoxifen (**118**).

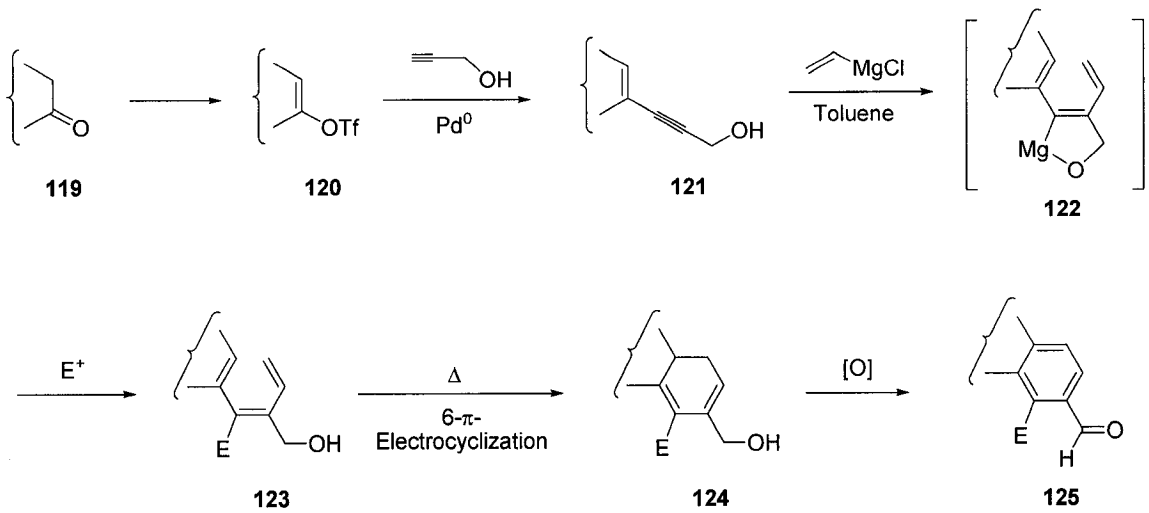
[57] Tessier, P.; Penwell, A. J.; Souza, F. E. S.; Fallis, A. G. *Org. Lett.* **2003,** *5*, 2989.



Scheme 41: Synthesis of (Z)-Tamoxifen *via* magnesium mediated carbometallation

3.3 Carbometallation of Vinyl Propargyl Alcohols

Further probing the scope of the methodology founded a new annualation procedure to attach functionalized benzene rings to cyclic ketones. The strategy involved carbometallation of a vinylpropargyl alcohol (**121**) with vinylmagnesium chloride. Six-π-electrocyclic ring closure of the resulting triene (**123**), followed by oxidation generated the functionalized benzaldehyde (Scheme 42). The vinylpropargyl alcohol can be obtained from the related vinyl triflate **119**, derived from an appropriate cyclic ketone, which was then coupled through a Sonogashira reaction with propargyl alcohol to give **121**. A desirable aspect of the method is that various functional groups can be attained depending on the electrophile used to quench magnesium chelate **122**.



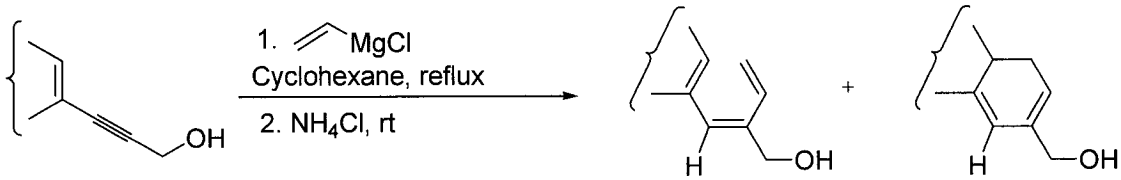
Scheme 42: Carbometallation of vinylpropargyl alcohols with vinylmagnesium chloride

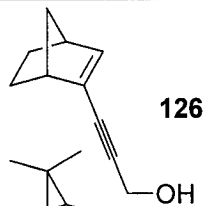
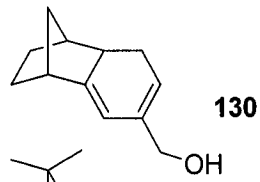
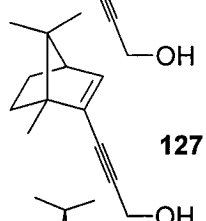
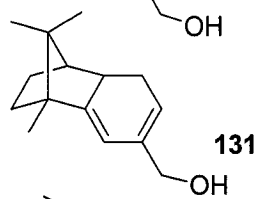
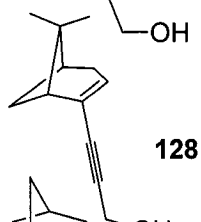
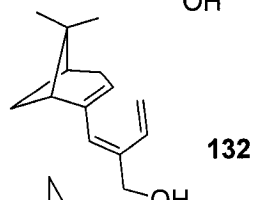
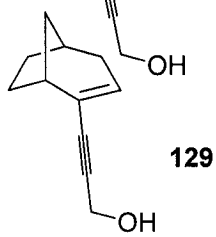
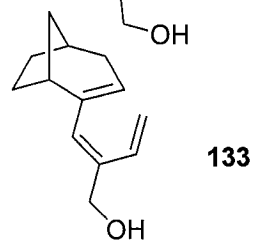
Of considerable interest were chiral bicyclic ketones due to their high potential for chiral asymmetric transformations. Norcamphor, camphor, nopinone and bicyclo[3.2.1]octan-2-one were chosen as substrates for this investigation. The vinylpropargyl alcohols were prepared *via* the general protocol: conversion of the corresponding ketone to the triflate using lithiumdiisopropyl amide (LDA) and trapping of the enolate with *N*-phenyltriflouromethanesulfonamide[58] ($PhN(Tf)_2$). The triflate underwent Sonogashira palladium coupling, with propargyl alcohol to give the desired vinylpropargyl alcohols **126**, **127**, **128**, and **129** (Table 4).

Carbometallation of the alkynols with vinylmagnesium chloride and subsequent quenching with a proton worked well with the chiral compounds. A pleasant surprise was that the trienes generated **126** and **127**, cyclized under the reaction conditions (Entry 1 and 2). The diene was formed in one pot from the vinyl propargyl alcohol. However, the more conformationally mobile ring systems, trienes generated from alkynols **128** and **129**, did not cyclize and only trienes **132** and **133** were isolated (Entry 3 and 4).

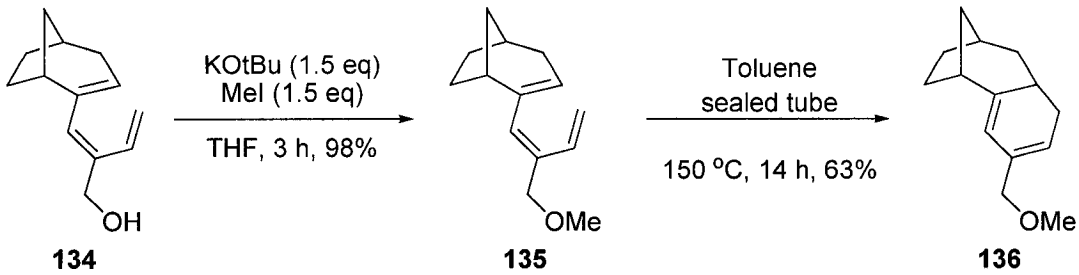
[58] Hendrickson, J. B.; Bair, K. W.; Bergeron, R.; Giga, A.; Skipper, P. L.; Sternbach, D. D.; Wareing, J. A. *Organic Preparations and Procedures Int.* **1977**, *9*, 173.

Table 4: Carbometallation of bicyclic vinyl propargyl alcohols



Entry	Propargyl Alcohol	Triene/Cyclized Product	Yield (%)
1	 **126**	 **130**	43
2	 **127**	 **131**	81
3	 **128**	 **132**	77
4	 **129**	 **133**	64

The cyclization of triene **133** was attempted in refluxing toluene; however, only starting material was obtained. The protection of the allylic alcohol as the methyl ether using sodium hydride and methyliodide, was necessary to induce cyclization at 150 °C in a sealed tube (Scheme 43).

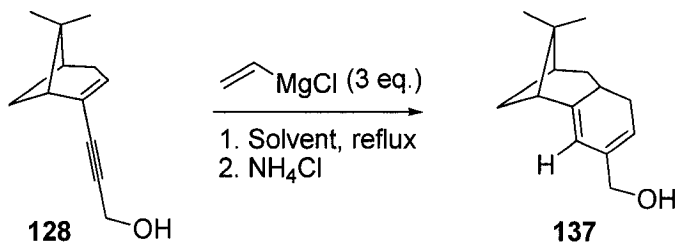


134 **135** **136**

Scheme 43: Thermal cyclization of triene **134**

3.4 Research Objectives

We were very close to completing the project and publishing the results. However, one question we wanted to answer before submitting the paper was whether reaction conditions could be found to allow for the tandem carbometallation-cyclization for the bicycle[3.1.1] based vinylpropargyl alcohol **128** (Scheme 44). If this could occur, this would make our general approach an attractive multi-component reaction.

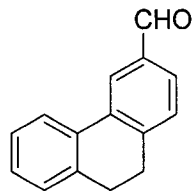


128 **137**

Scheme 44: One pot carbometallation-annulation of **128**

Given that electrocyclic ring closures are thermal reactions, the logical step was to increase the reaction temperatures for the carbometallation reaction.

It was also felt that another example could be synthesized to further demonstrate the novelty of carbometallation-annulation strategy. The target molecule dihydrophenanthrene **138** was to be synthesized (Figure 12).



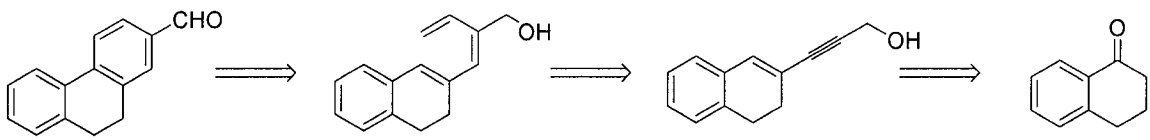
138

Figure 12: Target molecule **138** *via* carbometallation-annulation sequence

This is an attractive target since its core structure is part of a variety of natural products such as antibiotics pradimicin A and benanomicin A.[59] Also, the dihydrophenanthrene core is exhibited in discotic liquid crystals.[60]

3.5 Retrosynthesis

The approach to the molecule comes from the established route developed in our lab (Scheme 45). Dihydrophenanthrene **138** would originate from carbometallation of vinyl propargyl alcohol **140** and vinyl magnesium chloride followed by cyclization of the resulting triene **139**. Alkynol **140** would be prepared from tetralone (**141**).



138 **139** **140** **141**

Scheme 45: Retrosynthetic plan to dihydrophenanthrene **138**

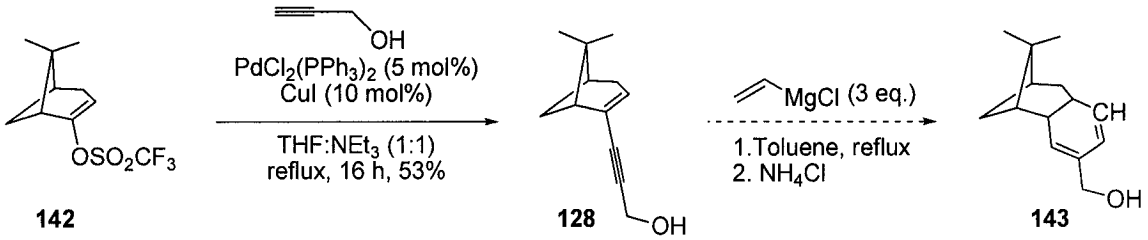
The next section discusses the results obtained from the cyclization of alcohol **128** and the synthesis of **138**.

[59] (a) Kelly, T. R.; Li, Q.; Bhushan, V. *Tetrahedron Lett.* **1990,** *31,* 161; (b) Kato, H.; Ohmori, K.; Suzuki, K. *Tetrahedron Lett.* **2000,** *41,* 6827.
[60] Foster, E. J.; Babuin, J.; Nguyen, N.; Williams, V.E. *Chem.Comm.* **2004,** *18,* 2052.

4 Results and Discussion – Magnesium-Mediated Carbometallation – Aryl Annulation Protocol for the Synthesis of Fused Rings

4.1 Tandem carbometalltion-annulation of nopinone based vinyl propargyl alcohol

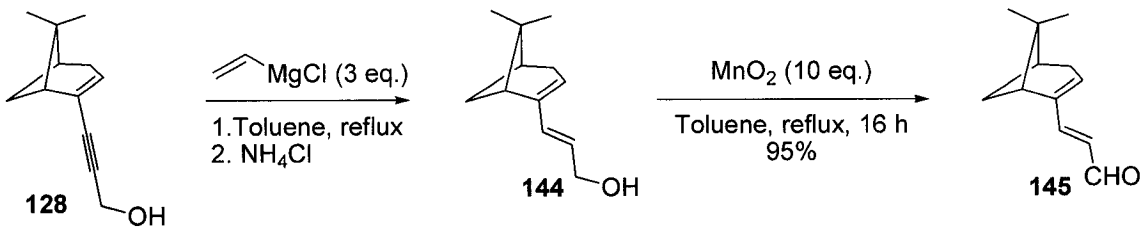
The plan was commenced by performing the carbometallation reaction of propargyl alcohol **128** in toluene. Alcohol **128** was prepared from the corresponding triflate **142** by palladium coupling with propargyl alcohol in 95% yield. We predicted that the carbometallation reaction would proceed smoothly to the desired cyclohexadiene **137**, or perhaps triene **132**. Under the initial reaction conditions, vinylmagnesium chloride (3 eq.) and cyclohexane, only the triene was recovered. Our initial attempt at switching to the higher boiling solvent toluene resulted in mysterious results. Obtaining an unknown product, preliminary characterization suggested cyclohexadiene **143** was obtained (Scheme 46). Compound **143** would have resulted from the olefin isomerization of the initially formed cyclohexadiene after thermal cyclization. However examination of the ^{13}C NMR spectrum suggested that **143** was not the compound isolated due to the absence a CH signal.



Scheme 46: Formation of originally suggested cyclohexadiene **143**

Initial characterization did not provide sufficient information for structure determination so it was subjected to oxidative conditions in hopes to obtain more insight. Upon treatment of compound "**143**" with MnO_2, ^1H NMR showed a distinct doublet in the region of a typical aldehyde. This suggested that the aldehyde proton was coupling to one α-hydrogen, signifying that an α,β-unsaturated carbonyl moiety was present. Based on this evidence it was concluded that reduction of propargyl alcohol **128** to allylic alcohol **144** had occurred during the carbometallation step and oxidation gave aldehyde

145 (Scheme 47). This also explains the missing CH_2 peak, unfortunately the vinyl group did not add across the alkyne.



Scheme 47: Oxidation of allylic alcohol

The geometry of the allylic alcohol is a *trans* orientaion, due to the two olefin protons having a coupling constant of 15.6 Hz. In an nOe difference experiment, irradiation of alkene proton H_2 generated an nOe at proton H_3 (Figure 13). Furthmore, irradiation of proton H_1 generated an nOe at bridgehead proton H_4. These interactions confirmed the *trans* orientation of the allylic alcohol.

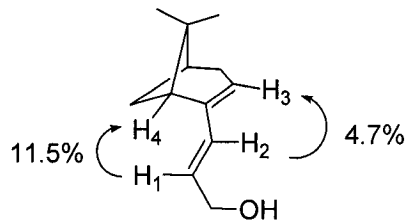
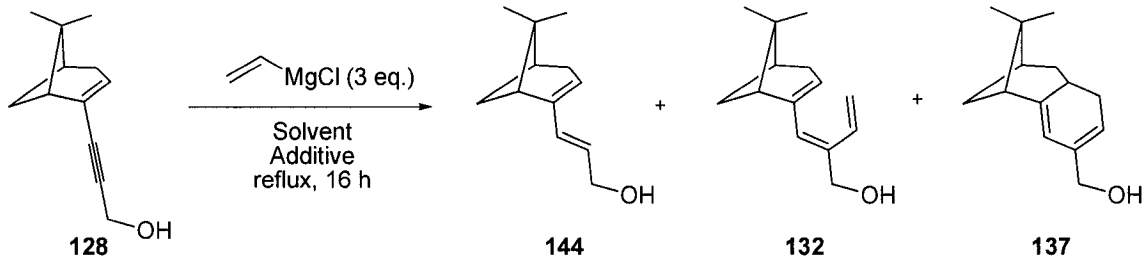


Figure 13 : nOe interactions of **144**

The attempts to add the vinyl piece across the propargyl alcohol are shown in Table 5. Adding $MgCl_2$ to the mixture has shown to improve reactions yields for carbometallation. It is proposed that the salt prevents aggregate formation from the Grignard reagent. However, the presence of the additive did not improve the reaction and only allylic alcohol **144** was obtained in 40% yield. It was also observed in our lab that reagents purchased from Fluka were superior than sources from other companies. Unfortunately, changing the source from Aldrich to Fluka, running the reaction in toluene or cyclohexane gave only the reduced product (Entry 4 and 5). Finally, a bottle from

Acros was obtained and in cyclohexane, to our excitement, the desired triene (**132**) was formed in 77% (Entry 6).

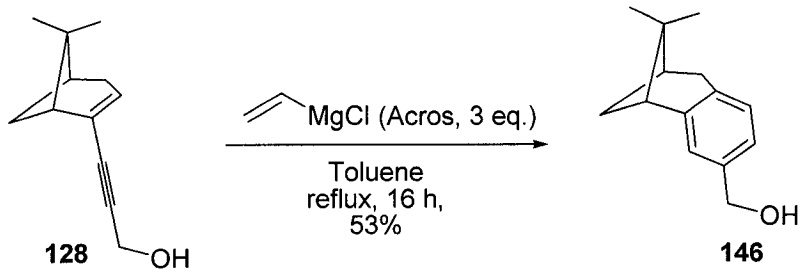
Table 5: Cyclization of [3.1.1] bicycle



128 **144** **132** **137**

Entry	Source	Solvent	Additive	Yield 144 (%)	Yield 132 (%)
1	Aldrich	Toluene	-	42	0
2	Aldrich	Cyclohexane	-	38	0
3	Aldrich	Toluene	$MgCl_2$	40	0
4	Fluka	Toluene	$MgCl_2$	35	0
5	Fluka	Cyclohexane	$MgCl_2$, CuI	30	0
6	Acros	Cyclohexane	-	0	77

With these results, the reaction was performed again, this time using Acros Organics and toluene as solvent (Scheme 48). Refluxing the mixture overnight did not provide the predicted products, triene **132** or cyclohexadiene **137.** Interestingly, instead the fully aromatized product **137** was obtained. Once electrocyclization occurred, the diene oxidized in the presence of air. This was favorable as now we were able to obtain the final, functionalized aromatic ring from the vinylpropargyl alcohol in one pot.



Scheme 48: Carbometallation-Annulation of vinylpropargyl alcohol **128**

4.2 Hydromagnesiation of the Propargyl Alcohol

We are still in the process of trying to explain the reduction of propargyl alcohol **128** to the allylic alcohol **144**. A hydride source must be present in the bottle of vinylmagnesium chloride purchased from Aldrich Chemicals and Fluka Chemicals. However, where the hydride originates from, we cannot determine. Calling customer service at Aldrich Chemicals, we were informed that both bottles of vinylmagnesium chloride contain no stabilizers and certificate of analysis states that no impurities are present.

All that we can state is that due to the *trans* geometry of the allylic alcohol, the addition of the hydride is possibly a regiocontrolled, *anti*-hydromagnesiation. The intermediate is most likely magnesium chelate **147**, a similar intermediate to that of the carbometallation reactions (Figure 14). Hydroalumination of propargyl alcohols with $LiAlH_4$ are also considered to involve intermediates like **148** to furnish the *trans* alkene.

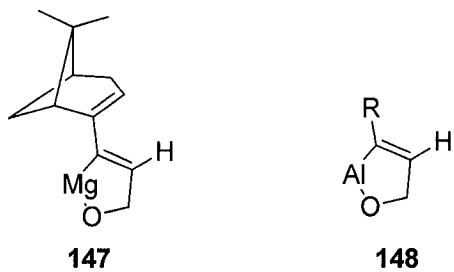
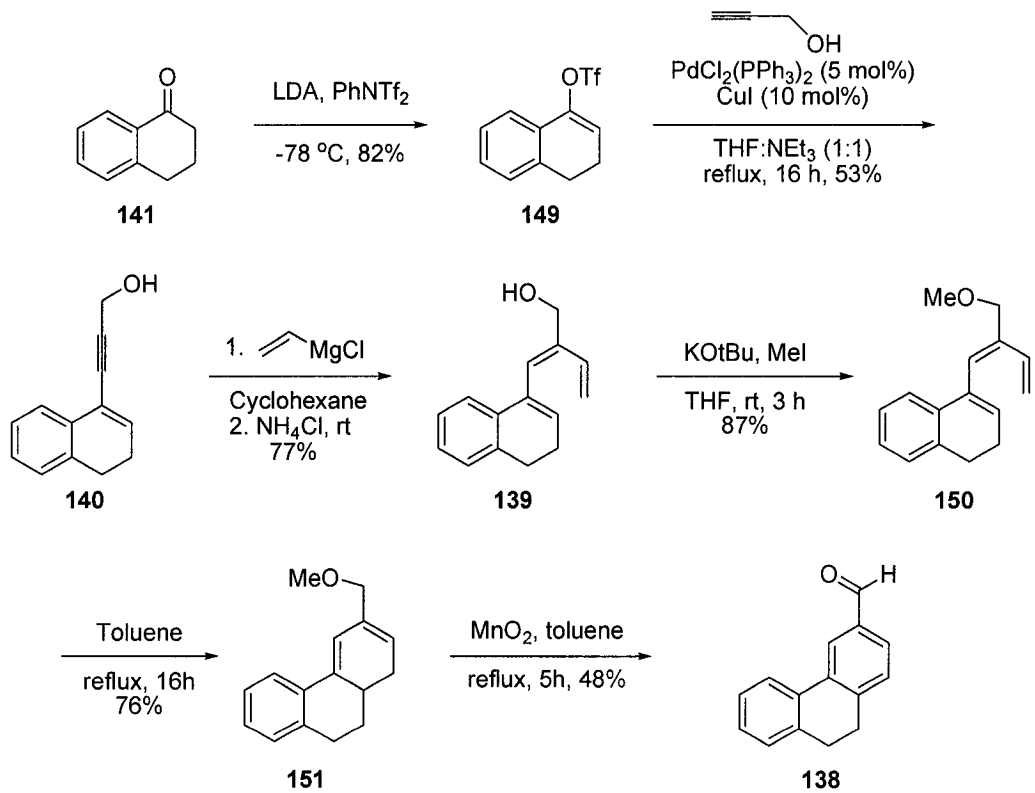


Figure 14: Proposed intermediate for hydromagnesiation hydralumination of propargyl alcohols

4.3 Synthesis of Dihydrophenanthrene 129

The first step towards **138** started with treating tetralone (**141**) with LDA and trapping the resulting enolate with $PhN(Tf)_2$ to furnish triflate **149** in 82% yield (Scheme 49).[61] Sonogashira palladium coupling reaction of the triflate with propargyl alcohol gave alcohol **140** in 53%. Carbometallation with vinylmagnesium chloride (Acros Organics) and quenching the reaction with saturated aqueous ammonium chloride provided triene **139** in 77% yield. Heating the triene directly in toluene was attempted; however, only decomposition of the compound was observed. It was necessary to methylate the alcohol with sodium hydride and methyl iodide. Refluxing methyl ether **150** in toluene gave cyclohexadiene **151** in 76% yield. To complete the synthesis, aromatization with MnO_2 provided the desire dihydrophenanthrene **138** in 48% yield.



Scheme 49: Synthesis of **138**

[61] Comins, D. L.; Dehghani, A. *Tetrahedron Lett.* **1997,** *74,* 77.

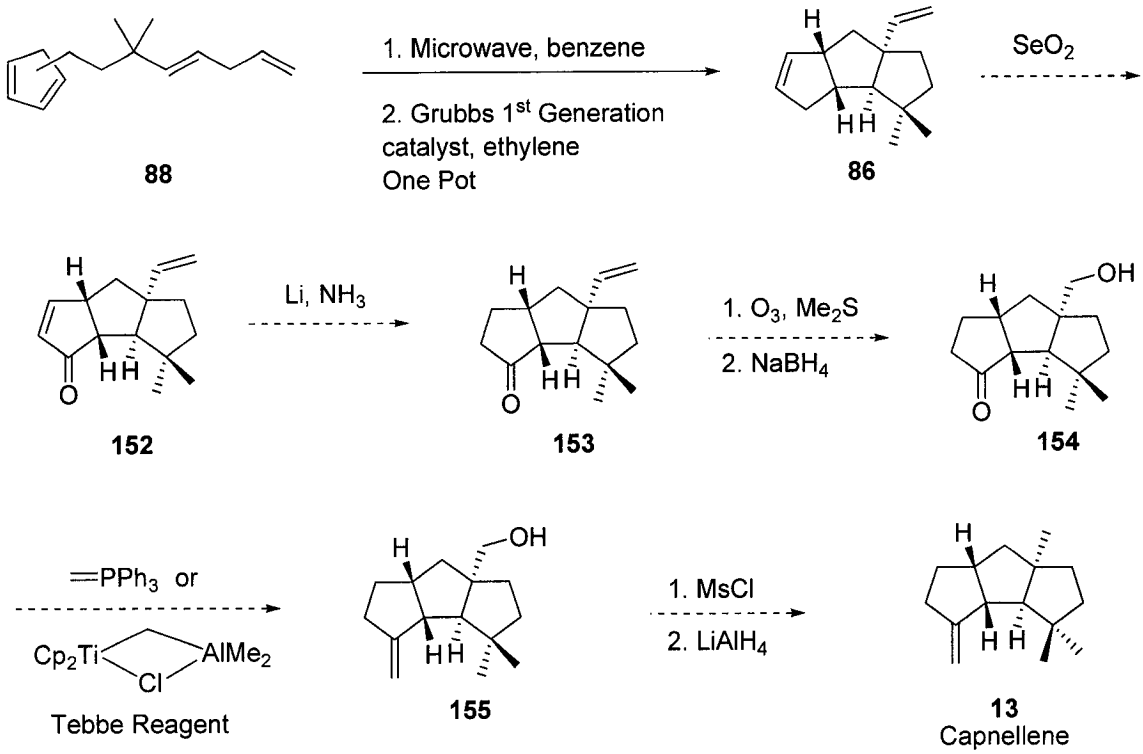
5 Conclusions and Future Work

5.1 Synthesis of Linear Triquinanes

Studies towards the synthesis of linear triquinanes were described. Triquinane core **85** was synthesized *via* a novel one pot IMDA-ROM-RCM approach from substituted cyclopentadiene **76**. This was a one pot reaction that assembled the triquinane core with the requisite *cis-anti-cis* ring junction. Also, the IMDA reaction utilized microwave accelerated conditions for improved yields.

Pleased with our initial success, this approach was applied to the synthesis of natural product capnellene (**13**). Triquinane core **86** was successfully built albeit in low yields. Fortunately, optimization of the IMDA microwave conditions, using chlorobenzene as solvent, improved the yields for this step. It was also found that the tandem ROM-RCM sequence worked best with Grubbs 1st generation catalyst under an atmosphere of ethylene. The combination of the two optimized reaction conditions provided the unsubstituted triquinane core **85** in 65% yield.

The one pot reaction to the capnellene core must be repeated with the optimized reaction conditions. Once this is prepared, the completion of the total synthesis of **13** is envisioned first with allylic oxidation of the olefin with selenium oxide to give enone **152** (Scheme 50). However, it must be aware that a tertiary alcohol may form from this reaction. Reduction of the enone using lithium/ammonia gives carbonyl **153**. The terminal alkene would then be converted to the aldehyde through ozonolysis and then reduction of the resulting aldehyde with sodium borohydride or a milder reducing agent, would provide alcohol **154**. Lastly, Wittig olefination would give exo cyclic compound **155**, mesylation of the remaining alcohol, followed by reduction with $LiAlH_4$ should provide us with the total synthesis of capnellene (**13**).



Scheme 50: Proposed total synthesis of capnellene

5.2 Magnesium-Mediated Carbometallation – Annulation Protocol

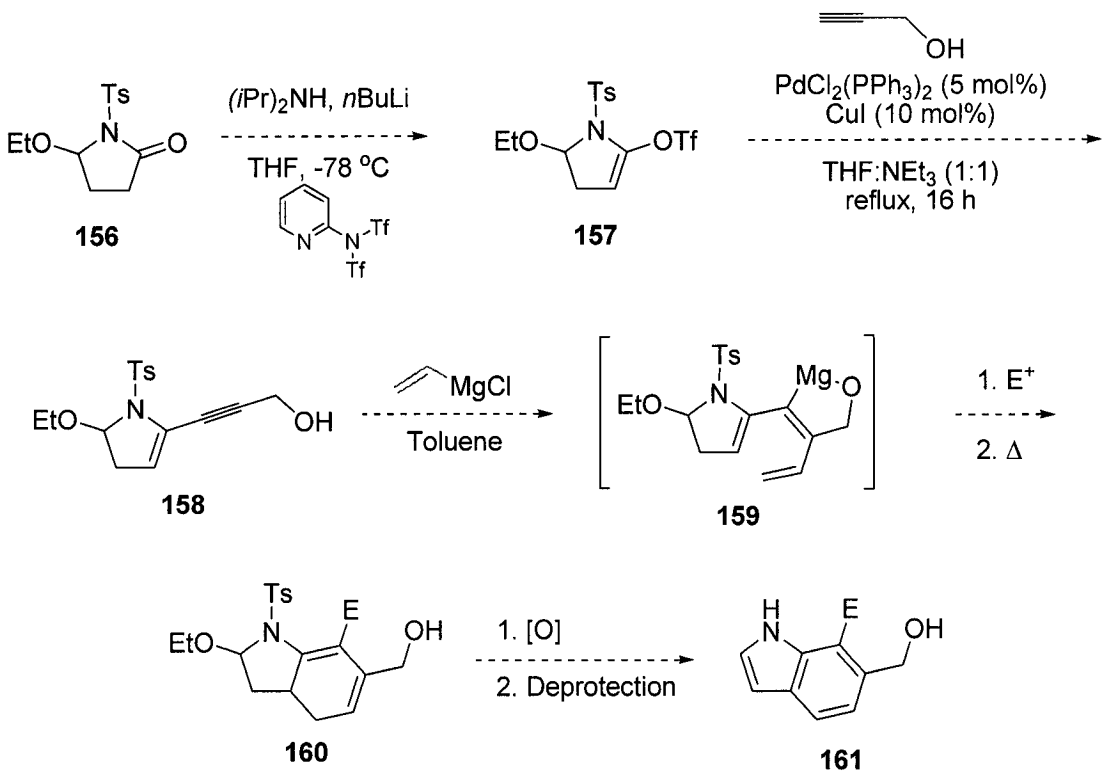
A carbometallation-annulation protocol was applied towards the nopinone based propargyl alcohol **128** to give the functionalized aromatic compound **146** in one pot. Through the investigations we found that the quality of the Grignard reagent is essential for the efficiency of the reaction. In our case, some sources of reagents caused reduction of the propargyl alcohol to allylic alcohol **144**. An explanation for the reduction is not known. Perhaps deuterium studies can be performed to determine the mechanism of the reaction.

With the completion of the last project, a spin off project could be the synthesis of the indoles through the carbometallation-annulation protocol. Speckamp and coworkers have done palladium catalyzed couplings on pyrrolidinone system **157** including Stille couplings, Sonogashira couplings and CO insertions.[62]

---

[62] (a) Bernabé, P.; Rutjes, F. P. J. T.; Hiemstra, H.; Speckamp, W. N. *Tetrahedron Lett.* **1996,** *37,* 3561; (b) Luker, T.; Hiemstra, H.; Speckamp, W. N. *Tetrahedron Lett.* **1996,** *37,* 8257; (c) Luker, T.; Hiemstra, H.; Speckamp, W. N. *J. Org. Chem.* **1997,** *62,* 8131.

The plan for the synthesis of indoles would start with the converstion to triflate **157** from **156** with LDA and Comin's reagent[63] (Scheme 51). Sonogashira coupling with propargyl alcohol would give vinylpropargyl alcohol **158**. The next step is to add vinyl magnesium chloride across propargyl alcohol **158** and quench the chelate **159** with a variety of electrophiles. Heating the resulting compound should induce electrocyclization to provide cyclic product **160**. Subsequent oxidation and deprotection would furnish the desired substituted indole **161**.



Scheme 51: Proposed synthesis of substituted indoles

[63] Comins, D. L.; Dehghani, A. *Tetrahedron Lett.* **1992,** *33,* 6299.

5.3 Claims to Original Research

1. Developed an efficient route to linear triquinane core **85** through a one pot intramolecular Diels-Alder – ring opening metathesis – ring closing metathesis sequence.

2. Applied the new methodology towards the synthesis to the core structure of capnellene (**86**).

3. Prepared substrates through the carbometallation-annulation protocol, including a one pot synthesis of chiral compound **137**.

4. Completed the basic studies required for the successful application of the carbometallation protocol for indole syntheses.

5. Publication: Tessier, P.; Nguyen, N.; Clay. M. D.; Fallis, A. G. *Organic Lett.* **2005,** *7,* 767.

6 Experimental

General Experimental

All non-aqueous reactions were performed under a positive pressure of dry nitrogen in flame-dried glassware using dry solvents. Tetrahydrofuran and diethyl ether were distilled from sodium/benzophenone. Dichloromethane, dimethyl formamide, benzene, toluene and triethylamine were distilled from calcium hydride. Standard inert atmosphere techniques were employed in handling air and moisture sensitive reagents. All starting material was purchased from Aldrich Chemical Company, all transition metal catalysts were purchased from Strem Chemical, Inc. and all were used without purification unless otherwise stated.

Reactions were monitored by thin layer chromatography (TLC) using commercial aluminum-backed silica gel sheets coated with silica gel 60 F_{254} (E. Merck). TLC spots were visualized under ultraviolet light or developed by heating the plate after treatment with potassium permanganate, phospomolybdic acid or ninhydrin stains. Room temperature corresponds to 21 °C. Anhydrous magnesium sulfate ($MgSO_4$) was used to dry solutions in organic solvents. Excess solvents were removed *in vacuo* at pressures obtained by a water or air aspirator connected to a Büchi rotary evaporator. Trace solvents were removed on a vacuum pump. Product purification by flash chromatography was performed with VWR Silica Gel 60 (230-400 mesh). Petroleum ether refers to a mixture of hydrocarbons with boiling range of 30-60 °C.

The base *n*-butyllithium (*n*-BuLi) was tritrated by dissolving diphenyl acetic acid (180 mg, 0.848 mmol) in THF (5 mL). The solution was cooled to 0 °C and *n*-BuLi was added dropwise until a yellow colour persisted.

Grignard reagents were titrated by dissolving diphenyl ditelluride (100 mg, 0.244 mmol) in THF (5 mL). Grignard reagent was added dropwise until a yellow colour persisted.

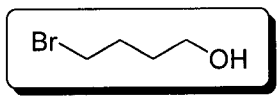
Microwave reactions were performed in a CEM Model ESP-1500 Plus oven equipped with a pressure monitoring device and an EST-300 Plus fiber optic temperature

probe. All reactions were heated in a quartz tube and when non-polar solvents were employed, such as benzene and toluene, a carboflon™ was added.

Infrared (IR) spectra were obtained as neat films in a sodium chloride cell. All IR spectra were recorded on an ABB Bomem MB Series Fourier transform infrared spectrometer (FTIR). ^{1}H NMR (300 or 500 MHz) and ^{13}C NMR (75 or 125 MHz) were run on Bruker AMX300 spectrometer, Bruker AMX500 spectrometer or Varian INOVA500 spectrometer. Chemical shifts are reported downfield from tetramethylsilane (δ scale) in ppm. ^{1}H NMR data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad), coupling constants (Hz), and integration. Low resolution mass spectroscopy (MS), using either electron impact (EI) or chemical ionization (CI), was performed on a V. G. Micromass 7070 HS mass spectrometer with an electron beam energy of 70 eV (for EI). High resolution mass spectroscopy (HRMS) was performed on a Kratos Concept-11A mass spectrometer with an electron beam of 70 eV. Melting points were determined with a Thomas –Hoover Unit melting point apparatus and uncorrected.

Compounds were named using ACD/I-Lab Web service (ACD/IUPAC Name 6.04).

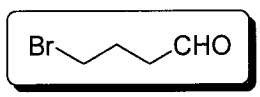
4-Bromobutan-1-ol (67)



The compound was prepared according to the procedure described in Ref. 39. Tetrahydrofuran (5.62 mL, 69.3 mmol) was added dropwise to a solution of BBr_3 (2.18 mL, 23.1 mmol) in CH_2Cl_2 (30 mL) at 0 °C. The mixture was heated at reflux and stirred for 1.5 h. The reaction was cooled to rt, quenched with MeOH and heated at reflux for an additional 1 h. Removal of methyl borate and methanol *in vacuo* provided pure bromoalcohol **67** as an orange oil (7.74g, 73%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 3.67 (t, J = 6.3 Hz, 2H), 3.43 (t, J = 6.6 Hz, 2H), 1.99-1.89 (m, 3H), 1.74-1.64 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 62.3, 34.0, 31.4, 29.5; HRMS (EI) *m/z* calcd for C_4H_9BrO (M^+ - 18) 133.9731, found 133.9725. ^{1}H NMR and ^{13}C NMR spectra of this sample were in good agreement with that reported for this compound[64]

4-Bromobutanal (68)



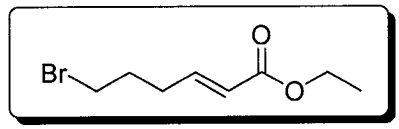
The compound was prepared according to the procedure described in Ref. 40. PDC (1.86 g, 4.94 mmol) was added to a solution of alcohol **67** (500 mg, 3.29 mmol) in CH_2Cl_2 (5 mL). The reaction stirred at rt for 2 h. The mixture was filtered through a pad of silica gel, washing with Et_2O. The filtrate was concentrated. Chromatography (pet ether/Et_2O, 3:1) afforded **68** as a yellow oil (520 mg, 100%). Aldehyde **68** was carried to the next reaction immediately after purification.

^{1}H NMR (300 MHz, $CDCl_3$) δ 9.77 (s, 1H), 3.42 (t, J = 3.9 Hz, 2H), 2.63 (t, J = 4.2 Hz, 2H), 2.14 (quintet, J = 4.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 200.8, 42.3, 32.8, 25.1; HRMS (EI) *m/z* calcd for C_4H_7BrO (M^+) 149.9968, found 149.9613. ^{1}H NMR and ^{13}C

[64] Tauh, P.; Fallis, A. G. *J. Org. Chem.* **1999,** *64,* 6960.

NMR spectra of this sample were in good agreement with that reported for this compound.[40]

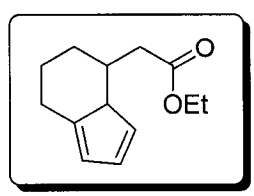
Ethyl-(2*E*)-6-bromohex-2-enoate (70)



The compound was prepared according to the procedure described in Ref. 40. Triethyl phosphonoacetate (3.10 mL, 15.6 mmol) was added to a suspension of sodium hydride (375 mg, 15.6 mmol) in THF (25 mL). The milky white solution stirred at rt until gas evolution ceased. A solution of **68** (2.13 g, 14.2 mmol) in THF (25 mL) was added to the mixture and the reaction stirred for 3 h. Diluted mixture with H_2O and the aqueous phase was extracted with CH_2Cl_2 (3x). Combined CH_2Cl_2 extracts were washed with H_2O (3x), brine, dried and concentrate. Chromatography (pet ether/Et_2O, 3:1) afforded **70** as a yellow oil (1.42 g, 45%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.88 (ddd, J = 15.6, 7.0, 7.0 Hz, 1H), 5.85 (ddd, J = 14.1, 1.5, 1.5 Hz, 1H), 4.16 (q, J = 7.1 Hz, 2H), 3.54 (t, J = 6.5 Hz, 2H), 2.35 (q, J = 7.1 Hz, 2H), 1.99 (quintet, J = 7.0 Hz, 2H), 1.26 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.8, 147.1, 122.9, 60.7, 33.0, 31.1, 30.8, 14.6; HRMS (EI) *m/z* calcd for $C_8H_{13}BrO_2$ (M^+) 220.0098, found 220.0094. ^{1}H NMR and ^{13}C NMR spectra of this sample were in good agreement with that reported for this compound.[40]

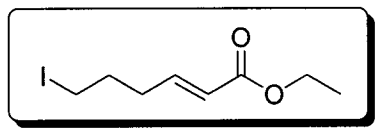
Ethyl-4,5,6,7-tetrahydro-3a*H*-inden-4-ylacetate (72)



Ethylmagnesium bromide (1.09 mL, 1.09 mmol, 1 M in THF) was added to a solution of freshly distilled cyclopentadiene (81.8 μL, 0.994 mmol) in THF (2 mL) at 0 °C. The solution was heated at reflux for 4 h. The reaction was cooled to 0 °C and to this was added a solution of **70** (200 mg, 0.904 mmol) in THF (2 mL). After 2 h of stirring at rt the reaction was diluted with with Et_2O. The organic phase was washed with HCl (10% aq, 3x), $NaHCO_3$ (sat. aq, 3x), brine, dried and concentrated. Chromatography (petroleum ether/Et_2O, 19:1) afforded **72** as a colorless oil (74 mg, 40%). Starting material was also recovered (54 mg, 54%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.38-6.17 (m, 3H), 4.09 (qd, *J* = 7.2, 2.1 Hz, 2H), 3.20-3.10 (m, 1H), 2.88 (d, *J* = 1.5 Hz, 2H), 2.63 (q, 9.0 Hz, 1H), 2.06-1.71 (m, 5H), 1.63-1.50 (m, 1H), 1.20 (t, 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.6, 151.3, 132.5, 131.3, 126.4, 60.6, 51.1, 46.1, 42.3, 34.1, 30.8, 25.0, 14.6; IR (neat) υ = 2957, 2873, 1729 cm^{-1}; MS (EI) *m/z* (relative intensity) 206 (M^+, 50), 177 (6), 132 (100), 91 (23), 69 (23); HRMS (EI) *m/z* calcd for $C_{13}H_{18}O_2$ (M^+) 206.1306, found 206.1290.

Ethyl-(2*E*) -6-iodohex-2-enoate (70a)

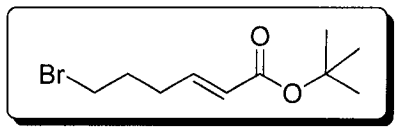


The compound was prepared according to the procedure described in Ref. 42. A mixture of **70** (500 mg, 2.26 mmol), sodium iodide (1.01 g, 6.78 mmol) and acetone (5mL) was heated at reflux and stirred for 3 h. The heterogeneous mixture was filtered through a pad a silica gel, washing with Et_2O. Concentration of the filtrate afforded **70a** as a clear oil (540 mg, 89%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.86 (ddd, *J* = 15.6, 7.0, 7.0 Hz, 1H), 5.85 (ddd, *J* = 15.6, 1.5, 1.5 Hz, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.16 (t, *J* = 6.8 Hz, 2H), 2.31 (q, *J* = 7.2 Hz, 2H), 1.95 (quintet, *J* = 6.9 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.8, 146.9, 122.9, 60.7, 33.1, 31.8, 14.6, 5.9; HRMS (EI) *m/z* calcd for $C_8H_{13}IO_2$

(M^+) 267.9960, found 267.9956. ^{1}H NMR and ^{13}C NMR spectra of this sample were in good agreement with that reported for this compound.[42]

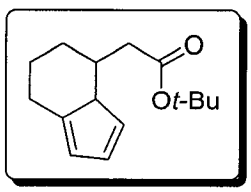
tert-Butyl-(2*E*)-6-iodohex-2-enoate (70b)



(*t*-Butoxycarbonylmethyl)triphenylphosphonium bromide (1.5 g, 3.28 mmol)) was added to a suspension of sodium hydride (78 mg, 3.28 mmol) in THF (5 mL). The milky white solution stirred at rt until gas evolution ceased and then heated to reflux for 45 min. The reaction cooled to rt and a solution of aldehyde **68** (492 mg, 3.28 mmol) in THF (5 mL) was added and the reaction continued to stir for an additional 16 h. Diluted mixture with H_2O and the aqueous phase was extracted with Et_2O (3x). Combined Et_2O extracts were washed with H_2O (3x), brine, dried and concentrate. Chromatography (pet ether/Et_2O, 3:1) afforded **70b** as yellow oil (390 mg, 48%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.77 (ddd, J = 15.6, 7.0, 7.0 Hz, 1H), 5.77 (ddd, J = 15.6, 1.5, 1.5 Hz, 1H), 3.38 (t, J = 6.6 Hz, 2H), 2.32 (q, J = 7.2 Hz, 2H), 1.98 (quintet, J = 6.6 Hz, 2H), 1.45 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.1, 145.8, 124.6, 80.6, 33.1, 31.2, 30.6, 28.5; IR (neat) υ = 2981, 1712, 1652, 1159 cm^{-1}; MS (EI) *m/z* (relative intensity) 192 (M^+-57, 10), 177 (31), 57 (100);

tert-Butyl-4,5,6,7-tetrahydro-3a*H*-inden-4-ylacetate (72a, Table 1, Entry 5)

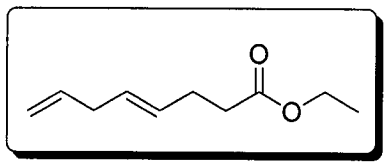


Ethylmagnesium bromide (1.18 mL, 1.18 mmol, 1 M in THF) was added to a solution of freshly distilled cyclopentadiene (0.097 mL, 1.18 mmol) in THF (3 mL) at 0 °C. The

solution was heated to reflux for 4 h. The reaction was cooled to 0 °C and to this was added a solution of **70b** (270 mg, 1.08 mmol) in THF (3 mL). After 2 h of stirring at rt the reaction was diluted with with Et_2O. The organic phase was washed with HCl (10% aq, 3x), $NaHCO_3$ (sat. aq, 3x), brine, dried and concentrated. Chromatography (petroleum ether/Et_2O, 19:1) afforded **72a** as a colorless oil (101 mg, 40%). Starting material was also recovered (136 mg, 51%).

^1H NMR (300 MHz, $CDCl_3$) δ 6.40-6.18 (m, 3H), 3.11-3.16 (m, 1H), 2.8 (d, J = 1.4 Hz, 2H), 2.53 (q, J = 5.4 1H), 2.02-1.94 (m, 2H), 1.86-1.82 (m, 1H), 1.75-1.69 (m, 2H), 1.59-1.53 (m, 1H), 1.39 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.5, 151.3, 132.1, 130.8, 126.0, 79.9, 51.9, 45.8, 41.8, 33.8, 30.3, 28.1, 24.7; IR (neat) υ = 3501, 3071, 2953, 1652 cm^{-1}; MS (EI) *m/z* (relative intensity) 177 (M^+-53, 45), 132 (100), 91 (21), 69 (23);

Ethyl-(4*E*)-octa-4,7-dienoate (81)

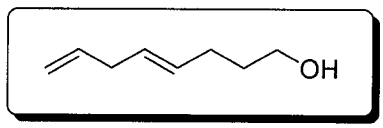


The compound was prepared according to the procedure described in Ref. 44a. A solution of 1,5-hexadien-3-ol (2 mL, 17.9 mmol) and propionic acid (80 μL, 1.07 mmol) in triethyl orthoacetate (22.9 ml, 125 mmol) was heated to 145 °C under conditions for distillative removal of ethanol. When distillation of ethanol was complete (ca 3 h), the reaction was cooled to rt and diluted with Et_2O. The organic phase was washed with HCl (10% aq, 3x), $NaHCO_3$ (sat. aq, 3x), brine, dried and concentrated. Chromatography (pet ether/Et_2O, 19:1) afforded **81** as a colorless oil (2.38 g, 93%).

^1H NMR (300 MHz, $CDCl_3$) δ 5.78 (ddt, J = 17.1, 10.2, 6.3 Hz, 1H), 5.52-5.39 (m, 2H), 5.03-4.93 (m, 2H), 4.10 (q, J = 7.1 Hz, 2H), 2.73-2.69 (m, 2H), 2.36-2.28 (m, 4H), 1.23 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.6, 137.4, 129.7, 129.3, 115.4, 60.6, 37.0, 34.6, 28.3, 14.6; IR (neat) υ = 2980, 1737 cm^{-1}; MS (EI) *m/z* (relative intensity) 168 (M^+, 13), 123 (11), 94 (34), 80 (100); HRMS (EI) *m/z* calcd for $C_{10}H_{16}O_2$ (M^+) 168.1150,

found 168.1171. ^{1}H NMR and ^{13}C NMR spectra of this sample were in good agreement with that reported for this compound.[44a]

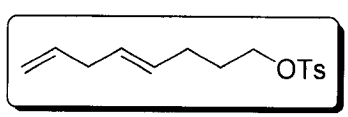
(4*E*)-Octa-4,7-dien-1-ol (82)



The compound was prepared according to the procedure described in Ref. 44a. A solution of ester **81** (1 g, 5.94 mmol) in dry THF (10 mL) was added dropwise to a suspension of $LiAlH_4$ (450 mg, 11.9 mmol) in dry THF (20 mL) at rt. After 30 min, H_2O was added dropwise until mixture turned white. HCl (10% aq) was added until the solution turned clear. Et_2O extracts (3x) were combined and washed with H_2O and brine, dried and concentrated. Chromatography (pet ether/Et_2O, 3:1) afforded **82** as a colorless oil (690 mg, 92%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.79 (ddt, J = 17.1, 10.2, 6.6 Hz, 1H), 5.46-5.42 (m, 2H), 5.03-4.92 (m, 2H), 3.62 (t, J = 6.6 Hz, 2H), 2.73-2.70 (m, 2H), 2.11-2.05 (m, 2H), 1.62 (quintet, J = 6.9 Hz, 2H), 1.50 (bs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.6, 131.2, 128.8, 115.3, 62.9, 37.1, 32.7, 29.2; IR (neat) υ = 3352, 2929, 912 cm^{-1}; too unstable for MS. ^{1}H NMR and ^{13}C NMR spectra of this sample were in good agreement with that reported for this compound.[44]

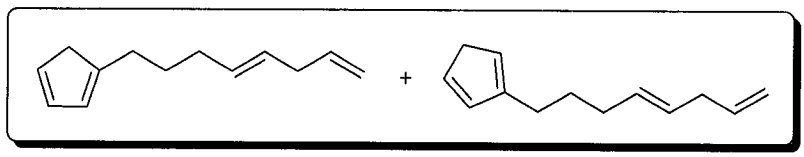
(4*E*)-Octa-4,7-dien-1-yl-4-methylbenzenesulfonate (83)



Triethylamine (1.78 mL, 12.78 mmol), *p*-toluenesulfonyl chloride (1.63 g, 8.53 mmol) and DMAP (26 mg, 0.213 mmol) were added to a solution of alcohol **82** (538 mg, 4.26 mmol) in CH_2Cl_2 (20 mL). The mixture stirred at rt for 24 h. The reaction was washed

with HCl (10% aq, 3x), H_2O, brine, dried and concentrated. Chromatography (pet ether/Et_2O, 19:1 or pure CH_2Cl_2) afforded **83** as a colorless oil (948 mg, 79%).
^1H NMR (300 MHz, $CDCl_3$) δ 7.76 (d, J = 8.3 Hz, 2H), 7.32 (d, J = 8.0 Hz, 2H), 5.73 (ddt, J = 16.7, 10.4, 6.4 Hz, 1H), 5.38-5.22 (m, 2H), 4.99-4.92 (m, 2H), 3.99 (t, J = 6.4 Hz, 2H), 2.67-2.63 (m, 2H), 2.42 (s, 3H), 2.04-1.98 (m, 2H), 1.68 (quintet, J = 6.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.0, 137.3, 133.5, 130.2, 129.7, 129.6, 128.3, 115.4, 70.2, 36.9, 28.8, 28.5, 22.1; IR (neat) ν = 3076, 2925, 1362, 1177 cm^{-1}; too unstable for MS.

1-((4*E*)-Octa-4,7-dien-1-yl)cyclopenta-1,3-diene
and **2-((4*E*)-Octa-4,7-dien-1-yl)cyclopenta-1,3-diene (84)**

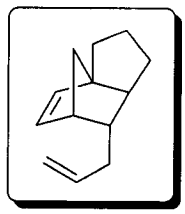


Procedure A: Sodium hydride (51.4 mg, 2.14 mmol) was added to a solution of freshly distilled cyclopentadiene (0.176 mL, 2.14 mmol) in THF (5 mL) at 0 °C. Bubbling started due to hydrogen gas evolution and the solution turned red due to the formation of cyclopentadienylsodium. Once bubbling ceased, tosylate **83** (300 mg, 1.07 mmol) in THF (5 mL) was added *via* cannula. The reaction slowly warmed to rt and stirred for 6 h. Diluted with HCl (10% aq) and the aqueous phase was extracted with pet ether (3x). Combined pet ether extracts (3x) were washed with H_2O, brine, dried and concentrated. Chromatography (pure pet ether) afforded **84** as a colorless oil (186 mg, 99%).
Procedure B: Ethylmagnesium bromide (5.25 mL, 1 M in THF, 5.25 mmol) was added to a solution of freshly distilled cyclopentadiene (0.432 mL, 5.25 mmol) in THF (5 mL) at 0 °C. The solution was heated at reflux for 4 h. The solution was cooled to 0 °C and to this was added a solution of tosylate **83** (500 mg, 1.75 mmol) in THF (5 mL). The reaction stirred at rt for 16 h. Diluted with HCl (10% aq) and the aqueous phase was extracted with pet ether (3x). Combined pet ether extracts (3x) were washed with H_2O,

brine, dried and concentrated.. Chromatography (pure pet ether) afforded **84** as a colorless oil (186 mg, 99%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.43-5.98 (m, 3H), 5.87-5.74 (m, 1H), 5.50-5.36 (m, 2H), 5.03-4.94 (m, 2H), 2.92 (bs, 1H), 2.85 (bs, 1H), 2.72-2.70 (m, 2H), 2.41-2.31 (m, 2H), 2.03-2.01 (m, 2H), 1.65-1.52 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.2, 147.4, 137.8, 135.1, 134.0, 132.8, 131.8, 131.7, 130.8, 128.34, 128.29, 126.7, 126.3, 115.1, 43.6, 41.6, 37.1, 32.7, 32.6, 30.5, 29.8, 29.7, 28.9; IR (neat) ν = 2929, 1432, 972 cm^{-1}; MS (EI) *m/z* (relative intensity) 174 (M^+, 8), 119 (10), 80 (100), 67 (12), 41 (12); HRMS calcd for $C_{13}H_{18}$ (M^+) 174.1408, found 174.1400.

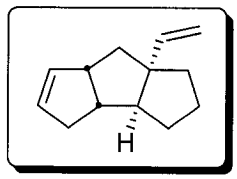
7-Allyl-1,2,3,6,7,7a-hexahydro-3a,6-methanoindene (75)



A microwave quartz vessel was charged with substituted cyclopentadiene **84** (100 mg, 0.572 mmol), chlorobenzene (5 mL) and a carboflon™. The solution was degassed with argon for 15 min. The microwave apparatus was quickly assembled and the reaction was heated at 210 °C and 310 psi for 2 h. The solution was directly loaded onto the chromatographic column. Purification using pure pet ether afforded **75** as a clear oil (80 mg, 80%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.16 (d, J = 5.6 Hz, 1H), 5.92 (dd, J = 5.6, 2.9 Hz, 1H), 5.77 (ddt, J = 17.1, 10.3, 6.7 Hz, 1H), 4.96-4.89 (m, 2H), 2.77 (bs, 1H), 1.97-1.77 (m, 7H), 1.66-1.61 (m, 1H), 1.38 (d, J = 8.1 Hz, 1H), 1.30-1.22 (m, 1H), 1.21 (d, J = 8.1 Hz, 1H), 1.12-1.07 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 141.7, 138.5, 132.6, 114.4, 63.5, 53.0, 52.0, 49.0, 47.2, 39.2, 31.5, 27.1, 27.0; IR (neat) ν = 2951, 2906, 2864 cm^{-1}; MS (EI) *m/z* (relative intensity) 174 (M^+, 35), 159 (14), 145 (16), 133 (28), 119 (23), 92 (100), 80 (72), 97 (21); HRMS calcd for $C_{13}H_{18}$ (M^+) 174.1408, found 174.1411.

7a-Vinyl-2,3,3a,3b,4,6a,7,7a-octahydro-1H-cyclopenta[a]pentalene (85)



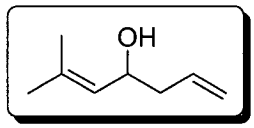
Procedure A: A microwave quartz vessel was charged with substituted cyclopentadiene **84** (100 mg, 0.572 mmol), chlorobenzene (5 mL) and a carboflon™. The solution was degassed with argon for 15 min. The microwave apparatus was quickly assembled and the reaction was heated at 210 °C and 310 psi for 2 h. The quartz vessel was removed from the apparatus, placed with a septum and the solution was degassed with argon for 10 min. The solution was then purged with ethylene for another 10 min. While maintaining an ethylene atmosphere, Grubbs 1st generation catalyst (24.3 mg, 0.0286 mmol) was added. After being stirred at rt for 2 h under ethylene atmosphere the reaction was quenched with DMSO (0.100 mL). The mixture was concentrated *in vacuo* and chromatography (pure pet ether) afforded **85** as a clear oil (65 mg, 65%).

Procedure B: A solution of Diels-Alder adduct **75** (50.0 mg, 0.287 mmol) in benzene (5 mL) was degassed with argon for 15 min. The solution was purged with ethylene for another 10 min. While maintaining the ethylene atmosphere, Grubbs 1st generation catalyst was added (12.2 mg, 0.0144 mmol) and after being stirred at rt for 2 h under ethylene atmosphere the reaction was quenched with DMSO (0.050 mL). The mixture was concentrated *in vacuo* and chromatography (pure pet ether) afforded **85** as a clear oil (49.5 mg, 99%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 5.87 (dd, J = 17.5, 10.7 Hz, 1H), 5.61-5.49 (m, 2H), 4.87 (dd, J = 17.4, 1.4 Hz, 1H), 4.80 (dd, J = 10.6, 1.4 Hz, 1H), 3.19-3.14 (m, 1H), 2.55-2.49 (m, 1H), 2.33-2.29 (m, 1H) 2.16-2.11 (m, 1H), 1.90 (dd, J = 13.0, 8.5 Hz, 1H), 1.82-1.59 (m, 6H), 1.58-1.48 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.3, 135.5, 128.0, 109.0, 58.6, 58.2, 50.8, 49.8, 43.4, 39.4, 36.4, 31.4, 23.9; IR (neat) ν = 2953, 2927, 2856 cm^{-1}; MS (EI) *m/z* (relative intensity) 174 (M^+, 100), 159 (40), 145 (48), 131 (95), 119 (70),

108 (68), 91 (96), 79 (76), 67 (50); HRMS calcd for $C_{13}H_{18}$ (M^+) 174.1408, found 174.1393.

6-Methylhepta-1,5-dien-4-ol (90)

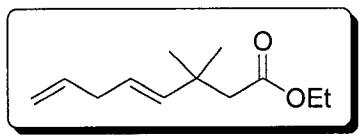


The compound was prepared according to the procedure described in Ref. 46. Allylmagnesium bromide (100 mL, 100 mmol, 1M in Et_2O), *via* syringe pump was slowly added to a solution of 3-methyl-2-butenal (5.51 mL, 57.1 mmol) in Et_2O (115 mL) at 0 °C. The reaction stirred at rt for 16 h. The grey solution was cooled to 0 °C and slowly quenched with HCl (10% aq, 25 mL) until a white ppt started to form. The aqueous phase was extracted with Et_2O (3x), the combined Et_2O extracts were washed with H_2O, dried and concentrated. Chromatography (pure CH_2Cl_2) afforded **90** as a colorless oil (5.98 g, 83%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.78 (ddt, J = 17.1, 10.1, 7.1 Hz, 1H), 5.19-5.06 (m, 3H), 4.37 (dt, J = 8.6, 6.4 Hz, 1H), 2.26-2.21 (m, 2H), 1.70 (d, J = 1.2 Hz, 3H), 1.66 (d, J = 1.3, 3H), 1.08 (bs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 135.8, 134.9, 127.5, 118.2, 68.1, 42.5, 30.1, 26.1, 18.6; MS (EI) *m/z* (relative intensity) 108 (M^+-18, 2), 85 (100), 67 (9), 55 (7), 41 (25); HRMS calcd for C_8H_{12} (M^+ – 18) 108.0935, found 108.0952. Characterization of this sample was in good agreement with that reported for this compound.[65]

[65] Gau, A. -H.; Lin, G. –L.; Uang, B. –J.; Liao, F. –L.; Wang, S. –L. *J. Org. Chem.* **1999,** *64,* 2194.

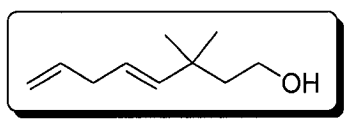
Ethyl-(4*E*)-3,3-dimethylocta-4,7-dienoate (91)



The compound was prepared according to the procedure described in Ref. 47. A solution of alcohol **90** (3.00 g, 23.8 mmol) and phenol (111 mg, 1.18 mmol) in triethyl orthoacetate (30.5 ml, 166 mmol) was heated to 145 °C under conditions for distillative removal of ethanol. When distillation of ethanol was complete (ca 24 h), the reaction was cooled to rt and diluted with Et_2O. The organic phase was washed with HCl (10% aq, 3x), NaOH (10% aq, 3x), brine, dried and concentrated. Chromatography (petroleum ether/Et_2O gradient, 19:1 (200 mL), 9:1 (200 mL), 3:1) afforded **91** as a colorless oil (3.03 g, 65%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 5.80 (ddt, J = 17.1, 10.1, 6.3 Hz, 1H), 5.50 (dt, J = 14.3, 1.2 Hz, 1H) 5.34 (dt, J = 15.6, 6.3 Hz, 1H), 5.02-4.93 (m, 2H), 4.06 (q, J = 7.1 Hz, 2H), 2.72 (tq, J = 6.3, 1.4 Hz, 2H), 2.24 (s, 2H), 1.21 (t, J = 7.1 Hz, 3H), 1.10 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.2, 140.2, 137.6, 129.6, 124.4, 116.3, 115.2, 60.3, 47.6, 37.0, 35.8, 27.9, 14.7; IR (neat) ν = 2962, 2930, 1735 cm^{-1}; MS (EI) *m/z* (relative intensity) 196 (M^+, 11), 162 (11), 129 (15), 109 (95), 108 (100), 93 (64), 81 (28), 67 (46), 55 (21); HRMS calcd for $C_{12}H_{20}O_2$ (M^+) 196.1463, found 196.1492.

(4*E*)-3,3-Dimethylocta-4,7-dien-1-ol (92)

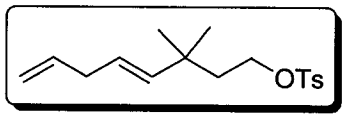


A solution of ester **91** (500 mg, 2.55 mmol) in THF (10 mL) was added dropwise to a suspension of $LiAlH_4$ (193 mg, 5.09 mmol) in THF (10 mL) at rt. After 30 min, H_2O was added dropwise until mixture turned white. HCl (10% aq) was added until the solution turned colourless. Et_2O extracts (3x) were combined and washed with H_2O and brine,

dried and concentrated. Chromatography (petroleum ether/Et_2O, 3:1) afforded **92** as a colorless oil (340 mg, 87%).

^1H NMR (300 MHz, $CDCl_3$) δ 5.79 (ddt, J = 17.1, 10.3, 6.4 Hz, 1H), 5.45 (d, J = 15.8 Hz, 1H), 5.34 (dt, J = 9.6, 6.0 Hz, 1H), 5.02-4.95 (m, 2H), 3.62 (t, J = 7.1 Hz, 2H), 2.73 (bt, J = 5.9 Hz, 2H), 1.57 (t, J = 7.1 Hz, 2H), 1.37 (bs, 1H), 0.99 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.5, 137.6, 124.5, 115.3, 68.3, 60.6, 45.8, 37.1, 35.3, 28.0; IR (neat) ν = 3345, 2959, 2936, 2899 cm^{-1}; too unstable for MS.

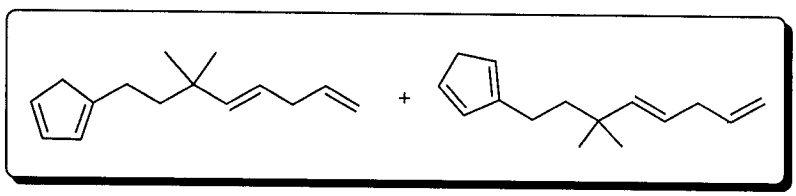
(4*E*)-3,3-Dimethylocta-4,7-dien-1-yl 4-methylbenzenesulfonate (93)



Triethylamine (5.96 mL, 42.8 mmol), *p*-toluenesulfonyl chloride (5.44 g, 28.5 mmol) and DMAP (86 mg, 0.710 mmol) were added to a solution of alcohol **92** (2.20 g, 14.2 mmol) in CH_2Cl_2 (30 mL). The mixture stirred at rt for 24 h. The reaction was washed with HCl (10% aq, 3x), H_2O, brine, dried and concentrated. Chromatography (petroleum ether/Et_2O, 19:1or pure CH_2Cl_2) afforded **93** as a colorless oil (4.07 g, 93%).

^1H NMR (300 MHz, $CDCl_3$) δ 7.75 (d, J = 8.3 Hz, 2H), 7.31 (d, J = 8.4 Hz, 2H), 5.72 (m, 1H), 5.24 (m, 2H), 4.95 (m, 2H), 3.98 (t, J = 7.4 Hz, 2H), 2.66 (m, 2H), 2.42 (s, 3H), 1.63 (t, J = 7.4 Hz, 2H), 0.93 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.0, 139.8, 137.5, 133.5, 130.1, 128.2, 125.3, 115.4, 68.7, 41.2, 37.0, 35.2, 27.9, 22.0; IR (neat) ν = 2962, 1363 cm^{-1}; too unstable for MS

1-((4*E*)-3,3-Dimethylocta-4,7-dien-1-yl)cyclopenta-1,3-diene
and 2-((4*E*)-3,3-Dimethylocta-4,7-dien-1-yl)cyclopenta-1,3-diene (88)

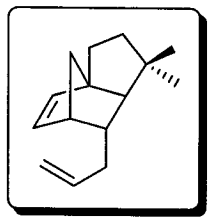


Procedure A: Sodium hydride (51.4 mg, 2.14 mmol) was added to a solution of freshly distilled cyclopentadiene (0.18 mL, 2.14 mmol) in THF (5 mL) at 0 °C. The solution turned red due to the formation of cyclopentadienyl anion. Once bubbling ceased, tosylate **93** (300 mg, 1.07 mmol) in THF (5 mL) was added via cannula. The reaction slowly warmed to rt and stirred for 1.5 hr. The mixture was extracted with petroleum ether (3x). Petroleum ether extracts (3x) were combined and washed with H_2O and brine, dried and concentrated.. Chromatography (petroleum ether) afforded **88** as a colorless oil (186 mg, 99%).

Procedure B: Ethylmagnesium bromide (4.86 mL, 1 M in THF, 4.86 mmol) was added to a solution of freshly distilled cyclopentadiene (0.400 mL, 4.86 mmol) in THF (5 mL) at 0 °C. The solution was heated at reflux for 4 h. The solution was cooled to 0 °C and to this was added a solution of tosylate **93** (500 mg, 1.62 mmol) in THF (5 mL). The reaction stirred at rt for 16 h. Diluted with HCl (10% aq) and the aqueous phase was extracted with pet ether (3x). Combined pet ether extracts (3x) were washed with H_2O, brine, dried and concentrated. Chromatography (pure pet ether) afforded **88** as a colorless oil (194 mg, 60%).

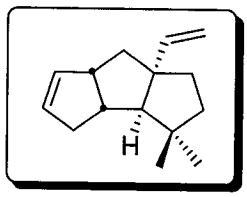
^{1}H NMR (300 MHz, $CDCl_3$) δ 6.42-5.92 (m, 3H), 5.84 (ddt, J = 17.1, 103, 6.3 Hz, 1H), 5.47-5.27 (m, 2H), 5.04-4.95 (m, 2H), 2.92 (s, 1H) 2.85 (s, 1H), 2.77 (bt, 2H), 2.33-2.22 (m, 2H), 1.53-1.42 (m, 2H), 1.00 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.0, 148.1, 141.6, 141.5, 138.1, 135.3, 134.0, 132.8, 130.7, 126.0, 125.5, 124.1, 115.1, 43.8, 43.1, 42.3, 41.6, 37.2, 36.1, 36.1, 27.7, 26.3, 25.5; IR (neat) ν = 2959, 2917 cm^{-1}; MS (EI) *m/z* (relative intensity) 202 (M^+, 14), 187 (13), 161 (21), 109 (78), 92 (100), 67 (77), 43 (25); HRMS calcd for $C_{15}H_{22}$ (M^+) 202.1721, found 202.1730.

7-Allyl-1,1-dimethyl-1,2,3,6,7,7a-hexahydro-3a,6-methanoindene (87)



A microwave quartz vessel was charged with substituted cyclopentadiene **88** (100 mg, 0.495 mmol), benzene (5 mL) and a carboflon™. The solution was degassed with argon for 15 min. The microwave apparatus was quickly assembled and the reaction was heated at 210 °C and 310 psi for 2 h. The solution was directly loaded onto the chromatographic column. Purification using pure pet ether afforded **87** as a clear oil (45 mg, 45%).
^{1}H NMR (500 MHz, $CDCl_3$) δ 6.18 (d, J = 5.7 Hz, 1H), 5.90 (dd, J = 5.7, 2.8 Hz, 1H), 5.76 (ddt, J = 17.0, 10.0, 7.2 Hz, 1H), 4.96-4.89 (m, 2H), 2.75 (bs, 1H), 2.04-1.99 (m, 1H), 1.93-1.87 (m, 1H), 1.81-1.52 (m, 5H), 1.38 (broad dd, 1H), 1.12 (dt, J = 7.9, 1.9 Hz, 1H), 0.97 (s, 6H), 0.82 (dd, J = 5.1, 2.1 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.2, 138.7, 132.3, 114.7, 65.2, 62.6, 50.8, 47.8, 44.3, 42.3, 40.6, 36.5, 32.9, 28.1, 26.8; IR (neat) ν = 2957, 2864, 908 cm^{-1}; MS (EI) *m/z* (relative intensity) 202 (M^+, 16), 187 (20), 161 (17), 109 (26), 92 (100), 67 (24); HRMS calcd for $C_{15}H_{22}$ (M^+) 202.1721, found 202.1712.

3,3-Dimethyl-7a-vinyl-2,3,3a,3b,4,6a,7,7a-octahydro-1*H*-cyclopenta[*a*]pentalene (86)



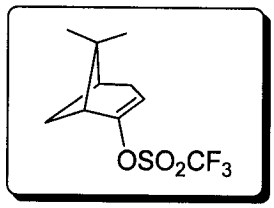
Procedure A: A microwave quartz vessel was charged with substituted cyclopentadiene **88** (100 mg, 0.495 mmol), benzene (5 mL) and a carboflon™. The solution was degassed with argon for 15 min. The microwave apparatus was quickly assembled and the reaction was heated at 210 °C and 310 psi for 2 h. The quartz vessel was removed from the apparatus, placed with a septum and the solution was degassed with argon for 10 min. The solution was then purged with ethylene for another 10 min. While maintaining the ethylene atmosphere, Grubbs 1st generation catalyst (21.0 mg, 0.0248 mmol) was added. After being stirred at rt for 2 h under ethylene atmosphere the reaction was quenched

with DMSO (0.100 mL). The mixture was concentrated *in vacuo* and chromatography (pure pet ether) afforded **86** as a clear oil (15.1 mg, 15%).

Procedure B: A solution of Diels-Alder adduct **87** (50.0 mg, 0.247 mmol) in benzene (5 mL) was degassed with argon for 15 min. The solution was purged with ethylene for another 10 min. While maintaining the ethylene atmosphere, Grubbs 1st generation catalyst was added (10.5 mg, 0.0124 mmol) and after being stirred at rt for 2 h under ethylene atmosphere the reaction was quenched with DMSO (0.050 mL). The mixture was concentrated *in vacuo* and chromatography (pure pet ether) afforded **86** as a clear oil (49.2 mg, 99%).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.00 (dd, J = 17.5, 10.5 Hz, 1H), 5.61-5.52 (m, 1H), 4.90 (dd, J = 17.5, 1.0 Hz, 1H), 4.75 (dd, J = 10.5, 1.5 Hz, 1H), 3.11-3.09 (m, 1H), 2.56-2.53 (m, 2H), 2.14-2.10 (m, 1H),1.88-1.84 (m, 2H), 1.77 (dd, J = 13.5, 8.0 Hz, 1H), 1.57 (bd, J = 3.3 Hz, 1.53-1.46 (m, 3H), 1.43-1.40 (m, 1H), 1.01 (s, 3H), 0.95 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 150.0, 136.0, 128.7, 107.8, 69.7, 58.5, 52.3, 45.6, 45.1, 41.7, 41.1, 40.0, 36.4, 30.3, 25.8; IR (neat) ν = 2943, 2863, 1467, 900 cm^{-1}; MS (EI) *m/z* (relative intensity) 202 (M^+, 10), 187 (100), 161 (6), 148 (33), 105 (22), 91 (22), 79 (16); HRMS calcd for $C_{15}H_{22}$ (M^+) 202.1721, found 202.1726.

(1*R*)-6,6-Dimethylbicyclo[3.1.1]hept-2-en-2-yl trifluoromethanesulfonate (142)

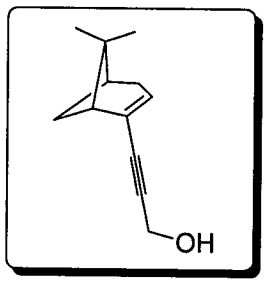


n-Butyllithium (10.9 mL, 2.5 M in hexanes, 27.1 mmol) was added dropwise to a solution of diisopropylamine (3.80 ml, 27.1 mmol) in THF (10 mL) at -78 °C and the solution stirred for 30 min. At -78 °C nopinone (2.5 mL, 18.1 mmol) was added. The solution was warmed to rt and stirred for an additional 40 min. The clear solution cooled to -78 °C again and to this was added a solution of *N*-phenyltrifluoromethanesulfonimide (7.10 g, 27.1 mmol) in THF (20 mL). The reaction was warmed to rt and stirred for 16 h.

The reaction was quenched with H_2O and the aqueous phase was extracted with Et_2O (3x). The combined organic phases were washed with H_2O (3x), brine, dried and concentrated. Chromatography (pure pet ether) provided **142** as a colourless oil (3.03 g, 62%).

^1H NMR (300 MHz, $CDCl_3$) δ 5.53-5.50 (m, 1H), 2.54 (dt, J = 9.2, 5.7 Hz, 1H), 2.40-2.22 (m, 2H), 2.15-2.09 (m, 1H). 1.36 (d, J = 9.2 Hz, 1H), 1.32 (s, 3H), 0.91 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.4, 121.0, 116.8, 111.8, 46.6, 40.5, 40.1, 32.1, 28.6, 25.9, 21.2; IR (neat) υ = 2949, 1658, 1414 cm^{-1}; MS (EI) *m/z* (relative intensity) 270 (M^+, 3), 226 (16), 162 (9), 77 (52), 55 (100); HRMS (EI) *m/z* calcd for $C_{10}H_{13}F_3O_3S$ (M^+) 270.0537, found 270.0496.

(1*R*)-3-(6,6-Dimethylbicyclo[3.1.1]hept-2-en-2-yl)prop-2-yn-1-ol (128)

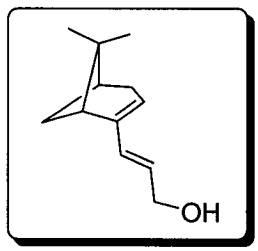


A round bottom flask equipped with a water condenser was charged with $Pd(PPh_3)_2Cl_2$ (130 mg, 0.18 mmol), copper(I)iodide (70 mg, 0.37 mmol), triflate **142** (1.00 g g, 3.7 mmol), triethylamine (18.5 mL) and THF (18.5 mL). The yellow mixture was degassed with argon for 15 min. To the mixture was added propargyl alcohol (0.236 mL, 4.1 mmol) and quickly the mixture turned from yellow to orange, to red and then to black. The mixture stirred at refluxed for 16 h. The mixture was filtered through a pad of silica gel washing with Et_2O. The filtrate was concentrate. Chromatography (pet ether/Et_2O, 3:1) afforded propargyl alcohol **128** as a dark yellow oil (619 mg, 95%).

^1H NMR (300 MHz, $CDCl_3$) δ 5.96 (bs, 1H), 4.37 (s, 2H), 2.38 (dt, J = 9.0, 5.6 Hz, 1H), 2.31 (quintet, J = 3 Hz, 3H), 2.23 (td, J = 5.7, 1.2 Hz, 1H), 2.08 (bs, 1H), 1.67 (s, 1H), 1.26 (s, 3H), 1.20 (d, J = 9.0 Hz, 1H) 0.86 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 131.9,

129.7, 87.3, 86.7, 52.1, 47.3, 40.5, 38.3, 32.4, 31.7, 26.4, 21.4; IR (neat) υ 3607, 2955, 1375 cm^{-1}; MS (EI) *m/z* (relative intensity) 176 (M^+, 82), 161 (16), 145 (44), 133 (100), 103 (79), 77 (55); HRMS (EI) *m/z* calcd for $C_{12}H_{16}O$ (M^+) 176.1201, found 176.1213.

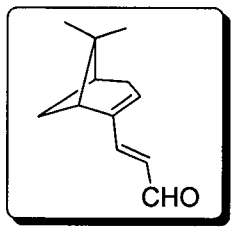
(1*R*, 2*E*)-3-(6,6-Dimethylbicyclo[3.1.1]hept-2-en-2-yl)prop-2-en-1-ol (144)



Vinylmagnesium chloride (4.12 mL, Aldrich Chemicals batch #02813AB, 1.6 M in THF, 6.60 mmol) was added dropwise to a solution of vinylpropargyl alcohol **128** (363 mg, 2.06 mmol) in toluene (20 mL). The brown reaction mixture stirred at reflux for 16 h. The reaction was quenched with saturated aqueous NH_4Cl (10 mL) at 0°C and the mixture stirred for 10 min. Dichloromethane was added followed by water and the aqueous phase was extracted with dichloromethane (3x). The combined organic phases were washed with H_2O (2x), brine, dried with $MgSO_4$ and concentrated. Chromatography (petroleum ether/Et_2O, 3:1) afforded **144** as a clear oil (154 mg, 42%).

^1H NMR (300 MHz, $CDCl_3$) δ 6.22 (d, J = 15.6 Hz, 1H), 5.67 (dt, J = 9.5, 6.1 Hz, 1H), 5.54 (bs, 1H), 4.17 (d, J = 5.9 Hz, 2H), 2.53-2.47 (m, 3H), 2.40 (dt, J = 8.7, 5.7 Hz, 1H), 2.33-2.27 (m, 1H), 2.11-2.09 (m, 1H), 1.30 (s, 3H), 1.11 (d, J = 8.7 Hz, 1H), 0.78 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.0, 133.4, 125.2, 124.6, 64.4, 41.6, 41.3, 38.1, 32.3, 31.6, 26.7, 21.2; IR (neat) υ = 3348, 2920 cm^{-1}; MS (EI) *m/z* (relative intensity) 178 (M^+, 18), 163 (7), 147 (38), 135 (13), 105 (64), 91 (100), 69 (28), 43 (97); HRMS (EI) *m/z* calcd for $C_{12}H_{18}O$ (M^+) 178.1357, found 178.1350.

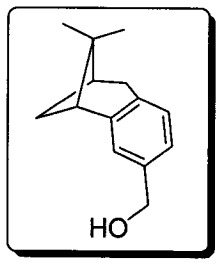
(1*R*, 2*E*)-3-(6,6-Dimethylbicyclo[3.1.1]hept-2-en-2-yl)acrylaldehyde (145)



Manganese (II) oxide (742 mg, 8.52 mmol) was added to a solution of allylic alcohol **144** (152 mg, 0.852 mmol) in toluene (10 mL). The black mixture stirred at reflux for 16 h. The mixture was filtered through a pad of silica washing with Et_2O. The filtrate was concentrated. Chromatography (pet ether/Et_2O, 19:1) afforded **145** as a yellow oil (142 mg, 95%).

^1H NMR (500 MHz, $CDCl_3$) δ 9.55 (d, J = 7.8 Hz, 1H), 7.08 (d, J = 15.6 Hz, 1H), 6.17 (bs, 1H), 6.01 (dd, J = 15.6, 7.8 Hz, 2.57-2.51 (m, 1H), 2.49-2.44 (m, 3H), 2.17-2.13 (m, 1H), 1.56 (s, 1H), 1.32 (s, 3H), 1.32 (d, J = 9 Hz, 1H), 0.75 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.7, 153.7, 146.6, 137.3, 125.9, 41.7, 40.8, 38.2, 33.4, 31.5, 26.4, 21.2; IR (neat) υ = 2949, 2821, 1682, 1612cm^{-1}; MS (GCMS) *m/z* (relative intensity) 176 (M^+, 7), 133 (73), 105 (100), 91 (72), 77 (52).

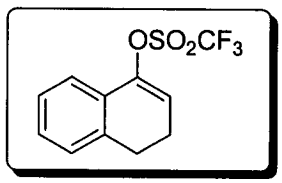
(1*R*)-(2,2-Dimethyl-1,2,3,4-tetrahydro-1,3-methanonaphthalen-7-yl)methanol (146)



Vinylmagnesium chloride (2.6 mL, Acros Organics, 15% wt in THF, 4.34 mmol) was added dropwise to a solution of **145** (191 mg, 1.08 mmol) in toluene (13 mL). The brown reaction mixture stirred at reflux for 16 h. The reaction was quenched with saturated aqueous NH_4Cl (10 mL) at 0°C and the mixture stirred for 10 min. Dichloromethane was added followed by water and the aqueous phase was extracted with dichloromethane

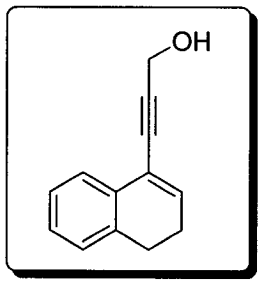
(3x). The combined organic phases were washed with H_2O (2x), brine, dried with $MgSO_4$ and concentrated. Chromatography (petroleum ether/Et_2O, 3:1) afforded **146** as a clear oil (115 mg, 53%). ^1H NMR (500 MHz, $CDCl_3$) δ 7.11-7.07 (m, 2H), 6.90 (s, 1H), 4.60 (s, 2H), 2.94 (bs, 2H), 2.71 (t, 5.5 Hz, 1H), 2.60 (dt, 9.3, 5.9 Hz, 1H), 2.25 (m, 1H), 1.35 (s, 3H), 1.23 (bs, 1H), 1.21 (d, 9.3 Hz, 1H), 0.61 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.1, 137.3, 134.4, 127.8, 124.7, 124.5, 62.4, 47.7, 40.4, 39.0, 32.6, 31.8, 26.0, 21.2; IR (neat) ν = 3336, 2980, 2916, 2867 cm^{-1}; MS (EI) *m/z* 202.1 (M^+, 8), 159 (14), 129 (100), 115 (7); HRMS calcd for $C_{14}H_{18}O$ (M^+) 202.1356, found 202.1353.

3,4-Dihydronaphthalen-1-yl trifluoromethanesulfonate (149)



The compound was prepared according to the procedure described in Ref. 69. *n*-Butyllithium (7.42 mL, 2.3 M, 16.7 mmol) was added dropwise to a solution of diisopropylamine (2.18 ml, 16.7 mmol) in THF (5 mL) at -78 °C and the solution stirred for 30 min. At -78 °C was added tetralone (2.02 mL, 15.2 mmol). The solution warmed to rt and stirred for an additional 30 min. The clear solution cooled to -78 °C again and to this was added a solution of *N*-phenyltrifluoromethanesulfonimide (5.7 g, 16.0 mmol) in THF (10 mL). The reaction was warmed to rt and stirred for 3 h. The reaction was quenched with H_2O and the aqueous phase was extracted with Et_2O (3x). The combined organic phases were washed with H_2O (3x), brine, dried and concentrated. Chromatography (pet ether) provided **149** as a colourless oil (3.29g, 78%).
^1H NMR (500 MHz, $CDCl_3$) δ 7.37-7.35 (m, 1H), 7.27-7.25 (m, 2H), 7.18-7.17 (m, 1H), 6.02 (t, J = 4.8 Hz, 1H), 2.86 (t, J = 8.0 Hz, 2H), 2.52-2.48 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 146.4, 136.2, 129.1, 128.6, 127.7, 126.9, 122.4, 121.2, 119.9, 117.7, 26.8, 22.3. ^1H NMR and ^{13}C NMR spectra of this sample were in good agreement with that reported for this compound.[61]

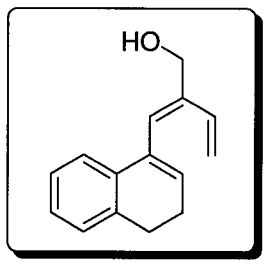
3-(3,4-Dihydronapthalen-1-yl)prop-2-yn-1-ol (140)



A round bottom flask equipped with a water condenser was charged with $Pd(PPh_3)_2Cl_2$ (414 mg, 0.591 mmol), copper(I)iodide (225 mg, 1.18 mmol), triflate **149** (3.29 g, 11.8 mmol), triethylamine (25 mL) and THF (25 mL). The yellow mixture was degassed with argon for 15 min. To the mixture was added propargyl alcohol (0.755 mL, 13.0 mmol) and quickly the mixture turned from yellow to orange, then to red and then to black. The mixture stirred at refluxed for 16 h. The mixture was filtered through a pad of silica gel washing with Et_2O. The filtrate was concentrate. Chromatography (pet ether/Et_2O, 3:1) afforded propargyl alcohol **140** as a dark yellow oil (1.71 g, 79%).

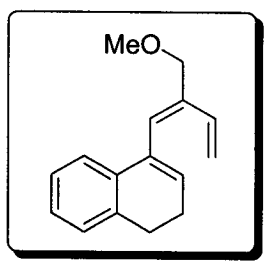
^1H NMR (500 MHz, $CDCl_3$) δ 7.59 (d, J = 7.5 Hz, 1H), 7.23 (td, J = 7.4, 0.8 Hz, 1H), 7.18 (td, J = 7.4, 1.4 Hz, 1H), 7.10 (d, J = 7.3 Hz, 1H), 6.47 (t, J = 4.8 Hz, 1H), 4.52 (s, 2H), 2.78 (t, J = 7.9 Hz, 2H), 2.75 (bs, 1H), 2.38-2.34 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.8, 134.8, 132.3, 127.6, 127.2, 126.5, 124.8, 121.1, 88.1, 83.3, 51.3, 26.9, 23.4; IR (neat) υ = 3359, 2935, 2830, 1487 cm^{-1}; MS (EI) *m/z* (relative intensity) 184 (M^+,100), 152 (63), 141 (52), 115 (41); HRMS (EI) *m/z* calcd for $C_{13}H_{12}O$ (M^+) 184.0888, found 184.0832.

2-(3,4-Dihydronapthalen-1-ylmethylene)but-3-en-1-ol (139)



Vinylmagnesium chloride (2.45 mL, Acros Organics, 15% wt in THF, 4.12 mmol) was added to a solution of **140** (190 mg, 1.03 mmol) in toluene (5 mL) at rt. A water condenser was quickly placed on the round bottom flask and the dark brown solution was stirred at reflux for 16 h. The solution was cooled to 0 °C and the reaction was quenched with saturated aqueous NH_4Cl (10 mL) and the yellow solution stirred for 30 min at rt. Dilution with H_2O and the aqueous phase was extracted with EtOAc (3x). The combined organic extracts were washed with H_2O (3x), dried and concentrated. Flash chromatography (pet ether/Et_2O, 3:1) afforded **139** as a yellow oil (168 mg, 77%).
^1H NMR (500 MHz, $CDCl_3$) δ 7.17 (s, 4H), 6.73 (ddd, J = 18.0, 11.3, 0.9 Hz, 1H), 6.49 (s, 1H), 5.98 (td, J = 4.7, 1.6 Hz, 1H) 5.39 (dt, J = 18.0, 0.9 Hz, 1H), 5.13 (dt, J = 11.3, 1.4 Hz, 1H), 4.48 (d, J = 1.1 Hz, 2H), 2.80 (t, J = 7.7 Hz, 2H), 2.42 – 2.37 (m, 2H) 2.20 (bs, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.7, 135.9, 134.6, 133.4, 132.9, 129.8, 128.2, 127.4, 127.1, 126.4, 124.2, 114.2, 64.0, 27.8, 23.2; IR (neat) υ = 3606, 3448, 3054, 2987, 2306, 1422 cm^{-1}; MS (EI) *m/z* (relative intensity) 212 (M^+, 55), 181 (100), 165 (53), 141 (35), 128 (26); HRMS (EI) *m/z* calcd for $C_{15}H_{16}O$ (M^+) 212.1201, found 212.1199.

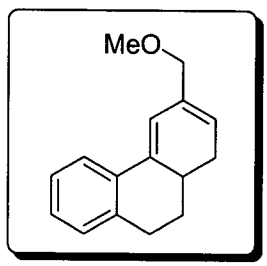
4-[2-(Methoxymethyl)buta-1,3-dien-1-yl]-1,2-dihydronaphthalene (150)



triene **139** (160 mg, 0.754 mmol) and methyl iodide (0.24 mL, 3.95 mmol) were added to a suspension of NaH (60 mg, 60% suspension in mineral oil, 1.58 mmol) in THF (20 mL) at rt. The solution stirred at rt for 16 h. Diluted the reaction with H_2O and the aqueous phase was extracted with Et_2O (3x). The combined Et_2O extracts were washed with H_2O (3x), brine, dried and concentrated. Flash chromatography (pet ether/Et_2O, 19:1) afforded methyl ether **150** as a colourless oil (155 mg, 87%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.14 (s, 4H), 6.70 (ddd, J = 17.9, 11.4, 0.9 Hz, 1H), 6.41 (s, 1H), 5.98 (td, J = 5.7, 1.5 Hz, 1H), 5.39 (d, J = 17.8 Hz, 1H), 5.10 (dt, J = 11.2, 1.5 Hz, 1H), 2.79 (t, J = 6.7 Hz, 2H), 2.42-2.35 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.4, 135.1, 133.9, 133.4, 130.3, 130.2, 127.9, 127.5, 126.8, 124.7, 115.0, 74.4, 58.4, 28.3, 23.6; IR (neat) υ = 3161, 2936, 2865, 2814, 1468 cm^{-1}; MS (EI) *m/z* (relative intensity) 226 (M^+, 56), 196 (38), 181 (100), 165 (75), 141 (40), 115 (41); HRMS (EI) *m/z* calcd for $C_{16}H_{18}O$ (M^+) 226.13577, found 226.1394.

3-(Methoxymethyl)-1,9,10,10a-tetrahydrophenanthrene (151)

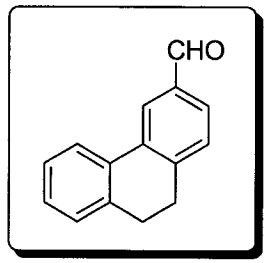


Methyl ether **150** (110 mg, 0.49 mmol) was dissolved in toluene (20 mL) and the solution refluxed for 16 h. Toluene was removed *in vacuo* and flash chromatography (pet ether/Et_2O, 29:1) afforded cyclohexadiene **151** as a yellow oil (83 mg, 76%).

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.77 (d, J = 9.0 Hz, 1H), 7.20-7.10 (m, 3H), 6.65 (d, J = 2.2 Hz, 1H), 5.86-5.90 (m, 1H), 3.99 (q, J = 11.5 Hz, 2H), 3.34 (s, 3H), 2.86-2.77 (m, 2H), 2.68-2.54 (m, 1H), 2.31 (dt, J = 16.8, 6.4 Hz, 1H), 2.11-1.98 (m, 2H), 1.58-1.45 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.3, 137.0, 134.8, 133.6, 129.5, 127.4, 126.5, 125.1, 123.7, 117.6, 75.4, 58.1, 36.5, 31.4, 31.0, 30.3; IR (neat) υ = 3155, 2936, 1803,

1377 cm^{-1}; MS (EI) *m/z* (relative intensity) 224 (M^+, 75), 193 (65), 179 (100), 165 (54), 152 (23); HRMS (EI) *m/z* calcd for $C_{16}H_{18}O$ (M^+) 226.1357, found 226.1352.

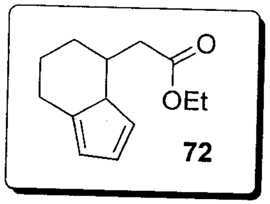
9,10-Dihydrophenanthrene-3-carbaldehyde (138)



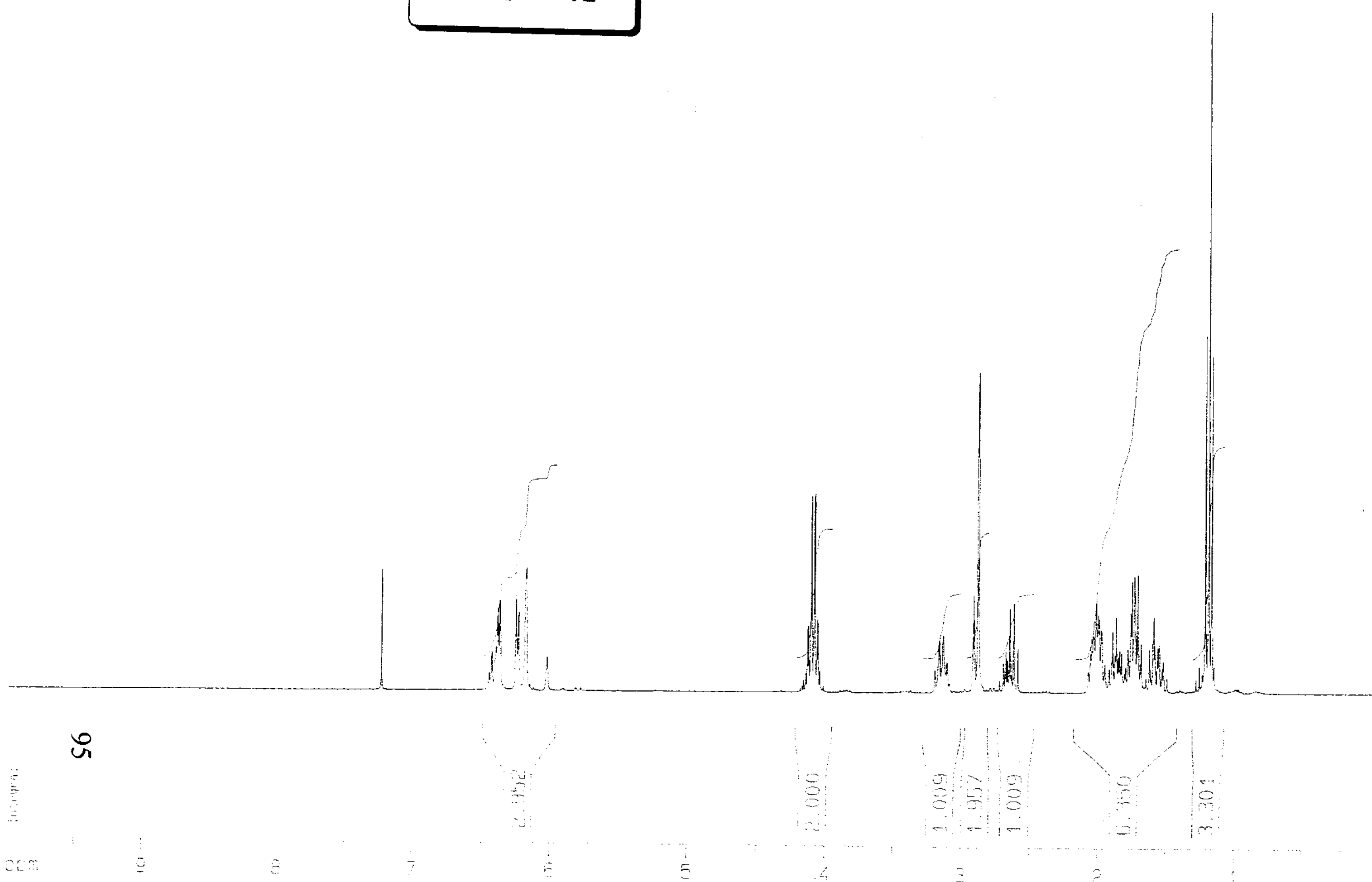
Manganese (II) oxide (115 mg, 1.33 mmol) was added to a solution of **151** (30 mg, 0.133 mmol) in toluene (5 mL) at rt. The mixture stirred at refluxed for 16 h. The mixture was filtered through a pad of silica gel washing with CH_2Cl_2. The filtrate was concentrated. Chromatography (pet ether/Et_2O, 19:1) afforded aldehyde **138** as a colourless oil (22 mg, 80%).

^1H NMR (500 MHz, $CDCl_3$) δ 10.01 (s, 1H), 8.23 (d, J = 1.5 Hz, 1H), 7.83 (d, J = 7.5 Hz, 1H), 7.72 (dd, J = 7.6, 1.6 Hz, 1H), 7.38 (d, J = 7.6 Hz, 1H), 7.34 (dt, J = 7.3, 1.8 Hz, 1H), 7.28-7.25 (m, 2H), 2.96-2.87 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 192.0, 144.4, 139.8, 137.0, 135.5, 135.3, 133.1, 128.8, 128.7, 128.1, 127.1, 124.7, 123.8, 29.3, 28.3; IR (neat) υ = 2930, 2835, 1698 cm^{-1}; MS (EI) *m/z* (relative intensity) 208 (M^+, 100), 179 (70), 162 (8), 89 (10); HRMS (EI) *m/z* calcd for $C_{15}H_{12}O$ (M^+) 226.0888, found 208.0887.

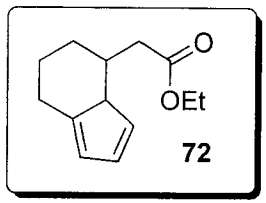
Appendix I



72




```
Current Data Parameters
NAME        NNbicyclo-clean
EXPNO                     1
PROCNO                    1

F2 - Acquisition Parameters
Date_            20050414
Time                14.39
INSTRUM             av300
PROBHD   5 mm QNP  1H/1
PULPROG              zg30
TD                  30720
SOLVENT             CDCl3
NS                     16
DS                      0
SWH              5081.301 Hz
FIDRES           0.165407 Hz
AQ              3.0228980 sec
RG                  456.1
DW                 98.400 usec
DE                   6.00 usec
TE                  300.0 K
D1             1.00000000 sec

============ CHANNEL f1 ============
NUC1                   1H
P1                  10.50 usec
PL1                 [illegible] dB
SFO1          300.131[illegible] MHz

F2 - Processing parameters
SI                  65536
SF            300.1300[illegible] MHz
WDW                    EM
SSB                     0
LB                   [illegible] Hz
GB                      0
PC                   [illegible]

1D NMR plot parameters
CX                   [illegible] cm
CY                   [illegible] cm
F1P                  [illegible] ppm
F1                   [illegible] Hz
F2P                  [illegible] ppm
F2                   [illegible] Hz
PPMCM                [illegible] ppm/cm
HZCM                 [illegible] Hz/cm
```



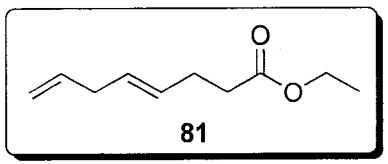
72

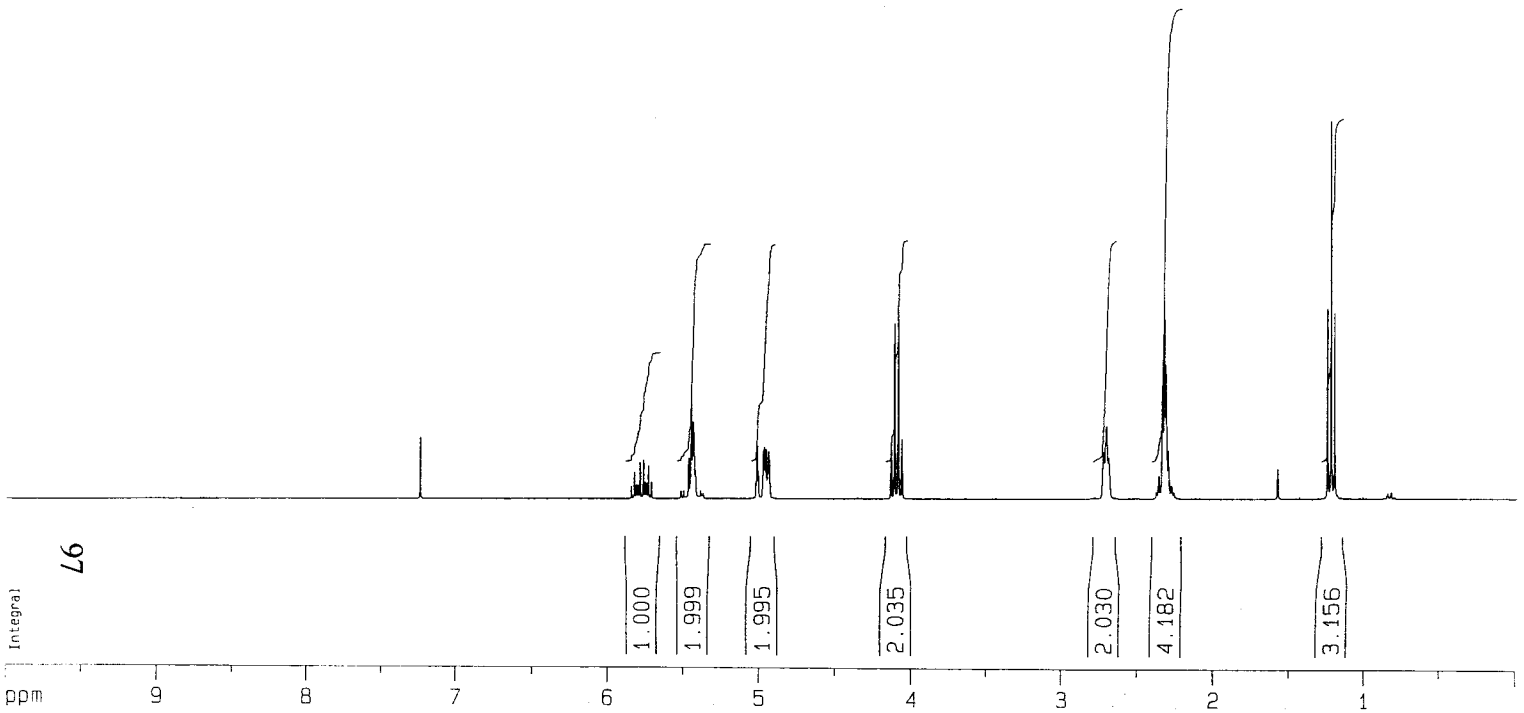
2000
1500
1000
500
0

96

150
100
50

ppm (f1)





Current Data Parameters

NAME	NN02-128
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20041214
Time	11.20
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	256
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

========== CHANNEL f1 ==========

NUC1	1H
P1	10.50 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

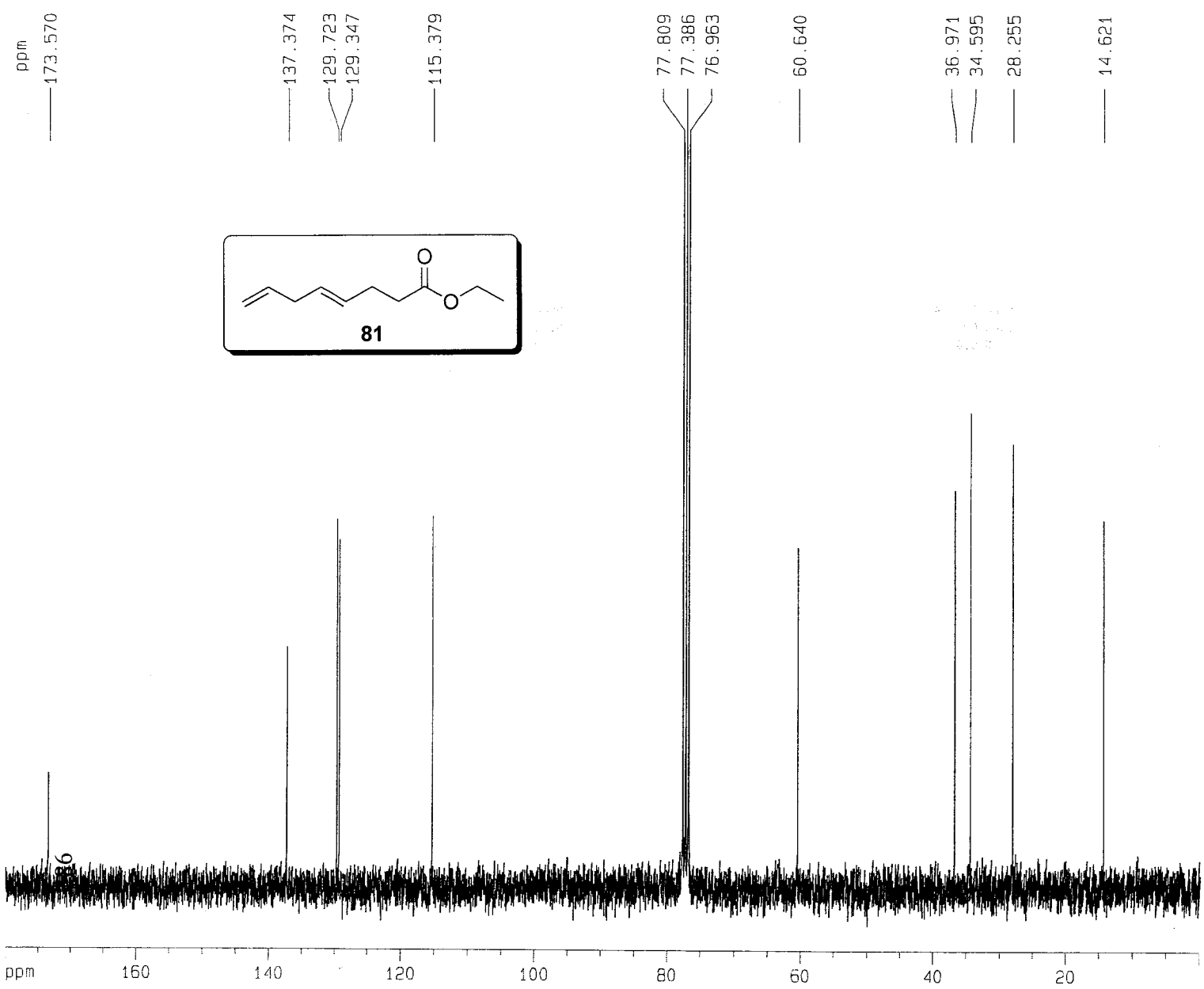
F2 - Processing parameters

SI	65536
SF	300.1300000 MHz
WDW	EM
SSB	0
LB	0.10 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	20.00 cm
CY	5.00 cm
F1P	10.000 ppm
F1	3001.30 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	0.50000 ppm/cm
HZCM	150.06500 Hz/cm

13C with proton decoupling



Current Data Parameters

NAME	NN02-128
EXPNO	3
PROCNO	1

F2 - Acquisition Parameters

Date_	20041214
Time	11.23
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zgpg30
TD	32768
SOLVENT	CDCl3
NS	189
DS	0
SWH	17985.611 Hz
FIDRES	0.548877 Hz
AQ	0.9110004 sec
RG	6502
DW	27.800 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec
d11	0.03000000 sec
d12	0.00002000 sec

========== CHANNEL f1 ==========

NUC1	13C
P1	5.00 usec
PL1	-6.00 dB
SFO1	75.4752653 MHz

========== CHANNEL f2 ==========

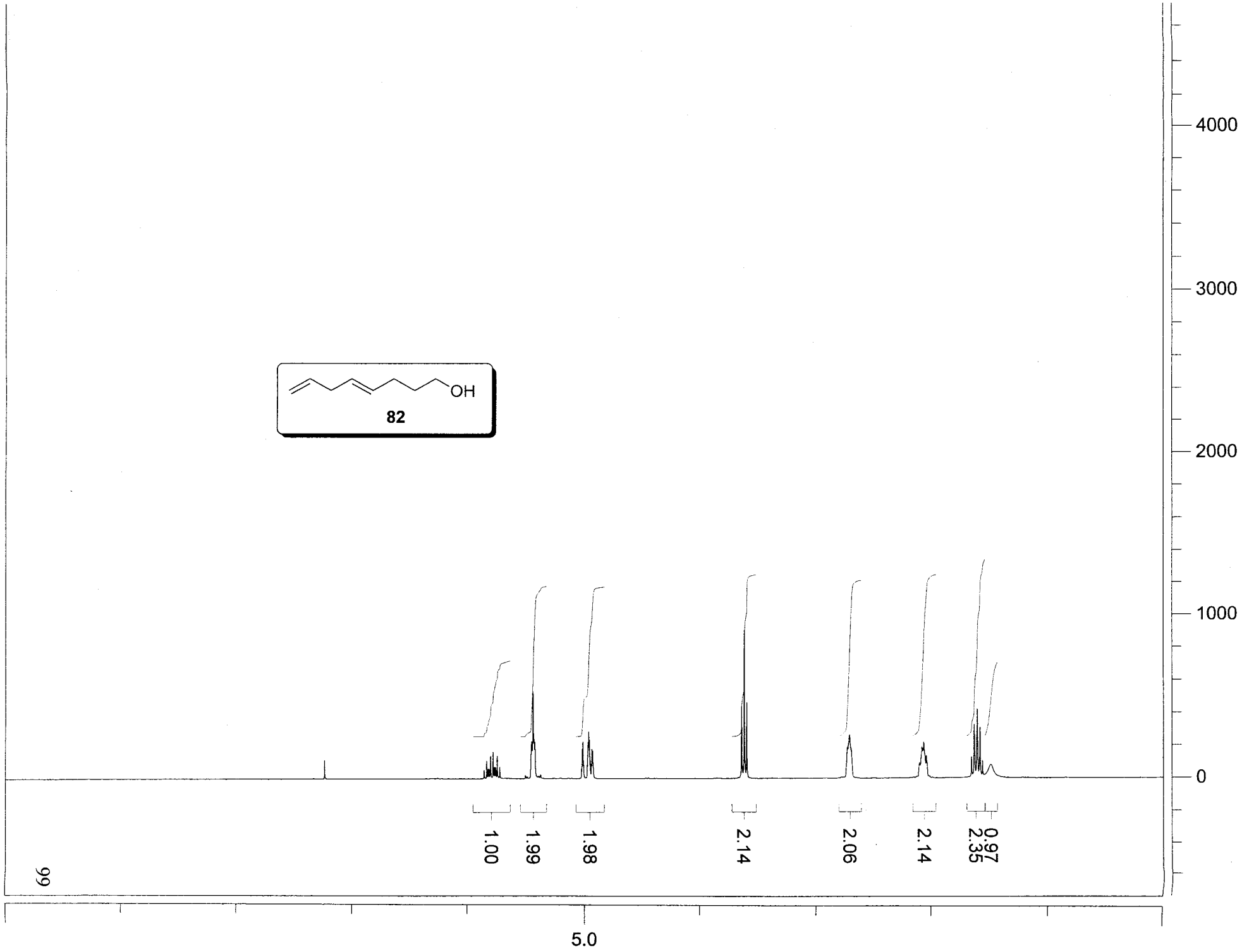
CPDPRG2	waltz16
NUC2	1H
PCPD2	70.00 usec
PL2	-3.00 dB
PL12	13.48 dB
PL13	15.63 dB
SFO2	300.1314860 MHz

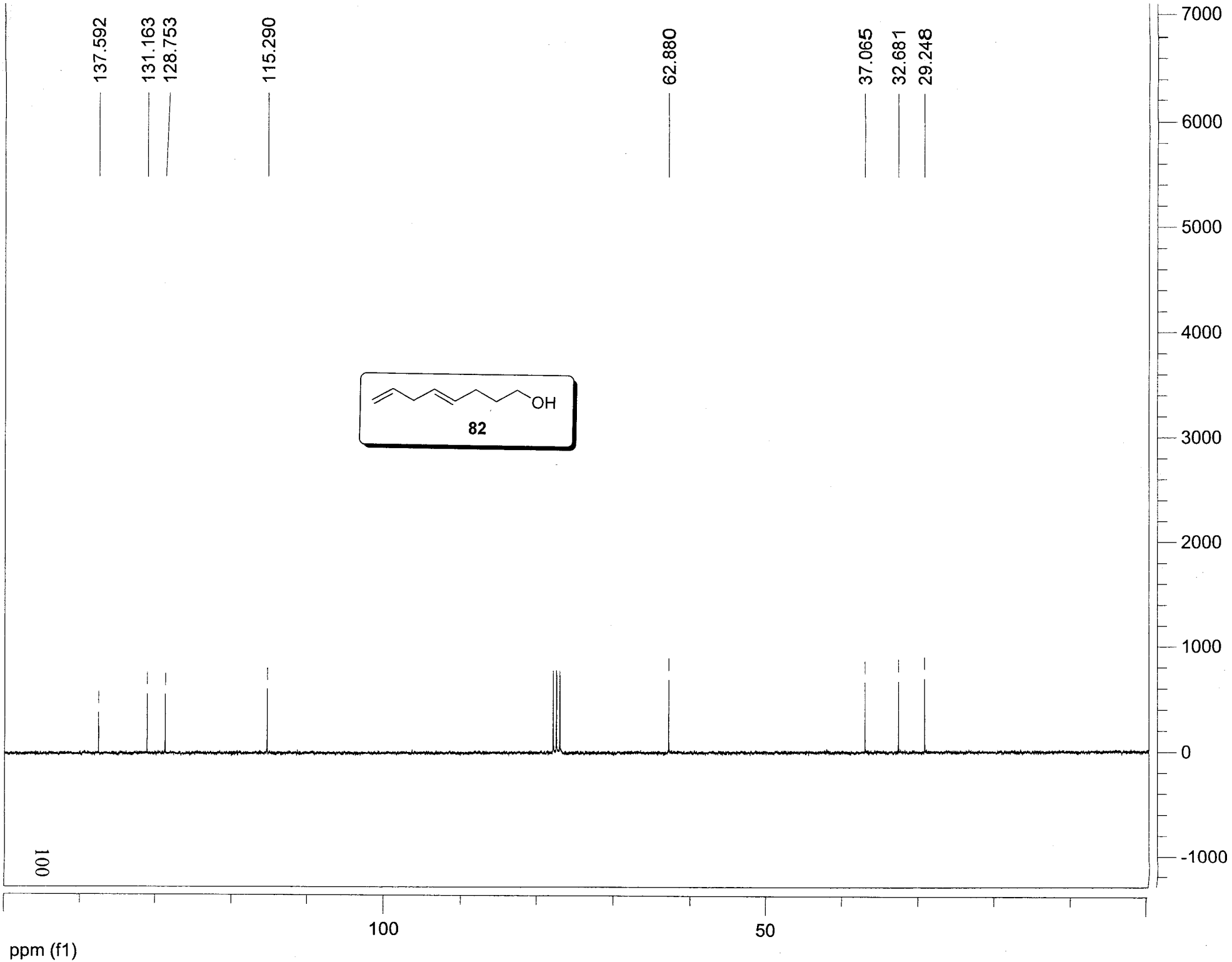
F2 - Processing parameters

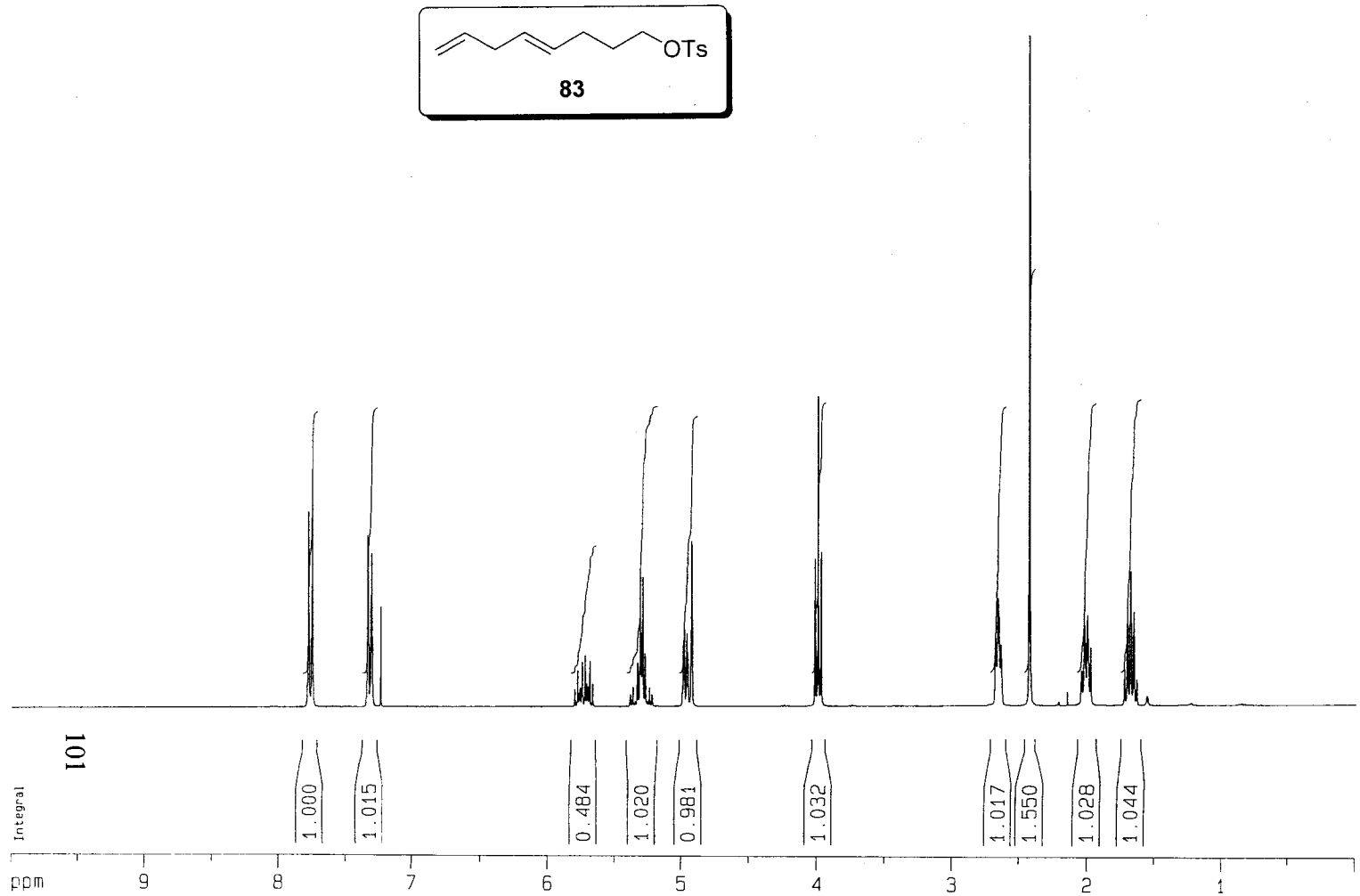
SI	65536
SF	75.4677190 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

1D NMR plot parameters

CX	20.00 cm
CY	8.00 cm
F1P	180.000 ppm
F1	13584.19 Hz
F2P	-0.000 ppm
F2	-0.00 Hz
PPMCM	9.00000 ppm/cm
HZCM	679.20959 Hz/cm


OH
82
4000
3000
2000
1000
0
1.00
1.99
1.98
2.14
2.06
2.14
0.97
2.35
99
5.0
ppm (f1)


137.592
131.163
128.753
115.290
62.880
37.065
32.681
29.248
OH
82
7000
6000
5000
4000
3000
2000
1000
0
-1000
100
100
50
ppm (f1)



Current Data Parameters

NAME	NN02-112
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20041023
Time	18.56
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	228.1
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

========== CHANNEL f1 ==========

NUC1	1H
P1	10.50 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

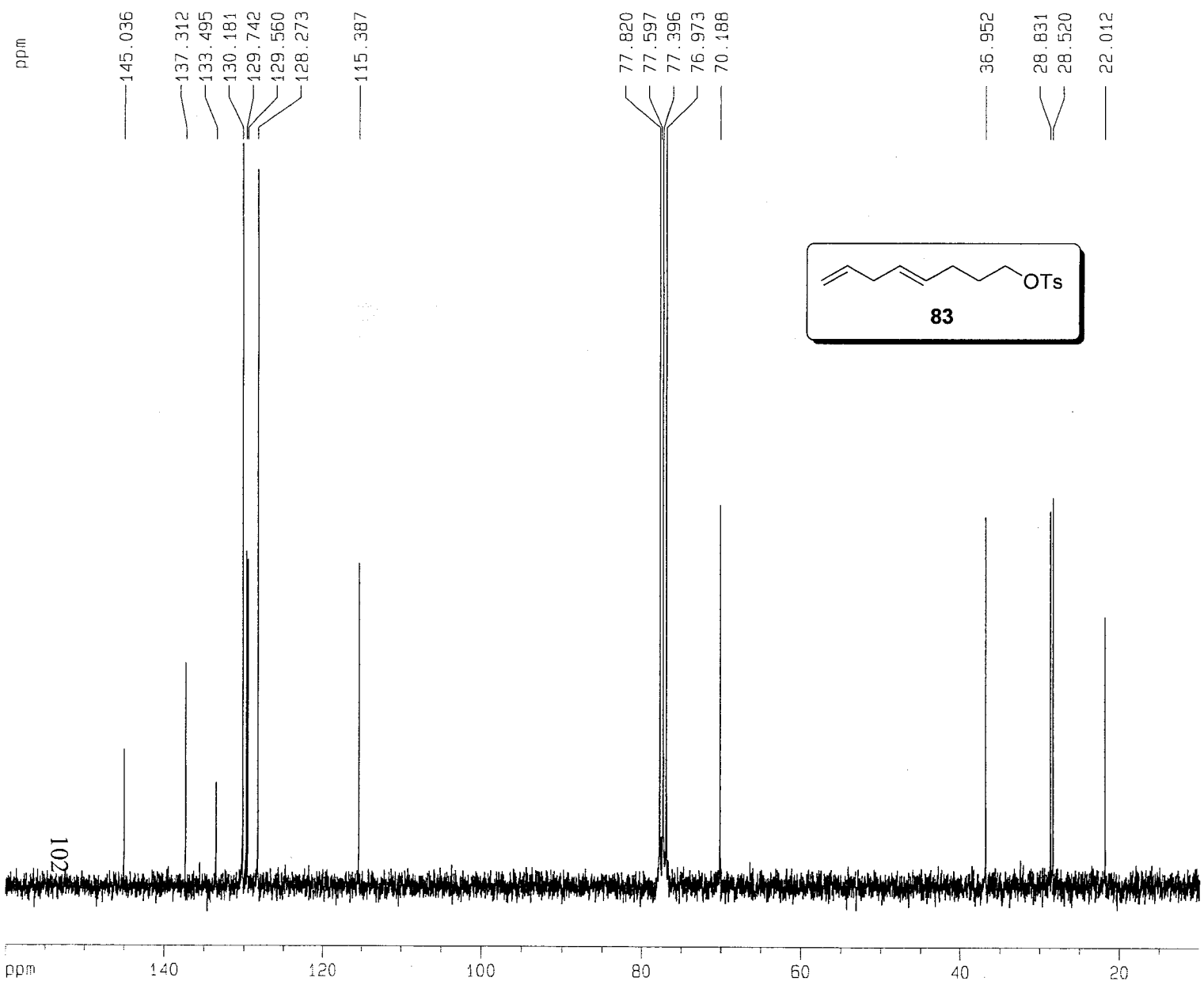
F2 - Processing parameters

SI	65536
SF	300.1300000 MHz
WDW	EM
SSB	0
LB	0.10 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	20.00 cm
CY	10.00 cm
F1P	10.000 ppm
F1	3001.30 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	0.50000 ppm/cm
HZCM	150.06500 Hz/cm

13C with proton decoupling



Current Data Parameters

NAME	NN02-112
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20041023
Time	19.07
INSTRUM	av300
PROBHD	5 mm GNP 1H/1
PULPROG	zgpg30
TD	32768
SOLVENT	CDCl3
NS	366
DS	0
SWH	17985.611 Hz
FIDRES	0.548877 Hz
AQ	0.9110004 sec
RG	3649.1
DW	27.800 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec
d11	0.03000000 sec
d12	0.00002000 sec

========== CHANNEL f1 ==========

NUC1	13C
P1	5.00 usec
PL1	-6.00 dB
SF01	75.4752653 MHz

========== CHANNEL f2 ==========

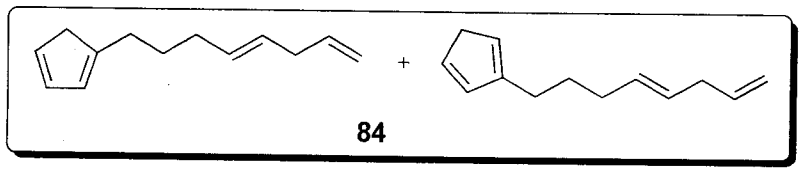
CPDPRG2	waltz16
NUC2	1H
PCPD2	70.00 usec
PL2	-3.00 dB
PL12	13.48 dB
PL13	15.63 dB
SF02	300.1314860 MHz

F2 - Processing parameters

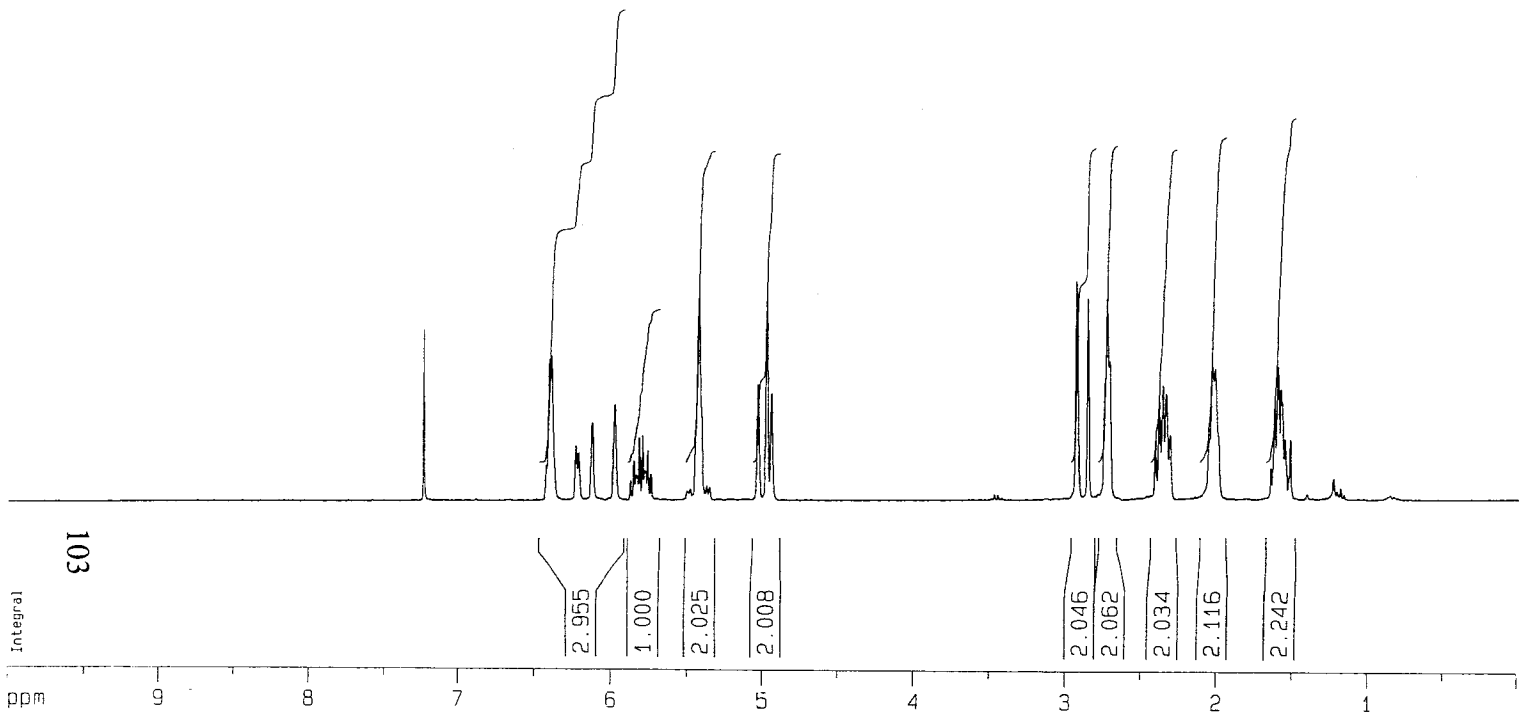
SI	65536
SF	75.4677190 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

1D NMR plot parameters

CX	20.00 cm
CY	12.50 cm
F1P	160.000 ppm
F1	12074.83 Hz
F2P	10.000 ppm
F2	754.68 Hz
PPMCM	7.50000 ppm/cm
HZCM	566.00787 Hz/cm



84



Current Data Parameters

NAME	NN02-130
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20041201
Time	17.45
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	406.4
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

========== CHANNEL f1 ==========

NUC1	1H
P1	10.50 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

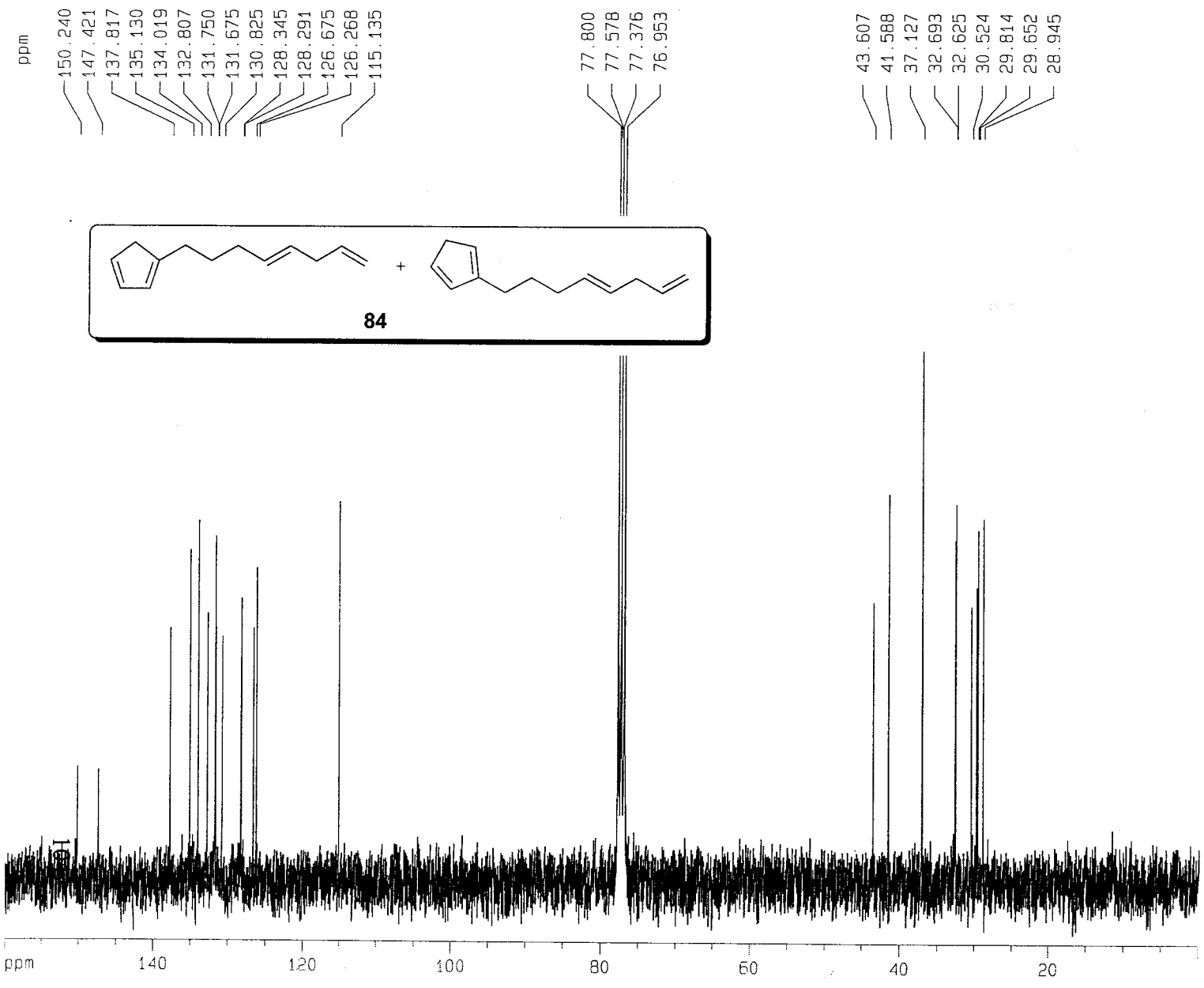
F2 - Processing parameters

SI	65536
SF	300.1300000 MHz
WDW	EM
SSB	0
LB	0.10 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	20.00 cm
CY	3.00 cm
F1P	10.000 ppm
F1	3001.30 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	0.50000 ppm/cm
HZCM	150.06500 Hz/cm

13C with proton decoupling



Current Data Parameters

NAME	NN02-130
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20041201
Time	17.51
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zgpg30
TD	32768
SOLVENT	CDCl3
NS	1024
DS	0
SWH	17985.611 Hz
FIDRES	0.548877 Hz
AQ	0.9110004 sec
RG	5792.6
DW	27.800 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec
d11	0.03000000 sec
d12	0.00002000 sec

========== CHANNEL f1 ==========

NUC1	13C
P1	5.00 usec
PL1	-6.00 dB
SFO1	75.4752653 MHz

========== CHANNEL f2 ==========

CPDPRG2	waltz16
NUC2	1H
PCPD2	70.00 usec
PL2	-3.00 dB
PL12	13.48 dB
PL13	15.63 dB
SFO2	300.1314860 MHz

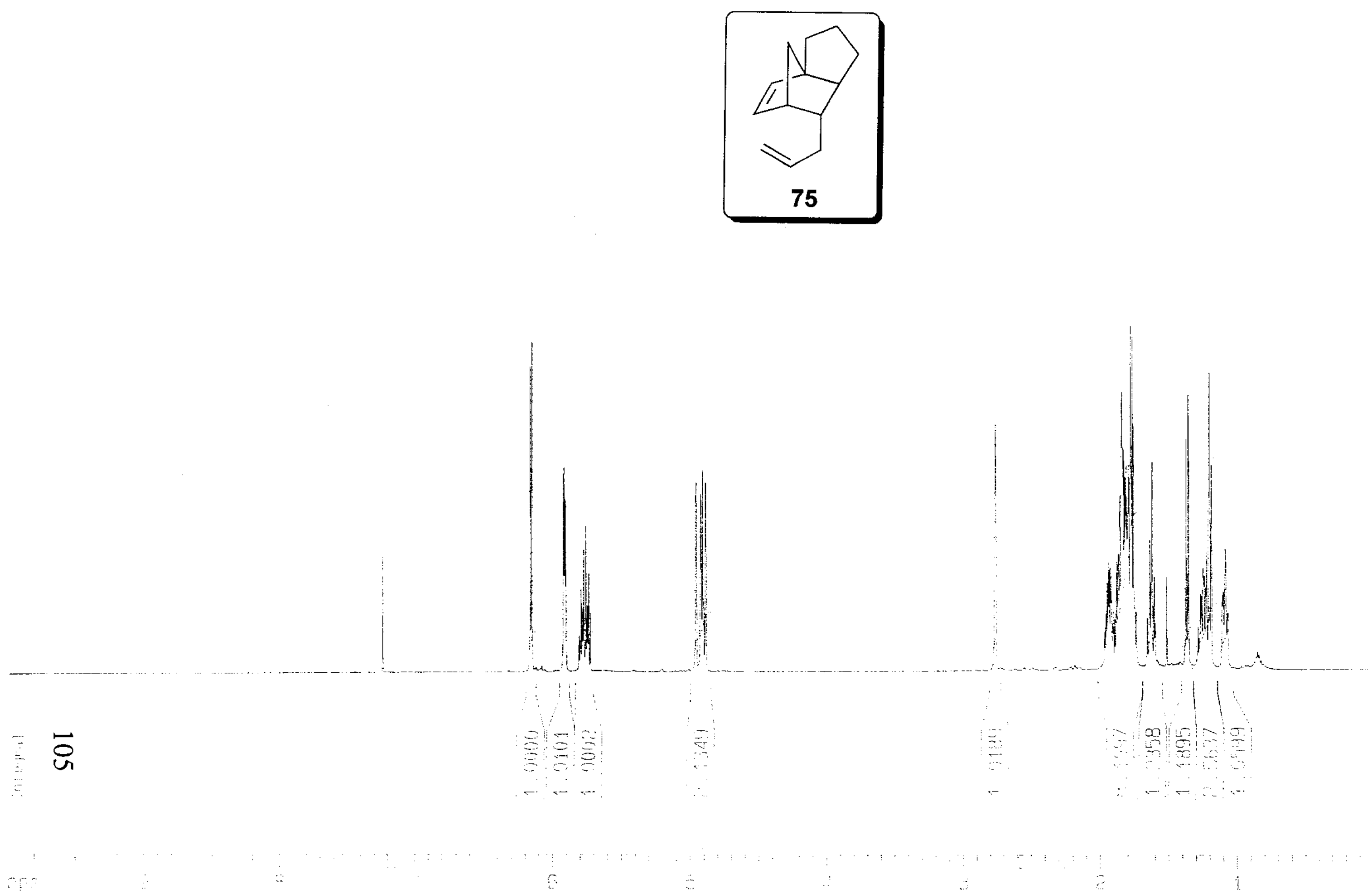
F2 - Processing parameters

SI	65536
SF	75.4677190 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

1D NMR plot parameters

CX	20.00 cm
CY	9.00 cm
F1P	160.000 ppm
F1	12074.83 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	8.00000 ppm/cm
HZCM	603.74176 Hz/cm

NNDA proton



Current Data Parameters
NAME nnda
EXPNO 1
PROCNO 1

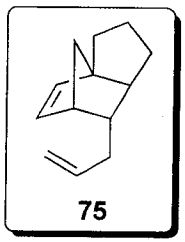
F2 - Acquisition Parameters
Date_ 20050427
Time 0.00
INSTRUM varian
PROBHD
PULPROG seqfil
TD 64000
SOLVENT solvent
NS 1
DS 0
SWH 8002.401 Hz
FIDRES 0.125038 Hz
AQ 3.9680500 sec
RG 4
DW 62.481 usec
DE 115.71 usec
TE 293.0 K

F2 - Processing parameters
SI 65536
SF 500.1144578 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters

Archive directory: /export/home/vnmr1/vnmrsys/data
Sample directory:
File: CARBON

Pulse Sequence: s2pul



75

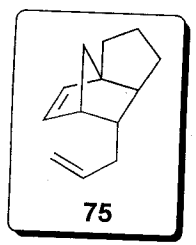
STANDARD PROTON PARAMETERS

Archive directory: /export/home/vnmr1/vnmrsys/data
Sample directory:
File: PROTON

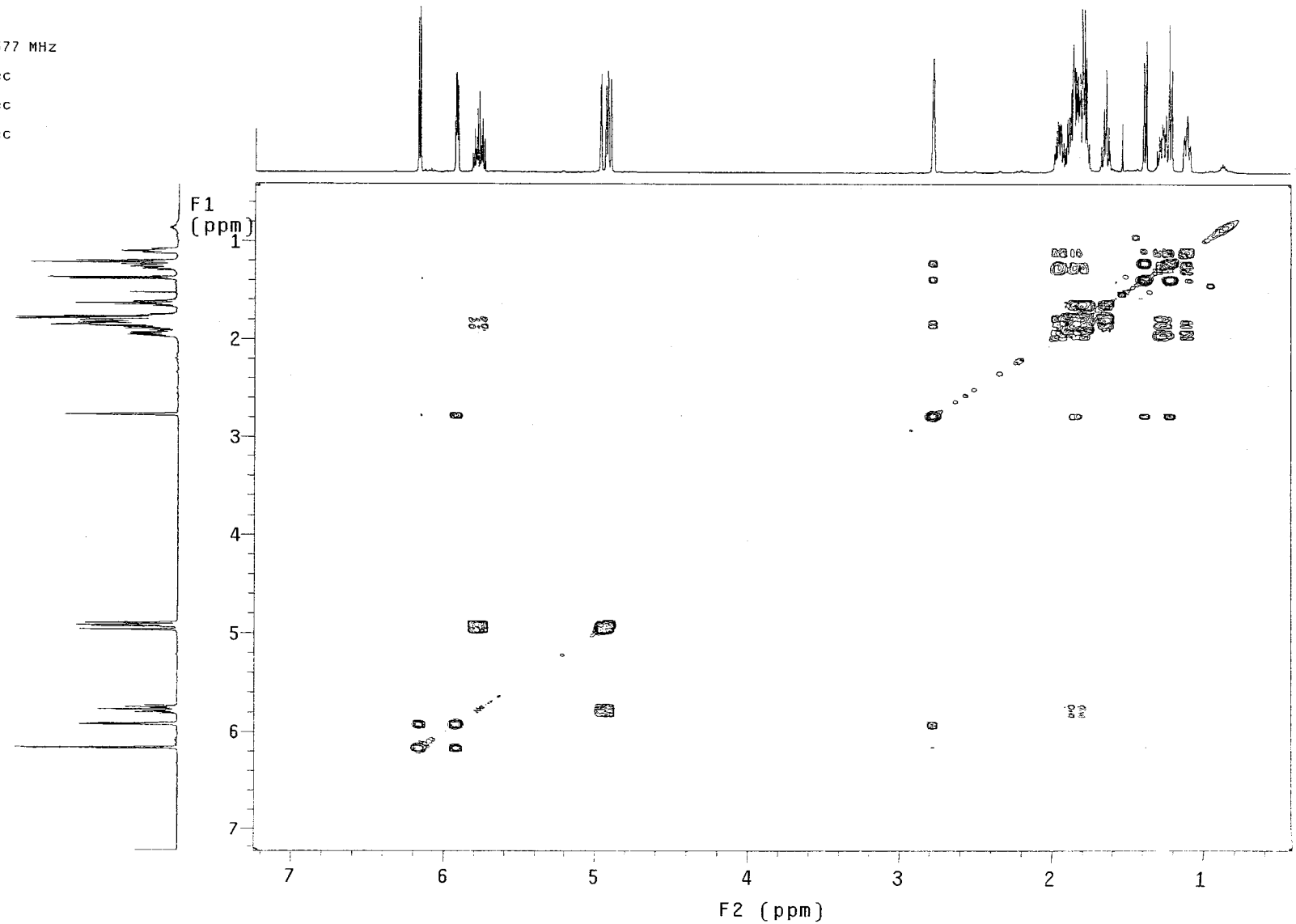
Pulse Sequence: gCOSY

Solvent: CDCl3
Temp. 20.0 C / 293.1 K
INOVA-500 "inova500"

Relax. delay 1.000 sec
Acq. time 0.150 sec
Width 3417.5 Hz
2D Width 3417.5 Hz
Single scan
256 increments
OBSERVE H1, 500.1739577 MHz
DATA PROCESSING
Sq. sine bell 0.075 sec
F1 DATA PROCESSING
Sq. sine bell 0.037 sec
FT size 1024 x 1024
Total time 5 min, 25 sec



75



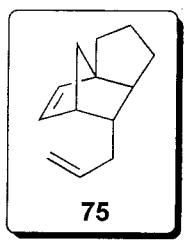
STANDARD PROTON PARAMETERS

Archive directory: /export/home/vnmr1/vnmrsys/data
Sample directory:
File: PROTON

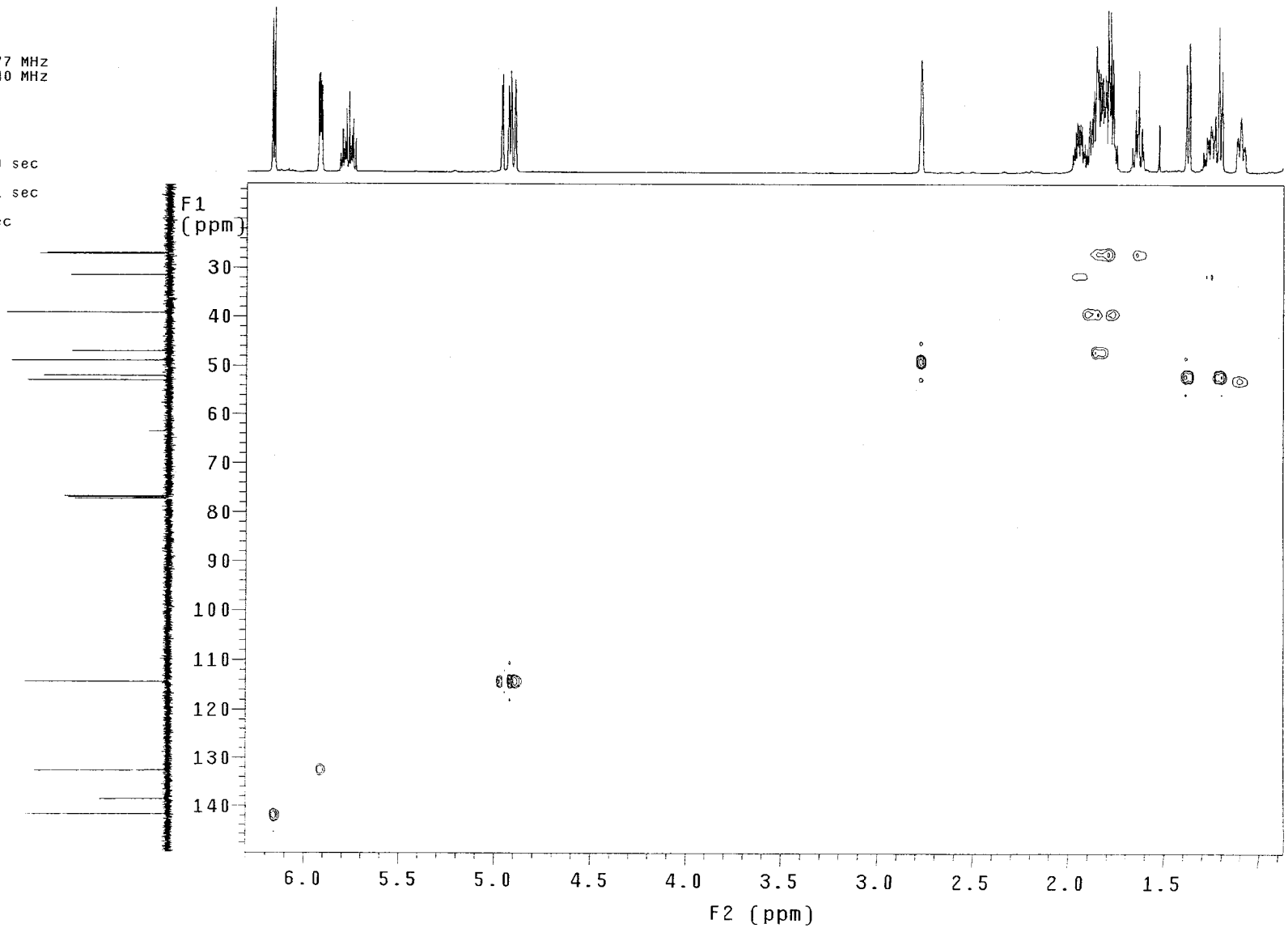
Pulse Sequence: gHMQC

Solvent: CDCl3
Temp. 20.0 C / 293.1 K
User: 1-14-87
INOVA-500 "inova500"

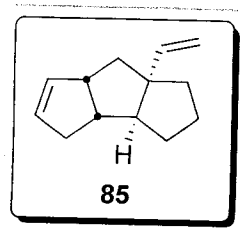
Relax. delay 1.000 sec
Acq. time 0.149 sec
Width 3438.5 Hz
2D Width 20207.1 Hz
4 repetitions
2 x 128 increments
OBSERVE H1, 500.1739577 MHz
DECOUPLE C13, 125.7788840 MHz
Power 44 dB
on during acquisition
off during delay
W40_tr7302 modulated
DATA PROCESSING
Gauss apodization 0.069 sec
F1 DATA PROCESSING
Gauss apodization 0.011 sec
FT size 1024 x 2048
Total time 21 min, 10 sec



75



1H NMR



Current Data Parameters

NAME	NN02-115-500
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20041029
Time	13.18
INSTRUM	AV500WB
PROBHD	5 mm TBO BB/1H
PULPROG	zg30
TD	65536
SOLVENT	Acetone
NS	1
DS	0
SWH	7440.476 Hz
FIDRES	0.113533 Hz
AQ	4.4040694 sec
RG	203.2
DW	67.200 usec
DE	6.00 usec
TE	300.0 K
D1	0.01000000 sec

======== CHANNEL f1 ========

NUC1	1H
P1	14.00 usec
PL1	0.00 dB
SFO1	500.1327766 MHz

F2 - Processing parameters

SI	65536
SF	500.1300049 MHz
WDW	EM
SSB	0
LB	0.00 Hz
GB	0
PC	1.00

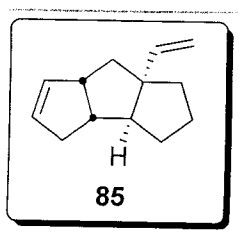
1D NMR plot parameters

CX	20.00 cm
CY	3.00 cm
F1P	10.000 ppm
F1	5001.30 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	0.50000 ppm/cm
HZCM	250.06500 Hz/cm

13C with proton decoupling

ppm

147.353
135.492
128.008
108.955
77.115
76.861
76.607
58.642
58.161
50.801
49.784
43.406
39.477
36.459
31.422
23.926



85

110

ppm 140 120 100 80 60 40 20

Current Data Parameters

NAME	NNO2-115-500
EXPNO	3
PROCNO	1

F2 - Acquisition Parameters

Date_	20041029
Time	13.23
INSTRUM	AV500WB
PROBHD	5 mm TBO BB/1H
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	349
DS	0
SWH	30030.029 Hz
FIDRES	0.458222 Hz
AQ	1.0912244 sec
RG	1824
DW	16.650 usec
DE	22.00 usec
TE	300.0 K
D1	1.00000000 sec
d11	0.03000000 sec
d12	0.00002000 sec

======== CHANNEL f1 ========

NUC1	13C
P1	8.00 usec
PL1	-0.20 dB
SF01	125.7703643 MHz

======== CHANNEL f2 ========

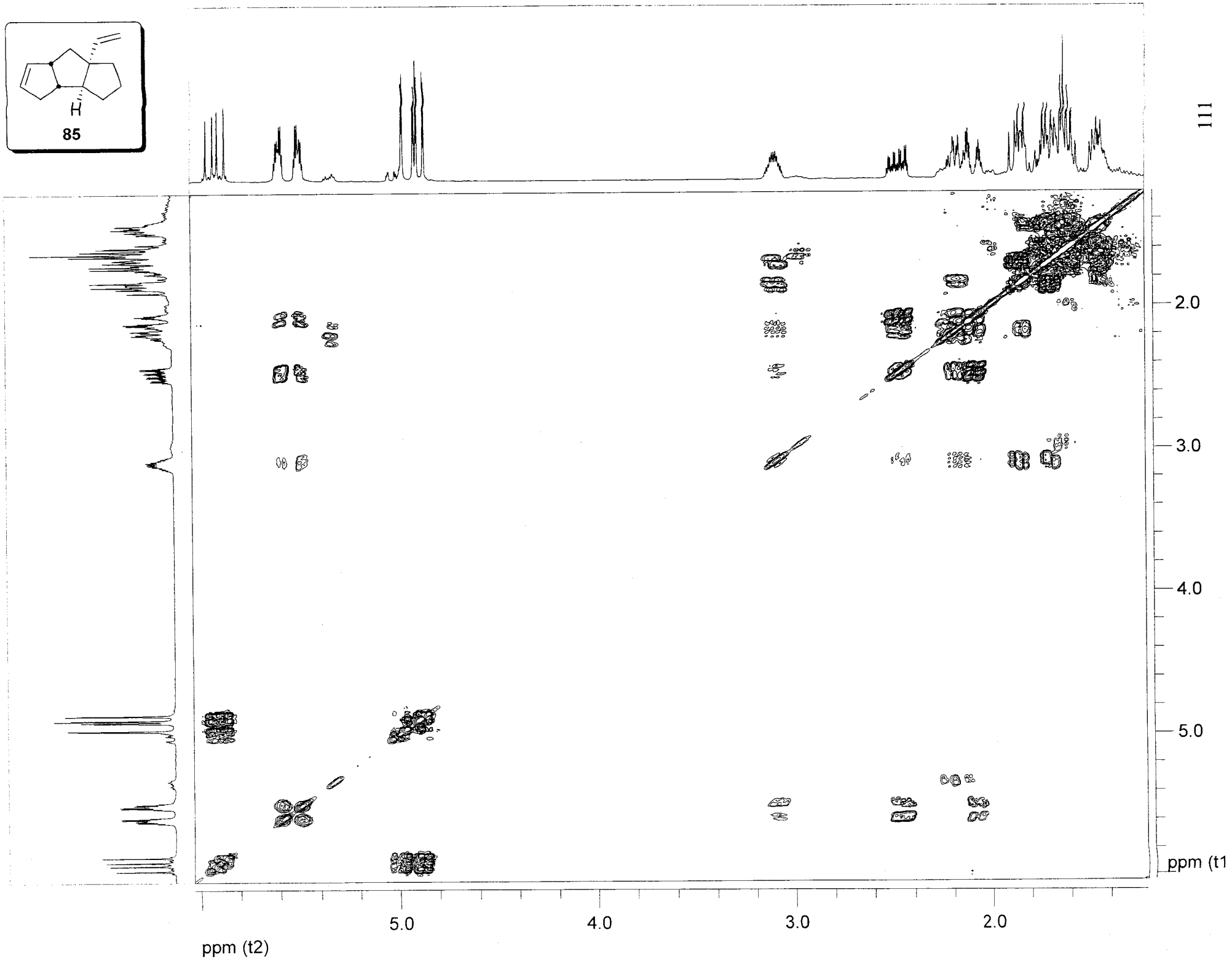
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	-0.20 dB
PL12	14.94 dB
PL13	14.90 dB
SF02	500.1320005 MHz

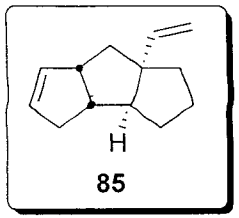
F2 - Processing parameters

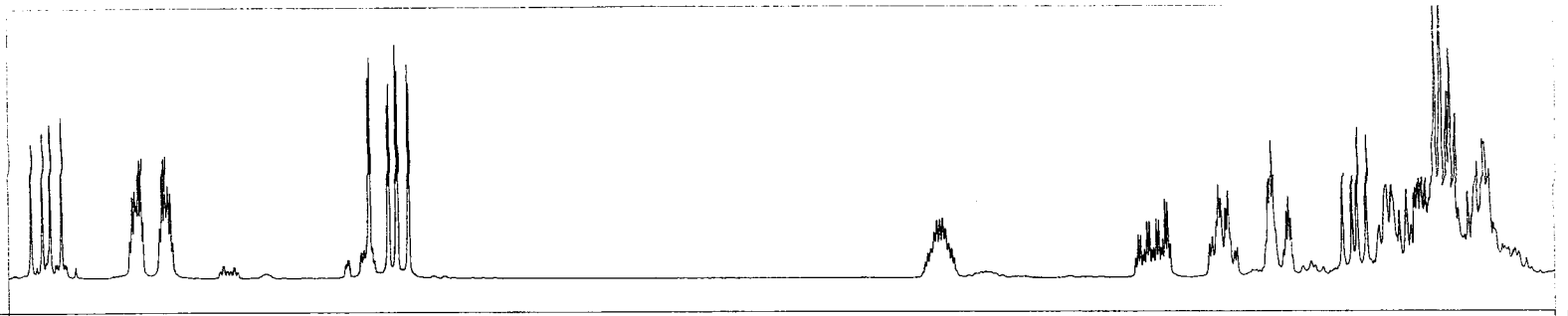
SI	32768
SF	125.7578051 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.00

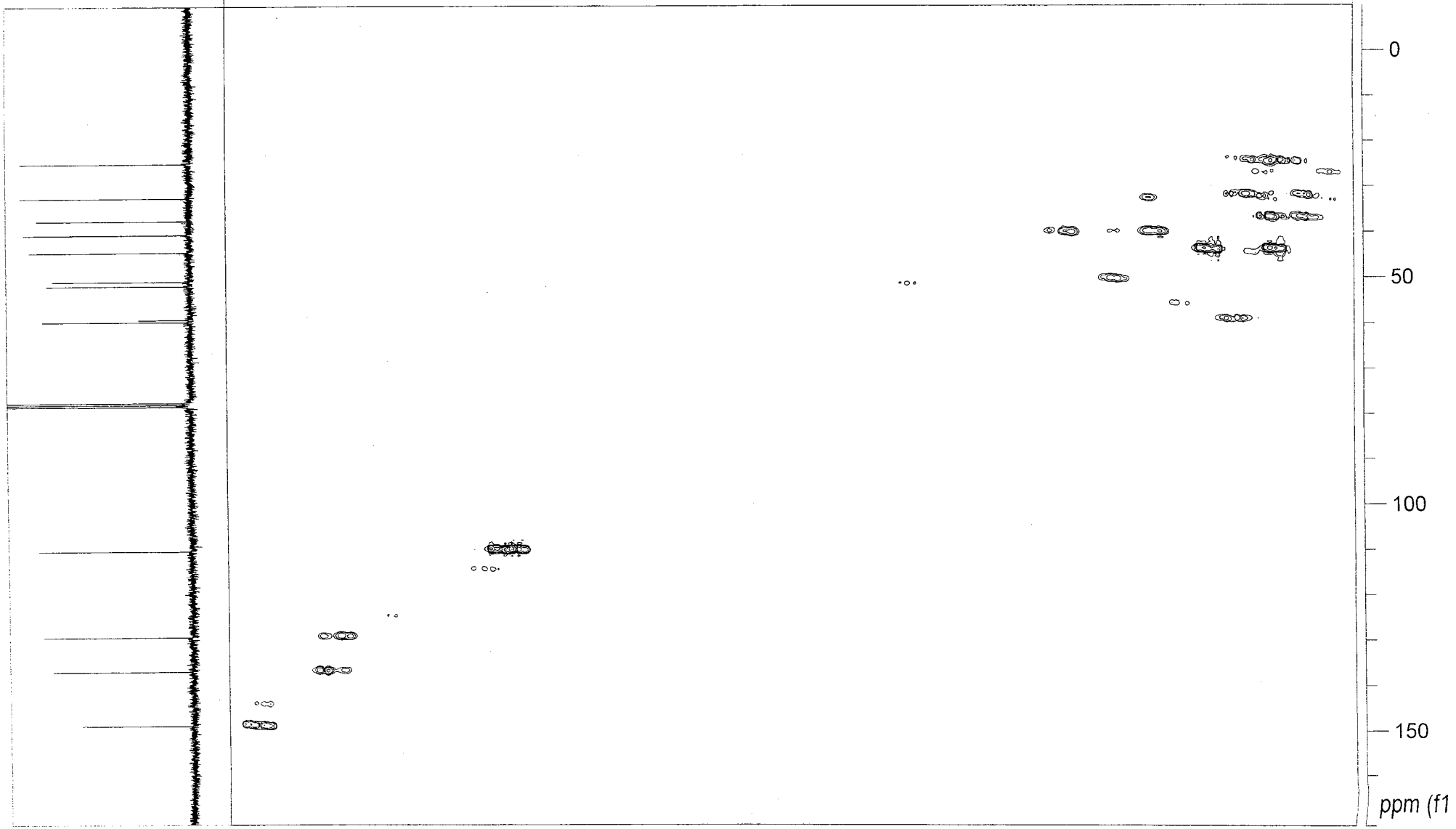
1D NMR plot parameters

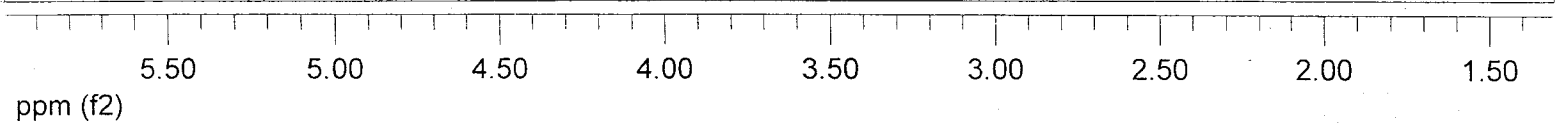
CX	20.00 cm
CY	10.00 cm
F1P	160.000 ppm
F1	20121.25 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	8.00000 ppm/cm
HZCM	1006.06244 Hz/cm

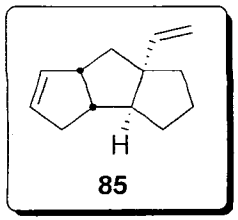

H
85
111
2.0
3.0
4.0
5.0
ppm (t1
5.0
4.0
3.0
2.0
ppm (t2)


H
85


112


0
50
100
150
ppm (f1


5.50
5.00
4.50
4.00
3.50
3.00
2.50
2.00
1.50
ppm (f2)


H

85

113
0
50
100
150
ppm (f1
5.50
5.00
4.50
4.00
3.50
3.00
2.50
2.00
1.50
ppm (f2)

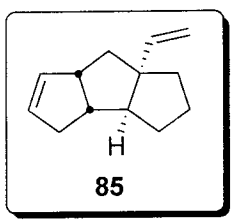
STANDARD PROTON PARAMETERS

Archive directory: /export/home/vnmr1/vnmrsys/data
Sample directory:

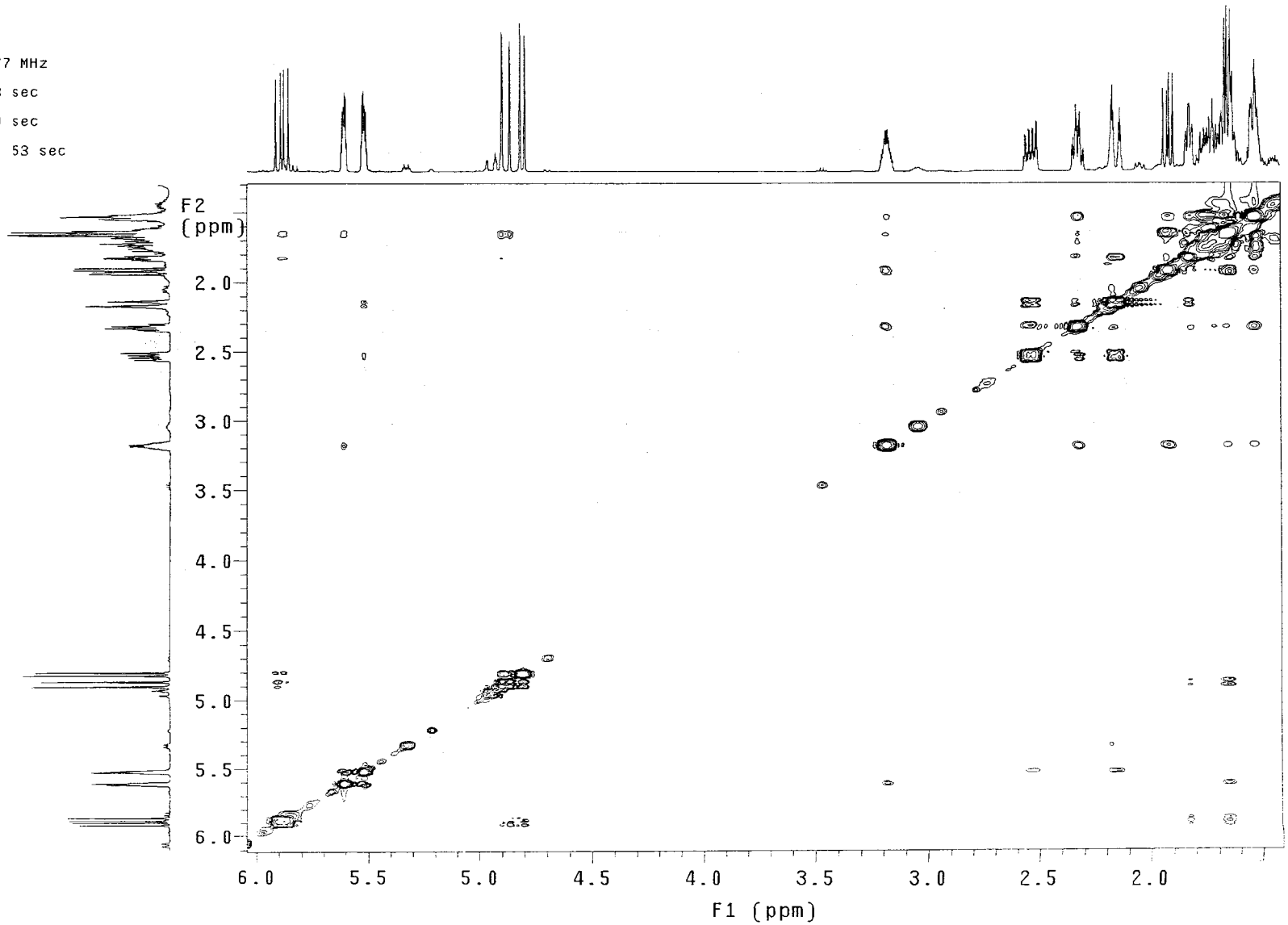
Pulse Sequence: NOESY

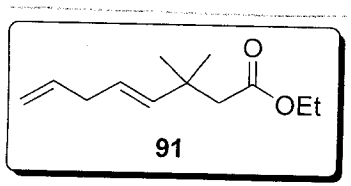
Solvent: CDCl3
Temp. 20.0 C / 293.1 K
File: NNnougan-noesy
INOVA-500 "inova500"

Relax. delay 1.000 sec
Mixing 2.600 sec
Acq. time 0.137 sec
Width 3732.9 Hz
2D Width 3732.9 Hz
16 repetitions
2 x 160 increments
OBSERVE H1, 500.1739577 MHz
DATA PROCESSING
Gauss apodization 0.063 sec
F1 DATA PROCESSING
Gauss apodization 0.079 sec
FT size 2048 x 2048
Total time 5 hr, 23 min, 53 sec



85





91

115

Current Data Parameters

NAME	NN02-56
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20041208
Time	13.27
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	181
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

========== CHANNEL f1 ==========

NUC1	1H
P1	10.50 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

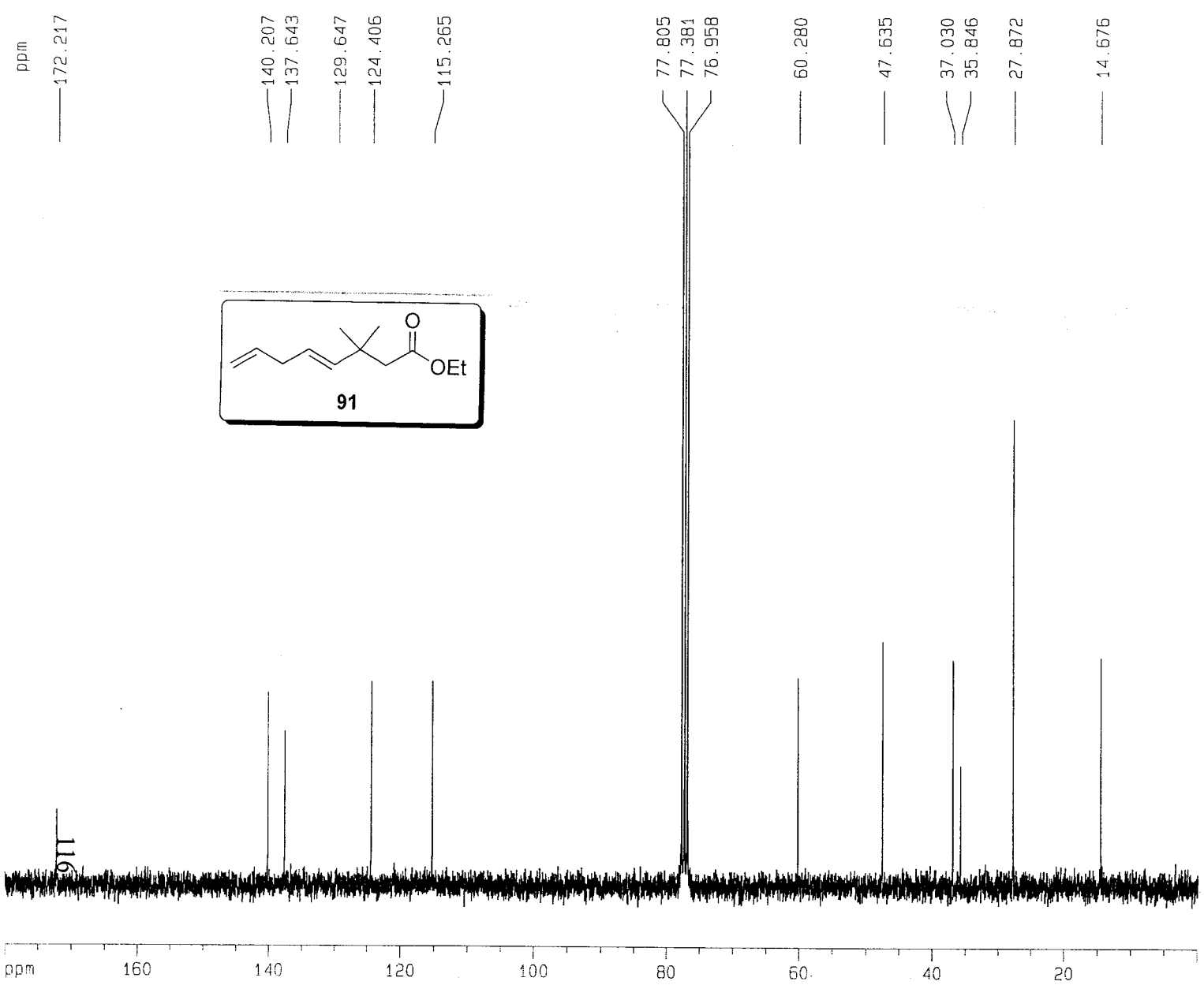
F2 - Processing parameters

SI	65536
SF	300.1300000 MHz
WDW	EM
SSB	0
LB	0.10 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	20.00 cm
CY	8.00 cm
F1P	10.000 ppm
F1	3001.30 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	0.50000 ppm/cm
HZCM	150.06500 Hz/cm

13C with proton decoupling



Current Data Parameters

NAME	NN02-137
EXPNO	8
PROCNO	1

F2 - Acquisition Parameters

Date_	20041205
Time	17.58
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zgpg30
TD	32768
SOLVENT	CDCl3
NS	299
DS	0
SWH	17985.611 Hz
FIDRES	0.548877 Hz
AQ	0.9110004 sec
RG	3649.1
DW	27.800 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec
d11	0.03000000 sec
d12	0.00002000 sec

========== CHANNEL f1 ==========

NUC1	13C
P1	5.00 usec
PL1	-6.00 dB
SFO1	75.4752653 MHz

========== CHANNEL f2 ==========

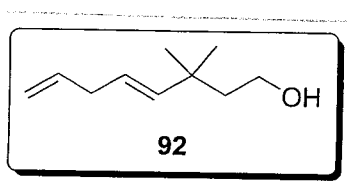
CPDPRG2	waltz16
NUC2	1H
PCPD2	70.00 usec
PL2	-3.00 dB
PL12	13.48 dB
PL13	15.63 dB
SFO2	300.1314860 MHz

F2 - Processing parameters

SI	65536
SF	75.4677190 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

1D NMR plot parameters

CX	20.00 cm
CY	8.00 cm
F1P	180.000 ppm
F1	13584.19 Hz
F2P	-0.000 ppm
F2	-0.00 Hz
PPMCM	9.00000 ppm/cm
HZCM	679.20959 Hz/cm



Current Data Parameters
NAME NN02-144
EXPNO 1
PROCNO 1

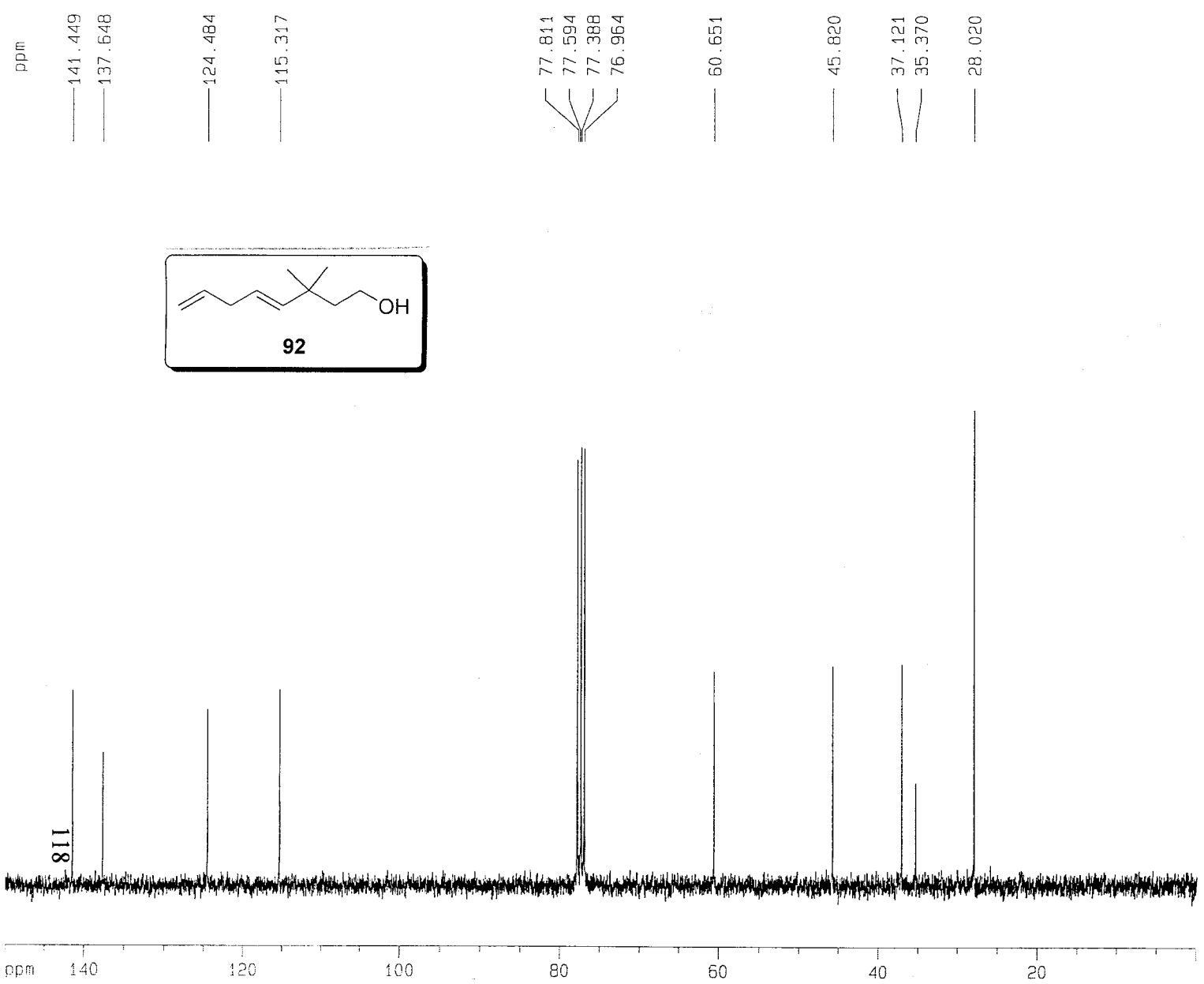
F2 - Acquisition Parameters
Date_ 20050112
Time 13.41
INSTRUM av300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 203.2
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

========== CHANNEL f1 ==========
NUC1 1H
P1 10.50 usec
PL1 -3.00 dB
SF01 300.1319477 MHz

F2 - Processing parameters
SI 65536
SF 300.1300000 MHz
WDW EM
SSB 0
LB 0.10 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 20.00 cm
CY 10.00 cm
F1P 10.000 ppm
F1 3001.30 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.50000 ppm/cm
HZCM 150.06500 Hz/cm

13C with proton decoupling



Current Data Parameters

NAME	NN02-141
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20041208
Time	13.14
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zgpg30
TD	32768
SOLVENT	CDCl3
NS	307
DS	0
SWH	17985.611 Hz
FIDRES	0.548877 Hz
AQ	0.9110004 sec
RG	3649.1
DW	27.800 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec
d11	0.03000000 sec
d12	0.00002000 sec

========== CHANNEL f1 ==========

NUC1	13C
P1	5.00 usec
PL1	-6.00 dB
SFO1	75.4752653 MHz

========== CHANNEL f2 ==========

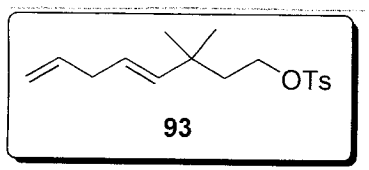
CPDPRG2	waltz16
NUC2	1H
PCPD2	70.00 usec
PL2	-3.00 dB
PL12	13.48 dB
PL13	15.63 dB
SFO2	300.1314860 MHz

F2 - Processing parameters

SI	65536
SF	75.4677190 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

1D NMR plot parameters

CX	20.00 cm
CY	8.00 cm
F1P	150.000 ppm
F1	11320.16 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	7.50000 ppm/cm
HZCM	566.00793 Hz/cm



93

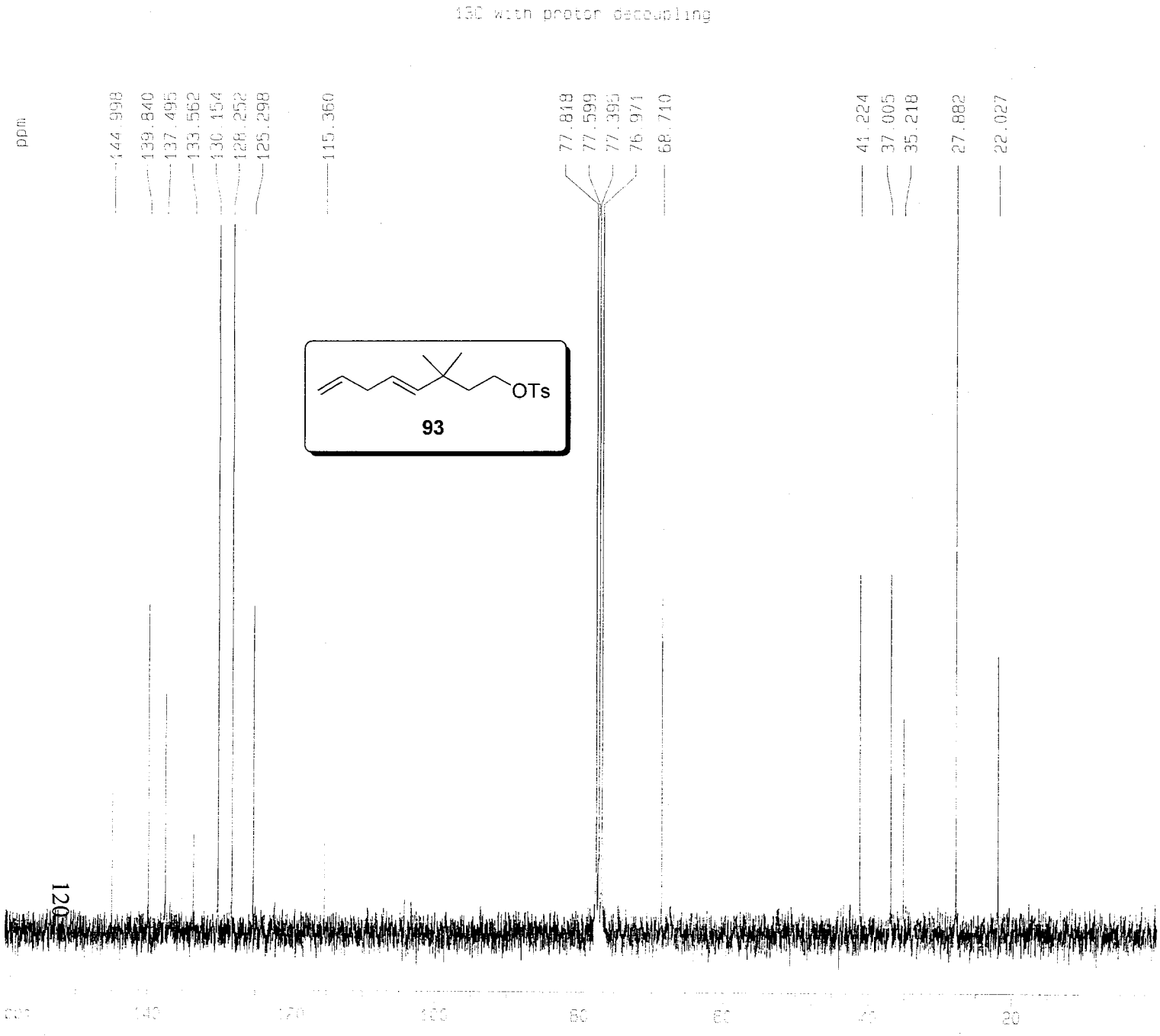
Current Data Parameters
NAME NNtosyl-methyl
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20050417
Time 15.02
INSTRUM av300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 256
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

========== CHANNEL f1 ==========
NUC1 1H
P1 10.50 usec
PL1 -3.00 dB
SFO1 300.1319477 MHz

F2 - Processing parameters
SI 65536
SF 300.1300000 MHz
WDW EM
SSB 0
LB 0.10 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 20.00 cm
CY 10.00 cm
F1P 10.000 ppm
F1 3001.30 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.50000 ppm/cm
HZCM 150.06500 Hz/cm



Current Data Parameters
NAME 10Nbenzylmethyl
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
Date_ 20050417
Time 15.06
INSTRUM av300
PROBHD 5 mm DUL 1H/1
PULPROG zgpg30
TD 32768
SOLVENT CDCl3
NS 464
DS 0
SWH 17985.611 Hz
FIDRES 0.548877 Hz
AQ 0.9110004 sec
RG 6502
DW 27.800 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec
d11 0.03000000 sec
d12 0.00002000 sec

CHANNEL f1
NUC1 13C
P1 5.00 usec
PL1 -6.00 dB
SFO1 75.4752653 MHz

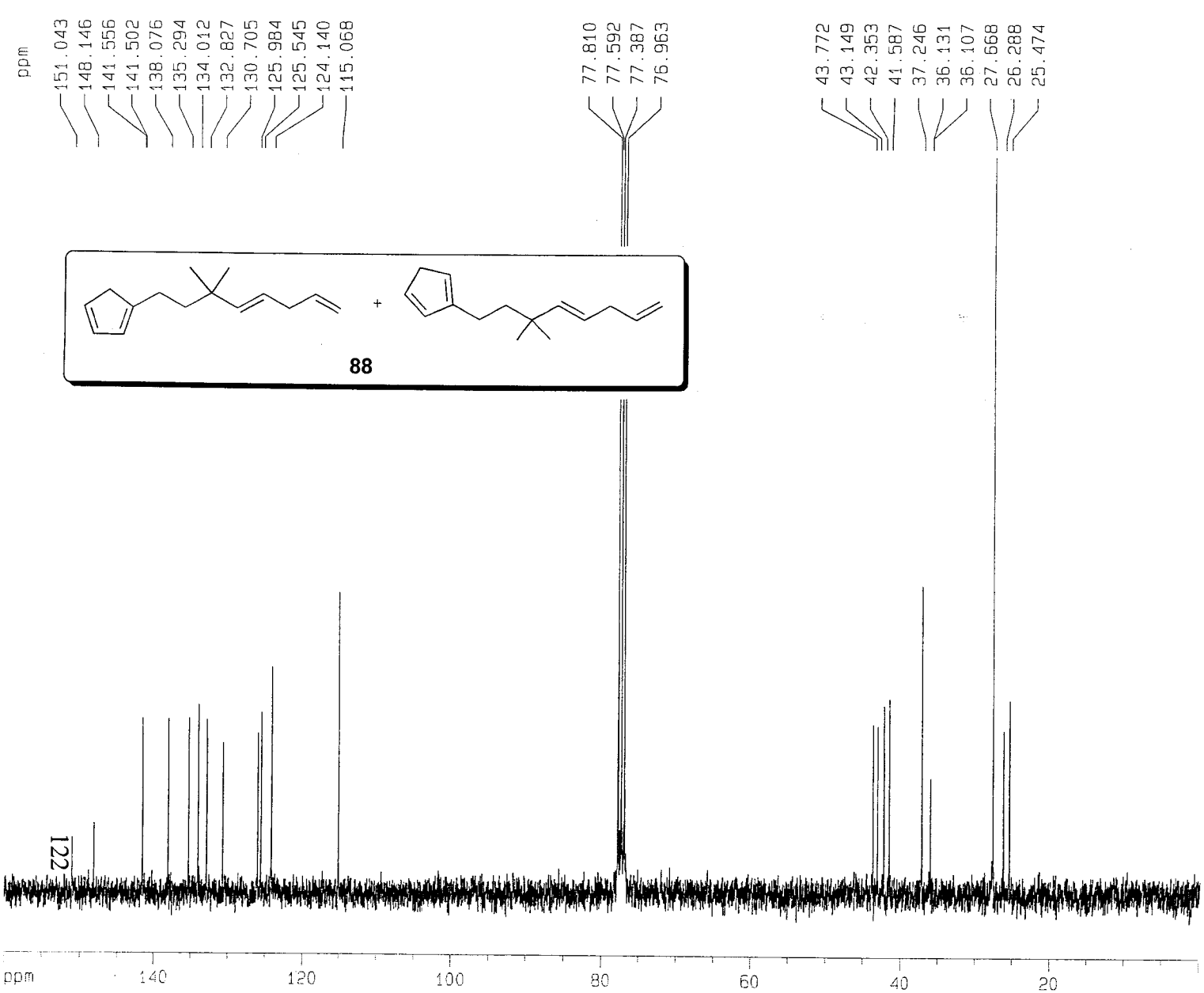
CHANNEL f2
CPDPRG2 waltz16
NUC2 1H
PCPD2 70.00 usec
PL2 -1.00 dB
PL12 13.08 dB
PL13 16.63 dB
SFO2 300.1312869 MHz

F2 - Processing parameters
SI 65536
SF 75.4677446 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

1D NMR plot parameters
CX 20.61 cm
CY 19.81 cm
F1P 190.000 ppm
F1 14374.83 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 9.00000 ppm/cm
HZCM 679.74176 Hz/cm

88

13C with proton decoupling



Current Data Parameters

NAME	NN02-158
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20050126
Time	22.32
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zgpg30
TD	32768
SOLVENT	CDCl3
NS	471
DS	0
SWH	17985.611 Hz
FIDRES	0.548877 Hz
AQ	0.9110004 sec
RG	8192
DW	27.800 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec
d11	0.03000000 sec
d12	0.00002000 sec

========== CHANNEL f1 ==========

NUC1	13C
P1	5.00 usec
PL1	-6.00 dB
SFO1	75.4752653 MHz

========== CHANNEL f2 ==========

CPDPRG2	waltz16
NUC2	1H
PCPD2	70.00 usec
PL2	-3.00 dB
PL12	13.48 dB
PL13	15.63 dB
SFO2	300.1314860 MHz

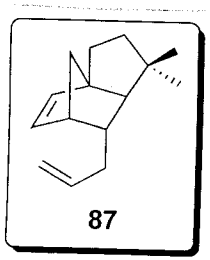
F2 - Processing parameters

SI	65536
SF	75.4677190 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

1D NMR plot parameters

CX	20.00 cm
CY	12.50 cm
F1P	160.000 ppm
F1	12074.83 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	8.00000 ppm/cm
HZCM	603.74176 Hz/cm

1H NMR



87

Current Data Parameters
NAME NNDA-methyl
EXPNO 1
PROCNO 1

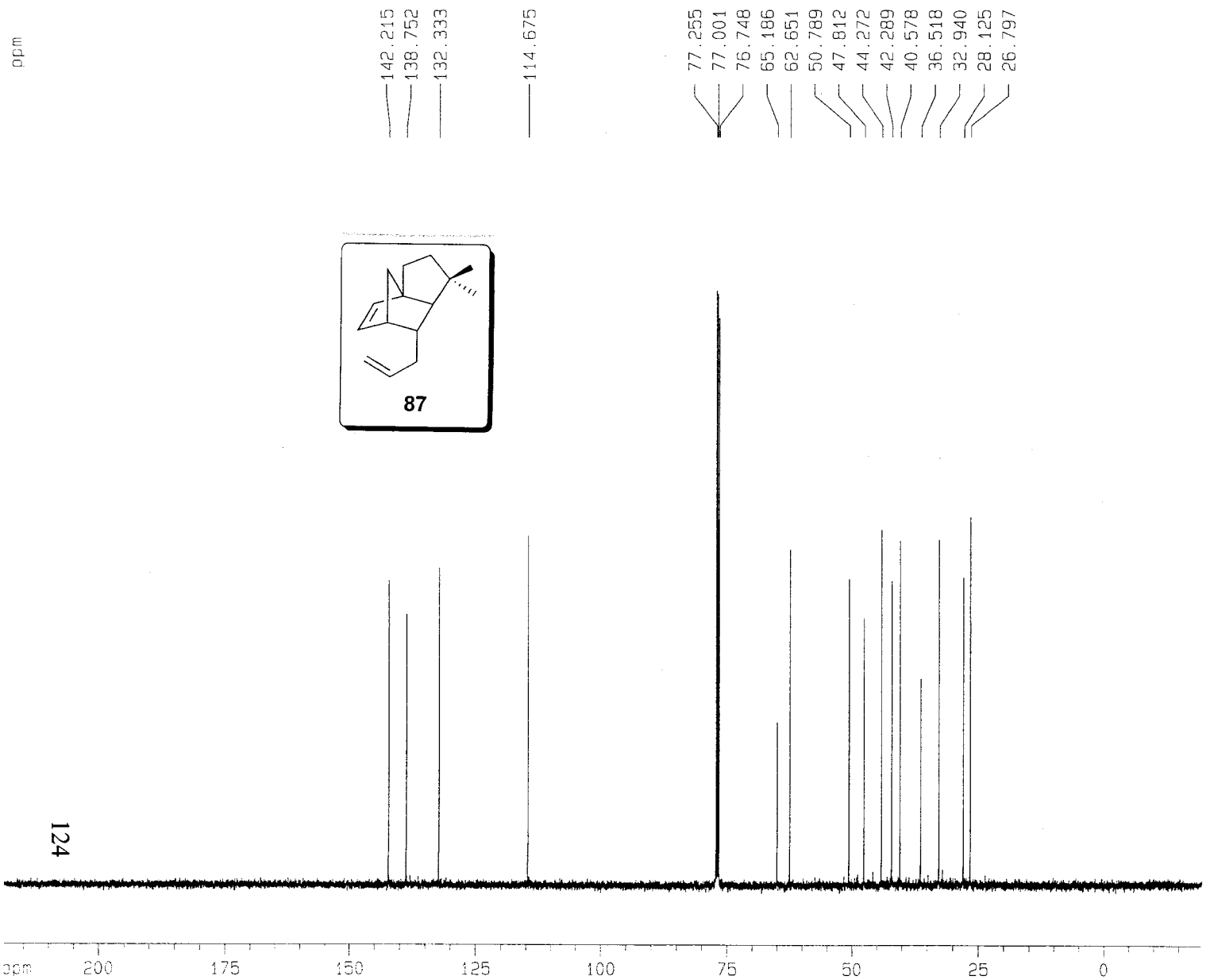
F2 - Acquisition Parameters
Date_ 20050502
Time 10.52
INSTRUM AV500WB
PROBHD 5 mm TBO BB/1H
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 0
SWH 7440.476 Hz
FIDRES 0.113533 Hz
AQ 4.4040694 sec
RG 114
DW 67.200 usec
DE 6.00 usec
TE 300.0 K
D1 0.01000000 sec

======== CHANNEL f1 ========
NUC1 1H
P1 14.00 usec
PL1 0.00 dB
SFO1 500.1327766 MHz

F2 - Processing parameters
SI 65536
SF 500.1300049 MHz
WDW EM
SSB 0
LB 0.00 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 20.00 cm
CY 30.00 cm
F1P 10.000 ppm
F1 5001.30 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.50000 ppm/cm
HZCM 250.06500 Hz/cm

NNDA-methyl 13C with proton decoupling



Current Data Parameters

NAME	NNDA-methyl
EXPNO	4
PROCNO	1

F2 - Acquisition Parameters

Date_	20050502
Time	12.00
INSTRUM	AV500WB
PROBHD	5 mm TBO BB/1H
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	512
DS	0
SWH	30030.029 Hz
FIDRES	0.458222 Hz
AQ	1.0912244 sec
RG	23170
DW	16.650 usec
DE	40.00 usec
TE	300.0 K
D1	1.00000000 sec
d11	0.03000000 sec
d12	0.00002000 sec

======== CHANNEL f1 ========

NUC1	13C
P1	8.00 usec
PL1	-0.20 dB
SFO1	125.7703643 MHz

======== CHANNEL f2 ========

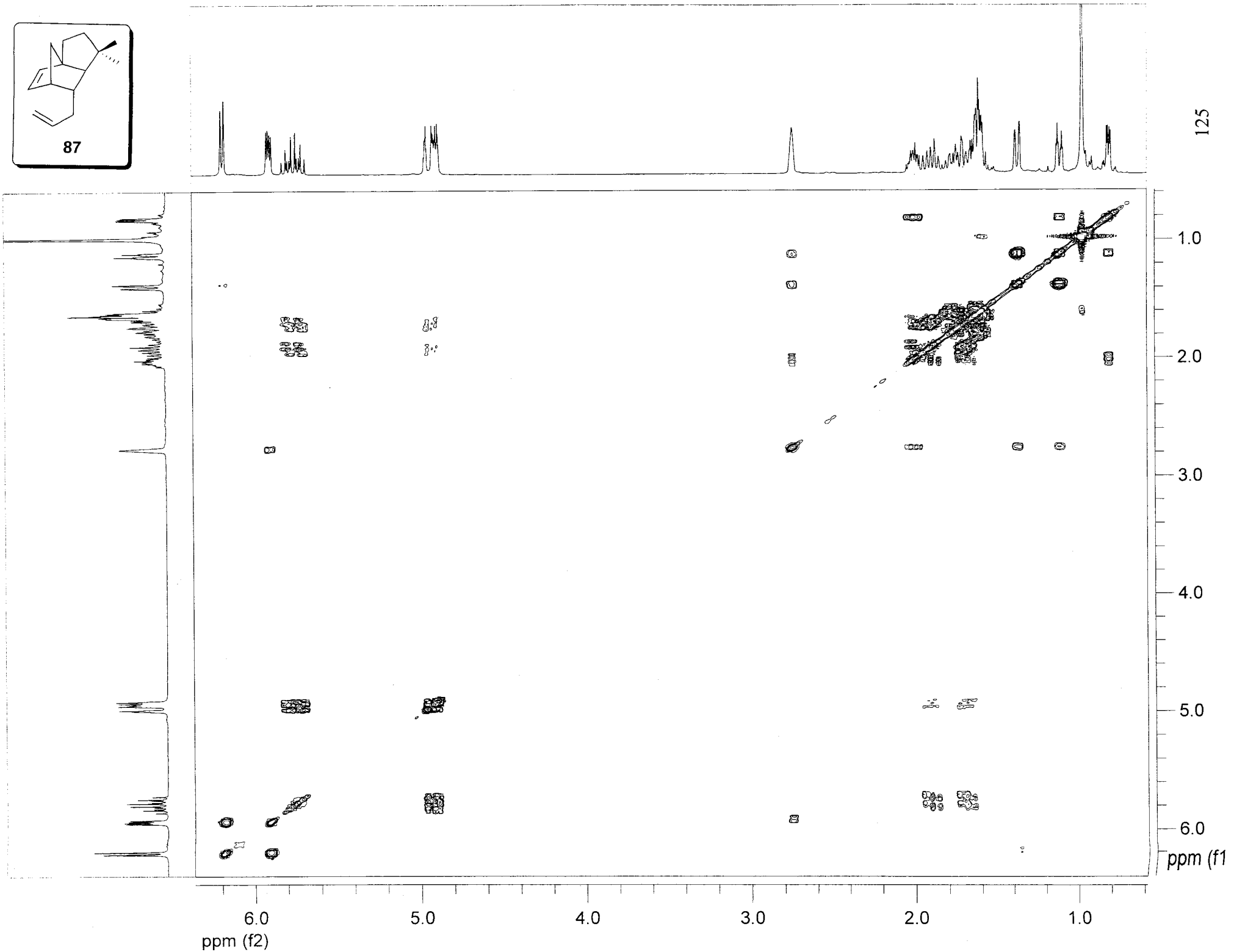
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	-0.20 dB
PL12	14.94 dB
PL13	14.90 dB
SFO2	500.1320005 MHz

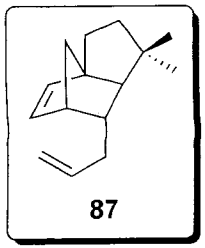
F2 - Processing parameters

SI	32768
SF	125.7577877 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.00

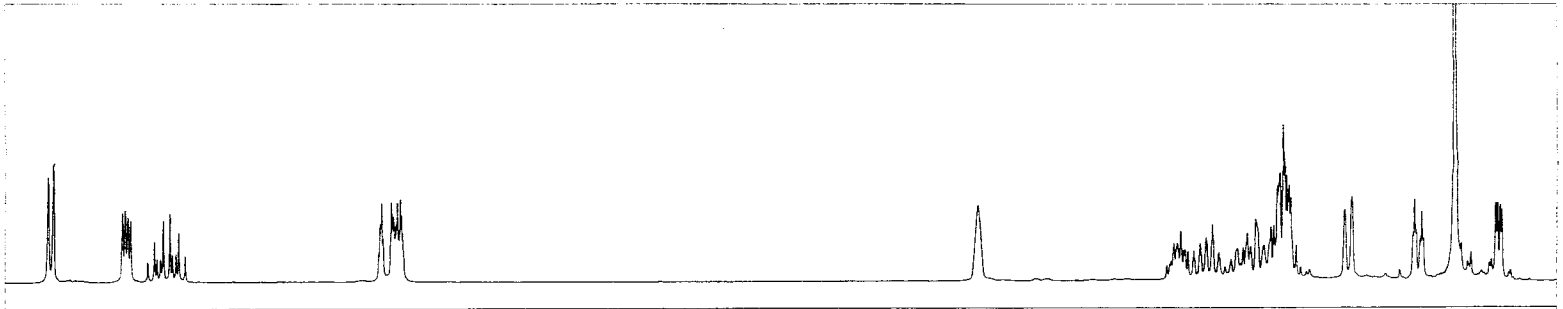
1D NMR plot parameters

CX	20.00 cm
CY	10.00 cm
F1P	219.402 ppm
F1	27591.57 Hz
F2P	-19.390 ppm
F2	-2438.46 Hz
PPMCM	11.93963 ppm/cm
HZCM	1501.50146 Hz/cm

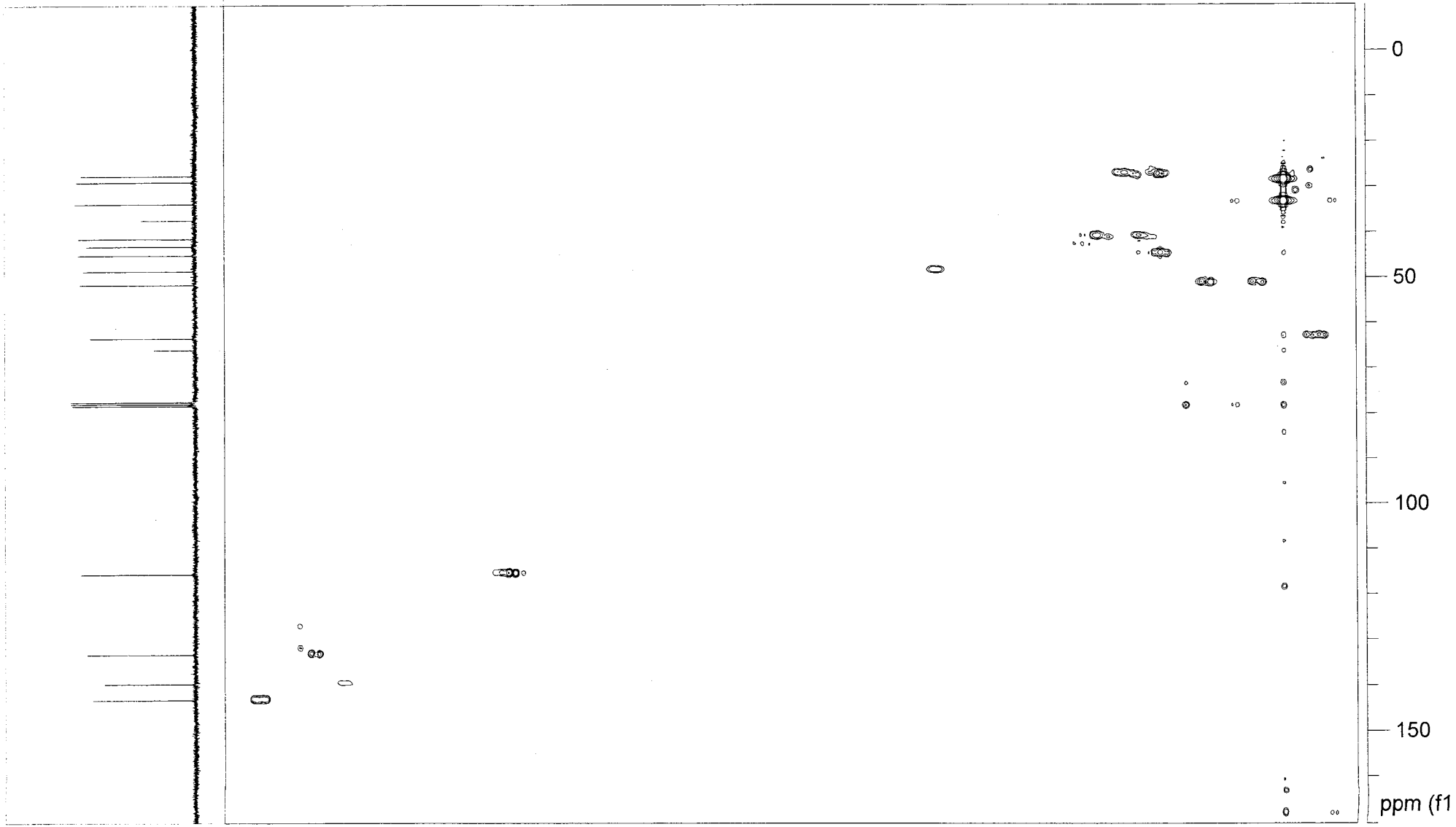

87
125
1.0
2.0
3.0
4.0
5.0
6.0
ppm (f1
6.0
5.0
4.0
3.0
2.0
1.0
ppm (f2)

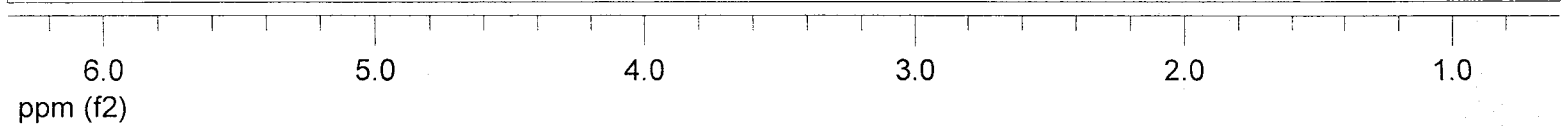


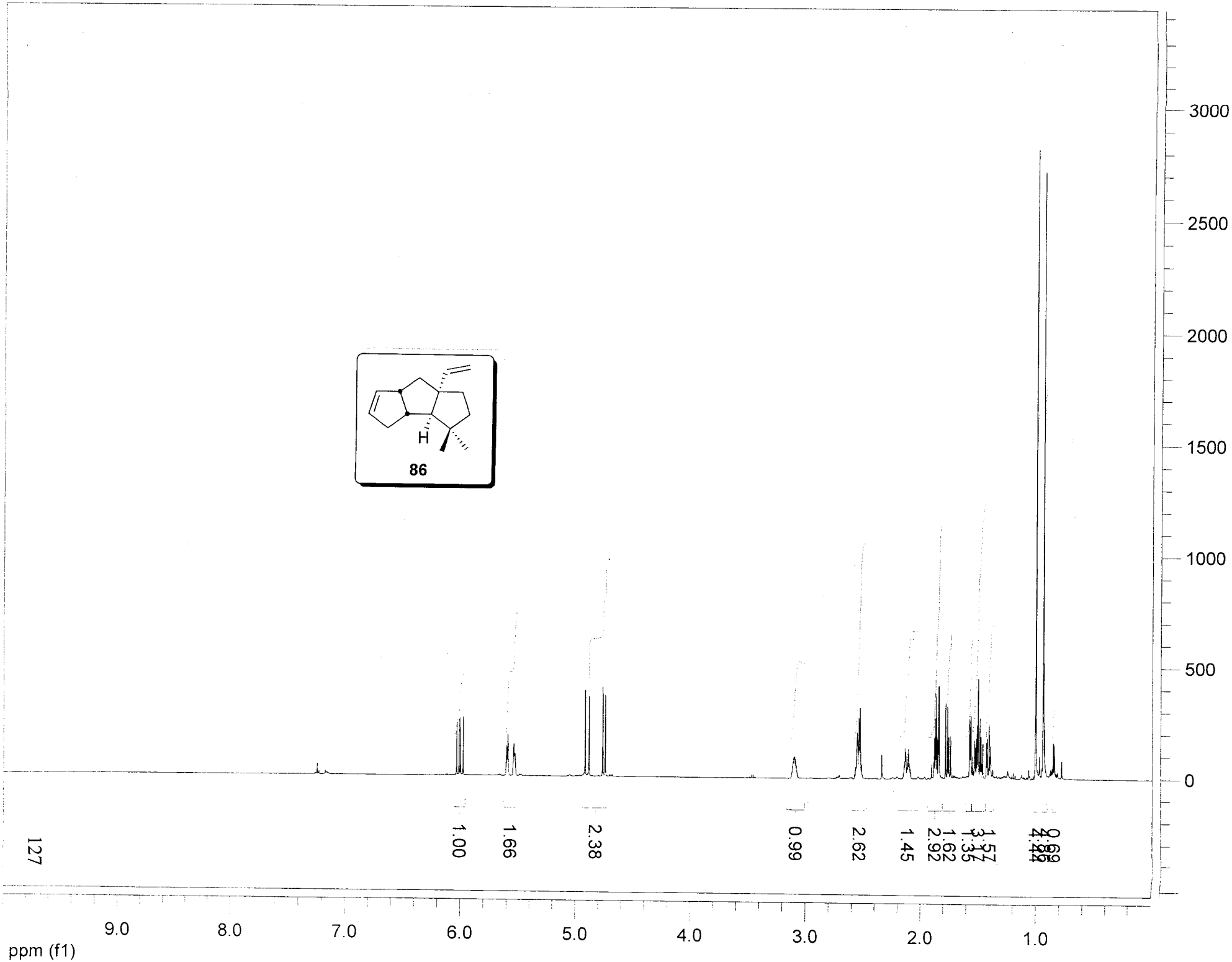
87

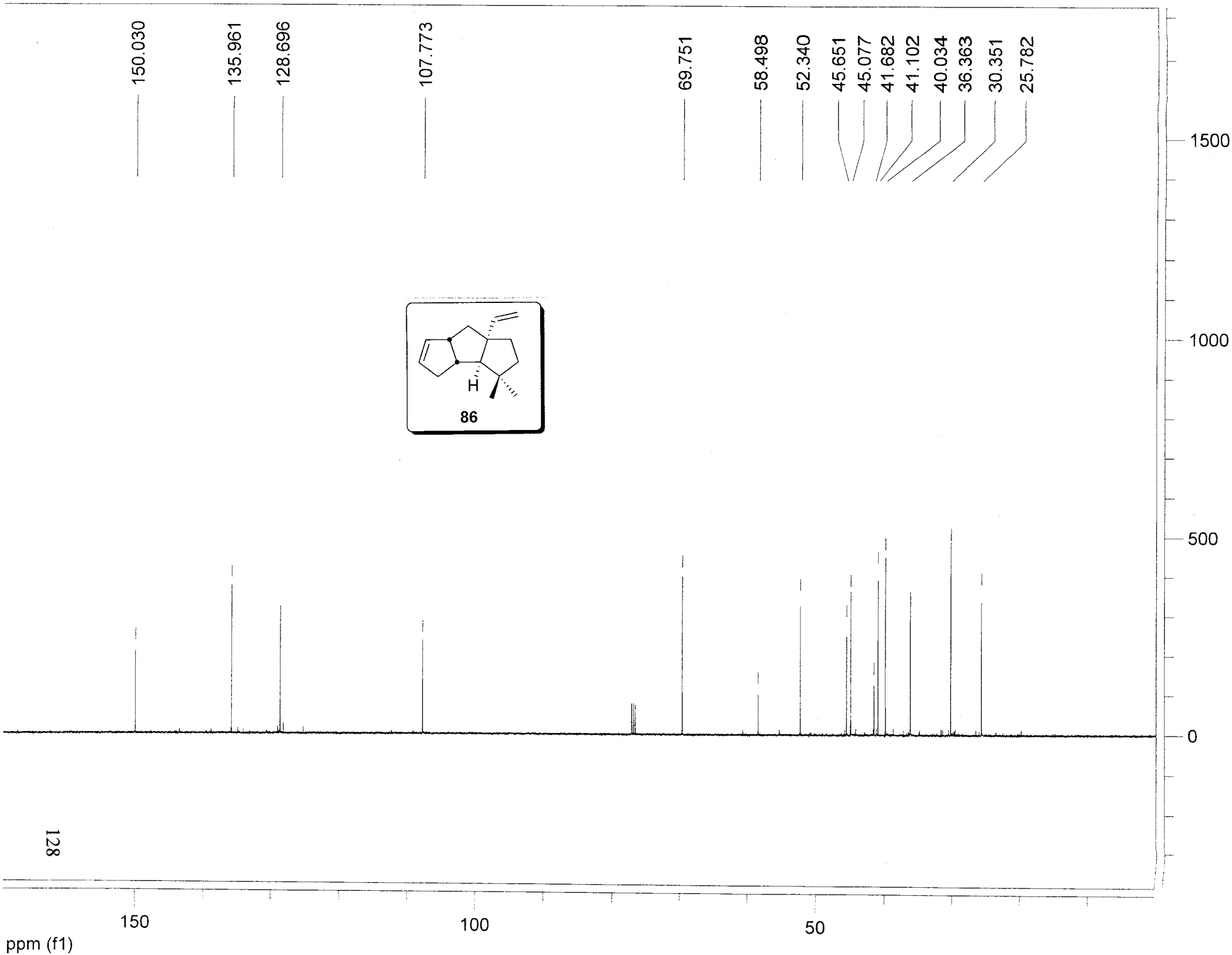


126

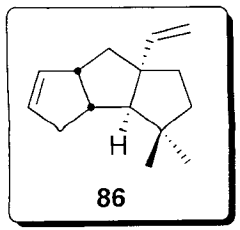




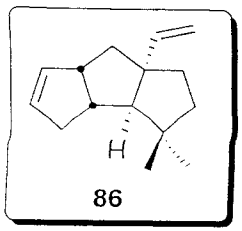

86
3000
2500
2000
1500
1000
500
0
127
1.00
1.66
2.38
0.99
2.62
1.45
1.62
2.92
1.57
1.35
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (f1)


150.030
135.961
128.696
107.773
69.751
58.498
52.340
45.651
45.077
41.682
41.102
40.034
36.363
30.351
25.782
86
1500
1000
500
0
128
150
100
50
ppm (f1)

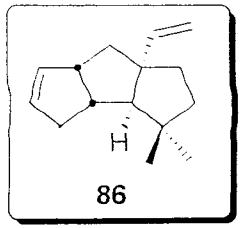
1500
1000
500
0
25.782
30.351
36.363
40.034
41.102
41.682
45.077
45.651
52.340
58.498
69.751
107.773
128.696
135.961
150.030
H
86
50
100
150
ppm (f1)



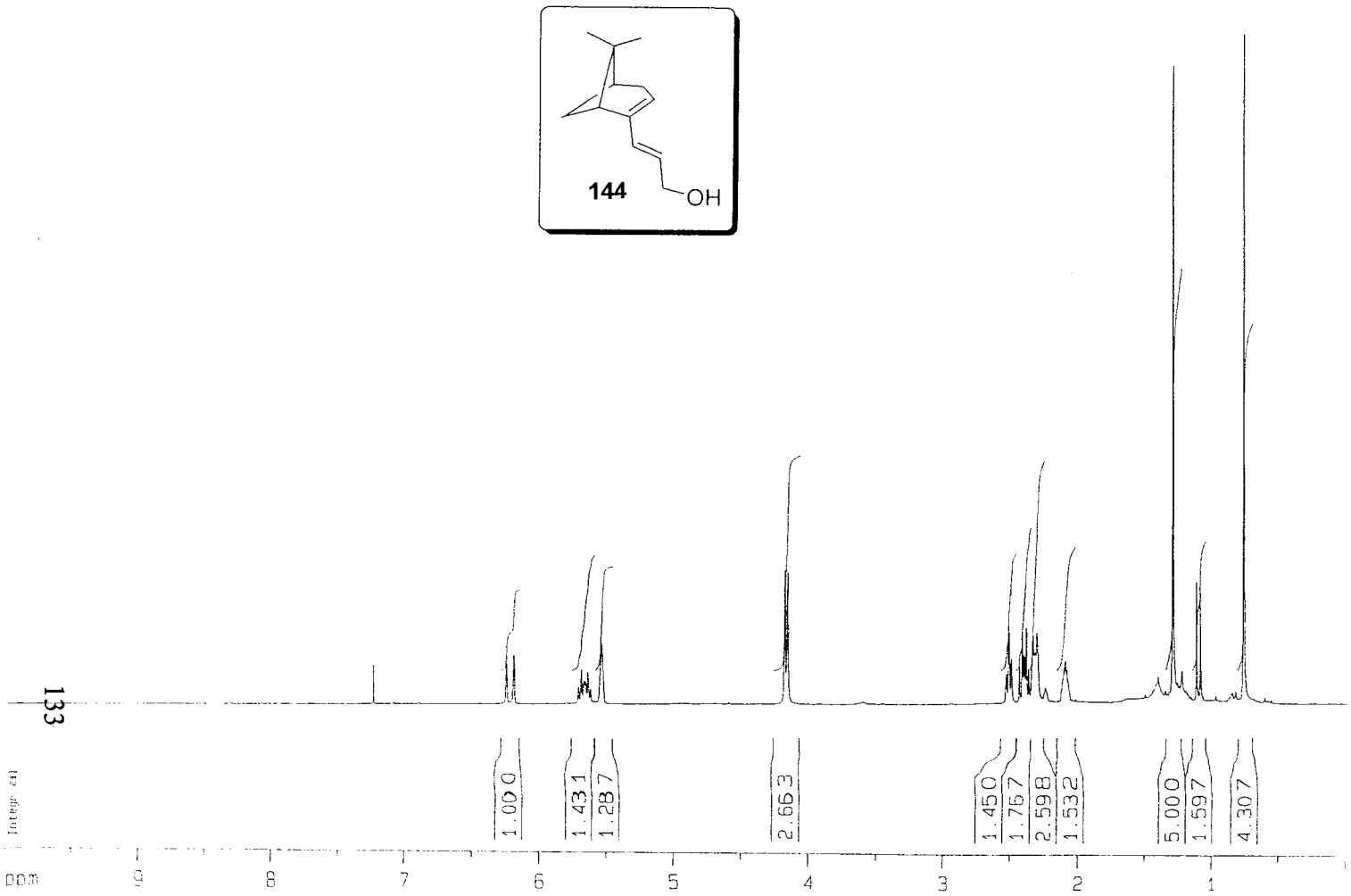
86



86

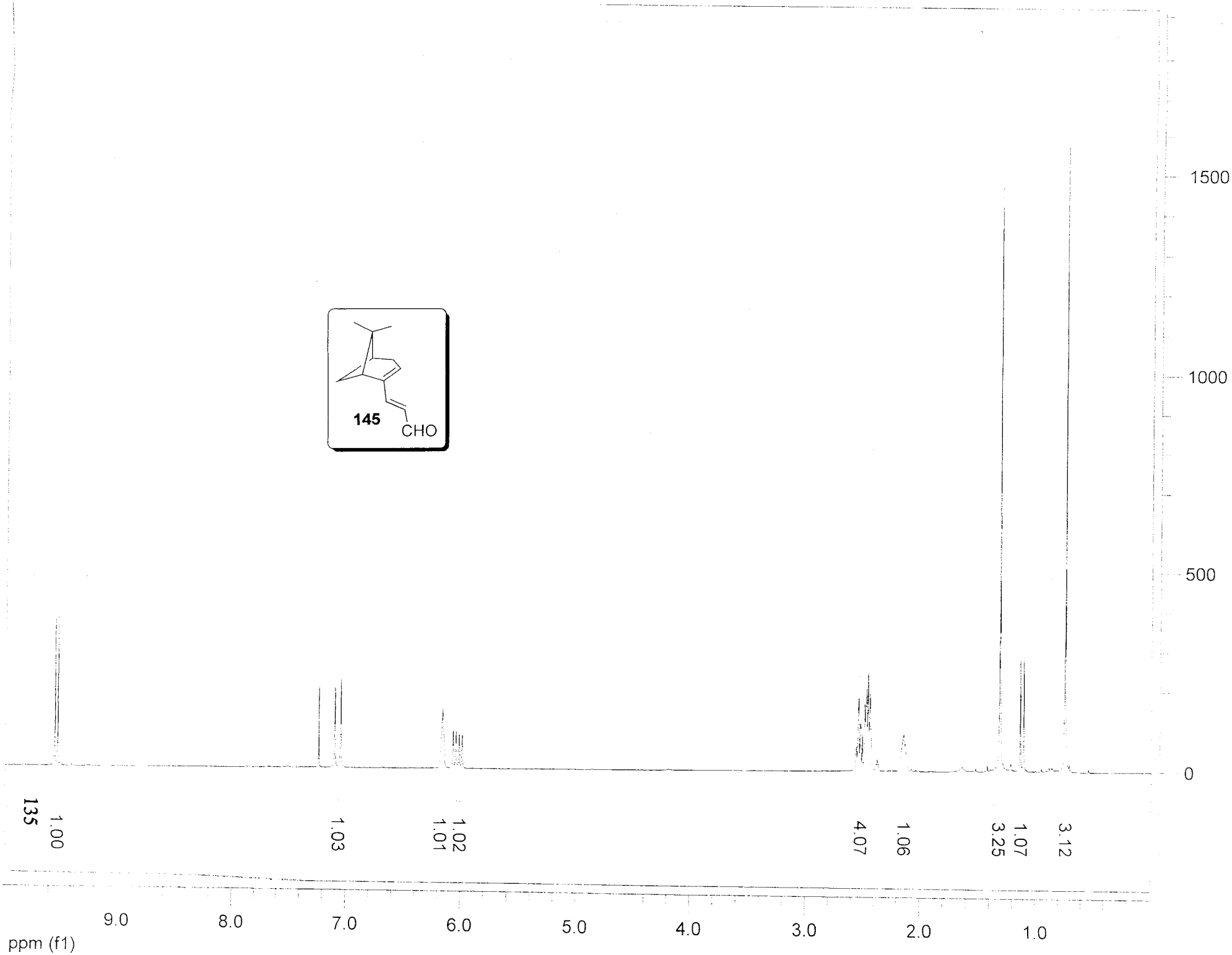

H
86

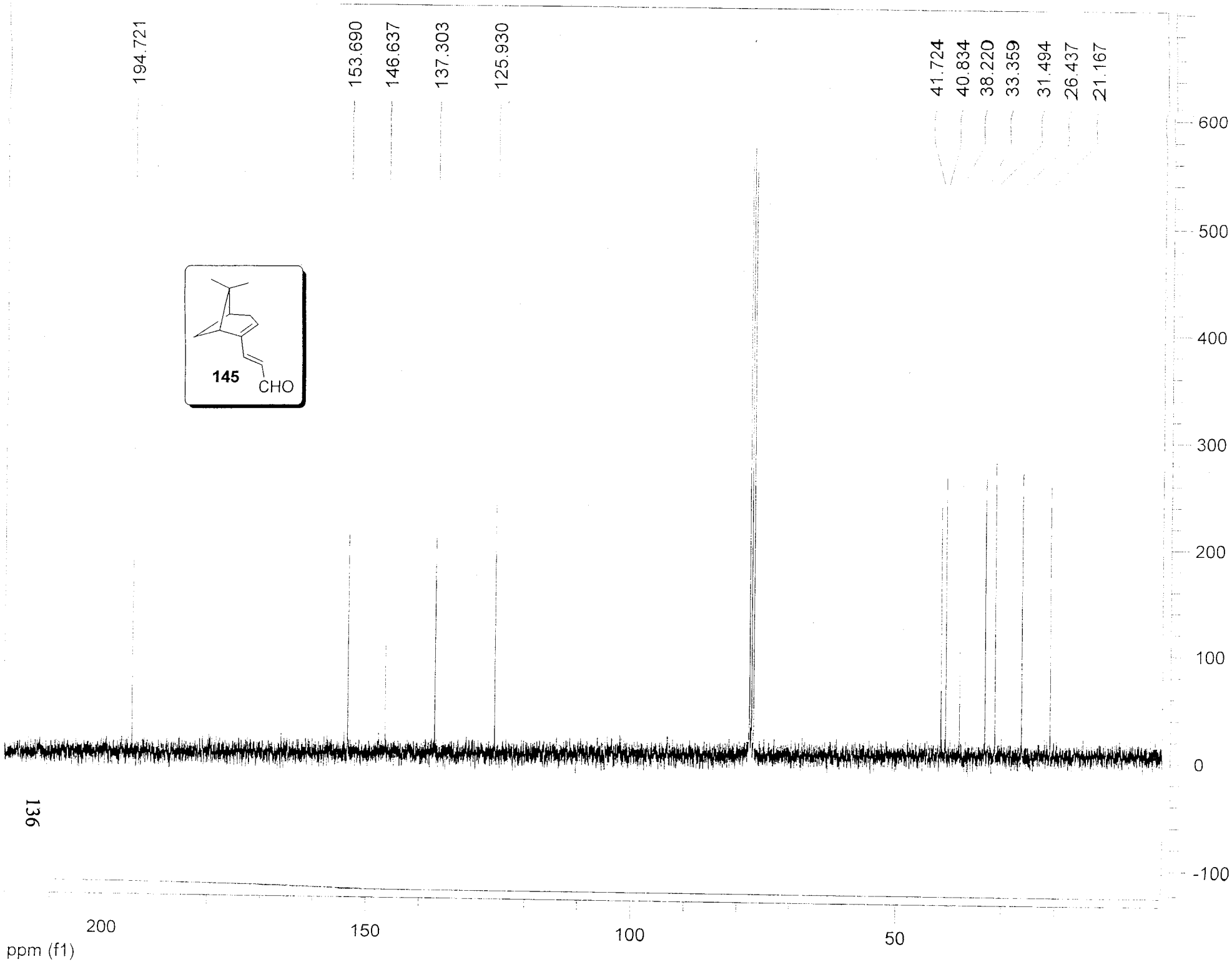
1.0
2.0
3.0
4.0
5.0
6.0
ppm (f1
6.0
5.0
4.0
3.0
2.0
1.0
ppm (f2)

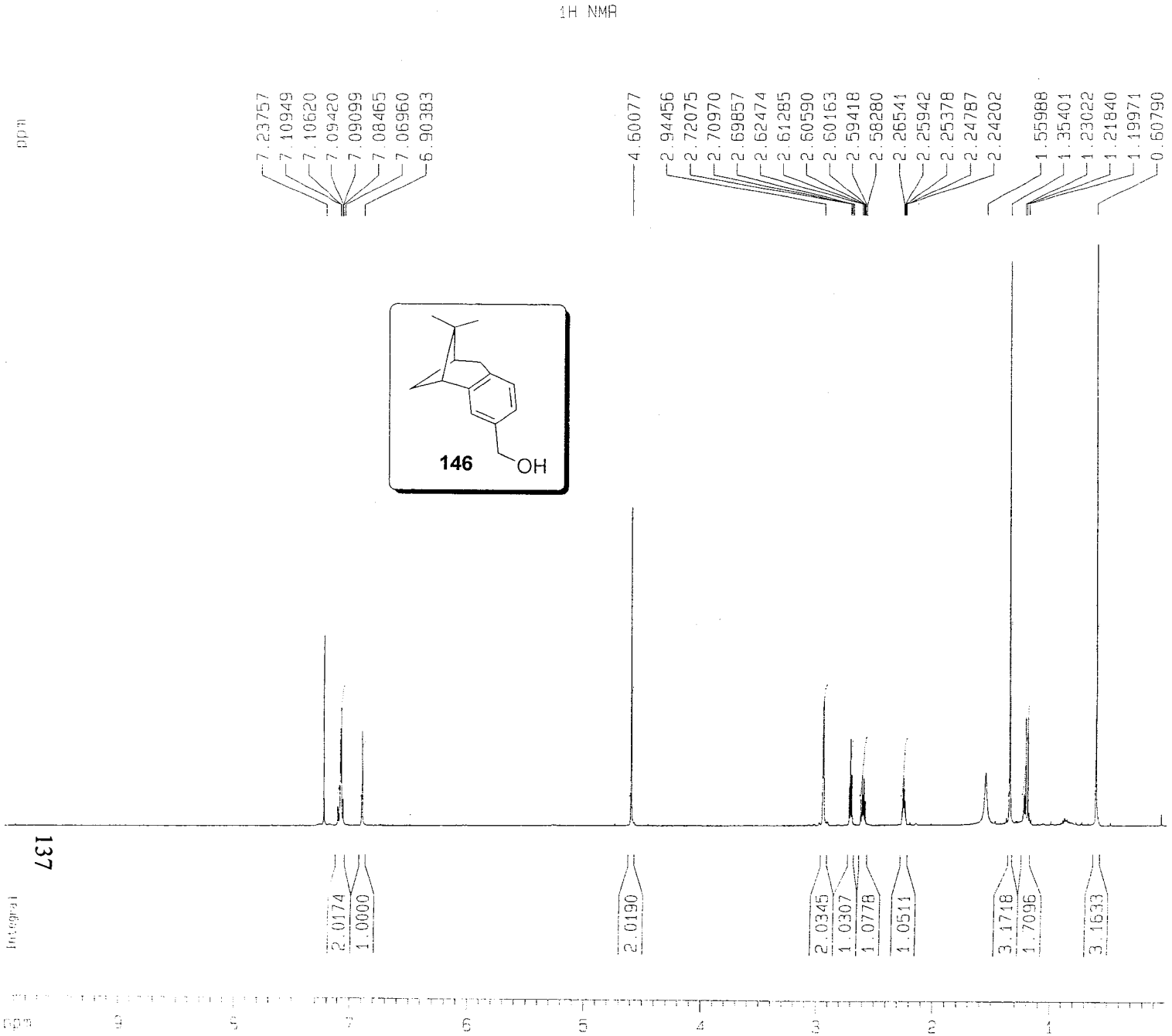



```
Current Data Parameters
NAME      NMnopinone-red-D
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_           20050503
Time              19.24
INSTRUM           av300
PROBHD   5 mm QNP  1H/1
PULPROG             zg30
TD                 30720
SOLVENT            CDCl3
NS                    16
DS                     0
SWH            5081.301 Hz
FIDRES         0.165407 Hz
AQ             3.0228980 sec
RG                   181
DW                98.400 usec
DE                 6.00 usec
TE                300.0 K
D1             1.00000000 sec

============ CHANNEL f1 =============
NUC1                 1H
P1                10.50 usec
PL1               -3.00 dB
SFO1         300.1319477 MHz

F2 - Processing parameters
SI                65536
SF          300.1300000 MHz
WDW                  EM
SSB                   0
LB                 0.10 Hz
GB                    0
PC                 1.00

1D NMR plot parameters
CX                20.00 cm
CY                10.00 cm
F1P               10.000 ppm
F1              3001.30 Hz
F2P               0.000 ppm
F2                0.00 Hz
PPMCM          0.50000 ppm/cm
HZCM         150.06500 Hz/cm
```

144
OH


145
CHO
1500
1000
500
0
135
1.00
1.03
1.02
1.01
4.07
1.06
3.25
1.07
3.12
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (f1)


194.721
153.690
146.637
137.303
125.930
41.724
40.834
38.220
33.359
31.494
26.437
21.167
145
CHO
600
500
400
300
200
100
0
-100
136
200
150
100
50
ppm (f1)



137

Current Data Parameters

NAME	NN02-105
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20041018
Time	14.18
INSTRUM	AV500WB
PROBHD	5 mm TBO BB/1H
PULPROG	zg30
TD	65536
SOLVENT	Acetone
NS	16
DS	0
SWH	7440.476 Hz
FIDRES	0.113533 Hz
AQ	4.4040694 sec
RG	203.2
DW	67.200 usec
DE	6.00 usec
TE	300.0 K
D1	0.01000000 sec

======== CHANNEL f1 ========

NUC1	1H
P1	14.00 usec
PL1	0.00 dB
SF01	500.1327766 MHz

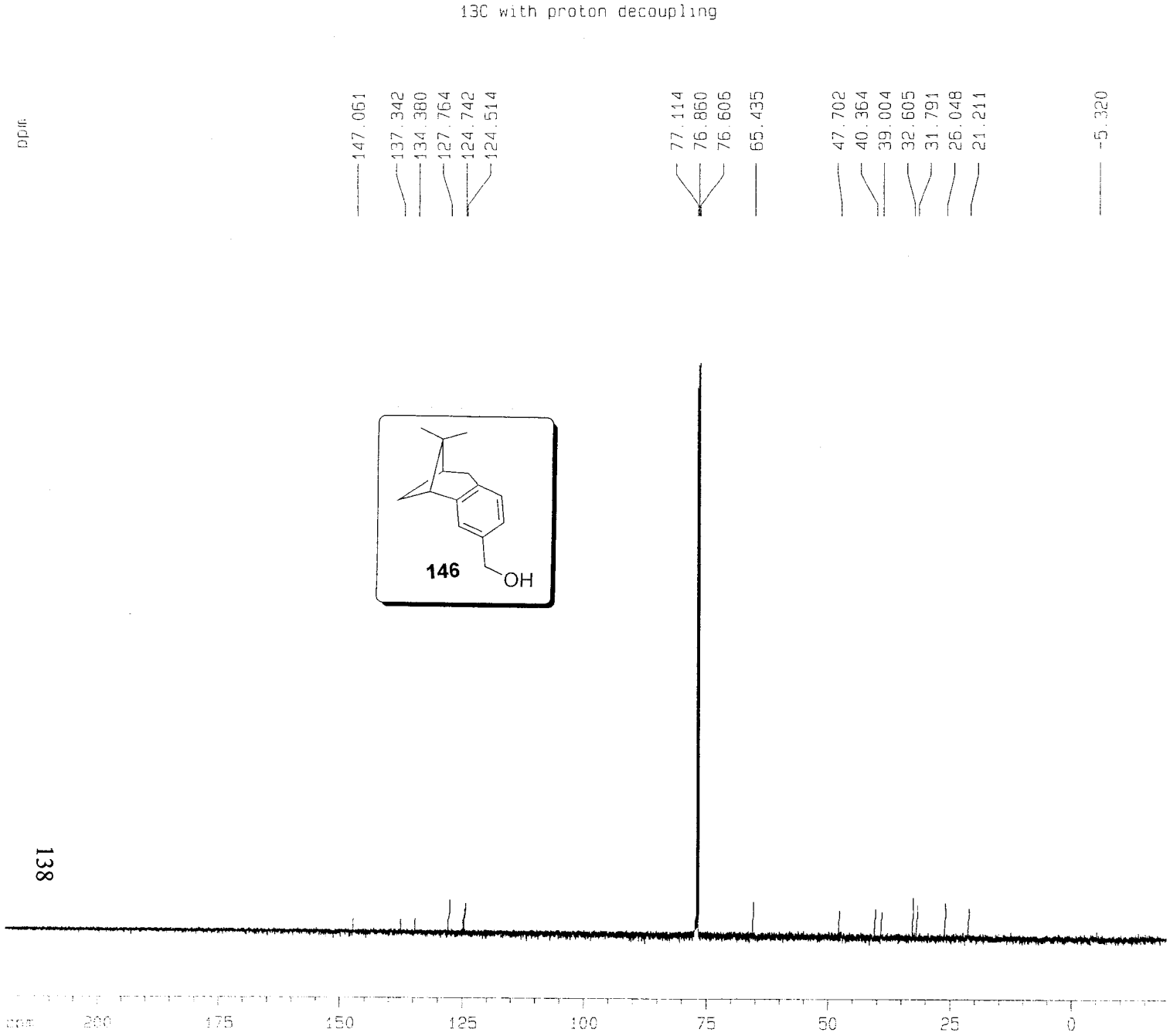
F2 - Processing parameters

SI	65536
SF	500.1300049 MHz
WDW	EM
SSB	0
LB	0.00 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	20.00 cm
CY	10.00 cm
F1P	10.000 ppm
F1	5001.30 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	0.50000 ppm/cm
HZCM	250.06500 Hz/cm

13C with proton decoupling



Current Data Parameters

NAME	MN02-105
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20041016
Time	14.23
INSTRUM	AV500W6
PROBHD	5 mm TBO BB/1H
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	476
DS	0
SWH	30030.029 Hz
FIDRES	0.458222 Hz
AQ	1.0912244 sec
RG	1824
DW	16.650 usec
DE	22.00 usec
TE	300.0 K
D1	1.00000000 sec
d11	0.03000000 sec
d12	0.00002000 sec

======== CHANNEL f1 ========

NUC1	13C
P1	8.00 usec
PL1	-0.20 dB
SFO1	125.7703643 MHz

======== CHANNEL f2 ========

CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	-0.20 dB
PL12	14.94 dB
PL13	14.90 dB
SFO2	500.1320005 MHz

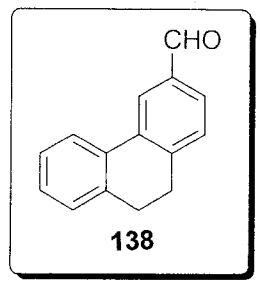
F2 - Processing parameters

SI	32768
SF	125.7578051 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	20.00 cm
CY	10.00 cm
F1P	219.264 ppm
F1	27574.17 Hz
F2P	-19.528 ppm
F2	-2455.86 Hz
PPMCM	11.93963 ppm/cm
HZCM	1501.50159 Hz/cm

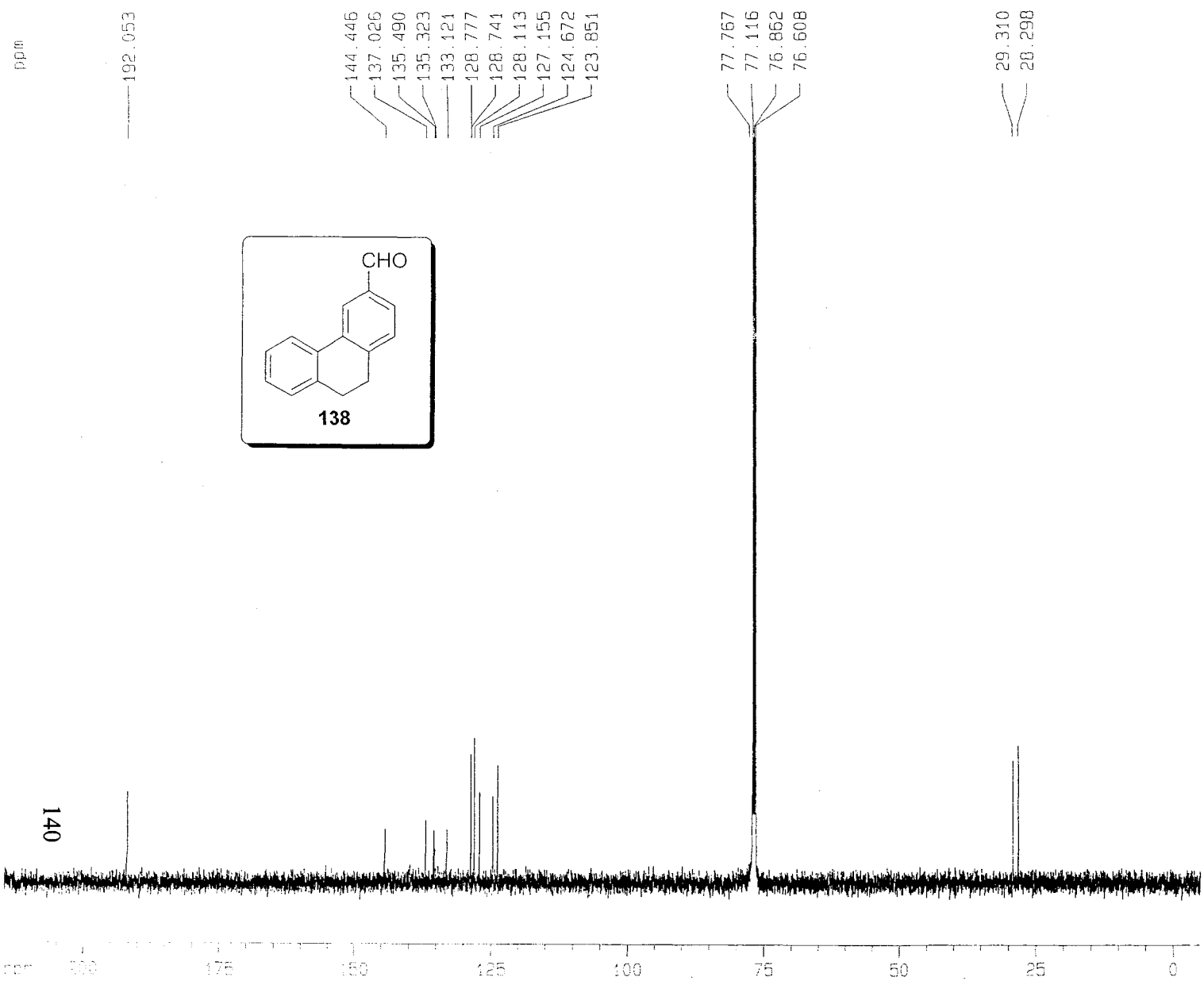
1H NMR



138


```
Current Data Parameters
NAME          NN02-148-500
EXPNO                    1
PROCNO                   1

F2 - Acquisition Parameters
Date_          20050118
Time                11.09
INSTRUM          AV500WB
PROBHD   5 mm 1H0 BB/1H
PULPROG             zg30
TD                 65536
SOLVENT          Acetone
NS                    16
DS                     0
SWH           7440.476 Hz
FIDRES        0.113533 Hz
AQ            4.4040694 sec
RG                   181
DW              67.200 usec
DE               6.00 usec
TE              300.0 K
D1            0.01000000 sec

======== CHANNEL f1 ========
NUC1                 1H
P1              14.00 usec
PL1              0.00 dB
SF01        500.1327766 MHz

F2 - Processing parameters
SI                 65536
SF          500.1300048 MHz
WDW                   EM
SSB                    0
LB               0.00 Hz
GB                     0
PC                  1.00

1D NMR plot parameters
CX                20.00 cm
CY                10.00 cm
F1P              10.500 ppm
F1             5251.37 Hz
F2P               0.000 ppm
F2                0.00 Hz
PPMCM          0.52500 ppm/cm
HZCM         262.56824 Hz/cm
```

13C with proton decoupling



Current Data Parameters

NAME	NN02-148-500
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20050118
Time	12.25
INSTRUM	AV500WB
PROBHD	5 mm TBO BB/1H
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	3036
DS	0
SWH	30030.029 Hz
FIDRES	0.458222 Hz
AQ	1.0912244 sec
RG	2896
DW	16.650 usec
DE	22.00 usec
TE	300.0 K
D1	1.00000000 sec
d11	0.03000000 sec
d12	0.00002000 sec

======== CHANNEL f1 ========

NUC1	13C
P1	8.00 usec
PL1	-0.20 dB
SFO1	125.7703643 MHz

======== CHANNEL f2 ========

CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	-0.20 dB
PL12	14.94 dB
PL13	14.90 dB
SFO2	500.1320005 MHz

F2 - Processing parameters

SI	32768
SF	125.7578051 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	20.00 cm
CY	100.00 cm
F1P	215.000 ppm
F1	27037.93 Hz
F2P	-5.000 ppm
F2	-628.79 Hz
PPMCM	11.00000 ppm/cm
HZCM	1383.33582 Hz/cm