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POSTDOCTORAL STUDIES

MACLEAN, Ross

AUTEUR DE LA THÈSE - AUTHOR OF THESIS

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and Oxy-Cope/ENE/Claisen Reactions

L. Barriault

DIRECTEUR DE LA THÈSE - THESIS SUPERVISOR

EXAMINATEURS DE LA THÈSE - THESIS EXAMINERS

P. Arya

W. Ogilvie

J.-M. De Koninck, Ph.D.

LE DOYEN DE LA FACULTÉ DES ÉTUDES
SUPÉRIEURES ET POSTDOCTORALES

SIGNATURE

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**APPLICATIONS OF A HYDROXY-DIRECTED DIELS-ALDER REACTION
AND FURTHER INVESTIGATION OF THE TANDEM OXY-COPE/ENE, AND
OXY-COPE/ENE/CLAISEN REACTIONS**

By

PETER ROSS MACLEAN

B.Sc. (Honours), University of Western Ontario, 2001.

A Thesis submitted to the School of Graduate Studies and Research In Partial Fulfillment
of the Requirements for the Degree of Master of Science

Ottawa-Carleton Chemistry Institute
Department of Chemistry
University of Ottawa
Ottawa, Ontario
Canada

Candidate

Supervisor

Peter Ross MacLean

Dr. Louis Barriault

University of Ottawa

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TABLE OF CONTENTS

List of Schemes.....	4
List of Figures.....	7
List of Tables.....	8
List of Abbreviations.....	9
Abstract.....	11
Acknowledgements.....	12
Chapter 1: Introduction.....	14
1.1 The Diels-Alder Reaction: π -Facial Diastereoselectivity.....	14
1.2 Disposable Tethers.....	16
1.3 A Hydroxy-Directed Diels-Alder.....	18
1.4 Tandem Reactions.....	20
1.5 Tandem Oxy-Cope/Ene Reaction.....	22
1.6 Tandem Oxy-Cope/Ene Reaction/Claisen Reaction.....	25
1.7 Microwave Heating.....	26
Chapter 2: A Highly Diastereoselective Approach To Polycyclic Molecules.....	29
2.1 Aim Of The Project.....	29
2.2 Preparation Of The Diene Precursors.....	29
2.3 Preparation Of The Dienes.....	32
2.4 Hydroxy-Directed Diels-Alder Results.....	34
2.5 Explanation Of Results.....	38
2.6 Future Directions.....	39
Chapter 3: Application Of The Tandem Oxy-Cope/Ene/Claisen Reaction	
Towards The Synthesis Of A Rosane.....	41
3.1 Background.....	41
3.2 Retrosynthetic Analysis.....	42
3.3 Synthesis Of A Divinyl-Cyclohexanol.....	44
3.4 Tandem Oxy-Cope/Ene/Claisen Results.....	47
3.5 Explanation Of Results.....	50
3.6 Installing Functionality At C8.....	54

Chapter 4: Working Towards The Synthesis Of Isovelleral Analogues.....	58
4.1 Background.....	58
4.2 Approach To Isovelleral Analogues.....	59
4.3 Preparation Of The Dienes.....	60
4.4 Results And Discussion.....	61
4.5 Future Work.....	65
Experimental.....	67
Claims To Original Research.....	89
References.....	90
Appendix.....	93

LIST OF SCHEMES

Scheme 1: Facial Selectivity Using Dienes Containing Allylic Substituents	14
Scheme 2: Facial Selectivity Using Allylically Substituted Vinylcyclohexenes	15
Scheme 3: Tamao's Silicon Tethered Diels-Alder	16
Scheme 4: Stork's Use of a Silicon Tethered Diels-Alder	17
Scheme 5: Stork's Use of a Magnesium Tethered Diels-Alder	17
Scheme 6: Ward's Use of a Magnesium Tethered Diels-Alder	18
Scheme 7: Hydroxy-Directed Diels-Alder Reaction	19
Scheme 8: Synthesis of β -sinesal; Tandem Claisen/Cope Reaction	21
Scheme 9: Tandem Transannular Diels-Alder/Aldol Reaction	21
Scheme 10: Total Synthesis of (+)-Isovelleral via tandem Rearrangement- Cyclopropanation Reaction	22
Scheme 11: Tandem oxy-Cope/transannular ene Reaction	23
Scheme 12: Competing Retroene Reaction	24
Scheme 13: Total Synthesis of (+)-Arteannium M	24
Scheme 14: Tandem Oxy-Cope/Ene/Claisen Reaction	25
Scheme 15: Determining The Diastereoselectivity of The Reaction	26
Scheme 16: An Absence of Microwave Effects	28
Scheme 17: Oxy-Cope/Transannular Ene Followed by a Tether Controlled Diels-Alder	29
Scheme 18: Corey-Fuchs Approach to Diene Precursors	30
Scheme 19: Preparation of Unsubstituted Diene	31
Scheme 20: Preparation of Dienes	32
Scheme 21: Second Approach to Diene System	34
Scheme 22: Attempts at a Hydroxy-Directed Diels-Alder	34

Scheme 23: Trace Amounts of Diels-Alder Products	35
Scheme 24: Aromatization of Dienes	36
Scheme 25: Oxy-Cope/Ene/Claisen Method of Generating Dienes	36
Scheme 26: Tethered Diels-Alder Results	37
Scheme 27: Preparing a Diene Featuring a Cis-Ring-Junction	39
Scheme 28: Tandem Oxy-Cope/Ene/Claisen Reaction	42
Scheme 29: Retrosynthetic Approach to the Rosane Core	43
Scheme 30: Predicted Stereochemical Outcome of Oxy-Cope/Ene/Claisen Reaction	44
Scheme 31: Preparation of the Side-chain	45
Scheme 32: Attempted 1,2-Rearrangement	45
Scheme 33: Stille or Negishi Coupling Strategy	46
Scheme 34: Epoxide Opening Strategy	47
Scheme 35: Oxy-Cope/Ene/Claisen Results	48
Scheme 36: Similar Oxy-Cope/Ene/Claisen Results	49
Scheme 37: Ring Closing Metathesis	50
Scheme 38: Mechanism of the Oxy-Cope/Ene Reaction	52
Scheme 39: Formation of an Aldehyde Side-Product	53
Scheme 40: Mechanism of the Claisen Rearrangement	54
Scheme 41: Preparation of The Epoxide	55
Scheme 42: Ireland-Claisen Approach	56
Scheme 43: Attempted Epoxide Opening	57
Scheme 44: Attempted Epoxide Opening With DIBAL	57
Scheme 45: Approach Using Two Types of Dienes	60
Scheme 46: Approach Using Alkynyl Dienophile	61
Scheme 47: Decomposition of Dienophile	61

LIST OF FIGURES

Figure 1: Mechanism For The Tandem Oxy-Cope/ene Reaction	33
Figure 2: Comparison with Previous Work	38
Figure 3: 3.2.5. 5 β ,20-Epoxy-hydroxy-ros-15-ene	41
Figure 4: Application of the Curtin-Hammett Principle	51
Figure 5: The Marasmane Sesquiterpene Isovelleral	58
Figure 6: Retrosynthetic Analysis of Isovelleral	59
Figure 7: Approach Using Two Types of Dienes	59

LIST OF TABLES

Table 1: Corey-Fuchs Products	30
Table 2: Results Using Alkynyl Dienophile	62
Table 3: Results Using Alkenyl Dienophile	64
Table 4: Results Using a Grignard Reagent	65

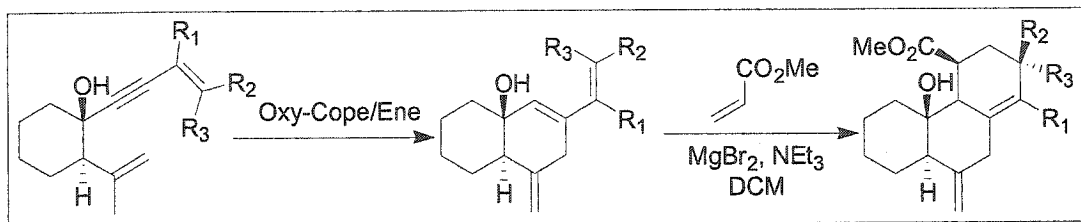
LIST OF ABBREVIATIONS

Bn	benzyl
BuLi	butyl lithium
DBU	1,8-diazobicyclo[5.4.0]undec-7-ene
DCM	dichloromethane
DMAP	4-dimethylaminopyridine
DMF	N,N-dimethylformamide
Eq.	equivalents
EtOAc	ethylacetate
Et ₂ O	diethylether
Et ₃ N	triethylamine
GC	gas chromatography
GC/MS	gas chromatography/mass spectrometry
HMDS	hexamethyldisilazane
HPLC	high pressure liquid chromatography
HRMS	high resolution mass spectrum
iPrOH	isopropanol
IR	infrared
LDA	lithiumdiisopropylamide
Me	methyl
MgBr ₂ ·OEt ₂	magnesium bromide diethyletherate
mp	melting point
NMR	nuclear magnetic resonance
PG	protecting group
Ph	phenyl
PMB	para-methoxy benzyl
Pyr	pyridine
ppm	parts per million
PTSA	para- toluene sulfonic acid
RCM	ring-closing metathesis

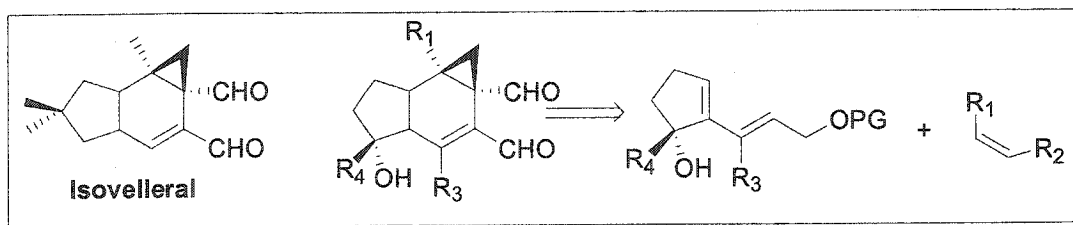
SAR	structure-activity relationship
TBAF	tetrabutylammonium fluoride
TBDMS	<i>tert</i> -butyldimethylsilyl
TBDPS	<i>tert</i> -butyldiphenylsilyl
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl

ABSTRACT

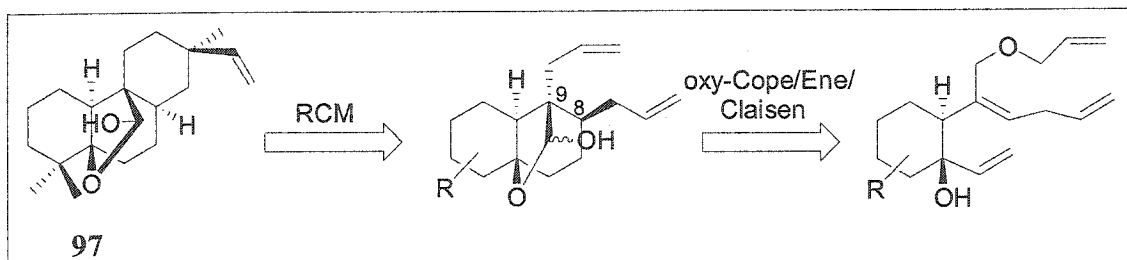
The recent development of a hydroxy-directed Diels-Alder reaction, which enables control of both regio- and diastereoselectivity, has prompted an investigation of potential applications. Extending the methodology to more complicated dienes, such as those created via the tandem oxy-Cope/Ene reaction, offers the potential for rapid construction of polycyclic molecules with significant stereochemical complexity.



The simplicity and efficiency of this technique has also inspired its employment as the primary disconnection in the production of a library of analogues of the unsaturated dialdehyde Isovelleral.



Also examined herein is the recently discovered tandem oxy-Cope/Ene/Claisen reaction; a highly diastereoselective method for generating *trans*-decalin systems containing quaternary carbon centers. Showing potential as a tool in diterpene synthesis, the scope and limitations of this reaction were further investigated by attempting the synthesis of a rosane derivative **97**, recently isolated from the liverwort *Gackstroemia decipiens*.



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Finally and most importantly, I would like to acknowledge the constant love and support I have received from my wife Tammy. It's hard to believe how far we've come together; I look forward to what the future will bring.

“To my parents, Peter and Cindy MacLean...”

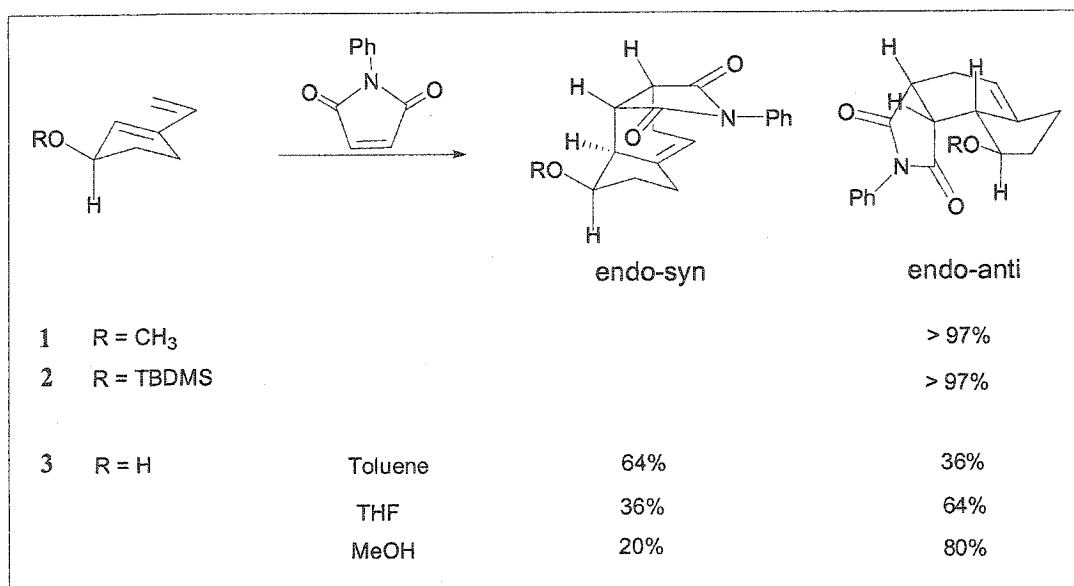
Chapter 1: Introduction

1.1 The Diels-Alder Reaction: π -Facial Diastereoselectivity

One of the most significant challenges that the Diels-Alder reaction presents is finding methods of controlling the π -facial diastereoselectivity when asymmetric dienes or dienophiles are used. An area showing some favorable results has been research on semicyclic dienes containing heteroatomic substitutions at the α -allylic position.

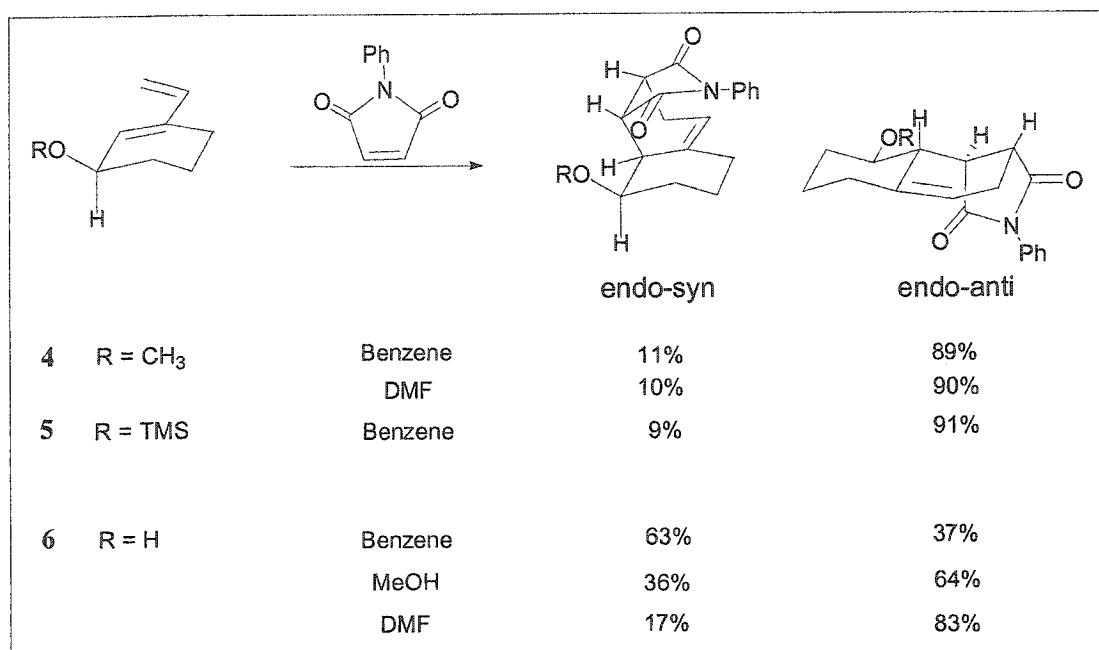
Some interesting observations were made by Overman et al. in their study of facial selectivity in Diels-Alder cycloadditions of dienes **1**, **2**, and **3**.¹ Treating dienes **1** and **2** with *N*-phenylmaleimide in a variety of solvents resulted in cycloaddition occurring exclusively from the diene face anti to the allylic substituent. The authors attributed these results to the unfavourable steric interactions which would result should the dienophile approach syn to the methoxy or -OTBDMS group.

Interestingly, when a hydroxyl-substituted diene **3** was used, the facial selectivity of the cycloaddition showed a solvent dependency. The formation of some syn-adduct was attributed to a stabilizing hydrogen bond between the OH substituent and the proximal carbonyl oxygen on the imide dienophile. This would be expected to be of least importance in MeOH where external solvation of the carbonyl and hydroxyl substituent would dominate.



Scheme 1: Facial Selectivity Using Dienes Containing Allylic Substituents

The same trends were later observed by Franck² when using similarly substituted vinylcyclohexenes. Once again, the presence of a methoxy or O-silyl substituent at the α -allylic position resulted in preferential formation of the endo-anti adduct while the diene **6** containing a hydroxyl group showed a similar solvent dependence in facial selectivity.

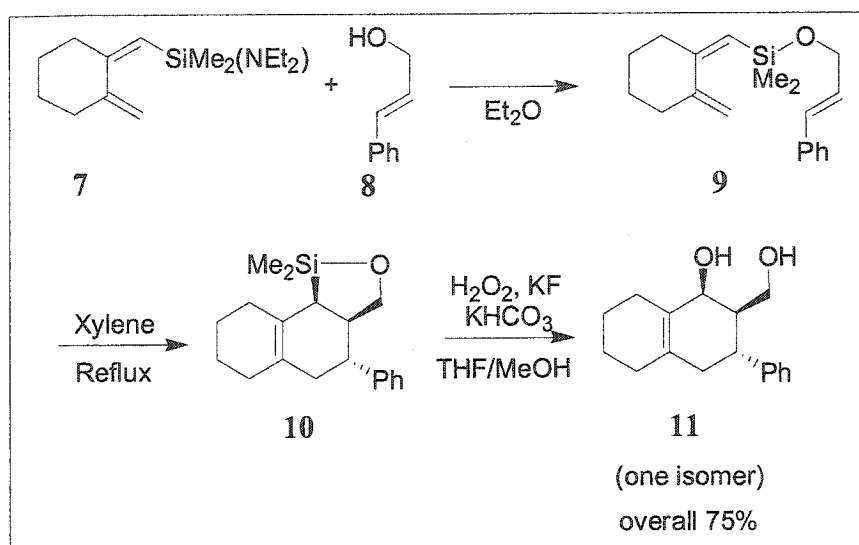


Scheme 2: Facial Selectivity Using Allylically Substituted Vinylcyclohexenes

While choice of solvent appears to give some anti/syn selectivity in the case of dienes **3** and **6**, it does not offer the high level of diastereoselectivity often required in modern organic synthesis. Furthermore, in examples using a tertiary allylic alcohol, facial selectivity is even less discriminate.² To solve this problem, the Barriault group turned their attention to the possibility of using a temporary metal tether to direct the approach of the dienophile.

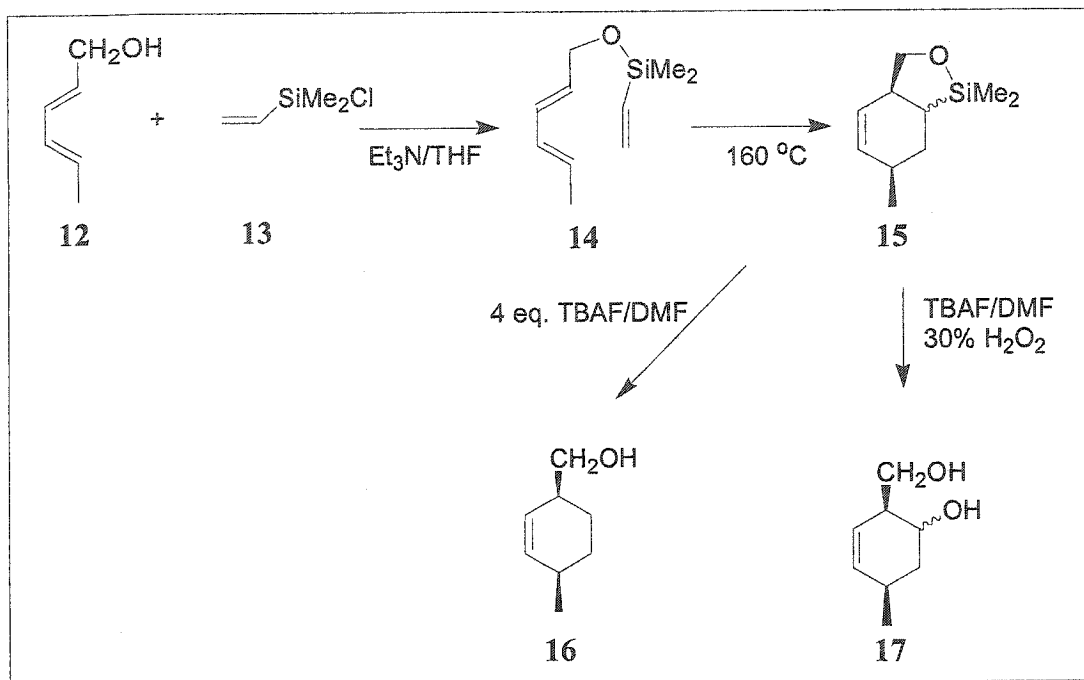
1.2 Disposable Tethers:

One of the first examples of a tethered controlled [4+2] cycloaddition was reported by Tamao³ in 1989. After preparing the exocyclic silyl diene **7**, it was condensed with cinnamyl alcohol **8** to give Diels-Alder precursor **9**. As a result of this tether, the reaction becomes an intramolecular process and the cycloaddition can occur with regio- and diastereocontrol. After heating, adduct **10** was obtained and further transformed to diol **11** by hydrogen peroxide oxidation of the silicon-carbon bond.



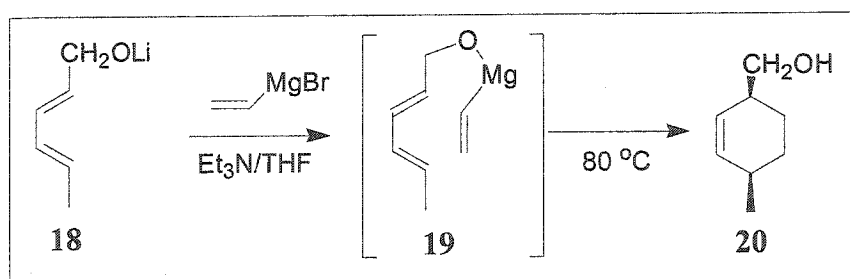
Scheme 3: Tamao's Silicon Tethered Diels-Alder

As reported independently by Stork⁴ and Sieburth⁵, silicon can also be employed as a disposable tether in the Diels-Alder reaction when a vinyl silane is used as a dienophile. A prototypical case is shown in Scheme 4 below; by tethering diene **12** to the silyl-substituted dienophile **13**, triene **14** is obtained and upon heating gives rise to a mixture of *endo/exo* products **15**. The tether can then be fluorodesilylated to give **16** or oxidatively cleaved to give diol **17**. (Scheme 5)



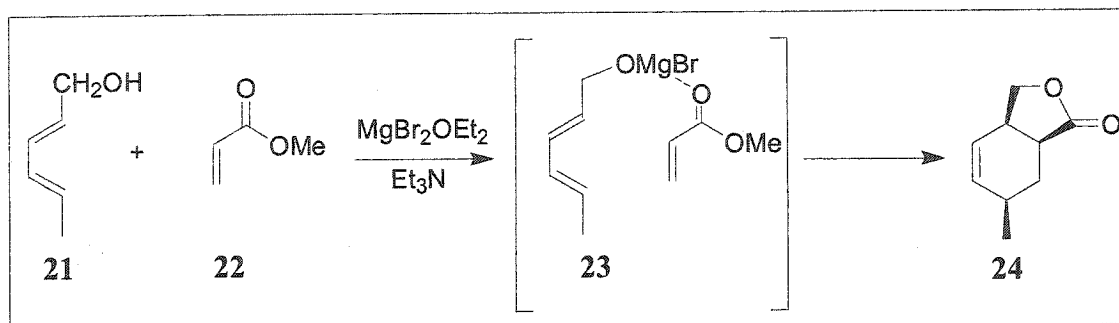
Scheme 4: Stork's Use of a Silicon Tethered Diels-Alder

Stork later expanded on this work to show that magnesium could also serve as the temporary tether.⁶ This was accomplished by first treating the allylic alcohol **12** with *n*-BuLi at -78 °C to give lithium alkoxide **18**, and then adding 1 equivalent of vinylmagnesium bromide at room temperature. After heating for 1 hour at 80 °C cycloadduct **20** was obtained.



Scheme 5: Stork's Use of a Magnesium Tethered Diels-Alder

Ward later demonstrated that temporary magnesium tethers could also be generated from Lewis acids like $\text{MgBr}_2 \cdot \text{OEt}_2$.⁷ Shown below, treatment of diene **21** with $\text{MgBr}_2 \cdot \text{OEt}_2$ and NEt_3 ⁸ followed by addition of methyl acrylate **22** resulted in an intermediate **23** capable of undergoing an “intramolecular” cycloaddition to give lactone **24** after workup.



Scheme 6: Ward's Use of a Magnesium Tethered Diels-Alder

More recently, other types of disposable tethers such as Al,⁹ Zn,¹⁰ and B,¹¹ have been employed in the Diels-Alder reaction. A common trend with these examples however, is that they require harsh conditions and elevated temperatures to form the metal-alkoxide diene species and they seem limited to dienes possessing a primary alcohol.

1.3 A Hydroxy-Directed Diels-Alder

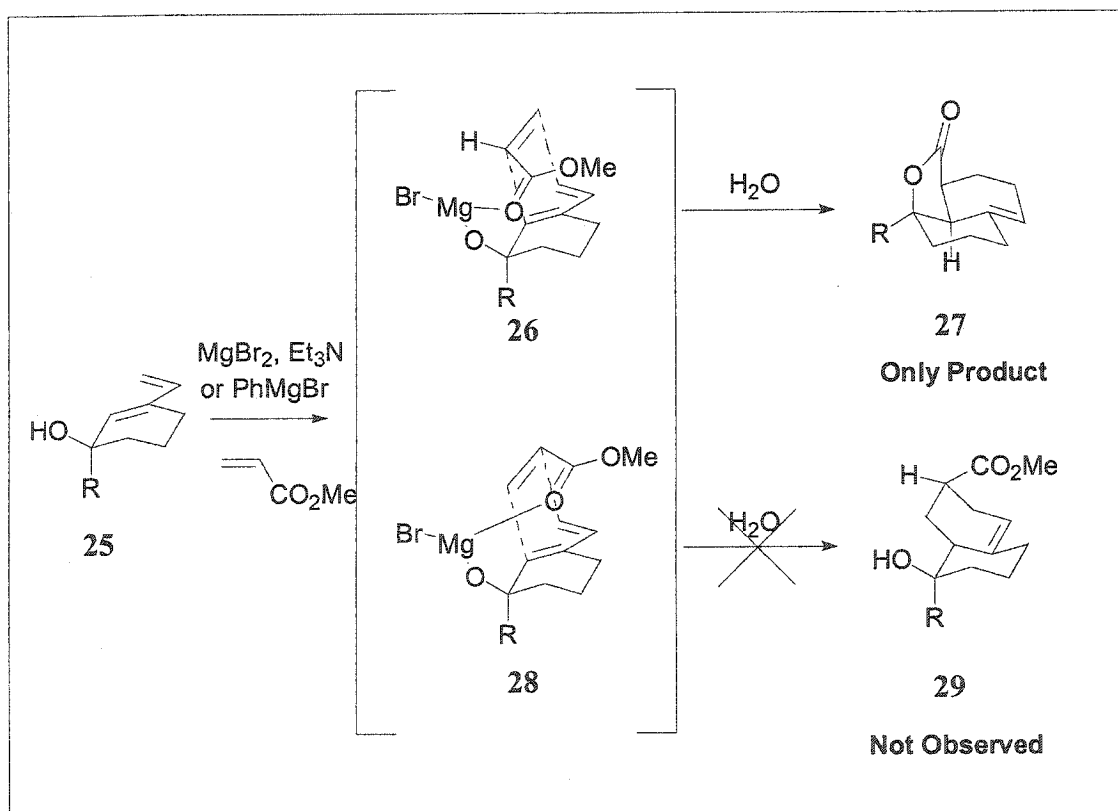
Recognizing an absence of examples in the literature, the Barriault lab began to examine the possibility of employing temporary metal tethers with dienes possessing secondary and tertiary alcohols.¹² The goal was to develop a protocol for converting the alcohol to a magnesium alkoxide, which could then tether to a dienophile and direct its approach.

Originally this was done by treating the diene with a Grignard reagent at $-78\text{ }^\circ\text{C}$ in toluene, and then allowing the flask to warm to room temperature. However, because of inconsistent results and the uncertain shelf-lives of Grignard reagents, a new method was developed based upon some of Ward's results.⁷ This technique involved adding the diene to a solution of $\text{MgBr}_2 \cdot \text{OEt}_2$ and NEt_3 in DCM at room temperature and then stirring for

approximately 30 minutes. Using either method the result is the same; deprotonation of the alcohol and complexation of the magnesium, which can then serve as a tether-point to which a carbonyl-containing dienophile can complex.

As demonstrated below, facial selectivity is controlled by the magnesium tether, resulting in a preferential approach of the dienophile from the same face as the alcohol. Regioselectivity for the reaction can be explained by examination of the two transition states shown. The only observed product, cycloadduct **27**, is formed via a seven-membered transition state **26**. The lack of formation of its regio-isomer **29** can be explained by the fact that the cycloaddition would need to occur via a more strained eight-membered transition state **28**. (Scheme 7)

Therefore, the methodology allows control of both the regio- and stereofacial approach of the dienophile, resulting in the preferential formation of only one of the four possible Diels-Alder adducts.



Scheme 7: Hydroxy-Directed Diels-Alder Reaction

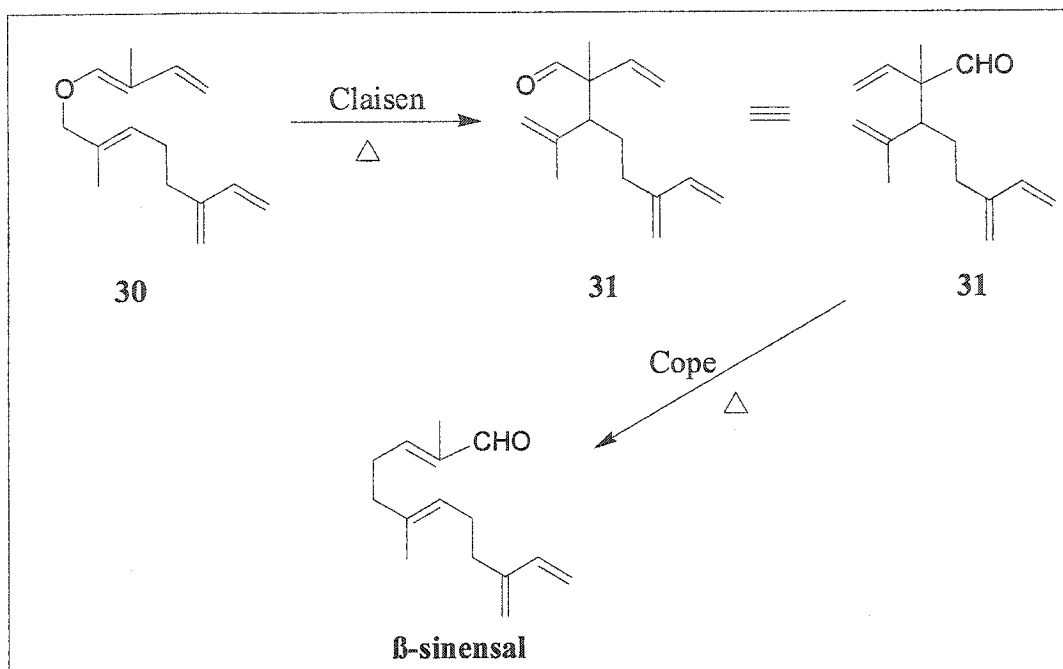
1.4 Tandem Reactions

One of the major challenges that today's synthetic organic chemists face is creating a maximum degree of molecular complexity in a minimal number of synthetic steps.¹³ An obvious approach to achieving this kind of synthetic efficiency is to find methods of combining two or more reactions into a single step, or operation.¹⁴ These types of reactions are often referred to as "tandem reactions."

By definition, tandem reactions are combinations of two or more "ordinary" reactions whose occurrence is in a specific order. Also, if they involve sequential addition of reagents, the secondary reagents must be integrated into the products.¹⁴ For instance, if a tandem reaction is a combination of two sigmatropic rearrangements, then the product of the first rearrangement will have a structure, which under the synthetic conditions, undergoes a second rearrangement.

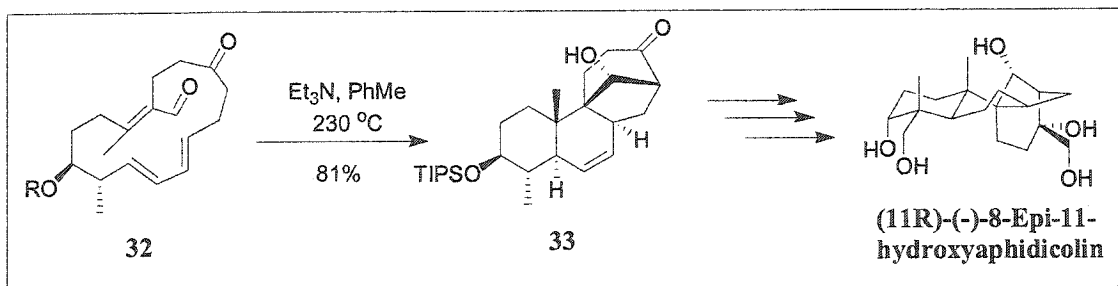
An early example of this type of tandem sigmatropic rearrangement was the synthesis of β -sinensal, an important sensory component of the sweet orange oil. As shown in Scheme 8, the ether **30** first undergoes a Claisen rearrangement to furnish the intermediate aldehyde **31**. This aldehyde **31** subsequently undergoes a Cope reaction to provide the α,β -unsaturated aldehyde product, β -sinensal.¹⁵

Without a doubt, the most useful tandem reactions are those which combine the construction of a desired skeletal framework, along with the controlled formation of as many stereogenic centers as possible. An illustrative example of how two well-known reactions can be combined in tandem to give a structurally complex molecule is shown in Deslongchamps' asymmetric synthesis of the unnatural aphidicolin derivative, (11R)-(-)-8-epi-11-hydroxyaphidicolin.¹⁶ (Scheme 9)



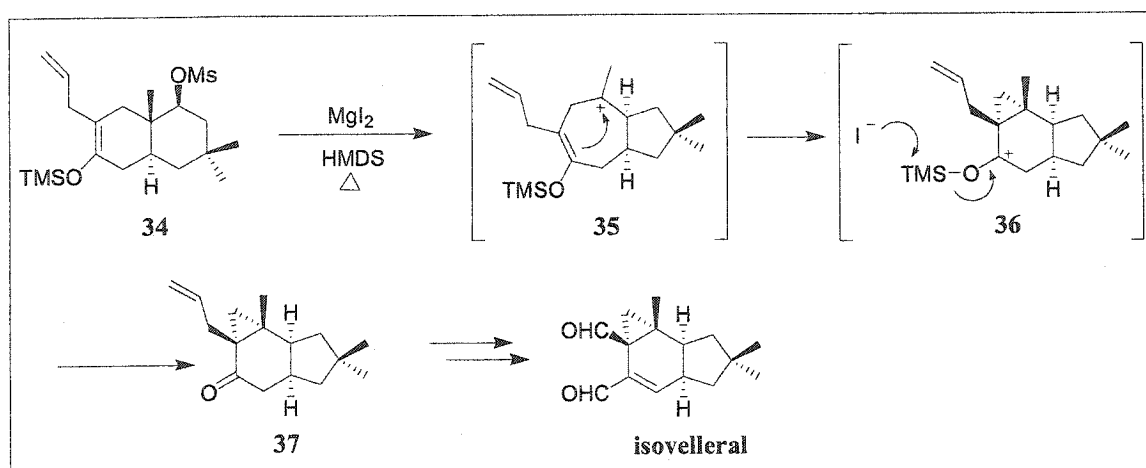
Scheme 8: Synthesis of β -sinensal; Tandem Claisen/Cope Reaction

As shown below, when the macrocyclic aldehyde **32** was heated at 220 °C for 30 hours in a sealed tube it underwent a tandem transannular Diels-Alder/aldol reaction to provide tetracycle **33** as the sole diastereomer, in 81% yield. With the tetracyclic backbone of the molecule in hand, a series of simple transformations were then used to complete the synthesis.



Scheme 9: Tandem Transannular Diels-Alder/Aldol Reaction

In their recent total synthesis of (+)-Isovelleral, Wijnberg and de Groot,¹⁷ made use of a novel tandem rearrangement-cyclopropanation. In this reaction an appropriately functionalized bicyclic octahydronaphthalene was used to not only generate the marasmane core, but to also install all of the stereogenic centers present in the natural product. As shown below, treatment of the silyl enol ether **34** with MgI_2 first gives rearrangement to the tertiary cation **35**. This can then further rearrange via a ring contraction to give cyclopropane **36**, which upon loss of the TMS group gives ketone **37**. Obtaining the complete core of the molecule with one step, only a few transformations are then required to generate the dialdehyde isovelleral.



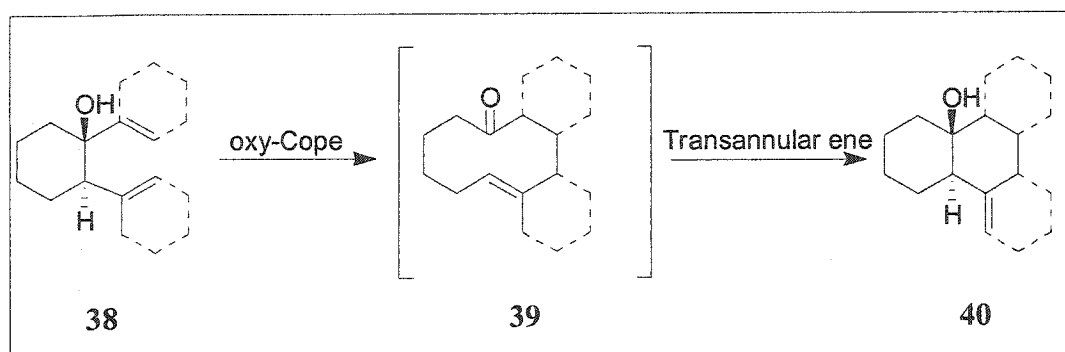
Scheme 10: Total Synthesis of (+)-Isovelleral via tandem Rearrangement-Cyclopropanation Reaction

1.5 Tandem Oxy-Cope/Ene Reaction

As previously mentioned, the principle focus of the Barriault group has been the development of novel methods for creating new carbon-carbon bonds. The aim of this endeavor has been to find new ways of quickly and easily assembling molecules with a high degree of stereochemical complexity.

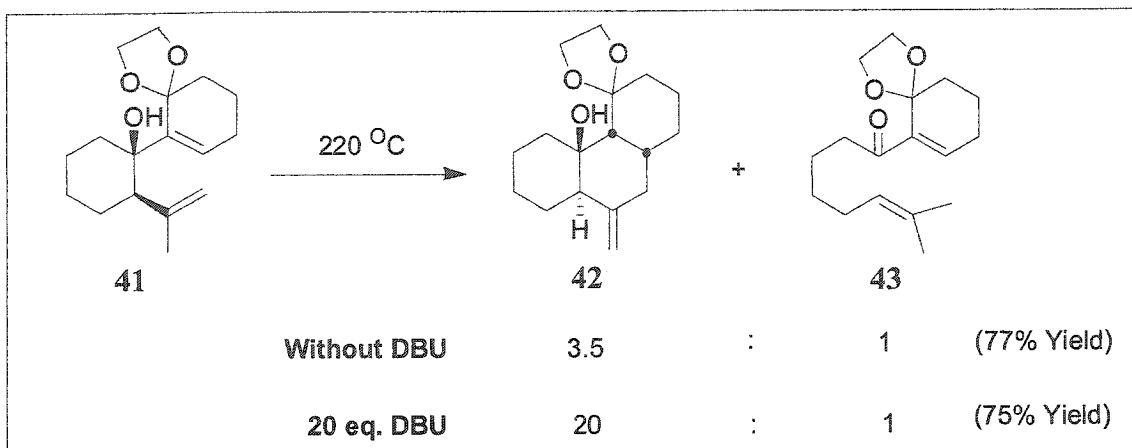
The first methodology to be examined by the Barriault group was the tandem oxy-Cope/transannular ene reaction of 1,2-divinylcyclohexanols.¹⁸ This reaction was first reported by Sutherland¹⁹ as an undesired side reaction of the oxy-Cope rearrangement and others such as Paquette²⁰ and Rajagopalan²¹ have also reported cases of undesired transannular ene byproducts when attempting anionic oxy-Cope rearrangements.

As shown in Scheme 11, early studies by Warrington and Barriault¹⁸ found that upon heating in toluene to temperatures ranging from 180 °C to 220 °C, 1,2-divinylcyclohexanols **38** undergo rearrangement to give polycyclic structures **40** featuring a tertiary alcohol at the ring junction. This is actually a two-step reaction whereby the 1,2-divinylcyclohexanols **38** first go through an oxy-Cope rearrangement to give an intermediate macrocyclic ketone **39**, which then readily undergoes a transannular ene reaction to yield bi- and tricyclic skeletons **40** with high diastereoselectivity.



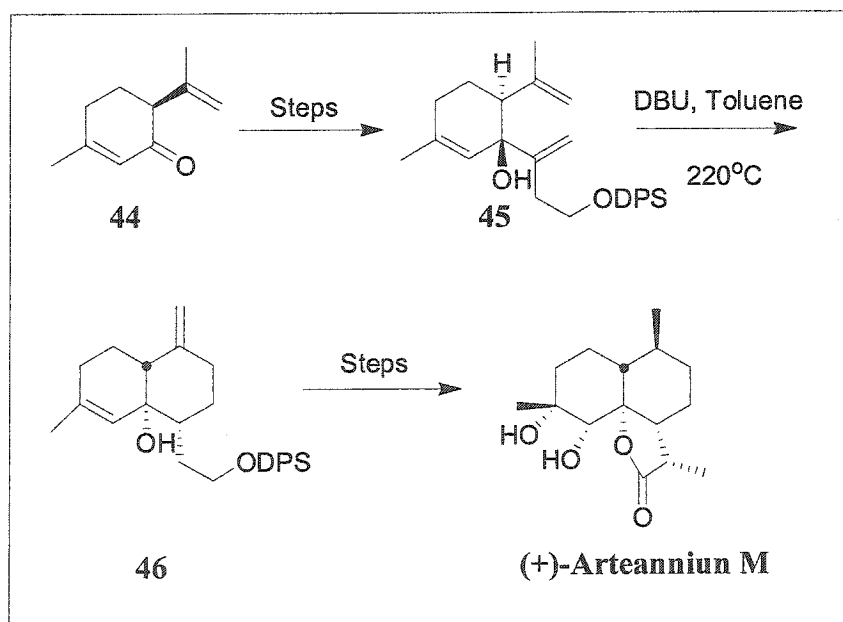
Scheme 11: Tandem oxy-Cope/transannular ene Reaction

One of the early downsides of this methodology was that when the vinyl group attached to the tertiary alcohol was part of a six membered ring, as shown in Scheme 12, a considerable amount of retroene product was also observed.¹⁸ Fortunately, it was discovered that the formation of this side-product could be greatly reduced by the addition of DBU to the reaction.²²



Scheme 12: Competing Retroene Reaction

To showcase the utility of this methodology it was later used as the key-step in the short total synthesis of (+)-Arteannium M.²³ Heating the 1,2-divinylcyclohexanol **45** in toluene to 220 °C in a sealed tube in the presence of DBU provided the bicyclic compound **46** in 55-60% yield, with both high diastereoselectivity (de >98%) and enantioselectivity (ee=78%). Overall, (+)-Arteannium M was synthesized in just 10 steps and 14.1% overall yield from the known ketone **44**. (Scheme 13)

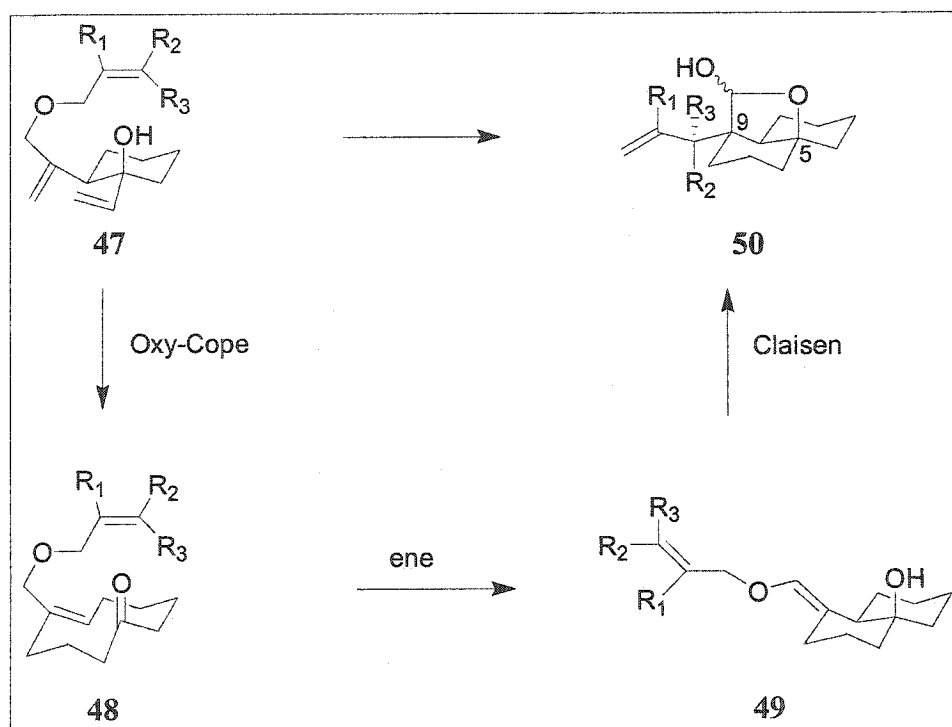


Scheme 13: Total Synthesis of (+)-Arteannium M

1.6 Tandem Oxy-Cope/Ene/Claisen Reaction

After successfully proving the synthetic potential of the tandem oxy-Cope/ene reaction, the group began exploring the possibility of addressing an even greater synthetic challenge; the creation of asymmetric quaternary carbon centers. The result was the discovery of a new tandem reaction, the tandem oxy-Cope/ene/Claisen.

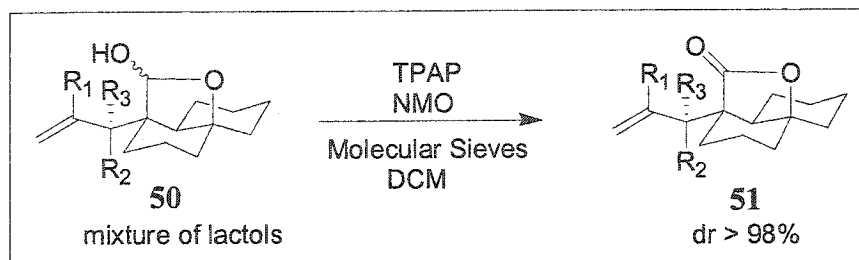
As illustrated in Scheme 14, it was shown that upon heating, 1,2-divinylcyclohexanol allyl and propargyl ethers **47** undergo a cascade of three successive thermal pericyclic reactions to yield bicyclic lactols **50**.



Scheme 14: Tandem Oxy-Cope/Ene/Claisen Reaction

The starting material **47** first undergoes one thermally allowed [3,3] sigmatropic rearrangement to generate the oxy-Cope product **48** in situ. This of course, like the substrates already shown, readily undergoes an ene reaction to give a second intermediate **49**, which is set up to undergo a second [3,3] rearrangement, this time a Claisen rearrangement. The aldehyde obtained readily lactonizes to give the final product **50**, featuring quaternary carbons at C5 and C9.²⁴

In order to determine the diastereoselectivity of the reaction, the mixture of lactols **50** was next oxidized with TPAP to give the corresponding lactones **51**. (Scheme 15) In each case the results indicated the formation of only a single diastereomer (dr > 98%) with yields ranging from good (60%) to excellent (98%)



Scheme 15: Determining The Diastereoselectivity of The Reaction

1.7 Microwave Heating

In the electromagnetic spectrum, microwave radiation is located between infrared radiation and radio waves. This corresponds to wavelengths of 1mm – 1m or frequencies between 0.3 and 300GHz. While many of the band frequencies in this region are used for telecommunications and radar, one of the most popular uses of microwave radiation is for heating materials.²⁵

When a polar liquid, such as water, is placed in a microwave oven, it is subjected to an electric field that rapidly oscillates back and forth. This oscillating field exerts oscillating torques on the polar molecules, continually rotating them back and forth to align their dipole moments with the field direction.²⁶

Microwave frequency, however, is not high enough for the rotation to follow the field. As the dipole re-orientates to align itself with the electric field, the field is already changing and generates a phase difference between the orientation of the field and that of the dipole. This phase difference causes energy to be lost from the dipole by molecular friction and collisions, giving rise to dielectric heating.²⁵

The use of microwave activation by organic chemists, as a non-conventional energy source, has grown steadily since the mid-1980s. In many publications, authors have claimed that microwave irradiation has led to large reductions in reaction times, improved yields, as well as enhanced selectivity in certain instances.²⁷

Unsurprisingly, these claims have led to debates concerning what the exact microwave effects actually are and how they might alter the outcome of a reaction. In their review of microwave-assisted organic synthesis, Lidström *et al* conclude that in most examples the specific microwave effects claimed can be attributed to thermal effects.²⁵ They state that:

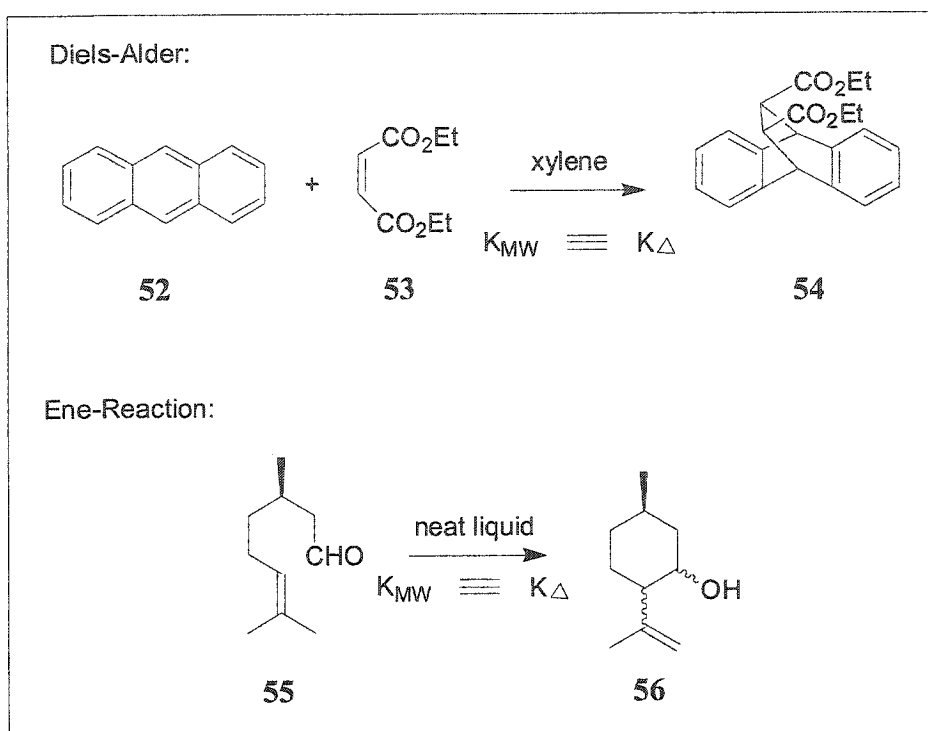
Microwave heating can be very rapid, producing heat profiles not easily accessible by other heating techniques. Experiments performed using microwave-assisted organic synthesis may therefore result in a different outcome when compared to conventionally heated reactions, even if the final temperature is the same.²¹

When using microwave heating, it is often possible for 'hot spots' to be encountered; situations where localized temperatures can actually be much higher than the overall temperature measured in the system

The vast majority of experiments carried out with a microwave heat-source in the Barriault lab, in fact all those described herein, are run in non-polar solvents such as toluene. Such solvents are transparent to microwave irradiation and only weakly absorb microwaves.

In order to actually heat the contents of the reaction vessel, a carboflon™ bar is added. This carboflon bar is a chemically inert fluoropolymer filled with carbon black, a strong microwave absorber. The carboflon™ absorbs the microwave energy and transfers its generated thermal energy to the nonpolar solvent.

It is also important to note that the tandem reactions being studied within the Barriault lab are all comprised of pericyclic reactions such as the Claisen rearrangement, the oxy-Cope reaction, and the ene reaction. These reactions all have isopolar activated complexes which differ very little, or not at all, in charge separation or charge distribution from the corresponding initial reactants. Therefore, ground and transition states have identical polarities; no charges are developed during the reaction path. Because of this, *no specific microwave effects should be expected* for these types of reactions.



Scheme 16: An Absence of Microwave Effects

Although the area still requires a great deal of investigation, studies on the Diels-Alder³⁰ and the ene-reaction³¹ do support the theory. As shown above in Scheme 16, no difference in reaction rate, or in fact even product distribution for the ene reaction [55→56], was observed when comparing conventional heating with microwave irradiation when using non-polar solvent, or no solvent at all.

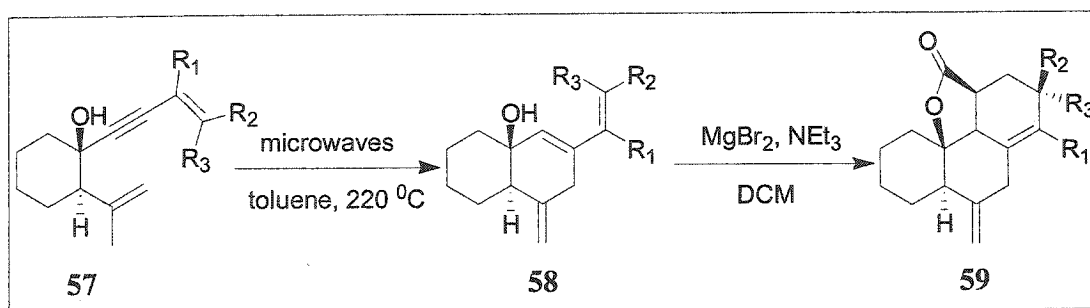
In spite of this many groups still report improved reaction results when using microwave heating as opposed to conventional heating sources. In fact, within the Barriault lab several examples have shown improved yield and a dramatic decrease in reaction time, even when the theory shows that neither solvent, nor reaction-type should support the notion.²²

One explanation currently being examined is the possibility that the surface of the carboflonTM, being used as a heat source, might actually be reaching temperatures much greater than that of the overall reaction vessel. In effect, this could be considered a “hot spot” in the system. As a result, the change in observed reaction times and yields could be attributed to the non-conventional heat profiles obtained within the microwave.

Chapter 2: A Highly Diastereoselective Approach to Polycyclic Molecules

2.1 Aim Of The Project

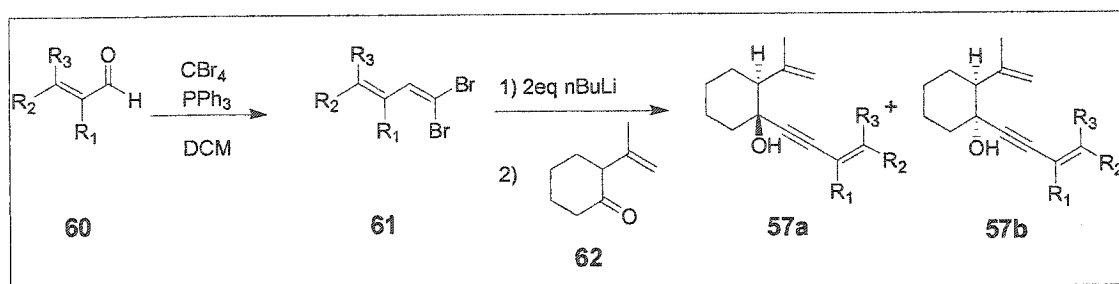
In light of the success of the recently developed tandem reactions^{18,24} and hydroxy-directed Diels-Alder reaction¹², it was envisioned that a combination of these two techniques might prove to be a fast and efficient method for generating polycyclic compounds of significant stereochemical complexity. As outlined in Scheme 17, the oxy-Cope/ene product of an ene/yne substituted cyclohexanol, such as **57**, would provide a diene **58** with a properly placed tertiary alcohol to allow for a tether controlled Diels-Alder reaction to take place. In the end, this new methodology would permit the rapid generation of steroid or diterpene skeletons with high diastereoselective control by means of two simple reactions.



Scheme 17: Oxy-Cope/Transannular Ene Followed by a Tether Controlled Diels-Alder

2.2 Preparation of the Diene Precursors

In order to investigate the tandem-reaction component of this methodology, a series of 1-alkynyl-2-vinyl-cyclohexanols **57** needed to be prepared. The first approach to these molecules was to begin with readily available α,β -unsaturated aldehydes. Using the methodology of Corey and Fuchs²⁸, these aldehydes **60** were first converted to their respective dibromides **61**, which upon treatment with one equivalent of *n*-butyllithium undergo a carbene rearrangement to yield a terminal alkyne. However, by adding a second equivalent of *n*-butyllithium to the reaction, the terminal alkyne can then be deprotonated and used to alkylate the known ketone **62**, giving a diastereomeric mixture of alcohols **57a** and **57b**.



Scheme 18: Corey-Fuchs Approach to Diene Precursors

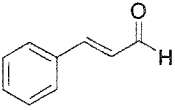
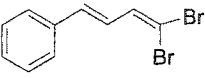
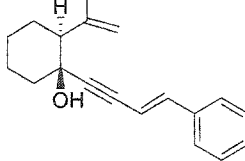
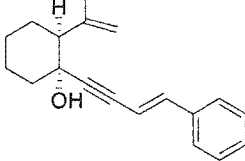
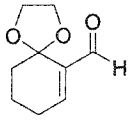
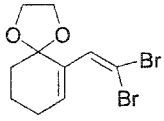
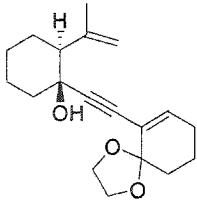
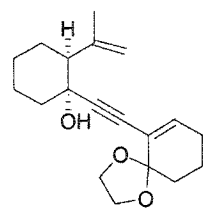
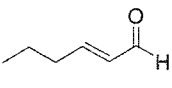
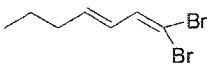
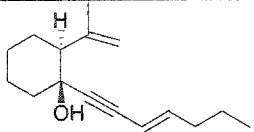
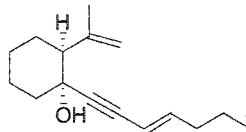
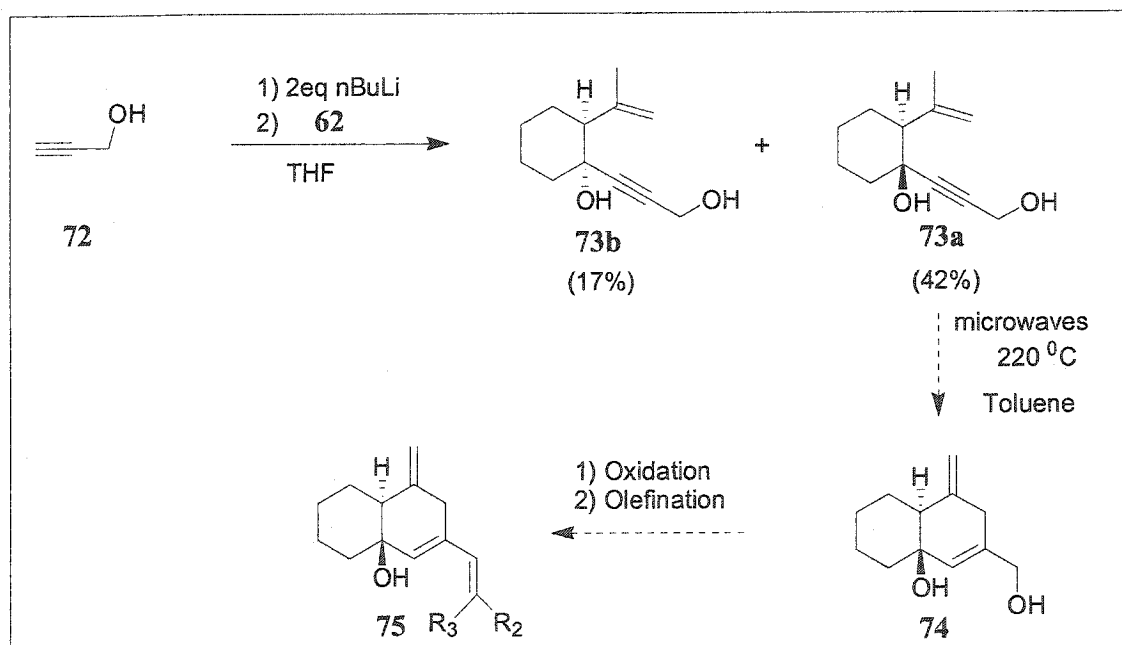
Aldehyde	Dibromide (Yield)	Cyclohexanol (Yield)	
 63	 64	 65a (42%)	 65b (33%)
 66	 67 (65%)	 68a (41%)	 68b (38%)
 69	 70 (76%)	 71a (29%)	 71b (42%)

Table 1: Corey-Fuchs Products

This strategy was used on a few α,β -unsaturated aldehydes to give the cyclohexanols listed above in Table 1. Other examples were also examined; however, the ease of formation, as well as stability of the dibromides **61** once formed showed some dependence on the nature of the aldehyde used. While aromatic, or highly conjugated aldehydes, gave relatively stable dibromide products, aliphatic or low molecular weight

aldehydes tended to be less reactive and their products were usually unstable. Preparation of a diene lacking substitution was attempted using this method; however, neither the preparation of the dibromide **61**, nor alkylation of the ketone **62** proceeded cleanly or in significant yield when acrolein (**60**, R₁, R₂, R₃ = H) was used as a starting aldehyde.

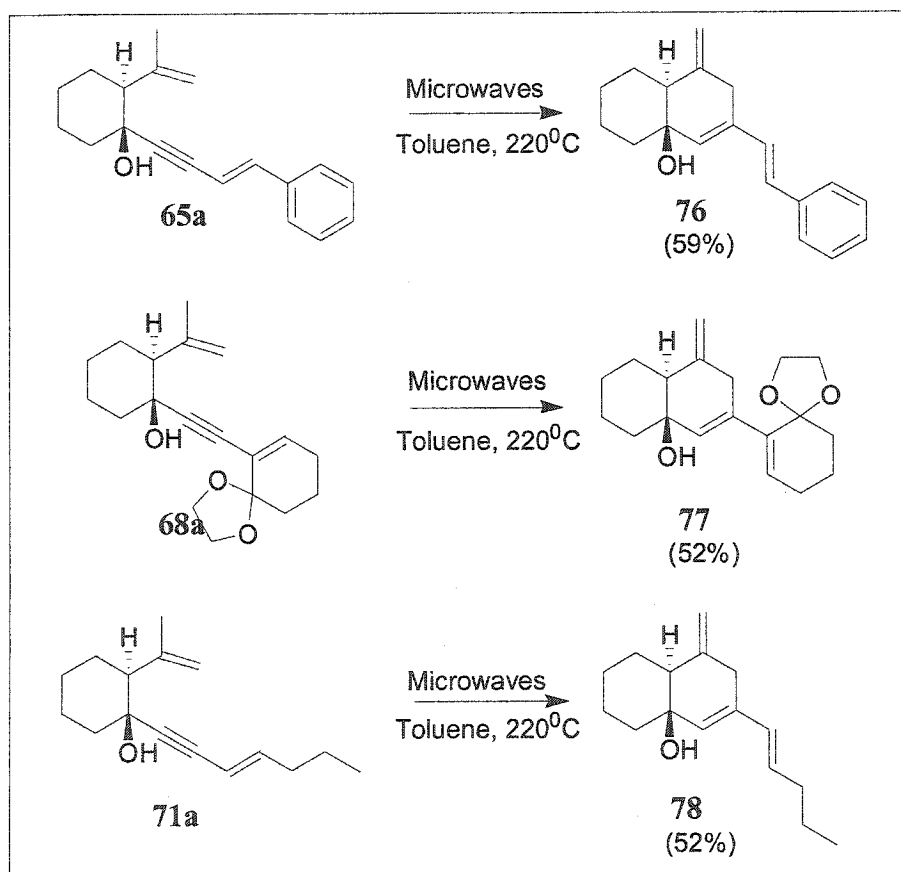
Therefore, the unsubstituted diene was approached from an alternative route. Propargyl alcohol **72** was first treated with 2 equivalents of *n*BuLi at -78 °C to generate the C-O-dianion; this was then quenched with ketone **62** to give a mixture of diastereomers **73a** and **73b**. Best results were obtained when the THF and propargyl alcohol **78** were freshly distilled, the ketone **62** was highly pure, and the scale was less than 10 mmol. Once the desired cyclohexanol **73a** was isolated by flash chromatography, oxidation, followed by Wittig or Horner-Wadsworth-Emmons condensation, could then be employed, before or after the tandem Oxy-Cope/transannular ene reaction, to give a variety of dienes **75**. (Scheme 19)



Scheme 19: Preparation of Unsubstituted Diene

2.3 Preparation of the Dienes

The conversion of the 1-alkynyl-2-vinyl-cyclohexanols **65a**, **68a**, and **71a** to their respective dienes was accomplished by heating with either a sealed tube and wax bath, or more commonly, microwave irradiation. The general protocol for these reactions involved dissolving between 10 to 200 mg of the starting material in 12-20 mL of toluene and adding 5 to 20 equivalents of DBU as well as the carboflon. The mixture would then be degassed with argon for 10 minutes and then heated with microwaves to 220 °C for between 30 minutes and 3 hours, depending on the amount of substrate and its reactivity. Although precise conditions varied with each molecule, in the end each of the dienes was obtained with high diastereoselectivity and in fair yields. (Scheme 20)



Scheme 20: Preparation of Dienes

Shown in Figure 1, the mechanism for this reaction accounts for the exclusive formation of a *trans* ring-junction in these molecules. The ene/yne substituted cyclohexanol **57a** first undergoes a thermal oxy-Cope rearrangement to produce the

allene-enol **79**. This readily tautomerizes to give the ketone intermediate **80** in situ, which undergoes a transannular ene reaction to yield the diene **58** as a single diastereomer. The exclusive formation of the *trans* ring junction is attributed to the E-olefin geometry of the macrocycle (**79**, **80**), a direct result of the anti relationship between the isopropenyl and alkynyl substituents in the starting material.

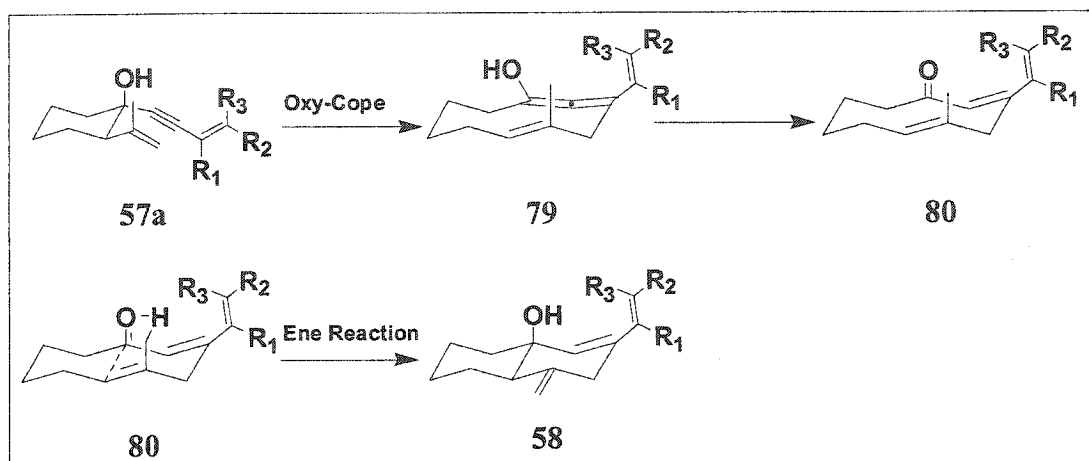
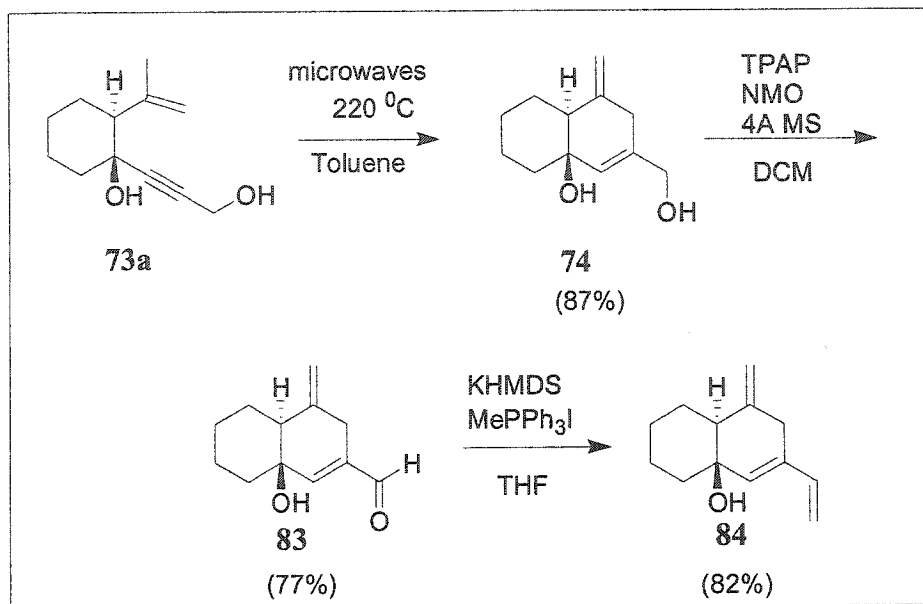


Figure 1: Mechanism For The Tandem Oxy-Cope/ene Reaction

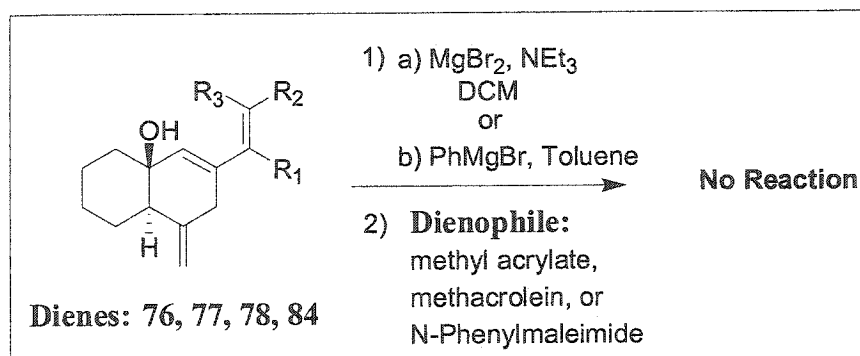
For the alternative approach, diol **73a** was also heated in the microwave to give the *trans*-decalin product **74** in 87% yield. This was then converted to the simplest diene of the series ($R_1, R_2, R_3 = H$) using two simple transformations. The primary alcohol was first oxidized using either TPAP/NMO or Dess-Martin periodinane to give aldehyde **83**; after a quick workup, the crude aldehyde was then subjected to Wittig condensation with $MePPh_3I$ to provide diene **84**. (Scheme 21)



Scheme 21: Second Approach to Diene System

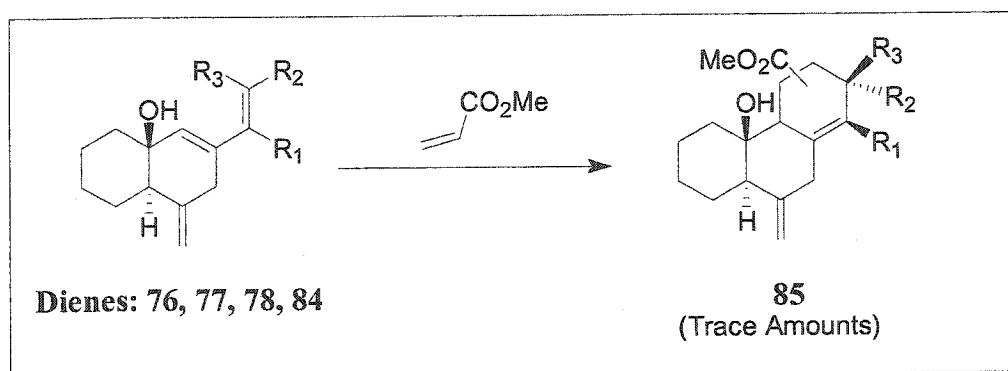
2.4 Hydroxy-Directed Diels-Alder Results

Having successfully prepared a small series of dienes using the oxy-Cope/ene reaction, the Diels-Alder component of the project was next to be examined. Surprisingly, initial attempts at a hydroxy-directed Diels-Alder reaction using two well proven protocols¹² were completely unsuccessful. Dienes **76, 77, 78, 84**, were each treated to conditions 1 a) or 1 b) and then subjected to a wide variety of dienophiles. (Scheme 22) In no case was any of the desired Diels-Alder adduct ever observed by TLC, GC/MS, or NMR. Even treatment with a powerful dienophile like N-phenylmaleimide proved to be unsuccessful.



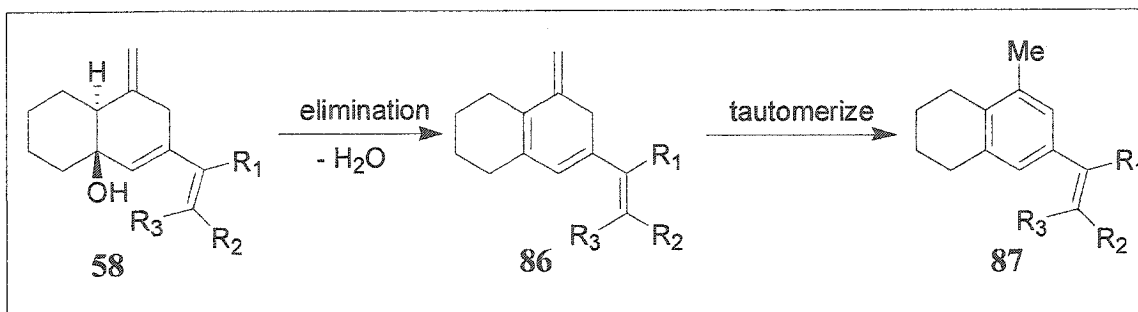
Scheme 22: Attempts at a Hydroxy-Directed Diels-Alder

In some cases when methyl acrylate was used as a dienophile, trace amounts of an *un-lactonized* Diels Alder product **85**, could be observed by GC/MS or proton NMR. However, these products were never isolated in sufficient quantity or purity for definitive structure assignment and characterization. It is therefore not known whether any regio- or stereofacial control was attained. Simple model studies and comparison with previous work¹¹ suggested the desired product should lactonize.



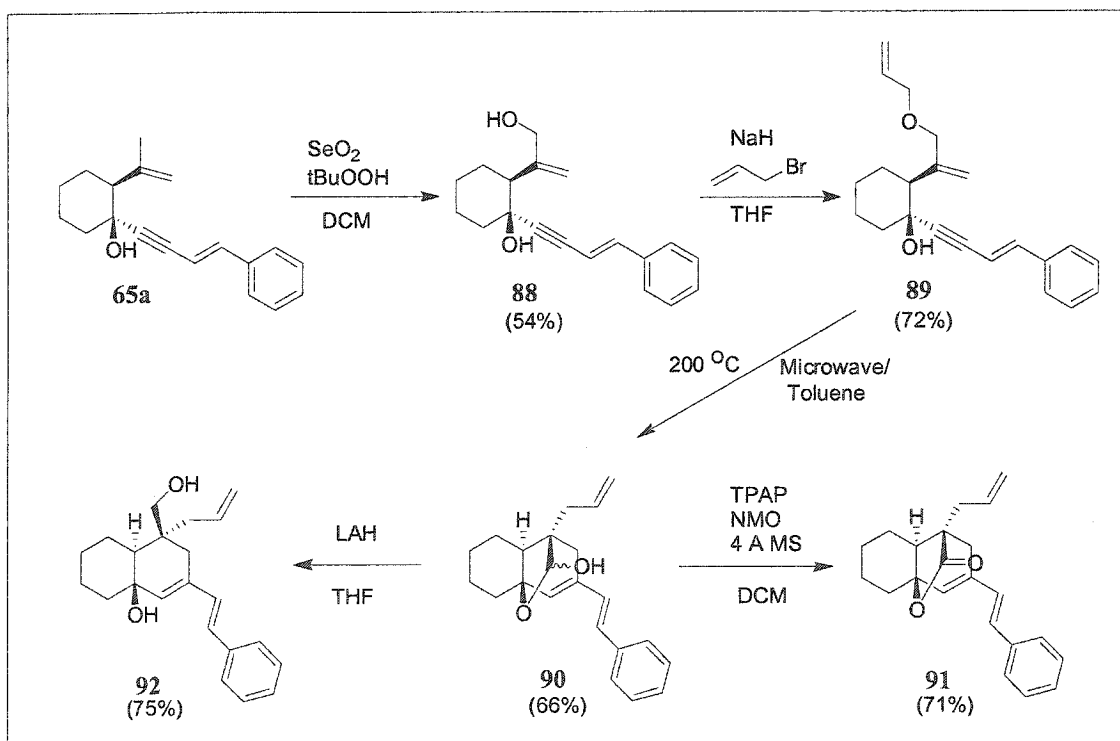
Scheme 23: Trace Amounts of Diels-Alder Products

Upon stirring the reaction for prolonged amounts of time, the diene would usually begin to decompose, resulting in a product which was less polar than the starting material and very UV-active in the TLC. Upon isolation of these products, identification by GC/MS and ¹HNMR revealed an aromatic product, presumably formed by the elimination of water. As shown below in Scheme 24, the tertiary alcohol functionality in all of these compounds can be readily eliminated under mildly acidic conditions. Once this occurs, the molecule **86** can tautomerize to give the thermodynamically favoured aromatic ring **87**.



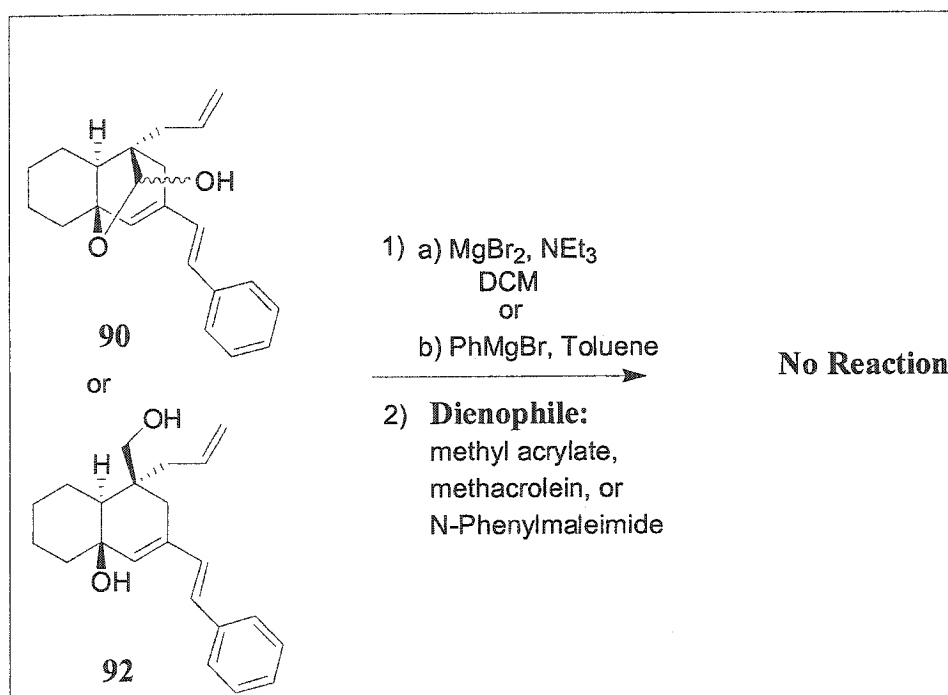
Scheme 24: Aromatization of Dienes

It was believed that this decomposition route could be avoided by replacing the exocyclic double bond with a quaternary centre. This was accomplished using the more recently developed oxy-Cope/ene/Claisen tandem reaction.¹⁷ Subjecting the already prepared alcohol **65a** to an allylic oxidation using SeO_2 , diol **88** could be obtained and then selectively allylated at the newly formed primary alcohol to give the tandem reaction precursor **89**. Subjecting **89** to microwaves and heating to 200°C gave lactol **90** as a diastereomeric mixture which could be resolved by oxidizing to the lactone **91**, or reducing to the diol **92**. (Scheme 25)



Scheme 25: Oxy-Cope/ene/Claisen Method of Generating Dienes

Shown in Scheme 26 below, dienes **90** and **92** were both investigated for reactivity under the hydroxy-directed Diels Alder conditions. It was unknown what directing effects that lactol **90** might have should a tethered Diels-Alder be possible. Diol **90** would also present an interesting case, as two tether sites were now available. Unfortunately, questions of the stereochemical outcome would not be answered. These dienes proved to be completely unreactive, and in each case only starting material was ever observed or recovered.



Scheme 26: Tethered Diels-Alder Results

2.5 Explanation of Results

An interesting observation was made with the detection by GC/MS of trace amounts of Diels-Alder products on some occasions using dienes **77** and **84**. However, in contrast to previous work in this area,⁵ the identified masses suggested that the expected lactonization was not occurring. An obvious reason for this might be that in the rare instance that a cycloaddition did occur, it either occurred with the wrong regiochemistry or from the face opposite to the alkoxide tether.

Careful examination using molecular models eventually led to the hypothesis that perhaps locking the tertiary alcohol axially at the *trans* ring-junction of the decalin framework was a problem. Comparison with the six-membered single-ring systems previously used by Thomas and Clement¹¹ suggested that a bit more flexibility in the molecule might be required to permit a proper approach by the dienophile. This hints that perhaps using similar dienes with a *cis* ring-junction might be more favourable. (Figure 2)

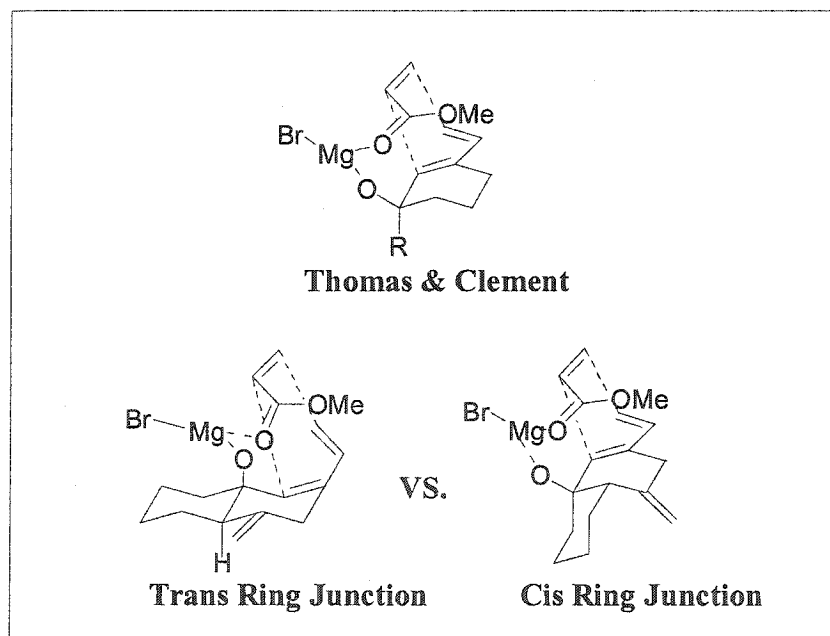


Figure 2: Comparison with Previous Work

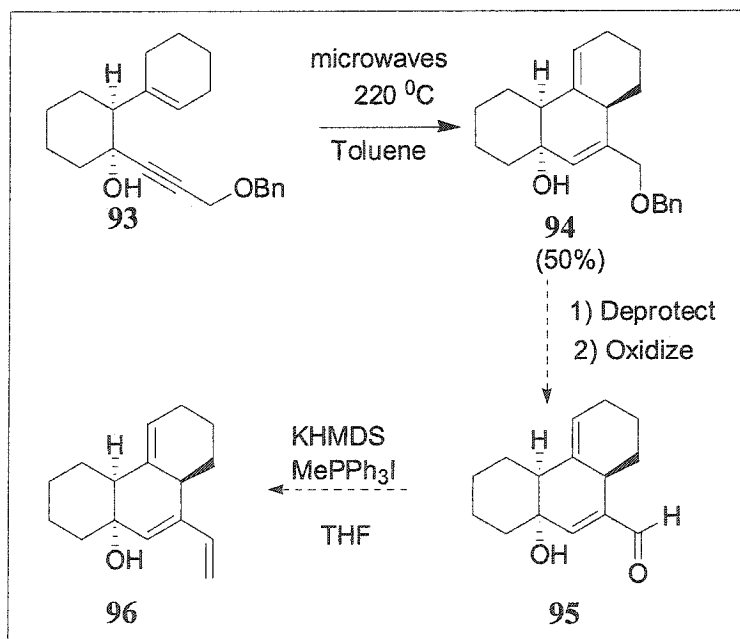
Unfortunately, preparing dienes featuring a *cis* ring-junction was not as straightforward as it was for the corresponding cases containing a *trans* ring-junction. Oxy-Cope/ene precursors **65b**, **68b**, and **71b** were all unreactive after up to 3 hours in the

microwave at 220 °C, while diol **73b** degraded entirely after 1 hour giving a mess of products by TLC.

2.6 Future Directions

While the formation of dienes featuring a *cis* ring-junction was not favourable using the ene/yne substituted cyclohexanols available, there is some favourable precedence to warrant future investigation. Previous work in the Barriault lab has shown that with prolonged heating in the microwave, a decalin with a *cis* ring-junction can be obtained in modest amounts.

In his M.Sc.thesis,¹⁵ Deon showed that he was able to make tricyclic compound **94** featuring a *cis* ring-junction when the oxy-Cope/ene precursor **93** was heated for 3 hours in the microwave. Upon further investigation this result was reproducible; but as previously observed, after as long as 9 hours in the microwave at 220 °C, only a 50% yield (based upon recovered starting material) of the desired **94** was obtained. (Scheme 27)



Scheme 27: Preparing a Diene Featuring a Cis-Ring-Junction

If this yield could be improved, and the method extended to further examples, this might prove to be a beneficial new direction for the project. For example, if the benzyl

group were to be replaced with a PMB group, then after a simple deprotection with DDQ, the primary alcohol could be liberated without disturbing the rest of the molecule. Following with an oxidation/Wittig procedure similar to that shown previously, the end result would be a tri-cyclic diene like **96**, featuring a *cis* ring-junction. Being less rigid than the previously examined dienes with a *trans* ring-junction, molecules resembling **96** may be more suitable for a hydroxy-directed Diels-Alder reaction.

Chapter 3: Application of the Tandem Oxy-Cope/Ene/Claisen Reaction Towards the Total Synthesis of a Rosane

3.1 Background:

To demonstrate its synthetic usefulness, it was decided to apply the tandem Oxy-Cope/Ene/Claisen reaction toward the total synthesis of a diterpene. Recently isolated²² from the liverwort *Gackstroemia decipiens*, the rosane **97** features several structural challenges that could be readily addressed by the newly developed tandem reaction. (Figure 3)

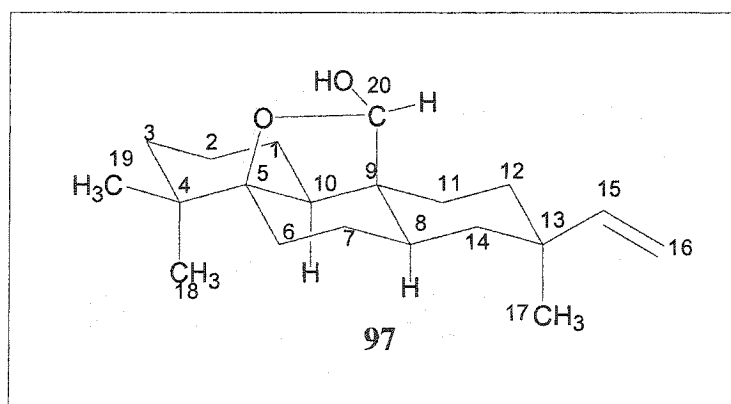
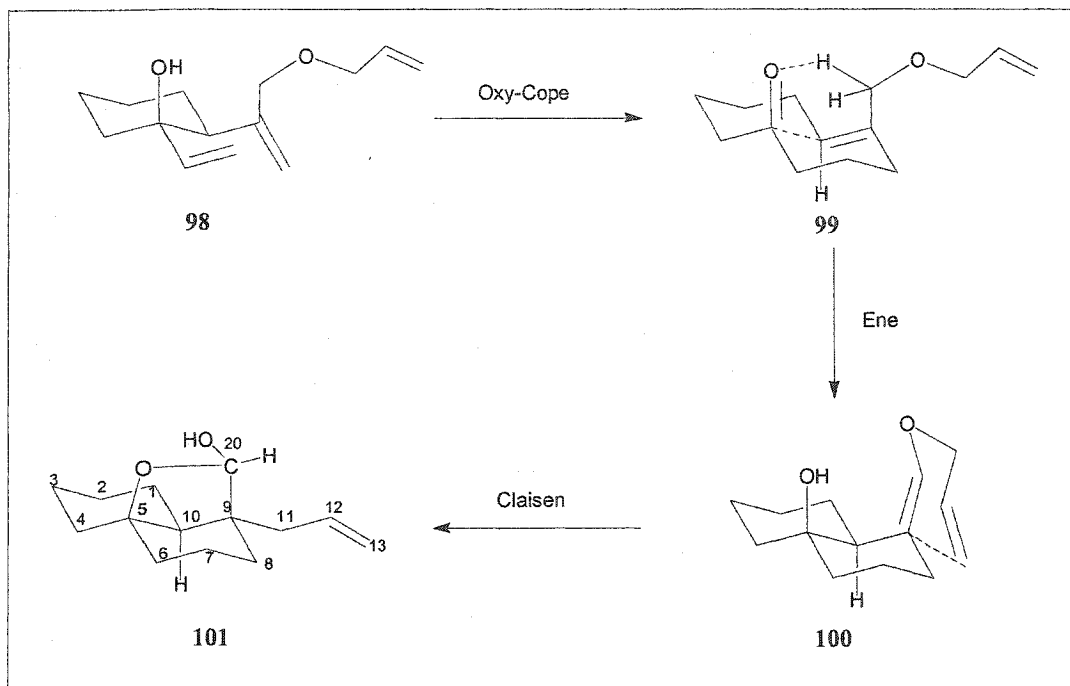


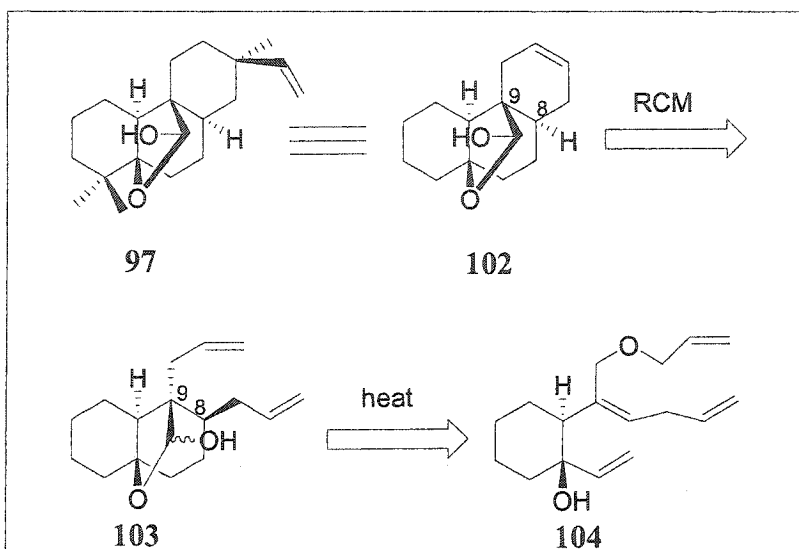
Figure 3: 3.2.5. 5 β ,20-Epoxy-hydroxy-ros-15-ene

Based upon previous work in the lab by Denissova¹⁷, it was known that the tandem oxy-Cope/Ene/Claisen reaction would provide a quick route to the *trans*-decalin skeleton containing the desired C9 quaternary centre as well as the C20 lactol. (Scheme 28) Further investigation would be required to determine whether or not the reaction would be amenable to the incorporation of functionality at C8 without having a negative impact on the diastereoselectivity. If so, this methodology would prove to be a reliable route to not only the rosane **97**, but to a wide variety of diterpenoids as well.



3.2 Retrosynthetic Analysis

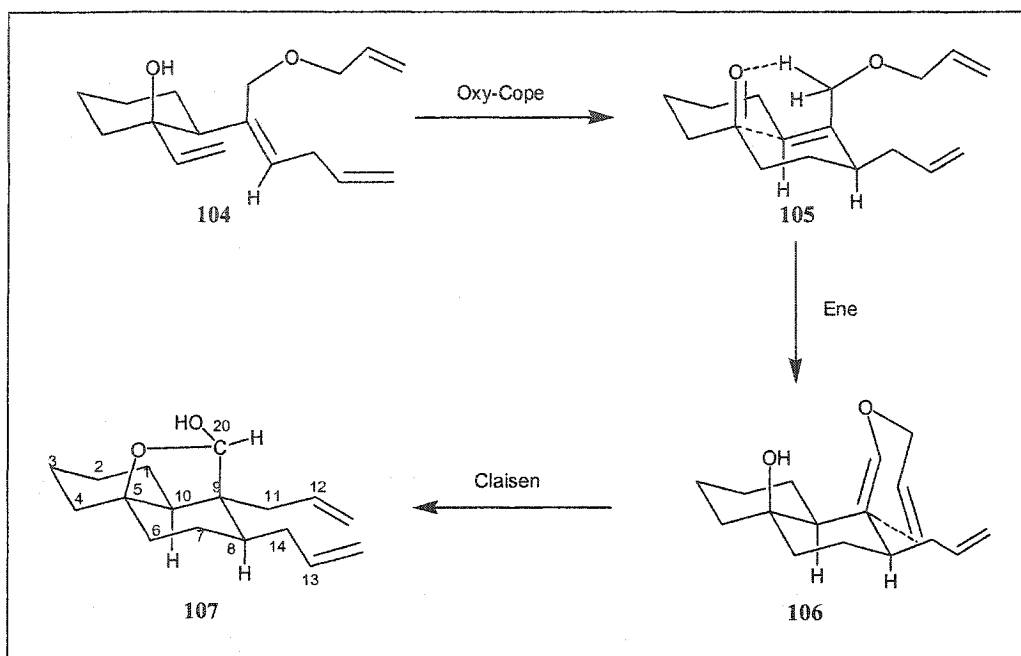
Before tackling the natural product itself, it was decided to simplify the problem by first working towards the core of the molecule. By removing the C4 geminal dimethyls as well as the vinyl and methyl groups at the C13 stereocentre, one is left with a simple tetracyclic structure **102**, which should be available in essentially two steps from the alcohol **104**. A ring-closing metathesis of **103** was not a major concern; however, introduction of the C8 stereocentre was an issue that had not previously been examined. It was hoped that the addition of an allyl substituent at C8 in **103** would not complicate the reactivity or stereoselectivity of the three-step tandem sequence. (Scheme 29)



Scheme 29: Retrosynthetic Approach to the Rosane Core

Preliminary examination of the issue using molecular models appeared to favour the desired C8 and C9 stereochemistry. (Scheme 30) Upon heating, ether **104** should first undergo an oxy-Cope reaction to give, after tautomerization, the macrocyclic ketone **105**. This would ideally prefer to adopt the configuration shown below, placing the C8-allyl group in an equatorial position and undergoing a transannular ene reaction to give the intermediate enol ether **106**.

This would then be properly setup to next undergo a Claisen rearrangement via a chair-like transition state, which should preferentially proceed anti to the bridgehead alcohol at C5 to afford the desired bicyclic lactol **107**.

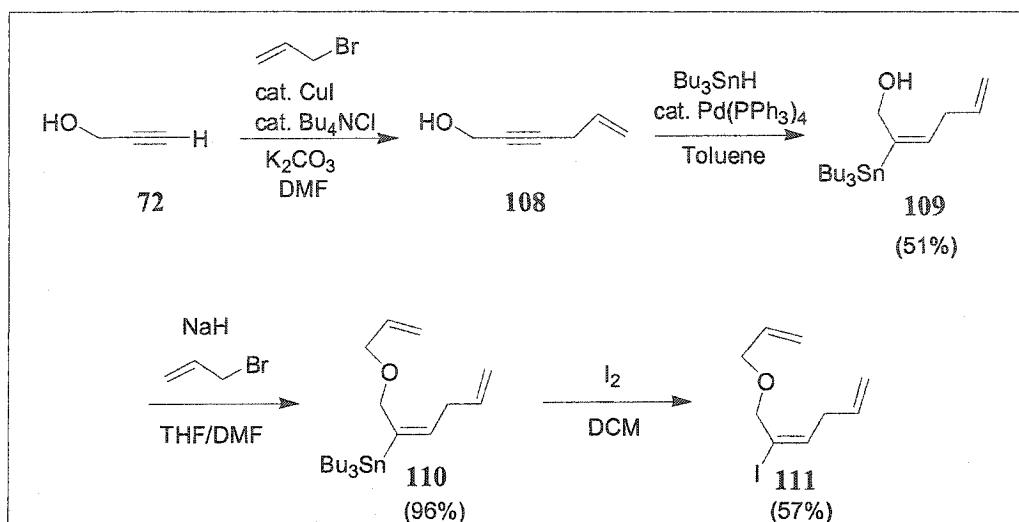


Scheme 30: Predicted Stereochemical Outcome of Oxy-Cope/Ene/Claisen Reaction

3.3 Synthesis of a Divinyl-Cyclohexanol

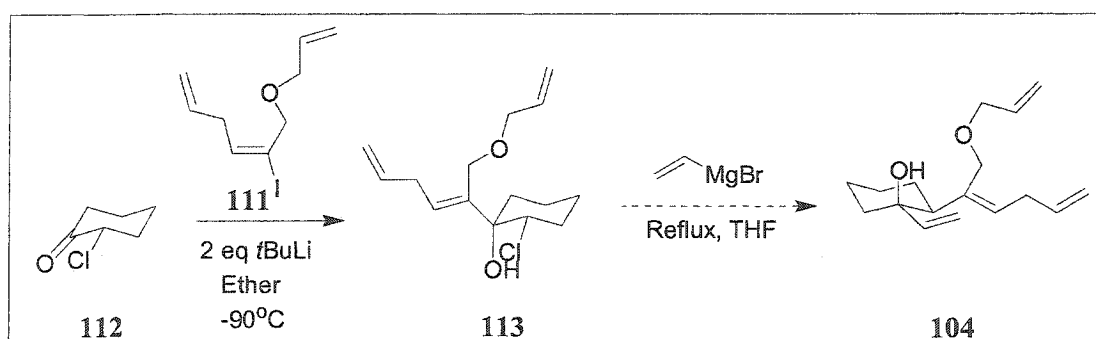
In planning the synthesis of the tandem reaction precursor **104**, it was decided that the simplest disconnection would be a cleavage of the large side chain from the six-membered ring. With this, a variety of coupling strategies could then be examined for placing the substituted vinyl group on the ring.

Shown in Scheme 31, synthesis of the side-chain itself was relatively easy. To begin, propargyl alcohol **72** was selectively C-allylated using a Cu(I) catalyst and solid-liquid phase transfer conditions.³⁰ Directed addition of Bu₃SnH with catalytic palladium then gave the preferential formation of vinyl-stannane **109**. To complete the side-chain, the primary alcohol was next deprotonated with NaH and then capped with an allyl group to give the stannane **110**. In the event that the tin-substituted species was of no use, it could readily be converted to its iodo-analogue. Stirring compound **110** in DCM with 1.2 equivalents of I₂ for five minutes readily gave the unstable vinyl iodide **111**. Because of the general instability of this compound, it was always prepared and purified immediately before its use.



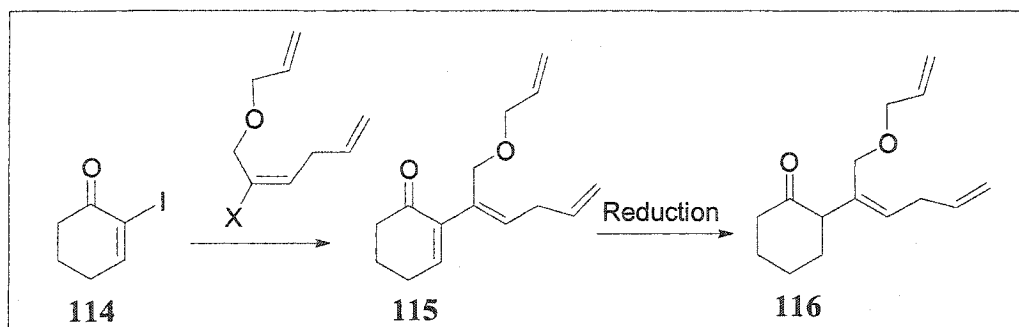
Scheme 31: Preparation of the Side-chain

Several approaches were considered for attaching the side-chain to the cyclohexanol, using either vinyl-stannane **110**, or vinyl iodide **111**. The original approach considered was to make use of an alkylation-1,2-rearrangement protocol starting with chloroketone **112**.³¹ Metal-halogen exchange was accomplished by treating vinyl-iodide **111** with 2 equivalents of *t*BuLi in THF and $-90\text{ }^{\circ}\text{C}$, and addition of chloroketone **112** to the reaction mixture afforded a vinyl alcohol **113**. However, the attempted 1,2-rearrangement by treatment with vinyl magnesium bromide was largely unsuccessful. In the end, the approach was abandoned because of its low yields and poor reproducibility. (Scheme 32)



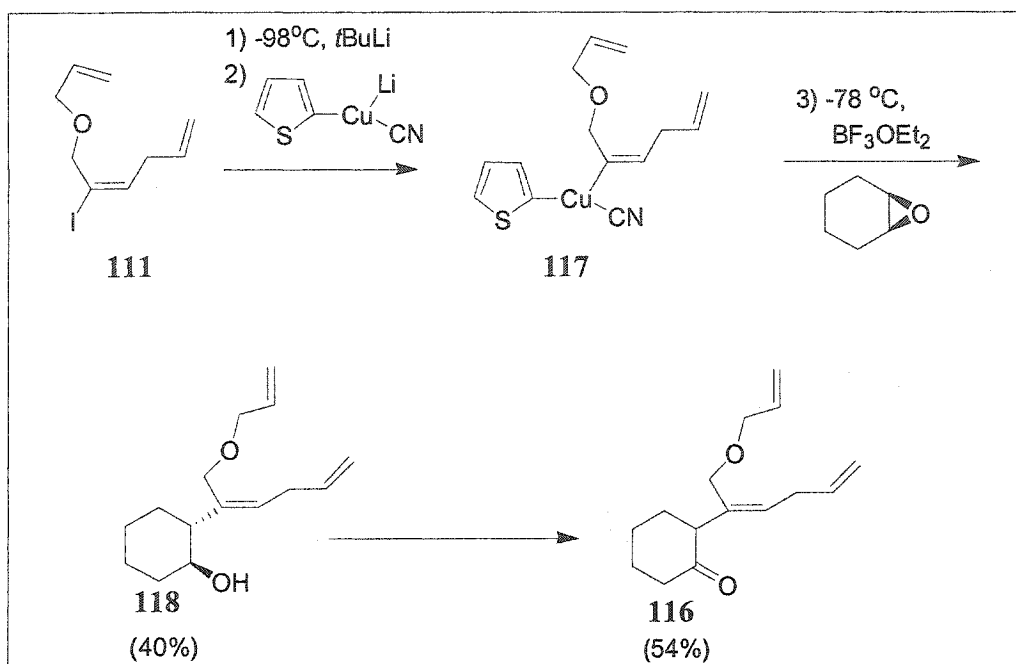
Scheme 32: Attempted 1,2-Rearrangement

A second approach considered was to attempt either a Stille or Negishi coupling reaction with an iodo-enone **114**, followed by a reduction of the conjugated double bond. (Scheme 33) These two approaches were both already under investigation in the lab, but unfortunately the results were not encouraging. While coupling reactions were successful with simple substrates, the presence of additional substituents on the vinyl-tin or vinyl-iodo compounds appeared to dramatically reduce the reactivity.



Scheme 33: Stille or Negishi Coupling Strategy

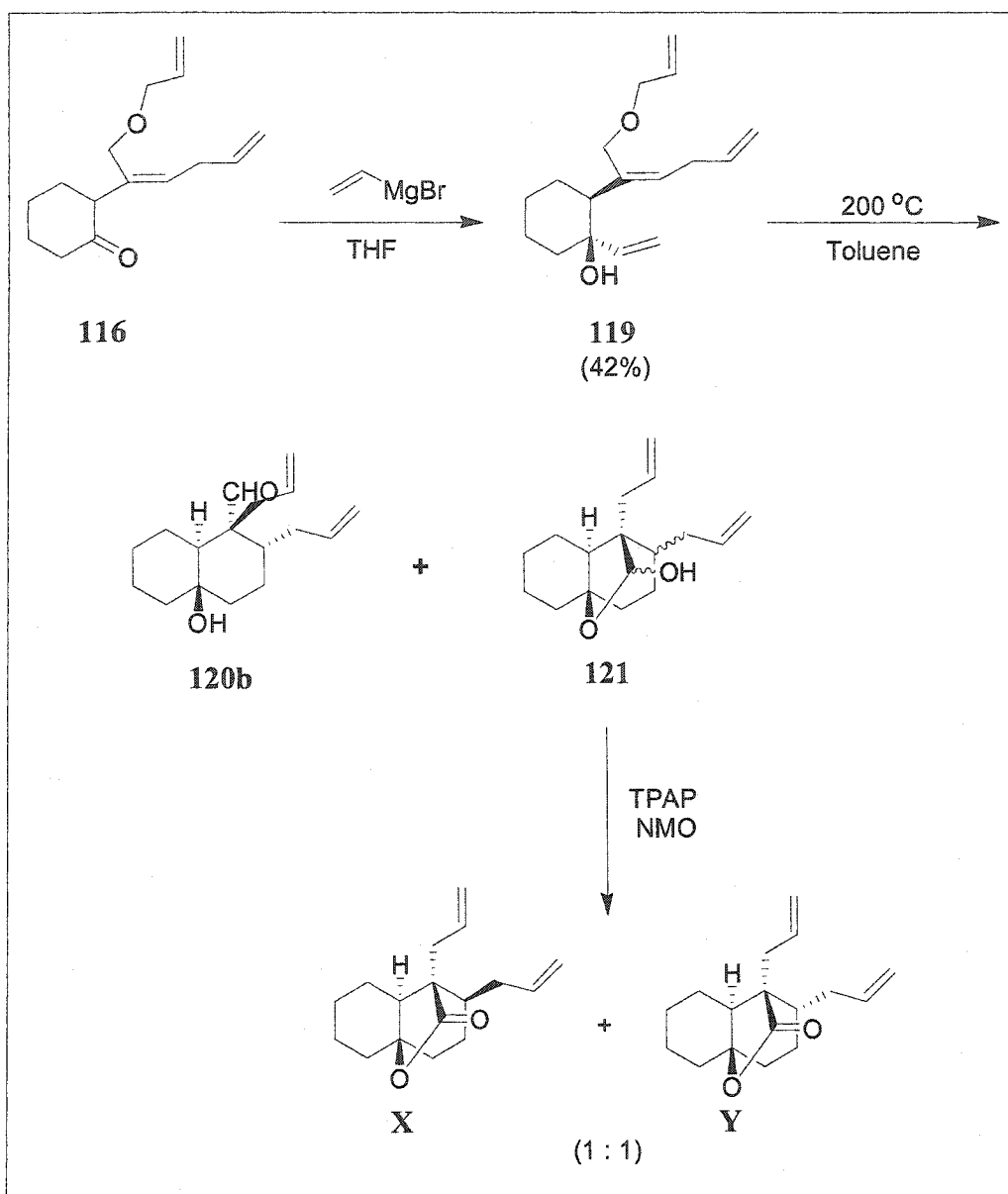
In the end, it was decided to attempt an epoxide opening strategy to obtain the desired cyclohexanol **104**. The vinyl iodide **111** was first subjected to halogen metal exchange, and then treated with 2-thienyl-lithiumcyanocuprate to form the higher order cuprate **117**. To this was added cyclohexene oxide and an equivalent of the Lewis acid $\text{BF}_3 \cdot \text{OEt}_2$ to promote epoxide opening. Following the workup and column chromatography, the desired alcohol **118** was obtained in modest yields. This could then be subjected to either TPAP or Dess-Martin oxidation to give the desired ketone **116**. (Scheme 34)



Scheme 34: Epoxide Opening Strategy

3.4 Tandem Oxy-Cope/Ene/Claisen Results

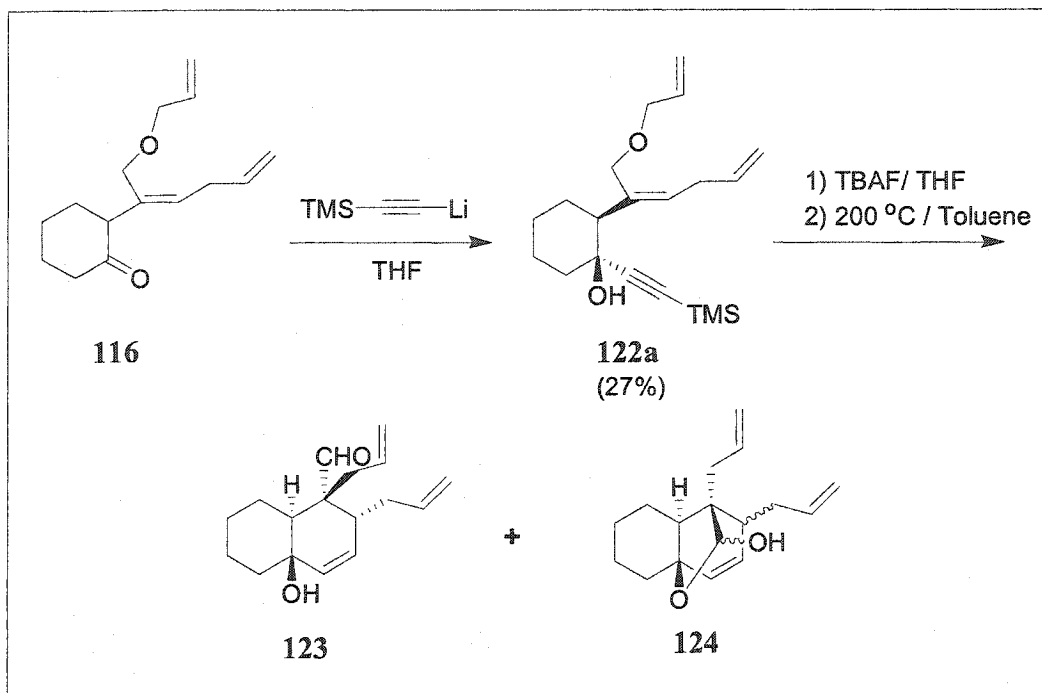
Ketone **116** was next treated with vinyl magnesium bromide to afford tertiary alcohol **119**. This was then placed in a microwave cell containing a carboflon, diluted with toluene, and heated to 200°C for 30 minutes. Subsequent examination of the reaction by TLC showed complete conversion of the starting material to two new spots, both of lower R_f . After isolation of the two spots, $^1\text{H NMR}$, GC, and GC/MS studies revealed that the top spot was in fact an aldehyde, believed to have the stereochemistry shown in compound **120b**. The bottom spot was determined to be a mixture of lactols **121** which upon oxidation gave a 1:1 mixture of lactones **X** and **Y**. (Scheme 35)



Scheme 35: Oxy-Cope/Ene/Claisen Results

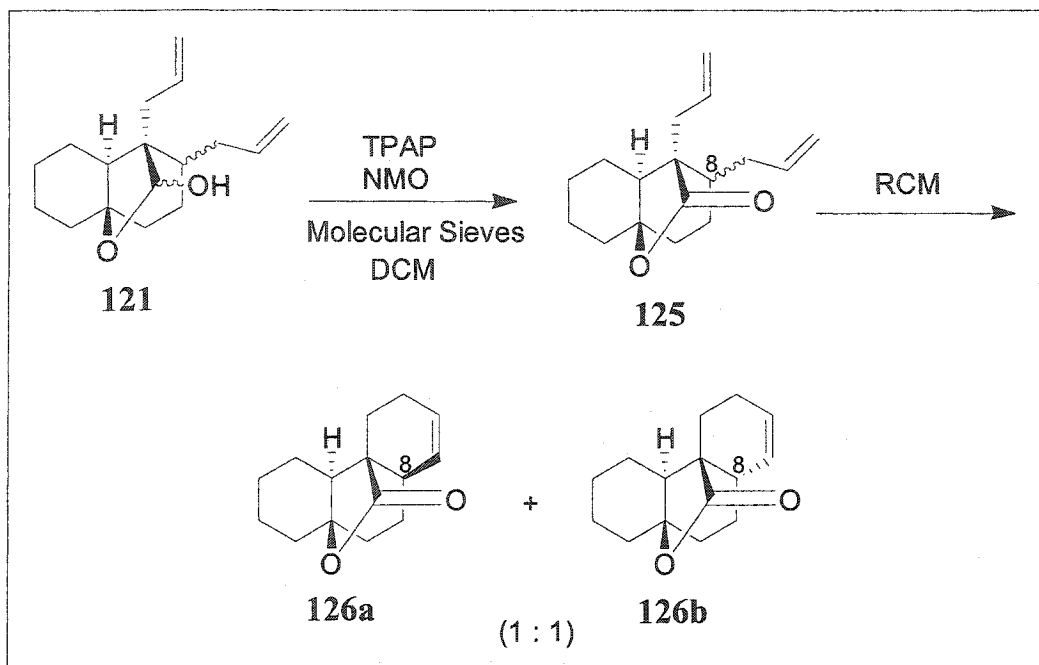
In repeating the experiment with an ethynyl substituent in place of the vinyl, it was hoped that the macrocyclic ketone intermediate might become slightly more rigid, and less likely to invert prior to the ene reaction, resulting in improved diastereoselectivity. Ketone **116** was treated with a TMS-ethynyl-lithium nucleophile to give a mixture of alcohols from which the desired diastereomer **122a** was isolated by column chromatography. The silyl-appendage was then cleaved with TBAF and after purification the resulting product was subjected to heating in the microwave. (Scheme 36)

The result was once again the complete conversion of starting material to two new spots in the TLC, the second of which, once again appeared to be a mixture of products upon examination by GC/MS. Unfortunately, due to the small scale of the reactions, and the difficulty of purification, an accurate determination of product ratios and yields was not obtained at the time.



Scheme 36: Similar Oxy-Cope/Ene/Claisen Results

In spite of the non-selectivity of the tandem oxy-Cope/Ene/Claisen reaction, the diastereomeric mixture **121** was subjected to further study. As previously mentioned, upon oxidation of the lactol mixture **121** with TPAP it was confirmed by GC and GC/MS that there was in fact a mixture of C8 epimers, in almost a 1:1 ratio. While the tandem reaction had failed in terms of diastereoselectivity, it was decided to at least qualitatively examine the last step of the project. When the lactone **125** was treated with Grubbs catalyst in DCM, a ring closing metathesis was successful, resulting in the formation of the tricyclic molecule **126**. Examination by GC, GC/MS and ¹HNMR confirmed the success of the ring-closure, but once again indicated a 1:1 mixture of diastereomers. (Scheme 37)



Scheme 37: Ring Closing Metathesis

3.5 Explanation of Results

In order to understand where the diastereoselectivity of the reaction was lost, it was necessary to further examine the mechanism of the reaction. To begin with, the divinyl cyclohexanol should undergo an oxy-Cope rearrangement to produce a macrocyclic ketone, after tautomerization. This ketone however, can adopt one of two interconvertible conformers, **A** or **B**. In conformer **A**, there is a unfavourable gauche-like interaction between the R group and the ether chain, while in conformer **B**, the R group occupies an axial position on the ring. (Scheme 38)

It was hoped that the equilibrium between the two conformers would lie to the left, favoring conformer **A**. Conformer **A**, could then undergo the transannular-ene reaction shown to give the trans-decalin **128**, where R would be occupying an equatorial position. If conformer **B** were to further react, it would provide intermediate **129** where R is now in an axial position. Unfortunately, it appears that when R = allyl, the selectivity between the two conformers (**A** or **B**) is not that great, and the result is that after the ene reaction occurs, there is a mixture of C8 epimers, **128** and **129**.

This mechanism could also be interpreted using the Curtin-Hammett principle. Assuming conformers **A** and **B** where in rapid equilibrium but the subsequent ene reaction occurs relatively slowly, then the product distribution of **128** to **129** will depend totally on the difference in energies between transition states **A'** and **B'**. If the difference is high enough, good selectivity should be seen. However, if these transition states are similar in energies the product distribution of **128** and **129** should be roughly 1:1. (Figure 4)

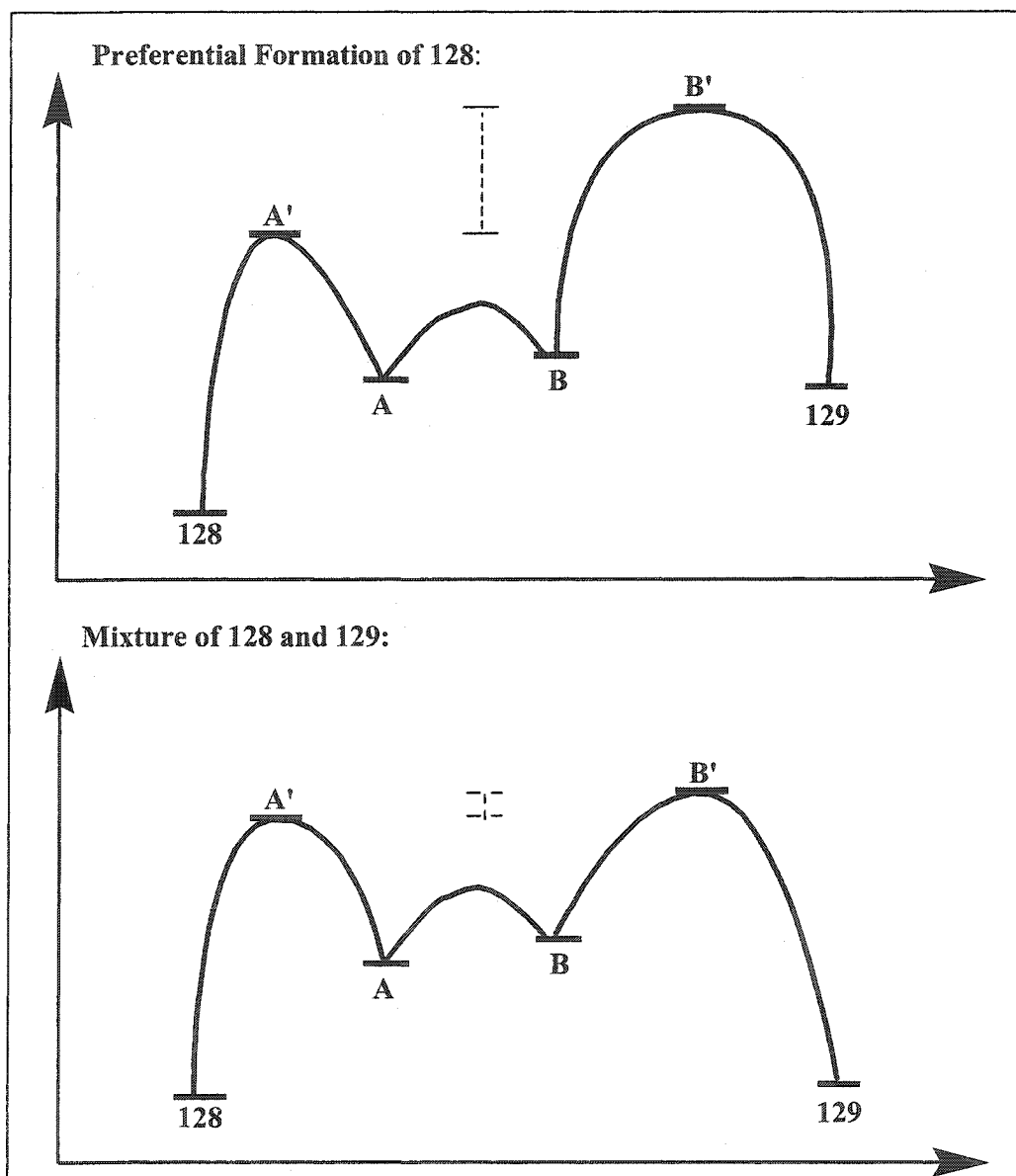
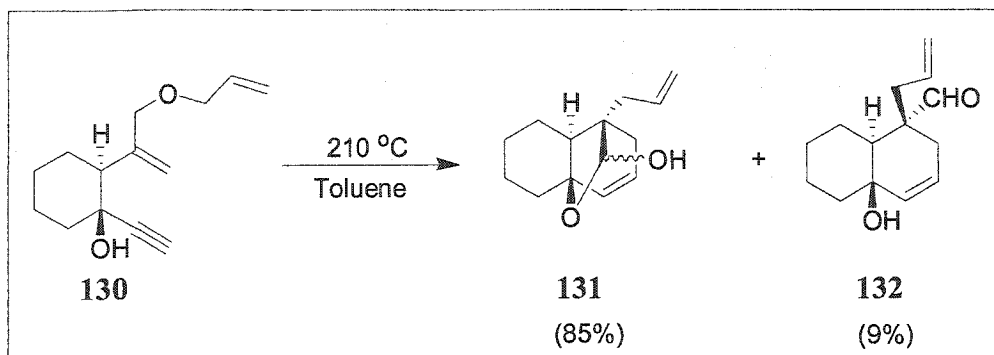


Figure 4: Application of the Curtin-Hammett Principle

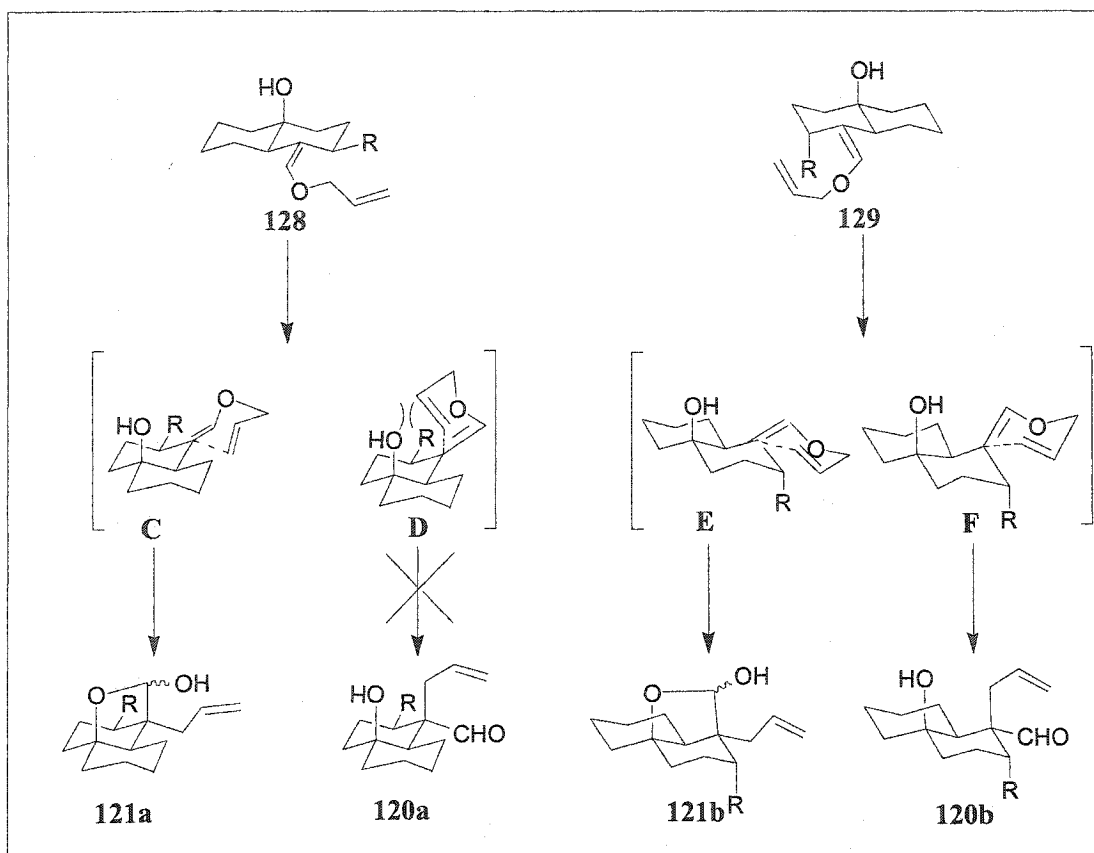
epimerization is not a possibility.) The formation of the aldehyde side-product **132** was explained by the fact that the Claisen rearrangement can take place either from the top face or the bottom face of the molecule. While preferential attack should occur anti to the bridgehead alcohol of the molecule, it does not occur with complete selectivity (Scheme 39)



Scheme 39: Formation of an Aldehyde Side-Product

A similar explanation can be applied to the system under investigation. As shown below in Scheme 40, both oxy-Cope/ene products **128** and **129** are setup to further undergo a Claisen rearrangement. However, this can occur from either face of the molecule and therefore two products can potentially arise in each case. In the case of **128**, the Claisen rearrangement should prefer to occur anti to the bridgehead alcohol as shown in transition state **C**. As a result lactol **121a** is formed while aldehyde **120a** is not.

For intermediate **129** however, the R group is also axial and both transition state **E** and transition state **F** should have similar energies. Therefore, both lactol **121b** and aldehyde **120b** are formed.



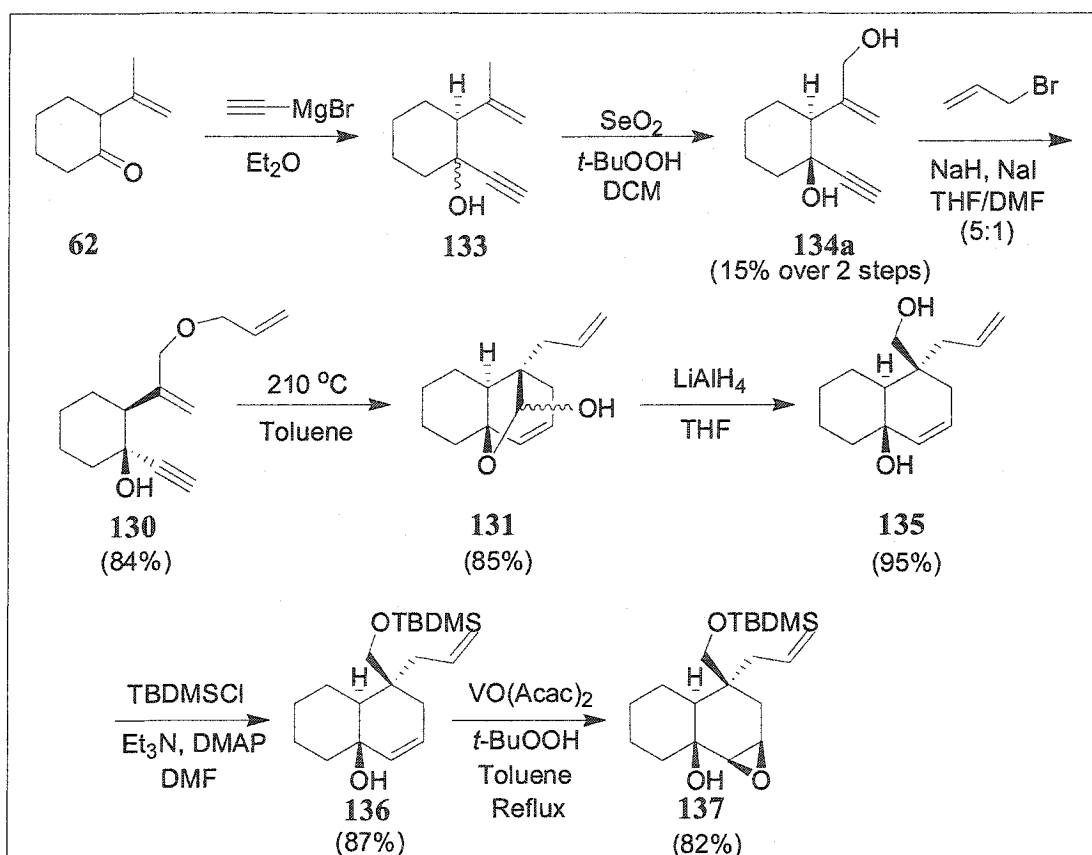
Scheme 40: Mechanism of the Claisen Rearrangement

3.6 Installing Functionality at C8

In order to circumvent the diastereoselectivity problems encountered with the first approach to the Rosane structure, an alternative route was investigated. If successful, this would involve installation of the C8 center after the tandem oxy-Cope/Ene/Claisen reaction. Using a sequence already optimized by J. Warrington, it was possible to quickly produce epoxide **137**. (Scheme 41)

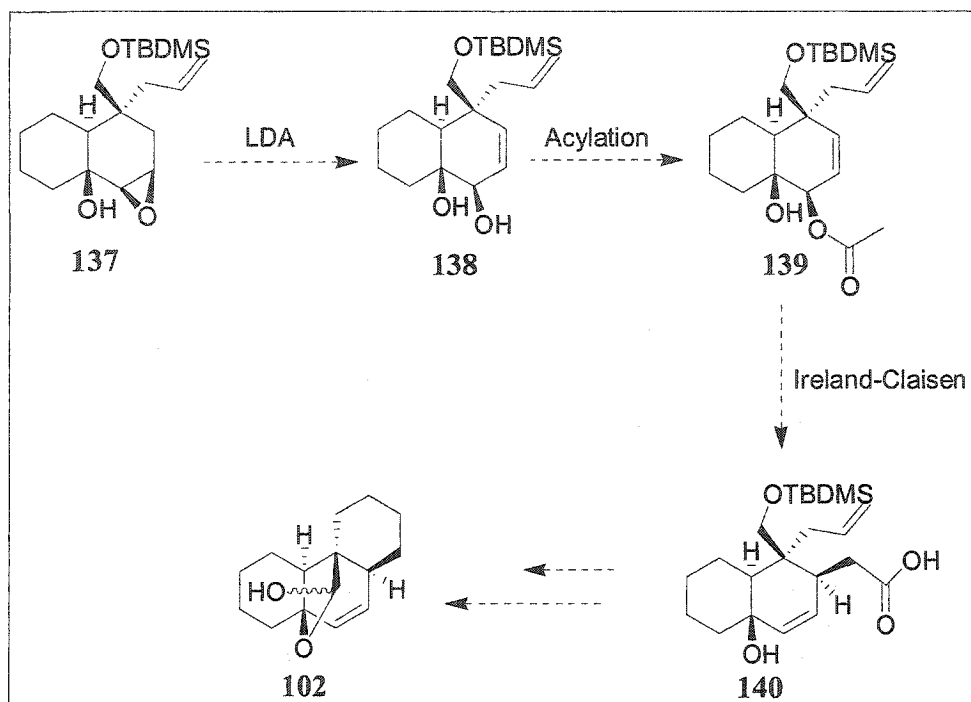
To begin with, ketone **62** was alkylated with ethynyl magnesium bromide to give a mixture of diastereomeric alcohols **133**. The crude mixture was then treated with selenium dioxide to give a mixture of allylic alcohols from which diol **134a** was isolated by column chromatography. Next, the primary alcohol was selectively capped by treatment with NaH and allyl bromide to afford ether **130**. As was previously shown in Scheme 39, this was then placed in the microwave and heating to 210 °C gave rearrangement to the desired lactol **131** in 85% yield.

The lactol **131** was then reduced with LiAlH_4 to give diol **135** and the primary alcohol was next protected with a silyl group to give molecule **136**. Finally, an allylic epoxidation with vanadium oxide acetylacetonide provided the desired epoxide **137** stereoselectively.



Scheme 41: Preparation of The Epoxide

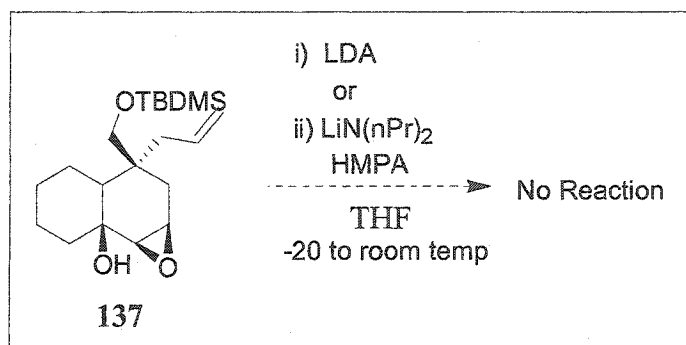
It was hoped that by treating with LDA, the epoxide would open to give an allylic alcohol **138** which could serve as a handle for installing the desired functionality at C8. If allylic alcohol **138** was first acylated and then subjected to Ireland-Claisen conditions³³, rearrangement should give allylic transposition to the acid **139**, with the desired C8 stereochemistry. After a few simple manipulations, the molecule could then be converted to the targeted tricyclic lactol **102**. (Scheme 42)



Scheme 42: Ireland-Claisen Approach

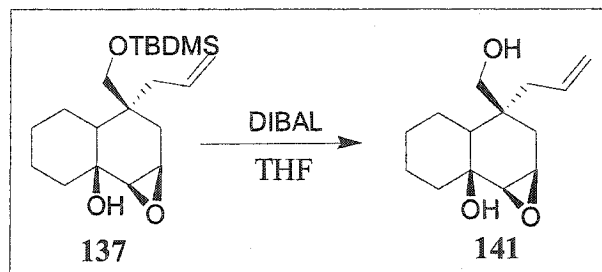
Regrettably, all attempts at an epoxide opening were unsuccessful. The epoxide 137 was stirred at $-20\text{ }^{\circ}\text{C}$ in THF and up to 6 equivalents of LDA were added. When no reaction was observed after 30 minutes the flask was warmed to $0\text{ }^{\circ}\text{C}$. With still no observable reaction, the flask was next allowed to warm to room temperature. Even after further addition of LDA, or stirring the reaction for several days, only starting material was observed. Addition of excess nBuLi at $-78\text{ }^{\circ}\text{C}$ and subsequent warming (in case the LDA was possibly quenched) also gave no reaction. Attempts at refluxing the reaction led to complete decomposition of the starting material.

The epoxide opening was also attempted using several equivalents of lithium di-n-propylamine and HMPA. Even after warming to room temperature and stirring overnight, no conversion to product was observed.



Scheme 43: Attempted Epoxide Opening

At the same time as the above approaches were being investigated, another student in the laboratory had come across a procedure for opening epoxides with DIBAL.³⁴ However, upon stirring the epoxide **137** with DIBAL in THF at 0 °C for 1 hour, and then allowing the reaction to warm to room temperature overnight, none of the desired product **138** was formed. While the starting material was completely consumed the major product was unfortunately only the diol **141**, resulting from cleavage of the silyl protecting group. (Scheme 44)



Scheme 44: Attempted Epoxide Opening With DIBAL

Chapter 4: Working Towards The Synthesis of Isovelleral Analogues

4.1 Background

Isovelleral is a mutagenic marasmane sesquiterpene which has been isolated from basidiomycetes of several genera, including *Lactarius* and *Russula*, and is known to play a role in the complicated chemical defence mechanism of these fungi.³⁵ Although the exact mechanism of its action is not fully understood, it is believed that the α,β -unsaturated dialdehyde functionality is strongly connected to the potent antifungal, antibacterial and antifeedant activities of this molecule.³⁶

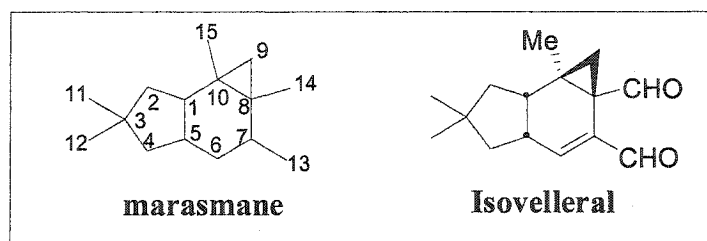


Figure 5: The Marasmane Sesquiterpene Isovelleral

Like capsaicin, isovelleral is a vanilloid receptor agonist which first elicits a response of pain or inflammation, and is then followed by a desensitization of the receptor. As a result of its biological properties, some pharmaceutical companies have taken an interest in examining the structure/activity relationship of this molecule. A search of the literature reveals however, that while there have been a few total syntheses of Isovelleral published,³⁷ relatively few synthetic studies have been carried out on simpler derivatives of the natural product.³⁸

This prompted the Barriault group to develop a general and efficient strategy for producing a variety of isovelleral analogues which will later undergo SAR studies at AstraZeneca. The overall aim of the project was to create a library of analogues that maintained the tricyclic marasmane core and the unsaturated dialdehyde functionality, which are believed to be important to the biological activity of the molecule, while at the same time allowing for several points of structural diversity.

4.2 Approach To Isovelleral Analogues

Upon examination of the marasmane core **142**, it was determined that a Diels-Alder strategy using diene **143** and dienophile **144** might allow for the rapid construction of a variety of analogues. (Figure 6) If diene **143** were to feature a secondary or tertiary alcohol at either of the two allylic positions on the ring, we could utilize a hydroxy-directed Diels-Alder protocol to control the regio- and facial- selectivity of the reaction.

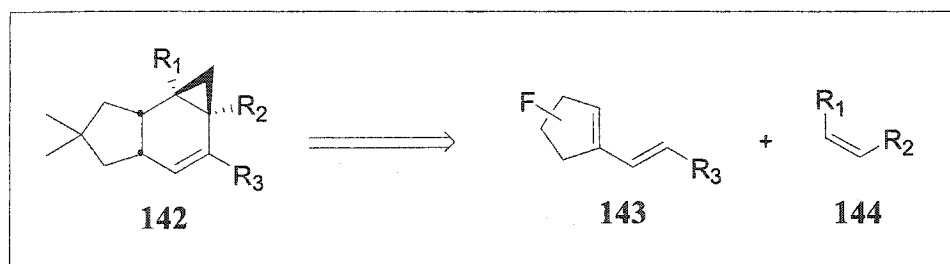


Figure 6: Retrosynthetic Analysis of Isovelleral

A benefit of this strategy is that it allows for a synthetic approach to the formation of isovelleral analogues from two different types of semicyclic dienes. To permit a rapid creation of twice as many compounds, the project was divided, allowing one student to work with dienes of Type I and another to work with dienes of Type II. (Figure 7)

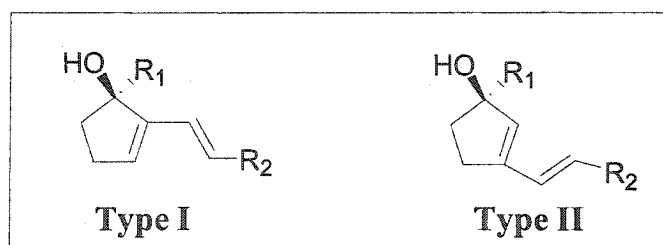
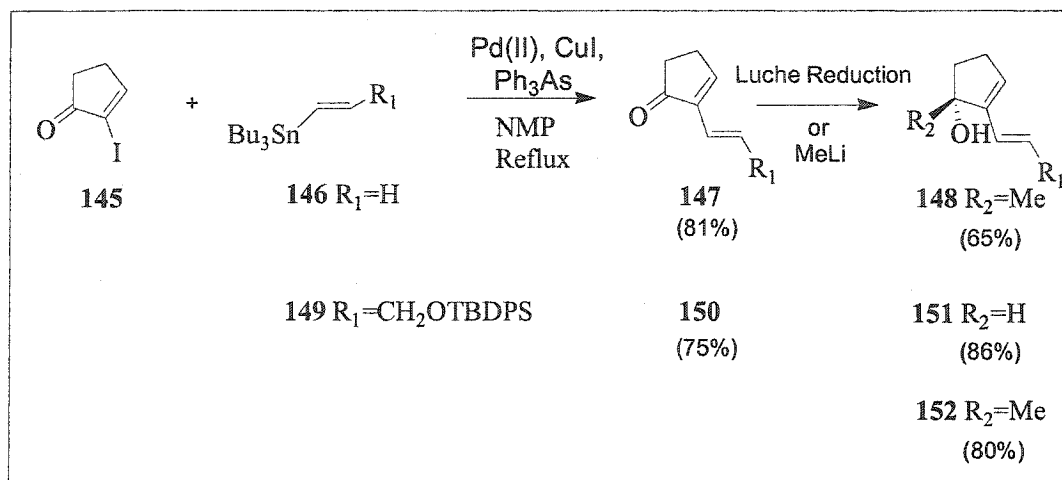


Figure 7: Approach Using Two Types of Dienes

4.3 Preparation Of The Dienes

For preparation of the Type I dienes it was decided to start from readily available 2-iodo-2-cyclopentenone **145** and install a substituted vinyl group using either a Negishi³⁹ or a Stille⁴⁰ coupling. In the end, a modified Stille protocol⁴¹ (Scheme 45) was chosen for its ease of setup and consistent yields.

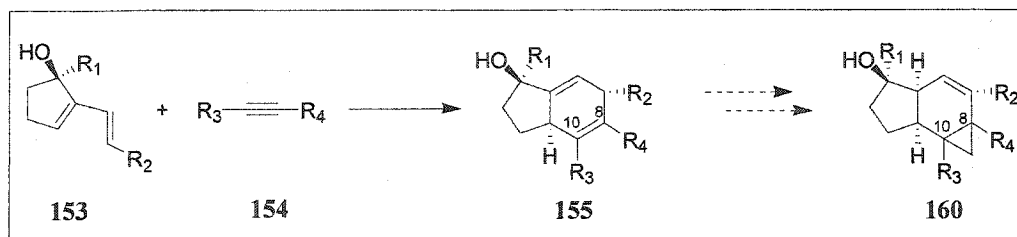


Scheme 45: Approach Using Two Types of Dienes

The possibility of other tertiary alcohols was also examined, ($R_2 = -nBu, -tBu, -CH=CH_2$); however, addition of the corresponding Grignard or Lithium species all produced significant amounts of 1,4-addition to enone **150**. In any event, the desired 1,2-addition products also proved to be a great deal less stable than **152** to the reaction conditions of the subsequent Diels-Alder reactions. Degradation was presumed to be occurring via an elimination of the tertiary alcohol.

4.4 Results and Discussion

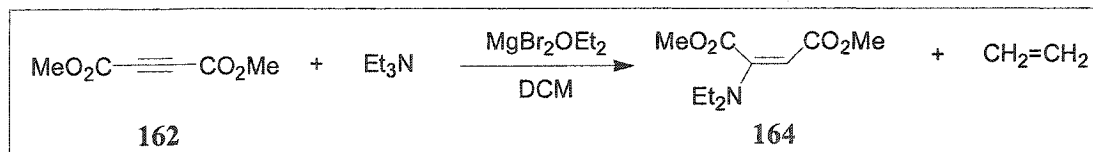
In disconnecting isovelleral we immediately took into consideration the need to construct a cyclopropane ring bridging C8 and C10. The most direct route to this challenge appeared point towards the use of an alkynyl dienophile **154**. Resultantly, the Diels-Alder adduct **155** would contain a C8-C10 double bond. As shown below in Scheme 46, this could then be used to install the necessary cyclopropyl unit.



Scheme 46: Approach Using Alkynyl Dienophile

Summarized in Table 2, a few Diels-Alder reactions were attempted using dienes **151** and **152** with an alkynyl dienophile. Much to our surprise, no product was observed in any case. While diene **151** bearing a secondary alcohol could be recovered for additional trials, the less stable **152** usually decomposed when the reaction was left for prolonged amounts of time.

Another source of difficulty with these reactions was the decomposition of the most powerful dienophile in the series, diester **162**. It appears that the symmetric diester was susceptible to an interesting addition reaction with triethylamine under the experimental conditions. To confirm this, the reaction was run without adding the diene, and complete conversion to **164** was observed. (Scheme 47)



Scheme 47: Decomposition of Dienophile

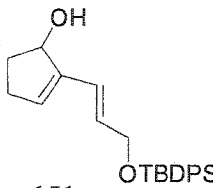
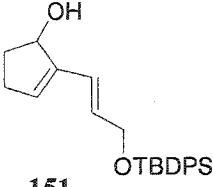
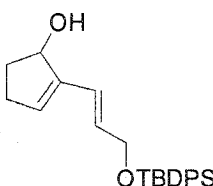
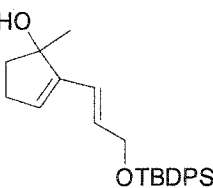
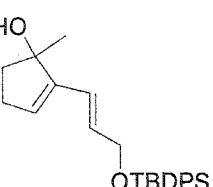
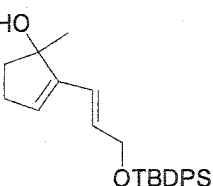
Diene	Dienophile	Conditions	Results
 151	$\text{MeO}_2\text{C}-\text{C}\equiv\text{C}-\text{Me}$ 161	MgBr_2 , OEt_2 , 2,6-lutidine, DCM	No Reaction
 151	$\text{MeO}_2\text{C}-\text{C}\equiv\text{C}-\text{Me}$ 161	MgBr_2 , OEt_2 , 2,6-lutidine, DCM 80°C/1hr (Microwave)	No Reaction
 151	$\text{MeO}_2\text{C}-\text{C}\equiv\text{C}-\text{CO}_2\text{Me}$ 162	MgBr_2 , OEt_2 , 2,6-lutidine, DCM	No Reaction (Dienophile Decomposed)
 152	$\text{EtO}_2\text{C}-\text{C}\equiv\text{C}-\text{OTBDPS}$ 163	MgBr_2 , OEt_2 , Et_3N , DCM	Decomposition of Diene
 152	$\text{MeO}_2\text{C}-\text{C}\equiv\text{C}-\text{CO}_2\text{Me}$ 162	MgBr_2 , OEt_2 , Et_3N , DCM	Decomposition of Diene (Dienophile Decomposed)
 152	$\text{MeO}_2\text{C}-\text{C}\equiv\text{C}-\text{CO}_2\text{Me}$ 162	MgBr_2 , OEt_2 , 2,6-lutidine, DCM	Decomposition of Diene

Table 2: Results Using Alkynyl Dienophile

At this stage, it was decided to explore other options for the project. While the addition of a triple bond had not previously been examined using this methodology, the addition of more common dienophiles such as *n*-phenylmaleimide **165** or methacrolein

166 had been well proven with related six-membered semicyclic dienes.¹² However, as shown below in Table 3, even these dienophiles failed to give any product. Once again, diene 151 failed to give any product, while diene 152 eventually decomposed.

It seemed to be that the five-membered ring was dramatically less reactive than the six-membered ring already examined using this methodology. Similar results were also being observed in the Type II dienes by J. Farrand.

Fortunately, upon modifying the reaction conditions, positive results began to appear. By simply treating the diene with vinyl magnesium bromide in Toluene, instead of using the usual $\text{MgBr}_2 \cdot \text{OEt}_2$ / NEt_3 / DCM technique for preparing the magnesium alkoxide, the reactions began to work. Interestingly, this approach proved to be less successful when used on the related six-membered semicyclic dienes.¹²

Shown in Table 4, the methodology has been successful with dienes 148 and 152, both featuring a tertiary alcohol. Surprisingly, when the same approach was tried with diene 151, which contains a secondary alcohol, only trans-esterification to product 172 was observed. For the time being stereochemistry of products 169 – 171 has been assigned based upon the positive results of previous work, assuming tether control. Further NMR or crystallography experiments will be required to verify stereochemistry.

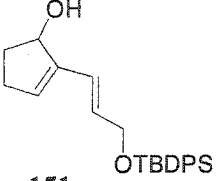
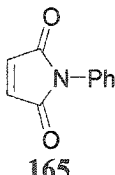
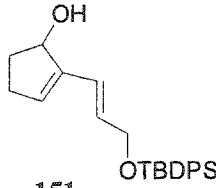
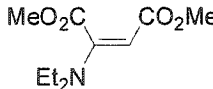
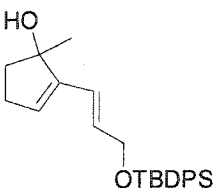
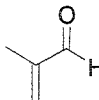
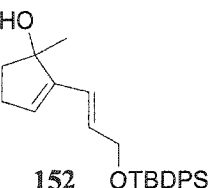
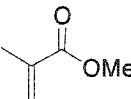
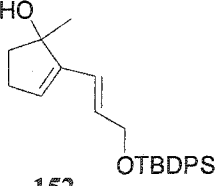
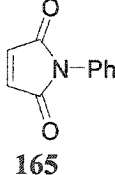
Diene	Dienophile	Conditions	Results
 151	 165	MgBr ₂ OEt ₂ 2,6-lutidine DCM	No Reaction
 151	 164	MgBr ₂ OEt ₂ 2,6-lutidine DCM	No Reaction
 152	 166	MgBr ₂ OEt ₂ 2,6-lutidine DCM	Decomposition of Diene
 152	 166	MgBr ₂ OEt ₂ Et ₃ N, DCM	Decomposition of Diene
 152	 165	MgBr ₂ OEt ₂ Et ₃ N, DCM	Decomposition of Diene

Table 3: Results Using Alkenyl Dienophile

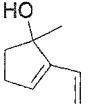

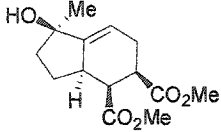
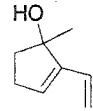
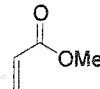
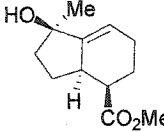
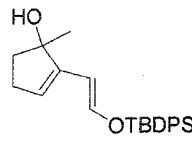
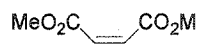
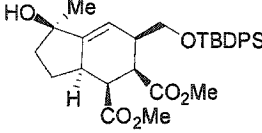
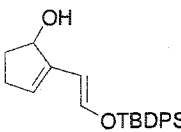
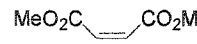
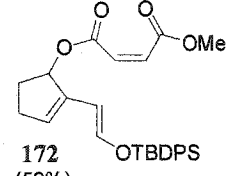
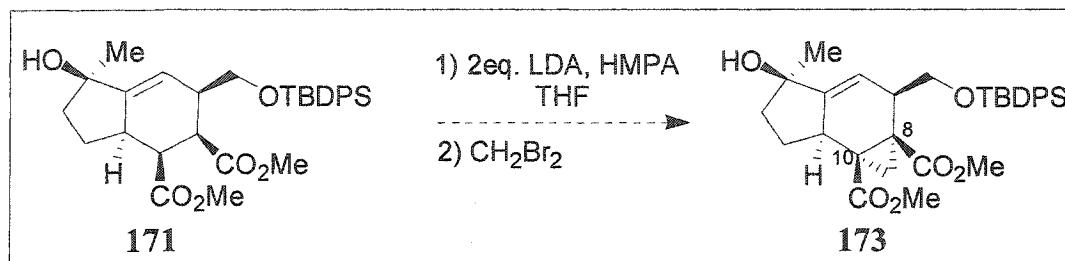
Diene	Dienophile	Conditions	Results
 148	 167	$\text{H}_2\text{C}=\text{CHMgBr}$, Toluene -78 °C to R.T.	 169 (60%)
 148	 168	$\text{H}_2\text{C}=\text{CHMgBr}$, Toluene -78 °C to R.T.	 170 (40%)
 152	 167	$\text{H}_2\text{C}=\text{CHMgBr}$, Toluene -78 °C to R.T.	 171 (43%)
 151	 167	$\text{H}_2\text{C}=\text{CHMgBr}$, Toluene -78 °C to R.T.	 172 (53%)

Table 4: Results Using a Grignard Reagent

4.5 Future Work

Having found proper conditions for carrying out the hydroxy-directed Diels-Alder reactions, a great deal of work now lays ahead in synthesizing the desired isovelleral analogues. If accessing the C8-C10 double bond is no longer possible via a direct route, then a major challenge will be in finding another method for installing the desired cyclopropane.

One idea currently being examined is to start with a diester such as **171**, and treat it with two equivalents of LDA, followed by one equivalent of dibromomethane.⁴² If successful, this would generate the desired cyclopropane **173**. (Scheme 48)



Scheme 48: Cyclopropanation of Diester

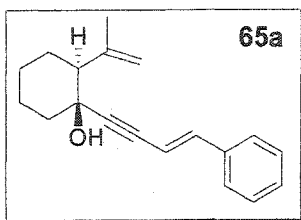
Once the methodology is worked out, other structural modifications are also planned. These include the incorporation of heteroatoms into core of the molecule, as well as replacing the cyclopropane by an epoxide or aziridine. Because of the procedural simplicity of the hydroxy-directed Diels-Alder reaction a multitude of isovelleral analogs will be prepared, featuring several points of diversity.

Experimental

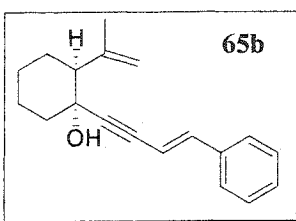
All reactions were carried out under dry N₂ atmosphere in flame-dried glassware equipped with a magnetic stir bar and a rubber septum, unless otherwise indicated. THF and Et₂O were freshly distilled from sodium/benzophenone. Dichloromethane, triethylamine and DMF were freshly distilled from CaH₂. MgBr₂·OEt₂ was prepared in-house and stored in the glove box. The other commercially available reagents were used without purification, unless otherwise indicated.

Reactions were monitored by thin layer chromatography (TLC) analysis of aliquots using aluminum sheets pre-coated (0.2 mm layer thickness) with silica gel 60 F₂₅₄ (E. Merck). Flash chromatography was carried out on 230- 400 mesh silica gel 60. For purification of compounds containing tertiary alcohol functionality, the silica gel was doped with 2% Et₃N. TLC plates were viewed under UV light and stained with phosphomolybdic acid or p-anisaldehyde staining solutions. GC/MS was performed on a HP 6890 Gas Chromatograph using a HP-5MS (cross linked 5% PH ME siloxane) column (30 m x0.25 mm, 0.25 μm film). ¹H and ¹³C NMR spectra were recorded on a Bruker 300 MHz or Bruker 500 MHz spectrometer. IR spectra were recorded on a Bomen Michaelson 100 FTIR spectrometer. Melting points were recorded on a Gallenkamp Melting Point Apparatus P 1106G.

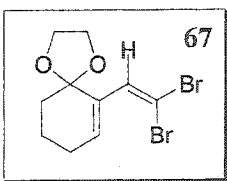
Microwave reactions were conducted in a CEM Model ESP-1500 Plus oven equipped with a pressure monitoring device and an EST-300 Plus fibre optic temperature probe. All experiments were performed in sealed quartz tubes. When using non-polar solvents such as Toluene, a carboflon™ bar was added.



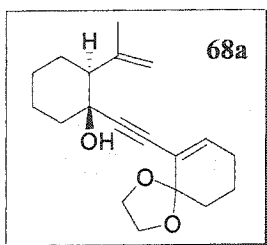
2-Isopropenyl-1-(4-phenyl-but-3-en-1-ynyl)-cyclohexanol (65): To a solution of the dibromide **64** (3.00 g, 10.42 mmol) stirring in THF (15 mL) at -78°C was added *n*-BuLi (8.02 mL, 20.84 mmol). The solution was stirred for 45 minutes allowing the formation of the alkynyl lithium *in situ*. To this was added a solution of ketone **62** (0.9646 g, 6.9797mmol) in THF (10 mL). This was stirred for 1 hour, warmed to room temperature and quenched with NH_4Cl (sat. aq.). The mixture was extracted with EtOAc (3x) and the combined organic layers were dried over MgSO_4 and concentrated. Flash chromatography with 10% EtOAc/Hexanes gave **65a** as a yellow oil (0.7727 g, 42%). IR (neat, cm^{-1}) 3554, 3464, 2942, 2559, 1641, 1442; $^1\text{H-NMR}$ (300 MHz, CDCl_3) * 7.37-7.22 (m, 5H), 6.88 (d, $J = 16.3$ Hz, 1H), 6.18 (d, $J = 16.3$ Hz, 1H), 5.02 (s, 1H), 4.87 (s, 1H), 2.28 (s, 1H), 2.25-2.17 (m, 1H), 2.02 (s, 3H), 1.77-1.18 (m, 8H); ^{13}C NMR (75 MHz, CDCl_3) * 148.3, 141.0, 136.1, 128.6, 128.4, 126.1, 112.3, 107.7, 96.3, 82.4, 67.4, 52.6, 39.6, 26.7, 26.0, 25.7, 20.6; HRMS (EI) m/z (M^+) calcd 266.1671 for $\text{C}_{19}\text{H}_{22}\text{O}$, obsd 266.1671.



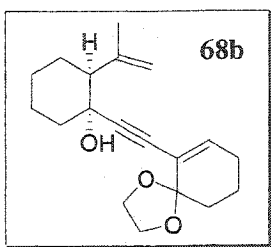
Compound **65b** was also obtained as a yellow oil (0.6135 g, 33%). IR (neat, cm^{-1}) 3541, 3445, 2934, 2858, 1635, 1492, 1448, 1327; $^1\text{H-NMR}$ (300 MHz, CDCl_3) * 7.38-7.23 (m, 5H), 6.90 (d, $J = 16.3$ Hz, 1H), 6.18 (d, $J = 16.3$ Hz, 1H), 5.00 (s, 1H), 4.94 (s, 1H), 2.77 (s, 1H), 2.22-2.12 (m, 2H), 1.91 (s, 3H), 1.90-1.17 (m, 7H); ^{13}C NMR (75 MHz, CDCl_3) * 154.5, 141.1, 136.1, 128.7, 128.5, 126.1, 115.1, 107.8, 93.5, 85.4, 70.3, 56.4, 40.5, 28.5, 25.6, 24.0, 20.9; HRMS (EI) m/z (M^+) calcd 266.1671 for $\text{C}_{19}\text{H}_{22}\text{O}$, obsd 266.1656.



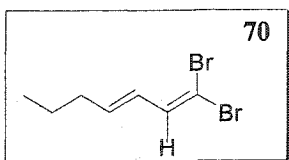
6-(2,2-Dibromo-vinyl)-1,4-dioxaspiro[4.5]dec-6-ene (67): To zinc dust (1.1540 g, 17.65 mmol) and triphenylphosphine (4.63 g, 17.65 mmol) stirring in DCM (20 mL) at 0 °C was added via canula CBr₄ (5.85 g, 17.65 mmol) in DCM (15 mL). The resulting dark green solution was allowed to warm to room temperature and stirred for 24 hours resulting in a pink solution. The aldehyde **66** (0.7423 g, 4.4130 mmol) in DCM (15 mL) was then canulated into the flask and stirred for 3 hours. The solution was then diluted with petroleum ether (200 mL) and filtered through a pad of Celite. The solution was then concentrated and flashed with 15 % EtOAc/Hexanes to yield **73** as a yellow oil (0.9217 g, 65%). IR (neat, cm⁻¹) 2946, 2880, 1586, 1438, 1365, 1340, 1265, 1174, 1117, 1071, 1021, 946; ¹H-NMR (300 MHz, CDCl₃) * 6.89-6.88 (m, 1H), 6.36 (dt, J = 1.3, 2.70 Hz, 1H), 3.96 (s, 4H), 2.12-2.09 (m, 2H), 1.75-1.72 (m, 2H); ¹³C NMR (75 MHz, CDCl₃) * 135.5, 134.5, 133.8, 106.2, 89.8, 65.1, 33.5, 25.3, 20.0; HRMS (EI) *m/z* (M⁺ - C₂H₄) calcd 293.8891 for C₈H₈Br₂O₂, obsd 293.8895.



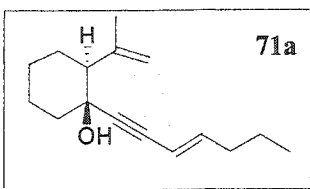
1-(1,4-Dioxaspiro[4.5]dec-6-en-6-ylethynyl)-2-isopropenyl-cyclohexanol (68a): To a solution of the dibromide **67** (0.9000 g, 2.77 mmol) stirring in THF (5 mL) at -78 °C was added n-BuLi (2.26 mL, 5.54 mmol). The solution was stirred for 45 minutes allowing the formation of the alkynyl lithium *in situ*. To this was added a solution of ketone **62** (0.2680 g, 1.94 mmol) in THF (5 mL). This was stirred for 1 hour, warmed to room temperature and quenched with NH₄Cl (sat. aq.). The mixture was extracted with EtOAc (3x) and the combined organic layers were dried over MgSO₄ and concentrated. Flash chromatography with 10% EtOAc/Hexanes gave **68a** as a white crystals (0.2410 g, 41%). IR (neat, cm⁻¹) 3464, 2937, 1639, 1442, 1352, 1268, 1176, 1073; ¹H-NMR (500 MHz, CDCl₃) * 6.21 (t, J = 4.1 Hz, 1H), 4.94 (s, 1H), 4.81 (s, 1H), 4.18-4.12 (m, 2H), 3.97-3.92 (m, 2H), 2.2-1.9 (m, 5H), 1.74 (s, 3H), 1.75-1.4 (m, 9H); ¹³C NMR (125 MHz, CDCl₃) * 148.4, 139.8, 123.9, 112.1, 105.9, 93.4, 81.0, 67.3, 65.7 (2 CH₂), 52.7, 39.8, 34.4, 26.8, 25.77, 25.76, 25.6, 20.6, 20.2; HRMS (EI) *m/z* (M⁺) calcd 302.1882 for C₁₉H₂₆O₃, obsd 302.1879, mp: 51-54 °C.



Compound **68b** was also obtained as a colorless oil (0.2201 g, 38%). IR (neat, cm^{-1}) 3459, 2928, 2855, 1445, 1373, 1351, 1073; $^1\text{H-NMR}$ (300 MHz, C_6D_6) * 6.10 (t, $J = 3.9$ Hz, 1H), 4.96 (s, 1H), 4.91-4.90 (m, 1H), 4.01-3.94 (m, 2H), 3.61-3.54 (m, 2H), 2.58 (s, 1H), 2.28-2.12 (m, 2H) 1.95 (s, 3H), 1.89-1.03; (m, 11H); $^{13}\text{C NMR}$ (75 MHz, C_6D_6) * 146.0, 139.2, 122.3, 114.8, 111.2, 95.9, 85.4, 70.6, 65.7(2 CH_2), 56.8, 41.3, 34.9, 30.2, 29.0, 26.1, 25.7, 21.5, 20.6; HRMS (EI) m/z (M^+) calcd 302.1882 for $\text{C}_{19}\text{H}_{26}\text{O}_3$, obsd 302.1885.

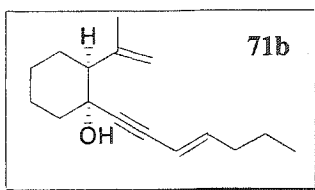


1,1-Dibromo-hepta-1,3-diene (70): CBr_4 (8.06 g, 24.3 mmol) was slowly added to a solution of Ph_3P (12.06 g, 45.98 mmol) in DCM (15 mL) at 0°C , and the mixture was stirred for 30 min. A solution of aldehyde **69** (1.00 g, 10.19 mmol) in DCM (10 mL) was then added and stirring was maintained for 1 hour. The mixture was diluted with petroleum ether and filtered through Celite. The filtrate was washed with NaHCO_3 (sat. aq.), H_2O , and brine, dried over MgSO_4 , and concentrated. Flash chromatography with 1% EtOAc/ Hexane gave **70** as a yellow oil (1.96 g, 76%). IR (neat, cm^{-1}) 2960, 2932, 2873, 1706, 1651, 1463; $^1\text{H-NMR}$ (300 MHz, CDCl_3) * 6.87 (d, $J = 9.9$ Hz, 1H), 6.11-6.01 (m, 1H), 5.93-5.83 (m, 1H), 2.09-2.02 (m, 2H), 1.53-1.18 (m, 2H), 0.89 (t, $J = 7.4$ Hz, 3H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3) * 139.4, 137.1, 127.2, 88.3, 35.0, 22.0, 13.7; HRMS (EI) m/z (M^+) calcd 251.9149 for $\text{C}_7\text{H}_{10}\text{Br}_2$, obsd 251.9152.

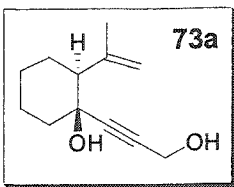


1-Hept-3-en-1-ynyl-2-isopropenyl-cyclohexanol (71): To a solution of the dibromide **70** (0.5000 g, 1.97 mmol) stirring in THF (15 mL) at -78°C was added $n\text{-BuLi}$ (1.75 mL, 4.14 mmol). The solution was stirred for 45 minutes allowing the formation of the alkynyl lithium *in situ*. To this was added a solution of ketone **62** (0.2450 g, 1.77 mmol) in THF (5 mL). This was stirred for 1 hour, warmed to room temperature and quenched with NH_4Cl (sat. aq.). The mixture was extracted with EtOAc (3x) and the combined organic layers were dried over MgSO_4 and concentrated. Flash

chromatography with 10% EtOAc/Hexanes gave **71a** as a colorless oil (0.1194 g, 29%). IR (neat, cm^{-1}) 3556, 3079, 2934, 1638, 1447, 1371, 1266, 1177, 1138, 1070; $^1\text{H-NMR}$ (500 MHz, CDCl_3) * 6.05 (dt, $J = 7.1, 15.9$ Hz, 1H), 5.43 (dt, $J = 1.6, 15.9$ Hz, 1H), 4.97 (t, $J = 1.6$ Hz, 1H), 4.81 (s, 1H), 2.23-1.94 (m, 7H), 1.77-1.15 (m, 10H), 0.87 (t, $J = 7.3$ Hz, 3H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) * 148.4, 144.5, 112.1, 109.1, 92.4, 81.9, 67.2, 52.6, 39.6, 35.1, 26.7, 26.0, 25.8, 21.9, 20.6, 13.6; HRMS (EI) m/z (M^+) calcd 232.1827 for $\text{C}_{16}\text{H}_{24}\text{O}$, obsd 232.1840.

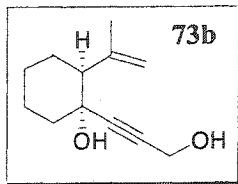


Compound **71b** was also obtained as a colorless oil (0.1725 g, 42%). IR (neat, cm^{-1}) 3452, 3073, 3019, 2933, 2860, 1634, 1447, 1375, 1060, 1013; $^1\text{H-NMR}$ (300 MHz, CDCl_3) * 6.08 (dt, $J = 7.1, 15.9$ Hz, 1H), 5.47 (dt, $J = 1.6, 15.9$ Hz, 1H), 4.97-4.95 (m, 1H), 4.89-4.88 (m, 1H), 2.68 (s, 1H), 2.16-1.95 (m, 3H), 1.85 (s, 3H), 1.75-1.17 (m, 10H), 0.88 (t, $J = 7.4$ Hz, 3H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3) * 145.6, 144.5, 114.9, 109.2, 89.4, 85.0, 70.1, 56.4, 40.5, 35.0, 28.5, 25.7, 24.0, 21.9, 20.8, 13.6; HRMS (EI) m/z (M^+) calcd 232.1827 for $\text{C}_{16}\text{H}_{24}\text{O}$, obsd 232.1808.



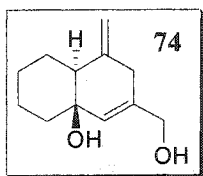
2-Isopropenyl-1-(4-phenyl-but-3-en-1-ynyl)-cyclohexanol (73): To a solution of propargyl alcohol **72** (0.2000 g, 3.57 mmol) stirring in THF (20 mL) at -78 °C was added $n\text{-BuLi}$ (3.06 mL, 7.49 mmol). The solution was stirred for 1 hour and allowed to warm to -20 °C permitting the formation of the dianion *in situ*. The reaction was then cooled again to -78 °C and a solution of ketone **62** (0.4437 g, 3.21 mmol) in THF (10 mL) was added via canula. This was stirred for 1 hour, warmed to room temperature and quenched with NH_4Cl (sat. aq.). The mixture was extracted with EtOAc (3X) and the combined organic layers were dried over MgSO_4 and concentrated. Flash chromatography with 10-60% EtOAc/Hexanes gradient gave **73a** as white crystals (0.2618 g, 42%). IR (neat, cm^{-1}) 3372, 2935, 2851, 1641, 1445, 1371, 1162, 1112, 1030; $^1\text{H-NMR}$ (500 MHz, CDCl_3) * 4.98-4.97 (m, 1H), 4.82 (s, 1H), 4.25 (s, 2H), 2.20-2.15 (m, 2H), 2.12-2.09 (m, 1H), 1.95 (s, 3H), 1.74-1.44 (m, 8H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) * 148.1, 112.4, 90.7, 81.3, 67.1,

52.6, 51.2, 39.7, 29.7, 26.7, 25.8, 25.7, 20.5; HRMS (EI) m/z (M^+) calcd 194.1307 for $C_{12}H_{18}O_2$, obsd 194.1313, mp: 86-87 °C.



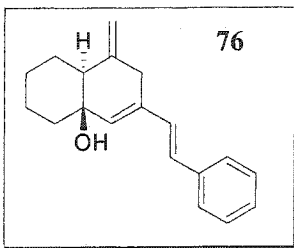
Compound **73b** was also obtained as a white powder (0.1064 g, 17%). IR (neat, cm^{-1}) 3376, 2933, 2859, 1728, 1641, 1446, 1264; 1H -NMR (300 MHz, $CDCl_3$) * 4.93 (s, 1H), 4.85 (s, 1H), 4.25 (s, 2H), 2.74 (br. s, 1H), 2.10-2.00 (m, 2H), 1.81 (s, 3H), 1.65-1.43 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$) * 145.3, 115.1, 87.6, 84.4, 69.8, 56.1, 51.1, 40.4, 28.4, 25.5, 23.8, 21.0; HRMS (EI) m/z (M^+) calcd 194.1307 for $C_{12}H_{18}O_2$, obsd 194.1278.

6-Hydroxymethyl-8-methylene-1,3,4,7,8,8a-hexahydro-2H-naphthalen-4a-ol (**74**):



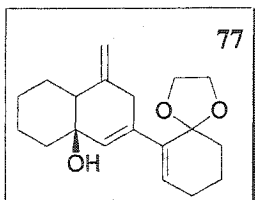
To a solution of **73a** (0.4487 g, 2.31 mmol) in toluene (20 mL) was added DBU (1.04 mL, 6.93 mmol). The solution was degassed with argon for 10 minutes and then heated with microwaves at 200 °C for 1 hour. The toluene was evaporated and the crude product was crystallized from ethyl acetate to yield **74** as white crystals (0.3910 g, 87%). IR (neat, cm^{-1}) 3321, 2920, 2845, 1654, 1078 ; 1H -NMR (300 MHz, $CDCl_3$) * 5.62 (s, 1H), 4.96 (s, 1H), 4.76 (s, 1H), 4.00 (s, 2H), 2.87-2.67 (m, 2H), 2.19-1.20 (m, 11H); ^{13}C NMR (75 MHz, $CDCl_3$) * 145.7, 139.3, 129.8, 109.1, 69.5, 65.8, 48.3, 37.1, 36.1, 25.8, 22.8, 20.9; HRMS (EI) m/z (M^+) calcd 194.1307 for $C_{12}H_{18}O_2$, obsd 194.1296, mp: 114-117 °C.

8-Methylene-6-styryl-1,3,4,7,8,8a-hexahydro-2H-naphthalen-4a-ol (**76**):

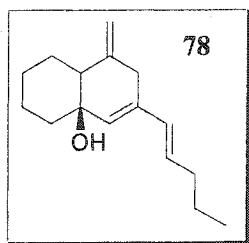


of **65a** (0.2196 g, .0.8244 mmol) in toluene (15 mL) was added DBU (1.23 mL, 8.24mmol). The solution was degassed with argon for 10 minutes and then heated with microwaves at 220 °C for 90 minutes. The toluene was evaporated and the crude product was flashed with 10% ethylacetate/hexanes to yield **76** as a yellow oil (0.1303 g, 59%). IR (neat, cm^{-1}) 3561, 3451, 3026, 2931, 2855, 1938, 1873, 1796, 1725, 1649, 1493, 1448, 1262, 1075; 1H -NMR (300 MHz, $CDCl_3$) * 7.42-7.37 (m, 2H), 7.34-7.28 (m, 2H), 7.24-7.19 (m, 1H), 6.75 (d, $J = 16.3$ Hz, 1H), 6.55 (d, J

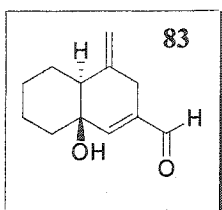
= 16.3 Hz, 1H), 5.78 (s, 1H), 5.06 (s, 1H), 4.82 (s, 1H), 3.20-3.10 (m, 2H), 2.22-2.18 (m, 1H), 1.92-1.24 (m, 9H); ^{13}C NMR (75 MHz, CDCl_3) * 145.7, 137.1, 136.3, 136.2, 130.4, 128.6, 128.0, 127.5, 126.3, 109.3, 69.7, 48.3, 37.1, 35.4, 25.8, 22.9, 20.9; HRMS (EI) m/z (M^+) calcd 266.1671 for $\text{C}_{19}\text{H}_{22}\text{O}$, obsd 266.1671.



6-(1,4-Dioxo-spiro[4.5]dec-6-en-6-yl)-8-methylene-1,3,4,7,8,8a-hexahydro-2H-naphthalen-4a-ol (77): To a solution of **68a** (0.0783 g, .02589 mmol) in toluene (20 mL) was added DBU (0.39 mL, 2.59 mmol). The solution was degassed with argon for 10 minutes and then heated with microwaves at 220 °C for 180 minutes. The toluene was evaporated and the crude product was flashed with 10% ethylacetate/hexanes to yield **77** as a yellow oil (0.0409 g, 52%). (Characterization not possible due to product instability; tertiary alcohol very unstable to traces of acid.)



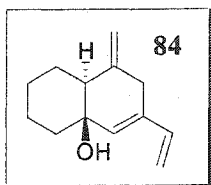
8-Methylene-6-pent-1-enyl-1,3,4,7,8,8a-hexahydro-2H-naphthalen-4a-ol (78): To a solution of **71a** (0.0930 g, .04002 mmol) in toluene (12 mL) was added DBU (0.300 mL, 2.01 mmol). The solution was degassed with argon for 10 minutes and then heated with microwaves at 220 °C for 120 minutes. The toluene was evaporated and the crude product was flashed with 10% ethylacetate/hexanes to yield **78** as a yellow oil (0.0482 g, 52%). IR (neat, cm^{-1}) 3387, 2927, 2852, 1642, 1443, 1364, 1048; ^1H -NMR (300 MHz, CDCl_3) * 6.00 (d, $J = 15.7$ Hz, 1H), 5.68 (dt, $J = 6.9, 15.7$ Hz, 1H), 5.52 (s, 1H), 4.98 (s, 1H), 4.75 (d, $J = 1.4$ Hz, 1H), 2.98-2.84 (m, 2H), 2.16-2.02 (m, 3H), 1.86-1.16 (m, 11H), 0.89 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) * 146.1, 136.4, 133.3, 131.7, 130.5, 108.9, 69.7, 48.4, 37.2, 35.5, 34.9, 25.8, 22.9, 22.5, 20.9, 13.7; HRMS (EI) m/z (M^+) calcd 232.1827 for $\text{C}_{16}\text{H}_{24}\text{O}$, obsd 232.1815.



8a-Hydroxy-4-methylene-3,4,4a,5,6,7,8,8a-octahydro-naphthalene-2-carbaldehyde (83): To a flask containing TPAP (5 mg, 0.0257 mmol), NMO (45 mg, 0.3861 mmol), and 4 Å molecular sieves (130

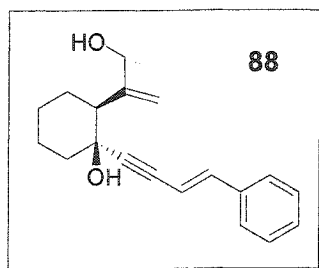
mg), and a stirring bar, was added diol **74** (50 mg, 0.2574 mmol) in DCM (5 mL). This was stirred for 30 minutes and then the reaction was filtered through a pad of silica and washed with EtOAc. The solvent was evaporated leaving the crude aldehyde **83** as a colorless oil (38 mg, 77%) which was immediately carried on to the next step. HRMS (EI) m/z (M^+) calcd 192.1150 for $C_{12}H_{16}O_2$, obsd 192.1133.

8-Methylene-6-vinyl-1,3,4,7,8,8a-hexahydro-2H-naphthalen-4a-ol (84): To a solution



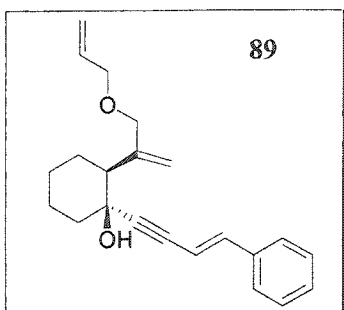
of $MePPh_3I$ (0.1036 g, 0.2563 mmol) in THF (3 mL) at 0 °C was added KHMDS (0.47 mL, 0.2366 mmol). This was allowed to stir at 0°C for 30 minutes, after which time was added aldehyde **83** (38 mg, 0.1971 mmol) in THF (3 mL) via canula. This was stirred for 1 hour, after

which was added NaCl (sat. aq.). The mixture was extracted with EtOAc (3x) and the combined organic extracts were dried over $MgSO_4$ and concentrated. Flash chromatography with 10% EtOAc/Hexanes (1% NEt_3) gave **84** as a colorless oil (30.6 mg, 82%). IR (neat, cm^{-1}) 3556, 3453, 3083, 2931, 2855, 1651, 1604, 1445, 1262, 1081; 1H -NMR (500 MHz, C_6D_6) * 6.26 (dd, $J = 17.3, 10.8$ Hz, 1H), 5.58 (s, 1H), 5.08 (d, $J = 17.5$ Hz, 1H), 4.95 (d, $J = 10.8$ Hz, 1H), 4.80 (s, 1H), 4.68 (s, 1H), 2.78-2.69 (m, 2H), 1.97-1.86 (m, 3H), 1.77-1.69 (m, 2H), 1.47-1.41 (m, 2H), 1.27-1.08 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) * 146.0, 139.1, 136.7, 136.5, 113.0, 109.0, 69.4, 48.6, 37.6, 34.9, 26.3, 23.2, 21.3; HRMS (EI) m/z (M^+) calcd 190.1358 for $C_{13}H_{18}O$, obsd 190.1377.



2-(1-Hydroxymethyl-vinyl)-1-(4-phenyl-but-3-en-1-ynyl)-cyclohexanol (88): To a solution of **65a** (101 mg, 0.379 mmol) stirring in DCM (5 mL) was added $tBuOOH$ (0.145 mL, 1.517 mmol) and SeO_2 (21 mg, 0.190 mmol). The reaction was stirred for 2 days and then diluted with DCM (20 mL) and quenched with $NaHCO_3$ (sat. aq.). The organic phase was then washed with $NaHCO_3$ (1x), H_2O (2x), and NaCl (sat. aq.) (1x). The organic phase was then dried with $MgSO_4$, concentrated and flashed with 10% ethylacetate/hexanes to yield **88** as a white powder (57.8 mg, 54%). IR (neat, cm^{-1}) 3391, 2927, 2859, 1761, 1646, 1442, 1022; 1H -NMR (300 MHz, $CDCl_3$) * 7.68-7.26 (m, 5H), 6.85 (d, $J = 16.3$ Hz, 1H), 6.13 (d, $J = 16.3$

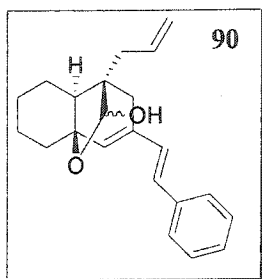
Hz, 1H), 5.22 (s, 1H), 5.11 (s, 1H), 4.20 (s, 2H), 3.83 (br s, 1H), 2.41 (dd, $J = 3.3, 12.9$ Hz, 1H), 2.16-1.21 (m, 9H); ^{13}C NMR (75 MHz, CDCl_3) * 149.3, 141.1, 136.1, 128.7, 128.5, 126.2, 116.6, 107.7, 96.1, 83.0, 68.1, 65.5, 52.1, 39.7, 26.3, 25.8, 20.6; HRMS (EI) m/z (M^+) calcd 282.1620 for $\text{C}_{19}\text{H}_{22}\text{O}_2$, obsd 282.1639, mp: 130-134 °C.



2-(1-Allyloxymethyl-vinyl)-1-(4-phenyl-but-3-en-1-ynyl)-cyclohexanol (89) To a flask at 0 °C, containing diol **88** (58.0 mg, 0.2054 mmol) stirring in THF (5 mL), was added NaH (10.8 mg, 0.4519 mmol). This was stirred for 30 minutes after which time allyl bromide (0.027 mL, 0.3081 mmol) was added. The reaction was stirred for 90 minutes

and then quenched at 0 °C with NH_4Cl (sat. aq.). The aqueous phase was extracted with EtOAc (3x), and the combined organic fractions were dried with MgSO_4 , concentrated, and flashed with 10% ethylacetate/hexanes to yield **89** as a colorless oil (47.9 mg, 72%). IR (neat, cm^{-1}) 3400, 2931, 2856, 1635, 1067, 925, 748; ^1H -NMR (300 MHz, CDCl_3) * 7.35-7.21 (m, 5H), 6.84 (d, $J = 16.3$ Hz, 1H), 6.14 (d, $J = 16.3$ Hz, 1H), 5.98-5.85 (m, 1H), 5.32-5.26 (m, 1H), 5.20-5.17 (m, 3H), 4.42 (d, $J = 1.3$ Hz, 1H), 4.21-4.11 (m, 2H), 3.95-3.86 (m, 2H), 2.43 (dd, $J = 3.4, 12.8$ Hz, 1H), 2.18-2.14 (m, 1H), 1.91-1.62 (m, 4H), 1.56-1.41 (m, 2H), 1.35-1.19 (m, 1H); ^{13}C NMR (75 MHz, CDCl_3) * 145.3, 140.6, 136.3, 133.8, 128.6, 128.4, 126.1, 119.3, 117.7, 108.0, 96.5, 82.7, 71.8, 70.4, 68.0, 53.0, 39.5, 25.9, 25.8, 20.6; HRMS (EI) m/z ($\text{M}^+ - \text{H}_2\text{O}$) calcd 304.1827 for $\text{C}_{22}\text{H}_{24}\text{O}$, obsd 304.1839.

7-Allyl-9-styryl-11-oxa-tricyclo[5.3.2.01,6]dodec-9-en-12-ol (90): To a solution of **89**

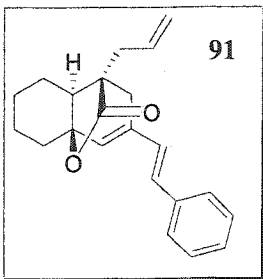


(0.0191 g, 0.5914 mmol) in toluene (20 mL) was added DBU (0.300 mL, 2.01 mmol). The solution was degassed with argon for 10 minutes and then heated with microwaves at 200 °C for 90 minutes. The toluene was evaporated and the crude product was flashed with 20% ethylacetate/hexane to yield **90** as white crystals (0.1263 g, 66%). (Mixture of Diastereomers) IR (neat, cm^{-1}) 3381, 3067, 3029,

2929, 2856, 1944, 1878, 1830, 1640, 1619, 1595, 1446, 1142, 1107; ^1H -NMR (300 MHz, CDCl_3) * 7.40-7.12 (m, 5H), 6.78- 6.55 (m, 2H), 5.94-5.74 (m, 2H), 5.30-4.96 (m, 3H),

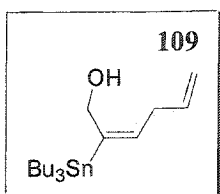
3.12-2.09 (m, 4H), 2.03-1.17 (m, 10H); ^{13}C NMR (75 MHz, CDCl_3) * 137.27, 137.20, 137.16, 136.22, 135.21, 134.83, 134.63, 130.12, 129.70, 128.56, 128.45, 137.73, 127.47, 126.50, 126.32, 117.84, 117.77, 104.68, 103.68, 78.91, 49.34, 49.21, 49.12, 46.44, 37.63, 37.42, 35.37, 32.71, 32.47, 32.29, 24.90, 24.67, 23.33, 21.05, 20.89; HRMS (EI) m/z (M^+) calcd 322.1933 for $\text{C}_{22}\text{H}_{26}\text{O}_2$, obsd 322.1916, mp:162-163 °C.

7-Allyl-9-styryl-11-oxa-tricyclo[5.3.2.01,6]dodec-9-en-12-one (91): To a flask



containing TPAP (2 mg, 0.0052 mmol), NMO (18.4 mg, 0.1568 mmol), and 4 Å molecular sieves (50 mg), and a stirring bar, was added **90** (33.7 mg, 0.1045 mmol) in DCM (5 mL). This was stirred for 30 minutes and then the reaction mixture was filtered through a pad of silica and washed with EtOAc. The solvent was evaporated leaving the crude product which was flashed with 10%

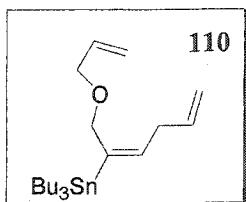
ethylacetate/hexane to give lactone **91** as white crystals (23.6 mg, 71%). IR (neat, cm^{-1}) 2935, 2859, 1765, 1493, 1165, 1126; ^1H -NMR (500 MHz, CDCl_3) * 7.39-7.20 (m, 5H), 6.69 (d, $J = 16.3$ Hz, 1H), 6.53 (d, $J = 16.3$ Hz, 1H), 5.91 (s, 1H), 5.86-5.78 (m, 1H), 5.27-5.19 (m, 2H), 2.65 (dd, $J = 1.4, 17.8$ Hz, 1H), 2.48-2.40 (m, 3H), 2.26 -2.23 (m, 1H), 2.08-2.02 (m, 1H), 1.86-1.77 (m, 2H), 1.65-1.44 (m, 3H), 1.27 -1.14 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3) * 180.6, 137.4, 136.7, 133.5, 132.9, 129.3, 128.74, 128.67, 128.3, 127.9, 126.6, 119.4, 80.8, 50.8, 47.2, 35.1, 33.4, 31.9, 24.0, 23.8, 20.3; HRMS (EI) m/z (M^+) calcd 320.1776 for $\text{C}_{22}\text{H}_{24}\text{O}_2$, obsd 320.1757, mp:124-127 °C.



2-Tributylstannanyl-hexa-2,5-dien-1-ol (109): The alcohol **108**

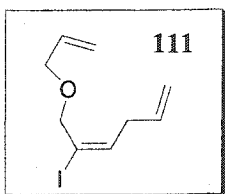
(6.70 g, 69.7 mmol) was diluted with toluene (20 mL) and then canulated into a flask containing $\text{Pd}(\text{PPh}_3)_4$ (0.4030 g, 0.3485 mmol) stirring in toluene (50 mL) under argon. The flask was stirred for 1 hour, and then cooled to 0 °C. Tributyltin hydride (20.7 mL, 77.0 mmol) was added and the reaction was allowed to stir for 20 minutes and then the toluene was evaporated. The crude mixture was flashed with 5% EthylAcetate/Hexanes to give **109** as a clear oil (13.80 g, 51 %) IR (neat, cm^{-1}) 3421, 3081, 2956, 2924, 2871, 2854, 1639, 1608, 1464, 1376, 1071, 1021; ^1H -NMR (300 MHz, CDCl_3) * 5.87- 5.73 (m, 1H), 5.70-5.42 (m, 1H),

5.05-4.95 (m, 2H), 4.44- 4.26 (m, 2H), 2.82 (t, J = 6.3 Hz, 2H), 1.58-1.21 (m, 13H), 0.99-0.77 (m, 15H) ; ^{13}C NMR (75 MHz, CDCl_3) *147.2, 136.6, 136.2, 114.8, 63.4, 33.8, 29.2, 27.4, 13.7, 10.0; HRMS (EI) m/z (M^+ - C_4H_9) calcd 331.1084 for $\text{C}_{14}\text{H}_{27}\text{OSn}$, obsd 331.1091.



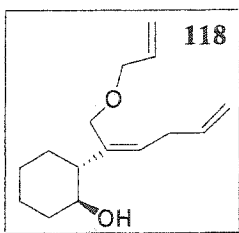
(1-Allyloxymethyl-penta-1,4-dienyl)-tributyl-stannane (110):

The alcohol 109 (4.00 g, 10.33 mmol) was added to a flask containing NaH (0.62 g, 15.50 mmol), and NaI (0.465 g, 3.1 mmol), stirring in a 1:1 mixture of THF/DMF (50 mL) at 0°C . This was stirred for 30 minutes and then allyl bromide (1.77 mL, 20.66 mmol) was added. The mixture was stirred for 24 hours and then quenched with 100 mL H_2O . The mixture was extracted with 1:1 Ether/Hexanes (4 x 50 mL) and the combined organic layers were dried over MgSO_4 . The solvent was evaporated and the crude oil was flashed with 5% EtOAc/Hexanes to give the product 110 (4.23 g, 96%) as a colorless oil.



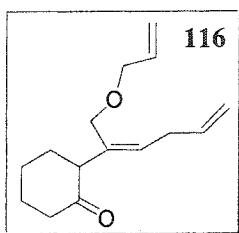
6-Allyloxy-5-iodo-hexa-1,4-diene (111): Iodine (2.76 g, 10.88 mmol) was added to a flask containing the vinylstannane 110 (4.23 g, 9.89 mmol) stirring in DCM (30 mL). This was allowed to stir for 30 minutes and then TBAF (10 mL, 10 mmol) was added. The mixture

was stirred for an additional 30 minutes and then the reaction was quenched with Na_2SO_3 (sat. aq.) (40 mL). The aqueous layer was extracted with DCM (3 x 40 mL) and the combined organic layers were dried over MgSO_4 and concentrated. The crude product was flashed with 1-10% EtOAc/Hexanes to give colorless oil 111 (1.49 g, 57%). [Note: this compound decomposes quickly at room temperature, as well as under refrigeration for longer than a few days] IR (neat, cm^{-1}) 3080, 3008, 2979, 2912, 2852, 1640, 1426, 1355, 1089, 919; ^1H -NMR (500 MHz, CDCl_3) * 6.42 (t, J = 7.8 Hz, 1H), 5.95-5.87 (m, 1H), 5.76-5.68 (m, 1H), 5.29 (dd, J = 1.6, 17.3 Hz, 1H), 5.19 (dd, J = 1.3, 10.4 Hz, 1H), 5.06-5.01 (m, 2H), 4.11 (s, 2H), 3.96-3.94 (m, 2H), 2.87-2.84 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3) * 141.9, 134.4, 117.6, 116.2, 99.6, 71.1, 70.3, 35.1; HRMS (EI) m/z (M^+) calcd 264.0011 for $\text{C}_9\text{H}_{13}\text{IO}$, obsd 263.9977.



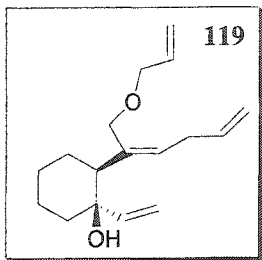
2-(1-Allyloxymethyl-penta-1,4-dienyl)-cyclohexanol (118):

Freshly prepared 6-Allyloxy-5-iodo-hexa-1,4-diene **111** (270 mg, 1.02 mmol) was dissolved in 15 mL of dry and degassed [with Argon] ether and then the mixture was cooled to $-98\text{ }^{\circ}\text{C}$. Next, *t*-BuLi (1.62 mL, 2.10 mmol) was added, and the reaction was stirred for 5 minutes. Freshly prepared 2-thienyl-lithiumcyanocuprate (4.40 mL, 0.25 M in THF, 1.10 mmol) was next added and this was stirred for 2 minutes. Cyclohexene oxide (0.3 mL, 3.00 mmol) was added along with $\text{BF}_3 \cdot \text{OEt}_2$ (0.36 mL, 3.00 mmol) and the reaction was allowed to warm to $-78\text{ }^{\circ}\text{C}$. This was stirred at $-78\text{ }^{\circ}\text{C}$ for 1 hour, and then quenched at $-78\text{ }^{\circ}\text{C}$ with saturated basic ammonium chloride solution (15 mL), warmed to room temperature and extracted with ethyl acetate (45 mL, 3 x 15 mL). The combined extracts were dried (MgSO_4) and concentrated *in vacuo* and column chromatography with 5% EtOAc/Benzene gave alcohol **118** as yellow crystals (96.8 mg, 40%).



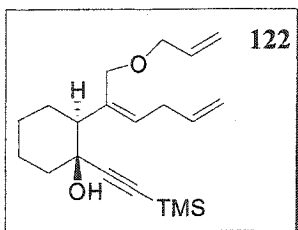
2-(1-Allyloxymethyl-penta-1,4-dienyl)-cyclohexanone (116): To a flask containing TPAP (6 mg, 0.0154 mmol), NMO (54 mg, 0.4634 mmol), 4 Å molecular sieves (160 mg), and a stirring bar, was added **118** (73 mg, 0.3089 mmol) in DCM (5 mL). This was stirred for 3 hours and then the reaction mixture was filtered through a pad of

silica and washed with EtOAc. The solvent was evaporated leaving the crude product which was flashed with 10% ethylacetate/hexane to give ketone **116** as a colorless oil (39.3 mg, 54%). IR (neat, cm^{-1}) 3074, 2934, 2861, 1709, 1450, 1126, 1077; $^1\text{H-NMR}$ (500 MHz, CDCl_3) * 5.89-5.75 (m, 2H), 5.35 (t, $J = 7.3\text{ Hz}$, 1H), 5.22 (dd, $J = 1.5, 17.2\text{ Hz}$, 1H), 5.13 (d, $J = 10.4\text{ Hz}$, 1H), 5.04 (dd, $J = 1.6, 17.2\text{ Hz}$, 1H), 4.97 (dd, $J = 1.4, 10.1\text{ Hz}$, 1H), 4.03 (d, $J = 11.6\text{ Hz}$, 1H), 3.93 (d, $J = 11.6\text{ Hz}$, 1H), 3.90-3.83 (m, 2H), 3.23-3.19 (m, 1H), 2.88-2.83 (m, 2H), 2.41-2.30 (m, 2H), 2.09-1.63 (m, 6H); $^{13}\text{C NMR}$ (125 MHz, CDCl_3) * 211.2, 136.5, 135.5, 134.9, 128.2, 116.9, 115.2, 71.1, 67.4, 55.6, 42.3, 32.5, 31.9, 27.7, 25.3; HRMS (EI) m/z ($\text{M}^+ - \text{C}_3\text{H}_5$) calcd 193.1229 for $\text{C}_{12}\text{H}_{17}\text{O}_2$, obsd 193.1257.



2-(1-Allyloxymethyl-penta-1,4-dienyl)-1-vinyl-cyclohexanol (119): Ketone 116 (39.3 mg, 0.1677 mmol) was dissolved in THF (4 mL) and cooled to 0 °C with stirring. Vinyl magnesium bromide (0.3354 mmol, 0.38 mL) was added to the reaction and this was allowed to stir for 3 hours. The reaction was then quenched with NH₄Cl (sat. aq.), extracted with EtOAc (3x) and the combined organic layers were dried over MgSO₄ and concentrated. Flash chromatography with 10% EtOAc/Hexanes gradient gave **119** as a colorless oil (18.5 mg, 42%). IR (neat, cm⁻¹) 3412, 3082, 3006, 2932, 2855, 1638, 1446, 1349, 1271, 1172, 1065; ¹H-NMR (300 MHz, CDCl₃) * 5.94-5.68 (m, 3H), 5.45 (t, J = 7.53 Hz, 1H), 5.32-4.89 (m, 6H), 4.10 (d, J = 2.4 Hz, 1H), 4.03-3.93 (m, 2H), 3.89 –3.79 (m, 2H), 2.84-2.78 (m, 2H), 2.24 (dd, J = 3.03, 12.64 Hz, 1H), 1.96-1.18 (m, 8H); ¹³C NMR (75 MHz, CDCl₃) *146.9, 136.8, 136.4, 133.8, 132.0, 117.5, 115.2, 110.8, 73.0, 70.9, 64.3, 54.8, 38.5, 31.9, 26.7, 26.4, 21.3; HRMS (EI) *m/z* (M⁺) 262.1933 for C₁₇H₂₆O₂, obsd 262.1908.

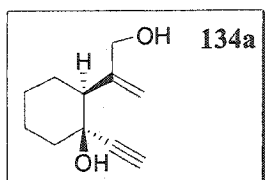
2-(1-Allyloxymethyl-penta-1,4-dienyl)-1-trimethylsilanylethynyl-cyclohexanol



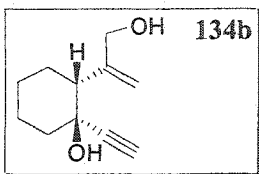
(122): In a 25 mL roundbottom flask, TMS acetylene (0.1536 mmol, 0.03 mL) was added to 3 mL of dry THF and the flask was then cooled to -78 °C. To this was then added *n*-BuLi (0.1408 mmol, 0.06 mL), and the reaction was allowed to stir for 15 minutes. Ketone 116, dissolved in 2 mL of THF, was then cannulated into the flask and the reaction was stirred for 30 minutes. This was then quenched at 0 °C with saturated NH₄Cl (aq), and then extracted with ethyl acetate (3X). The combined organic layers were dried over MgSO₄, filtered, and concentrated. The residue was purified on a short column (10% EtOAc/Hexanes) to give **122a** (11 mg, 27%) as a colorless oil. IR (neat) 3340, 2935, 2860, 1727, 1448, 1340, 1250, 1074; ¹H NMR (CDCl₃) * 5.92-5.75 (m, 2H), 5.65 (t, J = 7.5 Hz, 1H), 5.29 (dd, J = 1.6, 17.3 Hz, 1H), 5.19 (dd, J = 1.1, 20.4 Hz, 1H), 5.06 (dd, J = 1.7, 17.1 Hz, 1H), 4.99 (dd, J = 1.6 Hz, 10.1 Hz, 1H), 4.86 (br. s, 1H), 4.16-4.08 (m, 2H), 3.94-3.87 (m, 2H), 2.89 (br. t, J = 5.6

Hz, 2H), 2.32 (dd, $J = 3.0, 12.7$ Hz, 1H), 2.10-2.06 (m, 1H), 1.86-0.81 (m, 7H), 0.10 (s, 9H); ^{13}C NMR (CDCl_3) * 136.4, 135.8, 134.0, 133.2, 117.6, 115.4, 87.0, 80.2, 70.2, 68.5, 63.9, 55.5, 39.7, 32.1, 26.1, 25.7, 20.6, 0.1; HRMS (EI) m/z ($\text{M}^+ - \text{C}_3\text{H}_5$) calcd 291.1780 for $\text{C}_{17}\text{H}_{27}\text{O}_2\text{Si}$, obsd 291.1799.

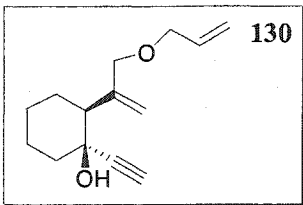
1-Ethynyl-2-(1-hydroxymethyl-vinyl)-cyclohexanol (134a):



To a solution of ketone **62** (1.50 g, 10.8 mmol) in ether (100 mL) at 0 °C was added ethynylmagnesium bromide (26 mL, 13 mmol) dropwise. The mixture was warmed to room temperature and allowed to stir for 3 hrs. The reaction was quenched with a saturated aqueous solution of ammonium chloride. The mixture was extracted with ethyl acetate (3X) and the combined organic layers were dried over MgSO_4 , filtered and concentrated. The residue was purified by flash chromatography (5% ethyl acetate in 95% hexanes) to give a mixture of diastereomers **133** (dr = 1.5:1) as a yellow oil. The oil (450 mg) was dissolved in DCM (40 mL) at room temperature and SeO_2 (0.205 g, 1.85 mmol) was added to the mixture, followed by *t*-BuOOH (2.0 mL, 14.5 mmol). After 48 hrs, SeO_2 (0.201 g, 1.81 mmol) was added and 24 hrs later, *t*-BuOOH (1.0 mL, 7.3 mmol) was added. The reaction was quenched 48 hrs later with a saturated aqueous solution of ammonium chloride. The mixture was extracted with ethyl acetate (3X) and the organic layers were combined and washed with Na_2CO_3 , water and saturated solution of sodium chloride. The combined organic layers were dried over MgSO_4 , filtered and concentrated. The residue was purified by flash chromatography (12% ethyl acetate in 88% hexanes) to give **134a** (296.0 mg, 15% for 2 steps), the major diastereomer, as a colorless oil. IR (neat) 3200 (w), 2927 (m), 2847 (w), 1654 (w), 1264 (m), 1129 (m), 1071 (w), 1048 (s), 971 (m); ^1H NMR (300 MHz, CDCl_3) * 5.17 (s, 1H), 5.06 (s, 1H), 4.41 (s, 1H), 4.13 (s, 2H), 2.87 (s, 1H), 2.41 (s, 1H), 2.34 (dd, $J = 3.4\text{Hz}, 12.9\text{Hz}$, 1H), 2.14-2.06 (m, 1H), 1.87-1.24 (m, 3H), 1.50-1.17 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3) *. 148.5(C4), 117.4(CH₂), 88.5(C4), 71.8(C4), 67.6(CH), 64.8(CH₂), 52.4(CH), 39.5(CH₂), 26.0(CH₂), 25.6(CH₂), 20.4(CH₂); HRMS (EI) m/z calcd for $\text{C}_{11}\text{H}_{14}\text{O}$ ($[\text{M}-\text{H}_2\text{O}]^+$) 162.1045 for $\text{C}_{11}\text{H}_{14}\text{O}$, found 162.1050.



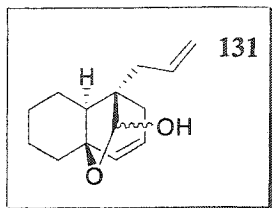
Compound **134b**, the minor diastereomer, was also obtained as colorless oil (197.0 mg, 10% for 2 steps). IR (neat) 3300 (m), 2934 (s), 2859 (m), 1651 (w), 1445 (w), 1124 (w), 1064 (m), 1004 (w), 906 (w); ^1H NMR (300 MHz, CDCl_3) * 5.25 (d, $J = 0.9\text{Hz}$, 1H), 5.19 (s, 1H), 4.36 (s, 1H), 4.18 (d, $J = 12.4\text{Hz}$, 1H), 4.02 (d, $J=12.4\text{Hz}$, 1H), 3.18 (s, 1H), 2.49 (s, 1H), 2.18-2.05 (m, 2H), 1.77-1.47 (m, 6H), 1.32-1.13 (m, 1H); ^{13}C NMR (75 MHz, CDCl_3) * 148.2(C4), 116.0(CH₂), 85.2(C4), 74.7(CH), 72.0(C4), 67.4(CH₂), 51.7(CH), 41.3(CH₂), 30.0(CH₂), 25.7(CH₂), 23.7(CH₂); HRMS (EI) m/z calcd (M^+) 180.11503 for $\text{C}_{11}\text{H}_{16}\text{O}_2$, found 180.11467.



2-(1-Allyloxymethyl-vinyl)-1-ethynyl-cyclohexanol (130):

To a solution of diol **134a** (96.8 mg, 0.537 mmol) in a mixture of THF/DMF (5 / 1.7 mL) was added sodium hydride 60% in oil (23.0 mg, 0.575 mmol) at 0 °C. After 10 min, allyl bromide (0.055 mL, 0.636 mmol) was added to the mixture. The mixture was stirred at 0 °C for 1 hr. The reaction was quenched with a saturated aqueous solution of ammonium chloride. The mixture was extracted with ethyl acetate (3X) and the combined organic layers were dried over MgSO_4 , filtered and concentrated. The residue was purified by flash chromatography (30% diethyl ether in 70% hexanes) to give **130** (99.8 mg, 84%) as a colorless oil. IR (neat) 3306 (s), 3300 (m), 3079 (m), 2936 (s), 2857 (s), 1644 (m), 1446 (m), 1351 (m), 1144 (m), 1070 (s), 977 (s), 922 (s), 648 (m); ^1H NMR (CDCl_3) * 5.92-5.79 (m, 1H), 5.24 (d, $J = 17.2\text{Hz}$, 1H), 5.17-5.13 (m, 3H), 4.48 (s, 1H), 4.11-4.06 (m, 2H), 3.91-3.78 (m, 2H), 2.35-2.27 (m, 2H), 2.10-2.04 (m, 1H), 1.83-1.50 (m, 4H), 1.48-1.13 (m, 3H); ^{13}C NMR (CDCl_3) * 144.8(C4), 133.6(CH), 119.6(CH₂), 117.7(CH₂), 88.5(C4), 71.5(CH₂), 71.2(C4), 70.4(CH₂), 67.3(CH), 52.9(CH), 39.4(CH₂), 25.7(2CH₂), 20.3(CH₂); HRMS (EI) m/z calcd ($[\text{M}-\text{C}_3\text{H}_6\text{O}]^+$) 162.10447 for $\text{C}_{11}\text{H}_{14}\text{O}$, found 162.1061.

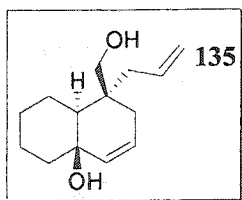
7-Allyl-11-oxa-tricyclo[5.3.2.01,6]dodec-9-en-12-ol (131): A clean, dry microwave cell



was charged with a solution of compound 130 (1.04 g, 4.73 mmol) and DBU (0.050 mL) in toluene (17 mL). This mixture was degassed by bubbling it with argon for 20 minutes. The microwave cell was then sealed, and the reaction was heated from room temperature to 210 °C over 15 minutes and then held

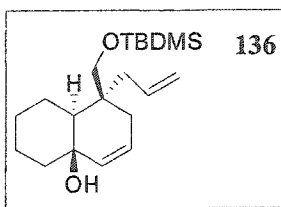
at this temperature for 40 minutes. After cooling, the reaction mix was concentrated and the residue was subjected to flash chromatography (20% EtOAc/Hexanes) to obtain lactol 131 (850 mg, 85%) as an off white solid. (Mixture of Diastereomers) IR (neat, cm^{-1}) 3379, 3074, 3025, 2930, 2855, 1822, 1727, 1640, 1143, 1100; $^1\text{H-NMR}$ (300 MHz, CDCl_3) * 5.83-5.51 (m, 3H), 5.24 (d, $J = 6.9$, 0.55H) + 5.07-4.96 (m, 2.45H), 4.97 (d, $J = 4.3$ Hz, 0.45H), 4.07 (d, $J = 4.3$ Hz, 0.55H), 2.40-2.11 (m, 3H), 1.98-1.85 (m, 2H), 1.73-1.23 (m, 8H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3) * 137.2, 136.6, 135.4, 134.7, 128.1, 126.5, 117.4, 117.3, 105.1, 103.8, 78.5, 49.3, 49.1, 48.8, 45.9, 38.7, 37.3, 35.3, 33.3, 32.6, 32.4, 29.6, 25.0, 24.7, 23.3, 23.2, 21.0, 20.9; Mp: 55-57 °C.

8-Allyl-8-hydroxymethyl-1,3,4,7,8,8a-hexahydro-2H-naphthalen-4a-ol (135): To a



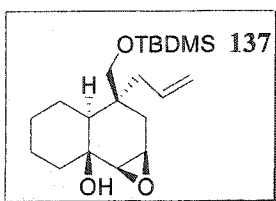
solution of lactol 131 (83 mg, 0.37 mmol) in THF (5 mL) at 0 °C was added LiAlH_4 (20 mg) This was stirred for 1.5 hours, and then 10 mL of H_2O was added carefully. The organic phase was extracted with EtOAc (3X), dried over MgSO_4 , and concentrated.

The crude product was flashed on a short column (40% EtOAc/Hexanes) to give diol 135 (80 mg, 95%) as a white solid.



8-Allyl-8-(tert-butyl-dimethyl-silanyloxymethyl)-1,3,4,7,8,8a-hexahydro-2H-naphthalen-4a-ol (136): To a solution of diol 135 (335 mg, 1.51 mmol) in dry DMF (10 mL) stirring at room temperature was added NEt₃ (4.53 mmol) and DMAP (0.15

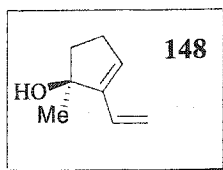
mmol), followed by TBDMSCl (1.81 mmol). This was stirred for 12 hours and then poured into 150 mL of water, and extracted with Et₂O (4 x 30 mL). The combined organic phases were dried over MgSO₄. The residue was subjected to flash chromatography (10% EtOAc/Hexanes) to afford 136 (442 mg, 87%) as a viscous yellow oil. IR (neat, cm⁻¹) 3428, 2075, 3015, 2929, 2857, 1445, 1255, 1081; ¹H-NMR (300 MHz, CDCl₃) * 5.73-5.59 (m, 1H), 5.57-5.51 (m, 1H), 5.46-5.42 (m, 1H), 5.04-4.93 (m, 2H), 4.55 (d, J = 1.8 Hz, 1H), 3.63 (d, J = 10.2, 1H), 3.19 (d, J = 10.6 Hz, 1H), 2.09-2.02 (m, 1H), 1.95-1.1.85 (m, 1H), 1.79-1.58 (m, 6H), 1.43-1.38 (m, 3H), 1.21-1.12 (m, 2H), 0.81 (s, 9H), -0.01 (s, 6H); ¹³C NMR (75 MHz, CDCl₃) * 134.0, 133.7, 126.3, 118.3, 67.7, 66.6, 48.3, 41.5, 39.2, 38.5, 33.6, 27.0, 25.7, 21.2, 20.2, 18.0, -5.6. HRMS (EI) *m/z* (M⁺ -18) calcd 318.2379 for C₂₀H₃₄OSi, obsd 318.2375.



3-Allyl-3-(tert-butyl-dimethyl-silanyloxymethyl)-octahydro-1-oxa-cyclopropa[a]naphthalen-7a-ol (137):

A clean dry re-sealable pressure tube was charged with compound 136 (200 mg, 0.59 mmol) and toluene (10 mL). This was degassed for 10 minutes by bubbling with argon, and a solution of VO(Acac)₂ (2 mg/mL in toluene, 1 mL) was added followed by *t*-BuOOH (70% in H₂O, 1.52 mmol) at which point the solution turned dark red. The tube was sealed and heated to 120 °C for 24 hours, during which time the reaction turned orange. The mixture was cooled, and a saturated solution of Na₂S₂O₃ was added (1 mL). After one minute of stirring, the solution was extracted with EtOAc (3 X 10 mL), dried over MgSO₄ and concentrated. The residue was subjected to flash chromatography (0 to 40% EtOAc/Hexane) to afford

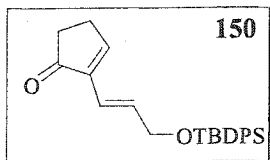
epoxide **137** (170 mg, 82%) as a white solid. IR (neat, cm^{-1}) 3583, 3452, 3075, 2930, 2855, 1638, 1471, 1447, 1255, 1085; $^1\text{H-NMR}$ (300 MHz, CDCl_3) * 5.69-6.66 (m, 1H), 5.04-4.94 (m, 2H), 3.52-3.41 (m, 2H), 3.25-3.23 (m, 1H), 2.85 (d, $J = 3.9$ Hz, 1H), 2.65 (d, $J = 1.2$ Hz, 1H), 2.04-1.91 (m, 3H), 1.83-1.67 (m, 3H), 1.64-1.46 (m, 4H), 1.39-1.24 (m, 1H), 1.20-1.03 (m, 1H), 0.95 (dd, $J = 3.1, 11.9$ Hz, 1H), 0.83 (s, 9H), -0.02 (s, 6H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3) * 134.2, 118.3, 67.9, 67.1, 58.7, 55.1, 47.9, 41.2, 39.6, 39.4, 29.5, 26.9, 25.8, 21.4, 20.8, 18.1; HRMS (EI) m/z ($\text{M}^+ - \text{C}(\text{CH}_3)_3$) calcd 295.1729 for $\text{C}_{16}\text{H}_{27}\text{O}_3\text{Si}$, obsd 295.1753.



1-Methyl-2-vinyl-cyclopent-2-enol (148): 2-Vinyl-cyclopent-2-enone **147** (101 mg, 0.934 mmol) was stirred in THF (10 mL) at -78 $^\circ\text{C}$. To this was added MeLi in THF (1.12 mmol, 1.4 M, 0.80 mL).

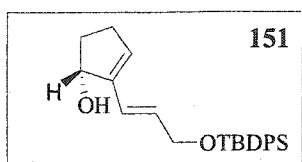
The reaction was stirred for 20 minutes, and then warmed to 0 $^\circ\text{C}$ and quenched with saturated NH_4Cl (10 mL). The mixture was extracted with EtOAc (3x) and the combined organic layers were dried over MgSO_4 and concentrated. Flash chromatography with 20% EtOAc/Hexanes gave **148** as a colorless oil (75 mg, 65 %). IR (neat, cm^{-1}) 3382, 2926, 2851, 1438, 1097, 1028; $^1\text{H-NMR}$ (300 MHz, C_6D_6) * 6.29 (dd, $J = 11.3, 17.9$ Hz, 1H), 5.75 (dd, $J = 1.1, 17.9$ Hz, 1H), 5.45 (t, 2.4Hz, 1H), 5.08 (dd, $J = 1.5, 11.3$ Hz, 1H), 2.02-1.78 (m, 3H), 1.71-1.55 (m, 1H), 1.35 (s, 3H), 1.03 (s, 1H); $^{13}\text{C NMR}$ (75 MHz, C_6D_6) * 146.7, 130.6, 130.2, 115.3, 83.3, 42.6, 28.7, 25.8, 15.3.

2-[3-(tert-Butyl-diphenyl-silanyloxy)-propenyl]-cyclopent-2-enone (150): In an argon



flushed flask fitted with a condenser, 2-iodo-2-cyclopentenone **145** (679 mg, 3.26 mmol), copper (I) iodide (62 mg, 3.26 mmol), triphenylarsine (100 mg, 3.26 mmol) and *bis*(benzonitrile) palladium(II) chloride (62 mg, 1.63 mmol) were placed and NMP (1.5 mL) was added. The flask was next lowered into an oil bath maintained at 100 $^\circ\text{C}$ and stannane **149** (2.29 g, 3.92 mmol) was cannulated in with 1.5 mL of NMP. After 1 hour, the flask and contents were cooled to room temperature and the mixture was dissolved in EtOAc (100

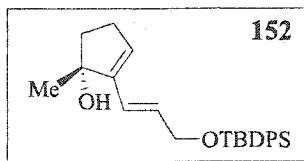
mL) and washed successively with aqueous KF solution (0.67 satd, 3 x 30 mL) and water (2 x 30mL). The aqueous layers were combined and back-extracted with EtOAc (60 mL), and the combined organic layers were dried over MgSO₄ and then concentrated. The dark oily residue was next flashed with 2-10% Ether/Pet.Ether to give enone **150** (918 mg, 75%) as a yellow oil. IR (neat, cm⁻¹) 3071, 2937, 2859, 1971, 1902, 1826, 1707, 1448, 1376, 1093; ¹H-NMR (300 MHz, CDCl₃) * 7.67 (d, J = 7.1 Hz, 4H), 7.43-7.34 (m, 7H), 6.79 (dt, J = 4.1, 15.9 Hz, 1H), 6.42 (d, J = 15.9 Hz, 1H), 4.30 (d, J = 2.39 Hz, 2H), 2.60 (s, 2H), 2.47-2.45 (m, 2H), 1.06 (s, 9H) ; ¹³C NMR (75 MHz, CDCl₃) * 208.3, 158.5, 140.5, 135.5, 133.5, 133.3, 129.6, 127.7, 118.7, 64.1, 35.7, 26.8, 26.3, 19.3; HRMS (EI) *m/z* (M⁺ - C(CH₃)₃) calcd 319.1154 for C₂₀H₁₉O₂Si, obsd 319.1175.



2-[3-(tert-Butyl-diphenyl-silyloxy)-propenyl]-cyclopent-2-

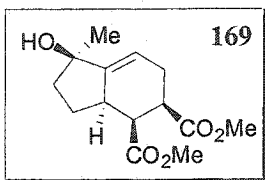
enol (151): Ketone **150** (32.5 mg, 0.0864 mmol) was stirred in MeOH (5 mL) at 0 °C and CeCl₃·7H₂O was added. This was

allowed to stir for 5 minutes and then NaBH₄ (4 mg, 0.1058 mmol) was added. The reaction was allowed to stir for another 5 minutes and then it was quenched with saturated NH₄Cl (5 mL). The stir bar was removed and the flask was placed on the rotovap to remove the solvent. The dry residue was diluted with Et₂O (5 mL) and H₂O (5 mL). The aqueous phase was extracted with Et₂O (3X) and then the combined organic layers were dried over MgSO₄. Evaporation of solvent left alcohol **151** (28.1 mg, 86%) as a colorless oil. IR (neat, cm⁻¹) 3382, 3074, 3044, 2936, 2851; 1967, 1896, 1470, 1438, 1115, 1028; ¹H-NMR (300 MHz, CDCl₃) * 7.71-7.66 (m, 4H), 7.45-7.34 (m, 6H), 6.41 (d, J = 15.9 Hz, 1H), 5.97 (dt, J = 4.6, 15.9 Hz, 1H), 5.84-5.82 (m, 1H), 4.95-4.93 (m, 1H), 4.29 (d, J = 4.6 Hz, 2H), 2.62-2.50 (m, 1H), 2.35-2.18 (m, 2H), 1.87-1.80 (m, 1H), 1.50 (br s, 1H), 1.06 (s, 9H); ¹³C NMR (75 MHz, CDCl₃) * 143.4, 135.5, 133.6 (2C's), 133.1, 129.6, 127.6, 123.9, 76.1, 64.3, 34.0, 30.2, 26.8, 19.2; HRMS (EI) *m/z* (M⁺ - H₂O) calcd 360.1909 for C₂₄H₂₈OSi, obsd 360.1922.



2-[3-(tert-Butyl-diphenyl-silanyloxy)-propenyl]-1-methylcyclopent-2-enol (152): Ketone **150** (45 mg, 0.1194 mmol) was stirred in THF (5 mL) at $-78\text{ }^{\circ}\text{C}$. To this was added MeLi in

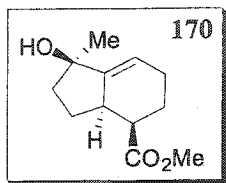
THF (0.182 mmol, 1.4 M, 0.13 mL). The reaction was stirred for 20 minutes, and then warmed to $0\text{ }^{\circ}\text{C}$ and quenched with saturated NH_4Cl (5 mL). The mixture was extracted with EtOAc (3x) and the combined organic layers were dried over MgSO_4 and concentrated. Flash chromatography with 20% EtOAc/Hexanes gave **148** as a colorless oil (37.5 mg, 80%). IR (neat, cm^{-1}) 3402, 3070, 3040, 2962, 2924, 2865, 1961, 1890, 1830, 1700, 1587, 1437, 1109; $^1\text{H-NMR}$ (300 MHz, CDCl_3) * 7.69-7.64 (m, 4H), 7.43-7.32 (m, 6H), 6.21-6.18 (m, 2H), 5.71 (t, $J = 2.6\text{ Hz}$, 1H), 4.25 (d, $J = 3.7\text{ Hz}$, 2H), 2.50-2.05 (m, 3H), 1.97-1.92 (m, 1H), 1.52 (s, 1H), 1.39 (s, 3H), 1.05 (s, 9H); $^{13}\text{C NMR}$ (75 MHz, CDCl_3) *145.9, 135.6, 133.7, 129.8, 129.7, 129.6, 127.6, 122.6, 83.3, 64.7, 42.6, 26.7, 26.8, 25.8, 19.3; HRMS (EI) m/z ($\text{M}^+ - \text{H}_2\text{O}$) calcd 374.2066 for $\text{C}_{25}\text{H}_{30}\text{OSi}$, obsd 374.2062.



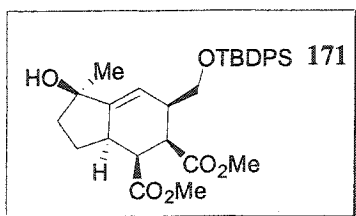
1-Hydroxy-1-methyl-2,3,3a,4,5,6-hexahydro-1H-indene-4,5-dicarboxylic acid dimethyl ester (169): Diene **148** (20 mg, 0.1611 mmol) was stirred in toluene (4 mL) at $-78\text{ }^{\circ}\text{C}$. To this was added vinyl magnesium bromide in THF (0.1772 mmol, 0.71

M, 0.25 mL) and after 15 minutes of stirring dimethyl maleate **167** (0.4833 mmol, 0.06 mL) was added. The reaction was allowed to warm to room temperature over 45 minutes after which time it was quenched with saturated NH_4Cl (5 mL). The mixture was extracted with EtOAc (3x) and the combined organic layers were dried over MgSO_4 and concentrated. Flash chromatography with 20% EtOAc/Hexanes gave **169** as a colorless oil (26.0 mg, 60 %). IR (neat, cm^{-1}) 3504, 2955, 2925, 2852, 1739, 1732, 1437, 1206, 1164; $^1\text{H-NMR}$ (300 MHz, C_6D_6) * 5.64-5.61 (m, 1H), 3.34 (s, 3H), 3.30 (s, 3H), 2.89-2.78 (m, 1H), 2.46-2.27 (m, 2H), 2.15-2.06 (m, 2H), 1.92-1.85 (m, 1H), 1.71-1.49 (m, 2H), 1.40-1.25 (m, 5H); $^{13}\text{C NMR}$ (75 MHz, C_6D_6) * 173.6, 172.1, 148.5, 117.6, 76.6,

51.4, 50.9, 42.7, 42.3, 42.2, 41.3, 27.2, 26.7, 25.8; HRMS (EI) m/z ($M^+ - H_2O$) calcd 250.1205 for $C_{14}H_{18}O_4$, obsd 250.1194.



1-Hydroxy-1-methyl-2,3,3a,4,5,6-hexahydro-1H-indene-4-carboxylic acid methyl ester (170): Diene 148 (22 mg, 0.1779 mmol) was stirred in toluene (5 mL) at $-78\text{ }^\circ\text{C}$. To this was added vinyl magnesium bromide in THF (0.2136 mmol, 0.70 M, 0.31 mL) and after 15 minutes of stirring methyl acrylate 168 (0.5337 mmol, 0.05 mL) was added. The reaction was allowed to warm to room temperature and then stirred for 2 hours after which time it was quenched with saturated NH_4Cl (5 mL). The mixture was extracted with EtOAc (3x) and the combined organic layers were dried over $MgSO_4$ and concentrated. Flash chromatography with 10-20% EtOAc/Hexanes gave 170 as a colorless oil (14.8 mg, 40%). IR (neat, cm^{-1}) 34.12, 2958, 2924, 2852, 1732, 1433, 1162; 1H -NMR (300 MHz, $CDCl_3$) * 5.76-5.72 (m, 1H), 3.62 (s, 3H), 2.98 (dd, $J = 4.8, 8.2$ Hz, 1H), 2.55-2.45 (m, 2H), 2.16-2.01 (m, 3H), 1.88-1.47 (m, 5H), 1.36 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) * 174.3, 148.9, 118.2, 77.1, 51.3, 41.4, 41.0, 40.6, 26.1, 25.9, 25.7, 22.6; HRMS (EI) m/z ($M^+ - H_2O$) calcd 192.1150 for $C_{12}H_{16}O_2$, obsd 192.1155.



6-(tert-Butyl-diphenyl-silyloxymethyl)-1-hydroxy-1-methyl-2,3,3a,4,5,6-hexahydro-1H-indene-4,5-dicarboxylic acid dimethyl ester (171): Diene 152 (45 mg, 0.1144 mmol) was stirred in toluene (5 mL) at $-78\text{ }^\circ\text{C}$. To this was added vinyl magnesium bromide in THF (0.1258 mmol, 0.71 M, 0.18 mL) and after 15 minutes of stirring dimethyl maleate 167 (0.3432 mmol, 0.04 mL) was added. The reaction was allowed to warm to room temperature over 45 minutes after which time it was quenched with saturated NH_4Cl (5 mL). The mixture was extracted with EtOAc (3x) and the combined organic layers were dried over $MgSO_4$ and concentrated. Flash chromatography with 10-20% EtOAc/Hexanes gave 171 as a colorless oil (26.6 mg, 43%). IR (neat, cm^{-1}) 3498, 3071,

3048, 2954, 2931, 2892, 2857, 1962, 1898, 1830, 1738, 1434 1196, 1170, 1083; $^1\text{H-NMR}$ (300 MHz, C_6D_6) * 7.82-7.78 (m, 4H), 7.25-7.18 (m, 6H), 6.09-6.06 (m, 1H), 4.09-4.03 (m, 1H), 3.92-3.87 (m, 1H), 3.25 (s, 3H), 3.23 (s, 3H), 2.88-2.83 (m, 3H), 2.23-2.16 (m, 2H), 1.96-1.89 (m, 1H), 1.72-1.56 (m, 2H), 1.46-1.36 (m, 4H), 1.19 (s, 9H) ; $^{13}\text{C NMR}$ (75 MHz, C_6D_6) * 173.1, 173.0, 151.1, 136.1, 134.1, 130.0, 128.4, 118.9, 76.8, 65.5, 51.2, 50.9, 43.8, 43.1, 41.6, 41.3, 40.3, 27.2, 27.0, 26.8, 19.6; HRMS (EI) m/z ($\text{M}^+ - \text{C}(\text{CH}_3)_3$) calcd 479.1890 for $\text{C}_{27}\text{H}_{31}\text{O}_6\text{Si}$, obsd 479.1911.

CLAIMS TO ORIGINAL RESEARCH

1. Developed a series of dienes using the tandem oxy-Cope/ene and oxy-Cope/ene/Claisen reactions. Examined their reactivity under hydroxy-directed Diels-Alder conditions.
2. Examined an approach toward 3.2.5.β,20-Epoxy-hydroxy-ros-15-ene based upon the tandem oxy-Cope/ene/Claisen reaction.
3. Conducted preliminary research into the synthesis of Isovelleral analogues using a hydroxy-directed Diels-Alder Reaction.
4. Poster Presentation: 'Applications of a Hydroxy-Directed Diels Alder Reaction'
R. MacLean and L. Barriault, 13th Québec-Ontario Minisymposium in Synthetic and Bioorganic Chemistry, November 8-10, 2002, Queen's University, Kingston, Ontario.

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APPENDIX

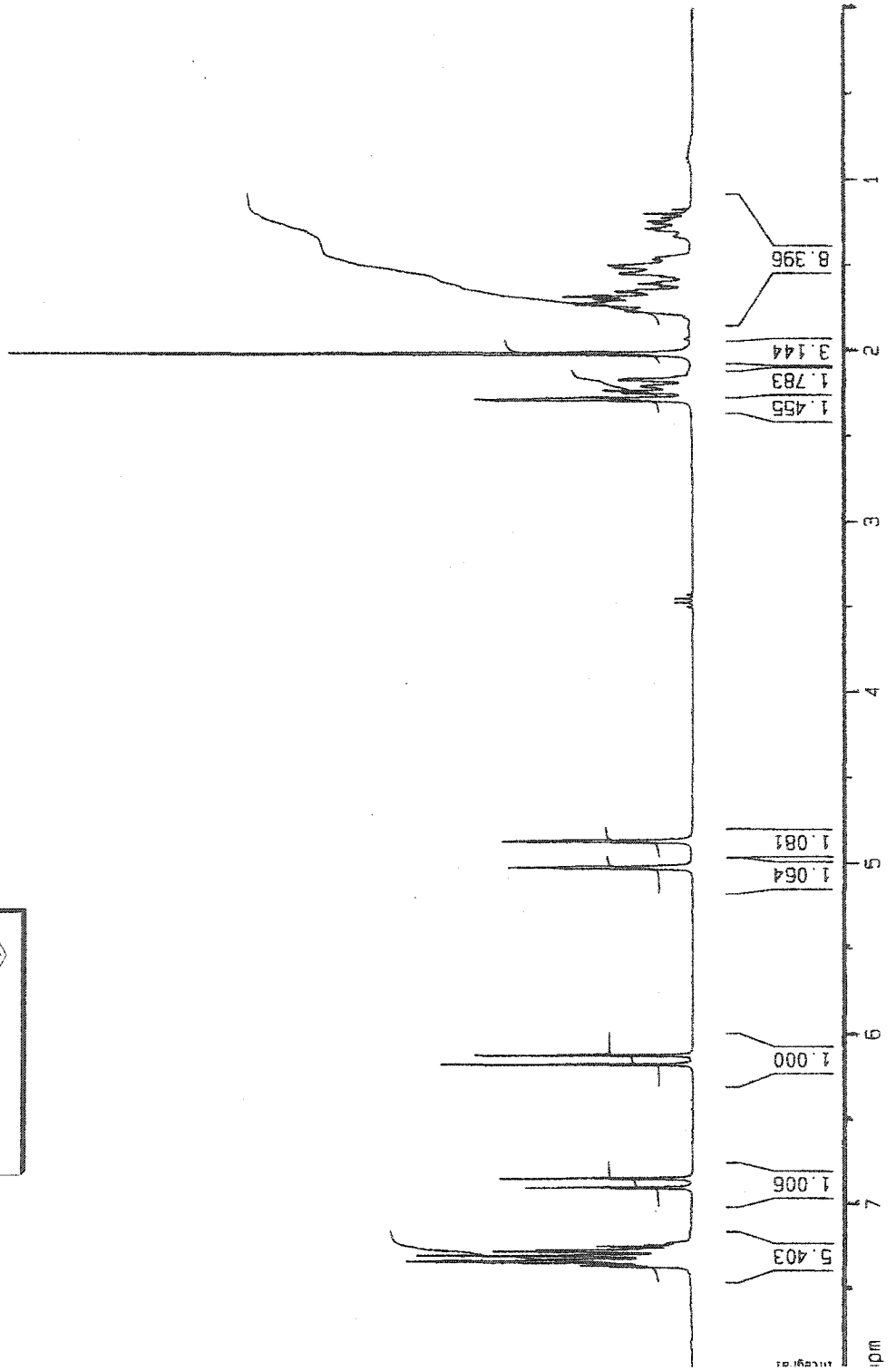
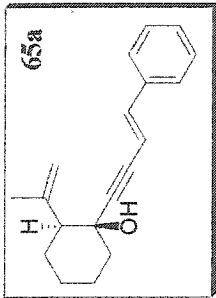
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 DE 5.00 usec
 TE 300.0 K
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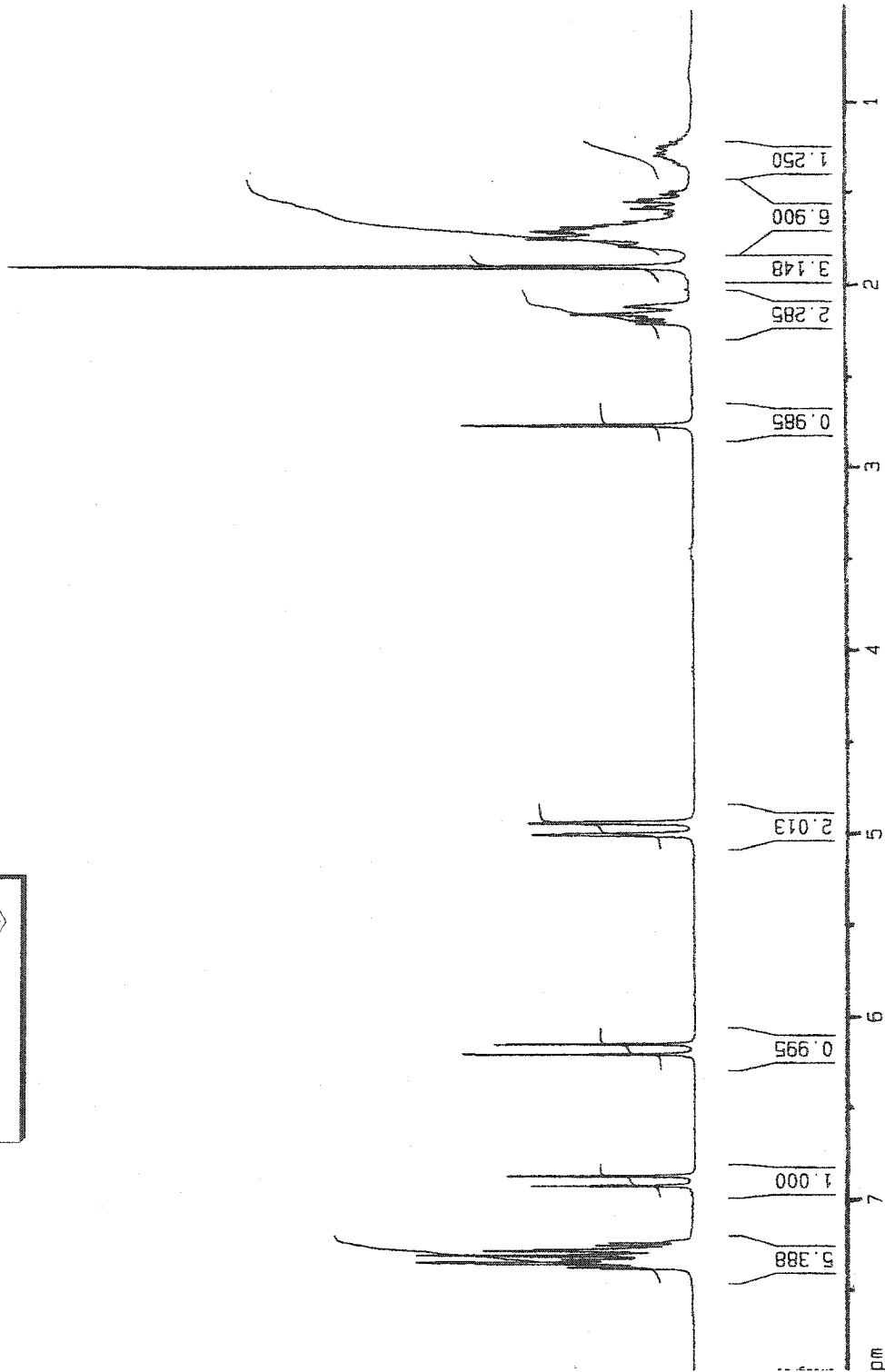
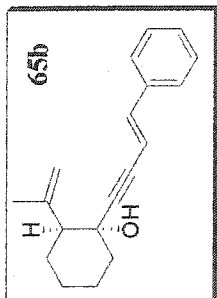
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 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
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 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

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 GB 0
 PC 1.00

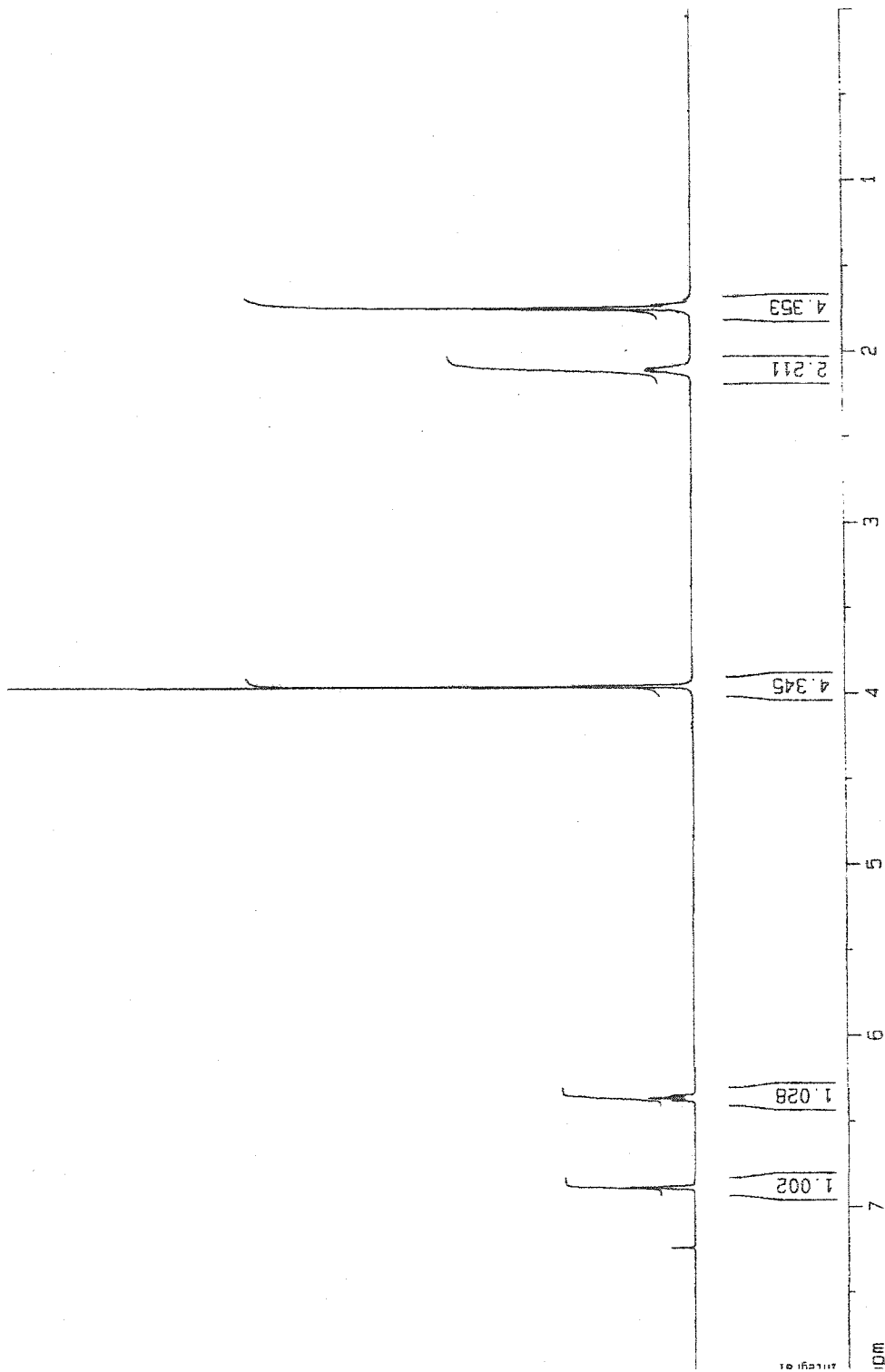
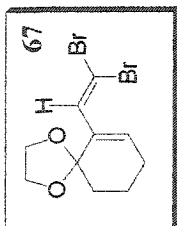
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 TD 30720
 SOLVENT CDCl3
 NS 48
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 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
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 TE 300.0 K
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 SSB 0
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 GB 0
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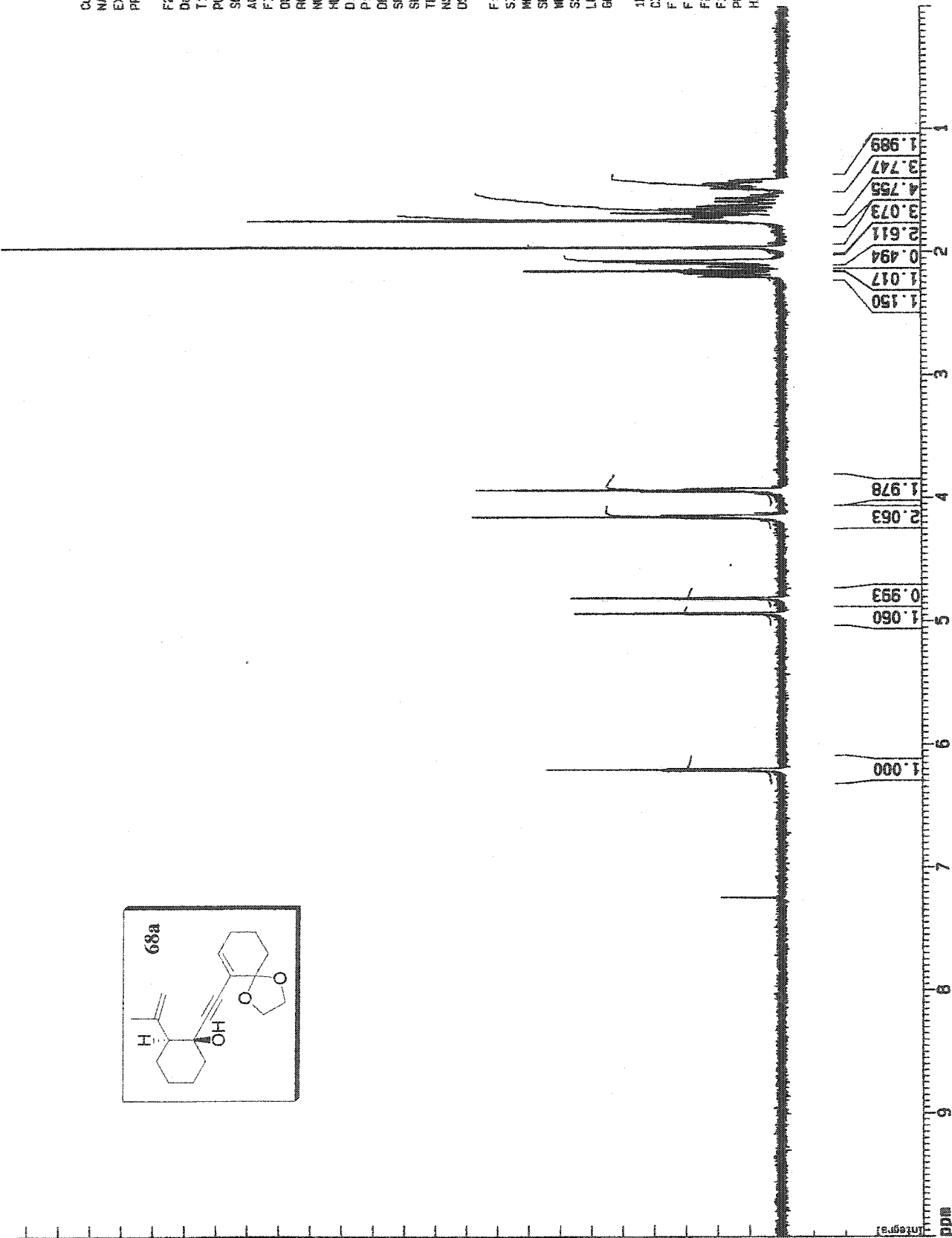
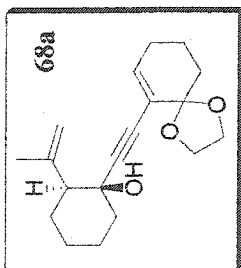


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 D1 0.0100000 sec
 P1 5.6 usec
 DE 88.8 usec
 SF01 500.1381707 MHz
 SWH 7042.25 Hz
 TD 65536
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 DS 0

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 LB 0.00 Hz
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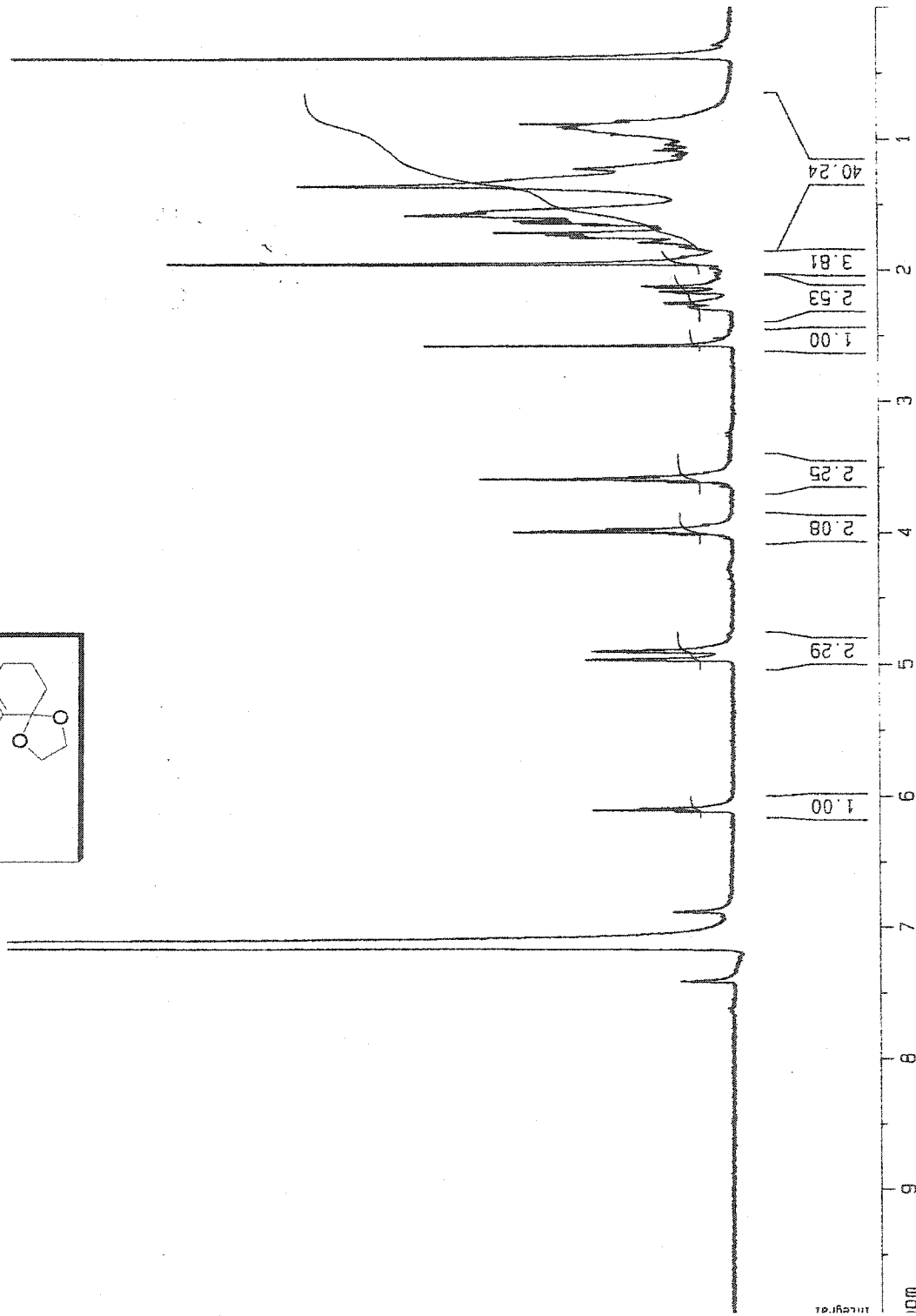
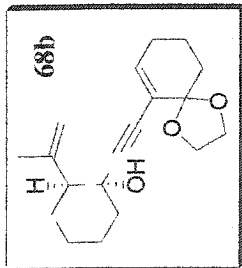
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 AQ 3.0228980 sec
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F2 - Processing parameters
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 SF 300.1299999 MHz
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 SSB 0
 LB 0.10 Hz
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1D NMR plot parameters
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 CY 150.00 cm
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 F1 3001.30 Hz
 F2P 0.000 ppm
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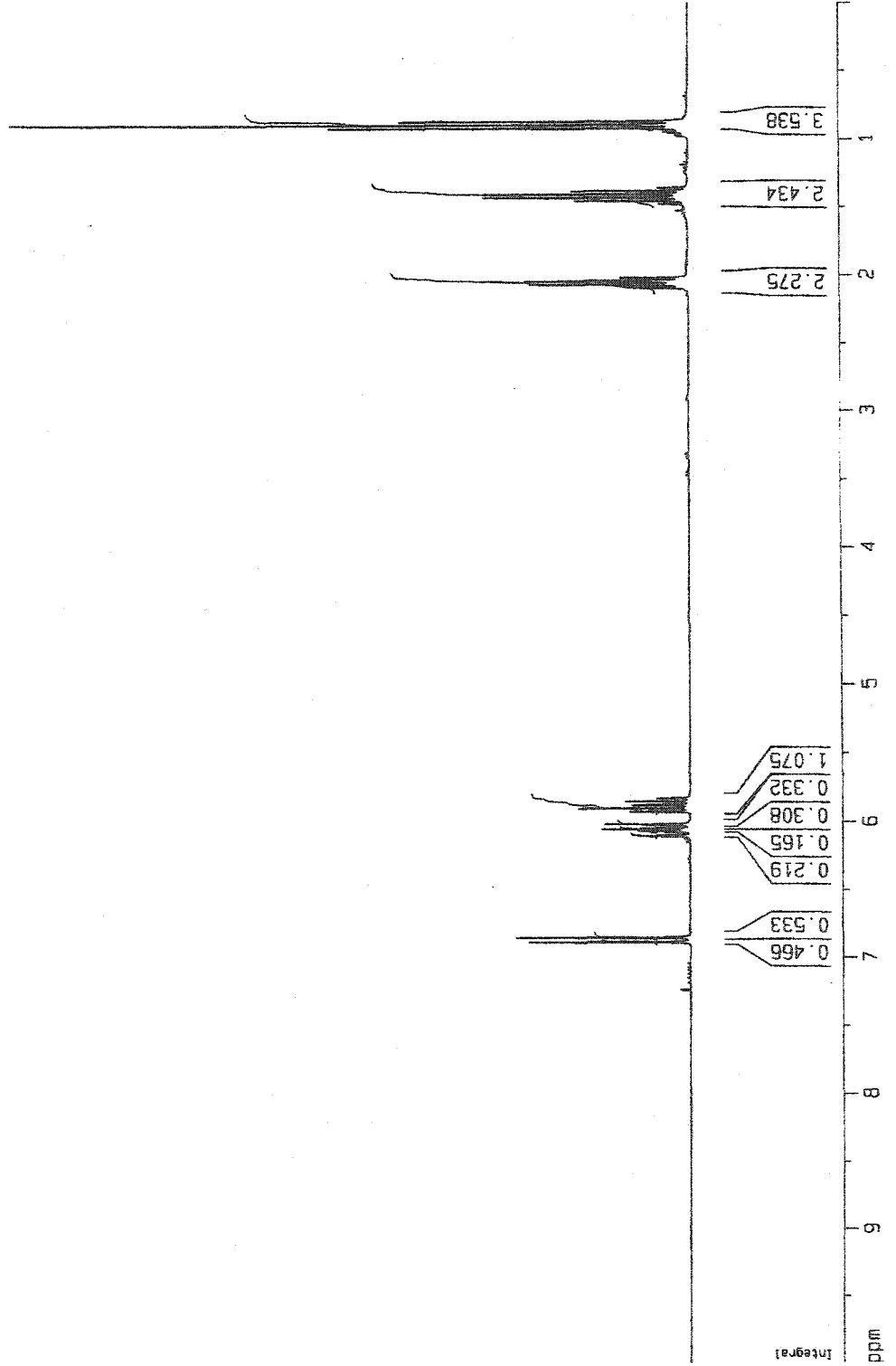
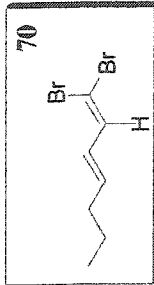
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 CY 10.00 cm
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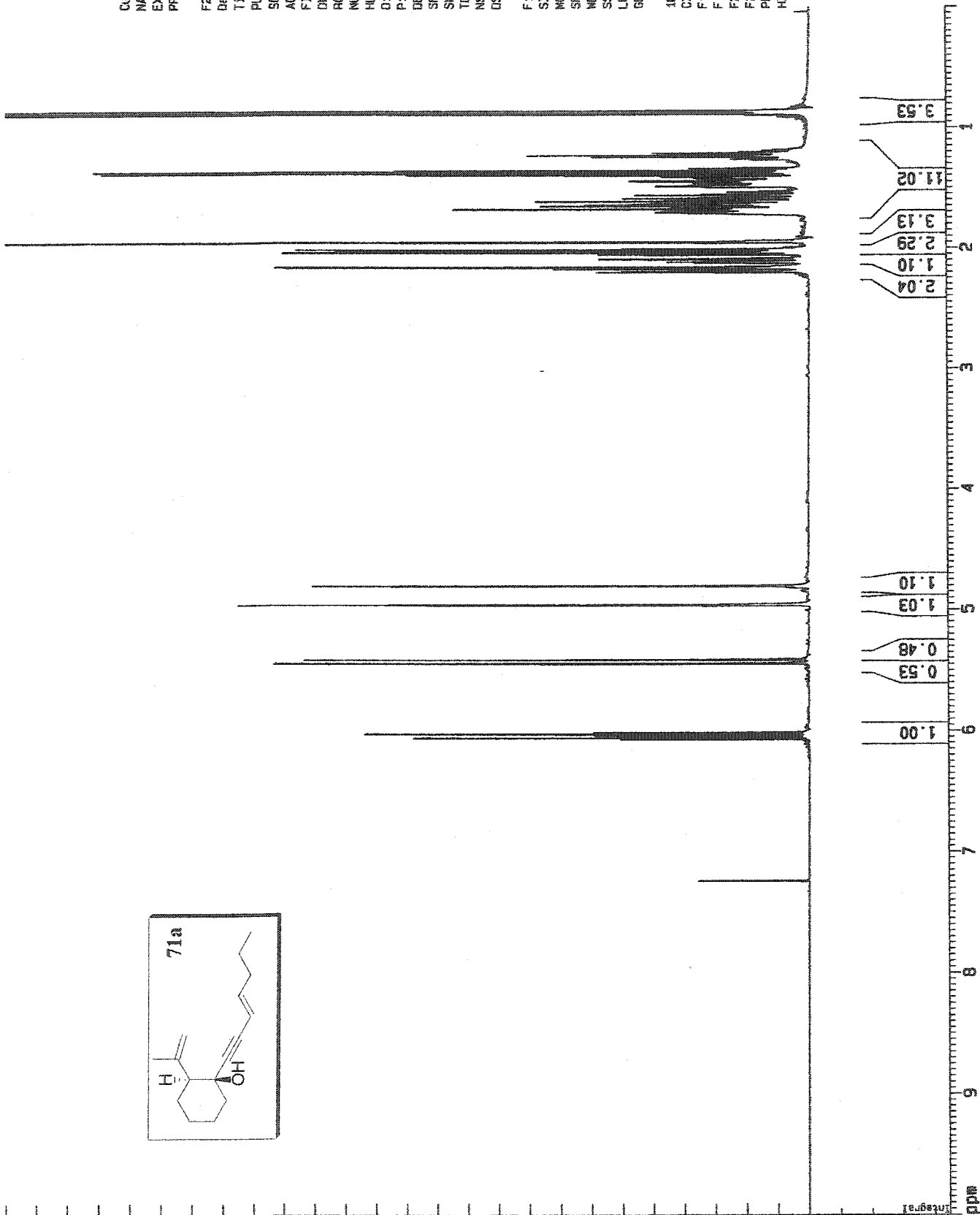
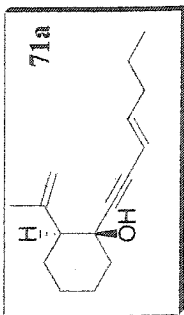


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 P1 3.0 usec
 DE 88.8 usec
 SF01 500.1381707 MHz
 SSW 7042.25 Hz
 TD 65536
 NS 16
 DS 0

F1 - Processing parameters
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 LB 0.00 Hz
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1D NMR plot parameters
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 F2P 0.000 ppm
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 PROCNO 1

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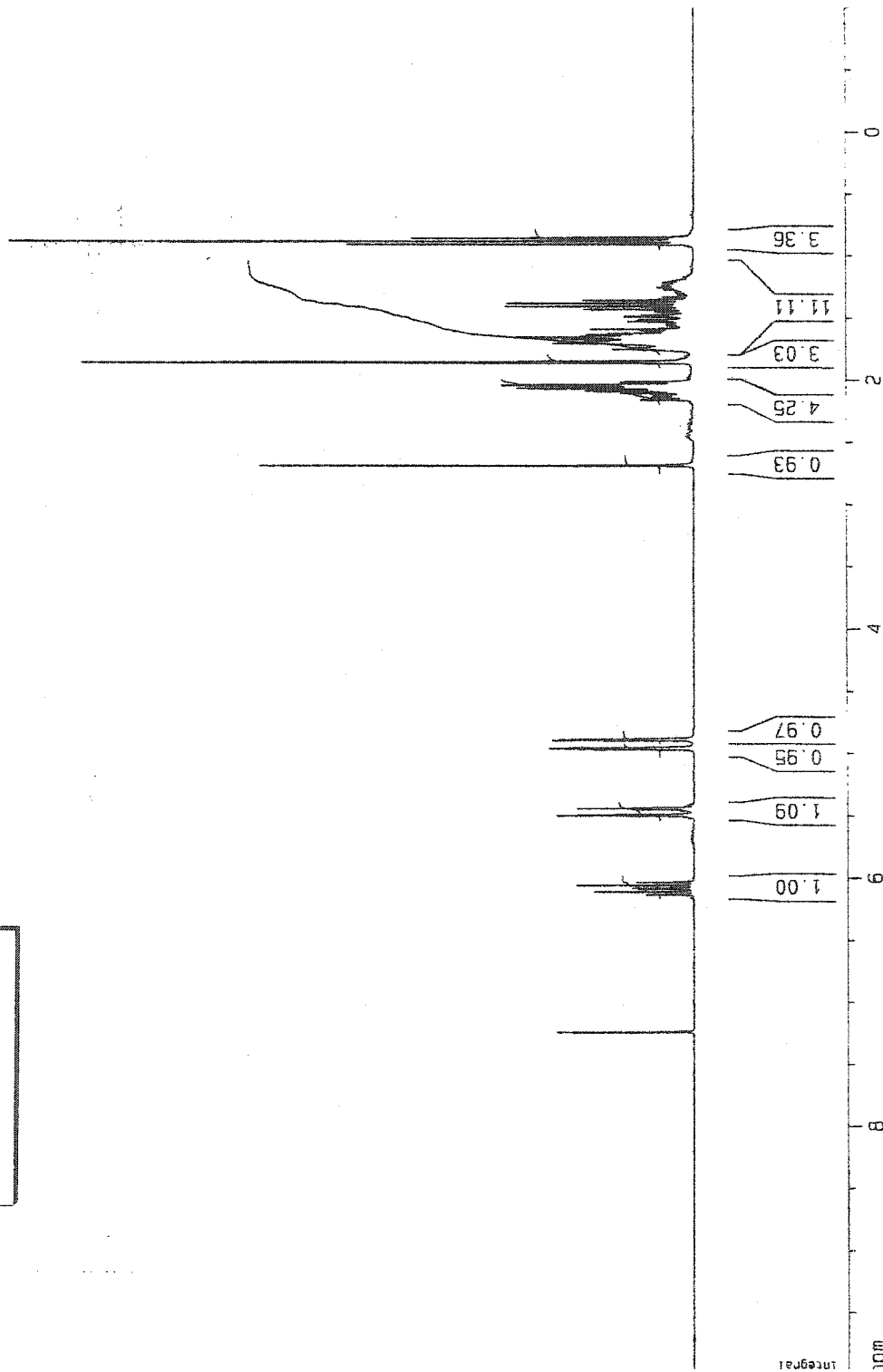
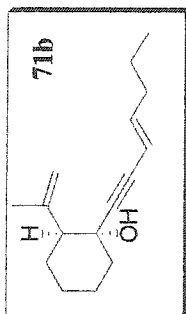
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 RG 181
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 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

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F2 - Processing parameters

SI 65536
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 LB 0.10 Hz
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1D NMR plot parameters
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 CY 10.00 cm
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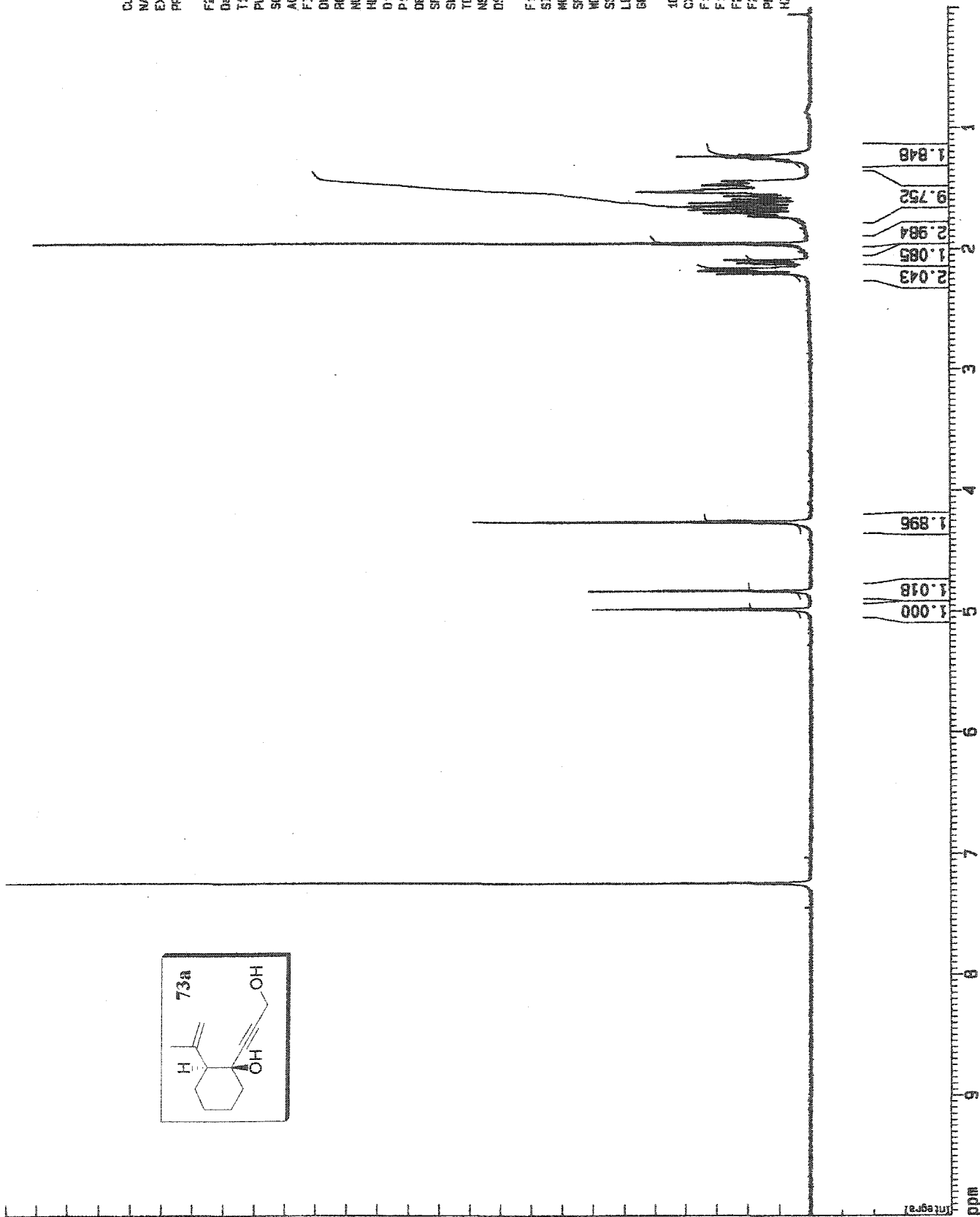
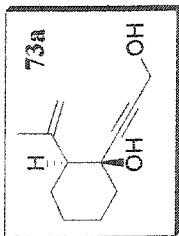


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 TD 65536
 NS 16
 DS 0

F1 - Processing parameters
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1D NMR plot parameters
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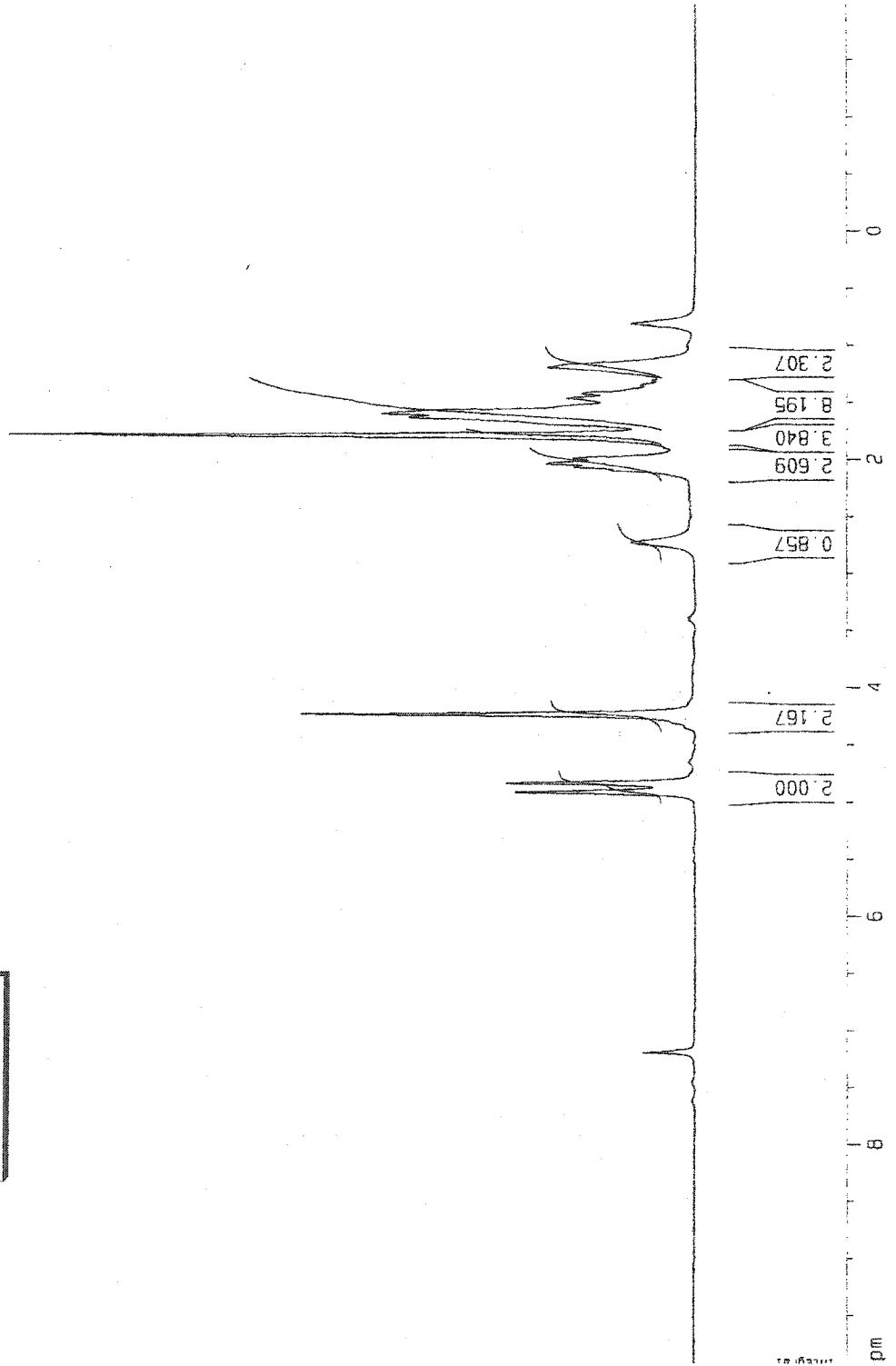
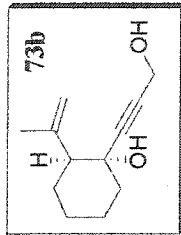
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 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl3
 NS 32
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 228.1
 JW 98.400 usec
 JE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

***** CHANNEL f1 *****
 NUC1 1H
 P1 9.50 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
 DC 1.00

1D NMR plot parameters
 CX 20.00 cm
 CY 10.00 cm
 F1P 10.000 ppm
 F1 3001.30 Hz
 F2P -2.000 ppm
 F2 -600.26 Hz
 ppmCM 0.60000 ppm/cm
 HzCM 180.07800 Hz/cm



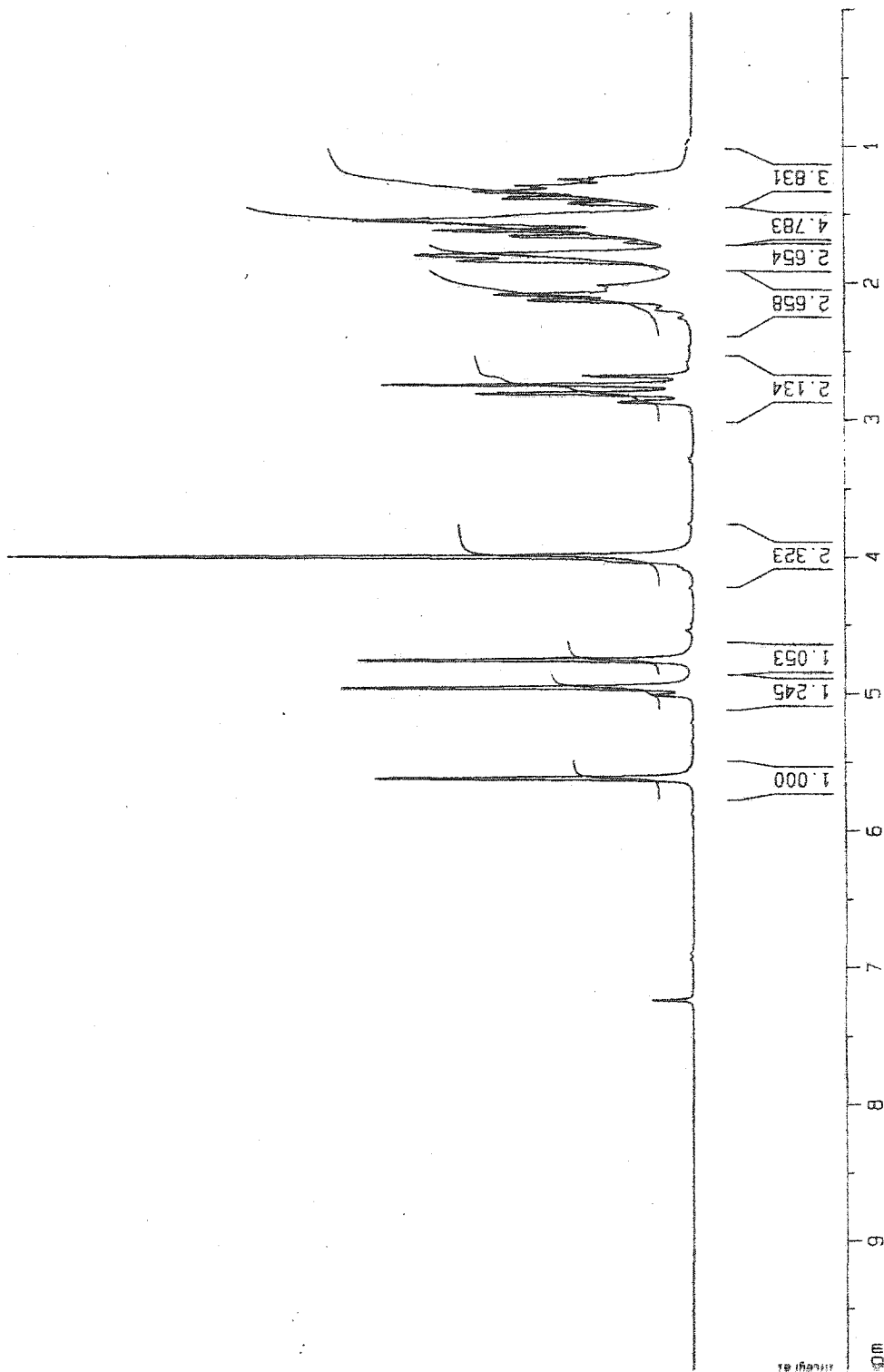
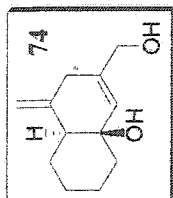
Current Data Parameters
 NAME prm-diol
 EXPNO 1
 PROCNO 1

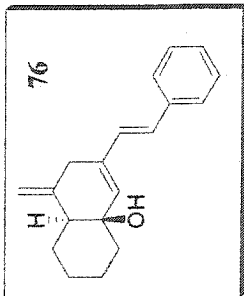
F2 - Acquisition Parameters
 Date_ 20020514
 Time 14.21
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl3
 NS 32
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 143.7
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.0000000 sec

===== CHANNEL f1 =====
 NUC1 1H
 P1 13.20 usec
 PL1 -3.00 dB
 SF01 300.1319477 MHz

F2 - Processing parameters
 SI 65536
 SF 300.1299994 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 prm-29
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters

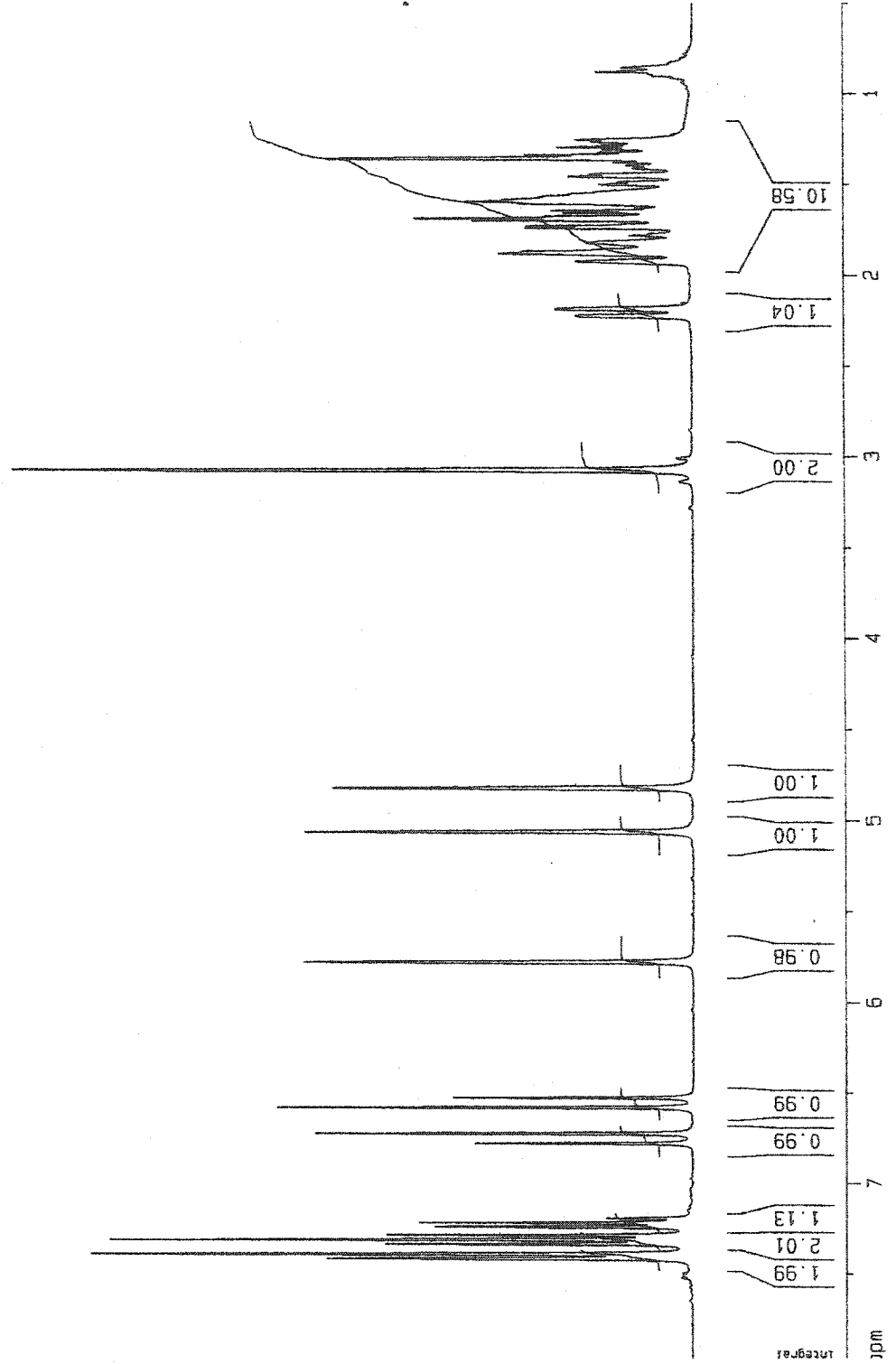
Date_ 20010614
 Time 18.30
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl3
 NS 16
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228960 sec
 RG 90.5
 DM 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.0000000 sec

***** CHANNEL f1 *****
 NUC1 1H
 P1 9.50 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 8.000 ppm
 F1 2401.04 Hz
 F2P 0.500 ppm
 F2 150.06 Hz
 PPMCM 0.37500 ppm/cm
 HZCM 112.54875 Hz/cm



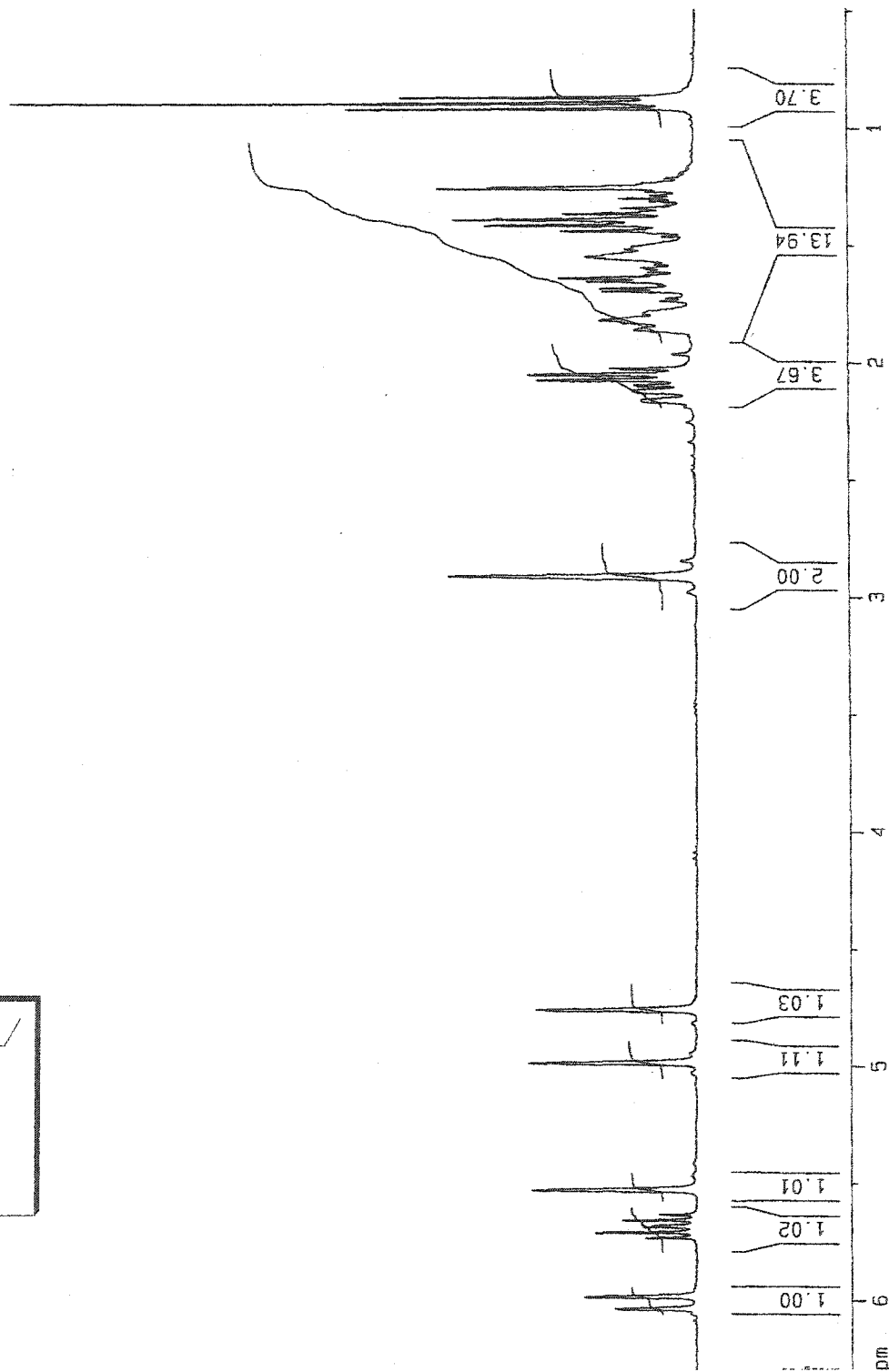
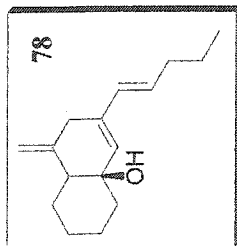
Current Data Parameters
 NAME prm-158
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20011106
 Time 17.20
 INSTRUM av300
 PROBRD 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 114
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.0000000 sec

***** CHANNEL f1 *****
 NUC1 1H
 P1 11.00 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

ID NMR plot parameters
 CX 20.00 cm
 CY 10.00 cm
 F1P 6.346 ppm
 F1 1904.65 Hz
 F2P 0.487 ppm
 F2 146.29 Hz
 PPMCM 0.29293 ppm/cm
 HZCM 87.91798 Hz/cm

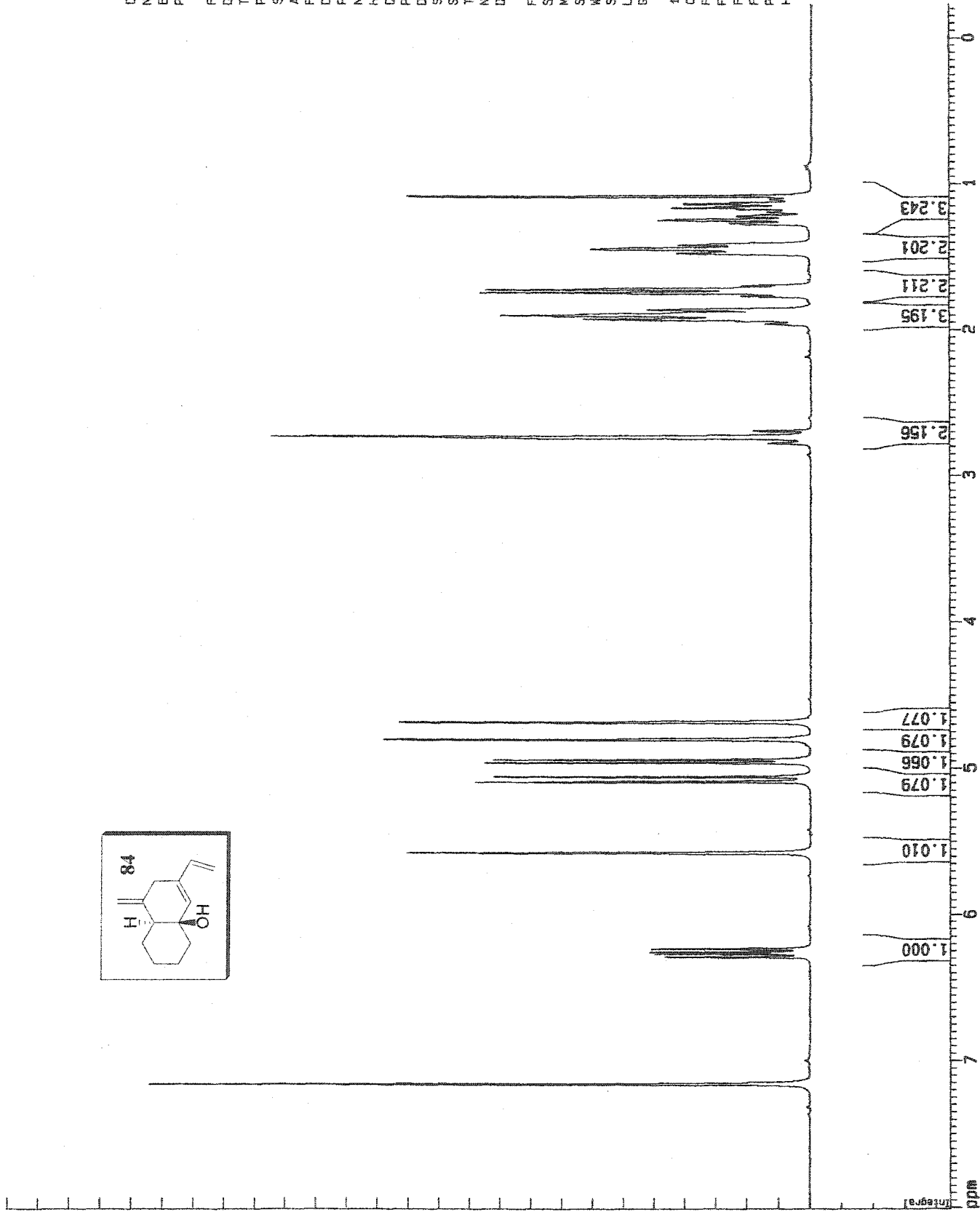
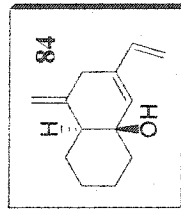


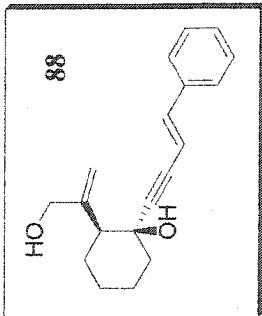
Current Data Parameters
 NAME prM-diene
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters
 Date 20010914
 Time 5.44
 PULPROG zg
 SOLVENT CDCl3
 AQ 4.6530805 sec
 FIDRES 0.107456 Hz
 DM 71.0 usec
 RG 128
 NUCLEUS 1H
 HL1 0 dB
 D1 0.0100000 sec
 P1 3.0 usec
 DE 88.8 usec
 SF01 500.1381707 MHz
 SWH 7042.25 Hz
 TD 65536
 NS 16
 DS 0

F1 - Processing parameters
 SI 32768
 MC2 GF
 SF 500.1354449 MHz
 WDW EM
 SSB 0
 LB 0.00 Hz
 GB 0

1D NMR plot parameters
 CX 22.00 cm
 F1P 8.009 ppm
 F1 4005.62 Hz
 F2P -0.235 ppm
 F2 -117.71 Hz
 PPMCM 0.37477 ppm/
 HZCM 187.43330 Hz/°C





Current Data Parameters
 NAME prm-dio1
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters

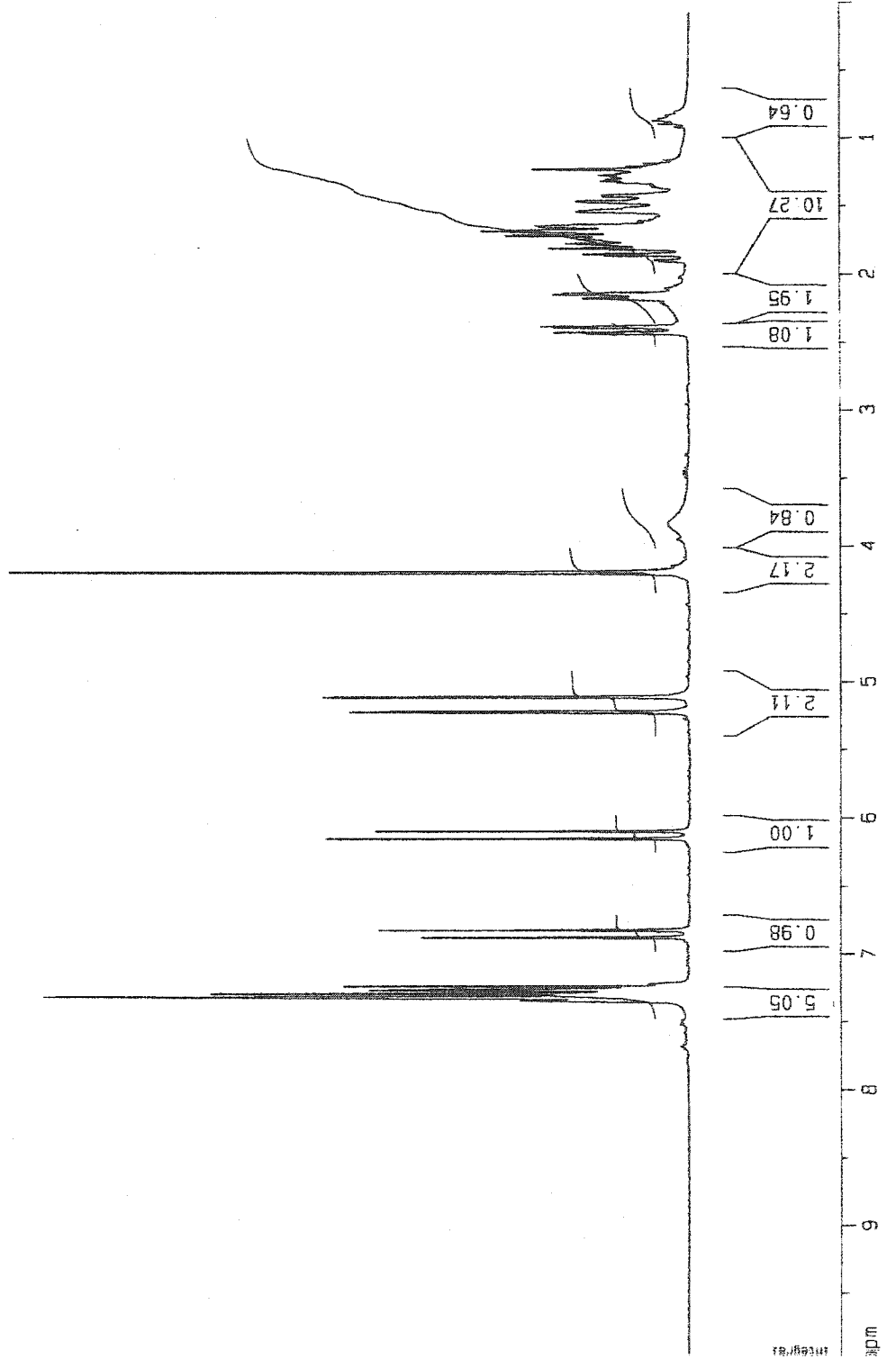
Date_ 20011018
 Time 15.26
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl3
 NS 48
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 256
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

===== CHANNEL f1 =====
 NUC1 1H
 P1 11.00 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 prn-247
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters

Date_ 20020416
 Time 19.34
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl3
 NS 32
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 456.1
 DW 98.400 usec
 DE 5.00 usec
 TE 300.0 K
 D1 1.00000000 sec

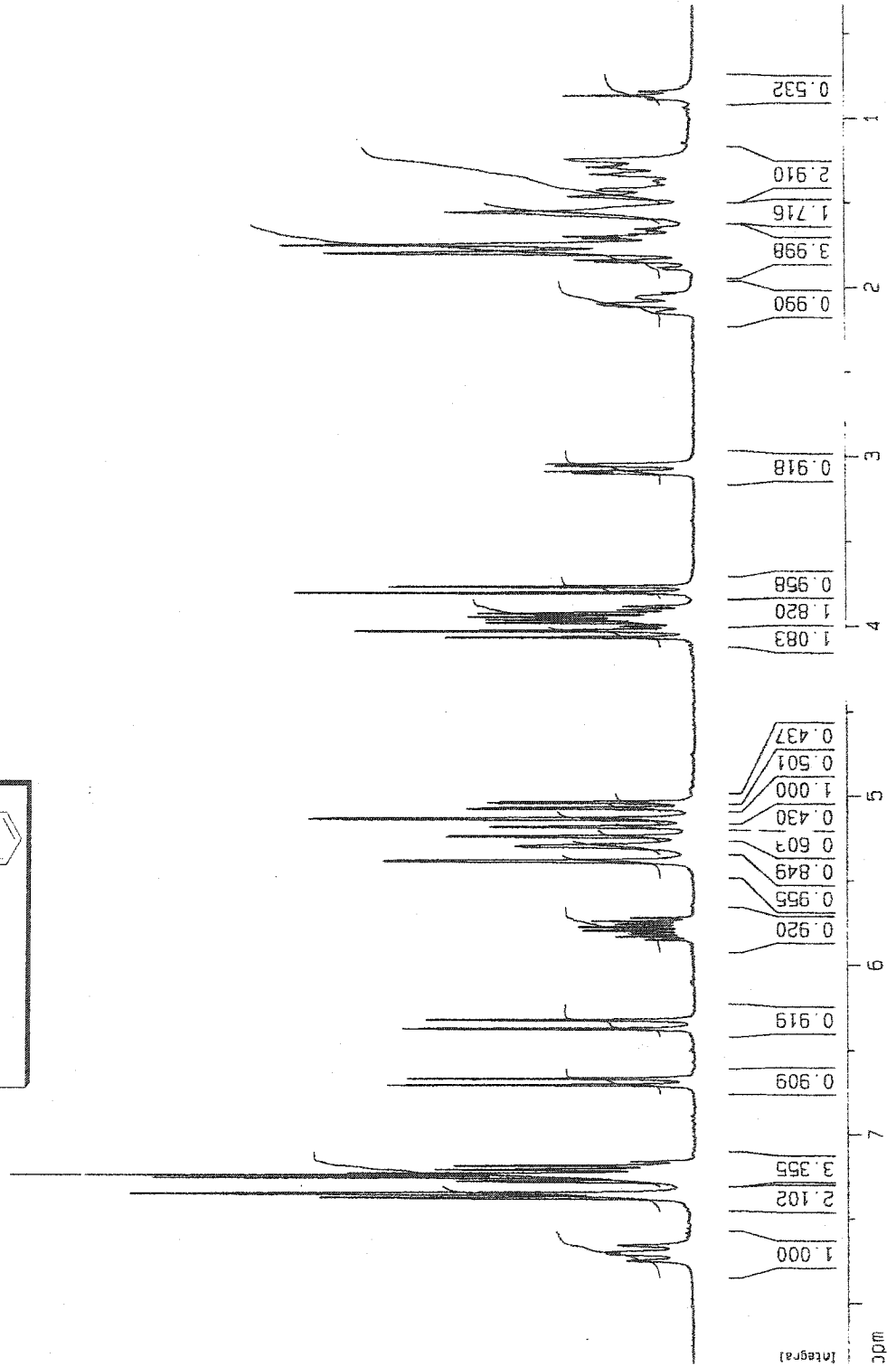
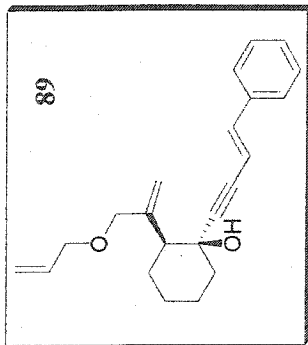
***** CHANNEL f1 *****
 NUC1 1H
 P1 10.00 usec
 PL1 -3.00 dB
 SF01 300.1319477 MHz

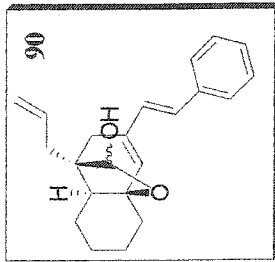
F2 - Processing parameters

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 8.367 ppm
 F1 2511.29 Hz
 F2P 0.328 ppm
 F2 98.59 Hz
 PRMCM 0.40194 ppm/cm
 HZCM 120.63484 Hz/cm





Current Data Parameters
 NAME prm-lactol
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters

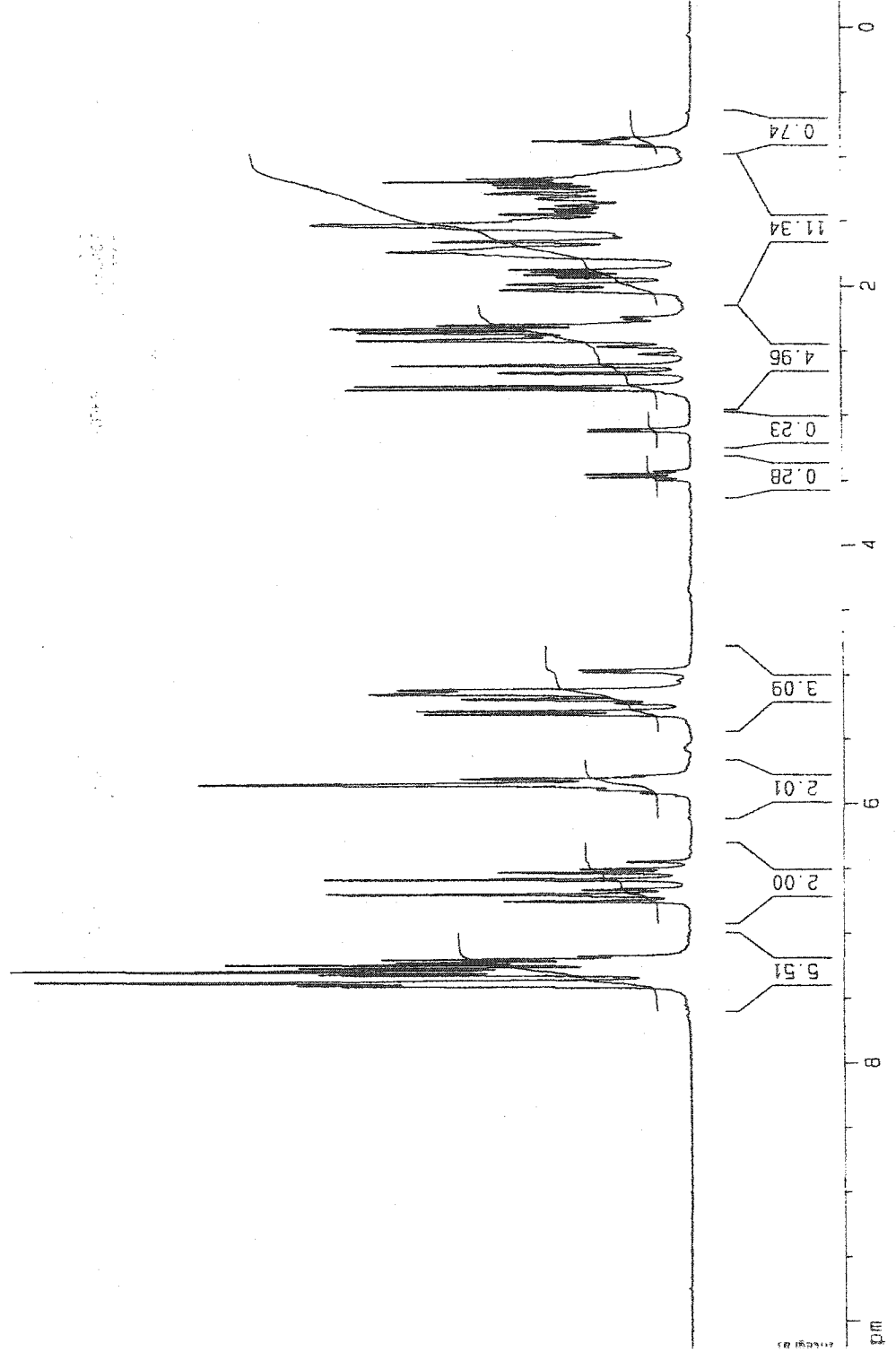
Date_ 20030407
 Time 20.43
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl3
 NS 32
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 143.7
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

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

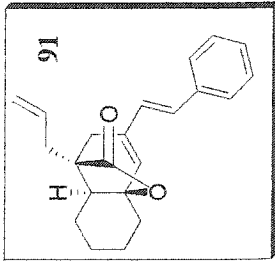
F2 - Processing parameters
 SI 65536
 SF 300.1300000 MHz
 WDW EM
 SSB 0
 LB 0.10 Hz
 GB 0
 PC 1.00

1D NMR plot parameters

CX 20.00 cm
 CY 10.00 cm
 F1P 10.267 ppm
 F1 3081.46 Hz
 F2P -0.205 ppm
 F2 -61.61 Hz
 PPMCM 0.52362 ppm/cm
 HZCM 157.15363 Hz/cm



SEP 28 2001



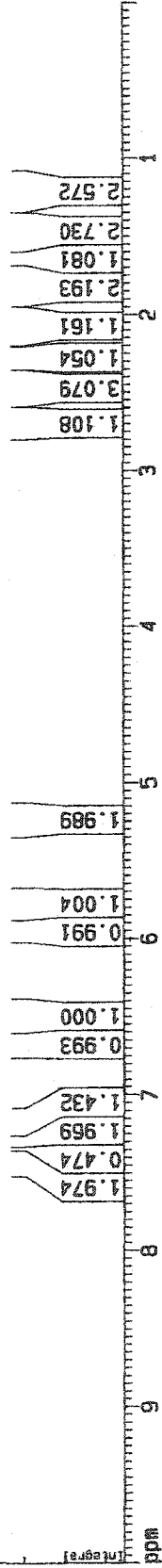
Current Data Parameters
NAME ross_12
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date 20010928
Time 4.24

PULPROG zg
SOLVENT CDCl3
AQ 4.6530805 sec
FIDRES 0.107466 Hz
AQ 71.0 usec
RG 512
NUCLEUS 1H
HL1 0 dB
D1 0.0100000 sec
P1 3.0 usec
DE 88.8 usec
SFO1 500.1361707 MHz
SWH 7042.25 Hz
TD 65536
NS 16
DS 0

F1 - Processing parameters
SI 32768
NC2 DF
SF 500.1354311 MHz
WDW EM
SSB 0
LB 0.00 Hz
GB 0

1D NMR plot parameters
CX 22.00 cm
F1P 10.000 ppm
F1 5001.35 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.45455 ppm/
HZCM 227.33429 Hz/1



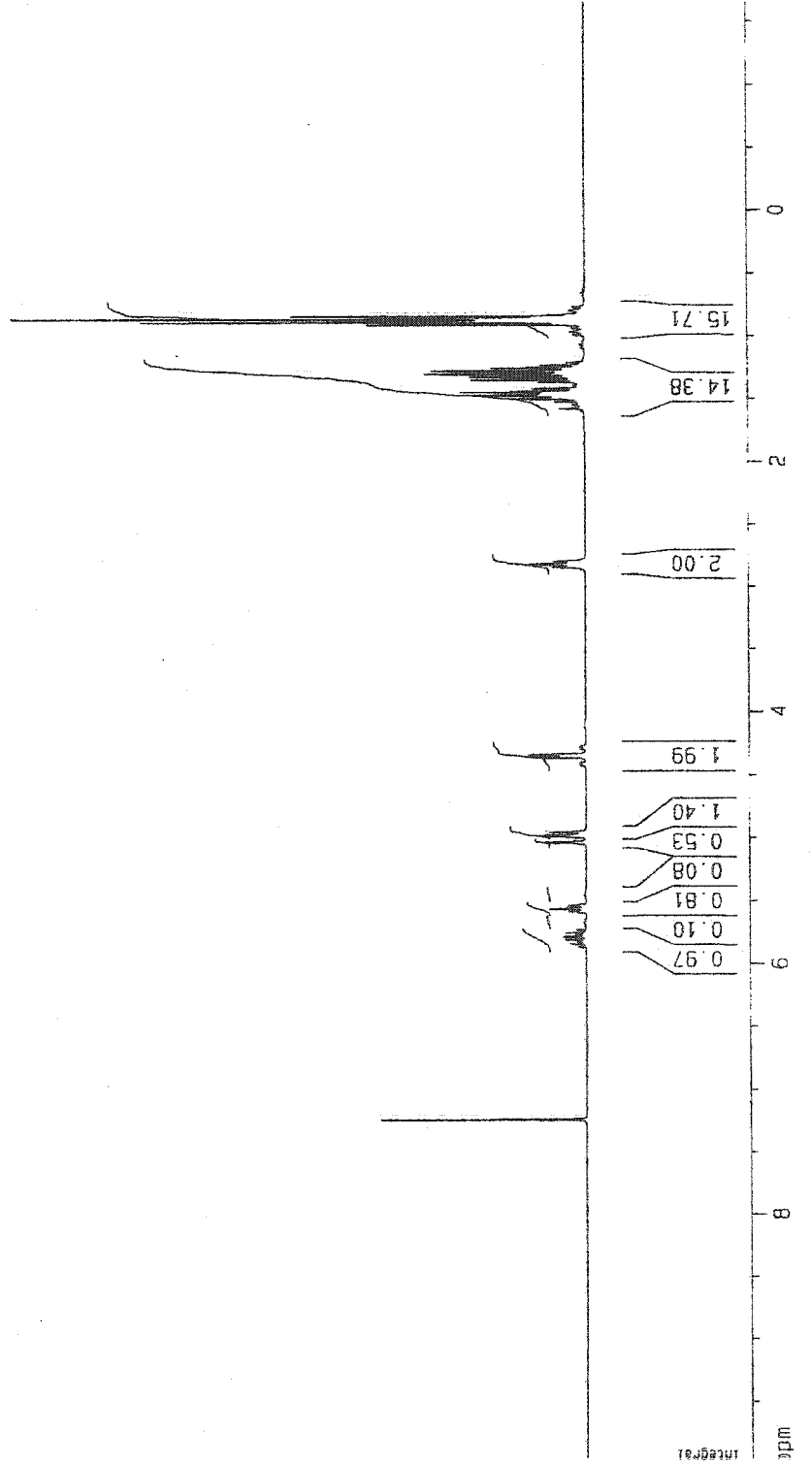
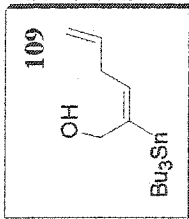
Current Data Parameters
 NAME prm-tin1
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20030408
 Time 16.31
 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 101.6
 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 -1.655 ppm
 F2 -496.64 Hz
 PRMCM 0.58274 ppm/cm
 HZCM 174.89720 Hz/cm

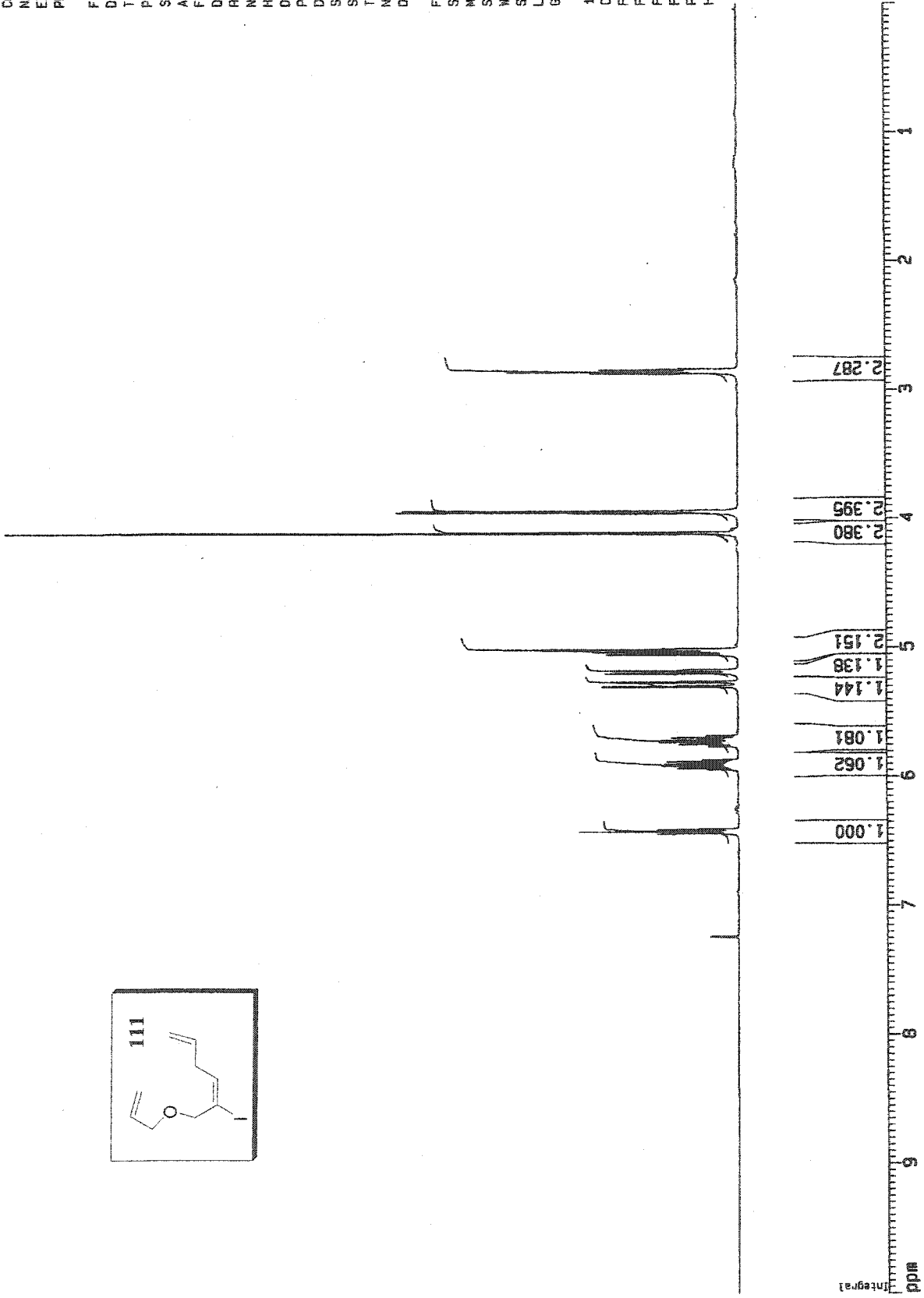
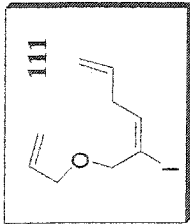


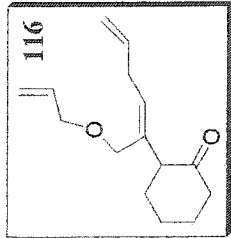
Current Data Parameters
 NAME prn-1000
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters
 Date 20020528
 Time 5.27
 PULPROG zg
 SOLVENT CDCl3
 AG 4.6530805 sec
 FIDRES 0.107456 Hz
 DM 71.0 usec
 RG 256
 NUCLEUS 1H
 HL1 0 dB
 O1 0.0100000 sec
 P1 5.6 usec
 DE 66.8 usec
 SFO1 500.1361707 MHz
 SMH 7042.25 Hz
 TD 65536
 NS 16
 DS 0

F1 - Processing parameters
 SI 32768
 MC2 EF
 SF 500.1354307 MHz
 NDW EM
 SSB 0
 LB 0.00 Hz
 GB 0

1D NMR plot parameters
 CX 22.00 cm
 F1P 10.000 ppm
 F1 5001.35 Hz
 F2P 0.000 ppm
 F2 0.00 Hz
 PPMCM 0.45455 ppm/
 HZCM 227.33429 Hz/1



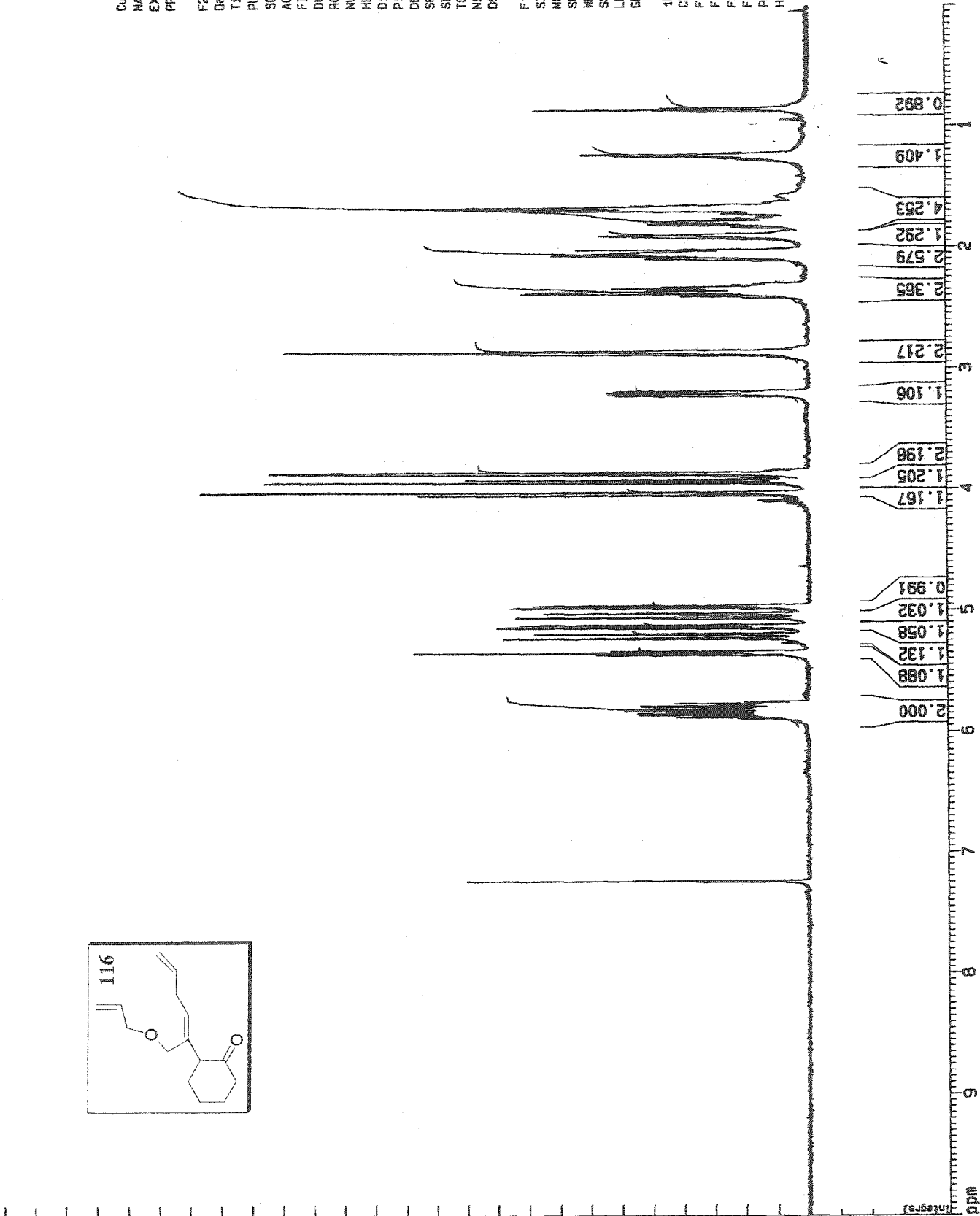


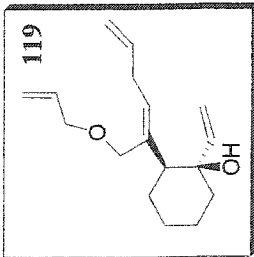
Current Data Parameters
 NAME PMP-235
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters
 Date 20020326
 Time 18.31
 PULPROG zg
 SOLVENT CDCl3
 AQ 4.6530905 sec
 FIDRES 0.107456 Hz
 DN 71.0 usec
 RG 1024
 NUCLEUS 1H
 HL1 0 dB
 D1 0.0100000 sec
 P1 5.6 usec
 DE 88.0 usec
 SFO1 500.1381707 MHz
 SHH 7042.25 Hz
 TD 65536
 NS 16
 DS 0

F1 - Processing parameters
 SI 32768
 MC2 GF
 SF 500.1354311 MHz
 WDW EM
 SSB 0
 LB 0.00 Hz
 GB 0

1D NMR plot parameters
 CX 22.00 cm
 F1P 10.000 ppm
 F1 5001.35 Hz
 F2P 0.000 ppm
 F2 0.00 Hz
 PPMCM 0.45455 ppm/
 HZCM 227.33429 Hz/°C





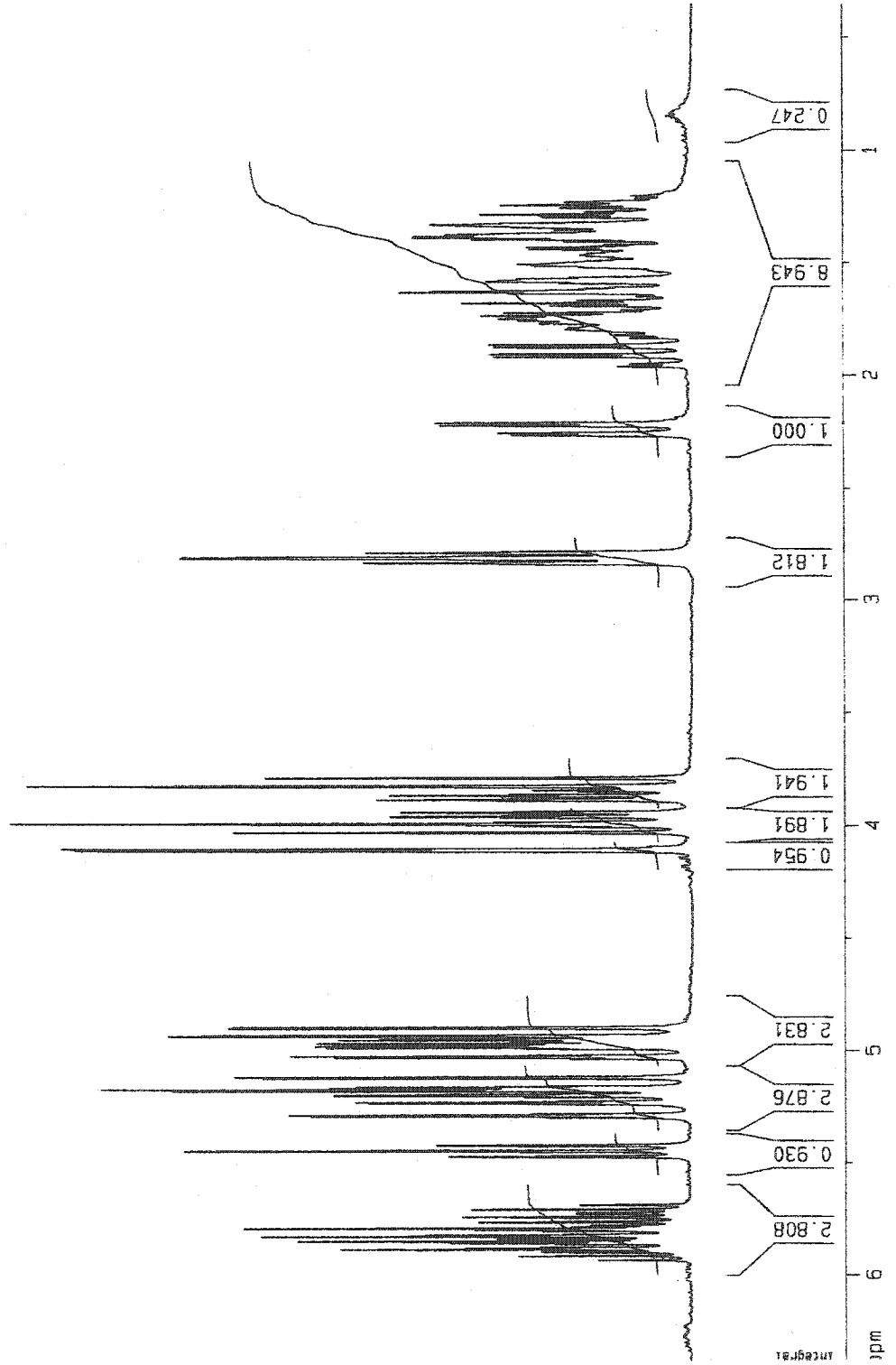
Current Data Parameters
 NAME prm-277
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20020607
 Time 12.44
 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
 OW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

***** CHANNEL f1 *****
 NUC1 1H
 P1 20.00 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
 CK 20.00 cm
 CY 10.00 cm
 F1P 6.406 ppm
 F1 1922.51 Hz
 F2P 0.350 ppm
 F2 104.94 Hz
 PPMCM 0.30280 ppm/cm
 HZCM 90.87852 Hz/cm



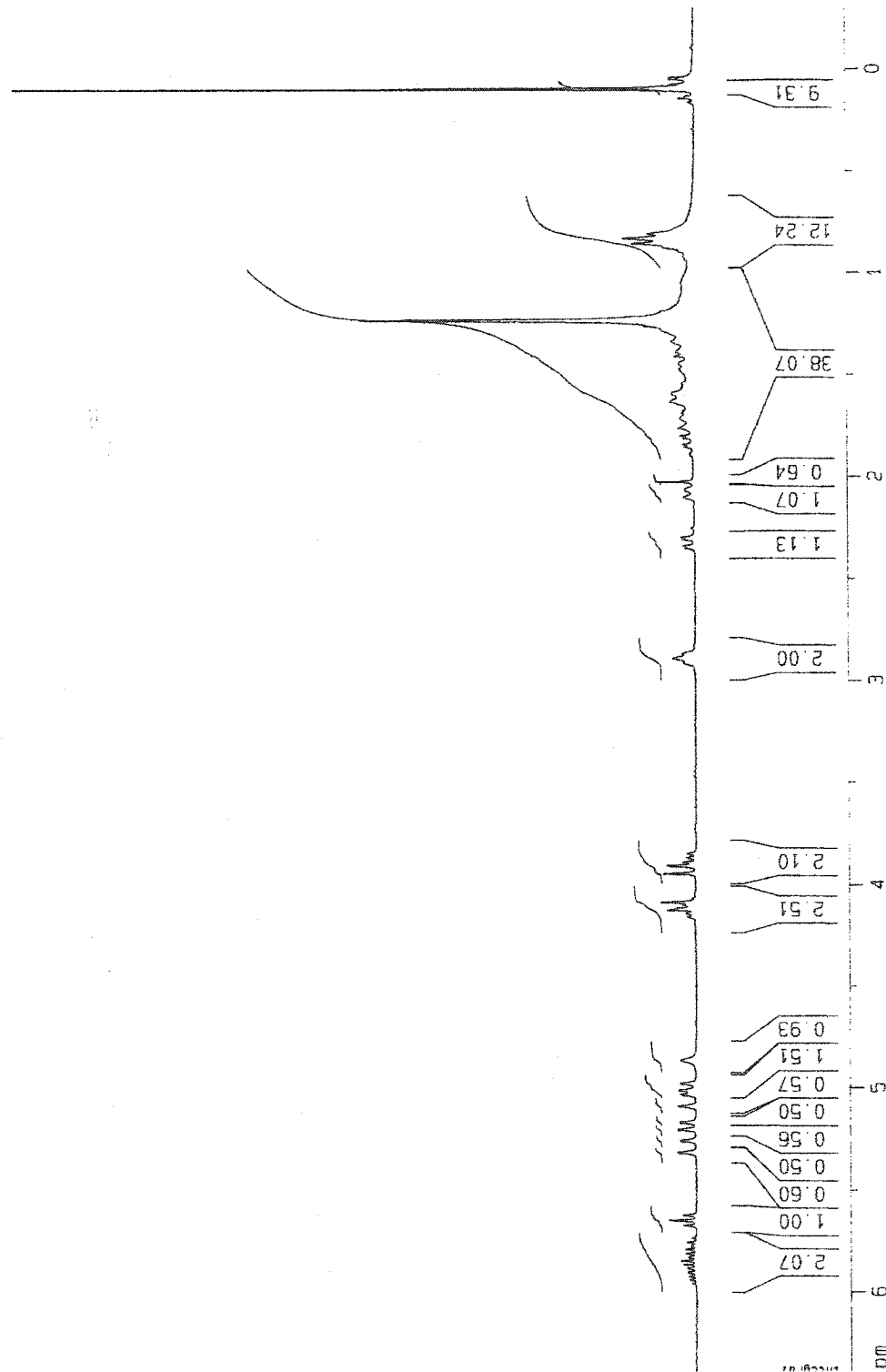
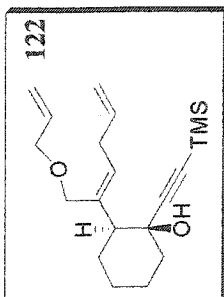
Current Data Parameters
 NAME prm-236a
 EXPNO 1
 PROCNO 1

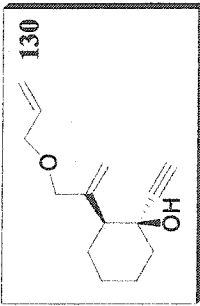
F2 - Acquisition Parameters
 Date_ 20020403
 Time 14.06
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl3
 NS 64
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 362
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 2.00000000 sec

***** CHANNEL f1 *****
 NUC1 1H
 P1 10.00 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 6.435 ppm
 F1 1931.47 Hz
 F2P -0.299 ppm
 F2 -89.87 Hz
 PPMCM 0.33674 ppm/cm
 HZCM 101.06676 Hz/cm





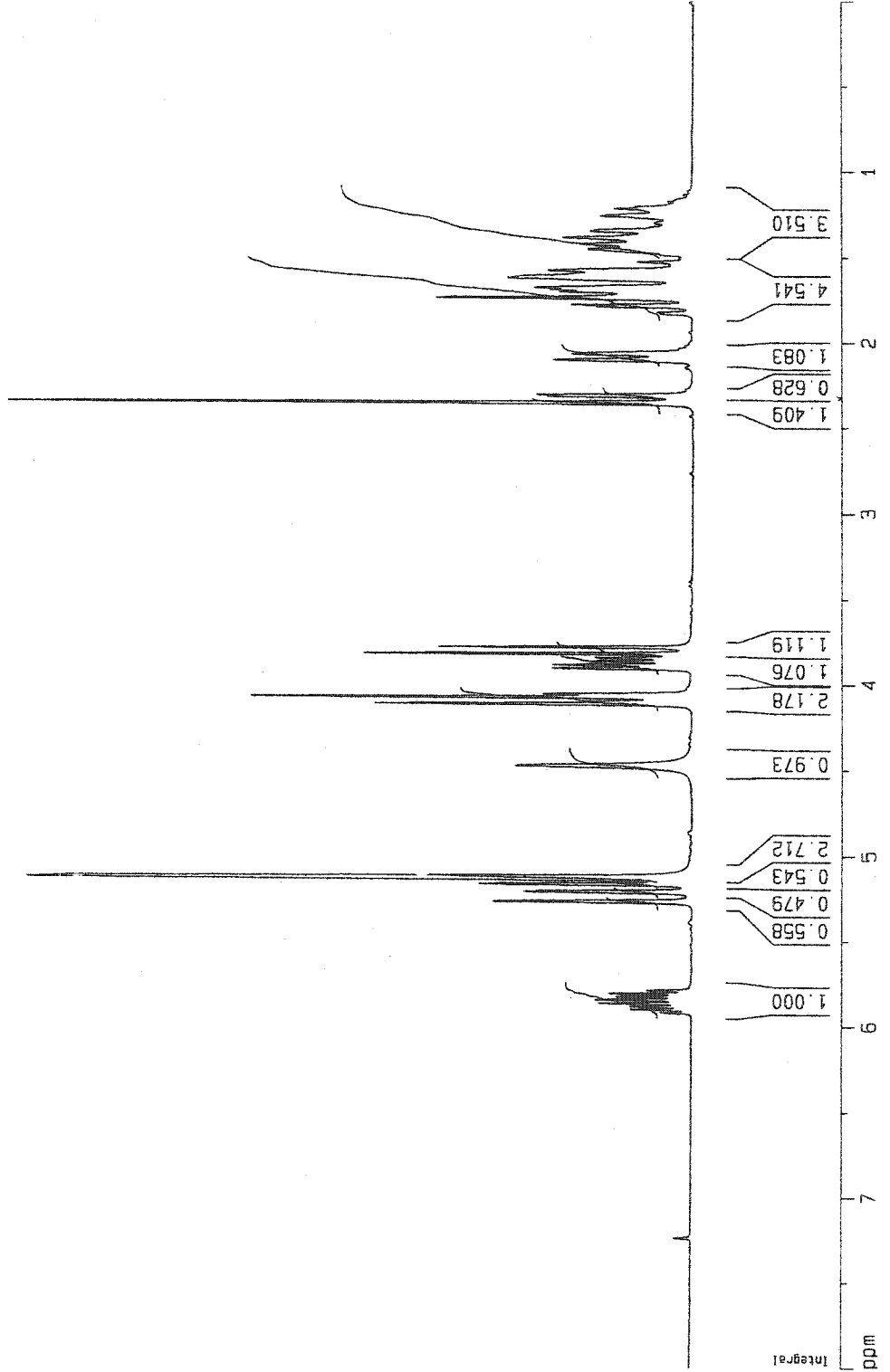
Current Data Parameters
 NAME jmw3-123
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20020222
 Time 10.26
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl3
 NS 16
 DS 0
 SWH 5081.501 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 45.3
 CW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

==== CHANNEL f1 =====
 NUC1 1H
 P1 13.50 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 8.000 ppm
 F1 2401.04 Hz
 F2P 0.000 ppm
 F2 0.00 Hz
 PPMCM 0.40000 ppm/cm
 HZCM 120.05200 Hz/cm



Current Data Parameters
 NAME prm-ylactol
 EXPNO 1
 PROCNO 1

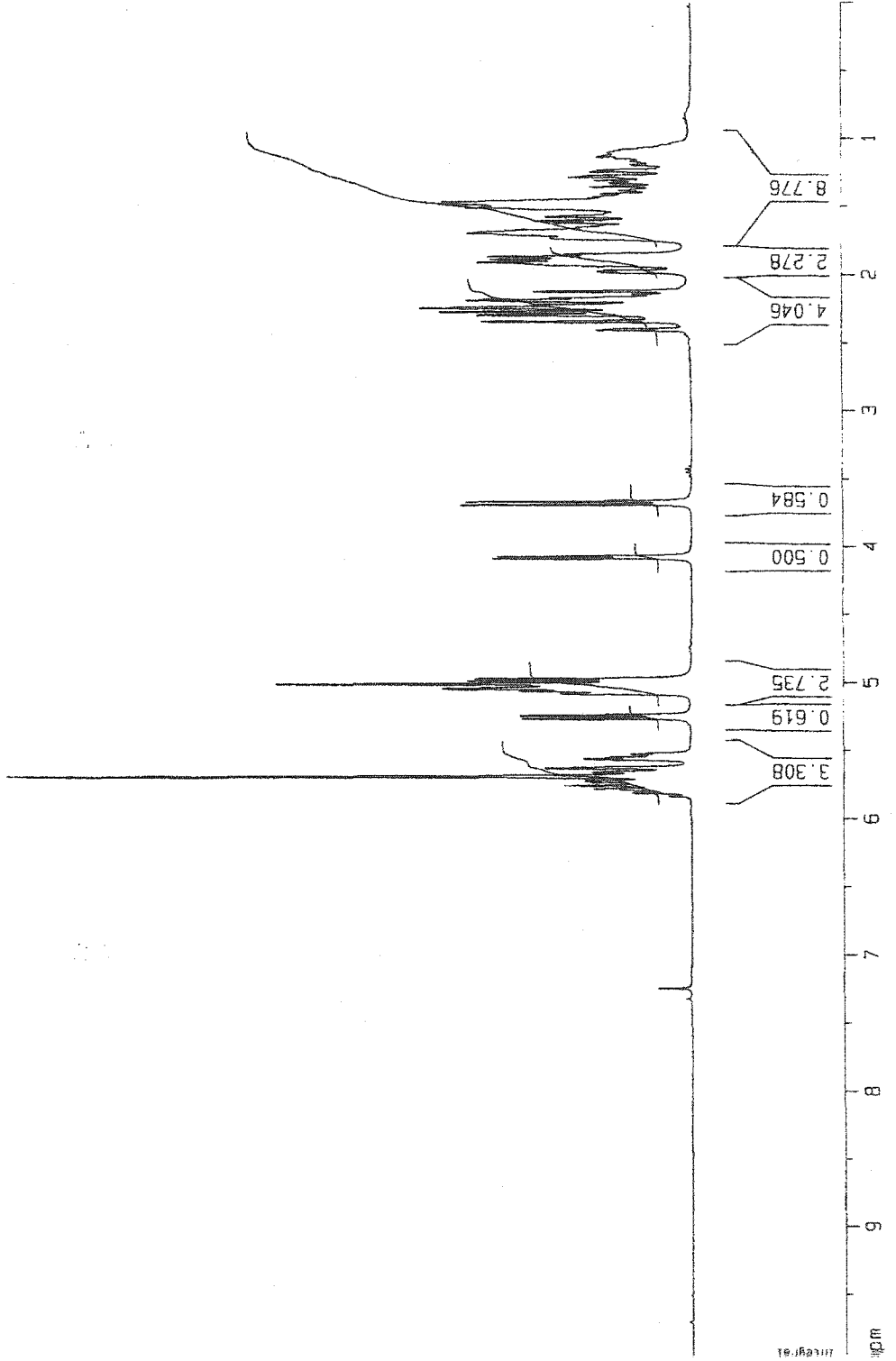
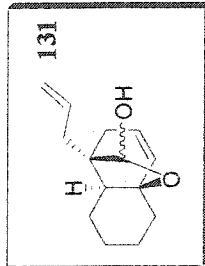
F2 - Acquisition Parameters

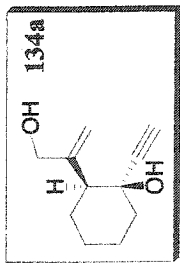
Date... 20030407
 Time 21.10
 INSTRUM av300
 PROBHD 5 mm GNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDC13
 NS 32
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 45.3
 DW 96.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

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

F2 - Processing parameters

SI 65536
 SF 300.1299995 MHz
 WDW EM
 SSB 0
 LB 0.10 Hz
 GB 0
 PC 1.00
 ID 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





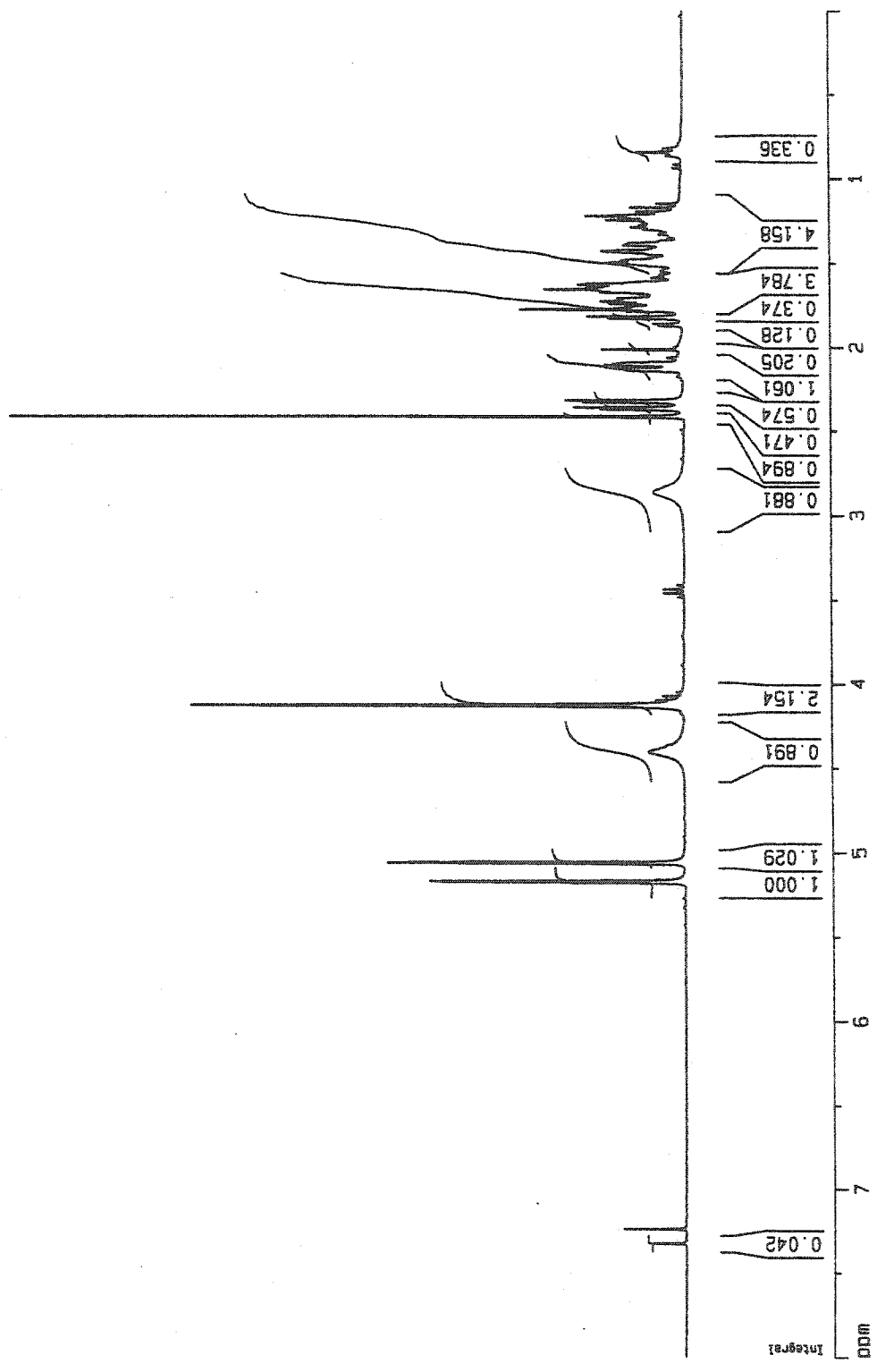
Current Data Parameters
 NAME jmw3-64
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20011206
 Time 8.28
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl3
 NS 16
 DS 0
 SMH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 101.6
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

***** CHANNEL f1 *****
 NUC1 1H
 P1 11.00 usec
 PL1 -3.00 dB
 SF01 300.1319477 MHz

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

1D NMR plot parameters
 CX 20.00 cm
 CY 10.00 cm
 FIP 8.000 ppm
 F1 2401.04 Hz
 F2P 0.000 ppm
 F2 0.00 Hz
 PPMCM 0.40000 ppm/cm
 HZCM 120.05200 Hz/cm



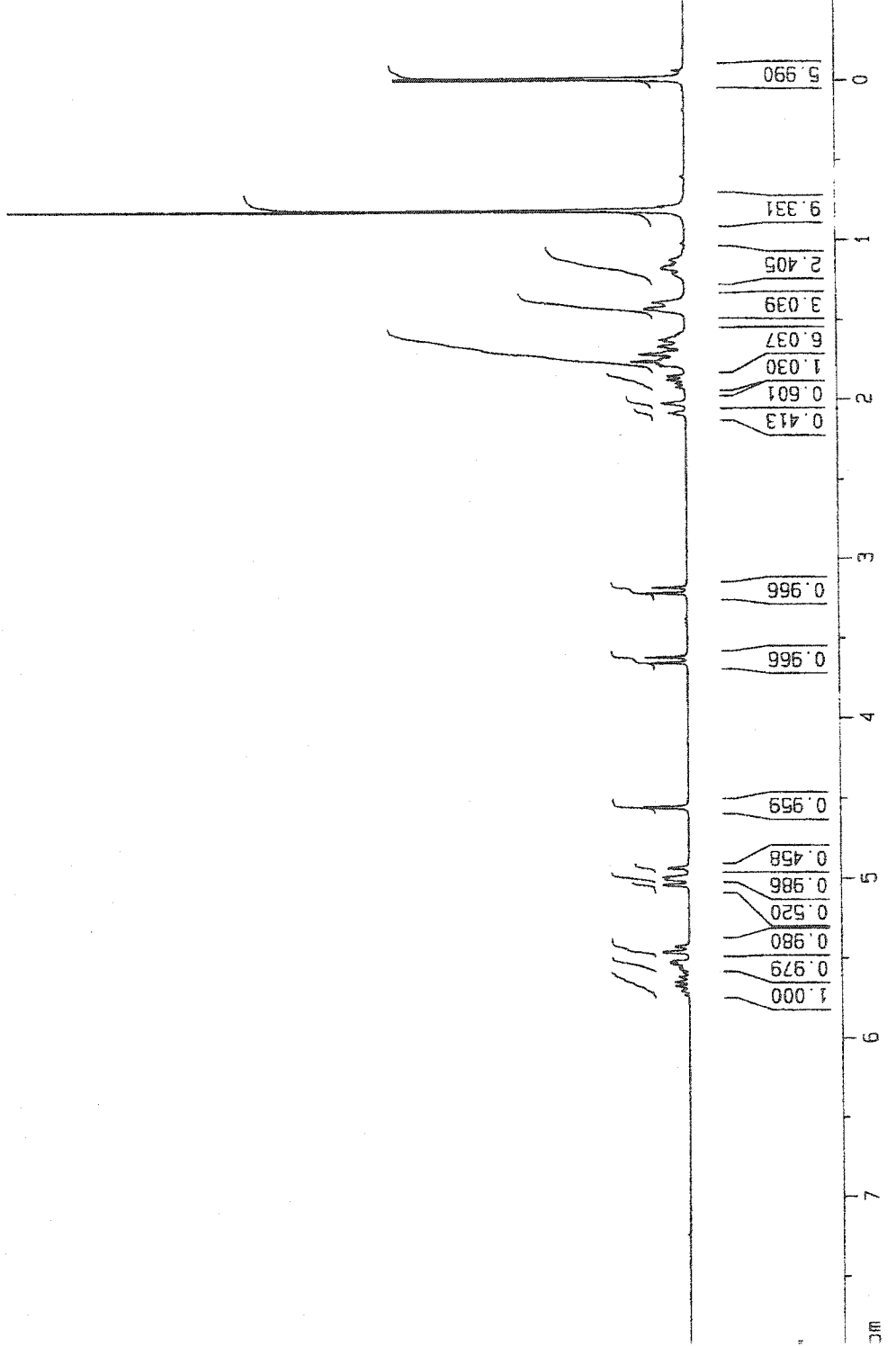
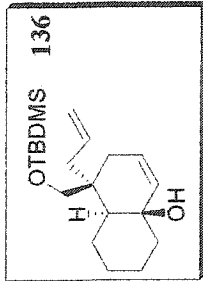
Current Data Parameters
 NAME jmw4-17
 EXPNO 1
 PROCNO 1

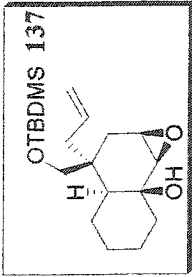
F2 - Acquisition Parameters
 Date_ 20020516
 Time 12.36
 INSTRUM av300
 PROBHD 5 mm GNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDC13
 NS 16
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 18
 DM 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

***** CHANNEL f1 *****
 NUC1 1H
 P1 15.00 usec
 PL1 -3.00 dB
 SF01 300.1319477 MHz

F2 - Processing parameters
 SI 65536
 SF 300.1299993 MHz
 WDW EM
 SSB 0
 LB 0.10 Hz
 GB 0
 PC 1.00

ID NMR plot parameters
 CX 20.00 cm
 CY 10.00 cm
 F1P 8.000 ppm
 F1 2401.04 Hz
 F2P -0.500 ppm
 F2 -150.06 Hz
 PPHCM 0.42500 ppm/cm
 HZCM 127.55524 Hz/cm





Current Data Parameters
 NAME jmw4-15
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters

Date_ 20020517
 Time 10.47
 INSTRUM av300
 PROBHD 5 mm GNP 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 16
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

***** CHANNEL f1 *****

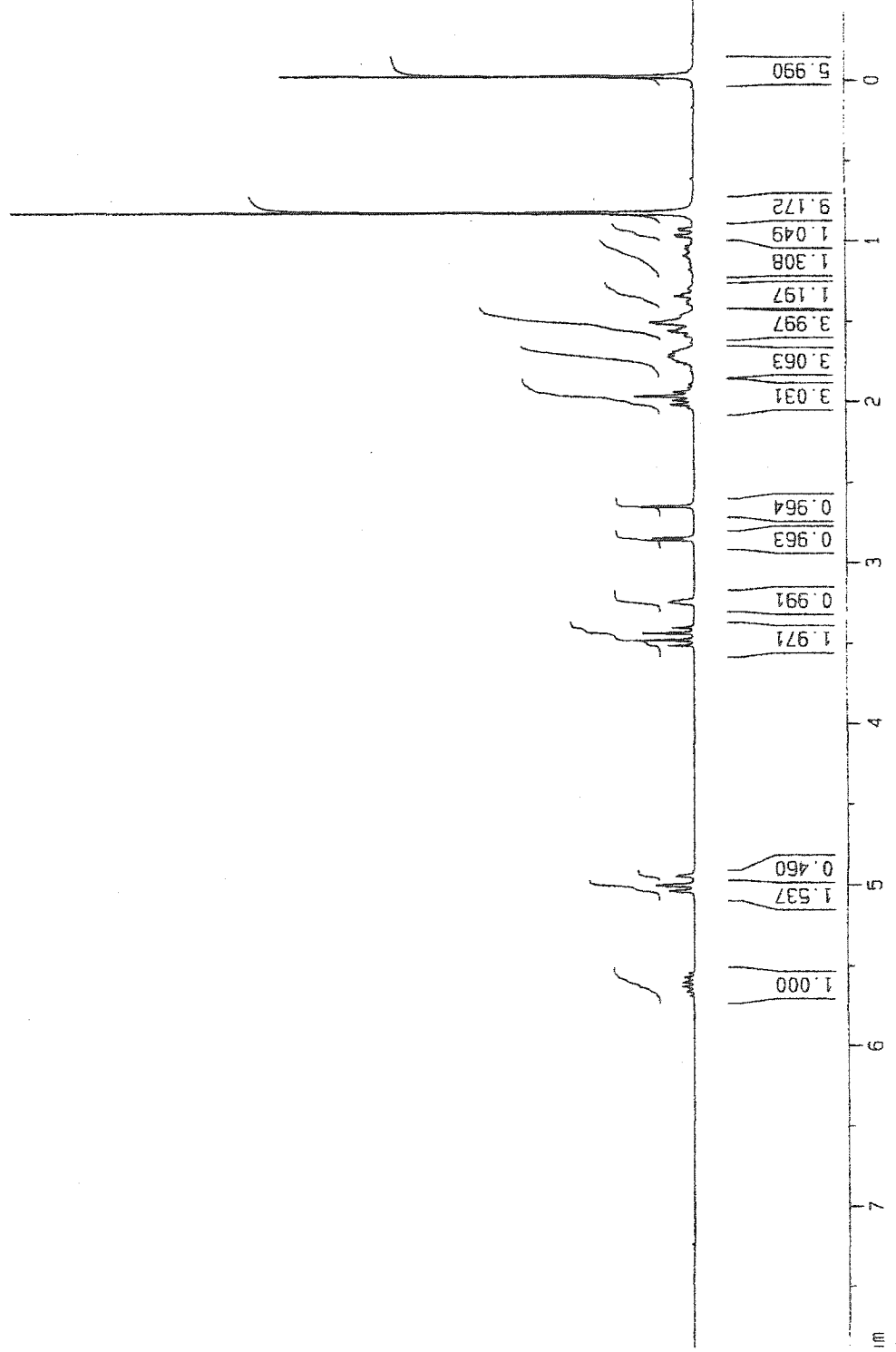
NUC1 1H
 P1 15.00 usec
 PL1 -3.00 dB
 SF01 300.1319477 MHz

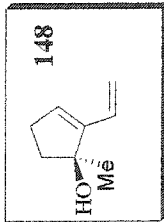
F2 - Processing parameters

SI 65536
 SF 300.1299992 MHz
 WDM 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 8.000 ppm
 F1 2401.04 Hz
 F2P -150.06 ppm
 F2 -150.06 Hz
 PPMCM 0.42500 ppm/cm
 HZCM 127.55524 Hz/cm





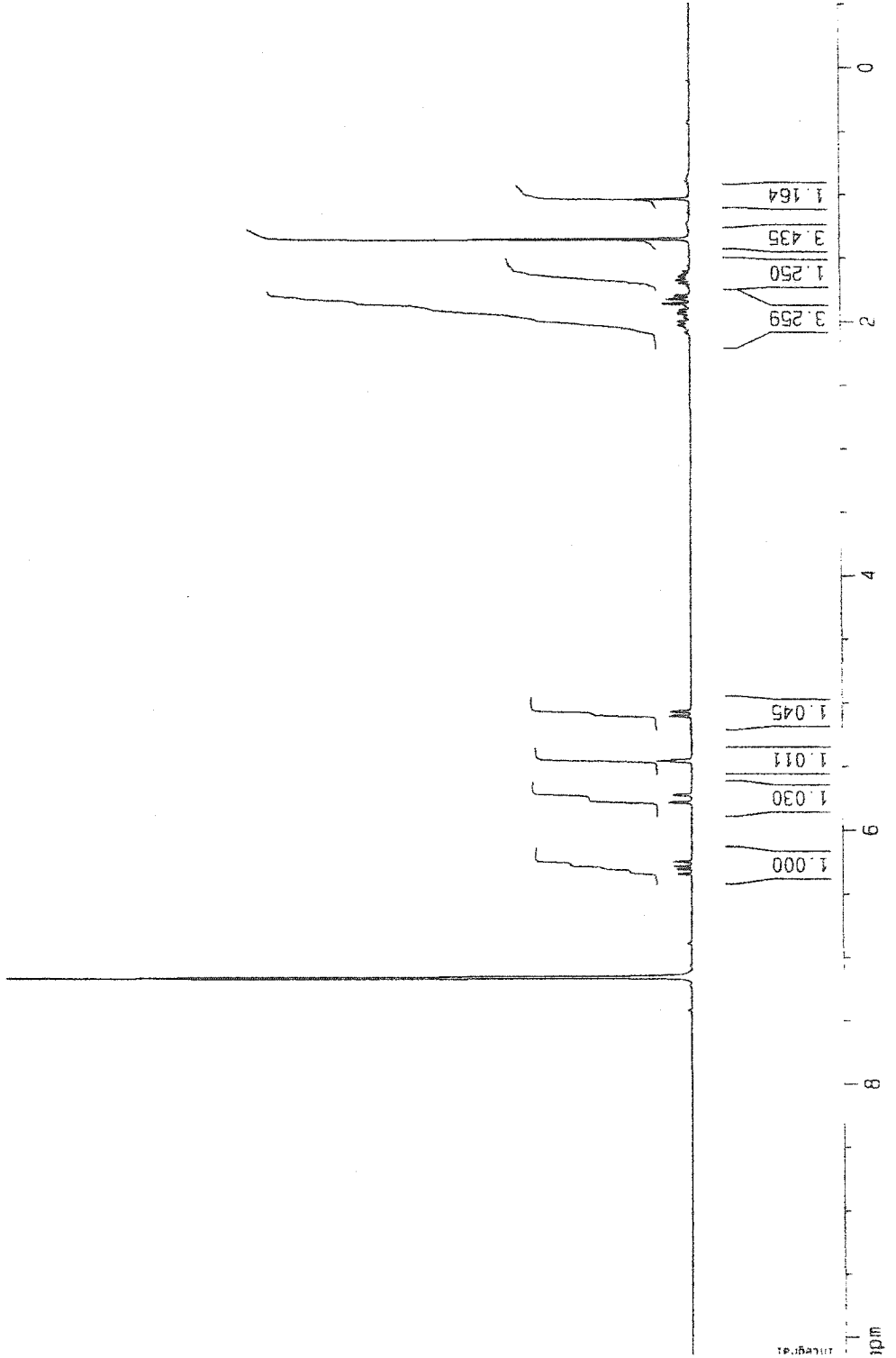
Current Data Parameters
 NAME prm-418 (again)
 EXPNO 1
 PROCNO 1

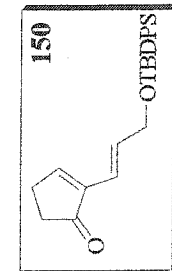
F2 - Acquisition Parameters
 Date_ 20030203
 Time 14.51
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl3
 NS 16
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228960 sec
 RG 456.1
 DM 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

===== CHANNEL f1 =====
 NUC1 1H
 P1 9.75 usec
 PL1 -3.00 dB
 SFO1 300.1319477 MHz

F2 - Processing parameters
 SI 65536
 SF 300.1299998 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 10.188 ppm
 F1 3057.80 Hz
 F2P -0.519 ppm
 F2 -155.90 Hz
 PPMCM 0.53538 ppm/cm
 HZCM 160.68504 Hz/cm





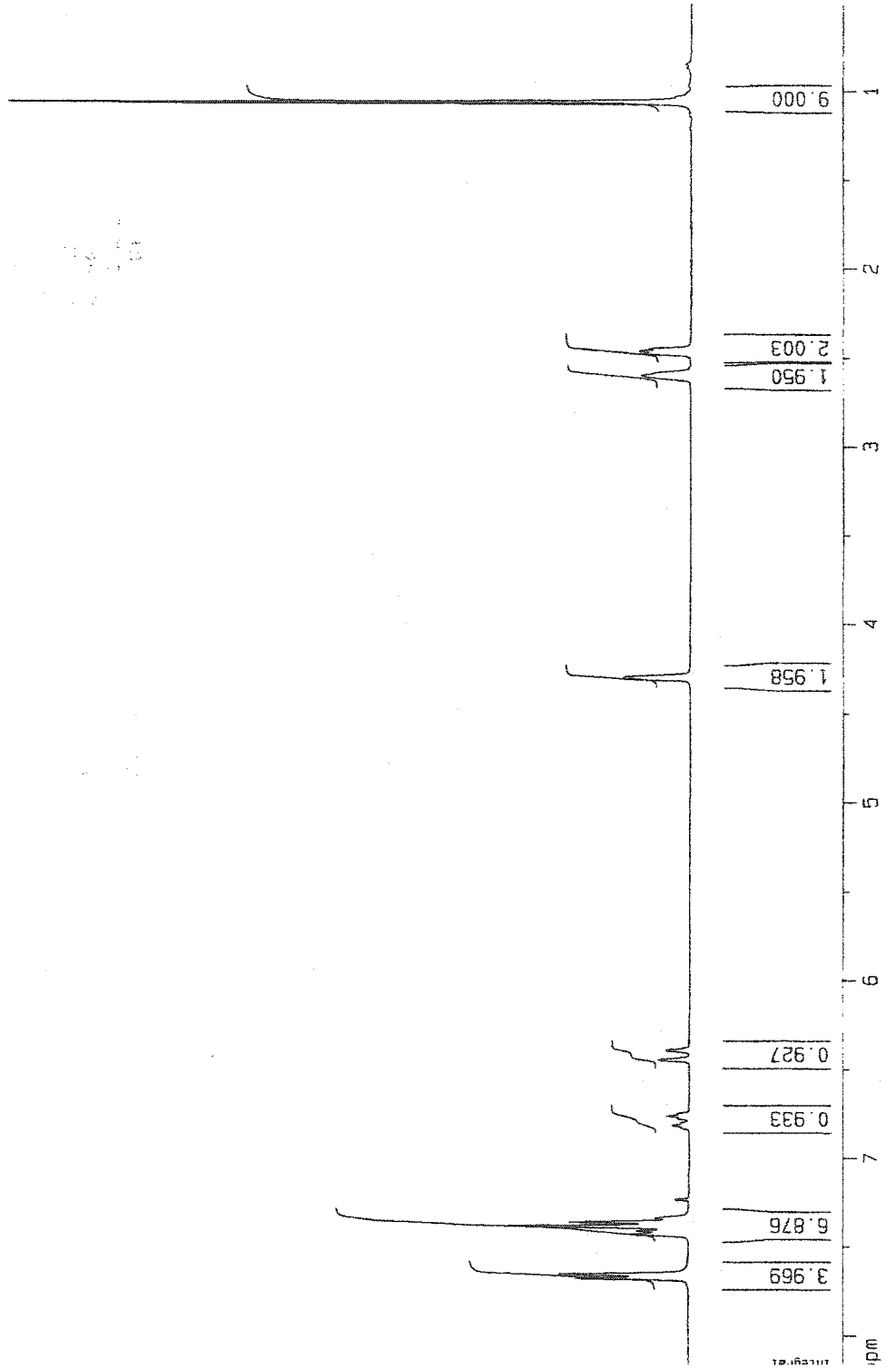
Current Data Parameters
 NAME prm-374
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20021104
 Time 14.31
 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 128
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

***** CHANNEL f1 *****
 NUC1 1H
 P1 9.75 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

10 NMR plot parameters
 CX 20.00 cm
 CY 10.00 cm
 F1P 8.211 ppm
 F1 2464.46 Hz
 F2P 0.511 ppm
 F2 153.47 Hz
 PPMCM 0.38500 ppm/cm
 HZCM 115.54935 Hz/cm



Current Data Parameters
 NAME prm-424(20H)
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters

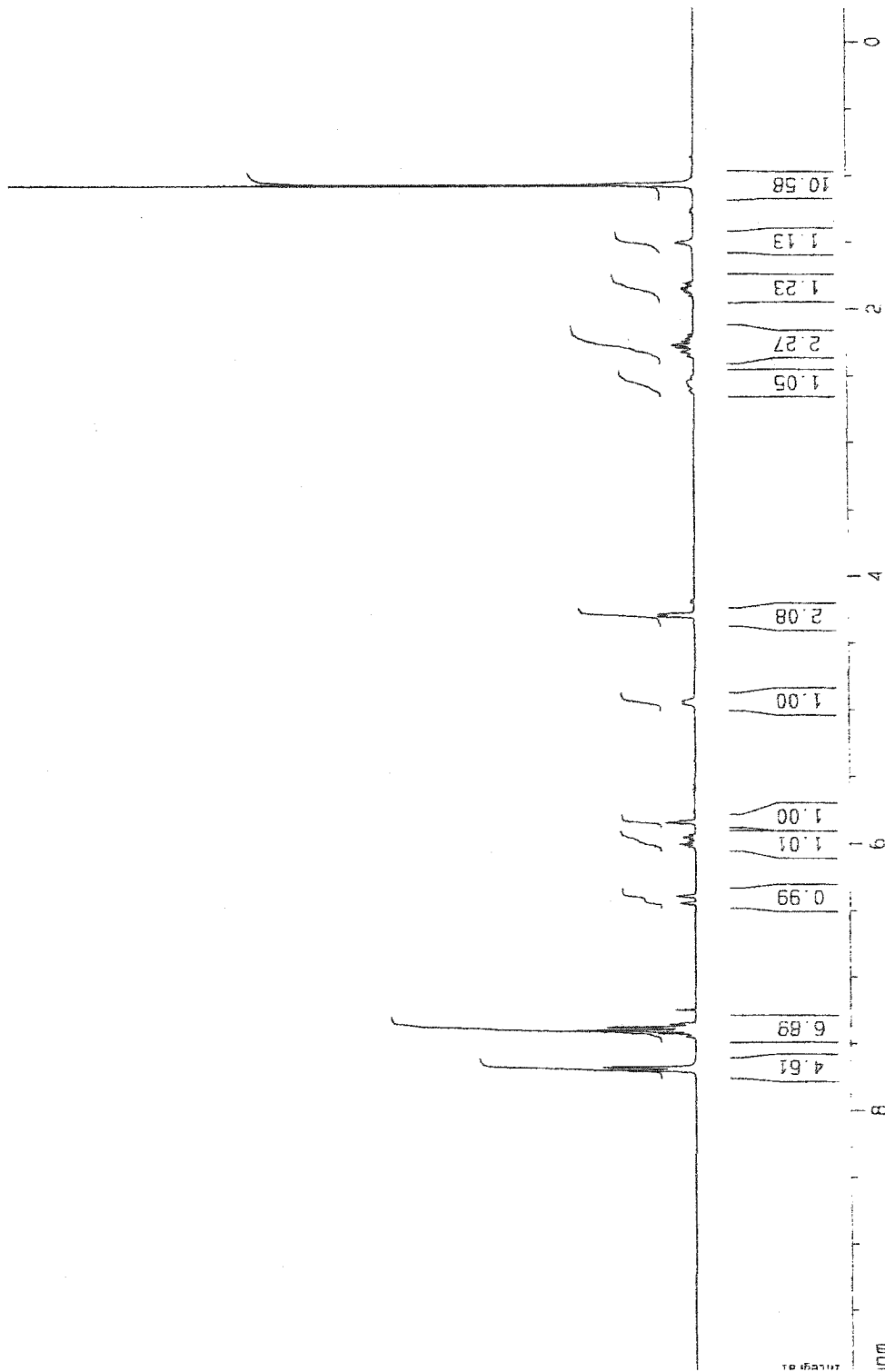
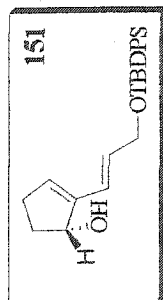
Date_ 20030205
 Time 15 50
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl3
 NS 16
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 101.6
 CW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.0000000 sec

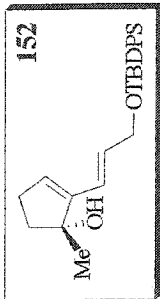
***** CHANNEL f1 *****
 NUC1 1H
 P1 9.75 usec
 PL1 -3.00 dB
 SF01 300.1319477 MHz

F2 - Processing parameters

SI 65536
 SF 300.1299999 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 10.007 ppm
 F1 3003.51 Hz
 F2P -0.258 ppm
 F2 -77.31 Hz
 PPMCM 0.51325 ppm/cm
 HZCM 154.04128 Hz/cm





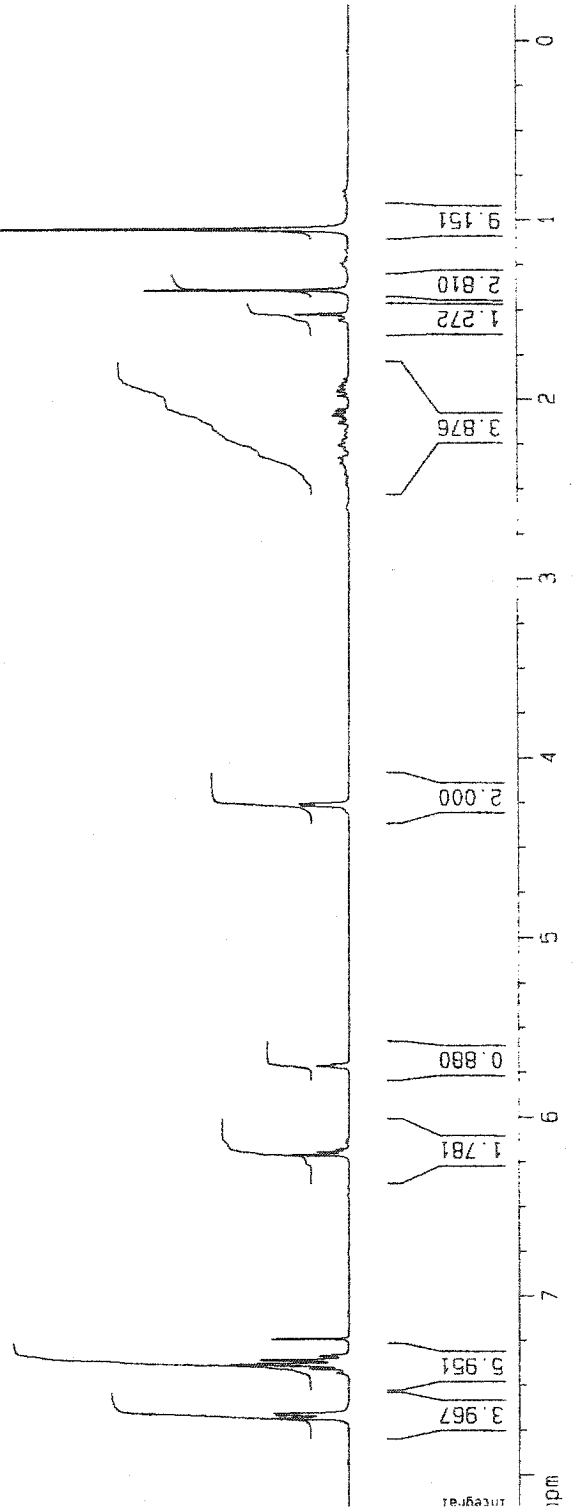
Current Data Parameters
 NAME prm-375
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20021105
 Time 12.24
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 36720
 SOLVENT CDCl3
 NS 32
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 362
 DK 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

***** CHANNEL f1 *****
 NUC1 1H
 P1 9.75 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 8.216 ppm
 F1 2465.94 Hz
 F2P -0.203 ppm
 F2 -61.01 Hz
 PPMCM 0.42097 ppm/cm
 HZCM 126.34714 Hz/cm



Current Data Parameters
 NAME 8cm-422gain
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters

Date_ 20030204
 Time 14.34
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl3
 NS 32
 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

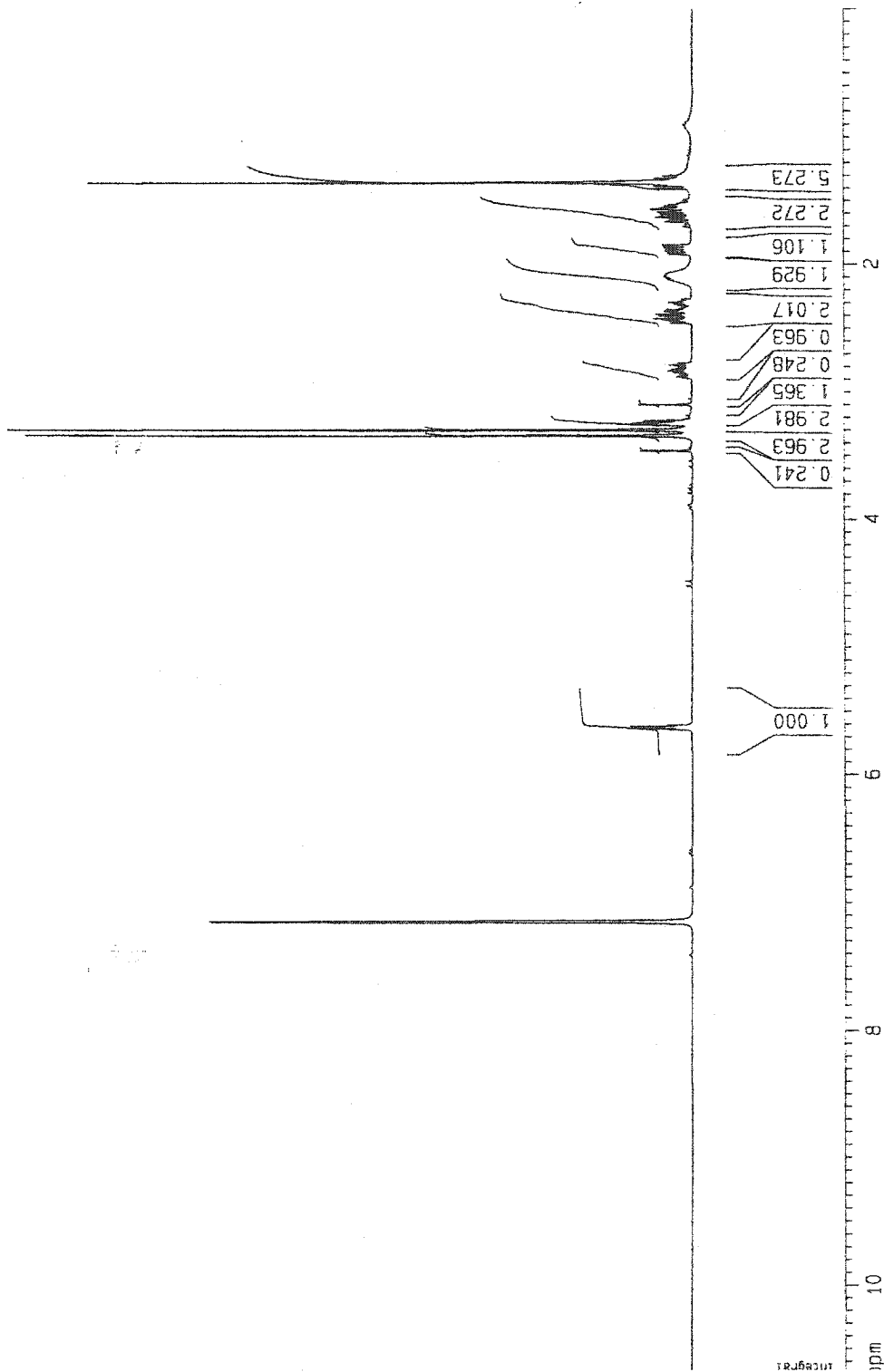
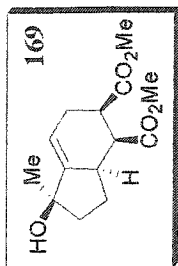
***** CHANNEL f1 *****
 NUC1 1H
 P1 9.75 usec
 PL1 -3.00 dB
 SFO1 300.1319477 MHz

F2 - Processing parameters

SI 65536
 SF 300.1299997 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 10.723 ppm
 F1 3218.39 Hz
 F2P -0.000 ppm
 F2 -0.00 Hz
 PPMCH 0.53617 ppm/cm
 HZCM 160.91931 Hz/cm



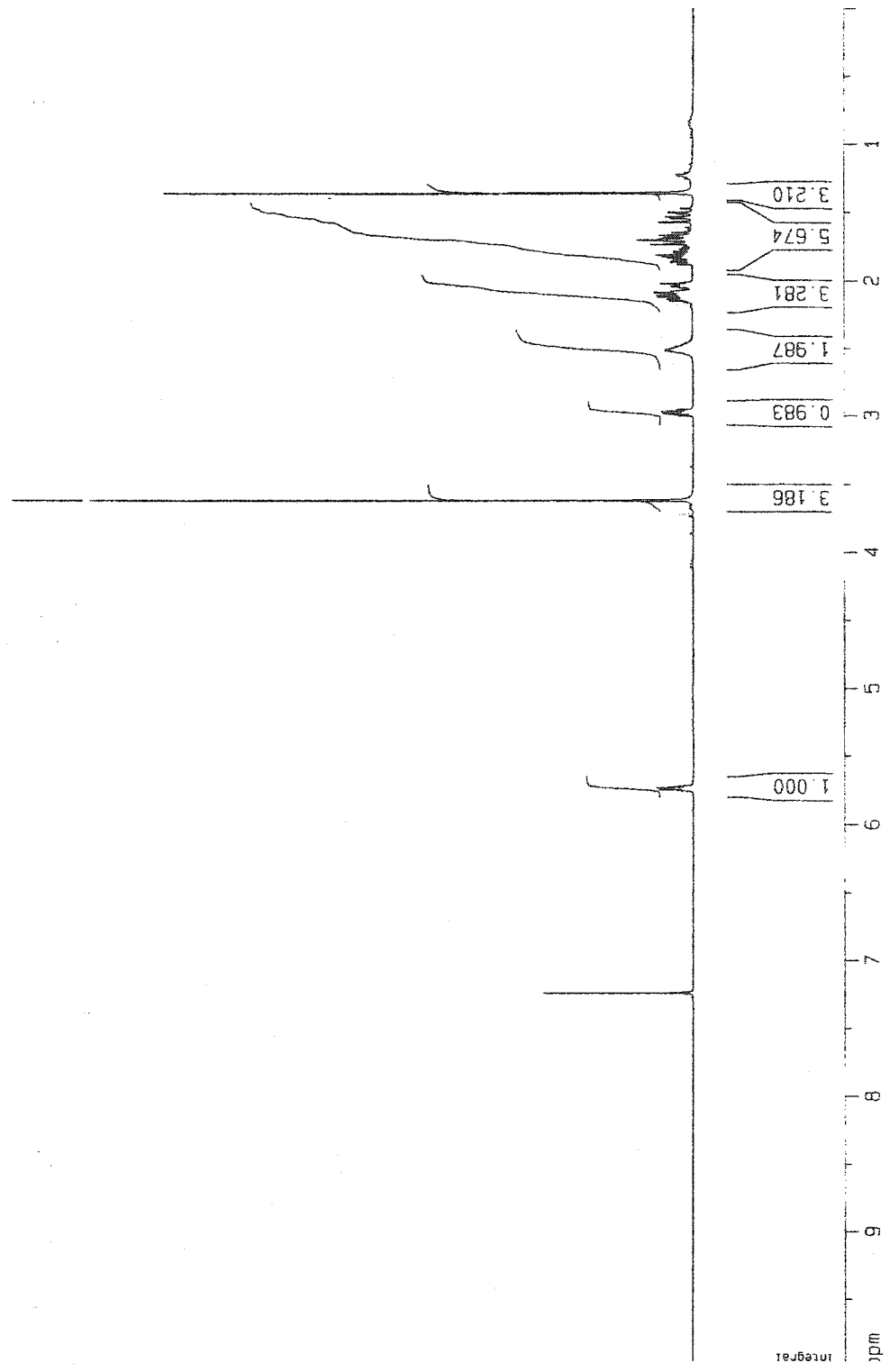
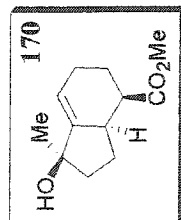
Current Data Parameters
 NAME prm-419
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20030129
 Time 12.10
 INSTRUM av300
 PROBHD 5 mm GNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl3
 NS 64
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 512
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

***** CHANNEL f1 *****
 NUC1 1H
 P1 9.75 usec
 PL1 -3.00 dB
 SF01 300.1319477 MHz

F2 - Processing parameters
 SI 65536
 SF 300.1300001 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 prm-428
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20030407
 Time 21:51
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl3
 NS 32
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 322.5
 DK 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

