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**STUDIES INTO THE DEVELOPMENT OF NOVEL TANDEM REACTIONS
AIMED AT THE CONSTRUCTION OF COMPLEX POLYCYCLIC
STRUCTURES**

By

ROXANNE CLÉMENT

B.Sc. (Honours), University of Ottawa, 2002

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

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TABLE OF CONTENTS

List of Schemes.....	4
List of Figures	6
List of Tables	7
List of Abbreviations	8
Abstract.....	10
Acknowledgments.....	12
Chapter 1: Introduction.....	16
1.1 The Diels-Alder Reaction	16
1.1.1 The Classic Diels-Alder Reaction: Regio-, Stereo- and Facial Selectivity	16
1.1.2 Use of Disposable Tethers in Diels-Alder Reactions	21
1.1.3 Hydroxy-Directed Diels-Alder Reaction	25
1.2 Tandem Reactions.....	26
1.3 Steroids in Natural Products: Synthesis of 14- β -Hydroxysteroids	29
1.4 Aim of the Current Project.....	32
Chapter 2: Studies Into the Tandem Oxy-Cope/Claisen/Ene/Claisen and Oxy-Cope/Claisen/Ene Reactions.....	34
2.1 Background	34
2.2 Preparation and Reaction of Benzyl Ether Derivatives	40
2.3 Preparation and Reaction of 1,3-Enyne Derivatives.....	43
2.4 Conclusion	47
Chapter 3: Studies Into the Tandem Oxy-Cope/Claisen/Ene/Hydroxy-Directed Diels-Alder Reaction	48
3.1 Background	48
3.2 Preparation and Reaction of 5- and 6-Membered Propargyl Ethers	49
3.3 Preparation and Reaction of Cyclohexenyl and C-2 Methyl Analogs.....	68
3.4 Additional Studies.....	76
3.4.1 Functionalization of the Propargyl Group	76
3.4.2 Functionalization of the C-1 Alkyne.....	78
3.4.3 Functionalization of the Cyclohexenyl Ring of 3.32	79

3.4.4 Tandem Oxy-Cope/Claisen/Ene/HDDA Reaction with 2-Phenylthio-2-Cyclopentenone and α -Methylene- γ - Butyrolactone	80
3.4.5 Attempts at a Tandem Oxy-Cope/Claisen/Ene/Claisen/ Diels-Alder Reaction	82
3.5 Conclusion	83
3.6 Future Studies	84
Chapter 4: Experimental	87
4.1 General Method and Materials.....	87
4.2 Experimental Method and Data Relating to Compounds of Chapter 2	88
4.3 Experimental Method and Data Relating to Compounds of Chapter 3	101
4.3.1 General Method for the Tandem Oxy-Cope/Claisen/Ene/ HDDA Reaction.....	110
Claims to Original Research	138
Spectra.....	139

LIST OF SCHEMES

Scheme 1.1: Facial Selectivity in the Diels-Alder Reaction with Allylic Substituents on Semicyclic Dienes	21
Scheme 1.2: Use of Silicon as a Disposable Tether in a Diels-Alder Reaction	22
Scheme 1.3: Alkenyl Boronic Esters in IMDA Reactions	23
Scheme 1.4: Use of Magnesium and Aluminium as Tethering Units in Diels-Alder Reactions	24
Scheme 1.5: Lewis Acids and Grignard Reagents as Tethering Agents in Diels-Alder Reactions	25
Scheme 1.6: Hydroxy-Directed Diels-Alder Reaction	26
Scheme 1.7: Shindo's Tandem [2+2]/Michael Reaction	28
Scheme 1.8: Kraus' Tandem Diels-Alder/Ene Reaction	28
Scheme 1.9: First Synthesis of the A/B Ring Structure of Ouabain	31
Scheme 1.10: Deslongchamps' Synthesis of 14- β -Hydroxysteroids	32
Scheme 2.1: Discovery of the Tandem Oxy-Cope/Claisen/Ene/Claisen Reaction	36
Scheme 2.2: Preparation and Reaction of Benzyl Ether Derivatives 2.13 and 2.14	41
Scheme 2.3: Preparation and Reaction of Cyclohexenyl Derivatives 2.17 and 2.18	42
Scheme 2.4: Preparation and Reaction of 1,3-Enyne 2.21	44
Scheme 2.5: Preparation and Reaction of 1,3-Enyne 2.24	45
Scheme 2.6: Preparation and Reaction of 1,3-Enyne 2.28	46
Scheme 3.1: Tandem Oxy-Cope/Claisen/Ene/Claisen Reaction of 2.4 and 3.1	49
Scheme 3.2: Preparation and Tandem Oxy-Cope/Claisen/Ene Reaction of Propargyl Ether 3.3	50
Scheme 3.3: First Attempt at a Tandem Oxy-Cope/Claisen/Ene/Diels-Alder Reaction	51
Scheme 3.4: Investigation of the Mechanism for the Formation of 3.6	53
Scheme 3.5: First Tandem Oxy-Cope/Claisen/Ene/Diels-Alder Reaction with N-Phenylmaleimide	54
Scheme 3.6: Tandem Oxy-Cope/Claisen/Ene/Diels-Alder Reaction with Methyl Acrylate	55
Scheme 3.7: First Tandem Oxy-Cope/Claisen/Ene/HDDA Reaction with Methyl Acrylate	56
Scheme 3.8: Method for the Tandem Oxy-Cope/Claisen/Ene/HDDA Reaction	59

Scheme 3.9: Preparation of Propargyl Ether 3.24	66
Scheme 3.10: Preparation of Propargyl Ether 3.32	69
Scheme 3.11: Alkylation of 2-Isopropenyl-Cyclohexanone 2.9	72
Scheme 3.12: Preparation of Propargyl Ether 3.40	73
Scheme 3.13: Attempts at Functionalizing the Propargyl Group	77
Scheme 3.14: Preparation and Attempted Reaction of 3.50	78
Scheme 3.15: Preparation of Propargyl Ether 3.52	78
Scheme 3.16: Preparation of Propargyl Ether 3.59	80
Scheme 3.17: Attempt at a Tandem Oxy-Cope/Claisen/Ene/HDDA Reaction with 2-Phenylthio-2-Cyclopentenone	81
Scheme 3.18: Preparation of α -Methylene- γ -Butyrolactone	81
Scheme 3.19: Tandem Oxy-Cope/Claisen/Ene/HDDA Reaction with α -Methylene- γ -Butyrolactone	82
Scheme 3.20: Attempts at a Tandem Oxy-Cope/Claisen/Ene/Claisen/ Diels-Alder Reaction	83
Scheme 3.21: Cis-Decalin Formation Through a Tandem Oxy-Cope/Claisen/Ene Reaction	85

LIST OF FIGURES

Figure 1.1: Regioselectivity in the Diels-Alder Reaction	17
Figure 1.2: The Klopman-Salem Equation	17
Figure 1.3: Interaction of Orbital Coefficients	18
Figure 1.4: Secondary Orbital Effects in the Diels-Alder Reaction	19
Figure 1.5: Two Important 14- β -Hydroxysteroids: Actodigin and Ouabain	30
Figure 1.6: Anticipated Pathway for the Generation of the B/C/D Ring System of the Steroid Core Structure	33
Figure 2.1: Application of the Oxy-Cope/Ene, the Oxy-Cope/Ene/Claisen and the Oxy-Cope/Claisen/Ene in the Total Syntheses of (+)-Arteannuin M, Tetrodecamycin and a Wiedemannic Acid Analog	35
Figure 2.2: Crystallographic Structure of 2.6	37
Figure 2.3: Proposed Mechanism for the Tandem Oxy-Cope/Claisen/Ene/Claisen Reaction	38
Figure 2.4: Study of the Tandem Oxy-Cope/Claisen/Ene/Claisen Reaction with Various Substrates	39
Figure 2.5: Anticipated Tandem Reaction of 1,3-Enyne 2.21	43
Figure 2.6: Intramolecular [4+2] Cycloaddition of 1,3-Enynes	47
Figure 3.1: Proposed Mechanism for the Tandem Oxy-Cope/Claisen/Ene Reaction	50
Figure 3.2: Proposed Mechanism for the Formation of 3.6	52
Figure 3.3: Transition States for the HDDA Reaction with Methyl Acrylate	57
Figure 3.4: Structure Elucidation of 3.18b by 2-D NMR Experiments	62
Figure 3.5: Structure Elucidation of 3.18a by 2-D NMR Experiments	62
Figure 3.6: Experimental Evidence for the Epimerization of 3.19	63
Figure 3.7: Structure Elucidation of 3.20/3.20b by 2-D NMR Experiments	64
Figure 3.8: Transition States for the HDDA Reaction with Dimethyl Fumarate	65
Figure 3.9: Single Crystal Structure of 3.26	68
Figure 3.10: Structure Elucidation of 3.34 by 2-D NMR Experiments	71
Figure 3.11: Structure Elucidation of 3.37 by 2-D NMR Experiments	71
Figure 3.12: Structure Elucidation of 3.42 by 2-D NMR Experiments	75
Figure 3.13: Structure Elucidation of 3.44 by 2-D NMR Experiments	75
Figure 3.14: Anticipated Application of the Oxy-Cope/Claisen/Ene/HDDA Reaction to the Synthesis of 14- β -Hydroxysteroids	86

LIST OF TABLES

Table 3.1: Results of the Tandem Oxy-Cope/Claisen/Ene/HDDA Reaction with Propargyl Ether 3.3	59
Table 3.2: Results of the Tandem Oxy-Cope/Claisen/Ene/HDDA Reaction with Propargyl Ether 3.24	66
Table 3.3: Results of the Tandem Oxy-Cope/Claisen/Ene/HDDA Reaction with Propargyl Ether 3.32	69
Table 3.4: Alkylation of 2-Isopropenyl-Cyclohexanone 2.9	72
Table 3.5: Results of the Tandem Oxy-Cope/Claisen/Ene/HDDA Reaction with Propargyl Ether 3.40	73

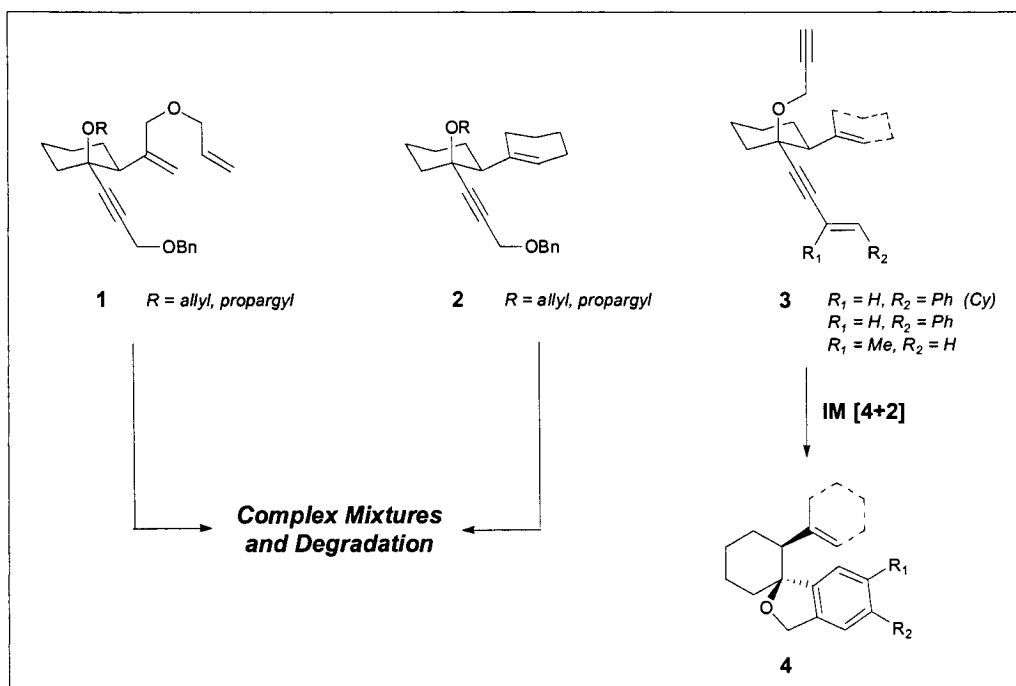
LIST OF ABBREVIATIONS

aq.	aqueous
Bn	benzyl
br.	broad
brsm	based on recovered starting material
DA	Diels-Alder
DBU	1,8-diazobicyclo[5.4.0]undec-7-ene
DCM	dichloromethane
DDQ	2,3-dichloro-5,6-dicyano- <i>p</i> -benzoquinone
DME	1,2-dimethoxyethane
DMF	N,N-dimethylformamide
DMSO	dimethyl sulfoxide
dr	diastereomeric ratio
eq.	equivalents
Et ₂ O	diethyl ether
EtOAc	ethyl acetate
Et ₃ N	triethylamine
DDA	hydroxy-directed Diels-Alder
HRMS	high resolution mass spectrum
IM	intramolecular
IMDA	intramolecular Diels-Alder
<i>i</i> -PrMgBr	isopropylmagnesium bromide

IR	infrared
KHMDS	potassium hexamethyldisilazane
LAH	lithium aluminium hydride
Me	methyl
MgBr ₂ ·OEt ₂	magnesium bromide diethyl etherate
mp	melting point
<i>n</i> -BuLi	<i>n</i> -butyllithium
NMR	nuclear magnetic resonance
NPM	N-phenylmaleimide
PA	<i>p</i> -anisaldehyde
Ph	phenyl
PMBCl	<i>p</i> -methoxybenzyl chloride
ppm	parts per million
PTSA	<i>para</i> -toluene sulfonic acid
sat.	saturated
SM	starting material
TBAF	tetrabutylammonium fluoride
<i>t</i> -BuLi	<i>tert</i> -butyllithium
<i>t</i> -BuOK	potassium <i>tert</i> -butoxide
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl

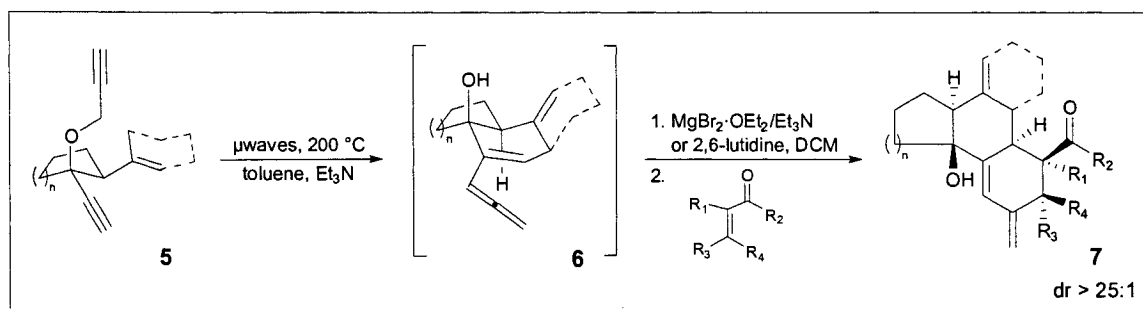
ABSTRACT

The scope and limitations of the tandem oxy-Cope/Claisen/ene/Claisen and the oxy-Cope/Claisen/ene reactions were investigated through the synthesis of various substrates possessing both allyl and propargyl moieties on the tertiary hydroxyl group. Substrates **1** and **2** led to degradation or the isolation of complex mixtures, indicating that the tandem pericyclic sequences were very sensitive to functionality. The 1,3-enynes **3** were found to undergo an intramolecular [4+2] cycloaddition in place of the expected oxy-Cope/Claisen/ene rearrangement, thus generating aromatic compounds **4**.



The tandem oxy-Cope/Claisen/ene/HDDA reaction was developed over the course of this research. Microwave irradiation of propargyl ethers **5** provided the diene intermediates **6** via a tandem oxy-Cope/Claisen/ene reaction. The corresponding

magnesium alkoxides of **6**, generated *in situ* by treatment with a solution of $\text{MgBr}_2 \cdot \text{OEt}_2$ /base, reacted upon the addition of various dienophiles to afford the diterpenes **7** as sole diastereoisomers [dr > 25:1]. The scope and limitations of this reaction were investigated through the preparation of various derivatives.



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Whatever road we choose in life, whatever goals we achieve, in the end I strongly believe that the warmest memories arise from the people the days were shared with. In these past 5 years, I have been blessed by being surrounded by incredible people, and it is something I shall never forget.

***« There is a theory which states that if ever anyone discovers
exactly what the Universe is for and why it is here,
it will instantly disappear and be replaced by something even more
bizarre and inexplicable.***

There is another theory which states that this has already happened. »

- D. Adams

« Dédée à mes parents, Ghislaine et Jean-Guy »

Chapter 1: Introduction

1.1 The Diels-Alder Reaction

1.1.1 The Classic Diels-Alder Reaction: Regio-, Stereo- and Facial Selectivity

The Diels-Alder reaction is, without a doubt, one of the most studied and applied methodologies of all time in organic synthesis. Its mechanism was first reported in 1928¹ and Otto Diels and Kurt Alder were awarded the Nobel prize in 1950. Since then, it has been the subject of intense research and has found a direct application in countless total syntheses. Woodward and Hoffman were pioneers in predicting the reaction's selectivity based on FMO interactions² and their findings ultimately led to the fine-tuning of this cycloaddition. The Diels-Alder reaction has thus become an invaluable method for the regio- and stereoselective generation of rings systems bearing up to four chiral centers.

Regioselectivity in Diels-Alder reactions is controlled by the size of the frontier molecular orbital coefficients such that both large and small coefficients are matched together. For example, **1.1** and **1.2** react regioselectively to afford **1.3**. (*Figure 1.1*).

¹ Diels, O.; Alder, K. *Ann.* **1928**, 460, 98.

² Woodward, R. B.; Hoffman, R. *The Conservation of Orbital Symmetry*, Verlag Chemie: Weinheim, 1970.

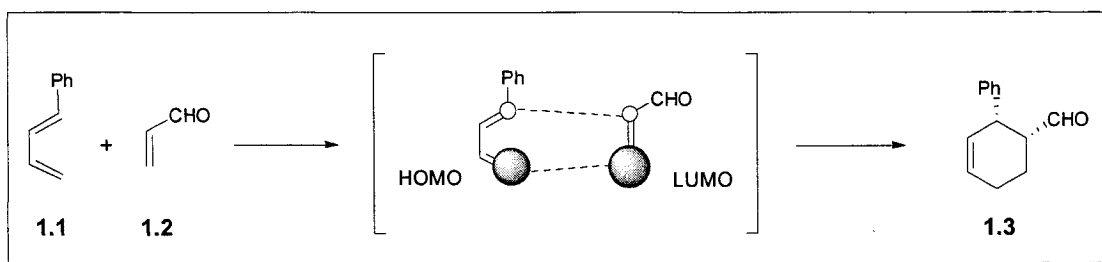


Figure 1.1: Regioselectivity in the Diels-Alder Reaction

The explanation for this matching is found in the Klopman-Salem equation, which expresses the interaction of two molecules in terms of their molecular orbitals³ (Figure 1.2).

$$\Delta E = \left[-\sum_{ab} (q_a + q_b) \beta_{ab} S_{ab} \right] + \left[\sum_{k,l} \frac{Q_k Q_l}{\epsilon R_{kl}} \right] + \left[\sum_r^{\text{occ.}} \sum_s^{\text{unocc.}} - \sum_s^{\text{occ.}} \sum_r^{\text{unocc.}} \frac{2 \left(\sum_{ab} c_{ra} c_{sb} \beta_{ab} \right)^2}{E_r - E_s} \right]$$

c_{ra}/c_{sb} = atomic orbital coefficients

Figure 1.2: The Klopman-Salem Equation

The first term of the equation consists of the first-order closed-shell repulsion that reflects the interaction between the filled orbitals of two molecules and is consequently an overall antibonding effect. For many reactions, this constitutes a great deal of the activation barrier. The second term addresses Coulombic repulsion/attraction and is especially important in ionic or polar reactions. Of primary interest in pericyclic reactions is the third term, which reflects the interaction of all the filled orbitals with all the unfilled orbitals of correct symmetry. It is from this last term that the small/small and large/large preference arises: the larger the value of the numerator, the more favourable

³ (a) Klopman, G. *J. Am. Chem. Soc.* **1968**, 90, 223. (b) Salem, L. *J. Am. Chem. Soc.* **1968**, 90, 543 and 553.

the reaction. Depicted in *Figure 1.3* are the two possible cases of coefficient matching: *Case A* consists of a favoured small/small-large/large interaction while *Case B* is a disfavoured small/large-large/small interaction. The smallest coefficients have been assigned the arbitrary values of x and y , while m and n represent the increase to a larger coefficient. The difference between the sums of the products of the interacting coefficients in *Case A* and *Case B* is the positive value nm , indicating that *Case A* generates a larger value than *Case B*. Due to the third term's negative sign, the energy will be lowered by a greater amount in *Case A*, leading to the observed coefficient matching.⁴

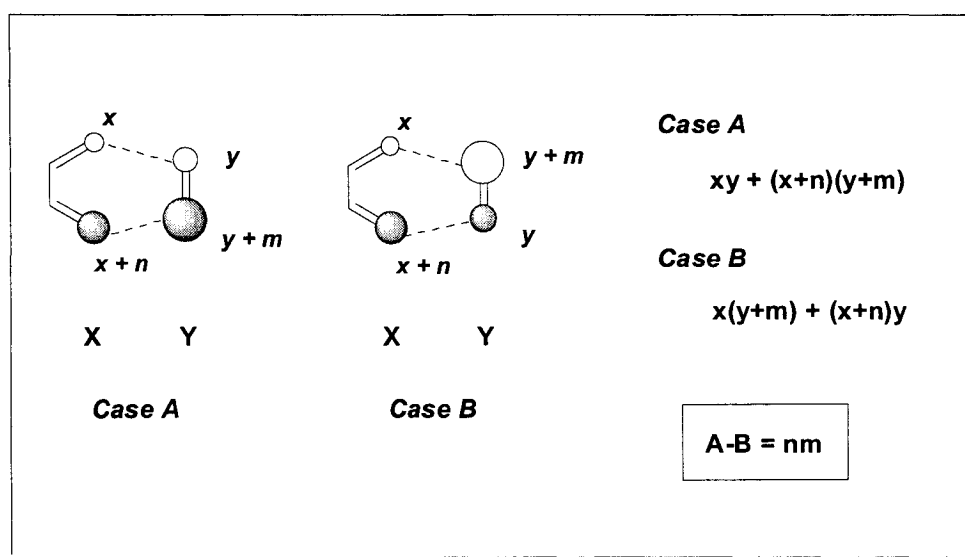


Figure 1.3: Interaction of Orbital Coefficients

The reaction between 1.1 and 1.2 in *Figure 1.1* leads specifically to the *cis*-adduct 1.3. This stereoselectivity is related to secondary orbital interactions and can be better exemplified with cyclopentene and maleic anhydride. As illustrated in *Figure 1.4*, the

⁴ Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*, John Wiley and Sons: New York, 1976.

dienophile can theoretically approach the diene in two specific orientations, resulting in either *endo* product **1.4** or *exo* product **1.5**. The transition state leading to the *endo* product has an additional secondary bonding orbital interaction between the carbonyl groups of the dienophile and the forming double-bond (represented by double-headed solid arrows). This added stability lowers the energy of the *endo* transition state, which accelerates its reaction. Overall, the effect is kinetic and the *endo* product is obtained at a faster rate than the *exo* product, despite the fact that the *exo* product is thermodynamically favoured.⁵

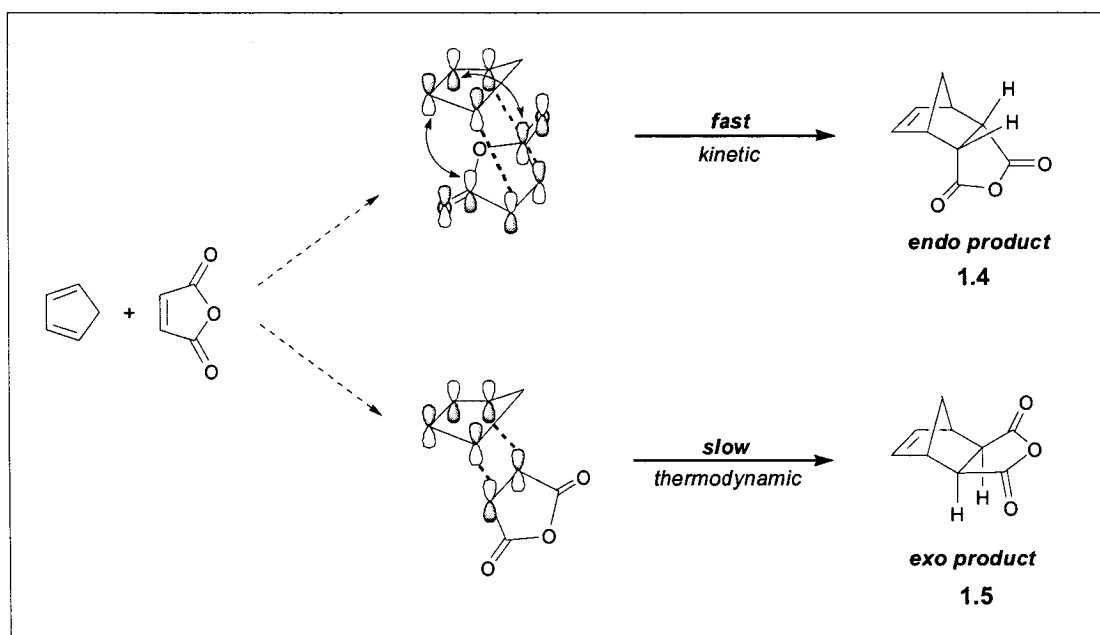


Figure 1.4: Secondary Orbital Effects in the Diels-Alder Reaction

The last issue in Diels-Alder reactions concerns the facial selectivity of the cycloaddition. Overman *et al.*⁶ reported that facial selectivity could be controlled by the presence of heteroatomic allylic substituents on specific semicyclic dienes. In particular,

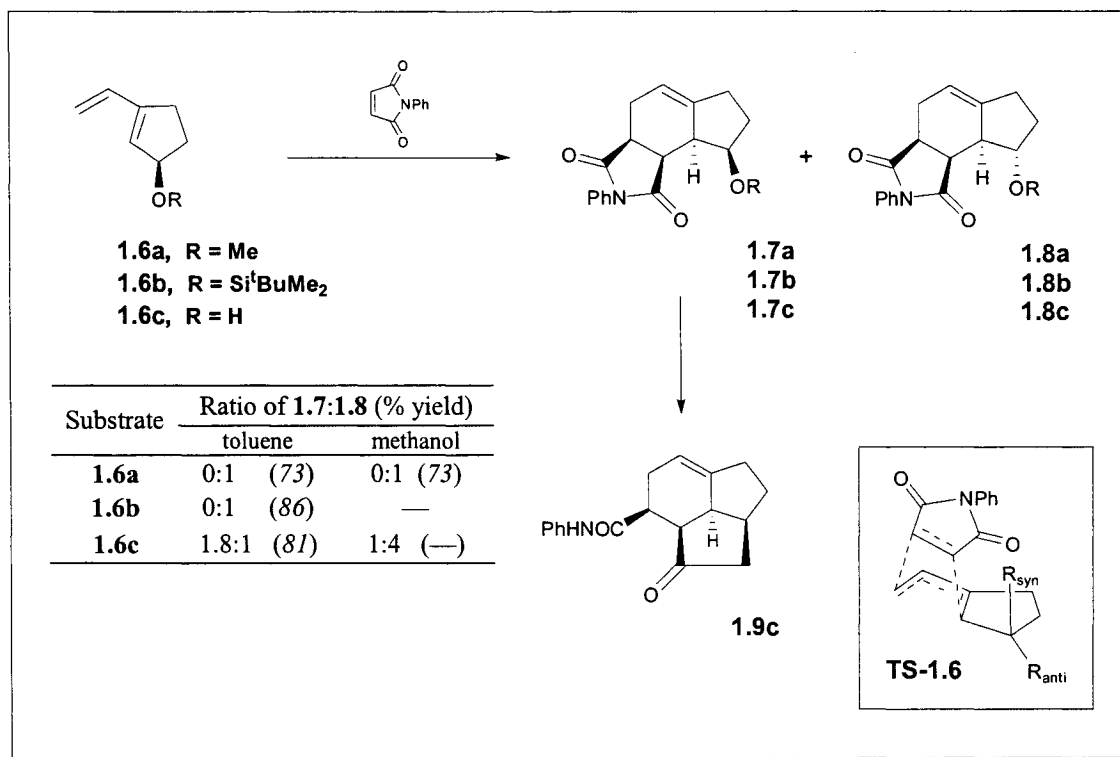
⁵ Clayden, J.; Greeves, N.; Warren, S.; Wothers, P. *Organic Chemistry*, Oxford University Press: New York, 2001.

⁶ Overman, L. E.; Kahn, S. D.; Hehre, W. J.; Fisher, M. J. *J. Am. Chem. Soc.* **1988**, *110*, 4625.

when **1.6a** and **1.6b** were reacted with N-phenylmaleimide in toluene, the adducts **1.8a** and **1.8b**, resulting from the addition of the dienophile *anti* to the allylic substituent, were isolated as the sole products in yields of 73% and 86% respectively (*Scheme 1.1*). The reaction of **1.6a** and N-phenylmaleimide in methanol proceeded similarly. Reaction of semicyclic diene **1.6c**, on the other hand, generated both **1.7c** and **1.8c** in ratios which were dependant on the solvent. When the reaction was conducted in toluene, a ratio of 1.8:1 for **1.7c** to **1.8c** was observed. Conversely, the use of methanol led to an inverse selectivity of 1:4. Extended reaction times with **1.6c** led to the conversion of the *syn* adduct **1.7c** to the tricyclic lactone **1.9c**. These results were rationalized through steric and electrostatic repulsions in the transition state (**TS-1.6**, *Scheme 1.1*). Steric interactions between the dienophile and a *syn* allylic substituent, along with electrostatic repulsion between the carbonyl of N-phenylmaleimide and the allylic substituent would overall disfavour the *syn* approach, leading to the selective formation of the *anti* adducts **1.8**. Indeed, this was the case for **1.6a** and **1.6b**. With **1.6c**, H-bonding between the carbonyl group of the dienophile and the allylic hydroxyl substituent on the semicyclic diene would favour the formation of the *syn* adduct **1.7c** in toluene. The use of a protic solvent such as methanol, however, reverses this selectivity due to H-bonding between the solvent molecules and the hydroxyl group which overall increases the steric interactions between the dienophile and the allylic substituent, thus favouring the formation of the *anti* adduct **1.8c**. Further studies conducted by Franck *et al.*,⁷ however, suggest a simple steric model, as their results indicated that polar aprotic solvents

⁷ Datta, S. C.; Franck, R. W.; Tripathy, R.; Quigley, G. J.; Huang, L.; Chen, S.; Sihaed, A. *J. Am. Chem. Soc.* **1990**, *112*, 8472.

increased the yield of *anti* adduct; an observation contradicting the electrostatic theory of Overman.



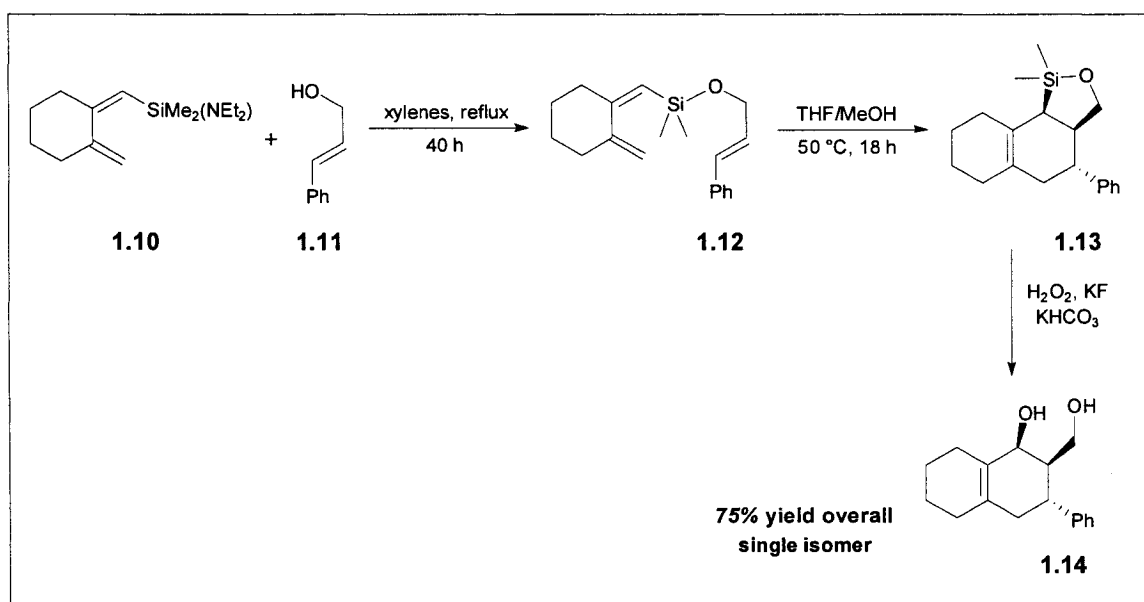
Scheme 1.1: Facial Selectivity in the Diels-Alder Reaction with Allylic Substituents on Semicyclic Dienes

1.1.2 Use of Disposable Tethers in Diels-Alder Reactions

In order to solve facial selectivity problems and promote regioselectivity, the use of temporary tethers⁸ was applied to Diels-Alder reactions. Temporary tethers allow a reaction to occur pseudo-intramolecularly by linking the two reacting entities together, allowing for a faster and more complete reaction. The total entropy of the system is thus lowered and the decrease in the degrees of freedom leads to a more selective reaction.

⁸ For a review on the use of disposable tethers in organic chemistry, see: Gauthier, D. R. Jr.; Zandi, K. S.; Shea, K. J. *Tetrahedron* **1998**, 54, 2289.

One of the first examples of a disposable tether in Diels-Alder reactions was reported with silicon in 1989.⁹ Diene **1.10** was condensed with cinnamyl alcohol **1.11** (*Scheme 1.2*). The intramolecular Diels-Alder reaction of the resulting system **1.12** led exclusively to cycloadduct **1.13**. The latter was then oxidatively cleaved to diol **1.14** in an overall yield of 75%. It is to note that the use of silicon as a tethering agent in [4+2] cycloadditions has also been reported by other groups.¹⁰



Scheme 1.2: Use of Silicon as a Disposable Tether in a Diels-Alder Reaction

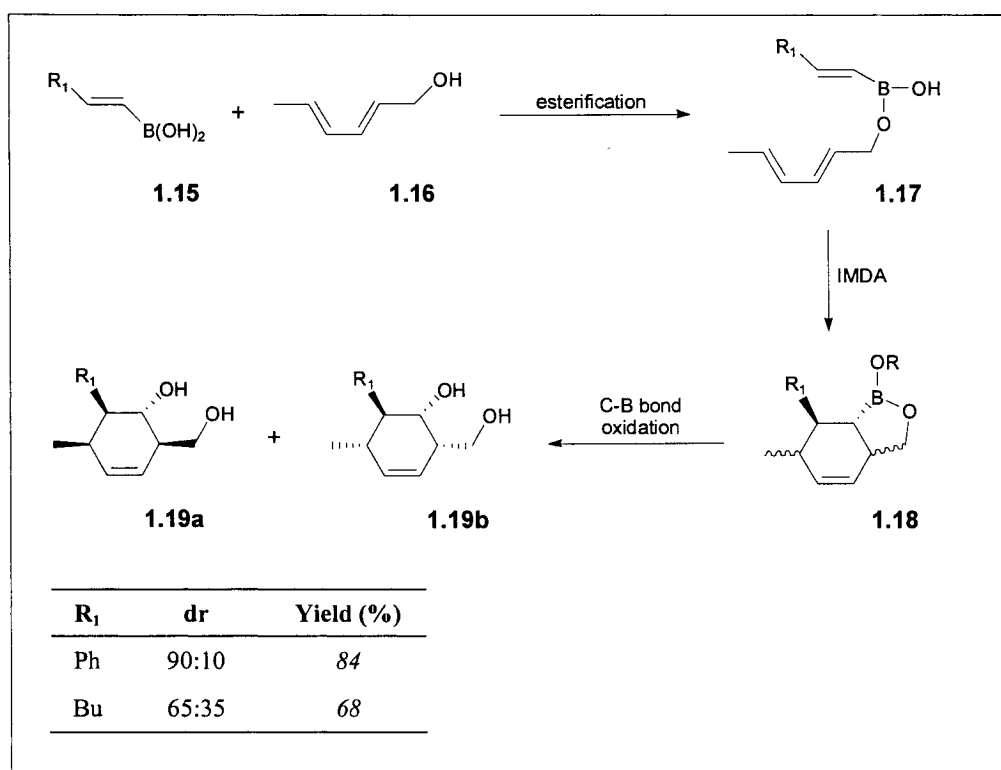
Similarly, a temporary covalent connection using boron was reported in 1999.¹¹ Alkenyl boronic acids **1.15** were connected to diene **1.16** to form the corresponding alkenyl boronic esters **1.17** (*Scheme 1.3*). Intramolecular Diels-Alder (IMDA) reaction of

⁹ Tamao, K.; Kobayashi, K.; Yoshihiko, I. *J. Am. Chem. Soc.* **1989**, *111*, 6478.

¹⁰ (a) Shea, K. J.; Zandi, K. S.; Staab, A. J.; Carr, R. *Tetrahedron Lett.* **1990**, *31*, 5885. (b) Stork, G.; Chan, T. Y.; Breault, G. A. *J. Am. Chem. Soc.* **1992**, *114*, 7578. (c) Craig, D.; Reader, J. C. *Tetrahedron Lett.* **1990**, *31*, 6585. (d) Craig, D.; Reader, J. C. *Tetrahedron. Lett.* **1992**, *33*, 4073. (e) Sieburth, S. M.; Fensterbank, L. *J. Org. Chem.* **1992**, *57*, 5279.

¹¹ Batey, R. A.; Thadani, A. N.; Lough, A. J. *J. Am. Chem. Soc.* **1999**, *121*, 450.

substrates **1.17** led to boracycles **1.18**, which were cleaved to diols **1.19a-b** in overall yields of 68-84%. Complete regioselectivity was observed and the *endo* product was formed preferentially with diastereomeric ratios of 90:10 and 65:35 with $R_1 = \text{Ph}$ and $R_1 = \text{Bu}$ respectively.

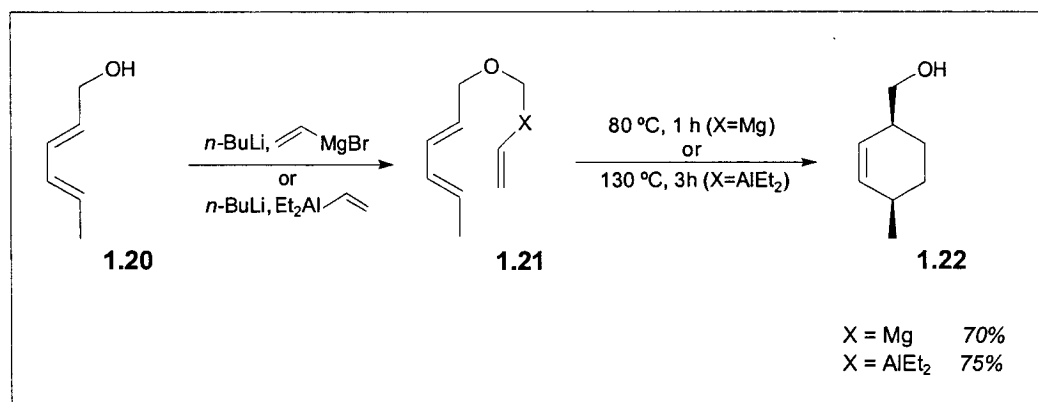


Scheme 1.3: Alkenyl Boronic Esters in IMDA Reactions

In 1995, Stork *et al.* reported the use of magnesium and aluminium as tethering agents.¹² Diene **1.20** was treated with *n*-BuLi at -78 °C and a solution of either vinylmagnesium bromide or vinyl diethylaluminium was subsequently added to generate the tethered intermediate **1.21** (*Scheme 1.4*). It was found that the reaction proceeded despite the fact that the dienophile was now formally a vinyl carbanion. In fact, the

¹² Stork, G.; Chan, T. Y. *J. Am. Chem. Soc.* **1995**, *117*, 6595.

reaction with magnesium as a tether was complete in a single hour at 80 °C to afford **1.22**, as opposed to the silicon analog, which necessitated 3 hours at 180 °C .



Scheme 1.4: Use of Magnesium and Aluminium as Tethering Units in Diels-Alder Reactions

Titanium compounds,¹³ as well as aluminium and zinc tethers,¹⁴ have also been reported with similar results. The exploitation of metals as tethering agents has the advantage of resulting in shorter pathways to regio- and stereoselective IMDA reactions. Conversely, covalent tethering systems require additional synthetic steps to install and cleave the agent.

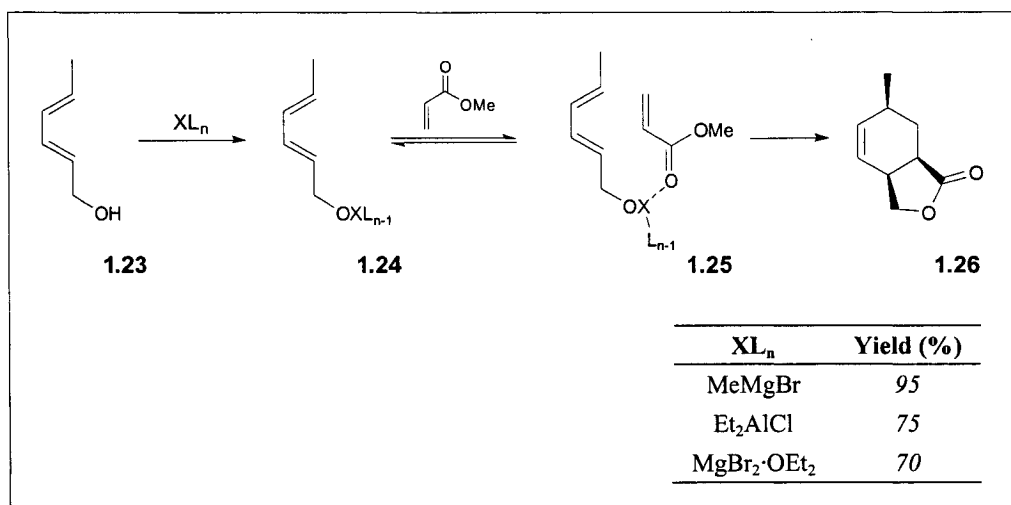
Finally, in 2000, Ward *et al.* published results concerning the use of different Lewis acids and Grignard reagents as tethering agents.¹⁵ Treatment of **1.23** with methylmagnesium bromide led to the generation of magnesium alkoxide **1.24** (Scheme 1.5). The carbonyl group of methyl acrylate complexes onto the magnesium and the two components are effectively linked (**1.25**) for the [4+2] cycloaddition, affording **1.26** as the sole product in 95% yield. Interchanging the metallic species for diethyl aluminium

¹³ Bienaymé, H. *Angew. Chem. Int. Ed.* **1997**, 36, 2670

¹⁴ Bertozzi, F.; Olsson, R; Fredj, T. *Org. Lett.* **2000**, 2, 1283.

¹⁵ Ward, D. E.; Abaee, M. S. *Org. Lett.* **2000**, 2, 3937.

chloride and magnesium bromide diethyl etherate led to the formation of **1.26** in yields of 75% and 70% respectively.

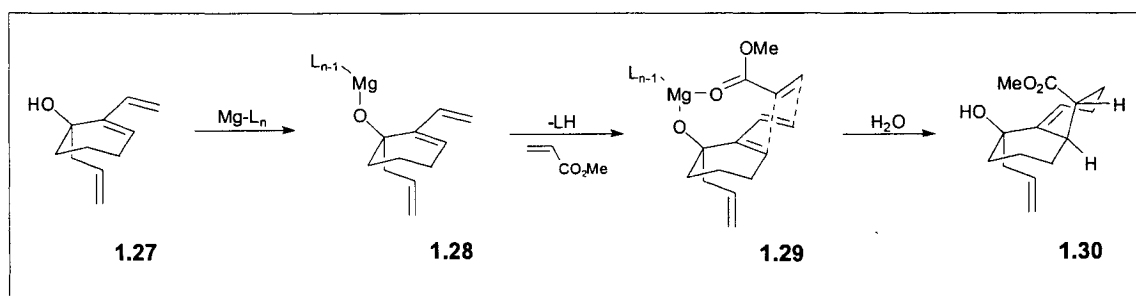


Scheme 1.5: Lewis Acids and Grignard Reagents as Tethering Agents in Diels-Alder Reactions

1.1.3 Hydroxy-Directed Diels-Alder Reaction

Secondary and tertiary allylic alcohols are sensitive by nature and their complexation to many Lewis acids or subjection to high temperatures leads to their degradation. In order to address these issues, Barriault *et al.*¹⁶ developed a highly regio- and stereoselective hydroxy-directed Diels-Alder reaction, which can be applied to semicyclic dienes possessing secondary or tertiary hydroxyl groups such as **1.27**, through the *in situ* generation of magnesium alkoxide **1.28** (Scheme 1.6). Upon addition of a dienophile, complex **1.29** is formed, and the subsequent [4+2] cycloaddition leads to **1.30**.

¹⁶ Barriault, L.; Thomas, J. D. O.; Clément, R. *J. Org. Chem.* **2003**, 68, 2317.



Scheme 1.6: Hydroxy-Directed Diels-Alder Reaction

The corresponding adducts were generally isolated in good yields, with complete regioselectivity and high diastereoselectivities [dr > 25:1]. Moreover, the methodology was applicable to a wide range of dienophiles. The magnesium alkoxide could be formed by treatment with phenylmagnesium bromide at $-78\text{ }^{\circ}\text{C}$, or by addition of a $\text{MgBr}_2\cdot\text{OEt}_2$ /base complex at room temperature. The reactions were accelerated due to Lewis acid complexation of the dienophile's carbonyl group, which activated the latter towards cycloaddition by donor-acceptor interactions between the dienophile and the catalyst.¹⁷

1.2 Tandem Reactions

Tandem reactions in organic chemistry increase the efficiency of a synthetic route by allowing two or more reactions to happen in “one-pot”, thus eliminating the need to isolate or purify the intermediates. Such sequences of reactions constitute in a rapid pathway to the formation of multiple carbon-carbon bonds, often with great selectivity, and find many an application in organic synthesis. The most descriptive definition of tandem reactions has been given by Ho¹⁸ as consisting of combinations of two or more

¹⁷ Pindur, U.; Lutz, G.; Otto, C. *Chem. Rev.* **1993**, 93, 741.

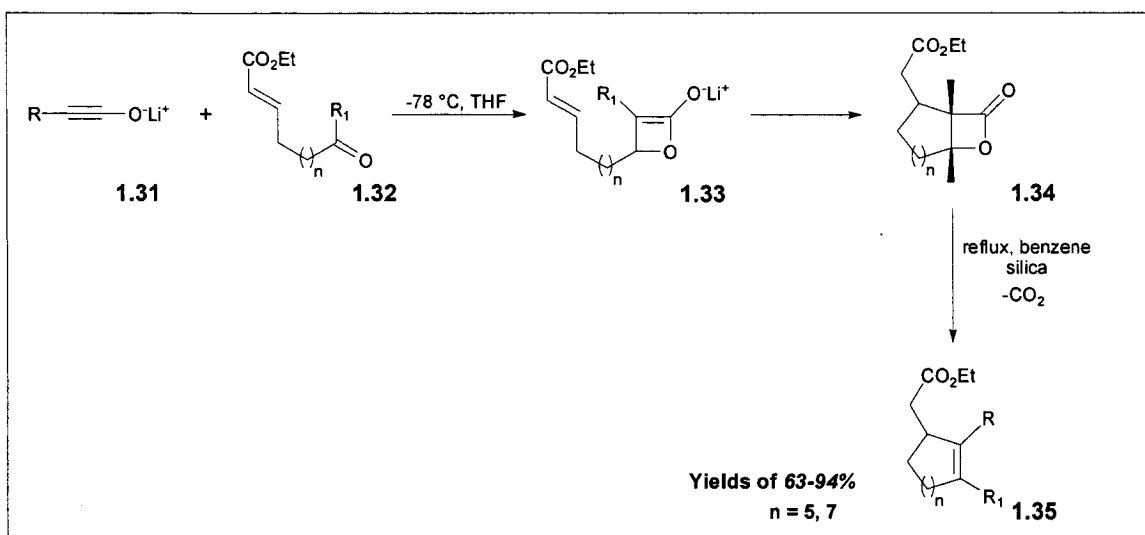
¹⁸ Ho, T.-L. *Tandem Organic Reactions*, John Wiley and Sons: New York, 1992.

reactions whose occurrence is in a specific order; if they should involve the sequential addition of reagents, these secondary reagents must be integrated into the products.

Tandem reactions are commonly divided into three distinct categories. The first embodies the **cascade** or **domino reactions**, designating those which take place on a single substrate, with no added reagents or modifications to the conditions. The second class, termed **consecutive reactions**, are those in which an intermediate requires additional energy to pursue the remaining reaction(s), while the final category is referred to as **sequential reactions**: reagents must be added in order for a subsequent reaction to occur. All tandem reactions have in common the fact that they offer simple routes for the construction of complex structures in as few steps as possible. Furthermore, since the intermediates are not isolated, it becomes much easier to work with unstable species as they can be generated and immediately reacted *in situ*.

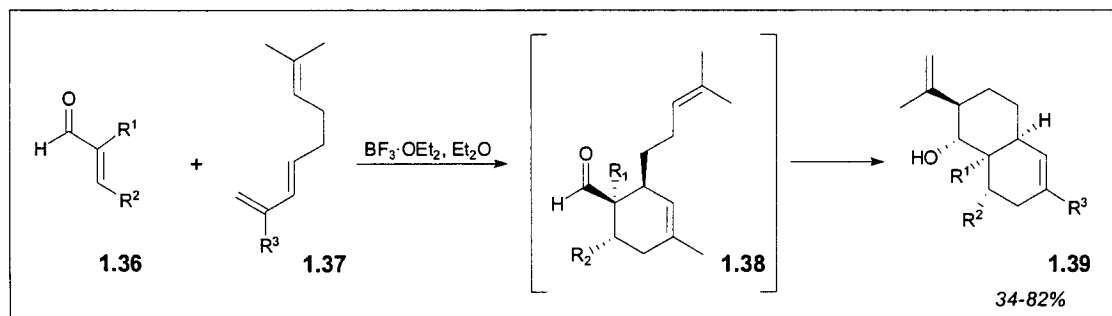
A recent tandem [2+2] cycloaddition/Michael reaction was reported by Shindo *et al.* in 2001.¹⁹ An ynoate anion (**1.31**) undergoes a [2+2] cycloaddition with the carbonyl moiety of a second molecule (**1.32**) to generate intermediate **1.33** (*Scheme 1.7*). The enolate created in the first step can then react to form the Michael 1,4-addition product **1.34** after work-up. Subsequent acid-catalyzed decarboxylation affords the polysubstituted 5-, 6- and 7-membered cycloalkenes **1.35** in 63-94% yield.

¹⁹ Shindo, M.; Matsumoto, K.; Sato, Y.; Shishido, K. *Org. Lett.* **2001**, *3*, 2029.



Scheme 1.7: Shindo's Tandem [2+2]/Michael Reaction

A second noteworthy example is the novel tandem Diels-Alder/ene reaction reported by Kraus and Kim in 2004.²⁰ Unsaturated aldehydes **1.36** react with trienes **1.37** to afford intermediates **1.38** through a [4+2] cycloaddition (*Scheme 1.8*). A subsequent ene reaction generates the corresponding bicyclic products **1.39**. Yields varied between 34% and 82% and the stereochemistry of the products was consistent with an *endo* approach of the dienophile, followed by a stereoselective ene reaction. Most cases studied afforded a single diastereoisomer.



Scheme 1.8: Kraus' Tandem Diels-Alder/Ene Reaction

²⁰ Kraus, G. A.; Kim, J. *Org. Lett.* **2004**, 6, 3115.

1.3 Steroids in Natural Products: Synthesis of 14- β -Hydroxysteroids

The steroid core is embedded in many natural products and hormonal compounds. The latter, which are produced in the adrenal cortex and reproductive organs of the human body, are responsible for several biological processes, including the regulation of blood pressure, sodium ion intake, as well as the control of metabolic and immunological activities. Steroids as drugs are extremely attractive due to their high biological activity and wide pharmacology;²¹ it is estimated that roughly a third of all prescription drugs contain a steroid derivative.²² Over the years, nearly all steroids and their analogs have been synthesized from partially degraded natural compounds. Case in point, corticosteroids,²³ an important class of anti-inflammatory compounds, have been synthesized from bile acid and the steroid diosgenin for several years.²⁴

An important class of steroids is the 14- β -hydroxysteroids, as they demonstrate tremendous potential in the treatment of heart disease. For example, extracts of *Digitalis Purpurea* have been used for over 200 years to increase the force of heart contractions, while decreasing their rate;²⁵ the three most abundant compounds of the extract belong to the 14- β -hydroxysteroid family. Actodigin and ouabain (*Figure 1.5*) have also drawn a considerable amount of attention as they have likewise proven to be highly relevant as cardiac glycosides.²⁶

²¹ Antead, G. M.; Carlson, K. E.; Katzenellenbogen, J. A. *Steroids* **1977**, *62*, 268.

²² Michellys, P.-Y.; Maurin, P.; Toupet, L.; Pellisier, H.; Santelli, M. *J. Org. Chem.* **2001**, *66*, 115 and references therein.

²³ Hench, P. S.; Kendall, E. C.; Slocumb, C. H.; Polley, H. F. *Proc. Staff Meetings Mayo Clinic* **1949**, *24*, 181.

²⁴ Herzog, H.; Oliveto, E. P. *Steroids* **1992**, *57*, 617.

²⁵ Erbarat, P. W. *J. Med. Chem.* **1987**, *30*, 231.

²⁶ (a) Gliklich, J. I.; Gaffney, R.; Rosen, M. R.; Hoffman, B. F. *Eur. J. of Pharm.* **1975**, *32*, 1. (b) Jacobs, W. A.; Bigelow, N. M. *J. Biol. Chem.* **1932**, *96*, 647.

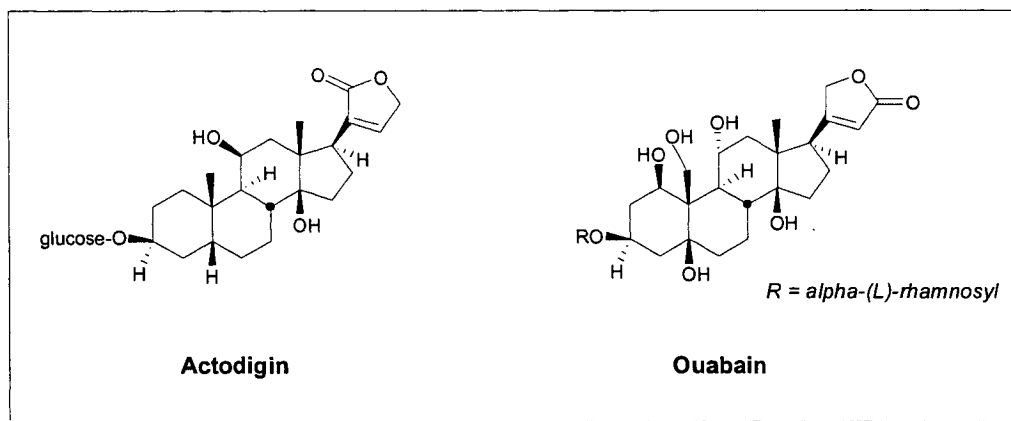


Figure 1.5: Two Important 14- β -Hydroxysteroids: Actodigin and Ouabain

Actodigin was first prepared from digitoxigenin in 1966,²⁷ and later from testosterone in 1979.²⁸ It demonstrates good activity as a cardioactive drug with little of the usual toxicity and side-effects associated with the digitalis glycosides. Ouabain was isolated from the bark and roots of the ouabaio tree in Africa by Arnaud in 1888²⁹ and has shown potential as a hypertensive and congestive heart failure drug.³⁰ In 2003, Jung *et al.* reported the first synthesis of the A/B ring of ouabain,³¹ which they constructed by a key Robinson annelation involving the α - β -unsaturated ketone **1.40** and the cyclohexanone **1.41** to generate the carbon framework observed in **1.45** (Scheme 1.9). Conversion of **1.42** to the bis-epoxy ketone **1.43** was effected through standard procedures and **1.43** was opened under aluminium amalgam conditions to afford **1.44**. Treatment of **1.44** with triethylformate and 5% HCl in methanol generated the tetraol **1.45** with the desired all-*cis* stereochemistry in an overall yield of 7.7% for 9 steps.

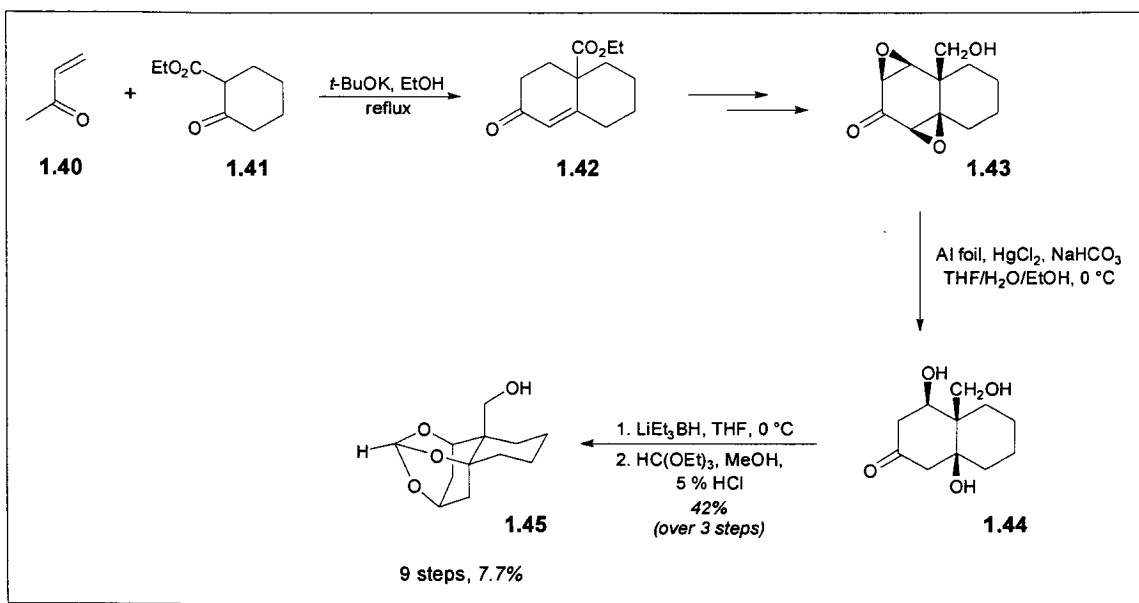
²⁷ Ferland, J. M.; Lefebvre, Y.; Deghengi, R.; Wiesner, K. *Tetrahedron Lett.* **1966**, 7, 3617.

²⁸ Tsai, T. Y. R.; Minta, A.; Wiesner, K. *Heterocycles* **1979**, 12, 1397.

²⁹ Arnaud, M. *Compt. Rend. Acad.* **1888**, 107, 1011.

³⁰ Thomas, R.; Gray, P.; Andrew, J. *Adv. Drug Res.* **1990**, 19, 312.

³¹ Jung, M. E.; Piizzi, G. *Org. Lett.* **2003**, 5, 137.

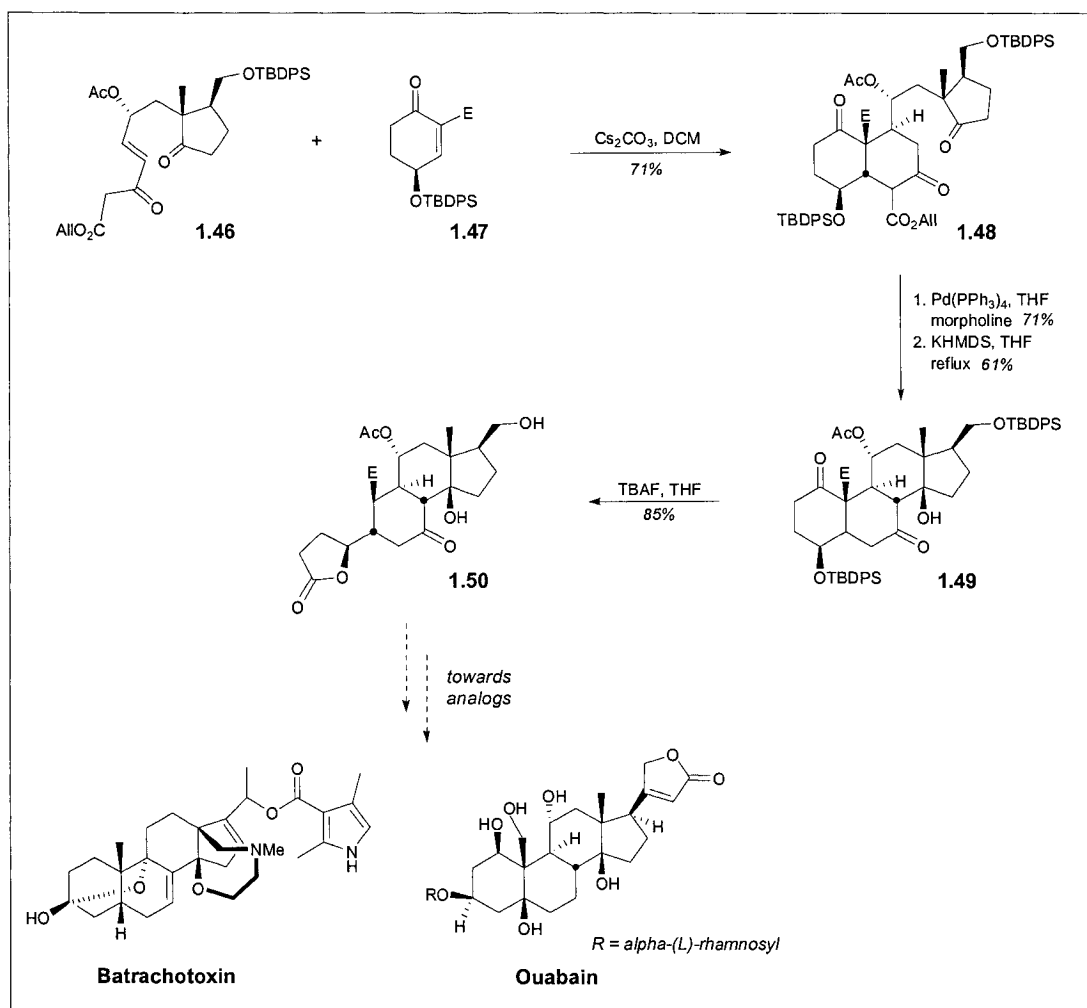


Scheme 1.9: First Synthesis of the A/B Ring Structure of Ouabain

Deslongchamps *et al.* devised an interesting asymmetric synthetic strategy for cardioactive steroids through anionic polycyclization.³² The sequence of reactions consisted of a double Michael addition/aldol condensation to give the desired compound **1.48** with high stereoselectivity (*Scheme 1.10*). Treatment of **1.46** with cyclohexenone **1.47** afforded tricycle **1.48** under basic conditions in 71% yield. Selective decarboxylation of the allyl ester, followed by exposure to KHMDS at reflux, generated **1.49** in 50% yield (over 2 steps). Diol **1.50** was obtained through deprotection of the silyl groups with TBAF in 85% yield. This intermediate was then used for the preparation of ouabain and batrachotoxin analogs.³³

³² Deslongchamps, P.; Yang, Z.; Shannon, D.; Truong, V.-L. *Org. Lett.* **2002**, *4*, 4693.

³³ Deslongchamps, P.; Trudeau, S. *J. Org. Chem.* **2004**, *69*, 832 and references therein.



Scheme 1.10: Deslongchamps' Synthesis of 14-β-Hydroxysteroids

1.4 Aim of the Current Project

The studies described herein focus on the development of novel tandem reactions aimed at the construction of complex polycyclic structures. Investigations were undertaken for the tandem oxy-Cope/Claisen/ene/Claisen and the oxy-Cope/Claisen/ene reactions in order to further evaluate the effect of substitution on the starting materials. Details of the development, as well as the study of the scope and limitations of the tandem oxy-Cope/Claisen/ene/hydroxy-directed Diels-Alder reaction are also described.

This particular methodology is expected to have a direct application in the synthesis of the B/C/D ring system of the steroid core structure (*Figure 1.6*).

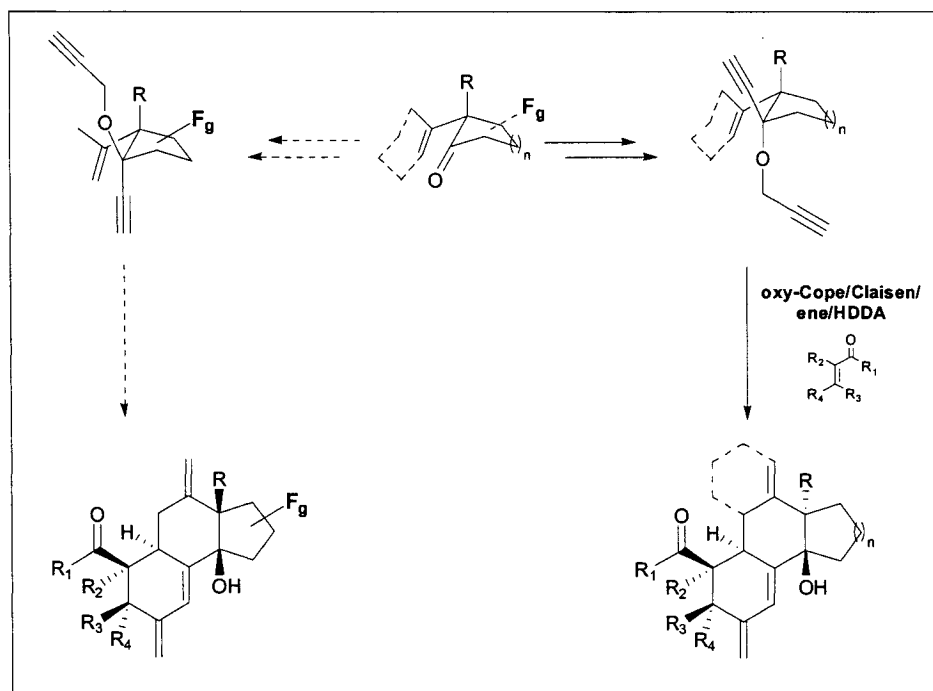


Figure 1.6: Anticipated Pathway for the Generation of the B/C/D Ring System of the Steroid Core Structure

Chapter 2: Studies Into the Tandem Oxy-Cope/Claisen/Ene/Claisen and Oxy-Cope/Claisen/Ene Reactions

2.1 Background

One of the primary interests in our group is the development of tandem reactions and their application to total synthesis. The first tandem reaction developed in our laboratory was the oxy-Cope/ene,³⁴ allowing the construction of bicyclic systems in one highly enantioselective and diastereoselective step. This methodology was directly applied to the synthesis of (+)-Arteannuin M (*Figure 2.1*).³⁵ The subsequent development of the tandem oxy-Cope/ene/Claisen reaction provided facile access to quaternary centers; this tandem sequence is currently been used in the total synthesis of Tetrodecamycin.³⁶ Finally, the recently reported oxy-Cope/Claisen/ene reaction,³⁷ which stereoselectively generates decalin skeletons bearing two contiguous quaternary centers, was exploited in the synthesis of a Wiedemannic acid analog.³⁸ Through the development of these cascade reactions, successive pericyclic rearrangements have proven to be a powerful method of generating complex skeletons in a stereoselective fashion from relatively simple substrates.

³⁴ Barriault, L.; Warrington, J. M.; Yap, G. P. A. *Org. Lett.* **2000**, 2, 663.

³⁵ Barriault, L.; Deon, D. H. *Org. Lett.* **2001**, 3, 1925.

³⁶ Barriault, L.; Warrington, J. M., *unpublished results*.

³⁷ (a) Gauvreau, D. Thesis. *Enantioselective Tandem Oxy-Cope/Ene Reaction*, University of Ottawa, 2003.

(b) Barriault, L.; Sauer, E. L. O. *J. Am. Chem. Soc.* **2004**, 126, 8569.

³⁸ Barriault, L.; Sauer, E. L. O. *Org. Lett.* **2004**, 6, 3329.

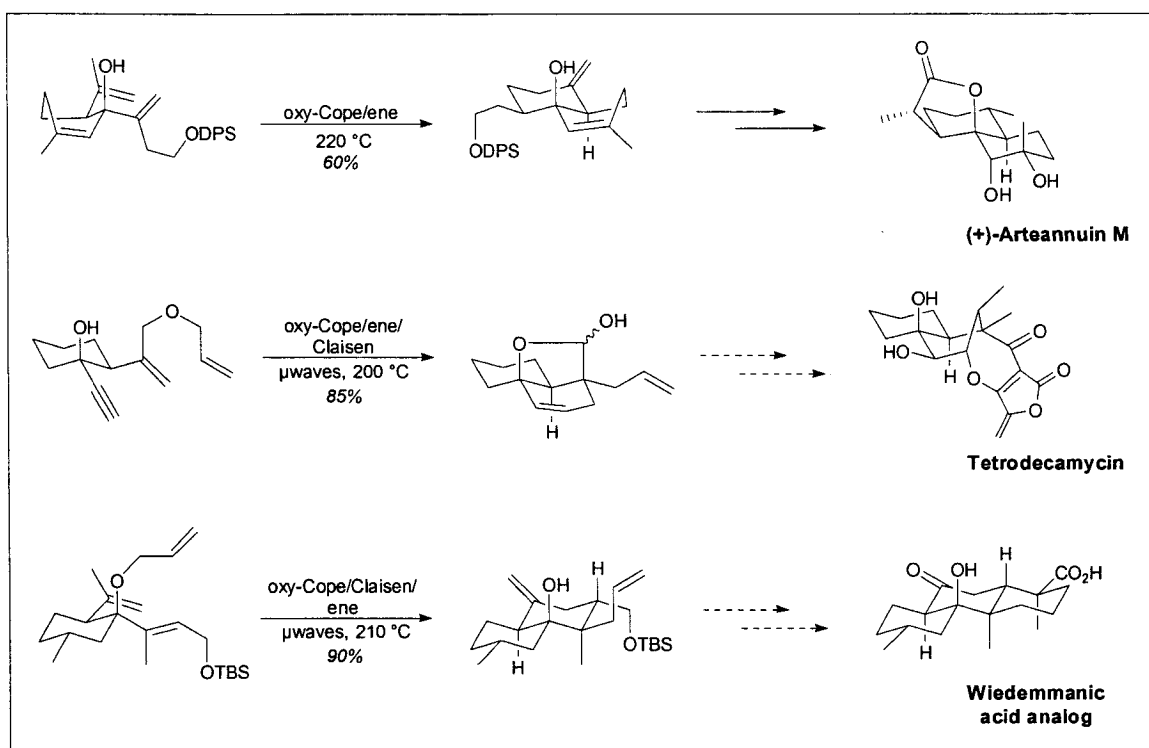
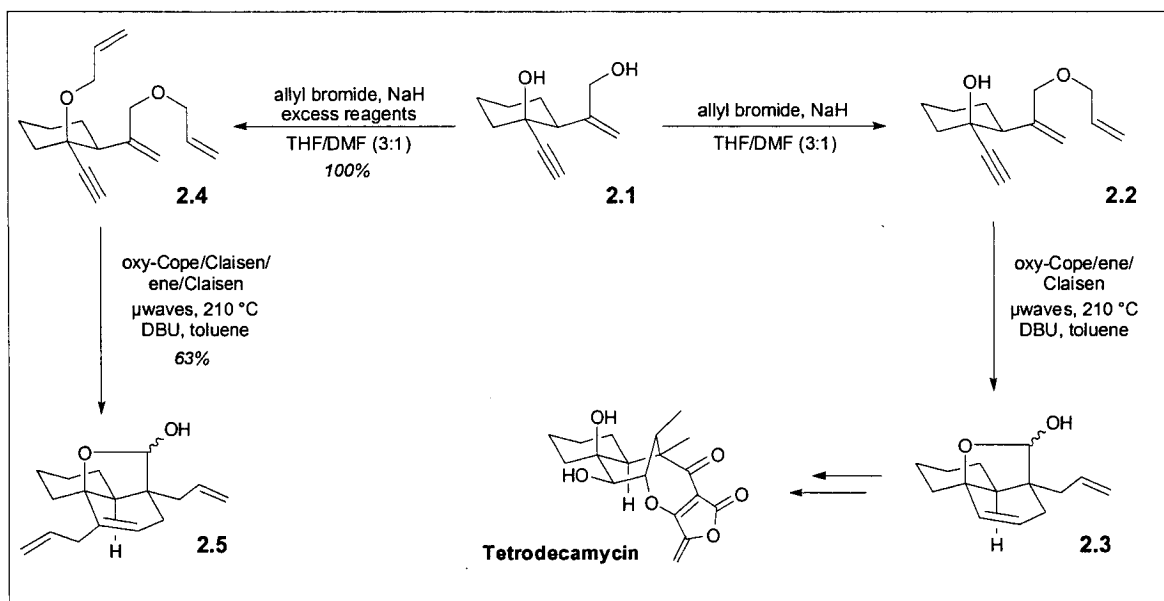


Figure 2.1: Application of the *Oxy-Cope/Ene*, the *Oxy-Cope/Ene/Claisen* and the *Oxy-Cope/Claisen/Ene* in the Total Syntheses of (+)-Arteannuin M, Tetrodecamycin and a Wiedemannic Acid Analog

While working on the total synthesis of Tetrodecamycin, a novel cascade of four pericyclic reactions was accidentally discovered. Usually, diol **2.1** was treated with allyl bromide and sodium hydride to afford the mono-allylated compound **2.2**, which underwent an *oxy-Cope/ene/Claisen* reaction to provide **2.3**, an intermediate to Tetrodecamycin (*Scheme 2.1*). When **2.1** was instead treated with a large excess of reagents, in an effort to accelerate the allylation step, bis-allylated **2.4** was obtained. Microwave irradiation of this compound (210 °C) led to **2.5**.



Scheme 2.1: Discovery of the Tandem Oxy-Cope/Claisen/Ene/Claisen Reaction

Based on the NMR data, it was assumed that **2.5** was a lactol. In fact, treatment of **2.5** with lithium aluminium hydride led to **2.6**, the crystallographic structure of which revealed the presence of an extra allyl group, as well as proved the relative stereochemistry of the compound (*Figure 2.2*). The established structure of **2.6** can easily be correlated to that of the corresponding lactol **2.5**.

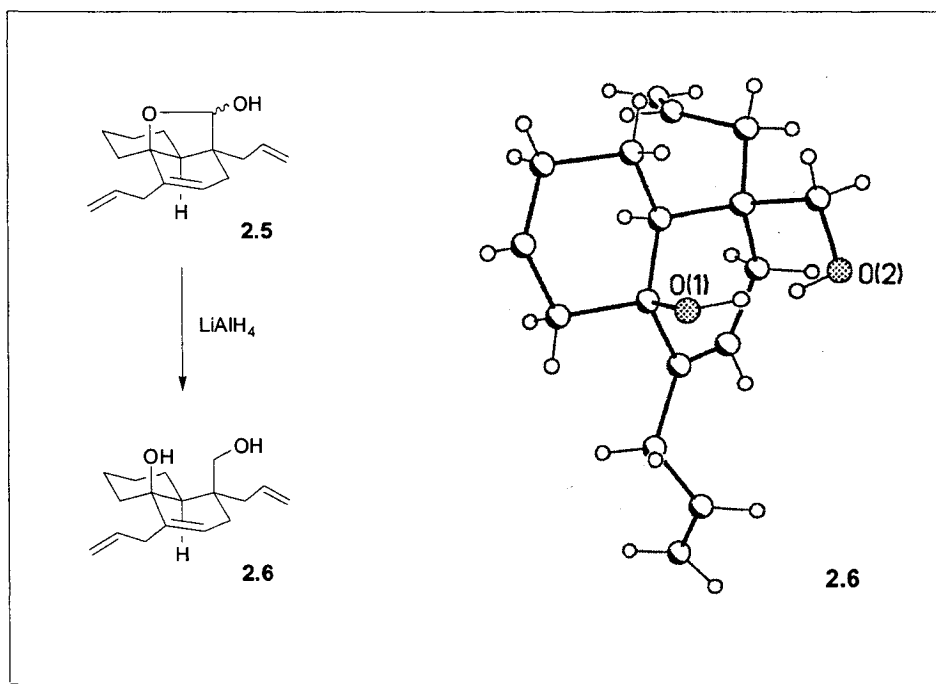


Figure 2.2: Crystallographic Structure of **2.6**

The formation of **2.5** can be explained by an oxy-Cope/Claisen/ene/Claisen reaction (*Figure 2.3*). The tandem sequence is triggered by an oxy-Cope rearrangement of **2.4** to give the highly-strained macrocycle **2.4A**. The latter is poised to rearrange *via* a Claisen [3,3]-shift to provide enone **2.4B**. Transannular ene reaction of **2.4B** gives enol ether **2.4C** and the presence of the allyl vinyl ether on **2.4C** allows for another Claisen rearrangement, leading to **2.4D**. The latter reacts to provide lactol **2.5** as an inseparable mixture of diastereoisomers. It becomes evident that this novel cascade of reactions can offer access to many types of complex molecules.

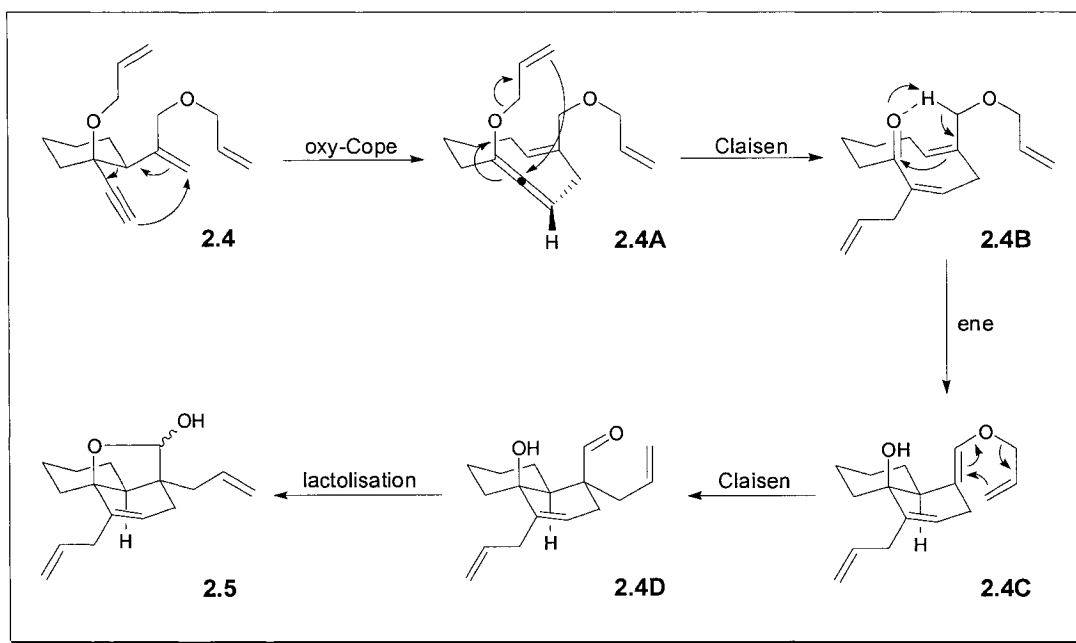


Figure 2.3: Proposed Mechanism for the Tandem Oxy-Cope/Claisen/Ene/Claisen Reaction

Initial investigations into this new tandem pericyclic sequence were undertaken by colleague D. Gauvreau.^{37a} His results, depicted in *Figure 2.4*, revealed that the replacement of the allyl moiety by a propargyl group decreased the chemical yield of the reaction (*Entry 1*). Additional functionalization of the substrates also led to low yields (*Entry 2*) or complex mixtures of inseparable products (*Entries 3-5*).

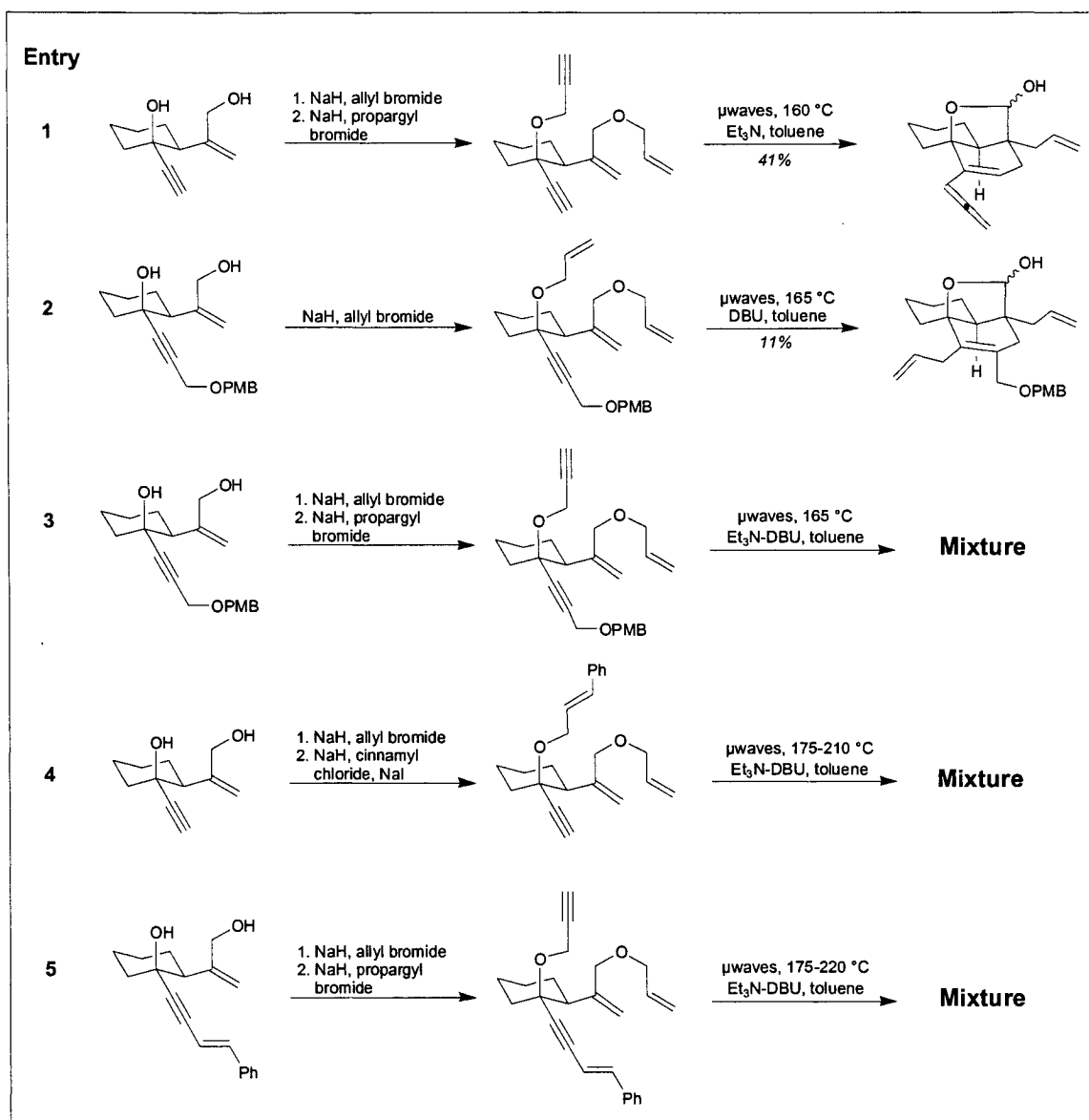


Figure 2.4: Study of the Tandem Oxy-Cope/Claisen/Ene/Claisen Reaction with Various Substrates

In order to further investigate the tandem oxy-Cope/Claisen/ene/Claisen and related oxy-Cope/Claisen/ene reactions, various substrates would need to be synthesized; related results are presented herein. It is to be noted that the variation of the allyl group on the primary alcohol had previously been investigated,³⁹ and thus was not explored. Another notable point is the fact that all cyclohexanol precursors bear the isopropenyl

³⁹ Barriault, L.; Denissova, I. *Org. Lett.* **2002**, 4, 1371.

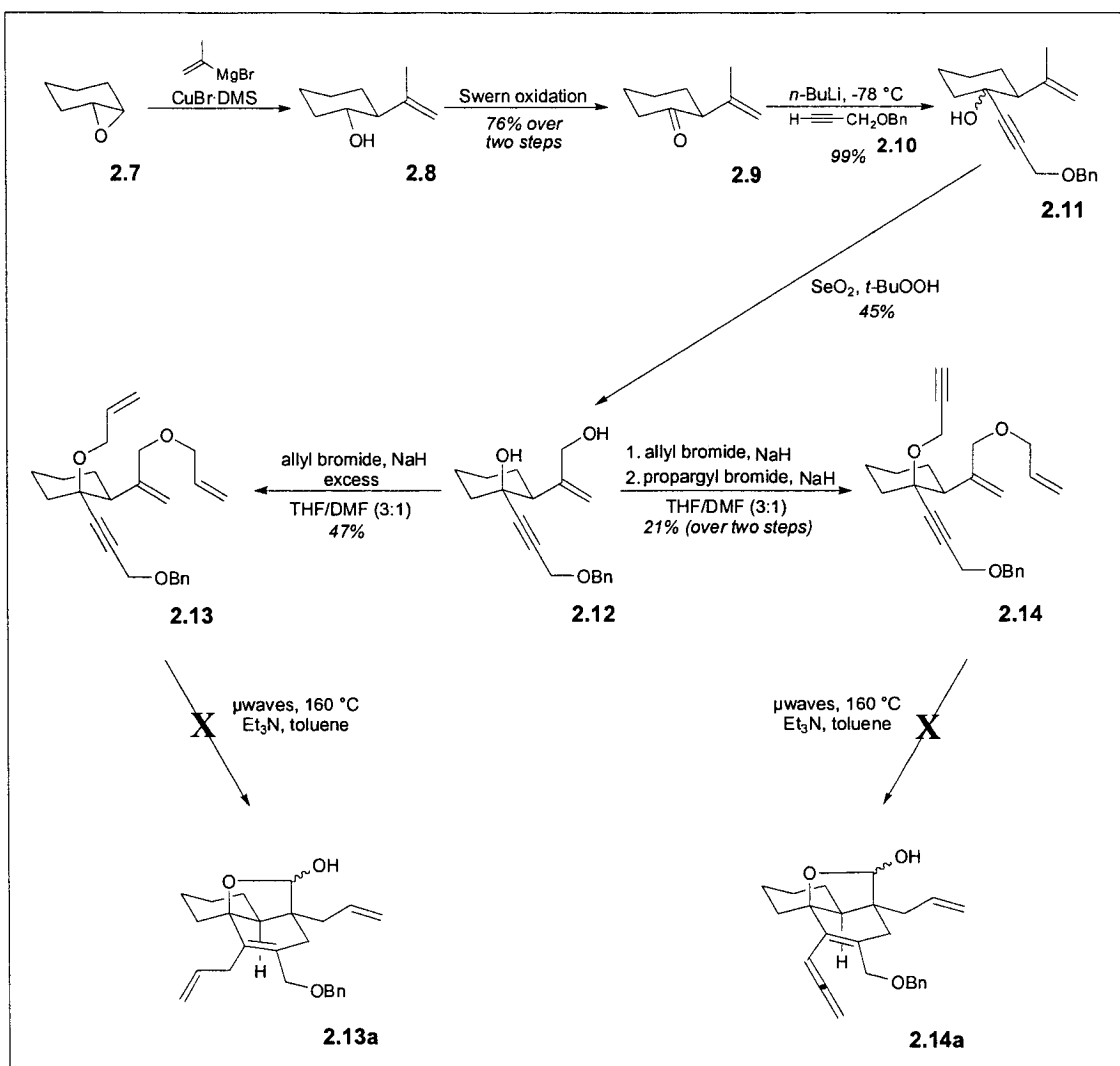
(cyclohexenyl) and ethynyl groups in an *anti* relationship, obtained as major diastereoisomers from addition of the ethynyl derivatives onto the parent ketone.

2.2 Preparation and Reaction of Benzyl Ether Derivatives

Allyl ethers **2.13** and **2.14** were prepared according to *Scheme 2.2*. Their synthesis began by the treatment of commercially available cyclohexene oxide **2.7** with isopropenylmagnesium bromide and copper bromide-dimethylsulfide to give the corresponding alcohol **2.8**, which was subsequently oxidized using the Swern procedure⁴⁰ to afford ketone **2.9** in 76% yield (over 2 steps). Deprotonation of benzylated propargyl alcohol **2.10** with *n*-BuLi at -78 °C, followed by the addition of ketone **2.9**, gave **2.11** as a mixture of two diastereoisomers (78:22) in 99% yield. Allylic oxidation of the mixture was effected with selenium dioxide and *t*-BuOOH to afford the desired diol **2.12** as the major diastereoisomer in 45% yield. The latter was treated with an excess of allyl bromide and sodium hydride to afford the bis-allylated compound **2.13** in 47 % yield. Alternatively, a sequential addition of allyl bromide and propargyl bromide to a solution of **2.12** in the presence of excess NaH provided propargyl ether **2.14** in 21% yield (over 2 steps). When **2.13** and **2.14** were heated with microwaves (160 °C) for 1 hour in the presence of triethylamine,⁴¹ they produced a complex mixture from which the desired products **2.13a** and **2.14a** were not isolated (*Scheme 2.2*).

⁴⁰ Swern, D.; Mancuso, A. J.; Huang, S.-L. *J. Org. Chem.* **1978**, *43*, 2480.

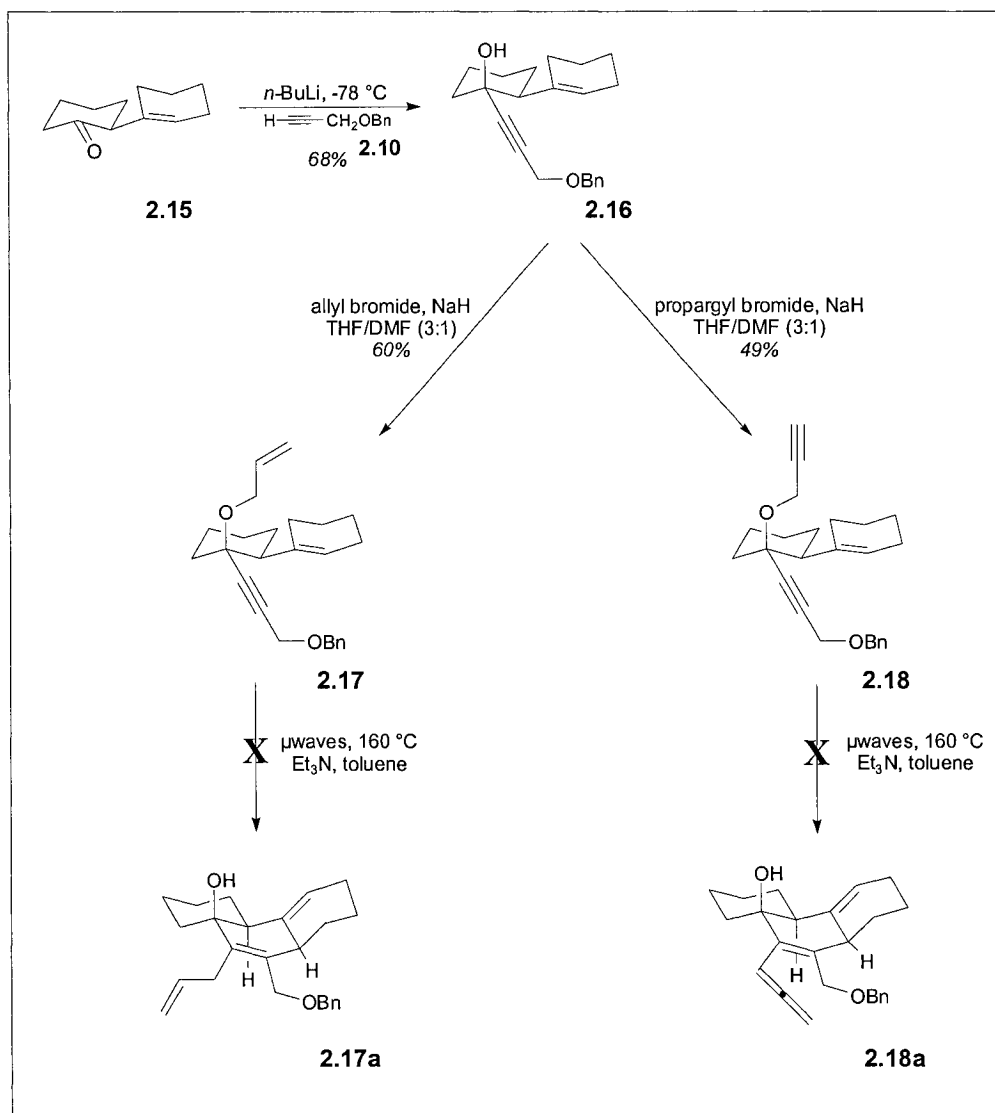
⁴¹ Grisé, C. *Stereoselective Formation of Quaternary Carbon Centers Using Macrocyclic Conformation*, University of Ottawa, 2004. For reviews on microwaves in organic synthesis, see: (a) Loupy, A.; Petit, A.; Hamelin, J.; Texier-Boullet, F.; Jacquault, P.; Mathé, D. *Synthesis* **1998**, *9*, 1213. (b) Majetich, G.; Hichs, R. J. *J. Microwave Power Electromagnetic Energy* **1995**, *30*, 27. (c) Loupy, A.; Perreux, L. *Tetrahedron* **2001**, *57*, 9199. (d) Lidström, P.; Tierny, J.; Wathey, B.; Westman, J. *Tetrahedron* **2001**, *57*, 9225.



Scheme 2.2: Preparation and Reaction of Benzyl Ether Derivatives **2.13** and **2.14**

In the hopes that the omission of the primary *O*-allyl moiety would allow the anticipated oxy-Cope/Claisen/ene reaction to occur, substrates **2.17** and **2.18** were synthesized from 2-(1-cyclohexenyl)-cyclohexanone (Scheme 2.3). Exposure of commercially available 2-(1-cyclohexenyl)-cyclohexanone **2.15** to lithiated alkyne **2.10** afforded **2.16** as the major diastereoisomer (77:33) in 68% yield. Subsequent allylation led to **2.17** in 49% yield, while alkylation with propargyl bromide gave **2.18** in 60% yield. Unfortunately, irradiation (160 °C) of **2.17** and **2.18** for 1 hour did not afford the

expected **2.17a** and **2.18a**; **2.17** led to degradation, while **2.18** gave a complex mixture of products from which **2.18a** was absent.



Scheme 2.3: Preparation and Reaction of Cyclohexenyl Derivatives **2.17** and **2.18**

The results summarized in *Schemes 2.2* and *2.3* indicate that the tandem oxy-Cope/Claisen/ene/Claisen and oxy-Cope/Claisen/ene reactions are not tolerant of additional substitution. Further investigations were thus abandoned.

2.3 Preparation and Reaction of 1,3-Enyne Derivatives

It was envisioned that **2.21** could undergo a tandem oxy-Cope/Claisen/ene reaction, generating intermediate **2.21a** (Figure 2.5). Probable electrocyclization, followed by aromatization could further afford **2.21b**, providing a rapid synthetic pathway to the generation of such complex polycyclic structures.

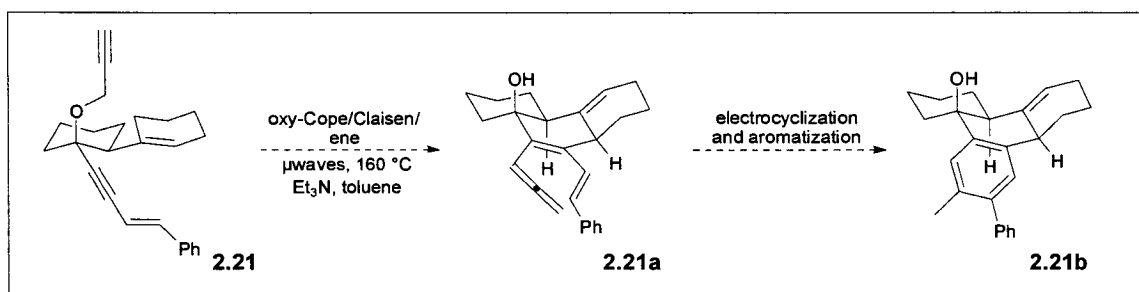
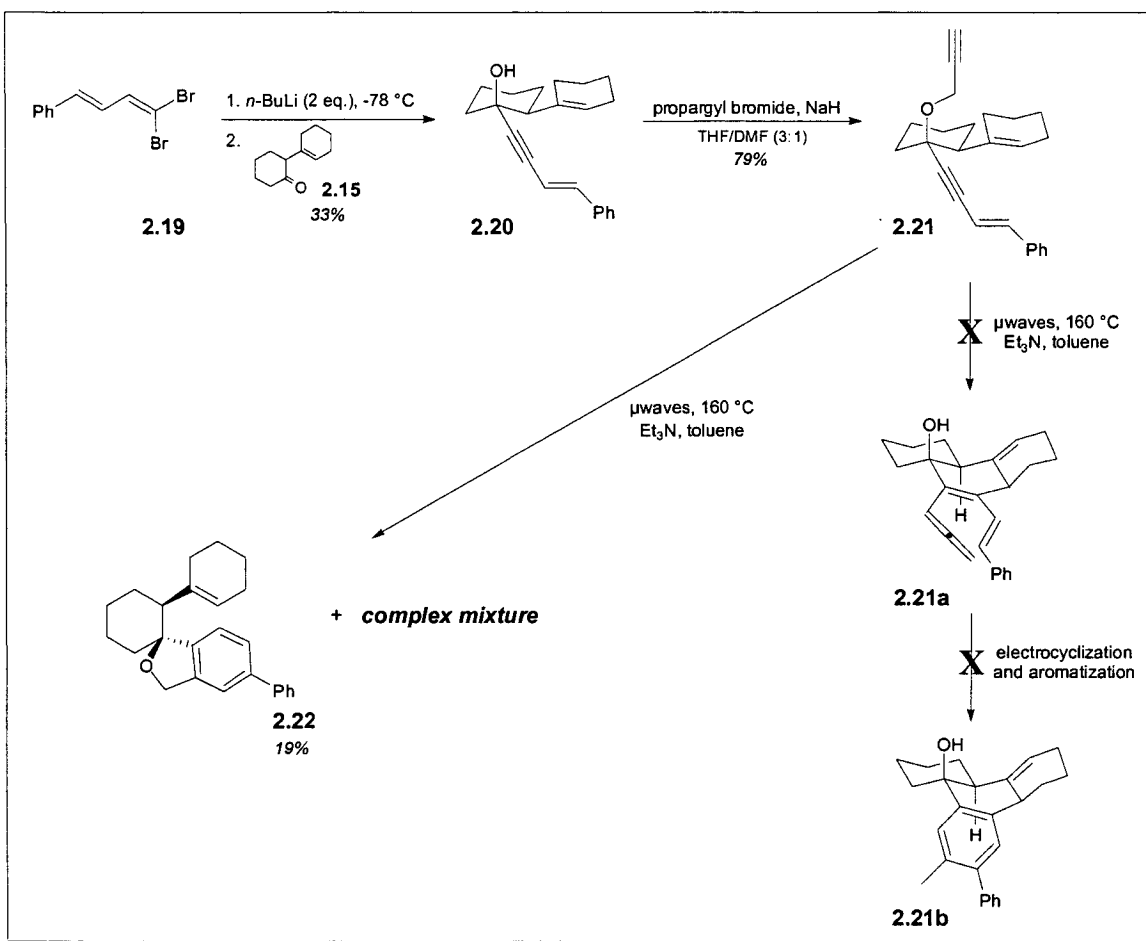


Figure 2.5: Anticipated Tandem Reaction of 1,3-Enyne 2.21

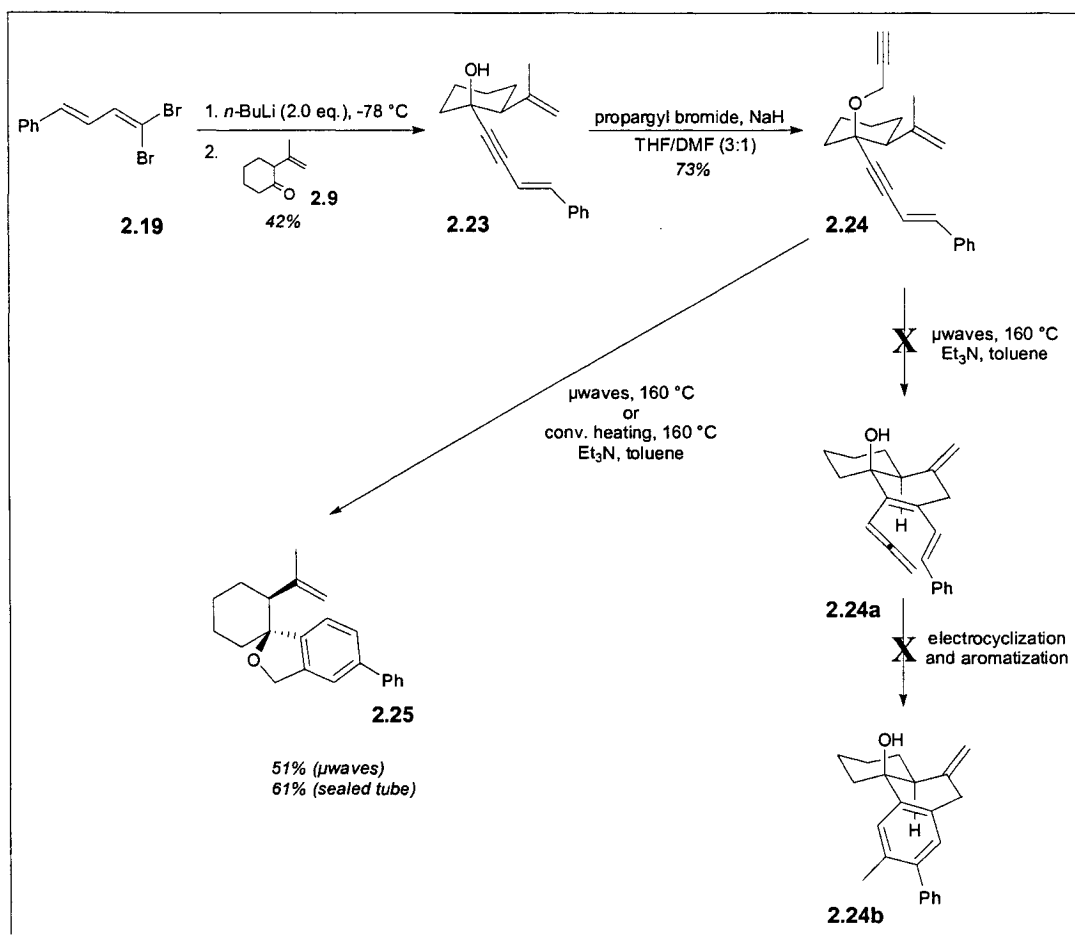
2.21 was prepared *via* the alkylation of 2-(1-cyclohexenyl)-cyclohexanone **2.15**. Dibromo **2.19**⁴² was treated with 2.0 equivalents of *n*-BuLi at -78 °C to generate the corresponding acetylenic anion and the latter was quenched with **2.15** to afford alcohol **2.20** as the major diastereoisomer (75:25) in 33% yield (Scheme 2.4). As previously described, **2.20** was converted to propargyl ether **2.21** in 79% yield. Microwave irradiation (160 °C) of **2.21** for 1 hour led to a mixture of products, however, neither **2.21a**, nor **2.21b**, were observed in the crude reaction mixture. The major product isolated (19%) corresponded to **2.22**.

⁴² Michel, P.; Gennet, D.; Rassat, A. *Tetrahedron Lett.* **1999**, 40, 8575.



Scheme 2.4: Preparation and Reaction of 1,3-Enyne **2.21**

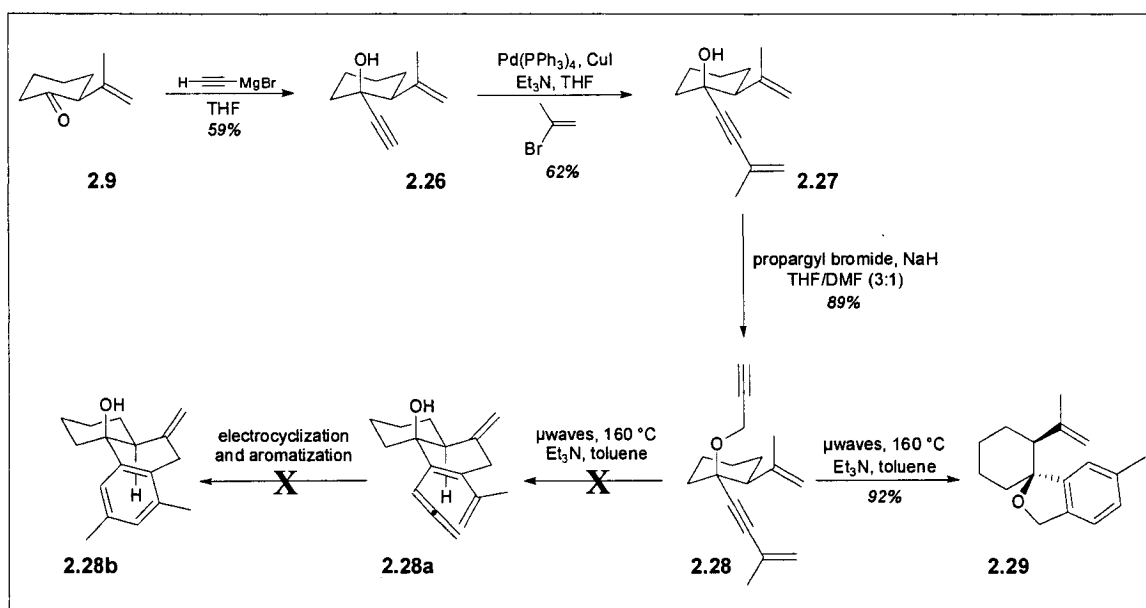
A second attempt at the oxy-Cope/Claisen/ene reaction was performed with **2.24**, the synthesis of which was analogous to that of **2.21** (*Scheme 2.5*). Irradiation (160 °C) of **2.24** for 1 hour led to the formation of **2.25** as the sole product in 51% yield. Alternatively, if the reaction was conducted by heating in a sealed tube immersed in a wax bath (160 °C) for 1 hour, **2.25** was isolated in 61% yield. In neither case was **2.24a** or **2.24b** observed in the reaction mixture.



Scheme 2.5: Preparation and Reaction of 1,3-Enyne 2.24

Finally, propargyl ether **2.28** was synthesized (Scheme 2.6). The treatment of ketone **2.9** with ethynylmagnesium bromide afforded the major diastereoisomer **2.26** (60:40) in 59% yield. Sonogashira coupling⁴³ with 2-bromopropene led to alcohol **2.27** (62% yield) and subsequent alkylation with propargyl bromide gave rise to propargyl ether **2.28** in 89% yield. Microwave irradiation (160 °C) for 1 hour afforded **2.29** exclusively in 92% yield. The fact that a considerably lower yield was obtained when a phenyl group was present seems to indicate that the aromatic system interferes with the course of the reaction.

⁴³ Sonogashira, K.; Tohda, T.; Hagihara, N. *Tetrahedron Lett.* **1975**, 50, 4467.



Scheme 2.6: Preparation and Reaction of 1,3-Enyne 2.28

At this point, literature research revealed that the rearrangement observed for conjugated enynes **2.21**, **2.24** and **2.28** had previously been reported.⁴⁴ As depicted in *Figure 2.6*, 1,3-enynes **2.30** undergo an intramolecular [4+2] cycloaddition to generate intermediates **2.31**, which thereon rearrange to aromatic products **2.32** through an intramolecular isomerization process. On account of these reports, additional studies were not pursued.

⁴⁴ (a) Danheiser, R. L.; Gould, A. E.; Fernández de la Pradilla, R.; Helgason, A. L. *J. Org. Chem.* **1994**, 59, 5514. (b) González, J. J.; Francesch, A.; Cárdenas, D. J.; Echavarren, A. M. *J. Org. Chem.* **1998**, 63, 2854. (c) Rodríguez, D.; Navarro-Vázquez, A.; Castedo, L.; Domínguez, D.; Saá, C. *J. Org. Chem.* **2003**, 68, 1938.

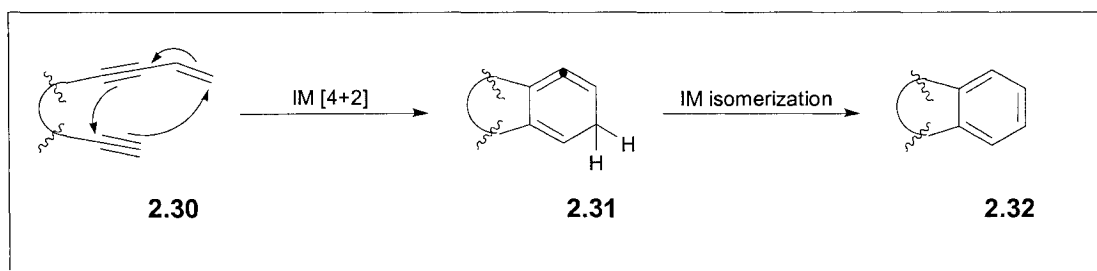


Figure 2.6: Intramolecular [4+2] Cycloaddition of 1,3-Enynes

2.4 Conclusion

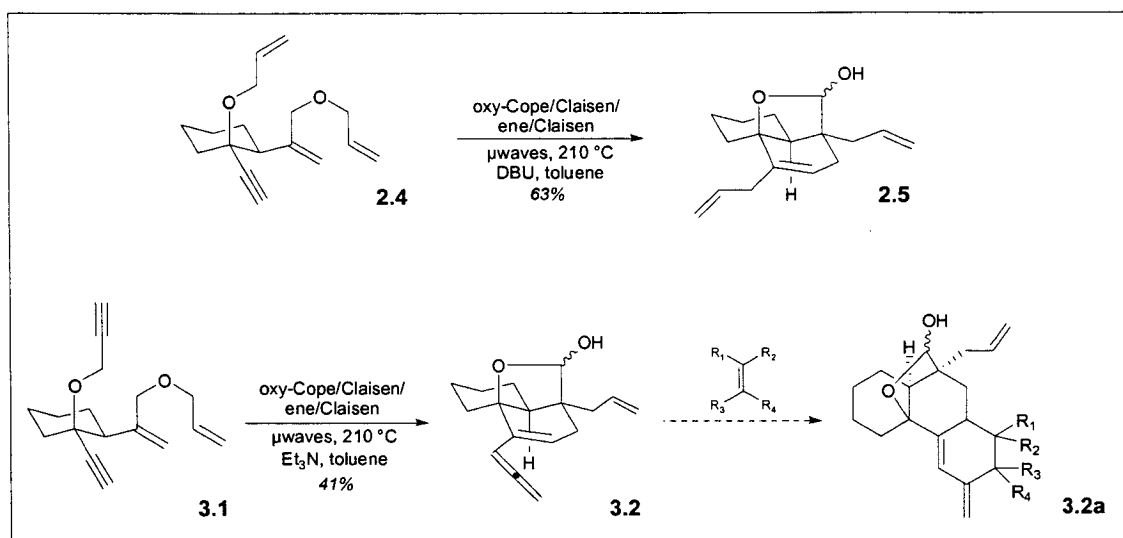
Initially, it was anticipated that the tandem oxy-Cope/Claisen/ene/Claisen and oxy-Cope/Claisen/ene reactions could provide functionalized tricyclic and tetracyclic compounds in a single synthetic step. Unfortunately, the results obtained in the present study indicate that the rearrangement is very sensitive to functionality. The presence of several double and triple bonds, along with aromatic rings on the substrates, seem to seriously hinder the rearrangement, inviting a plethora of side-reactions to occur in its place which translates into degradation and the isolation of complex mixtures.

Chapter 3: Studies Into the Tandem Oxy-Cope/Claisen/Ene/Hydroxy-Directed Diels-Alder Reaction

3.1 Background

As outlined in Chapter 2, the first oxy-Cope/Claisen/ene/Claisen reaction was observed for the conversion of bis-allylated **2.4** to lactol **2.5** (*Scheme 2.1, reproduced in Scheme 3.1*). Replacing the allyl moiety on the tertiary alcohol by a propargyl group led to the isolation of **3.2** in 41% yield. **3.2** possesses an allene function, which also constitutes an integral part of a diene, anticipated to undergo [4+2] cycloadditions in the presence of dienophiles to afford the corresponding adducts **3.2a** (*Scheme 3.1*). The goal of the present project was to add a Diels-Alder reaction to the cascade of pericyclic reactions, so as to generate diterpenes in one simple synthetic step. The methodology could eventually be applied to the generation of the B/C/D ring system of the steroid core and thus have a direct application in the synthesis of many biologically active compounds.⁴⁵

⁴⁵ Applezweig, N. *Steroid Drugs*, McGraw-Hill: New York, 1962.



Scheme 3.1: Tandem Oxy-Cope/Claisen/Ene/Claisen Reaction of **2.4** and **3.1**

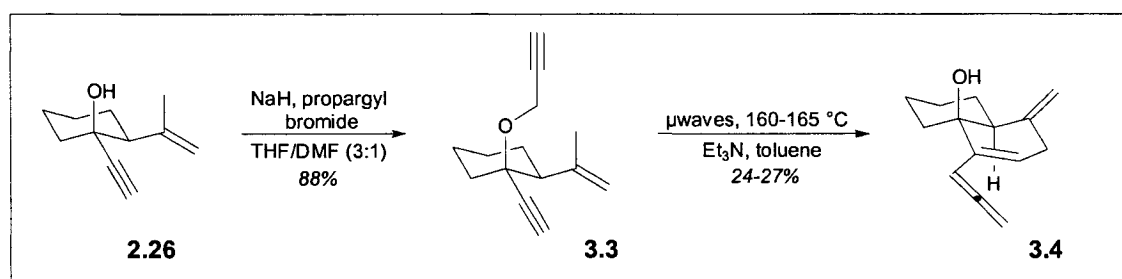
The use of vinyl allenes as dienes in Diels-Alder reactions has previously been reported.⁴⁶ Studies concluded that, in general, facial, as well as *endo/exo* selectivity, was mostly governed by steric interactions between the out-of-plane substituents of the vinyl allene and the incoming dienophile. Semi-empirical studies conducted on 1,2,4-pentatriene determined that the HOMO coefficients at the reacting sites of the vinyl allene were very similar in size.^{46c} However, the addition of substituents to the vinyl allene could no doubt modify the size of these coefficients and permit regioselectivity in the cycloaddition.^{46a}

3.2 Preparation and Reaction of 5- and 6-membered Propargyl Ethers

Since the rearrangement of **3.1** led to the generation of diastereomeric lactols **3.2**, propargyl ether **3.3** was synthesized as a simplified substrate for the study (*Scheme 3.2*).

⁴⁶ (a) Reich, H. J.; Eisenhart, E. K.; Whipple, W. L.; Kelly, M. J. *J. Am. Chem. Soc.* **1988**, *110*, 6432. (b) Spino, C.; Thibault, C.; Gingras, S. *J. Org. Chem.* **1998**, *63*, 5283. (c) Palenzuela, J. A.; Regás, D.; Afonso, M. M.; Rodríguez, M. L. *J. Org. Chem.* **2003**, *68*, 7845.

Alcohol **2.26** was converted to **3.3** by treatment with propargyl bromide and sodium hydride in THF/DMF (3:1). Microwave irradiation (160-165 °C) for 3 hours led to the isolation of the corresponding oxy-Cope/Claisen/ene product **3.4** in yields ranging between 24-27%.



Scheme 3.2: Preparation and Tandem Oxy-Cope/Claisen/Ene Reaction of Propargyl Ether **3.3**

As previously described, **3.3** undergoes an oxy-Cope rearrangement to afford macrocycle **3.3A**. The Claisen [3,3]-shift of **3.3A** generates enone **3.3B**, which rearranges to the bicyclic enol **3.4** by a transannular ene reaction (*Figure 3.1*).

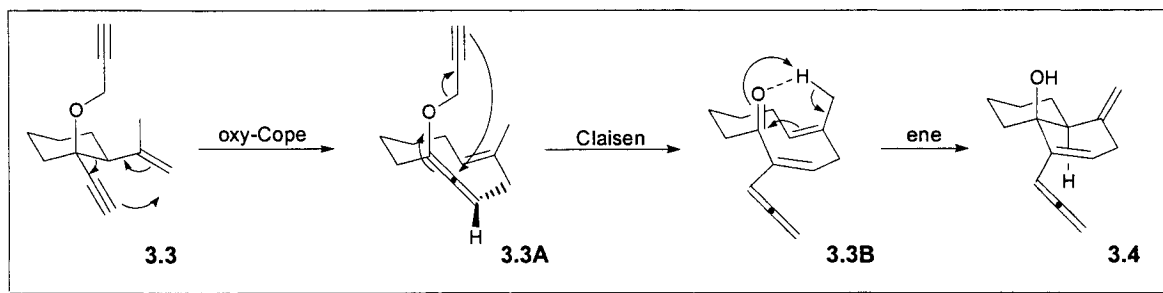
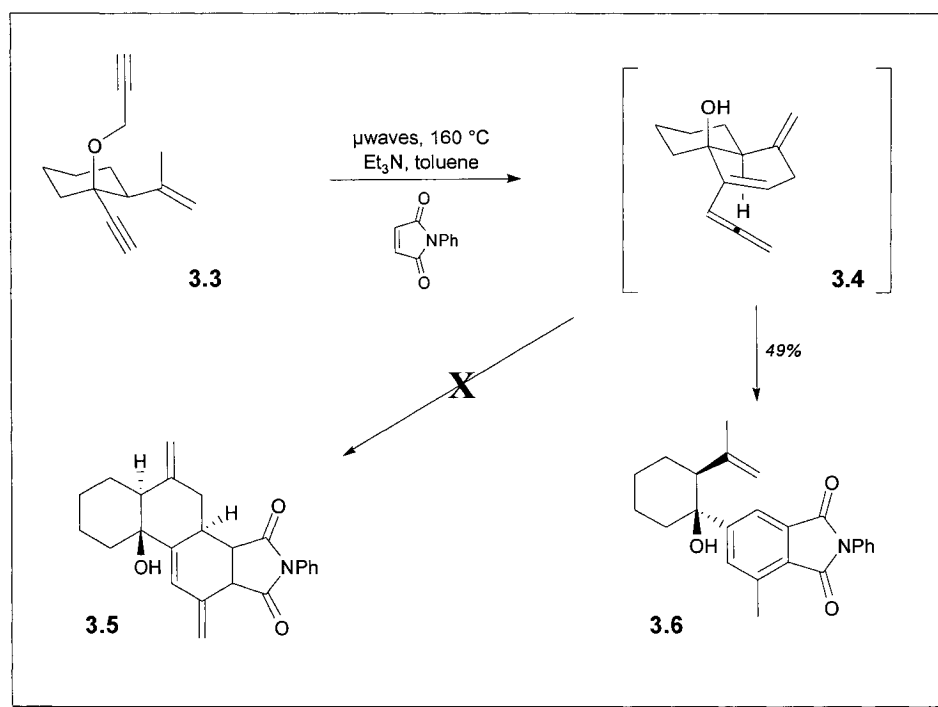


Figure 3.1: Proposed Mechanism for the Tandem Oxy-Cope/Claisen/Ene Reaction

The first attempt at a tandem oxy-Cope/Claisen/ene/Diels-Alder reaction was effected using N-phenylmaleimide as the dienophile. Propargyl ether **3.3**, N-phenylmaleimide and triethylamine were dissolved in dry toluene and the mixture was degassed with argon to be subsequently heated with microwaves (160 °C) for 2 hours and

20 minutes (*Scheme 3.3*). Unfortunately, the expected Diels-Alder adduct **3.5** was not observed in the crude reaction mixture. To our surprise, the aromatic compound **3.6** was isolated in its place in 49% yield. Repeating the reaction without triethylamine, or in a pressure tube heated with a wax bath also afforded **3.6** in similar yields.



Scheme 3.3: First Attempt at a Tandem Oxy-Cope/Claisen/Ene/Diels-Alder Reaction

The formation of **3.6** is suggested to occur through the mechanism illustrated in *Figure 3.2*. Propargyl ether **3.3** undergoes the oxy-Cope reaction, followed by the Claisen rearrangement to provide **3.3B**, at which point N-phenylmaleimide reacts with the substrate to generate **3.6i**. The latter undergoes a ring fragmentation to provide intermediate **3.6j**, which rapidly isomerizes to **3.6**. Since N-phenylmaleimide is a highly activated dienophile, the [4+2] cycloaddition occurs at a faster rate than the anticipated ene reaction.

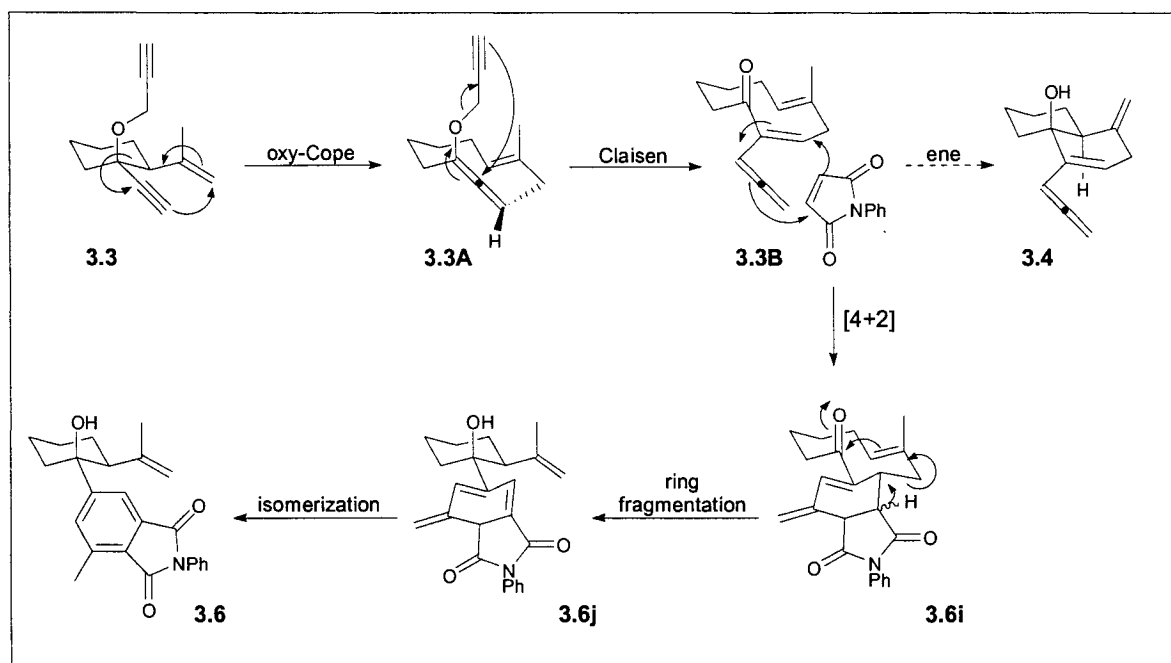
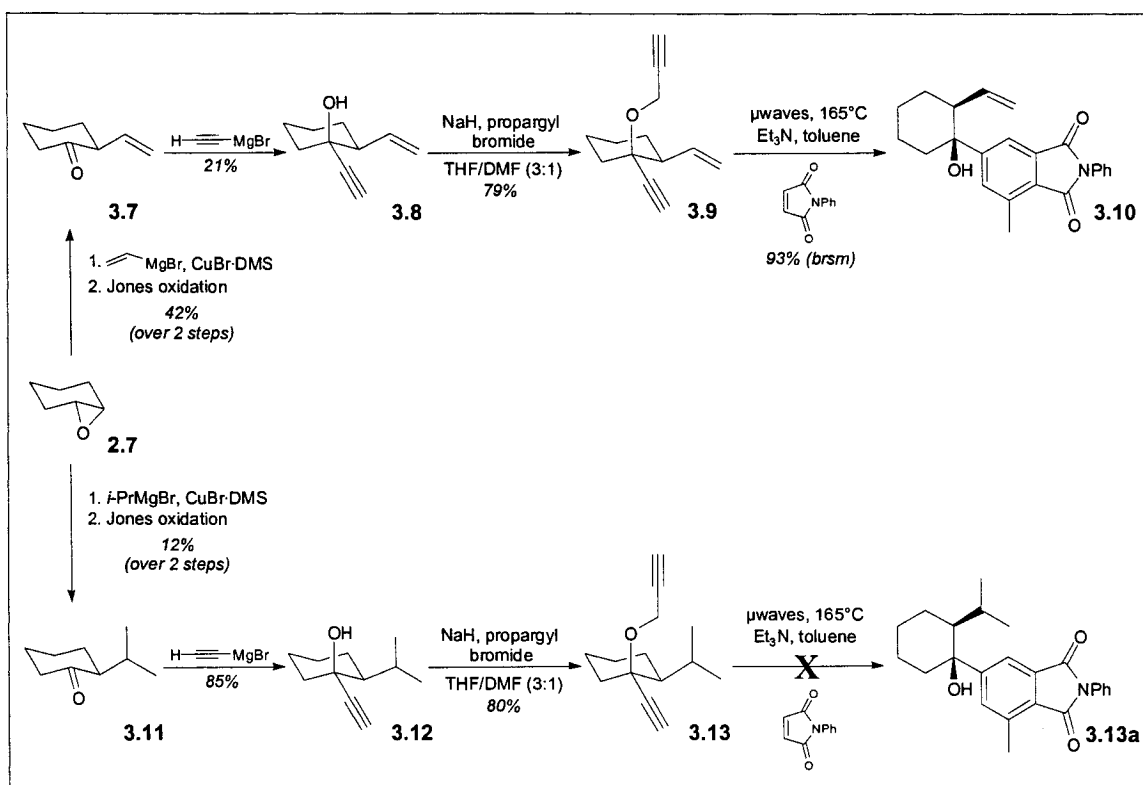


Figure 3.2: Proposed Mechanism for the Formation of 3.6

Compounds **3.9** and **3.13** were synthesized to further investigate the proposed mechanism (*Scheme 3.4*). Cyclohexene oxide **2.7** was treated with vinylmagnesium bromide and copper bromide-dimethylsulfide to give the corresponding alcohol, which was oxidized by the Jones procedure⁴⁷ to ketone **3.7** in 42% yield (over 2 steps). Exposure of **3.7** to ethynylmagnesium bromide afforded **3.8** as the major diastereoisomer (57:33) in 21% yield. Conversion of **3.8** to propargyl ether **3.9** was effected as previously described in 79% yield. **3.13** was synthesized analogously by the use of isopropylmagnesium bromide in the epoxide-opening step. If the proposed mechanism is faulty and an ene reaction does take place in the formation of **3.6**, compound **3.9** should not react, as it lacks the methyl group needed for the carbonyl-ene reaction. In the case of **3.13**, the results of irradiation would indicate whether or not the double bond of the isopropenyl group in **3.3** was involved in the generation of **3.6**. In fact, irradiation of **3.9**

⁴⁷ Jones, E. R. H.; Bowden, K.; Heilbron, I.M. *J. Chem. Soc.* **1946**, 39.

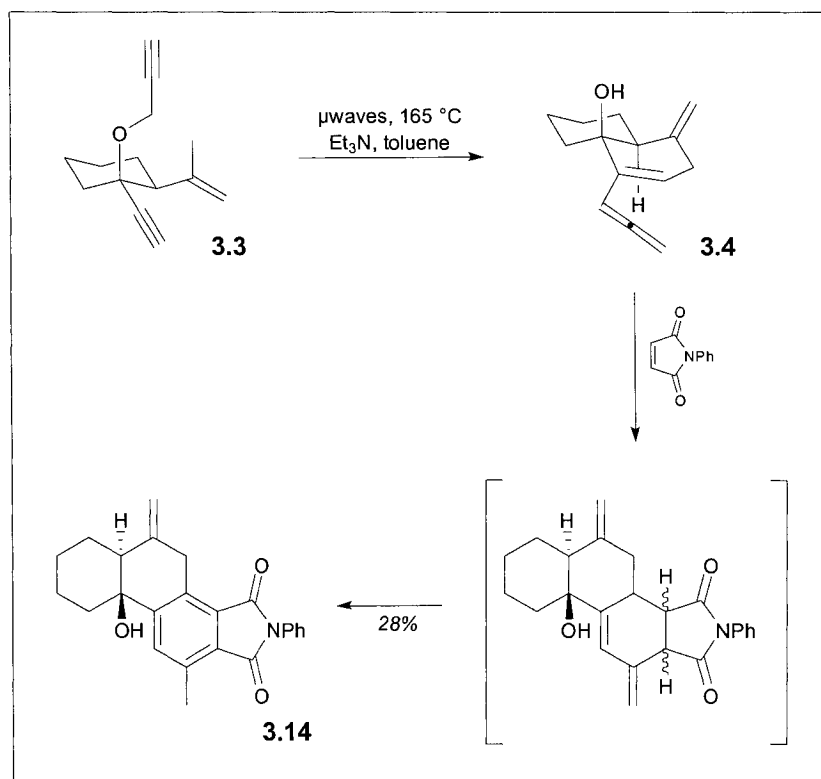
(165 °C) for 3 hours led to **3.10** in 93% yield (brsm), indicating that no ene reaction was occurring in the formation of **3.6**. Furthermore, irradiation of **3.13** (165 °C) for 4 hours led to the recovery of the starting material, attesting to the involvement of the double-bond of the isopropenyl moiety in the rearrangement of **3.3** to **3.6**. From these results, one can conclude that the reaction is triggered by an oxy-Cope and that the Diels-Alder reaction occurs once **3.3B** is formed.



Scheme 3.4: Investigation of the Mechanism for the Formation of **3.6**

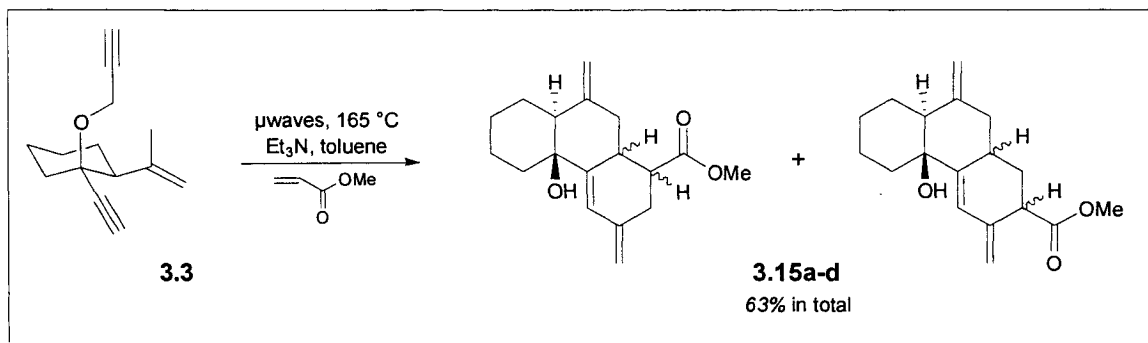
In order to obtain the desired Diels-Alder adduct, propargyl ether **3.3** was irradiated with microwaves (165 °C) for 4 hours in the absence of a dienophile in order to fully form the diene intermediate **3.4** (Scheme 3.5). N-Phenylmaleimide was subsequently added at room temperature and the solution was stirred overnight. Adduct **3.14** was isolated as the sole product in 28% yield. Although the aromatization of **3.14** is

not surprising, its mechanism is unclear. The presence of oxygen in the reaction mixture could possibly account for this result.



Scheme 3.5: First Tandem Oxy-Cope/Claisen/Ene/Diels-Alder Reaction with *N*-Phenylmaleimide

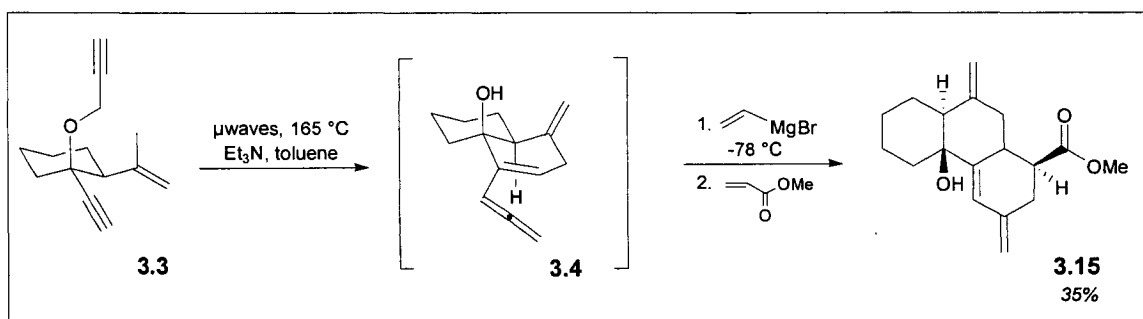
With this promising result in hand, we set out for a second attempt using methyl acrylate as the dienophile. Propargyl ether **3.3**, triethylamine and methyl acrylate were dissolved in dry toluene and the solution was degassed with argon to be subsequently irradiated with microwaves (165 °C) for 3 hours (*Scheme 3.6*). The corresponding oxy-Cope/Claisen/ene/Diels-Alder products **3.15a-d** were observed as a mixture of 4 diastereoisomers by NMR and isolated in a total yield of 63%. In this particular case, the tandem oxy-Cope/Claisen/ene reaction completes before the occurrence of the Diels-Alder reaction, owing to the lower reactivity of methyl acrylate as a dienophile.



Scheme 3.6: Tandem Oxy-Cope/Claisen/Ene/Diels-Alder Reaction with Methyl Acrylate

It becomes evident that for this methodology to be synthetically useful, however, only one diastereoisomer must be selectively obtained. It is thus at this point that the tandem oxy-Cope/Claisen/ene reaction meets the hydroxy-directed Diels-Alder (HDDA) reaction. Propargyl ether **3.3** was converted to **3.4** by microwave heating (165 °C). The solution was cooled to -78 °C and treated with 1.0 equivalent of vinylmagnesium bromide in order to generate the corresponding magnesium alkoxide *in situ* (Scheme 3.7). Following 20 minutes of stirring, 3.0 equivalents of methyl acrylate were added and the reaction was stirred at room temperature overnight. Much to our delight, a single Diels-Alder adduct, **3.15**, was isolated in 35% yield [dr > 25:1].⁴⁸ The relative stereochemistry of **3.15** was initially established based on results from the original HDDA research as well as NMR data, and was later confirmed by an X-ray crystallograph of a subsequent analog (see Figure 3.9).

⁴⁸ Diastereomeric ratios were determined by 300 and 500 MHz ¹H NMR of the crude reaction mixture.



Scheme 3.7: First Tandem Oxy-Cope/Claisen/Ene/HDDA Reaction with Methyl Acrylate

The two possible transition states for the hydroxy-directed Diels-Alder reaction are depicted in *Figure 3.3*. Following the generation of the magnesium alkoxide of **3.4**, the oxygen of the dienophile's carbonyl group complexes to the magnesium. As a result, the dienophile is effectively delivered *syn* to the tertiary alcohol of the diene, dictating the facial selectivity of the reaction. The *endo* approach of the dienophile can occur *via* **TS-3.15A** or **TS-3.15B**. The high regioselectivity of the HDDA reaction is rationalized through orbital interactions between the diene and dienophile and the exclusive formation of **3.15** indicates that **TS-3.15A** is kinetically favoured as a direct result of these interactions. Orbital effects aside, it is good to note that **TS-3.15A** could also consist of a lower-energy chelated form than **TS-3.15B**, due to a closer interaction between the metal, the oxygen and the carbonyl group.

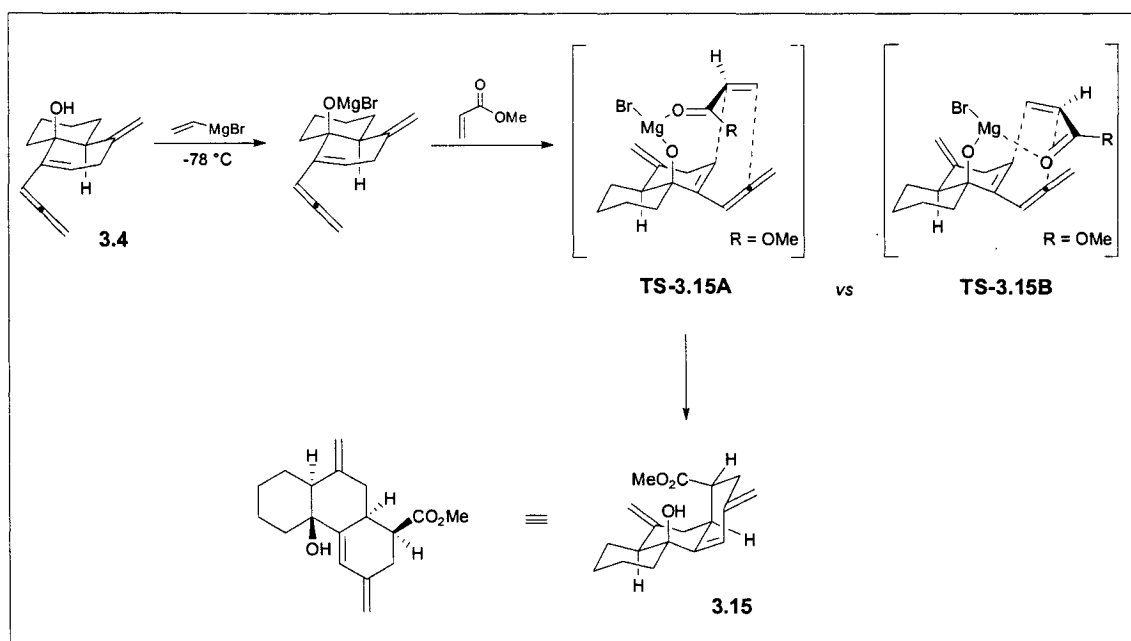


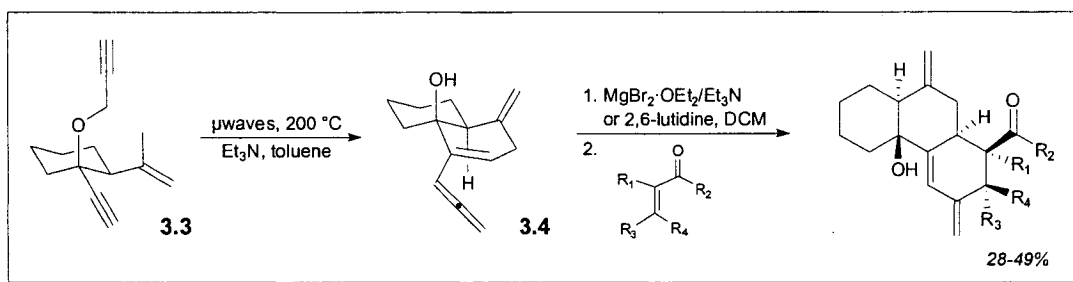
Figure 3.3: Transition States for the HDDA Reaction with Methyl Acrylate

Some problems arose with the use of organomagnesium reagents to generate the magnesium alkoxide. First, the degree of conversion from **3.3** to **3.4** could not be monitored with precision. Therefore, excess of Grignard reagent was often present in the solution and led to the formation of side-products. The addition of 0.8-0.9 equivalents of Grignard reagent, along with a large excess of dienophile greatly minimized these side-reactions. Secondly, in order to achieve reproducible yields, the organomagnesium reagent had to be prepared fresh, as previously reported by our group.¹⁶ It becomes evident that this requirement is rather inconvenient for the development of a methodology. Alternatively, one can use $\text{MgBr}_2 \cdot \text{OEt}_2$ in conjunction with a base (commonly triethylamine or 2,6-lutidine).⁴⁹ Unfortunately, the thermal reaction was conducted in toluene due to the high-temperature requirement and the $\text{MgBr}_2 \cdot \text{OEt}_2$ /base complex has a low solubility in non-polar solvents. In fact, when the reaction was

⁴⁹ Vedejs, E.; Daugulis, O. *J. Org. Chem.* **1996**, *61*, 5702.

conducted entirely in toluene, mixtures of diastereoisomers were obtained, suggesting that the poor solubility of the $\text{MgBr}_2 \cdot \text{OEt}_2$ /base complex prevented complete complexation of the tertiary alcohol. The use of 1,2-dichloroethane, as well as a toluene/ether solvent system, was investigated, but polymerization was obtained in the first case, and mixtures of diastereoisomers in the latter one. It was possible to conduct the reaction in a solvent system consisting of toluene and dichloromethane, but the reaction time was considerably longer (4 days) and a trace of a second diastereoisomer could be observed. Rather, it became customary to concentrate the solution in *vacuo* after the thermal reaction⁵⁰ and re-dissolve the crude **3.4** in dry dichloromethane to undergo the HDDA reaction. $\text{MgBr}_2 \cdot \text{OEt}_2$ and either triethylamine or 2,6-lutidine were stirred in dry dichloromethane for 20 minutes (a change of colour from beige to white or pink was noticed). The DCM solution of **3.4** was then cannulated into the $\text{MgBr}_2 \cdot \text{OEt}_2$ /base solution and the mixture was stirred for 2 hours, after which time the dienophile was added to afford the desired adducts in 28-49% yields (*Scheme 3.8*). The time for which the diene and the magnesium complex were stirred proved to be crucial, as insufficient stirring times led to the isolation of mixtures of diastereoisomers, a fact which is attributed to the complexation of a more sterically hindered tertiary alcohol to the magnesium.

⁵⁰ From this point, conversion of **3.3** to **3.4** was effected by microwave irradiation (200 °C) for 2 hours.

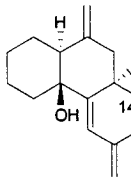
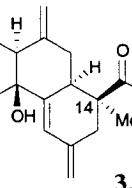
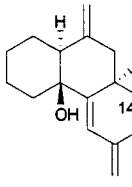
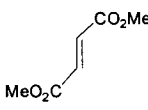
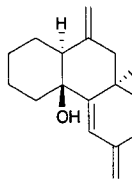
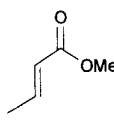
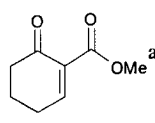
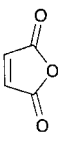
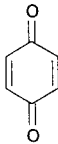


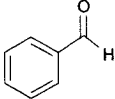
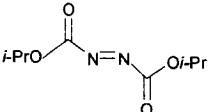
Scheme 3.8: Method for the Tandem Oxy-Cope/Claisen/Ene/HDDA Reaction

Using the newly developed conditions, the tandem oxy-Cope/Claisen/ene/HDDA reaction of propargyl ether **3.3** was studied with various dienophiles. Results are disclosed in *Table 3.1*.

Table 3.1: Results of the Tandem Oxy-Cope/Claisen/Ene/HDDA Reaction with Propargyl Ether 3.3

Entry	Dienophile	Product	Yield (%) [dr]
1			28 [> 25:1]
2			35 [> 25:1]
3			41 [> 25:1]
4			49 [> 25:1]

5		 3.18a  3.18b	30 [3:2 – 2:1]
6		 3.19 + C-14 epimer	39 [10:1 – 5:1]
7		 3.20	34 [> 25:1]
8		Failed	—
9		Failed	—
10		Failed	—
11		Failed	—
12		Failed	—

13		Failed	—
14	$\text{H}-\text{C}\equiv\text{C}-\text{CO}_2\text{Et}$	Failed	—
15		Failed	—

^a For synthesis, see: Liotta, D.; Barnum, C.; Puleo, R.; Zima, G.; Bayer, C.; Kezar, H. S. *J. Org. Chem.* **1981**, *46*, 2920.

As previously reported, the use of N-phenylmaleimide and methyl acrylate as dienophiles led to the corresponding products in yields of 28% and 35% respectively (*Table 3.1, Entries 1-2*). Similarly, methyl methacrylate and methyl vinyl ketone afforded **3.16** and **3.17** in respective yields of 41% and 49% (*Table 3.1, Entries 3-4*). The use of methacrolein as the dienophile led to the isolation of two distinct diastereoisomers, **3.18a** and **3.18b** in 30% overall yield (*Table 3.1, Entry 5*). The structures of these products were elucidated through 2-D NMR experiments.

3.18b corresponded to the expected product, with the aldehyde group *syn* to the hydroxyl (*Figure 3.4*).⁵¹ H_1/H_2 have a strong coupling with H_3 only (perpendicular to the *pi*-system of the double-bond; allylic coupling) [**A**]. The NOESY spectrum reveals correlations between H_4 and the methyl group, as well as between H_5 and the methyl group [**B**]. NOESY correlations are also displayed between H_3 and H_6 [**C**] (H_6 was

⁵¹ All 2-D NMR experiments were done on an Avance 300/500 MHz, in deuterated chloroform or acetone.

identified through allylic coupling with H₈/H₉) and between H₅ and H₁₀ [**D**]. Finally, a W-coupling is observed between H₃ and the methyl group in the COSY spectrum [**E**]. In order for this W-coupling to be present, the methyl group has to be *anti* to the alcohol.

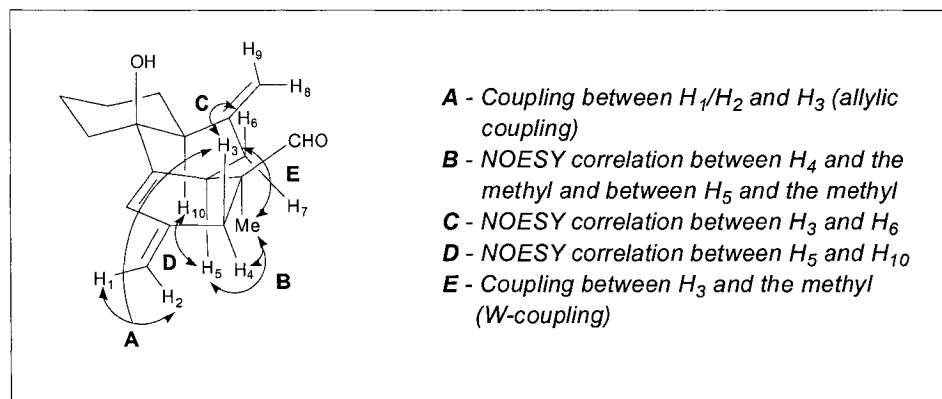


Figure 3.4: Structure Elucidation of **3.18b** by 2-D NMR Experiments

3.18a consisted of the C-14 stereoisomer of **3.18b**, bearing the aldehyde group *anti* to the hydroxyl (Figure 3.5). H₁ and H₂ are coupled with H₃ and H₄ [**A**], while the NOESY spectrum reveals a correlation between H₅ and H₆, thus indicating that they must be on the same side of the molecule [**B**]. This only leaves the stereochemistry of the C-14 carbon to be assigned. Since **3.18b** had the aldehyde *syn* to the hydroxyl group, by default, **3.18a** must bear the aldehyde group *anti* to the alcohol.

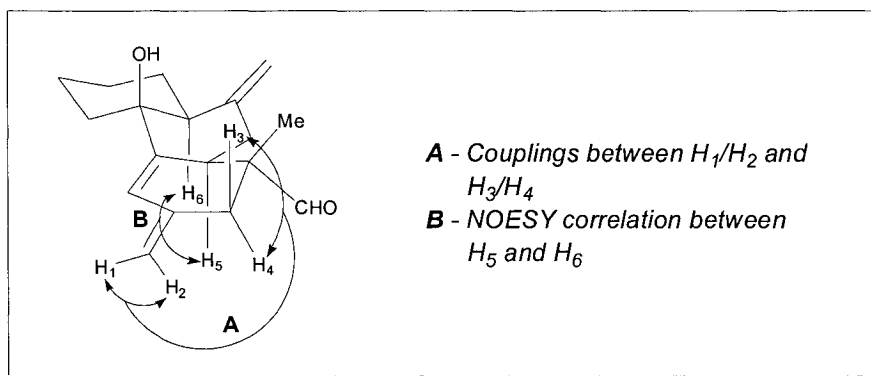


Figure 3.5: Structure Elucidation of **3.18a** by 2-D NMR Experiments

The diastereomeric ratio of **3.18a** and **3.18b** was variable between experiments, ranging from 3:2 to 2:1 with $\text{MgBr}_2 \cdot \text{OEt}_2 / \text{Et}_3\text{N}$ as the complexing agent. Repetition of the experiment with fresh vinylmagnesium bromide led to a ratio of 2:1. This peculiar result could not be explained and was determined as anomalous.

The use of acrolein as the dienophile also led to the formation of two diastereoisomers in 39% overall yield (*Table 3.1, Entry 6*), the diastereomeric ratio of which varied with reaction time.⁵² Suspecting that epimerization might be occurring, the major epimer **3.19** was stirred overnight in the presence of $\text{MgBr}_2 \cdot \text{OEt}_2$ and 2,6-lutidine. A drastic change in the diastereomeric ratio was observed (from 8.4:1 to 1:2.8) (*Figure 3.6*), clearly indicating that **3.19** undergoes epimerization at the C-14 center under the reaction conditions.

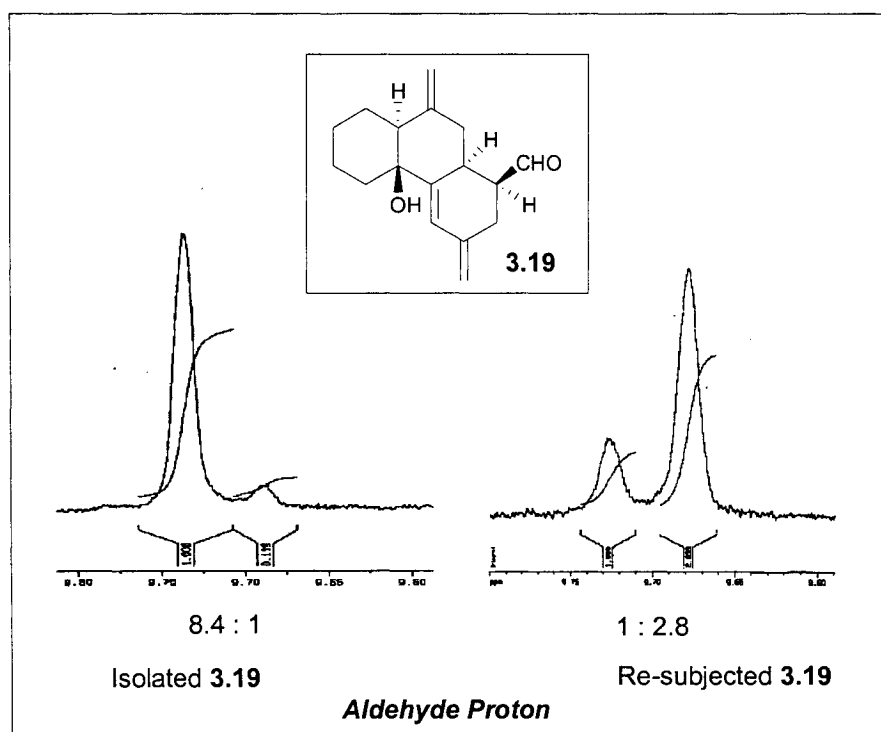


Figure 3.6: Experimental Evidence for the Epimerization of **3.19**

⁵² Ratio measured from the aldehyde protons in ^1H NMR.

Cycloadduct **3.20**, resulting from the tandem oxy-Cope/Claisen/ene/HDDA reaction of **3.3** with dimethyl fumarate (34% yield), possesses the ester group at C-14 *anti* to the hydroxyl group (*Table 3.1, Entry 7*). Structure elucidation of **3.20** was established on the triol **3.20b**, readily obtained from the reduction of the ester group of **3.20** with LAH (*Figure 3.7*). The NOESY spectrum indicates the following correlations: H₅ with H₆ [**A**], H₅ with CH₂^Y [**B**], H₃ with CH₂^Y [**C**], H₃ with H₄ [**D**]. The only way these correlations are possible is if the molecule has the structure depicted in *Figure 3.7*.

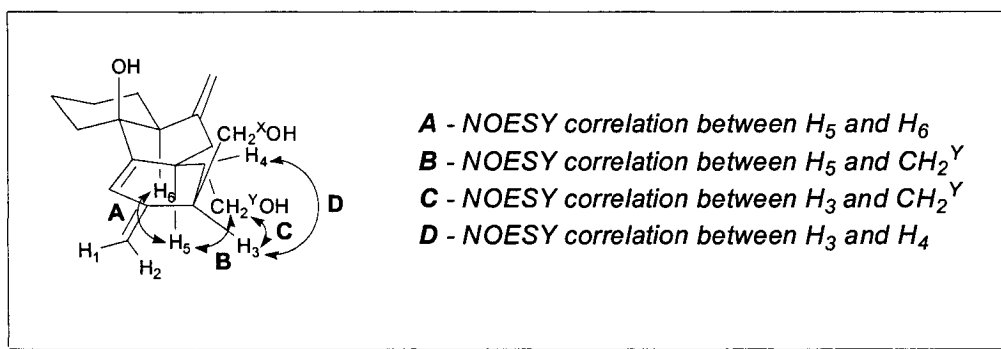


Figure 3.7: Structure Elucidation of **3.20/3.20b** by 2-D NMR Experiments

Dimethyl fumarate represents the only symmetrical dienophile within the successful entries of *Table 3.1*. The coefficients on both reacting sites are consequently equal. Furthermore, either of the two ester groups may complex to the magnesium, leading to an 8-membered tether in **TS-3.20A** or a 9-membered tether in **TS-3.20B** (*Figure 3.8*). According to the product obtained, **TS-3.20B** must be preferred, perhaps due to greater orbital overlap. The result observed in this specific case seems to contradict a transition state favoured solely on the basis of a lower-energy chelated form.

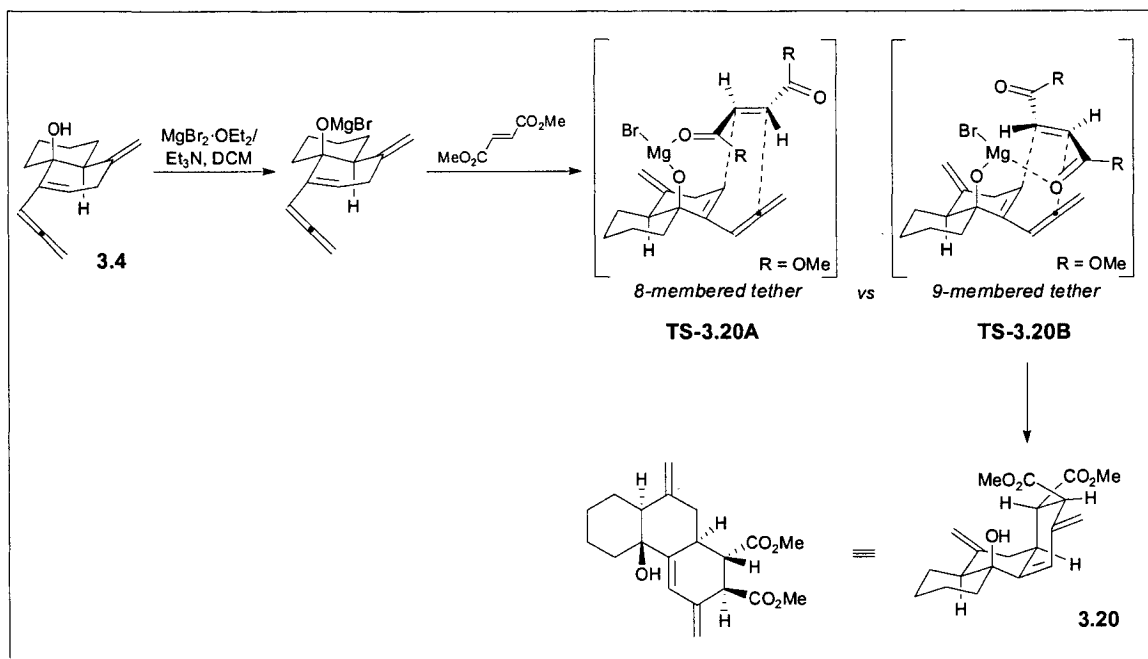
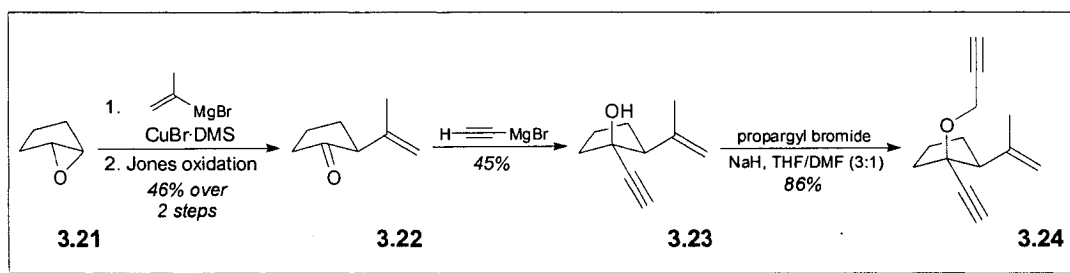


Figure 3.8: Transition States for the HDDA Reaction with Dimethyl Fumarate

The dienophiles studied in *Entries 8 to 15* (Table 3.1), including one bearing a triple-bond (*Entry 14*) and some hetero-dienophiles (*Entries 13 and 15*), did not react with the diene intermediate **3.4**; recovery of starting material along with degradation was observed in all cases.

Propargyl ether **3.24** was synthesized as the second substrate for the development of the tandem oxy-Cope/Claisen/ene/HDDA reaction. The chemical steps described for the synthesis of **3.3** were applied to commercially available cyclopentene oxide **3.21** to afford propargyl ether **3.24** (Scheme 3.9).

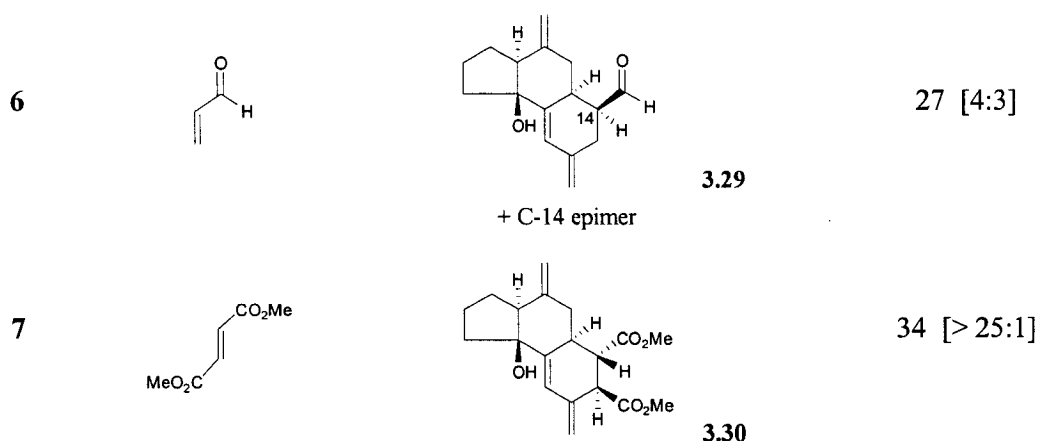


Scheme 3.9: Preparation of Propargyl Ether 3.24

The oxy-Cope/Claisen/ene/HDDA methodology developed with propargyl ether 3.3 was repeated with 3.24. The results are displayed in *Table 3.2*.

Table 3.2: Results of the Tandem Oxy-Cope/Claisen/Ene/HDDA Reaction with Propargyl Ether 3.24

Entry	Dienophile	Product	Yield (%) [dr]
1		 suggested structure (unstable)	unstable [> 25:1]
2		 3.25	47 [> 25:1]
3		 3.26	32 [> 25:1]
4		 3.27	39 [> 25:1]
5		 3.28	24 [> 25:1]



The use of N-phenylmaleimide as the dienophile led to the isolation of an unstable product whose NMR data matched the expected cycloadduct (*Table 3.2, Entry 1*). Attempts to aromatize the compound, and therefore generate a more stable product, were made using DDQ or oxygen but proved futile. Methyl acrylate, methyl methacrylate and methyl vinyl ketone as dienophiles led to the corresponding products **3.25**, **3.26** and **3.27** in 47%, 32% and 39% yields respectively (*Table 3.2, Entries 2-4*). X-ray analysis of crystalline **3.26** confirmed its structure (*Figure 3.9*), while reinforcing that of **3.15** (*Scheme 3.7*).

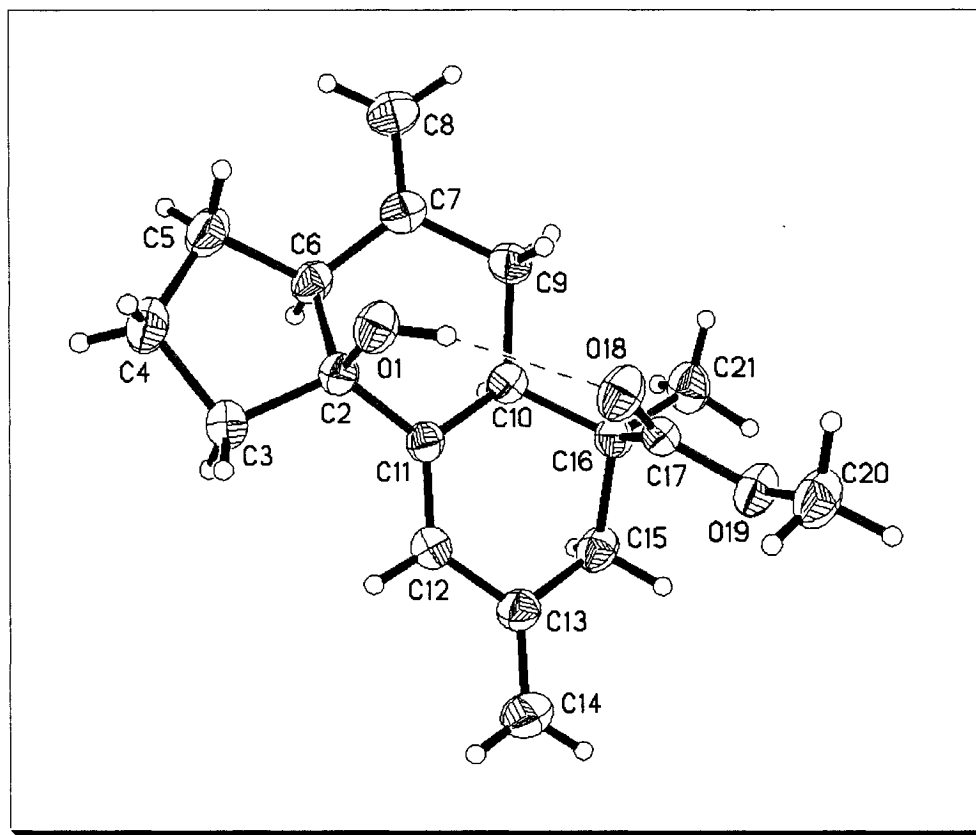


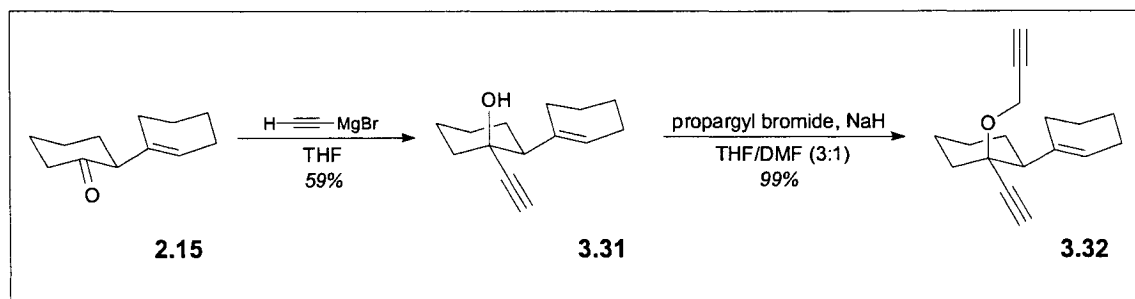
Figure 3.9: Single Crystal Structure of **3.26**

The use of methacrolein as the dienophile with propargyl ether **3.24** led to a single diastereoisomer, **3.28**, in 24% yield (*Table 3.2, Entry 5*). Conversely, propargyl ether **3.3** had led to a mixture of stereoisomers (*Table 3.1, Entry 5*). The adduct of acrolein, **3.29**, was isolated in 27% yield; again, epimerization at the C-14 center was observed (*Table 3.2, Entry 6*). Finally, dimethyl fumarate led to a single adduct, **3.30**, in 34% yield (*Table 3.2, Entry 7*).

3.3 Preparation and Reaction of Cyclohexenyl and C-2 Methyl Analogs

Treatment of 2-(1-cyclohexenyl)-cyclohexanone **2.15** with ethynylmagnesium bromide led to **3.31** as the major diastereoisomer (60:40) in 59% yield (*Scheme 3.10*).

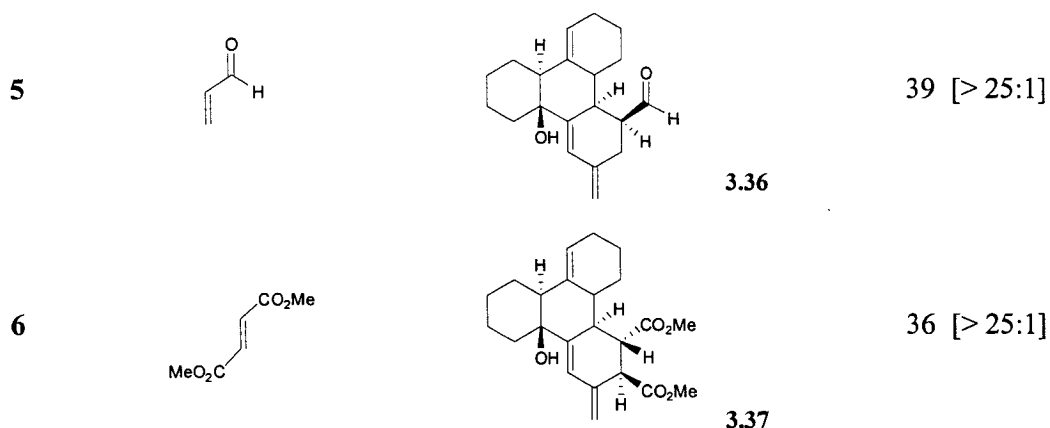
3.31 was subsequently alkylated with propargyl bromide and sodium hydride in THF/DMF (3:1) to afford **3.32** in 99% yield. Results of the tandem oxy-Cope/Claisen/ene/HDDA reaction for propargyl ether **3.32** are illustrated in *Table 3.3*.



Scheme 3.10: Preparation of Propargyl Ether 3.32

Table 3.3: Results of the Tandem Oxy-Cope/Claisen/Ene/HDDA Reaction with Propargyl Ether 3.32

Entry	Dienophile	Product	Yield (%) [dr]
1		 3.33	21 [$> 25:1$]
2		 3.34	37 [$> 25:1$]
3		Failed ^a	—
4		 3.35	44 [$> 25:1$]



^a The reaction was repeated 3 times, to no avail; mostly starting material was recovered.

The use of methyl acrylate and methyl methacrylate as dienophiles led to the corresponding products **3.33** and **3.34** as single diastereoisomers in yields of 21% and 37% respectively, while methyl vinyl ketone failed to react, despite several attempts (*Table 3.3, Entries 1-3*). The structure of **3.34** (*Table 3.3, Entry 2*) was confirmed by 2-D NMR experiments and details relating to the elucidation of its relative stereochemistry are illustrated in *Figure 3.10*. H_1/H_2 have a strong coupling with H_3 only (perpendicular to the π -system of the double-bond; allylic coupling) [**A**] and W-coupling is observed between H_3 and the methyl group [**B**]. The NOESY spectrum indicates the following correlations: H_5 with H_7 [**C**], H_5 with H_6 and H_5 with the methyl group [**D**]. Thus H_7 , H_6 , H_5 and the methyl group are all *syn* to one another and *anti* to the hydroxyl group.⁵³

⁵³ Diastereoselectivity of the oxy-Cope/ene rearrangement was investigated for analogous compounds in Deon, D. Thesis. *The Effect of DBU on the Tandem Oxy-Cope/Ene Reaction and Total Synthesis of (+)-Arteannuin M*, University of Ottawa, 2001.

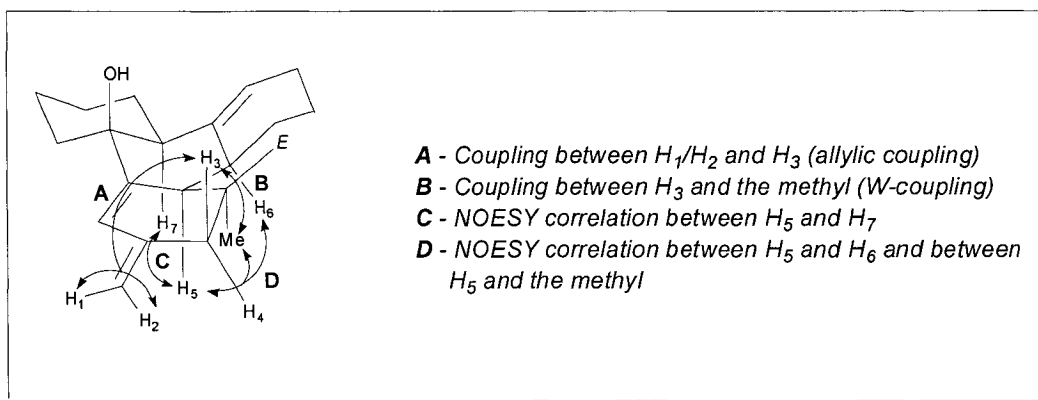


Figure 3.10: Structure Elucidation of 3.34 by 2-D NMR Experiments

Products **3.35** and **3.36**, arising from the use of methacrolein and acrolein as dienophiles, were isolated in respective yields of 44% and 39% (Table 3.3, Entries 4-5). Dimethyl fumarate as the dienophile similarly led to a single diastereoisomer, **3.37**, in 36% yield (Table 3.3, Entry 6). 2-D NMR experiments conducted on **3.37** confirmed the relative stereochemistry (Figure 3.11). NOESY correlations are observed between H₃ and H₅ [A], as well as between H₅ and H₆ [B] and H₅ and H₇ [C]. H₃ and H₄ are known to be *anti* to each other, due to the geometry of the dienophile.

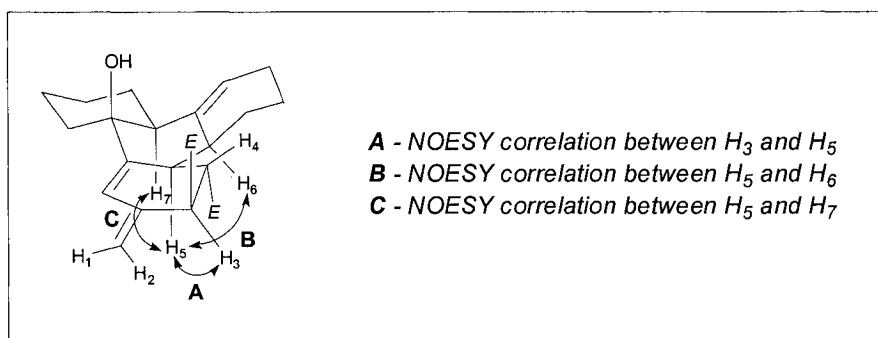
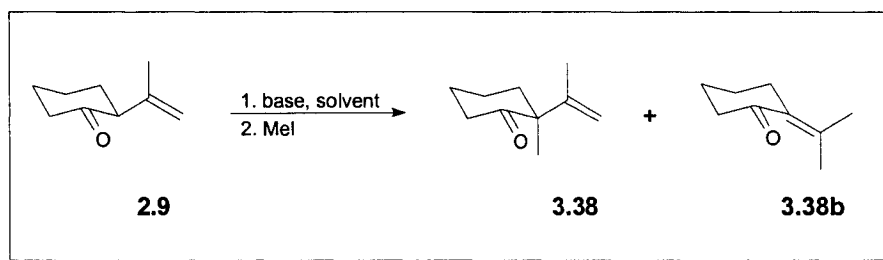


Figure 3.11: Structure Elucidation of 3.37 by 2-D NMR Experiments

The last substrate studied was a close analog of **3.3**, bearing an additional methyl group at C-2, thus introducing another quaternary center and taking a further step towards steroid synthesis. The synthesis of **3.40** began by the treatment of 2-isopropenyl-

cyclohexanone **2.9** with freshly sublimed potassium *tert*-butoxide in THF at 0 °C to generate the corresponding enolate, which was trapped with methyl iodide, affording **3.38** in 8% yield (*Scheme 3.11*). In addition, the conjugated system **3.38b** was obtained as a side-product in 5% yield. Various bases, solvents and equivalents of reagents were studied in order to optimize this reaction and eliminate side-product formation (*Table 3.4*).



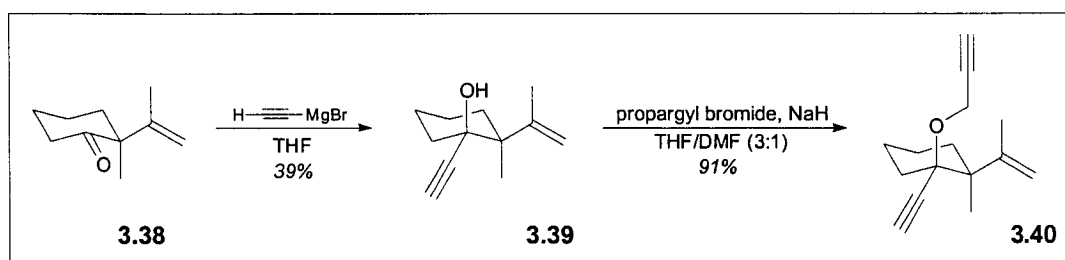
Scheme 3.11: Alkylation of 2-Isopropenyl-Cyclohexanone 2.9

Table 3.4: Alkylation of 2-Isopropenyl-Cyclohexanone 2.9

Entry	Base	Equivalents of base	Equivalents of MeI	Solvent	Temperature (°C)	Yield (%)	
						3.38	3.38b
1	<i>t</i> -BuOK	1.2	2.0	THF	0	8	5
2	<i>t</i> -BuOK	1.2	1.05	<i>t</i> -BuOH	-78	SM recovered	
3	NaOMe	1.0	1.3	THF	0	50	21
4	NaOMe	1.2	1.05	THF	0	64	18
5	NaOMe	1.05	1.5	MeOH	0	SM recovered	

Unfortunately, **3.38b** was consistently observed along with the desired **3.38**. The use of 1.2 eq. of NaOMe and 1.05 eq. of MeI in THF at 0 °C (*Table 3.4, Entry 4*) provided the best yield of **3.38** (64%), with a minor amount of **3.38b** (18%). These

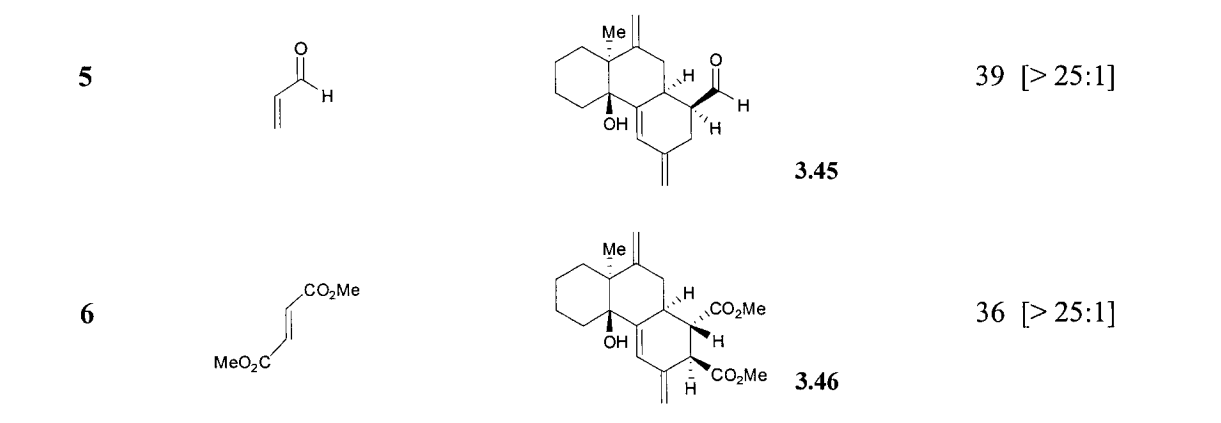
conditions were therefore applied to a larger scale to afford the necessary quantity of **3.38**. Exposure of **3.38** to ethynylmagnesium bromide generated alcohol **3.39** as the major diastereoisomer (63:37) in 39% yield (*Scheme 3.12*). Conversion of **3.39** to propargyl ether **3.40** was effected, using protocols previously described, in 91% yield. Results of the tandem oxy-Cope/Claisen/ene/HDDA reaction for propargyl ether **3.40** are presented in *Table 3.5*.



Scheme 3.12: Preparation of Propargyl Ether 3.40

Table 3.5: Results of the Tandem Oxy-Cope/Claisen/Ene/HDDA Reaction with Propargyl Ether 3.40

Entry	Dienophile	Product	Yield (%) [dr]
1		 3.41	26 [$> 25:1$]
2		 3.42	21 [$> 25:1$]
3		 3.43	48 [$> 25:1$]



Methyl acrylate and methyl methacrylate as dienophiles led to the corresponding products **3.41** and **3.42** in yields of 26% and 21% respectively (*Table 3.5, Entries 1-2*). The relative stereochemistry of **3.42** was confirmed by 2-D NMR experiments (*Figure 3.12*). NOESY correlations are displayed between H₅ and the ring junction methyl group [A], as well as between H₅ and the C-14 methyl group [B] and W-coupling is observed between H₃ and the C-14 methyl group [C], thus indicating that both methyl groups and H₅ are on the same side of the molecule. It should be noted that **3.42** is very similar in structure to **3.3**, with the exception of the additional C-2 methyl group. Since this center is relatively far from the reactive site, one can make the reasonable assumption that the difference in energy for the two HDDA transition states will be minor, thus, the product bearing the ester *syn* to the hydroxyl group is expected.

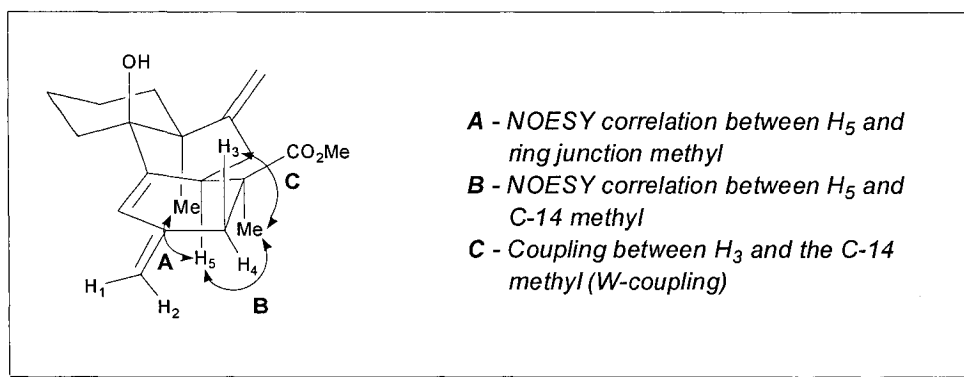


Figure 3.12: Structure Elucidation of 3.42 by 2-D NMR Experiments

The use of methyl vinyl ketone and methacrolein as dienophiles led to the corresponding adducts 3.43 and 3.44 in yields of 48% and 44% respectively (*Table 3.5, Entries 3-4*). 2-D NMR experiments were conducted on 3.44 (*Figure 3.13*). H₁/H₂ have a strong coupling with H₃ only (perpendicular to the *pi*-system of the double-bond; allylic coupling). NOESY correlations are reported between H₅ and the ring junction methyl group [**A**], between H₅ and the C-14 methyl group [**B**], between the C-14 and ring junction methyl groups [**C**], as well as between H₄ and H₅ [**D**], thus indicating their *syn* relationship.

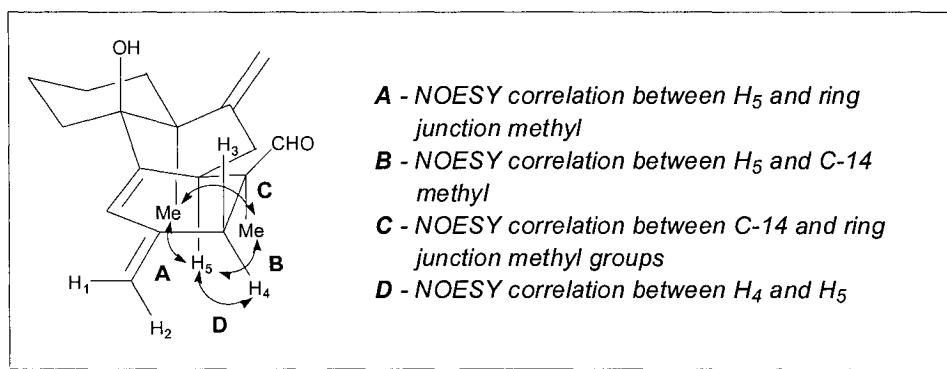


Figure 3.13: Structure Elucidation of 3.44 by 2-D NMR Experiments

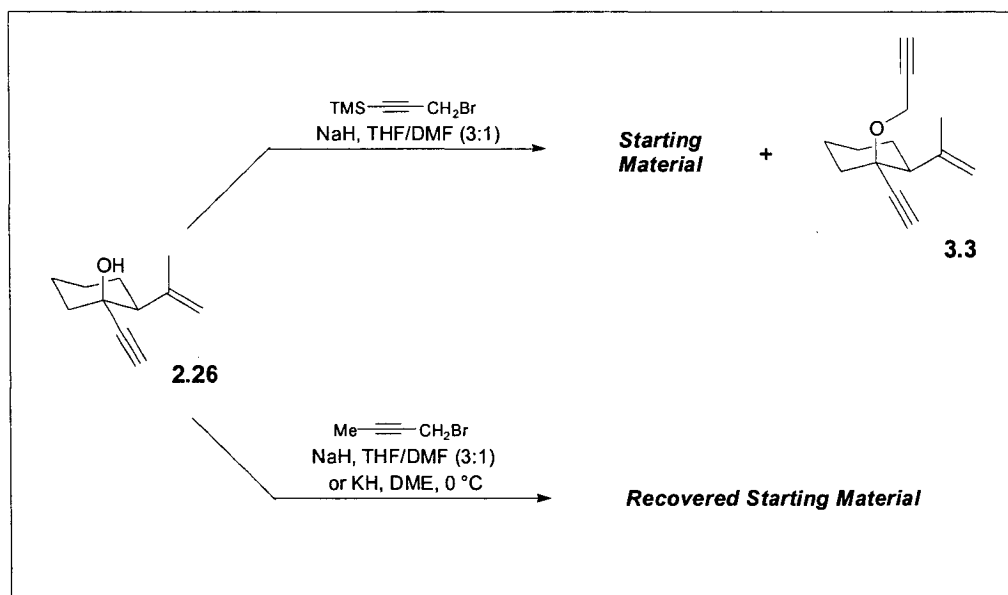
Finally, acrolein and dimethyl fumarate led to the corresponding products **3.45** and **3.46** as single diastereoisomers in respective yields of 39% and 36% (*Table 3.5, Entries 5-6*).

3.4 Additional Studies

Further studies were conducted through the addition of functionality to the triple bonds and the cyclohexenyl moiety of the substrate, and through the synthesis of more complex dienophiles, so as to further study the scope and limitations of the tandem oxy-Cope/Claisen/ene/HDDA reaction. Attempts at a tandem oxy-Cope/Claisen/ene/Claisen/Diels-Alder reaction were also made.

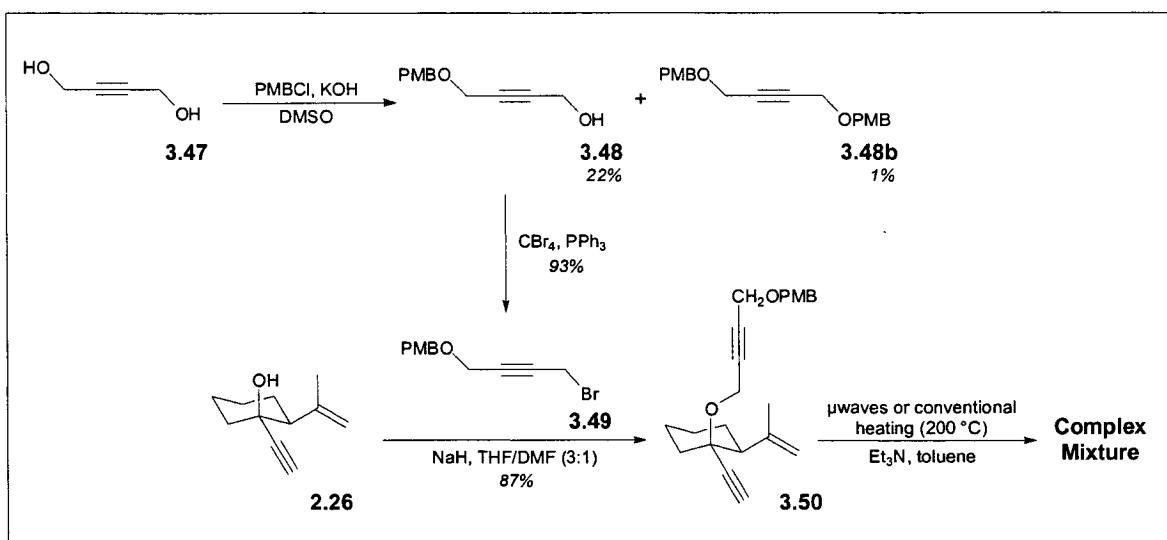
3.4.1 Functionalization of the Propargyl Group

In order to evaluate the effect of functionalization of the propargyl group, alkylation of **2.26** was attempted with TMS-propargyl bromide and sodium hydride (*Scheme 3.13*). Regrettably, starting material was recovered, along with **3.3**, suggesting that the TMS group was rather labile. The use of 1-bromo-2-butyne as alkylating agent, with sodium hydride in THF/DMF (3:1) or with potassium hydride in DME, only led to the recovery of the starting material.



Scheme 3.13: Attempts at Functionalizing the Propargyl Group

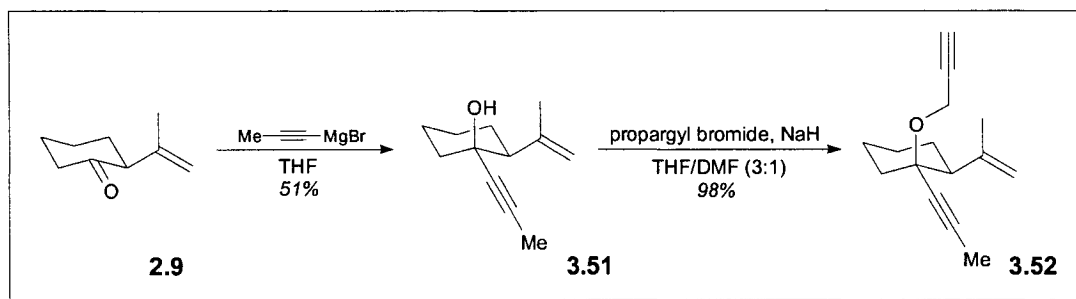
Treatment of commercially available 2-butyne-1,4-diol **3.47** with 1.1 equivalents of KOH and 1.0 equivalent of PMBCl in dry DMSO provided the mono-protected alkyne **3.48** in 22% yield, along with 1% of the bis-protected **3.48b**; the remainder consisting in unreacted starting material (*Scheme 3.14*). Conversion of **3.48** to propargyl bromide **3.49** was accomplished by exposure to CBr_4 and PPh_3 (93% yield). Alkylation of **2.26** with **3.49** in the presence of sodium hydride in THF/DMF (3:1) afforded **3.50** in 87% yield. Exposure of **3.50** to microwaves or to conventional heating ($200\text{ }^\circ\text{C}$) for 2 hours led, in both cases, to a complex mixture from which no desired product was isolated.



Scheme 3.14: Preparation and Attempted Reaction of 3.50

3.4.2 Functionalization of the C-1 Alkyne

Exposure of 2-isopropenyl-cyclohexanone **2.9** to 1-propynylmagnesium bromide generated **3.51** as the major diastereoisomer (71:29) in 51% yield, which was transformed to the corresponding propargyl ether **3.52** as previously described (*Scheme 3.15*).



Scheme 3.15: Preparation of Propargyl Ether 3.52

Irradiation (200 °C) of **3.52** for 2 hours led to a complex mixture of products, from which the expected oxy-Cope/Claisen/ene product was clearly absent. A possible side-reaction consists of a [1,5]-shift, although this has not yet been confirmed. Similar

to what was observed in the first part of the project, these preliminary results would suggest that the oxy-Cope/Claisen/ene reaction is not very tolerant of substitution at the alkynes, possibly due to increased steric hindrance at the transition state.

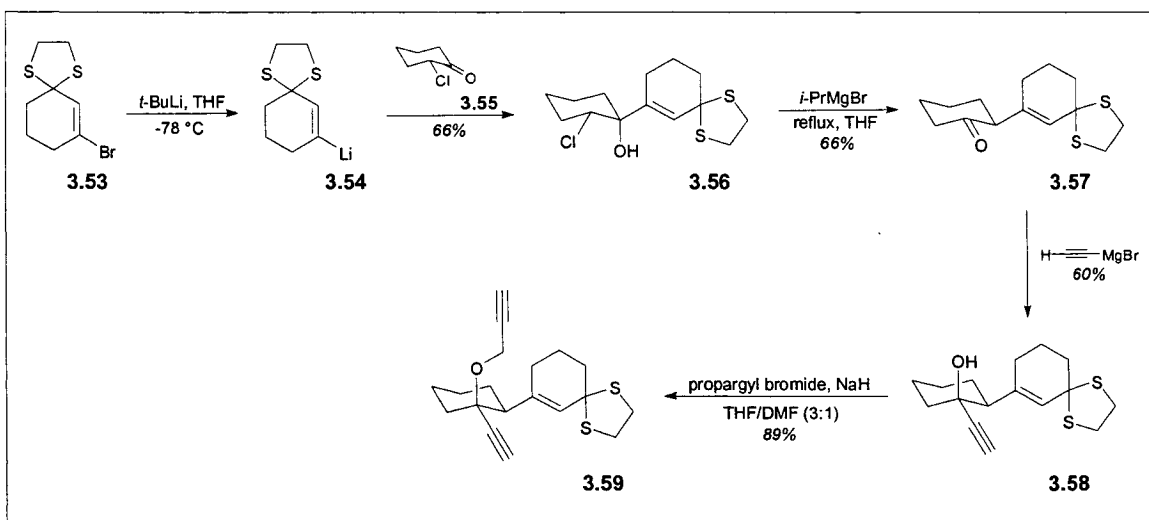
3.4.3 Functionalization of the Cyclohexenyl Ring of 3.32

The addition of a ketone functionality to the cyclohexenyl moiety of **3.32** was investigated so as to furnish additional chemical handles in the final products, thus widening the synthetic possibilities of this reaction. Exposure of commercially available 2-chlorocyclohexanone **3.55** to cyclohexenyllithium **3.54**,⁵⁴ generated by *t*-BuLi treatment of the parent bromide **3.53** in THF, afforded chlorohydrin **3.56** in 66% yield (*Scheme 3.16*).⁵⁵ Conversion of **3.56** to the corresponding ketone **3.57** in 66% yield was effected through a 1,2-migration using Holt's procedure.⁵⁶ Subsequent treatment of **3.57** with ethynylmagnesium bromide generated **3.58** as the sole diastereoisomer in 60% yield. Finally, alkylation with propargyl bromide afforded **3.59** in 89% yield.

⁵⁴ Shih, C.; Swenton, J. S. *J. Org. Chem.* **1982**, *47*, 2825.

⁵⁵ It is to note that this particular reaction was very sensitive and that results were often not reproducible.

⁵⁶ Holt, D. A. *Tetrahedron Lett.* **1981**, *22*, 2243.



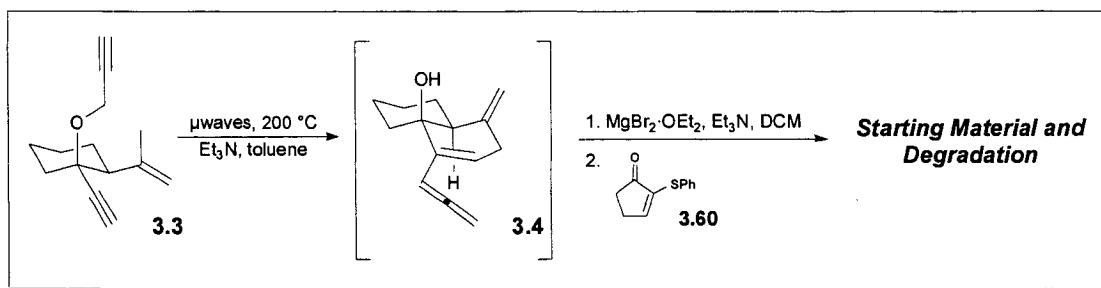
Scheme 3.16: Preparation of Propargyl Ether 3.59

Owing to the fact that microwaves generally cause the degradation of thioacetals,⁵³ **3.59** was conventionally heated in the presence of triethylamine at 200 °C for 48 hours and 230 °C for 6 hours. Unfortunately, only starting material was recovered. It would thus appear that the steric hindrance caused by the presence of the thioacetal group inhibits the reaction.

3.4.4 Tandem Oxy-Cope/Claisen/Ene/HDDA Reaction with 2-Phenylthio-2-Cyclopentenone and α -Methylene- γ -Butyrolactone

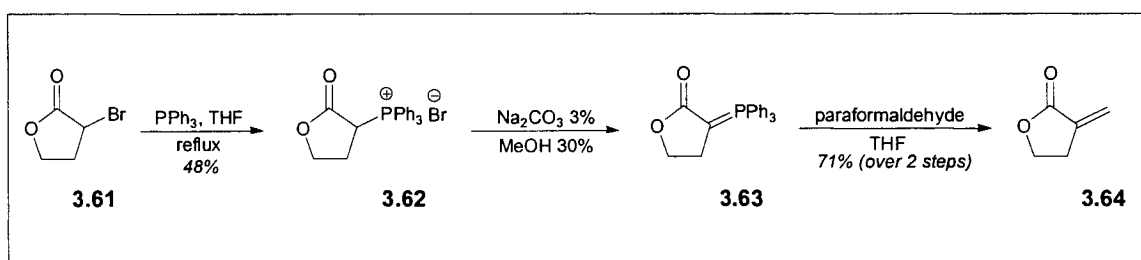
The tandem oxy-Cope/Claisen/ene/HDDA reaction was studied with two additional dienophiles. Specifically constructed with total synthesis in mind, these dienophiles possess additional chemical handles for further side-chain construction. In the first instance, 2-phenylthio-2-cyclopentenone **3.60**⁵⁷ was reacted with diene intermediate **3.4**, which led to degradation and recovery of the starting material (*Scheme 3.17*).

⁵⁷ Monteiro, H. J. *J. Org. Chem.* **1977**, *42*, 2324.



Scheme 3.17: Attempt at a Tandem Oxy-Cope/Claisen/Ene/HDDA Reaction with 2-Phenylthio-2-Cyclopentenone

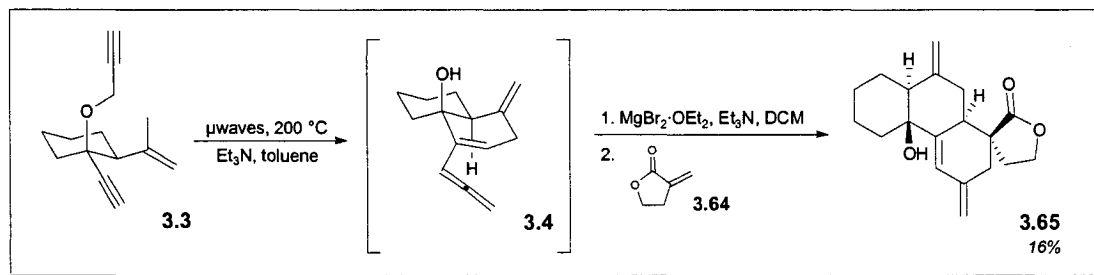
α -Methylene- γ -butyrolactone was also prepared as a more functionalized dienophile; its interest lay in the fact that the lactone could subsequently be opened, thus offering possibilities for side-chain additions. Following literary procedures,⁵⁸ commercially available α -bromo- γ -butyrolactone **3.61** was treated with triphenylphosphine in refluxing THF to afford the corresponding phosphonium bromide salt **3.62** (Scheme 3.18). Addition of a solution of 3% sodium carbonate in methanol (30%) led to phosphonium ylid **3.63**. Conversion of **3.63** to the desired α -methylene- γ -butyrolactone **3.64** was effected by treatment with paraformaldehyde (71% yield over 2 steps).



Scheme 3.18: Preparation of α -Methylene- γ -Butyrolactone

⁵⁸ (a) Fliszar, S.; Hudson, R. F.; Salvadori, G. *Helv. Chim. Acta* **1963**, *46*, 1580. (b) Grieco, P. A.; Pogonowski, S. *J. Org. Chem.* **1974**, *39*, 1958.

Reaction of diene intermediate **3.4** with the prepared α -methylene- γ -butyrolactone **3.64** led to the expected product **3.65** in 16% yield (*Scheme 3.19*). Despite the fact that the yield was relatively low, it is anticipated that the reaction could be optimized in the future.

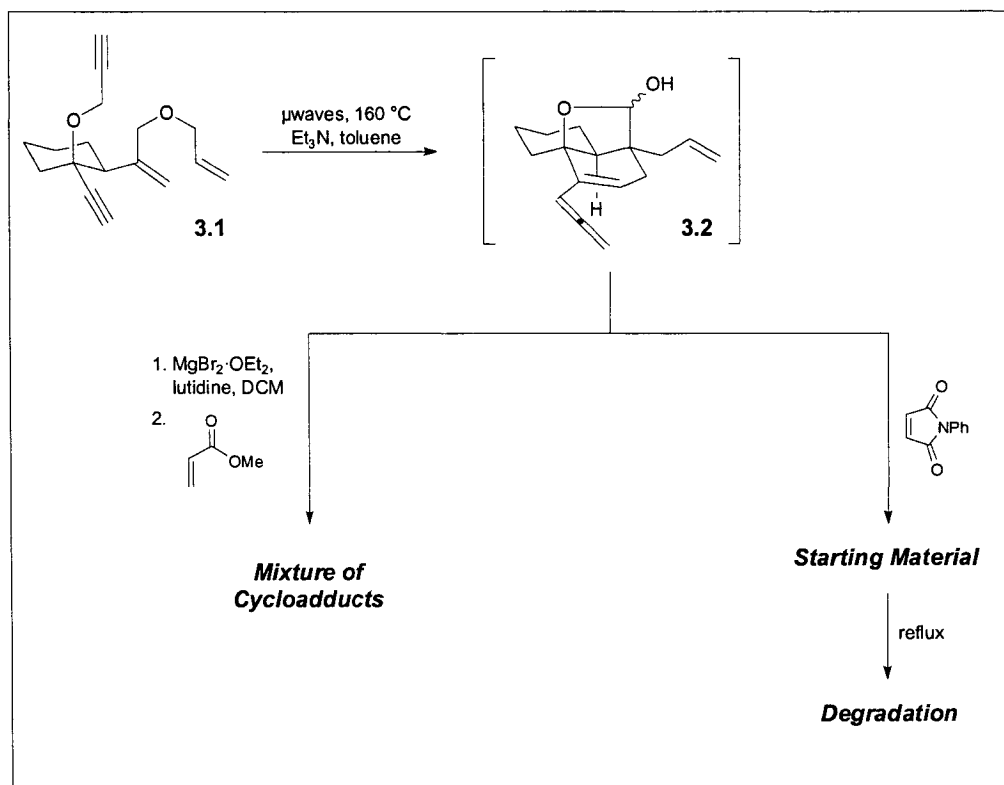


Scheme 3.19: Tandem Oxy-Cope/Claisen/Ene/HDDA Reaction with α -Methylene- γ -Butyrolactone

3.4.5 Attempts at a Tandem Oxy-Cope/Claisen/Ene/Claisen/Diels-Alder Reaction

As previously reported (*Scheme 3.1*), irradiation of **3.1** led to the generation of diastereomeric lactols **3.2** through a tandem oxy-Cope/Claisen/ene/Claisen reaction; the addition of a [4+2] cycloaddition to this pericyclic cascade of reactions was briefly investigated. To this end, **3.1** was irradiated with microwaves (160 °C) for 4 hours to effect its conversion to lactols **3.2** (*Scheme 3.20*). In the first case, N-phenylmaleimide was added and the reaction was stirred overnight; only starting material was observed by TLC. Refluxing the reaction mixture led to degradation. In the second case, **3.2** was treated with $\text{MgBr}_2\cdot\text{OEt}_2$ /lutidine in DCM, followed by the addition of methyl acrylate. A complex mixture containing at least 3 diastereoisomers arising from the subsequent [4+2] cycloaddition was observable by NMR. The fact that a mixture of diastereoisomers

was obtained is not surprising in light of previously reported results;⁵⁹ it was found that polyoxygenated precursors are not well-suited for the HDDA methodology due to difficulties with the magnesium tether occurring in an organized fashion.



Scheme 3.20: Attempts at a Tandem Oxy-Cope/Claisen/Ene/Claisen/Diels-Alder Reaction

3.5 Conclusion

In conclusion, the scope and limitations of the tandem oxy-Cope/Claisen/ene/HDDA reaction were investigated in the present research. The results presented in this thesis illustrate the successful development of a methodology that can convert simple propargyl ethers to functionalized polycyclic molecules, in a single

⁵⁹ Farand, J. Thesis. *Studies on the Tandem Oxy-Cope/Ene/Claisen Reaction. Applications of the HDDA Reaction Towards the Total Synthesis of Havellockate and Synthesis of Isovelleral Analogues*, University of Ottawa, 2004.

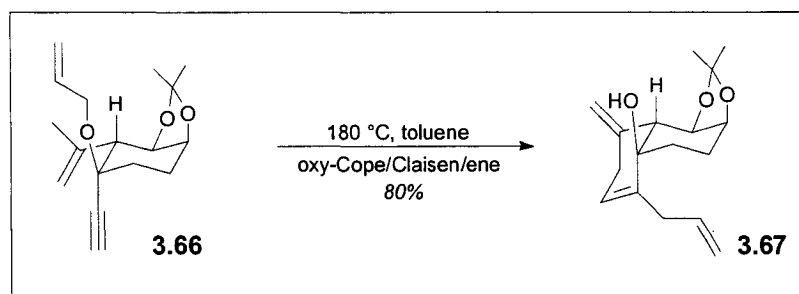
chemical step, with high regio- and stereoselectivity. The yields, which vary between 21% and 49%, are relatively good when considering that they reflect 4 tandem reactions and therefore average between 68% and 84% per pericyclic step. The methodology was found to be applicable to four classes of propargyl ethers, each with a wide variety of dienophiles. Propargyl ethers bearing additional substitution at the terminus of the triple bonds, or on the cyclohexenyl moiety, were not suitable for the reaction.

3.6 Future Studies

As previously noted, all examples in the present study are with cyclohexanol substrates bearing the isopropenyl (cyclohexenyl) and ethynyl groups in an *anti* relationship, consequently generating the *trans*-decalin systems through the oxy-Cope/Claisen/ene reaction. In fact, the *syn* substrates surveyed only led to degradation.⁶⁰ Such tandem pericyclic reactions have often been problematic in our laboratory. Notwithstanding, the example depicted in *Scheme 3.21*, wherein substrate **3.66** possesses an acetal function on the ring, generated the corresponding *cis*-decalin **3.67** through an oxy-Cope/Claisen/ene reaction in 80% yield.⁶¹

⁶⁰ Barriault, L.; Clément, R., *unpublished results*.

⁶¹ Barriault, L.; Morency, L. *Tetrahedron Lett.* **2004**, 45, 6105.



Scheme 3.21: *Cis-Decalin Formation Through a Tandem Oxy-Cope/Claisen/Ene Reaction*

In light of this result, it is conceivable that if a substrate akin to **3.68** (with added functionality on the ring) was synthesized, it could undergo an oxy-Cope/Claisen/ene reaction to provide **3.69**, ultimately leading to the generation of the corresponding diterpenes **3.70** upon subsequent addition of dienophiles (*Figure 3.14*). Structures such as **3.69** contain the B/C/D ring system of the 14- β -hydroxysteroids, as previously outlined in the *Introduction*. The methodology developed so far with the analogous *anti* compounds **3.71** provides two of the chiral centers found in the core structure of the 14- β -hydroxysteroids. The *syn* substrates could lead to the stereoselective formation of three of the necessary quaternary centers. Furthermore, the hydroxyl group could be used to direct hydrogenation of the endocyclic double-bond and afford the necessary stereochemistry at C-8. The tandem oxy-Cope/Claisen/ene/HDDA reaction would no doubt constitute in an ingenious way to generate such compounds and future research will be directed towards such objectives.

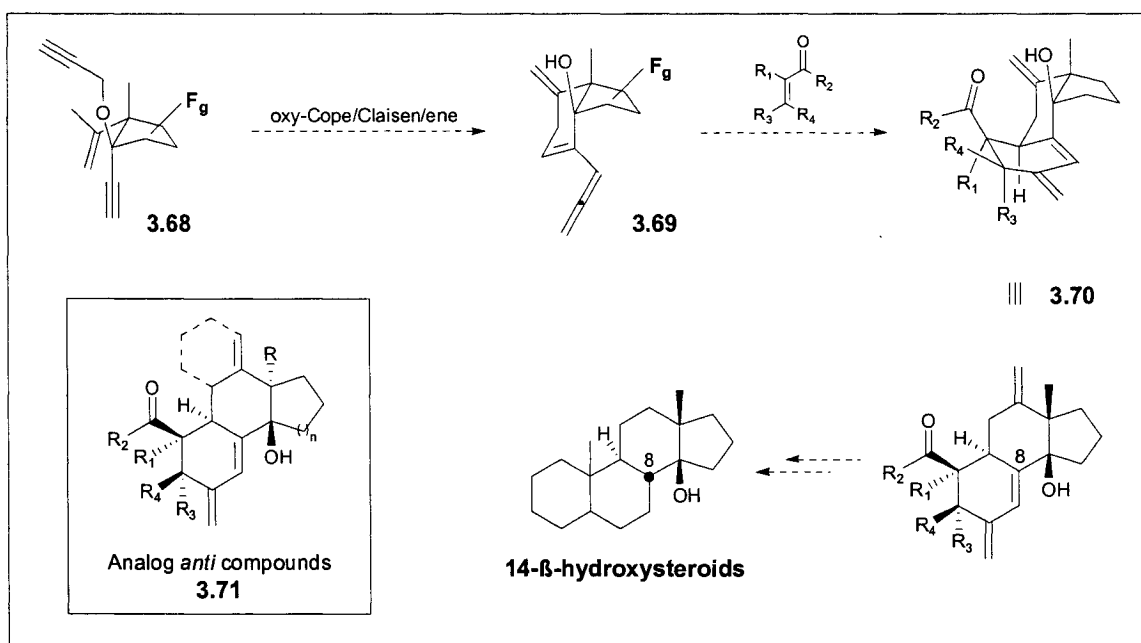


Figure 3.14: Anticipated Application of the Oxy-Cope/Claisen/Ene/HDDA Reaction to the Synthesis of 14-β-Hydroxysteroids

Chapter 4: Experimental

4.1 General Methods and Materials

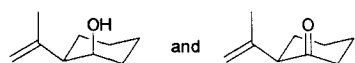
All reactions were performed under nitrogen or argon atmosphere in flame-dried glassware equipped with a magnetic stir bar and a rubber septum, unless otherwise indicated. All solvents were freshly distilled prior to use; diethyl ether and THF over sodium and benzophenone; toluene, DMF, triethylamine, DMSO, DME, and DCM over calcium hydride. $\text{MgBr}_2 \cdot \text{OEt}_2$ was prepared in our laboratory and stored in the glove box. All other commercial reagents were used without purification, unless otherwise noted.

Reactions were monitored by thin layer chromatography (TLC) analysis of aliquots using glass sheets pre-coated (0.2 mm layer thickness) with silica gel 60 F₂₅₄ (E. Merck). Thin layer chromatography plates were viewed under UV light and stained with phosphomolybdic acid or *p*-anisaldehyde staining solution. Column chromatographies were carried out with silica gel 60 (230-400 mesh, Merck). ¹H and ¹³C NMR spectra were recorded in deuterated solvents, on Bruker AMX 300 MHz and Bruker AMX 500 MHz spectrometers. IR spectra were recorded with a Bomem Michaelson 100 FTIR spectrometer. HRMS were obtained on a Kratos Analytical Concept instrument (University of Ottawa Mass Spectrum Centre). Melting points were recorded on a Gallenkamp melting point machine apparatus P 1106G and X-ray crystallographs were performed on a Bruker AX SMART 1k CCD diffractometer.

Microwave reactions were conducted in a CEM Model ESP-1500 Plus oven, equipped with a EST-300 Plus temperature probe. All experiments were effected in a quartz tube in the presence of two carboflons.TM

4.2 Experimental Method and Data Relating to Compounds of Chapter 2

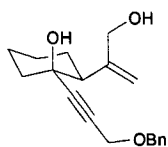
2-Isopropenyl-cyclohexanol (2.8) and 2-Isopropenyl-cyclohexanone (2.9)



A dry round bottom flask was charged with CuBr·DMS (4.810 g, 23.4 mmol) and THF (300 mL). The solution was cooled to -30 °C, followed by the addition of isopropenylmagnesium bromide (608.0 mL, 0.304 mol). The mixture was stirred for 20 minutes, at which point cyclohexene oxide **2.7** (22.967 g, 0.234 mol) was added and the solution was stirred to room temperature. The reaction was followed by TLC and quenched with NH₄Cl (sat. aq.) upon completion. The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO₄, filtered, and concentrated. A dry round bottom flask was charged with oxalyl chloride (9.69 mL, 0.111 mol) and DCM (200 mL). The solution was cooled to -78 °C, and DMSO (15.8 mL, 0.222 mol) was slowly added. After 20 minutes of stirring, the crude alcohol **2.8** in DCM (20 mL) was added to give an opaque white mixture. The latter was stirred at -78 °C for 1.5 hours, followed by the addition of triethylamine (64.4 mL, 0.463 mol). The solution was again stirred at 0 °C for an additional hour and quenched with NH₄Cl (sat. aq.). The mixture was extracted with DCM (3x) and the combined organic layers were dried over MgSO₄, filtered, and concentrated. Flash chromatography (3-10% ethyl

acetate in hexanes) afforded **2.9** (9.690 g, 76% over two steps) as a yellow oil. Characterisation data is available through the literature.⁶²

1-(3-Benzyloxy-prop-1-ynyl)-2-(1-hydroxymethyl-vinyl)-cyclohexanol (2.11 and 2.12)

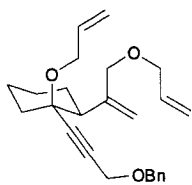


To a solution of prop-2-ynyloxymethyl-benzene **2.10** (3.603 g, 24.7 mmol) in THF (25 mL) at -78 °C was added *n*-BuLi (9.12 mL, 22.8 mmol). The solution was stirred for 15 minutes, allowing the formation of the alkynyl lithium *in situ*. To this was added ketone **2.9** (2.620 g, 19.0 mmol) *via* canula. The reaction was stirred overnight and quenched with NH₄Cl (sat. aq.). The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO₄, filtered, and concentrated. The residue was quickly flashed on a pad of silica to afford both diastereoisomers of **2.11** (5.401 g, 99%). To a solution of SeO₂ (1.082 g, 9.75 mmol) in DCM (95 mL) at 0 °C was added *t*-BuOOH (0.30 mL, 19.3 mmol). The mixture was stirred until the solid disappeared (15-60 minutes), and a DCM solution (5 mL) of **2.11** (5.401 g, 19.0 mmol) was added at 0 °C. The reaction was stirred overnight at room temperature and quenched with Na₂SO₃ (sat. aq.). The mixture was extracted with DCM (3x) and the combined organic layers were washed with brine, dried over MgSO₄, filtered and concentrated. Flash chromatography (25-100% ethyl acetate in hexanes) afforded the major diastereoisomer (78:22) **2.12** (2.576 g, 45%) as a yellow oil. IR (neat, cm⁻¹) 3346 (br), 3088 (w), 3068 (w), 3035 (w), 2935 (s), 2857 (m), 1691 (m), 1453 (m), 1354 (m), 1072 (s); ¹H NMR (CDCl₃, 300 MHz) δ 7.35-7.27 (m, 5H), 5.24 (s, 1H), 5.18 (s, 1H),

⁶² (a) Onishi, T.; Nishida, T. *J. Chem. Soc.* **1978**, 651. (b) Fujita, Y.; Onishi, T.; Nishida, T. *Synthesis* **1978**, 12, 934. (c) Utagawa, A.; Hirota, H.; Ohno, S.; Takahashi, T. *Bull. Chem. Soc. Jpn.* **1988**, 61, 1207.

4.57 (s, 2H), 4.21-4.01 (m, 4H), 3.52 (br, s), 3.40-2.08 (m, 2H), 2.02 (s, 1H), 1.87-1.33 (m, 5H), 1.26-1.21 (m, 2H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 149.0 (C_4), 137.7 (C_4), 128.8 (CH), 128.5 (CH), 128.3 (CH), 116.1 (CH_2), 88.3 (C_4), 82.9 (C_4), 72.6 (C_4), 71.8 (CH_2), 67.8 (CH_2), 57.8 (CH_2), 52.2 (CH), 41.8 (CH_2), 30.6 (CH_2), 26.1 (CH_2), 24.3 (CH_2); HRMS (EI) m/z calcd for $\text{C}_{11}\text{H}_{15}\text{O}_2$ ($[\text{M}-\text{CH}_2\text{OBn}]^+$) 179.1072, found 179.1060.

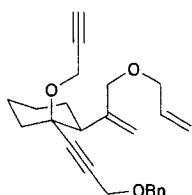
{3-[1-Allyloxy-2-(1-allyloxymethyl-vinyl)-cyclohexyl]-prop-2-ynylloxymethyl}-benzene (2.13)



To a solution of **2.12** (0.803 g, 2.67 mmol) and allyl bromide (1.16 mL, 13.4 mmol) in THF/DMF (9:3 mL) was added sodium hydride 60% in oil (0.534 g, 13.4 mmol) slowly at room temperature. The reaction was followed by TLC and quenched with NH_4Cl (sat. aq.) upon completion. The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO_4 , filtered, and concentrated. Flash chromatography (5% ethyl acetate in hexanes) afforded **2.13** (0.974 g, 99%) as a yellow oil. IR (neat, cm^{-1}) 3080 (m), 3067 (m), 3015 (m), 2983 (m), 2936 (s), 2856 (s), 1646 (m), 1496 (w), 1454 (s), 1353 (s), 1258 (m), 1167 (s), 1092 (s); ^1H NMR (CDCl_3 , 300 MHz) δ 7.37-7.24 (m, 5H), 6.02-5.86 (m, 2H), 5.34-5.12 (m, 4 H), 5.13 (t, $J = 8.7$ Hz, 2H), 4.58 (s, 2H), 4.19-4.14 (m, 4H), 4.06-3.91 (m, 4H), 2.37-2.19 (dd, $J = 12.7, 3.3$ Hz, 1H), 2.27-2.21 (m, 1H), 1.1 (qd, $J = 12.9, 3.7$ Hz, 1H), 1.71-1.67 (m, 1H), 1.56-1.47 (m, 4H), 1.36-1.32 (m, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 147.2 (C_4), 137.9 (C_4), 135.8 (CH), 135.5 (CH), 128.8 (CH), 128.7 (CH), 128.5 (CH), 128.2 (CH), 116.9 (CH_2), 115.6 (CH_2), 114.2 (CH_2), 88.3 (C_4), 82.1 (C_4), 74.5 (C_4), 73.5 (CH_2), 71.7 (C_4), 71.6 (CH_2), 71.3 (CH_2), 64.6 (CH_2), 57.7 (CH_2), 51.8 (CH), 35.9

(CH₂), 27.5 (CH₂), 26.3 (CH₂), 20.9 (CH₂); HRMS (EI) m/z calcd for C₂₂H₂₇O₃ ([M-C₃H₅]⁺) 339.1960, found 339.2006.

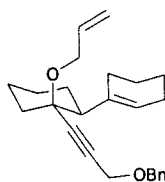
{3-[2-(1-Allyloxymethyl-vinyl)-1-prop-2-ynyloxy-cyclohexyl]-prop-2-nyloxymethyl}-benzene (2.14)



To a solution of **2.12** (0.887 g, 2.95 mmol) and allyl bromide (0.27 mL, 3.10 mmol) in THF/DMF (9:3 mL) was added sodium hydride 60% in oil (0.124 g, 3.10 mmol) slowly at room temperature. The reaction was followed by TLC and quenched with NH₄Cl (sat. aq.) upon completion. The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO₄, filtered, and concentrated. The residue and propargyl bromide (0.69 mL, 7.40 mmol) were dissolved in THF/DMF (9:3 mL) and sodium hydride 60% in oil (0.295 g, 7.40 mmol) was slowly added at room temperature. The reaction was followed by TLC and quenched with NH₄Cl (sat. aq.) upon completion. The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO₄, filtered, and concentrated. Flash chromatography (5% ethyl acetate in hexanes) afforded **2.14** (0.469 g, 42% over two steps) as a yellow oil. IR (neat, cm⁻¹) 3293 (m), 3084 (w), 3068 (w), 3031 (w), 2936 (m), 2857 (m), 1644 (w), 1496 (m), 1453 (m), 1353 (m), 1259 (m), 1167 (m), 1079 (m); ¹H NMR (CDCl₃, 300 MHz) δ 7.36–7.27 (m, 5H), 5.96–5.83 (m, 1H), 5.28–5.10 (m, 4H), 4.55 (s, 2H), 4.30–4.11 (m, 5H), 4.02–3.94 (m, 3H), 2.36 (t, J = 2.3 Hz, 1H); 3.40 (dd, J = 12.4, 3.1 Hz, 1H), 2.21 (d, J = 11.2 Hz, 1H), 1.85 (qd, J = 13.0, 3.7 Hz, 1H), 1.77–1.69 (m, 1H), 1.61–1.43 (m, 4H), 1.34–1.22 (m, 1H); ¹³C NMR (CDCl₃, 75 MHz) δ 146.8 (C₄), 137.8 (C₄), 135.4 (CH), 128.8 (CH), 128.5 (CH), 128.2 (CH), 116.9 (CH₂), 114.4 (CH₂), 87.3 (C₄), 83.1 (C₄), 81.3 (C₄), 75.8 (C₄), 73.6 (C₄), 73.3 (CH), 71.7

(CH), 71.2 (CH), 57.6 (CH₂), 52.3 (CH₂), 51.6 (CH), 36.1 (CH₂), 27.3 (CH₂), 26.2 (CH₂), 20.9 (CH₂); HRMS (EI) *m/z* calcd for C₁₈H₂₃O₃ ([M-Bn]⁺) 287.1647, found 287.1627.

2'-Allyloxy-2'-(3-benzyloxy-prop-1-ynyl)-bicyclohexyl-1-ene (2.16 and 2.17)

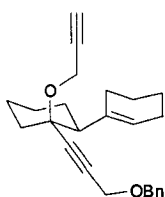


To a solution of prop-2-ynyloxymethyl-benzene **2.10** (2.460 g, 16.8 mmol) in THF (25 mL) at -78 °C was added *n*-BuLi (6.56 mL, 15.5 mmol). The solution was stirred for 15 minutes, allowing the formation of the alkynyl lithium *in situ*. To this was added 2-(1-cyclohexenyl)cyclohexanone **2.15** (2.32 mL, 13.0 mmol) *via* canula. The reaction was stirred overnight, quenched with NH₄Cl (sat. aq.), and the mixture was extracted with diethyl ether (3x). The combined organic layers were dried over MgSO₄, filtered, and concentrated. Flash chromatography (15% ethyl acetate in hexanes) afforded the major diastereoisomer (77:33) **2.16**⁶³ as a yellow oil (2.852 g, 68%). To a solution of **2.16** (1.420 g, 4.38 mmol) and allyl bromide (1.90 mL, 21.9 mmol) in THF/DMF (9:3 mL) was added sodium hydride 60% in oil (0.876 g, 21.9 mmol) slowly at room temperature. The reaction was followed by TLC and quenched with NH₄Cl (sat. aq.) upon completion. The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO₄, filtered, and concentrated. Flash chromatography (5% ethyl acetate in hexanes) afforded **2.17** (0.787 g, 49%) as a yellow oil. IR (neat, cm⁻¹) 3065 (w), 3030 (w), 2931 (s), 2855 (s), 1447 (m), 1353 (m), 1090 (m), 1073 (m); ¹H NMR (CDCl₃, 300 MHz) δ 7.37-7.25 (m, 5H), 6.00-5.88 (m, 1H), 5.60 (s, 1 H), 5.30 (dd, *J* = 17.4, 1.9 Hz, 1 H), 5.10 (dd, *J* = 10.5, 1.9 Hz, 1H), 4.58 (s, 2H), 4.20 (s, 2H), 4.18-4.11 (m, 1H), 3.94-3.89 (m, 1H), 2.31-2.16 (m, 2H), 2.10-1.84 (m, 5H), 1.75-1.65 (m, 1H), 1.63-1.35 (m, 8H), 1.31-1.21 (m, 1H); ¹³C NMR

⁶³ Characterisation data for **2.15** is available through reference 53.

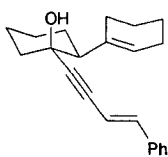
(CDCl₃, 75 MHz) δ 139.7 (C₄), 138.0 (C₄), 136.2 (CH), 128.8 (CH), 128.6 (CH), 128.2 (CH), 124.4 (CH), 115.2 (CH₂), 89.0 (C₄), 81.8 (C₄), 75.7 (C₄), 71.2 (CH₂), 64.5 (CH₂), 57.6 (CH₂), 55.8 (CH), 36.1 (CH₂), 28.2 (CH₂), 26.7 (CH₂), 26.4 (CH₂), 25.9 (CH₂), 23.8 (CH₂), 23.1 (CH₂), 21.0 (CH₂); HRMS (EI) m/z calcd for C₂₂H₂₇O₂ ([M-C₃H₅]⁺) 323.2011, found 323.2026.

2'-(3-Benzyloxy-prop-1-ynyl)-2'-prop-2-ynyloxy-bicyclohexyl-1-ene (2.18)



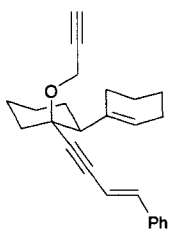
To a solution of **2.16** (1.432 g, 4.42 mmol) and propargyl bromide (1.97 mL, 2.21 mmol) in THF/DMF (9:3 mL) was added sodium hydride 60% in oil (0.884 g, 2.21 mmol) slowly at room temperature. The reaction was followed to completion and quenched with NH₄Cl (sat. aq.) upon completion. The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO₄, filtered, and concentrated. Flash chromatography (5% ethyl acetate in hexanes) afforded **2.18** (0.947 g, 60%) as a yellow oil. IR (neat, cm⁻¹) 3295 (m), 3088 (w), 3064 (w), 3031 (w), 2931 (s), 2856 (s), 1447 (m), 1353 (m), 1072 (m); ¹H NMR (CDCl₃, 300 MHz) δ 7.34 (m, 5H), 5.61 (s, 1H), 4.60 (s, 2H), 4.29 (dd, J_{AB} = 15.2 Hz, J_{AX} = 2.5 Hz, 1H), 4.17 (dd, J_{AB} = 15.2 Hz, J_{BX} = 2.5 Hz, 1H), 4.21 (s, 2H), 2.37 (t, J = 2.4 Hz, 1H), 2.24-2.16 (m, 2H), 2.09-2.04 (m, 2H), 2.00-1.95 (m, 2H), 1.91 (qd, J = 13.0, 3.7 Hz, 1H), 1.77-1.73 (m, 1H), 1.68-1.40 (m, 8H), 1.36-1.22 (m, 1H); ¹³C NMR (CDCl₃, 75 MHz) δ 139.5 (C₄), 137.9 (C₄), 128.8 (CH), 128.5 (CH), 128.2 (CH), 124.6 (CH), 88.0 (C₄), 82.9 (C₄), 81.7 (C₄), 77.0 (CH), 73.4 (C₄), 71.3 (CH₂), 57.5 (CH₂), 55.7 (CH), 52.3 (CH₂), 36.4 (CH₂), 28.0 (CH₂), 26.6 (CH₂), 26.4 (CH₂), 25.9 (CH₂), 23.8 (CH₂), 23.0 (CH₂), 21.1 (CH₂); HRMS (EI) m/z calcd for C₂₅H₂₈O (M⁺) 362.2246, found 362.2250.

2-(4-Phenyl-but-3-en-1-ynyl)-bicyclohexyl-1'-en-2-ol (2.20)



To a solution of (4,4-Dibromo-buta-1,3-dienyl)-benzene **2.19** (24.153 g, 84.5 mmol) in THF (100 mL) at -78 °C was added *n*-BuLi (58.9 mL, 169.0 mmol). The solution was stirred for 60 minutes at -78 °C and warmed to -25 °C for 30 minutes, allowing the formation of the alkynyl lithium *in situ*. The reaction was cooled back -78 °C and a solution of 2-(1-cyclohexenyl)cyclohexanone **2.15** (12.6 mL, 70.4 mmol) in THF (5 mL) was added *via* canula. The reaction was stirred for 60 minutes and quenched with NH₄Cl (sat. aq.). The mixture was extracted with ethyl acetate (3x) and the combined organic layers were dried over MgSO₄, filtered, and concentrated. Flash chromatography (20% ethyl acetate in hexanes) afforded the major diastereoisomer (75:25) **2.20** (14.454 g, 67%) as a yellow oil. IR (neat, cm⁻¹); 3546 (br), 3462 (br), 3027 (m), 2931 (s), 2855 (s), 1447 (m), 1063 (m), 968 (s), 952 (s); ¹H NMR (CDCl₃, 300 MHz) δ 7.41-7.26 (m, 5H), 6.87 (d, J = 16.3 Hz, 1H), 6.16 (d, J = 16.3 Hz, 1H), 5.59 (s, 1H), 2.55 (d, J = 16.9 Hz, 1H), 2.33 (s, 1H), 2.21-2.01 (m, 5H), 1.77-1.42 (m, 10H), 1.38-1.19 (m, 1H); ¹³C NMR (CDCl₃, 75 MHz) δ 141.3 (CH), 141.1 (C₄), 136.7 (C₄), 128.1 (CH), 128.9 (CH), 123.7 (CH), 108.4 (CH), 97.2 (C₄), 82.6 (C₄), 68.2 (C₄), 53.5 (CH), 29.8 (CH₂), 32.4 (CH₂), 26.9 (CH₂), 26.4 (CH₂), 25.8 (CH₂), 23.6 (CH₂), 23.6 (CH₂), 22.9 (CH₂), 21.1 (CH₂); HRMS (EI) *m/z* calcd for C₂₂H₂₆O (M⁺) 306.1984, found 306. 2032.

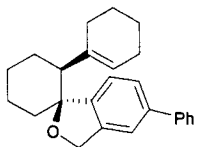
2'-(4-Phenyl-but-3-en-1-ynyl)-2'-prop-2-ynyloxy-bicyclohexyl-1-ene (2.21)



To a solution of **2.20** (1.041 g, 3.40 mmol) and propargyl bromide (0.38 mL, 5.10 mmol) in THF/DMF (9:3 mL) was added sodium hydride 60% in oil (0.204 g, 5.10 mmol) slowly at room temperature. The reaction was followed by TLC and quenched with NH_4Cl (sat. aq.) upon completion.

The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO_4 , filtered, and concentrated. Flash chromatography (5% ethyl acetate in hexanes) afforded **2.21** (0.972 g, 79%) as a yellow oil. IR (neat, cm^{-1}) 3303 (m), 3031 (w), 2931 (s), 2856 (m), 1447 (w), 1060 (m); ^1H NMR (CDCl_3 , 300 MHz) δ 7.41-7.27 (m, 5H), 6.93 (d, $J = 16.2$ Hz, 1H), 6.20 (d, $J = 16.2$ Hz, 1H), 5.67 (s, 2H), 4.35 (dd, $J_{\text{AB}} = 15.2$ Hz, $J_{\text{AX}} = 2.5$ Hz, 1H), 4.25 (dd, $J_{\text{AB}} = 15.2$ Hz, $J_{\text{BX}} = 2.5$ Hz, 1H), 2.42 (t, $J = 2.4$ Hz, 1H), 2.33-2.23 (m, 2H), 2.15-2.10 (m, 4H), 1.97 (qd, $J = 12.6, 3.3$ Hz, 1H), 1.82-1.78 (m, 1H), 1.70-1.58 (m, 5H), 1.54-1.46 (m, 3H), 1.40-1.27 (m, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 141.7 (CH), 139.3 (C_4), 136.7 (C_4), 129.1 (CH), 129.0 (CH), 126.6 (CH), 124.8 (CH), 108.3 (CH), 93.1 (C_4), 86.4 (C_4), 81.9 (C_4), 77.4 (CH), 73.4 (CH_2), 55.7 (CH), 52.5 (CH_2), 36.5 (CH_2), 28.5 (CH_2), 26.7 (CH_2), 26.5 (CH_2), 26.1 (CH_2), 23.9 (CH_2), 23.2 (CH_2), 21.3 (CH_2); HRMS (EI) m/z calcd for $\text{C}_{25}\text{H}_{28}\text{O}$ (M^+) 344.2140, found 344.2133.

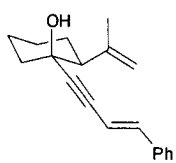
2-Cyclohex-1-enyl-5'-phenyl-3'H-spiro[cyclohexane-1,1'-isobenzofuran] (2.22)



To a solution of **2.21** (2.031 g, 5.90 mmol) in toluene (12 mL) in a microwave cell was added Et_3N (8.21 mL, 59.0 mmol). The solution was degassed with argon (20 minutes) and subsequently heated with microwaves at 160 $^\circ\text{C}$ for 1 hour. The solution was concentrated and flash

chromatography of the residue (50% benzene in hexanes) afforded **2.22** (0.381 g, 19%) as a yellow oil. IR (neat, cm^{-1}) 3033 (m), 2929 (s), 2854 (s), 1600 (w), 1480 (s), 1446 (s), 1052 (2), 1033 (s), 762 (s), 697 (s), 677 (s); ^1H NMR (CDCl_3 , 300 MHz) δ 7.59 (d, J = 6.8 Hz, 2H), 7.48-7.32 (m, 5H), 7.11 (d, J = 7.4 Hz, 1H), 5.38 (s, 1H), 5.09 (d, J_{AB} = 12.4 Hz, 1H), 5.02 (d, J_{AB} = 12.1 Hz, 1H), 2.14 (dd, J = 12.4, 2.5 Hz, 1H), 1.96 (qd, J = 13.0, 3.1 Hz), 1.90-1.15 (m, 15H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 144.5 (C_4), 141.2 (C_4), 140.4 (C_4), 138.8 (C_4), 138.5 (C_4), 128.7 (CH), 128.3 (CH), 127.1 (CH), 125.9 (CH), 123.9 (CH), 121.8 (CH), 119.2 (CH), 90.3 (C_4), 72.3 (CH_2), 53.7 (CH), 39.3 (CH_2), 29.3 (CH_2), 28.1 (CH_2), 26.4 (CH_2), 25.6 (CH_2), 23.4 (CH_2), 22.5 (CH_2), 22.4 (CH_2); HRMS (EI) m/z calcd for $\text{C}_{25}\text{H}_{28}\text{O}$ (M^+) 344.2140, found 344.2137.

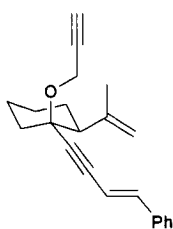
2-Isopropenyl-1-(4-phenyl-but-3-en-1-ynyl)-cyclohexanol (**2.23**)



To a solution of (4,4-Dibromo-buta-1,3-dienyl)-benzene **2.19** (2.546 g, 8.91 mmol) in THF (40 mL) at $-78\text{ }^{\circ}\text{C}$ was added $n\text{-BuLi}$ (7.42 mL, 17.8 mmol). The solution was stirred for 60 minutes at $-78\text{ }^{\circ}\text{C}$ and warmed to $-25\text{ }^{\circ}\text{C}$ for 30 minutes, allowing the formation of the alkynyl lithium *in situ*. The reaction was cooled back to $-78\text{ }^{\circ}\text{C}$ and a solution of **2.9** (1.172 g, 8.48 mmol) in diethyl ether (5 mL) was added *via* canula. The reaction was stirred for 60 minutes and quenched with NH_4Cl (sat. aq.). The mixture was extracted with ethyl acetate (3x) and the combined organic layers were dried over MgSO_4 , filtered, and concentrated. Flash chromatography (10% ethyl acetate in hexanes) afforded the major diastereoisomer (56:44) **2.23** (0.952 g, 42%) as a yellow oil. IR (neat, cm^{-1}) 3554 (m), 3464 (m), 2942 (s), 2559 (m), 1641 (m), 1442 (s), 1371 (m); ^1H NMR (CDCl_3 , 300 MHz) δ 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 (CDCl_3 , 75 MHz) δ 148.3 (C_4), 141.0 (CH), 136.1 (C_4), 128.6 (CH), 128.4 (CH), 126.1 (CH), 112.3 (CH_2), 107.7 (CH), 96.3 (C_4), 82.4 (C_4), 67.4 (C_4), 52.6 (CH), 39.6 (CH_2), 26.7 (CH_2), 26.0 (CH_3), 25.7 (CH_2), 20.6 (CH_2); HRMS (EI) m/z calcd for $\text{C}_{19}\text{H}_{22}\text{O}$ (M^+) 266.1671, found 266.1671.

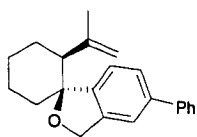
[4-(2-Isopropenyl-1-prop-2-ynyloxy-cyclohexyl)-but-1-en-3-ynyl]-benzene (2.24)



To a solution of **2.23** (0.952 g, 3.57 mmol) and allyl bromide (0.48 mL, 5.36 mmol) in THF/DMF (9:3 mL) was added sodium hydride 60% in oil (0.220 g, 5.36 mmol) slowly at room temperature. The reaction was followed by TLC and quenched with NH_4Cl (sat. aq.) upon completion.

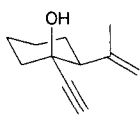
The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO_4 , filtered, and concentrated. Flash chromatography (40% benzene in hexanes) afforded **2.24** (0.793 g, 73%) as a yellow oil. IR (neat, cm^{-1}) 3299 (m), 3070 (w), 3029 (w), 2935 (s), 2857 (m), 1448 (m), 1062 (s); ^1H NMR (CDCl_3 , 300 MHz) δ 7.39-7.24 (m, 5H), 6.90 (d, $J = 16.3$ Hz, 1H), 6.18 (d, $J = 16.3$ Hz, 1H), 4.90 (s, 2H), 4.33 (dd, $J_{\text{AB}} = 14.9$ Hz, $J_{\text{AX}} = 2.5$ Hz, 1H), 4.22 (dd, $J_{\text{AB}} = 14.9$ Hz, $J_{\text{BX}} = 2.5$ Hz, 1H), 2.39 (t, $J = 2.4$ Hz, 1H), 2.32-2.23 (m, 2H), 1.94 (qd, $J = 13.0, 3.7$ Hz, 1H), 1.87 (s, 3H), 1.81-1.72 (m, 1H), 1.68-1.46 (m, 4H), 1.39-1.23 (m, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) 147.2 (C_4), 141.8 (CH), 136.6 (C_4), 129.1 (CH), 129.0 (CH), 126.6 (CH), 113.8 (CH_2), 108.1 (CH), 92.6 (C_4), 86.6 (C_4), 81.7 (C_4), 77.0 (CH), 73.5 (C_4), 54.9 (CH), 52.4 (CH_2), 36.4 (CH_2), 26.8 (CH_2), 26.2 (CH_2), 22.8 (CH_3), 21.2 (CH_2); HRMS (EI) m/z calcd for $\text{C}_{22}\text{H}_{24}\text{O}$ (M^+) 304.1827, found 304.1804.

2-Isopropenyl-6'-phenyl-3'H-spiro[cyclohexane-1,1'-isobenzofuran] (2.25)



Microwave version: To a solution of **2.24** (61.2 mg, 0.204 mmol) in toluene (12 mL) in a microwave cell was added Et₃N (0.28 mL, 2.04 mmol). The solution was degassed with argon (20 minutes) and subsequently heated with microwaves at 160 °C for 1 hour. The solution was concentrated and flash chromatography (5% ethyl acetate in hexanes) afforded **2.25** (31.1 mg, 51%) as off-white crystals. *Pressure tube version:* To a solution of **2.24** (65.1 mg, 0.214 mmol) in toluene (12 mL) in a dry pressure tube was added Et₃N (0.30 mL, 2.14 mmol). The solution was degassed using argon (20 minutes) and the tube was subsequently sealed and heated in a wax bath to 160 °C for 1 hour. The mixture was concentrated and flash chromatography of the residue (5% ethyl acetate in hexanes) afforded **2.25** (39.7 mg, 61%) as off-white crystals. IR (neat, cm⁻¹) 3308 (w), 3065 (w), 3032 (w), 2927 (s), 2854 (s), 1448 (m), 1052 (m), 1035 (m); ¹H NMR (CDCl₃, 300 MHz) δ 7.56 (d, J = 8.1 Hz, 2H), 7.47-7.38 (m, 3H), 7.34-7.28 (m, 2H), 7.12 (d, J = 8.1 Hz, 1H), 5.07 (s, 2H), 4.65 (s, 1H), 4.57 (s, 1H), 2.35 (dd, J = 12.6, 3.4 Hz, 1H), 1.97 (qd, J = 13.0, 3.7 Hz, 1H), 1.89-1.55 (m, 6H), 1.47 (s, 3H), 1.45-0.67 (m, 2H); ¹³C NMR (CDCl₃, 75 MHz) δ 147.4 (C₄), 144.7 (C₄), 141.4 (C₄), 140.9 (C₄), 140.1 (C₄), 129.1 (CH), 127.5 (CH), 126.5 (CH), 122.1 (CH), 119.9 (CH), 113.3 (CH₂), 90.4 (C₄), 72.3 (CH₂), 53.3 (CH), 39.8 (CH₂), 30.1 (CH₂), 28.9 (CH₂), 26.6 (CH₂), 23.4 (CH₃), 22.9 (CH₂); HRMS (EI) m/z calcd for C₂₂H₂₄O (M⁺) 304.1827, found 304.1807, m.p. 98.7-99.4 °C.

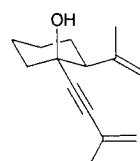
1-Ethynyl-2-isopropenyl-cyclohexanol (2.26)



To a solution of ketone **2.9** (1.055 g, 15.9 mmol) in THF (40 mL) at 0 °C was added dropwise ethynylmagnesium bromide (94.8 mL, 47.4 mmol).

The solution was warmed to room temperature and allowed to stir overnight. The reaction was quenched with NH₄Cl (sat. aq.) and the mixture was extracted with diethyl ether (3x). The combined organic layers were dried over MgSO₄, filtered, and concentrated. Flash chromatography (5% ethyl acetate in hexanes) afforded the major diastereoisomer (60:40) **2.26** as a yellow oil (2.421 g, 59%). IR (neat, cm⁻¹) 3548 (m), 3468 (br), 3307 (s), 3079 (w), 2938 (s), 2856 (s), 1639 (m), 1447 (m), 1071 (m), 972 (s); ¹H NMR (CDCl₃, 300 MHz) δ 4.95 (s, 1H), 4.79 (s, 1H), 2.37 (s, 1H), 2.23 (s, 1H), 2.18-2.08 (m, 2 H), 1.92 (s, 3H), 1.72-1.37 (m, 6H), 1.28-1.12 (m, 1H); ¹³C NMR (CDCl₃, 75 MHz) δ 148.4 (C₄), 112.8 (CH₂), 89.0 (C₄), 71.7 (CH), 67.4 (C₄), 52.8 (CH), 40.1 (CH₂), 27.0 (CH₂), 26.1 (CH₃), 26.1 (CH₂), 20.8 (CH₂); HRMS (EI) m/z calcd for C₁₁H₁₄ [(M-H₂O)⁺] 146.1095, found 146.1095.

2-Isopropenyl-1-(3-methyl-but-3-en-1-ynyl)-cyclohexanol (2.27)



2-bromo-propene (0.36 mL, 2.94 mmol), Pd(PPh₃)₄ (68.0 mg, 0.0590 mmol),

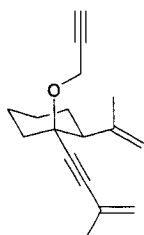
CuI (12.0 mg, 0.0590 mmol) and Et₃N (1.84 mL, 13.2 mmol) were dissolved

in THF and the solution was degassed with argon (20 minutes). Alcohol

2.26 was subsequently added (0.483 g, 2.94 mmol) at room temperature. The reaction was stirred overnight and concentrated. The residue was purified by flash chromatography (15% ethyl acetate in hexanes) to afford **2.27** (0.371 g, 62%). IR (neat, cm⁻¹) 3552 (br), 2467 (br), 3095 (w), 3080 (w), 2938 (s), 2855 (s), 1639 (m), 1615 (m),

1448 (m), 1373 (m), 1293 (m), 971 (m), 895 (m); ^1H NMR (CDCl_3 , 300 MHz) δ 5.20 (d, $J = 1.2$ Hz, 1H), 5.15 (t, $J = 1.9$ Hz, 1H), 4.97 (t, $J = 1.9$ Hz, 1H), 4.81 (s, 1H), 2.22-2.17 (m, 2H), 2.14-2.09 (m, 1H), 1.96 (s, 3H), 1.82 (t, $J = 1.4$ Hz, 3H), 1.74-1.39 (m, 6H), 1.29-1.16 (m, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 148.7 (C_4), 126.8 (C_4), 122.0 (CH_2), 122.6 (CH_2), 93.4 (C_4), 84.6 (C_4), 67.5 (C_4), 53.0 (CH), 39.9 (CH_2), 27.1 (CH_2), 26.3 (CH_3), 26.1 (CH_2), 23.7 (CH_3), 21.0 (CH_2); HRMS (EI) m/z calcd for $\text{C}_{14}\text{H}_{20}\text{O}$ (M^+) 204.1514, found 204.1514.

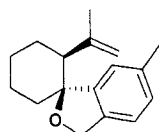
2-Isopropenyl-1-(3-methyl-but-3-en-1-ynyl)-1-prop-2-ynyloxy-cyclohexane (2.28)



To a solution of **2.27** (0.371 g, 1.80 mmol) and propargyl bromide (0.81 mL, 9.10 mmol) in THF/DMF (9:3 mL) was added sodium hydride 60% in oil (0.363 g, 9.10 mmol) slowly at room temperature. The reaction was followed by TLC and quenched with NH_4Cl (sat. aq.) upon completion. The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO_4 , filtered, and concentrated. Flash chromatography (20% benzene in hexanes) afforded **2.28** (389.2 mg, 89%) as a yellow oil. IR (neat, cm^{-1}) 3303 (m), 3095 (w), 3072 (w), 2936 (s), 2858 (m), 1063 (s); ^1H NMR (CDCl_3 , 300 MHz) δ 5.22 (s, 1H), 5.18 (s, 1H), 4.82 (s, 2H), 4.29 (dd, $J_{\text{AB}} = 15.2$ Hz, $J_{\text{AX}} = 2.5$ Hz, 1H), 4.21 (dd, $J_{\text{AB}} = 15.2$ Hz, $J_{\text{BX}} = 2.5$ Hz, 1H), 2.34 (s, 1H), 2.27-2.15 (m, 2H) 2.05-1.85 (m, 1H), 1.84 (s, 3H), 1.81 (s, 3H), 1.75-1.72 (m, 1H), 1.62-1.41 (m, 4H), 1.34-1.19 (m, 1H); ^{13}C NMR (CDCl_3 75 MHz) δ 146.7 (C_4), 128.3 (C_4), 126.5 (C_4), 121.6 (CH_2), 113.2 (CH_2), 89.0 (C_4), 81.3 (C_4), 76.3 (CH), 72.9 (C_4), 54.5 (CH), 52.0 (CH_2), 36.0 (CH_2), 26.4 (CH_2), 25.8

(CH₂), 23.4 (CH₃), 22.3 (CH₃), 20.8 (CH₂); HRMS (EI) m/z calcd for C₁₇H₂₂O (M⁺) 242.1671, found 242.1583.

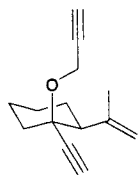
2-Isopropenyl-6'-methyl-3'H-spiro[cyclohexane-1,1'-isobenzofuran] (2.29)



To a solution of **2.28** (46.6 mg, 0.192 mmol) in toluene (12 mL) in a microwave cell was added Et₃N (0.27 mL, 1.92 mmol). The solution was degassed with argon (20 minutes) and subsequently heated with microwaves at 160 °C for 1 hour. The solution was concentrated and flash chromatography of the residue (5% ethyl acetate in hexanes) afforded **2.29** (42.7 mg, 92%) as a colourless oil. IR (neat, cm⁻¹) 3072 (w), 3011 (w), 2932 (s), 2856 (m), 1446 (m), 1029 (m); ¹H NMR (CDCl₃, 300 MHz) δ 7.01 (s, 2H), 6.86 (s, 1H), 4.97 (s, 2H), 4.58 (d, J = 20.6 Hz, 2H), 2.34 (s, 3H), 2.33-2.26 (dd, J = 13.0, 3.7 Hz, 1H), 1.94 (qd, J = 13.0, 3.1 Hz, 1H), 1.87-1.24 (m, 7H), 1.43 (s, 3H); ¹³C NMR (CDCl₃, 75 MHz) δ 147.5 (C₄), 145.7 (C₄), 136.7 (C₄), 136.3 (C₄), 128.5 (CH), 122.4 (CH), 120.9 (CH), 113.1 (CH₂), 90.3 (C₄), 72.2 (CH₂), 53.2 (CH), 39.8 (CH₂), 28.9 (CH₂), 26.6 (CH₂), 23.4 (CH₃), 22.9 (CH₂), 21.8 (CH₃); HRMS (EI) m/z calcd for C₁₇H₂₂O (M)⁺ 242.1671, found 242.1676.

4.3 Experimental Method and Data Relating to Compounds of Chapter 3

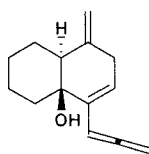
1-Ethynyl-2-isopropenyl-1-prop-2-ynyloxy-cyclohexane (3.3)



To a solution of **2.26** (2.545 g, 15.5 mmol) and propargyl bromide (5.16 mL, 46.0 mmol) in THF/DMF (9:3 mL) was added sodium hydride 60% in oil

(1.860 g, 46.0 mmol) slowly at room temperature. The reaction was followed by TLC and quenched with NH_4Cl (sat. aq.) upon completion. The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO_4 , filtered, and concentrated. Flash chromatography (5% ethyl acetate in hexanes) afforded **3.3** (2.568 g, 81%) as a yellow oil. IR (neat, cm^{-1}) 3303 (s), 3073 (m), 2934 (s), 2858 (s), 1641 (m), 1448 (m), 1376 (m), 1143 (m), 1094 (s), 1063 (s), 892 (s); ^1H NMR (CDCl_3) δ 4.81 (d, $J = 1.2$ Hz, 2H), 4.24 (dd, $J_{\text{AB}} = 15.2$ Hz, $J_{\text{AX}} = 2.5$ Hz, 1H), 4.13 (dd, $J_{\text{AB}} = 15.2$ Hz, $J_{\text{BX}} = 2.5$ Hz, 1H), 2.48 (s, 1H), 2.34 (t, $J = 2.5$ Hz, 1H), 2.25-2.12 (m, 2H), 1.86 (qd, $J = 12.4, 3.7$ Hz, 1H), 1.78 (s, 3H), 1.75-1.67 (m, 1H), 1.60-1.38 (m, 4H), 1.33-1.16 (m, 1H); ^{13}C NMR (CDCl_3) δ 146.6 (C_4), 113.5 (CH_2), 84.2 (C_4), 80.9 (C_4), 75.9 (C_4), 74.9 (CH), 73.1 (CH), 54.3 (CH), 51.9 (CH_2), 35.8 (CH_2), 26.2 (CH_2), 25.7 (CH_2), 22.1 (CH_3), 20.6 (CH_2); HRMS (EI) m/z calcd for $\text{C}_{14}\text{H}_{18}\text{O}$ (M^+) 202.1358, found 202.1348.

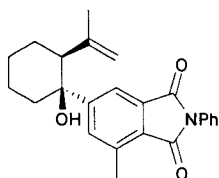
8-Methylene-5-propa-1,2-dienyl-1,3,4,7,8,8a-hexahydro-2H-naphthalen-4a-ol (**3.4**)



To a solution of **3.3** (160.7 mg, 0.795 mmol) in toluene (12 mL) in a microwave cell was added Et_3N (1.11 mL, 7.95 mmol). The solution was degassed with argon and subsequently heated with microwaves at 160 °C for 2 hours and at 165 °C for 1 hour. The solution was concentrated and flash chromatography of the residue (5% hexanes in benzene) afforded **3.4** (39.0 mg, 24%) as a yellowish oil. IR (neat, cm^{-1}) 3441 (br), 2932 (s), 2855 (m), 1954 (w), 1713 (w), 1687 (w), 1447 (m); ^1H NMR (CDCl_3) δ 5.80-5.75 (m, 2H), 4.93 (s, 1H), 4.90 (s, 1H), 4.88 (s, 1H), 4.74 (d, $J = 1.2$ Hz, 1H), 2.94 (d, $J_{\text{AB}} = 19.2$ Hz), 2.77 (dd, $J_{\text{AB}} = 19.2$ Hz, $J_{\text{AX}} = 5.0$ Hz), 2.23-2.19 (m, 2H), 1.82-1.22 (m, 8H); ^{13}C NMR δ 209.8 (C_4), 146.2 (C_4), 137.9

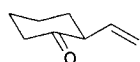
(C₄), 126.7 (CH), 108.8 (CH₂), 90.3 (CH), 77.0 (CH₂), 72.3 (C₄), 49.1 (CH), 36.6 (CH₂), 35.0 (CH₂), 26.0 (CH₂), 23.6 (CH₂), 21.5 (CH₂); HRMS (EI) m/z calcd for C₁₄H₁₈O (M⁺) 202.1358, found 202.1359.

6-(1-Hydroxy-2-isopropenyl-cyclohexyl)-4-methyl-2-phenyl-isoindole-1,3-dione (3.6)



To a solution of **3.3** (0.241 g, 1.20 mmol) in toluene (12 mL) in a microwave cell was added Et₃N (1.67 mL, 12.0 mmol) and N-phenylmaleimide (0.518 g, 3.0 mmoles). The solution was degassed with argon (20 minutes) and subsequently heated with microwaves at 160 °C for 2 hours and 20 minutes. The solution was concentrated and flash chromatography of the residue (15% ethyl acetate in hexanes) afforded **3.6** (98.6 mg, 26%) as a yellowish oil/foam. IR (neat, cm⁻¹) 3521 (br), 3074 (w), 2934 (m), 2857 (m), 1772 (m), 1712 (s), 1502 (m), 1376 (s), 1112 (m); ¹H NMR (CDCl₃) δ 7.84 (s, 1H), 7.62 (s, 1H), 7.50-7.31 (m, 5H), 4.725 (s, 1H), 4.70 (s, 1H), 2.70 (s, 3H), 2.54 (dd, J = 12.4, 3.7 Hz, 1H), 2.40 (s, 1H), 1.93-1.55 (m, 7H), 1.51-1.31 (m, 1H), 1.26 (s, 3H); ¹³C NMR (CDCl₃) δ 168.3 (C₄), 168.0 (C₄), 156.2 (C₄), 147.4 (C₄), 138.5 (C₄), 133.6 (CH), 132.5 (C₄), 132.2 (C₄), 129.4 (CH), 128.7 (CH), 128.3 (CH), 127.0 (CH), 126.9 (C₄), 118.9 (CH), 113.7 (CH₂), 75.2 (C₄), 53.4 (CH), 40.8 (CH₂), 28.2 (CH₂), 26.3 (CH₂), 25.3 (CH₃), 21.9 (CH₂), 18.4 (CH₃); HRMS (EI) m/z calcd for C₂₄H₂₃NO₂ [(M-H₂O)⁺] 357.1728, found 357.1728.

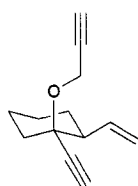
2-Vinyl-cyclohexanone (3.7)



A dry round bottom flask was charged with CuBr·DMS (1.256 g, 6.11 mmoles) and THF (150 mL). The solution was cooled to -30 °C, followed by the

addition of vinylmagnesium bromide (99.3 mL, 79.4 mmol). The mixture was stirred for 20 minutes, at which point cyclohexene oxide **2.7** (6.18 mL, 61.1 mmol) was added and the solution was stirred to room temperature. The reaction was followed by TLC and quenched with NH₄Cl (sat. aq.) upon completion. The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO₄, filtered, and concentrated. The residue was re-dissolved in diethyl ether (100 mL) and Jones' reagent (70.5 mL, 91.7 mmol) was slowly added at 0 °C. The reaction was allowed to reach room temperature. Upon completion, as observed by TLC analysis, the reaction was quenched with NH₄Cl (sat. aq.). The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO₄, filtered, and concentrated. Flash chromatography (15% ethyl acetate in hexanes) afforded **3.7** (3.210 g, 42%) as a yellow oil. Characterisation data is available through the literature.⁶⁴

1-Ethynyl-2-vinyl-cyclohexanol and 1-Ethynyl-1-prop-2-ynoxy-2-vinyl-cyclohexane (3.8 and 3.9)

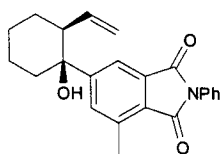


To a solution of ketone **3.7** (0.295 g, 23.7 mmol) in THF (10 mL) at 0 °C was added dropwise ethynylmagnesium bromide (9.50 mL, 47.5 mmol). The reaction was warmed to room temperature and followed to completion by TLC, at which point it was quenched with NH₄Cl (sat. aq.). The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO₄, filtered, and concentrated. Flash chromatography (15% ethyl acetate in hexanes) afforded the major diastereoisomer (57:33) **3.8** as a yellow oil (73.8 mg, 21%). To a solution of **3.8** (73.8 mg, 0.492 mmol) and propargyl bromide (0.11 mL, 0.983 mmol) in THF/DMF (3:1

⁶⁴ Sunggak, K.; Sangphil, L. *Tetrahedron Lett.* **1991**, *32*, 6575.

mL) was added sodium hydride 60% in oil (39.0 mg, 0.983 mmol) slowly at room temperature. The reaction was followed by TLC and quenched with NH_4Cl (sat. aq.) upon completion. The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO_4 , filtered, and concentrated. Flash chromatography (5% ethyl acetate in hexanes) afforded **3.9** (73.4 mg, 74%) as a yellow oil. IR (neat, cm^{-1}) 3298 (s), 3076 (w), 2938 (s), 2861 (m), 1640 (w), 1447 (w), 1079 (s), 1070 (s), 1052 (m), 915 (w); ^1H NMR (CDCl_3) δ 6.09-5.97 (m, 1H), 5.09 (s, 1H), 5.05 (m, 1H), 4.23 (q, $J = 1.2$ Hz, 2H), 2.51 (s, 1H), 2.36 (t, $J = 2.5$ Hz, 1H), 2.34-2.25 (m, 1H), 2.23-2.06 (m, 1H), 1.71-1.44 (m, 6H), 1.40-1.18 (m, 1H); ^{13}C (CDCl_3) δ 138.8 (CH), 116.1 (CH_2), 84.6 (C_4), 81.2 (C_4), 75.9 (C_4), 75.6 (CH), 73.7 (CH), 52.3 (CH_2), 50.3 (CH), 35.1 (CH_2), 27.8 (CH_2), 24.3 (CH_2), 21.5 (CH_2); HRMS (EI) m/z calcd for $\text{C}_{13}\text{H}_{16}\text{O}$ [(M- C_2H) $^+$] 163.1123, found 163.1149.

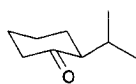
6-(1-Hydroxy-2-vinyl-cyclohexyl)-4-methyl-2-phenyl-isoindole-1,3-dione (**3.10**)



To a solution of **3.9** (63.5 mg, 0.338 mmol) in toluene (12 mL) in a microwave cell was added Et_3N (0.47 mL, 3.38 mmol) and N-phenylmaleimide (0.175 g, 1.01 mmol). The solution was degassed with argon and subsequently heated with microwaves at 165 $^\circ\text{C}$ for 3 hours. Reaction was not complete, but the solution was concentrated and flash chromatography of the residue (15% ethyl acetate in hexanes) afforded **3.10** (12.9 mg, 11%) as a yellow oil (56.3 mg, 89% of the starting material **3.9** was recovered). IR (neat, cm^{-1}) 3525 (br), 3072 (w), 3035 (w), 2929 (m), 2856 (s), 1772 (m), 1713 (s), 1502 (m), 1406 (m), 1374 (s), 1110 (m); ^1H NMR (CDCl_3) δ 7.84 (s, 1H), 7.66 (s, 1H), 7.53-7.44 (m, 2H), 7.43-7.33 (m, 3H),

5.57-5.45 (m, 1H), 5.02 (s, 1H), 4.98 (d, $J = 8.7$ Hz, 1H), 2.72 (s, 3H), 2.69-2.65 (m, 1H), 1.98-1.84 (m, 2H), 1.83-1.36 (m, 7H); ^{13}C NMR (CDCl_3) δ 168.2 (C_4), 168.0 (C_4), 156.1 (C_4), 138.7 (C_4), 138.0 (CH), 133.6 (CH), 132.8 (C_4), 132.2 (C_4), 129.4 (CH), 128.3 (CH), 127.0 (CH), 118.5 (CH), 117.8 (CH_2), 77.6 (C_4), 75.6 (C_4), 48.8 (CH), 40.6 (CH_2), 26.2 (CH_2), 25.7 (CH_2), 21.9 (CH_2), 18.4 (CH_3); HRMS (EI) m/z calcd for $\text{C}_{18}\text{H}_{24}\text{O}_3$ (M^+) 361.1678, found 361.1699.

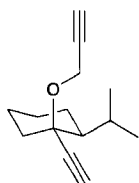
2-Isopropyl-cyclohexanone (3.11)



A dry round bottom flask was charged with $\text{CuBr}\cdot\text{DMS}$ (1.047 g, 5.10 mmol) and THF (50 mL). The solution was cooled to $-30\text{ }^\circ\text{C}$, followed by the addition of isopropylmagnesium bromide (132.5 mL, 66.3 mmol). The mixture was stirred for 20 minutes, at which point cyclohexene oxide **2.7** (5.15 mL, 51.0 mmol) was added and the solution was stirred to room temperature. The reaction was followed by TLC and quenched with NH_4Cl (sat. aq.) upon completion. The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO_4 , filtered, and concentrated. The residue was re-dissolved in diethyl ether (100 mL) and Jones' reagent (28.6 mL, 76.4 mmol) was slowly added at $0\text{ }^\circ\text{C}$. The reaction was allowed to reach room temperature. Upon completion, as observed by TLC analysis, the reaction was quenched with NH_4Cl (sat. aq.). The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO_4 , filtered, and concentrated. Flash chromatography (15% ethyl acetate in hexanes) afforded **3.11** (0.855 g, 12%) as a yellow oil. Characterisation data is available through the literature.⁶⁵

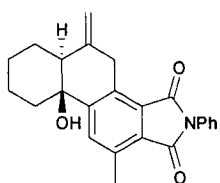
⁶⁵ Epstein, W. W.; Grua, J. R.; Gregonis, D. *J. Org. Chem.* **1982**, *47*, 1128.

1-Ethynyl-2-isopropyl-cyclohexanol and 1-Ethynyl-2-isopropyl-1-prop-2-ynyloxy-cyclohexane (3.12 and 3.13)



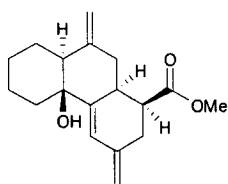
To a solution of ketone **3.11** (0.855 g, 6.10 mmol) in THF (20 mL) at 0 °C was added dropwise ethynylmagnesium bromide (24.4 mL, 12.2 mmol). The reaction was warmed to room temperature and followed to completion by TLC, at which point it was quenched with NH₄Cl (sat. aq.). The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO₄, filtered, and concentrated. Flash chromatography (15% ethyl acetate in hexanes) afforded the major diastereoisomer (75:15) **3.12** as a yellow oil (0.654 g, 65%). To a solution of **3.12** (0.654 g, 3.44 mmol) and propargyl bromide (1.15 mL, 10.3 mmol) in THF/DMF (9:3 mL) was added sodium hydride 60% in oil (0.413 g, 10.3 mmol) slowly at room temperature. The reaction was followed by TLC and quenched with NH₄Cl (sat. aq.) upon completion. The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO₄, filtered, and concentrated. Flash chromatography (5% ethyl acetate in hexanes) afforded **3.13** (0.441 g, 80%) as a colourless oil. IR (neat, cm⁻¹) 3306 (s), 2935 (s), 2868 (s), 1448 (m), 1370 (m), 1255 (m), 1148 (s), 1068 (s), 1046 (s), 930 (m); ¹H NMR (CDCl₃) δ 4.25 (dd, J_{AB} = 15.5 Hz, J_{AX} = 2.5 Hz, 1H), 4.12 (dd, J_{AB} = 15.5 Hz, J_{BX} = 2.5 Hz, 1H), 2.48 (s, 1H), 2.41-2.28 (m, 2H), 2.18 (d, J = 13.0 Hz, 1H), 1.79-1.68 (m, 1H), 1.60-1.30 (m, 5H), 1.26-1.09 (m, 2H), 0.91 (s, 3H), 0.88 (s, 3H); ¹³C NMR (CDCl₃) δ 85.3 (C₄), 81.5 (C₄), 78.1 (C₄), 74.9 (CH), 73.3 (CH), 52.0 (CH₂), 51.9 (CH), 36.5 (CH₂), 29.1 (CH), 26.4 (CH₂), 24.1 (CH₃), 21.4 (CH₂), 20.6 (CH₂), 18.8 (CH₃); HRMS (EI) m/z calcd for C₁₁H₁₃O [(M-(*i*-Pr))⁺] 161.0966, found 161.0961.

10-Hydroxy-12-methyl-6-methylene-16-phenyl-1,2,3,4,5,6,7,10-octahydro-16-azacyclopenta[a]phenanthrene-15,17-dione (3.14)



To a solution of **3.3** (51.1 mg, 0.253 mmol) in toluene (12 mL) in a microwave cell was added Et₃N (0.35 mL, 2.53 mmol). The solution was degassed with argon (20 minutes) and subsequently heated with microwaves at 165 °C for 4 hours. N-Phenylmaleimide (0.131 g, 0.758 mmol) was added and the solution was stirred overnight at room temperature. The reaction was quenched with NH₄Cl (sat. aq.) and the mixture was extracted with hexanes/ether (3x). The combined organic layers were dried over MgSO₄, filtered, and concentrated. Flash chromatography (25% ethyl acetate in hexanes) afforded **3.14** (26.7 mg, 28%) as a yellow oil. IR (neat, cm⁻¹) 3519 (br), 2931 (w), 2858 (w), 1764 (2), 1712 (s), 1501 (2), 1375 (m), 1114 (w); ¹H NMR (CDCl₃) δ 7.69 (s, 1H), 7.52-7.42 (m, 2H), 7.41-7.29 (m, 3H), 5.20 (s, 1H), 4.95 (s, 1H), 4.15 (d, J_{AB} = 19.8 Hz, 1H), 3.85 (d, J_{AB} = 19.8 Hz, 1H), 2.68 (s, 3H), 2.67-2.64 (m, 1H), 2.43 (d, J = 11.8 Hz, 1H), 1.91-1.46 (m, 8H); ¹³C NMR (CDCl₃) δ 168.1 (C₄), 149.6 (C₄), 144.5 (C₄), 136.5 (C₄), 134.6 (CH), 134.3 (C₄), 132.1 (C₄), 129.5 (C₄), 129.4 (CH), 128.5 (C₄), 128.3 (CH), 127.1 (CH), 126.4 (C₄), 111.3 (CH₂), 71.4 (C₄), 48.0 (CH), 36.5 (CH₂), 36.1 (CH₂), 25.5 (CH₂), 23.9 (CH₂), 21.9 (CH₂), 18.1 (CH₃); HRMS (EI) m/z calcd for C₂₃H₂₀NO₃ [(M-CH₃)⁺] 358.1443, found 358.1432.

4b-Hydroxy-3,9-dimethylene-1,2,3,4b,5,6,7,8,8a,9,10,10a-dodecahydrophenanthrene-1-carboxylic acid methyl ester (3.15) Method A and B.



Method A: To a solution of **3.3** (51.1 mg, 0.253 mmol) in toluene (12 mL) in a microwave cell was added Et₃N (0.35 mL, 2.53 mmol). The

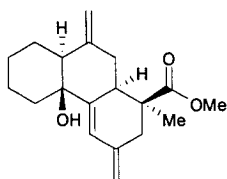
solution was degassed with argon (20 minutes) and subsequently heated with microwaves at 165 °C for 4 hours. The solution was cooled to -78 °C and vinylmagnesium bromide (0.29 mL, 0.253 mmol) was added dropwise. The solution was stirred for 20 minutes, methyl acrylate (68 µL, 0.759 mmol) was added, and the reaction was stirred overnight at room temperature. The reaction was quenched with NH₄Cl (sat. aq.) and the mixture was extracted with hexanes/ether (3x). The combined organic layers were dried over MgSO₄, filtered, and concentrated. Flash chromatography (15% ethyl acetate in hexanes) afforded **3.15** (25.6 mg, 35%) as a yellow oil. **Method B:** To a solution of **3.3** (48.1 mg, 0.238 mmol) in toluene (12 mL) in a microwave cell was added Et₃N (0.33 mL, 2.38 mmol). The solution was degassed with argon (20 minutes) and subsequently heated with microwaves at 200 °C for 2 hours. The solution was concentrated and the resulting residue re-dissolved in DCM (2 mL). In a separate flask, lutidine (0.11 mL, 0.952 mmoles) was added to a solution of MgBr₂·OEt₂ (0.123 g, 0.476 mmoles) in DCM (4 mL). The solution was stirred for 30 minutes and **3.4** was cannulated into the flask. The solution was stirred for 2 hours at room temperature and methyl acrylate (0.14 mL, 1.19 mmoles) was added. The reaction was stirred overnight and quenched with NH₄Cl (sat. aq.). The mixture was extracted with DCM (3x) and the combined organic layers were dried over MgSO₄, filtered, and concentrated. Flash chromatography (10% ethyl acetate in hexanes) afforded **3.15** (25.2 mg, 35%) as a yellow oil. IR (neat, cm⁻¹) 3517 (br), 3079 (w), 2931 (s), 2856 (m), 1737 (s), 1644 (m), 1608 (w), 1437 (m), 1276 (m), 1203 (m), 1165 (m), 891 (m); ¹H NMR (CDCl₃, 300 MHz) δ 6.42 (s, 1H), 4.89 (s, 1H), 4.85 (s, 2H), 4.71 (s, 1H), 3.69 (s, 3H), 2.96 (quint., J = 6.2 Hz, 1H), 2.84 (quint., J = 5.6 Hz, 1H), 2.48-2.11 (m, 6H), 1.90-1.40 (m, 8H); ¹³C NMR (CDCl₃, 75 Hz) δ 174.4 (C₄), 150.2 (C₄),

146.4 (C₄), 141.5 (C₄), 125.3 (CH), 113.0 (CH₂), 110.1 (CH₂), 73.0 (C₄), 52.0 (CH₃), 46.9 (CH), 42.4 (CH), 37.3 (CH₂), 33.5 (CH₂), 33.0 (CH), 28.5 (CH₂), 26.1 (CH₂), 23.0 (CH₂), 21.8 (CH₂); HRMS (EI) m/z calcd for C₁₈H₂₂O₂ [(M-H₂O)⁺] 270.1620, found 270.1565.

4.3.1 General Method for the Tandem Oxy-Cope/Claisen/Ene/HDDA Reaction

Below is one example of the MgBr₂·OEt₂/base method, as applied to compound 3.3. For the following 3.3, 3.24, 3.32 and 3.40 cycloadducts, only the number of equivalents of MgBr₂·OEt₂, base and dienophile are indicated (along with the base and dienophile used).

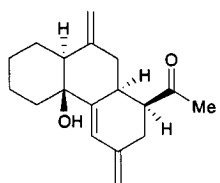
4b-Hydroxy-1-methyl-3,9-dimethylene-1,2,3,4b,5,6,7,8,8a,9,10,10a-dodecahydrophenanthrene-1-carboxylic acid methyl ester (3.16)



To a solution of **3.3** (27.4 mg, 0.136 mmol) in toluene (12 mL) in a microwave cell was added Et₃N (0.19 mL, 1.36 mmol). The solution was degassed with argon (20 minutes) and subsequently heated with microwaves at 200 °C for 2 hours, at which point it was concentrated and the resulting residue was re-dissolved in DCM (2 mL). In a separate flask, triethylamine (76 µL, 0.544 mmoles) was added to a solution of MgBr₂·OEt₂ (70.2 g, 0.272 mmoles) in DCM (4 mL). The solution was stirred for 30 minutes and **3.4** was cannulated into the flask. The solution was stirred for an additional 2 hours at room temperature and methyl methacrylate (50 µL, 0.408 mmoles) was added. The reaction was stirred overnight and quenched with NH₄Cl (sat. aq.). The mixture was extracted with DCM (3x) and the combined organic layers were dried over MgSO₄, filtered, and concentrated. Flash chromatography (5% ethyl acetate in hexanes) afforded **3.16** (16.8 mg, 41%) as a yellow

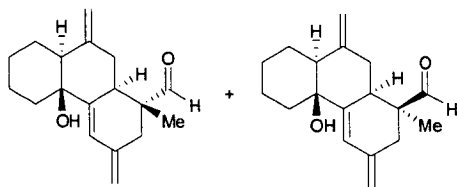
oil. IR (neat, cm^{-1}) 3524 (br), 3078 (w), 2933 (s), 2857 (m), 1732 (s), 1644 (m), 1435 (m), 1255 (m), 1236 (m), 1109 (m), 891 (m); ^1H NMR (CDCl_3 , 300 MHz) δ 6.38 (s, 1H), 4.93 (s, 1H), 4.88 (s, 1H), 4.82 (s, 1H), 4.68 (s, 1H), 3.67 (s, 3H), 2.58-2.50 (m, 2H), 2.46-2.36 (m, 2H), 2.19 (d, $J = 14.9$ Hz, 1H), 2.15-2.04 (m, 1H), 1.86-1.25 (m, 9H), 1.16 (s, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 148.3 (C_4), 146.1 (C_4), 140.3 (C_4), 123.6 (CH), 113.5 (CH_2), 109.1 (CH_2), 76.4 (C_4), 72.4 (C_4), 51.5 (CH_3), 46.4 (CH), 43.7 (C_4), 39.7 (CH), 36.5 (CH_2), 34.8 (CH_2), 34.2 (CH_2), 25.5 (CH_2), 23.1 (CH_3), 22.4 (CH_2), 21.2 (CH_2); HRMS (EI) m/z calcd for $\text{C}_{19}\text{H}_{26}\text{O}_3$ (M^+) 302.1882, found 302.1863.

1-(4b-Hydroxy-3,9-dimethylene-1,2,3,4b,5,6,7,8,8a,9,10,10a-dodecahydro-phenanthren-1-yl)-ethanone (3.17)



2.0 equivalents of $\text{MgBr}_2 \cdot \text{OEt}_2$, along with 4.0 equivalents of lutidine were used; 2.5 equivalents of methyl vinyl ketone were added. Flash chromatography (15% ethyl acetate in hexanes) afforded **3.17** (31.0 mg, 49%) as a yellow oil. IR (neat, cm^{-1}) 3498 (br), 3078 (w), 2931 (s), 2856 (m), 1709 (s), 1644 (m), 1608 (w), 1436 (m), 1355 (m), 971 (m), 888 (s); ^1H NMR (CDCl_3 , 300 MHz) δ 6.43 (s, 1H), 4.88 (s, 1H), 4.85-4.83 (m, 2H), 4.71 (s, 1H), 2.99 (quint., $J = 6.2$ Hz, 1H), 2.89 (quint., $J = 5.6$ Hz, 1H), 2.44 (d, $J = 9.9$ Hz, 1H) 2.39-2.08 (m, 4H), 2.18 (s, 3H), 1.91-1.25 (m, 9 H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 209.4 (C_4), 149.7 (C_4), 145.7 (C_4), 141.3 (C_4), 125.2 (CH), 112.6 (CH_2), 109.9 (CH_2), 72.6 (C_4), 49.9 (CH), 46.6 (CH), 37.0 (CH_2), 32.9 (CH_2), 32.5 (CH), 28.8 (CH_3), 27.6 (CH_2), 25.7 (CH_2), 22.6 (CH_2), 21.4 (CH_2); HRMS (EI) m/z calcd for $\text{C}_{18}\text{H}_{24}\text{O}_2$ (M^+) 272.1776, found 272.1813.

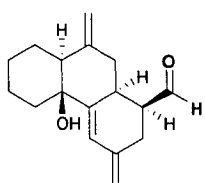
4b-Hydroxy-1-methyl-3,9-dimethylene-1,2,3,4b,5,6,7,8,8a,9,10,10a-dodecahydro-phenanthrene-1-carbaldehyde and 4b-Hydroxy-2-methyl-3,9-dimethylene-1,2,3,4b,5,6,7,8,8a,9,10,10a-dodecahydro-phenanthrene-2-carbaldehyde (3.18a and 3.18b)



2.0 equivalents of $\text{MgBr}_2 \cdot \text{OEt}_2$, along with 4.0 equivalents of lutidine were used; 3.0 equivalents of methacrolein were added. Flash chromatography

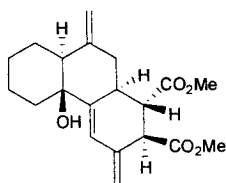
(15% ethyl acetate in hexanes) afforded **3.18** as two stereoisomers (**3.18a**, 4.1 mg; **3.18b**, 4.9 mg, 30%) as yellow oils. **3.18a**: IR (neat, cm^{-1}) 3466 (br), 2931 (s), 2853 (m), 2736 (w), 1720 (s), 1641 (m), 1452 (m), 949 (w), 885 (m); ^1H NMR (CDCl_3 , 300 MHz) δ 9.58 (s, 1H), 6.44 (s, 1H), 4.95 (s, 1H), 4.91 (s, 1H), 4.87 (s, 1H), 4.77 (s, 1H), 2.61-2.44 (m, 3H), 2.34-2.28 (m, 1H), 2.23 (s, 1H), 2.03-1.99 (m, 1H), 1.85-1.78 (m, 1H), 1.73-1.24 (m, 8H), 1.09 (s, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 205.3 (CH), 146.8 (C_4), 146.0 (C_4), 139.3 (C_4), 124.6 (CH), 114.0 (CH_2), 109.6 (CH_2), 71.6 (C_4), 47.4 (C_4), 45.1 (CH), 39.1 (CH), 36.8 (CH_2), 35.9 (CH_2), 32.3 (CH_2), 25.3 (CH_2), 23.4 (CH_2), 21.3 (CH_2), 20.2 (CH_3); HRMS (EI) m/z calcd for $\text{C}_{18}\text{H}_{24}\text{O}_2$ (M^+) 272.1776, found 272.1772. **3.18b**: IR (neat, cm^{-1}) 3455 (br), 2929 (s), 2853 (m), 1723 (s), 1646 (m), 1451 (w), 884 (m); ^1H NMR (CDCl_3 , 300 MHz) δ 9.64 (s, 1H), 6.17 (s, 1H), 5.00 (s, 1H), 4.95 (s, 1H), 4.94 (s, 1H), 4.76 (s, 1H), 2.68 (dd, $J = 13.7, 3.7$ Hz, 1H), 2.48 (d, $J = 14.9$ Hz, 1H), 2.35 (dd, $J = 12.4, 4.3$ Hz, 1H), 2.13 (d, $J = 14.9$ Hz, 1H), 2.00-1.90 (m, 3H), 1.84-1.49 (m, 8H), 1.04 (s, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 205.5 (CH), 147.3 (C_4), 144.8 (C_4), 139.6 (C_4), 120.9 (CH), 114.5 (CH_2), 110.4 (CH_2), 72.6 (C_4), 50.3 (CH), 47.5 (C_4), 41.5 (CH), 39.6 (CH_2), 34.0 (CH_2), 33.4 (CH_2), 25.3 (CH_2), 24.0 (CH_2), 21.1 (CH_2), 19.9 (CH_3); HRMS (EI) m/z calcd for $\text{C}_{18}\text{H}_{24}\text{O}_2$ (M^+) 272.1776, found 272.1769.

4b-Hydroxy-3,9-dimethylene-1,2,3,4b,5,6,7,8,8a,9,10,10a-dodecahydro-phenanthrene-1-carbaldehyde (3.19)



2.0 equivalents of $\text{MgBr}_2 \cdot \text{OEt}_2$, along with 4.0 equivalents of lutidine were used; 10.0 equivalents of acrolein were added. Flash chromatography (15% ethyl acetate in hexanes) afforded **3.19** (17.6 mg, 39%) as a yellow oil. IR (neat, cm^{-1}) 3476 (br), 2931 (s), 2854 (m), 2718 (w), 1721 (s), 1642 (m), 1445 (m), 1073 (m), 890 (m); ^1H NMR (CDCl_3 , 300 MHz) δ 9.75 (d, $J = 1.2$ Hz, 1H), 6.44 (d, $J = 1.9$ Hz, 1H), 4.93 (s, 1H), 4.91 (s, 1H), 4.88-4.87 (m, 1H), 4.78-4.77 (m, 1H), 3.02 (quint., $J = 6.8$ Hz, 1H), 2.76-2.69 (m, 1H), 2.55-2.29 (m, 4H), 1.99 (d, $J = 13.0$ Hz, 1H), 1.84-1.41 (m, 8H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 203.6 (CH), 148.1 (C_4), 145.8 (C_4), 139.9 (C_4), 125.1 (CH), 113.4 (CH_2), 109.7 (CH_2), 71.8 (C_4), 49.1 (CH), 45.4 (CH), 36.7 (CH_2), 33.1 (CH_2), 32.1 (CH), 27.8 (CH_2), 25.3 (CH_2), 23.2 (CH_2), 21.2 (CH_2); HRMS (EI) m/z calcd for $\text{C}_{17}\text{H}_{22}\text{O}_2$ (M^+) 258.1620, found 258.1634.

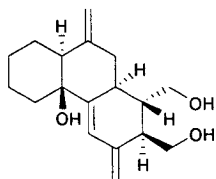
4b-Hydroxy-3,9-dimethylene-1,2,3,4b,5,6,7,8,8a,9,10,10a-dodecahydro-phenanthrene-1,2-dicarboxylic acid dimethyl ester (3.20)



3.0 equivalents of $\text{MgBr}_2 \cdot \text{OEt}_2$, along with 6.0 equivalents of lutidine were used; 10.0 equivalents of dimethyl fumarate were added. Flash chromatography (10% ethyl acetate in hexanes) afforded **3.20** (18.1 mg, 34%) as a yellow oil. IR (neat, cm^{-1}) 3535 (br), 3084 (w), 2931 (m), 2855 (w), 1739 (s), 1643 (w), 1436 (m), 1280 (m), 1260 (m), 1225 (m), 1165 (m), 894 (m); ^1H NMR (CDCl_3 , 300 MHz) δ 6.41 (s, 1H), 5.03 (d, $J = 2.5$ Hz, 1H), 4.91 (s, 1H), 4.81 (s, 2H), 3.72 (s, 3H), 3.70 (s, 3H), 3.59-3.53 (m, 1H), 2.78-2.64 (m, 3H), 2.30-2.17 (m, 2H), 2.10-2.02 (m, 1H), 1.84-1.69 (m, 2H), 1.66-1.29 (m, 6H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 174.8

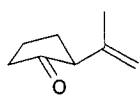
(C₄), 173.1 (C₄), 147.4 (C₄), 145.8 (C₄), 139.6 (C₄), 125.3 (CH), 113.6 (CH₂), 110.3 (CH₂), 71.3 (C₄), 52.5 (CH₃), 52.4 (CH₃), 50.0 (CH), 48.5 (CH), 44.9 (CH), 38.6 (CH₂), 35.8 (CH₂), 35.5 (CH), 25.6 (CH₂), 24.1 (CH₂), 22.0 (CH₂); HRMS (EI) m/z calcd for C₂₀H₂₄O₄ [(M- H₂O)⁺] 328.1675, found 328.1668.

7,8-Bis-hydroxymethyl-6,10-dimethylene-1,3,4,6,7,8,8a,9,10,10a-decahydro-2H-phenanthren-4a-ol (3.20b)



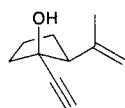
To a solution of **3.20** (32.6 mg, 0.0942 mmoles) in THF (5 mL) at -78 °C was added DIBAL-H (0.38 mL, 0.565 mmoles). The solution was stirred at for 30 minutes at -78 °C, for 30 minutes at 0 °C, for 60 minutes at room temperature. The reaction was quenched with a 1M solution of sodium tartrate and stirred overnight. The mixture was extracted with ethyl acetate (3x), and the combined organic layers were dried over MgSO₄, filtered, and concentrated. Flash chromatography (40% ethyl acetate in hexanes) afforded **3.20b** as a yellow oil. IR (neat, cm⁻¹) 3390 (br), 2929 (s), 2850 (m), 1707 (m), 1651 (m), 1447 (m), 1034 (m), 890 (w); ¹H NMR (CDCl₃; 300 MHz) δ 6.37 (d, J = 1.9 Hz, 1H), 4.99 (s, 1H), 4.93 (s, 1H), 4.87 (s, 1H), 4.74 (s, 1H), 3.43-3.57 (m, 4H), 2.84-2.74 (m, 1H), 2.58 (quint., J = 6.8 Hz, 1H), 2.44 (q, J = 6.2 Hz, 1H), 2.36 (t, J = 7.4 Hz, 1H), 2.15-1.22 (m, 13H); ¹³C NMR (CDCl₃, 75 MHz) δ 149.0 (C₄), 146.5 (C₄), 142.6 (C₄), 124.6 (CH), 112.3 (CH₂), 109.2 (CH₂), 71.9 (C₄), 63.9 (CH₂), 63.1 (CH₂), 45.7 (CH), 43.3 (CH), 43.3 (CH), 38.0 (CH₂), 37.4 (CH₂), 32.3 (CH), 25.5 (CH₂), 22.8 (CH₂), 21.6 (CH₂); HRMS (EI) m/z calcd for C₁₈H₂₄O₂ [(M-H₂O)⁺] 272.1776, found 272.1738.

2-Isopropenyl-cyclopentanone (3.22)



A dry round bottom flask was charged with CuBr·DMS (0.733 g, 3.57 mmoles) and THF (100 mL). The solution was cooled to -30 °C, followed by the addition of isopropenylmagnesium bromide (92.7 mL, 46.4 mmoles). The mixture was stirred for 20 minutes, at which point cyclopentene oxide **3.21** (3.11 mL, 36.0 mmoles) was added and the solution was stirred to room temperature. The reaction was followed by TLC and quenched with NH₄Cl (sat. aq.) upon completion. The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO₄, filtered, and concentrated. The residue was re-dissolved in diethyl ether (50 mL) and Jones' reagent (20.6 mL, 53.5 mmoles) was slowly added at 0 °C. The reaction was allowed to reach room temperature. Upon completion, as observed by TLC analysis, the reaction was quenched with NH₄Cl (sat. aq.). The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO₄, filtered, and concentrated. Flash chromatography (15% ethyl acetate in hexanes) afforded **3.22** (2.145 g, 48%) as a yellow oil. Characterisation data is available through the literature.⁶⁶

1-Ethynyl-2-isopropenyl-cyclopentanol (3.23)

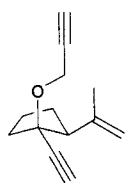


To a solution of ketone **3.22** (2.145 g, 17.3 mmol) in THF (40 mL) at 0 °C was added dropwise ethynylmagnesium bromide (69.1 mL, 34.6 mmol). The reaction was warmed to room temperature and stirred until completion by TLC, at which point it was quenched with NH₄Cl (sat. aq.). The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO₄, filtered, and

⁶⁶ Sate, T.; Takezoe, K. *Tetrahedron Lett.* **1991**, 32, 4003.

concentrated. Flash chromatography (10% ethyl acetate in hexanes) afforded the major diastereoisomer (66:34) **3.23** as a yellow oil (0.989 g, 38%). IR (neat, cm^{-1}) 3496 (br), 3305 (s), 3085 (w), 2969 (s), 2923 (m), 2875 (m), 1640 (m), 1450 (m), 1376 (m), 1019 (m), 896 (m), 649 (m); ^1H NMR (CDCl_3 , 300 MHz) δ 5.03 (s, 1H), 4.89 (s, 1H), 2.60 (m, 1H), 2.41 (s, 1H), 2.19-1.97 (m, 3H), 1.92 (s, 3H), 1.85-1.53 (m, 4H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 143.9 (C_4), 113.5 (CH), 87.9 (C_4), 73.2 (C_4), 71.8 (CH), 57.9 (CH), 42.2 (CH_2), 28.4 (CH_2), 25.2 (CH_3), 21.8 (CH_2); HRMS (EI) m/z calcd for $\text{C}_{10}\text{H}_{14}\text{O}$ (M^+) 150.1045, found 150.1016.

1-Ethynyl-2-isopropenyl-1-prop-2-ynyloxy-cyclopentane (**3.24**)

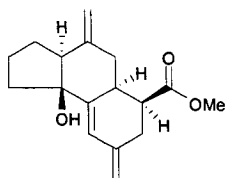


To a solution of **3.23** (2.070 g, 13.8 mmol) and propargyl bromide (4.61 mL, 41.4 mmol) in THF/DMF (30:10 mL) was added sodium hydride 60% in oil (1.656 g, 41.4 mmol) slowly at room temperature. The reaction was followed by TLC and quenched with a saturated aqueous solution of NH_4Cl upon completion. The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO_4 , filtered, and concentrated. Flash chromatography (5% ethyl acetate in hexanes) afforded **3.24** (2.234 g, 86%) as a yellow oil. IR (neat, cm^{-1}) 3297 (s), 3076 (w), 2970 (s), 2875 (m), 1640 (m), 1451 (m), 1375 (m), 1185 (m), 1065 (s), 894 (s); ^1H NMR (CDCl_3 , 300 MHz) 4.88-4.86 (m, 2H), 4.25 (dd, $J_{\text{AB}} = 15.5$ Hz, $J_{\text{AX}} = 25$ Hz, 1H), 4.16 (dd, $J_{\text{AB}} = 15.5$ Hz, $J_{\text{BX}} = 2.5$ Hz, 1H), 2.62-2.54 (m, 1H), 2.54 (s, 1H), 2.33 (t, $J = 2.5$ Hz, 1H), 2.32-2.24 (m, 1H), 2.03-1.86 (m, 2H), 1.85 (s, 3H), 1.83-1.56 (m, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 143.7 (C_4), 113.7 (CH_2), 84.2 (C_4), 82.6 (C_4), 81.4 (C_4), 75.2

(CH), 73.7 (CH), 58.3 (CH), 53.3 (CH₂), 38.9 (CH₂), 28.1 (CH₂), 23.0 (CH₃), 21.6 (CH₂);

HRMS (EI) *m/z* calcd for C₁₃H₁₆O (M⁺) 188.1201, found 188.1117.

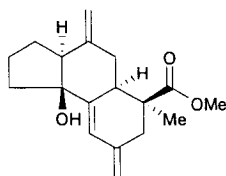
9b-Hydroxy-4,8-dimethylene-2,3,3a,4,5,5a,6,7,8,9b-decahydro-1H-cyclopenta[a]naphthalene-6-carboxylic acid methyl ester (3.25)



2.0 equivalents of MgBr₂·OEt₂, along with 4.0 equivalents of triethylamine were used; 5.0 equivalents of methyl acrylate were added. Flash chromatography (10% ethyl acetate in hexanes) afforded

3.25 (36.6 mg, 47%) as a colorless oil. IR (neat, cm⁻¹) 3490 (m, br), 3080 (w), 2952 (s), 2870 (m), 1729 (s), 1647 (m), 1429 (m), 1196 (s), 1172 (s), 882 (m); ¹H NMR (CDCl₃, 300 MHz) δ 6.21 (s, 1H), 4.93 (s, 1H), 4.90 (s, 1H), 4.85 (s, 1H), 4.77 (s, 1H), 3.61 (s, 3H), 2.93-2.89 (m, 1H), 2.78-2.60 (m, 4H), 2.46-2.37 (m, 2H), 2.18 (br. s, 1H), 2.10-1.71 (m, 6H); ¹³C NMR (CDCl₃, 75 MHz) δ 173.6 (C₄), 146.7 (C₄), 143.3 (C₄), 140.0 (C₄), 124.3 (CH), 113.4 (CH₂), 109.5 (CH₂), 80.5 (C₄), 51.5 (CH₃), 49.4 (CH), 43.1 (CH), 36.0 (CH), 35.9 (CH₂), 34.4 (CH₂), 33.4 (CH₂), 25.6 (CH₂), 21.3 (CH₂); HRMS (EI) *m/z* calcd for C₁₇H₂₂O₃ (M⁺) 274.1569, found 274.1583.

9b-Hydroxy-6-methyl-4,8-dimethylene-2,3,3a,4,5,5a,6,7,8,9b-decahydro-1H-cyclopenta[a]naphthalene-6-carboxylic acid methyl ester (3.26)

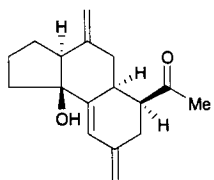


2.0 equivalents of MgBr₂·OEt₂, along with 4.0 equivalents of lutidine were used; 3.0 equivalents of methyl methacrylate were added. Flash chromatography (12% ethyl acetate in hexanes) afforded **3.26** (17.9

mg, 32%) as a white powder. IR (neat, cm⁻¹) 3503 (br, w), 3075 (w), 2966 (m), 2950 (m), 2871 (m), 2836 (m), 1716 (s), 1643 (m), 1436 (m), 1200 (s), 1123 (m), 923 (m); ¹H

NMR (CDCl₃, 300 MHz) δ 6.17 (s, 1H), 4.91 (s, 1H), 4.87 (s, 1H), 4.80 (s, 1H), 4.78 (s, 1H), 3.58 (s, 3H), 2.84 (t, J = 13.3 Hz, 1H), 2.73 (d, J = 15.5 Hz, 1H), 2.62-2.47 (m, 2 H), 2.42-2.33 (m, 3H), 2.09-1.90 (m, 3H), 1.84-1.72 (m, 3H), 1.32 (s, 3H); ¹³C NMR (CDCl₃, 75 MHz) δ 175.6 (C₄), 147.0 (C₄), 144.3 (C₄), 140.7 (C₄), 124.2 (CH), 112.6 (CH₂), 109.5 (CH₂), 80.6 (C₄), 51.8 (CH₃), 49.3 (CH), 46.4 (C₄), 44.0 (CH₂), 43.2 (CH), 36.0 (CH₂), 30.2 (CH₂), 25.7 (CH₂), 24.1 (CH₃), 21.4 (CH₂); HRMS (EI) m/z calcd for C₁₈H₂₄O₃ (M⁺) 288.1725, found 288.1738; m.p. 112.2-113.4 °C.

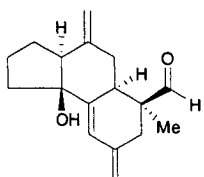
1-(9b-Hydroxy-4,8-dimethylene-2,3,3a,4,5,5a,6,7,8,9b-decahydro-1H-cyclopenta[a]naphthalen-6-yl)-ethanone (3.27)



2.0 equivalents of MgBr₂·OEt₂, along with 4.0 equivalents of lutidine were used; 5.0 equivalents of methyl vinyl ketone were added. Flash chromatography (15% ethyl acetate in hexanes) afforded **3.27** (17.1 mg, 39%) as a yellow oil.

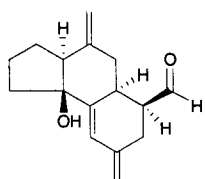
IR (neat, cm⁻¹) 3486 (br, m), 2986 (w), 2945 (m), 2859 (m), 1700 (s), 1644 (m), 1361 (m), 1160 (m), 884 (m); ¹H NMR (CDCl₃, 300 MHz) δ 6.14 (s, 1H), 4.91 (s, 1H), 4.87 (s, 1H), 4.84 (s, 1H), 4.77 (s, 1H), 2.98-2.94 (m, 1H), 2.79-2.74 (m, 4H), 2.58 (s, 1H), 2.45-2.36 (m, 1H), 2.31 (d, J = 11.2 Hz, 1H), 2.11 (s, 3H), 2.06-1.91 (m, 3H), 1.84-1.69 (m, 3H); ¹³C NMR (CDCl₃, 75 MHz) δ 209.6 (C₄), 146.8 (C₄), 144.3 (C₄), 139.7 (C₄), 123.7 (CH), 113.5 (CH₂), 109.5 (CH₂), 80.5 (C₄), 50.9 (CH), 49.4 (CH), 36.0 (CH), 35.8 (CH₂), 32.9 (CH₂), 28.8 (CH₂), 25.6 (CH₃), 21.3 (CH₂); HRMS (EI) m/z calcd for C₁₇H₂₂O₂ (M⁺) 258.1620, found 258.1620.

9b-Hydroxy-6-methyl-4,8-dimethylene-2,3,3a,4,5,5a,6,7,8,9b-decahydro-1H-cyclopenta[a]naphthalene-6-carbaldehyde (3.28)



2.0 equivalents of $\text{MgBr}_2 \cdot \text{OEt}_2$, along with 4.0 equivalents of lutidine were used; 5.0 equivalents of methacrolein were added. Flash chromatography (10% ethyl acetate in hexanes) afforded **3.28** (17.8 mg, 24%) as a yellow oil. IR (neat, cm^{-1}) 3456 (br), 3076 (2), 2964 (s), 2872 (m), 2736 (w), 1719 (s), 1645 (m), 1445 (m), 1374 (m), 1158 (m), 884 (m); ^1H NMR (CDCl_3 , 300 MHz) δ 9.56 (s, 1H), 6.28 (s, 1H), 4.94 (s, 2H), 4.89 (s, 1H), 4.81 (s, 1H), 2.61-2.57 (m, 3H), 2.53-2.36 (m, 3H), 2.10-1.67 (m, 7H), 1.16 (s, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 205.6 (CH), 146.1 (C_4), 143.9 (C_4), 139.4 (C_4), 125.7 (CH), 113.8 (CH_2), 110.2 (CH_2), 80.6 (C_4), 49.2 (CH), 48.0 (C_4), 41.6 (CH), 41.0 (CH_2), 34.5 (CH_2), 29.7 (CH_2), 25.3 (CH_3), 21.3 (CH_2), 20.6 (CH_3); HRMS (EI) m/z calcd for $\text{C}_{17}\text{H}_{22}\text{O}_2$ (M^+) 258.1620, found 258.1559.

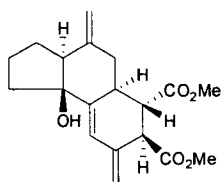
9b-Hydroxy-4,8-dimethylene-2,3,3a,4,5,5a,6,7,8,9b-decahydro-1H-cyclopenta[a]naphthalene-6-carbaldehyde (3.29)



2.0 equivalents of $\text{MgBr}_2 \cdot \text{OEt}_2$, along with 4.0 equivalents of lutidine were used; 10.0 equivalents of acrolein were added. Flash chromatography (15% ethyl acetate in hexanes) afforded **3.29** (15.7 mg, 27%) as a yellow oil. IR (neat, cm^{-1}) 3449 (br), 2931 (s), 2875 (m), 2852 (m), 1719 (s), 1652 (s), 1605 (w), 1439 (w), 1239 (w), 1068 (m), 893 (m); ^1H NMR (CDCl_3 , 300 MHz) δ 9.68 (d, $J = 1.9$ Hz, 1H), 6.25 (s, 1H), 4.96 (s, 1H), 4.93 (s, 2H), 4.81 (s, 1H), 2.91-2.75 (m, 3H), 2.66-2.59 (m, 2H), 2.53-2.44 (m, 3H), 2.09-1.69 (m, 6H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 204.5 (CH), 146.0 (C_4), 143.9 (C_4), 139.1 (C_4), 125.5 (CH), 114.4 (CH_2), 110.2

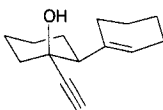
(CH₂), 80.5 (C₄), 49.4 (CH), 49.0 (CH), 36.2 (CH₂), 35.6 (CH), 33.0 (CH₂), 32.5 (CH₂), 25.2 (CH₂), 21.2 (CH₂); HRMS (EI) m/z calcd for C₁₆H₂₀O₂ (M⁺) 244.1463, found 244.1461.

9b-Hydroxy-4,8-dimethylene-2,3,3a,4,5,5a,6,7,8,9b-decahydro-1H-cyclopenta[a]naphthalene-6,7-dicarboxylic acid dimethyl ester (3.30)



3.0 equivalents of MgBr₂·OEt₂, along with 6.0 equivalents of lutidine were used; 10.0 equivalents of dimethyl fumarate were added. Flash chromatography (15% ethyl acetate in hexanes) afforded **3.30** (26.9 mg, 34%) as a yellow oil. IR (neat, cm⁻¹) 3517 (br, w), 3076 (w), 2952 (m), 2869 (w), 2850 (w), 1739 (s), 1436 (m), 1260 (m), 1199 (m), 1168 (m), 894 (m); ¹H NMR (CDCl₃, 300 MHz) δ 6.26 (s, 1H), 5.05 (d, J = 2.5 Hz, 1H), 4.93 (s, 1H), 4.87 (d, J = 2.5 Hz, 1H), 4.80 (s, 1H), 3.72 (s, 3H), 3.71 (s, 3H), 3.67-3.64 (m, 1H), 2.77-2.72 (m, 2H), 2.48-2.38 (m, 3H), 2.09-1.69 (m, 7H); ¹³C NMR (CDCl₃, 75 MHz) δ 174.4 (C₄), 172.5 (C₄), 144.8 (C₄), 144.5 (C₄), 138.9 (C₄), 124.9 (CH), 113.5 (CH₂), 110.5 (CH₂), 80.2 (C₄), 52.1 (CH₃), 52.0 (CH₃), 49.3 (CH), 49.1 (CH), 49.0 (CH), 36.8 (CH), 36.7 (CH₂), 33.8 (CH₂), 24.6 (CH₂), 21.2 (CH₂); HRMS (EI) m/z calcd for C₁₉H₂₄O₅ (M⁺) 332.1624, found 332.1635.

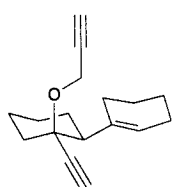
2-Ethynyl-bicyclohexyl-1'-en-2-ol (3.31)



To a solution of 2-(1-cyclohexenyl)-cyclohexanone **2.15** (3.990 g, 22.4 mmol) in THF (60 mL) at 0 °C was added dropwise ethynylmagnesium bromide (67.2 mL, 33.6 mmol). The reaction was warmed to room temperature and stirred until completion by TLC, at which point it was quenched with NH₄Cl (sat. aq.).

The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO₄, filtered, and concentrated. Flash chromatography (5% ethyl acetate in hexanes) afforded the major diastereoisomer (60:40) **3.31** as a white solid (2.454 g, 54%). IR (neat, cm⁻¹) 3439 (br), 3253 (m), 2939 (w), 1642 (m); ¹H NMR (CDCl₃, 300 MHz) δ 5.53 (s, 1H), 2.51-2.40 (m, 1H), 2.34 (s, 1H), 2.25 (s, 1H), 2.13-2.06 (m, 1H), 2.04-1.89 (m, 4H), 1.71-1.32 (m, 10H), 1.26-1.11 (m, 1H); ¹³C NMR (CDCl₃, 75 MHz) 140.8 (C₄), 123.8 (CH), 89.4 (C₄), 71.4 (CH), 67.6 (C₄), 53.0 (CH), 39.9 (CH₂), 32.3 (CH₂), 26.8 (CH₂), 26.3 (CH₂), 25.7 (CH₂), 23.4 (CH₂), 22.8 (CH₂), 20.9 (CH₂); HRMS (EI) m/z calcd for C₁₄H₂₀O (M⁺) 204.1514, found 204.1498; m.p. 77.5-78.3 °C.

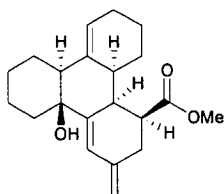
2'-Ethynyl-2'-prop-2-ynyloxy-bicyclohexyl-1-ene (3.32)



To a solution of **3.31** (0.800 g, 3.92 mmol) and propargyl bromide (1.53 mL, 13.7 mmol) in THF/DMF (9:3 mL) was added sodium hydride 60% in oil (0.548 g, 13.7 mmol) slowly at room temperature. The reaction was followed by TLC and quenched with NH₄Cl (sat. aq.) upon completion. The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO₄, filtered, and concentrated. Flash chromatography (5% ethyl acetate in hexanes) afforded **3.32** (0.938 g, 99%) as a colourless oil. IR (neat, cm⁻¹) 3307 (s), 2930 (s), 2856 (s), 1447 (m), 1137 (m), 1091 (m), 1072 (m), 1056 (m); ¹H NMR (CDCl₃, 300 MHz) δ 5.54 (s, 1H), 4.26 (dd, J_{AB} = 15.2 Hz, J_{AX} = 2.5 Hz, 1H), 4.15 (dd, J_{AB} = 15.2 Hz, J_{BX} = 2.5 Hz, 1H), 2.44 (s, 1H), 2.34 (t, J = 2.4 Hz, 1H), 2.17 (m, 2H), 1.98 (m, 4H), 1.85 (qd, J = 12.6, 3.5 Hz, 1H), 1.73-1.69 (m, 1H), 1.58-1.36 (m, 8H), 1.32-1.21 (m, 1H); ¹³C NMR (CDCl₃, 75 MHz) δ 138.9 (C₄), 124.7 (CH), 84.8 (C₄), 81.5 (C₄), 76.7 (C₄), 75.1 (CH),

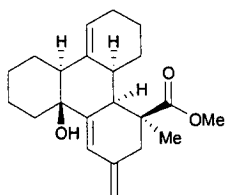
73.4 (CH), 55.3 (CH), 52.3 (CH₂), 36.5 (CH₂), 28.1 (CH₂), 26.5 (CH₂), 26.3 (CH₂), 25.8 (CH₂), 23.7 (CH₂), 23.0 (CH₂), 20.1 (CH₂); HRMS (EI) m/z calcd for C₁₇H₂₂O (M⁺) 242.1671, found 242.1625.

4-Hydroxy-1-methyl-3-methylene-1,2,3,4b,5,6,7,8,8a,10,11,12,12a,12b-tetradecahydro-triphenylene-1-carboxylic acid methyl ester (3.33)



2.0 equivalents of MgBr₂·OEt₂, along with 4.0 equivalents of triethylamine were used; 5.0 equivalents of methyl acrylate were added. Flash chromatography (3% ethyl acetate in hexanes) afforded **3.33** (20.0 mg, 23%) as off-white crystals. IR (neat, cm⁻¹) 3530 (w br), 2929 (s), 2857 (m), 1736 (s), 1435 (m), 1272 (m), 1199 (m); ¹H NMR (CDCl₃, 300 MHz) δ 6.48 (s, 1H), 5.25 (s, 1H), 4.89 (s, 1H), 4.83 (s, 1H), 3.73 (s, 3H), 3.28 (t, J = 7.1 Hz, 1H), 2.87 (quint., J = 6.2 Hz, 1H) 2.70-2.59 (m, 1H), 2.57-2.51 (m, 3H), 1.99 (br. s, 2H), 1.82-0.98 (m, 13 H); ¹³C NMR (CDCl₃, 75 MHz) δ 174.4 (C₄), 148.9 (C₄), 141.3 (C₄), 139.9 (C₄), 126.2 (CH), 120.6 (CH), 112.4 (CH₂), 73.1 (C₄), 51.7 (CH₃), 45.8 (CH), 41.4 (CH), 40.6 (CH), 37.1 (CH₂), 34.7 (CH), 28.8 (CH₂), 25.9 (CH₂), 24.9 (CH₂), 24.6 (CH₂), 22.6 (CH₂), 22.0 (CH₂), 21.6 (CH₂); HRMS (EI) m/z calcd for C₂₁H₂₆O₂ [(M-H₂O)⁺] 310.1933, found 310.1957; m.p. 133.7-134.2 °C.

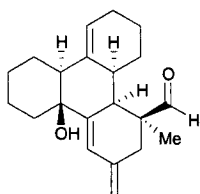
4b-Hydroxy-1-methyl-3-methylene-1,2,3,4b,5,6,7,8,8a,10,11,12,12a,12b-tetradecahydro-triphenylene-1-carboxylic acid methyl ester (3.34)



2.0 equivalents of MgBr₂·OEt₂, along with 4.0 equivalents of triethylamine were used; 3.0 equivalents of methyl methacrylate were added. Flash chromatography (10% ethyl acetate in hexanes) afforded

3.34 (17.8 mg, 24%) as a yellow oil. IR (neat, cm^{-1}) 3561 (br w), 2931 (s), 2858 (m), 1732 (s), 1434 (m), 1237 (s), 1112 (s); ^1H NMR (CDCl_3 , 300 MHz) δ 6.44 (s, 1H), 5.21 (s, 1H), 4.93 (s, 1H), 4.86 (s, 1H), 3.71 (s, 3H), 2.85 (d, $J = 6.8$ Hz, 1H), 2.75-2.67 (m, 1H), 2.64 (d, $J = 15.5$ Hz, 1H), 2.53 (d, $J = 11.8$ Hz, 1H), 2.30 (d, $J = 15.5$ Hz, 1H), 1.97 (br. s, 2H), 1.80-1.21 (m, 12H), 1.13 (s, 3H), 1.09-0.95 (m, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 177.5 (C_4), 147.1 (C_4), 140.4 (C_4), 140.2 (C_4), 124.8 (CH), 120.2 (CH), 113.6 (CH_2), 73.1 (C_4), 51.7 (CH_3), 45.8 (CH), 43.1 (C_4), 42.2 (CH), 41.0 (CH), 36.8 (CH_2), 35.1 (CH_2), 26.7 (CH_3), 25.9 (CH_2), 24.6 (CH_2), 24.5 (CH_2), 22.6 (CH_2), 21.9 (CH_2), 21.5 (CH_2); HRMS (EI) m/z calcd for $\text{C}_{22}\text{H}_{30}\text{O}_3$ (M^+) 342.2195, found 342.2209.

4b-Hydroxy-1-methyl-3-methylene-1,2,3,4b,5,6,7,8,8a,10,11,12,12a,12b-tetradecahydro-triphenylene-1-carbaldehyde (3.35)

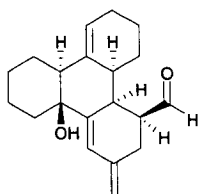


3.0 equivalents of $\text{MgBr}_2 \cdot \text{OEt}_2$, along with 6.0 equivalents of triethylamine were used; 8.0 equivalents of methacrolein were added.

Flash chromatography (10% ethyl acetate in hexanes) afforded **3.35**

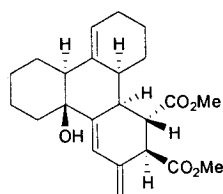
(33.4 mg, 44%) as a yellow oil. IR (neat, cm^{-1}) 3454 (br w), 2929 (s), 2858 (m), 1720 (s), 1449 (w); ^1H NMR (CDCl_3 , 300 MHz) δ 9.74 (s, 1H), 6.11 (s, 1H), 5.53 (s, 1H), 4.97 (s, 1H), 4.93 (s, 1H), 2.66 (d, $J = 11.2$ Hz, 1H), 2.36 (q, $J = 14.7$ Hz, 1H), 2.18-2.08 (m, 1H), 2.03-1.97 (m, 2H), 1.91 (d, $J = 11.8$ Hz, 1H), 1.84-1.06 (m, 14H), 1.01 (s, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 205.0 (CH), 146.9 (C_4), 140.2 (C_4), 139.2 (C_4), 123.2 (CH), 120.6 (CH), 114.2 (CH_2), 72.5 (C_4), 51.7 (CH), 48.9 (C_4), 47.1 (CH), 43.4 (CH), 34.0 (CH_2), 33.2 (CH_2), 29.7 (CH_2), 25.7 (CH_2), 25.6 (CH_2), 24.2 (CH_2), 21.4 (CH_2), 21.3 (CH_3), 20.7 (CH_2); HRMS (EI) m/z calcd for $\text{C}_{21}\text{H}_{28}\text{O}_2$ (M^+) 312.2089, found 312.2077.

4b-Hydroxy-1,8a-dimethyl-3-methylene-1,2,3,4b,5,6,7,8,8a,10,11,12,12a,12b-tetradecahydro-triphenylene-1-carbaldehyde (3.36)



3.0 equivalents of $\text{MgBr}_2 \cdot \text{OEt}_2$, along with 6.0 equivalents of lutidine were used; 10.0 equivalents of acrolein were added. Flash chromatography (10% ethyl acetate in hexanes) afforded **3.36** (21.4 mg, 33%) as a yellow oil. IR (neat, cm^{-1}) 3423 (br w), 2930 (s), 2856 (m), 1718 (m), 1447 (w), 896 (w); ^1H NMR (CDCl_3 ; 300 MHz) δ 9.69 (d, $J = 4.3$ Hz, 1H), 6.32 (d, 1.9 Hz, 1H), 5.64-5.59 (m, 1H), 4.96 (s, 1H), 4.90 (s, 1H), 2.84 (quint., $J = 4.3$ Hz, 1H), 2.69-2.62 (m, 1H), 2.54-2.50 (m, 2H), 2.12-1.17 (m, 17H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 205.5 (CH), 144.6 (C_4), 139.3 (C_4), 138.3 (C_4), 123.4 (CH), 123.3 (CH), 114.2 (CH_2), 72.0 (C_4), 48.9 (CH), 47.2 (CH), 42.3 (CH), 39.6 (CH), 34.2 (CH_2), 31.3 (CH_2), 27.8 (CH_2), 25.6 (CH_2), 25.5 (CH_2), 24.1 (CH_2), 21.5 (CH_2), 20.7 (CH_2); HRMS (EI) m/z calcd for $\text{C}_{20}\text{H}_{24}\text{O}$ $[(\text{M}-\text{H}_2\text{O})^+]$ 280.1827, found 280.1824.

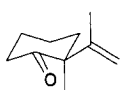
4b-Hydroxy-3-methylene-1,2,3,4b,5,6,7,8,8a,10,11,12,12a,12b-tetradecahydro-triphenylene-1,2-dicarboxylic acid dimethyl ester (3.37)



3.0 equivalents of $\text{MgBr}_2 \cdot \text{OEt}_2$, along with 6.0 equivalents of triethylamine were used; 8.0 equivalents of dimethyl fumarate were added. Flash chromatography (10% ethyl acetate in hexanes) afforded **3.37** (30.8 mg, 36%) as a yellow oil. IR (neat, cm^{-1}) 3533 (br w), 2931 (m), 2858 (m), 1739 (s), 1436 (m), 1265 (m), 1167 (m); ^1H NMR (CDCl_3 , 300 MHz) δ 6.47 (s, 1H), 5.36 (s, 1H), 4.97 (s, 1H), 4.71 (s, 1H), 3.74 (s, 3H), 3.69 (s, 3H), 3.47 (d, $J = 11.2$ Hz, 1H), 3.18-3.04 (m, 2H), 2.61-2.50 (m, 1H), 2.32 (d, $J = 11.8$ Hz, 1H), 2.19-1.99 (m, 3H), 1.88-1.17 (m, 11H), 0.97-0.82 (m, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 174.7 (C_4), 173.0 (C_4),

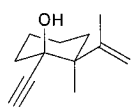
147.3 (C₄), 139.6 (C₄), 139.5 (C₄), 127.0 (CH), 121.3 (CH), 111.8 (CH₂), 71.3 (C₄), 52.1 (CH₃), 51.7 (CH₃), 48.2 (CH), 44.9 (CH), 43.5 (CH), 39.1 (CH₂), 38.5 (CH), 38.0 (CH), 25.4 (CH₂), 24.2 (CH₂), 24.1 (CH₂), 22.1 (CH₂ x 2), 21.5 (CH₂); HRMS (EI) m/z calcd for C₂₃H₃₀O₅ (M⁺) 386.2093, found 386.2071.

2-Isopropenyl-2-methyl-cyclohexanone (3.38)



To a solution of sodium methoxide (5.330 g, 38.6 mmol) in THF (100 mL) at 0 °C was added ketone **2.9** (2.633 g, 46.3 mmol) in THF (20 mL) *via* canula. The solution was stirred for 20 minutes and freshly distilled methyl iodide (2.40 mL, 38.6 mmol) was added. The reaction was followed by TLC and quenched with NH₄Cl (sat. aq.) upon completion. The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO₄, filtered, and concentrated. Flash chromatography (3% hexanes in benzene) afforded **3.38** as a yellow oil. (3.736, 64%) with **3.38b** (0.9763 g, 17%). IR (neat, cm⁻¹) 2967 (m), 2937 (s), 2865 (m), 1710 (s), 1638 (m), 1449 (m), 898 (m); ¹H NMR (CDCl₃, 300 MHz) δ 4.90 (s, 1H), 4.69 (s, 1H), 2.52-2.42 (m, 1H), 2.27-2.17 (m, 2H), 1.97-1.87 (m, 1H), 1.72-1.53 (m, 3H), 1.63 (s, 3H), 1.44-1.33 (m, 1H), 1.06 (s, 3H); ¹³C NMR (CDCl₃, 75 MHz) δ 214.5 (C₄), 146.7 (C₄), 112.3 (CH₂), 55.2 (C₄), 39.8 (CH₂), 37.9 (CH₂), 27.9 (CH₂), 24.5 (CH₃), 21.8 (CH₂), 19.5 (CH₃); HRMS (EI) m/z calcd for C₁₀H₁₆O (M⁺) 152.1201, found 152.1329.

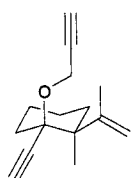
1-Ethynyl-2-isopropenyl-2-methyl-cyclohexanol (3.39)



To a solution of ketone **3.38** (3.736 g, 24.6 mmol) in THF (100 mL) at room temperature was added dropwise ethynylmagnesium bromide (73.7 mL, 36.9

mmol). The reaction was warmed to room temperature and allowed to stir until completion by TLC, at which point it was quenched with NH_4Cl (sat. aq.). The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO_4 , filtered, and concentrated. Flash chromatography (10% ethyl acetate in hexanes) afforded the major diastereoisomer (63:37) **3.39** as a yellow oil (1.712 g, 39%). IR (neat, cm^{-1}) 2537 (br m), 2206 (m), 2933 (s), 2867 (m), 1625 (m), 1445 (m), 981 (s); ^1H NMR (CDCl_3 , 300 MHz) δ 5.08 (s, 1H), 5.03 (s, 1H), 2.47 (s, 1H), 2.40 (s, 1H), 1.98 (s, 3H), 1.99-1.78 (m, 3H), 1.63-1.38 (m, 4H), 1.27 (s, 3H), 1.28-1.17 (m, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 150.6 (C_4), 114.5 (CH_2), 88.3 (C_4), 72.4 (CH), 70.1 (C_4), 45.5 (C_4), 35.3 (CH_2), 31.1 (CH_2), 23.0 (CH_3), 20.9 (CH_2), 20.1 (CH_2), 20.0 (CH_3); HRMS (EI) m/z calcd for $\text{C}_{11}\text{H}_{15}\text{O}$ $[(\text{M}-\text{CH}_3)^+]$ 163.1123, found 163.1130.

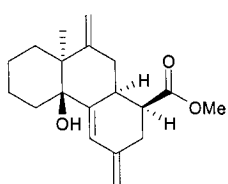
1-Ethynyl-2-isopropenyl-2-methyl-1-prop-2-ynyloxy-cyclohexane (**3.40**)



To a solution of **3.39** (1.712 g, 9.62 mmol) and propargyl bromide (5.36 mL, 48.1 mmol) in THF/DMF (18:6 mL) was added sodium hydride 60% in oil (1.924 g, 48.1 mmol) slowly at room temperature. The reaction was followed by TLC and quenched with NH_4Cl (sat. aq.) upon completion. The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO_4 , filtered, and concentrated. Flash chromatography (10% hexanes in benzene) afforded **3.40** (1.897 g, 91%) as a yellow oil. IR (neat, cm^{-1}) 3302 (s), 3095 (w), 2933 (s), 2886 (m), 1630 (m), 1445 (m), 1374 (m), 1087 (s), 1066 (s), 895 (m); ^1H NMR (CDCl_3 , 300 MHz) δ 5.01 (s, 1H), 4.94-4.93 (m, 1H), 4.26 (dd, $J_{\text{AB}} = 15.5$ Hz, $J_{\text{AX}} = 2.5$ Hz, 1H), 4.17 (dd, $J_{\text{AB}} = 15.5$ Hz, $J_{\text{BX}} = 2.5$ Hz, 1H), 2.54 (s, 1H), 2.33 (t, $J = 2.5$ Hz, 1H), 2.12-1.98 (m, 2H), 1.89 (s,

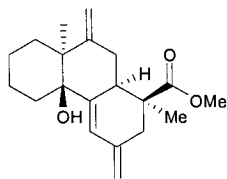
3H), 1.81-1.70 (m, 1H), 1.61-1.32 (m, 5H), 1.24 (s, 3H); ^{13}C NMR (CDCl_3 ; 75 MHz) δ 150.3 (C_4), 113.2 (CH_2), 83.7 (C_4), 81.1 (C_4), 80.5 (C_4), 76.5 (CH), 73.0 (CH), 52.0 (CH_2), 45.3 (C_4), 32.1 (CH_2), 31.4 (CH_2), 23.1 (CH_3), 22.3 (CH_3), 21.0 (CH_2), 20.8 (CH_2); HRMS (EI) m/z calcd for $\text{C}_{14}\text{H}_{17}\text{O}$ $[(\text{M}-\text{CH}_3)^+]$ 201.1279, found 201.1272.

4b-Hydroxy-8a-methyl-3,9-dimethylene-1,2,3,4b,5,6,7,8,8a,9,10,10a-dodecahydro-phenanthrene-1-carboxylic acid methyl ester (3.41)



3.0 equivalents of $\text{MgBr}_2 \cdot \text{OEt}_2$, along with 6.0 equivalents of lutidine were used; 20.0 equivalents of methyl acrylate were added. Flash chromatography (5% ethyl acetate in hexanes) afforded **3.41** (27.4 mg, 26%) as a yellow oil. IR (neat, cm^{-1}) 3499 (br w), 2935 (s), 2859 (m), 1725 (m), 1444 (m), 1197 (m), 1174 (m), 885 (m); ^1H NMR (CDCl_3 , 300 MHz) δ 6.21 (s, 1H), 4.92 (s, 1H), 4.84 (s, 2H), 4.81 (s, 1H), 3.60 (s, 3H), 3.07-2.94 (m, 1H), 2.86-2.81 (m, 2H), 2.77-2.70 (m, 2H), 2.29 (dd, $J = 14.9, 5.0$ Hz, 1H), 2.15 (s, 1H), 1.96-1.88 (m, 1H), 1.85-1.24 (m, 6H), 0.98 (s, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 174.3 (C_4), 156.0 (C_4), 143.2 (C_4), 140.3 (C_4), 123.5 (CH), 113.8 (CH_2), 108.2 (CH_2), 73.4 (C_4), 51.6 (CH_3), 43.6 (CH), 41.8 (C_4), 35.9 (CH), 34.4 (CH_2), 34.0 (CH_2), 32.9 (CH_2), 30.4 (CH_2), 26.1 (CH_3), 20.9 (CH_2), 20.6 (CH_2); HRMS (EI) m/z calcd for $\text{C}_{19}\text{H}_{26}\text{O}_3$ (M^+) 302.1882, found 302.1878.

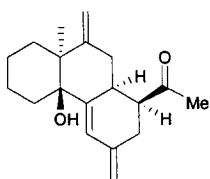
4b-Hydroxy-1,8a-dimethyl-3,9-dimethylene-1,2,3,4b,5,6,7,8,8a,9,10,10a-dodecahydro-phenanthrene-1-carboxylic acid methyl ester (3.42)



2.0 equivalents of $\text{MgBr}_2 \cdot \text{OEt}_2$, along with 4.0 equivalents of triethylamine were used; 3.0 equivalents of methyl methacrylate were added. Flash chromatography (5% ethyl acetate in hexanes) afforded

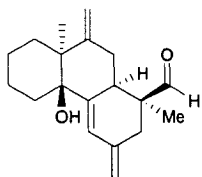
3.42 (12.6 mg, 21%) as a yellow oil. IR (neat, cm^{-1}) 2507 (br w), 2936 (s), 2861 (m), 1719 (s), 1633 (w), 1465 (w), 1444 (w), 199 (m), 888 (m); ^1H NMR (CDCl_3 , 300 MHz) δ 6.17 (s, 1H), 4.87 (s, 1H), 4.85 (s, 1H), 4.83 (s, 1H), 4.79 (s, 1H), 3.57 (s, 3H), 3.18 (s, 1H), 3.11-3.04 (m, 1H), 2.80 (d, $J = 15.4$ Hz, 1H), 2.52-2.39 (m, 3H), 1.89 (d, $J = 12.9$ Hz, 1H), 1.85-1.38 (m, 7H), 1.31 (s, 3H), 0.96 (s, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 176.2 (C_4), 156.0 (C_4), 144.0 (C_4), 140.8 (C_4), 123.6 (CH), 112.9 (CH_2), 108.3 (CH_2), 73.5 (C_4), 51.9 (CH_3), 46.8 (C_4), 44.3 (CH_2), 42.8 (CH), 41.8 (C_4), 33.1 (CH_2), 30.8 (CH_2), 30.7 (CH_2), 26.2 (CH_3), 23.6 (CH_3), 21.1 (CH_2), 21.0 (CH_2); HRMS (EI) m/z calcd for $\text{C}_{20}\text{H}_{28}\text{O}_3$ (M^+) 316.2038, found 316.2037.

1-(4b-Hydroxy-8a-methyl-3,9-dimethylene-1,2,3,4b,5,6,7,8,8a,9,10,10a-dodecahydrophenanthren-1-yl)-ethanone (3.43)



2.0 equivalents of $\text{MgBr}_2 \cdot \text{OEt}_2$, along with 4.0 equivalents of triethylamine were used; 10.0 equivalents of methyl vinyl ketone were added. Flash chromatography (8% ethyl acetate in hexanes) afforded **3.43** (41.4 mg, 48%) as a yellow oil. IR (neat, cm^{-1}) 3461 (br w), 2927 (s), 2859 (m), 1707 (m), 1445 (w), 1336 (w), 885 (m); ^1H NMR ($(\text{CD}_3)_2\text{CO}$, 500 MHz) δ 6.26 (s, 1H), 5.01 (s, 1H), 4.86 (s, 1H), 4.83 (s, 1H), 4.68 (s, 1H), 3.38 (d, $J = 11.6$ Hz, 1H), 2.71-2.65 (m, 1H), 2.55-2.48 (m, 1H), 2.41-2.37 (m, 1H), 2.23-2.11 (m, 1H), 2.15 (s, 3H), 1.98-1.90 (m, 2H), 1.78-1.46 (m, 8H), 1.02 (s, 3H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 210.2 (C_4), 154.9 (C_4), 147.7 (C_4), 140.7 (C_4), 123.6 (CH), 113.8 (CH_2), 108.5 (CH_2), 73.8 (C_4), 54.9 (CH), 41.6 (C_4), 36.2 (CH_2), 34.5 (CH_2), 33.6 (CH), 32.6 (CH_2), 30.4 (CH_2), 26.7 (CH_3), 25.9 (CH_3), 20.8 ($\text{CH}_2 \times 2$); HRMS (EI) m/z calcd for $\text{C}_{19}\text{H}_{26}\text{O}_2$ (M^+) 286.1933, found 286.1919.

4b-Hydroxy-1,8a-dimethyl-3,9-dimethylene-1,2,3,4b,5,6,7,8,8a,9,10,10a-dodecahydro-phenanthrene-1-carbaldehyde (3.44)

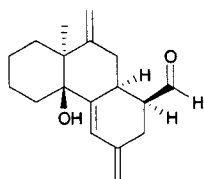


2.0 equivalents of $\text{MgBr}_2 \cdot \text{OEt}_2$, along with 4.0 equivalents of triethylamine were used; 5.0 equivalents of methacrolein were added.

Flash chromatography (10% ethyl acetate in hexanes) afforded **3.44**

(18.4 mg, 18%) as a yellow oil. IR (neat, cm^{-1}) 3463 (br w), 2930 (s), 2861 (m), 1718 (s), 1634 (w), 1458 (w), 1444 (w), 1372 (w), 888 (m); ^1H NMR (CDCl_3 , 300 MHz) δ 9.48 (s, 1H), 6.24 (d, $J = 2.5$ Hz, 1H), 4.92 (s, 1H), 4.89-4.85 (m, 3H), 2.95 (dddd, $J = 14.3, 14.3, 2.5, 2.5$ Hz, 1H), 2.69-2.35 (m, 5H), 2.07 (br. s, 1H), 1.95-1.89 (m, 1H), 1.78-1.52 (m, 6H), 1.18 (s, 3H), 1.01 (s, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 205.3 (CH), 155.3 (C_4), 143.9 (C_4), 139.7 (C_4), 124.7 (CH), 113.9 (CH_2), 108.8 (CH_2), 73.7 (C_4), 48.8 (C_4), 41.6 (C_4), 40.9 (CH, CH_2), 32.9 (CH_2), 30.8 (CH_2), 30.3 (CH_2), 26.2 (CH_3), 21.0 (CH_2), 20.9 (CH_2), 20.3 (CH_3); HRMS (EI) m/z calcd for $\text{C}_{19}\text{H}_{26}\text{O}_2$ (M^+) 286.1933, found 286.1928.

4b-Hydroxy-8a-methyl-3,9-dimethylene-1,2,3,4b,5,6,7,8,8a,9,10,10a-dodecahydro-phenanthrene-1-carbaldehyde (3.45)

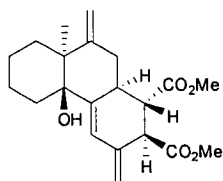


2.0 equivalents of $\text{MgBr}_2 \cdot \text{OEt}_2$, along with 4.0 equivalents of triethylamine were used; 20.0 equivalents of acrolein were added. Flash chromatography (5% ethyl acetate in hexanes) afforded **3.45** (20.2 mg,

30%) as a yellow oil. IR (neat, cm^{-1}) 3451 (br w), 2936 (s), 2863 (m), 1716 (s), 1634 (w), 1443 (w), 1009 (w), 886 (m); ^1H NMR (CDCl_3 , 300 MHz) δ 9.66 (s, 1H), 6.22 (s, 1H), 4.95 (s, 1H), 4.92 (s, 1H), 4.87 (d, $J = 2.5$ Hz, 1H), 4.85 (s, 1H), 3.15 (dddd, $J = 14.8, 14.8, 2.5, 2.5$ Hz, 1H), 2.88-2.79 (m, 2H), 2.68-2.63 (m, 2H), 2.35 (dd, $J = 15.0, 5.2$ Hz, 1H), 1.99-1.88 (m, 2H), 1.80-1.41 (m, 7H), 1.02 (s, 3H); ^{13}C NMR (CDCl_3 , 75 MHz)

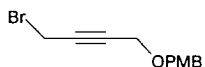
δ 204.3 (CH), 155.2 (C₄), 143.8 (C₄), 139.5 (C₄), 124.4 (CH), 114.6 (CH₂), 108.6 (CH₂), 73.7 (C₄), 49.8 (CH), 41.8 (C₄), 35.2 (CH), 33.5 (CH₂), 32.8 (CH₂), 32.0 (CH₂), 30.4 (CH₂), 26.2 (CH₃), 20.9 (CH₂ x 2); HRMS (EI) m/z calcd for C₁₈H₂₄O₂ (M⁺) 272.1776, found 272.1795.

4b-Hydroxy-8a-methyl-3,9-dimethylene-1,2,3,4b,5,6,7,8,8a,9,10,10a-dodecahydro-phenanthrene-1,2-dicarboxylic acid dimethyl ester (3.46)



4.0 equivalents of MgBr₂·OEt₂, along with 8.0 equivalents of triethylamine were used; 10.0 equivalents of dimethyl fumarate were added. Flash chromatography (5% ethyl acetate in hexanes) afforded **3.46** (26.6 mg, 22%) as a yellow oil. IR (neat, cm⁻¹) 3511 (br w), 2927 (s), 2861 (m), 1740 (s), 1437 (m), 1261 (m), 1201 (m), 1166 (s), 887 (m); ¹H NMR ((CD₃)₂CO, 500 MHz) δ 6.28 (s, 1H), 5.07 (d, J = 2.4 Hz, 1H), 4.96 (d, J = 2.4 Hz, 1H), 4.86 (s, 1H), 4.82 (s, 1H), 3.72 (s, 3H), 3.72 (s, 3H), 2.79-2.71 (m, 3H), 2.29-2.25 (m, 1H), 1.96-1.92 (m, 1H), 1.78-1.22 (m, 8H), 1.07 (s, 1H), 1.00 (s, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 174.4 (C₄), 172.6 (C₄), 153.9 (C₄), 144.8 (C₄), 139.0 (C₄), 123.5 (CH), 118.6 (CH₂), 109.0 (CH₂), 73.8 (C₄), 52.1 (CH₃), 52.0 (CH₃), 50.2 (CH), 49.2 (CH), 41.2 (C₄), 36.3 (CH), 33.8 (CH₂), 32.5 (CH₂), 30.7 (CH₂), 25.8 (CH₃), 20.8 (CH₂), 20.7 (CH₂); HRMS (EI) m/z calcd for C₂₁H₂₆O₄ [(M- H₂O)⁺] 342.1831, found 342.1851.

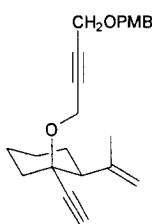
4-(4-Methoxy-benzyloxy)-but-2-yn-1-ol and 1-(4-Bromo-but-2-ynyloxymethyl)-4-methoxy-benzene (3.48 and 3.49)



To a solution of 2-butyne-1,4-diol **3.47** (4.999 g, 58.1 mmol) in DMSO (30 mL) at 0 °C was added grinded KOH (3.585 g, 63.0 mmol) and freshly distilled

PMBCl (4.532 g, 29.1 mmol). The reaction was stirred for 3 hours and followed by TLC to completion, at which point it was quenched with NH₄Cl (sat. aq.). The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO₄, filtered, and concentrated. Flash chromatography (30% ethyl acetate in hexanes) afforded **3.48** (2.943 g, 22%) and **3.48b** (0.211 g, 1%). To a solution of **3.48** (0.3956 g, 1.92 mmol) in DCM (60 mL) was added CBr₄ (0.7960 g, 2.40 mmol) and PPh₃ (0.7550 g, 2.88 mmol) at 0 °C. The solution was allowed to reach room temperature. The reaction was followed by TLC and concentrated upon completion. Hexanes (20 mL) was added to precipitate triphenylphosphine oxide, which was filtered out on a pad of celite. The residue was quickly flashed on a short pad of silica (5% ethyl acetate in hexanes) to afford **3.49** (0.4780 g, 93%). Characterisation data is available through the literature.⁶⁷

1-[4-(1-Ethynyl-2-isopropenyl-cyclohexyloxy)-but-2-ynyloxymethyl]-4-methoxy-benzene (3.50)

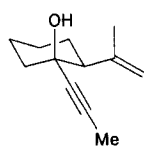


To a solution of **2.26** (74.7 mg, 0.455 mmol) and 1-(4-Bromo-but-2-ynyloxymethyl)-4-methoxy-benzene **3.49** (0.366 g, 1.37 mmol) in THF/DMF (3:1 mL) was added sodium hydride 60% in oil (54.6 mg, 1.37 mmol) slowly at room temperature. The reaction was followed by TLC and quenched with NH₄Cl (sat. aq.) upon completion. The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO₄, filtered, and concentrated. Flash chromatography (5% ethyl acetate in hexanes) afforded **3.50** (0.140 g, 87%) as a yellow oil. IR (neat, cm⁻¹) 3447 (br), 2932 (w), 2857 (w), 1613 (2), 1515 (m), 1249 (m), 1032 (w); ¹H NMR (CDCl₃, 500 MHz) δ 7.26 (d, J = 8.5 Hz, 2H), 6.83 (d,

⁶⁷ Banti, L.; Guanti, G.; Basso, A. *Eur. J. Org. Chem.* **2000**, 6, 939.

$J = 8.5$ Hz, 2H), 4.87 (s, 2H), 4.49 (s, 2H), 4.33 (ddd, $J_{AB} = 15.2$ Hz, $J_{AX} = 1.8$ Hz, $J_{AY} = 1.8$ Hz, 1H), 4.22 (ddd, $J_{AB} = 15.2$ Hz, $J_{BX} = 1.8$ Hz, $J_{BY} = 1.8$ Hz, 1H), 4.15 (t, $J = 1.8$ Hz, 2H), 3.78 (s, 3H), 2.50 (s, 1H), 2.28-2.23 (m, 1H), 2.19 (dd, $J = 12.7, 3.6$ Hz, 1H), 1.89 (qd, $J = 12.9, 3.5$ Hz, 1H), 1.82 (t, $J = 1.1$ Hz, 3H), 1.75 (d, $J = 13.0$ Hz), 1.61-1.21 (m, 5H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 159.3 (C_4), 146.8 (C_4), 129.8 (CH), 129.5 (C_4), 113.8 (CH), 113.3 (CH_2), 84.4 (C_4), 83.8 (C_4), 81.0 (C_4), 75.9 (C_4), 74.8 (CH), 71.0 (CH_2), 57.1 (CH_2), 55.3 (CH_3), 54.4 (CH), 52.2 (CH_2), 35.9 (CH_2), 26.3 (CH_2), 25.7 (CH_2), 22.2 (CH_3), 20.6 (CH_2); HRMS (EI) m/z calcd for $\text{C}_{11}\text{H}_{15}\text{O}$ $[(\text{M}-\text{C}_4\text{H}_4\text{OPMB})^+]$ 163.1123, found 163.1125.

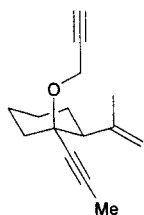
2-Isopropenyl-1-prop-1-ynyl-cyclohexanol (**3.51**)



To a solution of ketone **2.9** (7.800 g, 56.5 mmol) in THF (100 mL) at 0 °C was added dropwise 1-propynylmagnesium bromide (220.1 mL, 113.0 mmol). The reaction was warmed to room temperature and stirred until completion by TLC, at which point it was quenched with NH_4Cl (sat. aq.). The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO_4 , filtered, and concentrated. Flash chromatography (15% hexanes in benzene) afforded the major diastereoisomer (71:29) **3.51**, as a yellow oil (5.149 g, 51%). IR (neat, cm^{-1}) 3549 (br), 3079 (w), 2936 (s), 2855 (s), 1639 (m), 1447 (m), 1370 (m), 1286 (m), 969 (s), 893 (m); ^1H NMR (CDCl_3 , 300 MHz) δ 4.89 (s, 1H), 4.73 (s, 1H), 2.11 (s, 1H), 2.10-1.99 (m, 2H), 1.88 (s, 3H), 1.71 (s, 3H), 1.66-1.21 (m, 6H), 1.22-1.06 (m, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 148.5 (C_4), 111.9 (CH_2), 84.2 (C_4), 78.7 (C_4), 66.8 (C_4), 52.6 (CH), 39.8 (CH_2),

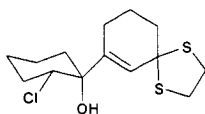
26.5 (CH₂), 25.6 (CH₂), 20.4 (CH₂), 3.1 (CH₃); HRMS (EI) *m/z* calcd for C₁₂H₁₈O (M⁺) 178.1358, found 178.1361.

2-Isopropenyl-1-prop-1-ynyl-1-prop-2-ynyloxy-cyclohexane (3.52)



To a solution of **3.51** (5.149 g, 28.9 mmol) and propargyl bromide (16.1 mL, 0.145 mol) in THF/DMF (36:12 mL) was added sodium hydride 60% in oil (5.784 g, 0.145 mol) slowly at room temperature. The reaction was followed by TLC and quenched with NH₄Cl (sat. aq.) upon completion. The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO₄, filtered, and concentrated. Flash chromatography (5% benzene in hexanes) afforded **3.52** (6.170 g, 99%) as a yellow oil. IR (neat, cm⁻¹) 3297 (s), 3072 (w), 2935 (s), 2857 (s), 1640 (m), 1448 (s), 1375 (m), 1179 (s), 1093 (s), 1065 (s), 890 (s); ¹H NMR (CDCl₃, 300 MHz) δ 4.79 (s, 2H), 4.22 (dd, J_{AB} = 15.2 Hz, J_{AX} = 2.5 Hz), 4.10 (dd, J_{AB} = 15.2 Hz, J_{BX} = 2.5 Hz), 2.31 (m, 1H), 2.18-2.08 (m, 2H), 1.84 (qd, J = 13.0, 3.7 Hz, 1H), 1.80 (s, 3H), 1.78 (s, 3H), 1.73-1.65 (m, 1H), 1.61-1.47 (m, 1H), 1.43-1.15 (m, 4H); ¹³C NMR (CDCl₃, 75 MHz) δ 147.1 (C₄), 113.0 (CH₂), 82.7 (C₄), 81.3 (C₄), 79.8 (C₄), 75.9 (C₄), 72.7 (CH), 54.5 (CH), 51.5 (CH₂), 36.0 (CH₂), 26.3 (CH₂), 25.6 (CH₂), 22.3 (CH₃), 20.6 (CH₂), 3.3 (CH₃); HRMS (EI) *m/z* calcd for C₁₂H₁₇O [(M-C₃H₃)⁺] 177.1279, found 177.1293.

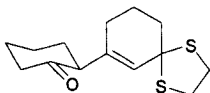
2-Chloro-1-(1,4-dithia-spiro[4.5]dec-6-en-7-yl)-cyclohexanol (3.56)



To a solution of dibromide **3.53** (0.688 g, 2.45 mmol) in THF (5 mL) at -78 °C was added *t*-BuLi (2.91 mL, 4.66 mmol). The solution was

stirred for 20 minutes, allowing the formation of the lithium reagent **3.54** *in situ* (turned forest green). To this was added 2-chlorocyclohexanone **3.55** (0.232 g, 1.72 mmol) in THF (2 mL) *via* canula (colour change to yellow). The solution was stirred for 10 minutes and quenched with NH₄Cl (sat. aq.) at -78 °C. The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO₄, filtered, and concentrated. Flash chromatography (5% ethyl acetate in hexanes) afforded **3.56** (0.345 g, 66%) as a yellow oil. IR (neat, cm⁻¹) 3561 (m), 3467 (br), 2936 (s), 2859 (s), 1446 (m), 1277 (m), 986 (m), 749 (m); ¹H NMR (CDCl₃, 300 MHz) δ 6.00 (s, 1H), 4.11-4.05 (m, 1H), 3.35-3.22 (m, 4H), 2.19-1.16 (m, 15 H); ¹³C NMR (CDCl₃, 75 MHz) δ 142.6 (C₄), 126.6 (CH), 75.6 (C₄), 65.4 (CH), 65.3 (C₄), 40.8 (CH₂), 40.0 (CH₂), 39.8 (CH₂), 36.1 (CH₂), 32.0 (CH₂), 26.0 (CH₂), 23.7 (CH₂), 22.9 (CH₂), 20.3 (CH₂); HRMS (EI) m/z calcd for C₁₄H₂₁OS₂Cl (M)⁺ 304.0722, found 304.0724.

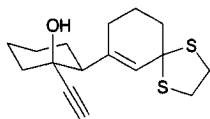
2-(1,4-Dithia-spiro[4.5]dec-6-en-7-yl)-cyclohexanone (**3.57**)



To a solution of the chlorohydrin **3.56** (0.345 g, 1.14 mmol) in THF (5 mL) was added isopropenylmagnesium bromide (2.39 mL, 1.19 mmol); the solution was refluxed with a condenser for ~2 hours. The reaction was followed by TLC and quenched with NH₄Cl (sat. aq.) upon completion. The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO₄, filtered, and concentrated. Flash chromatography (5% ethyl acetate in hexanes) afforded **3.57** (0.201 g, 66%) as a yellow oil. IR (neat, cm⁻¹) 2932 (s), 2859 (s), 1710 (s), 1448 (m), 1276 (w), 1123 (m), 887 (w); ¹H NMR (CDCl₃, 300 MHz) δ 5.47 (s, 1H), 3.33-3.18 (m, 4H), 2.88-2.83 (m, 1H), 2.31-1.58 (m, 14H); ¹³C NMR (CDCl₃, 75 MHz) δ 210.1 (C₄),

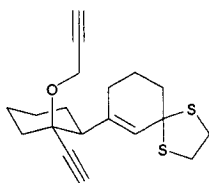
137.3 (C₄), 128.3 (CH), 65.4 (C₄), 58.0 (CH), 42.0 (CH₂), 41.2 (CH₂), 39.8 (2 x CH₂), 31.6 (CH₂), 27.5 (CH₂), 26.3 (CH₂), 24.6 (CH₂), 22.6 (CH₂); HRMS (EI) m/z calcd for C₁₄H₂₀OS₂ (M)⁺ 268.0956, found 268.0951.

2-(1,4-Dithia-spiro[4.5]dec-6-en-7-yl)-1-ethynyl-cyclohexanol (3.58)



To a solution of ketone **3.57** (0.437 g, 1.63 mmol) in THF (20 mL) at 0 °C was added dropwise ethynylmagnesium bromide (6.51 mL, 3.26 mmol). The reaction was warmed to room temperature and stirred until completion by TLC, at which point it was quenched with NH₄Cl (sat. aq.). The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO₄, filtered, and concentrated. Flash chromatography (5% ethyl acetate in hexanes) afforded **3.58** (only product), as a yellow oil (0.288 g, 60%). IR (neat, cm⁻¹) 3451 (br), 2386 (br), 2933 (s), 2857 (m), 1610 (w), 1446 (m), 1276 (m), 973 (m); ¹H NMR (CDCl₃, 500 MHz) δ 5.70 (s, 1H), 3.35-3.22 (m, 4H), 2.4-2.26 (m, 3H), 2.12-1.14 (m, 14H); ¹³C NMR (CDCl₃, 125 MHz) δ 140.7 (C₄), 129.2 (CH), 88.1 (C₄), 71.6 (CH), 67.6 (C₄), 65.4 (C₄), 52.4 (CH), 41.1 (CH₂), 39.9 (CH₂), 39.8 (CH₂), 39.7 (CH₂), 29.9 (CH₂), 25.8 (CH₂), 25.5 (CH₂), 22.9 (CH₂), 20.3 (CH₂); HRMS (EI) m/z calcd for C₁₆H₂₂OS₂ (M)⁺ 294.1112, found 294.1113.

7-(2-Ethynyl-2-prop-2-ynyloxy-cyclohexyl)-1,4-dithia-spiro[4.5]dec-6-ene (3.59)



To a solution of **3.58** (0.288 g, 0.978 mmol) and propargyl bromide (0.55 mL, 4.89 mmol) in THF/DMF (12:4 mL) was added sodium hydride 60% in oil (0.196 g, 4.89 mmol) slowly at room temperature.

The reaction was followed by TLC and quenched with NH_4Cl (sat. aq.) upon completion. The mixture was extracted with diethyl ether (3x) and the combined organic layers were dried over MgSO_4 , filtered, and concentrated. Flash chromatography (8% ethyl acetate in hexanes) afforded **3.59** (0.288 g, 89%) as a yellow oil. IR (neat, cm^{-1}) 3291 (s), 2933 (s), 2857 (s), 1446 (m), 1054 (s); ^1H NMR (CDCl_3 , 500 MHz) δ 5.70 (s, 1H), 4.25 (dd, $J_{\text{AB}} = 15.2$ Hz, $J_{\text{AX}} = 2.4$ Hz, 1H), 4.14 (dd, $J_{\text{AB}} = 15.2$ Hz, $J_{\text{BX}} = 2.4$ Hz, 1H), 3.36-3.24 (m, 4H), 2.50 (s, 1H), 2.34 (m, 1H), 2.22-1.94 (m, 6H), 1.85 (qd, $J = 12.9, 3.9$ Hz, 1H), 1.78-1.19 (m, 8H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 140.6 (C_4), 129.4 (CH), 83.6 (C_4), 81.0 (C_4), 76.2 (C_4), 75.5 (CH), 73.0 (CH), 66.2 (C_4), 54.7 (CH), 52.0 (CH_2), 41.6 (CH_2), 39.8 (CH_2), 39.7 (CH_2), 35.8 (CH_2), 26.3 (CH_2), 25.6 (CH_2), 25.4 (CH_2), 23.0 (CH_2), 20.4 (CH_2); HRMS (EI) m/z calcd for $\text{C}_{19}\text{H}_{24}\text{OS}_2$ (M) $^+$ 332.1269, found 332.1251.

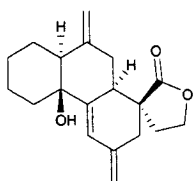
α -Methylene- γ -butyrolactone (3.64)



A solution of α -Bromo- γ -butyrolactone **3.61** (4.904 g, 29.4 mmol) and triphenylphosphine (7.795 g, 29.4 mmol) in THF was refluxed with a condenser for ~2 hours. The reaction mixture was cooled down to 0 °C and the precipitate was filtered out. The precipitate was dissolved in hot methanol (3 mL) and crystallisation was initiated by the addition of cold diethyl ether (4 mL). The white crystals **3.62** (6.051 g, 48%) were filtered out and dissolved in 30% methanol (10 mL). To this solution was added aqueous Na_2CO_3 (2.0 mL; 0.28 M) and the reaction was stirred for 40 minutes, at which point the phosphorane **3.63** was filtered out as off-white crystals. A solution of the crude **3.63** and paraformaldehyde (0.898 g, 28.4 mmol) in THF (10 mL) were refluxed with a condenser for ~2.5 hours. The solution was concentrated to a third of its original

volume and hexanes (10 mL) was added to precipitate out triphenylphosphine oxide. The remaining solution was quickly passed through a pad of silica and concentrated to afford α -methylene- γ -butyrolactone **3.64** (0.988 g, 71% over 2 steps). Characterisation data is available through the literature.^{57b}

Tetracyclic compound (**3.65**)



2.0 equivalents of $\text{MgBr}_2 \cdot \text{OEt}_2$, along with 4.0 equivalents of triethylamine were used; 5.0 equivalents of α -Methylene- γ -butyrolactone were added. Flash chromatography (15% ethyl acetate in hexanes) afforded **3.65** (29.4 mg, 16%) as a yellow oil. IR (neat, cm^{-1}) 3463 (br w), 2933 (s), 2856 (m), 1764 (s), 1173 (m), 1029 (m); ^1H NMR (CDCl_3 , 300 MHz) δ 6.49 (s, 1H), 4.98 (s, 1H), 4.90 (s, 2H), 4.72 (s, 1H), 4.34-4.25 (m, 2H), 2.67 (d, $J = 14.8$ Hz, 1H), 2.60-2.52 (m, 2H), 2.45-2.35 (m, 2H), 2.11-1.96 (m, 3H), 1.87-1.22 (m, 9 H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 148.1 (C_4), 145.6 (C_4), 138.9 (C_4), 124.9 (CH), 114.5 (CH_2), 110.1 (CH_2), 72.4 (C_4), 64.9 (CH_2), 46.5 (CH), 43.8 (C_4), 36.8 (CH_2), 36.5 (CH), 35.3 (CH_2), 35.2 (CH_2), 34.6 (CH_2), 34.0 (CH_2), 25.5 (CH_2), 22.3 (CH_2), 21.3 (CH_2); HRMS (EI) m/z calcd for $\text{C}_{19}\text{H}_{24}\text{O}_3$ (M^+) 300.1725, found 300.1733.

CLAIMS TO ORIGINAL RESEARCH

1. Studied the scope and limitations of the tandem oxy-Cope/Claisen/ene/Claisen and oxy-Cope/Claisen/ene reactions as applied to various substrates.
2. Developed a highly regio- and stereoselective tandem oxy-Cope/Claisen/ene/HDDA reaction. Four different types of substrates were surveyed with a wide variety of dienophiles; propargyl ethers were converted to the corresponding diterpenes as single diastereoisomers.
3. Oral Presentation: “An Expeditious Synthesis of Diterpenes: Cascade of Four Pericyclic Reactions - Oxy-Cope/Claisen/Ene/Hydroxy-Directed Diels-Alder Reaction” R. Clément and L. Barriault: November 6th, 2004, 15th Québec-Ontario Minisymposium in Synthetic and Bioorganic Chemistry (QOMSSBOC), University of Ottawa, Ottawa, Ontario, Canada.
4. Poster Presentations: “An Expeditious Synthesis of Diterpenes: Cascade of Four Pericyclic Reactions - Oxy-Cope/Claisen/Ene/Hydroxy-Directed Diels-Alder Reaction” R. Clément and L. Barriault (i) December 2003, 14th Québec-Ontario Minisymposium in Synthetic and Bioorganic Chemistry (QOMSSBOC), Université de Québec à Montréal (UQAM), Montréal, Québec, Canada. (ii) May 2004, Organic Synthesis Day, University of Ottawa, Ontario, Canada.

SPECTRA

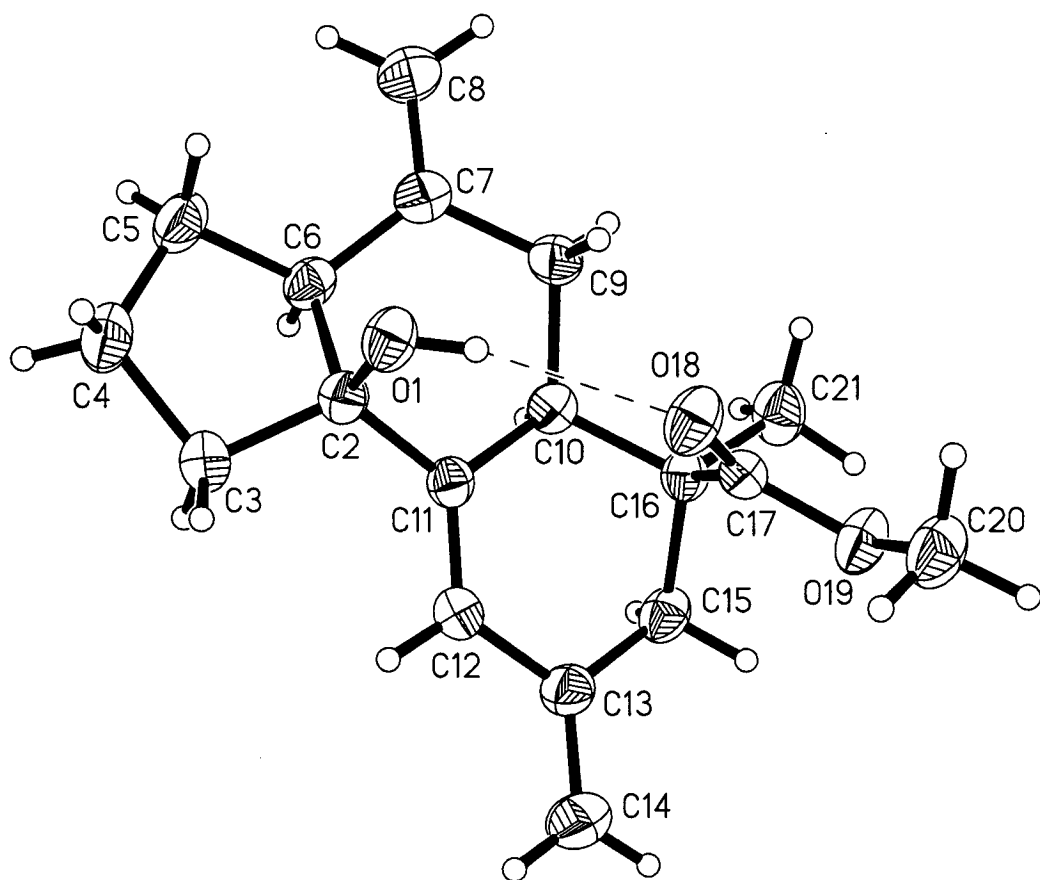


Table 1. Crystal data and structure refinement for lb403.

Identification code	lb403	
Empirical formula	C ₁₈ H ₂₄ O ₃	
Formula weight	288.37	
Temperature	206(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 6.4756(11) Å	α = 115.133(2)°.
	b = 11.3717(19) Å	β = 95.490(3)°.
	c = 12.327(2) Å	γ = 104.228(2)°.
Volume	775.6(2) Å ³	
Z	2	
Density (calculated)	1.235 Mg/m ³	
Absorption coefficient	0.082 mm ⁻¹	
F(000)	312	
Crystal size	0.55 x 0.35 x 0.05 mm ³	
Theta range for data collection	1.87 to 26.37°.	
Index ranges	-8 ≤ h ≤ 8, -14 ≤ k ≤ 14, -15 ≤ l ≤ 15	
Reflections collected	8270	
Independent reflections	3141 [R(int) = 0.0223]	
Completeness to theta = 26.37°	99.4 %	
Absorption correction	Multiscan, SADABS	
Max. and min. transmission	0.9957 and 0.9561	
Refinement method	Full-matrix least-squares on F ²	
Data / restraints / parameters	3141 / 0 / 194	
Goodness-of-fit on F ²	1.047	
Final R indices [I > 2σ(I)]	R1 = 0.0459, wR2 = 0.1077	
R indices (all data)	R1 = 0.0601, wR2 = 0.1136	
Extinction coefficient	0.023(4)	
Largest diff. peak and hole	0.252 and -0.167 e.Å ⁻³	

Table 2. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for lb403. $U(\text{eq})$ is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	$U(\text{eq})$
O(1)	5085(2)	1414(1)	7558(1)	33(1)
C(2)	6875(2)	2524(2)	8526(1)	28(1)
C(3)	5890(3)	3251(2)	9602(2)	36(1)
C(4)	5381(3)	2272(2)	10171(2)	41(1)
C(5)	6876(3)	1369(2)	9785(2)	40(1)
C(6)	8309(3)	1918(2)	9070(1)	30(1)
C(7)	9205(2)	963(2)	8115(1)	31(1)
C(8)	9646(3)	-90(2)	8171(2)	45(1)
C(9)	9571(3)	1271(2)	7052(1)	31(1)
C(10)	9888(2)	2781(2)	7358(1)	27(1)
C(11)	8189(2)	3350(2)	7999(1)	26(1)
C(12)	7834(3)	4469(2)	8018(1)	31(1)
C(13)	8907(3)	5182(2)	7379(1)	34(1)
C(14)	8384(4)	6223(2)	7334(2)	52(1)
C(15)	10603(3)	4647(2)	6746(2)	33(1)
C(16)	10085(2)	3083(2)	6253(1)	28(1)
C(17)	7922(2)	2350(2)	5286(1)	27(1)
O(18)	6286(2)	1598(1)	5320(1)	37(1)
O(19)	8050(2)	2656(1)	4352(1)	37(1)
C(20)	6078(3)	2033(2)	3388(2)	44(1)
C(21)	11933(3)	2647(2)	5654(2)	39(1)

Table 3. Bond lengths [Å] and angles [°] for lb403.

O(1)-C(2)	1.4488(18)
O(1)-H(1A)	0.8300
C(2)-C(11)	1.503(2)
C(2)-C(3)	1.529(2)
C(2)-C(6)	1.542(2)
C(3)-C(4)	1.539(2)
C(3)-H(3A)	0.9800
C(3)-H(3B)	0.9800
C(4)-C(5)	1.542(3)
C(4)-H(4A)	0.9800
C(4)-H(4B)	0.9800
C(5)-C(6)	1.538(2)
C(5)-H(5A)	0.9800
C(5)-H(5B)	0.9800
C(6)-C(7)	1.501(2)
C(6)-H(6A)	0.9900
C(7)-C(8)	1.324(2)
C(7)-C(9)	1.519(2)
C(8)-H(8A)	0.9400
C(8)-H(8B)	0.9400
C(9)-C(10)	1.548(2)
C(9)-H(9A)	0.9800
C(9)-H(9B)	0.9800
C(10)-C(11)	1.528(2)
C(10)-C(16)	1.547(2)
C(10)-H(10A)	0.9900
C(11)-C(12)	1.339(2)
C(12)-C(13)	1.460(2)
C(12)-H(12A)	0.9400
C(13)-C(14)	1.330(2)
C(13)-C(15)	1.508(2)
C(14)-H(14A)	0.9400
C(14)-H(14B)	0.9400
C(15)-C(16)	1.548(2)

C(15)-H(15A)	0.9800
C(15)-H(15B)	0.9800
C(16)-C(17)	1.530(2)
C(16)-C(21)	1.540(2)
C(17)-O(18)	1.2039(18)
C(17)-O(19)	1.3414(18)
O(19)-C(20)	1.447(2)
C(20)-H(20A)	0.9700
C(20)-H(20B)	0.9700
C(20)-H(20C)	0.9700
C(21)-H(21A)	0.9700
C(21)-H(21B)	0.9700
C(21)-H(21C)	0.9700

C(2)-O(1)-H(1A)	109.5
O(1)-C(2)-C(11)	109.09(11)
O(1)-C(2)-C(3)	106.94(12)
C(11)-C(2)-C(3)	118.66(13)
O(1)-C(2)-C(6)	108.90(12)
C(11)-C(2)-C(6)	110.64(12)
C(3)-C(2)-C(6)	102.12(12)
C(2)-C(3)-C(4)	104.20(13)
C(2)-C(3)-H(3A)	110.9
C(4)-C(3)-H(3A)	110.9
C(2)-C(3)-H(3B)	110.9
C(4)-C(3)-H(3B)	110.9
H(3A)-C(3)-H(3B)	108.9
C(3)-C(4)-C(5)	106.47(13)
C(3)-C(4)-H(4A)	110.4
C(5)-C(4)-H(4A)	110.4
C(3)-C(4)-H(4B)	110.4
C(5)-C(4)-H(4B)	110.4
H(4A)-C(4)-H(4B)	108.6
C(6)-C(5)-C(4)	105.39(13)
C(6)-C(5)-H(5A)	110.7
C(4)-C(5)-H(5A)	110.7

C(6)-C(5)-H(5B)	110.7
C(4)-C(5)-H(5B)	110.7
H(5A)-C(5)-H(5B)	108.8
C(7)-C(6)-C(5)	118.88(14)
C(7)-C(6)-C(2)	112.28(12)
C(5)-C(6)-C(2)	103.67(13)
C(7)-C(6)-H(6A)	107.1
C(5)-C(6)-H(6A)	107.1
C(2)-C(6)-H(6A)	107.1
C(8)-C(7)-C(6)	123.37(15)
C(8)-C(7)-C(9)	121.12(15)
C(6)-C(7)-C(9)	115.51(13)
C(7)-C(8)-H(8A)	120.0
C(7)-C(8)-H(8B)	120.0
H(8A)-C(8)-H(8B)	120.0
C(7)-C(9)-C(10)	114.00(13)
C(7)-C(9)-H(9A)	108.8
C(10)-C(9)-H(9A)	108.8
C(7)-C(9)-H(9B)	108.8
C(10)-C(9)-H(9B)	108.8
H(9A)-C(9)-H(9B)	107.6
C(11)-C(10)-C(16)	110.23(12)
C(11)-C(10)-C(9)	113.91(12)
C(16)-C(10)-C(9)	114.41(12)
C(11)-C(10)-H(10A)	105.8
C(16)-C(10)-H(10A)	105.8
C(9)-C(10)-H(10A)	105.8
C(12)-C(11)-C(2)	122.99(14)
C(12)-C(11)-C(10)	121.25(13)
C(2)-C(11)-C(10)	115.66(12)
C(11)-C(12)-C(13)	123.56(15)
C(11)-C(12)-H(12A)	118.2
C(13)-C(12)-H(12A)	118.2
C(14)-C(13)-C(12)	121.93(16)
C(14)-C(13)-C(15)	121.96(16)
C(12)-C(13)-C(15)	116.10(13)

C(13)-C(14)-H(14A)	120.0
C(13)-C(14)-H(14B)	120.0
H(14A)-C(14)-H(14B)	120.0
C(13)-C(15)-C(16)	112.97(12)
C(13)-C(15)-H(15A)	109.0
C(16)-C(15)-H(15A)	109.0
C(13)-C(15)-H(15B)	109.0
C(16)-C(15)-H(15B)	109.0
H(15A)-C(15)-H(15B)	107.8
C(17)-C(16)-C(21)	109.38(12)
C(17)-C(16)-C(10)	110.43(12)
C(21)-C(16)-C(10)	111.93(12)
C(17)-C(16)-C(15)	108.73(12)
C(21)-C(16)-C(15)	108.87(13)
C(10)-C(16)-C(15)	107.41(12)
O(18)-C(17)-O(19)	122.48(14)
O(18)-C(17)-C(16)	126.74(13)
O(19)-C(17)-C(16)	110.77(12)
C(17)-O(19)-C(20)	115.57(12)
O(19)-C(20)-H(20A)	109.5
O(19)-C(20)-H(20B)	109.5
H(20A)-C(20)-H(20B)	109.5
O(19)-C(20)-H(20C)	109.5
H(20A)-C(20)-H(20C)	109.5
H(20B)-C(20)-H(20C)	109.5
C(16)-C(21)-H(21A)	109.5
C(16)-C(21)-H(21B)	109.5
H(21A)-C(21)-H(21B)	109.5
C(16)-C(21)-H(21C)	109.5
H(21A)-C(21)-H(21C)	109.5
H(21B)-C(21)-H(21C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for lb403. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + \dots + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	30(1)	38(1)	28(1)	17(1)	3(1)	6(1)
C(2)	30(1)	29(1)	26(1)	13(1)	6(1)	10(1)
C(3)	42(1)	39(1)	31(1)	17(1)	14(1)	16(1)
C(4)	46(1)	46(1)	31(1)	21(1)	12(1)	10(1)
C(5)	51(1)	42(1)	32(1)	23(1)	9(1)	11(1)
C(6)	32(1)	30(1)	26(1)	15(1)	1(1)	7(1)
C(7)	27(1)	31(1)	33(1)	16(1)	0(1)	7(1)
C(8)	53(1)	45(1)	48(1)	28(1)	12(1)	24(1)
C(9)	33(1)	32(1)	34(1)	16(1)	9(1)	16(1)
C(10)	24(1)	30(1)	27(1)	14(1)	3(1)	8(1)
C(11)	28(1)	27(1)	22(1)	10(1)	3(1)	7(1)
C(12)	37(1)	30(1)	28(1)	12(1)	10(1)	13(1)
C(13)	43(1)	26(1)	31(1)	13(1)	6(1)	8(1)
C(14)	72(1)	45(1)	62(1)	37(1)	31(1)	26(1)
C(15)	34(1)	31(1)	32(1)	17(1)	5(1)	1(1)
C(16)	27(1)	30(1)	28(1)	14(1)	7(1)	8(1)
C(17)	31(1)	26(1)	26(1)	12(1)	10(1)	12(1)
O(18)	31(1)	44(1)	34(1)	22(1)	3(1)	3(1)
O(19)	38(1)	42(1)	30(1)	21(1)	3(1)	4(1)
C(20)	47(1)	48(1)	31(1)	21(1)	-1(1)	8(1)
C(21)	33(1)	52(1)	39(1)	24(1)	14(1)	17(1)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^{-3}$) for lb403.

	x	y	z	U(eq)
H(1A)	5308	1321	6879	49
H(3A)	4554	3393	9312	43
H(3B)	6936	4141	10201	43
H(4A)	3839	1704	9864	49
H(4B)	5682	2791	11069	49
H(5A)	7783	1446	10510	48
H(5B)	6003	406	9262	48
H(6A)	9575	2692	9683	36
H(8A)	9401	-269	8833	53
H(8B)	10206	-657	7549	53
H(9A)	8313	680	6354	38
H(9B)	10867	1042	6795	38
H(10A)	11311	3322	7958	33
H(12A)	6839	4814	8467	37
H(14A)	7294	6520	7721	63
H(14B)	9103	6663	6915	63
H(15A)	12031	5118	7328	40
H(15B)	10701	4862	6059	40
H(20A)	6361	2259	2730	65
H(20B)	4927	2377	3720	65
H(20C)	5624	1046	3069	65
H(21A)	11541	1656	5257	59
H(21B)	13277	3042	6281	59
H(21C)	12144	2968	5046	59

Table 6. Torsion angles [°] for lb403.

O(1)-C(2)-C(3)-C(4)	74.78(15)
C(11)-C(2)-C(3)-C(4)	-161.43(13)
C(6)-C(2)-C(3)-C(4)	-39.54(16)
C(2)-C(3)-C(4)-C(5)	22.52(18)
C(3)-C(4)-C(5)-C(6)	3.44(18)
C(4)-C(5)-C(6)-C(7)	-153.30(14)
C(4)-C(5)-C(6)-C(2)	-27.87(16)
O(1)-C(2)-C(6)-C(7)	58.48(16)
C(11)-C(2)-C(6)-C(7)	-61.42(17)
C(3)-C(2)-C(6)-C(7)	171.35(13)
O(1)-C(2)-C(6)-C(5)	-71.08(15)
C(11)-C(2)-C(6)-C(5)	169.03(12)
C(3)-C(2)-C(6)-C(5)	41.79(15)
C(5)-C(6)-C(7)-C(8)	-29.1(2)
C(2)-C(6)-C(7)-C(8)	-150.28(16)
C(5)-C(6)-C(7)-C(9)	150.49(14)
C(2)-C(6)-C(7)-C(9)	29.32(18)
C(8)-C(7)-C(9)-C(10)	-156.55(15)
C(6)-C(7)-C(9)-C(10)	23.85(19)
C(7)-C(9)-C(10)-C(11)	-47.49(17)
C(7)-C(9)-C(10)-C(16)	-175.56(12)
O(1)-C(2)-C(11)-C(12)	93.63(17)
C(3)-C(2)-C(11)-C(12)	-29.1(2)
C(6)-C(2)-C(11)-C(12)	-146.59(15)
O(1)-C(2)-C(11)-C(10)	-82.62(15)
C(3)-C(2)-C(11)-C(10)	154.65(13)
C(6)-C(2)-C(11)-C(10)	37.16(17)
C(16)-C(10)-C(11)-C(12)	-30.81(19)
C(9)-C(10)-C(11)-C(12)	-160.98(14)
C(16)-C(10)-C(11)-C(2)	145.52(13)
C(9)-C(10)-C(11)-C(2)	15.34(17)
C(2)-C(11)-C(12)-C(13)	-172.13(14)
C(10)-C(11)-C(12)-C(13)	3.9(2)
C(11)-C(12)-C(13)-C(14)	174.42(17)

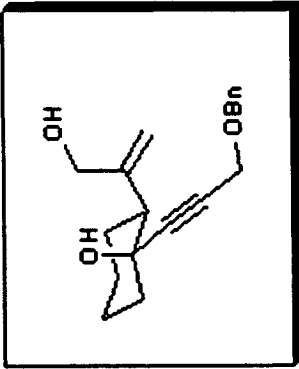
C(11)-C(12)-C(13)-C(15)	-4.2(2)
C(14)-C(13)-C(15)-C(16)	-146.57(17)
C(12)-C(13)-C(15)-C(16)	32.00(19)
C(11)-C(10)-C(16)-C(17)	-63.22(15)
C(9)-C(10)-C(16)-C(17)	66.68(16)
C(11)-C(10)-C(16)-C(21)	174.65(13)
C(9)-C(10)-C(16)-C(21)	-55.44(17)
C(11)-C(10)-C(16)-C(15)	55.20(15)
C(9)-C(10)-C(16)-C(15)	-174.89(12)
C(13)-C(15)-C(16)-C(17)	62.18(16)
C(13)-C(15)-C(16)-C(21)	-178.73(13)
C(13)-C(15)-C(16)-C(10)	-57.34(16)
C(21)-C(16)-C(17)-O(18)	121.07(17)
C(10)-C(16)-C(17)-O(18)	-2.5(2)
C(15)-C(16)-C(17)-O(18)	-120.15(16)
C(21)-C(16)-C(17)-O(19)	-59.21(16)
C(10)-C(16)-C(17)-O(19)	177.18(12)
C(15)-C(16)-C(17)-O(19)	59.56(15)
O(18)-C(17)-O(19)-C(20)	0.6(2)
C(16)-C(17)-O(19)-C(20)	-179.10(13)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for lb403 [$\text{\AA}$ and $^\circ$].

D-H...A	d(D-H)	d(H...A)	d(D...A)	$\angle(\text{DHA})$
O(1)-H(1A)...O(18)	0.83	2.20	3.0130(16)	166.6

Symmetry transformations used to generate equivalent atoms:



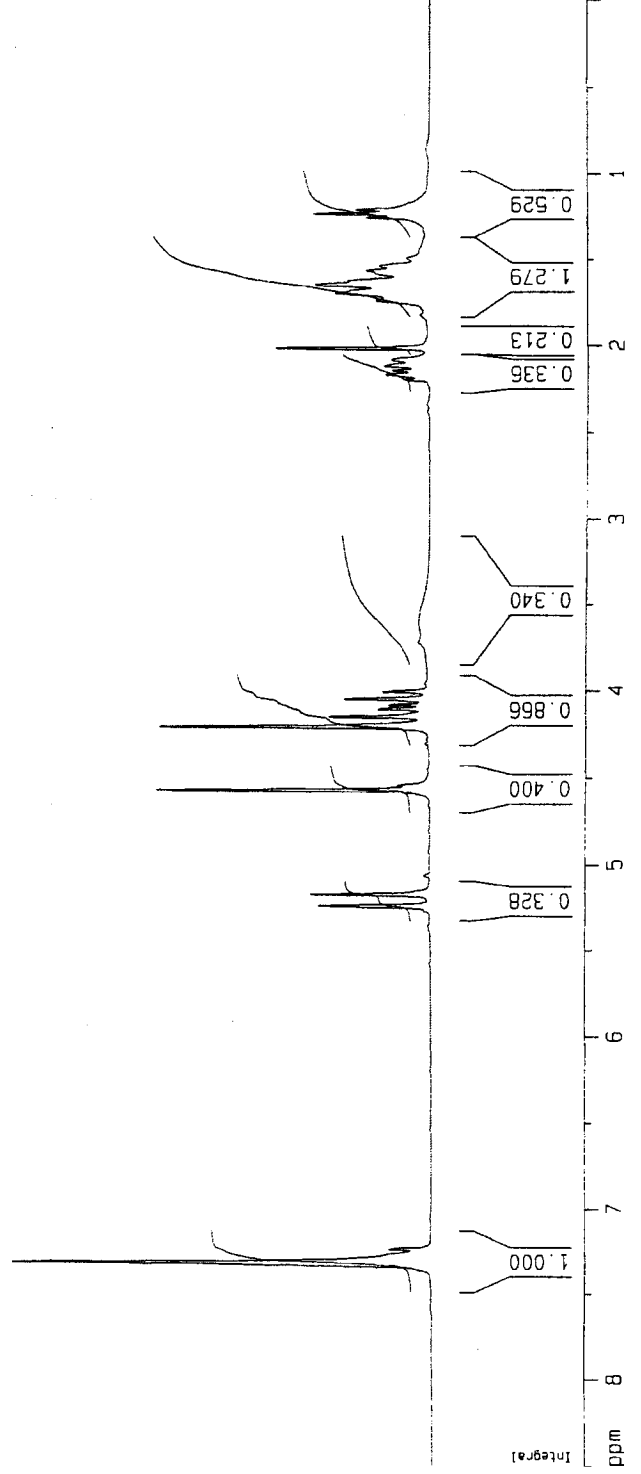
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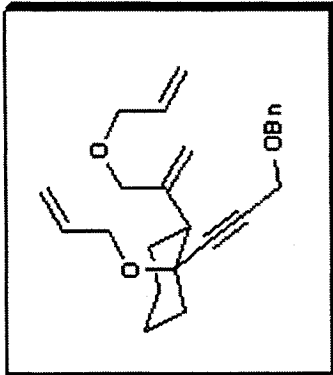
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 DE 6.00 usec
 TE 300.0 K
 D1 1.0000000 sec

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1D NMR plot parameters
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 HZCM 127.55524 Hz/cm





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 PROCNO 1

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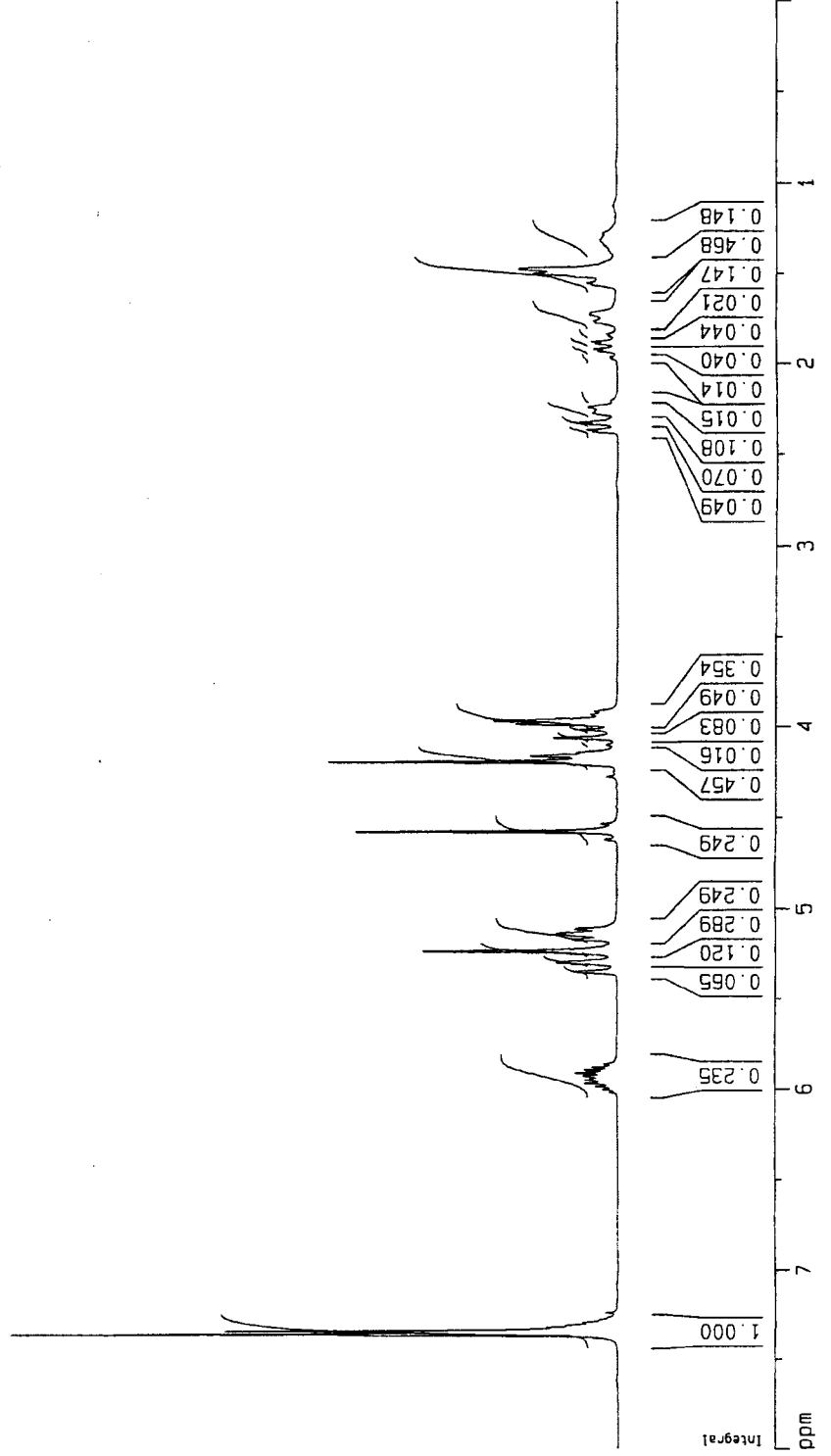
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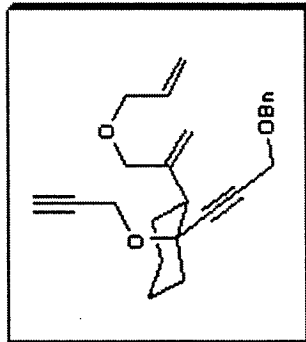
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 NQW EM
 SSB 0
 LB 0.10 Hz
 GB 0
 PC 1.00

ID NMR plot parameters

CX 20.00 cm
 CY 10.00 cm
 F1P 8.000 ppm
 F1 2401.04 Hz
 F2P 0.000 ppm
 F2 0.00 Hz
 PPMCM 0.40000 ppm/cm
 HZCM 120.05200 Hz/cm





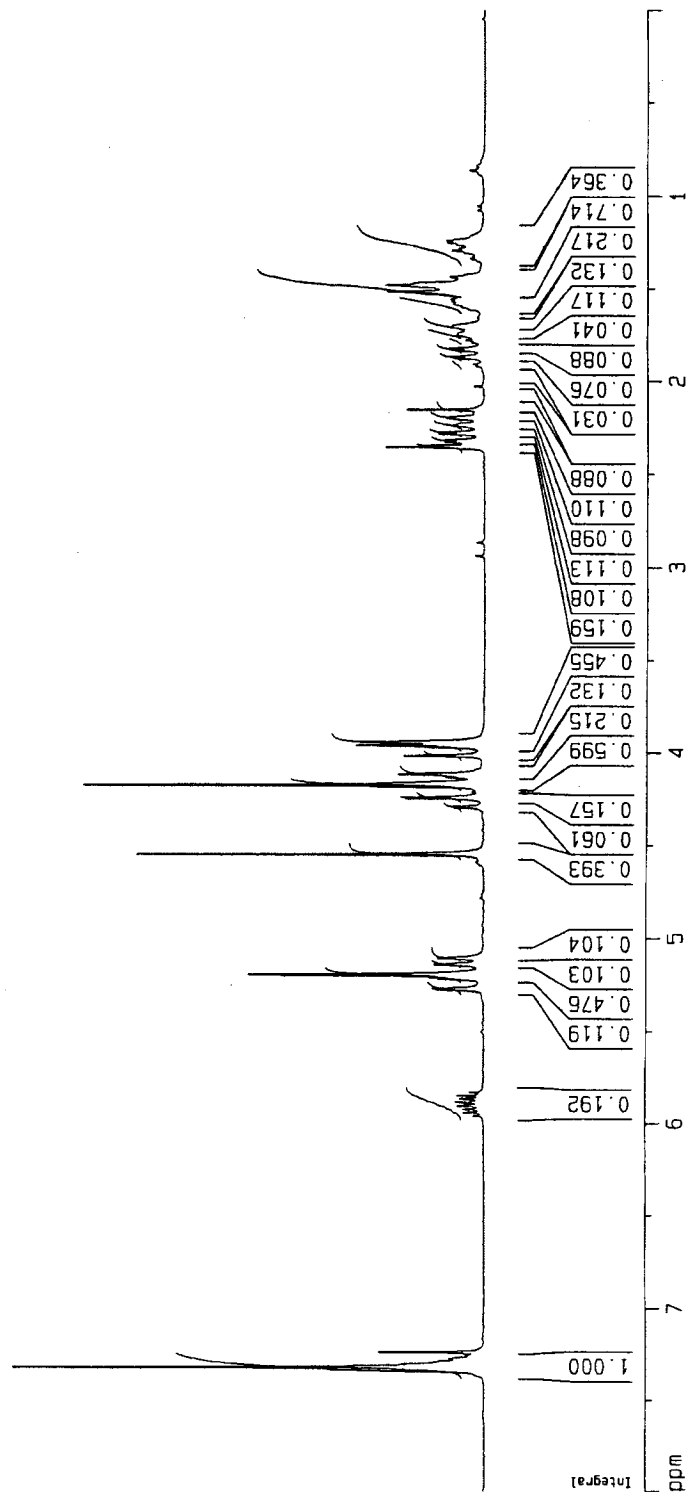
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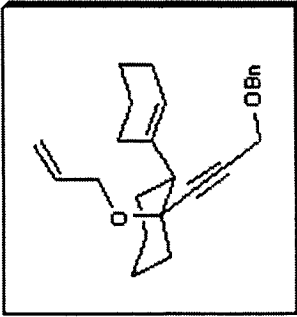
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 SOLVENT CDCl3
 NS 32
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 287.4
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

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





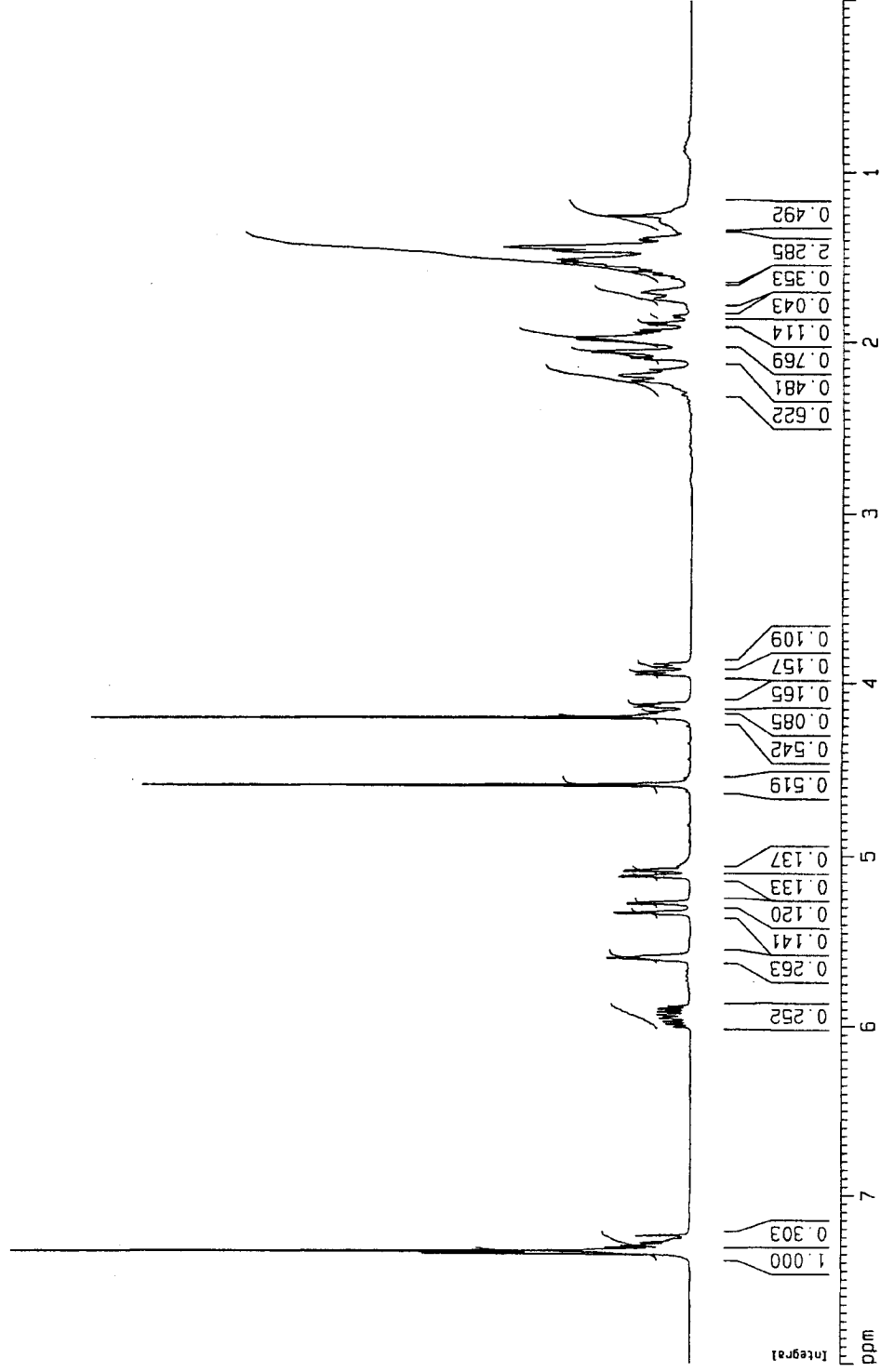
Current Data Parameters
 NAME rc_269
 EXPNO 1
 PROCNO 1

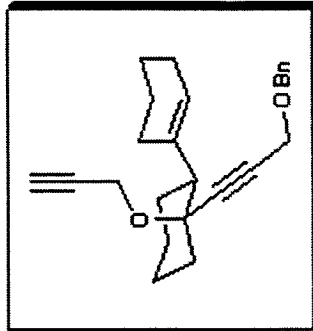
F2 - Acquisition Parameters
 Date_ 20030403
 Time 18.09
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl3
 NS 16
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 71.8
 DW 96.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

===== CHANNEL f1 =====
 NUC1 1H
 P1 10.50 usec
 PL1 -3.00 dB
 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 rc_270
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters

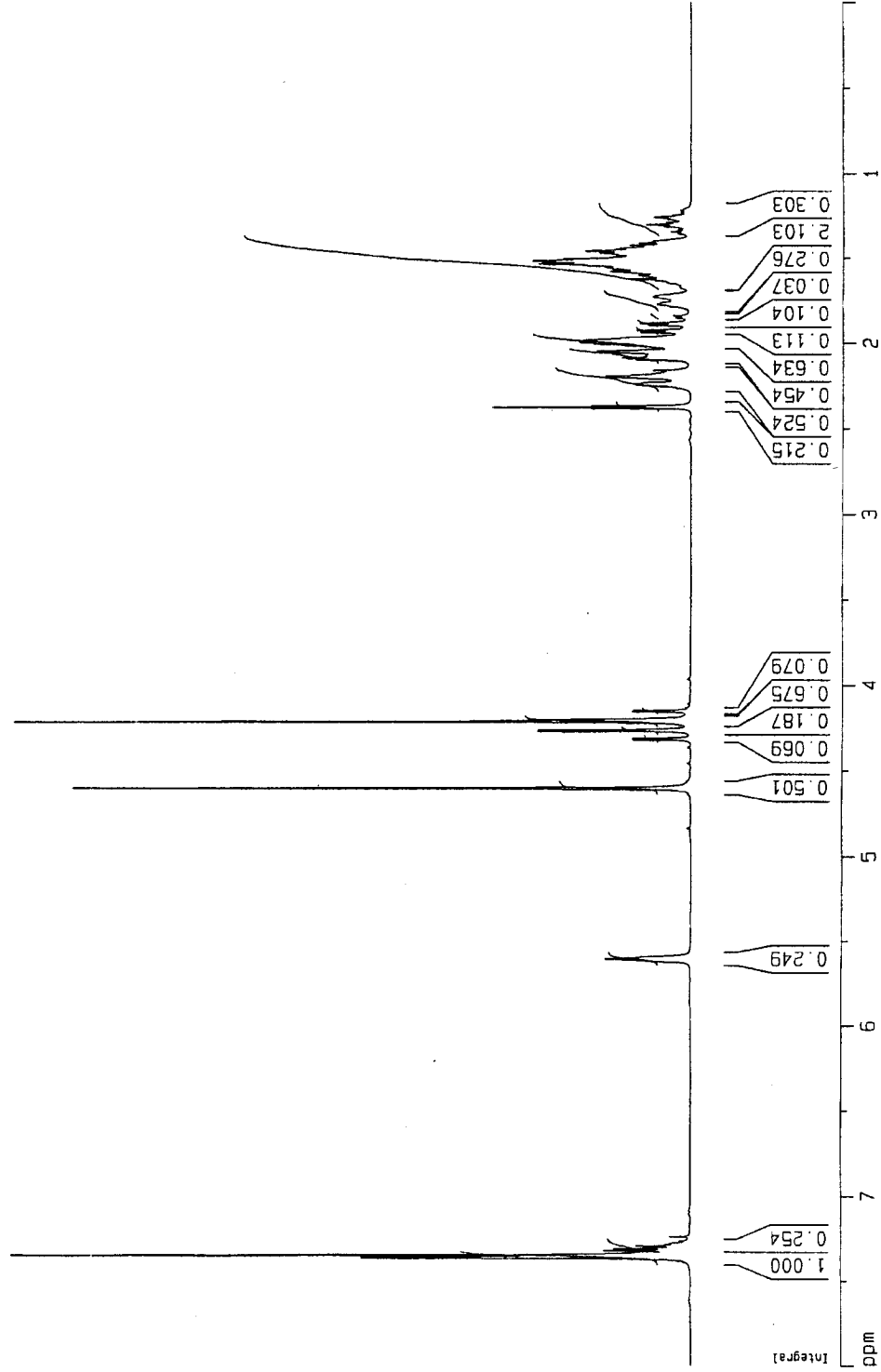
Date_ 20030404
Time 17.02
INSTRUM av300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 45.3
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.0000000 sec

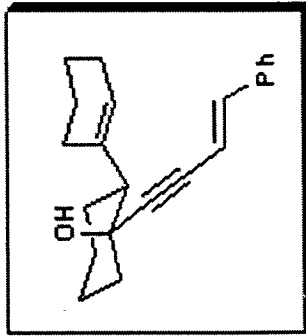
===== CHANNEL f1 =====

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 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





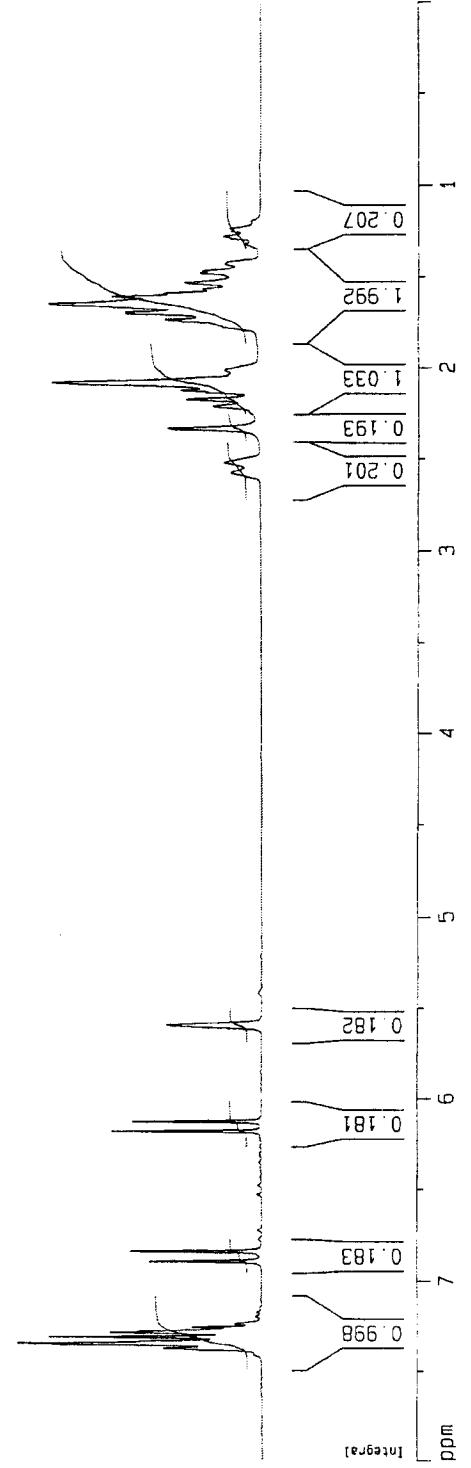
Current Data Parameters
 NAME rc_250-lp
 EXPNO 1
 PROCNO 1

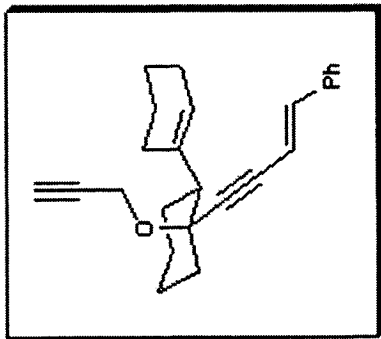
F2 - Acquisition Parameters
 Date_ 20030314
 Time 14.54
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl3
 NS 16
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 45.3
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

===== 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 8.00 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 rc_253b
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters

Date_ 20030319
 Time 13:33
 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 22.6
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.0000000 sec

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

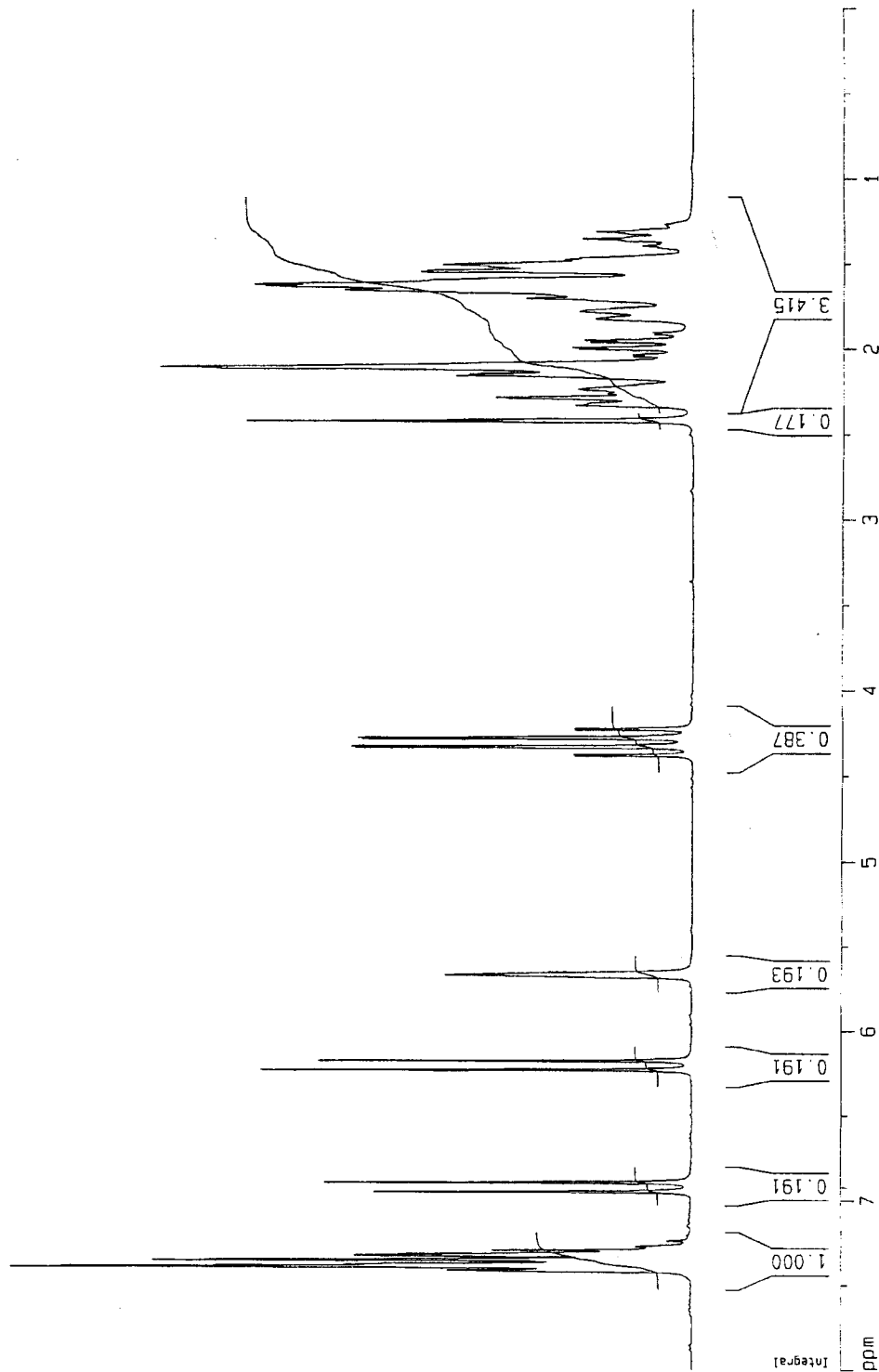
NUC1 1H
 P1 10.50 usec
 PL1 -3.00 dB
 SF01 300.1319477 MHz

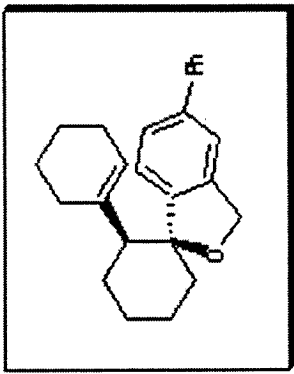
F2 - Processing parameters

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 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





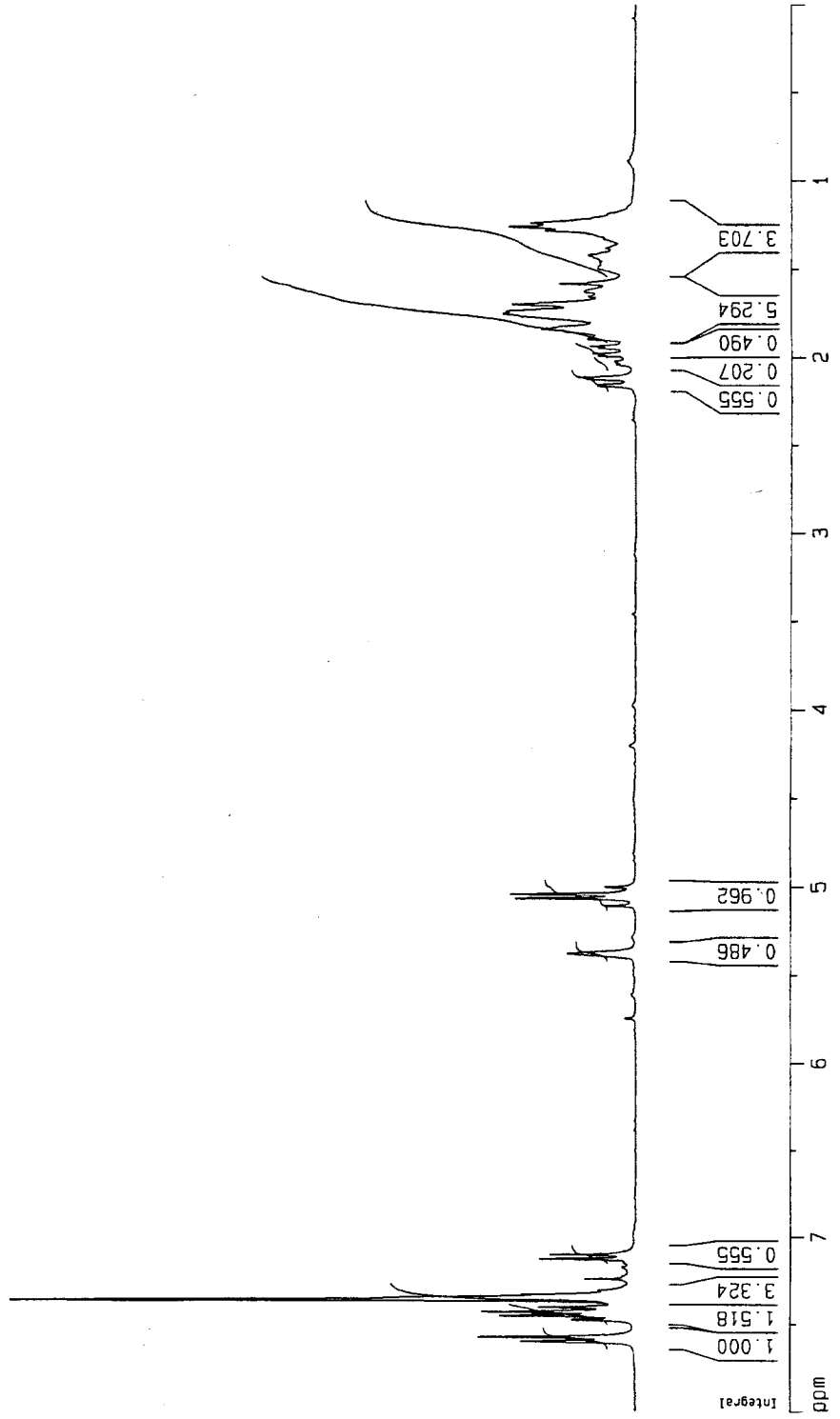
Current Data Parameters
NAME rc_302_2
EXPNO 1
PROCNO 1

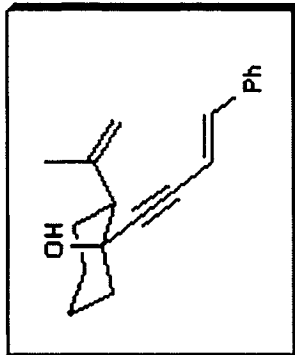
F2 - Acquisition Parameters
Date_ 20030513
Time 15.44
INSTRUM av300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 101.6
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.0000000 sec

===== 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 20.00 cm
FIP 8.000 ppm
F1 2401.04 Hz
F2 0.000 ppm
F2 0.00 Hz
PUNCH 0.40000 ppm/cm
HZCM 120.05200 Hz/cm





Current Data Parameters
 NAME prm-25
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters

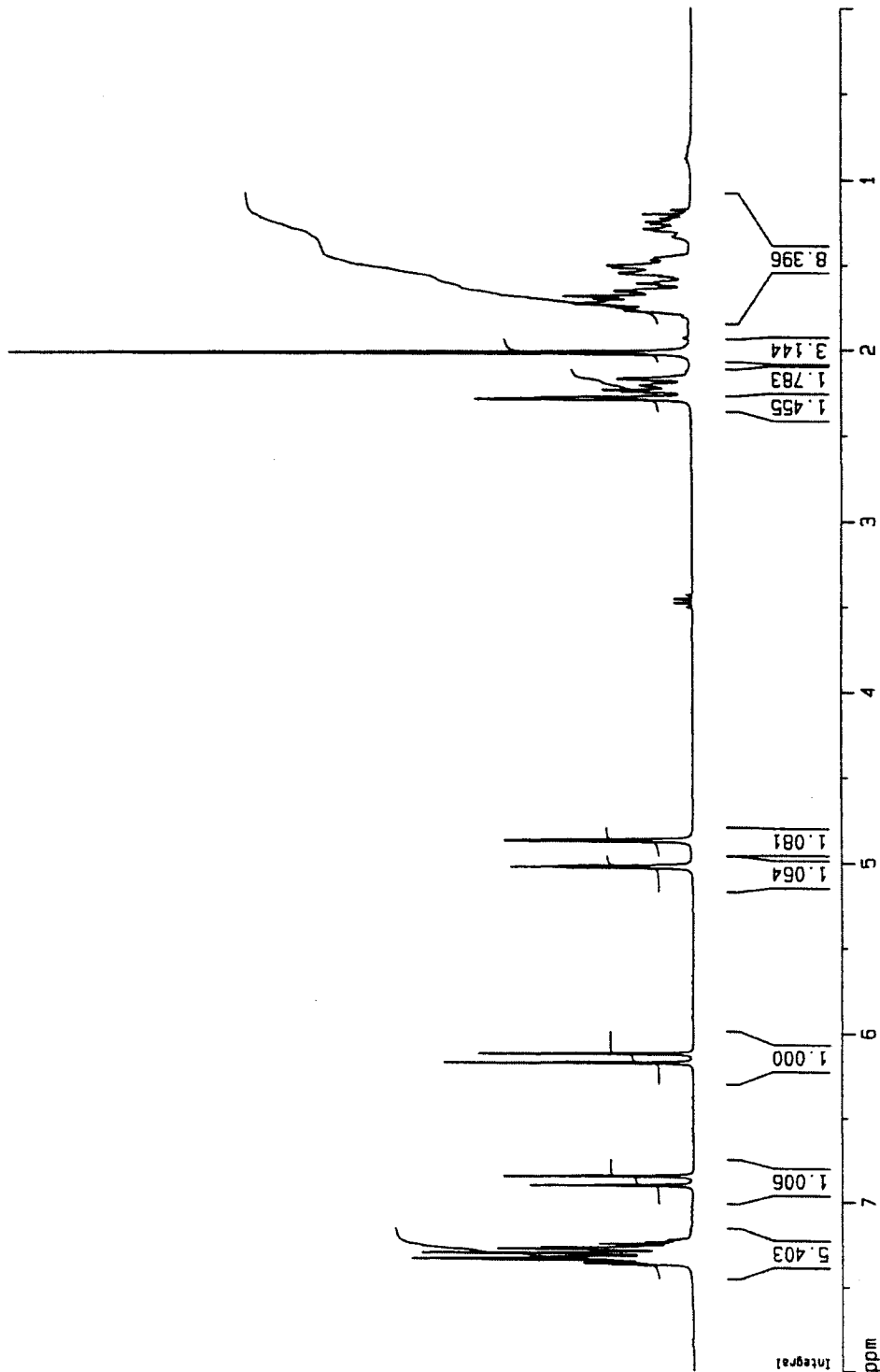
Date_ 20010606
 Time 17.31
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDC13
 NS 32
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 45.3
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.0000000 sec

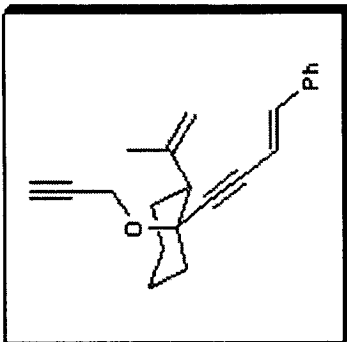
===== CHANNEL f1 =====

NUC1 1H
 P1 9.50 usec
 PL1 -3.00 dB
 SF01 300.1319477 MHz

F2 - Processing parameters

SF 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 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





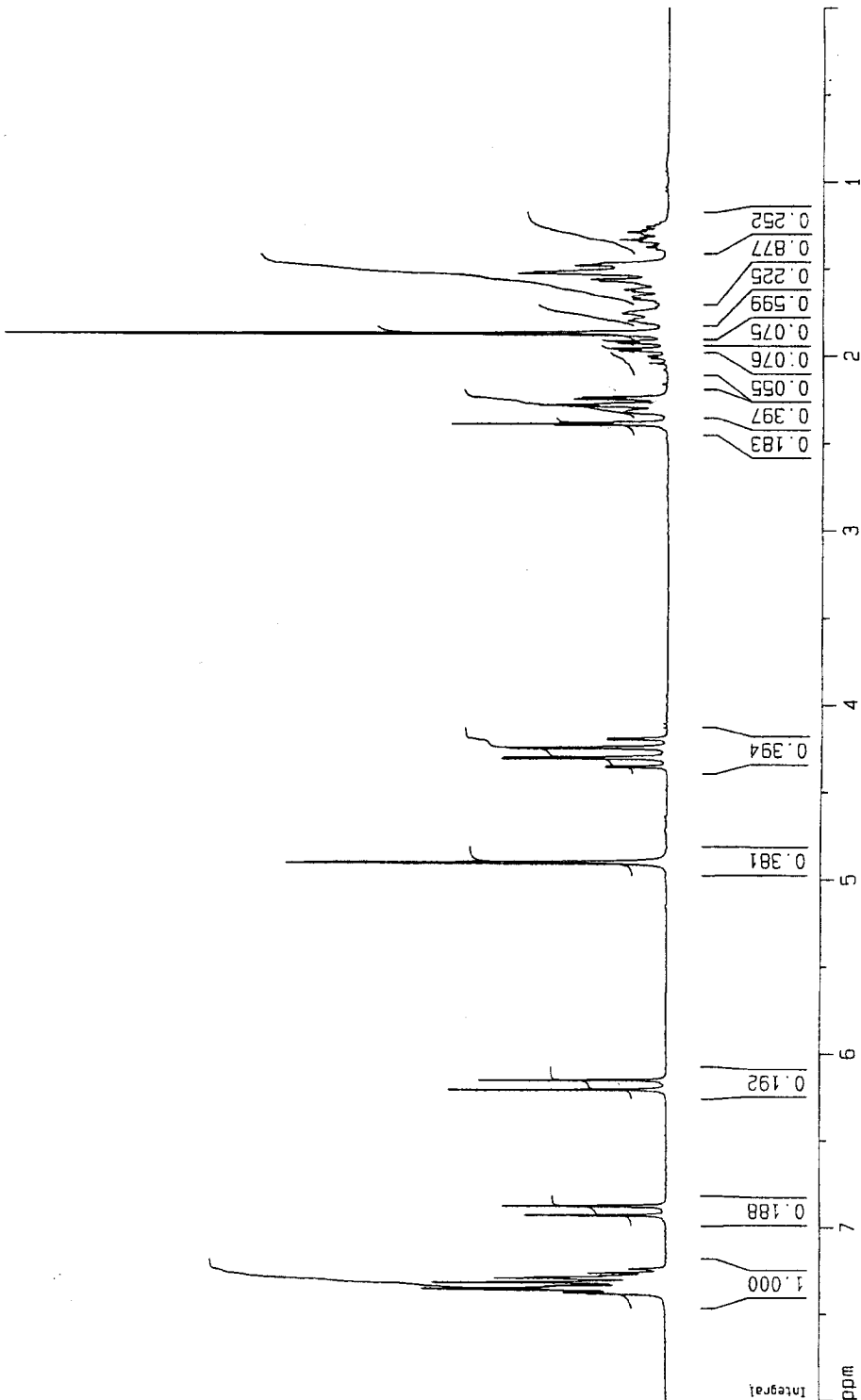
Current Data Parameters
 NAME rc_263
 EXPNO 1
 PROCNO 1

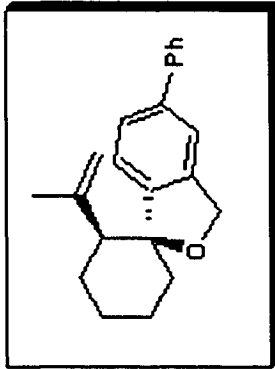
F2 - Acquisition Parameters
 Date_ 20030331
 Time 14.09
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl3
 NS 32
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 45.3
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.0000000 sec

===== 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 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 rc_267b
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters

Date_ 20030408
 Time 13.41
 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 256
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

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

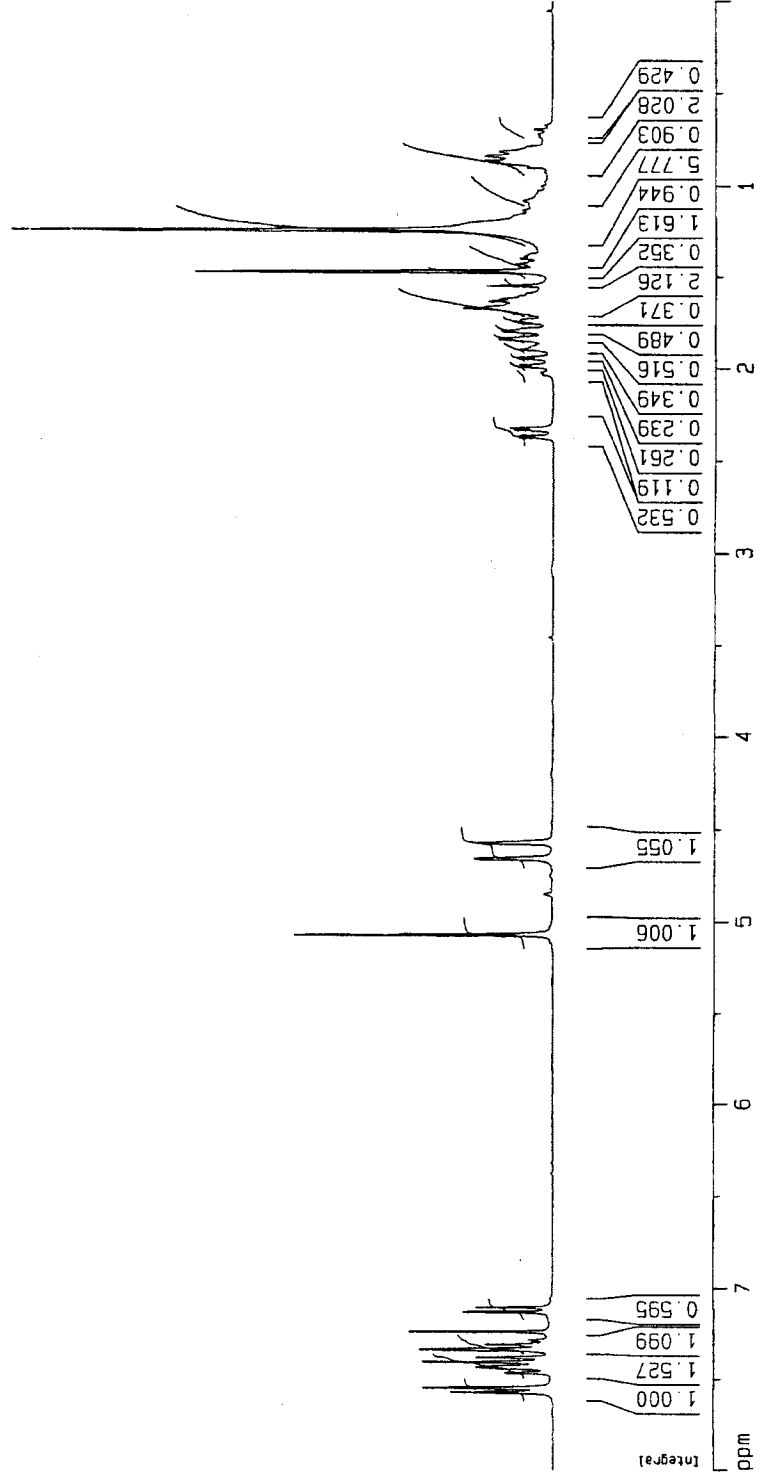
NUC1 1H
 P1 10.50 usec
 PL1 -3.00 dB
 SF01 300.1319477 MHz

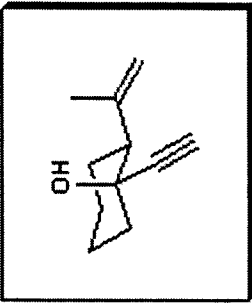
F2 - Processing parameters

SI 65536
 SF 300.1300000 MHz
 WDW EM
 SSF 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
 F2 0.000 ppm
 F2 0.00 Hz
 PPMCM 0.40000 ppm/cm
 HZCM 120.05200 Hz/cm





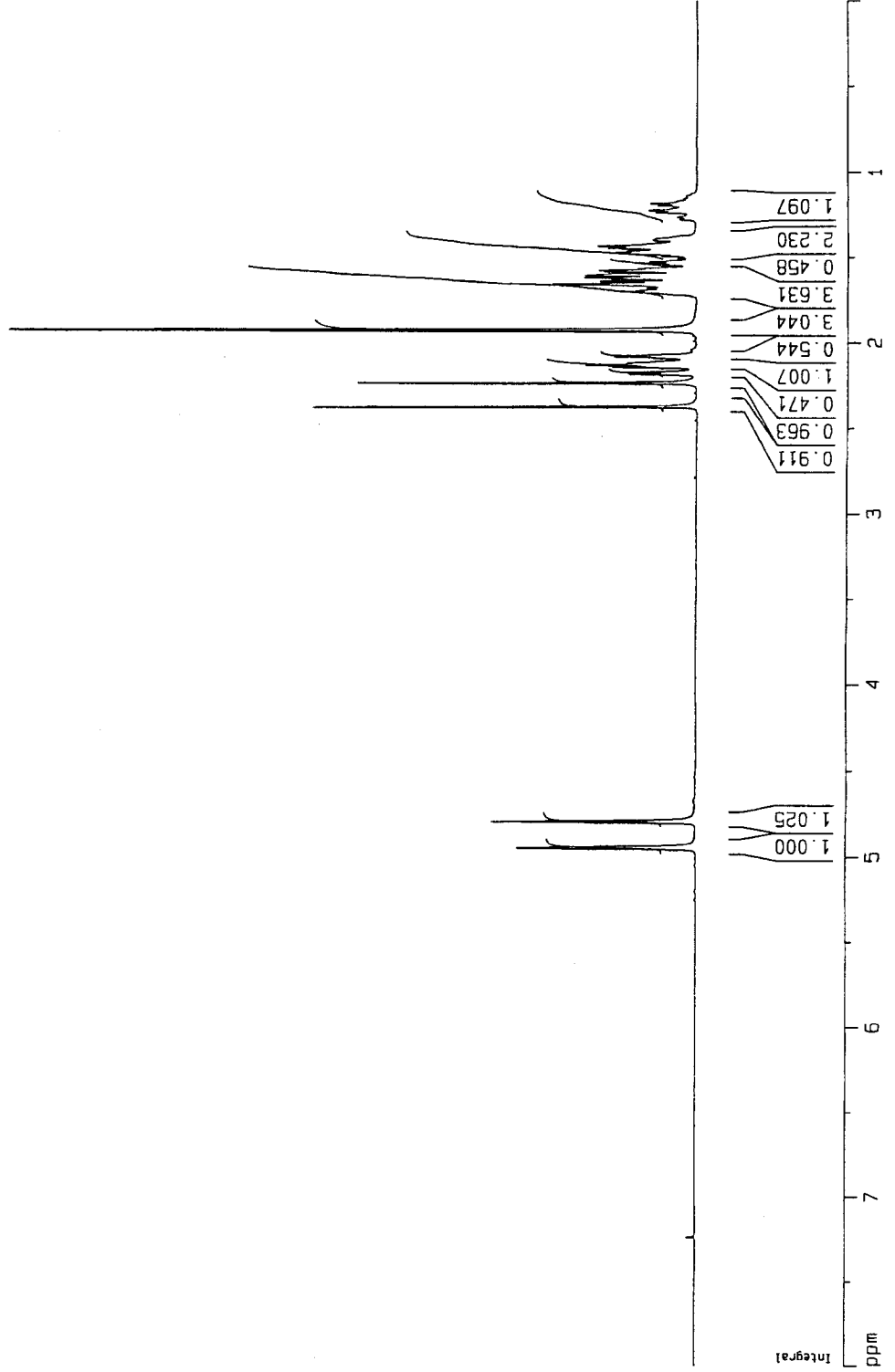
Current Data Parameters
 NAME rc_498_alcohol
 EXPNO 1
 PROCNO 1

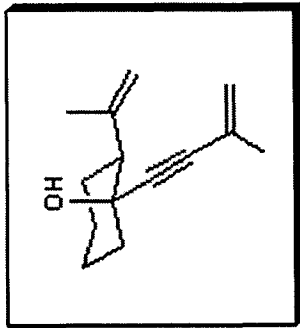
F2 - Acquisition Parameters
 Date_ 20031029
 Time 10.52
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl3
 NS 32
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 45.3
 DM 98.400 usec
 DE 5.00 usec
 TE 300.0 K
 D1 1.00000000 sec

===== 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 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





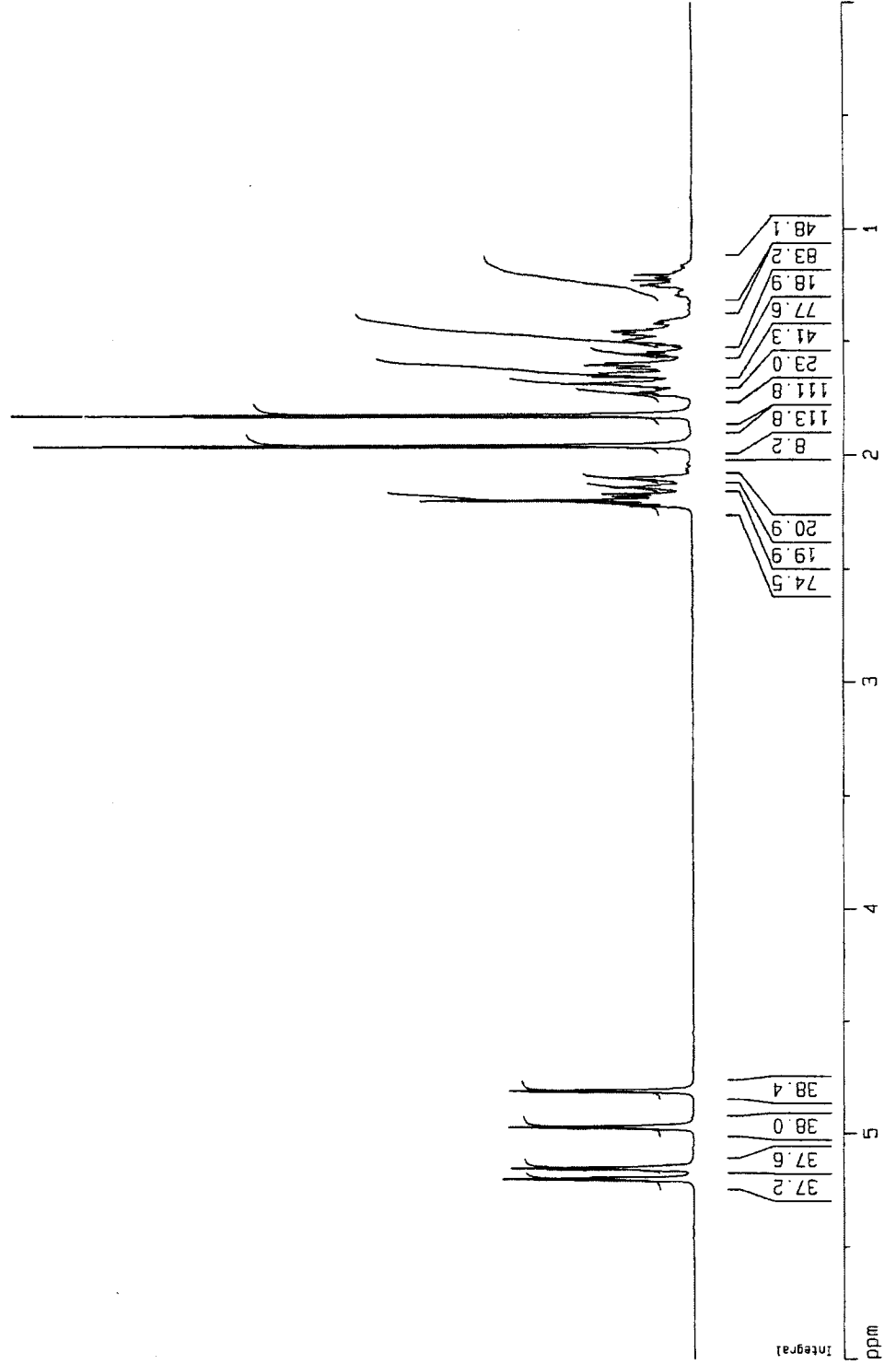
Current Data Parameters
 NAME rc_289
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20030425
 Time 16.24
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl₃
 NS 16
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 64
 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 6.000 ppm
 F1 1800.78 Hz
 F2P -0.000 ppm
 F2 -0.00 Hz
 PPMCM 0.30000 ppm/cm
 HZCM 90.03900 Hz/cm

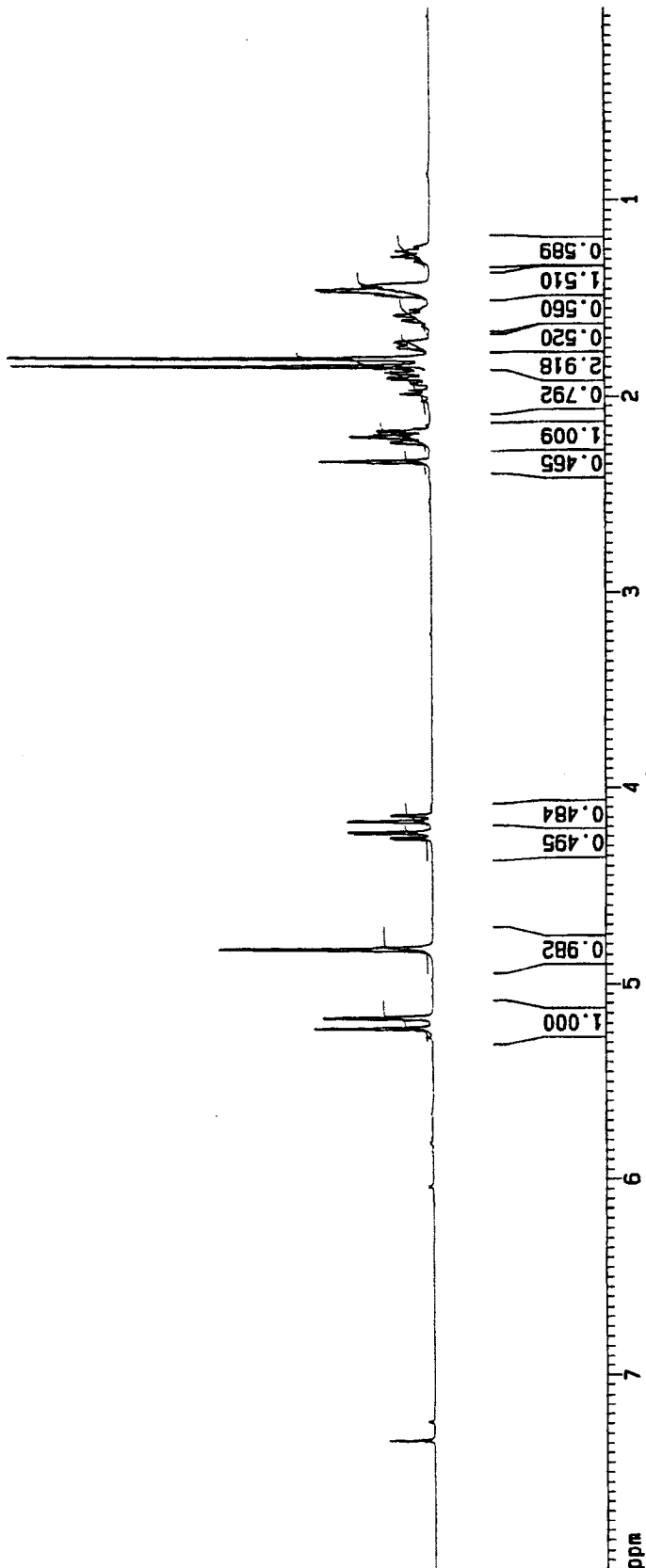
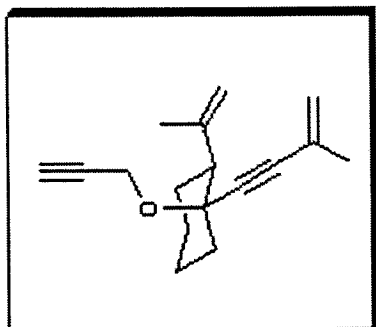


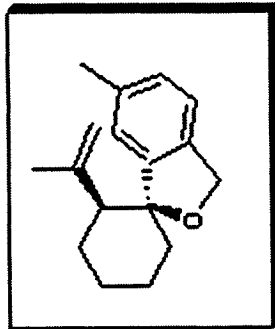
Current Data Parameters
NAME rox-misc
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date 20030424
Time 21.27
PULPROG zg
SOLVENT CDCl3
AQ 4.6530805 sec
FIDRES 0.107456 Hz
AQ 71.0 usec
RG 328
NUCLEUS 1H
HL1 0 dB
D1 0.0100000 sec
P1 5.6 usec
DE 88.8 usec
SF01 500.1381707 MHz
SNH 7042.25 Hz
TD 65536
NS 4
DS 0

F1 - Processing parameters
SI 32768
MC2 OF
SF 500.1354311 MHz
WDW EM
SSB 0
LB 0.10 Hz
GB 0

1D NMR plot parameters
CX 22.00 cm
F1P 8.000 ppm
F1 4001.08 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.36364 ppm/
HZCM 181.86743 Hz/c





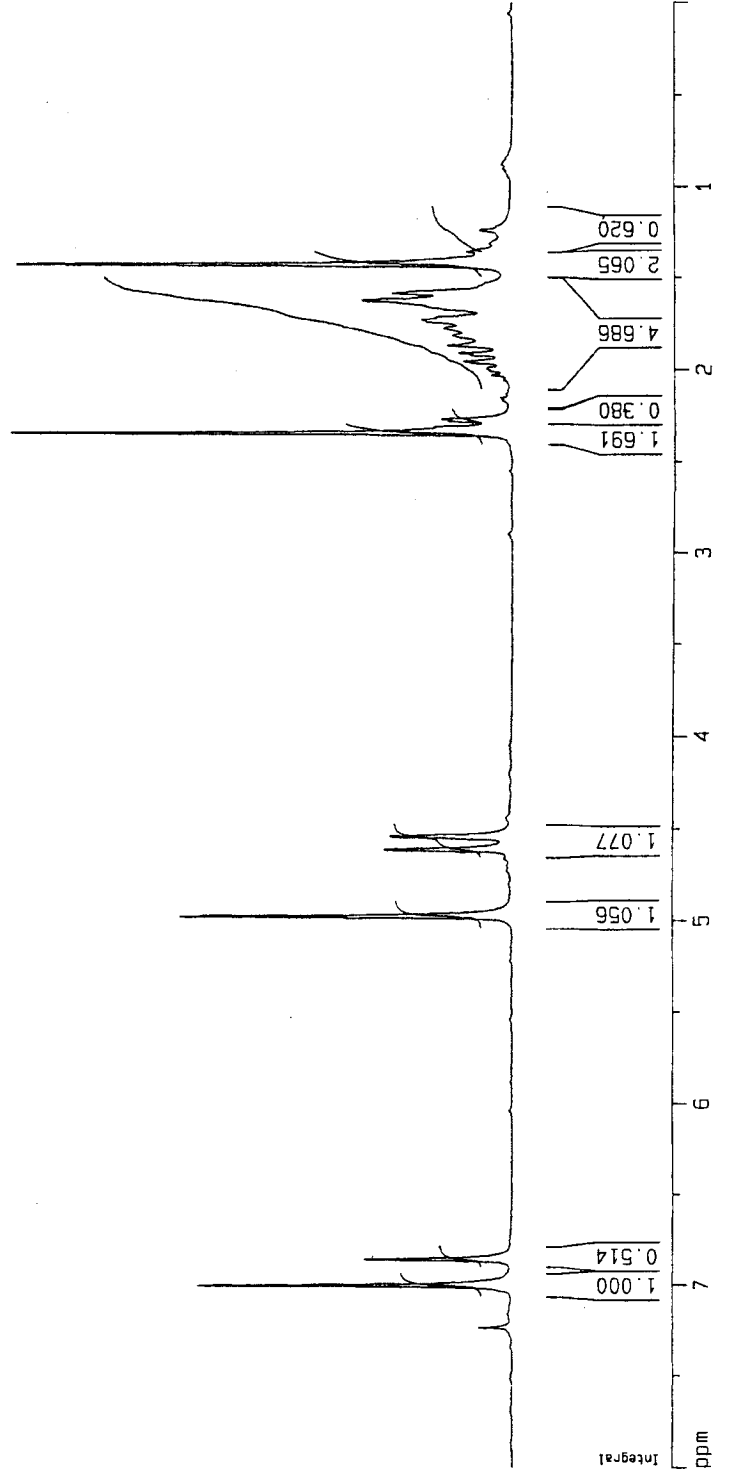
Current Data Parameters
NAME rc_293
EXPNO 1
PROCNO 1

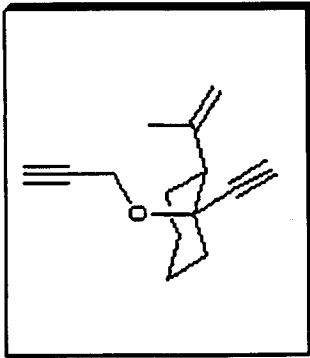
F2 - Acquisition Parameters
Date_ 20030430
Time 14.12
INSTRUM av300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 32
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 114
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

===== 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 8.00 cm
F1P 8.000 ppm
F1 2401.04 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.40000 ppm/cm
HZCM 120.05300 Hz/cm





Current Data Parameters
 NAME rc_502_280atch
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters

Date_ 20031104
 Time 17.29
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl3
 NS 32
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.155407 Hz
 AQ 3.0228980 sec
 RG 18
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

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

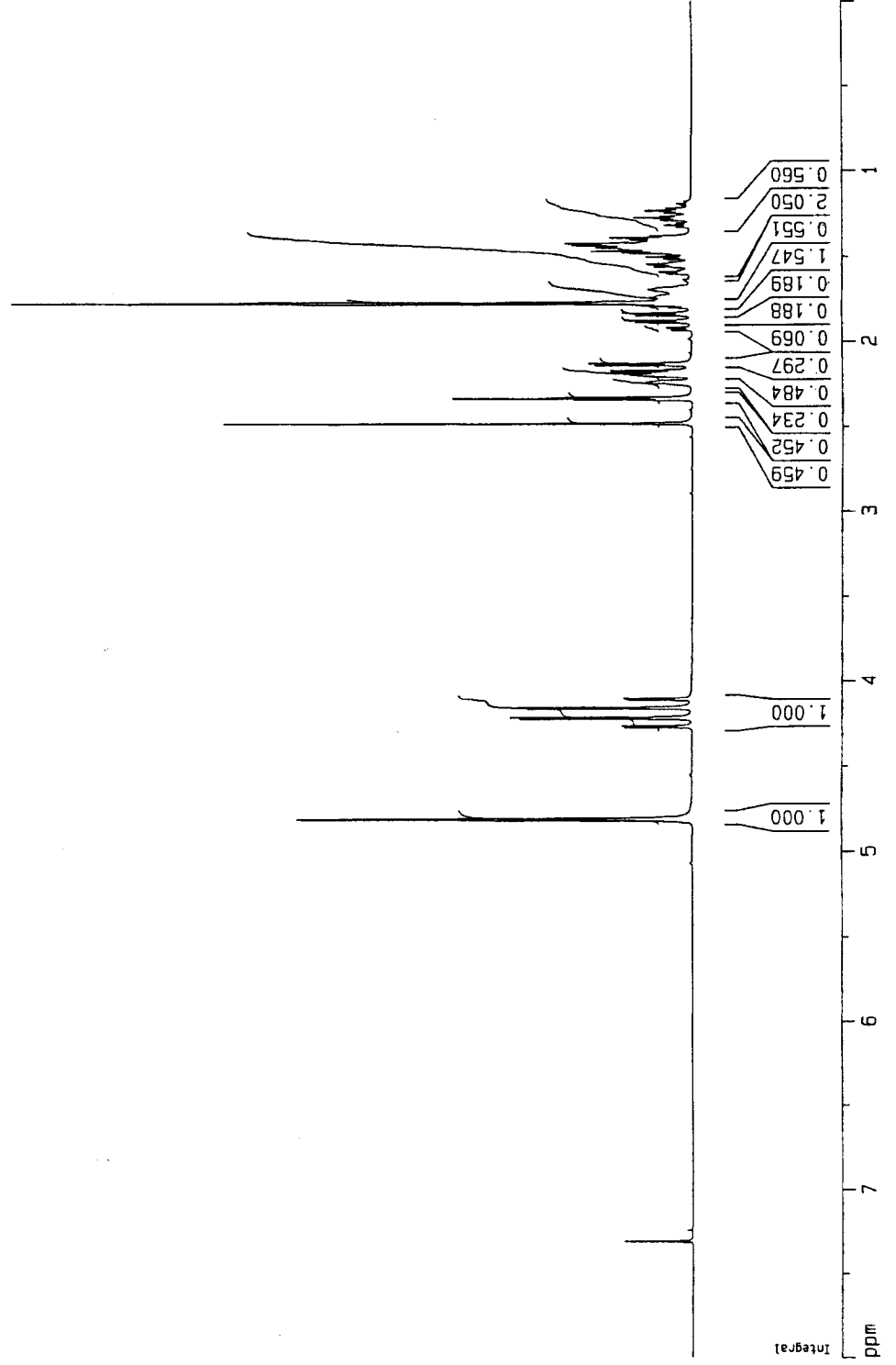
NUC1 1H
 P1 10.50 usec
 PL1 -3.00 dB
 SFO1 300.1319477 MHz

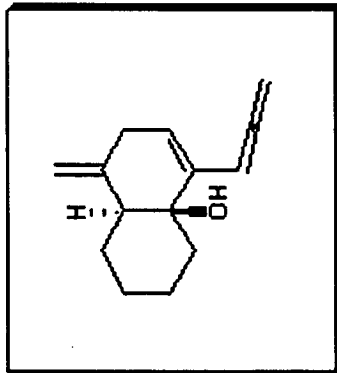
F2 - Processing parameters

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

1D NMR plot parameters

CX 20.00 cm
 CY 10.00 cm
 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





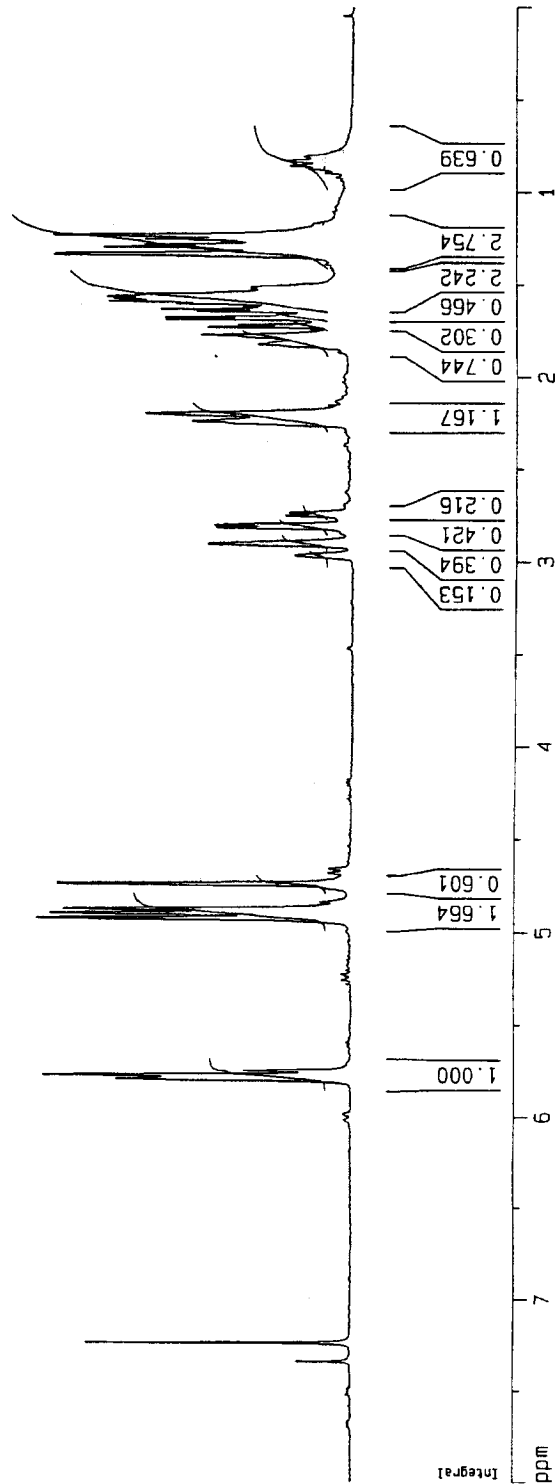
Current Data Parameters
 NAME rc_373b
 EXPNO 1
 PROCNO 1

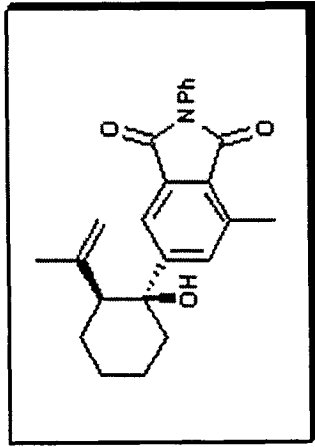
F2 - Acquisition Parameters
 Date_ 20030717
 Time 16.12
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl3
 NS 32
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 287.4
 DM 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

===== 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 6.00 cm
 F1P 8.000 ppm
 F1 2401.04 Hz
 F2P 0.000 ppm
 F2 0.00 Hz
 PPMCH 0.40000 ppm/cm
 HZCM 120.05200 Hz/cm





Current Data Parameters
 NAME rc_tandem (2)
 EXPNO 5
 PROCNO 1

F2 - Acquisition Parameters

Date_ 20030620
 Time 13.10
 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 1.0000000 sec

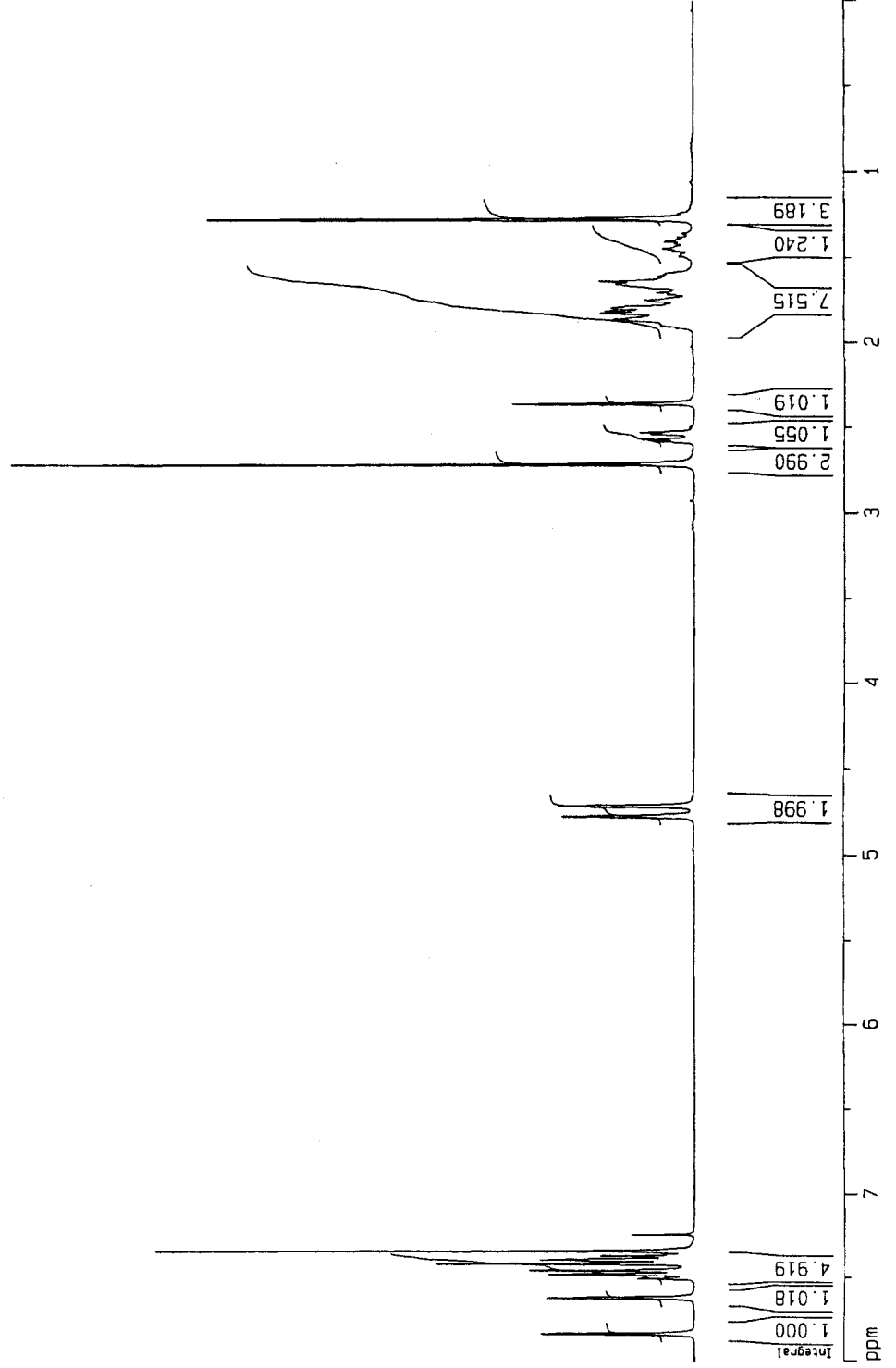
===== CHANNEL f1 =====
 NUC1 1H
 P1 10.50 usec
 PL1 -3.00 dB
 SF01 300.1319477 MHz

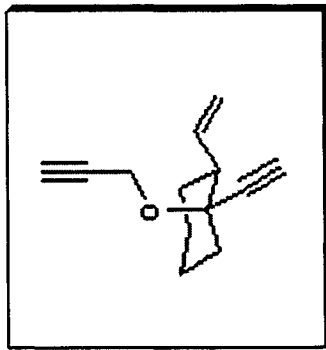
F2 - Processing parameters

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 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





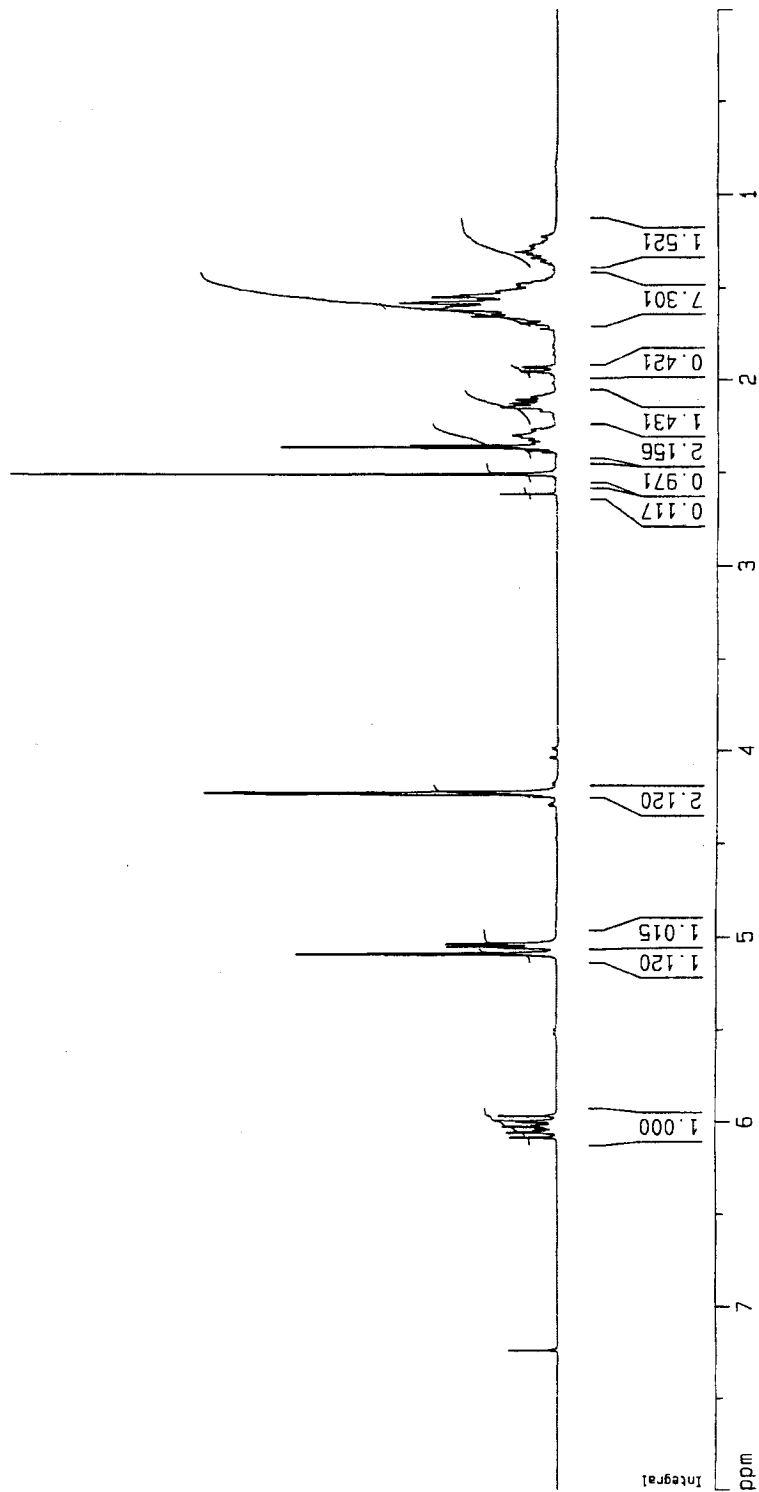
Current Data Parameters
NAME rc_375
EXPNO 1
PROCNO 1

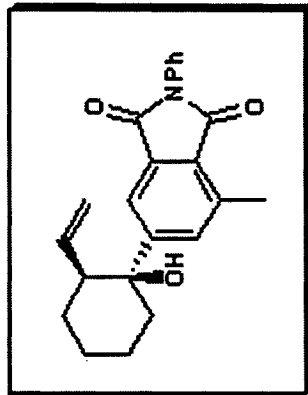
F2 - Acquisition Parameters
Date_ 20030716
Time 17.43
INSTRUM av300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 32
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 101.6
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

===== 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 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 rc_380
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters

Date_ 20030718
 Time 16.03
 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 406.4
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

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

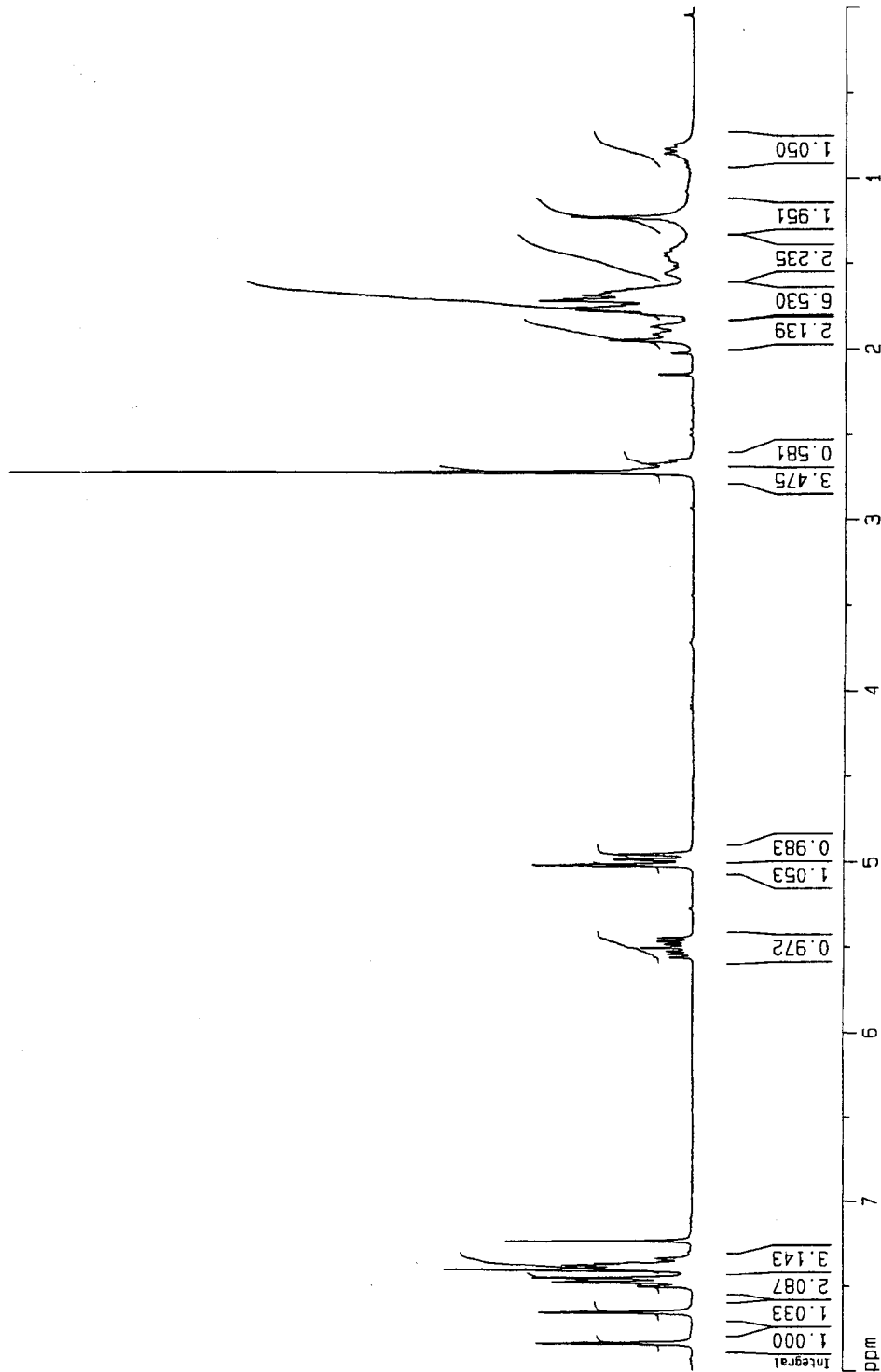
NUC1 1H
 P1 10.50 usec
 PL1 -3.00 dB
 SF01 300.1319477 MHz

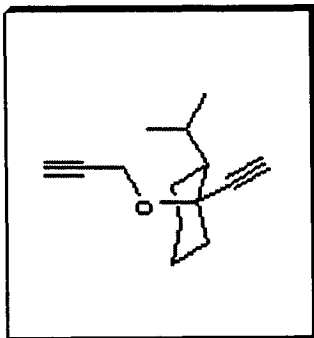
F2 - Processing parameters

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
 FIP 8.000 ppm
 F1 2401.04 Hz
 F2P 0.000 ppm
 F2 0.00 Hz
 PPMCM 0.40000 ppm/cm
 HZCM 0.05200 Hz/cm





Current Data Parameters
 NAME rc_alkipr
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters

Date_ 20030806
 Time 17.29
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TO 30720
 SOLVENT CDCl3
 NS 16
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 25.4
 DM 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

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

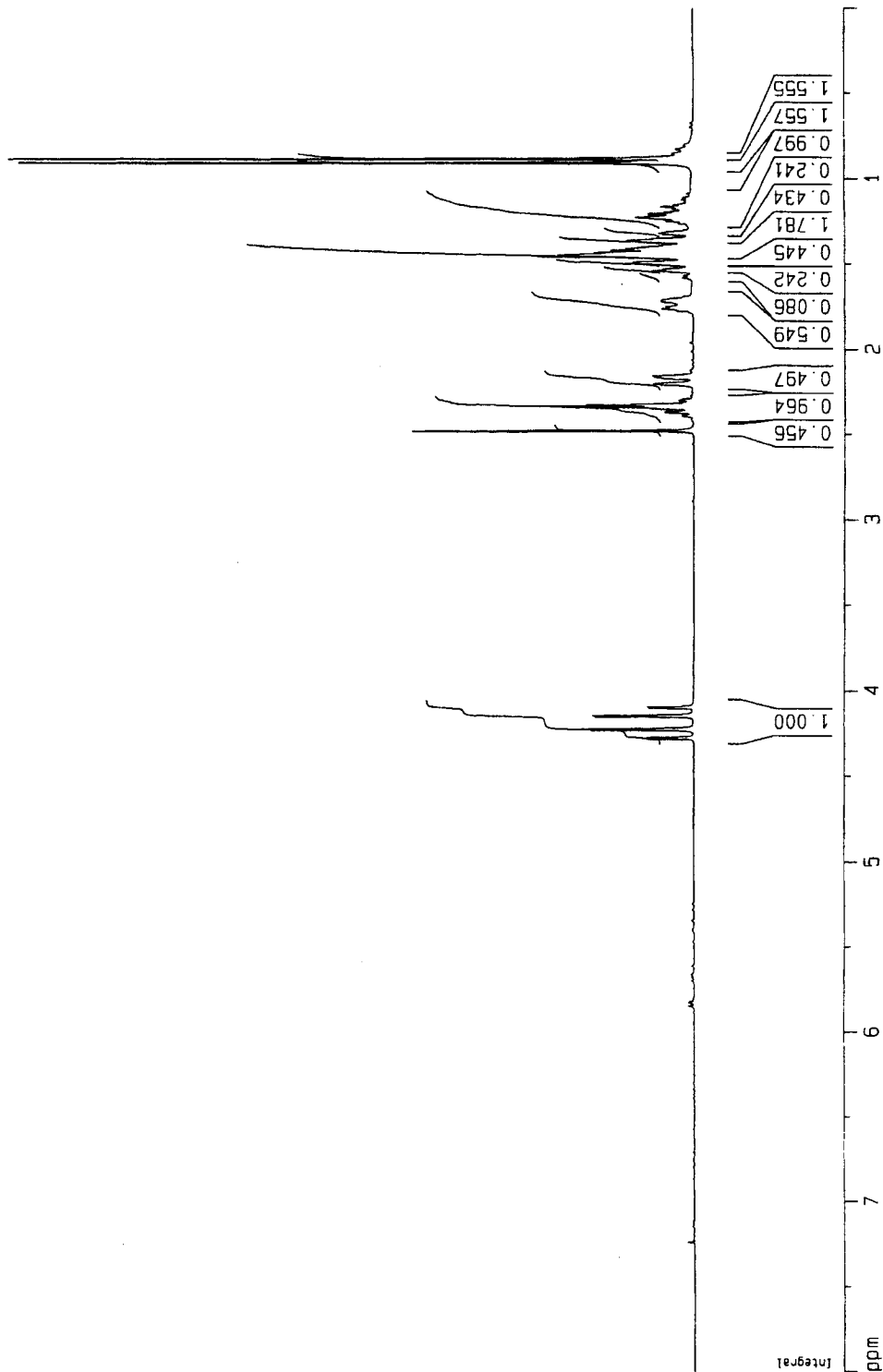
NUC1 1H
 P1 10.50 usec
 PL1 -3.00 dB
 SF01 300.1319477 MHz

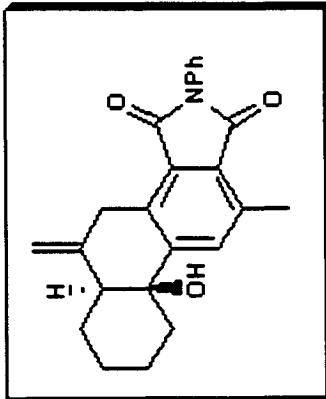
F2 - Processing parameters

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 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 rc_387
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters

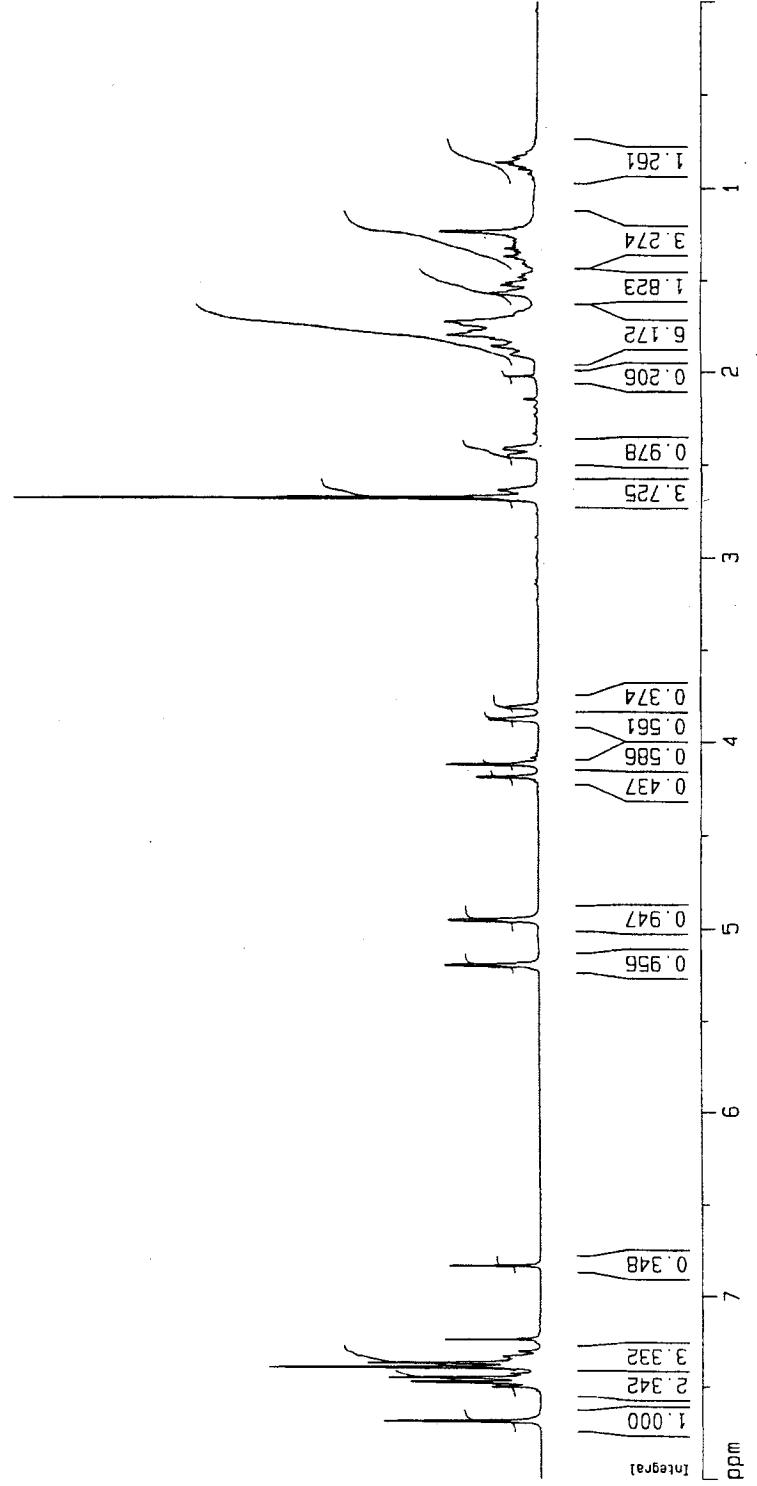
Date_ 20030805
 Time 16.45
 INSTRUM av300
 PROBHD 5 mm GNP 1H/1
 PULPROG zg30
 TO 30720
 SOLVENT CDCl3
 NS 32
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 256
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

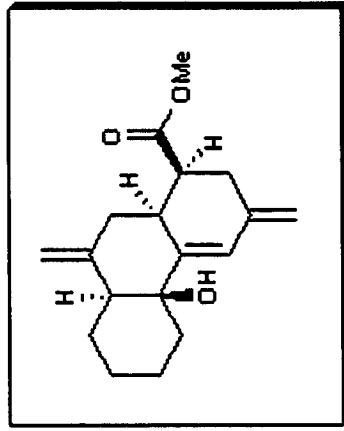
===== CHANNEL f1 =====
 NUC1 1H
 P1 10.50 usec
 PL1 -3.00 dB
 SF01 300.1319477 MHz

F2 - Processing parameters
 SI 65536
 SF 300.1300000 MHz
 WOH 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 rc_tandDA
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters

Date_ 20030724
 Time 16.46
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TO 30720
 SOLVENT CDCl3
 NS 32
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 256
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

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

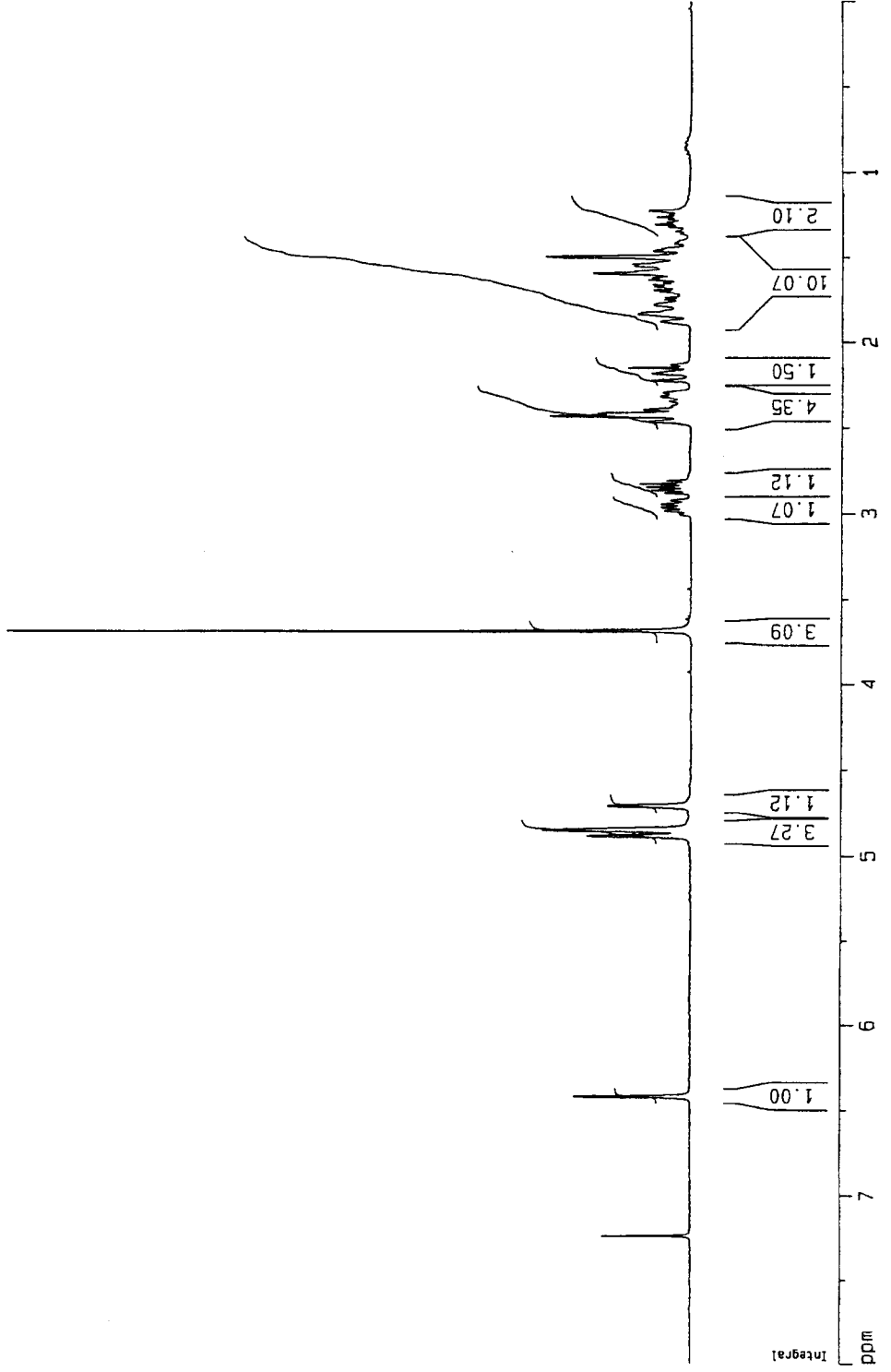
NUC1 1H
 P1 10.50 usec
 PL1 -3.00 dB
 SF01 300.1319477 MHz

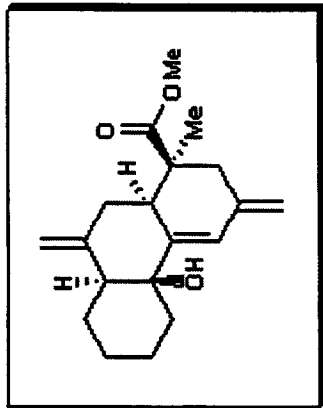
F2 - Processing parameters

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 rc_508
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters

Date_ 20031104
 Time 17.04
 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 362
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

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

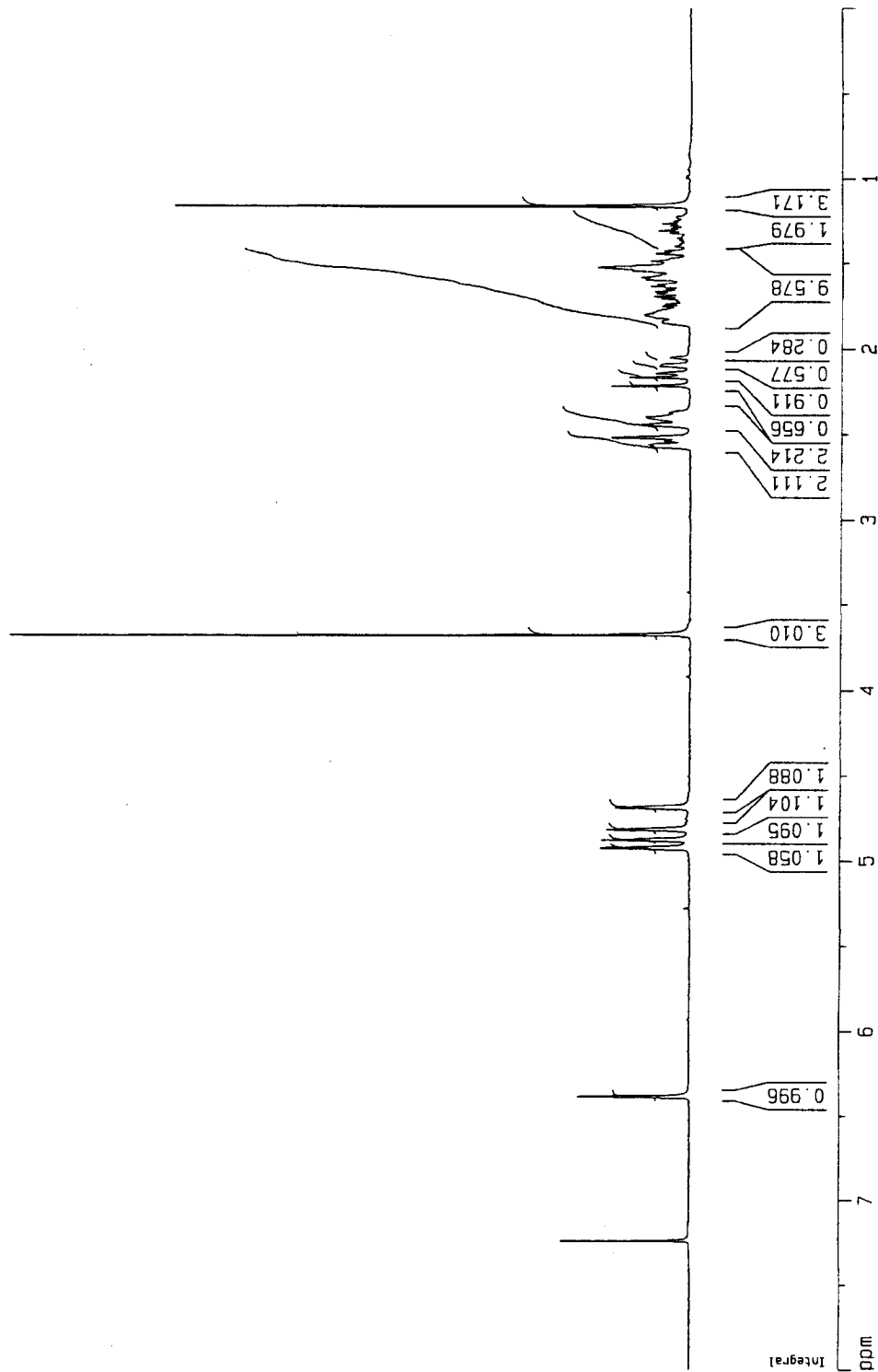
NUC1 1H
 P1 10.50 usec
 PL1 -3.00 dB
 SF01 300.1319477 MHz

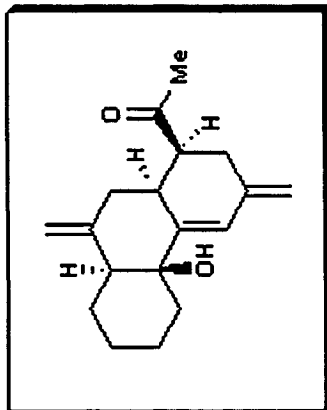
F2 - Processing parameters

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 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





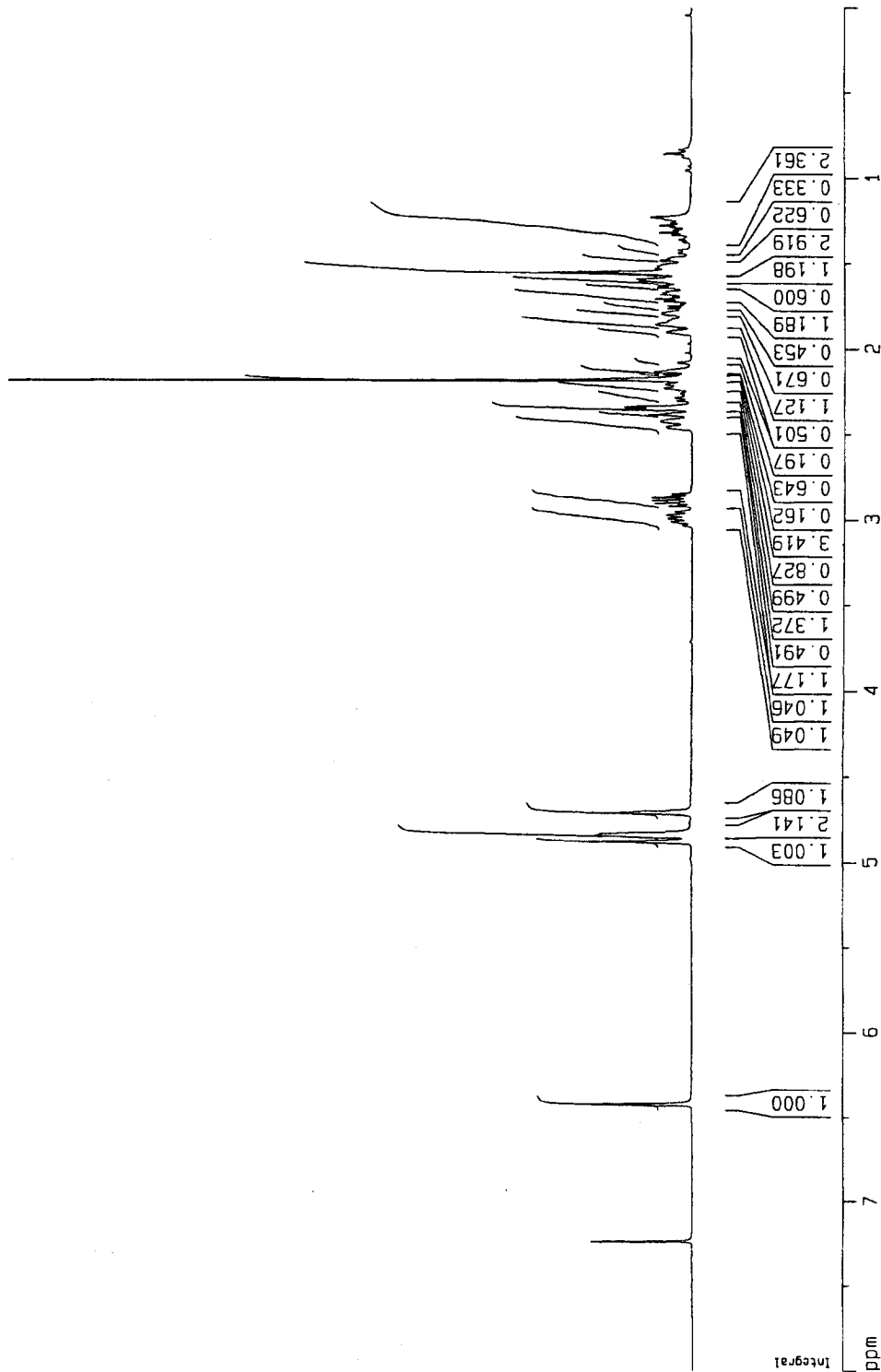
Current Data Parameters
 NAME rc_505
 EXPNO 1
 PROCNO 1

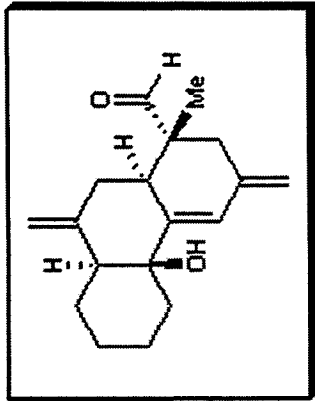
F2 - Acquisition Parameters
 Date_ 20031031
 Time 14.06
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl3
 NS 64
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 287.4
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

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

F2 - Processing parameters
 SI 65536
 SF 300.1300000 MHz
 WDW EM
 SSF 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





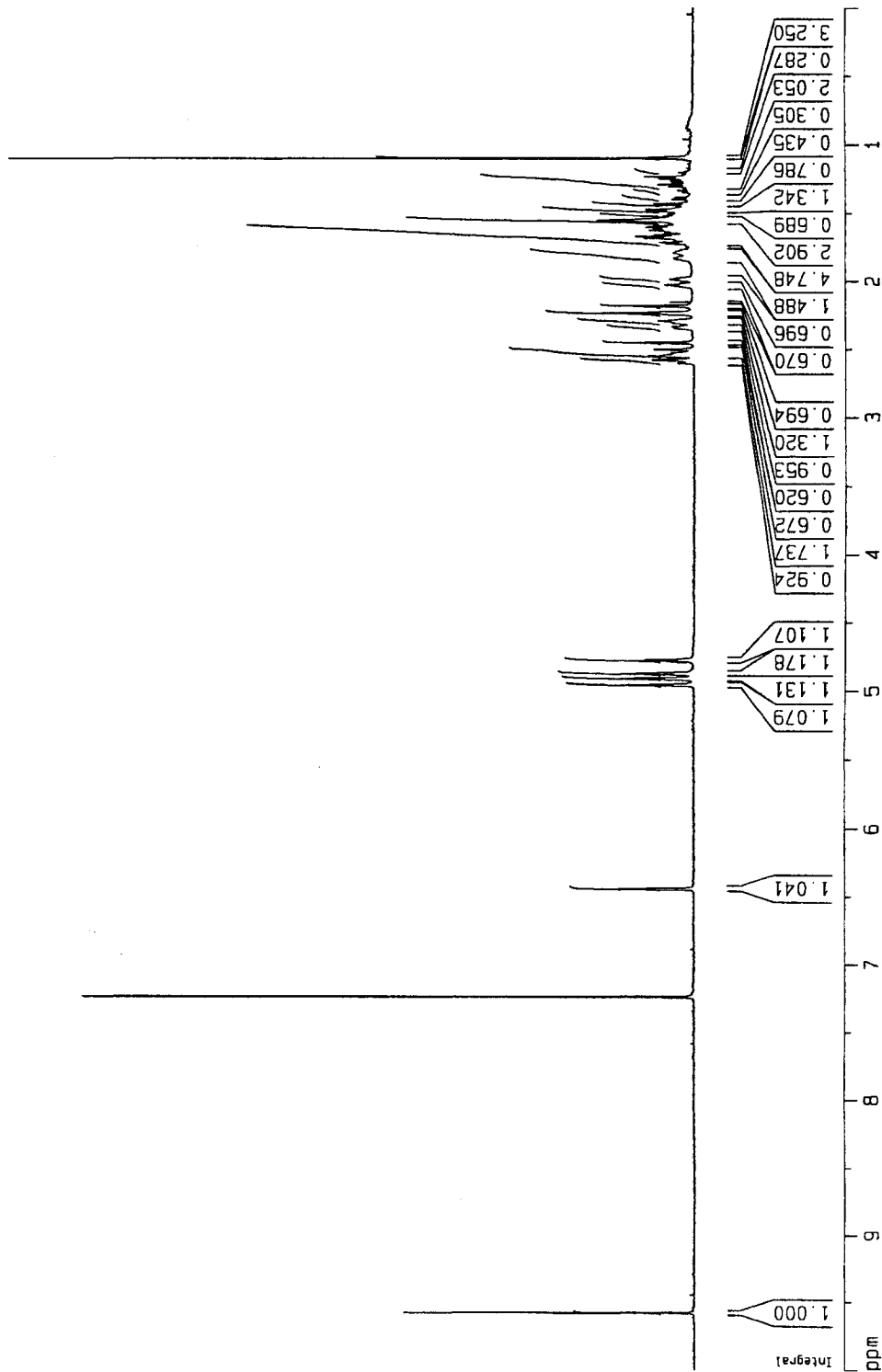
Current Data Parameters
 NAME rc_535
 EXPNO 1
 PROCNO 1

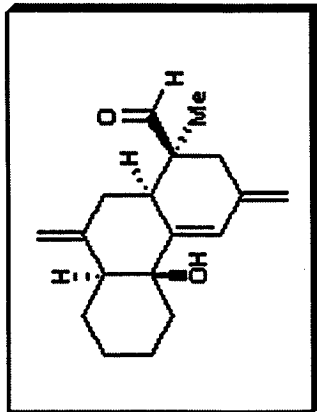
F2 - Acquisition Parameters
 Date_ 20031119
 Time 18.15
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl3
 NS 16
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 645.1
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

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

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

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





Current Data Parameters
 NAME rc_548_b
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters

Date_ 20031127
 Time 20.27
 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 724.1
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.0000000 sec

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

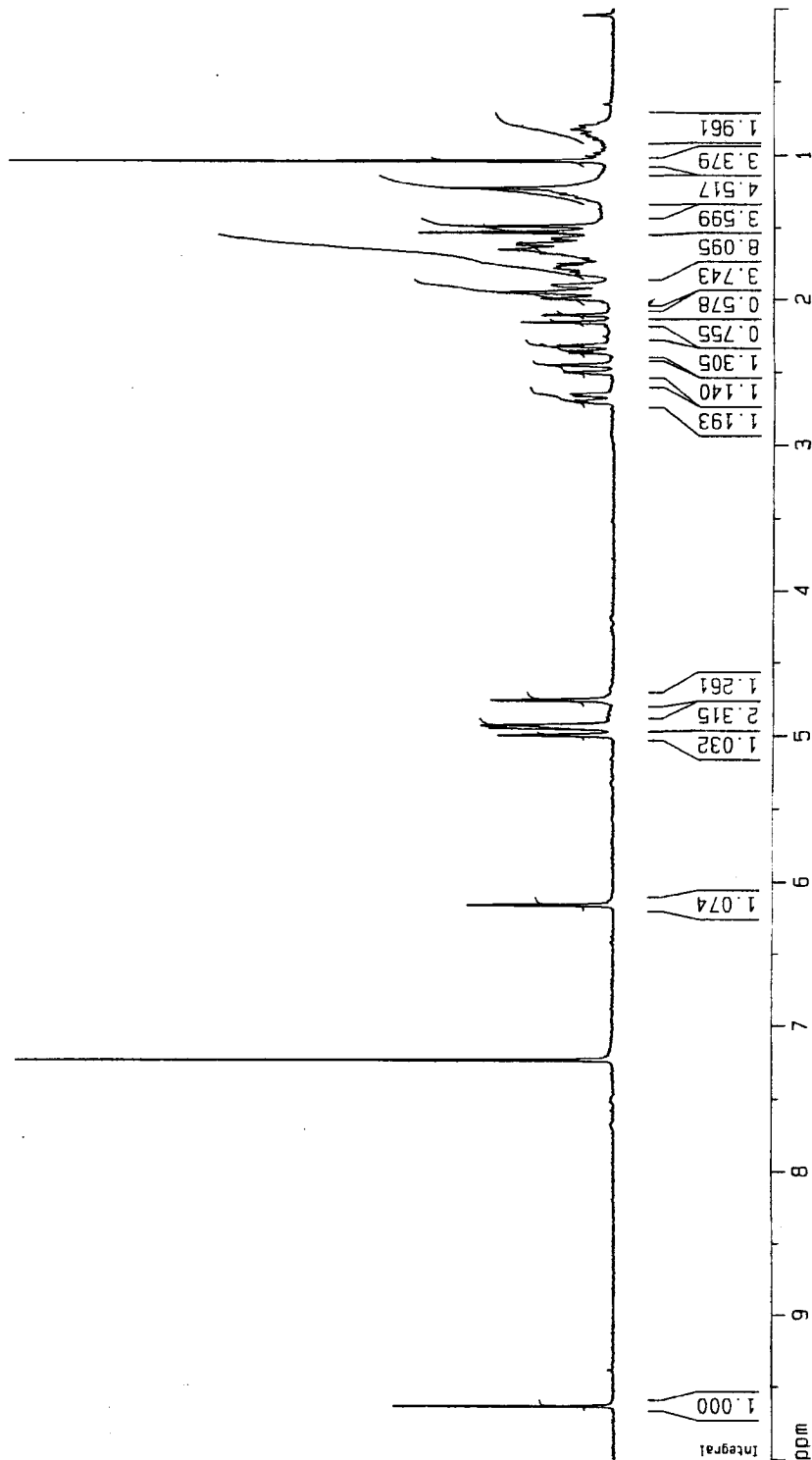
NUC1 1H
 P1 10.50 usec
 PL1 -3.00 dB
 SF01 300.1319477 MHz

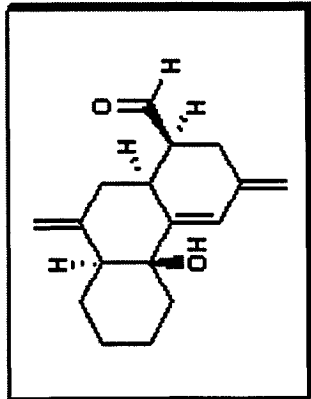
F2 - Processing parameters

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





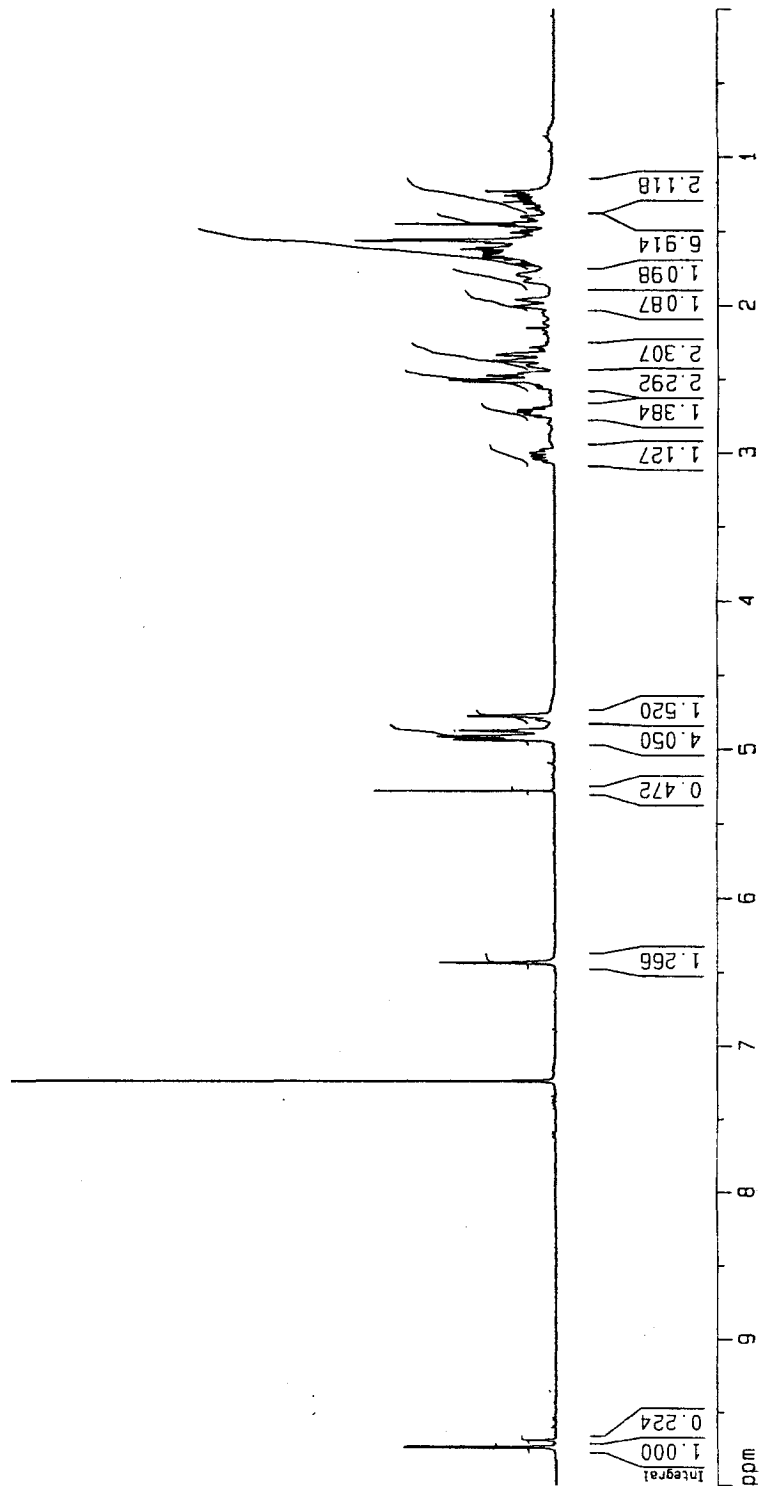
Current Data Parameters
 NAME rc_544_1
 EXPNO 1
 PROCNO 1

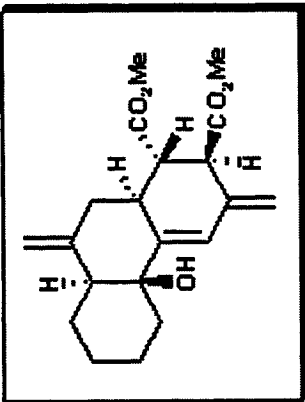
F2 - Acquisition Parameters
 Date_ 20031121
 Time 16:57
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl3
 NS 16
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 456.1
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

===== CHANNEL f1 =====
 NUC1 1H
 P1 10.50 usec
 PL1 -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





Current Data Parameters
 NAME rc_398
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters

Date_ 20030821
 Time 16.05
 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 203.2
 DM 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

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

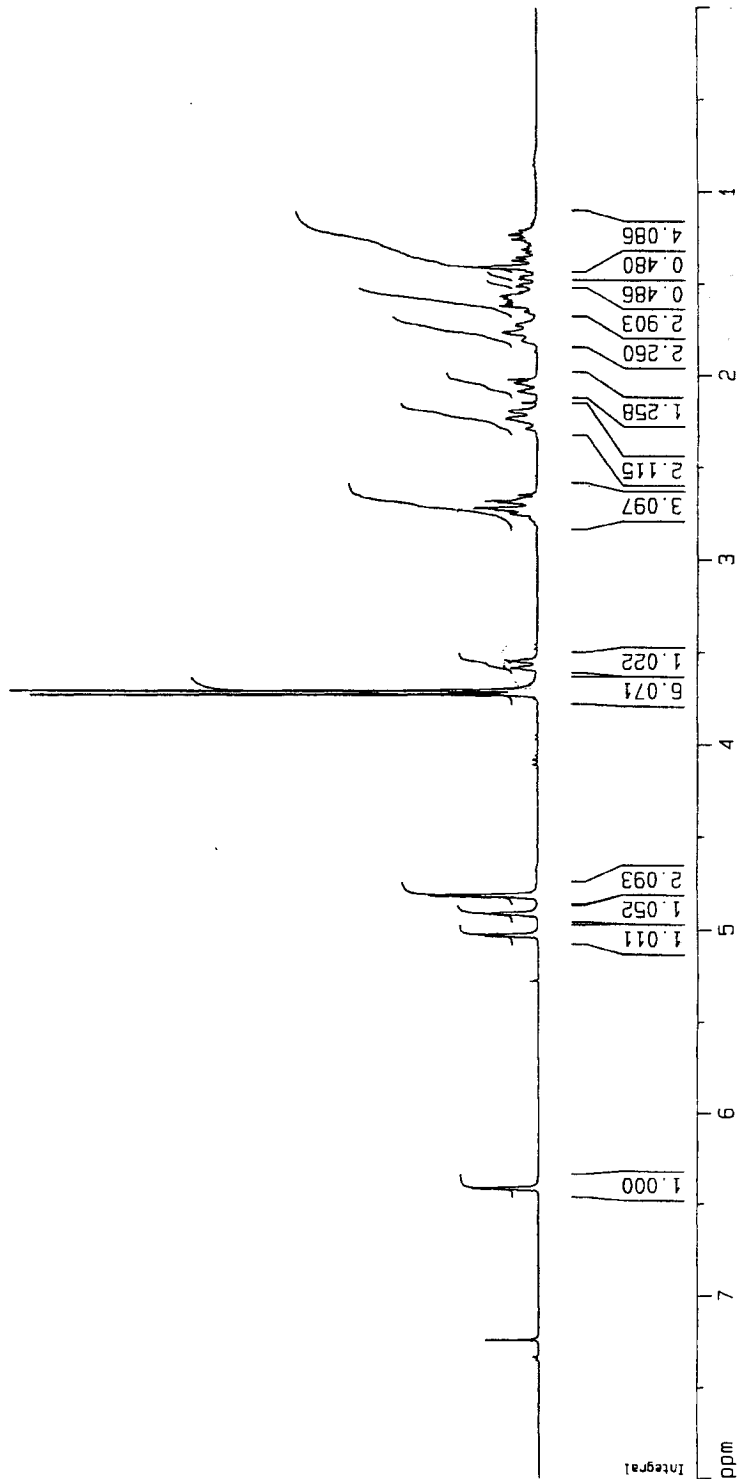
NUC1 1H
 P1 10.50 usec
 PL1 -3.00 dB
 SF01 300.1319477 MHz

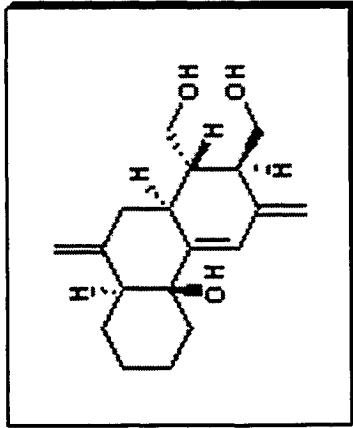
F2 - Processing parameters

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 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





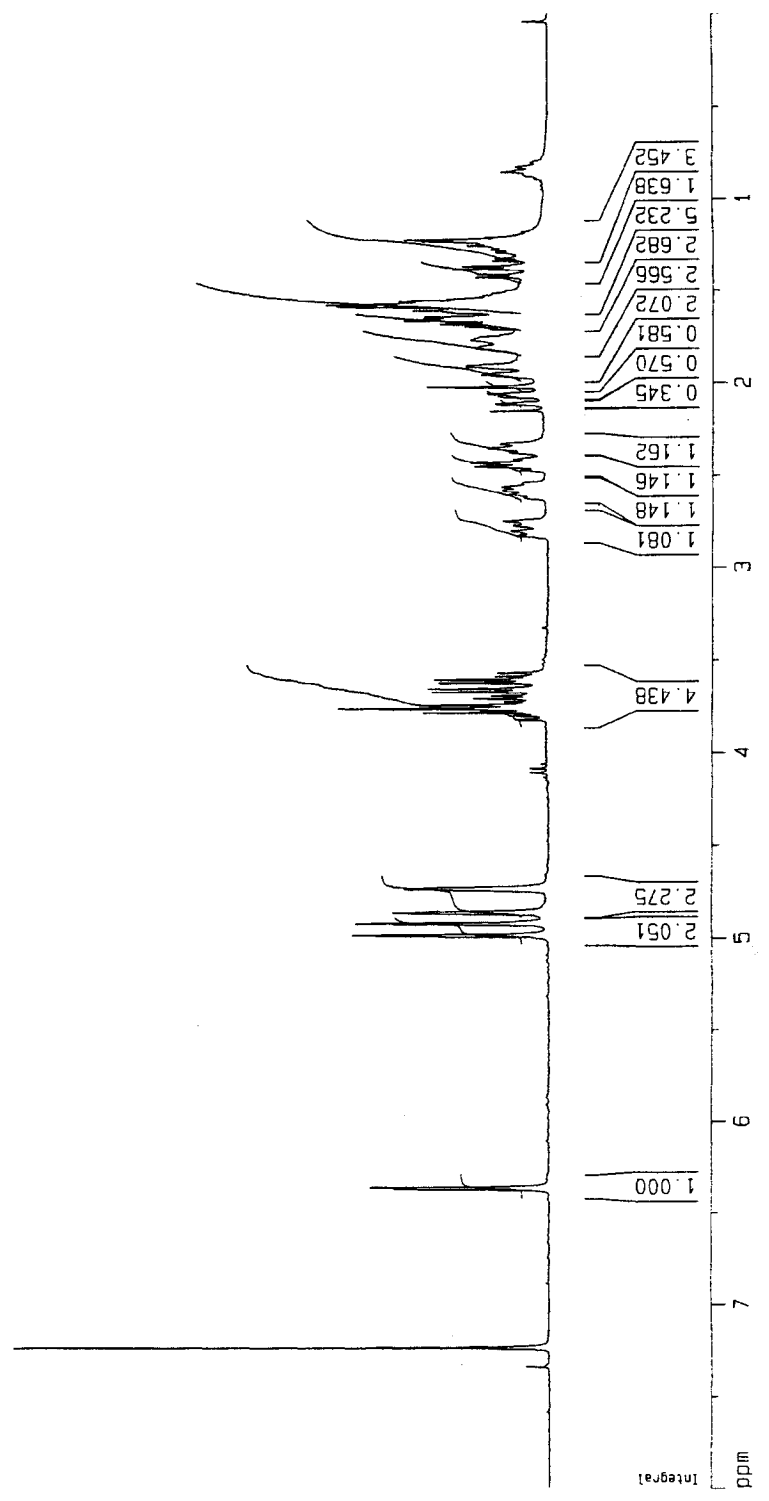
Current Data Parameters
NAME rc_434
EXPNO 1
PROCNO 1

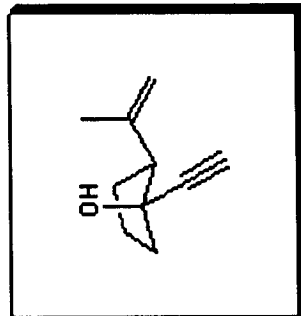
F2 - Acquisition Parameters
Date_ 20030919
Time 15.49
INSTRUM av300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 64
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 512
DM 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

===== 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

10 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 rc_374_1
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters

Date_ 20030819
 Time 13.24
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl3
 NS 16
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 25.4
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

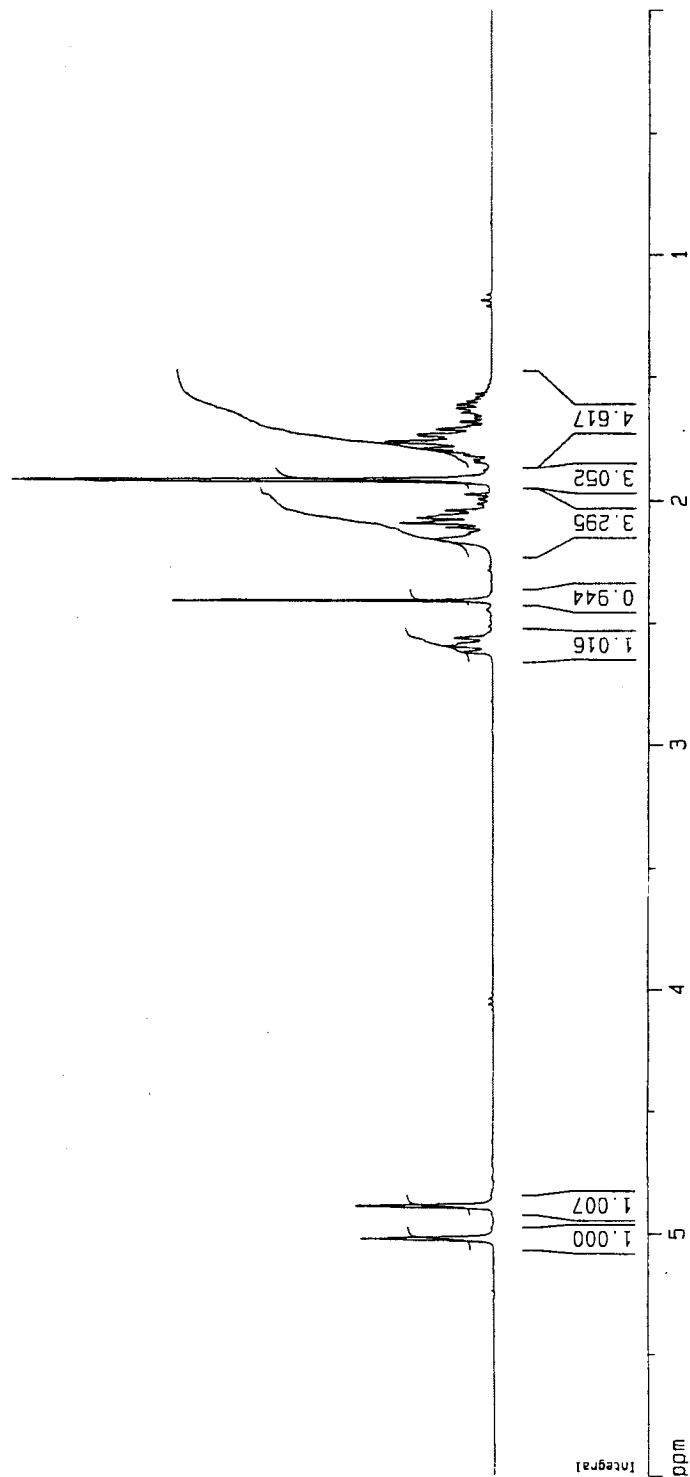
===== CHANNEL f1 =====

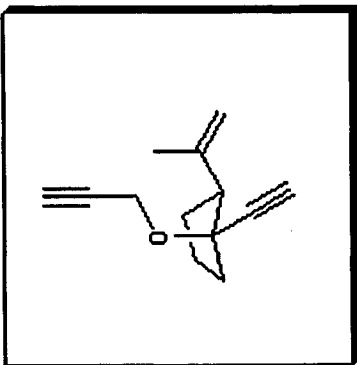
NUC1 1H
 P1 10.50 usec
 PL1 -3.00 dB
 SF01 300.1319477 MHz

F2 - Processing parameters

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

ID NMR plot parameters
 CX 20.00 cm
 CY 10.00 cm
 F1P 6.000 ppm
 F1 1800.78 Hz
 F2P -0.000 ppm
 F2 -0.00 Hz
 PPMCM 0.30000 ppm/cm
 HZCM 90.03900 Hz/cm





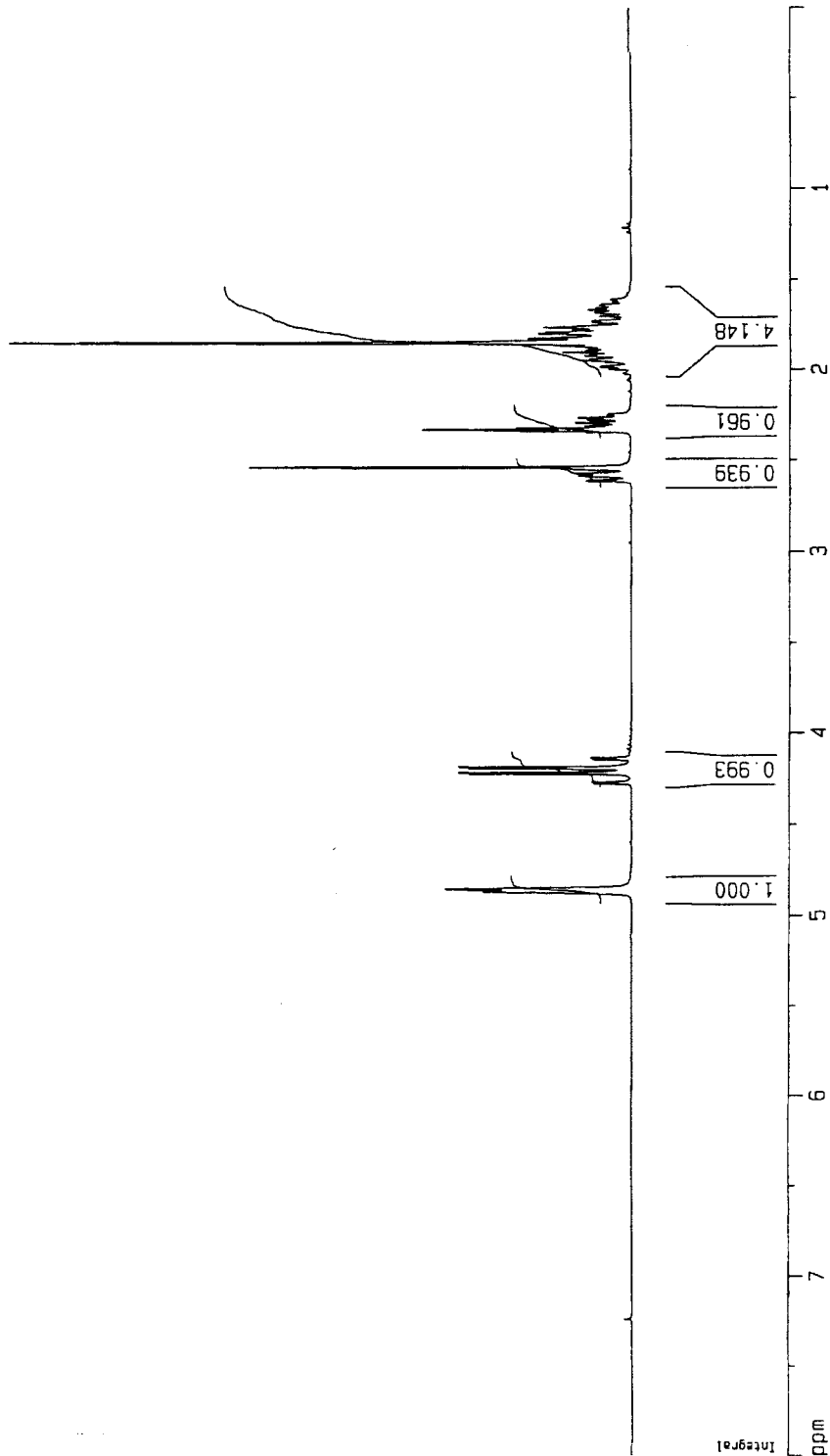
Current Data Parameters
 NAME rc_400
 EXPNO 1
 PROCNO 1

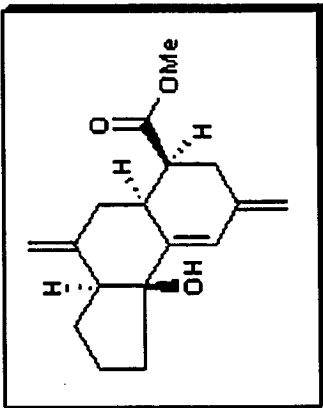
F2 - Acquisition Parameters
 Date_ 20030820
 Time 15.15
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl₃
 NS 16
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 28.5
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

===== 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 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





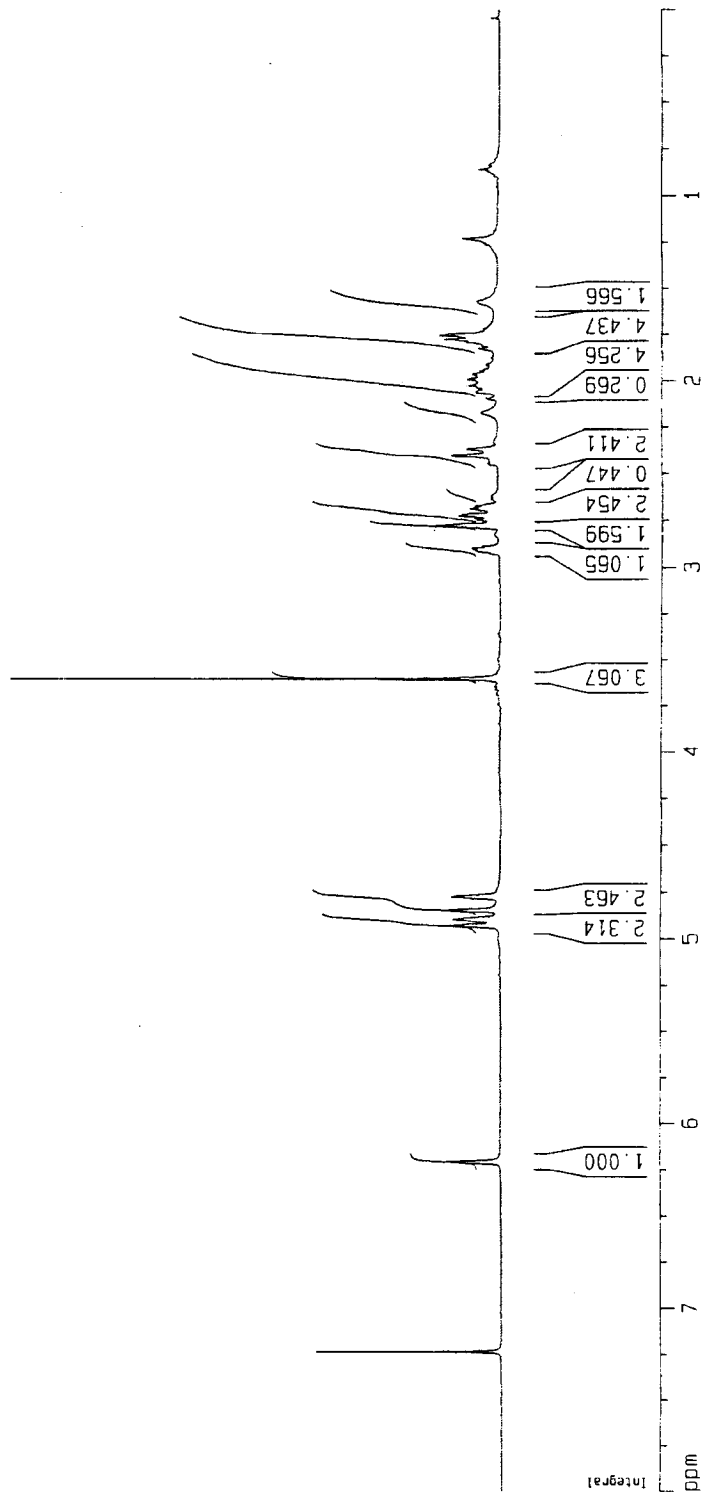
Current Data Parameters
 NAME rc_437 (_2)
 EXPNO 1
 PROCNO 1

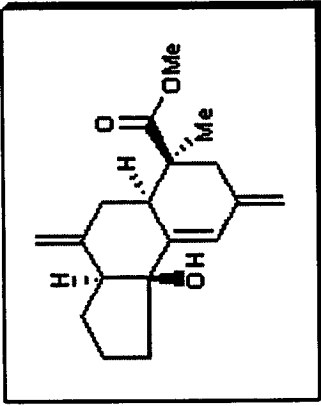
F2 - Acquisition Parameters
 Date_ 20030918
 Time 15.49
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl3
 NS 121
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 512
 DM 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

===== 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
 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 rc_xray
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters

Date_ 20031205
Time 13.45
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 574.7
DM 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.0000000 sec

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

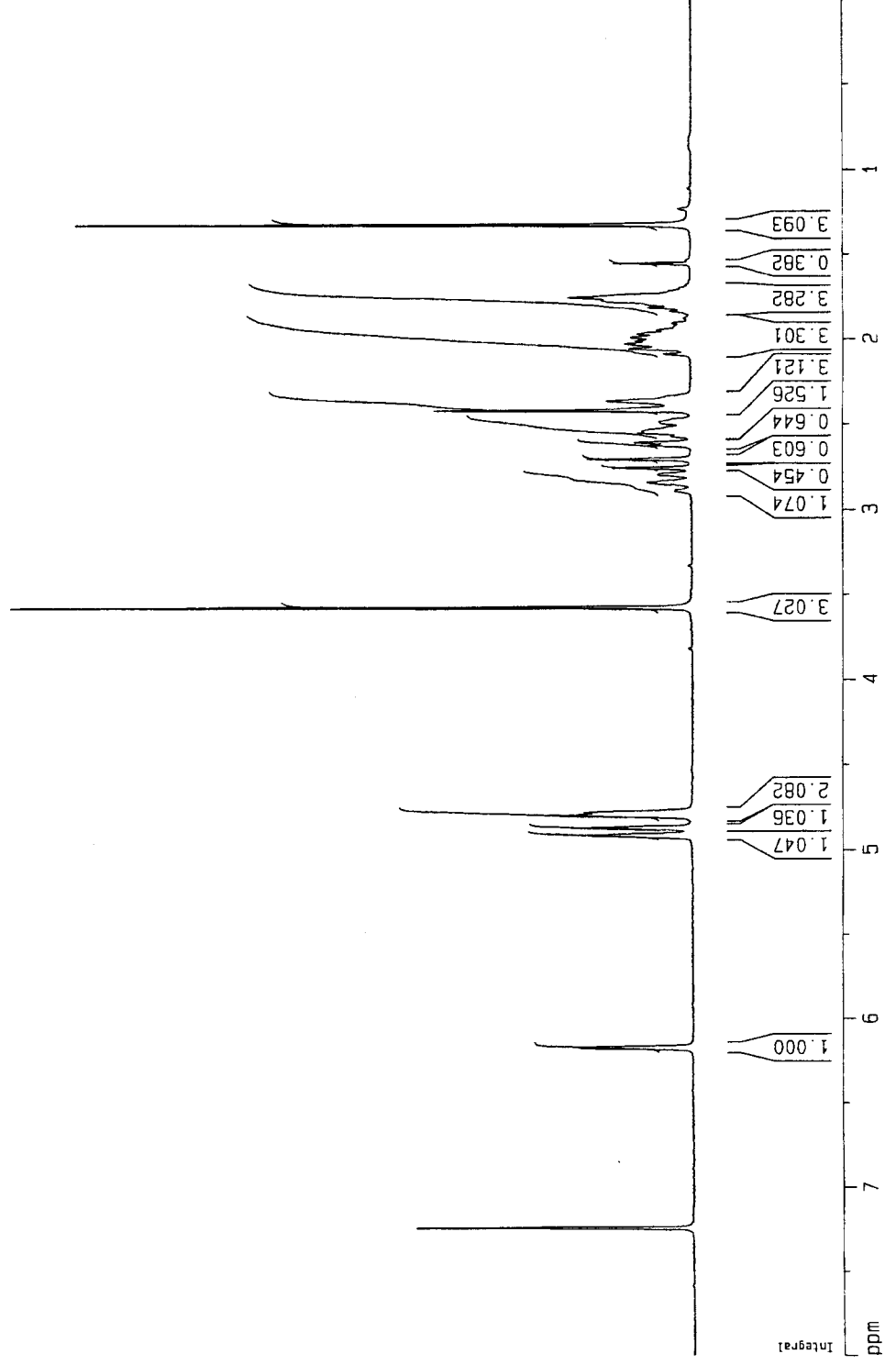
NUC1 1H
P1 10.50 usec
PL1 -3.00 dB
SF01 300.1319477 MHz

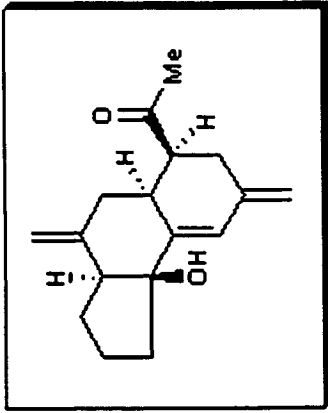
F2 - Processing parameters

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
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





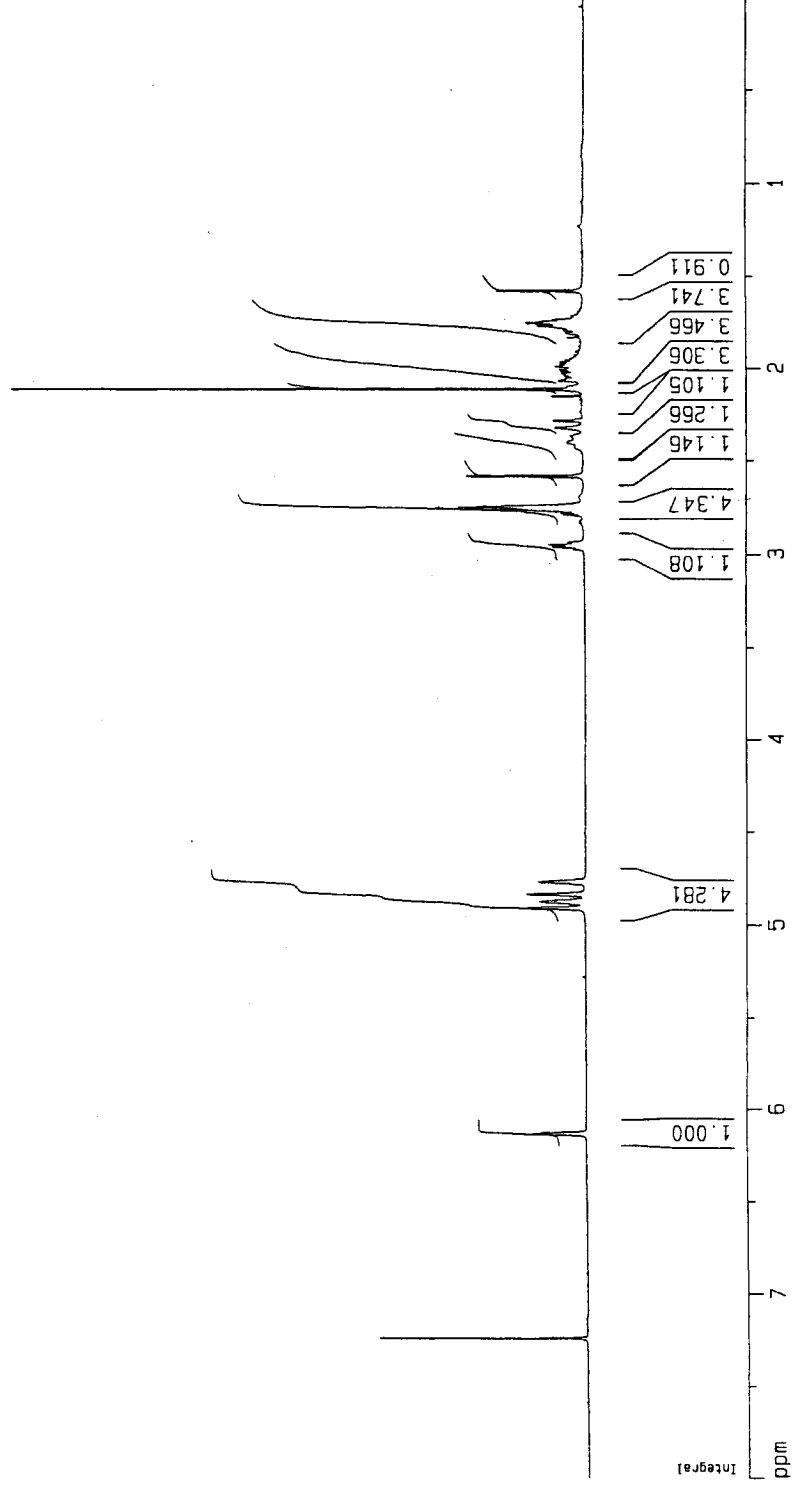
Current Data Parameters
NAME rc_550_a
EXPNO 1
PROCNO 1

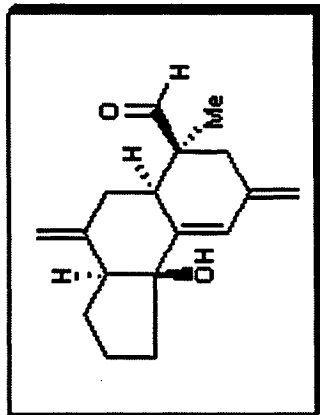
F2 - Acquisition Parameters
Date_ 20031125
Time 17.48
INSTRUM av300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 32
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 406.4
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

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





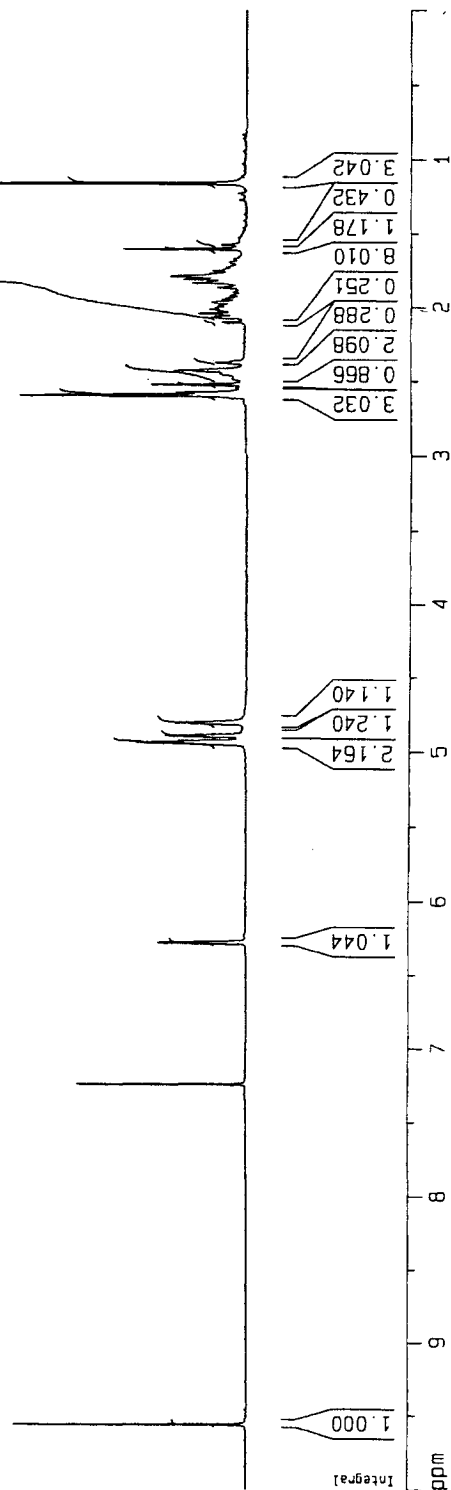
Current Data Parameters
 NAME rc_564_a
 EXPNO 1
 PROCNO 1

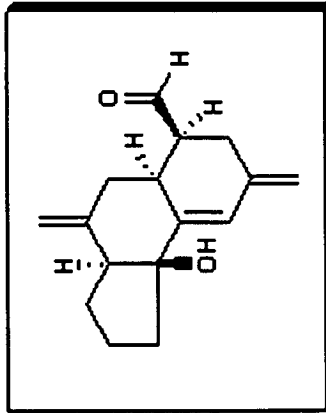
F2 - Acquisition Parameters
 Date_ 20031203
 Time 18.16
 INSTRUM av300
 PROBHD 5 mm GNP 1H/1
 PULPROG zg30
 TO 30720
 SOLVENT CDCl3
 NS 32
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 287.4
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.0000000 sec

===== 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





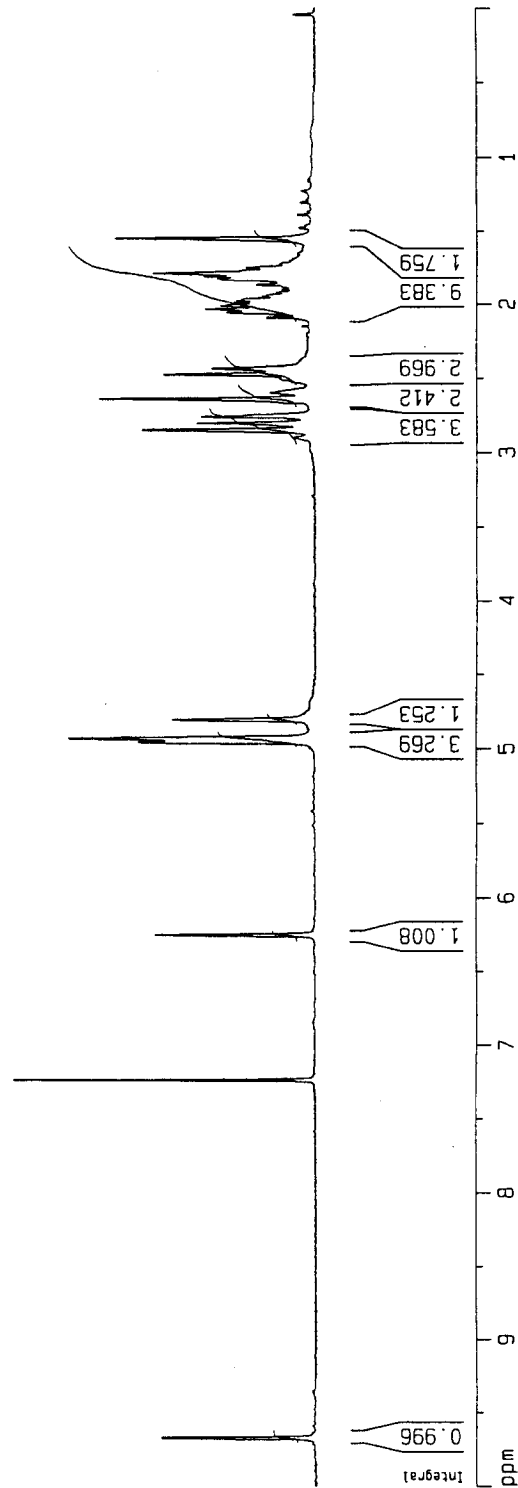
Current Data Parameters
NAME rc_558
EXPNO 1
PROCNO 1

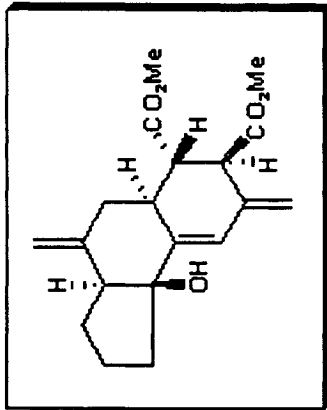
F2 - Acquisition Parameters
Date_ 20031128
Time 17:55
INSTRUM av300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 456.1
DM 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

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

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

1D NMR plot parameters
CX 20.00 cm
CY 8.00 cm
F1P 10.000 ppm
F1 3001.30 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCM 0.50000 ppm/cm
HZCM 150.06500 Hz/cm





Current Data Parameters
 NAME rc_556
 EXPNO 1
 PROCNO 1

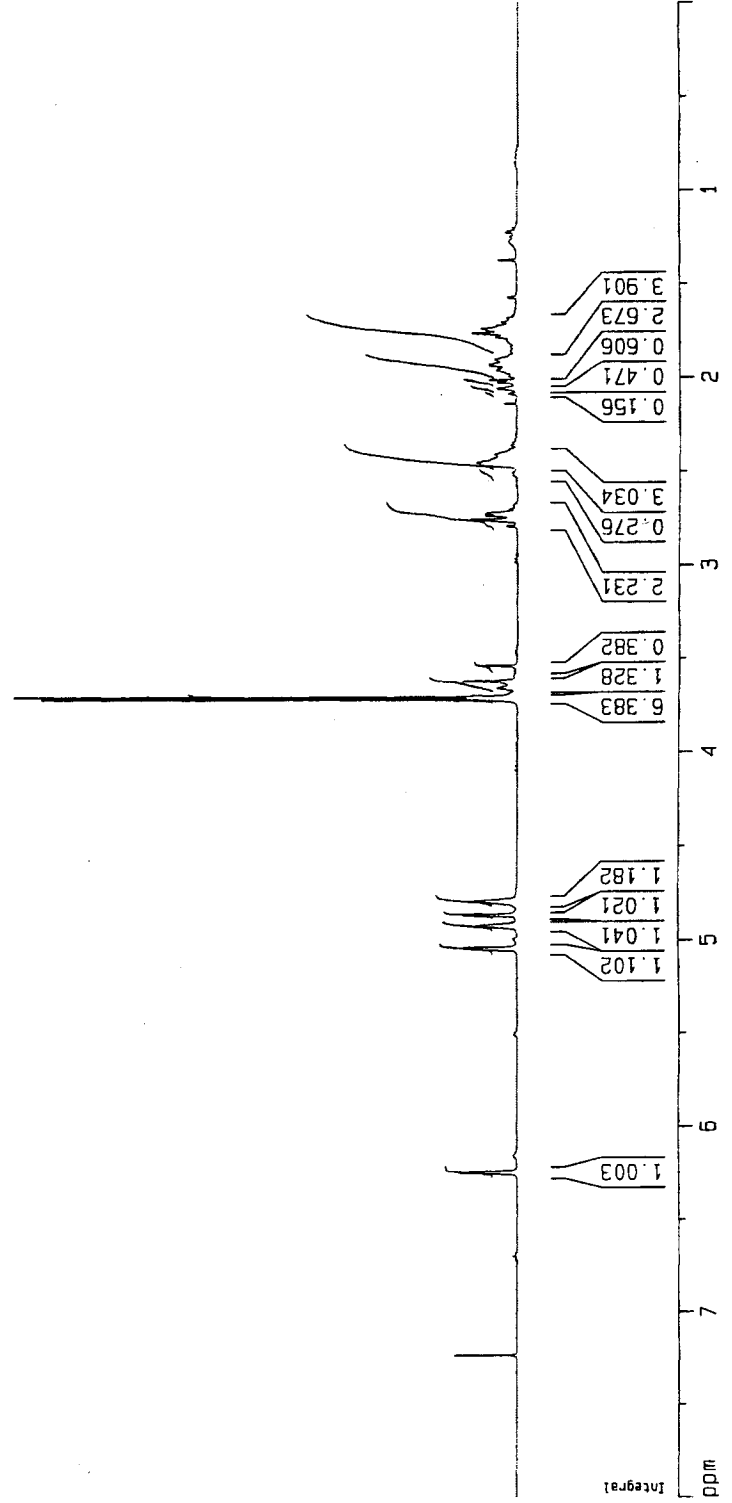
F2 - Acquisition Parameters
 Date_ 20031201
 Time 18.21
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TO 30720
 SOLVENT CDCl3
 NS 16
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 181
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.0000000 sec

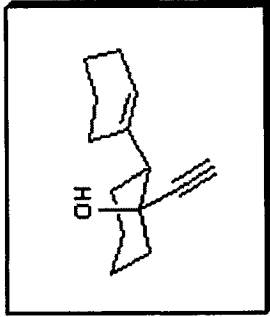
===== CHANNEL f1 =====

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 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





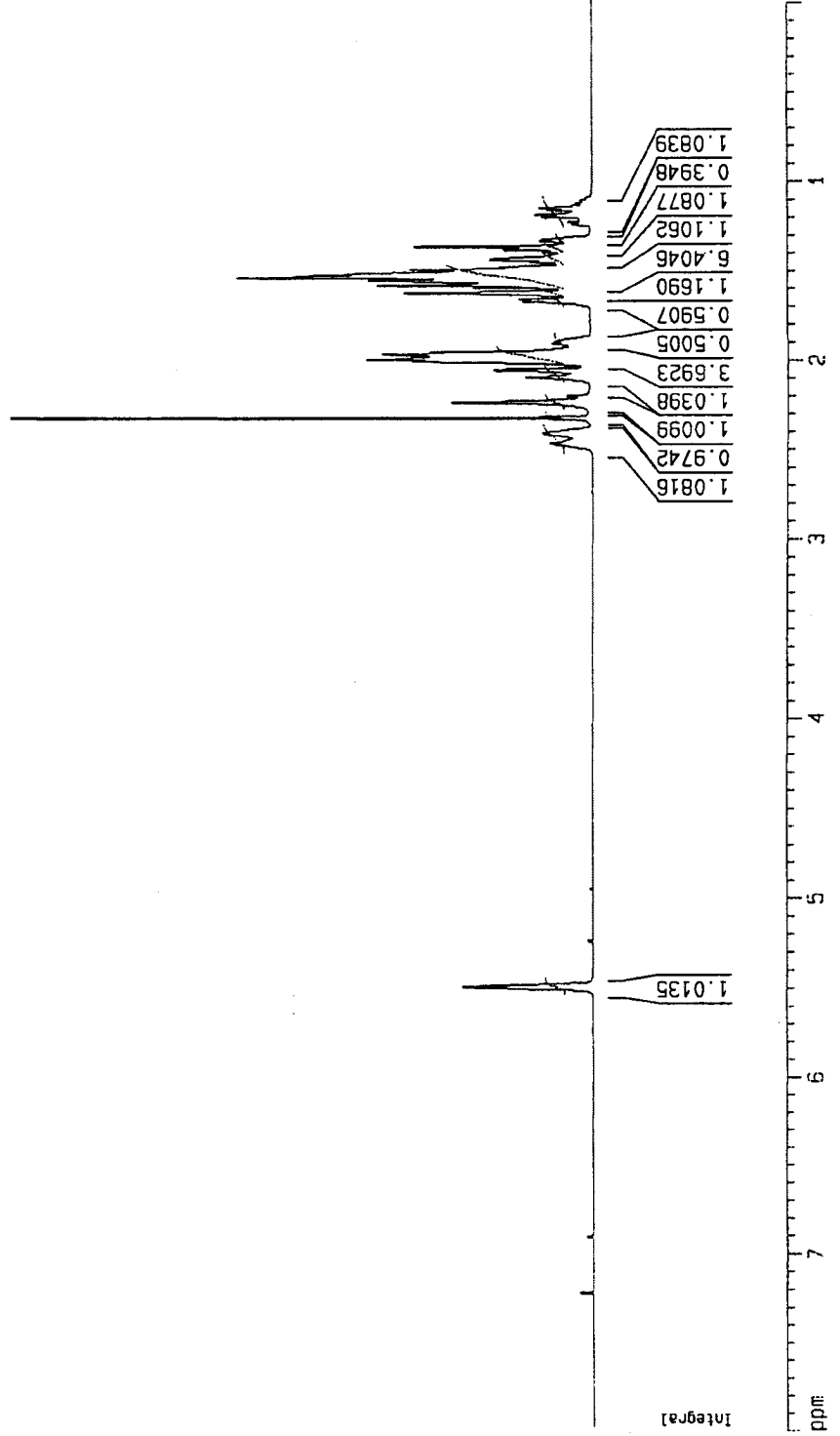
Current Data Parameters
 NAME rc_720
 EXPNO 1
 PROCNO 1

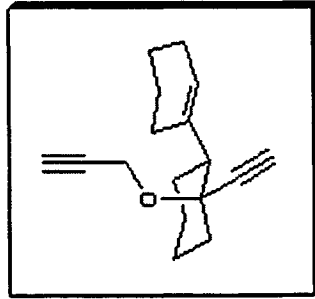
F2 - Acquisition Parameters
 Date_ 20040421
 Time 11.02
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl3
 NS 16
 DS 0
 SNH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228960 sec
 RG 28.5
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

===== 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
 FIP 8.000 ppm
 F1 2401.04 Hz
 F2 0.000 ppm
 F2P 0.00 Hz
 PPMCM 0.40000 ppm/cm
 HZCM 120.05200 Hz/cm





Current Data Parameters
 NAME rc_297all
 EXPNO 4
 PROCNO 1

F2 - Acquisition Parameters

Date_ 20030527
 Time 18.53
 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 45.3
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

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

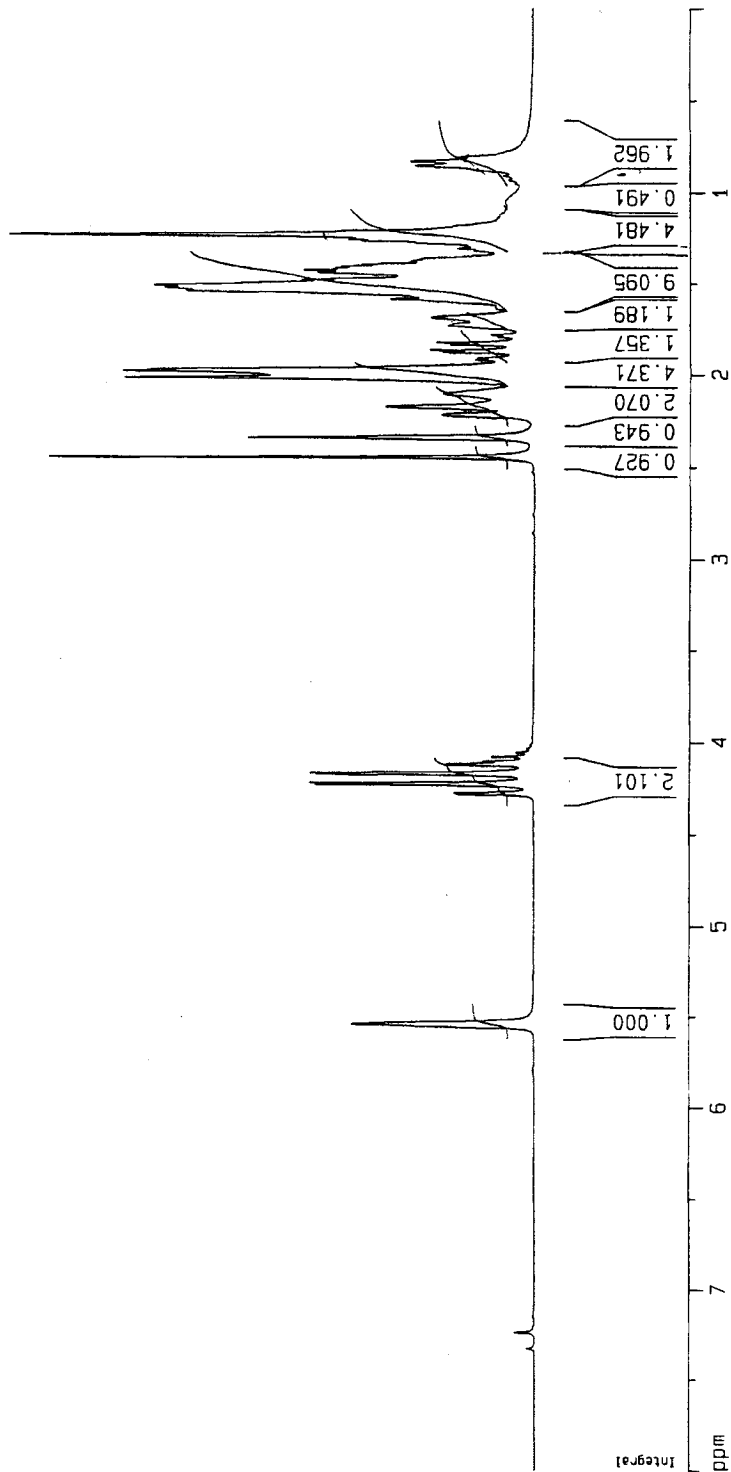
NUC1 1H
 P1 10.50 usec
 PL1 -3.00 dB
 SF01 300.1319477 MHz

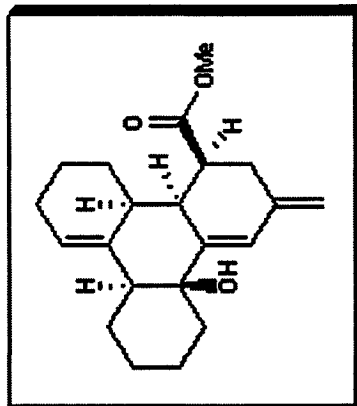
F2 - Processing parameters

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 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 rc_627_r
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters

Date_ 20040217
 Time 18.37
 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 512
 DM 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

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

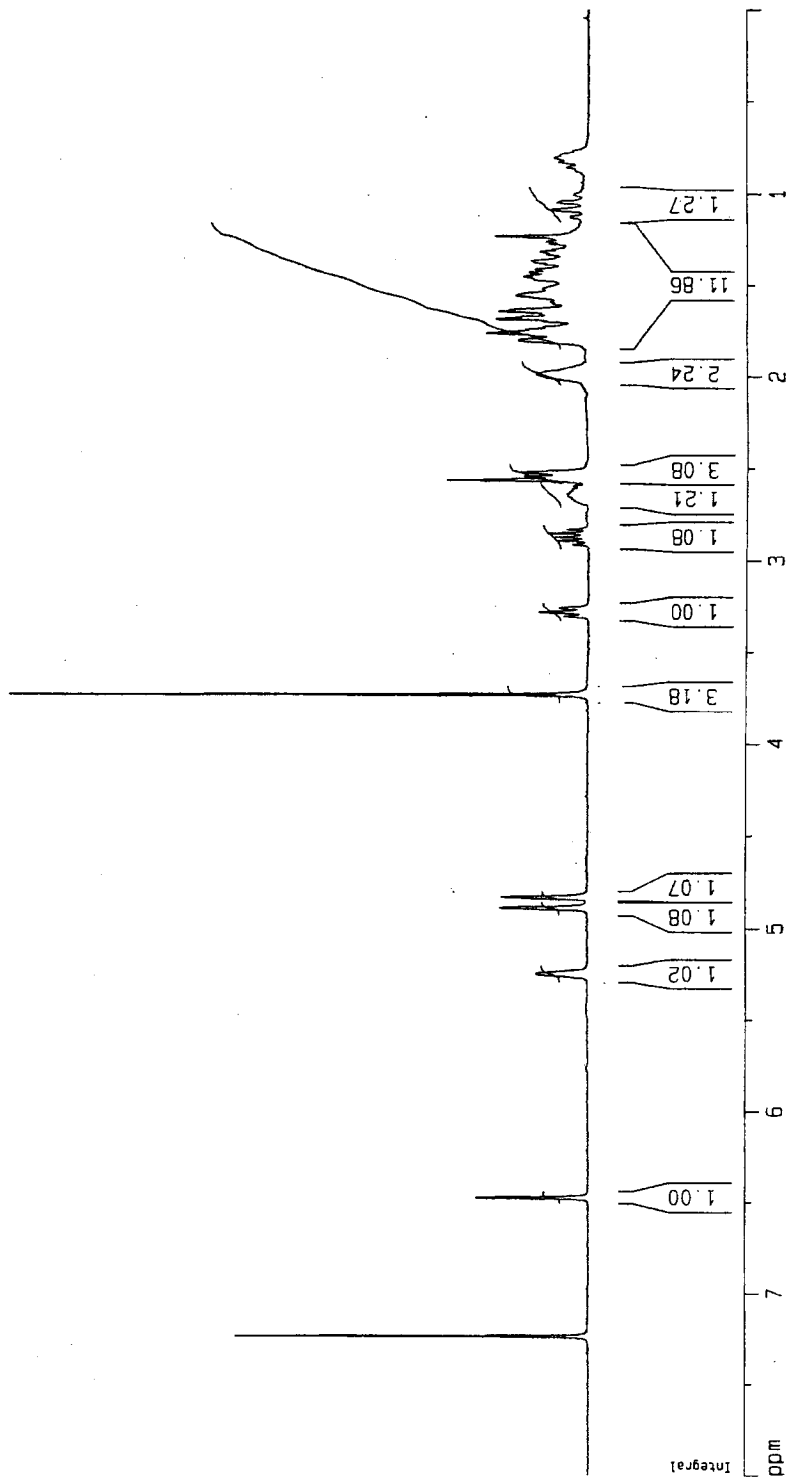
NUC1 1H
 P1 10.50 usec
 PL1 -3.00 dB
 SF01 300.1319477 MHz

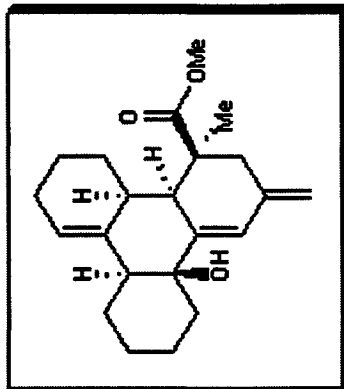
F2 - Processing parameters

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

10 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





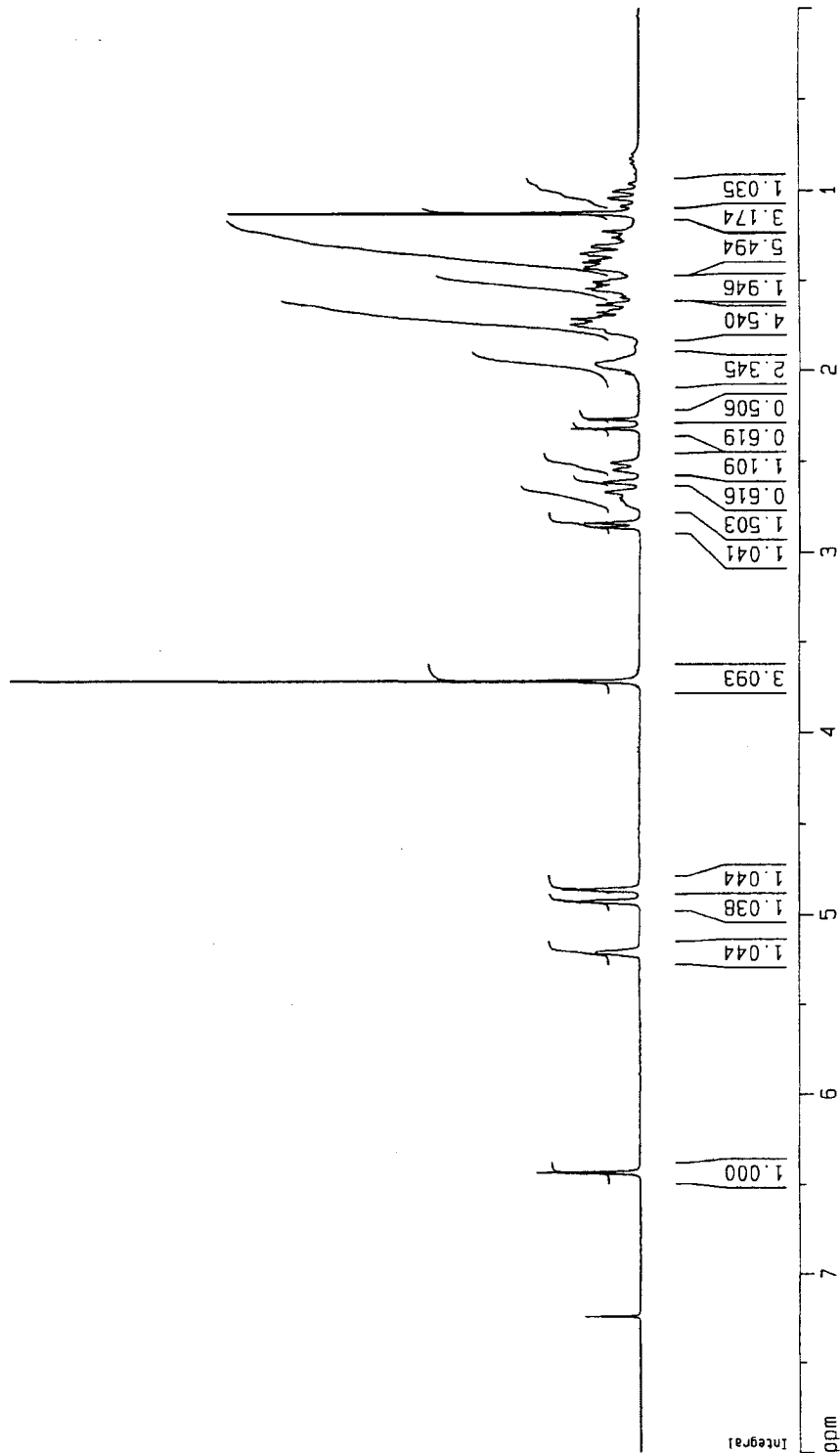
Current Data Parameters
 NAME rc_622p
 EXPNO 1
 PROCNO 1

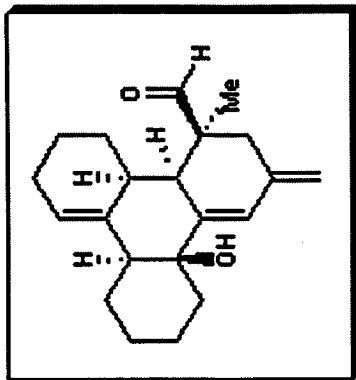
F2 - Acquisition Parameters
 Date_ 20040210
 Time 16.04
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl3
 NS 16
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 128
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

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





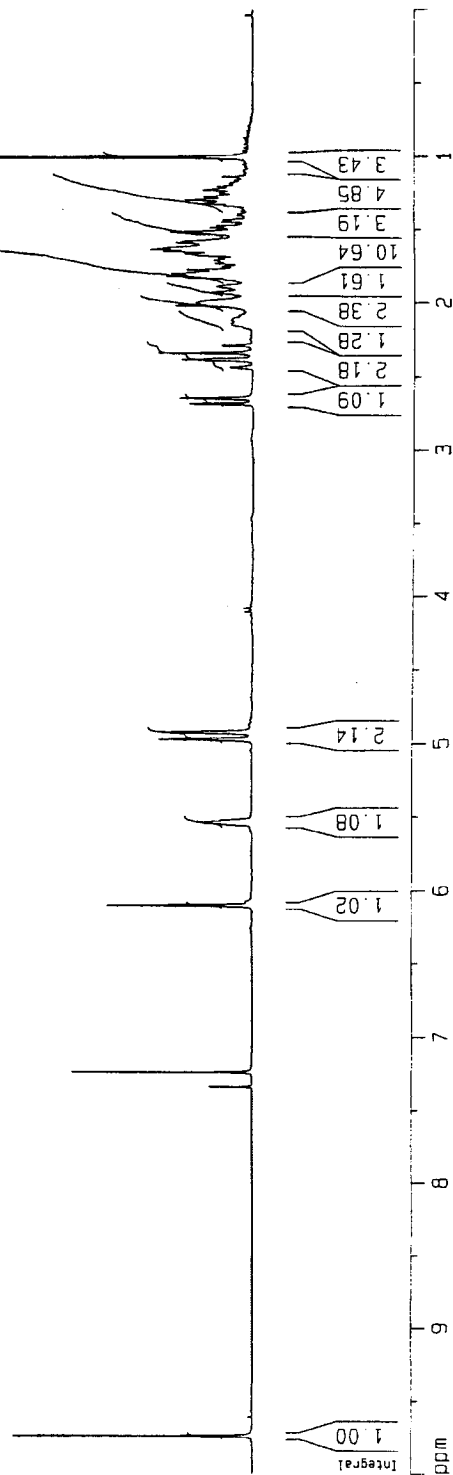
Current Data Parameters
 NAME rc_658_c
 EXPNO 1
 PROCNO 1

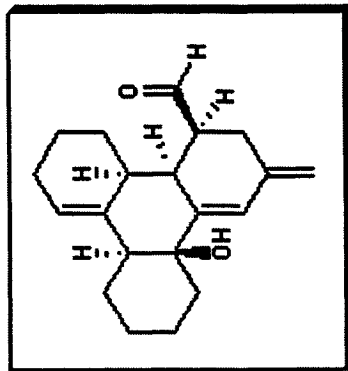
F2 - Acquisition Parameters
 Date_ 20040308
 Time 12.05
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl3
 NS 16
 DS 0
 SMH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 255
 DM 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

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

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

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





Current Data Parameters
NAME rc_651_b
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters

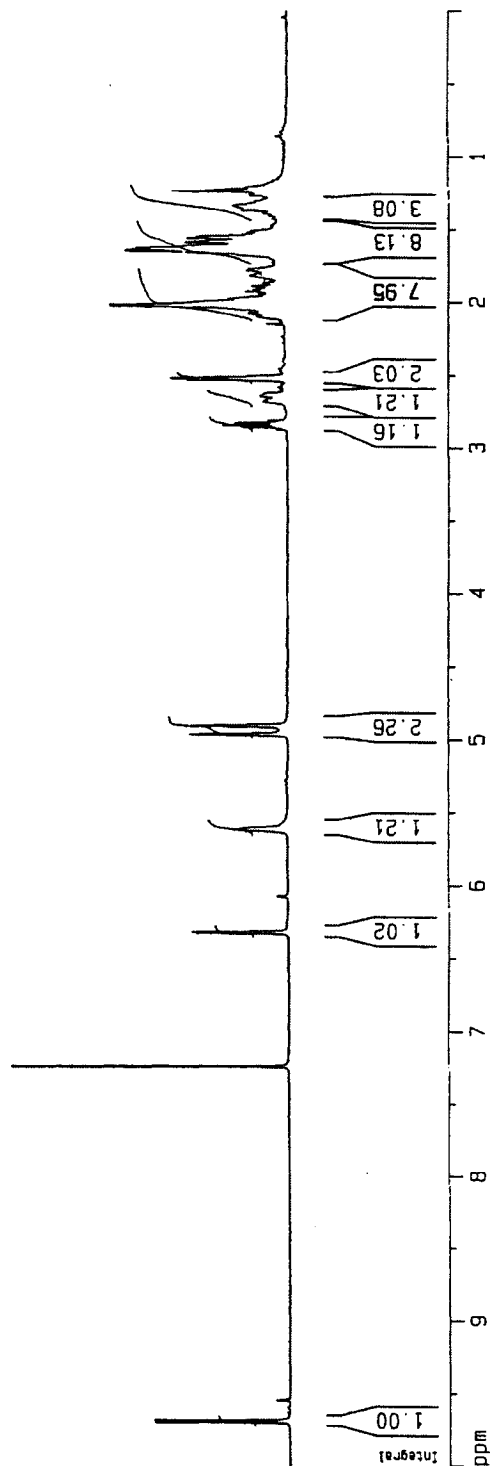
Date_ 20040301
Time 11.28
INSTRUM av300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 287.4
DM 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

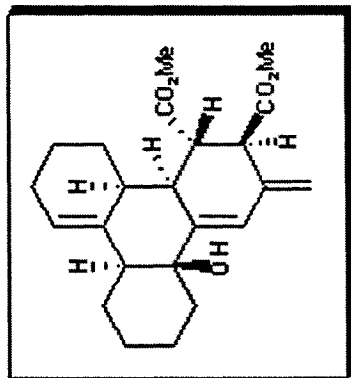
===== CHANNEL f1 =====

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
FIP 10.000 ppm
F1 3001.30 Hz
F2 0.000 ppm
F2 0.00 Hz
PPMCH 0.50000 ppm/cm
HZCM 150.06500 Hz/cm





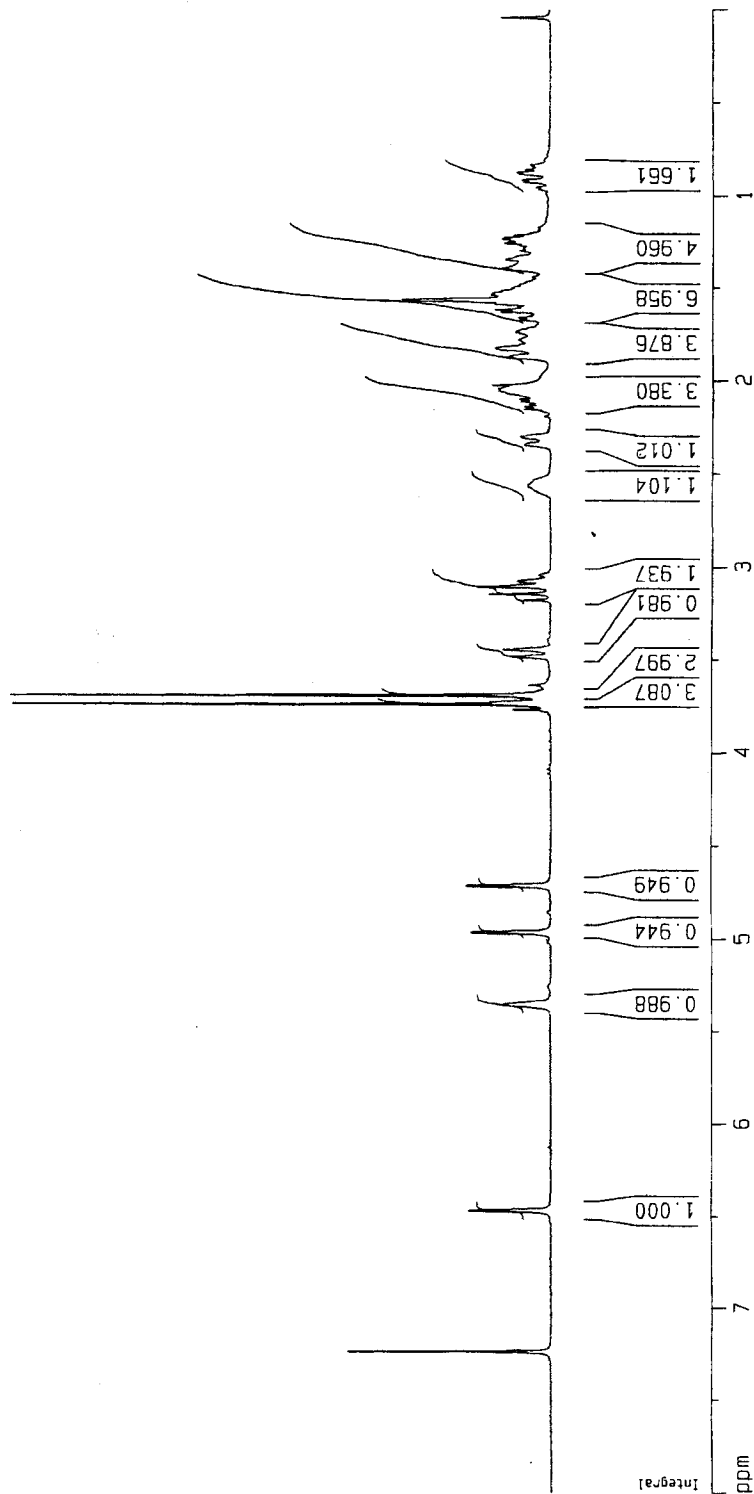
Current Data Parameters
 NAME rc_630
 EXPNO 1
 PROCNO 1

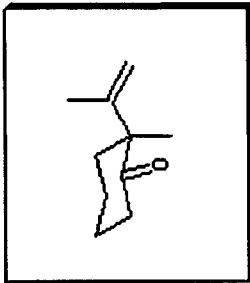
F2 - Acquisition Parameters
 Date_ 20040211
 Time 16.20
 INSTRUM av300
 PROBHD 5 mm GNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT COC13
 NS 16
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228960 sec
 RG 406.4
 DM 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.0000000 sec

===== 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 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



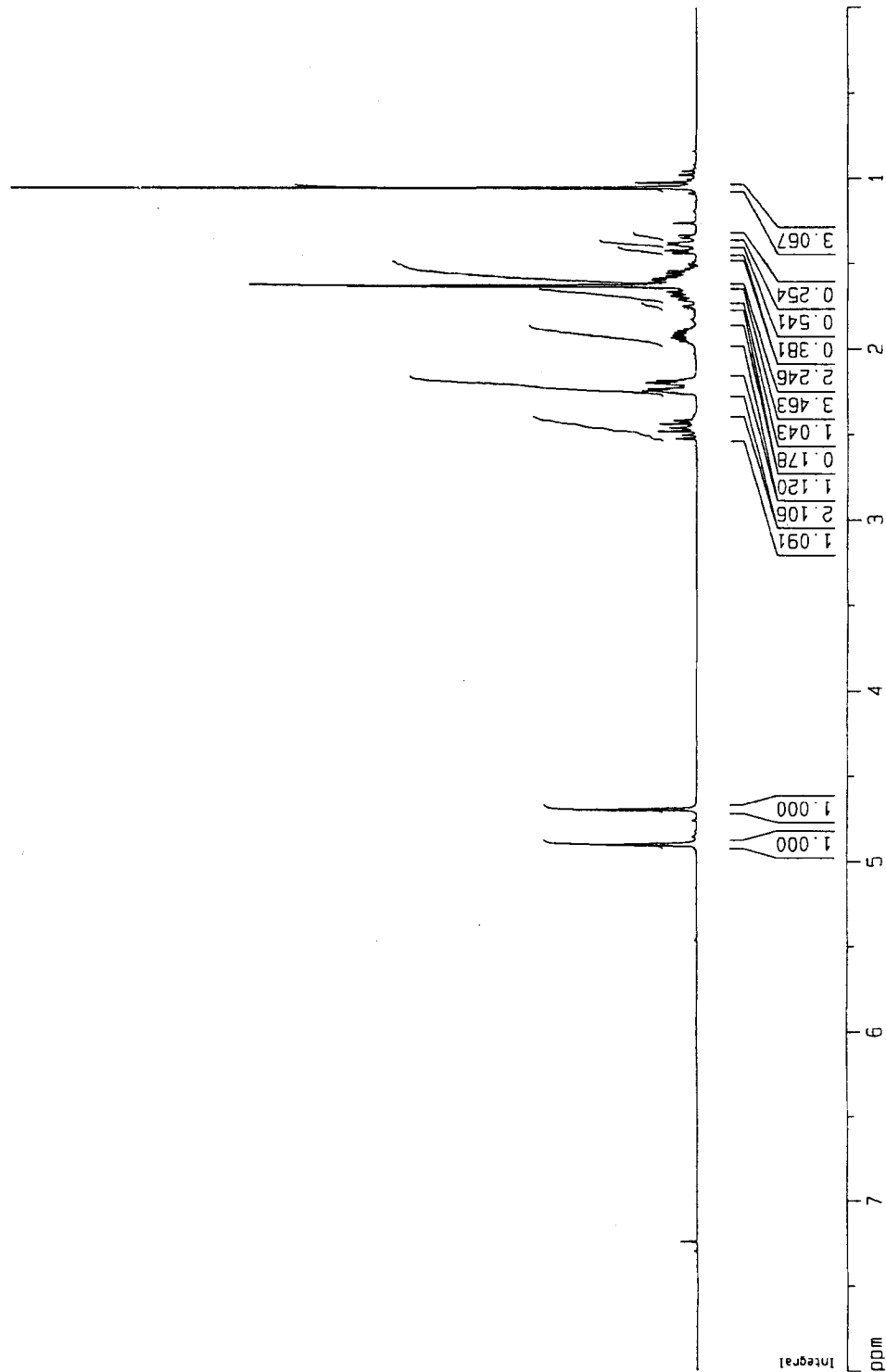


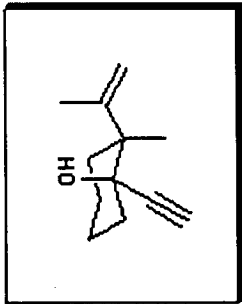
Current Data Parameters
 NAME rc_623_b
 EXPNO 1
 PROCNO 2

F2 - Acquisition Parameters
 Date_ 20040206
 Time 16.42
 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 45.3
 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
 ID NMR plot parameters
 CX 20.00 cm
 CY 10.00 cm
 F1P 8.000 ppm
 F1 2401.04 Hz
 F2 0.000 ppm
 F2 0.00 Hz
 PPMCM 0.40000 ppm/cm
 HZCM 120.05200 Hz/cm





Current Data Parameters
NAME rc_649_ip
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters

Date_ 20040405
Time 13.07
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 45.3
DM 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

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

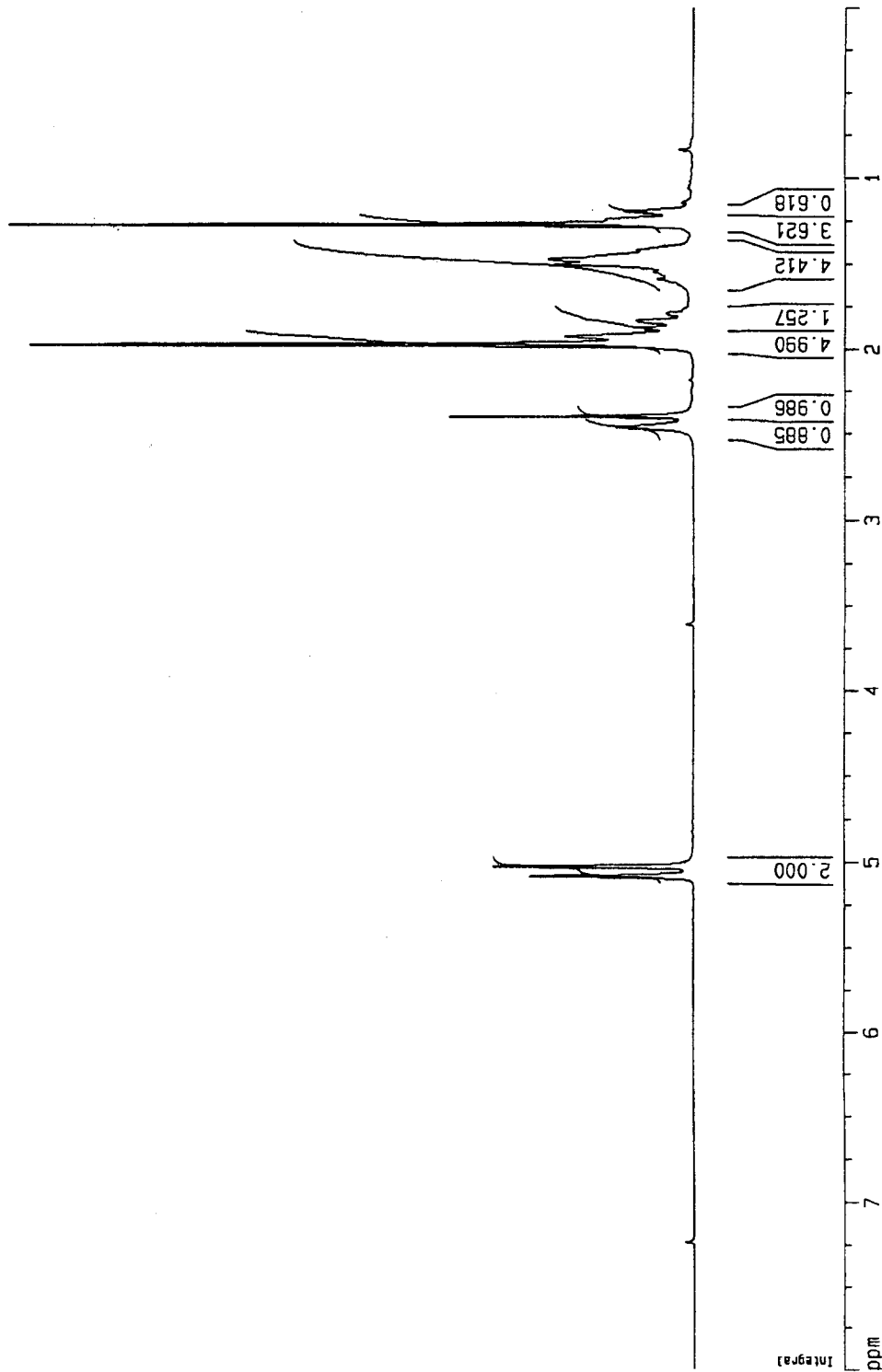
NUC1 1H
P1 10.50 usec
PL1 -3.00 dB
SF01 300.1319477 MHz

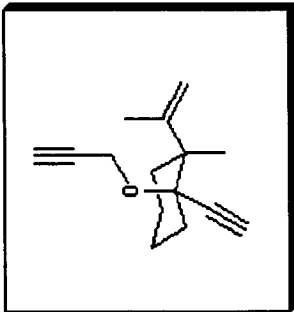
F2 - Processing parameters

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

10 NMR plot parameters

CX 20.00 cm
CY 10.00 cm
F1P 8.000 ppm
F1 2401.04 Hz
F2 0.000 ppm
F2P 0.00 Hz
PPHCH 0.40000 ppm/cm
HZCM 120.05200 Hz/cm





Current Data Parameters
 NAME rc_661
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters

Date_ 20040304
 Time 13.30
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl3
 NS 16
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.155407 Hz
 AQ 3.0228980 sec
 RG 45.3
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.0000000 sec

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

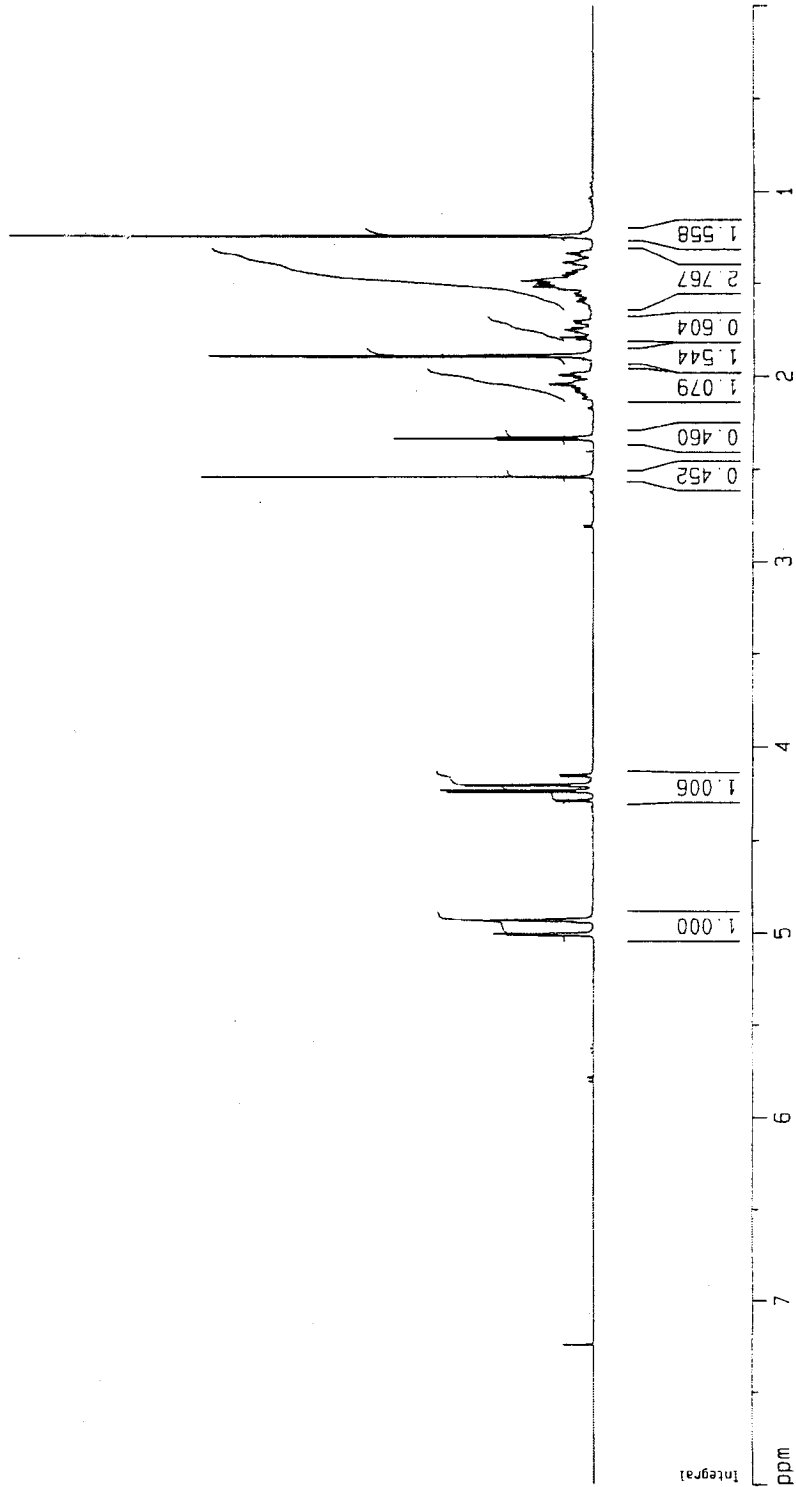
NUC1 1H
 P1 10.50 usec
 PL1 -3.00 dB
 SF01 300.1319477 MHz

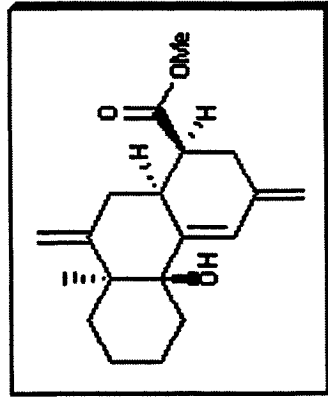
F2 - Processing parameters

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
 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 rc_724p_2
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters

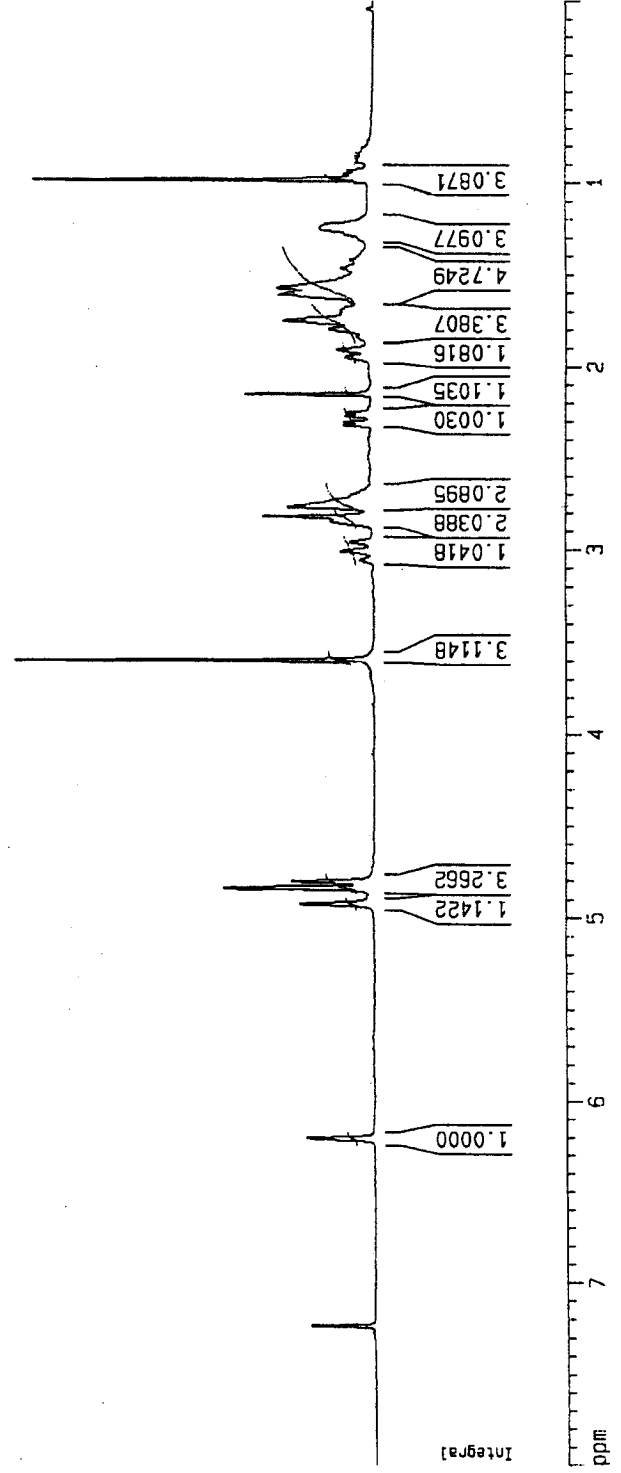
Date_ 20040427
 Time 12.16
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl3
 NS 16
 DS 0
 SMH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 203.2
 DM 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

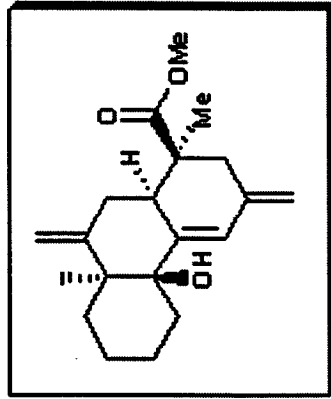
===== CHANNEL f1 =====

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

F2 - Processing parameters

SI 65536
 SF 300.1300000 MHz
 NDM EM
 SSB 0
 LB 0.10 Hz
 GB 0
 PC 1.00
 ID NMR plot parameters
 CX 20.00 cm
 CY 10.00 cm
 FIP 8.000 ppm
 F1 2401.04 Hz
 F2 0.000 ppm
 F2P 0.00 Hz
 PPMCM 0.40000 ppm/cm
 HZCM 120.05200 Hz/cm





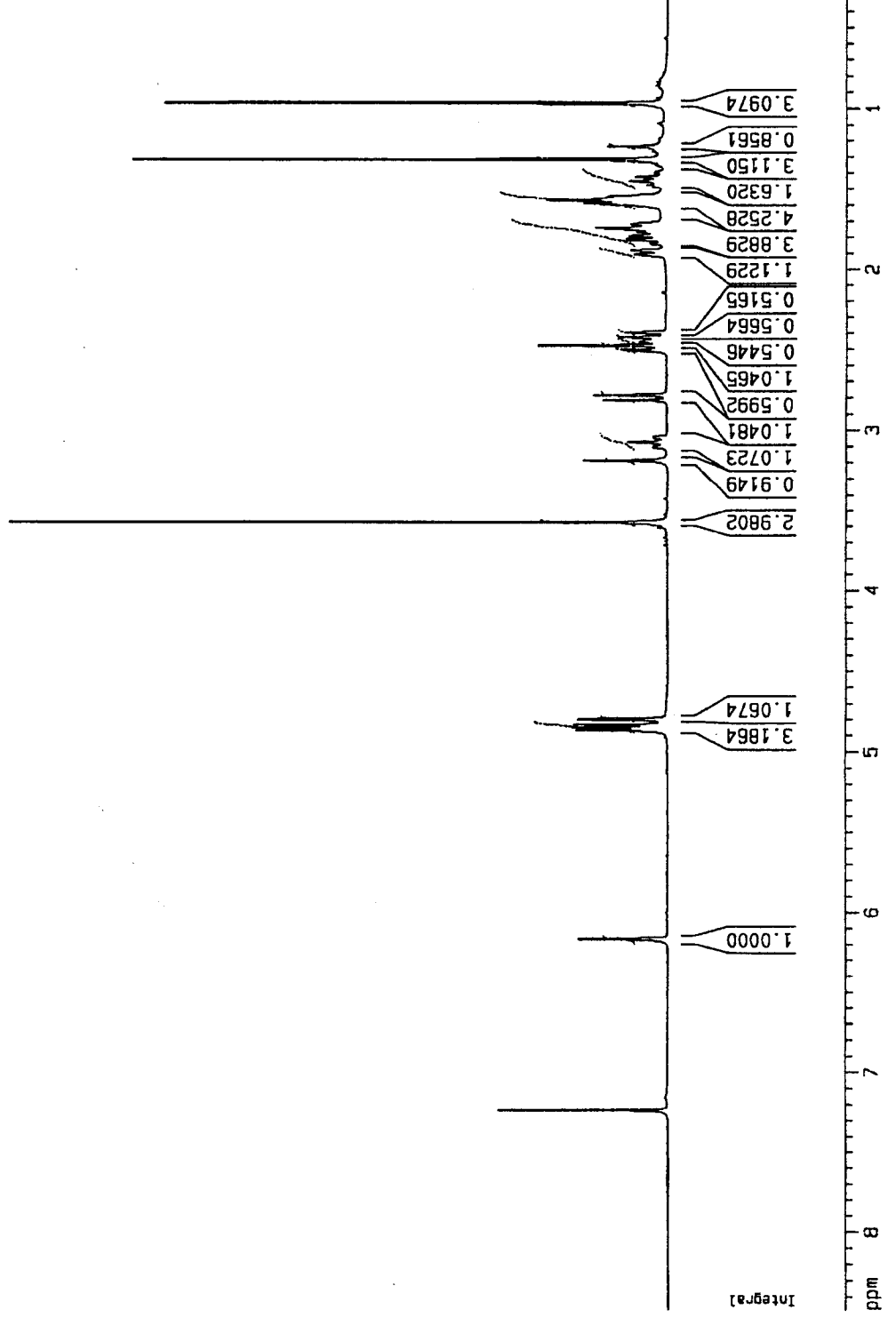
Current Data Parameters
NAME rc_666
EXPNO 1
PROCNO 1

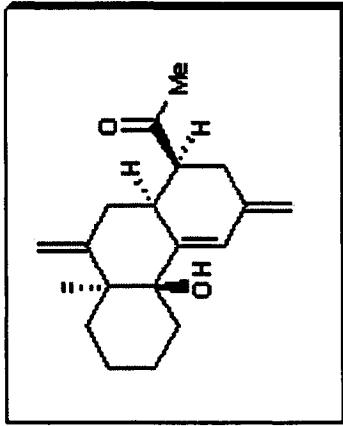
F2 - Acquisition Parameters
Date_ 20040310
Time 17.25
INSTRUM AV500MB
PROBHD 5 mm BBI 1H-BB
PULPROG zg30
TD 65536
SOLVENT H2O+D2O
NS 16
DS 0
SMH 7440.476 Hz
FIDRES 0.113533 Hz
AQ 4.4040694 sec
RG 101.6
DM 67.200 usec
DE 6.00 usec
TE 300.0 K
D1 0.01000000 sec

----- CHANNEL f1 -----
NUC1 1H
P1 10.50 usec
PL1 3.00 dB
SF01 500.1327766 MHz

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

1D NMR plot parameters
CX 20.00 cm
CY 10.00 cm
FIP 8.486 ppm
F1 4244.27 Hz
F2P 0.320 ppm
F2 160.10 Hz
PNUC1 0.40831 ppm/cm
HZCM 204.20851 Hz/cm





Current Data Parameters
 NAME rc_670p1
 EXPNO 1
 PROCNO 1

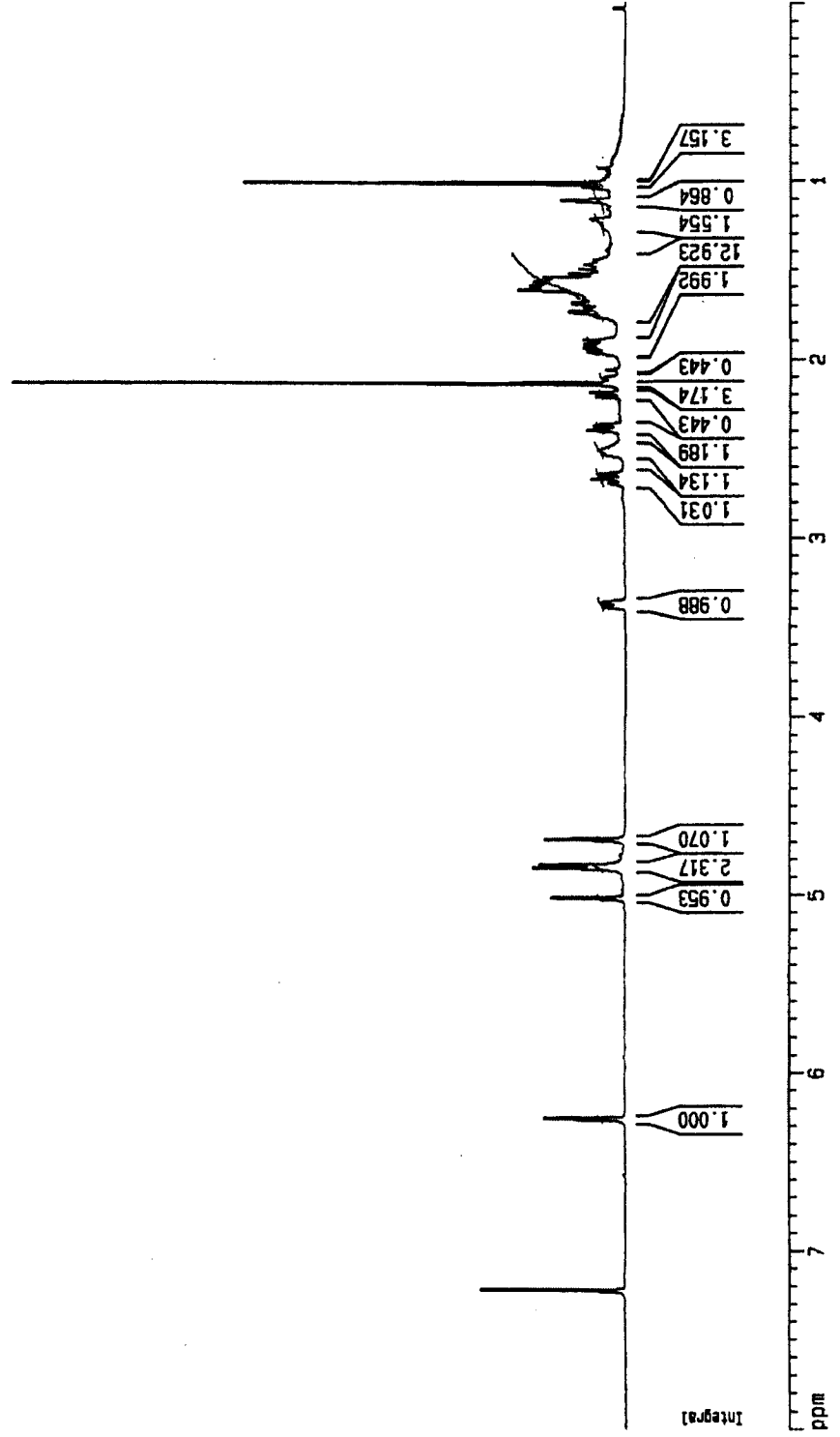
F2 - Acquisition Parameters

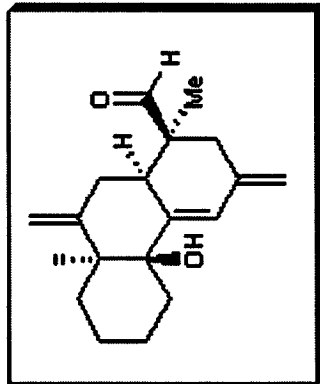
Date 20040322
 Time 9.24
 INSTRUM AV500NB
 PROBHD 5 mm BBI 1H-88
 PULPROG zg30
 TD 65536
 SOLVENT Acetone
 NS 32
 DS 0
 SWH 7440.476 Hz
 FIDRES 0.113533 Hz
 AQ 4.4040694 sec
 RG 45.25
 DM 67.200 usec
 DE 6.00 usec
 TE 300.0 K
 D1 0.01000000 sec

***** CHANNEL f1 *****
 NUC1 1H
 P1 10.50 usec
 PL1 3.00 dB
 SF01 500.1327766 MHz

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

1D NMR plot parameters
 CX 20.00 cm
 CY 10.00 cm
 FIP 8.000 ppm
 F1 4001.04 Hz
 F2 0.000 ppm
 F2 0.00 Hz
 PPMCH 0.40000 ppm/cm
 HZCM 200.05200 Hz/cm





Current Data Parameters
 NAME rc_668pb
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters

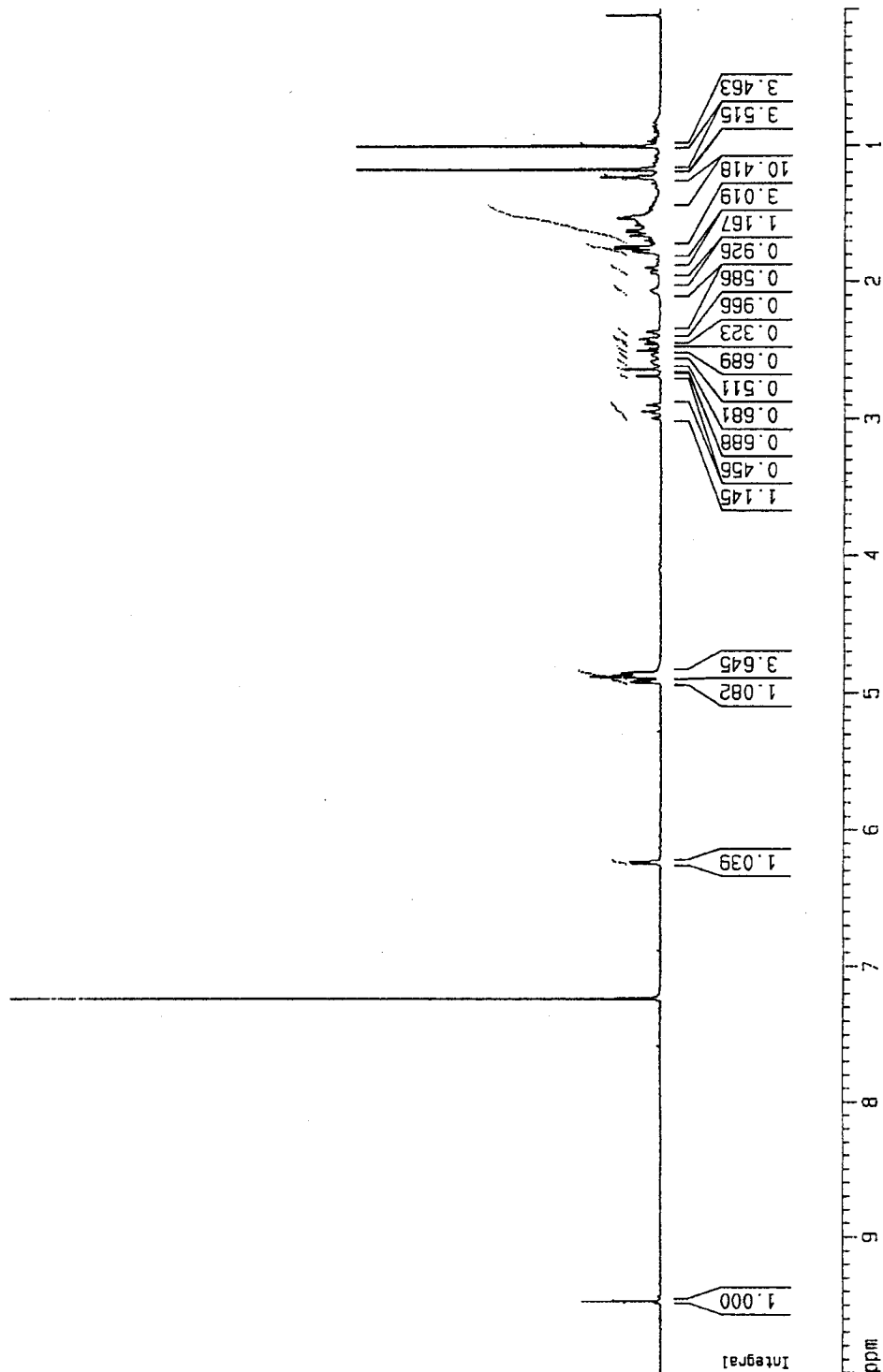
Date_ 20040401
 Time 9.49
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl3
 NS 32
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 912.3
 DN 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.0000000 sec

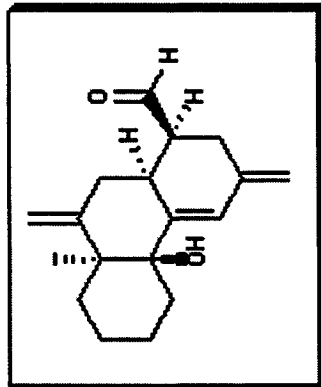
===== CHANNEL f1 =====

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





Current Data Parameters
 NAME rc_676_a
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters

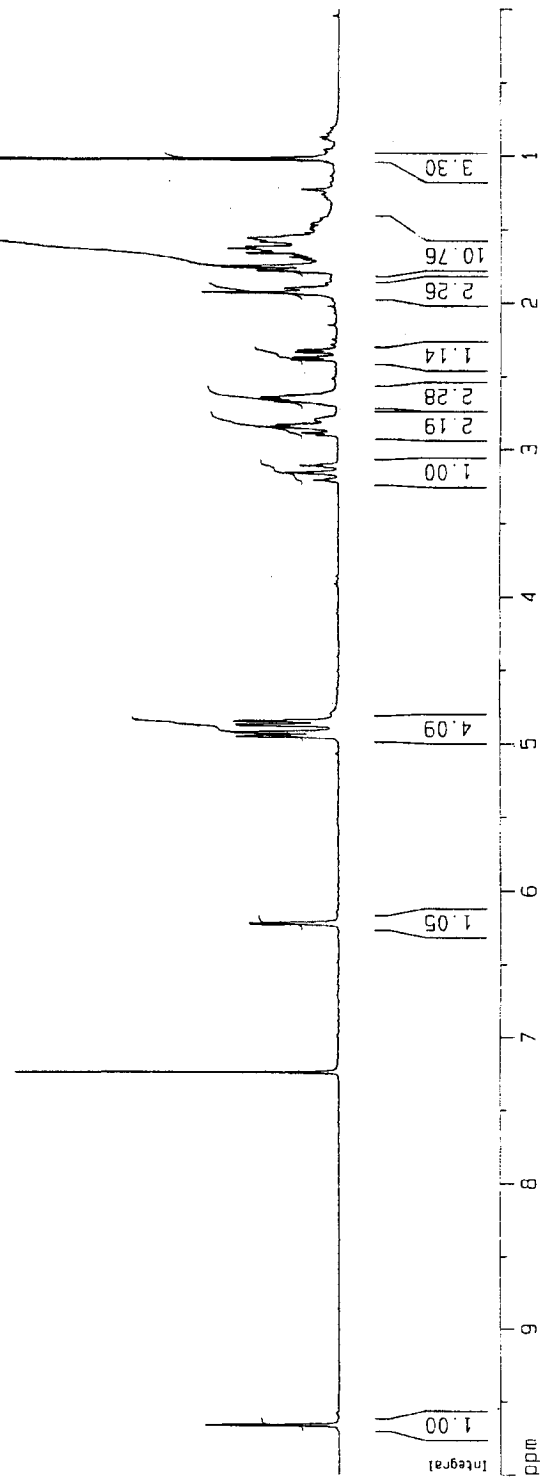
Date_ 20040319
 Time 10.31
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TO 30720
 SOLVENT CDCl3
 NS 32
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0229980 sec
 RG 456.1
 DM 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

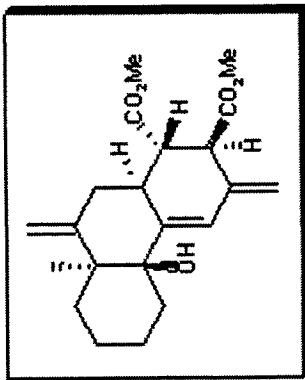
===== CHANNEL f1 =====

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

F2 - Processing parameters

SF 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 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 rc_678_a
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters

Date_ 20040323
Time 13.59
INSTRUM AV500WB
PROBHD 5 mm BBI 1H-BB
PULPROG zg30
TD 65536
SOLVENT Acetone
NS 32
DS 0
SWH 7440.476 Hz
FIDRES 0.113533 Hz
AQ 4.4040694 sec
RG 90.51
DN 67.200 usec
DE 6.00 usec
TE 300.0 K
D1 0.01000000 sec

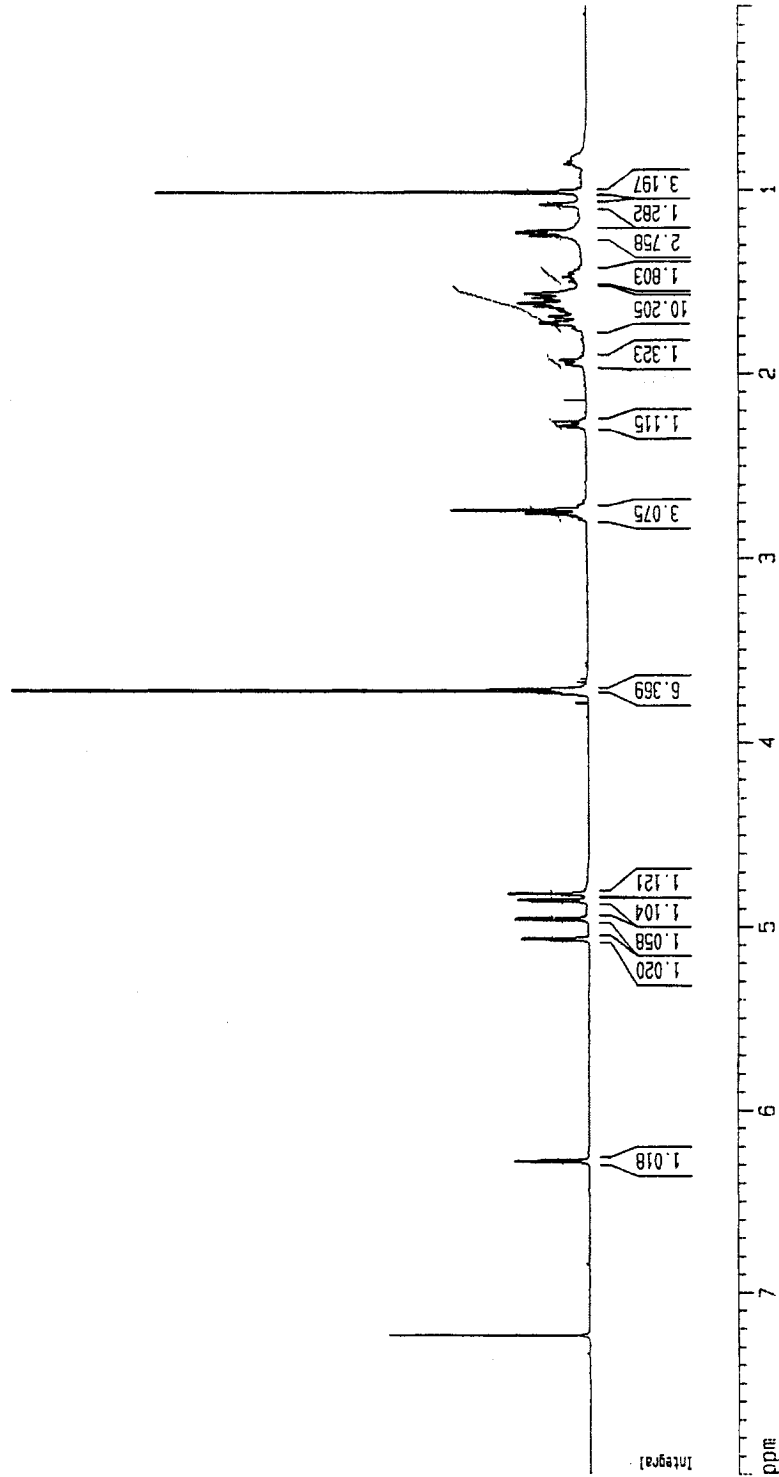
===== CHANNEL f1 =====
NUC1 1H
P1 10.50 usec
PL1 3.00 dB
SF01 500.1327766 MHz

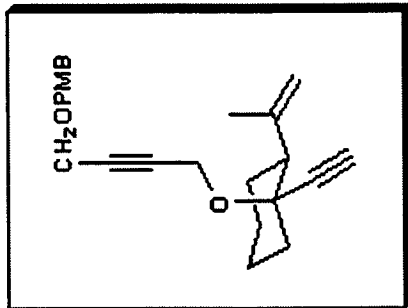
F2 - Processing parameters

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

1D NMR plot parameters

CX 20.00 cm
CY 14.00 cm
F1P 8.000 ppm
F1 4001.04 Hz
F2P 0.000 ppm
F2 0.00 Hz
PPMCH 0.40000 ppm/cm
HZCM 200.05200 Hz/cm





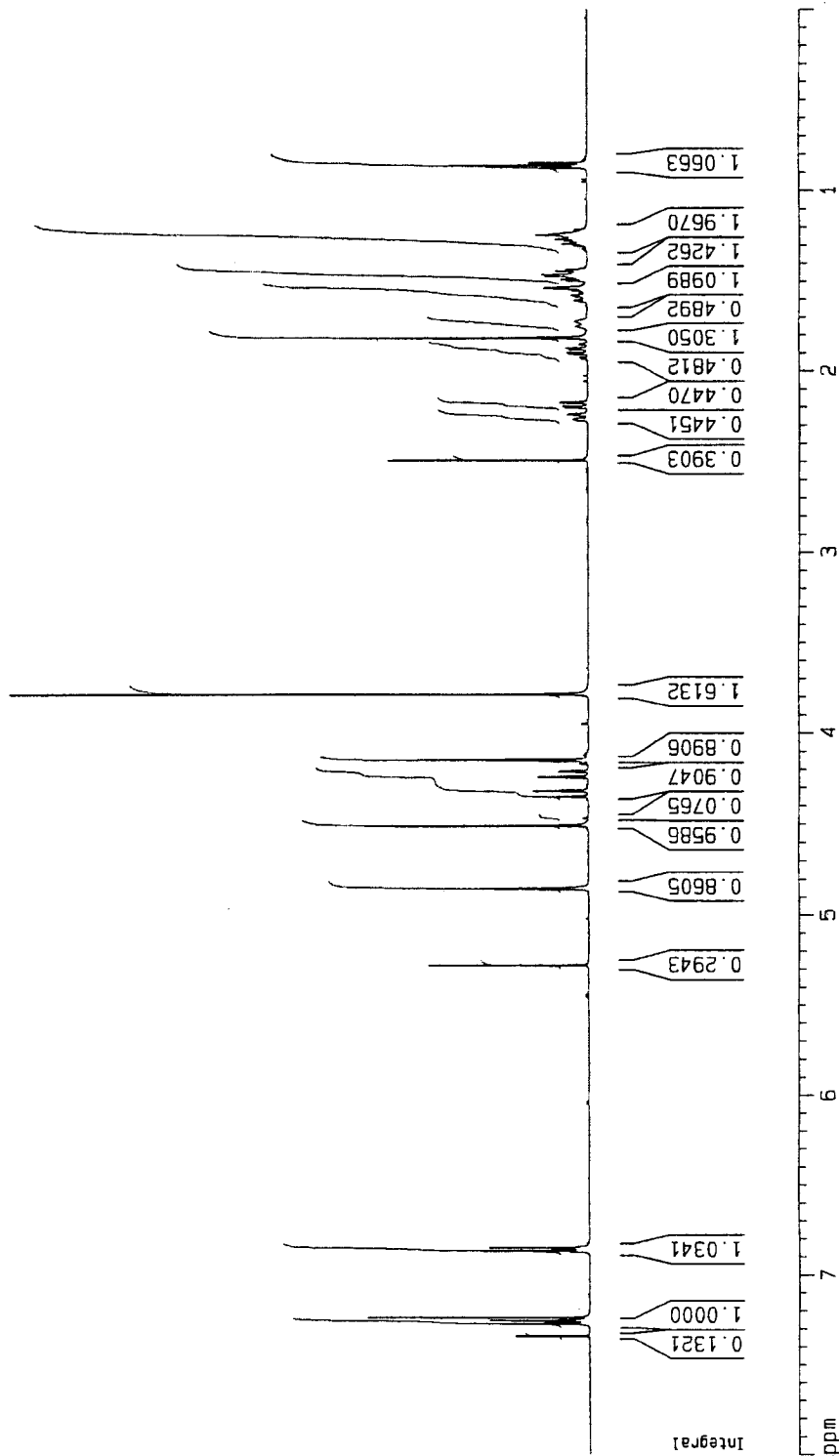
Current Data Parameters
 NAME rc_749_b
 EXPNO 1
 PROCNO 1

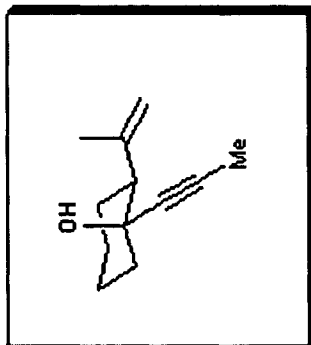
F2 - Acquisition Parameters
 Date_ 20040928
 Time 20:58
 INSTRUM AV500WB
 PROBHD 5 mm TBO BB/1H
 PULPROG zg30
 TD 65536
 SOLVENT Acetone
 NS 40
 DS 0
 SNH 7440.476 Hz
 FIDRES 0.113533 Hz
 AQ 4.4040694 sec
 RG 203.2
 DW 67.200 usec
 DE 5.00 usec
 TE 300.0 K
 D1 0.01000000 sec

===== CHANNEL f1 =====
 NUC1 1H
 P1 14.00 usec
 PL1 0.00 dB
 SF01 500.132756 MHz

F2 - Processing parameters
 SI 65536
 SF 500.130049 MHz
 WDW EM
 SSB 0
 LB 0.00 Hz
 GB 0
 PC 1.00

1D NMR plot parameters
 CX 20.00 cm
 CY 10.00 cm
 F1P 8.000 ppm
 F1 4001.04 Hz
 F2P 0.000 ppm
 F2 0.00 Hz
 PPMCM 0.40000 ppm/cm
 HZCM 200.05200 Hz/cm





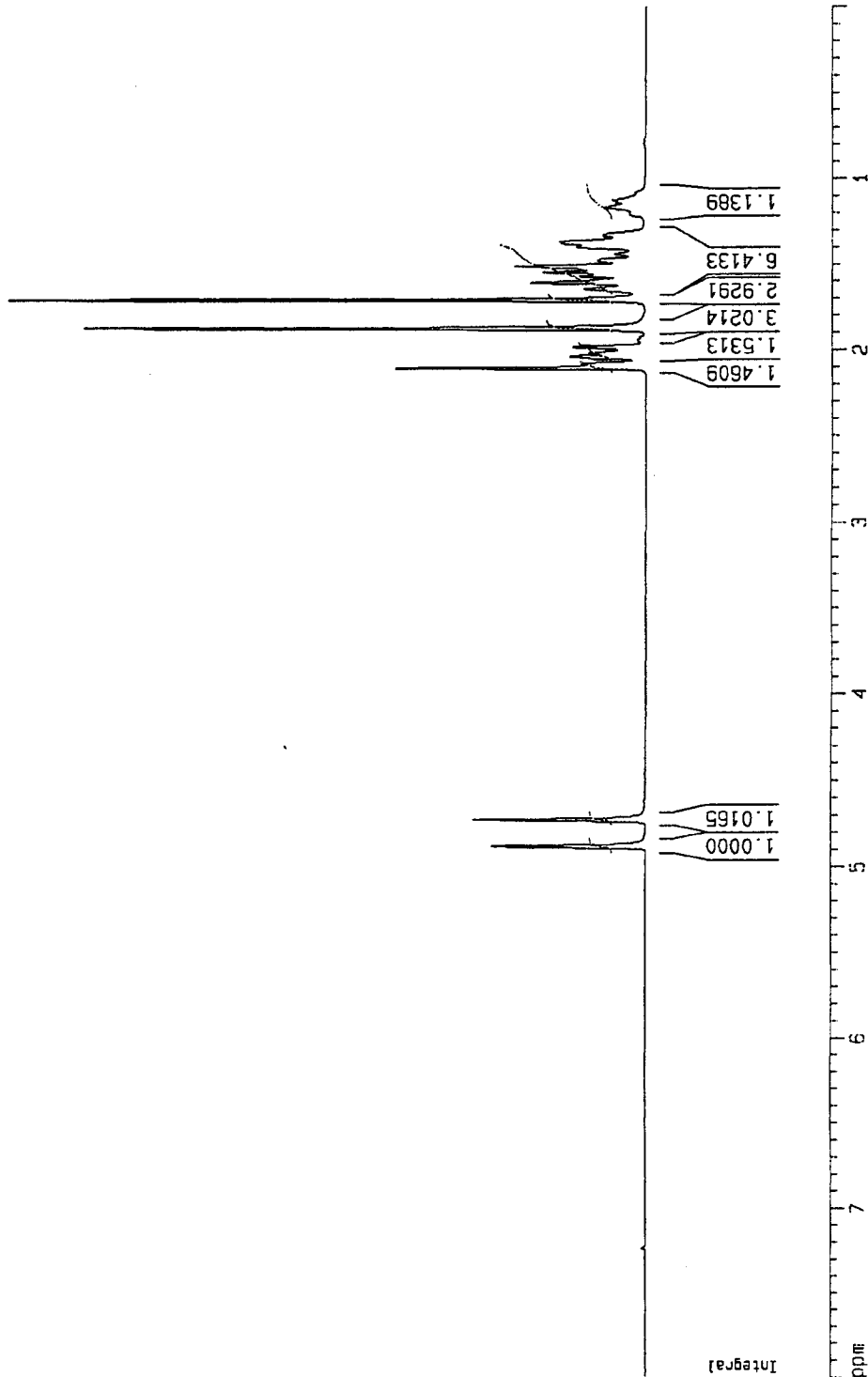
Current Data Parameters
 NAME rc_725_a
 EXPNO 1
 PROCNO 1

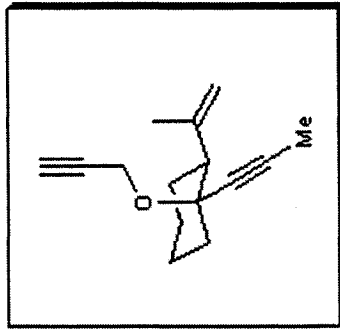
F2 - Acquisition Parameters
 Date_ 20040427
 Time 12.22
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TO 30720
 SOLVENT CDCl3
 NS 16
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 20.2
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

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

F2 - Processing parameters
 SI 65536
 SF 300.1300000 MHz
 NDW 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 rc_728pp
 EXPNO 1
 PROCNO 1

F2 - Acquisition Parameters
 Date_ 20040503
 Time 13.23
 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 22.6
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

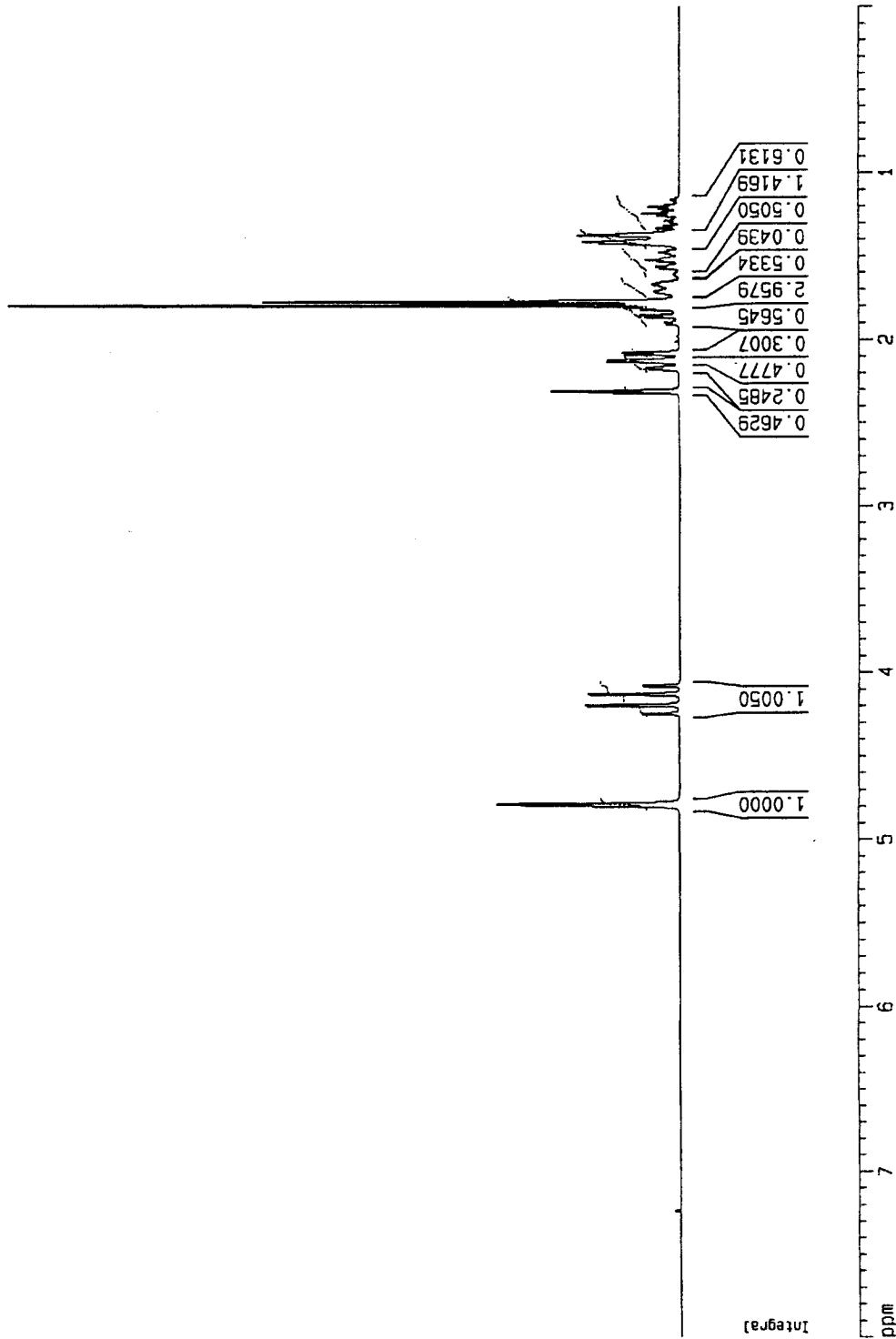
===== CHANNEL f1 =====

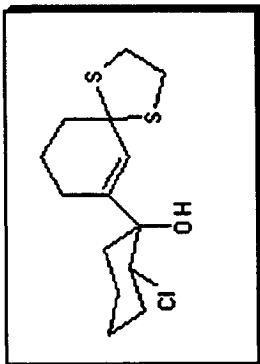
NUC1 1H
 P1 10.50 usec
 PL1 -3.00 dB
 SF01 300.1319477 MHz

F2 - Processing parameters

SI 65536
 SF 300.1300000 MHz
 NDM 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 0.000 ppm
 F2 0.00 Hz
 PPMCM 0.40000 ppm/cm
 HZCM 120.05200 Hz/cm





Current Data Parameters
 NAME jmw4-118
 EXPNO 1
 PROCNO 1

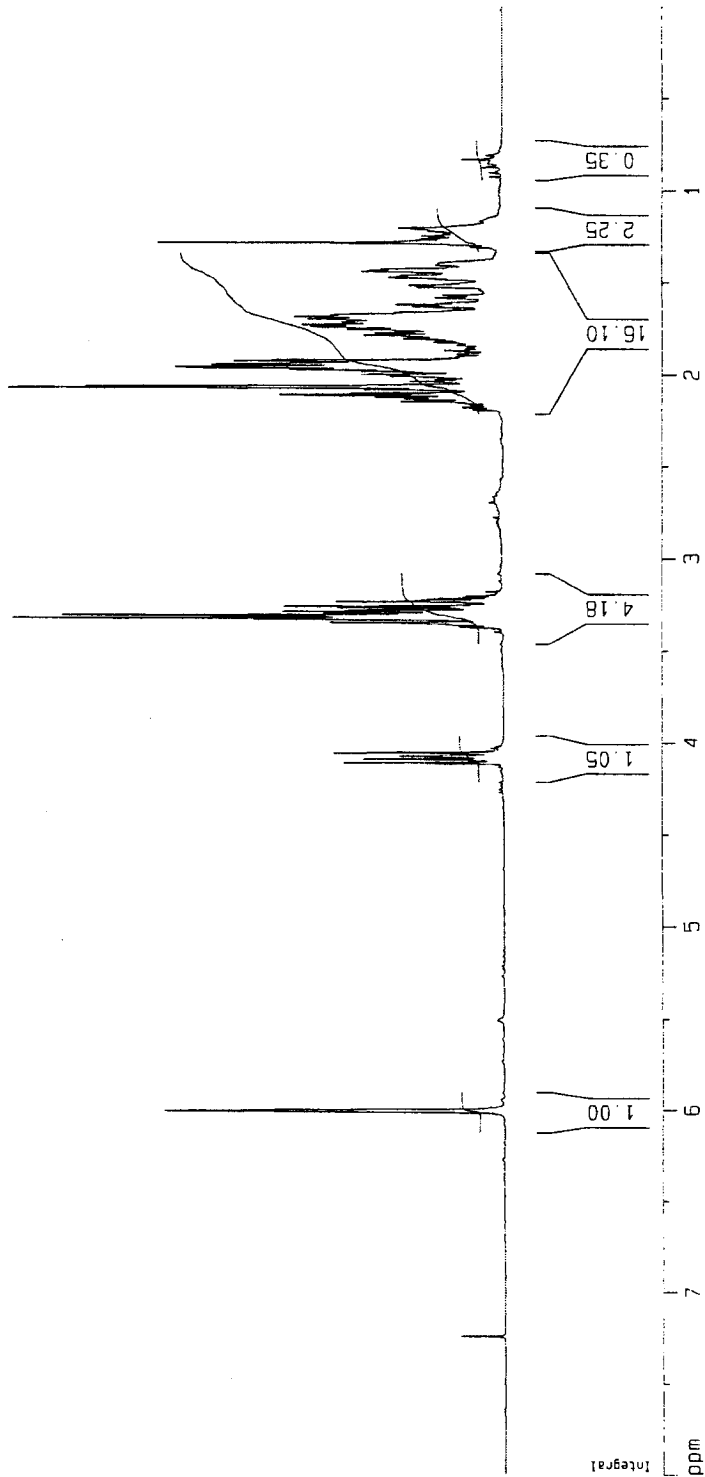
F2 - Acquisition Parameters

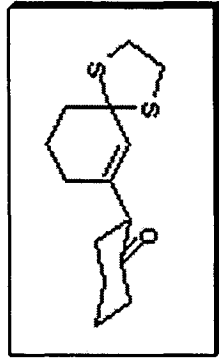
Date_ 20020905
 Time 17.55
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TD 30720
 SOLVENT CDCl3
 NS 16
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 45.3
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

===== 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
 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 jmw4-119
 EXPNO 1
 PROCNO 1

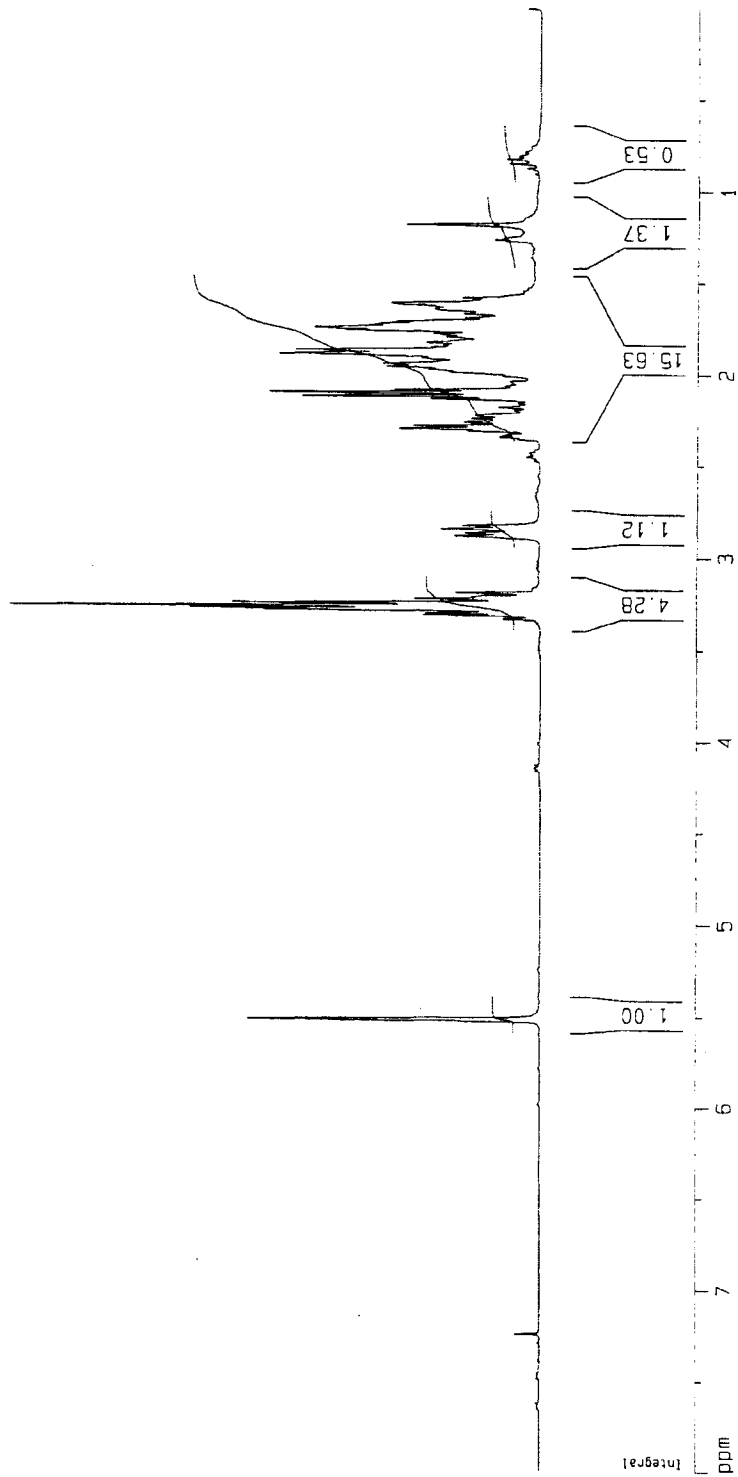
F2 - Acquisition Parameters

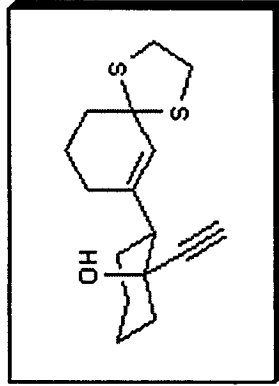
Date_ 20020906
 Time 16.23
 INSTRUM av300
 PROBHD 5 mm QNP 1H/1
 PULPROG zg30
 TO 30720
 SOLVENT CDCl3
 NS 16
 DS 0
 SWH 5081.301 Hz
 FIDRES 0.165407 Hz
 AQ 3.0228980 sec
 RG 45.3
 DW 98.400 usec
 DE 6.00 usec
 TE 300.0 K
 D1 1.00000000 sec

===== 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
 B 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
 FZCM 120.05200 Hz/cm





Current Data Parameters
 NAME rc_841a
 EXPNO 1
 PROCNO 1

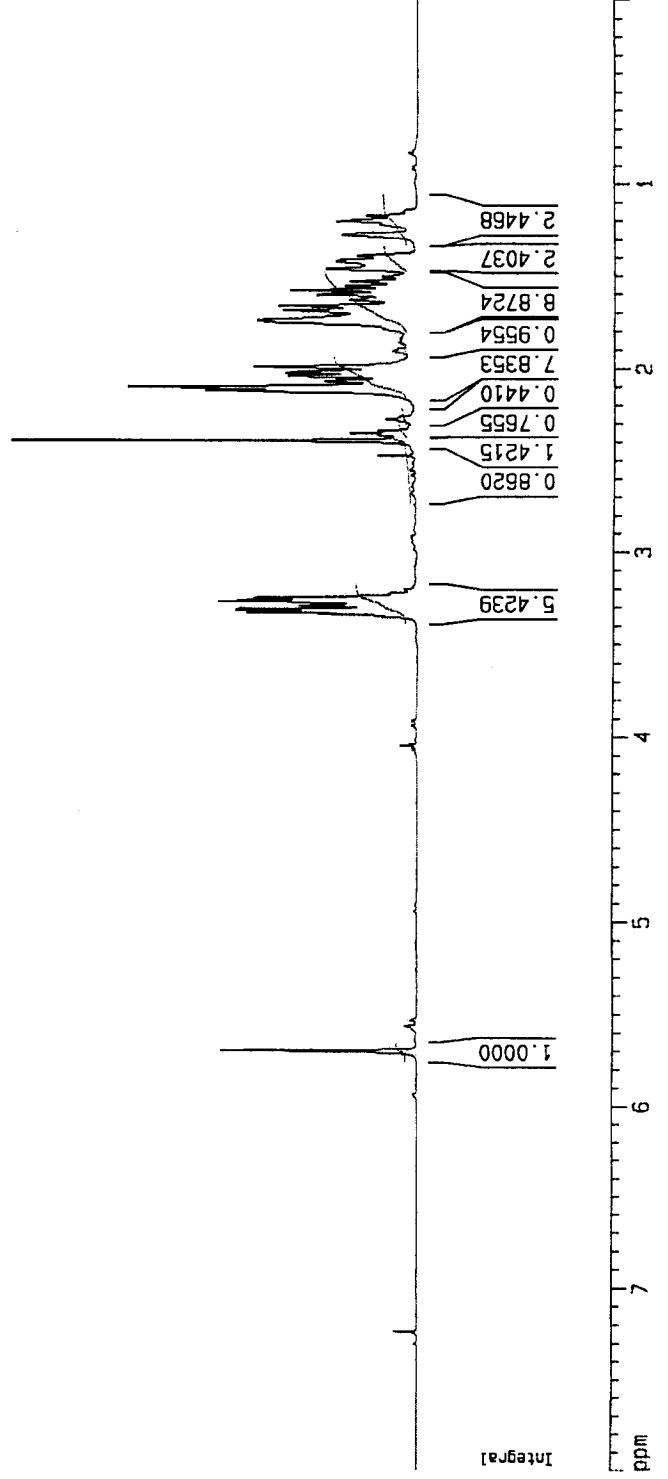
F2 - Acquisition Parameters

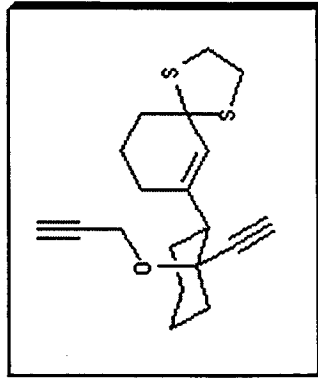
Date_ 20040727
 Time 13.10
 INSTRUM AV500WB
 PROBHD 5 mm BBI 1H-BB
 PULPROG zg30
 TO 65536
 SOLVENT Acetone
 NS 16
 DS 0
 SH 7440.476 Hz
 FIDRES 0.113533 Hz
 AQ 4.4040894 sec
 RG 15
 DW 67.200 usec
 DE 6.00 usec
 TE 300.0 K
 D1 0.01000000 sec

===== CHANNEL f1 =====
 NUC1 1H
 P1 9.50 usec
 PL1 3.00 dB
 SF01 500.1327766 MHz

F2 - Processing parameters

SI 65536
 SF 500.1300049 MHz
 WDW EM
 SSB 0
 LB 0.00 Hz
 GB 0
 PC 1.00
 ID NMR plot parameters
 CX 20.00 cm
 CY 10.00 cm
 FIP 8.000 ppm
 F1 4001.04 Hz
 F2 0.000 ppm
 F2 0.00 Hz
 PPMCM 0.40000 ppm/cm
 HZCM 200.05200 Hz/cm





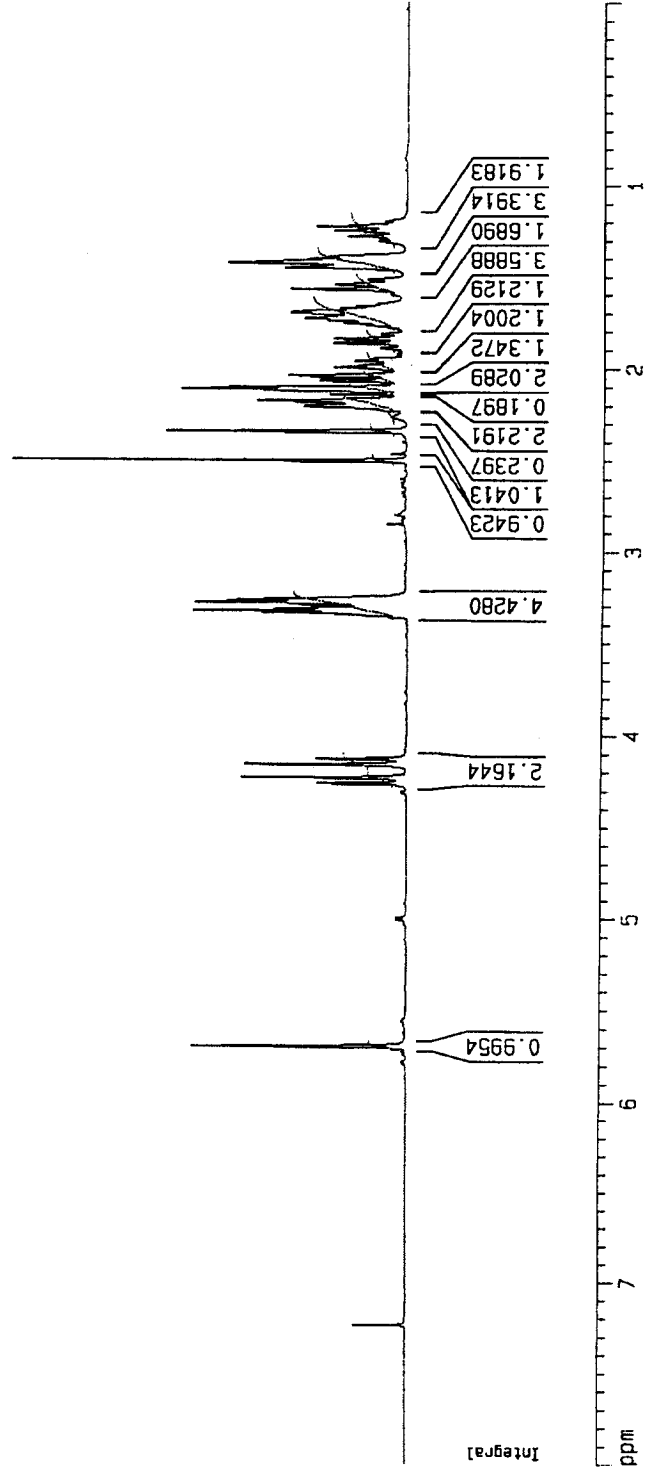
Current Data Parameters
NAME rc_B44a
EXPNO 1
PROCNO 1

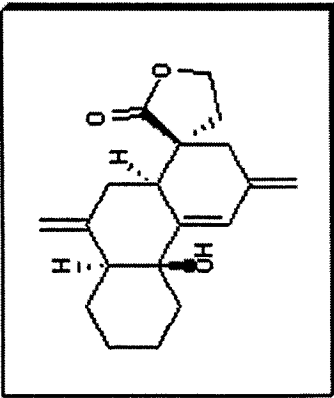
F2 - Acquisition Parameters
Date_ 20040728
Time 17.54
INSTRUM AV500WB
PROBHD 5 mm BBI 1H-BB
PULPROG zg30
TD 65536
SOLVENT Acetone
NS 16
DS 0
SWH 7440.476 Hz
FIDRES 0.113533 Hz
AQ 4.4040694 sec
RG 28.51
DW 67.200 usec
DE 6.00 usec
TE 300.0 K
D1 0.01000000 sec

===== CHANNEL f1 =====
NUC1 1H
P1 9.50 usec
PL1 3.00 dB
SF01 500.1327766 MHz

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

1D NMR plot parameters
CX 20.00 cm
CY 8.00 cm
FIP 8.000 ppm
F1 4001.04 Hz
F2 0.000 ppm
F2 0.00 Hz
PPMCM 0.40000 ppm/cm
HZCM 200.05200 Hz/cm





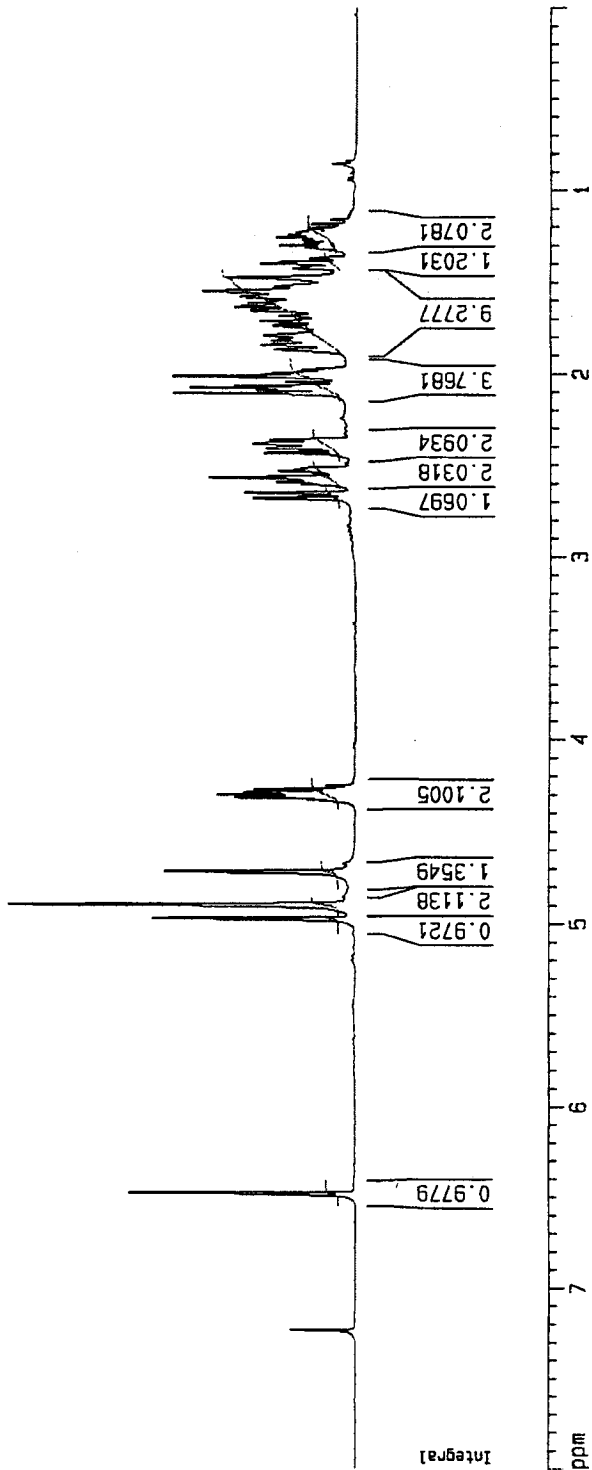
Current Data Parameters
NAME rc_850
EXPNO 1
PROCNO 1

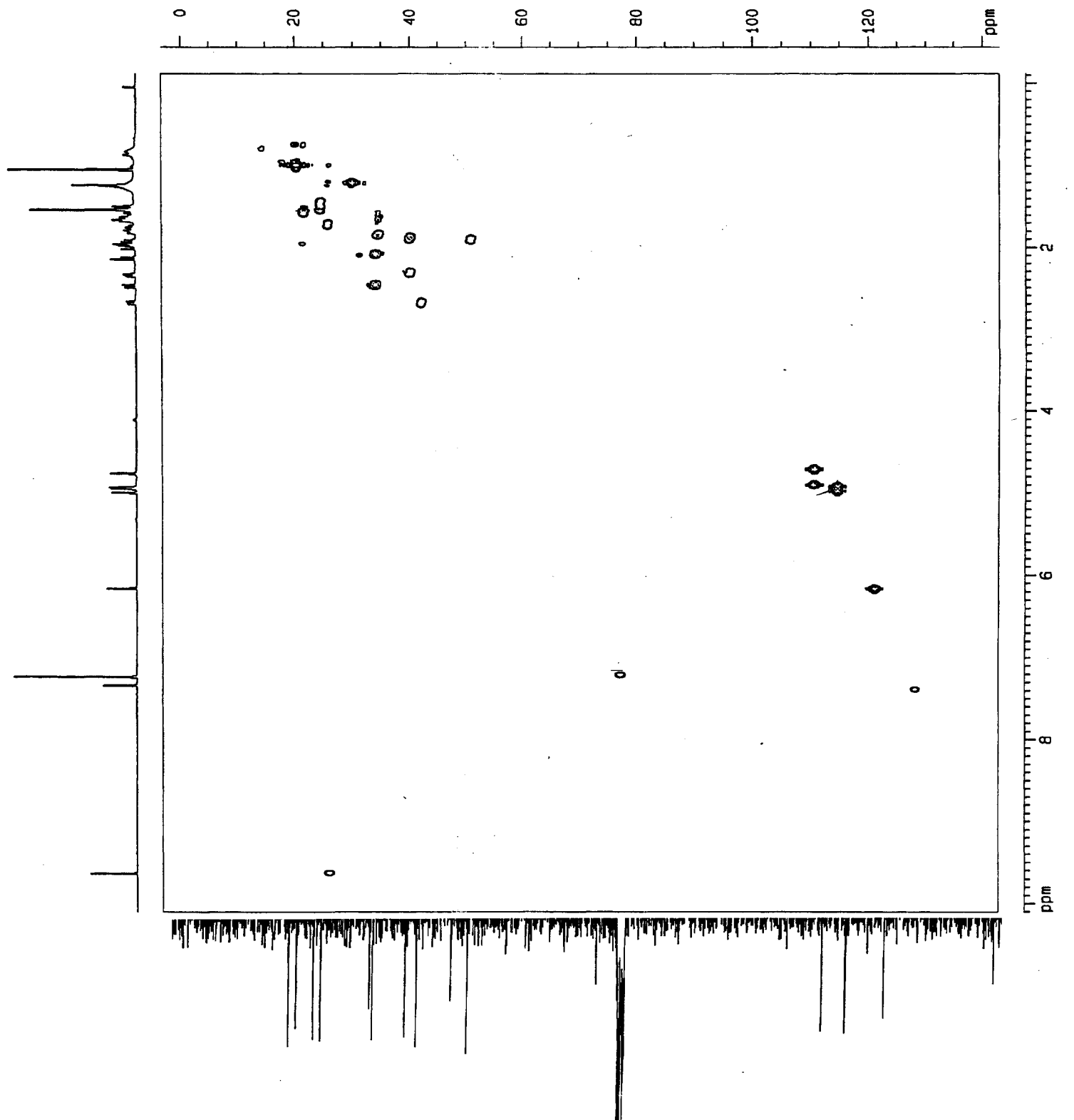
F2 - Acquisition Parameters
Date_ 20040819
Time 14.58
INSTRUM AV500NB
PROBHD 5 mm BBI 1H-BB
PULPROG zg30
TD 65536
SOLVENT Acetone
NS 32
DS 0
SWH 7440.476 Hz
FIDRES 0.113533 Hz
AQ 4.4040694 sec
RG 80.63
DN 67.200 usec
DE 6.00 usec
TE 300.0 K
D1 0.01000000 sec

===== CHANNEL f1 =====
NUC1 1H
P1 9.40 usec
PL1 3.00 dB
SF01 500.132766 MHz

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

1D NMR plot parameters
CX 20.00 cm
CY 6.00 cm
F1P 8.000 ppm
F1 4001.04 Hz
F2 0.000 ppm
F2P 0.00 Hz
PPNCH 0.40000 ppm/cm
HZCH 200.05200 Hz/cm





Current Data Parameters

Current Data Parameters	
NAME	rc_548b_2d
EXPNO	3
PROCNO	1

F2 - Acquisition Parameters

Time	20:04:22	20:22:11
INSTRUM	AV5000B	
PRGNOB	5 m 8B1 1H	
FILE_PDS	noesypsh	
TO	1054	
NO SOLVENT	CDC13	
NS	40	
SC	4807.852 Hz	
F1_FREQS	4.695012 Hz	
RG	0.1053400 sec	
RG	181	
DE	164.000 uS/c	
BE	5.00 uS/c	
TE	300.0 K	
D1	0.00000300 sec	
D1	1.00000000 sec	
D6	0.00000000 sec	
D6	0.99990000 sec	
IND	0.00120600 sec	
IND	0.00000000 sec	
IND	1.00000000 sec	

***** CHANNEL 11 *****

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,***** CHANNEL F1 *****
NUC1      1H
P1         9.50 usec
P2        19.00 usec
PL1        3.00 dB
SF01      500.1325829 MHz

```

***** GRADIENT CHANNEL *****

PRODUCT	UNIT	PRICE
GPAN1	SINE100	0.00 %
GPAN2	SINE100	0.00 %
GPX1	0.00 %	
GPX2	0.00 %	
GPY1	0.00 %	
GPY2	0.00 %	
GPZ1	40.00 %	
GPZ2	-40.00 %	
P16	1000.00	USEC

F1 - Acquisition parameters

NOO	1
10	255
SFO1	500.1325 MHz
FIDRES	18.780048 Hz

MC 9.019.5

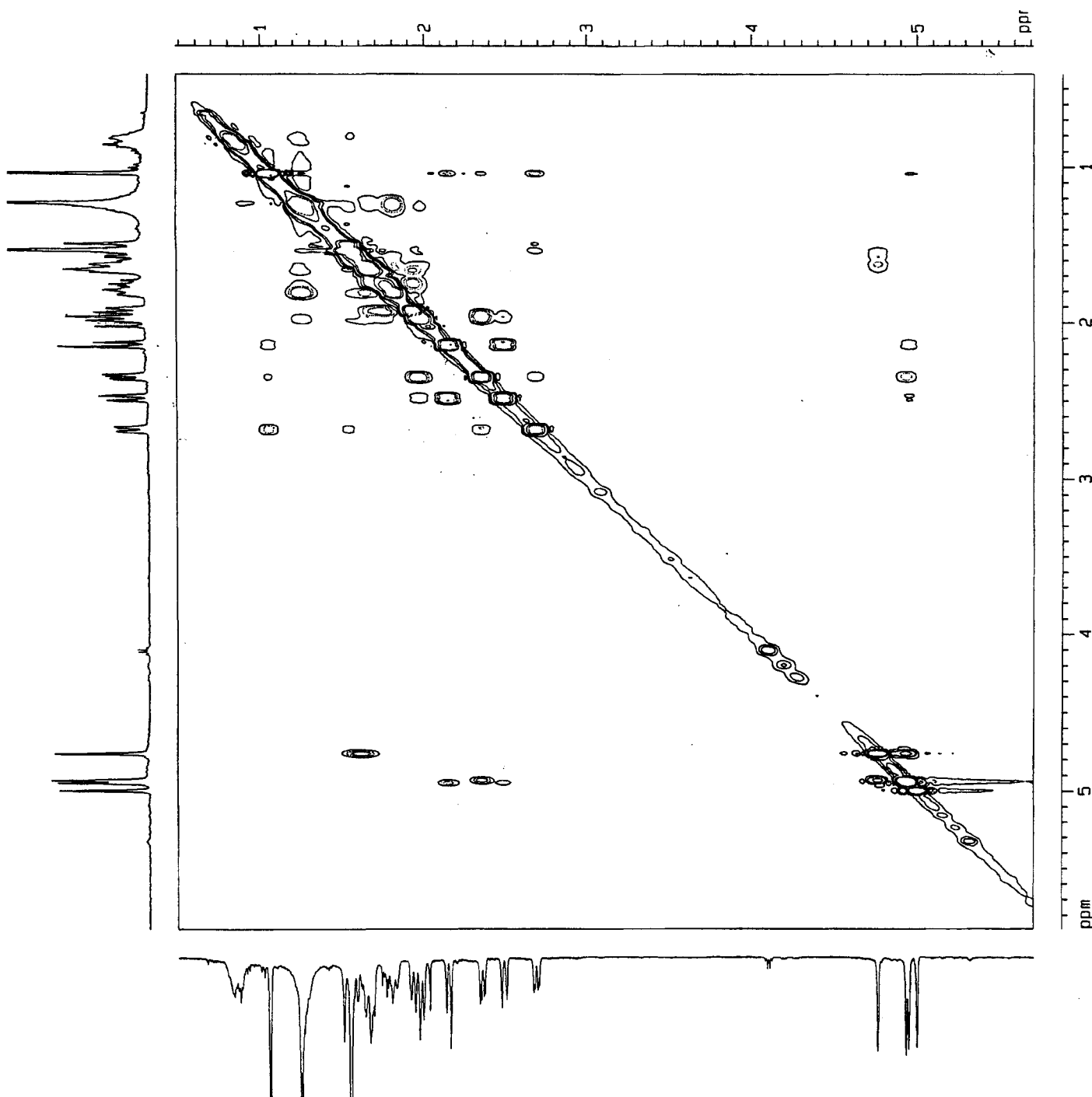
S1	1024
SF	500.130049 Mhz
MOD	QPSK
SSB	2
LB	0.00 Mhz
GB	0
PC	1.00

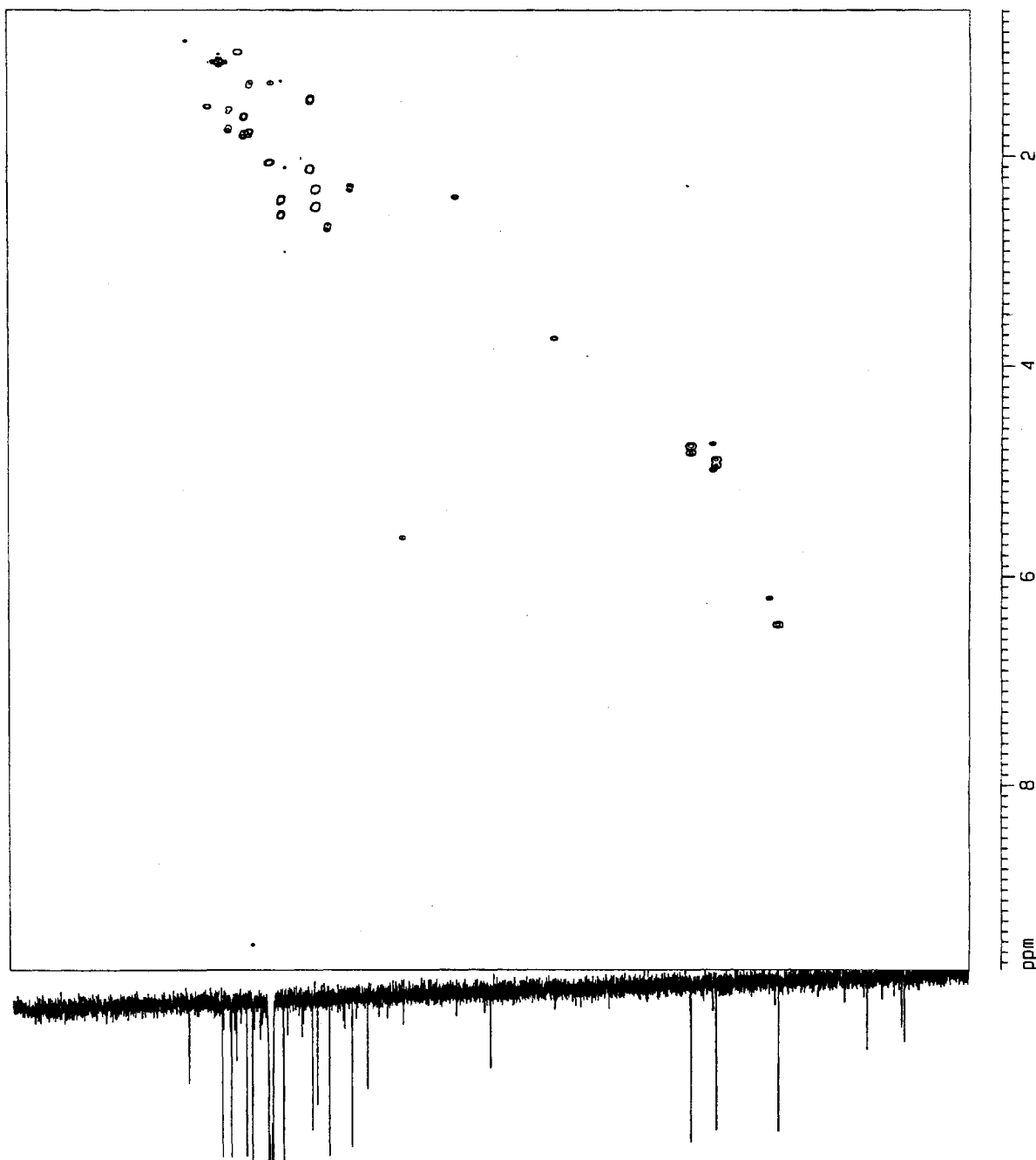
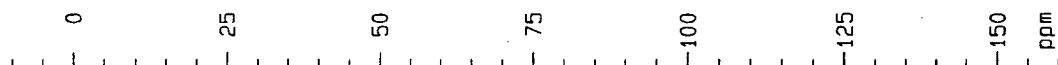
SI	1024
f1 - Processing parameters	

\$1	1024
NC2	TPPI
SF	500.130049 MHz
WOW	OSINE
SSB	2
LB	0.00 Hz
GB	0

20 mm plot parameters

cu nm plot parameters	
CRZ	15.00 cm
CK1	15.00 cm
W2P0	5.887 ppm
FZ0	2644.20 Hz
ZPM	0.405 ppm
ZH	202.31 Hz
F0	5.718 ppm
F00	2059.68 Hz
SPH	0.480 ppm
FHI	275.87 Hz
SPHON	0.30545 ppm/cm
FZ10	182.7362 Hz/cm
SPHON	0.34822 ppm/cm
FZ10N	174.65443 Hz/cm



[illegible]

```

***** CHANNEL 12 *****
CP0402      00P
INC2        13C
P3          8.00 usec
PO02       70.00 usec
PL3        -0.20 dB
PL12       15.51 dB
SF02      125.767498 MHz

```

[illegible]

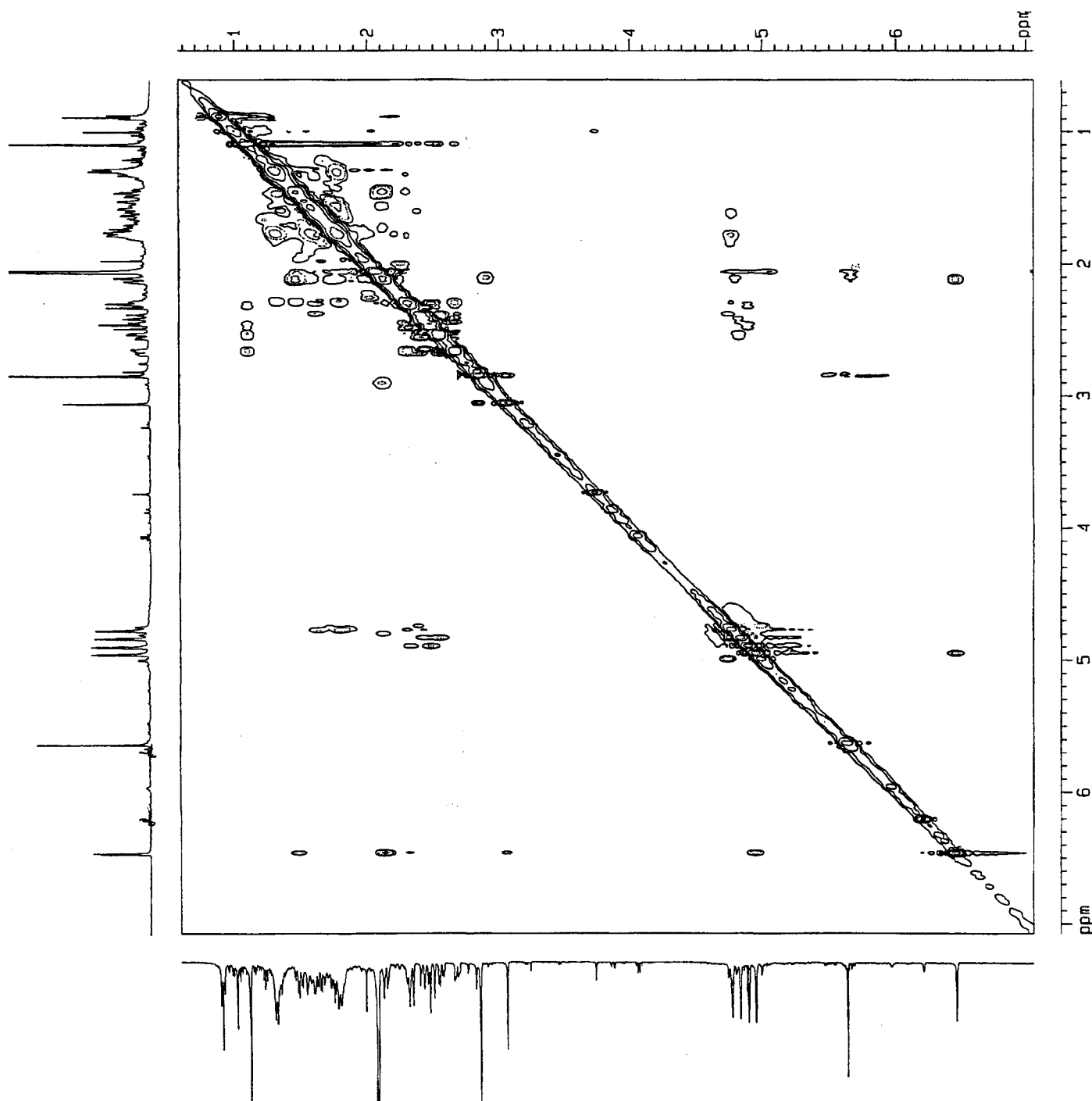
1000	2	
TD	256	
5F01	125.7678 MHz	
10T0RES	88.426712 Hz	
Su	179.992 pipe	

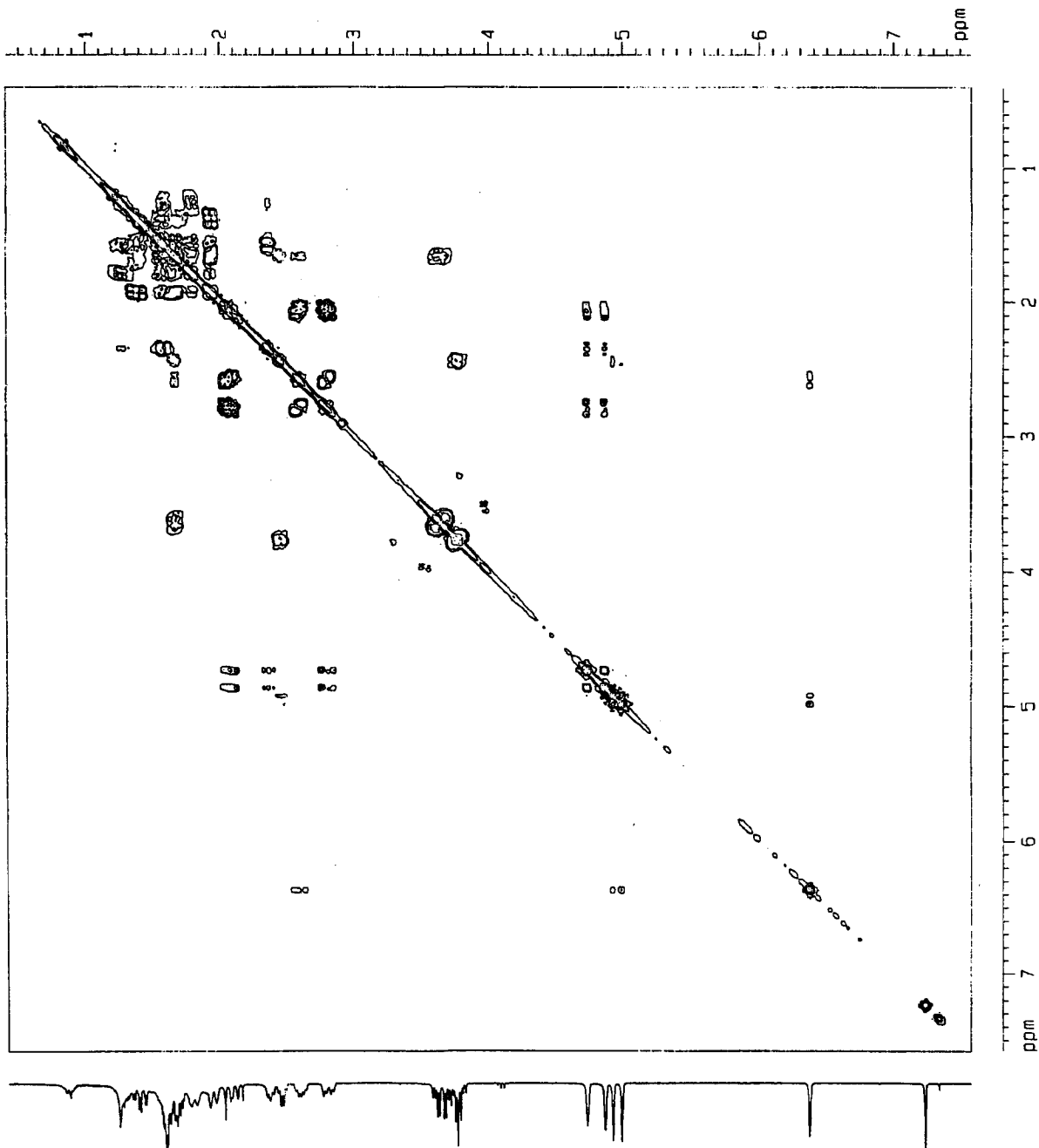
SI	Processing parameters
OF	1024
DOM	500.1300049 MHz
SSB	SINE
LB	0
CB	0.06 Hz
PC	0
	1.00

F1 - Processing parameters	
SI	1024
MC2	OF
PF	125.757854 MHz
MON	SDNC
SSB	D
LB	0.00 MHz
MA	0

[illegible]

Current Data Parameters		F2 - Acquisition Parameters		F1 - Processing Parameters		2D NMR plot parameters	
NAME	VALUE	NAME	VALUE	NAME	VALUE	NAME	VALUE
EXPNO	1	PROCNO	1	MD0	1	CX1	15.00 cm
RG	320.000	RG	320.000	TO	250	CX2	15.00 cm
RGUNIT	Hz	RGUNIT	Hz	FIDRES	500.1250 MHz	LO	15.00 cm
INSTRUM	zgpg30	INSTRUM	zgpg30	NUC1	13C	NUC2	13C
PULPROG	gm	PULPROG	gm	NUC2	13C	PRG1	zgpg30
PRG2	zgpg30	PRG2	zgpg30	NUC3	1H	PRG2	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC4	1H	PRG3	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC5	1H	PRG4	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC6	1H	PRG5	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC7	1H	PRG6	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC8	1H	PRG7	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC9	1H	PRG8	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC10	1H	PRG9	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC11	1H	PRG10	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC12	1H	PRG11	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC13	1H	PRG12	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC14	1H	PRG13	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC15	1H	PRG14	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC16	1H	PRG15	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC17	1H	PRG16	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC18	1H	PRG17	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC19	1H	PRG18	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC20	1H	PRG19	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC21	1H	PRG20	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC22	1H	PRG21	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC23	1H	PRG22	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC24	1H	PRG23	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC25	1H	PRG24	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC26	1H	PRG25	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC27	1H	PRG26	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC28	1H	PRG27	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC29	1H	PRG28	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC30	1H	PRG29	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC31	1H	PRG30	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC32	1H	PRG31	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC33	1H	PRG32	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC34	1H	PRG33	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC35	1H	PRG34	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC36	1H	PRG35	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC37	1H	PRG36	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC38	1H	PRG37	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC39	1H	PRG38	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC40	1H	PRG39	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC41	1H	PRG40	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC42	1H	PRG41	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC43	1H	PRG42	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC44	1H	PRG43	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC45	1H	PRG44	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC46	1H	PRG45	zgpg30
TO SOLVENT	DMSO	TO SOLVENT	DMSO	NUC47	1H	PRG46	zgpg30
TO SOLVENT	DMSO						





NAME	Current Data Parameters
RC_434 (2d)	4

F2 - Acquisition Parameters

Date	2042022	Time	21.34
INSTRUM	AS300	S	0
PROBND	H/I	cost	5000
PULLPROG	cost	5000	5000
TO	1024		
SOLVENT	CDCl3		
NS	1		
OS	0		
SWH	215.172 MHz		
NUC1	13C		
NUC2	13C		
PROBHD	0.273150 mm		
NUC1	13C		
NUC2	13C		
DE	232.000 ussec		
TE	6.00 ussec		
GE	300.0 K		
TO	0.0000300 sec		
OT	1.00000000 sec		
OT1	0.0000400 sec		
OT2	0.0010000 sec		
OT3	0.0300000 sec		
OT4	0.0000000 sec		
OT5	0.0000000 sec		
OT6	0.0000000 sec		
OT7	0.0000000 sec		
OT8	0.0000000 sec		
OT9	0.0000000 sec		
OT10	0.0000000 sec		
OT11	0.0000000 sec		
OT12	0.0000000 sec		
OT13	0.0000000 sec		
OT14	0.0000000 sec		
OT15	0.0000000 sec		
OT16	0.0000000 sec		
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OT18	0.0000000 sec		
OT19	0.0000000 sec		
OT20	0.0000000 sec		
OT21	0.0000000 sec		
OT22	0.0000000 sec		
OT23	0.0000000 sec		
OT24	0.0000000 sec		
OT25	0.0000000 sec		
OT26	0.0000000 sec		
OT27	0.0000000 sec		
OT28	0.0000000 sec		
OT29	0.0000000 sec		
OT30	0.0000000 sec		
OT31	0.0000000 sec		
OT32	0.0000000 sec		
OT33	0.0000000 sec		
OT34	0.0000000 sec		
OT35	0.0000000 sec		
OT36	0.0000000 sec		
OT37	0.0000000 sec		
OT38	0.0000000 sec		
OT39	0.0000000 sec		
OT40	0.0000000 sec		
OT41	0.0000000 sec		
OT42	0.0000000 sec		
OT43	0.0000000 sec		
OT44	0.0000000 sec		
OT45	0.0000000 sec		
OT46	0.0000000 sec		
OT47	0.0000000 sec		
OT48	0.0000000 sec		
OT49	0.0000000 sec		
OT50	0.0000000 sec		
OT51	0.0000000 sec		
OT52	0.0000000 sec		
OT53	0.0000000 sec		
OT54	0.0000000 sec		
OT55	0.0000000 sec		
OT56	0.0000000 sec		
OT57	0.0000000 sec		
OT58	0.0000000 sec		
OT59	0.0000000 sec		
OT60	0.0000000 sec		
OT61	0.0000000 sec		
OT62	0.0000000 sec		
OT63	0.0000000 sec		
OT64	0.0000000 sec		
OT65	0.0000000 sec		
OT66	0.0000000 sec		
OT67	0.0000000 sec		
OT68	0.0000000 sec		
OT69	0.0000000 sec		
OT70	0.0000000 sec		
OT71	0.0000000 sec		
OT72	0.0000000 sec		
OT73	0.0000000 sec		
OT74	0.0000000 sec		
OT75	0.0000000 sec		
OT76	0.0000000 sec		
OT77	0.0000000 sec		
OT78	0.0000000 sec		
OT79	0.0000000 sec		
OT80	0.0000000 sec		
OT81	0.0000000 sec		
OT82	0.0000000 sec		
OT83	0.0000000 sec		
OT84	0.0000000 sec		
OT85	0.0000000 sec		
OT86	0.0000000 sec		
OT87	0.0000000 sec		
OT88	0.0000000 sec		
OT89	0.0000000 sec		
OT90	0.0000000 sec		
OT91	0.0000000 sec		
OT92	0.0000000 sec		
OT93	0.0000000 sec		
OT94	0.0000000 sec		
OT95			

***** CHANNEL 1 *****

IN	OUT
5.25 usec	5.25 usec
10.50 usec	10.50 usec
-3.00 dB	-3.00 dB
300.1311882 MHz	300.1311882 MHz

***** GRADIENT CHANNEL *****

NAME	SIZE	UNIT
BPAN1	100	%
BPAN2	100	%
BPX1	0.00	%
BPX2	0.00	%
BPY1	0.00	%
BPY2	0.00	%
BPZ1	10.00	%
BPZ2	10.00	%
P16	1000.00	usec

5.1 - Acquisition parameters

400	1
TO	256
5F01	300.1312 MHz
FIDRES	0.410642 Hz
SM	7.181 ppm

F2 - Processing parameters

SI	1024
SF	300.1300000 MHz
MOD	SINE
FSR	0
GB	0.00 MHz
PC	0
	1.00

F1 - Progression assessment

SI	1024
MC2	OF
SF	300.130000 MHz
MOD	SINE
LSB	0
CS	0.00 Hz

10-10-68

[illegible]

1H NOESY

Current Data Parameters

NAME: PC_01_24

EXPNO: 1

PROCNO: 1

PRG: nmr

DATE_: 04.12

TIME: 09.30

PROBHD: 5 mm BBO 1H/1

NUC1: 1H

NUC2: 13C

NUC3: 15N

PC: 0.000000

PC2: 0.000000

PC3: 0.000000

PC4: 0.000000

PC5: 0.000000

PC6: 0.000000

PC7: 0.000000

PC8: 0.000000

PC9: 0.000000

PC10: 0.000000

PC11: 0.000000

PC12: 0.000000

PC13: 0.000000

PC14: 0.000000

PC15: 0.000000

PC16: 0.000000

PC17: 0.000000

PC18: 0.000000

PC19: 0.000000

PC20: 0.000000

PC21: 0.000000

PC22: 0.000000

PC23: 0.000000

PC24: 0.000000

PC25: 0.000000

PC26: 0.000000

PC27: 0.000000

PC28: 0.000000

PC29: 0.000000

PC30: 0.000000

PC31: 0.000000

PC32: 0.000000

PC33: 0.000000

PC34: 0.000000

PC35: 0.000000

PC36: 0.000000

PC37: 0.000000

PC38: 0.000000

PC39: 0.000000

PC40: 0.000000

PC41: 0.000000

PC42: 0.000000

PC43: 0.000000

PC44: 0.000000

PC45: 0.000000

PC46: 0.000000

PC47: 0.000000

PC48: 0.000000

PC49: 0.000000

PC50: 0.000000

PC51: 0.000000

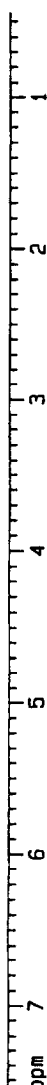
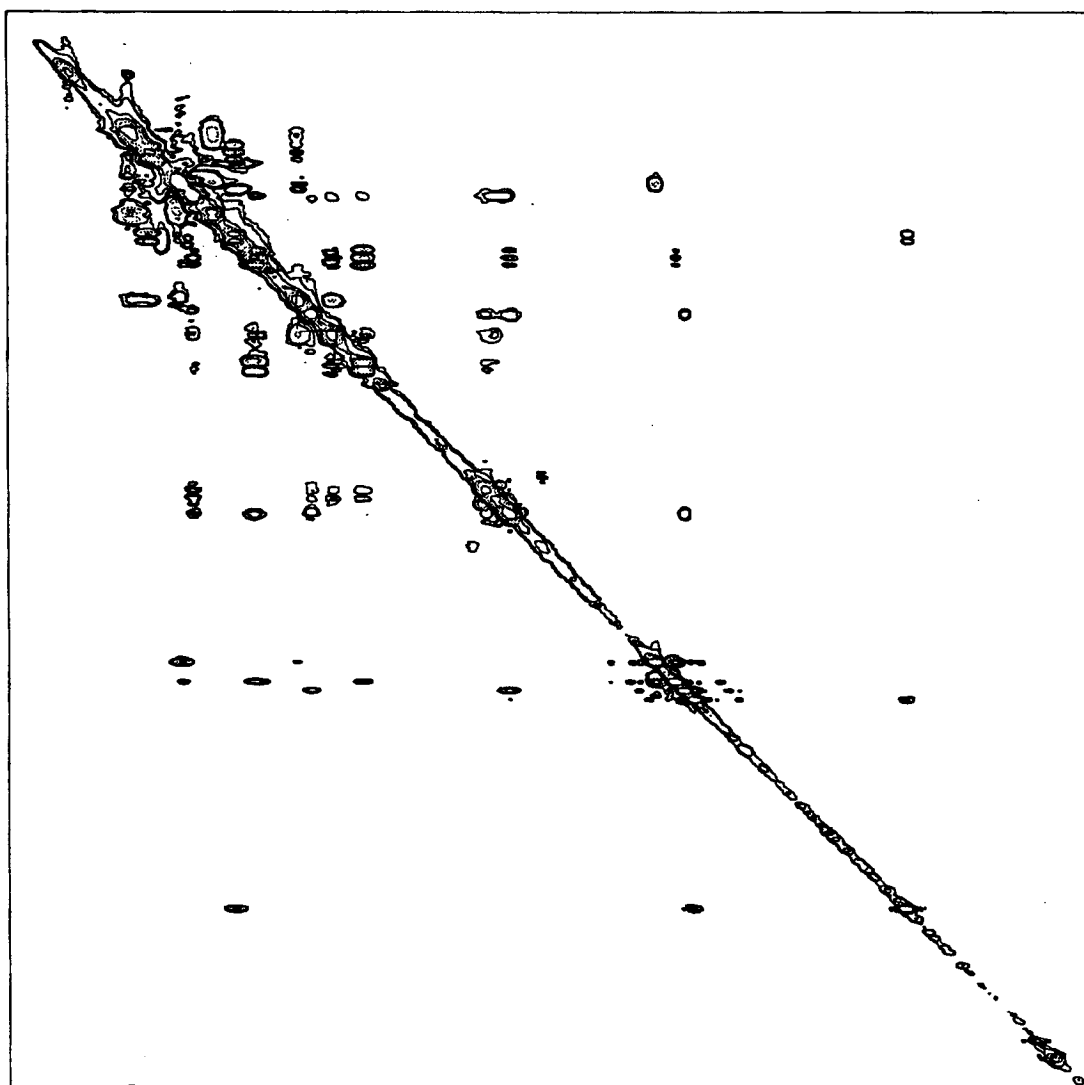
PC52: 0.000000

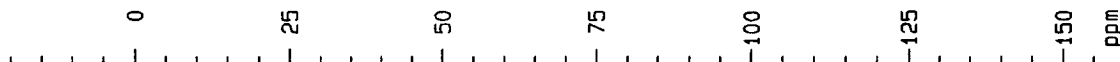
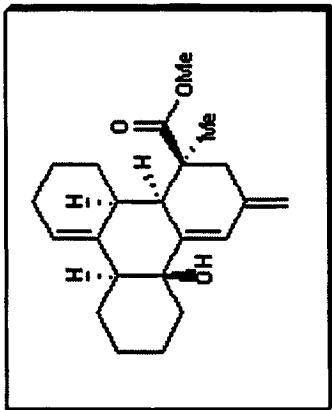
PC53: 0.000000

PC54: 0.000000

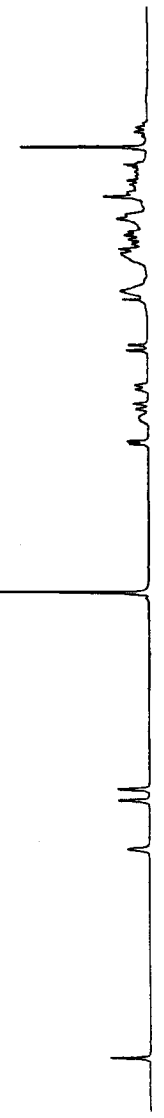
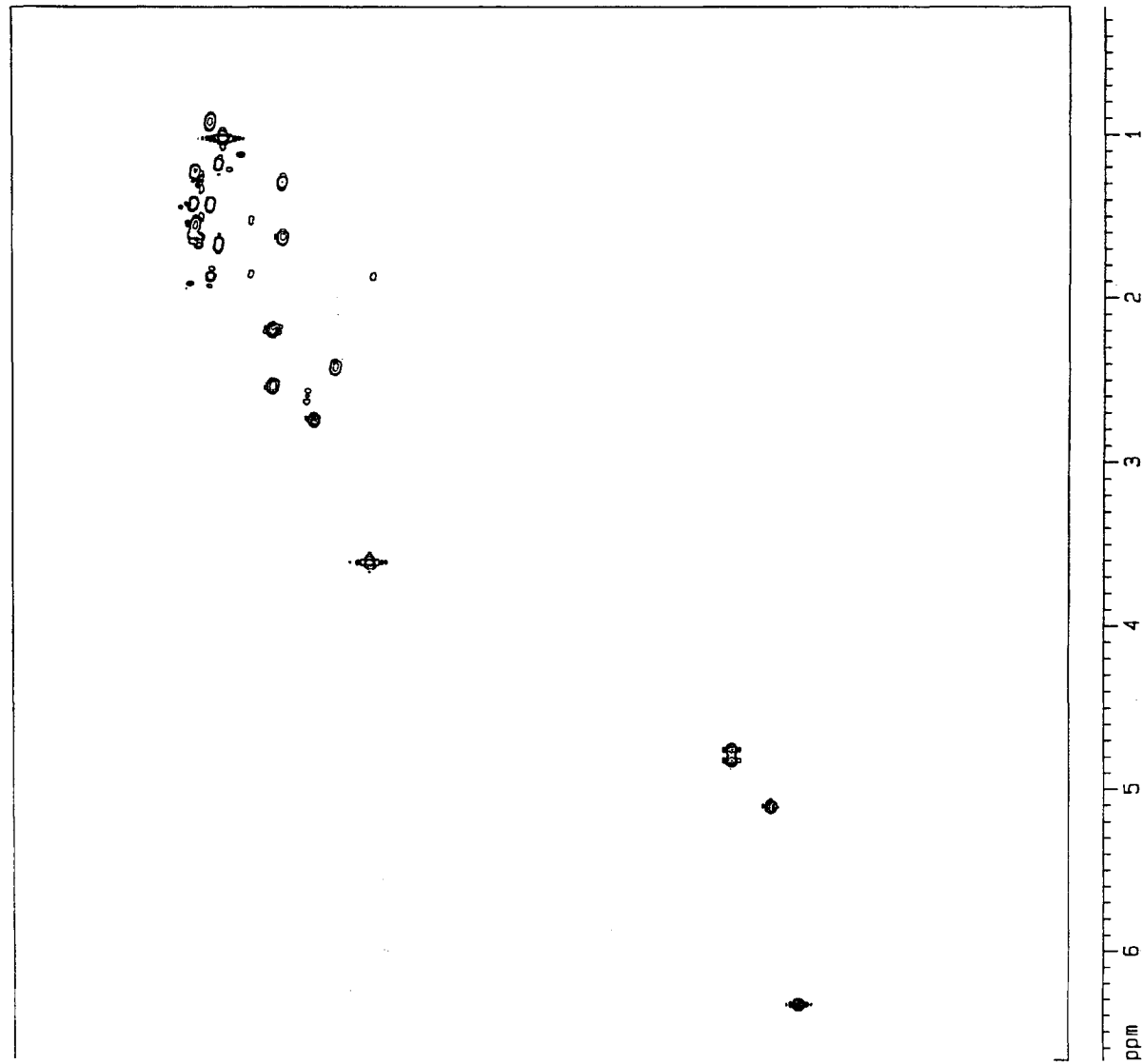
PC55: 0.000000

PC56: 0.000000





NAME	3729.574 Hz
FMRES	3.154672 Hz
NUC1	13C
NUC2	13C
NUC3	13C
NUC4	13C
NUC5	13C
NUC6	13C
NUC7	13C
NUC8	13C
NUC9	13C
NUC10	13C
NUC11	13C
NUC12	13C
NUC13	13C
NUC14	13C
NUC15	13C
NUC16	13C
NUC17	13C
NUC18	13C
NUC19	13C
NUC20	13C
NUC21	13C
NUC22	13C
NUC23	13C
NUC24	13C
NUC25	13C
NUC26	13C
NUC27	13C
NUC28	13C
NUC29	13C
NUC30	13C
NUC31	13C
NUC32	13C
NUC33	13C
NUC34	13C
NUC35	13C
NUC36	13C
NUC37	13C
NUC38	13C
NUC39	13C
NUC40	13C
NUC41	13C
NUC42	13C
NUC43	13C
NUC44	13C
NUC45	13C
NUC46	13C
NUC47	13C
NUC48	13C
NUC49	13C
NUC50	13C
NUC51	13C
NUC52	13C
NUC53	13C
NUC54	13C
NUC55	13C
NUC56	13C
NUC57	13C
NUC58	13C
NUC59	13C
NUC60	13C
NUC61	13C
NUC62	13C
NUC63	13C
NUC64	13C
NUC65	13C
NUC66	13C
NUC67	13C
NUC68	13C
NUC69	13C
NUC70	13C
NUC71	13C
NUC72	13C
NUC73	13C
NUC74	13C
NUC75	13C
NUC76	13C
NUC77	13C
NUC78	13C
NUC79	13C
NUC80	13C
NUC81	13C
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NUC83	13C
NUC84	13C
NUC85	13C
NUC86	13C
NUC87	13C
NUC88	13C
NUC89	13C
NUC90	13C
NUC91	13C
NUC92	13C
NUC93	13C
NUC94	13C
NUC95	13C
NUC96	13C
NUC97	13C
NUC98	13C
NUC99	13C
NUC100	13C



1H NOESY/EXSY

Current Data Parameters
NAME rc_784
EXPNO 4
PROCNO 1

F2 - Acquisition Parameters

Date_ 20040829
Time 0.27

INSTRUM APT500006
PROBHD 5 mm BBO/1H

PULPROG zgpg30
TD 131074

TO SOLVENT CDCl3
NS 40

DS 2
SWH 3180.662 Hz

FIDRES 3.106115 Hz
AQ 0.161026 sec

RG 64
DM 157.200 umsec

DE 6.00 umsec
TE 300.0 K

1E 0.0000300 sec
d0 0.0000000 sec

d1 1.0000000 sec
d8 0.0000000 sec

d16 0.0000000 sec
d18 0.0000000 sec

1M 0.0031440 sec
NOESPT 0.0000000 sec

NOESF 1.0000000 sec
MCHRG 1.0000000 sec

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

NUC1 1H

P1 14.00 umsec

P2 28.00 umsec

P4 0.00 dB

SFO1 500.1313655 MHz

***** GRADIENT CHANNEL *****

GRAM1 SINE100

GRAM2 SINE100

GPV1 0.00 X

GPV2 0.00 X

GPV3 0.00 X

GPV4 0.00 X

GPV5 0.00 X

GPV6 0.00 X

GPV7 0.00 X

GPV8 0.00 X

GPV9 0.00 X

GPV10 0.00 X

GPV11 0.00 X

GPV12 0.00 X

GPV13 0.00 X

GPV14 0.00 X

GPV15 0.00 X

GPV16 0.00 X

GPV17 0.00 X

GPV18 0.00 X

GPV19 0.00 X

GPV20 0.00 X

GPV21 0.00 X

GPV22 0.00 X

GPV23 0.00 X

GPV24 0.00 X

GPV25 0.00 X

GPV26 0.00 X

GPV27 0.00 X

GPV28 0.00 X

GPV29 0.00 X

GPV30 0.00 X

GPV31 0.00 X

GPV32 0.00 X

GPV33 0.00 X

GPV34 0.00 X

GPV35 0.00 X

GPV36 0.00 X

GPV37 0.00 X

GPV38 0.00 X

GPV39 0.00 X

GPV40 0.00 X

GPV41 0.00 X

GPV42 0.00 X

GPV43 0.00 X

GPV44 0.00 X

GPV45 0.00 X

GPV46 0.00 X

GPV47 0.00 X

GPV48 0.00 X

GPV49 0.00 X

GPV50 0.00 X

GPV51 0.00 X

GPV52 0.00 X

GPV53 0.00 X

GPV54 0.00 X

GPV55 0.00 X

GPV56 0.00 X

GPV57 0.00 X

GPV58 0.00 X

GPV59 0.00 X

GPV60 0.00 X

GPV61 0.00 X

GPV62 0.00 X

GPV63 0.00 X

GPV64 0.00 X

GPV65 0.00 X

GPV66 0.00 X

GPV67 0.00 X

GPV68 0.00 X

GPV69 0.00 X

GPV70 0.00 X

GPV71 0.00 X

GPV72 0.00 X

GPV73 0.00 X

GPV74 0.00 X

GPV75 0.00 X

GPV76 0.00 X

GPV77 0.00 X

GPV78 0.00 X

GPV79 0.00 X

GPV80 0.00 X

GPV81 0.00 X

GPV82 0.00 X

GPV83 0.00 X

GPV84 0.00 X

GPV85 0.00 X

GPV86 0.00 X

GPV87 0.00 X

GPV88 0.00 X

GPV89 0.00 X

GPV90 0.00 X

GPV91 0.00 X

GPV92 0.00 X

GPV93 0.00 X

GPV94 0.00 X

GPV95 0.00 X

GPV96 0.00 X

GPV97 0.00 X

GPV98 0.00 X

GPV99 0.00 X

GPV100 0.00 X

GPV101 0.00 X

GPV102 0.00 X

GPV103 0.00 X

GPV104 0.00 X

GPV105 0.00 X

GPV106 0.00 X

GPV107 0.00 X

GPV108 0.00 X

GPV109 0.00 X

GPV110 0.00 X

GPV111 0.00 X

GPV112 0.00 X

GPV113 0.00 X

GPV114 0.00 X

GPV115 0.00 X

GPV116 0.00 X

GPV117 0.00 X

GPV118 0.00 X

GPV119 0.00 X

GPV120 0.00 X

GPV121 0.00 X

GPV122 0.00 X

GPV123 0.00 X

GPV124 0.00 X

GPV125 0.00 X

GPV126 0.00 X

GPV127 0.00 X

GPV128 0.00 X

GPV129 0.00 X

GPV130 0.00 X

GPV131 0.00 X

GPV132 0.00 X

GPV133 0.00 X

GPV134 0.00 X

GPV135 0.00 X

GPV136 0.00 X

GPV137 0.00 X

GPV138 0.00 X

GPV139 0.00 X

GPV140 0.00 X

GPV141 0.00 X

GPV142 0.00 X

GPV143 0.00 X

GPV144 0.00 X

GPV145 0.00 X

GPV146 0.00 X

GPV147 0.00 X

GPV148 0.00 X

GPV149 0.00 X

GPV150 0.00 X

GPV151 0.00 X

GPV152 0.00 X

GPV153 0.00 X

GPV154 0.00 X

GPV155 0.00 X

GPV156 0.00 X

GPV157 0.00 X

GPV158 0.00 X

GPV159 0.00 X

GPV160 0.00 X

GPV161 0.00 X

GPV162 0.00 X

GPV163 0.00 X

GPV164 0.00 X

GPV165 0.00 X

GPV166 0.00 X

GPV167 0.00 X

GPV168 0.00 X

GPV169 0.00 X

GPV170 0.00 X

GPV171 0.00 X

GPV172 0.00 X

GPV173 0.00 X

GPV174 0.00 X

GPV175 0.00 X

GPV176 0.00 X

GPV177 0.00 X

GPV178 0.00 X

GPV179 0.00 X

GPV180 0.00 X

GPV181 0.00 X

GPV182 0.00 X

GPV183 0.00 X

GPV184 0.00 X

GPV185 0.00 X

GPV186 0.00 X

GPV187 0.00 X

GPV188 0.00 X

GPV189 0.00 X

GPV190 0.00 X

GPV191 0.00 X

GPV192 0.00 X

GPV193 0.00 X

GPV194 0.00 X

GPV195 0.00 X

GPV196 0.00 X

GPV197 0.00 X

GPV198 0.00 X

GPV199 0.00 X

GPV200 0.00 X

GPV201 0.00 X

GPV202 0.00 X

GPV203 0.00 X

GPV204 0.00 X

GPV205 0.00 X

GPV206 0.00 X

GPV207 0.00 X

GPV208 0.00 X

GPV209 0.00 X

GPV210 0.00 X

GPV211 0.00 X

GPV212 0.00 X

GPV213 0.00 X

GPV214 0.00 X

GPV215 0.00 X

GPV216 0.00 X

GPV217 0.00 X

GPV218 0.00 X

GPV219 0.00 X

GPV220 0.00 X

GPV221 0.00 X

GPV222 0.00 X

GPV223 0.00 X

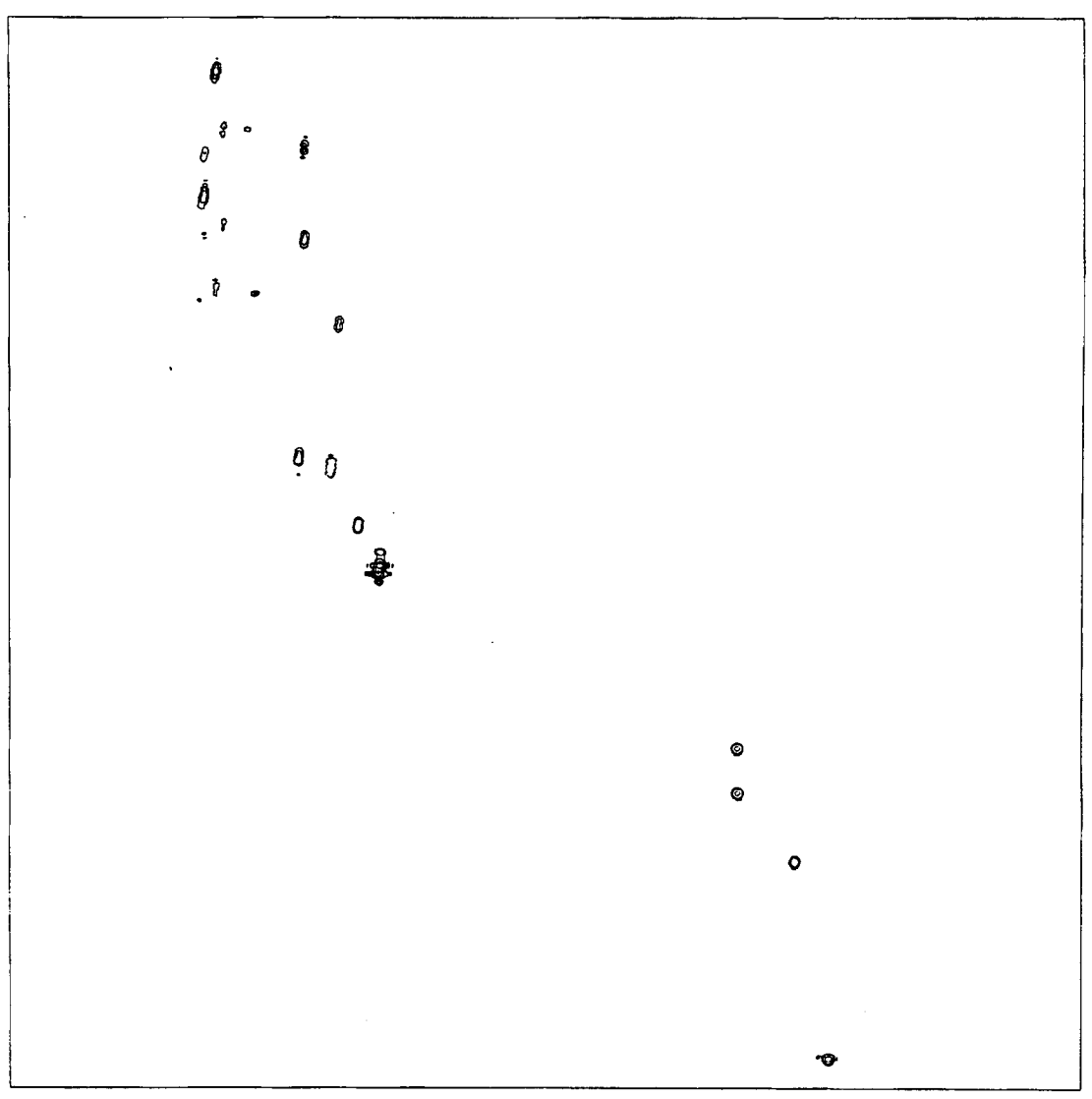
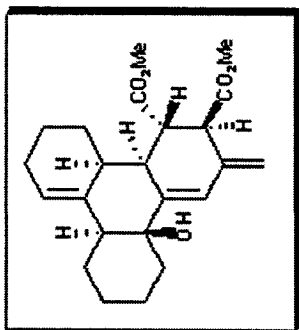
GPV224 0.00 X

GPV225 0.00 X

GPV226 0.00 X

GPV227 0.00 X

GPV228 0.00 X



NAME: C013
 SOLVENT: DMSO
 INSTR: 500
 FIDRES: 1.774276 Hz
 A2: 0.2018548 sec
 PC: 1.0014
 DE: 275.00 sec
 TE: 300.0 K
 DMSO2: 145.000000 sec
 D1: 1.00000000 sec
 D2: 0.03348000 sec
 D3: 0.00000000 sec
 D4: 0.00000000 sec
 D5: 0.00100000 sec
 D6: 0.00200000 sec
 D7: 0.00300000 sec
 D8: 0.00400000 sec
 D9: 0.00500000 sec
 D10: 0.00600000 sec
 D11: 0.00700000 sec
 D12: 0.00800000 sec
 D13: 0.00900000 sec
 D14: 0.01000000 sec
 D15: 0.01100000 sec
 D16: 0.01200000 sec
 D17: 0.01300000 sec
 D18: 0.01400000 sec
 D19: 0.01500000 sec
 D20: 0.01600000 sec
 D21: 0.01700000 sec
 D22: 0.01800000 sec
 D23: 0.01900000 sec
 D24: 0.02000000 sec
 D25: 0.02100000 sec
 D26: 0.02200000 sec
 D27: 0.02300000 sec
 D28: 0.02400000 sec
 D29: 0.02500000 sec
 D30: 0.02600000 sec
 D31: 0.02700000 sec
 D32: 0.02800000 sec
 D33: 0.02900000 sec
 D34: 0.03000000 sec
 D35: 0.03100000 sec
 D36: 0.03200000 sec
 D37: 0.03300000 sec
 D38: 0.03400000 sec
 D39: 0.03500000 sec
 D40: 0.03600000 sec
 D41: 0.03700000 sec
 D42: 0.03800000 sec
 D43: 0.03900000 sec
 D44: 0.04000000 sec
 D45: 0.04100000 sec
 D46: 0.04200000 sec
 D47: 0.04300000 sec
 D48: 0.04400000 sec
 D49: 0.04500000 sec
 D50: 0.04600000 sec
 D51: 0.04700000 sec
 D52: 0.04800000 sec
 D53: 0.04900000 sec
 D54: 0.05000000 sec
 D55: 0.05100000 sec
 D56: 0.05200000 sec
 D57: 0.05300000 sec
 D58: 0.05400000 sec
 D59: 0.05500000 sec
 D60: 0.05600000 sec
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 D64: 0.06000000 sec
 D65: 0.06100000 sec
 D66: 0.06200000 sec
 D67: 0.06300000 sec
 D68: 0.06400000 sec
 D69: 0.06500000 sec
 D70: 0.06600000 sec
 D71: 0.06700000 sec
 D72: 0.06800000 sec
 D73: 0.06900000 sec
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 D75: 0.07100000 sec
 D76: 0.07200000 sec
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 D78: 0.07400000 sec
 D79: 0.07500000 sec
 D80: 0.07600000 sec
 D81: 0.07700000 sec
 D82: 0.07800000 sec
 D83: 0.07900000 sec
 D84: 0.08000000 sec
 D85: 0.08100000 sec
 D86: 0.08200000 sec
 D87: 0.08300000 sec
 D88: 0.08400000 sec
 D89: 0.08500000 sec
 D90: 0.08600000 sec
 D91: 0.08700000 sec
 D92: 0.08800000 sec
 D93: 0.08900000 sec
 D94: 0.09000000 sec
 D95: 0.09100000 sec
 D96: 0.09200000 sec
 D97: 0.09300000 sec
 D98: 0.09400000 sec
 D99: 0.09500000 sec
 D100: 0.09600000 sec
 D101: 0.09700000 sec
 D102: 0.09800000 sec
 D103: 0.09900000 sec
 D104: 0.10000000 sec
 D105: 0.10100000 sec
 D106: 0.10200000 sec
 D107: 0.10300000 sec
 D108: 0.10400000 sec
 D109: 0.10500000 sec
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 D123: 0.11900000 sec
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 D125: 0.12100000 sec
 D126: 0.12200000 sec
 D127: 0.12300000 sec
 D128: 0.12400000 sec
 D129: 0.12500000 sec
 D130: 0.12600000 sec
 D131: 0.12700000 sec
 D132: 0.12800000 sec
 D133: 0.12900000 sec
 D134: 0.13000000 sec
 D135: 0.13100000 sec
 D136: 0.13200000 sec
 D137: 0.13300000 sec
 D138: 0.13400000 sec
 D139: 0.13500000 sec
 D140: 0.13600000 sec
 D141: 0.13700000 sec
 D142: 0.13800000 sec
 D143: 0.13900000 sec
 D144: 0.14000000 sec
 D145: 0.14100000 sec
 D146: 0.14200000 sec
 D147: 0.14300000 sec
 D148: 0.14400000 sec
 D149: 0.14500000 sec
 D150: 0.14600000 sec
 D151: 0.14700000 sec
 D152: 0.14800000 sec
 D153: 0.14900000 sec
 D154: 0.15000000 sec
 D155: 0.15100000 sec
 D156: 0.15200000 sec
 D157: 0.15300000 sec
 D158: 0.15400000 sec
 D159: 0.15500000 sec
 D160: 0.15600000 sec
 D161: 0.15700000 sec
 D162: 0.15800000 sec
 D163: 0.15900000 sec
 D164: 0.16000000 sec
 D165: 0.16100000 sec
 D166: 0.16200000 sec
 D167: 0.16300000 sec
 D168: 0.16400000 sec
 D169: 0.16500000 sec
 D170: 0.16600000 sec
 D171: 0.16700000 sec
 D172: 0.16800000 sec
 D173: 0.16900000 sec
 D174: 0.17000000 sec
 D175: 0.17100000 sec
 D176: 0.17200000 sec
 D177: 0.17300000 sec
 D178: 0.17400000 sec
 D179: 0.17500000 sec
 D180: 0.17600000 sec
 D181: 0.17700000 sec
 D182: 0.17800000 sec
 D183: 0.17900000 sec
 D184: 0.18000000 sec
 D185: 0.18100000 sec
 D186: 0.18200000 sec
 D187: 0.18300000 sec
 D188: 0.18400000 sec
 D189: 0.18500000 sec
 D190: 0.18600000 sec
 D191: 0.18700000 sec
 D192: 0.18800000 sec
 D193: 0.18900000 sec
 D194: 0.19000000 sec
 D195: 0.19100000 sec
 D196: 0.19200000 sec
 D197: 0.19300000 sec
 D198: 0.19400000 sec
 D199: 0.19500000 sec
 D200: 0.19600000 sec
 D201: 0.19700000 sec
 D202: 0.19800000 sec
 D203: 0.19900000 sec
 D204: 0.20000000 sec
 D205: 0.20100000 sec
 D206: 0.20200000 sec
 D207: 0.20300000 sec
 D208: 0.20400000 sec
 D209: 0.20500000 sec
 D210: 0.20600000 sec
 D211: 0.20700000 sec
 D212: 0.20800000 sec
 D213: 0.20900000 sec
 D214: 0.21000000 sec
 D215: 0.21100000 sec
 D216: 0.21200000 sec
 D217: 0.21300000 sec
 D218: 0.21400000 sec
 D219: 0.21500000 sec
 D220: 0.21600000 sec
 D221: 0.21700000 sec
 D222: 0.21800000 sec
 D223: 0.21900000 sec
 D224: 0.22000000 sec
 D225: 0.22100000 sec
 D226: 0.22200000 sec
 D227: 0.22300000 sec
 D228: 0.22400000 sec
 D229: 0.22500000 sec
 D230: 0.22600000 sec
 D231: 0.22700000 sec
 D232: 0.22800000 sec
 D233: 0.22900000 sec
 D234: 0.23000000 sec
 D235: 0.23100000 sec
 D236: 0.23200000 sec
 D237: 0.23300000 sec
 D238: 0.23400000 sec
 D239: 0.23500000 sec
 D240: 0.23600000 sec
 D241: 0.23700000 sec
 D242: 0.23800000 sec
 D243: 0.23900000 sec
 D244: 0.24000000 sec
 D245: 0.24100000 sec
 D246: 0.24200000 sec
 D247: 0.24300000 sec
 D248: 0.24400000 sec
 D249: 0.24500000 sec
 D250: 0.24600000 sec
 D251: 0.24700000 sec
 D252: 0.24800000 sec
 D253: 0.24900000 sec
 D254: 0.25000000 sec
 D255: 0.25100000 sec
 D256: 0.25200000 sec
 D257: 0.25300000 sec
 D258: 0.25400000 sec
 D259: 0.25500000 sec
 D260: 0.25600000 sec
 D261: 0.25700000 sec
 D262: 0.25800000 sec
 D263: 0.25900000 sec
 D264: 0.26000000 sec
 D265: 0.26100000 sec
 D266: 0.26200000 sec
 D267: 0.26300000 sec
 D268: 0.26400000 sec
 D269: 0.26500000 sec
 D270: 0.26600000 sec
 D271: 0.26700000 sec
 D272: 0.26800000 sec
 D273: 0.26900000 sec
 D274: 0.27000000 sec
 D275: 0.27100000 sec
 D276: 0.27200000 sec
 D277: 0.27300000 sec
 D278: 0.27400000 sec
 D279: 0.27500000 sec
 D280: 0.27600000 sec
 D281: 0.27700000 sec
 D282: 0.27800000 sec
 D283: 0.27900000 sec
 D284: 0.28000000 sec
 D285: 0.28100000 sec
 D286: 0.28200000 sec
 D287: 0.28300000 sec
 D288: 0.28400000 sec
 D289: 0.28500000 sec
 D290: 0.28600000 sec
 D291: 0.28700000 sec
 D292: 0.28800000 sec
 D293: 0.28900000 sec
 D294: 0.29000000 sec
 D295: 0.29100000 sec
 D296: 0.29200000 sec
 D297: 0.29300000 sec
 D298: 0.29400000 sec
 D299: 0.29500000 sec
 D300: 0.29600000 sec
 D301: 0.29700000 sec
 D302: 0.29800000 sec
 D303: 0.29900000 sec
 D304: 0.30000000 sec
 D305: 0.30100000 sec
 D306: 0.30200000 sec
 D307: 0.30300000 sec
 D308: 0.30400000 sec
 D309: 0.30500000 sec
 D310: 0.30600000 sec
 D311: 0.30700000 sec
 D312: 0.30800000 sec
 D313: 0.30900000 sec
 D314: 0.31000000 sec
 D315: 0.31100000 sec
 D316: 0.31200000 sec
 D317: 0.31300000 sec
 D318: 0.31400000 sec
 D319: 0.31500000 sec
 D320: 0.31600000 sec
 D321: 0.31700000 sec
 D322: 0.31800000 sec
 D323: 0.31900000 sec
 D324: 0.32000000 sec
 D325: 0.32100000 sec
 D326: 0.32200000 sec
 D327: 0.32300000 sec
 D328: 0.32400000 sec
 D329: 0.32500000 sec
 D330: 0.32600000 sec
 D331: 0.32700000 sec
 D332: 0.32800000 sec
 D333: 0.32900000 sec
 D334: 0.33000000 sec
 D335: 0.33100000 sec
 D336: 0.33200000 sec
 D337: 0.33300000 sec
 D338: 0.33400000 sec
 D339: 0.33500000 sec
 D340: 0.33600000 sec
 D341: 0.33700000 sec
 D342: 0.33800000 sec
 D343: 0.33900000 sec
 D344: 0.34000000 sec
 D345: 0.34100000 sec
 D346: 0.34200000 sec
 D347: 0.34300000 sec
 D348: 0.34400000 sec
 D349: 0.34500000 sec
 D350: 0.34600000 sec
 D351: 0.34700000 sec
 D352: 0.34800000 sec
 D353: 0.34900000 sec
 D354: 0.35000000 sec
 D355: 0.35100000 sec
 D356: 0.35200000 sec
 D357: 0.35300000 sec
 D358: 0.35400000 sec
 D359: 0.35500000 sec
 D360: 0.35600000 sec
 D361: 0.35700000 sec
 D362: 0.35800000 sec
 D363: 0.35900000 sec
 D364: 0.36000000 sec
 D365: 0.36100000 sec
 D366: 0.36200000 sec
 D367: 0.36300000 sec
 D368: 0.36400000 sec
 D369: 0.36500000 sec
 D370: 0.36600000 sec
 D371: 0.36700000 sec
 D372: 0.36800000 sec
 D373: 0.36900000 sec
 D374: 0.37000000 sec
 D375: 0.37100000 sec
 D376: 0.37200000 sec
 D377: 0.37300000 sec
 D378: 0.37400000 sec
 D379: 0.37500000 sec
 D380: 0.37600000 sec
 D381: 0.37700000 sec
 D382: 0.37800000 sec
 D383: 0.37900000 sec
 D384: 0.38000000 sec
 D385: 0.38100000 sec
 D386: 0.38200000 sec
 D387: 0.38300000 sec
 D388: 0.38400000 sec
 D389: 0.38500000 sec
 D390: 0.38600000 sec
 D391: 0.38700000 sec
 D392: 0.38800000 sec
 D393: 0.38900000 sec
 D394: 0.39000000 sec
 D395: 0.39100000 sec
 D396: 0.39200000 sec
 D397: 0.39300000 sec
 D398: 0.39400000 sec
 D399: 0.39500000 sec
 D400: 0.39600000 sec
 D401: 0.39700000 sec
 D402: 0.39800000 sec
 D403: 0.39900000 sec
 D404: 0.40000000 sec
 D405: 0.40100000 sec
 D406: 0.40200000 sec
 D407: 0.40300000 sec
 D408: 0.40400000 sec
 D409: 0.40500000 sec
 D410: 0.40600000 sec
 D411: 0.40700000 sec
 D412: 0.40800000 sec
 D413: 0.40900000 sec
 D414: 0.41000000 sec
 D415: 0.41100000 sec
 D416: 0.41200000 sec
 D417: 0.41300000 sec
 D418: 0.41400000 sec
 D419: 0.41500000 sec
 D420: 0.41600000 sec
 D421: 0.41700000 sec
 D422: 0.41800000 sec
 D423: 0.41900000 sec
 D424: 0.42000000 sec
 D425: 0.42100000 sec
 D426: 0.42200000 sec
 D427: 0.42300000 sec
 D428: 0.42400000 sec
 D429: 0.42500000 sec
 D430: 0.42600000 sec
 D431: 0.42700000 sec
 D432: 0.42800000 sec
 D433: 0.42900000 sec
 D434: 0.43000000 sec
 D435: 0.43100000 sec
 D436: 0.43200000 sec
 D437: 0.43300000 sec
 D438: 0.43400000 sec
 D439: 0.43500000 sec
 D440: 0.43600000 sec
 D441: 0.43700000 sec
 D442: 0.43800000 sec
 D443: 0.43900000 sec
 D444: 0.44000000 sec
 D445: 0.44100000 sec
 D446: 0.44200000 sec
 D447: 0.44300000 sec
 D448: 0.44400000 sec
 D449: 0.44500000 sec
 D450: 0.44600000 sec
 D451: 0.44700000 sec
 D452: 0.44800000 sec
 D453: 0.44900000 sec
 D454: 0.45000000 sec
 D455: 0.45100000 sec
 D456: 0.45200000 sec
 D457: 0.45300000 sec
 D458: 0.45400000 sec
 D459: 0.45500000 sec
 D460: 0.45600000 sec
 D461: 0.45700000 sec
 D462: 0.45800000 sec
 D463: 0.45900000 sec
 D464: 0.46000000 sec
 D465: 0.46100000 sec
 D466: 0.46200000 sec
 D467: 0.46300000 sec
 D468: 0.46400000 sec
 D469: 0.46500000 sec
 D470: 0.46600000 sec
 D471: 0.46700000 sec
 D472: 0.46800000 sec
 D473: 0.46900000 sec
 D474: 0.47000000 sec
 D475: 0.47100000 sec
 D476: 0.47200000 sec
 D477: 0.47300000 sec
 D478: 0.47400000 sec
 D479: 0.47500000 sec
 D480: 0.47600000 sec
 D481: 0.47700000 sec
 D482: 0.47800000 sec
 D483: 0.47900000 sec
 D484: 0.48000000 sec
 D485: 0.48100000 sec
 D486: 0.48200000 sec
 D487: 0.48300000 sec
 D488: 0.48400000 sec
 D489: 0.48500000 sec
 D490: 0.48600000 sec
 D491: 0.48700000 sec
 D492: 0.48800000 sec
 D493: 0.48900000 sec
 D494: 0.49000000 sec
 D495: 0.49100000 sec
 D496: 0.49200000 sec
 D497: 0.49300000 sec
 D498: 0.49400000 sec
 D499: 0.49500000 sec
 D500: 0.49600000 sec
 D501: 0.49700000 sec
 D502: 0.49800000 sec
 D503: 0.49900000 sec
 D504: 0.50000000 sec
 D505: 0.50100000 sec
 D506: 0.50200000 sec
 D507: 0.50300000 sec
 D508: 0.50400000 sec
 D509: 0.50500000 sec
 D510: 0.50600000 sec
 D511: 0.50700000 sec
 D512: 0.50800000 sec
 D513: 0.50900000 sec
 D514: 0.51000000 sec
 D515: 0.51100000 sec
 D516: 0.51200000 sec
 D517: 0.51300000 sec
 D518: 0.51400000 sec
 D519: 0.51500000 sec
 D520: 0.51600000 sec
 D521: 0.51700000 sec
 D522: 0.51800000 sec
 D523: 0.51900000 sec
 D524: 0.52000000 sec
 D525: 0.52100000 sec
 D526: 0.52200000 sec
 D527: 0.52300000 sec
 D528: 0.52400000 sec
 D529: 0.52500000 sec
 D530: 0.52600000 sec
 D531: 0.52700000 sec
 D532: 0.52800000 sec
 D533: 0.52900000 sec
 D534: 0.53000000 sec
 D535: 0.53100000 sec
 D536: 0.53200000 sec
 D537: 0.53300000 sec
 D538: 0.53400000 sec
 D539: 0.53500000 sec
 D540: 0.53600000 sec
 D541: 0.53700000 sec
 D542: 0.53800000 sec
 D543: 0.53900000 sec
 D544: 0.54000000 sec
 D545: 0.54100000 sec
 D546: 0.54200000 sec
 D547: 0.54300000 sec
 D548: 0.54400000 sec
 D549: 0.54500000 sec
 D550: 0.54600000 sec
 D551: 0.54700000 sec
 D552: 0.54800000 sec
 D553: 0.54900000 sec
 D554: 0.55000000 sec
 D555: 0.55100000 sec
 D556: 0.55200000 sec
 D557: 0.55300000 sec
 D558: 0.55400000 sec
 D559: 0.55500000 sec
 D560: 0.55600000 sec
 D561: 0.55700000 sec
 D562: 0.55800000 sec
 D563: 0.55900000 sec
 D564: 0.56000000 sec
 D565: 0.56100000 sec
 D566: 0.56200000 sec
 D567: 0.56300000 sec
 D568: 0.56400000 sec
 D569: 0.56500000 sec
 D570: 0.56600000 sec

Current Data Parameters
NAME: P1_524_24
EXPNO: 2
PROCNO: 1

F2 - Acquisition Parameters

Date_: 20040404
Time: 21:31
INSTRUM: spect
PROBHD: 5 mm QNP 1H/13C
PULPROG: zgpg30
TD: 1024
SOLVENT: CDCl3
NS: 20
DS: 0
SWH: 9816.360 Hz
FIDRES: 1.77478 Hz
AQ: 0.281856 sec
RG: 327.5
DM: 278.300 umsec
DE: 6.00 umsec
TE: 300.0 K
D0: 0.00100300 sec
d1: 1.00000000 sec
d13: 0.00010000 sec
d16: 0.00100000 sec
IN0: 0.00050040 sec
PCPRG2: 0.00000000 sec
PCPRG1: 1.00000000 sec

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

NUC1: 1H
P1: 5.25 umsec
PL1: 10.50 umsec
PL1: -3.00 dB
SF01: 300.1310812 MHz

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

CPDPRG2: gpcpg2
NUC2: 13C
P2: 10.00 umsec
PL2: 0.00 dB
SF02: 100.6281500 MHz

F1 - Acquisition parameters

WDW: EM
SSB: 0
GB: 0
PC: 1.00

F2 - Processing parameters

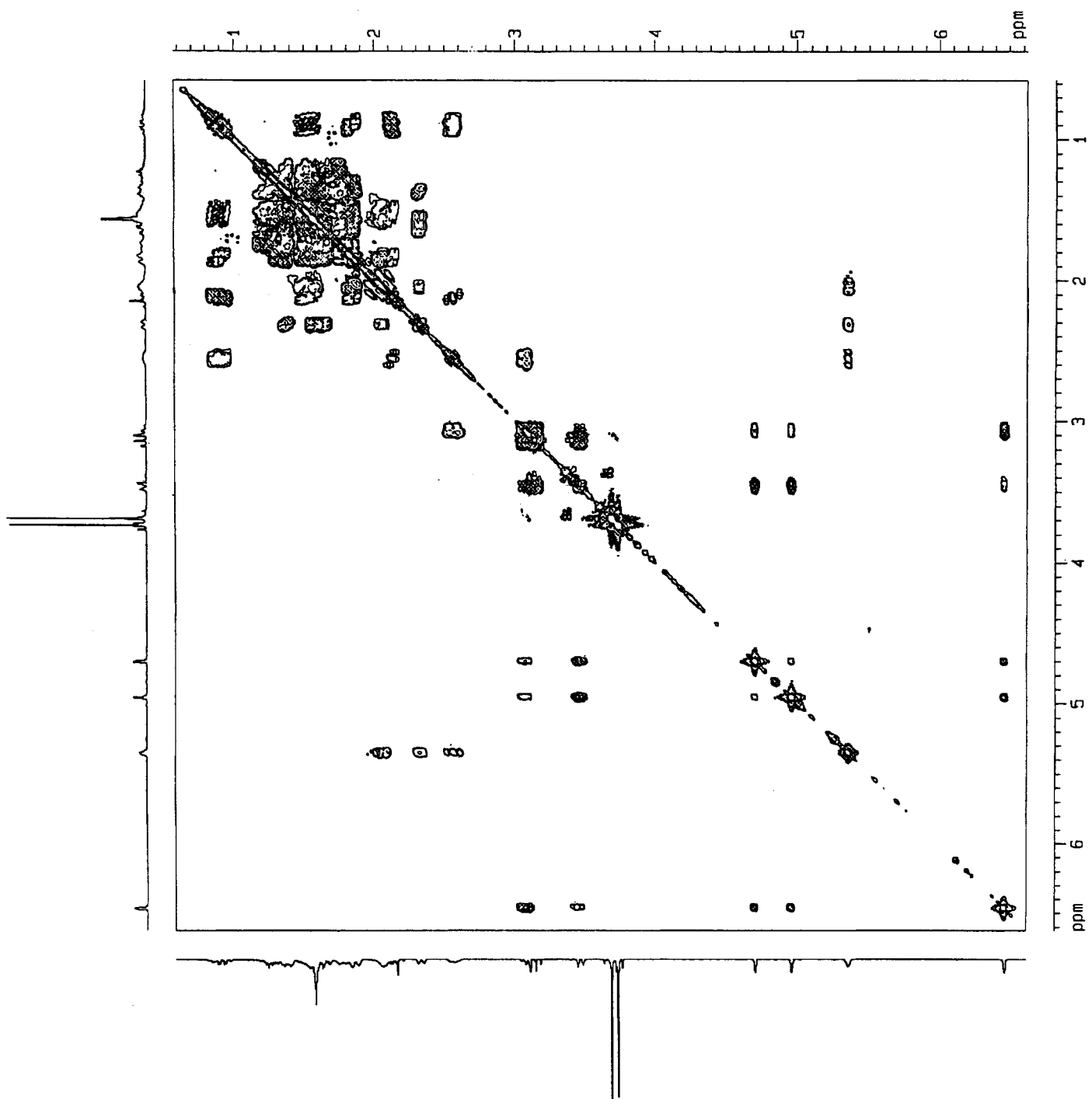
SI: 32768
SF: 300.1300000 MHz
WDW: EM
SSB: 0
GB: 0
PC: 1.00

F1 - Processing parameters

SI: 1024
SF: 300.1300000 MHz
WDW: EM
SSB: 0
GB: 0
PC: 1.00

===== 2D NMR plot parameters =====

C12: 15.00 cm
C11: 15.00 cm
F2P0: 0.000 ppm
F2P1: 1989.80 Hz
F2P2: 0.000 ppm
F2P3: 172.74 Hz
F2P4: 0.000 ppm
F2P5: 1989.80 Hz
F2P6: 0.576 ppm
F2P7: 172.74 Hz
F2P8: 0.40357 ppm/cm
F2P9: 12.12403 Hz/cm
F2P10: 0.40357 ppm/cm
F2P11: 12.12403 Hz/cm



1H NOESY

Current Meta Parameters

NAME
EXPNO
PROCNO

F2 - Acquisition Parameters

Date_

Time

INSTRUM

PROBHD

PULPROG

TD

DELTA

DELTA2

DELTA3

DELTA4

DELTA5

DELTA6

DELTA7

DELTA8

DELTA9

DELTA10

DELTA11

DELTA12

DELTA13

DELTA14

DELTA15

DELTA16

DELTA17

DELTA18

DELTA19

DELTA20

DELTA21

DELTA22

DELTA23

DELTA24

DELTA25

DELTA26

DELTA27

DELTA28

DELTA29

DELTA30

DELTA31

DELTA32

DELTA33

DELTA34

DELTA35

DELTA36

DELTA37

DELTA38

DELTA39

DELTA40

DELTA41

DELTA42

DELTA43

DELTA44

DELTA45

DELTA46

DELTA47

DELTA48

DELTA49

DELTA50

DELTA51

DELTA52

DELTA53

DELTA54

DELTA55

DELTA56

DELTA57

DELTA58

DELTA59

DELTA60

DELTA61

DELTA62

DELTA63

DELTA64

DELTA65

DELTA66

DELTA67

DELTA68

DELTA69

DELTA70

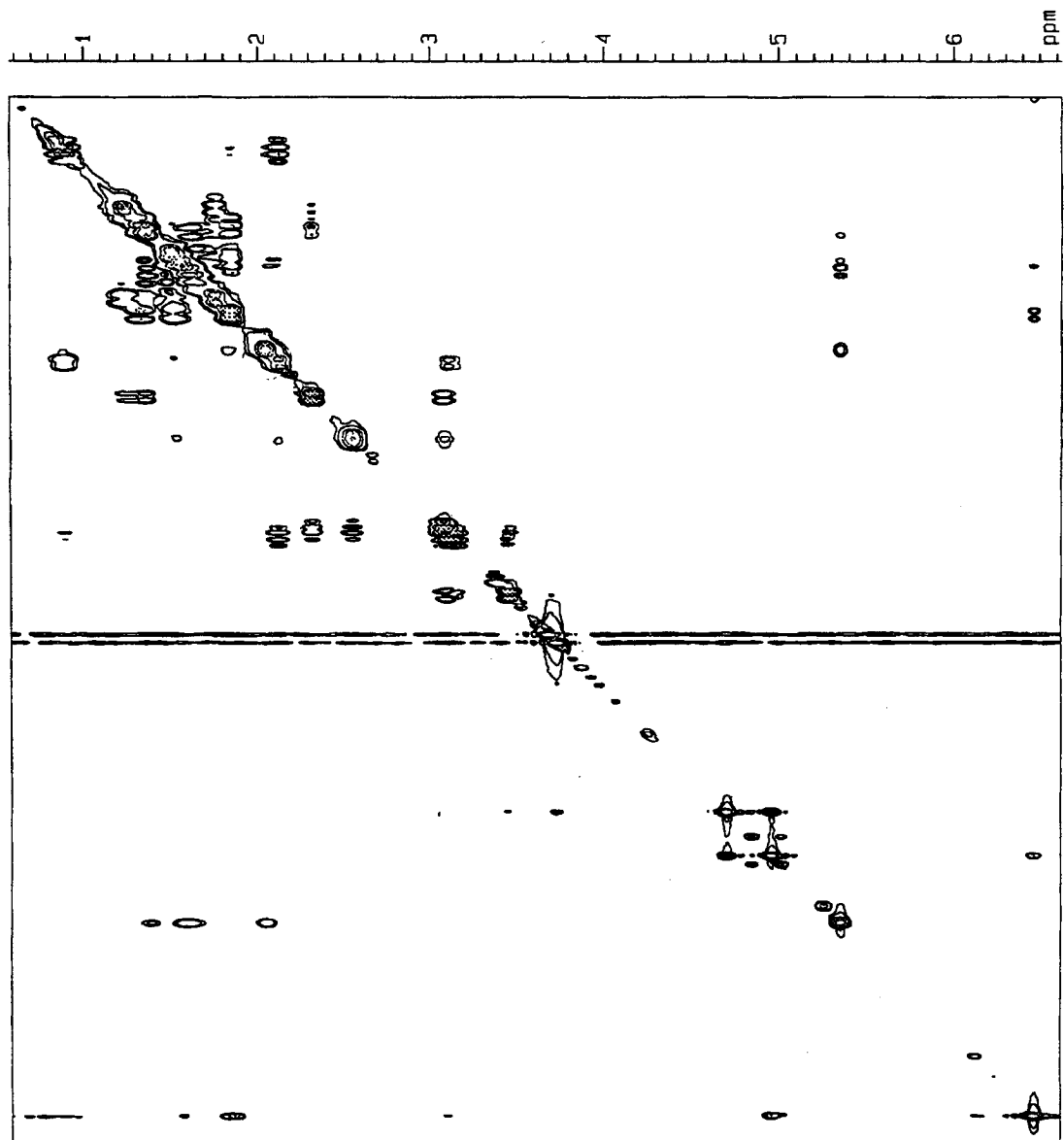
DELTA71

DELTA72

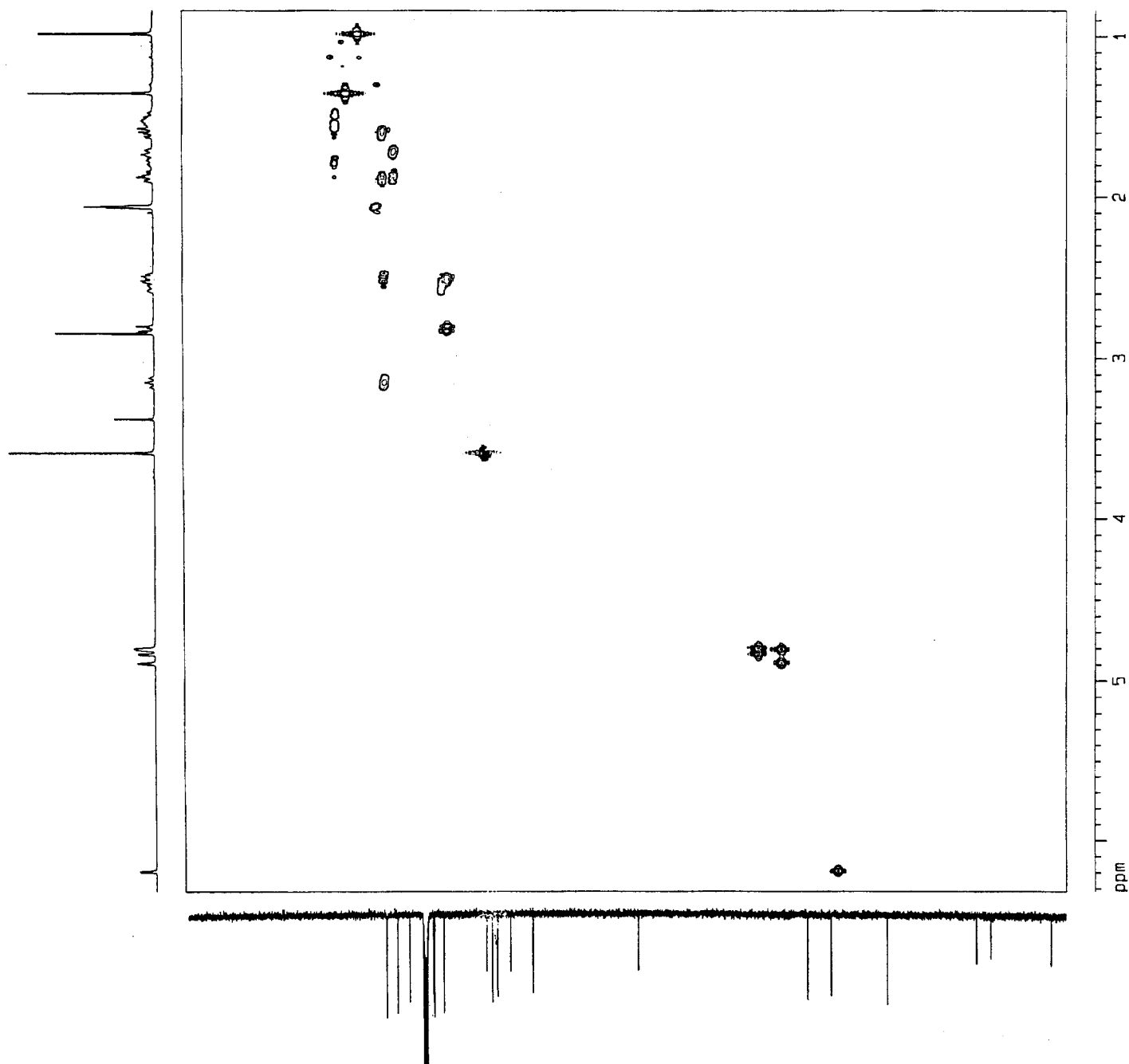
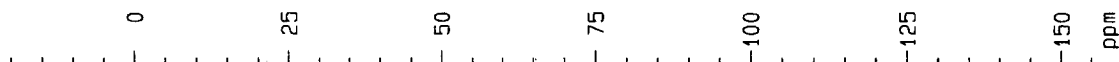
DELTA73

DELTA74

DELTA75



1 2 3 4 5 6 ppm



¹H COSY

Current Data Parameters
NAME EXPNO PROCNO
r02 2 1

F2 - Acquisition Parameters

Date_ 20040505
Time 13:19
INSTRUM AVANCE
PROBHD 5 mm BBO 1H/1H
PULPROG zgpg30
TD 1024
SOLVENT CDCl3
NS 40
DS 0
SWH 2566.972 Hz
FIDRES 2.793778 Hz
AQ 0.185355 sec
RG 327.5
WDW 174.400 usec
DE 6.00 usec
TE 300.0 K
D0 0.00000000 sec
D1 1.00000000 sec
d13 0.00000000 sec
D16 0.00010000 sec
D10 0.00348000 sec
MCREST 0.00000000 sec
PCPRG2 1.00000000 sec

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

MU1 1H
P0 14.00 usec
P1 14.00 usec
PL1 0.00 dB
SF01 500.1317677 MHz

***** GRADIENT CHANNEL *****

GP0A1 SINE100
GPMAG 5.00 %
GP12 0.00 %
GP11 0.00 %
GP12 0.00 %
GP21 10.00 %
GP22 10.00 %
P16 1000.00 usec

F1 - Acquisition Parameters

MU0 1H
TD 256
FIDRES 11.998111 Hz
SN 5.732 dB

F2 - Processing Parameters

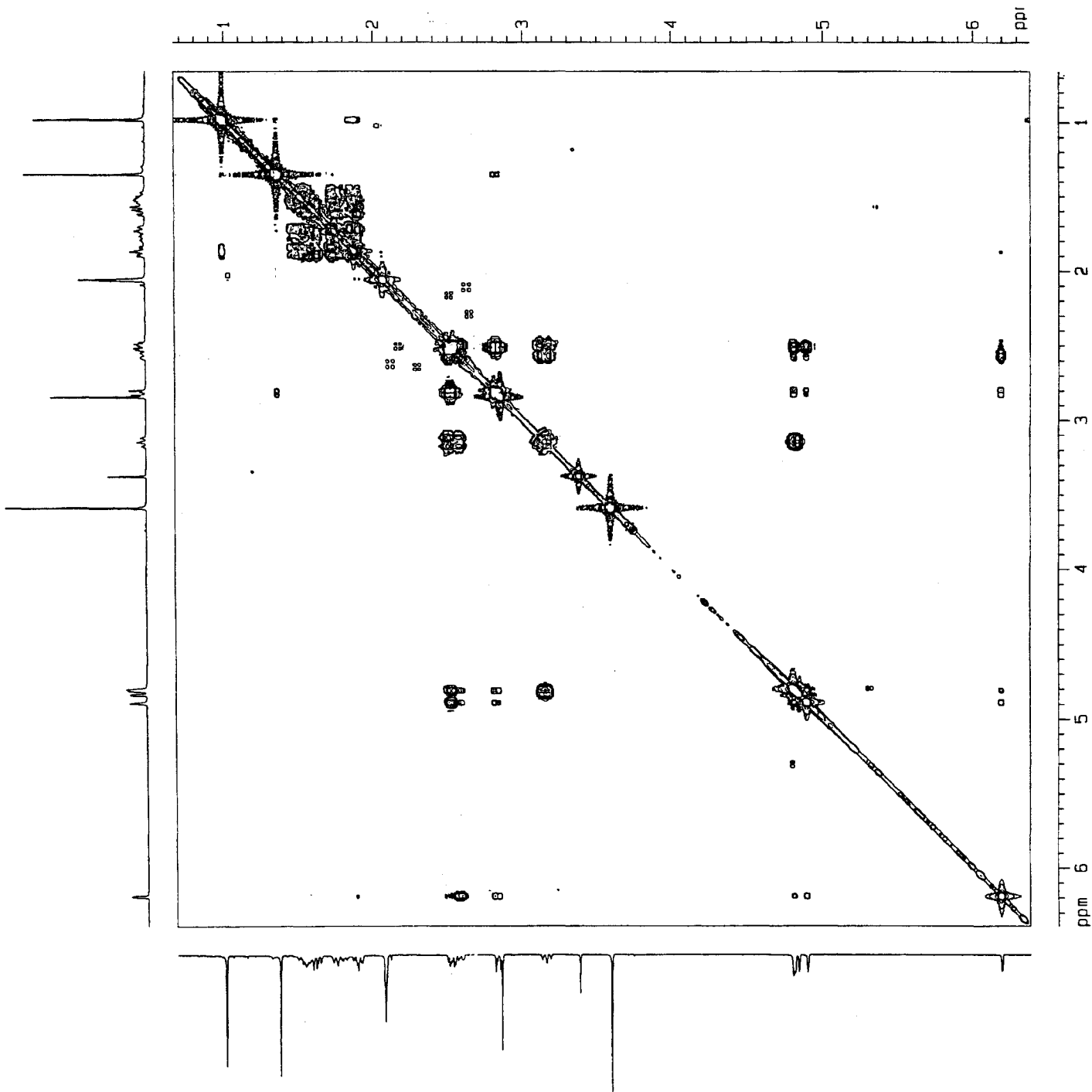
SF 500.1300649 MHz
WDW SINE
SSB 0
LB 0.00 Hz
GB 0.00 Hz
PC 1.00

F1 - Processing Parameters

SF 500.1300249 MHz
WDW SINE
SSB 0
LB 0.00 Hz
GB 0.00 Hz

20 MHz p100 parameters

CU2 15.00 usec
CU1 15.00 usec
FAPLO 6.391 dB
FAPLO 3190.36 Hz
FAPHI 0.659 dB
FAPHI 329.38 Hz
FAPLO 6.391 dB
FAPLO 3190.36 Hz
FAPHI 0.659 dB
FAPHI 329.38 Hz
FAPLO 0.38216 Hz/cg
FAPLO 191.13150 Hz/cg
FAPLO 0.38216 Hz/cg
FAPLO 191.13150 Hz/cg



STANDARD PROTON PARAMETERS.

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

Pulse Sequence: ghmqc

Solvent: Acetone
 Temp. 20.0 C / 293.1 K
 INOVA-500 "Inova500"

Relax. delay 1.000 sec
 Acq. time 0.200 sec
 Width 5110.5 Hz
 2D Width 20248.0 Hz

2 repetitions
 2 x 128 increments
 OBSERVE H1, 500.1765458 MHz
 DECOUPLE C13, 125.7794335 MHz

Power 44 dB
 on during acquisition
 off during delay
 w40-tr7502 modulated

DATA PROCESSING

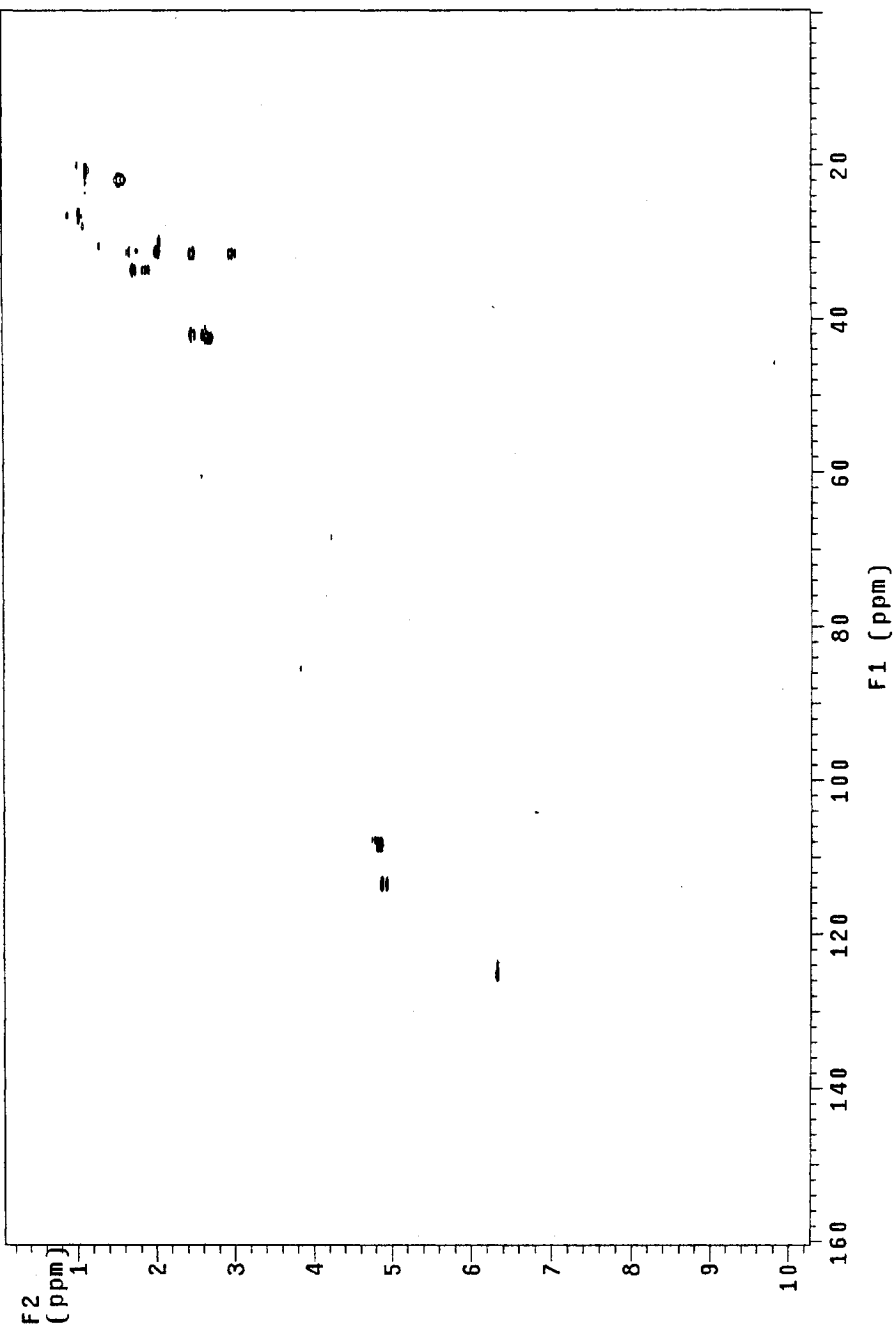
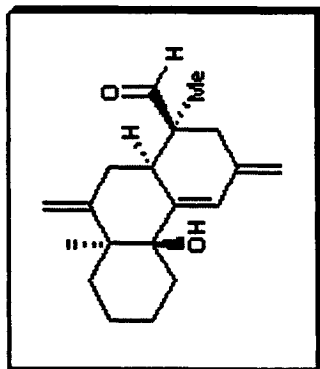
Gauss apodization 0.093 sec

F1 DATA PROCESSING

Gauss apodization 0.004 sec

FT size 2048 x 2048

Total time 11 min, 22 sec



STANDARD PROTON PARAMETERS

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

Pulse Sequence: gCDSY

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

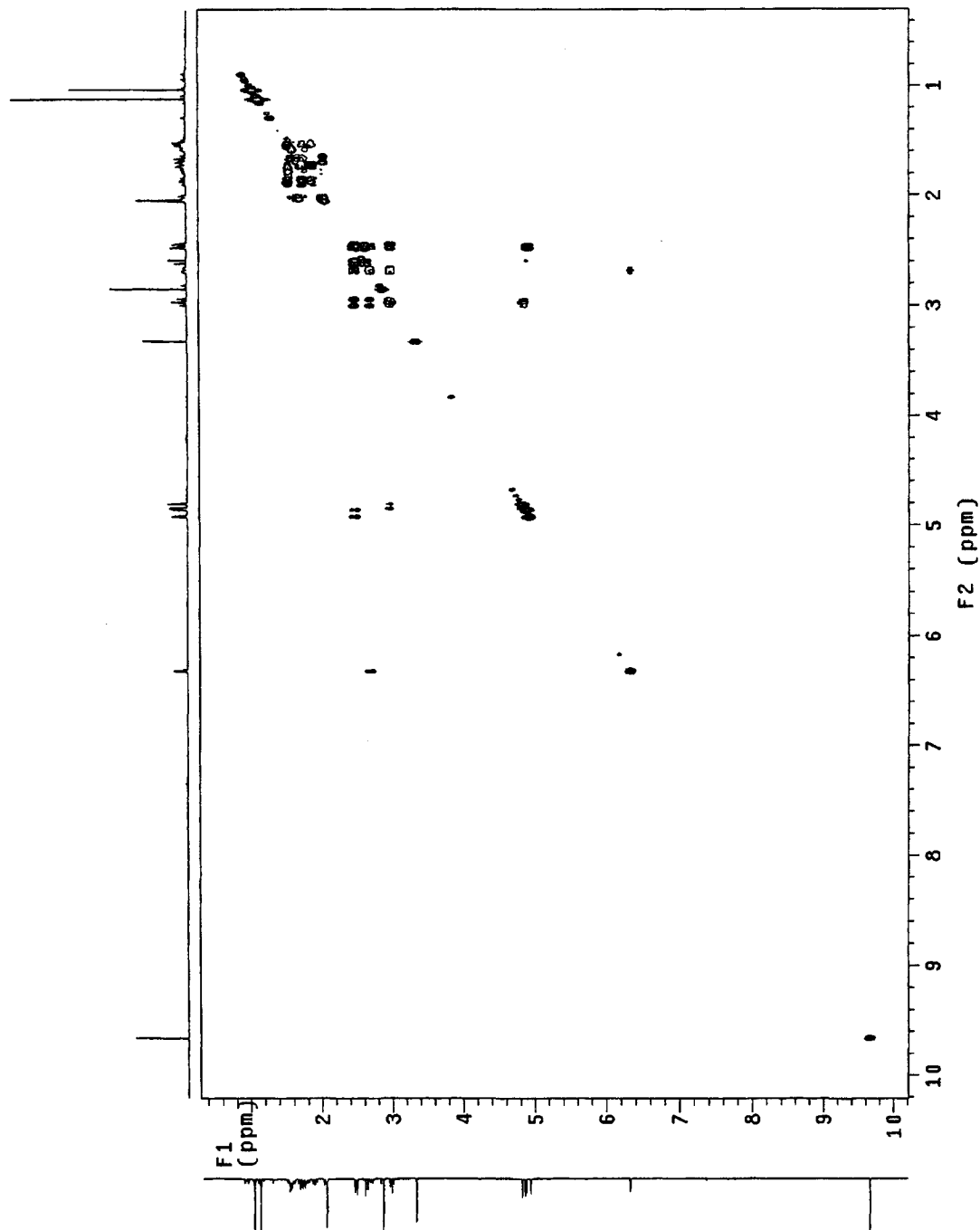
Relax. delay 1.000 sec
 Acq. time 0.206 sec
 Width 4983.1 Hz
 2D Width 4983.1 Hz
 4 repetitions

256 increments

OBSERVE H1, 500.1765458 MHz

DATA PROCESSING

Sq. sine bell 0.103 sec
 F1 DATA PROCESSING
 Sq. sine bell 0.026 sec
 FT size 2048 x 2048
 Total time 21 min, 34 sec



STANDARD PROTON PARAMETERS

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

Pulse Sequence: NOESY

Solvent: Acetone
Temp. 20.0 C / 293.1 K
INNOVA-500 "inova500"

Relax. delay 1.000 sec
Mixing 1.300 sec
Acq. time 0.205 sec
Width 5005.3 Hz
2D Width 5005.3 Hz
16 repetitions

2 x 200 increments

OBSERVE HI, 500.1765458 MHz

DATA PROCESSING

Gauss apodization 0.095 sec
F1 DATA PROCESSING
Gauss apodization 0.011 sec
F1 size 2048 x 2048
Total time 4 hr, 32 min, 4 sec

