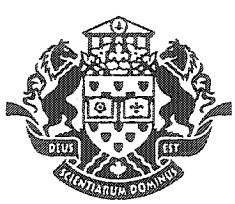

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FACULTÉ DES ÉTUDES SUPÉRIEURES ET POSTDOCTORALES

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STUDIES ON THE TANDEM OXY-COPE/ENE/CLAISEN REACTION. APPLICATIONS OF THE HYDROXY-DIRECTED DIELS-ALDER REACTION TOWARDS THE TOTAL SYNTHESIS OF HAVELLOCKATE AND SYNTHESIS OF ISOVELLERAL ANALOGUES

By

JULIE ALINE FARAND

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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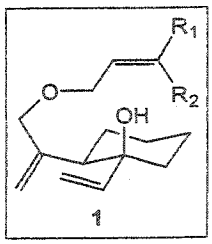
Bn	benzyl
BuLi	butyl lithium
Boc_2O	*tert*-butoxycarbonyl anhydride
DBU	1,8-diazobicyclo[5.4.0]undec-7-ene
DCM	dichloromethane
DIBAL-H	diisobutylaluminum hydride
DMAE	N,N-dimethylaminoethanol
DMAP	4-dimethylaminopyridine
DMF	N,N-dimethylformamide
Eq.	equivalents
EtOAc	ethylacetate
Et_2O	diethylether
Et_3N	triethylamine
GC	gas chromatography
GC/MS	gas chromatography/mass spectrometry
HPLC	high pressure liquid chromatography
HRMS	high resolution mass spectrum
HDDA	hydroxy-directed Diels-Alder
HMDS	hexamethyldisilazane
HMPA	hexamethylphosphoramide
IR	infrared
*i*PrOH	isopropanol

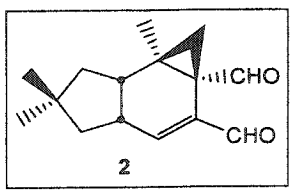
LDA	lithiumdiisopropylamide
Me	methyl
$MgBr_2 \cdot OEt_2$	magnesium bromide diethyletherate
mp	melting point
MS	molecular sieves
NMR	nuclear magnetic resonance
NOESY	nuclear overhauser and exchange spectroscopy
NPM	N-phenylmaleimide
ON	overnight
PG	protecting group
Ph	phenyl
Pyr	pyridine
ppm	parts per million
PTSA	*para*-toluene sulfonic acid
RP	reaction pathway
SAR	structure activity relationship
SM	starting material
TBAF	tetrabutylammonium fluoride
TBDMS	*tert*-butyldimethylsilyl
TBDPS	*tert*-butyldiphenylsilyl
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl

ABSTRACT



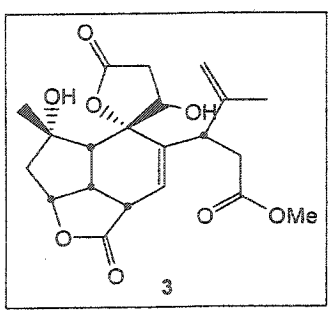
1

The synthesis of decalin systems possessing a quaternary carbon at C-9 was achieved via the tandem oxy-Cope/ene/Claisen rearrangement. Depending on the substitution pattern of the allyl ether **1**, different reaction pathways may be followed to generate the decalin cores. In the case of 1,2-divinylchyclohexanol having a 1,2-disubstituted allyl ether, the tandem reaction afforded the decalin system in good yield. However, trisubstituted allyl ethers produced unique decalin products via a radical 1,3-shift. In addition, microwave irradiation of 1,2-divinylcyclohexanol propargyl ethers generated tetracyclic acetals via the tandem oxy-Cope/ene/Claisen/5-exo *dig* cyclization.



2

The scope and limitations of the hydroxy-directed Diels-Alder (HDDA) reaction were studied on 5-membered semicyclic dienes possessing secondary or tertiary allylic alcohols. A temporary magnesium tether provided by $MgBr_2 \cdot OEt_2$ or vinylmagnesium bromide was utilized to regio- and stereoselectively control the Diels-Alder reaction. This methodology was applied towards the synthesis of the hydrindane moiety of isovelleral **2** in order to construct its analogues.



3

As well, the HDDA reaction was applied towards the total synthesis of havellockate **3**. The bicyclic core of the natural product was prepared with high regio- and stereocontrol and good yield.

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First and foremost, I would like to thank my professor and supervisor Dr Louis Barriault for giving me the opportunity to be a member of his group. Your dynamism, contagious motivation and passion for this science are tremendous assets to the University of Ottawa and the scientific community.

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graduate studies at U of O!). I wish you all the best in your future endeavours. Last but not least, I would like to express my sincerest gratitude to Dr Tony Durst for believing in my capabilities and devoting much effort and time to the biopharmaceutical program.

« Dédié à mes parents, Raymond et Ginette Farand,
et à mon grand-père Farand… »

Chapter 1: Introduction

1.1 History of the Tandem Oxy-Cope/Ene Reaction

The rapid construction of new carbon-carbon bonds has challenged many organic chemists. A variety of reactions have been developed, namely the pericyclic, ring closing metathesis polymerisation and metal-catalyzed cross-coupling reactions, and have been applied to devise distinctive synthetic strategies towards total syntheses. With these valuable and efficient reactions, the synthetic chemist must limit the number of steps without losing stereoselective and regioselective control. Reactions in tandem, where two or more reactions occur consecutively without purification, are remarkable tools for generating new carbon-carbon bonds and limiting the number of synthetic steps.

During a study on the construction of 8-membered rings, Sutherland *et al.*[1] observed the tandem oxy-Cope/transannular ene product as an unanticipated by-product of the oxy-Cope rearrangement. Paquette[2] and Rajagoplan[3] also reported observing the undesired tandem product as a result of a tandem anionic oxy-Cope/transannular ene reaction. Barriault and Warrington capitalized on these previous observations and studied the tandem oxy-Cope/transannular ene reaction of 1,2-divinylcyclohexanols.[4] When heated in a sealed tube for 5 h, the 1,2-divinylcyclohexanols **1.1** undergo a diastereoselective tandem oxy-Cope/ene reaction to rapidly afford bi- and tricyclic skeletons **1.2** in 44-86% yield (Figure 1.1).

---

[1] Chorlton, A. P.; Morris, G. A.; Sutherland, J. K. *J. Chem. Soc. Perkin Trans. 1* **1991**, 1205.
[2] Paquette, L.A.; Nakatani, S.; Zydowsky, T.M. ; Edmondson, S. D. ; Sun, Q.-L. ; Skerlj, R. *J. Org. Chem.* **1999**, *64*, 3244.
[3] Rajagopalan, K.; Janardhanam, S.; Balakumar, A. *J. Org. Chem.* **1993**, *58*, 5482
[4] Warrington, J. M.; Yap, G. P. A.; Barriault, L. *Org. Lett.* **2000**, *2*, 663.

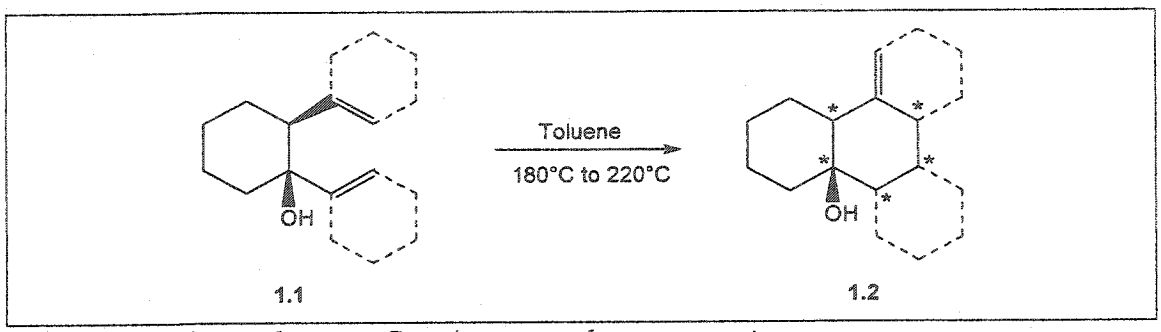


Figure 1.1: The tandem oxy-Cope/transannular ene reaction.

As illustrated in Figure 1.2, the thermally induced oxy-Cope rearrangement of **1.3** affords enol **1.4**, which rapidly tautomerizes to the stable ketone **1.5**. A consecutive transannular ene reaction occurs via a chair-like transition state and brings the hydrogen and oxygen atoms of the macrocycle **1.6** in close proximity.[5] The resulting bi- or tricyclic core **1.7** possessing up to five contiguous stereogenic centers may be created via the tandem reaction.

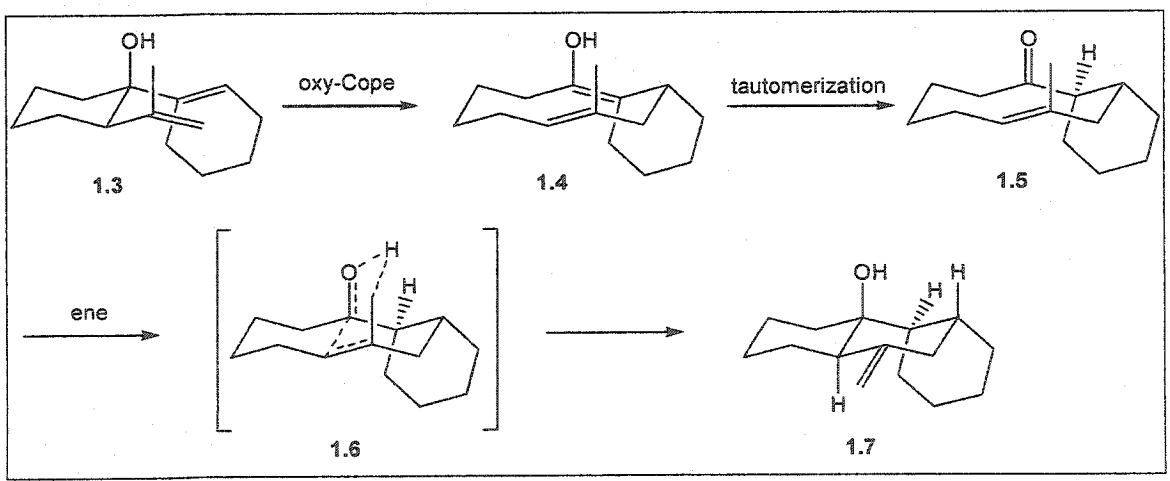
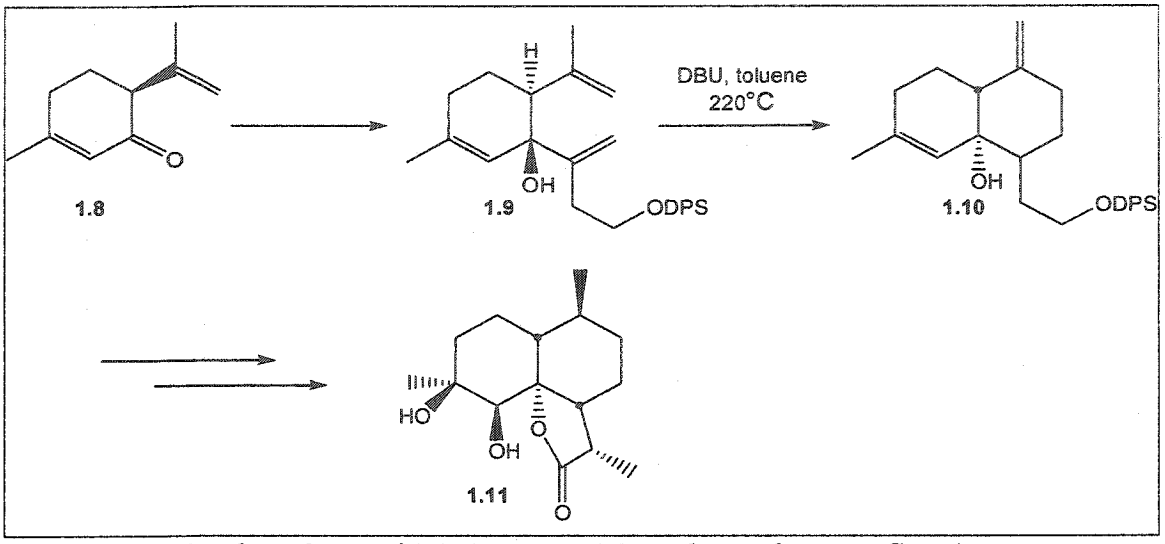


Figure 1.2: Mechanism and transition state of the tandem oxy-Cope/transannular ene.

A few years later, Barriault and Deon applied this methodology towards the total synthesis of (+)-arteanniun M **1.11**.[6] Isolated from *Artemisia annua L.* in the Sichuan province of China, artennniun M shares a similar skeleton with the anti-malaria drug

[5] Terada, Y.; Yamamura, S. *Tetrahedron Lett.* **1979**, *20*, 1623.
[6] Barriault, L.; Deon, D. H. *Org. Lett.* **2001**, *3*, 1925.

endoperoxide artemisin. The total synthesis of the natural product was completed in 10 steps via the tandem oxy-Cope/transannular ene reaction with high diastereo- and enantiomeric excess.



Scheme 1.1: *Total synthesis of (+)-Artennuin M via the tandem oxy-Cope/ene reaction.*

The total synthesis of agelasimine A **1.12** was also attempted by Barriault and Denissova via the tandem approach (Figure 1.3).[7] Bearing a *trans*-decalin system with a tertiary alcohol at the ring junction and four contiguous stereogenic centers, the tandem oxy-Cope/transannular ene reaction could offer an additional application in synthetic organic chemistry.

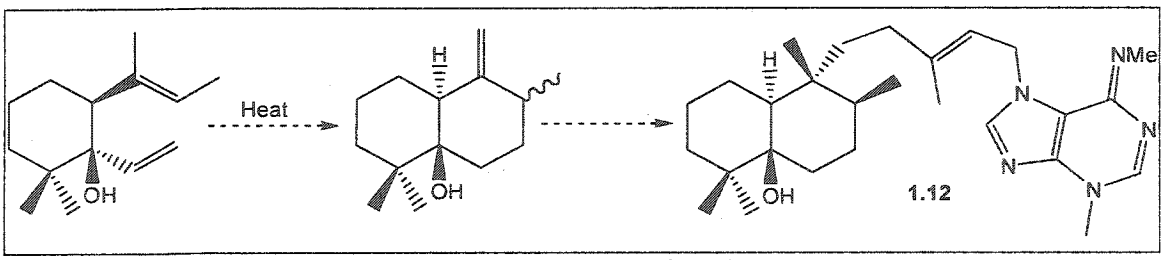


Figure 1.3: *Approach towards the total synthesis of agelasimine A.*

[7] Denissova, I. Ph. D. Thesis, University of Ottawa, **2004**.

During this study, the tandem oxy-Cope/transannular ene/Claisen reaction was discovered as an efficient method of generating diastereoselective decalin skeletons with quaternary carbon centers.[8] The scope and limitations of this methodology, including new discoveries, will be discussed in the following chapter.

1.2 The Diels-Alder Reaction

Since its discovery in 1928, the Diels-Alder reaction has been widely applied towards the total synthesis of numerous natural products. This cycloaddition has been extensively studied on various levels by many disciplines, ranging from the quantum chemist to the synthetic organic chemist. The shared curiosity and fascination for the Diels-Alder reaction primarily exists since improvement is still possible on many facets. Although it is a powerful synthetic tool, high regio- and diastereoselectivity has not been perfected with every diene and dienophile. Thus, the reaction conditions are highly dependent on the nature of the reacting partners.

Many organic chemists, namely Woodward and Hoffman,[9] have concentrated their efforts in order to rationalize the selectivity during the course of this reaction. More recently, Lewis acids and temporary tethers have been examined to improve the rate and selectivity of the Diels-Alder reaction. A brief overview regarding the frontier molecular orbital theory, use of Lewis acids and temporary tethers will be discussed. As well, the hydroxy-directed Diels-Alder reaction will be introduced as a powerful methodology for the construction of bicyclic skeletons from semicyclic dienes possessing tertiary alcohols.

---

[8] Barriault, L.; Denissova, I. *Org. Lett.* **2002**, *4*, 1371.
[9] Woodward, R. B.; Hoffman, R. *The Conservation of Orbital Symmetry*, Verlag Chemie, Weinheim, 1970.

1.2.1 Stereoselectivity, Regioselectivity and Diastereoselectivity

The stereoselectivity of the Diels-Alder reaction is governed by sterics, but mainly electronic factors when sterically hindering diene and dienophiles are not involved. Eventhough the *exo* adduct is the thermodynamic product during the Diels-Alder reaction, the *endo* product is more quickly obtained, and is therefore the kinetic product. The preferred *endo* product can be explained by the presence of secondary orbital interactions during the transition state (Figure 1.4).

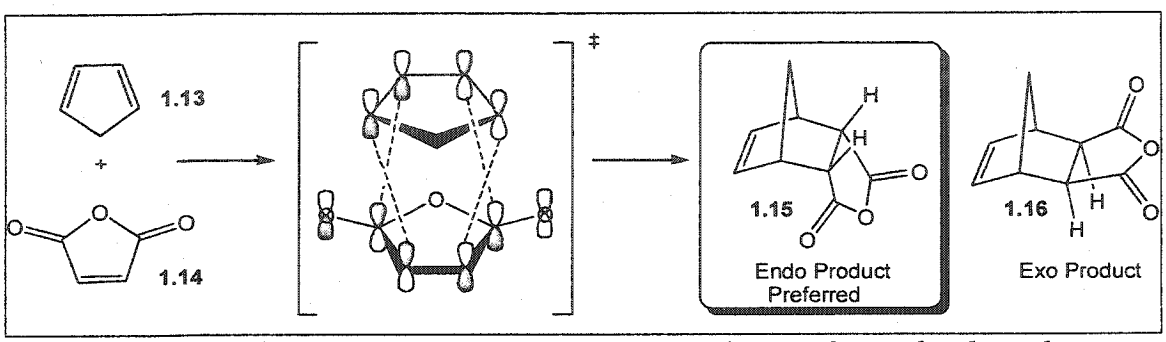


Figure 1.4: *Stabilization of the endo transition state with secondary orbital overlapping.*

During the reaction between cyclopentadiene **1.13** and maleic anhydride **1.14**, secondary orbital overlapping, represented by the dashed lines in Figure 1.4, are responsible for stabilizing and lowering the energy of the transition state, thus rendering the cycloaddition stereoselective. Although the *exo* product **1.16** can be observed, the *endo* product **1.15** is ultimately present in larger ratios. On similar grounds, the regioselectivity is determined by pairing the coefficients of the atomic orbitals between diene **1.17** and dienophile **1.18** that are similar in size and identical in sign (Figure 1.5). Many chemists prefer to rationalize the regioselectivity by allocating partial charges to

each atom concerned, however the frontier molecular orbital theory is preferred by theoreticians and numerous organic chemists.[10]

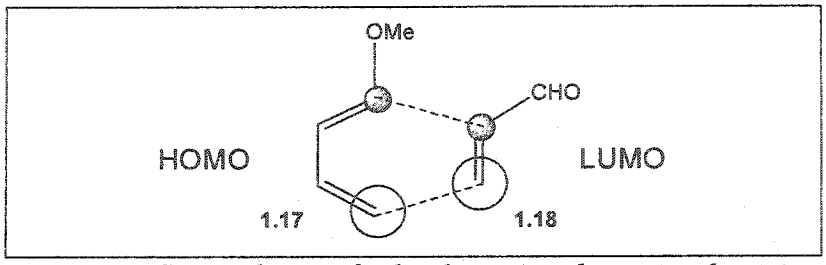
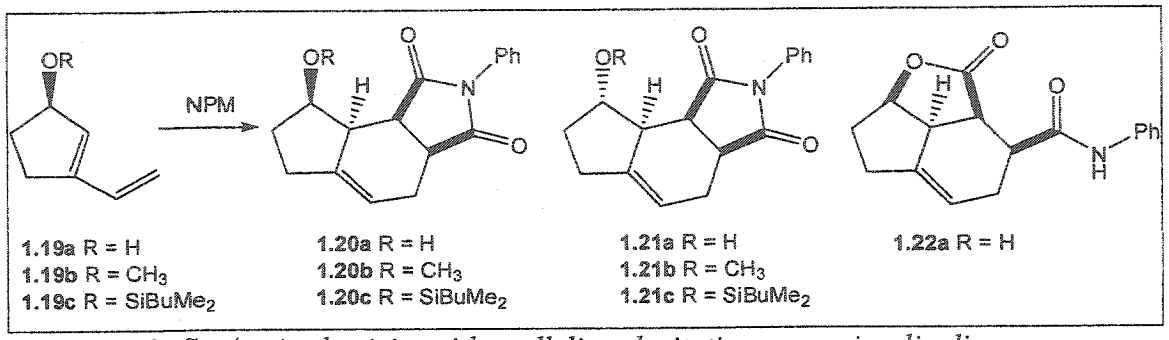


Figure 1.5: Size and sign of orbitals govern the regioselectivity

The diastereoselectivity (or facial selectivity) of the Diels-Alder reactions has been particularly studied by Overman[11] and Frank[12] during the last fifteen years. Overman illustrated that α- allylic substitutions on the semicyclic diene **1.19 a,b,c** can control the facial selectivity during the Diels-Alder reaction (Scheme 1.2). When diene **1.19a** was treated with NPM at room temperature in toluene, **1.20a** and **1.21a** were respectively observed by HPLC in a 1.8:1 ratio. However, after 5 hours and upon purification, **1.20a** was converted into **1.22a** to yield **1.21a** and **1.22a** in 28% and 53% yield. However, when the reaction was performed in methanol, the syn/anti selectivity of **1.20a** and **1.21a** was obtained in a 1:4 mixture by HPLC. In addition, THF slightly afforded a smaller anti preference (syn/anti = 1: 1.8) when utilized as solvent.

[10] For more details see Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*, John Wiley & Sons, Trowbridge, 2000.
[11] Fisher, M. J.; Hehre, W. J.; Overman, L. E.; Kahn, S. D. *J. Am. Chem. Soc.* **1988**, *110*, 4625.
[12] Datta, S. C.; Frank, R. W.; Tripathy, R.; Quigley, G. J.; Huang, L.; Chen, S.; Sihaed, A. *J. Am. Chem. Soc.* **1990**, *112*, 8472.



Scheme 1.2: *Syn/anti selectivity with α-allylic substitution on semicyclic dienes.*

Interestingly, when **1.19b** (R = CH_3) or **1.19c** (R = $SiBuMe_2$) were used as dienes, the anti products **1.21b** and **1.21c** were obtained as the sole diastereomers (anti/syn >25:1) in both cases in 73% and 84% yields, respectively. When toluene was substituted with methanol or THF, diene **1.19b** and NPM still provided **1.21b** in 73% yield. Thus, Overman demonstrated that heteroatomic substitution in the α-allylic position of the semicyclic diene and the solvent can control the facial selecitivity of the cycloaddition without additional reagents.

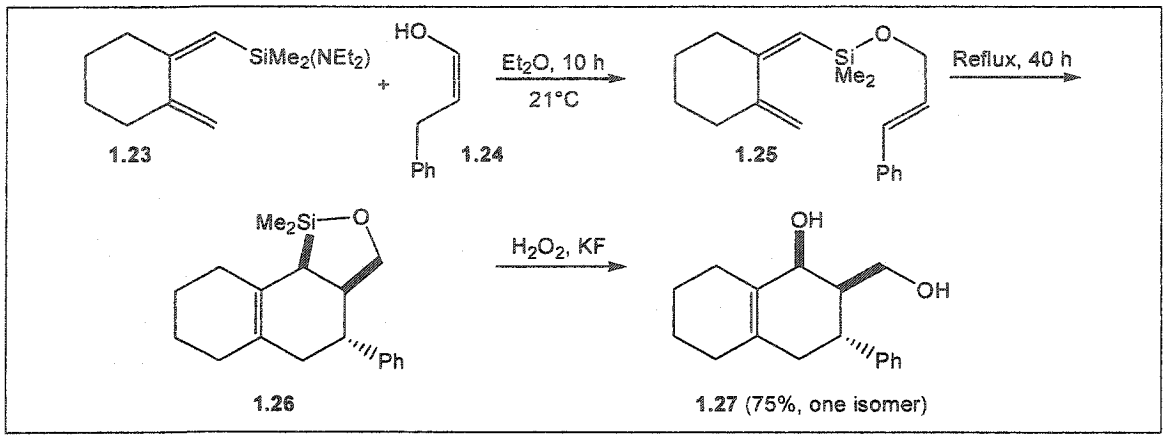
1.2.2 Lewis Acids and Temporary Tethers

The use of Lewis acids in the Diels-Alder reaction has been extensively studied.[13] In addition to their rate accelerating effect, Lewis acids can act as temporary tethering units. Their ability to complex to heteroatoms can be advantageous in order to control the regio- and facialselectivity during the Diels-Alder reactions. Aluminium,[14] silicon,[15] boron[16] and zinc[14b] tethers have been widely used and all display particular advantages and disadvantages. Pioneer work by Tamao *et al.* illustrated that the regio- and stereoselectivity of an intramolecular Diels-Alder reaction could be controlled via a

---

[13] Shea, K. J.; Zandi, K. S.; Gauthier, D. R. *Tetrahedron* **1998**, *54*, 2289.
[14] (a) Stork, G.; Chan, T.Y. *J. Am. Chem. Soc.* **1995**, *117*, 6595. (b) Olsson, R.; Bertozzi, F.; Frejd, T. *Org. Lett.* **2000**, *2*, 1283.
[15] (a) Tamao, K.; Kobayashi, K.; Ito, Y. *J. Am. Chem. Soc.* **1989**, *111*, 6478. (b) Stork, G.; Chan, T.Y.; Breault, G.A. *J. Am. Chem. Soc.* **1992**, *114*, 7578.
[16] Batey, R. A.; Thadani, A. N.; Lough, A. J. *J. Am. Chem. Soc.* **1999**, *121*, 450.

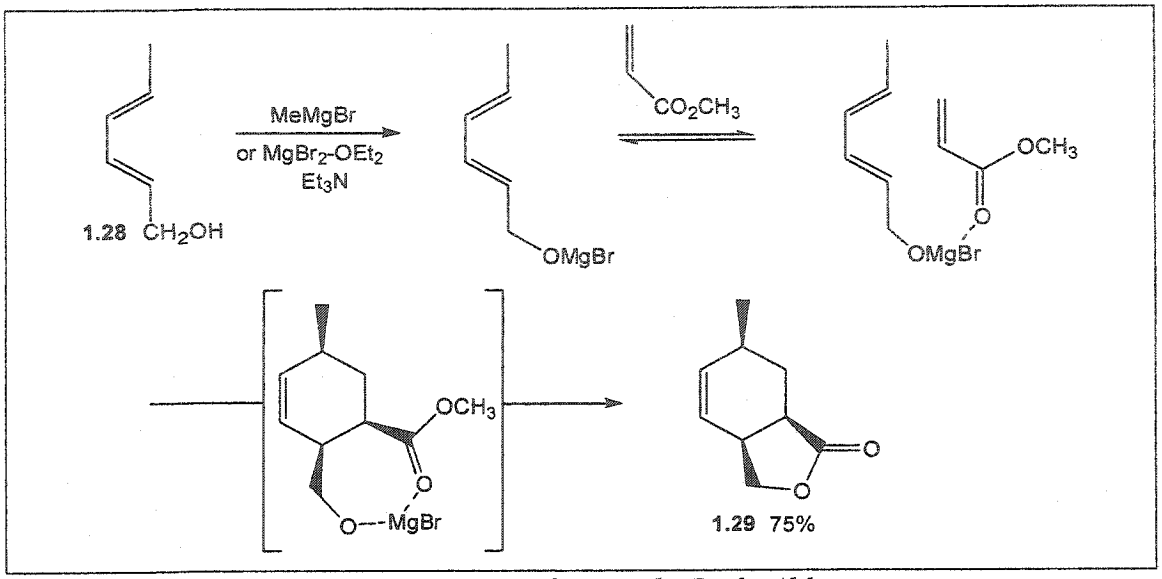
covalent bond between the silicon and oxygen atoms of diene **1.23** and dienophile **1.24** (Scheme 1.3). Cycloadduct **1.26** was generated during reflux in xylene after 40 hours.



Scheme 1.3: *Tamao and co-workers' temporary silicon tether.*

An additional reaction was required to cleave the Si-O bond and presented a drawback to this methodology. However, the stereochemistry was retained during this process and oxidative desilylation afforded **1.27** in 75% yield as the sole isomer. Stork[13] and Ward[17] have illustrated the use of magnesium as temporary tethering unit and Lewis acid. As depicted in Scheme 1.4, Ward applied Vedejs' methodology by using $MgBr_2 \cdot OEt_2$ and triethylamine,[18] or a Grignard reagent as source of magnesium. The desired cycloadduct **1.29** was obtained in 75% yield with high regio- and stereocontrol from sorbic alcohol **1.28**.

[17] Ward, D. E.; Abaee, M. S. *Org. Lett.* **2000**, *2*, 3937.
[18] Vedejs, E.; Daugulis, O. *J. Org. Chem.* **1996**, *61*, 5702.



Scheme 1.4: *Ward's use of magnesium tethers in the Diels-Alder reaction.*

1.2.3 The Hydroxy-Directed Diels-Alder Reaction (HDDA)

As mentioned previously, Overman studied the use of semicyclic dienes with symmetrical dienophiles, such as N-phenylmaleimide. However, when a non-symmetrical dienophile is used, it is difficult to control both the facial and regioselectivity of the cycloaddition. Semicyclic dienes bearing a tertiary alcohol at the α-allylic position were of particular interest in our laboratory. With the intention of applying such dienes in future total syntheses, a method needed to be developed in order to accommodate such sensitive precursors and control both the regio- and stereoselectivity of the Diels-Alder reaction.

Barriault, Thomas and Clément[19] have recently developed a highly stereoselective hydroxy-directed Diels-Alder reaction using semicyclic dienes possessing tertiary alcohols. The use of magnesium tethers allows the dienophiles, both symmetrical or asymmetrical, to add *syn* to the tertiary alcohol in the α-allylic position of the diene. In

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

addition, the regioselectivity was controlled when asymmetric dienophiles were utilized. Their studies were concentrated on two types of 6-membered semicyclic dienes, types **A** and **B** (Figure 1.6).

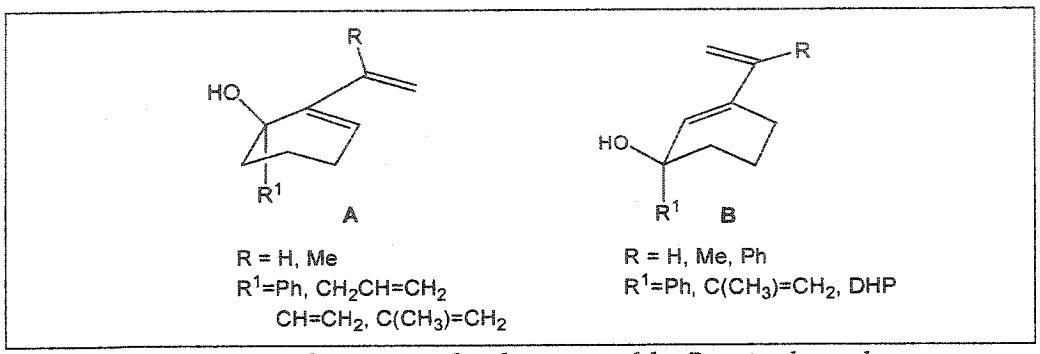
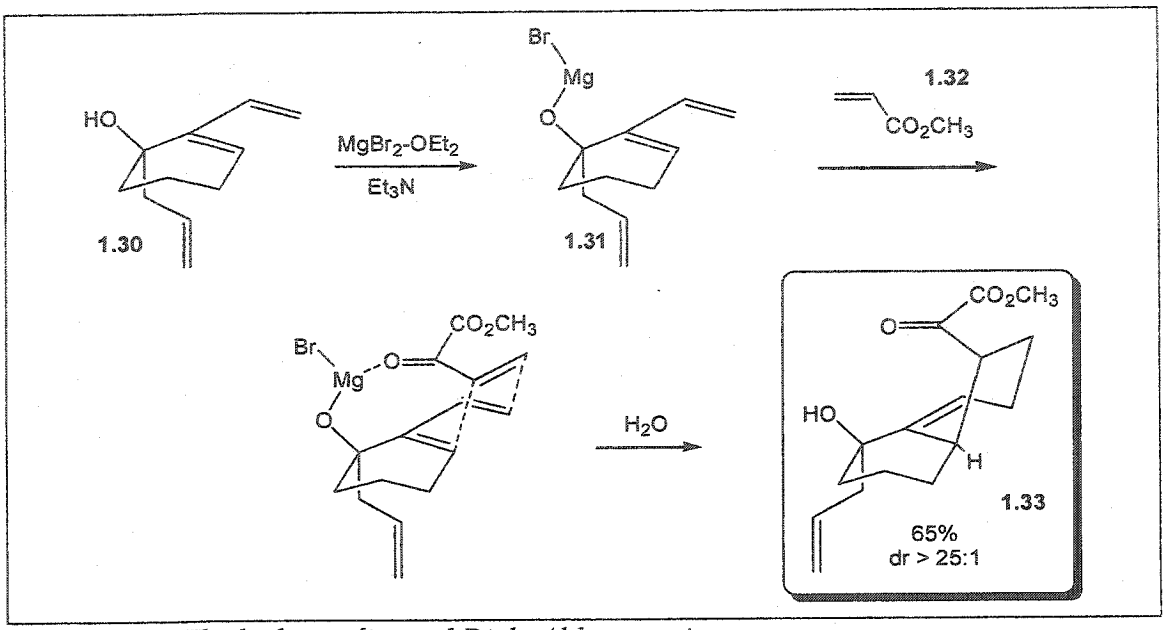


Figure 1.6: *Type A and B semicyclic dienes used by Barriault et al.*

In the presence of $MgBr_2 \cdot OEt_2$ and triethylamine, the tertiary alcohol **1.30** forms a magnesium alkoxide **1.31** (Scheme 1.5). After the addition of the dienophile **1.32**, the same magnesium unit complexes to, the oxygen of the carbonyl group from the dienophile, and lowers the LUMO of the latter. This temporary tethering unit allows the dienophile **1.32** to add *syn* to the hydroxyl group of diene **1.30**, hence the hydroxy-directed Diels-Alder reaction. During this process, the regio- and facialselectivity of cycloadduct **1.33** are respectively controlled (dr >25:1) by the favourable overlapping of atomic orbitals and the presence of the magnesium tethering unit.



Scheme 1.5: *The hydroxy-directed Diels-Alder reaction.*

Various Lewis acids were examined in order to optimize the yield of the reaction. Even though the halogens on the magnesium were varied, i.e. Cl and I, and other metals were scanned, such as Zn, B and V, the $MgBr_2{\cdot}OEt_2/Et_3N$ combination afforded the best yields. Depending on the diene (type **A** or **B**) and dienonophile used, such as NPM, methylacrylate, acrolein and methacrolein, the desired cycloadducts **1.33** were obtained in 30-89% yield. More details on this methodology will be provided in the following chapters which will illustrate the use of the HDDA reaction with 5-membered semicyclic dienes.

1.3 Application of the Diels-Alder Reaction Towards the Synthesis of Marasmic Acid and Isovelleral

Many fungal metabolites, such as marasmic acid **1.34** and isovelleral **1.35**, have been isolated from the mushroom Basidiomycetes (Figure 1.7).[20,21] Due to their antibacterial properties, these natural products rapidly became synthetic targets in many laboratories.[22] Although various synthetic strategies have been published, the Diels-Alder reaction was frequently chosen as a key step for the construction of the *cis*-hydrindane ring skeleton. Thus, a brief summary of the Diels-Alder reaction applied towards the total synthesis of marasmic acid and isovelleral follows.

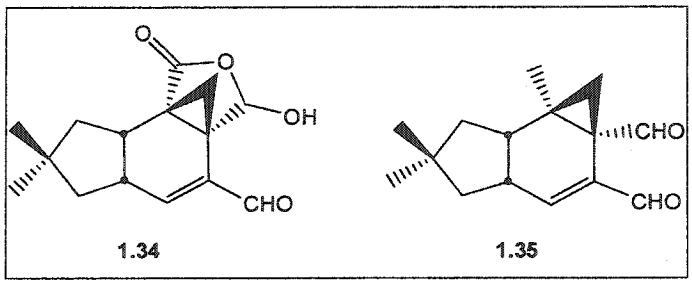


***Figure 1.7:** Marasmic acid and isovelleral.*

Wilson and Turner[23] attempted to achieve the first stereospecific synthesis of the marasmic acid skeleton via a Diels-Alder reaction (Scheme 1.6). When diene **1.36** and dimethylacetylene dicarboxylate **1.37** were heated in a glass tube under vacuum, the desired cycloadduct **1.38** was obtained in >95% purity. If the precursors were refluxed in

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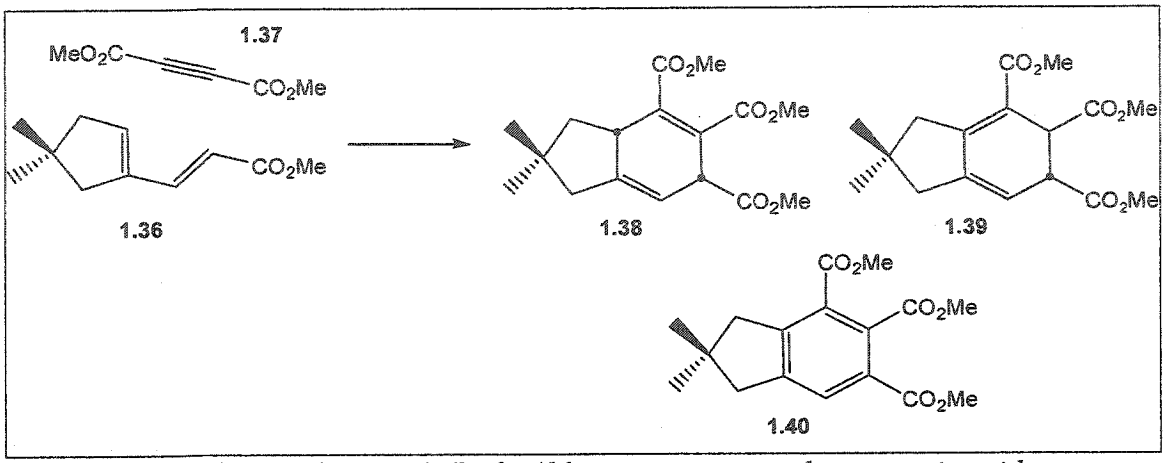
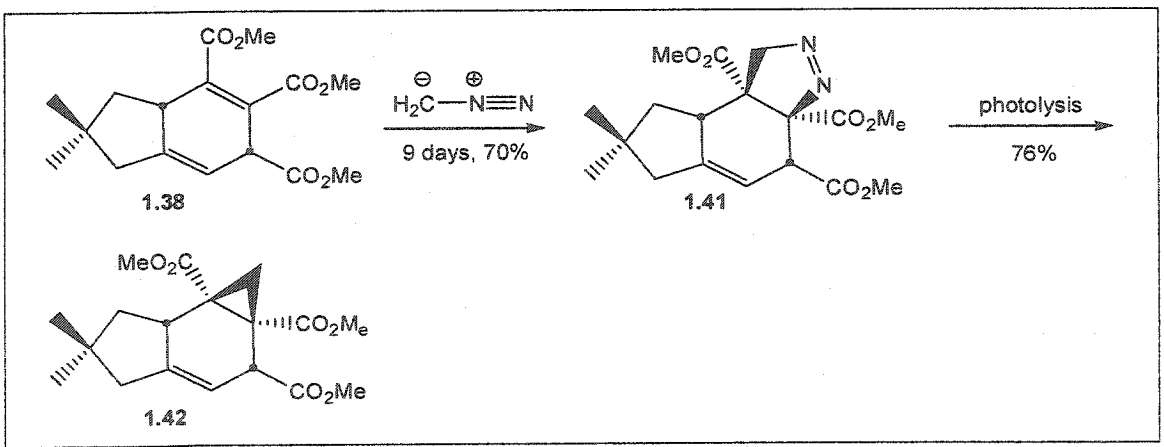
[20] Isolation of marasmic acid see Dugan, J. J.; de Mayo, P.; Nisbet, M. ; Robinson, J. R. ; Anchel, M. *J. Am. Chem. Soc.* **1966**, *88*, 2383 and references therein.
[21] Isolation of isovelleral, see Magnusson, G.; Thorén, S.; Wickberg, B. *Tetrahedron Lett.* **1972**, 1105. For a review on marasmanes and lactaranes, see Ayer, W. A.; Browne, L. M. *Tetrahedron Lett.* **1981**, *37*, 2199.
[22] Total synthesis of marasmic acid : (a) Greenlee, W. J.; Woodward, R. B. *J. Am. Chem. Soc.* **1976**, *98*, 6075; *Tetrahedron* **1980**, *36*, 3367. (b) Boeckman, R. K., Jr.; Ko, S. S. *J. Am. Chem. Soc.* **1980**, *102*, 7146. (c) Tobe, Y.; Yamashita, D.; Takahashi, T.; Inata, M.; Sato, J.; Kakinchi, K.; Kobiro, K.; Odaira, Y. *J. Am. Chem. Soc.* **1990**, *112*, 775. Total synthesis of isovelleral : (d) Bergman, R.; Hansson, T.; Sterner, O.; Wickberg, B. *J. Chem. Soc., Chem. Commun.* **1990**, 865. (e) Thompson, S.K.; Heathcock, C.H. *J. Org. Chem.* **1990**, *55*, 3004. (f) Thompson, S.K.; Heathcock, C.H. *J. Org. Chem.* **1992**, *57*, 5979. (g) Bell, R. P. L.; Wijnberg, J. B. P. A.; de Groot, A. *J. Org. Chem.* **2001**, *66*, 2350.
[23] Wilson, S. R.; Turner, R. B. *J. Org. Chem.* **1973**, *38*, 2870.

benzene overnight, or stirred neat for 3 days under N_2, products **1.39** and **1.40** were obtained in 60% yield and 40% yield respectively.



Scheme 1.6: Wilson and Turner's Diels-Alder reaction towards marasmic acid.

In this example, the selective formation of stereogenic centers during the Diels-Alder reaction was not problematic since the symmetrical alkyne **1.37** was utilized as dienophile. Furthermore, they envisioned creating the cyclopropane via a 1,3-dipolar cycloaddition with diazomethane, followed by photolysis (Scheme 1.7). Due to steric interactions, Wilson and Turner anticipated the *exo* product to be the predominant cycloadduct. Stereospecific decomposition of pyrazoline **1.41** presumably afforded the desired cyclopropane **1.42**.



Scheme 1.7: Installation of the cyclopropane via a 1,3-dipolar cycloaddition.

Over a period of seven years, Wilson and Turner believed that they had constructed the first stereospecific skeleton of marasmic acid. During that time frame, Greenlee and Woodward[22a] were also actively attempting the total synthesis of marasmic acid via the same approach as described above.

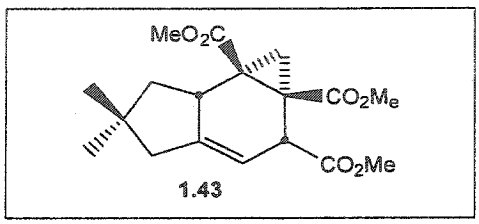
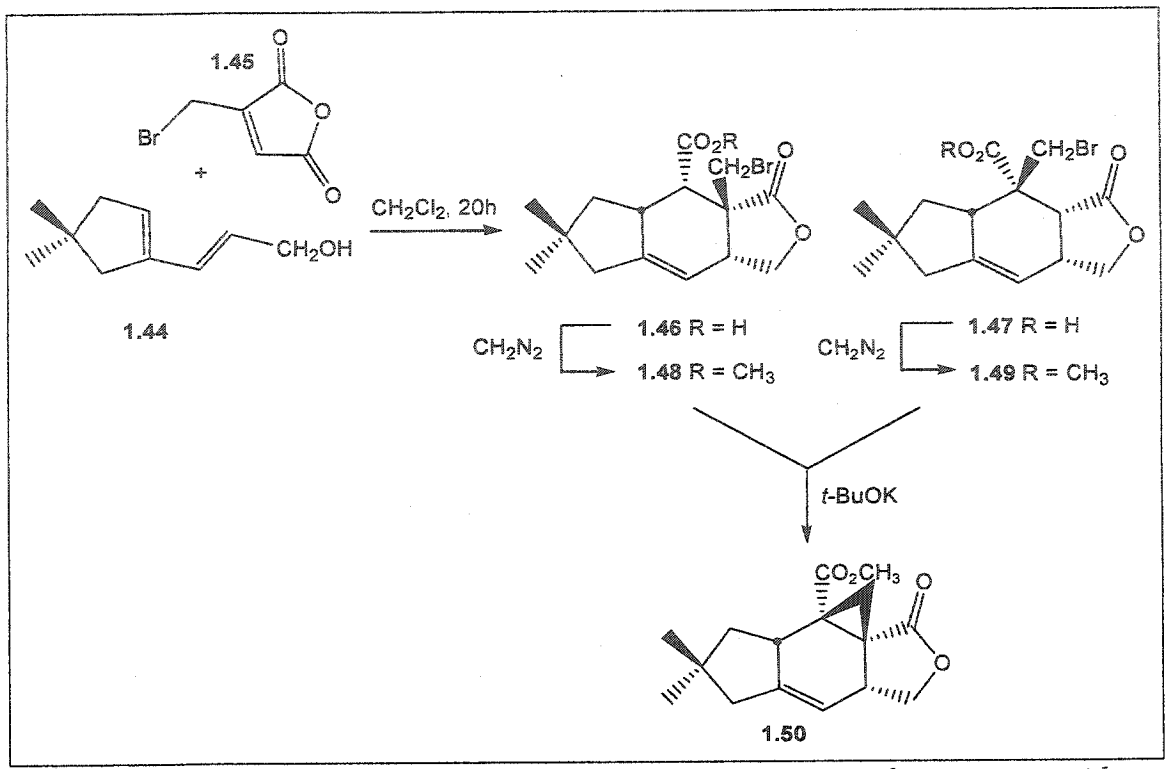


Figure 1.8: *(±)-Isomarasmic acid*

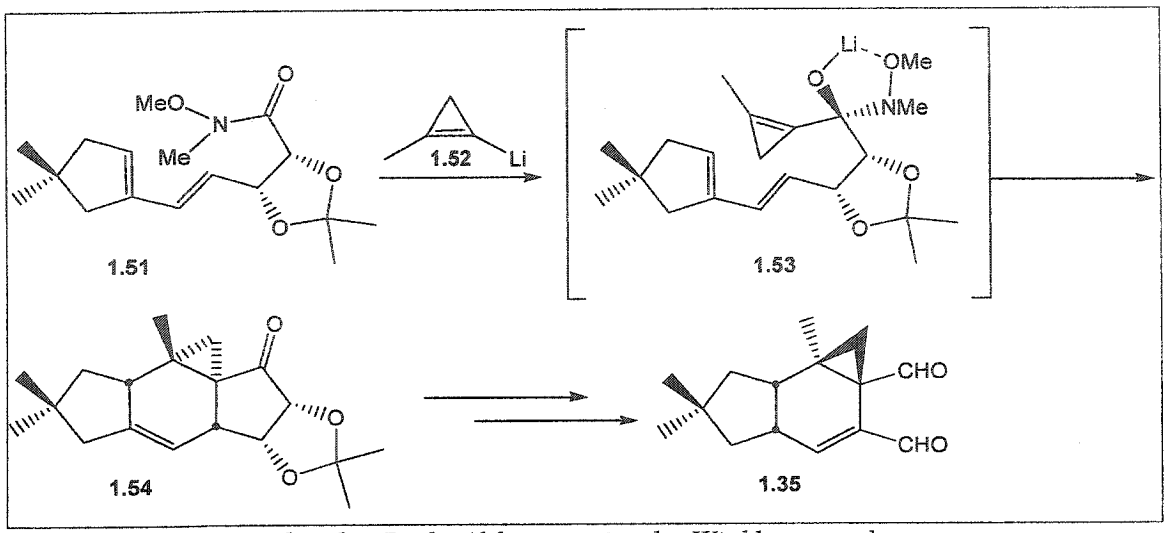
NMR studies with a lanthanide shift reagent showed that Wilson and Turner's stereochemical assignment was questionable and their cycloadduct is currently believed to be the (±)-isomarasmic acid skeleton **1.43** (Figure 1.8). The selectivity during the Diels-Alder reaction puzzled both groups since they both anticipated the cycloaddition to occur from the least hindered face.

With that result in hand, Greenlee and Woodward successfully synthesized both (±)-isomarasmic acid **1.43** and (±)-marasmic acid **1.34**. The former was achieved by reproducing Wilson and Turner's Diels-Alder and 1,3-dipolar cycloadditions and correctly assigning the resulting stereochemistry. The total synthesis of (±)-marasmic acid **1.34** was achieved via an *endo*-selective Diels-Alder reaction (Scheme 1.8). Using diene alcohol **1.44** and bromomethylmaleic anhydride **1.45**, a non-symmetrical dienophile, cycloadducts **1.46** (39%) and **1.47** (61%) were obtained after 20 hours. Due to the preferred *endo* selectivity, the bromomethylene group was conveniently located *cis* to the ring junction proton. Upon treatment with potassium *tert*-butoxide, bromines **1.48** and **1.49** were displaced to afford the cyclopropane **1.50** in 47% overall yield (from **1.44**).



Scheme 1.8: *Greenlee and Woodward's Diels-Alder reaction towards marasmic acid.*

A parallel approach can also give rise to the hydrindane ring skeleton of (+)-isovelleral **1.35**. Wickberg *et al.*[22d] utilized a sophisticated intramolecular Diels-Alder approach to construct the tricyclic core of isovelleral **1.35** (Scheme 1.9). Treatment of Weinreb amide **1.51** with methylcyclopropenyl-lithium **1.52** in ether at -70°C formed intermediate **1.53**. As the reaction mixture was warmed to room temperature, a spontaneous intramolecular Diels-Alder reaction afforded the pentacyclic ketone **1.54** in 65% yield. Similar to Wilson and Turner's approach, the *exo*-selectivity was preferred and afforded a diastereomer of the isovelleral core. The efficiency of this total synthesis was diminished since additional steps were required to transform **1.54** into isovelleral **1.35**.



Scheme 1.9: *Intramolecular Diels-Alder reaction by Wickberg et al.*

As demonstrated above, the Diels-Alder reaction is a powerful tool for the construction of polycyclic skeletons bearing stereogenic centers. The hydroxy-directed Diels-Alder reaction will be studied towards the synthesis of isovelleral analogues and the total synthesis of havellockate, and will therefore be discussed in the corresponding chapters.

Chapter 2: Studies on the Tandem Oxy-Cope/Ene/Claisen Reaction

2.1 Background

The construction of asymmetric quaternary carbon centers has perplexed synthetic chemists for numerous years. Several methods have been developed[24] in order to generate these challenging quaternary centers during carbon-carbon bond formation. Denissova and Barriault[8] have recently reported a method to construct decalin skeletons possessing quaternary carbon centers (Figure 2.1). This domino reaction is triggered by an oxy-Cope rearrangement of allyl-1,2-divinylcyclohexanol **2.1** followed by tautomerization to provide the 10-membered cycle **2.2**. The successive stereoselective transannular ene reaction of **2.2** gives exclusively *E* enol ether **2.3**, which can subsequently undergo a Claisen rearrangement to afford lactol **2.4**.

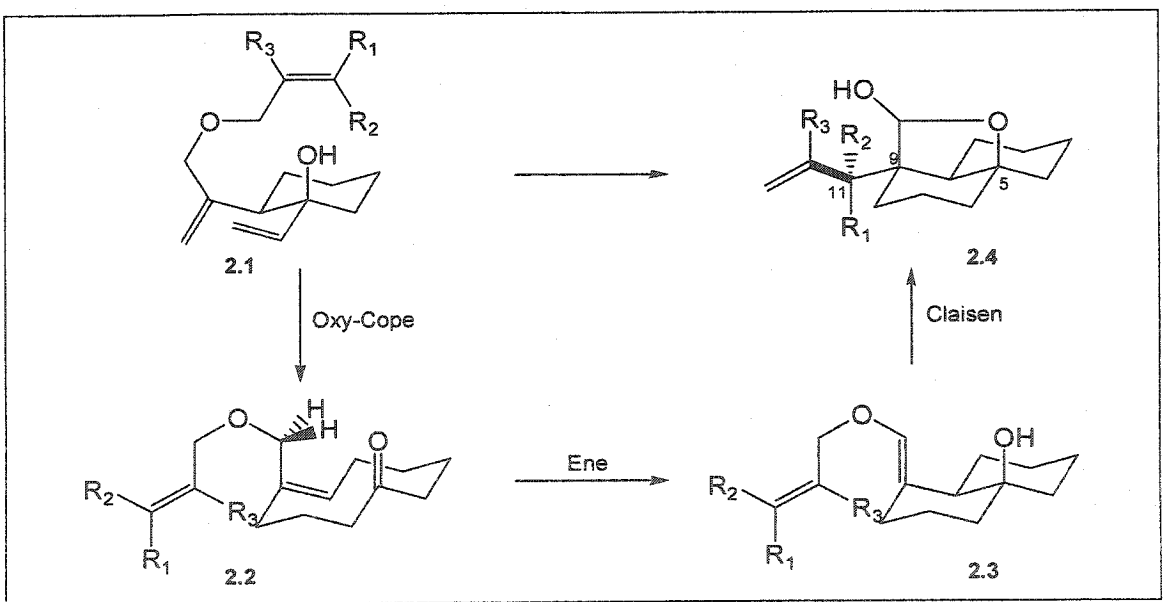
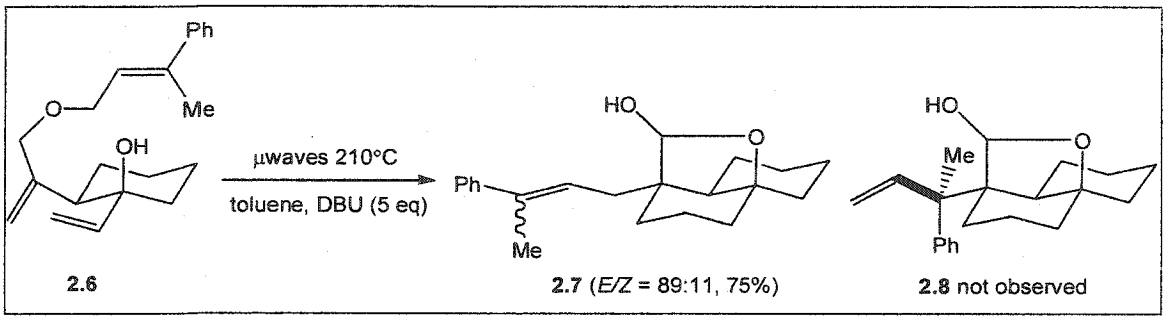


Figure 2.1: *The Tandem Oxy-Cope/Ene/Claisen Reaction.*

[24] For a review see (a) Denissova, I.; Barriault, L. *Tetrahedron* **2003**, *59*, 10105. (b) Martin, S. F. *Tetrahedron* **1980**, *36*, 419. (c) Corey, E. J.; Guzman-Perez, A. *Angew. Chem. Int. Ed.* **1998**, *110*, 402. (d) Christoffers, J.; Mann, A. *Angew. Chem. Int. Ed.* **2001**, *40*, 4591. (e) Christoffers, J.; Baro, A. *Angew. Chem. Int. Ed.* **2003**, *42*, 1688.

In cases using *trans*-disubstituted allyl ethers, lactols **2.4** were obtained in good chemical yields and high diastereoselectivity at C-5, C-9 and C-11. When R_1 and R_2 = Me, the desired lactol **2.4** and enol ether **2.3** were afforded in 76% and 15% yield respectively. Surprisingly, when trisubstituted allyl ether **2.6** was irradiated with microwaves, decalin **2.8** was not produced. Instead, lactol **2.7** was isolated in 75% yield (Scheme 2.1). In addition, isomerization of the trisubstituted olefin (*E*/*Z* = 89:11) was observed during the course of the reaction. These results suggest that a competing radical 1,3-shift is involved in the thermal process.



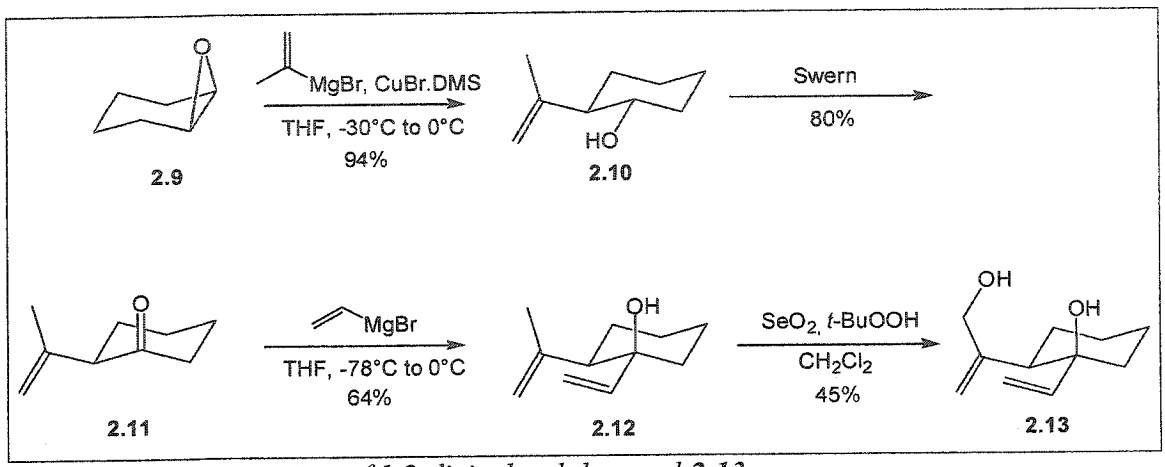
Scheme 2.1: *Microwave irradiation of the trisubstituted allyl ether* ***2.6****.*

The scope and limitations of this method have been studied to elucidate mechanistic pathways and competing reactions. The substitution pattern of the terminal alkene has been varied and the precursors have been subjected to microwave irradiation and conventional heating in a sealed tube immersed in a wax bath.

2.2 Preparation of the Allyl Ethers

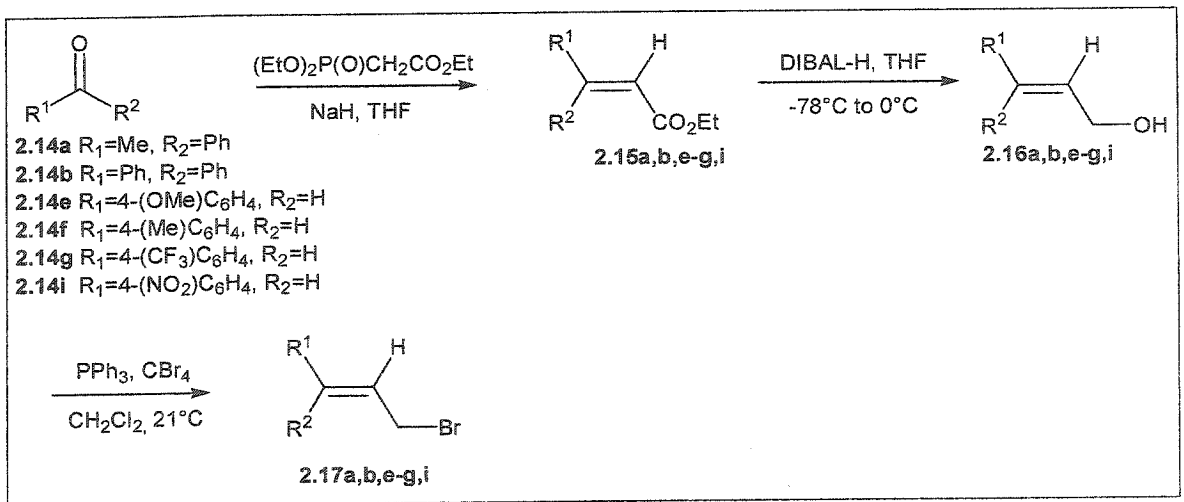
The 1,2-divinylcyclohexanol **2.13** was prepared via a series of Grignard and oxidation reactions (Scheme 2.2). Initially, cyclohexene oxide **2.9** was treated with copperbromide dimethylsulfide and isopropenylmagnesium bromide to afford alcohol **2.10** in 94% yield. The alcohol subsequently underwent a Swern oxidation to provide ketone **2.11** in 80% yield. A second Grignard reaction was performed on **2.11** in order to

introduce an equatorial vinyl group adjacent to the isopropenyl group to give alcohol **2.12** in 64% yield. Allylic oxidation of **2.12** with selenium dioxide afforded the desired 1,2-divinylcyclohexanol **2.13** in 45% yield.



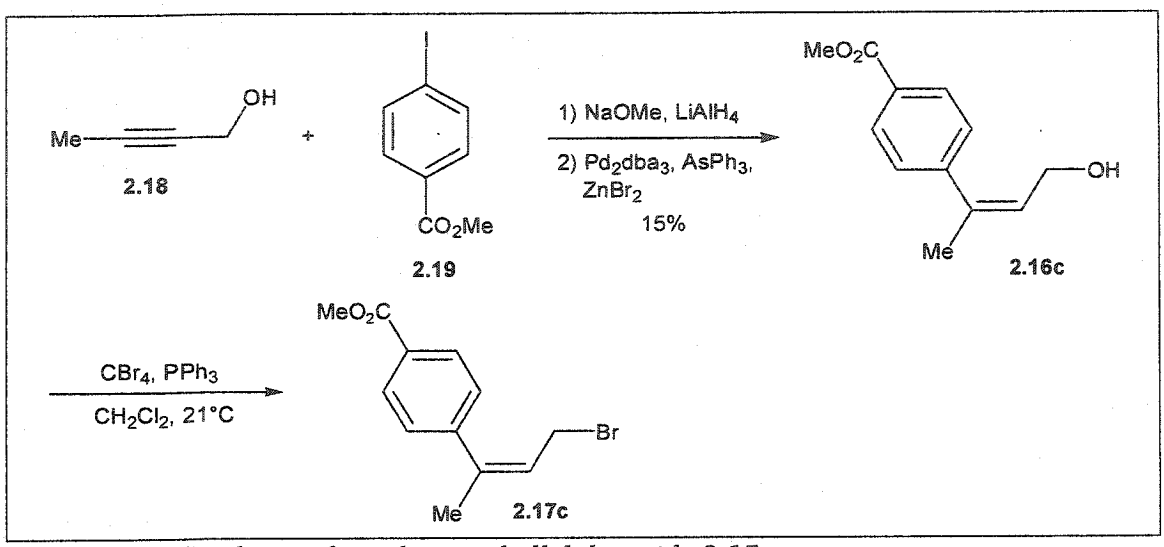
Scheme 2.2: *Preparation of 1,2-divinylcyclohexanol 2.13.*

At this stage, various allylbromides were prepared according to Schemes 2.3, 2.4, 2.5 and 2.6 Exposure of ketones (**2.14a,b,e-g,i**) to triethylphosphonoacetate and sodium hydride in THF afforded di- and trisubstituted alkenes **2.15a,b,e-g,i** in 10%-93% yields (Scheme 2.3). Following reduction of the ethyl ester groups with DIBAL-H, the allylic alcohols **2.16a,b,e-g,i** were transformed into the corresponding allyl bromides **2.17a,b,e-g,i** using CBr_4 and PPh_3 and were used without purification towards the next step.



Scheme 2.3: *General procedure for the synthesis of allyl bromides 2.17.*

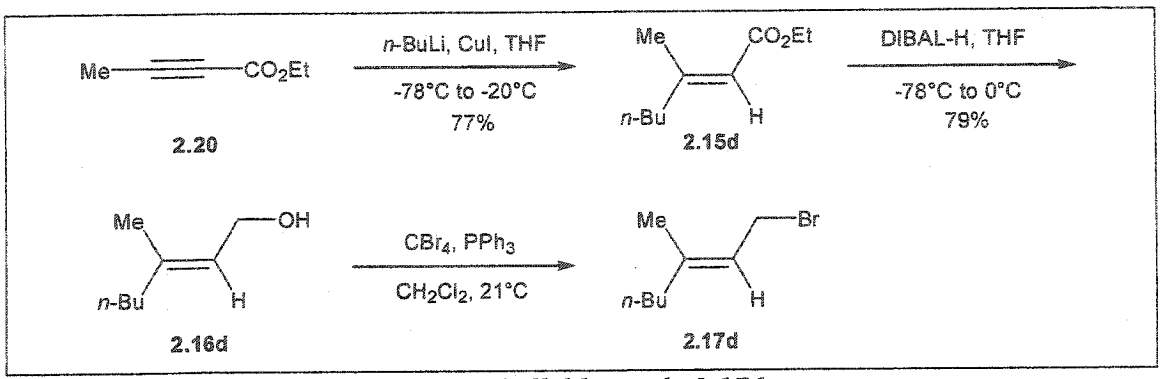
Trisubstituted allyl bromides **2.17c** and **2.17d** were synthesized using different procedures described in Scheme 2.4 and Scheme 2.5. According to Dvorak's methodology[25], hydroalumination and subsequent palladium-catalyzed coupling of butynol **2.18** and 4-iodobenzoic acid **2.19** generated allylic alcohol **2.16c** in 15% yield (Scheme 2.4). Exposure of allylic alcohol **2.16c** to CBr_4 and PPh_3 afforded allylic bromide **2.17c** which was used without purification towards the next step.



***Scheme 2.4:** Synthesis of trisubstituted allyl bromide **2.17c**.*

Stereoselective addition of the organocopper reagent to acetylenic ester **2.20** afforded the olefin **2.15d** in 77% yield (Scheme 2.5).[26] The conjugated ester **2.15d** subsequently underwent a reduction and bromination to provide the crude allylic bromide **2.17d**.

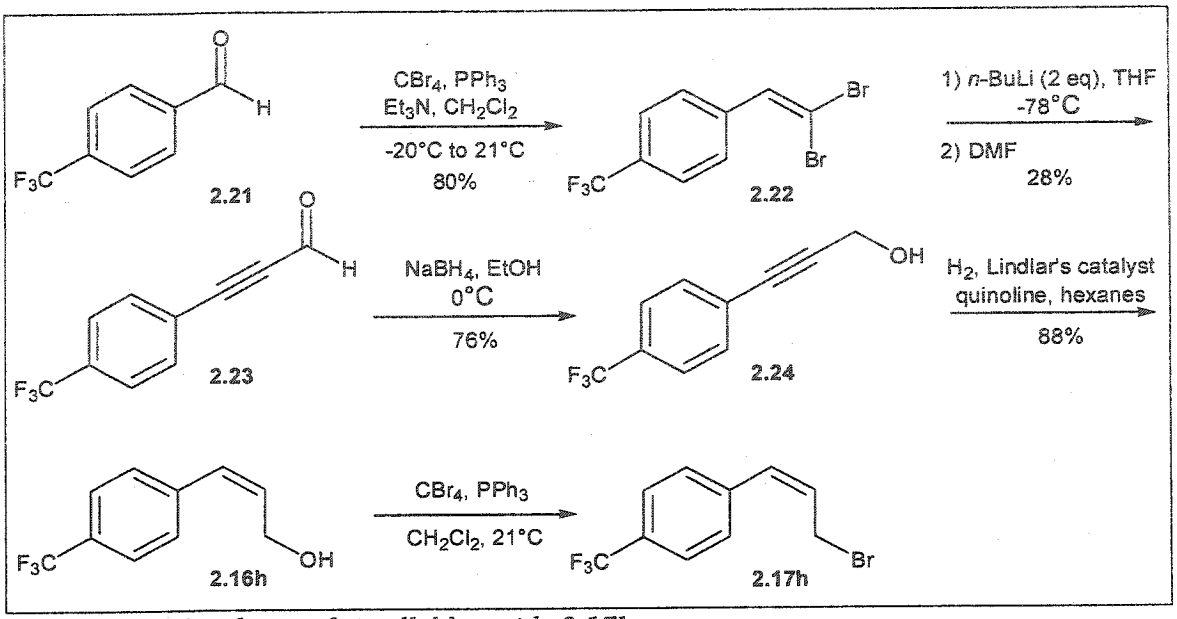
[25] Dvorak, D.; Havranek, M. *J. Am. Chem. Soc.* **2002**, *67*, 2125-2130.
[26] Anderson, R.J.; Corbin, V.L.; Cotterell, G.; Cox, G.R.; Henrick, C.A.; Schaub, F.; Siddall, J.B. *J. Am. Chem. Soc.* **1975**, *97*, 1197-1204.



Scheme 2.5: Synthesis of trisubstituted allyl bromide 2.17d.

In order to prepare *cis* alkene **2.17h** bearing an electron withdrawing group on the aryl, a different procedure was also required (Scheme 2.6). A modified Corey-Fuchs[27] reaction with 4-trifluoromethylbenzaldehyde **2.21** afforded dibromo **2.22** (80% yield) and the latter was reacted with 2 equivalents of *n*-BuLi. After the formation of the acetylenic anion, dimethylformamide was added to generate aldehyde **2.23**. After reduction with sodium borohydride, the alkyne **2.24** was reduced to *cis* alkene **2.16h** using Lindlar's catalyst and H_2. In order to control the reaction and avoid complete reduction to the alkane, the catalyst was poisoned with quinoline. As previously described, the resulting allylic alcohol **2.16h** was converted to allyl bromide **2.17h** and was used without purification for the etherification of diol **2.13**.

[27] Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, *36*, 3769.

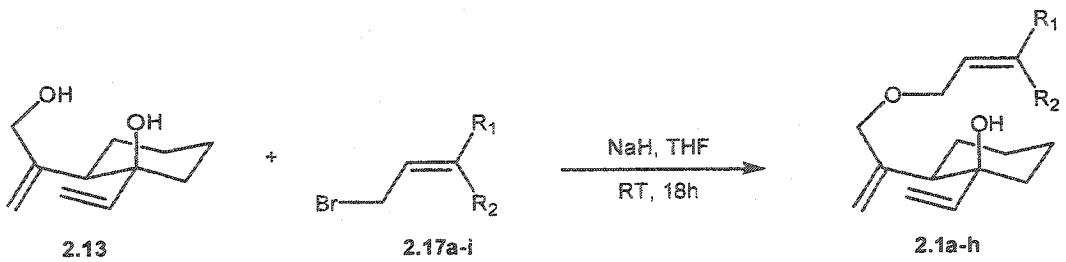


Scheme 2.6: Synthesis of cis allyl bromide 2.17h.

2.3 The Tandem oxy-Cope/Ene/Claisen Reaction: Results and Discussion

Exposure of 1,2-divinylcyclohexanol **2.13** to various allylbromides **2.17a-i** and sodium hydride in THF afforded the desired allyl ethers **2.1a-h** in yields ranging from 46% to 95% (Table 2.1). Surprisingly, etherification reaction of **2.13** with allyl bromide **17i** gave a complex mixture from which no allyl ether **2.1i** was isolated.

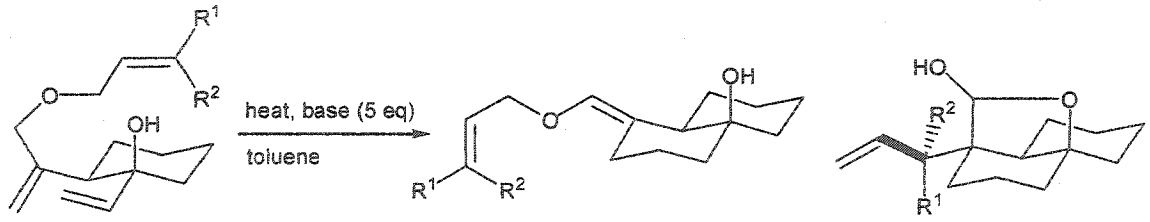
Table 2.1: Preparation of the tandem reaction precursors.



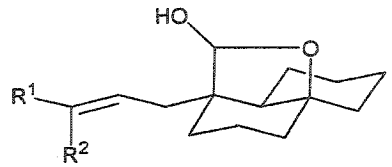
entry	allyl bromide	R_1	R_2	product	Yield %
1	**2.17a**	Me	Ph	**2.1a**	65
2	**2.17b**	Ph	Ph	**2.1b**	68
3	**2.17c**	4-$(CO_2Me)C_6H_4$	Me	**2.1c**	46
4	**2.17d**	Bu	Me	**2.1d**	76
5	**2.17e**	4-$(OMe)C_6H_4$	H	**2.1e**	71
6	**2.17f**	4-$(Me)C_6H_4$	H	**2.1f**	75
7	**2.17g**	4-$(CF_3)C_6H_4$	H	**2.1g**	95
8	**2.17h**	H	4-$(CF_3)C_6H_4$	**2.1h**	55
9	**2.17i**	4-$(NO_2)C_6H_4$	H	**2.1i**	degradation

The allyl-1,2-divinylcyclohexanols **2.1a-h** were dissolved in toluene in the presence of 5 equivalents of base (Et_3N or DBU). After degassing the solution with argon for 15 minutes, the reaction mixture was irradiated with microwaves in a quartz cell at 210°C for 1h (method A) or heated at 210°C in a sealed tube immersed in a wax bath for 18-24h (method B). The results are summarized in Table 2.2. All resulting lactols **2.4a-e** and **2.5a,b** were oxidized to the lactones with TPAP to correctly identify the isomerization and epimerization ratios.

Table 2.2: Tandem Oxy-Cope/Ene/Claisen Reaction of Allyl-1,2-divinylcyclohexanols.



2.1a-h 2.3 2.4



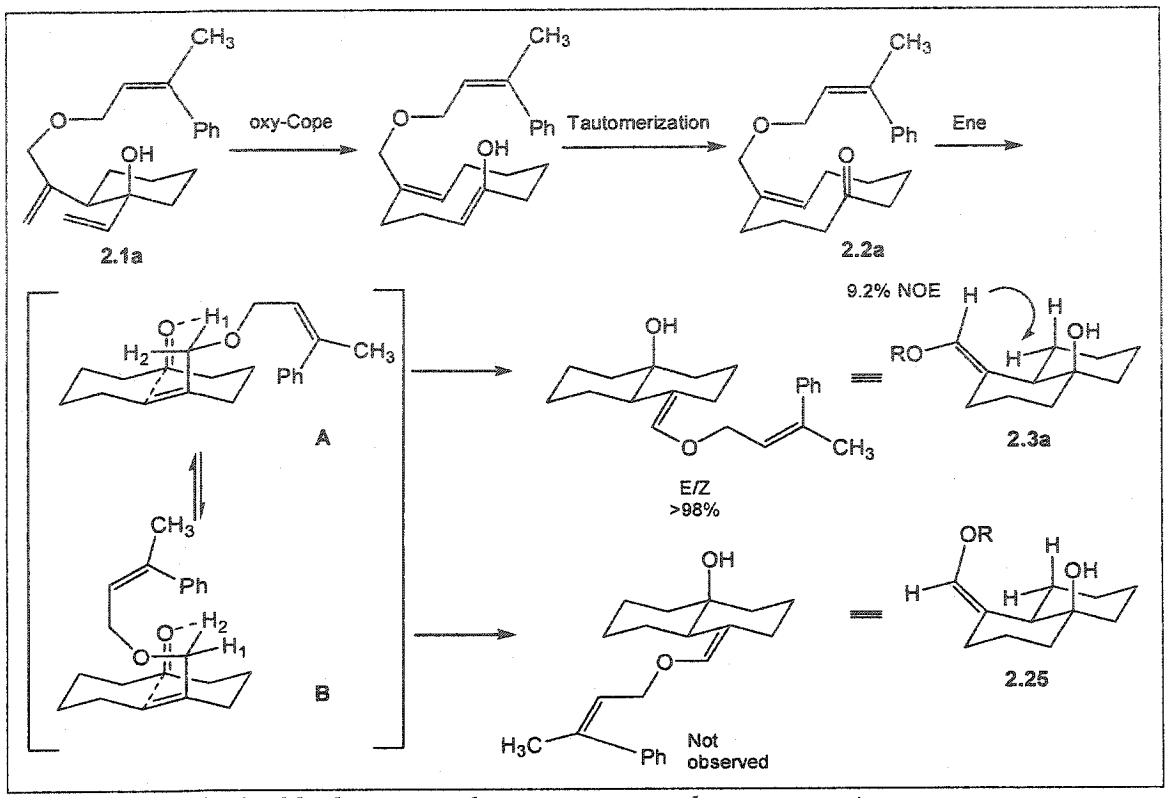
2.5

entry	substrate	R_1	R_2	method	product	yield
1	**2.1a**	Me	Ph	A[a]	**2.5a** and **2.3a**	34% (*E*/*Z* = 56:44) and 51%
2	**2.1b**	Ph	Ph	A[a]	**2.5b**[e]	24%
3	**2.1b**	Ph	Ph	B[b]	**2.5b** and **2.3b**	13% and 10%
4	**2.1c**	4-$(CO_2Me)C_6H_4$	Me	A[b] or B[b]	degradation	---
5	**2.1d**	Bu	Me	A[b]	**2.3d**	24%
6	**2.1d**	Bu	Me	B[b]	**2.3d**	51%
7	**2.1e**	4-$(MeO)C_6H_4$	H	A[b]	degradation	---
8	**2.1e**	4-$(MeO)C_6H_4$	H	B[b]	**2.4e**	50% (*dr* = 9:1)[f]
9	**2.1e**	4-$(MeO)C_6H_4$	H	B[c]	degradation	---
10	**2.1e**	4-$(MeO)C_6H_4$	H	B[d]	degradation	---
11	**2.1f**	4-$(Me)C_6H_4$	H	A[b]	**2.4f**	36% (*dr* = 4:1)[f]
12	**2.1f**	4-$(Me)C_6H_4$	H	A[d]	**2.4f**	63% (*dr* >25:1)[f]
13	**2.1f**	4-$(Me)C_6H_4$	H	B[d]	degradation	---
14	**2.1g**	4-$(CF_3)C_6H_4$	H	A[b]	degradation	---
15	**2.1g**	4-$(CF_3)C_6H_4$	H	B[b]	**2.4g**	98% (*dr* >25:1)[f]
16	**2.1h**	H	4-$(CF_3)C_6H_4$	A[b]	**2.4h**	99% (dr >25:1)[f]
17	**2.1h**	H	4-$(CF_3)C_6H_4$	B[b]	**2.4h**	51% (dr >25:1)[f]

[a] DBU. [b] Et_3N. [c] 2,6-Lutidine. [d] No base. [e] The dimer **(2.26b)** $(C(Ph)_2{=}CHCH_2)_2$ was isolated in 20%. [f] Diastereomeric ratios at C-11 were determined by 300 MHz ^1H NMR spectrum of the corresponding lactone.

Microwave irradiation of **2.1a**, bearing a *Z*-trisubstituted alkene, afforded the 1,3-shift product **2.5a** (*E*/*Z* = 56:44) and *E*-enol ether **2.3a** in 34% and 51% yields respectively (entry1). This result was slightly different than the reaction depicted in Scheme 2.1. When the corresponding *E*-trisubstituted alkene **2.6** was irradiated with microwaves, lactol **2.7** was obtained with isomerization (*E*/*Z* = 89:11) and the enol ether intermediate nor the 3,3-shift product **2.8** were never observed. Isolation and characterization of *E*-enol ether **2.3a** by NOE demonstrated the high diastereoselectivity of the transannular ene process (Scheme 2.7).

After the oxy-Cope reaction, macrocyclic ketone **2.2a** can adopt two reactive conformations at the transition state, **A** and **B**. A close examination of transition state **A** reveals that the O-allyl group is oriented in the pseudo-equatorial position where as in transition state **B**, it is in the pseudo-axial position. This causes severe steric interactions which favours an energetically lower transition state, such as **A**. The formation of **2.3a** over **2.25** is then readily explained.



Scheme 2.7: *The highly diastereoselective transannular ene reaction.*

Irradiation of **2.1b** also gave the 1,3-shift product **2.5b** along with dimer **2.26b** in 24% and 20% yield respectively (entry 2). Irradiation or heating of **2.1d** afforded exclusively *E*-enol ether **2.3d** in 24% (method A) and 51% (method B) (entries 5 and 6). In order to drive the reaction to completion, enol ether intermediates **2.3d** were subjected to prolonged heating, which unfortunately led to degradation. In both cases, no products resulting from a 1,3- or 3,3-shift were observed in the crude reaction mixture.

Much to our delight, the formation of dimer **2.26b** and decalins **2.5a** and **2.7** confirmed our assumption that the 1,3-shift implied formation of an oxaallyl-allyl radical pair (Figure 2.2).[28]

[28] (a) Gajewski, J.J.; Conrad, N.D. *J. Am. Chem. Soc.* **1979**, *101*, 2747. (b) Barluenga, J.; Aznar, F.; Liz, R.; Bayod, M. *J. Org. Chem.* **1987**, *52*, 5190. (c) Gajewski, J.J. *Acc. Chem. Res.* **1997**, *30*, 219.

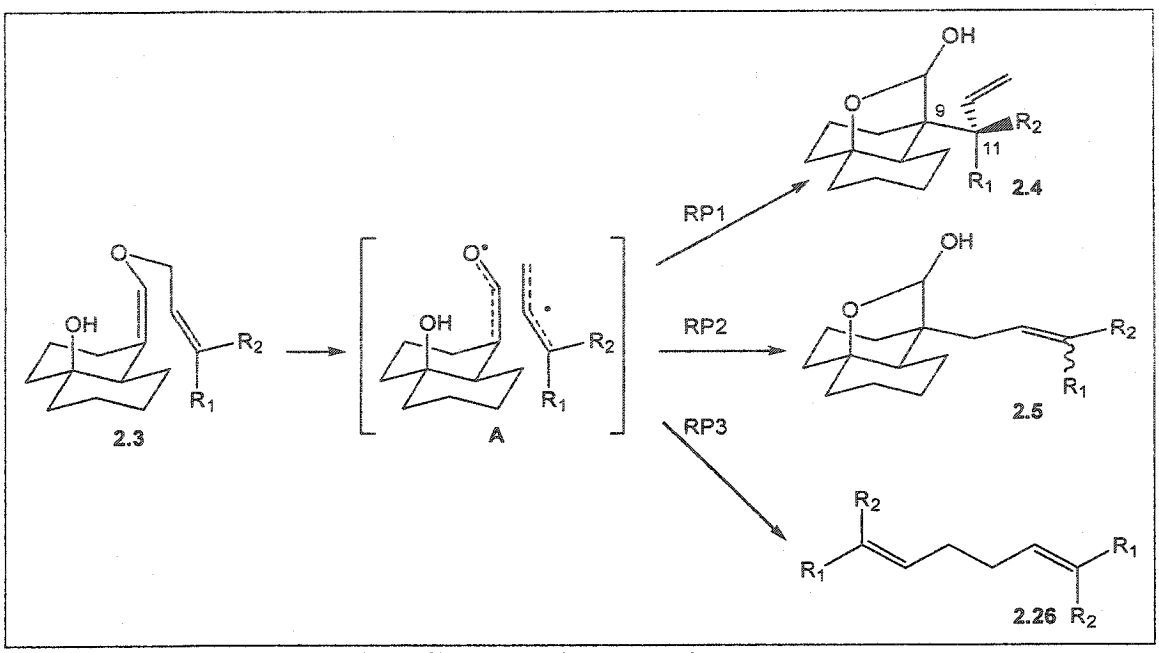


Figure 2.2: *Proposed oxaallyl-allyl radical pair mechanism.*

As illustrated in Figure 2.3, Gajewski's model depicts that the Claisen rearrangement occurs via an early chair-like transition state. During his study, the use of kinetic isotope effects demonstrated that the C_4-O bond breaks faster than the formation of the C_1-C_6 bond when radical stabilizing subtituents are present on the carbon skeleton **2.27**. These results indicate the formation of an oxaally-allyl radical pair may be preferred over the traditional concerted mechanism.

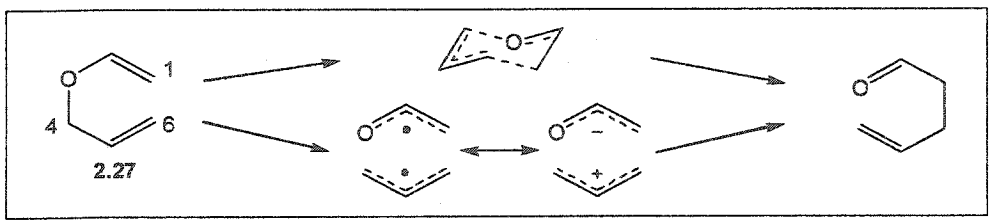


Figure 2.3: *Gajewski's model.*

Homolytic cleavage of the C-O bond in **2.3** would produce the oxallyl-allyl radical intermediate **A** which can recombine to form the 3,3-, 1,3- or dimer products (**2.4**, **2.5** and **2.26**) respectively *via* three energetically distinct reaction pathways RP1, RP2 and RP3 (Figure 2.2).

In the case of disubtituted allyl ethers **2.1e-h**, the substrate undergoes the tandem oxy-Cope/ene/Claisen reaction to afford the desired lactols **2.4e-h**. Since the terminal alkene of the enol ether **2.3e-h** of this process does bear radical stabilizing substituents, the 3,3-shift may involve a radical pair which recombines via RP1 to generate decalins **2.4a-h**. In contrast, when the precursors to the tandem reaction carry sterically demanding subtituents, i.e. trisubstituted allyl ethers (entries 1-6), the energetically lower 1,3-shift competes with the 3,3-shift to afford **2.5** via RP2. In the case of trisubstituted allyl ether **2.1b** having gem-diphenyl (R_1=R_2=Ph), the formation of dimer **2.26** via RP3 was also observed. As illustrated in Figure 2.2, severe steric interactions are developed between the enol ether rings **2.3** and substituents R_1 and R_2 in the transition state. These interactions are responsible for increasing the energy level of the [3,3]-sigmatropic rearrangement and thus favouring the 1,3-shift (Figure 2.4).

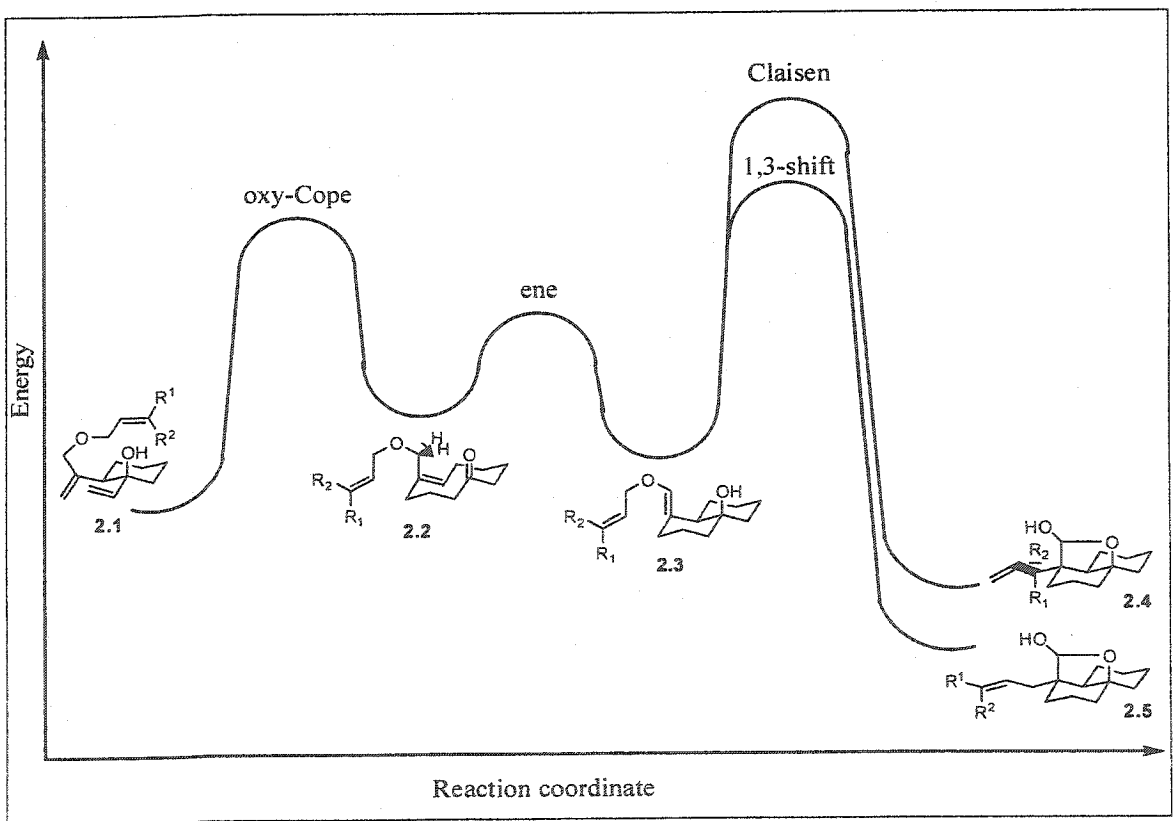
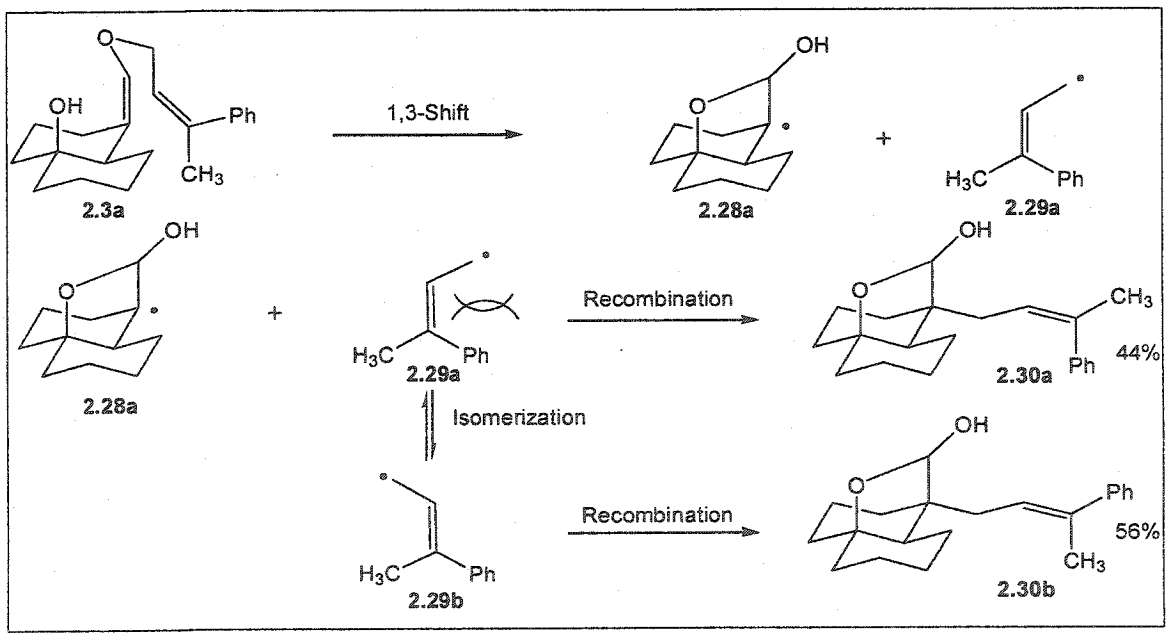


Figure 2.4: Energy diagram of the oxy-Cope/ene/Claisen and 1,3-shift reaction.

During this sequence of events, homolytic cleavage of the C-O bond in **2.3a** generates two radical species **2.28a** and **2.29a** (Scheme 2.8). The oxygen radical quickly rearranges to afford a stabilized tertiary radical and lactol **2.28a**. During this time, the allyl radical **2.29a** can isomerizes to **2.29b** before recombining with the radical decalin **2.28a**. Due to the fact that both decalins **2.30a** and **2.30b** are not obtained with an identical *E/Z* ratio (89:11 vs 56:44), this result indicates that the recombination rate of the oxaallyl-allyl radical pairs competes with the allyl radical isomerization rate. In other words, if this reaction followed Curtin-Hammett's principle[29] and the isomerization equilibrium of the allyl radicals was fast, both allyl ethers **2.3a** and **2.6** should have given decalins **2.5a** and **2.7** in identical *E/Z* ratios.



Scheme 2.8: Isomerization and recombination of the radical pairs.

As mentioned previously, isolation of dimer **2.26b**, which was created by the recombination of both allyl radical moieties, also indicated the presence of radical

[29] Curtin, D.Y. *Rec. Chem. Prog.* **1954**, *15*, 111.

intermediates. These general results demonstrated that the reaction pathway is highly dependent on the degree of substitution of the allyl moiety.

In addition to steric interactions, the heating source greatly influenced the outcome of the reaction. Irradiation of **2.1b** with microwaves afforded **2.5b** (24%) and the dimer **2.26b** (20%) whereas heating **2.1b** in the sealed tube generated **2.5b** (13%) and enol ether **2.3b** (10%). Interestingly, enol ether **2.3b** was diluted in dichloromethane with catalytic trimethylaluminum and afforded the 1,3-shift product **2.5b** at room temperature.

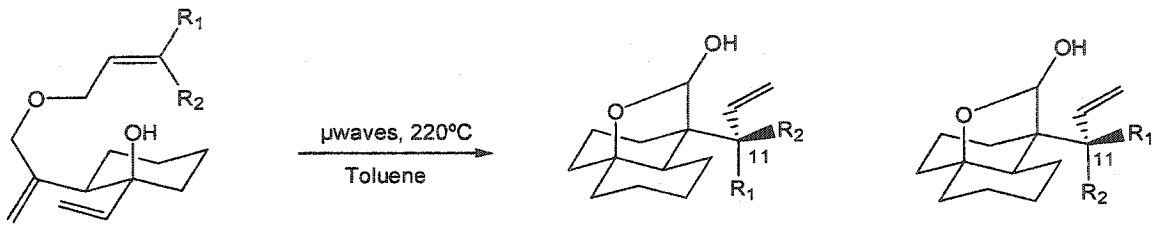
Irradiation of **2.1e** with microwaves gave a complex mixture from which no decalin **2.4e** was isolated (entry 7). In contrast, heating of **2.1e** in a sealed tube at 210°C gave the desired product **2.4e** in 50% yield as a mixture of diasteromers (9:1) at C-11 (entry 8). When triethylamine was replaced by 2,6-lutidine (entry 9) or performing the reaction without base (entry 10), starting material **2.1e** degraded without observing a trace of product. In the case of allyl ether **2.1f**, decalin **2.4f** was only obtained when microwave irradiation was used as source of heating (method A) (entries 11-13). Interestingly, *trans*-allyl ether **2.1g** was completely converted to desired decalin **2.4g** in 98% yield (dr > 25:1) using method B (entries 14 and 15). On the other hand, method A was required to convert **2.1h** to **2.4h** in quantitative yield (entry 16), since method B afforded **2.4h** in 51% yield (entry 17).

In some cases, a loss of selectivity was observed at C-11 (entries 8 and 11). It was initially hypothesized that the epimerization was due to the presence of base. Therefore, an experiment was conducted without base (entry 12) and the resulting lactol **2.4f** was generated in excellent diastereoselectivity (dr > 25:1). These results were

puzzling because the presence of electron donating substituents on the aryl group should decrease stabilization of the anion at C-11 and thus disfavoured epimerization.

On the other hand, when electron withdrawing subtituents were present on the aryl group (entries 15-17), the diastereoselectivity observed was surprisingly excellent (dr > 25:1). One would expect greater epimerization in these cases since the anion created on C-11 during epimerization would be stabilized by the withdrawing effect of trifluoromethane.

Table 2.3: Denissova's deuterium and temperature study.



2.31 **2.33** **2.35**

entry	substrate	R_1	R_2	T °C	Yield[a]	Ratio A:B
1	**2.31a**	Ph	D	220[b]	44%	2 : 1
2	**2.31a**	Ph	D	220	N.D.	2 : 1
3	**2.31b**	Ph	H	200	40%	11 : 1
4	**2.31b**	Ph	H	180	55%[c]	13 : 1
5	**2.31b**	Ph	H	160	N.R.	--

[a] Yield after oxidation of the lactol with TPAP. [b] 5 Equiv. of triethylamine were used. [c] Reaction not complete, 35% of **2.31b** was recovered.

In order to explain the formation of minor epimer **2.35** at C-11, Denissova conducted as series of experiments (Table 2.3).[30] Deuterium allyl ether **2.31a** was irradiated for 1h at 220°C with and without triethylamine (entries 1 and 2, Table 2.2). In both cases, decalins **2.33a** and **2.35a** were isolated in a ratio of 2:1 and no exchange of deuterium at C-11 was observed. These results were a clear indication that the base was not responsible for the epimerization. When the irradiation temperatures were varied

[30] Farand, J.A.; Denissova, I.; Barriault, L. *Heterocycles* **2004**, *62*, 735.

(entries 3-5), the diastereoselectivity of the Claisen was found to be dependent on the reaction temperature. This suggests that at high temperatures, the boat-like transition state **B** competes with the chair-like transition state **A**, to afford decalins **2.33b** and **2.35b** (Figure 2.5). In other words, less epimerization is observed at lower temperatures since the boat-like transition state, which would afford the undesired epimer **2.35b**, is energetically inaccessible.

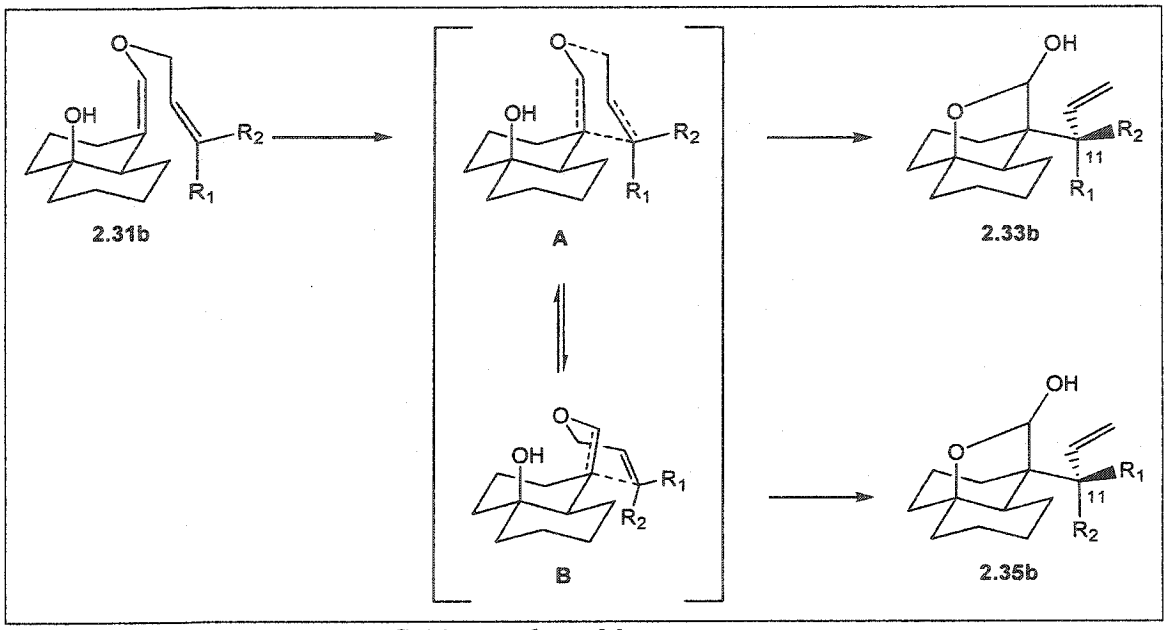


Figure 2.5: *Epimerization at C-11 via a boat-like transition state.*

As depicted in Figure 2.6, energetically higher transition state **B** may afford *Z*-enol ether **2.34** to provide epimer **2.35**. In order to provide evidence that the latter reaction pathway is not followed, ether **2.36** was heated at 220°C for 1 h (Scheme 2.10). ^{1}H NMR of the crude reaction mixture indicated the formation of only one enol ether **2.37** (*E*/*Z* > 98%). These results confirm that the epimerization occurs during the boat-like transition state of the Claisen rearrangement.

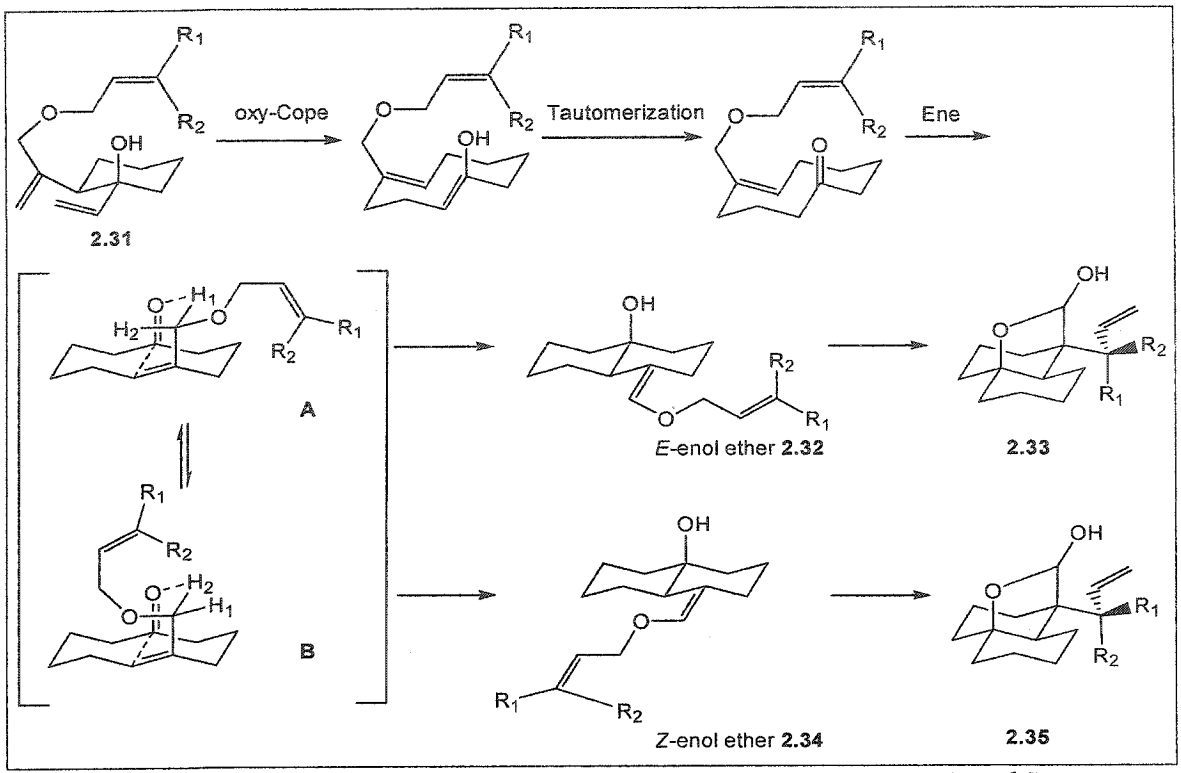
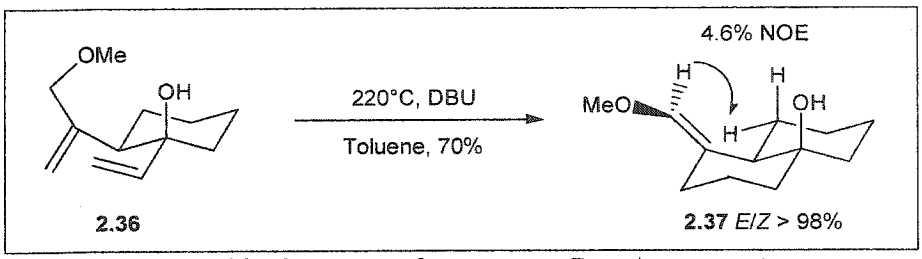


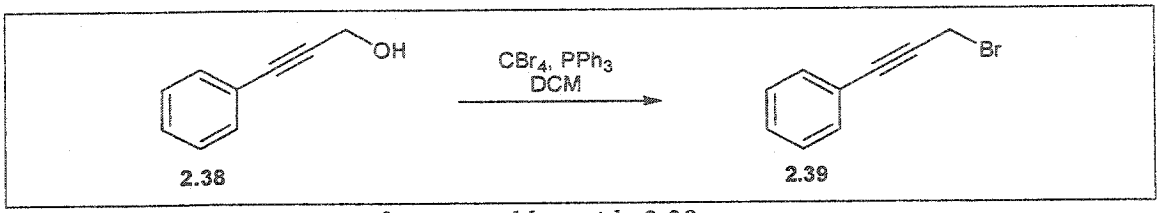
Figure 2.6: *Formation of enol ethers* ***2.32*** *and* ***2.34*** *via transition states* ***A*** *and* ***B****.*



Scheme 2.9: *Highly diastereoselective oxy-Cope/ene reaction.*

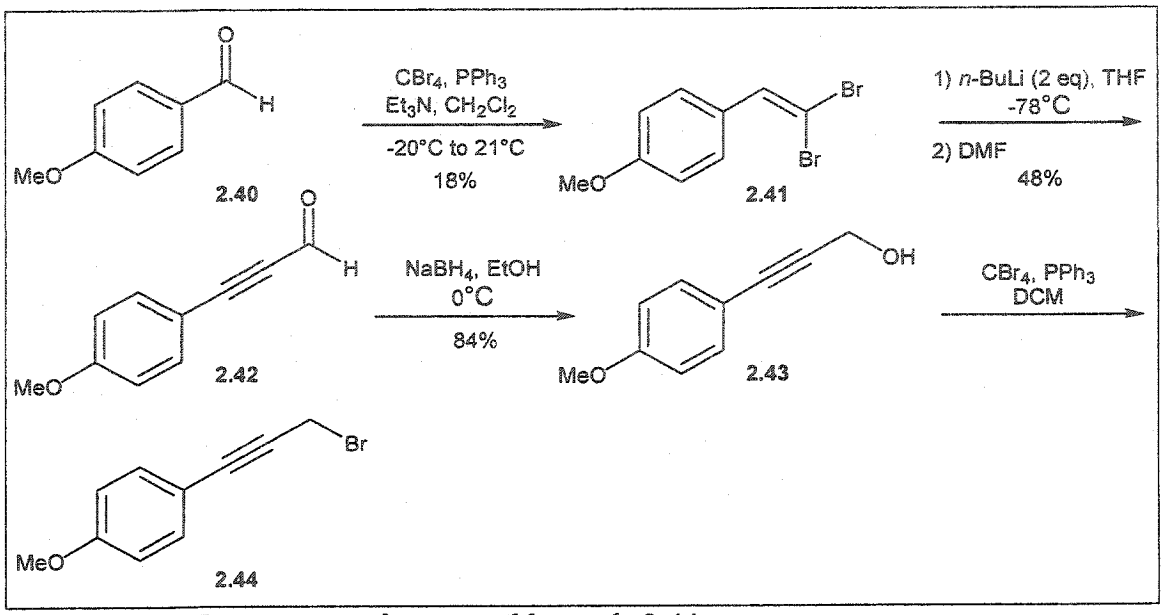
2.4 The Tandem Oxy-Cope/Ene/Claisen Reaction of Propargyl Ethers

In addition to allyl ethers, propargyl ethers can also undergo the tandem oxy-Cope/ene/Claisen reaction. The preparation of the allylic bromides required for the etherification is depicted in Scheme 2.10 and Scheme 2.11.



Scheme 2.10: Preparation of propargyl bromide 2.39.

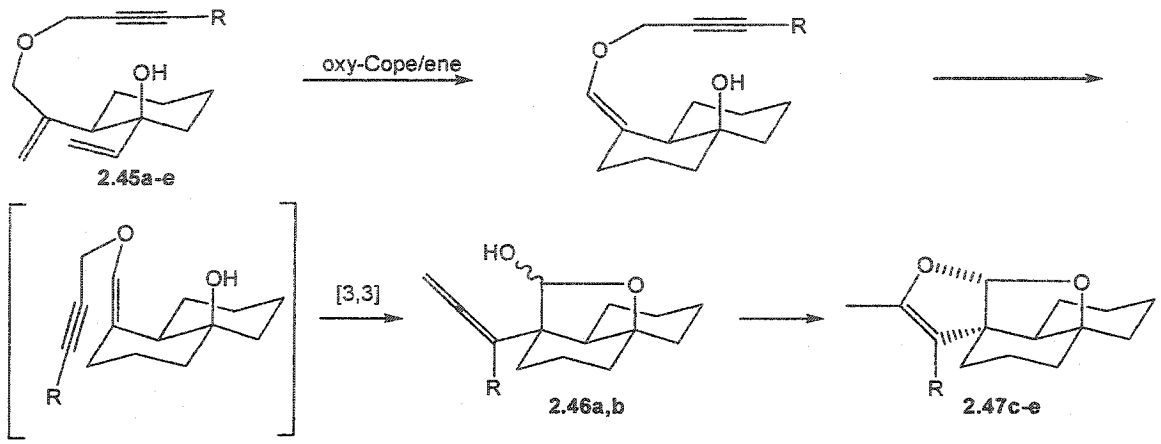
Exposure of the commercially available alkyne **2.38** to carbon tetrabromide and triphenylphosphine in CH_2Cl_2 afforded propargyl bromide **2.39** (Scheme 2.10). The product was subsequently utilized without additional purification. As well, *p*-anisaldehyde **2.40** was treated overnight with carbon tetrabromide, triphenylphosphine and triethylamine in CH_2Cl_2 to yield dibromo **2.41** in 18% yield (Scheme 2.11). The lengthy reaction time was responsible for the degradation of the majority of the product and should therefore not exceed 5 hours. Dibromo **2.41** reacted with *n*-BuLi and the intermediate was quenched with DMF to afford aldehyde **2.42** in 48% yield. Reduction of aldehyde **2.42** with sodium borohydride in ethanol generated alcohol **2.43** in 84% yield. Bromination of alcohol **2.43** afforded propargyl bromide **2.44** and was used without purification towards the etherification with diol **2.13**.



Scheme 2.11: *Preparation of propargyl bromide 2.44.*

Etherification of 1,2-divinylcyclohexanol **2.13** and propargyl bromides **2.39** and **2.44** in the presence of sodium hydride afforded the precursors to the tandem reaction **2.45a** and **2.45b** in 59% and 80% yields respectively. Propargyl ethers **2.45a-e** were irradiated with microwaves for 1h to provide decalins **2.46a,b** and **2.47c-e** in high yield (dr > 25:1) (Table 2.4). The formation of tetracyclic acetal **2.47** was observed when R was a withdrawing or aromatic group (entries 3-5). In the presence of these substituents, the allene intermediate **A** is activated and the hydroxyl group cyclizes onto the *sp*-hybridized carbon to afford the desired acetal **2.47** (Figure 2.7). The other lactol **B** can not cyclize to the *trans* acetal due to the formation of a highly strained 5-membered ring. Since this process is under thermodynamic control and an equilibrium exists between **A** and **B**, the 5-exo *dig* cyclization solely affords tetracyclic acetal **2.47**.

Table 2.4: The tandem oxy-Cope/ene/Claisen/exo-dig cyclization.



entry	substrate	R	product	Yield % (dr)
1[a]	**2.45a**	H	**2.46a**	98 (>25:1)
2[a]	**2.45b**	Me	**2.46b**	68 (>25:1)
3[a]	**2.45c**	CH_2OBn	**2.47c**	81 (>25:1)
4	**2.45d**	Ph	**2.47d**	85 (>25:1)
5	**2.45e**	4-$(MeO)C_6H_4$	**2.47e**	81 (>25:1)

[a] These experiments were performed by Irina Denissova

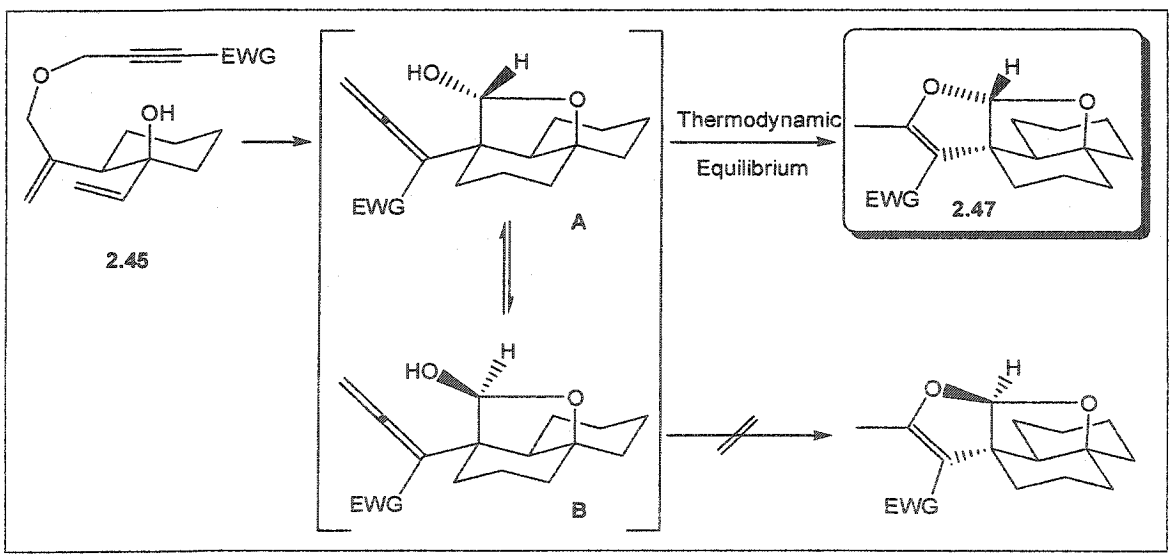


Figure 2.7: Thermodynamic control of the 5-exo dig cyclization.

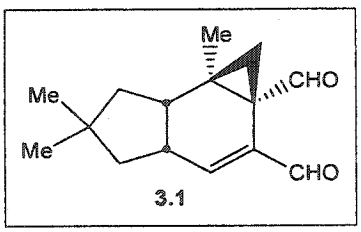
2.5 Conclusion

In conclusion, the scope and limitations of the tandem oxy-Cope/transannular ene/Claisen reaction were studied. Disubstituted allyl ethers afforded the desired lactols via a 3,3-shift whereas trisubstituted allyl ethers afforded lactols through a 1,3-shift. Due to sterically demanding substituents, the latter followed an energetically lower oxaallyl-allyl radical pair transition state. The presence of radical intermediates was supported by the isolation of a dimer and observation of isomerization at the resulting terminal alkene during the 1,3-shift. Propargyl ethers were also utilized to synthesize allenes and tetracyclic acetals via the tandem oxy-Cope/ene/Claisen and 5-exo *dig* cyclization. The acetals were generated when the allene intermediate was activated by electron withdrawing groups or aromatics. Since the reaction is under thermodynamic control, only the *cis* tetracyclic acetal was observed. These tandem reactions efficiently afforded decalin structures possessing a quaternary carbon at C-9 and they are currently being applied towards the total synthesis of natural products.

Chapter 3: Applications of the Hydroxy-Directed Diels-Alder Reactions Towards the Synthesis of Isovelleral Analogues

3.1 Background and Biological Activity

As the study on the oxy-Cope/ene/Claisen reaction was being finalized, the synthesis of isovelleral analogues was pursued in collaboration with AstraZeneca. Due to the intriguing biological activity of isovelleral **3.1**, the synthesis of its analogues was undertaken to ultimately conduct structure activity relationship (SAR) studies. Isovelleral is a mutagenic sesquiterpene dialdehyde found in the chemical defence mechanism of many basidiomycetes. This compound formed enzymatically in the fruit bodies of *Lactarius vellereus* is the result of a response to injury.



3.1

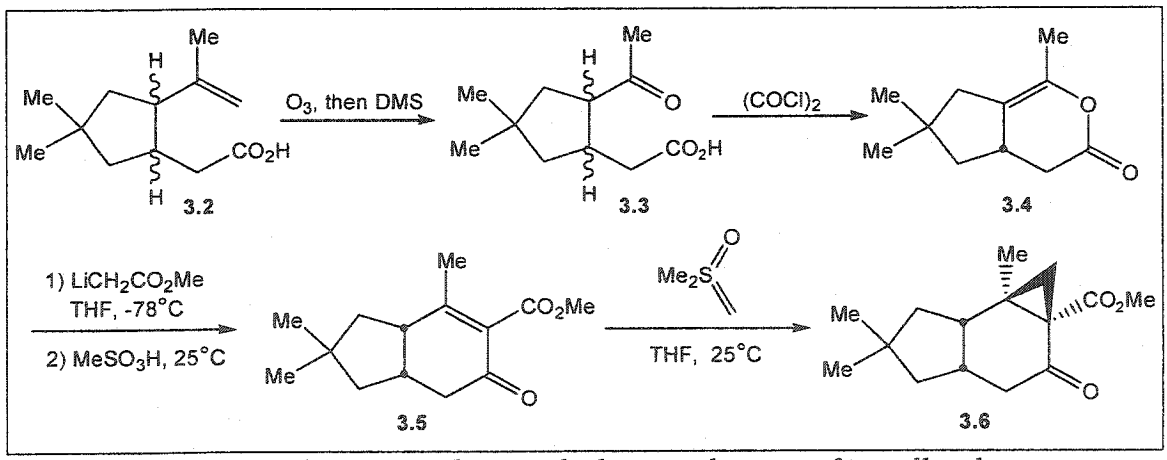
In addition to displaying a wide range of biological activities[31], such as strong antibiotic and antifeedant properties, isovelleral **3.1** has a high affinity for the dopamine D1 and vanilloid receptors.[32] Sterner *et al* have reported IC_{50} = 0.29 μM for the binding of ^{3}H-SCH 23390 to the dopamine receptor and IC_{50} = 2.7 μM for the binding of ^{3}H-resiniferatoxin to the vanilloid receptor. Due to its high affinity for the vanilloid receptor, this natural product is responsible for activation of the receptor, and subsequently creates a painful response to the organism in question. Sterner's group also established that the biological activity of isovelleral mainly focused on the presence of the dialdehyde moiety. In order to determine by structure activity relationship (SAR)

[31] Camazine, S.M.; Resh, J.F.; Eisner, T.; Meiwald, J. *J. Chem. Ecol.*, **1993**, *9*, 1439.
[32] Sterner, O. *et al*, *Bioorg. Med. Chem.*, **1997**, *5*, 1363.

studies whether other functional groups, such as the cyclopropane, are crucial for such biological activity, the synthesis of isovelleral analogues was attempted.

3.2 Previous Total Syntheses of Isovelleral

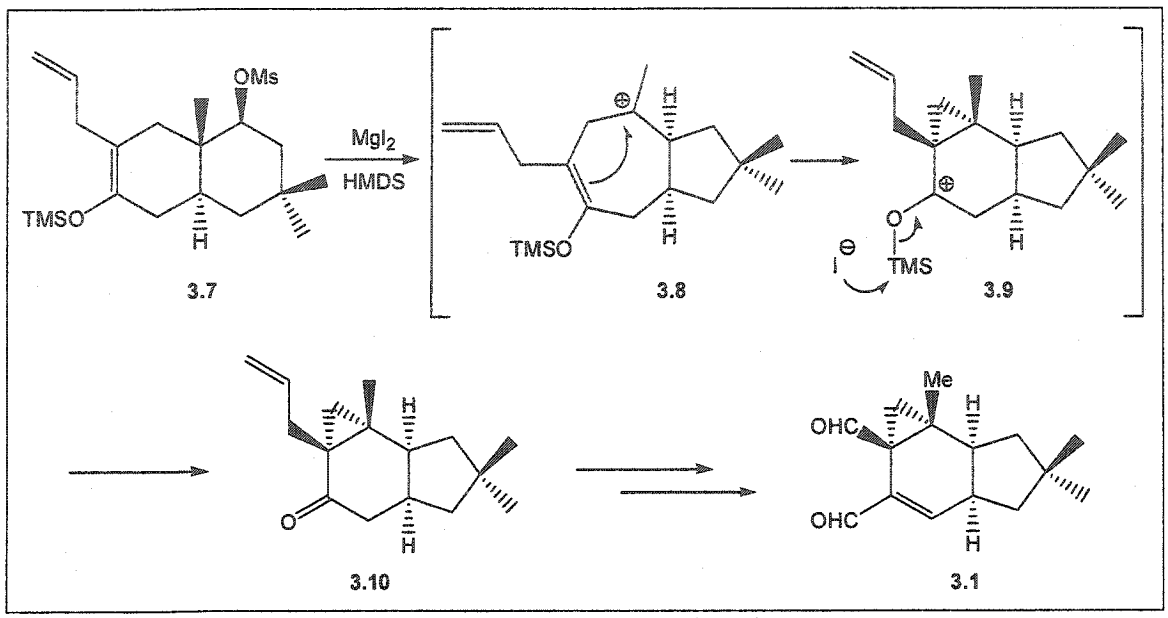
In addition to Wickberg *et al.*,[22d] two other groups have been successful with the total synthesis of isovelleral. Heathcock[22e,f] and Wijnberg's[22g] synthetic strategies differ from the traditional Diels-Alder route for the construction of the *cis*-hydrindane core. In Heathcock's racemic approach, keto-acid **3.3** afforded enol lactone **3.4** after treatment with oxalyl chloride. The *cis* ring junction was created when **3.4** was exposed to the lithium enolate of methyl acetate followed by methanesulfonic acid. Using Corey-Chaykovsky's reagent with alkene **3.5**, cyclopropane **3.6** was quickly generated on the most accessible face.



Scheme 3.1: *Heathcock's approach towards the tricyclic core of isovelleral.*

Wijnberg's enantioselective approach towards the total synthesis of isovelleral involved a MgI_2-induced rearrangement-cyclopropanation reaction (Scheme 3.2). Optically active mesylate **3.7** afforded intermediate **3.8** upon quick addition of MgI_2 and HMDS. It is believed that MgI_2 induces ionization of the sulfonate ester bond in

refluxing benzene or toluene to afford homoallylic cation **3.8** which cyclizes to ketone **3.10**. Thus, cyclopropane **3.10** was created diastereoselectively in 82% yield from **3.7**.

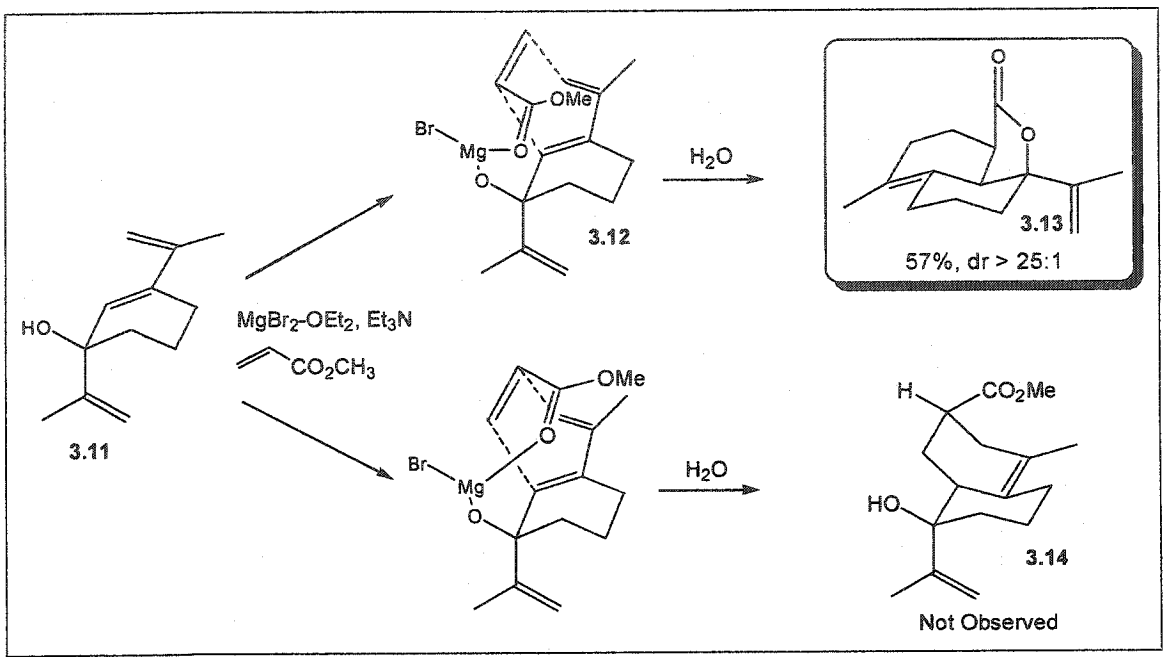


Scheme 3.2: *Wijnberg's approach towards (+)-isovelleral.*

3.3 Retrosynthetic Analysis

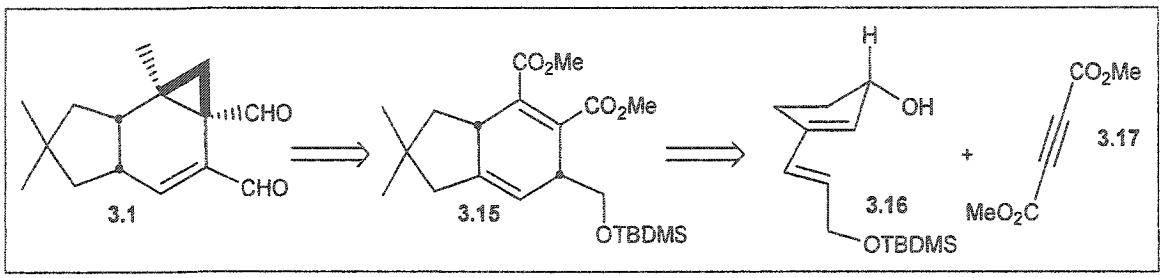
Although many total syntheses of isovelleral have been completed in the past fifteen years,[22d-g] our principal goal was to generate isovelleral analogues to conduct SAR studies. During the last two years, our laboratory has focused much attention onto the hydroxy-directed Diels-Alder reaction (HDDA). In 2003, Thomas and Clément demonstrated a highly regio- and stereoselective Diels-Alder reaction of semicyclic dienes in the presence of a temporary magnesium tethering unit.[19] This method consists of an *in situ* formation of pseudo-cyclic complexes **3.12** using $MgBr_2 \cdot OEt_2$ and Et_3N in dichloromethane.[18] The magnesium acts as both a Lewis acid and a temporary tethering unit between dienes, such as diene **3.11**, and dienophile. Mild reaction conditions were utilized in reactions involving sensitive tertiary alcohols to afford **3.13** as a sole diastereomer (Scheme 3.3). Since the magnesium tether binds to both the alcohol of

diene **3.11** and carbonyl of the dienophile, the facial selectivity is dictated as the dienophile is delivered *syn* to the hydroxyl group. In addition to methyl acrylate, other dienophiles such as N-phenylmaleimide (NPM) and various type **B** dienes gave the corresponding cycloadducts in 57-80% yield and dr > 25:1.



Scheme 3.3: *Hydroxy-Directed Diels-Alder Reaction with semicyclic dienes* ***B****.*

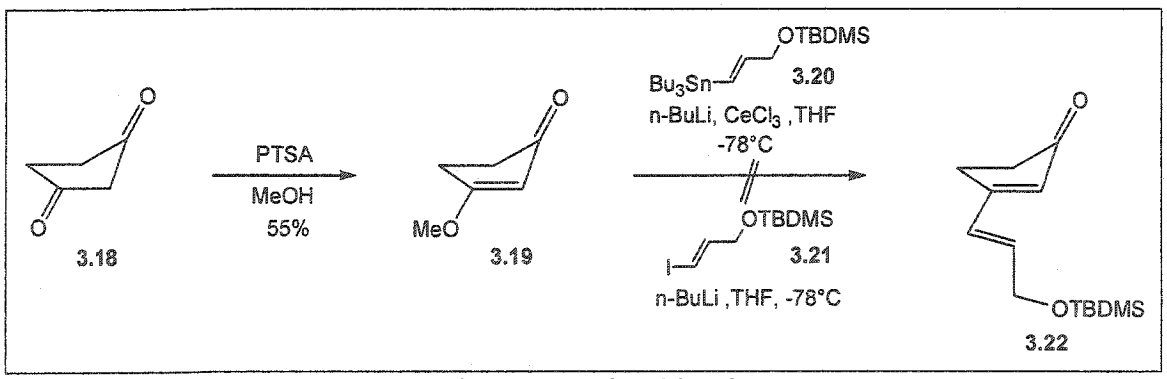
The synthesis of the bicyclo[4.3.0]nonane core of isovelleral analogues was envisioned using the regio- and stereoselective hydroxy-directed Diels-Alder reaction. By applying the methodology presented in Scheme 3.3 to a 5-membered cyclic diene, the desired cycloadduct was visualized as the core of the natural product. The retrosynthetic analysis took cognizance of a Diels-Alder reaction between diene **3.16** and dimethyl acetylenedicarboxylate **3.17** (Scheme 3.4) to generate the hydrindane core of isovelleral. The alkyne **3.17** was chosen as dienophile since it would create an electrophilic alkene in **3.15** that should react with the Corey-Chaykovsky reagent to install the cyclopropane.



Scheme 3.4: Retrosynthetic analysis of isovelleral analogues.

3.4 Synthesis of Various Dienes and Hydroxy-Directed Diels-Alder Results

The initial synthesis of diene **3.16** was attempted by reacting commercially available 1,3-cyclopentadione **3.18** with a catalytic amount of *p*-toluenesulfonic acid in methanol (Scheme 3.5) to afford enol ether **3.19** in 55% yield. Vinylstannane **3.20** underwent tin-lithium exchange in the presence of *n*-butyllithium. This solution was canulated into a heterogeneous solution containing anhydrous cerium trichloride and enol ether **3.19**. Even though thin layer chromatography revealed the formation of tetrabutylstannane, which indicated a successful tin-lithium exchange, the desired diene **3.22** was never observed. Therefore, vinyl iodide **3.21** was also subjected to a iodine-lithium exchange with *n*-butyllithium. Unfortunately, addition of the vinyllithium to the enol ether **3.19** did not afford the desired product **3.22**.



Scheme 3.5: Attempted synthesis of type B Diels-Alder diene.

The problem was overcome by initially treating 1,3-cyclopentadione **3.18** with phosphorus tribromide in refluxing dichloromethane for 24 hours to give vinyl bromide **3.23** in 57% yield (Scheme 3.6).[33] In the meantime, alkenylcatecholborane **3.24** was prepared by hydroboration between *tert*-butyl-dimethyl-prop-2-ynyloxy-silane and catecholborane. With vinyl bromide **3.23** and boronic ester **3.24** in hand, diene **3.22** was synthesized via a Suzuki coupling reaction mediated by $(Ph_3P)_2PdCl_2$[34] and sodium acetate in 85% yield. At this stage, ketone **3.22** was used to generate hydroxy dienes **3.25** and **3.26**. Thus, ketone **3.22** was quantitatively reduced to alcohol **3.25** using Luche's conditions[35] and ketone **3.22** was treated with methyllithium in THF to give diene **3.26** in 84% yield.

In the absence of an alkyl chain, diene **3.28** and **3.29** required an alternative procedure for their synthesis (Scheme 3.7). Enol ether **3.19** was cooled to -78°C, then treated with vinylmagnesium bromide in THF to produce the corresponding 1,2-addition product. The latter was subjected to an acidic work-up giving enone **3.27** in 100% yield.[11] Reduction of **3.27** gave the volatile secondary alcohol **3.28** and treatment with vinylmagnesium bromide afforded volatile alcohol **3.29** in 41% yield.

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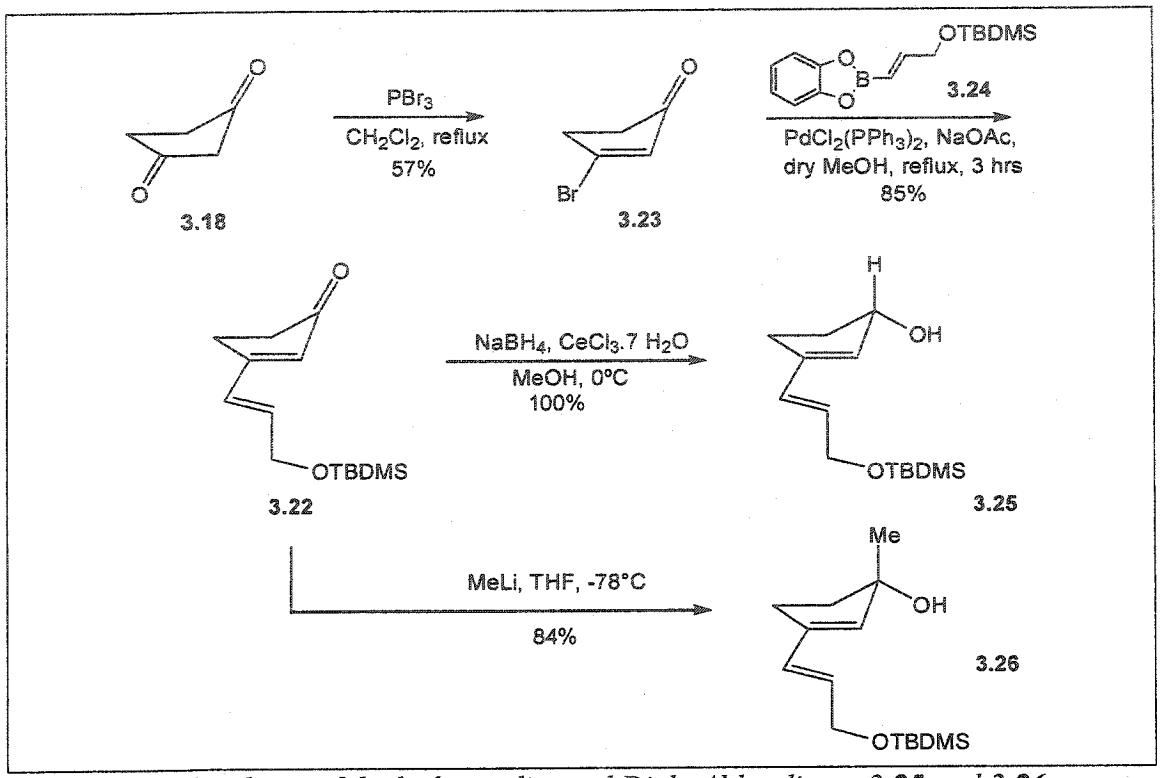
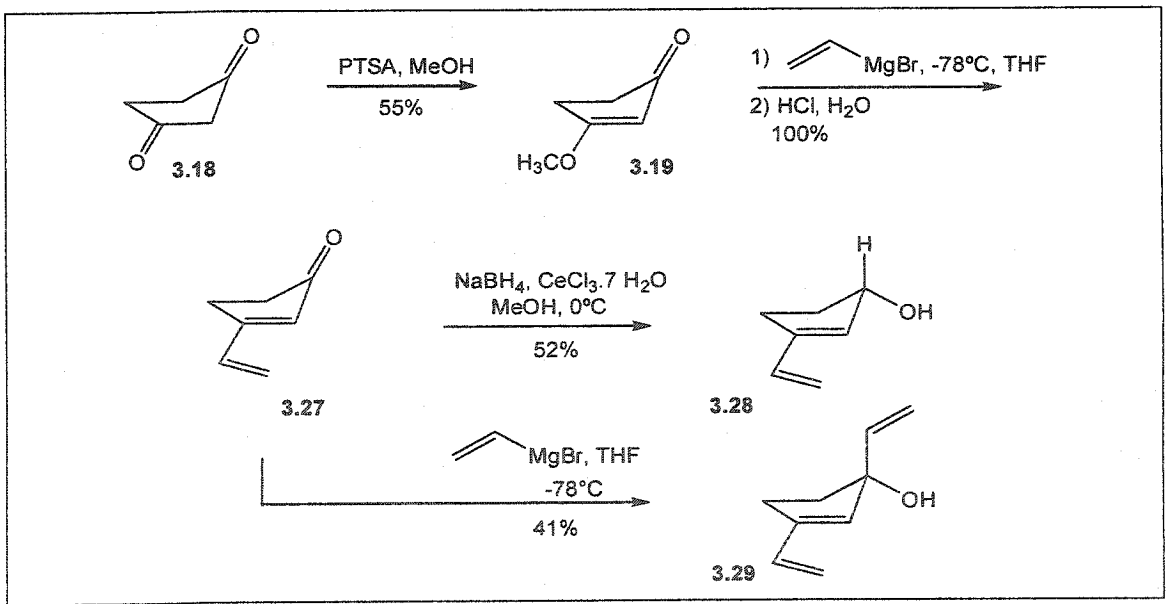
[33] Shih, C.; Swenton, J. S. *J. Org. Chem.* **1982**, *47*, 2825.
[34] Itatani, H.; Bailar, J.C.Jr. *American Oil Chemist's Society*, **1967**, *44*, 147
[35] Luche, J.-L. *J. Am. Chem. Soc.* **1998**, *100*, 2226



Scheme 3.6: *Synthesis of the hydroxy-directed Diels-Alder dienes* ***3.25*** *and* ***3.26****.*

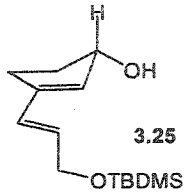
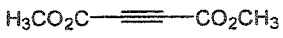
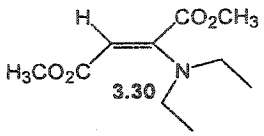
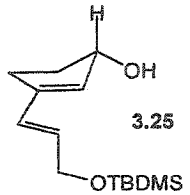
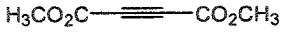
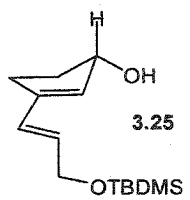
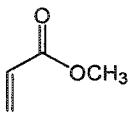
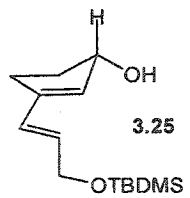
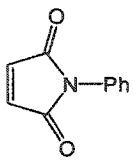
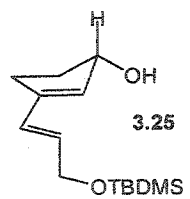
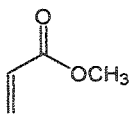
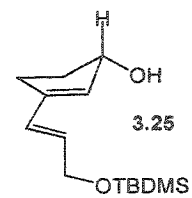


Scheme 3.7: *Synthesis of the hydroxy-directed Diels-Alder dienes* ***3.28*** *and* ***3.29****.*

The hydroxy-directed Diels-Alder reaction was attempted with dienes **3.25**, **3.26**, **3.28** and **3.29** with various dienophiles. Two reaction conditions were tried to generate the corresponding magnesium alkoxide diene, $MgBr_2{\cdot}OEt_2$ and Et_3N in DCM

(method A) or vinylmagnesium bromide in toluene (method B). The results are summarized in Tables 3.1, 3.2 and 3.3.

Table 3.1: The hydroxy-directed Diels-Alder reaction between diene **3.25** and activated dienophiles.

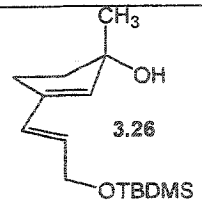
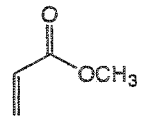
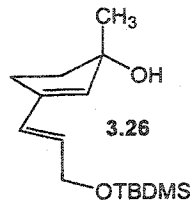
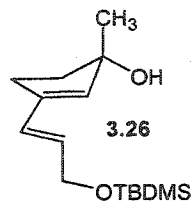
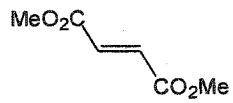
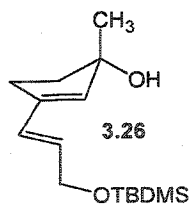
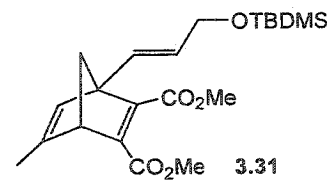
Entry	Diene	Dienophile	Method	Results
1	 **3.25**	 **3.17**	A	 **3.30**
2	 **3.25**	 **3.17**	A[a]	Decomposition
3	 **3.25**		A[a]	Decomposition
4	 **3.25**		A[a]	Decomposition
5	 **3.25**		A	Decomposition
6	 **3.25**		B	Mixture of esters and lactones

[a]2,6-Lutidine was used as base.

Diene **3.25** was treated with $MgBr_2 \cdot OEt_2$ and Et_3N in dichloromethane followed by the addition of dimethylacetylene dicarboxylate **3.17** (entry 1, Table 3.1). Surprisingly, alkene **3.30** was generated within minutes with no trace of desired product in the crude mixture. Since alkyne **3.17** was an excellent Michael acceptor, triethylamine quickly acted as a nucleophile onto the conjugated system to generate the undesired product **3.30** after loss of ethylene. In order to overcome this problem, triethylamine was substituted with bulkier base 2,6-lutidine, but no product was isolated and diene **3.25** readily decomposed under these conditions (entry 2).

Methyl acrylate and N-phenylmaleimide with $MgBr_2 \cdot OEt_2$ and 2,6-lutidine (entries 3 and 4) and methylacrylate with $MgBr_2 \cdot OEt_2/Et_3N$ (entry 5) were unsuccessfully scanned with diene **3.25** possessing a secondary alcohol. A cycloaddition did occur between diene **3.25** and dimethyl maleate when vinylmagnesium bromide was used as base and source of magnesium (entry 6). However, a mixture of esters and lactones gave rise to a complex ^1H NMR spectrum from which no desired cycloadducts were isolated. Even though dienophiles and bases were varied, all these reactions were unsuccessful and led to decomposition of the starting material.

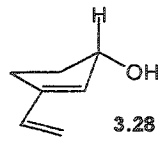
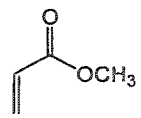
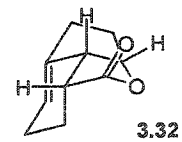
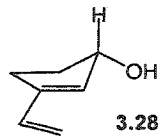
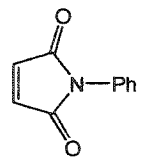
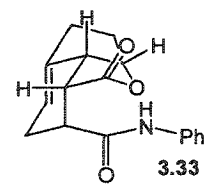
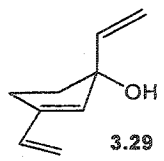
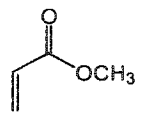
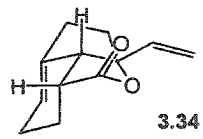
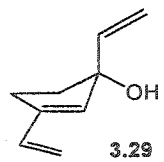
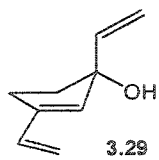
Table 3.2: The hydroxy-directed Diels-Alder reaction between diene **3.26** and activated dienophiles.

Entry	Diene	Dienophile	Method	Results
1			A	Decomposition
2			B	Decomposition
3			B	No desired product
4			B	 Possible structure

Tertiary alcohol **3.26** was utilized with $MgBr_2 \cdot OEt_2/Et_3N$ and methyl acrylate, however this very acid sensitive diene decomposed in the reaction mixture (entry 1, Table 3.2). The use of vinylmagnesium bromide as source of magnesium and base was tried with diene **3.26** and dimethyl maleate, dimethyl fumarate and dimethyl acetylenedicarboxylate as dienophiles (entry 2-4). The results of these reactions were respectively decomposition of the diene, a mixture of unknown products and the possible formation of diester **3.31**. The latter was isolated on a small scale and further NMR studies were abandoned.

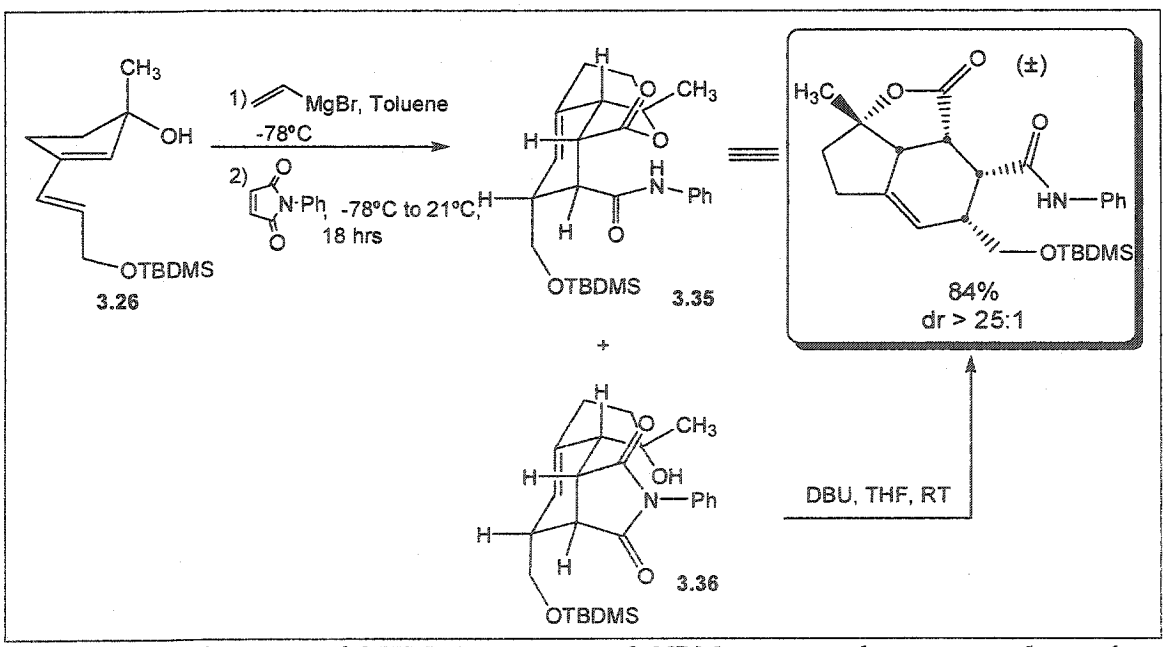
In every case presented above, dienes bearing an alkyl chain were unsuccessfully scanned with Grignards and $MgBr_2 \cdot OEt_2/Et_3N$. In order to determine whether the alkyl chain was responsible for the lack of success, diene **3.28** and **3.29** were subjected to similar reaction conditions (entries 1-5, Table 3.3).

Table 3.3 The hydroxy-directed Diels-Alder reaction between various 5-membered dienes and activated dienophiles.

Entry	Diene	Dienophile	Method	Results
1	 **3.28**		A	 **3.32** 32%, dr > 25:1
2	 **3.28**		A	 **3.33** 54%, dr > 25:1
3	 **3.29**		A	 **3.34** 23%, dr > 25:1
4	 **3.29**		A[a]	No reaction
5	 **3.29**		B[b]	Decomposition

[a] 36 hours at 21°C. [b] Reflux.

After much anticipation, reaction between diene **3.28**, methyl acrylate or N-phenylmaleimide and $MgBr_2{\cdot}OEt_2/Et_3N$ afforded desired cycloadducts **3.32** (32% yield) and **3.33** (54% yield) in excellent diasteromeric ratio (>25:1) (entries 1 and 2). Due to the presence of the magnesium tether, the facial selectivity was governed as the activated dienophile was delivered *syn* to the alcohol of diene **3.28**. The regioisoselectivity was controlled by the preferred overlap of the frontier molecular orbitals between diene and dienophile and their corresponding coefficients. Tertiary alcohol **3.29** also generated the preferred cycloadduct **3.34** in 23% yield with methyl acrylate as dienophile (entry 3). No reaction was observed when diene **3.29** and dimethyl maleate, a less activated dienophile, were stirred with $MgBr_2{\cdot}OEt_2/Et_3N$ for 36 hours. When vinylmagnesium bromide was employed as base and source of magnesium, no HDDA occurred at room temperature and heating at 110°C resulted in degradation of diene **3.29**.

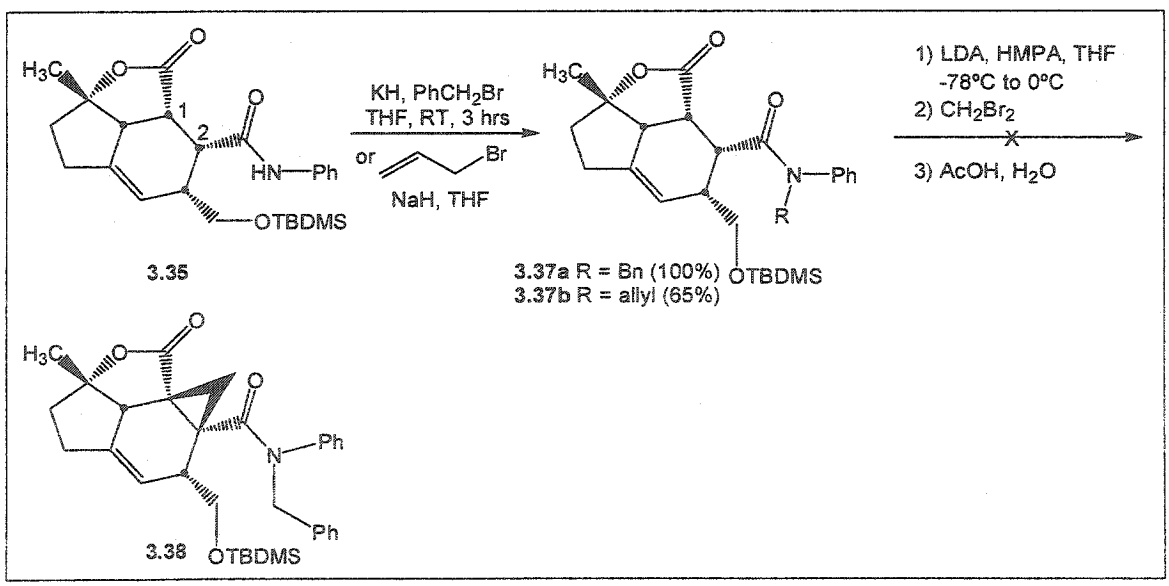


Scheme 3.8: *The successful HDDA reaction with NPM using vinylmagnesium bromide.*

As a last attempt, diene **3.26** was reacted with N-phenylmaleimide and vinylmagnesium bromide (Scheme 3.8). Due to its exceptional reactivity, this dienophile afforded cycloadducts **3.35** and **3.36**. After treatment of imide **3.36** with DBU, lactonisation provided cycloadduct **3.35** in 84% yield from diene **3.26** (dr > 25:1). As predicted, the regio- and stereoselectivity were controlled when the magnesium is tethered to both the alcohol of diene **3.26** and the carbonyl group of the dienophile.

In general, dienes **3.25** and **3.26** were not compatible with this methodology, unless a powerful dienophile such as N-phenylmaleimide was chosen. Even though the reaction medium was alkaline, the presence of a Lewis acid may have promoted the decomposition of the sensitive diene. In contrast, dienes **3.28** and **3.29** which reflect those used by Thomas and Clément, displayed a wider range of applications and are useful precursors for the synthesis of cycloadducts using the HDDA reaction.

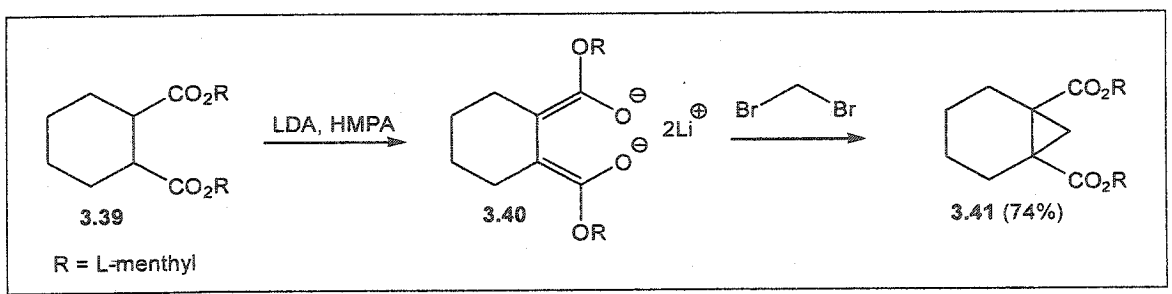
Since the HDDA was not successful with dimethyl acetylenedicarboxylate **3.17** as dienophile, the acidic protons at C-1 and C-2 in **3.35** were the remaining useful structural feature on the cycloadduct for the installation of the cyclopropane (Scheme 3.9).



Scheme 3.9: *Attempts towards the cyclopropanation.*

Since the cycloprotonation step required the use of LDA, protection of amide **3.35** was attempted using various conditions. Protection of amide **3.35** with Boc_2O was unsuccessful and the product seemed to be sensitive to the basic work-up conditions. In addition, iodomethane and sodium hydride failed to protect amide **3.35**. Protection with allylbromide and sodium hydride afforded the desired product **3.37b** in 65% accompanied with unknown byproducts (Scheme 3.9). During a modification of this reaction, using *tetrakis*-triphenylphosphine palladium (0), allylbromide and triethylamine, the starting material was recovered.[36] The desired amide **3.37a** was successfully protected in quantitative yield in the presence of benzyl bromide and potassium hydride[37].

According to Garratt and Porter,[38] cyclopropanes can be generated in the presence of a diester **3.39**, LDA and the electrophilic dibromo- or diiodomethane (Scheme 10).

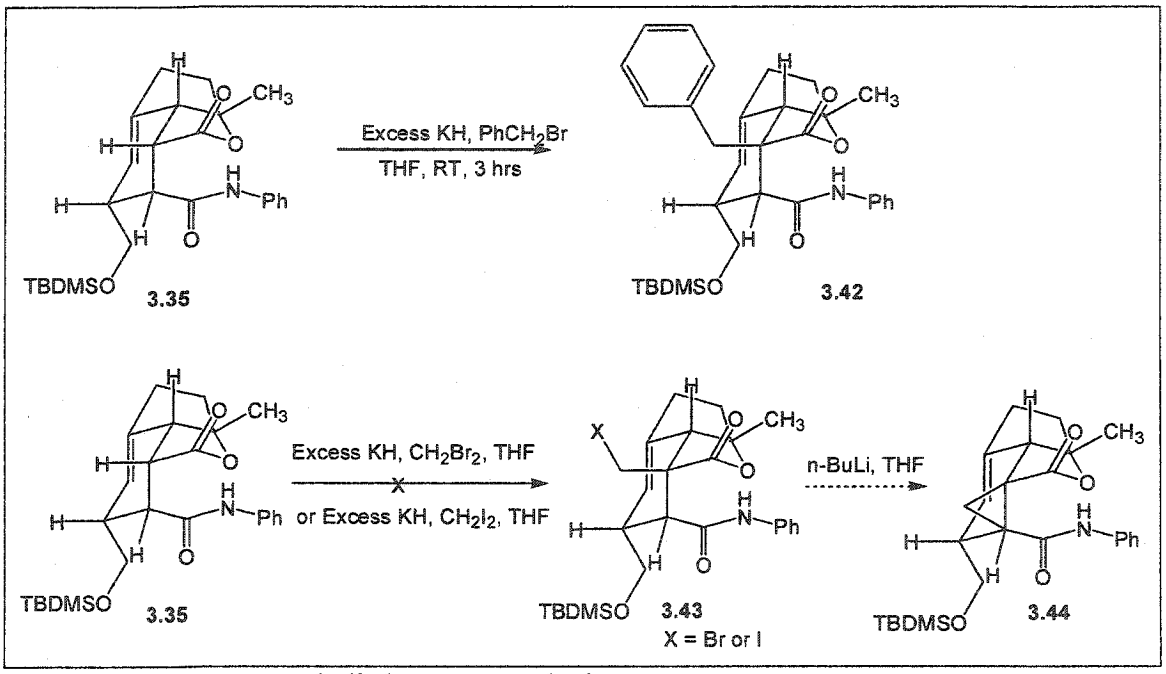


Scheme 3.10: *Garratt and Porter's cyclopropanation with diester **3.39**.*

Subjecting **3.37a** or **3.37b**, bearing a lactone and amide to the same reaction conditions with CH_2I_2 or CH_2Br_2, did not afford the desired cyclopropane **3.38**. When the protection of amide **3.35** towards amide **3.37a** was repeated on a larger scale, an excess of potassium hydride was utilized and product **3.42** was obtained in 73% yield (Scheme 3.11). With an excess of base, the most acidic proton of the amide **3.35** was initially

[36] Kimura, M.; Fugami, K.; Tanaka, S.; Tamaru, Y. *J. Org. Chem.* **1993**, *57*, 6377
[37] Xia, Y.; Kozikowski, A.P. *J. Am. Chem. Soc.* **1989**, *111*, 4116
[38] Garratt, P.; Porter, J. *J. Chem. Research, Synopses.* **1987**, *4*, 108

removed, followed by removal of the proton α to the lactone. As the electrophile was added to the reaction medium, the last anion formed acted as the first nucleophile to afford α-lactone alkylation. This result seemed promising because benzylbromide could be substituted with dibromo- or diiodomethane in order to install the cyclopropane after additional treatment with base. As depicted in scheme 3.11, these reactions were ineffective.

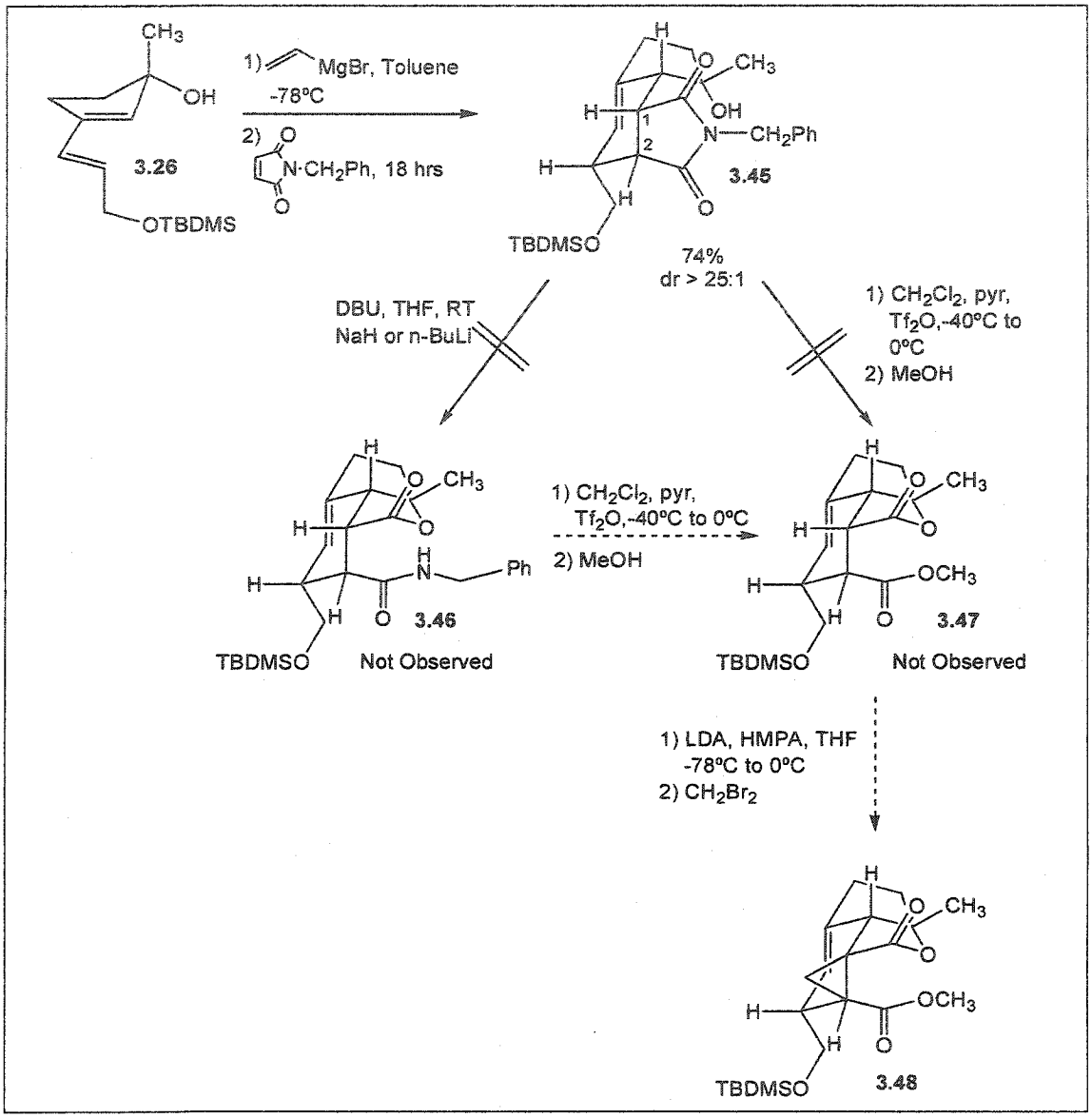


Scheme 3.11: *Attempted alkylations α to the lactone.*

Since the acidic protons were α to a lactone and an amide, and Garratt's study illustrated the use of acidic protons α to esters, transformation of the amide to an ester was envisioned to increase the acidity of proton on C-2 (Scheme 3.12). According to Charette's methodology,[39] primary and secondary amides with a methylene group next to the nitrogen (C(O)NHCH$_2$R) can be transformed into a methyl ester in the presence of triflic anhydride, pyridine and methanol. Since the methylene group seemed to be crucial

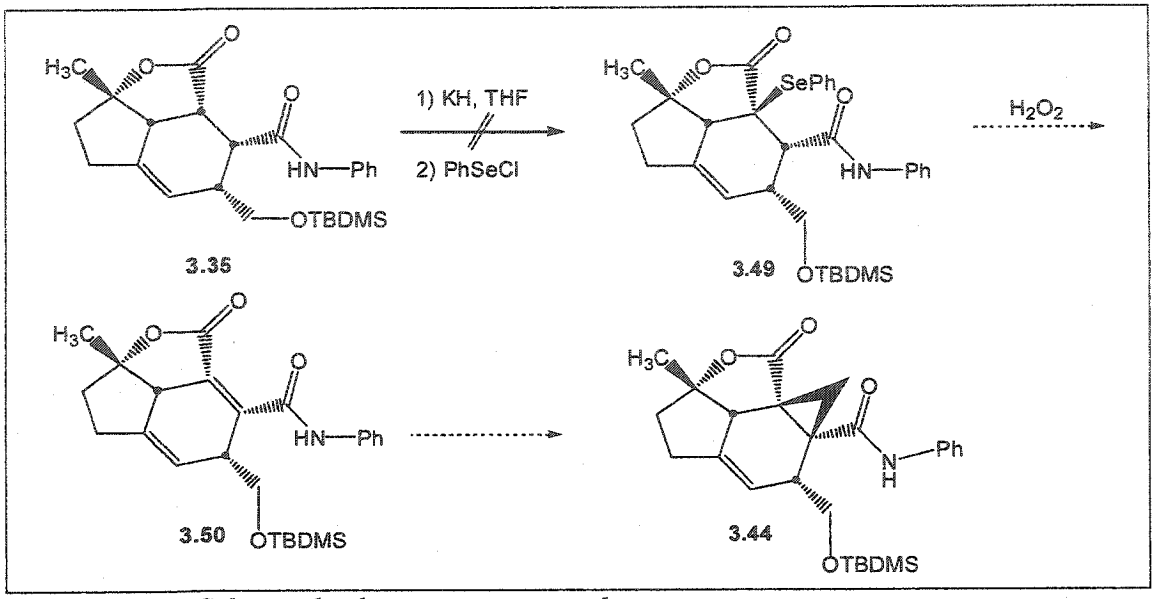
[39] Charette, A.B.; Chua, P. *Synlett.* **1998**, 163.

for such transformation, a hydroxy-directed Diels-Alder reaction was conducted using N-benzylmaleimide as dienophile. The mixture of diene **3.26**, dienophile and vinylmagnesium bromide solely afforded cycloadduct **3.45** in 74% yield (dr > 25:1). In this particular case, lactonisation was not observed. Since Charette's methodology required primary or secondary amides, tertiary amide **3.45** was therefore subjected to basic conditions (NaH, DBU and *n*-BuLi) to drive the lactonisation towards amide **3.46**. These attempts were not successful and can be rationalized using pKa concepts. During lactonisation, an anion would be developed on the nitrogen of the amide. Due to the presence of the benzyl group, the anion is not as stabilized as was the case with N-phenylmaleimide. The additional methylene group increased the pKa, destabilized the charge on the nitrogen and rendered lactonisation unfavorable. Nevertheless, Charette's esterification was tried with tertiary amide **3.45**. No reaction occurred and the starting material was recovered.



Scheme 3.12: *HDDA reaction with N-benzylmaleimide and attempted esterification.*

In addition to these reactions, selenium chemistry was undertaken to insert an endocyclic alkene **3.50** between the lactone and amide (Scheme 3.13). Treating cycloadduct **3.35** with an excess of potassium hydride and phenylselenyl chloride resulted in decomposition of the starting material. A similar reaction was conducted with the N-allyl amide, LDA, HMPA and PhSeCl, which yielded a mixture of undesired products.



Scheme 3.13: Selenoxide elimination proposal.

3.5 Conclusion

In conclusion, the scope and limitations of the HDDA reaction applied towards 5-membered cyclic dienes were investigated. Dienes **3.25** and **3.26** bearing an alkyl chain were unreactive unless a powerful dienophile, such as N-phenylmaleimide or N-benzylmaleimide, were employed with a Grignard as source of magnesium and base. Dienes **3.28** and **3.29**, which resembled the previously studied 6-membered semicyclic dienes, were compatible with N-phenylmaleimide and methylacrylate when $MgBr_2 \cdot OEt_2$ and Et_3N were utilized as tethering agent. Reaction between diene **3.25** and dimethyl acetylenedicarboxylate **3.17** was most likely unfavorable due to a resulting ring strain in the product, caused by two endocyclic alkenes and an sp^2-hybridized carbon at the ring junction. All attempts towards cyclopropanation failed. Dimethyl cyclopropene 1,2-dicarboxylate is currently being studied as dienophile as a route to the tricyclic core of isovelleral.

Chapter 4: Studies Towards the Total Synthesis of Havellockate

4.1 Background

Marine origin diterpenes are particularly interesting as synthetic targets due to their complex structures and numerous stereochemical centers. During their search for bio-active secondary metabolites in 1998, Anjaneyulu *et al.* discovered a novel diterpenoid, havellockate **4.1**, from the soft coral *Sinularia granosa*, located on the Havellock Island of the Andaman and Nicobar group of Islands of the Indian Ocean Figure 4.1). Structure elucidation of the diterpenoid was conducted using spectral data and X-ray analysis. Interestingly, havellockate has structural resemblance with the recently isolated tetracyclic diterpenoids isomandapamate **4.2** from *Sinularia maxima*[40] and mandapamate **4.3** from *Sinularia dissecta*.[41]

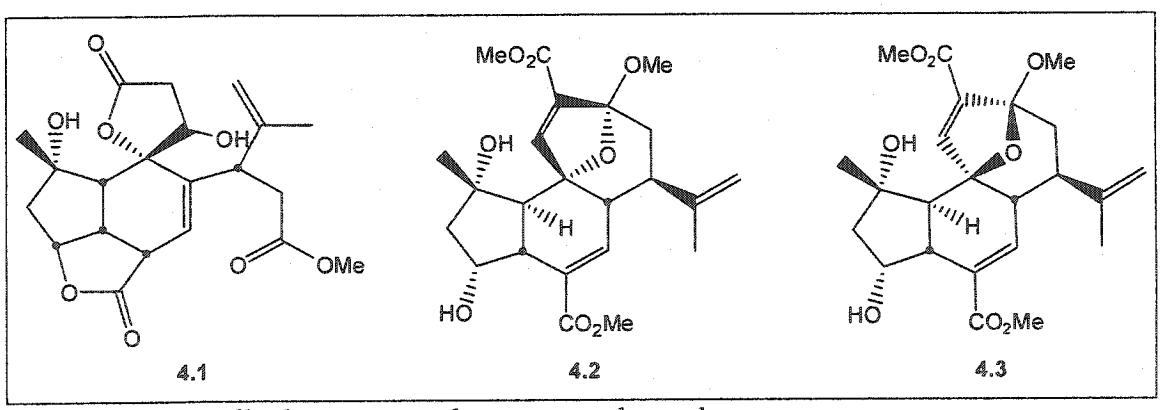


Figure 4.1: *Havellockate, isomandapamate and mandapamate.*

The complex skeleton of mandapamate **4.3** is believed to be the result of a biosynthetic transannular Diels-Alder reaction (Figure 4.2).[46] Therefore, the application

[40] (a) Anjaneyulu, A.S.R.; Sagar, K.S.; Venugopal, M.J.R.V. *Tetrahedron*, **1995**, *51*, 10997. (b) Anjaneyulu, A.S.R.; Krishna Murthy, M.V.R.; Rao, G.V. *Tetrahedron*, **1997**, *53*, 9301.
[41] Venkateswarlu, Y.; Farooq Biabani, M.A.; Venkata Rami Reddy, M.; Prabhakar Rao, T.; Kunwar, A.C.; Faulkner, D.J. *Tetrahedron Lett.* **1994**, 2249.

of a Diels-Alder reaction towards the synthesis of these complex cores presents an attractive and feasible synthetic route.

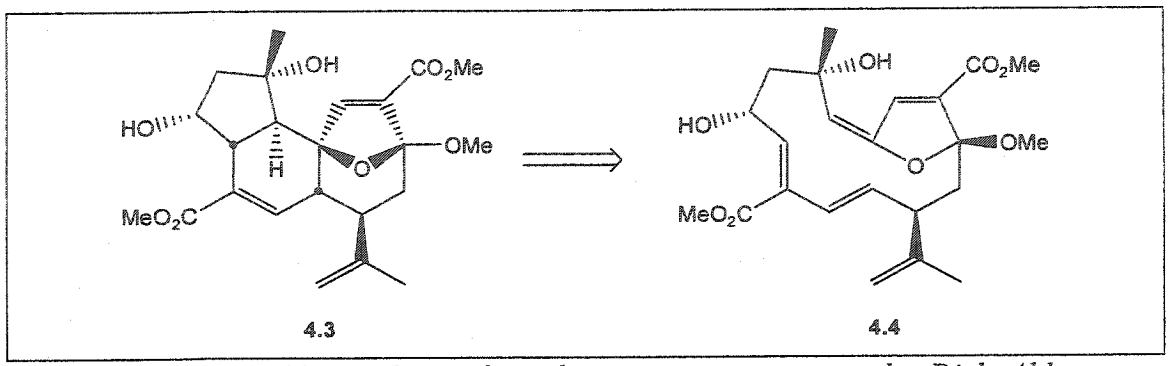
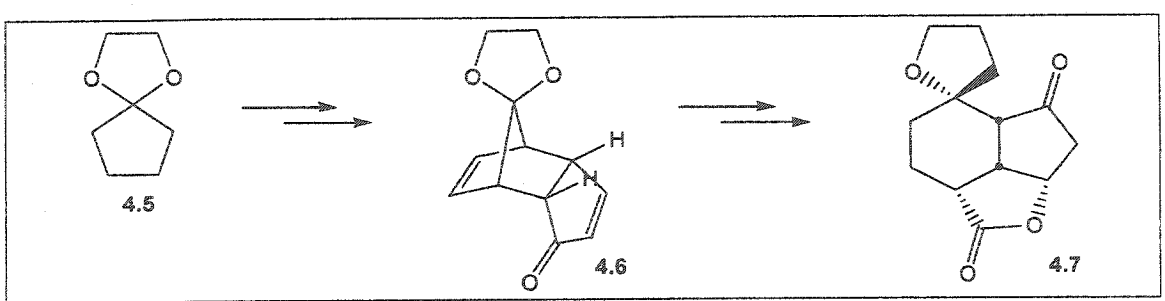


Figure 4.2: *Proposed biosynthesis of mandapamate via a transannular Diels-Alder.*

Amongst the three natural products, the key structural features which render havellockate **4.1** synthetically challenging and compatible with our developped methodology are: the eight stereogenic centers, a *cis*-fused hydrindane moiety and two γ-lactones, where one of them is spiro-fused. Since its isolation, Mehta *et al.* have been, to the best of our knowledge, the only group to attempt the total synthesis of havellockate.[42] The synthesis of the tetracyclic core **4.7** of the diterpenoid was accomplished from 1,4-dioxa-spiro[4.4]nonane **4.5**, via an *endo*-dicyclopentadienone-10-ethylene ketal **4.6** to afford **4.7** in 23 synthetic steps (Scheme 4.1). With the intention of efficiently completing the total synthesis of havellockate, we chose to apply the hydroxy-directed Diels-Alder reaction to stereoselectively construct the hydrindane moiety of havellockate.



Scheme 4.1: *Mehta's approach towards the tetracyclic core of havellockate.*

[42] Mehta, G.; Senthil Kumaran, R. *Tetrahedron Lett.* **2001**, *42*, 8097.

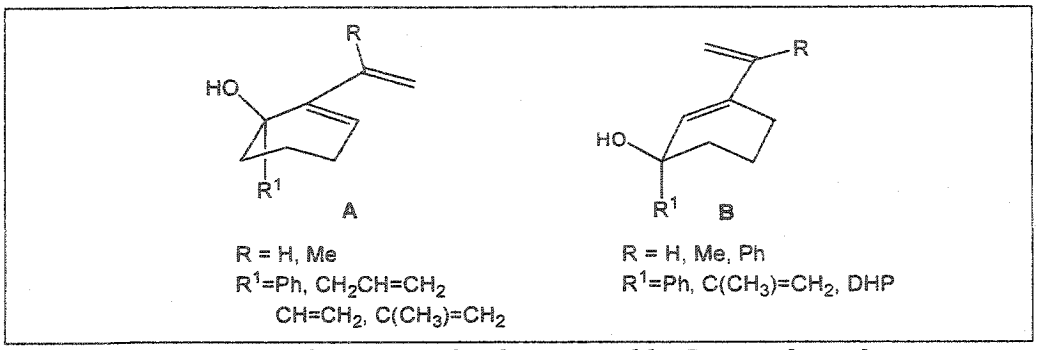
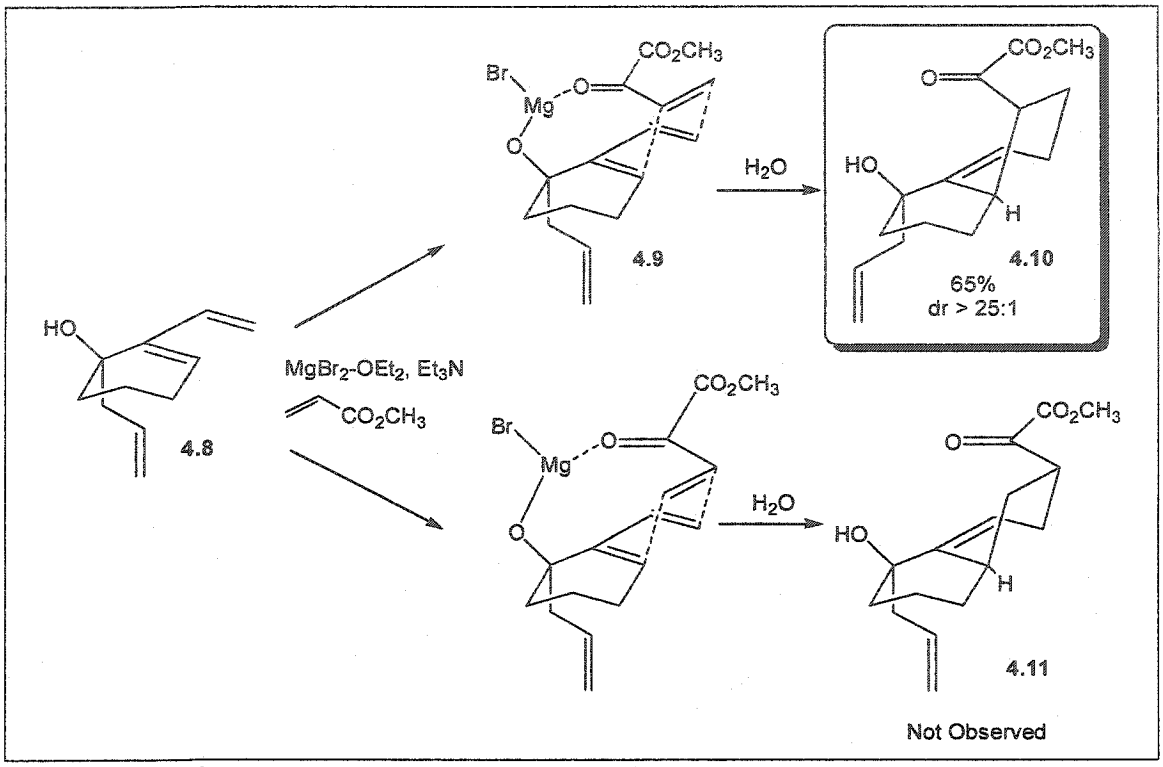


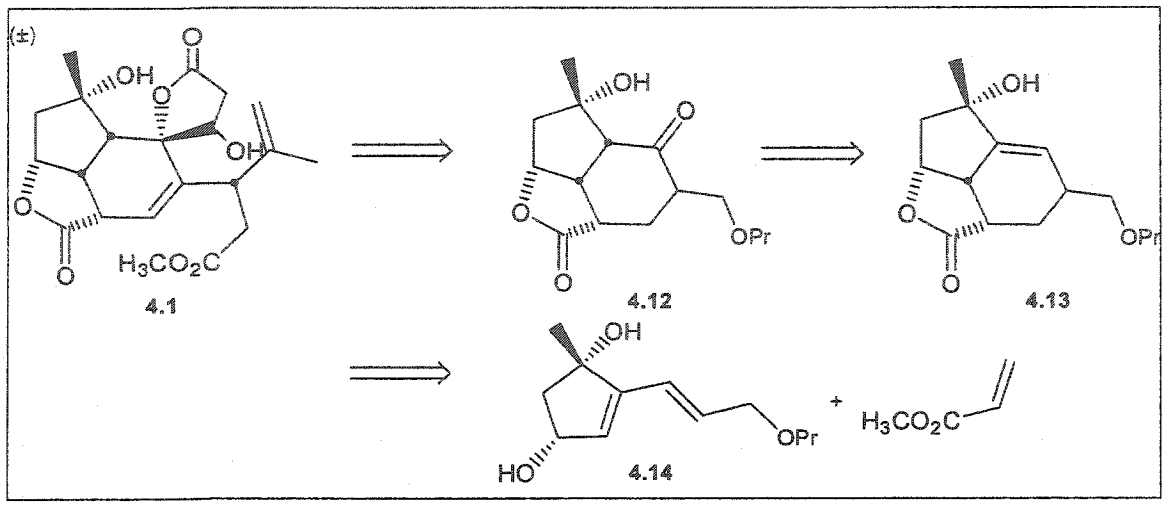
Figure 4.3: *Type A and B semicyclic dienes used by Barriault et al.*

In addition to type **B** dienes, Barriault, Thomas and Clément[19] also studied the compatibility of various type **A** dienes **4.8** with many dienophiles, such as acrolein, methylacrylate and N-phenylmaleimide, in the hydroxy-directed Diels-Alder reaction (39-89% yield, dr > 25:1) (Figure 4.3 and Scheme 4.2). As previously discussed, cycloadducts **4.10** were obtained regio- and stereoselectively due to the presence of a magnesium tethering unit which is responsible for delivering the dienophile *syn* to the hydroxyl group of the diene. Using this methodology, a retrosynthetic analysis of havellockate was designed and is depicted in Scheme 4.3.



Scheme 4.2: *The HDDA reaction with a type A diene.*

The side alkyl chain of havellockate **4.1** was envisionned to be installed via a Claisen rearrangement. Ketone **4.12** would be prepared via a hydroboration and subsequent oxidation of alkene **4.13**. The tricyclic core **4.13** can be regio- and stereoselectively constructed via the hydroxy-directed Diels-Alder reaction between diene **4.14** and methylacrylate. The lactone would spontaneously be generated during the course of the reaction to afford the carbon skeleton of havellockate **4.1**.



Scheme 4.3: Retrosynthetic analysis of havellockate via the HDDA reaction.

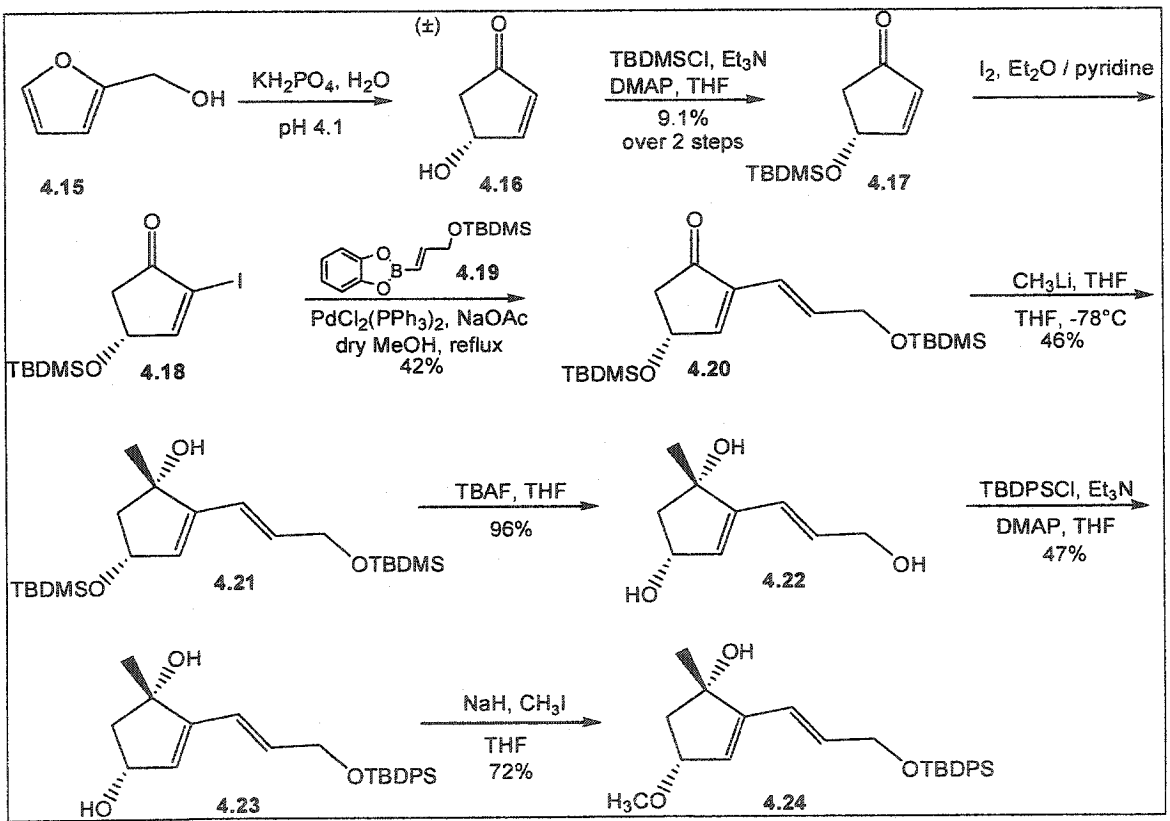
4.2 Synthesis of Various Dienes and Hydroxy-Directed Diels-Alder Results

The synthesis of various dienes began by refluxing commercially available furfuryl alcohol **4.15**[43] in water in a controlled pH environment to afford enone **4.16** (Scheme 4.4).[44] The secondary alcohol was protected with TBDMSCl, triethylamine and DMAP to generate silylether **4.17**. The crude vinyl iodide **4.18**,[45] obtained upon treatment of **4.17** with iodine and a mixture of ether and pyridine (1:1), underwent a Suzuki coupling reaction with alkenylboronic ester **4.19** to provide diene **4.20** in 42% yield over two steps. Nucleophilic attack of methyllithium onto the least hindered face of ketone **4.20** afforded HDDA reaction precursor **4.21**. The stereochemistry of **4.21** was proven by a ^{1}H NMR NOESY experiment which illustrated a *syn* relationship between the hydrogen at 4.61 ppm and the methyl hydrogens at 1.35 ppm (Scheme 4.5).

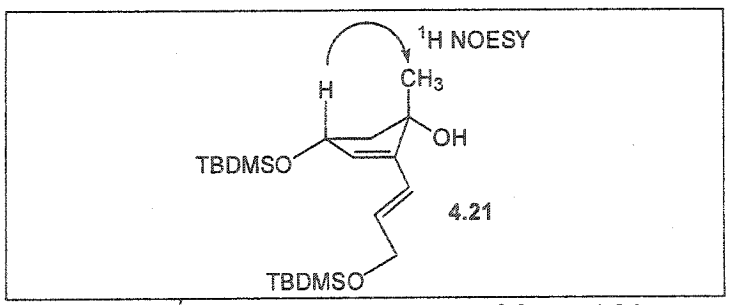
Since precursor **4.21** possessed three oxygen atoms to which magnesium could create a tether, the protection pattern of diene **4.21** was varied to explore the scope and limitation of the HDDA reaction. The masked hydroxyl groups **4.21** were initially

[43] 250g/10.50$ from Aldrich
[44] Curran, T. T.; Hay, D. A.; Koegel, C. P.; Evans, J. C. *Tetrahedron*, **1997**, *53*, 1983
[45] Johnson, C.R.; Adams, J.P.; Matthew, P.B.; Senanayake, C.B.W. *Tetrahedron Lett.* **1992**, *33*, 917

deprotected with three equivalents of TBAF. The resulting triol **4.22** was treated with TBDPSCl to selectively protect the primary alcohol in 47% yield. Since a trace of di-protected product was beginning to appear by TLC, the uncompleted reaction was quenched with saturated ammonium chloride. Finally, secondary alcohol **4.23** was protected with iodomethane and sodium hydride to provide methylether **4.24** in 72% yield.



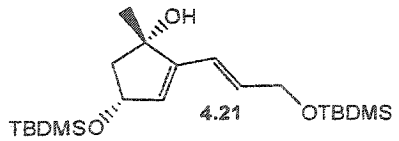
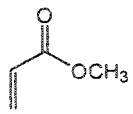
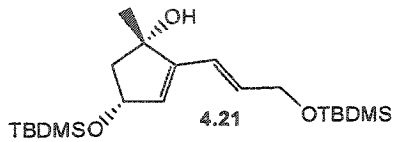
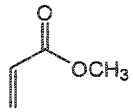
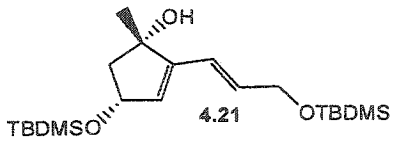
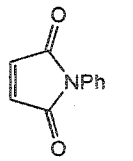
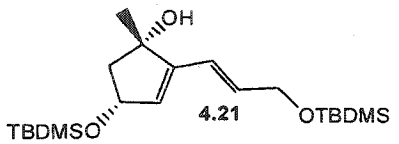
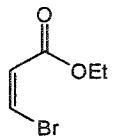
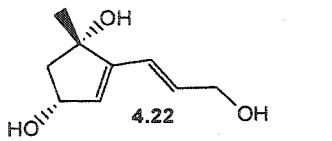
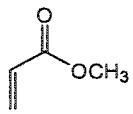
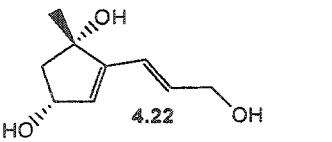
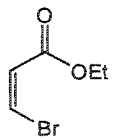
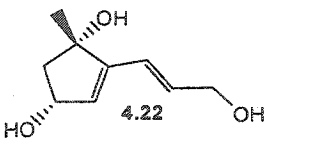
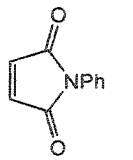
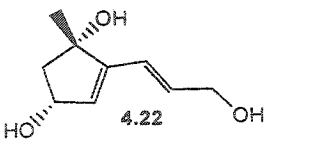
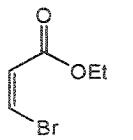
Scheme 4.4: Synthesis of dienes 4.21, 4.22, 4.23 and 4.24 for the HDDA reaction.



Scheme 4.5: ^{1}H NOESY correlation of diene 4.21.

With the Diels-Alder precursors in hand, the dienes were reacted with various dienophiles and $MgBr_2 \cdot OEt_2$ /Et_3N in DMC (method A) or vinylmagnesium bromide in toluene (method B) (Table 4.1, 4.2 and 4.3).

Table 4.1: Attempted Diels-Alders with dienes **4.21** and **4.22** with various dienophiles.

Entry	Diene	Dienophile	Conditions	Product
1			A	SM
2			B	SM
3			B	SM
4			B	SM
5			B[a]	SM
6			B[a]	SM
7			B[a]	SM
8			A	Decomposition

[a] THF was used as solvent.

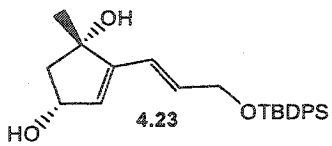
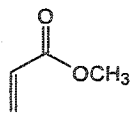
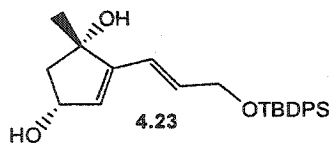
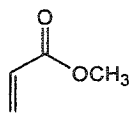
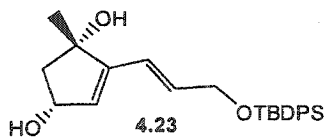
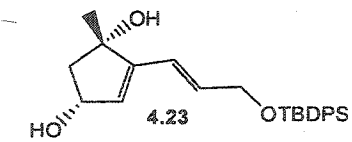
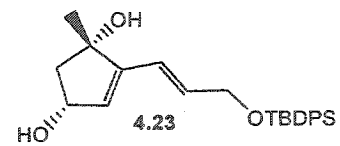
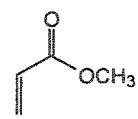
As listed in Table 3.1, diene **4.21** was treated with methyl acrylate and $MgBr_2 \cdot OEt_2$/ Et_3N (entry 1). In contrast with previous HDDA reactions, no reaction occurred and the starting material was recovered. The source of magnesium was changed from the Lewis acid salt to vinylmagnesium bromide with hope of undergoing a HDDA reaction (entry 2-4). Methyl acrylate, N-phenylmaleimide and ethyl (*Z*)-3-bromo-2-propenoate[46] were scanned as dienophiles with diene **4.21** and vinylmagnesium bromide without success. Ethyl (*Z*)-3-bromo-2-propenoate was chosen as an activated dienophile, bearing an electron withdrawing halogen and ester, with the potential of installing the endocyclic alkene of havellockate **4.1** after elimination. Since diene **4.21** was not offering results, triol **4.22** was considered as diene. Interestingly, one, two or all three hydroxyls could tether to the magnesium unit and facilitate the HDDA process. However, the solubility of **4.22** was one variable that had not immediately been considered. Therefore, non-polar toluene was substituted with tetrahydrofuran when the reaction conditions required vinylmagnesium bromide. The change in solvents could have possibly been responsible for the lack of productivity between diene **4.22** and methyl acrylate, ethyl (*Z*)-3-bromo-2-propenoate and N-phenylmaleimide (entries 5-7). Knowing that triol **4.22** was partially soluble in dichloromethane, the reaction was attempted between triol **4.22**, ethyl (*Z*)-3-bromo-2-propenoate and $MgBr_2 \cdot OEt_2/Et_3N$ but led to decomposition of the starting material (entry 8).

At this point in time, the primary alcohol of triol **4.22** was selectively protected with TBDPSCl to focus the magnesium tethering onto the resulting accessible secondary and tertiary alcohols. The hydroxy-directed Diels-Alder reaction (HDDA) was tried between diene **4.23**, methyl acrylate, dimethyl maleate, $MgBr_2 \cdot OEt_2/Et_3N$ and

[46] For the preparation, see Ma, S; Lu. X. *Organic Syntheses,* **1995**, *72*, 112

vinylmagnesium bromide (entries 1-4, Table 3.2). These esters were chosen as dienophiles in order to directly afford a cycloadduct bearing the 5-membered γ-lactone. Since these reactions were not productive, diol **4.23** was lastly reacted with methyl acrylate and an aggressive Lewis acid (entry 5). Not surprisingly, the diene decomposed in the presence of dimethylaluminum chloride.

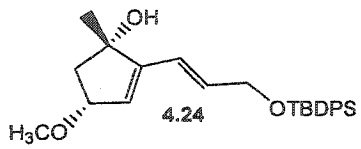
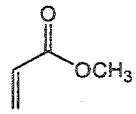
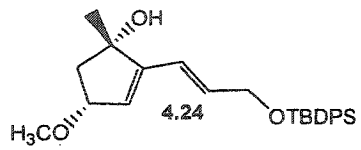
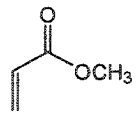
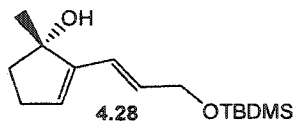
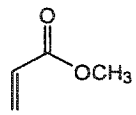
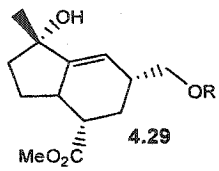
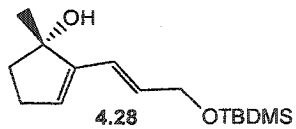
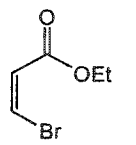
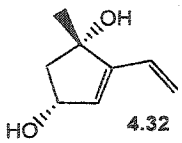
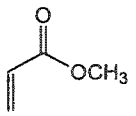
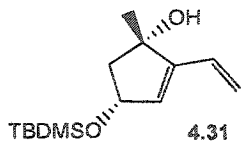
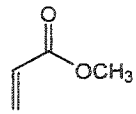
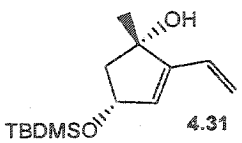
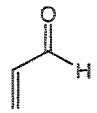
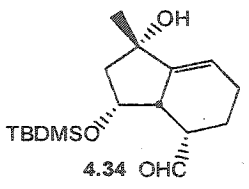
Table 4.2: Attempted Diels-Alders with diene **4.23** and various dienophiles.

Entry	Diene	Dienophile	Conditions	Product
1			A	SM
2			B	SM
3			A	SM
4			B	SM
5			$(CH_3)_2AlCl$ Toluene	Decomposition

At this point, the protecting groups were changed from the initial diene **4.21**. Instead of protecting 1° and 2° alcohols with *tert*-butyldimethylsilyl groups, the 1° alcohol was protected with *tert*-butyldiphenylsilyl and the 2° alcohol was protected as a less

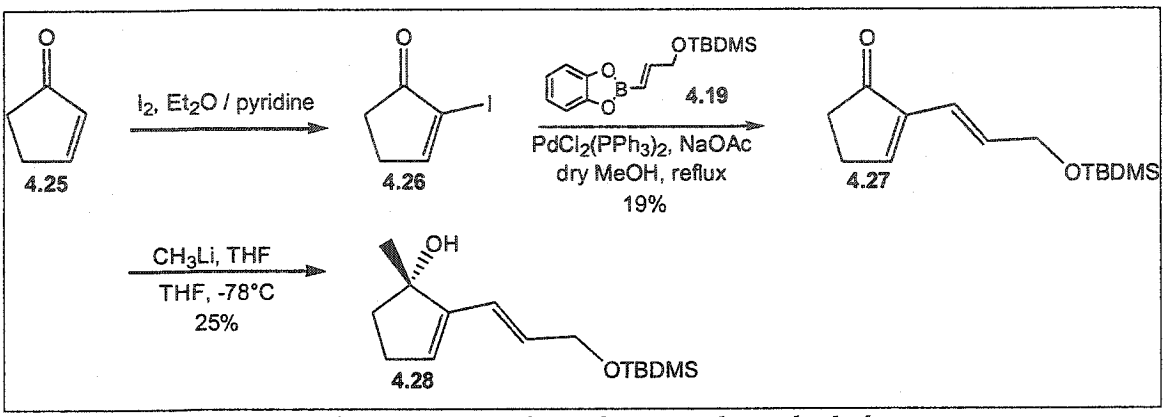
hindering methyl ether. Only recovered starting material was obtained when diene **4.24** was treated with methyl acrylate, the $MgBr_2{\cdot}OEt_2/Et_3N$ or vinylmagnesium bromide (entry 1 and 2, Table 4.3).

Table 4.3: Attempted Diels-Alders with dienes **4.24**, **4.28**, **4.31** and **4.32** with dienophiles.

Entry	Diene	Dienophile	Conditions	Product
1	 **4.24**		A	SM
2	 **4.24**		B	SM
3	 **4.28**		B	 **4.29** Regioisomers 4:1
4	 **4.28**		B	Decompostion
5	 **4.32**		A	SM
6	 **4.31**		A	SM
7	 **4.31**		A[a]	 **4.34** Epimers 9:1

[a] 2,6-Lutidine was used as base.

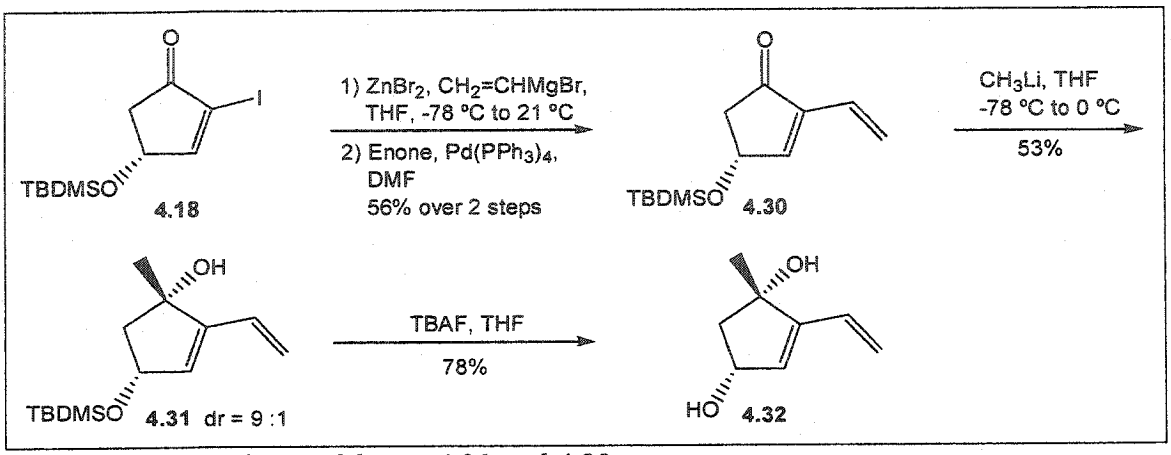
Due to the fact that all dienes bearing a secondary alcohol were not compatible with the chosen dienophiles, a diene lacking the secondary alcohol was synthesized. α-Iodination of commercially available enone **2.25** followed by a Suzuki coupling reaction afforded diene **2.27** (Scheme 4.6). Tertiary alcohol **2.28** was obtained by treating the resulting ketone **2.27** with methyllithium in 25% yield. These products were obtained in low yields given that they are susceptible to decomposition with an excess of base.



Scheme 4.6: *Synthesis of diene* ***2.28*** *without the secondary alcohol.*

The HDDA reaction was attempted between diene **2.28**, dienophile (methyl acrylate and ethyl (*Z*)-3-bromo-2-propenoate) with vinylmagnesium bromide to respectively afford an inseperable mixture of regioisomers **4.29** in >90% yield and decomposition of diene **4.28** (entries 3 and 4). With all these attempts, it was clear that dienes **4.21**, **4.22**, **4.23**, **4.24** and **4.28** were not compatible with the chosen dienophiles and reaction conditions to afford the desired cycloadducts. Mimicking the 6-membered semicyclic dienes of Barriault, Thomas and Clément and the successful 5-membered semicyclic dienes (Table 3.3), dienes **4.31** and **4.32** were synthesized (Scheme 4.7).

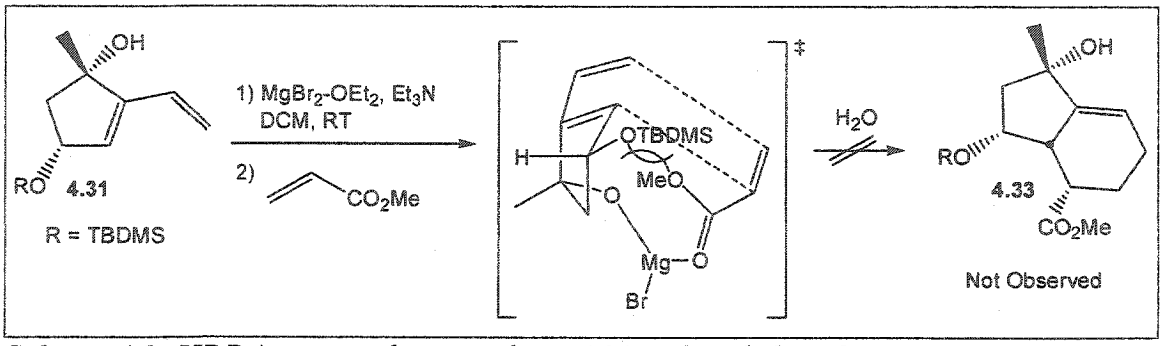
Palladium-catalyzed cross-coupling of vinyl iodide **4.18** under Negishi conditions[47] afforded diene **4.30** in 56% over 2 steps. Next, nucleophilic attack with methyllithium was anticipated to occur *anti* to the silylether. Tertiary alcohol **4.31** was obtained in 53% yield with a diastereomeric *anti/syn* ratio of 9:1. Upon deprotection with TBAF, diol **4.32** was also generated in 78% yield.



***Scheme 4.7:** Synthesis of dienes **4.31** and **4.32**.*

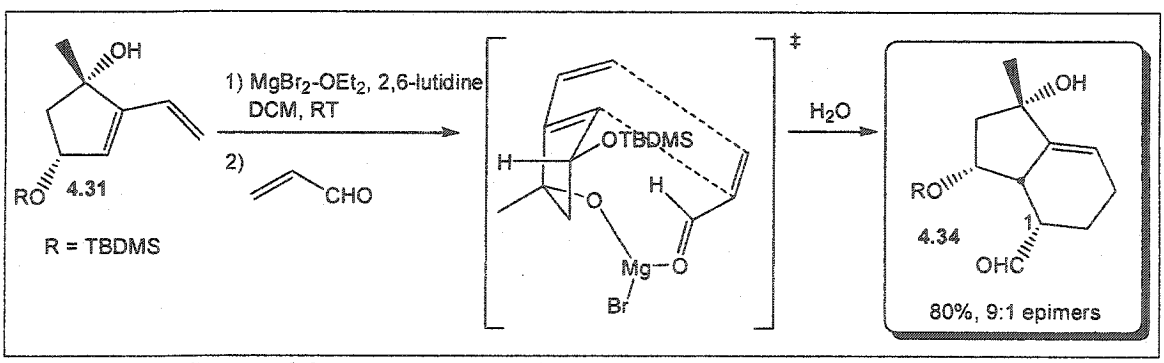
Diene **4.32**, bearing a diol, was envisioned reacting with methylacrylate and $MgBr_2 \cdot OEt_2/Et_3N$ to directly afford the tricyclic core of havellockate **4.1** after spontaneous lactonisation (Table 4.3, entry 5). The lack of product can possibly be explained by the presence of the diols, which can create unfavorable aggregates with magnesium and can promote difficulties during the reaction. In order to overcome this problem, the monoprotected diene **4.31** was reacted with methyl acrylate and $MgBr_2 \cdot OEt_2/Et_3N$ without success (entry 6).

[47] (a) Pour, M.; Negishi, E. *Tetrahedron Lett.* **1996**, *37*, 4679. (b) Negishi, E. ; Owczarczyk, Z.R.; Swanson, D. *Tetrahedron Lett.* **1991**, *32*, 4453.



Scheme 4.8: HDDA reaction between diene 4.31 and methylacrylate.

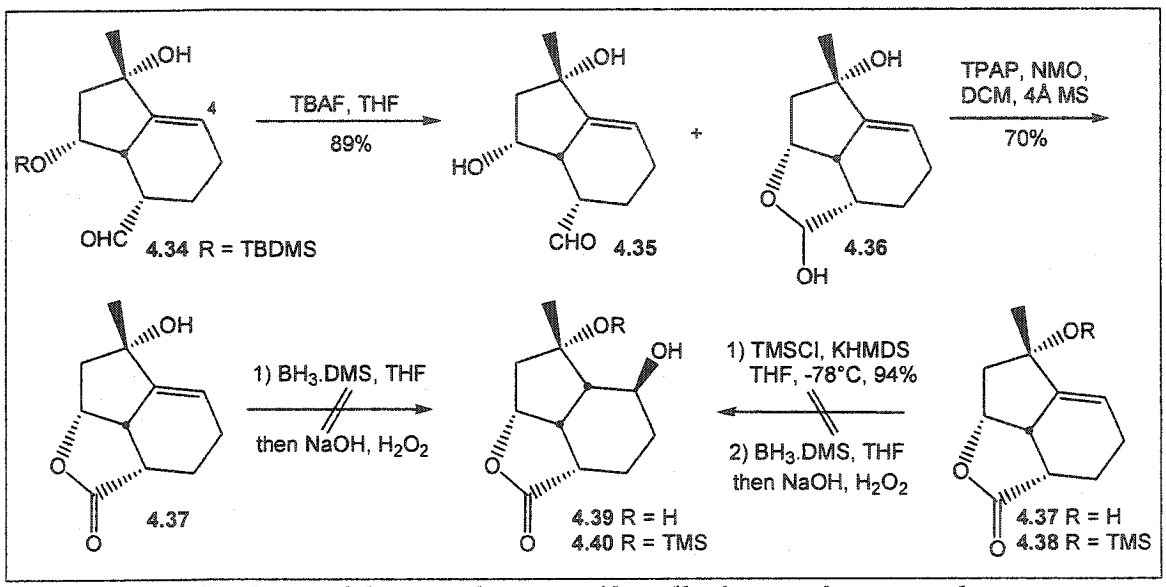
However, visualization of the transition state of this reaction offers insight on the lack of reaction. As illustrated in Scheme 4.8, when the dienophile is delievered *syn* to the alcohol during the HDDA, steric interactions are developed between the bulky TBDMS group and the methylester. This unfavorable interaction is a plausible explanation for the absence of product **4.33**. In order to decrease the steric bulk of the dienophile, acrolein was tested as dienophile with $MgBr_2 \cdot OEt_2$/2,6-lutidine (Table 4.3, entry 7). As demonstrated by Thomas and Clément, 2,6-lutidine was required as base when acrolein was used as dienophile to decrease the epimerization at the vulnerable C-1. Much to our delight, the HDDA reaction regio- and stereoselectively afforded bicyclic core **4.34** of havellockate **4.1** in 80% yield (α/β = 9:1) (Scheme 4.9).



Scheme 4.9: Successful HDDA reaction between diene 4.31 and acrolein.

4.3 Towards the Synthesis of the Tetracyclic Core of Havellockate

With the bicyclic core of havellockate in hand, the next challenge was the formation of the γ-lactone followed by a stereoselective hydroboration of the endocyclic alkene. Deprotection of silylether **4.34** with TBAF afforded a mixture of alcohol **4.35** and lactol **4.36** in a combined yield of 89% (Scheme 4.10). Oxidation of the mixture with NMO, 4Å MS and catalytic TPAP provided lactone **4.37** in 70% yield.



Scheme 4.10: *Synthesis of the tricyclic core of havellockate and attempted hydroboration.*

In order to control the stereogenic centers found on havellockate **4.1**, a stereoselective hydroboration was envisioned to, primarily afford the required *cis* ring junction, and secondly insert an alcohol on C-4. The facial selectivity of the hydroboration would hopefully be controlled by steric factors and afford the desired *cis* ring junction. However, there was the possibility of a complexation between the tertiary alcohol and the borane reagent to provide the *trans* ring junction. If this were the case, one could simply protect the alcohol to avoid such problems. The regioselectivity of the hydroboration would be dictated by the anti-Markovnikov addition of the boron onto the

less substituted carbon of the alkene. As illustrated in Table 3.4, many hydroboration conditions were scanned with alkene **4.37**. Unless otherwise indicated, no reaction occurred and the starting material was recovered and purified.

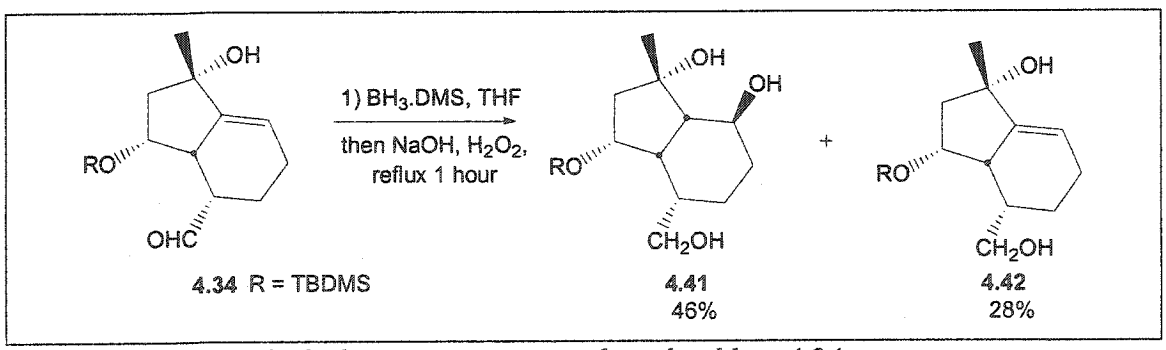
Table 4.4: Attempted hydroborations to generate the cis-ring junction.

Entry	R	Hydroboration	Conditions	Oxidation	Conditions
1	H	BH_3.DMS	CH_2Cl_2, reflux for 2 hrs RT for 18 hrs	NaOH, H_2O_2, EtOH	RT 18 hrs
2	H	BH_3.DMS	hexanes, RT for 1 hr	NaOH, H_2O_2, EtOH	RT 18 hrs, Reflux 1 hr
3	H	BH_3.DMS	THF, reflux for 18 hrs	NaOH, H_2O_2, EtOH	Reflux for 2 hrs, RT 18 hrs
4	H	BH_3.DMS	THF, RT for 6 hrs	NaOH, H_2O_2, EtOH	RT for 18 hrs, Reflux for 1 hr
5	H	9-BBN dimer	THF, reflux for 6 hrs RT for 18 hrs	NaOH, H_2O_2	Reflux for 1 hr
6	TMS	BH_3.DMS	THF, reflux for 3 hrs	NaOH, H_2O_2, EtOH	RT for 18 hrs
7	TMS	9-BBN.THF	THF, RT for 30 minutes Reflux for 18 hrs Solvent evaporated ON	---	---
8	TMS	BH_3.THF	THF, 0°C for 1 hr RT for 18 hrs	NaOH, H_2O_2	Decomposed
9	TMS	Catecholborane	THF, reflux for 8 hrs	NaOH, H_2O_2	RT for 18 hrs

In entries 1 to 4, alkene **4.37** and borane·DMS were combined in various solvents such as dichloromethane, hexanes and THF. Even though the length and temperature of the reaction were varied, no reaction occurred. As expected, alkene **4.37** and the bulky 9-BBN dimer did not afford the desired alcohol due to the size and inaccessibility of the borane towards the reactive site on the substrate (entry 5). Bearing in mind that the free

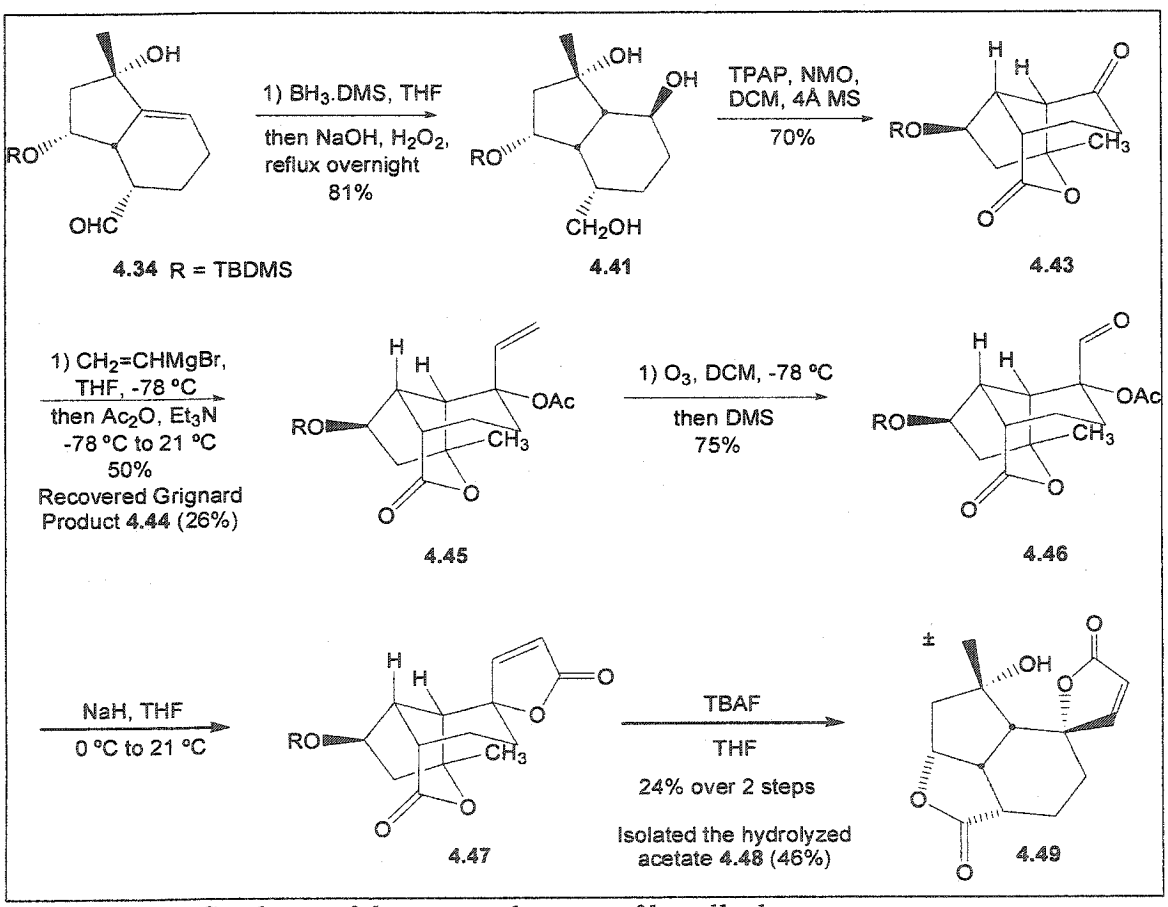
tertiary alcohol might be responsible for the lack of results, the later was protected with TMSCl and KHMDS in 94% yield (Scheme 4.10). The resulting alkene **4.38** was treated with various borane reagents, such as BH_3·THF, 9-BBN·THF, BH_3·DMS and catecholborane, with THF as solvent without success (entries 6-9). Since the substrate is polyoxegenated, an excess of borane would always be used to insure the presence of the reactive reagent after possible complexation to the oxygen atoms.

After many hydroboration attempts, it was apparent that the synthetic strategy would require some modifications. Instead of deprotecting alcohol **4.34** and generating γ-lactone **4.37**, the hydroboration was directly attempted with the HDDA cycloadduct **4.34** and BH_3·THF, followed by oxidation of the trialkylborane with $NaOH/H_2O_2$ (Scheme 4.11). After oxidation, the heterogeneous mixture was refluxed for 1 hour and afforded the desired triol **4.41** in 46% yield and diol **4.42** in 28% yield.



Scheme 4.11: *First hydroboration attempt with cycloadduct 4.34.*

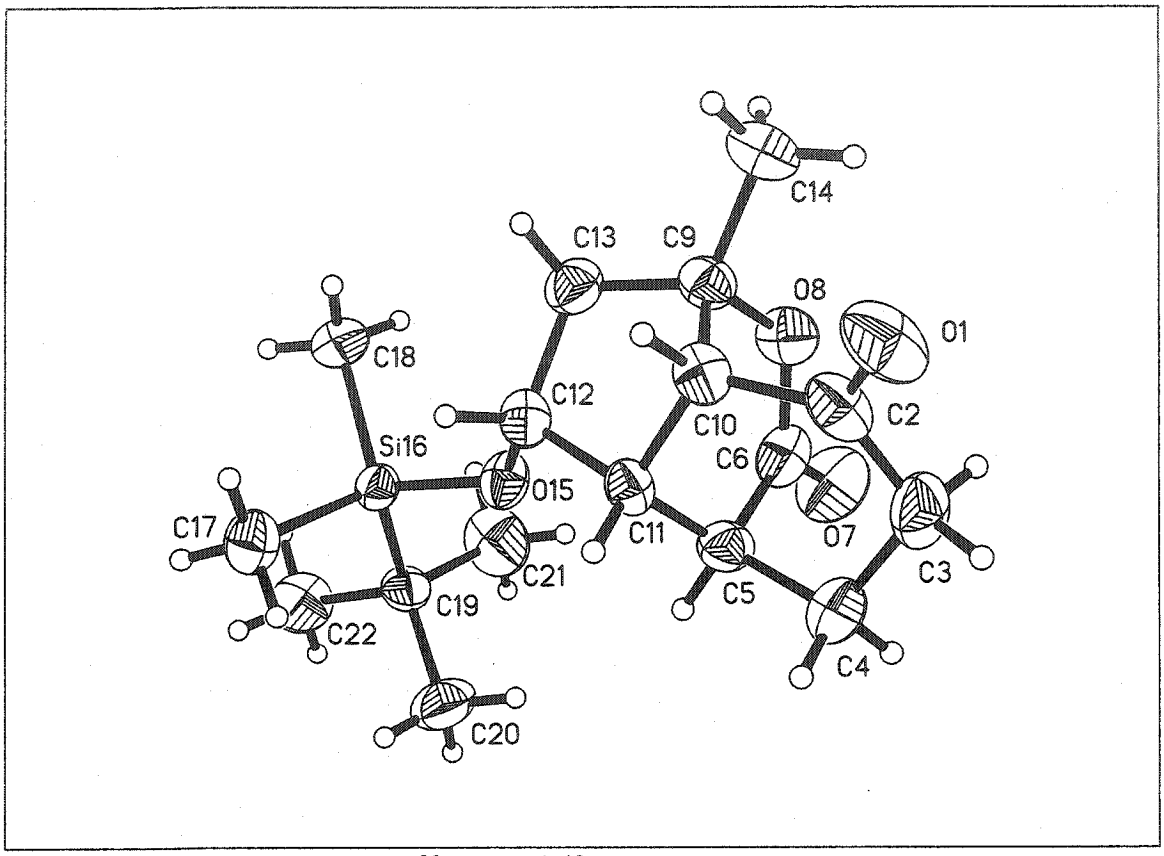
In order to drive the reaction to completion, the procedure was modified and the oxidation mixture was refluxed overnight. Astonishingly, hydroboration of **4.34** provided **4.41** in 81% yield as the sole isomer (Scheme 4.12). In addition to the hydroboration, the aldehyde was reduced *in situ* to the primary alcohol. Close examination of the progression of the reaction showed that the aldehyde was first reduced, followed by the hydroboration of the resulting product. After this accomplishment, the main focus was the construction of the spirolactone.



Scheme 4.12: *Synthesis of the tetracyclic core of havellockate.*

Secondary alcohol **4.41** was oxidized to the ketone with NMO and TPAP (cat.). In addition, the primary alcohol of **4.41** was oxidized to the aldehyde, whereupon the tertiary alcohol and aldehyde cyclized to form the lactol. The resulting lactol was further

oxidized to provide lactone **4.43** in 70% yield. The generation of this rigid product confirmed the presence of a *cis* ring junction and protected *in situ* the tertiary alcohol as a lactone. The X-ray structure of lactone **4.43** is illustrated in Scheme 4.13.



Scheme 4.13: *X-ray structure of lactone* ***4.43****.*

Ketone **4.43** was treated with vinylmagnesiumbromide and the reaction was quenched with acetic anhydride to afford acetate **4.45** in 50% yield over two steps. The acetalisation reaction did no go to completion and the tertiary alcohol **4.44**, resulting from the Grignard addition, was recovered in 26% yield. Due to the presence of the lactone and the *cis* ring junction, the Grignard reagent is believed to selectively attack on the top face. Even in the presence of an excess of vinylmagnesium bromide, TLC and ^{1}H NMR

never indicated a second product (attack from the bottom face) or opening of the lactone. Ozone was bubbled into a solution of **4.45** in dichloromethane to transform the terminal alkene into aldehyde **4.46** in 75% yield.

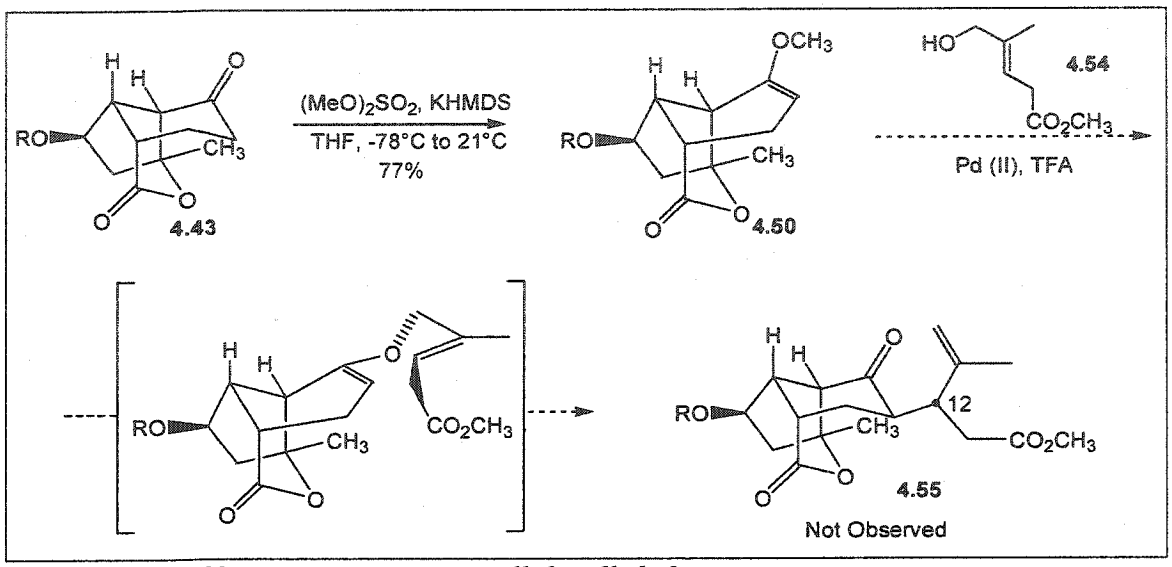
The closure of the spirolactone was envisioned via an intramolecular aldol condensation without elimination to afford the secondary alcohol of the spiro-lactone on havellockate **4.1**. Acetate **4.46** was initially treated with LDA but the desired product was not observed by ^{1}H NMR. KHMDS and DBU afforded the starting material whereas freshly sublimed potassium *tert*-butoxide hydrolyzed the acetate. However, treatment of acetate **4.46** with NaH, followed by deprotection of the secondary alcohol afforded the aldol product with elimination and the 5-membered γ-lactone **4.47** (Scheme 4.12). Upon deprotection, the secondary alcohol spontaneously attacks the rigid 6-membered lactone to relieve strain and liberate the tertiary alcohol. In addition to obtaining the desired spirolactone **4.49** in 24% over two steps, the hydrolyzed acetate **4.48** bearing the 5-membered lactone was also isolated in 46% yield. After observing the facile elimination of the hydroxyl after condensation, it was established that the spirolactone would be installed after the addition of the side alkyl chain during the total synthesis of havellockate **4.1**.

4.4 Installation of the Side Alkyl Chain of Havellockate via a Claisen Rearrangement

According to Nakai,[48] a palladium-catalyzed Claisen reaction can occur via an *in situ* enol ether exchange in the presence of TFA. This methodology was attempted in order to install the side alkyl chain on the tricyclic core of havellockate. In addition,

[48] Nakai, T.; Sugiura, M. *Tetrahedron Lett.* **1996**, *37*, 7991.

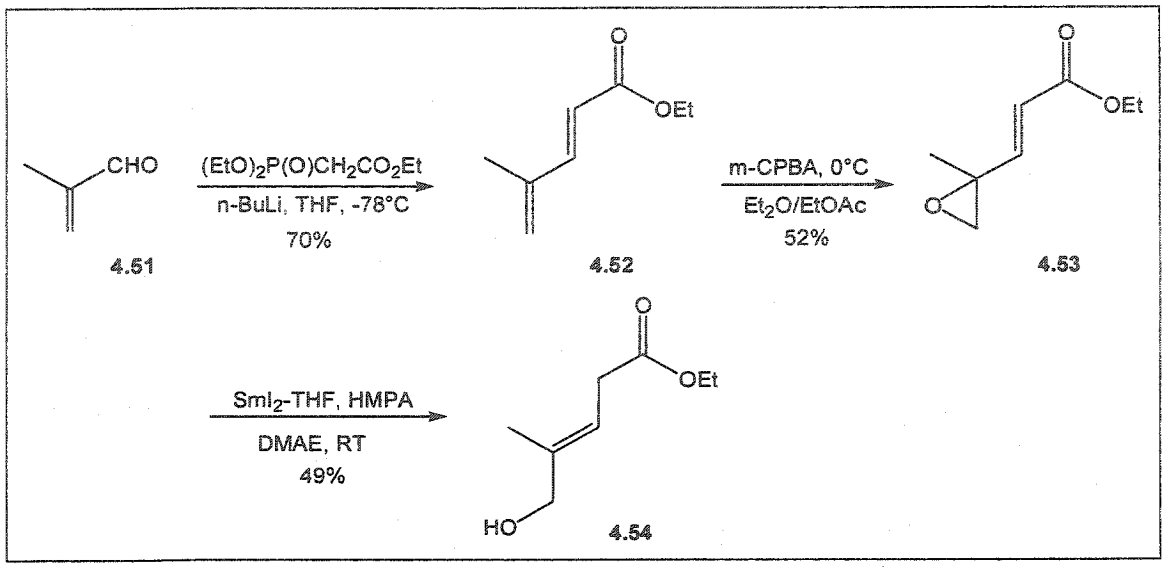
since the 6-membered lactone was hindering the bottom face of the complex, the Claisen rearrangement would occur from the top face to afford the desired stereogenic center on C-12. The enol ether **4.50** was obtained from ketone **4.43** with KHMDS and dimethylsulfate in 77% yield (Scheme 4.14).



Scheme 4.14: *Claisen attempts to install the alkyl chain.*

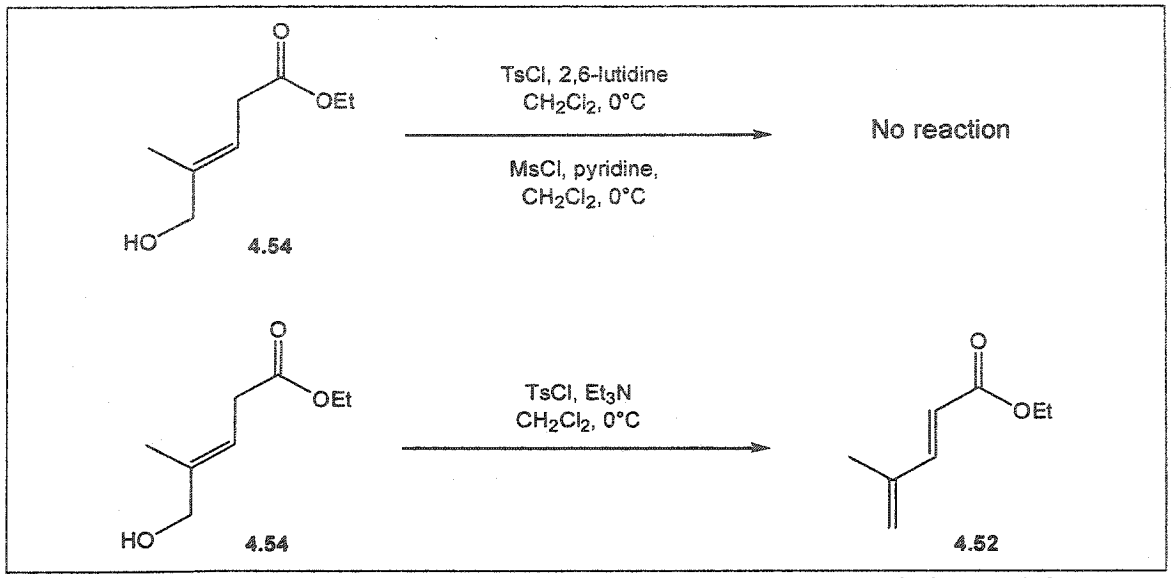
Allylic alcohol **4.54** was prepared in three steps starting with a Horner-Wadsworth-Emmons reaction between triethylphosphonoactetate and commercially available methacrolein **4.51** (Scheme 4.15).[49] The most electron rich alkene of ester **4.52** underwent epoxidation in the presence of *m*CPBA to afford epoxide **4.53** in 52% yield. The highly regioselective samarium(II) iodide-induced reduction of γ,δ-epoxy-α,β-unsaturated ester **4.53** with HMPA and DMAE afforded the allylic alcohol **4.54** in 49% yield. Unfortunately, the anticipated Claisen reaction via the enol ether exchange between methylenol ether **4.50** and allylic alcohol **4.54** was not successful. Upon many attempts, the methyl enol ether **4.50** would simply hydrolyze to ketone **4.43** with addition of allylic alcohol **4.54**.

[49] Etemad-Moghadam, G.; Seyden-Penne, J. *Tetrahedron*, **1984**, *40*, 5153



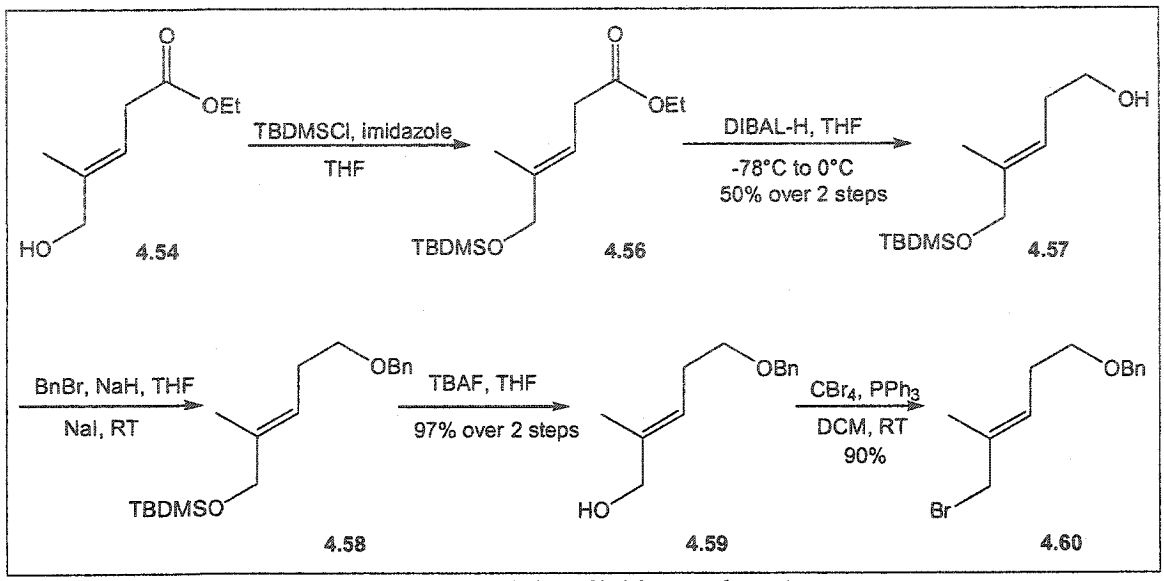
Scheme 4.15: *Preparation of the allylic alcohol* ***4.54*** *via a* SmI_2*-induced reduction.*

In order to overcome this problem, *O*-alkylation of ketone **4.43** with the tosylated version of allylic alcohol **4.54** was suggested. This would have directly created the enol ether which could subsequently undergo a Claisen rearrangement to afford the desired side alkyl chain **4.55** of havellockate. Activation of allylic alcohol **4.54** was considered using tosyl chloride and base (Scheme 4.16). To avoid the unfavoured elimination product **4.52**, 2,6-lutidine was chosen as a hindered base, but no reaction occurred. A similar result was obtained with mesyl chloride and pyridine. Allylic alcohol **4.54** was activated with tosyl chloride and triethylamine, however the undesired conjugated system **4.52** was isolated due to elimination.



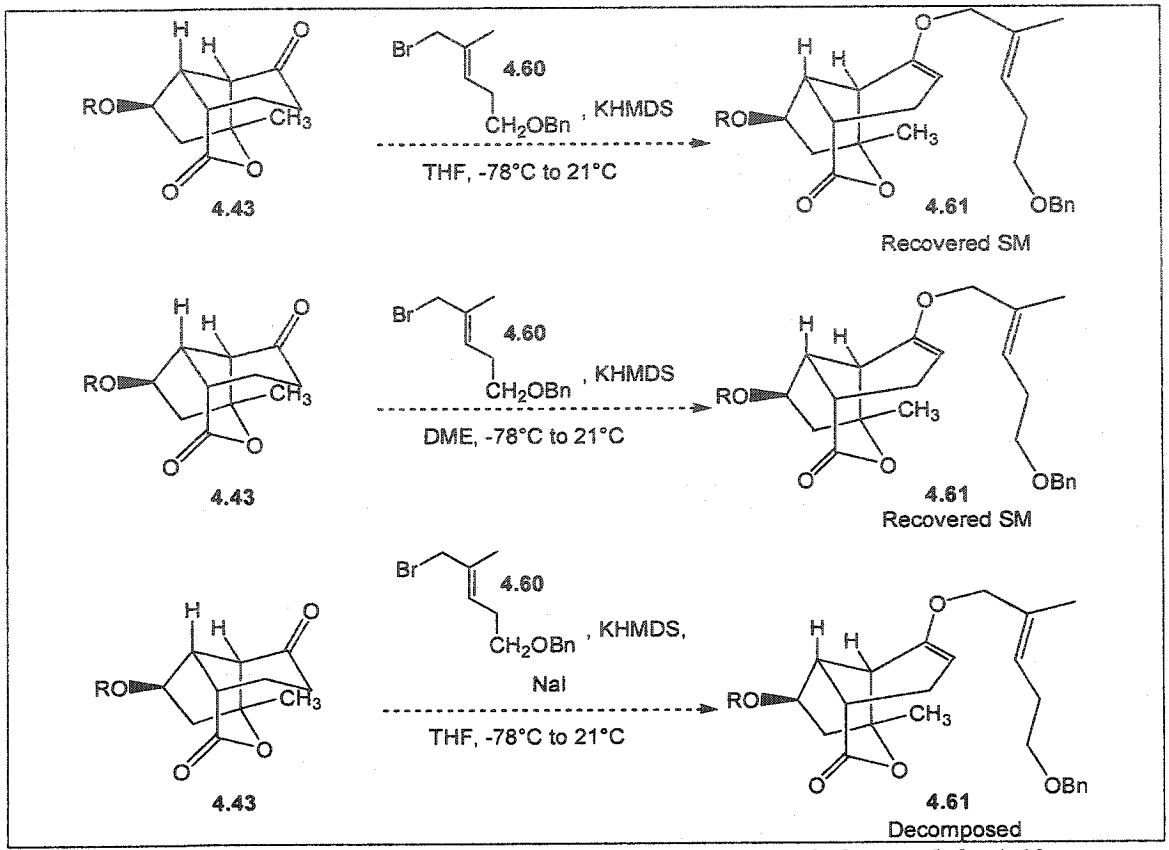
Scheme 4.16: *Attempts to prepare the mesylate and tosylate activated electrophiles.*

Due to the fact that allylic alcohol **4.54** readily eliminated to the conjugated ester **4.52** with tosylchloride, allyl bromide **4.60** was considered as an electrophile (Scheme 4.17). However, in order to avoid elimination, the ester needed to be reduced to the primary alcohol. The primary alcohol **4.54** was protected with TBDMSCl to provide silyl ether **4.56**. Crude ester **4.56** was reduced in the presence of DIBAL-H to afford alcohol **4.57** in 50% yield over two steps. The later was protected with benzylbromide and the silyl protecting group was subsequently removed with TBAF to generate allylic alcohol **4.59** in 97% yield over two steps. In the presence of carbon tetrabromide and triphenylphosphine, bromine-activated electrophile **4.60** was afforded in 90% yield.



Scheme 4.17: *Synthesis of the electrophilic allyl bromide* ***4.60.***

Although some *C*-alkylation was anticipated, the bromine-activated electrophile was tested with ketone **4.43** and KHMDS to provide the Claisen precursor **4.61** (Scheme 4.18). When THF and DME were used as solvents, no reaction occurred and the starting materials were recovered. As a final attempt, allyl bromide **4.60** was used with a catalytic amount of sodium iodide in THF, but under such conditions, ketone **4.43** decomposed.



Scheme 4.18: *Attempts of O-alkylation with bromine-activated electrophile* ***4.60****.*

4.5 Conclusion

In conclusion, the scope and limitations of the hydroxy-directed Diels-Alder reaction were established during the course of this study. In general, dienes which bear the alkyl chain are not compatible with the HDDA reaction. In addition, polyoxygenated precursors are not well-suited with this methodology due to, their insolubility in non-polar solvents and, the difficulty of the magnesium to tether the diene and dienophile in an organized fashion. However, semicyclic diene **4.31** afforded the desired regio- and stereoselective Diels-Alder cycloadduct with acrolein. With this result in hand, the tetracyclic core of havellockate was obtained in 12 steps from furfuryl alcohol. The formation of the 6-membered lactone was unexpected but proved to be helpful in the subsequent reactions in terms of selectivity and protecting the tertiary alcohol. Since the

aldol condensation afforded the enone after spontaneous elimination, installation of the side alkyl chain will be performed before functionalizing the spirolactone. The Claisen reaction is currently being studied as a route for adding the alkyl chain with the desired stereogenic center.

Chapter 5: Experimental

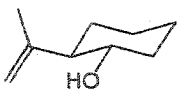
5.1 General Methods and Materials

All reactions were carried out under dry atmospheres in flame-dried glassware or sealed tubes equipped with a magnetic bar and a rubber septum, unless otherwise indicated. THF and Et_2O were freshly distilled from sodium/benzophenone. Dichloromethane, DMF, toluene and triethylamine were freshly distilled from CaH_2. $MgBr_2 \cdot OEt_2$ was prepared in our laboratory and stored in the glove box. The other commercially available reagents were used without purification, unless otherwise indicated.

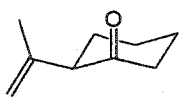
Reactions were monitered by TLC analysis of aliquots, using aluminum sheets precoated (0.2 mm layer thickness) with silica gel 60 F_{254} (E. Merck). Flash chromatography was carried out on 230-400 mesh silica gel 60. TLC plates were viewed under UV light and stained with *p*-anisaldehyde staining solution. GC (Agilent 6890 Series) was equipped with a crosslinked 5% PH ME siloxane column (30 m x 0.32 mm, 0.25 μm film). ^1H and ^{13}C NMR spectra were recorded on Bruker Avance 300 MHz and Bruker AMX 500 MHz spectrometers. IR spectra were recorded on a Bomen Michaelson 100 FTIR spectrometer. HRMS spectra were obtained on a Kratos Analytical Concept instrument. Melting points were recorded on a Gallenkamp Melting Point Apparatus P 1106G. 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 pressure monitoring device and an EST-300 Plus fibre optic temperature probe. All experiments were performed in a quartz tube (previously washed with

aqueous iPrOH/NaOH solution, water and acetone). When using non-polar solvents such as toluene, a carboflon™ bar was added.

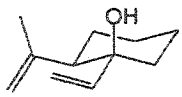


2-isopropenyl-cyclohexanol (2.10) A dry 500 mL round bottom flask was charged with CuBr·DMS (1.05 g, 5.09 mmol) and THF (150 mL). The solution was cooled to -30°C followed by the addition of isopropenylmagnesium bromide (132.4 mL, 66.23 mmol). The mixture was stirred for 15 minutes. Cyclohexene oxide **2.9** (5.00 g, 50.9 mmol) was added and the solution was warmed to 0°C and stirred for 1.5 hours. The reaction mixture was quenched with saturated NH_4Cl (200 mL) and extracted with ether (3x). The combined organic phases were dried over anhydrous $MgSO_4$, concentrated *in vacuo* and purified by flash column chromatography (20% EtOAc in hexanes) to provide alcohol **2.10** as a yellow oil (7.14 g, 94%). Spectral data: Warrington, J. M.; Yap, G. P. A.; Barriault, L. *Org. Lett.* **2000**, *2*, 663.



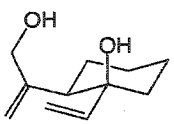
2-isopropenyl-cyclohexanone (2.11) A 500 mL dry round bottom flask was charged with oxalyl chloride (5.33 mL, 61.1 mmol) and dichloromethane (200 mL). The solution was cooled to –78°C, and DMSO (8.67 mL, 122 mmol) was slowly added. After 20 minutes of stirring, alcohol **2.10** (7.136 g, 50.90 mmol) was added to give an opaque white mixture. The later was stirred at –78°C for 1.5 hours, followed by the addition of triethylamine (35.47 mL, 254.5 mmol). The solution was again stirred at 0°C for an additional hour and quenched with saturated NH_4Cl. The aqueous layer was extracted with CH_2Cl_2 (3x) and the combined organic phases were dried over anhydrous $MgSO_4$. The solution was concentrated and purified by flash column chromatography (20 % EtOAc in hexanes) to afford ketone **2.11** as a yellow oil

(5.63 g, 80%). Spectral data: Warrington, J. M.; Yap, G. P. A.; Barriault, L. *Org. Lett.* **2000**, *2*, 663.



2-isopropenyl-1-vinyl-cyclohexanol (2.12)

To a dry 500 mL round bottom flask was added 2-isopropenylcyclohexanone **2.11** (3.90 g, 28.2 mmol) and THF (150 mL). The solution was cooled to –78°C, followed by the addition of vinylmagnesium bromide (84.0 mL, 84.6 mmol). The mixture was stirred at –78°C for 30 minutes. The solution was subsequently stirred at 0°C for 1 hour. The reaction was quenched with saturated NH_4Cl, and the aqueous phase was extracted with ethyl acetate (3x). The solution was dried over anhydrous $MgSO_4$, concentrated and purified by flash column chromatography (10% EtOAc in hexanes), to afford alcohol **2.12** as a yellow oil (2.98 g, 64%). Spectral data: Warrington, J. M.; Yap, G. P. A.; Barriault, L. *Org. Lett.* **2000**, *2*, 663.

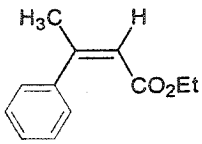


2-(1-hydroxymethyl-vinyl)-1-vinyl-cyclohexanol (2.13)

A solution of 2-isopropenyl-1-vinyl-cyclohexanol **2.12** (2.98 g, 17.92 mmol) in CH_2Cl_2 (50 mL) was canulated into a dry 250 mL round bottom flask. Selenium dioxide (0.994 g, 8.96 mmol) and *t*-BuOOH 70% (9.22 mL, 71.7 mmol) were added and the mixture was stirred overnight. The reaction mixture was diluted with CH_2Cl_2 and water. The organic layer was washed with saturated sodium bicarbonate (2 x 30 mL), brine (30 mL), water (30 mL) and another 30 mL of brine. The organic layer was dried over $MgSO_4$ and the solvent was evaporated *in vacuo*. The crude product was purified by flash column chromatography (35% EtOAc in hexanes) to afford diol **2.13** as colorless crystals (1.48 g, 45%). IR (cm^{-1}) 3310 (br), 3201 (br), 3073 (m), 3010 (m),

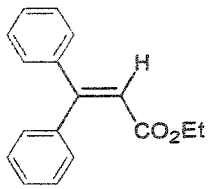
2978 (m), 2934 (s), 2855 (s), 1638 (m), 1448 (m). ^{1}H NMR (300 MHz, $CDCl_3$) δ_{ppm} 5.83 (dd, J = 17.2 Hz, J =10.7 Hz, 1H), 5.14 (d, J = 17.2 Hz, 1H), 5.03 (s, 1H), 4.96 (d, J = 10.7 Hz, 1H), 4.86 (s, 1H), 4.03 (d, J = 12.5 Hz, 1H), 3.90 (d, J = 12.5 Hz, 1H), 3.46 (bs, 2H), 2.21 (dd, J = 3.1 Hz, J = 12.8 Hz, 1H), 1.92-1.19 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 149.8 (C_4), 146.4 (CH), 116.7 (CH_2), 111.7 (CH_2), 73.3 (C_4), 65.1 (CH_2), 52.4 (CH), 38.7 (CH_2), 27.2 (CH_2), 26.4 (CH_2), 21.5 (CH_2). HRMS (EI), *m/z* (M^+-H_2O) calculated for $C_{11}H_{16}O$ 164.1247 found 164.1223. mp = 77.9-80.1°C.

5.2 General Procedure A for the Horner-Wadsworth-Emmons Reaction



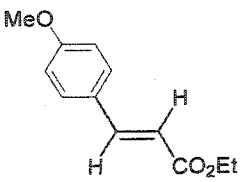
(*Z*)-3-Phenyl-but-2-enoic acid ethyl ester (2.15a)

To a dry 250 mL round bottom flask was added NaH (4.996 g, 124.9 mmol) and THF (125.0 mL). The mixture was cooled to 0°C followed by the addition of triethylphosphonoacetate (16.52 mL, 83.24 mmol). The solution was stirred for 40 minutes. After adding acetophenone **2.14a** (5.00 g, 41.6 mmol) to the solution, the reaction mixture was warmed to room temperature (21°C) and stirred overnight. The solution was quenched with saturated NH_4Cl (100 mL), and the aqueous phase was extracted with ether (3 x 50 mL). The combined organic layers were dried over anhydrous $MgSO_4$, and the organic solvent was evaporated. The *E* and *Z* isomers were seperated by column chromatography (10% EtOAc in hexanes) to afford the *Z* isomer **2.15a** (0.79 g, 10%). Spectral analysis: Kobayashi, Y.; William, A. D.; Mizojiri, R. *J. Organomet. Chem.* **2002**, *653(1-2)*, 91.



3,3-Diphenyl-acrylic acid ethyl ester (2.15b)

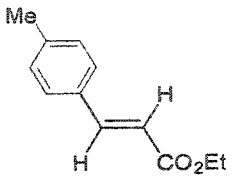
To a dry round bottom flask was added NaH (0.823 g, 34.3 mmol) and THF (35.0 mL) under an atmosphere of nitrogen. Triethylphosphonoacetate was slowly added to the solution. The mixture was refluxed for 15 minutes and a solution of benzophenone **2.14b** (1.25 g, 6.86 mmol) in THF (5.0 mL) was slowly cannulated into the solution. The reaction mixture was refluxed for an additional 3 hours, cooled to room temperature and poured into 200 mL of 1 N aqueous citric acid. The aqueous phase was extracted with ether (3 x 25 mL) and the combined organic layers were washed with water and brine. The organic phase was dried over anhydrous $MgSO_4$ and the solvent was evaporated. The crude product was purified by flash column chromatography (35% EtOAc in hexanes) to yield ester **2.15b** as a colorless oil (1.86 g, >98%). Spectral analysis: Groundwater, P. W.; Garnett, I.; Morton, A. J.; Sharif, T.; Coles, S. J.; Hursthouse, M. B.; Nyerges, M.; Anderson, R. J.; Bendell, D.; McKillop, A.; Zhang, W. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2781.



***trans*-3-(4-Methoxy-phenyl)-acrylic acid ethyl ester (2.15c)**

Prepared using general procedure **A**

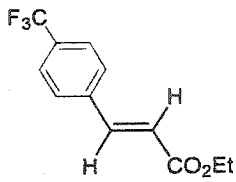
Sodium hydride (1.10 g, 27.5 mmol); triethylphosphonoacetate (4.12 mL, 18.4 mmol); *p*-anisaldehyde **2.14c**(1.25 g, 9.18 mmol) in THF (30.0 mL) to provide ester **2.15c** as a colorless oil (1.76 g, 93%). Spectral data: Huang, Z-Z.; Tang, Y. *J. Org. Chem.* **2002**, *67*, 5320.



***trans*-3-*p*-Tolyl-acrylic acid ethyl ester (2.15f)**

Prepared using general procedure **A**

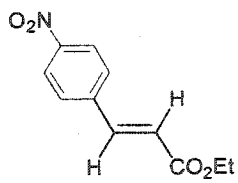
Sodium hydride (1.25 g, 31.2 mmol); triethylphosphonoacetate (4.13 mL, 20.8 mmol); *p*-tolualdehyde **2.14f** (1.25 g, 10.4 mmol) in THF (60.0 mL) to provide ester **2.15f** as a colorless oil (1.76 g, 89%). Spectral data: Huang, Z-Z.; Tang, Y. *J. Org. Chem.* **2002**, *67*, 5320.



***trans*-3-(4-Trifluoromethyl-phenyl)-acrylic acid ethyl ester (2.15g)**

Prepared using general procedure **A**

Sodium hydride (0.696 g, 17.4 mmol); triethylphosphonoacetate (2.30 mL, 11.6 mmol); *p*-(trifluoromethyl)benzaldehyde **2.14g** (1.01 g, 5.80 mmol) in THF (30.0 mL) to provide ester **2.15g** as colorless crystals (1.22 g, 86%). Spectral data: Huang, Z-Z.; Tang, Y. *J. Org. Chem.* **2002**, *67*, 5320.

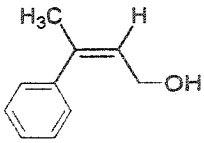


***trans*-3-(4-Nitro-phenyl)-acrylic acid ethyl ester (2.15i)**

Prepared using general procedure **A**

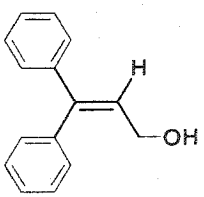
Sodium hydride (15.9 mg, 0.398 mmol); triethylphosphonoacetate (0.05 mL, 0.3 mmol); *p*-nitrobenzaldehyde **2.14i** (20.0 mg, 0.132 mmol) in THF (5.0 mL) to provide ester **2.15i** as a colorless crystals (15.3 mg, 52%). Spectral data: Masllorens, J.; Moreno-Manas, M.; Pla-Quintana, A.; Roglans, A. *Org. Lett.* **2003**, *5*, 1559.

5.3 General Procedure B for the DIBAL-H Reduction



(*Z*)-3-Phenyl-but-2-en-1-ol (2.16a)

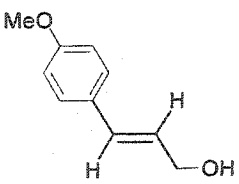
A solution of (*Z*)-3-phenyl-but-2-enoic acid ethyl ester **2.15a** (0.793 g, 4.17 mmol) in THF (60.0 mL) was canulated into a dry 250 mL round bottom flask. The mixture was cooled to –78°C. DIBAL-H (7.11 mL, 12.5 mmol) was added, and the solution was stirred at 0°C for 2.5 hours. The reaction was quenched with a 0.1 M aqueous solution of sodium tartrate and was stirred overnight. The clear aqueous layer was extracted with EtOAc (3 x 50 mL), dried over $MgSO_4$, and the solvent was evaporated to afford alcohol **2.16a** as a colorless oil (0.60 g, 97%). Spectral data: Carruthers, W.; Evans, N.; Pooranamoorthy, R. *J. Chem. Soc., Perkin Trans. 1* **1975**, 76.



3,3-Diphenyl-prop-2-en-1-ol (2.16b)

Prepared using general procedure **B**

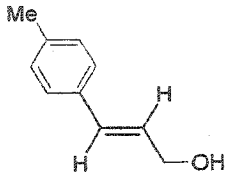
3,3-Diphenyl-acrylic acid ethyl ester **2.15b** (1.86 g, 7.38 mmol); DIBAL-H (14.8 mL, 22.2 mmol) in THF (100 mL) to afford alcohol **2.16b** as a colorless oil (1.17 g, 75%). Spectral data: Wang, Z.-X.; Shi, Y. *J. Org. Chem.* **1998**, *63*, 3099.



***trans*-3-(4-Methoxy-phenyl)-prop-2-en-1-ol (2.16e)**

Prepared using general procedure **B**

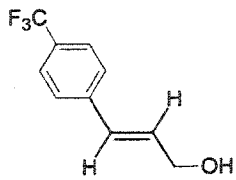
trans-3-(4-methoxy-phenyl)-acrylic acid ethyl ester **2.15e** (1.76 g, 8.52 mmol); DIBAL-H (17.0 mL, 25.5 mmol) in THF (100 mL) to afford alcohol **2.16e** as colorless crystals (1.25 g, 90%). Spectral data: Charette, A. B.; Molinaro, C.; Brochu, C. *J. Am. Chem. Soc.* **2001**, *123*, 12168.



***trans*-3-*p*-Tolyl-prop-2-en-1-ol (2.16f)**

Prepared using general procedure **B**

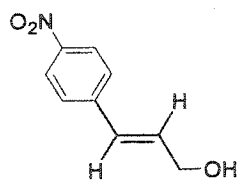
trans-3-p-tolyl-acrylic acid ethyl ester **2.15f** (1.76 g, 9.23 mmol); DIBAL-H (18.5 mL, 27.7 mmol) in THF (100 mL) to afford alcohol **2.16f** as colorless crystals (1.09 g, 80%). Spectral data: Takeuchi, R.; Ue, N.; Tanabe, K.; Yamashita, K.; Shiga, N. *J. Am. Chem. Soc.* **2001**, *123*, 9525.



***trans*-3-(4-Trifluoromethyl-phenyl)-prop-2-en-1-ol (2.16g)**

Prepared using general procedure **B**

trans-3-(4-Trifluoromethyl-phenyl)-acrylic acid ethyl ester **2.15g** (0.323 g, 1.32 mmol); DIBAL-H (2.65 mL, 3.97 mmol) in THF (50.0 mL) to afford alcohol **2.16g** as yellow crystals (0.266 g, 99%). Spectral data: Imai, N.; Nomura, T.; Yamasoto, S.; Ninomiya, Y.; Nokami, J. *Tetrahedron: Asymmetry* **2002**, *13*, 2433.

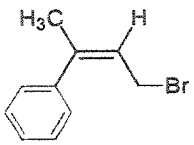


***trans*-3-(4-Nitro-phenyl)-prop-2-en-1-ol (2.16i)**

Prepared using general procedure **B**

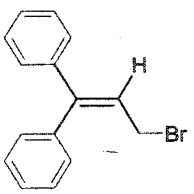
trans-3-(4-Nitro-phenyl)-acrylic acid ethyl ester **2.15i** (0.934 g, 4.22 mmol); DIBAL-H (8.44 mL, 12.7 mmol) in THF (60.0 mL) to afford alcohol **2.16i** as a colorless oil (0.399 g, 53%). Spectral data: Malet, R.; Moreno-Manas, M.; Parella, T.; Pleixats, R. *Organometallics* **1995**, *14*, 2463.

5.4 General procedure C for bromination of allylic alcohols



(*Z*)-(3-Bromo-1-methyl-propenyl)-benzene (2.17a)

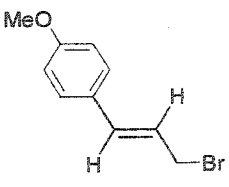
To a dry 100 mL round bottom flask was added (*Z*)-3-phenyl-but-2-en-1-ol **2.16a** (792.7 mg, 5.349 mmol) in 100.0 mL of dichloromethane at room temperature (21°C). Carbon tetrabromide (2.217 g, 6.686 mmol) was added and the mixture was stirred for 5 minutes. A solution of triphenylphosphine (2.104 g, 8.023 mmol) in dichloromethane (10.0 mL) was cannulated into the reaction mixture which subsequently became yellow. The solution was stirred at room temperature for one hour, followed by the removal of dichloromethane *in vacuo*. The residue was diluted with hexanes, and the triphenylphosphine oxide precipitated from solution. The mixture was filtered through celite (3x), and the organic solvent was evaporated on the rotary evaporator to provide **2.17a**. The product was used in the following reaction without further purification.



1-Bromo-3,3-diphenyl-prop-2-ene (2.17b)

Prepared using general procedure C

3,3-Diphenyl-prop-2-en-1-ol **2.16b** (509.6 mg, 2.423 mmol); carbon tetrabromide (100.0 mg, 3.029 mmol); triphenylphosphine (953.3 mg, 3.635 mmol) in CH_2Cl_2 (50.0 mL). The product was used in the following reaction without further purification.

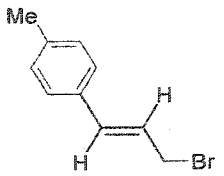


***trans*-1-(3-Bromo-propenyl)-4-methoxy-benzene (2.17e)**

Prepared using general procedure C

trans-3-(4-Methoxy-phenyl)-prop-2-en-1-ol **2.16e** (150.0 mg, 0.914 mmol); carbon tetrabromide (378.7 mg, 1.142 mmol); triphenylphosphine (359.4 mg,

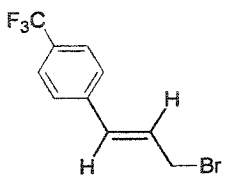
1.370 mmol) in CH_2Cl_2 (25.0 mL). The product was used in the following reaction without further purification.



***trans*-1-(3-Bromo-propenyl)-4-methyl-benzene (2.17f)**

Prepared using general procedure **C**

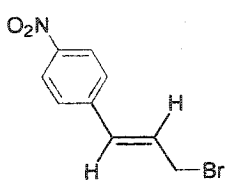
trans-3-*p*-Tolyl-prop-2-en-1-ol **2.16f** (304.8 mg, 2.057 mmol); carbon tetrabromide (852.5 mg, 2.571 mmol); triphenylphosphine (809.1 mg, 3.085 mmol) in CH_2Cl_2 (30.0 mL). The product was used in the following reaction without further purification.



***trans*-1-(3-Bromo-propenyl)-4-trifluoromethyl-benzene (2.17g)**

Prepared using general procedure **C**

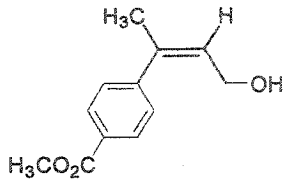
trans-3-(4-Trifluoromethyl-phenyl)-prop-2-en-1-ol **2.16g** (100.0 mg, 0.495 mmol); carbon tetrabromide (205.1 mg, 0.6185 mmol); triphenylphosphine (194.6 mg, 0.7419 mmol) in CH_2Cl_2 (10.0 mL). The product was used in the following reaction without further purification.



***trans*-1-(3-Bromo-propenyl)-4-nitro-benzene (2.17i)**

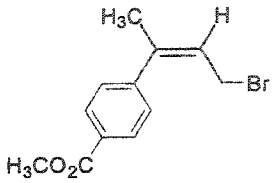
Prepared using general procedure **C**

trans-3-(4-Nitro-phenyl)-prop-2-en-1-ol **2.16i** (200.0 mg, 1.116 mmol); carbon tetrabromide (462.7 mg, 1.395 mmol); triphenylphosphine (439.1 mg, 1.674 mmol) in CH_2Cl_2 (30.0 mL). The product was used in the following reaction without further purification.



(*Z*)-3-(4-Methoxycarbonylphenyl)but-2-en-1-ol (2.16c)

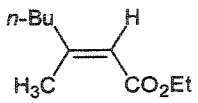
Sodium methoxide (3.5 mg, 0.065 mmol) was added to a 1 M solution of $LiAlH_4$ (34.4 mg, 0.901 mmol) in THF (0.9 mL). The mixture was cooled to 0°C, and a solution of but-2-yn-1-ol **2.18** (60.3 mg, 0.860 mmol) in THF (1.0 mL) was slowly added. The reaction mixture was stirred for 4 h at room temperature. After hydroalumination was completed, the reaction was cooled to 0°C; dimethylcarbonate (0.08 mL, 0.1 mmol) was added, and the mixture was stirred for 10 minutes without cooling. 4-iodobenzoic acid **2.19** (157.7 mg, 0.6018 mmol), $Pd_2dba_3{\cdot}CHCl_3$ (15.6 mg, 0.0151 mmol), $ArPh_3$ (18.4 mg, 0.0601 mmol) and zinc (II) chloride (49.2 mg, 0.361 mmol) were added to the reaction mixture under an argon atmosphere. The reaction was stirred for 3 h at room temperature followed by heating at 50°C for 1.5 h. Methanol (1 mL) was then added, and after 2 h at room temperature, the reaction mixture was poured into brine/water (1:1), acidified with 5% hydrochloric acid to become slightly acidic (pH = 5-6), and extracted with ether (3x). The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated *in vacuo*. The crude product was purified by flash column chromatography (petroleum ether/ether/acetone 8:1:1) to afford alcohol **2.16c** (44.0 mg, 35%). Spectral data: Havranek, M.; Dvorak, D. *J. Org. Chem.* **2002**, *67*, 2125.



(*Z*)-4-(3-Bromo-1-methyl-propenyl)-benzoic acid methyl ester (2.17c)

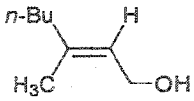
Prepared using general procedure **C**

(*Z*)-3-(4-Methoxycarbonylphenyl)but-2-en-1-ol **2.16c** (58.1 mg, 0.282 mmol); carbon tetrabromide (116.8 mg, 0.3522 mmol); triphenylphosphine (110.8 mg, 0.4224 mmol) in CH_2Cl_2 (10.0 mL). The product was used in the following reaction without further purification.



(*Z*)-3-Methyl-hept-2-enoic acid ethyl ester (2.15d)

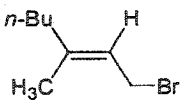
To CuI suspended in dry THF (8.0 mL) at –40°C under an atmosphere of N_2 was added n-BuLi (1.46 mL, 2.97 mmol). The solution was stirred for 30 minutes, followed by cooling to –78°C. A solution of ethyl 2-butynoate **2.20** (0.30 g, 2.68 mmol) in THF (2.0 mL) was cannulated dropwise into the reaction mixture. After 1.5 hours, the reaction was quenched by dropwise addtion of 1 mL of methanol. The mixture was warmed to –20°C and 2 mL of saturated NH_4Cl (aq) was added with stirring. The solution was filtered through a celite pad and the remaining gray solid was washed with ether. The aqueous phase was extracted with ether (3x). The combined organic layers were washed with brine and dried over anhydrous $MgSO_4$. The solvent was evaporated and the crude product was purified by flash column chromatography (10% EtOAc in hexanes) to yield ester **2.15d** as a colorless oil (0.352 g, 77.3%). Spectral data: Anderson, R.J.; Corbin, V.L.; Cotterell, G.; Cox, G.R.; Henrick, C.A.; Schaub, R.; Siddall, J.B. *J. Am. Chem. Soc.* **1975**, *97*, 1197.



(Z)-3-Methyl-hept-2-en-1-ol (2.16d)

Prepared using general procedure **B**

(Z)-3-Methyl-hept-2-enoic acid ethyl ester **2.15d** (352.0 mg, 2.068 mmol); DIBAL-H (4.14 mL, 6.20 mmol) in THF (40.0 mL) to afford alcohol **2.16d** as a colorless oil (209.2 mg, 79%). Spectral data: Hu, T.; Schaus, J.V.; Lam, K.; Palfreyman, M.G.; Wuonola, M.; Gustafson, G.; Panek, J.S. *J. Org. Chem.* **1998**, *63*, 2401.

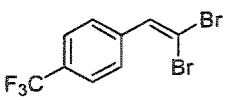


(Z)-1-Bromo-3-methyl-hept-2-ene (2.17d)

Prepared using general procedure **C**

(Z)-3-Methyl-hept-2-en-1-ol **2.16d** (120.6 mg, 0.9406 mmol); carbon tetrabromide (389.9 mg, 1.176 mmol); triphenylphosphine (370.1 mg, 1.411 mmol) in CH_2Cl_2 (20.0 mL). The product was used in the following reaction without further purification.

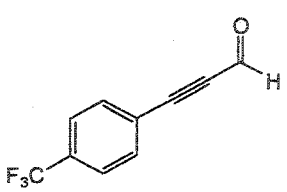
5.5 General Procedure D for the preparation of propargyl alcohols



1-(2,2-Dibromo-vinyl)-4-trifluoromethyl-benzene (2.22)

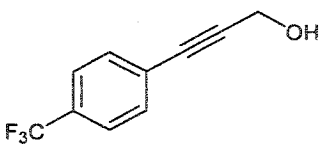
Carbon tetrabromide (1.943 g, 5.858 mmol) was dissolved in dichloromethane (10.0 mL) under N_2, and the solution was stirred at –20°C for 10 minutes. A solution of triphenylphosphine (1.537 g, 5.858 mmol) in dichloromethane (8.0 mL) was slowly cannulated into the reaction mixture. The yellow solution was stirred at –20°C for one hour. A solution of *p*-(trifluoromethyl)-benzaldehyde **2.21** (0.4 mL, 3 mmol) with triethylamine (0.41 mL, 3.0 mmol) and dichloromethane (5.0 mL) was cannulated into the reaction mixture. The latter was stirred at room temperature (21°C) for 4 hours. The mixture was diluted with petroleum ether and triphenylphosphine oxide

precipitated out of the solution. The mixture was filtered through a silica pad, concentrated *in vacuo* and purified by flash column chromatography (5% EtOAc in hexanes) to provide dibromo **2.22** as a light yellow oil (0.966 g, >98%). Spectral data: Huh, D.H.; Jeong, J.S.; Lee, H.B.; Ryu, H.; Kim, Y.G. *Tetrahedron* **2002**, *58*, 9925.



(4-Trifluoromethyl-phenyl)-propynal (2.23)

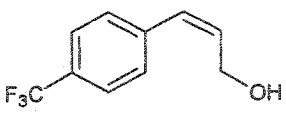
1-(2,2-Dibromo-vinyl)-4-trifluoromethyl-benzene **2.22** (1.710 g, 5.193 mmol) was dissolved in dry THF (50.0 mL) under an atmosphere of nitrogen and the solution was cooled to –78°C. After addition of n-BuLi (5.71 mL, 10.9 mmol), the solution was stirred at –78°C for 40 minutes. A solution of dry DMF (0.94 mL, 7.8 mmol) in dry THF (10.0 mL) was cannulated into the reaction mixture and the latter was stirred at –78°C for 20 minutes, followed by 40 minutes at room temperature (21°C). The reaction was quenched with saturated NH_4Cl (aq) and the aqueous layer was extracted with ether (3x). The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The crude volatile aldehyde **2.23** (288.2 mg, 28%) was used towards the next reaction.



3-(4-Trifluoromethyl-phenyl)-prop-2-yn-1-ol (2.24)

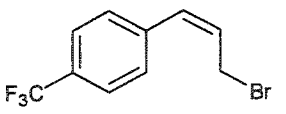
To a round bottom flask was added (4-trifluoromethyl-phenyl)-propynal **2.23** (288.2 mg, 1.455 mmol) and EtOH (30.0 mL). The solution was cooled to 0°C and sodium borohydride (275.1 mg, 7.273 mmol) was slowly added. The solution was stirred for one hour and was quenched with saturated NH_4Cl (aq). The aqueous layer was extracted with ether (3x) and the combined organic layers were dried over anhydrous $MgSO_4$ and concentrated. The residue was purified by flash column chromatography (20% EtOAc in hexanes) to yield alcohol **2.24** as a volatile brown oil (220.2 mg, 76%).

Spectral data: Scott, E.E.; Donnelly, E.T.; Welker, M.E. *J. Organomet. Chem.* **2003**, *673(1-2)*, 67.



3-(4-Trifluoromethyl-phenyl)-*cis*-prop-2-en-1-ol (2.16h)

To a solution of 3-(4-trifluoromethyl-phenyl)-prop-2-yn-1-ol **2.24** (100.8 mg, 0.5036 mmol) in dry hexanes (3.0 mL) was added 3 drops of quinoline and a crystal of Lindlar's catalyst. The flask was initially purged with H_2, followed by a constant presence of H_2 in the atmosphere. The reaction was monitored by TLC. If the reaction was not complete, another crystal of the catalyst was added to the reaction mixture. When the TLC revealed no presence of starting material, the reaction mixture was filtered through a silica pad and the flask was rinsed with DCM and its contents was poured onto the pad. The yellow solution was concentrated to afford the crude alkene **2.16h** as brownish orange crystals (162.5 mg, 88%).

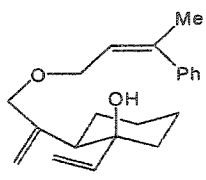


1-(3-Bromo-propenyl)-4-trifluoromethyl-benzene (2.17h)

Prepared using general procedure **C**

3-(4-Trifluoromethyl-phenyl)-*cis*-prop-2-en-1-ol **2.16h** (162.5 mg, 0.804 mmol); carbon tetrabromide (333.2 mg, 1.005 mmol); triphenylphosphine (316.2 mg, 1.206 mmol) in CH_2Cl_2 (15.0 mL). The product was used in the following reaction without further purification.

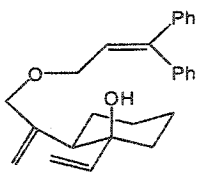
5.6 General Procedure E for Etherification between diol 2.13 and allylbromides 2.17



2-[1-(3-Phenyl-1-but-2-enyloxymethyl)-vinyl]-cyclohexanol (2.1a)

To a dry round bottom flask was added NaH (in 60% oil) (0.218 g, 5.46 mmol) and THF (10.0 mL) under an atmosphere of nitrogen. A

solution of diol **2.13** (0.200 g, 1.09 mmol) in THF (5.0 mL) was cannulated into the reaction mixture. The solution was stirred for 5 minutes, which was followed by the addition of the crude allyl bromide **2.17a** (>2 eq). The mixture was stirred overnight, quenched with saturated NH_4Cl and extracted with ether (3x). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash column chromatography (15 % EtOAc in Hexanes) and provided **2.1a** as a yellowish oil (0.22 g, 65%). IR (neat) 3402 (m), 2931 (s), 2855 (m), 1648 (w), 1442 (m), 1093 (m), 1050 (m), 975 (w), 915 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ_{ppm} 7.37-7.13 (m, 5H), 5.80 (dd, J = 17.2, 10.7 Hz, 1H), 5.68-5.62 (m, 1H), 3.60 (d, J = 17.2, 1.68 Hz, 1H), 4.95-4.88 (m, 3H), 3.96-3.87 (m, 2H), 3.82-3.74 (m, 2H), 3.60 (d, J = 12.6, 3.15 Hz, 1H), 2.23 (dd, J = 11.6 Hz, 1H), 2.07 (s, 3H), 2.04-1.21 (m, 8H). ^{13}C NMR (300 MHz, $CDCl_3$) δ_{ppm} 146.5 (CH), 146.1 (C_4), 141.4 (C_4), 140.8 (C_4), 128.0 (2 x CH), 127.7 (2 x CH), 127.1 (CH), 122.9 (CH), 118.0 (CH_2), 110.9 (CH_2), 72.5 (C_4), 72.1 (CH_2), 67.5 (CH_2), 51.9 (CH), 38.2 (CH_2), 26.5 (CH_2), 26.1 (CH_2), 25.3 (CH_3), 21.2 (CH_2). HRMS *m/z* (M^+ - $C_{11}H_{17}O_2$) calcd 131.0861 found 131.0859.

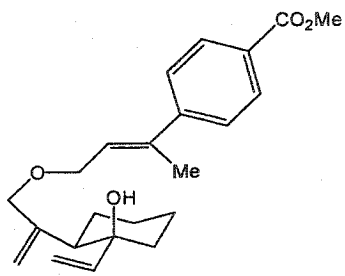


2-[1-(3,3-Diphenyl-allyloxymethyl)-vinyl]-1-vinyl-cyclohexanol (2.1b)

Followed using general procedure **E**

Sodium hydride (109.0 mg, 2.729 mmol); 1,2-divinylcyclohexanol **2.13** (100.0 mg, 0.5460 mmol); 1-bromo-3,3-diphenyl-prop-2-ene **2.17b** (theoretically 661.9 mg, 2.423 mmol) to afford **2.1b** as a light yellow oil (124.5 mg, 68%). IR (neat) 3399 (m), 3058 (w), 2931 (s), 2852 (m), 1654 (w), 1685 (w), 1590 (w), 1494 (m), 1444 (m), 1274 (w),

1062 (s), 965 (m), 917 (m), 753 (m), 700 (s) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ_{ppm} 7.36-7.13 (m, 10H), 6.18 (t, J = 6.8 Hz, 1H), 5.82 (dd, J = 17.2, 10.7 Hz, 1H), 5.17 (dd, J = 17.2, 1.65 Hz, 1H), 5.00-4.89 (m, 3H), 4.09-3.91 (m, 3H), 3.67 (d, J = 14.2 Hz, 1H), 3.65 (s, 1H), 2.25 (dd, J = 12.9, 3.23 Hz, 1H), 1.90-1.18 (m, 10H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 146.5 (CH), 146.1 (C_4), 145.2 (C_4), 141.6 (C_4), 139.1 (C_4), 129.8 (2 x CH), 128.1 (4 x CH), 127.6 (2 x CH), 127.5 (2 x CH), 124.5 (CH), 118.0 (CH_2), 111.0 (CH_2), 72.5 (C_4), 72.3 (CH_2), 67.8 (CH_2), 51.8 (CH), 38.2 (CH_2), 26.6 (CH_2), 26.1 (CH_2), 21.2 (CH_2). HRMS *m/z* (M^+ - $C_{11}H_{17}O_2$) calcd 193.1017 found 193.1042.

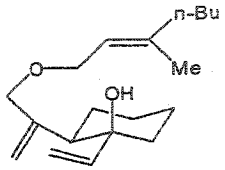


4-{3-[2-(2-Hydroxy-2-vinyl-cyclohexyl)-allyloxy]-1-methyl-propenyl}-benzoic acid methyl ester (2.1c)

Followed using general procedure **E**

Sodium hydride (19.0 mg, 0.469 mmol); 1,2-divinylcyclohexanol **2.13** (17.2 mg, 0.0949 mmol); (*Z*)-4-(3-bromo-1-methyl-propenyl)-benzoic acid methyl ester **2.17c** (theoretically 75.8 mg, 0.282 mmol) to afford **2.1c** as a light yellow oil (16.1 mg, 46%) and a trace of the *Z* isomer. IR (neat) 3402 (w), 3080 (w), 2929 (m), 2853 (w), 1724 (s), 1639 (w), 1608 (w), 1436 (m), 1278 (s), 1177 (w), 1105 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$), δ_{ppm} 8.00 and 7.99 (2d, J = 8.3 Hz and 8.4 Hz, 2H), 7.27 and 7.23 (2d, J = 8.4 Hz and 8.0 Hz, 2H), 5.88-5.77 and 5.79 (m and dd, J = 17.2 Hz, 10.7Hz, 1H), 5.70 (dt, J = 7.1, 1.3 Hz, 1H), 5.14 and 5.11 (2dd, J = 17.2, 1.6 Hz and J = 17.2, 1.6 Hz, 1H), 5.01-4.87 (m, 3H), 3.90 and 3.90 (2s, 3H), 2.25-2.16 (m, 1H), 2.08 and 2.07 (2s, 3H), 1.86-0.80 (m, 13H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 166.9 (C_4), 146.5 (CH), 146.1 (CH), 140.5 (C_4), 129.4 and 129.0 (2 x CH), 127.8 (2 x CH),

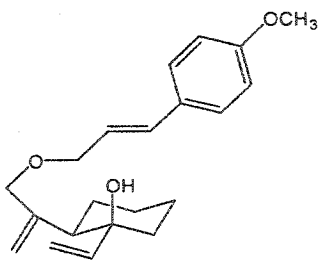
124.2 (CH), 117.9 (CH_2), 110.9 (CH_2), 72.5 and 72.4 (CH_2), 67.3 (CH_2), 52.1 and 51.8 (2 x CH_3), 38.2 (CH_2), 26.7 (CH_2), 26.1 (CH_2), 25.0 (CH_3), 21.2 (CH_2). HRMS *m/z* M^+-($C_{11}H_{17}O_2$) calcd 189.0915 found 189.0939.



2-[1-(3-Methyl-hept-2-enyloxymethyl)-vinyl]-1-vinyl-cyclohexanol (2.1d)

Followed using general procedure E

Sodium hydride (94.1 mg, 2.35 mmol); 1,2-divinylcyclohexanol **2.13** (86.1 mg, 0.470 mmol); (Z)-1-bromo-3-methyl-hept-2-ene **2.17d** (theoretically 179.8 mg, 0.9406 mmol) to afford **2.1d** as a colorless oil (0.104 g, 76%). IR ($CDCl_3$) 3402 (m), 2929 (s), 2859 (m), 1629 (w), 1436 (m), 1088 (m), 1056 (m), 979 (m), 914 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ_{ppm} 5.82 (dd, J = 17.2, 10.6 Hz, 1H), 5.28 (t, J = 6.6 Hz, 1H), 5.16 (dd, J = 17.2, 1.4 Hz, 1H), 5.03 (s, 1H), 4.94-4.90 (m, 2H), 4.00-3.83 (m, 4H), 3.66 (d, J = 11.5 Hz, 1H), 2.26 (dd, J = 12.8, 3.0 Hz, 1H), 1.97 (t, J = 7.1 Hz, 2H), 1.92-1.14 (m, 15H), 0.85 (t, J = 7.2 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 146.5 (CH), 146.2 (C_4), 141.1 (C_4), 119.7 (CH), 118.2 (CH_2), 110.9 (CH_2), 72.4 (C_4), 71.6 (CH_2), 66.5 (CH_2), 52.2 (CH), 39.2 (CH_2), 38.3 (CH_2), 29.8 (CH_2), 26.6 (CH_2), 26.1 (CH_2), 22.3 (CH_2), 21.2 (CH_2), 16.4 (CH_3), 13.9 (CH_3). HRMS *m/z* M^+-($C_{11}H_{17}O_2$) : 111.0596.

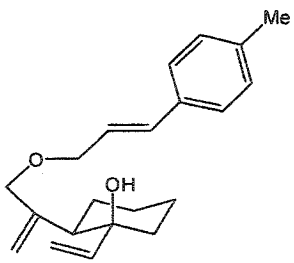


2-{1-[3-(4-Methoxy-phenyl)-allyloxymethyl]-vinyl}-1-vinyl-cyclohexanol (2.1e)

Followed using general procedure E

Sodium hydride (60.9 mg, 1.52 mmol); 1,2-divinylcyclohexanol **2.13** (55.8 mg, 0.305 mmol); *trans*-1-(3-bromo-propenyl)-4-

methoxy-benzene **2.17e** (theoretically 207.5 mg, 0.9135 mmol) to afford **2.1e** as a light yellow oil (71.1 mg, 71.1%). IR (neat) 3400 (m), 3084 (w), 2933 (s), 2855 (m), 1648 (m), 1603 (s), 1583 (w), 1572 (s), 1463 (m), 1352 (w), 1300 (m), 1249 (s), 1175 (m), 1100 (m), 1036 (m), 971 (m), 916 (m), 840 (m), 802 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$), δ_{ppm} 7.30 (d, J = 8.7 Hz, 2H), 6.83 (d, J = 8.8 Hz, 2H), 6.52 (d, J = 15.9 Hz, 1H), 6.11 (dt, J = 15.9, 6.3 Hz, 1H), 5.86 (dd, J = 17.2, 10.7 Hz, 1H), 5.20 (dd, J = 17.2, 1.7 Hz, 1H), 5.09 (s, 1H), 4.99 (d, J = 1.6 Hz, 1H), 4.96 (dd, J = 10.7, 1.7 Hz, 1H), 4.17-3.98 (m, 3H), 3.79 (s, 3H), 3.68 (d, J = 2.2 Hz, 1H), 2.28 (dd, J = 12.7, 3.1 Hz, 1H), 2.02-1.19 (m, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 159.3 (C_4), 146.5 (C_4), 146.1 (CH), 132.8 (CH), 129.2 (C_4), 127.7 (2 x CH), 122.8 (CH), 118.1 (CH_2), 113.9 (2 x CH), 111.0 (CH_2), 72.6 (CH_3), 71.8 (CH_2), 70.8 (CH_2), 55.3 (CH), 52.0 (CH), 38.3 (CH_2), 26.7 (CH_2), 26.1 (CH_2), 21.2 (CH_2). HRMS *m/z* M^+ ($C_{21}H_{28}O_3$) : 328.2033.

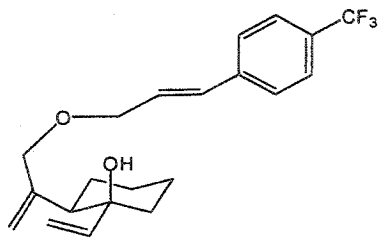


2-[1-(3-p-Tolyl-allyloxymethyl)-vinyl]-1-vinylcyclohexanol (2.1f)

Followed using general procedure **E**

Sodium hydride (205.7 mg, 5.142 mmol); 1,2-divinylcyclohexanol **2.13** (188.3 mg, 1.028 mmol); *trans*-1-(3-bromo-propenyl)-4-methyl-benzene **2.17f** (theoretically 434.2 mg, 2.056 mmol) to afford **2.1f** as a light yellow oil (241.6 mg, 75%). IR (neat) 3554 (w), 3402 (s), 3084 (w), 3020 (w), 2929 (s), 2855 (s), 1899 (w), 1835 (w), 1638 (m), 1513 (s), 1446 (s), 1410 (m), 1352 (m), 1287 (w), 1204 (w), 1101 (m), 1056 (m), 971 (s), 916 (s), 830 (m), 792 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ_{ppm} 7.27 (d, J = 8.1 Hz, 2H), 7.11 (d, J = 8.0 Hz, 2H), 6.55 (d, J = 15.9 Hz, 1H), 6.20 (dt, J = 15.9, 6.2 Hz, 1H), 5.87 (dd, J = 17.2, 10.7 Hz, 1H), 5.21 (dd, J

= 17.2, 1.6 Hz, 1H), 5.10 (s, 1H), 5.01 (d, J = 1.8 Hz, 1H), 4.97 (dd, J = 10.7, 1.6 Hz, 1H), 4.18-4.02 (m, 3H), 3.77 (d, J = 11.7 Hz, 1H), 3.67 (d, J = 2.2 Hz, 1H), 2.32 (s, 3H), 2.29 (dd, J = 12.9, 3.3 Hz, 1H), 2.03-1.22 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 146.5 (CH), 146.1 (C_4), 137.5 (C_4), 133.6 (C_4), 133.0 (CH), 129.2 (2 x CH), 126.4 (2 x CH), 123.9 (CH), 118.1 (CH_2), 111.0 (CH_2), 72.5 (C_4), 71.8 (CH_2), 70.6 (CH_2), 51.9 (CH), 38.2 (CH_2), 26.7 (CH_2), 26.1 (CH_2), 21.2 (CH_2), 21.1 (CH_3). HRMS *m/z* M^+ - ($C_{11}H_{17}O_2$) calcd 131.0861 found 131.0849.

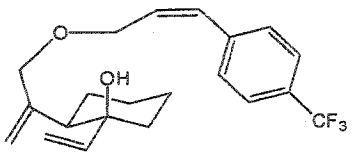


2-{1-[3-(4-Trifluoromethyl-phenyl)-*trans*-allyloxymethyl]-vinyl}-1-vinyl-cyclohexanol (2.1g)

Followed using general procedure **E**

Sodium hydride (33.0 mg, 0.825 mmol); 1,2-divinylcyclohexanol **2.13** (30.2 mg, 0.165 mmol); *trans*-1-(3-bromo-propenyl)-4-trifluoromethyl-benzene **2.17g** (theoretically 131.1 mg, 0.4946 mmol) to afford **2.1g** as a light yellow oil (57.0 mg, 95%). IR (neat) 3411 (m), 3080 (w), 2934 (m), 2855 (m), 1639 (w), 1616 (m), 1444 (w), 1415 (m), 1326 (s), 1166 (s), 1124 (s), 1068 (s), 1016 (m), 972 (m), 919 (m), 857 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ_{ppm} 7.54 (d, J = 8.3 Hz, 2H), 7.44 (d, J = 8.2 Hz, 2H), 6.62 (d, J = 16.0 Hz, 1H), 6.33 (dt, J = 16.0, 5.69 Hz, 1H), 5.86 (dd, J = 17.2, 10.7 Hz, 1H), 5.19 (dd, J = 17.2, 1.59 Hz, 1H), 5.12 (s, 1H), 5.02 (d, J = 1.73 Hz, 1H), 4.96 (dd, J = 10.7, 1.59 Hz, 1H), 4.21-4.02 (m, 3H), 3.78 (d, J = 11.8 Hz, 1H), 3.49 (d, J = 2.2 Hz, 1H), 2.28 (dd, J = 12.8, 3.3 Hz, 1H), 1.94-1.20 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 146.5 (CH), 146.0 (C_4), 140.0 (C_4), 131.0 (CH), 128.0 (CH), 126.6 (2 x CH), 125.5 (q, J = 3.8 Hz, 2 x CH), 118.1 (CH_2), 111.0 (CH_2), 72.6 (C_4),

72.4 (CH_2), 70.1 (CH_2), 51.8 (CH), 38.3 (CH_2), 26.8 (CH_2), 26.1 (CH_2), 21.2 (CH_2). HRMS *m/z* M^+- ($C_{11}H_{13}O_2$) calcd 185.0578 found 185.0572.



2-{1-[3-(4-Trifluoromethyl-phenyl)-*cis*-allyloxymethyl]-vinyl}-1-vinyl-cyclohexanol (2.1h)

Followed using general procedure **E**

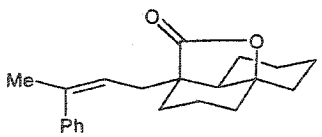
Sodium hydride (80.4 mg, 2.01 mmol); 1,2-divinylcyclohexanol **2.13** (73.6 mg, 0.402 mmol); 1-(3-bromo-propenyl)-4-trifluoromethyl-benzene **2.17h** (theoretically 213.1 mg, 0.8038 mmol) to afford **2.1h** as a a colorless oil (87.3 mg, 55%). IR (neat) 3411 (w), 3083 (w), 2938 (m), 2859 (w), 1607 (w), 1406 (w), 1322 (s), 1164 (m), 1121 (s), 1067 (m), 915 (w), 854 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ_{ppm} 7.57 (d, J = 8.2 Hz, 2H), 7.26 (d, J = 8.2 Hz, 2H), 6.61 (d, J = 11.8 Hz, 1H), 5.97-5.89 (m, 1H), 5.81 (dd, J = 17.2, 10.7 Hz, 1H), 5.13 (dd, J = 17.2, 1.6 Hz, 1H), 5.02 (s, 1H), 4.96 (d, J = 1.6 Hz, 1H), 4.87 (dd, J = 10.7, 1.6 Hz, 1H), 4.23 (ddd, J = 12.6, 6.1, 1.7 Hz, 1H), 4.11 (ddd, J = 12.5, 6.5, 1.6 Hz, 1H), 4.03 (dd, J = 11.7, 0.7 Hz, 1H), 3.72 (d, J = 11.8 Hz, 1H), 3.49 (d, J = 2.2 Hz, 1H), 2.25 (dd, J = 13.0, 3.3 Hz, 1H), 1.90-1.16 (m, 8H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 146.4 (CH), 145.8 (C_4), 139.9 (C_4), 130.7 (CH), 130.2 (CH), 129.4 (2 x CH), 125.1 (q, J = 3.8 Hz, 2 x CH), 118.1 (CH_2), 110.9 (CH_2), 72.6 (C_4), 72.5 (CH_2), 66.4 (CH_2), 51.7 (CH), 38.2 (CH_2), 26.7 (CH_2), 26.1 (CH_2), 21.2 (CH_2). HRMS *m/z* M^+ - (H_2O) calcd 348.1701 found 348.1694.

5.7 General Procedure F for the Tandem Reactions

Method A. A solution of allyl ether **2.1a** (133.0 mg, 0.4257 mmol) in dry deoxygenated toluene (12.0 mL) and DBU (196 mg, 1.20 mmol) was heated in a quartz tube for 60 min at 210°C. The solution was cooled to room temperature and concentrated *in vacuo*. The residue was purified by flash column chromatography (20% EtOAc in hexanes) to afford lactol **2.5a** (45.0 mg, 34%) and enol ether **2.3a** (66.5 mg, 51%) as colorless oils. In order to determine the diastereomeric ratios, lactols were oxidized with TPAP to afford the corresponding lactones.

Method B. A solution of allyl ether **2.1b** (119.0 mg, 0.3177 mmol) in dry deoxygenated toluene (5.0 mL) and triethylamine (97.1 mg, 0.960 mmol) was heated in a sealed tube for 18 h at 210°C. The solution was cooled to room temperature and concentrated *in vacuo*. The residue was purified by flash column chromatography (20% EtOAc in hexanes) to afford lactol **2.5b** (15.9 mg, 13%) and enol ether **2.3b** (12.4 mg, 10%) as colorless oils. In order to determine the diastereomeric ratios, lactols were oxidized with TPAP to afford the corresponding lactones.

5.8 General Procedure G for the Oxidation of the Lactols

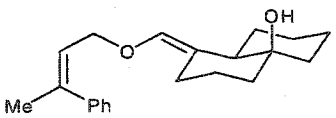


7-(3-Phenylbut-2-enyl)-10-oxatricyclo[5.3.3.0^{1,6}]tridecan-8-one (Lactone from 2.5a).

Lactol **2.5a** was prepared using general procedure F: method A.

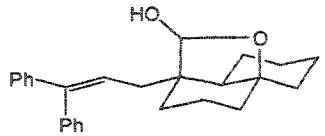
To a solution of lactol **2.5a** (13.2 mg, 0.04 mmol) in DCM (1.0 mL) was respectively added 4 Å molecular sieves (21.1 mg), 4-methylmorpholine *N*-oxide (7.5 mg, 0.06 mmol) and TPAP (0.7 mg, 0.002 mmol). After completion, the reaction mixture was poured over a pad of silica and the later was washed with 5%MeOH in EtOAc. The organic

solvent was evaporated and flash column chromatography (20% EtOAc in hexanes) afforded **lactone of 2.5a** as a colorless oil (11.2 mg, 90%). IR (neat, cm^{-1}) 3053 (w), 2929 (s), 2856 (m), 1770 (s), 1444 (m), 1261 (m), 1168 (m), 1128 (m), 1025 (w), 948 (m), 915 (m). ^1H NMR (300 MHz, $CDCl_3$), δ_{ppm} 7.68-7.08 (m, 10H), 5.64 (t, J = 7.07 Hz, 1H), 5.40 (t, J = 7.31 Hz, 1H), 2.55-0.75 (m, 40H). ^{13}C NMR (300 MHz, $CDCl_3$) δ_{ppm} 181.0 (C_4), 180.9 (C_4), 144.2 (C_4), 141.9 (C_4), 139.9 (C_4), 138.2 (C_4), 128.6 (2 x CH), 128.2 (2 x CH), 127.3 (2 x CH), 127.1 (CH), 126.1 (2 x CH), 122.7 (CH), 121.6 (CH), 83.6 (C_4), 83.4 (C_4), 77.6 (CH), 53.5 (C_4), 53.2 (C_4), 49.5 (CH), 49.5 (CH), 36.1 (CH_2), 33.6 (CH_2), 32.5 (CH_2), 32.2 (CH_2), 30.2 (CH_2), 30.1 (CH_2), 29.7 (CH_2), 26.4 (CH_3), 24.8 (CH_2), 24.5 (CH_2), 24.2 (CH_2), 24.2 (CH_2), 21.2 (CH_2), 19.8 (CH_2), 16.7 (CH_3). LRMS (EI) *m/z* (M^+) calcd for $C_{21}H_{26}O_2$ 310, found 310.



1-(3-Phenylbut-2-enyloxymethylene) octahydro-naphthalene -4a-ol (2.3a).

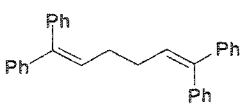
IR (neat, cm^{-1}) 3554 (w), 3052, (w), 2929 (s), 2859 (m), 1674 (m), 1493 (w), 1448 (m), 1377 (w), 1255 (w), 1229 (w), 1159 (s), 1094 (m), 1030 (m), 953 (m), 830 (w), 760 (m), 708 (m). ^1H NMR (300 MHz, $CDCl_3$) δ_{ppm} 7.36-7.14 (m, 5H), 5.66 (dt, J = 6.91, 1.32 Hz, 1H), 5.57 (s, 1H), 4.13 (d, J = 6.93 Hz, 2H), 2.85 (d, J = 10.6 Hz, 1H), 2.09 (s, 3H), 1.91-1.18 (m, 15H). ^{13}C NMR (300 MHz, $CDCl_3$) δ_{ppm} 142.1 (C_4), 141.0 (C_4), 139.9 (CH), 128.6 (2 x CH), 128.1 (2 x CH), 127.7 (CH), 123.4 (CH), 118.9 (C_4), 71.3 (C_4), 69.6 (CH_2), 47.4 (CH), 40.3 (CH_2), 38.5 (CH_2), 26.4 (CH_2), 26.4 (CH_2), 25.8 (CH_3), 23.7 (CH_2), 22.9 (CH_2), 21.7 (CH_2). LRMS (EI) *m/z* (M^+ - $C_{11}H_{17}O_2$) calcd for $C_{10}H_{11}$ 131, found 131.



7-(3,3-Diphenylallyl)-11-oxatricyclo[5.3.2.$0^{1,6}$]dodecan-12-ol (2.5b)

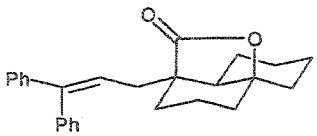
Prepared using general procedure **F**: method A.

2.1b (104.5 mg, 0.28 mmol), DBU (127.9 mg, 0.84 mmol) and toluene (12 mL) to give **2.5b** (25.0 mg, 24%) and dimer **2.26b** (20.0 mg, 20%) as colorless oils. 10b : IR (neat, cm^{-1}) 3374 (m), 3058 (w), 2928 (s), 2852 (m), 1944 (w), 1880 (w), 1719 (w), 1667 (w), 1596 (w), 1494 (m), 1444 (m), 1444 (m), 1358 (w), 1255 (w), 1107 (m), 968 (m), 911 (m), 760 (m), 699 (s). ^{1}H NMR (300 MHz, $CDCl_3$) δ_{ppm} 7.39-7.07 (m, 10H), 6.08-6.05 (t, J = 7.4 Hz, 1H), 5.28 and 5.08 (2d, J = 4.6 and 2.8 Hz, 1H), 3.04 and 2.82 (2 br s, 1H), 2.40-2.16 (m, 2H), 1.84-0.81 (m, 15H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 143.1 (C_4), 142.9 (C_4), 140.2 (C_4), 130.0 (CH), 129.9 (CH), 128.3 (C_4), 128.2 (CH), 128.1 (CH), 128.1 (CH), 127.2 (CH), 127.1 (CH), 126.9 (CH), 126.8 (CH), 126.8 (CH), 126.7 (CH), 125.9 (CH), 104.1 (CH), 101.7 (CH), 83.7 (C_4), 82.1 (C_4), 51.0 (C_4), 50.5 (CH), 49.4 (C_4), 48.9 (CH), 39.2 (CH_2), 38.6 (CH_2), 34.5 (CH_2), 34.1 (CH_2), 32.0 (CH_2), 31.6 (CH_2), 31.4 (CH_2), 30.7 (CH_2), 29.7 (CH_2), 25.8 (CH_2), 24.9 (CH_2), 24.6 (CH_2), 23.8 (CH_2), 23.6 (CH_2), 22.6 (CH_2), 21.6 (CH_2), 21.3 (CH_2), 19.5 (CH_2). HRMS (EI) *m/z* (M^+ - $C_{11}H_{17}O_2$) calcd for $C_{15}H_{13}$ 193.1017 found 193.1038.



1,1,6,6-Tetraphenylhexa-1,5–diene (2.26b) : IR (neat, cm^{-1}) 3080 (w), 3062 (w), 3028 (w), 2957 (w), 2920 (w), 2853 (w), 1494 (m), 1444 (m), 762 (m), 697 (s). ^{1}H NMR (300 MHz, $CDCl_3$) δ_{ppm} 7.37-7.12 (m, 20H), 6.06-6.01 (m, 2H), 2.24 (d, J = 7.2 Hz, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 142.6 (C_4),

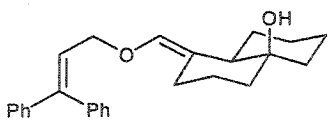
142.0 (C_4), 140.1 (C_4), 129.9 (2 x CH), 129.0 (CH), 128.1 (2 x CH), 127.2 (2 x CH), 126.9 (CH), 126.8 (CH), 30.1 (CH_2). HRMS (EI) *m/z* (M^+- $C_{15}H_{13}$) calcd for $C_{15}H_{13}$ 193.1017, found 193.1011.



7-(3,3-Diphenyl-allyl)-11-oxa-tricyclo[5.3.2.01,6]dodecan-12-one (Lactone from 2.5a)

Prepared using general procedure **G**

Lactol **2.5a** (12.4 mg, 0.0331 mmol); 4 Å molecular sieves (16.6 mg); NMO (5.8 mg, 0.050 mmol) and TPAP (0.6 mg, 0.002 mmol) in dry dichloromethane (1.0 mL) provided **lactone of 2.5a** (9.3 mg, 75%) as a yellow oil. IR (neat) 3050 (w), 3020 (w), 2936 (m), 2859 (m), 1764 (s), 1590 (w), 1494 (w), 1436 (m), 1352 (w), 1236 (w), 1152 (w), 1126 (m), 920 (m), 759 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ_{ppm} 7.36-7.11 (m, 10H), 6.02 (t, J = 7.4 Hz, 1H), 2.48-2.31 (m, 2H), 2.00 (d, J = 11.6 Hz, 1H), 1.87-0.79 (m, 14H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 180.2 (C_4), 144.4 (C_4), 142.6 (C_4), 139.5 (C_4), 129.8 (2 x CH), 128.3 (2 x CH), 128.1 (2 x CH), 127.2 (2 x CH), 127.6 (CH), 127.2 (CH), 123.7 (CH), 83.1 (C_4), 53.0 (C_4), 49.3 (CH), 35.6 (CH_2), 33.2 (CH_2), 32.1 (CH_2), 30.4 (CH_2), 24.3 (CH_2), 23.8 (CH_2), 20.8 (CH_2), 19.5 (CH_2). HRMS *m/z* M^+ ($C_{26}H_{28}O_2$) calcd 372.2089 found 372.2128.

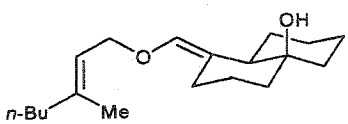


1-(3,3-Diphenylallyloxymethylene)octahydronaphthalen-4a-ol (2.3b)

Prepared using general procedure **F**: method B.

Allyl ether **2.1b** (119.4 mg, 0.3188 mmol), triethylamine (97.1 mg, 0.960 mmol) and toluene (5.0 mL) to give (**2.5b**) (12.4 mg, 13%) and (**2.3b**) (15.9 mg, 10%) as colorless oils. **2.3b** : IR (neat, cm^{-1}) 3354 (w), 3065 (w), 3026 (w), 2923 (s), 2846 (m), 1673 (w),

1487 (w), 1435 (m), 1364 (w), 1145 (s), 1087 (m), 1029 (w), 952 (m), 843 (w). ^{1}H NMR (500 MHz, $CDCl_3$) δ_{ppm} 7.39-7.31 (m, 3H), 7.29-7.23 (m, 5H), 7.17-7.14 (m, 2H), 6.20 (t, J = 3.8 Hz, 1H), 5.64 (s, 1H), 4.27 (d, J = 6.8 Hz, 2H), 2.90 (ddd, J = 9.1, 8.8, 4.1 Hz, 1H), 1.92 (d, J = 11.9 Hz, 1H), 1.75-1.17 (m, 14H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 145.3 (C_4), 141.5 (C_4), 139.4 (CH), 138.9 (C_4), 129.7 (2 x CH), 128.2 (2 x CH), 128.2 (2 x CH), 127.7 (CH), 127.7 (CH), 127.6 (2 x CH), 124.5 (CH), 118.8 (C_4), 71.0 (C_4), 69.6 (CH_2), 47.0 (CH), 39.9 (CH_2), 38.1 (CH_2), 26.0 (CH_2), 26.0 (CH_2), 23.3 (CH_2), 22.5 (CH_2), 21.2 (CH_2). HRMS (EI) *m/z* M^+- ($C_{11}H_{17}O_2$) calcd for $C_{15}H_{13}$ 193.1017, found 193.0960.

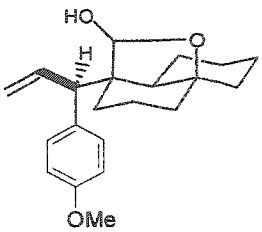


1-(3-Methylhept-2-enyloxymethylene)octahydronaphthalen-4a-ol (2.3d)

Prepared using general procedure **F**: method A and B

Reagent and quantities for A: Allyl ether **2.1d** (19.0 mg, 0.0650 mmol), triethylamine (18.2 mg, 0.180 mmol) and toluene (12.0 mL) to afford **(2.3d)** (4.5 mg, 24%) as a colorless oil. Reagents and quantities for B: Allyl ether **2.1d** (26.2 mg, 0.0896 mmol), triethylamine (29.0mg, 0.269 mmol) and toluene (5.0 mL) to afford **(2.3d)** (13.3 mg, 51%) as a colorless oil. IR (neat, cm^{-1}) 3388 (m), 2927 (s), 2858 (m), 1723 (w), 1663 (w), 1453 (m), 1371 (w), 1242 (w), 1144 (m), 1074 (m), 1031 (m), 944 (w). ^{1}H NMR (500 MHz, $CDCl_3$) δ_{ppm} 5.70 (s, 1H), 5.34-5.30 (m, 1H), 4.22 (d, J = 6.8 Hz, 2H), 2.85 (dt, J = 8.9, 2.0 Hz, 1H), 2.01 (t, J = 7.4 Hz, 2H), 1.92 (dd, J = 12.6, 3.6 Hz, 1H), 1.81-1.20 (m, 19H), 0.88 (t, J = 7.3 Hz, 5H). ^{13}C NMR (125 MHz, $CDCl_3$) δ_{ppm} 141.3 (C_4), 139.5 (CH), 120.0 (CH), 118.5 (C_4), 70.9 (C_4), 68.4 (CH_2), 47.1 (CH), 40.0 (CH_2), 39.3 (CH_2), 38.1 (CH_2), 29.8 (CH_2), 26.1 (CH_2), 26.0 (CH_2), 23.4 (CH_2), 22.6 (CH_2), 22.3

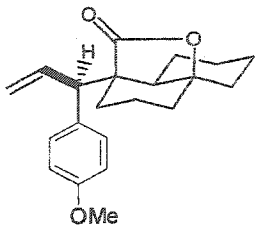
(CH_2), 21.3 (CH_2), 16.4 (CH_3), 13.9 (CH_3). HRMS (EI) *m/z* (M^+- $C_8H_{16}O$) calcd for $C_{11}H_{16}O$ 164.1201, found 164.1184.



7-[1-(4-Methoxyphenyl)allyl]-11-oxatricyclo[5.3.2.0^{1,6}]dodecan-12-ol (2.4e)

Prepared using general procedure **F**: method B.

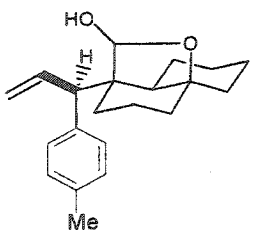
Allyl ether **2.1e** (26.5 mg, 0.0807 mmol), Et_3N (24.3 mg, 0.240 mmol) and toluene (5.0 mL) to provide lactol (**2.4e**) (16.4 mg, 50%) as a light yellow oil. IR (neat, cm^{-1}) 3373 (m), 3075 (w), 2928 (s), 2854 (w), 1610 (m), 1511 (s), 1449 (m), 1297 (w), 1247 (s), 1180 (m), 1107 (m), 1032 (s), 978 (m), 907 (m), 826 (m). ^1H NMR (300 MHz, $CDCl_3$) δ_{ppm} 7.22 and 7.15 (2d, J = 9.4 and 8.5 Hz, 2H), 6.82 (d, J = 8.5 Hz, 2H), 6.38 and 6.23-6.12 (dt and m, J = 16.9, 9.7 Hz, 1H), 5.50 and 5.24 (2d, J = 4.8 and 3.3 Hz, 1H), 5.10-4.91 (m, 2H), 3.98 and 3.56 (2d, J = 7.1 and 9.2 Hz, 1H), 3.77 (2s, 3H), 3.01 (br s, 1H), 2.31-0.81 (m, 15H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 157.9 (C_4), 139.9 (CH), 139.6 (CH), 133.6 (C_4), 133.4 (C_4), 131.5 (2 x CH), 131.5 (2 x CH), 130.1 (CH), 116.6 (CH_2), 115.3 (CH_2), 113.4 (CH), 113.2 (CH), 112.9 (CH), 103.7 (CH), 101.4 (CH), 83.9 (C_4), 82.2 (C_4), 55.1 (CH_3), 54.6 (C_4), 52.7 (C_4), 50.9 (CH), 50.1 (CH), 48.9 (CH), 47.8 (CH), 39.4 (CH_2), 38.5 (CH_2), 34.8 (CH_2), 34.5 (CH_2), 30.5 (CH_2), 28.6 (CH_2), 24.9 (CH_2), 24.8 (CH_2), 24.6 (CH_2), 23.3 (CH_2), 21.4 (CH_2), 21.4 (CH_2), 19.7 (CH_2), 19.6 (CH_2). HRMS (EI) *m/z* (M^+ - $C_{11}H_{17}O_2$) calcd for $C_{10}H_{11}O$ 147.0810, found 147.0825.



7-[1-(4-Methoxyphenyl)allyl]-11-oxatricyclo[5.3.2.0^{1,6}]dodecan-12-one (Lactone from 2.4e)

Prepared using general procedure **G**

Lactol **2.4e** (13.5 mg, 0.0411 mmol); 4 Å molecular sieves (20.6 mg); NMO (7.2 mg, 0.062 mmol) and TPAP (0.7 mg, 0.002 mmol) in dry dichloromethane (1.0 mL) provided **lactone of 2.4e** (8.7 mg, 65%) as a colorless oil. IR (neat, cm^{-1}), 3082 (w), 2933 (m), 2861 (w), 1764 (s), 1610 (m), 1512 (s), 1448 (w), 1301 (w), 1248 (s), 1182 (m), 1157 (m), 1124 (m), 1075 (w), 1035 (m), 949 (m), 925 (m). ^{1}H NMR (300 MHz, $CDCl_3$), δ_{ppm} 7.16 (d, J = 8.3 Hz, 2H), 6.82 (d, J = 8.2 Hz, 2H), 6.71-6.60 (m, 1H), 5.11 and 5.02 (2d, J = 10.4 and 10.2 Hz, 1H), 4.88 and 4.64 (2d, J = 17.4 and 17.4 Hz, 1H), 3.78 (s, 3H), 3.74 (d, J = 3.9 Hz, 1H), 52.15-0.82 (m, 15H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 179.5 (C_4), 158.1 (C_4), 139.5 (CH), 132.2 (C_4), 131.1 (2 x CH), 116.7 (CH_2), 113.5 (2 x CH), 82.5 (C_4), 55.9 (C_4), 55.2 (CH_3), 50.9 (CH), 48.6 (CH), 35.9 (CH_2), 33.5 (CH_2), 29.5 (CH_2), 24.2 (CH_2), 23.9 (CH_2), 20.7 (CH_2), 20.0 (CH_2). HRMS (EI) *m/z* (M^+) calcd for $C_{21}H_{26}O_3$ 326.1882, found 326.1843.

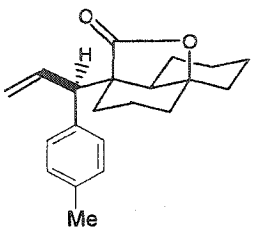


7-(1-*p*-Tolylallyl)-11-oxatricyclo[5.3.2.0^{1,6}]dodecan-12-ol (2.4f).

Prepared using general procedure **F**: method A.

Allyl ether **2.1f** (19.6 mg, 0.0631 mmol) and toluene (12.0 mL) to afford lactol **2.4f** (12.3 mg, 63 %) as a colorless oil. IR (neat, cm^{-1}) 3385 (m), 3078 (w), 3014 (w), 2927 (s), 2855 (m), 1635 (w), 1513 (w), 1449 (w), 1339 (w), 1262 (w), 1115 (m), 979 (m), 911 (m). ^{1}H NMR (300 MHz, $CDCl_3$) δ_{ppm} 7.21-7.07 (m, 4H), 6.45-6.33 and 6.26-6.14 (2m, 1H), 5.50 and 5.23 (2d, J = 4.8 and 3.1 Hz, 1H), 5.12-4.94 (m, 2H), 3.99 and 3.57 (2d, J = 9.3 and 7.5, 1H), 2.76-2.72 (m, 1H), 2.31 and 2.30 (2s, 3H), 2.18-

0.76 (m, 15H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 139.7 (CH), 139.6 (CH), 138.6 (C_4), 138.5 (C_4), 138.4 (C_4), 135.8 (C_4), 135.8 (C_4), 130.1 (2 x CH), 129.0 (2 x CH), 128.8 (2 x CH), 128.6 (2 x CH), 116.8 (CH_2), 115.4 (CH_2), 103.7 (CH), 101.5 (CH), 83.9 (C_4), 82.2 (C_4), 54.5 (C_4), 52.7 (C_4), 50.8 (CH), 50.5 (CH), 48.9 (CH), 48.3 (CH), 39.3 (CH_2), 38.4 (CH_2), 34.8 (CH_2), 34.5 (CH_2), 30.5 (CH_2), 29.7 (CH_2), 28.6 (CH_2), 24.9 (CH_2), 24.8 (CH_2), 24.6 (CH_2), 23.3 (CH_2), 21.4 (CH_2), 21.4 (CH_2), 21.0 (CH_3), 19.7 (CH_2). HRMS (EI) *m/z* (M^+ - $C_{11}H_{17}O_2$) calcd for $C_{10}H_{11}$ 131.0861, found 131.0868.

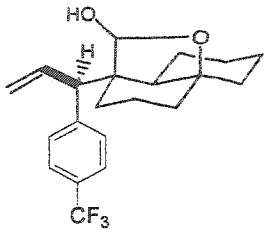


7-(1-*p*-Tolylallyl)-11-oxatricyclo[5.3.2.$0^{1,6}$]dodecan-12-one

(Lactone from 2.4f)

Prepared using general procedure **G**

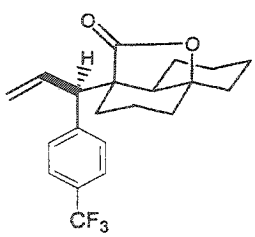
Lactol **2.4f** (8.0 mg, 0.026 mmol); 4 Å molecular sieves (12.9 mg); NMO (4.5 mg, 0.039 mmol) and TPAP (0.5 mg, 0.001 mmol) in dry dichloromethane (1.0 mL) provided **lactone of 2.4f** (6.0 mg, 75%) as a colorless oil. IR (neat, cm^{-1}) 3084m (w), 3020 (w), 2931 (m), 2859 (m), 1766 (s), 1629 (w), 1513 (w), 1448 (w), 1352 (w), 1236 (w), 1159 (w), 1124 (m), 946 (m), 920 (w). ^1H NMR (500 MHz, $CDCl_3$) δ_{ppm} 7.13 (d, J = 8.0 Hz, 2H), 7.08 (d, J = 7.8 Hz, 2H), 6.68-6.62 (m, 1H), 5.11 (d, J = 1.6 Hz, 1H), 4.66 (dd, J = 17.3, 1.6 Hz, 1H), 3.75 (d, J = 5.4 Hz, 1H), 2.31 (s, 3H), 2.15 (dd, J = 12.1, 3.9 Hz, 1H), 1.95 (d, J = 13.1 Hz, 1H), 1.86-0.05 (m, 13H). ^{13}C NMR (125 MHz, $CDCl_3$) δ_{ppm} 179.4 (C_4), 139.4 (CH), 137.2 (C_4), 136.2 (C_4), 130.0 (2 x CH), 129.0 (2 x CH), 116.7 (CH_2), 82.5 (C_4), 55.8 (C_4), 51.0 (CH), 49.2 (CH), 36.0 (CH_2), 33.6 (CH_2), 29.6 (CH_2), 24.2 (CH_2), 23.9 (CH_2), 21.0 (CH_3), 20.7 (CH_2), 20.0 (CH_2). HRMS (EI) *m/z* (M^+) calcd for $C_{21}H_{26}O_2$ 310.1933 found 310.1949.



7-[1-(4-Trifluoromethylphenyl)allyl]-11-oxatricyclo[5.3.2.0^{1,6}]dodecan-12-ol (2.4g)

Prepared using general procedure F: method B.

Allyl ether **2.1g** (15.2 mg, 0.0415 mmol), Et_3N (12.1 mg, 0.120 mmol) and toluene (5.0 mL) to provide lactol **2.4g** (14.9 mg, 98%) as colorless crystals. mp 122.3-125.1°C. IR (neat, cm^{-1}) 3387 (w), 2930 (m), 2859 (w), 1616 (w), 1448 (w), 1410 (w), 1326 (s), 1159 (m), 1120 (s), 1069 (m), 908 (w). ^{1}H NMR (500 MHz, $CDCl_3$) δ_{ppm} 7.53 and 7.52 (2d, J = 8.1 Hz and 8.1 Hz, 2H), 7.43 and 7.34 (2d, J = 8.2 Hz and 8.3 Hz, 2H), 6.45-6.38 and 6.21-6.14 (2m, 1H), 5.52 and 5.26 (2d, J = 4.7 Hz, and 3.2 Hz, 1H), 5.14 and 5.09 (dt and dd, J = 10.4, 1.4 Hz and 10.1, 1.7 Hz, 1H), 4.99 and 4.93 (2dt, J = 16.9, 2.88 Hz and 17.2, 1.5 Hz, 1H), 4.12 and 3.68 (2d, J = 7.1 Hz, and 9.1 Hz, 1H), 2.88 and 2.82 (2 br s, 1H), 2.31-0.79 (m, 15H). ^{13}C NMR (125 MHz, $CDCl_3$) δ_{ppm} 145.9 (CH_4), 145.6 (C_4), 138.8 (CH), 138.5 (CH), 130.6 (2 x CH), 129.4 (2 x CH), 125.0-124.8 (q, J = 6.5 Hz, 2 x CH), 117.6 (CH_2), 116.3 (CH_2), 103.4 (CH), 101.2 (CH), 84.0 (C_4), 82.4 (C_4), 54.4 (C_4), 50.8 (CH), 48.9 (CH), 39.3 (CH_2), 38.3 (CH_2), 34.7 (CH_2), 34.4 (CH_2), 29.6 (CH_2), 29.2 (CH_2), 24.8 (CH_2), 24.8 (CH_2), 24.7 (CH_2), 23.4 (CH_2), 21.4 (CH_2), 21.3 (CH_2), 19.6 (CH_2), 19.5 (CH_2). HRMS (EI) *m/z* (M^+- $C_{11}H_{17}O_2$) calcd for $C_{10}H_8F_3$ 185.0578, found 185.0576.

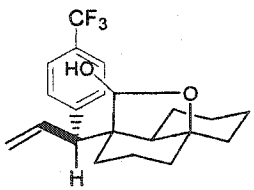


7-[1-(4-Trifluoromethylphenyl)allyl]-11-oxatricyclo[5.3.2.0^{1,6}]dodecan-12-one (Lactone from 2.4g)

Prepared using general procedure **G**

Lactol **2.4g** (10.3 mg, 0.0281 mmol); 4 Å molecular sieves (14.1 mg); NMO (4.9 mg, 0.042 mmol) and TPAP (0.5 mg, 0.001 mmol) in dry

dichloromethane (2.0 mL) provided **lactone of 2.4g** (9.8 mg, 96%) as a colorless oil. IR (neat, cm^{-1}) 3078 (w), 2929 (s), 2854 (m), 1760 (s), 1617 (w), 1450 (w), 1324 (s), 1164 (w), 1124 (s), 1072 (m), 1009 (w), 946 (w). ^1H NMR (300 MHz, $CDCl_3$) δ_{ppm} 7.54 (d, J = 8.1 Hz, 2H), 7.39 (d, J = 6.6 Hz, 2H), 6.71-6.59 (m, 1H), 5.15 (dd, J = 10.5, 1.5 Hz, 1H), 4.61 (dd, J = 17.3, 1.5 Hz, 1H), 3.86-3.85 (m, 1H), 2.18-2.11 (m, 1H), 1.97 (d, J = 13.3 Hz, 1H), 1.91-0.63 (m, 11H). ^{13}C NMR (125 MHz, $CDCl_3$) δ_{ppm} 178.9 (C_4), 144.7 (C_4), 138.6 (CH), 130.4 (2 x CH), 125.2 (q, J = 3.5 Hz, 2 x CH), 117.5 (CH_2), 82.6 (C_4), 55.7 (C_4), 51.0 (CH), 49.7 (CH), 35.9 (CH_2), 33.5 (CH_2), 29.9 (CH_2), 24.5 (CH_2), 23.8 (CH_2), 20.6 (CH_2), 20.0 (CH_2). HRMS (EI) *m/z* (M^+) calcd for $C_{21}H_{23}F_3O_2$ 364.1650, found 364.1633.

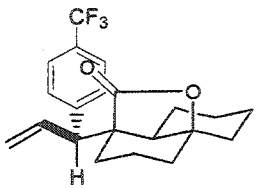


7-[1-(4-Trifluoromethylphenyl)allyl]-11-oxatricyclo[5.3.2.0^{1,6}]dodecan-12-ol (2.4h)

Prepared using general procedure **F**: method A and B.

Reagents and quantities for method A : Allyl ether **2.1h** (19.6 mg, 0.0535 mmol), triethylamine (15.2 mg, 0.161 mmol) and toluene (12.0 mL) to provide lactol **2.4h** (19.4 mg, 99%) as colorless crystals. Reagents and quantities for method B: Allyl ether **2.1h** (47.8 mg, 0.131 mmol), triethylamine (36.3 mg, 0.391 mmol) and toluene (5.0 mL) to provide lactol **2.4h** (24.3 mg, 51%) as colorless crystals. mp 126.6-128.5°C. IR ($CDCl_3$, cm^{-1}) 3371 (w), 3073 (w), 2930 (m), 2855 (w), 1623 (w), 1451 (w), 1411 (w), 1326 (s), 1164 (m), 1124 (m), 1070 (m), 986 (w). ^1H NMR (300 MHz, $CDCl_3$) δ_{ppm} 7.51-7.48 and 7.28 (m and d, J = 8.1 Hz, 4H), 6.34-6.16 (m, 1H), 5.53, 5.19-5.03 and 4.75 (d, m and s, J = 4.4 Hz, 3H), 4.14 and 3.64 (2d, J = 9.2 Hz and 8.5 Hz, 1H), 2.98 and 2.52 (2s (br), 1H), 2.15-0.81 (m, 15H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 146.5 (C_4), 137.5 and 136.9 (CH),

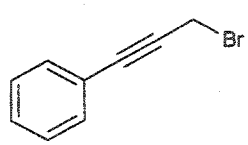
130.9 and 127.7 (2 x CH), 124.9-124.4 (q, J = 3.8 Hz, 2 x CH), 117.9 (CH_2), 102.6 and 101.0 (CH), 84.0 and 81.8 (C_4), 54.2 and 52.5 (C_4), 50.9 (CH), 49.0 (CH), 47.7 (CH), 39.3 and 38.4 (CH_2), 34.7 and 34.5 (CH), 29.7 and 28.8 (CH), 26.6 (CH), 24.9 (CH), 24.7 (CH), 23.9 (CH), 22.5 (CH), 21.6 (CH), 19.3 (CH). HRMS (EI) *m/z* (M^+) calcd for $C_{21}H_{25}F_3O_2$ 366.1807, found 366.1691.



7-[1-(4-Trifluoromethylphenyl)allyl]-11-oxatricyclo[5.3.2.0^{1,6}]dodecan-12-one (Lactone from 2.4h)

Prepared using general procedure **G**

Lactol **2.4h** (9.4 mg, 0.026 mmol); 4 Å molecular sieves (12.9 mg); NMO (4.5 mg, 0.039 mmol) and TPAP (0.5 mg, 0.001 mmol) in dry dichloromethane (2.0 mL) provided **lactone of 2.4h** (9.3 mg, 99%) as a colorless oil. IR (neat, cm^{-1}) 3076 (w), 2932 (m), 2860 (m), 1770 (s), 1617 (w), 1454 (m), 1326 (s), 1162 (s), 1123 (s), 1068 (m), 1018 (m), 939 (m). ^1H NMR (300 MHz, $CDCl_3$) δ_{ppm} 7.55 (d, J = 8.1 Hz, 2H), 7.37 (d, J = 8.1 Hz, 2H), 6.26-6.14 (m, 1H), 5.10 (dt, J = 10.4, 1.3 Hz, 1H), 4.93 (dt, J = 17.1, 1.4 Hz, 1H), 3.85 (d, J = 7.8 Hz, 1H), 2.07-1.92 (m, 3H), 1.79-0.81 (m, 12H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 178.2 (C_4), 144.2 (C_4), 137.6 (CH), 130.8 (2 x CH), 124.8 (q, J = 3.5 Hz, 2 x CH), 117.6 (CH_2), 82.4 (C_4), 55.8 (C_4), 51.5 (CH), 50.7 (CH), 35.7 (CH_2), 33.6 (CH_2), 30.6 (CH_2), 25.7 (CH_2), 24.1 (CH_2), 20.8 (CH_2), 19.3 (CH_2). HRMS (EI) *m/z* (M^+) calcd for $C_{21}H_{25}F_3O_2$ 364.1650, found 364.1653.

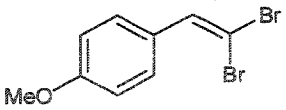


(3-Bromo-prop-1-ynyl)-benzene (2.39)

Prepared using general procedure **C**

Commercially available 3-phenyl-prop-2-yn-1-ol **2.38** (210.5 mg, 1.593 mmol); carbon tetrabromide (660.0 mg, 1.991 mmol); triphenylphosphine (626.6 mg, 2.389 mmol) in

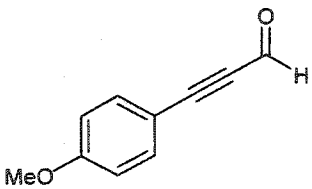
CH_2Cl_2 (30.0 mL). The product was used in the following reaction without further purification.



1-(2,2-Dibromo-vinyl)-4-methoxy-benzene (2.41)

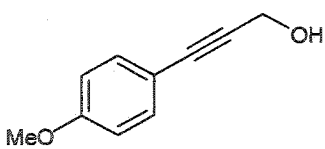
Prepared using general procedure **D**

Carbon tetrabromide (24.34 g, 73.39 mmol); triphenylphosphine (19.25 g, 73.39 mmol); *p*-anisaldehyde **2.40** (5.00 g, 36.72 mmol); triethylamine (5.12 mL, 36.7 mmol) in DCM (80.0 mL). The reaction was stirred overnight to afford **2.41** as yellow crystals (1.96 g, 18%). Spectral data: Huh, D.H.; Jeong, J.S.; Lee, H.B.; Ryu, H.; Kim, Y.G. *Tetrahedron* **2002**, *58*, 9925.



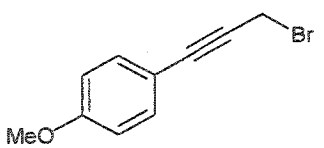
(4-Methoxy-phenyl)-propynal (2.42)

1-(2,2-Dibromo-vinyl)-4-methoxy-benzene **2.41** (1.96 g, 6.71 mmol); *n*-BuLi (5.8 mL, 13 mmol); DMF (0.53 mL, 6.8 mmol) in THF (60.0 mL) provided aldehyde **2.42** as yellow crystals (0.52 g, 48%). Spectral data: Wadsworth, D.H.; Geer, S.M.; Detty, M.R. *J. Org. Chem.* **1987**, *52*, 3662.



3-(4-Methoxy-phenyl)-prop-2-yn-1-ol (2.43)

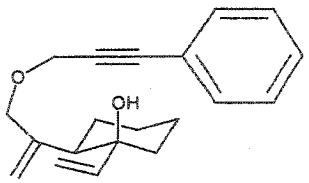
(4-Methoxy-phenyl)-propynal **2.42** (0.469 g, 2.92 mmol); $NaBH_4$ (0.552 g, 14.6 mmol) in EtOH (50.0 mL) to generate alcohol **2.43** as light yellow crystals (0.40 g, 84%). Spectral data: Wadsworth, D.H.; Geer, S.M.; Detty, M.R. *J. Org. Chem.* **1987**, *52*, 3662.



1-(3-Bromo-prop-1-ynyl)-4-methoxy-benzene (2.44)

3-(4-Methoxy-phenyl)-prop-2-yn-1-ol **2.43** (396.3 mg, 2.443 mmol); carbon tetrabromide (1.01 g, 3.05 mmol); triphenylphosphine (0.962 g, 3.67

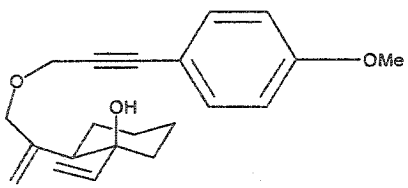
mmol) in DCM (50.0 mL). The product was used in the following reaction without further purification.



2-[1-(3-Phenyl-prop-2-ynyloxymethyl)-vinyl]-1-vinyl-cyclohexanol (2.45d)

Followed using general procedure **E**

Sodium hydride (109.0 mg, 2.729 mmol); 1,2-divinylcyclohexanol **2.13** (100.0 mg, 0.5460 mmol); (3-bromo-prop-1-ynyl)-benzene **2.39** (theoretically 310.7 mg, 1.593 mmol) to afford **2.45d** as a colorless oil (95.0 mg, 59%). IR (neat) 3426 (m), 3078 (w), 2931 (s), 2855 (m), 2228 (w),1637 (w), 1490 (m), 1443 (m), 1355 (w), 1256 (w), 1068 (s), 972 (m), 916 (s), 757 (s), 691 (m) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$), δ_{ppm} 7.45-7.39 (m, 2H), 7.33-7.27 (m, 3H), 5.87 (dd, J = 17.2, 10.7 Hz, 1H), 5.24-5.15 (m, 2H), 5.05-4.95 (m, 2H), 4.30 (dd, J = 29.6, 15.7 Hz, 2H), 4.14 (dd, J = 11.9, 0.9 Hz, 1H), 3.93 (d, J = 12.1 Hz, 1H), 3.11 (d, J = 2.15 Hz, 1H), 2.28 (dd, J = 12.7, 3.3 Hz, 1H), 1.94-1.16 (m, 8H). ^{13}C NMR (300 MHz, $CDCl_3$) δ_{ppm} 146.8 (CH), 146.2 (C_4) 132.1 (2 x CH), 128.9 (CH), 128.7 (2 x CH), 122.9 (C_4), 118.4 (CH_2), 111.5 (CH_2), 87.0 (C_4), 84.9 (C_4), 73.0 (C_4), 72.2 (CH_2), 58.0 (CH_2), 51.5 (CH), 38.7 (CH_2), 27.2 (CH_2), 26.5 (CH_2), 21.6 (CH_2). HRMS *m/z* (M^+ - $C_{11}H_{17}O_2$) calcd 115.0548 found 115.0521.

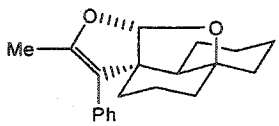


2-{1-[3-(4-Methoxy-phenyl)-prop-2-ynyloxymethyl]-vinyl}-1-vinyl-cyclohexanol (2.45e)

Followed using general procedure **E**

Sodium hydride (109.0 mg, 2.729 mmol); 1,2-divinylcyclohexanol **2.13** (100.0 mg, 0.5460 mmol); 1-(3-bromo-prop-1-ynyl)-4-methoxy-benzene **2.44** (theoretically 549.2 mg, 2.440 mmol) to afford **2.45e** as a colorless oil (142.8 mg, 80%). IR (Ether) 3423

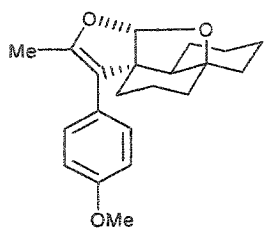
(m), 3071 (w), 2932, (s), 2859 (m), 2228 (w), 1607 (s), 1510 (s), 1442 (w), 1292 (m), 1249 (s), 1174 (m), 1062 (m), 917 (m), 833 (s) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$), δ_{ppm} 7.34 (d, J = 8.56 Hz, 2H), 6.79 (d, J = 8.56 Hz, 2H), 5.85 (dd, J = 17.2, 10.7 Hz, 1H), 5.21-5.12 (m, 2H), 5.02-4.93 (m, 2H), 4.26 (dd, J = 29.9, 15.6 Hz, 2H), 4.00 (dd, J = 63.8, 11.9 Hz, 2H), 3.75 (s, 3H), 3.14 (s, 1H), 2.25 (d, J = 12.8 Hz, 1H), 1.99-1.14 (m, 8H). ^{13}C NMR (300 MHz, $CDCl_3$) δ_{ppm} 169.1 (C_4), 146.8 (CH), 146.2 (C_4), 133.6 (2 x CH), 118.3 (CH), 115.0 (C_4), 114.3 (2 x CH), 111.4 (CH_2), 87.0 (C_4), 83.5 (C_4), 73.0 (C_4), 72.1 (CH_2), 58.0 (CH_2), 55.6 (CH_3), 51.5 (CH), 38.7 (CH_2), 27.2 (CH), 26.5 (CH_2), 21.7 (CH_2). HRMS *m/z* (M^+) calcd 326.1882 found 326.



Tetracyclic acetal (2.47d).

Prepared using general procedure **F**: method A.

Propargyl ether **2.45d** (76.8 mg, 0.259 mmol), DBU (119 mg, 0.78 mmol) and toluene (12.0 mL) generated tetracyclic acetal **2.47d** (65.3 mg, 85%) as a colorless oil. IR (neat, cm^{-1}) 3030 (w), 2927 (s), 2859 (m), 1648 (m), 1445 (w), 1237 (w), 1208 (m), 1076 (m), 977 (m), 903 (m), 757 (m), 699 (m). ^1H NMR (300 MHz, $CDCl_3$), δ_{ppm} 7.33-7.12 (m, 5H), 5.82 (s, 1H), 1.96 (s, 3H), 1.93-1.16 (m, 15H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 150.3 (C_4), 135.5 (C_4), 128.7 (2 x CH), 127.4 (2 x CH), 125.8 (CH), 113.8 (C_4), 112.7 (C_4), 89.3 (C_4), 62.4 (C_4), 52.1 (CH), 39.4 (CH_2), 33.9 (CH_2), 31.2 (CH_2), 25.3 (CH_2), 24.5 (CH_2), 21.7 (CH_2), 19.8 (CH_2), 13.4 (CH_3). LRMS (EI) *m/z* (M^+) calcd for $C_{20}H_{24}O_2$ 296, found 296.

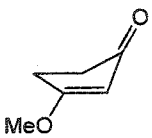


Tetracyclic acetal (2.47e).

Prepared using general procedure **F**: method A.

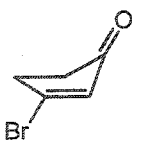
Propargyl ether **2.45e** (142.2 mg, 0.4356 mmol), DBU (201 mg,

1.32 mmol) and toluene (12.0 mL) afforded tetracyclic acetal **2.47e** (115.0 mg, 81%) as colorless crystals. mp 102-104°C. IR (neat, cm^{-1}) 3045 (w), 2927 (s), 2865 (m), 1655 (w), 1609 (w), 1513 (s), 1442 (w), 1346 (w), 1288 (m), 1244 (s), 1178 (m), 978 (m). ^1H NMR (300 MHz, $CDCl_3$), δ_{ppm} 7.04 (dd, J = 8.87, 2.10 Hz, 2H), 6.85 (dd, J = 6.83, 2.11 Hz, 2H), 5.80 (s, 1H), 3.78 (s, 3H), 1.92 (s, 3H), 1.88 (m, 15H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 157.9 (C_4), 149.1 (C_4),128.6 (2 x CH), 127.8 (C_4), 114.2 (2 x CH), 113.2 (C_4), 112.6 (CH), 89.3 (C_4), 62.4 (C_4), 55.6 (CH_3), 51.9 (CH), 39.4 (CH_2), 33.9 (CH_2), 31.3 (CH_2), 25.3 (CH_2), 24.5 (CH_2), 21.7 (CH_2), 19.8 (CH_2), 13.2 (CH_3). HRMS (EI) *m/z* (M^+) calcd for $C_{21}H_{26}O_3$ 326.1883, found 326.1884.



3-methoxycyclopent-2-enone (3.19)

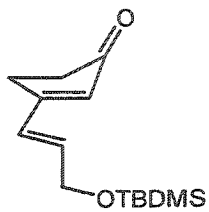
To a solution of 1,3-cyclopentadione **3.18** (1.0688 g, 10.895 mmol) and methanol (15.0 mL) was added recrystallized PTSA (207.2 mg, 1.090 mmol). The solution was stirred for 2.5 hours. The reaction was quenched with saturated $NaHCO_3$ (aq) until a pH of 8 was obtained. The aqueous layer was extracted with ether (3x) and the organic layers were combined, dried over $MgSO_4$ and concentrated. Purification by flash column chromatography (70% EtOAc in hexanes) generated methylenol ether **3.19** (671.5 mg, 55%) as colorless crystals. Spectral data: House, H. O.; Rasmusson, G. H. *J. Org. Chem.* **1963**, *28*, 27.



3-Bromo-cyclopent-2-enone (3.23)

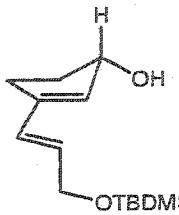
A 100 mL flame dried round bottom flask was charged with 1,3-cyclopentadione **3.18** (0.750 mg, 7.65 mmol), phosphorus tribromide (15.3 mmol, 1.45 mL), and dichloromethane (40.0 mL). The solution was heated to reflux under N_2 for 24 hours. The reaction was cooled to room temperature, poured over ice water and extracted

with ether (3x). The organic layers were combined, dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. Flash column chromatography (40% EtOAc in hexanes) afforded **3.23** as a colorless oil (0.69 g, 57%). Spectral data: Shih, C.; Swenton, J. S. *J. Org. Chem.* **1982**, *47*, 2825.



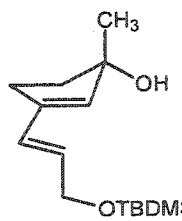
3-[3-(tert-Butyl-dimethyl-silanyloxy)-propenyl]-cyclopent-2-enone (3.22)

To a dry 25 mL round bottom flask with a magnetic stirrer were placed $PdCl_2(PPh_3)_2$ (19.7 mg, 0.0281 mmol) and NaOAc (11.5 mg, 0.141 mmol). The flask was flushed with N_2 and charged with dry methanol (1.0 mL), boronic ester **3.24** (29.9 mg, 0.103 mmol) and 3-bromo-cyclopent-2-enone **3.23** (15.0 mg, 0.0938 mmol). The reaction mixture was refluxed for 3 hours. The solution was cooled to room temperature and the boronate ester was oxidized by addition of 3 drops of 3 M NaOH (aq) and 3 drops of 30% hydrogen peroxide. The aqueous layer was extracted with benzene (3x) and the combined organic layer was washed with a saturated solution of brine. The organic layer was dried over $MgSO_4$, concentrated and flash chromatography (20% EtOAc/hexanes) generated **3.22** as colorless crystals (20.12 mg, 85%). IR (neat) 2923 (m), 2852 (m), 1700 (s), 1673 (s), 1646 (s), 1583 (m), 1441 (s), 1252 (m), 969 (s), 836 (s) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ_{ppm} 6.74 (d, J = 15.7 Hz, 1H), 6.34 (dt, J = 15.7, 4.2 Hz, 1H), 6.00 (s, 1H), 4.34 (dd, J = 4.1, 1.8 Hz, 2H), 2.74-2.71 (m, 2H), 2.45-2.42 (m, 2H), 0.91 (s, 9H), 0.08 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 209.7 (C_4), 171.9 (C_4), 138.7 (CH), 130.1 (CH), 124.7 (CH), 63.0 (CH_2), 34.8 (CH_2), 27.1 (CH_2), 2.5.9 (3 x CH_3), 18.4 (C_4), -5.36 (2 x CH_3). HRMS *m/z* M^+- (C_4H_9) calcd 195.0813 found 195.0866. mp 50.4-52.4 °C.



3-[3-(tert-Butyl-dimethyl-silanyloxy)-propenyl]-cyclopent-2-enol (3.25)

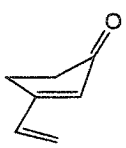
To a solution of ketone **3.22** (0.0400 mmol, 10.1 mg) in MeOH (1.5 mL) was added $CeCl_3 \cdot 7H_2O$ (0.0400 mmol, 14.9 mg) at 0°C, followed by $NaBH_4$ (0.0400 mmol, 1.51 mg). The solution was stirred for 5 minutes after which a TLC revealed no starting material. The reaction was quenched with saturated NH_4Cl (aq) and the MeOH was removed under vacuum. The solution was diluted with water and Et_2O and the aqueous layer was extracted with Et_2O (3x). The organic layers were combined, dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash chromatography (30 % EtOAc in hexanes) to afford **3.25** as a colorless oil (10.2 mg) in a quantitative yield. ^{1}H NMR (300 MHz, $CDCl_3$) δ_{ppm} 6.51 (d, 15.5 Hz, 1H), 5.66 (dt, J = 15.7 Hz, 4.8 Hz, 1H), 5.58 (s, 1H), 4.64 (s, 1H), 4.11 (d, J = 4.7 Hz, 2H), 2.43-2.36 (m, 1H), 2.12-1.99 (m, 2H), 1.63-1.54 (m, 1H), 0.98 (s, 9H), 0.06 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 144.4 (C_4), 132.3 (CH), 132.1 (CH), 126.2 (CH), 77.2 (CH), 63.7 (CH_2), 33.9 (CH_2), 29.8 (CH_2), 26.1 (3 x CH_3), 18.5 (C_4), -5.1 (2 x CH_3). IR ($CHCl_3$, cm^{-1}) 3342 (m), 2962 (s), 2923 (s), 2859 (s), 1603 (w), 1468 (m), 1242 (s), 1126 (m), 1056 (m), 966 (s), 837 (s), 772 (s). HRMS (EI) *m/z* (M^+) calcd 236.1596 found 236.1574.



3-[3-(tert-Butyl-dimethyl-silanyloxy)-propenyl]-1-methyl-cyclopent-2-enol (3.26)

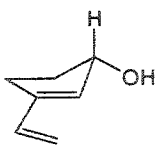
To a solution of ketone **3.22** (0.137 mmol, 34.5 mg) in THF (4.0 mL) cooled at -78°C was added methyllithium (0.21 mmol, 0.13 mL). The reaction was stirred for 3 hours and monitered by TLC. The reaction was quenched at 0°C with water and the aqueous layer was extracted with EtOAc (3x). The combined organic layers were

dried over anhydrous $MgSO_4$, concentrated, and purified by basified flash chromatography (Et_3N, 30% EtOAc in hexanes) to afford the tertiary alcohol **3.26** as a colorless oil (30.9 mg, 84%). ^1H NMR (300 MHz, C_6D_6) δ_{ppm} 6.48 d, J = 15.4 Hz, 1H), 5.67 (dt, J = 15.6 Hz, 4.9 Hz, 1H), 5.63 (s, 1H), 4.13 (dd, J = 4.9 Hz, 1.4 Hz, 2H), 2.43-2.34 (m, 1H), 2.22-2.11 (m, 1H), 1.81 (t, J = 6.8 Hz, 2H), 1.27 (s, 3H), 0.99 (s, 9H), 0.07 (s, 6H). ^{13}C NMR (75 MHz, C_6D_6) δ_{ppm} 142.3 (C_4), 136.7 (CH), 131.7 (CH), 126.3 (CH), 83.6 (C_4), 63.7 (CH_2), 40.1 (CH_2), 30.0 (CH_2), 27.7 (CH_3), 26.1 (3 x CH_3), 18.5 (C_4), -5.1 (2 x CH_3). IR (C_6D_6, cm^{-1}) 3359 (w), 2958 (s), 2929 (s), 2854 (s), 1468 (m), 1383 (m), 1250 (s), 1106 (s), 1066 (s), 969 (m), 837 (s), 768 (m). HRMS (EI) *m/z* (M^+) calcd 268.1859 found 268.1837.



3-Vinyl-cyclopent-2-enone (3.27)

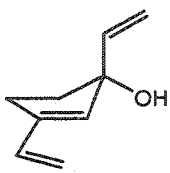
Vinylmagnesium bromide (1.58 mL, 1.42 mmol) was added dropwise at -78°C to a solution of 3-methoxycyclopent-2-enone **3.19** (132.5 mg, 1.182 mmol) in dry THF (3.0 mL). The solution was stirred for 1 hour at -78°C and was subsequently allowed to warm up to room temperature. The solution was slowly poured over ice (16 g) and concentrated HCl (0.5 mL), and was stirred for 2 hours. The aqueous layers were dried over anhydrous $MgSO_4$ and concentrated to provide diene **3.27** (127.8 mg, >99%) as a yellow oil. No purification was required. Spectral data: Fisher, M. J.; Hehre, W. J.; Overman, L. E.; Kahn, S. D. *J. Am. Chem. Soc.* **1988**, *110*, 4625.



3-Vinyl-cyclopent-2-enol (3.28)

To a solution of enone **3.27** (0.971 mmol, 150 mg) in MeOH (5.0 mL) was added $CeCl_3 \cdot 7H_2O$ (0.971 mmol, 362 mg) at 0°C, followed by $NaBH_4$ (0.971 mmol, 36.7

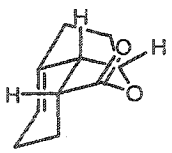
mg). The solution was stirred for 5 minutes after which a TLC revealed no starting material. The reaction was quenched with saturated NH_4Cl (aq) and the MeOH was removed under vacuum. The solution was diluted with water and Et_2O and the aqueous layer was extracted with Et_2O (3x). The organic layers were combined, dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash column chromatography (30 % EtOAc in hexanes) to afford **3.28** as a colorless oil (56.0 mg, 52%). Spectral data: Fisher, M.J.; Hehre, W.J.; Overman, L.E.; Kahn, S.D. *J. Am. Chem. Soc.* **1988**, *110*, 4625.



1,3-Divinyl-cyclopent-2-enol (3.29)

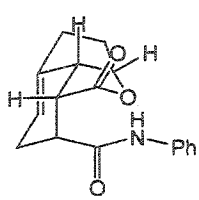
A dry round bottom flask was charged with the ketone **3.27** (0.761 mmol, 82.3 mg) in THF (8.0 mL) and the solution was cooled to -78°C. Vinylmagnesium bromide (1.52 mmol, 1.69 mL) was added and the solution was stirred for 10 minutes. The reaction was quenched at 0°C with saturated NH_4Cl. The aqueous layer was extracted with EtOAc (3x), the combined organic layers were dried over $MgSO_4$ and were concentrated *in vacuo*. Purification by flash chromatography (20% EtOAc in hexanes) yielded **3.29** as a volatile colorless oil (42.1 mg, 41%). ^1H NMR (300 MHz, $CDCl_3$) δ_{ppm} 6.54 (dd, J = 17.4 Hz, 10.6 Hz, 1H), 6.01 (dd, J = 17.3 Hz, 10.6 Hz, 1H), 5.58 (s, 1H), 5.24 (dd, J = 7.2 Hz, 0.7 Hz, 1H), 5.19 (s, 1H), 5.16 (dd, J = 7.0 Hz, J = 0.7 Hz, 1H), 5.02 (dd, J = 10.6 Hz, 0.7 Hz, 1H), 2.67-2.58 (m, 1H), 2.46-2.36 (m, 1H), 2.23-2.14 (m, 1H), 2.05-1.96 (m, 1H), 1.78 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 145.4 (C_4), 142.5 (CH), 133.7 (CH), 133.0 (CH), 116.8 (CH_2), 111.7 (CH_2), 85.3 (C_4), 38.9 (CH_2), 29.1 (CH_2). IR ($CDCl_3$, cm^{-1}) 3381 (m), 2932 (m), 2853 (w), 1761 (s), 1647 (w), 1447 (s), 1148 (s). HRMS (EI) *m/z* (M^+) calcd 136.0888 found 136.0877.

5.9 General Procedure H for the Hydroxy-Directed Diels-Alder Reaction



3,4,6,7,7a,7b-Hexahydro-2aH-2-oxa-cyclopenta[cd]inden-1-one (3.32)

Method A. To a solution of $MgBr_2 \cdot Et_2O$ (1.032 mmol, 266.6 mg) in CH_2Cl_2 (5.0 mL) at room temperature (21°C) was added Et_3N (1.7 mmol, 0.24 mL) under an atmosphere of nitrogen. The solution became pink and was stirred for 30 minutes. Diene **3.28** (0.344 mmol, 37.9 mg) in CH_2Cl_2 (3.0 mL) was subsequently cannulated into the reaction mixture and was stirred for and additional 30 minutes, during which the solution became orange. Dienophile (methylacrylate) (1.7 mmol, 0.16 mL) was added and the solution was stirred overnight. The solution was quenched with saturated NH_4Cl (aq), extracted with CH_2Cl_2 (3x), dried over anhydrous $MgSO_4$ and concentrated under vacuum. Purification by flash column chromatography (20% EtOAc in hexanes) afforded lactone **3.32** as a volatile colorless oil (18.2 mg, 32 %). ^1H NMR (300 MHz, $CDCl_3$) δ_{ppm} 5.64 (s, 1H), 4.84 (t, J = 5.8 Hz, 1H), 3.05-3.00 (m, 1H), 2.86 (broad s, 1H), 2.37 (t, J = 7.5 Hz and 8.4 Hz, 2H), 2.17-1.75 (m, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 178.0 (C_4), 137.0 (C_4), 122.4 (CH), 82.6 (CH), 42.6 (CH), 39.1 (CH), 31.1 (CH_2), 28.8 (CH_2), 21.1 (CH_2), 18.8 (CH_2). IR ($CHCl_3$, cm^{-1}) 2942 (w), 2844 (w), 1761 (s), 1440 (w), 1303 (w), 1148 (m), 1022 (m), 953 (m), 896 (m). HRMS (EI) *m/z* (M^+) calcd 164.0837 found 164.0837.

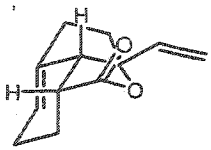


Reaction of 3.28 with N-phenylmaleimide (3.33)

Prepared using general procedure **H**: method A

$MgBr_2 \cdot Et_2O$ (0.232 mmol, 59.8 mg); Et_3N (0.386 mmol, 0.05 mL); diene

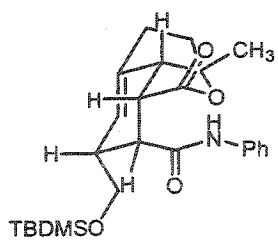
3.28 (0.077 mmol, 8.5 mg) ; N-phenylmaleimide (0.386 mmol, 66.8 mg) in DCM (5.0 mL) afforded amide **3.33** as colorless crystals (11.9 mg, 54%). Spectral data: Fisher, M.J.; Hehre, W.J.; Overman, L.E.; Kahn, S.D. *J. Am. Chem. Soc.* **1988**, *110*, 4625.



2a-Vinyl-3,4,6,7,7a,7b-hexahydro-2aH-2-oxa-cyclopenta[cd]inden-1-one (3.34)

Prepared using general procedure **H**: method A

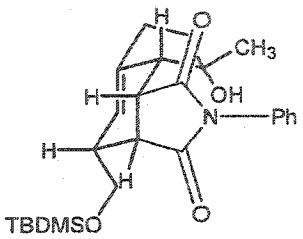
$MgBr_2 \cdot Et_2O$ (0.139 mmol, 35.8 mg); Et_3N (0.2 mmol, 0.03 mL); diene **3.29** (0.046 mmol, 6.3 mg); methylacrylate (0.2 mmol, 0.02 mL) in DCM (5.0 mL) afforded lactone **3.34** as a colorless oil (2.0 mg, 23%). ^1H NMR (300 MHz, $CDCl_3$) δ_{ppm} 5.93 (dd, J = 17.1 Hz, 10.8 Hz, 1H), 5.62 (broad s, 1H), 5.32 (dd, J = 17.1 Hz, 1.0 Hz, 1H), 5.16 (dd, J = 10.8 Hz, J = 1.0 Hz, 1H), 2.95 (dddd, J = 6.5 Hz, 5.2 Hz, 2.7 Hz, 1H), 2.72-2.69 (m, 1H), 2.51-2.35 (m, 2H), 2.19-1.96 (m, 5H), 1.83-1.71 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 177.8 (C_4), 138.1 (CH), 137.8 (C_4), 122.4 (CH), 114.1 (CH_2), 92.2 (C_4), 47.0 (CH), 37.8 (CH), 34.4 (CH_2), 31.1 (CH_2), 21.0 (CH_2), 18.6 (CH_2). IR (neat, cm^{-1}) 2959 (w), 2922 (s), 2851 (m), 1775 (s), 1448 (w), 1158 (w). HRMS (EI) *m/z* (M^+) calcd 190.0994 found 190.0988.



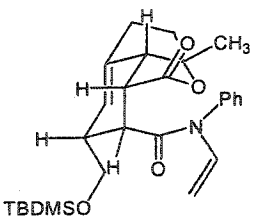
6-(tert-Butyl-dimethyl-silanyloxymethyl)-2a-methyl-1-oxo-1,2a,3,4,6,7,7a,7b-octahydro-2-oxa-cyclopenta[cd]indene-7-carboxylic acid phenylamide (3.35)

Method B. Vinylmagnesium bromide (0.56 mmol, 0.62 mL) was added dropwise to a solution of diene **3.26** (0.4675 mmol, 125.5 mg) in toluene (6.0 mL) cooled to -78°C under N_2. The reaction mixture was stirred for 30 minutes, followed by

cannulation of N-phenylmaleimide (1.403 mmol, 242.9 mg) in toluene (4.0 mL). The yellow solution was warmed up to room temperature and was stirred for 36 hours. A TLC revealed the presence of two products, the spontaneously lactonized amide and the free alcohol, and a trace of starting material. The orange solution was quenched with saturated NH_4Cl (aq), extracted with CH_2Cl_2 (3x), dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The crude products were purified by flash chromatography (20% EtOAc in hexanes) to afford the amide **3.35** with a trace of NPM as a light yellow oil (91.0 mg, 44%). The imide **3.36** was subsequently diluted in THF and 0.5 mL of DBU was added to the reaction flask. After stirring for 30 minutes, the organic solvent was removed under vacuum and the crude amide was purified by flash column chromatography (30% EtOAc in hexanes) to afford the pure amide **3.35** as a colorless foam (80.9 mg, 39%). The reaction yielded the amide (83%, dr > 25:1) after all manipulations. Amide **3.35**: ^{1}H NMR (300 MHz, $CDCl_3$) δ_{ppm} 9.98 (s, 1H), 7.55 (dd, J = 8.7 Hz, 0.8 Hz, 2H), 7.29 (t, J = 7.6 Hz, 2H), 7.06 (t, J = 7.4 Hz, 1H), 5.70 (s, 1H), 3.74 (m, 2H), 3.43 (dd, J = 7.9 Hz, 4.9 Hz, 1H), 3.31 (dd, J = 6.7 Hz, 4.9 Hz, 1H), 2.84 (broad s, 1H), 2.73 (d, J = 7.8 Hz, 1H), 2.46 (t, J = 6.9 Hz, 2H), 2.28-2.17 (m, 1H), 2.04-1.97 (m, 1H), 1.55 (s, 3H), 0.83 (s, 9H), -0.02 (d, J = 4.0 Hz, 6H). ^{13}C NMR (75 MHz, C_6D_6) δ_{ppm} 178.8 (C_4), 170.1 (C_4), 140.1 (C_4), 138.2 (C_4), 128.9 (2 x CH), 124.0 (CH), 121.8 (CH), 120.0 (2 x CH), 92.6 (C_4), 63.8 (CH_2), 49.4 (CH), 44.7 (CH), 40.2 (CH), 39.5 (CH), 36.5 (CH_2), 31.2 (CH_2), 25.9 (3 x CH_3), 24.9 (CH_3), 18.2 (C_4), -5.4 (2 x CH_3). IR (neat, cm^{-1}) 3316 (w), 3052 (w), 2954 (m), 2930 (m), 2887 (m), 2853 (m), 1740 (s), 1681 (m), 1597 (s), 1555 (m), 1499 (m), 1440 (m), 1248 (m), 1098 (s), 838 (s). HRMS (EI) *m/z* (M^+ - $(CH_3)_3$) calcd 384.1631 found 384.1624. mp 87.1-88.5°C.



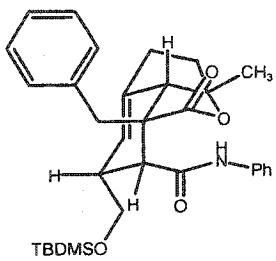
Imide **3.36** ^{1}H NMR (300 MHz, $CDCl_3$) δ_{ppm} 7.49-7.34 (m, 3H), 7.13 (d, J = 7.4 Hz, 2H), 5.55 (s, 1H), 4.96 (s, 1H), 4.18 (dd, J = 10.0 Hz, 7.1 Hz, 1H), 3.88 (t, J = 9.0 Hz, 1H), 3.64 (t, J = 7.6 Hz, 1H), 3.40 (t, J = 7.6 Hz, 1H), 2.51 (broad s, 1H), 2.40-2.28 (m, 3H), 1.97-1.79 (m, 2H), 1.40 (s, 3H), 0.89 (s, 9H), 0.07 (d, J = 1.5 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 180.6 (C_4), 176.0 (C_4), 146.4 (C_4), 131.5 (C_4), 129.2 (2 x CH), 128.9 (CH), 126.6 (2 x CH), 119.7 (CH), 79.0 (C_4), 63.0 (CH_2), 51.3 (CH), 42.5 (CH), 41.3 (CH), 41.1 (CH), 40.6 (CH_2), 29.2 (CH_3), 27.8 (CH_2), 25.9 (3 x CH_3), 18.3 (C_4), -5.3 (2 x CH_3). IR (neat, cm^{-1}) 3436 (w), 3050 (w), 2957 (m), 2932 (m), 2890 (w), 2856 (m), 1777 (w), 1695 (s), 1606 (w), 1500 (m), 1390 (m), 1253 (m), 1216 (m), 1110 (m), 838 (s). HRMS (EI) *m/z* (M^+ - ($C(CH_3)_3$) calcd 384.1631 found 348.1585.



6-(tert-Butyl-dimethyl-silanyloxymethyl)-2a-methyl-1-oxo-1,2a,3,4,6,7,7a,7b-octahydro-2-oxa-cyclopenta[cd]indene-7-carboxylic acid phenyl-vinyl-amide (3.37b)

A flame dried round bottom flask was charged with NaH (0.074 mmol, 3.0 mg). Amide **3.35** (0.0706 mmol, 31.2 mg) in THF (3.0 mL) was cannulated into the flask, followed by the addition of allybromide (0.078 mmol, 7.0 μL). The reaction was stirred for 4 hours. The excess reagents were quenched with saturated NH_4Cl (aq). The aqueous layer was extracted with EtOAc (3x). The organic layers were combined, dried over anhydrous $MgSO_4$ and concentrated. The product was purified by flash column chromatography (20% EtOAc in hexanes) to afford **3.37b** as a colorless oil (22.0 mg, 65%). ^{1}H NMR (300 MHz, $CDCl_3$) δ_{ppm} 7.39-7.29 (m, 5H), 5.91-5.82 (m, 1H), 5.63 (broad s, 1H), 5.05-

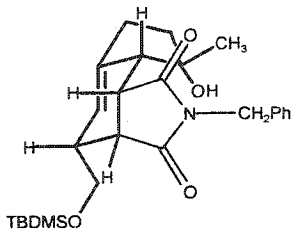
4.98 (m, 2H), 4.21 (d, J = 6.3 Hz, 2H), 3.63 (d, J = 7.5 Hz, 2H), 3.31-3.17 (m, 2H), 2.64 - 2.32 (m, 3H), 2.29-2.20 (m, 1H), 2.09 (broad s, 1H), 2.00-1.90 (m, 1H), 1.48 (s, 3H), 0.86 (s, 9H), 0.02 (d, J = 2.4 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 176.6 (C_4), 170.8 (C_4), 143.1 (C_4), 141.9 (C_4), 133.5 (2 x CH), 129.3 (2 x CH), 128.6 (CH), 127.6 (CH), 121.9 (CH), 117.5 (CH_2), 91.7 (C_4), 64.4 (CH_2), 52.7 (CH_2), 48.6 (CH), 43.6 (CH), 42.7 (CH), 38.3 (CH), 38.2 (CH_2), 29.7 (CH_2), 26.0 (3 x CH_3), 25.6 (CH_3), 18.4 (C_4), -5.3 (2 x CH_3). IR (neat, cm^{-1}) 3067 (w), 2954 (m), 2927 (s), 2858 (m), 1764 (s), 1661 (s), 1599 (m), 1250 (s), 1103 (m). HRMS (EI) *m/z* (M^+) calcd 481.2648 found 481.2656.



7a-Benzyl-6-(tert-butyl-dimethyl-silanyloxymethyl)-2a-methyl-1-oxo-1,2a,3,4,6,7,7a,7b-octahydro-2-oxa-cyclopenta[cd]indene-7-carboxylic acid phenylamide (3.42)

A solution of amide **3.35** (0.195 mmol, 85.7 mg) in THF (1.5 mL) was cannulated into a flask containing dried KH (1.14 mmol, 45.7 mg) and THF (1.5 mL). Benzylbromide (0.21 mmol, 0.030 mL) was added to the solution and was stirred for 1.5 hours. The TLC revealed no starting material. The reaction was quenched with saturated NH_4Cl (aq), the aqueous layers were extracted with EtOAc (3x) and the combined organic layers were dried over anhydrous $MgSO_4$. The solution was concentrated and the product was purified by flash column chromatography (20 % EtOAc in hexanes) to afford amide **3.42** as yellow crystals (75.1 mg, 73%). ^1H NMR (300 MHz, $CDCl_3$) δ_{ppm} 8.14 (s, 1H), 7.39-7.22 (m, 9H), 7.03 (t, J = 7.3 Hz, 1H), 4.99 (d, J = 2.2 Hz, 1H), 4.06 (dd, J = 11.1 Hz, 6.2 Hz, 1H), 3.61 (t, J = 11.6 Hz, 1H), 3.34 (d, J = 13.0 Hz, 1H), 3.20 (d, J = 4.3 Hz, 1H), 2.79 (d, J = 13.0 Hz, 1H), 2.68 (broad s, 1H), 2.46 (s, 1H),

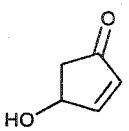
2.43-2.28 (m, 2H), 2.18-2.06 (m, 1H), 1.86-1.79 (m, 1H), 0.99 (s, 9H), 0.40 (s, 3H), 0.17 (d, J = 3.8 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 180.2 (C_4), 168.8 (C_4), 146.4 (C_4), 137.6 (C_4), 135.4 (C_4), 131.0 (2 x CH), 128.9 (2 x CH), 128.7 (2 x CH), 127.6 (CH), 124.0 (CH), 120.0 (2 x CH), 113.9 (CH), 89.7 (C_4), 63.5 (CH_2), 53.4 (C_4), 51.5 (CH), 50.5 (CH), 44.1 (CH_2), 40.1 (CH), 39.8 (CH_2), 31.6 (CH_2), 25.9 (3 x CH_3), 25.1 (CH_3), 18.1 (C_4), -5.1 (2 x CH_3). IR (neat, cm^{-1}) 3345 (w), 3062 (w), 2953 (m), 2926 (w), 2883 (w), 2857 (m), 1754 (s), 1693 (s), 1600 (s), 1538 (s), 1497 (s), 1380 (w), 1309 (m), 1250 (s), 1092 (s), 1076 (s), 838 (s). HRMS (EI) *m/z* (M^+-$(CH_3)_3$) calcd 474 found 474. mp = 67.1-70.8°C.



6-(tert-Butyl-dimethyl-silanyloxymethyl)-2a-methyl-1-oxo-1,2a,3,4,6,7,7a,7b-octahydro-2-oxa-cyclopenta[cd]indene-7-carboxylic acid benzylamide (3.45)

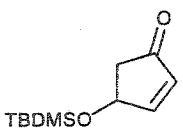
Vinylmagnesium bromide (0.12 mmol, 0.14 mL) was added dropwise to a solution of diene **3.26** (0.0577 mmol, 15.5 mg) in toluene (2.0 mL) cooled to -78°C under N_2. The reaction mixture was stirred for 30 minutes, followed by cannulation of N-benzylmaleimide (0.173 mmol, 32.5 mg) in toluene (1.0 mL). The lightly green solution was warmed up to room temperature and was stirred overnight (14 hours). The pink solution was quenched with saturated NH_4Cl (aq), extracted with CH_2Cl_2 (3x), dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by flash column chromatography (20% EtOAc in hexanes) to afford imide **3.45** as colorless crystals (19.6 mg, 74 %, dr > 25:1). ^{1}H NMR (300 MHz, $CDCl_3$) δ_{ppm} 7.27-7.18 (m, 5H), 5.38 (d, J = 2.5 Hz, 1H), 5.13 (s, 1H), 4.63 (d, J = 14.3 Hz, 1H), 4.53 (d, J = 14.3 Hz, 1H), 4.14 (dd, J = 10.0 Hz, 7.0 Hz, 1H), 3.81 (dd, J = 10.0 Hz, 8.1 Hz, 1H), 3.45 (dd, J =

8.3 Hz, 7.0 Hz, 1H), 3.23 (dd, J = 8.3 Hz, 6.6 Hz, 1H), 2.40 (broad s, 1H), 2.28 (d, J = 6.7 Hz, 1H), 2.20-2.00 (m, 2H), 1.70-1.61 (m, 2H), 1.33 (s, 3H), 0.89 (s, 9H), 0.07 (d, J = 1.7 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 181.1 (C_4), 176.7 (C_4), 146.2 (C_4), 135.4 (C_4), 128.5 (2 x CH), 128.0 (2 x CH), 127.8 (CH), 119.9 (CH), 78.9 (C_4), 63.0 (CH_2), 51.2 (CH), 42.4 (CH_2), 41.2 (CH), 41.1 (CH), 40.3 (CH_2), 29.3 (CH_3), 27.6 (CH_2), 26.0 (3 x CH_3), 18.4 (C_4), -5.3 (2 x CH_3). IR (neat, cm^{-1}) 3433 (w), 3036 (w), 2960 (m), 2033 (m), 2856 (w), 1767 (w), 1700 (s), 1687 (s), 1434 (m), 1397 (m), 1344 (m), 1254 (w), 834 (m). HRMS (EI) *m/z* (M^+) calcd 398.1787 found 398.1789. mp 67.1-70.8°C.



4-Hydroxy-cyclopent-2-enone (4.16)

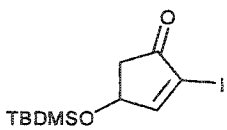
A solution of furfuryl alcohol **4.15** (0.102 mol, 10.0 g), KH_2PO_4 (3.670 mmol, 499.4 mg) in water (300.0 mL) at pH 4.1 (adjusted by addition of KOH and/or H_3PO_4) was refluxed for 48 hours. After cooling, the aqueous solution was saturated with NaCl, extracted with EtOAc (5x) and the combined organic phases were dried over $MgSO_4$. The organic solvent was removed in vacuo to afford the enone **4.16** as a brown oil and the crude product was used towards the next reaction.



4-(tert-Butyl-dimethyl-silanyloxy)-cyclopent-2-enone (4.17)

A solution of 4-hydroxy-2-cyclopentenone **4.16** (52.30 mmol, 5.131 g) and triethylamine (83.2 mmol, 11.6 mL) in THF (30.0 mL) was treated with DMAP (1.046 mmol, 127.8 mg). The solution was cooled to 0°C and treated portionwise with TBDMSCl (49.7 mmol, 7.49 g) to keep the temperature at or below 10°C (10 minutes). The resulting mixture was stirred at room temperature overnight. A 0.5 N solution of

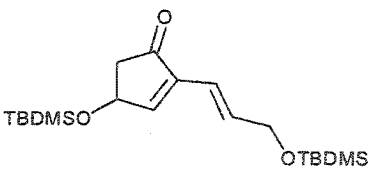
HCl was poured into the reaction mixture. The aqueous phase was extracted with hexanes (3x). The combined organic phase was washed with HCl (0.5 N), 5% $NaHCO_3$, brine and were dried over anhydrous $MgSO_4$. The solvent was concentrated *in vacuo* and the product was purified by flash column chromatography (100% hexanes to 10% EtOAc/hexanes) to afford silyl ether **4.17** as a yellow oil (1.988 g, 9.1 % over 2 steps). Spectral data: Curran, T. T.; Hay, D. A.; Koegel, C. P.; Evans, J. C. *Tetrahedron*, **1997**, *53*, 1983



4-(tert-Butyl-dimethyl-silanyloxy)-2-iodo-cyclopent-2-enone (4.18)

Iodine (12.997 mmol, 3.2986 g) dissolved in 1:1 Et_2O/pyridine (11.8 mL) was added dropwise, under an atmosphere of argon, to a solution of enone **4.17** (10.8 mmol, 2.30 g) in 1:1 Et_2O/pyridine (40.0 mL) at 0°C. The mixture was stirred for 1.5 hours at room temperature. The mixture was diluted with Et_2O and washed successively with H_2O, 1 N HCl (2x), H_2O, 20% aqueous $Na_2S_2O_3$ and the organic layer was dried over anhydrous $MgSO_4$. After concentration, the crude vinyl iodide **4.18** a yellow oil, (3.23 g, 88%) was used without further purification.

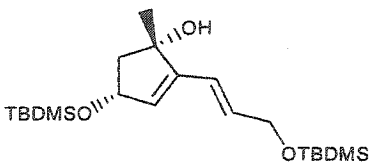
5.10 General procedure I for the Suzuki Coupling Reaction



4-(tert-Butyl-dimethyl-silanyloxy)-2-[3-(tert-butyl-dimethyl-silanyloxy)-propenyl]-cyclopent-2-enone (4.20)

To a dry 50 mL round bottom flask with a magnetic stirrer were placed $PdCl_2(PPh_3)_2$ (502.8 mg, 0.7164 mmol) and NaOAc (881.3 mg, 10.75 mmol). The flask was flushed with N_2 and charged with dry methanol (20.0 mL), boronic ester **4.19** (2.292g, 7.881

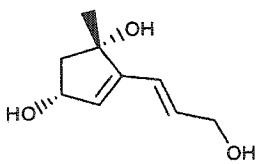
mmol) and vinyl iodide **4.18** (2.423g, 7.164 mmol). The reaction mixture was refluxed for 1 hour. The solution was cooled to room temperature and the boronate ester was oxidized by addition of 3 M NaOH (aq) (3 mL) and 30% hydrogen peroxide (3 mL). The aqueous layer was extracted with benzene (3x) and the combined organic layer was washed with a saturated solution of brine. The organic layer was dried over $MgSO_4$, concentrated and flash column chromatography (100% hexanes to 5% EtOAc/hexanes) generated diene **4.20** as a yellow oil (1.159 g, 42.3%). ^{1}H NMR (300 MHz, $CDCl_3$) δ_{ppm} 7.13 (d, J = 2.5 Hz, 1H), 6.80 (dt, J = 15.9, 4.3 Hz, 1H), 6.27 (d, J = 15.9 Hz, 1H), 4.90-4.88 (m, 1H), 4.27-4.26 (m, 2H), 2.78 (dd, J = 18.3, 6.0 Hz, 1H), 2.33 (dd, J = 18.3, 2.3 Hz, 1H), 0.90 (s, 9H), 0.89 (s, 9H), 0.10 (d, J = 3.8 Hz, 6H), 0.05 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 204.7 (C_4), 156.6 (CH), 140.6 (C_4), 136.2 (CH), 117.8 (CH), 68.5 (CH), 63.3 (CH_2), 46.6 (CH_2), 25.9 ($3xCH_3$), 25.8 ($3xCH_3$), 18.4 (C_4), 18.1 (C_4), -4.7 ($2xCH_3$), -5.3 ($2xCH_3$). IR (neat, cm^{-1}) 2955 (m), 2930 (m), 2893 (w), 2856 (m), 1717 (s), 1471 (w), 1255 (m), 1073 (m), 833 (s). HRMS (EI) *m/z* (M^+ - [C_4H_9]) calcd 325.1655 found 325.1640.



4-(tert-Butyl-dimethyl-silanyloxy)-2-[3-(tert-butyl-dimethyl-silanyloxy)-propenyl]-1-methyl-cyclopent-2-enol (4.21)

To a 10 mL flame-dried round bottom flask was canulated the ketone **4.20** (48.3 mg, 0.126 mmol) in THF (1.3 mL). The solution was cooled to -78 °C and methyllithium was added dropwise. The reaction mixture was stirred for 2 hours and was quenched with H_2O at 0°C. The aqueous layer was extracted with EtOAc (3x) and the combined organic

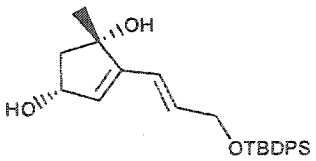
layers were dried over anhydrous $MgSO_4$. The product was purified by flash column chromatography (100% hexanes to 5% EtOAc/hexanes) to afford alcohol **4.21** (15.0 mg, 46%) as a yellow oil. ^1H NMR (300 MHz, $CDCl_3$) δ_{ppm} 6.29 (dt, J = 16.1, 3.9 Hz, 1H), 6.17 (d, J = 16.3 Hz, 1H), 5.66 (s, 1H), 4.61 (bs, 1H), 4.24 (d, J = 3.7 Hz, 2H), 2.44 (dd, J = 13.2, 6.7 Hz, 1H), 1.84-1.79 (m, 2H), 1.35 (s, 3H), 0.88 (d, J = 6.9 Hz, 18 H), 0.06 (s, 12H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 147.6 (C_4), 132.8 (CH), 131.2 (CH), 121.6 (CH), 80.9 (C_4), 72.9 (CH), 63.8 (CH_2), 53.4 (CH_2), 26.1 (CH_3), 25.9 ($3xCH_3$), 25. ($3xCH_3$), 18.4 (C_4), 18.2 (C_4), -4.6 ($2xCH_3$), -5.2 ($2xCH_3$). IR (neat, cm^{-1}) 3422 (w), 2956 (s), 2930 (s), 2886 (m), 2857 (m), 1472 (m), 1463 (w), 1361 (m), 1256 (m), 1125 (m), 1075 (s), 836 (s). HRMS (EI) *m/z* (M^+ - [C_4H_9]) calcd 341.1968 found 341.1926.



5-(3-Hydroxy-propenyl)-1-methyl-cyclopent-4-ene-1,3-diol (4.22)

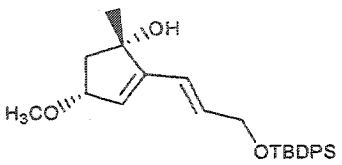
To a solution of diene **4.21** (0.2761 mmol, 110.1 mg) in THF (2.8 mL) was added TBAF (0.97 mmol, 0.97 mL). The solution was stirred for 2.5 hours, concentrated *in vacuo* and purified by flash column chromatography (10% MeOH in EtOAc) to afford triol **4.22** as a colorless oil (45.3 mg, 96%). ^1H NMR (300 MHz, acetone-d_6) δ_{ppm} 6.39 (dt, J = 16.1, 5.2 Hz, 1H), 6.17 (d, J = 16.1 Hz, 1H), 5.64 (d, J = 1.7 Hz, 1H), 4.53 (t, J = 6.4 Hz, 1H), 4.11 (d, J = 7.1 Hz, 2H), 3.89 (bs, 2H), 2.93 (bs, 1H), 2.42 (dd, J = 12.7, 7.0 Hz, 1H), 1.81 (dd, J = 10.9, 4.4 Hz, 1H), 1.28 (s, 3H). ^{13}C NMR (75 MHz, acetone-d_6) δ_{ppm} 148.5 (C_4), 133.5 (CH), 131.4 (CH), 122.8 (CH), 80.3 (C_4), 72.2 (CH), 63.1 (CH_2), 53.6 (CH_2), 27.3 (CH_3). IR (neat, cm^{-1}) 3313 (s), 2967 (w), 2937 (w), 2864 (w), 1668 (w), 1608 (w), 1425 (w), 1371 (m), 1331 (m), 1271 (w), 1205 (w),

1091 (m), 1051 (m), 1018 (m), 972 (m). HRMS (EI) *m/z* (M^+) calcd 170.0943 found 170.0947.



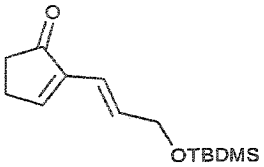
5-[3-(tert-Butyl-diphenyl-silanyloxy)-propenyl]-1-methyl-cyclopent-4-ene-1,3-diol (4.23)

A solution of triol **4.22** (56.5 mg, 0.332 mmol) and triethylamine (0.06 mL, 0.4 mmol) in THF (3.3 mL) was treated with DMAP (1.6 mg, 0.013 mmol). The solution was cooled to 0°C and was treated protionwise with TBDPSCl (92.2 mg, 0.335 mmol). The resulting mixture was stirred at room temperature overnight. A 0.5 N solution of HCl was poured into the reaction mixture. The aqueous phase was extracted with hexanes (3x). The combined organic phase was washed with HCl (0.5 N), 5% $NaHCO_3$ and brine. The organic layer was dried over anhydrous $MgSO_4$, concentrated and purified by flash column chromatography (50% EtOAc in hexanes) to afford diol **4.23** as a colorless oil (63.3 mg, 47%). ^1H NMR (300 MHz, $CDCl_3$) δ_{ppm} 7.66 (d, J = 7.5 Hz, 4H), 7.43-7.33 (m, 6H), 6.28-6.26 (s, 2H), 5.73 (d, J = 1.8 Hz, 1H), 4.59 (bs, 1H), 4.27 (d, J = 2.6 Hz, 2H), 2.74 (bs, 2H), 2.49 (dd, J = 13.9, 7.0 Hz, 1H), 1.85 (dd, J = 13.9, 4.2 Hz, 1H), 1.34 (s, 3H), 1.05 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 148.5 (C_4), 135.5 (4xCH), 133.5 (C_4), 133.5 (C_4), 132.8 (CH), 130.2 (CH), 129.7 (2xCH), 127.6 (4xCH), 121.6 (CH), 81.0 (C_4), 72.7 (CH), 64.4 (CH_2), 52.2 (CH_2), 26.8 ($3xCH_3$), 26.7 (CH_3), 19.2 (C_4). IR (neat, cm^{-1}) 3360 (m), 3072 (w), 3051 (w), 2967 (m), 2929 (m), 2861 (m), 1468 (w), 1428 (m), 1112 (s). HRMS (EI) *m/z* (M^+ - [H_2O + (C_4H_9)]) calcd 333.1311 found 333.1304.



2-[3-(tert-Butyl-diphenyl-silanyloxy)-propenyl]-4-methoxy-1-methyl-cyclopent-2-enol (4.24)

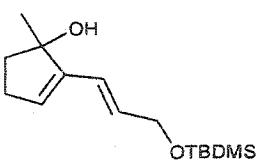
To a solution of NaH (2.7 mg, 0.068 mmol) in THF (0.2 mL) was canulated the diol **4.23** (13.9 mg, 0.0340 mmol) in THF (0.75 mL) at room temperature. The solution immediately turned yellow. Iodomethane (2.3 μL, 0.037 mmol) was added and the solution was stirred at room temperature for 48 hours. The reaction was quenched with saturated NH_4Cl (aq), the aqueous layer was extracted with CH_2Cl_2 (3x) and the combined organic layers were dried over anhydrous $MgSO_4$. After concentration, the product was purified by flash column chromatography (30% EtOAc in hexanes) to generate methyl ether **4.24** as a colorless oil (10.3 mg, 72%) ^{1}H NMR (300 MHz, $CDCl_3$) δ_{ppm} 7.66 (d, J = 6.8 Hz, 4H), 7.43-7.33 (m, 6H), 6.30-6.28 (m, 2H), 5.81 (d, J = 1.9 Hz, 1H), 4.27 (d, J = 2.5 Hz, 2H), 4.21-4.18 (m, 1H), 3.34 (s, 3H), 2.44 (dd, J = 13.5, 6.6 Hz, 1H), 1.88 (dd, J = 13.5, 4.7 Hz, 2H), 1.36 (s, 3H), 1.05 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 149.3 (C_4), 135.5 (4xCH), 133.6 (2xC_4), 132.8 (CH), 129.7 (2xCH), 127.7 (CH), 127.7 (4xCH), 121.5 (CH), 81.1 (CH), 80.8 (C_4), 64.3 (CH_2), 56.3 (CH_3), 49.2 (CH_2), 26.8 (3xCH_3), 26.4 (CH_3), 19.3 (C_4). IR (neat, cm^{-1}) 3430 (w), 3076 (w), 3045 (w), 2963 (m), 2932 (m), 2856 (m), 2822 (w), 1465 (w), 1431 (m), 1355 (m), 1115 (s). HRMS (EI) *m/z* (M^+ - [C_4H_9]) calcd 365.1573 found 365.1569.



2-[3-(tert-Butyl-dimethyl-silanyloxy)-propenyl]-cyclopent-2-enone (4.27)

Prepared using general procedure I

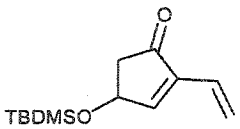
Vinyl iodide **4.26** (2.151g, 10.34 mmol), boronate ester **4.19** (3.3015 g, 11.375 mmol), $PdCl_2(PPh_3)_2$ (363.0 mg, 0.5170 mmol) and sodium acetate (1.272 g, 15.51 mmol). The product was purified by flash column chromatography (20% EtOAc in hexanes) to generate diene **4.27** (390.1 mg, 19%) as colorless crystals. ^{1}H NMR (300 MHz, $CDCl_3$) δ_{ppm} 7.43 (dd, J = 2.9, 2.5 Hz, 1H), 6.76 (dt, J = 15.9, 4.5 Hz, 1H), 6.29 (d, J = 15.9 Hz, 1H), 4.26 (d, J = 4.4 Hz, 2H), 2.63-2.55 (m, 2H), 2.46-2.43 (m, 2H), 0.89 (s, 9H), 0.06 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 208.3 (C_4), 158.4 (CH), 140.5 (C_4), 133.7 (CH), 118.6 (C_4), 63.5 (CH_2), 35.7 (CH_2), 26.3 (CH_2), 25.9 (3xCH_3), 18.4 (C_4), -5.3 (2xCH_3). IR (neat, cm^{-1}) 2954 (m), 2928 (m), 2896 (w), 2858 (m), 1706 (s), 1465 (w), 1347 (m), 1257 (m), 1087 (m), 984 (m), 840 (s), 775 (s). HRMS (EI) *m/z* (M^+ - [C_4H_9]) calcd 195.0841 found 195.0855. mp = 50.8-52.3 °C.



2-[3-(tert-Butyl-dimethyl-silanyloxy)-propenyl]-1-methyl-cyclopent-2-enol (4.28)

To a solution of ketone **4.27** (0.9124 mmol, 230.3 mg) in THF (9.1 mL) cooled at -78°C was added methyllithium (2.28 mmol, 1.42 mL). The reaction was stirred for 3 hours and monitered by TLC. The reaction was quenched at 0°C with water and the aqueous layer was extracted with EtOAc (3x). The combined organic layers were dried over anhydrous $MgSO_4$ and concentrated. Two purifications by flash chromatography (20% EtOAc in hexanes) afforded alcohol **4.28** as a yellow oil (60.5 mg, 25%). ^{1}H NMR (300 MHz, $CDCl_3$) δ_{ppm} 6.18 (s, 2H), 5.72 (t, J = 2.7 Hz, 1H), 4.22 (d,

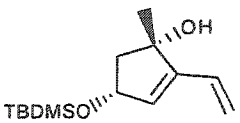
1.3 Hz, 2H), 2.46-2.31 (m, 1H), 2.28-2.16 (m, 1H), 2.13-2.05 (m, 1H), 2.02-1.88 (m, 1H), 1.61 (s, 1H), 1.40 (s, 3H), 0.89 (s, 9H), 0.06 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 145.9 (C_4), 130.1 (CH), 129.7 (CH), 122.6 (CH), 83.3 (C_4), 64.0 (CH_2), 42.6 (CH_2), 28.6 (CH_2), 25.9 ($3xCH_3$), 25.8 (CH_3), 18.4 (C_4), -5.2 ($2xCH_3$). IR (neat, cm^{-1}) 3378 (w), 2957 (m), 2929 (m), 2860 (m), 1476 (m), 1371 (w), 1250 (m), 1114 (m). HRMS (EI) *m/z* (M^+ - [H_2O]) calcd 250.1753 found 250.1759.



4-(tert-Butyl-dimethyl-silanyloxy)-2-vinyl-cyclopent-2-enone (4.30)

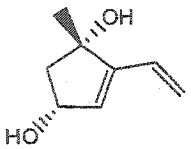
THF (20.0 mL) was degassed with one balloon of argon and was added to a 250 mL flask containing flame-dried $ZnBr_2$ (4.300 g, 19.10 mmol). Vinylmagnesium bromide (21.95 mL, 19.10 mmol) was added at -78°C and the mixture was warmed up to room temperature (21°C) over 1 hour. To the resulting white solution was canulated the iodoenone **4.18** (3.23 g, 9.55 mmol) and $Pd(PPh_3)_4$ (331.0 mg, 0.2865 mmol) in DMF (80.0 mL) degassed with argon. The orange solution was stirred for 1 hour, quenched with saturated NH_4Cl (aq), extracted with 1:1 hexanes/ether. The organic layer was washed with H_2O (2x) and the aqueous layer was extracted once again with 1:1 hexanes/ether. The combined organic layer was dried over anhydrous $MgSO_4$, concentrated and the product was purified by flash column chromatography (100% hexanes to 5% EtOAc/hexanes) to afford diene **4.30** as a colorless oil (1.5402 g, 56% over 2 steps). ^1H NMR (300 MHz, $CDCl_3$) δ_{ppm} 7.19 (d, J = 2.6 Hz, 1H), 6.34 (dd, J = 17.8, 11.2 Hz, 1H), 6.11 (dd, J = 17.8, 1.5 Hz, 1H), 5.38 (dd, J = 11.2, 1.6 Hz, 1H), 4.91-4.87 (m, 1H), 2.78 (dd, J = 18.3, 6.1 Hz, 1H), 2.32 (dd, J = 18.3, 2.3 Hz, 1H), 0.88 (s, 9H), 0.09 (d, J = 3.9 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 204.4 (C_4), 157.1 (CH),

141.2 (C_4), 126.0 (CH), 121.1 (CH_2), 68.5 (CH), 46.4 (CH_2), 25.7 ($3xCH_3$), 18.1 (C_4), -4.7 ($2xCH_3$). IR (neat, cm^{-1}) 2957 (m), 2930 (m), 2893 (w), 2859 (m), 1723 (s), 1472 (w), 1348 (m), 1253 (m), 1077 (s), 834 (s). HRMS (EI) *m/z* (M^+) calcd 238.1389 found 238.1379.



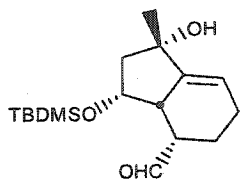
4-(tert-Butyl-dimethyl-silanyloxy)-1-methyl-2-vinyl-cyclopent-2-enol (4.31)

To a 10 mL flame-dried round bottom flask was canulated ketone **4.30** (0.226 mmol, 53.9 mg) in THF (3.0 mL). The solution was cooled to -78 °C and methyllithium (0.90 mmol, 0.57 mL) was added dropwise. The reaction mixture was stirred for 2 hours and was quenched with H_2O at 0°C. The aqueous layer was extracted with EtOAc (3x) and the combined organic layers were dried over anhydrous $MgSO_4$. The product was purified by flash column chromatography (20% EtOAc in hexanes) basified with triethylamine to afford diene **4.31** as a colorless oil (30.3 mg, 53%, dr = 9:1). ^1H NMR (300 MHz, $CDCl_3$) δ_{ppm} 6.28 (dd, J = 17.9, 11.3 Hz, 1H), 5.73-5.67 (m, 2H), 5.21 (dd, J = 16.3, 1.8 Hz, 1H), 4.64-4.59 (m, 1H), 2.45 (dd, J = 13.2, 6.7 Hz, 1H), 1.99 (s, 1H), 1.84 (dd, J = 13.3, 5.0 Hz, 1H), 1.36 (s, 3H), 0.87 (s, 9H), 0.06 (d, J = 0.8 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 148.3 (C_4), 131.8 (CH), 129.5 (CH), 117.8 (CH_2), 80.8 (C_4), 72.9 (CH), 53.3 (CH_2), 26.1 (CH_3), 25.9 ($3xCH_3$), 18.2 (C_4), -4.7 ($2xCH_3$). IR (neat, cm^{-1}) 3409 (w), 2962 (s), 2935 (s), 2897 (w), 2859 (m), 1468 (w), 1358 (m), 1255 (m), 1083 (s), 833 (s). HRMS (EI) *m/z* (M^+- H_2O) calcd 236.1597 found 236.1564.



1-Methyl-5-vinyl-cyclopent-4-ene-1,3-diol (4.32)

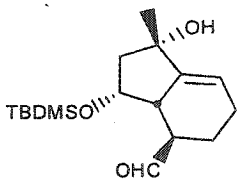
To a solution of diene **4.31** (0.119 mmol, 30.3 mg) in THF (0.5 mL) was added TBAF (0.18 mmol, 0.18 mL). The solution was stirred for 2.5 hours, concentrated *in vacuo* and purified by flash column chromatography (100% EtOAc) to afford diol **4.32** as colorless crystals (13.0 mg, 78%). ^{1}H NMR (300 MHz, acetone-d_6) δ_{ppm} 6.30 (dd, J = 17.9, 11.2 Hz, 1H), 5.78-5.70 (m, 1H), 5.70 (d, J = 1.9 Hz, 1H), 5.13 (dd, J = 11.3, 2.3 Hz, 1H), 4.54 (dd, J = 12.2, 6.1 Hz, 1H), 3.93-3.89 (m, 1H), 2.92 (s, 1H), 2.42 (dd, J = 12.7, 6.7 Hz, 1H), 1.82 (ddd, J = 12.7, 6.3, 0.8 Hz, 1H), 1.29 (s, 3H). ^{13}C NMR (75 MHz, acetone-d_6) δ_{ppm} 149.0 (C_4), 132.5 (CH), 131.0 (CH), 116.9 (CH_2), 80.3 (C_4), 72.2 (CH), 53.6 (CH_2), 27.2 (CH_3). IR (neat, cm^{-1}) 3338 (m), 2957 (w), 2928 (w), 2860 (w), 1439 (m), 1261 (m), 1055 (s). HRMS (EI) *m/z* (M^+) calcd 140.0837 found 140.0857. m.p. 102.5-104.1°C.



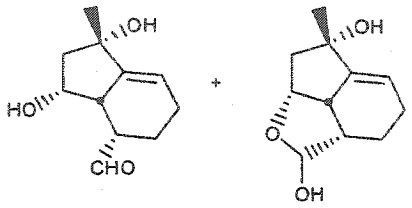
3-(tert-Butyl-dimethyl-silanyloxy)-1-hydroxy-1-methyl-2,3,3a,4,5,6-hexahydro-1H-indene-4-carbaldehyde (4.34a)

To a solution of $MgBr_2 \cdot Et_2O$ (6.9564 mmol, 1.7964 g) in CH_2Cl_2 (10.0 mL) at room temperature (21°C) was added 2,6-lutidine (11.6 mmol, 1.35 mL) under an atmosphere of argon. The white heterogeneous solution was stirred for 30 minutes. Diene **4.31** (2.319 mmol, 590.0 mg) in CH_2Cl_2 (12.0 mL) was subsequently canulated into the reaction mixture and was stirred for an additional 30 minutes. Acrolein (12 mmol, 0.78 mL) was added and the solution was stirred overnight. The solution was quenched with saturated NH_4Cl (aq), extracted with CH_2Cl_2 (3x), dried over anhydrous $MgSO_4$ and concentrated under vacuum. Purification by flash column

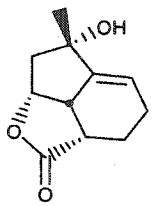
chromatography (20% EtOAc in hexanes) afforded the desired aldehyde **4.34a** and epimer **4.34b** (9:1) as colorless crystals (509.0 mg, 71 %) and as a colorless oil (50.5 mg, 7%) respectively. **4.34a** : ^{1}H NMR (300 MHz, $CDCl_3$) δ_{ppm} 9.78 (d, J = 5.2 Hz, 1H), 5.99 (dd, J = 6.6, 3.3 Hz, 1H), 4.36 (t, J = 3.6 Hz, 1H), 2.95 (s, 1H), 2.71-2.63 (m, 2H), 2.22-2.14 (m, 2H), 2.02-1.96 (m, 1H), 1.97 (dd, J = 14.0, 1.3 Hz, 1H), 1.90-1.81 (m, 1H), 1.82 (dd, J = 14.0, 3.5 Hz, 1H), 1.38 (s, 3H), 0.83 (s, 9H), 0.04 (d, J = 14.1 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 205.6 (CH), 147.4 (C_4), 121.0 (CH), 77.0 (C_4), 74.6 (CH), 49.4 (CH_2), 48.9 (CH), 45.8 (CH), 26.4 (CH_2), 25.9 (CH_3), 25.8 (3xCH_3), 21.9 (CH_2), 17.9 (C_4), -4.9 (CH_3), -5.4 (CH_3). IR ($CHCl_3$, cm^{-1}) 3481 (w), 2952 (m), 2931 (s), 2851 (m), 1713 (s), 1472 (m), 1360 (m), 1255 (m). HRMS (EI) *m/z* (M^+- [C_4H_9]) calcd 253.1260 found 253.1278. mp = 68.6-69.0 °C.



4.34b: ^{1}H NMR (300 MHz, $CDCl_3$) δ_{ppm} 6.69 (d, J = 1.7 Hz, 1H), 5.93 (dd, J = 6.7, 3.1 Hz, 1H), 4.25 (t, J = 3.4 Hz, 1H), 2.86 (bs, 1H), 2.60-2.45 (m, 1H), 2.45-2.15 (m, 3H), 2.04-1.89 (m, 2H), 1.76 (dd, J = 13.9, 3.0 Hz, 1H), 1.33 (s, 3H), 0.85 (s, 9H), 0.06 (d, J = 6.6 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 203.9 (CH), 150.3 (C_4), 119.4 (CH), 76.6 (C_4), 74.4 (CH), 49.5 (CH_2), 46.8 (CH), 46.6 (CH), 26.3 (CH_3), 25.8 (3xCH_3), 24.7 (CH_2), 23.7 (CH_2), 18.1 (C_4), -4.8 (CH_3), -5.0 (CH_3). IR (neat, cm^{-1}) 2957 (m), 2927 (s), 2860 (m), 2714 (w), 1727 (s), 1475 (m), 1258 (m), 1115 (m), 1031 (m). HRMS (EI) *m/z* (M^+- [C_4H_9 + H_2O]) calcd 235.1155 found 235.1139.



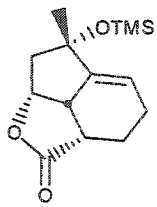
1,3-Dihydroxy-1-methyl-2,3,3a,4,5,6-hexahydro-1H-indene-4-carbaldehyde (4.35) and **4-Methyl-1,2a,3,4,6,7,7a,7b-octahydro-2-oxa-cyclopenta-[cd]indene-1,4-diol (4.36)** To a solution of silyl ether **4.34** (0.0725 mmol, 22.5 mg) in THF (1.0 mL) was added TBAF (0.11 mmol, 0.11 mL). The solution was stirred for 2.5 hours, concentrated *in vacuo* and purified by flash column chromatography (5% MeOH in EtOAc) to afford aldehyde **4.35** and lactol **4.36** as a colorless oil (13.1 mg, 92%). The mixture of products was used without full characterization towards the next step.



4-Hydroxy-4-methyl-3,4,6,7,7a,7b-hexahydro-2aH-2-oxa-cyclopenta[cd]inden-1-one (4.37)

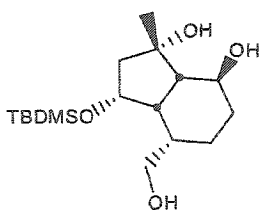
To a solution of aldehyde **4.35** and lactol **4.36** (0.223 mmol, 43.7 mg) in CH_2Cl_2 (4.0 mL) was added 4Å MS (111.4 mg), NMO (0.341 mmol, 39.9 mg) and TPAP (0.011 mmol, 3.9 mg) respectively. The dark green solution was stirred for 3 hours, filtered through a pad of silica and the latter was washed with 5% MeOH in EtOAc. The organic solvent was evaporated *in vacuo* and the product was purified by flash column chromatography (80% EtOAc in hexanes) to generate lactone **4.37** as a colorless oil (31.5 mg, 73%). ^{1}H NMR (300 MHz, $CDCl_3$) δ_{ppm} 5.88 (bs, 1H), 4.76 (t, J = 5.1 Hz, 1H), 3.07-3.02 (m, 2H), 2.30 (dd, J = 15.7, 6.2 Hz, 1H), 2.15-2.08 (m, 3H), 1.97 (d, J = 15.7 Hz, 1H), 1.98-1.76 (m, 2H), 1.33 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 177.8 (C_4), 143.5 (C_4), 120.4 (CH), 79.8 (CH), 78.8 (C_4), 46.6 (CH_2), 41.1 (CH), 39.0 (CH), 28.6 (CH_3), 20.5 (CH_2), 18.7 (CH_2). IR (neat, cm^{-1}) 3451 (w), 2973 (w), 2929 (w), 2843 (w), 1761

(s), 1440 (w), 1364 (m), 1241 (m), 1156 (m), 1101 (m), 965 (m). HRMS (EI) *m/z* (M^+) calcd 194.0943 found 194.0971.



4-Methyl-4-trimethylsilanyloxy-3,4,6,7,7a,7b-hexahydro-2aH-2-oxa-cyclopenta[cd]inden-1-one (4.38)

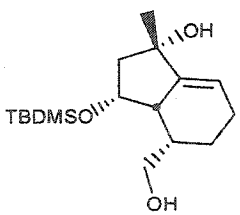
To a solution of alcohol **4.37** (0.132 mmol, 25.6 mg) in THF (5.0 mL) at -78°C under argon was added freshly distilled TMSCl (0.7 mmol, 0.09 mL) and KHMDS (0.461 mmol, 92.0 mg). The solution was stirred at -78°C for 2 hours, warmed to room temperature (21°C) and was quenched with saturated $NaHCO_3$ (aq). The aqueous layer was extracted with dichloromethane (3x) and the combined organic layers were dried over anhydrous $MgSO_4$. The organic solvent was removed *in vacuo* and the product was purified by flash column chromatography (20% EtOAc in hexanes) to yield lactone **4.38** as colorless crystals (33.4 mg, 94%). ^1H NMR (300 MHz, $CDCl_3$) δ_{ppm} 5.79 (s, 1H), 4.77 (t, J = 5.4 Hz, 1H), 3.00 (s, 2H), 2.23 (dd, J = 14.9, 6.6 Hz, 1H), 2.15-2.08 (m, 3H), 1.97 (d, J = 14.9 Hz, 1H), 1.86-1.78 (m, 1H), 1.32 (s, 3H), 0.11 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 117.7 (C_4), 141.8 (C_4), 119.7 (CH), 80.6 (C_4), 79.7 (CH), 46.1 (CH_2), 39.4 (CH), 38.6 (CH), 30.0 (CH_3), 20.4 (CH_2), 19.0 (CH_2), 2.2 (3xCH_3). IR ($CHCl_3$, cm^{-1}) 2958 (m), 2934 (w), 1766 (s), 1446 (w), 1299 (w), 1153 (s), 843 (m). HRMS (EI) *m/z* (M^+) calcd 266.1338 found 266.1318. mp = 48.4-48.0 °C.



3-(tert-Butyl-dimethyl-silanyloxy)-4-hydroxymethyl-1-methyl-octahydro-indene-1,7-diol (4.41)

To a solution of alkene **4.34** (1.691 mmol, 524.6 mg) in THF (16.9 mL) was added BH_3·DMS (4 mmol, 0.4 mL) dropwise during which bubbles were

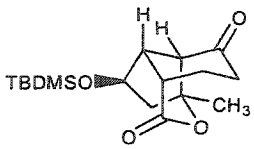
produced in solution. The jelly-like solution was stirred at room temperature (21°C) for 4 hours after which the borane was oxidized with 3N NaOH (1 mL) and 30% H_2O_2 (1 mL). The resulting solution was refluxed overnight and the aqueous layer was extracted with EtOAc (3x). The combined organic layers were dried over anhydrous $MgSO_4$, concentrated *in vacuo* and the product was purified by flash column chromatography (60 % EtOAc in hexanes) to afford triol **4.41** as colorless crystals (455.1 mg, 81%). ^{1}H NMR (300 MHz, $CDCl_3$) δ_{ppm} 4.29 (t, J = 4.1 Hz, 1H), 4.22 (dt, J = 11.1, 4.7 Hz, 1H), 3.67-3.64 (m, 2H), 2.38 (bs, 2H), 2.14-2.09 (m, 1H), 2.01-1.79 (m, 4H), 1.71-1.50 (m, 3H), 1.35 (s, 3H), 1.32-1.21 (m, 2H), 0.87 (s, 9H), 0.05 (d, J = 3.8 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 81.1 (C_4), 74.5 (CH), 70.2 (CH), 65.3 (CH_2), 57.4 (CH), 52.3 (CH), 45.1 (CH), 40.2 (CH), 33.1 (CH_2), 32.2 (CH_3), 25.9 (3xCH_3), 25.0 (CH_2), 17.7 (C_4), -3.9 (CH_3), -4.8 (CH_3). IR ($CHCl_3$, cm^{-1}) 3342 (m), 2961 (m), 2925 (s), 2861 (m), 1466 (m), 1333 (w), 1256 (m), 1099 (m), 1045 (s), 903 (w), 839 (m), 775 (m). HRMS (EI) *m/z* (M^+- [C_4H_9 + 2(H_2O)]) calcd 237.1309 found 237.1333. mp = 163.1-163.8 °C.



3-(tert-Butyl-dimethyl-silanyloxy)-4-hydroxymethyl-1-methyl-2,3,3a,4,5,6-hexahydro-1H-inden-1-ol (4.42)

To a solution of alkene **4.34** (1.654 mmol, 513.1 mg) in THF (16.0 mL) was added BH_3·DMS (1.2406 mmol, 0.22 mL) dropwise during which bubbles were produced in solution. The solution was stirred at room temperature (21°C) for 1 hour after which the borane was oxidized with 3N NaOH (1 mL) and 30% H_2O_2 (1 mL). The resulting solution was refluxed for 1 hour and the aqueous layer was extracted with EtOAc (3x). The combined organic layers were dried over anhydrous $MgSO_4$,

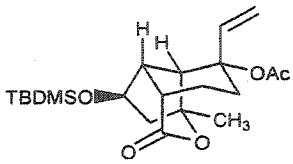
concentrated in vacuo and the product was purified by flash column chromatography (80 % EtOAc in hexanes) to afford alcohol **4.42** as a colorless foam (145.5 mg, 28%) and triol **4.41** as colorless crystals (250.1 mg, 46%). ^{1}H NMR (300 MHz, $CDCl_3$) δ_{ppm} 5.86 (dd, J = 7.0, 3.5 Hz, 1H), 4.40 (dd, J = 8.5, 3.7 Hz, 1H), 3.83 (dd, J = 11.0, 6.9 Hz, 1H), 3.55 (dd, J = 11.0, 6.7 Hz, 1H), 2.61-2.55 (m, 1H), 2.48 (bs, 2H), 2.24-2.11 (m, 1H), 2.10-2.00 (m, 2H), 1.81 (d, J = 1.1 Hz, 2H), 1.80-1.70 (m, 1H), 1.59-1.51 (m, 1H), 1.30 (s, 3H), 0.86 (s, 9H), 0.10 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 147.6 (C_4), 119.9 (CH), 76.3 (C_4), 74.5 (CH), 62.5 (CH_2), 50.0 (CH_2), 47.6 (CH), 37.0 (CH), 26.7 (CH_3), 25.9 (3xCH_3), 25.6 (CH_2), 22.3 (CH_2), 17.9 (C_4), -4.2 (CH_3), -5.0 (CH_3). IR ($CHCl_3$, cm^{-1}) 3401 (m), 2956 (s), 2930 (s), 2861 (s), 1474 (m), 1363 (m), 1249 (m), 1120 (m), 1094 (m), 1029 (s), 835 (s), 774 (s). HRMS (EI) *m/z* (M^+- [C_4H_9 + H_2O]) calcd 237.1311 found 237.1324.



6-(tert-Butyl-dimethyl-silanyloxy)-4-methyl-3-oxa-tricyclo[5.4.0.04,8]undecane-2,9-dione (4.43)

To a solution of triol **4.41** (0.027 mmol, 9.0 mg) in CH_2Cl_2 (2.0 mL) was added 4Å MS (13.6 mg), NMO (0.041 mmol, 5.0 mg) and TPAP (0.001 mmol, 0.5 mg) respectively. The dark green solution was stirred for 3 hours, filtered through a pad of silica and the latter was washed with 5% MeOH in EtOAc. The organic solvent was evaporated *in vacuo* and the product was purified by flash column chromatography (60% EtOAc in hexanes) to generate ketone **4.43** as colorless crystals (6.1 mg, 70%). ^{1}H NMR (300 MHz, $CDCl_3$) δ_{ppm} 4.43 (ddd, J = 9.2, 6.6, 2.8 Hz, 1H), 3.17 (s, 1H), 2.77-2.72 (m, 1H), 2.56 (dd, J = 16.3, 5.6 Hz, 1H), 2.43 (d, J = 4.8 Hz, 1H), 2.40-2.22 (m, 2H), 2.12 (dd, J =

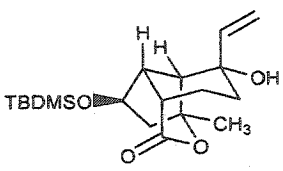
14.7, 9.1 Hz, 1H), 2.00 (dd, J = 14.7, 2.7 Hz, 1H), 1.95-1.88 (m, 1H), 1.34 (s, 3H), 0.85 (s, 9H), 0.03 (s, 6H). ^{13}C NMR (75 MHz, C_6D_6) δ_{ppm} 206.0 (C_4), 170.7 (C_4), 87.5 (C_4), 80.0 (CH), 57.5 (CH), 48.7 (CH_2), 47.4 (CH), 37.9 (CH_2), 37.5 (CH_2), 27.9 (CH_2), 25.8 (3xCH_3), 22.0 (CH_3), 18.1 (C_4), -4.8 (CH_3), -5.1 (CH_3). IR ($CHCl_3$, cm^{-1}) 2960 (m), 2935 (m), 2858 (w), 1747 (s), 1708 (m), 1466 (m), 1228 (m), 1094 (s). HRMS (EI) *m/z* (M^+-[C_4H_9]) calcd 267.1053 found 267.1048. mp = 104.8-105.4 °C.



Acetic acid 6-(tert-butyl-dimethyl-silanyloxy)-4-methyl-2-oxo-9-vinyl-3-oxa-tricyclo[5.4.0.04,8]undec-9-yl ester (4.45)

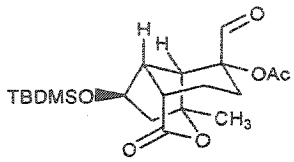
To a solution of ketone **4.43** (32.8 mg, 0.0992 mmol) in THF (4.0 mL) at -78°C was added vinylmagnesium bromide (0.25 mmol, 0.31 mL). The reaction mixture was stirred at -78°C for 30 minutes. Acetic anhydride (0.30 mmol, 30 μL) and triethylamine (0.298 mmol, 41.5 μL) were added and the yellow solution was warmed to room temperature. The reaction was quenched with saturated NH_4Cl (aq), the aqueous phase was extracted with CH_2Cl_2 (3x) and the combined organic phases were dried over anhydrous $MgSO_4$. The organic solvent was removed *in vacuo* and the product was purified by flash column chromatography (20% EtOAc in hexanes) to afford acetate **4.45** as colorless crystals (16.6 mg, 42%) and alcohol **4.44** as colorless crystals (9.0 mg, 26%). ^1H NMR (300 MHz, $CDCl_3$) δ_{ppm} 6.18 (dd, J = 17.6, 10.9 Hz, 1H), 5.33 (d, J = 17.3 Hz, 1H), 5.29 (d, J = 10.7 Hz, 1H), 4.33 (ddd, J = 9.2, 6.6, 2.4 Hz, 1H), 4.01-4.06 (m, 1H), 2.85 (d, J = 2.8 Hz, 1H), 2.54 (d, J = 4.0 Hz, 1H), 2.38-2.33 (m, 1H), 2.30-2.25 (m, 1H), 2.19-2.07 (m, 1H), 2.03 (d, J = 6.4 Hz, 1H), 1.99-1.96 (m, 3H), 1.85 (dd, J = 14.9, 2.2 Hz, 1H), 1.68-1.58 (m, 1H), 1.47 (s, 3H), 0.84 (s, 9H), -2.6 (s, 6H). ^{13}C NMR

(75 MHz, $CDCl_3$) δ_{ppm} 173.6 (C_4), 169.9 (C_4), 140.3 (CH), 116.3 (CH_2), 88.3 (C_4), 82.0 (C_4), 69.3 (CH), 51.0 (CH_2), 46.9 (CH), 45.5 (CH), 37.8 (CH), 31.1 (CH_2), 26.8 (CH), 25.7 (3xCH_3), 22.4 (CH_3), 22.2 (CH_3), 17.9 (C_4), -4.8 (CH_3), -5.1 (CH_3). IR ($CHCl_3$, cm^{-1}) 2952 (m), 2929 (s), 2891 (m), 2853 (m), 1739 (s), 1492 (m), 1375 (m), 1249 (s), 1219 (s), 1166 (m), 1112 (s), 975 (s), 835 (s), 774 (m). HRMS (EI) *m/z* (M^+) calcd 394.2176 found 394.2208. mp = 141.5-142.5 °C.



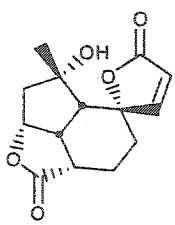
6-(tert-Butyl-dimethyl-silanyloxy)-9-hydroxy-4-methyl-9-vinyl-3-oxa-tricyclo[5.4.0.04,8]undecan-2-one (4.44)

^1H NMR (300 MHz, $CDCl_3$) δ_{ppm} 6.13 (dd, J = 17.3, 10.8 Hz, 1H), 5.33 (d, J = 17.4 Hz, 1H), 5.15 (d, J = 10.8 Hz, 1H), 4.33 (ddd, J = 9.2, 6.5, 2.3 Hz, 1H), 2.89 (d, J = 3.0 Hz, 1H), 2.35 (ddd, J = 7.1, 4.0, 4.0 Hz, 1H), 2.15-2.01 (m, 2H), 1.94 (dd, J = 13.8, 4.8 Hz, 1H), 1.88 (d, J = 2.2 Hz, 1H), 1.83-1.62 (m, 4H), 1.58 (s, 3H), 0.85 (s, 9H), 0.00 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 173.9 (C_4), 143.9 (CH), 113.4 (CH_2), 89.0 (C_4), 73.9 (C_4), 69.7 (CH), 51.1 (CH_2), 50.3 (CH), 45.6 (CH), 37.9 (CH), 32.9 (CH_2), 27.5 (CH_2), 25.7 (3xCH_3), 23.9 (CH_3), 18.0 (C_4), -4.8 (CH_3), -5.1 (CH_3). IR ($CHCl_3$, cm^{-1}) 3431 (w), 2952 (s), 2932 (s), 2888 (m), 2862 (m), 1737 (s), 1720 (s), 1469 (w), 1362 (m), 1248 (s), 1171 (s), 1060 (s), 934 (m), 829 (s). HRMS (EI) *m/z* (M^+ - [C_4H_9]) calcd 295.1366 found 295.1396. mp = 133.2-135.5 °C.



Acetic acid 6-(tert-butyl-dimethyl-silanyloxy)-9-formyl-4-methyl-2-oxo-3-oxa-tricyclo[5.4.0.04,8]undec-9-yl ester (4.46)

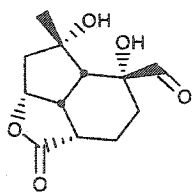
A solution of alkene **4.45** (0.0421 mmol, 16.6 mg) in CH_2Cl_2 (5.0 mL) was degassed with O_2 for 10 minutes at room temperature. The solution was cooled to -78°C and ozone was bubbled into the solution. After 5 minutes, dimethylsulfide (0.21 mmol, 15 μL) was added to the blue solution and the reaction mixture was warmed to room temperature. The solution was concentrated and the product was purified by flash column chromatography (30% EtOAc in hexanes) to yield aldehyde **4.46** as colorless crystals (12.2 mg, 73%). ^{1}H NMR (300 MHz, $CDCl_3$) δ_{ppm} 9.27 (s, 1H), 4.39 (ddd, J = 9.3, 6.6, 2.5 Hz, 1H), 2.92-2.83 (m, 2H), 2.45 (d, J = 4.3 Hz, 1H), 2.15-1.95 (m, 6H), 1.86 (dd, J = 15.1, 2.4 Hz, 1H), 1.67-1.58 (m, 2H), 1.45 (s, 3H), 0.85 (s, 9H), 0.00 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 195.7 (CH), 173.0 (C_4), 170.8 (C_4), 88.6 (C_4), 83.9 (C_4), 69.5 (CH), 50.2 (CH_2), 44.9 (CH), 41.8 (CH), 37.2 (CH), 25.7 (3xCH_3), 25.6 (CH_2), 25.2 (CH_2), 22.7 (CH_3), 20.8 (CH_3), 17.9 (C_4), -4.9 (CH_3), -5.1 (CH_3). IR ($CHCl_3$, cm^{-1}) 2955 (m), 2932 (m), 2888 (w), 2857 (m), 2721 (w), 1740 (s), 1460 (w), 1370 (m), 1290 (w), 1252 (s), 1222 (m), 1169 (m), 1104 (s), 1060 (m), 979 (m), 942 (m), 836 (m), 777 (m). HRMS (EI) *m/z* (M^+ - [TBDMS + H_2O + OAc]) calcd 193.0865 found 193.0880. mp = 113.7-116.1°C.



Tetracyclic Core (4.49)

To a solution of NaH (0.031 mmol, 1.2 mg) in THF (1.0 mL) at 0°C was canulated the aldehyde **4.46** (0.021 mmol, 8.2 mg) in THF (2.0 mL). The solution was gradually warmed to room temperature and was quenched with H_2O. The

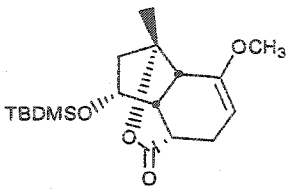
aqueous layer was extracted with EtOAc (3x), the combined organic layers were dried over anhydrous $MgSO_4$ and the solvent was evaporated *in vacuo*. The crude product **4.47** was diluted in THF (2.0 mL) and TBAF (0.030 mmol, 30 μL) was added to the solution. After 1 hour, the reaction mixture was concentrated *in vacuo* and the product was purified by flash column chromatography (60% EtOAc in hexanes) using a Pasteur pipette to afford the tetracyclic core **4.49** (1.3 mg, 24%) as a colorless oil and tricyclic core **4.48** (2.3 mg, 46%) as a colorless oil.. ^{1}H NMR (300 MHz, $CDCl_3$) δ_{ppm} 7.71 (d, J = 5.7 Hz, 1H), 6.90 (d, J = 5.7 Hz, 1H), 5.00 (dd, J = 6.6, 4.9 Hz, 1H), 3.25 (dt, J = 10.5, 6.6 Hz, 1H), 2.90-2.84 (m, 1H), 2.68 (dt, J = 14.2, 4.6 Hz, 1H), 2.49-2.43 (m, 1H), 2.32 (d, J = 10.1 Hz, 1H), 1.94-1.76 (m, 3H), 1.68 (s, 1H), 1.50 (s, 3H), 1.44-1.37 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 176.9 (C_4), 171.1 (C_4), 159.1 (CH), 119.9 (CH), 89.4 (C_4), 81.9 (C_4), 81.6 (C_4), 49.9 (CH_2), 47.7 (CH), 41.6 (CH), 37.2 (CH), 29.6 (CH_3), 28.8 (CH_2), 21.4 (CH_2). IR (neat, cm^{-1}) 3443 (w), 2964 (w), 2930 (w), 2854 (w), 1750 (s), 1466 (w), 1372 (w), 1250 (w), 1182 (w), 1121 (m), 1026 (w), 946 (w), 923 (w). HRMS (EI) *m/z* (M^+ - H_2O) calcd 246.0892 found 246.0892.



4,5-Dihydroxy-4-methyl-1-oxo-decahydro-2-oxa-cyclopenta[cd]indene-5-carbaldehyde (4.48)

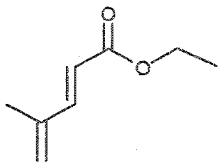
^{1}H NMR (300 MHz, $CDCl_3$) δ_{ppm} 9.51 (s, 1H), 4.95 (t, J = 5.9 Hz, 1H), 3.49 (bs, 1H), 3.22 (dt, J = 10.7, 6.7 Hz, 1H), 2.87-2.80 (m, 1H), 2.30 (d, J = 3.4 Hz, 1H), 2.26 (s, 1H), 2.23-2.15 (m, 1H), 1.96 (dd, J = 15.3, 5.2 Hz, 1H), 1.91-1.84 (m, 1H), 1.81-1.59 (m, 2H), 1.48 (s, 3H), 1.23 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 202.8 (CH), 178.5 (C_4), 82.7 (C_4), 82.5 (CH), 78.2 (C_4), 47.8 (CH_2), 47.5 (CH_2), 41.3 (CH), 37.8

(CH), 30.0 (CH_3), 28.7 (CH_2), 18.7 (CH_2). IR (neat, cm^{-1}) 3443 (m), 2969 (w), 2932 (m), 2869 (w), 1733 (s), 1454 (w), 1373 (m), 1231 (w), 1181 (m), 1112 (m), 1006 (m). HRMS (EI) *m/z* (M^+ - [H_2O + CHO]) calcd 193.0865 found 193.0857.



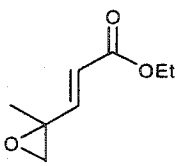
6-(tert-Butyl-dimethyl-silanyloxy)-9-methoxy-4-methyl-3-oxa-tricyclo[5.4.0.04,8]undec-9-en-2-one (4.50)

To a solution of KHMDS (0.115 mmol, 23.0 mg) in THF (1.0 mL) at -78°C was canulated the ketone **4.43** (0.0660 mmol, 21.8 mg) in THF (2.0 mL). The solution became yellow and was stirred at -78° C for 20 minutes. Freshly distilled dimethylsulfate (0.1320 mmol, 12 μL) was added and the reaction was warmed to room temperature over a period of 30 minutes. The orange solution was quenched with H_2O, extracted with CH_2Cl_2 and dried over $MgSO_4$. After concentration, the product was purified by flash column chromatography (20% EtOAc in hexanes) basified with triethylamine to afford methyl enol ether **26** as colorless crystals (17.1 mg, 77%). ^1H NMR (300 MHz, acetone-d_6) δ_{ppm} 4.82 (dd, J = 5.0, 2.3 Hz, 1H), 4.63 (ddd, J = 9.3, 6.7, 2.3 Hz, 1H), 3.53 (s, 3H), 2.95 (bs, 1H), 2.52-2.47 (m, 1H), 2.38-2.26 (m, 4H), 3.65 (dd, J = 14.7, 2.2 Hz, 1H), 1.30 (s, 3H), 0.88 (s, 9H), 0.06 (d, J = 1.3 Hz, 6H). ^{13}C NMR (75 MHz, acetone-d_6) δ_{ppm} 173.5 (C_4), 153.6 (C_4), 94.7 (CH), 88.8 (C_4), 71.2 (CH), 54.6 (CH), 49.6 (CH_2), 47.1 (CH), 44.7 (CH), 38.1 (CH), 30.1 (CH_2), 26.1 (3xCH_3), 22.7 (CH_3), 18.6 (C_4), -4.8 (CH_3), -5.0 (CH_3). IR ($CHCl_3$, cm^{-1}) 2957 (m), 2934 (s), 2900 (m), 2855 (m), 1736 (s), 1664 (m), 1470 (w), 1387 (m), 1252 (m), 1151 (s), 1091 (m), 1039 (s), 837 (s), 777 (m). HRMS (EI) *m/z* (M^+ - [C_4H_9]) calcd 281.1209 found 281.1201. mp = 127.5-129.2°C.



4-Methyl-penta-2,4-dienoic acid ethyl ester (4.52)

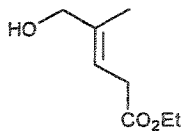
A solution of triethylphosphonoacetate (29 mmol, 5.7 mL) in THF (200 mL) was cooled to -78°C. *n*-BuLi (37.1 mmol, 12.0 mL) was added dropwise and the solution was stirred for 15 minutes, during which the solution became light orange. Methacrolein **4.51** (28.5 mmol, 2.36 mL) was added dropwise and the solution became light green. The reaction mixture was stirred for 2 hours, quenched with saturated NH_4Cl (aq) and the aqueous layer was extracted with Et_2O (3x). The organic layer was dried over anhydrous $MgSO_4$ and the product was purified by flash column chromatography (10% EtOAc in hexanes) to generate a colorless oil (2.81 g, 70%). Spectral data: Kover, B. W.; de Souza, N. A. *J. Org. Chem.* **1980**, *45*, 4225.



3-(2-Methyl-oxiranyl)-acrylic acid ethyl ester (4.53)

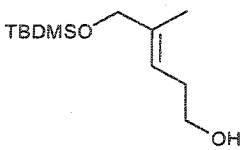
To a solution of MCPBA (24.0548 mmol, 5.3911 g) in ether (32.0 mL) at 0°C was added dropwise alkene **4.52** (20.0457 mmol, 2.81 g) in EtOAc (43.0 mL). The solution was stirred and warmed gradually to room temperature during 24 hours. The reaction was quenched with sodium sulfite (80.18 mmol, 10.11 g), the aqueous layer was extracted with Et_2O (3x) and the combined organic layers were washed with 10% Na_2CO_3 (3x). The organic solvent was removed *in vacuo* and the product was purified by flash column chromatography (20% EtOAc in hexanes) to yield epoxide **4.53** as a yellow oil (1.64 g, 52%). ^1H NMR (300 MHz, $CDCl_3$) δ_{ppm} 6.68 (d, J = 15.8 hz, 1H), 6.04 (d, J = 15.8 Hz, 1H), 4.18 (q, J = 7.1 Hz, 2H), 2.88 (d, J = 5.3 Hz, 1H), 2.78 (d, J = 5.3 Hz, 1H), 1.48 (s, 3H), 1.27 (t, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 165.8 (C_4), 148.3 (CH), 122.6 (CH), 60.5 (CH_2), 55.9 (CH_2), 54.7 (C_4), 18.9 (CH_3), 14.1 (CH_3). IR (neat, cm^{-1}) 2986 (s), 2937 (m), 1724 (s), 1660 (m), 1450 (m),

1368 (s), 1304 (s), 1267 (s), 1222 (s), 1181 (s), 1038 (s). HRMS (EI) *m/z* (M^+) calcd 156.0786 found 156.0746.



5-Hydroxy-4-methyl-pent-3-enoic acid ethyl ester (4.54)

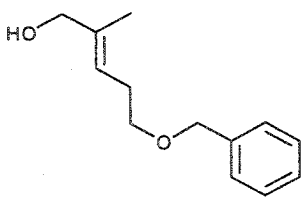
To a solution of epoxide **4.53** (1.28 mmol, 0.200 g), HMPA (1.28 mL) and DMAE (2.6 mmol, 0.26 mL) was added SmI_2-THF (2.74 mmol, 27.4 mL) at room temperature. Every drop of blue samarium iodide disappeared upon contact with the solution, which in turn became yellow. The reaction mixture was stirred overnight and became brown. The solution was quenched with saturated $NaHCO_3$ (aq) and the aqueous layer was extracted with EtOAc (3x). The combined organic layers were dried over anhydrous $MgSO_4$, concentrated and the product was purified by flash column chromatography (40% EtOAc in hexanes) to afford alcohol **4.54** as a colorless oil (100.0 mg, 49%). ^1H NMR (300 MHz, $CDCl_3$) δ_{ppm} 5.61 (t, J = 7.3 Hz, 1H), 4.12 (q, J = 7.4 Hz, 2H), 4.03 (s, 2H), 3.07 (d, J = 7.1 Hz, 2H), 1.67 (s, 3H), 1.51 (bs, 1H), 1.25 (t, J = 7.1 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 172.0 (C_4), 138.4 (C_4), 117.1 (CH), 68.3 (CH_2), 60.7 (CH_2), 33.3 (CH_2), 14.2 (CH_3), 13.9 (CH_3). IR (neat, cm^{-1}) 3375 (s), 2922 (w), 2850 (w), 1733 (s), 1622 (m), 1444 (m), 1155 (s). HRMS (EI) *m/z* (M^+-[H_2O + CH_2CH_3]) calcd 111.0446 found 111.0432.



5-(tert-Butyl-dimethyl-silanyloxy)-4-methyl-pent-3-en-1-ol (4.57)

To a solution of alcohol **4.54** (0.120 mmol, 18.9 mg) in THF (1.0 mL) was added imidazole (0.359 mmol, 24.4 mg). The solution was stirred for 5 minutes and TBDMSCl (0.143 mmol, 21.6 mg) was added and the reaction mixture was stirred for 1 hour. The reaction was quenched with saturated NH_4Cl (aq) and the aqueous layer

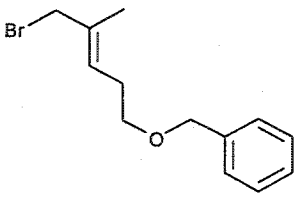
was extracted with ether (3x). The combined organic layers were dried over anhydrous $MgSO_4$, concentrated and the resulting ester **4.56** (colorless oil) was used without further purification. To a solution ester **4.56** (0.120 mmol, 32.5 mg) in THF (1.5 mL) at -78°C was added DIBAL-H (0.36 mmol, 0.24 mL). The solution was stirred at 0°C for 30 minutes, quenched with a 1:1 solution of 1M NaOH and 1M sodium tartrate (2.0 mL) and was stirred overnight. The aqueous layer was extracted with EtOAc (3x), the combined organic layers were dried over anhydrous $MgSO_4$ and concentrated in vacuo. The product was purified by flash column chromatography (40% EtOAc in hexanes) to afford alcohol **4.57** as a colorless oil (13.8 mg, 50% over 2 steps). ^{1}H NMR (300 MHz, $CDCl_3$) δ_{ppm} 5.39 (t, J = 7.2 Hz, 1H), 4.01 (s, 2H), 3.63 (t, J = 6.5 Hz, 2H), 2.31 (q, J = 6.9 Hz, 2H), 1.61 (s, 3H), 1.48 (bs, 1H), 0.89 (s, 9H), 0.05 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 137.9 (C_4), 119.6 (CH), 68.3 (CH_2), 62.4 (CH_2), 31.1 (CH_2), 25.9 (3xCH_3), 18.4 (C_4), 13.6 (CH_3), -5.3 (2xCH_3). IR (neat, cm^{-1}) 3367 (w), 2956 (m), 2930 (m), 2892 (m), 2861 (m), 1466 (w), 1257 (m), 1109 (m), 1063 (s), 839 (s), 774 (m). HRMS (EI) *m/z* (M^+-[C_4H_9]) calcd 173.0998 found 173.1010.



5-Benzyloxy-2-methyl-pent-2-en-1-ol (4.59)

To a solution of NaH (1.30 mmol, 51.4 mg) in THF (1.0 mL) was canulated the alcohol **4.57** (0.300 mmol, 69.1 mg) in THF (2.0 mL). Benzylbromide (0.60 mmol, 70 μL) and NaI (cat.) were added and the solution was stirred at room temperature overnight. The reaction was quenched with saturated NH_4Cl (aq) and the aqueous layer was extracted with CH_2Cl_2. The organic layer was dried over anhydrous $MgSO_4$, concentrated and the silyl ether **4.58** (yellow oil) was used in the next reaction without further purification. The silyl ether **4.58** (0.300 mmol, 96.2

mg) was diluted in THF (3.0 mL) and TBAF (0.75 mmol, 0.75 mL) was added to the solution. After 1 hour, the solution was concentrated and the product was purified by flash column chromatography (50% EtOAc in hexanes) to yield alcohol **4.59** as a colorless oil (60.0 mg, 97% over 2 steps). ^{1}H NMR (300 MHz, $CDCl_3$) δ_{ppm} 7.36-7.26 (m, 5H), 5.43 (t, J = 7.1 Hz, 1H), 4.50 (s, 2H), 3.99 (s, 2H), 3.47 (t, J = 6.9 Hz, 2H), 2.36 (q, J = 6.8 Hz, 2H), 1.66 (s, 3H), 1.46 (bs, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 138.4 (C_4), 136.7 (C_4), 128.4 (2xCH), 127.7 (2xCH), 127.6 (CH), 122.0 (CH), 72.9 (CH_2), 69.7 (CH_2), 68.7 (CH), 28.3 (CH_2), 13.8 (CH_3). IR (neat, cm^{-1}) 3389 (m), 3066 (w), 3032 (w), 2922 (m), 2865 (s), 1493 (w), 1458 (w), 1360 (w), 1097 (s), 1002 (m), 732 (s), 691 (s). HRMS (EI) *m/z* (M^+) calcd 206.1307 found 206.1280.



(5-Bromo-4-methyl-pent-3-enyloxymethyl)-benzene (4.60)

To a solution of carbon tetrabromide (0.0891 mmol, 29.6 mg) in CH_2Cl_2 (0.5 mL) was canulated the alcohol **4.59** (0.0713 mmol, 14.7 mg) in CH_2Cl_2 (1.0 mL). The solution was stirred for 5 minutes and triphenylphosphine (0.107 mmol, 28.0 mg) in CH_2Cl_2 (0.5 mL) was canulated into the solution. The reaction mixture was stirred for 4 hours and hexanes were added to precipitate the triphenylphosphine oxide from solution. The product was filtered through celite (3x), concentrated and purified by flash column chromatography (20% EtOAc in hexanes) to yield allyl bromide **4.60** as a colorless oil (17.3 mg, 90%). ^{1}H NMR (300 MHz, $CDCl_3$) δ_{ppm} 7.36-7.26 (m, 5H), 5.63 (t, J = 7.1 Hz, 1H), 4.50 (s, 2H), 3.96 (s, 2H), 3.47 (t, J = 6.8 Hz, 2H), 2.34 (q, J = 6.9 Hz, 2H), 1.76 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_{ppm} 137.7 (C_4), 133.8 (C_4), 128.4 (2xCH), 127.6 (2xCH), 127.6 (CH), 127.5

(CH), 72.9 (CH_2), 69.1 (CH_2), 41.4 (CH_2), 29.0 (CH_2), 14.8 (CH_3). IR (neat, cm^{-1}) 3033 (w), 2956 (m), 2930 (m), 2861 (m), 1726 (w), 1605 (w), 1496 (w), 1451 (m), 1100 (s). HRMS (EI) *m/z* (M^+-Br) calcd 189.1279 found 189.1259.

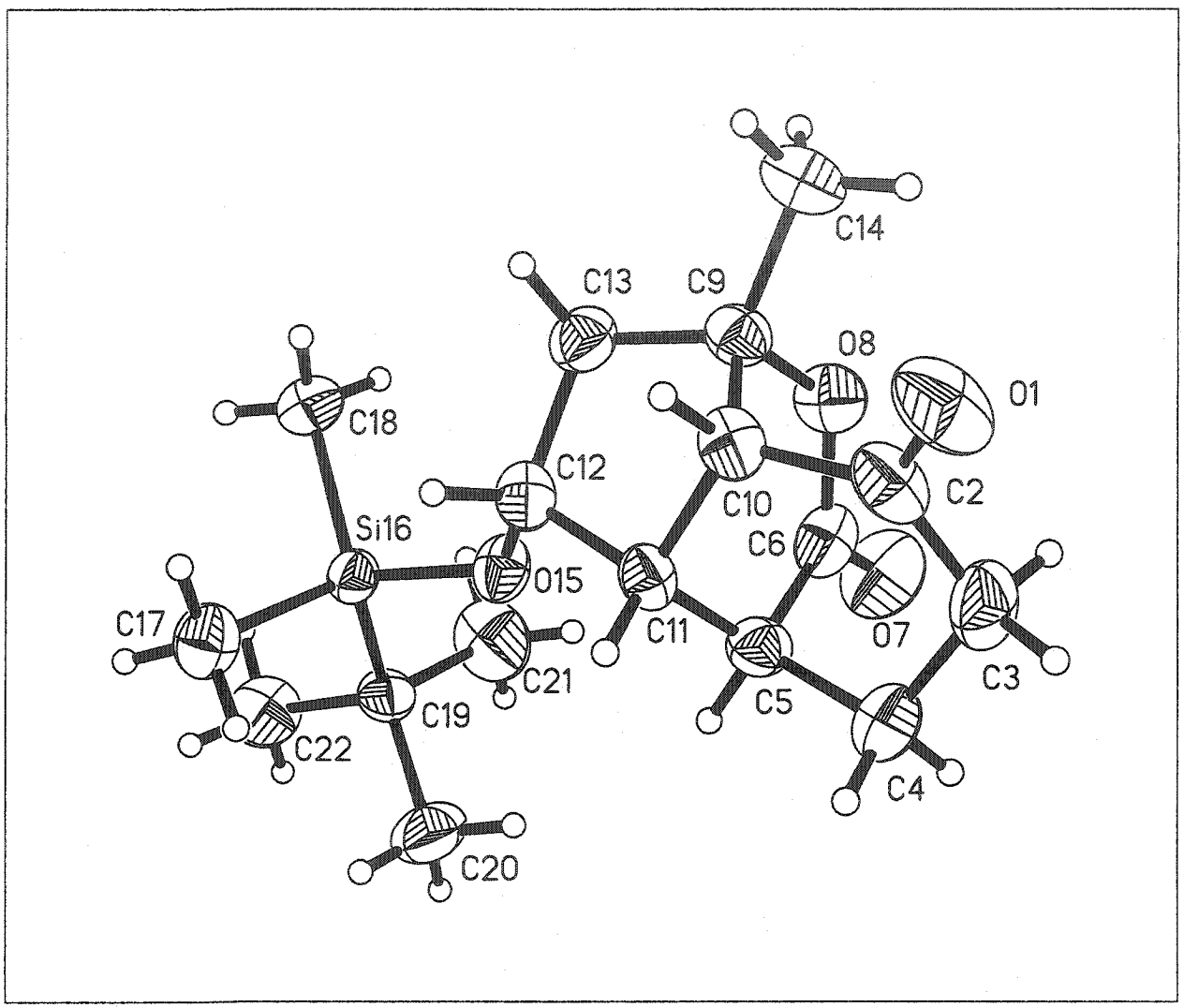
CLAIMS TO ORIGINAL RESEARCH

1. Studied the scope and limitations of the tandem oxy-Cope/ene/Claisen reaction applied towards allyl and propargyl ethers. By isolating a dimer, proved that a 1,3-radical shift competes with the Claisen reaction.
2. Studied the hydroxy-directed Diels-Alder reaction reaction with 5-membered semicyclic dienes and applied the methodology towards the construction of the isovelleral hydrindane core.
3. Applied the highly regio- and stereoselective hydroxy-directed Diels-Alder reaction towards the synthesis of the tetracyclic core of havellockate.
4. Publication : J. Farand, L. Barriault and I. Denissova, "Microwave Assisted Pericyclic Reactions in Cascade to Construct Decalin Frameworks Possesing Quaternary Center. Scope and Limitations", *Heterocycles* **2004**, *62*, 735.
5. Oral presentations : 1) "Studies on the Tandem Oxy-Cope/Ene/Claisen Reaction" J. Farand, I. Denissova and L. Barriault. May 2002. University of Ottawa. Ottawa, Ontario. Canada. 2) "Applications of the Hydroxy-Directed Diels-Alder Reaction Towards the Total Synthesis of Havellockate and the Synthesis of Isovelleral Analogues" J. Farand and L. Barriault. December 5, 2003. Québec-Ontario Minisymposium in Synthetic and Bio-organic Chemistry (QOMSBOC). Université du Québec à Montréal (UQAM). Montréal, Québec. Canada. 3) "Studies on the Tandem Oxy-Cope/Ene/Claisen Reaction. Applications of the Hydroxy-Directed Diels-Alder Towards the Total Synthesis of Havellockate and the Synthesis of Isovelleral Analogues." J. Farand, I. Denissova and L. Barriault.

(i) January 22, 2004. Boehringer-Ingelheim. Laval, Québec. Canada. (ii) January 29, 2004. Merck-Frosst. Kirkland, Québec. Canada. (iii) February 3, 2004. MethylGene. St-Laurent, Québec. Canada.

6. Poster Presentations : 1) "Studies Towards the Total Synthesis of Isovelleral and Analogues" J. Farand and L. Barriault. i) August 2003, IUPAC, Ottawa, Canada. ii) May 2003, Ottawa-Carleton Chemical Institute Symposium (OCCI), Ottawa, Canada iii) May 2003, Organic Synthesis Day, Ottawa, Canada. 2) "Etudes sur les reactions péricycliques en cascades" J. Farand, I. Denissova and L. Barriault. October 2002. 14e Colloque annuel de chimie des étudiantes et étudiants de l'Université de Sherbrooke. Sherbrooke, Québec. Canada.

SPECTRA


C14
C13
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O8
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C12
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C3
C5
C19
C22
C4
C20

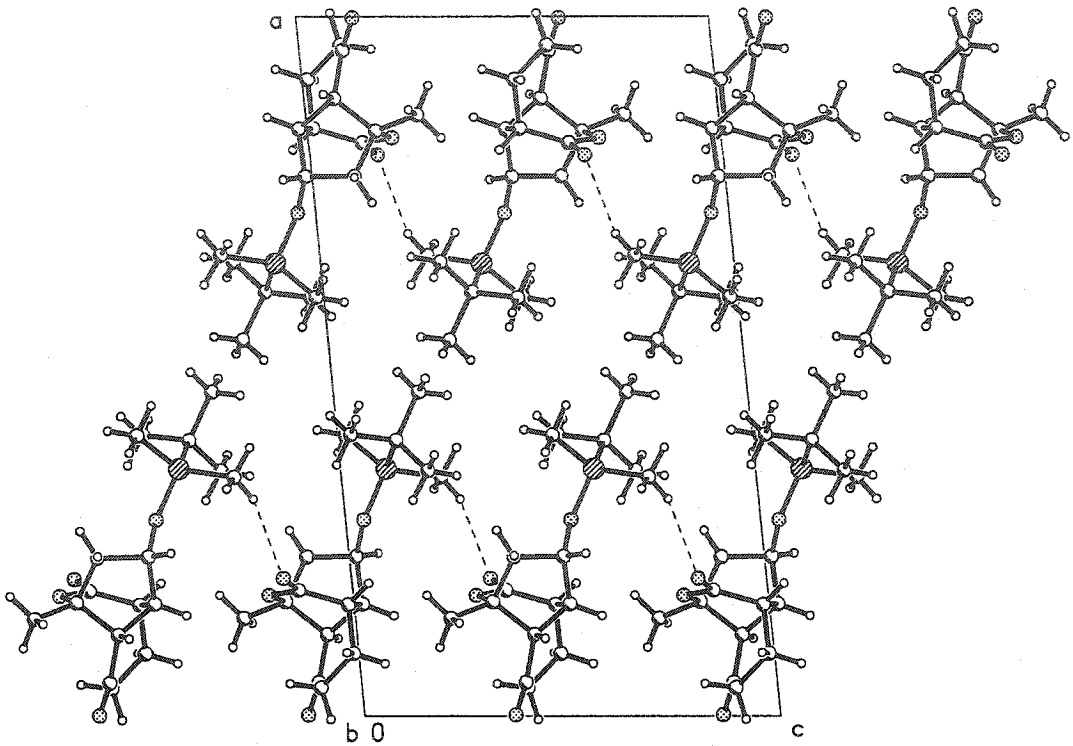

a
b 0
c

Table 1. Crystal data and structure refinement for lb404.

Identification code	lb404	
Empirical formula	C17 H28 O4 Si	
Formula weight	324.48	
Temperature	205(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/c	
Unit cell dimensions	a = 20.267(4) Å	α= 90°.
	b = 7.4833(14) Å	β= 95.913(4)°.
	c = 12.041(2) Å	γ = 90°.
Volume	1816.4(6) $Å^3$	
Z	4	
Density (calculated)	1.187 Mg/m^3	
Absorption coefficient	0.144 mm^{-1}	
F(000)	704	
Crystal size	0.40 x 0.22 x 0.18 mm^3	
Theta range for data collection	1.01 to 25.68°.	
Index ranges	-24<=h<=22, -8<=k<=9, -14<=l<=10	
Reflections collected	9671	
Independent reflections	3452 [R(int) = 0.0789]	
Completeness to theta = 25.68°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.0 and 0.835	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3452 / 0 / 206	
Goodness-of-fit on F^2	1.055	
Final R indices [I>2sigma(I)]	R1 = 0.0767, wR2 = 0.1391	
R indices (all data)	R1 = 0.1426, wR2 = 0.1555	
Largest diff. peak and hole	0.286 and -0.295 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for lb404. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	18(1)	4408(4)	-1355(2)	63(1)
C(2)	480(2)	5389(6)	-1036(3)	44(1)
C(3)	405(2)	7370(6)	-994(3)	52(1)
C(4)	894(2)	8302(5)	-127(3)	49(1)
C(5)	1593(2)	7530(5)	-142(3)	37(1)
C(6)	1797(2)	7828(5)	-1299(3)	40(1)
O(7)	1970(1)	9247(4)	-1645(2)	63(1)
O(8)	1725(1)	6436(3)	-2033(2)	42(1)
C(9)	1632(2)	4597(5)	-1646(3)	36(1)
C(10)	1163(2)	4596(5)	-717(3)	37(1)
C(11)	1600(2)	5586(5)	205(3)	32(1)
C(12)	2283(2)	4687(5)	168(3)	34(1)
C(13)	2277(2)	3948(5)	-1028(3)	42(1)
C(14)	1395(2)	3567(6)	-2693(3)	54(1)
O(15)	2806(1)	5944(3)	435(2)	36(1)
Si(16)	3536(1)	5436(1)	1102(1)	29(1)
C(17)	3419(2)	4170(5)	2399(3)	46(1)
C(18)	4018(2)	4045(5)	190(3)	48(1)
C(19)	3942(2)	7659(5)	1412(3)	34(1)
C(20)	3512(2)	8796(6)	2108(4)	59(1)
C(21)	4025(2)	8641(6)	318(3)	67(1)
C(22)	4629(2)	7403(5)	2065(3)	55(1)

Table 3. Bond lengths [Å] and angles [°] for lb404.

O(1)-C(2)	1.220(4)
C(2)-C(3)	1.492(6)
C(2)-C(10)	1.518(5)
C(3)-C(4)	1.531(5)
C(4)-C(5)	1.530(5)
C(5)-C(6)	1.510(5)
C(5)-C(11)	1.513(5)
C(6)-O(7)	1.206(4)
C(6)-O(8)	1.364(4)
O(8)-C(9)	1.471(4)
C(9)-C(14)	1.513(5)
C(9)-C(13)	1.515(5)
C(9)-C(10)	1.542(5)
C(10)-C(11)	1.538(5)
C(11)-C(12)	1.543(5)
C(12)-O(15)	1.428(4)
C(12)-C(13)	1.542(5)
O(15)-Si(16)	1.654(2)
Si(16)-C(18)	1.861(4)
Si(16)-C(17)	1.863(4)
Si(16)-C(19)	1.877(4)
C(19)-C(20)	1.529(5)
C(19)-C(21)	1.533(5)
C(19)-C(22)	1.538(5)

O(1)-C(2)-C(3)	122.1(4)
O(1)-C(2)-C(10)	119.6(4)
C(3)-C(2)-C(10)	118.2(3)
C(2)-C(3)-C(4)	114.5(3)
C(5)-C(4)-C(3)	110.8(3)
C(6)-C(5)-C(11)	113.6(3)
C(6)-C(5)-C(4)	107.3(3)
C(11)-C(5)-C(4)	110.0(3)
O(7)-C(6)-O(8)	117.7(4)

O(7)-C(6)-C(5)	124.5(4)
O(8)-C(6)-C(5)	117.6(3)
C(6)-O(8)-C(9)	121.2(3)
O(8)-C(9)-C(14)	104.7(3)
O(8)-C(9)-C(13)	108.9(3)
C(14)-C(9)-C(13)	115.4(3)
O(8)-C(9)-C(10)	109.8(3)
C(14)-C(9)-C(10)	115.9(3)
C(13)-C(9)-C(10)	102.0(3)
C(2)-C(10)-C(11)	115.9(3)
C(2)-C(10)-C(9)	115.5(3)
C(11)-C(10)-C(9)	99.8(3)
C(5)-C(11)-C(10)	106.0(3)
C(5)-C(11)-C(12)	113.3(3)
C(10)-C(11)-C(12)	102.8(3)
O(15)-C(12)-C(13)	112.4(3)
O(15)-C(12)-C(11)	110.7(3)
C(13)-C(12)-C(11)	105.2(3)
C(9)-C(13)-C(12)	105.5(3)
C(12)-O(15)-Si(16)	124.3(2)
O(15)-Si(16)-C(18)	109.88(15)
O(15)-Si(16)-C(17)	109.84(14)
C(18)-Si(16)-C(17)	109.29(18)
O(15)-Si(16)-C(19)	104.21(14)
C(18)-Si(16)-C(19)	111.54(17)
C(17)-Si(16)-C(19)	111.98(17)
C(20)-C(19)-C(21)	108.8(3)
C(20)-C(19)-C(22)	109.1(3)
C(21)-C(19)-C(22)	109.0(3)
C(20)-C(19)-Si(16)	109.8(3)
C(21)-C(19)-Si(16)	109.8(2)
C(22)-C(19)-Si(16)	110.3(2)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for lb404. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	36(2)	94(3)	56(2)	-14(2)	-3(1)	-21(2)
C(2)	35(2)	66(3)	32(2)	0(2)	3(2)	-8(2)
C(3)	30(2)	65(3)	58(3)	5(2)	2(2)	10(2)
C(4)	39(2)	51(3)	56(3)	0(2)	4(2)	11(2)
C(5)	33(2)	40(2)	37(2)	-8(2)	1(2)	-1(2)
C(6)	30(2)	33(3)	57(3)	4(2)	3(2)	-2(2)
O(7)	68(2)	37(2)	85(2)	14(2)	17(2)	-12(2)
O(8)	49(2)	40(2)	38(2)	5(1)	12(1)	-6(1)
C(9)	37(2)	35(2)	35(2)	-3(2)	1(2)	-6(2)
C(10)	37(2)	36(2)	38(2)	4(2)	1(2)	-7(2)
C(11)	29(2)	39(2)	27(2)	4(2)	2(2)	0(2)
C(12)	32(2)	29(2)	41(2)	3(2)	-4(2)	-7(2)
C(13)	43(2)	33(2)	48(3)	-2(2)	3(2)	1(2)
C(14)	62(3)	60(3)	39(3)	-12(2)	0(2)	-7(2)
O(15)	33(1)	30(2)	45(2)	4(1)	-1(1)	-2(1)
Si(16)	27(1)	29(1)	32(1)	0(1)	1(1)	3(1)
C(17)	47(2)	43(3)	48(3)	9(2)	5(2)	2(2)
C(18)	53(3)	45(3)	48(3)	-9(2)	5(2)	12(2)
C(19)	37(2)	30(2)	34(2)	-5(2)	0(2)	-5(2)
C(20)	60(3)	46(3)	69(3)	-22(2)	-2(2)	10(2)
C(21)	87(4)	50(3)	64(3)	13(2)	4(3)	-20(3)
C(22)	44(3)	49(3)	68(3)	-11(2)	-8(2)	-12(2)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for lb404.

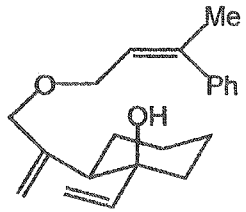
	x	y	z	U(eq)
H(3A)	-47	7649	-830	62
H(3B)	461	7860	-1732	62
H(4A)	902	9585	-289	58
H(4B)	748	8147	617	58
H(5A)	1899	8203	400	44
H(10A)	1107	3347	-472	44
H(11A)	1433	5431	943	38
H(12A)	2328	3686	708	41
H(13A)	2657	4401	-1383	50
H(13B)	2293	2639	-1021	50
H(14A)	981	4076	-3028	81
H(14B)	1325	2326	-2504	81
H(14C)	1726	3638	-3218	81
H(17A)	3105	4797	2815	69
H(17B)	3841	4069	2855	69
H(17C)	3251	2986	2204	69
H(18A)	3772	2964	-20	72
H(18B)	4442	3733	590	72
H(18C)	4090	4714	-477	72
H(20A)	3735	9918	2299	88
H(20B)	3439	8159	2786	88
H(20C)	3089	9032	1680	88
H(21A)	4241	9782	483	101
H(21B)	3593	8839	-88	101
H(21C)	4294	7925	-133	101
H(22A)	4823	8562	2256	82
H(22B)	4914	6751	1608	82
H(22C)	4583	6735	2743	82

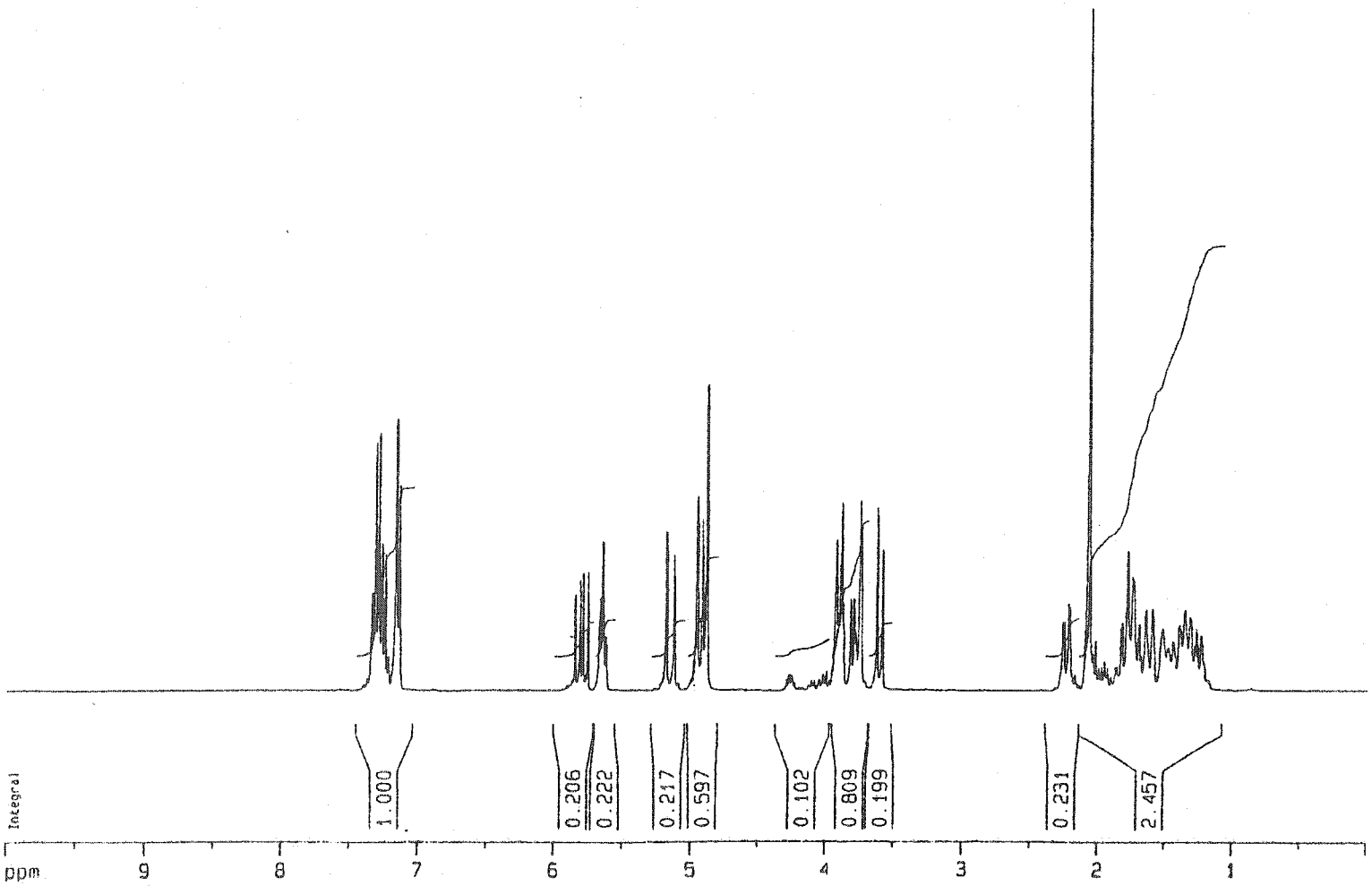
Table 6. Torsion angles [°] for lb404.

O(1)-C(2)-C(3)-C(4)	153.6(3)
C(10)-C(2)-C(3)-C(4)	-29.2(5)
C(2)-C(3)-C(4)-C(5)	43.2(5)
C(3)-C(4)-C(5)-C(6)	60.0(4)
C(3)-C(4)-C(5)-C(11)	-64.0(4)
C(11)-C(5)-C(6)-O(7)	-162.5(3)
C(4)-C(5)-C(6)-O(7)	75.7(5)
C(11)-C(5)-C(6)-O(8)	23.7(4)
C(4)-C(5)-C(6)-O(8)	-98.1(4)
O(7)-C(6)-O(8)-C(9)	169.1(3)
C(5)-C(6)-O(8)-C(9)	-16.7(5)
C(6)-O(8)-C(9)-C(14)	165.6(3)
C(6)-O(8)-C(9)-C(13)	-70.4(4)
C(6)-O(8)-C(9)-C(10)	40.5(4)
O(1)-C(2)-C(10)-C(11)	-148.7(3)
C(3)-C(2)-C(10)-C(11)	34.0(5)
O(1)-C(2)-C(10)-C(9)	95.0(4)
C(3)-C(2)-C(10)-C(9)	-82.3(4)
O(8)-C(9)-C(10)-C(2)	58.1(4)
C(14)-C(9)-C(10)-C(2)	-60.2(5)
C(13)-C(9)-C(10)-C(2)	173.5(3)
O(8)-C(9)-C(10)-C(11)	-66.9(3)
C(14)-C(9)-C(10)-C(11)	174.8(3)
C(13)-C(9)-C(10)-C(11)	48.4(3)
C(6)-C(5)-C(11)-C(10)	-54.5(4)
C(4)-C(5)-C(11)-C(10)	65.8(4)
C(6)-C(5)-C(11)-C(12)	57.5(4)
C(4)-C(5)-C(11)-C(12)	177.8(3)
C(2)-C(10)-C(11)-C(5)	-50.6(4)
C(9)-C(10)-C(11)-C(5)	74.2(3)
C(2)-C(10)-C(11)-C(12)	-169.7(3)
C(9)-C(10)-C(11)-C(12)	-44.9(3)
C(5)-C(11)-C(12)-O(15)	32.6(4)
C(10)-C(11)-C(12)-O(15)	146.5(3)

C(5)-C(11)-C(12)-C(13)	-89.0(3)
C(10)-C(11)-C(12)-C(13)	24.9(3)
O(8)-C(9)-C(13)-C(12)	82.7(3)
C(14)-C(9)-C(13)-C(12)	-159.9(3)
C(10)-C(9)-C(13)-C(12)	-33.3(4)
O(15)-C(12)-C(13)-C(9)	-115.2(3)
C(11)-C(12)-C(13)-C(9)	5.3(4)
C(13)-C(12)-O(15)-Si(16)	-95.8(3)
C(11)-C(12)-O(15)-Si(16)	146.9(2)
C(12)-O(15)-Si(16)-C(18)	69.6(3)
C(12)-O(15)-Si(16)-C(17)	-50.6(3)
C(12)-O(15)-Si(16)-C(19)	-170.7(2)
O(15)-Si(16)-C(19)-C(20)	58.4(3)
C(18)-Si(16)-C(19)-C(20)	176.9(3)
C(17)-Si(16)-C(19)-C(20)	-60.3(3)
O(15)-Si(16)-C(19)-C(21)	-61.3(3)
C(18)-Si(16)-C(19)-C(21)	57.2(3)
C(17)-Si(16)-C(19)-C(21)	-179.9(3)
O(15)-Si(16)-C(19)-C(22)	178.6(2)
C(18)-Si(16)-C(19)-C(22)	-62.9(3)
C(17)-Si(16)-C(19)-C(22)	60.0(3)

Symmetry transformations used to generate equivalent atoms:





Current Data Parameters

NAME	jaf-33
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20020121
Time	10.18
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 ==========

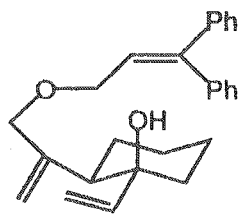
NUC1	1H
P1	11.00 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

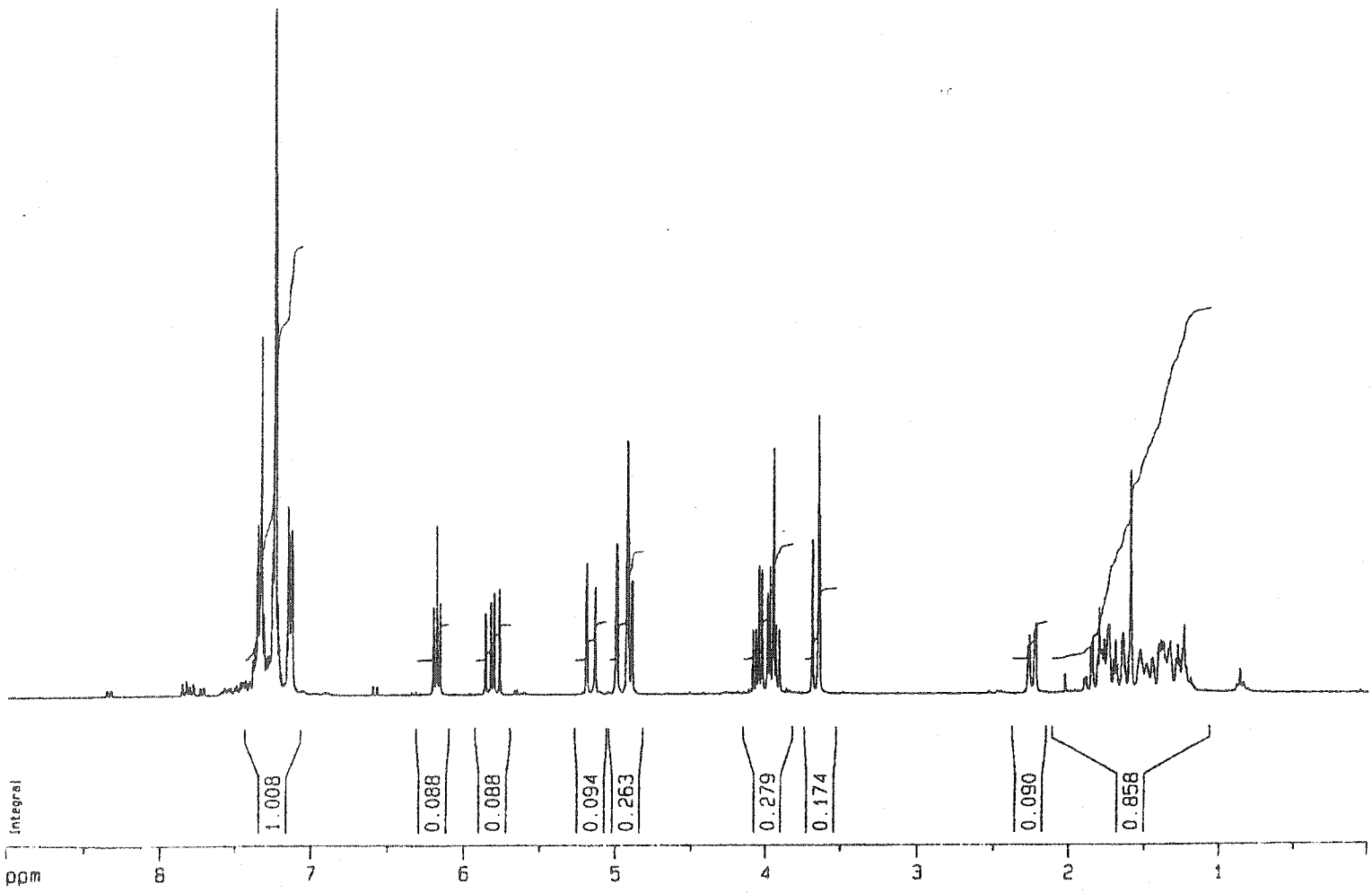
F2 - Processing parameters

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

1D NMR plot parameters

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





Current Data Parameters

NAME	jaf-51
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20020610
Time	18.26
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	256
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

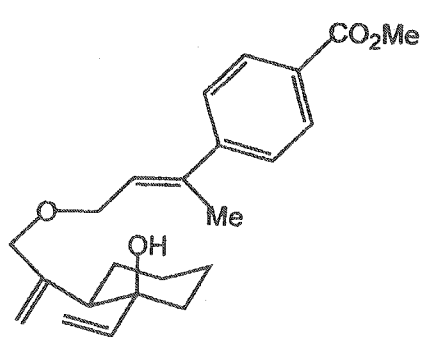
NUC1	1H
P1	20.00 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

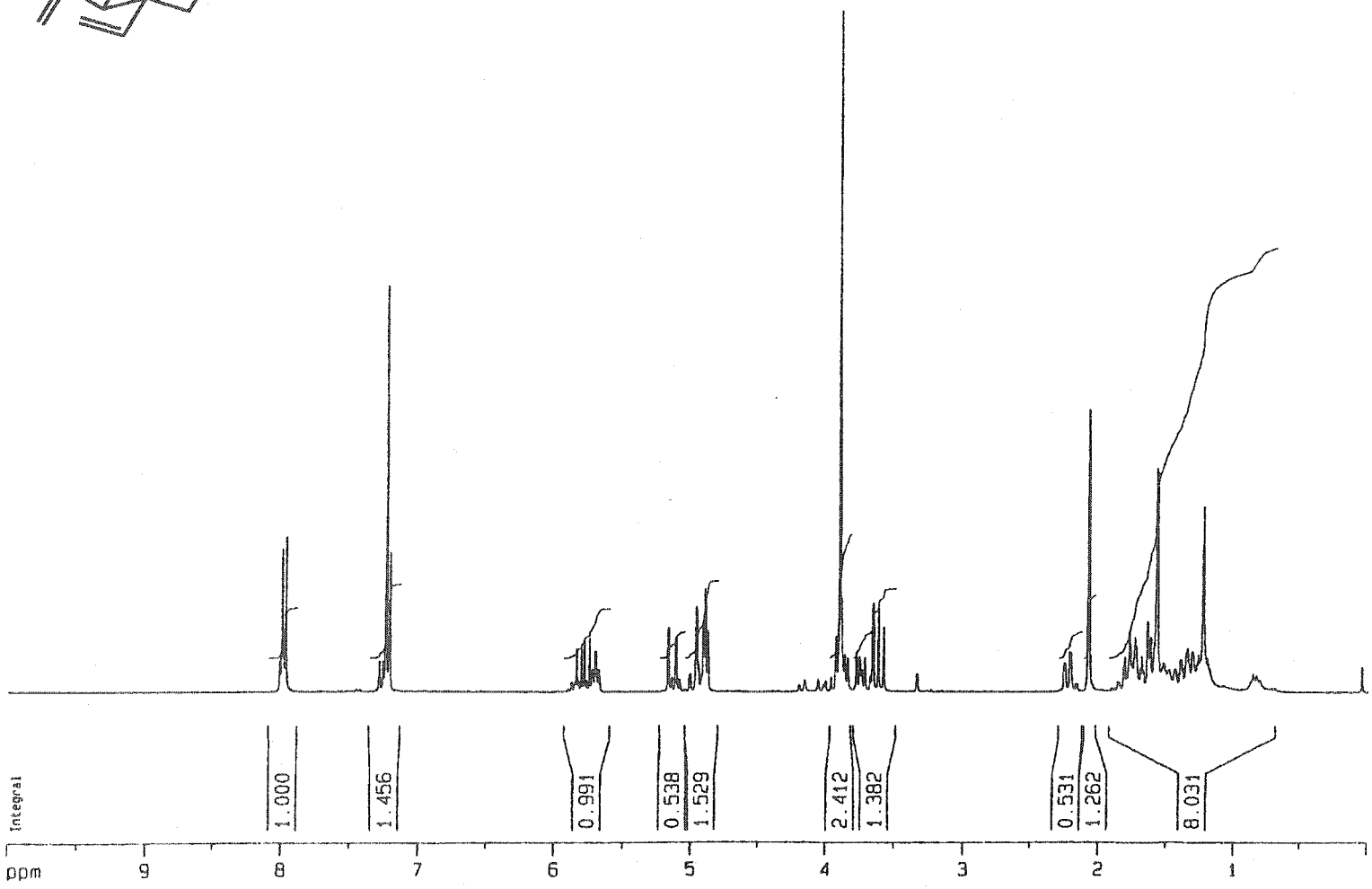
F2 - Processing parameters

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

1D NMR plot parameters

CX	20.00 cm
CY	10.00 cm
F1P	9.000 ppm
F1	2701.17 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	0.45000 ppm/cm
HZCM	135.05850 Hz/cm





Current Data Parameters

NAME	jaf-82
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20020722
Time	22.24
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	456.1
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

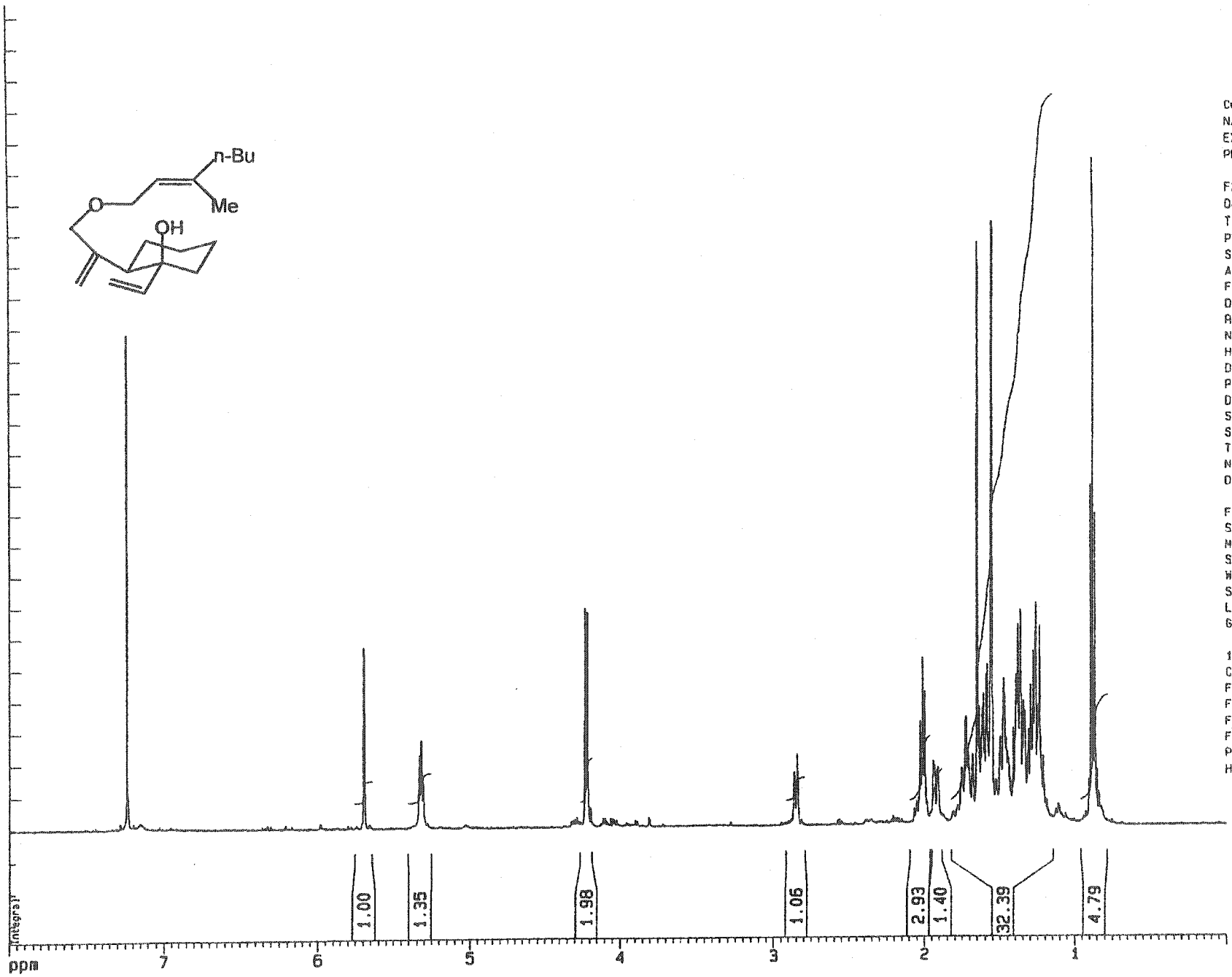
NUC1	1H
P1	8.00 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

F2 - Processing parameters

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

1D NMR plot parameters

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



Current Data Parameters

NAME	jaf-183
EXPNO	1
PROCNO	1

F2 - Acquisition Paramet

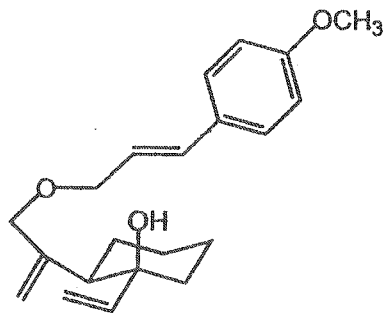
Date	20021016
Time	13.02
PULPROG	zg
SOLVENT	CDCl3
AQ	4.6530805
FIDRES	0.107456
DW	71.0
RG	2048
NUCLEUS	1H
HL1	0
D1	0.0100000
P1	3.3
DE	98.8
SFO1	500.1381707
SWH	7042.25
TD	65536
NS	16
DS	0

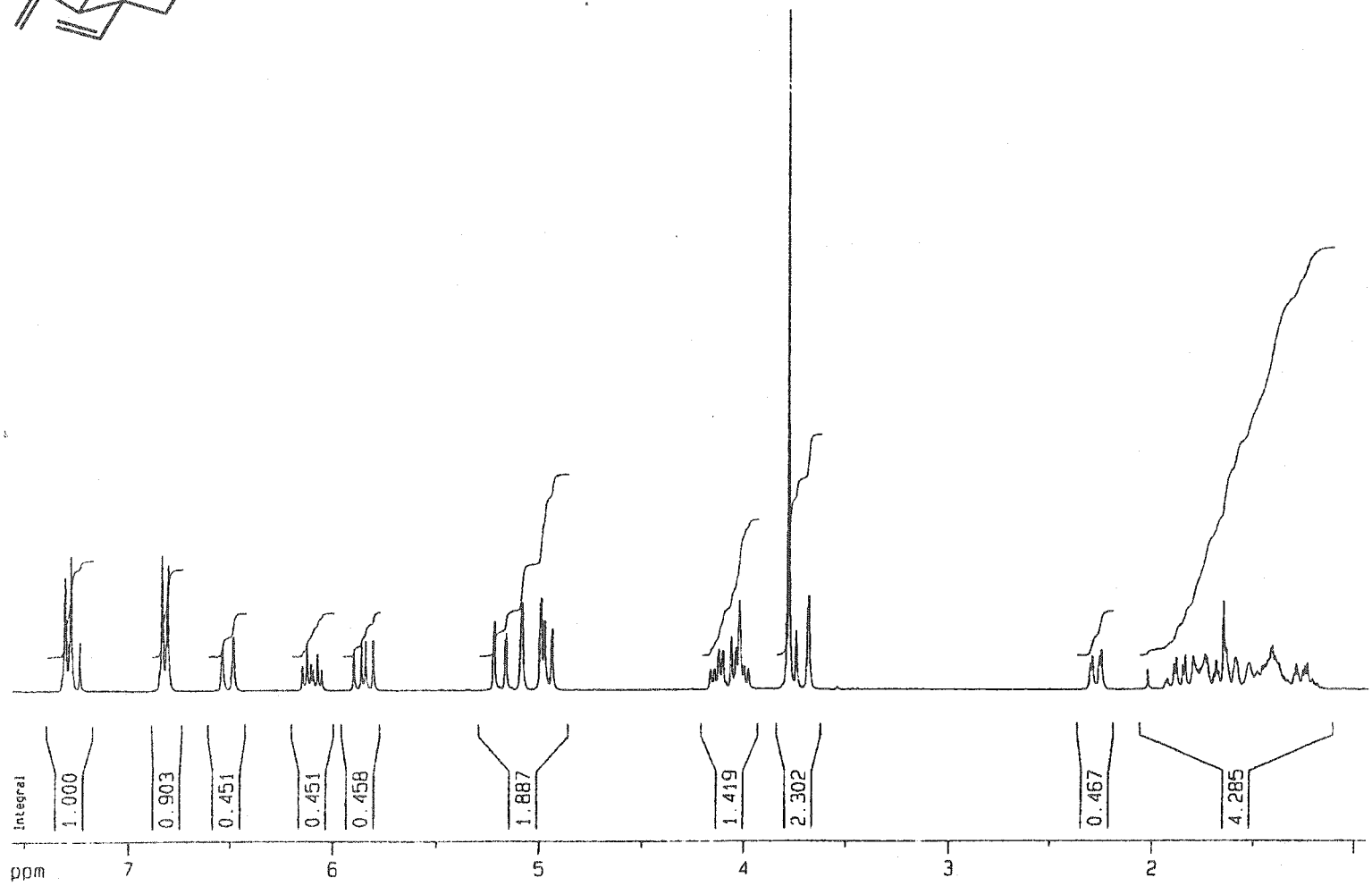
F1 - Processing paramete

SI	32768
MC2	QF
SF	500.1354311
WDW	EM
SSB	0
LB	0.30
GB	0

1D NMR plot parameters

CX	22.00
F1P	8.000
F1	4001.08
F2P	0.000
F2	0.00
PPMCM	0.36364
HZCM	181.86743





Current Data Parameters

NAME	jaf-83
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20020710
Time	10.31
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	161.3
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

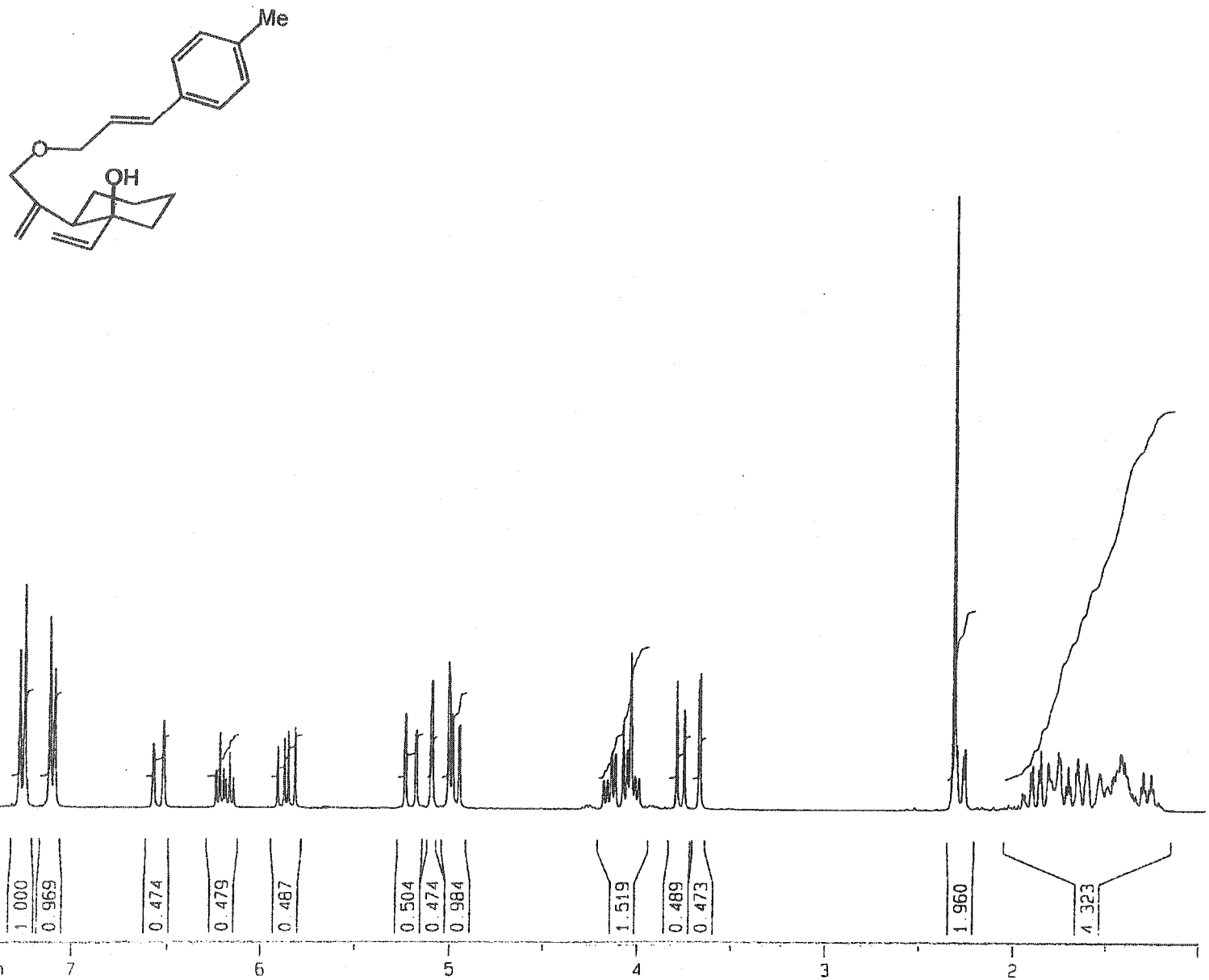
NUC1	1H
P1	26.00 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

F2 - Processing parameters

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

1D NMR plot parameters

CX	20.00 cm
CY	10.00 cm
F1P	7.567 ppm
F1	2271.07 Hz
F2P	0.937 ppm
F2	281.19 Hz
PPMCM	0.33150 ppm/cm
HZCM	99.49400 Hz/cm



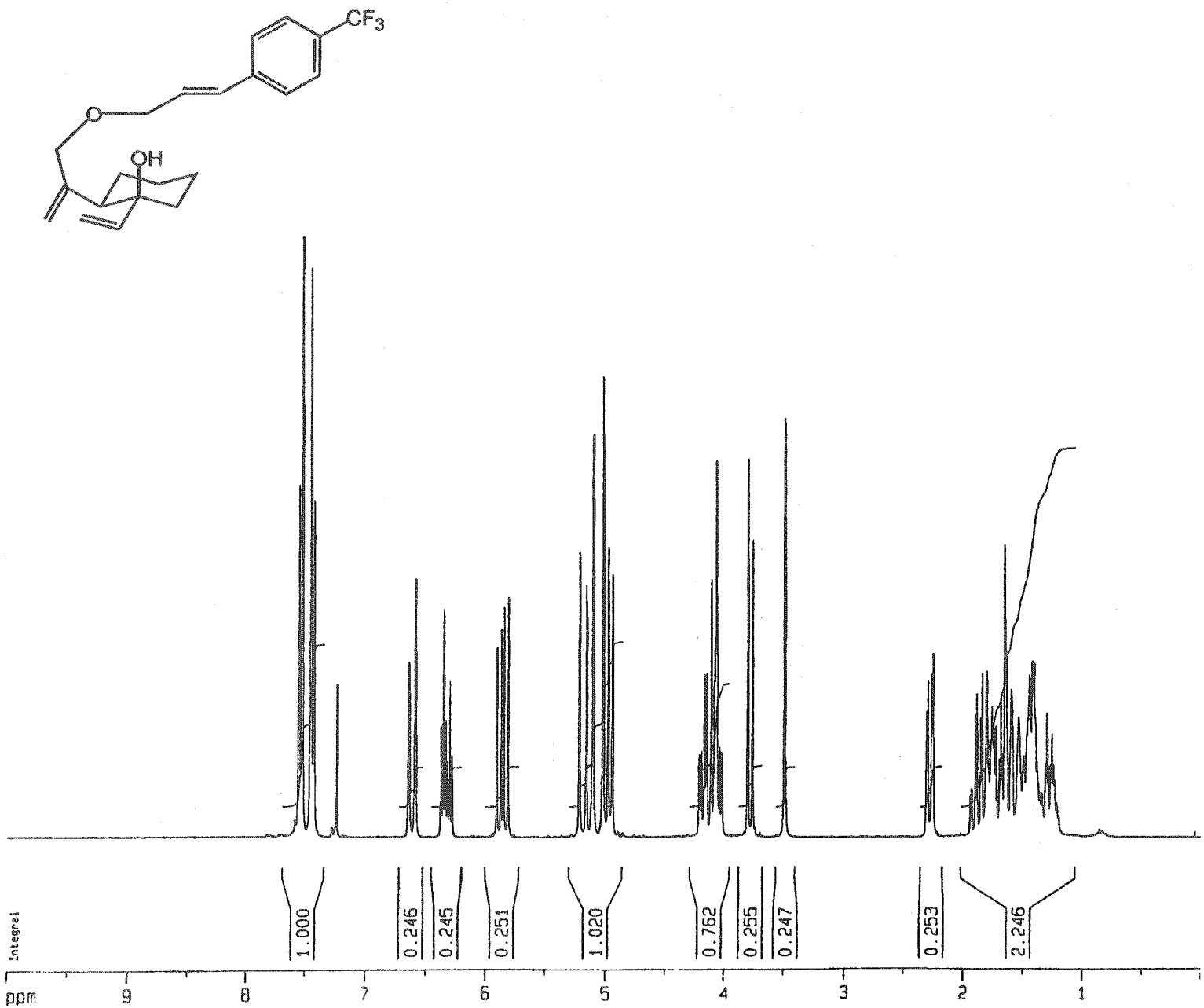
Current Data Parameters
NAME jaf-150a
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20020828
Time 10.39
INSTRUM av300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 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
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 7.518 ppm
F1 2256.32 Hz
F2P 0.966 ppm
F2 289.83 Hz
PPMCM 0.32761 ppm/cm
HZCM 98.32460 Hz/cm



Current Data Parameters

NAME	jaf-104
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20020728
Time	15.30
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	128
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

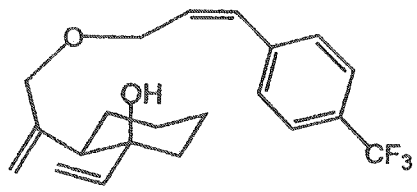
NUC1	1H
P1	8.00 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

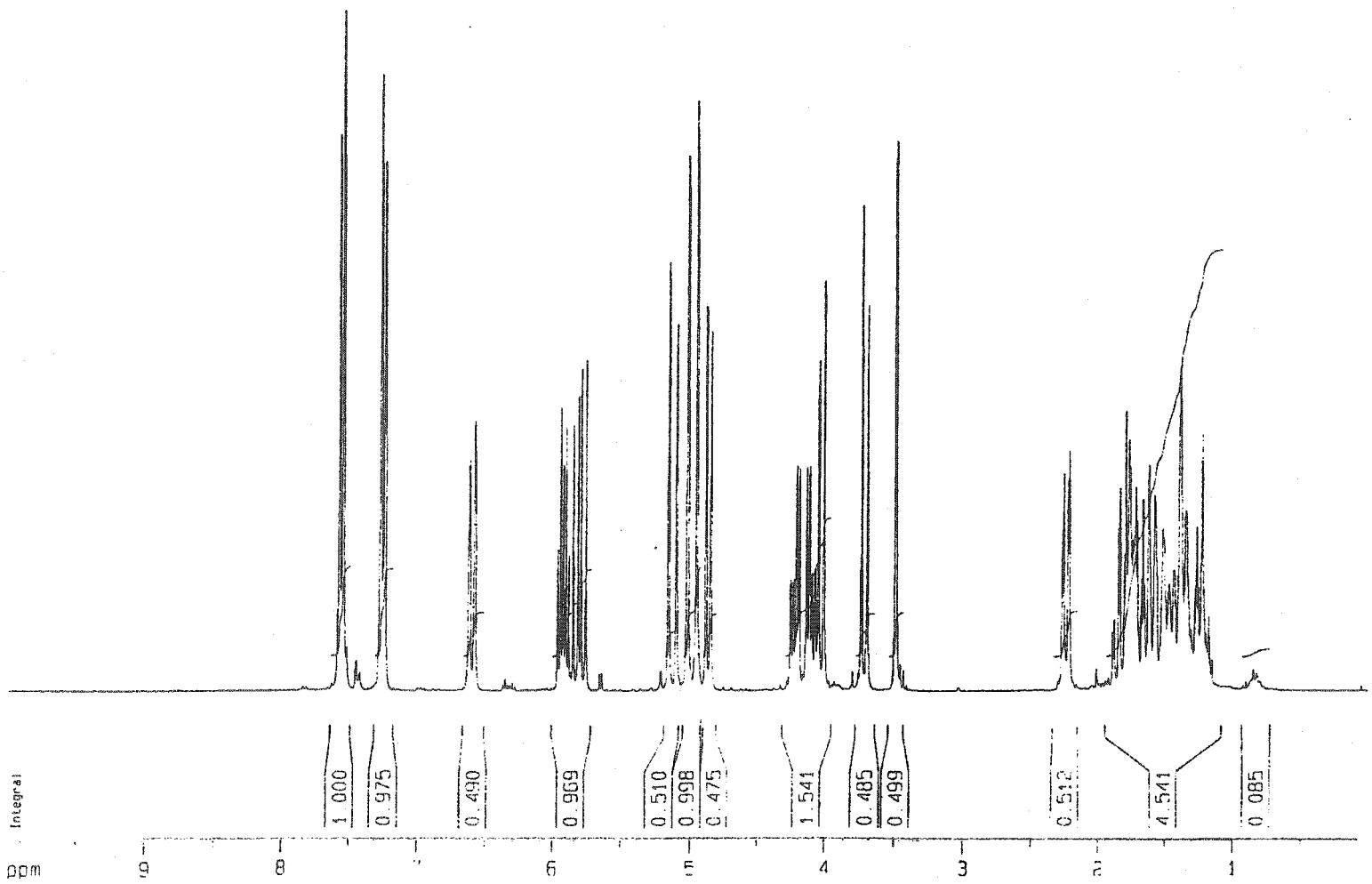
F2 - Processing parameters

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

1D NMR plot parameters

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





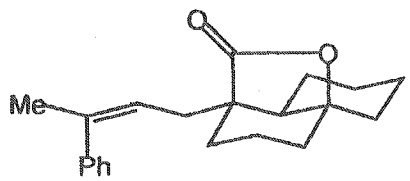
Current Data Parameters
NAME jaf-176
EXPNO 1
PROCNO 1

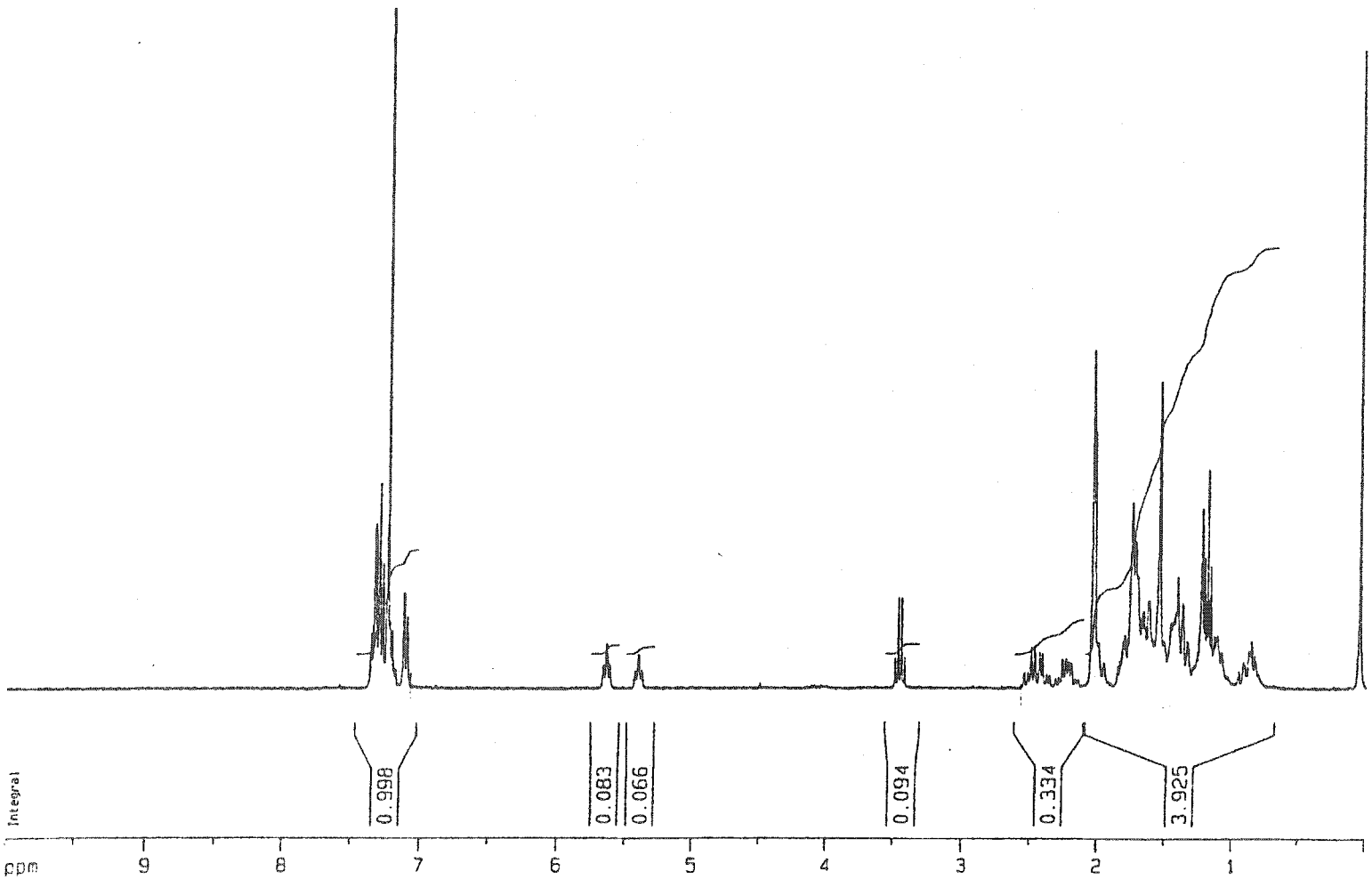
F2 - Acquisition Parameters
Date_ 20020924
Time 10.55
INSTRUM av300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 71.8
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

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

F2 - Processing parameters
SI 65536
SF 300.1300000 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 20.00 cm
CY 15.00 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	JF-22
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20011109
Time	11.49
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	724.1
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

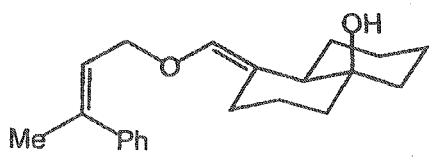
NUC1	1H
P1	11.00 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

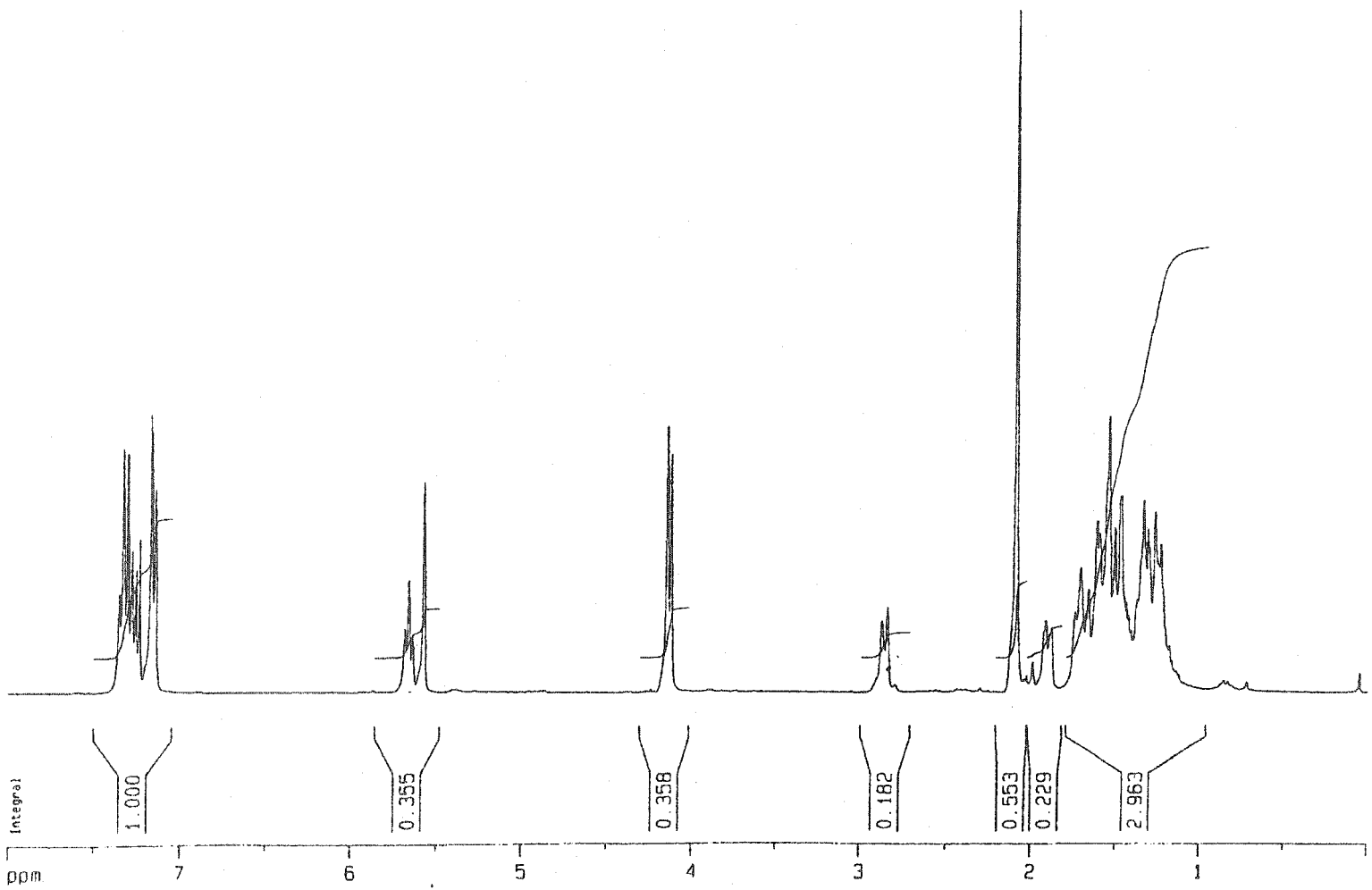
F2 - Processing parameters

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

1D NMR plot parameters

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





Current Data Parameters

NAME	jf-34
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20020130
Time	9.03
INSTRUM	av300
PROBHD	5 mm ONP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	181
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

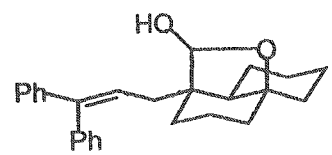
NUC1	1H
P1	11.00 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

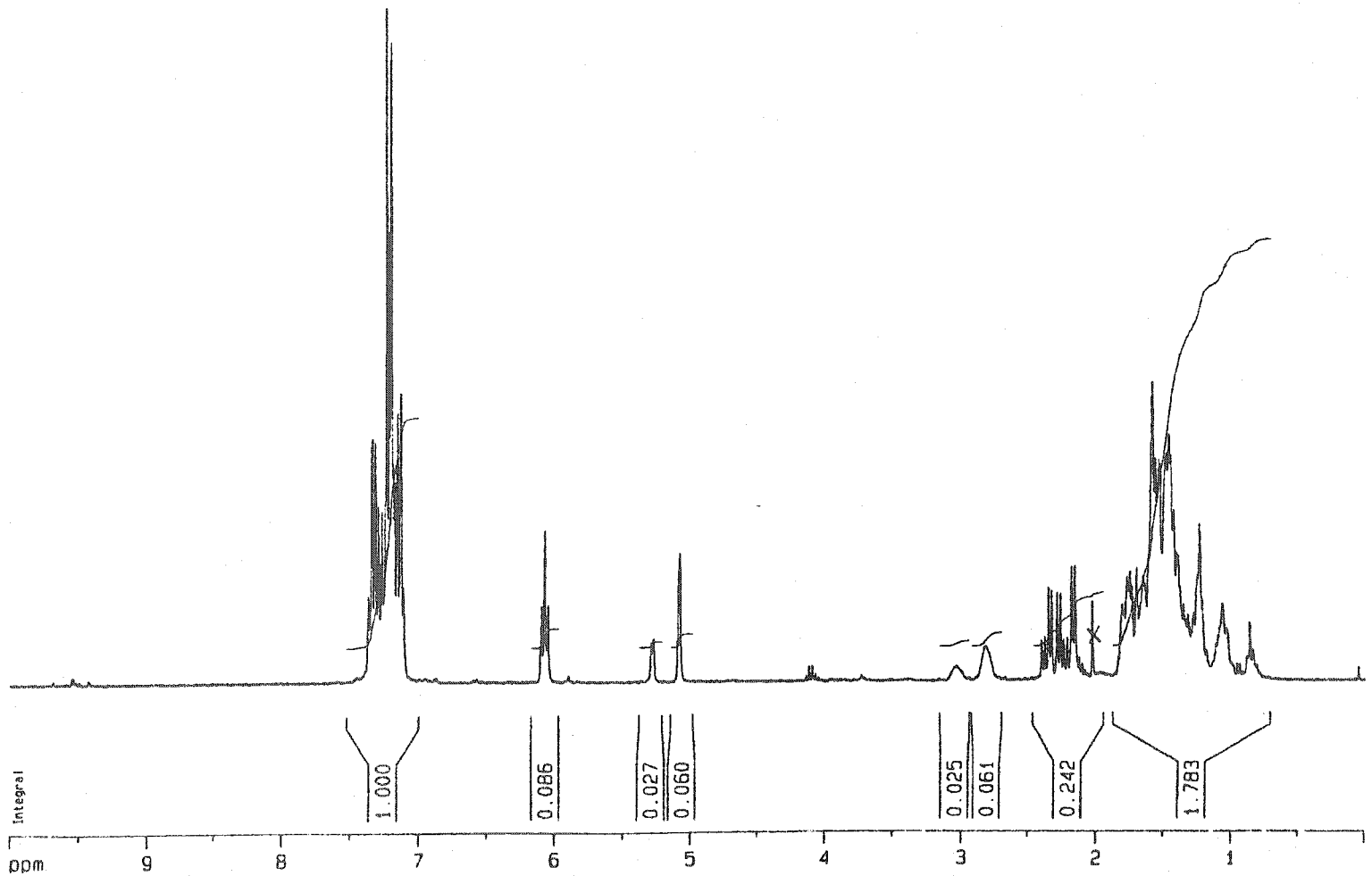
F2 - Processing parameters

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

1D NMR plot parameters

CX	20.00 cm
CY	10.00 cm
F1P	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	jaf-52
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20020611
Time	11.16
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 ==========

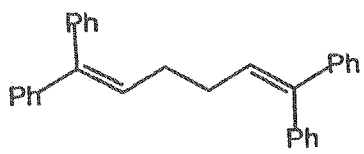
NUC1	1H
P1	20.00 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

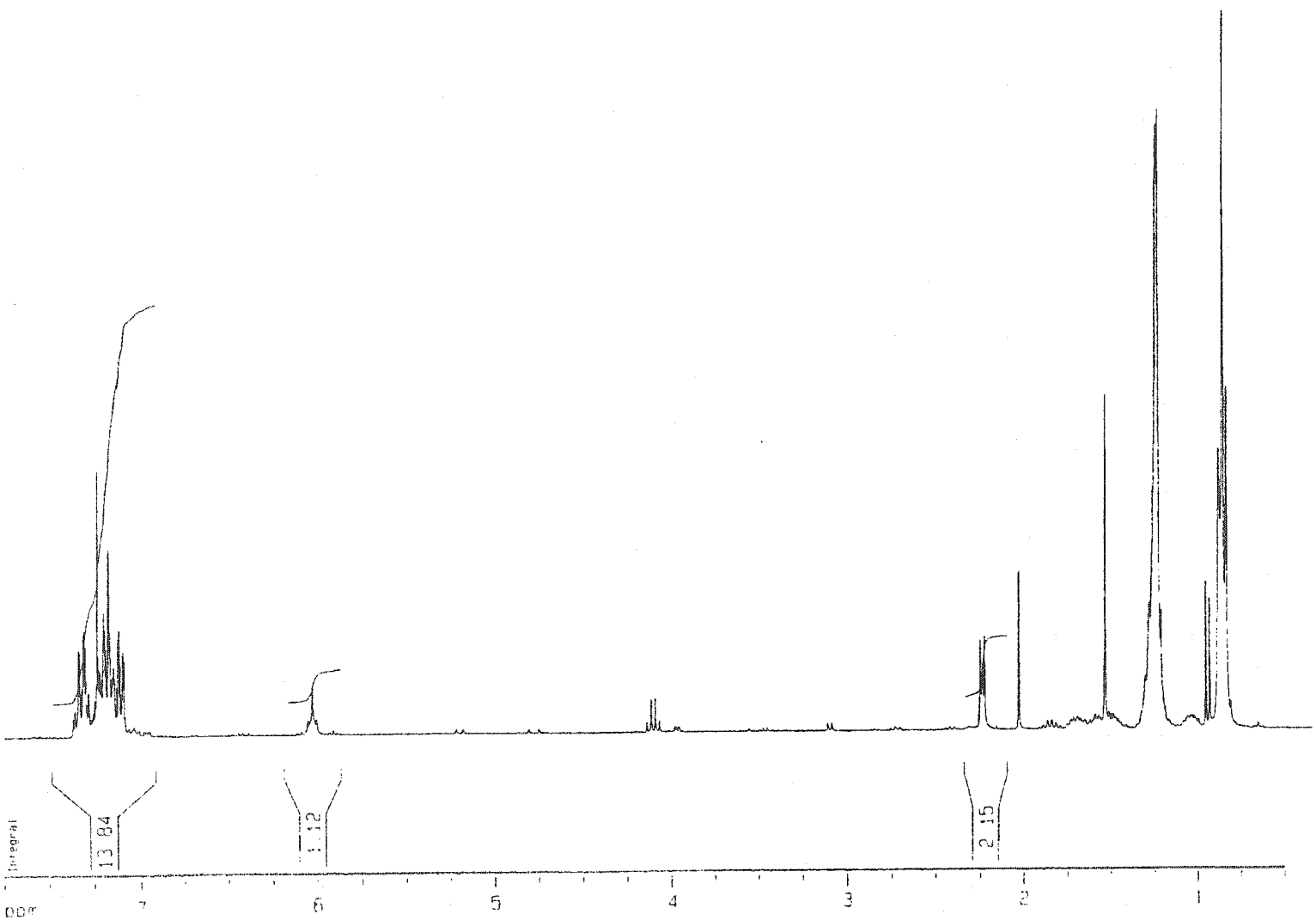
F2 - Processing parameters

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

1D NMR plot parameters

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





Current Data Parameters

NAME	jaf-dimer
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20030930
Time	17.43
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	256
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

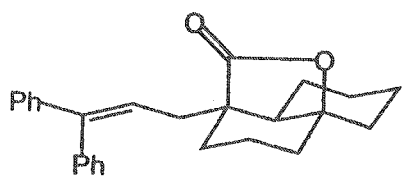
NUC1	1H
P1	10.50 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

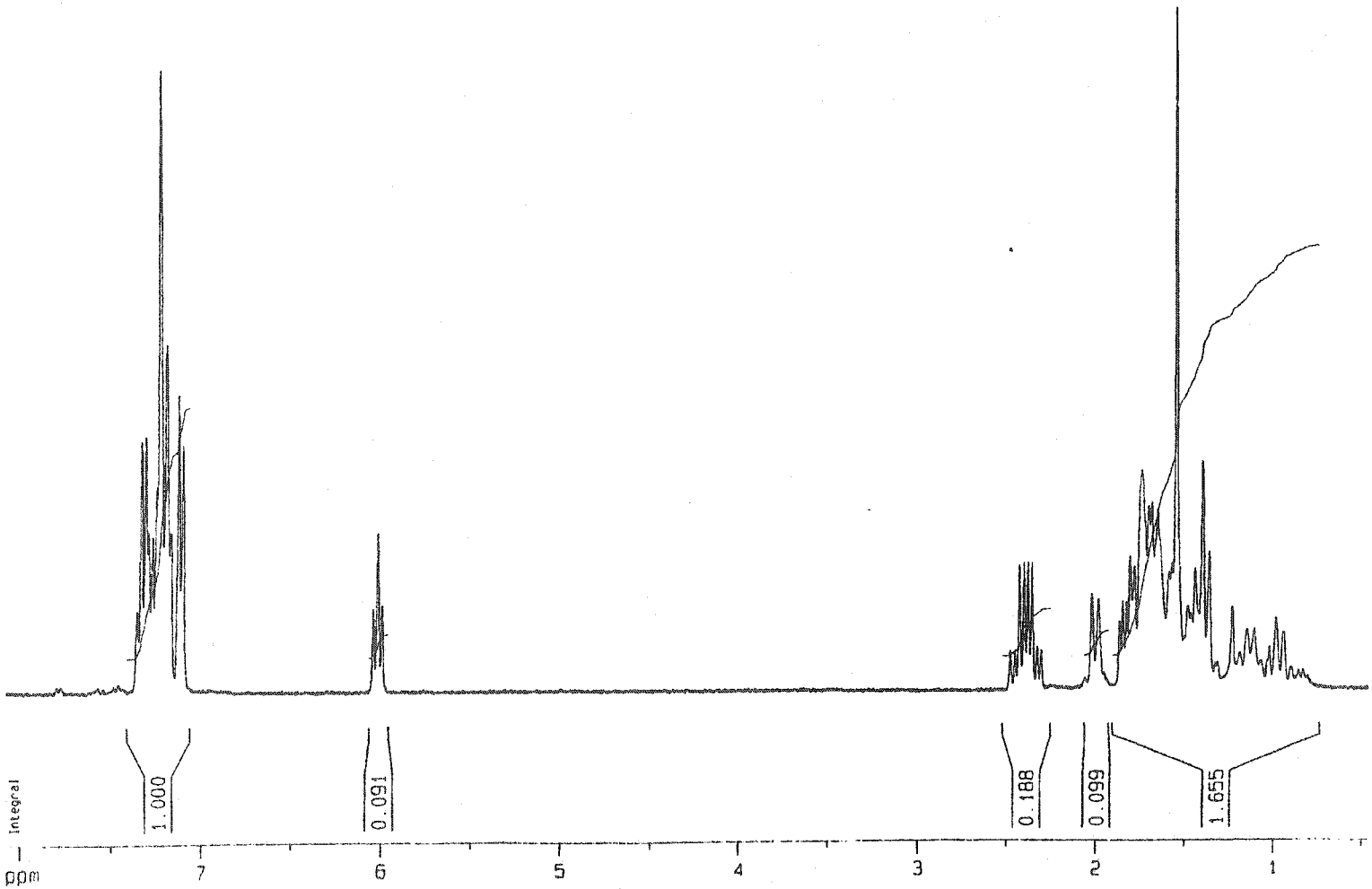
F2 - Processing parameters

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

1D NMR plot parameters

CX	20.00 cm
CY	15.00 cm
F1P	7.755 ppm
F1	2327.43 Hz
F2P	0.346 ppm
F2	104.36 Hz
PPMCM	0.37035 ppm/cm
HZCM	111.15346 Hz/cm





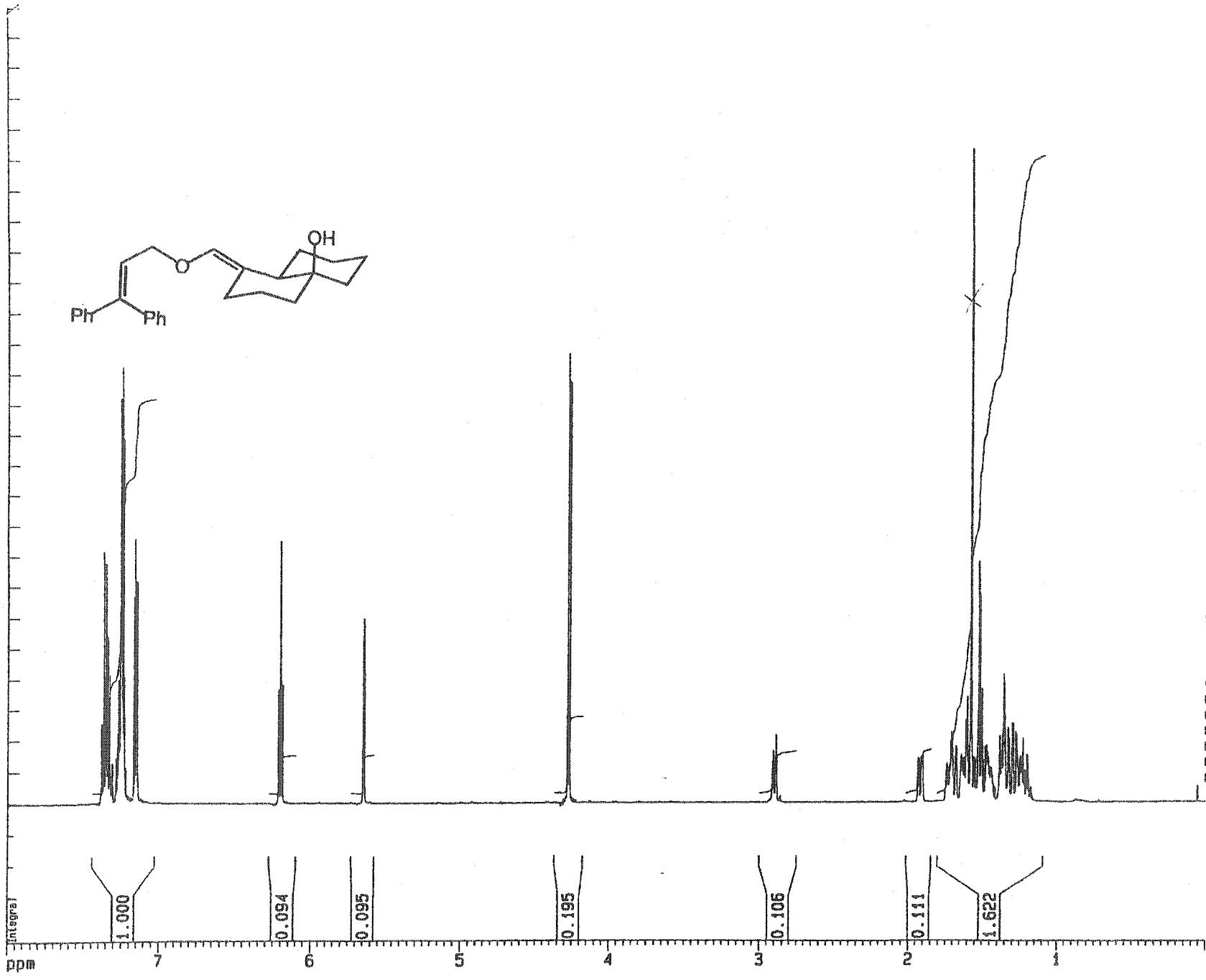
Current Data Parameters
NAME jaf-135
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20020816
Time 11.04
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 512
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

========== CHANNEL f1 ==========
NUC1 1H
P1 8.00 usec
PL1 -3.00 dB
SFO1 300.1319477 MHz

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

1D NMR plot parameters
CX 20.00 cm
CY 10.00 cm
F1P 8.080 ppm
F1 2425.17 Hz
F2P 0.463 ppm
F2 138.94 Hz
PPMCM 0.38087 ppm/cm
HZCM 114.31184 Hz/cm



Current Data Parameters

NAME	jaf-132a
EXPNO	1
PROCNO	1

F2 - Acquisition Parame

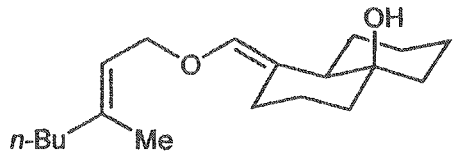
Date	20020812
Time	12.19
PULPROG	zg
SOLVENT	CDCl3
AQ	4.6530805
FIDRES	0.107456
DW	71.0
RG	512
NUCLEUS	1H
HL1	0
D1	0.0100000
P1	3.0
DE	88.8
SFO1	500.1381707
SWH	7042.25
TD	65536
NS	16
DS	0

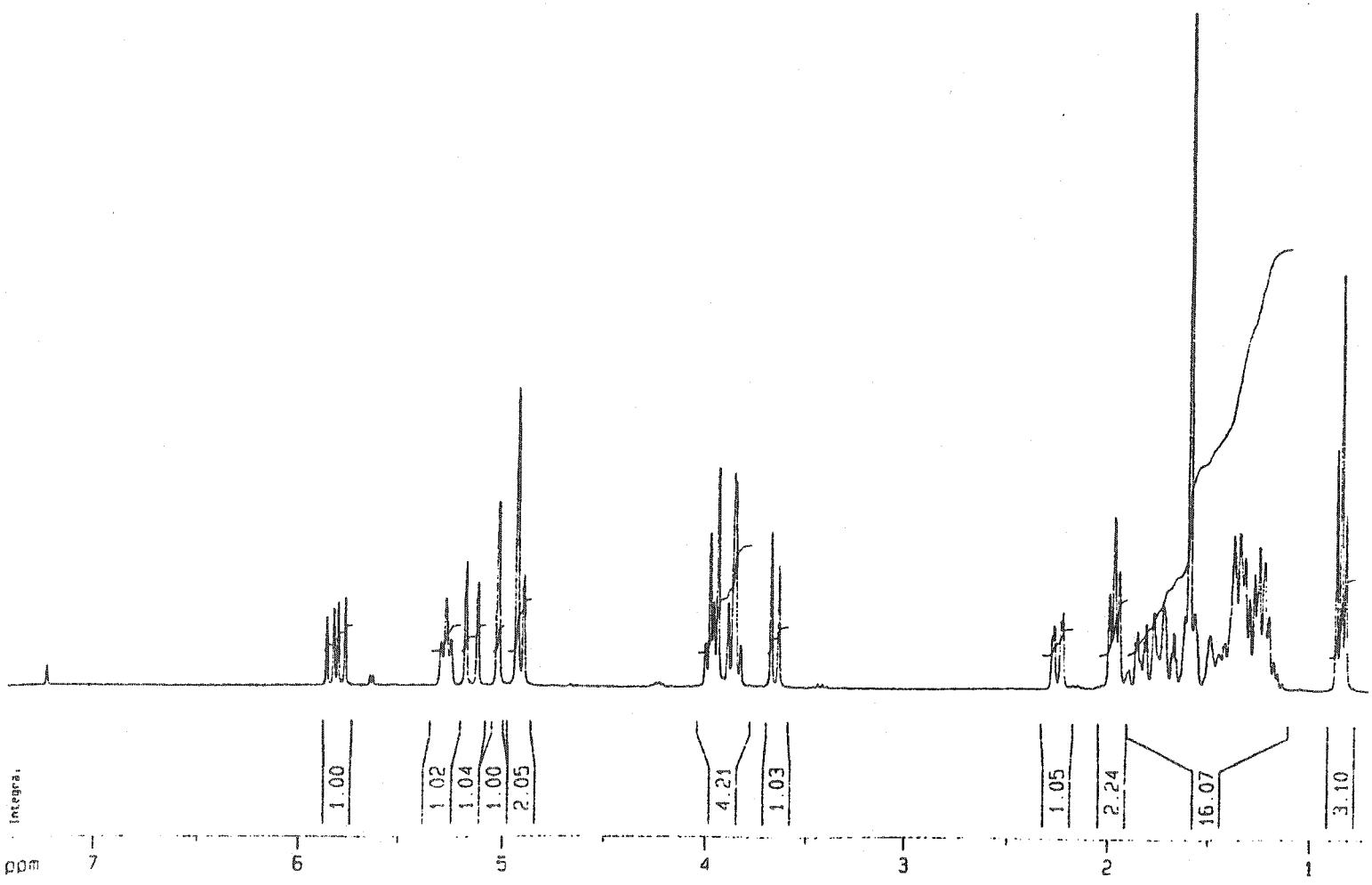
F1 - Processing paramet

SI	32768
MC2	QF
SF	500.1354311
WDW	EM
SSB	0
LB	0.00
GB	0

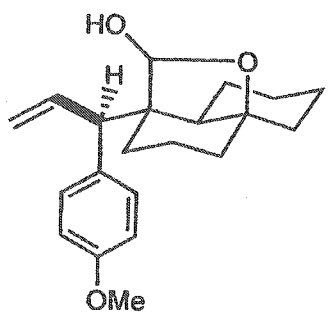
1D NMR plot parameters

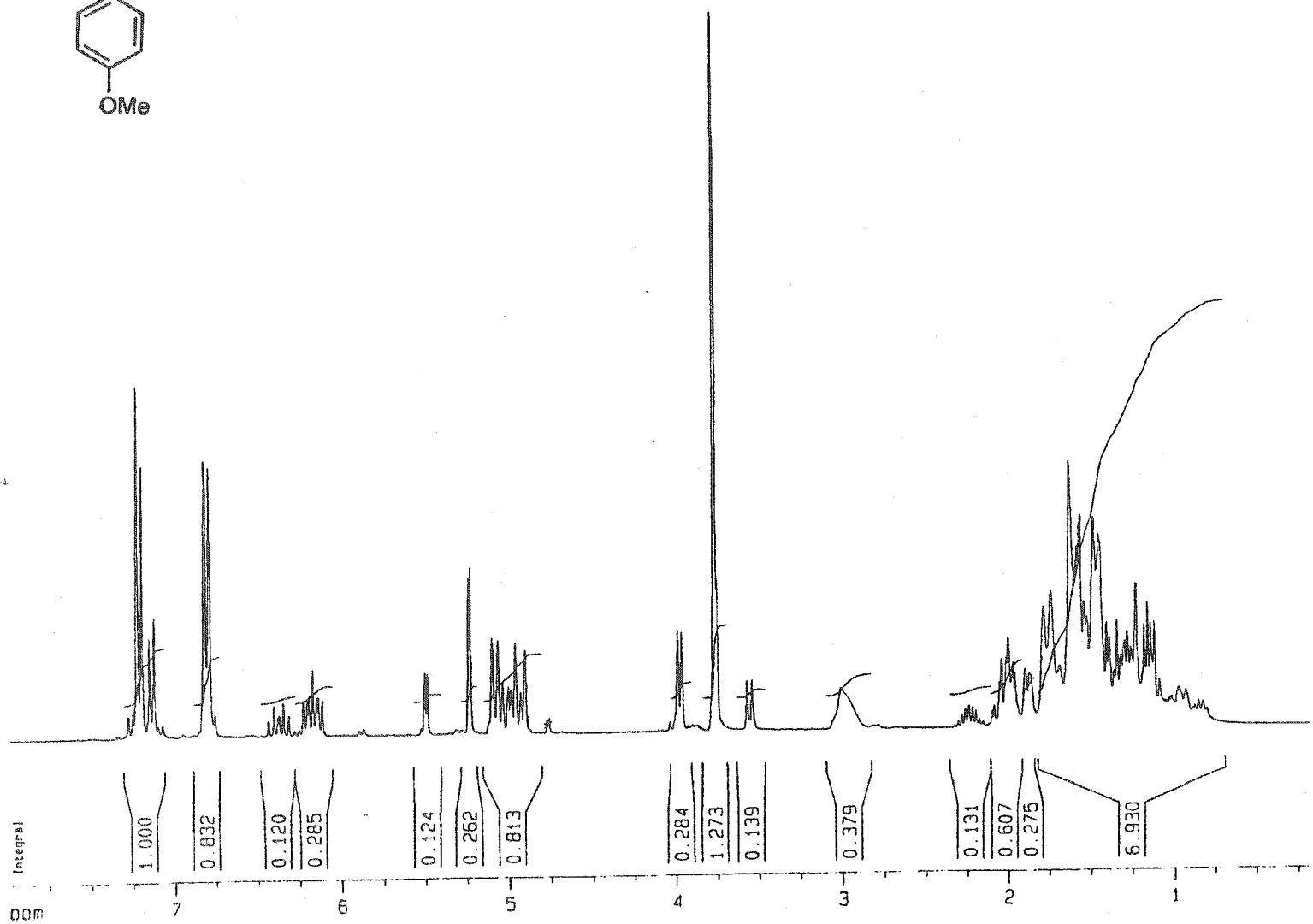
CX	22.00
F1P	8.000
F1	4001.08
F2P	0.000
F2	0.00
PPMCM	0.36364
HZCM	181.86743






```
Current Data Parameters
NAME                  jaf-182
EXPNO                       1
PROCNO                      1

F2 - Acquisition Parameters
Date_              20021003
Time                  11.48
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
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                   7.435 ppm
F1                 2230.80 Hz
F2P                   0.709 ppm
F2                  212.73 Hz
PPMCM              0.33620 ppm/cm
HZCM             100.90379 Hz/cm
```





Current Data Parameters

NAME	jaf-114
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20020802
Time	22.15
INSTRUM	av300
PROBHD	5 mm GNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	64
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	228.1
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

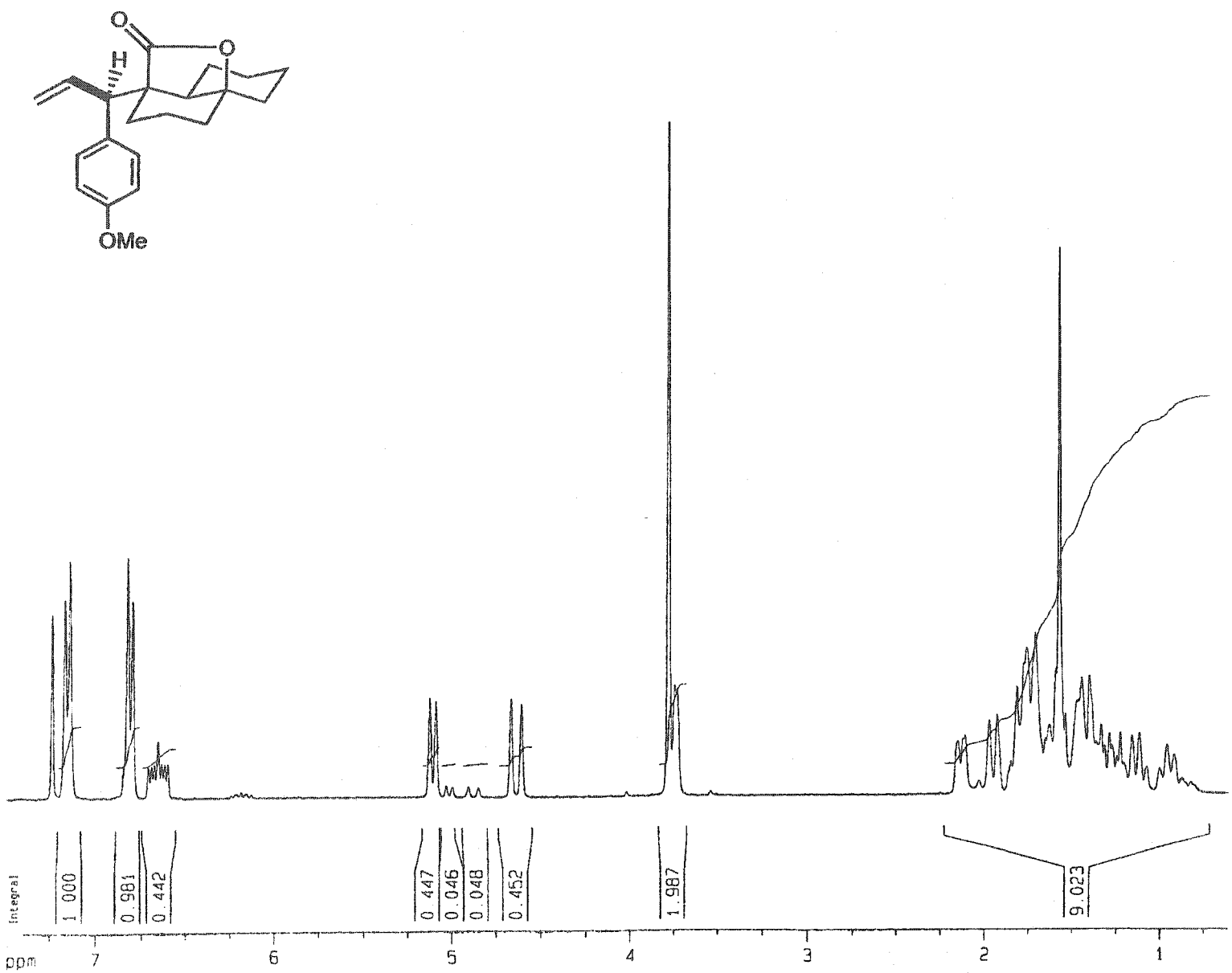
NUC1	1H
P1	8.00 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

F2 - Processing parameters

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

1D NMR plot parameters

CX	20.00 cm
CY	15.00 cm
F1P	7.988 ppm
F1	2397.29 Hz
F2P	0.184 ppm
F2	55.29 Hz
PPMCM	0.39016 ppm/cm
HZCM	117.09995 Hz/cm



Current Data Parameters

NAME	jaf-141
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20020821
Time	10.02
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	362
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

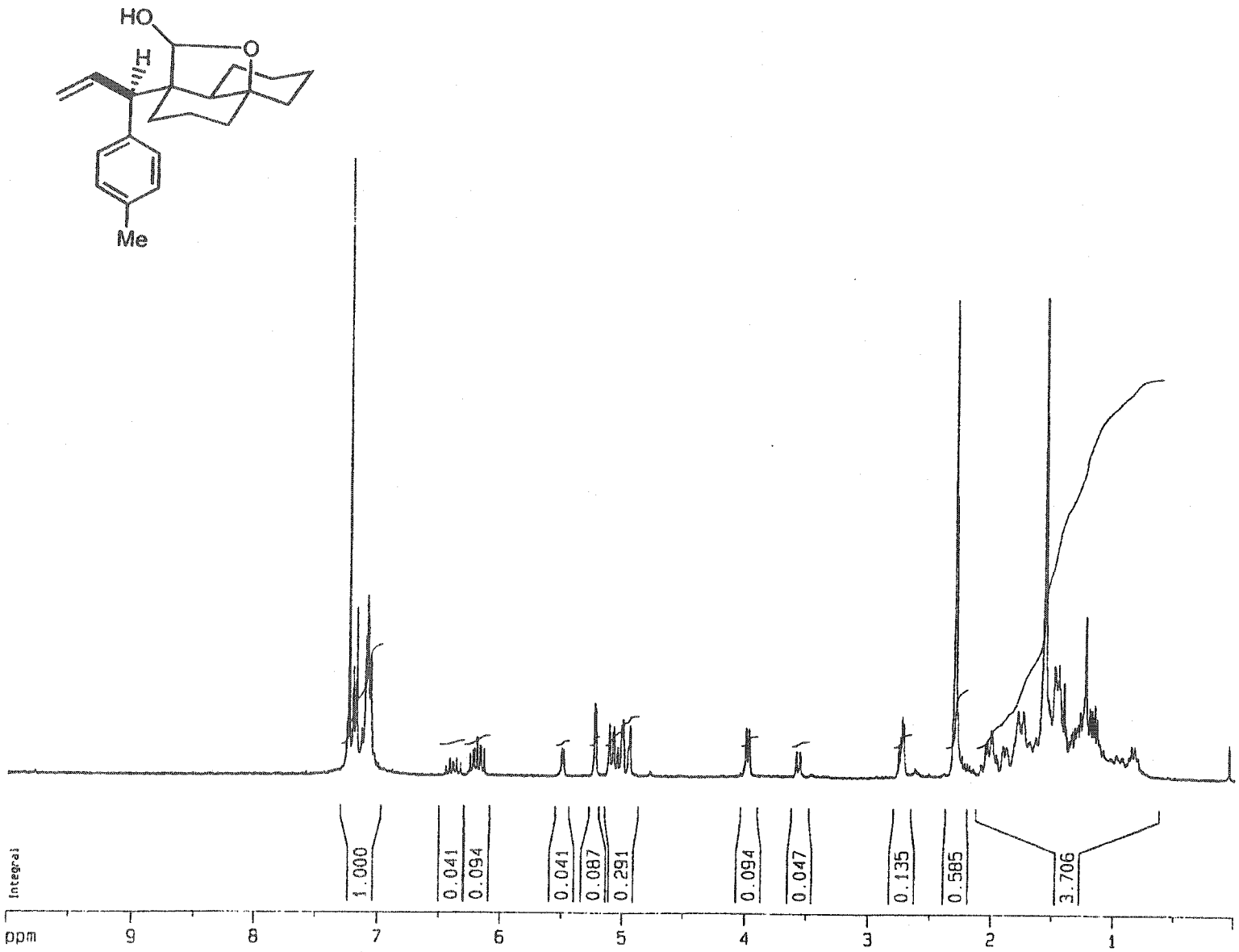
NUC1	1H
P1	8.00 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

F2 - Processing parameters

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

1D NMR plot parameters

CX	20.00 cm
CY	13.00 cm
F1P	7.494 ppm
F1	2249.15 Hz
F2P	0.607 ppm
F2	182.18 Hz
PPMCM	0.34435 ppm/cm
HZCM	103.34849 Hz/cm



Current Data Parameters

NAME	jaf-154
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20021008
Time	9.05
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
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

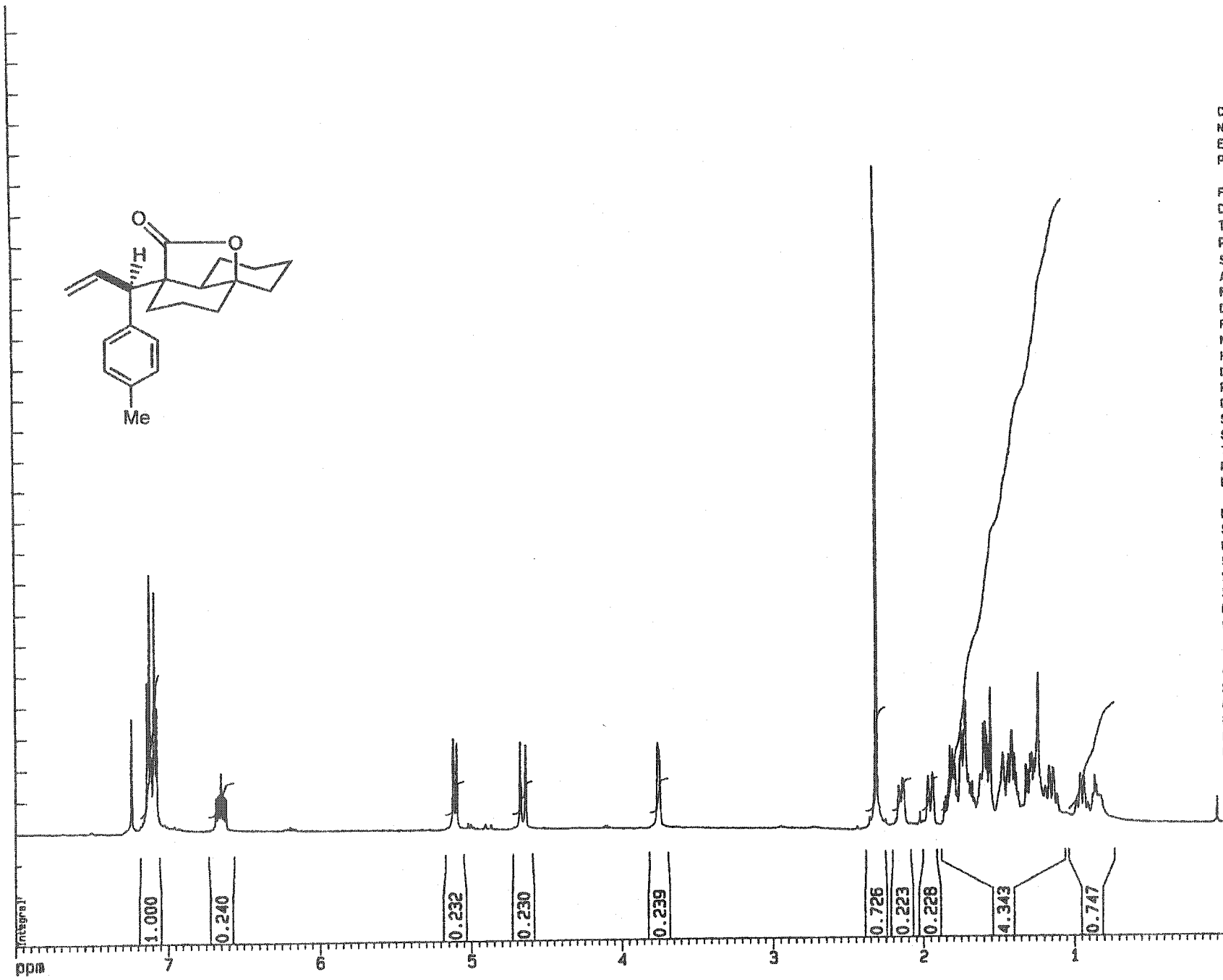
NUC1	1H
P1	9.75 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

F2 - Processing parameters

SI	65536
SF	300.1300000 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	jaf_186
EXPNO	1
PROCNO	1

F2 - Acquisition Paramet

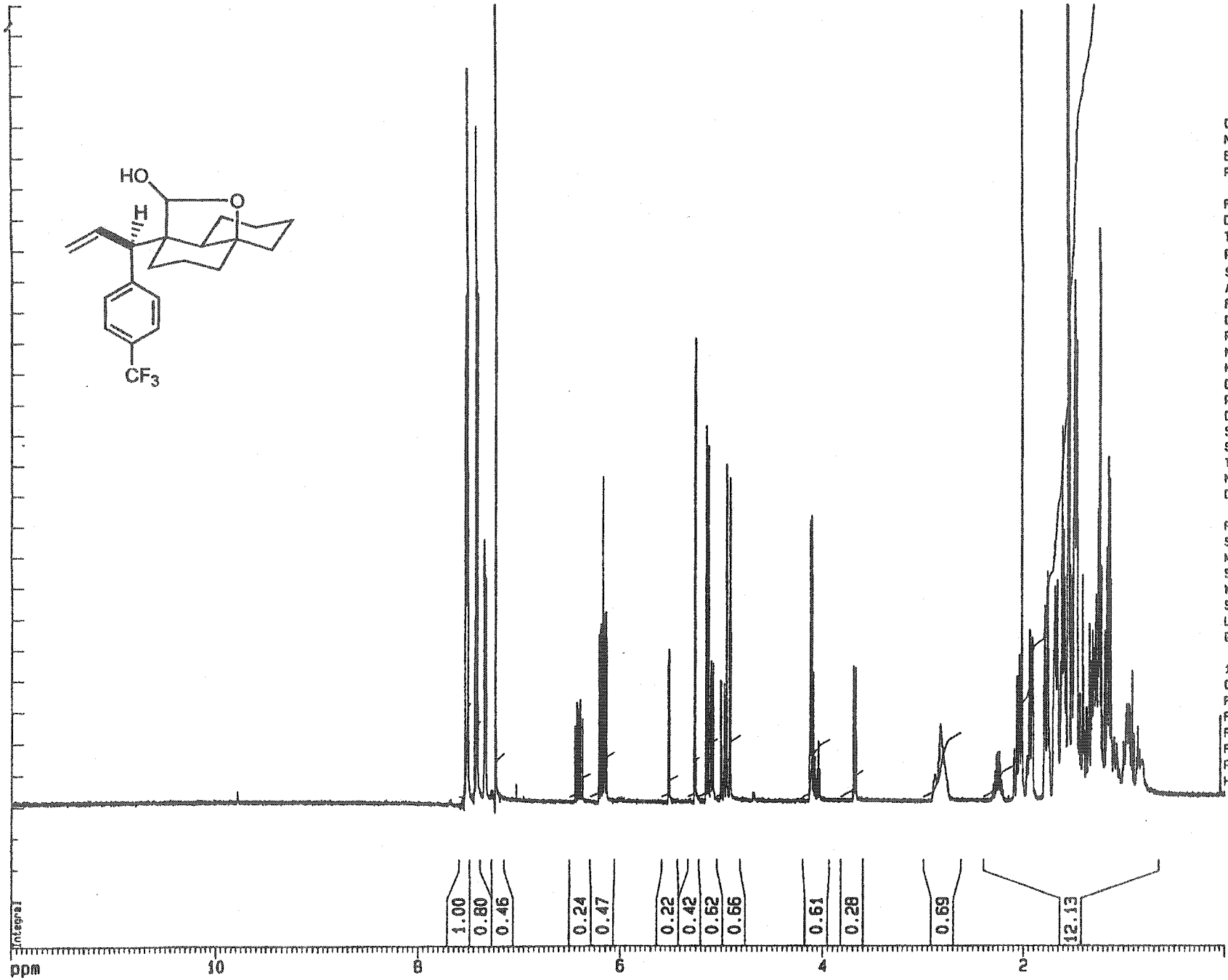
Date	20021016
Time	10.25
PULPROG	zg
SOLVENT	CDCl3
AQ	4.6530805
FIDRES	0.107456
DW	71.0
RG	1024
NUCLEUS	1H
HL1	0
D1	0.0100000
P1	3.3
DE	88.8
SFO1	500.1381707
SWH	7042.25
TD	65536
NS	16
DS	0

F1 - Processing paramet

SI	32768
MC2	DF
SF	500.1354311
WDW	EM
SSB	0
LB	0.30
GB	0

1D NMR plot parameters

CX	22.00
F1P	8.000
F1	4001.08
F2P	0.000
F2	0.00
PPMCM	0.3636
HZCM	181.8674



Current Data Parameters

NAME	jef-110
EXPNO	1
PROCNO	1

F2 - Acquisition Paramet

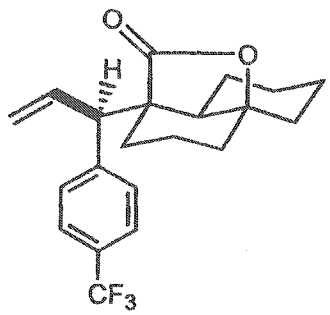
Date	20020730
Time	11.57
PULPROG	zg
SOLVENT	CDCl3
AQ	4.6530805
FIDRES	0.107456
DW	71.0
RG	512
NUCLEUS	1H
HL1	0
D1	0.0100000
P1	3.0
DE	88.8
SFO1	500.1381707
SWH	7042.25
TD	65536
NS	16
DS	0

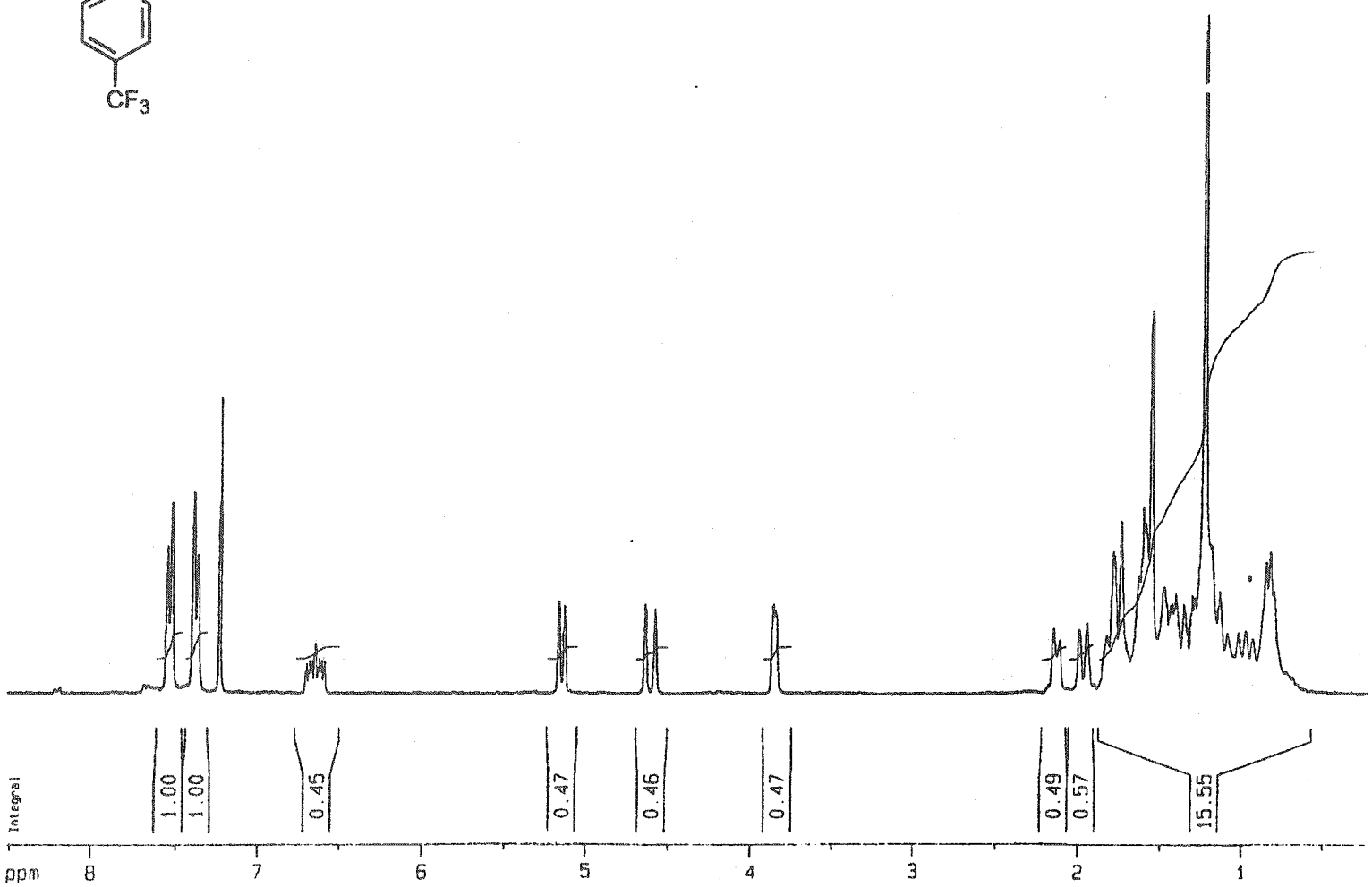
F1 - Processing paramet

SI	32768
MC2	QF
SF	500.1354311
NDN	EM
SSB	0
LB	0.00
GB	0

1D NMR plot parameters

CX	22.00
F1P	12.000
F1	6001.63
F2P	0.000
F2	0.00
PPMCM	0.54545
HZCM	272.80115





Current Data Parameters

NAME	jaf-146
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20020826
Time	13.36
INSTRUM	av300
PROBHD	5 mm GNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	512
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

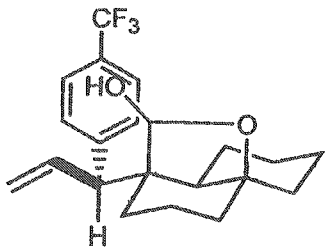
NUC1	1H
P1	9.75 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

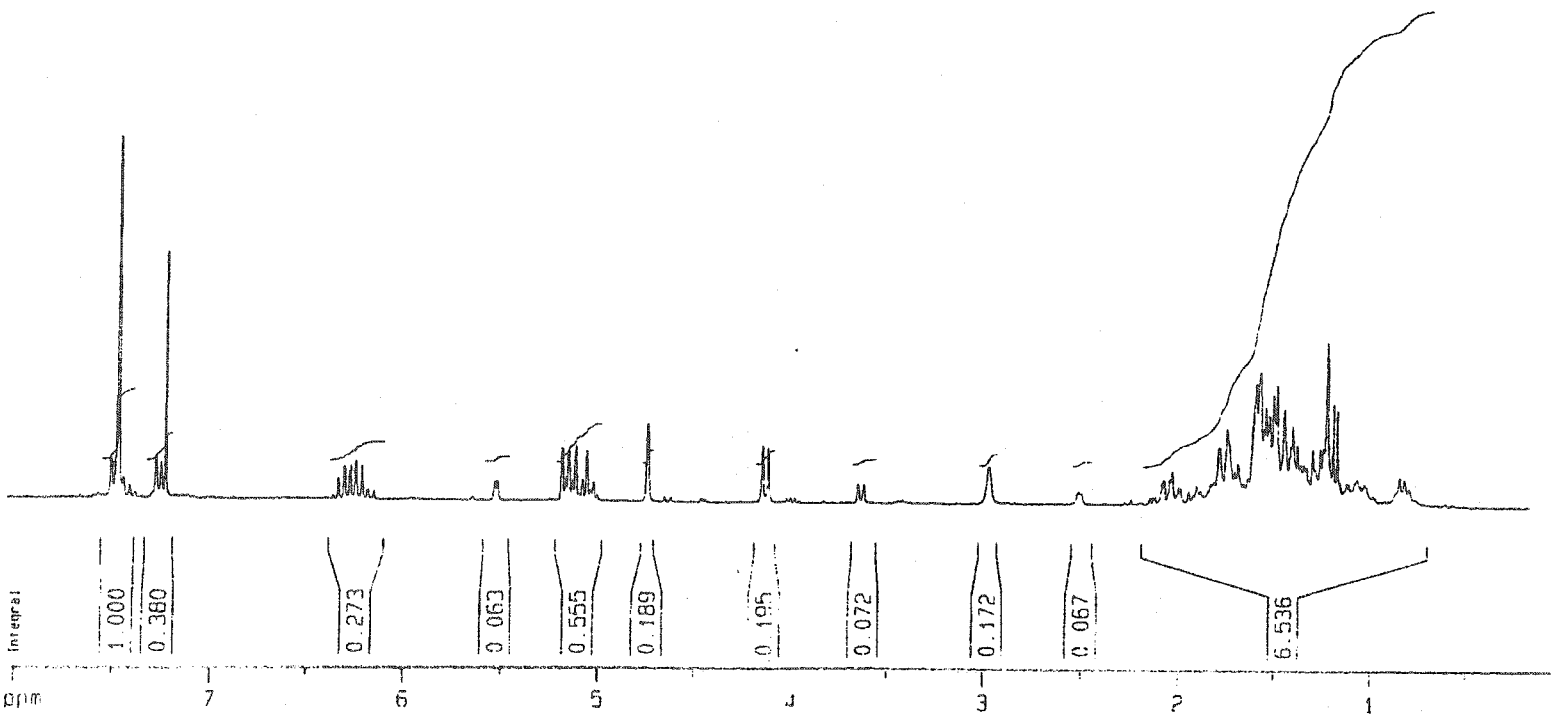
F2 - Processing parameters

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

1D NMR plot parameters

CX	20.00 cm
CY	10.00 cm
F1P	8.522 ppm
F1	2557.76 Hz
F2P	0.224 ppm
F2	67.34 Hz
PPMCM	0.41489 ppm/cm
HZCM	124.52057 Hz/cm





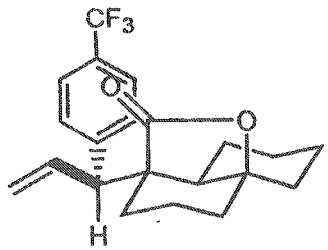
Current Data Parameters
NAME jaf-177
EXPNO 1
PROCNO 1

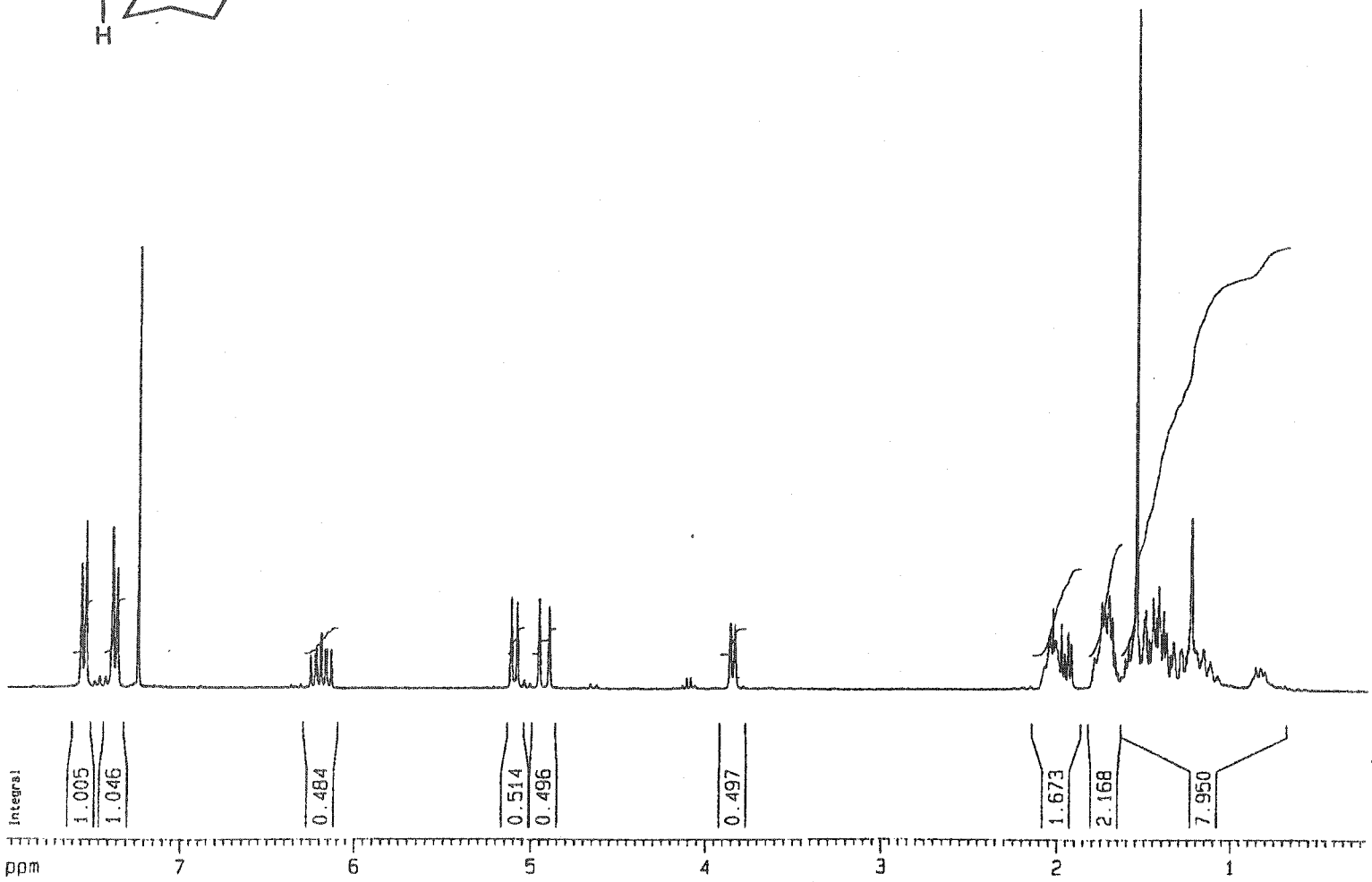
F2 - Acquisition Parameters
Date_ 20020930
Time 13.24
INSTRUM av300
PROBHD 5 mm DNP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 406.4
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

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

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

1D NMR plot parameters
CX 20.00 cm
CY 10.00 cm
F1P 8.047 ppm
F1 2415.19 Hz
F2P 0.168 ppm
F2 50.69 Hz
PPMCM 0.39991 ppm/cm
HZCM 116.22493 Hz/cm





Current Data Parameters

NAME	jaf-180
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20021007
Time	12.10
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	574.7
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

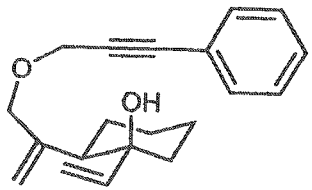
NUC1	1H
P1	9.75 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

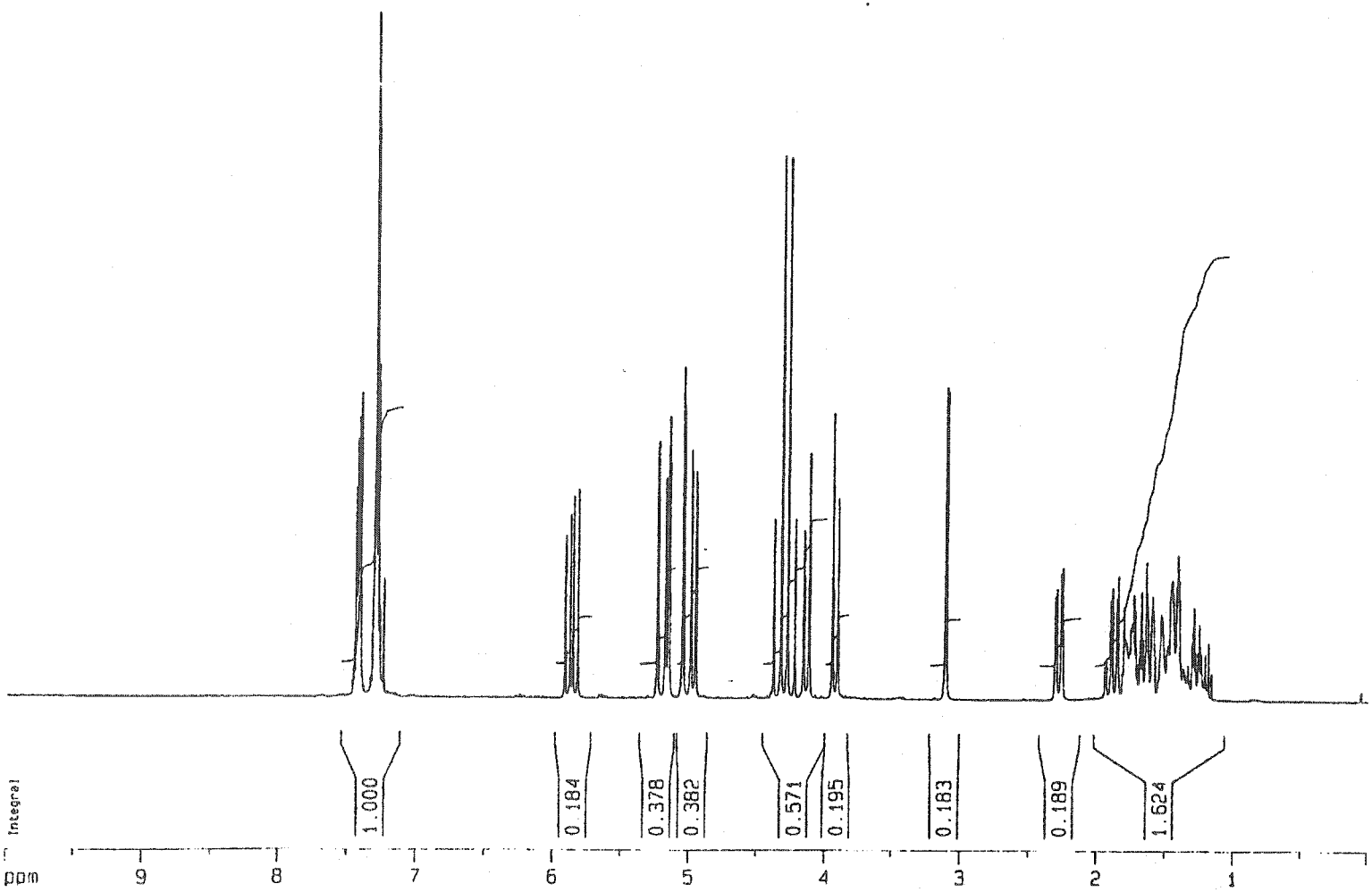
F2 - Processing parameters

SI	65536
SF	300.1300000 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	7.982 ppm
F1	2395.66 Hz
F2P	0.212 ppm
F2	63.60 Hz
PPMCM	0.38851 ppm/cm
HZCM	116.60320 Hz/cm





Current Data Parameters

NAME	jaf-37
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20020211
Time	11.18
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	101.6
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

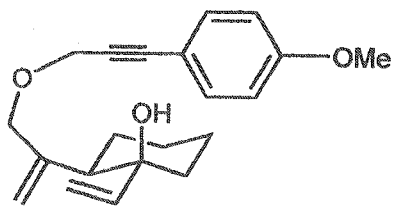
NUC1	1H
P1	11.00 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

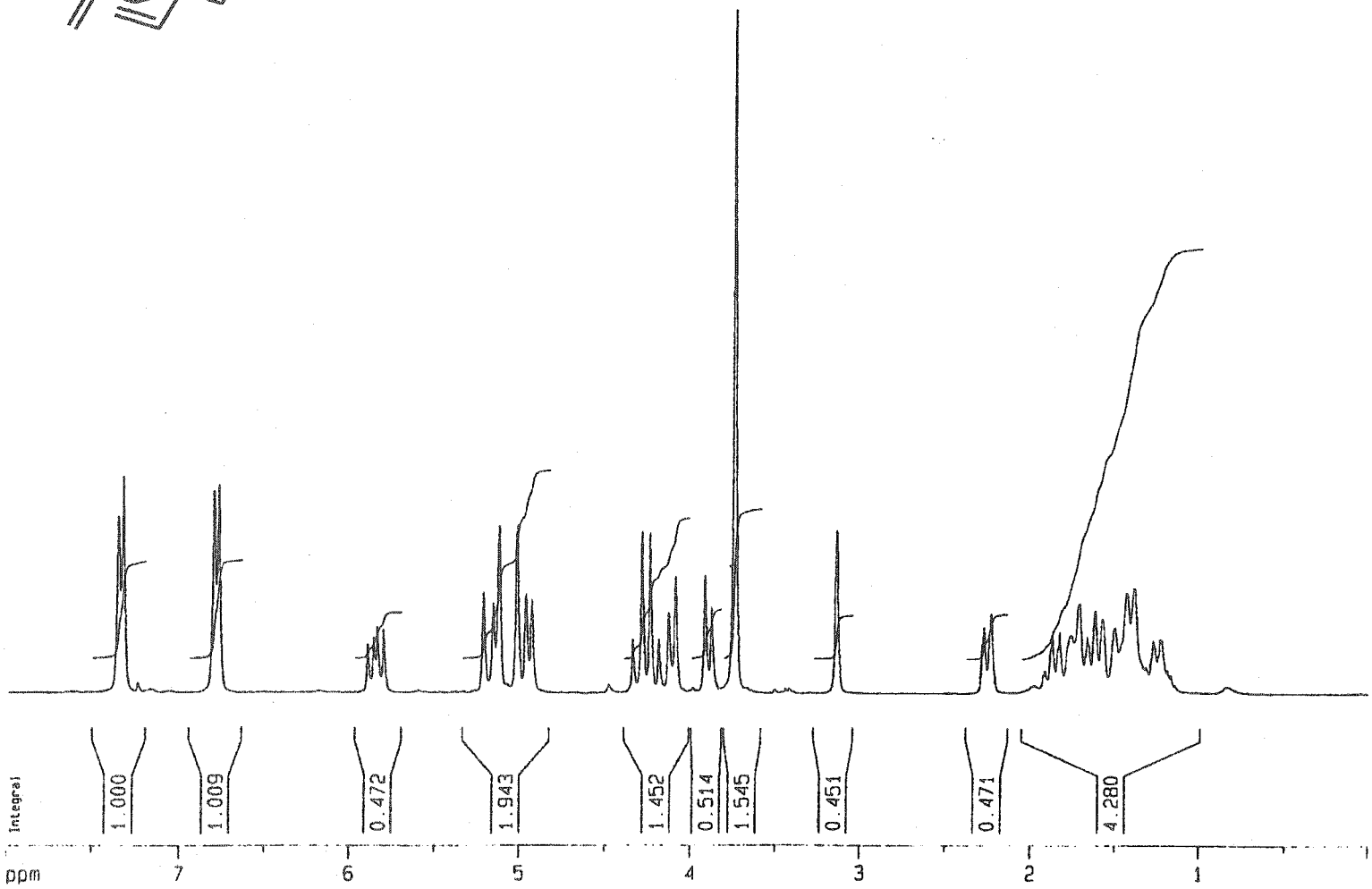
F2 - Processing parameters

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

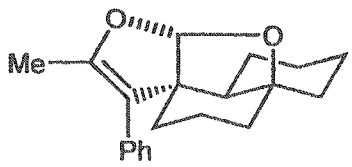
1D NMR plot parameters

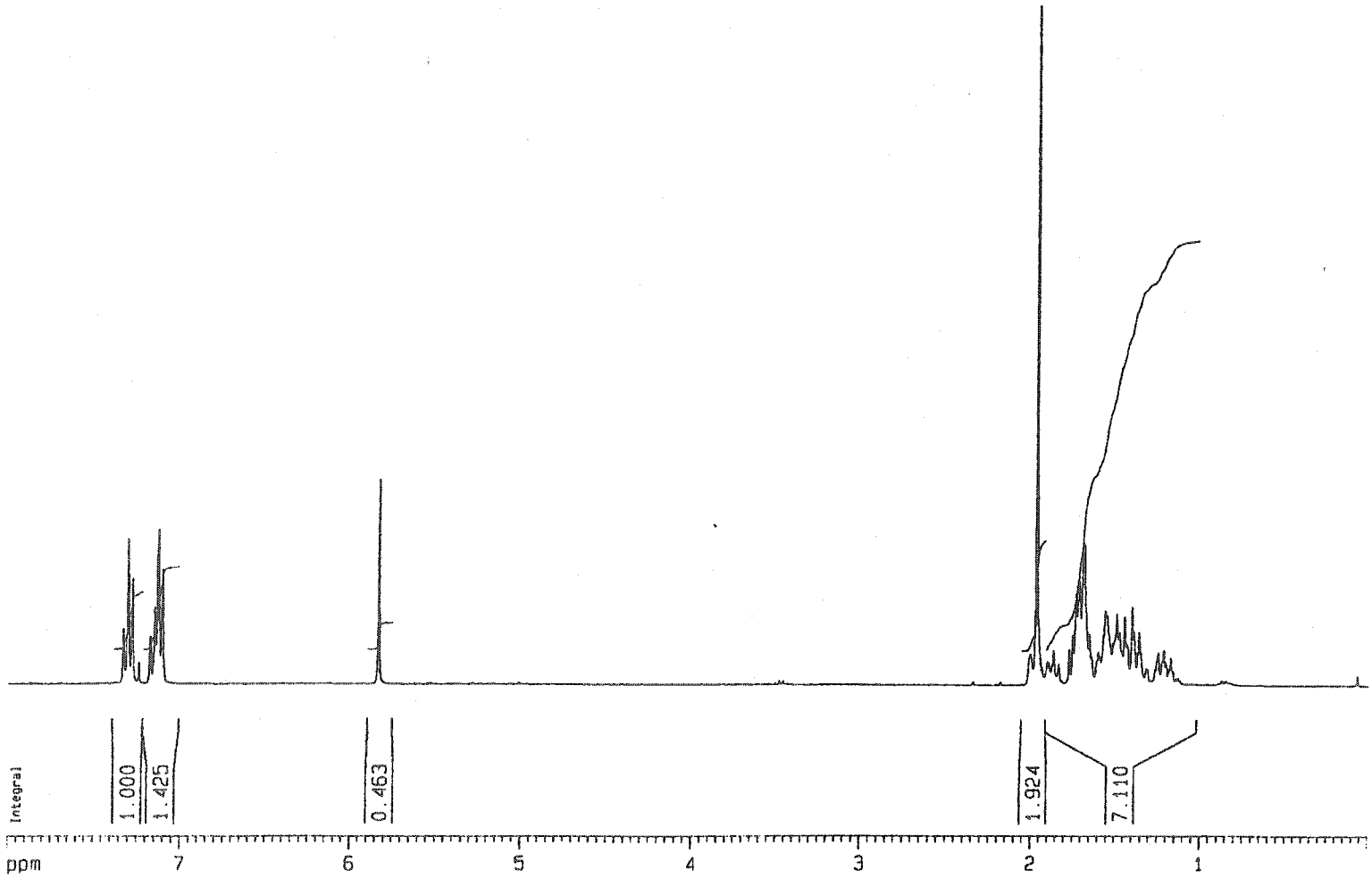
CX	20.00 cm
CY	10.00 cm
F1P	10.000 ppm
F1	3001.30 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	0.50000 ppm/cm
HZCM	150.06500 Hz/cm






```
Current Data Parameters
NAME                  jaf-43
EXPNO                      1
PROCNO                     1

F2 - Acquisition Parameters
Date_              20020313
Time                   9.00
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                    10.00 usec
PL1                   -3.00 dB
SFO1              300.1319477 MHz

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

1D NMR plot parameters
CX                    20.00 cm
CY                    10.00 cm
F1P                   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	jaf-38
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20020215
Time	11.56
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	71.8
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

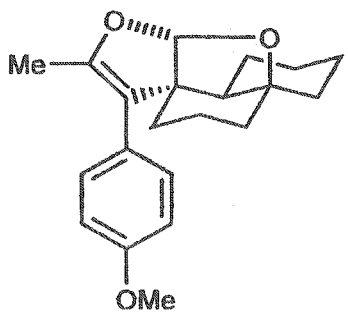
NUC1	1H
P1	11.00 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

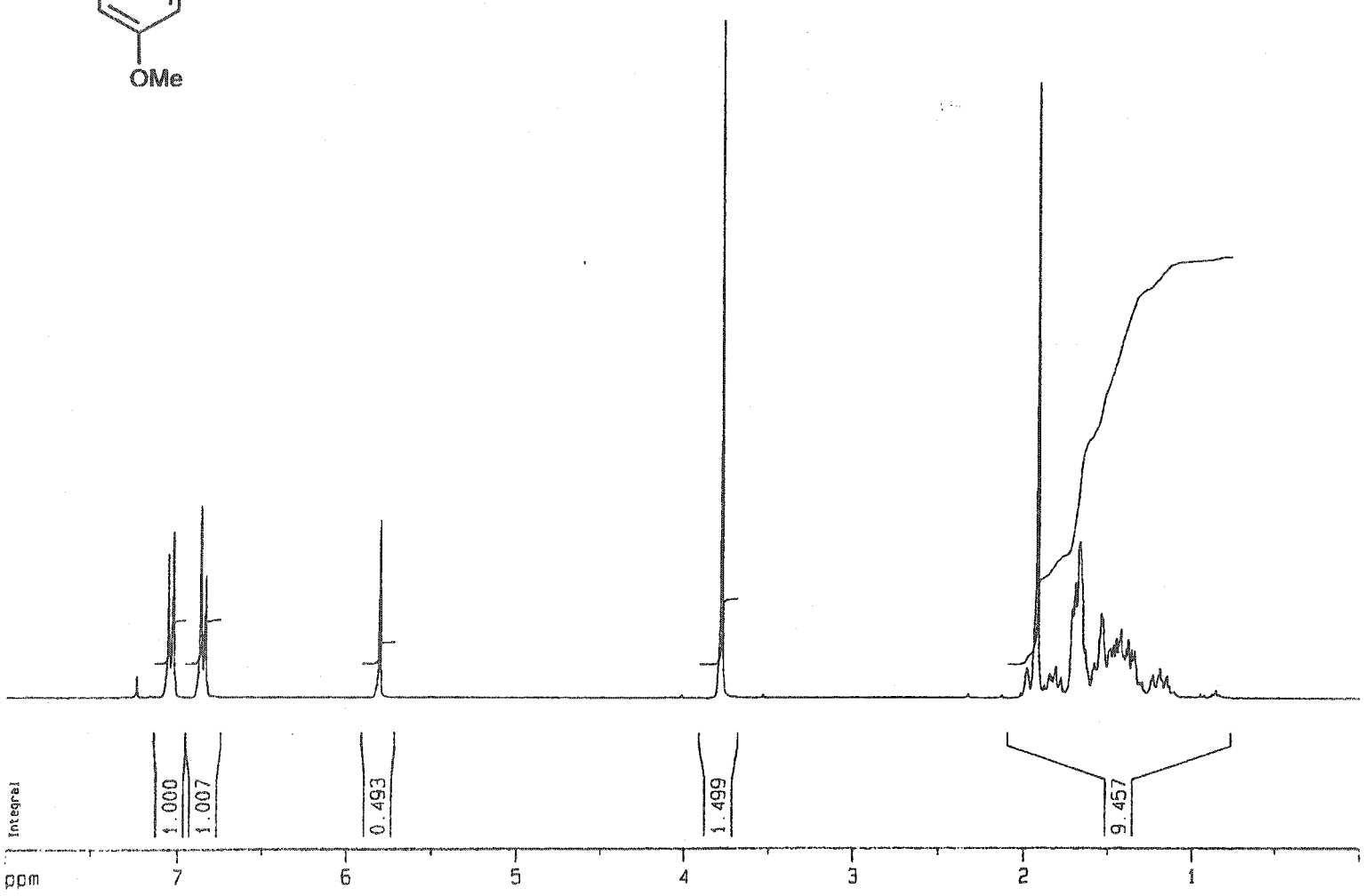
F2 - Processing parameters

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

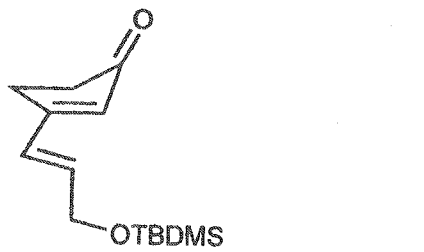
1D NMR plot parameters

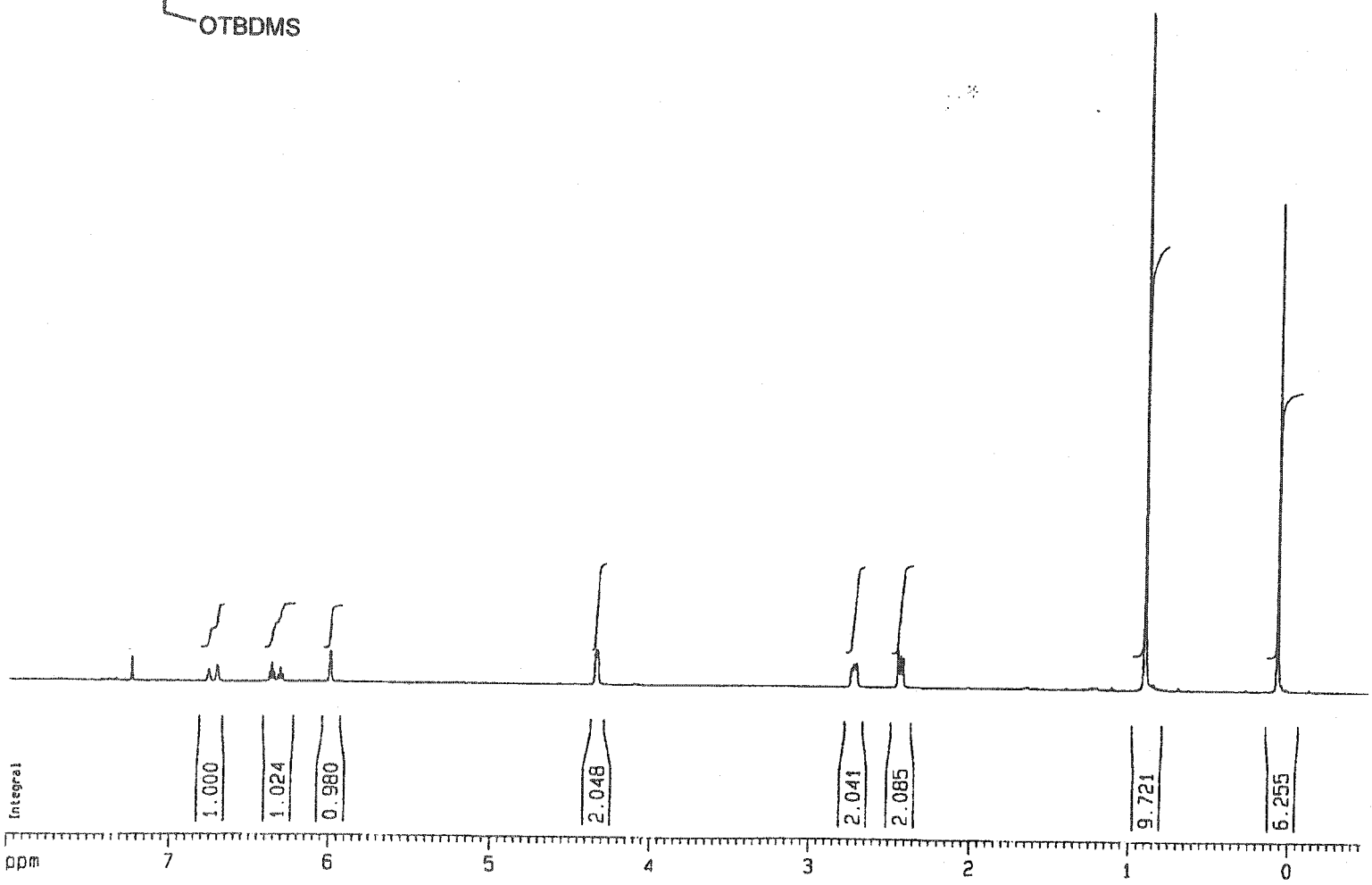
CX	20.00 cm
CY	10.00 cm
F1P	8.000 ppm
F1	2401.04 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	0.40000 ppm/cm
HZCM	120.05200 Hz/cm






```
Current Data Parameters
NAME                  jaf-44
EXPNO                      1
PROCNO                     1

F2 - Acquisition Parameters
Date_              20020314
Time                   10.47
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                   98.400 usec
DE                    6.00 usec
TE                   300.0 K
D1                 1.00000000 sec

============ CHANNEL f1 ==========
NUC1                       1H
P1                    10.00 usec
PL1                   -3.00 dB
SFO1              300.1319477 MHz

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

1D NMR plot parameters
CX                    20.00 cm
CY                    10.00 cm
F1P                    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
```





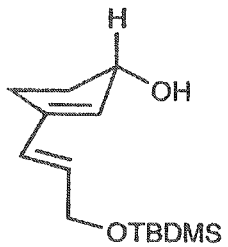
Current Data Parameters
NAME jaf-200
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20021119
Time 11.48
INSTRUM av300
PROBHD 5 mm ONP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 228.1
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

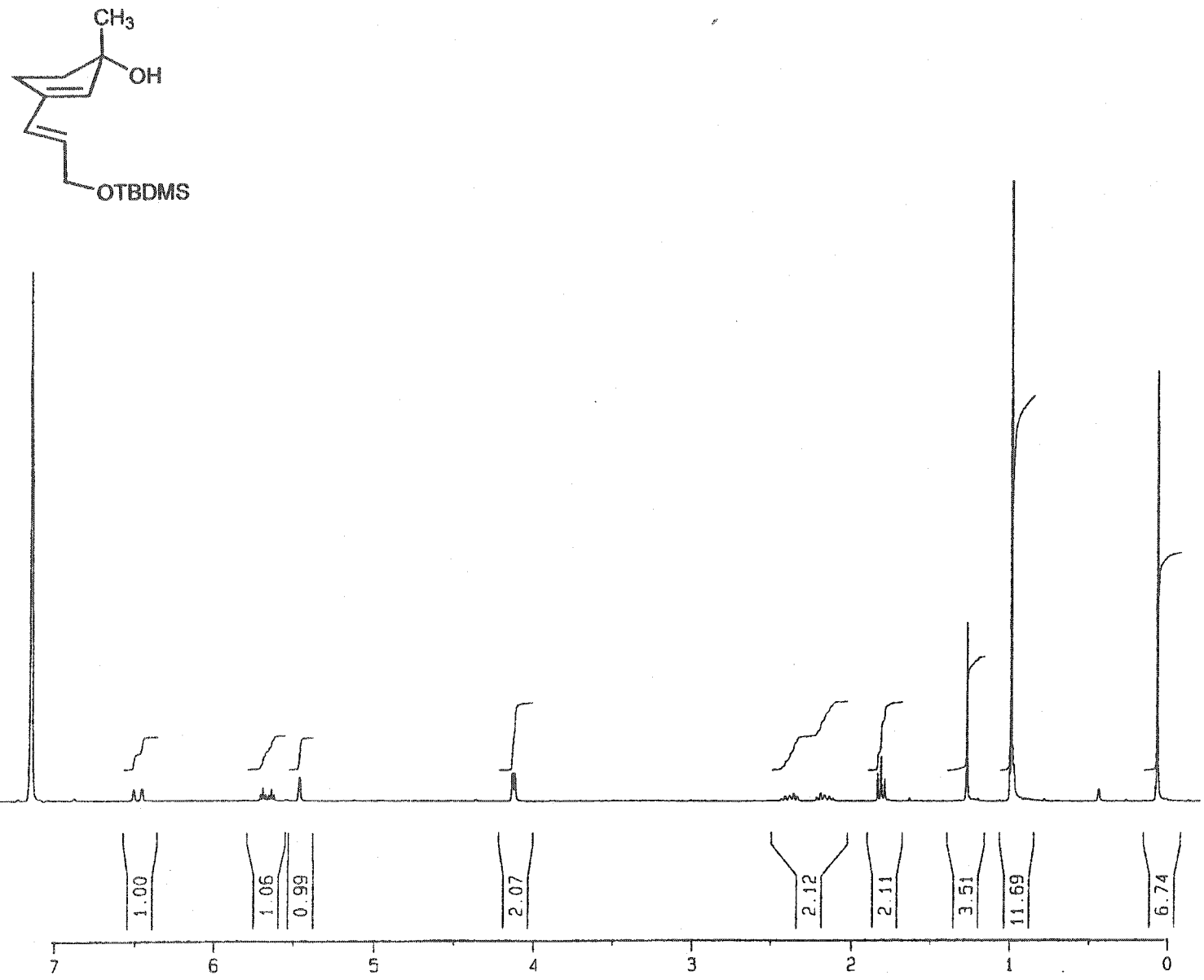
========== CHANNEL f1 ==========
NUC1 1H
P1 9.75 usec
PL1 -3.00 dB
SFO1 300.1319477 MHz

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

1D NMR plot parameters
CX 20.00 cm
CY 10.00 cm
F1P 8.000 ppm
F1 2401.04 Hz
F2P -0.500 ppm
F2 -150.06 Hz
PPMCM 0.42500 ppm/cm
HZCM 127.55524 Hz/cm




```
Current Data Parameters
NAME                  jaf-277
EXPNO                       1
PROCNO                      1

F2 - Acquisition Parameters
Date_              20030303
Time                   11.30
INSTRUM                av300
PROBHD   5 mm QNP  1H/1
PULPROG                zg30
TD                    30720
SOLVENT               CDCl3
NS                        16
DS                         2
SWH                5081.301 Hz
FIDRES             0.165407 Hz
AQ                 3.0228980 sec
RG                       181
DW                  98.400 usec
DE                   6.00 usec
TE                  300.0 K
D1                1.00000000 sec

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

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

1D NMR plot parameters
CX                   20.00 cm
CY                   10.00 cm
F1P                  7.590 ppm
F1                 2277.85 Hz
F2P                 -0.302 ppm
F2                  -90.55 Hz
PPMCM              0.39456 ppm/cm
HZCM             118.42014 Hz/cm
```



benzene

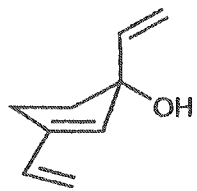
Current Data Parameters
NAME jaf-267b
EXPNO 1
PROCNO 1

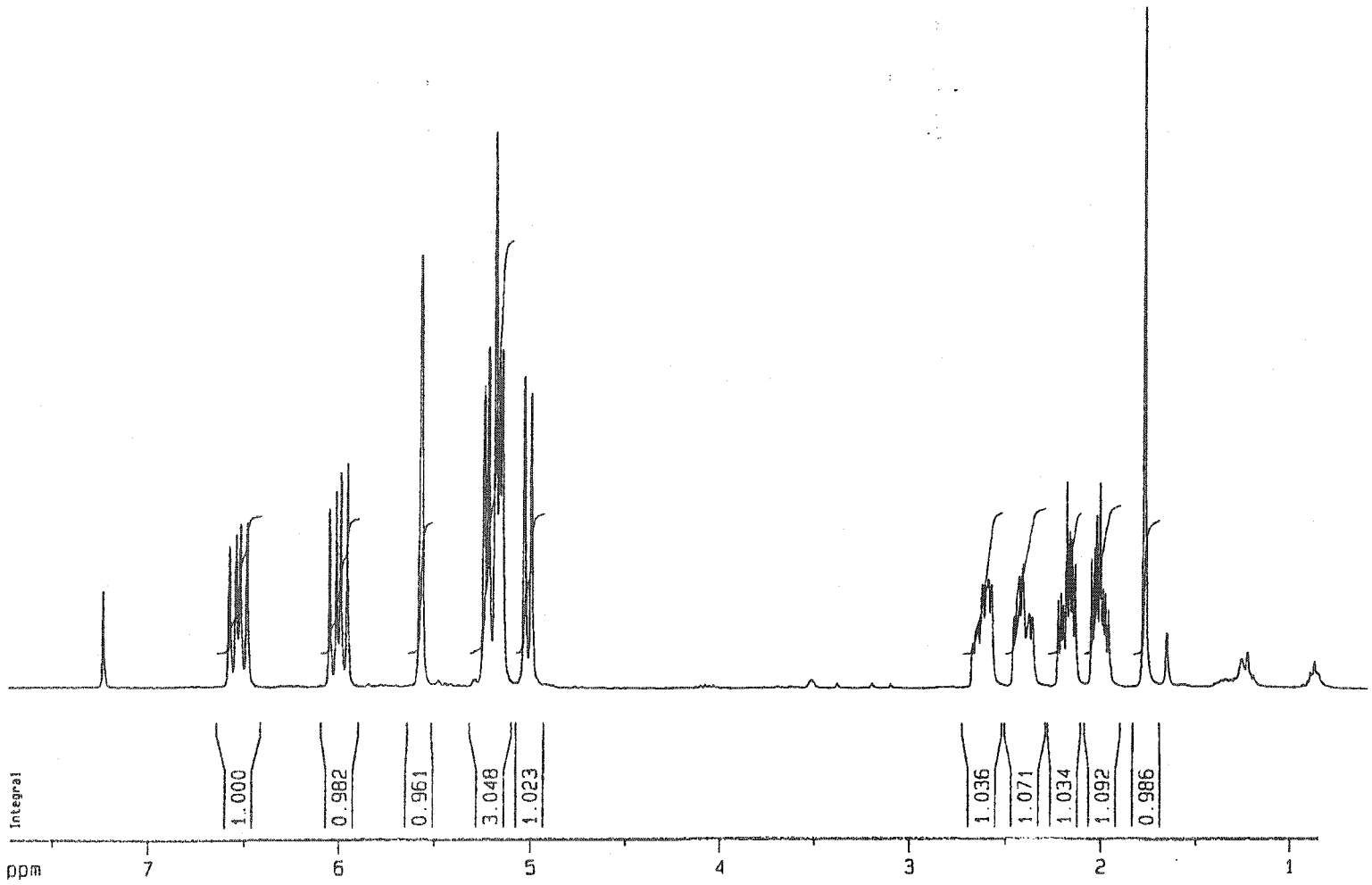
F2 - Acquisition Parameters
Date_ 20030221
Time 9.57
INSTRUM av300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 362
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

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

F2 - Processing parameters
SI 65536
SF 300.1300000 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 7.596 ppm
F1 2279.78 Hz
F2P -0.207 ppm
F2 -62.25 Hz
PPMCM 0.39017 ppm/cm
HZCM 117.10131 Hz/cm





Current Data Parameters

NAME	jaf-248
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20030126
Time	15.29
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	181
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

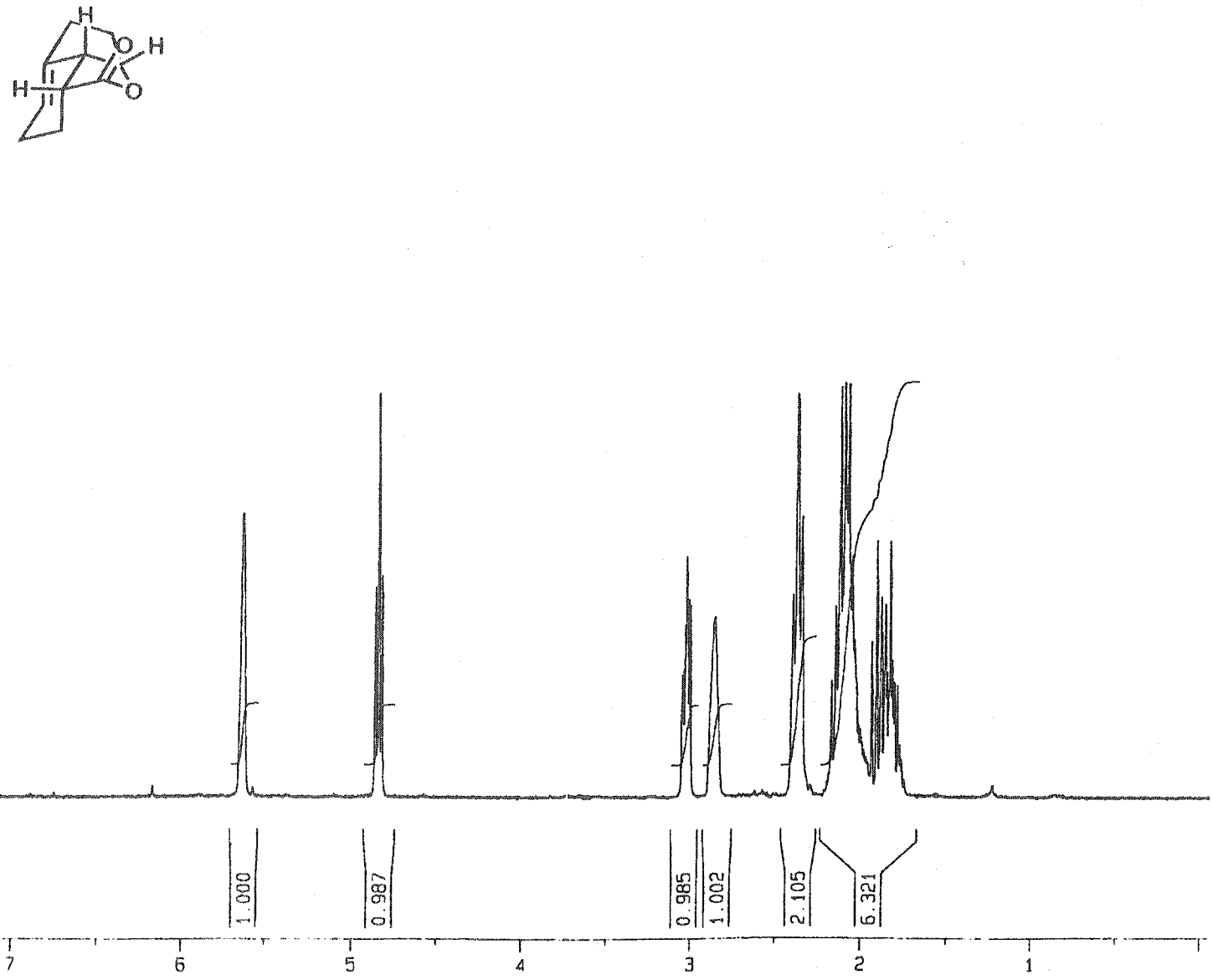
NUC1	1H
P1	9.75 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

F2 - Processing parameters

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

1D NMR plot parameters

CX	20.00 cm
CY	10.00 cm
F1P	7.739 ppm
F1	2322.67 Hz
F2P	0.588 ppm
F2	176.37 Hz
PPMCM	0.35756 ppm/cm
HZCM	107.31502 Hz/cm



Current Data Parameters

NAME	jaf-242e
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20030123
Time	16.07
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5091.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	512
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

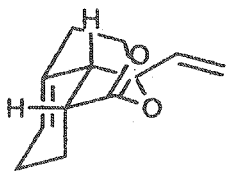
NUC1	1H
P1	9.75 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

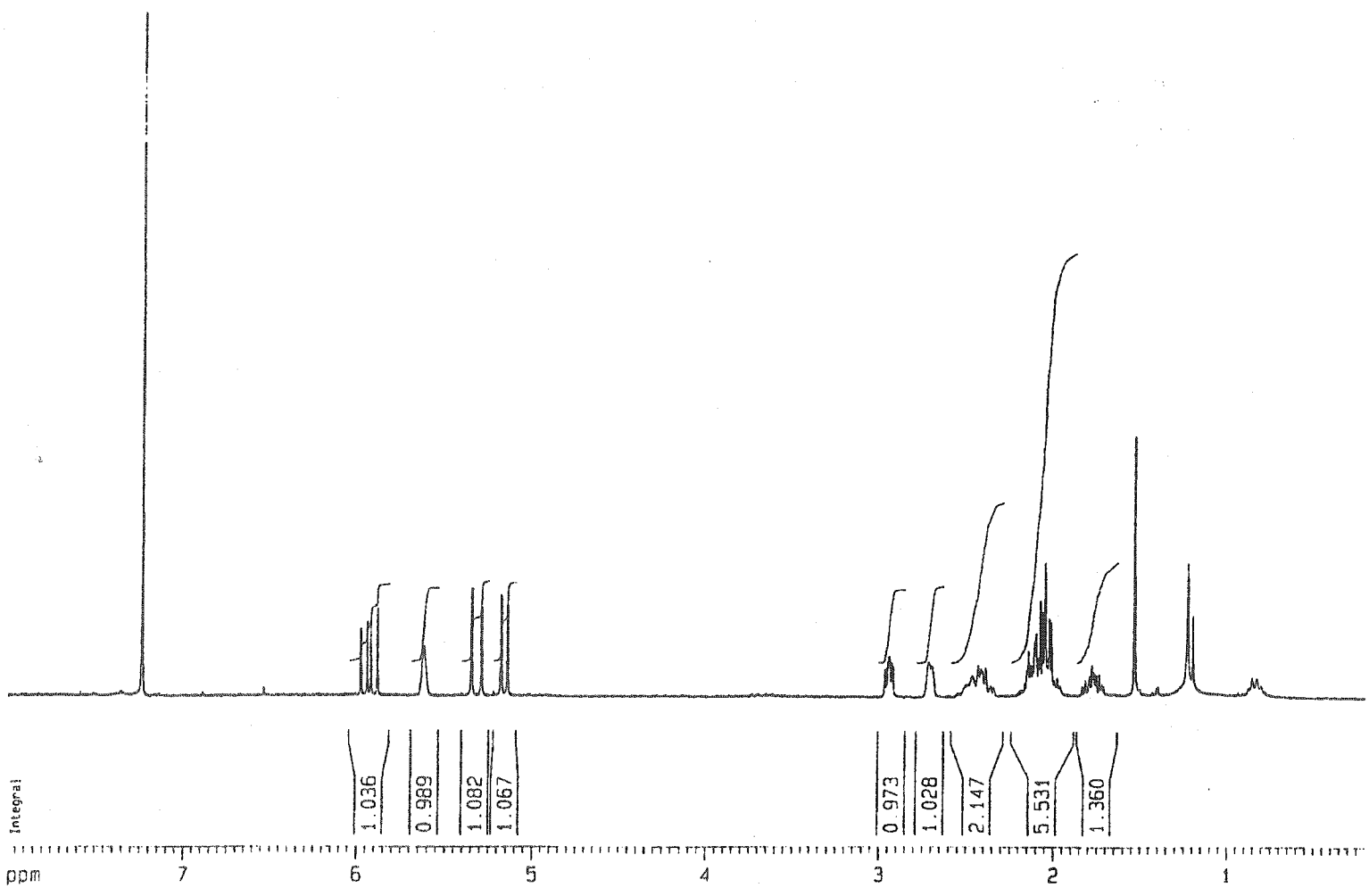
F2 - Processing parameters

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	7.459 ppm
F1	2238.63 Hz
F2P	-0.059 ppm
F2	-17.57 Hz
PPMCM	0.37587 ppm/cm
HZCM	112.81006 Hz/cm





Current Data Parameters

NAME	jaf-249
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20030131
Time	11.55
INSTRUM	av300
PROBHD	5 mm GNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	912.3
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

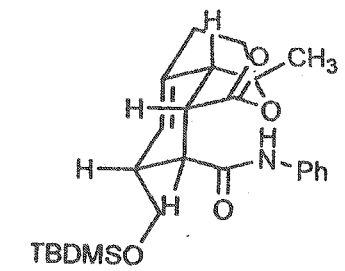
NUC1	1H
P1	9.75 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

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	7.997 ppm
F1	2400.25 Hz
F2P	0.200 ppm
F2	60.00 Hz
PPMCM	0.38987 ppm/cm
HZCM	117.01215 Hz/cm



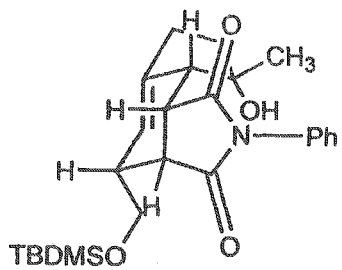
Current Data Parameters
NAME jaf-281cosy
EXPNO 1
PROCNO 1

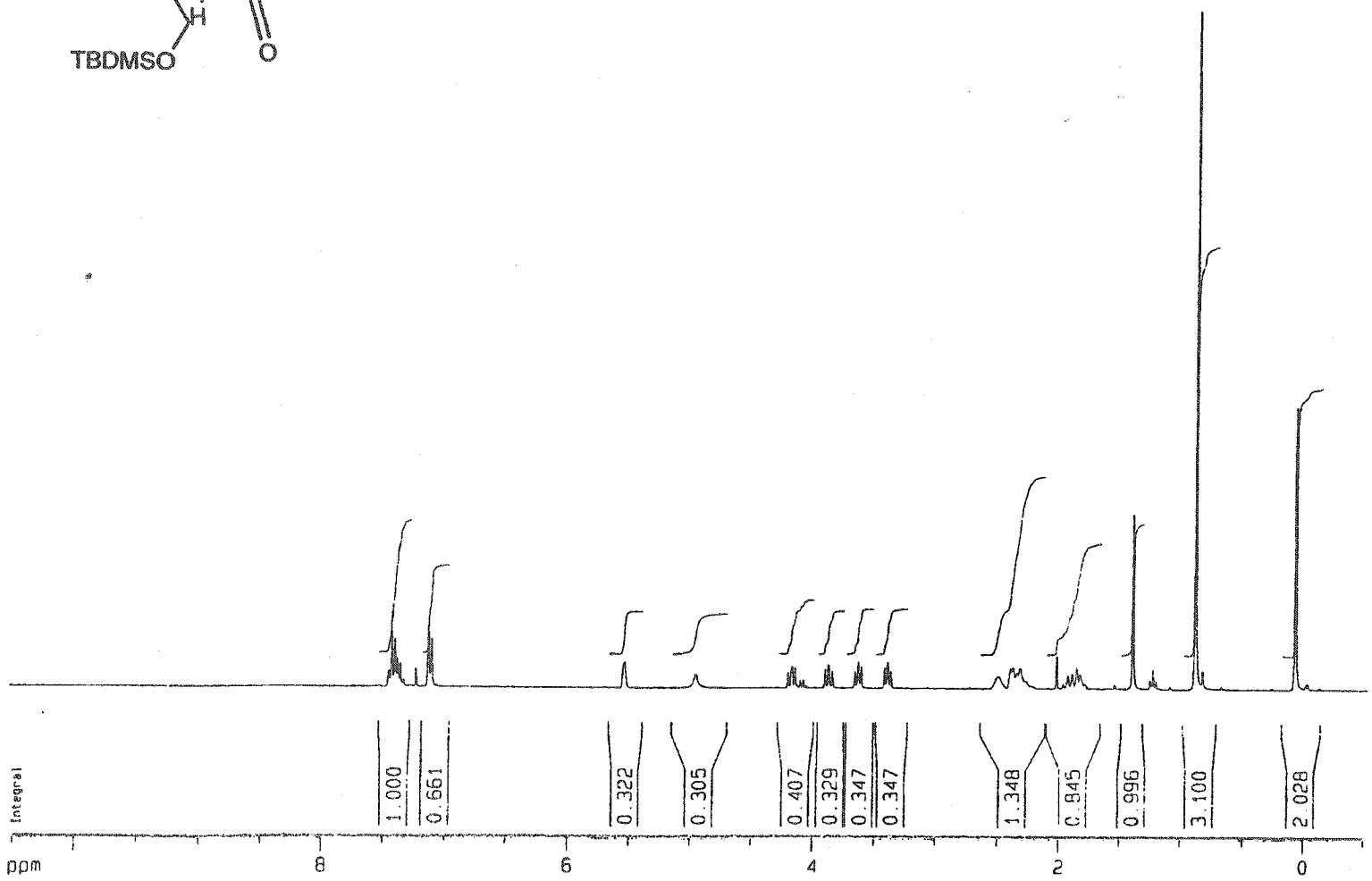
F2 - Acquisition Parameters
Date_ 20030404
Time 16.31
INSTRUM av300
PROBHD 5 mm GNP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 80.6
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

========== CHANNEL f1 ==========
NUC1 1H
P1 10.50 usec
PL1 -3.00 dB
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 15.00 cm
F1P 10.417 ppm
F1 3126.36 Hz
F2P -0.405 ppm
F2 -121.48 Hz
PPMCM 0.54107 ppm/cm
HZCM 162.39207 Hz/cm





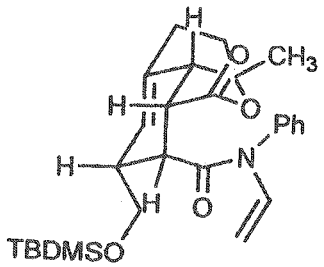
Current Data Parameters
NAME jaf-290
EXPNO 1
PROCNO 1

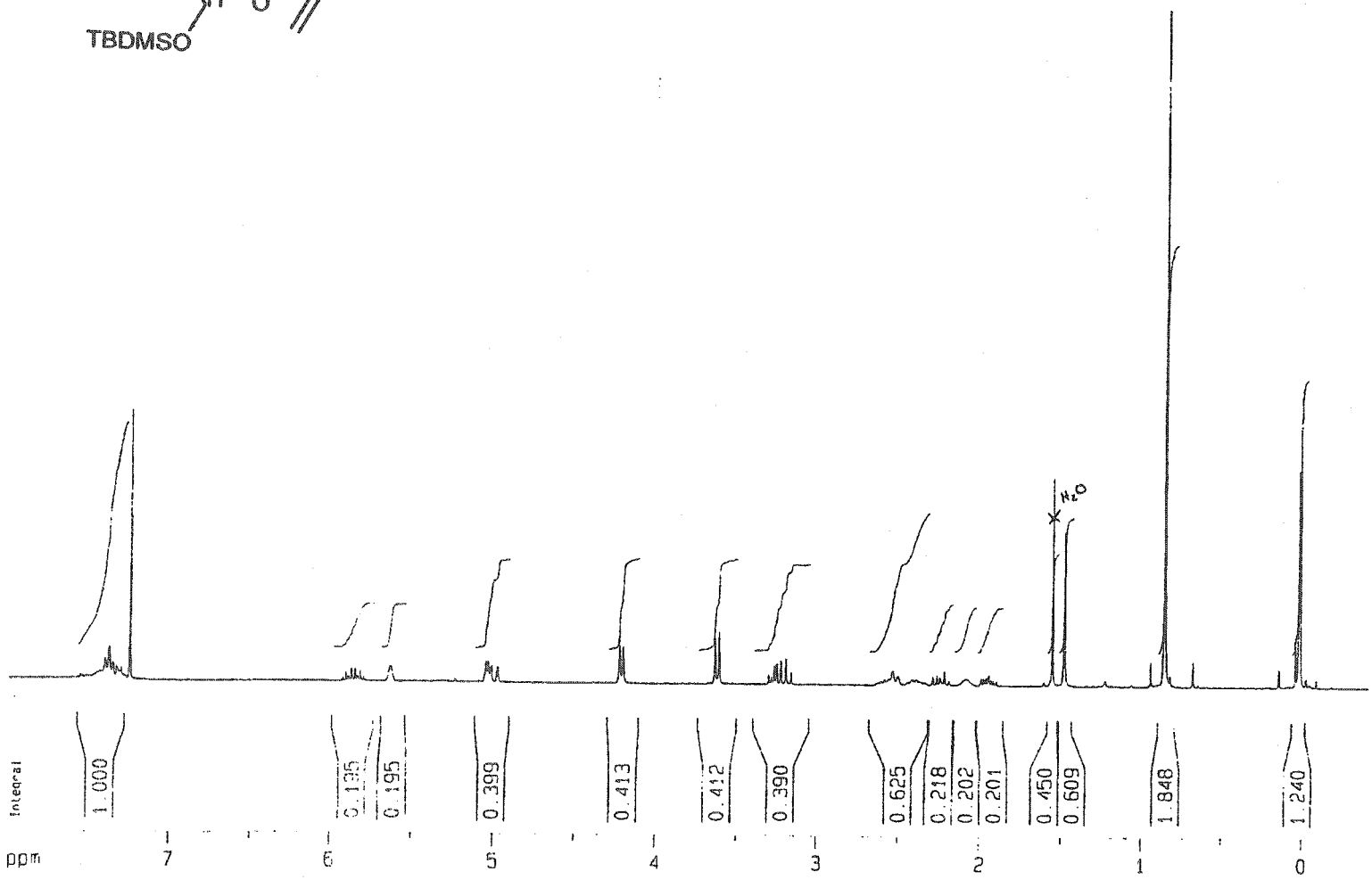
F2 - Acquisition Parameters
Date_ 20030313
Time 12.10
INSTRUM av300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165403 Hz
AQ 3.0228980 sec
RG 128
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

========== CHANNEL f1 ==========
NUC1 1H
P1 10.50 usec
PL1 -3.00 dB
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 10.539 ppm
F1 3163.12 Hz
F2P -0.536 ppm
F2 -160.95 Hz
PPMCM 0.55377 ppm/cm
HZCM 166.20393 Hz/cm





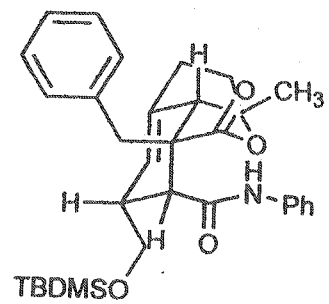
Current Data Parameters
NAME jaf-299a
EXPNO 1
PROCNO 1

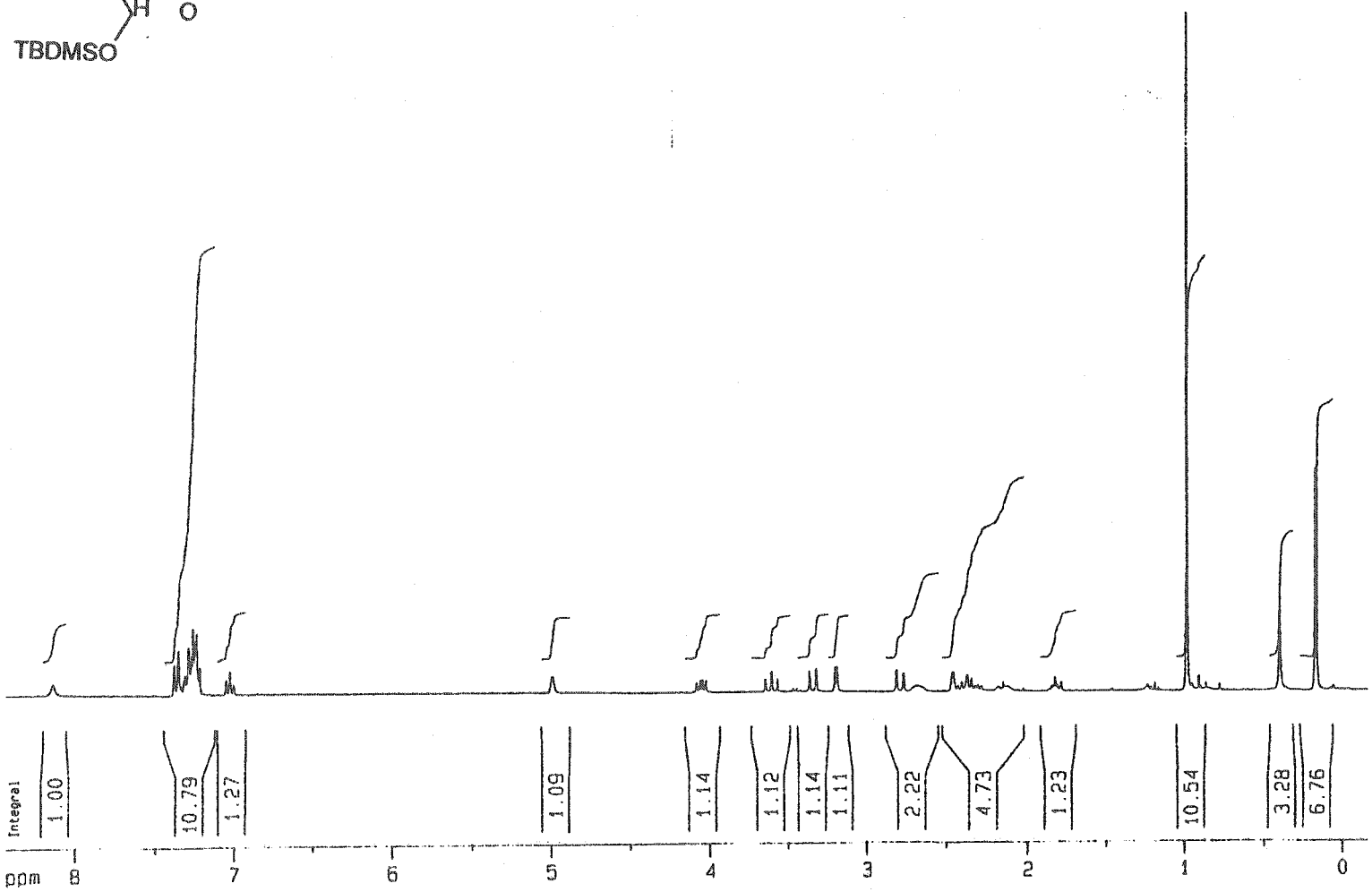
F2 - Acquisition Parameters
Date_ 20030325
Time 22.38
INSTRUM av300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 724.1
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

========== 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 7.978 ppm
F1 2394.34 Hz
F2P -0.414 ppm
F2 -124.35 Hz
PPMCM 0.41960 ppm/cm
HZCM 125.93426 Hz/cm





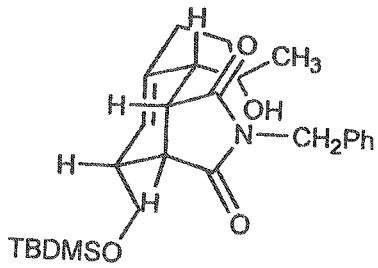
Current Data Parameters
NAME jaf-322a
EXPNO 1
PROCNO 1

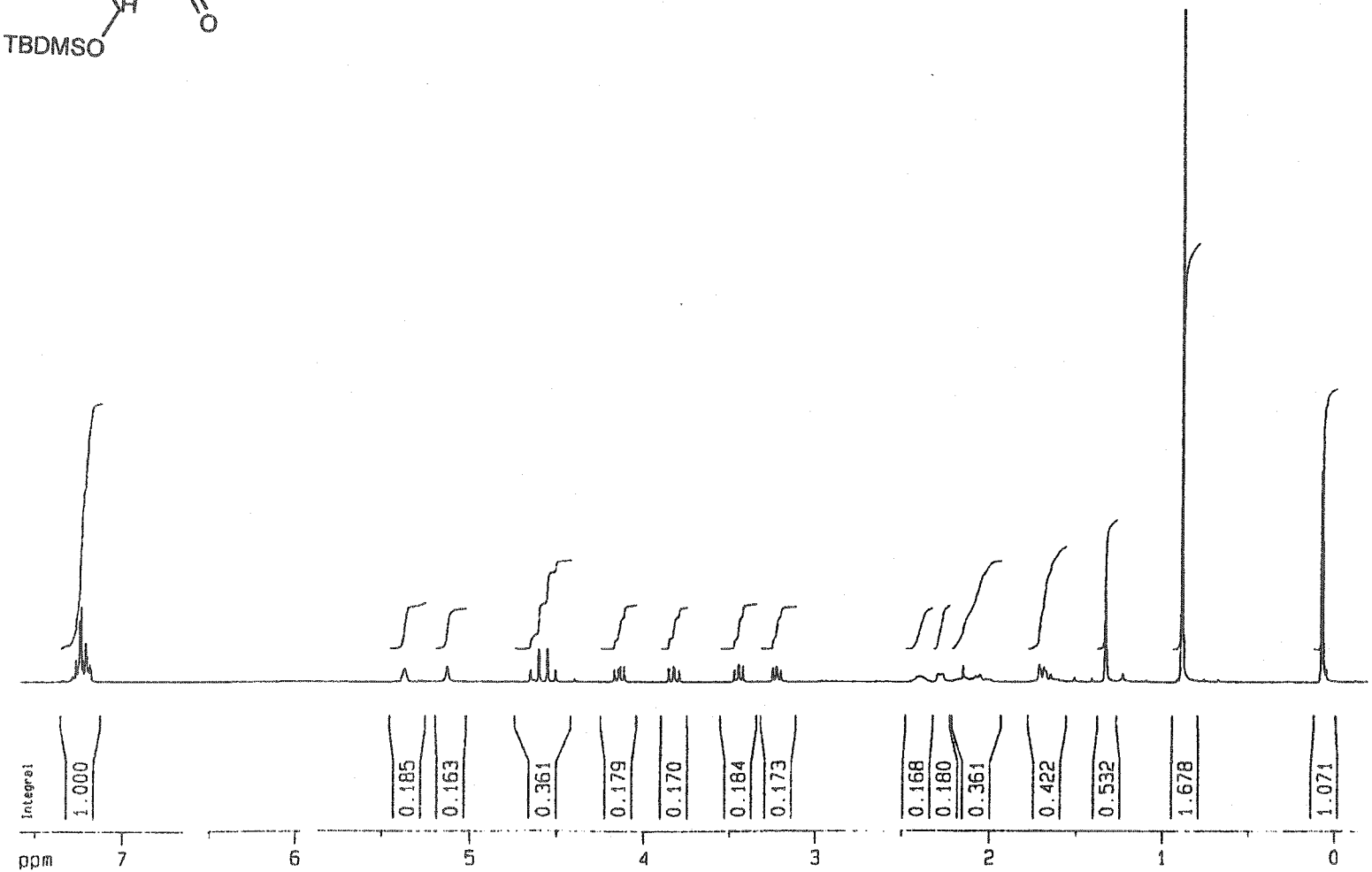
F2 - Acquisition Parameters
Date_ 20030413
Time 12.57
INSTRUM av300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 161.3
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

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

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

1D NMR plot parameters
CX 20.00 cm
CY 10.00 cm
F1P 8.436 ppm
F1 2531.85 Hz
F2P -0.170 ppm
F2 -51.03 Hz
PPMCM 0.43029 ppm/cm
HZCM 129.14386 Hz/cm





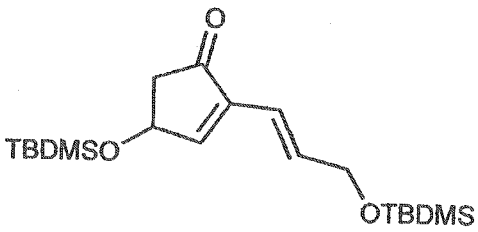
Current Data Parameters
NAME jaf-336
EXPNO 1
PROCNO 1

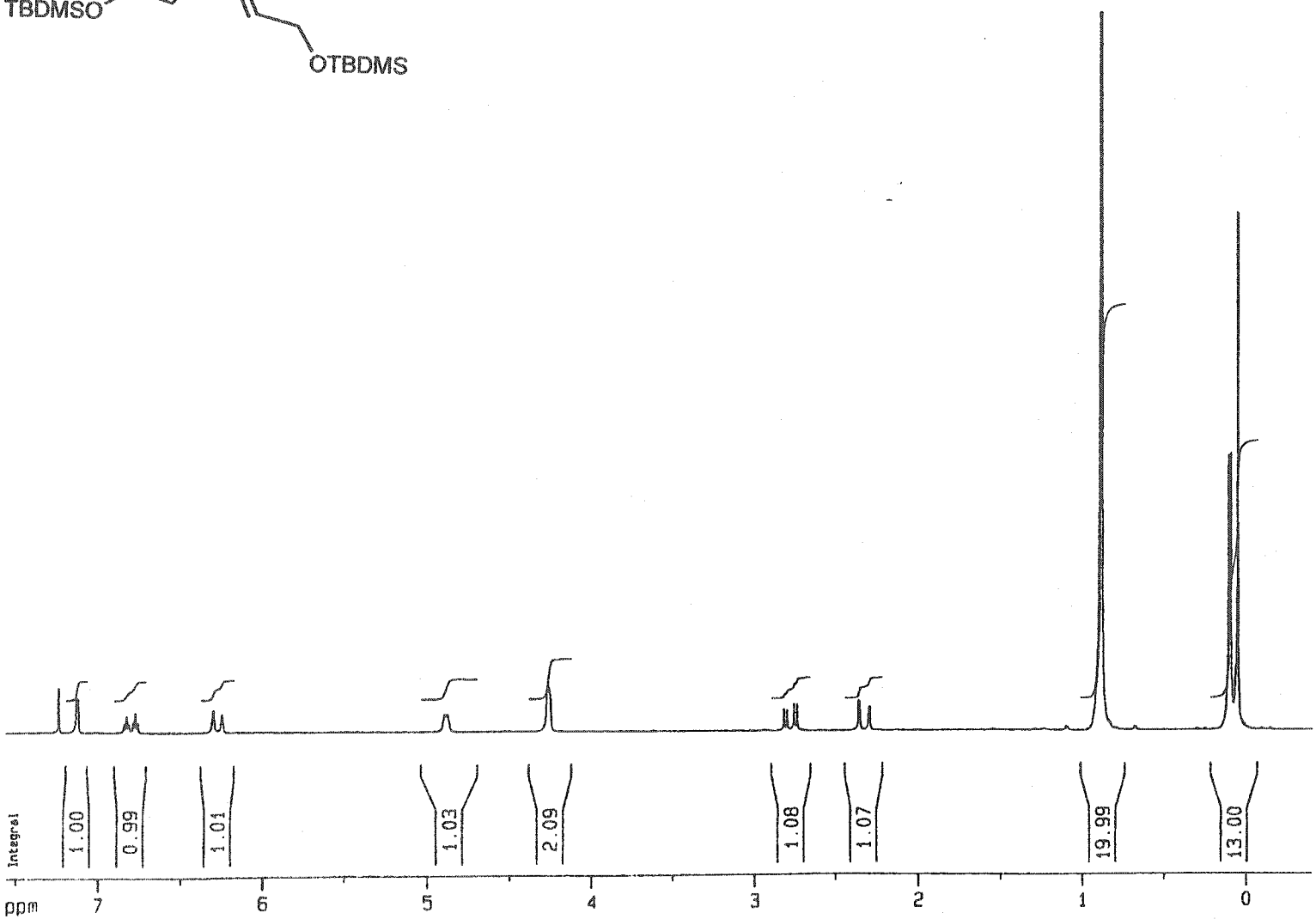
F2 - Acquisition Parameters
Date_ 20030425
Time 10.43
INSTRUM av300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 287.4
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

========== 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 7.592 ppm
F1 2278.49 Hz
F2P -0.193 ppm
F2 -58.06 Hz
PPMCM 0.38926 ppm/cm
HZCM 116.82769 Hz/cm





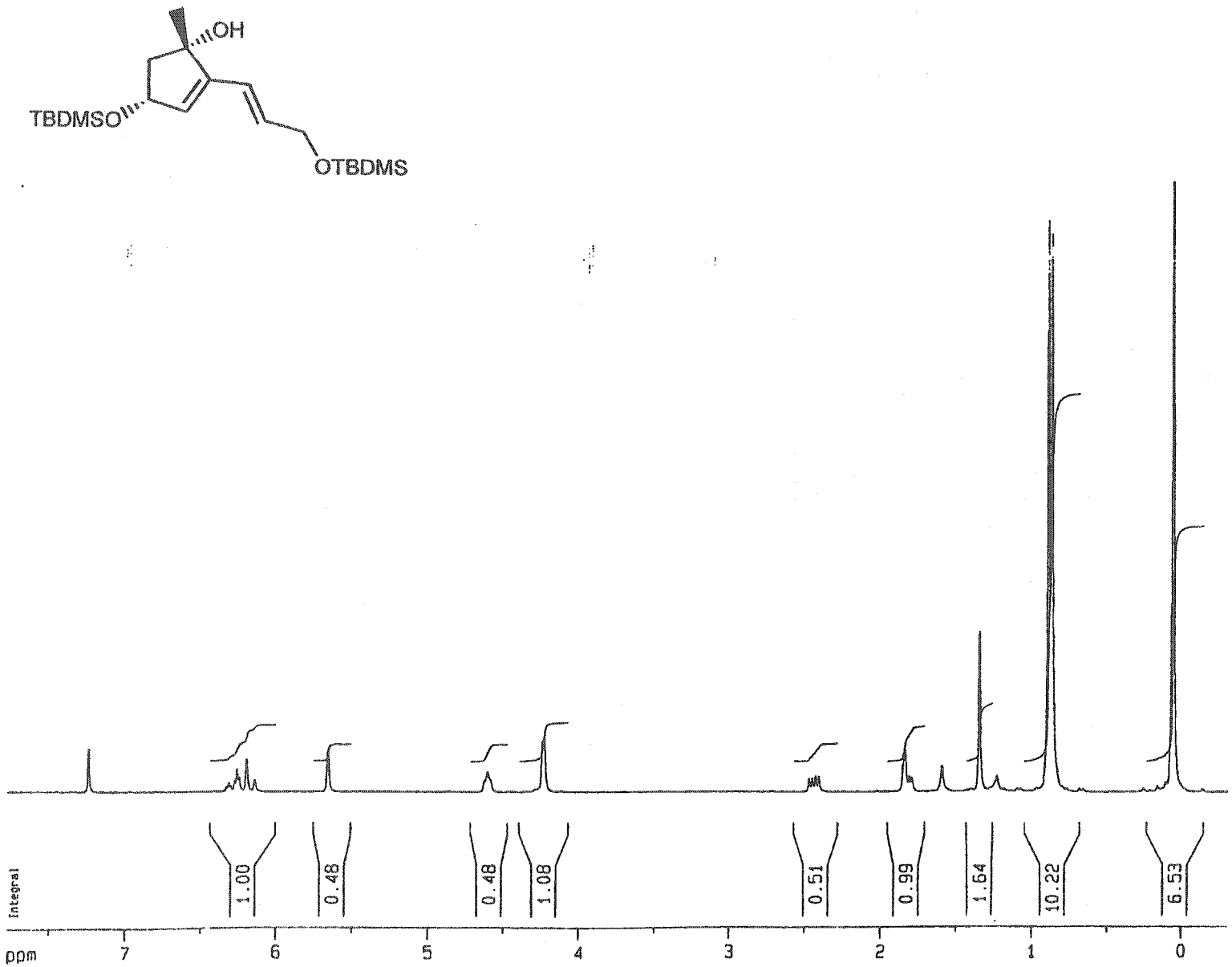
Current Data Parameters
NAME jaf-422a
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20030715
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 203.2
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

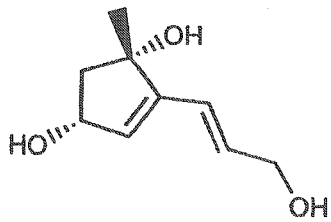
========== CHANNEL f1 ==========
NUC1 1H
P1 10.50 usec
PL1 -3.00 dB
SFO1 300.1319477 MHz

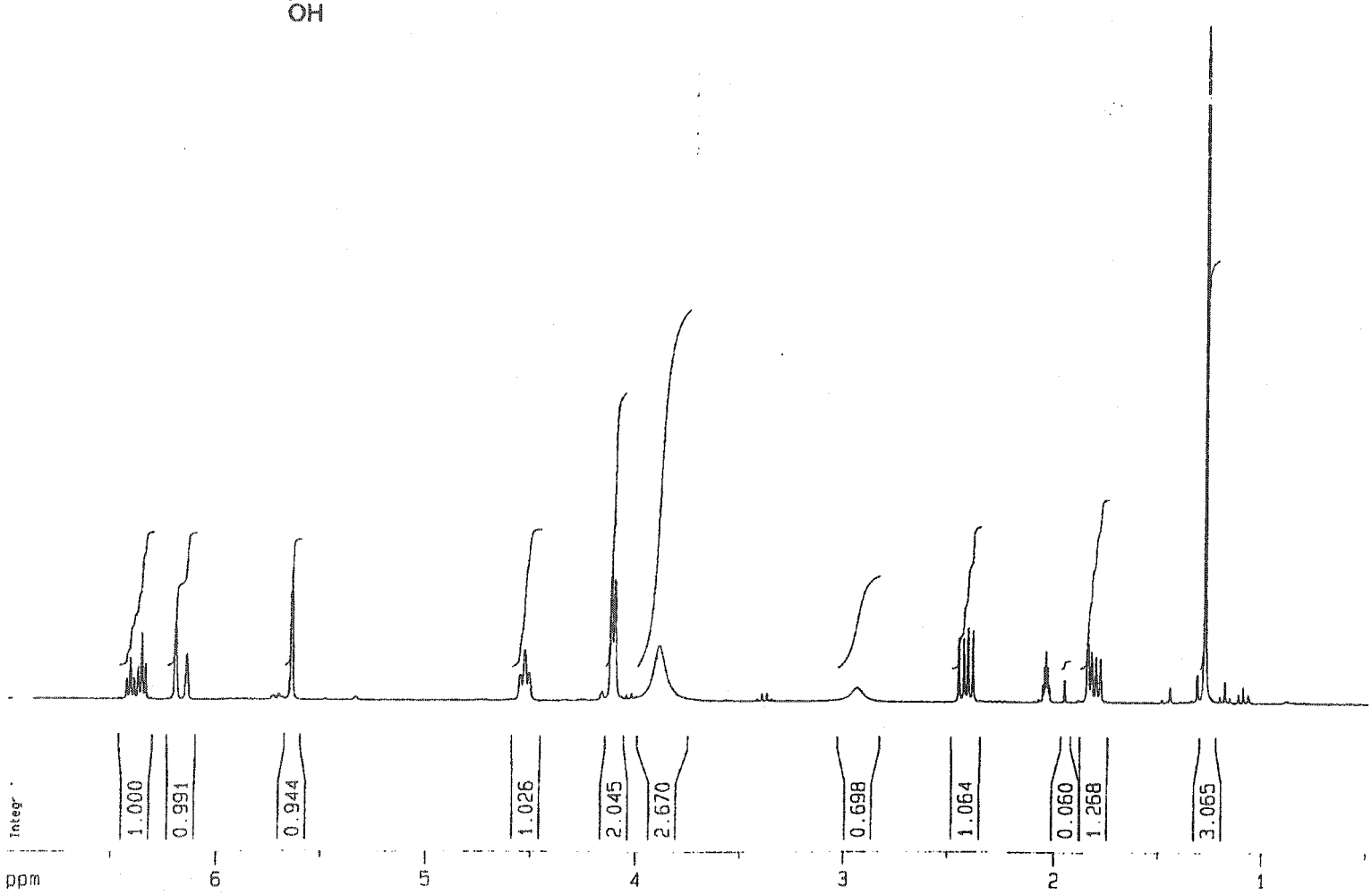
F2 - Processing parameters
SI 65536
SF 300.1300000 MHz
WDW EM
SSB 0
LB 0.10 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 20.00 cm
CY 15.00 cm
F1P 7.564 ppm
F1 2270.28 Hz
F2P -0.406 ppm
F2 -121.78 Hz
PPMCM 0.39850 ppm/cm
HZCM 119.60267 Hz/cm




```
Current Data Parameters
NAME                  jaf-415
EXPNO                       1
PROCNO                      1

F2 - Acquisition Parameters
Date_              20030710
Time                  14.39
INSTRUM               av300
PROBHD   5 mm QNP  1H/1
PULPROG                zg30
TD                    30720
SOLVENT               CDCl3
NS                       16
DS                        0
SWH                5081.301 Hz
FIDRES            0.165407 Hz
AQ                3.0228980 sec
RG                      256
DW                   98.400 usec
DE                    6.00 usec
TE                   300.0 K
D1              1.00000000 sec

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

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

1D NMR plot parameters
CX                   20.00 cm
CY                   10.00 cm
F1P                  7.782 ppm
F1                 2335.52 Hz
F2P                 -0.309 ppm
F2                  -92.78 Hz
PPMCM              0.40454 ppm/cm
HZCM             121.41483 Hz/cm
```





Current Data Parameters

NAME	jaf-631
EXPNO	3
PROCNO	1

F2 - Acquisition Parameters

Date_	20040226
Time	11.09
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	203.2
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

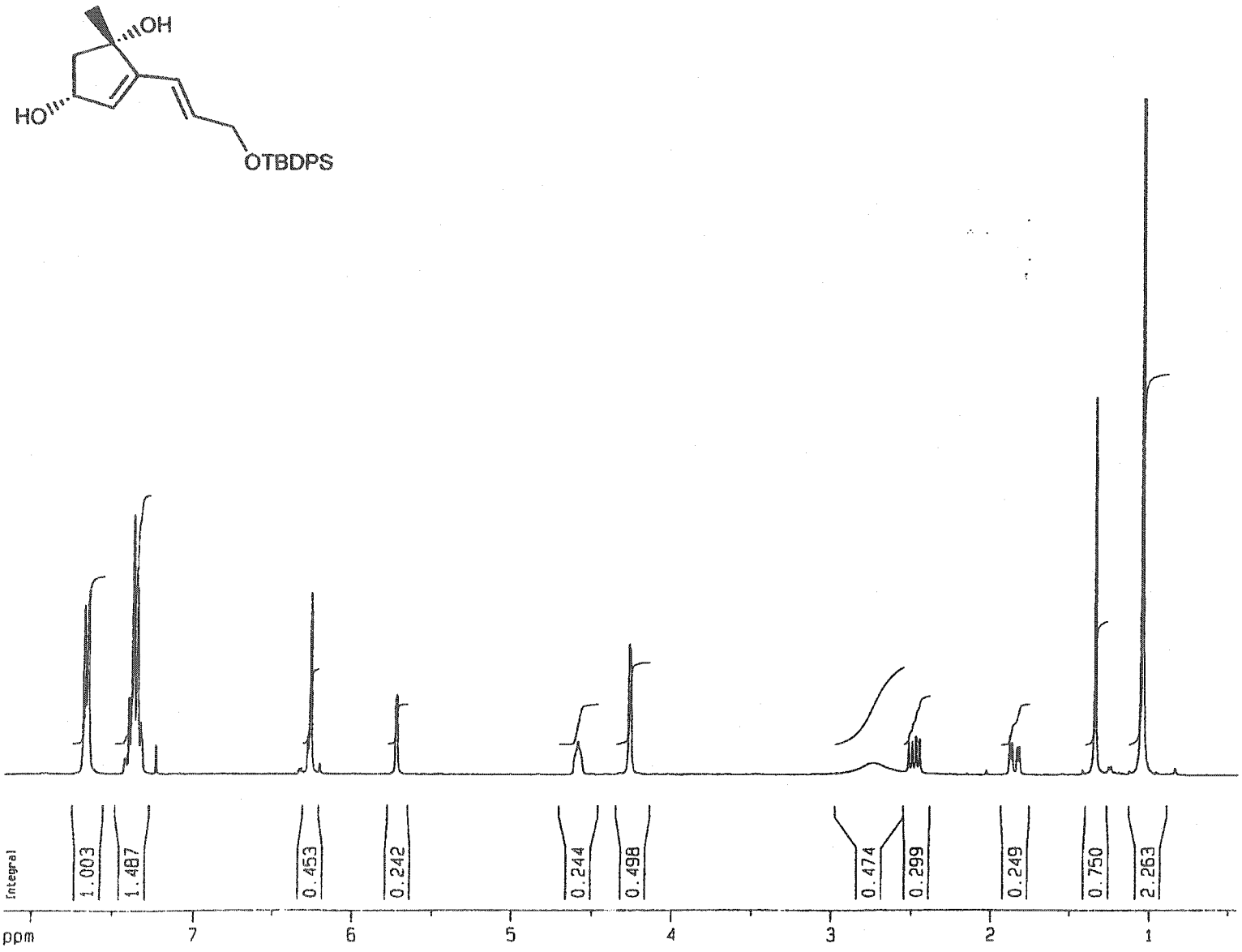
NUC1	1H
P1	10.50 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

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	6.995 ppm
F1	2099.34 Hz
F2P	0.489 ppm
F2	146.70 Hz
PPMCM	0.32530 ppm/cm
HZCM	97.63198 Hz/cm



Current Data Parameters

NAME	jaf-454
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20030801
Time	10.16
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	101.5
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

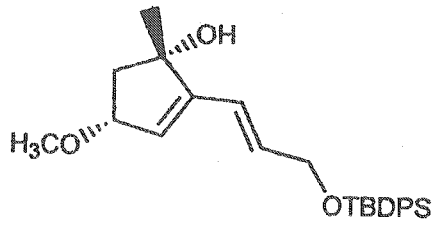
NUC1	1H
P1	10.50 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

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	20.00 cm
F1P	6.173 ppm
F1	2452.91 Hz
F2P	0.440 ppm
F2	131.92 Hz
PPMCM	0.38667 ppm/cm
HZCM	116.04988 Hz/cm



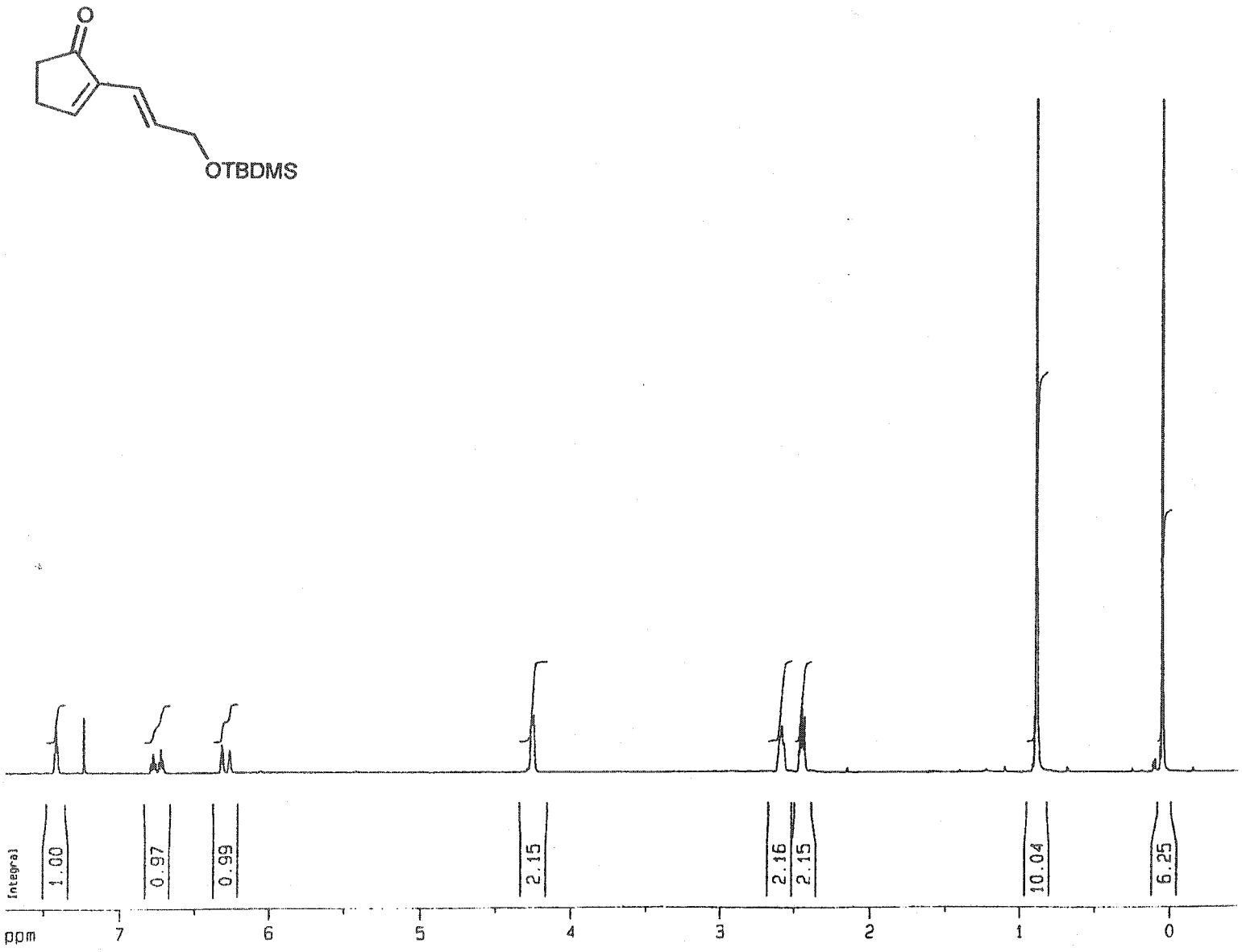
Current Data Parameters
NAME jaf-475
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20030902
Time 10.51
INSTRUM av300
PROBHD 5 mm ONP 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 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
SFO1 300.1319477 MHz

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

1D NMR plot parameters
CX 20.00 cm
CY 10.00 cm
F1P 8.201 ppm
F1 2461.47 Hz
F2P 0.580 ppm
F2 174.18 Hz
PPMCM 0.38105 ppm/cm
HZCM 114.36446 Hz/cm



Current Data Parameters

NAME	jaf-469
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20030827
Time	14.06
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	256
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

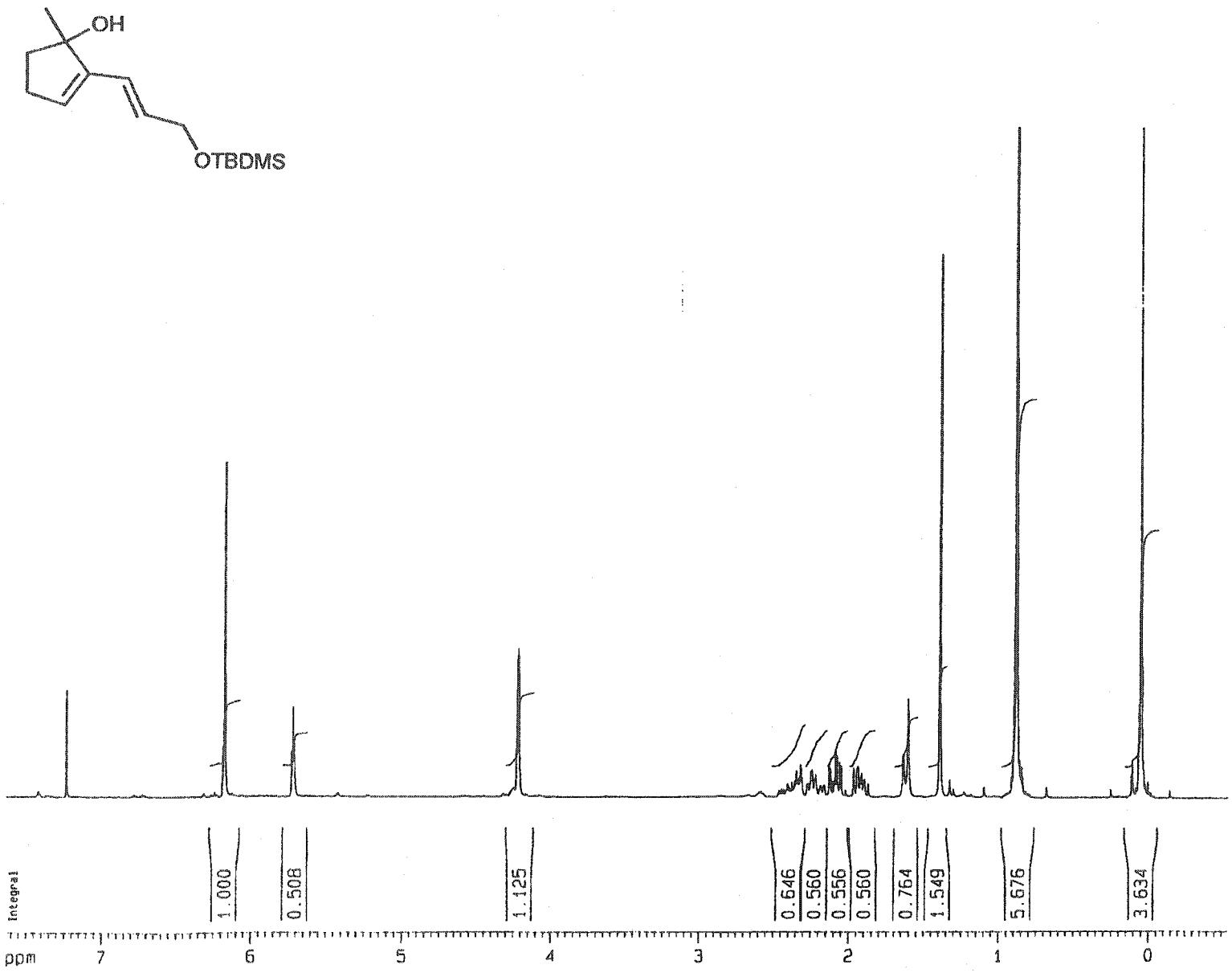
NUC1	1H
P1	10.50 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

F2 - Processing parameters

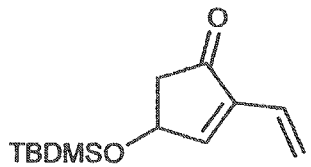
SI	65536
SF	300.1300000 MHz
WDW	EM
SSB	0
LB	0.10 Hz
GB	0
PC	1.00

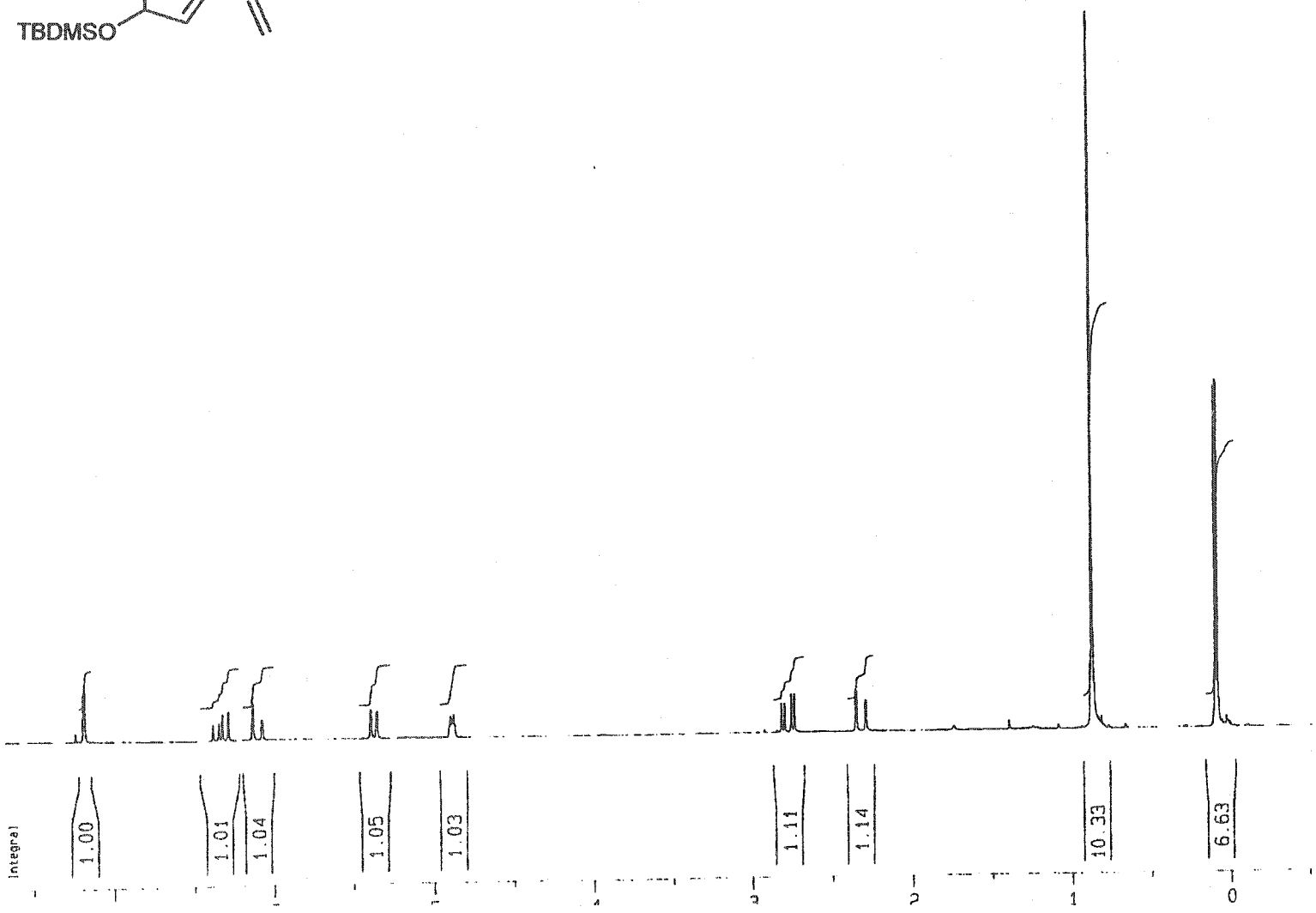
1D NMR plot parameters

CX	20.00 cm
CY	20.00 cm
F1P	7.756 ppm
F1	2327.75 Hz
F2P	-0.428 ppm
F2	-128.44 Hz
PPMCM	0.40919 ppm/cm
HZCM	122.80983 Hz/cm

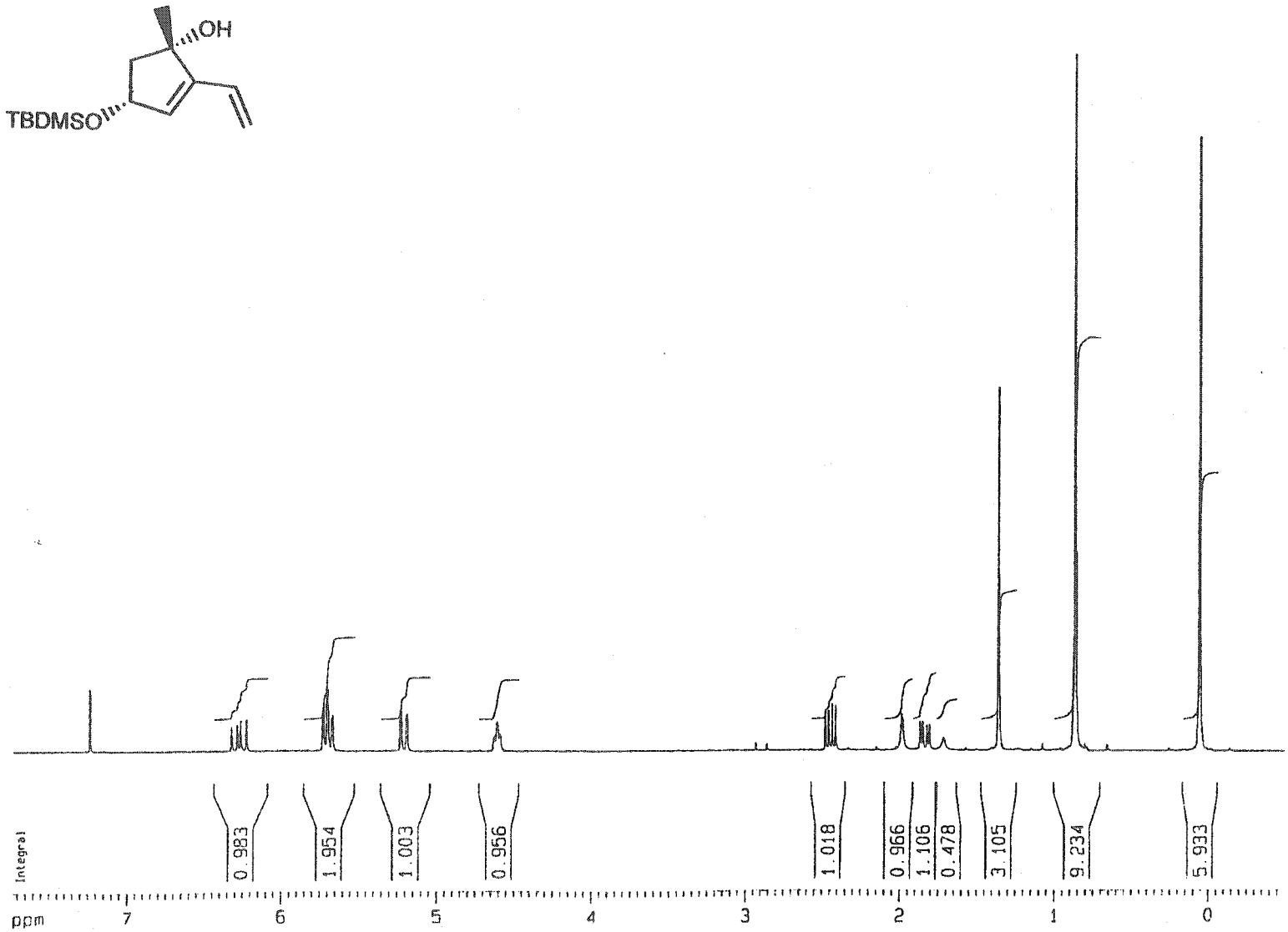



```
Current Data Parameters
NAME                  jaf-470
EXPNO
PROCNO                     1

F2 - Acquisition Parameters
Date_              20030829
Time                  11.14
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                    161.3
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
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                   45.00 cm
F1P                  7.639 ppm
F1                2292.57 Hz
F2P                 -0.545 ppm
F2                -163.63 Hz
PPMCM             0.40919 ppm/cm
HZCM            122.80983 Hz/cm
```






```
Current Data Parameters
NAME                  jaf-487a
EXPNO                        1
PROCNO                       1

F2 - Acquisition Parameters
Date_              20030917
Time                   14.16
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
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                     15.00 cm
F1P                     7.685 ppm
F1                   2306.64 Hz
F2P                    -0.522 ppm
F2                   -156.59 Hz
PPMCM                0.41036 ppm/cm
HZCM               123.16173 Hz/cm
```



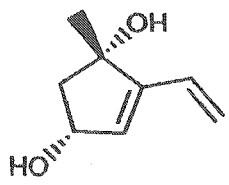
Current Data Parameters
NAME jaf-492
EXPNO 1
PROCNO 1

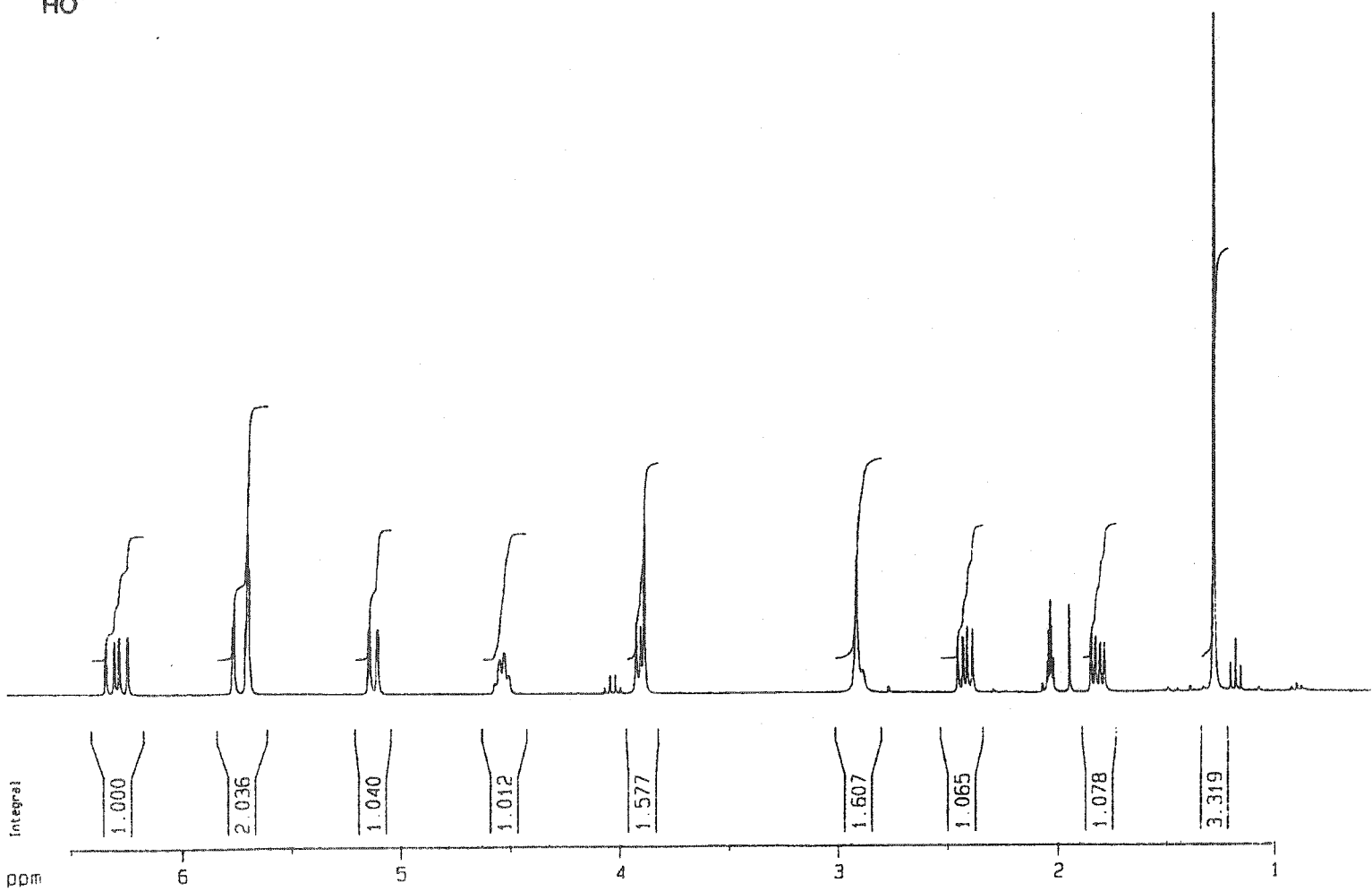
F2 - Acquisition Parameters
Date_ 20030919
Time 12.36
INSTRUM av300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 181
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

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

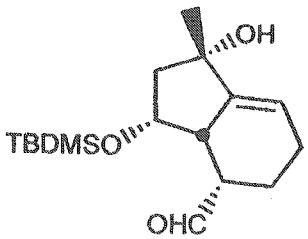
F2 - Processing parameters
SI 65536
SF 300.1300000 MHz
WDW EM
SSB 0
LB 0.10 Hz
GB 0
PC 1.00

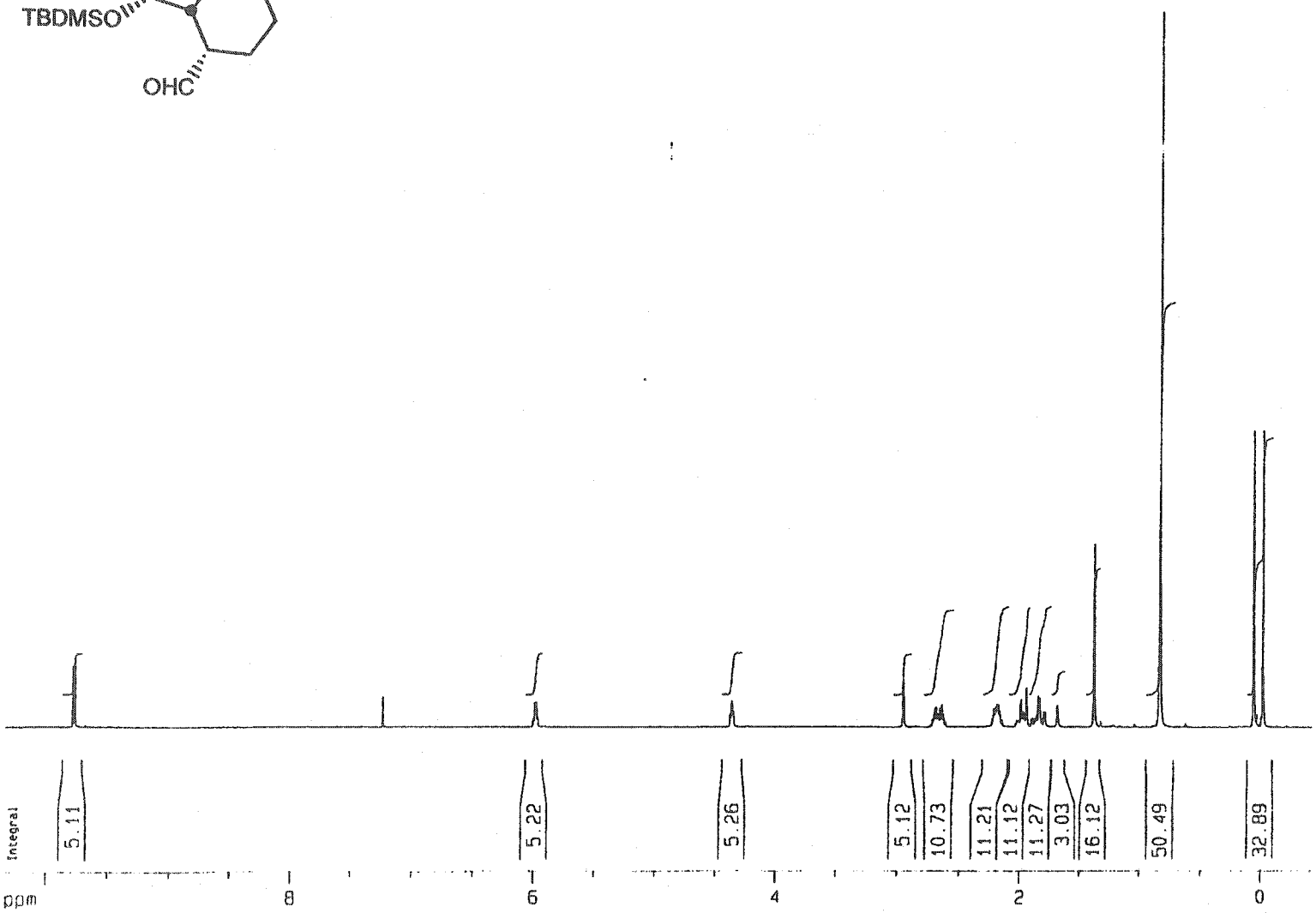
1D NMR plot parameters
CX 20.00 cm
CY 30.00 cm
F1P 7.732 ppm
F1 2320.72 Hz
F2P -0.498 ppm
F2 -149.56 Hz
PPMCM 0.41153 ppm/cm
HZCM 123.51362 Hz/cm






```
Current Data Parameters
NAME                  jaf-495
EXPNO                       1
PROCNO                      1

F2 - Acquisition Parameters
Date_              20030919
Time                   18.33
INSTRUM                av300
PROBHD   5 mm QNP  1H/1
PULPROG                zg30
TD                    30720
SOLVENT               ~~CDCl3~~ Aceton
NS                        16
DS                         0
SWH                5081.301 Hz
FIDRES            0.165407 Hz
AQ                3.0228980 sec
RG                    228.1
DW                   98.400 usec
DE                    6.00 usec
TE                   300.0 K
D1                1.00000000 sec

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

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

1D NMR plot parameters
CX                    20.00 cm
CY                    10.00 cm
F1P                   6.794 ppm
F1                  2039.20 Hz
F2P                   0.557 ppm
F2                   167.15 Hz
PPMCM              0.31187 ppm/cm
HZCM              93.60291 Hz/cm
```





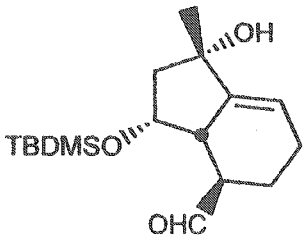
Current Data Parameters
NAME jaf-490bot
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20030917
Time 12.23
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 143.7
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

========== CHANNEL f1 ==========
NUC1 1H
P1 10.50 usec
PL1 -3.00 dB
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 15.00 cm
F1P 10.335 ppm
F1 3101.91 Hz
F2P -0.428 ppm
F2 -128.44 Hz
PPMCM 0.53816 ppm/cm
HZCM 161.51781 Hz/cm



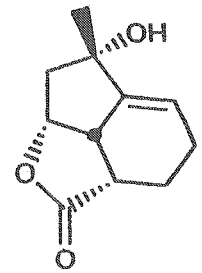
Current Data Parameters
NAME jaf-490top
EXPNO 1
PROCNO 1

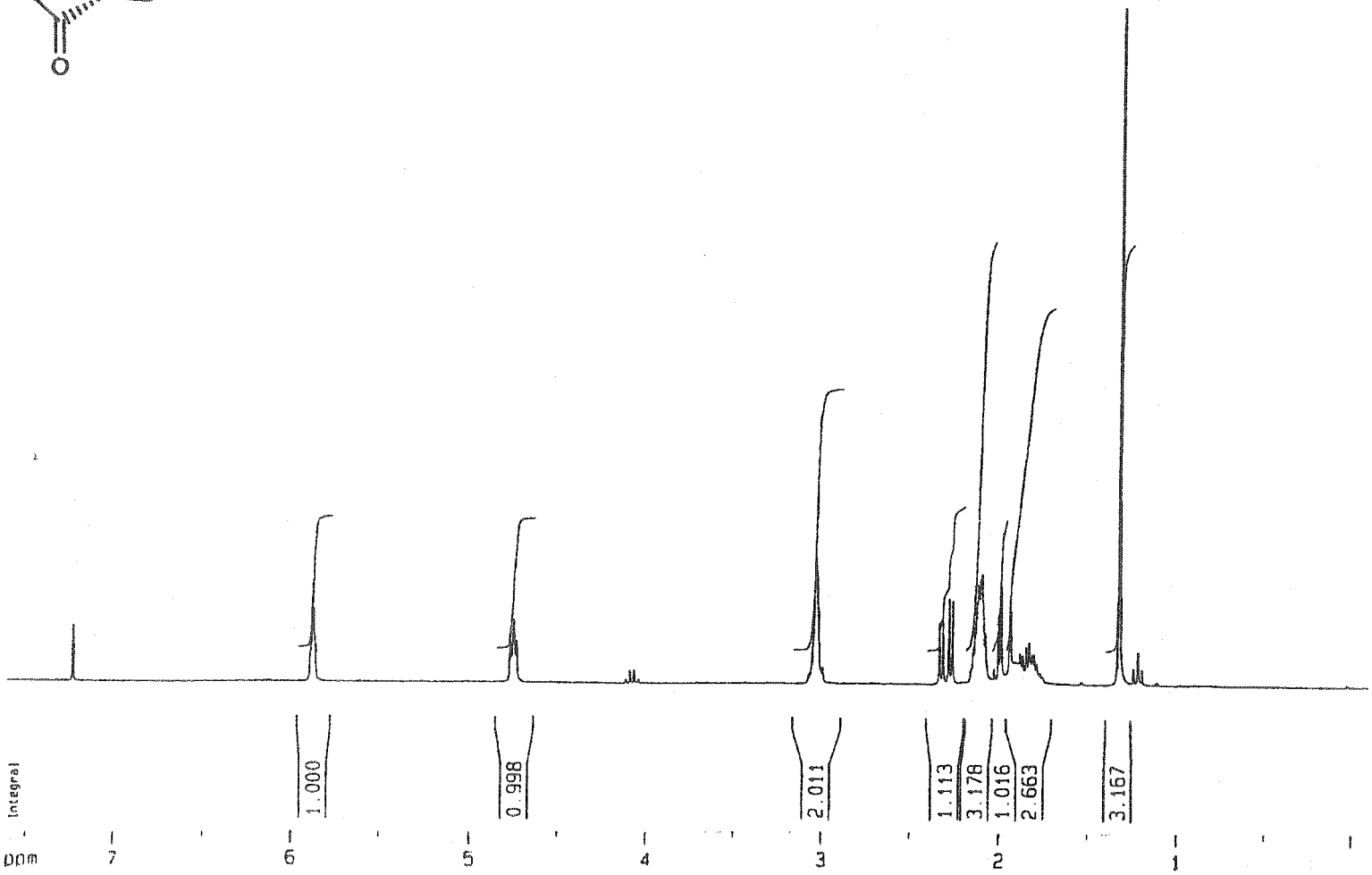
F2 - Acquisition Parameters
Date_ 20030918
Time 14.07
INSTRUM av300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 512
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

========== 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 15.00 cm
F1P 10.406 ppm
F1 3123.03 Hz
F2P -0.733 ppm
F2 -219.93 Hz
PPMCM 0.55692 ppm/cm
HZCM 167.14806 Hz/cm





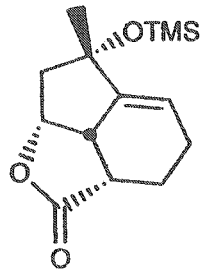
Current Data Parameters
NAME jaf-504
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20030927
Time 13.31
INSTRUM av300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 203.2
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

========== CHANNEL f1 ==========
NUC1 1H
P1 10.50 usec
PL1 -3.00 dB
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 7.617 ppm
F1 2286.01 Hz
F2P -0.089 ppm
F2 -26.81 Hz
PPMCM 0.38530 ppm/cm
HZCM 115.64102 Hz/cm



Current Data Parameters

NAME	jaf-522
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20031016
Time	9.20
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	322.5
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

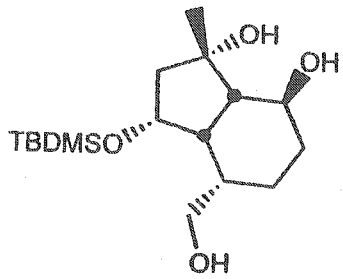
NUC1	1H
P1	10.50 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

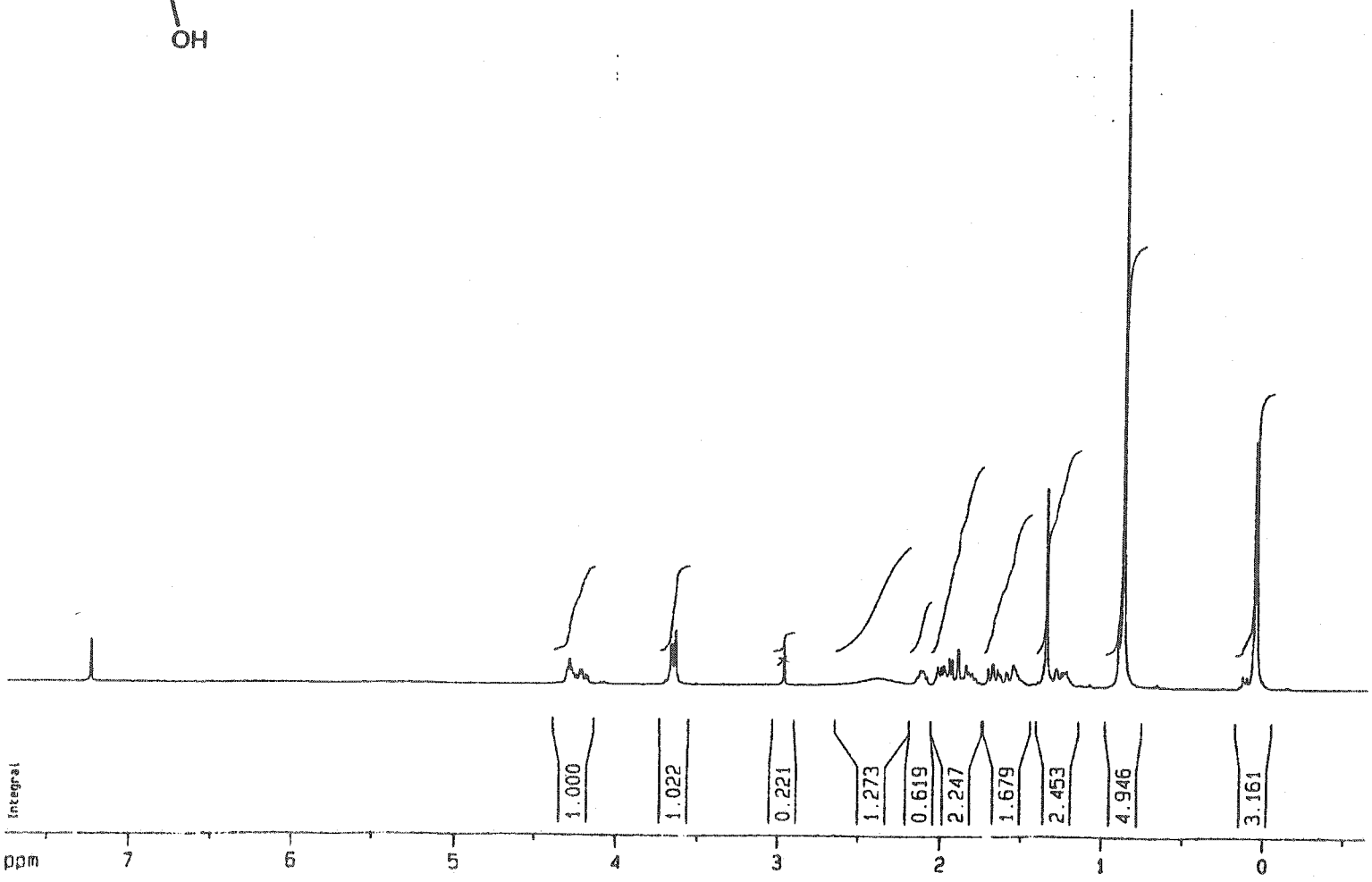
F2 - Processing parameters

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	15.00 cm
F1P	7.636 ppm
F1	2291.64 Hz
F2P	-0.423 ppm
F2	-126.97 Hz
PPMCM	0.40293 ppm/cm
HZCM	120.93053 Hz/cm





Current Data Parameters

NAME	jaf-530
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20031022
Time	10.59
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	228.1
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

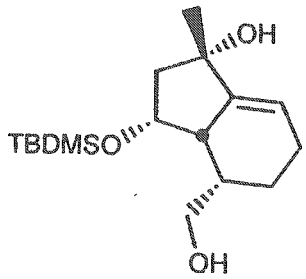
NUC1	1H
P1	10.50 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

F2 - Processing parameters

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

1D NMR plot parameters

CX	20.00 cm
CY	10.00 cm
F1P	7.756 ppm
F1	2327.92 Hz
F2P	-0.650 ppm
F2	-194.96 Hz
PPMCM	0.42030 ppm/cm
HZCM	126.14417 Hz/cm



Current Data Parameters

NAME	jaf-546pur
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20031107
Time	9.51
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	90.5
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

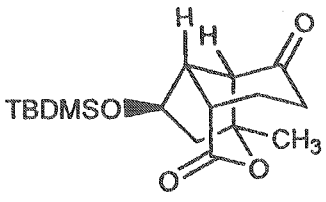
NUC1	1H
P1	10.50 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

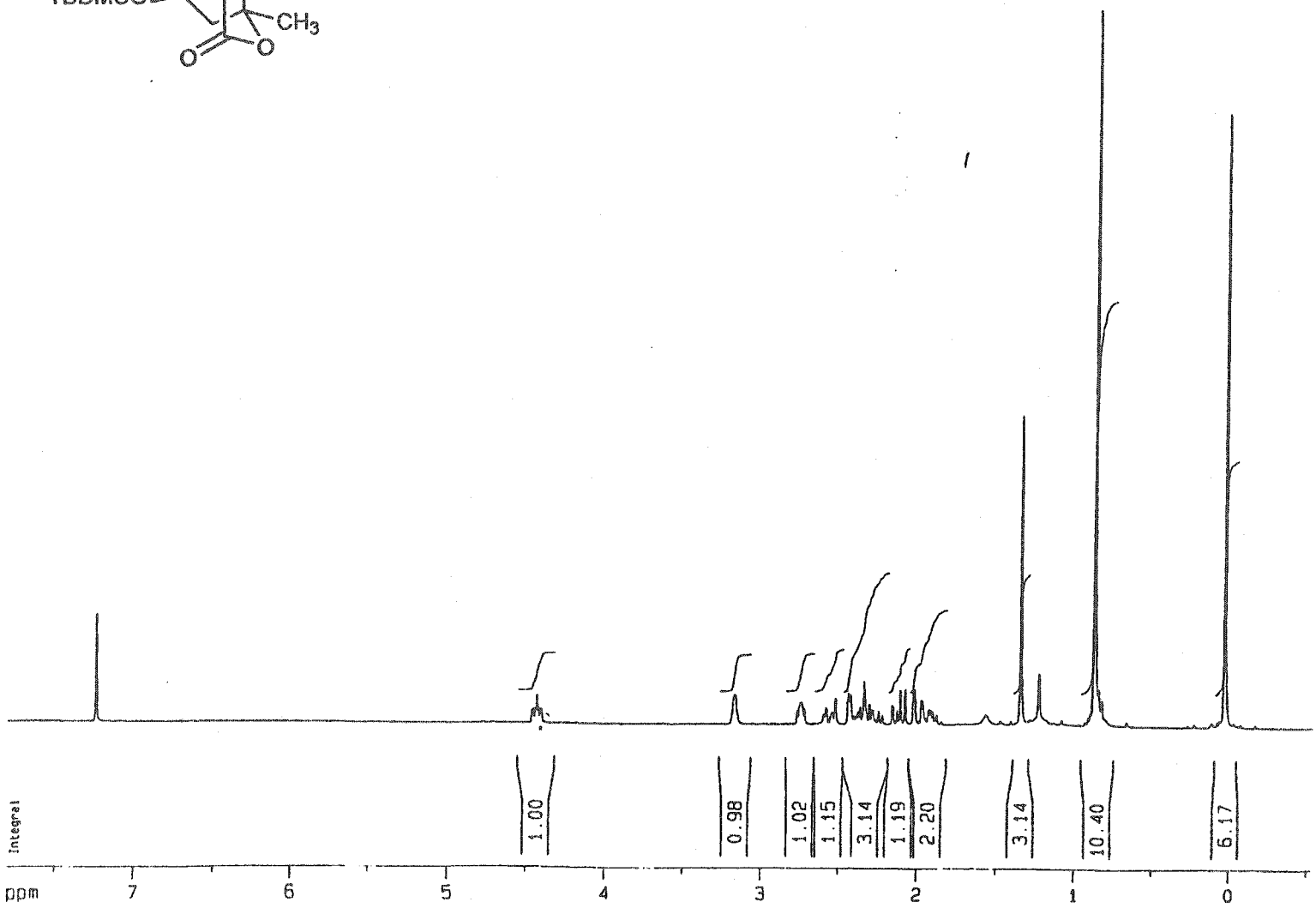
F2 - Processing parameters

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	15.00 cm
F1P	7.613 ppm
F1	2284.77 Hz
F2P	-0.527 ppm
F2	-158.02 Hz
PPMCM	0.40696 ppm/cm
HZCM	122.13970 Hz/cm





Current Data Parameters

NAME	jaf-531
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20031022
Time	13.44
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	406.4
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

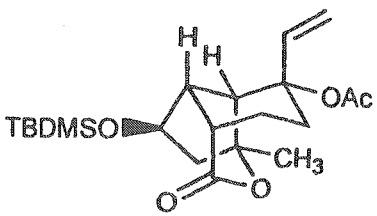
NUC1	1H
P1	10.50 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

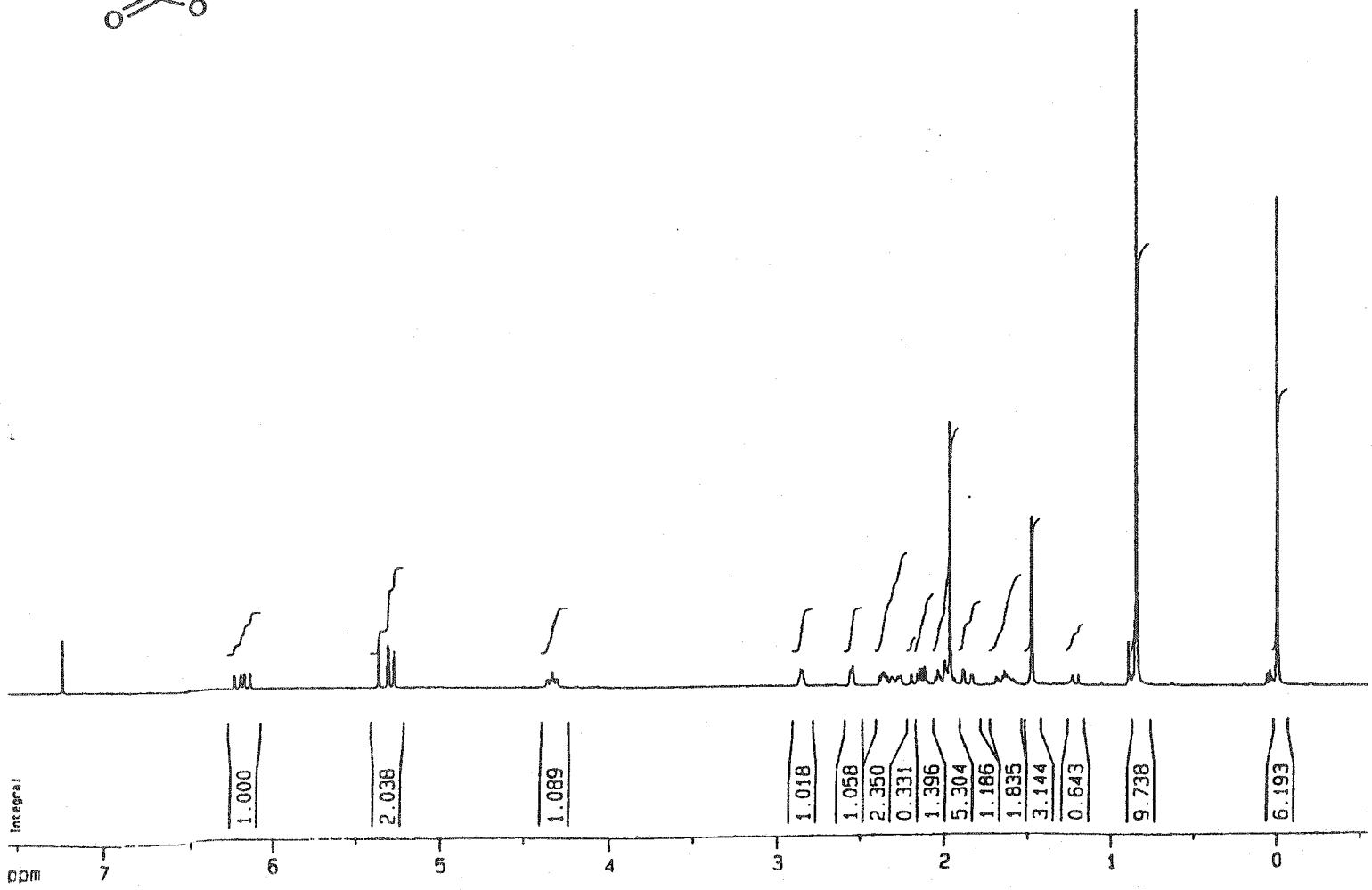
F2 - Processing parameters

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

1D NMR plot parameters

CX	20.00 cm
CY	15.00 cm
F1P	7.804 ppm
F1	2342.14 Hz
F2P	-0.531 ppm
F2	-159.43 Hz
PPMCM	0.41675 ppm/cm
HZCM	125.07818 Hz/cm





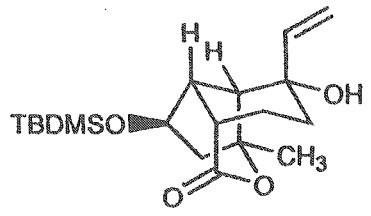
Current Data Parameters
NAME jaf-552
EXPNO 1
PROCNO 1

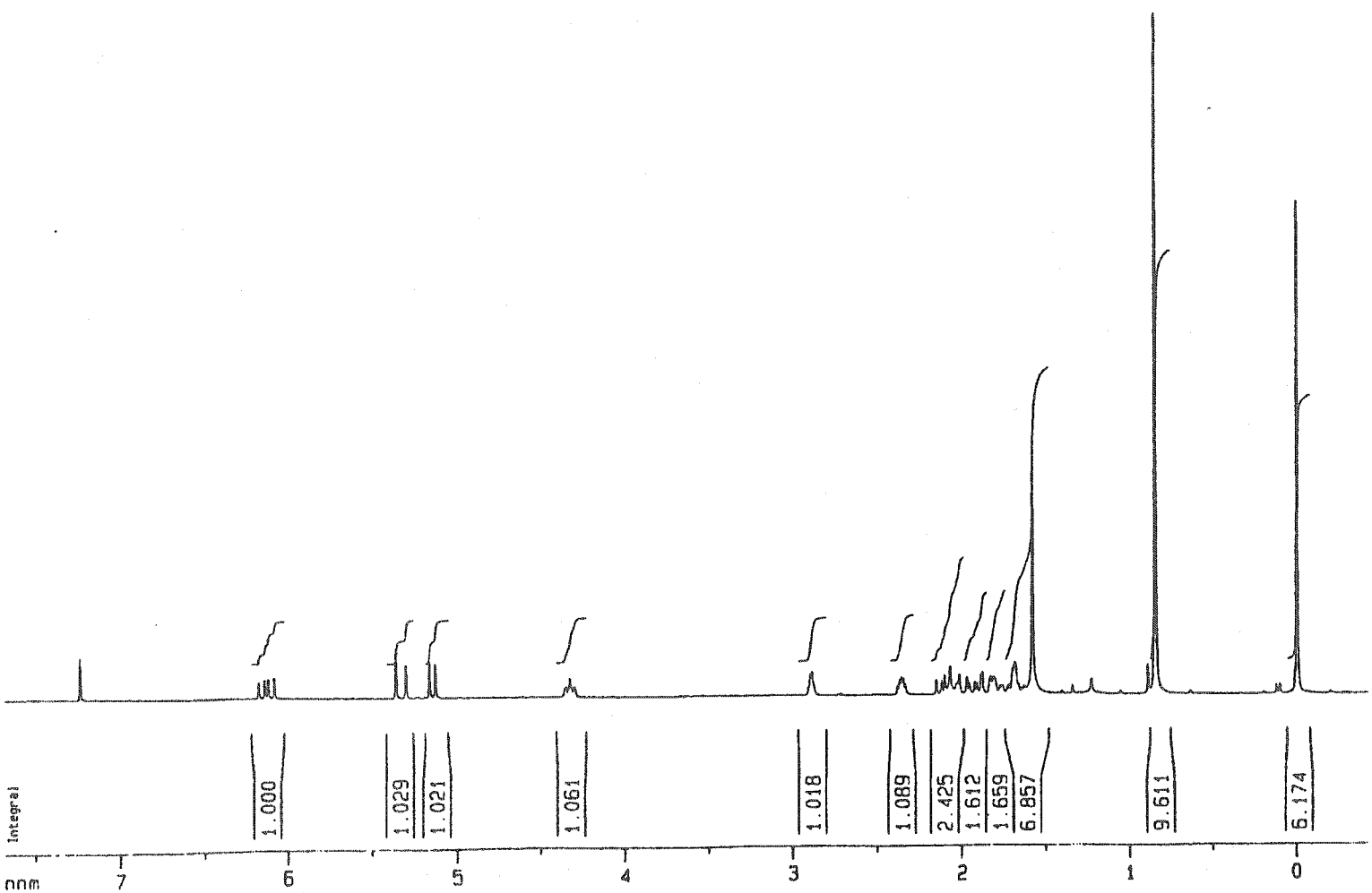
F2 - Acquisition Parameters
Date_ 20031112
Time 11.01
INSTRUM av300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 287.4
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

========== 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 7.564 ppm
F1 2270.28 Hz
F2P -0.551 ppm
F2 -165.27 Hz
PPMCM 0.40575 ppm/cm
HZCM 121.77727 Hz/cm





Current Data Parameters

NAME	jaf-552grig
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20031113
Time	12.15
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	256
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

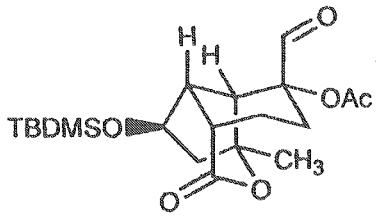
NUC1	1H
P1	10.50 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

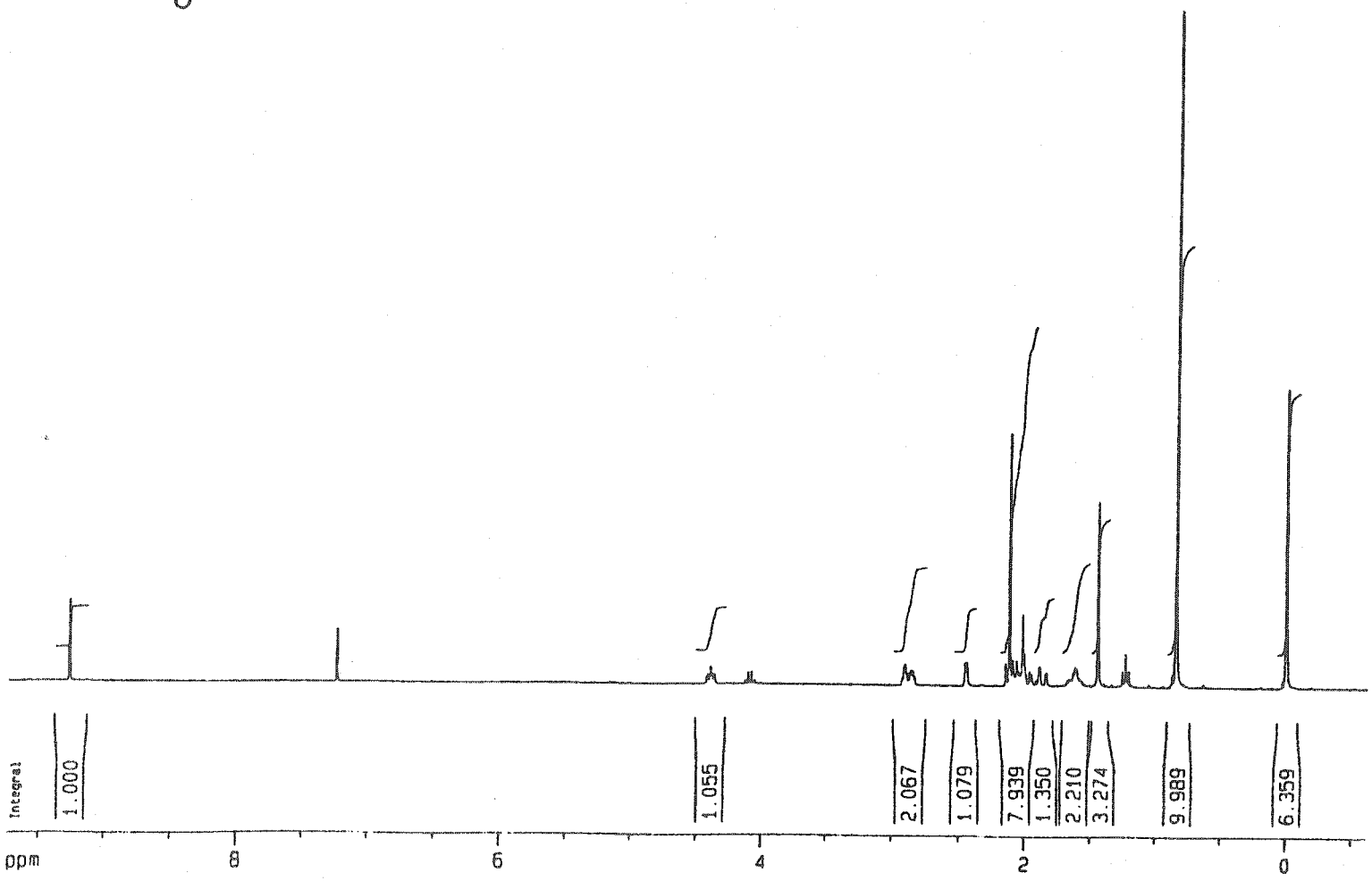
F2 - Processing parameters

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

1D NMR plot parameters

CX	20.00 cm
CY	10.00 cm
F1P	7.685 ppm
F1	2306.52 Hz
F2P	-0.430 ppm
F2	-129.02 Hz
PPMCM	0.40575 ppm/cm
HZCM	121.77727 Hz/cm





Current Data Parameters

NAME	jaf-553
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20031113
Time	9.27
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	287.4
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

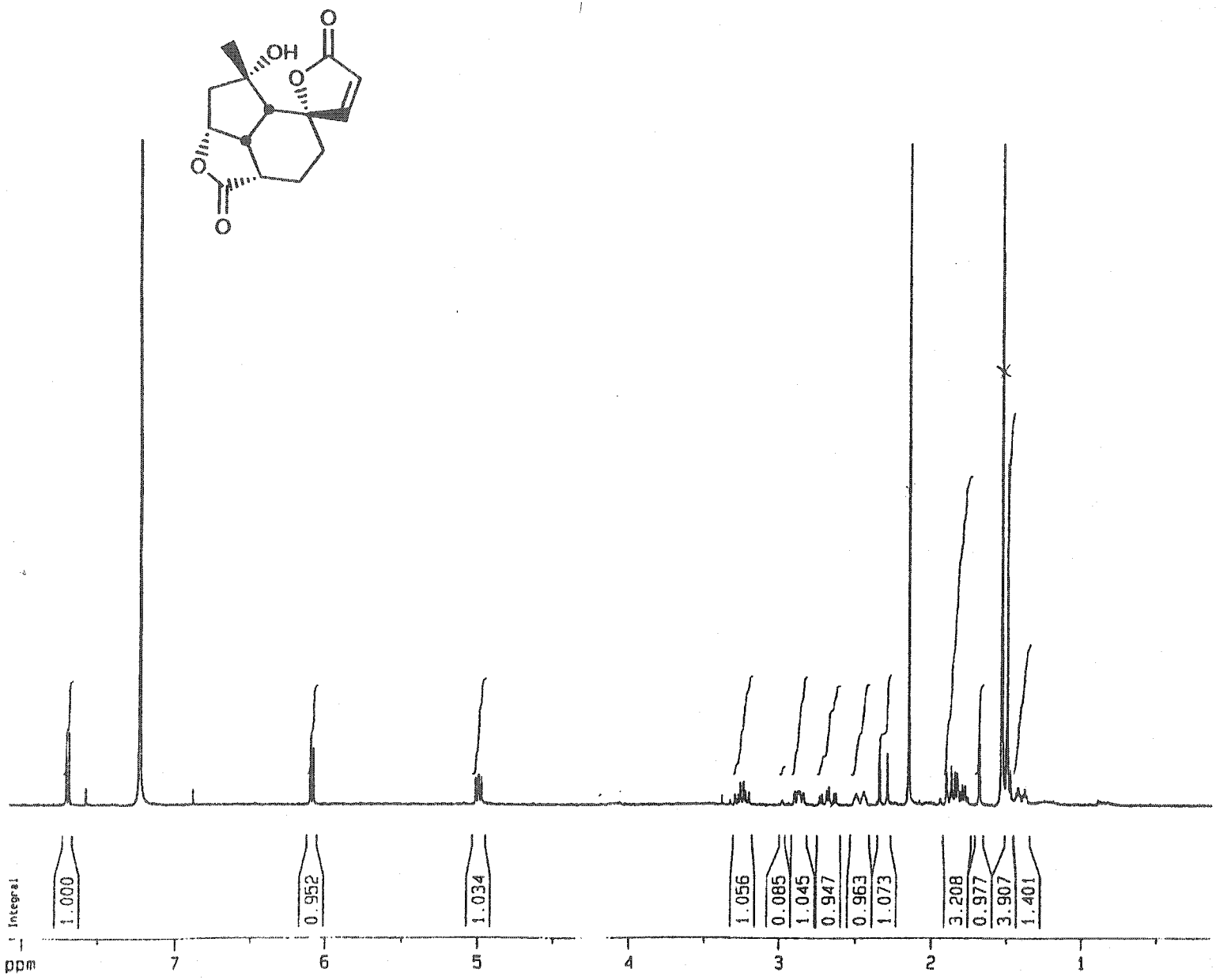
NUC1	1H
P1	10.50 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

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	9.738 ppm
F1	2922.66 Hz
F2P	-0.623 ppm
F2	-187.01 Hz
PPMCM	0.51805 ppm/cm
HZCM	155.48346 Hz/cm



Current Data Parameters

NAME	jaf-571b
EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

Date_	20031126
Time	15.57
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	200
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	1290.2
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

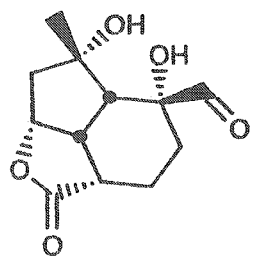
NUC1	1H
P1	10.50 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

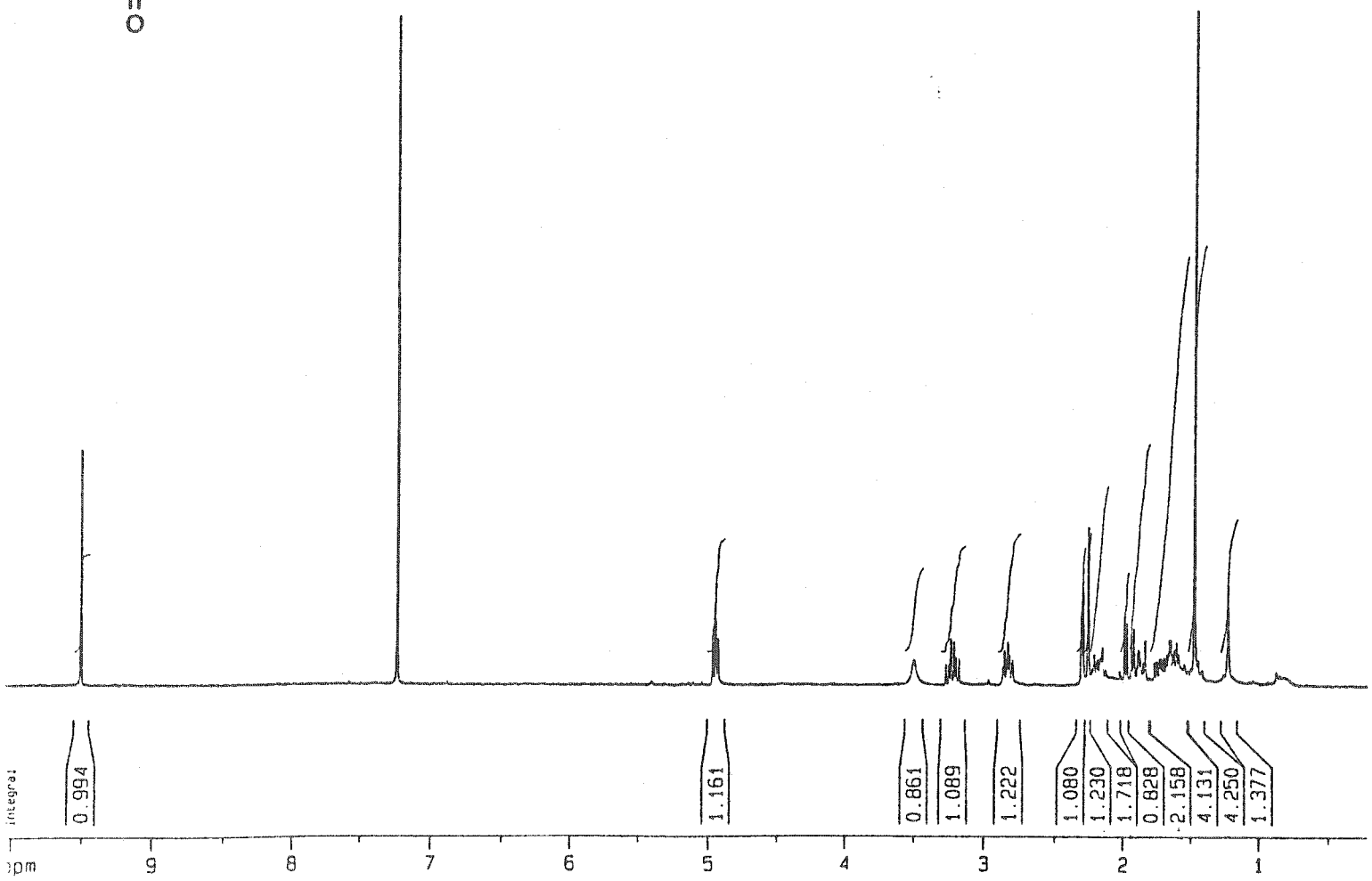
F2 - Processing parameters

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	50.00 cm
F1P	8.106 ppm
F1	2432.92 Hz
F2P	0.138 ppm
F2	41.27 Hz
PPMCM	0.39844 ppm/cm
HZCM	119.58250 Hz/cm





Current Data Parameters

NAME	jaf-577
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20031203
Time	10.10
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	912.3
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

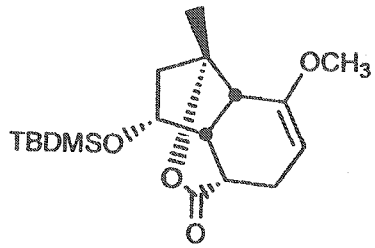
NUC1	1H
P1	10.50 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

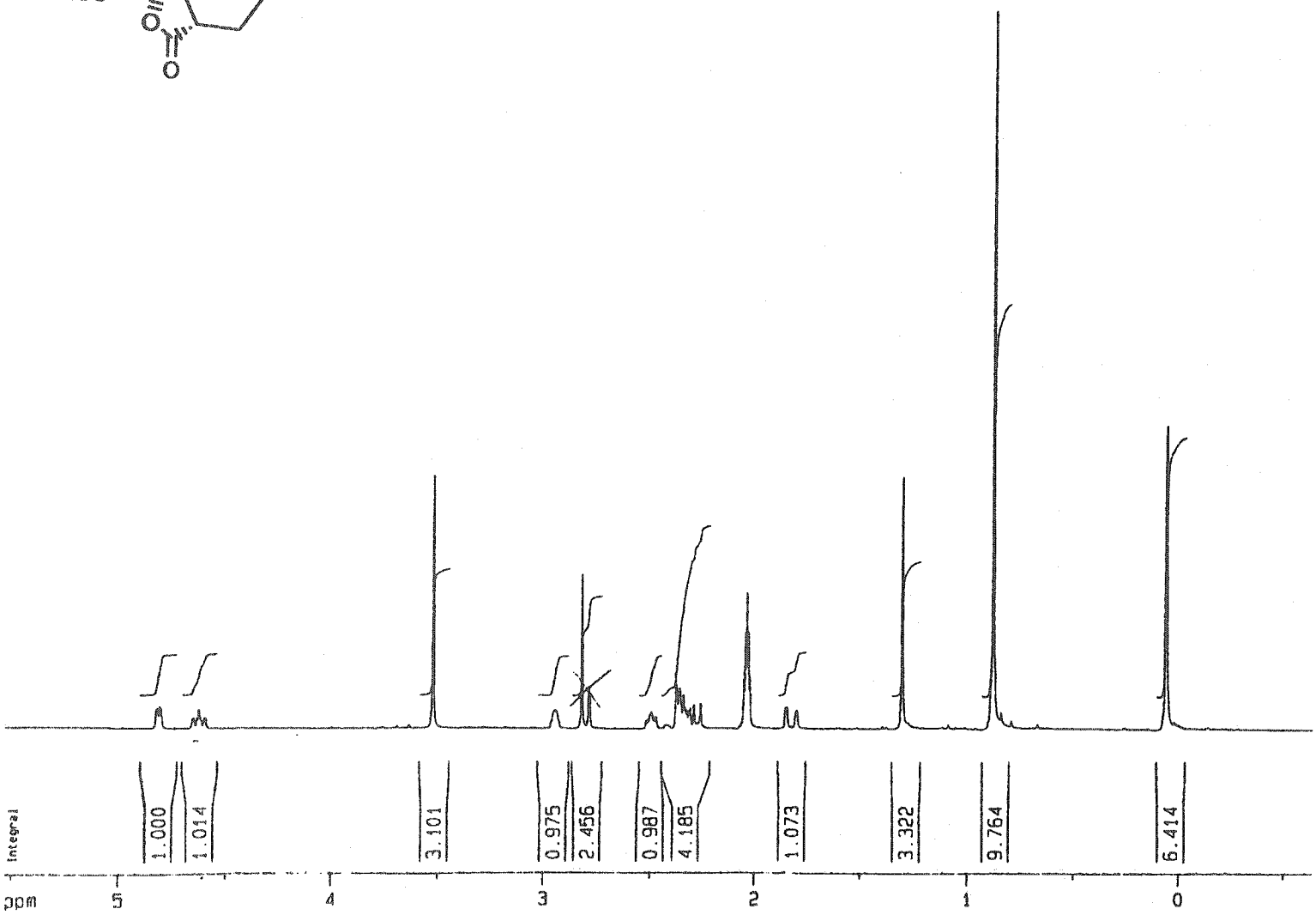
F2 - Processing parameters

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	10.067 ppm
F1	3021.28 Hz
F2P	0.214 ppm
F2	64.19 Hz
PPMCM	0.49263 ppm/cm
HZCM	147.85440 Hz/cm





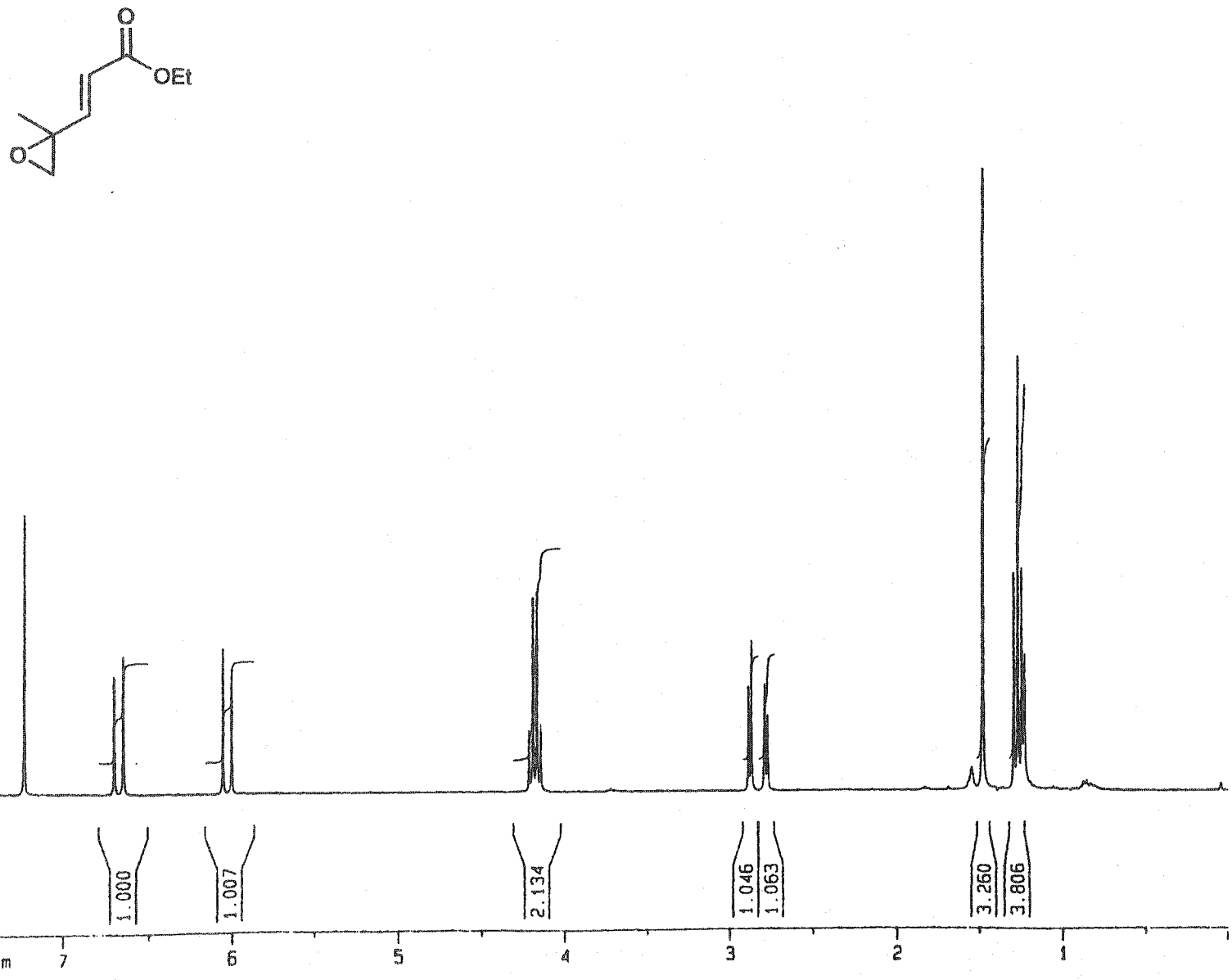
Current Data Parameters
NAME jaf-604
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20040209
Time 12.05
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 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
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 12.00 cm
F1P 5.532 ppm
F1 1660.38 Hz
F2P -0.640 ppm
F2 -192.18 Hz
PPMCM 0.30863 ppm/cm
HZCM 92.62788 Hz/cm



Current Data Parameters

NAME	jaf-595proton
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20040204
Time	16.12
INSTRUM	av300
PROBHD	5 mm ONP 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	724.1
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

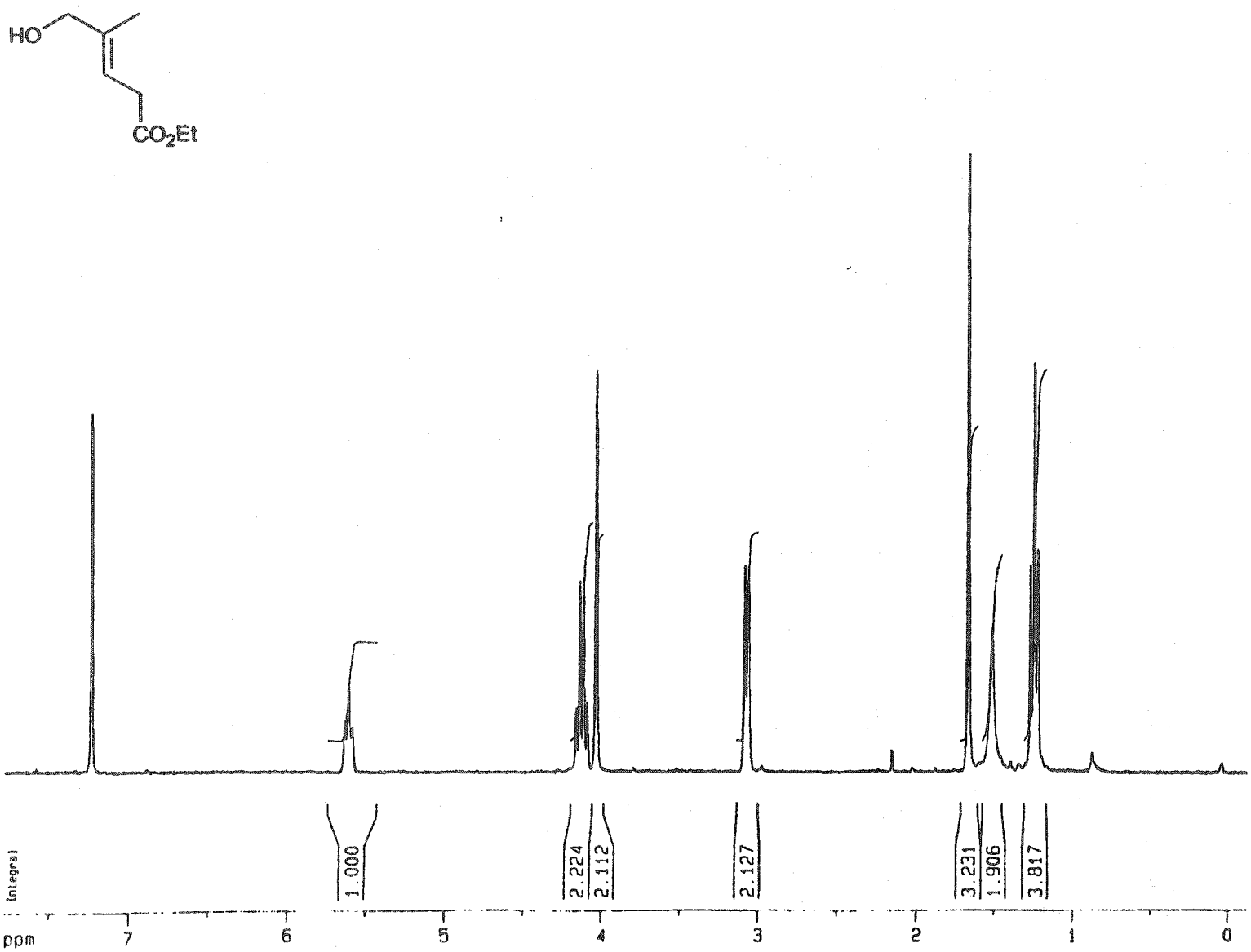
NUC1	1H
P1	10.50 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

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	7.500 ppm
F1	2250.98 Hz
F2P	0.000 ppm
F2	0.00 Hz
PPMCM	0.37500 ppm/cm
HZCM	112.54875 Hz/cm



Current Data Parameters

NAME	jaf-609
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20040219
Time	12.30
INSTRUM	av300
PROBHD	5 mm ONP 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	724.1
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

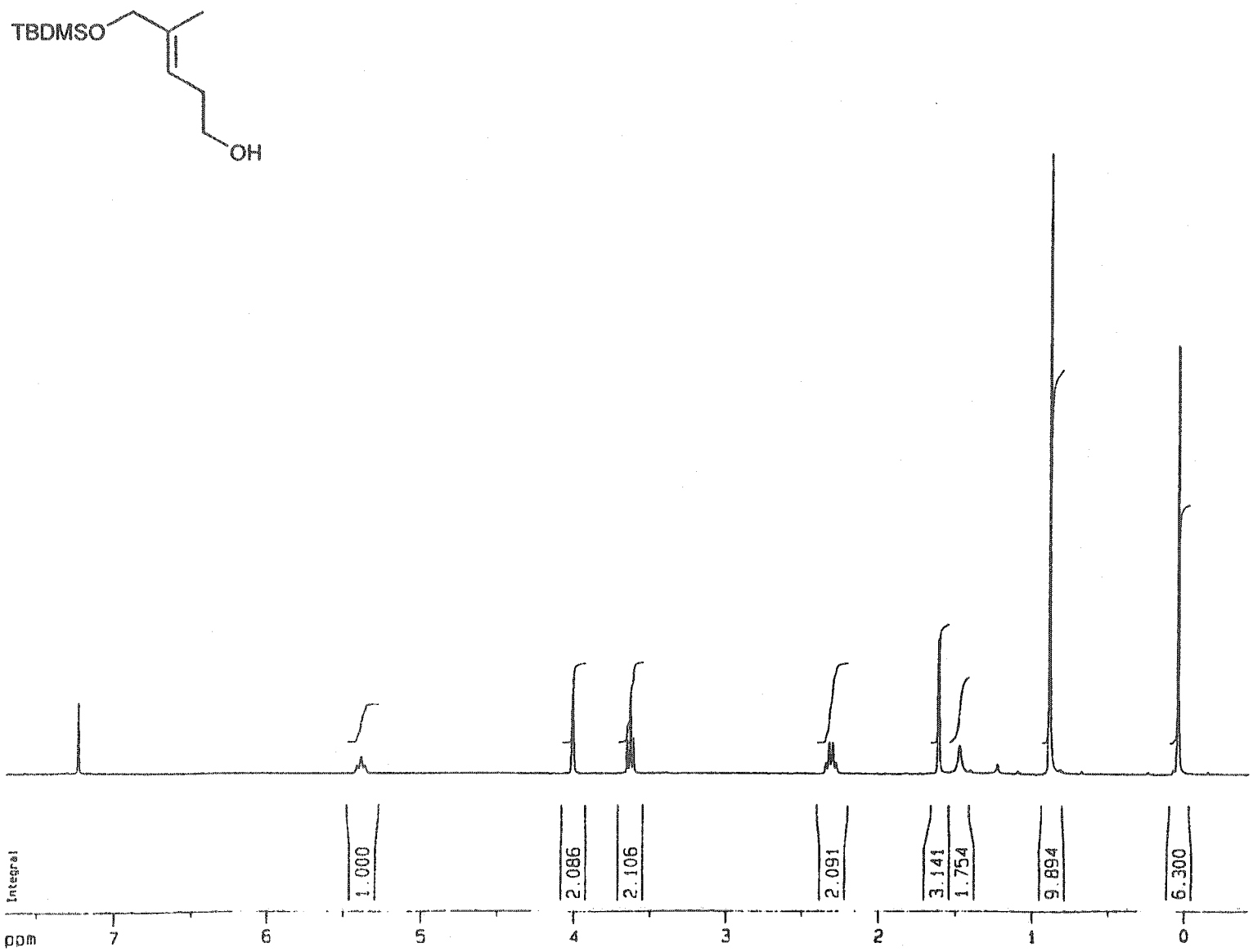
NUC1	1H
P1	10.50 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

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	7.783 ppm
F1	2336.02 Hz
F2P	-0.127 ppm
F2	-38.21 Hz
PPMCM	0.39553 ppm/cm
HZCM	118.71162 Hz/cm



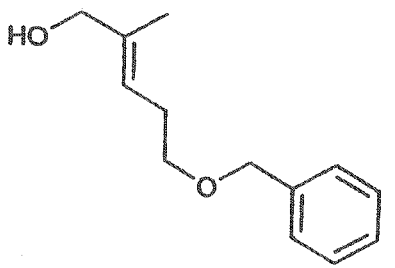
Current Data Parameters
NAME jaf-616
EXPNO 1
PROCNO 1

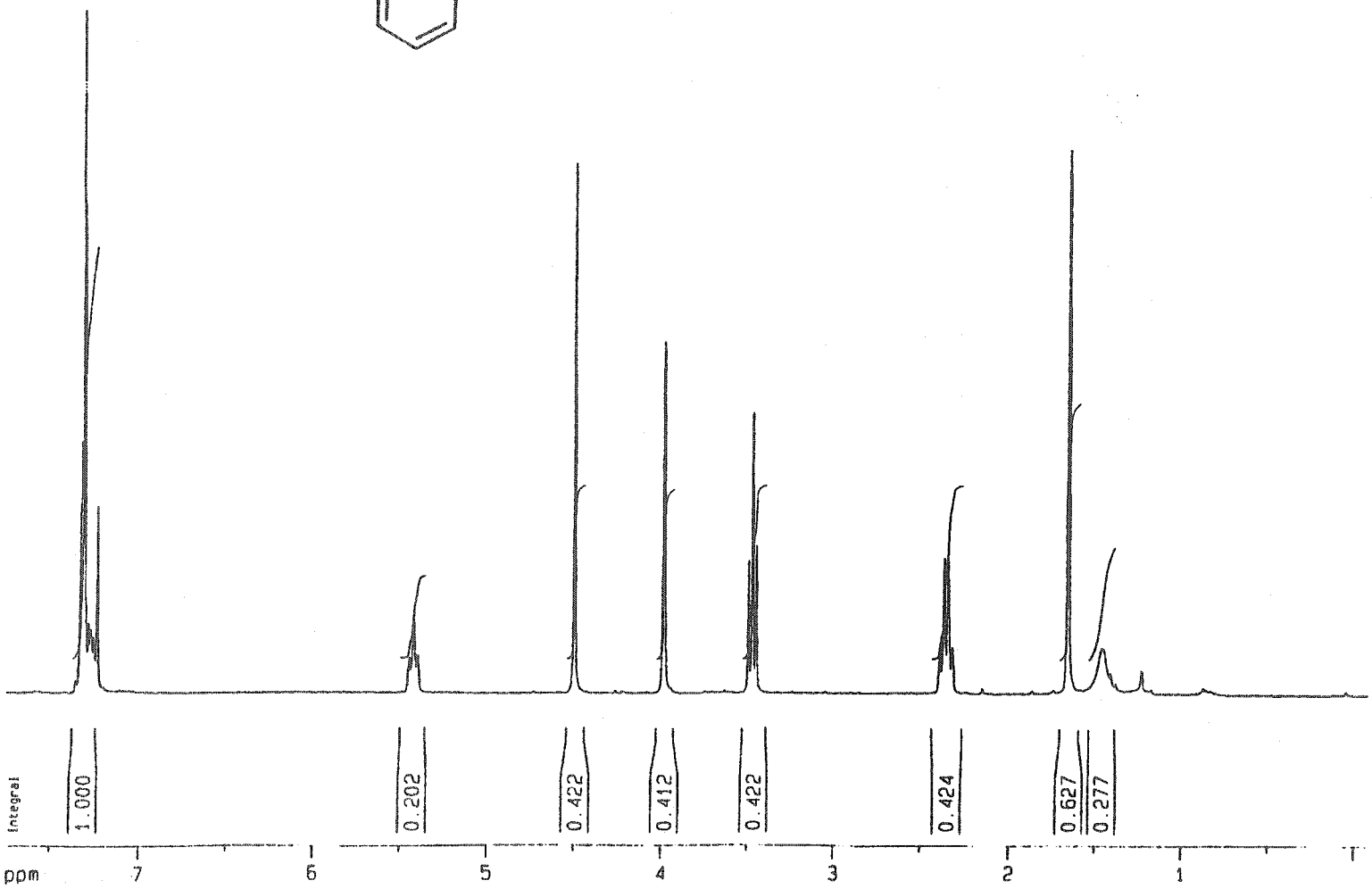
F2 - Acquisition Parameters
Date_ 20040216
Time 10.26
INSTRUM av300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 406.4
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

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

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

1D NMR plot parameters
CX 20.00 cm
CY 10.00 cm
F1P 7.709 ppm
F1 2313.68 Hz
F2P -0.428 ppm
F2 -128.44 Hz
PPMCM 0.40684 ppm/cm
HZCM 122.10606 Hz/cm





Current Data Parameters

NAME	jaf-618
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20040216
Time	13.01
INSTRUM	av300
PROBHD	5 mm ONP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	406.4
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

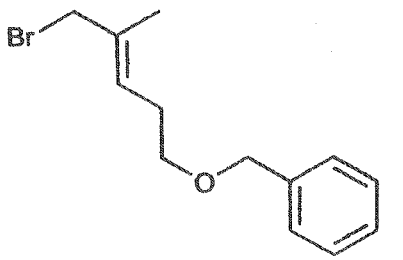
NUC1	1H
P1	10.50 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

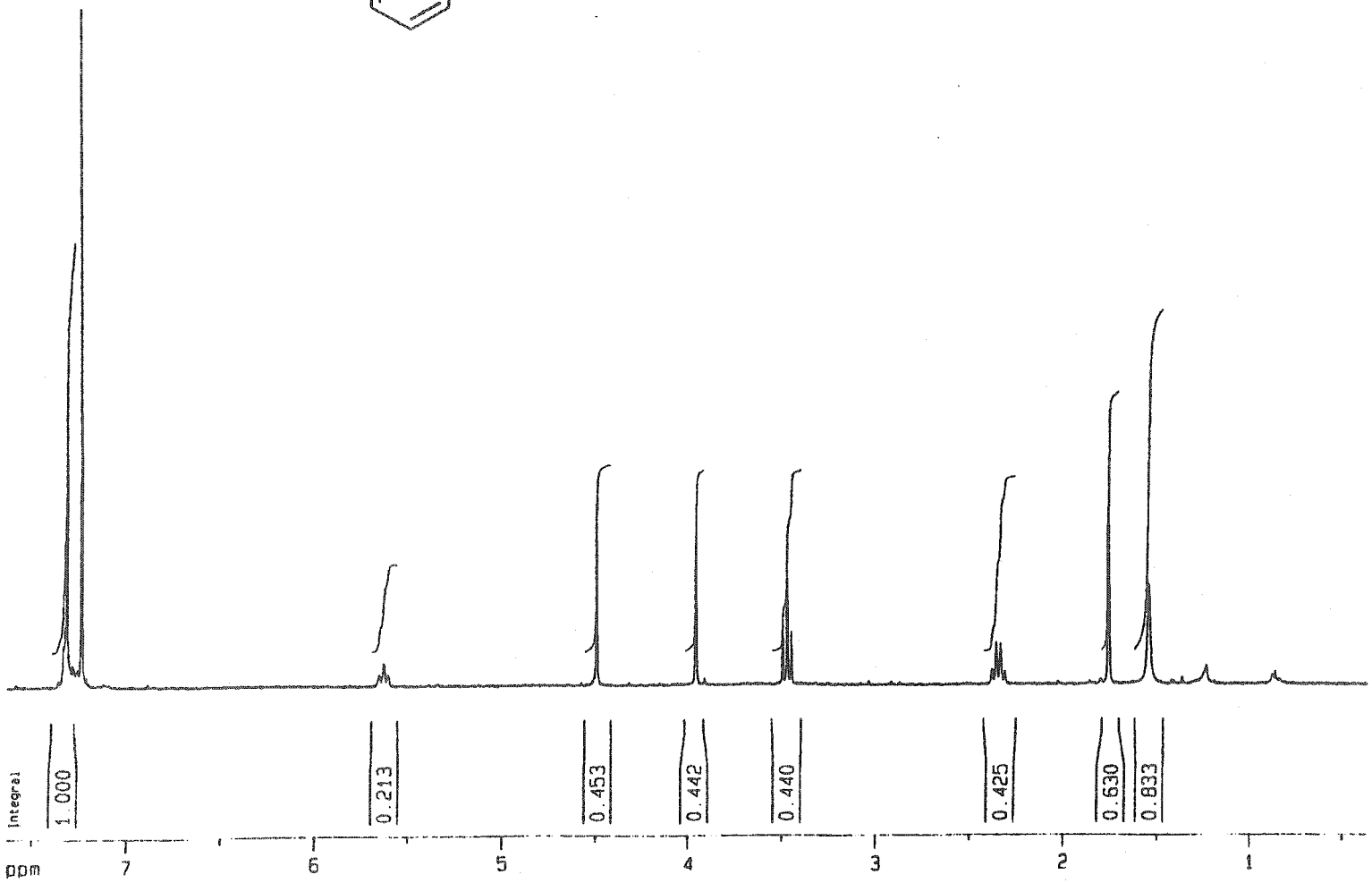
F2 - Processing parameters

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

1D NMR plot parameters

CX	20.00 cm
CY	10.00 cm
F1P	7.751 ppm
F1	2326.44 Hz
F2P	-0.083 ppm
F2	-24.84 Hz
PPMCM	0.39171 ppm/cm
HZCM	117.56426 Hz/cm





Current Data Parameters

NAME	jaf-623
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20040219
Time	14.34
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	1290.2
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
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	7.636 ppm
F1	2291.64 Hz
F2P	0.366 ppm
F2	109.72 Hz
PPMCM	0.36350 ppm/cm
HZCM	109.09634 Hz/cm