MODULAR STRATEGIES FOR THE SYNTHESIS OF TETRAHYDROFURAN AND TETRAHYDROPYRAN CONTAINING ACETOGENINS

by

FENG WANG

A dissertation submitted to the Graduate Faculty in Chemistry in partial fulfillment of the requirements for the degree of Doctor of Philosophy, The City University of New York

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Abstract

MODULAR STRATEGIES FOR THE SYNTHESIS OF TETRAHYDROFURAN AND TETRAHYDROPYRAN CONTAINING ACETOGENINS

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Feng Wang

Advisor: Professor David R. Mootoo

Annonaceous acetogenins, a family of naturally occurring polyketides, are well known for their cytotoxic, antitumoral, insecticidal, and immunosuppresive activities. The majority of structures contain one or more stereochemically complex tetrahydrofuran (THF) rings. A smaller subset referred to as non-classical congeners contain a highly substituted tetrahydropyran (THP). This thesis describes modular strategies for both THF and THP containing acetogenins, using as test cases the mono-THF acetogenin, 4-deoxyannoreticuin and the THF-THP congener muconin. 4-Deoxyannoreticuin, a typical member of the mono-THF acetogenin with two flanking carbinol groups at C-15 and C-20, shows cytotoxicity at the micromolar level against several human cancer cell lines, including MCF-7, HT-29, A-498, PC-3 and PACA. Muconin shows micromolar and selective cytotoxicity against PACA-2 and MCF-7.

Chapter 1 presents a review of the different structural types and bioactivity of the acetogenins.

Chapter 2 describes an olefin cross metathesis strategy for coupling of cyclic ether and butenolide segments of the acetogenins. This approach was applied to alcohol epimers of 4-deoxyannoreticuin in an attempt to assign the configuration at the C9 carbinol in the natural product. The activity of these compounds against two human tumor cell lines, PC3 and Jurkat, was also evaluated. Unfortunately, identification of one or the other epimeric structures with the natural product was not possible because of the closeness of the physical and cytotoxicity data for all three compounds.

Chapter 3 deals with a tandem, iodonium ion promoted, cyclization on acetals of dihydroxydienes diene-acetals. These precursors are assembled in a modular fashion from aldehydes and easily accessible dihydroxydienes and the reaction products are stereochemically complex THF-THP subunits as found in the non-classical acetogenins. Vicinal or 1,3- diol precursors produced adjacently or methylene linked cyclic ethers in good to moderate yield. In all cases the cascade appears to be initiated by a 5-exo trig type cyclization to give a 2,5-disubstituted THF connected to an oxocarbenium ion which undergoes attack by the second alkene to form the THP ring. The substitution pattern and connectivity of the second alkene determines the mechanism of formation and constitution of the THP, i.e. a 2,5,6-tri-alkylated or 2,6-dialkyl-4-halogenated. Altogether, three new stereogenic centers are generated in the THF-THP products. The feasibility of this tandem reaction for non-classical acetogenin synthesis was illustrated in the preparation of an advanced precursor to muconin.

Acknowledgment

It would not have been possible to write this doctoral thesis without the help and support of the kind people around me, to only some of whom it is possible to give particular mention here.

Above all, I would like to thank my mentor, Dr. David R. Mootoo, for his support and patience, not to mention his advice and unsurpassed knowledge of chemistry. He has showed me what kind of qualities a chemist should have and what the true professionalism is. I will continue the journey of chemistry without him nearby, but his advice would never be forgotten.

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CHAPTER ONE

Acetogenins: classification, biosynthesis and bioactivity

1.1 Structure

Annonaceous acetogenins, a family of naturally occurring polyketides, are well known for their cytotoxic, antitumoral, insecticidal, and immunosuppresive activities.[1] Since the discovery of uvaricin in 1982 (**Figure 1.1**),[2] 417 annonaceous acetogenins have been isolated. Their highly potent bioactivities and structural complexity have attracted the attention of synthetic and medicinal chemists. A notable feature of several acetogenins is the ability to inhibit multiple drug resistant (MDR) tumor cell lines.[3] The cytotoxic effects exhibited by acetogenins are at least in part due to the inhibition of NADH-ubiquinone oxidoreductase (mitochondrial complex I) of the respiratory chain. This inhibition results in a depletion of ATP levels which may cause arrest in the cell cycle at the G1 phase, and consequently induce apoptosis.[4] However, the exact details of this mechanism remains elusive.

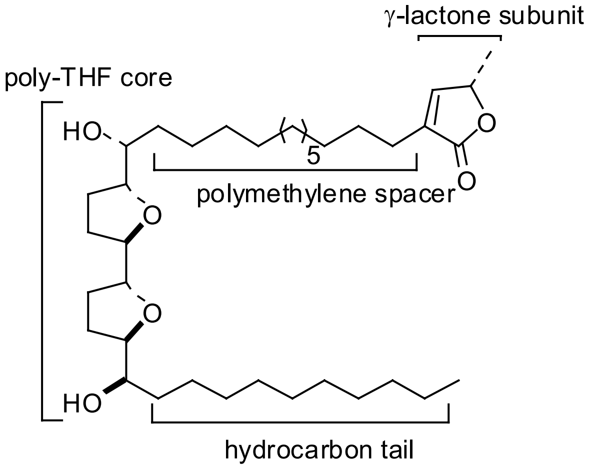


FIGURE 1.1 Structure of uvaricin.

Structurally, the simplest acetogenins contain linear C_{32} or C_{34} hydrocarbon chain ending in a γ-lactone (**Figure 1.2**). In the more complex structures, a variety of oxygenated functions, such as hydroxyl, ketone, epoxide, tetrahydrofuran (THF) and tetrahydropyran (THP) are present, as well as double and triple bonds. The classical cyclic ether acetogenins contain one or more epoxide, a mono- THF, an adjacently linked bis- or tris- THF, or non-adjacently linked bis- THF. The less common or non-classical acetogenins are those containing a THP ring. Among the 417 acetogenins isolated to date, 40 are linear, 16 are epoxy (E-1, E-2 and E-3), 206 are mono-THF (T-1 and T-2), 146 are bis-THF (T-3 ~ T6), one is a tris-THF (T-7), and the remaining eight are non-classical structures (T8 ~ T10) (**Figure 1.3**).[4]

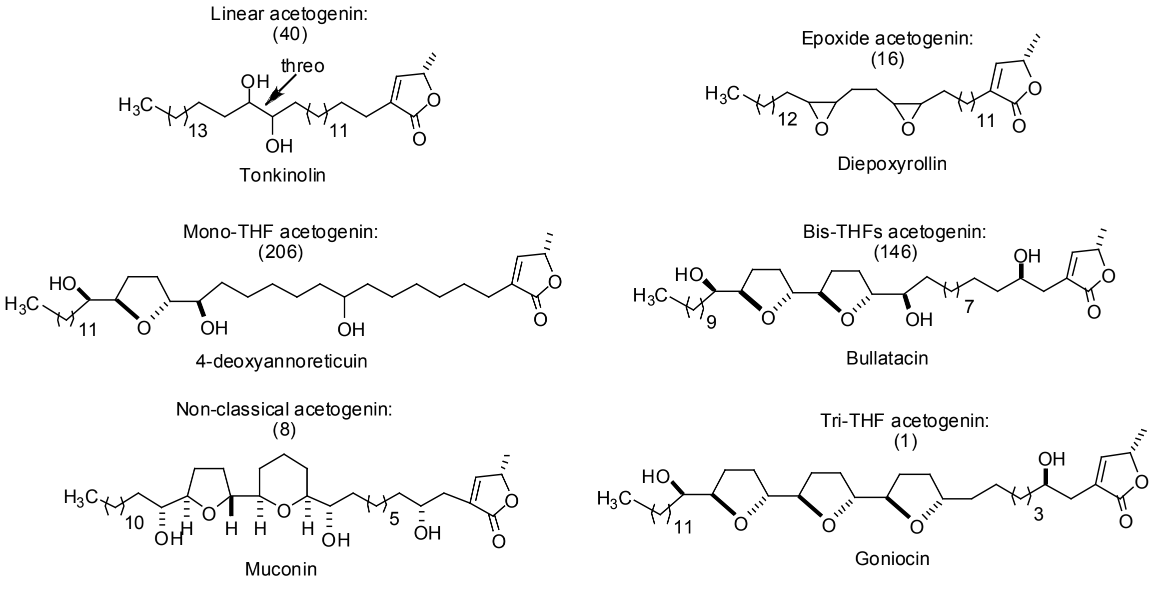


Figure 1.2 Representative acetogenins

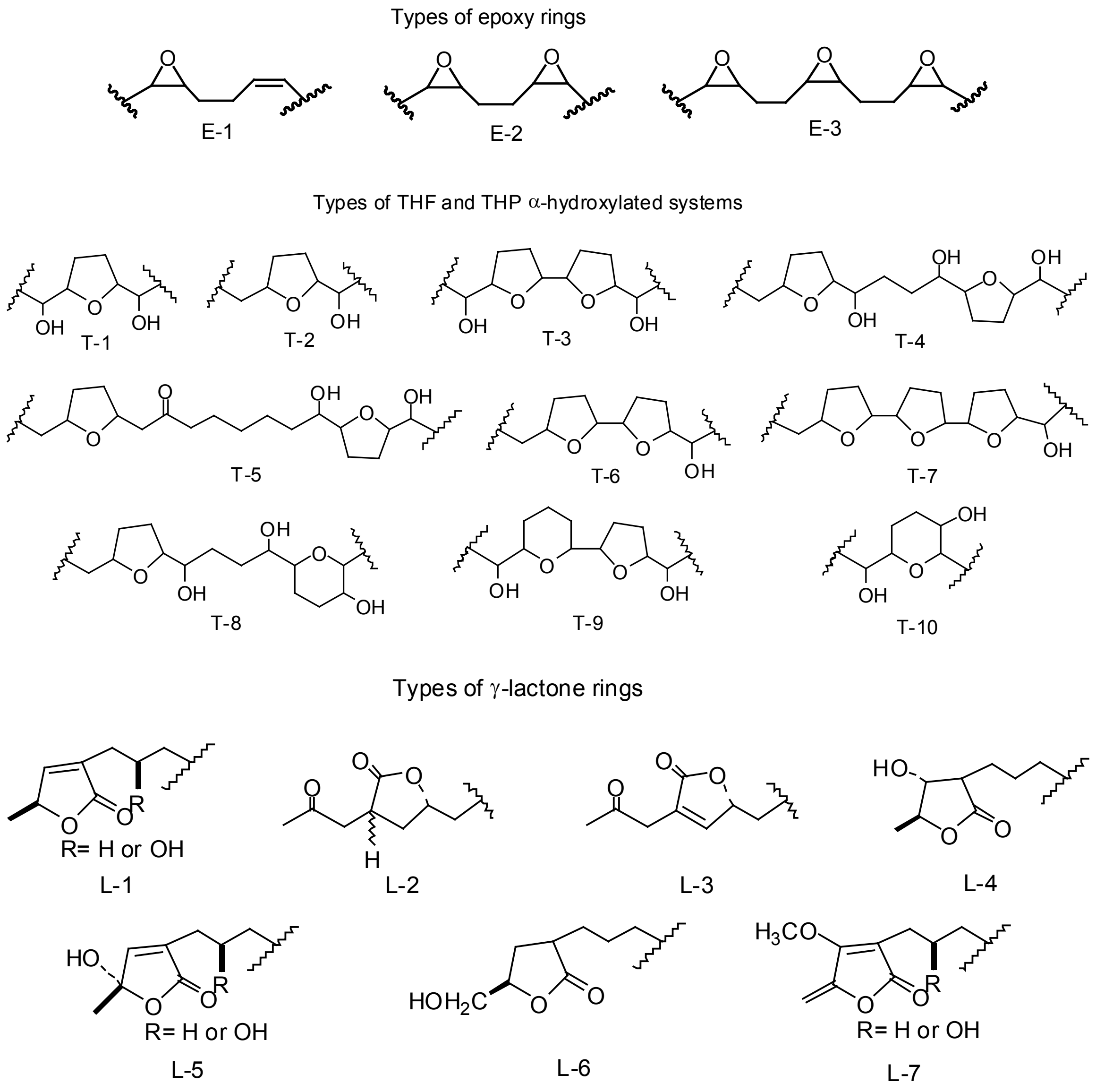


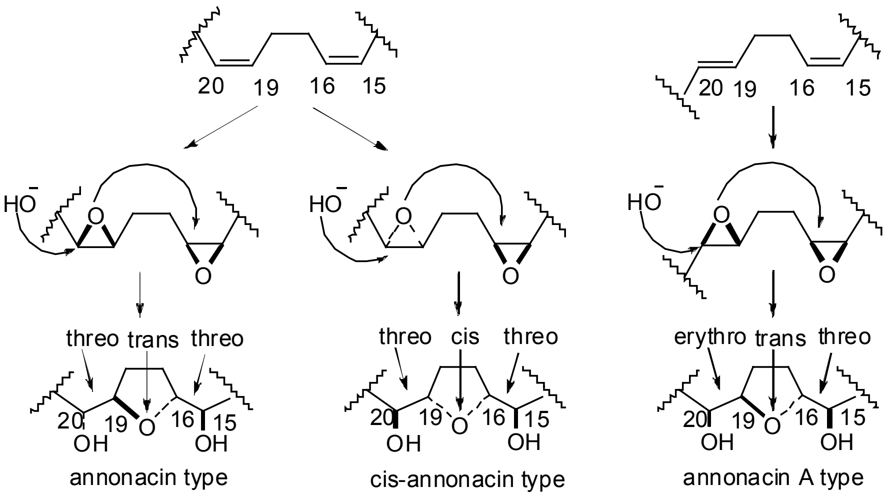
FIGURE 1.3 Subtypies of cyclic ether containing acetogenins with different lactone residues

1.2 Biosynthesis

Although acetogenins are very varied in terms of the position, number and the size of the cyclic ether ring, the number and the position of hydroxyl groups and the structures of the *γ*-lactones, they are believed to be all derived from related polyketide pathways.[1c,5]

Recent discoveries of muridienins (presumed precursors of mono-THF acetogenins) and chatenaytrienins (presumed precursors of bis-THF acetogenins) provided strong evidence that the lactone moiety arises through enzymatic combination of lacceroic (C32) and ghedoic (C34) fatty acids with a three-carbon unit.[6,7] However, these free acids or their esterified products have not been isolated, which might suggest that they are actually short-term intermediates.[1c] The sequence of these processes remains unknown. The THF, THP and epoxide rings are suggested to arise from the epoxidation of isolated alkenes and subsequent epoxide cyclizations (**Scheme 1.1**).[1c] This hypothesis is strongly supported by the discovery of possible linear acetogenin precursors with double bonds in appropriate positions.

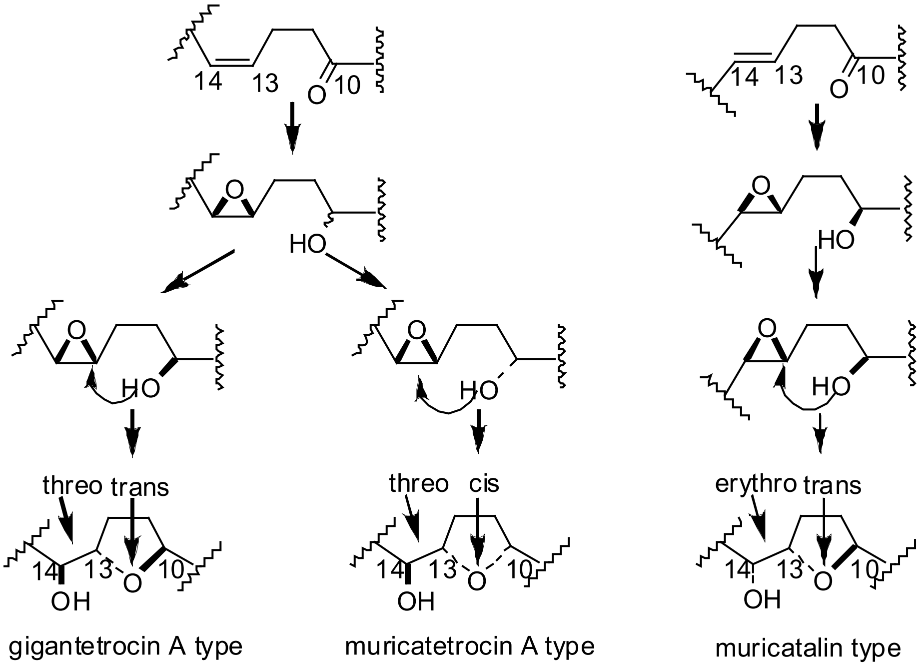
SCHEME 1.1 Proposed biosynthetic pathways of three types of mono-THF acetogenins bearing flanking carbinols.



Acetogenins bearing a mono-THF ring with two flanking carbinols (the annonacin,[8, 9] cis-annonacin[9] and annonacin A[10] types) are considered to be formed from cis-cis or trans-cis dienes, through epoxidation followed by cyclization starting from the left side of each precursor.

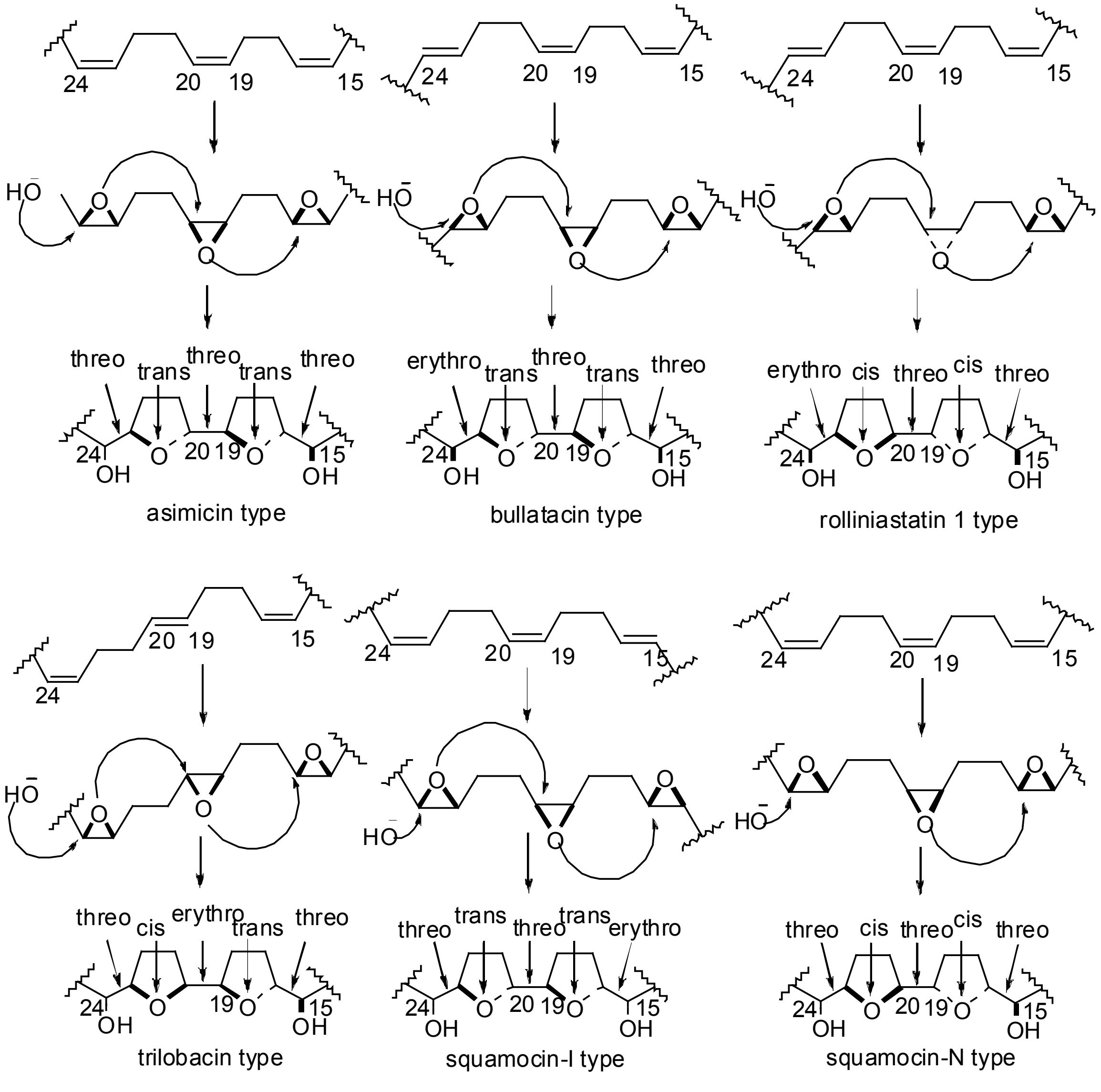
The three types of acetogenins bearing a mono-THF ring with one flanking carbinol (gigantetrocin A,[11] muricatetrocin A[12] and muricatelin[13] types) can be formed from oxidation of one of the alkenes to give a keto *cis*-alkene or keto *trans*-alkene, followed by reduction of the keto group and cyclization of the resulting hydroxy epoxide (**Scheme 1.2**).

SCHEME 1.2 Proposed biosynthetic pathways of three types of mono-THF acetogenins.



Six types of adjacent bis-THF ring acetogenins having two flanking hydroxyls (asimicin,[14] bullatacin,[15] rolliniastatin,[16] trilobacin,[17] squamocin-I[18] and squamocin-N[18] types) can be generated via epoxide opening cascade reactions similar to those described for the annonacin series (**Scheme 1.3**).

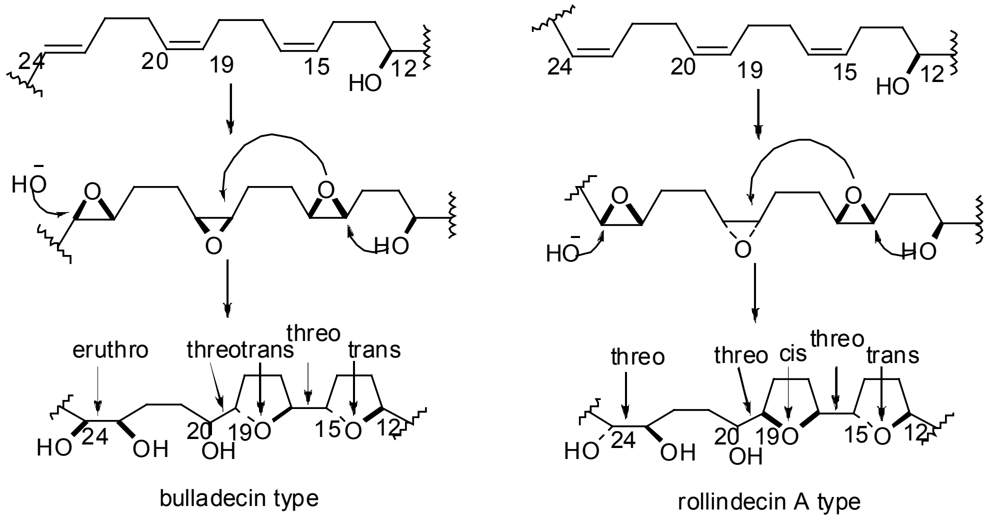
SCHEME 1.3 Proposed biosynthetic pathways of six types of bis-THF acetogenins.



Two other types of acetogenins, bearing adjacent bis-THF rings with one flanking carbinol (bulladecin and rollindecin A types), can be formed from hydroxylated *cis-cis-*

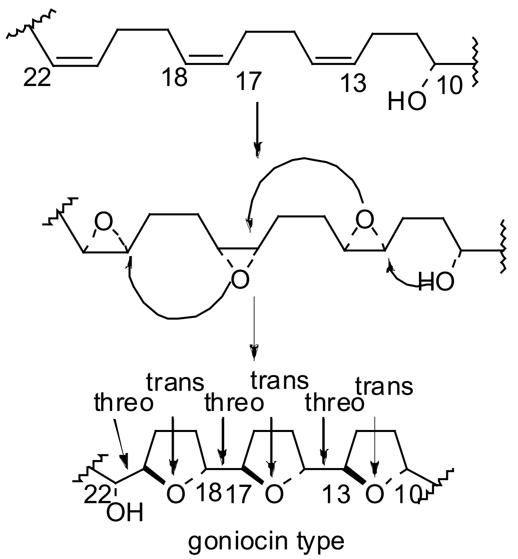
trans or hydroxylated *cis-cis-cis* trienes, through epoxidation and cyclization starting from the right side (**Scheme 1.4**).

SCHEME 1.4 Proposed biosynthetic pathways of bis-THF acetogenins with one flanking carbinol.



The formation of acetogenin, bearing adjacent tri-THF rings (goniocin type) which was found recently in *Goniothalamus giganteus*,[19] can also be explained via an epoxide opening cascade, in this case on a *tris*-epoxy alcohol precursor (**Scheme 1.5**).

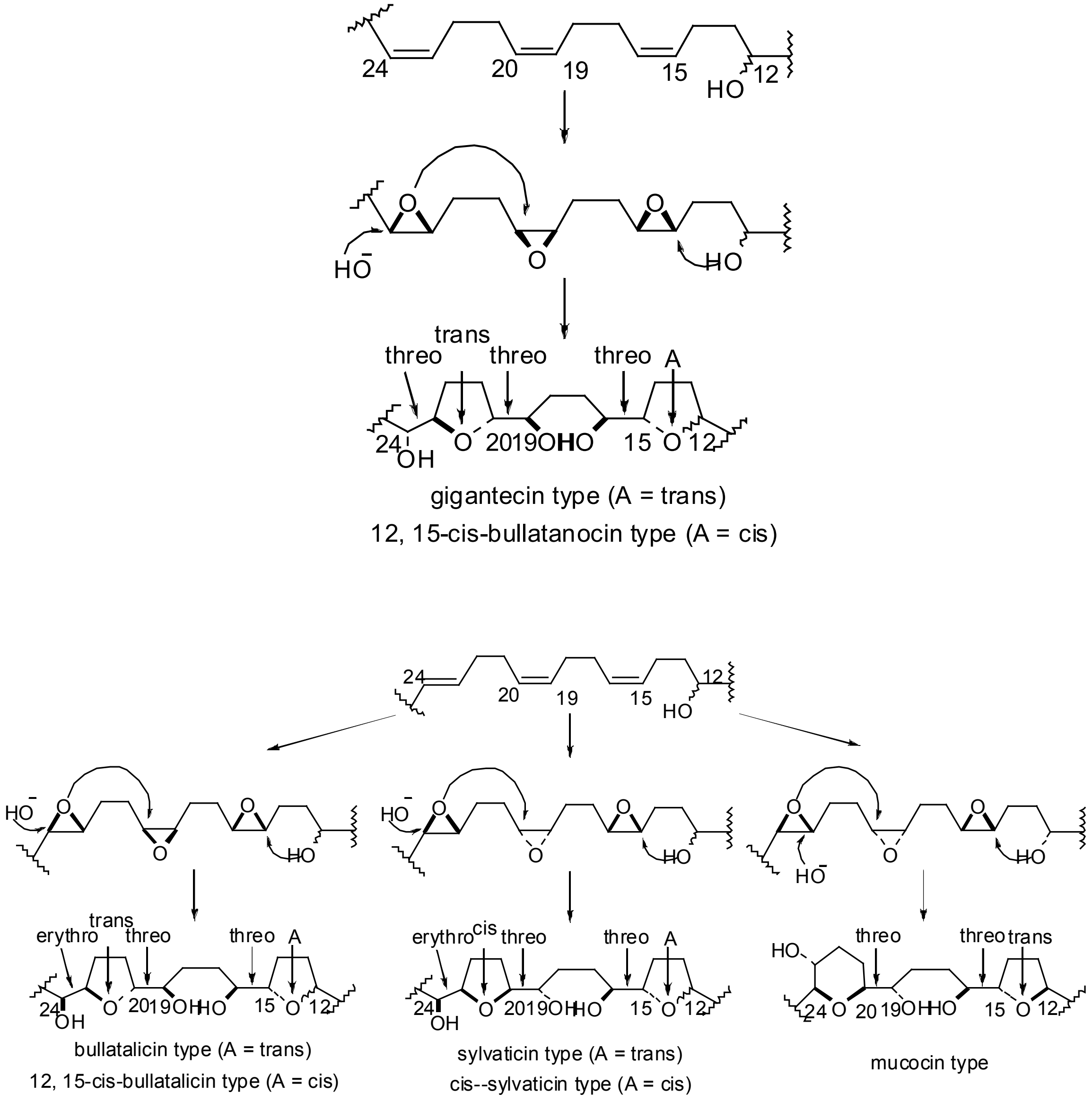
SCHEME 1.5 Proposed biosynthetic pathways of goniocin.



Six types of acetogenins having non-adjacent bis-THF rings (gigantecin,[20] 12,15-*cis*-bullatanocin,[21] bullutalicin,[22] 12,15-*cis*-bullatalicin,[21] sylvaticin[23] and cis-sylvaticin.[21]) have been found. These compounds consist of one THF ring bearing one flanking carbinol and another THF ring bearing two flanking carbinols, separated by two methylenes. The formations of these acetogenins can be considered to result from two separate epoxide opening cascades that start from ends of a tris- epoxide precursor. Non-classical acetogenins, like mucocin, which have non-adjacent THF and tetrahydropyran (THP) rings, may arise from a similar biogenetic pathway (**Scheme 1.6**).

The biosynthesis of acetogenins remains elusive. The epoxide opening cascade sequence is one of the more plausible pathways. The laboratory syntheses of several THF containing acetogenins have mimicked this mechanism.[24]

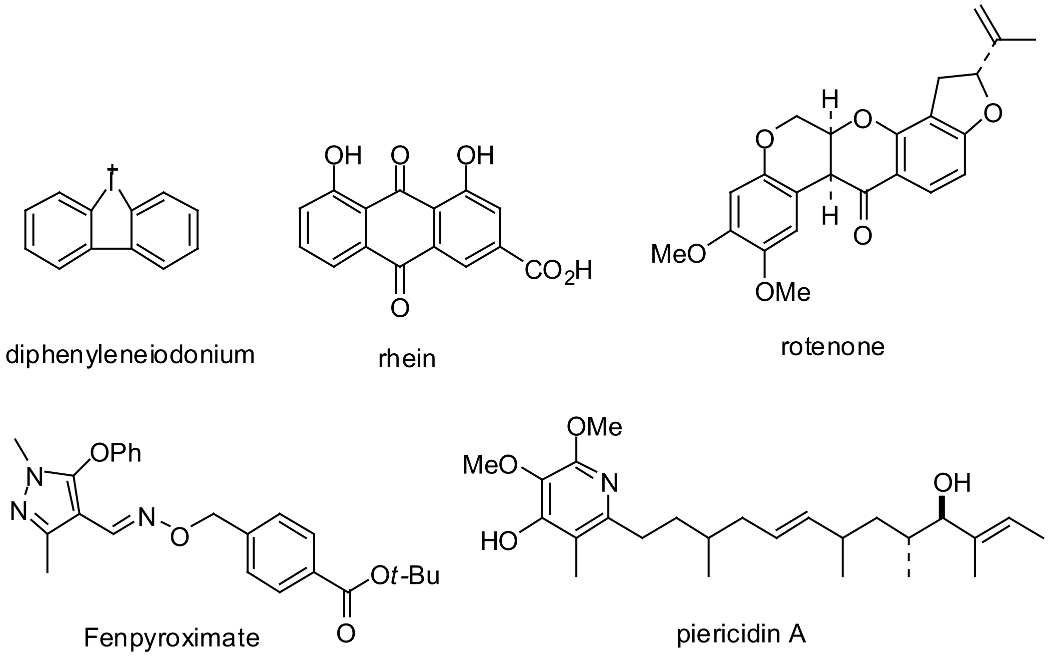
SCHEME 1.6 Proposed biosynthetic pathways of six types of bis-THF acetogenins and mucocin.



1.3 Bioactivity

Annonaceous acetogenins are the most potent inhibitors of mitochondrial NADH-ubiquinone oxidoreductase (complex I).[25] Except rhein[26] and diphenyleneiodonium,[27] which inhibit electron input into the enzyme, all inhibitors are believed to act on the terminal electron transfer step to ubiquinone. Ordinary complex I inhibitors such as piericidin A, rotenone, and several synthetic agrochemicals like Fenpyroximate have structural features in common, notably a polar and/or heterocyclic ring processing hydrogen bond ability and a hydrophobic "tail" structure (**Scheme 1.7**).[28] The former may play an important role in binding to the enzyme through specific interactions. The tail moiety may be important for attaching to and penetrating through the membrane-embedded segment of the enzyme. Therefore a critical degree of hydrophobicity may be required.

SCHEME 1.7 Some common inhibitors of mitochondrial complex I.



For acetogenins, the inhibitory mechanism might be different from that of the inhibitors mentioned above since two toxophores of acetogenins (the hydroxylated THF and γ-lactone moieties) are separated by a long alkyl spacer. Based on NMR spectroscopy and differential scanning calorimetry studies on acetogenins in liposomal membranes, MacLaughlin and colleagues proposed a model for an active conformation of acetogenins in the mitochondrial membrane environment, wherein the THF ring(s) with flanking carbinol groups resides near the glycerol backbone of phosphatidylcholine irrespective of the number of THF rings, and act as a hydrophilic anchor at the membrane surface. The γ-lactone ring directly interacts with the target site of complex I by lateral diffusion in the mitochondrial membrane interior.[29] This model has been challenged by recent structural-activity studies on acetogenin mimtics.[30] According to this model, the γ-lactone is the only species that interacts directly with the enzyme. Therefore structural modification of this moiety is expected to result in a drastic decrease in inhibitory potency. However, the structural modifications of γ-lactone moiety, such as deletion of the γ-methyl group, transformation of the γ-lactone ring to a six-membered δ-lactone ring and complete removal of γ-lactone ring did not significantly affect the inhibitory potency. [29] Moreover, the observation that OH groups adjacent to the THF ring is not crucial for the potent activity is in disagreement with the supposed important function of these OH groups as hydrophilic anchors at the membrane surface. On the contrary, OH groups and lactone may be crucial for cellular uptake and localization, because the degree and location of hydroxylation and the presence of lactone have a marked effect on cytoxicity.

CHAPTER TWO

Synthesis and antitumor activity of 4-deoxyannoreticuin

2.1 Introduction

4-deoxyannoreticuin,[30] a white amorphous powder, is similar to annoreticuin[31] except that it does not have a hydroxyl group at C-4 (**Figure 2.1**). It shows cytotoxicity at the micromolar level against several human cancer cell lines, including MCF-7, HT-29, A-498, PC-3 and PACA.[30] 4-deoxyannoreticuin is a typical member of the mono-THF acetogenin with two flanking carbinol groups at C-15 and C-20. The MH^+ peak in the FABMS at *m/z* 581 established the molecular weight as 580. The elemental composition of $C_{35}H_{64}O_6$ was confirmed by high resolution EIMS of the molecular ion which gave an exact mass of *m/z* 581.4763 (calcd 581.4781). NMR data indicated the presence of an α,β-unsaturated γ-lactone which was corroborated by an absorption band in the IR at 1760 cm^{-1} and the UV λ_{max} at 215 nm.

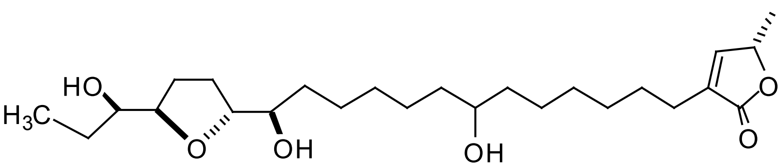


FIGURE 2.1 Structure of 4-deoxyannoreticuin.

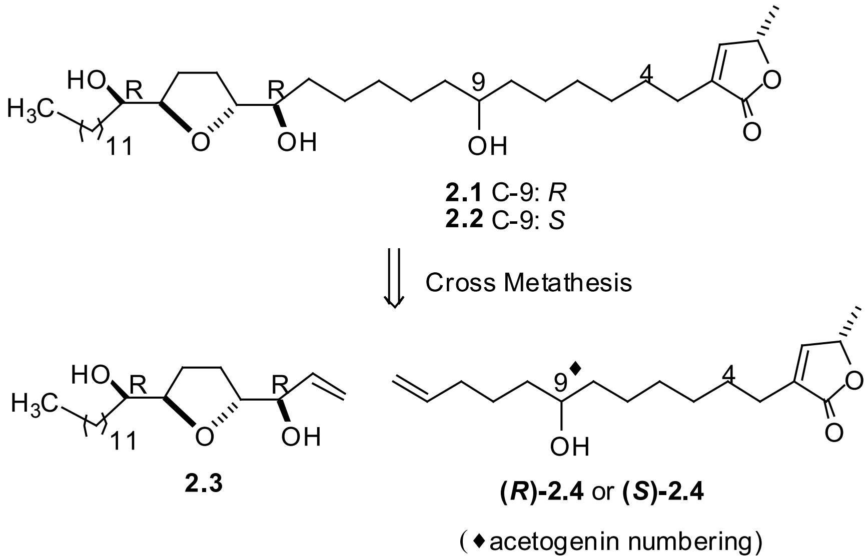
The presence of a single THF ring with two flanking carbinols in a *threo/trans/threo* relative configuration was evidenced by ^1H NMR signals at δ 3.41 (H-15/20) and 3.80 (H-16/19), each integrating for two protons, as well as ^{13}C NMR peaks at δ 74.06 (C-15/20), 82.58 (C-16/19), and 82.64 (C-16/19).[32] The ring was located between C-15 and C-20 based on peaks in the EIMS as *m/z* 311 and 381. The hydroxyl located between THF ring and lactone was confirmed by EIMS at *m/z* 311. A small EIMS peak at m/z

211 suggested that the location might be at C-9. A high resolution EIMS of the peak at *m/z* 211 gave the exact mass of *m/z* 211.1342 (calcd 211.1334), established the molecular composition of the fragment as $C_{12}H_{19}O_3$, and confirmed that hydroxyl group was at C-9. Unfortunately, insufficient material was available to complete Mosher ester derivatives, which would be helpful in resolving the stereochemistry of C-9.

2.2 Synthetic strategy

We were particularly in a synthetic plan that would be practical for assigning an unambiguous structure to 4-deoxyannoreticuin and in the longer term would be applicable to other mono-THF acetogenin congeners. The gross structure of 4-deoxyannoreticuin is represented as in **2.1** or **2.2** but the configuration at C-9 was not determined. The relative stereochemistry of the C-15-C20 portion was deduced as the threo-trans-threo motif on the basis of the known ^{1}H and ^{13}C NMR trends. The absolute stereochemistry of the THF core was assigned as 15*R*, 16*R*, 19*R*, 20*R* because this configuration was determined for the analogous segment in 2,4-*trans*-squamoxinone, a co-isolate from the same plant material, and several other mono-THF containing acetogenins.[30] It was also assumed that the configuration at C-34 is *S* by analogy with all the other acetogenins for which this center has been determined.[9] In order to establish the configuration at C-9, we set as synthetic goals the C-9 epimeric structures **2.1** and **2.2**, with the plan of matching one or the other to the natural product on the basis of its physical properties. Accordingly, a modular synthesis in which a fixed THF segment x could be paired with epimeric-C-9-hydroxy-butenolide components (*R*)-4 and (*S*)-4 (or appropriately protected alcohol derivatives), via an olefin cross metathesis, was conceived (**Scheme 2.1**).[33, 34]

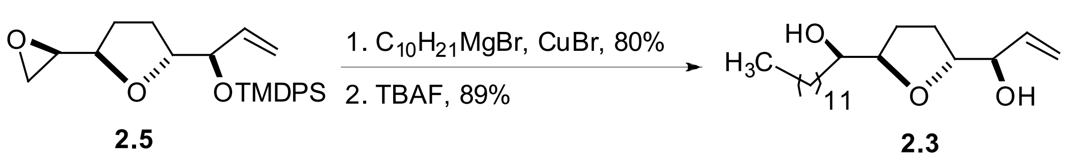
SCHEME 2.1 Retrosynthesis for 4-deoxyannoreticuin.



2.3 Synthesis

The synthesis of the THF segment followed our earlier work on the analog of **2.3** that contained a hydrocarbon chain with two carbons less.[33b] Thus, the copper (I)-mediated reaction of undecylmagnesium bromide with the known epoxide **2.5**, followed by desilylation of the product provided diol 2.**3** (**Scheme 2.2**).

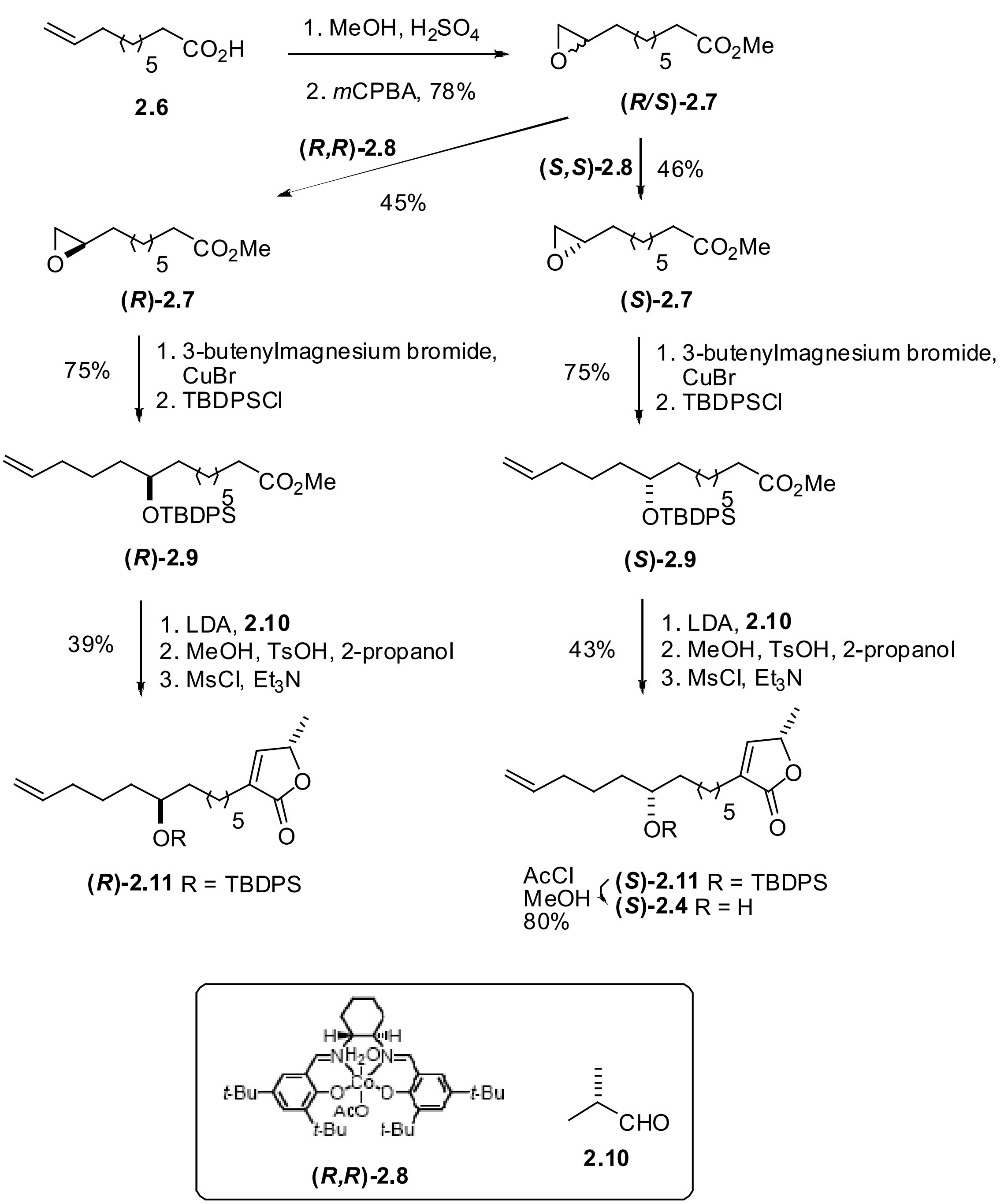
SCHEME 2.2 Synthesis of THF segment.



The epimeric butenolide segment (*R*)-**2.4** and (*S*)-**2.4**, originated from the racemic mixture of epoxides *rac*-**2.7** are derived from the raction of methyl dec-9-enoate with *m*CPBA (**Scheme 2.3**). Treatment of rac-**2.7** under Jacobson's Hydrolytic Kinetic Resolution (HKR) conditions using (*R, R*)-**2.8**, or its enantiomer gave either (*R*)-**2.7** or (*S*)-**2.7** in 45% and 46% yields, respectively.[35] Epoxides (*R*)-**2.7** and (*S*)-**2.7** were next converted to the silyl ethers (*R*)-**2.9** and (*S*)-**2.9**, respectively, via a two-step epoxide opening-alcohol silylation sequence. The *ee* of these products were deduced to be over 95% by H^1 NMR analysis of their Mosher ester derivatives.[36] Silyl ether (*R*)-**2.9** and (*S*)-**2.9** were individually partnered with aldehyde **2.10** and forwarded into a known aldol reaction-elimination protocol to give butenolide alkenes (*R*)-**2.11** and (*S*)-**2.11**, respectively, in 39% and 43% overall yield from (*R*)-**2.9** and (*S*)-**2.9**.[37] To compare the use of protected versus deprotected alcohol butenolide partners in the CM and subsequent reactions (vide infra), one of the silyl ether (*S*)-**2.11** was converted to the derived alcohol (*S*)-**2.4**.

The CM and subsequent steps were first evaluated for TBDPS-protected butenolide (*R*)-**2.11** (**Scheme 2.4**). The optimal CM conditions were found to be methylene chloride as the solvent, a 1:2 molar ratio of 3: (*R*)-**2.11,** 10 mol % Grubbs II catalyst, at room temperature for approximately 20h. The desired product (*R*)-**2.12** was obtained in 73% isolated yield based on THF segment **2.3**. The homodimer of (*R*)-**2.11** was also isolated in 20% yield together with approximately 15% of unreacted (*R*)-**2.11.** Selective hydrogenation of isolated alkene in (*R*)-**2.12** using $RhCl(PPh_3)_3$ as a catalyst provided an inseparable 7:1 mixture of the desired hydrogenated product and the completely hydrogenated material in 70% combined yield.

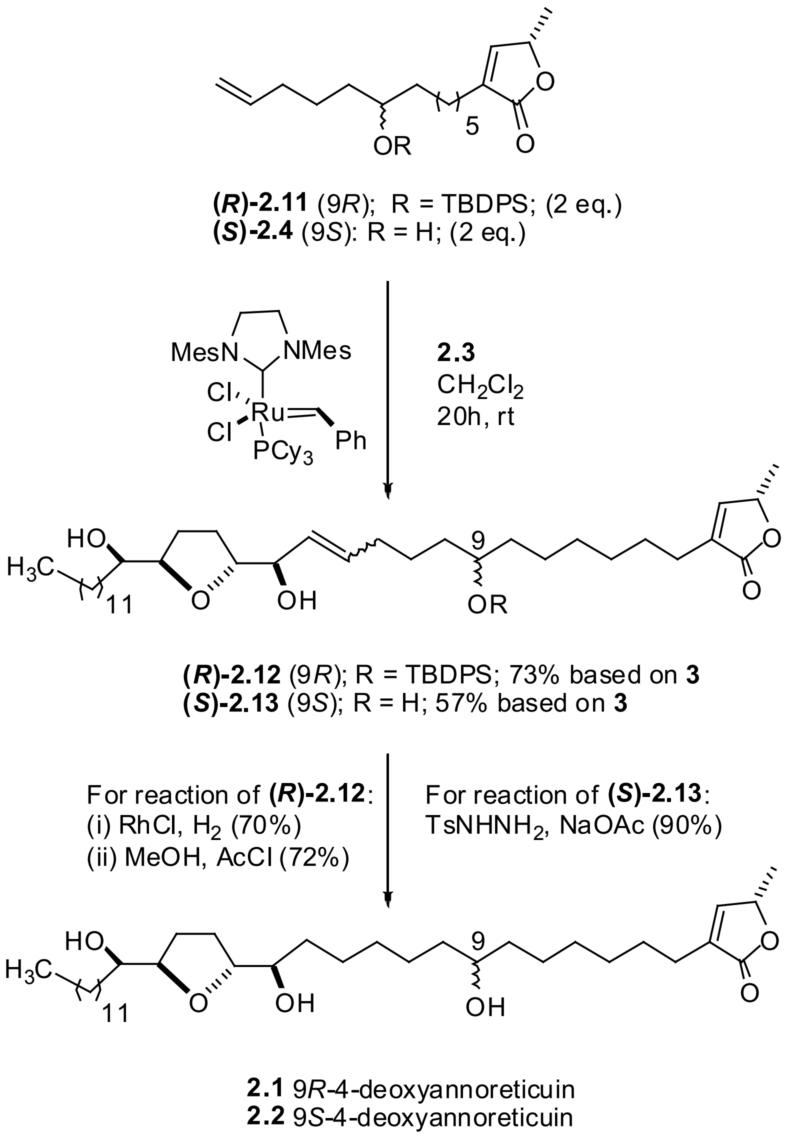
SCHEME 2.3 Synthesis of butenolide segements.



Exposure of this mixture to methanolic HCl led to 9*R*-4-deoxyannoreticuin (**2.1**) that contained approximately 10% of the corresponding over-reduced product. For the synthesis of 9*S*-4-deoxyannoreticuin (**2.2**), the CM reaction was performed with the desilylated butenolide (*S*)-**2.4** thereby obviating the desilylation step in a more advanced THF-butenolide synthetic intermediate. Accordingly, application of the CM conditions to **2.3** and (*S*)-**2.4** gave (*S*)-**2.13** in 57% isolated yield based on **2.3**. Given the difficulty in controlling the $RhCl(PPh_3)_3$-catalyzed hydrogenation of (*R*)-**2.12**, the diimide reduction of (*S*)-**2.13** was explored and found to be superior, giving 9*S*-4-deoxyannoreticuin (**2.2**) in 90% yield with no evidence of the over-reduced product.

In the absence of an actual sample of 4-deoxyannoreticuin we attempted to assign the configuration at C-9 in the natural product by comparison of NMR data for synthetic **2.1** and **2.2** with the reported listings for the natural 4-deoxyannoreticuin. All three sets of data were essentially identical, which corroborated the gross structure assigned to the natural product, but at the same time made assignment of the C-9 configuration impossible. This scenario was not completely surprising giving the close similarity (albeit noticeably different) of the NMR data for the analogous epimers of corossolin, the C-10 regioisomer of 4-deoxyannoreticuin.[38, 39] Similar observations have been made in a recent rigorous investigation on acetogenin diastereomers that vary with respect to the configuration at the remote stereogenic centers. Examination of the optical rotations were also inconclusive because the values obtained for **2.1** and **2.2** were appreciably different from that reported for the natural product, ($[\alpha]_D$ = + 19°, + 25° and + 6.8° for **2.1**, **2.2** and natural 4-deoxyannoreticuin, respectively). Parenthetically, the optical otation for **2.1** and **2.2** were essentially identical to the values observed for the respective C-10 epimers of corossolin.[38]

SCHEME 2.4 Cross metathesis and final products.



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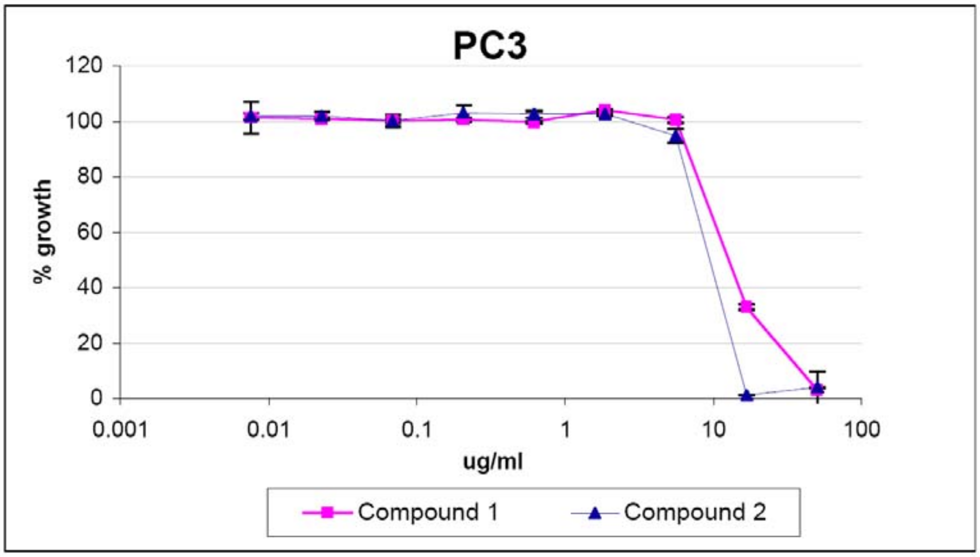
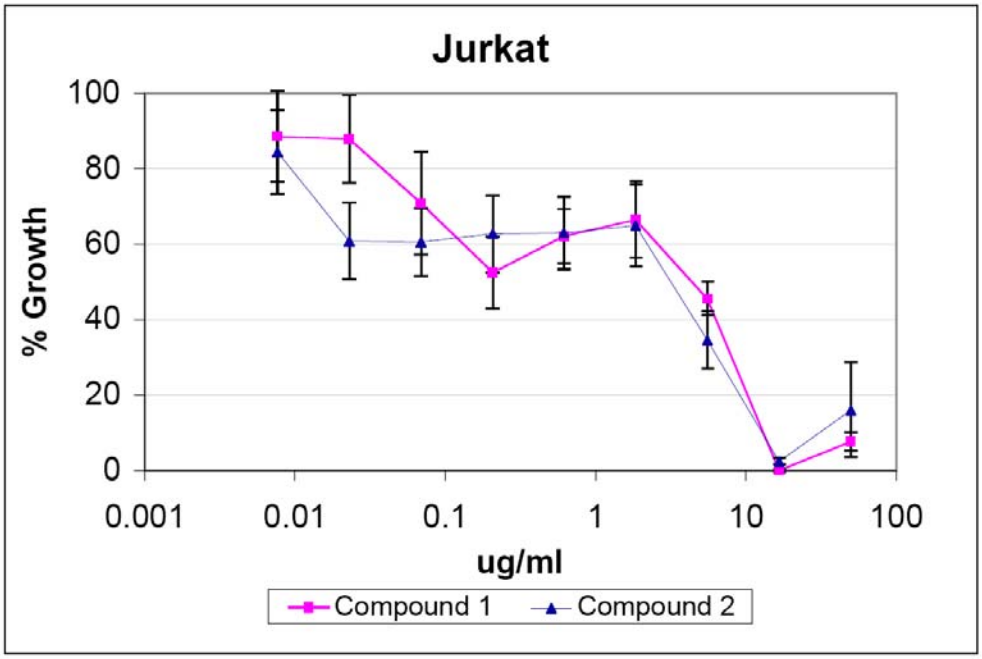
2.4 Biological assay

In the case of corossolin,[38] the cytotoxic activities of the C-10 epimers were significantly different. Therefore, we next attempted to identify **2.1** or **2.2** with the natural product by comparing their cytotoxicity against PC-3 (human prostate) with the expectation that the activity of one or the other would more closely match the reported data for the natural product. The GI 50 values for **2.1** and **2.2** were found to be approximately 15 and 10 μg/mL in a 7-day MTT assay. Thus, preliminary biological evaluation was also not structurally insightful. Epimers **2.1** and **2.2** also showed similar activity against Jurkat cells (human T-cell leukemia), with GI_{50} values in the range of 5-10 μg/mL. These data suggest that the notion a change in the configuration at such remoter carbinol centers leads to significant difference in cytotoxic activity may hold only for certain cell lines and is not general.

MTS assays for 1 and 2 against PC-3 and Jurkat cell lines





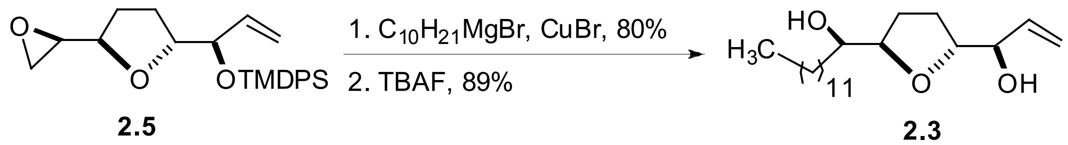
2.5 Conclusion

In conclusion we have developed a highly convergent synthesis for the mono-THF containing acetogenins that is based on the CM coupling of THF and butenolide components. This methodology was applied to the epimeric analogous of the natural product 4-deoxyannoreticuin, in an attempt to resolve the unassigned configuration at C-9. Unfortunately, identification of one or the other epimeric structures with the natural product was not possible because of the closeness of the physical data for all three compounds, illustrating the limitation of this strategy for the assignment of stereochemistry at remote stereogenic centers. In contrast to observations made for closely related THF acetogenins, the cytotoxicity of the epimeric analogues of 4-deoxyannoreticuin was found to be very similar.

2.6 Experimental section

General. Solvents were purified by standard procedures or used from commercial sources as appropriate. Petroleum ether refers to the fraction of petroleum ether boiling between 40 and 60 °C. Ether refers to diethyl ether. Unless otherwise stated thin layer chromatography (TLC) was done on 0.25 mm thick precoated silica gel 60 (HF-254, Whatman) aluminium sheets and flash column chromatography (FCC) was performed using Kieselgel 60 (32-63 mesh, Scientific Adsorbents). Elution for FCC usually employed a stepwise solvent polarity gradient, correlated with TLC mobility. Chromatograms were observed under UV (short and long wavelength) light, and/or were visualized by heating plates that were dipped in a solution of ammonium (VI) molybdate tetrahydrate (12.5 g) and cerium (IV) sulfate tetrahydrate (5.0 g) in 10% aqueous sulphuric acid (500 mL). Optical rotations ($[\alpha]_D$ were recorded using a Rudolph Autopol III polarimeter which has a thermally jacketed 10 cm cell (path length of 1 dm) and are given in units of 10^{-1} degcm^{2}g at 589 nm (sodium D-line). NMR spectra were recorded using either Varian Unity Plus 500 or Bruker Ultra Shield instruments (^{1}H and ^{13}C; 500 and 125 MHz respectively). Spectra were recorded in $CDCl_3$ solutions with residual $CHCl_3$ as internal standard (H 7.27 and C 77.0 ppm). Chemical shifts are quoted in ppm relative to tetramethysilane (H 0.00) and coupling constants (*J*) are given in Hertz. First order approximations are employed throughout. High-resolution mass spectrometry was performed on an Ultima Micromass Q-Tof instrument at the Mass Spectrometry Laboratory of the University of Illinois, Urbana-Champaign.

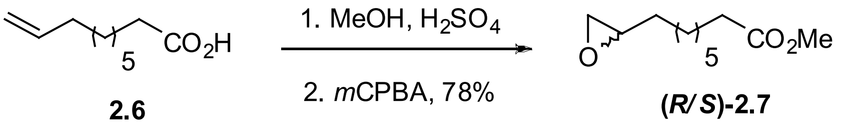
Synthesis of (2R, 5R, 1'R, 1"R)-2-[1'-Hydroxy-2'-propenyl]-5-[1"-hydroxytridecyl]-tetrahydrofuran (2.3)



In a 50 mL round-bottom flask equipped with magnetic stirring bar, were placed CuBr (36.3 mg, 0.253 mmol) and anhydrous THF (10 mL). Pre-prepared, $C_{11}H_{23}MgBr$ (11.5 mL, ca 0.4 M in THF) was added dropwise at 0 °C, and then epoxide **2.5** (120 mg, 0.422 mmol) was introduced. The reaction was stirred at 0 °C for 3 h, then poured into ice cold saturated aqueous NH_4Cl, and extracted with ether. The organic phase was washed with brine, dried (Na_2SO_4), filtered, and evaporated under reduced pressure. The residue was purified by FCC (2-5% EtOAc:petroleum ether) to give the derived alcohol (160 mg, 86%): R_f= 0.45 (5% EtOAc: petroleum ether); ^{1}H NMR ($CDCl_3$) δ 5.81 (m, 1H), 5.24-5.28 (dd, 2H, *J* = 17.1Hz, 10.6 Hz), 4.10 (t, 1H), 3.88-3.89 (q, 1H), 3.75-3.76 (q, 1H), 3.35 (m, 1H), 2.31 (d, 1H, *J* = 4.1 Hz), 1.86-1.89 (m, 2H), 1.52-1.70 (m, 2H), 1.36 (m, 1H), 1.36-1.38 (m, 2H), 1.23 (s, br, 20H), 0.88 (s, br, 9H), 0.85 (t, *J* = 6.7 Hz, 3H), 0.05 (s, 3H), 0.03 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 137.6, 115.7, 82.7, 82.4, 76.0, 74.0, 33.6, 31.9, 29.7, 29.7, 29.6, 29.6, 29.6, 29.4, 28.4, 27.8, 25.8, 25.6, 22.7, 18.3, 14.1, 1.0, -4.6, -4.8; HRMS (FAB) calcd for $C_{26}H_{53}O_3Si$ (M + H$^+$) 441.3764, found 441.3744.

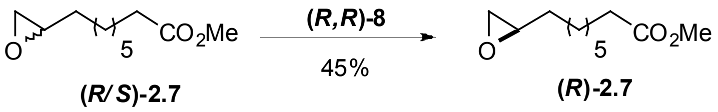
To a solution of the product from the previous step (64 mg, 0.145 mmol) in THF (10 mL) was added Bu_4NF (1.45 mL, 1M in THF) at 0 °C. The reaction was stirred at rt until TLC indicated complete disappearence of the starting material, at which time the mixture was diluted with water and extracted with EtOAc. The organic phase was dried (Na_2SO_4), filtered and evaporated under reduced pressure. The residue was purified by FCC to give **2.3** (40 mg, 85%): white powder; $R_f = 0.3$ (25% EtOAc: petroleum ether); ^{1}H NMR δ ($CDCl_3$) 5.78 (m, 1H), 5.18-5.36 (dd, 2H, $J = 17.5, 10.5$ Hz), 3.93 (m, 1H), 3.80-3.88 (m, 2H), 3.39 (m, 1H), 2.45 (b, 1H), 2.25 (b, 1H), 1.94-1.98 (m, 2H), 1.68-1.73 (m, 2H), 1.40-1.41 (m, 1H), 1.29-1.38 (m, 3H), 1.24 (s, br, 20H), 0.86 (t, $J = 6.8$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 136.7, 117.1, 82.9, 82.2, 75.5, 74.0, 33.6, 31.9, 29.7, 29.7, 29.7, 29.6, 29.6, 29.6, 29.3, 28.5, 28.4, 25.6, 22.7, 14.1; HRMS (FAB) calcd for $C_{20}H_{38}O_3Na$ (M + Na^+) 349.2719, found 349.2708.

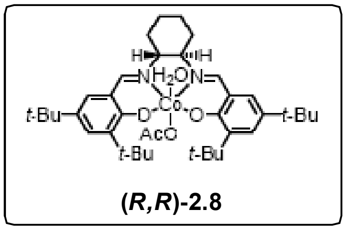
Synthesis of methyl 8-(oxiran-2-yl)octanoate (2.7)



To a solution of methyl dec-9-enoate (1.40 g, 7.60 mmol) in CH_2Cl_2 (25 mL) was added *m*CPBA (4.26 g, 19 mmol, 77% purity) at room temperature. The mixture was stirred for 1h and quenched by adding saturated aqueous $NaHCO_3$ and saturated aqueous $Na_2S_2O_3$, and extracted with EtOAc. The organic phase was dried (Na_2SO_4), filtered and evaporated under reduced pressure. The residue was purified by FCC to give **2.7** (1.31 g, 86.4%): as a yellow oil; $R_f = 0.70$ (10% EtOAc: petroleum ether); ^{1}H NMR ($CDCl_3$) δ 3.69 (s, 3H), 2.92 (m, 1H), 2.75-2.77 (m, 1H), 2.47-2.48 (m, 1H), 2.32 (t, $J = 7.5$ Hz, 2H), 1.60-1.62 (m, 2H), 1.34-1.55 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 174.2, 52.3, 51.4, 47.1, 34.1, 32.4, 29.2, 29.1, 29.0, 25.9, 24.9.

Synthesis of (R)- Methyl 8-(oxiran-2-yl)octanoate [(*R*)-2.7]

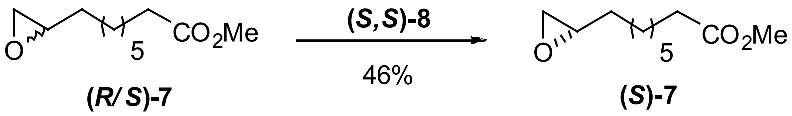




(*R,R*)-2.8

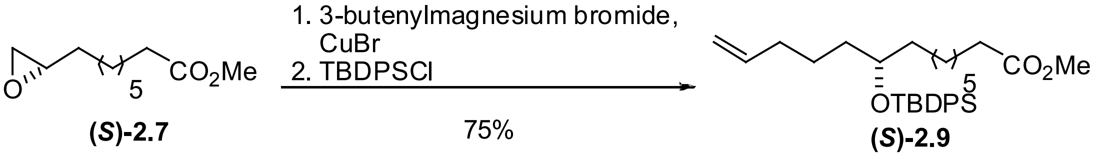
A solution of **(*R*/*S*)-2.7** (1.83 g, 9.17 mmol) in DME (10 mL) was treated with (*R,R*)-salen-Co(OAc) (182 mg, 0.275 mmol) and distilled water (0.091 mL, 5.06 mmol). The mixture was stirred at room temperature for 72 h, then purified by FCC to give **(*R*)-2.7** (677 mg, 37%) and the derived diol (765 mg, 38%). The TLC and NMR data for **(*R*)-2.7** was as listed for **(*R*/*S*)-2.7**.

Synthesis of (S)-Methyl 8-(oxiran-2-yl)octanoate [(*S*)-2.7]



(*S*)-2.7 (4.2 g, 46%) was obtained from **(*R*/*S*)-2.7** (9.2 g. 46 mmol) using **(*S*, *S*)-2.8**, following the procedure described for **(*R*)-2.7.** For **(*S*)-2.7**: The TLC and NMR data for **(*S*)-*2.*7** was as listed for **(*R*/*S*)-2.7**.

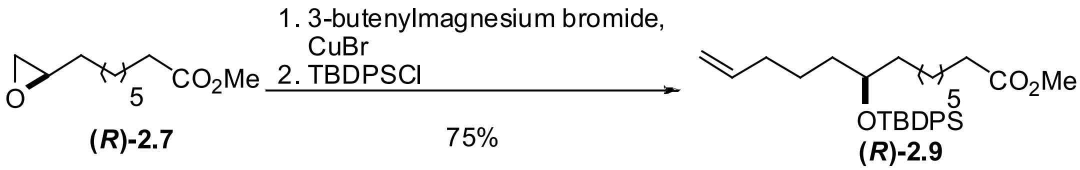
Synthesis of (S)-methyl 9-tert-butyldiphenylsilyloxytetradec-13-enoate [(*S*)-2.9]



To a suspension of CuBr (258 mg, 1.8 mmol) in THF (15 mL) at 0 ˚C was added 3-butenylmagnesium bromide (18 mL, 0.5 M in THF, 9.0 mmol) over 5 min. A solution of **(*S*)-2.7** (600 mg, 3.00 mmol) in anhydrous THF (3 mL) was then introduced, dropwise over 5 min. The reaction was stirred at 0 ˚C for 10 min at which time saturated aqueous NH_4Cl was added and the mixture extracted with ether. The organic phase was washed with brine, dried (Na_2SO_4), filtered, and evaporated under reduced pressure. The residue was purified by FCC to give the derived alcohol: R_f = 0.50 (20% EtOAc: petroleum ether).

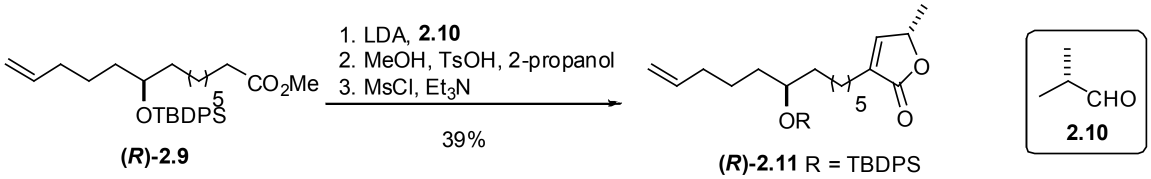
A solution of the product from the previous step (358 mg, 1.4 mmol), TBDPSCl (769 mg, 2.8 mmol) and imidazole (477 mg, 7.00 mmol) in anhydrous CH_2Cl_2 (20 mL) was stirred under nitrogen at room temperature for 2 h. The mixture was quenched with brine and extracted with ether (3 x 50 mL). The organic phase was dried (Na_2SO_4) filtered, and evaporated under reduced pressure. The residue was purified by FCC to afford **2.9** (600 mg, 87%): R_f = 0.50 (5% EtOAc: petroleum ether); ^1H NMR ($CDCl_3$) δ 7.69-7.70 (m, 4H), 7.37-7.44 (m, 6H), 4.91-4.96 (m, 2H), 3.75 (m, 1H), 3.70 (s, 3H), 2.30 (t, *J* = 7.5 Hz, 2H), 1.92-1.93 (m, 2H), 1.59-1.60 (m, 2H), 1.40-1.45 (m, 6H), 1.14-1.23 (m, 8H); ^{13}C δ NMR ($CDCl_3$) 174.5, 139.2, 136.2, 135.1, 135.0, 129.6, 127.6, 114.5, 77.0, 73.3, 51.6, 36.5, 36.0, 34.3, 34.0, 29.7, 29.3, 29.3, 27.3, 25.2, 25.0, 24.4, 19.7.

Synthesis of (R)-methyl 9-tert-butyldiphenylsilyloxytetradec-13-enoate [(*R*)-2.9]



(*R*)-2.9 (600 mg, 75%) was obtained from ***(R)*-2.7** (324 mg. 1.62 mmol) following the two step reaction sequence described for **(*S*)-2.9**. The TLC and NMR data for **(*R*)-2.9** was as listed for **(*S*)-2.9**.

Synthesis of butenolide (*R*)-2.11

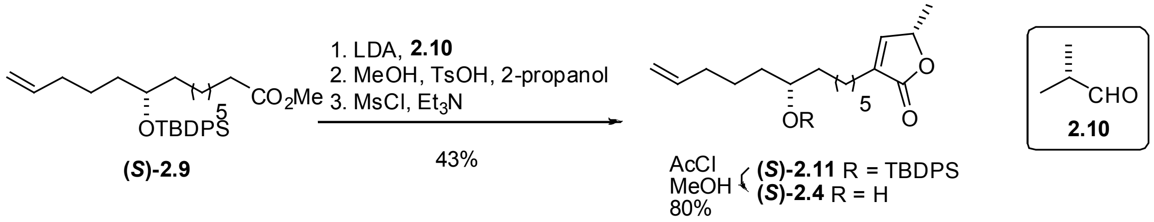


To a solution of diisopropylamine (1.2 mL, 8.5 mmol) in anhydrous THF (15 mL) at –78 ˚C, was added BuLi (2.4 mL, 2.5 M in hexane, 6 mmol). The mixture was warmed to 0 ˚C and stirred at this temperature for 10 min, then cooled to –78 ˚C, at which time a solution of **(*R*)-2.9** (600 mg, 1.21 mmol) in anhydrous THF (6 mL) was added. The reaction mixture was stirred at –78 ˚C for 1 h and a solution of aldehyde **2.10** (574 mg, 3.63 mmol) in anhydrous THF (6 mL) was slowly introduced. After 30 min, the reaction was quenched with saturated aqueous NH_4Cl and extracted with ether. The organic extract was dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by FCC to afford the aldol product (400 mg, 70% based on consumed **(*R*)-2.9**.

To the solution of product from the previous step (400 mg, 0.613 mmol) in a mixture of MeOH (10 mL) and 2-propanol (1 mL) was added TsOH (12 mg, 0.06 mmol) at 0 ˚C. The reaction mixture was stirred at room temperature for 20 h, then concentrated under reduced pressure. The residue was purified by FCC to afford the derived lactone as a yellow oil (227 mg, 69%).

To a solution of the material from the previous step (227 mg, 0.42 mmol) in CH_2Cl_2 (10 mL) was added Et_3N (0.3 mL, 2.1 mmol) and MsCl (0.07 mL, 0.84 mmol) at 0 ˚C. After stirring at room temperature for 14 h, the reaction was diluted wth saturated aqueous NH_4Cl and extracted with ether. The organic phase was dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by FCC to afford **(*R*)-2.11** (176 mg, 81%): R_f= 0.75 (15% EtOAc: petroleum ether); ^{1}H NMR ($CDCl_3$) δ 7.66-7.68 (m, 4H), 7.35- 7.41 (m, 6H), 6.94 (d, *J* = 1.5 Hz, 1H), 5.69- 5.72 (m, 1H), 4.97-4.99 (m, 1H), 4.88-4.94 (m, 2H), 3.70-3.74 (m, 1H), 2.20- 2.24 (m, 2H), 1.90-1.91 (m, 2H), 1.38-1.47 (m, 11H), 1.14- 1.1.23 (m, 6H), 1.05 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 173.8, 148.8, 138.9, 135.9, 134.8, 134.7, 134.3, 129.4, 129.4, 127.4, 114.3, 73.1, 36.3, 35.8, 33.8, 29.3, 29.1, 27.3, 27.1, 25.1, 24.7, 24.2, 19.4, 19.2; HRMS (FAB) calcd for $C_{33}H_{46}O_3Si$ (M + H$^+$) 519.3294, found 519.3282.

Synthesis of butenolide (*S*)-2.11

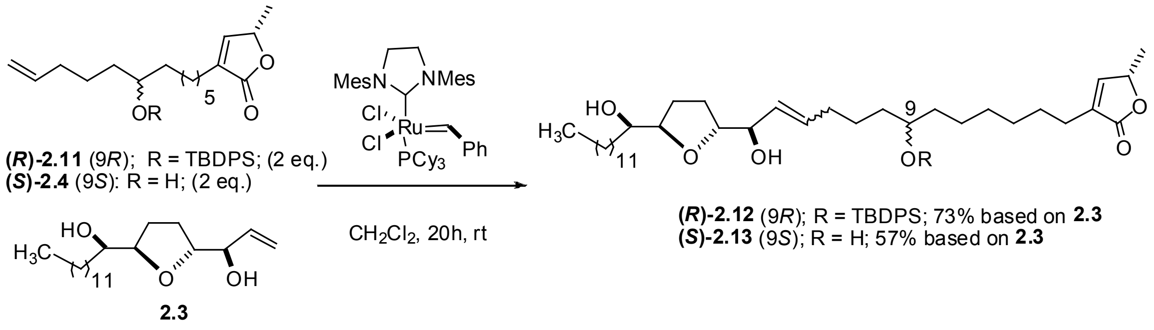


R_f= 0.70 (15% EtOAc: petroleum ether); ^{1}H NMR ($CDCl_3$) *δ* 7.69- 7.70 (m, 4H), 7.37-7.45 (m, 6H), 6.96 (d, *J* = 1.4 Hz, 1H), 5.71- 5.76 (m, 1H), 5.00- 5.01 (m, 1H), 4.91- 4.96 (m, 2H), 3.74- 3.76 (m, 1H), 2.23- 2.26 (t, *J* = 8.1 Hz, 2H), 1.92- 1.93 (m, 2H), 1.25- 1.49 (m, 11H), 1.16- 1.23 (m, 6H), 1.08 (s, 9H); ^{13}C NMR ($CDCl_3$) *δ* 173.8, 148.7, 138.9, 135.9, 134.8, 134.7, 134.4, 129.4, 127.4, 114.3, 73.1, 36.3, 35.8, 33.8, 29.3, 29.1, 27.3, 27.1, 25.1, 24.7, 24.2, 19.4, 19.2; HRMS (FAB) calcd for $C_{33}H_{46}O_3Si$ (M + H^+) 519.3294, found 519.3293.

Synthesis of butenolide (*S*)-2.4

5% AcCl in MeOH (2.1 mL) was added at room temperature to a solution of **(*S*)-2.11** in CH_2Cl_2 (5 mL). The mixture was stirred for 16 h, then diluted with CH_2Cl_2 and washed with saturated aqueous $NaHCO_3$. The organic phase was dried (Na_2SO_4) and concentrated under reduced pressure. FCC of the residue afforded **(*S*)-2.4** (50 mg, 82%): R_f= 0.45 (30% EtOAc: petroleum ether); ^{1}H NMR ($CDCl_3$) δ 7.00 (s, 1H), 5.81- 5.86 (m, 1H), 4.97- 5.06 (m, 3H), 3.61- 3.62 (m, 1H), 2.27- 2.31 (m, 2H), 2.02- 2.11 (m, 2H), 1.37- 1.58 (m, 17H); ^{13}C NMR ($CDCl_3$) δ 173.8, 148.8, 138.7, 134.3, 114.6, 71.8, 37.4, 36.9, 33.7, 29.3, 29.1, 27.4, 25.5, 25.2, 24.9, 19.2; HRMS (FAB) calcd for $C_{17}H_{28}O_3$ (M + H^+) 281.2117, found 281.2111.

Synthesis of THF-butenolide (*R*)-2.12



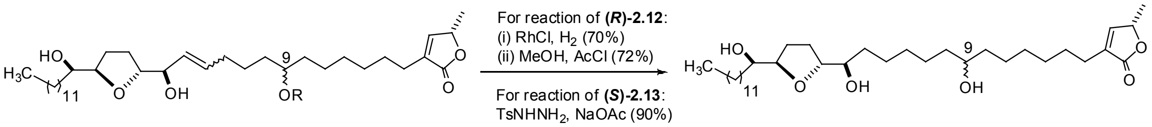
Grubb's II catalyst (6 mg, 0.007 mmol) in CH_2Cl_2 (1 mL) was injected, at rt, into a degassed solution of alcohol **2.3** (23 mg, 0.07 mmol) and **(*R*)-2.11** (74 mg, 0.14 mmol), in CH_2Cl_2 (2 mL). The reaction was stirred for 20 h at rt, then quenched by addition of

DMSO (50 μL) and concentrated *in vacuo*. FCC of the residue afforded **(*R*)-2.12** (42 mg, 73% based on **2.3**), recovered **(*R*)-2.11** (ca 15%) and the homodimer ***(R)-2.*11** (ca 20 %). For **(*R*)-2.12**: R_f= 0.50 (30% EtOAc: petroleum ether); ^{1}H NMR ($CDCl_3$) *δ* 7.65- 7.67 (m, 4H), 7.34- 7.42 (m, 6H), 6.94 (s, 1H), 5.65- 5.68 (m, 1H), 5.32- 5.34 (m, 1H), 4.97- 4.99 (m, 1H), 3.81- 3.85 (m, 3H), 3.70- 3.73 (m, 1H), 3.41 (m, 1H), 2.43- 2.44 (m, 1H), 2.20- 2.21 (m, 3H), 1.88- 1.89 (m, 4H), 1.20- 1.47 (m, 36H), 1.04 (s, 9H), 0.89 (t, *J* = 3.2 Hz, 3H); ^{13}C NMR ($CDCl_3$) *δ* 173.8, 149.5, 149.3, 149.1, 148.7, 135.9, 134.7, 134.5, 134.3, 129.4, 128.3, 127.4, 123.1, 123.0, 122.7, 82.7, 82.6, 75.6, 74.0, 73.0, 33.6, 31.9, 29.7 (three signals), 29.6 (three signals), 29.3 (two signals), 29.1, 28.4 (two signals), 27.3, 27.1, 25.1, 22.7, 19.2, 14.1; HRMS (FAB) calcd for $C_{51}H_{80}O_6Si$ (M + Na^+) 839.5622, found 839.5613.

Synthesis of THF-butenolide (*S*)-2.13

Grubb's II catalyst (9.3 mg, 0.01 mmol) in CH_2Cl_2 (1 mL) was injected, at rt, into a degassed solution of alcohol **2.3** (36 mg, 0.11 mmol), and **(*S*)-2.4** (50 mg, 0.178 mmol), in CH_2Cl_2 (2 mL). The reaction was stirred for 20 h at rt, then quenched by addition of DMSO (50 μL) and concentrated *in vacuo*. FCC of the residue provided **(*S*)-2.13** (36 mg, 57% based on **2.3**), and the homodimer of **(*S*)-2.4** (ca 27%). For **(*S*)-2.13**: R_f= 0.50 (80% EtOAc: petroleum ether); ^{1}H NMR ($CDCl_3$) *δ* 7.01 (s, 1H), 5.76- 5.82 (m, 1H), 5.41-5.46 (m, 1H), 5.02- 5.03 (m, 1H), 3.85- 3.92 (m, 3H), 3.61 (s, br, 1H), 3.42- 3.44 (m, 1H), 2.29 (t, *J* = 7.5 Hz, 2H), 2.10 (m, 2H), 1.97- 2.01 (m, 2H), 1.28-1.70 (m, 44H), 0.90 (t, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$) *δ* 173.9, 148.9, 134.3, 128.6, 82.8, 82.5, 76.8, 76.7, 75.5, 74.0, 71.7, 37.4, 36.9, 32.3, 31.9, 29.7 (five signals), 29.6, 29.4, 29.3, 29.2, 27.4, 25.6, 25.5, 25.2, 22.7, 19.2, 14.2; HRMS (FAB) calcd for $C_{35}H_{62}O_6$ (M + H^+) 579.4614, found 579.4625.

Synthesis of (9*R*)-4-deoxyannoreticuin (2.1)



(*R*)-2.12 (9*R*); R = TBDPS; 73% based on **2.3**
(*S*)-2.13 (9*S*); R = H; 57% based on **2.3**

2.1 9*R*-4-deoxyannoreticuin
2.2 9*S*-4-deoxyannoreticuin

Chlorotris(triphenylphosphine)-rhodium (I) (7.1 mg, 0.0077 mmol) was added to a degassed solution of **(*R*)-2.12** (23 mg, 0.028 mol) in a mixture of benzene-EtOH (2 mL, 50% v/v). The mixture was stirred under an atmosphere of hydrogen for 12 h, at which time the solvent was removed under reduced pressure. FCC of the residue gave an inseparable mixture of the 13,14-dihydro- and tetrahydro derivatives of **(*R*)-2.12** (16 mg, 70%): R_f = 0.50 (30% EtOAc: petroleum ether).

A mixture of 5% AcCl in MeOH (0.5 mL) was added at room temperature to a solution of the material obtained in the previous step (10 mg, 12.2 mmol) in CH_2Cl_2 (1 mL). The mixture was stirred at this temperature for 3 h, diluted with CH_2Cl_2, and washed with a saturated aqueous $NaHCO_3$. The organic layer was dried (Na_2SO_4), filtered, and concentrated under reduced pressure. FCC of the residue afforded a mixture of **2.1** and the completely hydrogenated product (7.2 mg, 72%) in an approximate 7:1 ratio: R_f = 0.35 (60% EtOAc: petroleum ether); Repeated FCC provided a sample of **2.1** that contained less than 10% of the completely reduced material: $[\alpha]^{22}_D$ +19 (c 2.00, CH_2Cl_2). ^1H NMR ($CDCl_3$) δ 6.96 (s, 1H), 4.96- 4.98 (m, 1H), 3.76- 3.80 (m, 2H), 3.56 (s, br, 1H), 3.36- 3.41 (m, 2H), 2.25- 2.27 (m, 4H, CH_2, 2xOH, D_2O ex.), 1.96- 1.97 (m, 2H), 1.24-

1.52 (m, 48H), 0.87 (t, J = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 173.8, 148.9, 134.3, 82.7, 77.4, 74.0 (two signals), 71.9, 37.4, 33.5, 33.4, 31.9, 29.7 (three signals), 29.6 (three signals), 29.3, 29.1, 28.7, 27.3, 25.6 (three signals), 25.5, 25.2, 22.7, 19.2, 14.1; HRMS (FAB) calcd for $C_{35}H_{64}O_6$ ($M+H^+$) 581.4781, found 581.4794.

Synthesis of (9S)-4-deoxyannoreticuin (2.2)

A solution of sodium acetate (280 mg, 3.41 mmol) in water (5 mL) was addead via a syringe pump, over 4 h, to a mixture of **(*S*)-2.13** (24 mg, 0.041 mmol), p-toluenesulfonyl hydrazide (511 mg, 2.74 mmol) and DME (4 mL) at reflux. After cooling to rt, the reaction mixture was poured into water and extracted with EtOAc. The combined organic extract was washed with 2M HCl, water and brine, dried (Na_2SO_4), filtered, concentrated under reduced pressure and purified by FCC to give **2.2** as a white solid (21.5 mg, 90%). $R_f = 0.50$ (80% EtOAc: petroleum ether); $[\alpha]^{22}_D$ +25 (c 4.00, CH_2Cl_2); ^{1}H NMR ($CDCl_3$) δ 6.96 (s, 1H), 4.95- 4.99 (m, 1H), 3.76- 3.80 (m, 2H), 3.56 (s, br, 1H), 3.36- 3.40 (m, 2H), 2.23- 2.24 (m, 2H), 1.95- 1.96 (m, 2H), 1.66 (m, 2H), 1.23- 1.53 (m, 48H), 0.86 (t, $J = 6.8$ Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 173.8, 148.9, 134.3, 82.7, 82.6, 77.4, 74.0, 71.9, 37.4, 33.5, 33.4, 31.9, 29.7, 29.6, 29.6, 29.6, 29.3, 29.3, 29.1, 28.7, 27.3, 25.6, 25.6, 25.5, 22.7, 19.2, 14.1; HRMS (FAB) calcd for $C_{35}H_{64}O_6$ ($M + H^+$) 581.4781, found 581.4789.

2.7 Cytotoxicity Assay

Cells were cultured in RPMI medium supplemented with 10% fetal bovine serum and penicillin-streptomycin-fungizone mixture (100 units/mL, 100 μg/mL and 0.25 μg.mL respectively) and maintained in a 37 °C humidified 5% CO_2 incubator. On the day before the drug treatment, cells were plated onto each well of 96-well plate at 2,000 cells/well (200 μl of the medium per well). After 24 hours, cells were treated with different concentrations of compounds and incubated for 72 hours. After the incubation, cell growth was evaluated using a CellTiter 96 AQueous One Solution Cell Proliferation Assay (Promega). UV absorption (490 nm) of each well was quantified by SpectraMax Plus 384 microplate reader (Molecular Devices).

CHAPTER THREE

Tandem cyclization of diene-acetals to THF-THP subunits: synthetic studies on muconin

3.1 Syntheses of muconin and jimenezin

Non-classical acetogenins, which are characterized by the presence of a THP ring, represents a minor subgroup in the acetogenin family. They can be classified into three categories: mono-THP (pyrinicin and pyragonicin type),[40] non-adjacent-bis-THF-THP (mucocin type)[41] and adjacent-bis-THF-THP (jimenezin and muconin type).[42] The syntheses of these non-classical acetogenins is interesting to synthetic chemists because of their structural uniqueness and potent biological activities. Among the non-classical acetogenins, muconin stands out for its potent and selective in vitro cytotoxicity against PACA-2 ($ED_{50} = 5.4 \times 10^{-4}$ μg/mL) and MCF-7 ($ED_{50} = 2.4 \times 10^{-4}$ μg/mL).[43] Muconin was first isolated by the MacLaughlin group in 1996.[43] With eight stereogenic centers, six of which are found in the THF/THP core unit, muconin poses a significant synthetic challenge (**Figure 3.1**). Muconin has attracted considerable synthetic interest, with four published total syntheses.[44]

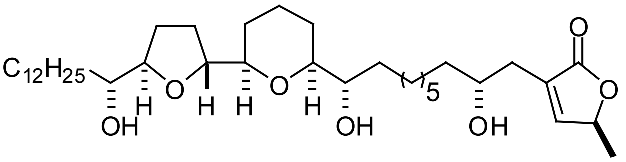
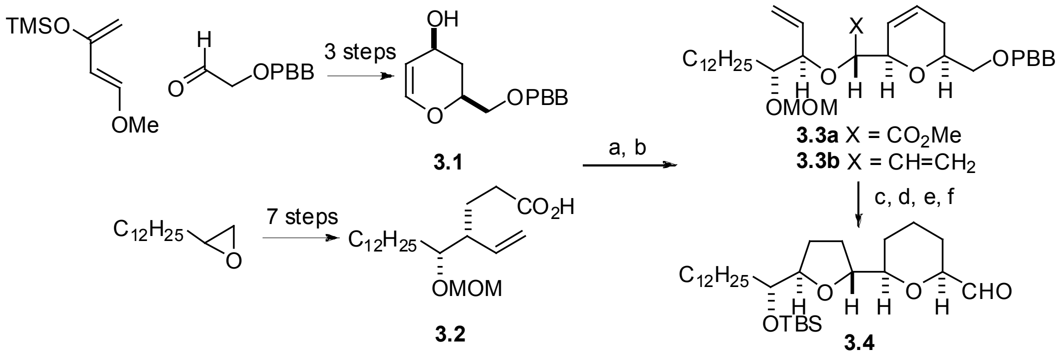


Figure 3.1 Structure of muconin

Jacobsen's group achieved the first total synthesis of muconin in 1998 (**Scheme 3.1**).[44a] Building block **3.1** was readily accessed through a hetero-Diels-Alder reaction and intermediate **3.2** was obtained in seven steps, starting with the Kinetic Hydrolytic Resolution on racemic tetradecene oxide.[35] Esterification of **3.1** with acid **3.2** was effected and the silyl ketene acetal of the ester was generated. Ireland-Claisen rearrangement[45] on the latter afforded a 2,6-*cis*-disubstituted dihydropyran, which was isolated as the methyl ester **3.3a** in 81% yield. The methyl ester was converted to the terminal olefin **3.3b** in 70% yield through a one-pot DIBALH reduction/Wittig olefination sequence. The THF ring was constructed in excellent yield through a ring-closing metathesis on **3.3b**. Deprotection of the silyl ether followed by alcohol oxidation with Dess-Martin periodinane furnished THF-THP subunit **3.4**.

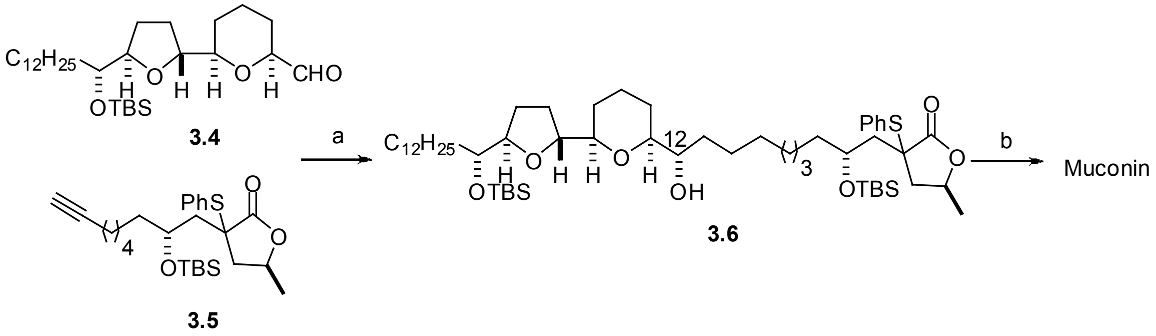
SCHEME 3.1



(a) (i) EDC, cat. DMAP, CH_2Cl_2; (ii) LDA, TMSCl, THF/HMPA 4:1; (iii) CH_2N_2, 82%; (b) (i) DIBALH, PhMe; (ii) $CH_2=PPh_3$, 70%; (c) (i) TMSBr, 4Å molecular sieves, 82%; (ii) TBSOTf, 2,6-lutidine, 99%; (d) 5 mol%, $Mo(CHMe_2Ph)(NAr)(OCMe(CF_3)_2)_2$, 99%; (e) 10% Pd/C, $NaHCO_3$, EtOH, H_2(5 atm), 95%; (f) DMP, pyridine, 95%.

The butenolide segment **3.5** was synthesized through a route which has been widely used in acetogenin syntheses (**Scheme 3.2**).[46] The key fragment coupling was accomplished by hydroboration of **3.5** and transmetalation, followed by addition of the resulting vinylzinc derivative to aldehyde **3.4**. However, this provided the undesired alcohol configuration at C-12. A swern oxidation/$Zn(BH_4)_2$ reduction sequence ensured the desired (*S*) stereochemistry at C-12. Oxidation of the thiophenyl group with *m*CPBA, followed by thermally induced elimination to the butenolide and alcohol deprotection completed the synthesis of muconin. The longest linear sequence was 25 steps and had an overall yield of 7.3%.

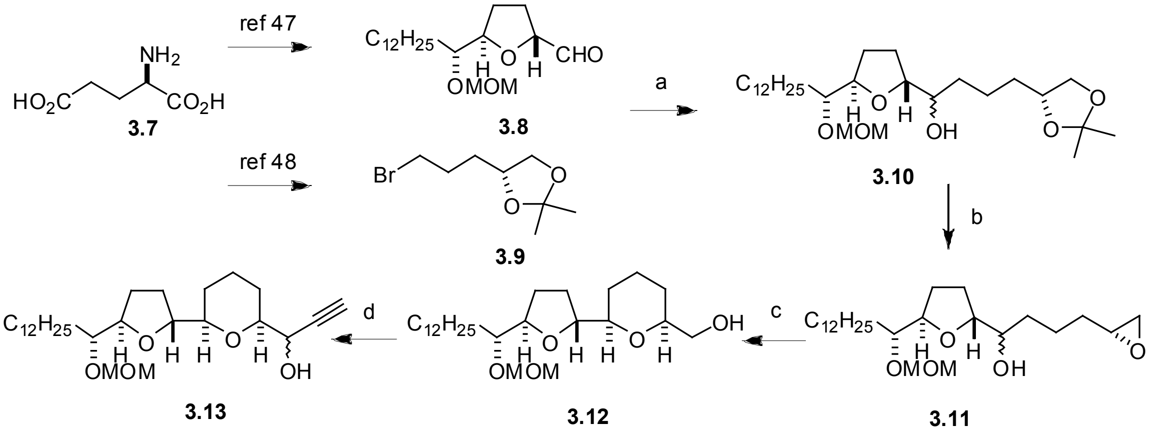
SCHEME 3.2



(a) (i) $(Cyclohexyl)_2BH$, hexane; (ii) $ZnEt_2$, hexane, 73%; (iii) Swern oxidation; (iv) $Zn(BH_4)_2$, Et_2O, cyclohexane, CH_2Cl_2; (v) 10mol% PtO_2, THF, H_2, 63%; (b) (i) *m*-CPBA, CH_2Cl_2; (ii) PhMe, heat; (iii) 5% AcCl in MeOH, 70%.

Subsequently, the Kitahara's synthesis of muconin was reported (**Scheme 3.3**).[44b, 44c] The two building blocks **3.8** and **3.9** were prepared from D-glutamic acid (**3.7**).[47, 48] The chelation-controlled addition of a Grignard reagent derived from **3.9** gave the coupling product **3.10** as an inseparable mixture with a 3:1 diastereoselectivity favoring the desired α–epimer. The mixture was transformed to the corresponding epoxide mixture **3.11**. Treatment of **3.11** with CSA afforded the desired *cis*-THP **3.12** together with the *trans*-THP isomer. Dess-Martin periodinane oxidation of **3.12** gave the aldehyde, which was reacted with ethnylmagnesium bromide to afford the THF-THP segment **3.13** in 80% yield as a 1:1.4 mixture of alcohol epimers.

SCHEME 3.3

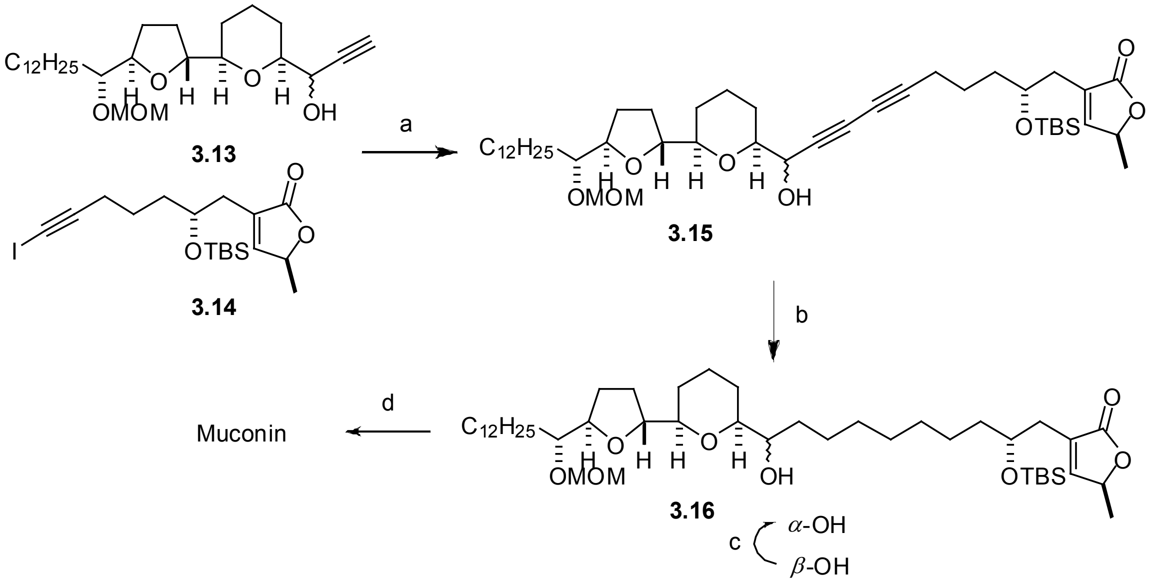


(a) Mg, Et_2O, 80%, *threo:erythro* = 3:1; (b) (i) AcOH, H_2O, THF, 70%; (ii) Triisopropylbenzenesulfonyl chloride, Py, DCM, 79%; (iii) NaOMe, MeOH, DCM, 90%; (c) CSA, DCM, 80%, *cis:trans* = 3:1; (d) (i) DMP, $NaHCO_3$, DCM; (ii) HCCMgBr, Tol, THF, 80%(2 steps), α–isomer:β–isomer = 1:1.4.

Palladium(0)-mediated coupling of the alkyne **3.13** with the iodoalkyne **3.14** using Schreiber's protocol afforded a separable mixture of diyne alcohols **3.15** with α/β selectivity of 1/1.4 (**Scheme 3.4**). Following hydrogenation of the diyne, the β alcohol epimer was converted to the desired α product by an oxidation-reduction sequence. Alcohol protecting group removal then furnished muconin with a longest linear step of 24 and 0.73% overall yield.

The Takahashi's synthesis of muconin was reported in 2002 (**Scheme 3.5**).[44d, 44e] The intermediate **3.17** was prepared by the Sharpless asymmetric oxidation on a triene precursor, which was prepared in 10 steps from ethyl (*E*)-heptadec-4-enoate. Tetraol **3.18** was obtained via a double Sharpless dihydroxylation on the silyl ether derivative of **3.17**.

SCHEME 3.4

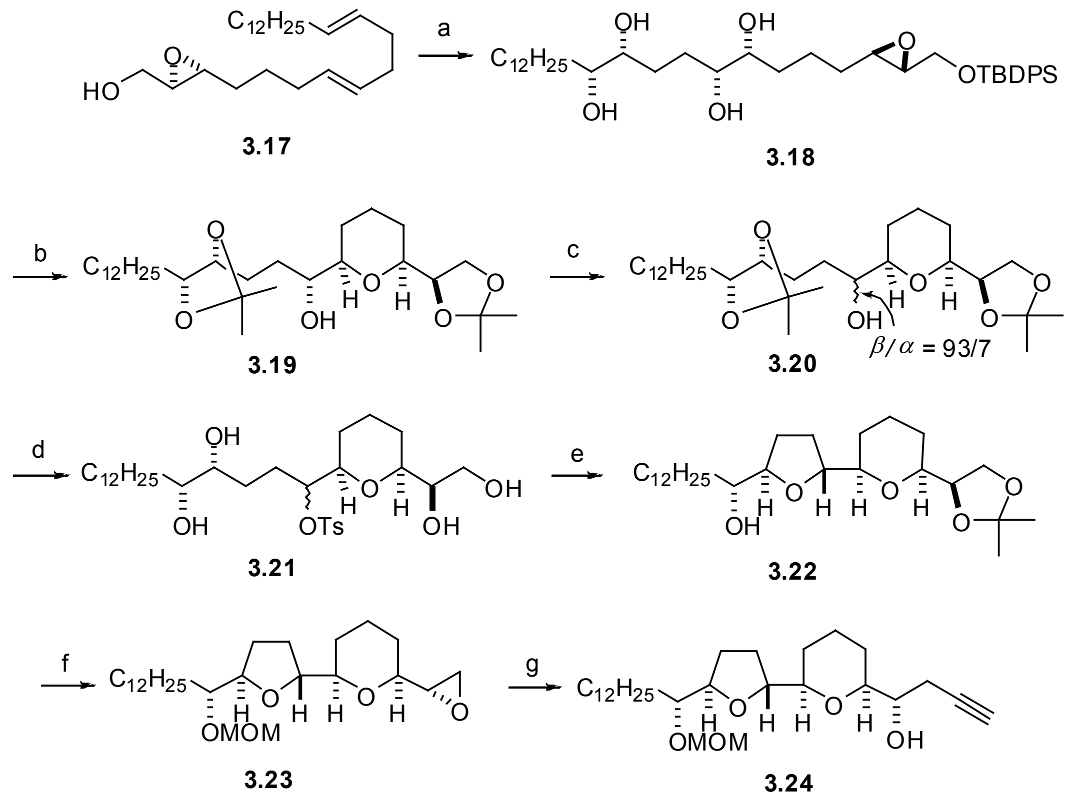


(a) $Pd_2(dba)_3$, CuI, i-Pr_2NH, (2-furyl)$_3$P, C_6H_6, 55%;
(b) $(Ph_3P)_3RhCl$, H_2, 77%; (c) (i) DMP, DMC; (ii) LiAl(O*t*-Bu)$_3$H,
THF, 80%; (d) BF_3• Et_2O, Me_2S, 82%.

Exposure of **3.18** to CSA gave the THP resulting from a 6-*exo* cyclization of the hydroxy epoxide. Treatment of this product with dimethoxypropane under acidic condition afforded **3.19** in 85% yield. DMP oxidationof **3.19** followed by $Zn(BH_4)_2$ reduction of the derived ketone afforded alcohol **3.20** with dominant *β*-selectivity. Formation of the THF ring in **3.22** was achieved by heating tosylate **3.21** with sodium methoxide in methanol. Compound **3.22** was transformed to **3.24** by a straightforward reaction sequence.

Coupling of fragment **3.24** and butenolide **3.25** provided **3.26**. Selective hydrogenation of **3.26** with Wilkinson's catalyst, followed by global deprotection gave the final product. The longest linear sequence was 28 steps and had an overall yield of 9.7% (**Scheme 3.6**).

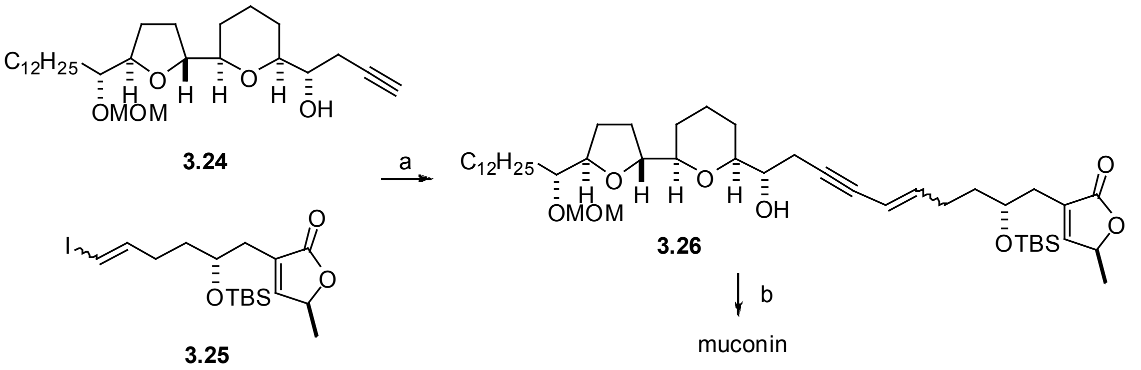
SCHEME 3.5



(a) (i) TBDPSCl, CH_2Cl_2; (ii) AD-mix-β, $MeSO_2NH_2$, t-BuOH-H_2O, quant.; (b) CSA, then MeOH, conc., and $(MeO)_2CMe_2$, 85%; (c) (i) DMP, $NaHCO_3$; (ii) $Zn(BH_4)_2$, Et_2O, 98%; (d) (i) p-TsCl, DMAP, Et_3N; (ii) AcOH-H_2O, 97%; (e) (i) NaOMe, MeOH, 50°C; (ii) $(MeO)_2CMe_2$, CSA, 78%; (f) (i) MOMBr, i-Pr_2NEt; (ii) AcOH-H_2O; (iii) BzCl, pyridine, and then MsCl; (iv) aq. NaOH, MeOH-THF, 74%; (g) (i) Lithium (trimethylsilyl)acetylide, BF_3•Et_2O, THF; (ii) K_2CO_3, MeOH, 97%.

The most recent total synthesis of muconin was reported by Yoshimitsu in 2004 (**Scheme 3.7**).[44f] The synthesis started with (-)-muricatacin (**3.27**), which was obtained through a novel radical α-C-H hydroxyalkylation on tetrahydrofuran.[49] Muricatacin was converted to the TBS ether which was subjected to a one-pot reduction/acetylation sequence to an acetylated lactol.

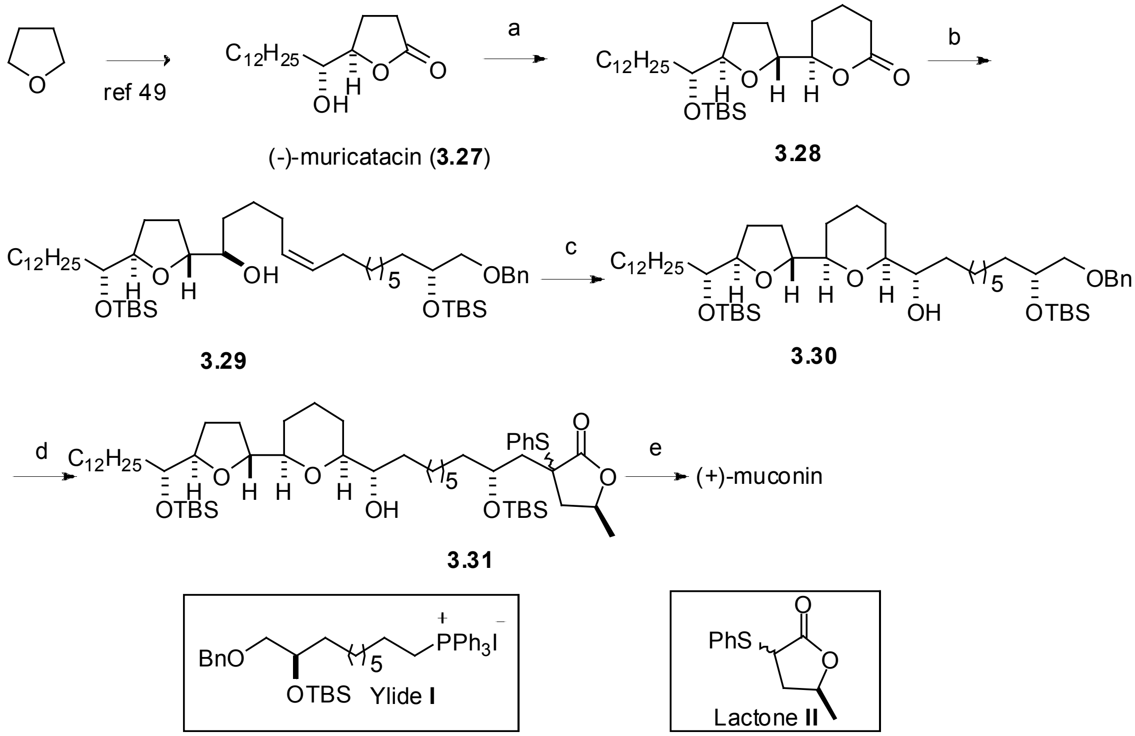
SCHEME 3.6



(a) $(Ph_3P)_2PdCl_2$, CuI, Et_3N, 79%; (b) (i) $(Ph_3P)_3RhCl$, H_2, benzene-EtOH; (ii) 10% HCl-MeOH, CH_2Cl_2, 66%.

The Lewis acid-catalyzed reaction of the product with 1-(trimethylsilyloxy)cyclopentene followed by Baeyer-Villiger oxidation of the resulting ketone afforded *δ*-lactone **3.28**. Reduction of **3.28** with DIBALH provided the lactol derivative, which subsequently underwent Wittig olefination with phosphonium ylide **I** to give the hydroxy *Z*-olefin **3.29** in 83% yield. Olefin **3.29** was oxidized with *m*CPBA to provide a mixture of epoxides, which upon exposure to CSA gave the desired tetrahydropyran **3.30** (39%) along with the diastereomeric THF-THP (59%). The latter was converted to **3.30** by a three-step sequence: alcohol oxidation/base catalyzed epimerization/ketone reduction. Treatment of a triflate derivative of **3.30** with the lithium enolate generated from the lactone **II** gave **3.31** in 86% yield. Compound **3.31** was transformed to the butenolide as described earlier and removal of the silyl ether provided muconin. The synthesis was completed with a longest linear sequence of 19 steps and 2.1% overall yield.

SCHEME 3.7



(a) (i) TBSCl, imidazole, DMF, 98%; (ii) DIBAL, CH_2Cl_2, then Ac_2O, Et_3N, DMAP, 96%; (iii) 1-(trimethylsilyloxy)cyclopentene, propionitrile, 93%; (iv) *m*CPBA, Na_2HPO_4, CH_2Cl_2, 89%; (b) (i) DIBAL, CH_2Cl_2, quant.; (ii) NaHMDS, THF, then ylide **I**, *n*-BuLi, THF; (c) (i) *m*CPBA, CH_2Cl_2, rt; (ii) CSA, CH_2Cl_2; (d) (i) TBSCl, imidazole, DMF, 98%; (ii) $Pd(OH)_2$-C, H_2, AcOEt, quant.; (iii) Tf_2O, 2,6-lutidine, CH_2Cl_2, 99%; (iv) LiHMDS, lactone **II**, HMPA, THF, 86%; (e) (i) *m*CPBA, CH_2Cl_2, (ii) toluene, reflux, 97% overall; (iii) cat. AcCl, MeOH, 96%.

Synthetic studies on the structurally related non-classical acetogenin jimenezin have also been reported (**Figure 3.2**). Jimenezin was isolated from the seeds of *Rollinia mucosa* and exhibited potent cytotoxic activity against six human solid tumor cell lines.[42] In 1999, Takahashi's group reported the first total synthesis of jimenezin and corrected the stereochemistry of the THF ring from *trans* to *cis* (**Scheme 3.8**).[50]

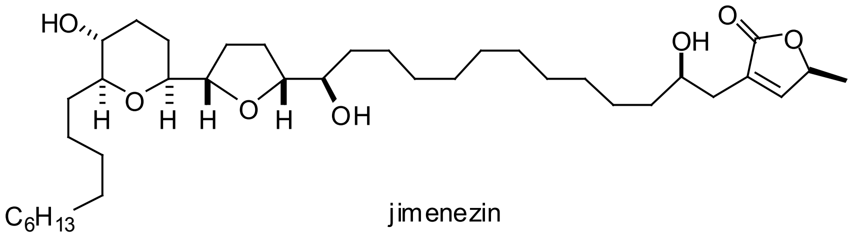
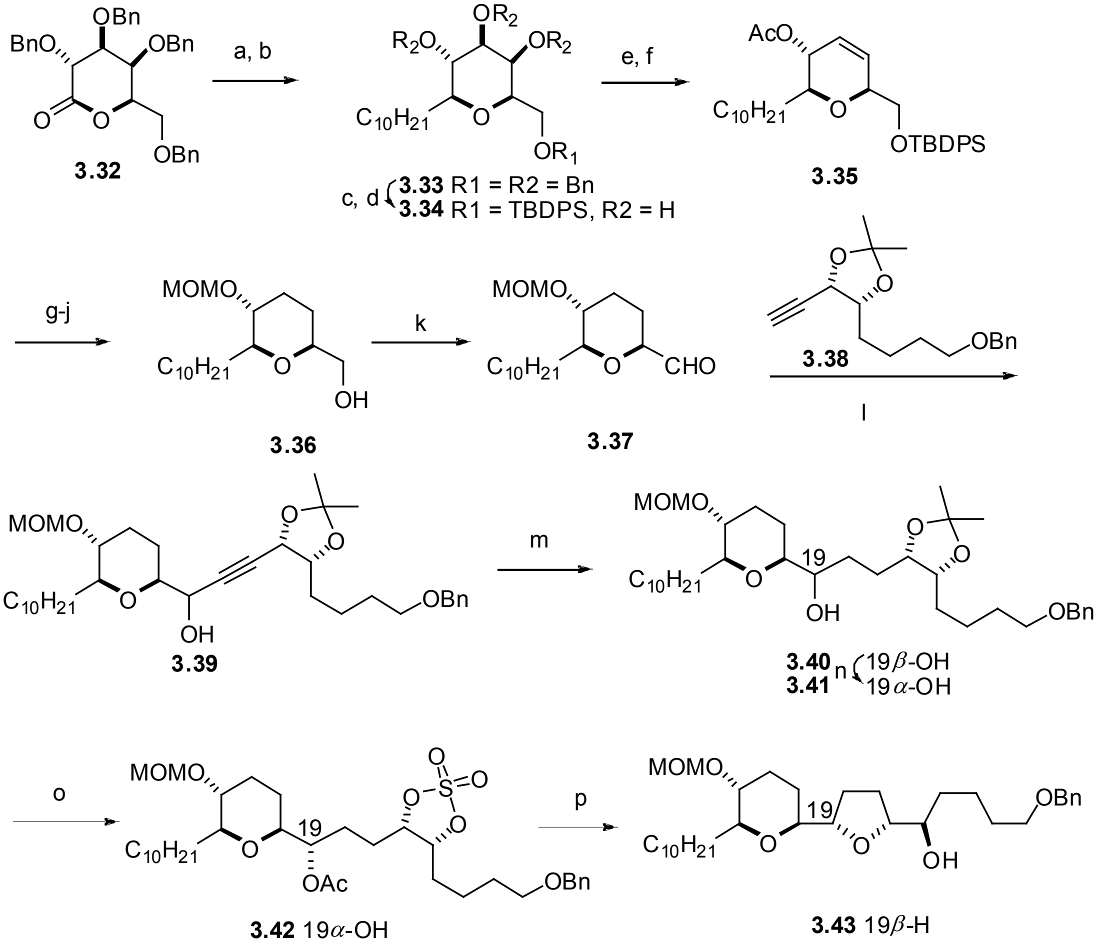


Figure 3.2 Structure of jimenezin

The Takahashi's synthesis was achieved by using carbohydrate **3.32** as the chiral building block.[51] The key steps include an efficient construction of the THF-THP fragment **3.43** through a stereoselective condensation between the pyranyl aldehyde **3.37** and the acetylene derivative **3.38** and a sulfate cyclization to form THF ring in the presence of a ruthenium catalyst. The aldehyde **3.37** was prepared from 2,3,4,6-tetra-*O*-benzyl-D-galactono-1,5-lactone (**3.32**) as follows. Reaction of **3.32** with decylmagnesium bromide in ether afforded a hemiacetal, which was treated with triethylsilane to give a β-glycoside **3.33** in 80% yield. Subsequent debenzylation and mono-silylation of **3.33** afforded a triol **3.34** in 78% yield. Deoxygenation of **3.34** was accomplished through an orthoester to provide an olefin **3.35** in 78% yield, which was converted to a primary alcohol **3.36** by the following sequence: (i) hydrogenation, (ii) deacetylation, (iii) formation of a methoxymethyl ether, (iv) desilylation (93% overall yield). Swern oxidation of **3.36** gave the aldehyde **3.37** in quantitative yield. Coupling reaction of **3.37** and **3.38** was achieved by using THF-HMPA (6:1) as the solvent at -78° C, giving a 92:8 mixture of the undesired *β*-carbinol and its diastereoisomer in 72% yield. Dess-Martin oxidation of the mixture (**3.40** and **3.41**), and subsequent reduction with L-Selectride in THF produced the **3.41** (94% de) in 97% overall yield.

Scheme 3.8

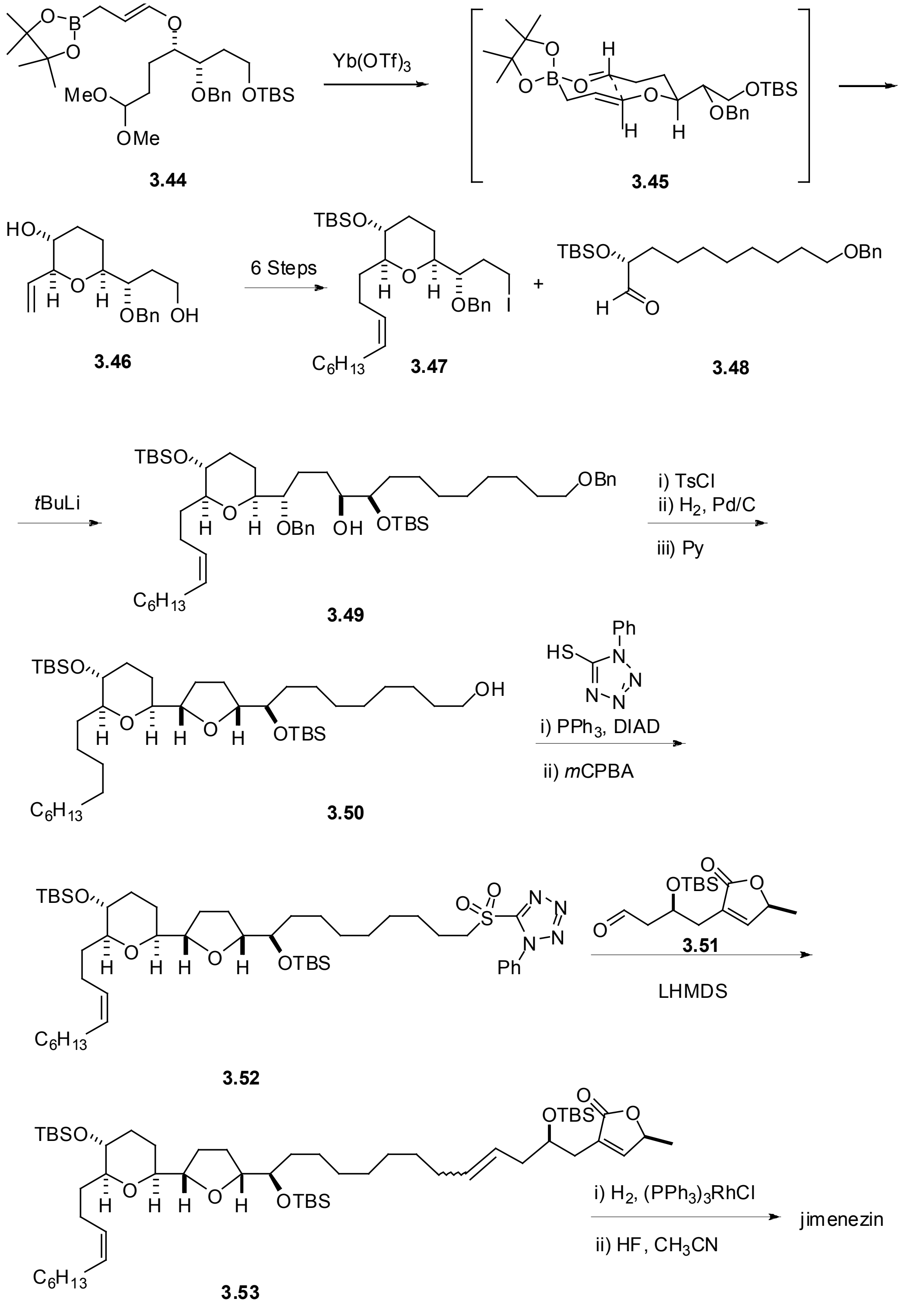


(a) Decylmagnesium bromide, Et_2O; (b) Et_3SiH, BF_3Et_2O, CH_2Cl_2, 80 %; (c) 10 % Pd/C, H_2, EtOAc-MeOH, rt; (d) TBDPSCl, imidazole, DMF, rt, 78 %; (e) $HC(OMe)_3$, CSA, CH_2Cl_2, rt; (f) Ac_2O, 78 %; (g) 0 % Pd/C, H_2, EtOAc, rt; (h) NaOMe, MeOH, rt; (i) MOMCl, *i*-Pr_2NEt, CH_2Cl_2, (j) TBAF, THF, rt, 93 %; (k) Swern oxidation, quant.; (l) *n*-BuLi, THF/HMPA; 72 %; (m) 10 % PtO_2, H_2, EtOAc, rt, 88 %; (n) (i) Dess-Martin periodinane, CH_2Cl_2, rt; (ii) L-Selectride, THF, 97%; (o) (i) Ac_2O, pyr, rt; (ii) aqu. AcOH, rt, 95%; (iii) $SOCl_2$, Et_3N, CH_2Cl_2, rt; (iv) cat. $RuCl_3$, $NaIO_4$, rt; (p) (i) NaOMe, MeOH, rt; (ii) aqu. H_2SO_4-Et_2O, rt, 83%.

The THF ring formation proceeded as follows. The 19α-alcohol **3.41** was acetylated, and then hydrolysis under acidic conditions afforded a diol, which was then treated with thionyl chloride and triethylamine. The resulting sulfite was oxidized with $NaIO_4$-$RuCl_3$, giving a cyclic sulfate **3.42**. Upon treatment with a base, **3.42** afforded the THF-THP core structure of jimenezin **3.43** in 83% yield from **3.42**.

Hoffmann's group reported the second total synthesis of jimenezin in 2006.[52] A highly stereoselective intramolecular allylboration was used to establish the THP ring and an intramolecular Williamson ether synthesis closed the THF ring (**Scheme 3.9**). Treatment of the *E*-allyl boronate **3.44** with Yb(OTf)$_3$ in acetonitrile led to the THP **3.46**. The organolithium derived from iodide **3.47** was treated with aldehyde **3.48** to afford the alcohol **3.49** as a single epimer. Tosylation of the secondary alcohol followed by one-pot alkene hydrogenation and benzylether cleavage afforded the derived dihydroxytosylate, which when treated with pyridine at reflux gave the THP-THF fragment **3.50**. The alcohol was converted to sulfone **3.51**, which was subjected to Julia-Kocienski olefination with butenolide aldehyde **3.52**, to give **3.53**. Chemoselective hydrogenation of the double bond followed by cleavage of the silyl ethers furnished jimenezin.

SCHEME 3.9


3.44
Yb(OTf)$_3$
3.45
3.46
6 Steps
3.47
+
3.48
tBuLi
3.49
i) TsCl
ii) H$_2$, Pd/C
iii) Py
3.50
i) PPh$_3$, DIAD
ii) mCPBA
3.52
3.51
LHMDS
3.53
i) H$_2$, (PPh$_3$)$_3$RhCl
ii) HF, CH$_3$CN
jimenezin

3.2 Summary of THF synthesis

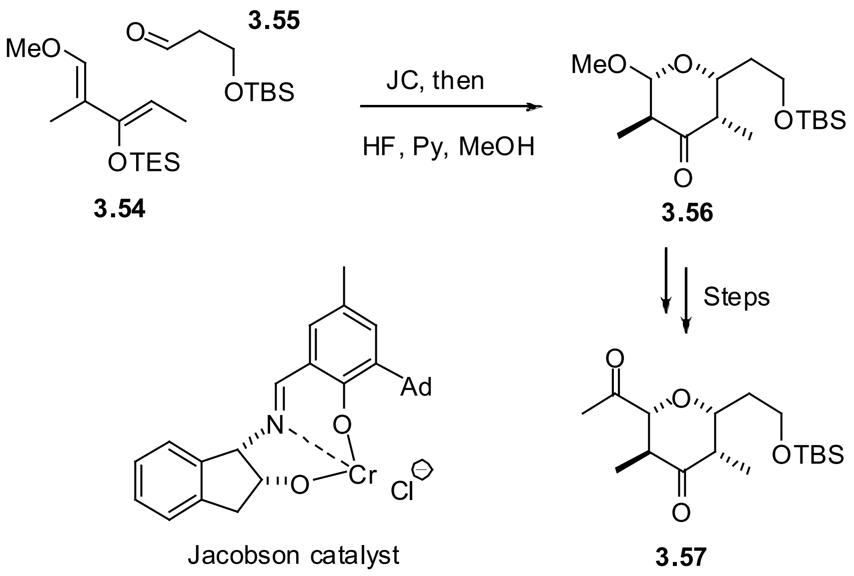
Our synthesis of 4-deoxyannoreticuin (Chapter 2) and the foregoing routes to the THF-THP acetogenins illustrate several of the more common strategies for introduction of the THF rings in the acetogenins: (i) halocyclization of hydroxyalkene derivatives,[53] (ii) cyclization of hydroxy epoxides,[54] (iii) Williamson ether synthesis on hydroxy tosylates[55] and (iv) Ring-Closing Metathesis on bis-allyl ethers.[56a] The oxidative cyclization of 4-alken-1-ols has also been widely used.[56b] This approach has also been applied to adjacently linked bis-THFs.[57]

3.3 Summary of THP synthesis

As illustrated in the synthesis of muconin, the cyclization of hydroxy epoxides is one of the more popular approaches for THP synthesis (**Scheme 3.3**, **3.5** and **3.7**). The other common strategies for THP synthesis are based on the hetero-Diels-Alder[58] and Prins reactions.[59]

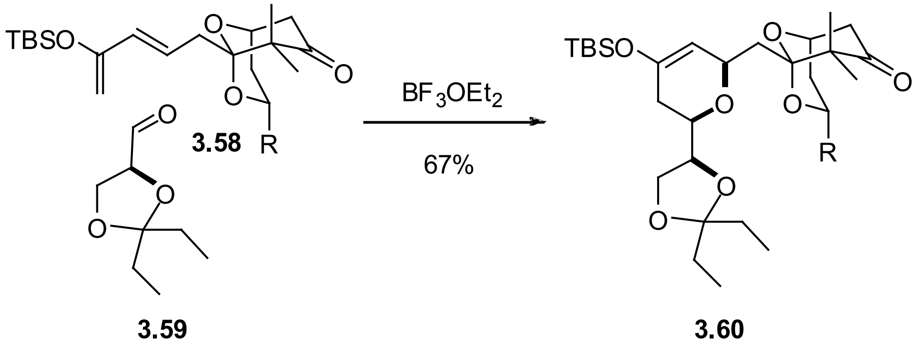
Jacobsen's synthesis of muconin is illustrative of the hetero-Diels-Alder approach (**Scheme 3.1**). A recent synthesis of phorboxazoles by Burke is another example of hetero-Diels-Alder reaction with Jacobsen catalyst.[60] The silyl enol ether, which was the product of the Diels-Alder reaction, was immediately treated with HF and pyridine to furnish the penta-substituted THP ring of the phorboxazoles in 77% yield and 91% ee (**Scheme 3.10**).

Scheme 3.10



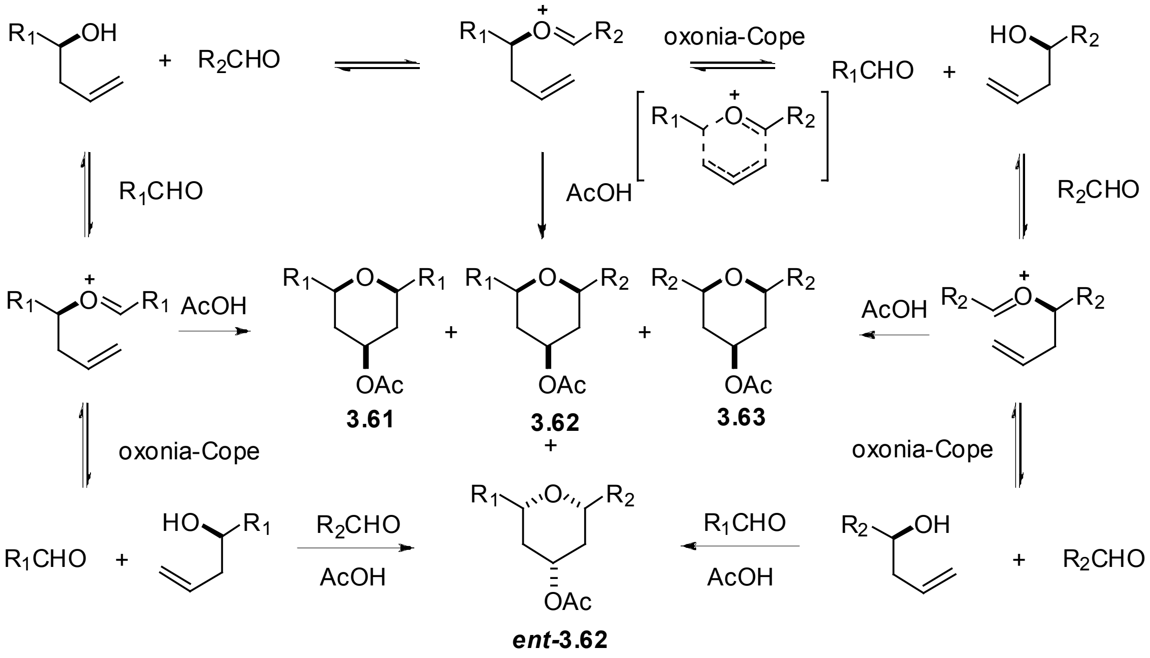
The hetero-Diels-Alder reaction has also been used in the synthesis of the B ring in the northern C1-C16 section of bryostatin I (**Scheme 3.11**).[61] The 15:4:1 mixture of diastereoisomers obtained from this reaction was readily separated to give the major product as the needed isomer for continuation of the synthesis.

SCHEME 3.11



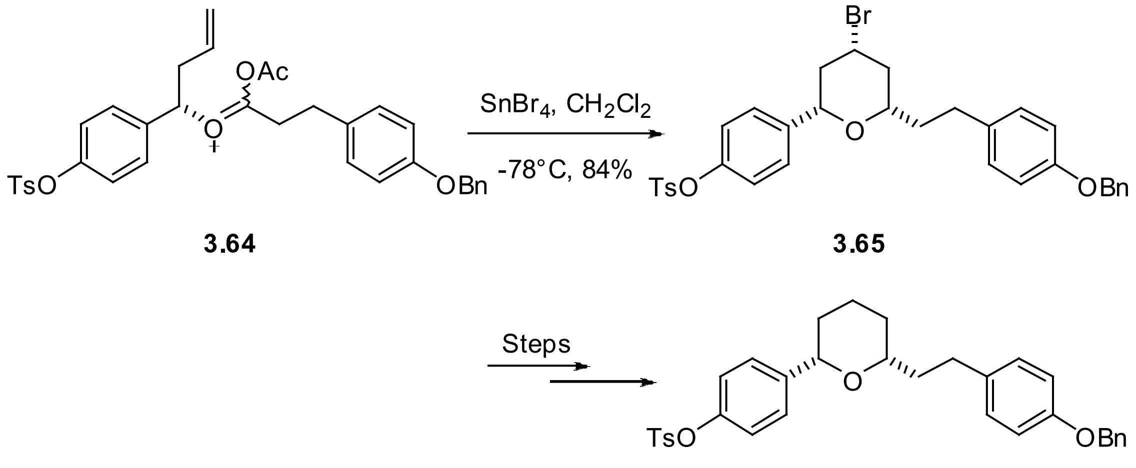
Prins cyclization has been widely used in the synthesis of THP containing natural products due to the convergent and efficient nature of the reaction.[59] However, a major drawback of the Prins reaction is that it requires acidic conditions, which are often not compatible with complex systems. Secondly, there is a potential for formation of diasteromeric products because of a competing 2-oxonia Cope rearrangement.[62] Alder proposed that 2-oxonia Cope rearrangement proceeds via a delocalised cationic transition state (**Scheme 3.12**). As illustrated by the scheme, a mixture of 4 cyclization products (**3.61**, **3.62**, ***ent*-3.62** and **3.63**) was expected to form.

SCHEME 3.12



Rychnovsky overcame this problem by using $SnBr_4$ instead of traditional acid promoters such as BF_3OEt.[63] The possible explanation might be the cyclization promoted by $SnBr_4$ is much faster than that promoted by BF_3OEt and thus suppresses the competing 2-oxonia Cope rearrangement. The use of $SnBr_4$ to promote the α-acetoxy ether Prins cyclisation in the synthesis of (-)-centrolobin showed significant improvement in both enantiomeric excess and overall yield (**Scheme 3.13**).

SCHEME 3.13



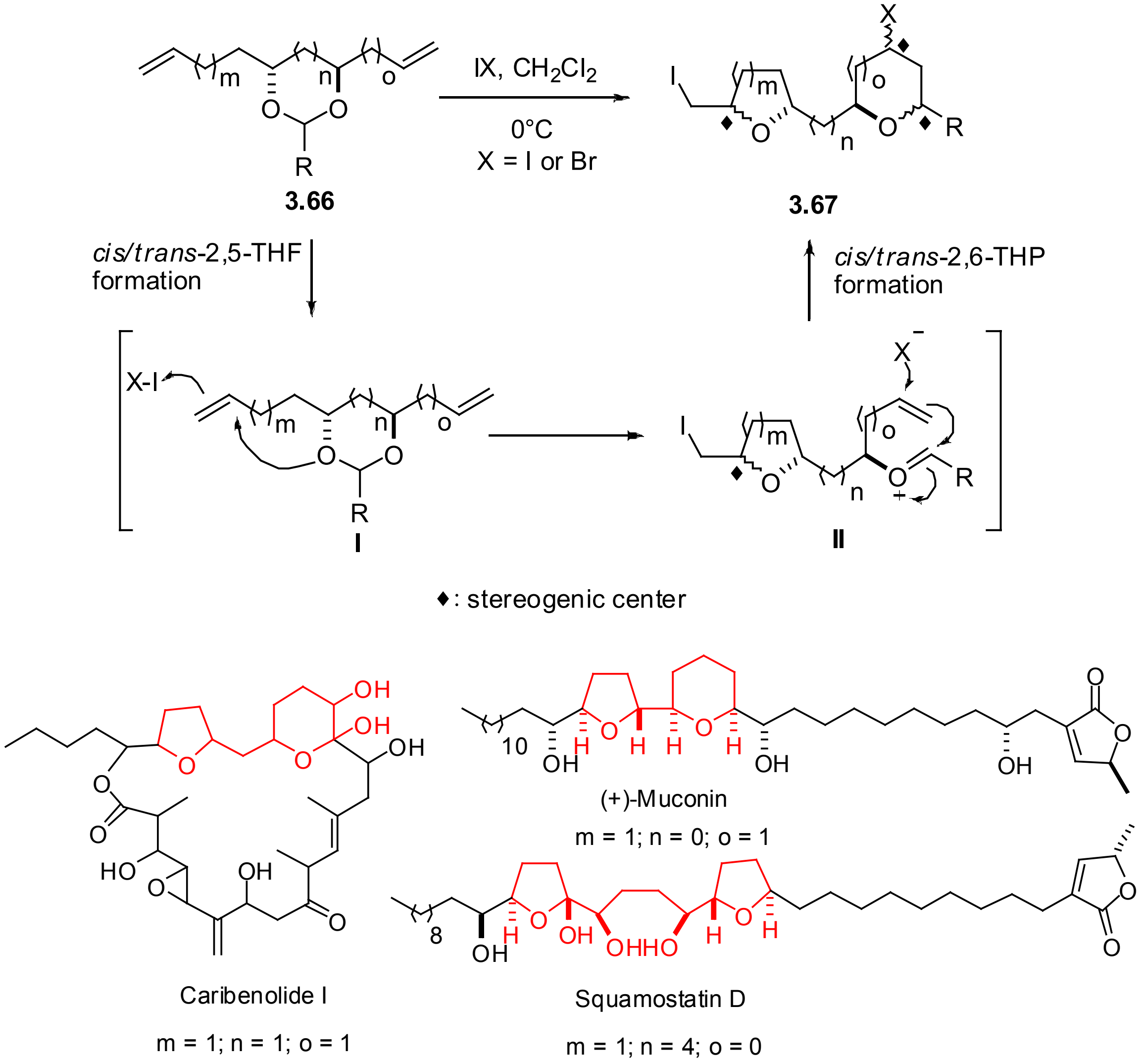
3.64 **3.65**

(-)-Centrolobine

3.4 Tandem cyclization of diene-acetals to THF-THP segments

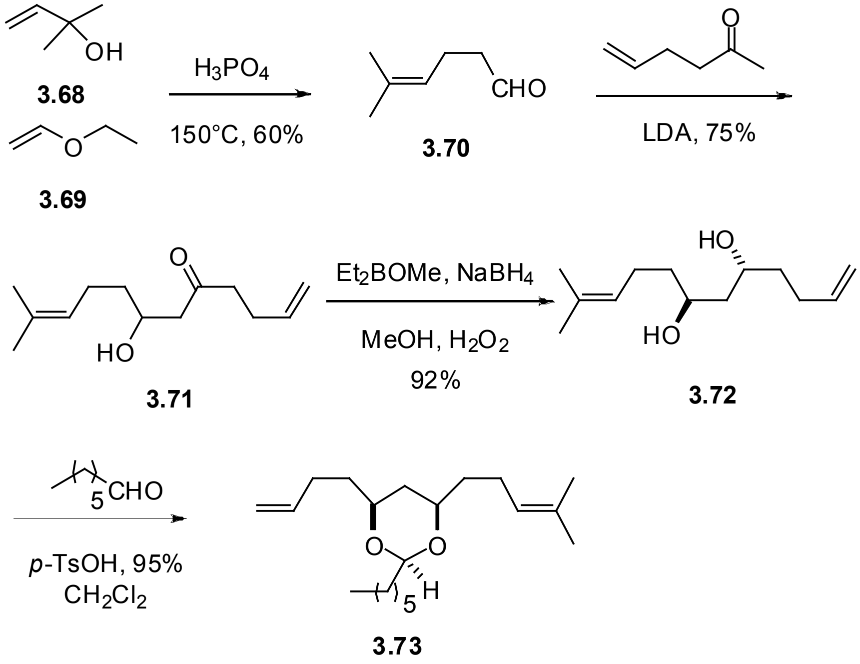
Our strategy for synthesis of the non-classical THF-THP subunits found in acetogenins such as muconin, centers on a tandem reaction for formation of the cyclic ethers (**Scheme 3.14**). This approach may be also applied to the THF-THP subunit found in other antitumor natural products such as caribenolide-I.[64] Thus reaction of an acetal-diene like **3.66** with an electrophile (I^+) proceeds via formation of the first cyclic ether and generation of an oxocarbenium ion (**I → II**). An alkene-oxocarbenuim ion cyclization on **II** gives the second ether ring leading to **3.67**. This reaction provides a convergent and rapid entry to stereochemically complex bis-cyclic ethers. Key questions on the feasibility of this plan are: (i) selective reaction of one of the two alkenes in the first step and (ii) stereoselectivity of the key C-O and C-C bond forming reactions.

SCHEME 3.14



The tandem strategy was first tested on acetal alkene **3.73**. The precursor to **3.73** was diol **3.72**. The synthesis of **3.72** started from the alkylation of aldehyde **3.70**[52] with the lithioenolate from hex-5-en-2-one. The aldol product **3.71** was subjected to stereoselective reduction using Et$_2$BOMe and NaBH$_4$ to give *syn*-diol **3.72.** Due to the closeness of chemical shifts of the carbinol hydrogens in **3.72**, the 1, 3-diol configuration solely relies on literature examples of this reaction.[65, 66] Reaction of diol **3.72** with heptaldehyde under acidic conditions gave the racemic acetal diene **3.73** as a single acetal diastereomer (**Scheme 3.15**).

SCHEME 3.15



The acetal configuration in **3.73** was presumed to correspond to the more stable diastereomer, i.e. the one in which the ring substituents were all equatorial. (**Figure 3.3**).

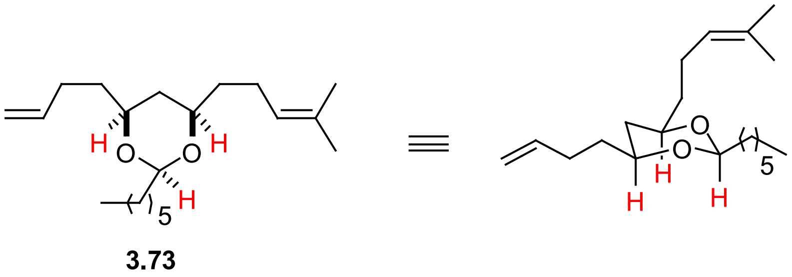
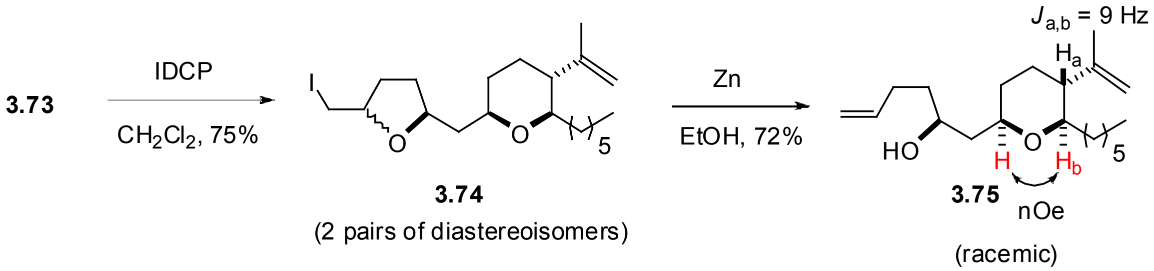


Figure 3.3 Presumed configuration of **3.73**

With acetal diene **3.73** in hand, the key cyclisation was next attempted. Treatment of **3.73** with IDCP gave the THF-THP ether **3.74** as an approximate 1:1 mixture of two diastereoiosmers in 75 % yield. To simplify the stereochemical analysis, **3.74** was converted to **3.75** by exposure to zinc. A single diastereoisomer **3.75** was obtained, indicating that the mixture **3.74** was due to *cis* and *trans* THF rings. A 2, 6-*cis*-THP ring was deduced from a nOe. The isopropenyl substituent was assigned as *trans* to the other THP substituents from a vicinal $J_{a,b}$ value of 9 Hz (**Scheme 3.16**).

SCHEME 3.16

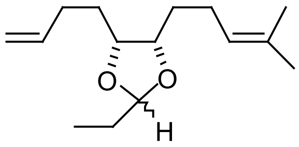
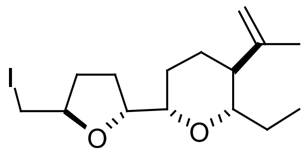


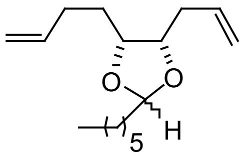
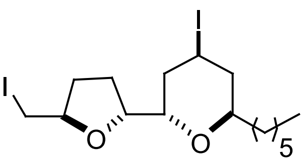
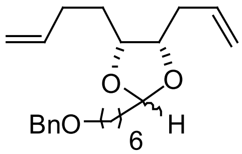
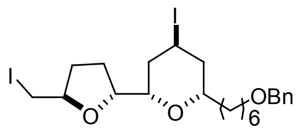
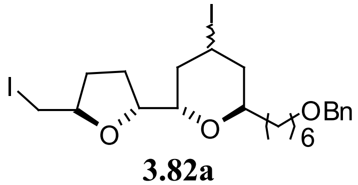
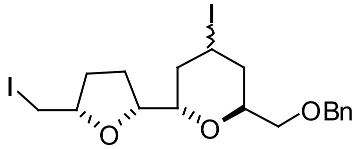
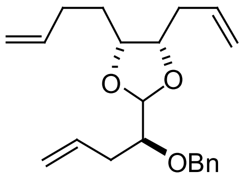
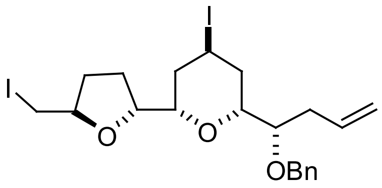
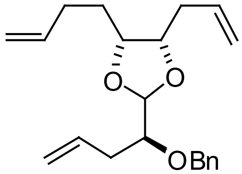
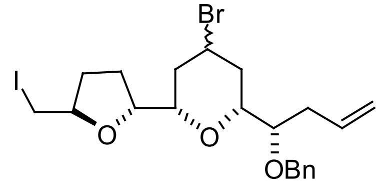
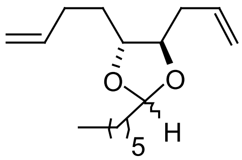
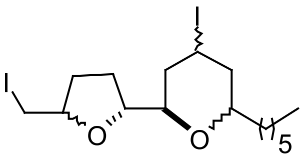
3.74
(2 pairs of diastereoisomers)

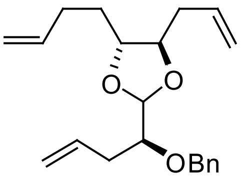
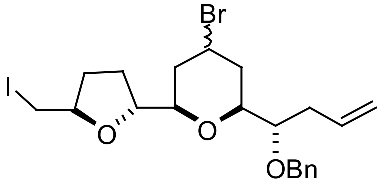
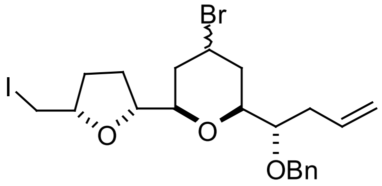
3.75
(racemic)

Inspired by this result, we next evaluated the tandem cyclisation of a variety of acetal diene substrates. The substrates, reaction conditions and cyclisation results are summarized in **Table 3.1**.

Table 3.1

Entry	Substrates	Conditions	Cyclised products	Yields
1	 **3.76** (±) (3:1 ratio of 2 isomers)	IDCP CH_2Cl_2 rt	 **3.77** (Proposed Stereochemistry)	50%

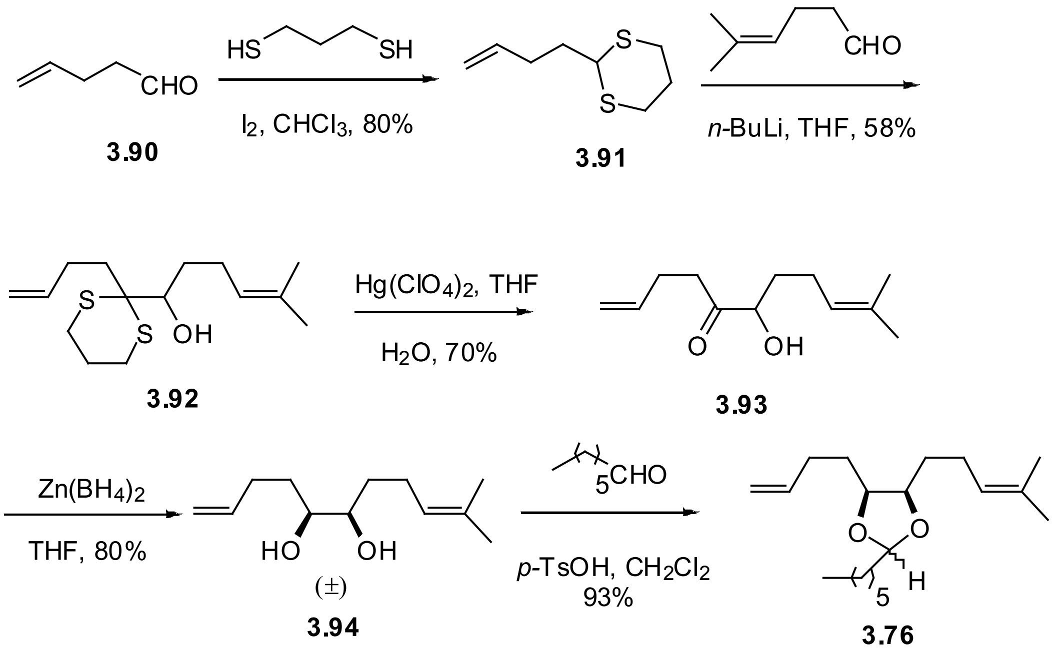
2	 **3.78** (Single isomer)	I_2 CH_2Cl_2 -40ºC	 **3.79**	14%
3	 **3.80** (3:1 ratio of 2 isomers)	I_2 CH_2Cl_2 0ºC	 **3.81**  **3.82a**  **3.82b** (3:7 ratio of **3.82a** : **3.82b**)	8.5% 43%
4	 **3.83** (Single isomer)	I_2 CH_2Cl_2 0ºC	 **3.84**	15%
5	 **3.83** (Single isomer)	IBr CH_2Cl_2 0ºC	 **3.85**	51%
6	 **3.86** (1:1 ratio of 2 isomers)	I_2 CH_2Cl_2 0ºC	 **3.87** (1:5:5 of 3 isomers)	60%

7	 **3.88** (1:1 ratio of 2 isomers)	IBr CH_2Cl_2 0°C	 **3.89a**  **3.89b** (2 isomers)	45%

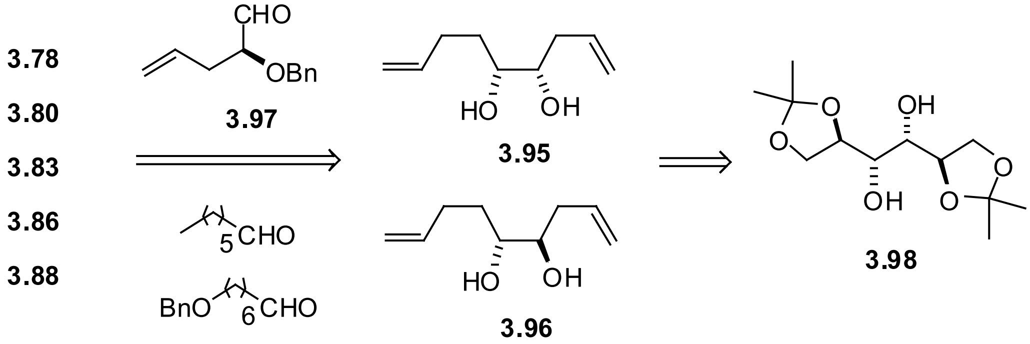
Synthesis of the 5, 6-*anti*-diol acetal **3.76** started from pent-4-enal (**3.90**) (**Scheme 3.17**). First, the aldehyde was protected as dithioacetal **3.91** by treating it with propane-1,3-dithiol in the presence of iodine. Deprotonation of **3.91** with *n*-butyllithium and alkylation with 5-methylhex-4-enal gave the product **3.92**. The α-hydroxy ketone **3.93** was obtained upon removal of the dithioacetal protecting group in **3.92**. Selective reduction of **3.93** with zinc borohydride gave the racemic **3.94** as the single diastereoisomer, which was presumed to be the anti diastereoisomer based on literature precedence.[66] Finally, A 3:1 ratio of acetal diastereoisomers **3.76** of undetermined configuration was obtained by treating diol **3.94** with heptaldehyde under acidic conditions.

The other acetal precursors listed in **Table 3.1** were all synthesized from commercially available 1,2:5,6-di-*O*-isopropylidene-D-mannitol **3.98** (**Scheme 3.18**).

SCHEME 3.17

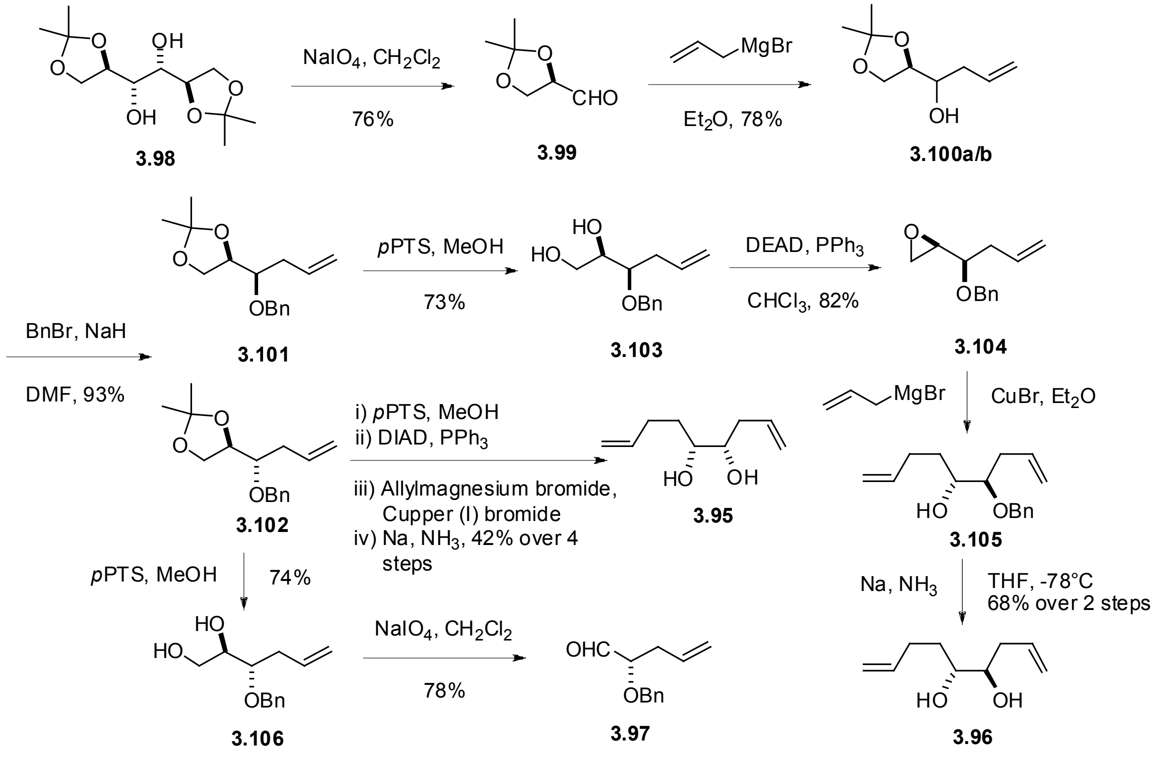


SCHEME 3.18



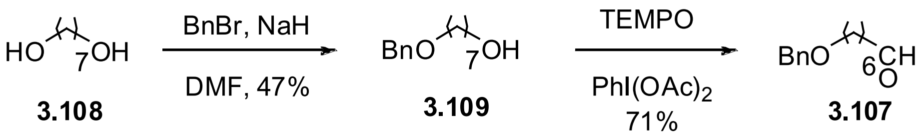
Treating **3.98** with $NaIO_4$ afforded aldehyde **3.99**, which was then treated with allylmagnesium bromide to give an inseparable 1:1 mixture of diastereoisomers **3.100a/b** (**Scheme 3.19**). Fortunately, the derived benzyl ethers **3.101** and **3.102** were chromatographically separable. Debenzylation of **3.101** and **3.102** gave the corresponding alcohols whose NMR information matches that of known alcohols perfectly. The isopropylidene in **3.101** was easily removed under acidic conditions to give diol **3.103**. Diol **3.103** was then transformed to epoxide **3.104** under Mitsunobu conditions. Treatment of **3.104** with allylmagnesium bromide provided (4*R*, 5*R*)-4-benzyloxynona-1,8-dien-5-ol (**3.105**). Upon exposure of **3.105** to sodium in the liquid ammonia, the benzyl group was cleanly removed to give (4*R*, 5*R*)-nona-1,8-diene-4,5-diol (**3.96**). (4*S*, 5*R*)-nona-1,8-diene-4,5-diol (**3.95**) was obtained in 42 % yield through a similar reaction sequence from benzyl ether **3.102**. Aldehyde **3.97** was synthesized from **3.102** via the removal of the isopropylidene and oxidative cleavage of the resulting vicinal diol in **3.106**.

SCHEME 3.19



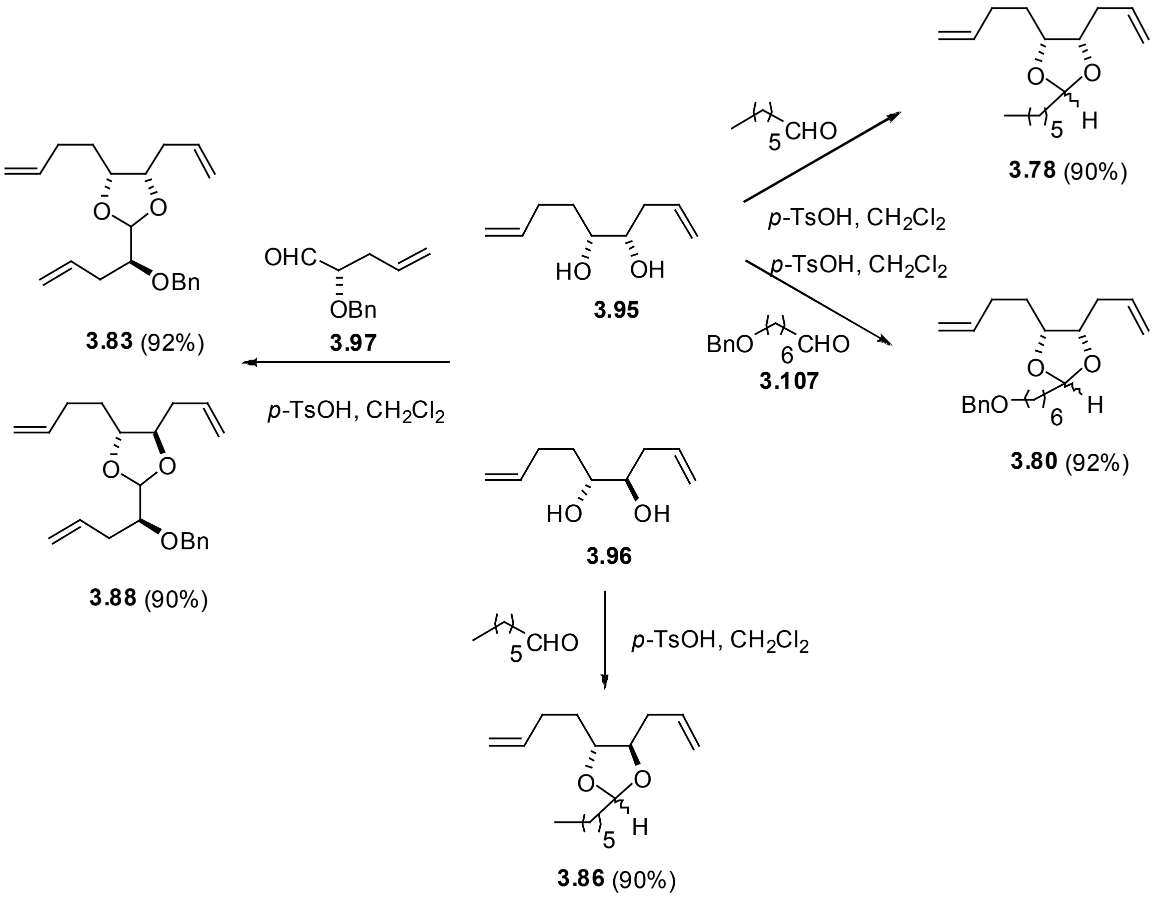
Aldehyde **3.107** was prepared from heptan-1, 7-diol (**3.108**) throughoxidation of the mono-benzyl ether **3.109** (**Scheme 3.20**).

SCHEME 3.20



Acetal diene **3.78**, **3.80**, **3.83**, **3.86** and **3.88** were obtained by the acetalization of diols **3.95** and **3.96** with the corresponding aldehydes **3.97**, heptanal or 7-benzyloxyheptanal (**Scheme 3.21**).

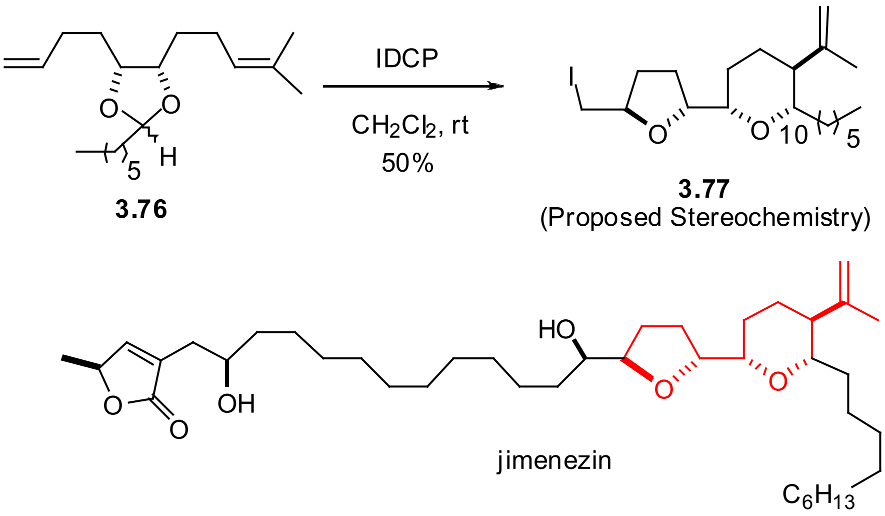
SCHEME 3.21



The diastereoselectivity of the acetalization reaction varied with the relative stereochemistry of the diol precursor. The *anti* diols gave predominantly a single acetal isomer whereas the *syn* diols gave an approximately 1:1 mixture of acetals. The configuration at the acetal carbons was not determined.

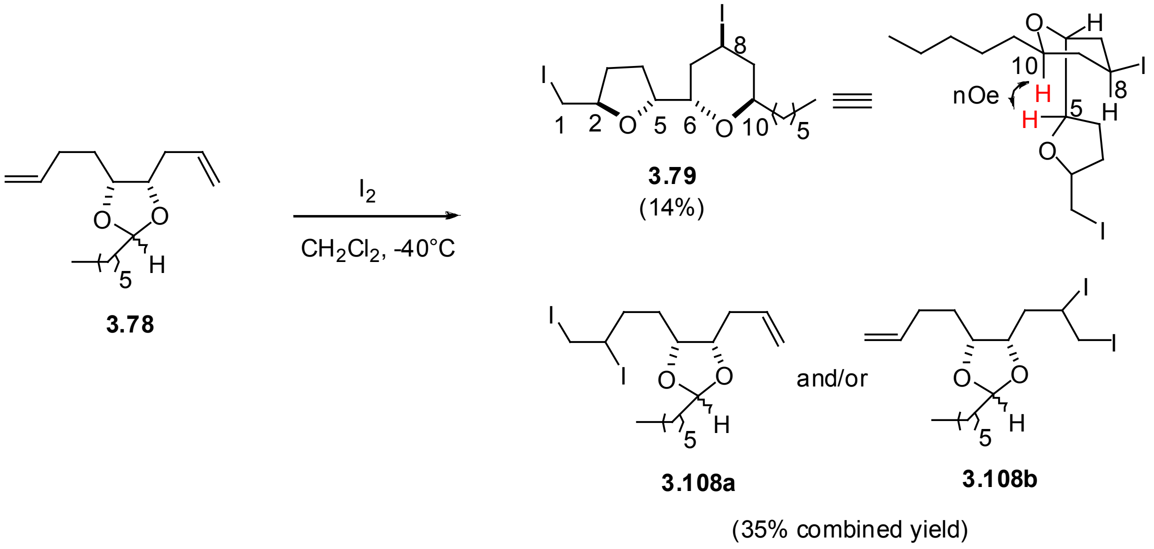
The tandem cyclization of the *anti* diol subsrates were first examined. Treatment of acetal mixture **3.76** with IDCP in dichloromethane at room temperature gave a single THF-THP diastereoisomer **3.77** in 55 % yield (**Scheme 3.22**). The gross structure of **3.77** was assigned by NMR but signal overlap did not permit stereochemical assignment. The stereochemistry of the THP ring was tentatively assigned by comparison with the reaction of the related 1, 3-diol substrate **3.73**. The 2, 5-*trans* THF stereochemistry was assigned following our observation that the iodoetherification reactions of 1, 2-*O*-isopropylidene-5-alkenes give the 2,5-*trans* THF motif. The conversion of **3.76** to **3.77** is relevant to the synthesis of the THF-THP core structure of the jimenezin subgroup of the acetogenins.

SCHEME 3.22



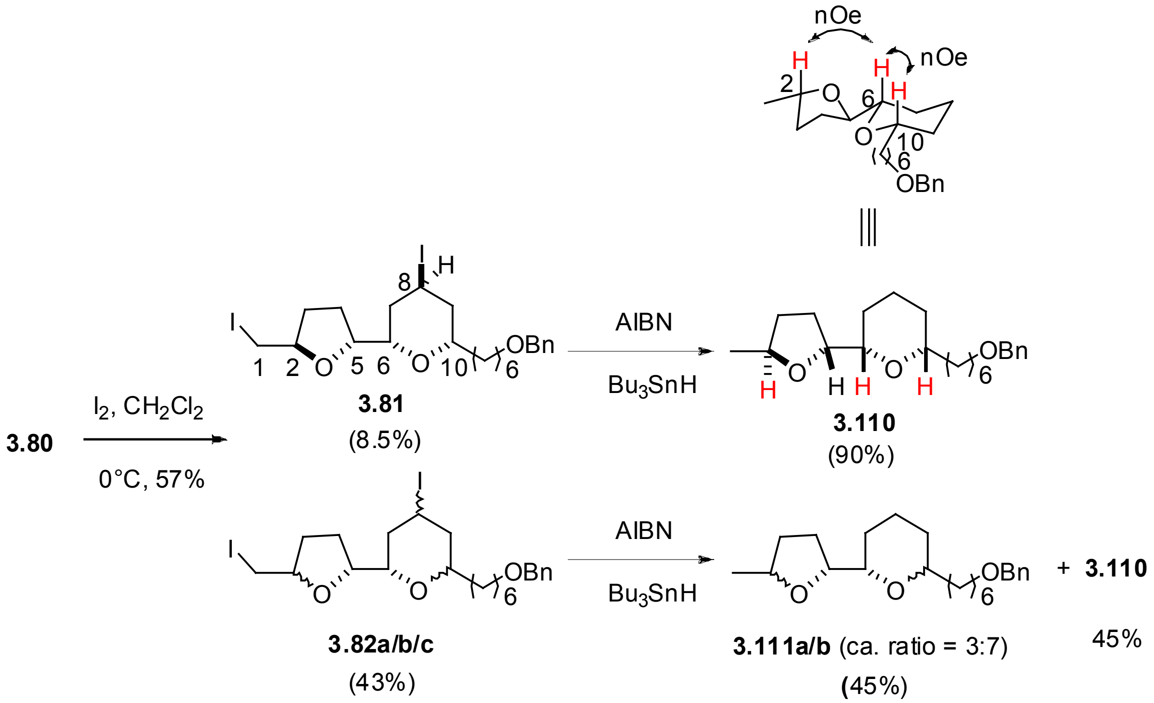
The tandem cyclization on the enantiopure acetal diene **3.78** was next examined. In this case the second ether ring formation involves a Prins-like cyclisation. Treating **3.78** with iodine at –40˚C gave THF-THP product **3.79** (14%) and uncyclized diiodides **3.108a** and/or **3.108b** as the major products (**Scheme 3.23**). Unexpectedly, the *trans*-THP ring was obtained instead of *cis*-THP ring, which is the normal product in Prins cyclization reactions. A nOe effect was observed between H5 and H10, which indicated that the THP ring was *trans*. The stereochemistry of THF ring was presumed as *trans* based on the cyclization result on **3.80** under the similar condition (vide infra). The equatorial iodide on C8 was deduced from a *J* value of 8 Hz, which was attributed to a *trans* diaxial relationship between H8 and one of the protons on the adjacent carbons.

SCHEME 3.23



Application of the identical cyclization conditions that were used on **3.78** to **3.80** gave **3.81** (8.5%) and **3.82** as a mixture of diastereoisomers (43%) (**Scheme 3.24**). To simply the analysis of stereochemistry of the products, **3.81** and **3.82** were treated with tributyltin hydride to give **3.110** and **3.111** respectively. Configuration of **3.110** was confirmed by the nOe effects observed between H2 and H6, H6 and H10. The equatorial iodide at C8 in **3.81** was assigned on the basis of a *Jvic* value of 8 Hz, as in the case of **3.79**. Removal of iodines in **3.82** yielded three products, **3.110** and the inseparable mixture of two isomers **3.111a/b**.

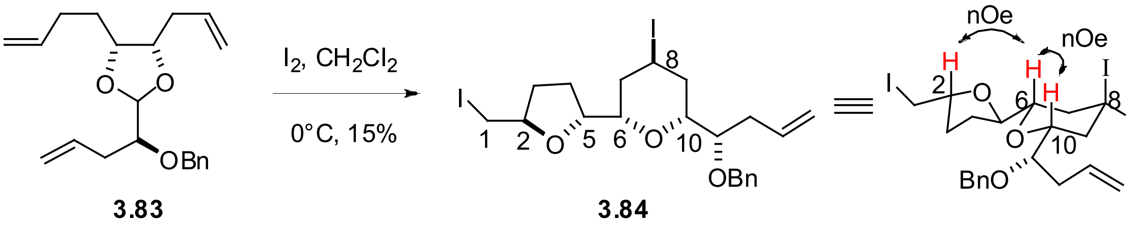
SCHEME 3.24



The results on **3.78** and **3.80** indicate that the tandem cyclization of *anti*-1, 2-diol acetal substrates with simple aldehyde components favor the formation of the 2, 6-*trans*-THP pattern with moderate stereoselectivity. The reaction of *anti*-1, 2-diol acetals with an α-alkoxy aldehyde component were next examined.

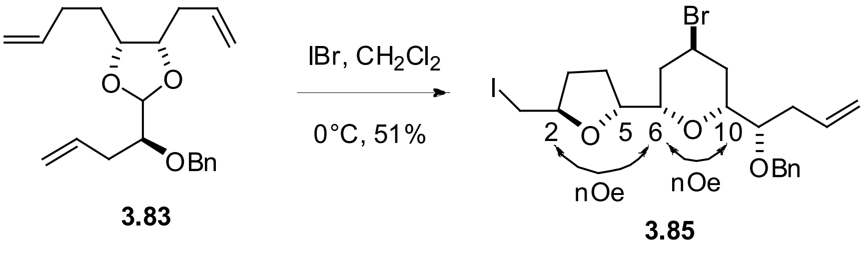
Acetal diene **3.83** was treated with iodine at 0˚C in CH_2Cl_2 (**Scheme 3.25**). To our pleasant surprise a single cyclization product **3.84** containing a *trans* THF and a *cis* THP was obtained. The configurations at the newly formed stereogenic carbons in **3.84** were deduced from nOe and vicinal *J* values. However, this reaction was sluggish and low yielding.

SCHEME 3.25



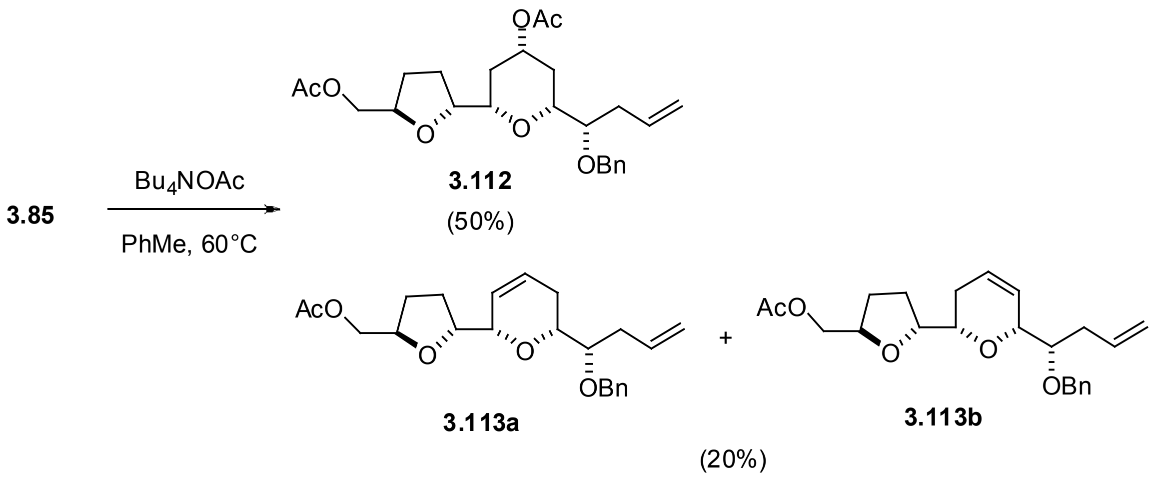
To improve the efficiency, we replaced iodine with iodine monobromide which is a more reactive specie of I^+ (**Scheme 3.26**). The reaction time was significantly shortened from 40 h to 10 min. The major product **3.85** was obtained in 51% yield as a single diastereoisomer. As for **3.84**, the stereochemistry of **3.85** was deduced from nOe effects observed between H2 and H6, H6 and H10.

SCHEME 3.26



In view of further elaboration of the product, **3.85** was treated with tetrabutylammonium acetate. A major single product **3.112** was obtained along with elimination products **3.113a** and **3.113b** in 20% yield (**Scheme 3.27**).

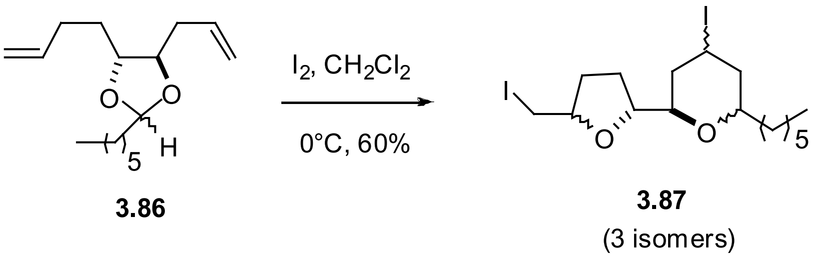
SCHEME 3.27



The afore-mentioned substrates are derived from 1, 2-*anti*-diols. To evaluate the effect of the stereochemistry of the 1, 2-diol, *syn*-diol substrates were next examined.

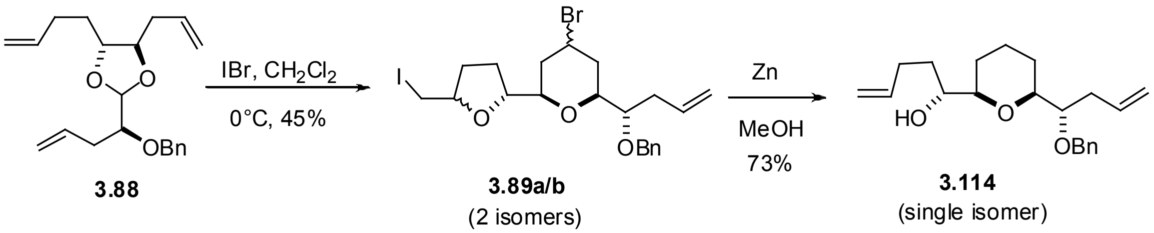
Treatment of 4, 5-*syn*-diol acetal **3.86** with iodine in dichloromethane at 0°C gave THF-THP **3.87** as a mixture of 3 diastereoisomers (**Scheme 3.28**). Although we were able to separate them, signal overlap in the NMR did not permit stereochemical assignment.

SCHEME 3.28



Treatment of 4, 5-*syn*-diol acetal **3.88** with iodine monobromide in dichloromethane at 0°C afforded a mixture of 2 diastereoisomers of very similar chromatographic mobility (**Scheme 3.29**). Exposure of **3.89a/b** to zinc provided a single product **3.114**. The THP ring in **3.114** was assigned the *cis* stereochemistry from a nOe between the carbinol protons of the THP. As will be discussed later, selective removal of the bromide in a subsequent derivative of **3.89** confirmed that the mixture **3.89a/b** was due to *cis* and *trans* THFs.

SCHEME 3.29



3.88

3.89a/b
(2 isomers)

3.114
(single isomer)

3.5 Synthetic studies on muconin

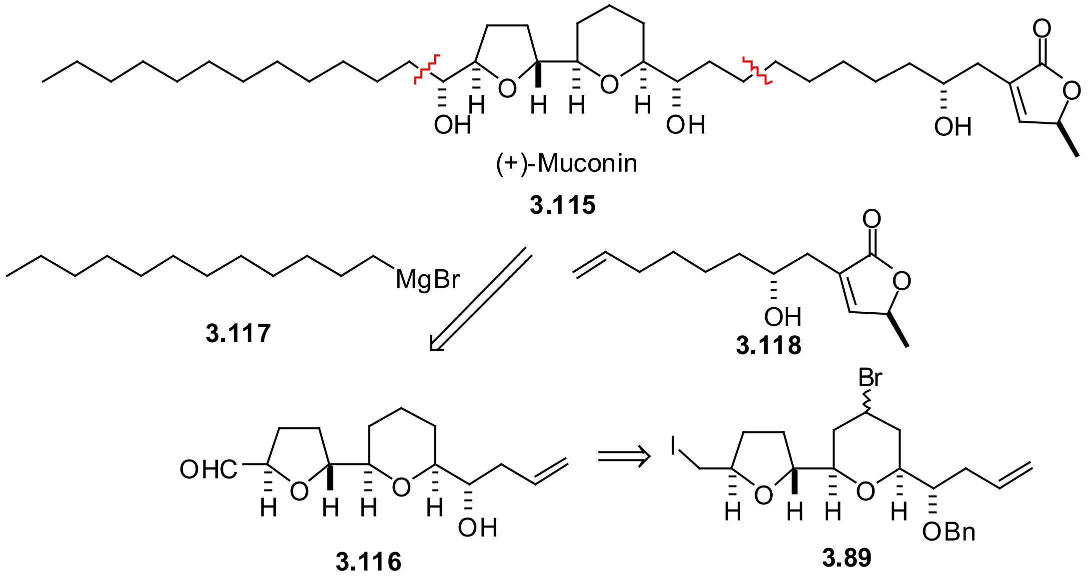
The results from the cyclization of acetal diene **3.88** was next applied to the synthesis of muconin (**Scheme 3.30**). Appropriate functionization of **3.89** would transform **3.89** to aldehyde **3.116**, which can be converted to muconin (**3.115**) using established reactions (vide infra).

Treatment of the *cis/trans* THF mixture **3.89** with thiophenol led to selective substitution of the primary iodide to give **3.119** (**Scheme 3.31**). Reduction of **3.119** with zinc afforded mixture **3.120**. Compound **3.120** was then oxidized to sulfoxide **3.121** by *m*CPBA. Pummerer rearrangement went smoothly to give thioacetal **3.122**.

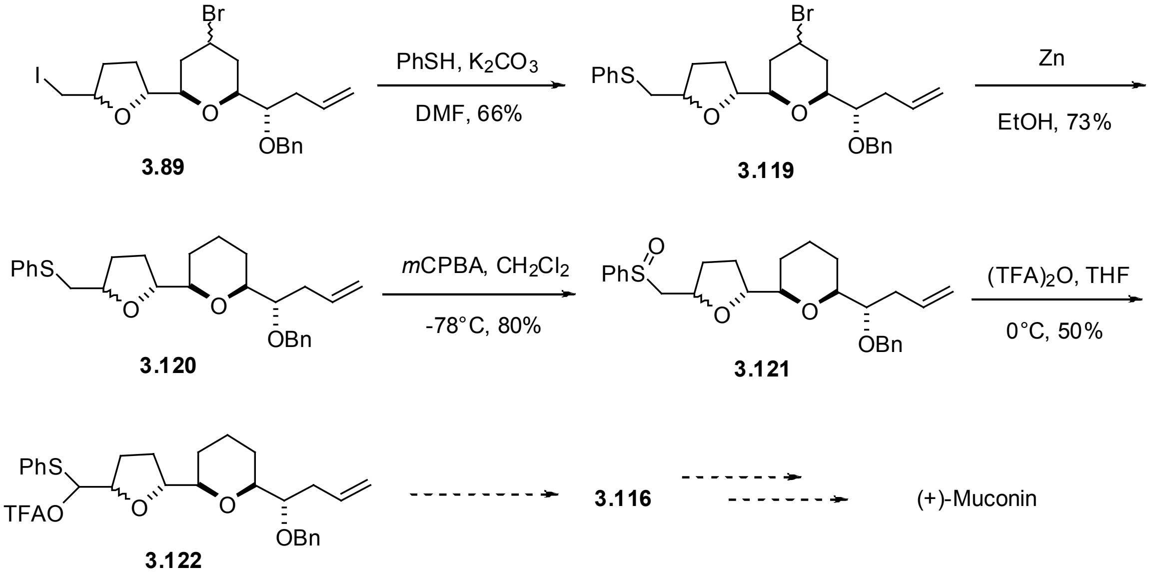
Completion of the synthesis of muconin requires the following key transformations: (i) conversion of thioacetal **3.122** to aldehyde **3.116**, (ii) alkylation of **3.116** with Grignard reagent **3.120**, (iii) olefin cross metathesis with butenolide **3.121** on the product from the

Grignard reaction and (iv) selective hydrogenation of the metathesis product (**Scheme 3.31**).[68] It may be possible to achieve the first two steps in a single reaction by treatment of **3.112** with excess Grignard reagent.[69]

SCHEME 3.30



SCHEME 3.31

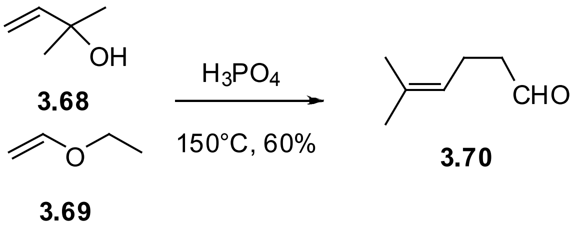


3.6 Conclusion

In conclusion a tandem, iodonium ion triggered, THF-THP forming reaction on acetals of dihydroxy-dienes was investigated. Vicinal or 1,3- diol precursors produced adjacently or methylene linked cyclic ethers in good to moderate yield. In all cases the cascade appears to be initiated by a 5-exo trig type cyclization to give a 2,5-disubstituted THF connected to an oxocarbenium ion which undergoes attack by the second alkene to form the THP ring. The substitution pattern and connectivity of the second alkene determines the mechanism of formation and constitution of the THP, i.e. a 2,5,6-tri-alkylated or 2,6-dialkyl-4-halogenated. IDCP was the reagent of choice for the first and IBr was optimal for the second. Altogether, three new stereogenic centers are generated in the THF-THP products. The anti-diol substrates showed high selectivity for the trans-2,5-disubstituted THF ring, whereas the selectivity for syn diol precursors was poor. Generally, the THP segments were formed in moderate to high selectivity depending on the operative mechanism in the oxocarbenium ion cyclization. Finally, the feasibility of using this tandem reaction for non-classical THF-THP containing acetogenins was illustrated by preparation of an advanced precursor to muconin. The modular nature of this synthesis and the rapid entry to such stereochemically rich frameworks from relatively simple precursors are noteworthy attributes in the context of future applications.

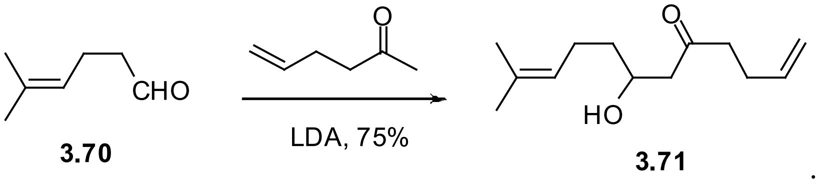
3.7 Experimental section

Synthesis of 5-methylhex-4-enal (3.70)



In a 500 mL high-pressure tolerant beer bottle with secured hitch cork were added in 2-methylbut-3-en-2-ol (**3.68**) (10 mL, 95.7 mmol) and ethylvinyl ether (**3.69**) (18.3 mL, 191 mmol) and 3 drops of H_3PO_4. The reaction mixture was heated up to 150 ˚C for 2 h. Then it was cooled down to 0 ˚C and distilled at 110 ˚C under the hood vacuum to give the desired product **3.70** as a coloreless liquid (6.4 g, 60%). ^{1}H NMR ($CDCl_3$) δ 9.77 (s, 1H), 5.09 (s, 1H), 2.46 (s, 2H), 2.32 (s, 2H), 1.70 (s, 3H), 1.63 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 202.7, 122.1, 70.6, 43.9, 25.6, 20.9, 17.7

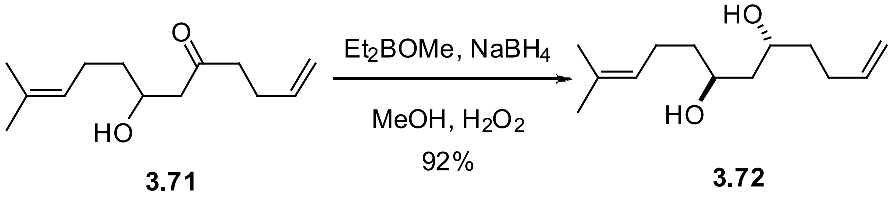
Synthesis of 7-hydroxy-11-methyldodeca-1, 10-dien-5-one (3.71)



To LDA prepared from *n*-BuLi (7.7 mL, 19.3 mmol, 2.5 M in hexane) and *i*-Pr_2NH (3.3 mL, 23.5 mmol) of in THF (53.2 mL) at –78 ˚C was added a solution of hex-5-en-2-one (0.42 g, 4.28 mmol) in THF (32 mL). The reaction mixture was stirred at -78 ˚C for 1 h, and to it was added a solution of aldehyde **3.70** (0.96 g, 8.56 mmol) of in THF (32 mL).

The reaction mixture was stirred at -78 ˚C for 1 h, quenched with saturated aqueous NH_4Cl, and diluted with ether. The aqueous layer was extracted with ether, and the combined extracts were dried ($MgSO_4$). The solvent was removed under reduced pressure. The residue was subjected to column chromatography to give **3.71** (0.67 g, 75%) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 5.78- 5.85 (m, 1H), 5.11- 5.15 (m, 1H), 5.00- 5.08 (m, 2H), 4.05- 4.09 (m, 1H), 2.93 (d, 1H, *J* = 3.6 Hz), 2.52- 2.63 (m, 4H), 2.34- 2.38 (m, 2H), 2.09- 2.15 (m, 2H), 1.71 (s, 3H), 1.64 (s, 3H), 1.45- 1.59 (m, 1H), 1.42- 1.44 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 211.1, 136.8, 132.2, 123.8, 115.4, 67.3, 49.2, 36.5, 36.4, 27.5, 25.7, 24.1, 17.7.

Synthesis of 11-methyldodeca-1,10-diene-5,7-diol (3.72)

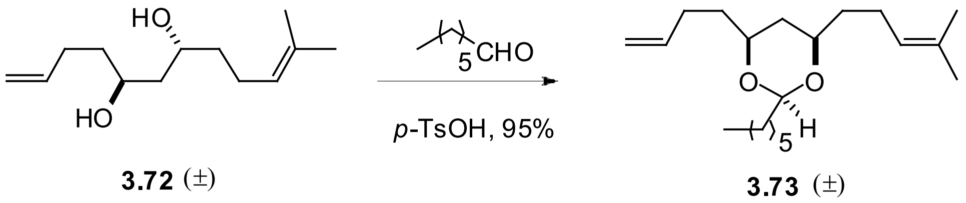


To a solution of ketone **3.71** (0.7 g, 3.33 mmol) in THF (37 mL) and MeOH (10 mL) was added in Et_2BOMe (3.8 mL, 3.83 mmol, 1.0 M in THF) at –78 ˚C. The reaction mixture was stirring at –78 ˚C for 0.5 h. Then $NaBH_4$ (151 mg, 4 mmol) was introduced and mixture stirred at –78 ˚C for an additional hour. MeOH (14 mL) was added followed by 1N aqueous NaOH (8.6 mL), and the mixture was maintained at 25 ˚C for 1 h. The mixture was cooled to 0 ˚C and 30% of H_2O_2 (4.3 mL) was added dropwise and the reaction mixture was allowed to warm to rt overnight. Brine (14 mL) was added and the mixture was concentrated to approximately 30 mL prior to extraction with Et_2O. The solvent was removed under reduced pressure. The residue was subjected to column chromatography. The product **3.72** (0.44 g, 92%) was obtained as colorless oil. ^{1}H NMR ($CDCl_3$) δ 5.81- 5.87 (m, 1H), 5.12- 5.15 (m, 1H), 4.97- 5.08 (m, 2H), 3.84- 3.90 (m, 2H), 3.39- 3.40 (m, 1H), 3.19- 3.20 (m, 1H), 2.06- 2.20 (m, 4H), 1.70 (s, 3H), 1.63 (s, 3H), 1.46- 1.60 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 138.4, 132.1, 123.9, 114.8, 72.8, 72.4, 42.9, 38.1, 37.2, 29.7, 25.7, 24.0, 17.7. HRMS (ESI) calcd for $C_{13}H_{24}O_2$ ($M + Na^+$) 235.1669, found 235.1671.

General procedure for synthesis of cyclic acetals from diol and aldehyde precursors

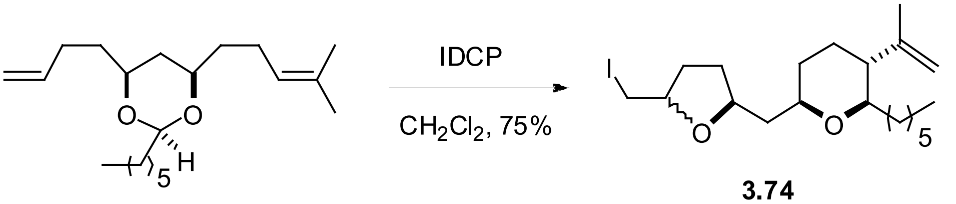
To a solution of the diol (1 mmol) in CH_2Cl_2 was added the aldehyde (2 mmol) and *p*-TsOH·H_2O (0.1 mmol) at 0 °C. The reaction mixture was stirring at rt for an additional hour, then quenched by adding saturated aqueous $NaHCO_3$, and extracted with CH_2Cl_2. The organic extract was dried (Na_2SO_4) and the solvent was removed under reduced pressure. The residue was subjected to column chromatography to give the desired acetal.

Synthesis of (2S, 4S, 6R)-4-(but-3-enyl)-2-ethyl-6-(4-methylpent-3-enyl)-1,3-dioxane (3.73)



^{1}H NMR ($CDCl_3$) δ 5.80- 5.86 (m, 1H), 5.11- 5.14 (m, 1H), 5.05- 5.06 (d, *J* = 5 Hz, 1H), 5.05- 5.05 (d, *J* = 1.6 Hz, 1H), 4.47- 4.48 (m, 1H), 3.53- 3.58 (m, 2H), 2.09- 2.21 (m, 4H), 1.70 (s, 1H), 1.64- 1.69 (m, 2H), 1.60 (s, 1H), 1.22- 1.54 (m, 14H), 0.88- 0.92 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 138.3, 131.8, 124.0, 114.6, 101.8, 75.5, 37.2, 36.0, 35.1, 35.1, 31.8, 29.2, 29.2, 25.7, 24.2, 23.5, 22.6, 17.6, 14.0. HRMS (ESI) calcd for $C_{20}H_{36}O_2$ ($M + H^+$) 309.2788, found 309.2790.

Synthesis of cyclised product 3.74

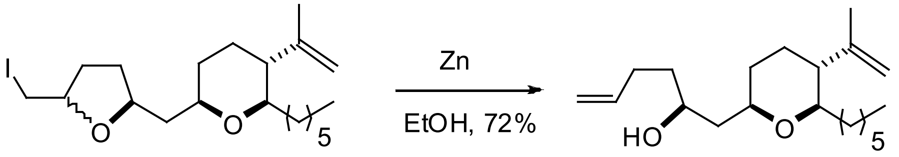


(±) **3.73**

3.74
(2 pairs of diastereoisomers)

To a solution of diol acetal **3.73** (70 mg, 0.227 mmol) in CH_2Cl_2 (10 mL) were added grinded molecular sieves (pre-activated, 1 g) and IDCP (160 mg, 0.341 mmol) at 0 °C. The reaction mixture was stirring at rt for 2 h. Then it was quenched by adding saturated $Na_2S_2O_3$, extracted by Et_2O, and dried (Na_2SO_4). The solvent was removed under reduced pressure. The residue was subjected to column chromatography to give **3.74** (74 mg, 75%) as a colorless oil. ^1H NMR ($CDCl_3$) δ 4.74 (s, 2H), 4.76 (s, 2H), 4.25- 4.28 (m, 1H), 4.11- 4.15 (m, 2H), 3.98- 4.00 (m, 1H), 3.40- 3.45 (m, 2H), 3.29- 3.32 (m, 2H), 3.17- 3.22 (m, 4H), 2.21- 2.24 (m, 1H), 2.07- 2.12 (m, 2H), 1.90- 2.02 (m, 4H), 1.50- 1.80 (m, 21H), 1.28- 1.37 (m, 20H), 0.87- 0.92 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 147.2, 111.6, 79.8, 79.8, 75.0, 49.9, 42.1, 41.9, 33.5, 32.6, 32.1, 31.9, 31.9, 21.9, 31.5, 30.8, 30.2, 29.2, 25.6, 22.7, 20.1, 14.1, 11.2, 11.0.

Synthesis of (*S*)-1-((2*R*, 5*R*, 6*R*)-6-ethyl-5-(prop-1-en-2-yl)tetrahydro-2H-pyran-2-yl)hex-5-en-2-ol (3.75)

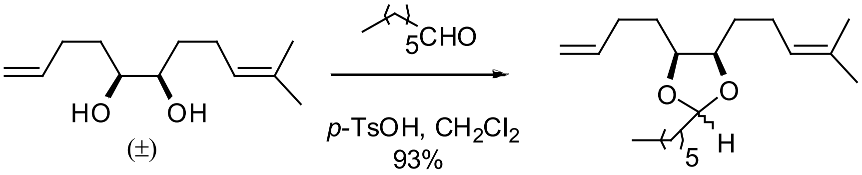


3.74
(2 pairs of diastereoisomers)

3.75
(racemic)

To a solution of **3.74** (15 mg, 0.035 mmol) in 95 % EtOH (5 mL) was added in Zinc (10.2 mg, 0.156 mmol). The mixture was kept refluxing for 1 h. The zinc was removed by filtration and solvent was removed under reduced pressure. The residue was subjected to column chromatography to give **3.75** (6.3 mg, 72%) as colorless oil. ^{1}H NMR ($CDCl_3$) δ 5.84- 5.90 (m, 1H), 5.04- 5.07 (d, J = 17.0 Hz, 1H), 4.96- 4.99 (d, J = 11.1 Hz, 1H), 4.78 (s, 1H), 4.75 (s, 1H), 3.98 (s, 1H), 3.88- 3.90 (m, 1H), 3.58- 3.62 (m, 1H), 3.33- 3.37 (dt, J = 2.0, 9.0 Hz, 1H), 2.15- 2.23 (m, 2H), 1.94- 2.00 (m, 1H), 1.73- 1.76 (m, 1H), 1.56- 1.65 (m, 6H), 1.28- 1.55 (m, 12H), 0.89- 0.90 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 146.8, 138.8, 114.4, 112.0, 80.2, 79.3, 71.7, 70.6, 50.0, 49.3, 42.6, 36.7, 33.4, 32.4, 31.7, 29.8, 29.7, 29.3, 25.6, 20.1, 14.0.

Synthesis of diol acetal 3.76

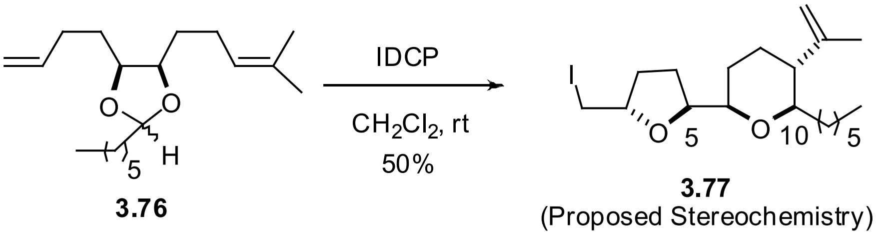


3.94

3.76

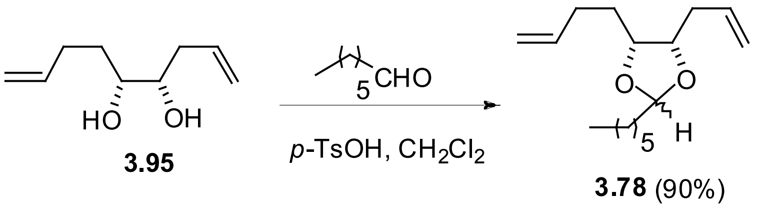
^{1}H NMR ($CDCl_3$) δ 5.84- 5.89 (m, 1H), 5.13- 5.17 (m, 1H), 5.01- 5.10 (m, 2H), 4.90- 4.92 (m, 1H), 3.93- 3.96 (m, 2H), 2.07- 2.31 (m, 5H), 1.72 (s, 3H), 1.62- 1.70 (m, 6H), 1.31- 1.61 (m, 10H), 0.89- 0.92 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 138.2, 132.2, 123.8, 123.7, 114.9, 114.8, 103.7, 102.5, 101.7, 77.9, 77.7, 77.6, 77.5, 35.3, 34.9, 34.4, 31.8, 31.8, 31.7, 31.7, 30.4, 30.1, 29.4, 29.2, 29.2, 29.0, 29.0, 28.9, 28.7, 27.9, 25.7, 24.8, 24.0, 22.6, 17.6, 17.6, 14.0.

Synthesis of compound 3.77



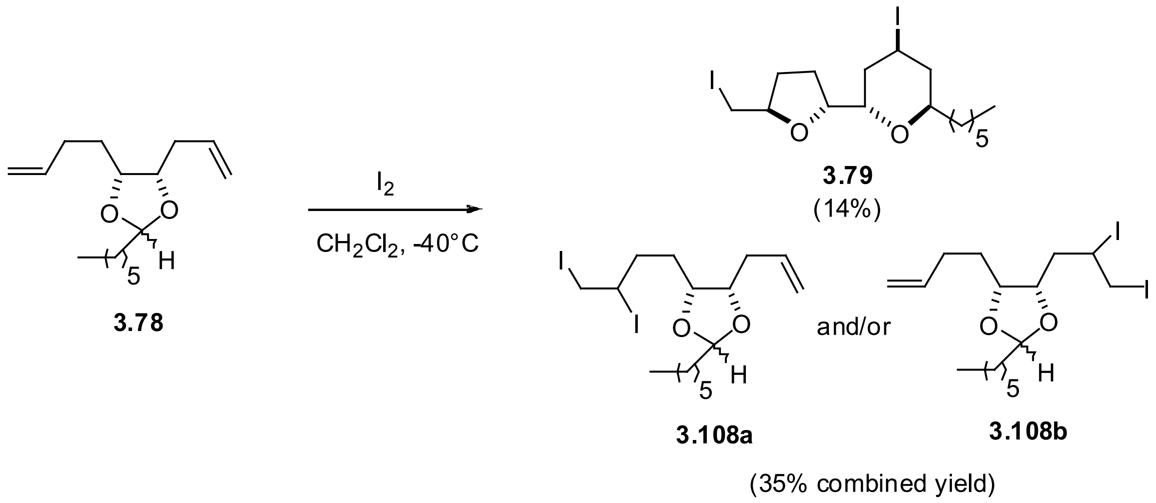
To a solution of acetal diene **3.76** (9 mg, 0.03 mmol) in CH_2Cl_2 (2 mL) were added grinded molecular sieves (pre-activated, 0.5 g) and IDCP (28.7 mg, 0.06 mmol) at 0 °C. The reaction mixture was stirring at rt for 2 h. Then it was quenched by adding saturated aqueous $Na_2S_2O_3$, extracted with Et_2O and dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue subjected to column chromatography to give **3.77** (12 mg, 50 %) as colorless oil. ^1H NMR ($CDCl_3$) δ 4.76 (s, 1H), 4.73 (s, 1H), 4.09- 4.11 (m, 1H), 3.98- 4.02 (m, 1H), 3.28- 3.31 (m, 1H), 3.23- 3.26 (m, 2H), 3.17- 3.22 (m, 1H), 2.18- 2.25 (m, 2H), 2.07- 2.10 (m, 1H), 1.91- 1.98 (m, 2H), 1.74- 1.80 (m, 2H), 1.62- 1.68 (m, 2H), 1.25- 1.41 (m, 10H), 0.91- 0.99 (m, 6H); ^{13}C NMR ($CDCl_3$) δ 147.2, 111.6, 101.7, 82.7, 79.9, 78.9, 70.6, 49.9, 34.4, 33.4, 32.1, 31.9, 29.8, 29.2, 29.0, 28.9, 28.4, 27.8, 25.6, 24.0, 23.5, 22.6, 22.5, 20.2, 14.1, 10.6. HRMS (ESI) calcd for $C_{19}H_{33}IO_2$ (M + NH_4^+) 438.1863, found 438.1866.

Synthesis of acetal diene 3.78



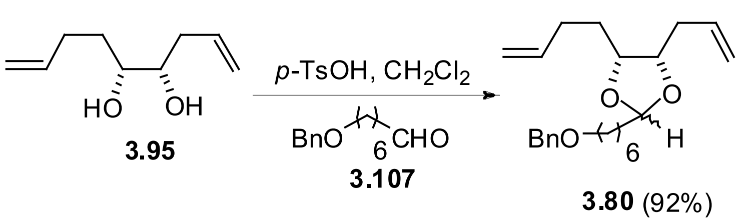
^{1}H NMR (CDCl$_3$) δ 5.84- 5.89 (m, 2H), 5.00- 5.16 (m, 4H), 5.05- 5.06 (t, *J* = 1.7 Hz, 1H), 3.97- 4.04 (m, 2H), 2.24- 2.32 (m, 3H), 2.13- 2.15 (m, 1H), 1.62- 1.70 (m, 2H), 1.31- 1.58 (m, 10H), 0.91- 0.94 (m, 3H); ^{13}C NMR (CDCl$_3$) δ 138.1, 134.8, 117.0, 114.9, 114.8, 103.8, 103.6, 78.4, 77.8, 34.9, 34.7, 31.9, 31.8, 30.4, 30.4, 29.4, 29.3, 29.2, 24.0, 23.9, 22.6, 19.6, 14.1, 14.1.

Synthesis of cyclized product 3.79



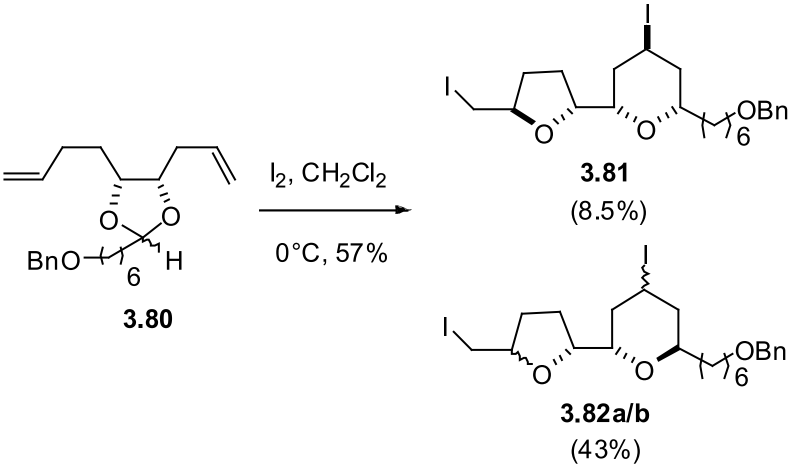
To a solution of acetal diene **3.78** (40 mg, 0.159 mmol) in CH$_2$Cl$_2$ (10 mL) were added grinded molecular sieves (pre-activated, 0.5 g) and I$_2$ (60 mg, 0.238 mmol) in CH$_2$Cl$_2$ (5 mL) at -40 °C. The reaction mixture was stirring at 0 °C for 2 h. Then it was quenched by adding saturated aqueous $Na_2S_2O_3$, extracted with Et_2O, and dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue was subjected to column chromatography to give **3.79** (10 mg, 14 %) and **3.108a/b** (25 mg, 35 %). For **3.79**: ^{1}H NMR ($CDCl_3$) δ 4.60 - 4.64 (tt, *J* = 4.0, 8.0 Hz, 1H), 4.40- 4.45 (m, 1H), 4.04- 4.10 (m, 1H), 3.50- 3.56 (m, 1H), 3.47- 3.49 (m, 1H), 3.26- 3.29 (m, 1H), 3.20- 3.24 (m, 1H), 2.58- 2.61 (m, 1H), 2.29- 2.36 (m, 2H), 2.11- 2.22 (m, 2H), 1.93- 2.00 (m, 1H), 1.82- 1.89 (m, 1H), 1.29- 1.47 (m, 10H), 0.90- 0.92 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 78.8, 78.2, 73.2, 45.2, 38.8, 36.2, 32.0, 31.8, 29.4, 29.2, 25.4, 22.6, 21.0, 14.1, 10.5, 1.0; For **3.108a/b**: ^{1}H NMR ($CDCl_3$) δ 5.86- 5.87 (m, 2H), 5.00- 5.17 (m, 4H), 4.91- 4.92 (m, 1H), 4.25- 4.32 (m, 1H), 3.97- 4.09 (m, 4H), 3.20- 3.30 (m, 3H), 3.17- 3.19 (m, 1H), 2.44- 2.45 (m, 1H), 2.09- 2.20 (m, 3H), 1.89- 1.92 (m, 2H), 1.29- 1.42 (m, 10H), 0.90- 0.97 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 138.1, 134.8, 117.0, 116.9, 114.9, 103.8, 103.7, 81.7, 80.9, 79.0, 45.4, 41.9, 35.6, 34.9, 34.8, 34.7, 32.1, 31.8, 30.4, 29.4, 29.3, 29.2, 28.6, 27.8, 25.4, 23.9, 22.7, 22.6, 14.1, 14.0, 10.4, 1.0.

Synthesis of acetal diene 3.80



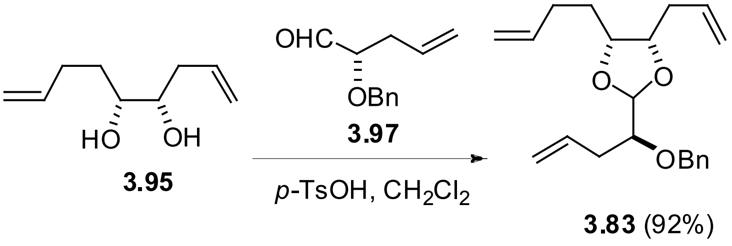
^{1}H NMR ($CDCl_3$) δ 7.30- 7.40 (m, 5H), 5.85- 5.88 (m, 2H), 5.00- 5.16 (m, 4H), 4.90- 4.92 (t, *J* = 4.8 Hz, 1H), 4.52 (s, 2H), 3.98- 4.04 (m, 2H), 3.47- 3.50 (t, *J* = 6.7 Hz, 2H), 2.20- 2.32 (m, 4H), 1.36- 1.69 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 138.7, 138.1, 128.4, 127.7, 127.5, 117.1, 115.0, 103.7, 77.8, 72.9, 70.5, 34.7, 34.6, 30.5, 29.7, 29.4, 29.1, 26.1, 23.9. HRMS (ESI) calcd for $C_{23}H_{34}O_3$ (M + H^+) 359.2581, found 359.2580.

Synthesis of 3.81 and 3.82a/b



The procedure refers to the synthesis of **3.79**. For **3.81**: ^{1}H NMR ($CDCl_3$) δ 7.30- 7.38 (m, 5H), 4.53 (s, 2H), 4.25- 4.27 (tt, *J* = 4.0, 8.0 Hz, 1H), 4.06- 4.07 (m, 1H), 3.98- 4.00 (m, 1H), 3.47- 3.50 (m, 2H), 3.24- 3.30 (m, 3H), 3.17- 3.20 (m, 1H), 2.44- 2.47 (m, 1H), 2.29- 2.31 (m, 1H), 2.08- 2.22 (m, 2H), 1.88- 1.92 (m, 3H), 1.58- 1.72 (m, 6H), 1.28- 1.42 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 128.4, 127.7, 127.5, 81.7, 80.8, 79.0, 72.9, 70.4, 45.4, 41.8, 35.5, 32.1, 29.7, 29.3, 27.8, 26.2, 25.4, 22.6, 10.5. For **3.82a/b**: ^{1}H NMR ($CDCl_3$) δ 7.29- 7.37 (m, 5H), 4.89- 4.90 (m, 1H), 4.52- 4.53 (m, 2H), 4.06- 4.09 (m, 2H), 3.75- 3.82 (m, 2H), 3.47- 3.50 (m, 3H), 3.17- 3.30 (m, 3H), 1.74- 2.22 (m, 4H), 1.61- 1.74 (m, 4H), 1.32- 1.57 (m, 8H); ^{13}C NMR ($CDCl_3$) δ 138.7, 128.4, 127.7, 127.5, 81.9, 78.8, 78.7, 78.2, 75.8, 73.6, 73.1, 72.9, 70.5, 45.2, 40.8, 38.8, 37.2, 36.1, 35.3, 34.1, 32.0, 30.9, 29.7, 29.4, 28.0, 26.2, 25.5, 22.4, 21.5, 21.0, 14.1, 10.7, 10.6, 10.3, 1.0.

Synthesis of acetal diene 3.83

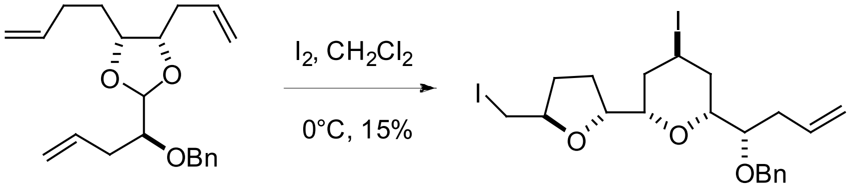


3.95

3.83 (92%)

^{1}H NMR (CDCl$_3$) δ 7.27- 7.40 (m, 5H), 5.85- 5.92 (m, 3H), 5.00- 5.17 (m, 6H), 4.91- 4.92 (d, *J* = 4.75 Hz, 1H), 4.80- 4.83 (d, *J* = 11.7 Hz, 1H), 4.63- 4.65 (d, *J* = 11.7 Hz, 1H), 3.45- 3.46 (m, 1H), 2.20- 2.39 (m, 6H), 1.54- 1.55 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 137.9, 135.0, 134.7, 128.2, 128.0, 127.5, 117.2, 116.9, 115.1, 104.2, 79.7, 78.0, 73.1, 35.0, 34.6, 30.4, 29.0.

Synthesis of 3.84

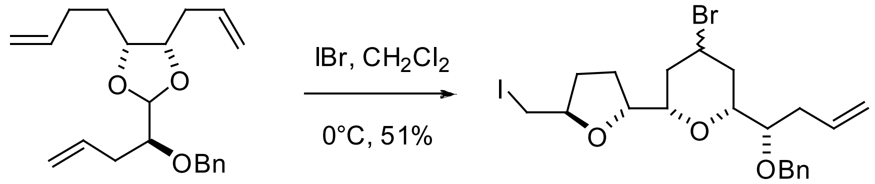


3.83

3.84

Compound **3.84** was prepared following the procedure used for **3.79**. ^{1}H NMR (CDCl$_3$) δ 7.30- 7.38 (m, 5H), 5.86- 5.90 (m, 1H), 5.11- 5.17 (m, 2H), 4.93- 4.94 (m, 1H), 4.62- 4.65 (m, 2H), 4.05- 4.09 (m, 2H), 3.87- 3.89 (m, 1H), 3.80- 3.83 (m, 1H), 3.58- 3.59 (m, 1H), 3.28- 3.31 (m, 1H), 3.19- 3.22 (m, 1H), 2.35- 2.37 (m, 2H), 2.09- 2.21 (m, 4H), 1.97- 1.99 (m, 1H), 1.67- 1.72 (m, 2H), 1.56- 1.59 (m, 1H); ^{13}C NMR (CDCl$_3$) δ 138.6, 134.5, 128.3, 127.9, 127.6, 117.4, 81.8, 80.1, 78.8, 75.9, 75.5, 72.4, 37.3, 35.9, 35.5, 32.1, 30.2, 27.8, 22.4, 14.1, 10.6.

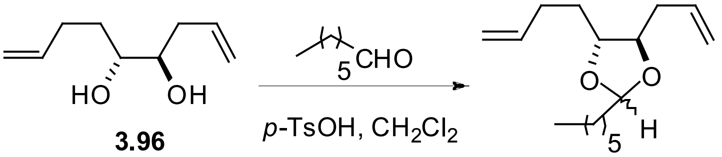
Synthesis of 3.85



3.83 **3.85**

To a solution of acetal diene **3.83** (110 mg, 0.345 mmol) in CH_2Cl_2 (15 mL) were added grinded molecular sieves (pre-activated, 0.5 g) and IBr (107 mg, 0.517 mmol, 1 M in CH_2Cl_2) at 0 °C. The reaction mixture was stirring at rt for 10 min. Then it was quenched by adding saturated aqueous $Na_2S_2O_3$, extracted with Et_2O, and dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue subjected to column chromatography to give product **3.85** (102 mg, 51 %). ^1H NMR ($CDCl_3$) δ 7.30- 7.38 (m, 5H), 5.86- 5.90 (m, 1H), 5.10- 5.16 (m, 2H), 4.81- 4.82 (m, 1H), 4.60- 4.66 (m, 2H), 4.02- 4.09 (m, 2H), 3.91- 3.93 (m, 1H), 3.86- 3.88 (m, 1H), 3.56- 3.57 (m, 1H), 3.28- 3.29 (m, 1H), 3.20- 3.22 (m, 1H), 2.36- 2.39 (m, 2H), 2.10- 2.20 (m, 4H), 1.89- 1.98 (m, 2H), 1.70- 1.79 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 135.2, 134.8, 134.6, 129.0, 128.8, 128.7, 128.6, 128.5, 128.4, 128.2, 128.1, 128.0, 127.9, 126.3, 117.5, 82.0, 81.9, 80.7, 80.2, 74.4, 74.1, 72.5, 50.4, 36.1, 36.0, 35.4, 35.3, 35.2, 34.7, 32.0, 31.9, 31.8, 27.7, 27.6, 27.5, 10.6. HRMS (ESI) calcd for $C_{21}H_{28}BrIO_3$ (M + H^+) 554.0587, found 554.0594.

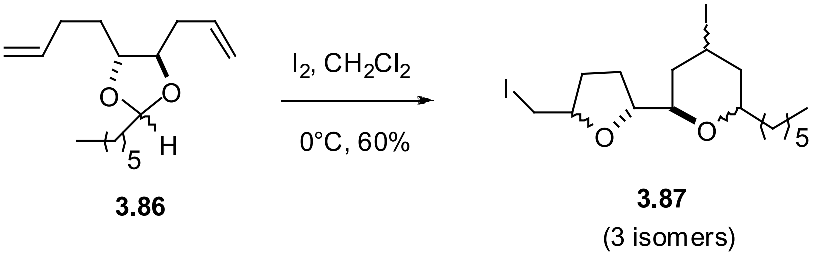
Synthesis of acetal diene 3.86



3.96 **3.86** (90%)

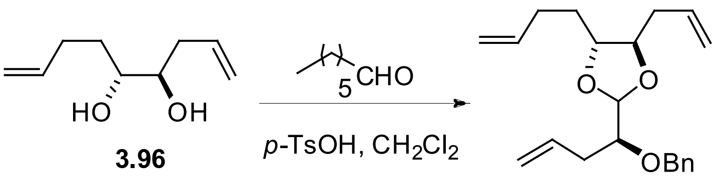
^{1}H NMR ($CDCl_3$) δ 5.82- 5.90 (m, 2H), 5.06- 5.18 (m, 3H), 5.00- 5.02 (m, 2H), 3.67- 3.72 (m, 2H), 2.19- 2.41 (m, 3H), 2.13- 2.18 (m, 1H), 1.63- 1.70 (m, 2H), 1.31- 1.60 (m, 10H), 0.89- 0.92 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 138.0, 138.0, 117.6, 117.6, 114.9, 103.6, 103.3, 81.1, 80.9, 79.8, 79.7, 37.6, 37.4, 34.4, 34.4, 32.3, 32.2, 32.2, 31.8, 30.1, 30.1, 29.3, 23.9, 23.9, 22.6, 14.1. HRMS (ESI) calcd for $C_{16}H_{28}O_2$ (M + H$^+$) 253.2162, found 253.2158.

Synthesis of 3.87



Compound **3.87** was prepared following the procedure used for **3.79**. ^{1}H NMR ($CDCl_3$) δ 4.27- 4.30 (m, 1H), 4.12- 4.14 (m, 1H), 4.03- 4.07 (m, 1H), 3.31- 3.34 (m, 1H), 3.26- 3.29 (m, 2H), 3.16- 3.20 (m, 1H), 2.31- 2.34 (m, 1H), 2.23- 2.27 (m, 2H), 2.09- 2.14 (m, 1H), 2.01- 2.03 (m, 1H), 1.83- 1.95 (m, 2H), 1.66- 1.70 (m, 1H), 1.29- 1.56 (m, 10H), 0.89- 0.92 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 81.4, 81.0, 79.1, 79.0, 45.1, 41.1, 35.7, 32.4, 31.8, 29.2, 28.0, 25.3, 22.9, 22.6, 14.1, 10.6. HRMS (ESI) calcd for $C_{16}H_{28}I_2O_2$ (M + NH$_4^+$) 524.0517, found 524.0518.

Synthesis of acetal diene 3.88

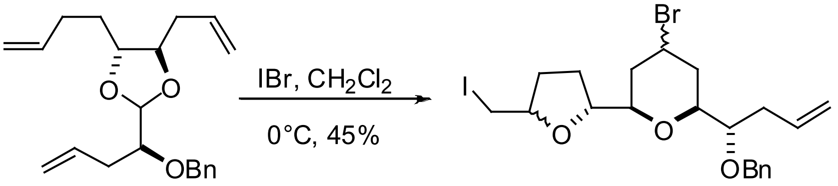


3.96

3.88 (90%)

^{1}H NMR (CDCl$_3$) δ 7.30- 7.40 (m, 5H), 5.82- 5.93 (m, 3H), 5.00- 5.18 (m, 7H), 4.78- 4.82 (t, *J* = 11.5 Hz, 1H,), 4.63- 4.66 (d, *J* = 11.7 Hz, 1H), 3.70- 3.76 (m, 2H), 3.46- 3.49 (m, 1H), 2.35- 2.40 (m, 4H), 2.17- 2.20 (m, 2H), 1.66- 1.70 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 138.7, 138.6, 137.9, 137.9, 135.0, 133.8, 133.7, 128.3, 128.0, 127.9, 127.5, 117.8, 117.7, 117.0, 115.0, 104.1, 104.0, 81.0, 80.8, 80.0, 79.8, 79.1, 73.1, 73.1, 37.2, 37.0, 34.9, 34.8, 31.9, 31.8, 30.2, 30.1. HRMS (ESI) calcd for $C_{21}H_{28}O_3$ (M + NH_4^+) 346.2377, found 346.2369.

Synthesis of 3.89a/b

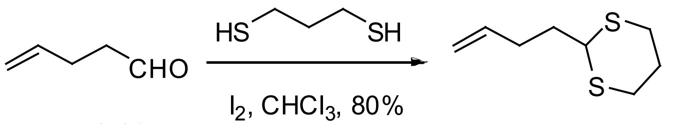


3.88

3.89a/b
(2 isomers)

Compound **3.89a/b** was prepared following the procedure used for **3.83**. ^{1}H NMR (C_6D_6) δ 7.36- 7.46 (m, 5H), 5.96- 5.97 (m, 1H), 5.25- 5.29 (m, 2H), 4.54- 4.56 (m, 2H), 4.40- 4.45 (m, 2H), 4.15- 4.17 (m, 1H), 4.03- 4.05 (m, 1H), 3.80- 3.82 (m, 1H), 3.69- 3.70 (m, 1H), 3.30- 3.31 (m, 1H), 3.22- 3.25 (m, 1H), 3.14- 3.16 (m, 1H), 2.50- 2.51 (m, 1H), 2.39- 2.40 (m, 1H), 1.96- 1.99 (m, 1H), 1.70- 1.81 (m, 5H), 1.48- 1.54 (m, 2H); ^{13}C NMR (C_6D_6) δ 139.1, 135.2, 117.1, 81.6, 80.3, 79.7, 74.2, 73.0, 72.3, 51.9, 36.0, 35.1, 24.7, 31.6, 27.4, 10.6. HRMS (ESI) calcd for $C_{21}H_{28}BrIO_3$ ($M + NH_4^+$) 552.0605, found 552.0608.

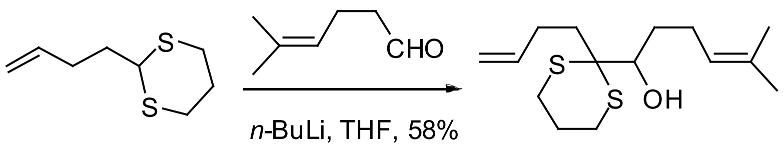
Synthesis of 2-(but-3-enyl)-1,3-dithiane (3.91)



3.90 **3.91**

To a solution of pent-4-enal (**3.90**) (450 mg, 5.36 mmol) in chloroform were added propane-1,3-dithiol (696 mg, 6.43 mmol) and iodine (136 mg, 0.536 mmol) at 0 °C. The reaction mixture was kept at rt for 2 h, then quenched with aqueous $Na_2S_2O_3$ and extracted with ether. The solvent was removed under reduced pressure and the residue was subjected to column chromatographyto give **3.91** (750 mg, 80 %) as a yellow oil. ^{1}H NMR ($CDCl_3$) δ 5.78- 5.86 (m, 1H), 5.07- 5.11 (d, J = 20.0 Hz, 1H), 5.02- 5.04 (d, J = 9.0 Hz, 1H), 4.05- 4.07 9 (t, J = 7 Hz, 1H), 2.80- 2.92 (m, 4H), 2.27- 2.32 (m, 2H), 2.11- 2.17 (m, 1H), 1.82- 1.99 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 137.1, 115.6, 70.6, 46.7, 34.6, 30.5, 30.3, 26.0.

Synthesis of 1-(2-(but-3-enyl)-1,3-dithian-2-yl)-5-methylhex-4-en-1-ol (3.92)

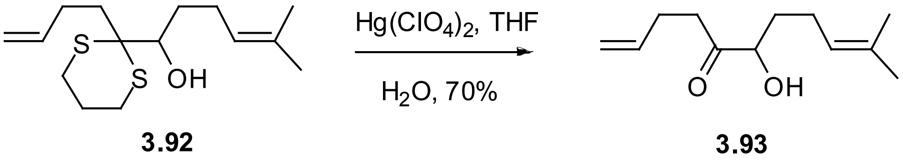


3.91 **3.92**

To the solution of **3.91** (240 mg, 1.38 mmol) in THF was added *n*-BuLi (0.44 mL, 1.1 mmol, 2.5 M in hexane) at –78 ˚C. The mixture was then warmed to 0 ˚C for 0.5 h and re-cooled to –78 ˚C, at which time 5-methylhex-4-enal (103 mg, 0.92 mmol) was added.

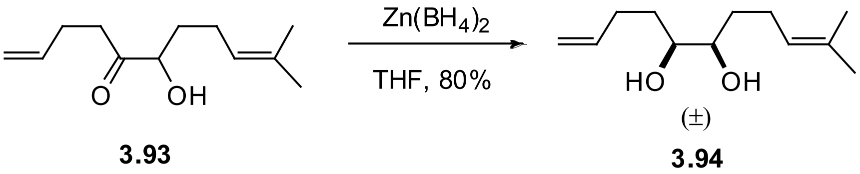
The reaction mixture was stirring at rt for 2 h, then quenched with saturated aqueous NH_4Cl and extracted with ether. The solvent was removed under reduced pressure and the residues subjected to column chromatography to give **3.92** (230 mg, 58 %) as colorless oil. ^{1}H NMR ($CDCl_3$) δ 5.80- 5.85 (m, 1H), 5.20- 5.22 (t, *J* = 6.6 Hz, 1H), 5.04- 5.08 (d, *J* = 17.1 Hz, 1H), 4.99- 4.97 (d, *J* = 10.2 Hz, 2H), 3.99- 4.01 (d, *J* = 10.0 Hz, 1H), 2.96- 3.01 (m, 2H), 2.73 (s, 1H), 2.63- 2.69 (m, 2H), 2.30- 2.38 (m, 3H), 2.18- 2.21 (m, 1H), 2.06- 2.09 (m, 1H), 1.94- 1.99 (m, 2H), 1.86- 1.88 (m, 1H), 1.74 (s, 3H), 1.71- 1.72 (m, 2H), 1.68 (s, 3H), 1.51- 1.53 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 138.2, 132.4, 124.2, 114.7, 71.2, 59.0, 33.8, 30.4, 28.9, 26.0, 25.9, 25.7, 25.1, 24.5, 17.8.

Synthesis of 6-hydroxy-10-methylundeca-1, 9-dien-5-one (3.93)



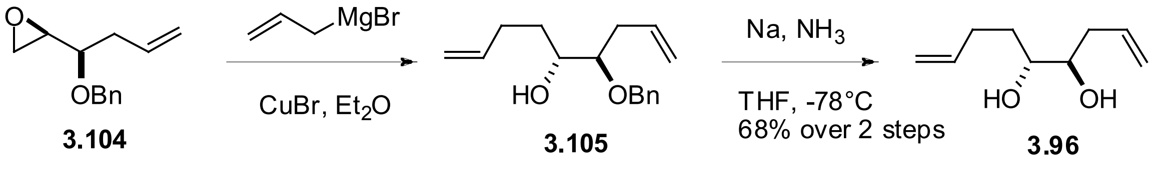
To a solution of **3.92** (85 mg, 0.3 mmol) in THF was added in $Hg(ClO_4)_2$ (143 mg, 0.36 mmol) at 0 ˚C. The mixture was stirring at 0 ˚C for 1 h and at rt for 2 h. Then it was quenched by saturated aqueous $NaHCO_3$ and extracted with ether. The solvent was removed under reduced pressure and the residue subjected to column chromatography to give **3.93** (41 mg, 70 %) as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 5.79- 5.87 (m, 1H), 5.11- 5.14 (m, 1H), 5.06- 5.09 (d, *J* = 18.6 Hz, 1H), 5.02- 5.04 (d, *J* = 9 Hz, 1 H), 4.16- 4.20 (m, 1H), 3.44-3.45 (d, *J* = 4.9 Hz, 1H), 2.52- 2.67 (m, 2H), 2.38- 2.41 (m, 2H), 2.19- 2.22 (m, 1H), 2.08- 2.18 (m, 1H), 1.85- 1.91 (m, 1H), 1.72 (s, 3H), 1.68 (s, 3H), 1.55- 1.64 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 211.6, 136.6, 133.3, 123.0, 115.8, 76.1, 37.0, 33.8, 27.5, 25.7, 23.4, 17.7.

Synthesis of (5*S*, 6*R*)-10-methylundeca-1, 9-diene-5, 6-diol (3.94)



To a solution of **3.93** (20 mg, 0.1 mmol) in THF (2 mL) was added $Zn(BH_4)_2$ (19 mg, 0.2 mmol) at 0 ˚C. The reaction mixture was stirring at rt for 0.5 h and quenched by adding 2 rops of H_2O at 0 ˚C. Then it was extracted with EtOAc and the solvent was removed under reduced pressure. The residue was subjected to column chromatography to give **3.94** (15.8 mg, 80 %) as a white powder. ^{1}H NMR ($CDCl_3$) δ 5.83- 5.92 (m, 1H), 5.16- 5.18 (m, 1H), 5.07- 5.11 (d, J = 17.1 Hz, 1H), 5.01- 5.03 (d, J = 10.2 Hz, 1H), 3.65- 3.72 (m, 1H), 2.28- 2.34 (m, 1H), 2.08- 2.24 (m, 3H), 1.85- 1.93 (m, 2H), 1.77 (s, 3H), 1.66 (s, 3H), 1.48- 1.60 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 138.4, 132.6, 123.9, 115.1, 74.5, 74.6, 31.3, 30.4, 30.2, 25.7, 24.5, 17.7.

Synthesis of (4*R*, 5*R*)-nona-1, 8-diene-4, 5-diol (3.96)

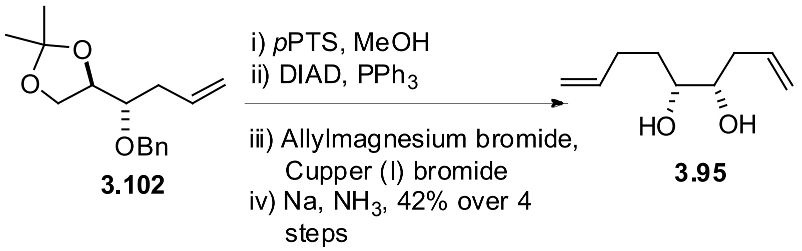


In a 100 mL round-bottom flask equipped with magnetic stirring bar, were placed CuBr (0.75 g, 5.22 mmol) and anhydrous THF (30 mL). Allylmagnesium bromide (87 mmol, 1

M in Et_2O) was added dropwise at 0 °C, and then epoxide **3.104** (1.77 g, 8.7 mmol) was introduced. The reaction was stirred at 0 °C for 3 h, then poured into ice cold saturated aqueous NH_4Cl, and extracted with ether. The organic phase was washed with brine, dried (Na_2SO_4), filtered, and evaporated under reduced pressure. The residue was purified by FCC to give the derived alcohol 3.105 (1.82 g, 85%); ^{1}H NMR ($CDCl_3$) δ 7.32- 7.40 (m, 5H), 5.82- 5.91 (m, 2H), 4.98- 5.19 (m, 4H), 4.73- 4.75 (m, 1H), 4.50- 4.75 (m, 1H), 3.59- 3.61 (m, 1H), 3.35- 3.39 (m, 1H), 2.50- 2.53 (m, 1H), 2.38- 2.40 (m, 1H), 2.29- 2.30 (m, 1H), 2.25- 2.28 (m, 1H), 2.15- 2.18 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 138.5, 138.1, 134.2, 128.5, 127.9, 127.8, 117.6, 114.8, 81.5, 72.3, 71.9, 34.8, 32.6, 29.9.

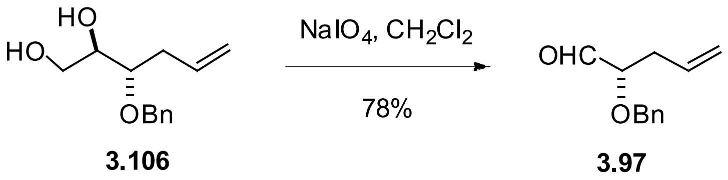
To a solution of **3.105** (294 mg, 1.2 mmol) in THF (20 mL) were added the liquidized NH_3 (c.a. 5 mL) and Na (55 mg, 2.4 mmol) at -78 °C. The reaction mixture was stirring for 10 min at -78 °C, and then solid NH_4Cl was added in to quench it until the dark blue color discharged. MeOH and H_2O were added in to ensure the absence of Na and it was extracted with EtOAc and dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue subjected to column chromatography to give **3.96** (0.156 g, 84 %). ^{1}H NMR ($CDCl_3$) δ 5.84- 5.90 (m, 2H), 5.21- 5.22 (m, 1H), 5.19 (s, 1H), 5.07- 5.17 (m, 1H), 5.00- 5.03 (m, 1H), 3.51- 3.55 (m, 1H), 2.37-2.39 (m, 1H), 2.19- 2.31 (m, 3H), 2.12- 2.13 (d, J = 5.2 Hz, 1H), 2.08- 2.09 (d, J = 4.4 Hz, 1H), 1.61- 1.66 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 138.3, 134.4, 118.5, 115.1, 73.4, 73.2, 38.3, 32.7, 29.9. HRMS (ESI) calcd for $C_9H_{16}O_2$ ($M + Na^+$) 179.1043, found 179.1036.

Synthesis of (4*S*, 5*R*)-nona-1, 8-diene-4, 5-diol (3.95)



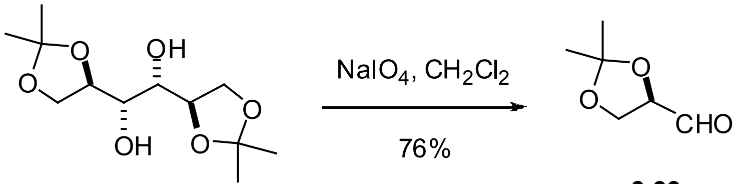
The procedure refers to the synthesis of **3.96**. ^{1}H NMR (CDCl$_3$) δ 5.83- 5.91 (m, 2H), 5.22- 5.23 (m, 1H), 5.21 (s, 1H), 5.08- 5.12 (m, 1H), 5.01- 5.04 (m, 1H), 3.71- 3.73 (m, 1H), 3.64- 3.67 (m, 1H), 2.17- 2.36 (m, 4H), 2.03- 2.04 (m, 2H), 1.58- 1.62 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 138.3, 134.8, 118.6, 115.2, 73.4, 73.1, 36.0, 30.8, 30.3. HRMS (ESI) calcd for $C_9H_{16}O_2$ (M + Na$^+$) 179.1043, found 179.1041.

Synthesis of (*S*)-2-(benzyloxy)pent-4-enal (3.97)



Compound **3.97** was prepared following the procedure used for **3.99**. ^{1}H NMR (CDCl$_3$) δ 9.69 (s, 1H), 7.33- 7.41 (m, 5H), 5.81- 5.90 (m, 1H), 5.15- 5.22 (m, 2H), 4.62- 4.72 (m, 2H), 3.86- 3.89 (m, 1H), 2.49- 2.57 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 203.3, 137.2, 132.4, 128.6, 128.2, 128.0, 118.5, 82.8, 72.5, 34.7.

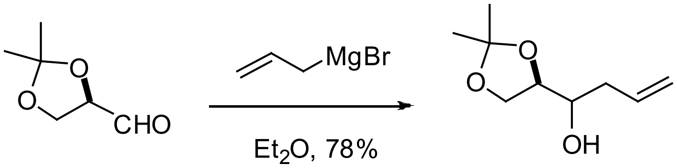
Synthesis of (*R*)-2, 2-dimethyl-1, 3-dioxolane-4-carbaldehyde (3.99)



3.98 **3.99**

To a solution of mannitol derivative **3.98** (5 g, 19 mmol) in CH_2Cl_2 was added a solution of saturated $NaHCO_3$ (2.3 mL) 0 ˚C. $NaIO_4$ (6.12 g, 28.6 mmol) was added slowly and suspension was stirred vigorously for 2 h until TLC analysis indicated the reaction was complete. Anhydrous $MgSO_4$ was added, and the reaction mixture was filtered and concentrated to provide **3.99** (3.75 g, 76%) as clear oil. ^1H NMR ($CDCl_3$) δ 9.71 (s, 1H), 4.36- 4.40 (m, 1H), 4.08- 4.20 (m, 2H), 1.50 (s, 3H), 1.42 (s, 3H).

Synthesis of alcohol 3.100

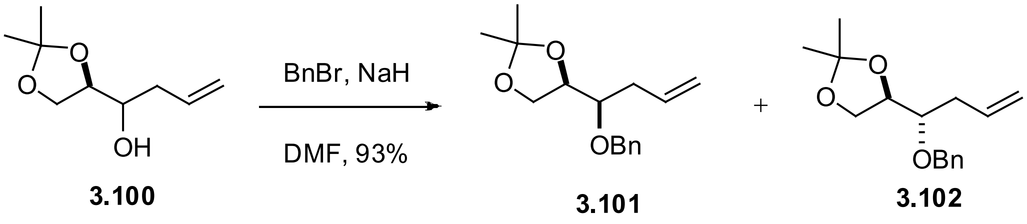


3.99 **3.100**

To a solution of aldehyde **3.99** (562 mg, 4.32 mmol) in anhydrous ether at 0 ˚C was added allylmagnesium bromide (8.65 mL, 1 M in Et_2O). The reaction mixture was stirred at rt for 0.5 h, and then was quenched by NH_4Cl and extracted with Et_2O and dried (Na_2SO_4). The solvent was removed under reduced pressure. The residue was subjected to column chromatography to give **3.100** (580 mg, 78 %) as a colorless oil. ^1H NMR ($CDCl_3$) δ 5.83- 5.91 (m, 1H), 5.14- 5.21 (m, 2H), 3.95- 4.07 (m, 2H), 3.77- 3.82 (m, 1H), 2.21- 2.37 (m, 2H), 2.00- 2.01 (d, J = 3.2 Hz, 1H), 1.46- 1.47 (m, 3H), 1.39- 1.40

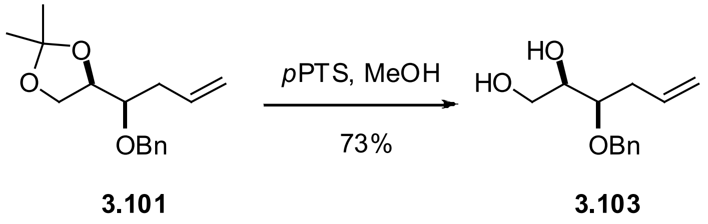
(m, 3H); ^{13}C NMR (CDCl$_3$) δ 134.0, 133.9, 117.9, 109.4, 109.1, 78.5, 77.2, 71.6, 70.4, 66.1, 38.3, 26.6, 25.3.

Synthesis of benzylether 3.101 and 3.102



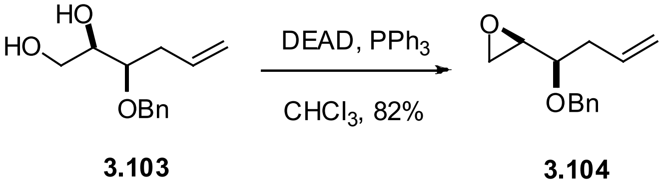
To a solution of alcohol **3.100** (4.1 g, 23.8 mmol) in DMF at 0 ˚C were added NaH (1.43 g, 35.7 mmol, 60 % in mineral oil) and BnBr (6.1 g, 35.7 mmol). The mixture was kept at rt for 2 h, and then quenched by saturated NH$_4$Cl solution, extracted with ether and dried (NaSO$_4$). The solvent was removed under reduced pressure. The residue was subjected to column chromatography to give **3.101** (2.68 g, 43 %) and **3.102** (3.1 g, 50 %). For **3.101**: ^{1}H NMR (CDCl$_3$) δ 7.29- 7.40 9m, 5 H), 5.86- 5.95 9m, 1H), 5.08- 5.15 (m, 2H), 4.68- 4.76 (m, 2H), 4.22- 4.26 (m, 1H), 4.00- 4.03 (m, 1H), 3.72- 3.75 (m, 1H), 3.52- 3.55 (m, 1H), 2.31- 2.37 (m, 1H), 2.20- 2.29 (m, 1H), 1.52 (s, 3H), 1.46 (1s, 3H); ^{13}C NMR (CDCl$_3$) δ 138.6, 134.6, 128.3, 127.8, 127.6, 117.2, 109.3, 79.3, 77.9, 72.6, 65.8, 35.3, 26.5, 25.4; For **3.102**: ^{1}H NMR (CDCl$_3$) δ 7.28- 7.50 (m, 5H), 5.88- 5.95 (m, 1H), 5.12- 5.20 (m, 2H), 4.61- 4.69 (m, 1H), 4.08- 4.14 (m, 1H), 4.05- 4.07 (m, 1H), 3.92- 3.94 (m, 1H), 3.58- 3.62 (m, 1H), 2.44- 2.48 (m, 1H), 2.35- 2.40 9m, 1H), 1.45 (s, 3H), 1.39 (s, 3H); ^{13}C NMR (CDCl$_3$) δ 138.3, 134.2, 128.5, 127.9, 127.8, 117.8, 109.1, 78.7, 72.6, 66.4, 35.5, 26.7, 25.4.

Synthesis of (2*R*, 3*R*)-3-(benzyloxy)hex-5-ene-1,2-diol (3.103)



To s solution of **3.101** (2 g, 7.63 mmol) in MeOH(130 mL) was added in *p*PTS (3.83g, 15.3 mmol) at 0 ˚C. The mixture was kept stirring overnight and the solvent was removed under reduced pressure. The residue was subjected to column chromatography to give **3.103** (1.24 g, 73 %) as colorless oil. ^{1}H NMR (CDCl$_3$) δ 7.29- 7.39 (m, 5H), 5.85- 5.93 (m, 1H), 5.14- 5.24 (m, 1H), 4.70- 4.80 (m, 1H), 4.50- 4.56 (m, 1H), 3.57- 3.74 (m, 4H), 2.63- 2.64 (m, 1H), 2.50- 2.61 (m, 1H), 2.40- 2.45 (m, 1H), 2.13- 2.17 (m, 1H); ^{13}C NMR (CDCl$_3$) δ 137.8, 133.8, 128.6, 128.1, 128.0, 118.0, 79.0, 72.5, 72.1, 63.8, 34.6.

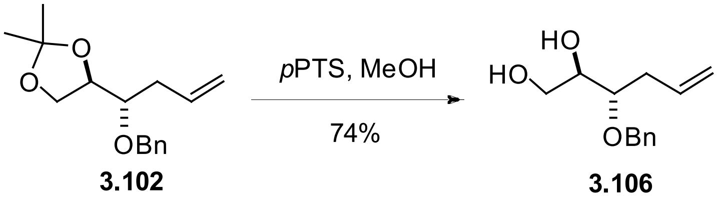
Synthesis of (*R*)-2-((*R*)-1-(benzyloxy)but-3-enyl)oxirane (3.104)



To a solution of **3.103** (1.15 g, 5.18 mmol) in CH$_3$Cl (30 mL) at 0 ˚C were added DEAD (1.65 g, 9.5 mmol) and PPh$_3$ (2.5 g, 9.5 mmol). The reaction mixture was heated to 60 ˚C for 2 h. Then the solvent was removed under reduced pressure. The residue was subjected to column chromatography to give **3.104** (0.87 g, 82 %) as colorless oil. ^{1}H

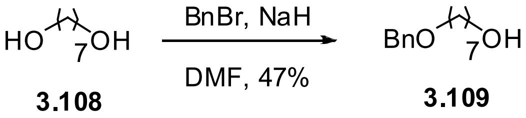
NMR ($CDCl_3$) δ 7.28- 7.41 (m, 5H), 5.84- 5.92 (m, 1H), 5.09- 5.17 (m, 2H), 4.81- 4.86 (m, 1H), 4.60- 4.62 (m, 1H), 3.12- 3.17 (m, 1H), 3.07- 3.09 (m, 1H), 2.80- 2.82 (m, 1H), 2.50- 2.54 (m, 1H), 2.37- 2.46 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 138.5, 133.9, 128.3, 127.7, 127.5, 117.5, 80.1, 71.7, 54.6, 43.4, 37.1.

Synthesis of (2*R*, 3*S*)-3-(benzyloxy)hex-5-ene-1,2-diol (3.106)



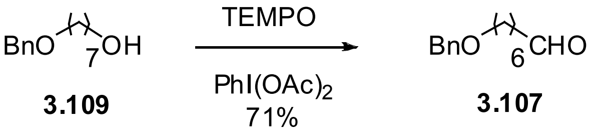
The procedure refers to the synthesis of **3.103**. ^1H NMR ($CDCl_3$) δ 7.31-m7.40 9m, 5H), 5.86- 5.93(m, 1H), 5.13- 5.21 (m, 2H), 4.70- 4.72 (d, *J* = 11.4Hz, 1H), 4.54- 4.56 (d, *J* = 11.4 Hz, 1H), 3.79- 3.82 (m, 1H), 3.73- 3.77 (m, 1H), 3.65- 3.69 (m, 1H), 2.49- 2.52 (m, 1H), 2.48- 2.49 (m, 1H), 2.39- 2.46 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 138.0, 134.1, 128.6, 128.0, 127.9, 117.8, 80.6, 72.6, 72.3, 63.2, 35.1.

Synthesis of 3.109



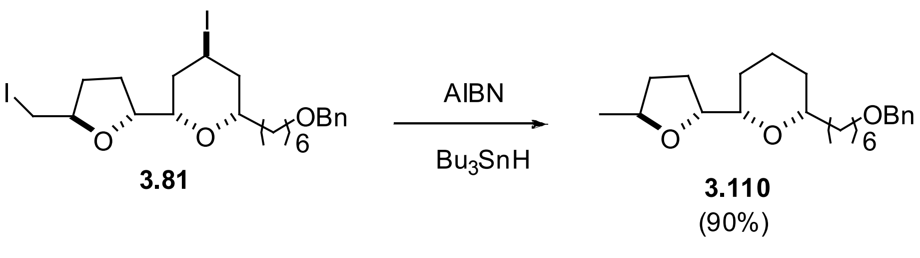
To a solution of **3.108** (1 g, 7.23 mmol) in DMF (30 mL) were added NaH (0.289 g, 7.23 mmol, 60 % in mineral oil) and BnBr (1.24 g, 7.23 mmol) at 0 °C. The reaction mixture was kept at rt for 2 h. Then it was quenched by adding saturated aqueous NH_4Cl, extracted with Et_2O, and dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue was subjected to column chromatography to give **3.109** (0.75 g, 45 %). ^{1}H NMR (CDCl$_3$) δ 7.28- 7.31 (m, 5H), 4.53- 4.56 (m, 2H), 3.61- 3.66 (m, 2H), 3.44- 3.50 (m, 2H), 1.58- 1.77 (m, 4H), 1.29- 1.53 (m, 6H); ^{13}C NMR (CDCl$_3$) δ 138.7, 128.4, 127.7, 127.5, 72.9, 70.4, 63.1, 32.7, 29.7, 29.3, 26.2, 25.7.

Synthesis of 3.107



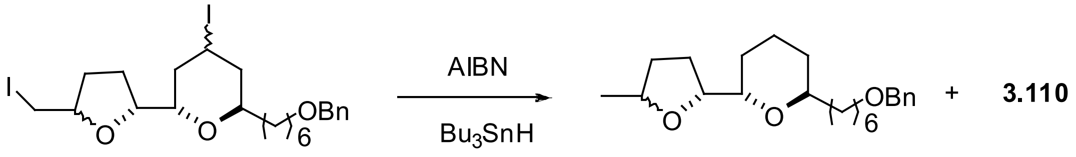
To a solution of **3.109** (0.75 g, 3.38 mmol) in pentane (20 mL) and CH$_2$Cl$_2$ (4 mL) were added TEMPO (53 mg, 0.338 mmol) and PhI(OAc)$_2$ (1.2 g, 3.72 mmol) at 0°C. The reaction mixture was stirring at rt for 1 h. Then it was quenched by adding saturated aqueous Na$_2$S$_2$O$_3$, extracted with Et$_2$O, and dried (Na$_2$SO$_4$). The solvent was removed under reduced pressure and the residue subjected to column chromatography to give **3.107** (0.53 g, 71 %). ^{1}H NMR (CDCl$_3$) δ 9.79 (s, 1H), 7.29- 7.44 (m, 5H), 4.56 (s, 2H), 3.48- 3.50 (m, 2H), 2.45- 2.47 (m, 2H), 1.63- 1.67 (m, 5H), 1.34- 1.40 (m, 5H); ^{13}C NMR (CDCl$_3$) δ 202.9, 238.6, 128.4, 127.7, 127.5, 72.9, 70.3, 43.9, 29.6, 29.0, 26.0, 22.0.

Synthesis of 3.110



To a solution of **3.81** (21 mg, 0.034 mmol) in benzene (5 mL) were added AIBN (1.69 mg, 0.01 mmol) and Bu_3SnH (30 mg, 0.102 mmol). The reaction mixture was heated to reflux for 2 h and the solvent was removed under the reduced pressure. The residue was subjected to column chromatography to give **3.110** (11 mg, 90 %). ^1H NMR ($CDCl_3$) δ 7.30- 7.38 (m, 5H), 4.53 (s, 2H), 4.05- 4.07 (m, 1H), 3.89- 3.91 (m, 1H), 3.46- 3.49 (m, 2H), 3.17- 3.20 (m, 2H), 2.02- 2.05 (m, 2H), 1.84- 1.88 (m, 2H), 1.75- 1.76 (1H), 1.64- 1.67 (m, 3H), 1.32- 1.67 (m, 10H), 1.21-1.22 (m, 3H), 1.18- 1.19 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 138.6, 128.4, 127.7, 127.6, 81.4, 80.3, 78.0, 75.6, 72.9, 70.5, 36.5, 33.7, 31.8, 29.8, 29.6, 29.2, 28.5, 28.4, 26.8, 26.3, 25.7, 23.4, 21.2, 16.4, 14.2, 13.8. HRMS (ESI) calcd for $C_{23}H_{36}O_3$ (M + NH_4^+) 378.3003, found 378.3009.

Synthesis of 3.111



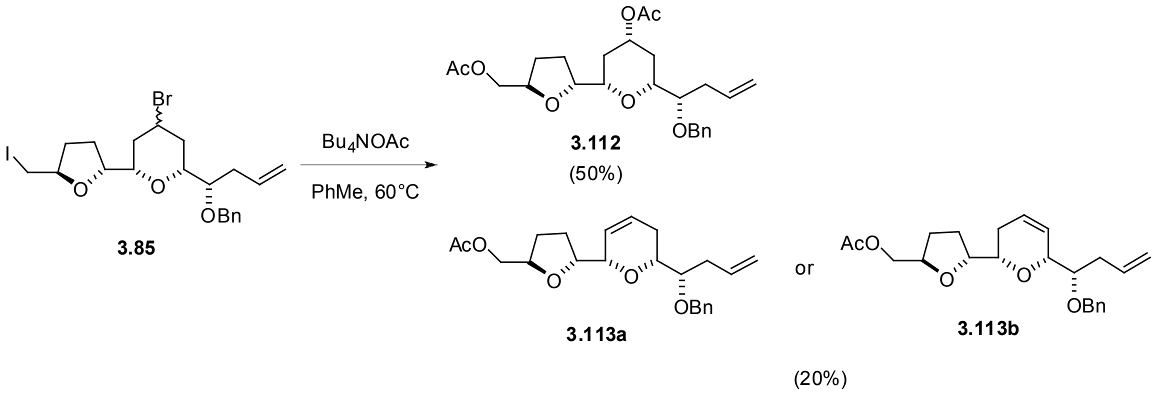
3.82a/b

3.111 (45%)
(3:7 ratio of 2 isomers)

3.110
45%

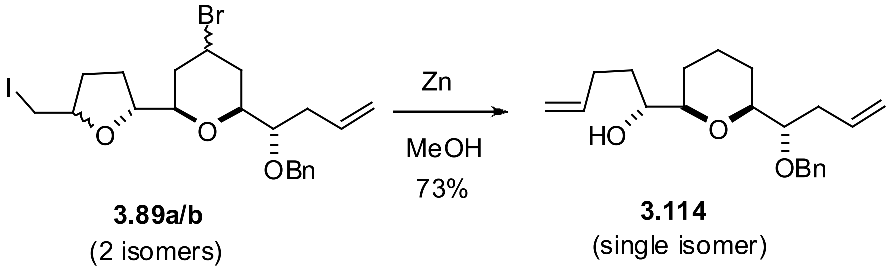
Compound **3.111** was prepared following the procedure used for **3.110**. For **3.111**: ^1H NMR (C_6D_6) δ 7.10- 7.33 (m, 5H), 4.35 (s, 2H), 4.15- 4.17 (m, 1H), 3.95- 4.03 (m, 1H), 3.52- 3.58 (m, 2H), 3.33- 3.35 (m, 2H), 1.70- 1.92 (m, 4H), 1.61- 1.68 (m, 4H), 1.22- 1.54 (m, 12H), 1.14- 1.15 (m, 3H); ^{13}C NMR (C_6D_6) δ 139.3, 128.5, 128.4, 128.3, 128.2, 128.1, 127.4, 127.2, 79.5, 78.8, 75.5, 75.0, 73.8, 73.4, 72.6, 71.5, 71.4, 70.2, 33.8, 33.2, 33.1, 32.7, 30.1, 30.0, 29.6, 28.8, 27.6, 27.6, 26.4, 25.9, 21.2, 18.6, 18.5. HRMS (ESI) calcd for $C_{23}H_{36}O_3$ (M + NH_4^+) 378.3003, found 378.3008.

Synthesis of 3.112 and 3.113a/b



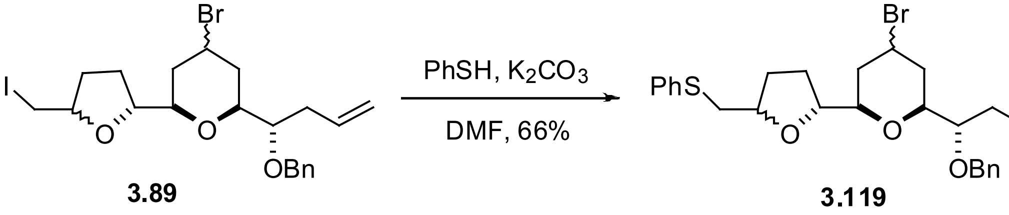
To a solution of **3.85** (65 mg, 0.106 mmol) in toluene (5 mL) was added Bu$_4$NOAc (224 mg, 0.743 mmol). The reaction was heated to 60 °C for 1 h. Then solvent was removed under reduced pressure. The residue was subjected to column chromatography to give the products **3.112** (24 mg, 50 %) and **3.113a/b** (9 mg, 20 %). For **3.112**: ^{1}H NMR (CDCl$_3$) δ 7.30- 7.37 (m, 5H), 5.85- 5.88 (m, 1H), 5.08- 5.15 (m, 2H), 4.63- 4.94 (m, 1H), 4.60- 4.63 (m, 2H), 4.22- 4.23 (m, 1H), 4.14- 4.17 (m, 1H), 3.98- 4.03 (m, 2H), 3.53- 3.55 (m, 1H), 3.37- 3.47 (m, 2H), 2.37- 2.39 (m, 2H), 2.11- 2.20 (m, 6H), 2.04 (s, 3H), 2.02 (s, 3H), 1.93- 1.94 (m, 1H), 1.59- 1.67 (m, 1H), 1.42- 1.45 (m, 1H), 1.28- 1.30 (m, 1H); ^{13}C NMR (CDCl$_3$) δ 171.1, 170.5, 138.5, 134.5, 128.3, 127.8, 127.6, 117.4, 81.5, 80.4, 77.7, 72.5, 70.4, 66.6, 35.4, 34.1, 32.7, 28.2, 27.2, 21.3, 21.0. For **3.113a/b**: ^{1}H NMR (CDCl$_3$) δ 7.30- 7.37 (m, 5H), 5.86- 5.95 (m, 2H), 5.72- 5.74 (m, 1H), 5.08- 5.15 (m, 2H), 4.67 (s, 2H), 4.27- 4.30 (m, 1H), 4.14- 4.19 (m, 2H), 3.99- 4.04 (m, 2H), 3.59- 3.65 (m, 2H), 2.40- 2.41 (m, 2H), 2.23- 2.25 (m, 1H), 1.97- 2.04 (m, 3H), 1.65- 1.68 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 171.2, 138.8, 134.8, 128.3, 127.8, 127.6, 126.9, 126.0, 117.1, 81.6, 80.8, 75.2, 72.6, 66.7, 35.6, 28.3, 26.7, 26.5, 21.0.

Synthesis of 3.114



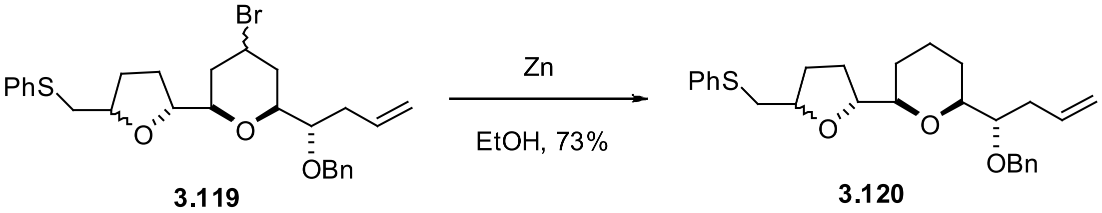
Compound **3.114** was prepared following the procedure used for **3.75**. ^{1}H NMR ($CDCl_3$) δ 7.30- 7.37 (m, 5H), 5.82- 5.92 (m, 2H), 4.98- 5.15 (m, 4H), 4.60- 4.68 (m, 2H), 3.42- 3.52 (m, 3H), 3.17- 3.21 (m, 1H), 2.16- 2.48 (m, 5H), 1.93- 1.95 (m, 1H), 1.45- 1.66 (m, 6H), 1.33- 1.35 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 138.6, 135.1, 128.4, 127.9, 127.7, 117.0, 114.7, 81.2, 80.7, 79.1, 73.6, 72.7, 34.8, 31.9, 29.7, 27.2, 26.6, 23.0.

Synthesis of 3.119



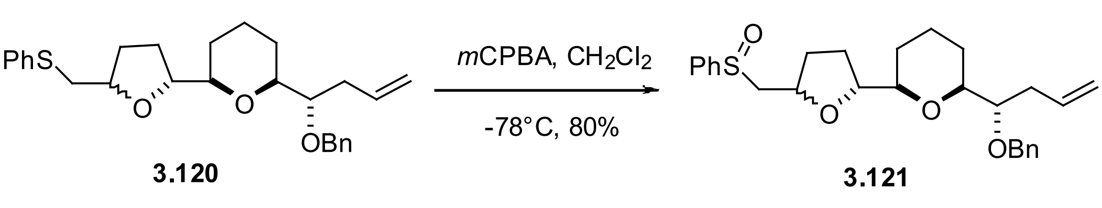
To a solution of **3.89** (80 mg, 0.142 mmol) in DMF (5 mL) were added in PhSH (17.2 mg, 0.156 mmol) and K_2CO_3 (21.5 mg, 0.156 mmol). The reaction mixture was kept at rt overnight. The solvent was removed under reduced pressure. The residue was subjected to column chromatography to give the products **3.119** (51 mg, 66 %). ^{1}H NMR ($CDCl_3$) δ 7.30- 7.40 (m, 10H), 5.83- 5.87 (m, 1H), 5.08- 5.15 (m, 2H), 4.83- 4.84 (m, 1H), 4.62- 4.65 (m, 2H), 3.96- 4.28 (m, 3H), 3.82- 3.85 (m, 1H), 3.50- 3.52 (m, 1H), 3.20- 3.30 (m, 2H), 2.97- 2.99 (m, 1H), 2.10- 2.50 (m, 3H), 1.86- 2.05 (m, 7H); ^{13}C NMR ($CDCl_3$) δ 135.0, 129.3, 129.1, 128.9, 128.8, 128.3, 128.3, 127.8, 127.8, 127.6, 126.0, 125.8, 117.2, 117.1, 81.3, 80.8, 80.1, 78.8, 78.5, 74.8, 74.5, 73.6, 73.1, 72.4, 72.3, 51.5, 51.3, 38.9, 38.6, 36.0, 35.9, 34.7, 34.6, 31.4, 30.8, 27.6, 27.4.

Synthesis of 3.120



Compound **3.120** was prepared following the procedure used for **3.75**. ^{1}H NMR (C_6D_6) δ 7.02- 7.53 (m, 10H), 6.07- 6.10 (m, 1H), 5.17- 5.29 (m, 2H), 4.64- 4.73 (m, 2H), 4.18- 4.40 (m, 1H), 3.89- 4.06 (m, 1H), 3.50- 3.53 (m, 2H), 3.18- 3.40 (m, 2H), 2.86- 3.06 (m, 1H), 2.50- 2.68 (m, 1H), 2.38- 2.48 (m, 1H), 1.73- 1.85 (m, 3H), 1.32- 1.65 (m, 7H); ^{13}C NMR (C_6D_6) δ 139.7, 137.5, 136.0, 129.0, 127.3, 125.6, 125.5, 116.5, 116.4, 81.8, 81.3, 81.2, 80.3, 79.8, 79.5, 79.2, 78.3, 78.2, 72.6, 72.5, 38.8, 38.6, 35.2, 31.6, 30.8, 27.5, 27.2, 27.0, 26.3, 23.4. HRMS (ESI) calcd for $C_{27}H_{34}O_3S$ (M + H^+) 439.2301, found 349.2290.

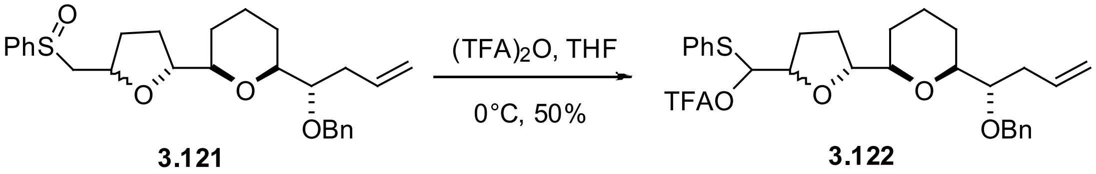
Synthesis of 3.121



To a solution of **3.120** (32 mg, 0.068 mmol) in CH_2Cl_2 (5 mL) was added in *m*CPBA (15.3 mg, 0.068 mmol, 77 %) at -78 °C. The reaction mixture was stirring for 10 min at

-78 °C before it was quenched by saturated aqueous $Na_2S_2O_3$. Then it was extracted with CH_2Cl_2, and dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue subjected to column chromatography to give product **3.121** (27 mg, 80 %). ^{1}H NMR (C_6D_6) δ 7.03- 7.77 (m, 10H), 5.92- 6.19 (m, 1H), 5.05- 5.18 (m, 2H), 4.54- 4.81 (m, 2H), 3.78- 4.21 (m, 2H), 3.40- 3.64 (m, 2H), 3.02- 3.38 (m, 1H), 2.68- 3.00 (m, 1H), 2.28- 2.62 (m, 2H), 1.30- 2.00 (m, 9H); ^{13}C NMR (C_6D_6) δ 135.9, 135.8, 135.7, 135.7, 130.1, 130.0, 130.0, 129.9, 128.9, 128.9, 128.8, 128.8, 128.8, 128.3, 128.3, 127.4, 127.3, 127.3, 124.4, 124.2, 123.7, 123.6, 116.6, 116.5, 116.5, 81.7, 81.5, 81.2 (3), 81.1 (2), 81.0, 79.7 (2), 79.6 (2), 79.5, 79.4, 79.1, 75.3, 75.0, 74.3, 74.2, 74.0, 73.7, 73.6, 72.7, 72.6, 72.4 (2), 65.0, 64.8, 62.8, 62.7, 35.2 (2), 35.1 (2), 32.4, 1.8, 31.4, 31.0, 27.4 (2), 27.3, 27.2, 27.1, 27.0.

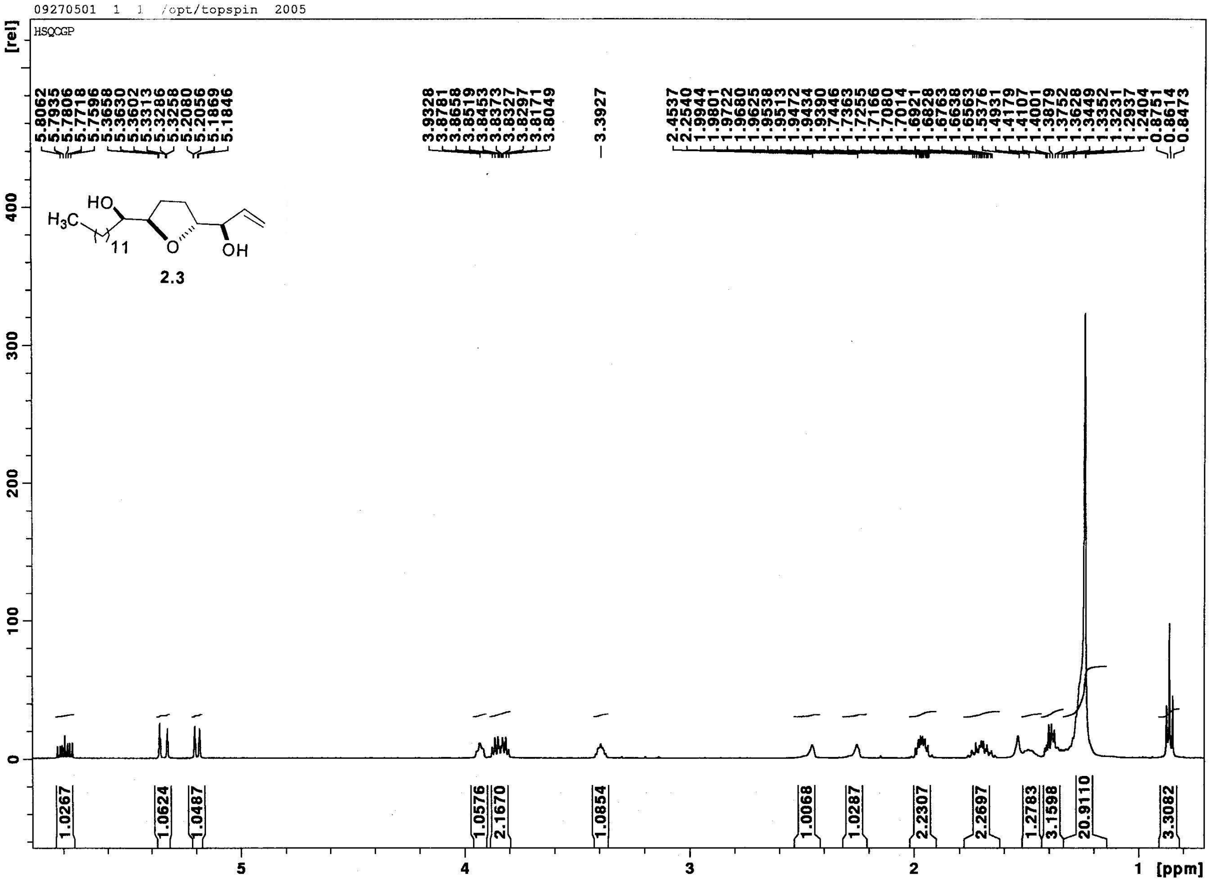
Synthesis of 3.122



To a solution of **3.121** (3 mg, 0.006 mmol) in THF (3 mL) was added in $(TFA)_2O$ (25 μL) at 0 °C. The reaction mixture was kept stirring at 0 °C for 10 min before it was quenched by saturated aqueous $NaHCO_3$. Then it was extracted with CH_2Cl_2, and dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue subjected to column chromatography to give product **3.122** (1.6 mg, 50 %). ^{1}H NMR (C_6D_6) δ 7.00- 7.70 (m, 10H), 6.68- 6.70 (m, 1H), 6.02- 6.04 (m, 1H), 5.17- 5.27 (m, 2H), 4.69 (s, 2H), 4.19- 4.24 (m, 1H), 3.74- 3.81 (m, 1H), 3.50- 3.53 (m, 1H), 3.38- 3.42 (m, 1H), 2.97- 3.01 (m, 1H), 2.40- 2.68 (m, 2H), 2.17- 2.22 (m, 1H), 1.75- 1.82 (m, 2H), 1.50- 1.64 (m, 2H), 1.21-

1.48 (m, 3H), 0.94- 1.08 (m, 2H); ^{13}C NMR (C_6D_6) δ 139.6, 135.6, 124.6, 132.8, 132.4, 129.2, 129.0, 128.9, 127.1, 116.7, 86.9, 82.4 (2), 81.3, 81.2, 81.1, 80.2, 79.6, 79.4, 77.5, 77.2, 77.0, 72.4, 53.1, 35.3, 35.2, 30.0, 29.0, 28.1, 27.3, 27.0, 26.4 (2), 23.4.

APPENDIX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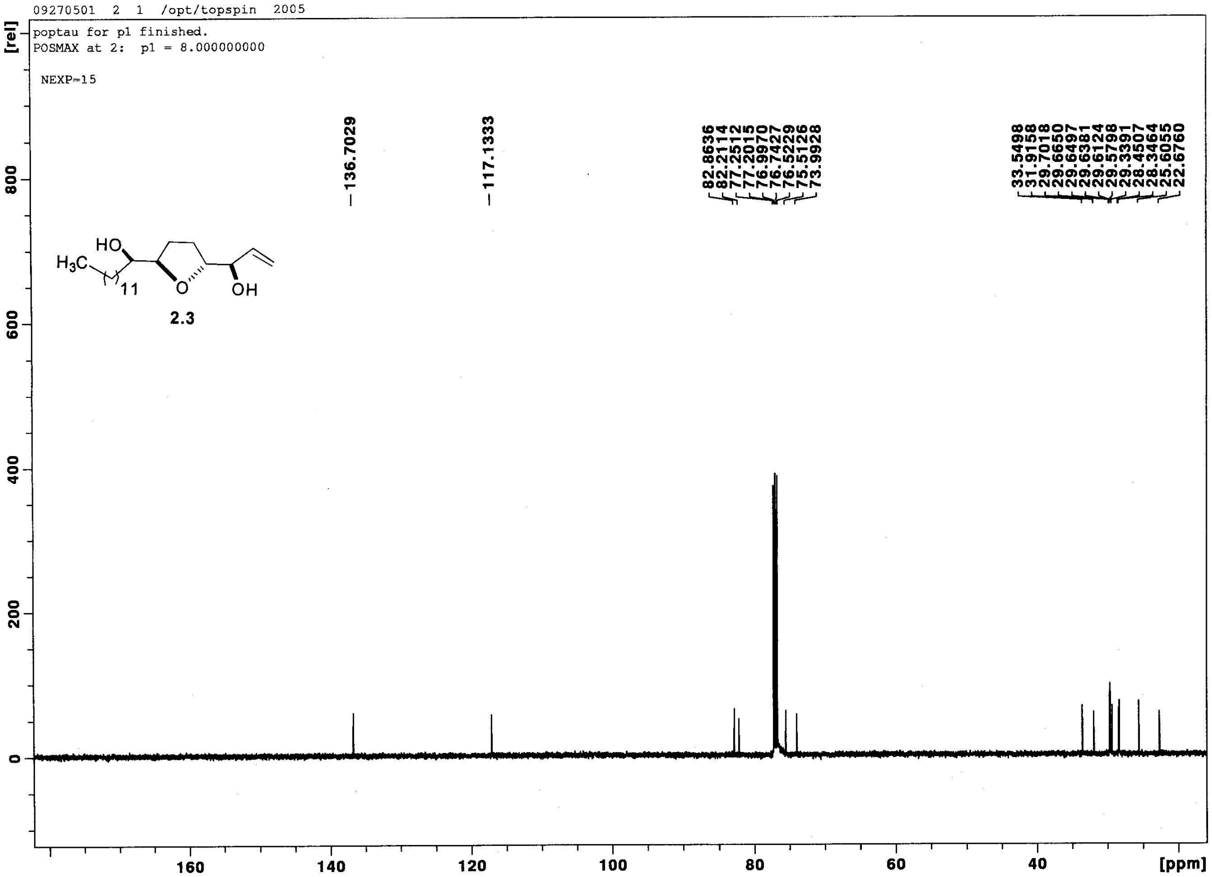
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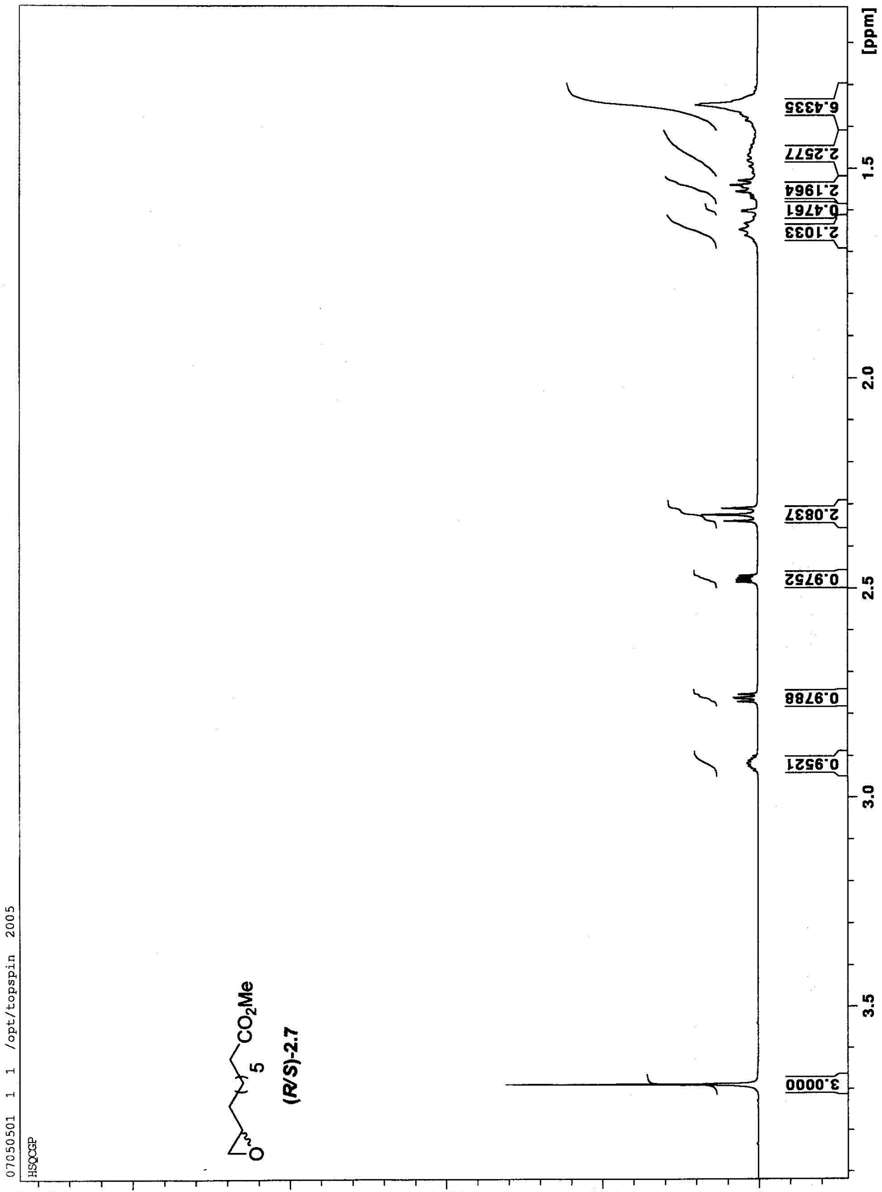
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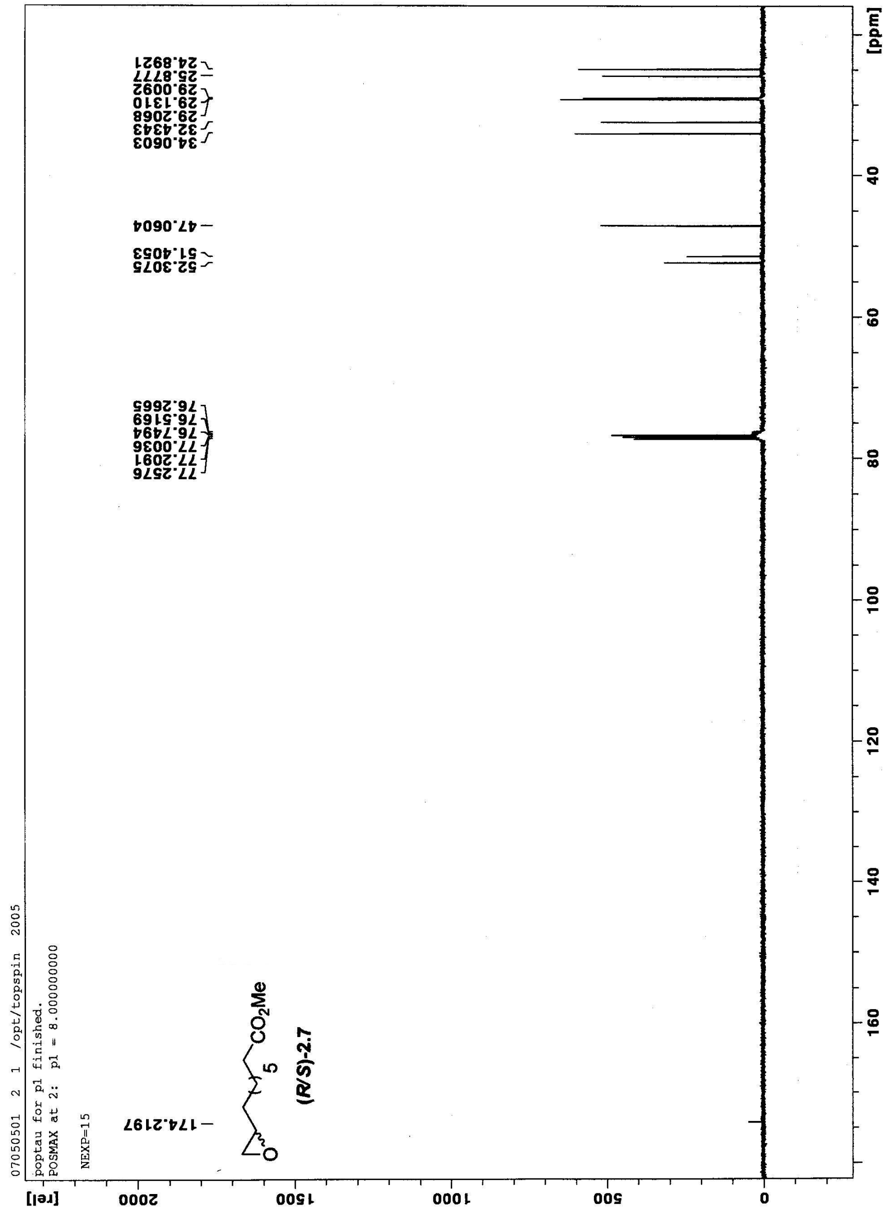
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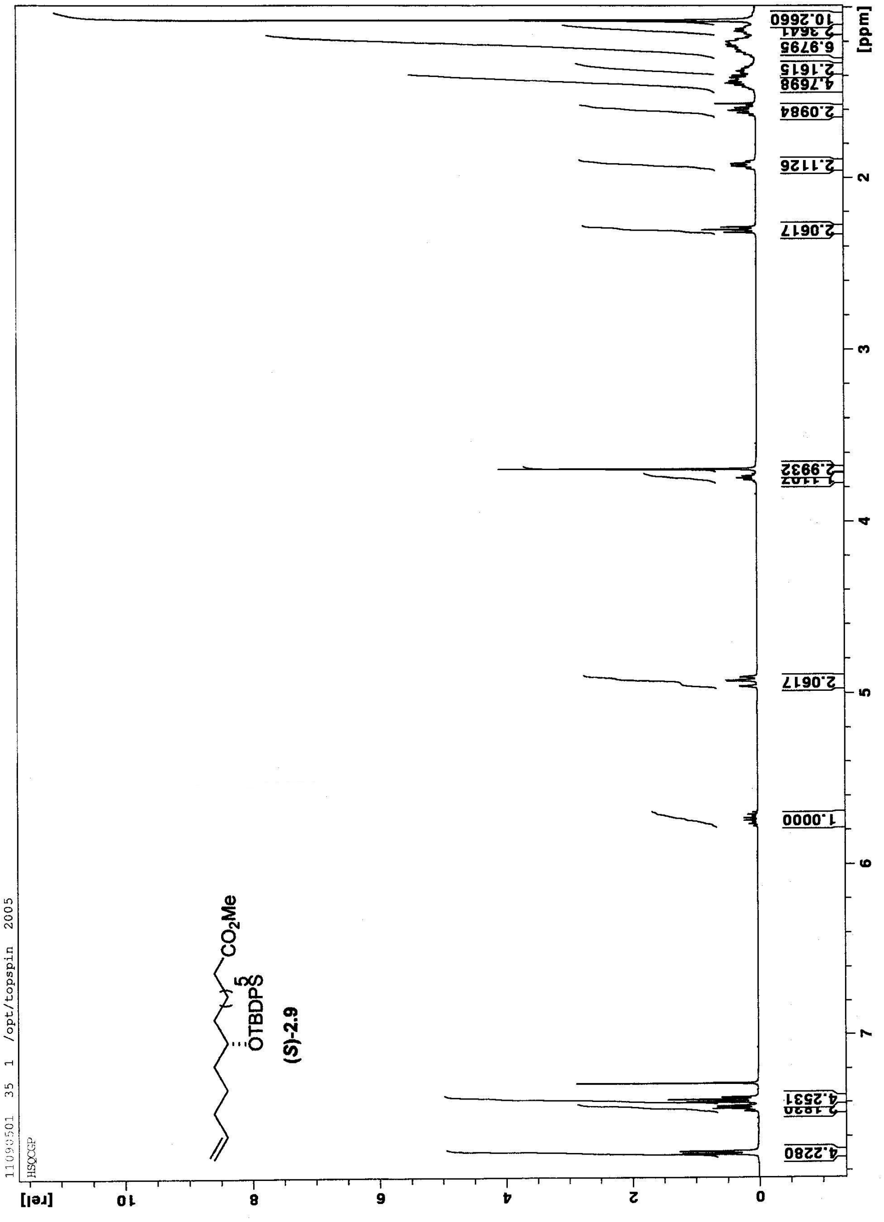
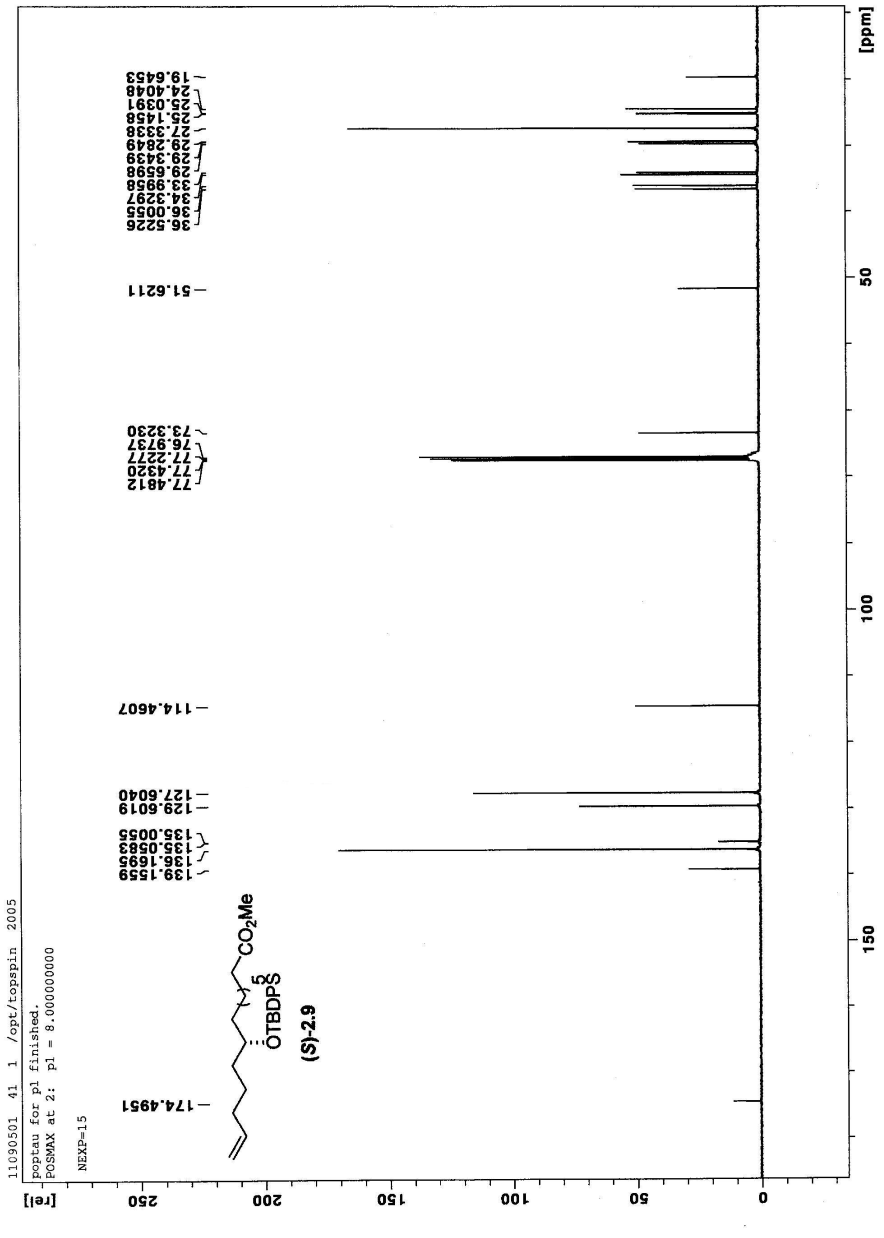
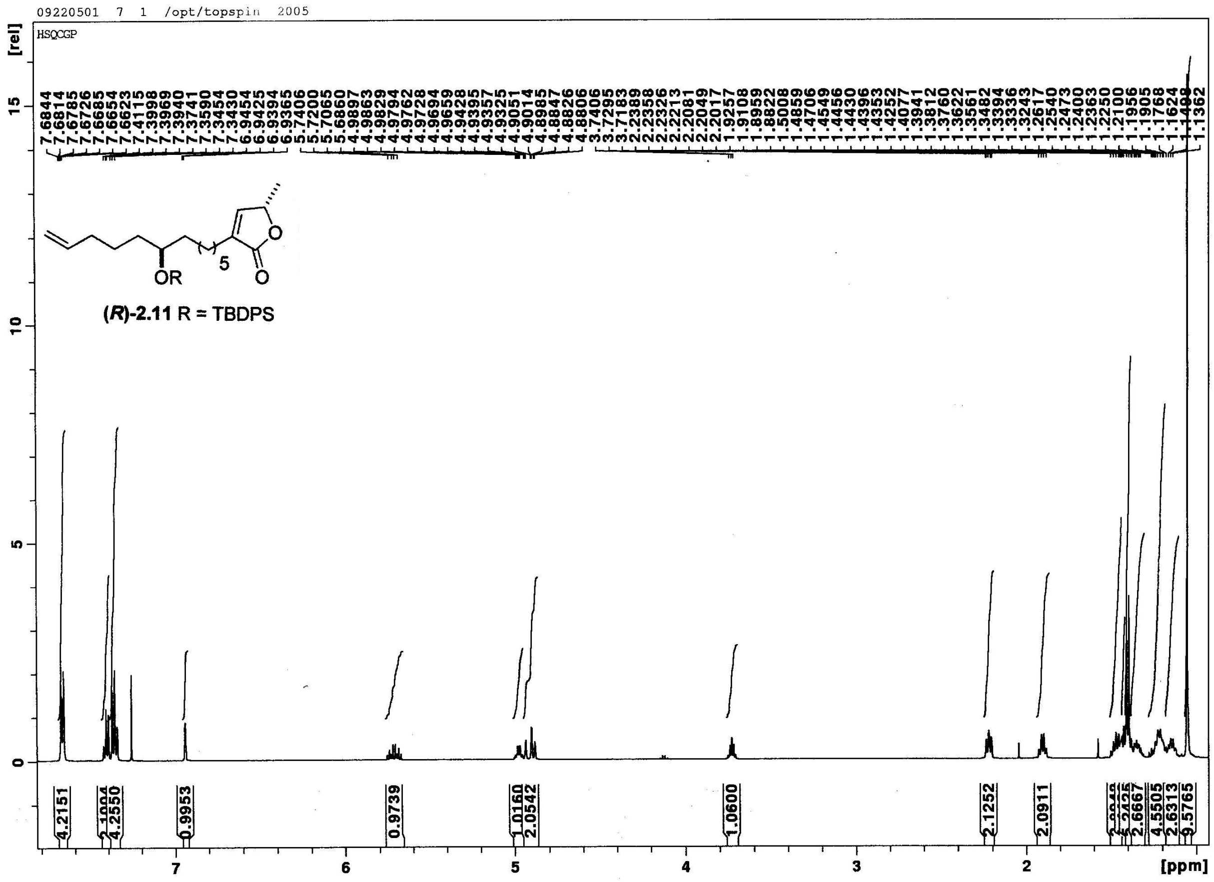
47.0604
34.0603
32.4343
29.2068
29.1310
29.0092
25.8777
24.8921
[rel]
2000
1500
1000
500
0
[ppm]
160
140
120
100
80
60
40

(R/S)-2.7

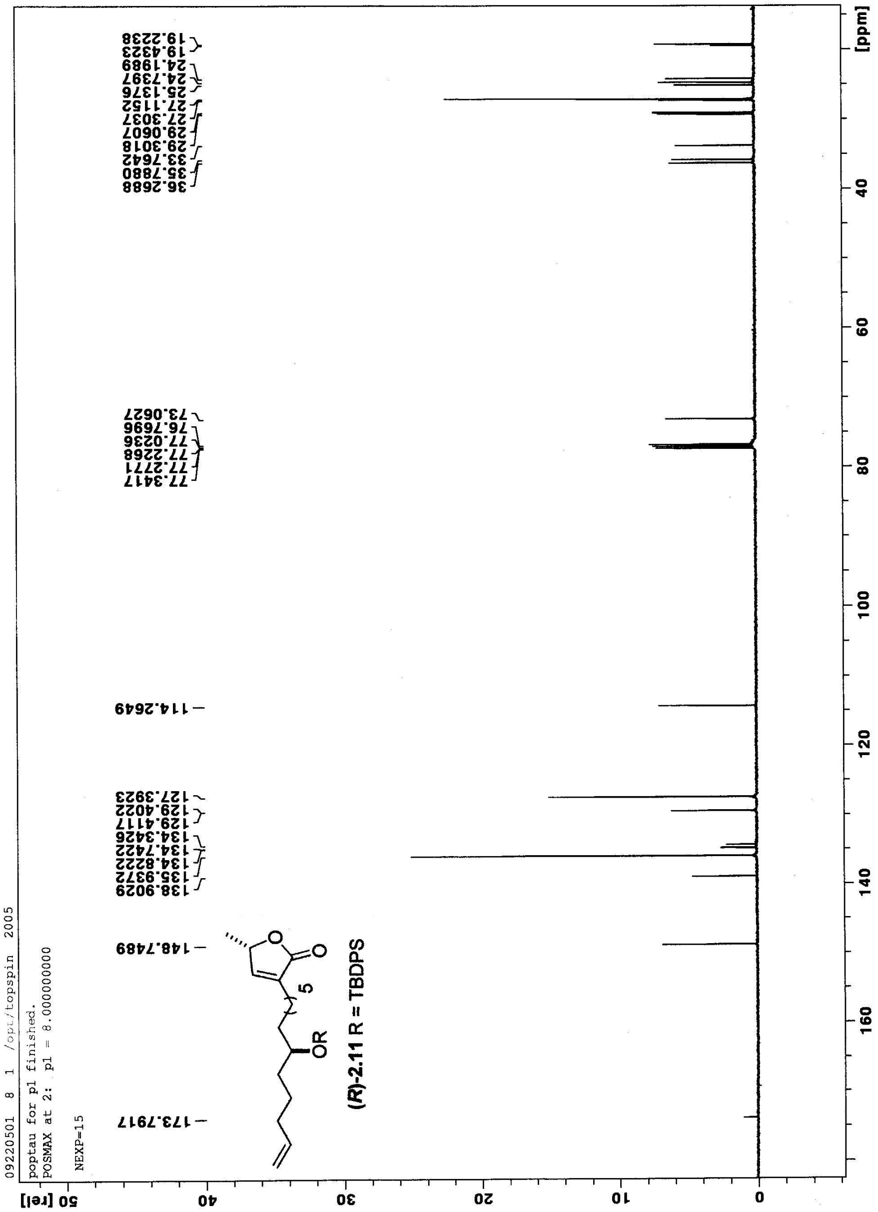

11090501 35 1 /opt/topspin 2005
HSQCGP
OTBDPS
CO2Me
5
10.2660
2.3641
6.9795
2.1615
4.7698
2.0984
2.1126
2.0617
2.9932
2.0617
1.0000
4.2531
4.2280
[ppm]
[rel]
0
1
2
3
4
5
6
7
0
2
4
6
8
10

(S)-2.9

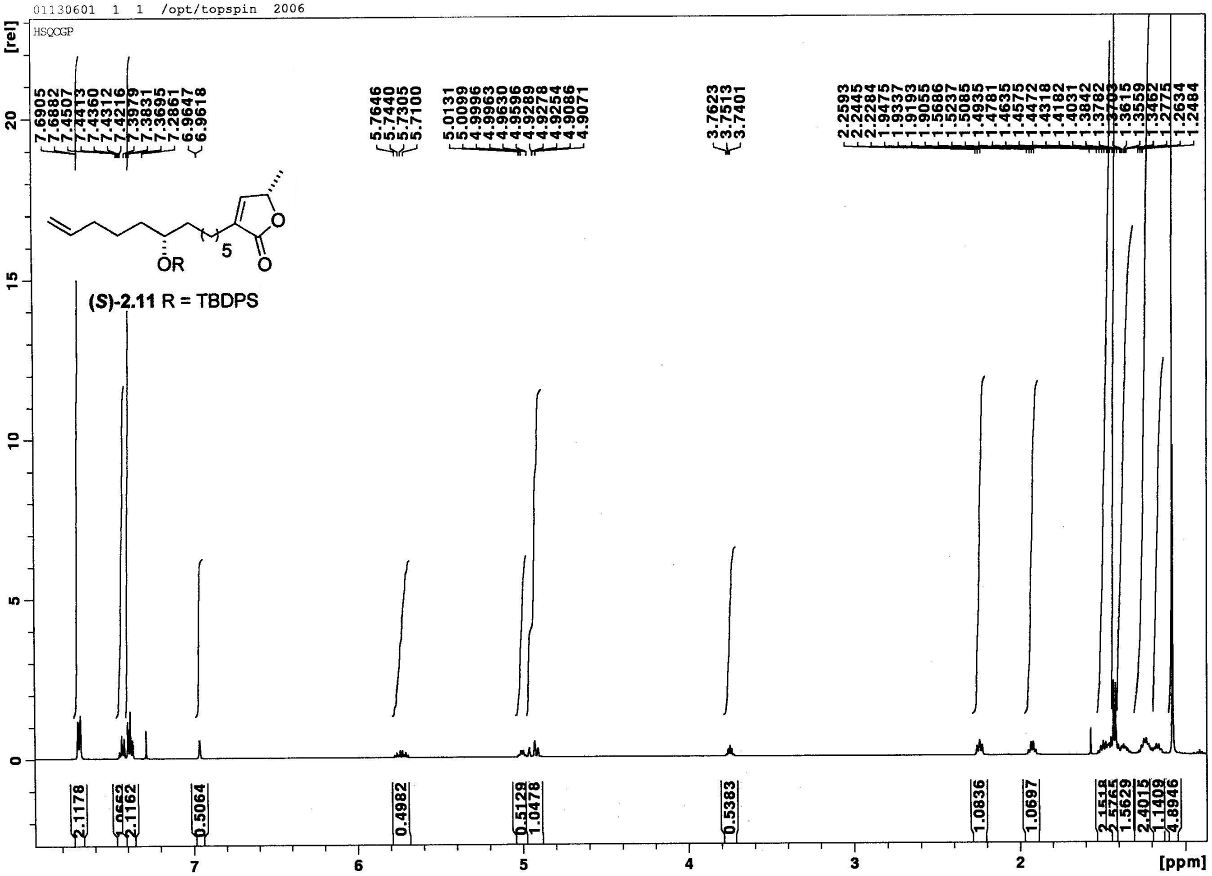

11090501 41 1 /opt/topspin 2005
poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
174.4951
139.1559
136.1695
135.0583
135.0055
129.6019
127.6040
114.4607
77.4812
77.4320
77.2277
76.9737
73.3230
51.6211
36.5226
36.0055
34.3297
33.9958
29.6598
29.3439
29.2849
27.3338
25.1458
25.0391
24.4048
19.6453
CO2Me
5
OTBDPS
(S)-2.9
[ppm]
150
100
50
[rel]
250
200
150
100
50
0


09220501 7 1 /opt/topspin 2005
HSQCGP
7.6844
7.6814
7.6785
7.6726
7.6685
7.6654
7.6623
7.4115
7.3998
7.3969
7.3940
7.3741
7.3590
7.3454
7.3430
6.9454
6.9425
6.9394
6.9365
5.7406
5.7200
5.7065
5.6860
4.9897
4.9863
4.9829
4.9794
4.9762
4.9728
4.9694
4.9659
4.9428
4.9395
4.9357
4.9325
4.9051
4.9014
4.8985
4.8847
4.8826
4.8806
3.7406
3.7295
3.7183
2.2389
2.2358
2.2326
2.2213
2.2081
2.2049
2.2017
1.9257
1.9108
1.8959
1.8822
1.5008
1.4859
1.4706
1.4549
1.4456
1.4430
1.4396
1.4353
1.4252
1.4077
1.3941
1.3812
1.3760
1.3622
1.3561
1.3482
1.3394
1.3336
1.3243
1.2617
1.2540
1.2473
1.2400
1.2363
1.2250
1.2100
1.1956
1.1905
1.1768
1.1624
1.1488
1.1362
OR
5
O
O
4.2151
2.1004
4.2550
0.9953
0.9739
1.0160
2.0542
1.0600
2.1252
2.0911
2.6667
4.5505
2.6313
9.5765
[rel]
15
10
5
0
7
6
5
4
3
2
[ppm]

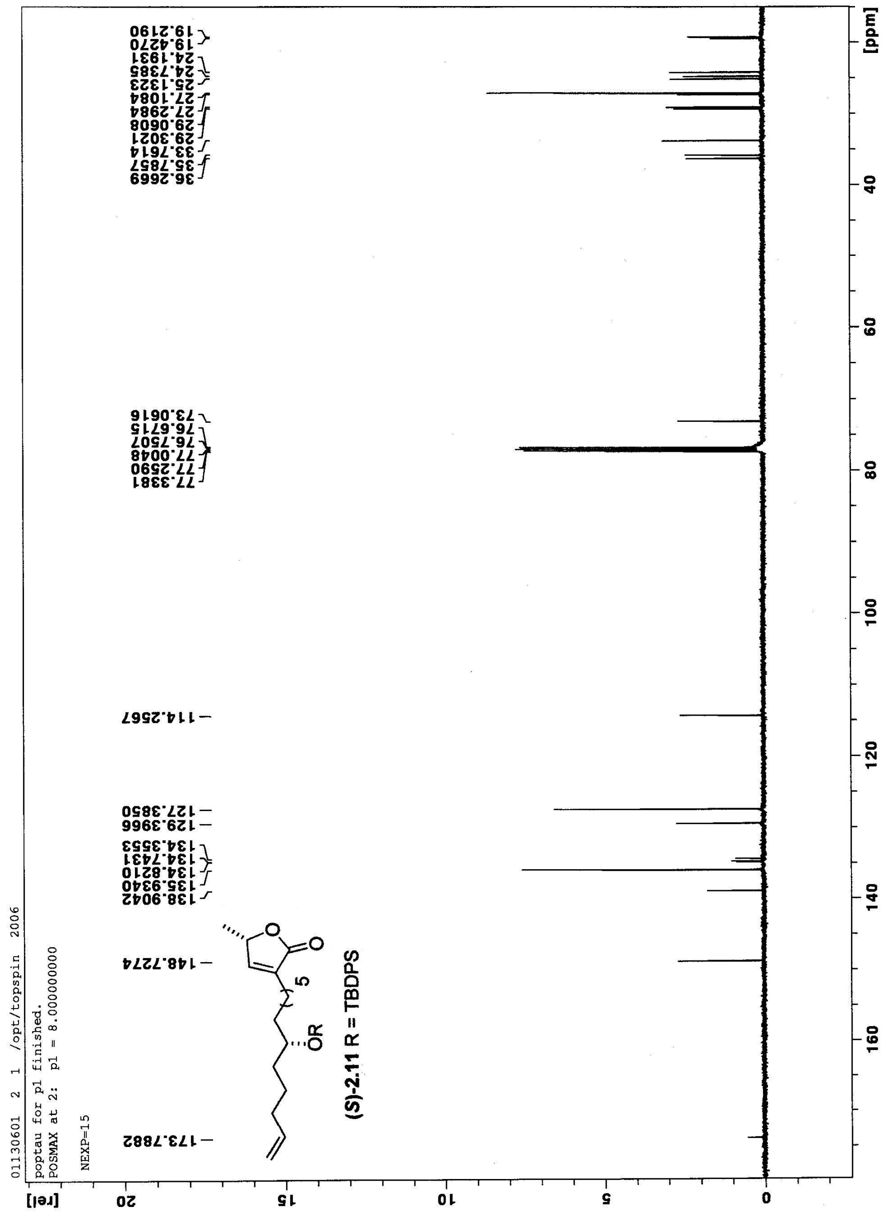
(*R*)-2.11 R = TBDPS


09220501 8 1 /opt/topspin 2005
poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
173.7917
148.7489
138.9029
135.9372
134.8222
134.7422
134.3426
129.4117
129.4022
127.3923
114.2649
77.3417
77.2771
77.2268
77.0236
76.7696
73.0627
36.2688
35.7880
33.7642
29.3018
29.0607
27.3037
27.1152
25.1376
24.7397
24.1989
19.4323
19.2238
OR
5
O
O
[ppm]
40
60
80
100
120
140
160
50 [rel]
40
30
20
10
0

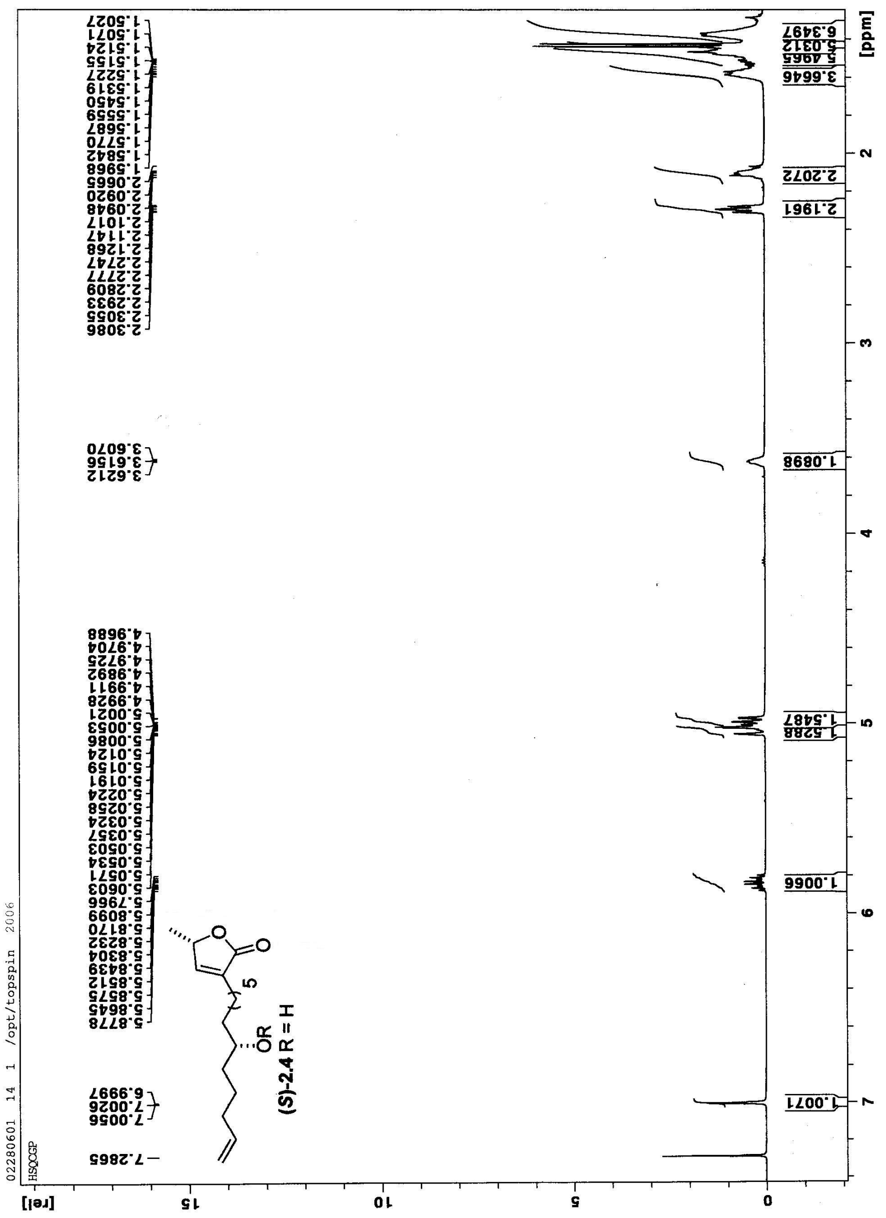
(*R*)-2.11 R = TBDPS


01130601 1 1 /opt/topspin 2006
HSQCGP
[rel]
20
15
10
5
0
7.6905
7.6882
7.4507
7.4413
7.4360
7.4312
7.4216
7.3979
7.3831
7.3695
7.2861
6.9647
6.9618
5.7646
5.7440
5.7305
5.7100
5.0131
5.0099
4.9996
4.9963
4.9630
4.9596
4.9289
4.9278
4.9254
4.9086
4.9071
3.7623
3.7513
3.7401
2.2593
2.2445
2.2284
1.9475
1.9337
1.9193
1.9055
1.5686
1.5237
1.5085
1.4935
1.4781
1.4635
1.4575
1.4472
1.4318
1.4182
1.4031
1.3842
1.3782
1.3703
1.3615
1.3559
1.3462
1.2775
1.2634
1.2484
OR
5
O
O
2.1178
1.0562
2.1162
0.5064
0.4982
0.5129
1.0478
0.5383
1.0836
1.0697
2.1518
2.5765
1.5629
2.4015
1.1409
4.8946
7
6
5
4
3
2
[ppm]

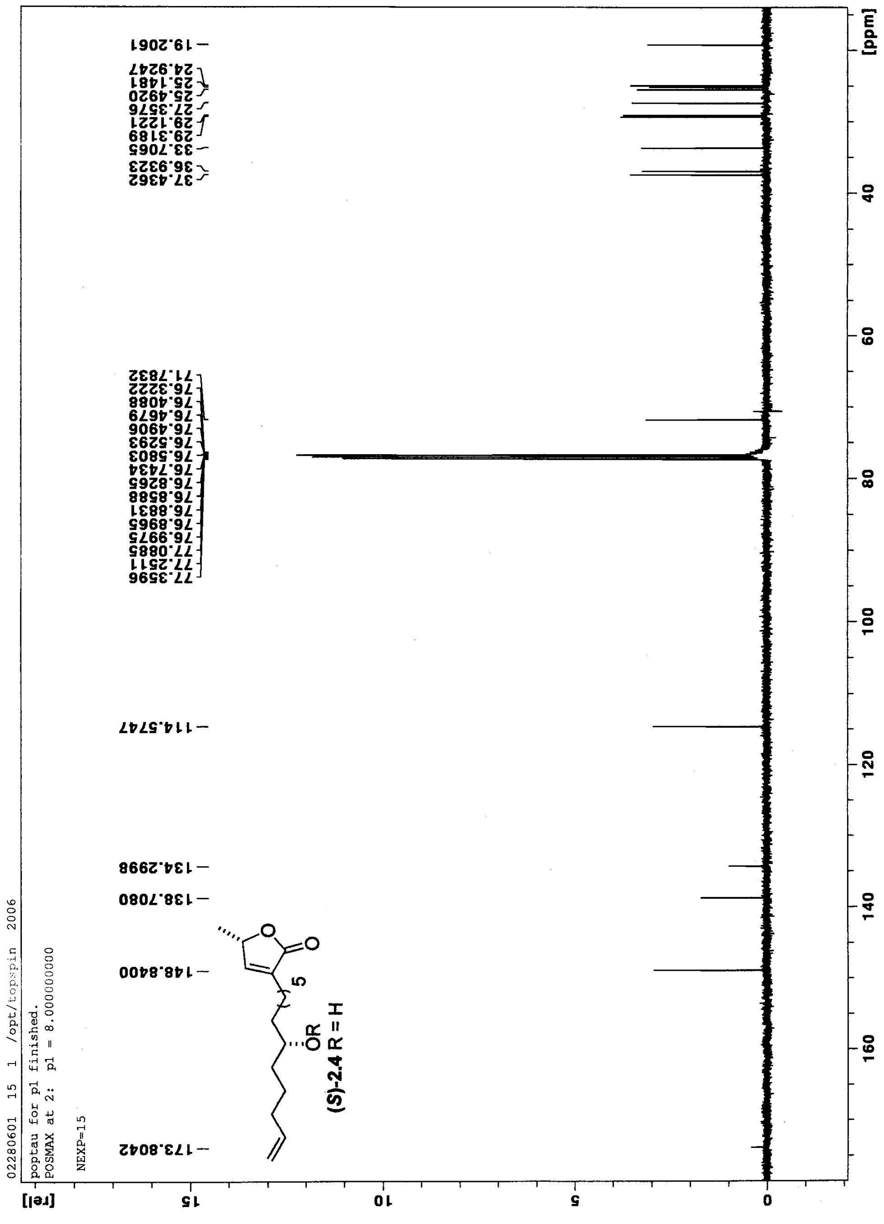
(*S*)-**2.11** R = TBDPS

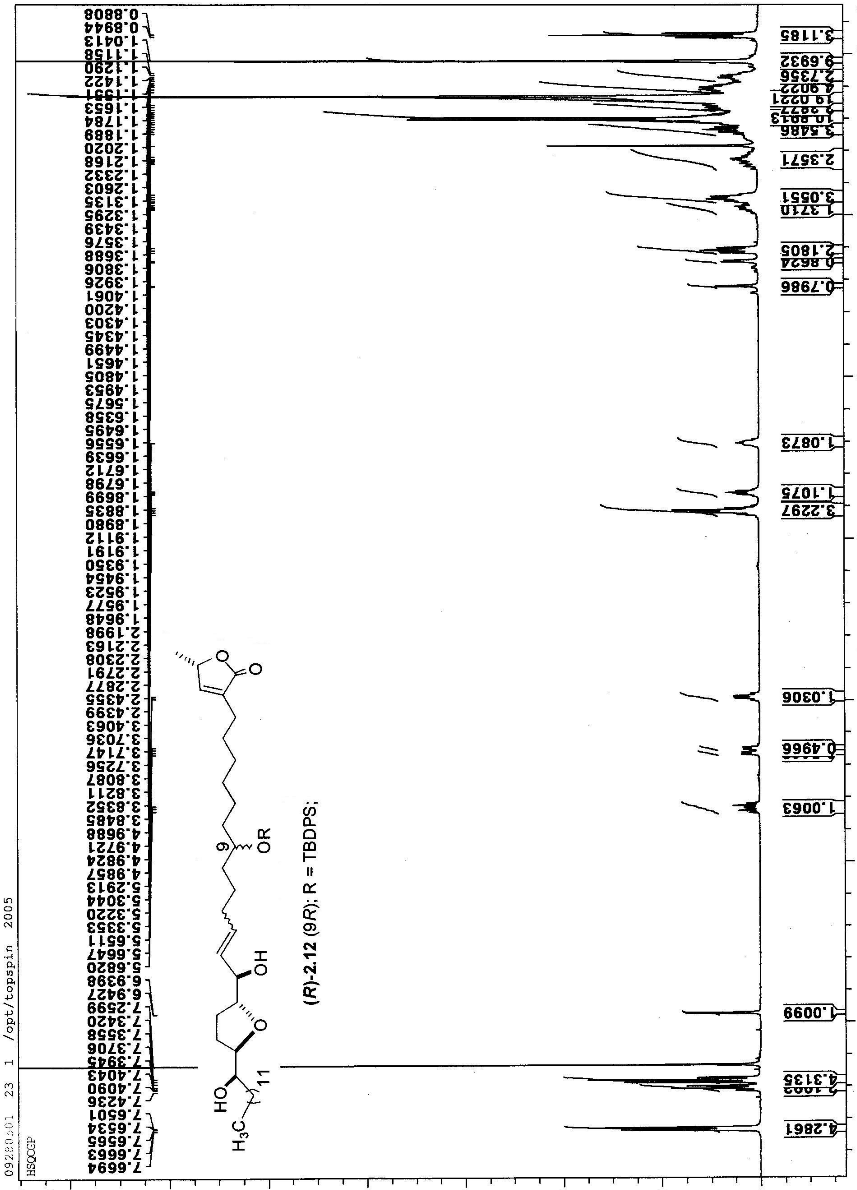

01130601 2 1 /opt/topspin 2006
poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
173.7882
148.7274
138.9042
135.9340
134.8210
134.7431
134.3553
129.3966
127.3850
114.2567
77.3381
77.2590
77.0048
76.7507
76.6715
73.0616
36.2669
35.7857
33.7614
29.3021
29.0608
27.2984
27.1084
25.1323
24.7385
24.1931
19.4270
19.2190
OR
O
O
5
[rel]
20
15
10
5
0
160
140
120
100
80
60
40
20
[ppm]

(S)-2.11 R = TBDPS

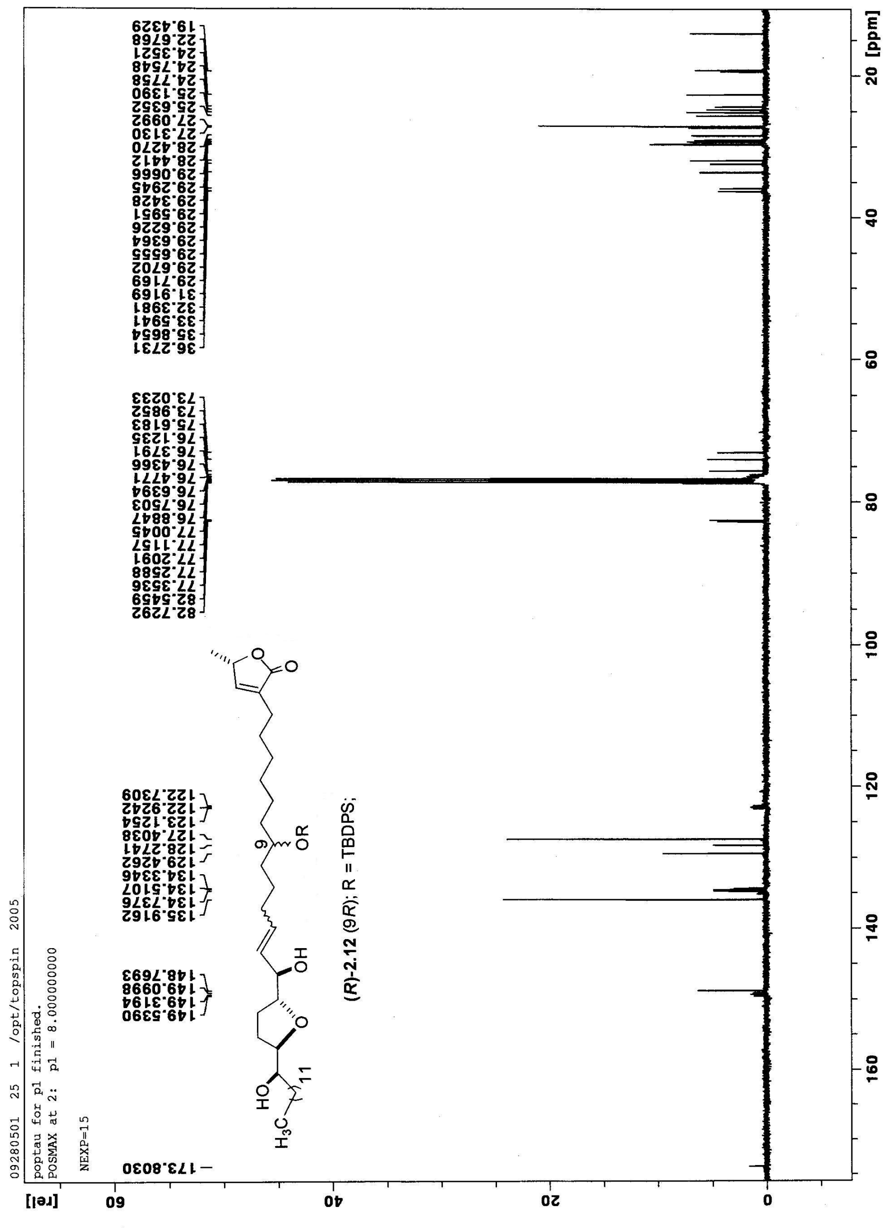


02280601 14 1 /opt/topspin 2006
HSQCGP
7.2865
7.0056
7.0026
6.9997
5.8778
5.8645
5.8575
5.8512
5.8439
5.8304
5.8232
5.8170
5.8099
5.7966
5.0603
5.0571
5.0534
5.0503
5.0357
5.0324
5.0258
5.0224
5.0191
5.0159
5.0124
5.0086
5.0053
5.0021
4.9928
4.9911
4.9892
4.9725
4.9704
4.9688
3.6212
3.6156
3.6070
2.3086
2.3055
2.2933
2.2809
2.2777
2.2747
2.1268
2.1147
2.1017
2.0948
2.0920
2.0665
1.5968
1.5842
1.5770
1.5687
1.5559
1.5450
1.5319
1.5227
1.5155
1.5124
1.5071
1.5027
O
O
5
OR
(S)-2.4 R = H
1.0071
1.0066
1.5288
1.5487
1.0898
2.1961
2.2072
3.6646
5.4965
5.0312
6.3497
7
6
5
4
3
2
[ppm]
0
5
10
15
[rel]

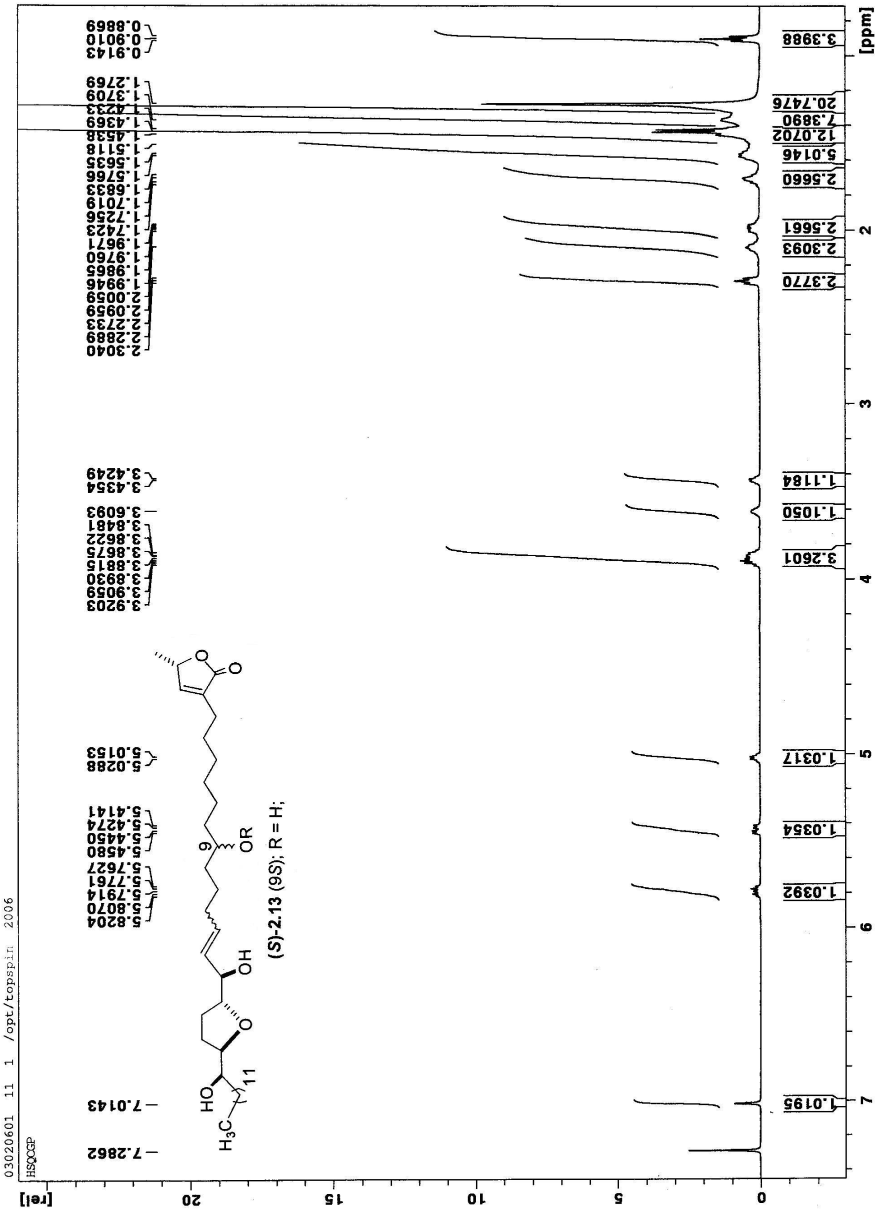

02280601 15 1 /opt/topspin 2006
poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
(S)-2.4 R = H
OR
O
O
5
173.8042
148.8400
138.7080
134.2998
114.5747
77.3596
77.2511
77.0885
76.9975
76.8965
76.8831
76.8588
76.8265
76.7434
76.5803
76.5293
76.4906
76.4679
76.4088
76.3222
71.7832
37.4362
36.9323
33.7065
29.3189
29.1221
27.3576
25.4920
25.1481
24.9247
19.2061
160
140
120
100
80
60
40
[ppm]
0
5
10
15
[rel]



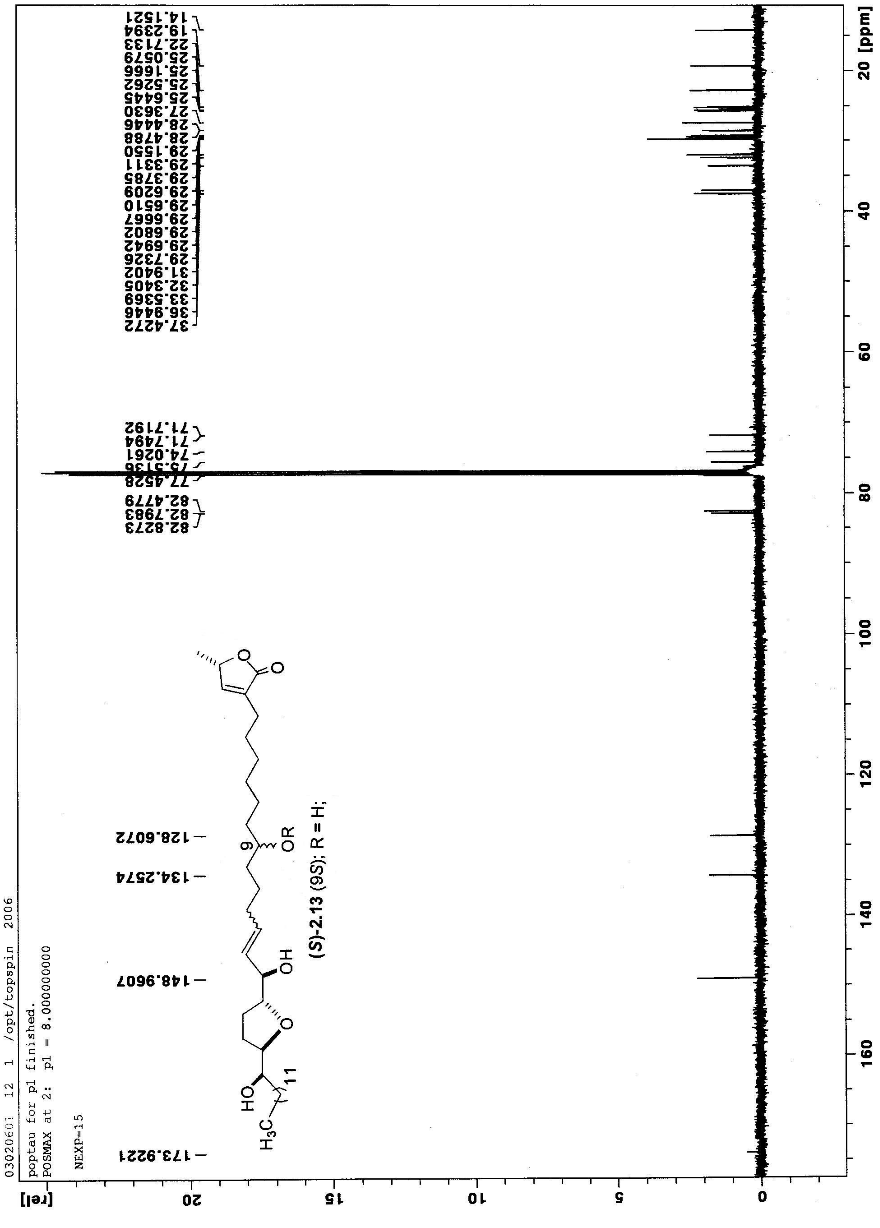
(*R*)-2.12 (9*R*); R = TBDPS;

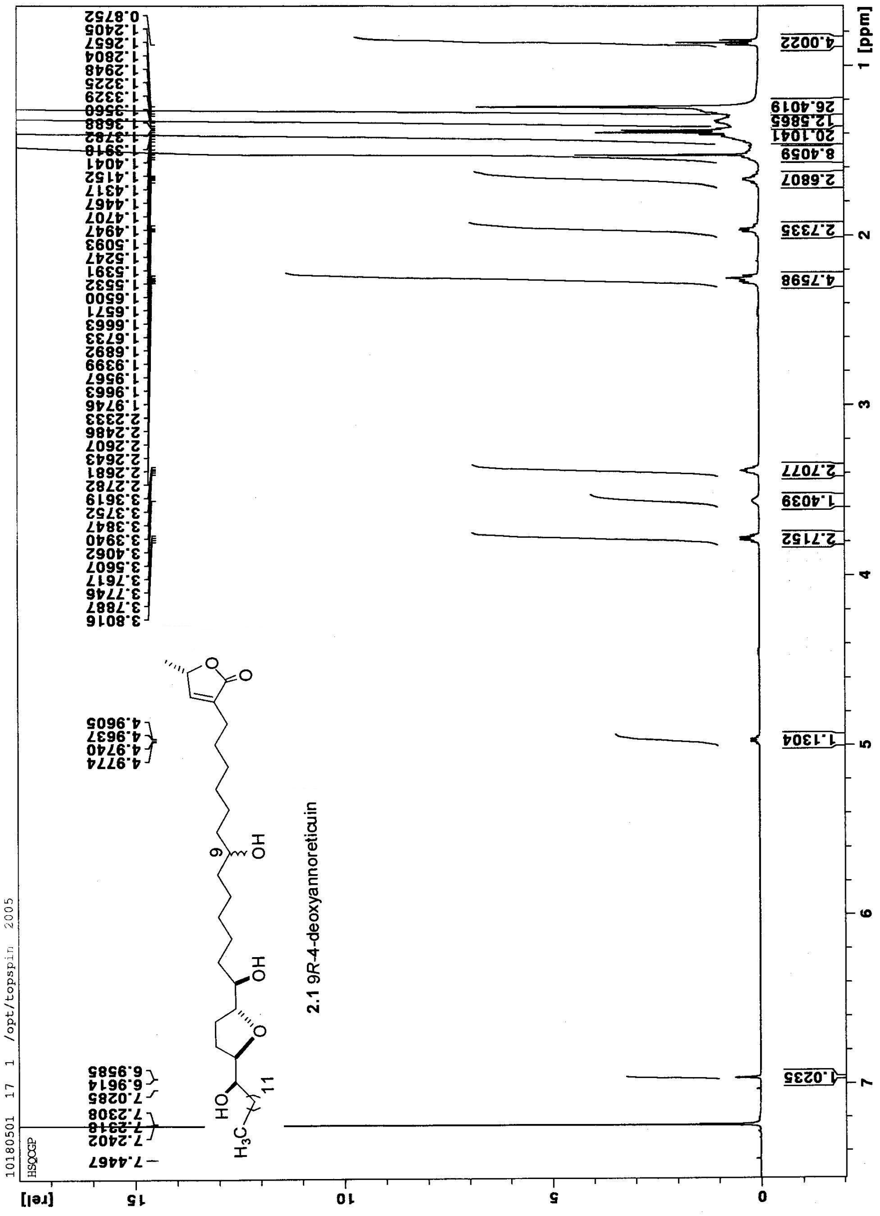


(R)-2.12 (9R); R = TBDPS;

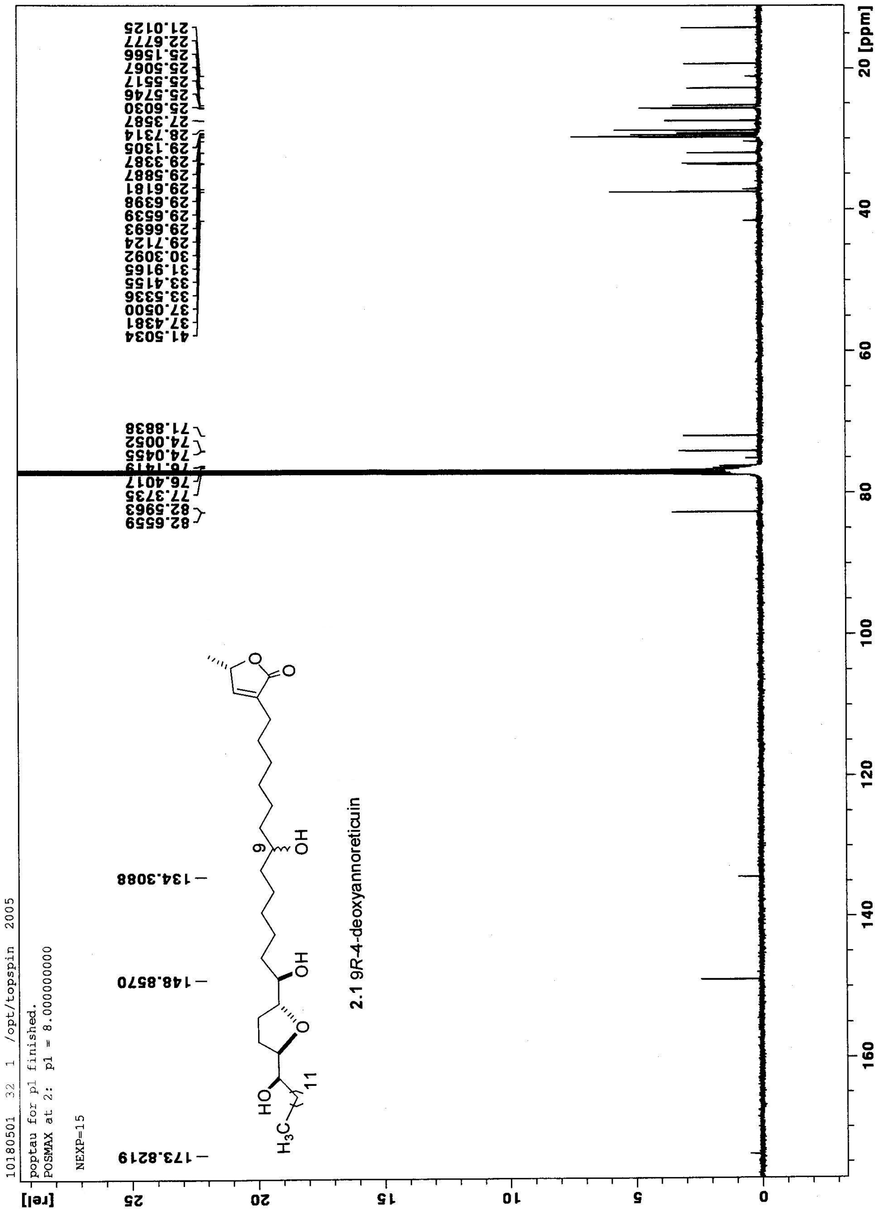

03020601 11 1 /opt/topspin 2006
HSQCGP
7.2862
7.0143
5.8204 5.8070 5.7914 5.7761 5.7627
5.4580 5.4450 5.4274 5.4141
5.0288 5.0153
3.9203 3.9059 3.8930 3.8815 3.8675 3.8622 3.8481
3.6093
3.4354 3.4249
2.3040 2.2889 2.2733 2.0959 2.0059 1.9946 1.9865 1.9760 1.9671 1.7423 1.7256 1.7019 1.6833 1.5766 1.5635 1.5118 1.4538 1.4369 1.4233 1.3709 1.2769
0.9143 0.9010 0.8869
1.0195
1.0392
1.0354
1.0317
3.2601
1.1050
1.1184
2.3770
2.3093
2.5661
2.5660
5.0146
12.0702
7.3890
20.7476
3.3988
[ppm]
7
6
5
4
3
2
1
[rel]
0
5
10
15
20
H3C
HO
11
O
OH
9
OR
O
O

(S)-2.13 (9S); R = H;

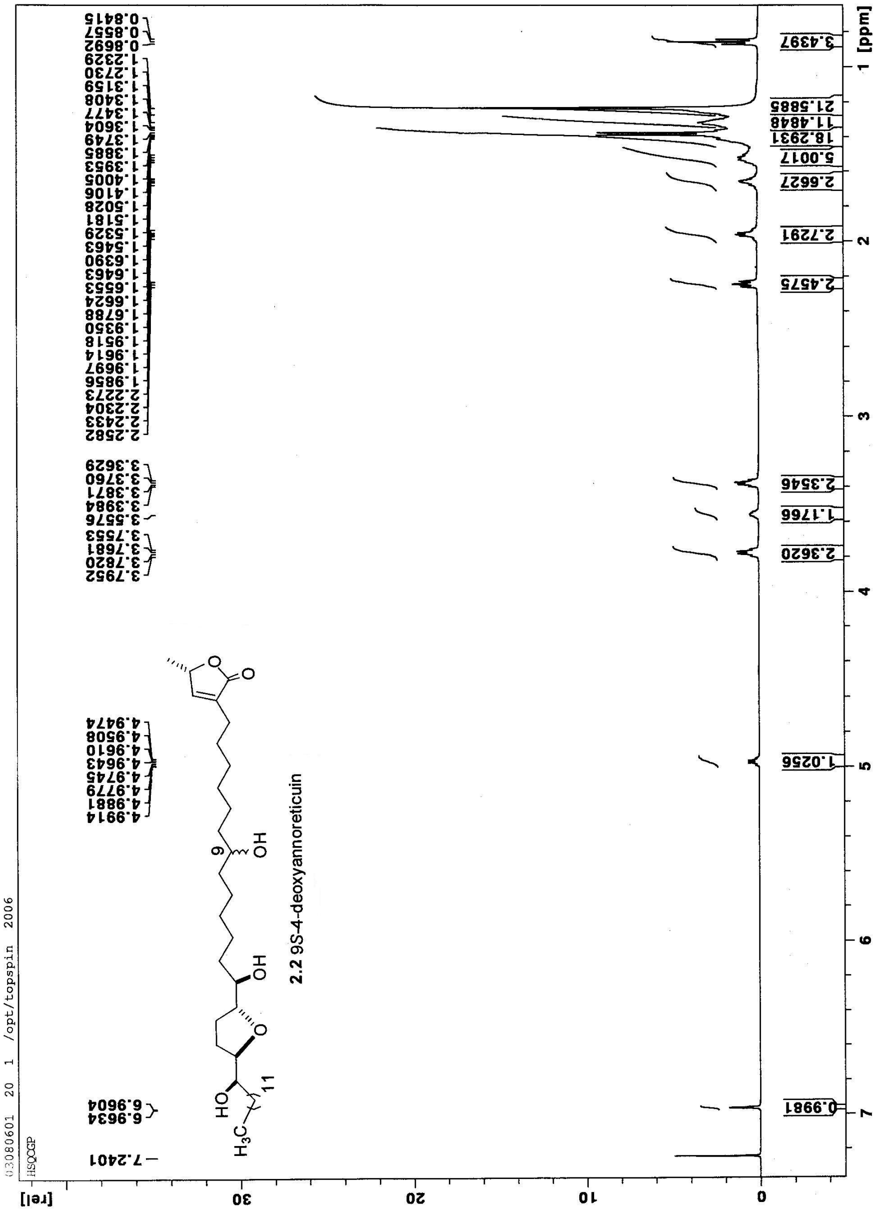

030206: 12 1 /opt/topspin 2006
poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
14.1521
19.2394
22.7133
25.0579
25.1666
25.5262
25.6445
27.3630
28.4446
28.4788
29.1550
29.3311
29.3785
29.6209
29.6510
29.6667
29.6802
29.6942
29.7326
31.9402
32.3405
33.5369
36.9446
37.4272
71.7192
71.7494
74.0261
75.5136
77.4528
82.4779
82.7983
82.8273
128.6072
134.2574
148.9607
173.9221
H3C
HO
11
O
OH
9
OR
O
O
(S)-2.13 (9S); R = H;
[rel]
20
15
10
5
0
[ppm]
160
140
120
100
80
60
40
20



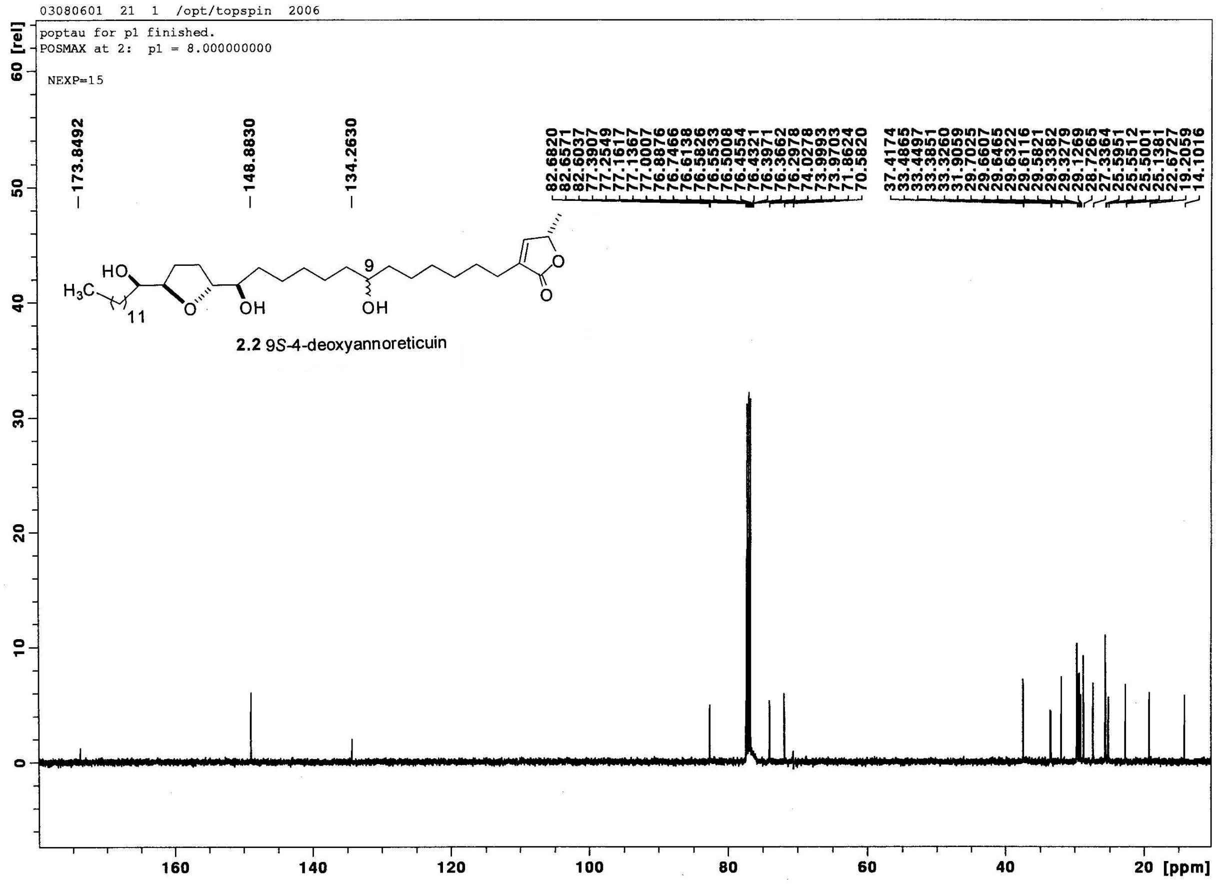
2.1 9*R*-4-deoxyannoreticuin

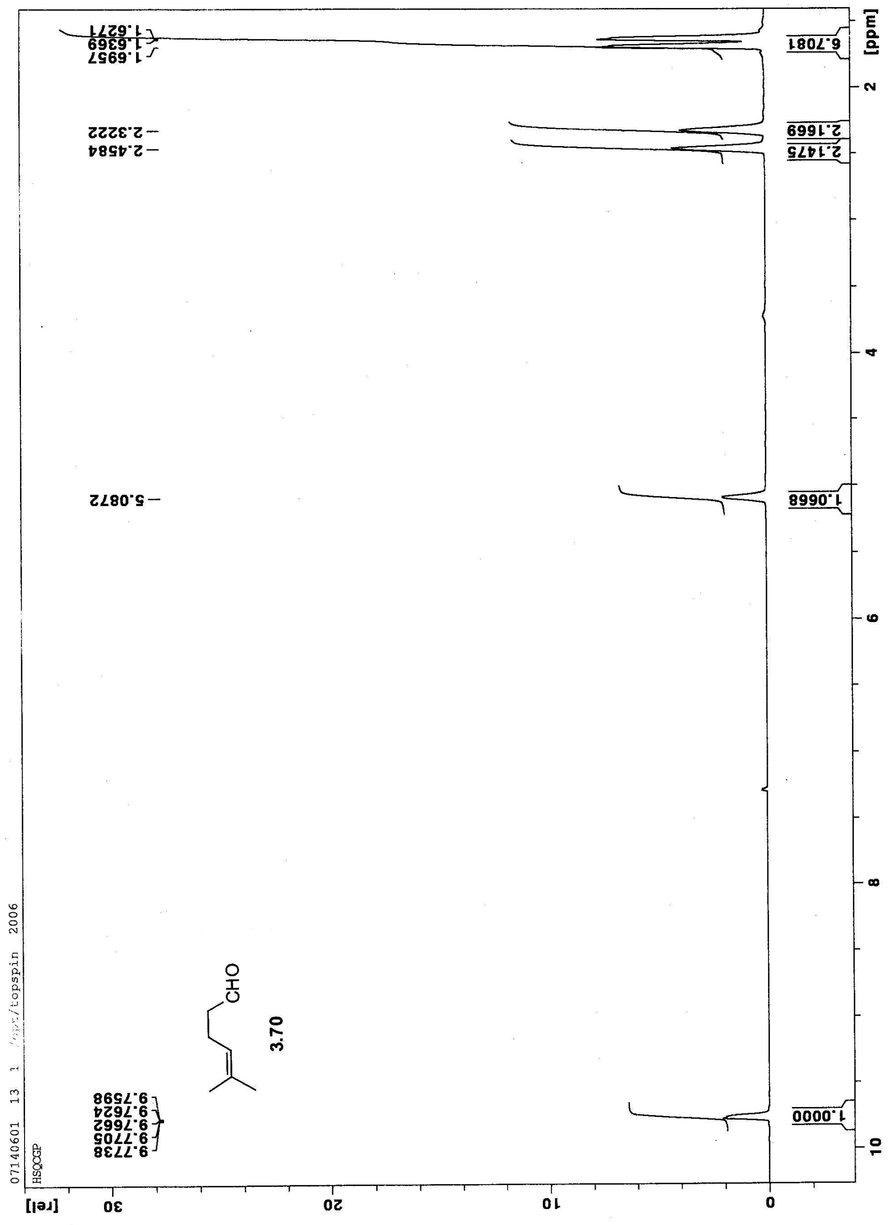


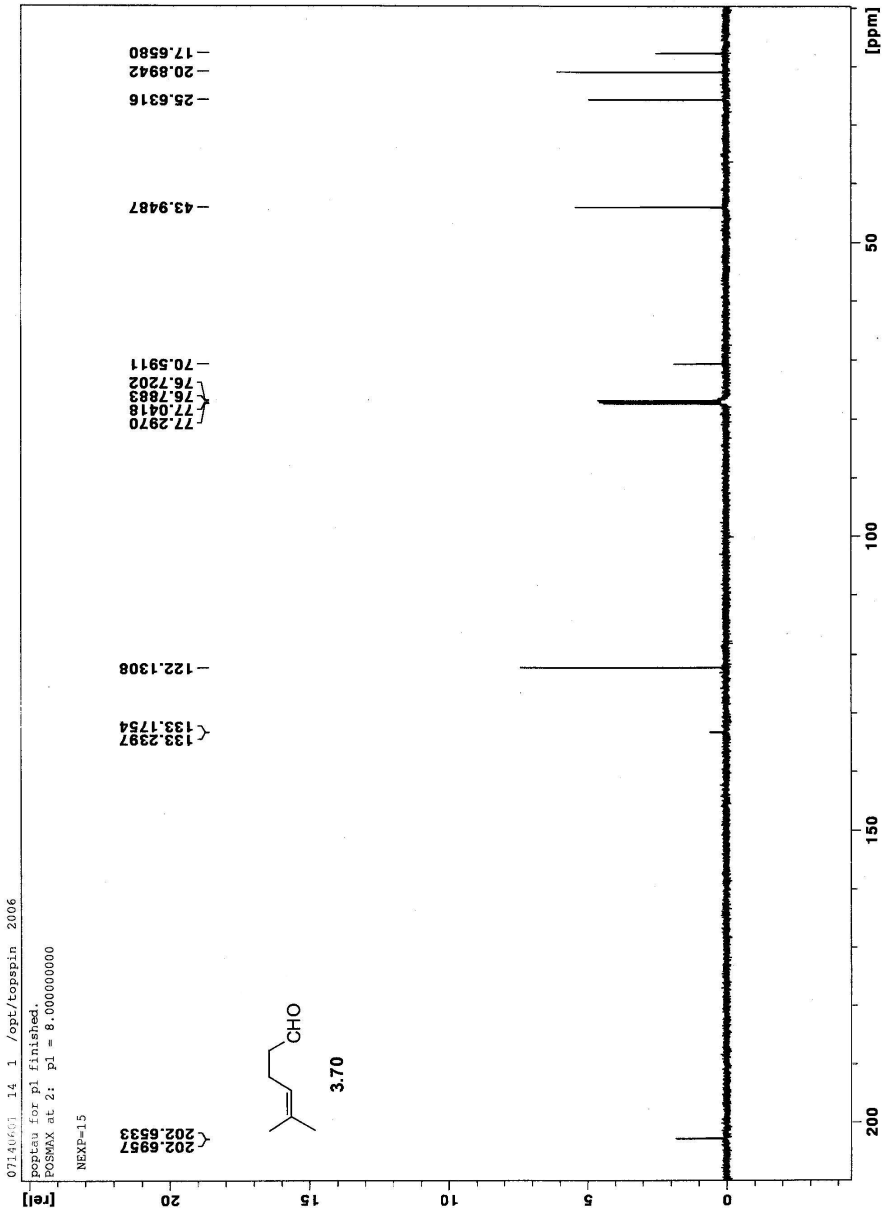
2.1 9R-4-deoxyannoreticuin



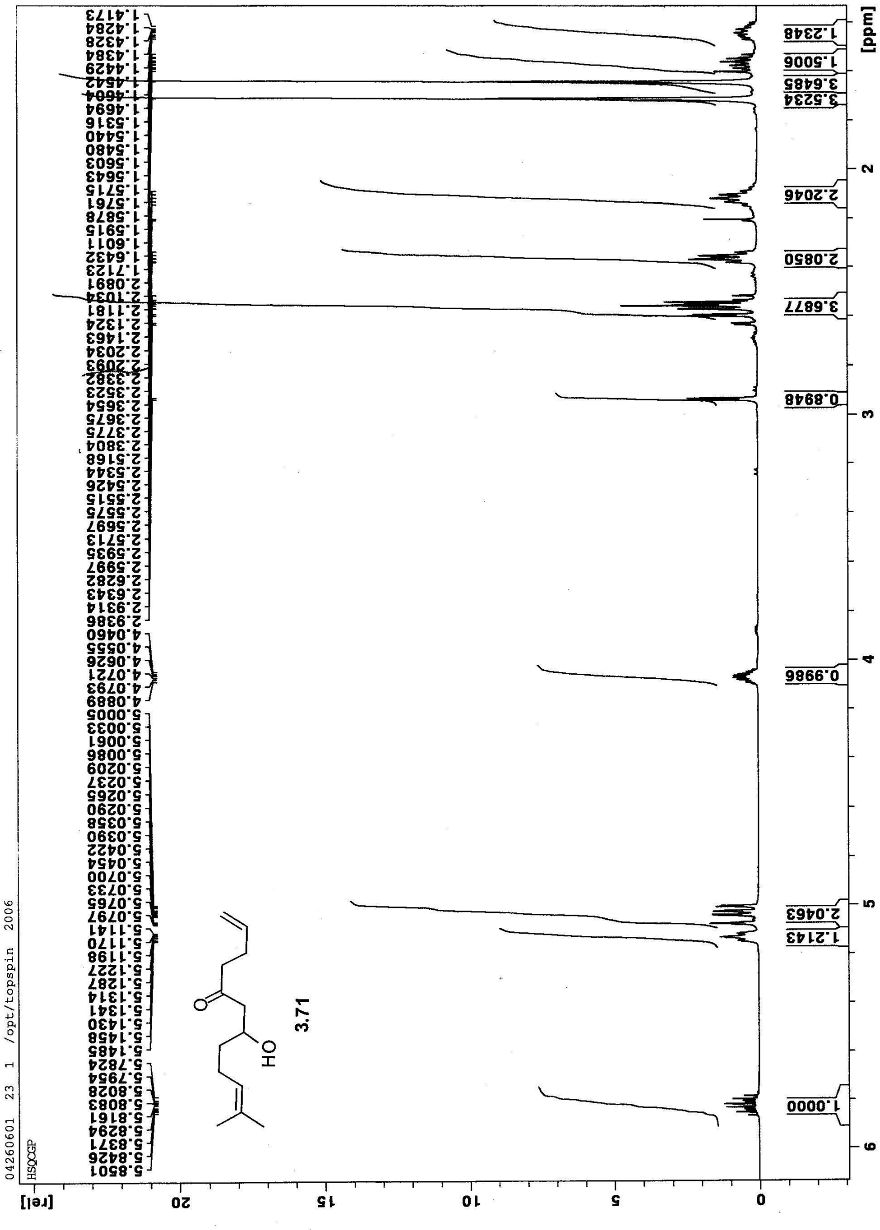
2.2 9S-4-deoxyannoreticuin

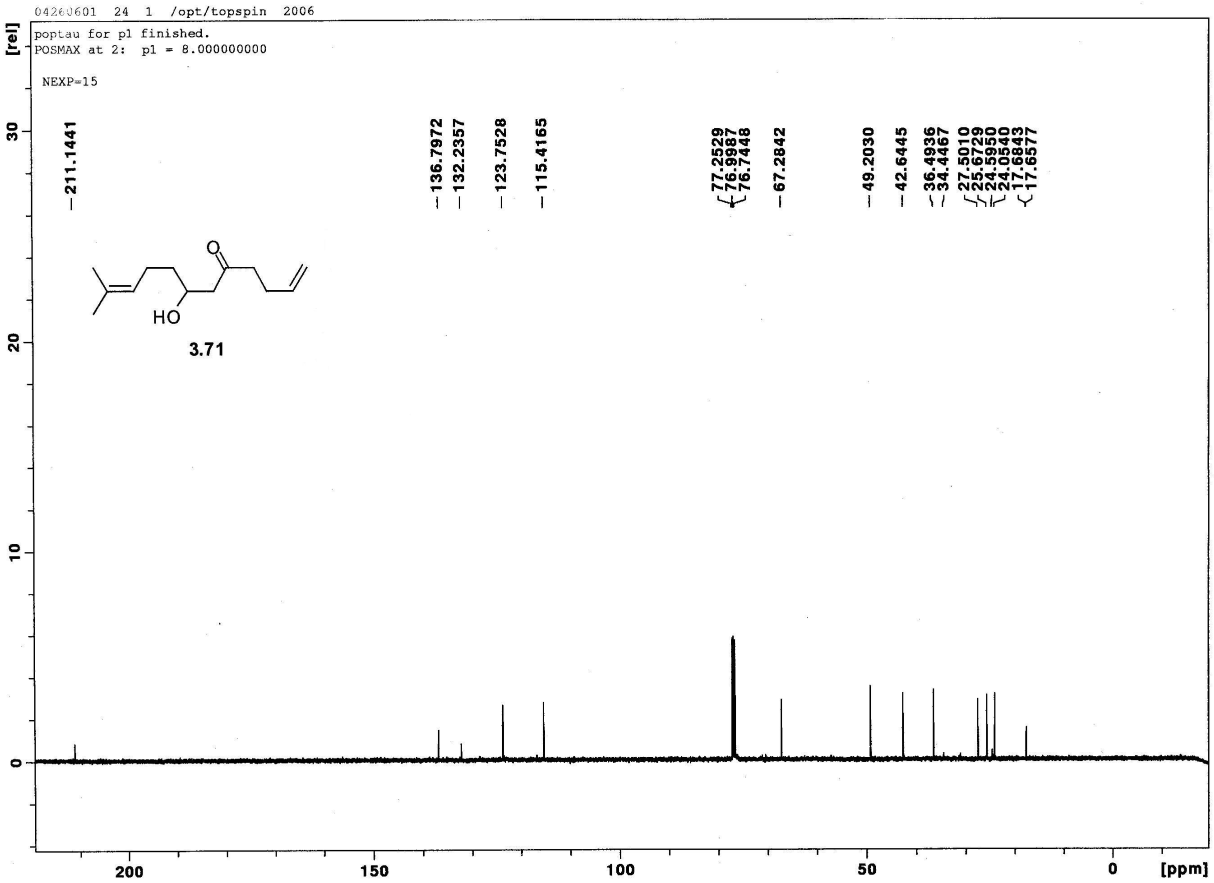

2.2 9*S*-4-deoxyannoreticuin

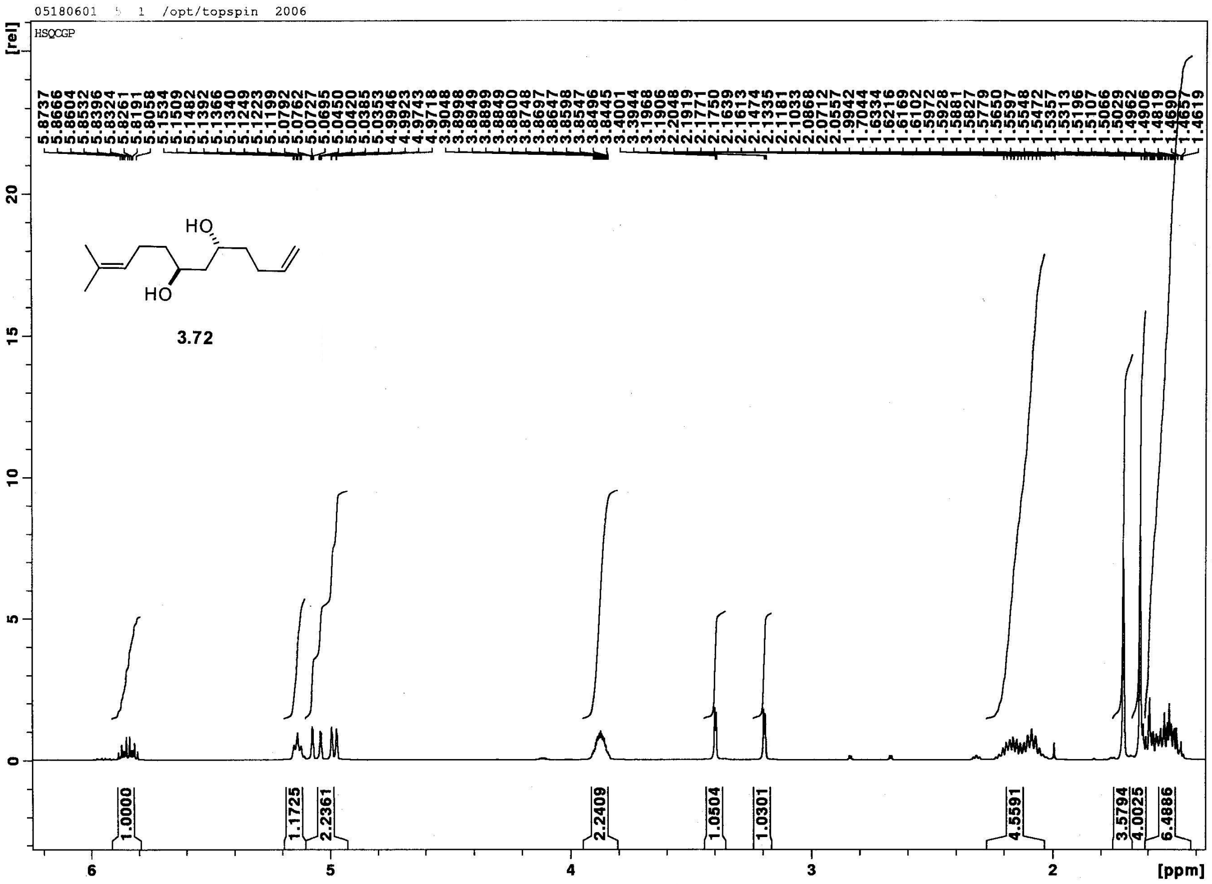

07140601 13 1 /opt/topspin 2006
HSQCGP
9.7738
9.7705
9.7662
9.7624
9.7598
5.0872
2.4584
2.3222
1.6957
1.6369
1.6271
1.0000
1.0668
2.1475
2.1669
6.7081
CHO
3.70
[ppm]
10
8
6
4
2
[rel]
30
20
10
0

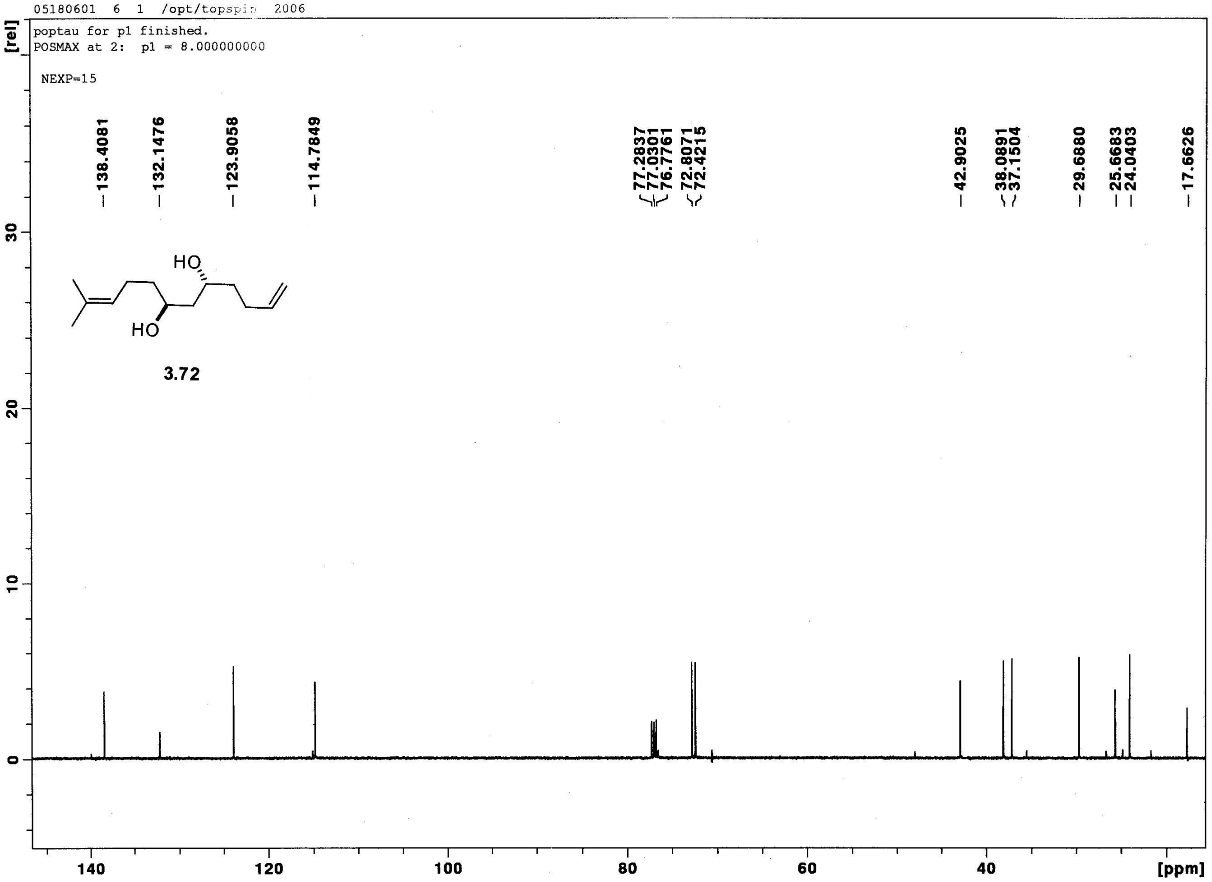

07140601 14 1 /opt/topspin 2006
poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
202.6957
202.6533
133.2397
133.1754
122.1308
77.2970
77.0418
76.7883
76.7202
70.5911
43.9487
25.6316
20.8942
17.6580
CHO
[ppm]
200
150
100
50
[rel]
20
15
10
5
0

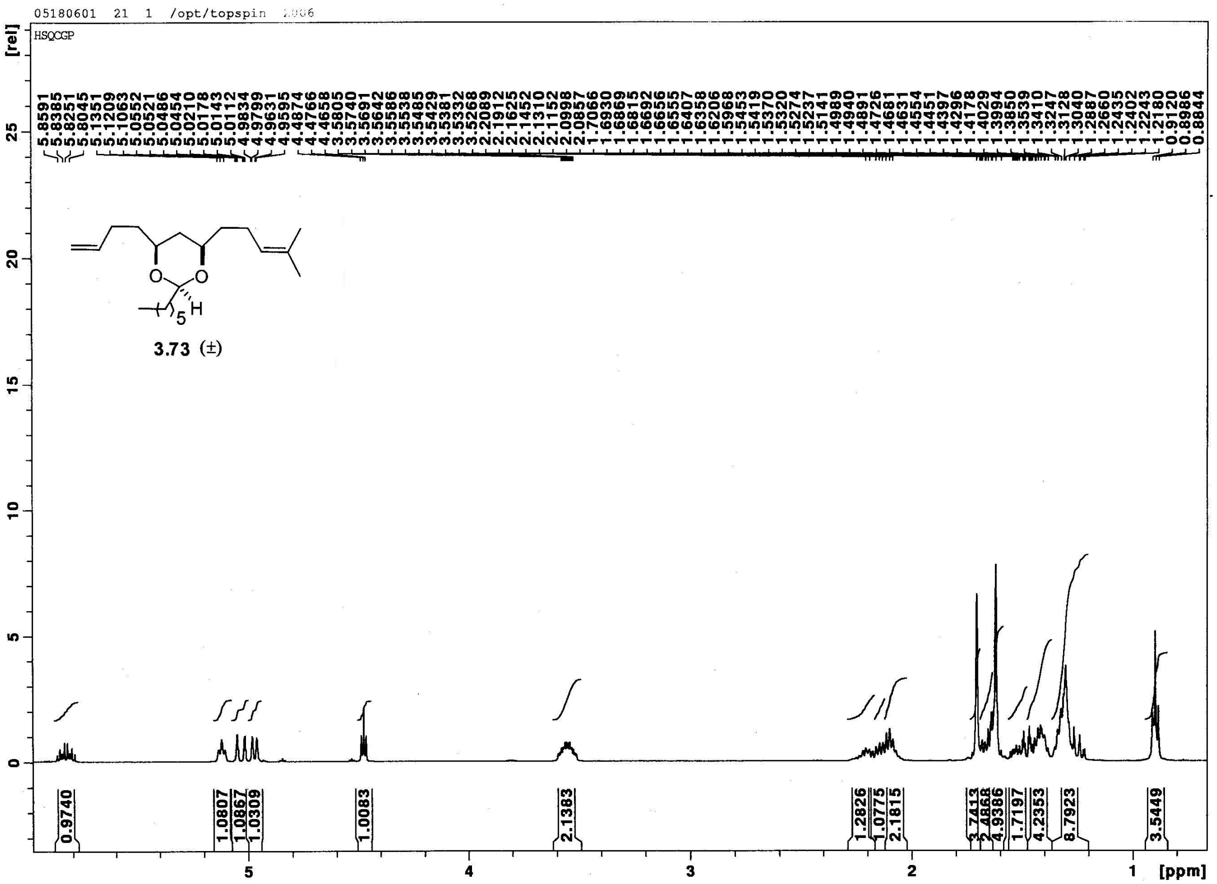
3.70

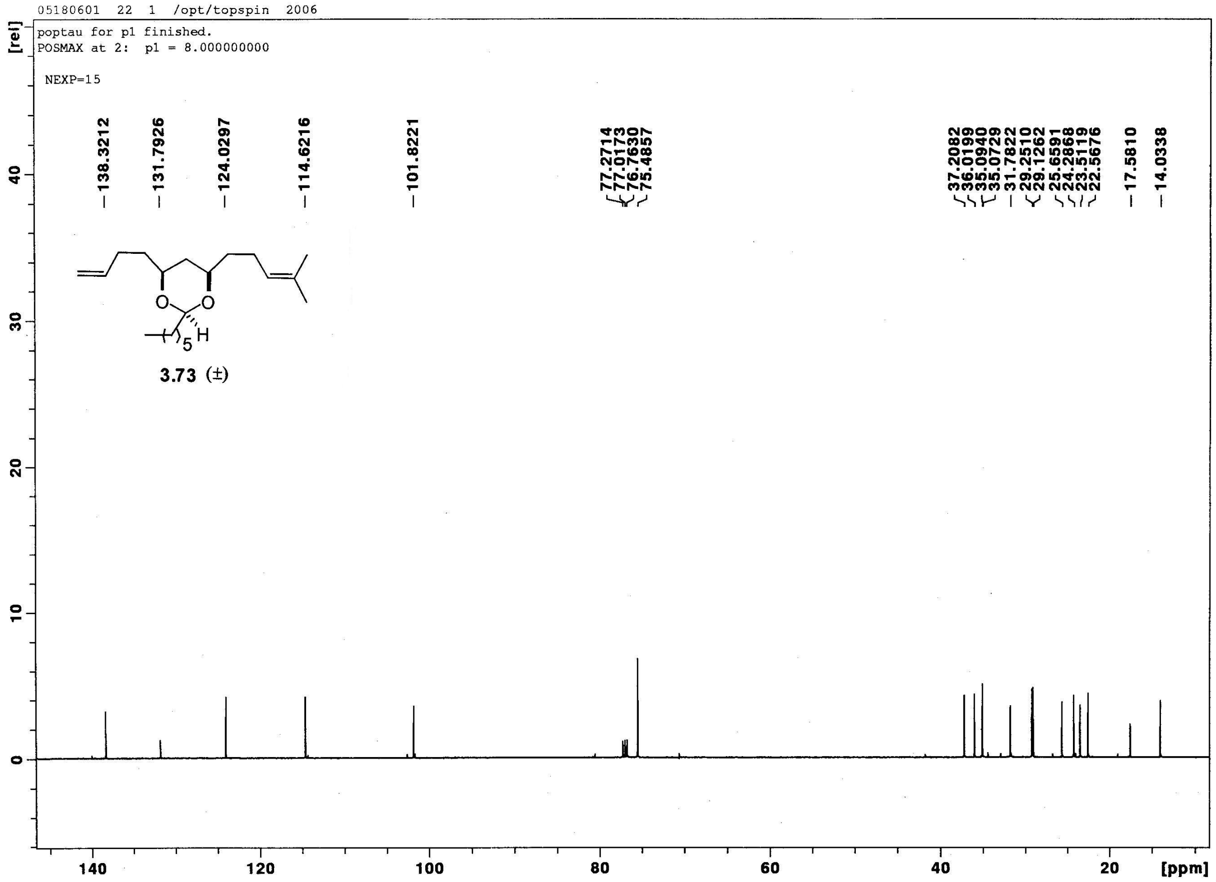

04260601 23 1 /opt/topspin 2006
HSQCGP
5.8501
5.8426
5.8371
5.8294
5.8161
5.8083
5.8028
5.7954
5.7824
5.1485
5.1458
5.1430
5.1341
5.1314
5.1287
5.1227
5.1198
5.1170
5.1141
5.0797
5.0765
5.0733
5.0700
5.0454
5.0422
5.0390
5.0358
5.0290
5.0265
5.0237
5.0209
5.0086
5.0061
5.0033
5.0005
4.0889
4.0793
4.0721
4.0626
4.0555
4.0460
2.9386
2.9314
2.6343
2.6282
2.5997
2.5935
2.5713
2.5697
2.5575
2.5515
2.5426
2.5344
2.5168
2.3804
2.3775
2.3675
2.3654
2.3523
2.3382
2.2093
2.2034
2.1463
2.1324
2.1181
2.1034
2.0891
1.7123
1.6432
1.6011
1.5915
1.5878
1.5761
1.5715
1.5643
1.5603
1.5480
1.5440
1.5316
1.4694
1.4604
1.4542
1.4429
1.4384
1.4328
1.4284
1.4173
O
HO
3.71
1.0000
1.2143
2.0463
0.9986
0.8948
3.6877
2.0850
2.2046
3.5234
3.6485
1.5006
1.2348
6
5
4
3
2
[ppm]
[rel]
20
15
10
5
0

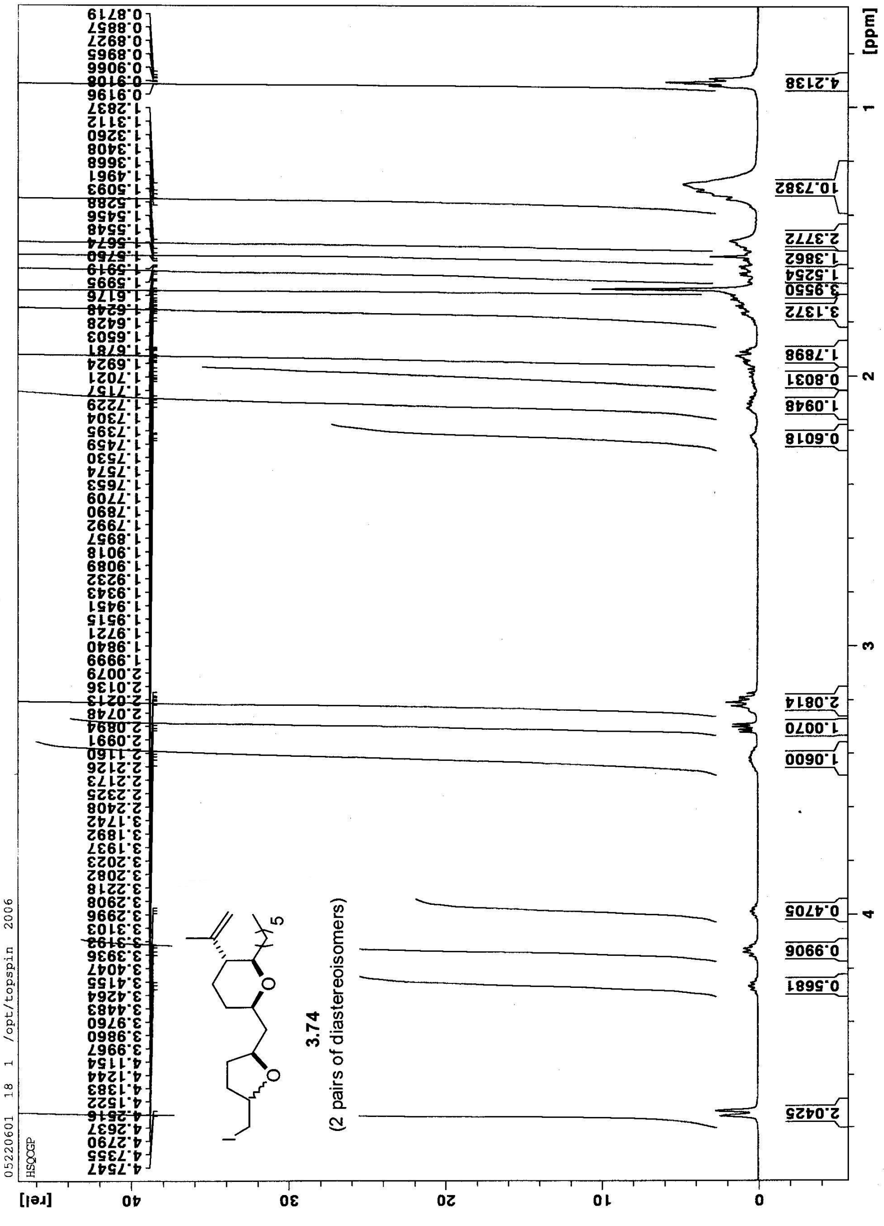

04260601 24 1 /opt/topspin 2006
poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
211.1441
136.7972
132.2357
123.7528
115.4165
77.2529
76.9987
76.7448
67.2842
49.2030
42.6445
36.4936
34.4467
27.5010
25.6729
24.5950
24.0540
17.6843
17.6577
O
HO
3.71
[rel]
30
20
10
0
200
150
100
50
0
[ppm]

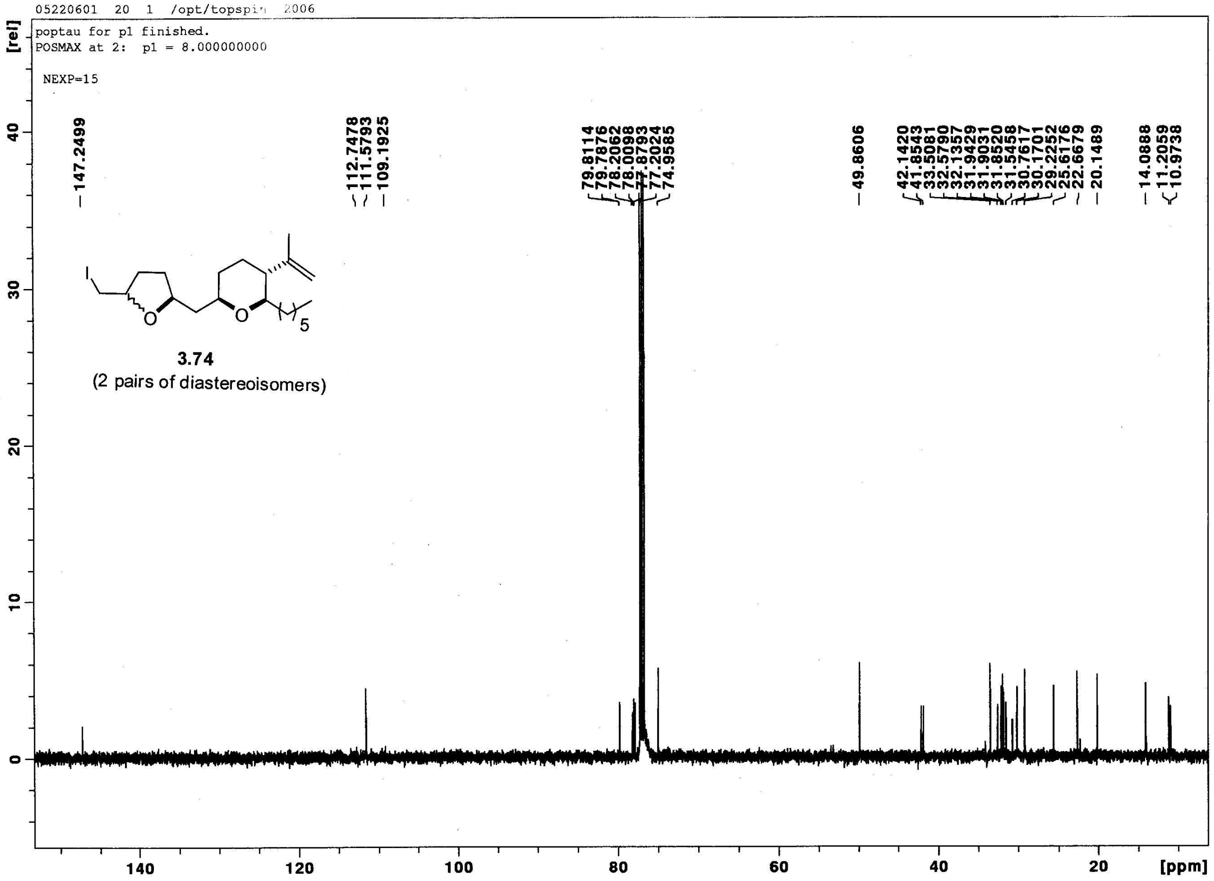

05180601 5 1 /opt/topspin 2006
HSQCGP
5.8737
5.8666
5.8604
5.8532
5.8396
5.8324
5.8261
5.8191
5.8058
5.1534
5.1509
5.1482
5.1392
5.1366
5.1340
5.1249
5.1223
5.1199
5.0792
5.0762
5.0727
5.0695
5.0450
5.0420
5.0385
5.0353
4.9946
4.9923
4.9743
4.9718
3.9048
3.8998
3.8949
3.8899
3.8849
3.8800
3.8748
3.8697
3.8647
3.8598
3.8547
3.8496
3.8445
3.4001
3.3944
3.1968
3.1906
2.2048
2.1919
2.1771
2.1750
2.1639
2.1613
2.1474
2.1335
2.1181
2.1033
2.0868
2.0712
2.0557
1.9942
1.7044
1.6334
1.6216
1.6169
1.6102
1.5972
1.5928
1.5881
1.5827
1.5779
1.5650
1.5597
1.5548
1.5472
1.5357
1.5313
1.5196
1.5107
1.5066
1.5029
1.4962
1.4906
1.4819
1.4690
1.4657
1.4619
HO
HO
3.72
1.0000
1.1725
2.2361
2.2409
1.0504
1.0301
4.5591
3.5794
4.0025
6.4886
[rel]
20
15
10
5
0
6
5
4
3
2
[ppm]


05180601 6 1 /opt/topspin 2006
poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
138.4081
132.1476
123.9058
114.7849
77.2837
77.0301
76.7761
72.8071
72.4215
42.9025
38.0891
37.1504
29.6880
25.6683
24.0403
17.6626
HO
HO
3.72
[rel]
30
20
10
0
140
120
100
80
60
40
[ppm]

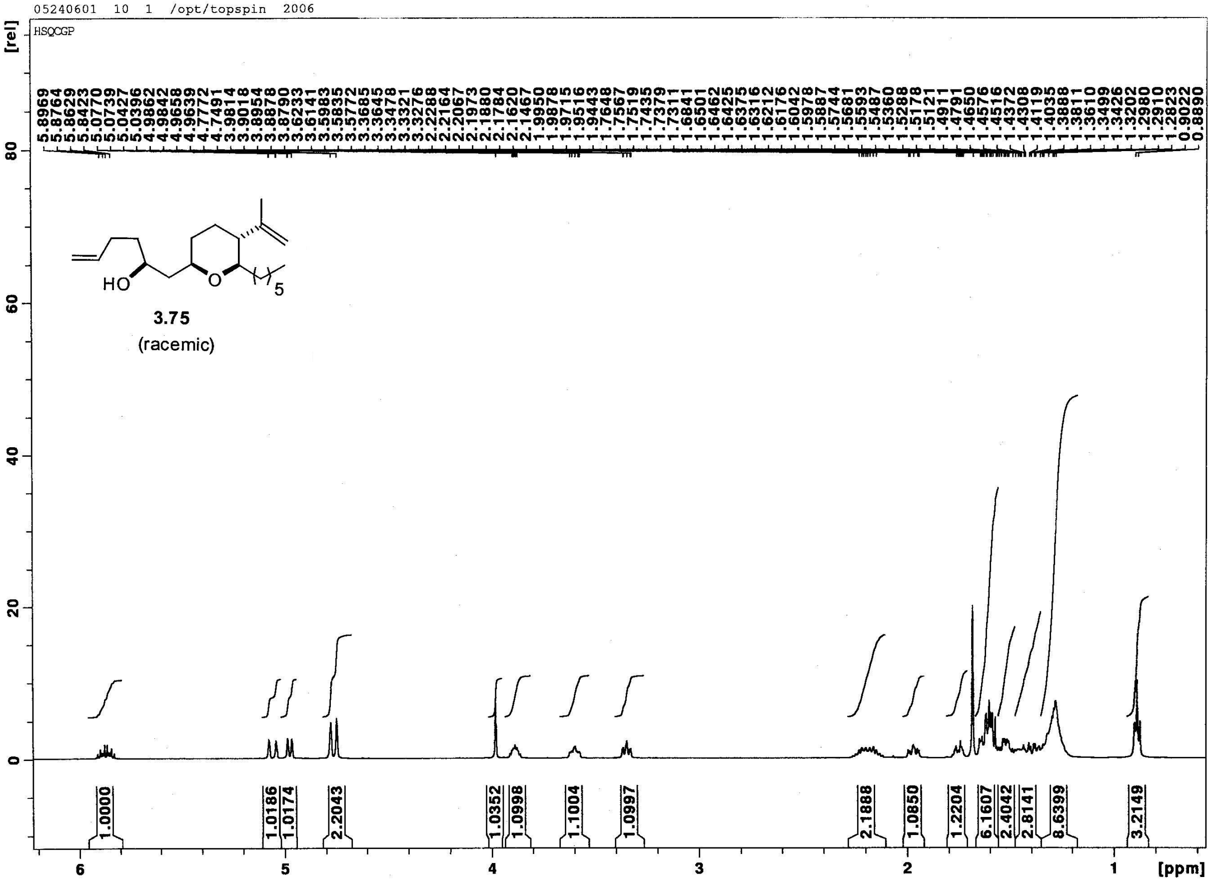

3.73 (±)
05180601 21 1 /opt/topspin 2006
HSQCGP
[rel]
25
20
15
10
5
0
5.8591
5.8385
5.8251
5.8045
5.1351
5.1209
5.1063
5.0552
5.0521
5.0486
5.0454
5.0210
5.0178
5.0143
5.0112
4.9834
4.9799
4.9631
4.9595
4.4874
4.4766
4.4658
3.5805
3.5740
3.5691
3.5642
3.5586
3.5538
3.5485
3.5429
3.5381
3.5332
3.5268
2.2089
2.1912
2.1625
2.1452
2.1310
2.1152
2.0998
2.0857
1.7066
1.6930
1.6869
1.6815
1.6692
1.6656
1.6555
1.6407
1.6358
1.6206
1.5968
1.5453
1.5419
1.5370
1.5320
1.5274
1.5237
1.5141
1.4989
1.4940
1.4891
1.4726
1.4681
1.4631
1.4554
1.4451
1.4397
1.4296
1.4178
1.4029
1.3994
1.3850
1.3539
1.3410
1.3247
1.3128
1.3040
1.2887
1.2660
1.2435
1.2402
1.2243
1.2180
0.9120
0.8986
0.8844
O
O
H
5
0.9740
1.0807
1.0867
1.0309
1.0083
2.1383
1.2826
1.0775
2.1815
3.7413
2.4868
4.9386
1.7197
4.2353
8.7923
3.5449
5
4
3
2
1
[ppm]


05180601 22 1 /opt/topspin 2006
poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
138.3212
131.7926
124.0297
114.6216
101.8221
77.2714
77.0173
76.7630
75.4857
37.2082
36.0199
35.0940
35.0729
31.7822
29.2510
29.1262
25.6591
24.2868
23.5119
22.5676
17.5810
14.0338
O
O
5
H
3.73 (±)
[rel]
40
30
20
10
0
140
120
100
80
60
40
20
[ppm]

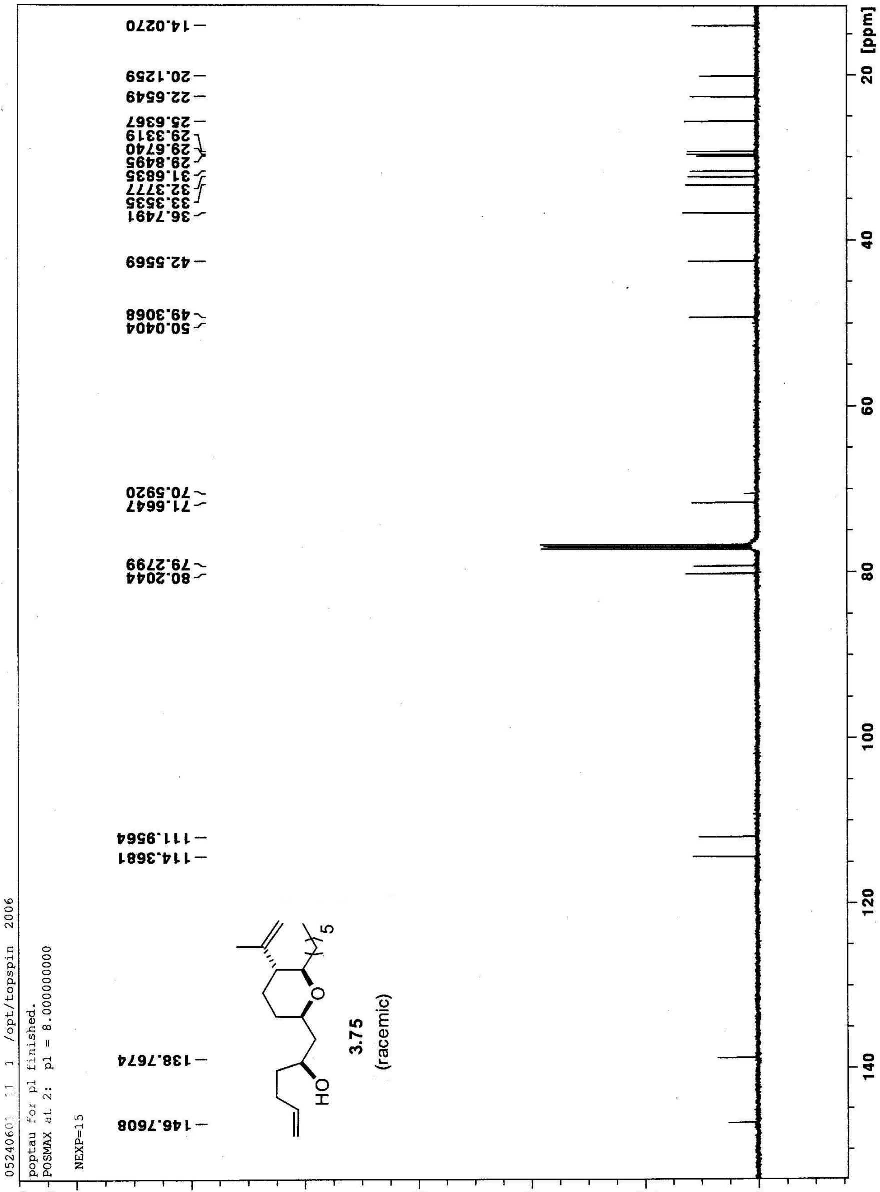

05220601 18 1 /opt/topspin 2006
HSQCGP
3.74
(2 pairs of diastereoisomers)
5
O
O
[ppm]
[rel]
0
10
20
30
40
1
2
3
4
0.8719
0.8857
0.8927
0.8965
0.9066
0.9108
0.9196
1.2837
1.3112
1.3260
1.3408
1.3668
1.4961
1.5093
1.5288
1.5456
1.5558
1.5674
1.5760
1.5919
1.5995
1.6176
1.6248
1.6428
1.6503
1.6781
1.6924
1.7021
1.7157
1.7229
1.7304
1.7395
1.7459
1.7530
1.7574
1.7653
1.7709
1.7890
1.7992
1.8957
1.9018
1.9069
1.9232
1.9343
1.9451
1.9515
1.9721
1.9840
1.9999
2.0079
2.0136
2.0213
2.0748
2.0894
2.0991
2.1160
2.2126
2.2173
2.2325
2.2408
3.1742
3.1892
3.1937
3.2023
3.2082
3.2218
3.2908
3.2996
3.3103
3.3919
3.3936
3.4047
3.4155
3.4264
3.4483
3.9760
3.9860
3.9967
4.1154
4.1244
4.1383
4.1522
4.2616
4.2637
4.2790
4.7355
4.7547
4.2138
10.7382
2.3772
1.3862
1.5254
3.9550
3.1372
1.7898
0.8031
1.0948
0.6018
2.0814
1.0070
1.0600
0.4705
0.9906
0.5681
2.0425



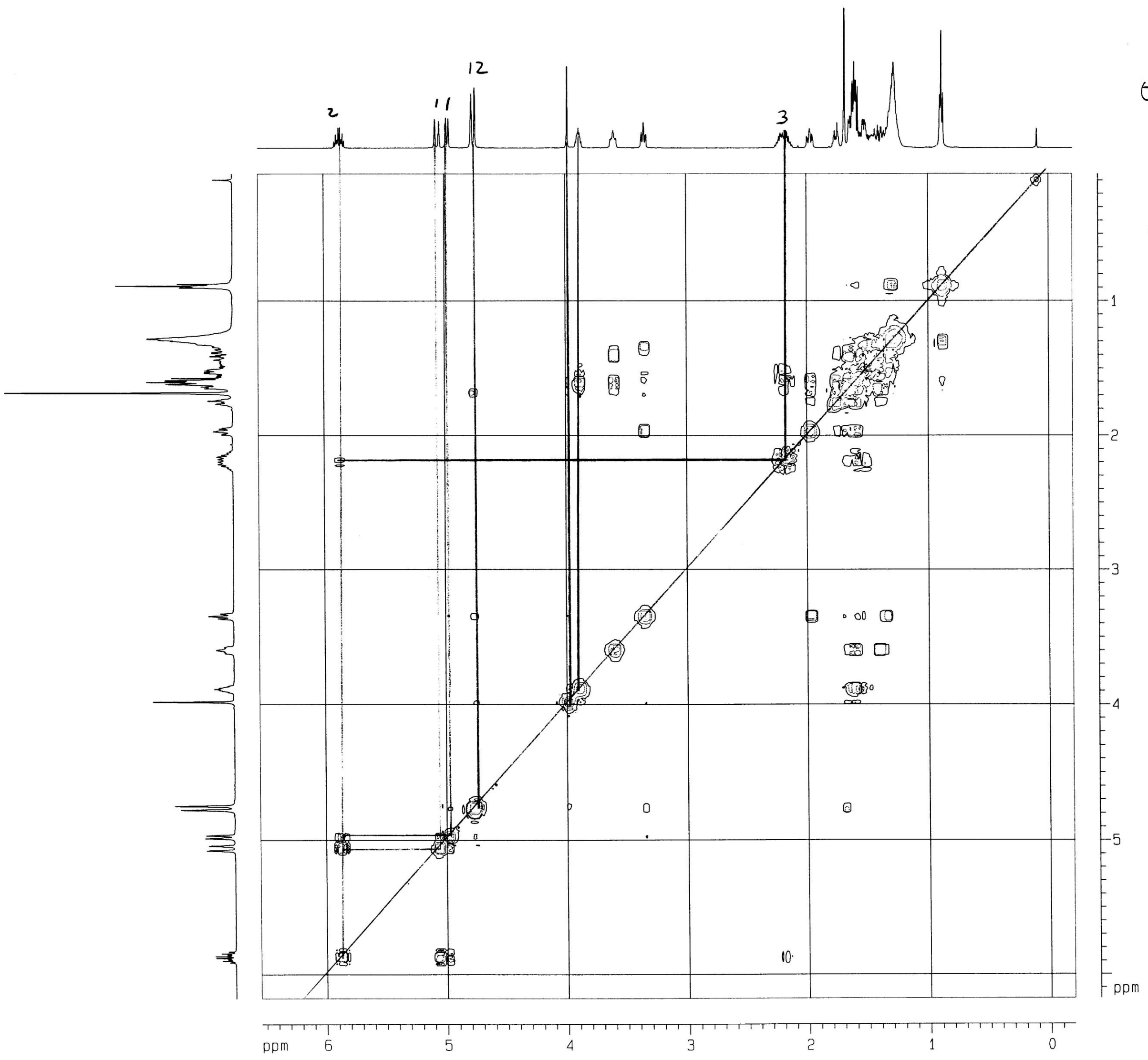
3.74
(2 pairs of diastereoisomers)


05240601 10 1 /opt/topspin 2006
HSQCGP
[rel]
80
60
40
20
0
5.8969
5.8764
5.8629
5.8423
5.0770
5.0739
5.0427
5.0396
4.9862
4.9842
4.9658
4.9639
4.7772
4.7491
3.9814
3.9018
3.8954
3.8878
3.8790
3.6233
3.6141
3.5983
3.5835
3.5772
3.3685
3.3645
3.3478
3.3321
3.3276
2.2288
2.2164
2.2067
2.1973
2.1880
2.1784
2.1620
2.1467
1.9950
1.9878
1.9715
1.9516
1.9443
1.7648
1.7567
1.7519
1.7435
1.7379
1.7311
1.6841
1.6501
1.6462
1.6425
1.6375
1.6316
1.6212
1.6176
1.6042
1.5978
1.5887
1.5744
1.5681
1.5593
1.5487
1.5360
1.5288
1.5178
1.5121
1.4911
1.4791
1.4650
1.4576
1.4516
1.4372
1.4308
1.4119
1.4035
1.3888
1.3811
1.3610
1.3499
1.3426
1.3202
1.2980
1.2910
1.2823
0.9022
0.8890
HO
O
5
1.0000
1.0186
1.0174
2.2043
1.0352
1.0998
1.1004
1.0997
2.1888
1.0850
1.2204
6.1607
2.4042
2.8141
8.6399
3.2149
6
5
4
3
2
1
[ppm]

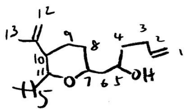
3.75
(racemic)


05240601 11 1 /opt/topspin 2006
poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
14.0270
20.1259
22.6549
25.6367
29.3319
29.6740
29.8495
31.6835
32.3777
33.3535
36.7491
42.5569
49.3068
50.0404
70.5920
71.6647
79.2799
80.2044
111.9564
114.3681
138.7674
146.7608
HO
O
5
20 [ppm]
40
60
80
100
120
140
0
20
40
60
80
100
120 [rel]

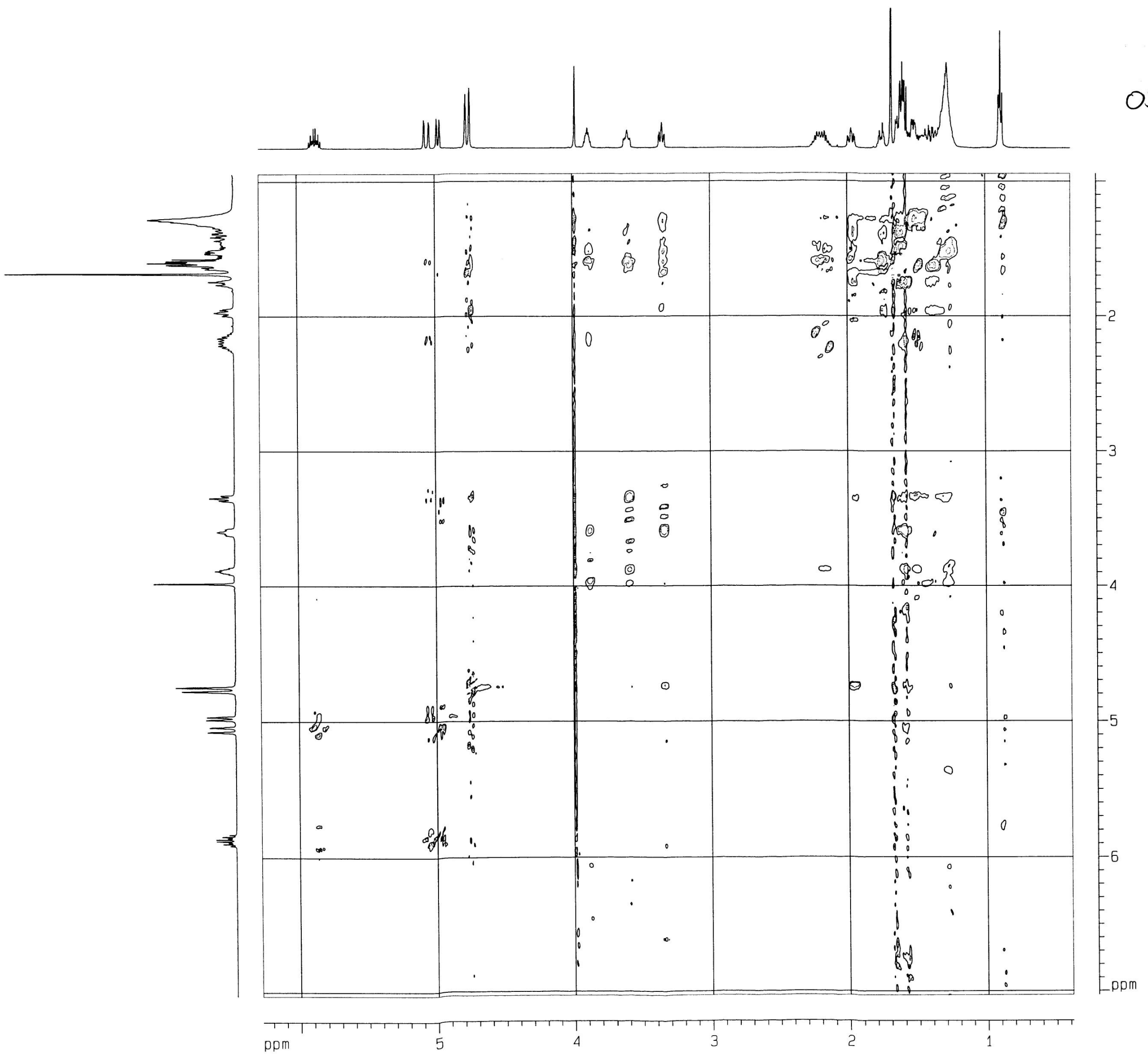
3.75
(racemic)



05300601-10



(3.15) COSY



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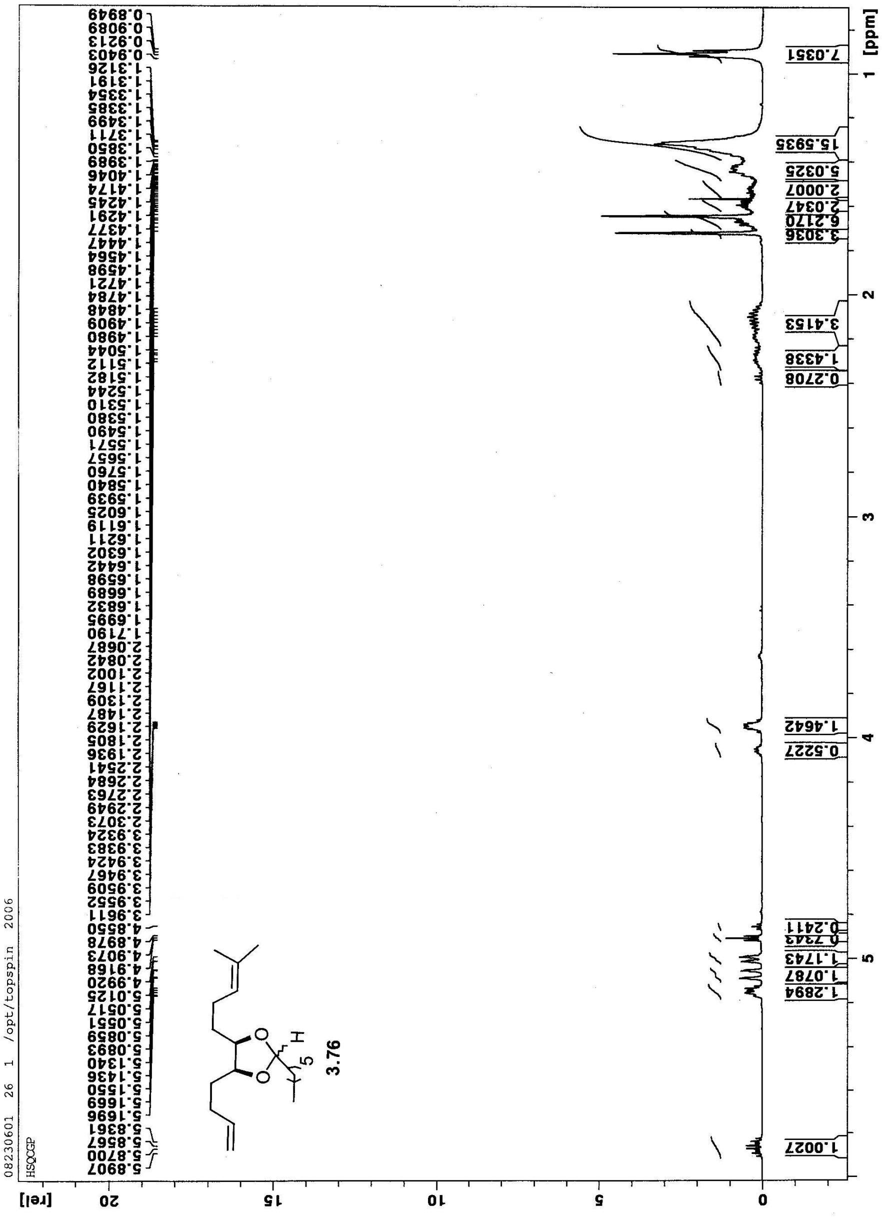
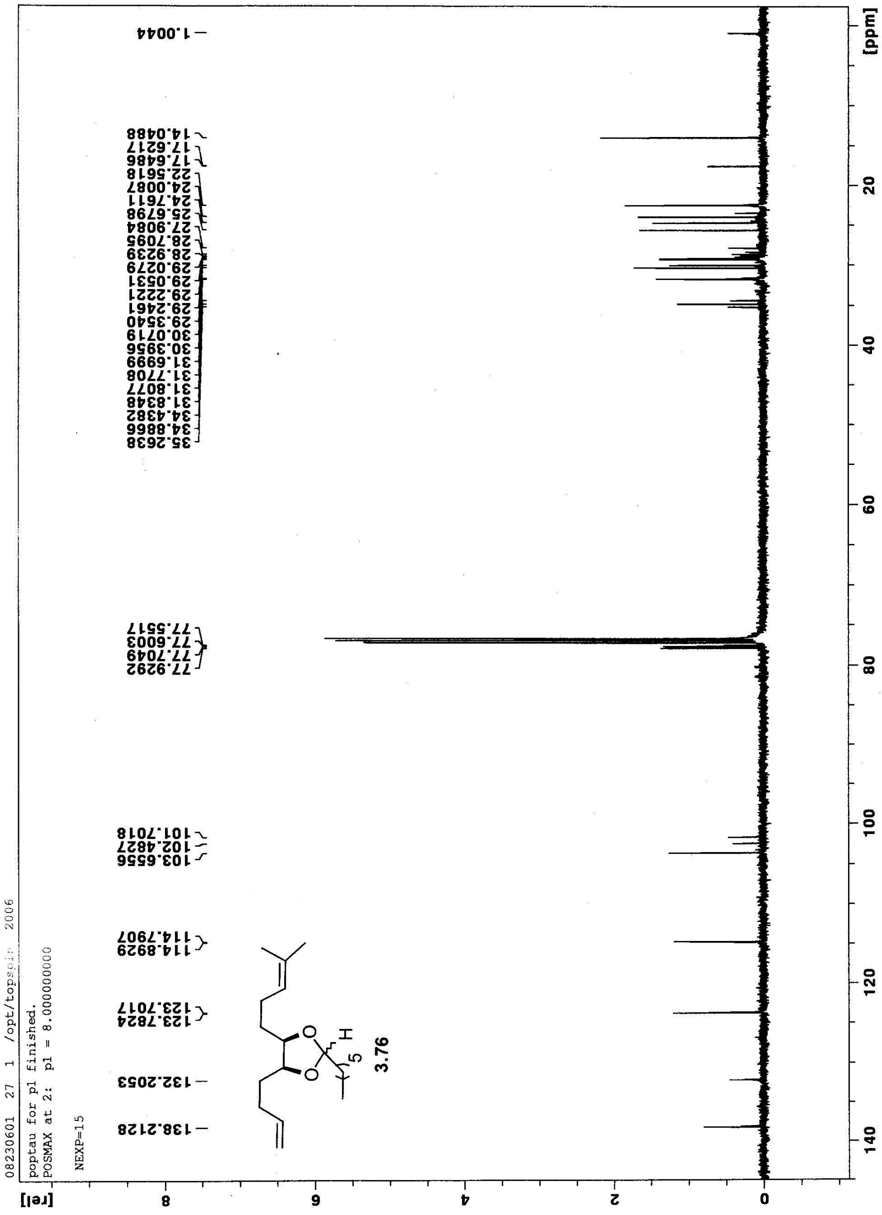
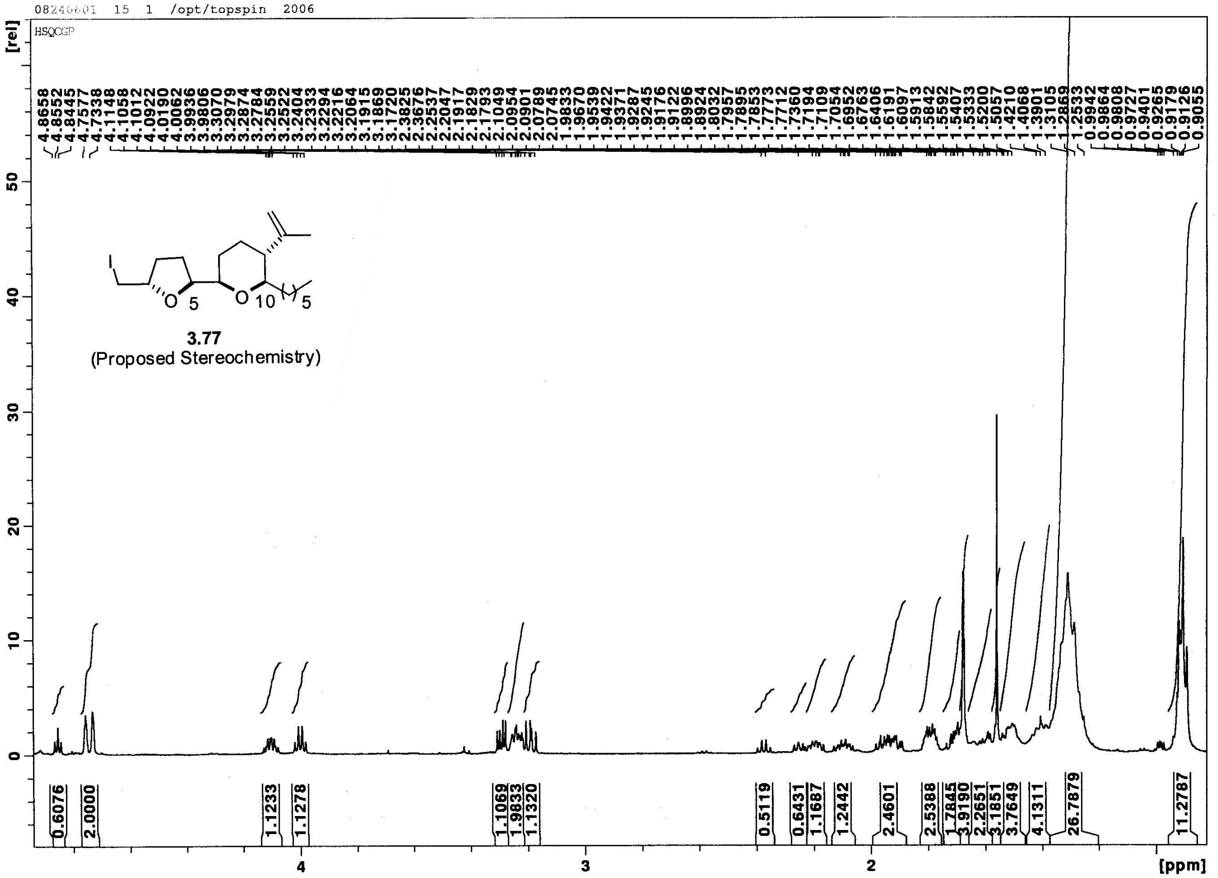
(3.75) NOESY

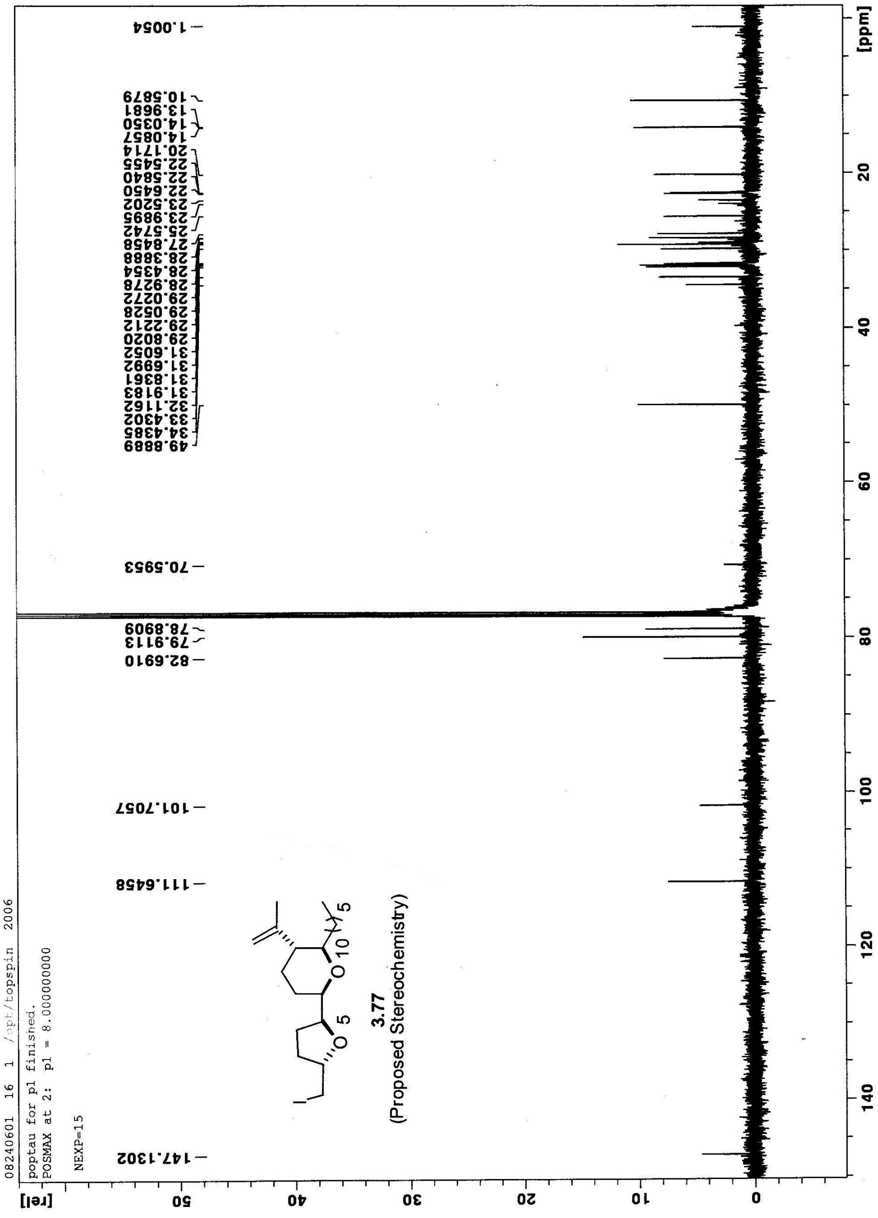

08230601 26 1 /opt/topspin 2006
HSQCGP
0.8949
0.9089
0.9213
0.9403
1.3126
1.3191
1.3354
1.3385
1.3499
1.3711
1.3850
1.3989
1.4046
1.4174
1.4245
1.4291
1.4377
1.4447
1.4564
1.4598
1.4721
1.4784
1.4848
1.4909
1.4980
1.5044
1.5112
1.5182
1.5244
1.5310
1.5380
1.5490
1.5571
1.5657
1.5760
1.5840
1.5939
1.6025
1.6119
1.6211
1.6302
1.6442
1.6598
1.6669
1.6832
1.6995
1.7190
2.0687
2.0842
2.1002
2.1167
2.1309
2.1487
2.1629
2.1805
2.1936
2.2541
2.2684
2.2763
2.2949
2.3073
3.9324
3.9383
3.9424
3.9467
3.9509
3.9552
3.9611
4.8850
4.8978
4.9073
4.9168
4.9920
5.0125
5.0517
5.0551
5.0859
5.0893
5.1340
5.1436
5.1550
5.1669
5.1696
5.8361
5.8567
5.8700
5.8907
7.0351
15.5935
5.0325
2.0007
2.0347
6.2170
3.3036
3.4153
1.4338
0.2708
1.4642
0.5227
0.2411
0.7343
1.1743
1.0787
1.2894
1.0027
H
5
1
2
3
4
5
[ppm]
0
5
10
15
20
[rel]

3.76

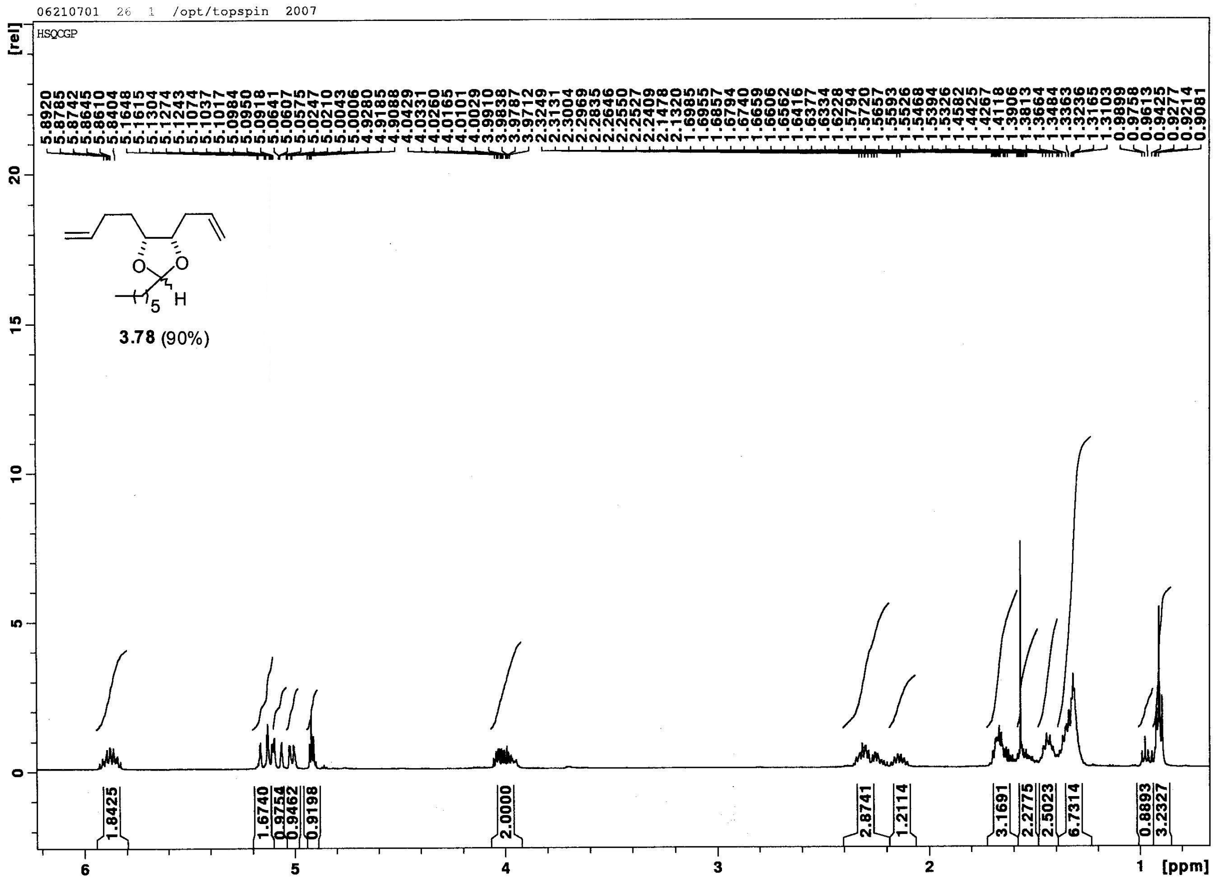

08230601 27 1 /opt/topspin 2006
poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
138.2128
132.2053
123.7824
123.7017
114.8929
114.7907
103.6556
102.4827
101.7018
77.9292
77.7049
77.6003
77.5517
35.2638
34.8866
34.4382
31.8348
31.8077
31.7708
31.6999
30.3956
30.0719
29.3540
29.2461
29.2221
29.0531
29.0279
28.9239
28.7095
27.9084
25.6798
24.7611
24.0087
22.5618
17.6486
17.6217
14.0488
1.0044
O
O
H
5
3.76
[rel]
8
6
4
2
0
140
120
100
80
60
40
20
[ppm]

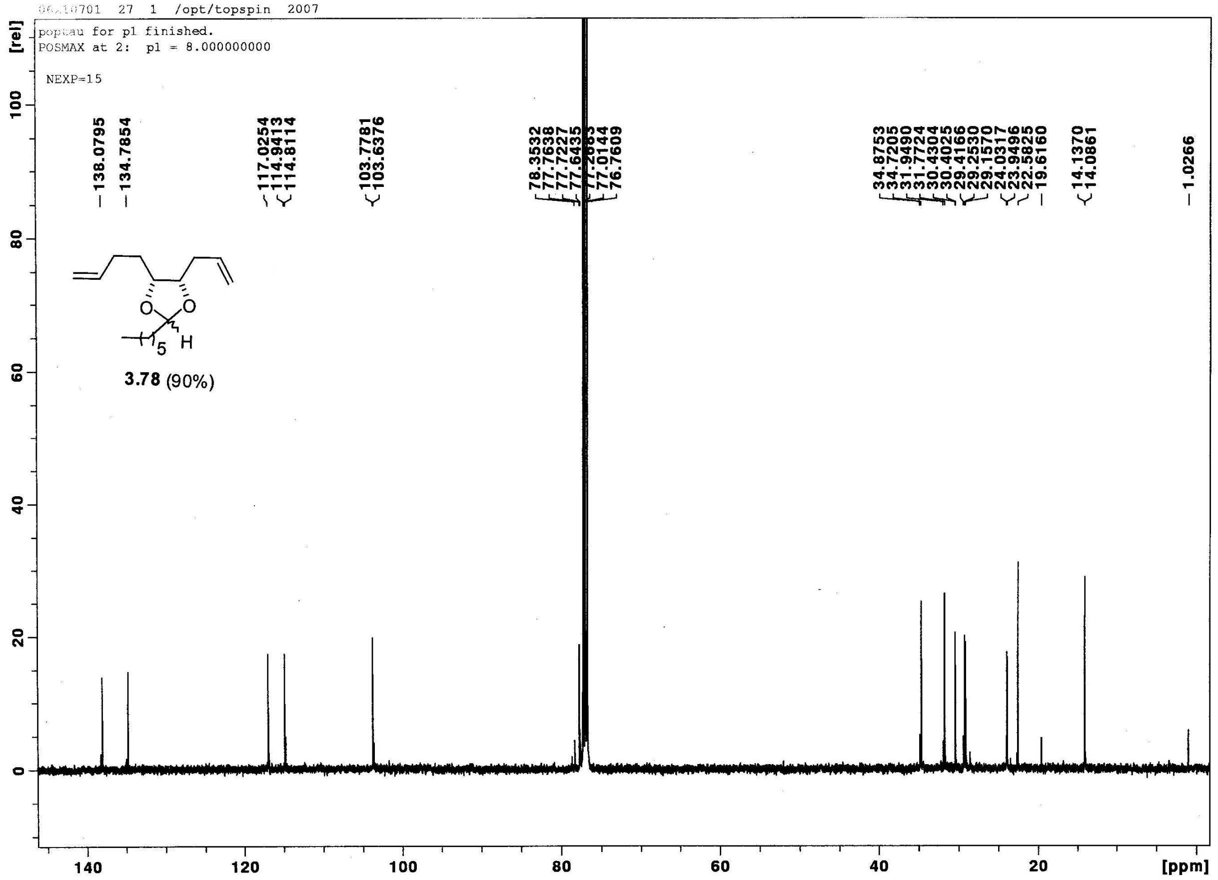


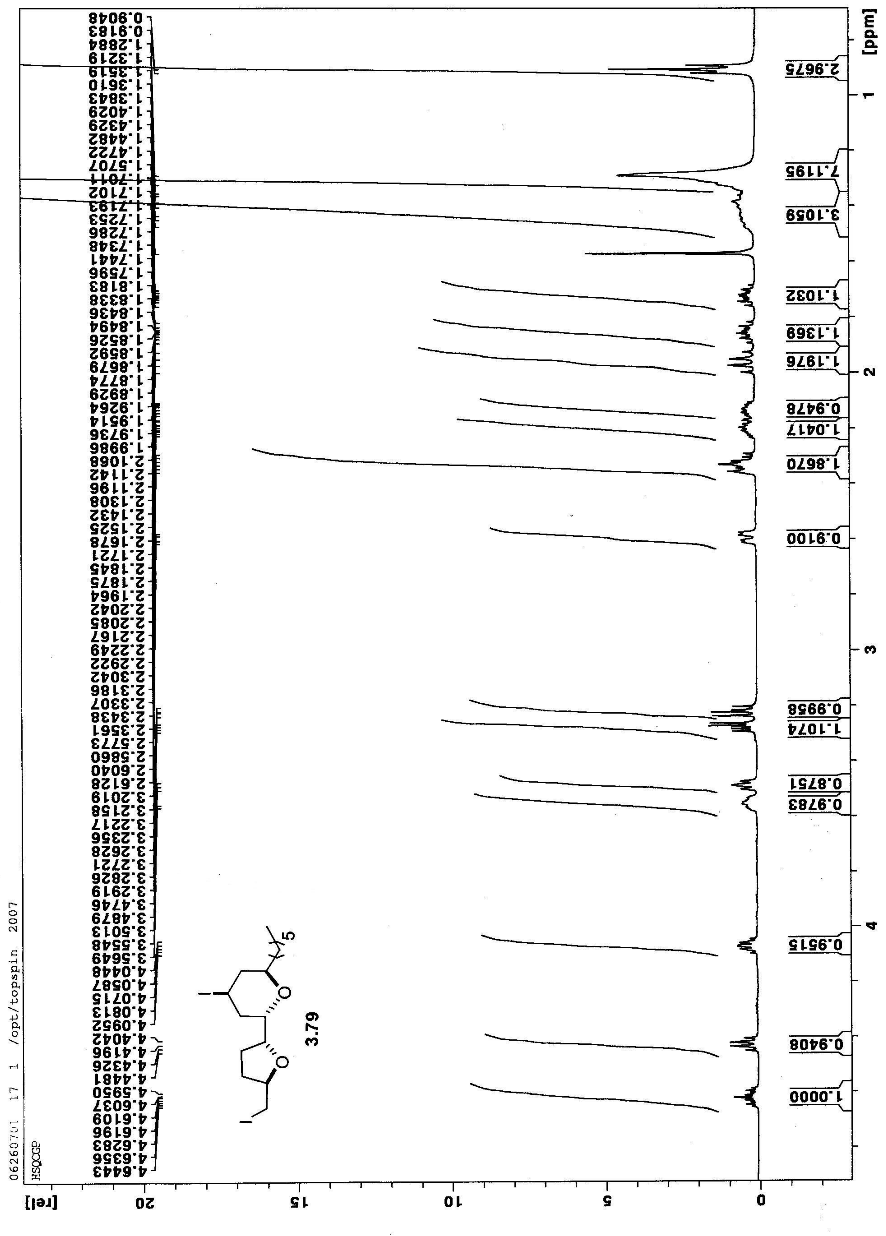
3.77
(Proposed Stereochemistry)



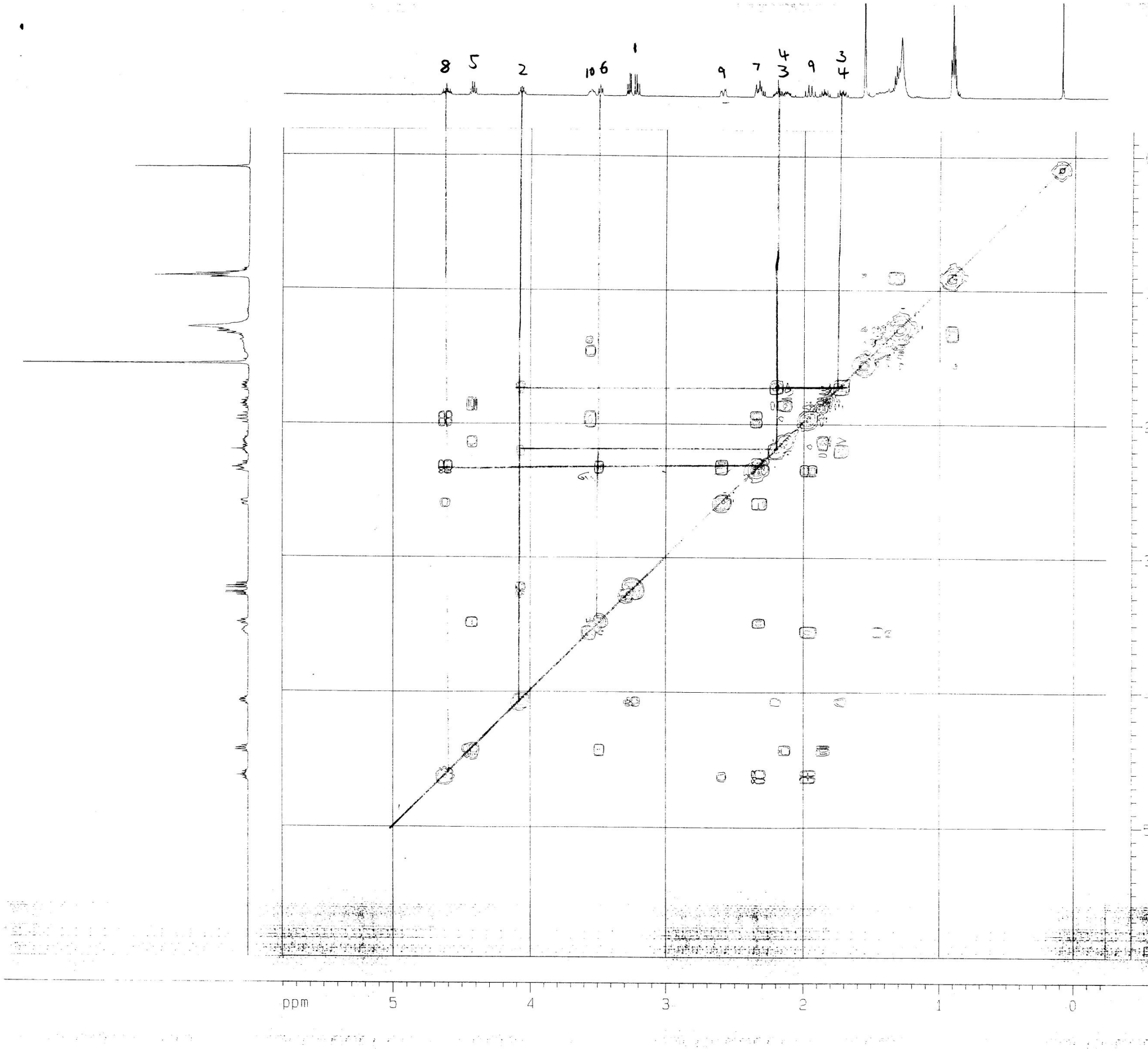
3.77
(Proposed Stereochemistry)

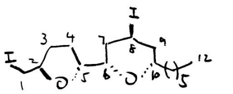

06210701 26 1 /opt/topspin 2007
HSQCGP
[rel]
5.8920 5.8785 5.8742 5.8645 5.8610 5.8404 5.1648 5.1615 5.1304 5.1274 5.1243 5.1074 5.1037 5.1017 5.0984 5.0950 5.0918 5.0641 5.0607 5.0575 5.0247 5.0210 5.0043 5.0006 4.9280 4.9185 4.9088 4.0429 4.0331 4.0260 4.0165 4.0101 4.0029 3.9910 3.9838 3.9787 3.9712 2.3249 2.3131 2.3004 2.2969 2.2835 2.2646 2.2550 2.2527 2.2409 2.1478 2.1320 1.6985 1.6955 1.6857 1.6794 1.6740 1.6659 1.6606 1.6562 1.6416 1.6377 1.6334 1.6228 1.5794 1.5720 1.5657 1.5593 1.5526 1.5468 1.5394 1.5326 1.4582 1.4425 1.4267 1.4118 1.3906 1.3813 1.3664 1.3484 1.3363 1.3236 1.3165 1.3103 0.9899 0.9758 0.9613 0.9425 0.9277 0.9214 0.9081
O
O
5
H
3.78 (90%)
1.8425
1.6740
0.9754
0.9462
0.9198
2.0000
2.8741
1.2114
3.1691
2.2775
2.5023
6.7314
0.8893
3.2327
20
15
10
5
0
6
5
4
3
2
1
[ppm]


06.10701 27 1 /opt/topspin 2007
popcau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
[rel]
138.0795
134.7854
117.0254
114.9413
114.8114
103.7781
103.6376
78.3532
77.7638
77.7227
77.6435
77.2683
77.0144
76.7609
34.8753
34.7205
31.9490
31.7724
30.4304
30.4025
29.4166
29.2530
29.1570
24.0317
23.9496
22.5825
19.6160
14.1370
14.0861
1.0266
O
O
5
H
3.78 (90%)
100
80
60
40
20
0
140
120
100
80
60
40
20
[ppm]

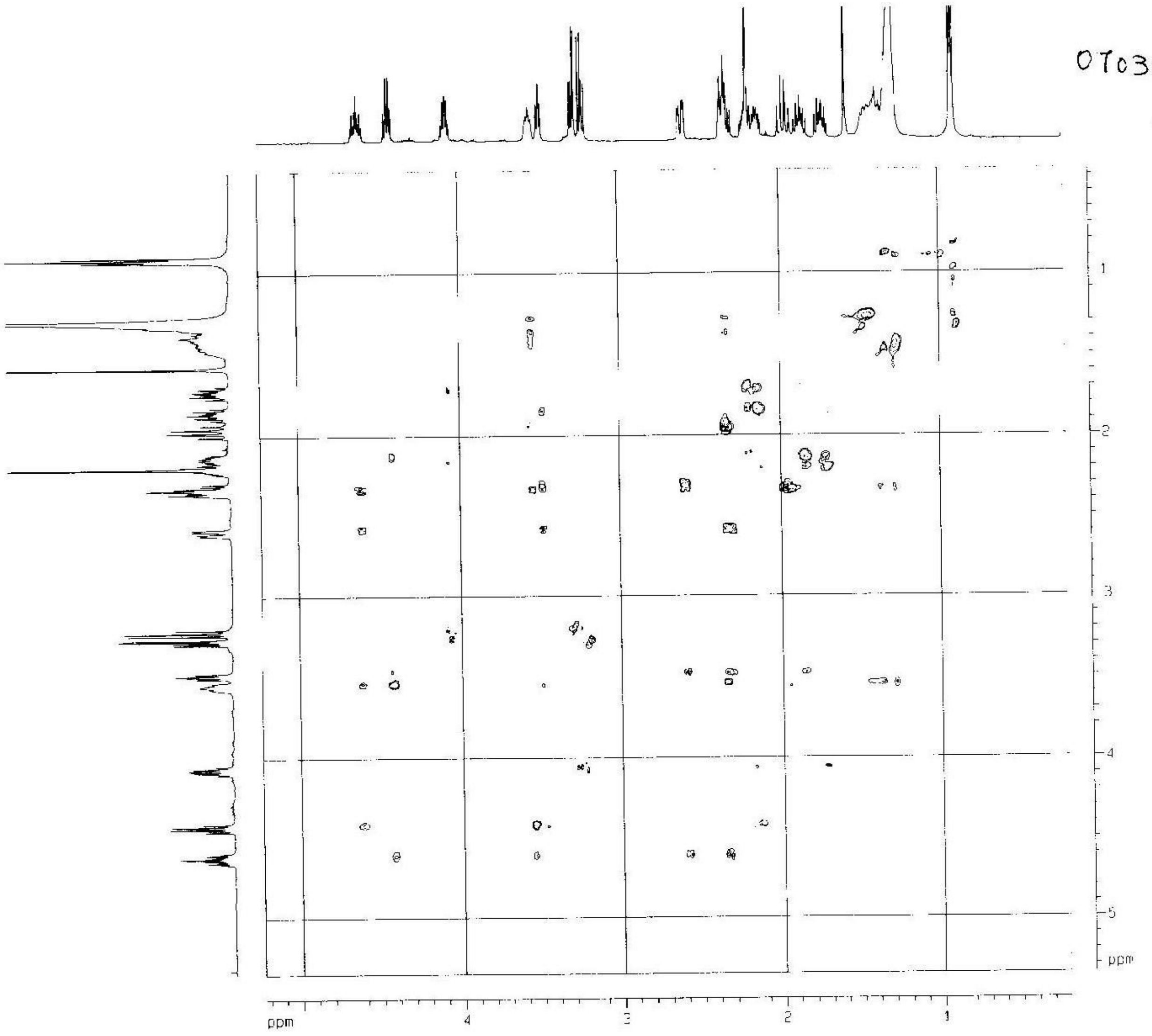

3.79
06260701 17 1 /opt/topspin 2007
HSQCGP
4.6443
4.6356
4.6283
4.6196
4.6109
4.6037
4.5950
4.4481
4.4326
4.4196
4.4042
4.0952
4.0813
4.0715
4.0587
4.0448
3.5649
3.5548
3.5013
3.4879
3.4746
3.2919
3.2826
3.2721
3.2628
3.2356
3.2217
3.2158
3.2019
2.6128
2.6040
2.5860
2.5773
2.3561
2.3438
2.3307
2.3186
2.3042
2.2922
2.2249
2.2167
2.2085
2.2042
2.1964
2.1875
2.1845
2.1721
2.1678
2.1525
2.1432
2.1308
2.1196
2.1142
2.1068
1.9986
1.9736
1.9514
1.9264
1.8929
1.8774
1.8679
1.8592
1.8526
1.8494
1.8436
1.8338
1.8183
1.7596
1.7441
1.7348
1.7286
1.7253
1.7193
1.7102
1.7011
1.5707
1.4722
1.4482
1.4329
1.4029
1.3843
1.3610
1.3519
1.3219
1.2884
0.9183
0.9048
5
1.0000
0.9408
0.9515
0.9783
0.8751
1.1074
0.9958
0.9100
1.8670
1.0417
0.9478
1.1976
1.1369
1.1032
3.1059
7.1195
2.9675
4
3
2
1
[ppm]
[rel]
20
15
10
5
0

06250701-29

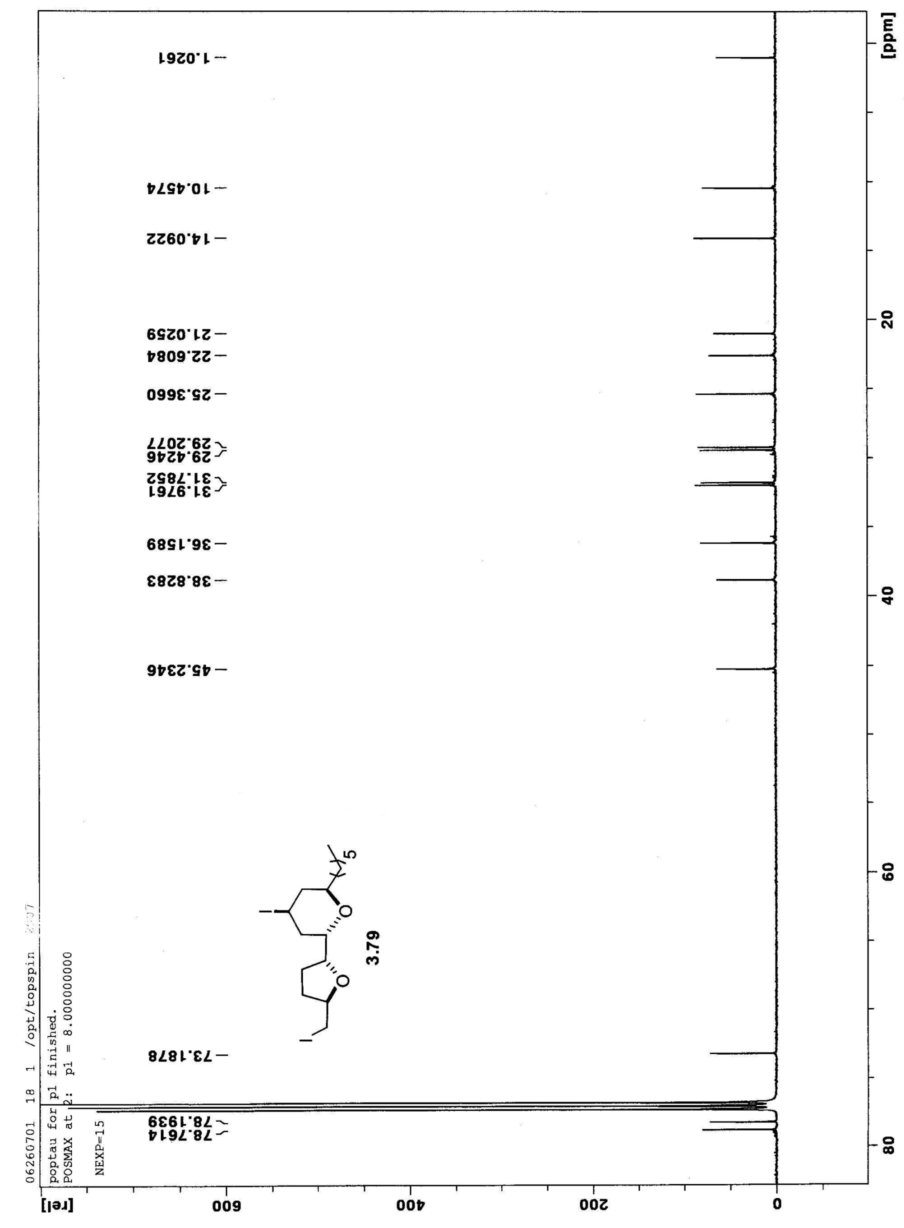




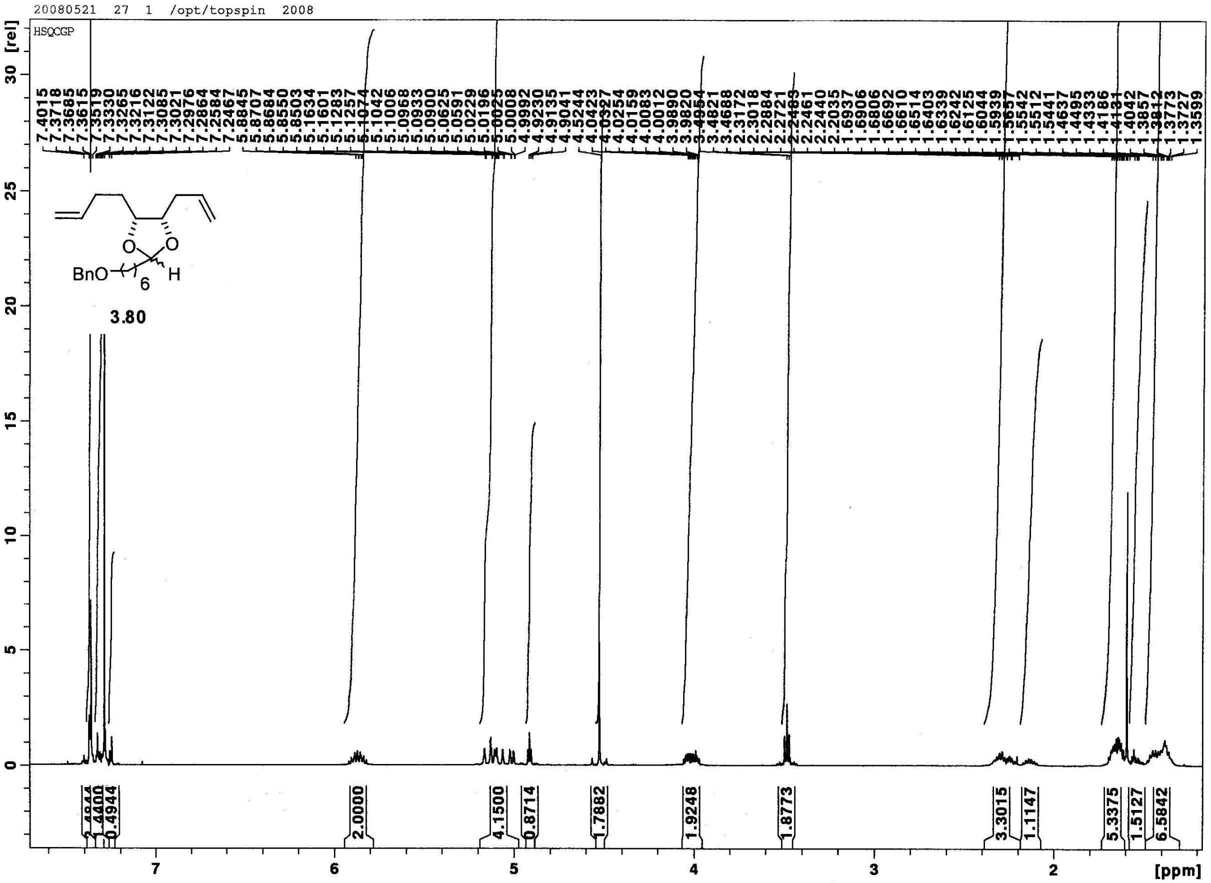
(3.79) COSY



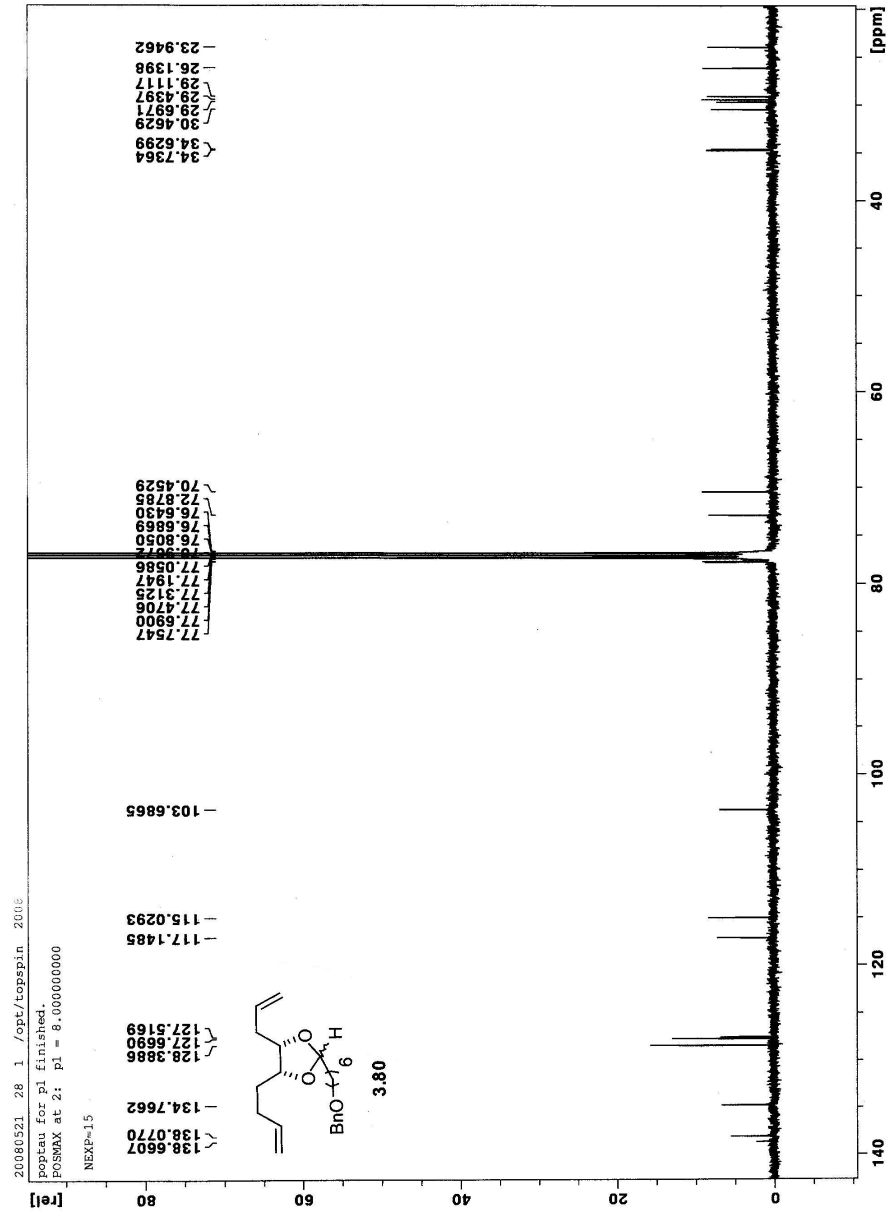
OT030701-10
(3.7a) NOESY

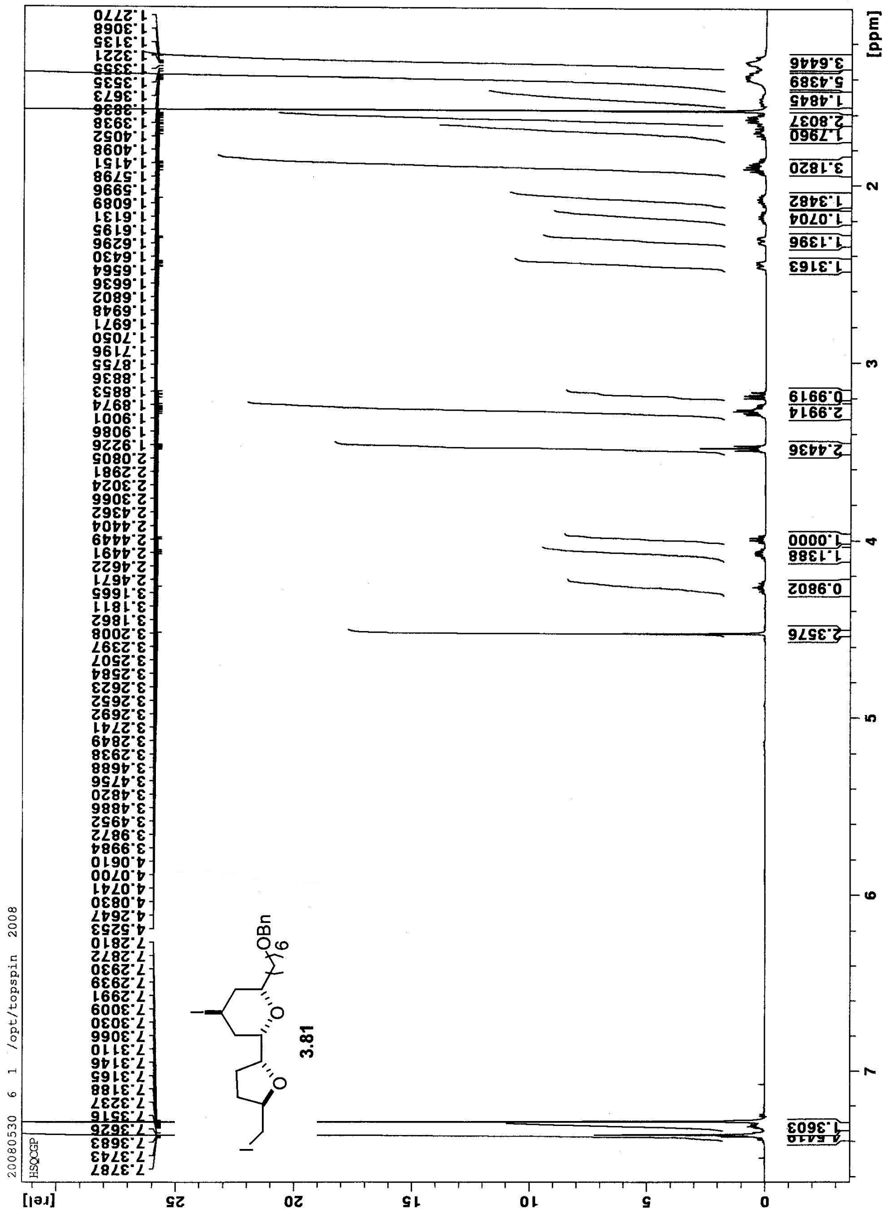

06260701 18 1 /opt/topspin
poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
1.0261
10.4574
14.0922
21.0259
22.6084
25.3660
29.2077
29.4246
31.7852
31.9761
36.1589
38.8283
45.2346
73.1878
78.1939
78.7614
5
80
60
40
20
[ppm]
0
200
400
600
[rel]

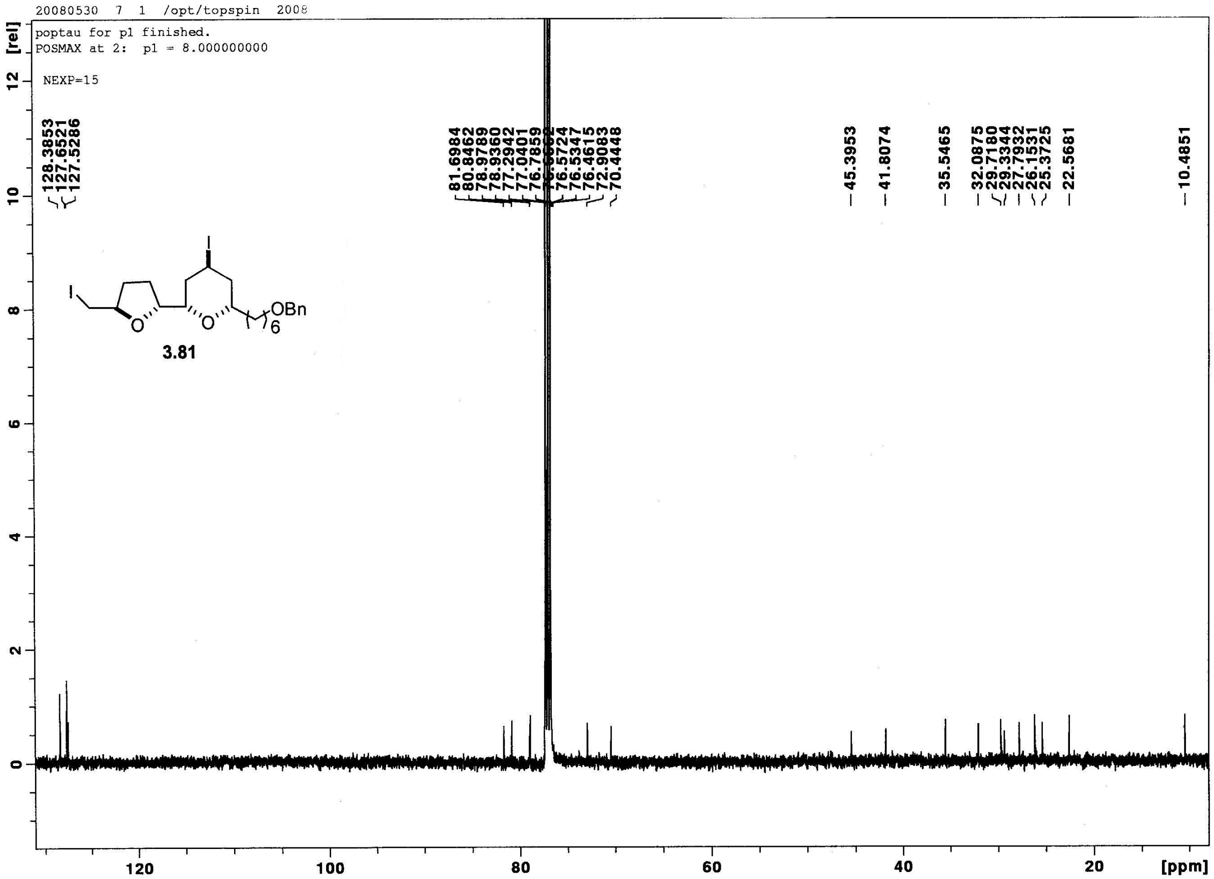
3.79

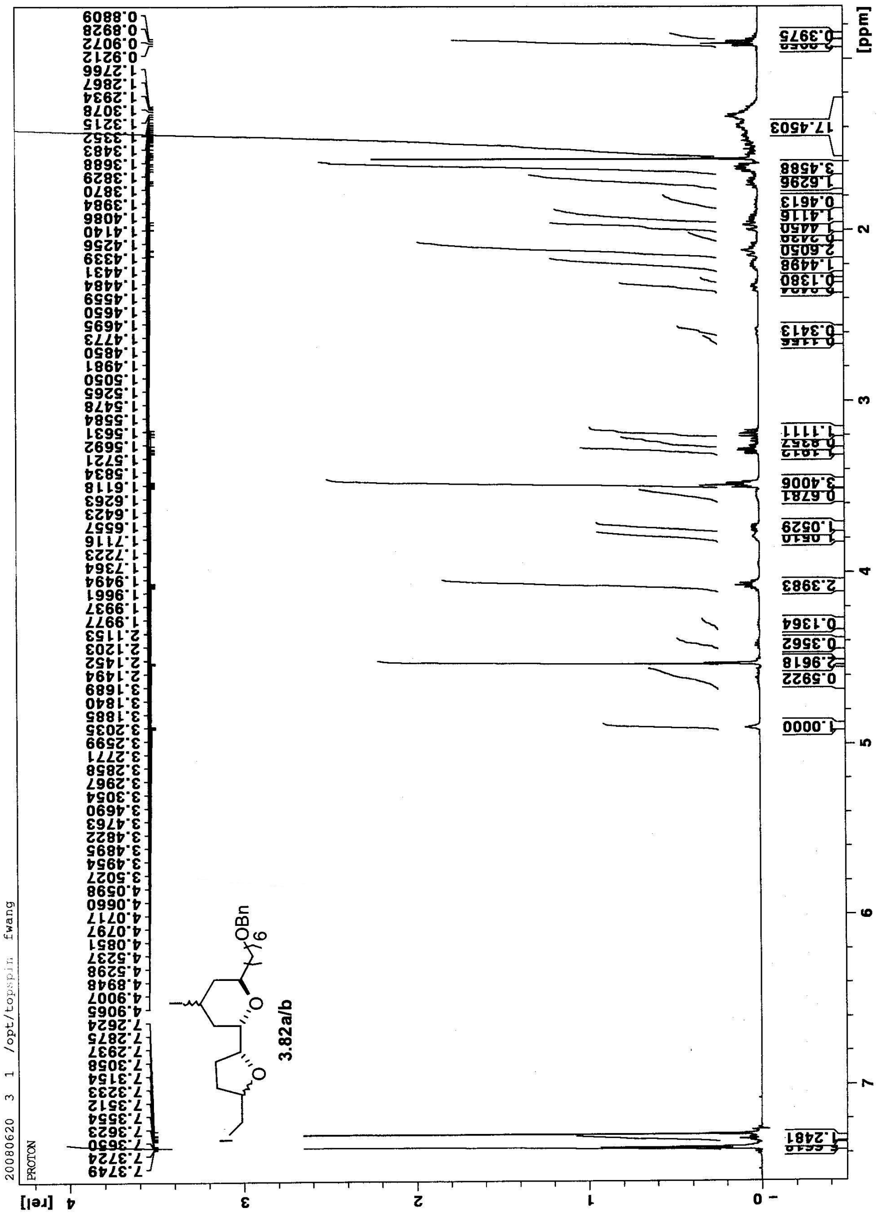

20080521 27 1 /opt/topspin 2008
HSQCGP
7.4015
7.3718
7.3685
7.3615
7.3519
7.3330
7.3265
7.3216
7.3122
7.3085
7.3021
7.2976
7.2864
7.2584
7.2467
5.8845
5.8707
5.8684
5.8550
5.8503
5.1634
5.1601
5.1283
5.1257
5.1074
5.1042
5.1006
5.0968
5.0933
5.0900
5.0625
5.0591
5.0229
5.0196
5.0025
5.0008
4.9992
4.9230
4.9135
4.9041
4.5244
4.0423
4.0327
4.0254
4.0159
4.0083
4.0012
3.9890
3.9820
3.4954
3.4821
3.4688
2.3172
2.3018
2.2884
2.2721
2.2483
2.2461
2.2440
2.2035
1.6937
1.6906
1.6806
1.6692
1.6610
1.6514
1.6403
1.6339
1.6242
1.6125
1.6044
1.5939
1.5657
1.5542
1.5512
1.5441
1.4637
1.4495
1.4333
1.4186
1.4131
1.4042
1.3857
1.3812
1.3773
1.3727
1.3599
BnO
O
O
6
H
1.4400
0.4944
2.0000
4.1500
0.8714
1.7882
1.9248
1.8773
3.3015
1.1147
5.3375
1.5127
6.5842
[rel]
30
25
20
15
10
5
0
7
6
5
4
3
2
[ppm]

3.80

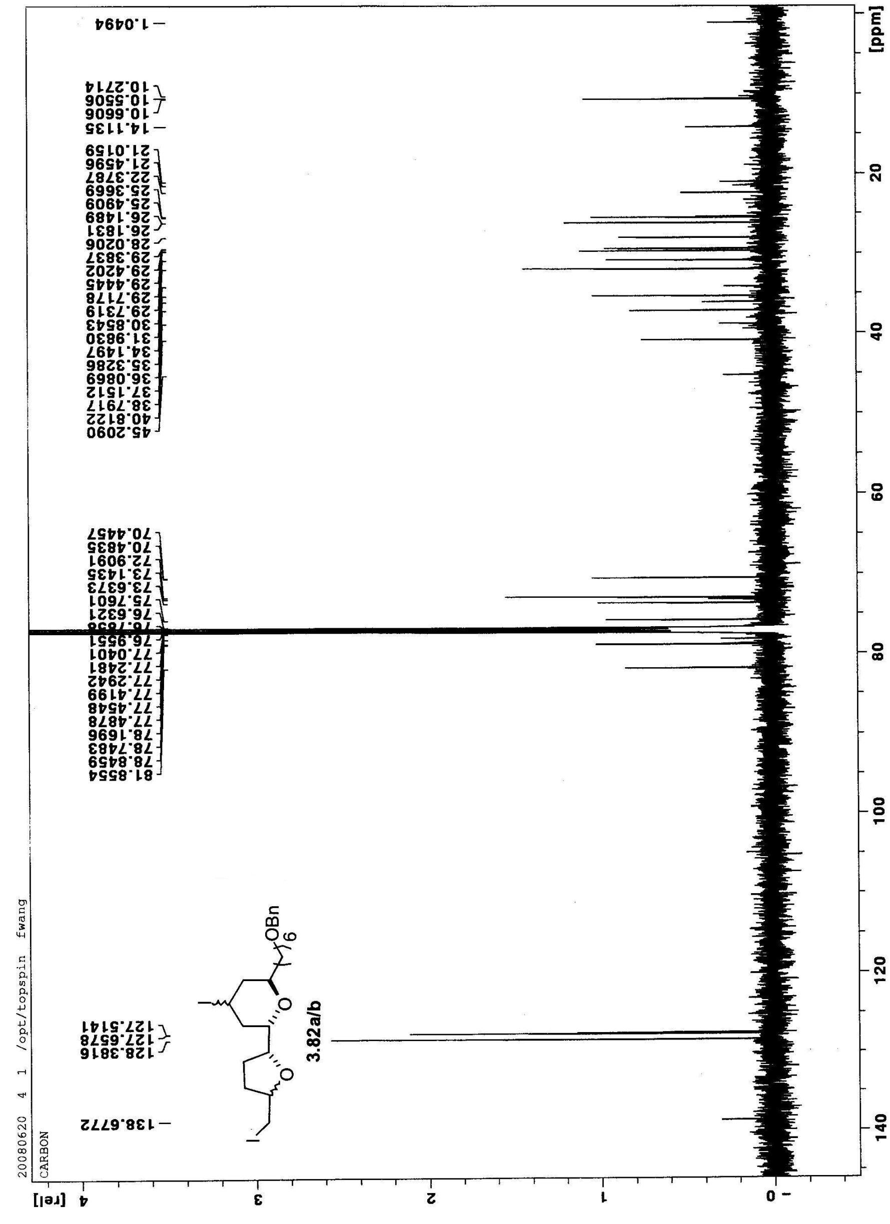

20080521 28 1 /opt/topspin 2008
poptau for p1 finished.
POSMAX at 2: p1 = 8.00000000
NEXP=15
138.6607
138.0770
134.7662
128.3886
127.6690
127.5169
117.1485
115.0293
103.6865
77.7547
77.6900
77.4706
77.3125
77.1947
77.0586
76.9872
76.8050
76.6869
76.6430
72.8785
70.4529
34.7364
34.6299
30.4629
29.6971
29.4397
29.1117
26.1398
23.9462
BnO
O
O
H
6
3.80
140
120
100
80
60
40
[ppm]
[rel]
80
60
40
20
0


20080530 6 1 /opt/topspin 2008
HSQCGP
3.81
OBn
6
[ppm]
[rel]
0
5
10
15
20
25
1
2
3
4
5
6
7
1.2270
1.3068
1.3135
1.3221
1.3335
1.3535
1.3673
1.3836
1.3938
1.4052
1.4098
1.4151
1.5798
1.5996
1.6089
1.6131
1.6195
1.6296
1.6430
1.6564
1.6636
1.6802
1.6948
1.6971
1.7050
1.7196
1.8755
1.8836
1.8853
1.8974
1.9001
1.9086
1.9226
2.0805
2.2981
2.3024
2.3066
2.4362
2.4404
2.4449
2.4491
2.4622
2.4671
3.1665
3.1811
3.1862
3.2008
3.2397
3.2507
3.2584
3.2623
3.2652
3.2692
3.2741
3.2849
3.2938
3.4688
3.4756
3.4820
3.4886
3.4952
3.9872
3.9984
4.0610
4.0700
4.0741
4.0830
4.2647
4.5253
7.2810
7.2872
7.2930
7.2939
7.2991
7.3009
7.3030
7.3066
7.3110
7.3146
7.3165
7.3188
7.3237
7.3516
7.3626
7.3683
7.3743
7.3787
3.6446
5.4389
1.4845
2.8037
1.7960
3.1820
1.3482
1.0704
1.1396
1.3163
0.9919
2.9914
2.4436
1.0000
1.1388
0.9802
2.3576
1.3603
4.5419

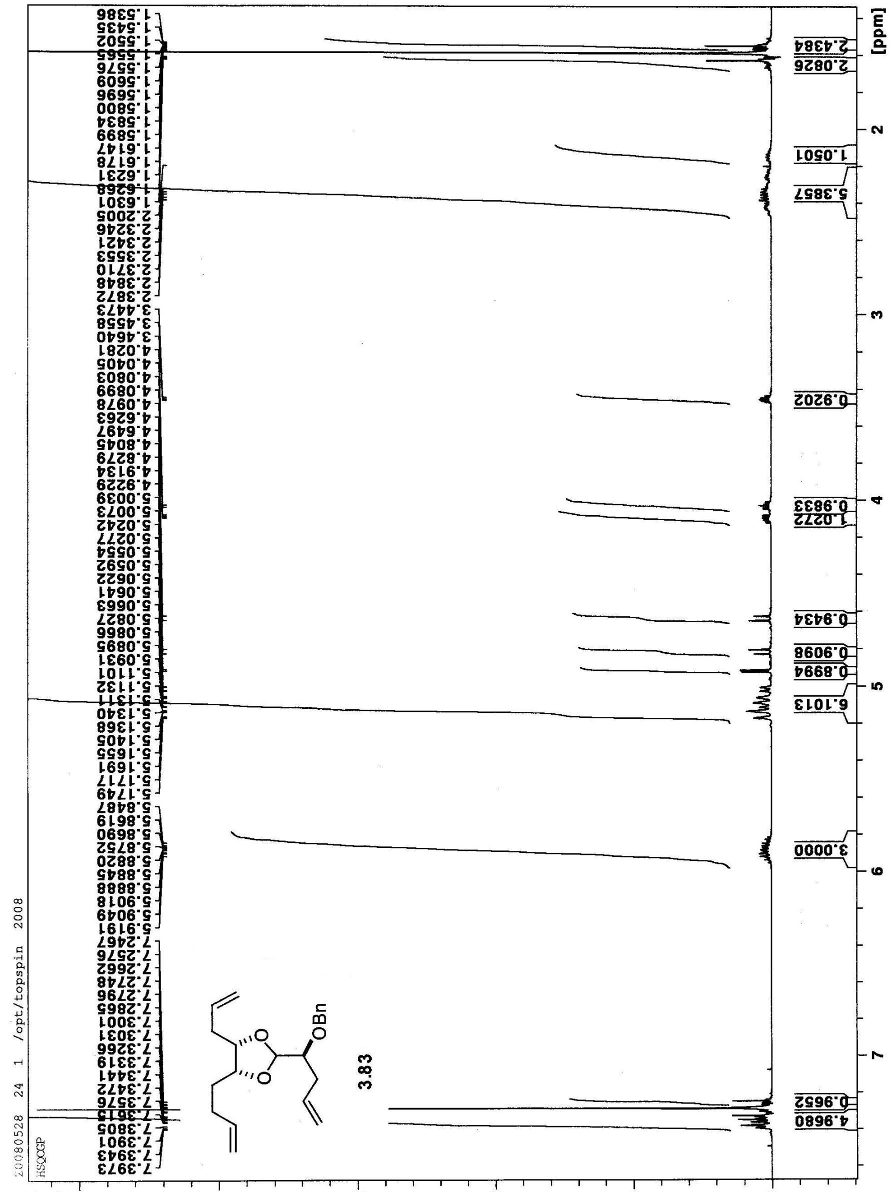

20080530 7 1 /opt/topspin 2008
poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
128.3853
127.6521
127.5286
81.6984
80.8462
78.9789
78.9360
77.2942
77.0401
76.7859
76.5724
76.5347
76.4615
72.9083
70.4448
45.3953
41.8074
35.5465
32.0875
29.7180
29.3344
27.7932
26.1531
25.3725
22.5681
10.4851
I
OBn
6
3.81
[rel]
12
10
8
6
4
2
0
120
100
80
60
40
20
[ppm]


20080620 3 1 /opt/topspin fwang
PROTON
7.3749
7.3724
7.3650
7.3623
7.3554
7.3512
7.3233
7.3154
7.3058
7.2937
7.2875
7.2624
4.9065
4.9007
4.8948
4.5298
4.5237
4.0851
4.0797
4.0717
4.0660
4.0598
3.5027
3.4954
3.4895
3.4822
3.4763
3.4690
3.3054
3.2967
3.2858
3.2771
3.2599
3.2035
3.1885
3.1840
3.1689
2.1494
2.1452
2.1203
2.1153
1.9977
1.9837
1.9661
1.9494
1.7364
1.7223
1.7116
1.6557
1.6423
1.6263
1.6118
1.5834
1.5721
1.5692
1.5631
1.5584
1.5478
1.5265
1.5050
1.4981
1.4850
1.4773
1.4695
1.4650
1.4559
1.4484
1.4431
1.4339
1.4256
1.4140
1.4086
1.3984
1.3870
1.3829
1.3688
1.3483
1.3352
1.3215
1.3078
1.2934
1.2867
1.2766
0.9212
0.9072
0.8928
0.8809
OBn
6
O
O
1.2481
1.0000
0.5922
2.9618
0.3562
0.1364
2.3983
1.0529
0.6781
3.4006
1.1111
0.3413
0.1380
1.4498
2.6050
1.4116
0.4613
1.6296
3.4588
17.4503
0.3975
7
6
5
4
3
2
1
[ppm]
0
1
2
3
4 [rel]

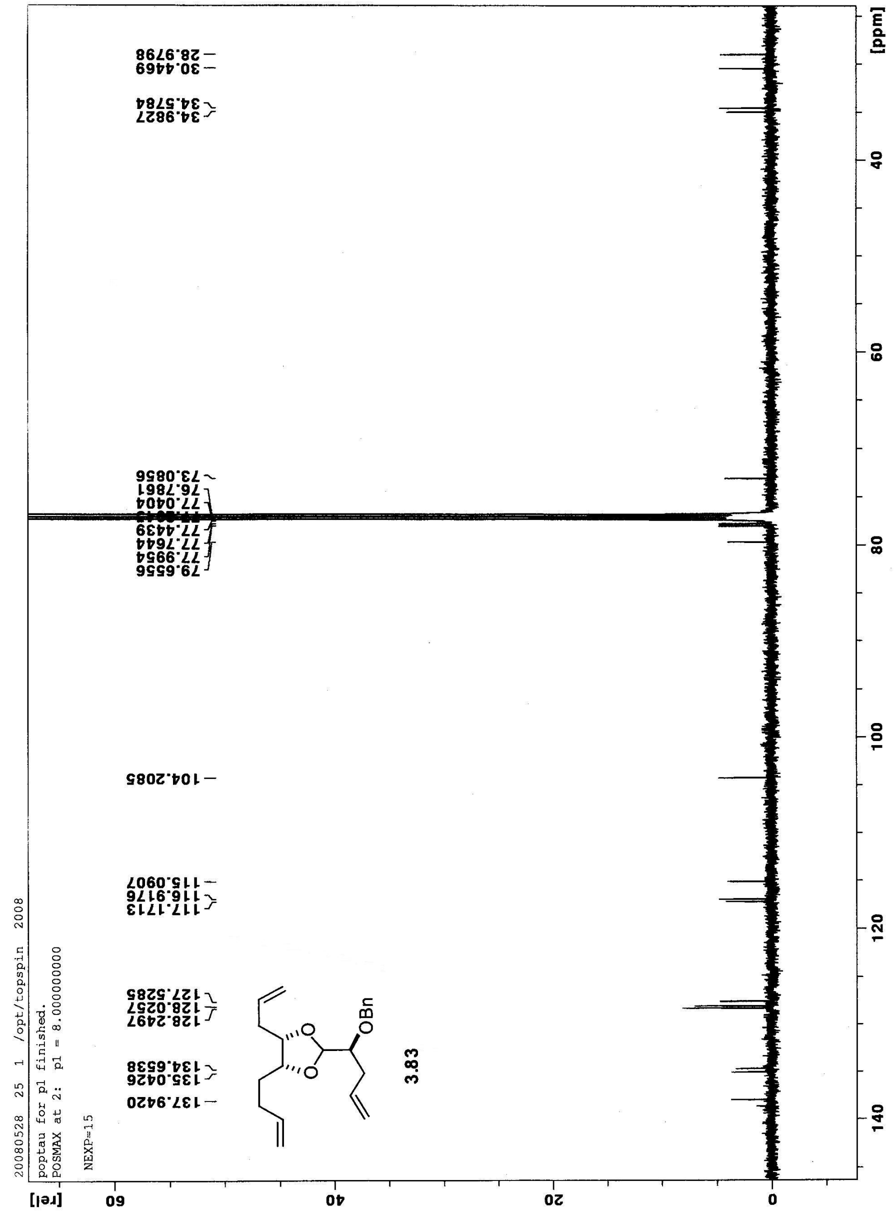
3.82a/b

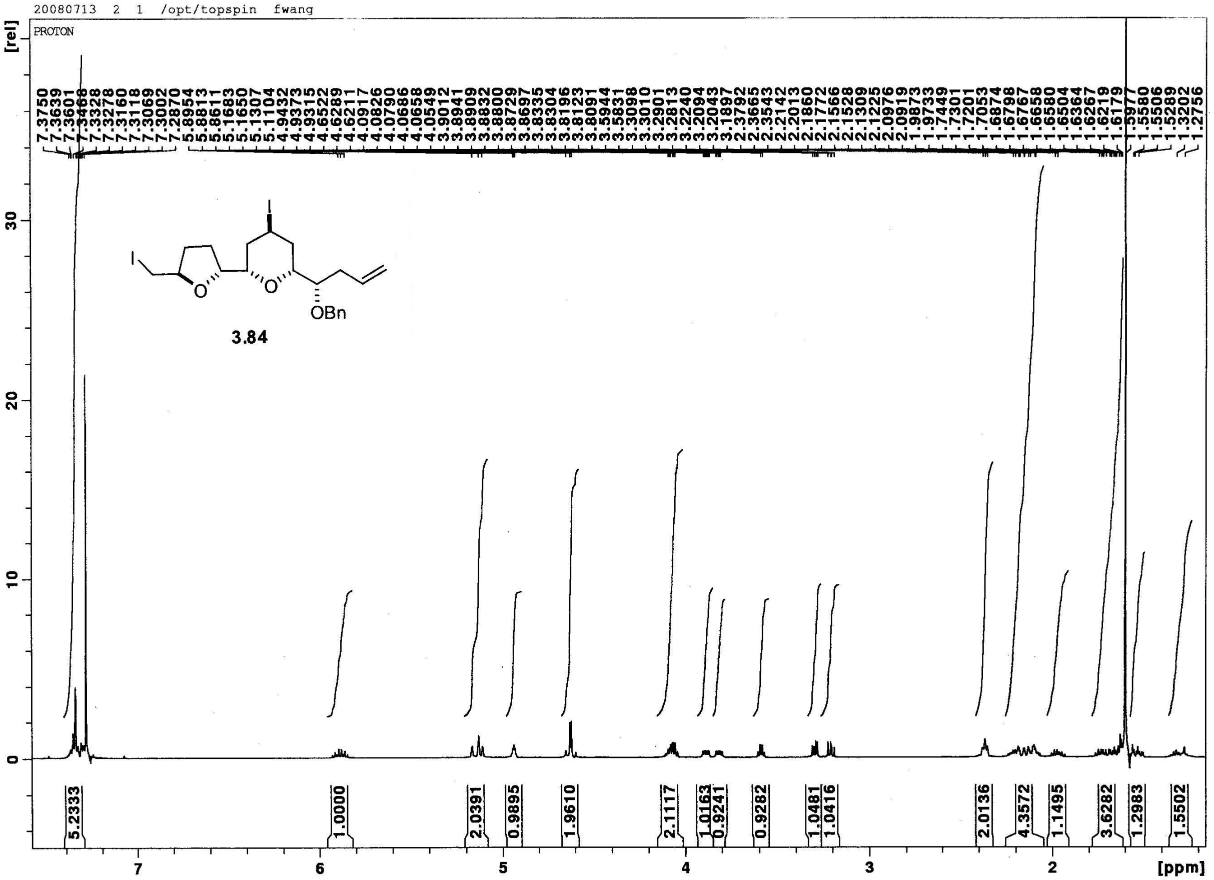

3.82a/b

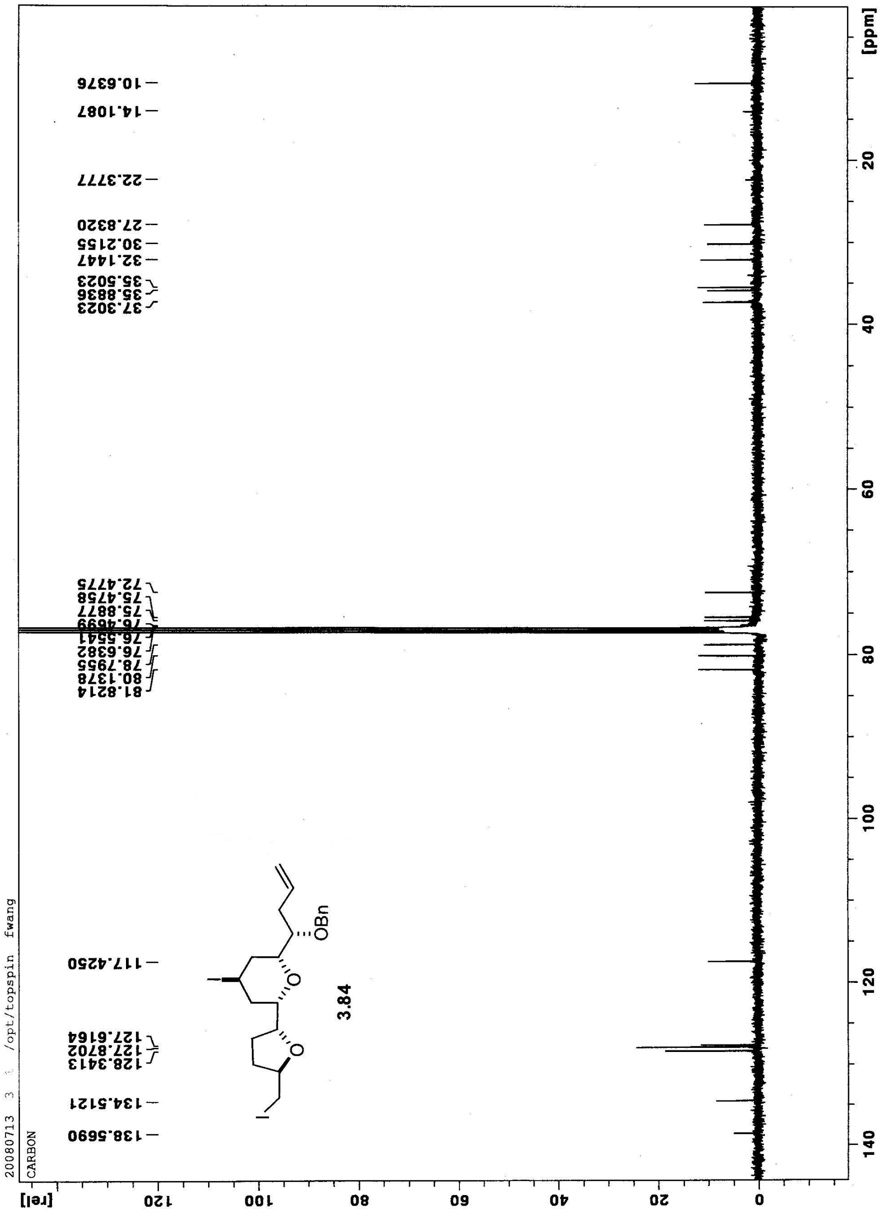
20080620 4 1 /opt/topspin fwang
CARBON
138.6772
128.3816
127.6578
127.5141
81.8554
78.8459
78.7483
78.1696
77.4878
77.4548
77.4199
77.2942
77.2481
77.0401
76.9551
76.6321
75.7601
73.6373
73.1435
72.9091
70.4835
70.4457
45.2090
40.8122
38.7917
37.1512
36.0869
35.3286
34.1497
31.9830
30.8543
29.7319
29.7178
29.4445
29.4202
29.3837
28.0206
26.1831
26.1489
25.4909
25.3669
22.3787
21.4596
21.0159
14.1135
10.6606
10.5506
10.2714
1.0494
OBn
6
O
O
I
0
1
2
3
4
[rel]
140
120
100
80
60
40
20
[ppm]


20080528 24 1 /opt/topspin 2008
HSQCCP
7.3973
7.3943
7.3901
7.3805
7.3615
7.3576
7.3472
7.3441
7.3319
7.3266
7.3031
7.3001
7.2865
7.2796
7.2748
7.2662
7.2576
7.2467
5.9191
5.9049
5.9018
5.8888
5.8845
5.8820
5.8752
5.8690
5.8619
5.8487
5.1749
5.1717
5.1691
5.1655
5.1405
5.1368
5.1340
5.1311
5.1132
5.1101
5.0931
5.0895
5.0866
5.0827
5.0663
5.0641
5.0622
5.0592
5.0554
5.0277
5.0242
5.0073
5.0039
4.9229
4.9134
4.8279
4.8045
4.6497
4.6263
4.0978
4.0899
4.0803
4.0405
4.0281
3.4640
3.4558
3.4473
2.3872
2.3848
2.3710
2.3553
2.3421
2.3246
2.2005
1.6301
1.6268
1.6231
1.6178
1.6147
1.5899
1.5834
1.5800
1.5696
1.5609
1.5576
1.5565
1.5502
1.5435
1.5386
O
O
OBn
4.9680
0.9652
3.0000
6.1013
0.8994
0.9098
0.9434
1.0272
0.9833
0.9202
5.3857
1.0501
2.0826
2.4384
7
6
5
4
3
2
[ppm]
25 [rel]
20
15
10
5
0

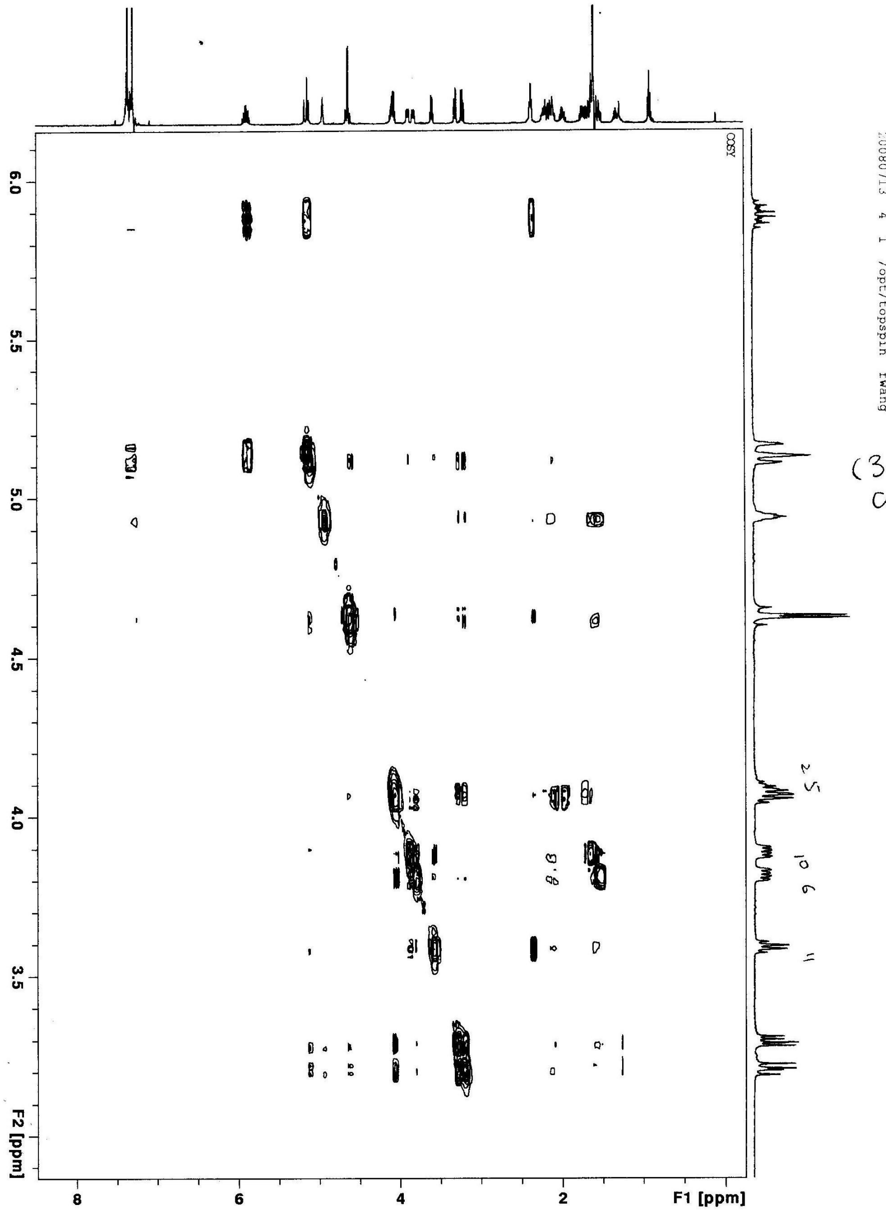
3.83


20080528 25 1 /opt/topspin 2008
poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
137.9420
135.0426
134.6538
128.2497
128.0257
127.5285
117.1713
116.9176
115.0907
104.2085
79.6556
77.9954
77.7644
77.4439
77.0404
76.7861
73.0856
34.9827
34.5784
30.4469
28.9798
O
O
OBn
3.83
[ppm]
140
120
100
80
60
40
[rel]
60
40
20
0

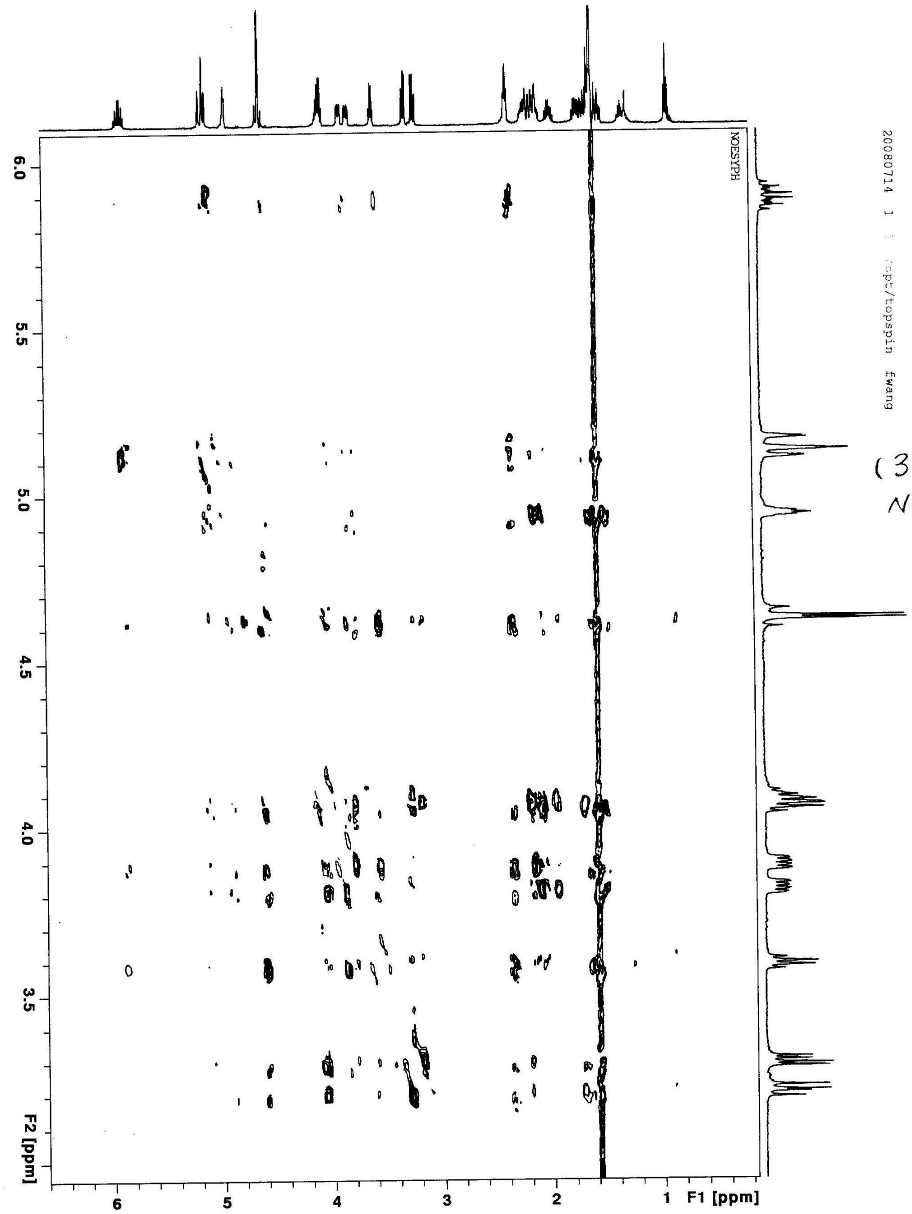

20080713 2 1 /opt/topspin fwang
PROTON
3.84
OBn
O
O
I
7.3750
7.3639
7.3601
7.3468
7.3328
7.3278
7.3160
7.3118
7.3069
7.3002
7.2870
5.8954
5.8813
5.8611
5.1683
5.1650
5.1307
5.1104
4.9432
4.9373
4.9315
4.6522
4.6289
4.6211
4.0917
4.0826
4.0790
4.0686
4.0658
4.0549
3.9012
3.8941
3.8909
3.8832
3.8800
3.8729
3.8697
3.8335
3.8304
3.8196
3.8123
3.8091
3.5944
3.5831
3.3098
3.3010
3.2901
3.2813
3.2240
3.2094
3.2043
3.1897
2.3792
2.3665
2.3543
2.2142
2.2013
2.1860
2.1772
2.1566
2.1528
2.1309
2.1225
2.0976
2.0919
1.9873
1.9733
1.7449
1.7301
1.7201
1.7053
1.6874
1.6798
1.6767
1.6658
1.6580
1.6504
1.6364
1.6267
1.6219
1.6179
1.5977
1.5580
1.5506
1.5289
1.3202
1.2756
5.2333
1.0000
2.0391
0.9895
1.9610
2.1117
1.0163
0.9241
0.9282
1.0481
1.0416
2.0136
4.3572
1.1495
3.6282
1.2983
1.5502
[rel]
30
20
10
0
7
6
5
4
3
2
[ppm]


20080713 3 /opt/topspin fwang
CARBON
138.5690
134.5121
128.3413
127.8702
127.6164
117.4250
81.8214
80.1378
78.7955
76.6382
76.5541
76.4699
75.8877
75.4758
72.4775
37.3023
35.8836
35.5023
32.1447
30.2155
27.8320
22.3777
14.1087
10.6376
O
O
OBn
[ppm]
140
120
100
80
60
40
20
[rel]
120
100
80
60
40
20
0

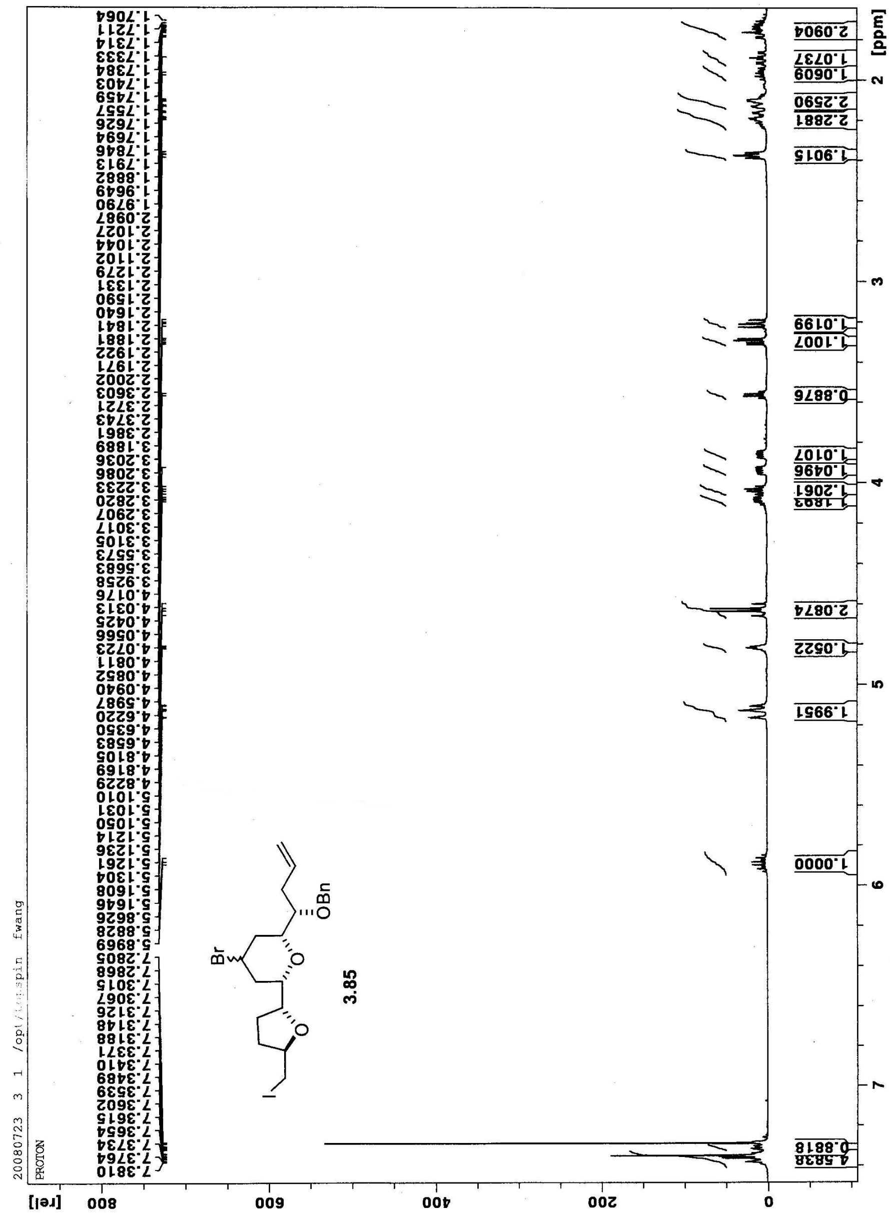
3.84


COSY
20080713 4 1 /opt/topspin fwang
6.0
5.5
5.0
4.5
4.0
3.5
F2 [ppm]
8
6
4
2
F1 [ppm]
2 5
10
9
11

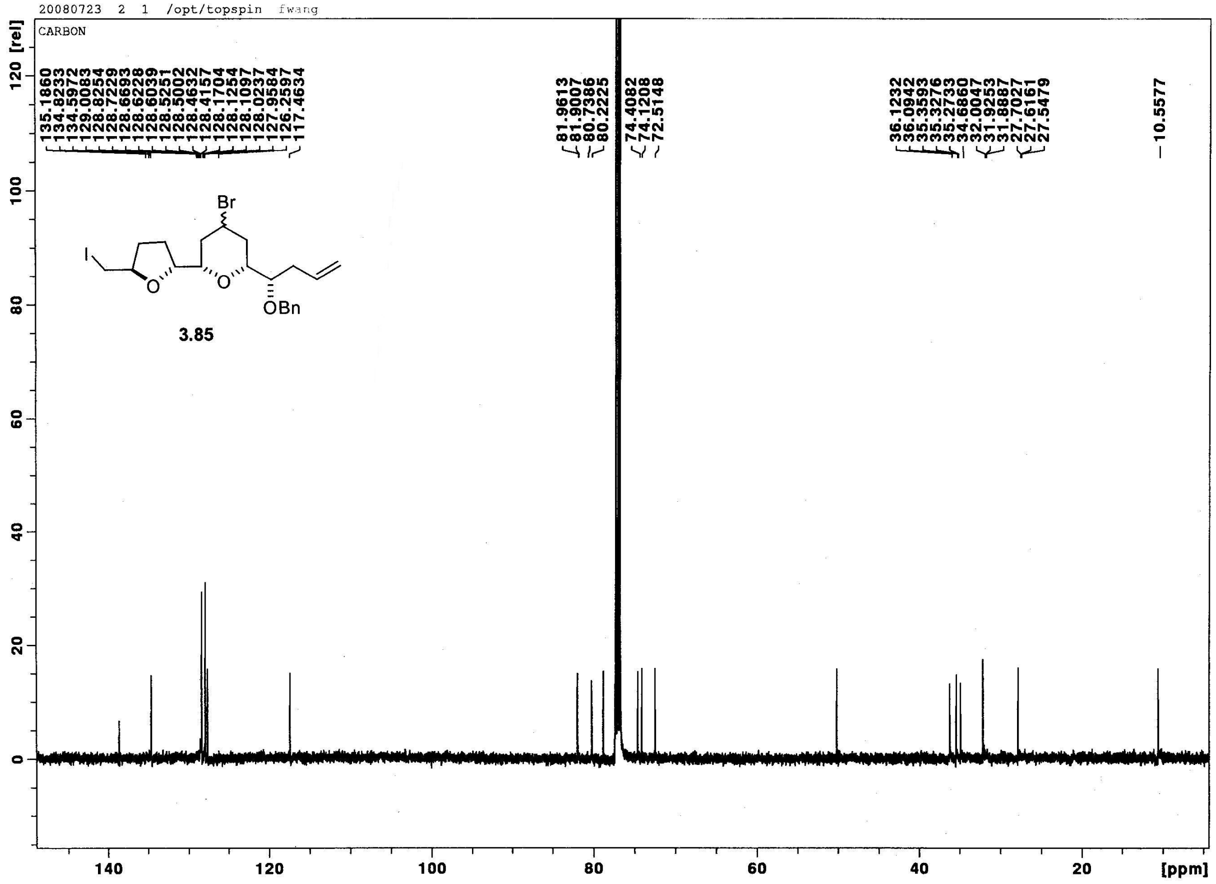
(3.84)
COSY

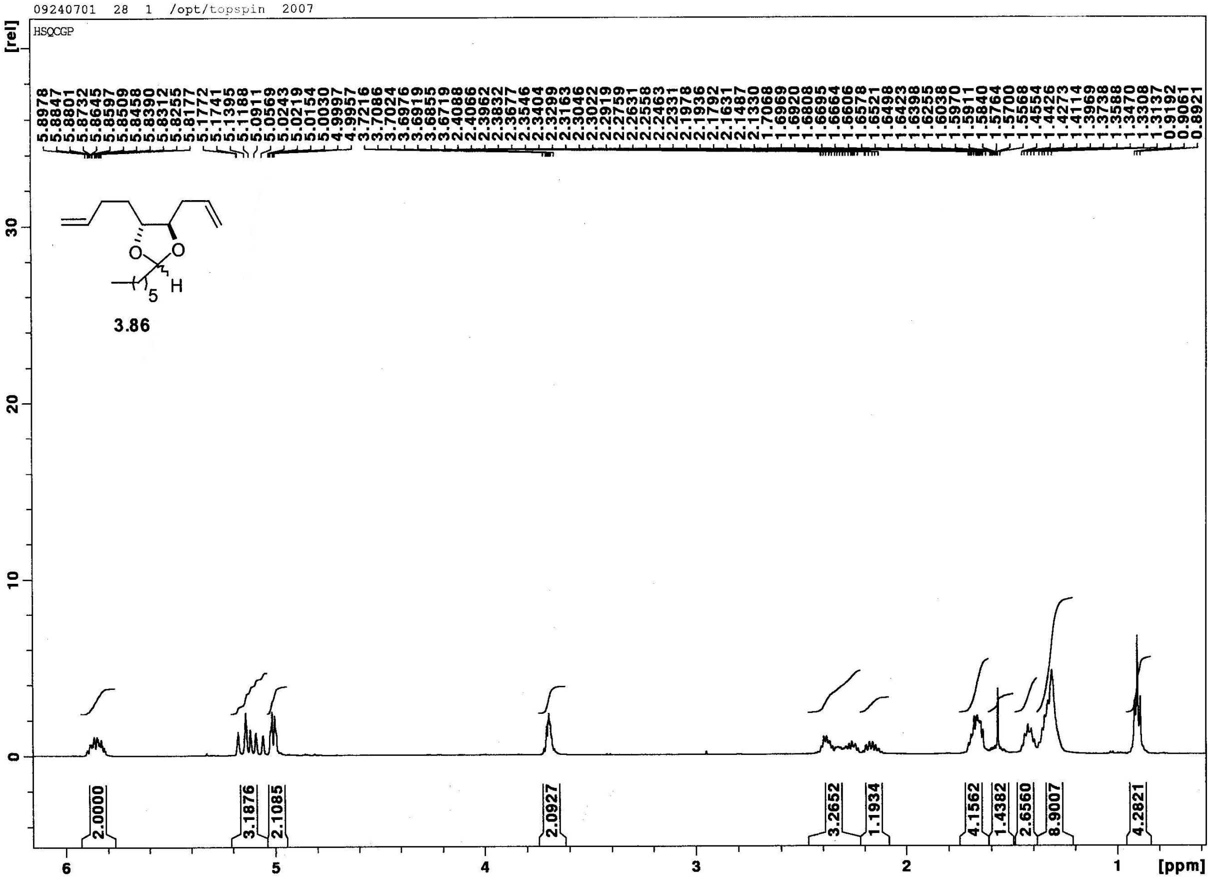

20080714 1 1 /opt/topspin fwang
NOESYPH
6.0
5.5
5.0
4.5
4.0
3.5
F2 [ppm]
6
5
4
3
2
1
F1 [ppm]

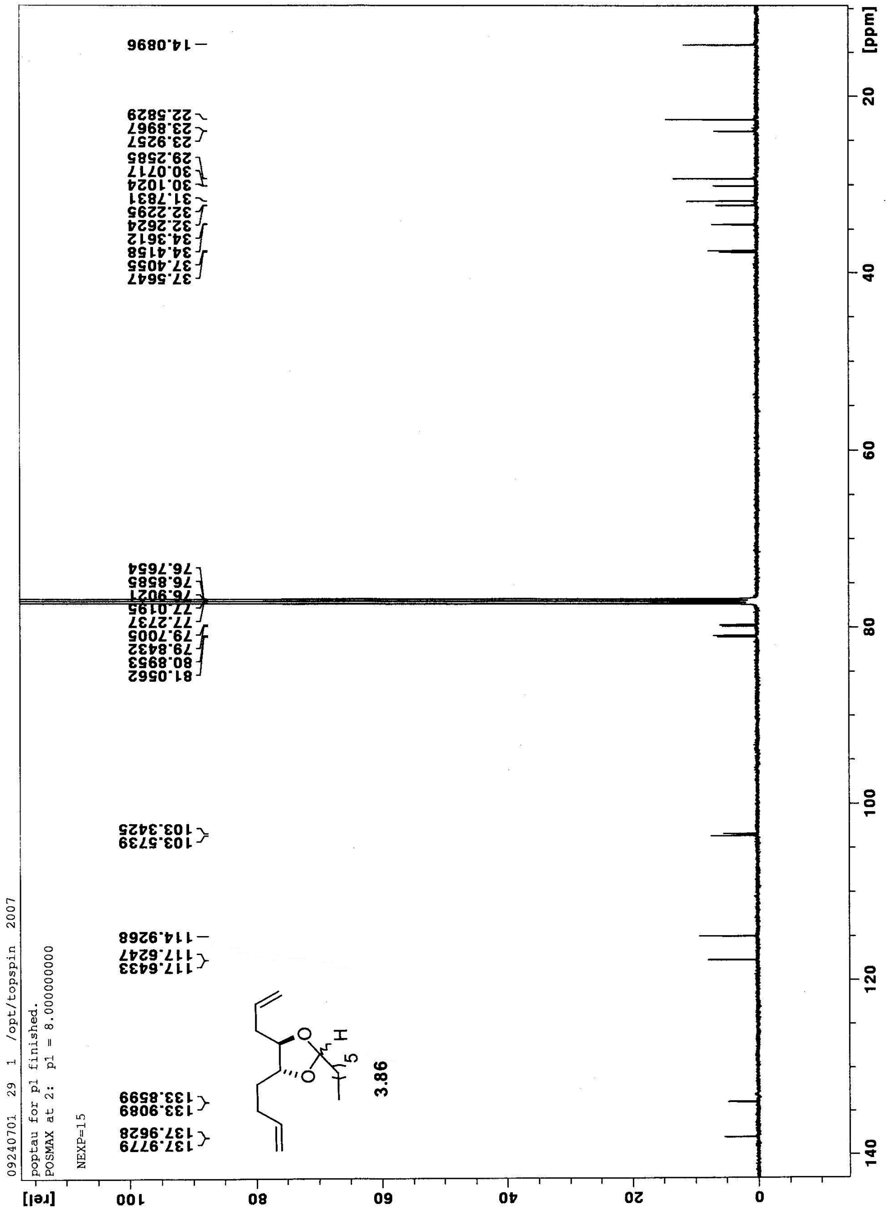
(3.84)
NOESY


20080723 3 1 /opt/topspin fwang
PROTON
7.3810
7.3764
7.3734
7.3654
7.3615
7.3602
7.3539
7.3489
7.3410
7.3371
7.3188
7.3148
7.3126
7.3067
7.3015
7.2868
7.2805
5.8969
5.8828
5.8626
5.1646
5.1608
5.1304
5.1261
5.1236
5.1214
5.1050
5.1031
5.1010
4.8229
4.8169
4.8105
4.6583
4.6350
4.6220
4.5987
4.0940
4.0852
4.0811
4.0723
4.0566
4.0425
4.0313
4.0176
3.9258
3.5683
3.5573
3.3105
3.3017
3.2907
3.2820
3.2233
3.2086
3.2036
3.1889
2.3861
2.3743
2.3721
2.3603
2.2002
2.1971
2.1922
2.1881
2.1841
2.1640
2.1590
2.1331
2.1279
2.1102
2.1044
2.1027
2.0987
1.9790
1.9649
1.8882
1.7913
1.7846
1.7694
1.7626
1.7557
1.7459
1.7403
1.7384
1.7333
1.7314
1.7211
1.7064
Br
O
O
OBn
I
4.5838
0.8818
1.0000
1.9951
1.0522
2.0874
1.1893
1.2061
1.0496
1.0107
0.8876
1.1007
1.0199
1.9015
2.2881
2.2590
1.0609
1.0737
2.0904
800
600
400
200
0
[rel]
7
6
5
4
3
2
[ppm]

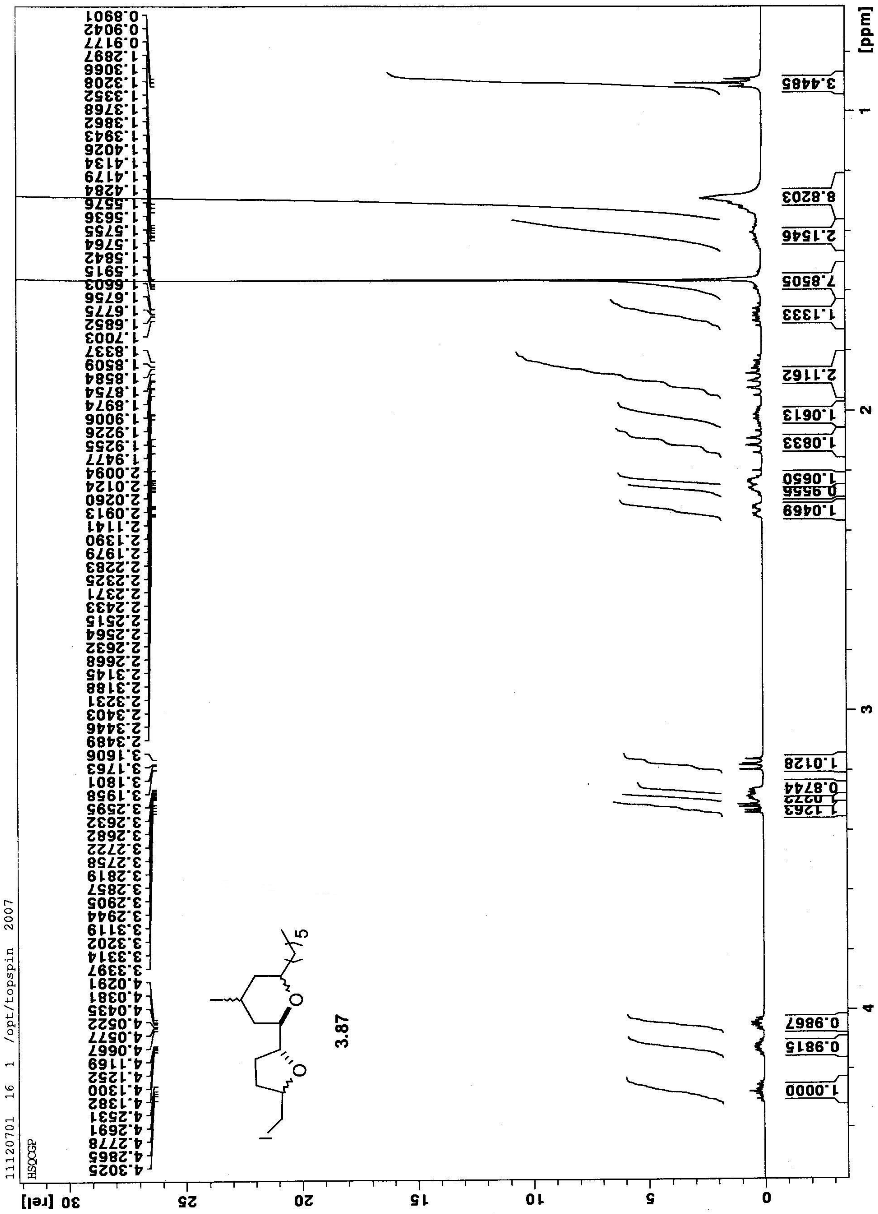
3.85


20080723 2 1 /opt/topspin fwang
CARBON
135.1860
134.8233
134.5972
129.0083
128.8254
128.7229
128.6693
128.6228
128.6039
128.5251
128.5002
128.4632
128.4157
128.1704
128.1254
128.1097
128.0237
127.9584
126.2597
117.4634
81.9613
81.9007
80.7386
80.2225
74.4082
74.1208
72.5148
36.1232
36.0942
35.3593
35.3276
35.2733
34.6860
32.0047
31.9253
31.8887
27.7027
27.6161
27.5479
10.5577
Br
I
O
O
OBn
3.85
120 [rel]
100
80
60
40
20
0
140
120
100
80
60
40
20
[ppm]

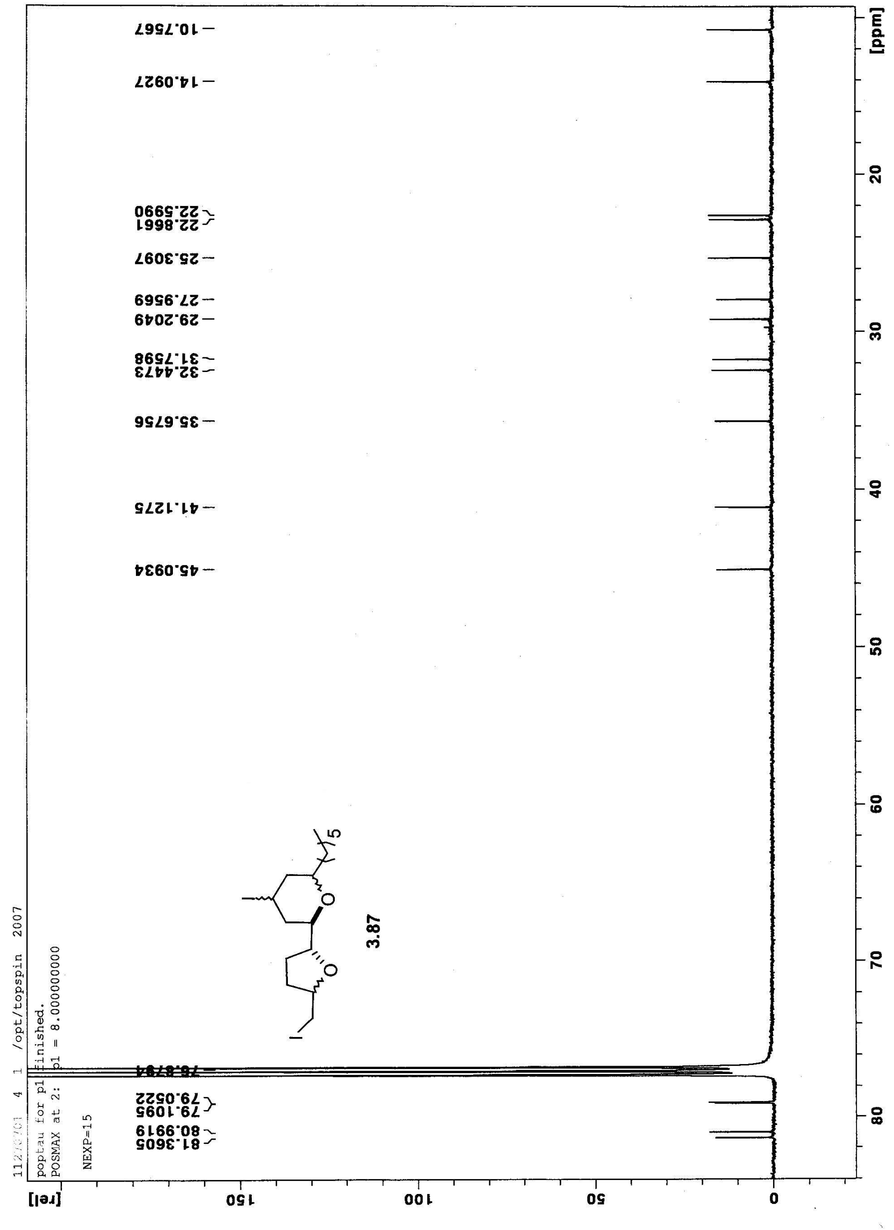

09240701 28 1 /opt/topspin 2007
HSQCGP
5.8978
5.8847
5.8801
5.8732
5.8645
5.8597
5.8509
5.8458
5.8390
5.8312
5.8255
5.8177
5.1772
5.1741
5.1395
5.1188
5.0911
5.0569
5.0243
5.0219
5.0154
5.0030
4.9997
4.9957
3.7216
3.7086
3.7024
3.6976
3.6919
3.6855
3.6719
2.4088
2.4066
2.3962
2.3832
2.3677
2.3546
2.3404
2.3299
2.3163
2.3046
2.3022
2.2919
2.2759
2.2631
2.2558
2.2463
2.2331
2.1978
2.1936
2.1792
2.1631
2.1487
2.1330
1.7068
1.6969
1.6920
1.6808
1.6695
1.6664
1.6606
1.6578
1.6521
1.6498
1.6423
1.6398
1.6255
1.6038
1.5970
1.5911
1.5840
1.5764
1.5700
1.5568
1.4554
1.4426
1.4273
1.4114
1.3969
1.3738
1.3588
1.3470
1.3308
1.3137
0.9192
0.9061
0.8921
O
O
5
H
3.86
[rel]
30
20
10
0
2.0000
3.1876
2.1085
2.0927
3.2652
1.1934
4.1562
1.4382
2.6560
8.9007
4.2821
6
5
4
3
2
1
[ppm]

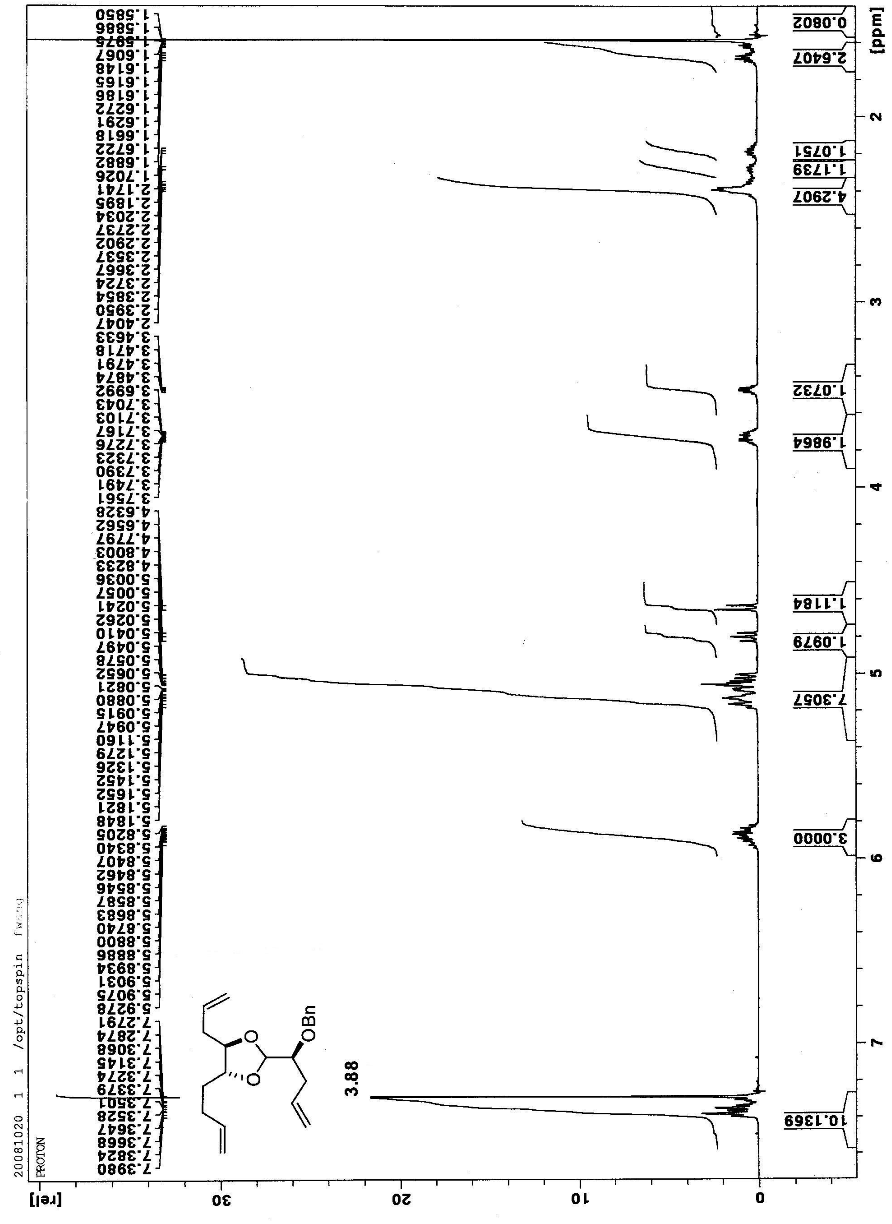

09240701 29 1 /opt/topspin 2007
poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
137.9779
137.9628
133.9089
133.8599
117.6433
117.6247
114.9268
103.5739
103.3425
81.0562
80.8953
79.8432
79.7005
77.2737
77.0195
76.9021
76.8585
76.7654
37.5647
37.4055
34.4158
34.3612
32.2624
32.2295
31.7831
30.1024
30.0717
29.2585
23.9257
23.8967
22.5829
14.0896
H
5
O
O
[rel]
100
80
60
40
20
0
140
120
100
80
60
40
20
[ppm]

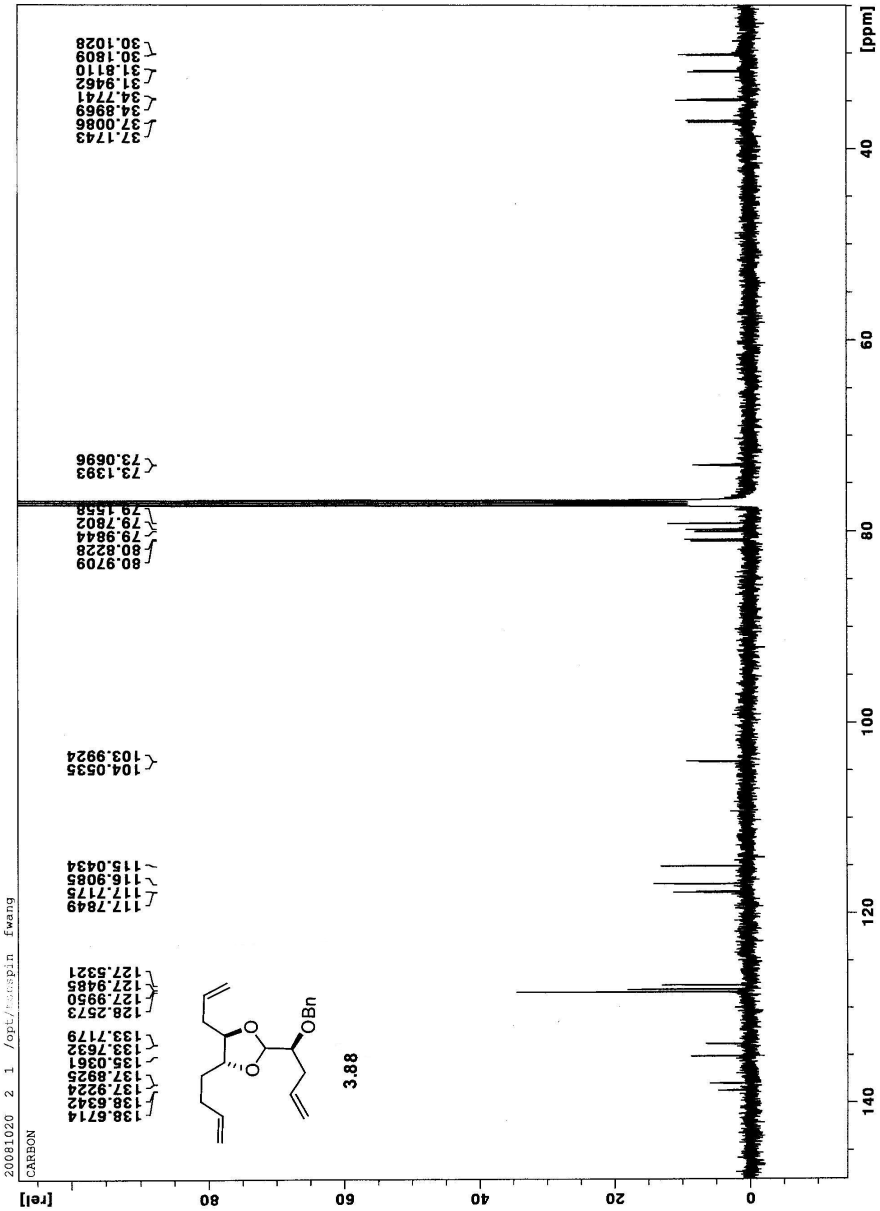
3.86


11120701 16 1 /opt/topspin 2007
HSQCGP
4.3025
4.2865
4.2778
4.2691
4.2531
4.1382
4.1300
4.1252
4.1169
4.0667
4.0577
4.0522
4.0435
4.0381
4.0291
3.3397
3.3314
3.3202
3.3119
3.2944
3.2905
3.2857
3.2819
3.2758
3.2722
3.2682
3.2632
3.2595
3.1958
3.1801
3.1763
3.1606
2.3489
2.3446
2.3403
2.3231
2.3188
2.3145
2.2668
2.2632
2.2564
2.2515
2.2433
2.2371
2.2325
2.2283
2.1979
2.1390
2.1141
2.0913
2.0260
2.0124
2.0094
1.9477
1.9255
1.9226
1.9006
1.8974
1.8754
1.8584
1.8509
1.8337
1.7003
1.6852
1.6775
1.6756
1.6603
1.5915
1.5842
1.5764
1.5755
1.5636
1.5576
1.4284
1.4179
1.4134
1.4026
1.3943
1.3862
1.3768
1.3352
1.3208
1.3066
1.2897
0.9177
0.9042
0.8901
1.0000
0.9815
0.9867
1.1263
1.0222
0.8744
1.0128
1.0469
0.9556
1.0650
1.0833
1.0613
2.1162
1.1333
7.8505
2.1546
8.8203
3.4485
5
4
3
2
1
[ppm]
30 [rel]
25
20
15
10
5
0

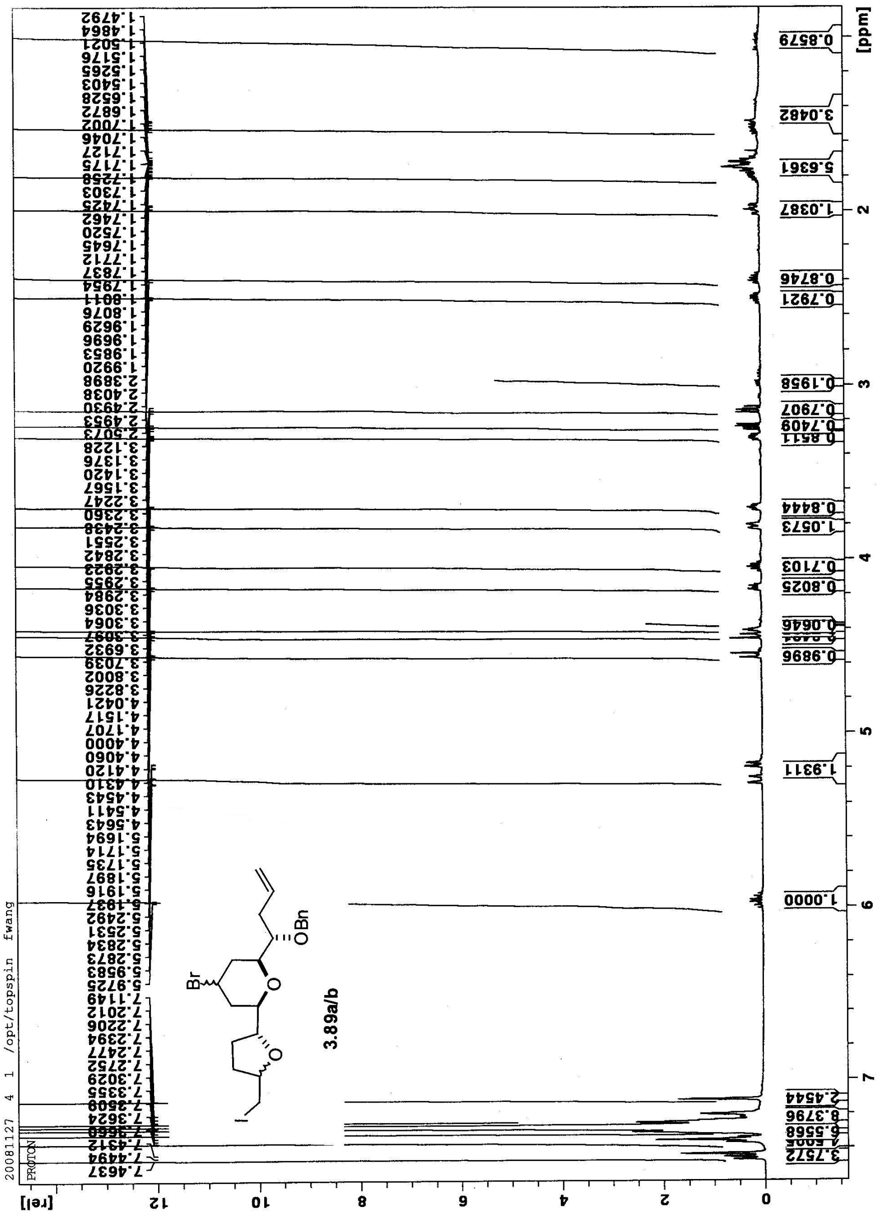
3.87

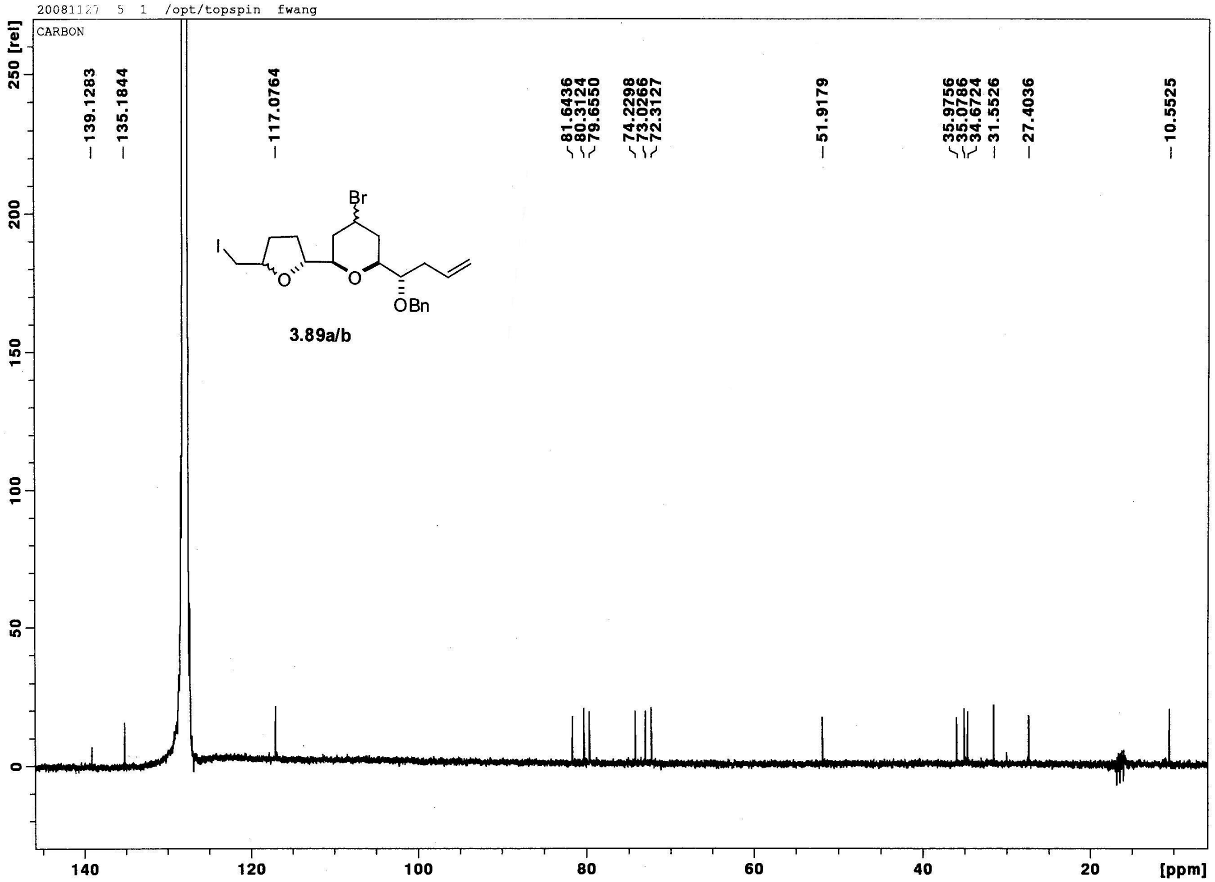

/opt/topspin 2007
poptau for pl finished.
POSMAX at 2: pl = 8.00000000
NEXP=15
10.7567
14.0927
22.5990
22.8661
25.3097
27.9569
29.2049
31.7598
32.4473
35.6756
41.1275
45.0934
76.8784
79.0522
79.1095
80.9919
81.3605
3.87
O
O
5
[ppm]
[rel]
20
30
40
50
60
70
80
0
50
100
150


20081020 1 1 /opt/topspin fwang
PROTON
7.3980
7.3824
7.3668
7.3647
7.3528
7.3501
7.3379
7.3274
7.3145
7.3068
7.2874
7.2791
5.9278
5.9075
5.9031
5.8934
5.8886
5.8800
5.8740
5.8683
5.8587
5.8546
5.8462
5.8407
5.8340
5.8205
5.1848
5.1821
5.1652
5.1452
5.1326
5.1279
5.1160
5.0947
5.0915
5.0880
5.0821
5.0652
5.0578
5.0497
5.0410
5.0262
5.0241
5.0057
5.0036
4.8233
4.8003
4.7797
4.6562
4.6328
3.7561
3.7491
3.7390
3.7323
3.7276
3.7167
3.7103
3.7043
3.6992
3.4874
3.4791
3.4718
3.4633
2.4047
2.3950
2.3854
2.3724
2.3667
2.3537
2.2902
2.2737
2.2034
2.1895
2.1741
1.7026
1.6882
1.6722
1.6618
1.6291
1.6272
1.6186
1.6165
1.6148
1.6067
1.5976
1.5886
1.5850
O
O
OBn
3.88
10.1369
3.0000
7.3057
1.0979
1.1184
1.9864
1.0732
4.2907
1.1739
1.0751
2.6407
0.0802
7
6
5
4
3
2
[ppm]
0
10
20
30
[rel]

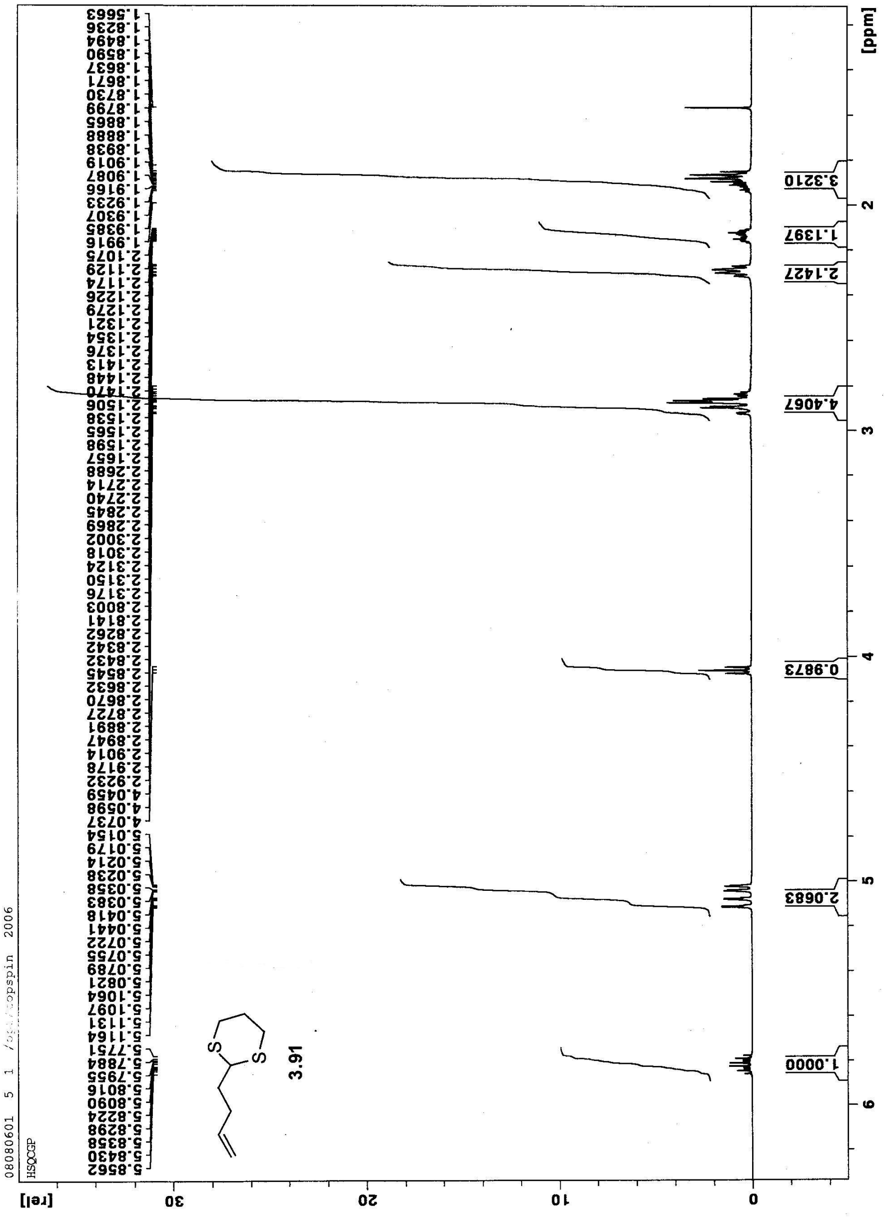

20081020 2 1 /opt/topspin fwang
CARBON
138.6714
138.6342
137.9224
137.8925
135.0361
133.7632
133.7179
128.2573
127.9950
127.9485
127.5321
117.7849
117.7175
116.9085
115.0434
104.0535
103.9924
80.9709
80.8228
79.9844
79.7802
79.1558
73.1393
73.0696
37.1743
37.0086
34.8969
34.7741
31.9462
31.8110
30.1809
30.1028
OBn
140
120
100
80
60
40
[ppm]
[rel]
80
60
40
20
0

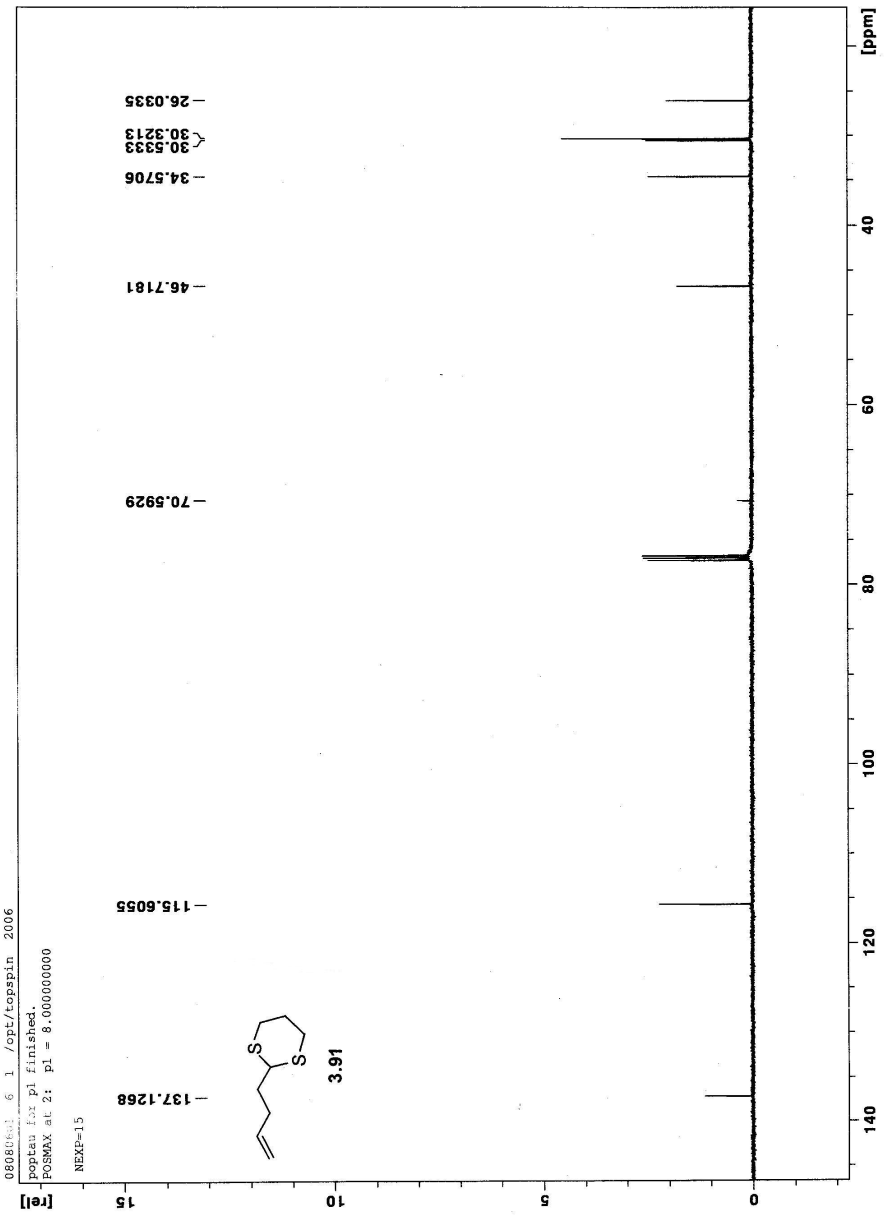
3.88

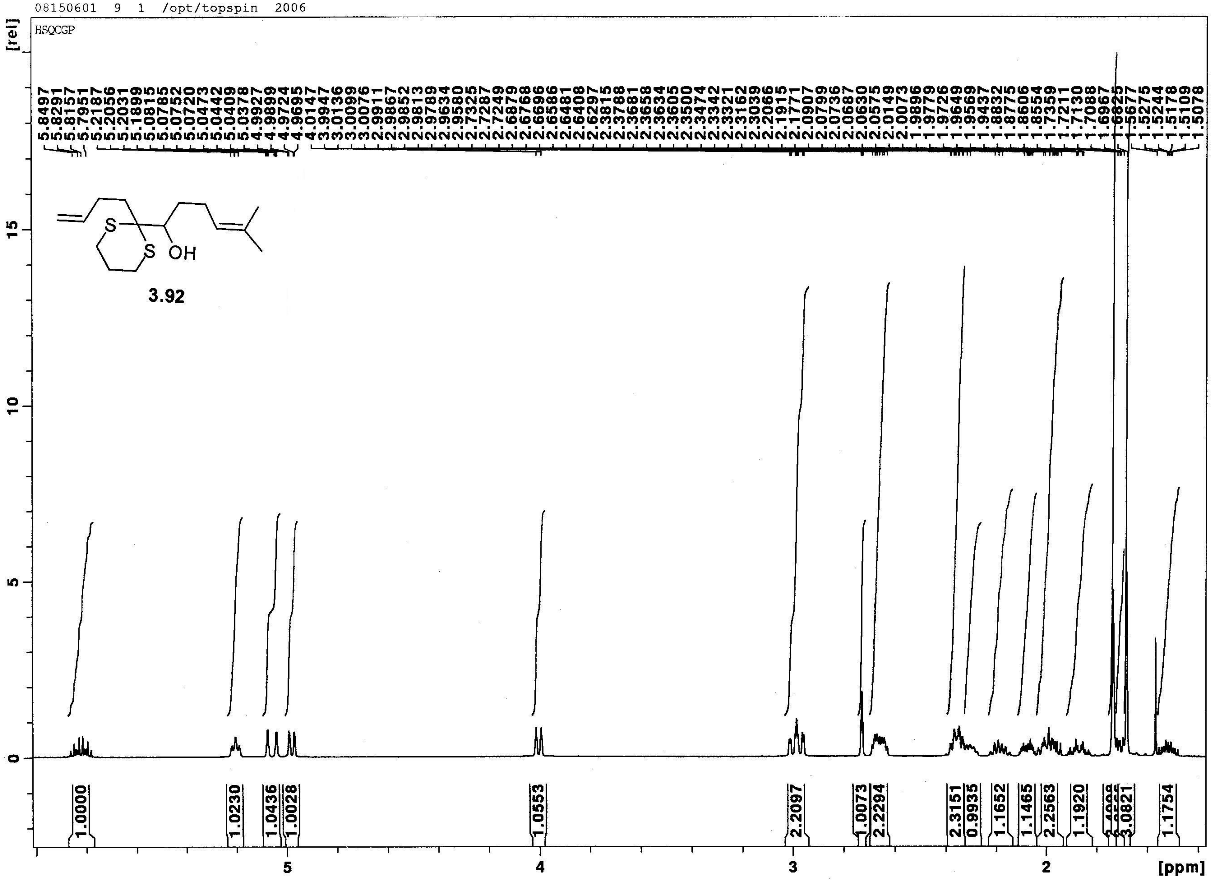

20081127 4 1 /opt/topspin fwang
PROTON
3.89a/b
Br
O
O
OBn
1.4792
1.4864
1.5021
1.5176
1.5265
1.5403
1.6528
1.6872
1.7002
1.7046
1.7127
1.7175
1.7258
1.7303
1.7425
1.7462
1.7520
1.7645
1.7712
1.7837
1.7954
1.8011
1.8076
1.9629
1.9696
1.9853
1.9920
2.3898
2.4038
2.4930
2.4953
2.5073
3.1228
3.1376
3.1420
3.1567
3.2247
3.2360
3.2438
3.2551
3.2842
3.2923
3.2955
3.2984
3.3036
3.3064
3.3097
3.6932
3.7039
3.8002
3.8226
4.0421
4.1517
4.1707
4.4000
4.4060
4.4120
4.4310
4.4543
4.5411
4.5643
5.1694
5.1714
5.1735
5.1897
5.1916
5.1937
5.2492
5.2531
5.2834
5.2873
5.9583
5.9725
7.1149
7.2012
7.2206
7.2394
7.2477
7.2752
7.3029
7.3355
7.3509
7.3624
7.3660
7.4312
7.4494
7.4637
0.8579
3.0482
5.6361
1.0387
0.8746
0.7921
0.1958
0.7907
0.7409
0.8511
0.8444
1.0573
0.7103
0.8025
0.0646
0.9896
1.9311
1.0000
2.4544
8.3796
6.5568
3.7572
[ppm]
2
3
4
5
6
7
[rel]
12
10
8
6
4
2
0


20081127 5 1 /opt/topspin fwang
CARBON
139.1283
135.1844
117.0764
81.6436
80.3124
79.6550
74.2298
73.0266
72.3127
51.9179
35.9756
35.0786
34.6724
31.5526
27.4036
10.5525
Br
I
O
O
OBn
250 [rel]
200
150
100
50
0
140
120
100
80
60
40
20
[ppm]

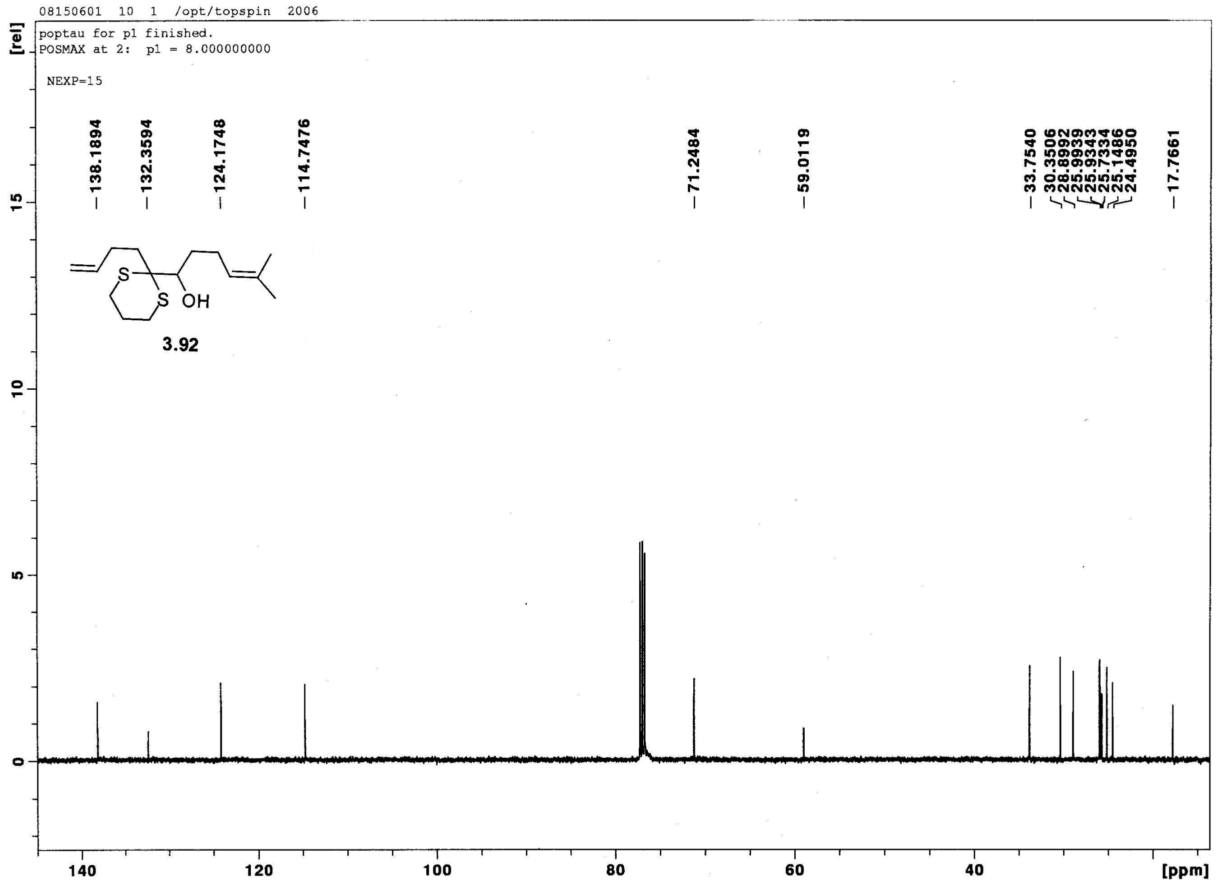
3.89a/b

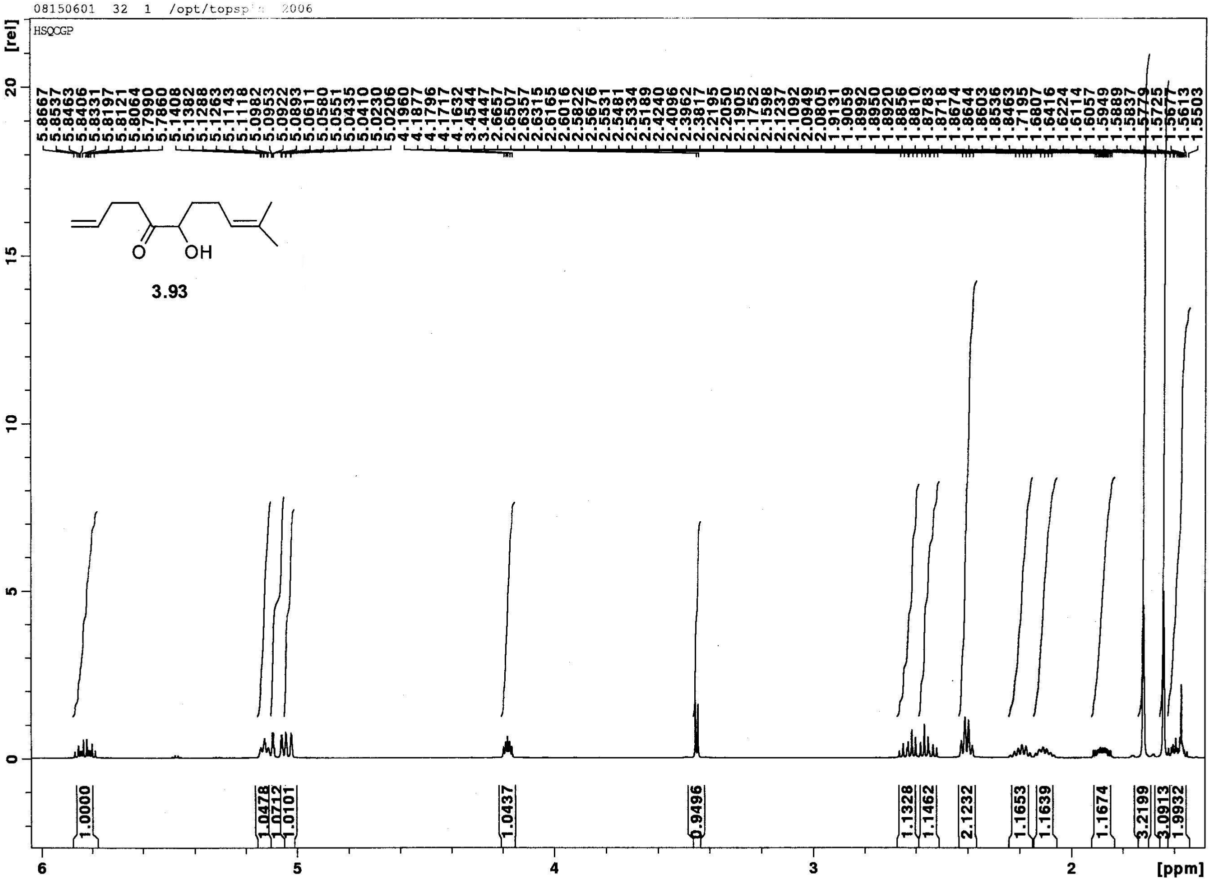

08080601 5 1 /opt/topspin 2006
HSQCGP
5.8562
5.8430
5.8358
5.8298
5.8224
5.8090
5.8016
5.7955
5.7884
5.7751
5.1164
5.1131
5.1097
5.1064
5.0821
5.0789
5.0755
5.0722
5.0441
5.0418
5.0383
5.0358
5.0238
5.0214
5.0179
5.0154
4.0737
4.0598
4.0459
2.9232
2.9178
2.9014
2.8947
2.8891
2.8727
2.8670
2.8632
2.8545
2.8432
2.8342
2.8262
2.8141
2.8003
2.3176
2.3150
2.3124
2.3018
2.3002
2.2869
2.2845
2.2740
2.2714
2.2688
2.1657
2.1598
2.1565
2.1538
2.1506
2.1470
2.1448
2.1413
2.1376
2.1354
2.1321
2.1279
2.1226
2.1174
2.1129
2.1075
1.9916
1.9385
1.9307
1.9233
1.9166
1.9087
1.9019
1.8938
1.8888
1.8865
1.8799
1.8730
1.8671
1.8637
1.8590
1.8494
1.8236
1.5663
S
S
3.91
1.0000
2.0683
0.9873
4.4067
2.1427
1.1397
3.3210
6
5
4
3
2
[ppm]
[rel]
30
20
10
0

0808061 6 1 /opt/topspin 2006
poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
137.1268
115.6055
70.5929
46.7181
34.5706
30.5333
30.3213
26.0335
3.91
S
S
[rel]
15
10
5
0
140
120
100
80
60
40
[ppm]

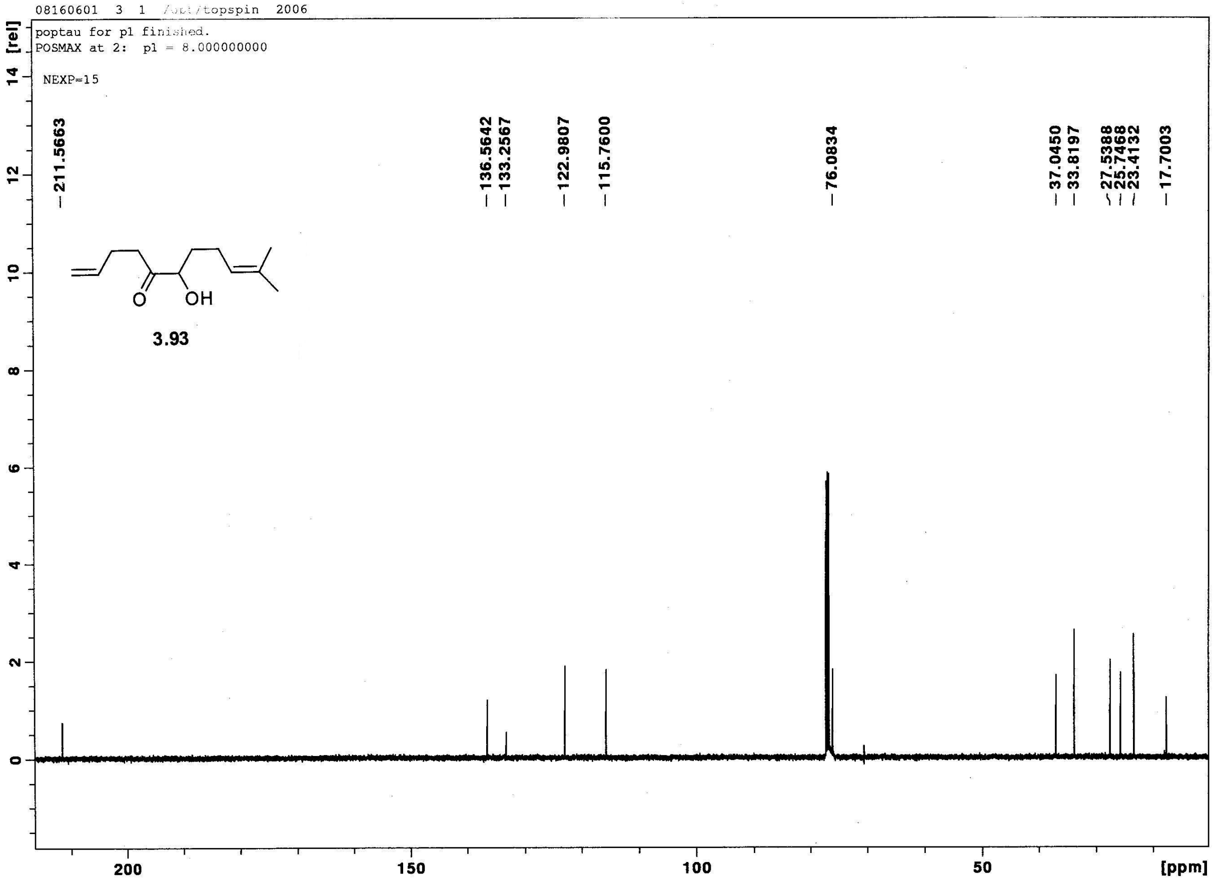

08150601 9 1 /opt/topspin 2006
HSQCGP
[rel]
5.8497
5.8291
5.8157
5.7951
5.2187
5.2056
5.2031
5.1899
5.0815
5.0785
5.0752
5.0720
5.0473
5.0442
5.0409
5.0378
4.9927
4.9899
4.9724
4.9695
4.0147
3.9947
3.0136
3.0099
3.0076
2.9911
2.9867
2.9852
2.9813
2.9789
2.9634
2.9580
2.7325
2.7287
2.7249
2.6879
2.6768
2.6696
2.6586
2.6481
2.6408
2.6297
2.3815
2.3788
2.3681
2.3658
2.3634
2.3605
2.3500
2.3474
2.3342
2.3321
2.3162
2.3039
2.2066
2.1915
2.1771
2.0907
2.0799
2.0736
2.0687
2.0630
2.0575
2.0149
2.0073
1.9896
1.9779
1.9726
1.9649
1.9569
1.9437
1.8832
1.8775
1.8606
1.8554
1.7359
1.7211
1.7130
1.7088
1.6967
1.6825
1.5677
1.5275
1.5244
1.5178
1.5109
1.5078
S
S
OH
15
10
5
0
1.0000
1.0230
1.0436
1.0028
1.0553
2.2097
1.0073
2.2294
2.3151
0.9935
1.1652
1.1465
2.2563
1.1920
3.0821
1.1754
5
4
3
2
[ppm]

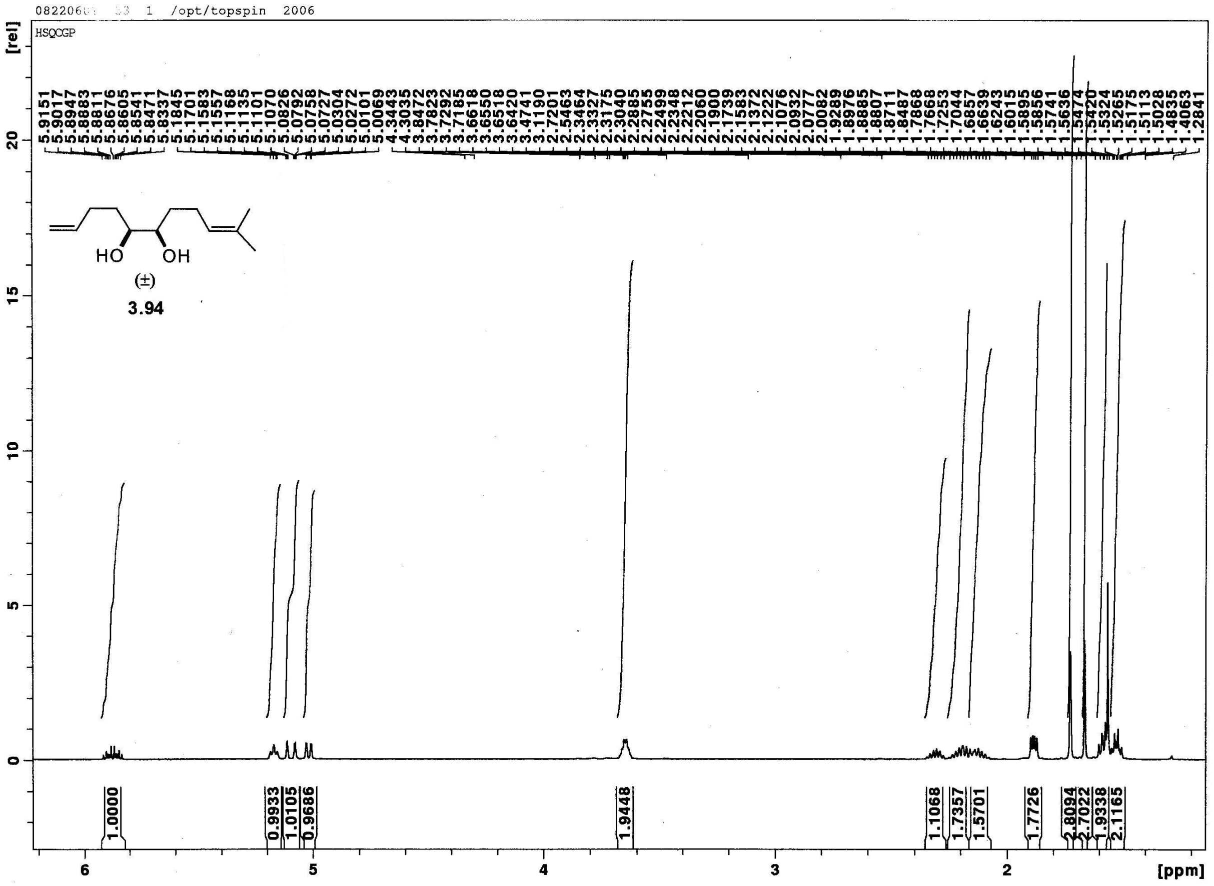
3.92

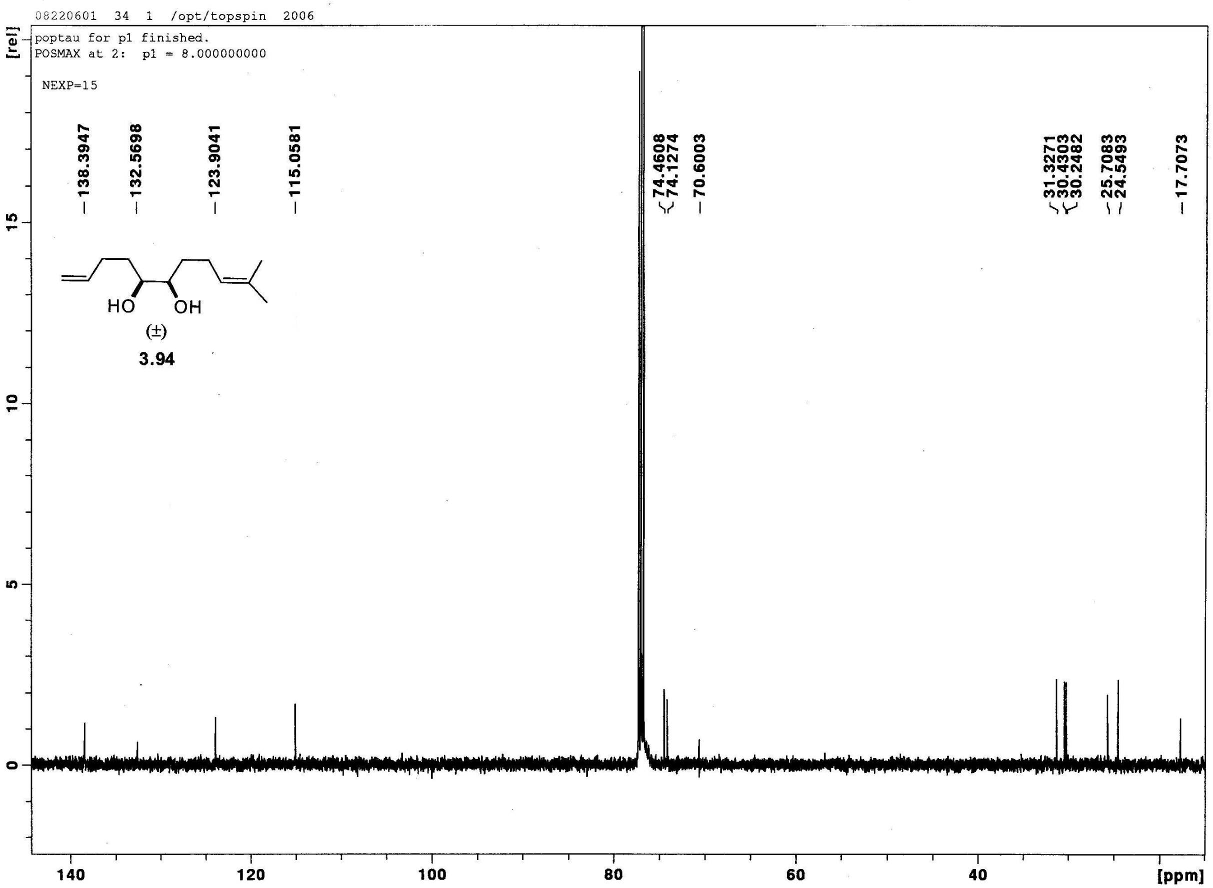

08150601 10 1 /opt/topspin 2006
poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
138.1894
132.3594
124.1748
114.7476
71.2484
59.0119
33.7540
30.3506
28.8992
25.9939
25.9343
25.7334
25.1486
24.4950
17.7661
S
S
OH
3.92
[rel]
15
10
5
0
140
120
100
80
60
40
[ppm]

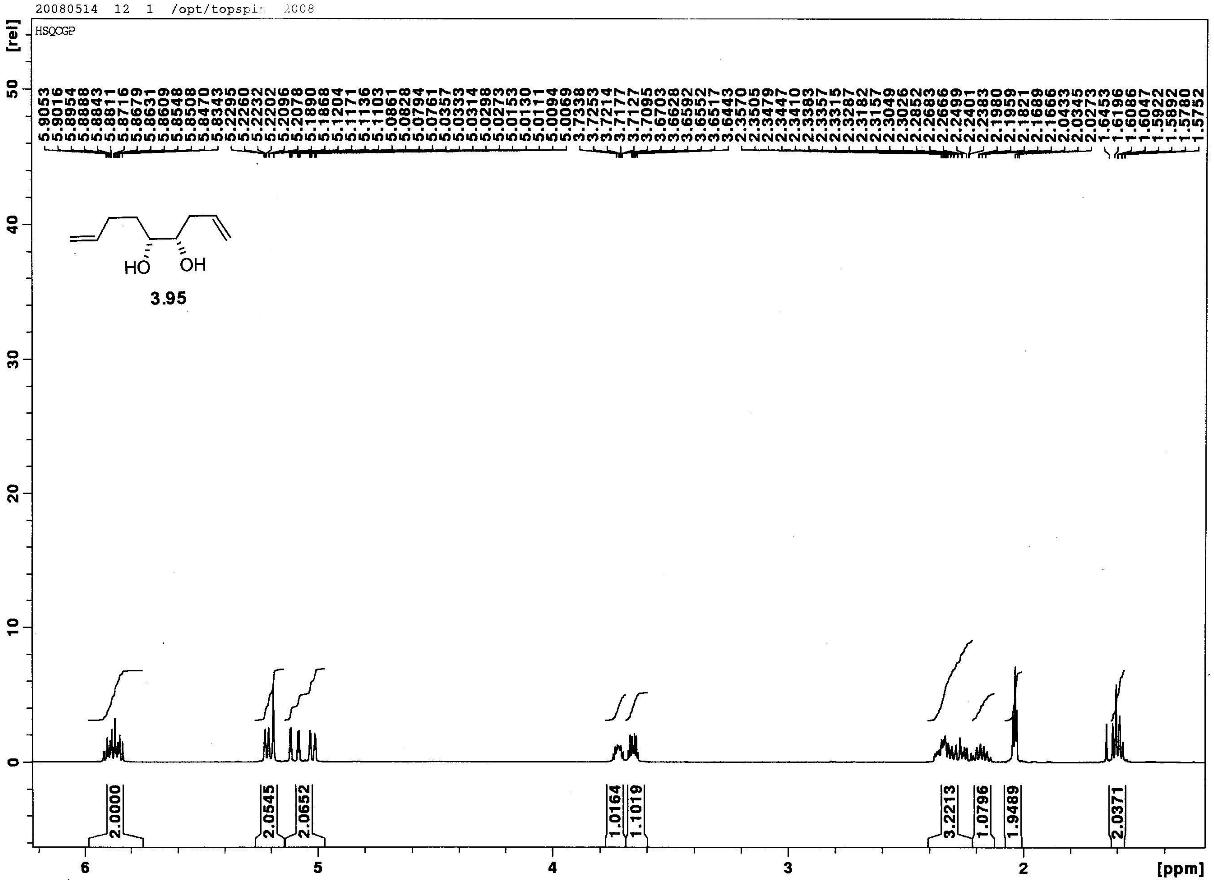
08150601 32 1 /opt/topspin 2006
HSQCGP
[rel]
20
15
10
5
0
5.8667
5.8537
5.8463
5.8406
5.8331
5.8197
5.8121
5.8064
5.7990
5.7860
5.1408
5.1382
5.1288
5.1263
5.1143
5.1118
5.0982
5.0953
5.0922
5.0893
5.0611
5.0580
5.0551
5.0435
5.0410
5.0230
5.0206
4.1960
4.1877
4.1796
4.1717
4.1632
3.4544
3.4447
2.6657
2.6507
2.6357
2.6315
2.6165
2.6016
2.5822
2.5676
2.5531
2.5481
2.5334
2.5189
2.4240
2.4096
2.3962
2.3817
2.2195
2.2050
2.1905
2.1752
2.1598
2.1237
2.1092
2.0949
2.0805
1.9131
1.9059
1.8992
1.8950
1.8920
1.8856
1.8810
1.8783
1.8718
1.8674
1.8644
1.8603
1.8536
1.8463
1.7195
1.6807
1.6416
1.6224
1.6114
1.6057
1.5949
1.5889
1.5837
1.5779
1.5725
1.5677
1.5613
1.5503
O
OH
1.0000
1.0478
1.0712
1.0101
1.0437
0.9496
1.1328
1.1462
2.1232
1.1653
1.1639
1.1674
3.2199
3.0913
1.9932
6
5
4
3
2
[ppm]

3.93

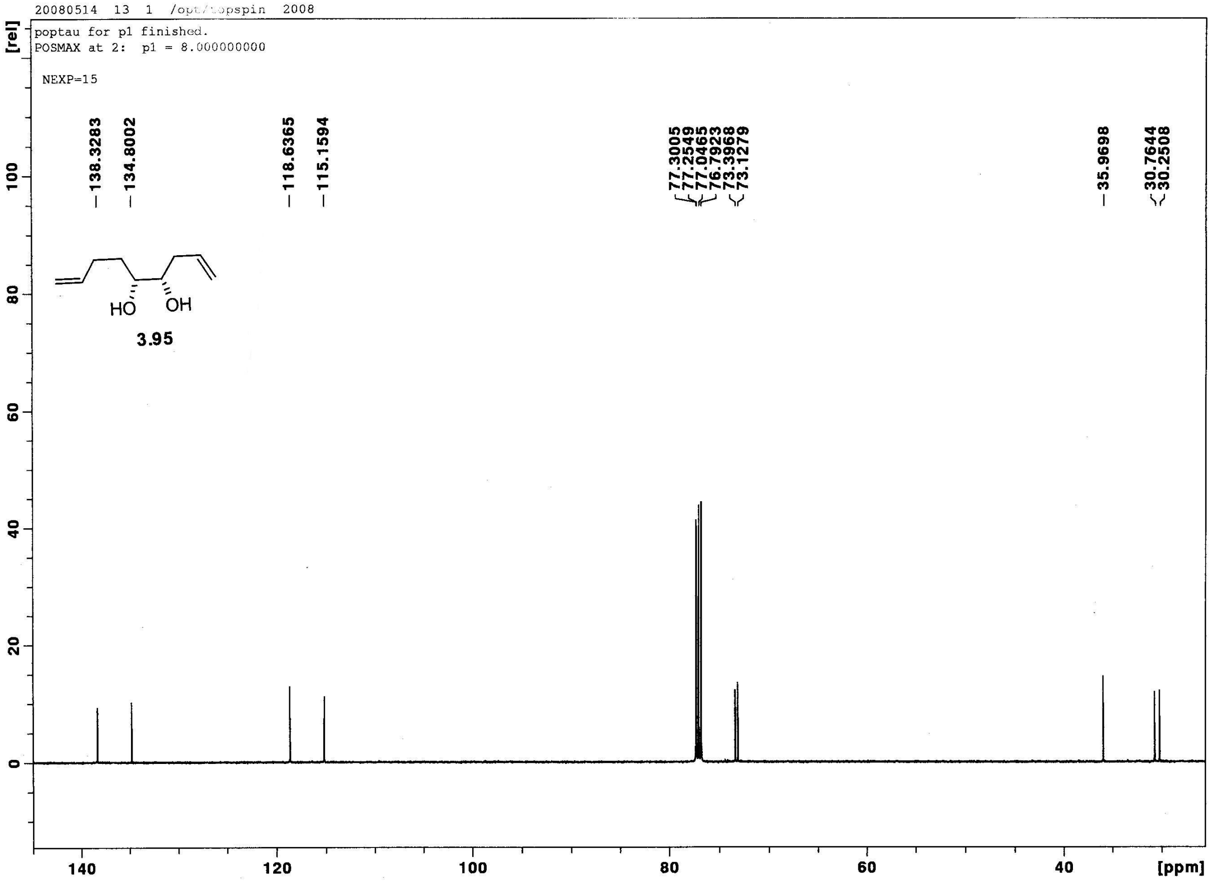

08160601 3 1 /opt/topspin 2006
poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
3.93
O
OH
211.5663
136.5642
133.2567
122.9807
115.7600
76.0834
37.0450
33.8197
27.5388
25.7468
23.4132
17.7003
[rel]
14
12
10
8
6
4
2
0
200
150
100
50
[ppm]

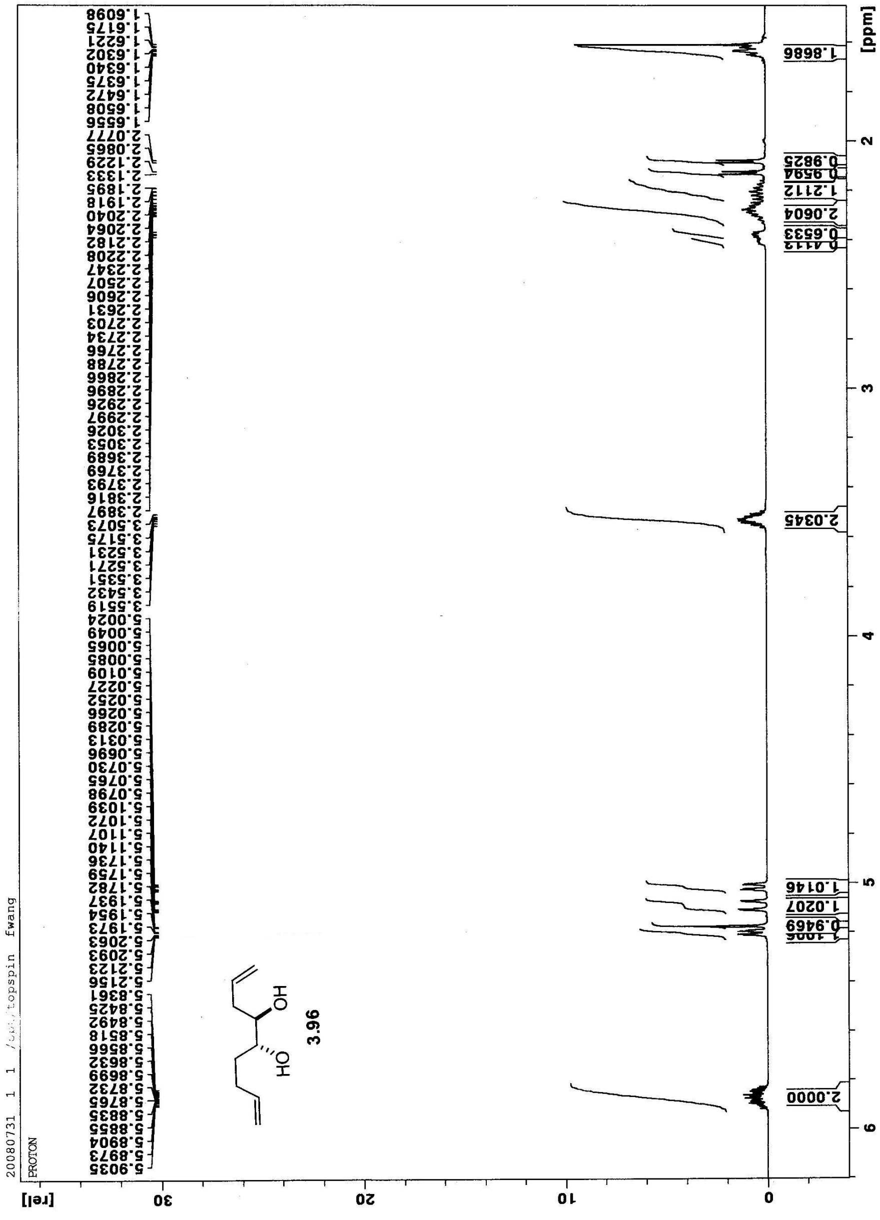

082206[illegible] 53 1 /opt/topspin 2006
HSQCGP
[rel]
20
15
10
5
0
5.9151
5.9017
5.8947
5.8883
5.8811
5.8676
5.8605
5.8541
5.8471
5.8337
5.1845
5.1701
5.1583
5.1557
5.1168
5.1135
5.1101
5.1070
5.0826
5.0792
5.0758
5.0727
5.0304
5.0272
5.0101
5.0069
4.3443
4.3035
3.8472
3.7823
3.7292
3.7185
3.6618
3.6550
3.6518
3.6420
3.4741
3.1190
2.7201
2.5463
2.3464
2.3327
2.3175
2.3040
2.2885
2.2755
2.2499
2.2348
2.2212
2.2060
2.1900
2.1739
2.1583
2.1372
2.1222
2.1076
2.0932
2.0777
2.0082
1.9289
1.8976
1.8885
1.8807
1.8711
1.8487
1.7868
1.7668
1.7253
1.7044
1.6857
1.6639
1.6243
1.6015
1.5895
1.5856
1.5741
1.5636
1.5474
1.5420
1.5324
1.5265
1.5175
1.5113
1.5028
1.4835
1.4063
1.2841
HO
OH
(±)
3.94
1.0000
0.9933
1.0105
0.9686
1.9448
1.1068
1.7357
1.5701
1.7726
2.8094
2.7022
1.9338
2.1165
6
5
4
3
2
[ppm]


08220601 34 1 /opt/topspin 2006
poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
[rel]
138.3947
132.5698
123.9041
115.0581
74.4608
74.1274
70.6003
31.3271
30.4303
30.2482
25.7083
24.5493
17.7073
HO
OH
(±)
3.94
15
10
5
0
140
120
100
80
60
40
[ppm]

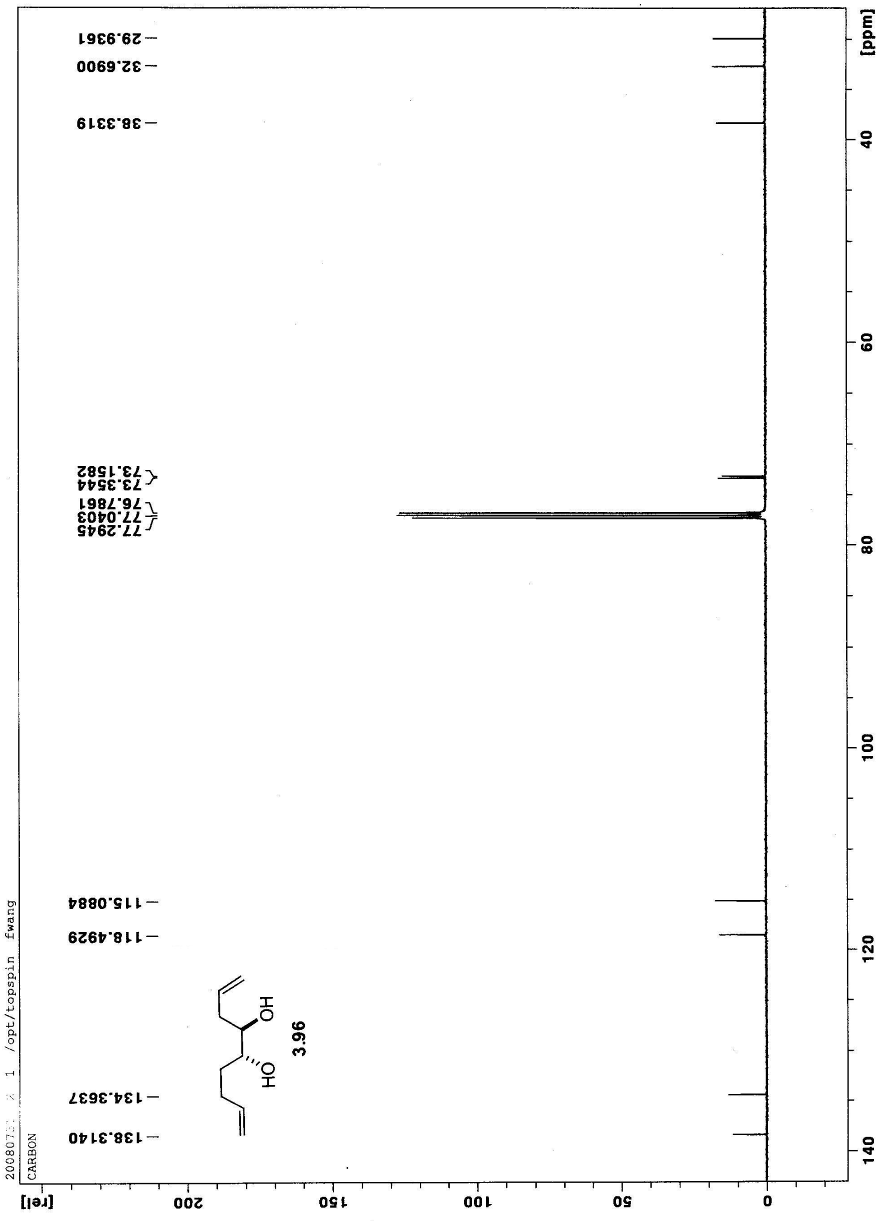

20080514 12 1 /opt/topspin 2008
HSQCGP
5.9053
5.9016
5.8954
5.8888
5.8843
5.8811
5.8716
5.8679
5.8631
5.8609
5.8548
5.8508
5.8470
5.8343
5.2295
5.2260
5.2232
5.2202
5.2096
5.2078
5.1890
5.1868
5.1204
5.1171
5.1136
5.1103
5.0861
5.0828
5.0794
5.0761
5.0357
5.0333
5.0314
5.0298
5.0273
5.0153
5.0130
5.0111
5.0094
5.0069
3.7338
3.7253
3.7214
3.7177
3.7127
3.7095
3.6703
3.6628
3.6592
3.6552
3.6517
3.6443
2.3570
2.3505
2.3479
2.3447
2.3410
2.3383
2.3357
2.3315
2.3287
2.3182
2.3157
2.3049
2.3026
2.2852
2.2683
2.2666
2.2499
2.2401
2.2383
2.1980
2.1959
2.1821
2.1689
2.1666
2.0433
2.0345
2.0273
1.6453
1.6196
1.6086
1.6047
1.5922
1.5892
1.5780
1.5752
HO
OH
2.0000
2.0545
2.0652
1.0164
1.1019
3.2213
1.0796
1.9489
2.0371
[rel]
50
40
30
20
10
0
6
5
4
3
2
[ppm]

3.95

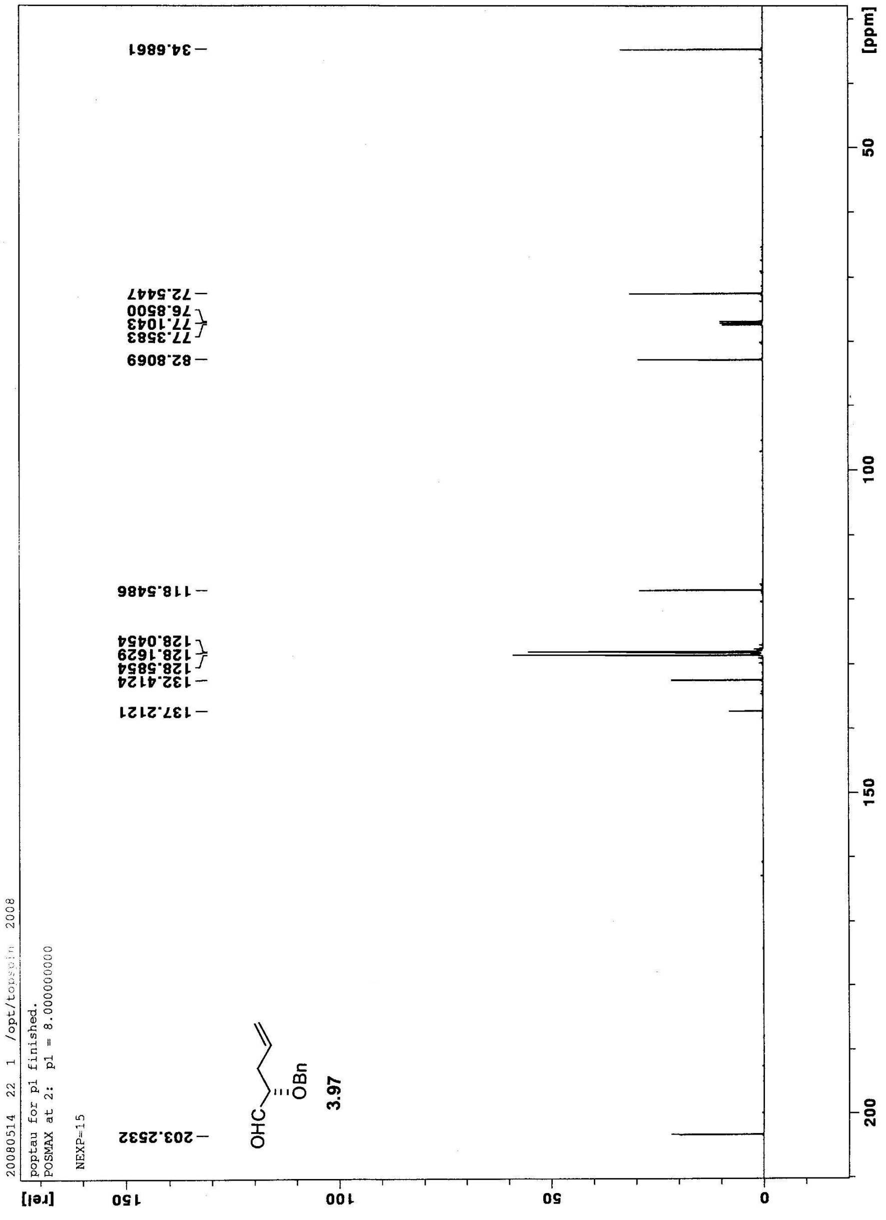

20080514 13 1 /opt/topspin 2008
poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
138.3283
134.8002
118.6365
115.1594
77.3005
77.2549
77.0465
76.7923
73.3968
73.1279
35.9698
30.7644
30.2508
HO
OH
3.95
[rel]
100
80
60
40
20
0
140
120
100
80
60
40
[ppm]

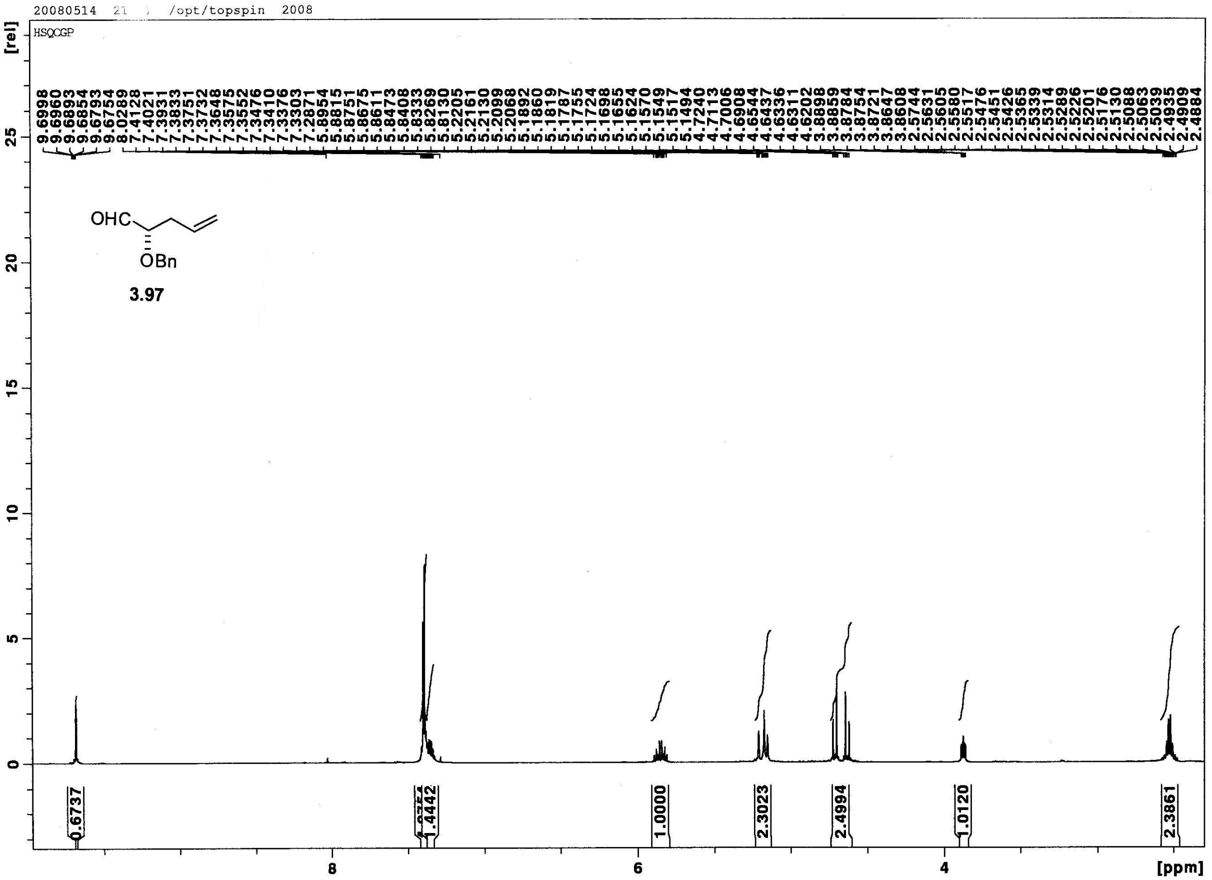

20080731 1 1 /... topspin fwang
PROTON
5.9035
5.8973
5.8904
5.8855
5.8835
5.8765
5.8732
5.8699
5.8632
5.8566
5.8518
5.8492
5.8425
5.8361
5.2156
5.2123
5.2093
5.2063
5.1973
5.1954
5.1937
5.1782
5.1759
5.1736
5.1140
5.1107
5.1072
5.1039
5.0798
5.0765
5.0730
5.0696
5.0313
5.0289
5.0266
5.0252
5.0227
5.0109
5.0085
5.0065
5.0049
5.0024
3.5519
3.5432
3.5351
3.5271
3.5231
3.5175
3.5073
2.3897
2.3816
2.3793
2.3769
2.3689
2.3053
2.3026
2.2997
2.2926
2.2896
2.2866
2.2788
2.2766
2.2734
2.2703
2.2631
2.2606
2.2507
2.2347
2.2208
2.2182
2.2064
2.2040
2.1918
2.1895
2.1333
2.1229
2.0865
2.0777
1.6556
1.6508
1.6472
1.6375
1.6340
1.6302
1.6221
1.6175
1.6098
OH
HO
2.0000
1.0056
0.9469
1.0207
1.0146
2.0345
0.4113
0.6533
2.0604
1.2112
0.9594
0.9825
1.8686
6
5
4
3
2
[ppm]
0
10
20
30
[rel]

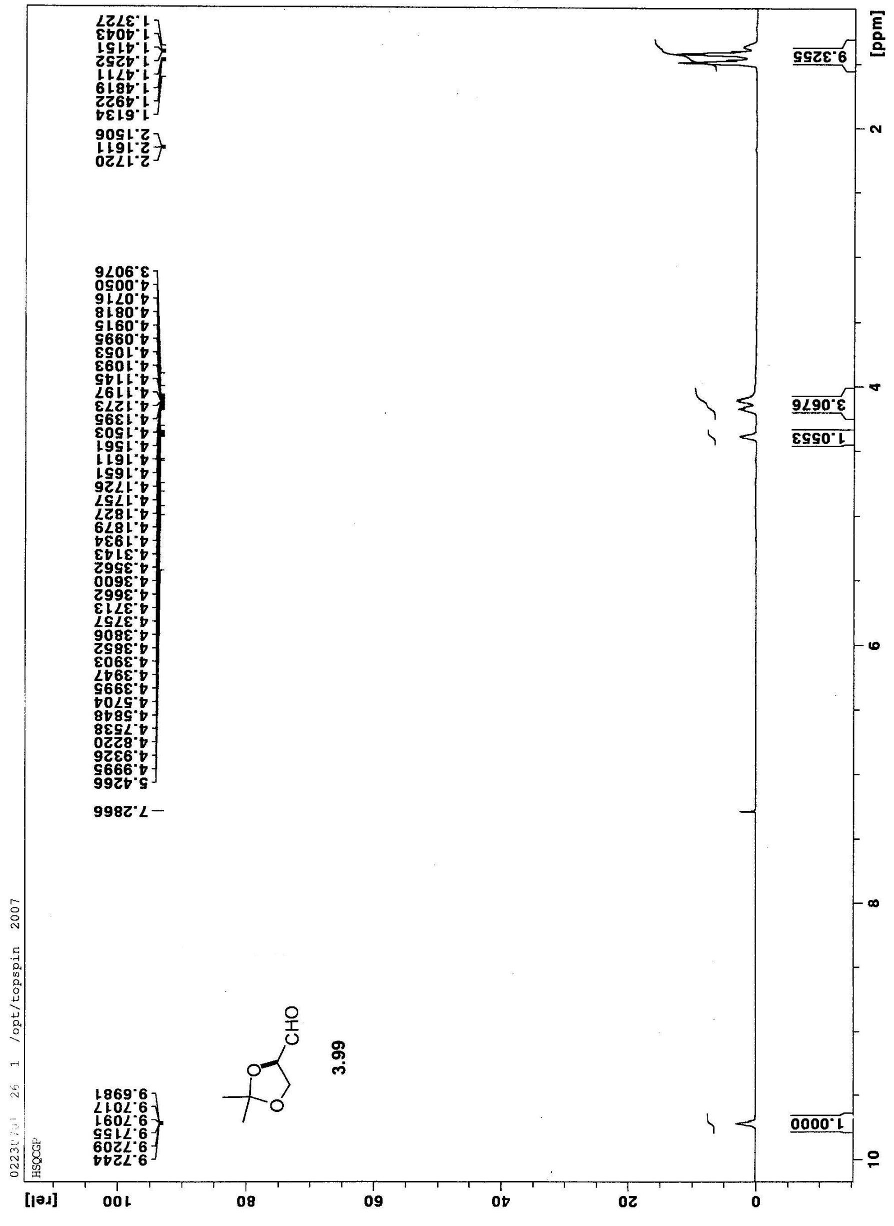
3.96

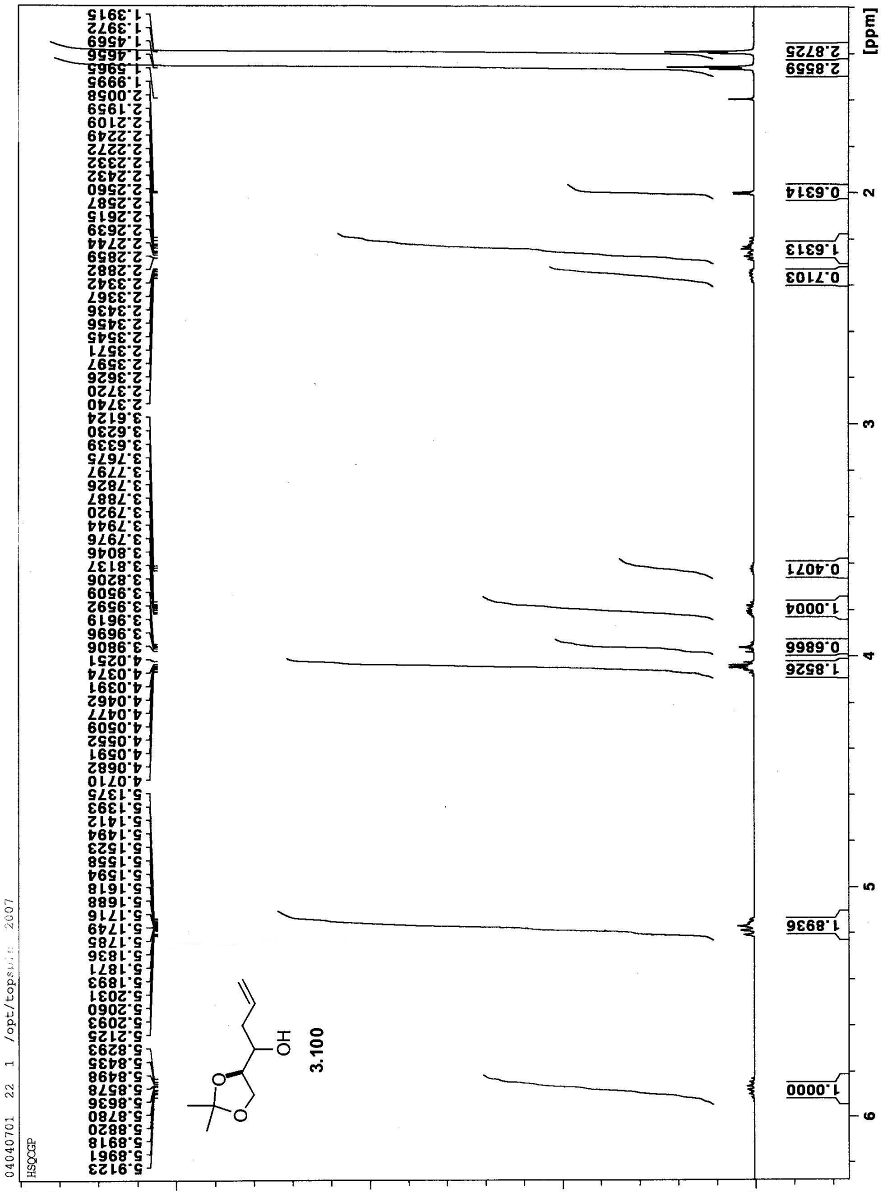

3.96

CARBON
1 /opt/topspin fwang
138.3140
134.3637
118.4929
115.0884
77.2945
77.0403
76.7861
73.3544
73.1582
38.3319
32.6900
29.9361
OH
HO
[ppm]
140
120
100
80
60
40
[rel]
200
150
100
50
0

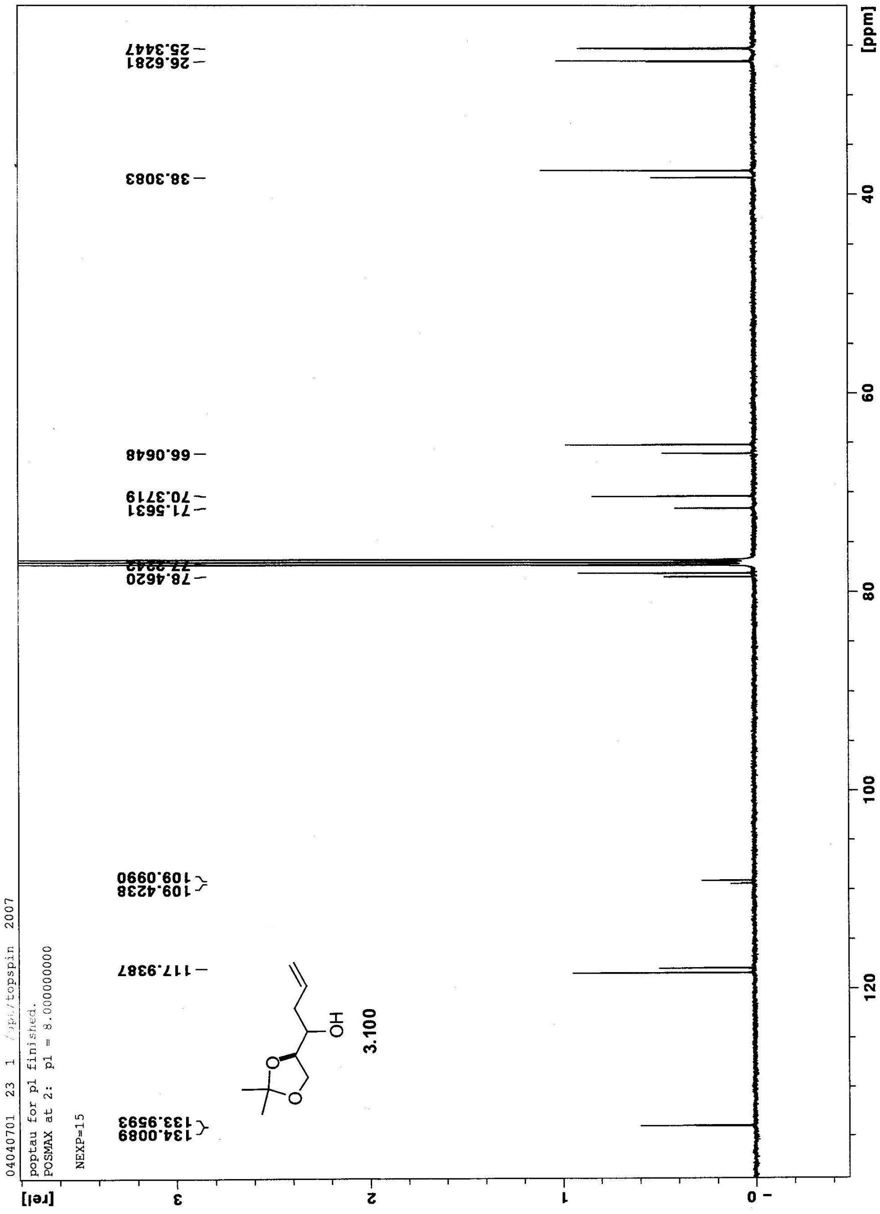

20080514 22 1 /opt/topspin 2008
poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
OHC
OBn
3.97
203.2532
137.2121
132.4124
128.5854
128.1629
128.0454
118.5486
82.8069
77.3583
77.1043
76.8500
72.5447
34.6861
200
150
100
50
[ppm]
[rel]
150
100
50
0

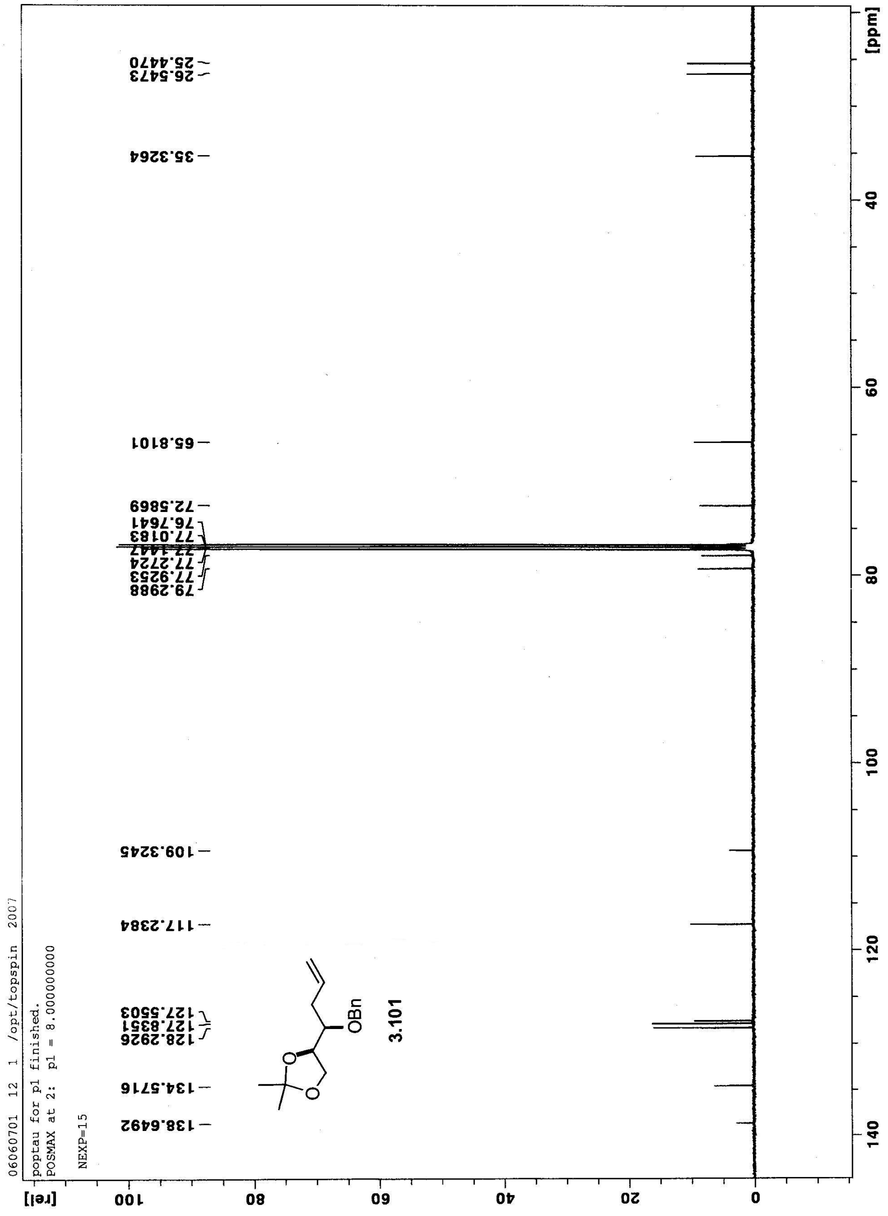

3.97
20080514 21 /opt/topspin 2008
HSQCGP
[rel]
25
20
15
10
5
0
9.6998
9.6960
9.6893
9.6854
9.6793
9.6754
8.0289
7.4128
7.4021
7.3931
7.3833
7.3751
7.3732
7.3648
7.3575
7.3552
7.3476
7.3410
7.3376
7.3303
7.2871
5.8954
5.8815
5.8751
5.8675
5.8611
5.8473
5.8408
5.8333
5.8269
5.8130
5.2205
5.2161
5.2130
5.2099
5.2068
5.1892
5.1860
5.1819
5.1787
5.1755
5.1724
5.1698
5.1655
5.1624
5.1570
5.1549
5.1517
5.1494
4.7240
4.7113
4.7006
4.6908
4.6544
4.6437
4.6336
4.6311
4.6202
3.8898
3.8859
3.8784
3.8754
3.8721
3.8647
3.8608
2.5744
2.5631
2.5605
2.5580
2.5517
2.5476
2.5451
2.5426
2.5365
2.5339
2.5314
2.5289
2.5226
2.5201
2.5176
2.5130
2.5088
2.5063
2.5039
2.4935
2.4909
2.4884
OHC
OBn
0.6737
1.4442
1.0000
2.3023
2.4994
1.0120
2.3861
8
6
4
[ppm]

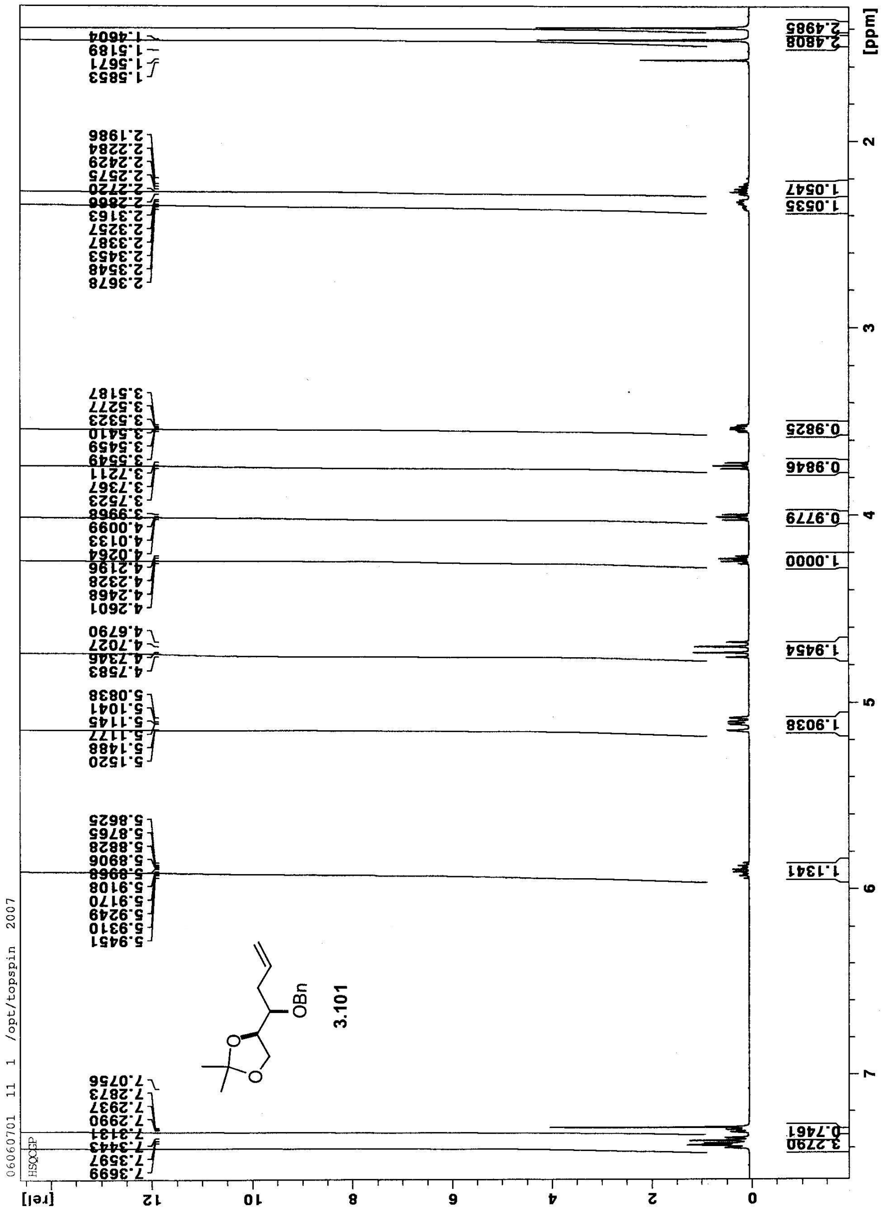
02230 26 1 /opt/topspin 2007
HSQCGP
3.99
CHO
O
O
9.7244
9.7209
9.7155
9.7091
9.7017
9.6981
7.2866
5.4266
4.9995
4.9326
4.8220
4.7538
4.5848
4.5704
4.3995
4.3947
4.3903
4.3852
4.3806
4.3757
4.3713
4.3662
4.3600
4.3562
4.3143
4.1934
4.1879
4.1827
4.1757
4.1726
4.1651
4.1611
4.1561
4.1503
4.1395
4.1273
4.1197
4.1145
4.1093
4.1053
4.0995
4.0915
4.0818
4.0716
4.0050
3.9076
2.1720
2.1611
2.1506
1.6134
1.4922
1.4819
1.4711
1.4252
1.4151
1.4043
1.3727
1.0000
1.0553
3.0676
9.3255
[rel]
100
80
60
40
20
0
10
8
6
4
2
[ppm]


04040701 22 1 /opt/topspin 2007
HSQCGP
5.9123
5.8961
5.8918
5.8820
5.8780
5.8636
5.8578
5.8498
5.8435
5.8293
5.2125
5.2093
5.2060
5.2031
5.1893
5.1871
5.1836
5.1785
5.1749
5.1716
5.1688
5.1618
5.1594
5.1558
5.1523
5.1494
5.1412
5.1393
5.1375
4.0710
4.0682
4.0591
4.0552
4.0509
4.0477
4.0462
4.0391
4.0374
4.0251
3.9806
3.9696
3.9619
3.9592
3.9509
3.8206
3.8137
3.8046
3.7976
3.7944
3.7920
3.7887
3.7826
3.7797
3.7675
3.6339
3.6230
3.6124
2.3740
2.3720
2.3626
2.3597
2.3571
2.3545
2.3456
2.3436
2.3367
2.3342
2.2882
2.2859
2.2744
2.2639
2.2615
2.2587
2.2560
2.2432
2.2332
2.2272
2.2249
2.2109
2.1959
2.0058
1.9995
1.5965
1.4656
1.4569
1.3972
1.3915
1.0000
1.8936
1.8526
0.6866
1.0004
0.4071
0.7103
1.6313
0.6314
2.8559
2.8725
6
5
4
3
2
[ppm]
0
1
2
3
[rel]

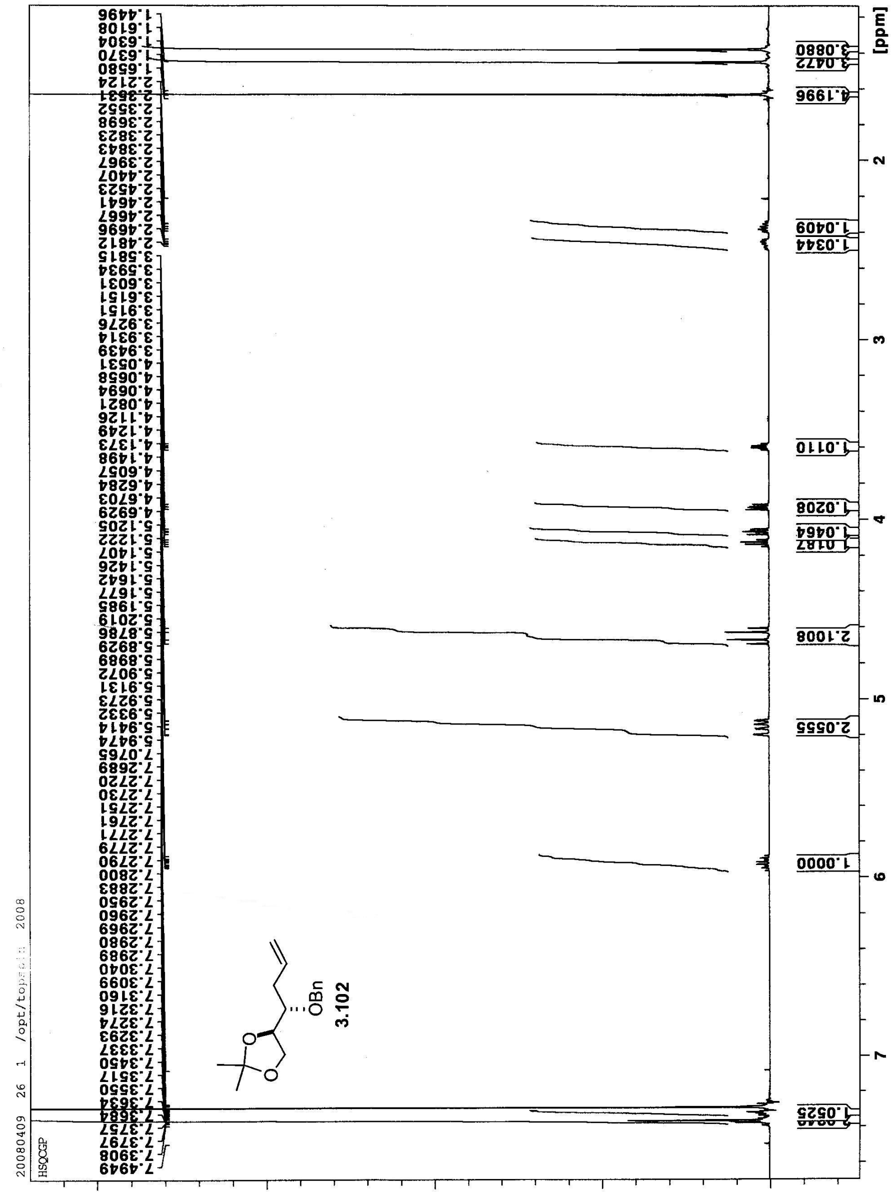
3.100


04040701 23 1 /opt/topspin 2007
poptau for p1 finished.
POSMAX at 2: p1 = 8.00000000
NEXP=15
134.0089
133.9593
117.9387
109.4238
109.0990
78.4620
77.2542
71.5631
70.3719
66.0648
38.3083
26.6281
25.3447
OH
O
O
3.100
[rel]
3
2
1
0
[ppm]
120
100
80
60
40

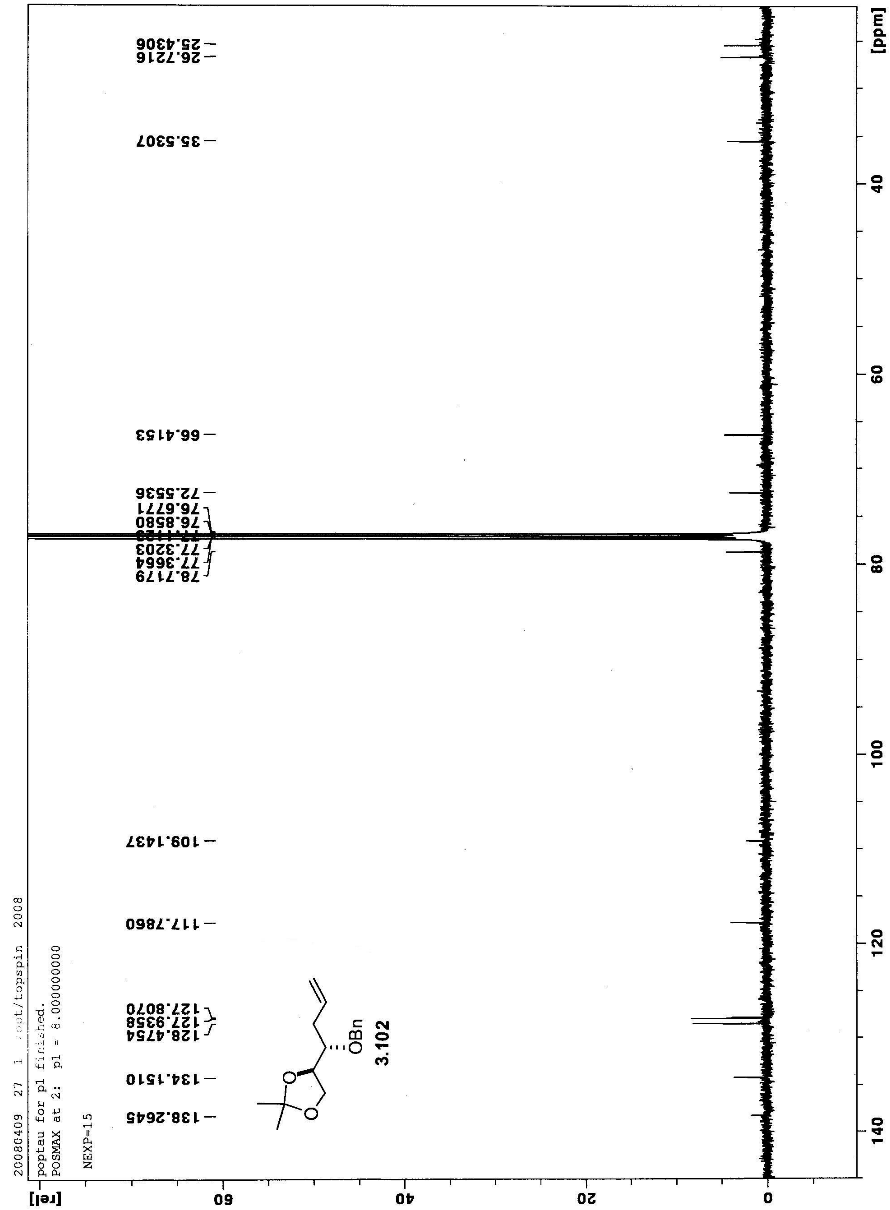

06060701 12 1 /opt/topspin 2007
poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
138.6492
134.5716
128.2926
127.8351
127.5503
117.2384
109.3245
79.2988
77.9253
77.2724
77.1442
77.0183
76.7641
72.5869
65.8101
35.3264
26.5473
25.4470
O
O
OBn
3.101
[rel]
100
80
60
40
20
0
140
120
100
80
60
40
[ppm]

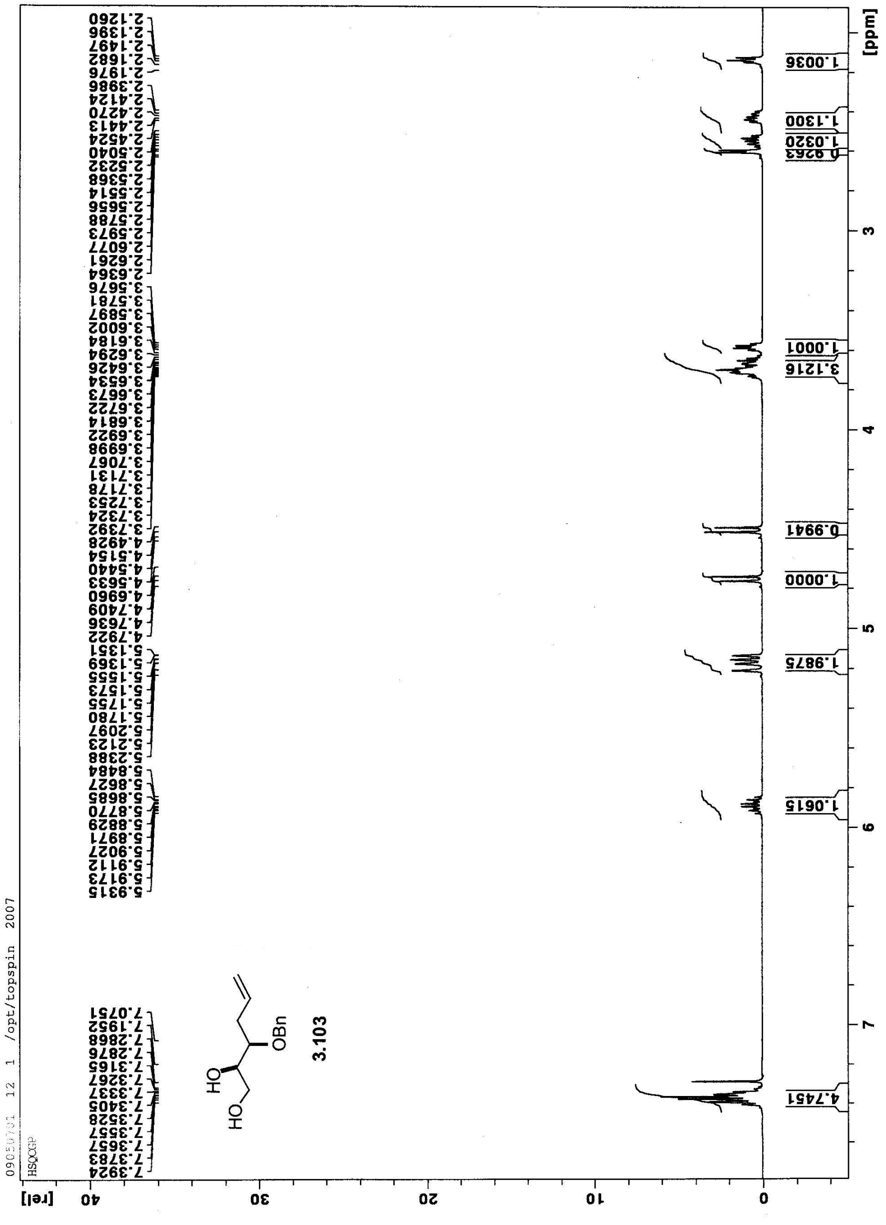

06060701 11 1 /opt/topspin 2007
HSQCCP
OBn
7.3699
7.3597
7.3443
7.3181
7.2990
7.2937
7.2873
7.0756
5.9451
5.9310
5.9249
5.9170
5.9108
5.8968
5.8906
5.8828
5.8765
5.8625
5.1520
5.1488
5.1177
5.1145
5.1041
5.0838
4.7583
4.7346
4.7027
4.6790
4.2601
4.2468
4.2328
4.2196
4.0264
4.0133
4.0099
3.9968
3.7523
3.7367
3.7211
3.5549
3.5459
3.5410
3.5323
3.5277
3.5187
2.3678
2.3548
2.3453
2.3387
2.3257
2.3163
2.2866
2.2720
2.2575
2.2429
2.2284
2.1986
1.5853
1.5671
1.5189
1.4604
3.2790
0.7461
1.1341
1.9038
1.9454
1.0000
0.9779
0.9846
0.9825
1.0535
1.0547
2.4808
2.4985
[ppm]
7
6
5
4
3
2
[rel]
12
10
8
6
4
2
0

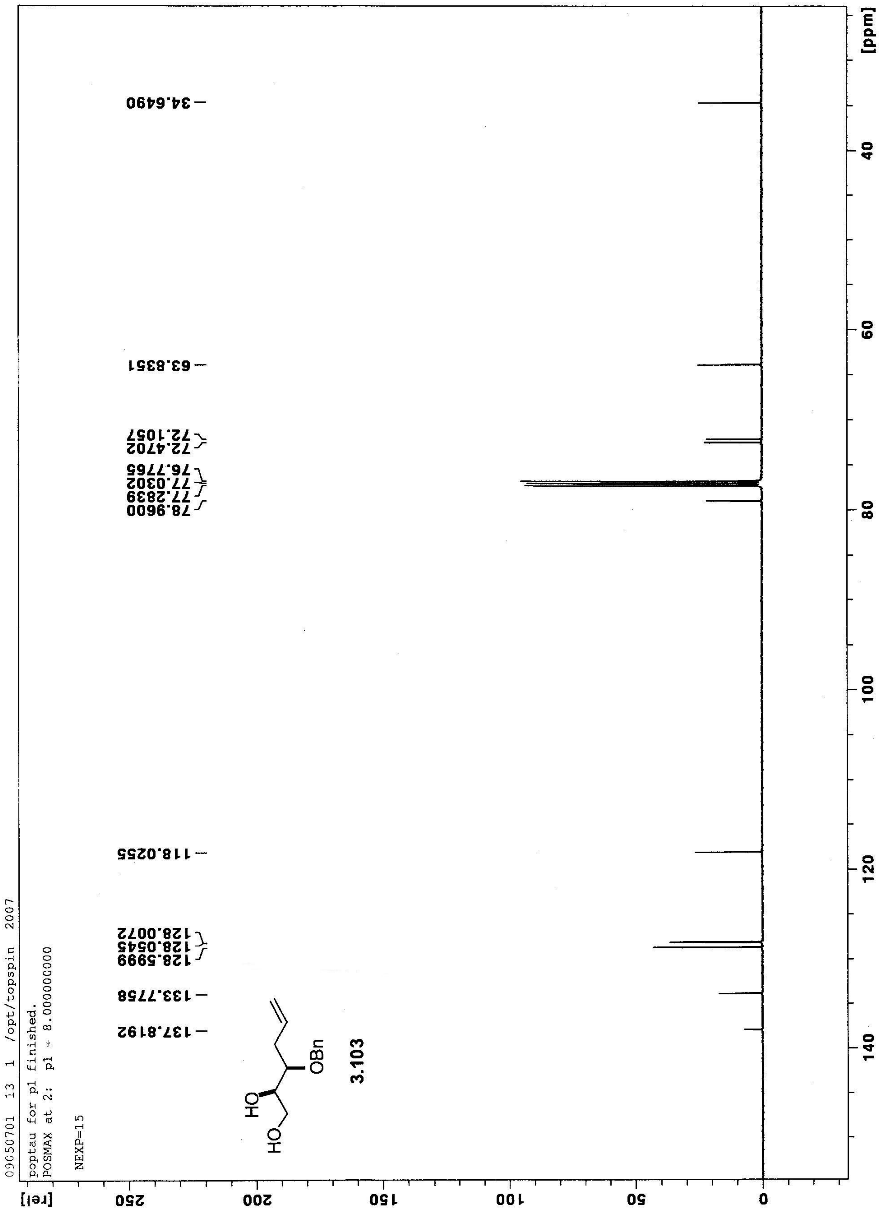
3.101


20080409 26 1 /opt/topspin 2008
HSQCGP
OBn
1.4496
1.6108
1.6304
1.6370
1.6580
2.2124
2.2631
2.3552
2.3698
2.3823
2.3843
2.3967
2.4407
2.4523
2.4641
2.4667
2.4696
2.4812
3.5815
3.5934
3.6031
3.6151
3.9151
3.9276
3.9314
3.9439
4.0531
4.0658
4.0694
4.0821
4.1126
4.1249
4.1373
4.1498
4.6057
4.6284
4.6703
4.6929
5.1205
5.1222
5.1407
5.1426
5.1642
5.1677
5.1985
5.2019
5.8786
5.8929
5.8989
5.9072
5.9131
5.9273
5.9332
5.9414
5.9474
7.0765
7.2689
7.2720
7.2730
7.2751
7.2761
7.2771
7.2779
7.2790
7.2800
7.2883
7.2950
7.2960
7.2969
7.2980
7.2989
7.3040
7.3099
7.3160
7.3216
7.3274
7.3293
7.3337
7.3450
7.3517
7.3550
7.3634
7.3684
7.3757
7.3797
7.3908
7.4949
3.0880
3.0472
4.1996
1.0409
1.0344
1.0110
1.0208
1.0464
1.0187
2.1008
2.0555
1.0000
1.0525
[ppm]
2
3
4
5
6
7
[rel]
20
15
10
5
0

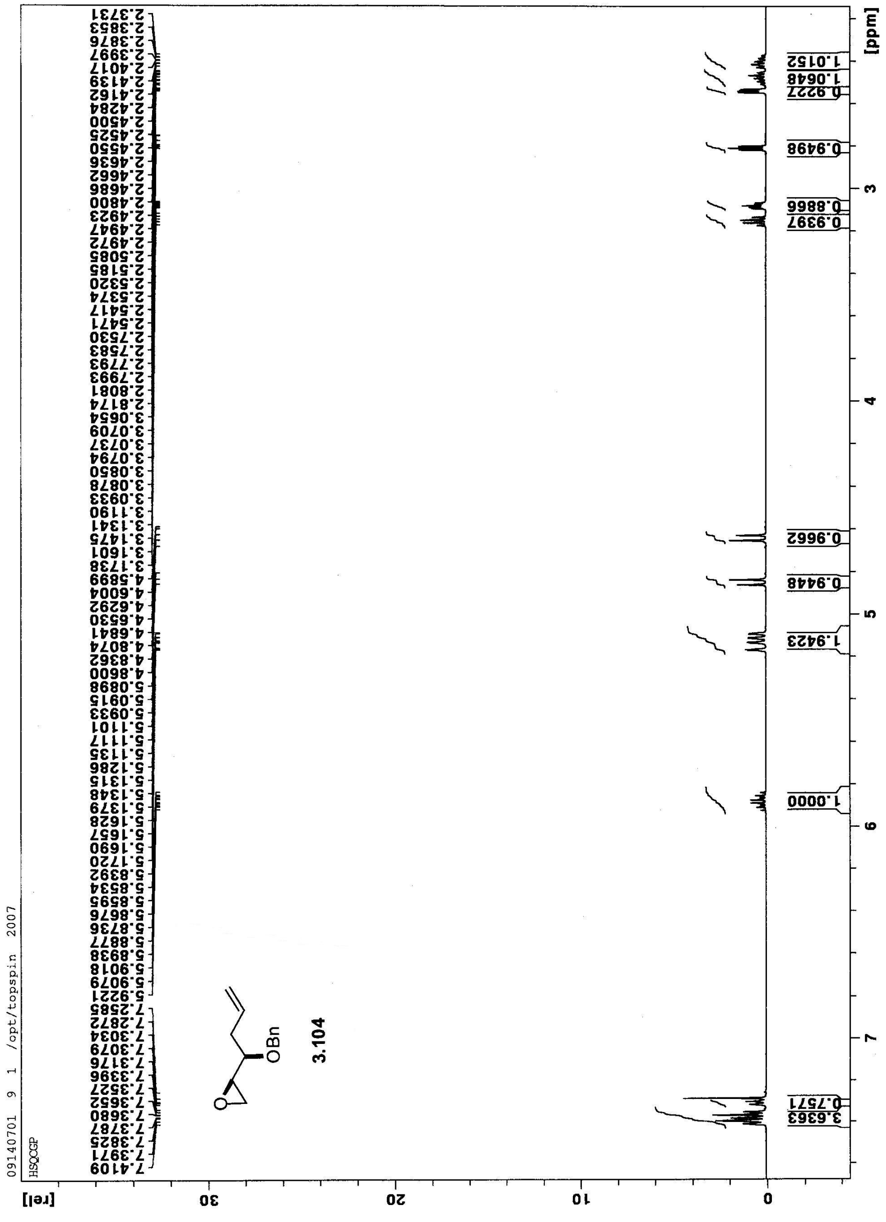
3.102

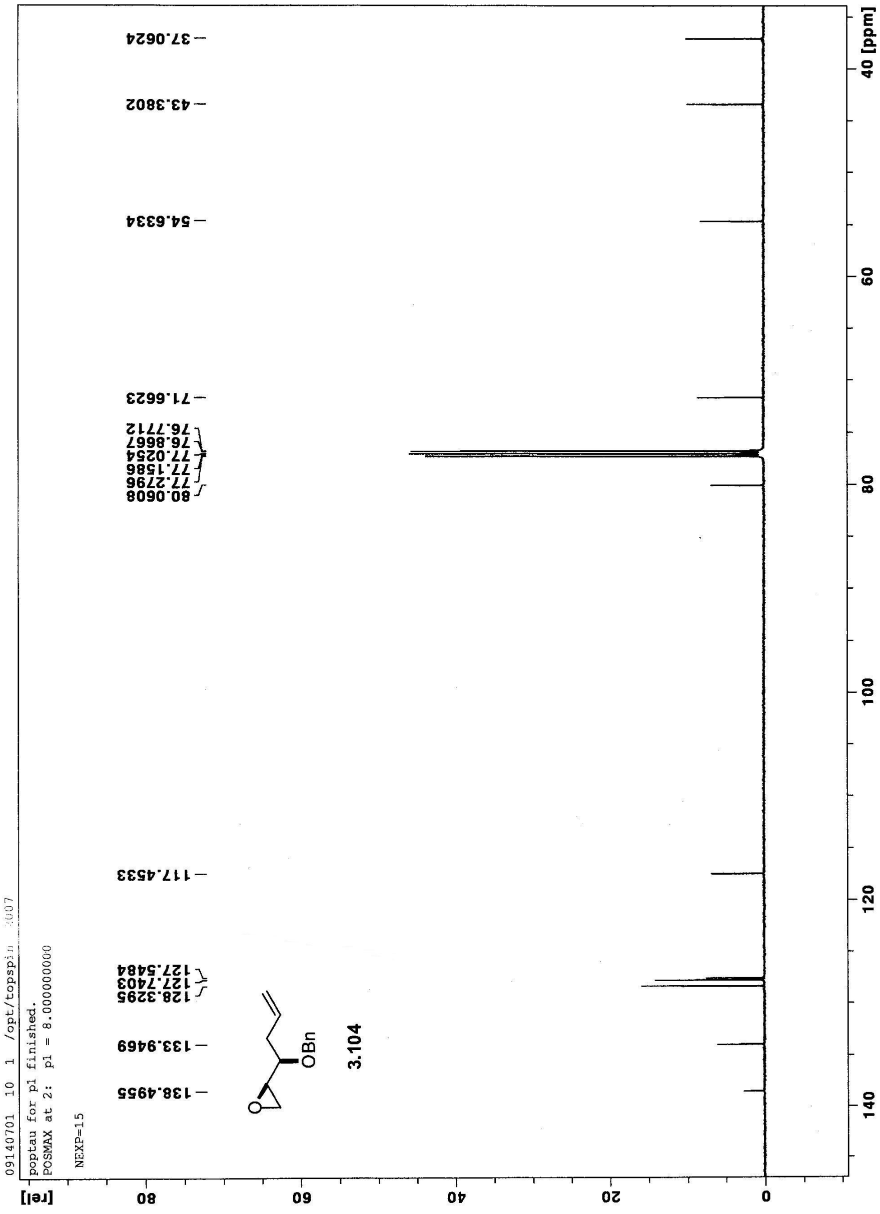

20080409 27 1 /opt/topspin 2008
poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
138.2645
134.1510
128.4754
127.9358
127.8070
117.7860
109.1437
78.7179
77.3664
77.3203
76.8580
76.6771
72.5336
66.4153
35.5307
26.7216
25.4306
OBn
3.102
[ppm]
140
120
100
80
60
40
[rel]
60
40
20
0

090507?? 12 1 /opt/topspin 2007
HSQCGP
3.103
HO
OH
OBn
7.3924
7.3783
7.3657
7.3557
7.3528
7.3405
7.3337
7.3267
7.3165
7.2876
7.2868
7.1952
7.0751
5.9315
5.9173
5.9112
5.9027
5.8971
5.8829
5.8770
5.8685
5.8627
5.8484
5.2388
5.2123
5.2097
5.1780
5.1755
5.1573
5.1555
5.1369
5.1351
4.7922
4.7636
4.7409
4.6960
4.5633
4.5440
4.5154
4.4928
3.7392
3.7324
3.7253
3.7178
3.7131
3.7067
3.6998
3.6922
3.6814
3.6722
3.6673
3.6534
3.6426
3.6294
3.6184
3.6002
3.5897
3.5781
3.5676
2.6364
2.6261
2.6077
2.5973
2.5788
2.5656
2.5514
2.5368
2.5232
2.5040
2.4524
2.4413
2.4270
2.4124
2.3986
2.1976
2.1682
2.1497
2.1396
2.1260
4.7451
1.0615
1.9875
1.0000
0.9941
3.1216
1.0001
0.9263
1.0320
1.1300
1.0036
[rel]
40
30
20
10
0
7
6
5
4
3
[ppm]

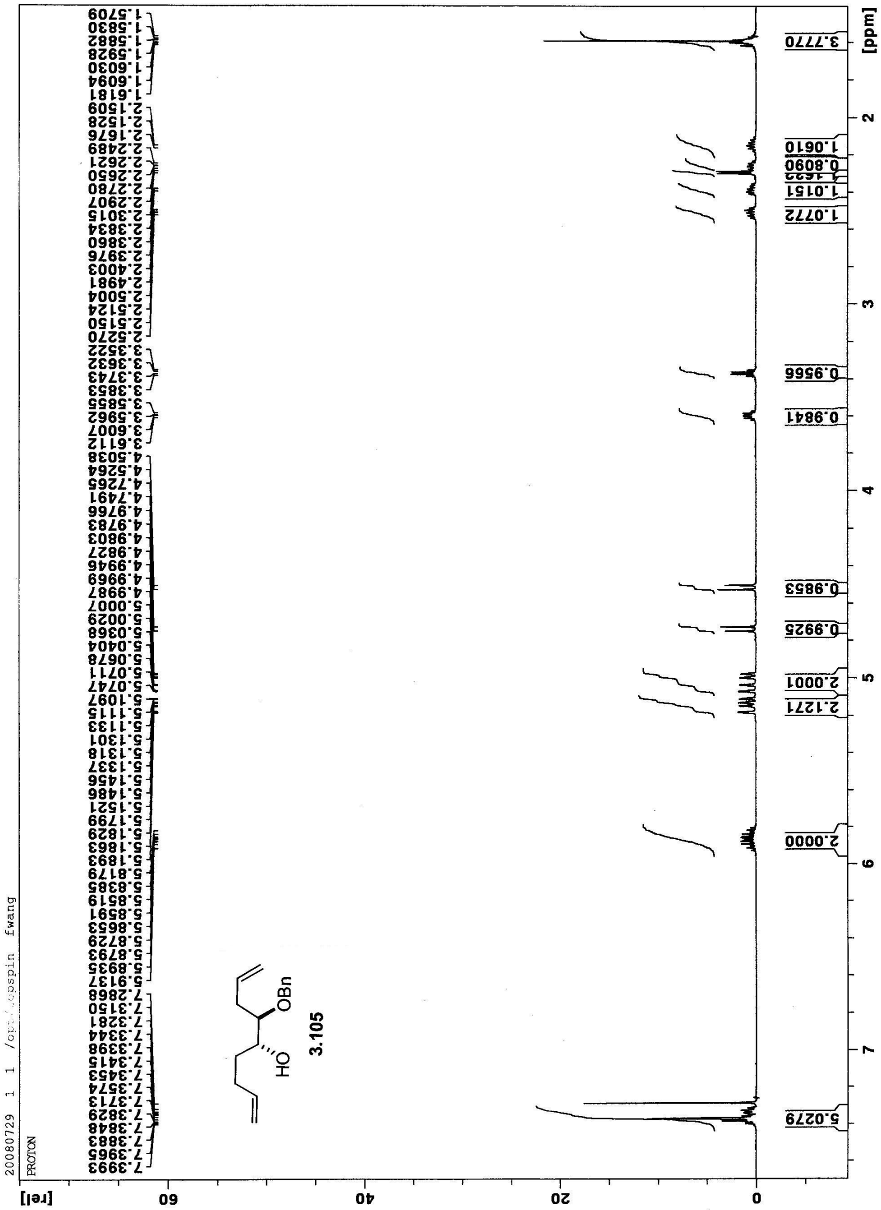

09050701 13 1 /opt/topspin 2007
poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
137.8192
133.7758
128.5999
128.0545
128.0072
118.0255
78.9600
77.2839
77.0302
76.7765
72.4702
72.1057
63.8351
34.6490
HO
HO
OBn
[rel]
250
200
150
100
50
0
140
120
100
80
60
40
[ppm]

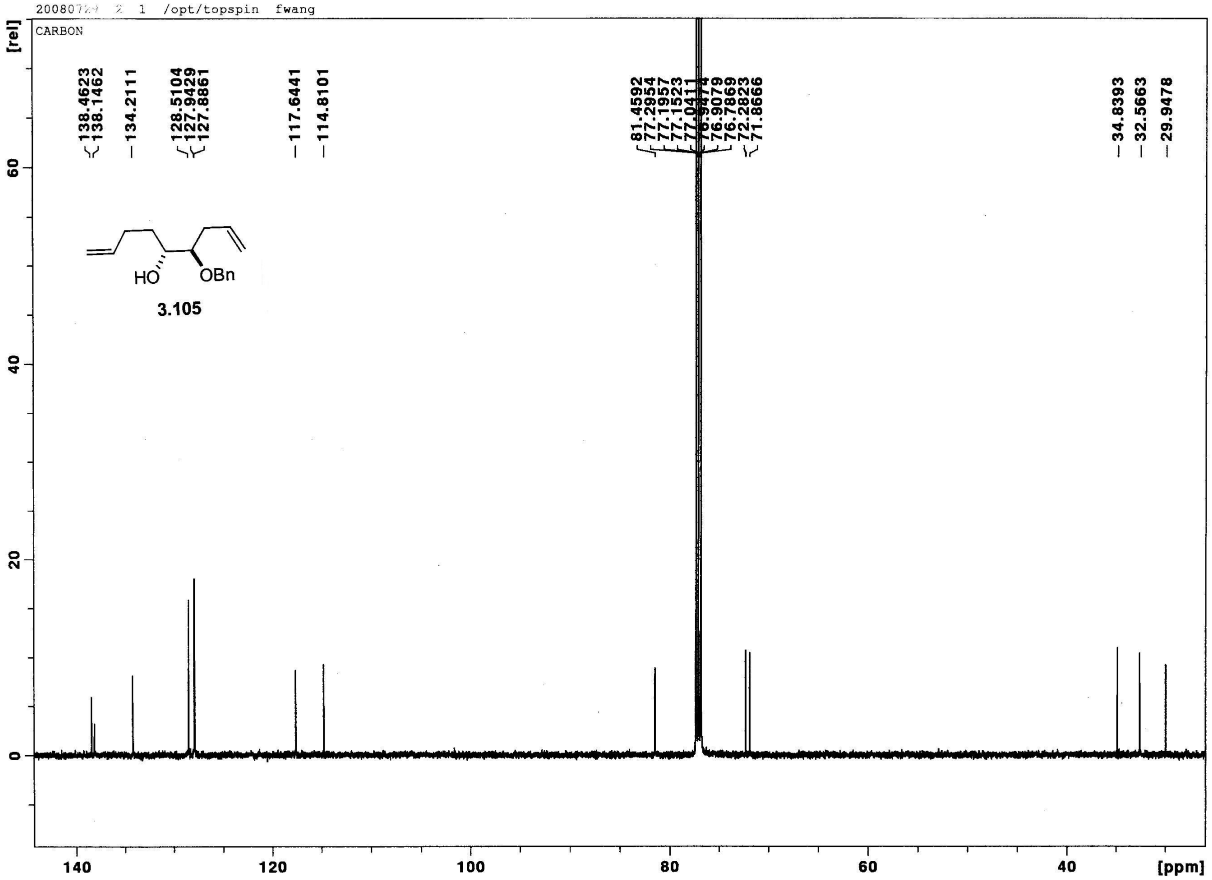
3.103

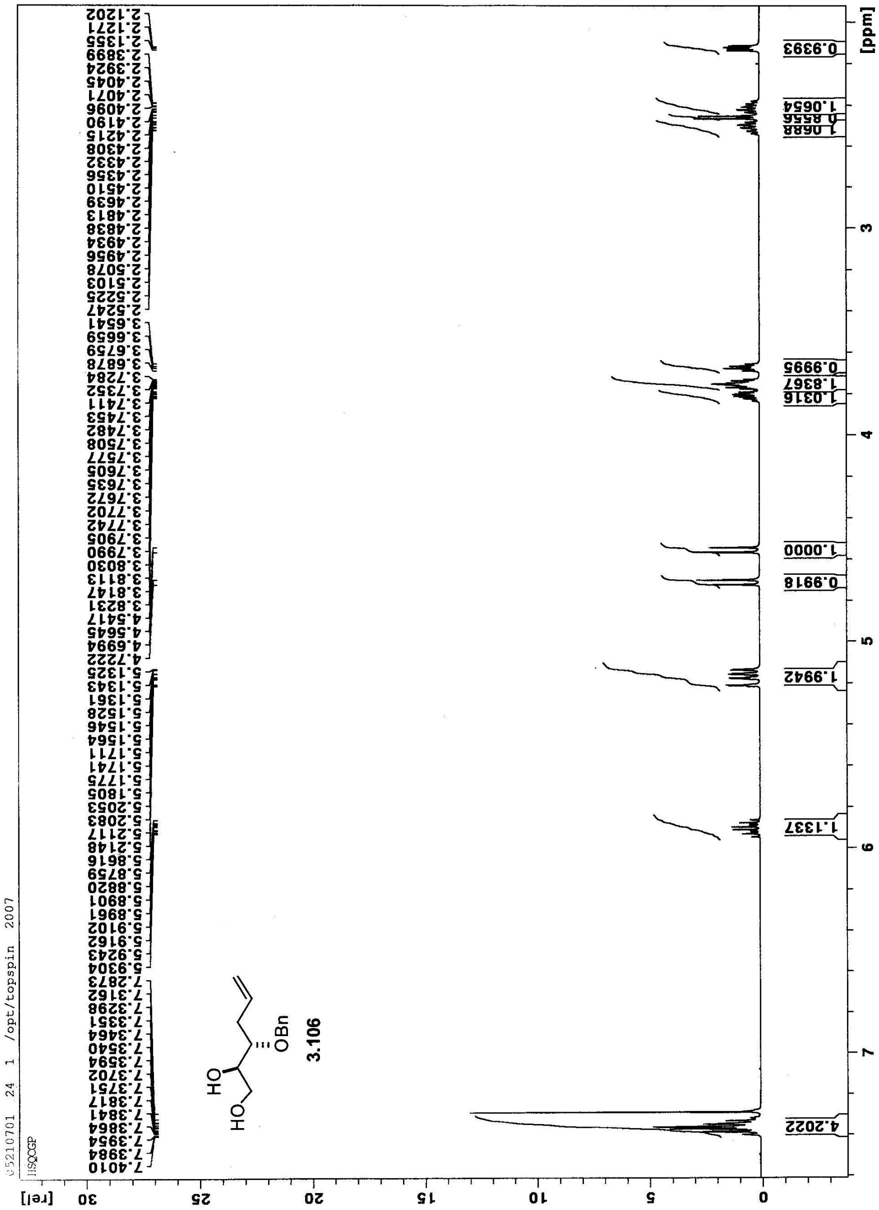

09140701 9 1 /opt/topspin 2007
HSQCGP
7.4109
7.3971
7.3825
7.3787
7.3680
7.3652
7.3527
7.3396
7.3176
7.3079
7.3034
7.2872
7.2585
5.9221
5.9079
5.9018
5.8938
5.8877
5.8736
5.8676
5.8595
5.8534
5.8392
5.1720
5.1690
5.1657
5.1628
5.1379
5.1348
5.1315
5.1286
5.1135
5.1117
5.1101
5.0933
5.0915
5.0898
4.8600
4.8362
4.8074
4.6841
4.6530
4.6292
4.6004
4.5899
3.1738
3.1601
3.1475
3.1341
3.1190
3.0933
3.0878
3.0850
3.0794
3.0737
3.0709
3.0654
2.8174
2.8081
2.7993
2.7793
2.7583
2.7530
2.5471
2.5417
2.5374
2.5320
2.5185
2.5085
2.4972
2.4947
2.4923
2.4800
2.4686
2.4662
2.4636
2.4550
2.4525
2.4500
2.4284
2.4162
2.4139
2.4017
2.3997
2.3876
2.3853
2.3731
O
OBn
3.104
3.6363
0.7571
1.0000
1.9423
0.9448
0.9662
0.9397
0.8866
0.9498
0.9227
1.0648
1.0152
[rel]
30
20
10
0
7
6
5
4
3
[ppm]

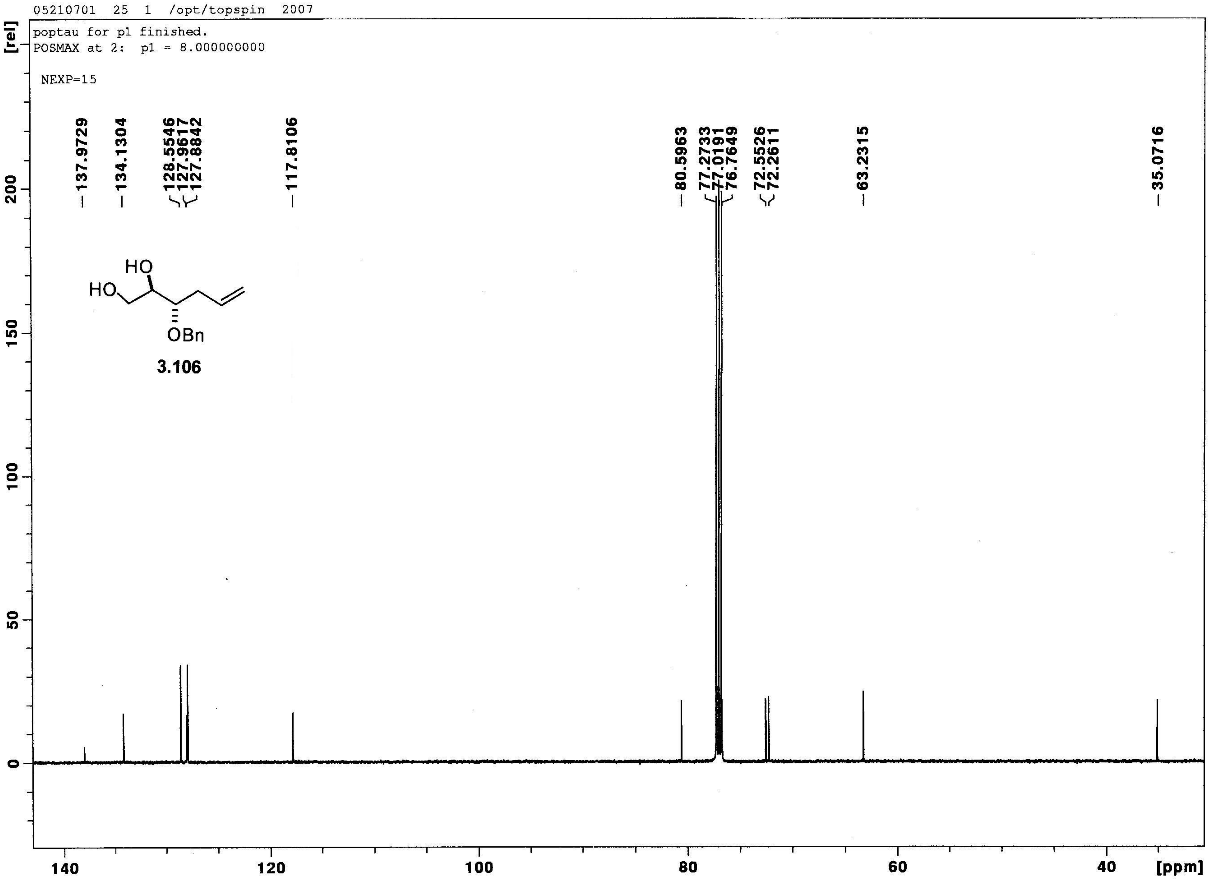

09140701 10 1 /opt/topspin 2007
poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
138.4955
133.9469
128.3295
127.7403
127.5484
117.4533
80.0608
77.2796
77.1586
77.0254
76.8667
76.7712
71.6623
54.6334
43.3802
37.0624
OBn
[rel]
80
60
40
20
0
140
120
100
80
60
40 [ppm]

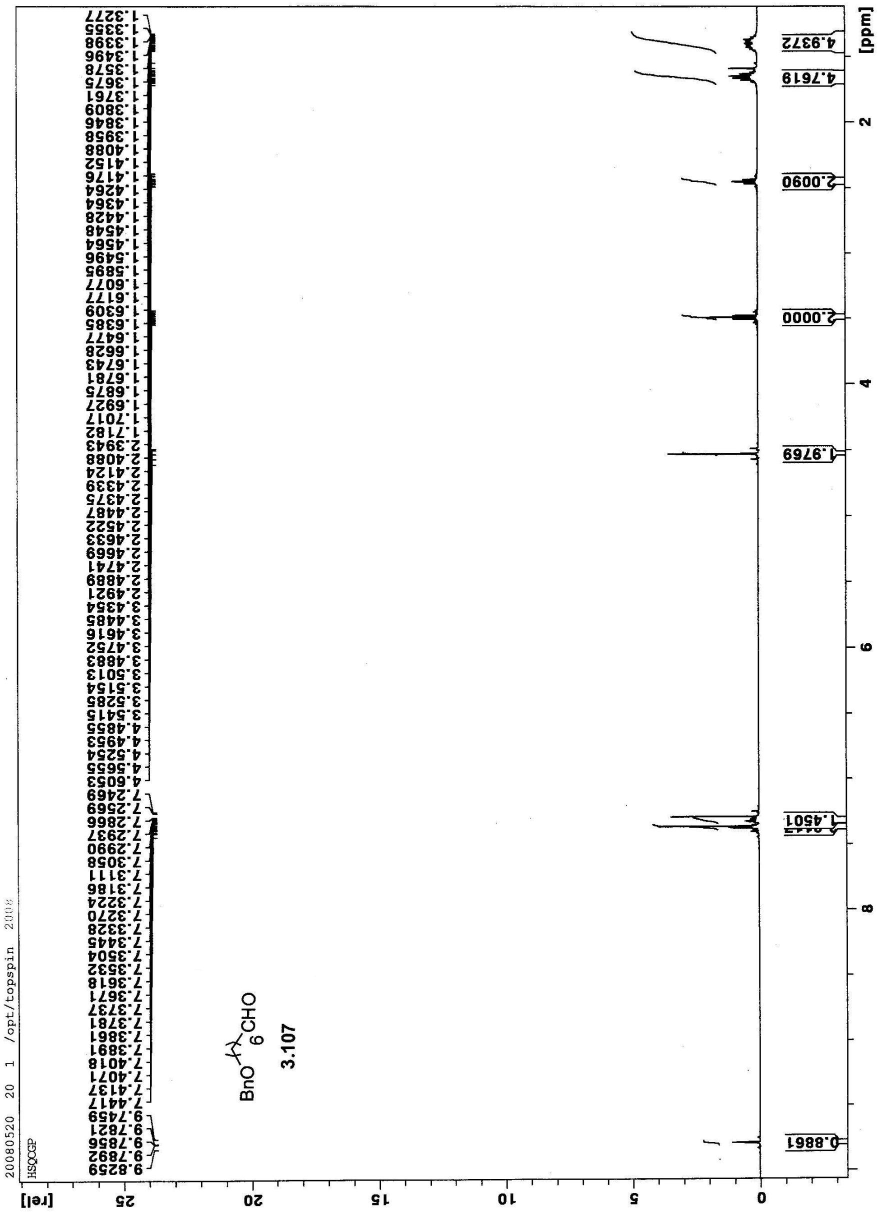
3.104


20080729 1 1 /opt/topspin fwang
PROTON
7.3993
7.3965
7.3883
7.3848
7.3829
7.3713
7.3574
7.3453
7.3415
7.3398
7.3344
7.3281
7.3150
7.2868
5.9137
5.8935
5.8793
5.8729
5.8653
5.8591
5.8519
5.8385
5.8179
5.1893
5.1863
5.1829
5.1799
5.1521
5.1486
5.1456
5.1337
5.1318
5.1301
5.1133
5.1115
5.1097
5.0747
5.0711
5.0678
5.0404
5.0368
5.0029
5.0007
4.9987
4.9969
4.9946
4.9827
4.9803
4.9783
4.9766
4.7491
4.7265
4.5264
4.5038
3.6112
3.6007
3.5962
3.5855
3.3853
3.3743
3.3632
3.3522
2.5270
2.5150
2.5124
2.5004
2.4981
2.4003
2.3976
2.3860
2.3834
2.3015
2.2907
2.2780
2.2650
2.2621
2.2489
2.1676
2.1528
2.1509
1.6181
1.6094
1.6030
1.5928
1.5882
1.5830
1.5709
HO
OBn
3.105
5.0279
2.0000
2.1271
2.0001
0.9925
0.9853
0.9841
0.9566
1.0772
1.0151
0.8090
1.0610
3.7770
7
6
5
4
3
2
[ppm]
0
20
40
60
[rel]

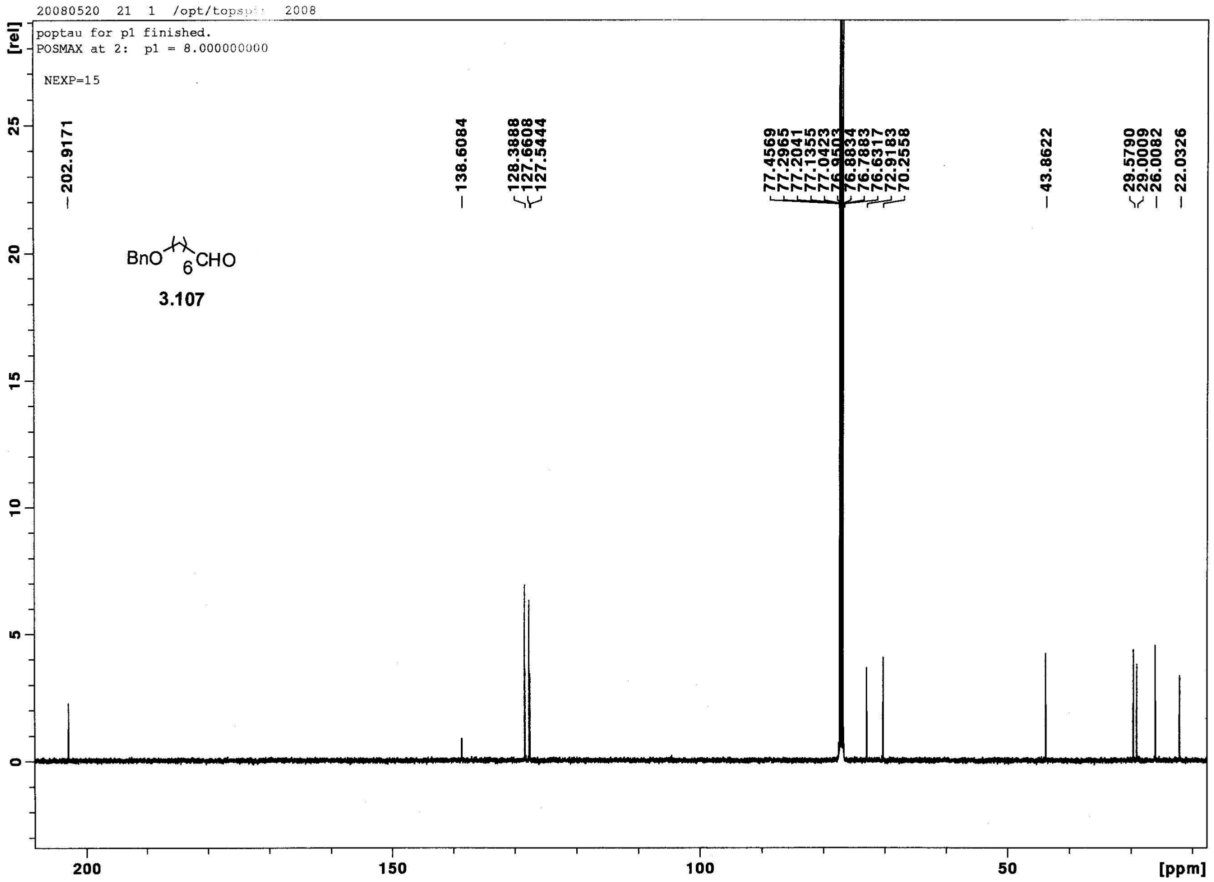

20080729 2 1 /opt/topspin fwang
CARBON
[rel]
60
40
20
0
138.4623
138.1462
134.2111
128.5104
127.9429
127.8861
117.6441
114.8101
81.4592
77.2954
77.1957
77.1523
77.0411
76.9474
76.9079
76.7869
72.2823
71.8666
34.8393
32.5663
29.9478
HO
OBn
3.105
140
120
100
80
60
40
[ppm]

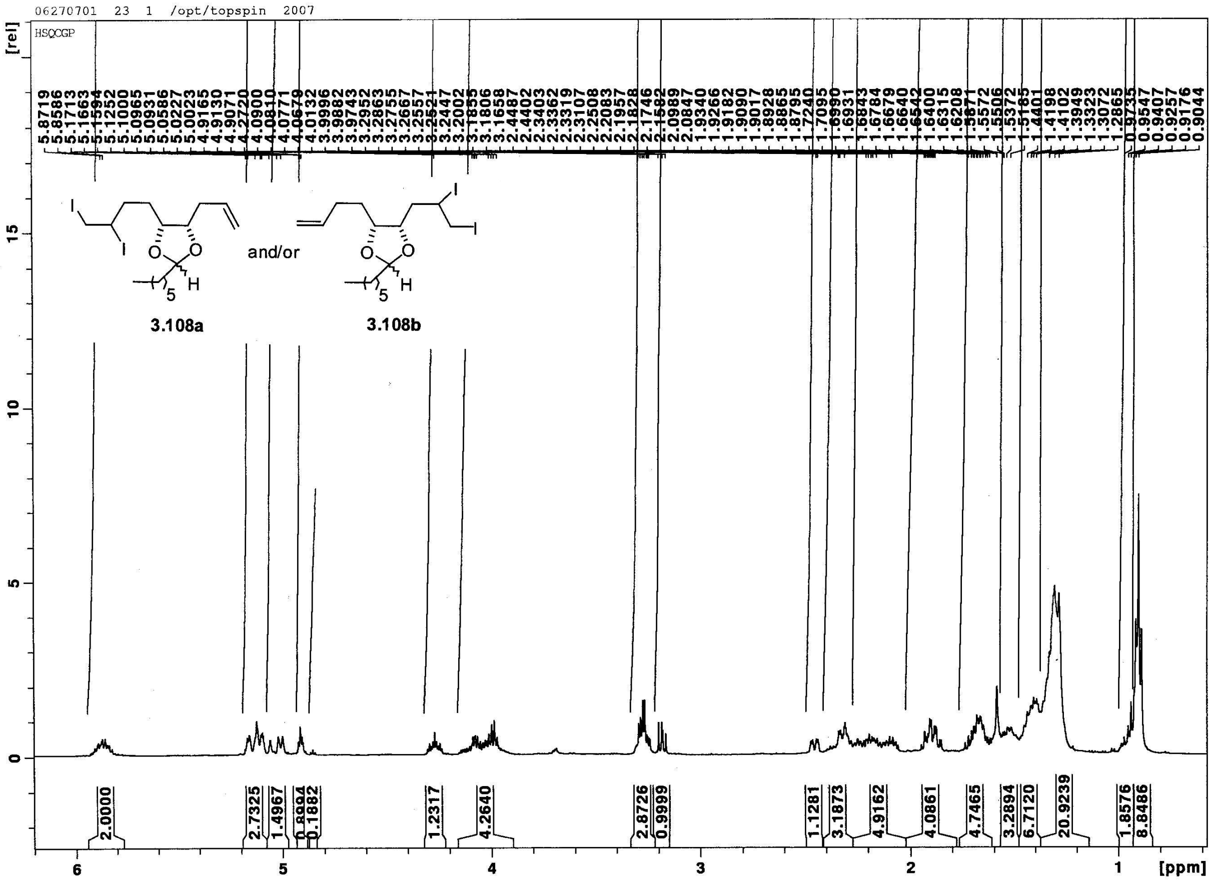

3.106
05210701 24 1 /opt/topspin 2007
zgpr
HO
HO
OBn
7.4010
7.3984
7.3954
7.3864
7.3841
7.3817
7.3751
7.3702
7.3594
7.3540
7.3464
7.3351
7.3298
7.3162
7.2873
5.9304
5.9243
5.9162
5.9102
5.8961
5.8901
5.8820
5.8759
5.8616
5.2148
5.2117
5.2083
5.2053
5.1805
5.1775
5.1741
5.1711
5.1564
5.1546
5.1528
5.1361
5.1343
5.1325
4.7222
4.6994
4.5645
4.5417
3.8231
3.8147
3.8113
3.8030
3.7990
3.7905
3.7742
3.7702
3.7672
3.7635
3.7605
3.7577
3.7508
3.7482
3.7453
3.7411
3.7352
3.7284
3.6878
3.6759
3.6659
3.6541
2.5247
2.5225
2.5103
2.5078
2.4956
2.4934
2.4838
2.4813
2.4639
2.4510
2.4356
2.4332
2.4308
2.4215
2.4190
2.4096
2.4071
2.4045
2.3924
2.3899
2.1355
2.1271
2.1202
4.2022
1.1337
1.9942
0.9918
1.0000
1.0316
1.8367
0.9995
1.0688
0.8556
1.0654
0.9393
7
6
5
4
3
[ppm]
0
5
10
15
20
25
30
[rel]

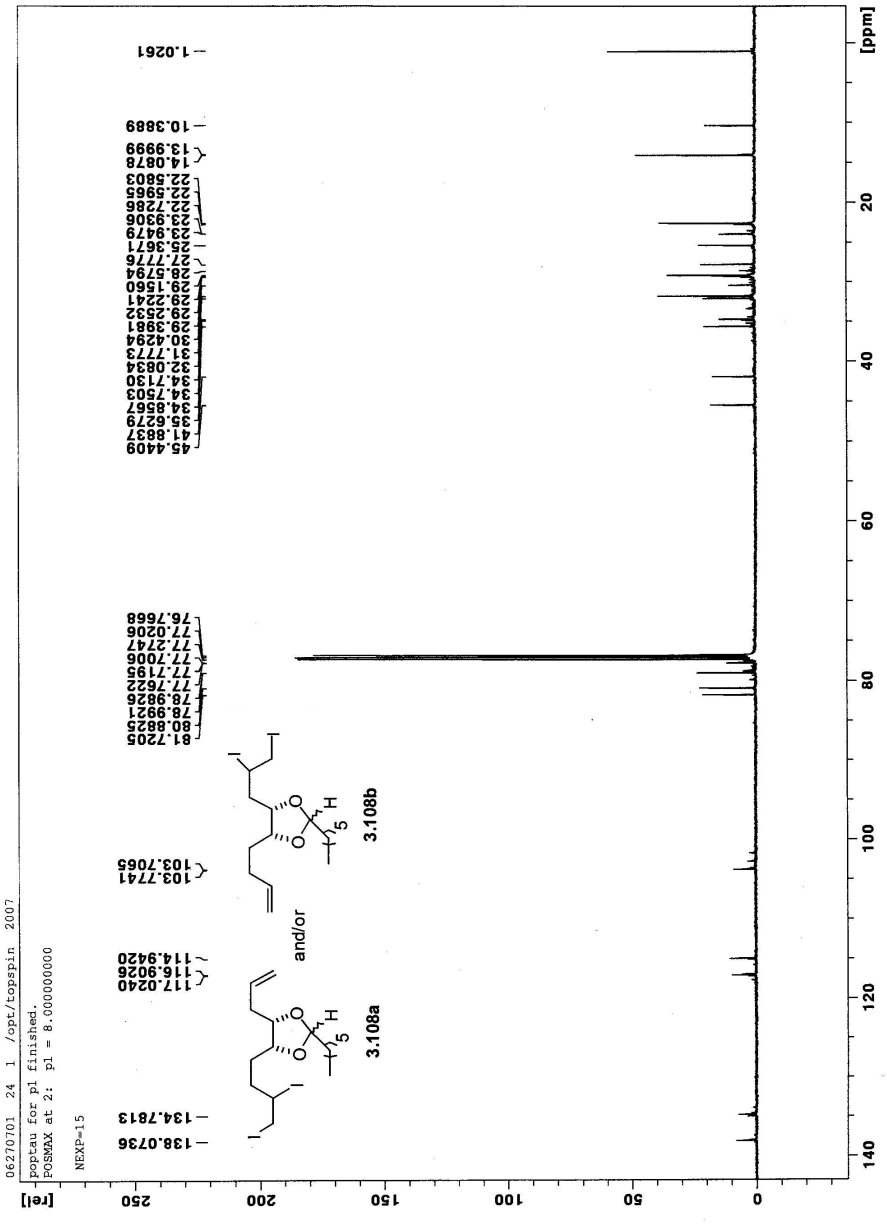

05210701 25 1 /opt/topspin 2007
poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
137.9729
134.1304
128.5546
127.9617
127.8842
117.8106
80.5963
77.2733
77.0191
76.7649
72.5526
72.2611
63.2315
35.0716
HO
HO
OBn
3.106
[rel]
200
150
100
50
0
140
120
100
80
60
40
[ppm]

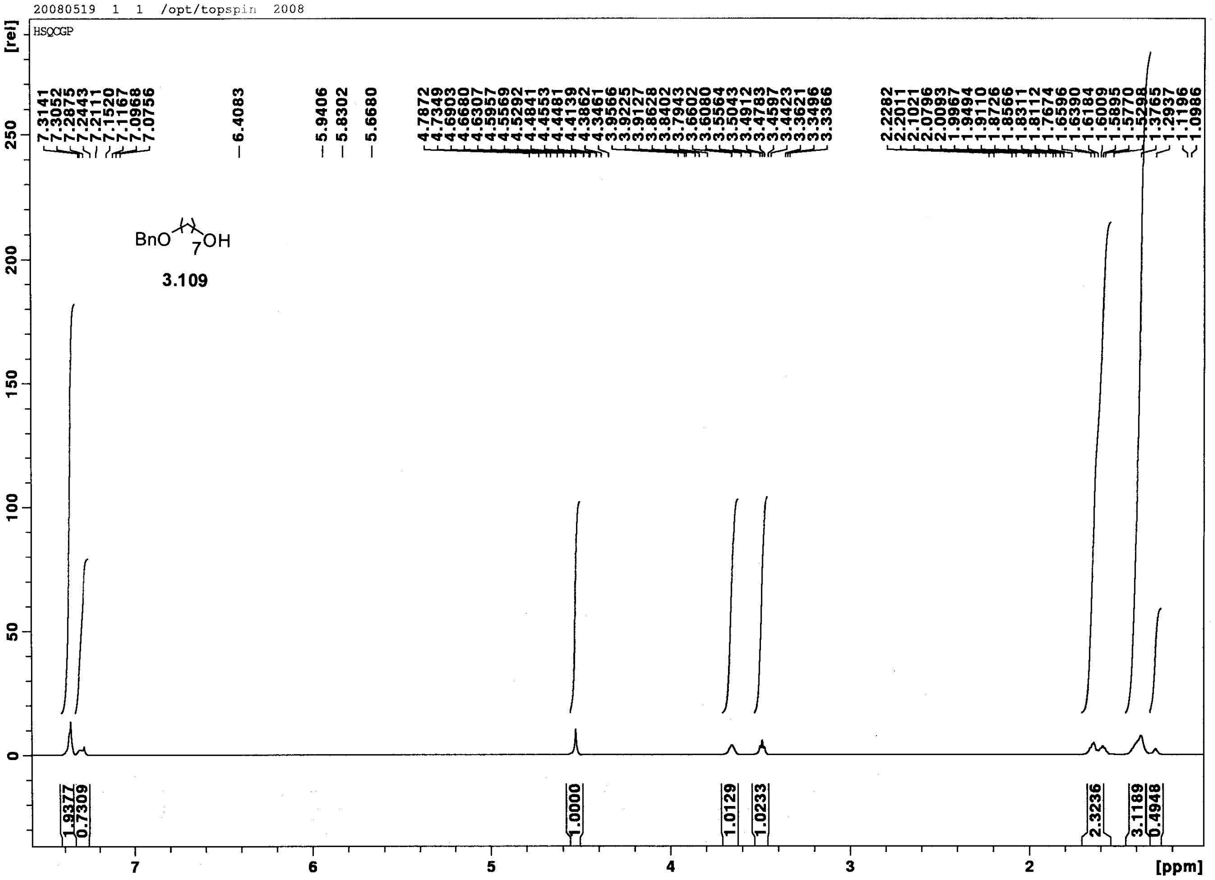

20080520 20 1 /opt/topspin 2008
HSQCGP
BnO
6
CHO
9.8259
9.7892
9.7856
9.7821
9.7459
7.4417
7.4137
7.4071
7.4018
7.3891
7.3861
7.3781
7.3737
7.3671
7.3618
7.3532
7.3504
7.3445
7.3328
7.3270
7.3224
7.3186
7.3111
7.3058
7.2990
7.2937
7.2866
7.2569
7.2469
4.6053
4.5655
4.5254
4.4953
4.4855
3.5415
3.5285
3.5154
3.5013
3.4883
3.4752
3.4616
3.4485
3.4354
2.4921
2.4889
2.4741
2.4669
2.4633
2.4522
2.4487
2.4375
2.4339
2.4124
2.4088
2.3943
1.7182
1.7017
1.6927
1.6875
1.6781
1.6743
1.6628
1.6477
1.6385
1.6309
1.6177
1.6077
1.5895
1.5496
1.4564
1.4548
1.4428
1.4364
1.4264
1.4176
1.4152
1.4088
1.3958
1.3846
1.3809
1.3761
1.3675
1.3578
1.3496
1.3398
1.3355
1.3277
0.8861
1.4501
1.9769
2.0000
2.0090
4.7619
4.9372
[rel]
25
20
15
10
5
0
8
6
4
2
[ppm]

3.107

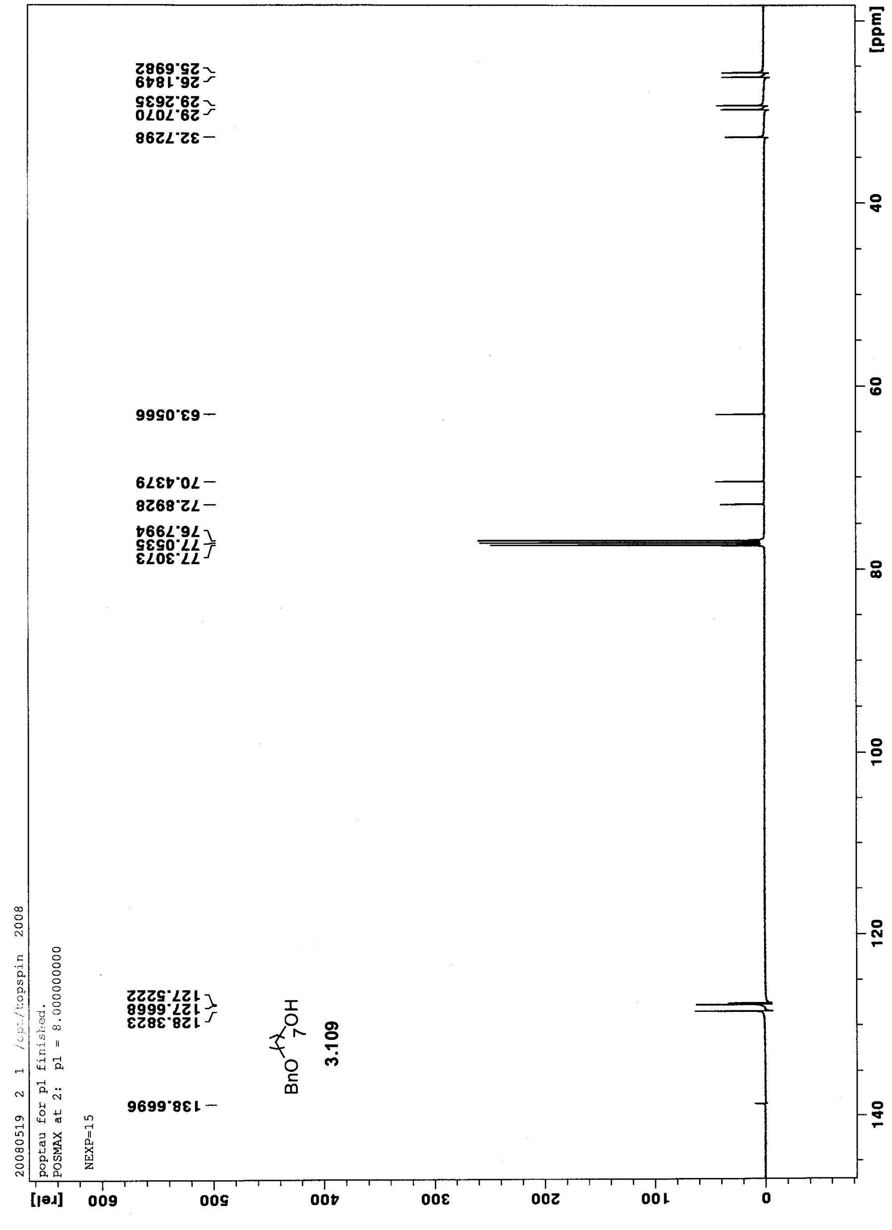

20080520 21 1 /opt/topspin 2008
poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
BnO
6
CHO
3.107
202.9171
138.6084
128.3888
127.6608
127.5444
77.4569
77.2965
77.2041
77.1355
77.0423
76.9503
76.8834
76.7883
76.6317
72.9183
70.2558
43.8622
29.5790
29.0009
26.0082
22.0326
[rel]
25
20
15
10
5
0
200
150
100
50
[ppm]

06270701 23 1 /opt/topspin 2007
HSQCGP
5.8719
5.8586
5.1713
5.1663
5.1594
5.1252
5.1000
5.0965
5.0931
5.0586
5.0227
5.0023
4.9165
4.9130
4.9071
4.2720
4.0900
4.0810
4.0771
4.0679
4.0132
3.9996
3.9882
3.9743
3.2952
3.2863
3.2755
3.2667
3.2557
3.2521
3.2447
3.2002
3.1855
3.1806
3.1658
2.4487
2.4402
2.3403
2.3362
2.3319
2.3107
2.2508
2.2083
2.1957
2.1828
2.1746
2.1582
2.0989
2.0847
1.9340
1.9266
1.9182
1.9090
1.9017
1.8928
1.8865
1.8795
1.7240
1.7095
1.6990
1.6931
1.6843
1.6784
1.6679
1.6640
1.6542
1.6400
1.6315
1.6208
1.5871
1.5572
1.5506
1.5372
1.5165
1.4401
1.4198
1.4102
1.3949
1.3323
1.3072
1.2865
0.9735
0.9547
0.9407
0.9257
0.9176
0.9044
I
I
O
O
5
H
3.108a
and/or
I
I
O
O
5
H
3.108b
2.0000
2.7325
1.4967
0.8994
0.1882
1.2317
4.2640
2.8726
0.9999
1.1281
3.1873
4.9162
4.0861
4.7465
3.2894
6.7120
20.9239
1.8576
8.8486
[rel]
15
10
5
0
6
5
4
3
2
1
[ppm]

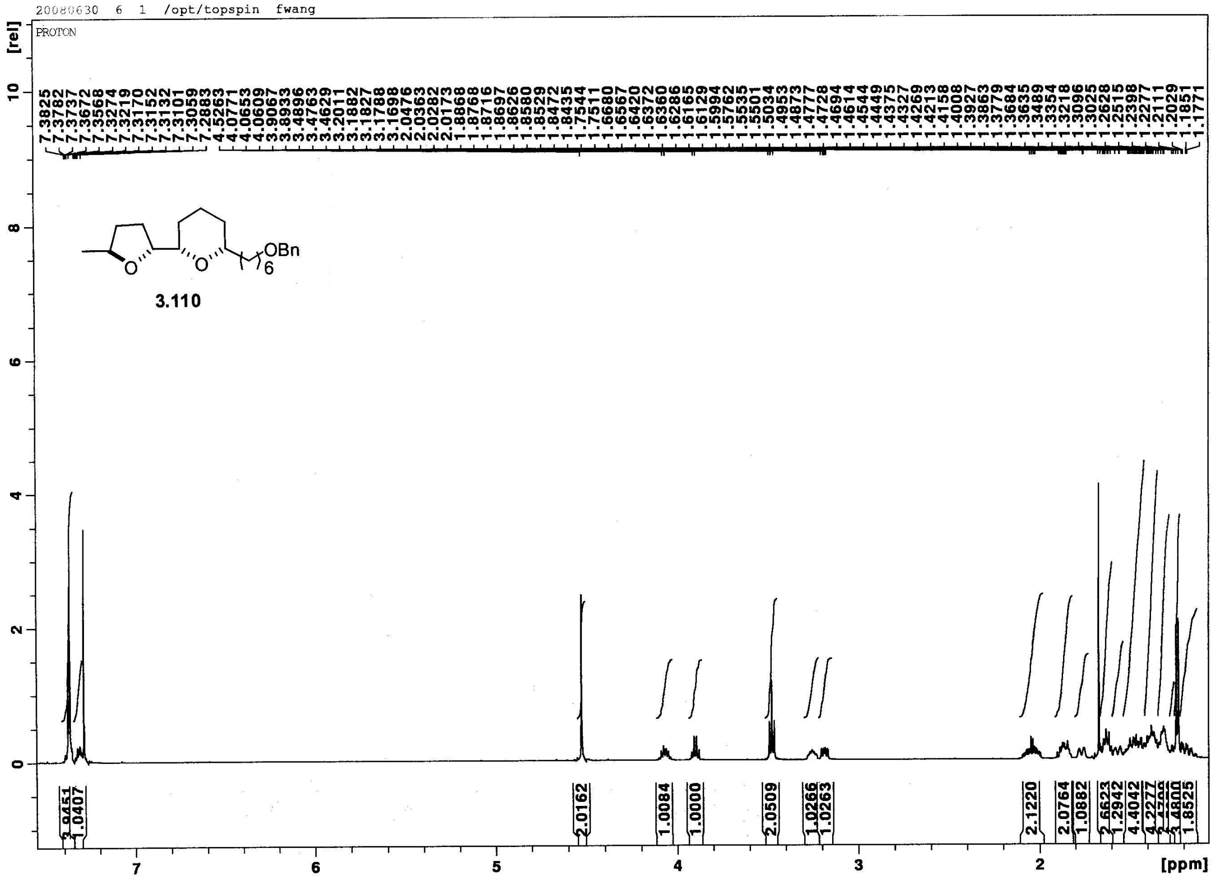

06270701 24 1 /opt/topspin 2007
poptau for p1 finished.
POSMAX at 2: p1 = 8.000000000
NEXP=15
138.0736
134.7813
117.0240
116.9026
114.9420
103.7741
103.7065
81.7205
80.8825
78.9921
78.9826
77.7622
77.7195
77.7006
77.2747
77.0206
76.7668
45.4409
41.8837
35.6279
34.8567
34.7503
34.7130
32.0834
31.7773
30.4294
29.3981
29.2532
29.2241
29.1560
28.5794
27.7776
25.3671
23.9479
23.9306
22.7286
22.5965
22.5803
14.0878
13.9999
10.3889
1.0261
3.108a
and/or
3.108b
O
O
H
5
[ppm]
140
120
100
80
60
40
20
[rel]
250
200
150
100
50
0


20080519 1 1 /opt/topspin 2008
HSQCGP
[rel]
250
200
150
100
50
0
7.3141
7.3052
7.2875
7.2443
7.2111
7.1520
7.1167
7.0968
7.0756
6.4083
5.9406
5.8302
5.6680
4.7872
4.7349
4.6903
4.6680
4.6307
4.5957
4.5569
4.5292
4.4841
4.4553
4.4481
4.4139
4.3862
4.3461
3.9566
3.9225
3.9127
3.8628
3.8402
3.7943
3.6602
3.6080
3.5564
3.5043
3.4912
3.4783
3.4597
3.4423
3.3621
3.3496
3.3366
2.2282
2.2011
2.1021
2.0796
2.0093
1.9967
1.9494
1.9110
1.8726
1.8566
1.8311
1.8112
1.7674
1.6596
1.6390
1.6184
1.6009
1.5895
1.5770
1.5298
1.3765
1.2937
1.1196
1.0986
BnO
7
OH
1.9377
0.7309
1.0000
1.0129
1.0233
2.3236
3.1189
0.4948
7
6
5
4
3
2
[ppm]

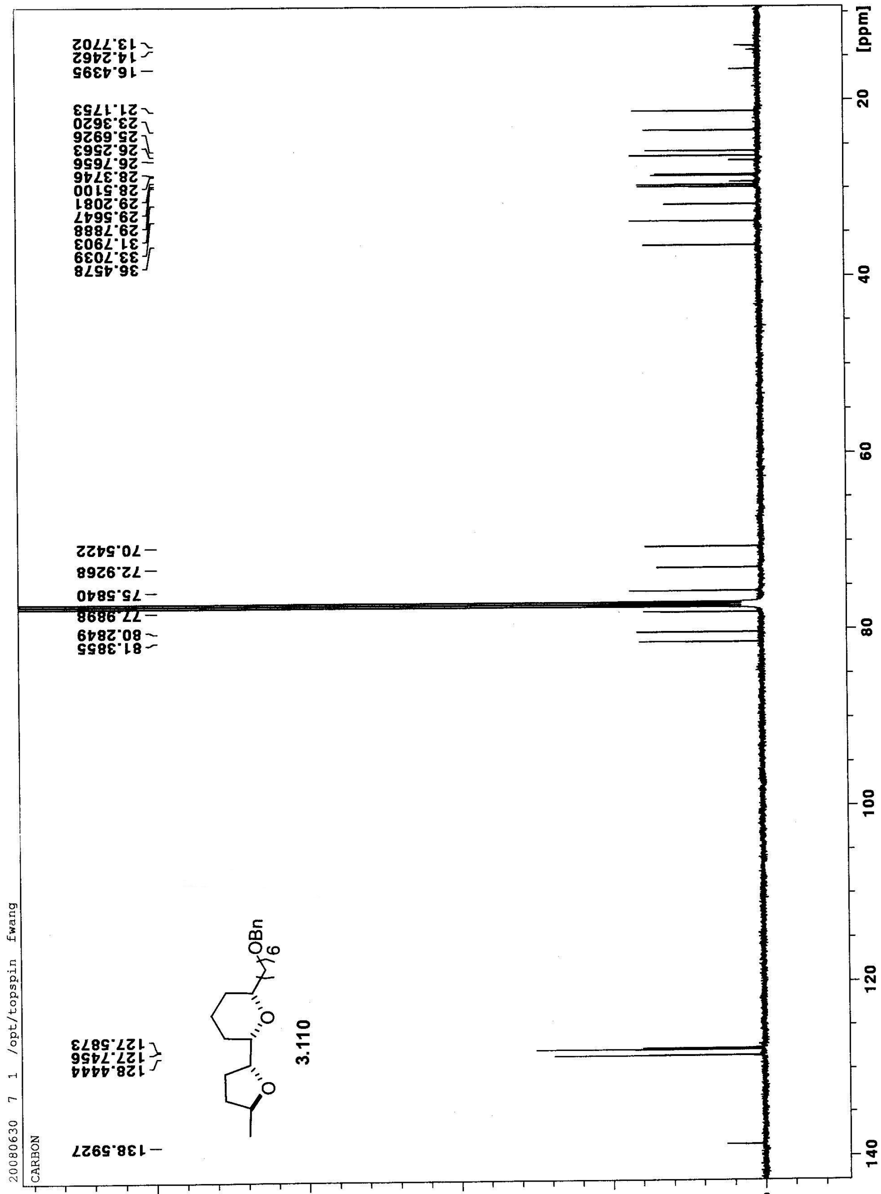
3.109

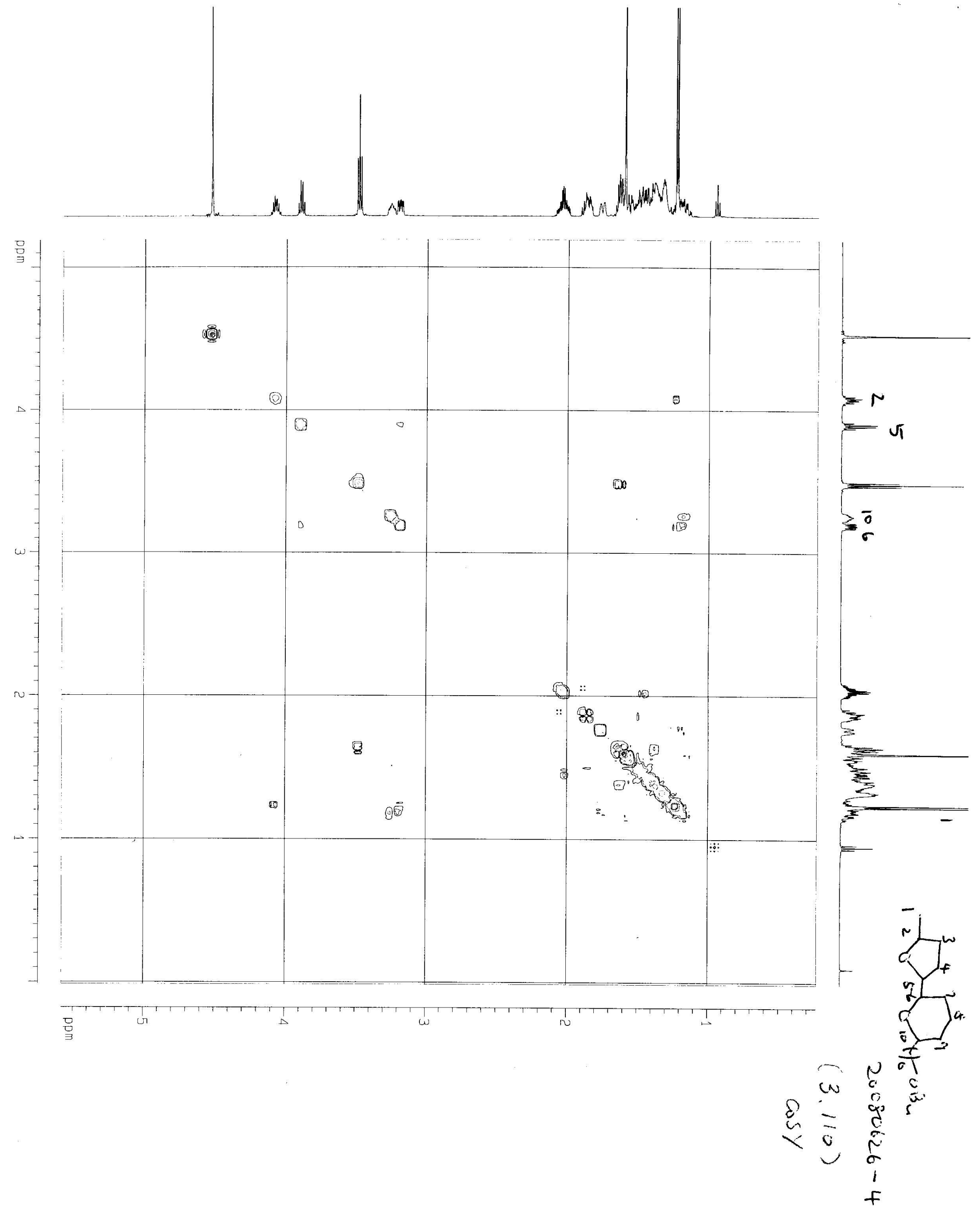


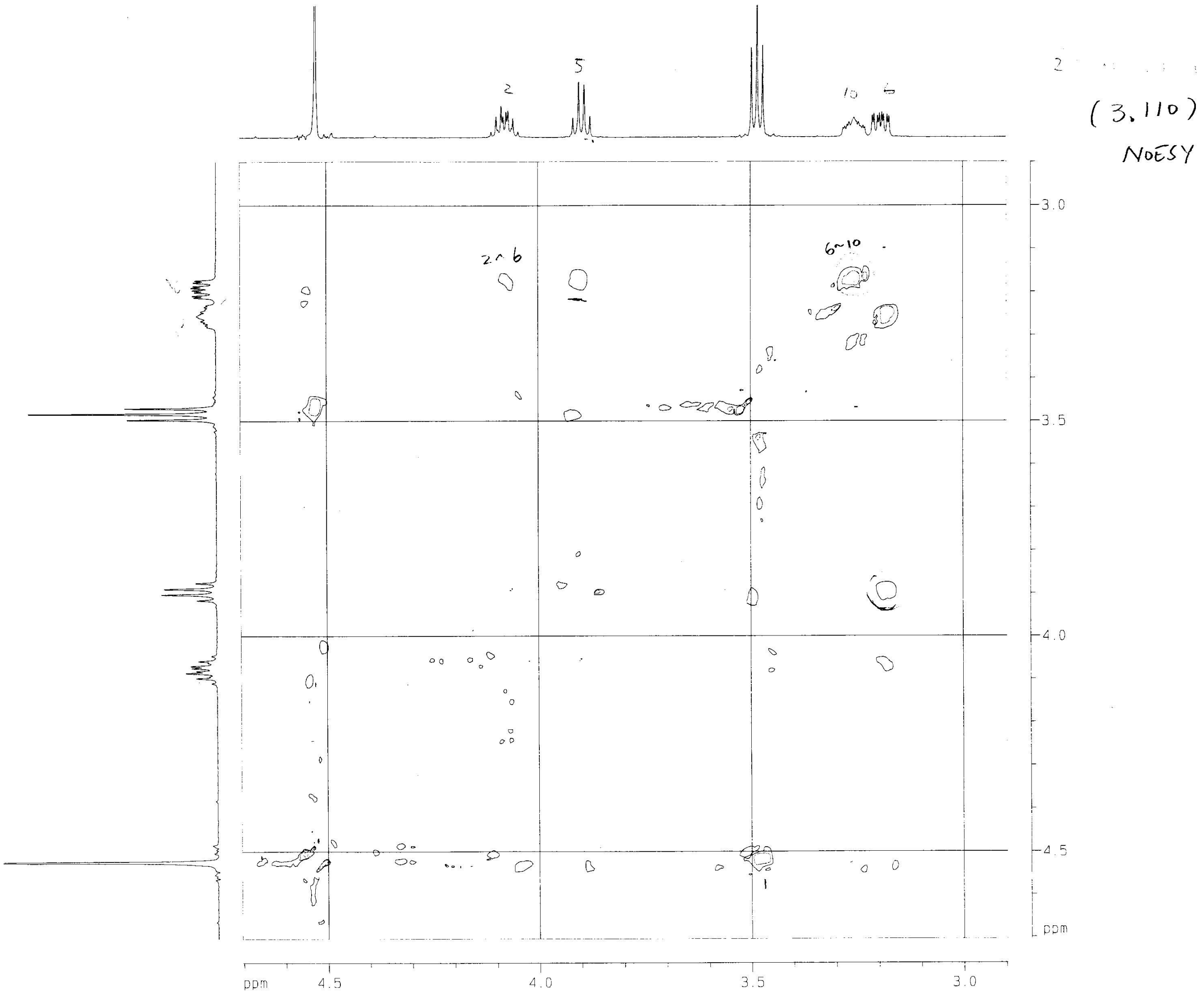
20080519 2 1 /opt/topspin 2008
poptau for p1 finished.
POSMAX at 2: p1 = 8.00000000
NEXP=15
138.6696
128.3823
127.6668
127.5222
77.3073
77.0535
76.7994
72.8928
70.4379
63.0566
32.7298
29.7070
29.2635
26.1849
25.6982
BnO
OH
7
3.109
[rel]
600
500
400
300
200
100
0
140
120
100
80
60
40
[ppm]

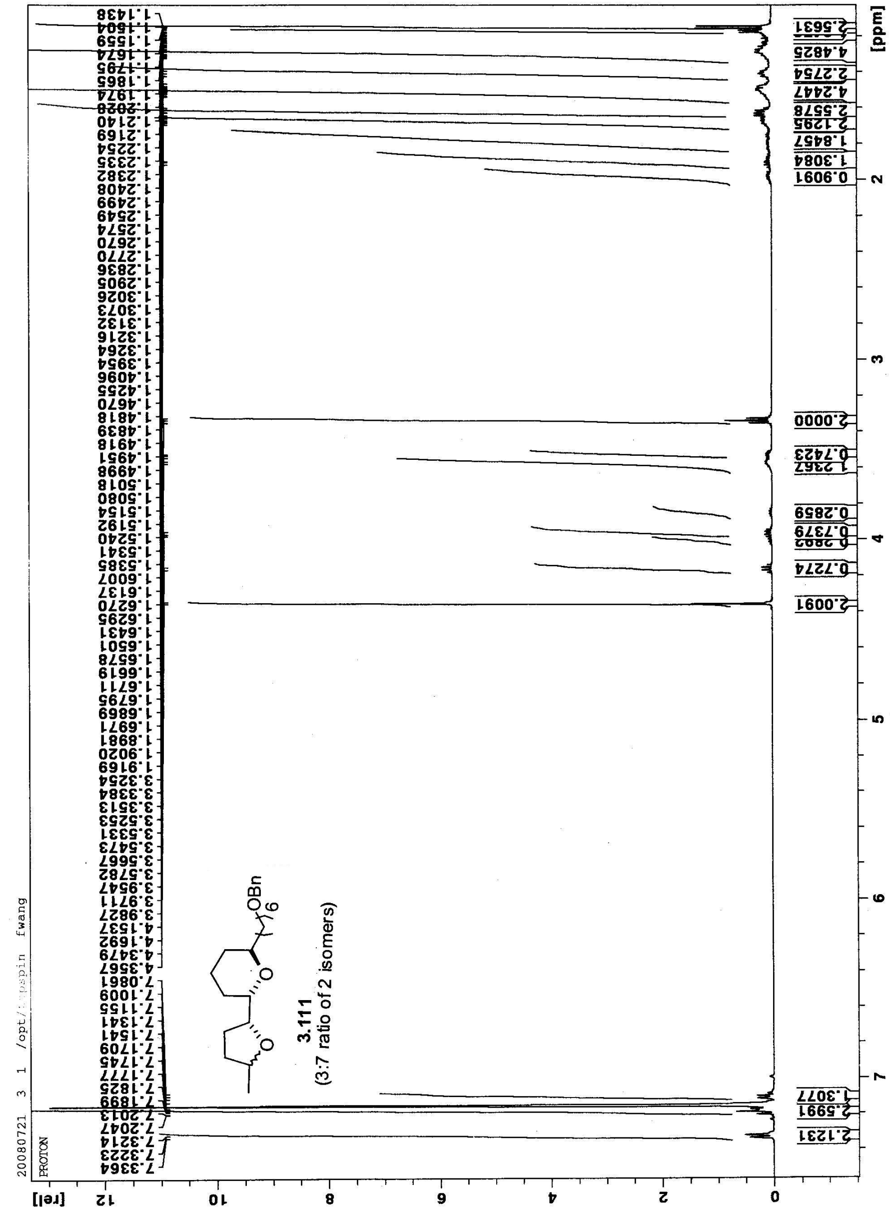

3.110

20080630 6 1 /opt/topspin fwang
PROTON
7.3825
7.3782
7.3737
7.3672
7.3568
7.3274
7.3219
7.3170
7.3152
7.3132
7.3101
7.3059
7.2883
4.5263
4.0771
4.0653
4.0609
3.9067
3.8933
3.4896
3.4763
3.4629
3.2011
3.1882
3.1827
3.1788
3.1698
2.0476
2.0363
2.0282
2.0173
1.8868
1.8768
1.8716
1.8697
1.8626
1.8580
1.8529
1.8472
1.8435
1.7544
1.7511
1.6680
1.6567
1.6420
1.6372
1.6360
1.6286
1.6165
1.6129
1.5994
1.5762
1.5535
1.5501
1.5034
1.4953
1.4873
1.4777
1.4728
1.4694
1.4614
1.4544
1.4449
1.4375
1.4327
1.4269
1.4213
1.4158
1.4008
1.3927
1.3863
1.3779
1.3684
1.3635
1.3489
1.3354
1.3218
1.3096
1.3025
1.2628
1.2515
1.2398
1.2277
1.2111
1.2029
1.1851
1.1771
OBn
6
O
O
3.9451
1.0407
2.0162
1.0084
1.0000
2.0509
1.0266
1.0263
2.1220
2.0764
1.0882
2.6623
1.2942
4.4042
4.2277
3.4800
1.8525
[rel]
10
8
6
4
2
0
7
6
5
4
3
2
[ppm]

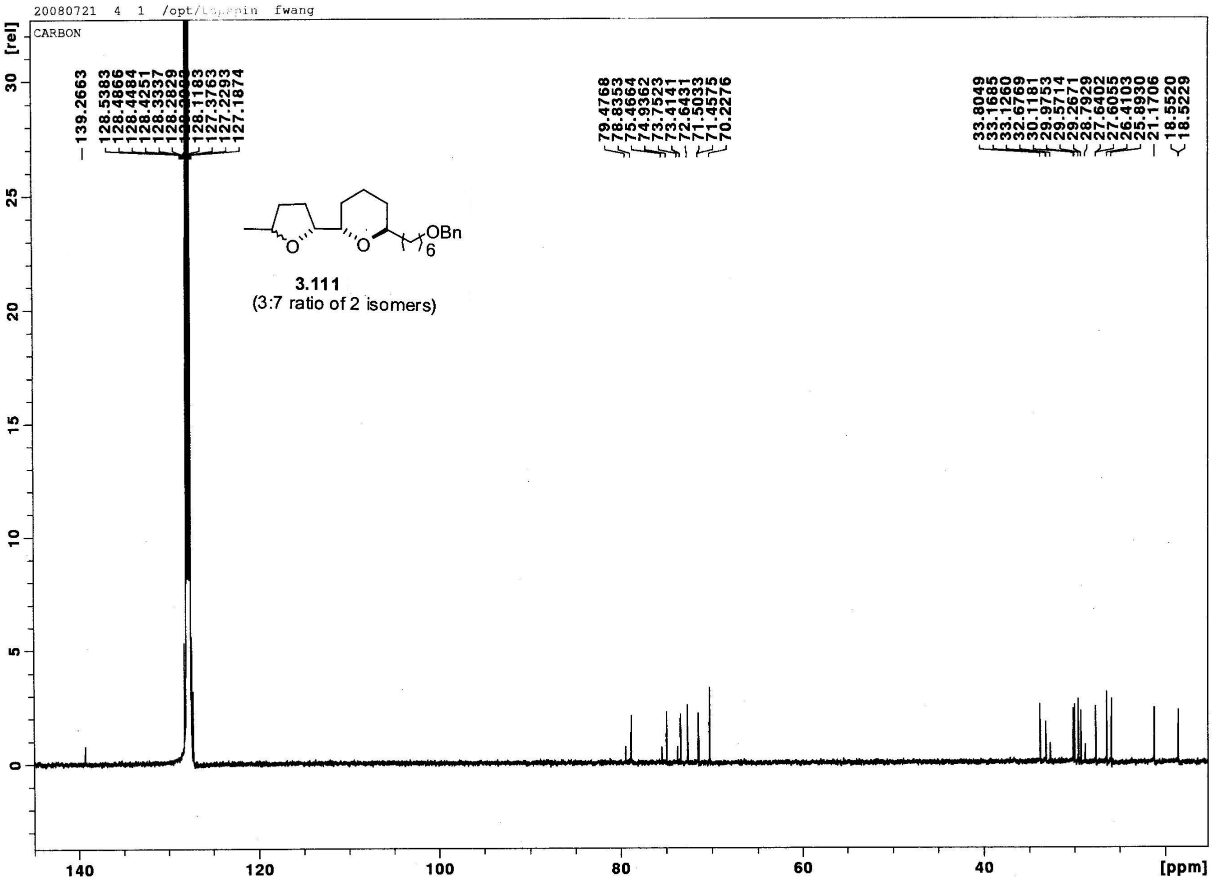

20080630 7 1 /opt/topspin fwang
CARBON
138.5927
128.4444
127.7456
127.5873
81.3855
80.2849
77.9898
75.5840
72.9268
70.5422
36.4578
33.7039
31.7903
29.7888
29.5647
29.2081
28.5100
28.3746
26.7656
26.2563
25.6926
23.3620
21.1753
16.4395
14.2462
13.7702
OBn
O
O
6
3.110
[ppm]
140
120
100
80
60
40
20
[rel]
20
15
10
5
0


ppm
5
4
3
2
1
ppm
1
2
3
4
2
5
10
6
1
1
2
3
4
5
6
7
8
9
10
20080626-4
(3,110)
COSY

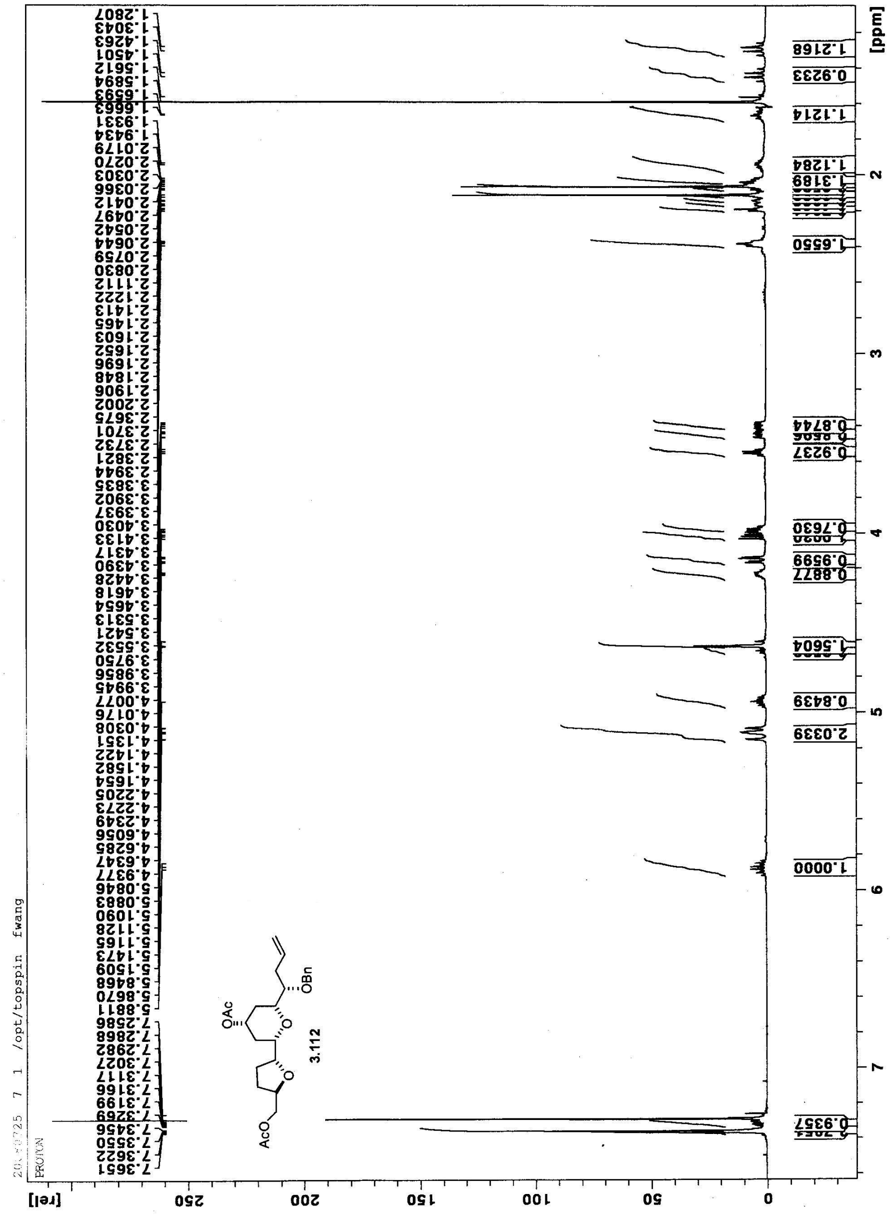

2
5
10
6
2
(3,110)
NOESY
2~6
6~10
1
3.0
3.5
4.0
4.5
ppm
ppm
4.5
4.0
3.5
3.0



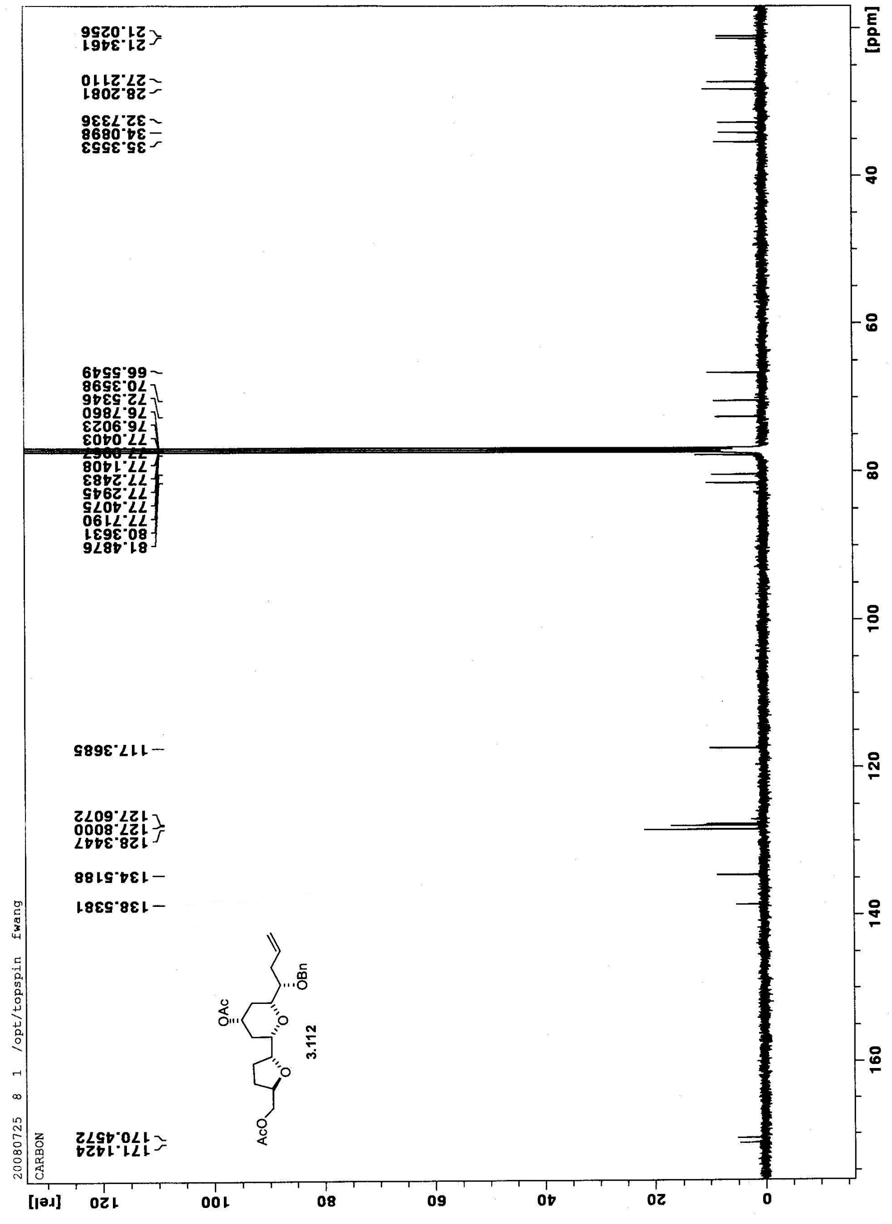
3.111
(3:7 ratio of 2 isomers)

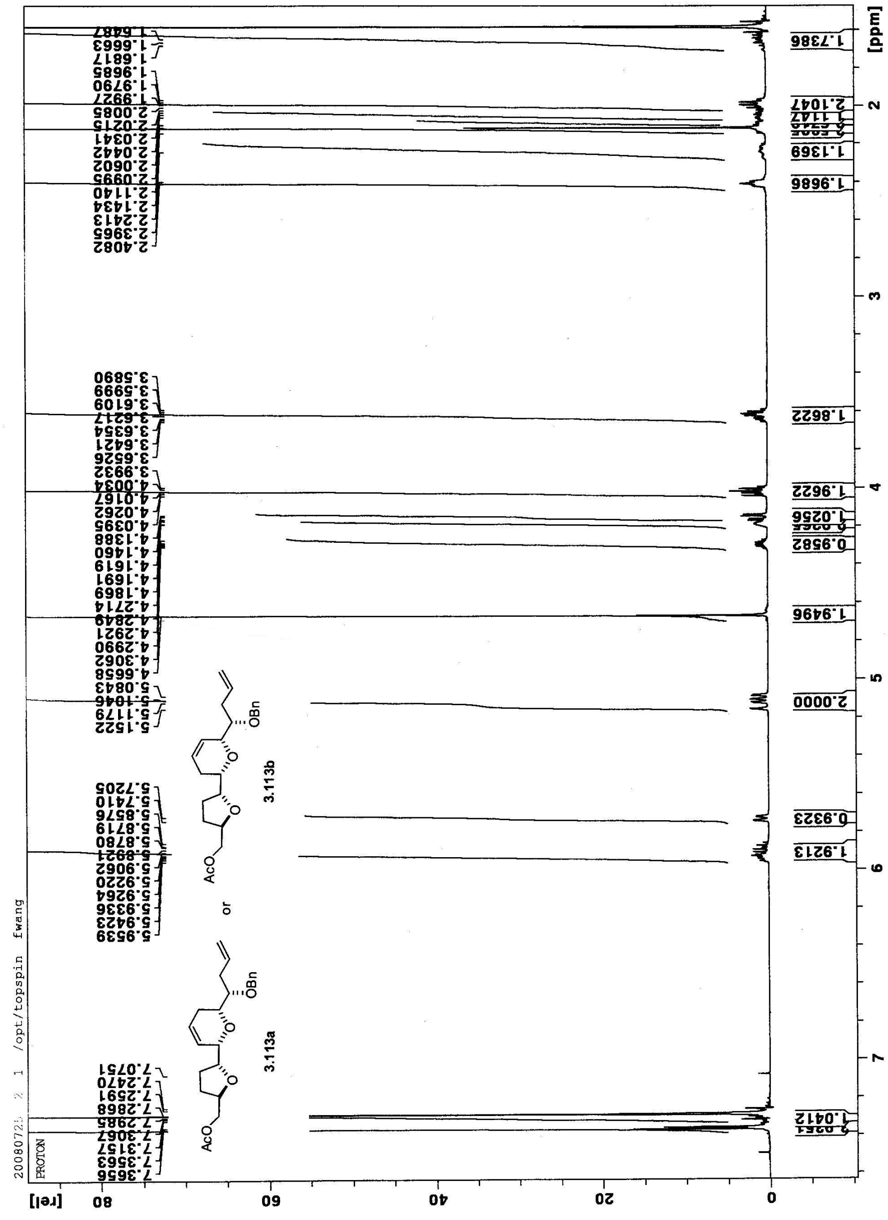


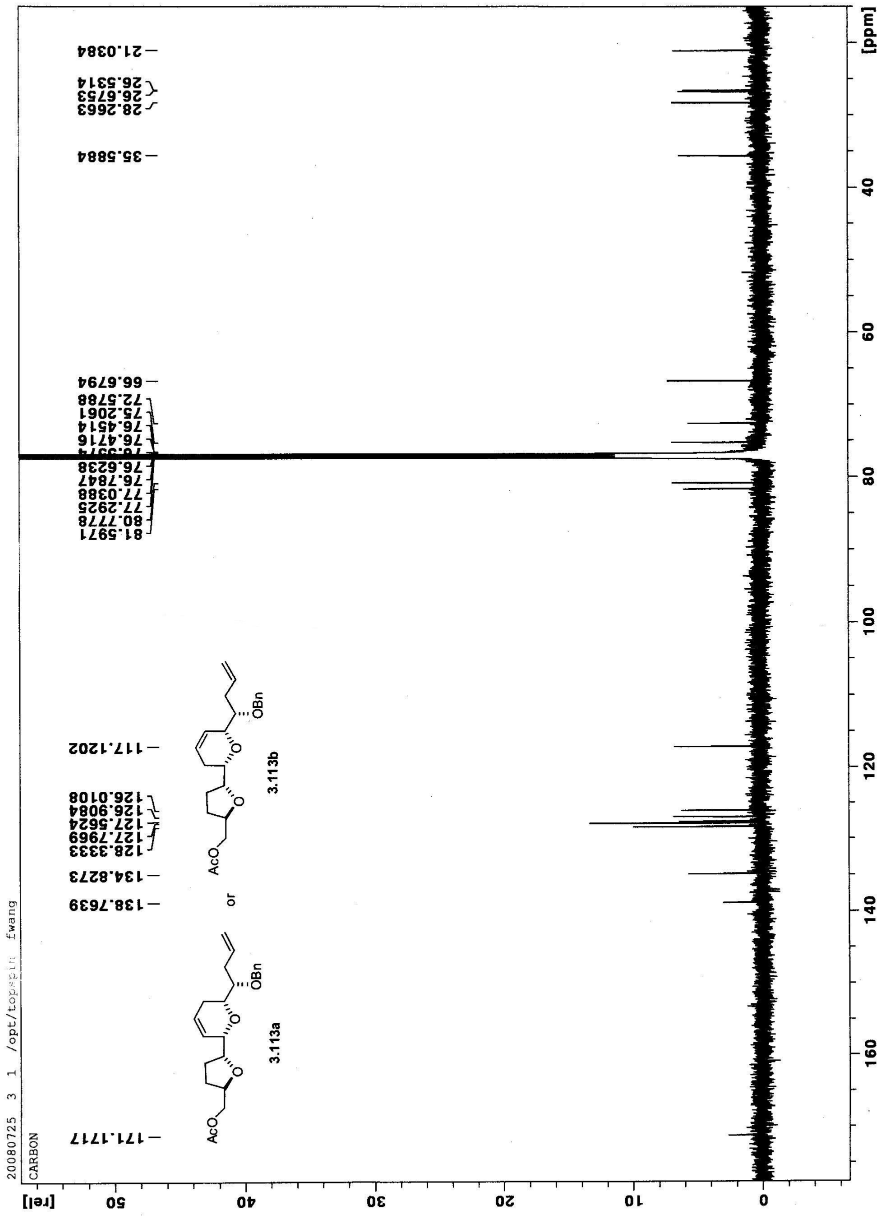
3.111
(3:7 ratio of 2 isomers)

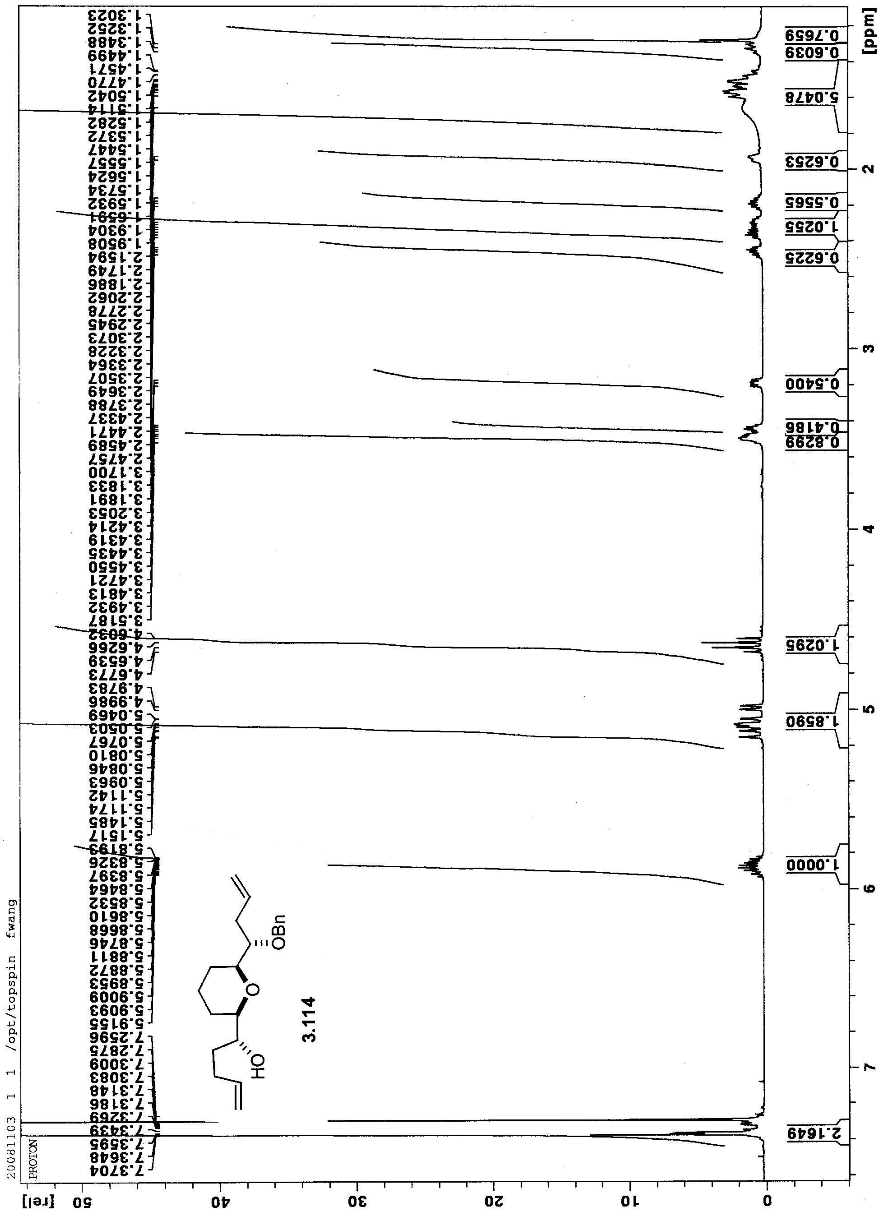


20..0725 7 1 /opt/topspin fwang
PROTON
7.3651
7.3622
7.3550
7.3456
7.3269
7.3199
7.3166
7.3117
7.3027
7.2982
7.2868
7.2586
5.8811
5.8670
5.8468
5.1509
5.1473
5.1165
5.1128
5.1090
5.0883
5.0846
4.9377
4.6347
4.6285
4.6056
4.2349
4.2273
4.2205
4.1654
4.1582
4.1422
4.1351
4.0308
4.0176
4.0077
3.9945
3.9856
3.9750
3.5532
3.5421
3.5313
3.4654
3.4618
3.4428
3.4390
3.4317
3.4133
3.4030
3.3937
3.3902
3.3835
2.3944
2.3821
2.3732
2.3701
2.3675
2.2002
2.1906
2.1848
2.1696
2.1652
2.1603
2.1465
2.1413
2.1222
2.1112
2.0830
2.0759
2.0644
2.0542
2.0497
2.0412
2.0366
2.0303
2.0270
2.0179
1.9434
1.9331
1.6663
1.6593
1.5894
1.5612
1.4501
1.4263
1.3043
1.2807
OAc
AcO
O
O
OBn
3.112
0.9357
1.0000
2.0339
0.8439
1.5604
0.8877
0.9599
0.7630
0.9237
0.8744
1.6550
1.3189
1.1284
1.1214
0.9233
1.2168
[rel]
250
200
150
100
50
0
7
6
5
4
3
2
[ppm]


20080725 8 1 /opt/topspin fwang
CARBON
171.1424
170.4572
138.5381
134.5188
128.3447
127.8000
127.6072
117.3685
81.4876
80.3631
77.7190
77.4075
77.2945
77.2483
77.1408
77.0967
77.0403
76.9023
76.7860
72.5346
70.3598
66.5549
35.3553
34.0898
32.7336
28.2081
27.2110
21.3461
21.0256
AcO
OAc
O
O
OBn
3.112
[ppm]
160
140
120
100
80
60
40
[rel]
120
100
80
60
40
20
0


20080723 2 1 /opt/topspin fwang
PROTON
3.113a
or
3.113b
AcO
OBn
1.6487
1.6663
1.6817
1.9685
1.9790
1.9927
2.0085
2.0215
2.0341
2.0442
2.0602
2.0995
2.1140
2.1434
2.2413
2.3965
2.4082
3.5890
3.5999
3.6109
3.6217
3.6354
3.6421
3.6526
3.9932
4.0034
4.0167
4.0262
4.0395
4.1388
4.1460
4.1619
4.1691
4.1869
4.2714
4.2849
4.2921
4.2990
4.3062
4.6658
5.0843
5.1046
5.1179
5.1522
5.7205
5.7410
5.8576
5.8719
5.8780
5.8921
5.9062
5.9220
5.9264
5.9336
5.9423
5.9539
7.0751
7.2470
7.2591
7.2868
7.2985
7.3067
7.3157
7.3563
7.3656
1.7386
2.1047
1.1142
1.1369
1.9686
1.8622
1.9622
1.0256
0.9582
1.9496
2.0000
0.9323
1.9213
1.0412
[ppm]
2
3
4
5
6
7
[rel]
0
20
40
60
80


20080725 3 1 /opt/topspin fwang
CARBON
171.1717
138.7639
134.8273
128.3333
127.7969
127.5624
126.9084
126.0108
117.1202
81.5971
80.7778
77.2925
77.0388
76.7847
76.6238
76.4716
76.4514
75.2061
72.5788
66.6794
35.5884
28.2663
26.6753
26.5314
21.0384
AcO
O
O
OBn
3.113a
or
3.113b
[ppm]
160
140
120
100
80
60
40
[rel]
50
40
30
20
10
0


20081103 1 1 /opt/topspin fwang
PROTON
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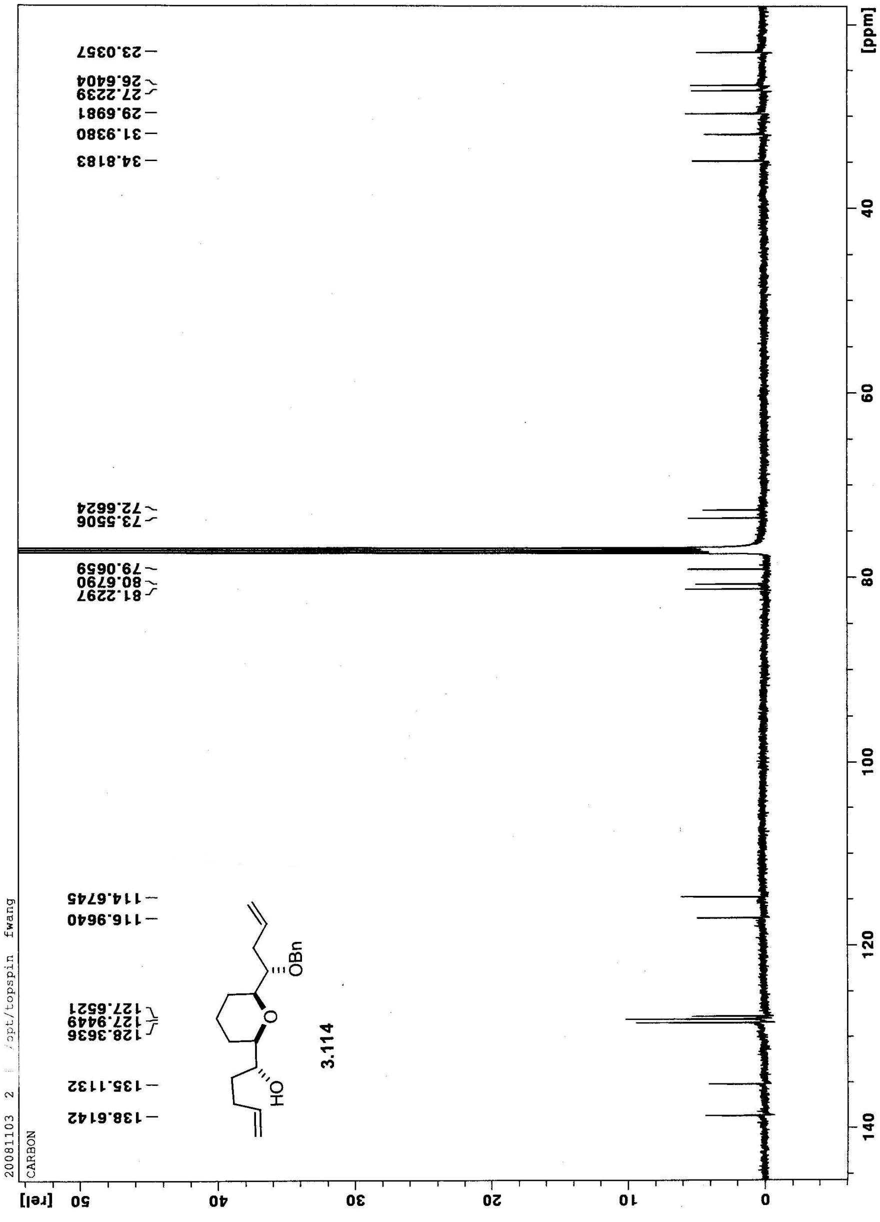
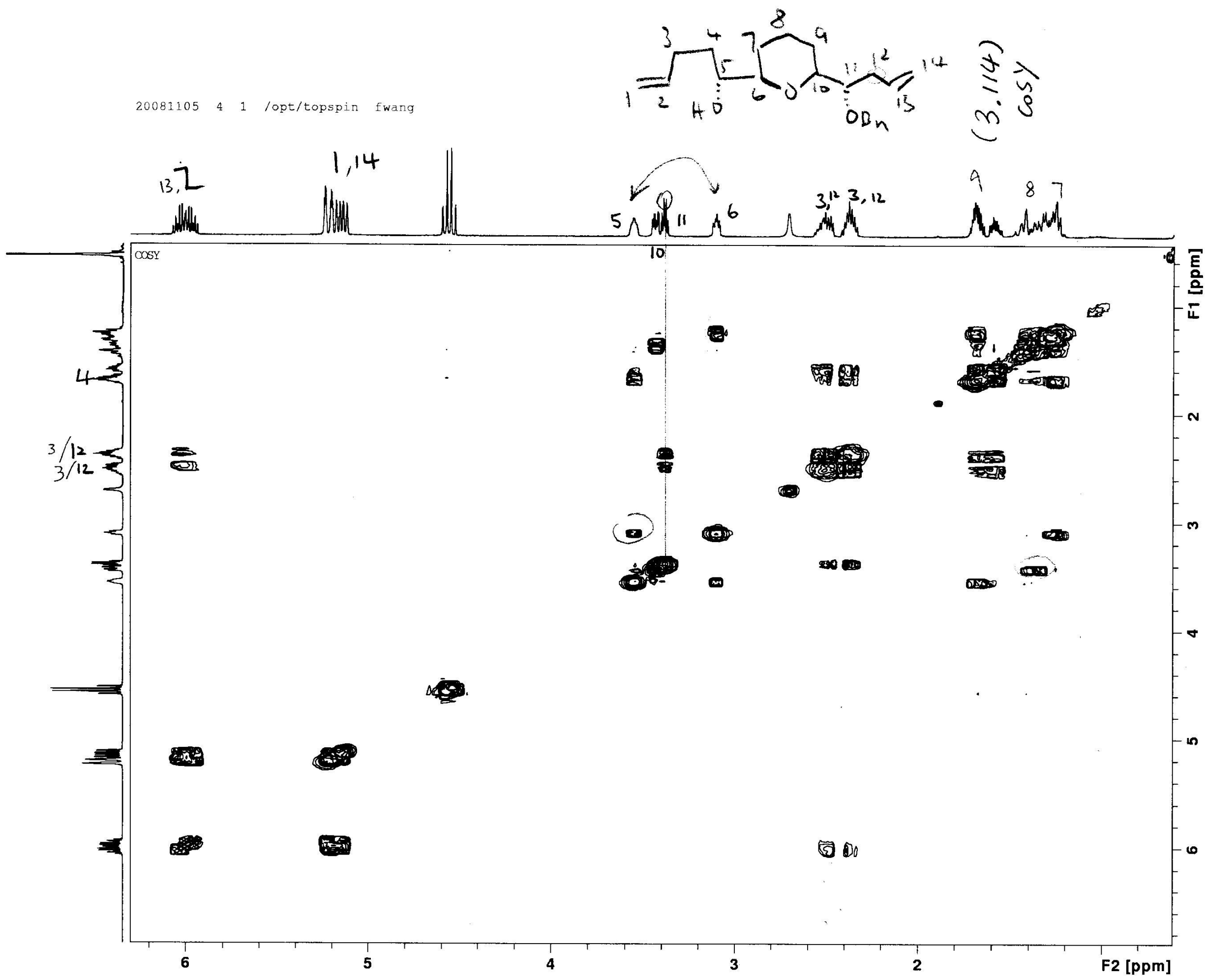
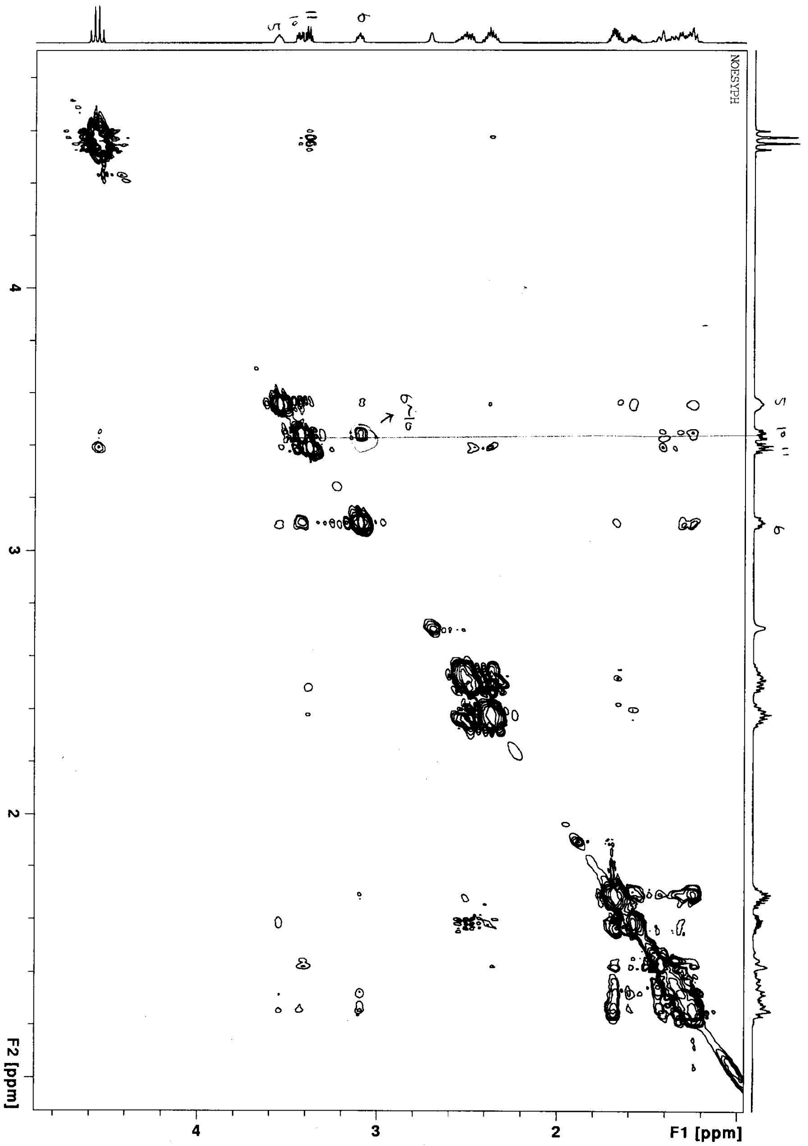
1.3252
1.3488
1.4499
1.4571
1.4770
1.5042
1.5114
1.5282
1.5372
1.5447
1.5557
1.5624
1.5734
1.5932
1.6591
1.9304
1.9508
2.1594
2.1749
2.1886
2.2062
2.2778
2.2945
2.3073
2.3228
2.3364
2.3507
2.3649
2.3788
2.4337
2.4471
2.4589
2.4757
3.1700
3.1833
3.1891
3.2053
3.4214
3.4319
3.4435
3.4550
3.4721
3.4813
3.4932
3.5187
4.6032
4.6266
4.6539
4.6773
4.9783
4.9986
5.0469
5.0503
5.0767
5.0810
5.0846
5.0963
5.1142
5.1174
5.1485
5.1517
5.8193
5.8326
5.8397
5.8464
5.8532
5.8610
5.8668
5.8746
5.8811
5.8872
5.8953
5.9009
5.9093
5.9155
7.2596
7.2875
7.3009
7.3083
7.3148
7.3186
7.3269
7.3439
7.3595
7.3648
7.3704
HO
O
OBn
0.7659
0.6039
5.0478
0.6253
0.5565
1.0255
0.6225
0.5400
0.4186
0.8299
1.0295
1.8590
1.0000
2.1649
2
3
4
5
6
7
[ppm]
0
10
20
30
40
50
[rel]

3.114

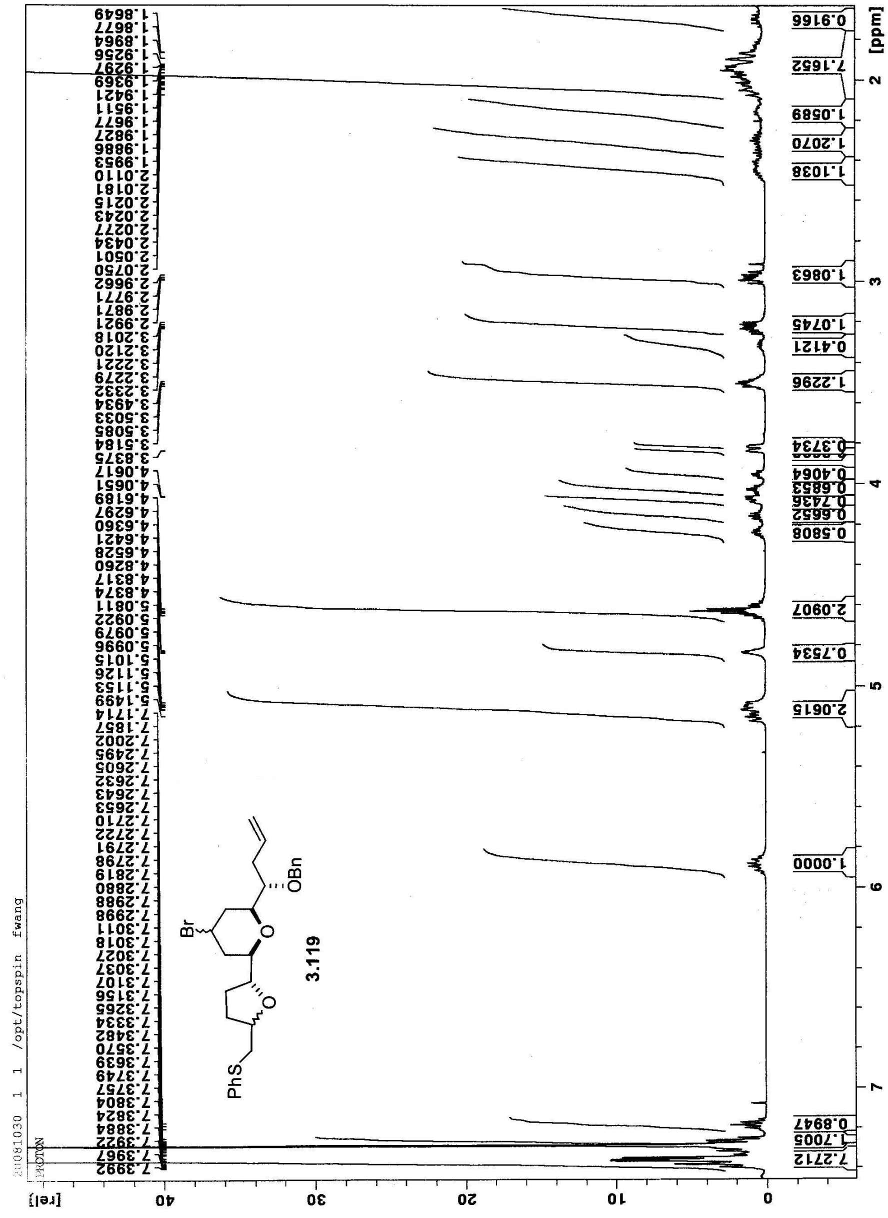

20081103 2 /opt/topspin fwang
CARBON
138.6142
135.1132
128.3636
127.9449
127.6521
116.9640
114.6745
81.2297
80.6790
79.0659
73.5506
72.6624
34.8183
31.9380
29.6981
27.2239
26.6404
23.0357
OH
O
OBn
[ppm]
140
120
100
80
60
40
[rel]
50
40
30
20
10
0

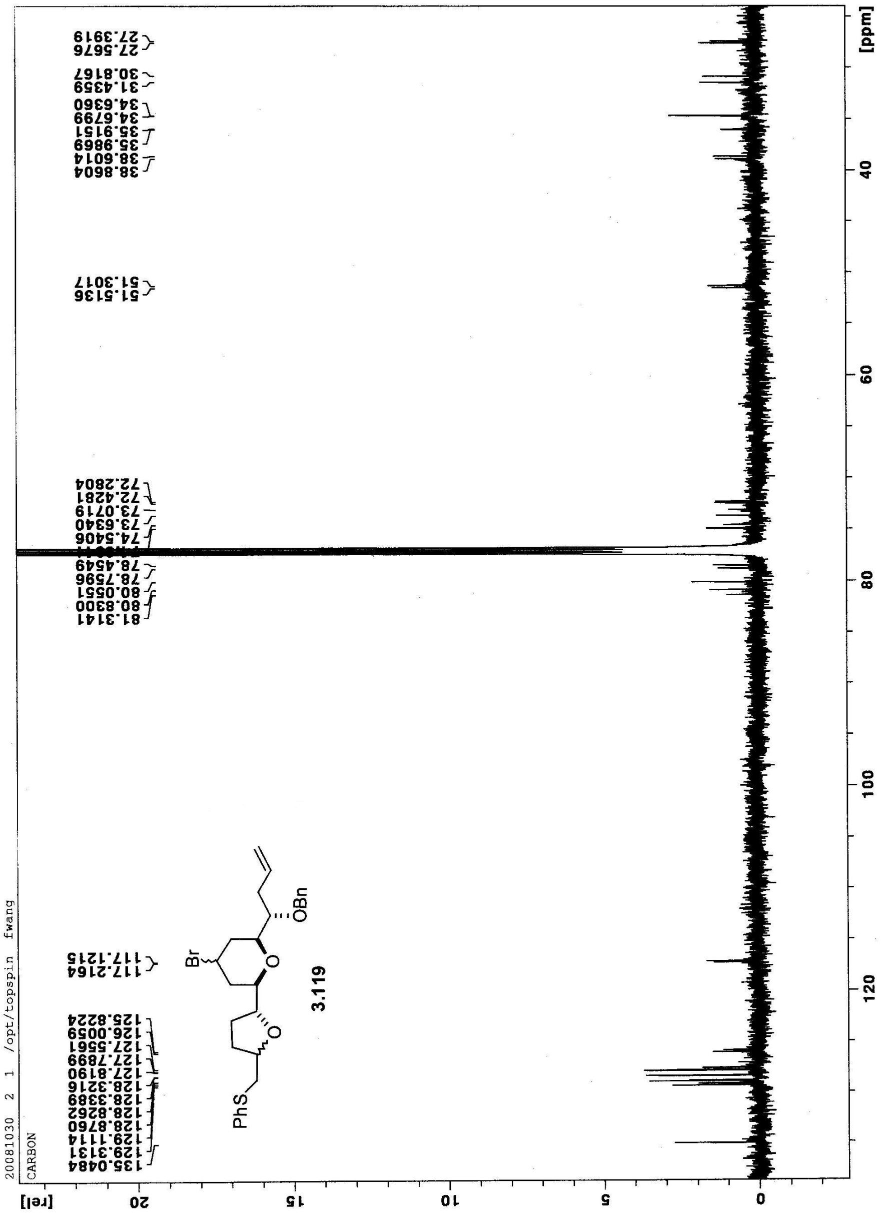
3.114

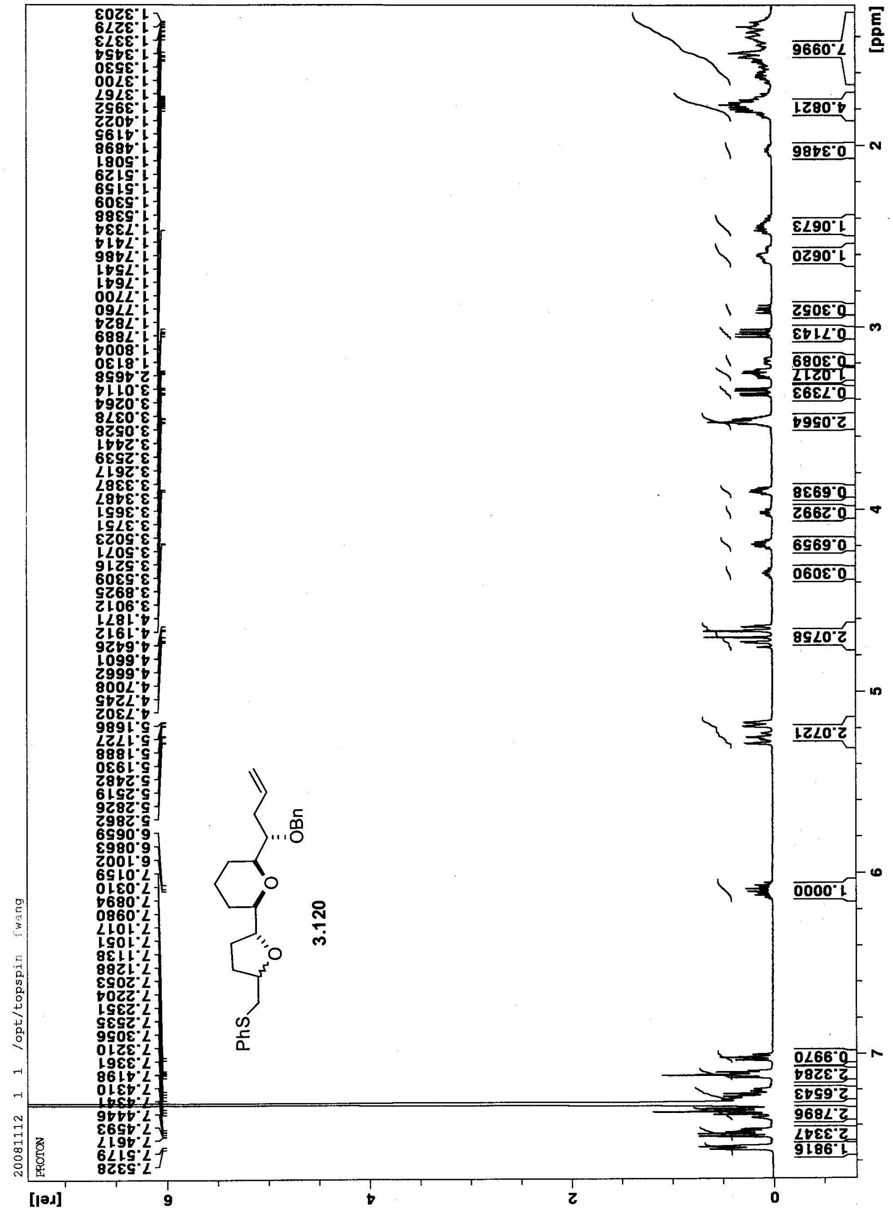

20081105 4 1 /opt/topspin fwang
COSY
(3.114)
COSY
1
2
3
4
5
6
7
8
9
10
11
12
13
14
HO
O
OBn
13, 2
1, 14
5
10
11
6
3', 12
3, 12
9
8
7
4
3/12
3/12
6
5
4
3
2
F2 [ppm]
F1 [ppm]

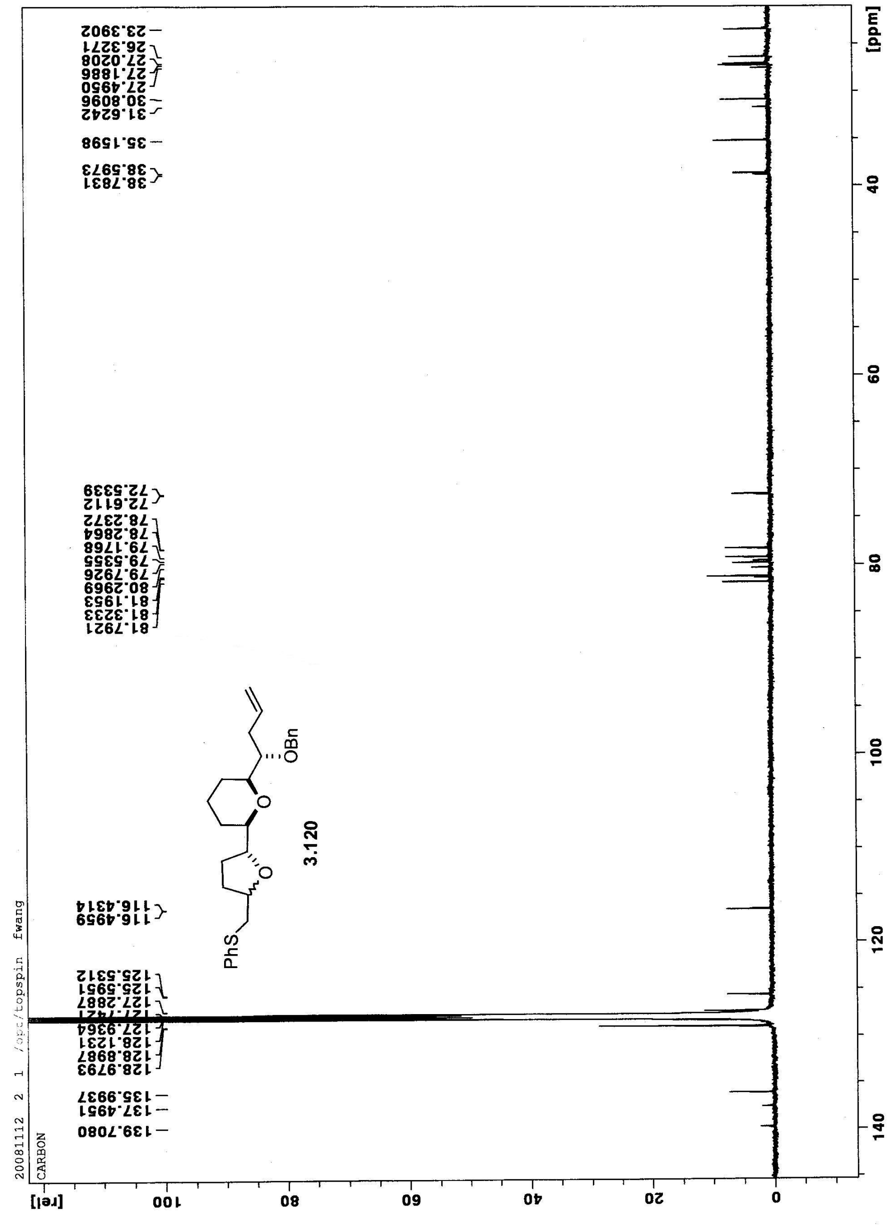

20081105 5 1 /opt/topspin fwang
NOESYPH
F2 [ppm]
F1 [ppm]
4
3
2
5
10
11
9
9~10

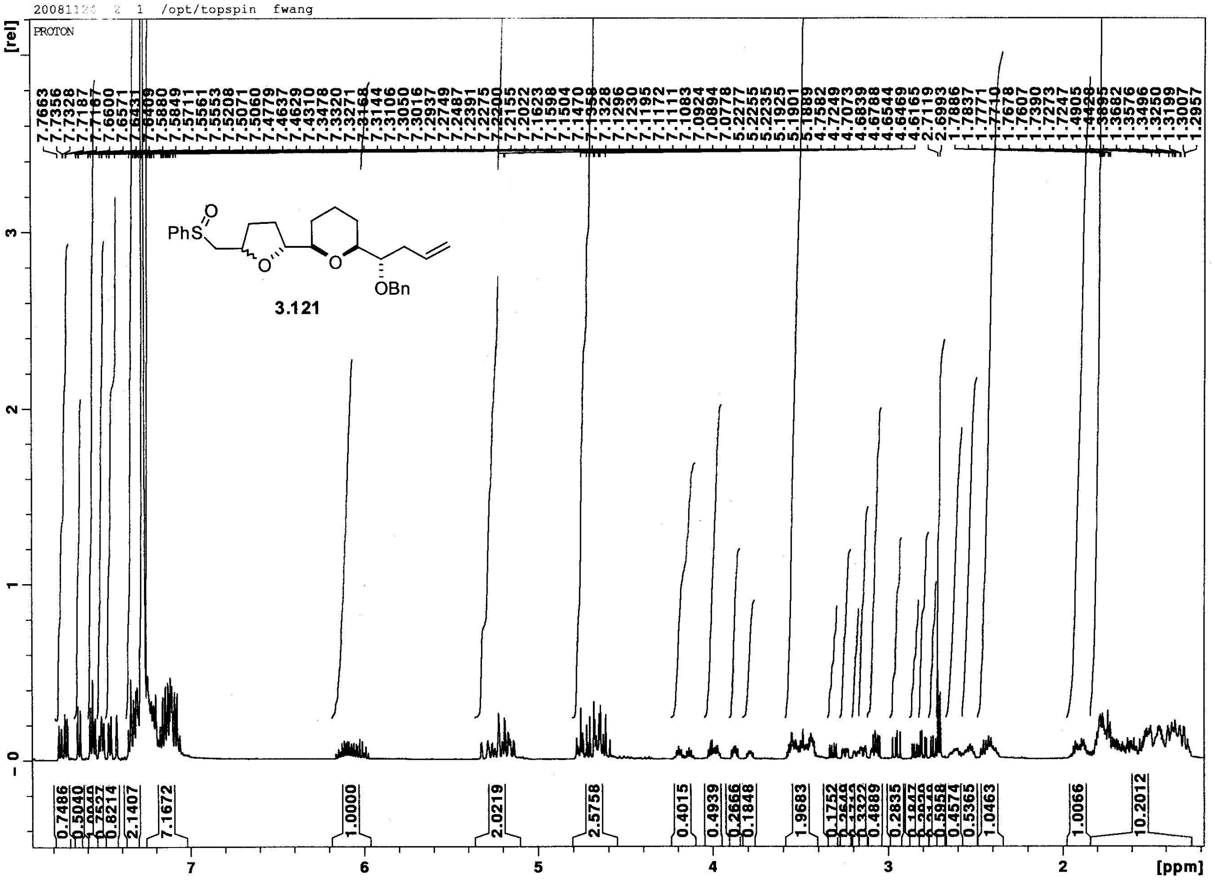
(3.114)
NOESY


20081030 1 1 /opt/topspin fwang
PROTON
PhS
Br
O
OBn
3.119
[ppm]
[rel]
0
10
20
30
40
2
3
4
5
6
7
0.9166
7.1652
1.0589
1.2070
1.1038
1.0863
1.0745
0.4121
1.2296
0.3734
0.4064
0.6853
0.7436
0.6652
0.5808
2.0907
0.7534
2.0615
1.0000
0.8947
1.7005
7.2712

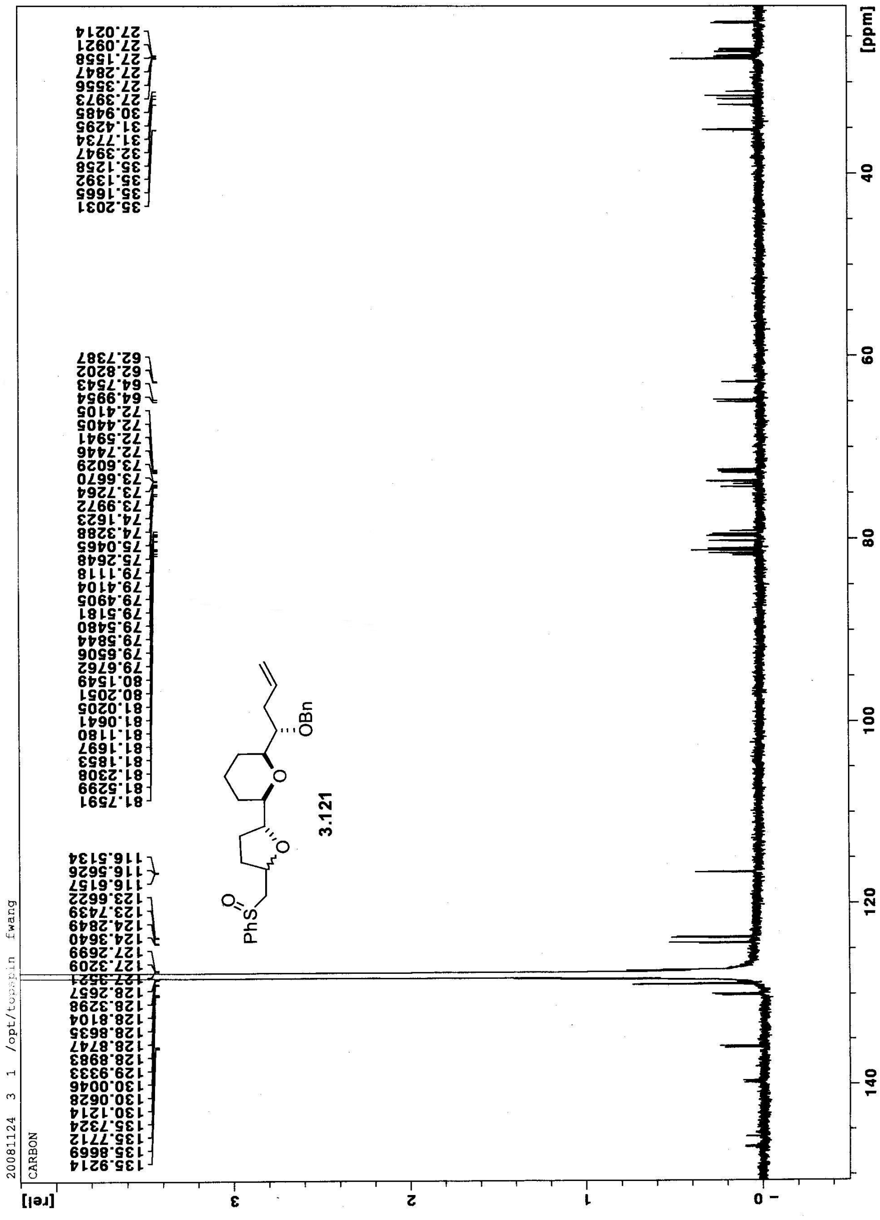

20081030 2 1 /opt/topspin fwang
CARBON
135.0484
129.3131
129.1114
128.8760
128.8262
128.3389
128.3216
127.8190
127.7899
127.5561
126.0059
125.8224
117.2164
117.1215
81.3141
80.8300
80.0551
78.7596
78.4549
74.5406
73.6340
73.0719
72.4281
72.2804
51.5136
51.3017
38.8604
38.6014
35.9869
35.9151
34.6799
34.6360
31.4359
30.8167
27.5676
27.3919
PhS
O
O
Br
OBn
3.119
[ppm]
40
60
80
100
120
[rel]
20
15
10
5
0

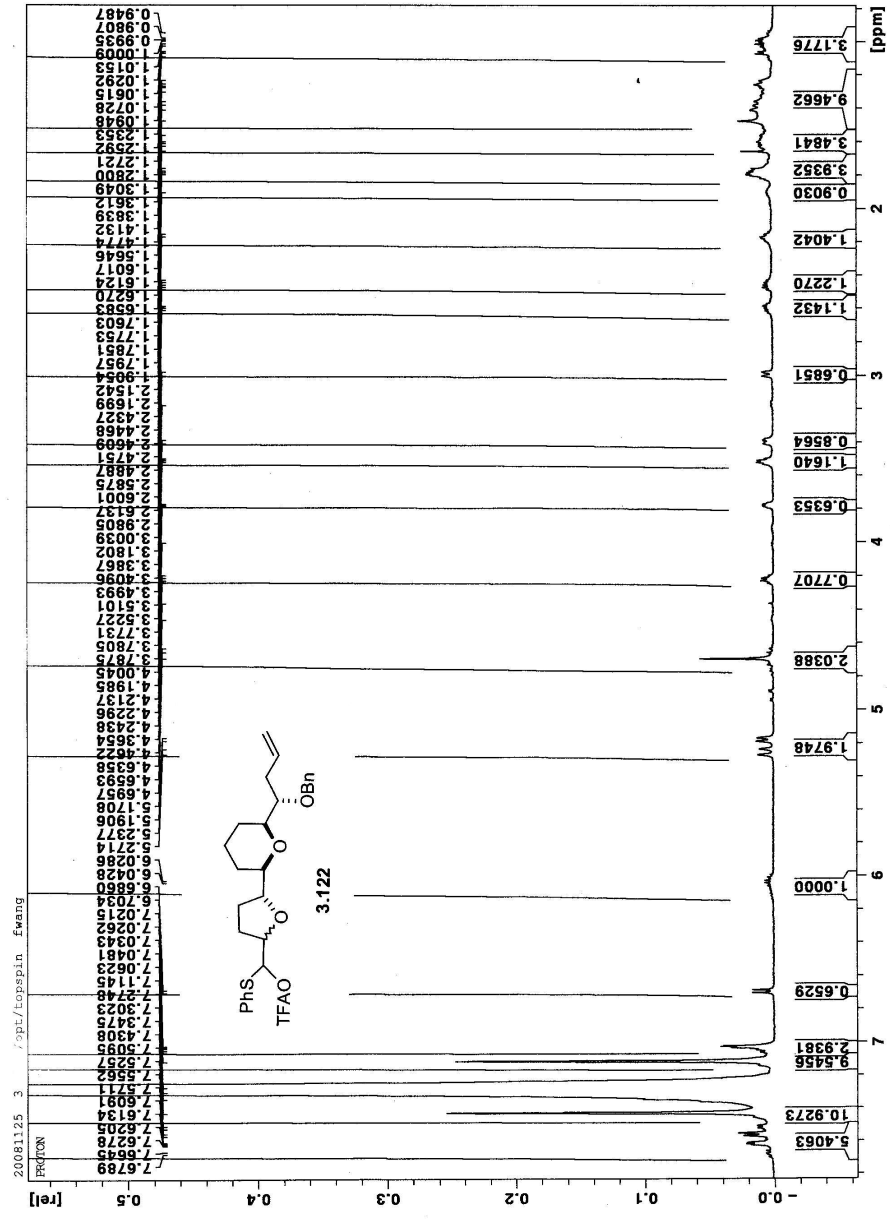

20081112 1 1 /opt/topspin fwang
PROTON
7.5328
7.5179
7.4617
7.4593
7.4446
7.4341
7.4310
7.4198
7.3361
7.3210
7.3056
7.2535
7.2351
7.2204
7.2053
7.1288
7.1138
7.1051
7.1017
7.0980
7.0894
7.0310
7.0159
6.1002
6.0863
6.0659
5.2862
5.2826
5.2519
5.2482
5.1930
5.1888
5.1727
5.1686
4.7302
4.7245
4.7008
4.6662
4.6601
4.6426
4.1912
4.1871
3.9012
3.8925
3.5309
3.5216
3.5071
3.5023
3.3751
3.3651
3.3487
3.3387
3.2617
3.2539
3.2441
3.0528
3.0378
3.0264
3.0114
2.4658
1.8130
1.8004
1.7889
1.7824
1.7760
1.7700
1.7641
1.7541
1.7486
1.7414
1.7334
1.5888
1.5309
1.5159
1.5129
1.5081
1.4898
1.4195
1.4022
1.3952
1.3767
1.3700
1.3530
1.3454
1.3373
1.3279
1.3203
PhS
O
O
OBn
3.120
1.9816
2.3347
2.7896
2.6543
2.3284
0.9970
1.0000
2.0721
2.0758
0.3090
0.6959
0.2992
0.6938
2.0564
0.7393
1.0217
0.3089
0.7143
0.3052
1.0620
1.0673
0.3486
4.0821
7.0996
7
6
5
4
3
2
[ppm]
6
4
2
0
[rel]


20081112 2 1 /opt/topspin fwang
CARBON
139.7080
137.4951
135.9937
128.9793
128.8987
128.1231
127.9364
127.7421
127.2887
125.5951
125.5312
116.4959
116.4314
81.7921
81.3233
81.1953
80.2969
79.7926
79.5355
79.1768
78.2864
78.2372
72.6112
72.5339
38.7831
38.5973
35.1598
31.6242
30.8096
27.4950
27.1886
27.0208
26.3271
23.3902
PhS
O
O
OBn
3.120
140
120
100
80
60
40
[ppm]
[rel]
100
80
60
40
20
0


20081124 2 1 /opt/topspin fwang
PROTON
[rel]
3
2
1
0
7.7663
7.7356
7.7328
7.7187
7.7167
7.6600
7.6571
7.6431
7.6409
7.5880
7.5849
7.5711
7.5561
7.5553
7.5208
7.5071
7.5060
7.4779
7.4637
7.4629
7.4310
7.3478
7.3320
7.3271
7.3168
7.3144
7.3106
7.3050
7.3016
7.2937
7.2749
7.2487
7.2391
7.2275
7.2200
7.2155
7.2022
7.1623
7.1598
7.1504
7.1470
7.1358
7.1328
7.1296
7.1230
7.1195
7.1172
7.1111
7.1083
7.0924
7.0894
7.0778
5.2277
5.2255
5.2235
5.1925
5.1901
5.1889
4.7582
4.7249
4.7073
4.6839
4.6788
4.6544
4.6469
4.6165
2.7119
2.6993
1.7886
1.7837
1.7771
1.7710
1.7678
1.7607
1.7390
1.7273
1.7247
1.4905
1.4428
1.3895
1.3682
1.3576
1.3496
1.3250
1.3199
1.3007
1.2957
PhS
O
O
O
OBn
0.7486
0.5040
0.7527
0.8214
2.1407
7.1672
1.0000
2.0219
2.5758
0.4015
0.4939
0.2666
0.1848
1.9683
0.1752
0.3322
0.4889
0.2835
0.1847
0.5958
0.4574
0.5365
1.0463
1.0066
10.2012
7
6
5
4
3
2
[ppm]

3.121


20081124 3 1 /opt/topspin fwang
CARBON
135.9214
135.8669
135.7712
135.7324
130.1214
130.0628
130.0046
129.9333
128.8983
128.8747
128.8635
128.8104
128.3298
128.2657
127.3521
127.3209
127.2699
124.3640
124.2849
123.7439
123.6622
116.6157
116.5626
116.5134
81.7591
81.5299
81.2308
81.1853
81.1697
81.1180
81.0641
81.0205
80.2051
80.1549
79.6762
79.6506
79.5844
79.5480
79.5181
79.4905
79.4104
79.1118
75.2648
75.0465
74.3288
74.1623
73.9972
73.7264
73.6670
73.6029
72.7446
72.5941
72.4405
72.4105
64.9954
64.7543
62.8202
62.7387
35.2031
35.1665
35.1392
35.1258
32.3947
31.7734
31.4295
30.9485
27.3973
27.3556
27.2847
27.1558
27.0921
27.0214
PhS
O
O
O
OBn
3.121
[rel]
3
2
1
0
140
120
100
80
60
40
[ppm]


20081125 3 /opt/topspin fwang
PROTON
7.6789
7.6645
7.6278
7.6205
7.6134
7.6091
7.5711
7.5562
7.5257
7.5095
7.4308
7.3475
7.3023
7.2748
7.1145
7.0623
7.0481
7.0343
7.0262
7.0215
6.7034
6.6880
6.0428
6.0286
5.2714
5.2377
5.1906
5.1708
4.6957
4.6593
4.6358
4.4622
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4.2438
4.2296
4.2137
4.1985
4.0045
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3.7805
3.7731
3.5227
3.5101
3.4993
3.4096
3.3867
3.1802
3.0039
2.9805
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2.4751
2.4609
2.4468
2.4327
2.1699
2.1542
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1.7957
1.7851
1.7753
1.7603
1.6583
1.6270
1.6124
1.6017
1.5646
1.4774
1.4132
1.3839
1.3612
1.3049
1.2800
1.2721
1.2592
1.2353
1.0948
1.0728
1.0615
1.0292
1.0153
1.0009
0.9935
0.9807
0.9487
PhS
TFAO
O
O
OBn
3.122
5.4063
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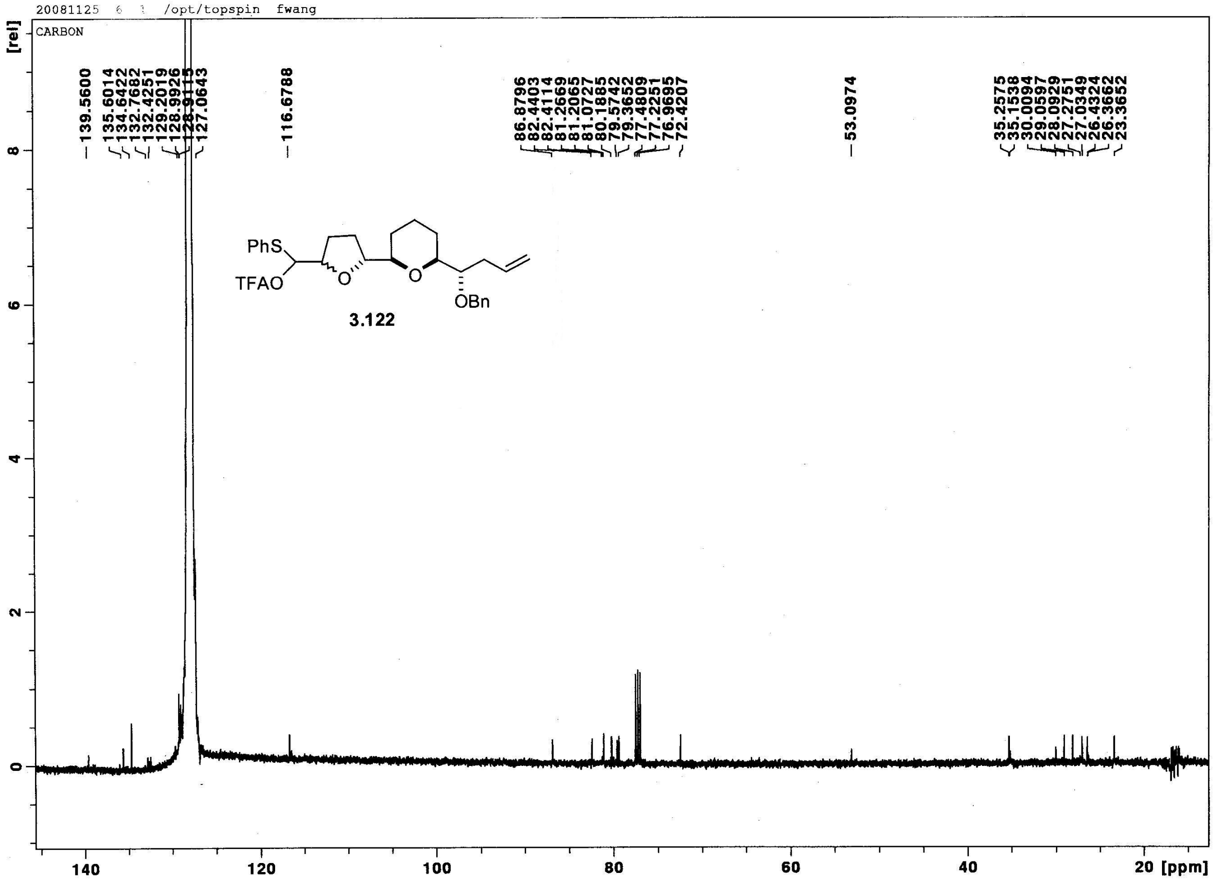
1.0000
1.9748
2.0388
0.7707
0.6333
1.1640
0.8564
0.6851
1.1432
1.2270
1.4042
0.9030
3.9352
3.4841
9.4662
3.1776
7
6
5
4
3
2
[ppm]
0.0
0.1
0.2
0.3
0.4
0.5
[rel]


20081125 6 1 /opt/topspin fwang
CARBON
[rel]
8
6
4
2
0
139.5600
135.6014
134.6422
132.7682
132.4251
129.2019
128.9926
128.9115
127.0643
116.6788
86.8796
82.4403
82.4114
81.2669
81.2065
81.0727
80.1885
79.5742
79.3652
77.4809
77.2251
76.9695
72.4207
53.0974
35.2575
35.1538
30.0094
29.0597
28.0929
27.2751
27.0349
26.4324
26.3662
23.3652
PhS
TFAO
O
O
OBn
140
120
100
80
60
40
20 [ppm]

3.122

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1. Recent reviews, see: (a) Rupprecht, J.K.; Hui, Y.H.; McLaughlin, J. L. *J. Nat. Prod.* **1990**, *53***,** 237; (b) Fang, X. P.; Rieser, M. J.; Gu, Z. M.; McLaughlin, J. L. *Phytochem. Anal.* **1993**, *4***,** 27 (part 1) 49 (part 2); (c) Alali, F. Q.; Liu, X. X.; McLaughlin, J. L. *J. Nat. Prod.* **1999**, *62***,** 504.

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