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Studies Toward the Total Synthesis of Vinigrol

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Studies Toward the Total Synthesis of Vinigrol

by

Louis Morency

A thesis submitted to the Faculty of Graduate and Postdoctoral Studies
In partial fulfillment of the requirements for the
Philosophiae Doctor (Ph.D.) degree in chemistry

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«C'est le temps que tu as perdu pour ta rose

qui fait ta rose si importante.

Antoine de Saint-exupéry, Le Petit Prince.

Abstract

This thesis presents the work done toward the total synthesis of vinigrol. The studies described here are divided into three main approaches.

First, the oxy-Cope/Claisen/ene and the oxy-Cope/ene reactions have been developed to provide *cis*-decalin systems. These methodologies have been applied for the synthesis of the core of vinigrol.

Second, a synthetic route that includes the exploitation of the hydroxy-directed Diels-Alder reaction to construct the vinigrol *cis*-decalin was developed. Two different strategies were developed to close the remaining eight-membered ring: a ring closing metathesis and a Claisen rearrangement.

Finally, the sequential hydroxy-directed Diels-Alder/Claisen reaction was adapted for the synthesis of the six- and eight-membered rings of vinigrol.

Remerciements

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Vinigrol: a Natural Product

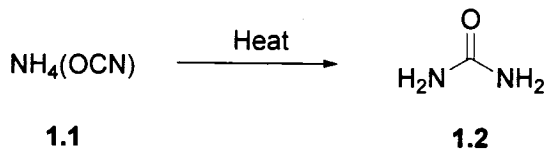
Introduction

"We must not forget that when radium was discovered no one knew that it would prove useful in hospitals. The work was one of pure science. And this is a proof that scientific work must not be considered from the point of view of the direct usefulness of it. It must be done for itself, for the beauty of science, and then there is always the chance that a scientific discovery may become like the radium a benefit for humanity."

Marie Curie

The field[1,3] of total synthesis within organic chemistry is very old. It is said to have started 178 years ago when Wöhler[2] synthesized urea, **1.2**, an organic compound, from inorganic material. That reaction is considered to be the birth of total synthesis.

Figure 1.1 – Wöhler's synthesis of urea



1.1 **1.2**

Since its beginning in 1828, total synthesis has been continually evolving. Long gone are the days when chemists had to chemically degrade their products in order to characterize them. Today, we benefit from state of the art instruments to help analyze and purify our compounds. Moreover, new catalysts and reagents are being developed every year which add to our chemical repertoire. With the acquisition of this modern arsenal, scientists have been able to target more and more complex natural products. Much to the delight of the synthetic chemist, Mother Nature has produced an large number of eye-catching structures to be tackled.

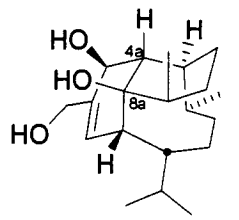
While part of the appeal of synthesizing new molecules undoubtedly lies in overcoming the unique challenges these structures present, natural product syntheses may be performed for other reasons as well. For example, one may be interested in verifying a proposed structure or gaining access to a variety of analogues. In some cases, it may also be possible to develop a synthetic route that will be cheaper or more accessible than obtaining the material from its natural source.

Regardless for the reasons behind this science, applications evolving from total syntheses are broad.[3] In addition to the obvious application in the pharmaceutical industry, there may be uses in the manufacturing of high-tech materials, polymers, fertilizers, pesticides, cosmetics and clothing.

Vinigrol

Vinigrol **1.3** is a diterpene isolated in 1987 from the fungal strain *Virgaria nigra* F-5408, found at the bottom of Mount Aso in the Kumamoto region of Japan.[4] Vinigrol bears a *cis*-decalin subunit traversed by an eight-membered ring that constitutes an unprecedented tricyclo[4.4.4.$0^{4a,8a}$]tetradecane. Moreover, the natural product possesses eight contiguous stereogenic centers.

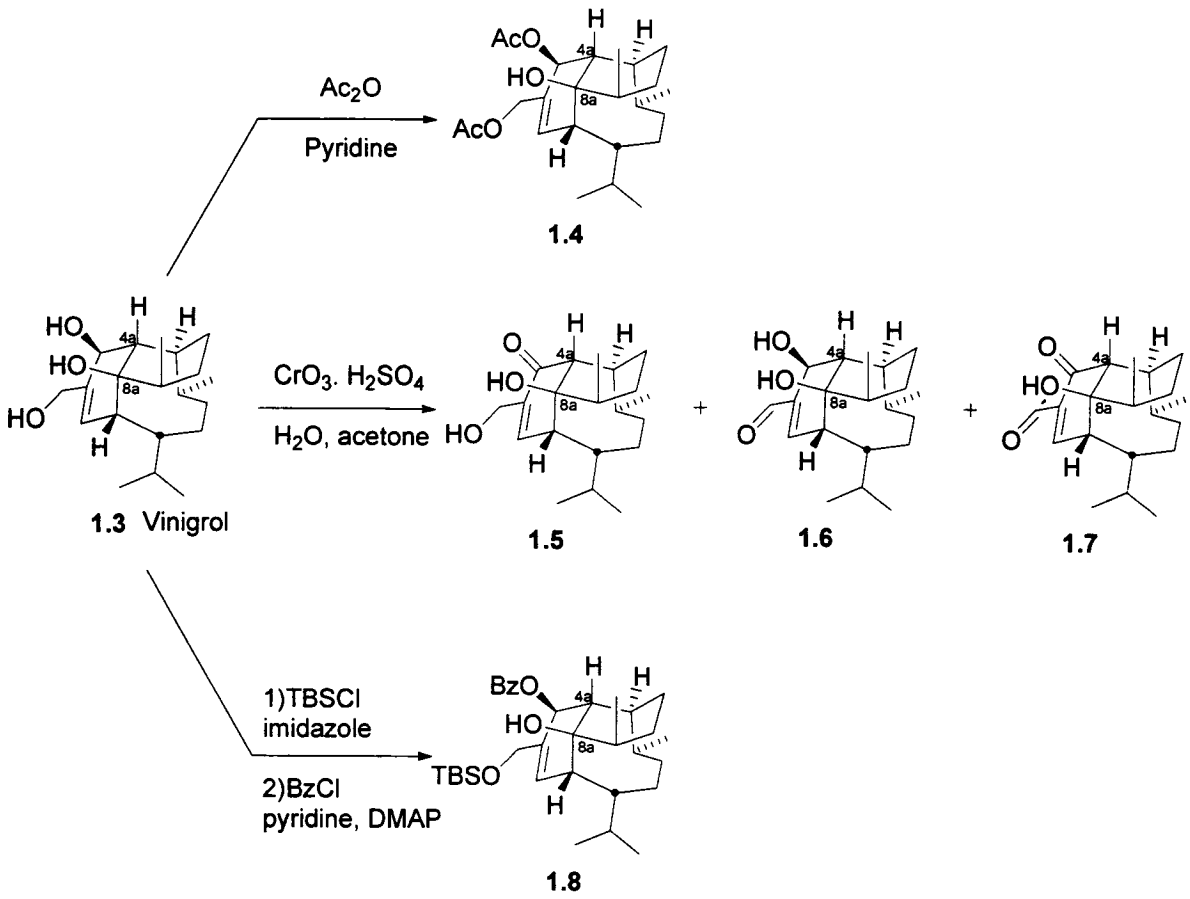
Figure 1.2 – Vinigrol



1.3 Vinigrol

Vinigrol was isolated from cultured mycelium by solvent extraction and silica gel chromatography to give colorless prisms (mp 108 °C), $[\alpha]_D$ –96.2° (*c* 1.05, $CHCl_3$) soluble in chloroform, ethyl acetate, and methanol, but not water. The structure of **1.3** was not easily elucidated and the use of NMR spectroscopy was insufficient. Many derivatives of the natural product had to be synthesized in order to confirm the structure.

Scheme 1.1 – Derivatives of vinigrol



X-ray diffraction of derivative **1.5** assigned all but one stereocentre; ^{1}H NMR and NOESY spectrum of **1.4** assigned the remaining secondary alcohol.

The biological activity

In addition to its attractive structure, vinigrol's diverse biological activity profile makes it a potentially interesting pharmaceutical substance as well. Vinigrol was first isolated as an antihypertensive and platelet aggregation-inhibiting substance.[5] The injection of 100 μg/kg of vinigrol on anesthetized normotensive rats caused their arterial blood pressure to decrease by 20%. When given orally at a higher dose of 2 mg/Kg, their blood pressure was reduced

by 15%. The effect of the drug lasted for 6 hours. Furthermore, its platelet aggregation inhibiting properties have been observed on rabbit and human models at low concentrations while at higher concentrations it induces aggregation.

Vinigrol showed some ability to induce the contraction of aortic smooth muscle strips in rats. This effect was compared to other vasodilators showing Ca^{2+} agonist activity on smooth muscle preparations.

Three years later, it was found that vinigrol is a tumor necrosis factor (TNF) antagonist[6] showing complete inhibition of the [^{125}I]-TNF at 2.1 nM in in-vitro binding studies on HL60 cells. Consequently, vinigrol would be a good lead for the treatment of endotoxic shock, inflammation, cachexia or to arrest the progression from AIDS-related complex to AIDS.

Similarly, vinigrol has potential for the treatment of HIV infectious diseases[7] owing to an EC_{50} of 0.092 μM for the antiviral activity of HIV-infected MT-4 cells. In comparison, azidothymidine (AZT), an existing drug for HIV, shows an EC_{50} of 0.2 nM.

Finally, a study done by Guglielmotti and coworkers showed that vinigrol could be used as an anti-inflammatory drug.[8] A follow-up study done by Keane showed that the natural product **1.3** combined with COX-2 inhibitors made a good candidate for the treatment of inflammatory diseases and arthritic disorders.[9]

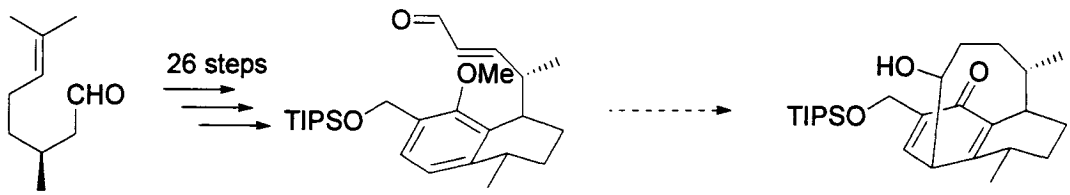
In light of its unusual and complex architecture, together with its promising biological activities, it is no surprise that vinigrol has stimulated the creativity of several synthetic chemists.

Previous work from other laboratories

Since vinigrol was isolated in 1987, many groups have begun working towards its total synthesis. One such group, Corey and coworkers, have developed two different strategies:

an electrophilic aromatic condensation[10] and an intramolecular Diels-Alder reaction.[11] The first approach started with (1*S*)-citronellal, **1.9**, and 26 steps later, precursor **1.10** was obtained. The key step did not produce the core of vinigrol **1.11** when Lewis acids such as trifluoroborane etherate, tribromoborane and trichloroborane were used.

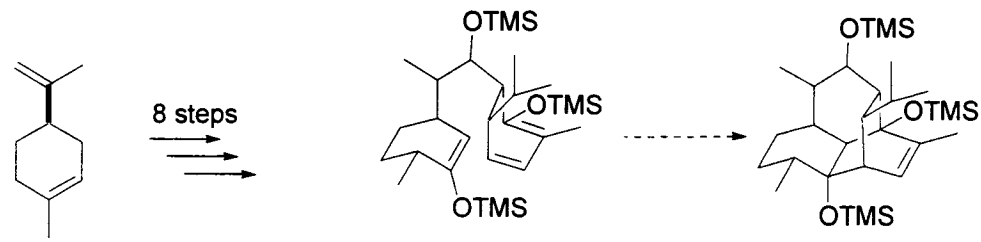
Scheme 1.2 – Corey's Electrophilic Aromatic Condensation



1.9 **1.10** **1.11**

The second approach started from limonene, **1.12**, which was converted to compound **1.13** in eight steps. The sequence was significantly shorter than the previous approach, however, the thermal Diels-Alder conditions did not give the desired compound **1.14**. The electron-rich character of both the diene and the dienophile, as well as the steric hindrance of the system, likely explains the unreactive nature of **1.13**.

Scheme 1.3 – Corey's intramolecular Diels-Alder reaction

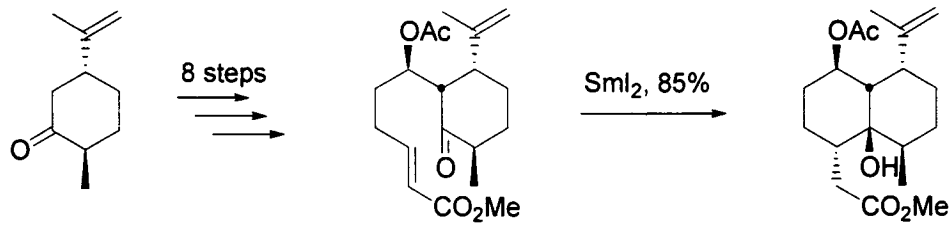


1.12 **1.13** **1.14**

Matsuda and coworkers have been working on a different approach to form the core of vinigrol. They performed a Barbier SmI_2-mediated cyclization to get to the *cis*-decalin[12] and the six- and eight-membered rings.[13] The synthesis of the decalin started from (+)-

dihydrocarvone **1.15** and eight steps later compound **1.16** was isolated. The Barbier cyclization allowed the isolation of the *cis*-decalin **1.17** in 85% yield.

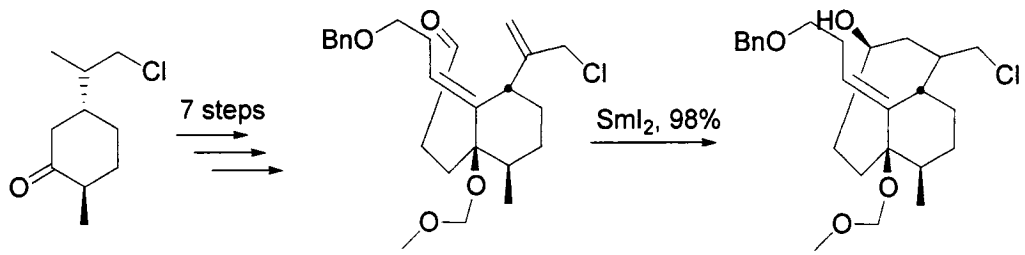
Scheme 1.4 – Matsuda's Barbier SmI_2-mediated cyclization, part 1



1.15 **1.16** **1.17**

This methodology was also applied to the formation of the eight-membered ring. The second sequence started from (+)-chlorodihydrocarvone **1.18** and seven steps were performed to give compound **1.19**. The Barbier cyclization was performed using SmI_2 and the six- and eight-membered rings were formed to give **1.20** in 98% yield. The Matsuda's methodology was able to synthesize all three rings found in the core of vinigrol, but only on different substrates. The entire tricyclic core has yet to be formed.

Scheme 1.5 – Matsuda's Barbier SmI_2-mediated cyclization, part 2

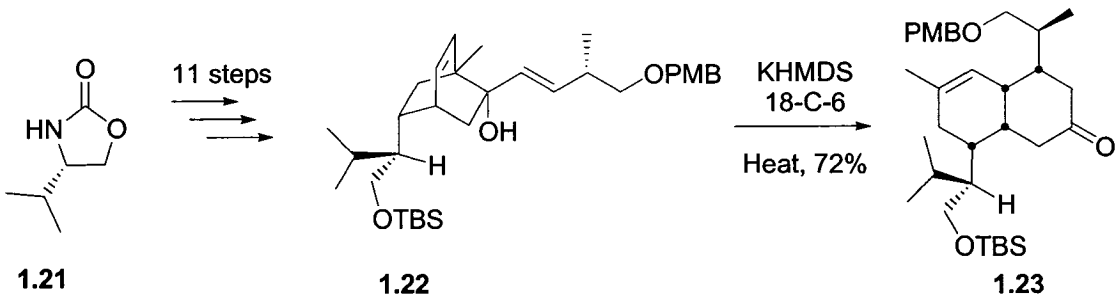


1.18 **1.19** **1.20**

Paquette and coworkers have worked for many years on the total synthesis of vinigrol.[14] Their strategy was to use an anionic oxy-Cope reaction to form the *cis*-decalin part of the natural product. Their synthesis started with (*S*)-oxazolidinone **1.21** and eleven steps were

performed to reach compound **1.22**. The bicyclo[2.2.2]octenol was then submitted to anionic oxy-Cope conditions to get *cis*-decalin **1.23** in 72% yield.

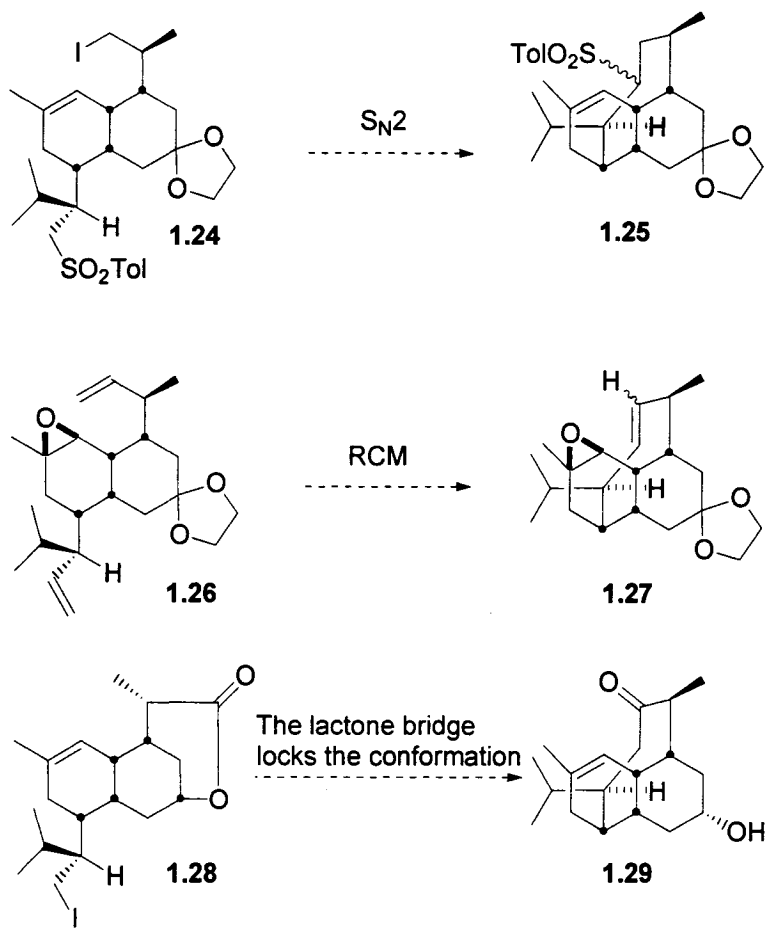
Scheme 1.6 – Paquette's approach



1.21 **1.22** **1.23**

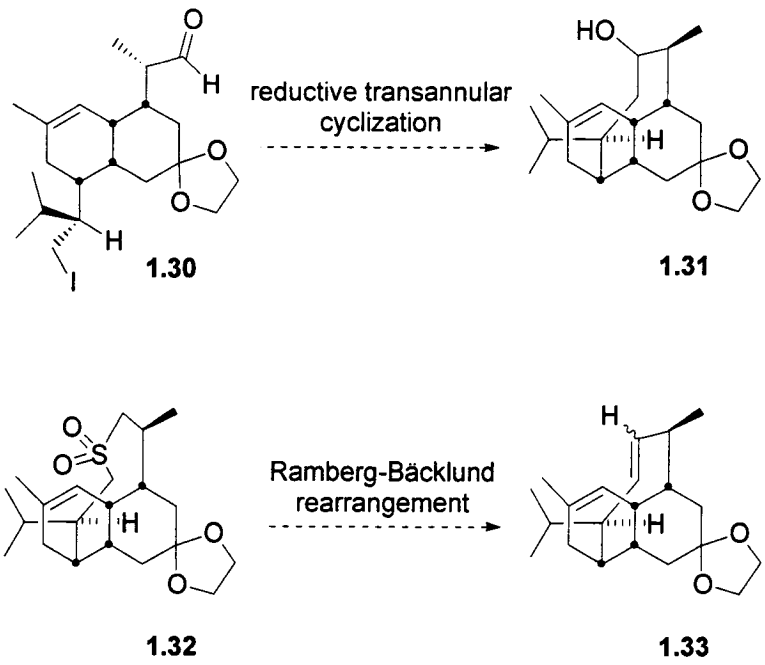
The above methodology provided two of vinigrol's rings with enough flexibility to functionalize the rest of the molecule and form the eight-membered ring. Several approaches were tried to assemble this last ring such as S_N2 substitutions and ring closing metathesis without success.[15] Paquette then tried a locked conformation of the *cis*-decalin to attempt the cyclization of the octalin ring,[16] however this too did not succeed.

Scheme 1.7 – Paquette's approaches to cyclize the eight-membered ring – part 1



Finally, two last strategies were implemented to try and form the desired cycle. A reductive transannular cyclization and a Ramberg-Bäcklund rearrangement both failed to give the desired core of vinigrol.[17] Paquette and coworkers have done a tremendous amount of work, however they have been unable to reach their goal: the total synthesis of vinigrol.

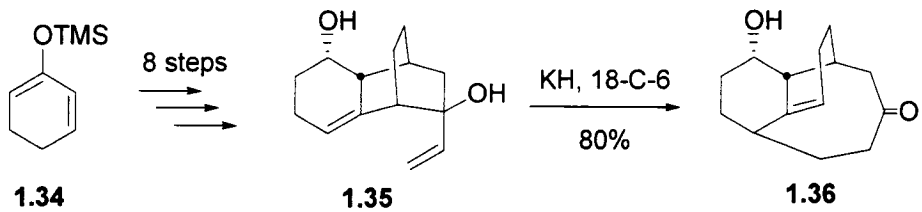
Scheme 1.8 - Paquette's approaches to cyclize the eight-membered ring – part 2



1.30 **1.31** **1.32** **1.33**

The first, and only, synthesis of the tricyclic ring system of vinigrol[18] was accomplished, in 1993, by Hanna and coworkers using an anionic oxy-Cope rearrangement to form the desired eight-membered ring. Their synthesis started from diene **1.34** to form the decalin using a Diels-Alder reaction. The anionic oxy-Cope precursor, **1.35**, was synthesized in eight steps and submitted to the reaction conditions to give the desired core of vinigrol **1.36** in 80% yield.

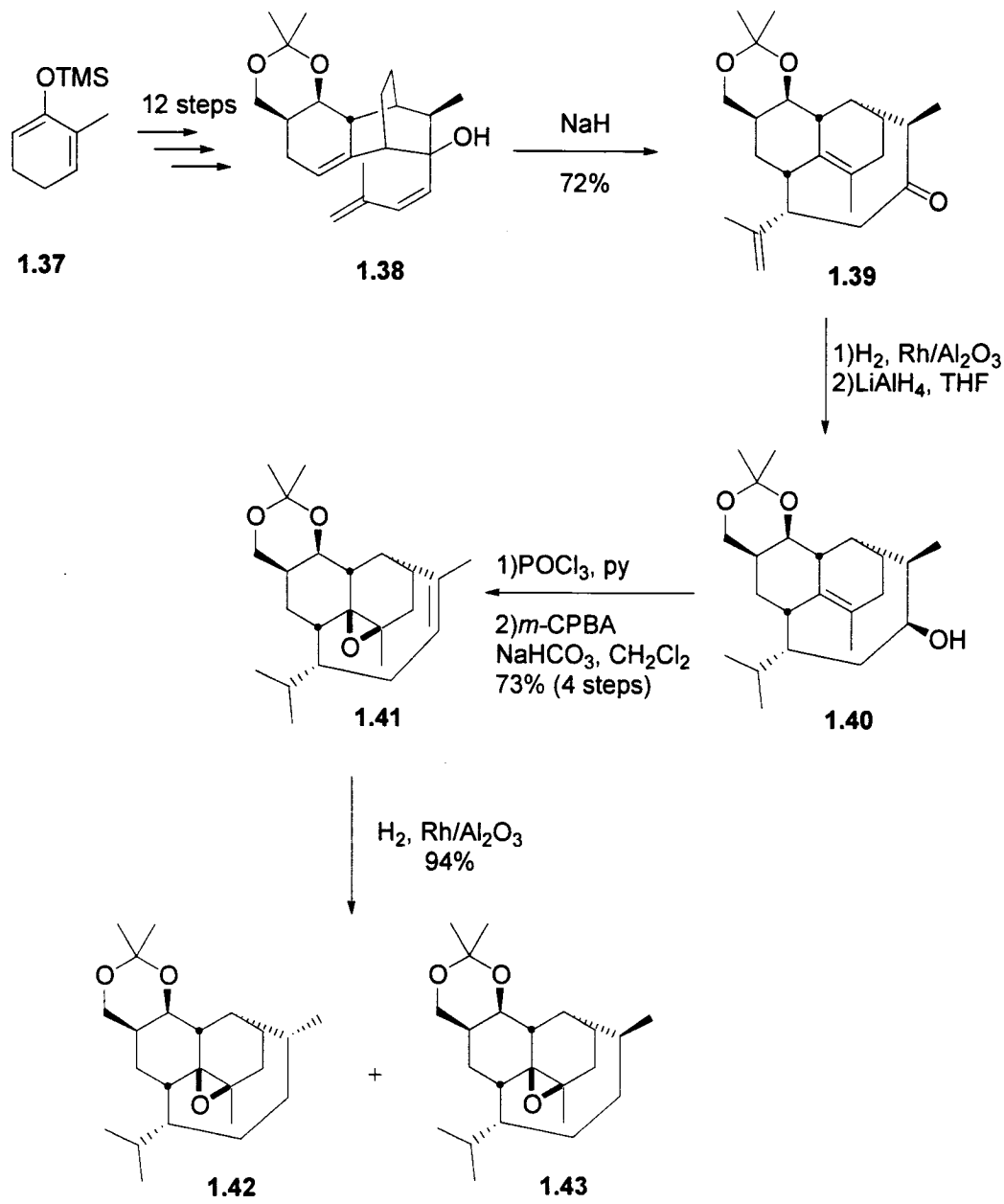
Scheme 1.9 – Hanna's synthesis of vinigrol's core



1.34 **1.35** **1.36**

In 2003, Hanna and coworkers published further developments on the functionalization of the core.[19] Their new approach started from diene **1.37** and was transformed into compound **1.38** in twelve steps. The anionic oxy-Cope conditions then gave the core of vinigrol, **1.39**, in 72% yield. The terminal alkene was then hydrogenated using catalytic rhodium on alumina and the ketone was reduced with $LiAlH_4$ to give compound **1.40**. The alcohol was dehydrated using $POCl_3$ and the alkene at the ring junction was selectively epoxidized to give compound **1.41**. The trisubstituted alkene was then reduced using hydrogen in the presence of rhodium on alumina. Unfortunately, the configuration of the methyl was obtained in a 2:3 ratio favoring the undesired isomer **1.43**. Despite the poor selectivity of the last step, Hanna's synthesis is the closest one to the natural product and the only one that has a completed tricyclic core.

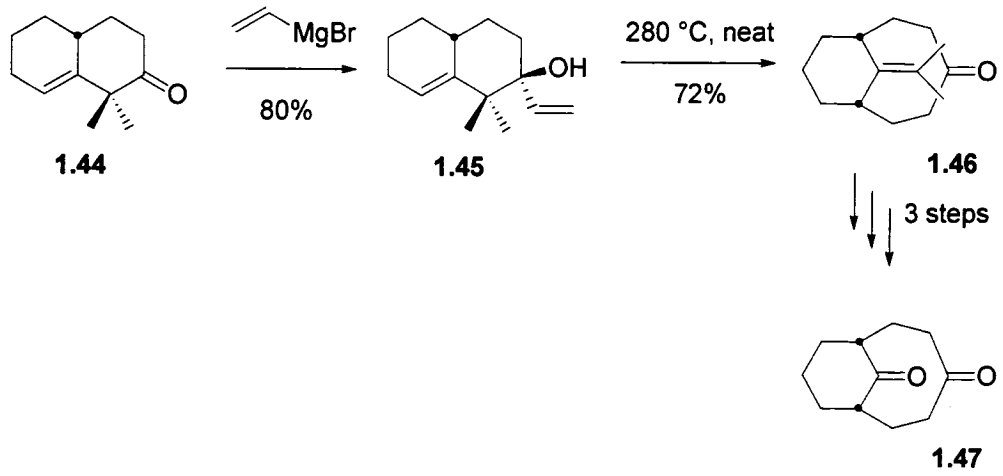
Scheme 1.10 – Functionalization of vinigrol's core



The research group of Mehta has also targeted the synthesis of vinigrol.[20] They used an oxy-Cope reaction to obtain bicyclo[5.3.1]undecanes which are present in the structure of vinigrol and Taxol®. The synthesis started from the readily available compound **1.44**[21] and vinylmagnesium bromide was added to give **1.45** in 80% yield. The next step was an oxy-

Cope reaction giving the desired six- and eight-membered rings of **1.46** in 72% yield. Three additional steps yielded diketone **1.47**. In this manner, two of the three rings found in vinigrol's core were rapidly created, however, the substrate lacks additional functionality from which to prepare vinigrol.

Scheme 1.11 – Mehta's oxy-Cope



1.44 **1.45** **1.46** **1.47**

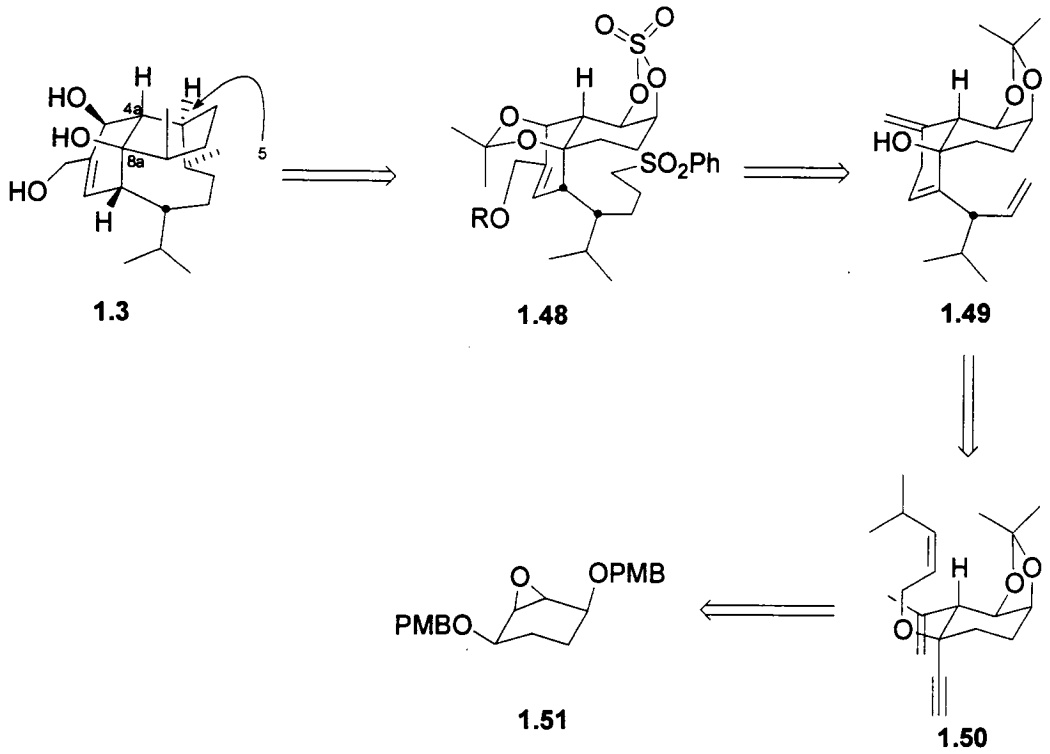
While the structure of vinigrol has been known for the last nineteen years, its total synthesis has yet to be accomplished. It was within that context that four years ago we embarked on our own efforts to succeed where others had failed before us. Herein, our own synthetic approaches toward the total synthesis of vinigrol will be described.

Retrosynthetic analysis

Our approaches toward vinigrol would rely on three different methodologies developed previously in our laboratory. Two methods were used to form the *cis*-decalin part of vinigrol while the third approach was used to build the six- and eight-membered rings of the natural product. Below are the retrosynthetic analyses for the approaches developed in the past years.

The first retrosynthesis, depicted in scheme 1.12, reveals that the eight-membered ring traversing the *cis*-decalin in **1.3** could be created via an intramolecular S_N2 displacement of the cyclic sulfate at C5 by a sulfone anion. Since *cis*-decalins can exist in two conformations, the acetonide moiety in **1.48** is essential to lock the *cis*-decalin in **1.48** into the conformer prone to cyclization. The latter could be obtained from *cis*-decalin **1.49**, which could be realized in one step from a tandem oxy-Cope/Claisen/ene reaction of allyl ether **1.50**. The tandem reaction precursor **1.50** could in turn, be generated from commercially available 1,3-cyclohexadiene.

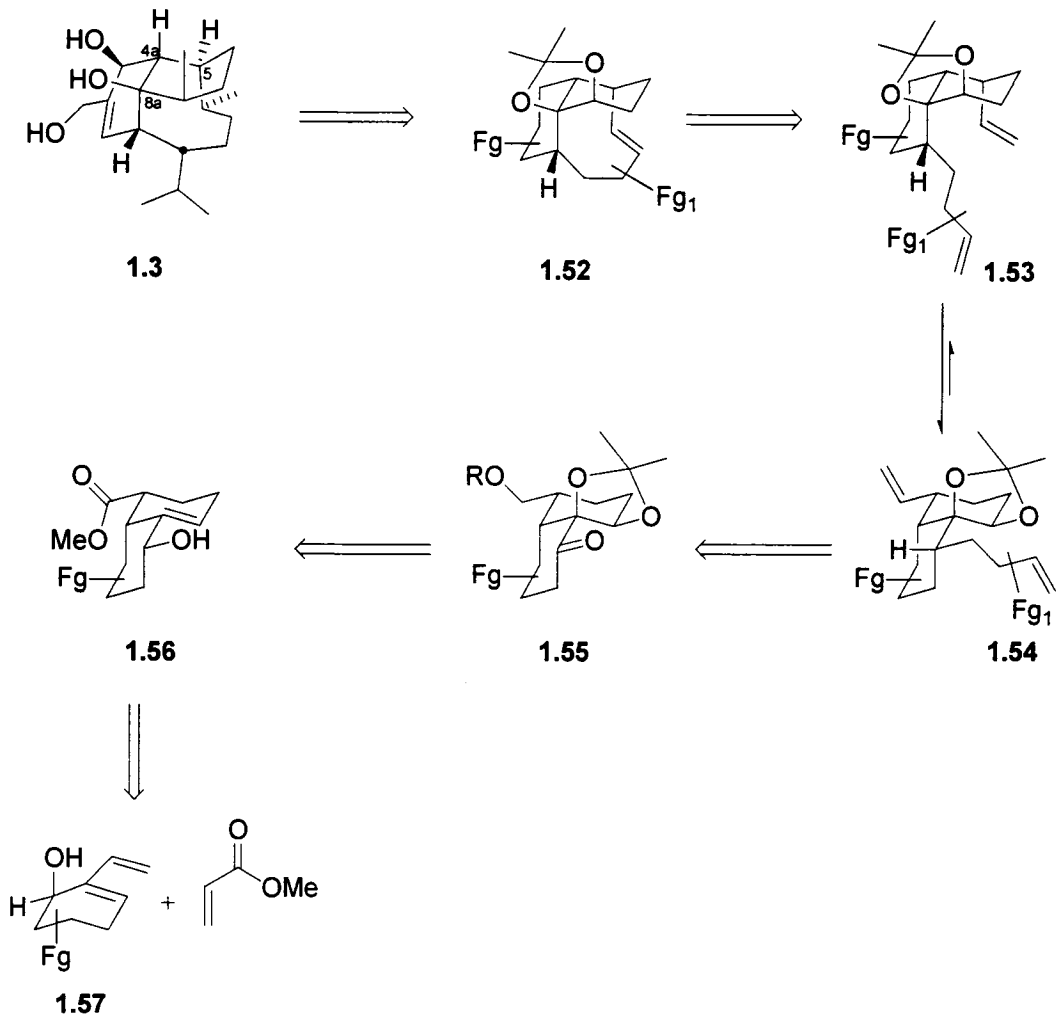
Scheme 1.12 – Retrosynthesis for the tandem oxy-Cope/Claisen/ene



In the second approach, we recognized that the octenyl ring in **1.52** could be generated from a ring closing metathesis of diene **1.53** (scheme 1.13). A cursory inspection revealed that conformer **1.54** should be favored at the ground state, but that the reactive species would be conformer **1.53**. Diene **1.54** could be prepared from ketone **1.55**, which could be obtained

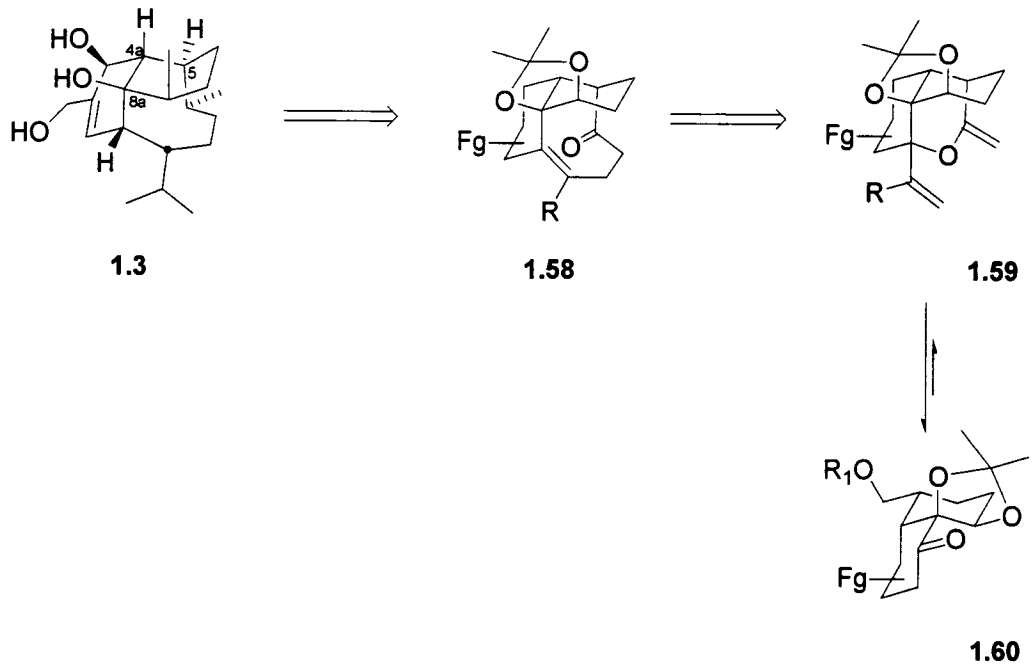
from the alkene **1.56**. The latter could be formed using the hydroxy-directed Diels-Alder reaction from semicyclic diene **1.57** and an activated dienophile.

Scheme 1.13 - Retrosynthesis for the hydroxy-directed Diels-Alder, part 1



A different approach to form the eight-membered ring was also envisioned. We proposed that the Claisen rearrangement of vinyl ether **1.59** could provide the tricyclic core of vinigrol **1.58** (scheme 1.14). The required vinyl ether **1.59** could be prepared from cycloadduct **1.60**. The latter could be formed in a few steps from an hydroxy-directed Diels-Alder reaction (scheme 1.13).

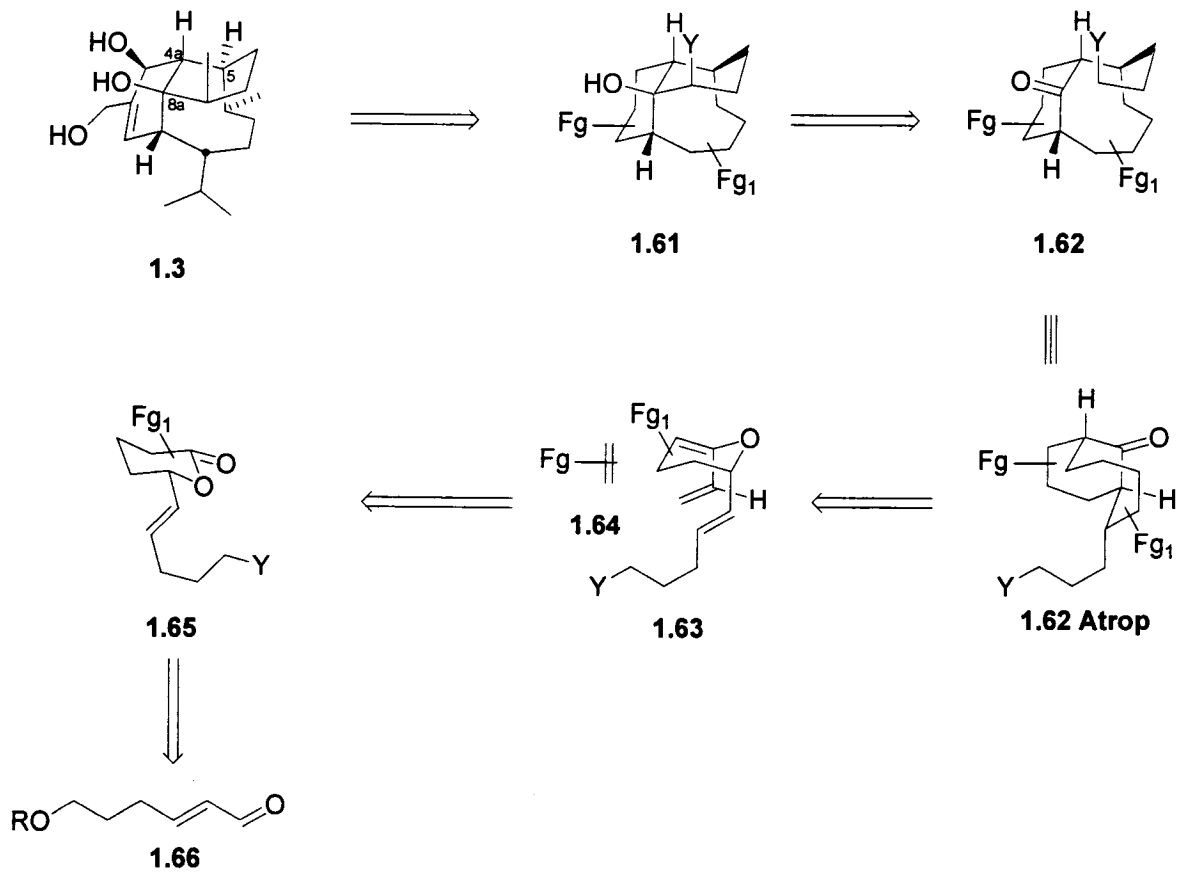
Scheme 1.14 - Retrosynthesis for the hydroxy-directed Diels-Alder, part 2



1.3 **1.58** **1.59** **1.60**

Since our attempts to generate the eight-membered ring in **1.3** via a [3,3]-rearrangement or through RCM were unsuccessful, we explored the creation of vinigrol core **1.61** via an intramolecular alkylation of **1.62** (scheme 1.15). The bicyclo[5.3.1]undecanone subunit **1.62** could be prepared from a sequential hydroxy-directed Diels-Alder/Claisen rearrangement between diene **1.63** and dienophile **1.64**. Diene **1.63** could be synthesized from lactone **1.65** derived from readily available aldehyde **1.66**.

Scheme 1.15 – Retrosynthesis for the sequential hydroxy-directed Diels-Alder/Claisen



2

First Approach:

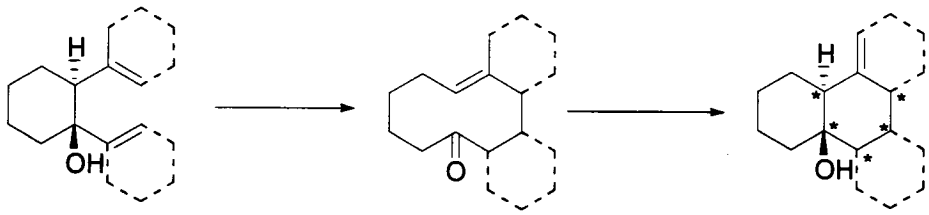
Pericyclic Reactions in Cascade

Introduction

The development of new methods to create highly functionalized decalins in only a few steps is a significant challenge. The use of cascade reactions[22] could solve this problem since many carbon-carbon bonds are formed in one step, thus rapidly creating molecular complexity.

Many scientists have contributed to this field by the development of different tandem sequences that produce highly functionalized decalins. Among these reactions, the oxy-Cope/ene has been used to synthesize various cores.[23] In 2000, Warrington and Barriault used the oxy-Cope/ene reaction on 1,2-divinylcyclohexanols[24] **2.1** to form advanced polycyclic molecules **2.3** with high diastereoselectivity.

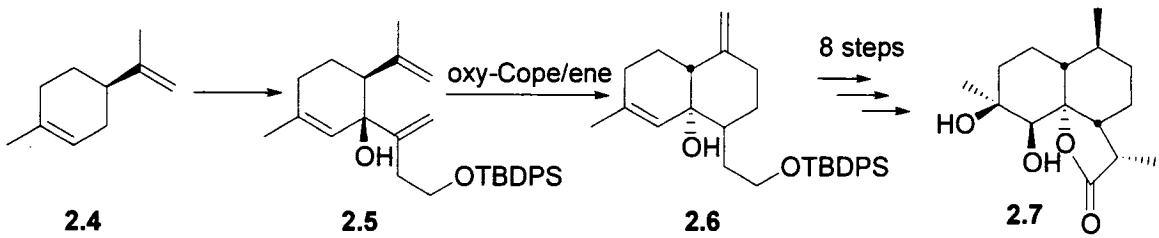
Scheme 2.1 – oxy-Cope/ene reaction developed by Warrington and Barriault



2.1 **2.2** **2.3**

This tandem reaction was then used to complete the total synthesis of (+)-arteanniun M **2.7** by Barriault and Deon.[25] The 1,2-divinylcyclohexanol **2.5** was heated in toluene for 5 hours to give *trans*-decalin **2.6**, the desired core of the natural product **2.7**. The total synthesis was achieved within ten steps from (+)-limonene **2.4**.

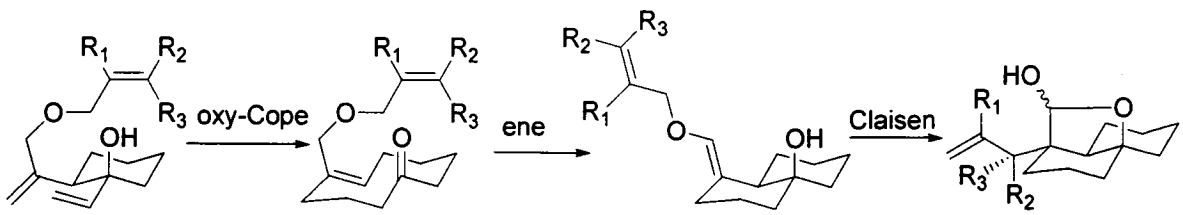
Scheme 2.2 – Synthesis of (+)-arteanniun M by Barriault and Deon



2.4 **2.5** **2.6** **2.7**

The oxy-Cope cascade reaction has since been extended by adding a Claisen [3,3] shift to further increase the complexity of the resulting product. The oxy-Cope/ene/Claisen was published for the first time by Barriault and Denissova[26] in 2002. The three successive reactions start with an oxy-Cope of 1,2-divinylcyclohexanol **2.8**. The resulting macrocycle **2.9** can then form the decalin via an ene reaction followed by a Claisen rearrangement to give **2.11**. This tandem reaction results in the synthesis of **2.11** bearing a new quaternary center.

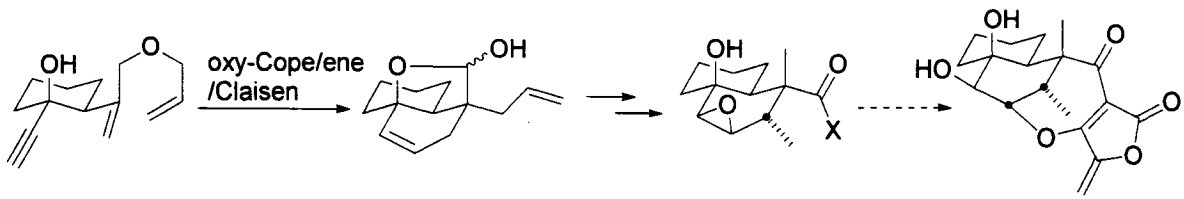
Scheme 2.3 – oxy-Cope/ene/Claisen reaction developed by Barriault and Denissova



2.8 **2.9** **2.10** **2.11**

Recently, Warrington and Barriault[27] published the synthesis of the C7-C15 *trans*-decalin portion of the natural antibiotic tetrodecamycin. They used the tandem oxy-Cope/ene/Claisen rearrangement to form the core **2.13** of the complex natural product **2.15**.

Scheme 2.4 – Approach to tetrodecamycin by Warrington and Barriault

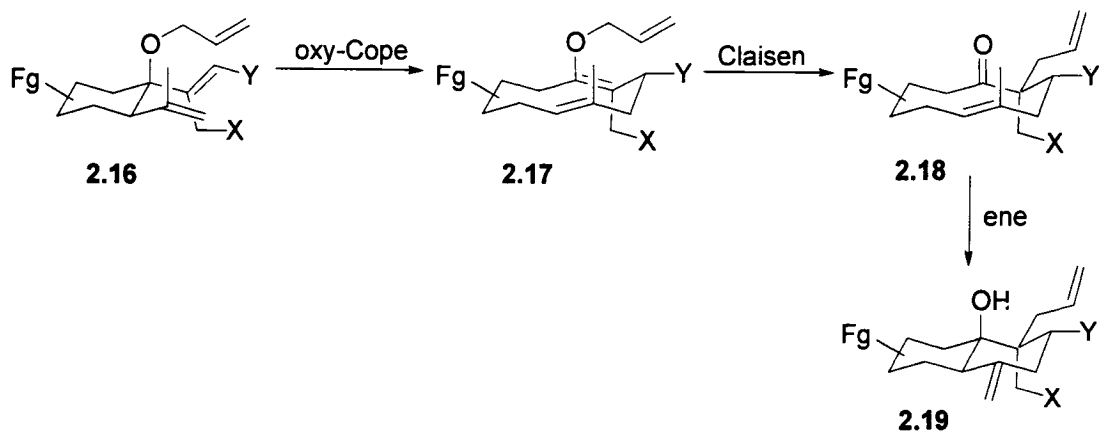


2.12 **2.13** **2.14** **2.15**

The cascade process happened when cyclohexanol **2.12** was submitted to microwave irradiation for 45 minutes in toluene. The resulting decalin **2.13** was obtained in 87% yield followed by 11 steps to get to their final point **2.14**.

Finally, this cascade reaction was further modified by Sauer and Barriault[28] by interchanging the Claisen and ene steps. They reported the oxy-Cope/Claisen/ene reaction to form *trans*-decalins such as **2.19**.

Scheme 2.5 –oxy-Cope/Claisen/ene reaction developed by Sauer and Barriault



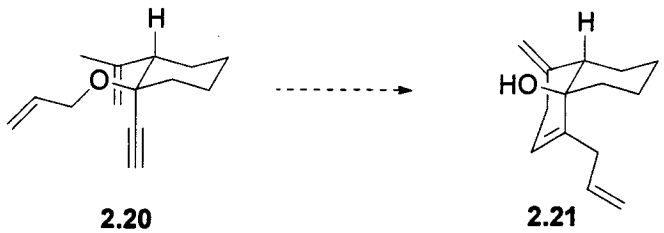
Similar to the previously detailed tandem reaction, compound **2.16** can undergo an oxy-Cope rearrangement followed by a Claisen [3,3] shift to give **2.18**. Finally, an ene rearrangement forms *trans*-decalin **2.19** as the desired compound.

Of these reported tandem reactions, none has produced a *cis*-decalin core. The methodology developed by Barriault *et al.* was not designed to synthesize a *cis* ring junction. Our goal was to find a way to make the *cis*-decalin and to apply it to the synthesis of vinigrol.

Synthesis of the cis-decalin via an oxy-Cope/Claisen/ene reaction

The development of a new application for the oxy-Cope/Claisen/ene reaction in order to produce a *cis*-decalin moiety was needed to pursue the total synthesis of vinigrol. A model study for the formation of the *cis* ring junction was mandatory to evaluate the feasibility of the rearrangement.

Figure 2.1 – Proposed cis*-decalin from an oxy-Cope/Claisen/ene*

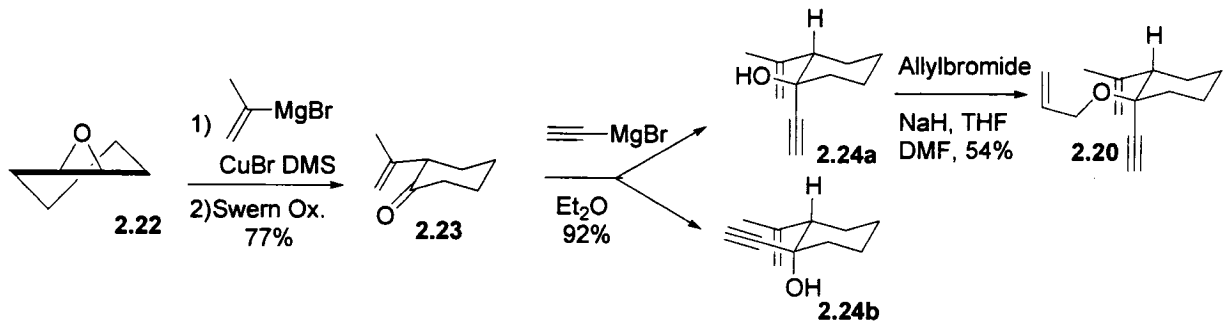


2.20 **2.21**

Compound **2.20** was chosen for a model due to its simplicity allowing fast formation of the rearrangement precursor. While decalin **2.21** was not appropriate for the synthesis of vinigrol because of its low degree of functionalization, it allowed a quick exploration of the reactivity of compounds such as **2.20**.

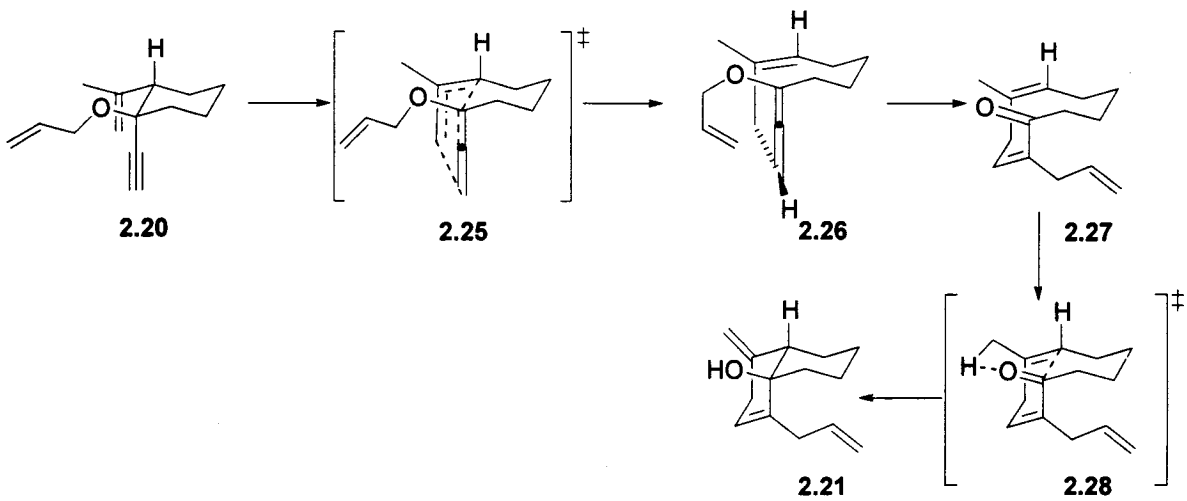
The oxy-Cope/Claisen/ene precursor **2.20** was synthesized by an allylation of known alcohol **2.24a**[27,29] using allylbromide in a mixture of THF and DMF.

Scheme 2.6 – Synthesis of precursor ***2.20***



The proposed mechanism is described in figure 2.2. Upon microwave irradiation,[30,31] the oxy-Cope product **2.26** was obtained, followed by a Claisen rearrangement to produce **2.27**. Finally, an ene reaction produced the desired compound **2.21**.

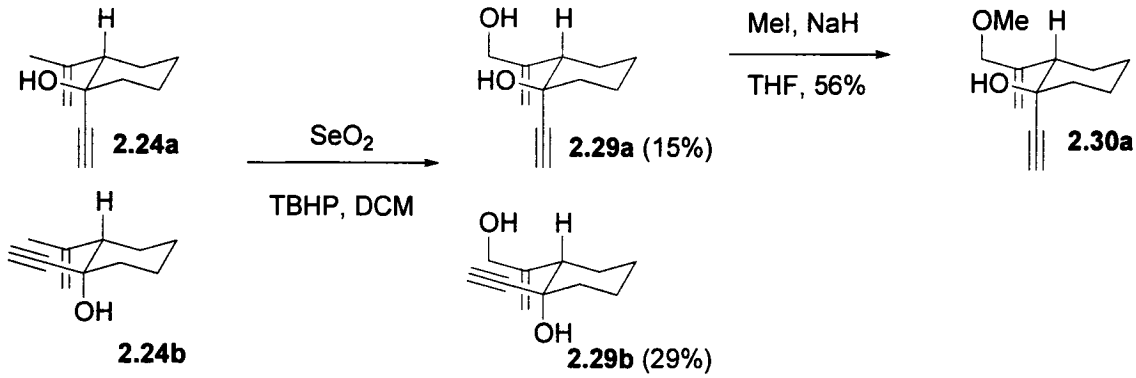
Figure 2.2 – Proposed mechanism



When the decalin precursor **2.20** was heated with microwave irradiation in toluene, a mixture of products was isolated. Some traces of product **2.21** may have been present but the geometry of the ring junction was not clarified. Different additives were added to help the reaction such as triethylamine, DBU,[32] and BHT.[33] None of the additives helped and the model was quickly abandoned.

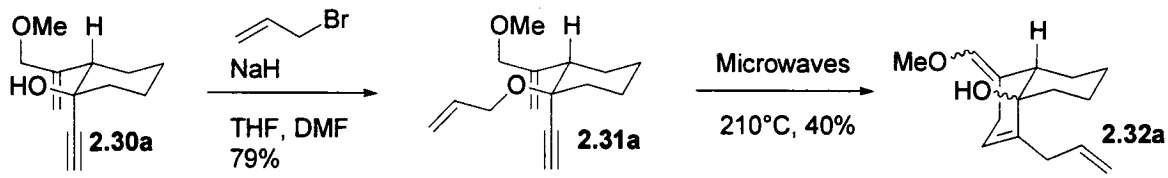
Meanwhile, a second model study to synthesize the *cis*-decalin was started. This new model, **2.30a,** is similar to the previous but bears an additional oxygen introduced by an allylic oxidation of **2.24** (mixture of **a** and **b**) with SeO_2. The primary alcohol[27] **2.29a** was selectively alkylated with iodomethane to provide **2.30a**.

Scheme 2.7 – Synthesis of precursor ***2.30a***



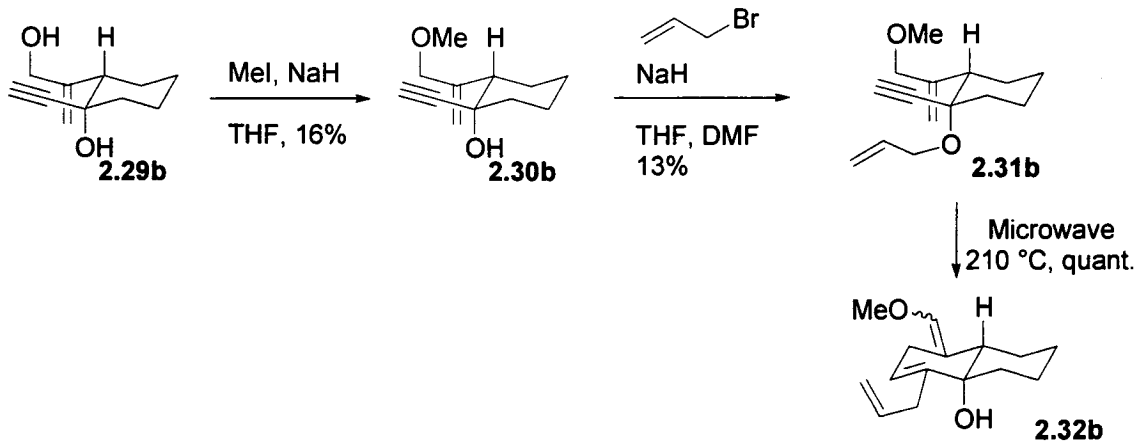
The tertiary alcohol was then alkylated with allyl bromide and the resulting compound **2.31a** was heated in toluene using a microwave. Decalin **2.32a** was isolated but the stereochemistry at the ring junction was not proved at this point.

Scheme 2.8 – Synthesis of decalin ***2.32a***



To verify the formation of the *cis*-decalin, the *trans*-decalin was made to compare with **2.32a**. In order to get a precursor that would allow a *trans*-ring junction, the same synthetic sequence has to be done with the diastereomer of **2.29b**. Despite the low yields of the alkylations (16 and 13%) the *trans* precursor **2.31b** was isolated. Heating **2.31b** in toluene for 1 hour at 210 °C yielded the *trans*-decalin in quantitative yield.

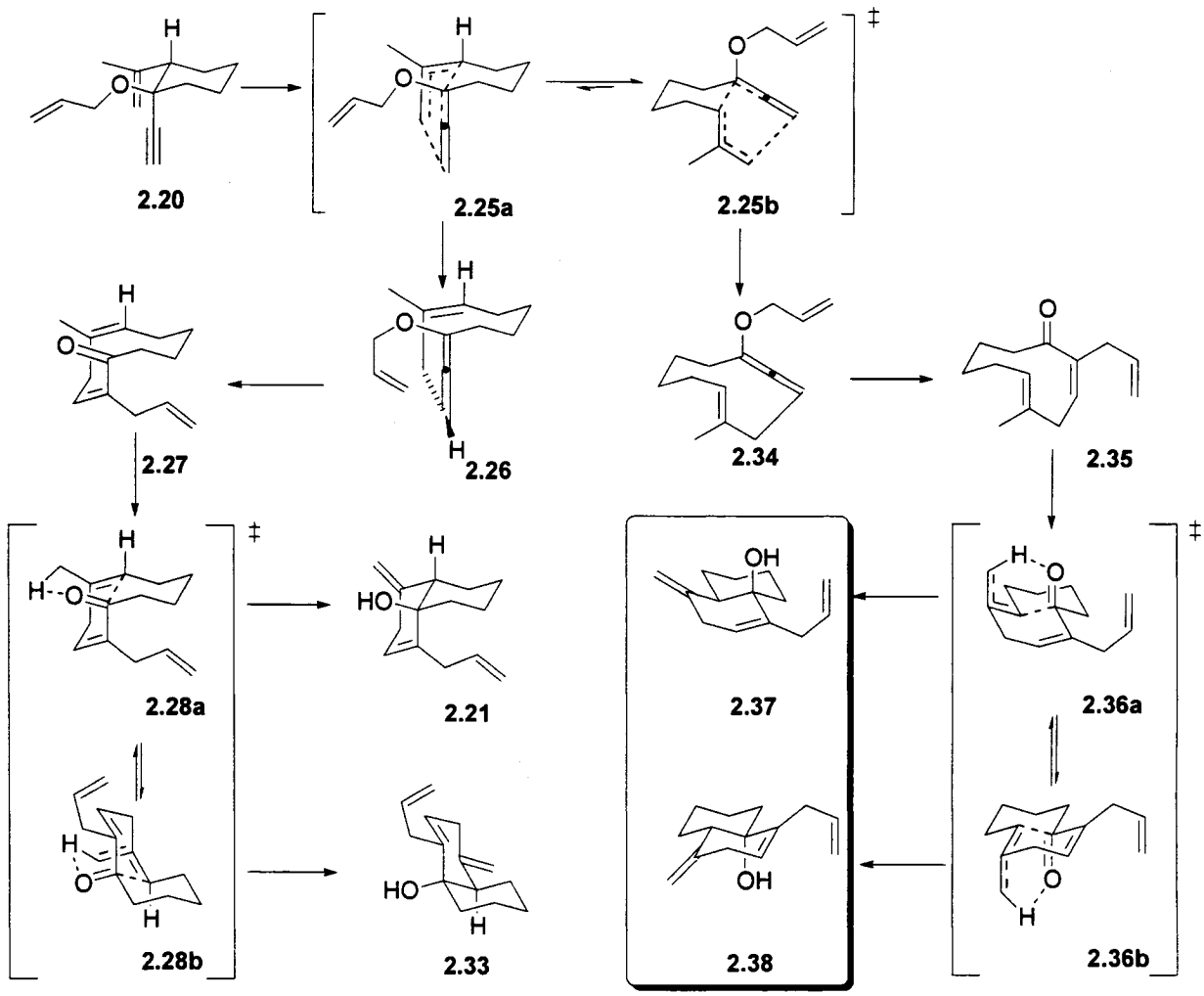
Scheme 2.9 – Synthesis of the trans-*decalin* **2.32b** *for comparison to the cis-decalin*



The ring junction of **2.32b** was unambiguous since compounds of that family had been synthesized before by this method and only *trans*-decalins were observed.[28] When the NMR spectra of **2.32a** and **2.32b** were compared, they were identical. This means that no *cis*-decalin was formed from **2.31a**.

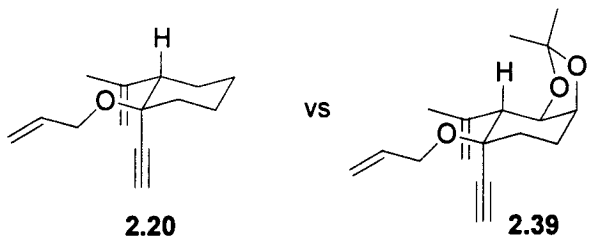
To understand this result, a closer look at the mechanism of the oxy-Cope/Claisen/ene reaction is necessary. The functionalized cyclohexane **2.20** exists in two different chair conformations. This means that the oxy-Cope rearrangement can proceed through **2.25a** or **2.25b** leading to two different macrocycles, **2.26** and **2.34** respectively. The Claisen rearrangements can then form products **2.27** and **2.35**. Before the ene cyclization, the macrocycles can equilibrate between **2.28a** and **2.28b** and between **2.36a** and **2.36b**. In this case, there is no substitution on the starting cyclohexane **2.20**, which implies that *cis*-decalins **2.21** and **2.33** are enantiomers, as are *trans*-decalins **2.37** and **2.38**. Clearly, in the case of the precursor **2.31a**, the transition state **2.25b** is favored over **2.25a** since only the *trans*-decalin **2.32b** was observed.

Figure 2.3 – Detailed mechanism of the oxy-Cope/Claisen/ene



In order to obtain the *cis*-decalin, it would be necessary to drive the equilibrium toward **2.25a**. To this end, we proposed using an acetonide to remotely control the conformation (figure 2.4).

Figure 2.4 – Adding substitution: acetonide

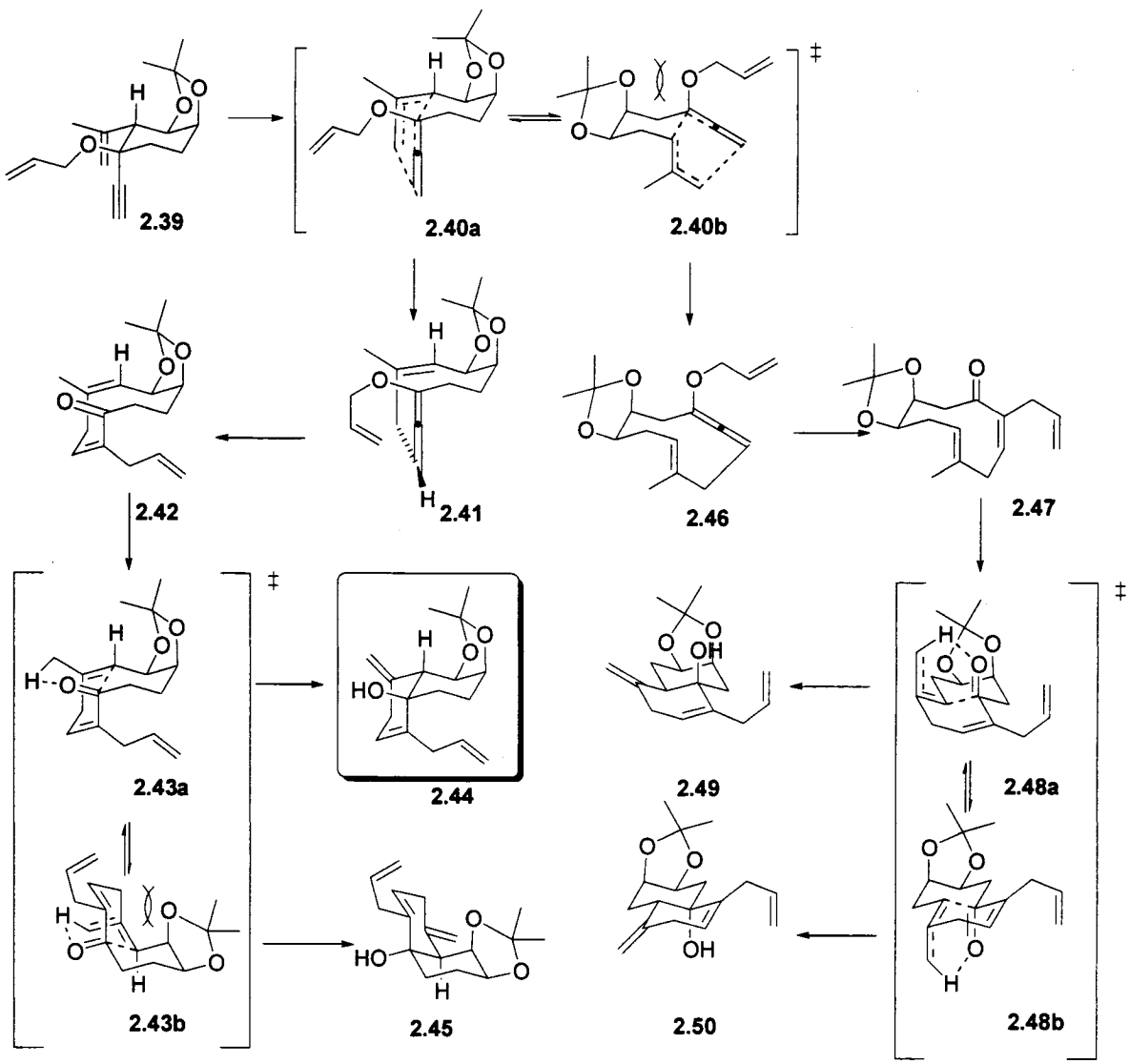


2.20 **2.39**

The Oxy-Cope/Claisen/ene and the control of the equilibrium

The acetonide moiety was introduced to favour transition state **2.40a** over **2.40b** by creating strong 1,3-diaxial interactions with the allyl ether in the case of **2.40b**. Macrocyclic allene **2.41** can undergo a Claisen [3,3]-shift to generate *in situ* 10-membered enone **2.42**. Following a carbonyl-ene reaction, the macrocyclic intermediate can adopt two possible reactive conformations, **2.43a** and **2.43b**. With an equilibrium between the two intermediates, the severe 1,3-diaxial interactions from the introduced acetonide can favour the desired *cis*-decalin **2.44** over **2.45**. In addition to forcing the oxy-Cope/Claisen/ene rearrangement to be selective, the acetonide would be useful to functionalize the decalin and allow further manipulations toward the synthesis of vinigrol.

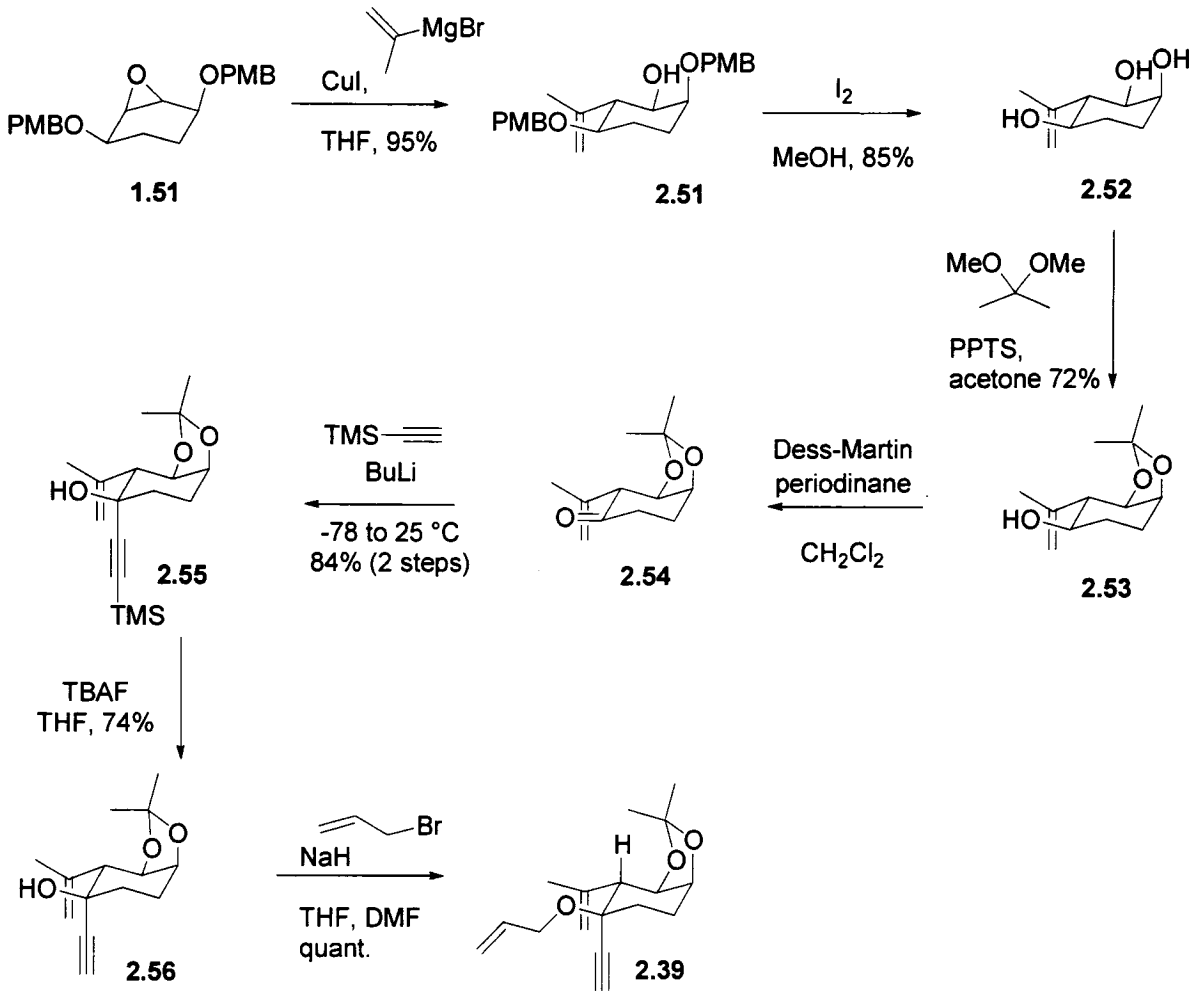
Figure 2.5 – Detailed mechanism of the oxy-Cope/Claisen/ene with the acetonide



The synthesis of precursor **2.39** commenced by the epoxide opening of *meso*-**1.51** with an organocuprate generated from isopropenylmagnesium bromide and CuI in THF to afford the corresponding homoallylic alcohol in 95% yield. The latter was treated with iodine in methanol[34] to provide racemic **2.52** free of benzyl groups in 85% yield. Following the protection of the *cis*-1,2-diol moiety in **2.52** with 2,2-dimethoxypropane and a catalytic amount of PPTS in acetone (72%), the corresponding acetonide was then oxidized using Dess-Martin's periodinane[35] to provide ketone **2.54**. Installation of the acetylene group on

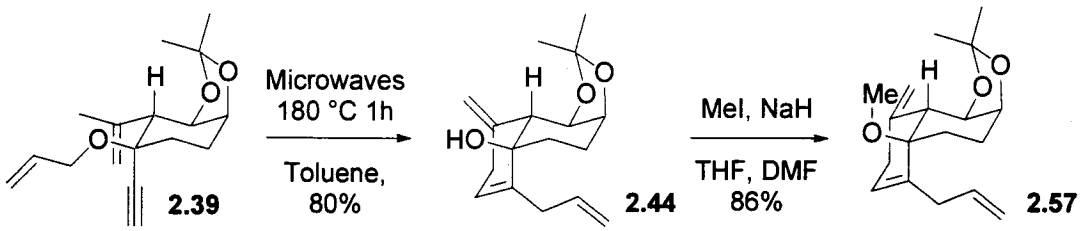
tandem reaction precursor **2.39** required the addition of lithium trimethylsilylacetylide to **2.54** in THF (84%, dr > 25:1) followed by treatment with fluoride ions to give alcohol **2.56** in 74% yield as the sole isomer. Allylation of tertiary alcohol **2.56** with allyl bromide and sodium hydride in THF-DMF (3:1) gave the desired allyl ether **2.39** in 100% yield.

*Scheme 2.10 – Synthesis of the precursor **2.39***



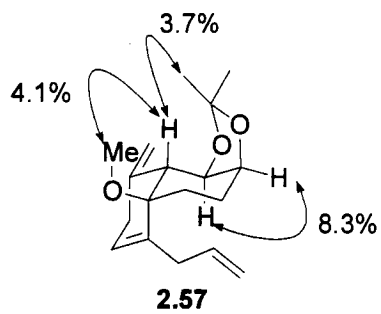
Compound **2.39** was then dissolved in degassed toluene and subjected to microwave irradiation (180 °C) for 1 hour to give the desired *cis*-decalin **2.44**. To prove the *cis* configuration of the ring junction, alcohol **2.44** was alkylated using iodomethane and sodium hydride in THF-DMF (2:1) to give **2.57** in 86% yield.

*Scheme 2.11 – Oxy-Cope/Claisen/ene on **2.39***



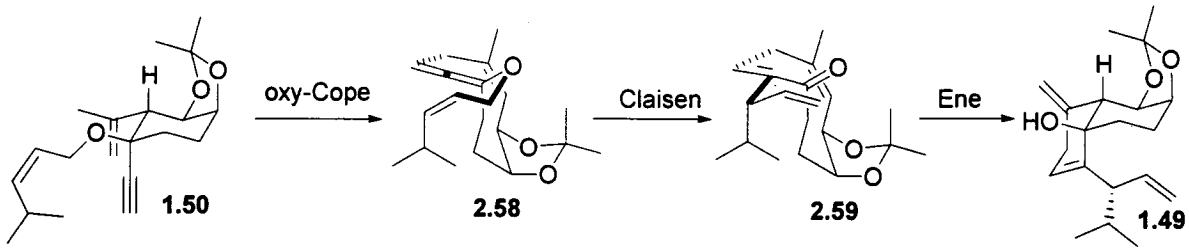
An NOE between the methoxy and the hydrogen at the ring junction (4.1%) proved the *cis*-decalin configuration while the NOE between the acetonide methyls and the H-ring junction (3.7%) proved that the isolated product was not the unwanted diastereoisomer **2.45** but the desired **2.44** (figure 2.5). A third strong NOE was observed between the acetonide hydrogens (8.3%). These experiments, combined with the COSY, ^{1}H NMR and ^{13}C NMR, supported the relative stereochemistry of *cis*-decalin **2.44**.

*Figure 2.6 – NOE experiments on **2.57***



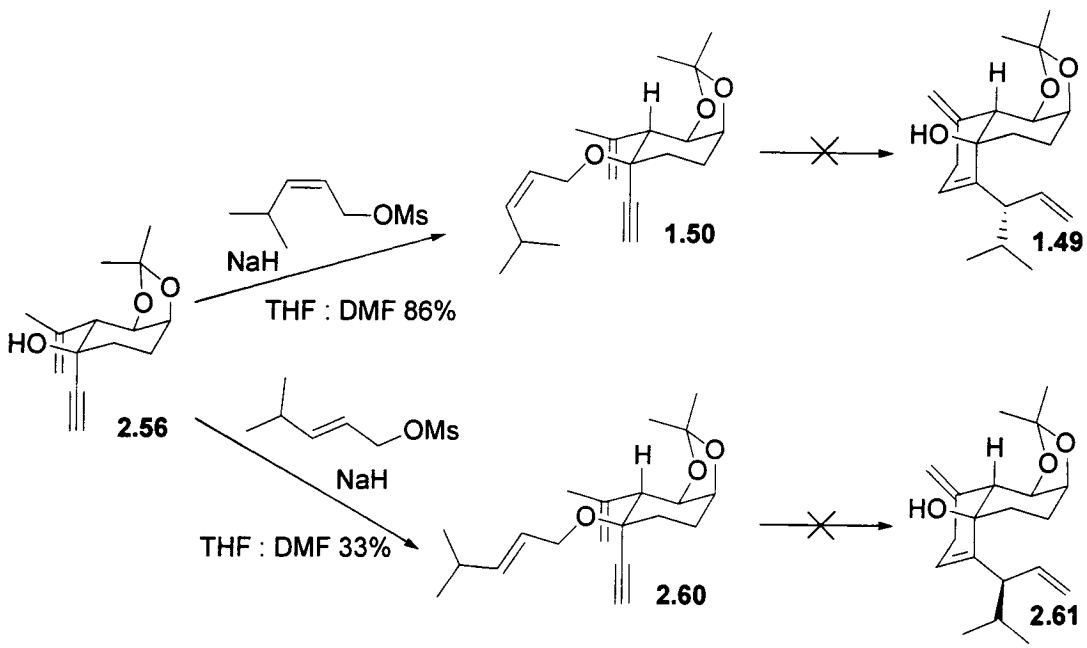
With a high yielding oxy-Cope/Claisen/ene rearrangement to form the *cis*-decalin in hand, we investigated the installation of the isopropyl unit. The rearrangement would set the proper stereochemistry of the isopropyl group as can be seen by looking at the oxy-Cope/Claisen/ene mechanism as in figure 2.7. Assuming that macrocyclic **2.58** is formed during the oxy-Cope process, Claisen rearrangement following by an ene reaction of **2.58** should give the desired product **1.49** bearing the proper isopropyl stereochemistry. The stereoselectivity appears to be controlled at the Claisen rearrangement step.

Figure 2.7 – Oxy-Cope/Claisen/ene bearing the isopropyl group



Precursor **1.50** was readily prepared from alcohol **2.56**, sodium hydride, and *cis*-mesylate-4-methyl-2-pentene[36] in 86% yield. Irradiation of **1.50** with microwaves at temperatures ranging from 160 to 200 °C gave a complex mixture of products from which no decalin product **1.49** was isolated. At first glance, steric interactions between the isopropyl group and the ring in **2.58** could elevate the activation energy of the rearrangement process thereby favouring other undesired lower energy processes. Similar results were reported by Hanna and co-workers[37] when attempting to rearrange *cis*-isopropyl tertiary bicyclo[2.2.2]octenols to the vinigrol skeleton via an anionic or thermal oxy-Cope reaction. In this case, the *trans*-isopropyl isomer, however, proceeded without any difficulties.

Scheme 2.12 – Alkylation of ***2.56*** *followed by oxy-Cope/Claisen/ene attempts*



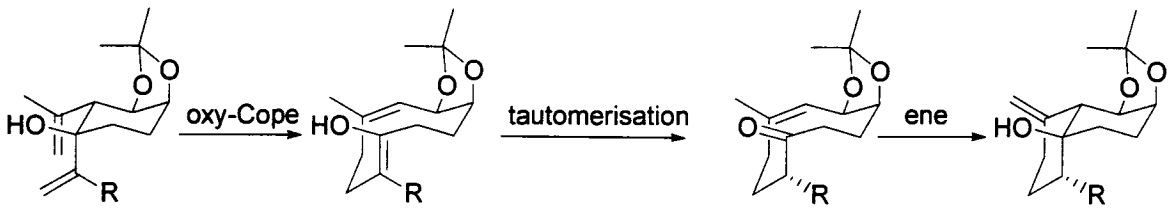
Trans-allyl ether **2.60** was thus prepared[38] from **2.56** and submitted to microwave irradiations. Surprisingly, no product **2.61** was observed and only decomposition was observed. *Trans*-allyl ether **2.60** would have given the wrong stereochemistry at the isopropyl position, but it would have been possible to invert it after. According to these results, it is clear that large substituents at the terminal position are detrimental to the rearrangement sequence.

Oxy-Cope/ene

Given the above failings, we needed to find another way to introduce the isopropyl group on the skeleton in order to synthesize vinigrol. Instead of an oxy-Cope/Claisen/ene rearrangement, a new approach could take the advantage of an oxy-Cope/ene reaction to form the *cis*-decalin. Like the oxy-Cope/Claisen/ene, no precedent existed for the formation of a *cis*-decalin,[24,27,39] however, the use of the acetonide could once again favour its formation. The introduction of a carbon chain R on **2.62** could be the anchor to install the

isopropyl group later on in the synthesis. From substrate **2.62**, an oxy-Cope would give enol **2.63** which would tautomerize to the ketone **2.64**. The transannular ene reaction would give the desired *cis*-decalin **2.65** with the right stereochemistry at R for the synthesis of vinigrol.

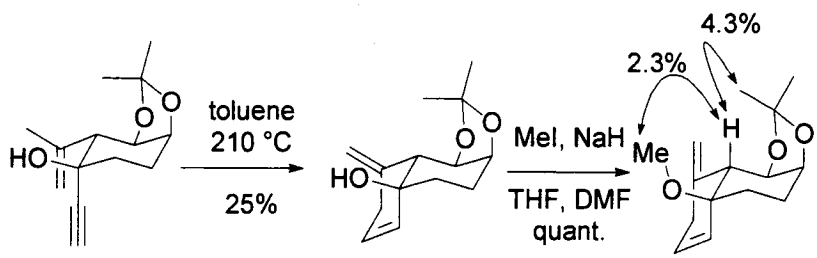
Figure 2.8 – Oxy-Cope/ene mechanism



2.62 **2.63** **2.64** **2.65**

The first experiment tried was on a simple model without the alkyl group, R, in order to verify the feasibility of the oxy-Cope/ene reaction.

*Scheme 2.13 – Oxy-Cope /ene on **2.56***

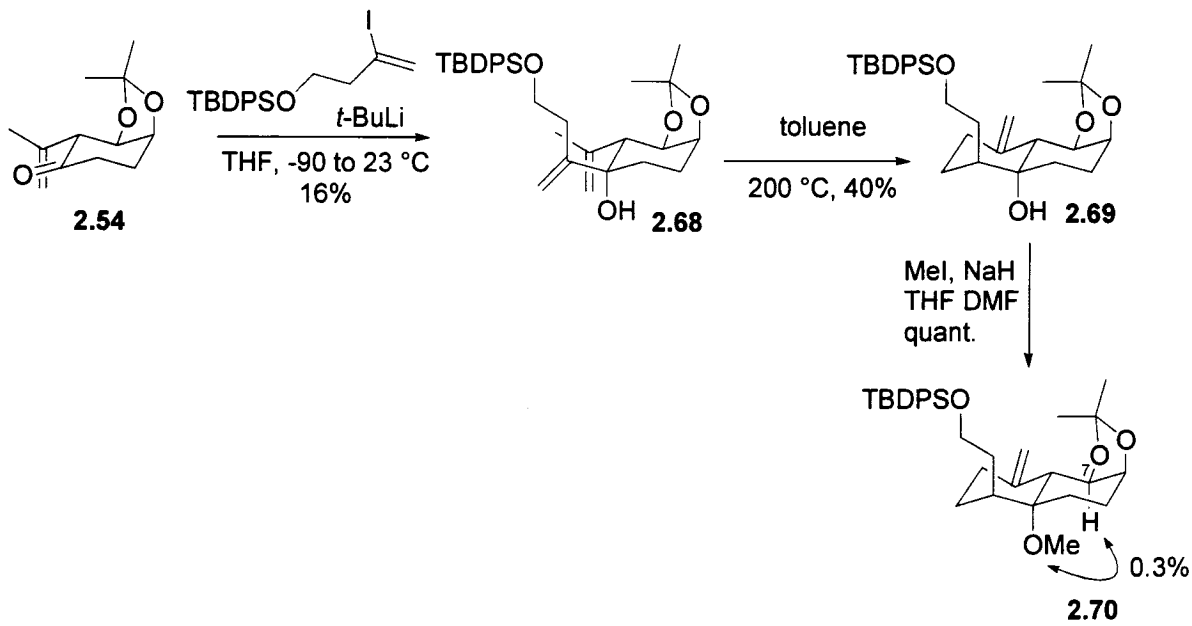


2.56 **2.66** **2.67**

Compound **2.56** was submitted directly to microwave irradiations. The isolated product **2.66** was the desired *cis*-decalin as proved by NOE experiments on the methylated compound **2.67**. A NOE of 2.3% between the hydrogen at the ring junction and the methoxy as well as with the acetonide (4.3%) proved the relative stereochemistry of **2.67**. Since the simple model of the oxy-Cope/ene worked, the introduction of a more functionalized side chain was tried next.

Alkylation of **2.54** by functionalized alkene *t*-butyldiphenylsilyloxy-3-iodobut-3-en-1-ol[39] could provide a model to verify the reactivity while still bearing functionality for introducing the desired isopropyl group. The alkylation, however, proceeded from the wrong face of the ketone and gave the undesired alcohol **2.68**. While this result was in opposition to the previous results with substrate **2.56**, this selectivity has been observed by S. Arns.[40] The *trans*-decalin **2.69** was thus isolated after microwave irradiations and the relative stereochemistry was proven by NOE (0.3%) between the methoxy and the hydrogen at C7.

Scheme 2.14 – Functionalized oxy-Cope/ene



Conclusions

The synthesis of *cis*-decalin cores was achieved through two different tandem processes: the oxy-Cope/Claisen/ene and the oxy-Cope/ene rearrangements. It has been demonstrated that a rearrangement precursor has to bear substituents that creates enough steric interaction to favour a *cis* transition state thus avoiding the formation of the *trans*-decalin. Once the *cis*-decalin **2.44** was obtained, we tried to functionalize the decalin core to make vinigrol. The

introduction of the isopropyl group, however, proved to be problematic for both of the tandem reaction sequences. Therefore, a different strategy was developed involving a hydroxy-directed Diels-Alder reaction to create the decalin portion of vinigrol.

3

Second Approach:

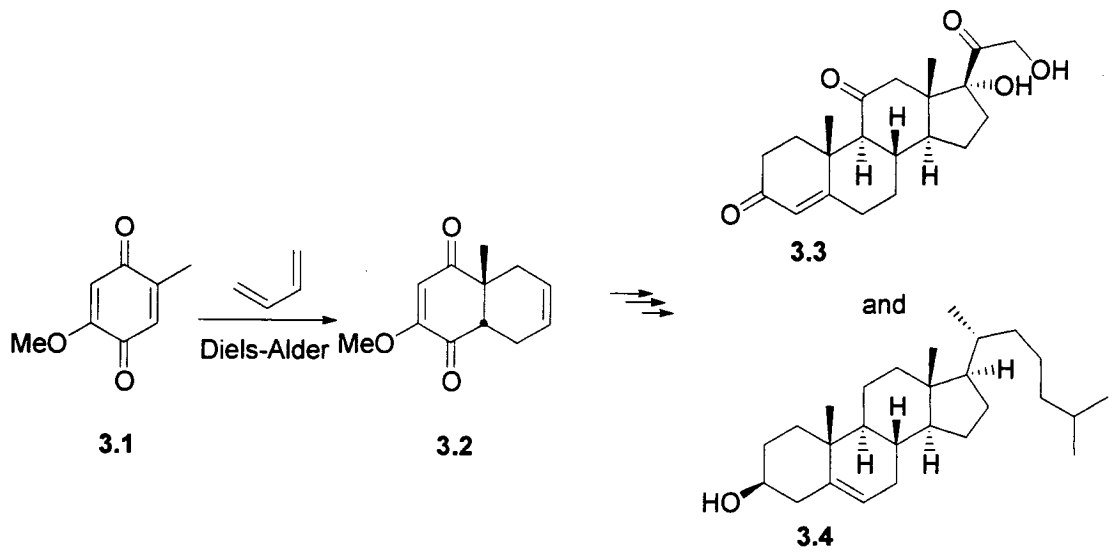
Hydroxy-Directed Diels-Alder

Introduction

In 1928, Diels and Alder[41] wrote: "Thus it appears to us that the possibility of synthesis of complex compounds related to or identical with natural products such as terpenes, sesquiterpenes, perhaps even alkaloids, has been moved to the near prospects."

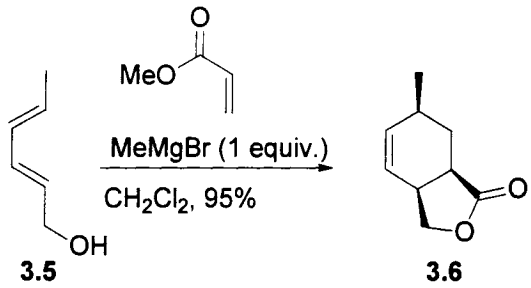
Obviously, since then, the Diels-Alder reaction has been intensely used for the synthesis of natural products.[42] Pioneers, such as Woodward, opened the way with syntheses of cortisone **3.3** and cholesterol **3.4**.[43]

Figure 3.1 – Woodward's approach to cortisone and cholesterol



For the decades following, chemists have used this powerful and versatile reaction to make complex molecules. Nonetheless, the [4+2] cycloaddition suffers some limitations. If the reaction is not controlled, many compounds may be formed simultaneously which is obviously not desirable for target-oriented synthesis. One of the problems regularly observed is the π-facial diastereoselectivity and consequently, it has been extensively studied.[44] A second problem frequently observed is the regioselectivity, especially when nonsymmetrical dienophiles are used. A solution for that problem is to use a temporary tether that binds the diene and the dienophile together. That Diels-Alder reaction would then be performed in an intramolecular way. To this end, the use of tethers[45] and Lewis acids[46] in the control of Diels-Alder reaction has also been studied. In 2000, Ward and Abaee[47] combined the two concepts to perform a [4+2] cycloaddition by self-assembly of the components on a Lewis acid template. They used different Lewis acids, but the one that gave the best results for the conversion of **3.5** into **3.6** was magnesium. They also developed an enantioselective version of the reaction.[48]

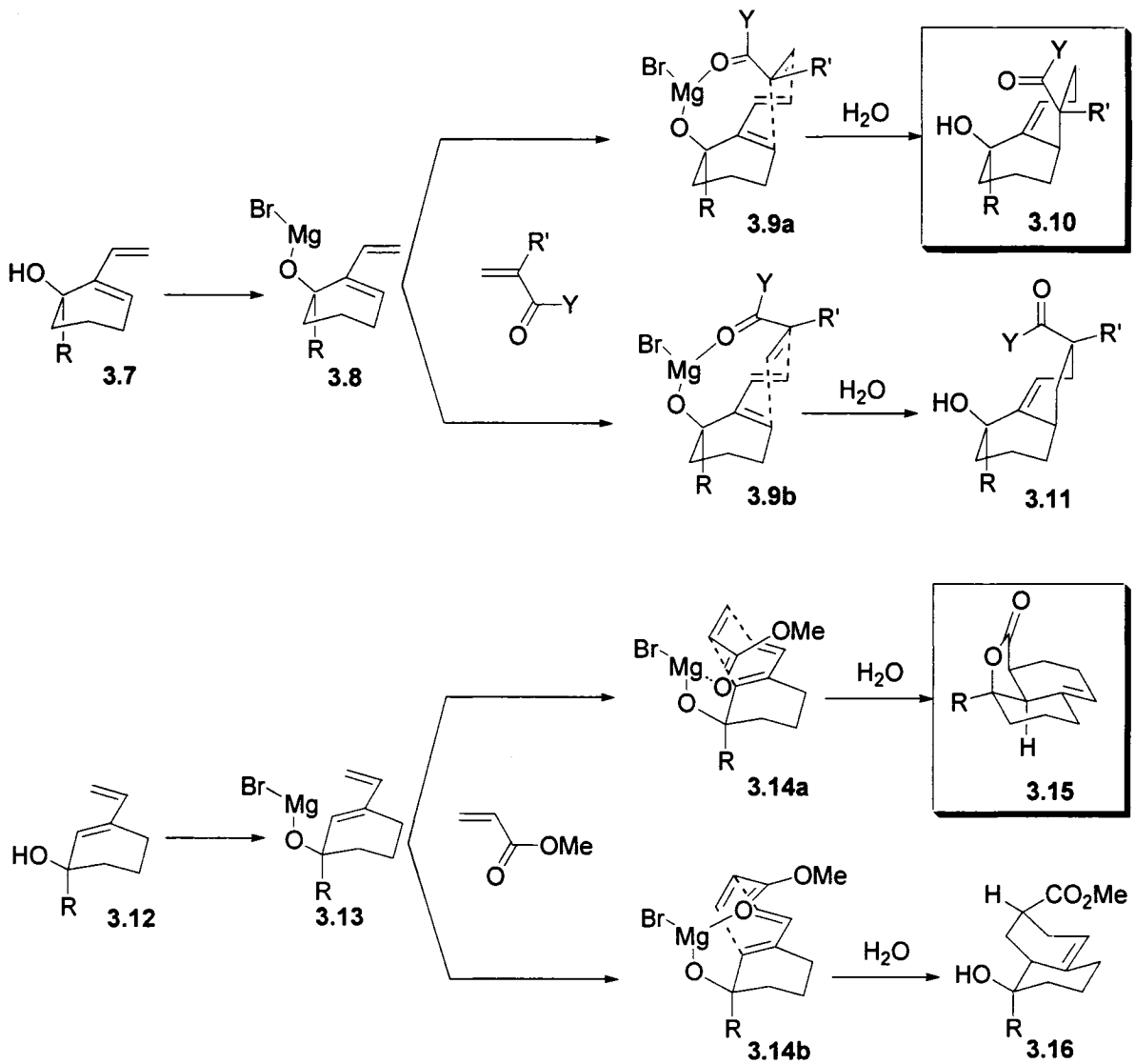
Figure 3.2 – Ward's Diels-Alder reaction using a Lewis acid template



3.5 **3.6**

Recently, Barriault *et al.* developed a hydroxy-directed variation of the Diels-Alder reaction (HDDA)[49] on two different types of dienes, **3.7** and **3.12**. This method controls the regio- and stereoselectivity via a magnesium tether through intermediates **3.9** and **3.14**. The dienophile and the diene are linked with the magnesium alkoxide and the Diels-Alder is forced to append syn with the alcohol.

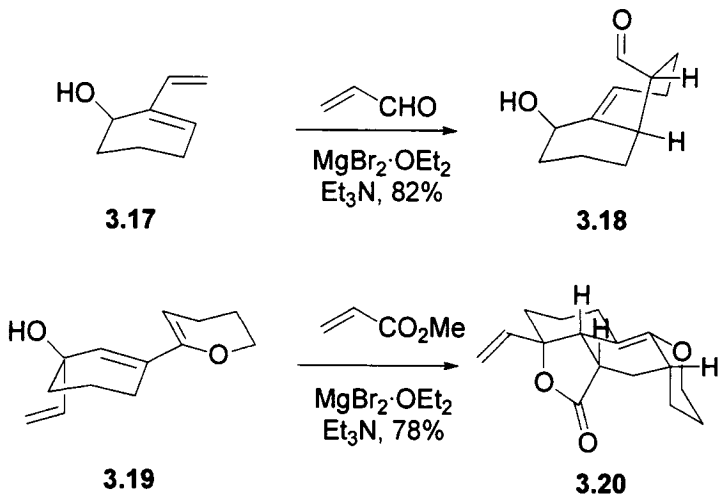
Figure 3.3 – Barriault's HDDA on two different types of dienes



In the case of **3.9**, the magnesium tether also controls the endo-facial selectivity. The differentiation between pathways leading to **3.10** versus **3.11** occurs because there is less strain when the dienophile approaches the diene. Transition state **3.9a** involves an eight-membered ring compared to **3.9b**, which goes through a nine-membered ring. For similar reasons, **3.15** is favoured over **3.16**. In transition state **3.14a**, a seven-membered-ring is formed compared to a nine-membered ring in **3.14b**. Interestingly, the proximity of the alkoxide and the dienophile in **3.14a** produces lactone **3.15**.

The HDDA has been applied to different substrates such as **3.17** and **3.19** affording diastereoselectivities of > 25:1. The efficiency of the HDDA attracted us to use it toward the synthesis of the decalin core of vinigrol.

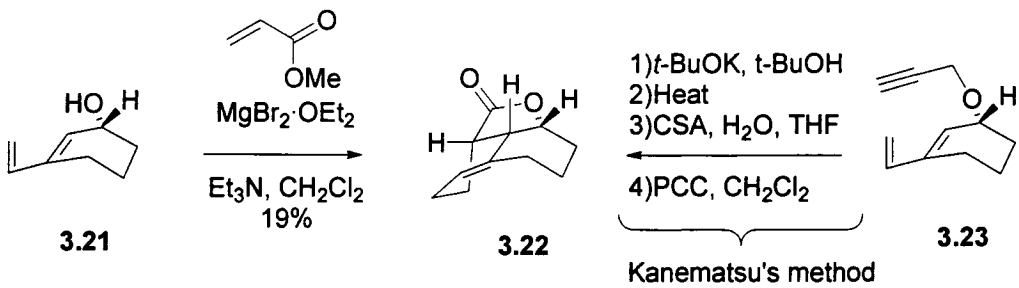
Figure 3.4 – Examples of HDDA



First attempt to generate the decalin core with an HDDA reaction

The first attempt to synthesize a *cis*-decalin moiety with an HDDA used a diene similar to **3.12**. Diene **3.21**[50] and the Diels-Alder adduct **3.22** are known from the literature, however the [4+2] cycloaddition of Kanematsu[51] was not as efficient as the HDDA and needed many additional steps to get to the desired lactone **3.22**. With the HDDA, a removable tether is formed by treating diene **3.21** with $MgBr_2$ and triethylamine to obtain a magnesium alkoxide.[52] The addition of the methyl acrylate forms the HDDA adduct **3.22** in 19% yield. Unfortunately, this yield could not be increased and compromised the synthetic route.

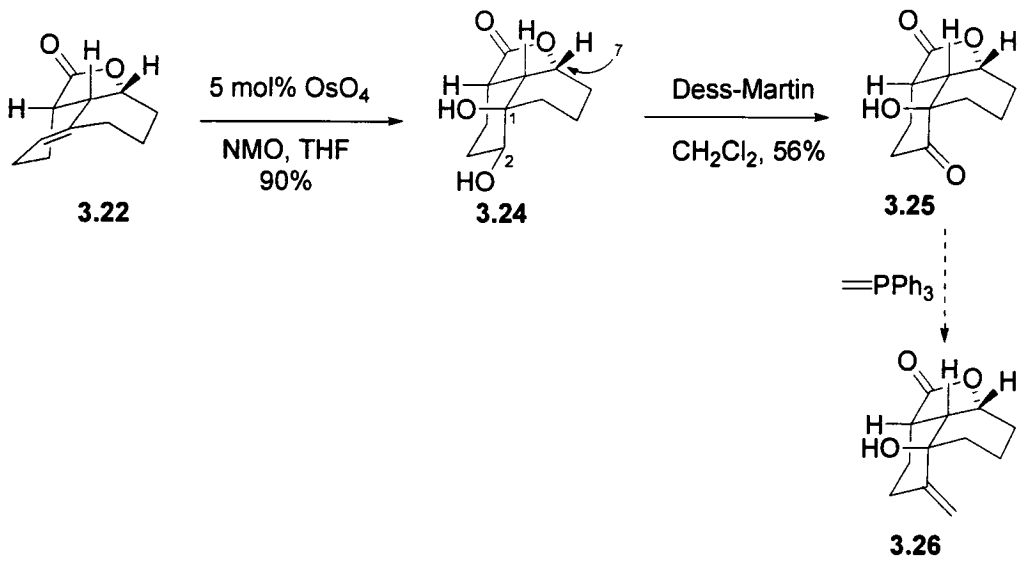
Scheme 3.1 – Barriault's HDDA vs. Kanematsu's method



3.21 **3.22** **3.23**

The goal of this Diels-Alder was to access a *cis*-decalin core such as **3.24** bearing functionality at the C-2 and C-7 positions. These two centers would be needed to install the eight-membered ring of vinigrol. Despite the low yield of the HDDA step, some exploratory experiments were performed to verify the reactivity of some later intermediates. The *cis*-decalin **3.24** was obtained by dihydroxylation of alkene **3.22** in 90% yield. The oxidation of the secondary alcohol to the ketone was performed under Dess-Martin periodinane conditions in 56% yield. This reaction was performed to verify the reactivity of the secondary alcohol and see the probability of installing the eight-membered ring at that position. Unfortunately, ketone **3.25** was not stable under basic conditions and therefore not stable to the Wittig reaction.

Scheme 3.2 – Functionalization of decalin ***3.22***

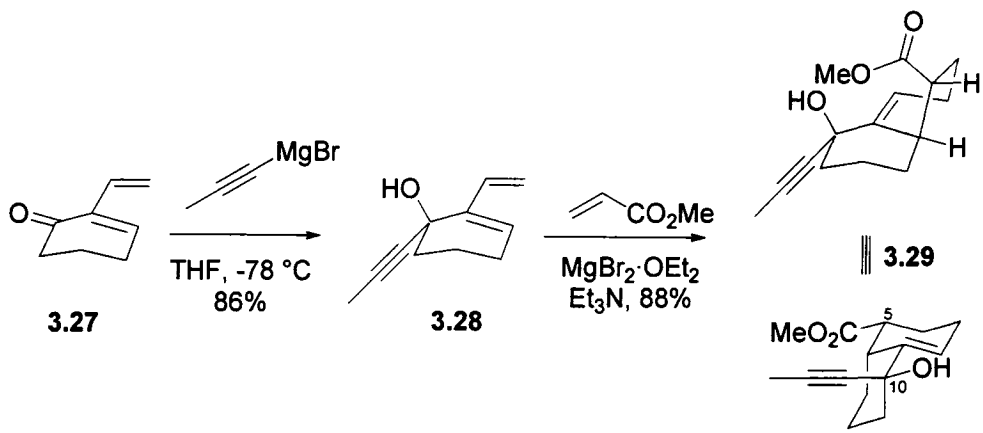


At this stage, our attention was turned to the low yield of the HDDA. By changing the starting diene, a better yield for the Diels-Alder could be expected.

Second attempt to generate the decalin core with an HDDA reaction

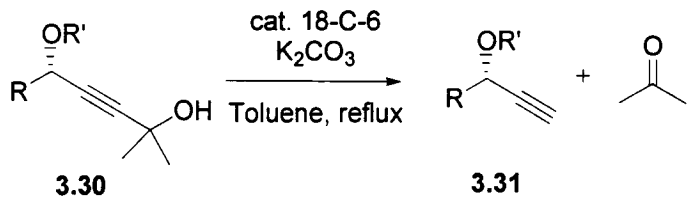
In order to change the diene, compound **3.27**[49] was alkylated with propynylmagnesium bromide to give **3.28** in 86% yield. The HDDA adduct **3.29** was then obtained with high reproducibility and in an excellent yield of 88% from the tertiary alcohol **3.28**. The yield of the HDDA confirmed that changing the diene was a good idea.

Scheme 3.3 – HDDA of ***3.28***



The resulting decalin possessed functional groups at C-5 and C-10, the proper location to install the desired eight-membered ring. Furthermore, C-10 is a tertiary alcohol that can be converted into a ketone. The propynyl group was added first to create the directing alcohol needed in the HDDA and to mask the ketone needed later on the synthesis. Carreira et al.[53] have demonstrated the formation of ketones from tertiary alcohols by treating compounds like **3.30** under basic conditions to obtain alkynes of type **3.31** and acetone. In their case, the method amounts to having protected an alkyne with acetone, but in our synthesis the goal was to protect the ketone with an alkyne.

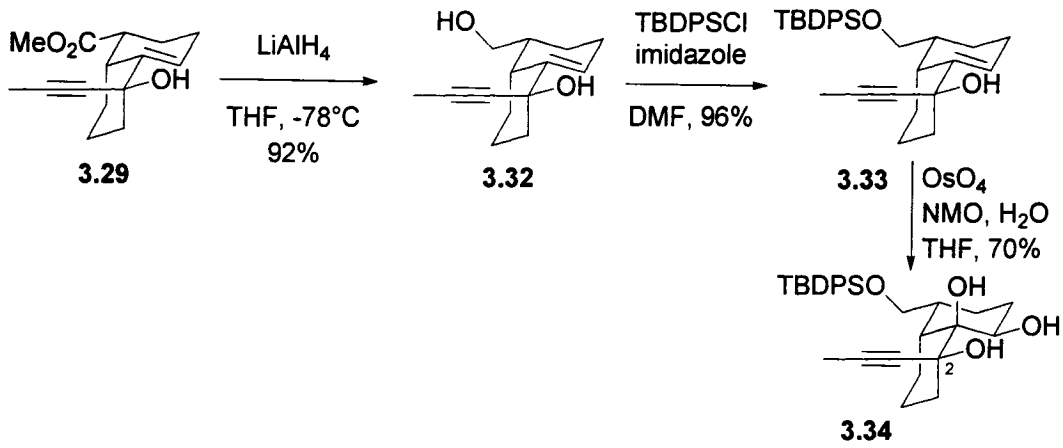
Figure 3.5 – Carreira's deprotection of alkyne ***3.30***



To avoid any epimerization of the ester on **3.29**, the reduction to the primary alcohol was performed directly after the HDDA step with $LiAlH_4$ in 92% yield. Alcohol **3.29** was then

selectively protected with TBDPSCl in 96% yield. The dihydroxylation of the resulting compound, **3.33**, led to triol **3.34** in 70% yield.

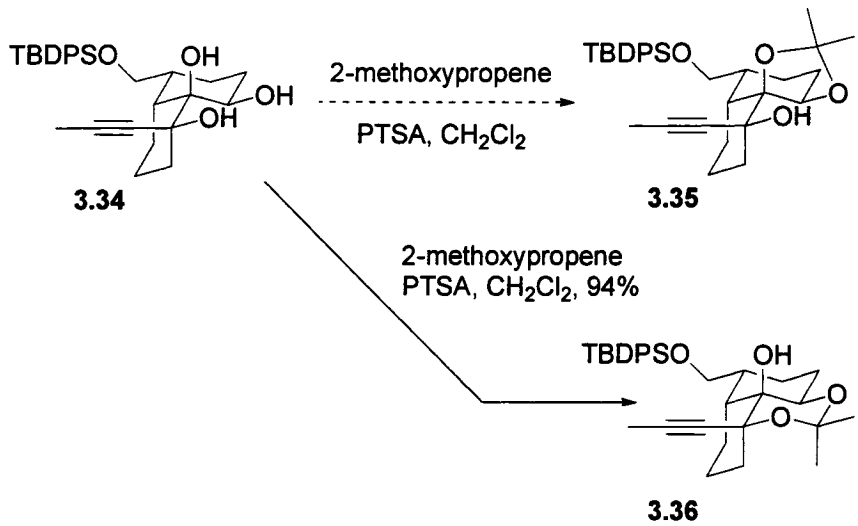
*Scheme 3.4 – Functionalization of decalin **3.29***



3.29 **3.32** **3.33** **3.34**

The next step was to selectively protect the 1,2-diol and leave the C-2 alcohol free to form a ketone. Treatment with 2-methoxypropene, however, did not produce the predicted acetonide **3.35**, but rather unproductive ketal **3.36**. The latter was not interesting since the propyne group would no longer be removable under basic conditions. Another protecting group, MOMCl, was then tried, but rather than mono-protection of the secondary alcohol, a complex mixture was isolated thus forcing a new strategy for the protecting groups.

*Scheme 3.5 – Protection of triol **3.34***



The stereochemistry of **3.36** was proven by X-ray crystallography on the deprotected alcohol **3.37** (figure 3.6). The primary alcohol **3.37** was isolated in quantitative yield upon the treatment of **3.36** with TBAF.

*Scheme 3.6 – Formation of diol **3.37***

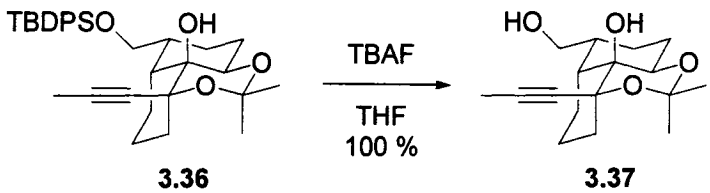
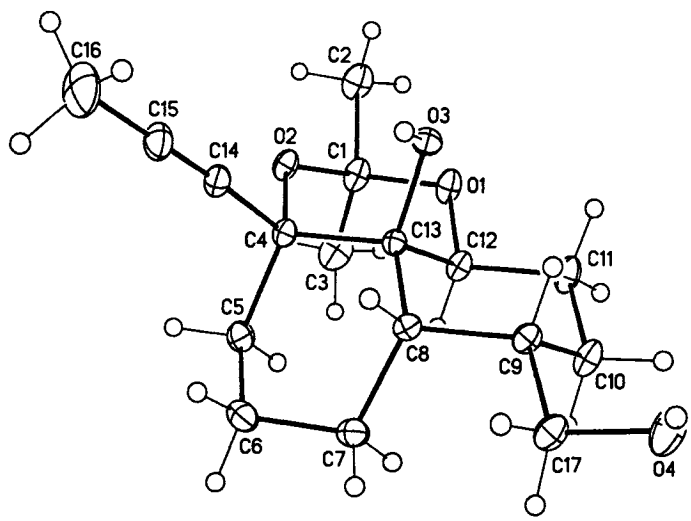
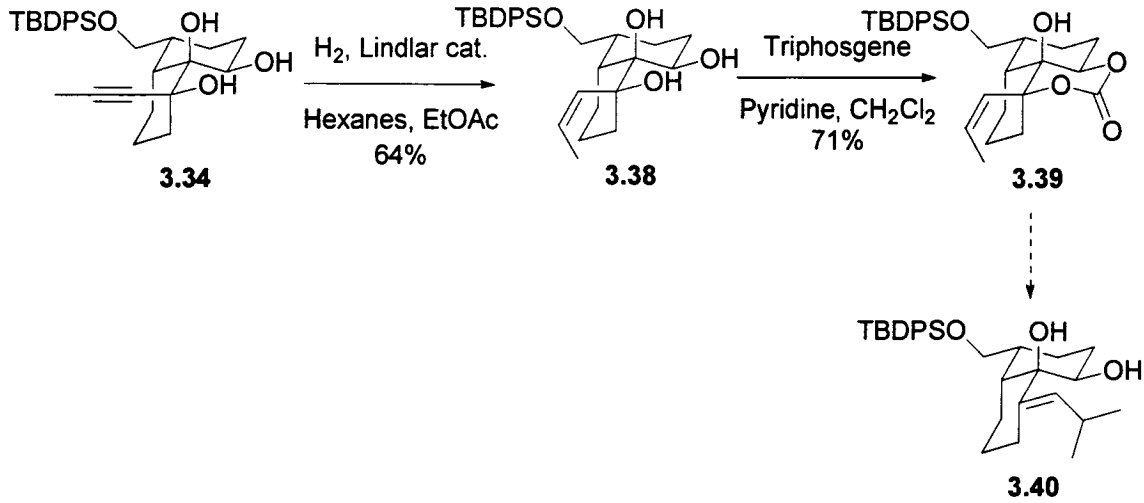


Figure 3.6 – ORTEP plot of ***3.37***



Finally, a short study was performed to see if the propyne moiety could have been used in an S_N2' reaction. Replacing the acetonide **3.36** by a good leaving group such as a carbonate would set up the substrate for a nucleophilic displacement. The first step was to reduce the alkyne to an alkene with hydrogenation using Lindlard's catalyst to yield **3.38**. The leaving group was then installed with triphosgene in 71% yield. Unfortunately, treatment with a Me_2CuLi or $MeCu(CN)MgBr$[54] failed to gave any of the S_N2' product **3.40**. If successful, the reaction could have been used to install the isopropyl functionality needed in the natural product.

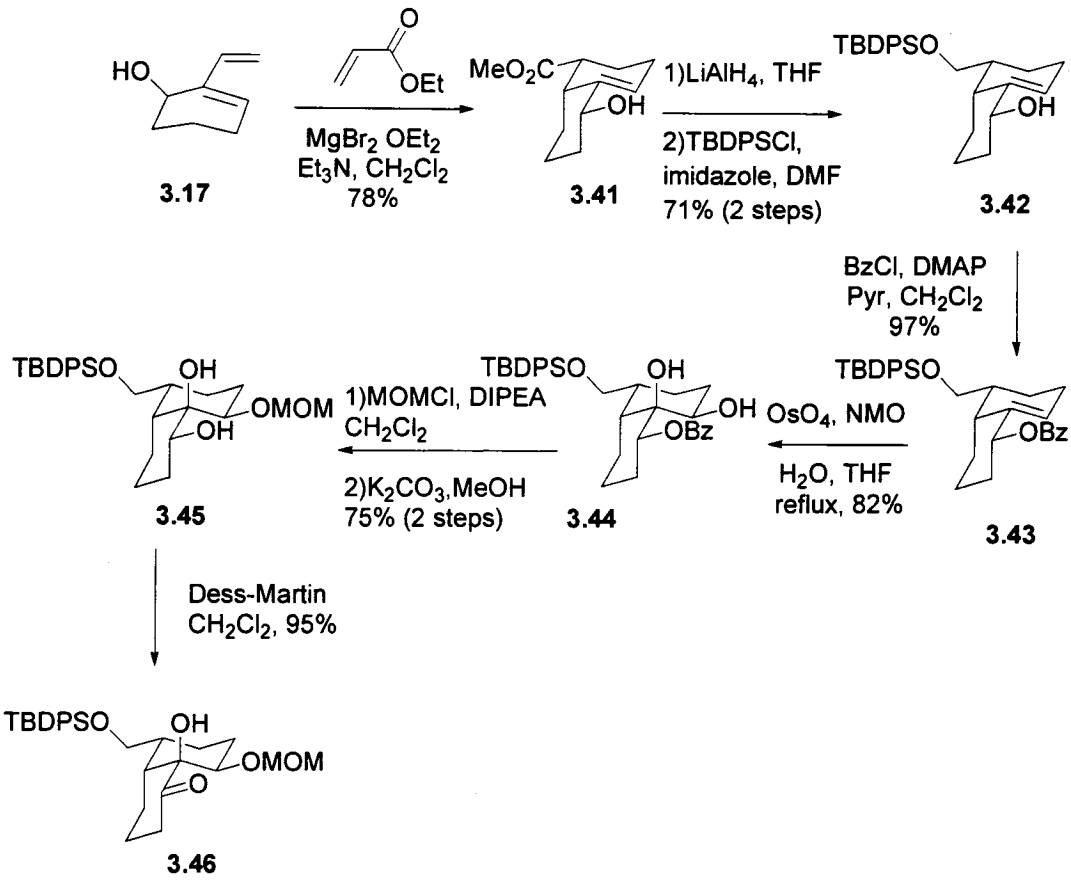
Scheme 3.7 – S_N2' strategy



A different HDDA to solve the problem

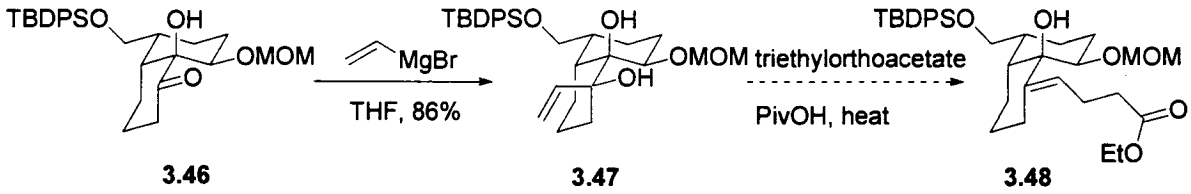
To remedy problems of the triol and unproductive propyne, a different diene was targeted for the HDDA. Known decalin **3.41**[49] was obtained from the HDDA with ethyl acrylate in 78% yield. The ester **3.41** was then reduced using $LiAlH_4$ and the crude primary alcohol was selectively protected using TBDPSCl in DMF with an overall yield of 71%. To avoid the previous problem of triol selectivity, the secondary alcohol **3.42** was protected in 97% yield with a benzoyl group before the dihydroxylation. The diol was installed with osmium tetroxide in refluxing THF (82% yield). The secondary alcohol **3.44** was selectively protected with MOMCl and the crude benzoate was deprotected to give diol **3.45** in 75% yield. In order to install a side chain on the decalin, secondary alcohol **3.45** was oxidized to the ketone to allow alkylation at that center. The oxidation afforded **3.46** in 95% yield.

Scheme 3.8 – A different HDDA



The next step was to alkylate on ketone **3.46** and install a functionalized carbon chain at that position. The goal of this transformation was to create a handle to install the desired eight-membered ring. The alkylation of the ketone went well using vinylmagnesium bromide to afford **3.47** in 86% yield. The subsequent step was to be an ortho-Johnson Claisen rearrangement,[55] but **3.48** was never isolated, only decomposition of the starting material was observed.

Scheme 3.9 – The ortho-Johnson Claisen rearrangement



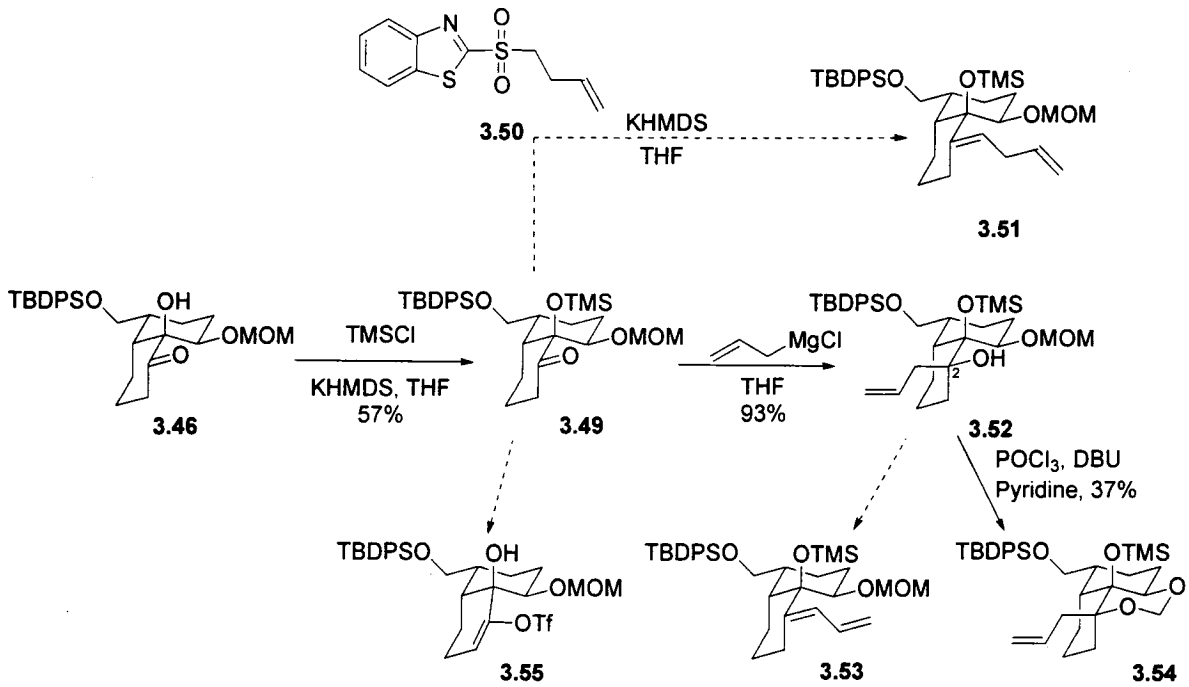
3.46 **3.47** **3.48**

Consequently, a new means of introducing the side chain was needed. To this end, TMS-protected **3.49**, obtained from **3.46** in 57% yield, was subjected to a variety of conditions. A modified Julia olefination[56] on **3.49** was tried using sulfone **3.50** but none of olefin **3.51** was observed.

Treatment with allylmagnesium chloride gave the desired tertiary alcohol **3.52** in 93% yield, however the relative stereochemistry of the allyl was inverted compared to the natural product which bears an eight-membered ring α at the C2 position. To invert this centre, alcohol **3.52** would have to be eliminated and the newly formed alkene hydrogenated from the β-face. To dehydrate compound **3.52**, $POCl_3$ was used but this led to **3.54** via cyclization of the MOM ether.

Finally, a palladium-coupling was planned to install the alkyl chain. However, the desired enol triflate **3.55** was not isolated using either triflic anhydride or *N*-phenyltrifluoromethanesulfonimide.

Scheme 3.10 – Alkylation of ketone ***3.49***

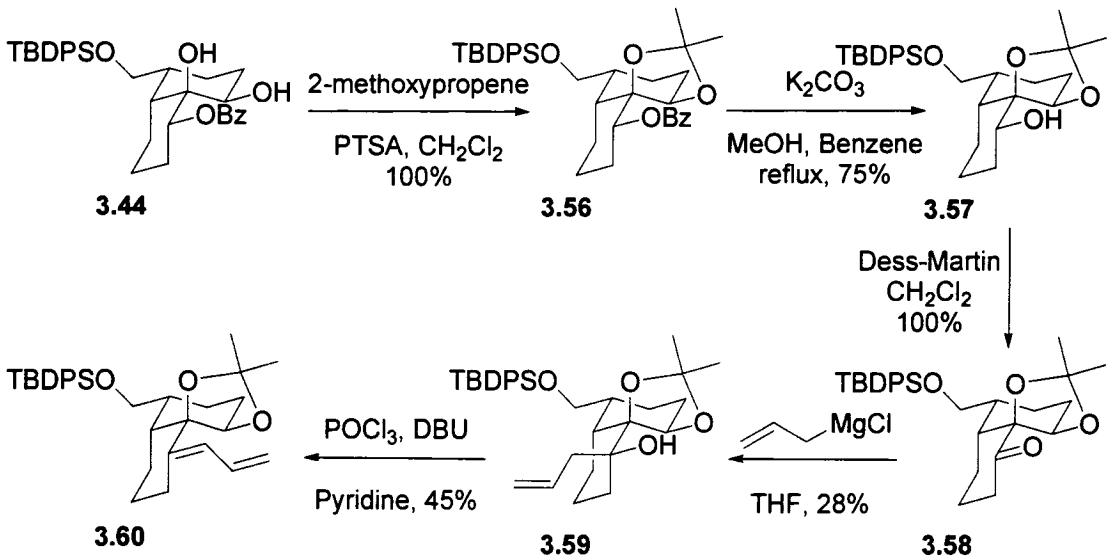


Changing the protecting group

In order to avoid cyclization products such as **3.54**, the synthetic sequence had to be changed to introduce a different protecting group. Treatment of diol **3.44** with 2-methoxypropene and PTSA in dichloromethane provided the corresponding acetonide **3.56** in quantitative yield. Removal of the benzoate group with potassium carbonate in methanol (75% yield) followed by a Dess-Martin periodinane oxidation produced ketone **3.57** in 100% yield. The alkylation using allylmagnesium chloride gave the tertiary alcohol **3.59** in a poor yield of 28%. To increase the yield, different conditions were tried such as adding $CeCl_3$ or changing the temperature and the solvent, however, none of those modifications improved the reaction yield. The resulting tertiary alcohol was then dehydrated using $POCl_3$ to give alkene **3.60** in 45% yield. The subsequent step would have been to selectively hydrogenate the tertiary substituted alkene using Crabtree's catalyst.[25] Since the allylmagnesium chloride step did not proceed well, the nucleophile would first need to be changed in order to increase

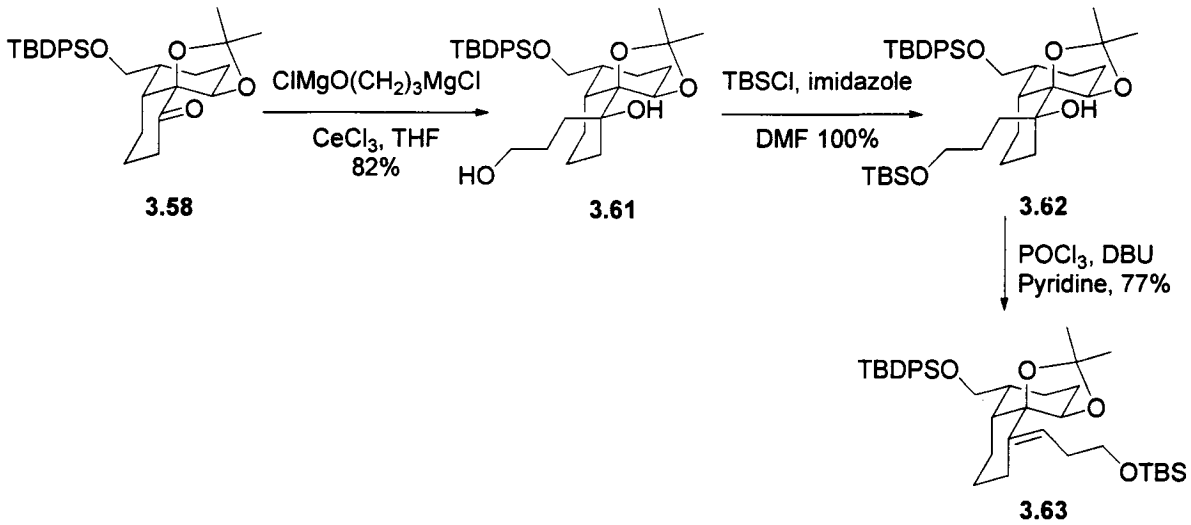
the yield. In addition, changing the nucleophile could avoid the problem of selective hydrogenation of the alkenes by not introducing the terminal alkene.

Scheme 3.11 – The use of an acetonide protecting group



The second nucleophile tried was $ClMg(CH_2)_3OMgCl$.[57] By treating ketone **3.58** with the above in the presence of $CeCl_3$ in THF, alcohol **3.61** was isolated in 82% yield. Protection of the primary alcohol as a TBS ether group (100%) and a subsequent elimination of the tertiary alcohol using $POCl_3$ and DBU in pyridine produced decalin **3.63** in 77% yield.

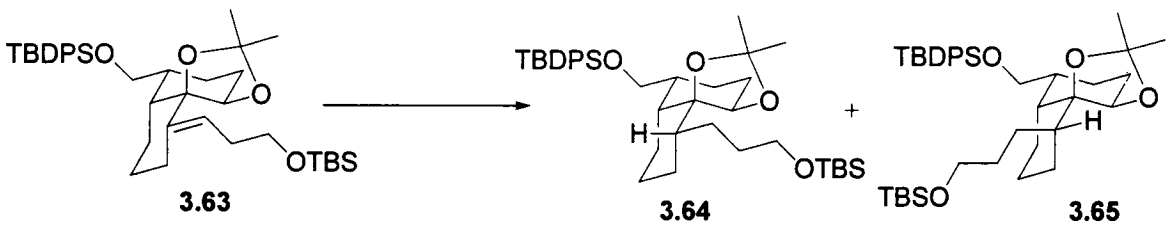
*Scheme 3.12 – Alkylation on ketone **3.58***

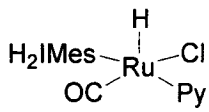


Hydrogenation of a hindered trisubstituted alkene

At this point, a stereoselective reduction of the trisubstituted exocyclic double **3.63** was investigated. A large number of hydrogenation protocols were scanned, though only hydrogenation methods using Pd/C, Raney Ni and Ru **3.66** were capable of reducing this olefin to yield decalins **3.64** and **3.65**.

Table 3.1 – Hydrogenation of ***3.63***



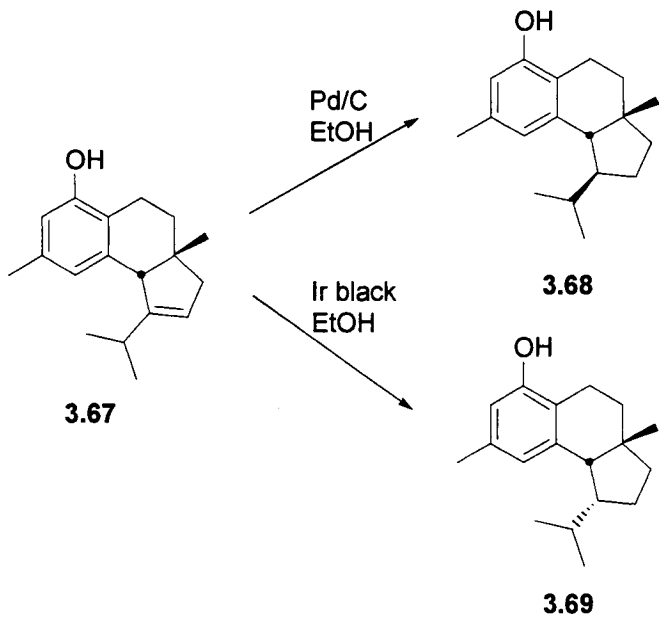
Entry	Catalyst	H_2 (psi)	Temp.(°C)	Time	Yield	Ratio **3.64** : **3.65**
1	Pd/C	15	25	15 h	S.M.	-
2	Pd/C	200	80	20 h	S.M.	-
3	Pd/C	1300	70	40 h	N.D.[a]	1:3[b]
4	Ir black	1500	80	40 h	S.M.[c]	-
5	Crabtree's	15	25	24 h	S.M.	-
6	Crabtree's	1250	120	48 h	Decomp.	-
7	Rh black	1225	79	18 h	S.M.[c]	-
8	$Rh(PPh_3)_3Cl$	1250	90	18h	Decomp.	-
9	$Ru(PPh_3)_3Cl$	100	60	24h	S.M.[b]	-
10	$Ru(PPh_3)_3Cl$	400	90	24h	Decomp.	-
11	Raney Ni	900	60	24h	99%[d]	4:1
12	 **3.66**	1300	80	5 days	99%	> 25:1

[a] N.D. = not determined. [b] The TBS group was partially removed during the reduction process. [c] Traces of **3.65** were observed. [d] Phenyls from the TBDPS group were reduced to the cyclohexanes.

A general observation from table 3.1 is that a high pressure of hydrogen was needed to reduce the double bond. Surprisingly, the reduction on Pd/C in ethanol afforded **3.65** as the

major product (entry 3). A similar result was reported by Trost.[58] They found that high-pressure hydrogenation of **3.67** with Pd/C afforded exclusively **3.68** (figure 3.7). They attributed the formation of **3.68** to "an equilibrium in the semihydrogenation step due to a slow final reductive elimination step." They circumvented this problem by hydrogenation of **3.67** over iridium black, yielding the desired product **3.69**. In our case, hydrogenation of **3.63** in the presence of iridium black did not give **3.64** (entry 4), rather, starting material was recovered along with traces of **3.65**.

Figure 3.7 – Trost's semihydrogenation

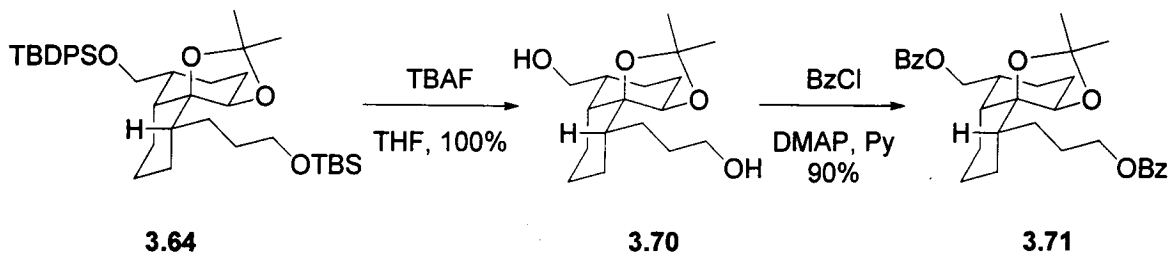


The use of Crabtree's[59] and Wilkinson's[60] catalysts (entries 5,6,8) also failed to give the desired decalin **3.64**. Raney Ni, however, gave a mixture of **3.64** and **3.65** in a ratio of 4:1 in 99% yield (entry 11). Fortunately, hydrogenation of **3.63** at 1300 psi in the presence of ruthenium-based catalyst **3.66** gave decalin **3.64** in a quantitative yield as the sole detectable isomer. The catalyst **3.66** was generated in situ from $H_2IMes(Cl)_2Py_2Ru{=}CHPh$ (6 mol%) in methanol with triethylamine.[61] This ruthenium-catalyzed reaction, however, suffered from two major problems. The autoclave had to be sealed in a glove box to avoid decomposition of the catalyst. Furthermore, the reaction gave a quantitative yield on a 15 mg scale, but did not go to completion on a larger scale such as 100 mg.

Non-metal-catalyzed reactions were also tried to reduce the alkene. Diimide[62] reduction using *p*-toluenesulfonhydrazide gave a mixture of starting material, **3.64** and **3.65**. The use of borane didn't give any reduced compound.

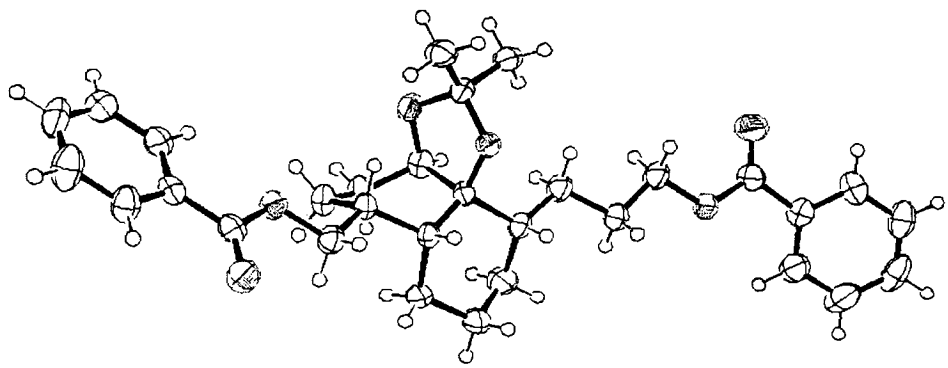
X-Ray diffraction was required to prove the relative stereochemistry of decalin **3.64**. Removal of both silicon protecting groups was realized with TBAF to afford the desired diol **3.70** in 100% yield. This diol was then esterified with benzoyl chloride in 90% yield. The crystal obtained from diester **3.71** proved that the hydrogenation happened from the β-face (figure 3.8).

*Scheme 3.13 – Synthesis of crystal **3.71***



3.64 **3.70** **3.71**

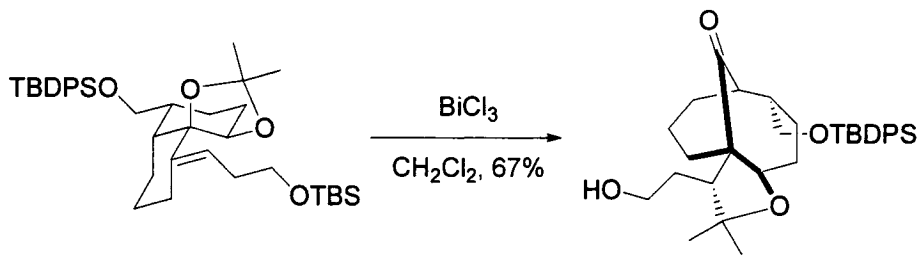
*Figure 3.8 – ORTEP plot of **3.71***



Removing the acetal...Prins/pinacol reaction instead

From the results described in table 3.1, the reduction of the alkene **3.63** no longer seemed appropriate for the total synthesis. The next option to help reduce the double bond was to remove the steric hindrance created by the acetonide. When the acetonide was treated with dilute protic acids, only decomposition was observed. Surprisingly, when a stoichiometric amount of $BiCl_3$ in dichloromethane was used instead, the bicyclo[4.3.1]decanone **3.72** was isolated in 67% yield.

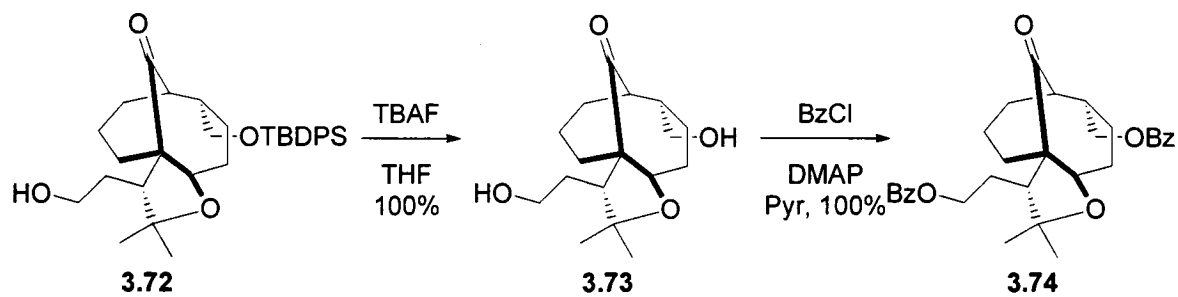
Scheme 3.14 – Discovered Prins/pinacol



3.63 **3.72**

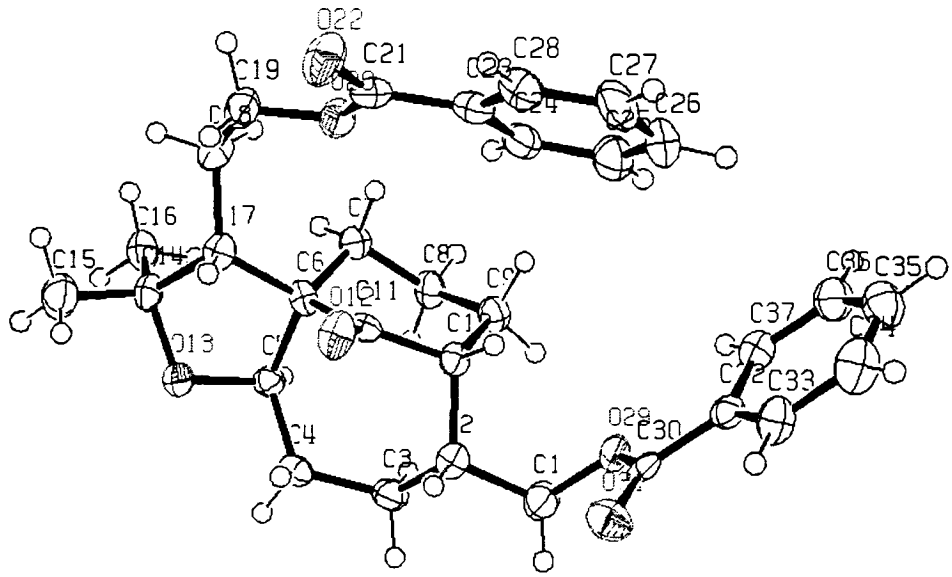
This acid-catalyzed rearrangement was unexpected and the structure had to be proved by an X-Ray diffraction (figure 3.9). The formation of a crystal was allowed by the removal of the silicon protecting group with TBAF in quantitative yield. The crystalline ester derivative **3.74** was obtained by treating the diol **3.73** with benzoyl chloride (100%).

*Scheme 3.15 – Synthesis of crystal **3.74***



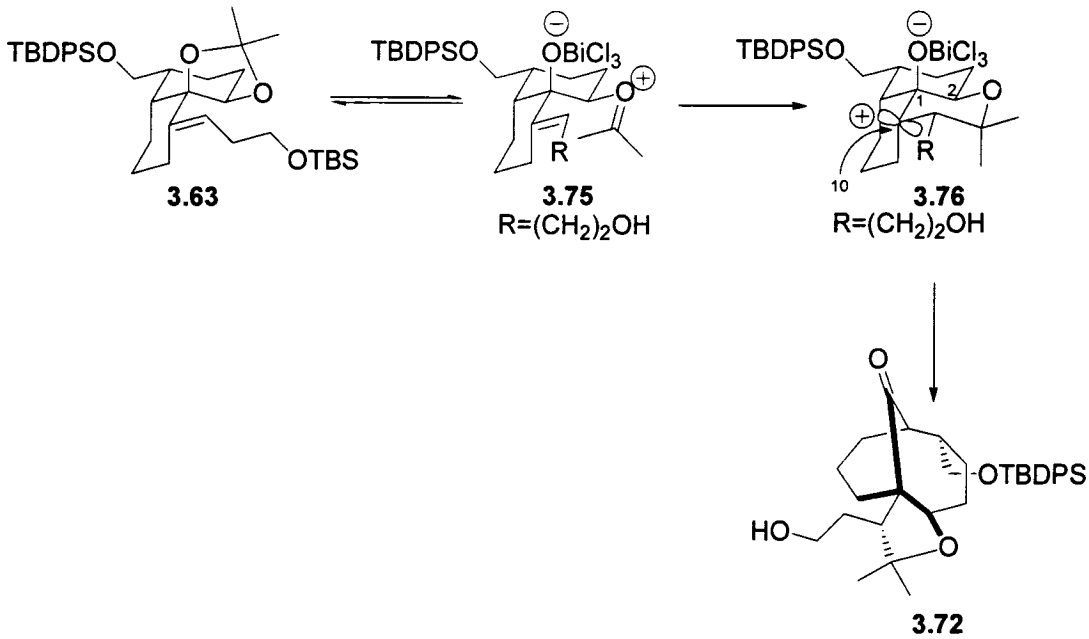
3.72 **3.73** **3.74**

Figure 3.9 – ORTEP plot of ***3.74***



With the structure of **3.72** confirmed, it was possible to rationalize the mechanism of the transformation (figure 3.10). Subjection of ketal **3.63** to a Lewis acid such as $BiCl_3$ gives the corresponding oxacarbenium **3.75** which is poised to undergo a Prins cyclization to furnish intermediate **3.76**. The empty p orbital in **3.76** (at C10) is aligned periplanar to the C1-C2 bond thus allowing this bond to migrate to form bicyclic ketone **3.72** bearing a quaternary center at C10. It is to be noted that the TBS ether was also removed under the Lewis acidic conditions.

Figure 3.10 – Mechanism of the Prins/pinacol



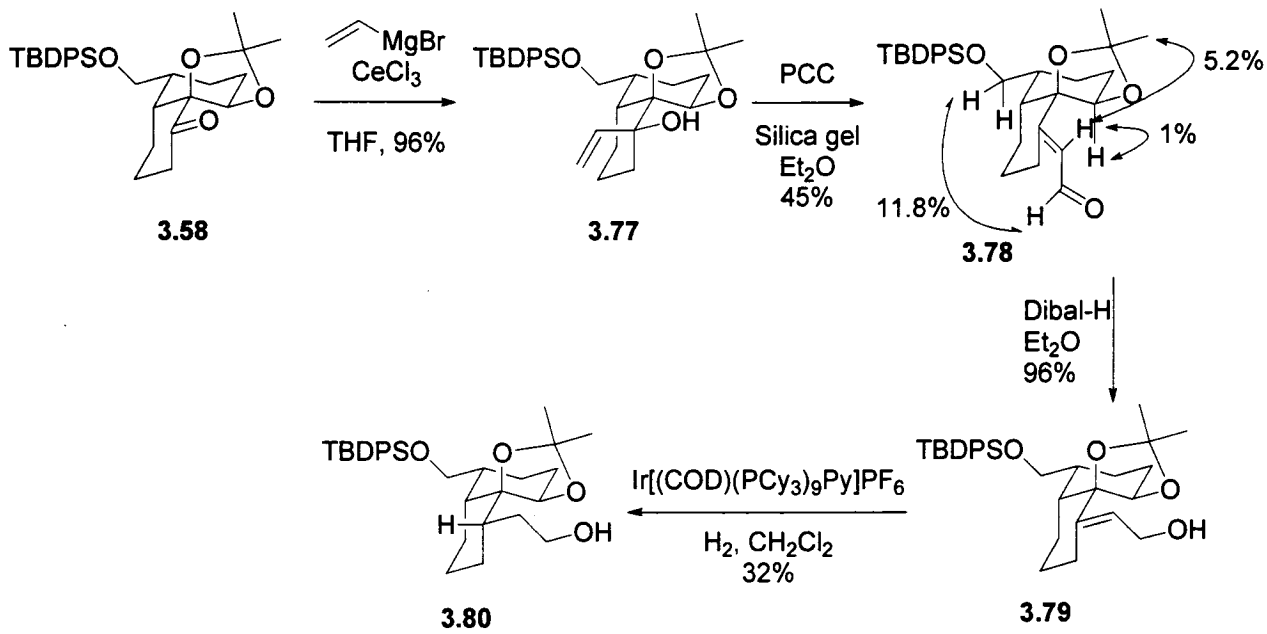
The Prins/pinacol rearrangement has the ability to generate bicyclic ketone systems as well as greatly increasing the molecular complexity. To the best of our knowledge, no examples for the synthesis of bicyclo[*m.n.*1]alkanones using the tandem Prins/pinacol reaction have been reported in the literature.[63] Further studies to explore and extend the scope of this method have been performed by colleagues[64] and are still underway.

A different substrate

Reexamining the reduction of the C10 alkene led us to consider Crabtree's catalyst. This catalyst has the property of binding to alcohols and delivering hydrogens to nearby alkenes. This complexation process has the advantage of bringing the reactive species close by and therefore favouring the hydrogenation. The use of Crabtree's catalyst, however, would require us to redesign the alkene and incorporate an allylic hydroxyl moiety. Allylic alcohol **3.79** was thus targeted and synthesized in three steps from ketone **3.58**. The addition of vinylmagnesium bromide to ketone **3.58** was realized in the presence of anhydrous cerium

chloride in THF at –78 °C to produce alcohol **3.77** in 96% yield. The resulting tertiary alcohol **3.77** was subjected to pyridinium chlorochromate and the 1,3-rearrangement[65] product **3.78** was obtained in a moderate yield of 45%. The *trans* alkene was isolated as the sole isomer as proved by NOE experiments: the aldehyde proton did not correlate with the hydrogen at C2 while the vinylic hydrogen did with an NOE of 1%.

Scheme 3.16 – 1,3-Rearrangement



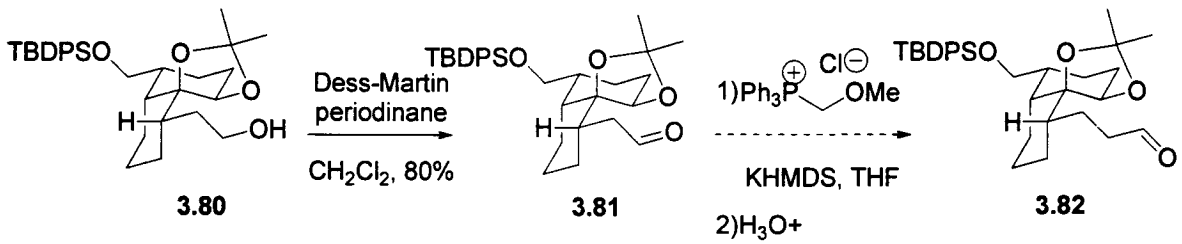
3.58 **3.77** **3.78** **3.79** **3.80**

Finally, the 1,2-reduction with Dibal-H gave allylic alcohol **3.79**, the desired substrate for the Crabtree reduction. The hydrogenation was only moderately successful, however. The reduced alkene **3.80** was isolated in only 32% yield. Moreover, the yield was inconsistent and various side products were frequently observed.

With the small amount of **3.80** produced, attention was turned to elongating the side chain by one carbon to form the eight-membered-ring. To install the extra carbon, alcohol **3.80** was oxidized to **3.81** with Dess-Martin periodinane in 90% yield. The Wittig reaction[66] was supposed to give aldehyde **3.82** after an acidic treatment but only starting material was

isolated. Taken together with the unreliable reduction using Crabtree's catalyst, this route was abandoned.

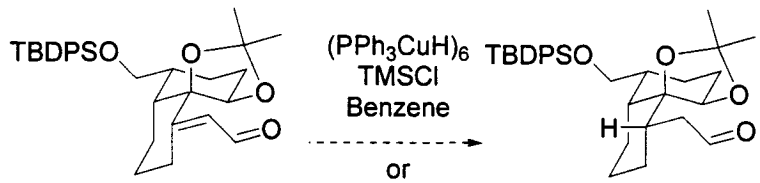
Scheme 3.17 – Elongation of the alkyl chain



3.80 **3.81** **3.82**

An alternative approach could be to reduce enone **3.78** using Strycker's reagent.[67] The 1,4-reduction of the enone would lead to **3.81** directly with no need for a subsequent oxidation. Unfortunately, the reaction led only to the recovery of starting material. The Birch reduction using sodium in ammonium led to exclusive decomposition of the enone **3.78.**

Scheme 3.18 – 1,4-Reduction of the enone 3.78



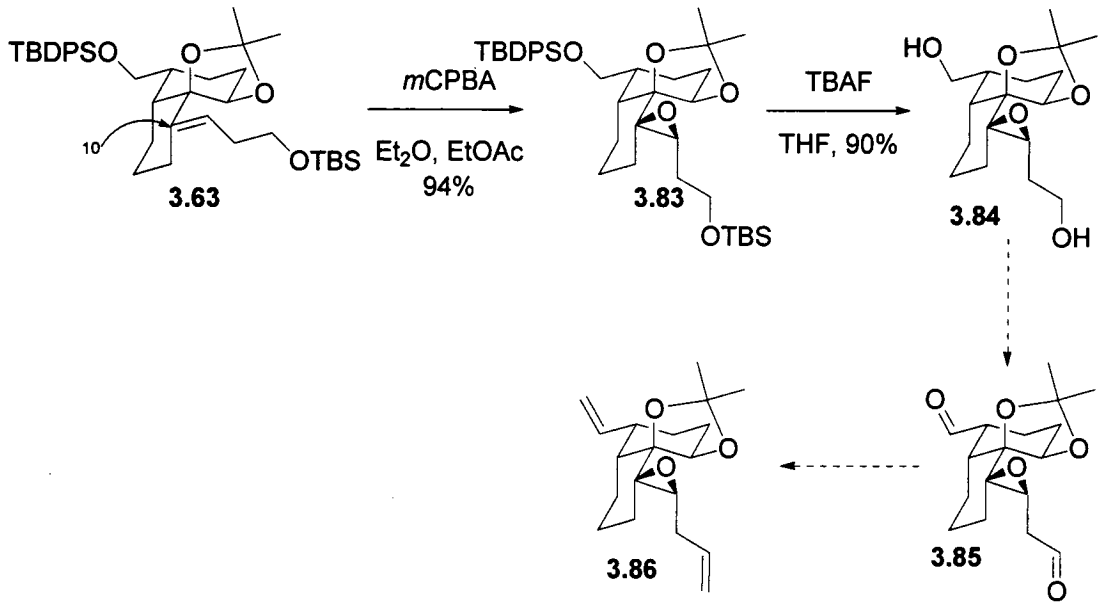
3.78 **3.81**

Epoxidation and cyclopropanation as the solution

As an alternative to the hydrogenation step, an epoxide was introduced to create the desired sp^3 carbon at C10. The alkene **3.63** was epoxidized using *m*CPBA to give compound **3.83** in 94% yield. The silicon-protecting groups were removed using TBAF in THF (90%). Different conditions to oxidize diol **3.84** were employed but the none of the common methods allowed the isolation of dialdehyde **3.85**, perhaps due to its possible instability.

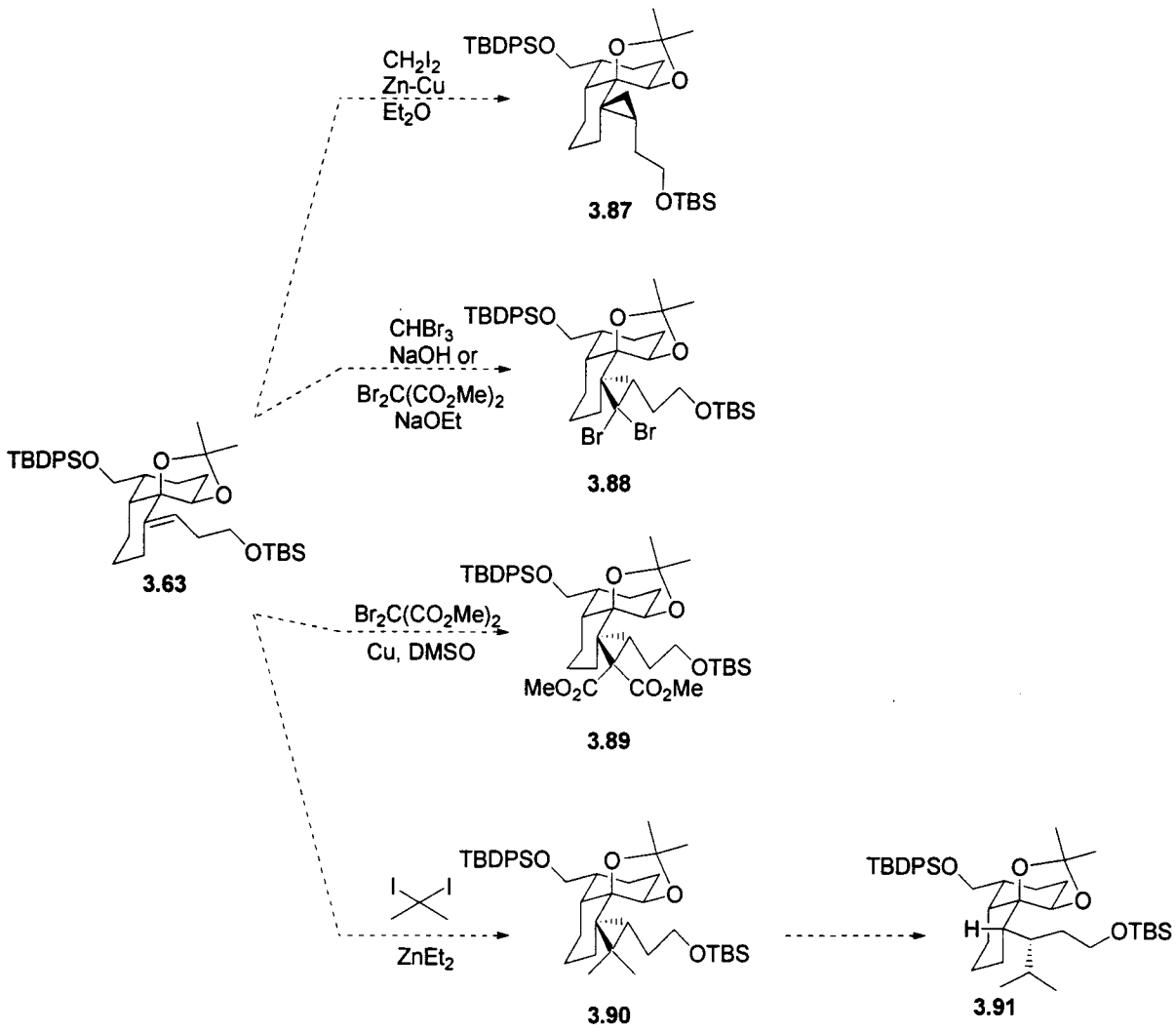
With dialdehyde **3.85**, it would have been be possible to alkylate to the dialkene **3.86** and try the ring closing metathesis.

Scheme 3.19 – Epoxidation approach



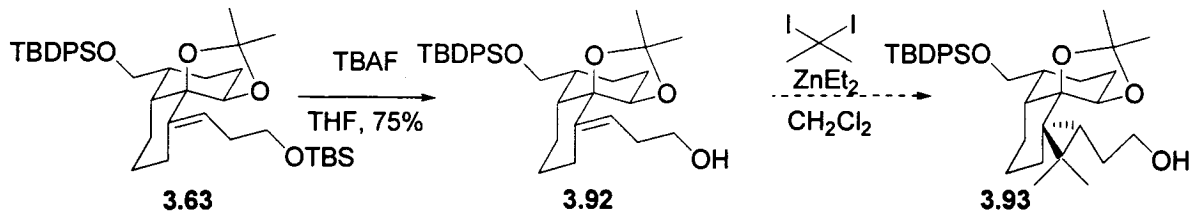
In parallel to the epoxide strategy, an alternative means of introducing an sp^3 carbon via a cyclopropane was envisioned. Treatment of **3.63** with diiodomethane and zinc-copper couple[68] gave none of the desired compound **3.87**. Similarly, both bromoform[69] and 2,2-dibromo-malonic acid dimethyl ester[70] led only to the recovery of starting material. The same 2,2-dibromo-malonic acid dimethyl ester was also used in combination with copper to try and form the diestercyclopropane,[71] **3.89**, however a complex mixture of unknown compounds was obtained instead. 2-Diazo-malonic acid dimethyl ester with $Rh_2(OAc)_4$[72] was used to try and obtain **3.89**, but a mixture of starting material and decomposition was isolated instead of the desired cyclopropane. Finally, formation of cyclopropane **3.90** was attempted with 2,2-diiodopropane and diethylzinc.[73] Once again, starting material alone was isolated. The latter example would have been particularly interesting since **3.90** bears the corresponding carbons for the isopropyl moiety of vinigrol. The opening of the cyclopropane would have given the desired isopropyl group **3.91** (scheme 3.20).

Scheme 3.20 – Cyclopropanation approach



As a last chance to get the cyclopropanation to work, the TBS protecting group was selectively removed by adding one equivalent of TBAF to give **3.92** in 75% yield. The goal of the deprotection was to help the reaction by complexing the free alcohol to the zinc thus aiding the formation of cyclopropane **3.93**. Unfortunately, this last attempt did not proceed as expected and gave only decomposition.

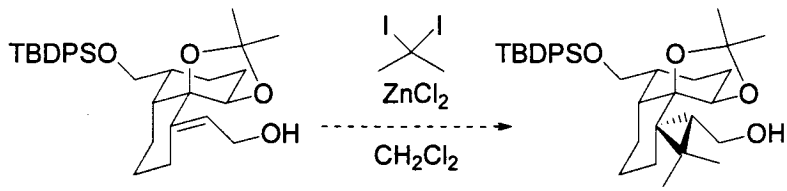
Scheme 3.21 – Cyclopropanation approach part 2



3.63 **3.92** **3.93**

The need for an sp^3 carbon at the C10 position led us to try the cyclopropanation on alkene **3.94**. In opposition to the cyclopropanation of **3.92** to **3.93**, the conversion of **3.94** to **3.95** would used an allylic alcohol to direct the reaction. The original procedure[73] was made for allylic alcohols therefore the reaction was more likely to be successful on this new substrate. Reacting with **3.94** with diiodomethane and zinc chloride, however, gave none of the desired compound **3.95**. Rather, decomposition of the starting material was observed. Therefore, the reduction of the double bond seemed to be the only way to form the sp^3 carbon at the C10 position.

*Scheme 3.22 – Cyclopropanation of **3.94***



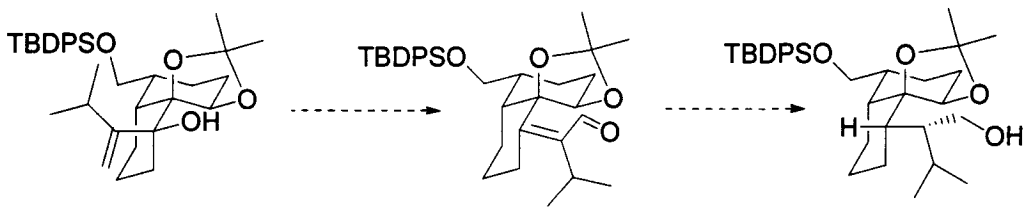
3.94 **3.95**

Attempt to introduce the isopropyl group

While the above chemistry was under investigation, some exploratory experiments were performed to functionalize the side chain and introduce the isopropyl moiety. The idea was to use the earlier PCC-induced 1,3-rearrangement of tertiary alcohol **3.77** to **3.78**. The use of a different Grignard reagent would allow the introduction of the desired isopropyl group on

tertiary alcohol **3.96**. The rearrangement would form enone **3.97** and subsequent reduction would set the proper stereochemistry of the isopropyl group.

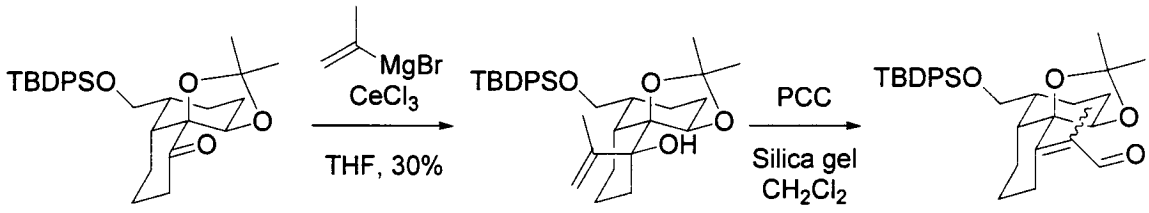
Scheme 3.23 – Proposed model to install the isopropyl moiety



3.96 **3.97** **3.98**

Initial experiments started with a simplified model of **3.96**, using a smaller Grignard reagent. Isopropenylmagnesium bromide was added to ketone **3.58** in the presence of anhydrous cerium chloride in THF at –78 °C to produce alcohol **3.99** in 30% yield. The addition of PCC produced a mixture of two different aldehydes **3.100**. Since the model study showed a mixture and the alkylation suffered from a low yield, no effort was made to move beyond the model substrate. Furthermore, by this time, the above results for the 1,4-reduction of enone **3.78** had been obtained making this approach futile.

Scheme 3.24 – Model study for 3,3-rearrangement



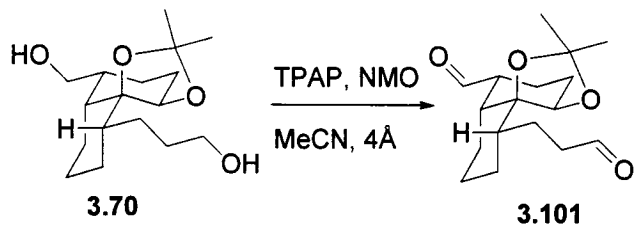
3.58 **3.99** **3.100**

Toward the eight-membered ring via ring-closing metathesis

Since all of the alternatives for the reduction of **3.63** to **3.64** failed, the eight-membered ring would have to be formed from the reduced alkene **3.64**. The planned strategy was to use ruthenium ring closing metathesis (RCM) to form the medium-size ring.

Diol **3.70** was subjected to TPAP oxidation,[74] thereby leading to the corresponding aldehyde **3.101**.

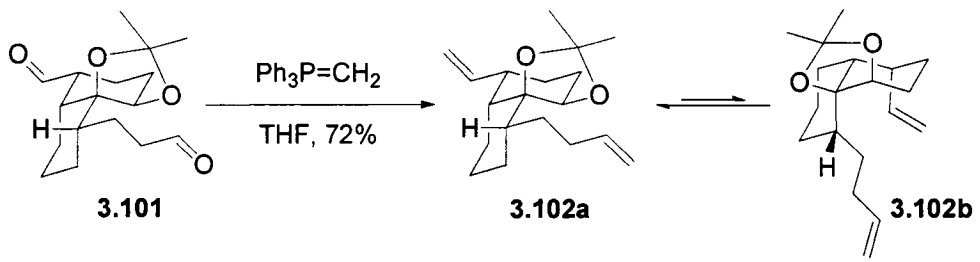
Scheme 3.25 – Functionalization of the side chains



3.70 **3.101**

Compound **3.101** was immediately treated with a slight excess of $Ph_3P{=}CH_2$ to provide diene **3.102** in 72% yield. We were now in position to explore the RCM approach aimed at forming the octalin belt.

Scheme 3.26 – An equilibrium



3.101 **3.102a** **3.102b**

A cursory inspection of the RCM revealed that **3.102a** should be the favored ground state conformation. Semiempirical calculations[75] (AM1) of model conformers **3.103** and **3.104** revealed that the heat of formation of **3.103** is 3.8 kcal/mol higher in energy than that of conformer **3.104** (Figure 3.11). The difference in energy between these two conformers suggests the interconversion between the two *cis*-decalin conformations should be feasible. Therefore, it is realistic to expect the presence of the productive conformer **3.102b** in the reaction media.

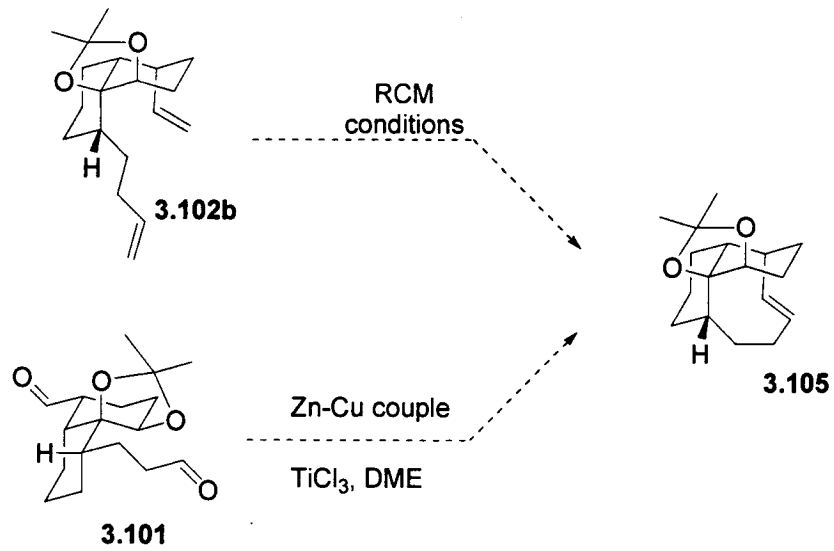
Figure 3.11 – Semiempirical calculations (AM1)

3.103 $\delta\Delta H_f$ (3.8 Kcal/mol)

3.104 ΔH_f (0 Kcal/mol)

Unfortunately, all attempts to cyclize **3.102** via metathesis[76] using either Grubbs' first- or second-generation catalyst were unproductive. We also tried to obtain the tricycle **3.105** by a $TiCl_3$-mediated coupling reaction of the two aldehydes in **3.101**. Exposure of dialdehyde **3.101** to the reaction conditions prescribed by McMurry,[77] however, gave only degradation products.

Scheme 3.27 – Attempt to cyclize the octalin ring



In accordance with our results, Paquette and co-workers recently reported unsuccessful approaches to generate the cyclooctane ring by assembling two side chains attached on a *cis*-decalin framework using various ring-closing methods.[14,15,16,17]

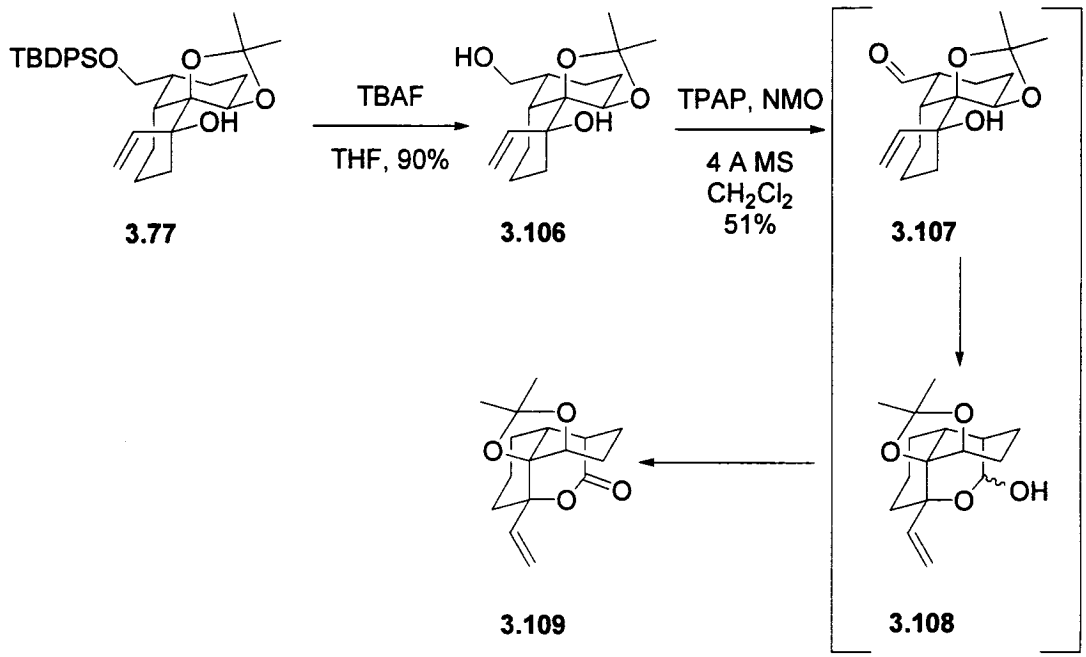
Helping the metathesis

The equilibrium between the conformers **3.102a** and **3.102b** seemed to be limiting the metathesis step. If the energy of the interconversion barrier between the two conformers is too high, none of the metathesis product **3.105** could be expected. To help the metathesis step, the equilibrium should be pushed toward a conformer that would favor the RCM. To this end, the conversion to the appropriate *cis*-decalin should be performed prior to the metathesis step.

Starting from compound **3.77**, cleavage of the silyl ether group employing TBAF followed by a ruthenium-mediated oxidation of the resulting diol **3.106** led to the formation *in situ* of

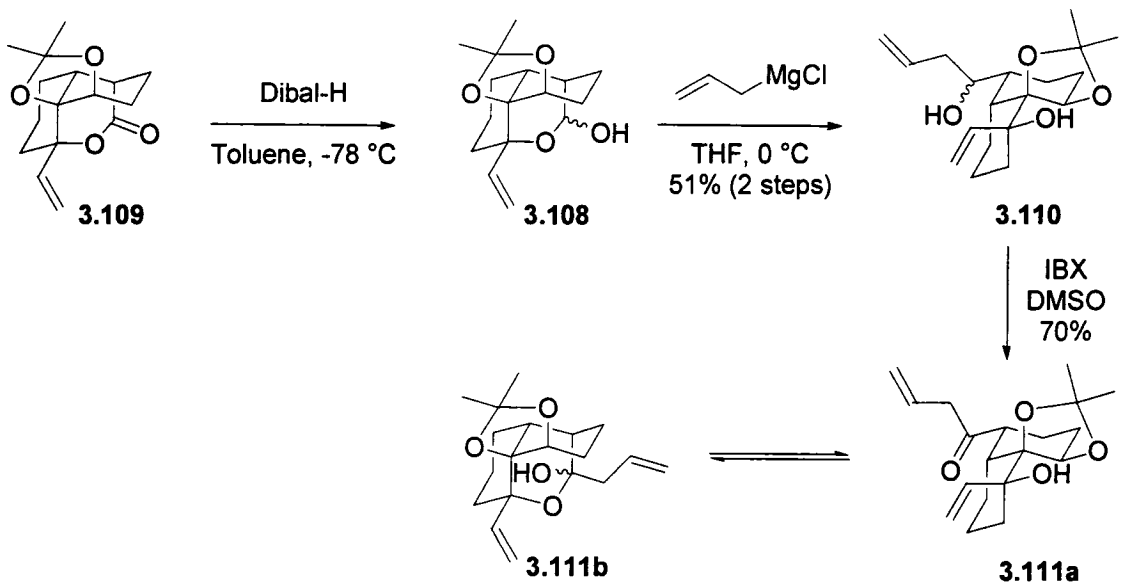
aldehyde **3.107** which exists in equilibrium with lactol **3.108**. The latter mixture was further oxidized to give lactone **3.109** in 51% yield.

*Scheme 3.28 – Synthesis of the lactone **3.109***



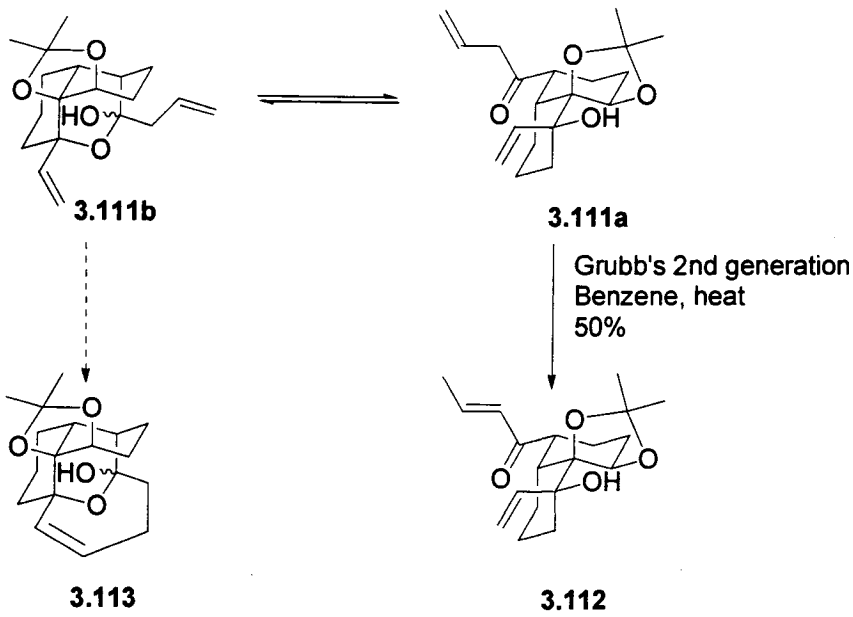
Lactone **3.109** was the appropriate *cis*-decalin conformer for the RCM reaction. Alkylation on the lactone would have led to the appropriate metathesis precursor. However, the alkylation on the lactone directly did not lead to the product **3.112b**, but to a mixture of compounds. Lactone **3.109** was thus selectively reduced to lactol **3.108** with Dibal-H at –78 °C. Compound **3.108** existed as the lactol and not the open form since no aldehyde peak was observed by ^{1}H NMR. The use of allylmagnesium chloride at 0 °C lead to diol in 51% yield (over 2 steps). The oxidation of the diol **3.110** was performed using iodoxybenzoic acid (IBX) in dimethyl sulfoxide to afford ketone **3.111a** in 70% yield. The ketone can exist as two different ketal diastereomers: **3.111a** and **3.111b**. In theory, there is an equilibrium between them, however, since no carbonyl peak was observed in the ^{13}C NMR, conformer **3.111b** seems to be favored.

*Scheme 3.29 – Preparation of diene **3.111***



Despite the NMR results, the RCM was tried using Grubbs' first- and second-generation catalysts, but none of the desired compound **3.113** was observed. Only isomerization of the terminal alkene to give **3.112** in 50% yield was observed. This last result convinced us that a different approach using an alternative to the RCM needed to be investigated.

Scheme 3.30 – Attempt to close the octalin ring

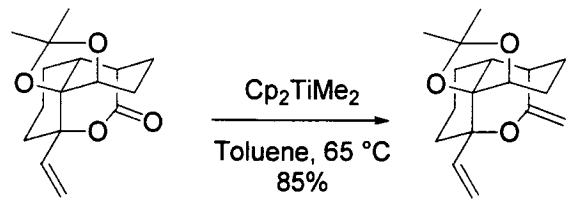


Toward the eight-membered ring through a Claisen rearrangement

Since our efforts to close the cyclooctane belt of vinigrol via RCM failed to provide any of the eight-membered ring, our attention was turned to the use of a Claisen rearrangement to complete the core of vinigrol.

The installation of the enol ether moiety, required for the subsequent Claisen rearrangement, was accomplished by treatment of lactone **3.109** with Petasis' reagent[78] in toluene at 65 °C. The desired enol ether **3.114** was obtained in 85% yield.

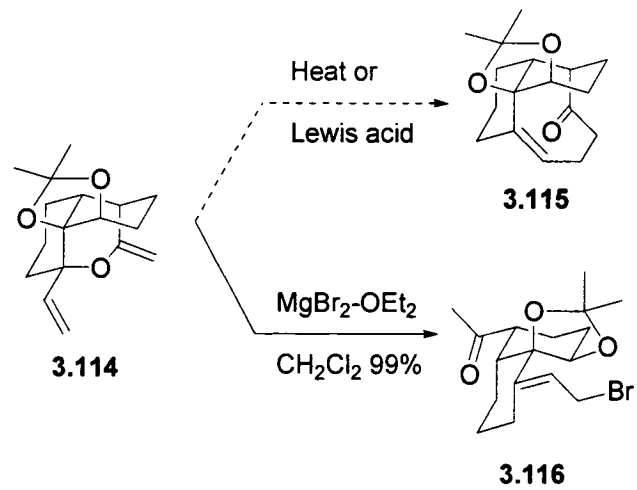
Scheme 3.31 – Formation of the enol ether ***3.114***



3.109 **3.114**

At this stage, all the requisite carbons embedded in the vinigrol skeleton were installed. The next objective was the creation of the eight-membered ring. Initial attempts to rearrange vinyl enol ether **3.114** to ketone **3.115** under thermal conditions were fruitless. Conventional heating of a solution of **3.114** in toluene at temperatures ranging from 160 to 210 °C in a sealed tube or using microwave irradiation led to recovery of the starting material or the formation of a complex mixture from which no Claisen rearrangement product **3.115** was isolated. We then turned our attention toward the use of hard and soft Lewis acids to catalyze this rearrangement.[79] Despite considerable experimental efforts, all runs using $Pd(0)L_4$, $Pd(II)L_2$,[80] $AgBF_4$, $AlMe_3$, $AlMe_2Cl$, Dibal-H, *i*-Bu_3Al,[81] bis(4-bromo-di-*tert*-butylphenoxyde (MABr),[82] and $Mg(OTf)_2$ in various solvents and conditions resulted in the degradation of **3.114** or its partial recovery. Interestingly, enol ether **3.114** was completely converted into ketone **3.116** in the presence of $MgBr_2$-OEt_2 in dichloromethane.

Scheme 3.32 – Attempt to from the eight-membered ring via a Claisen



Conclusions

The HDDA reaction proved to be a very effective means of synthesizing various decalin cores and more precisely the formation of *cis*-decalins. The method efficiently formed two cycles out of the three needed for the synthesis of vinigrol while providing sufficient functionality for the remainder of the synthesis. The third cyclization, however, to generate the cyclooctane belt, proved more difficult to accomplish. Efforts to close this ring by metathesis and by a Claisen rearrangement both failed. By keeping the medium-size ring formation until such a late stage of the synthetic sequence, the development of the previous decalin proved fruitless. Consequently, our next approach was to form a six- and eight-membered bicyclic compound and then cyclize the second six-membered ring. This way, the more challenging medium sized ring would be formed at the beginning.

4

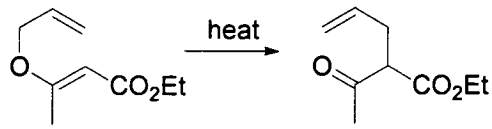
Third Approach:

Sequential Hydroxy-Directed Diels-Alder/Claisen Rearrangement

Introduction

Much of the chemistry used today in modern organic laboratories originates from reactions discovered many years ago. Modern scientists are now flavoring those reactions to make them more powerful and more efficient. In the previous chapter, we discussed the discovery of the Diels-Alder reaction in 1928. The reaction has since been upgraded to the HDDA allowing one to selectively obtain a single product from an intermolecular Diels-Alder. This reaction is not the only "old" reaction to have been revamped to meet today's needs. Fourteen years before the discovery of Diels and Alder, Ludwig Claisen published a [3+3] sigmatropic rearrangement of allyl vinylethers such as **4.1**.[83]

Figure 4.1 – Basic Claisen rearrangement

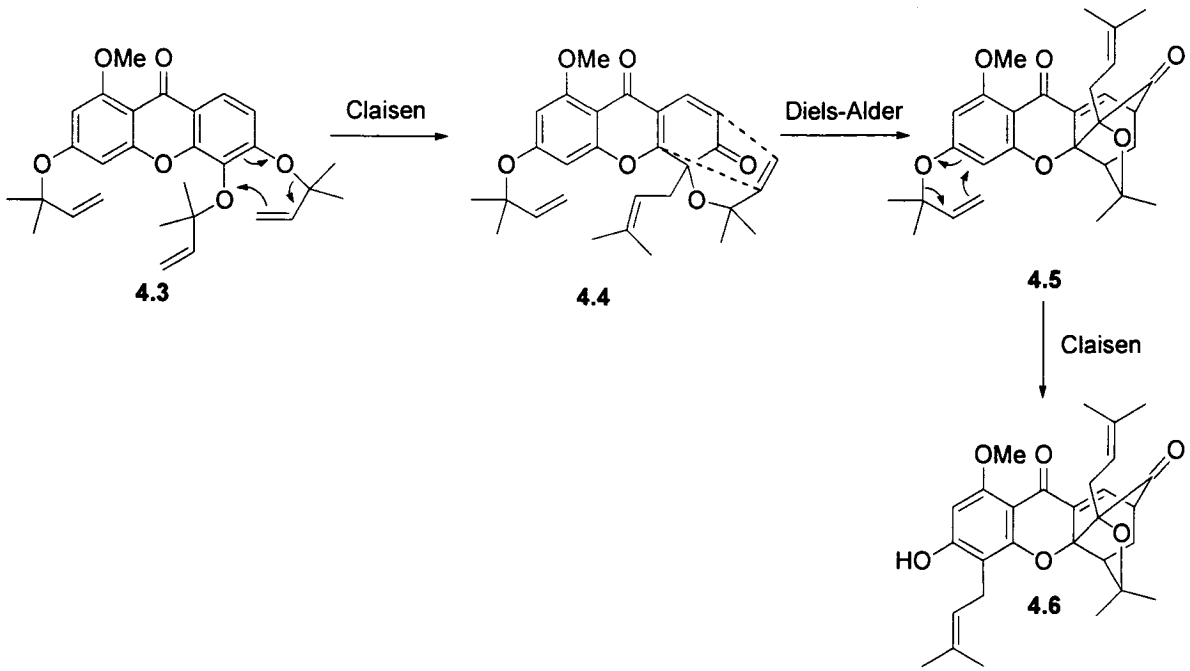


4.1 **4.2**

Since then, the Claisen reaction has had a huge impact on modern organic chemistry.[84] Many different asymmetric variations of the reaction have been developed[85] and the [3+3] sigmatropic rearrangement continues to be a great method to generate tertiary and quaternary carbon centers.

This powerful rearrangement can be combined with other reactions to generate even more complexity. For example, Nicolaou and Li[86,87] have developed a tandem Claisen/Diels-Alder rearrangement which they applied to the synthesis of 1-*O*-methylforbesione **4.6**. Their cascade reaction happened to be a useful strategy to construct fully substituted polycyclic systems such as **4.6**. Notably, according to the biosynthesis hypothesis[88] of similar compounds made by Quillian and Schienmann, this process likely represents a biomimetic synthesis.

Figure 4.2 – Nicolaou's approach to 1-O-methylforbesione

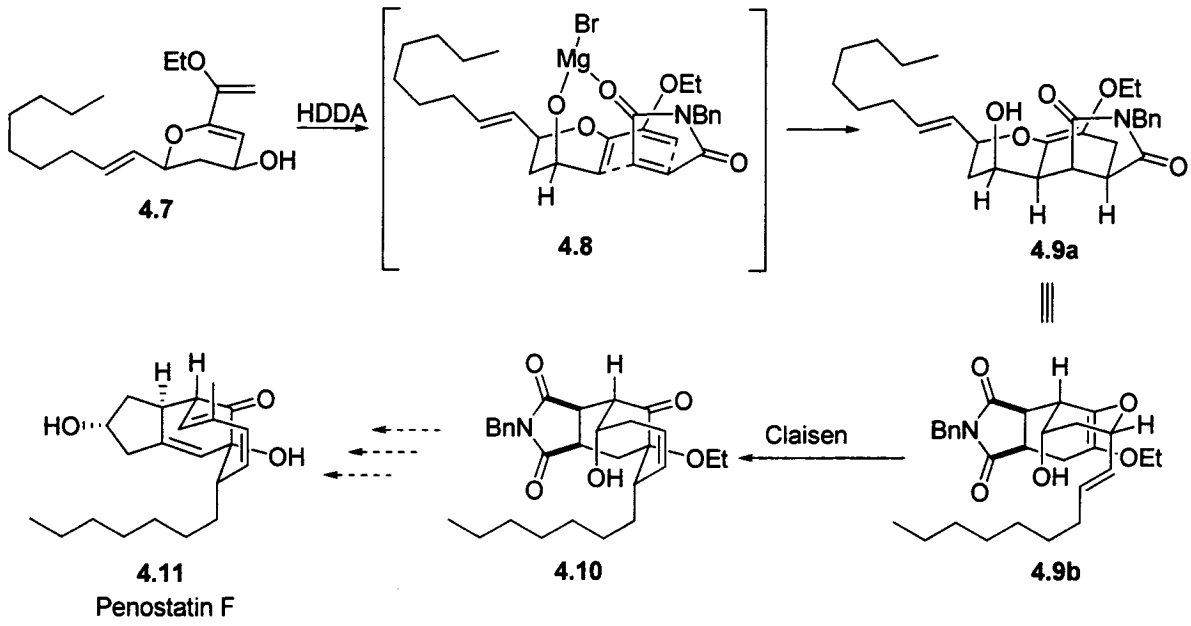


Their strategy started with Claisen precursor triallylether **4.3** which they heated in DMF at 120 °C for 20 minutes. The resulting intermediate **4.4** bears a quaternary center and is poised to do a [4+2] cycloaddition. The second part of the cascade reaction introduces both a quaternary and tertiary center to the molecule. Finally, a second Claisen on the other side of the molecule gives the natural product **4.6**. In summary, from a precursor of low complexity, **4.3**, the tandem Claisen/Diels-Alder produced a compound of high complexity, **4.5**, by performing two reactions at once.

Barriault and co-workers[89] recently published the synthesis of the core of penostatin F using a sequential hydroxy-directed Diels-Alder/Claisen reaction. The HDDA forces the dienophile (*N*-benzylmaleimide) to react with diene **4.7** on the β-face, the same side as the free secondary alcohol. This selectivity is assured by the magnesium tether and results in the exclusive production of *endo* compound **4.9**. This decalin intermediate, with its allyl vinylether moiety, is now set up for a subsequent Claisen rearrangement. The sequential HDDA/Claisen reaction gives bicyclic[5.3.1]undecenone **4.10**. In those two sequential

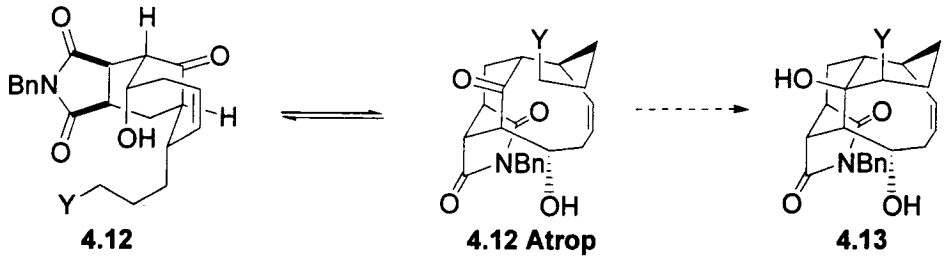
steps, the complexity is greatly increased while creating many stereogenic centers. Studies toward completing the total synthesis of penostatin F **4.11** are currently underway.

Figure 4.3 – Barriault's approach toward penostatin F via a HDDA/Claisen



The bicyclo[5.3.1]undecenone **4.10** formed via a sequential HDDA/Claisen could also be a useful approach to vinigrol. The six- and eight-membered rings in **4.10** would make it a very good intermediate to solve the problems detailed in the previous chapters, namely the late stage formation of the eight-membered ring. The previous approaches were forming the six-membered rings at the beginning but the subsequent formation of the medium sized ring was not successful. Using the sequential HDDA/Claisen, the six- and eight-membered rings would be formed first, leaving the more facile formation of a six-membered ring to be formed after. In order to form this last ring, the long alkyl chain in **4.10** would have to be replaced by a chain with a functional group such as in **4.12**. The functional group Y could be a connector such as a sulfone and could be used to intramolecularly alkylate the ketone. The alkylated product, **4.13**, would be the desired core of vinigrol.

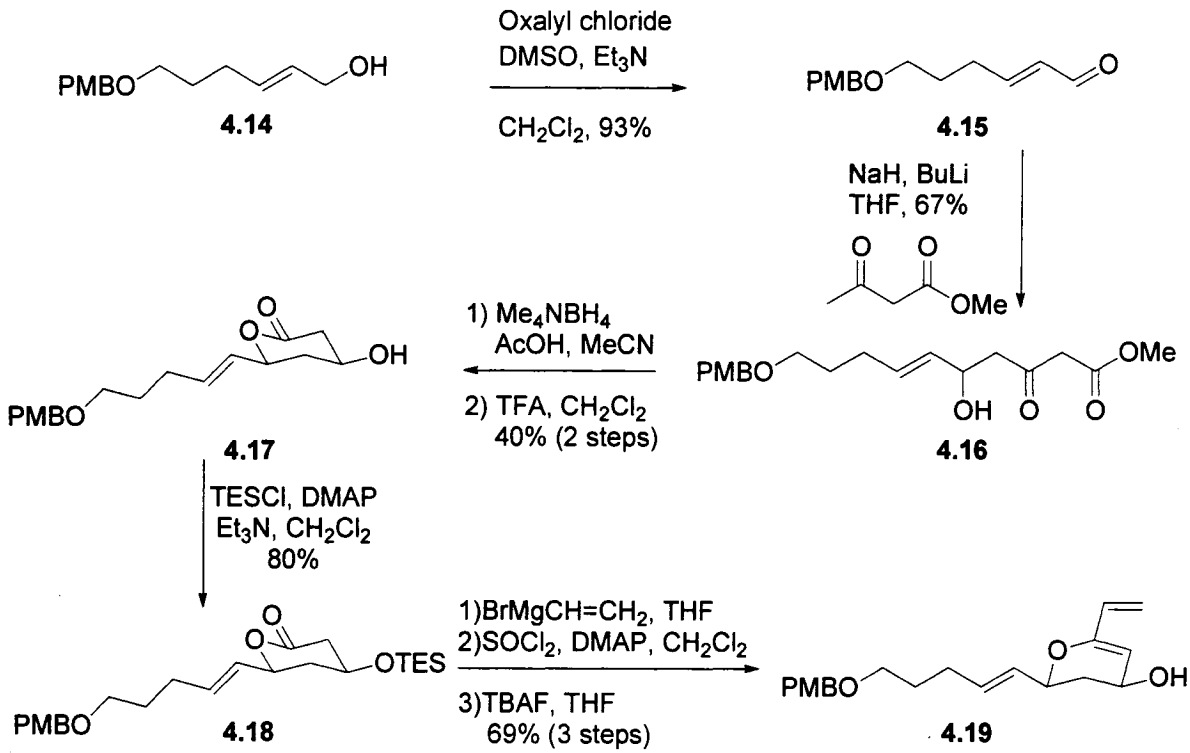
Figure 4.4 – Proposed use of the sequential HDDA/Claisen toward the vinigrol core



Synthesis of the HDDA/Claisen precursor

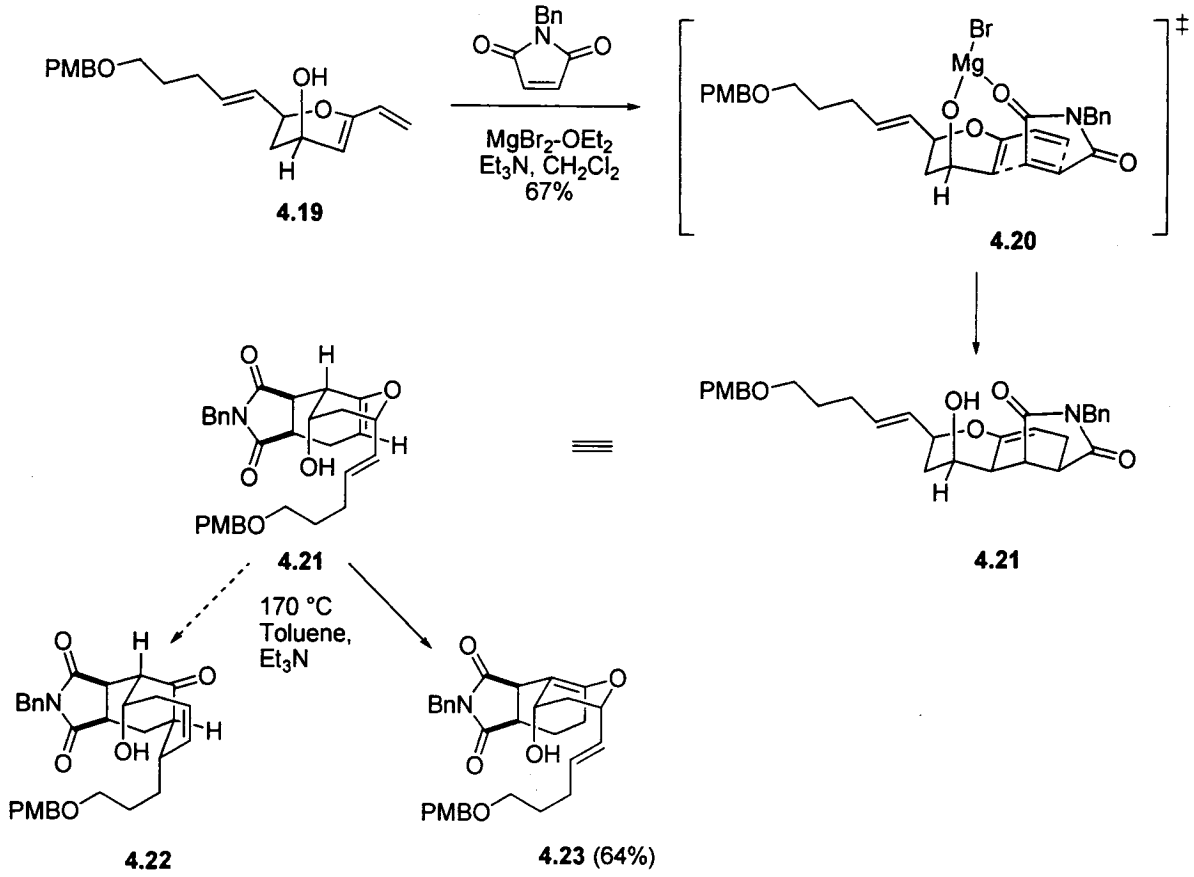
The sequential HDDA/Claisen was an attractive method to synthesize the six- and eight-membered rings of vinigrol. However, in opposition to the penostatin F approach, the alkyl chain had to be replaced by a propanol side chain. The choice of protecting group was crucial and PMB ether appeared to be more appropriate for the sequence. The allylic alcohol[90] **4.14** was oxidized using the Swern[91] protocol to give aldehyde **4.15** in 93% yield. Condensation of the Weiler[92] dianion with aldehyde **4.15** afforded the corresponding β-ketoester **4.16** in 67% yield. The latter was diastereoselectively reduced to the 1,3-anti diol using Me_4NBH_4 in a mixture of acetic acid/acetonitrile at –25 °C.[93] The resulting diol was treated with trifluoroacetic acid in dichloromethane to give lactone **4.17** in 40% yield (84% yield based on recovered starting material) over two steps as a single diastereomer. Protection of the secondary alcohol as a triethylsilyl ether in the presence of TESCl, DMAP, and triethylamine gave **4.18** in a good yield of 80%. The completion of diene **4.19** required addition of vinylmagnesium bromide in THF at –78 °C to produce the corresponding lactol which upon treatment with $SOCl_2$ and DMAP in methylene chloride and subsequent exposure to fluoride ions provided semicyclic diene **4.19** in 69% yield over three steps.

Scheme 4.1 – Synthesis of the diene ***4.16***



Hydroxy-directed Diels-Alder reaction of **4.19** and *N*-benzylmaleimide provided the desired bicyclo[4.4.0]decene **4.21** in 67% yield. The latter was poised to undergo a thermal Claisen [3,3]-shift. Surprisingly, the thermal rearrangement of **4.21** in the presence of triethylamine[94] gave only the 1,3-hydrogen shift byproduct **4.23** in 64% yield. The desired eight-membered ring **4.22** was not observed.

Scheme 4.2 – Sequential hydroxy-directed Diels-Alder/Claisen

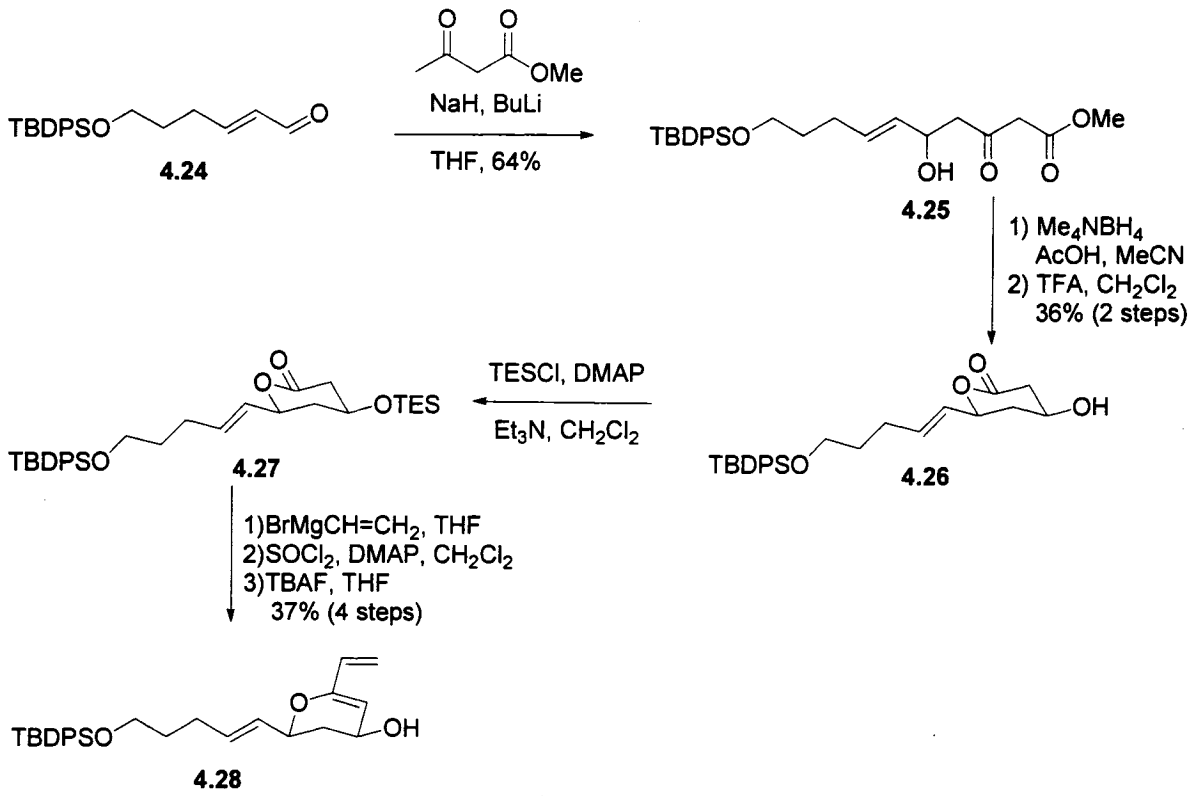


During their exploration toward penostatin F, Ang and Barriault[95] did not observe any isomerization of alkenes. The only difference between their sequential HDDA/Claisen and ours resides in the side chain. In their case, a heptane side chain was present on the molecule whereas in our case a PMB ether propane moiety was installed on the Diels-Alder adduct **4.21**. We were forced to conclude that this protected alcohol might be problematic for the Claisen reaction to occur.

Changing the protecting group

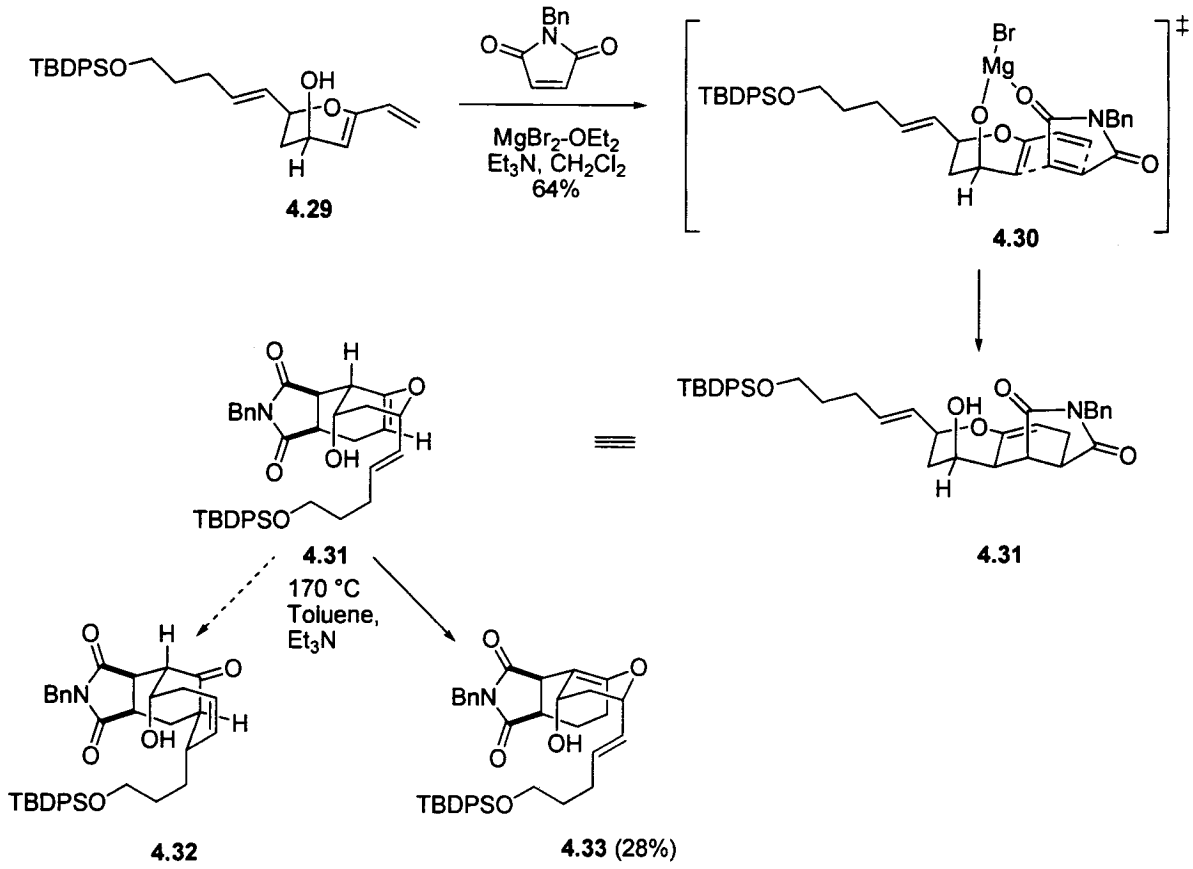
To solve this problem, the protecting group on the alcohol was replaced by a non-polar protecting group such as TBDPS ether. Using the same synthetic sequence as for aldehyde **4.15**, compound **4.24** was alkylated using the Weiler dianion to give β-ketoester **4.25** in 64% yield. The 1,3-anti diol was obtained by treating the β-ketoester **4.25** with tetramethylammonium borohydride at –25 °C in a mixture of acetic acid and acetonitrile. The lactone **4.26** was then formed by treating the crude diol with trifluoroacetic acid in dichloromethane. The two step process was performed with an overall yield of 36%, or 70% yield based on the recovered starting material. Secondary alcohol **4.26** was then protected using TESCl, DMAP and triethylamine in dichloromethane to give lactone **4.27**. Vinylmagnesium bromide was added at –78 °C and the lactol dehydrated with thionyl chloride and DMAP. Finally, diene **4.28** was obtained with fluoride treatment to remove the silicon-protecting group with an overall yield of 37% for the last four steps.

Scheme 4.3 – Changing the protecting group



The hydroxy-directed Diels-Alder reaction between diene **4.29** and *N*-benzylmaleimide afforded cycloadduct **4.31** in 64% yield. Compound **4.31** was then dissolved in toluene and heated in a sealed tube, however the [3,3] rearrangement product **4.32** was not observed. Instead, tetrasubstituted alkene **4.33** was isolated in 28% yield.

Scheme 4.4 – Sequential hydroxy-directed Diels-Alder/Claisen with the TBDPS ether



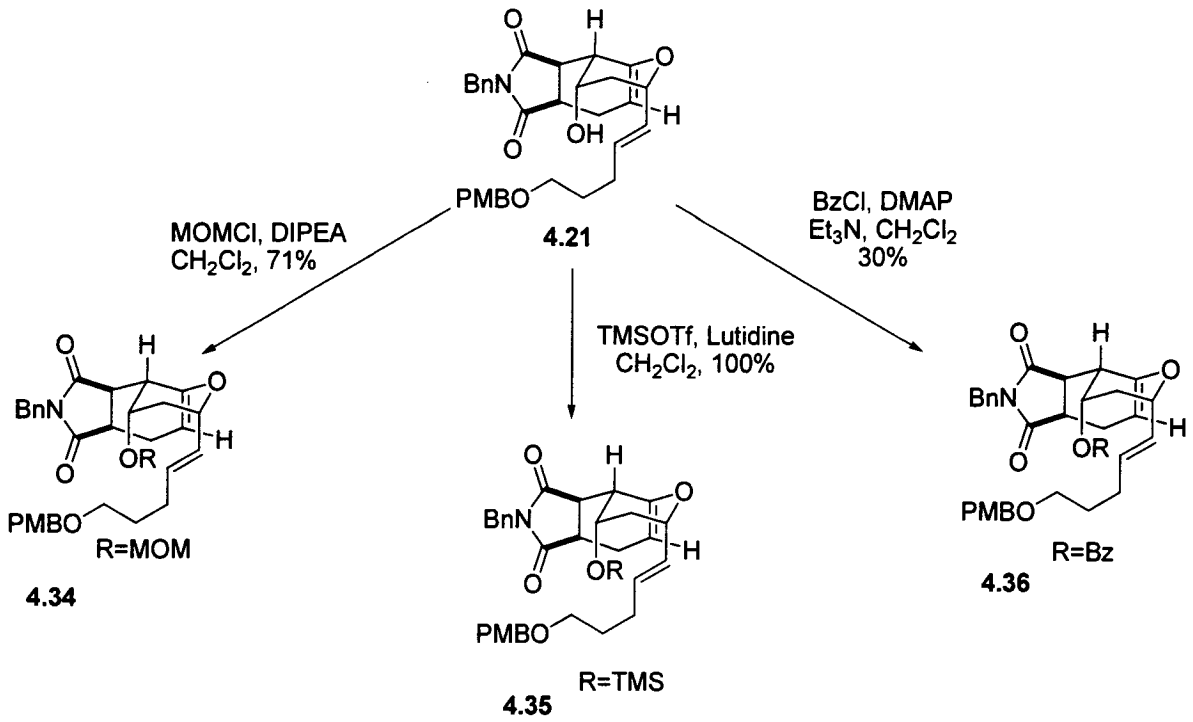
The proposed change in protecting group did not give the expected results. Obviously, the introduction of the TBDPS did not help to favour the Claisen rearrangement. Thinking that perhaps protection of the secondary alcohol on dienes **4.21** and **4.31** would solve the problem, a variety of protecting groups were explored.

Variation on the secondary alcohol

Three different types of protecting groups were installed on secondary alcohol **4.21**. First, a methoxymethylether (MOM) was put on using commercial MOMCl and diisopropylamine in dichloromethane (71% yield). A silicon-based protecting group was also installed by

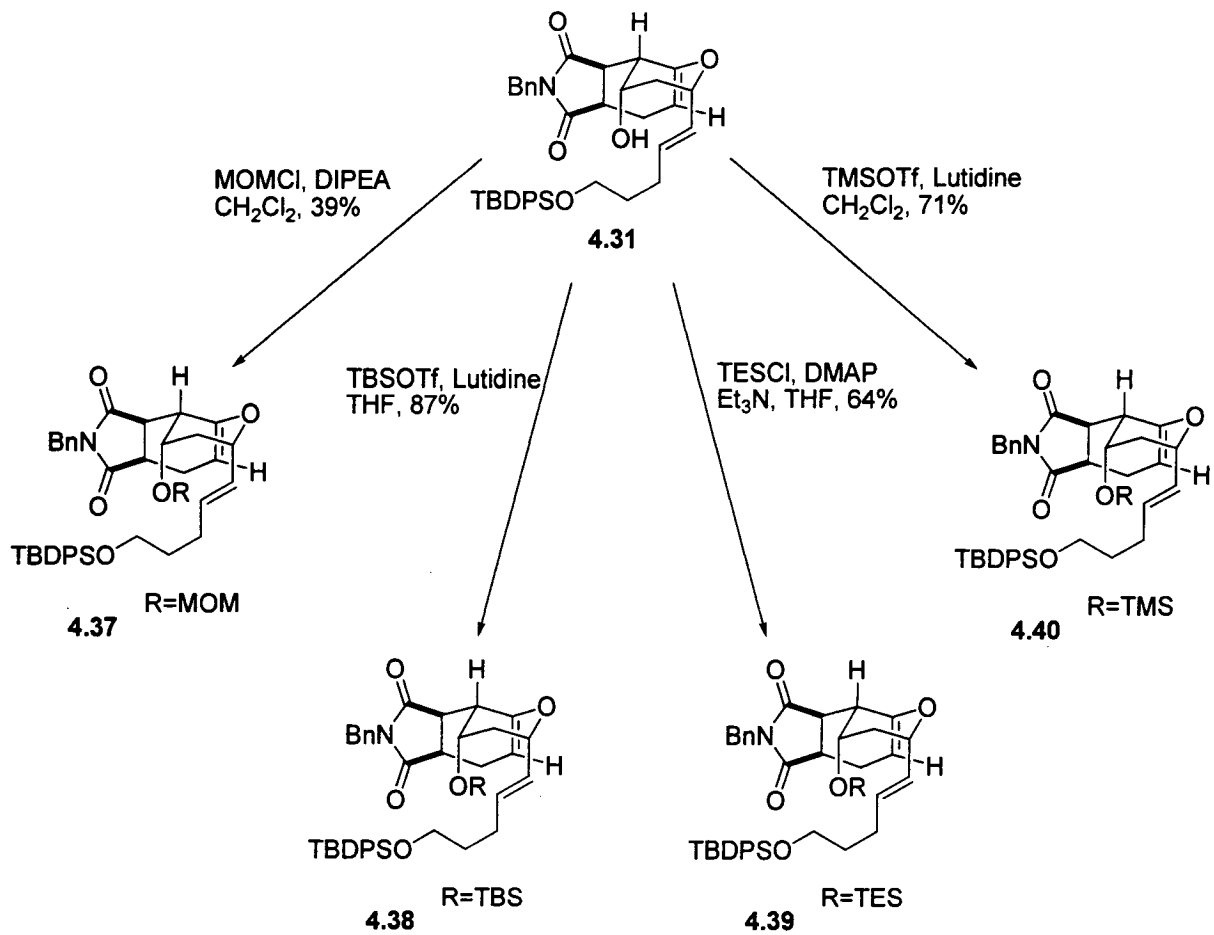
treating **4.21** with TMSOTf to afford **4.35** in quantitative yield. Finally, the secondary alcohol was benzoylated with a catalytic amount of DMAP, triethylamine in dichloromethane. Benzoate **4.36** was isolated in a modest yield of 30%.

*Scheme 4.5 – Protection of secondary alcohol **4.21***



The same strategy was employed for the secondary alcohol in **4.31**. Four different protecting groups were installed on **4.31**. The MOM group was installed using similar conditions as for alcohol **4.21**, but a lower yield of 39% was observed. Three different silicon-based protecting groups were also used to modify secondary alcohol **4.31**. First, alcohol **4.31** was treated with TBSOTf[96] to afford compound **4.37** in 87% yield. The TES ether was introduced using TESCl in tetrahydrofuran to give product **4.39** in 64% yield. Finally, the smallest silicon protecting group, TMS, was installed using TMSOTf to give compound **4.40** in 71% yield.

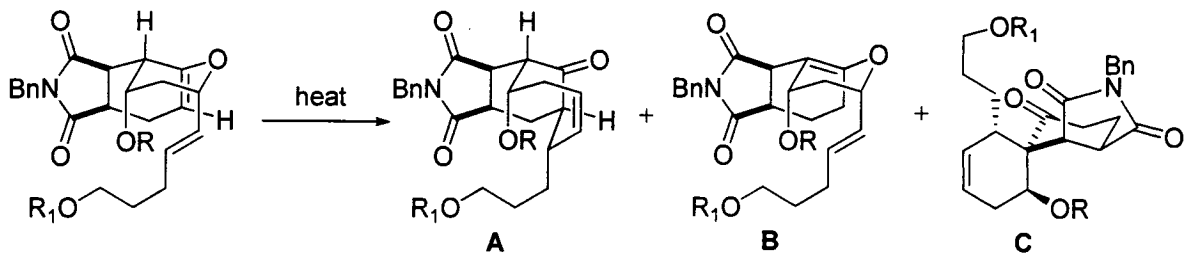
Scheme 4.6 – Protection of secondary alcohol ***4.31***



The next step consisted of heating the protected secondary alcohols **4.34-4.40** at 170 °C in toluene (sealed tube) in the presence of triethylamine.[97] The results are summarized in table 4.1.[98] Heating of 1,5-dienes **4.34-4.36** led to the double bond isomerized products **4.34B** and **4.35B** (entries 1 and 2) or a complex mixture from which no desired Claisen product **4.36A** was isolated (entry 3). Cycloadduct **4.37** was also submitted to the standard Claisen conditions, but only decomposition was observed (entry 4). We were gratified to find that diene **4.38** rearranged under the above reaction conditions to produce the expected Claisen product **4.38A** in 55% yield (entry 5). Different reaction conditions were tried including exposure of precursor **4.38** to microwave radiation (170 °C, 600 W) for 30 minutes in

acetonitrile. These conditions also furnished **4.38A**, albeit in a lower yield of 30% (entry 6). The installation of a TES protecting group on the secondary alcohol did not have a significant effect on the chemical yield for the transformation of **4.39** to the desired Claisen product **4.39A** (entries 7 and 8). When cycloadduct **4.39** was heated at 170 °C in a wax bath, a yield of 40% was obtained. However, when the same compound was heated in a microwave device, a lower yield of 33% was isolated. In both cases, a secondary compound was isolated in 15 and 33% yield respectively. This spiro compound is the result of a [3,3]-sigmatropic shift of **4.39B**. The replacement of toluene by a more polar solvent such as THF led to isomerization of alkene **4.39B** in 90% yield. Finally, the use of TMS protected **4.40** did not influence the chemical yield by much when used in toluene under conventional heat. Claisen product **4.40A** was isolated in 42% yield along with spiro compound **4.40C** (30% yield). Fortunately, the exposure of **4.40** to microwave irradiation furnished **4.40A** in 65% yield. In this case, we isolated **4.40B** as a side product in 14% yield. Interestingly, heating of **4.40** in acetonitrile in a sealed tube at 170 °C led to a complex mixture from which no desired Claisen product **4.40A** was isolated (entry 12). It is now clear that the choice of protecting groups R and R_1, the solvent as well as the heat source are crucial for the Claisen reaction to occur, however, their roles in the reaction remain elusive.

*Table 4.1 – Claisen rearrangement of cycloadduct **4.34-4.40***



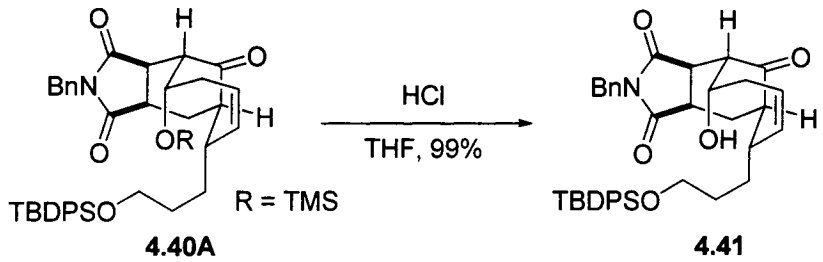
Entry	Starting material	R_1	R	Product (yield%)
1	**4.34**	PMB	MOM	**4.34B** (25)[a]
2	**4.35**	PMB	TMS	**4.35B** (35)[a]
3	**4.36**	PMB	Bz	degradation[a]

4	**4.37**	TBDPS	MOM	degradation[a, b]
5	**4.38**	TBDPS	TBS	**4.38A** (55)[a]
6	**4.38**	TBDPS	TBS	**4.38A** (30)[c]
7	**4.39**	TBDPS	TES	**4.39A** (40)[a] and **4.39C** (15)[a]
8	**4.39**	TBDPS	TES	**4.39A** (33)[c] and **4.39C** (33)[c]
9	**4.39**	TBDPS	TES	**4.39B** (90)[d]
10	**4.40**	TBDPS	TMS	**4.40A** (42)[a] and **4.40C** (30)[a]
11	**4.40**	TBDPS	TMS	**4.40A** (65)[c] and **4.40B** (14)[c]
12	**4.40**	TBDPS	TMS	Complex mixture[e]

[a]Heating in a sealed tube at 170 °C in toluene and 10 equiv of triethylamine. Traces of isomerized alkene B were observed. [c]Irradiation with microwaves at 600 W in acetonitrile at 170 °C for 30 min. [d]Heating in a sealed tube at 170 °C in THF and 10 equiv of triethylamine. [e]Heating in a sealed tube at 170 °C in THF and 10 equiv of triethylamine

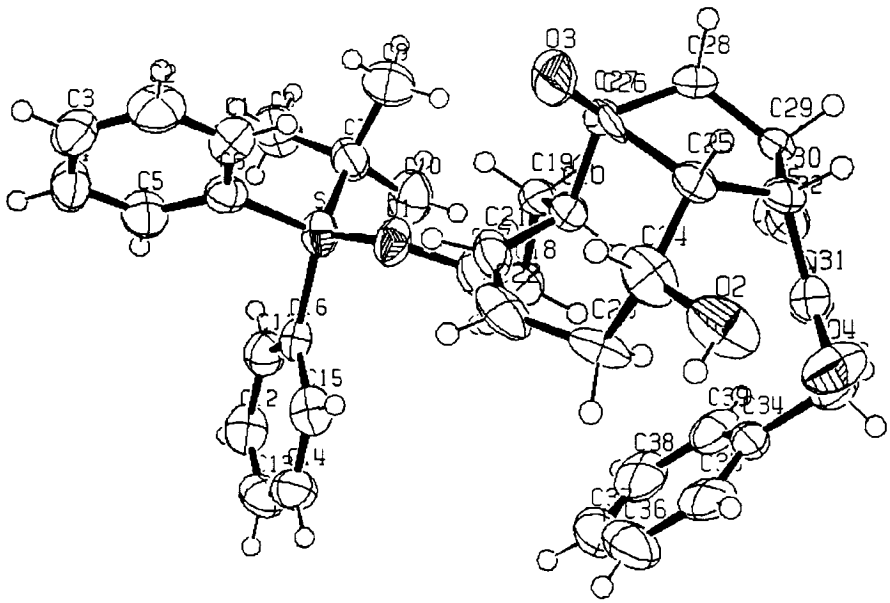
After the above screening for reactivity, the TMS protecting group was removed from **4.40A** with HCl in THF to afford the corresponding monoprotected alcohol **4.41** in 99% yield (scheme 4.7). At this stage, the stereochemistry of the bicyclo[5.3.1]undecenone **4.41** was established without ambiguity by X-ray diffraction (figure 4.5).

*Scheme 4.7 – Removal of the TMS group on **4.40A***



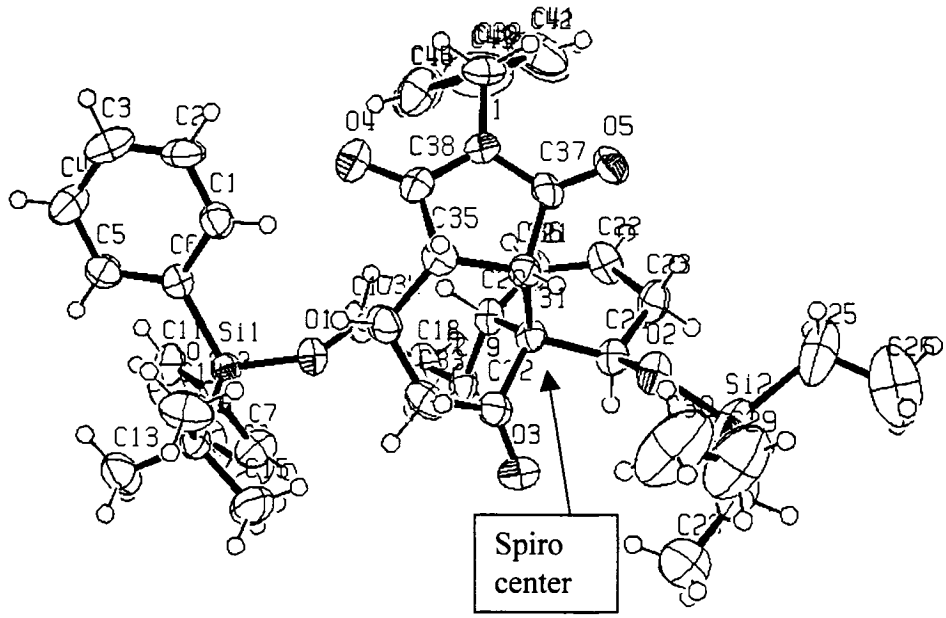
4.40A **4.41**

Figure 4.5 – ORTEP plot of ***4.41***



Likewise, the structure of spiro side product **C** was confirmed using X-ray diffraction. We were able to get a crystal from compound **4.39C** for which the ORTEP plot is shown below (figure 4.6).

Figure 4.6 – ORTEP plot of ***4.39C***

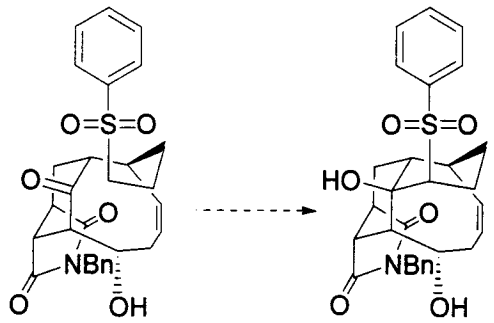


At this point, the sequential HDDA/Claisen had been optimized and we were ready to proceed with the total synthesis of vinigrol. The next step was to functionalize the side chain in order to form the last six-membered ring.

Attempt to form the six-membered ring via a sulfone alkylation

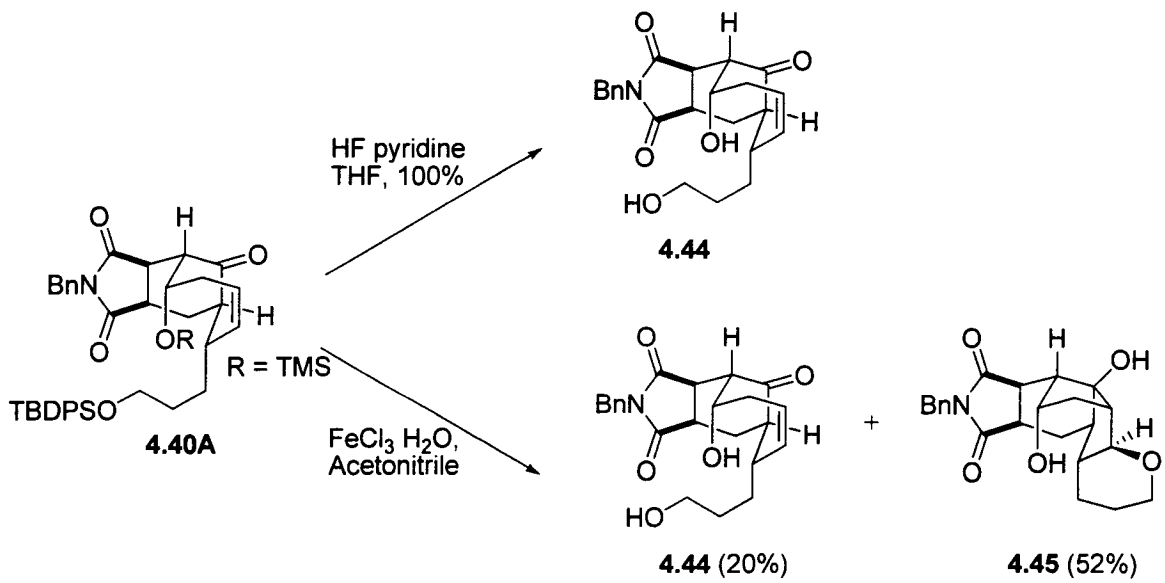
The first idea for forming the last ring was to modify the protected primary alcohol into a sulfone which could then alkylate intramolecular onto the ketone to give tricyclic core **4.43**.

Figure 4.7 – Proposed formation of the six-membered ring via a sulfone



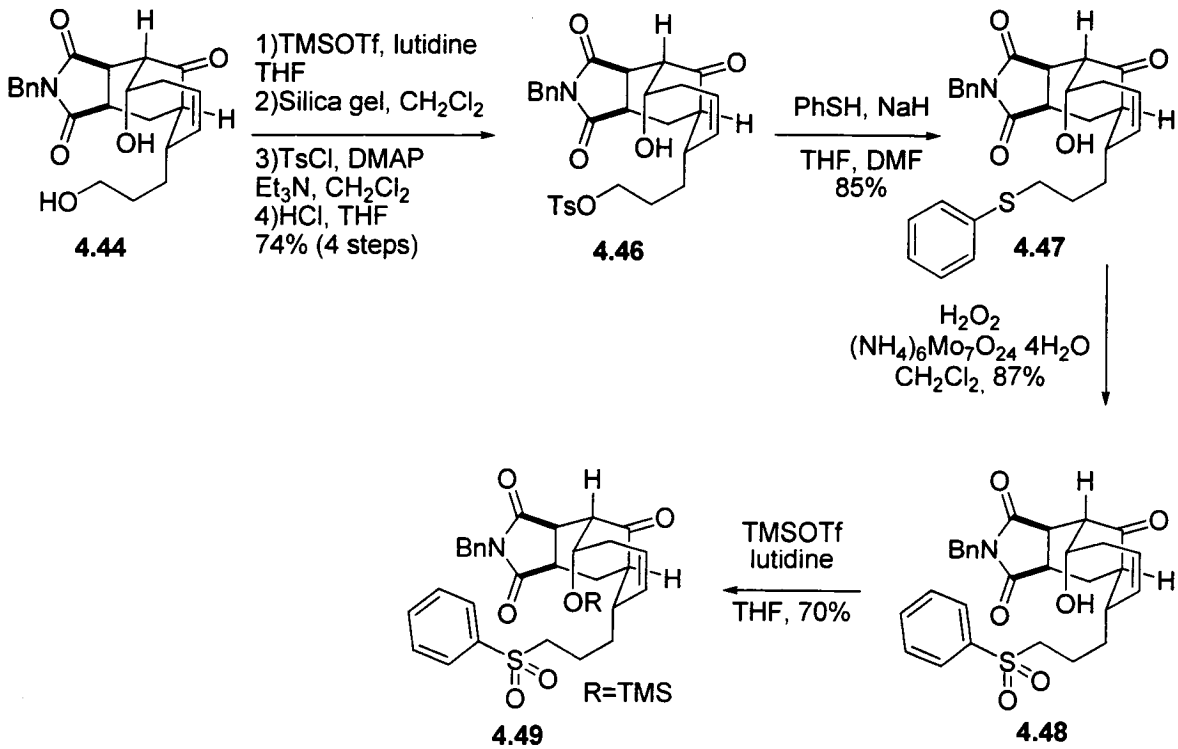
The synthesis started by the deprotection of TBDPS ether **4.40A** using fluoride ions. The use of TBAF led only to degradation of the starting material. To solve this problem, TBAF was replaced by HF pyridine to give diol **4.44** in 90% yield. Interestingly, when protected diol **4.40A** was treated with $FeCl_3$, both TMS and the TBDPS were removed to give **4.44** in 20% yield along with ether **4.45** in 52% yield. The polycyclic compound **4.45** was the result of a tandem deprotection/Prins reaction wherein the $FeCl_3$ acted as a Lewis acid.

*Scheme 4.8 – Removal of the silicon protecting groups on **4.40A***



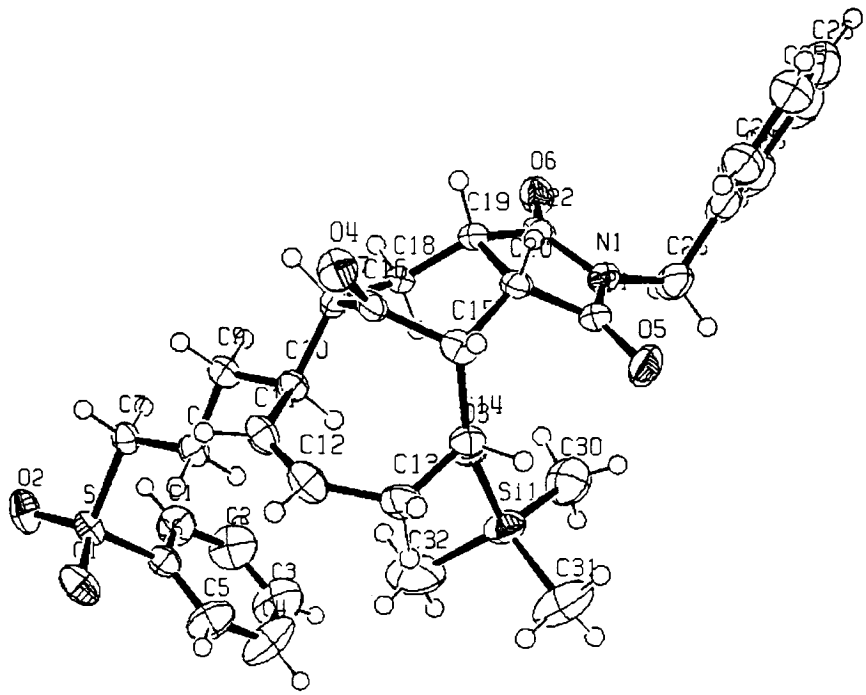
With diol **4.44** in hand, the next step was to selectively protect the more hindered alcohol and to install a tosylate on the primary alcohol. The strategy employed was to protect both alcohols with TMSOTf and to take advantage of the instability of the primary TMS ether on silica gel. By stirring the bis-protected alcohol with silica gel for 15 hours, the primary alcohol was selectively deprotected and transformed into a tosylate with *p*-toluenesulfonyl chloride, DMAP and triethylamine in dichloromethane. During the reaction workup, some of the secondary TMS was removed. The mixture was thus treated with HCl in tetrahydrofuran to remove the residual silicon-protecting group. The above four step sequence gave primary tosylate ester **4.46** in 74% overall yield. The S_N2 displacement of the tosylate with thiophenol gave thioether **4.47** in 85% yield which was oxidized with aqueous hydrogen peroxide in the presence of a catalytic amount of ammonium molybdate to give sulfone **4.48** in 87% yield. The secondary alcohol was reprotected using TMSOTf in the presence of lutidine to afford compound **4.49** in 70% yield.

*Scheme 4.9 – Synthesis of sulfone **4.49***



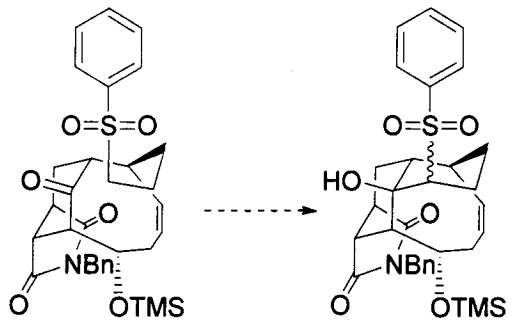
Sulfone **4.49** was a crystalline compound on which we were able to perform an X-Ray diffraction. The ORTEP plot below confirms the structure of cyclization precursor **4.49**.

Figure 4.8 – ORTEP plot of ***4.49***



Sulfone **4.49** was submitted to various strong bases such as LiHMDS, KHMDS and LDA in THF, but none of the desired tricyclic compound **4.50** was isolated. The number of experiments performed to get the cyclized product was minimal since we were running low on front line material. More effort could have been spent on this step, however, from the X-ray crystallographic obtained (figure 4.8), we realized that the sulfone lies far away from the ketone. Moreover, after building a model, it became apparent that the alkene in the eight-membered ring was reducing the flexibility of the ring. This rigidity certainly would not help bring the sulfone and ketone close together in space. As proof of this rigidity, a mixture of 4:1 of atropisomers was observed in the NMR.[99] This can be explained by rigidity of the ring, which creates two different isomers seen by the NMR.

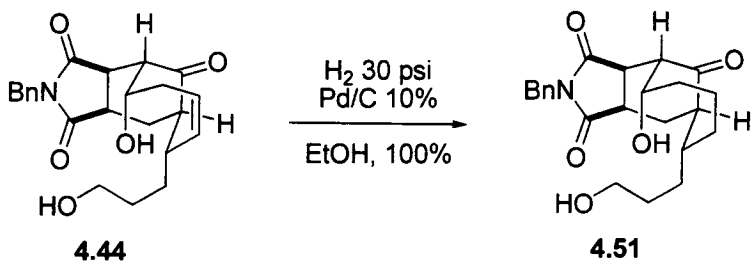
Scheme 4.10 – Attempt to perform the cyclization



Reduction of the alkene

To circumvent this problem, saturation of the double bond was considered. Alkene **4.44** was reduced using 30 psi of hydrogen, in the presence of a catalytic amount of 10% palladium on carbon, to give cyclooctane **4.51** in quantitative yield.

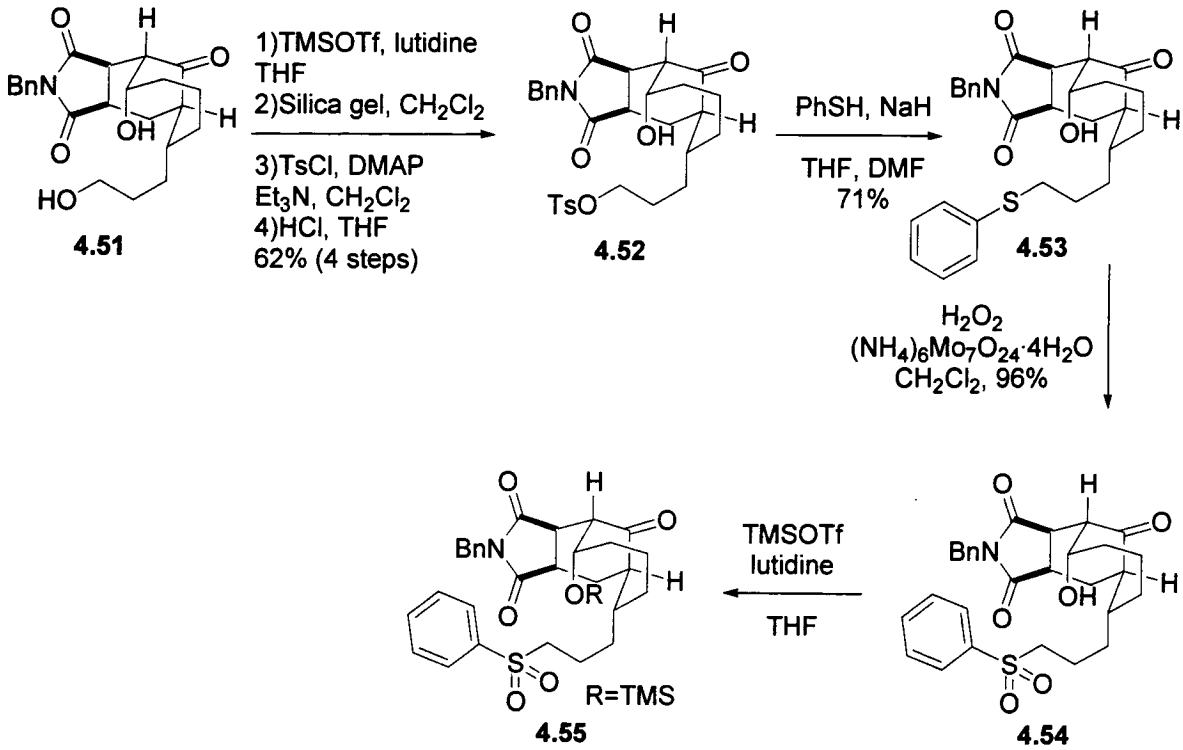
Scheme 4.11 – Hydrogenation of the alkene



The synthetic sequence for diol **4.51** is similar to the sequence for the previous diol **4.44**. The following four steps were performed to introduce a tosylate on the primary alcohol. The bis-protection of the diol with TMSOTf, followed by the deprotection of the primary alcohol with silica gel led to the precursor for the tosylate ester. The use of *p*-toluenesulfonyl chloride followed by an acidic treatment of the crude material allowed us to isolate compound **4.52** in an overall yield of 62% for the four step process. The S_N2 displacement

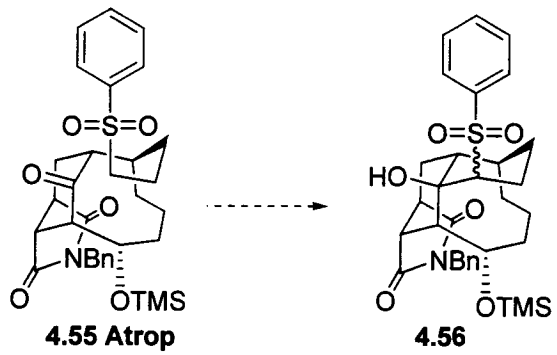
of the tosylate with thiophenol permitted the isolation of thioether **4.53** in 71% yield. The desired sulfone **4.54** was obtained, in 96% yield, after the oxidation of compound **4.53**. Secondary alcohol **4.54** was protected with a TMS group using standard conditions and the crude material was used directly for further steps.

*Scheme 4.12 – Synthesis of sulfone **4.55***



Sulfone **4.55** didn't suffer from the same flexibility problem as sulfone **4.49** as indicated by the lack of atropisomerism observed by NMR. This flexibility increases the probability of forming the atropisomer **4.55 Atrop**, and ultimately compound **4.56**. Unfortunately, despite the enhanced flexibility, treatment with different basic conditions like LDA, LiHMDS, and KHMDS led to decomposition or recovery of starting material. None of the desired tricyclic compound **4.56** was isolated.

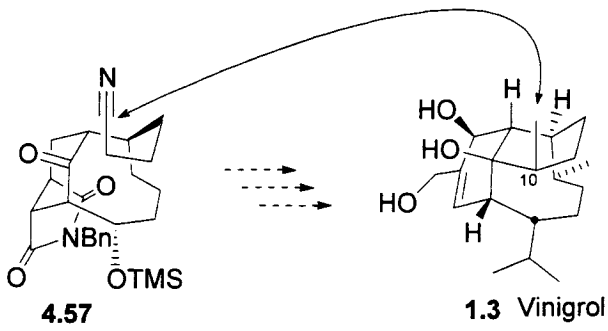
Scheme 4.13 – Attempt to perform the cyclization



Changing the sulfone for a cyanide

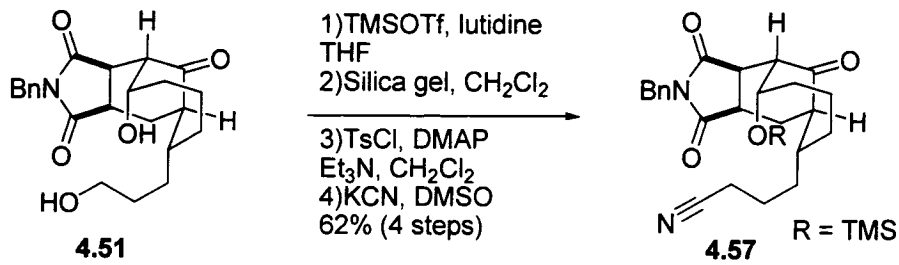
In light of the sulfone's lack of reactivity, steric hindrance was suspected to be a problem. A sulfone is considered to be a big nucleophile. The replacement of this electron-withdrawing group by a smaller one, a cyanide, would allow us to verify whether the cyclization could be performed with a smaller nucleophile. Furthermore, another advantage of the cyano group was the installation of the extra carbon needed for the synthesis of vinigrol. This carbon-carbon bond is needed for the formation of the methyl moiety at C-10 on vinigrol.

Figure 4.9 – Introduction of the needed carbon



To install the cyano group, the same strategy as for the sulfone was employed. The secondary alcohol was selectively protected from diol **4.51** in two steps. The primary alcohol was then tosylated using *p*-toluenesulfonyl chloride in dichloromethane. The S_N2 displacement was performed using potassium cyanide in dimethylsulfoxide. Cyano compound **4.57** was thus isolated in 62% yield over the 4 steps.

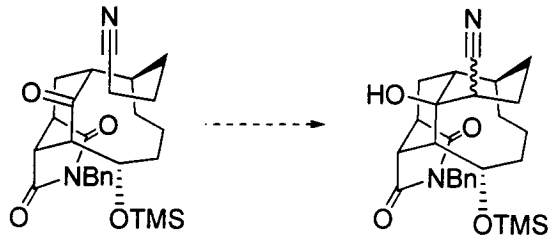
Scheme 4.14 – Introduction of the cyanide



4.51 **4.57**

The attempts to cyclize cyanide **4.57** intramolecularly onto the ketone to give the desired core of vinigrol did not give the desired results. None of tricyclic compound **4.58** was isolated from the various reactions conditions.[100] The use of LiHMDS, KHMDS, LDA, LDA and HMPA afforded either recovered starting material or degradation.

Scheme 4.15 – Attempt to perform the cyclization



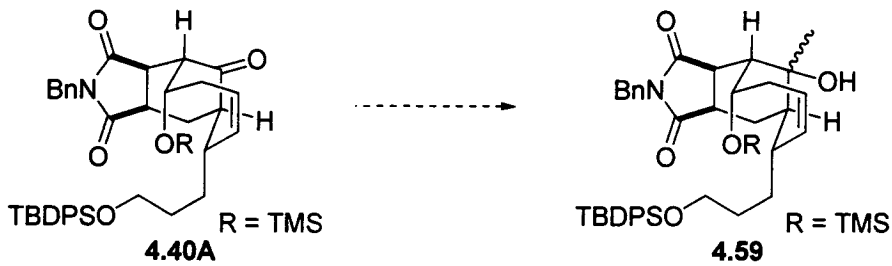
4.57 Atrop **4.58**

In light of the above results, the strategy involving the closure of the last ring was therefore abandoned. Meanwhile, some experiments were performed to verify the reactivity of the bridged ketone.

Reactivity of the bridged ketone

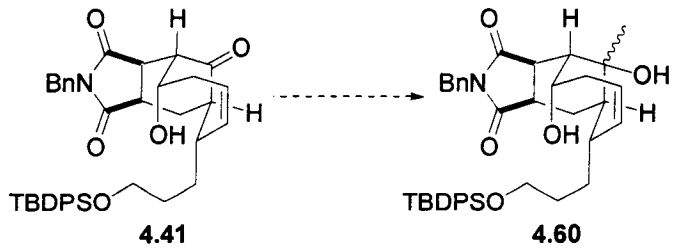
Transformation of the bridged ketone would open the door to alternative strategies aimed at constructing the vinigrol core. Initially, the use of a very good nucleophile to alkylate the ketone moiety was envisioned. To this end, methyllithium or methylmagnesium bromide were used, however, we did not isolate the desired alkylated product **4.59**. To activate the ketone moiety, anhydrous cerium chloride was employed with the previous two nucleophiles without any benefit. The starting material was recovered as well as decomposition material.

Scheme 4.16 – Attempt to alkylate on the ketone



The alkylation was also tried on the ketone **4.41**. Unfortunately, methyllithium and methylmagnesium bromide did not give the desired alkylated product **4.60**. Likewise, the use of anhydrous cerium chloride did not help the reactions.

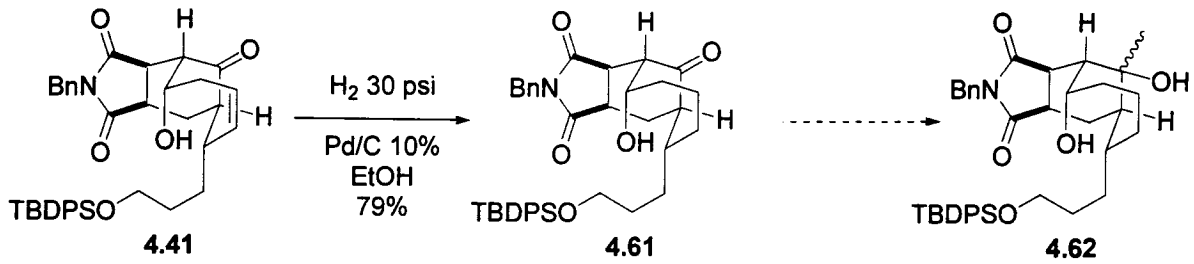
Scheme 4.17 – Attempt to alkylate on the ketone without the TMS



As previously detailed, the alkene gives rigidity to the eight-membered ring and hinders the ketone. Alkene **4.41** was thus reduced to cyclooctane **4.61** using 30 psi of hydrogen. The

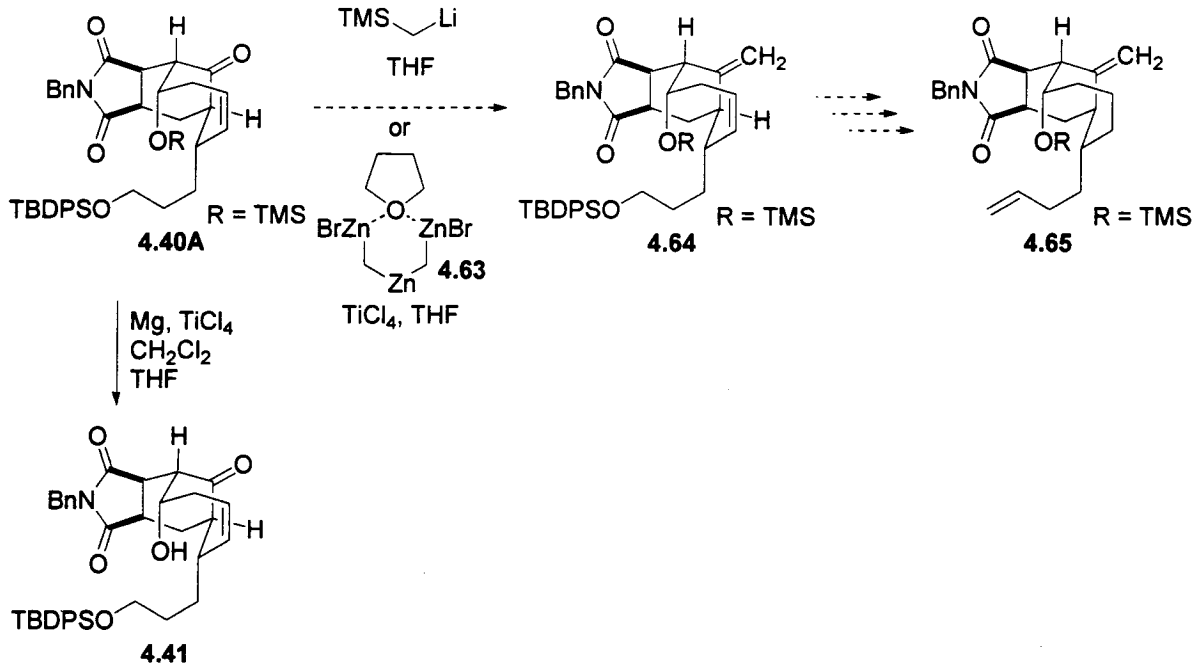
ketone was again submitted to the same nucleophiles (MeLi, MeMgBr) without any success; the desired alkylated product **4.62** was not isolated.

Scheme 4.18 – Attempt to alkylate on the ketone without the alkene



Finally, different reactions were tried to modify the ketone by introducing a double bond at that position to try a ring closing metathesis on a compound like **4.65**. First, the Peterson alkenylation reaction[101] was used to transform ketone **4.40A** into alkene **4.64**, though none of compound **4.64** was isolated. As well, the Petasis reagent[78] failed to produce the desired alkene. At this point we turned our attention to reagents specialized for hindered ketones. The use of Nysted's reagent[102] **4.63** was also unsuccessful. Similarly, when ketone **4.40A** was treated with powdered magnesium and $TiCl_4$ in dichloromethane,[103] the crude NMR showed the removal of the TMS group only.

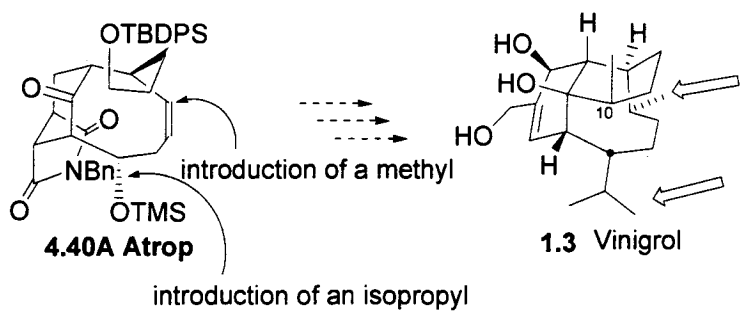
*Scheme 4.19 – Alkenylation of the ketone **4.40A***



Functionalization of the eight-membered ring: the isopropyl group

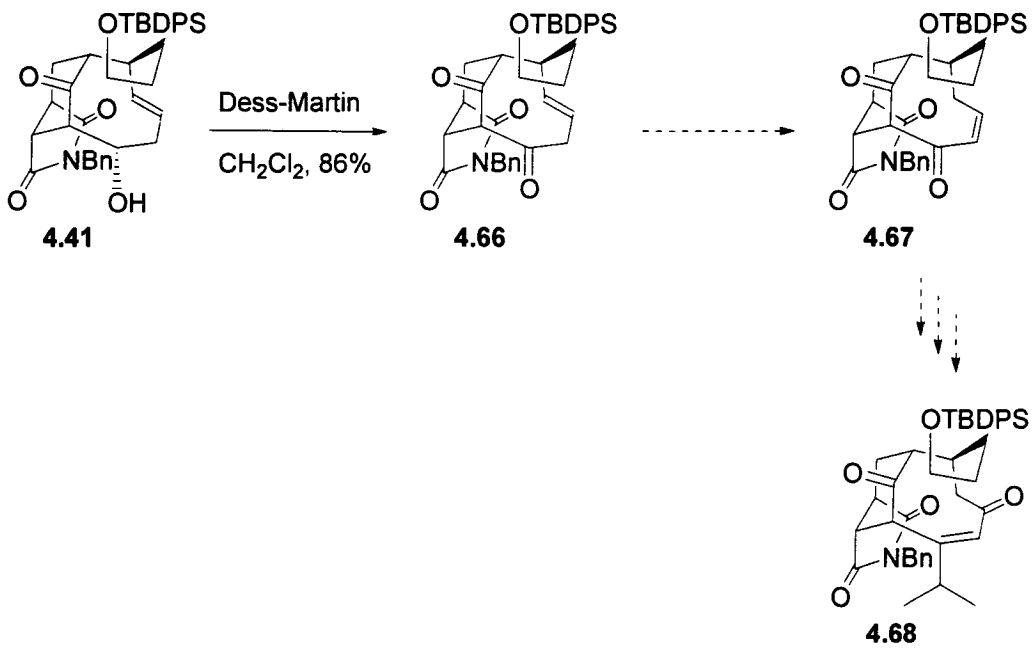
While experiments were being performed to obtain the tricyclic core of vinigrol, investigations toward the installation of the isopropyl and methyl units were performed. (figure 4.10).

Figure 4.10 – Work to be done on the eight-membered ring



First, we explored the installation of the isopropyl unit. Our approach was based on a 1,2 addition of isopropylmagnesium chloride onto an enone such as **4.67** followed by a subsequent 1,3-chromium rearrangement to give enone **4.68**. First, alcohol **4.41** was oxidized using Dess-Martin periodinane to give ketone **4.66** in 86% yield. Unfortunately, the use of PTSA in toluene to isomerize the alkene to give compound **4.67** led to decomposition of the starting material only. This result was explained by the rigidity of the eight-membered ring. Alkene **4.66** cannot isomerize since the resulting double bond cannot be in conjugation with the ketone. This means no overlap between the π-systems of the carbonyl and the olefin.

Scheme 4.20 – Attempt to install the isopropyl moiety

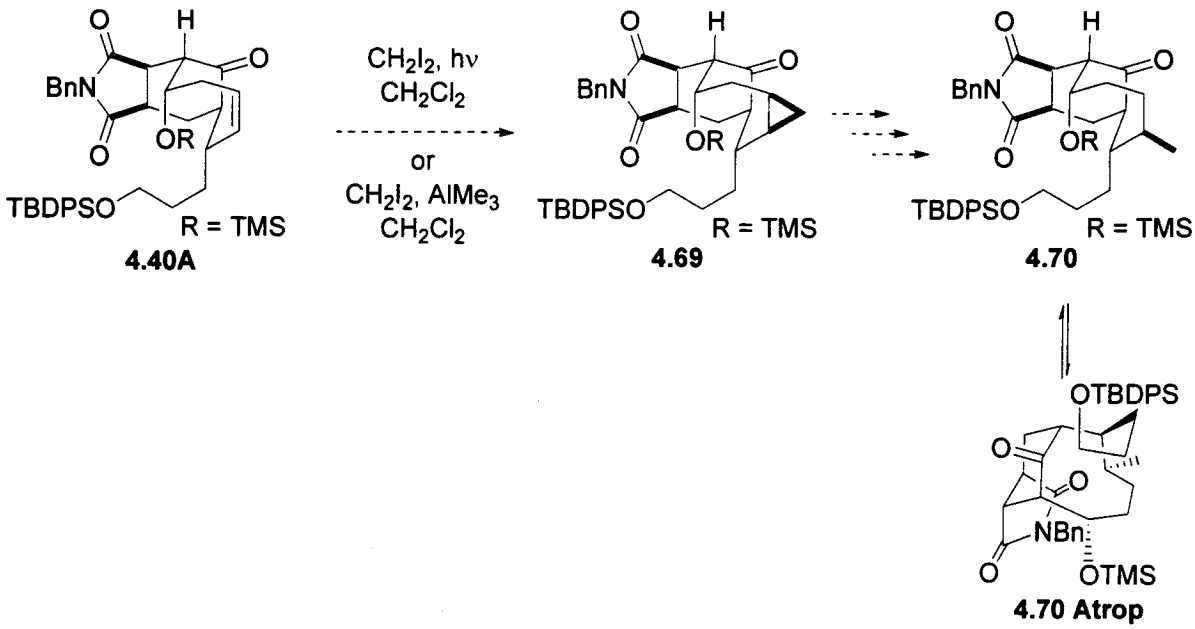


Functionalization of the eight-membered ring: the methyl group

The first attempt to install the methyl group was based on a cyclopropanation of alkene **4.40A** followed by a cyclopropane opening to afford compound **4.70** (scheme 4.21). The

additional methyl on the eight-membered ring may help the equilibration between **4.70** and its atropisomer **4.70 Atrop**. The latter is needed for a subsequent cyclization. The reaction was performed using diiodomethane and a hanovia 450W medium pressure mercury arc lamp.[104] Under these conditions, only starting material was isolated. A second procedure was tried using diiodomethane and trimethylaluminum in dichloromethane.[105] This procedure led to a complex mixture of products. Despite many efforts to obtain the cyclopropane, **4.69** was never observed and the approach was thus abandoned.

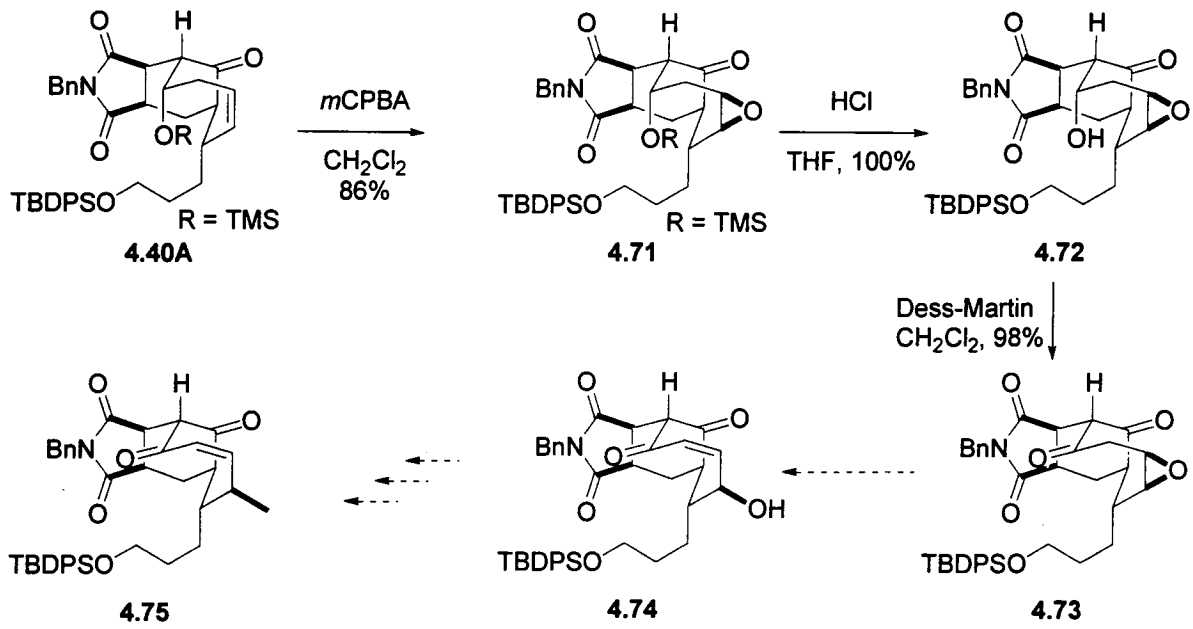
*Scheme 4.21 – Cyclopropanation of alkene **4.40A***



The functionalization of the eight-membered ring could also be done by using an epoxide moiety. Alkene **4.40A** was epoxidized using *m*-chloroperoxybenzoic acid to afford **4.71** in 86% yield. The latter was treated with aqueous HCl in tetrahydrofuran to give secondary alcohol **4.72** in quantitative yield. This alcohol was then oxidized using Dess-Martin periodinane to give ketone **4.73** in 98% yield. The next step was to open the epoxide using a strong base like LDA to give enone **4.74** with a secondary alcohol available for installing the required methyl group. Treatment with LDA, however, did not succeed in opening the

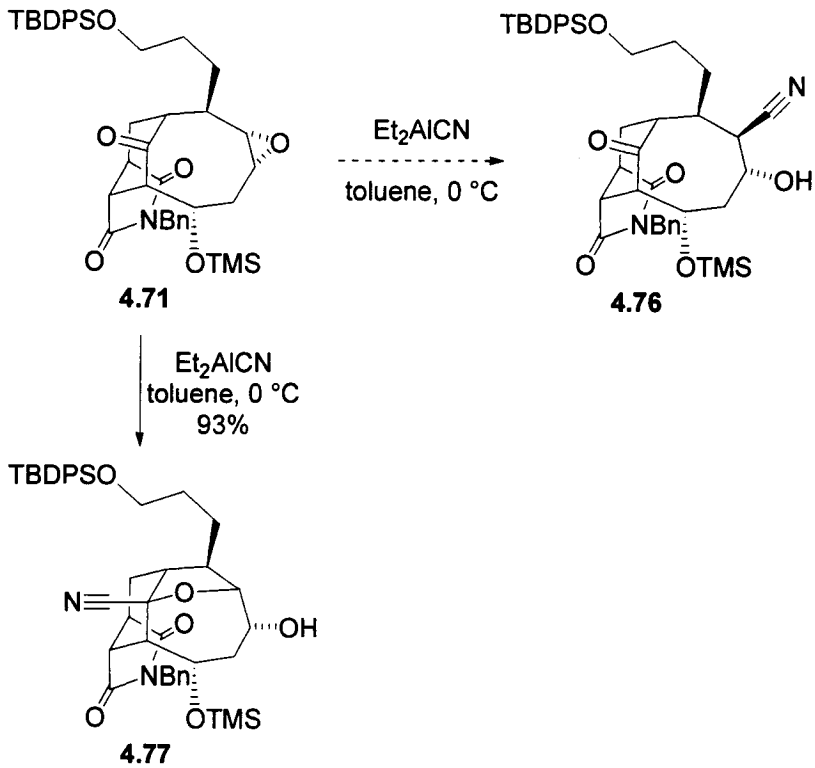
epoxide. As previously discussed, formation of an enone is difficult due to poor alignment of the π-orbitals. This could explain why compound **4.74** was not isolated.

Scheme 4.22 – Epoxide strategy



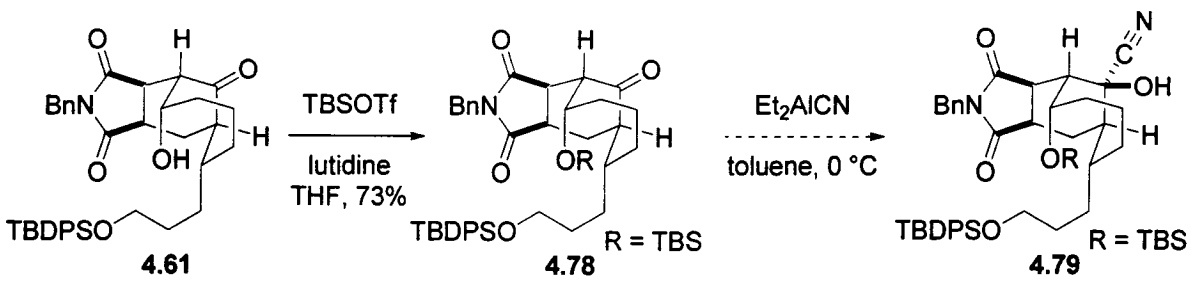
Alternatively, the opening of the epoxide could be accomplished using cyanide which could then be further transformed into the desired methyl group. Surprisingly, treatment of epoxide **4.71** with diethylaluminum cyanide[106,107] gave exclusively the cyanohydrin ether **4.77** in 93% yield. The expected product **4.76** was not observed. This result is explained by activation of the epoxide by the Lewis acid followed by opening of the epoxide by the carbonyl. The resulting oxacarbenium ion is attacked by the cyanide ion to give compound **4.77** in 93% yield.

Scheme 4.23 – Opening of epoxide ***4.71***



To verify the necessity of the epoxide in the reactivity of the ketone, the epoxide would have to be removed. To this end, the secondary alcohol was protected with TBSOTf to give compound **4.78** in 73% yield. This ketone was then submitted to the same conditions as **4.71**. Without the epoxide, however, no cyanohydrin **4.79** was observed. Only starting material was recovered, thereby proving the importance of the epoxide moiety in the carbonyl activation.

Scheme 4.24 – Diethylaluminum cyanide ***4.78***

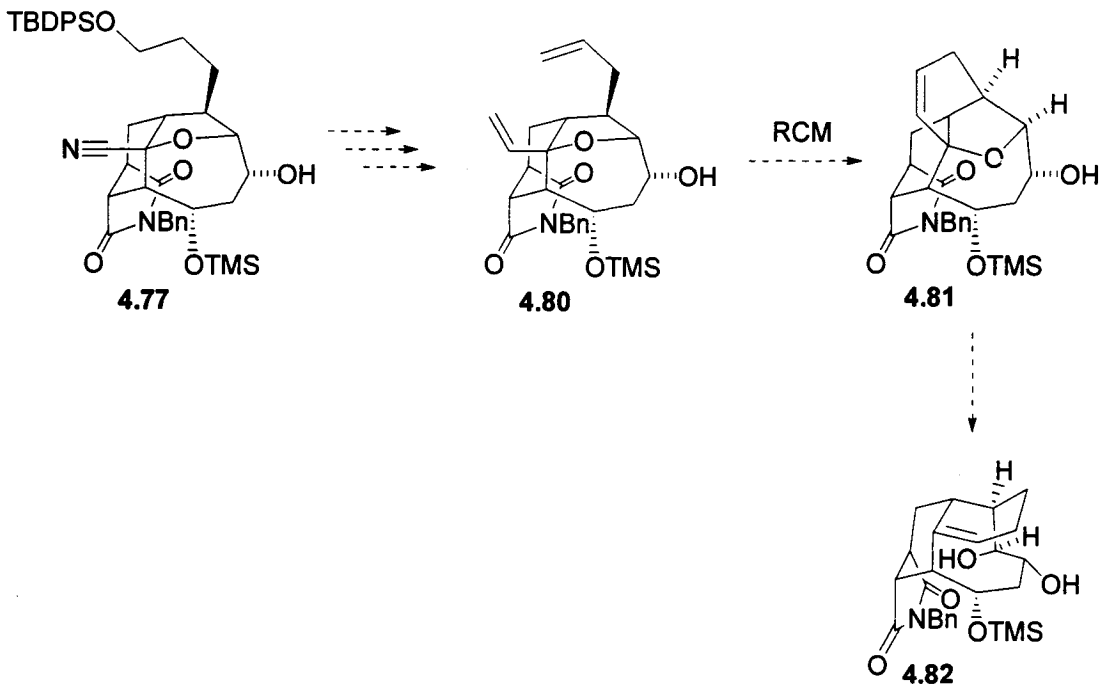


While product **4.79** was not obtained, the unexpected formation of **4.77** remained very interesting for the synthesis of vinigrol. For the first time, we were able to get the ketone to react with a nucleophile. The next step was to take advantage of this result and to use it to form the core of vinigrol. In light of the newly formed carbon-carbon bond, a new approach to the vinigrol core was envisioned.

Back to the synthesis of the core

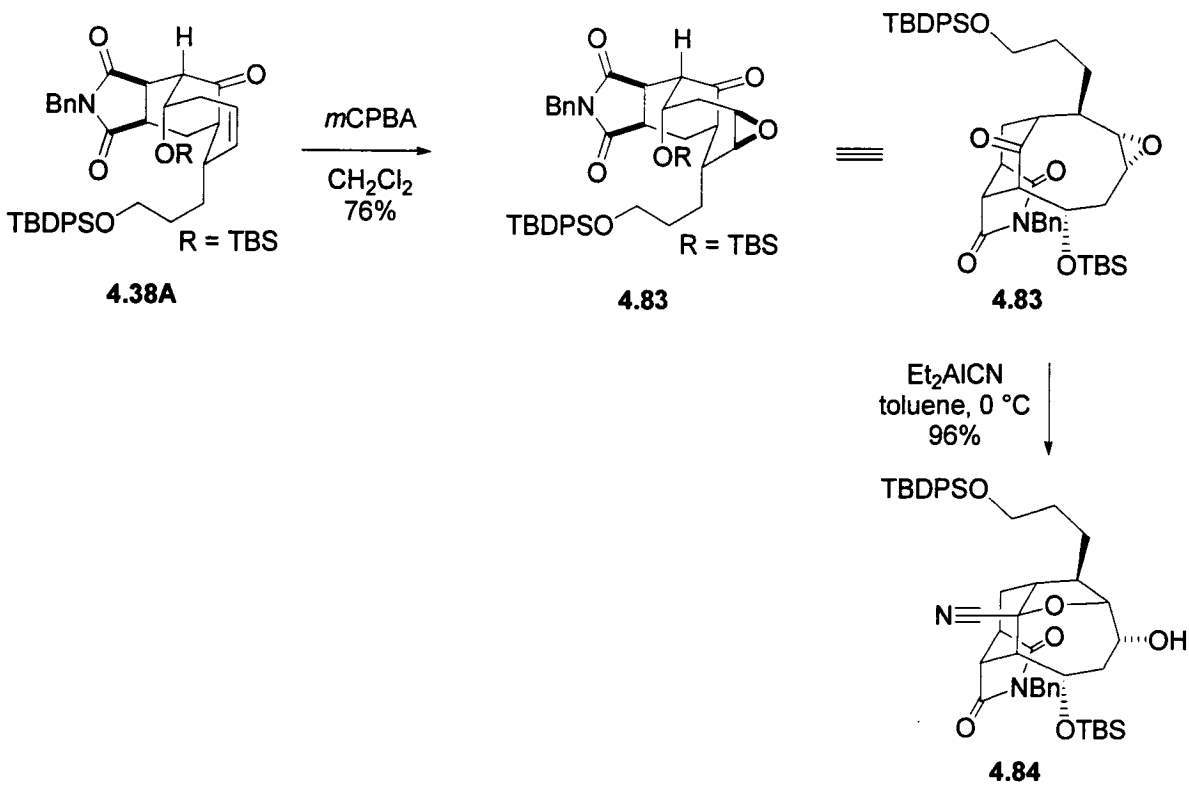
The new synthetic route was based on the ability to transform the cyanide in **4.77** into a double bond allowing a ring closing metathesis reaction to construct the last ring. A subsequent cleavage of the ether bond could be performed to give the isomerized alkene **4.82**.

Scheme 4.25 – Proposed strategy for the synthesis of the core



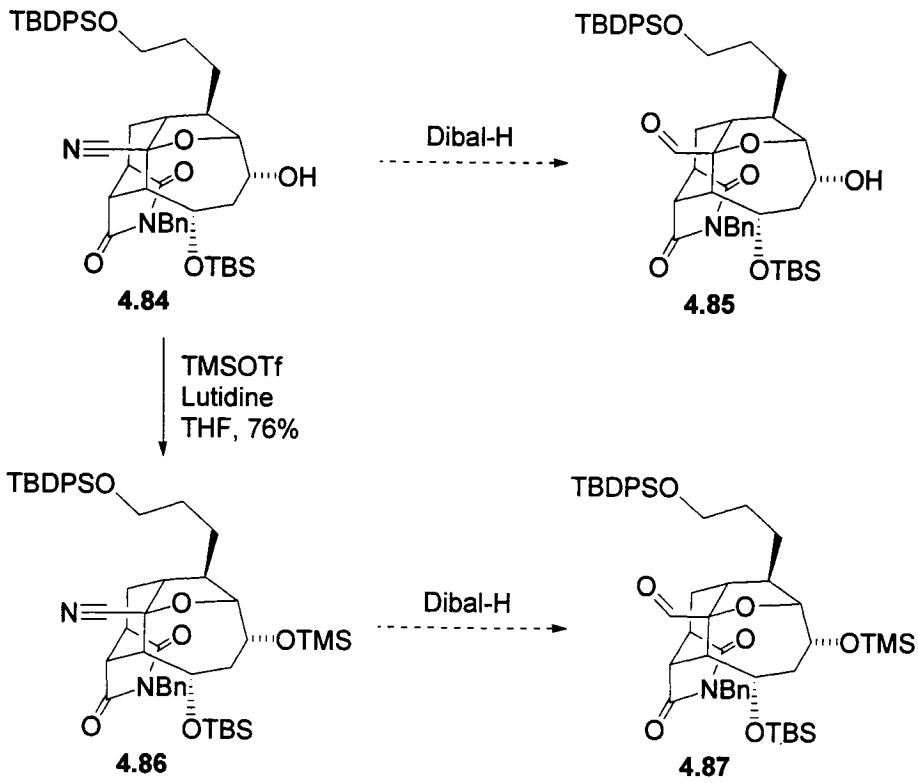
The cyanide opening of the epoxide was repeated on an analogous substrate to **4.71** wherein the TMS group was switched for a TBS group. To prepare this substrate, Claisen product **4.38A** was epoxidized with *m*-chloroperoxybenzoic acid to give epoxide **4.83** in 76% yield. Treatment with diethylaluminum cyanide in toluene at 0 °C gave compound **4.84** in 96% yield.

Scheme 4.26 – Synthesis of the TBS epoxide



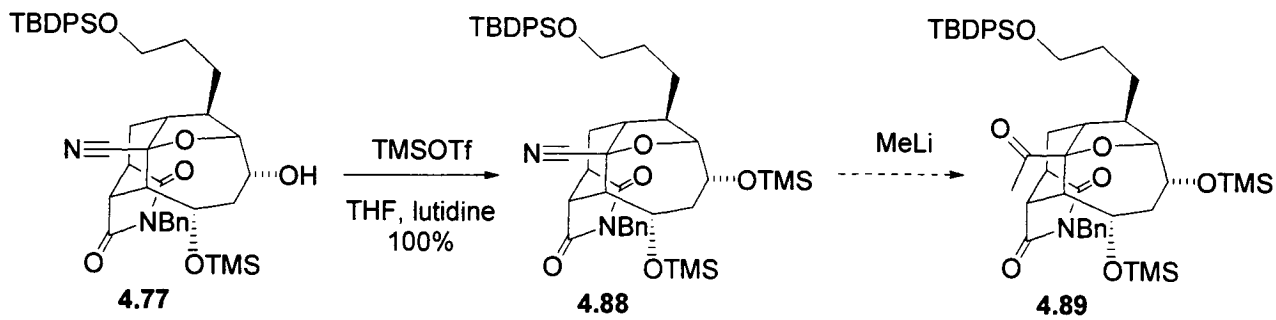
The conversion of cyanide **4.84** to the corresponding aldehyde proved to be challenging. Exposure of **4.84** to diisobutylaluminum hydride[108] in toluene at 0 °C led only to the recovery of the starting material. Obviously, stronger conditions had to be explored. Neat diisobutylaluminum hydride[109] was used, without any success. Suspecting that the free alcohol was interfering with the reaction, it was protected with TMSOTf to give compound **4.86** in 76% yield. This cyanide was thus submitted to neat diisobutylaluminum hydride, but none of **4.87** was isolated.

Scheme 4.27 – Reduction of the cyanide



The secondary alcohol in **4.77** was also protected using TMSOTf to give product **4.88** in quantitative yield. As an alternative to the reduction of the cyanide, **4.88** was treated with MeLi[110] in an effort to prepare ketone **4.89**. Unfortunately, methyl ketone **4.89** was not isolated.

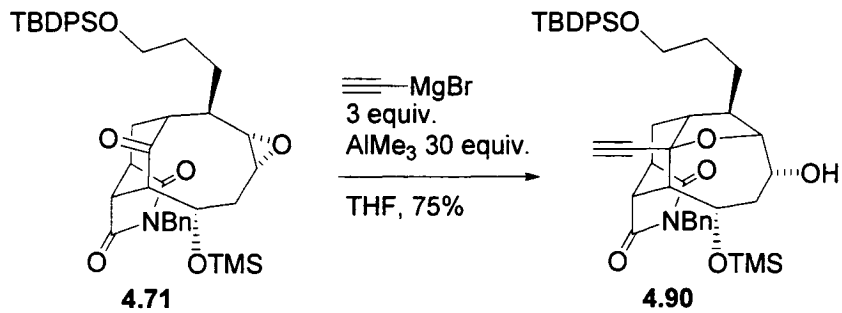
*Scheme 4.28 – Addition of MeLi to **4.88***



Variation of the nucleophile: replacing the cyanide

Considering the problems observed for the transformation of the cyanide into a carbonyl group, the nucleophilic cyanide was replaced by a nucleophilic alkyne. A new reaction was developed to mimic the diethylaluminum cyanide. Trimethylaluminum was used to activate the epoxide and ethynylmagnesium bromide was added. Epoxide **4.71** was treated with 30 equivalents of trimethylaluminum followed by 3 equivalents of ethynylmagnesium bromide to afford the desired compound **4.90** in 75% yield. For unknown reasons, the amount of Lewis acid required could not be reduced from 30 equivalents without hindering the reaction. Likewise, replacing the neat trimethylaluminum with a solution led to failure of the reaction. Finally, the use of other nucleophiles such as methyllithium, methylmagnesium bromide, vinylmagnesium bromide or propynylmagnesium bromide led to complete recovery of the starting material. Given the specificity of the discovered conditions, there was not much room for improving the reaction.

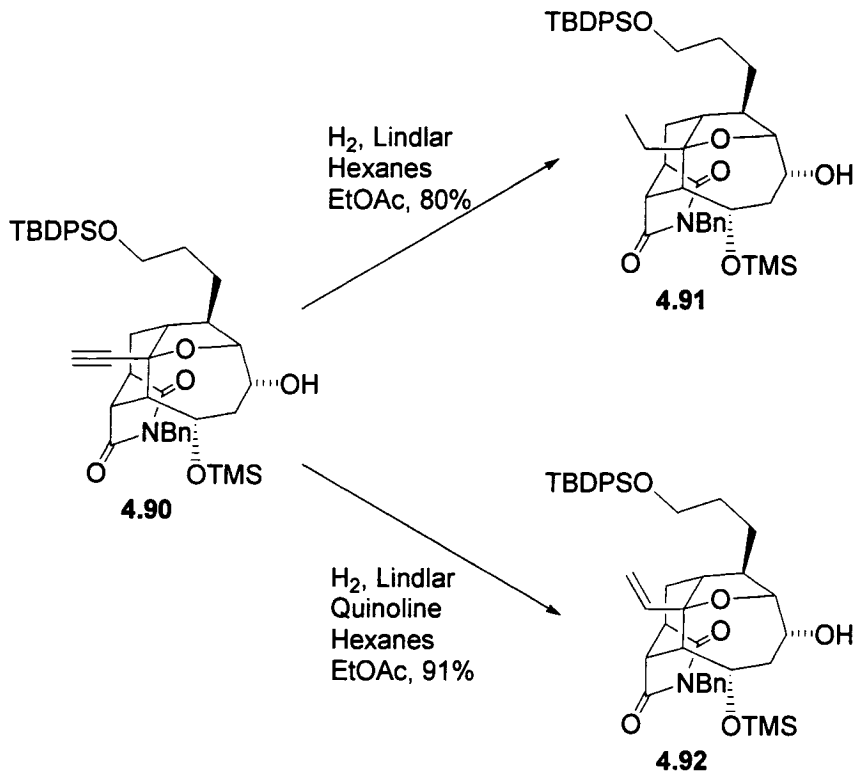
Scheme 4.29 – The use of ethynylmagnesium bromide



4.71 **4.90**

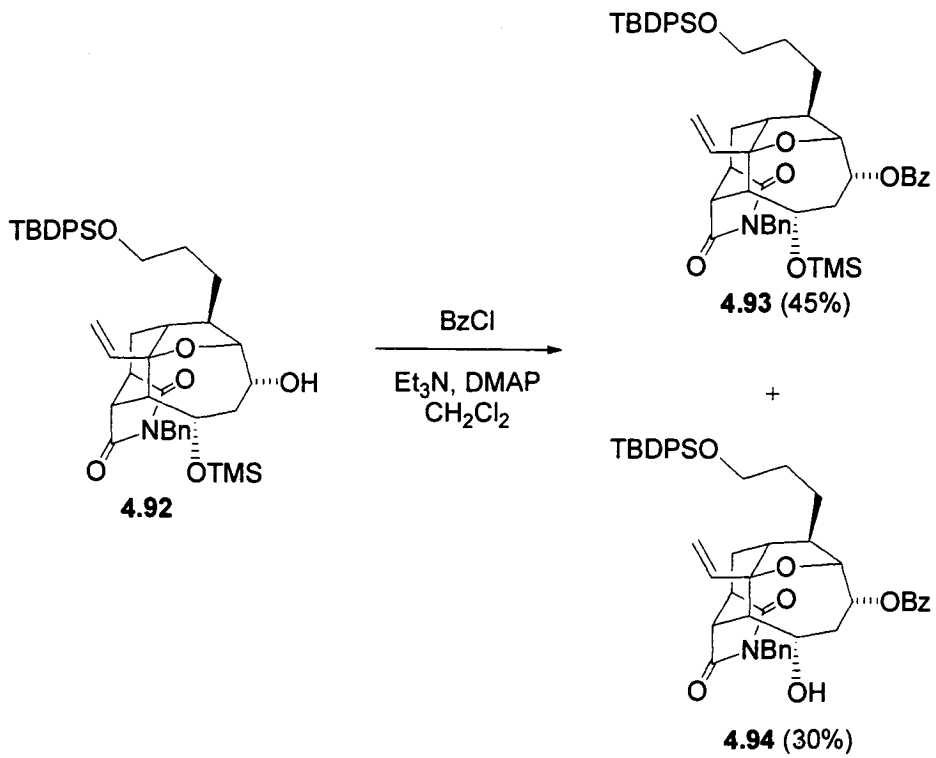
With alkyne **4.90** in hand, the next step was to partially hydrogenate the triple bond to the double bond. Terminal alkyne **4.90** was submitted to 15 psi of hydrogen with Lindlar's catalyst to give the unwanted fully reduced compound **4.91** in 80% yield. This unselective reduction has been observed before in our laboratory[111] with terminal alkynes. The use of Lindlar's catalyst in combination with quinoline fixed the problem and alkyne **4.90** was reduced to alkene **4.92** in 91% yield.

Scheme 4.30 – Lindlar reduction



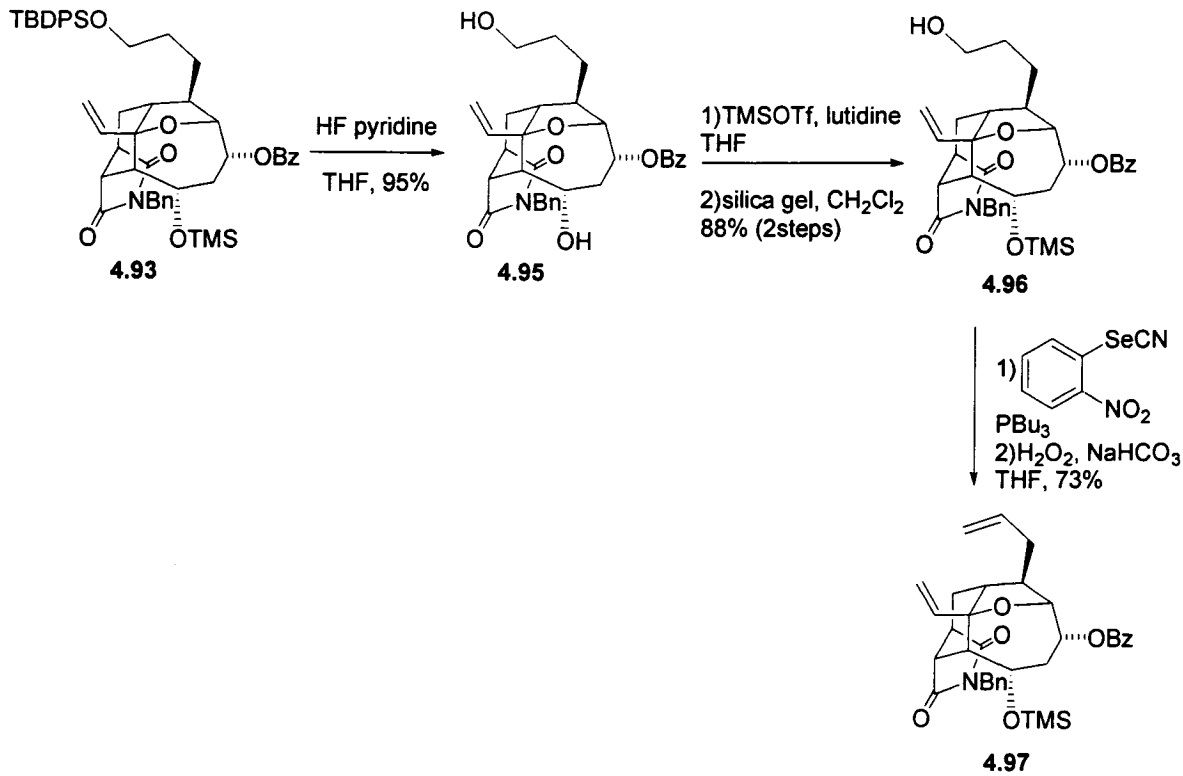
In order to reach the ring closing metathesis step, the second terminal alkene would need to be synthesized. To this end, secondary alcohol **4.92** was protected using benzoyl chloride, triethylamine and DMAP to give two compounds **4.93** (45%) and **4.94** (30%). Benzoate **4.93** is the expected protected product while benzoate **4.94** is the protected alcohol where the TMS group was also removed. The mixture was not a problem, however, since the subsequent step was to remove all the silicon groups.

Scheme 4.31 – Protection of the secondary alcohol



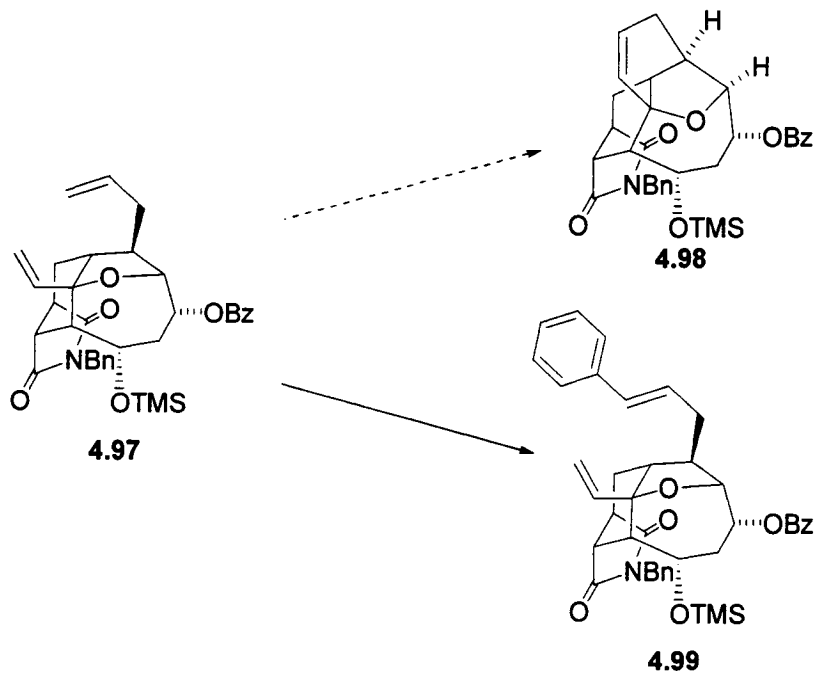
The removal of the silicon protecting groups was performed using HF pyridine to give diol **4.95** in 95% yield. To selectively reprotect the secondary alcohol only, diol **4.95** was bisprotected using TMSOTf and the crude material was stirred over silica gel for 15 hours. The free primary alcohol **4.96** was recovered in 88% overall yield for the two steps. Alcohol **4.96** was dehydrated using Grieco's reagent[112] (2-nitrophenyl selenocyanate) and tributylphosphine. Finally, treatment with hydrogen peroxide gave diene **4.97** in 73% yield.

Scheme 4.32 – Synthesis of the RCM precursor



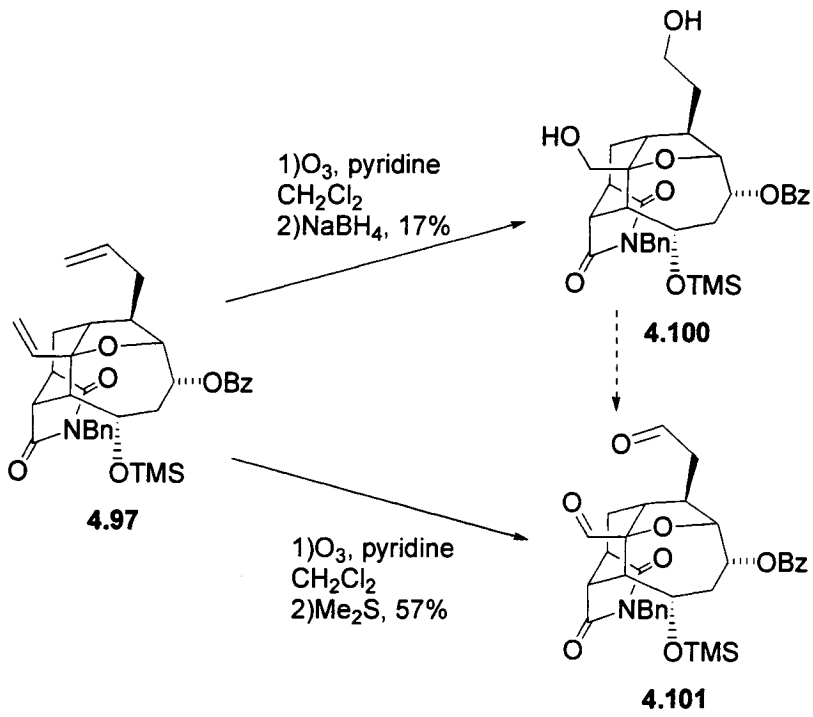
The remaining step was a ring closing metathesis.[113] The use of Grubbs first and second generation[76] catalysts, however, did not give the desired core **4.98** of vinigrol. Instead, the reaction led to the recovery of starting material with a small amount of **4.99** resulting from cross-metathesis with styrene from the catalyst. Given that cross-metathesis occurred only on the allyl group suggests that the more hindered vinyl group is inaccessible for the reaction. In order to try and avoid the cross-metathesis product, the reactions were also run in an ethylene atmosphere, but only starting material was recovered. A third metathesis catalyst was also tried, $RuCl(OC_6Br_5)CHPh)(IMes)(py)$,[114] giving results similar to Grubbs' second generation.

Scheme 4.33 – Attempt to perform the RCM of ***4.97***



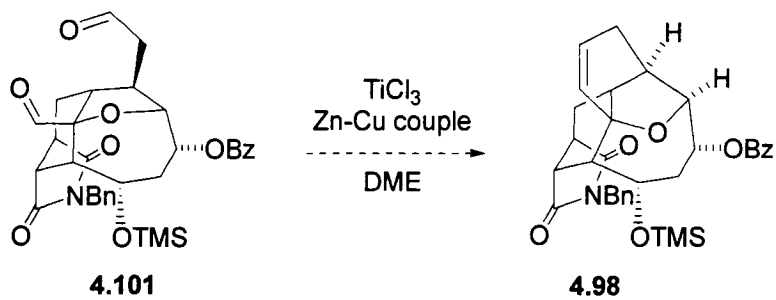
We next turned our attention to the McMurry coupling for forming the six-membered ring. Diene **4.97** was cleaved by ozone followed by a reductive workup with dimethylsulfide to give dialdehyde **4.101** in 57% yield. The yield was modest, but we had enough material to try the McMurry cyclization.

Scheme 4.34 – Ozonolysis of diene ***4.97***



The McMurry cyclization[115] was tried using $TiCl_3$ and a zinc-copper couple but a mixture of degradation products was observed. With the failure of both metathesis and McMurry strategy to form the tricyclic core, a new approach would be required for the synthesis of vinigrol.

Scheme 4.35 – Attempt to perform a McMurry cyclization



Conclusions

The synthesis of the six- and eight-membered rings of the core of vinigrol was accomplished from a sequential hydroxy-directed Diels-Alder/Claisen. The reaction had to be optimized to avoid isomerization of the alkene and the formation of a spiro compound. The last ring was to be formed with the intramolecular attack of a nucleophilic sulfone onto a ketone. In the meantime, we discovered that a nucleophilic cyanide could successfully attack the otherwise unreactive ketone. This reaction was modified for the formation of the missing six-membered ring. Unfortunately, this last ring was not formed despite many attempts.

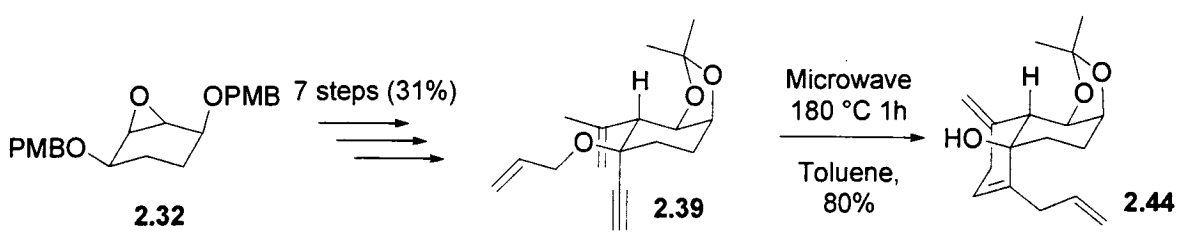
5

Summary and Outlook

Summary

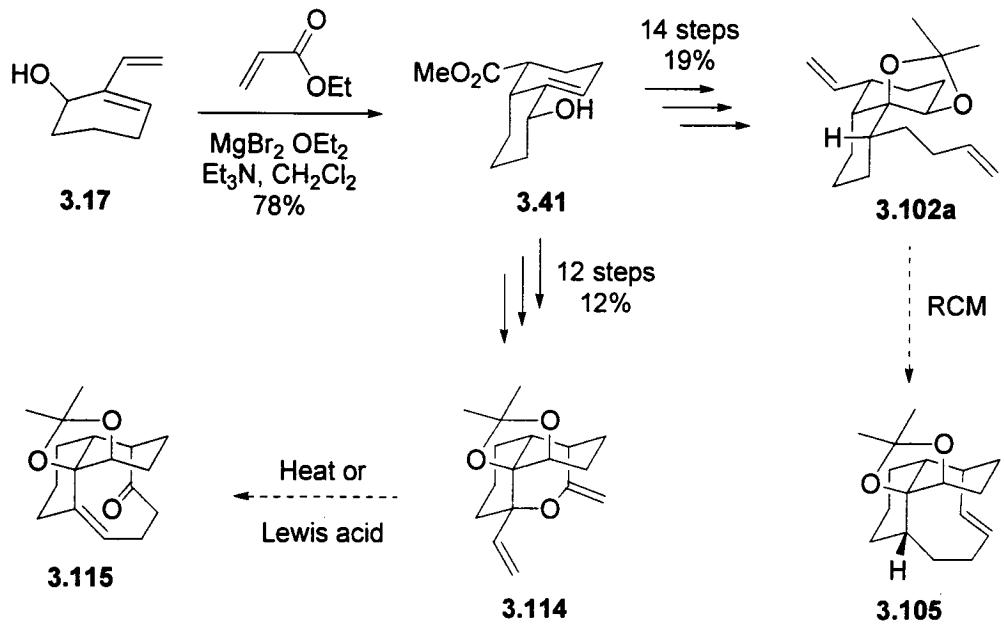
During the last four years, much effort was put forth toward the synthesis of vinigrol. Three different routes were designed and carried out, each using a different methodology developed in our laboratory: the tandem oxy-Cope/Claisen/ene, the hydroxy-directed Diels-Alder and the sequential hydroxy-directed Diels-Alder/Claisen. These approaches are summarized in schemes 5.1 to 5.3.

Scheme 5.1 – Summarized approach for the synthesis of the cis*-decalin part of vinigrol using an oxy-Cope/Claisen/ene*

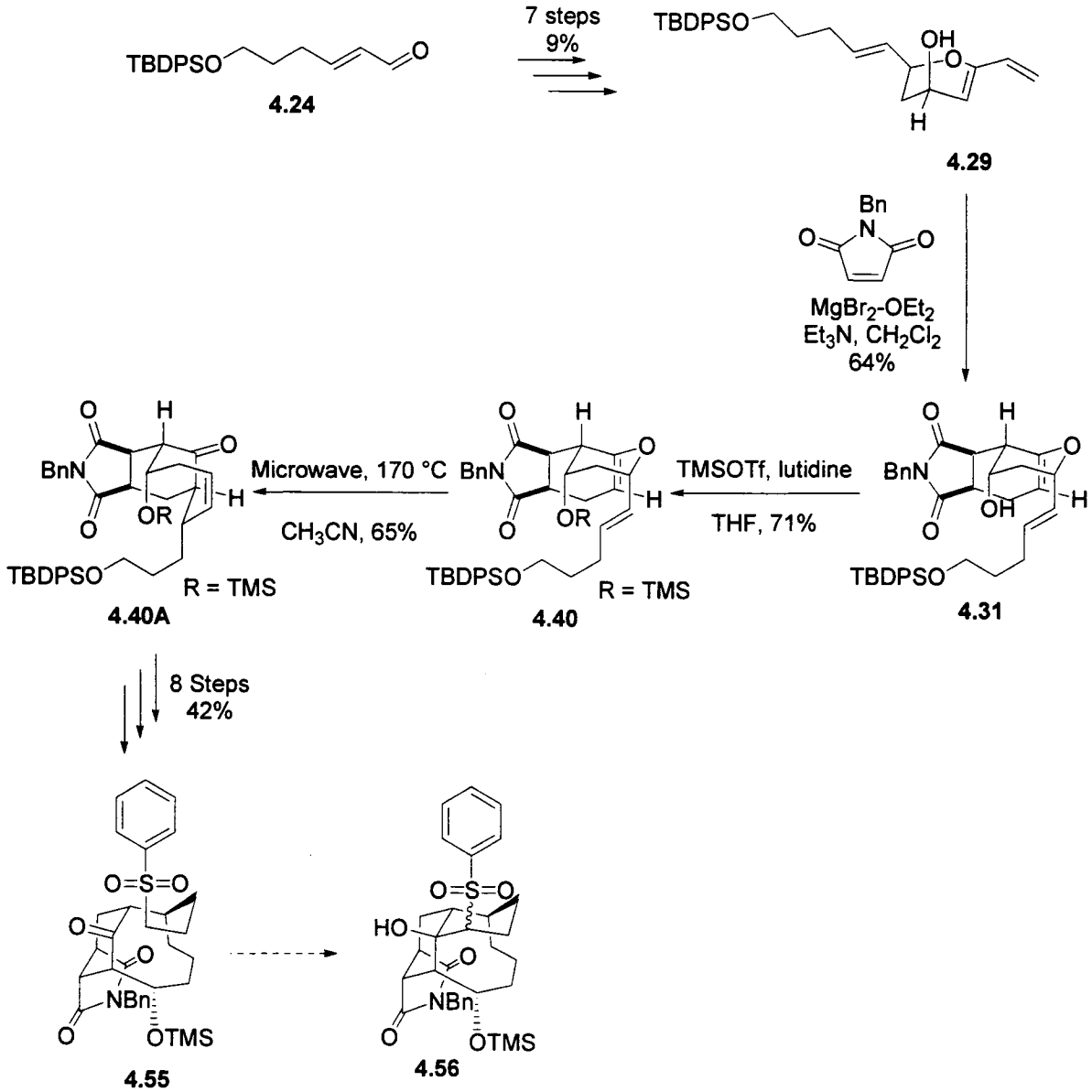


2.32 **2.39** **2.44**

Scheme 5.2 – Summarized approach for the synthesis of vinigrol using a hydroxy-directed Diels-Alder

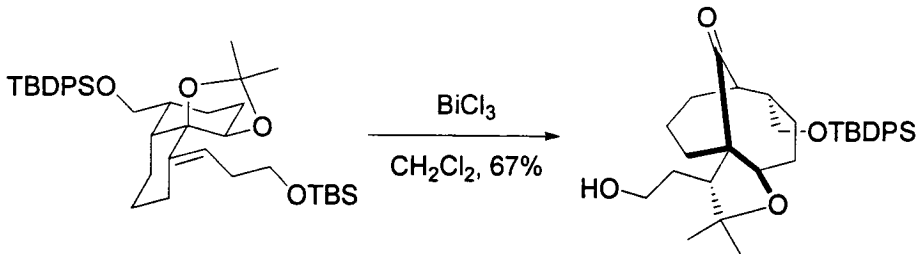


Scheme 5.3 - Summarized approach for the synthesis of vinigrol using a sequential HDDA/Claisen reaction



Finally, in addition to these three approaches, a novel method for the construction of highly functionalized bicyclo[*m.n.*1]alkanone **3.72** from acetal **3.63** was developed. This reaction is summarized in scheme 5.4.

Scheme 5.4 – A Prins/pinacol rearrangement

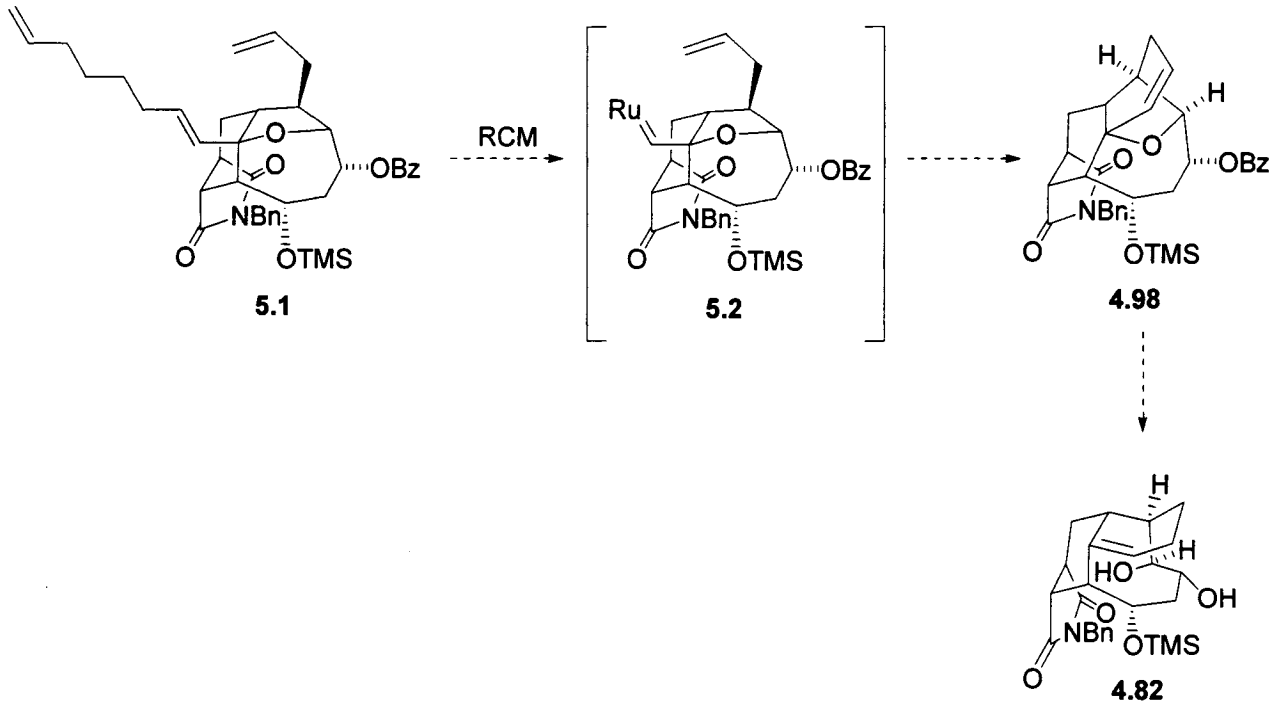


3.63 **3.72**

Outlook

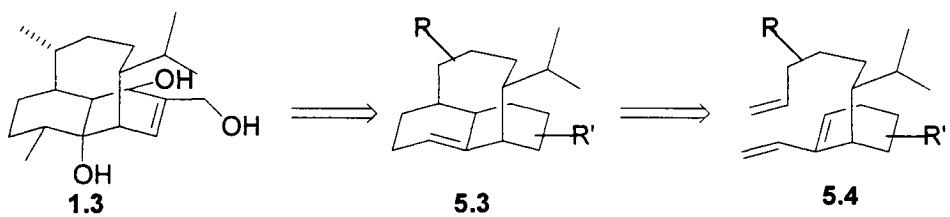
Future work on the metathesis avenue could be performed. One could consider a relay metathesis[116] to form the missing six-membered ring (scheme 5.5). In chapter four, it was demonstrated that the metathesis to form compound **4.98** was impeded by the steric hindrance of one of the alkenes. A ring closing metathesis of compound **5.1** would position the catalyst on the more hindered alkene thus helping the second ring closing metathesis to give **4.98**.

Scheme 5.5 – Relay metathesis strategy



In addition, a fourth route toward the synthesis of vinigrol has recently been started in our laboratory. This new approach is based on an intramolecular Diels-Alder of **5.4** to synthesize the core **5.3** of the natural product **1.3**.

Scheme 5.6 – Intramolecular Diels-Alder



Final Comments

Targeting a molecule as complex as vinigrol was not an easy task. The route along the way to the natural product was riddled with difficulties. Obstacles appeared where we did not expect them. Perseverance and creativity was needed to get around these problems.

Despite four years of work towards the total synthesis of vinigrol, we did not complete the molecule. That said, a lot of new chemistry was learned during those years. Three different routes were developed using three different strategies. Furthermore, an unexpected Prins/pinacol rearrangement was discovered, leading to projects for one Ph.D. and two masters students. As well, there are currently two different total syntheses projects now underway in our laboratory using the Prins/pinacol rearrangement.

Despite the fact that we did not complete the synthesis of vinigrol, we learned a lot along the way. Such is the beauty of this science: bad results let you learn as much as the good ones. From the expertise we have acquired from the first three routes to vinigrol, one can only believe that the next try is going to be the right one and that someday soon vinigrol will finally be synthesized.

Claims to Original Research

1. Development of the tandem oxy-Cope/Claisen/ene and tandem oxy-Cope/ene reactions to provide *cis*-decalin systems.
2. Development of a synthetic route that includes the exploitation of the hydroxy-directed Diels-Alder reaction to construct the vinigrol *cis*-decalin.
3. Development of two different synthetic strategies to target the formation of the eight-membered ring of vinigrol using a Claisen rearrangement or a ring closing metathesis.
4. Adaptation of the sequential hydroxy-directed Diels-Alder/Claisen for the synthesis of the six- and eight-membered rings of vinigrol.
5. Discovery of a Prins/pinacol rearrangement that allows the construction of functionalized bicyclo[m.n.1]alkanones.

Publications from this work

Morency, L.; Barriault, L. **"Stereoselective synthesis of the *cis*-decalin subunit of vinigrol via three pericyclic reactions in cascade"** *Tetrahedron Letters,* **2004,** *45* (32), 6105-6107.

Morency, L.; Barriault, L. "**Studies toward the Total Synthesis of Vinigrol. Synthesis of the Octalin Ring"** *Journal of Organic Chemistry*, **2005**, *70*, 8841-8853.

Lavigne, R. M. A.; Riou, M.; Girardin, M.; Morency, L.; Barriault, L. **"Synthesis of Highly Functionalized Bicyclo[m.n.1]alkanones via a Cationic Reaction Cascade",** *Organic Letters*, **2005**, *7*, 5921-5923.

Presentations from this work

1-**"Studies toward the total synthesis of Vinigrol"** December 2005, Pacifichem 2005, Honolulu, USA. Poster.

2-**"Studies toward the total synthesis of Vinigrol"** November 2005, QOMSBOC, Sainte-Adèle, Canada. Poster.

3-**"Studies toward the total synthesis of Vinigrol"** June 10 2005, Synthesis Day, Ottawa, Canada. Poster.

4-**"Studies toward the total synthesis of Vinigrol"** April 28-29 2005, SISOUM, Montréal, Canada. Oral presentation.

5-**"Studies toward the total synthesis of Vinigrol"** November 5-7 2004, QOMSBOC, Gatineau, Canada. Poster.

6-**"Studies toward the total synthesis of Vinigrol"** May 4 2004, Synthesis Day, Ottawa, Canada. Poster.

"Studies toward the total synthesis of Vinigrol" December 5-7, 2003, QOMSBOC, Montréal, Canada. Poster.

7-**"Studies toward the total synthesis of Vinigrol"** November 7-10, 2003, Banff Symposium in Organic Chemistry, Banff, Canada. Oral presentation, first prize winner (Gordon E. Young award).

8-**"Studies toward the total synthesis of Vinigrol"** August 10-15, 2003, The 39th IUPAC Congress and 86th Conference of The Canadian Society for Chemistry, Ottawa, Canada. Poster.

9-**"Studies toward the total synthesis of Vinigrol"** May 5 2003, Synthesis Day, Ottawa, Canada. Poster, second prize winner.

10-**"Studies toward the total synthesis of Vinigrol"** November 8-10, 2002, QOMSBOC, Kingston, Canada. Poster.

6

Experimental

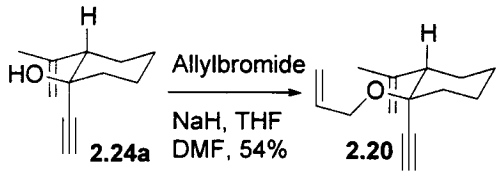
General Experimental

All reactions were performed under argon in flame-dried glassware equipped with a magnetic stirbar and a rubber septum unless otherwise indicated. Solvents were freshly distilled prior to use: diethylether, THF and 1,2-dimethoxyethane (DME) over sodium and benzophenone; dichloromethane, toluene and DMF over calcium hydride. All other commercial reagents were used without purification.

Microwave reactions were performed using a CEM Model ESP-1500 Plus microwave oven equipped with a pressure monitoring device and an EST-300 Plus fiber optic temperature probe. The reaction vessel was a quartz tube, and in each case a carboflon^{TM} was added to aid in the absorption of microwave radiation.

Reactions were monitored by TLC analysis using glass plates precoated (250 μm thickness) with silica gel 60 F_{254} (E. Merck). TLC plates were viewed using UV light, *p*-anisaldehyde staining solution, phosphomolybdic acid staining solution or potassium permanganate staining solution. Flash chromatography was carried out on 230-400 mesh silica gel 60.

^{1}H and ^{13}C NMR spectra were recorded on Bruker Avance 300 MHz, Bruker Avance 500 MHz or Varian INOVA 500 MHz spectrometers in the specified deuterated solvent. IR spectra were recorded on a Bomem Michaelson 100 FTIR spectrometer. HRMS spectra were obtained using a Kratos Analytical Concept spectrometer, and melting points were recorded using a Gallenkamp P1106G Melting Point Apparatus.



1-allyloxy-1-ethynyl-2-isopropenyl-cyclohexane (2.20)

Alcohol **2.24a** (280 mg, 1.7 mmol) was dissolved in THF (12.7 mL) and DMF (4.3 mL). NaH (136 mg, 3.4 mmol) was added followed by allylbromide (0.3 mL, 3.4 mmol). The reaction was stirred for 3 hours and quenched by adding saturated $NH_4Cl_{(aq)}$ (10 mL). The aqueous layer was extracted 3 times with diethyl ether (3 X 20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (5% EtOAc/hexanes) to afford 195 mg of **2.20** (54% yield) as a colourless oil.

Data for **2.20**

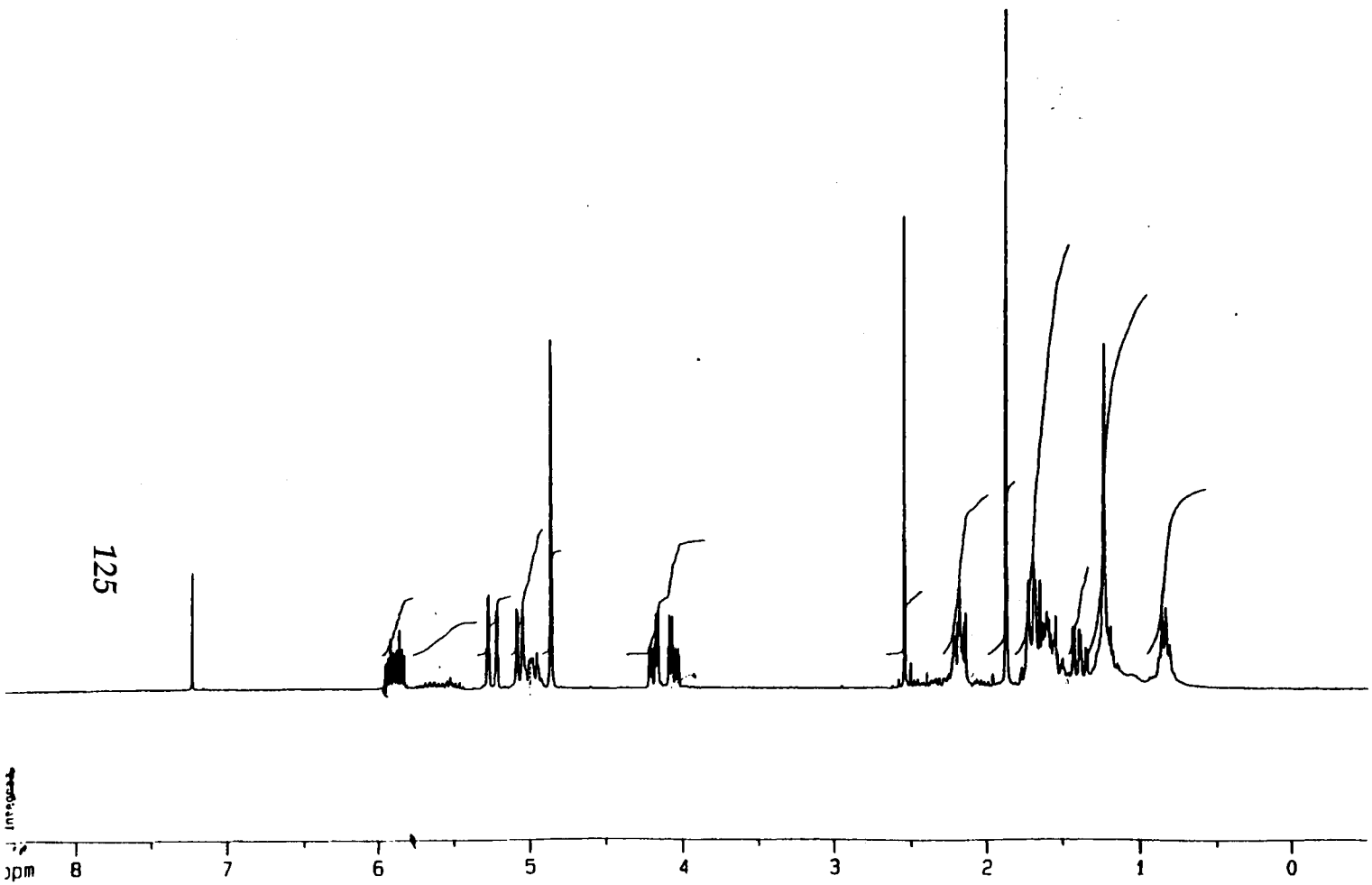
^{1}H NMR (300 MHz, $CDCl_3$): δ 5.96-5.84 (m, 1H), 5.25 (dq, J= 1.9 Hz, 17.2 Hz, 1H), 5.07 (dq, J= 1.8 Hz, 10.2 Hz, 1H), 4.87 (d, J= 1.2 Hz, 2H), 4.23-4.03 (m, 2H), 2.54 (s, 1H), 2.25-2.14 (m, 2H), 1.87 (s, 3H), 1.77-1.49 (m, 7H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 147.0, 135.7, 115.4, 112.3, 82.6, 78.3, 77.2, 64.6, 53.8, 38.5, 29.9, 25.9, 24.3, 23.6.

IR (neat) 3295, 3089, 2940, 2860, 1445, 1089 cm^{-1}.

EI HRMS calcd for $C_{14}H_{20}O$ (M+) 204.1514, obsd 204.1483 (M).

2.20



125

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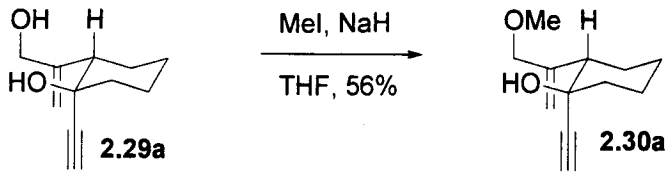


1-ethynyl-2-(1-methoxymethyl-vinyl)-cyclohexanol (2.30a)

Alcohol **2.29a** (280 mg, 1.55 mmol) was dissolved in THF (15 mL). NaH (62 mg, 1.55 mmol) was added followed by MeI (0.116 mL, 1.86 mmol). The reaction was stirred for 15 hours at room temperature. Saturated $NH_4Cl_{(aq)}$ (10 mL) was added and the aqueous layer was extracted 3 times with diethyl ether (3 X 40 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered, and the solvent was evaporated. The crude product was purified by flash column chromatography (20% EtOAc/hexanes) to afford 169 mg of **2.30a** (56% yield) as a colourless oil.

Data for **2.30a**

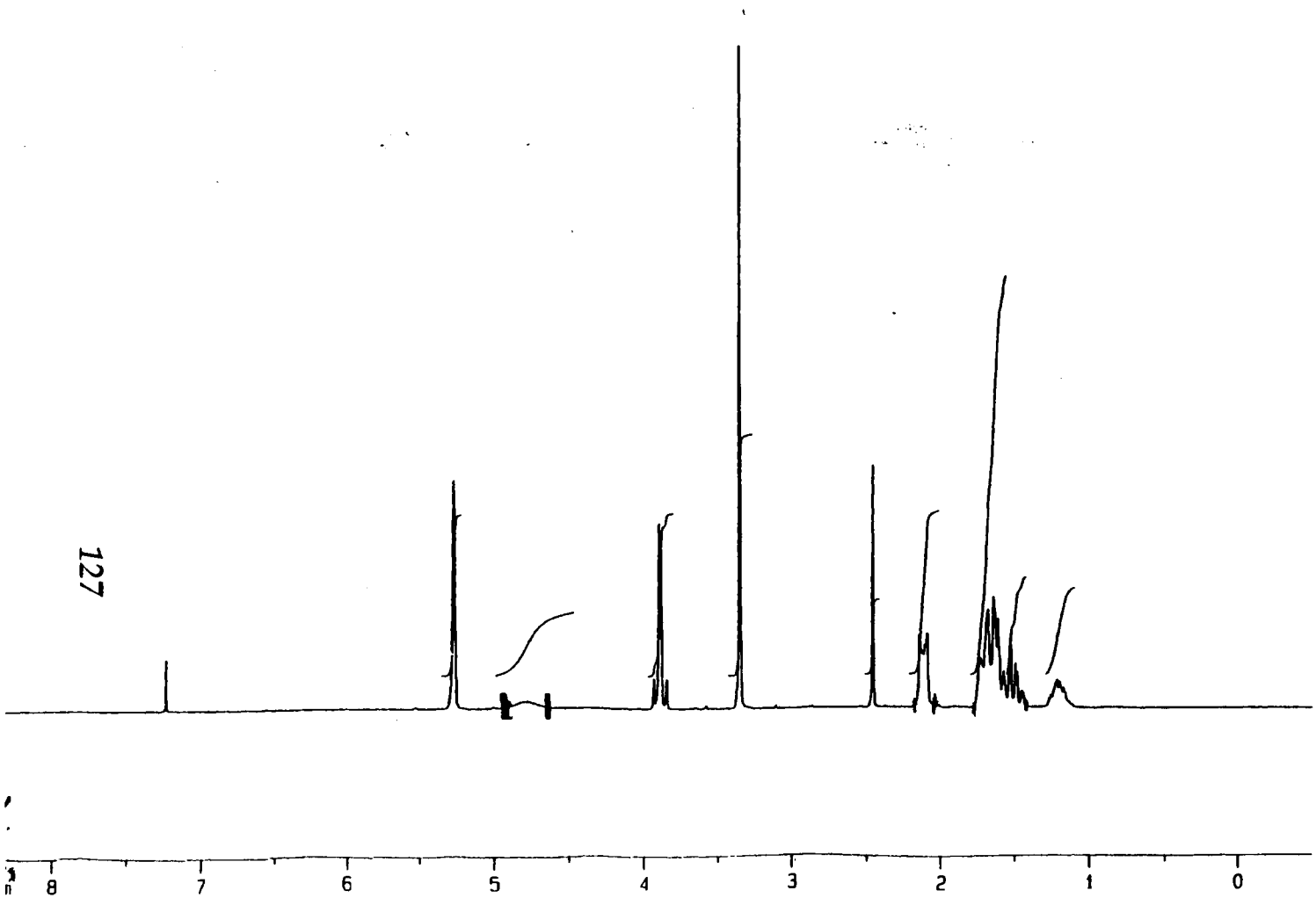
^{1}H NMR (300 MHz, $CDCl_3$): δ 5.27 (s, 2H), 4.7 (s, 1H), 3.89 (d, J= 4.2 Hz, 2H), 3.34 (s, 3H), 2.45 (s, 1H), 2.14-2.09 (m, 2H), 1.72-1.44 (m, 6H), 1.26-1.16 (m, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 144.8, 119.0, 85.6, 77.7, 74.0, 71.6, 57.8, 52.6, 40.9, 30.2, 25.8, 23.6.

IR (neat) 3393, 3304, 2933, 2860, 1450, 1095, 1057 cm^{-1}.

EI HRMS calcd for $C_{12}H_{16}O$ (M+ - H_2O) 176.12012, obsd 176.1174.

2.30a



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F2	-150.06	Hz
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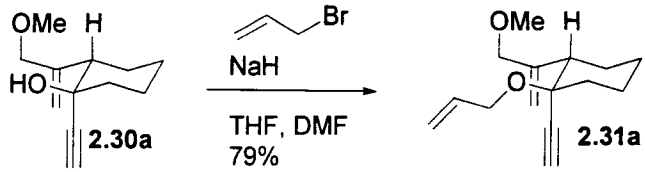


1-allyloxy-1-ethynyl-2-(1-methoxymethyl-vinyl)-cyclohexene (2.31a)

Alcohol **2.30a** (15 mg, 0.077 mmol) was dissolved in THF (0.75 mL) and DMF (0.25 mL). NaH (6 mg, 0.154 mmol) was added followed by allylbromide (0.013 mL, 0.154 mmol). The reaction was stirred for 3 hours and quenched with saturated $NH_4Cl_{(aq)}$ (2 mL). The aqueous layer was extracted 3 times with diethylether (3 X 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (10% EtOAc/hexanes) to afford 195 mg of **2.31a** (79% yield) as a colorless oil.

Data for **2.31a**

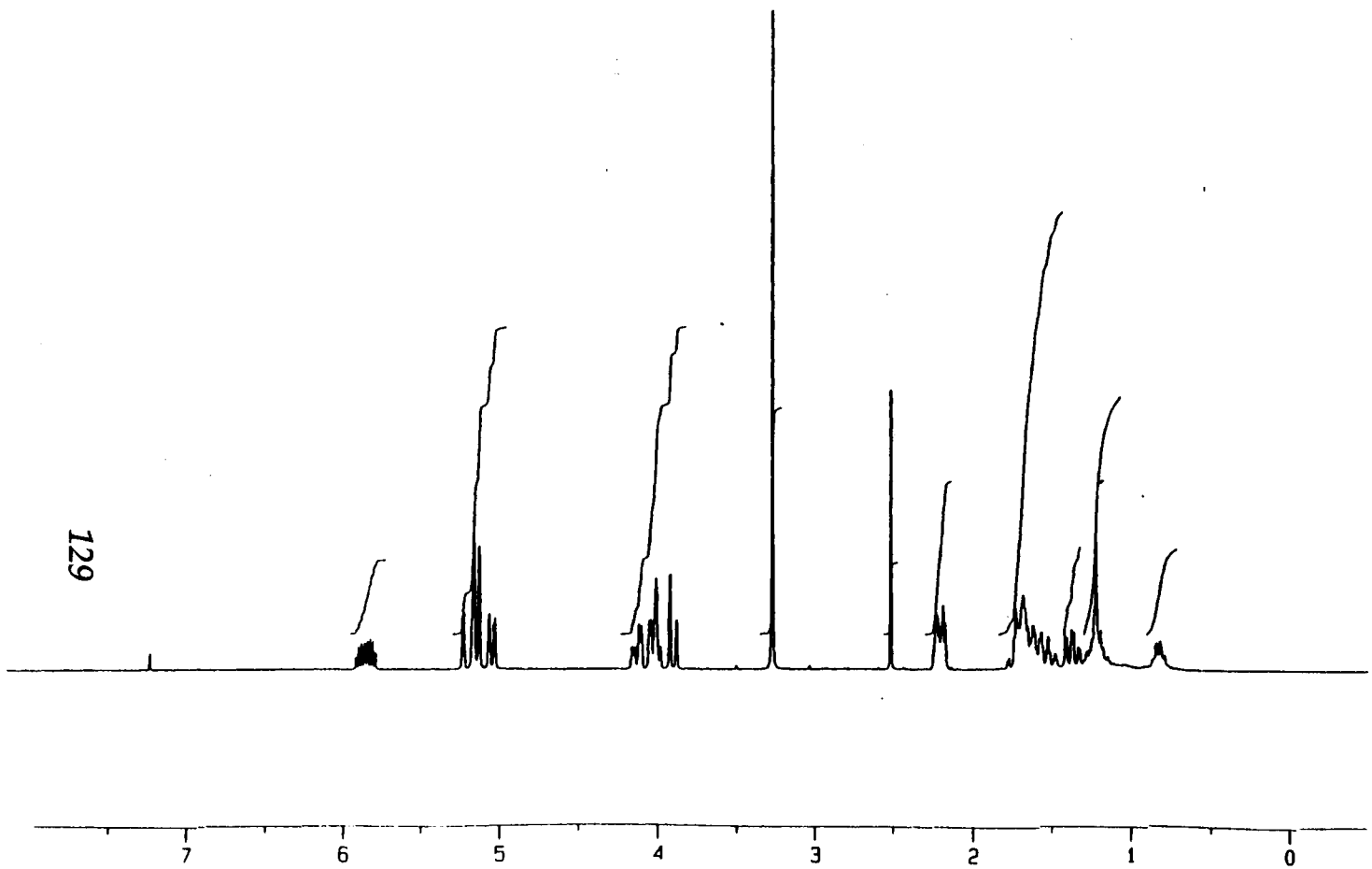
^{1}H NMR (300 MHz, $CDCl_3$): δ 5.93-5.80 (m, 1H), 5.24-5.04 (m, 4H), 4.13-3.88 (m, 4H), 3.27 (s, 3H), 2.52 (s, 1H), 2.24-2.17 (m, 2H), 1.73-1.52 (m, 6H), 1.42-1.36 (m, 1H).

^{13}C NMR (75 MHz, $CDCl_3$,) δ 147.2, 135.4, 115.5, 112.8, 82.1, 79.2, 77.8, 77.0, 64.5, 57.7, 48.5, 37.8, 29.9, 25.8, 23.4.

IR (neat) 3305, 2934, 2859, 1448, 1083 cm^{-1}.

EI HRMS calcd for $C_{14}H_{19}O_2$ (M+ - Me) 2199.13851, obsd 219.1372.

2.31a



129

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FIDRES	0.165407 Hz
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D1	1.00000000 sec

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F2 - Processing parameters

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1D NMR plot parameters

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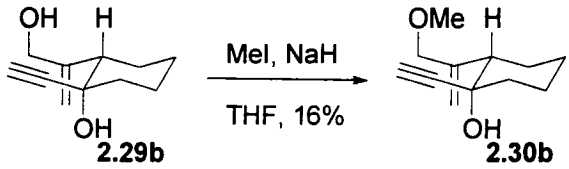


1-ethynyl-2-(1-methoxymethyl-vinyl)-cyclohexanol (2.30b)

Alcohol **2.29b** (140 mg, 0.78 mmol) was dissolved in THF (8 mL) and NaH (31 mg, 0.78 mmol) was added followed by MeI (0.058 mL, 0.93 mmol). The reaction was stirred for 15 hours at room temperature and quenched with saturated $NH_4Cl_{(aq)}$. (10 mL). The aqueous layer was extracted 3 times with ethylacetate (3 X 25 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (15% EtOAc/hexanes) to afford 25 mg of **2.30b** (16% yield) as a colourless oil.

Data for**2.30b**

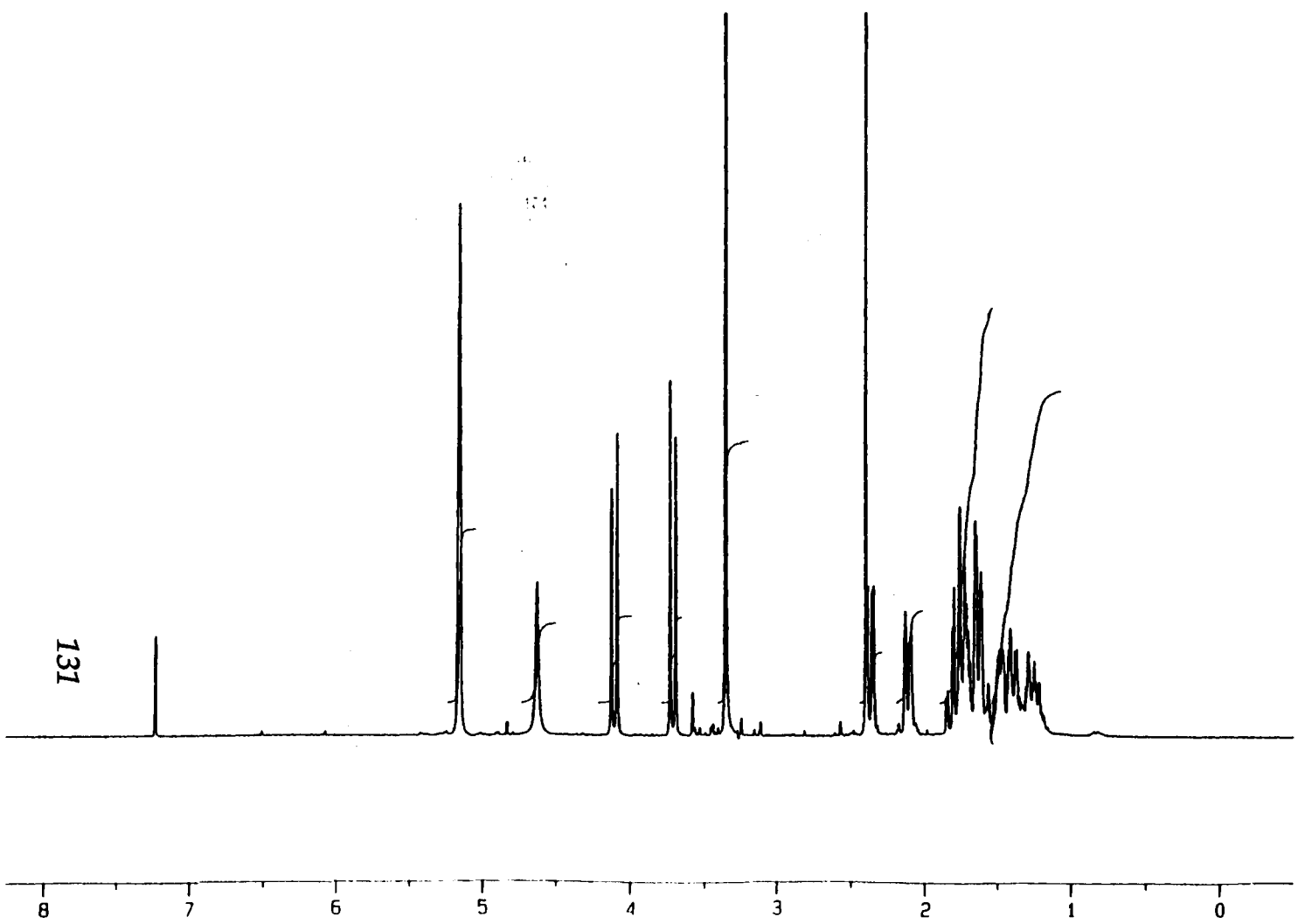
^{1}H NMR (300 MHz, $CDCl_3$): δ 5.16 (s, 2H), 4.63 (s, 1H), 4.11 (d, J= 11.4 Hz, 1H), 3.71 (d, J= 11.4 Hz, 1H), 3.34 (s, 3H), 2.40 (s, 1H), 2.39-2.35 (m, 1H), 2.14-2.09 (m, 1H), 1.81-1.56 (m, 4H), 1.50-1.22 (m, 3H)

^{13}C NMR ($CDCl_3$, 300 MHz) δ 144.7, 120.2, 88.7, 74.1, 71.4, 67.5, 57.5, 53.1, 39.5, 25.8, 25.7, 20.5.

IR (neat) 3377, 3300, 2935, 2859, 1449, 1079 cm^{-1}

EI HRMS calcd for $C_{11}H_{15}O_2$ (M+ - Me) 179.10721, obsd 179.1073.

2.30b



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SWH	5081.301 Hz
FIDRES	0.165407 Hz
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RG	161.3
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

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PL1	-3.00 dB
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1D NMR plot parameters

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F2P	-0.500 ppm
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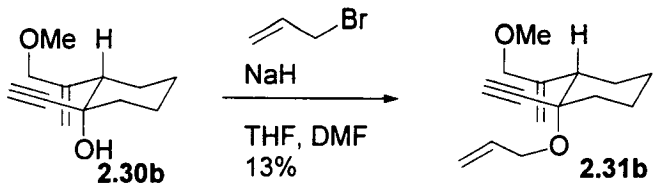


1-allyloxy-1-ethynyl-2-(1-methoxymethyl-vinyl)-cyclohexene (2.31b)

Alcohol **2.30b** (25 mg, 0.129 mmol) was dissolved in THF (1 mL) and DMF (0.3 mL). NaH (10 mg, 0.26 mmol) was added followed by allylbromide (0.022 mL, 0.26 mmol). The reaction was stirred for 3 hours and saturated $NH_4Cl_{(aq)}$ (2 mL) was added. The aqueous layer was extracted 3 times with diethylether (3 X 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (10% EtOAc/hexanes) to afford 4 mg of **2.31b** (13% yield) as a colourless oil.

Data for **2.31b**

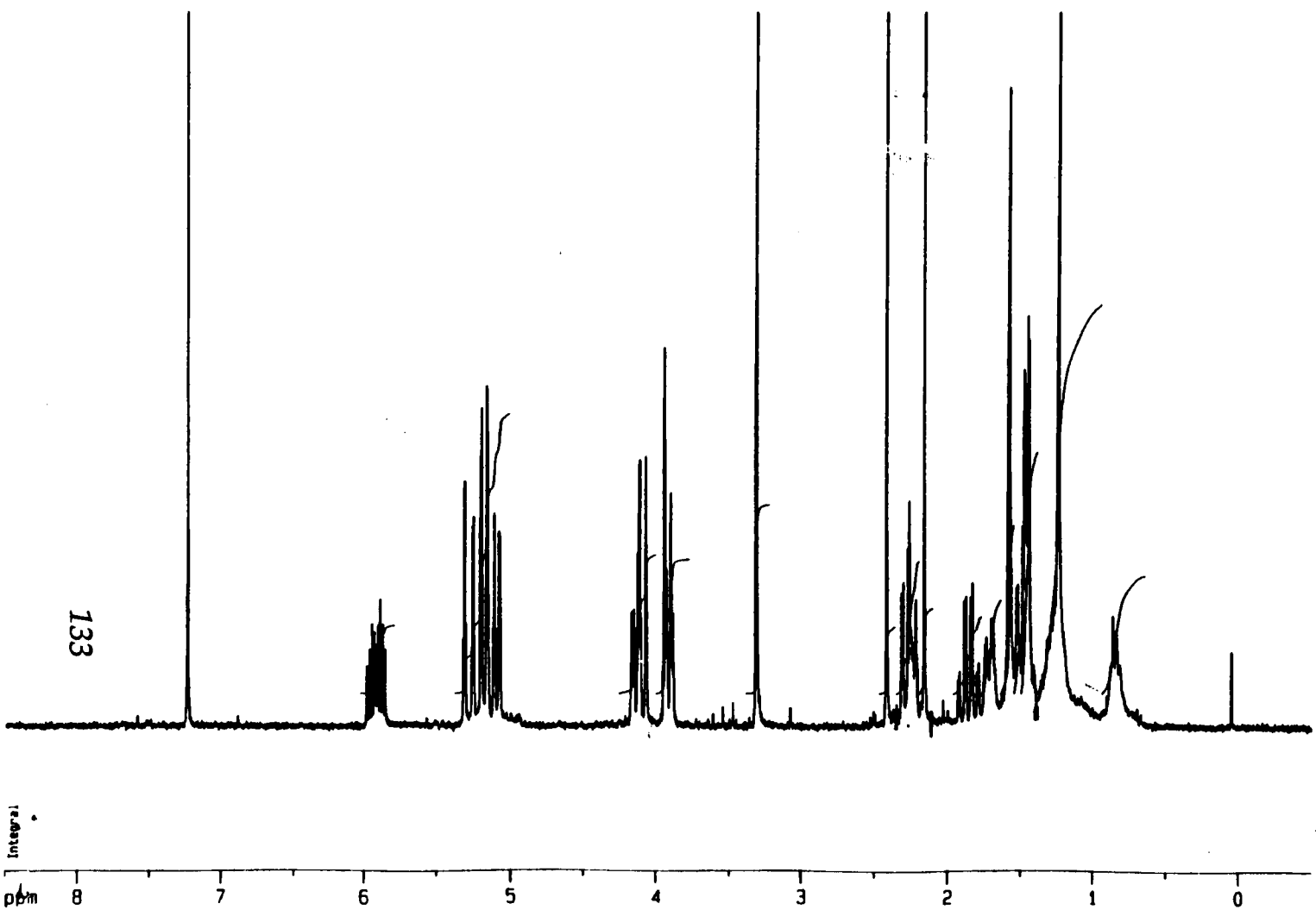
^{1}H NMR (300 MHz, $CDCl_3$): δ 5.99-5.86 (m, 1H), 5.32-5.07 (m, 4H), 4.17-4.06 (m, 2H), 3.94-3.88 (m, 2H), 3.31 (s, 3H), 2.41 (s, 1H), 2.31-2.15 (m, 2H), 1.92-1.74 (m, 1H), 1.74-1.26 (m, 6H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 146.4, 135.3, 115.3, 114.2, 85.0, 75.9, 73.9, 64.2, 57.9, 50.8, 35.5, 27.1, 25.8, 20.4.

IR (neat) 3299, 2931, 2856, 2360, 1440, 1092 cm^{-1}.

EI HRMS calcd for $C_{14}H_{19}O$ (M+ - OMe) 203.14359, obsd 203.1445.

2.31b



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FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	912.3
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

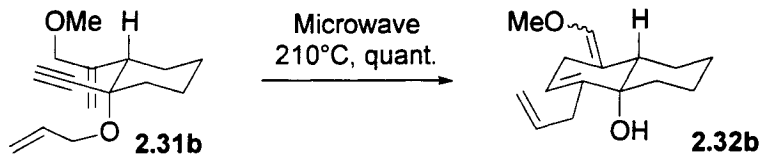
NUC1	1H
P1	10.00 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

F2 - Processing parameters

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

1D NMR plot parameters

CX	20.00 cm
CY	60.00 cm
F1P	8.500 ppm
F1	2551.10 Hz
F2P	-0.500 ppm
F2	-150.06 Hz
PPMCM	0.45000 ppm/cm
HZCM	135.05850 Hz/cm



5-Allyl-8-methoxymethylene-1,3,4,7,8,8a-hexahydro-2H-naphthalen-4a-ol (2.32b)

Product **2.31b** (4 mg, 0.017mmol) was dissolved in toluene (18 mL) and triethylamine (0.1 mL, 0.72 mmol) was added. The solution was sparged by bubbling with argon for 20 minut. The tube was sealed, fitted with temperature and pressure probes, and placed in the microwave. The temperature was ramped gradually to 210 °C, and was held there for 1 hour. The solvent was evaporated and the crude was purified by flash column chromatography (20% EtOAc/hexanes) to afford 4 mg of **2.32b** (100% yield) as a colourless oil.

Data for **2.32b**

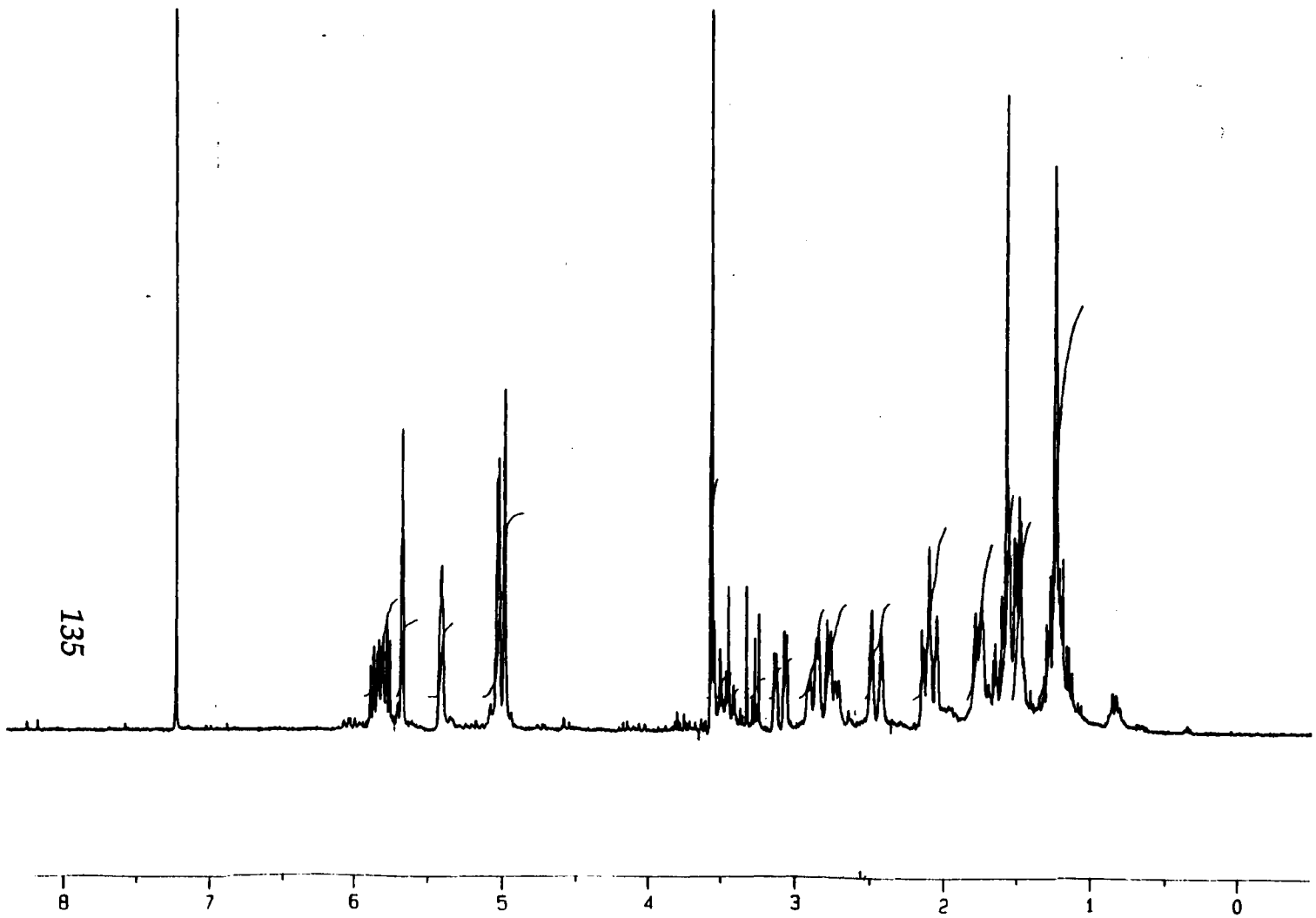
^{1}H NMR (300 MHz, $CDCl_3$): δ 5.90-5.76 (m, 1H), 5.68 (s, 1H), 5.41 (s, 1H), 5.05-4.98 (m, 2H), 3.57 (s, 3H), 3.55-3.25 (m, 1H), 3.14-3.06 (m, 1H), 2.92-2.71 (m, 2H), 2.51-2.42 (m, 1H), 2.15-2.05 (m, 2H), 1.79-1.73 (m, 2H), 1.70-1.41 (m, 2H), 1.33-1.13 (m, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 141.9, 141.1, 137.5, 123.6, 115.8, 114.3, 71.1, 59.7, 45.4, 35.4, 33.7, 26.4, 25.9. 23.2, 21.2.

IR (neat) 3443, 2933, 2856, 1730, 1687, 1446, 1216, 1103 cm^{-1}.

EI HRMS calcd for $C_{15}H_{22}O_2$ (M+) 234.16198, obsd 234.1644.

2.32b



Current Data Parameters

NAME	lmo_88A
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20020403
Time	8.10
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	456.1
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

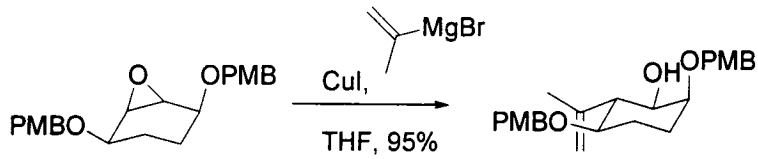
NUC1	1H
P1	10.00 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

F2 - Processing parameters

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

1D NMR plot parameters

CX	20.00 cm
CY	60.00 cm
F1P	8.500 ppm
F1	2551.10 Hz
F2P	-0.500 ppm
F2	-150.06 Hz
PPMCM	0.45000 ppm/cm
HZCM	135.05850 Hz/cm



1.51 **2.51**

2-Isopropenyl-3,6-bis-(4-methoxy-benzyloxy)-cyclohexanol (2.51)

To a suspension of CuI (0.102 g, 0.54 mmol) in diethylether (2.7 ml) at -10°C was added isopropenylmagnesium bromide 0.33 M (3.3 mL, 1.08 mmol) and stirred 20 minutes. Epoxide **1.51** (0.098 g, 0.54 mmol) was dissolved in diethylether (2.7 mL) and THF (1.5 mL) and canulated into the suspension of CuI. The reaction was allowed to warm to room temperature for 1 hour. A solution of saturated NH_4Cl-NH_4OH pH 8 was added to quench the reaction, and stirred for 30 minutes until the mixture turned light blue. The aqueous layer was extracted 3 times with diethylether (3 X 20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (45% EtOAc/hexanes) to afford 104 mg of **2.51** (95% yield) as a colourless oil.

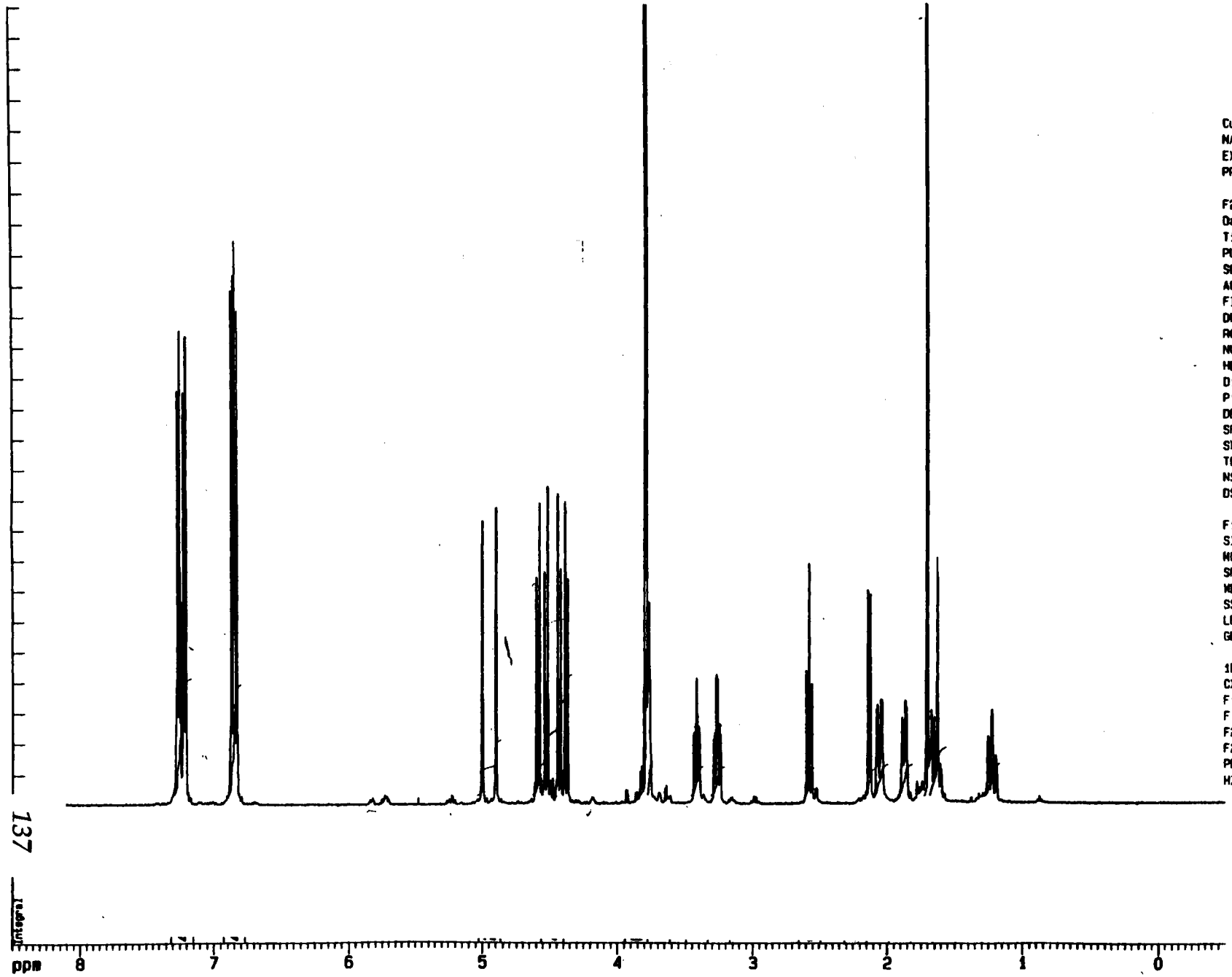
Data for **2.51**

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.26 (d, J= 8.7 Hz, 2H), 7.22 (d, J= 8.7 Hz, 2H), 6.86 (d, J= 8.7 Hz, 2H), 6.84 (d, J= 8.7 Hz, 2H), 5.00 (d, J= 1.4 Hz, 1H), 4.90 (d, J= 0.6 Hz, 1H), 4.61-4.36 (m, 4H), 3.79 (s, 3H), 3.78 (s, 3H), 3.76 (d, J= 2.3 Hz, 1H), 3.43-3.39 (m, 1H), 3.26 (dt, J= 4.2, 10.8 Hz, 1H), 2.57 (t, J= 10.6 Hz, 1H), 2.12 (d, J= 8.8 Hz, 1H), 2.05 (dq, 3.3, 14.5 Hz, 1H), 1.90 (s, 3H), 1.89-1.84 (m, 1H), 1.68-1.59 (m, 1H), 1.24-1.18 (m, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 159.2, 159.1, 143.5, 130.9, 130.8, 129.1 (x2), 114.6, 113.8, 113.7, 76.7, 75.6, 71.6, 70.8, 70.4, 55.2, 54.4, 24.7, 24.0, 19.4.

IR (neat) 3549, 2938, 2863, 1612, 1513, 1248, 1173, 1067.

EI HRMS calcd for $C_{25}H_{32}O_5$ (M+) 412.22498, obsd 412.2224.



Current Data Parameters
NAME lmo_193
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date 20020618
Time 7.36
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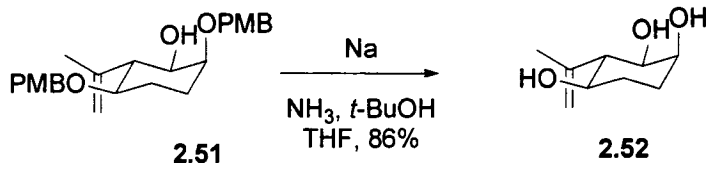
SOLVENT CDCl3
AQ 4.6530805 sec
FIDRES 0.107456 Hz
DW 71.0 usec
RG 256
NUCLEUS 1H
HL1 0 dB
D1 0.0100000 sec
P1 5.6 usec
DE 88.8 usec
SFO1 500.1381707 MHz
SWH 7042.25 Hz
TD 65536
NS 16
DS 0

F1 - Processing parameters
SI 32768
WC2 QF
SF 500.1354311 MHz
WDW EM
SSB 0
LB 0.00 Hz
GB 0

1D NMR plot parameters
CX 22.00 cm
F1P 8.500 ppm
F1 4251.15 Hz
F2P -0.500 ppm
F2 -250.07 Hz
PPMCM 0.40909 ppm/
HZCM 204.60086 Hz/



2.51 **2.52**

3-Isopropenyl-cyclohexane-1,2,4-triol (2.52)

Ammonia was condensed (12 mL) and sodium (0.417 g, 18 mmol) was added. The solution was stirred at -78°C for 30 minutes. tBuOH (0.57 mL, 6 mmol) was added followed by compound **2.51** (0.5 g, 1.2 mmol) in THF (4 mL). The reaction was allowed to warm to reflux and was stirred for 1 hour. The reaction was quenched by adding NH_4Cl. Ammonia was evaporated. The salts were stirred in methanol (20 mL), filtered and the solvent evaporated. The crude product was purified by flash chromatography (100% EtOAc to 10% MeOH/EtOAc) to afford 0.178 g of **2.52** (86% yield) as a yellow oil.

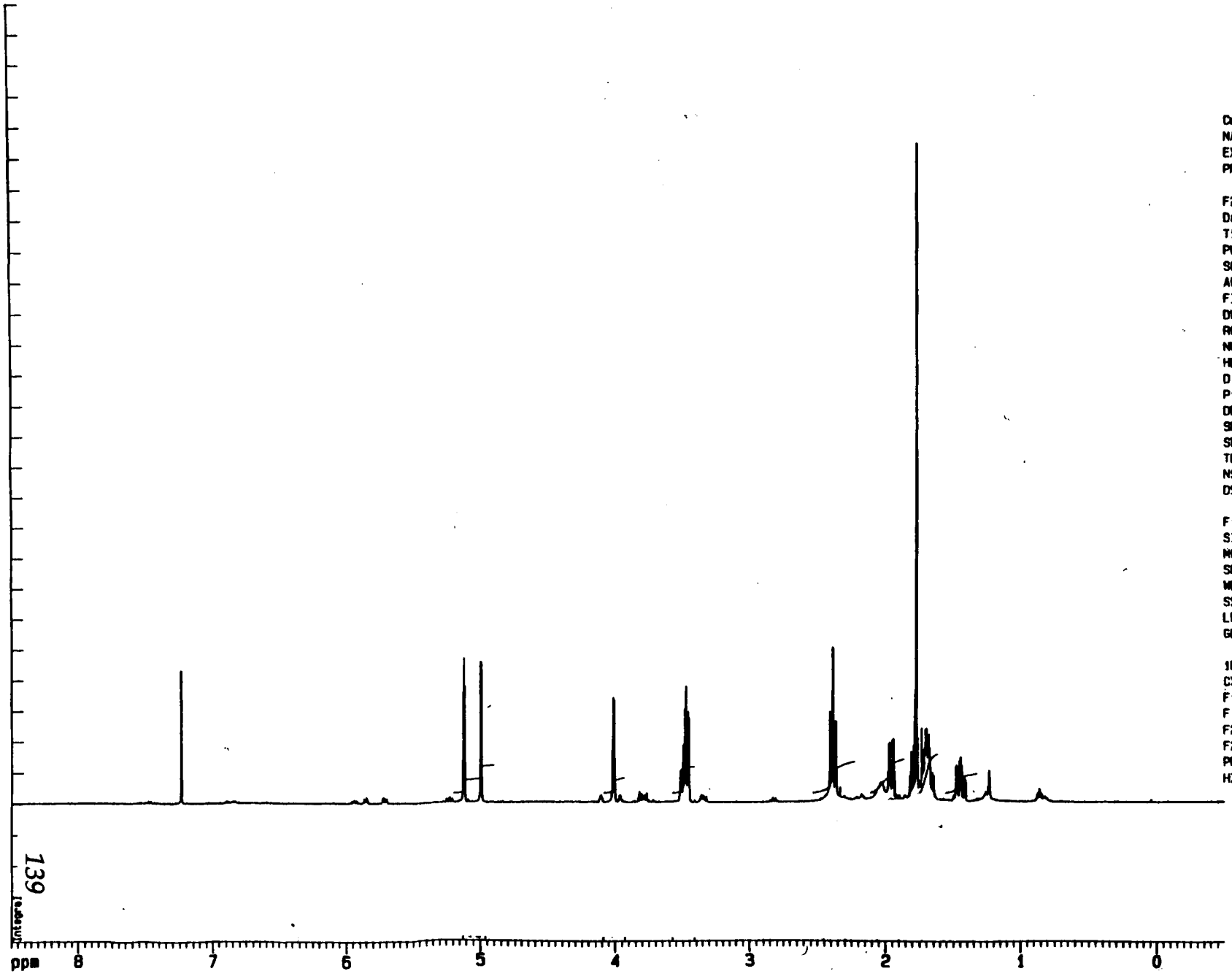
Data for **2.52**

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.12-5.11 (m, 1H), 4.99 (s, 1H), 4.01 (q, J= 3.0 Hz, 1H), 3.52-3.46 (m, 2H), 2.38 (t, J= 10.4 Hz, 2H), 2.03 (s, 1H), 1.95 (dq, 3.5, 14.6 Hz, 1H), 1.81-1.78 (m, 1H), 1.77 (s, 3H), 1.76-1.65 (m, 2H), 1.48-1.40 (m, 1H).

^{13}C NMR (500 MHz, $CDCl_3$) δ 142.3, 117.9, 70.8, 68.9, 67.5, 55.6, 27.3, 26.5, 17.9.

IR (neat) 3394, 2938, 1646, 1030.

EI HRMS calcd for $C_9H_{14}O_2$ (M+ - H_2O) 154.09938, obsd 154.0991.



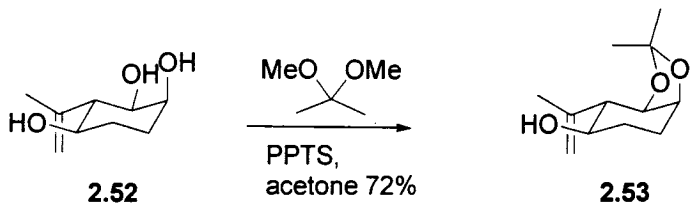
Current Data Parameters
NAME lmo_196
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date 20020620
Time 1.31
PULPROG zg
SOLVENT CDCl3
AQ 4.6530805 sec
FIDRES 0.107456 Hz
DW 71.0 usec
RG 512
NUCLEUS 1H
HL1 0 dB
D1 0.0100000 sec
P1 5.6 usec
DE 88.8 usec
SFO1 500.1381707 MHz
SWH 7042.25 Hz
TD 65536
NS 16
DS 0

F1 - Processing parameters
SI 32768
MC2 QF
SF 500.1354313 MHz
WDW EM
SSB 0
LB 0.00 Hz
GB 0

1D NMR plot parameters
CX 22.00 cm
F1P 8.500 ppm
F1 4251.15 Hz
F2P -0.500 ppm
F2 -250.07 Hz
PPMCM 0.40909 ppm/
HZCM 204.60086 Hz/

7.07



2.52 **2.53**

4-isopropropenyl-2,2-dimethyl-hexahydro-benzo[1,3]dioxol-5-ol (2.53)

Triol **2.52** (16 mg, .092 mmol) was dissolved in acetone (0.2 mL) amd 2,2-dimethoxypropane (0.115 mL, 0.93 mmol) was added, followed by PPTS (1 mg, 0.0046 mmol). The reaction was stirred for 4 hours and quenched by adding $NaHCO_{3sat.}$ The solvent was evaporated. The aqueous layer was extracted 3 times with ethylacetate (3 X 20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (30% EtOAc/hexanes to 80% EtOAc/hexanes) to afford 14 mg of **2.53** (72% yield) as a colourless oil.

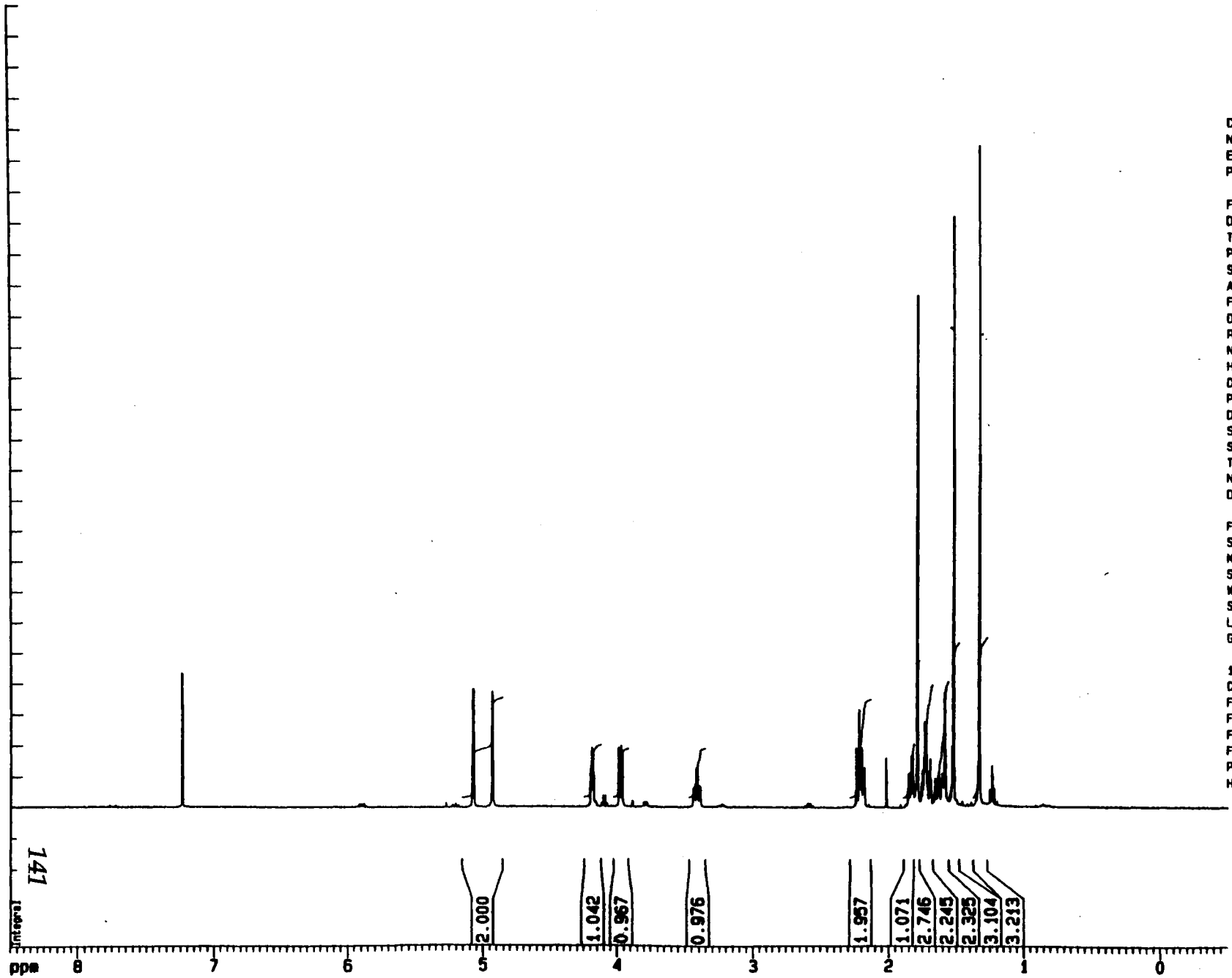
Data for **2.53**

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.08-5.07 (m, 1H), 4.93-4.92 (m, 1H), 4.20-4.18 (m, 1H), 3.97 (dd, J= 4.7, 9.4 Hz, 1H), 3.41 (dt, J= 3.7, 10.6 Hz, 1H), 2.24-2.17 (m, 2H), 1.86-1.81 (m, 1H), 1.79 (s, 3H), 1.76-1.65 (m, 1H), 1.63-1.58 (m, 2H), 1.52 (s, 3H), 1.33 (s, 3H).

^{13}C NMR ($CDCl_3$, 500 MHz) δ 142.7, 116.2, 108.7, 77.0, 72.8, 68.3, 57.3, 28.5, 28.1, 26.3, 23.7, 19.3.

IR (neat) 3443, 2933, 1647, 1035.

EI HRMS calcd for $C_{12}H_{18}O_2$ (M+ - H_2O) 194.13068, obsd 194.1301.

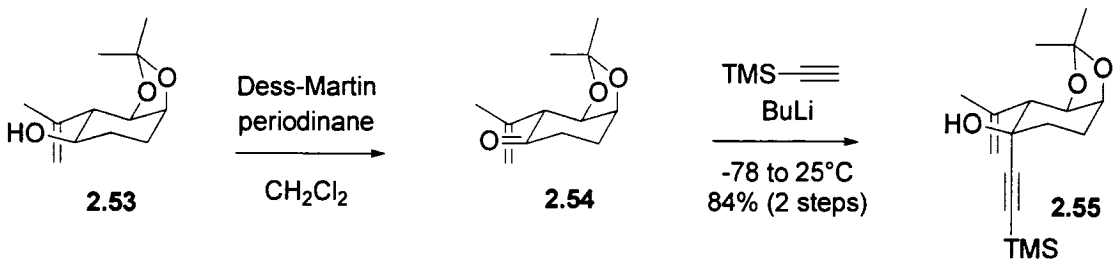


Current Data Parameters
NAME lmo_198
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date 20020626
Time 4.34
PULPROG zg
SOLVENT CDCl3
AQ 4.6530805 sec
FIDRES 0.107456 Hz
DW 71.0 usec
RG 1024
NUCLEUS 1H
HL1 0 dB
D1 0.0100000 sec
P1 5.6 usec
DE 88.8 usec
SFO1 500.1381707 MHz
SWH 7042.25 Hz
TD 65536
NS 32
DS 0

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

1D NMR plot parameters
CX 22.00 cm
F1P 8.500 ppm
F1 4251.15 Hz
F2P -0.500 ppm
F2 -250.07 Hz
PPMCM 0.40909 ppm/
HZCM 204.60086 Hz/



4-Isopropenyl-2,2-dimethyl-5-trimethylsilanylethynyl-hexahydro-benzo[1,3]dioxol-5-ol (2.55)

Alcohol **2.53** (0.014 g, 0.07 mmol) was dissolved in CH_2Cl_2 (1 mL) and Dess-Martin periodate (34 mg, 0.08 mmol) was added. The reaction was stirred for 3 hours at room temperature. A solution of $NaHCO_{3sat}$ was added, followed by Na_2SO_{3sat} and stirred for 20 minutes. The aqueous layer was extracted 3 times with dichloromethane (3 X 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (20% EtOAc/hexanes) to afford **2.54**, which was used directly for the next step.

Trimethylsilylacetylene (0.028 mL, 0.2 mmol) was dissolved in THF (1 mL) at -78°C, then butyllithium 2.7 M (0.07 mL, 0.196 mmol) was added dropwise. 15 minutes later, ketone **2.54** in THF (1 mL) was canulated into the solution of trimethylsilylacetylene. The reaction was stirred for 2 hours and quenched by adding methanol and saturated NH_4Cl_{aq}. The mixture was warmed to room temperature. The aqueous layer was extracted 3 times with diethylether (3 X 20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (10% EtOAc/benzene) to afford 18 mg of **2.55** (84% yield) as a colourless oil.

Data for **2.55**

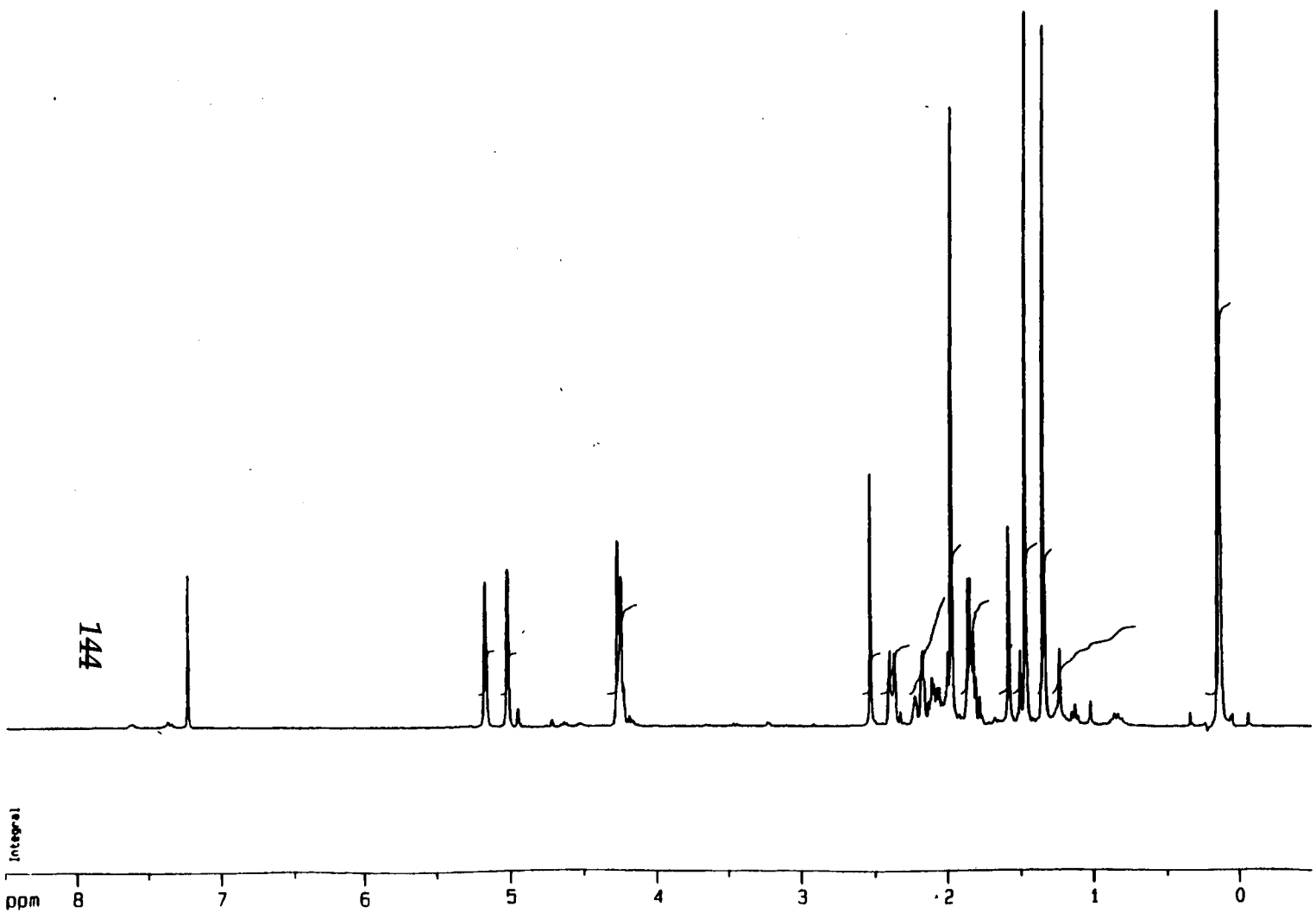
^{1}H NMR (300 MHz, $CDCl_3$): δ 5.02 (s, 1H), 4.27-4.23 (m, 2H), 2.52 (s, 1H), 2.40-2.36 (m, 1H), 2.22-2.02 (m, 2H), 1.97 (s, 3H), 1.86 (s, 2H), 1.46 (s, 3H), 1.34 (s, 3H), 0.14 (s, 1H), 0.14 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 141.6, 118.2, 108.4, 105.9, 92.3, 76.6, 72.6, 68.6, 57.6, 34.5, 28.5, 26.3, 23.8, 21.2, -0.3 (x3).

IR (neat) 3461, 2957, 2159, 1249, 1057.

EI HRMS indeterminable.

2.55



Current Data Parameters

NAME	1mo_222
EXPNO	5
PROCNO	1

F2 - Acquisition Parameters

Date_	20020806
Time	9.41
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PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	256
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

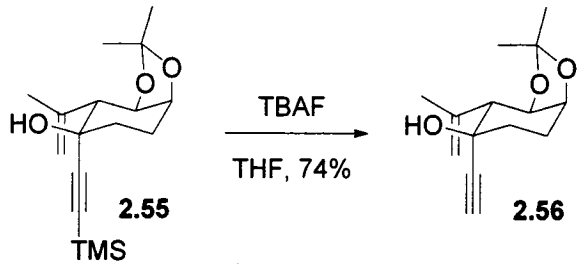
NUC1	1H
P1	8.00 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

F2 - Processing parameters

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

1D NMR plot parameters

CX	20.00 cm
CY	40.00 cm
F1P	8.500 ppm
F1	2551.10 Hz
F2P	-0.500 ppm
F2	-150.06 Hz
PPMCM	0.45000 ppm/cm
HZCM	135.05850 Hz/cm



5-Ethynyl-4-isopropenyl-2,2-dimethyl-hexahydro-benzo[1,3]dioxol-5-ol (2.56)

Compound **2.55** (0.018 g, 0.059 mmol) was dissolved in THF (1 mL), and TBAF 1 M (0.076 mL, 0.076 mmol) was added. The reaction was stirred for 1 hour and the solvent was evaporated. The crude product was purified by flash column chromatography (20% EtOAc/hexanes) to afford 10 mg of **2.56** (74% yield) as a colourless oil.

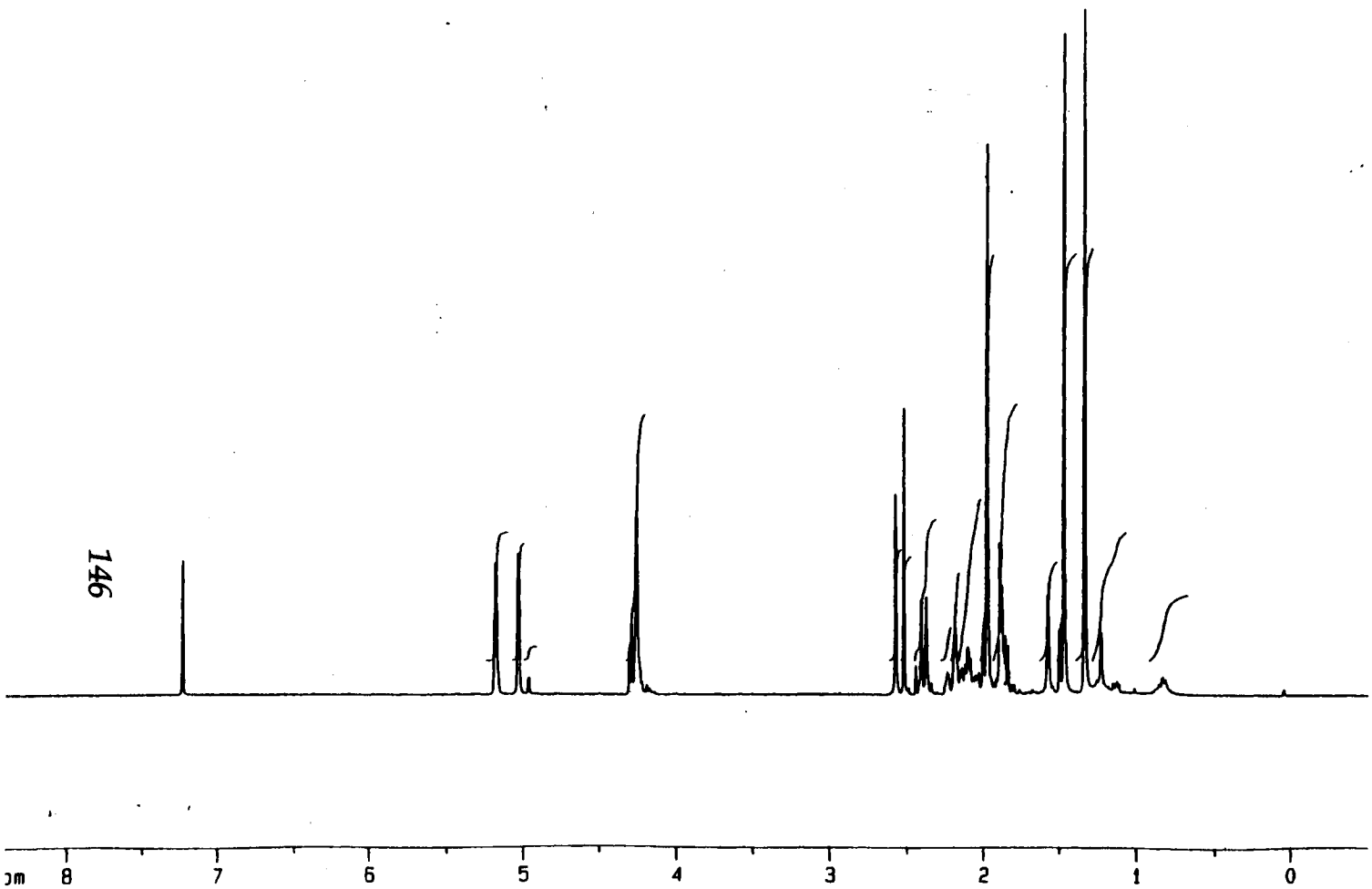
Data for **2.56**

^{1}H NMR (300 MHz, $CDCl_3$): δ 5.18 (s, 1H), 5.03 (s, 1H), 4.31-4.22 (m, 2H), 2.58 (s, 1H), 2.52 (s, 1H), 2.39 (d, J= 9.6 Hz, 1H), 2.24-2.03 (m, 2H), 1.97 (s, 3H), 1.89-1.79 (m, 2H), 1.49 (s, 3H), 1.34 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 141.5, 118.3, 108.4, 84.3, 76.5, 75.5, 72.6, 68.3, 57.5, 34.6, 28.5, 26.3, 23.6, 21.3.

IR (neat) 3460, 3261, 2944, 2869, 1059.

EI HRMS calcd for $C_{13}H_{17}O_3$ (M+ - Me) 221.11777, obsd 221.1182.



2.56

Current Data Parameters
NAME lmo_234
EXPNO 1
PROCNO 1

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PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 322.5
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

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

F2 - Processing parameters
SI 65536
SF 300.1300002 MHz
WDW EM
SSB 0
LB 0.10 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 20.00 cm
CY 10.00 cm
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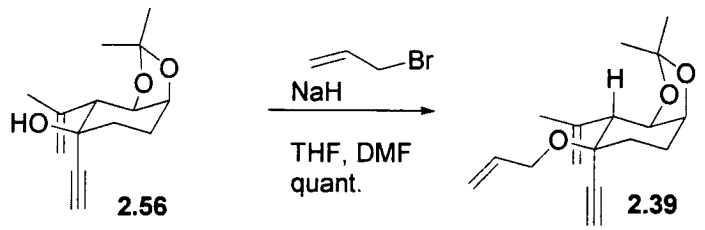
F1 2551.10 Hz
F2P -0.500 ppm
F2 -150.06 Hz
PPMCM 0.45000 ppm/cm
HZCM 135.05850 Hz/cm



5-Allyloxy-5-ethynyl-4-isopropenyl-2,2-dimethyl-hexahydro-benzo[1,3]dioxole (2.39)

Alcohol **2.56** (0.01 g, 0.042 mmol) was dissolved in THF (0.3 mL) and DMF (0.1 mL) The solution was cooled to 0°C. Sodium hydride 60 % (0.003 g, 0.085 mmol) was added, followed by allylbromide (0.014 mL, 0.085 mmol). The reaction was stirred for 3 hours, and quenched by adding saturated NH_4Cl_{aq}. The aqueous layer was extracted 3 times with diethylether (3 X 20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (20% EtOAc/hexanes) to afford 11 mg of **2.39** (94% yield) as a colourless oil.

Data for **2.39**

^{1}H NMR (300 MHz, $CDCl_3$): δ 5.94-5.82 (m, 1H), 5.29-5.22 (m, 1H), 5.11-5.02 (m, 3H), 4.32-4.15 (m, 3H), 4.04 (dd, J= 5.7, 13.0 Hz, 1H), 2.59 (s, 1H), 2.45 (d, J= 9.5 Hz, 1H), 2.37-2.15 (m, 1H), 2.10-2.03 (m, 1H), 1.93 (s, 3H), 1.81-1.65 (m, 2H), 1.49 (s, 3H), 1.33 (s, 3H).

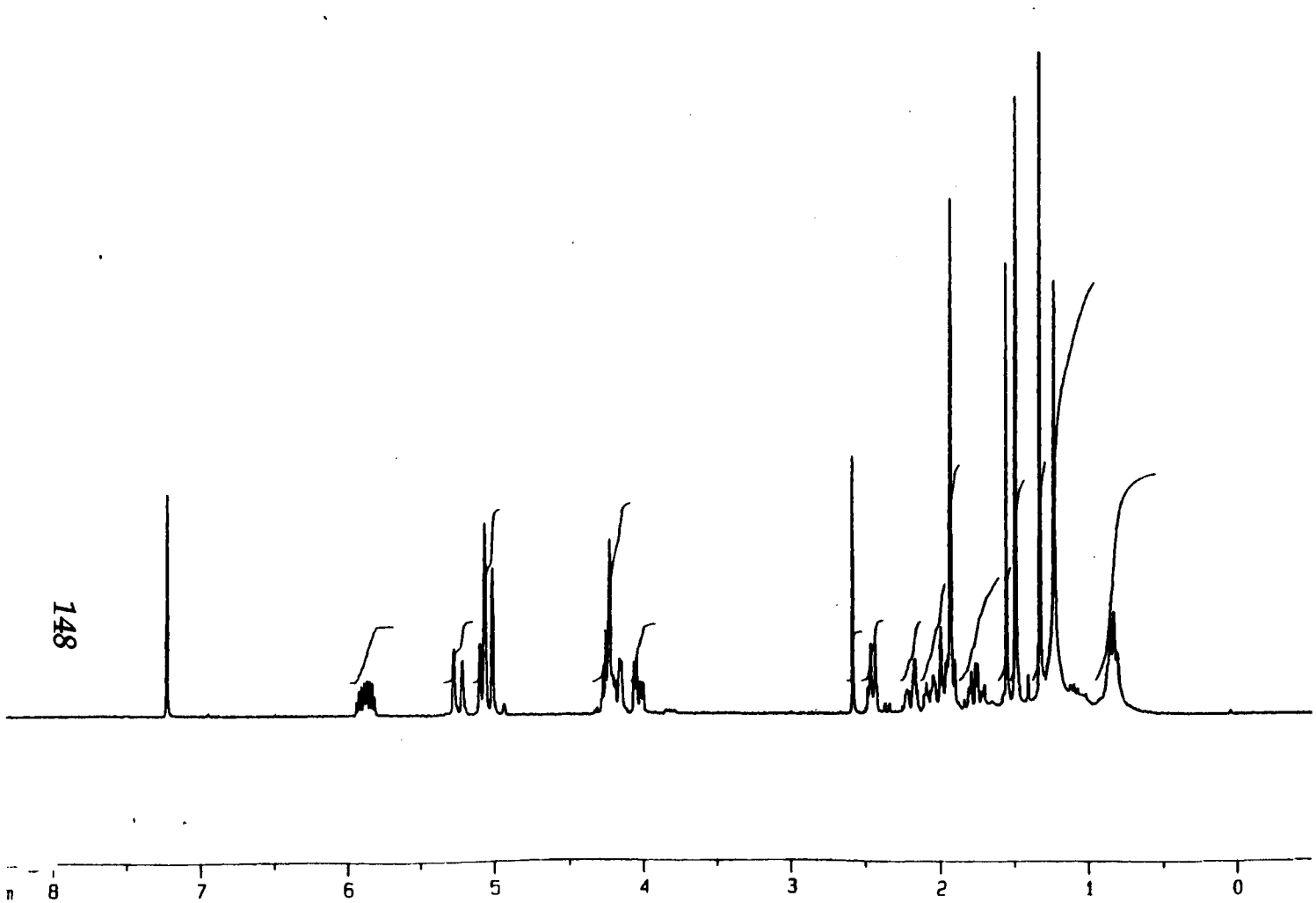
^{13}C NMR (75 MHz, $CDCl_3$) δ 142.7, 135.2, 115.7, 114.5, 108.2, 81.1, 78.3, 77.7, 72.5, 64.7, 55.4, 32.4, 29.7, 28.5, 26.3, 24.2, 23.7.

IR (neat) 3304, 2925, 2863, 1238, 1048.

HRMS EI calculated 276.1725, found 261.15045 (M+ -Me), 220.1466 (M+ -Me –Allyl).

EI HRMS calcd for $C_{16}H_{21}O_3$ (M+ - Me) 261.14907, obsd 261.15045

2.39



Current Data Parameters

NAME	Imo_236
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

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Time	9.02
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	322.5
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

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

F2 - Processing parameters

SI	65536
SF	300.1299999 MHz
WDW	EM
SSB	0
LB	0.10 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	20.00 cm
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F2P	-0.500 ppm
F2	-150.06 Hz
PPMCM	0.45000 ppm/cm
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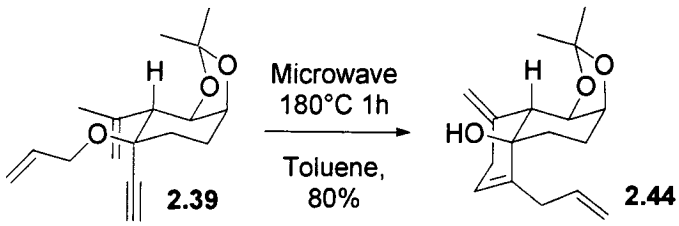


6-Allyl-2,2-dimethyl-9-methylene-4,5,8,9,9a,9b-hexahydro-3aH-naphtho[1,2-d][1,3]dioxol-5a-ol (2.44)

To a solution of **2.39** (0.081 g, 0.29 mmol) in toluene (18 mL) was added triethylamine (0.1 mL). The solution was sparged by bubbling with argon for 20 min. . The tube was sealed, fitted with temperature and pressure probes, and placed in the microwave. The temperature was ramped gradually to 210 °C, and was held there for 1 hour. The solvent was evaporated. The crude product was purified by flash column chromatography (20% EtOAc/hexanes) to afford 65 g of **2.44** (80% yield) as a colourless oil.

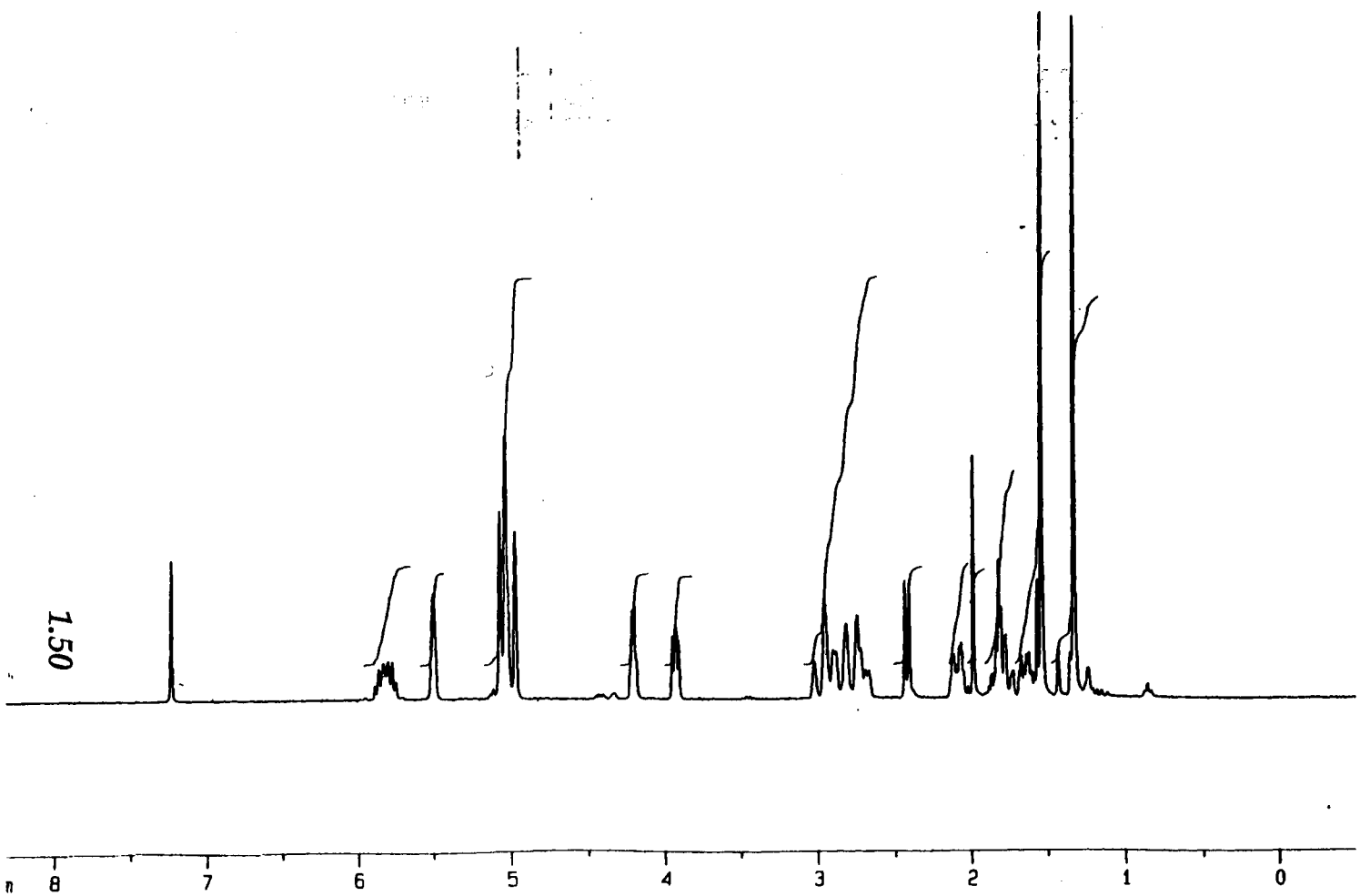
Data for **2.44**

^{1}H NMR (300 MHz, $CDCl_3$): δ 5.89-5.75 (m, 1H), 5.51 (s, 1H), 5.06 (d, J= 11 Hz, 2H), 5.0 (d, J= 19 Hz, 2H), 4.22-4.20 (m, 1H), 3.93 (dd, J= 8, 5 Hz, 1H), 3.02-2.67 (m, 4H), 2.42 (d, J= 8 Hz, 1H), 2.12-2.02 (m, 1H), 1.99 (s, 1H), 1.88-1.77 (m, 2H), 1.73-1.59 (m, 1H), 1.54 (s, 3H), 1.33 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$): 141.1, 139.1, 136.6, 127.5, 116.6, 113.7, 108.7, 75.2, 72.5, 72.4, 55.0, 34.9, 31.6, 28.4, 27.9, 26.2, 23.2.

IR (neat) 3502, 2983, 2942, 1228 cm^{-1}.

EI HRMS calcd for $C_{16}H_{21}O_3$ (M+) 276.17255, obsd 276.17404.



2.44

Current Data Parameters

NAME	lmo_813
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

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Time	16.46
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	322.5
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

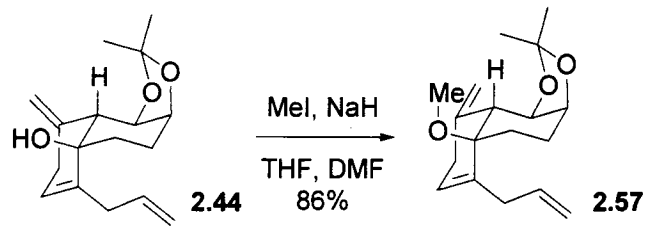
NUC1	1H
P1	10.50 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

F2 - Processing parameters

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

1D NMR plot parameters

CX	20.00 cm
CY	10.00 cm
F1P	8.500 ppm
F1	2551.10 Hz
F2P	-0.500 ppm
F2	-150.06 Hz
PPMCM	0.45000 ppm/cm
HZCM	135.05850 Hz/cm



2.44 **2.57**

6-Allyl-5a-methoxy-2,2-dimethyl-9-methylene-3a,4,5,5a,8,9,9a,9b-octahydro-naphtho[1,2-d][1,3]dioxole (2.57)

To a solution of alcohol **2.44** (0.011 g, 0.04 mmol) in THF (0.6 mL) and DMF (0.2 mL) was added NaH (0.003 g, 0.08 mmol). The reaction was stirred for 20 min. MeI (0.005 mL, 0.08 mmol) was added and the reaction was stirred for 24 hours. The solvent was evaporated. The crude product was purified by flash column chromatography (10% EtOAc/hexanes) to afford 10 mg of **2.57** (86% yield) as a colourless oil.

Data for **2.57**

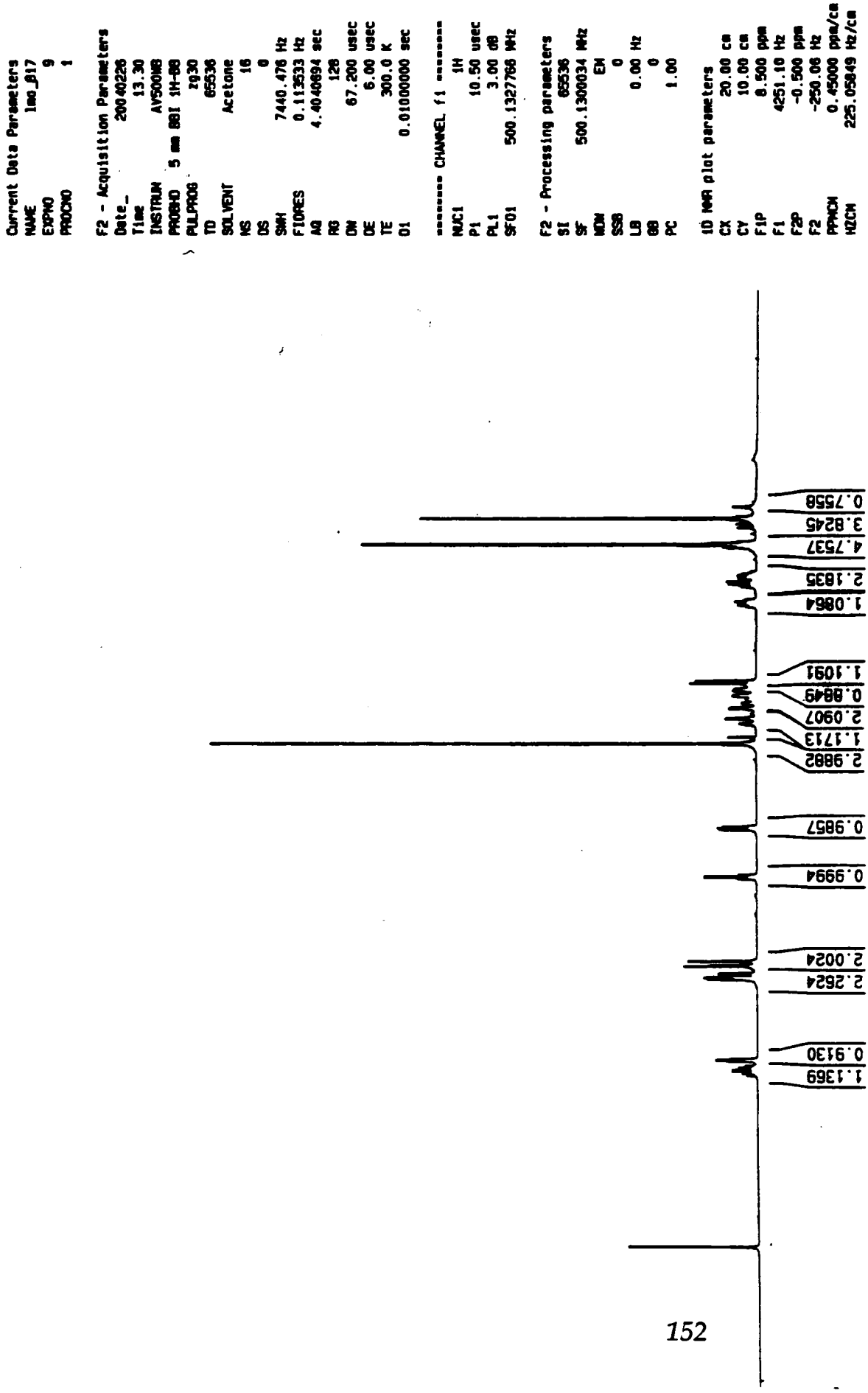
^{1}H NMR (500 MHz, $CDCl_3$): δ 5.84-5.76 (m, 1H), 5.72 (s, 1H), 5.06-5.01 (m, 2H), 4.94 (d, J= 19 Hz, 2H), 4.23 (q, J= 6 Hz, 1H), 3.84 (dd, J= 9, 6 Hz, 1H), 3.15 (s, 3H), 2.99-2.94 (m, 1H), 2.86-2.68 (m, 3H), 2.65 (d, J= 9 Hz, 1H), 2.04-1.99 (m, 1H), 1.87-1.76 (m, 2H), 1.58-1.51 (m, 1H), 1.54 (s, 3H), 1.33 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): 142.3, 136.3, 136.0, 127.2, 115.3, 112.0, 108.7, 77.5, 75.1, 72.9, 50.9, 50.8, 34.4, 31.2, 28.5, 28.1, 25.8, 23.1.

IR (neat) 2987, 2933, 1219, 1067 cm^{-1}.

EI HRMS calcd for $C_{17}H_{23}O_3$ (M+) 290.18820, obsd 290.18823.

2.57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EXPNO 9
PROCNO 1
F2 - Acquisition Parameters
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Time 13.30
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PROBHD 5 mm BBI 1H-BB
PULPROG zg30
TD 65536
SOLVENT Acetone
NS 16
DS 0
SWH 7440.476 Hz
FIDRES 0.113533 Hz
AQ 4.4040894 sec
RG 128
DW 67.200 usec
DE 6.00 usec
TE 300.0 K
D1 0.01000000 sec
======= CHANNEL f1 =======
NUC1 1H
P1 10.50 usec
PL1 3.00 dB
SFO1 500.1327768 MHz
F2 - Processing parameters
SI 65536
SF 500.1300034 MHz
WDW EM
SSB 0
LB 0.00 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 20.00 cm
CY 10.00 cm
F1P 8.500 ppm
F1 4251.10 Hz
F2P -0.500 ppm
F2 -250.06 Hz
PPMCM 0.45000 ppm/cm
HZCM 225.05849 Hz/cm
0.7558
3.8245
4.7537
2.1835
1.0864
1.1091
0.8849
2.0907
1.1713
2.9882
0.9857
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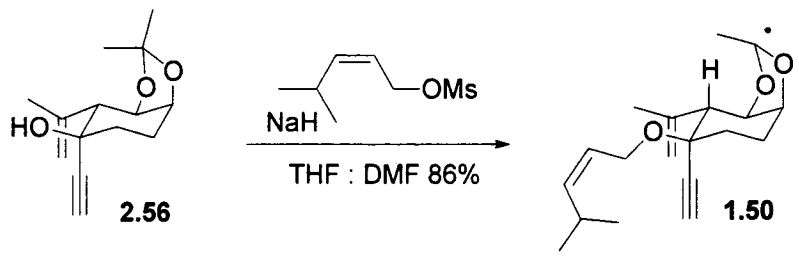
2.2624
0.9130
1.1369



5-Ethynyl-4-isopropenyl-2,2-dimethyl-5-(4-methyl-pent-2-enyloxy)-hexahydro-benzo[1,3]dioxole (1.50)

Z-4-methylpent-2-en-1-ol (0.04 g, 0.4 mmol) was dissolved in dichloromethane (4 mL) and triethylamine (0.178 mL, 1.28 mmol) was added. The solution was cooled to 0°C followed by addition of mesylchloride (0.031 mL, 0.4 mmol). The reaction was warmed to room temperature for 20 minutes. The reaction was done and quenched by adding saturated NH_4Cl_{aq}. The aqueous layer was extracted 3 times with dichloromethane (3 X 30 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was used directly to avoid decomposition. In the meantime a solution of alcohol **2.56** (0.010 g, 0.04 mmol) in THF (1 mL) and DMF (0.3 mL) was cooled to 0°C. NaH 60 % (0.024 g, 0.06 mmol) was added and the reaction was stirred at 0°C for 20 minutes. That solution was canulated in a solution of crude mesylated alcohol in THF (1 mL) (precooled at 0°C). The solution was warmed slowly to room temperature for 15 hours. The reaction was quenched by adding saturated NH_4Cl_{aq}. The aqueous layer was extracted 3 times with diethylether (3 X 20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (5% EtOAc /94% hexanes/1% Et_3N) to afford 11 mg of **1.50** (86% yield) as a colourless oil.

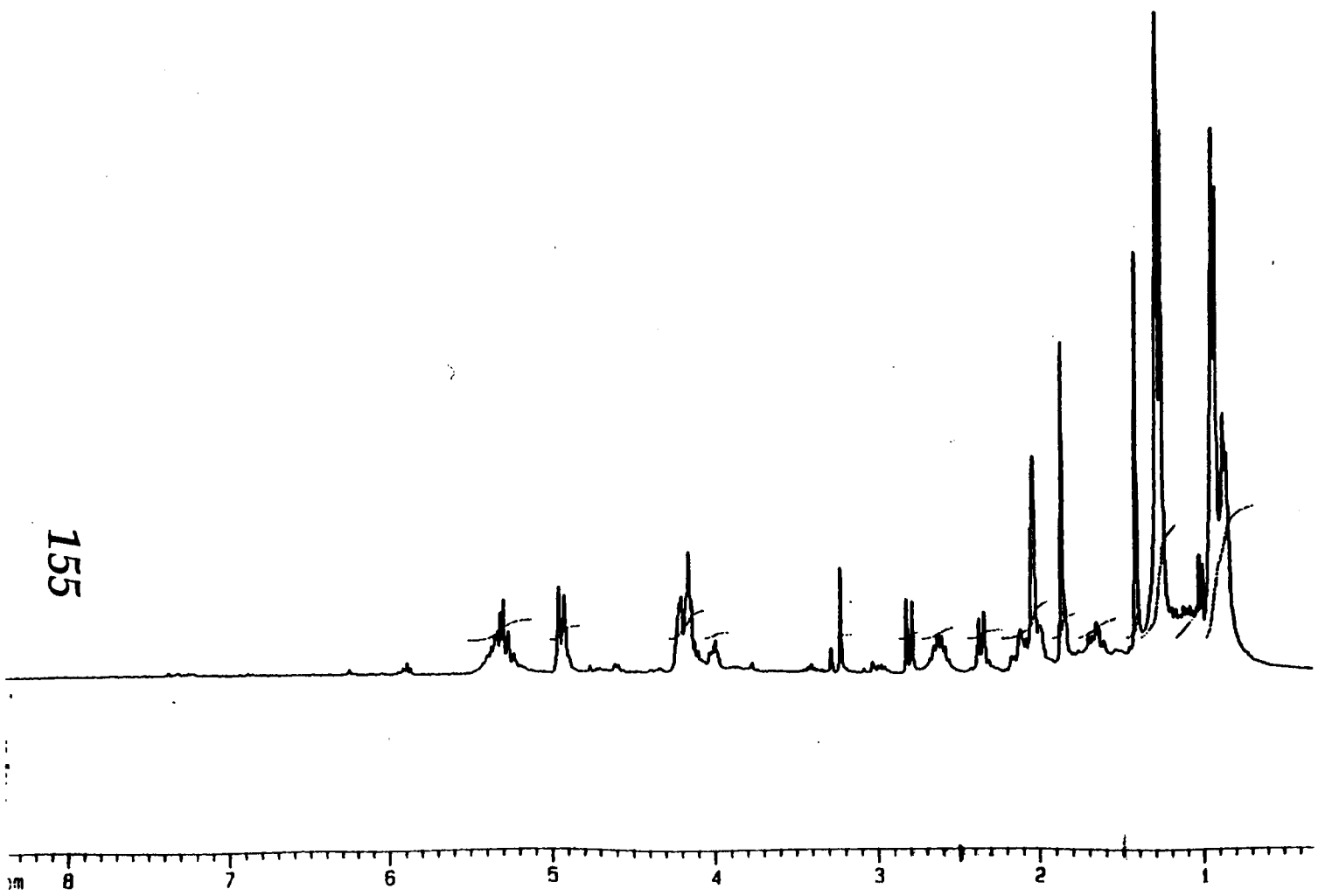
Data for **1.50**

^{1}H NMR (300 MHz, acetone-d_6): δ 5.42-5.19 (m, 2H), 4.94 (d, J= 10 Hz, 2H), 4.21-4.12 (m, 4H), 2.68-2.56 (m, 1H), 2.35 (d, J= 10 Hz, 1H), 2.18-2.00 (m, 4H), 1.84-1.54 (m, 1H), 1.41 (s, 3H), 1.28 (s, 3H), 1.25 (s, 3H), 1.02 (s, 3H), 1.00 (s, 3H).

^{13}C NMR (75 MHz, acetone-d_6) 143.1, 139.8, 125.0, 113.9, 107.8,81.5, 79.7, 78.1, 78.0, 72.8, 59.8, 55.8, 32.7, 28.4, 27.2, 26.1, 24.5, 23.9, 22.8, 22.7.

IR (neat) 2957, 2926, 2869, 1060 cm^{-1}.

EI HRMS calcd for $C_{19}H_{27}O_3$ (M+ - Me) 303.19602, obsd 303.19743.



Current Data Parameters

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EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

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PULPROG	zg30
TD	30720
SOLVENT	Acetone
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	143.7
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

---------- CHANNEL f1 ----------

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

F2 - Processing parameters

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

1D NMR plot parameters

CX	20.00 cm
CY	10.00 cm
F1P	8.486 ppm
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F2P	0.320 ppm
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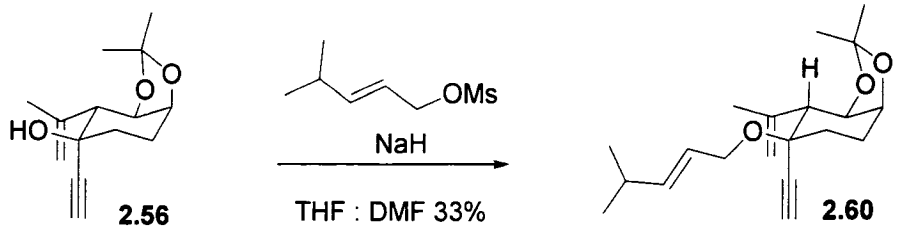
PPMCM	0.40831 ppm/cm
HZCM	122.54634 Hz/cm



2.56 **2.60**

5-Ethynyl-4-isopropenyl-2,2-dimethyl-5-(4-methyl-pent-2-enyloxy)-hexahydro-benzo[1,3]dioxole (2.60)

E-4-methylpent-2-en-1-ol (0.173 g, 1.73 mmol) was dissolved in dichloromethane (18 mL) and triethylamine (0.770 mL, 5.5 mmol) was added. The solution was cooled to 0°C and mesylchloride (0.133 mL, 1.73 mmol) was added. The reaction was warmed to room temperature for 30 minutes. The reaction was quenched by adding saturated NH_4Cl_{aq}. The aqueous layer was extracted 3 times with dichloromethane (3 X 40 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was used directly to avoid decomposition. In the meantime a solution of alcohol **2.56** (0.020 g, 0.085 mmol) in THF (1 mL) and DMF (0.6 mL) was cooled to 0°C and NaH (0.040 g, 1 mmol) was added. The reaction was stirred at 0°C for 20 minutes. That solution was canulated in a solution of crude mesylated alcohol in THF (1 mL) (precooled at 0°C). The solution was warmed slowly to room temperature for 15 hours. The reaction was quenched by adding saturated NH_4Cl_{aq}. The aqueous layer was extracted 3 times with diethylether (3 X 20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (10% Et_2O/hexanes) to afford 9 mg of **2.60** (33% yield) as a colorless oil.

Data for **2.60**

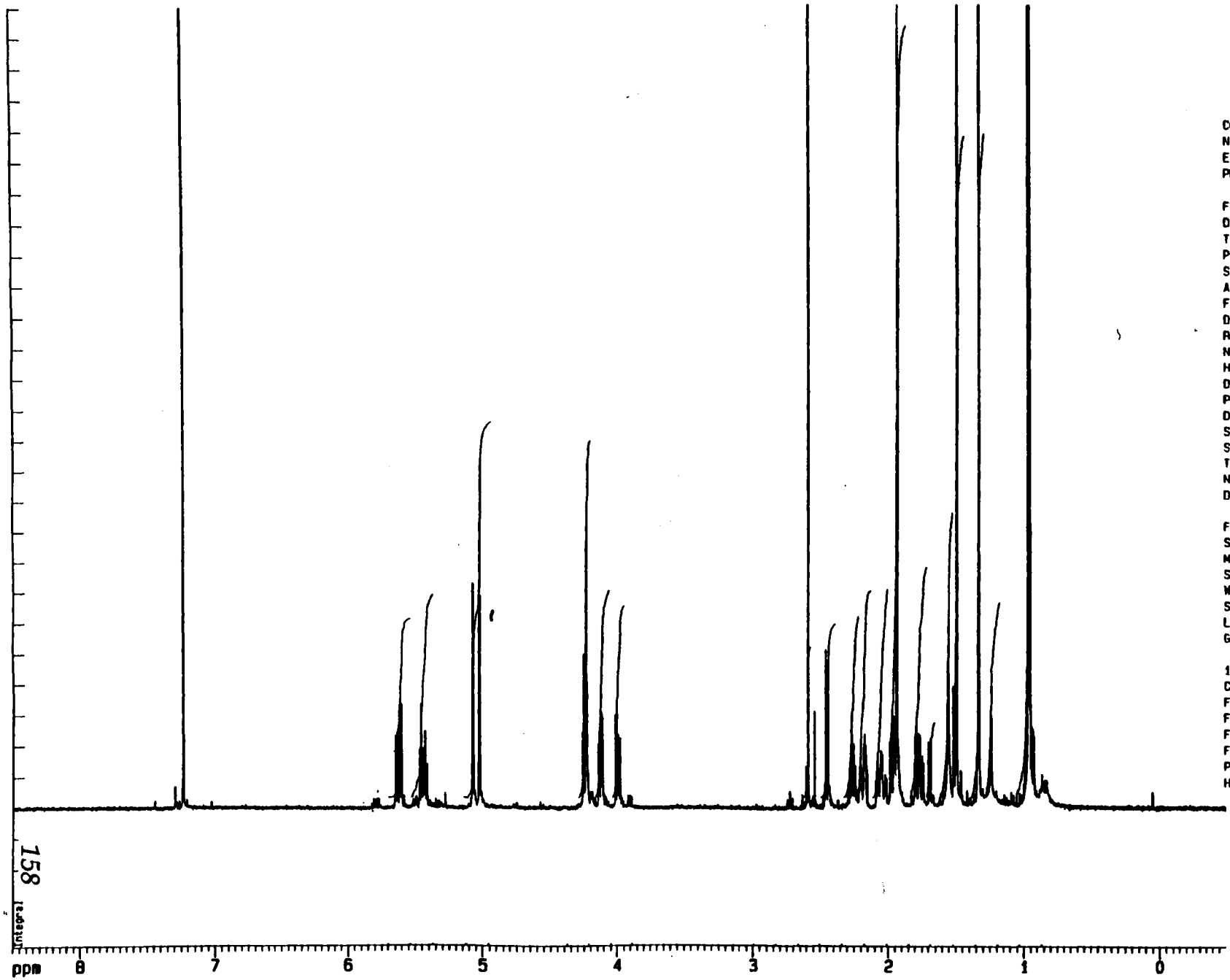
^{1}H NMR (500 MHz, $CDCl_3$): δ 5.62 (ddt, 16, 6, 1 Hz, 1H), 5.47-5.41 (m, 1H), 5.07 (t, J= 2 Hz, 1H), 5.02 (s, 1H), 4.26-4.22 (m, 2H), 4.12 (qt, 5, 2 Hz, 1H), 4.01-3.97 (m, 1H), 2.58 (s, 1H), 2.44 (d, J= 10 Hz, 1H), 2.28-2.21 (m, 1H), 2.20-2.15 (m, 1H), 2.08-2.02 (m, 1H), 1.98-

1.94 (m, 1H), 1.93 (s, 3H), 1.80-1.73 (m, 1H), 1.49 (s, 3H), 1.33 (s, 3H), 0.95 (d, J= 7 Hz, 6H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 142.8, 140.1, 123.9, 114.4, 108.1, 80.4, 78.2, 77.8, 76.4, 72.6, 65.0, 55.4, 32.6, 30.7, 28.5 x2, 26.3, 24.3, 23.7, 22.2.

IR (neat) 2958, 2933, 2871, 1061 cm^{-1}.

EI HRMS calcd for $C_{19}H_{27}O_3$ (M+ - Me) 303.19602, obsd 303.19418.



Current Data Parameters
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EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
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Time 17.07
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SOLVENT CDCl3
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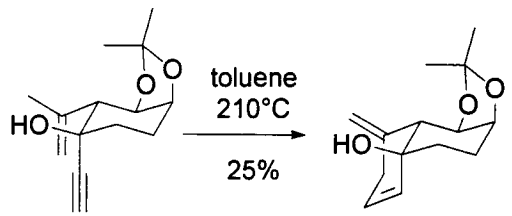
FIDRES 0.107456 Hz
DW 71.0 usec
RG 1024
NUCLEUS 1H
HL1 0 dB
D1 0.0100000 sec
P1 5.6 usec
DE 88.8 usec
SFO1 500.1381707 MHz
SWH 7042.25 Hz
TD 65536
NS 8
DS 0

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

1D NMR plot parameters
CX 22.00 cm
F1P 8.500 ppm
F1 4251.15 Hz
F2P -0.500 ppm
F2 -250.07 Hz
PPMCM 0.40909 ppm/
HZCM 204.60086 Hz/

7.0U



2.56 **2.66**

2,2-Dimethyl-9-methylene-4,5,8,9,9a,9b-hexahydro-3aH-naphtho[1,2-d][1,3]dioxol-5a-ol (2.66)

To a solution of alcohol **2.56** (0.012 g, 0.05 mmol) in toluene (1.5 mL) was added triethylamine (0.3 mL The tube was sealed, fitted with temperature and pressure probes, and placed in the microwave. The temperature was ramped gradually to 210 °C, and was held there for 1 hour. The solvent was evaporated. The crude product was purified by flash column chromatography (10% EtOAc/hexanes) to afford 3 g of **2.66** (25% yield) as a colourless oil.

Data for **2.66**

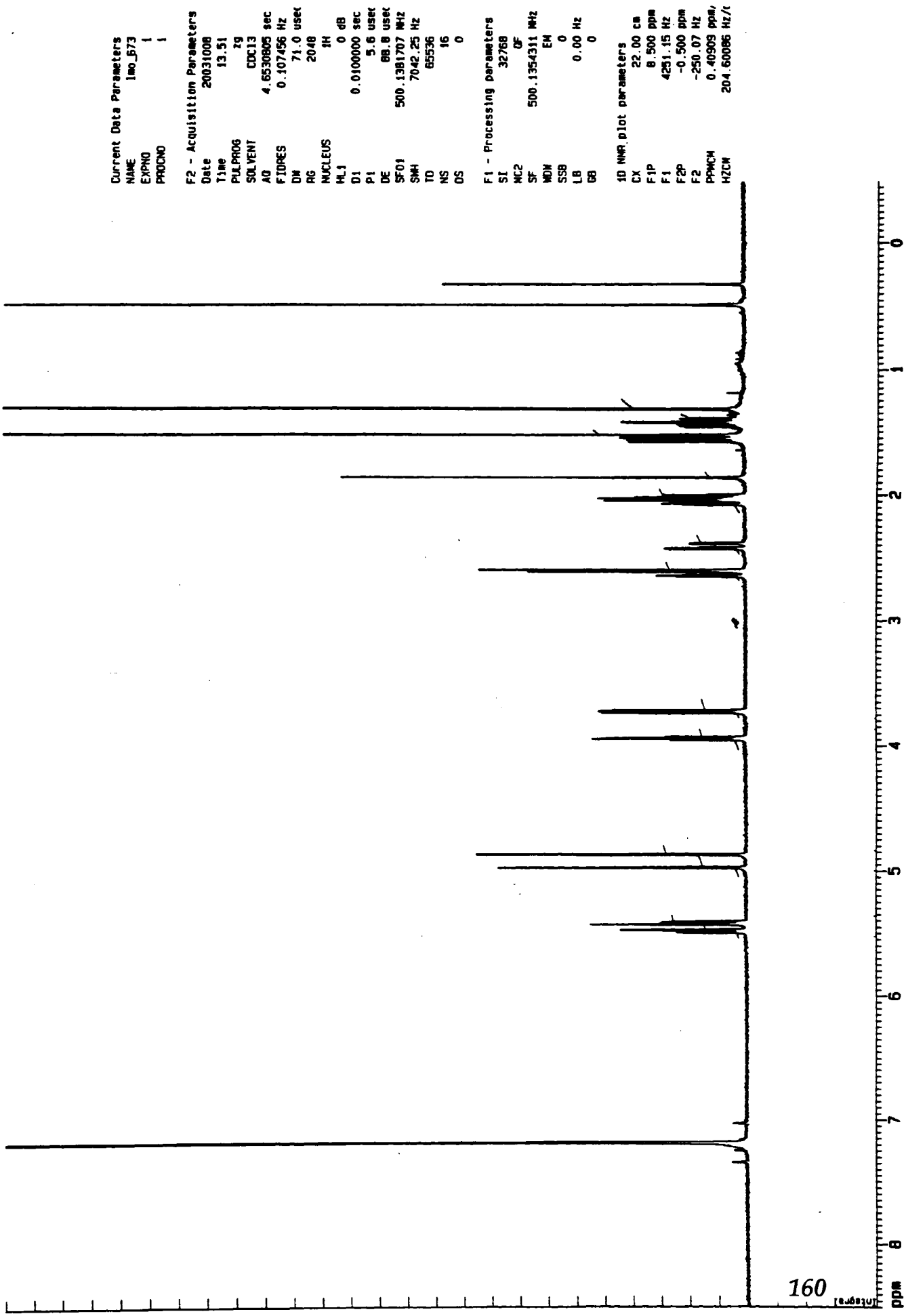
^{1}H NMR (500 MHz, C_6D_6): δ 5.50-5.46 (m, 1H), 5.41 (dt, J= 10, 3 Hz, 1H), 4.98-4.97 (m, 1H), 4.87-4.86 (m, 1H), 3.93 (q, J= 7 Hz, 1H), 3.72 (dd, J= 8, 5 Hz, 1H), 2.61-2.59 (m, 2H), 2.43-2.38 (m, 1H), 2.08-1.99 (m, 2H), 1.86 (s, 1H), 1.57-1.53 (m, 1H), 1.52 (s, 3H), 1.45-1.38 (m, 1H), 1.31 (s, 3H).

^{13}C NMR (125 MHz, C_6D_6) δ 141.8, 133.0, 129.1, 113.6, 108.3, 75.5, 72.7, 70.4, 55,2, 31.3, 31.2, 28.5, 26.5, 23.6.

IR (neat) 2480, 2983, 2935, 2869, 1217, 1052 cm^{-1}.

EI HRMS calcd for $C_{14}H_{18}O_2$ (M+ - H_2O) 218.13068, obsd 218.1261.

2.66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PROCNO 1
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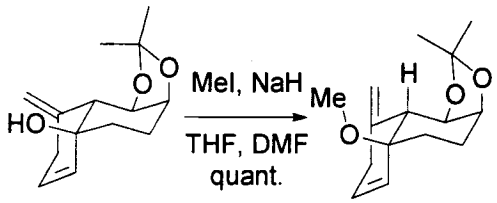
FIDRES 0.107456 Hz
DW 71.0 usec
RG 2048
NUCLEUS 1H
HL1 0 dB
D1 0.0100000 sec
P1 5.6 usec
DE 88.8 usec
SFO1 500.1381707 MHz
SWH 7042.25 Hz
TD 65536
NS 16
DS 0
F1 - Processing parameters
SI 32768
WC2 QF
SF 500.1354311 MHz
WDW EM
SSB 0
LB 0.00 Hz
GB 0
1D NMR plot parameters
CX 22.00 cm
F1P 8.500 ppm
F1 4251.15 Hz
F2P -0.500 ppm
F2 -250.07 Hz
PPMCM 0.40909 ppm/
HZCM 204.60086 Hz/
ppm
Integral



2.66 **2.67**

5a-Methoxy-2,2-dimethyl-9-methylene-3a,4,5,5a,8,9,9a,9b-octahydro-naphtho[1,2-d][1,3]dioxole (2.67)

To a solution of alcohol **2.67** (0.002 g, 0.008 mmol) in THF (0.1 mL) and DMF (0.3 mL) was added NaH (0.001 g, 0.016 mmol). The reaction was stirred for 5 minutes and MeI (0.005 mL, 0.016 mmol) was added. The reaction was stirred 2 hours. The solvent was evaporated. The crude product was purified by flash column chromatography (10% EtOAc/hexanes) to afford 2 mg of **2.67** (100% yield) as a colourless oil.

Data for**2.67**

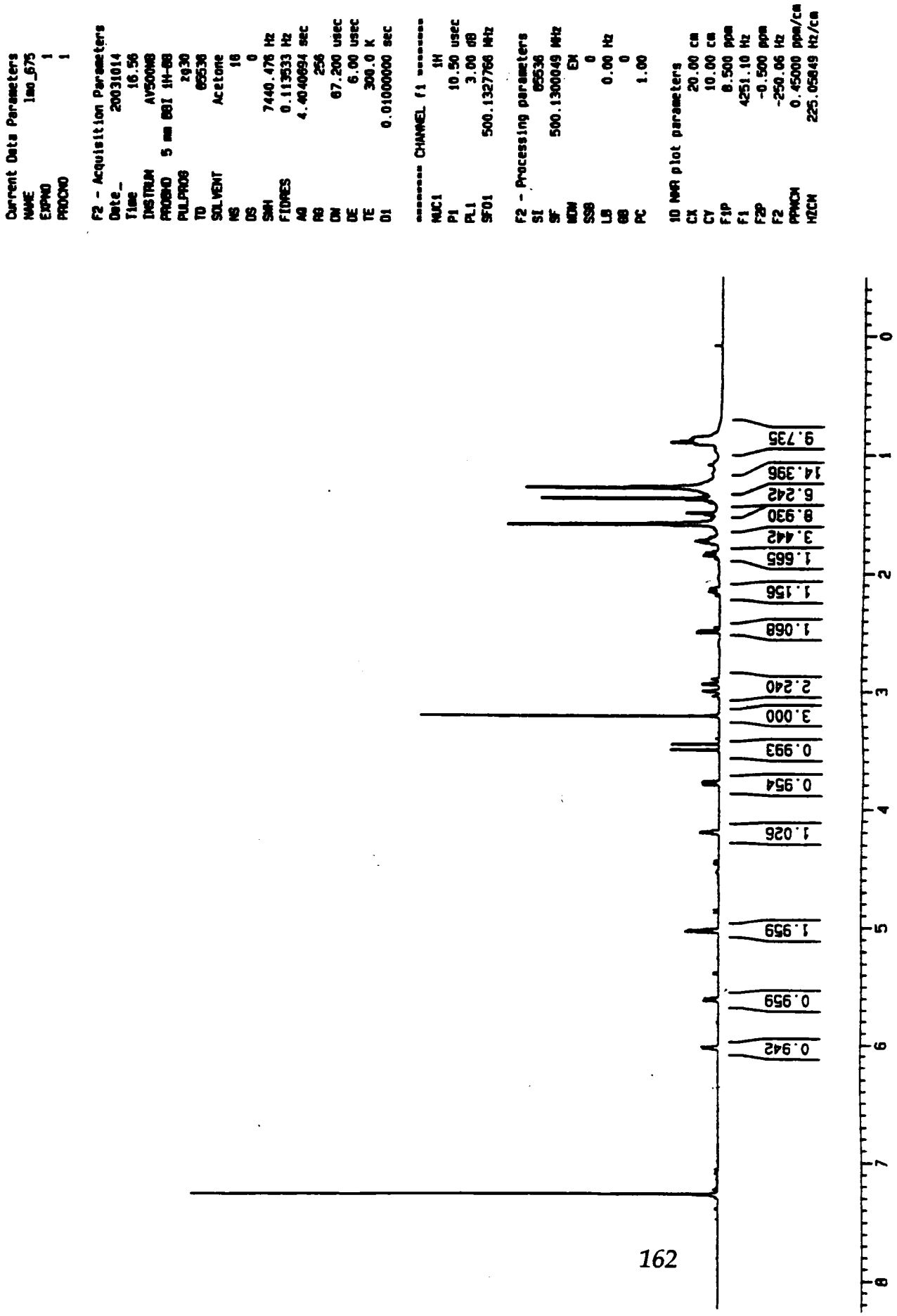
^{1}H NMR (500 MHz, $CDCl_3$): δ 6.04 (dt, J= 10, 4 Hz, 1H), 5.61 (d, J= 10 Hz, 1H), 5.03 (d, J= 9 Hz, 2H), 4.20 (dt, J= 5, 4 Hz, 1H), 3.79 (d, J= 9, 5 Hz, 1H), 3.48 (d, J= 25 Hz, 1H), 3.21 (s, 3H), 3.05-2.90 (m, 1H), 2.49 (d, J= 9 Hz, 1H), 2.17-2.12 (m, 1H), 1.87-1.81 (m, 1H), 1.75-1.68 (m, 2H), 1.36 (s, 3H), 1.27 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 141.2, 132.5, 128.4, 113.2, 108.6, 75.6, 74.4, 100.0, 72.6, 52.0, 30.2, 29.7, 28.3, 28.0, 26.2.

IR (neat) 2926, 2855, 1058 cm^{-1}.

EI HRMS calcd for $C_{14}H_{19}O_3$ (M+ - Me) 235.13342, obsd 235.13312.

2.67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SOLVENT Acetone
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DS 0
SWH 7440.476 Hz
FIDRES 0.113533 Hz
AQ 4.4040694 sec
RG 256
DW 67.200 usec
DE 6.00 usec
TE 300.0 K
D1 0.01000000 sec
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PL1 3.00 dB
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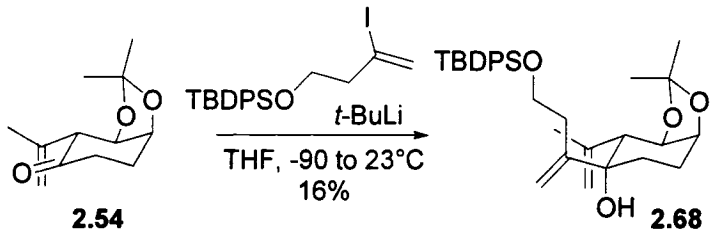
8



2.54 **2.68**

5-{1-[2-(tert-Butyl-diphenyl-silanyloxy)-ethyl]-vinyl}-4-isopropenyl-2,2-dimethyl-hexahydro-benzo[1,3]dioxol-5-ol (2.68)

*t*Butyldiphenylsilyloxy-3-iodobut-3-en-1-ol (0.087 g, 0.2 mmol) was dissolved in THF (3 mL) and the solution was cooled to -90°C. *t*BuLi 1.7 M (0.23 mL, 0.39 mmol) was added. The reaction was stirred at -90°C for 45 min. A solution of ketone **2.54** (0.020 g, 0.13 mmol) precooled at -90°C was canulated in the vinyl solution and stirred for 1 hour. The reaction was allowed to warm slowly to room temperature. The reaction was quenched by adding saturated NH_4Cl_{aq}. The aqueous layer was extracted 3 times with diethylether (3 X 20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (10% EtOAc/hexanes) to afford 11 mg of **2.68** (16% yield) as a colourless oil.

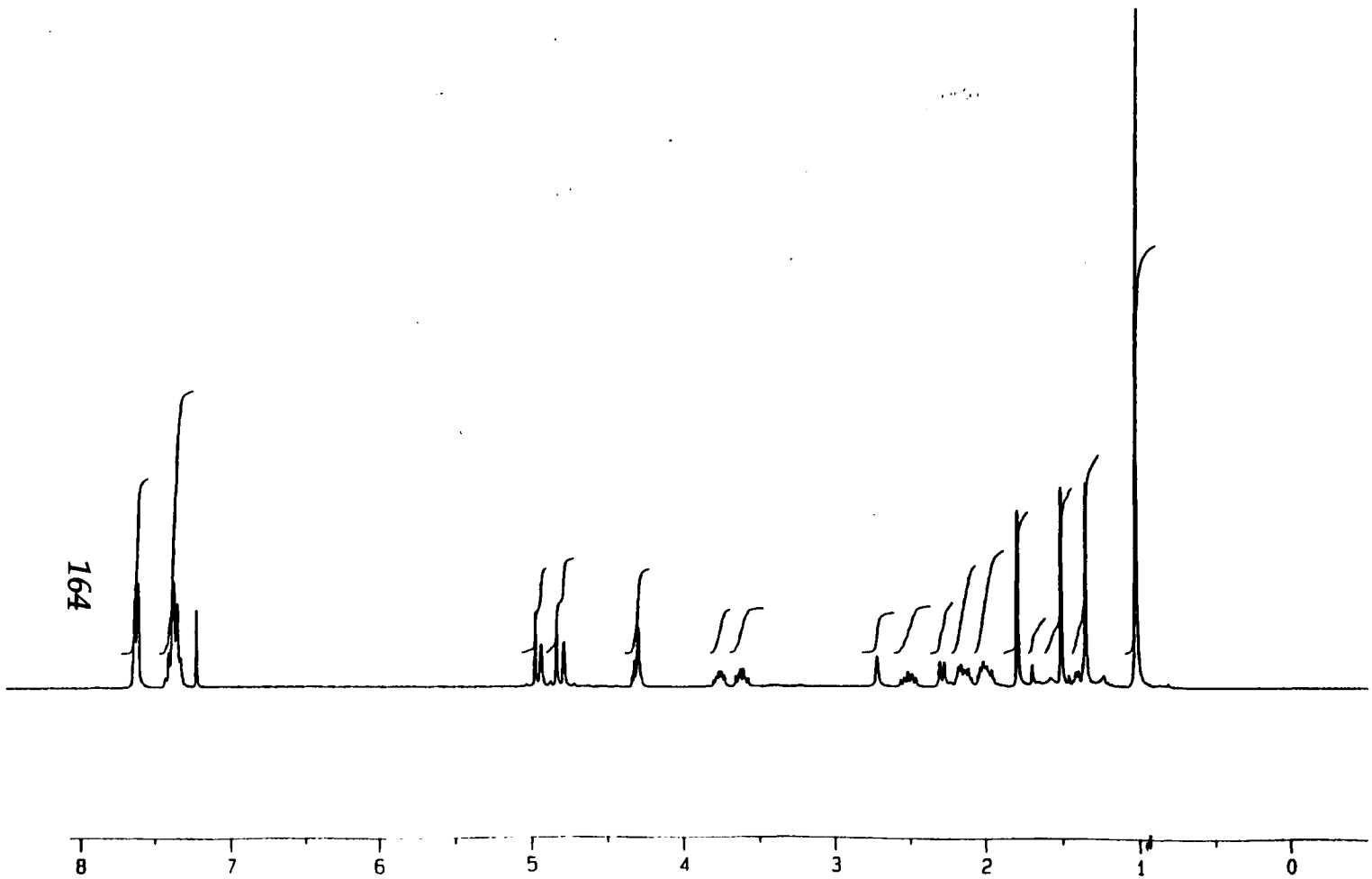
Data for **2.68**

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.63 (d, J= 7 Hz, 4H), 7.44-7.34 (m, 6H), 4.96 (d, J= 12 Hz, 2H), 4.81 (d, J= 14 Hz, 2H), 4.34-4.30 (m, 2H), 3.80-3.73 (m, 1H), 3.66-3.58 (m, 1H), 2.72 (s, 1H), 2.56-2.46 (m, 1H), 2.28 (d, J= 9 Hz, 1H), 2.18-2.10 (m, 2H), 2.05-1.95 (m, 2H), 1.79 (s, 3H), 1.70 (s, 1H), 1.51 (s, 3H), 1.35 (s, 3H), 1.02 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 153.2, 144.1, 135.6 (x4), 133.0 (x2), 129.8 (x2), 127.7 (x4), 114.9, 110.4, 107.7, 77.2, 77.1, 73.0, 65.5, 54.5, 35.2, 32.8, 28.8, 26.8 (x3), 26.4, 23.6, 22.4, 19.0.

IR (neat) 3431, 3071, 2931, 1064, 1112 cm^{-1}.

EI HRMS calcd for $C_{32}H_{44}O_4Si$ (M+) 520.30089, obsd 520.30208.



2.68

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PROCNO                        1

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PL1                     -3.00 dB
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F2 - Processing parameters
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1D NMR plot parameters
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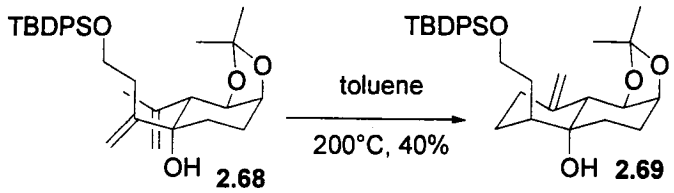


6-[2-(tert-Butyl-diphenyl-silanyloxy)-ethyl]-2,2-dimethyl-9-methylene-octahydro-naphtho[1,2-d][1,3]dioxol-5a-ol (2.69)

To a solution of alcohol **2.68** (0.011 g, 0.02 mmol) in toluene (2 mL) was added triethylamine (0.3 mL). The tube was sealed, fitted with temperature and pressure probes, and placed in the microwave. The temperature was ramped gradually to 200 °C, and was held there for 70 min. The solvent was evaporated. The crude product was purified by flash column chromatography (10% EtOAc/hexanes) to afford 4 mg of **2.69** (40% yield) as a colourless oil.

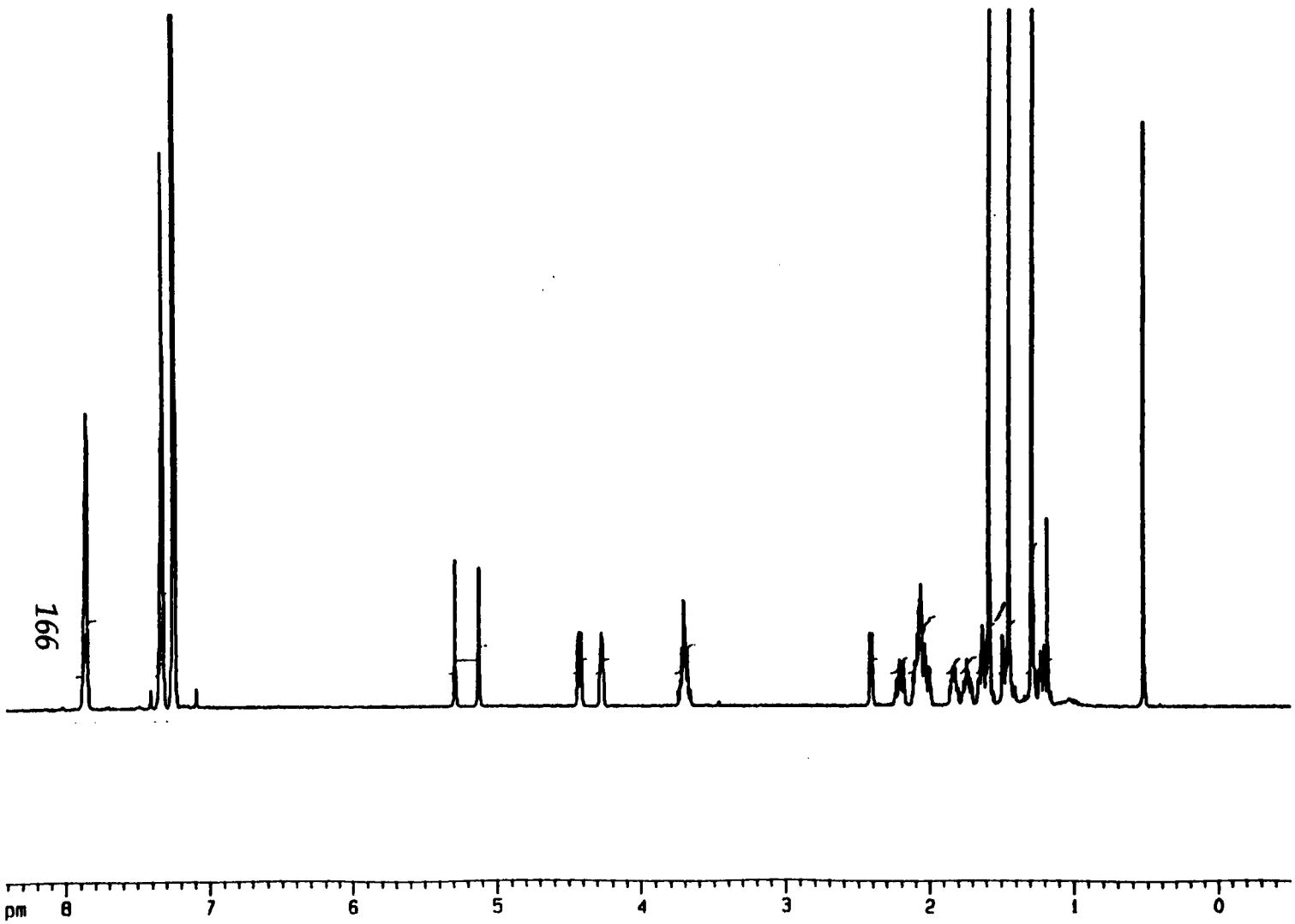
Data for **2.69**

^{1}H NMR (500 MHz, C_6D_6): δ 7.89-7.87 (m, 4H), 7.36-7.34 (m, 6H), 5.29 (s, 1H), 5.13 (s, 1H), 4.42 (dd, J= 8, 5 Hz, 1H), 4.27 (q, J= 4 Hz, 1H), 3.74-3.65 (m, 2H), 2.40 (d, J= 9 Hz, 1H), 2.24-2.17 (m, 1H), 2.11-1.99 (m, 4H), 1.86-1.80 (m, 1H), 1.77-1.70 (m, 1H), 1.65-1.60 (m, 2H), 1.58 (s, 3H), 1.49-1.46 (m, 1H), 1.45 (s, 3H), 1.28 (s, 9H), 1.21 (dt, J= 13, 5 Hz, 1H), 1.18 (s, 1H).

^{13}C NMR (125 MHz, C_6D_6) δ 146.1, 136.0 (x4), 134.2 (x2), 130.0 (x2), 128.3 (x4), 110.0, 107.7, 75.2, 74.6, 73.7, 63.1, 47.2, 44.1, 31.5, 31.1, 29.8, 29.0, 27.1 (x3), 26.5, 26.2, 22.5, 19.4.

IR (neat) 3560, 2982, 2880, 1055 cm^{-1}.

EI HRMS calcd for $C_{28}H_{35}O_4Si$ (M+ - tBu) 463.23046, obsd 463.2294.



2.69

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SOLVENT          Acetone
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SWH            7440.476 Hz
FIDRES         0.113533 Hz
AQ             4.4040694 sec
RG                 203.2
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1D NMR plot parameters
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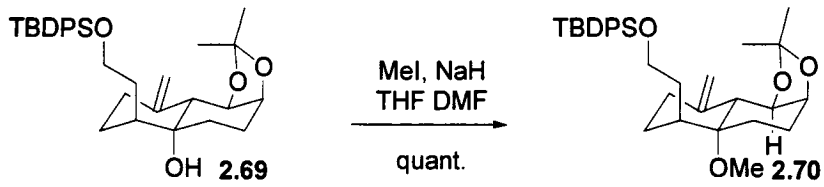


tert-Butyl-[2-(5a-methoxy-2,2-dimethyl-9-methylene-decahydro-naphtho[1,2-d][1,3]dioxol-6-yl)-ethoxy]-diphenyl-silane (2.70)

To a solution of alcohol **2.69** (0.004 g, 0.008 mmol) in THF (0.3 mL) and DMF (0.1 mL) was added NaH (0.002 g, 0.05 mmol). The reaction was stirred at 0°C for 20 minutes. MeI (0.010 mL, 0.16 mmol) was added and the reaction strirred for 2 hours at room temperature. The reaction was quenched by adding saturated NH_4Cl_{aq}. The aqueous layer was extracted 3 times with diethylether (3 X 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (10% EtOAc/hexanes) to afford 3 mg of **2.70** (100% yield) as a colourless oil.

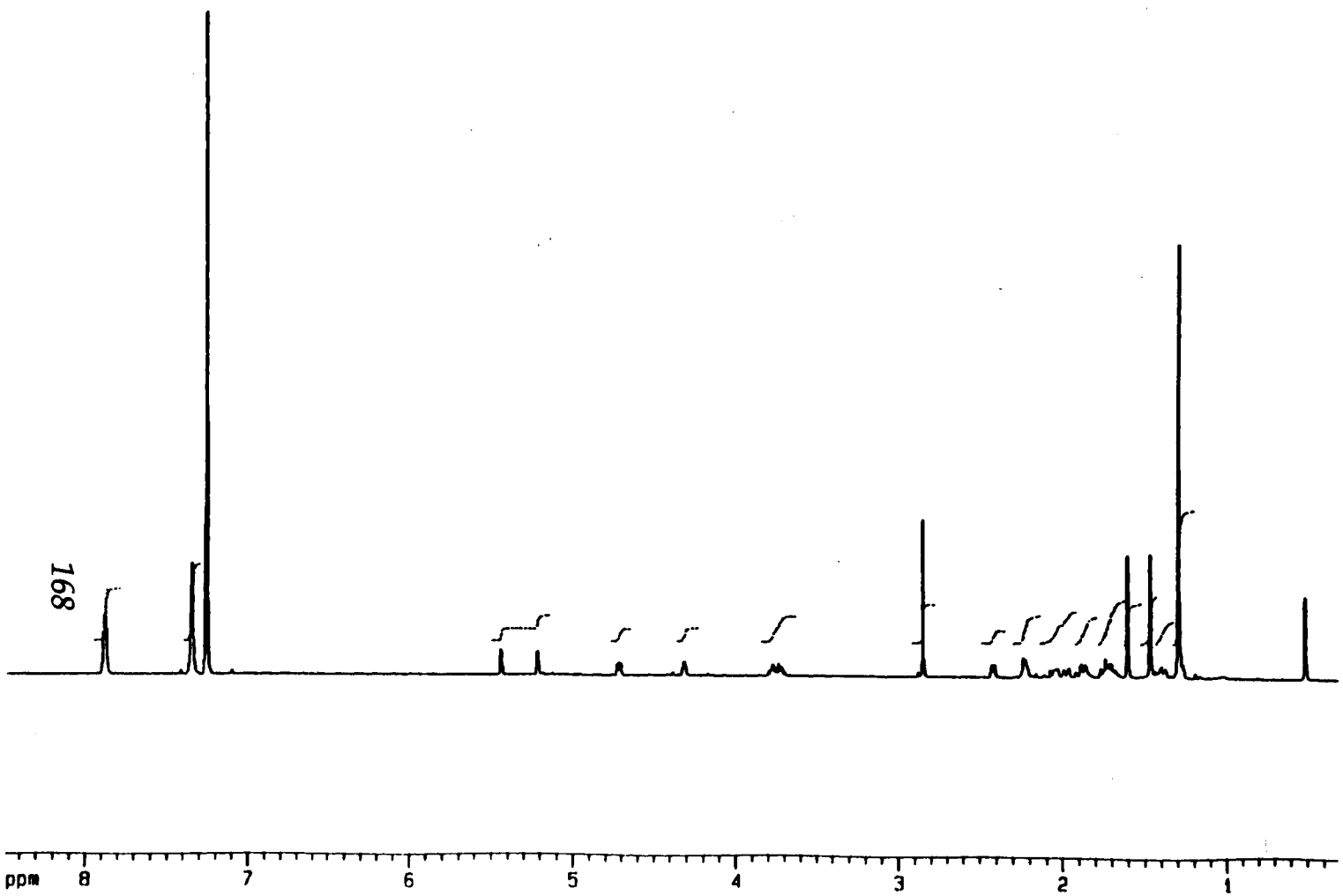
Data for **2.70**

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.68-7.60 (m, 4H), 7.42-7.33 (m, 6H), 4.92 (s, 1H), 4.87 (s, 1H), 4.35 (dd, J= 9, 5 Hz, 1H), 4.29-4.26 (m, 1H), 3.75-3.64 (m, 2H), 2.98 (s, 3H), 2.11-2.10 (m, 3H), 2.07-2.02 (m, 1H), 1.93-1.90 (m, 1H), 1.83-1.72 (m, 3H), 1.64-1.56 (m, 4H), 1.44 (s, 3H), 1.35 (s, 3H), 1.04 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 146.3, 135.6 (x4), 133.8 (x2), 129.7 (x2), 127.7 (x4), 108.5, 107.7, 79.8, 75.0, 73.3, 62.6, 47.1, 46.9, 33.3, 30.8, 30.3, 28.8, 26.9 (x3), 26.5, 24.6, 23.3, 21.9, 19.2.

IR (neat) 2930, 2857, 1113, 1071 cm^{-1}.

EI HRMS calcd for $C_{33}H_{46}O_4Si$ (M+ - tBu) 534.31654, obsd 534.31534.



2,70

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PROCNO 1

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F2 - Processing parameters
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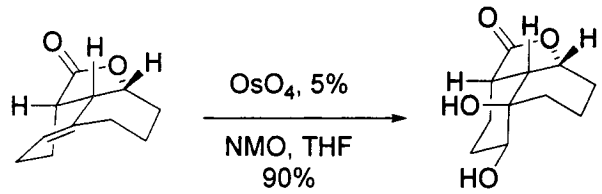


3.22 **3.24**

5,5a-dihydro-decahydronaphtho[1,8-bc]furan-2-one (3.24)

Compound **3.22** (22 mg, 0.12 mmol) was dissolved in THF (1.2 mL) and water (0.25 mL). NMO (29mg, 0.25 mmol) was added, followed by OsO_4 4% in water (0.039 mL, 0.006 mmol). The reaction was stirred for 15 hours and quenched by adding $Na_2SO_{3\ sat}$ (5 mL). The aqueous layer was extracted 3 times with ethylacetate (3 X 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (90% EtOAc/hexanes) to afford 23 mg of **3.24** (90% yield) as white crystals.

Data for **3.24**

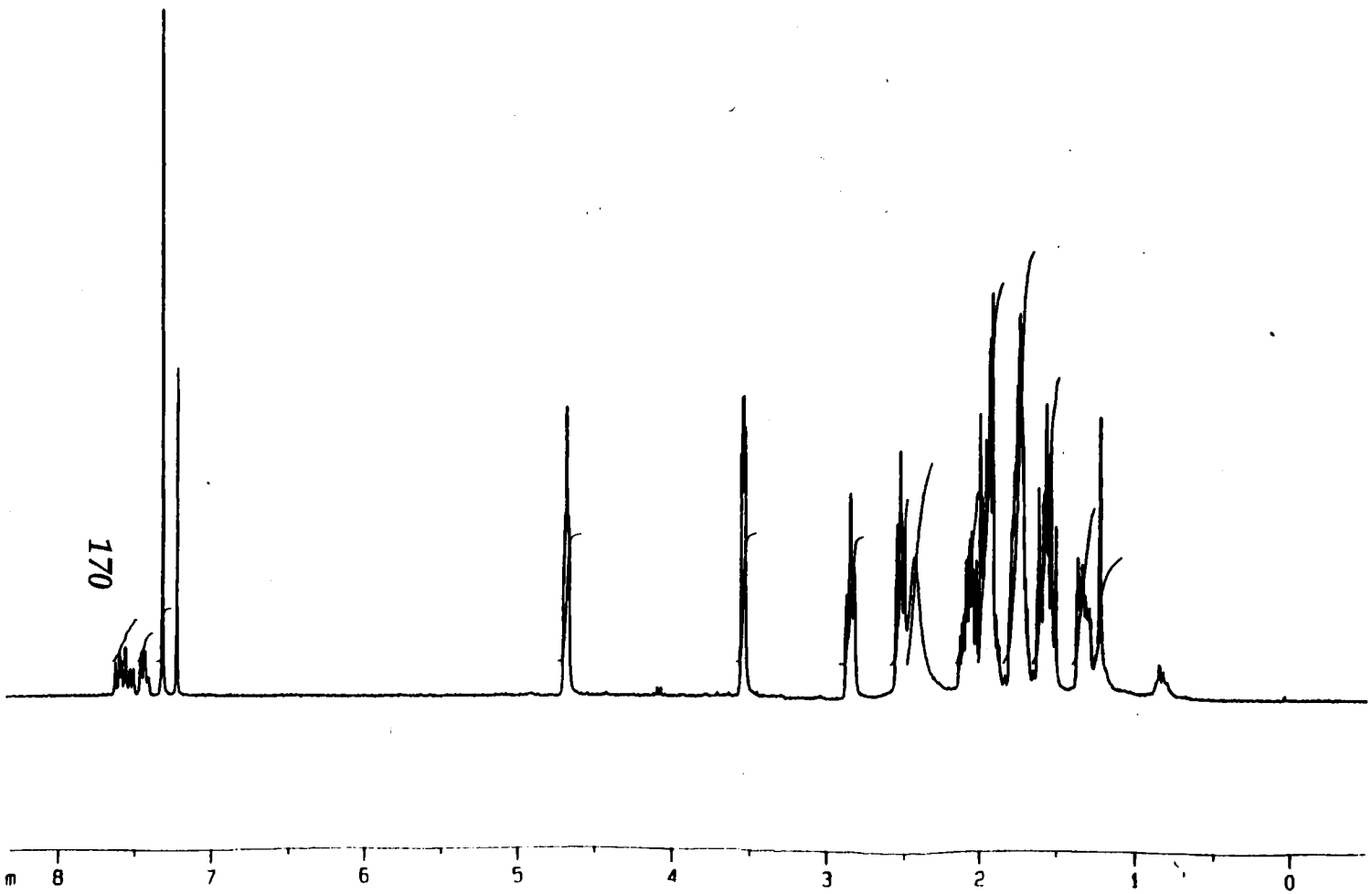
^{1}H NMR (300 MHz, $CDCl_3$): δ 4.71-4.67 (m, 1H), 3.55-3.53 (m, 1H), 2.88-2.82 (m, 1H), 2.55-2.43 (m, 3H), 2.14-1.87 (m, 4H), 1.80-1.68 (m, 3H), 1.62-1.51 (m, 2H), 1.37-1.25 (m, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 178.7, 78.1, 72.8, 70.7, 41.9, 39.9, 27.1, 25.8, 21.9, 15.1, 13.7.

IR (neat) 3444, 2936, 1754, 964 cm^{-1}.

EI HRMS calcd for $C_{11}H_{14}O_3$ (M+ - H_2O) 194.09430, obsd 194.0951.

3.24



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TE	300.0 K
D1	1.00000000 sec

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PL1	-3.00 dB
SFO1	300.1319477 MHz

F2 - Processing parameters

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1D NMR plot parameters

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F2	-150.06 Hz
PPMCM	0.45000 ppm/cm
HZCM	135.05850 Hz/cm

3.24 **3.25**

5a-hydroxy-octahydro-naphtho[1,8-bc]furan-2,5-dione (3.25)

Diol **3.24** (23 mg, 0.11 mmol) was dissolved in CH_2Cl_2 (1.1 mL) and Dess-Martin reagent (55 mg, 0.13 mmol) was added. The reaction was stirred for 24 hours at room temperature. $NaHCO_{3\ sat}$ (1 mL) was added followed by $Na_2SO_{3\ sat}$ (1 mL). Extracted 3 times with dichloromethane (3 X 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (100% EtOAc) to afford 13 mg of **3.25** (56% yield) as a colourless oil.

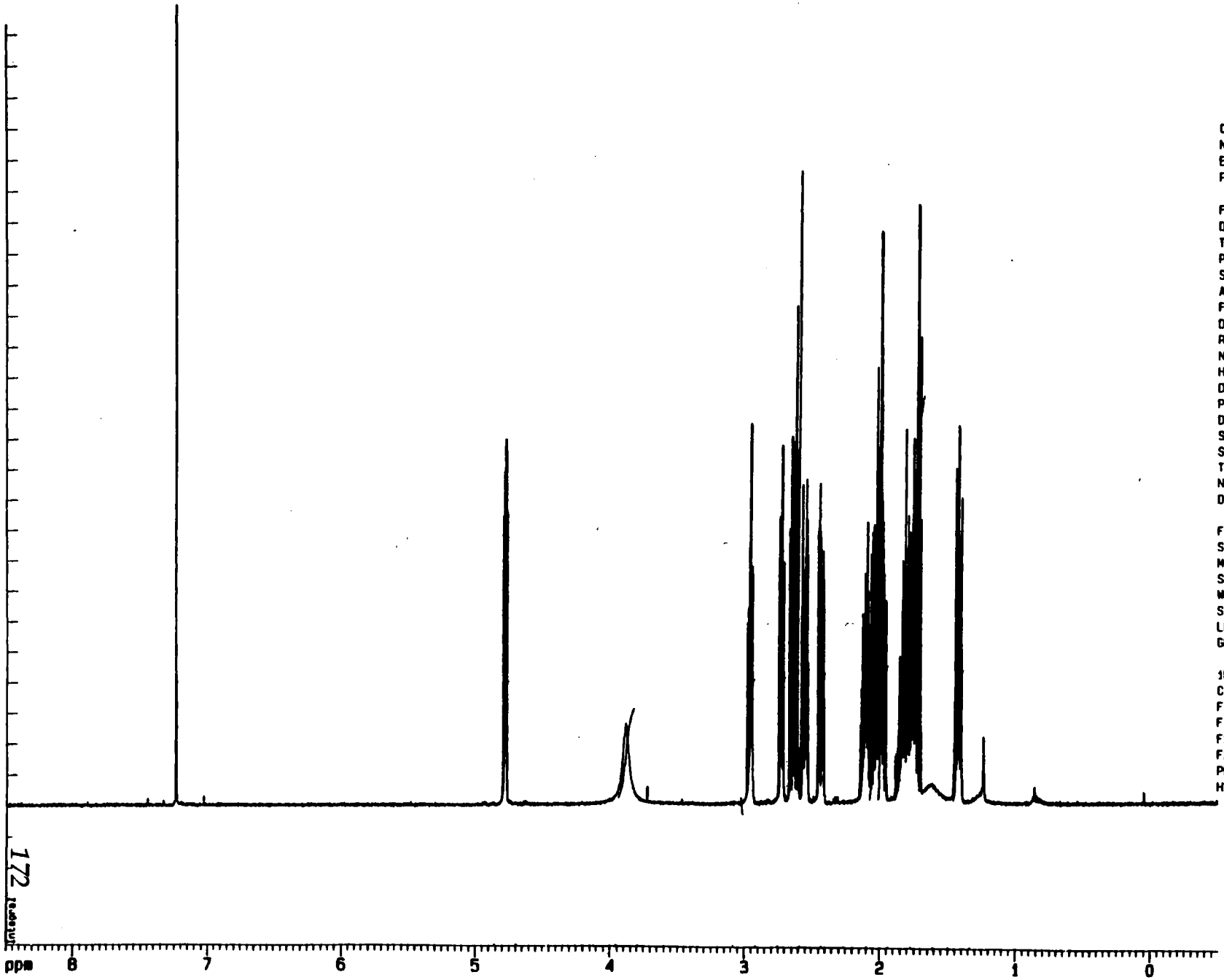
Data for **3.25**

^{1}H NMR (500 MHz, $CDCl_3$): δ 4.79-4.77 (m, 1H), 3.9 (s, 1H), 2.96-2.94 (m, 1H), 2.74-2.71 (m, 1H), 2.67-2.60 (m, 1H), 2.57-2.53 (m, 1H), 2.45-2.41 (m, 1H), 2.11-1.96 (m, 3H), 1.83-1.69 (m, 3H), 1.44-1.40 (m, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 211.9, 177.0, 77.3, 75.1, 48.1, 39.7, 33.7, 29.4, 22.7, 22.0, 13.4.

IR (neat) 3451, 2944, 1759, 1709, 1201, 974 cm^{-1}.

EI HRMS calcd for $C_{11}H_{14}O_4$ (M+) 210.0892, obsd 210.0898.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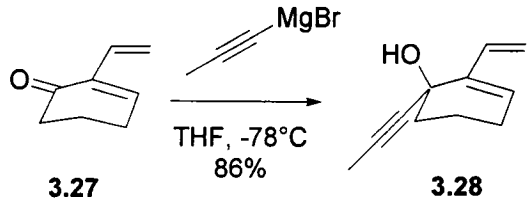


3.27 **3.28**

1-propynyl-2-vinyl-cylclohex-2-enol (3.28)

Ketone **3.27** (71 mg, 0.58 mmol) was dissolved in THF (6 mL) and cooled to -78°C. Propynylmagnesium bromide 0,5 M (1.75 mL, 0.87 mmol) was added dropwise and the reaction was stirred for 30 min. The solution was warmed to 0°C for 1 hour, then warmed to room temperature for 1 hour. The reaction was quenched by adding saturated NH_4Cl_{aq}. The aqueous layer was extracted 3 times with diethylether (3 X 20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (20% EtOAc/hexanes) to afford 81 mg of **3.28** (86% yield) as a colourless oil.

Data for **3.28**

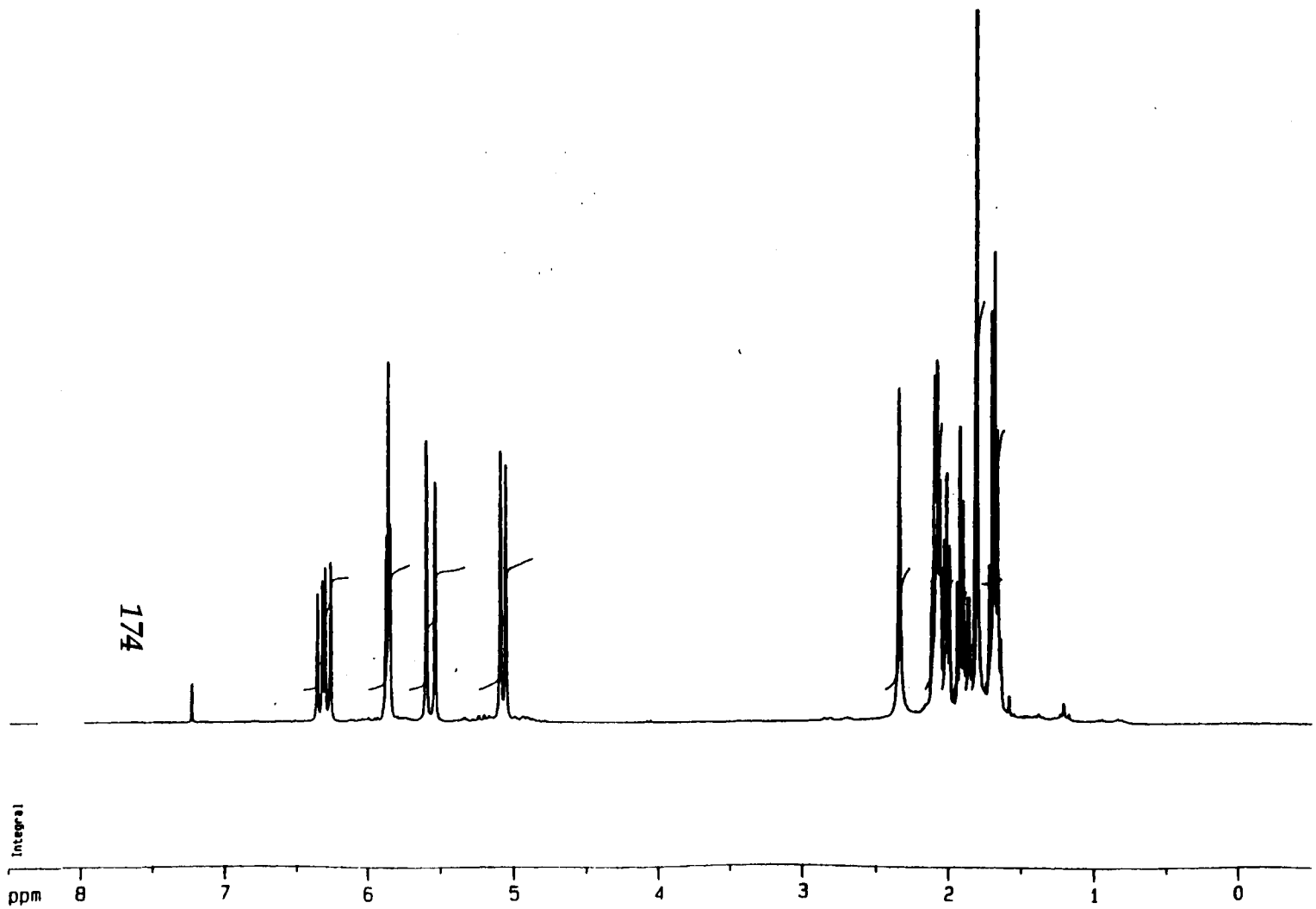
^{1}H NMR (300 MHz, $CDCl_3$): δ 6.37-6.27 (m, 1H), 5.87 (t, J= 4 Hz, 1H), 5.57 (d, J= 17.7 Hz, 1H), 5.08 (d, J= 11.3 Hz, 1H), 2.34 (s, 1H), 2.11-1.99 (m, 3H), 1.94-1.90 (m, 1H), 1.80 (s, 3H), 1.72-1.64 (m, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 138.5, 135.1, 128.9, 114.3, 82.6, 80.3, 66.6, 39.6, 25.6, 18.8, 3.6.

IR (neat) 3426, 2938, 2863, 1444, 989 cm^{-1}.

EI HRMS calcd for $C_{11}H_{14}O$ (M+) 162.10447, obsd 162.1026.

3.28



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F2 - Processing parameters

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1D NMR plot parameters

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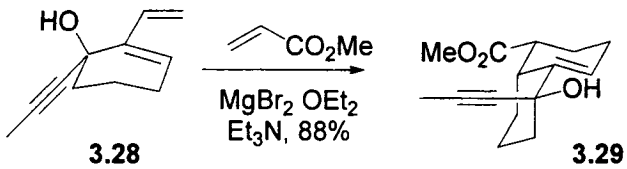


3.28 **3.29**

5-hydroxy-5-prop-1-ynyl-1, 2, 3, 5, 6, 7, 8, 8a, octahydro-naphthalene-1-carboxylique acid methylester (3.29)

To a suspension of $MgBr_2 \cdot Et_2O$ (2.4 g, 9.28 mmol) in dichloromethane (23 mL) triethylamine (1.9 mL, 13.92 mmol) was added and the reaction was stirred for 20 minutes at room temperature. The alcohol **3.28** (0.754 g, 4.64 mmol) in dichloromethane (5 mL) was canulated into the magnesium solution and the reaction was stirred for 20 minutes. Methylacrylate (0.920 mL, 10.2 mmol) was added and the reaction was stirred for 90 min. The reaction was quenched by adding saturated NH_4Cl_{aq}. The aqueous layer was extracted 3 times with dichloromethane (3 X 50 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (20% EtOAc/hexanes) to afford 1.02 g of **3.29** (88% yield) as a colourless oil.

Data for **3.29**

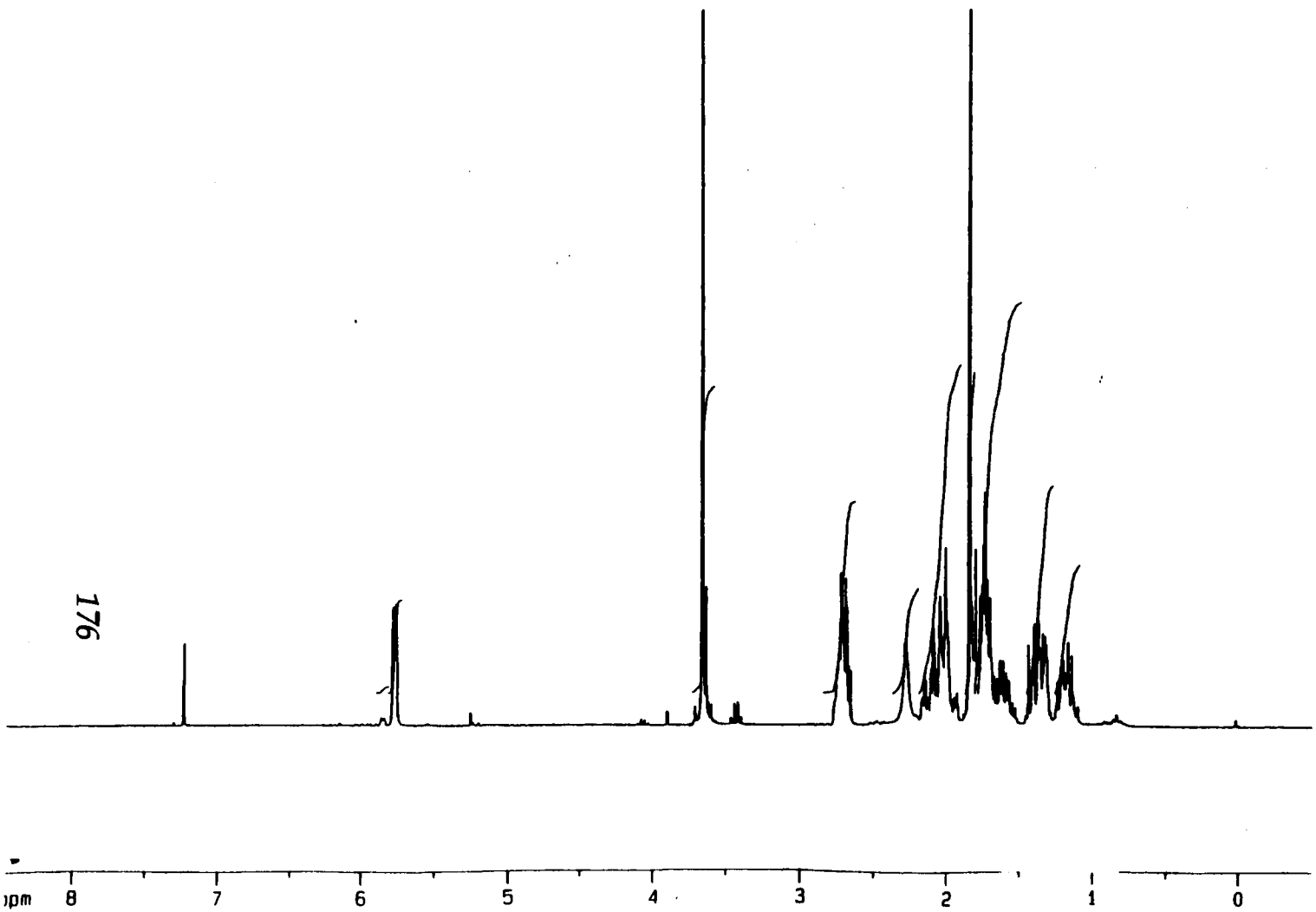
^1H NMR (300 MHz, $CDCl_3$): δ 5.77 (d, J= 4.9 Hz, 1H), 3.65 (s, 3H), 2.71-2.64 (m, 2H), 2.34 (s, 1H), 2.15-1.84 (m, 3H), 1.82 (s, 3H), 1.81-1.55 (m, 4H), 1.42-1.22 (m, 2H), 1.20-1.11 (m, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 175.1, 142.3, 116.1, 81.5, 80.9, 71.3, 51.4, 43.6, 43.4, 36.8, 29.2, 24.3, 23.3, 20.0, 3.7.

IR (neat) 3478, 2936, 2857, 1735, 1437, 1197 cm^{-1}.

EI HRMS calcd for $C_{15}H_{20}O_3$ (M+) 248.1214, obsd 248.1398.

3.29



Current Data Parameters
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EXPNO 3
PROCNO 1

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PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 90.5
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

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PL1 -3.00 dB
SFO1 300.1319477 MHz

F2 - Processing parameters
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SF 300.1300000 MHz
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SSB 0
LB 0.10 Hz
GB 0
PC 1.00

1D NMR plot parameters
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CY 40.00 cm
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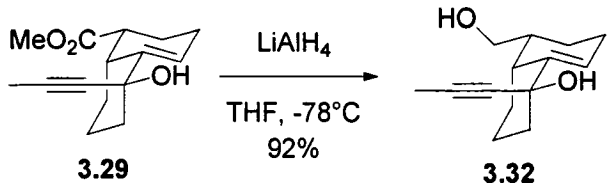
F2P -0.500 ppm
F2 -150.06 Hz
PPMCM 0.45000 ppm/cm
HZCM 135.05850 Hz/cm



3.29 **3.32**

5-Hydroxymethyl-1-prop-1-ynyl-1,2,3,4,4a,5,6,7-octahydro-naphthalen-1-ol (3.32)

Ester **3.29** (0.094 g, 0.38 mmol) was dissolved in THF (4 mL) and cooled to -78°C. Lithium aluminium hydride (0.043 g, 1.14 mmol) was added and the solution was warmed to room temperature for 30 minutes. The reaction was cooled to 0°C and 0.043 mL of water added dropwise, followed by 0.043 mL of NaOH 1M then 0.043 mL of water. Finally, 2 mL of sodium tartrate 0.5 M was added and stirred for 1 hour at room temperature. The aqueous layer was extracted 3 times with ethylacetate (3 X 20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (50% EtOAc/hexanes) to afford 77 mg of **3.32** (92 % yield) as a colourless oil.

Data for **3.32**

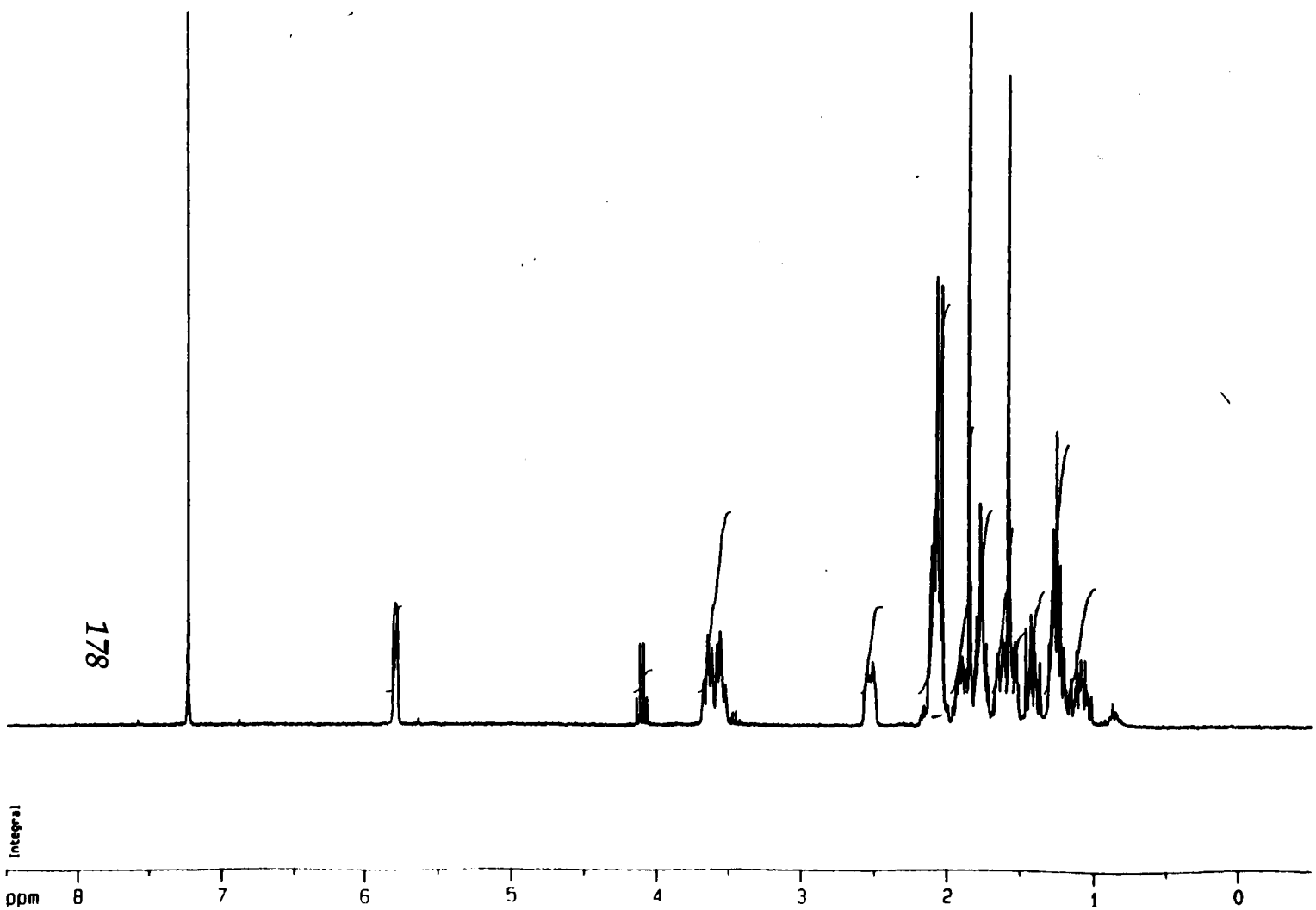
^{1}H NMR (300 MHz, $CDCl_3$): δ 5.79-5.78 (m, 1H), 3.67-3.52 (m, 2H), 2.54-2.50 (m, 1H), 2.12-2.02 (m, 4H), 1.93-1.85 (m, 1H), 1.84-1.71 (m, 2H), 1.84 (s, 3H), 1.67-1.60 (m, 1H), 1.45-1.35 (m, 1H), 1.29-1.17 (m, 3H), 1.15-1.00 (m, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 143.4, 116.2, 81.8, 80.7, 71.6, 65.4, 43.7, 39.9, 36.5, 27.5, 25.1, 23.7, 21.2, 3.8.

IR (neat) 3352, 2931, 2861 cm^{-1}.

EI HRMS calcd for $C_{14}H_{18}O$ (M+) 202.13576, obsd 202.1344.

3.32



Current Data Parameters
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EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20020724
Time 16.41
INSTRUM av300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 512
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

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

F2 - Processing parameters
SI 65536
SF 300.1300001 MHz
WDW EM
SSB 0
LB 0.10 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 20.00 cm
CY 40.00 cm
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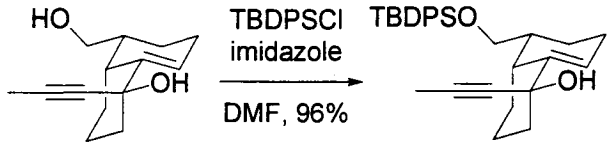
F1 2551.10 Hz
F2P -0.500 ppm
F2 -150.06 Hz
PPMCM 0.45000 ppm/cm
HZCM 135.05850 Hz/cm



3.32 **3.33**

5-(tert-Butyl-diphenyl-silanyloxymethyl)-1-prop-1-ynyl-1,2,3,4,4a,5,6,7-octahydro-naphthalen-1-ol (3.33)

Alcohol **3.32** (992 mg, 4.5 mmol) was dissolved in DMF (23 mL). Imidazole (0.674 g, 9.9 mmol) was added, followed by tert-Butyldiphenylsilylchloride (1.3 mL, 4.95 mmol). The reaction was stirred for 90 min. The reaction was quenched by adding saturated NH_4Cl_{aq}. The aqueous layer was extracted 3 times with a mixture of diethylether and hexanes (1:1) (3 X 50 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (10% EtOAc/hexanes to 15% EtOAc/hexanes) to afford 1.984 g of **3.33** (96% yield) as a colourless oil.

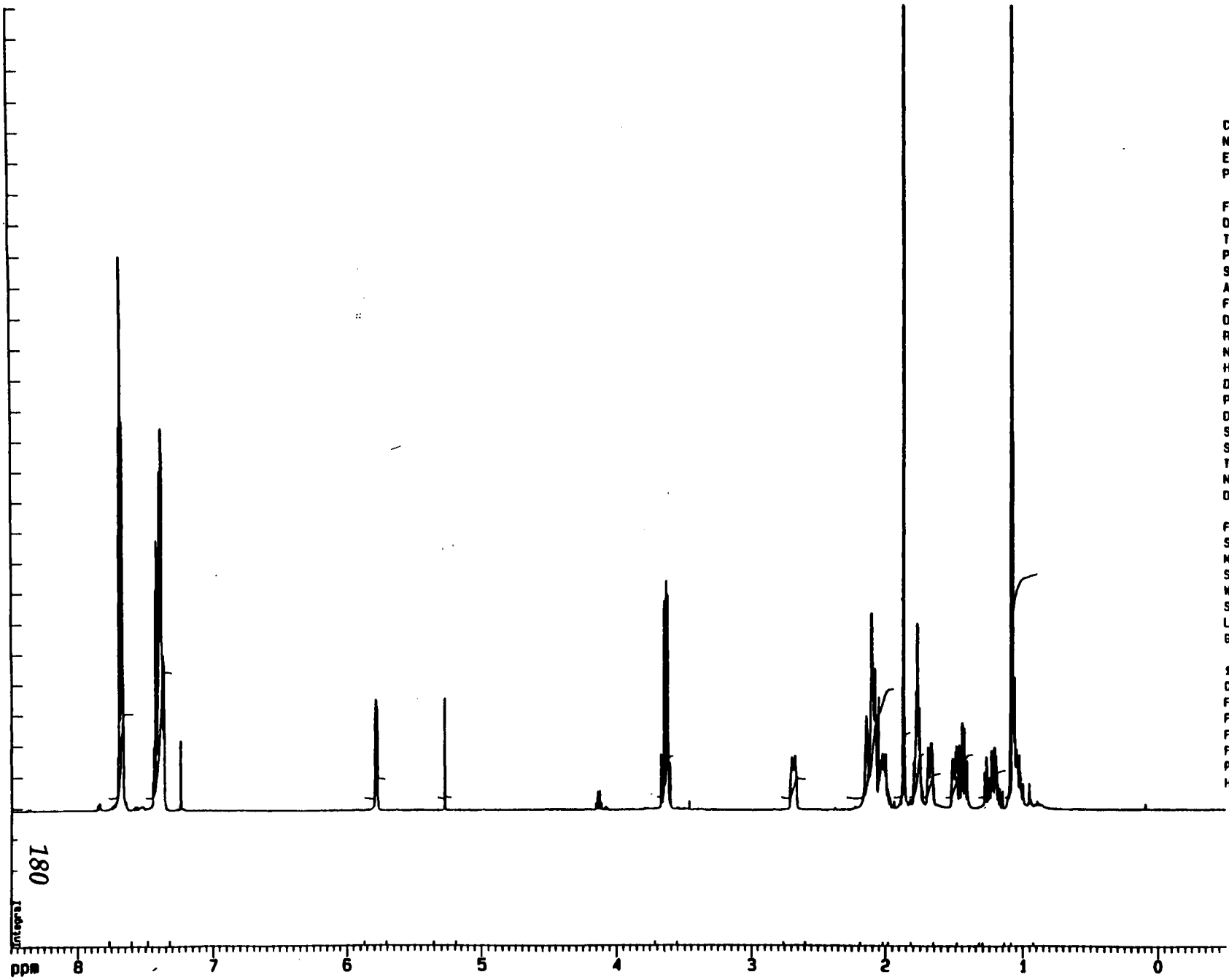
Data for **3.33**

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.70-7.67 (m, 4H), 7.44-7.36 (m, 6H), 5.78 (d, J= 3.2 Hz, 1H), 3.67-3.61 (m, 2H), 2.69-2.67 (m, 1H), 2.13-1.99 (m, 5H), 1.86 (s, 3H), 1.77-1.74 (m, 2H), 1.69-1.66 (m, 1H), 1.51-1.40 (m, 2H), 1.26-1.19 (m, 1H), 1.07-1.02 (m, 10H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 143.9, 135.5, 134.1, 129.5, 127.6, 115.7, 81.9, 80.6, 71.7, 65.8, 43.8, 39.7, 36.5, 27.5, 26.8, 25.1, 23.7, 21.0, 19.3, 3.5.

IR (neat) 3423, 3073, 2926, 2861, 1113.

EI HRMS calcd for $C_{30}H_{36}OSi$ (M+) 440.25354, obsd 440.2632.



Current Data Parameters
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EXPNO 1
PROCNO 1

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Date 20020610
Time 9.21
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SOLVENT CDCl3
AQ 4.6530805 sec
FIDRES 0.107456 Hz
DW 71.0 usec
RG 128
NUCLEUS 1H
HL1 0 dB
D1 0.0100000 sec
P1 5.6 usec
DE 88.8 usec
SFO1 500.1381707 MHz
SWH 7042.25 Hz
TD 65536
NS 16
DS 0

F1 - Processing parameters
SI 32768
WC2 QF
SF 500.1354311 MHz
WDW EM
SSB 0
LB 0.00 Hz
GB 0

1D NMR plot parameters
CX 22.00 cm
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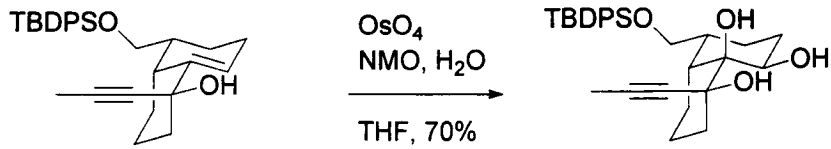
F1 4251.15 Hz
F2P -0.500 ppm
F2 -250.07 Hz
PPMCM 0.40909 ppm/
HZCM 204.60086 Hz/



3.33 **3.34**

5-(tert-Butyl-diphenyl-silanyloxymethyl)-1-prop-1-ynyl-octahydro-naphthalene-1,8,8a-triol (3.34)

Olefin **3.33** (91 mg, 0.19 mmol) was dissolved in THF (2 mL) and water (0.4 mL). NMO (0.047 g, 0.397 mmol) was added, followed by osmium tetroxide 4 % in water (0.063 mL, 0.01 mmol). The reaction was stirred for 24 hours. The reaction was not done, NMO (0.02 g, 0.17 mmol) was added, followed by more osmium tetroxide 4 % in water(0.02 mL, 0.003). The reaction was stirred for 8 hours. The reaction was quenched by adding $Na_2S_2O_3$. The aqueous layer was extracted 3 times with ethylacetate (3 X 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (15% to 50 %EtOAc/hexanes) to afford 69 mg of **3.34** (70% yield) as a colourless oil.

Data for **3.34**

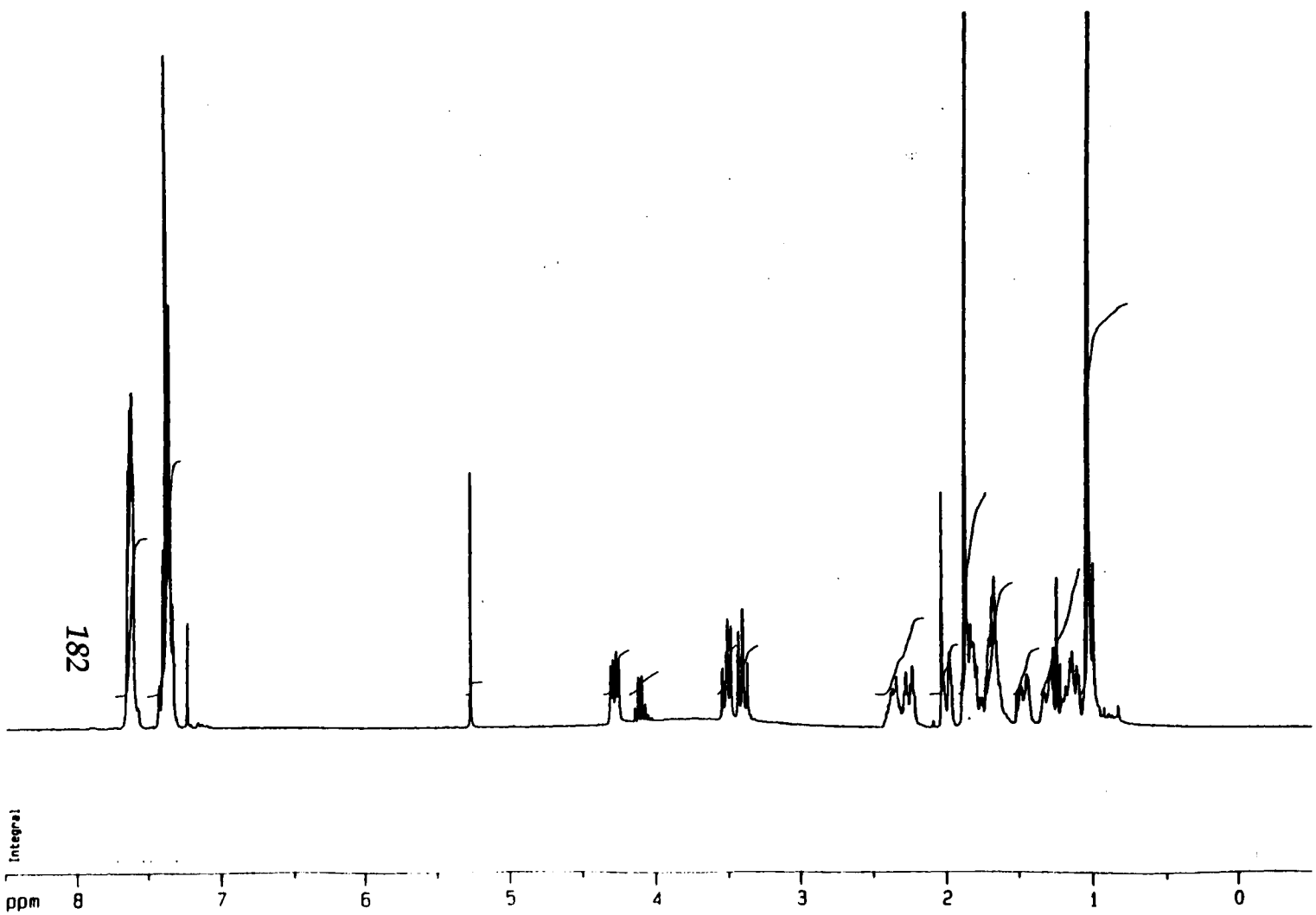
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.66-7.61 (m, 4H), 7.44-7.34 (m, 6H), 4.27 (dd, J= 5.2, 11.1 Hz, 1H), 3.46 (dt, J= 6.9, 34.1 Hz, 2H), 2.37-2.22 (m, 2H), 2.03-1.97 (m, 1H), 1.87 (s, 3H), 1.85-1.79 (m, 2H), 1.70-1.60 (m, 3H), 1.52-1.45 (m, 1H), 1.33-1.09 (m, 3H), 1.03 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 135.6, 135.5, 133.8, 129.6, 129.5, 127.6, 83.6, 79.7, 79.6, 75.3, 69.3, 65.6, 42.1, 37.2, 36.1, 30.2, 26.8, 22.8, 21.7, 21.1, 19.2, 3.6.

IR (neat) 3300, 2933, 2860, 1428, 1112 cm^{-1}.

EI HRMS calcd for $C_{26}H_{31}O_4Si$ (M+ - tBu) 435.19916, obsd 435.2062.

3.34



Current Data Parameters

NAME	lmo_187
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

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Time	10.24
INSTRUM	av300
PROBHD	5 mm GNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	90.5
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

NUC1	1H
P1	20.00 usec
PL1	-3.00 dB
SF01	300.1319477 MHz

F2 - Processing parameters

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

1D NMR plot parameters

CX	20.00 cm
CY	50.00 cm
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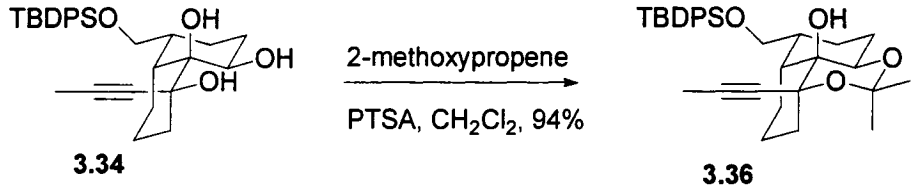
F1	2551.10 Hz
F2P	-0.500 ppm
F2	-150.06 Hz
PPMCM	0.45000 ppm/cm
HZCM	135.05850 Hz/cm



3.34 **3.36**

7-(tert-Butyl-diphenyl-silanyloxymethyl)-2,2-dimethyl-3a-prop-1-ynyl-octahydro-naphtho[1,8-de][1,3]dioxin-9b-ol (3.36)

Diol **3.34** (0.02 g, 0.04 mmol) was dissolved in CH_2Cl_2 (0.5 mL) and 2-methoxypropene (0.015 mL, 0.15 mmol) was added. TsOH (1 crystal) was added and the solution turned dark red. The reaction was done after 10 minutes of stirring. $NaHCO_{3sat}$ was added. The aqueous layer was extracted 3 times with dichloromethane (3 X 20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (10% EtOAc/hexanes) to afford 20 mg of **3.36** (94% yield) as yellow crystals. mp 154.0-154.3°C.

Data for **3.36**

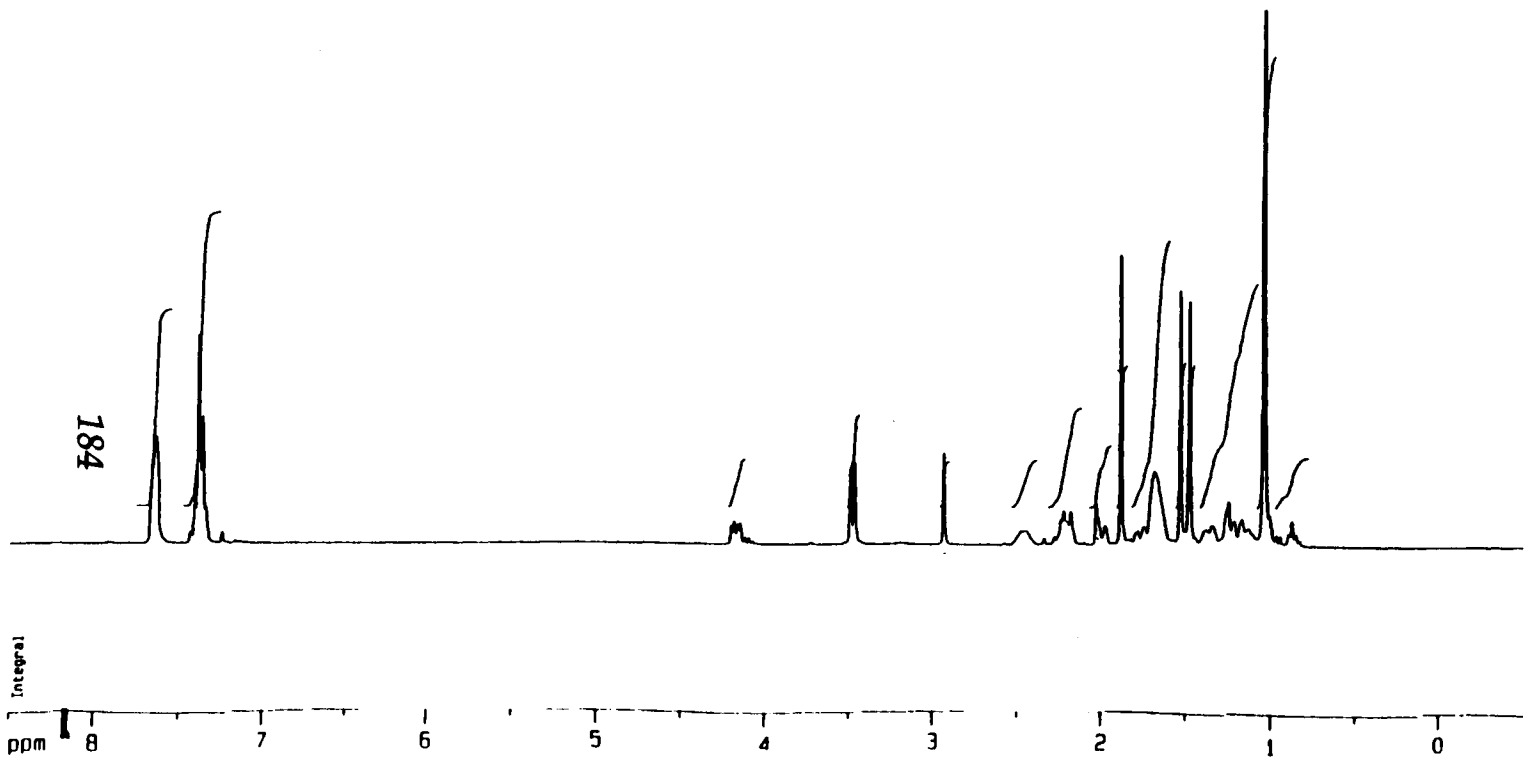
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.64-7.63 (m, 4H), 7.40-7.33 (m, 6H), 4.16 (dd, J= 5.0, 10.8 Hz, 1H), 3.47 (d, J= 3.47 Hz, 2H), 2.93 (s, 1H), 2.47-2.44 (m, 1H), 2.23-2.17 (m, 2H), 2.02-1.97 (m, 1H), 1.88 (s, 3H), 1.78-1.68 (m, 4H), 1.53 (s, 3H), 1.47 (s, 3H), 1.37-1.16 (m, 4H), 1.03 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 135.5 (x2), 135.5 (x2), 133.8 (x2), 129.5, 129.5, 127.5 (x4), 99.5, 81.9, 80.1, 79.3, 69.4, 66.4, 66.0, 40.2, 36.4, 36.2, 32.2, 26.8 (x3, 25.6, 23.1 (x2), 22.0, 21.5, 19.2, 3.8.

IR (neat) 3574, 2941, 2859, 1468, 1104.

EI HRMS calcd for $C_{32}H_{41}O_4Si$ (M+ - Me) 517.27741, obsd 517.2784.

3.36



Current Data Parameters

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EXPNO	1
PROCNO	1

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PULPROG	zg30
TD	30720
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SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	45.3
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

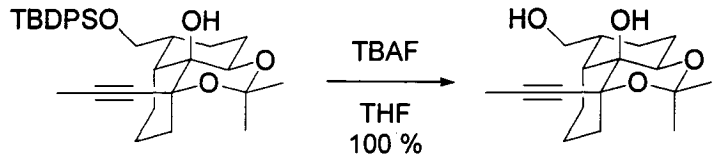
NUC1	1H
P1	8.00 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

F2 - Processing parameters

SI	65536
SF	300.1299999 MHz
WDW	EM
SSB	0
LB	0.10 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	20.00 cm
CY	10.00 cm
F1P	8.500 ppm
F1	2551.10 Hz
F2P	-0.500 ppm
F2	-150.06 Hz
PPMCM	0.45000 ppm/cm
HZCM	135.05850 Hz/cm



3.36 **3.37**

7-Hydroxymethyl-2,2-dimethyl-3a-prop-1-ynyl-octahydro-naphtho[1,8-de][1,3]dioxin-9b-ol (3.37)

Compound **3.36** (0.053 g, 0.1 mmol) was dissolved in THF (1 mL), and TBAF 1 M (0.13 mL, 0.13 mmol) added. The reaction was stirred for 4 hours. The solvent was evaporated. The crude product was purified by flash column chromatography (80% EtOAc/hexanes) to afford 31 mg of **3.37** (100% yield) as white crystals. Mp 181.0-182.0 °C.

Data for **3.37**

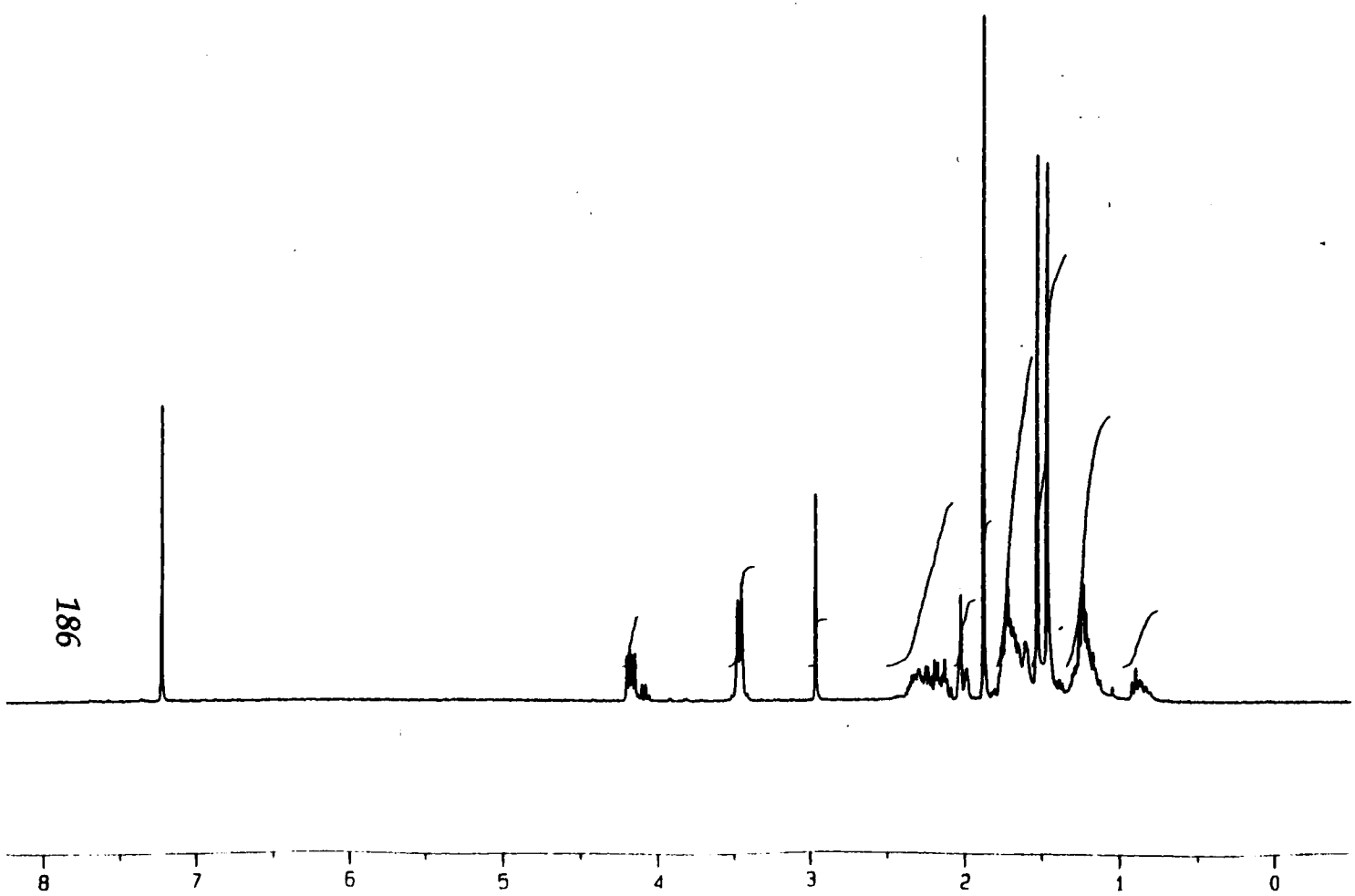
^{1}H NMR (300 MHz, $CDCl_3$): δ 4.16 (dd, J= 5.7, 10.6 Hz, 1H), 3.46 (d, J= 7.1 Hz, 2H), 2.97 (s, 1H), 2.38-2.09 (m, 3H), 2.02-1.99 (m, 1H), 1.88 (s, 3H), 1.78-1.59 (m, 5H), 1.53 (s, 3H), 1.47 (s, 3H), 1.30-1.12 (m, 4H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 99.6, 82.1, 80.1, 79.2, 69.4, 66.4, 65.4, 40.0, 37.1, 36.2, 32.2, 26.7, 25.6, 23.1, 22.0, 21.3, 4.0.

IR (neat) 3445, 2940, 2864,1198 cm^{-1}.

EI HRMS calcd for $C_{17}H_{26}O_4$ (M+) 294.18311, obsd 294.1841.

3.37



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PROCNO 1

F2 - Acquisition Parameters
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Time 14.50
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PULPROG zg30
TD 30720
SOLVENT COCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 812.7
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

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

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

1D NMR plot parameters
CX 20.00 cm
CY 10.00 cm
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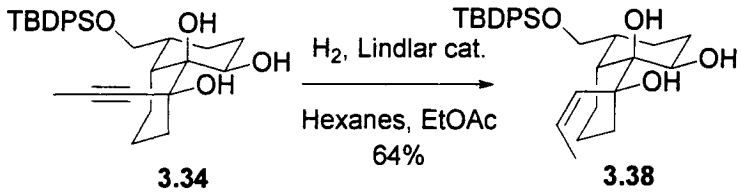
F1 2551.10 Hz
F2P -0.500 ppm
F2 -150.06 Hz
PPMCM 0.45000 ppm/cm
HZCM 135.05850 Hz/cm



3.34 **3.38**

5-(tert-Butyl-diphenyl-silanyloxymethyl)-1-propenyl-octahydro-naphthalene-1,8,8a-triol (3.38)

Alkyne **3.34** (0.017 g, 0.035 mmol) was dissolved in distilled hexanes (0.5 mL) and ethylacetate (0.3 mL). Lindlar's catalyst (a little spatula) was added and the flask was purged with H_2. The reaction was stirred for 2 hours, filtered trough a celite pad with dichloromethane. The solvent was evaporated to afford 11 mg of **3.38** (64 % yield) as a colourless oil.

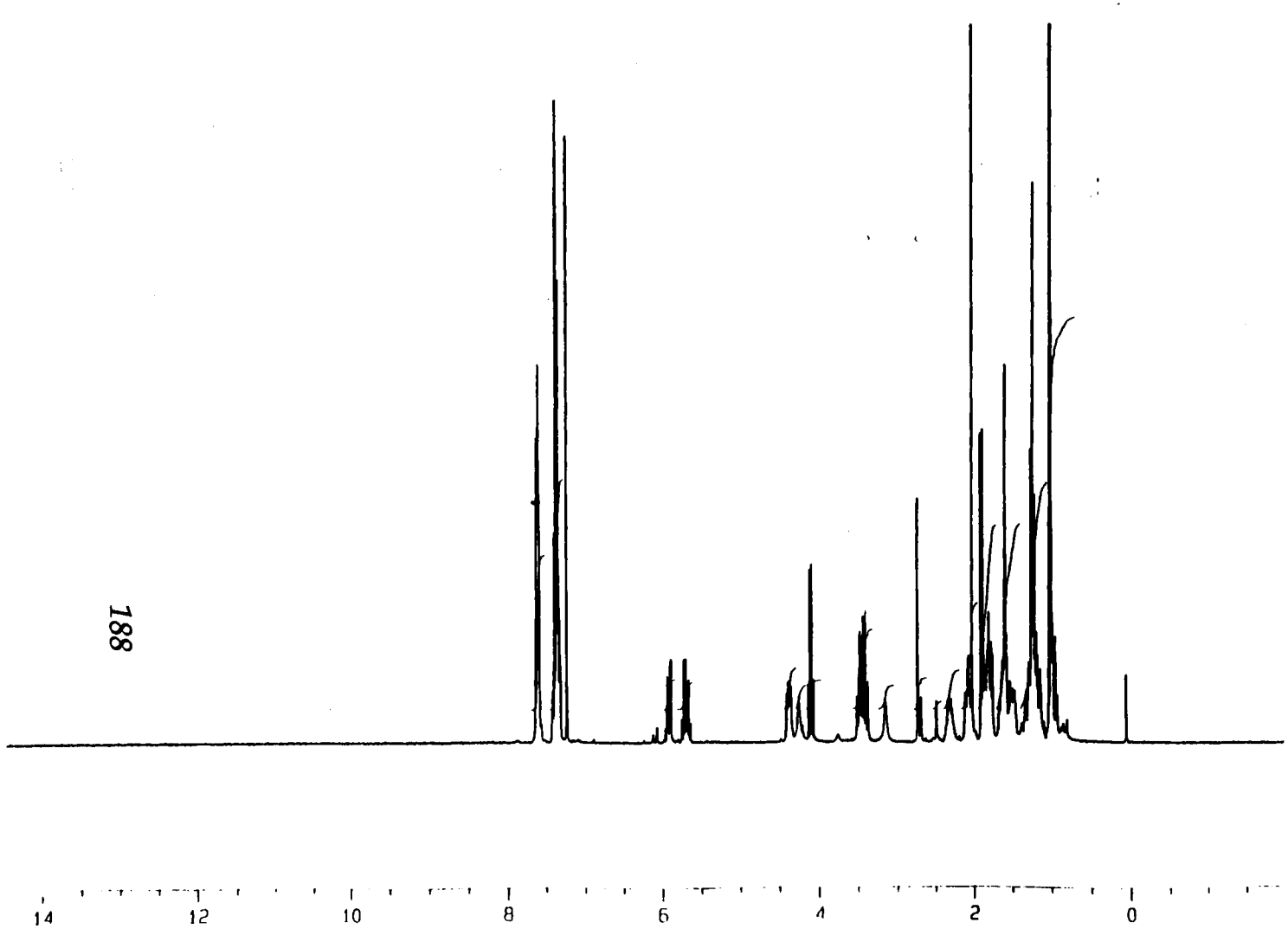
Data for **3.38**

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.64-7.60 (m, 4H), 7.43-7.32 (m, 6H), 5.92 (dd, J= 1.7, 12.1 Hz, 1H), 5.75-5.64 (m, 1H), 4.38 (dd, J= 5.1, 10.9 Hz, 1H), 4.26 (s, 1H), 3.52-3.37 (m, 2H), 3.15 (s, 1H), 2.73 (s, 1H), 2.36-2.27 (m, 1H), 2.11-2.04 (m, 2H), 1.90 (dd, J= 1.7, 7.2 Hz, 2H), 1.87-1.76 (m, 3H), 1.69-1.48 (m, 3H), 1.35-1.15 (m, 4H), 1.02 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 135.6 (x4), 133.8 (x2), 132.1, 129.5 (x2), 128.9, 127.6 (x4), 82.6, 75.6, 69.2, 66.1, 40.9, 36.2, 36.1, 30.1, 26.8 (x3), 22.7, 21.5, 21.3, 19.2, 14.9.

IR (neat) 3384, 2932, 2861, 1112 cm^{-1}.

EI HRMS calcd for $C_{30}H_{42}O_4Si$ (M+) 494.28524, obsd 494.2699.



188

3.38

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Current Data Parameters
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PROCNO                      1

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RG                      362
DW                  98.400 usec
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TE                   300.0 K
D1                1.00000000 sec

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PL1                   -3.00 dB
SFO1             300.1319477 MHz

F2 - Processing parameters
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SF               300.1300000 MHz
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1D NMR plot parameters
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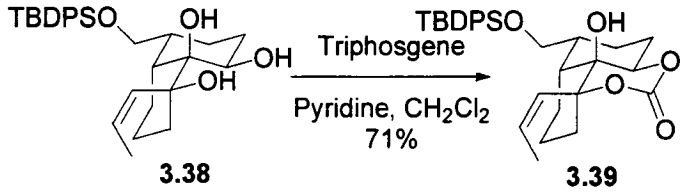


3.38 **3.39**

7-(tert-Butyl-diphenyl-silanyloxymethyl)-9b-hydroxy-3a-propenyl-decahydro-naphtho[1,8-de][1,3]dioxin-2-one (3.39)

Diol **3.38** (0.175 g, 0.35 mmol) was dissolved in dichloromethane (4 mL) and cooled to 0°C. Pyridine (0.028 mL, 0.35 mmol) was added followed by triphosgene (0.125 g, 0.42 mmol). The reaction was warmed to room temperature. The reaction was quenched by adding saturated NH_4Cl_{aq}. The aqueous layer was extracted 3 times with dichloromethane (3 X 20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (10% EtOAc/hexanes) to afford 130 mg of **3.39** (71% yield) as a colourless oil.

Data for **3.39**

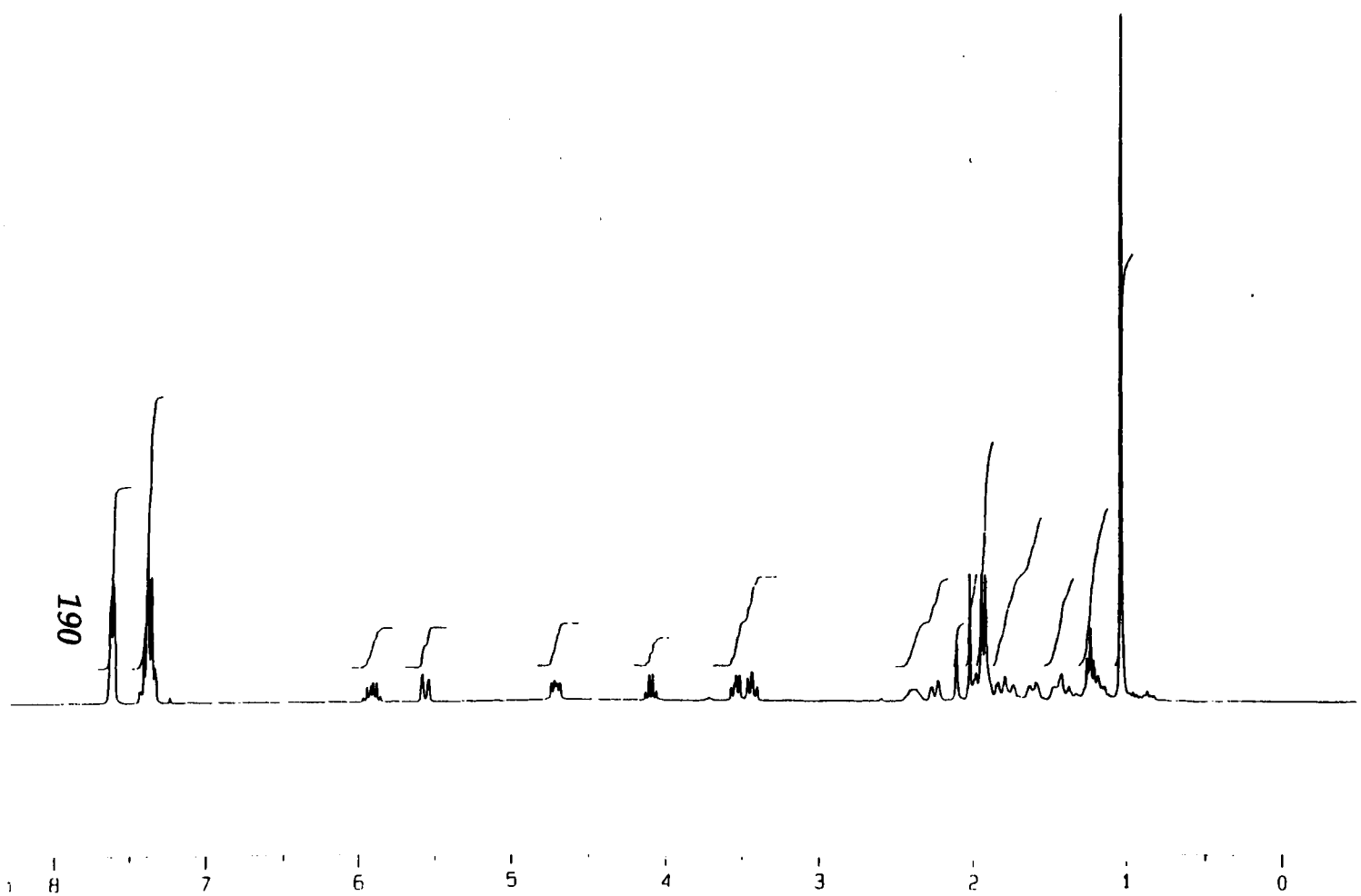
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.63-7.61 (m, 4H), 7.43-7.34 (m, 6H), 5.98-5.86 (m, 1H), 5.57 (d, J= 12.1 Hz, 1H), 4.71 (dd, J= 6.1, 10.5 Hz, 1H), 3.57-3.40 (m, 2H), 2.45-2.32 (m, 1H), 2.24 (d, J= 12.2 Hz, 1H), 2.10 (s, 1H), 2.01-1.97 (m, 2H), 1.92 (d, J= 7.3 Hz, 3H), 1.84-1.69 (m, 2H), 1.63-1.58 (m, 1H), 1.46-1.32 (m, 2H), 1.25-1.09 (m, 3H), 1.03 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 148.0, 135.4 (x2), 135.3 (x2), 133.4, 133.3, 132.9, 129.6 (x2), 127.6 (x4), 123.6, 89.3, 74.4, 68.5, 65.3, 60.3, 41.5, 36.6, 35.8, 26.7 (x3), 25.9, 21.7, 21.1, 19.1, 14.8.

IR (neat) 3445, 2941, 2861, 1731, 1105 cm^{-1}.

EI HRMS calcd for $C_{27}H_{31}O_5Si$ (M+ -tBu) 463.19408, obsd 463.1916.

3.39

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PROCNO                      1

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TD                    30720
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SWH                5081.301 Hz
FIDRES            0.165407 Hz
AQ                3.0228980 sec
RG                       32
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DE                   6.00 usec
TE                  300.0 K
D1                1.00000000 sec

============ CHANNEL f1 =============
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PL1                   -3.00 dB
SFO1             300.1319477 MHz

F2 - Processing parameters
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SF               300.1299995 MHz
WDW                       EM
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1D NMR plot parameters
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CY                     10.00 cm
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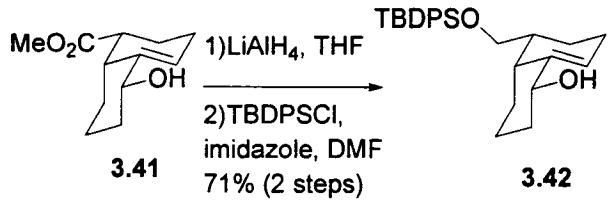


5-(*tert*-Butyl-diphenyl-silanyloxymethyl)-1,2,3,4,4a,5,6,7-octahydro-naphthalen-1-ol (3.42).

$LiAlH_4$ (0.075 g, 1.97 mmol) was added to a solution of ester **3.41** (0.41 g, 1.97 mmol) in THF (20 mL) at –78 °C. The reaction stirred for 30 min. A solution of sodium tartrate 1M (3 mL) was added and stirred for 15 h. The aqueous layer was extracted 3 times with ethylacetate (3 X 40 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent evaporated. The crude product was purified by flash silica column chromatography (EtOAc) to afford 360 mg of the primary alcohol (99% yield) as a white solid. The alcohol was dissolved in DMF (10 mL). Imidazole (0.293 g, 4.3 mmol) was added, followed by DPSCl (0.563 mL, 2.2 mmol). The reaction was stirred at room temperature for 1.5 h. The reaction was quenched using saturated $NH_4Cl_{(aq)}$. The aqueous layer was extracted 3 times with a mixture of 1:1 hexane: diethylether (3 X 30 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash silica column chromatography (10% to 80% EtOAc/hexanes, gradient elution) to afford 69 mg of starting material and 650 mg of **3.42** (78% yield) as a colourless oil.

Data for **3.42**

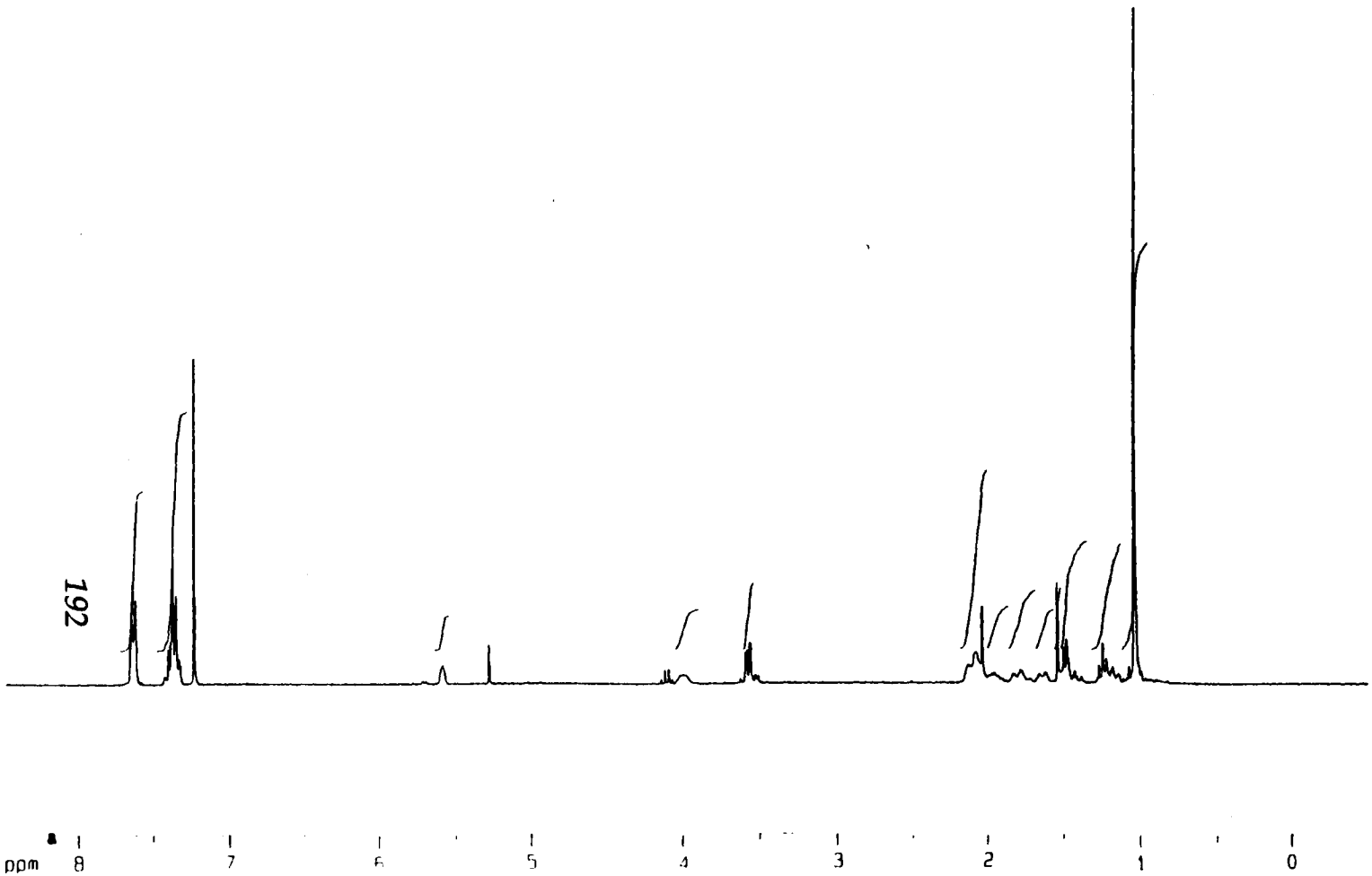
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.70-7.62 (m, 4H), 7.43-7.33 (m, 6H), 5.59 (s, 1H), 4.01-3.98 (m, 1H), 3.62-3.50 (m, 2H), 2.12-2.07 (m, 3H), 1.99-1.88 (m, 1H), 1.85-1.72 (m, 1H), 1.65-1.61 (m, 1H), 1.53 (d, J= 1.1 Hz, 1H), 1.52-1.48 (m, 3H), 1.26-1.14 (m, 3H), 1.03 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 144.4, 135.5 (x4), 134.0 (x2), 129.5 (x2), 127.6 (x4), 114.4, 73.2, 65.9, 39.5, 38.4, 38.2, 27.5, 26.8 (x3), 25.1, 24.4, 21.6, 19.3.

IR (neat) 3346, 2929, 2857, 1110 cm^{-1}.

EI HRMS calcd for $C_{23}H_{27}O_2Si$ (M^+ -*t*Bu) 363.1870, obsd 363.1874.

3.42



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PROCNO 1

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TD 30720
SOLVENT CDCl3
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DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 912.3
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

========== CHANNEL f1 ==========
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PL1 -3.00 dB
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F2 - Processing parameters
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SF 300.1300002 MHz
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LB 0.10 Hz
GB 0
PC 1.00

1D NMR plot parameters
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CY 10.00 cm
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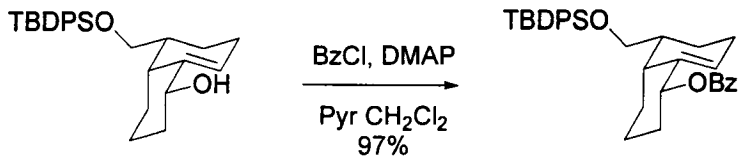
F2P -0.500 ppm
F2 -150.06 Hz
PPMCM 0.45000 ppm/cm
HZCM 135.05850 Hz/cm



3.42 **3.43**

Benzoic acid 5-(tert-butyl-diphenyl-silanyloxymethyl)-1,2,3,4,4a,5,6,7-octahydro-naphthalen-1-yl ester (3.43)

Alcohol **3.42** (0.729 g, 1.73 mmol) was dissolved in dichloromethane (9 mL). Pyridine (0.42 mL, 5.2 mmol), DMAP (1 crystal) and benzoyl chloride (0.3 mL, 2.6 mmol) were added and stirred for 15 h. HCl 2 N (4 mL) was added and the aqueous layer was extracted 3 times with dichloromethane (3 X 50 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash silica column chromatography (10% EtOAc/hexanes) to afford 84 mg of **3.43** (97% yield) as a colourless oil.

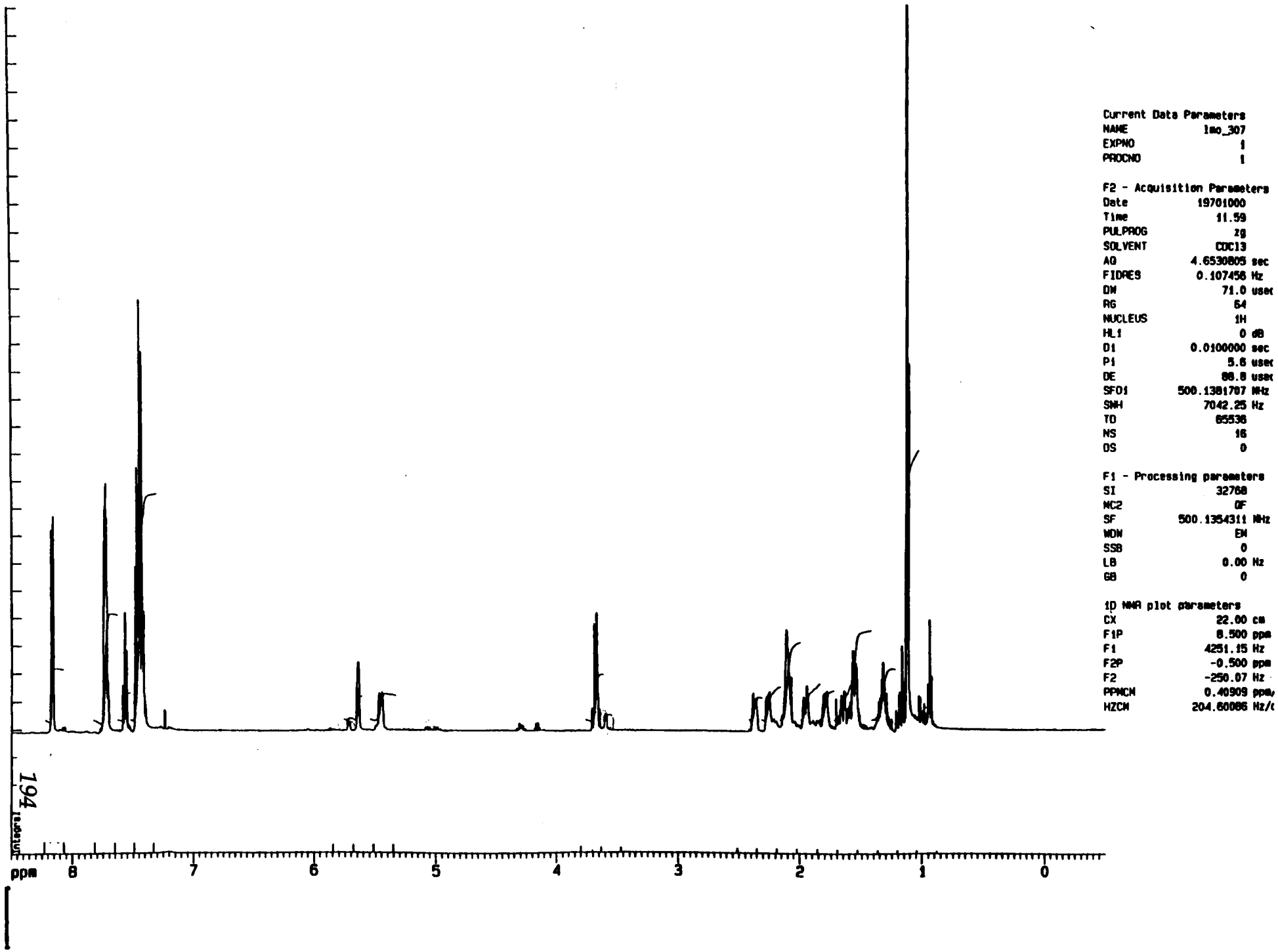
Data for **3.43**

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.18-8.15 (m, 2H), 7.76-7.71 (m, 4H), 7.59-7.53 (m, 1H), 7.49-7.39 (m, 8H), 5.64 (s, 1H), 5.46 (d, J= 11.0 Hz, 1H), 3.71-3.64 (m, 2H), 2.38-2.35 (m, 1H), 2.27-2.24 (m, 1H), 2.14-2.07 (m, 2H), 1.97-1.93 (m, 1H), 1.86-1.75 (m, 2H), 1.68-1.62 (m, 1H), 1.61-1.59 (m, 1H), 1.57-1.54 (m, 1H), 1.35-1.29 (m, 1H), 1.21-1.15 (m, 1H), 1.13 (s, 9H);).

^{13}C NMR (125 MHz, $CDCl_3$) δ 165.5, 139.8, 135.5 (x4), 134.0 (x2), 132.7 (x2), 130.7, 129.6 (x2), 129.5 (x2), 128.3 (x2), 127.6 (x2), 127.54, 115.6, 75.2, 65.8, 39.6, 38.4, 34.9, 27.4, 26.9 (x3), 25.0, 24.5, 21.5, 19.2.

IR (neat) 3063, 2937, 2854, 1722, 1267, 1102 cm^{-1}.

EI HRMS calcd for $C_{30}H_{31}O_3Si$ (M^+ -*t*Bu) 467.2042, obsd 467.1834.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PROCNO 1
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TD 65536
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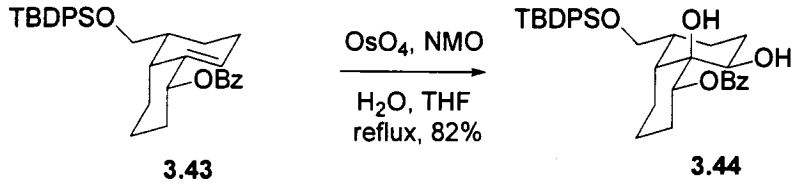


3.43 **3.44**

Benzoic acid 5-(*tert*-butyl-diphenyl-silanyloxymethyl)-8,8a-dihydroxy-decahydro-naphthalen-1-yl ester (3.44).

Compound **3.43** (84 mg, 0.16 mmol) was dissolved in THF (1.6 mL) and water (0.32 mL). NMO (0.037 g, 0.32 mmol) was added, followed by osmium tetroxide 4% in water (0.050 mL, 0.008 mmol). The reaction was stirred for 6 h at reflux and 18 h at room temperature. The reaction was not finished, NMO (0.02 g, 0.17 mmol) and osmium tetraoxide 4% in water (0.02 mL, 0.003) were added and stirred for 24 h at reflux. After completion, the reaction was quenched with a saturated aqueous solution of $Na_2S_2O_3$. The aqueous layer was extracted 3 times with ethylacetate (3 X 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash silica column chromatography (20% EtOAc/hexanes) to afford 73 mg of **3.44** (82% yield) as a colourless oil.

Data for **3.44**

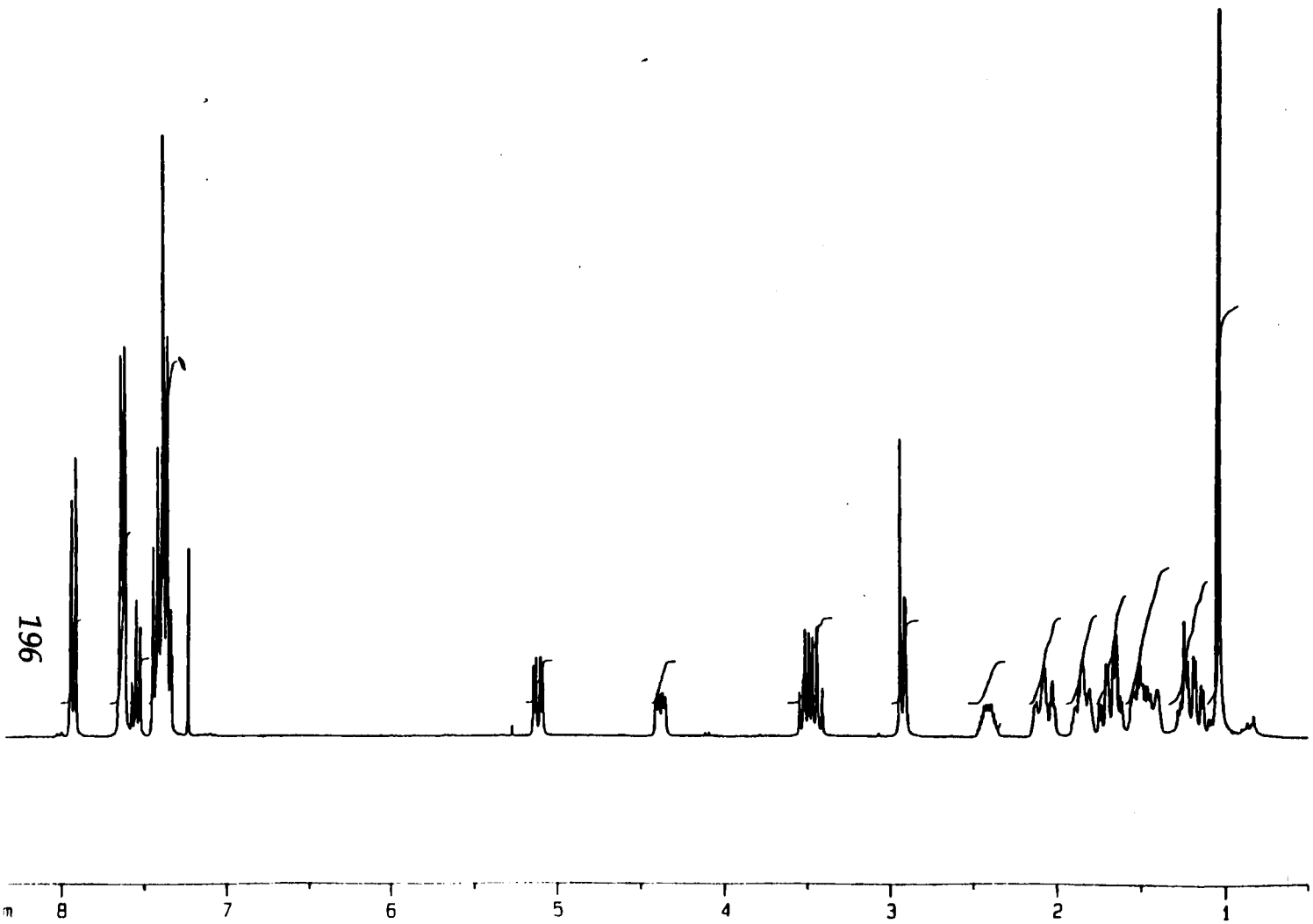
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.96-7.92 (m, 2H), 7.67-7.63 (m, 4H), 7.56 (tt, 1.3, 7.4 Hz, 1H), 7.44-7.34 (m, 8H), 5.12 (dd, J= 4.4, 12.1 Hz, 1H), 4.40-4.35 (m, 1H), 3.55-3.41 (m, 2H), 2.94 (s, 1H), 2.91 (d, J= 2.1 Hz, 1H), 2.46-2.35 (m, 1H), 2.13-2.01 (m, 2H), 1.91-1.80 (m, 2H), 1.75-1.61 (m, 2H), 1.56-1.40 (m, 3H), 1.28-1.13 (m, 2H), 1.04 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9, 135.6 (x4), 133.7 (x2), 133.3, 129.9, 129.6, 129.5, 129.3 (x2), 128.6 (x2), 127.6 (x4), 83.9, 73.6, 68.4, 65.8, 43.6, 35.8, 29.3, 28.8, 26.8 (x3), 23.6, 21.6, 21.3, 19.2.

IR (neat) 3470, 2921, 2854, 1722, 1272, 1106 cm^{-1}.

EI HRMS calcd for $C_{30}H_{33}O_5Si$ (M^+ -*t*Bu) 501.2097, obsd 501.1991.

3.44



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PROCNO	1

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FIDRES	0.165407 Hz
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========== CHANNEL f1 ==========

NUC1	1H
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PL1	-3.00 dB
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F2 - Processing parameters

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1D NMR plot parameters

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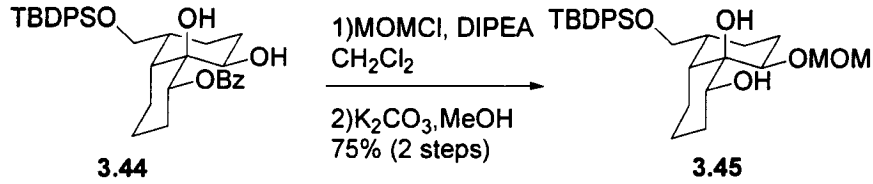


3.44 **3.45**

5-(tert-Butyl-diphenyl-silanyloxymethyl)-8-methoxymethoxy-octahydro-naphthalene-1,8a-diol (3.45)

Diol **3.44** (0.57 g, 1.02 mmol))was dissolved in dichloromethane (10 mL) and DIPEA (1.8 mL, 10.2 mmol) was added at 0°C. Chloromethyl methyl ether (0.23 mL, 3.06 mmol) was added. The reaction was warmed to 50 °C in a sealed tube for 60 min. The temperature was cooled to room temperature for 15 hours. The reaction was quenched by adding saturated NH_4Cl_{aq}. The aqueous layer was extracted 3 times with dichloromethane (3 X 30 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude material was dissolved in benzene (2 mL) and MeOH (2 mL). K_2CO_3 added until it didn't dissolved and heated to reflux for 6 hours, then cooled down to room temperature. Filtrated trough a celite pad with diethylether. The solvent was evaporated. The crude product was purified by flash column chromatography (50% EtOAc/hexanes) to afford 30 mg of **3.45** (75 % yield) as colourless oil.

Data for **3.45**

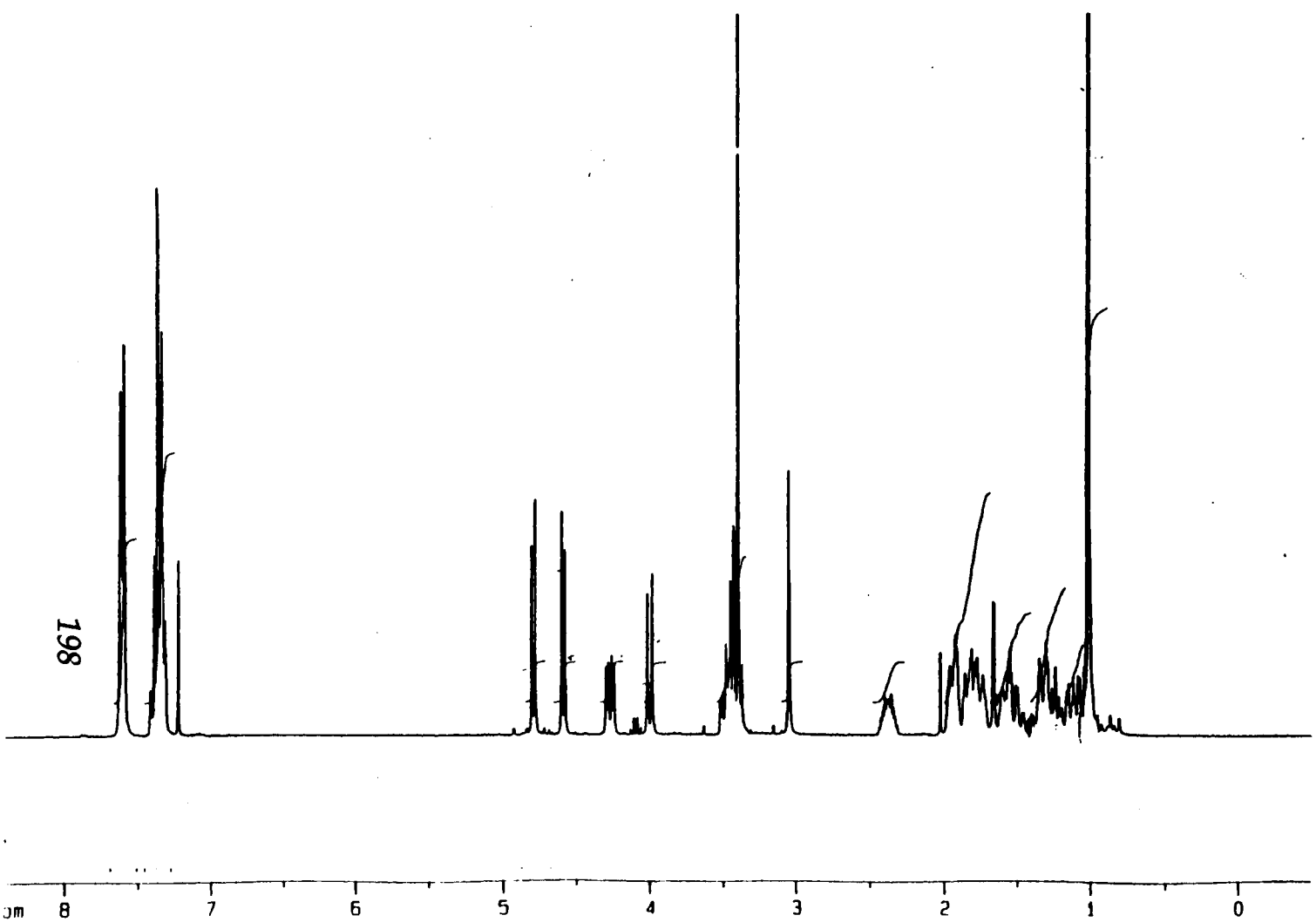
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.64-7.61 (m, 4H), 7.43-7.32 (m, 6H), 4.80 (d, J= 6.8 Hz, 1H), 4.59 (d, J= 6.8 Hz, 1H), 4.40 (dd, J= 4.8, 11.4 Hz, 1H), 4.090 (d, J= 9.9 Hz, 1H), 3.48-3.43 (m, 2H), 3.40 (s, 3H), 3.05 (s, 1H), 2.44-2.32 (m, 1H), 1.96-1.91 (m, 2H), 1.86-1.77 (m, 3H), 1.66 (s, 1H), 1.61-1.54 (m, 2H), 1.35-1.20 (m, 3H), 1.16-1.04 (m, 1H), 1.01 (s, 9H).

^{13}C NMR ($CDCl_3$, 300 MHz) δ 135.6, 135.5, 133.8, 129.6, 129.5, 127.6, 93.8, 80.8, 75.3, 74.0, 66.0, 56.4, 44.3, 36.1, 31.8, 26.8, 25.4, 24.0, 21.8, 21.6, 19.2.

IR (neat) 3487, 2932, 2859, 1425, 1111, 1023 cm^{-1}.

EI HRMS indeterminable.

3.45



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PROCNO 1

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TD 30720
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FIDRES 0.165407 Hz
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RG 143.7
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DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

========== CHANNEL f1 ==========
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PL1 -3.00 dB
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F2 - Processing parameters
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1D NMR plot parameters
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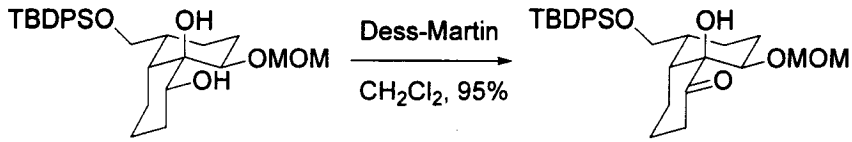


3.45 **3.46**

5-(tert-Butyl-diphenyl-silanyloxymethyl)-8a-hydroxy-8-methoxymethoxy-octahydro-naphthalen-1-one (3.46)

Alcohol **3.45** (0.510 g, 1.03 mmol) was dissolved in CH_2Cl_2 (10 mL) and Dess-Martin periodinane (540 mg, 1.27 mmol) was added. The reaction was stirred for 3 hours at room temperature. The reaction was quenched by adding a solution of $NaHCO_{3sat.}$ followed by $Na_2SO_{3sat.}$ The aqueous layer was extracted 3 times with dichloromethane (3 X 30 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (20% EtOAc/hexanes) to afford 480 mg of **3.46** (95% yield) as a colourless oil.

Data for **3.46**

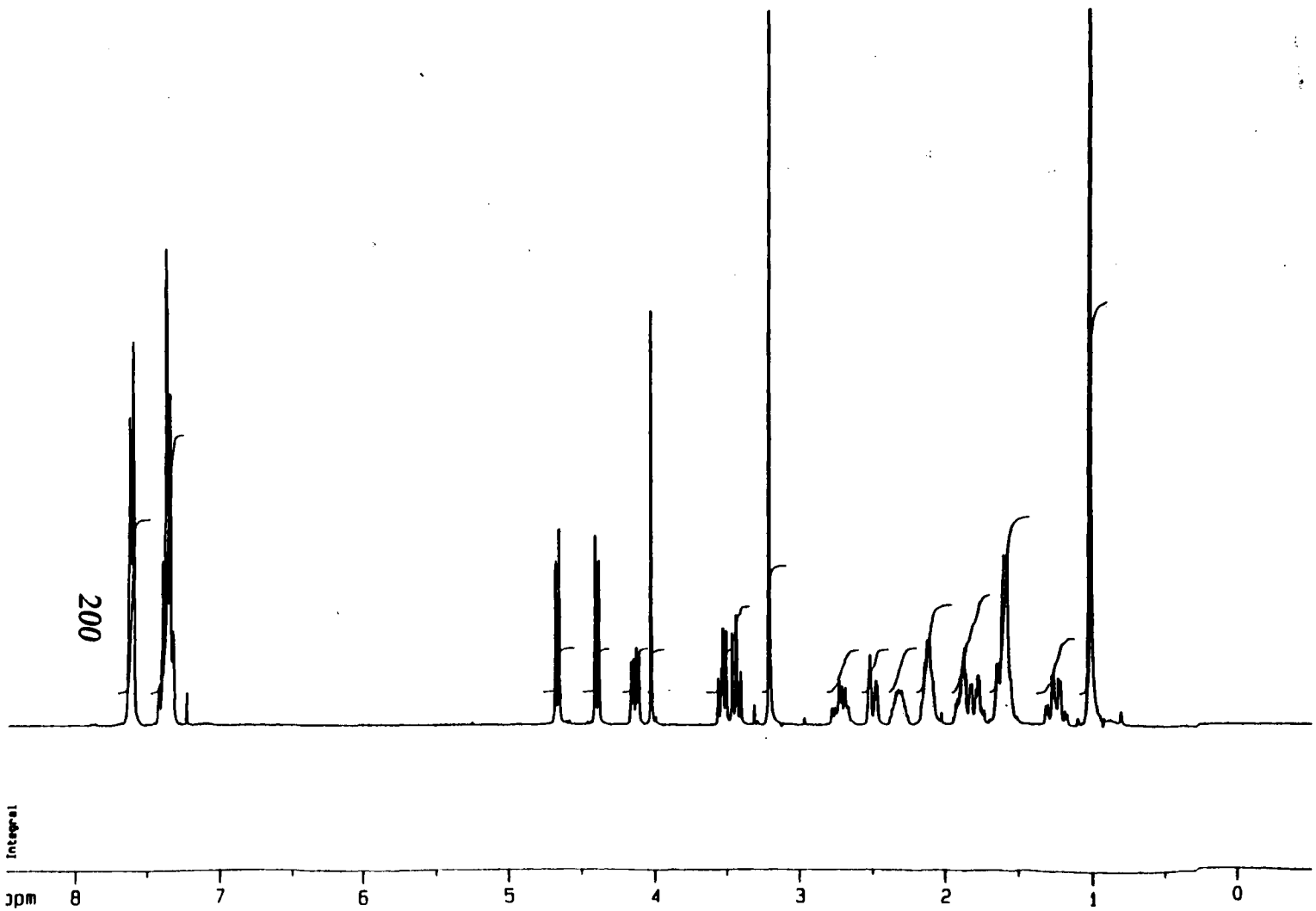
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.64-7.61 (m, 4H), 7.43-7.34 (m, 6H), 4.67 (d, J= 7.3 Hz, 1H), 4.40 (d, J= 7.2 Hz, 1H), 4.14 (dd, J= 5.0, 11.2 Hz, 1H), 4.03 (s, 1H), 3.57-3.41 (m, 2H), 3.21 (s, 3H), 2.78-2.67 (m, 1H), 2.52-2.47 (m, 1H), 2.38-2.26 (m, 1H), 2.14-2.02 (m, 2H), 1.94-1.73 (m, 2H), 1.70-1.50 (m, 4H), 1.25 (dq, 4.3, 13.2 Hz, 1H), 1.01 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 211.9, 135.5, 133.6, 133.5, 129.6, 129.5, 127.6, 94.1, 80.7, 74.9, 65.6, 55.6, 48.1, 37.4, 36.4, 26.7, 26.3, 25.9, 22.4, 21.4, 19.1.

IR (neat) 3488, 2932, 2860, 1715, 1428, 1110, 1035.

EI HRMS calcd for $C_{29}H_{40}O_5Si$ (M^+) 496.26450, obsd 496.26028.

3.46



Current Data Parameters
NAME lmo221
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20020729
Time 18.01
INSTRUM av300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 45.3
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

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

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

1D NMR plot parameters
CX 20.00 cm
CY 40.00 cm
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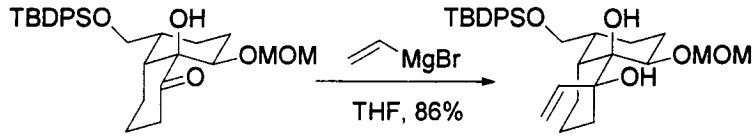
F2P -0.500 ppm
F2 -150.06 Hz
PPMCM 0.45000 ppm/cm
HZCM 135.05850 Hz/cm



3.46 **3.47**

5-(tert-Butyl-diphenyl-silanyloxymethyl)-8-methoxymethoxy-1-vinyl-octahydro-naphthalene-1,8a-diol (3.47)

Ketone **3.46** (0.01 g, 0.02 mmol) was dissolved in THF and cooled to -78°C. Vinylmagnesium bromide 0.7 M (0.063 mL, 0.044 mmol) was added and warmed to room temperature for 1 hour. More grignard reagent added (0.063 mL) and stirred for 2 hours. The reaction was quenched by adding saturated $NH_4Cl_{sat.}$ The aqueous layer was extracted 3 times with ethylacetate (3 X 20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (20% EtOAc/hexanes) to afford 9 mg of **3.47** (86% yield) as a colourless oil.

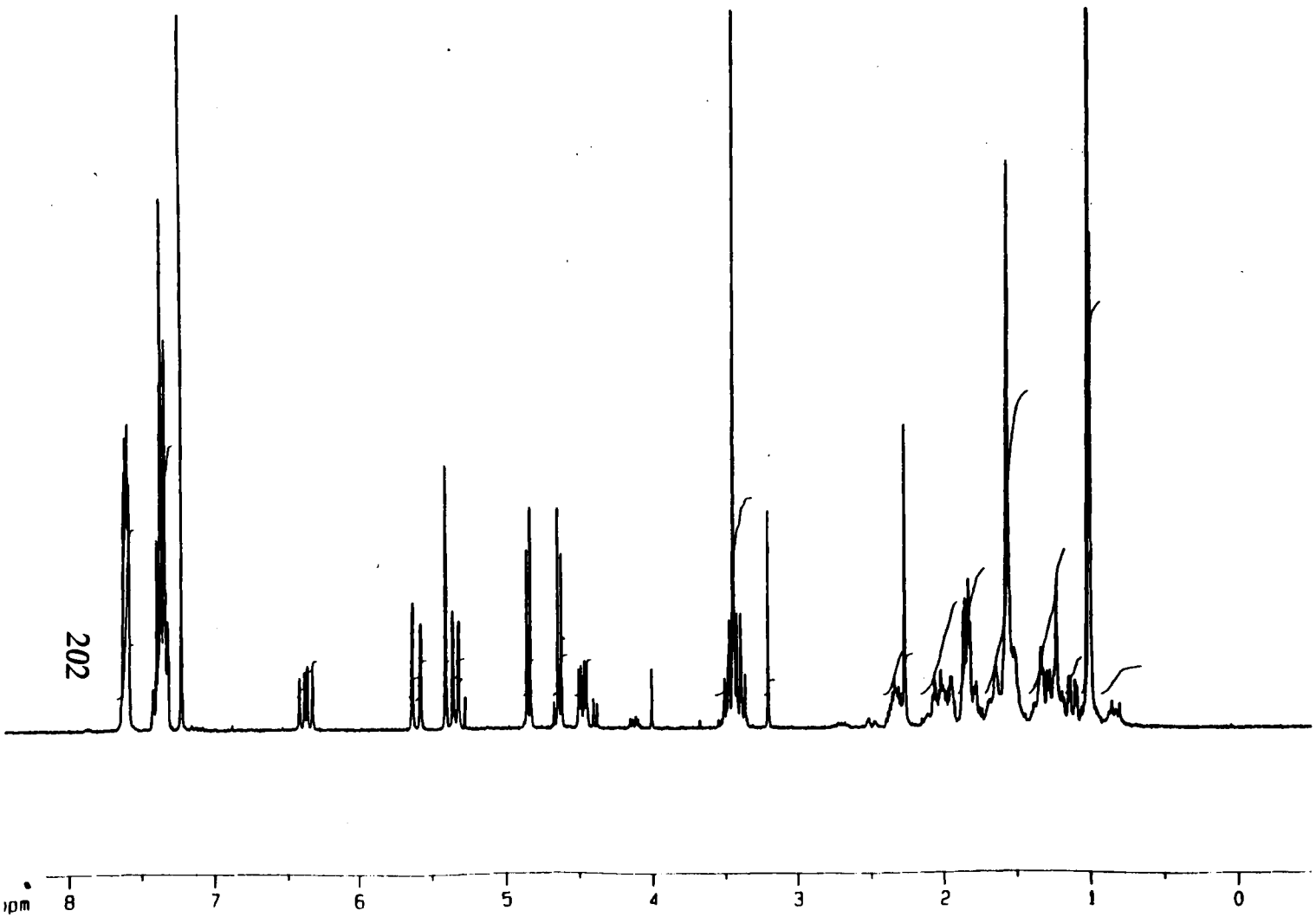
Data for **3.47**

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64-7.60 (m, 4H), 7.43-7.33 (m, 6H), 6.42-6.33 (m, 1H), 5.61 (dd, J= 2.2, 17.0 Hz, 1H), 5.41 (d, J= 1.0 Hz, 1H), 5.34 (dd, J= 2.2, 10.8 Hz, 1H), 4.85 (d, J= 7.1 Hz, 1H), 4.63 (d, J= 7.1 Hz, 1H), 4.48 (dd, J= 4.9, 11.4 Hz, 1H), 3.52-3.36 (m, 5H), 2.38-2.29 (m, 1H), 2.27 (s, 1H), 2.08-1.93 (m, 2H), 1.87-1.74 (m, 3H), 1.68-1.61 (m, 1H), 1.53-1.47 (m, 1H), 1.38-1.18 (m, 3H), 1.13 (dd, J= 4.3, 13.5 Hz, 1H), 1.02 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 138.5, 135.6, 135.6, 133.1, 129.6, 127.6, 116.9, 94.0, 79.1, 75.3, 75.2, 65.9, 56.9, 42.3, 36.8, 35.9, 26.8, 26.0, 22.0, 21.7, 21.5, 19.3.

IR (neat) 3442, 2931, 2859, 1646, 1112, 1017.

EI HRMS indeterminable.



3.47

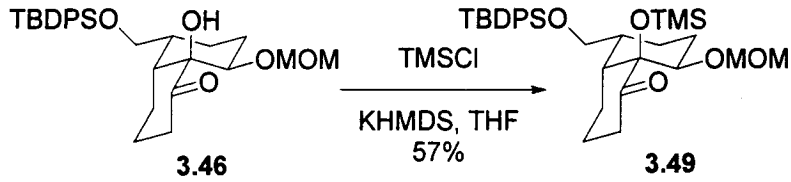
Current Data Parameters
NAME 1mo_243
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20020814
Time 9.47
INSTRUM av300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 406.4
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

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

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

1D NMR plot parameters
CX 20.00 cm
CY 50.00 cm
F1P 8.500 ppm
F1 2551.10 Hz
F2P -0.500 ppm
F2 -150.06 Hz
PPMCM 0.45000 ppm/cm
HZCM 135.05850 Hz/cm



3.46 **3.49**

5-(tert-Butyl-diphenyl-silanyloxymethyl)-8-methoxymethoxy-8a-trimethylsilanyloxy-octahydro-naphthalen-1-one (3.49)

Alcohol **3.46** (0.02 g, 0.04 mmol) was dissolved in THF (0.5 mL) and cooled to -78°C. KHMDS 0.5 M (0.32 mL, 0.16 mmol) was added, followed by trimethylsilylchloride (0.02 mL, 0.16 mmol). The reaction was allowed to warm to room temperature for 15 hours. The reaction was cooled back to -78°C and KHMDS (0.32 mL, 0.16 mmol) was added, followed by trimethylsilylchloride (0.03 mL, 0.24 mmol). The reaction was allowed to warm to room temperature for 24 hours. The crude mixture was purified directly by flash column chromatography (10% EtOAc/hexanes) to afford 13 mg of **3.49** (57% yield) as a colourless oil.

Data for **3.49**

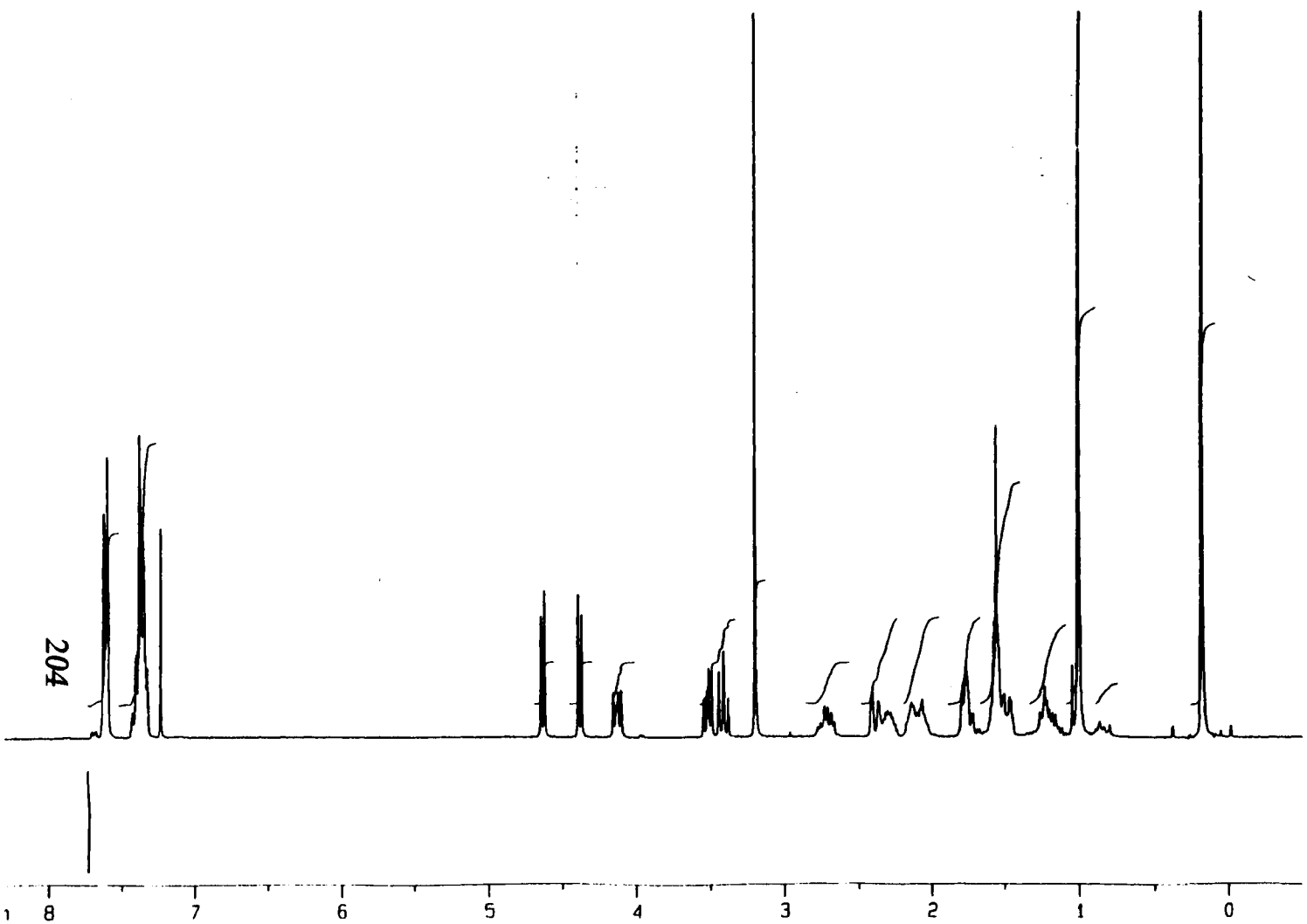
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.63-7.61 (m, 4H), 7.41-7.33 (m, 6H), 4.64 (d, J= 7.2 Hz, 1H), 4.38 (d, J= 7.2 Hz, 1H), 4.16-4.10 (m, 1H), 3.55-3.38 (m, 2H), 3.20 (s, 3H), 2.77-2.66 (m, 1H), 2.41-2.25 (m, 2H), 2.14-2.03 (m, 2H), 1.80-1.72 (m, 2H), 1.56-1.46 (m, 4H), 1.26-1.05 (m, 1H), 1.01 (s, 9H), 0.18 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 210.5, 135.5 (x4), 133.8, 133.7, 129.6, 127.6 (x4), 94.1, 85.2, 75.5, 65.7, 55.6, 49.3, 38.8, 36.5, 26.8 (x3), 26.5, 25.9, 22.4, 21.9, 19.2, 2.8 (x3).

IR (neat) 2953, 1727, 1106, 1036 cm^{-1}.

EI HRMS calcd for $C_{32}H_{48}O_3Si_2$ (M^+) 568.30403, obsd 568.27461.

3.49



Current Data Parameters

NAME	lmo_269
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20020830
Time	17.42
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	287.4
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

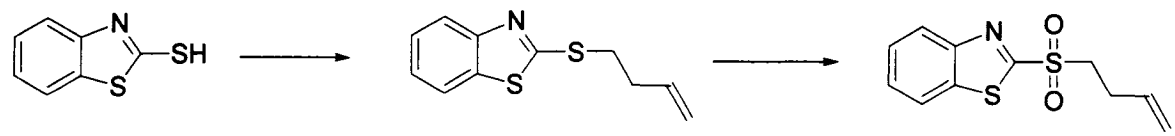
NUC1	1H
P1	9.75 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

F2 - Processing parameters

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

1D NMR plot parameters

CX	20.00 cm
CY	40.00 cm
F1P	8.500 ppm
F1	2551.10 Hz
F2P	-0.500 ppm
F2	-150.06 Hz
PPMCM	0.45000 ppm/cm
HZCM	135.05850 Hz/cm



3.50

2-But-3-enylsulfanyl-benzothiazole

3-buten-1-ol (0.1 g, 1.39 mmol), triphenylphosphine (0.546 g, 2.08 mmol), 2-mercaptobenzothiazole (0.348 g, 2.08 mmol) were dissolved in dichloromethane (6 mL) at 0°C. Diisopropylazodicarboxylate (0.41 mL, 2.08 mmol) was added dropwise and stirred at 0°C for 1 hour. The reaction was warmed to room temperature for 1 hour. The reaction was loaded directly on flash column chromatography (10% EtOAc/hexane) to afford 330 mg of **thioether** (100% yield) as colourless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.85 (d, J= 8.1 Hz, 1H), 7.73 (d, J= 7.9 Hz, 1H), 7.42-7.27 (m, 2H), 5.91-5.82 (m, 1H), 5.17-5.07 (m, 2H), 3.40 (t, J= 7.3 Hz, 2H), 2.57 (q, J= 7.1 Hz, 2H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 153.3, 135.7, 135.2, 126.0, 124.2, 121.5, 120.9, 116.9, 33.3, 32.7; IR (neat) 2986, 2925, 1458, 1427, 994; EI HRMS calcd for $C_{11}H_{11}NS_2$ (M^+) 221.03329, obsd 221.03430.

2-(But-3-ene-1-sulfonyl)-benzothiazole (3.50)

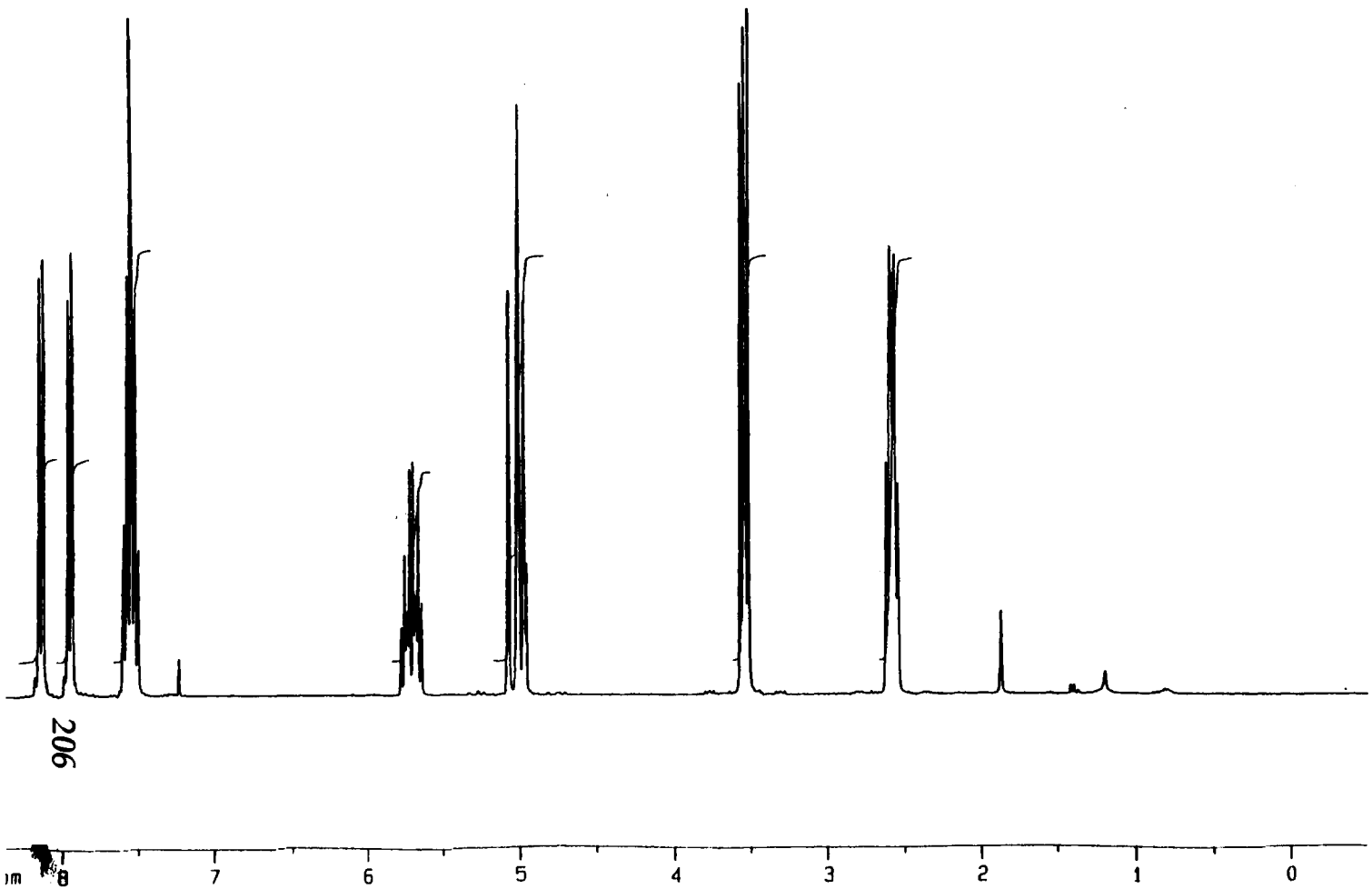
The **thioether** (0.33 g, 1.49 mmol) was dissolved in ethanol (15 mL) and cooled to 0 °C. Ammonium heptamolybdate tetrahydrate (0.46 g, 0.37 mmol) was added followed by H_2O_2 30 % (19 mL, 5.67 mmol). The reaction was stirred for 24 hours. The ethanol was evaporated. The aqueous layer was extracted 3 times with dichloromethane (3 X 30 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (10% EtOAc/hexanes to 20% EtOAc/hexanes) to afford 187 mg of **3.50** (50% yield) as white crystals. Mp 74.9-75.4°C.

Data for **3.50**

^{1}H NMR (300 MHz, $CDCl_3$): δ 8.14 (dd, J= 1.3, 8.1 Hz, 1H), 7.96 (dd, J= 1.4, 7.9 Hz, 1H), 7.56 (dq, 1.4, 7.2 Hz, 2H), 5.78-5.65 (m, 1H), 5.09-4.96 (m, 2H), 3.57-3.52 (m, 2H), 2.60 (q, J= 6.6 Hz, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 165.3, 152.4, 136.5, 133.0, 127.9, 127.5, 125.2, 122.2, 117.5, 53.6, 26.3.

IR (neat) 3082, 2988, 2925, 1476, 1330, 1154 cm^{-1}. **EI HRMS** indeterminable.



3.50

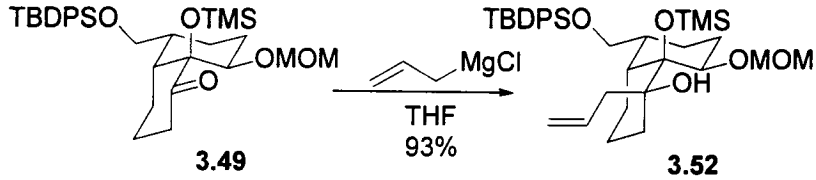
Current Data Parameters
NAME lmo_233
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20020808
Time 9.32
INSTRUM av300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 45.3
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

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

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

1D NMR plot parameters
CX 20.00 cm
CY 10.00 cm
F1P 8.500 ppm
F1 2551.10 Hz
F2P -0.500 ppm
F2 -150.06 Hz
PPMCM 0.45000 ppm/cm
HZCM 135.05850 Hz/cm



1-Allyl-5-(tert-butyl-diphenyl-silanyloxymethyl)-8-methoxymethoxy-8a-trimethylsilanyloxy-decahydro-naphthalen-1-ol (3.52)

Ketone **3.49** (0.024 g, 0.042 mmol) was dissolved in THF (0.5 mL) and cooled to –78 °C. Allylmagnesium chloride was added and stirred for 1 hour. The reaction was allowed to warm to room temperature. The reaction was quenched by adding $NaHCO_{3sat}$ The aqueous layer was extracted 3 times with diethylether (3 X 20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (10% EtOAc/hexanes) to afford 24 mg of **3.52** (93 % yield) as colourless oil.

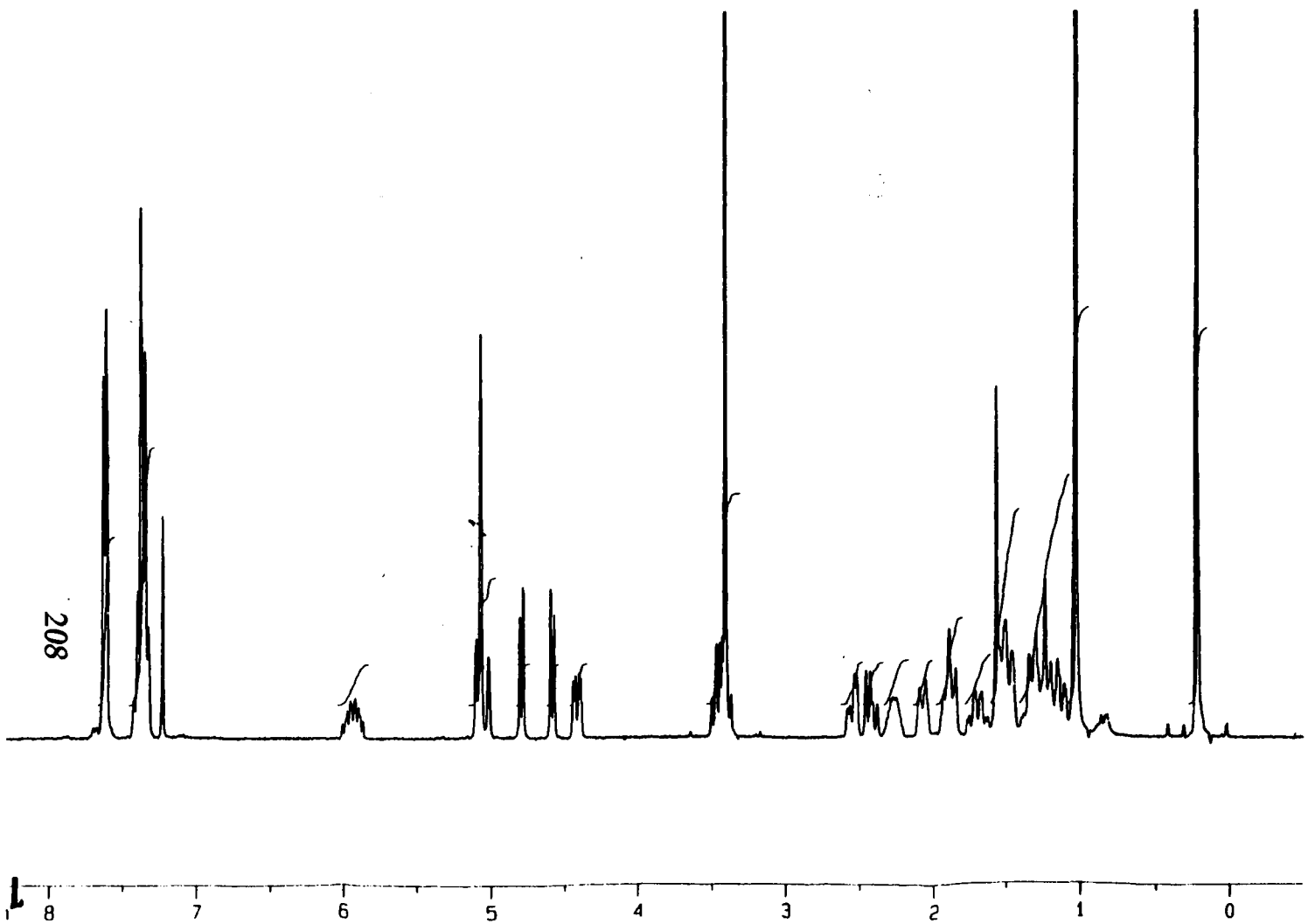
Data for **3.52**

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.63 (d, J= 6.8 Hz, 4H), 7.43-7.33 (m, 6H), 6.01-5.87 (m, 1H), 5.10-5.02 (m, 3H), 4.80 (d, J= 7.1 Hz, 1H), 4.59 (d, J= 7.1 Hz, 1H), 4.42 (dd, J= 4.7, 11.7 Hz, 1H), 3.50-3.37 (m, 2H), 3.41 (s, 3H), 2.58-2.52 (m, 1H), 2.46-2.38 (m, 1H), 2.29-2.24 (m, 1H), 2.10-2.05 (m, 1H), 1.93-1.85 (m, 2H), 1.77-1.63 (m, 1H), 1.54-1.46 (m, 3H), 1.39-1.09 (m, 4H), 1.03 (s, 9H), 0.22 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 135.5 (x4), 135.1, 134.0 (x2), 129.6 (x2), 127.6 (x4), 116.8, 94.1, 81.2, 78.9, 76.3, 66.1, 56.9, 42.6, 37.2, 36.6, 34.0, 26.8 (x3), 26.2, 21.8, 21.7, 21.6, 19.3, 3.2 (x3).

IR (neat) 3474, 2961, 2855, 1112, 1025 cm^{-1}.

HRMS EI indeterminable.



3.52

Current Data Parameters
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EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
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Time 17.04
INSTRUM av300
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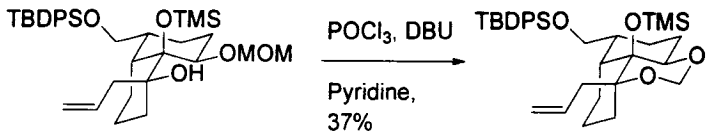
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 322.5
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

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

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

1D NMR plot parameters
CX 20.00 cm
CY 40.00 cm
F1P 8.500 ppm
F1 2551.10 Hz
F2P -0.500 ppm
F2 -150.06 Hz
PPMCM 0.45000 ppm/cm
HZCM 135.05850 Hz/cm



3.52 **3.54**

3a-Allyl-7-(tert-butyl-diphenyl-silanyloxymethyl)-9b-trimethylsilanyloxy-decahydro-naphtho[1,8-de][1,3]dioxine (3.54)

Alcohol **3.52** (0.011 g, 0.018 mmol) was dissolved in pyridine (0.5 mL) and DBU (0.073 mL, 0.054 mmol) and cooled to 0°C. $POCl_3$ (0.05 mL, 0.054 mmol) was added and the reaction was heated in a sealed tube at 65°C for 24 hours. Diethylether and water were added. The aqueous layer was extracted 3 times with ethylacetate (3 X 20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (5% EtOAc/hexanes) to afford 4 mg of **3.54** (37% yield) as a colourless oil.

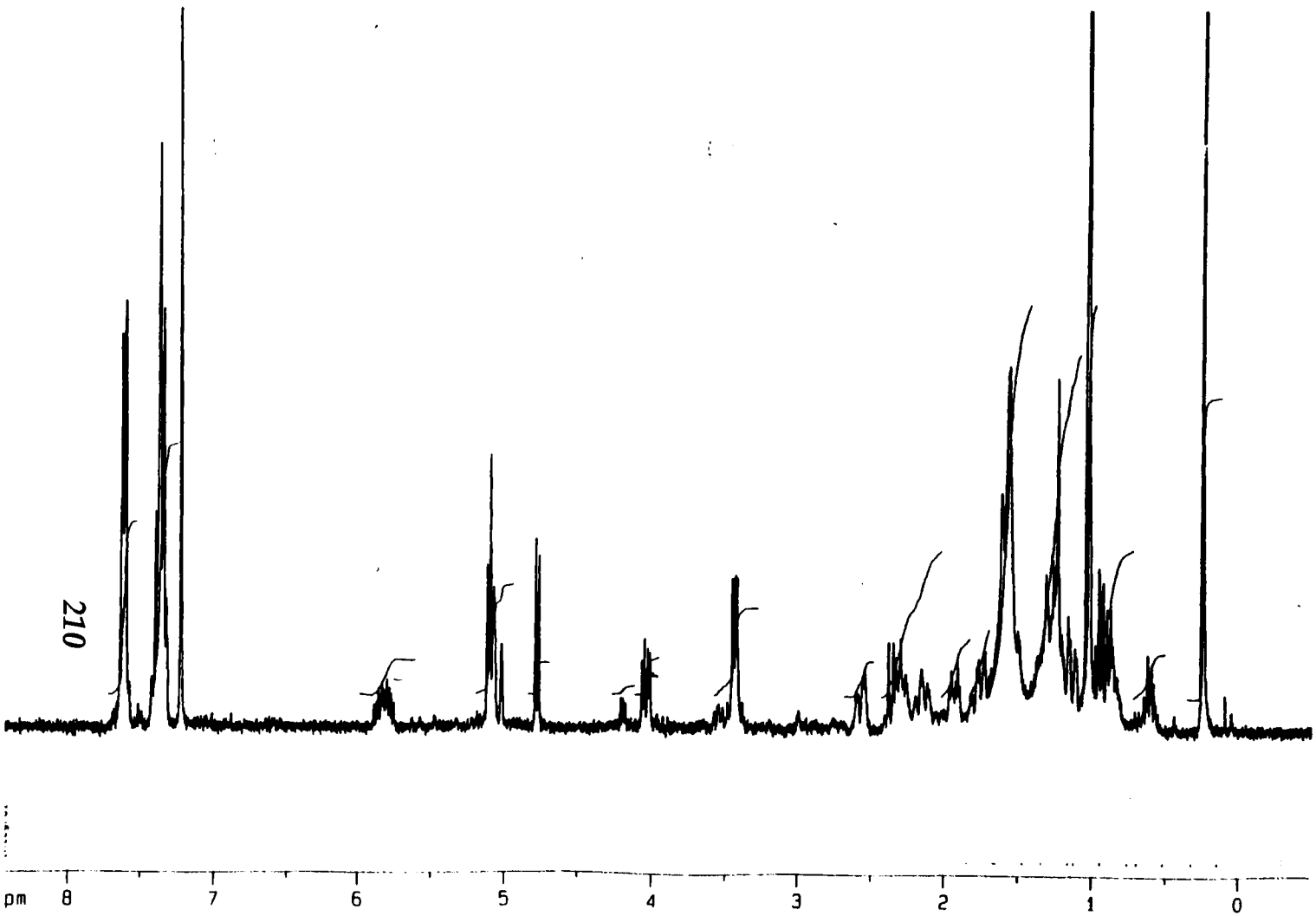
Data for **3.54**

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.70-7.50 (m, 4H), 7.43-7.34 (m, 6H), 5.90-5.76 (m, 1H), 5.195 (s, 2H), 4.78 (d, J= 6.5 Hz, 1H), 4.04 (dd, J= 4.6, 11.3 Hz, 1H), 3.43 (dd, J= 2.9, 7.0 Hz, 2H), 2.61-2.54 (m, 1H), 2.41-2.41 (m, 3H), 1.96-1.68 (m, 2H), 1.61-1.50 (m, 3H), 1.41-1.10 (m, 3H), 1.03 (s, 9H), 1.01-0.84 (m, 3H), 0.24 (s, 9H)

^{13}C NMR (125 MHz, $CDCl_3$) δ 135.5, 134.3, 134.0 (x2), 129.5 (x2), 127.6 (x4), 117.3, 86.9, 79.3, 76.8, 73.3, 66.2, 41.9, 37.1, 36.8, 26.8 (x3), 26.6, 25.9, 22.0, 21.8, 21.4, 19.3, 3.3 (x3).

IR (neat) 3424, 2954, 2859, 1037 cm^{-1}.

EI HRMS calcd for $C_{30}H_{41}O_4Si_2$ (M^+ -tBu) 521.25434, obsd 521.2616.



3.54

Current Data Parameters
NAME lmo_277
EXPNO 2
PROCNO 1

F2 - Acquisition Parameters
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Time 16.57
INSTRUM av300
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PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 1024
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

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

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

1D NMR plot parameters
CX 20.00 cm
CY 60.00 cm
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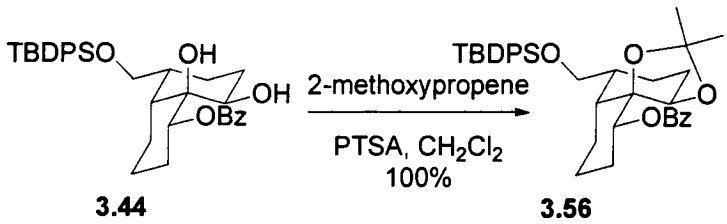
F1 2551.10 Hz
F2P -0.500 ppm
F2 -150.06 Hz
PPMCM 0.45000 ppm/cm
HZCM 135.05850 Hz/cm



3.44 **3.56**

Benzoic acid 6-(*tert*-butyl-diphenyl-silanyloxymethyl)-2,2-dimethyl-octahydro-naphtho[1,8a-d][1,3]dioxol-10-yl ester (3.56).

Diol **3.44** (0.693 g, 1.24 mmol) was dissolved in CH_2Cl_2 (12 mL). 2-methoxypropene (0.356 mL, 3.72 mmol) and TsOH (1 crystal) were added, then the solution turned dark red. The reaction was done after 10 min. $NaHCO_{3sat}$ was added. The aqueous layer was extracted 3 times with dichloromethane (3 X 60 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated by rotary evaporation under vacuum. The crude product was purified by flash silica column chromatography (20% EtOAc/hexanes) to afford 751 mg of **3.56** (100% yield) as a colourless oil.

Data for **3.56**

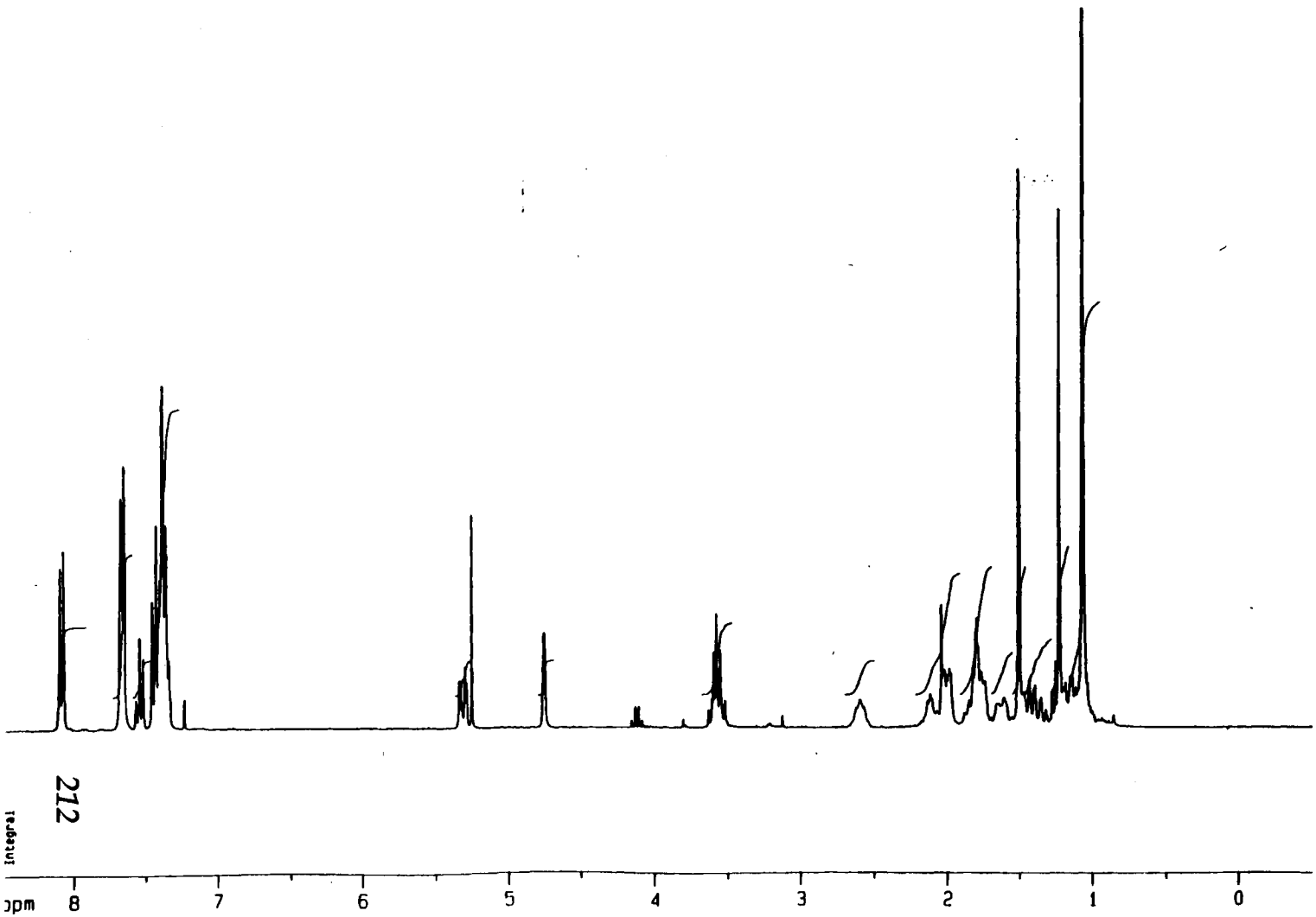
^{1}H NMR (300 MHz, $CDCl_3$): δ 8.09 (d, J= 7.1 Hz, 2H), 7.69-7.66 (m, 4H), 7.58-7.53 (m, 1H), 7.47-7.34 (m, 8H), 5.32 (dd, J= 4.2, 12.0 Hz, 1H), 4.76 (s, 1H), 3.63-3.52 (m, 2H), 2.62-2.57 (m, 1H), 2.17-1.97 (m, 3H), 1.87-1.74 (m, 3H), 1.69-1.55 (m, 1H), 1.50 (s, 3H), 1.47-1.25 (m, 2H), 1.23 (s, 3H), 1.19-1.09 (m, 2H), 1.06 (s, 9H).

^{13}C NMR ($CDCl_3$, 75 MHz) δ 165.4, 135.5 (x4), 133.9, 133.9, 132.9, 130.5, 129.6 (x2), 129.5, 129.5, 128.3 (x2), 127.6 (x4), 107.3, 83.8, 76.8, 72.6, 66.2, 40.8, 32.4, 29.6, 27.5, 26.9, 26.8 (x3), 22.6, 22.5, 19.2, 17.3.

IR (neat) 2945, 2856, 1716, 1266, 1101 cm^{-1}.

EI HRMS calcd for $C_{37}H_{46}O_5Si$ (M^+) 598.31145, obsd 598.31267.

3.56



Current Data Parameters

NAME	lmo_322
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20021010
Time	18.03
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	45.3
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

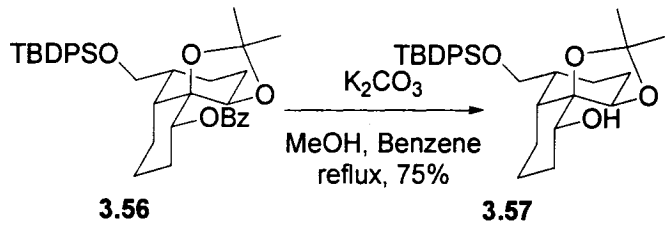
NUC1	1H
P1	9.75 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

F2 - Processing parameters

SI	65536
SF	300.1299996 MHz
WDW	EM
SSB	0
LB	0.10 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	20.00 cm
CY	30.00 cm
F1P	8.500 ppm
F1	2551.10 Hz
F2P	-0.500 ppm
F2	-150.06 Hz
PPMCM	0.45000 ppm/cm
HZCM	135.05850 Hz/cm



3.56 **3.57**

6-(*tert*-Butyl-diphenyl-silanyloxymethyl)-2,2-dimethyl-octahydro-naphtho[1,8a-d][1,3]dioxol-10-ol (3.57).

Benzoate **3.56** (0.818 g, 1.37 mmol) was dissolved in benzene (5 mL) and MeOH (5 mL). K_2CO_3 was added until it didn't dissolve and heated to reflux for 6 h, then cooled down to room temperature for 72 h, and filtered through a celite pad with diethylether. The solvent was evaporated. The crude product was purified by flash silica column chromatography (20% EtOAc/hexanes) to afford 510 mg of **3.57** (75% yield) as a colourless oil.

Data for **3.57**

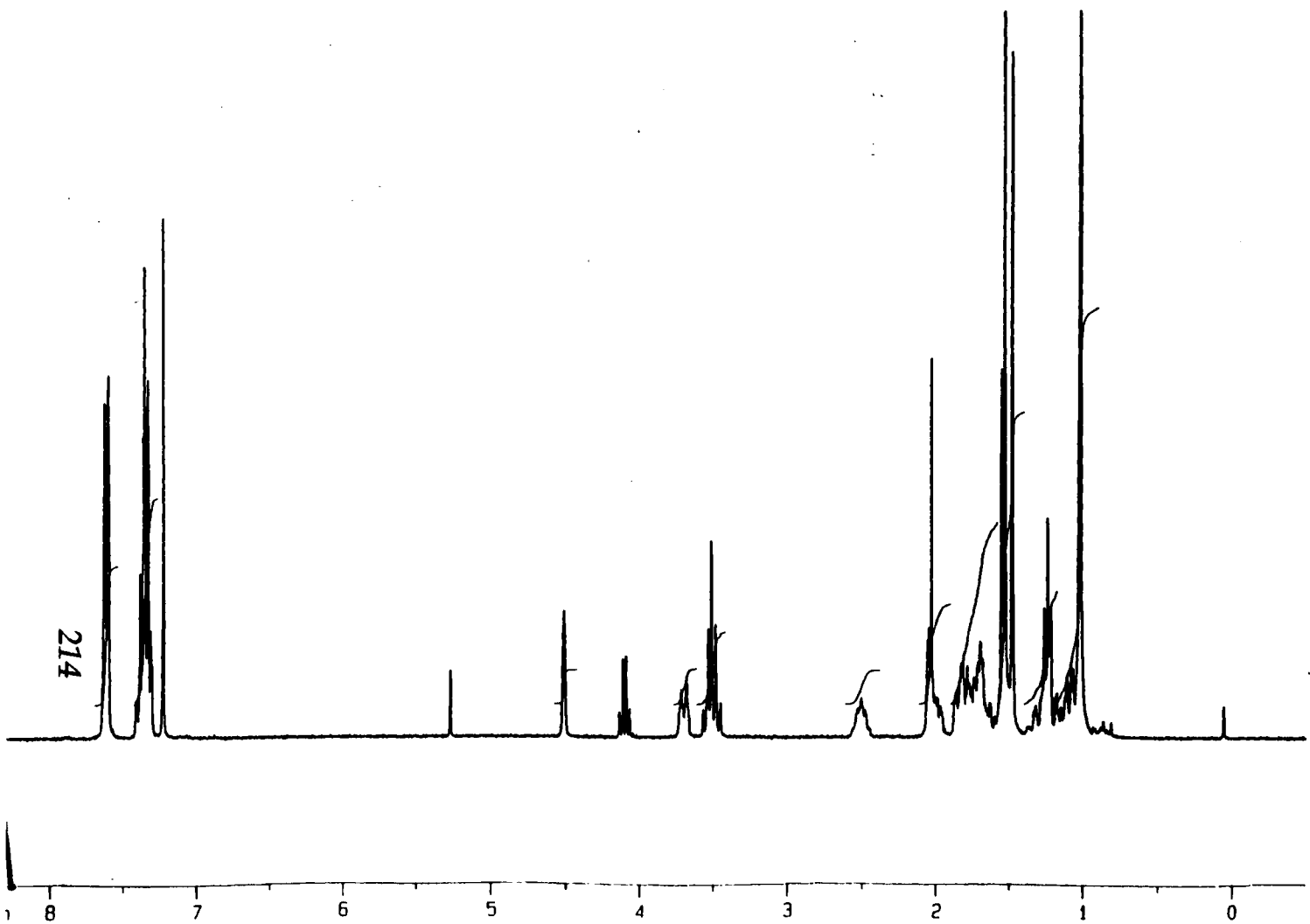
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.65-7.62 (m, 4H), 7.42-7.32 (m, 6H), 4.50 (s, 1H), 3.71-3.68 (m, 1H), 3.56-3.45 (m, 2H), 2.53-2.47 (m, 1H), 2.05-1.94 (m, 2H), 1.86-1.62 (m, 5H), 1.53 (s, 3H), 1.48 (s, 3H), 1.36-1.22 (m, 3H), 1.19-1.07 (m, 2H), 1.02 (s, 9H).

^{13}C NMR ($CDCl_3$, 75 MHz) δ 135.5 (x4), 134.1 (x2), 129.5 (x2), 127.6 (x4), 106.7, 85.9, 75.0, 71.6, 66.3, 40.1, 32.7, 31.1, 27.7, 27.2, 26.8 (x3), 23.6, 23.0, 22.6, 19.3, 17.6.

IR (neat) 3456, 2935, 2858, 1103, 1039 cm^{-1}.

EI HRMS calcd for $C_{30}H_{42}O_4Si$ (M^+) 494.28524, obsd 494.28459.

3.57



Current Data Parameters

NAME	lmo_324
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20021016
Time	15.08
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	574.7
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

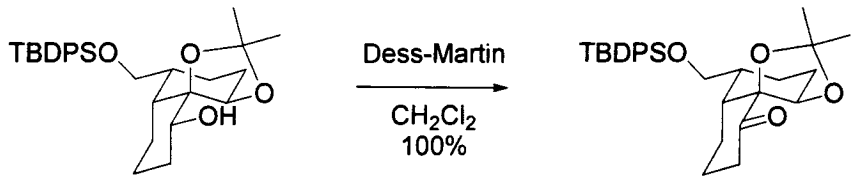
NUC1	1H
P1	9.75 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

F2 - Processing parameters

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

1D NMR plot parameters

CX	20.00 cm
CY	40.00 cm
F1P	8.500 ppm
F1	2551.10 Hz
F2P	-0.500 ppm
F2	-150.06 Hz
PPMCM	0.45000 ppm/cm
HZCM	135.05850 Hz/cm



3.57 **3.58**

6-(*tert*-Butyl-diphenyl-silanyloxymethyl)-2,2-dimethyl-octahydro-naphtho[1,8a-d][1,3]dioxol-10-one (3.58).

Alcohol **3.57** (0.004 g, 0.008 mmol) was dissolved in CH_2Cl_2 (10 mL). Dess-Martin periodinane (4 mg, 0.009 mmol) was added and the reaction was stirred for 3 h at room temperature. A solution of $NaHCO_{3sat}$ was added, followed by $Na_2S_2O_{3sat}$ and stirred for 20 min. The aqueous layer was extracted 3 times with dichloromethane (3 X 20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash silica column chromatography (20% EtOAc/hexanes) to afford 4 mg of **3.58** (100% yield) as white crystals. mp 76.7-77.5°C.

Data for **3.58**

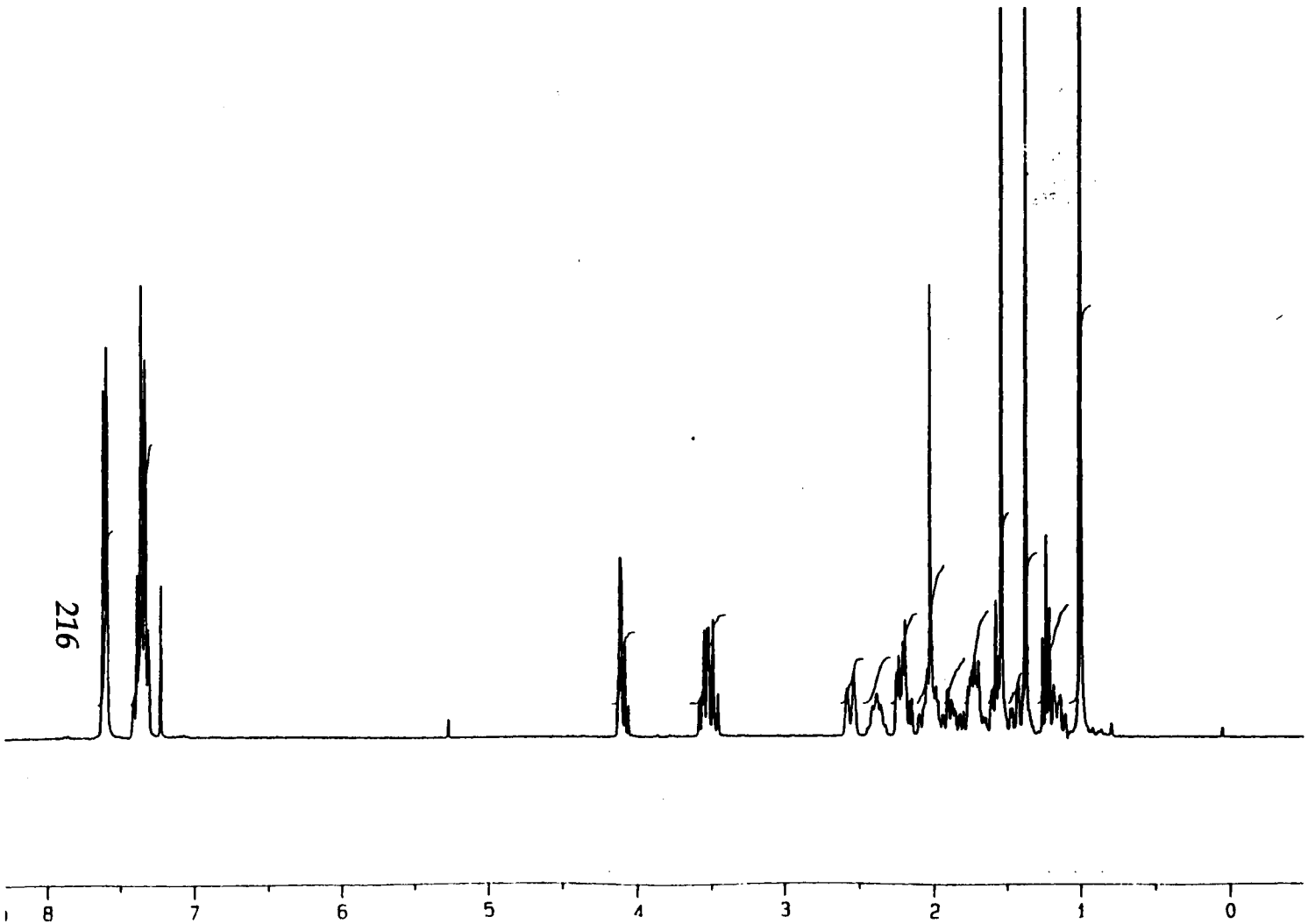
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.64-7.59 (m, 4H), 7.43-7.32 (m, 6H), 4.12 (t, J= 2.7 Hz, 1H), 3.58-3.45 (m, 2H), 2.58-2.53 (m, 1H), 2.41-2.36 (m, 1H), 2.25-2.15 (m, 2H), 2.10-1.90 (m, 2H), 1.89-1.80 (m, 1H), 1.77-1.60 (m, 2H), 1.54 (s, 3H), 1.52-1.39 (m, 1H), 1.38 (s, 3H), 1.23-1.10 (m, 2H), 1.01 (s, 9H).

^{13}C NMR ($CDCl_3$, 75 MHz) δ 209.8, 135.5 (x4), 133.9, 133.8, 129.6 (x2), 127.6 (x4), 109.1, 87.2, 74.3, 65.7, 42.9, 41.1, 32.7, 26.8 (x3), 26.7, 25.3, 25.2, 23,3, 21.3, 19.3, 16.9.

IR (neat) 2939, 2861, 1724, 1110 cm^{-1}.

EI HRMS calcd for $C_{30}H_{40}O_4Si$ (M^+) 492.26959, obsd 492.27021.

3.58



216

Current Data Parameters

NAME	lmo_328
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20021017
Time	11.35
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	203.2
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

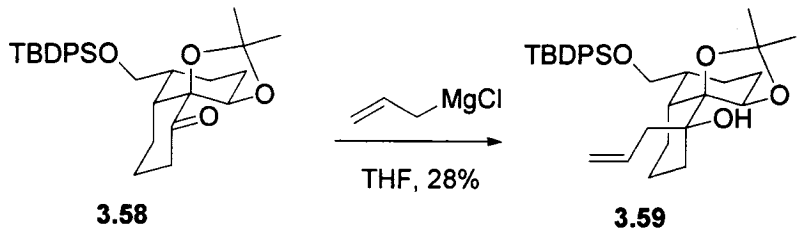
NUC1	1H
P1	9.75 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

F2 - Processing parameters

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

1D NMR plot parameters

CX	20.00 cm
CY	40.00 cm
F1P	8.500 ppm
F1	2551.10 Hz
F2P	-0.500 ppm
F2	-150.06 Hz
PPMCM	0.45000 ppm/cm
HZCM	135.05850 Hz/cm



3.58 **3.59**

10-Allyl-6-(tert-butyl-diphenyl-silanyloxymethyl)-2,2-dimethyl-octahydro-naphtho[1,8a-d][1,3]dioxol-10-ol (3.59)

Ketone **3.58** (0.057 g, 0.116 mmol) was dissolved in THF (0.2 mL) at -78°C. Allylmagnesium chloride 2M (0.3 mL, 0.579 mmol) was added and the reaction was stirred for 10 minutes. The reaction was allowed to warm to room temperature for 15 hours. Allylmagnesium bromide (0.3 mL, 0.579 mmol) was added and the reaction was stirred for 24 hours. The reaction was quenched by adding saturated NH_4Cl_{aq} The aqueous layer was extracted 3 times with diethylether (3 X 20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (20% EtOAc/hexanes) to afford 20 mg of **3.59** (28% yield) as a colourless oil.

Data for **3.59**

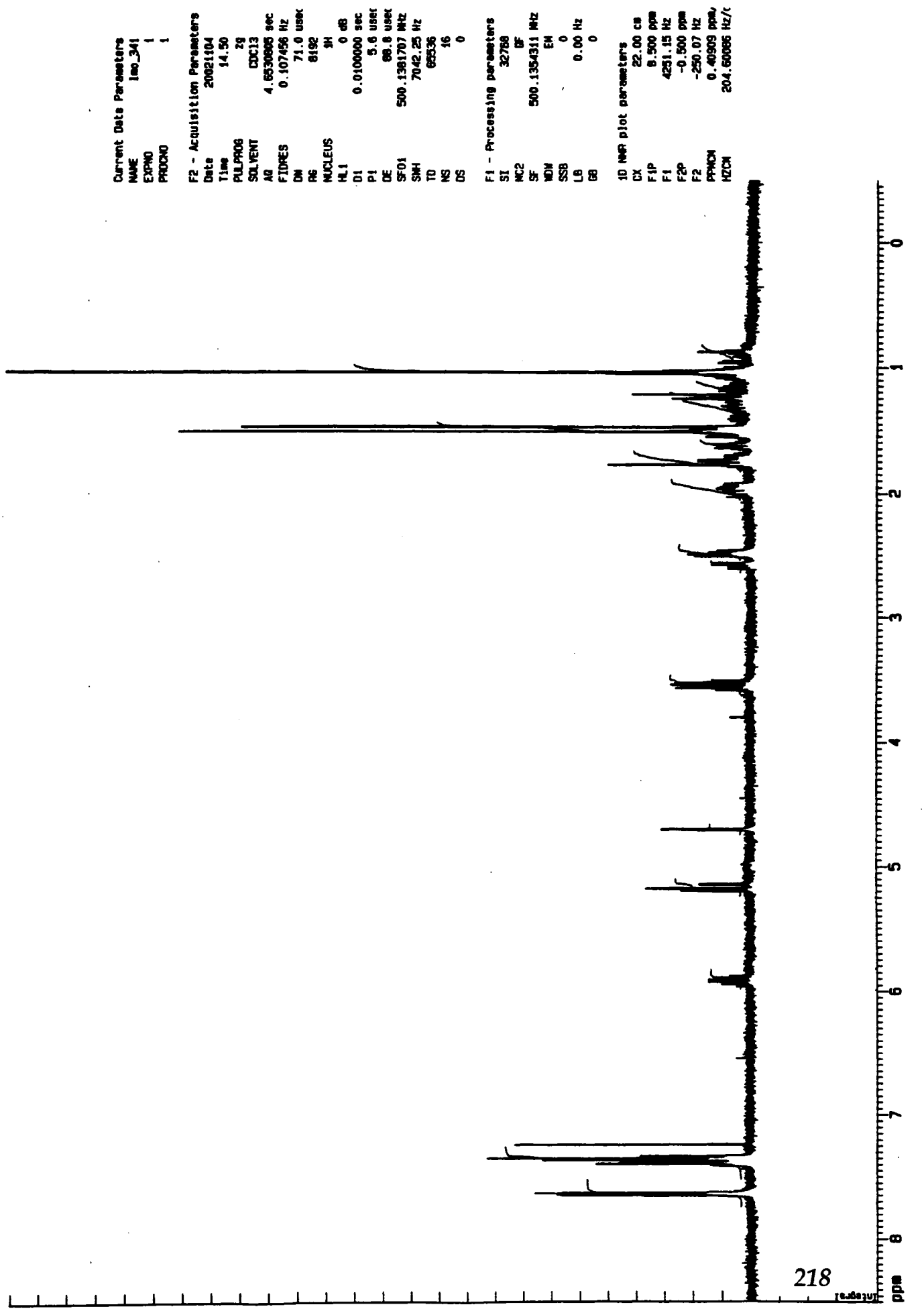
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.66-7.63 (m, 4H), 7.41-7.33 (m, 6H), 5.96-5.87 (m, 1H), 5.19-5.14 (m, 2H), 4.70 (s, 1H), 3.58-3.49 (m, 2H), 2.60-2.56 (m, 1H), 2.50-2.46 (m, 2H), 2.03-1.92 (m, 2H), 1.80-1.68 (m, 3H), 1.64-1.61 (m, 1H), 1.55-1.48 (m, 2H), 1.51 (s, 3H), 1.47 (s, 3H), 1.36-1.27 (m, 1H), 1.24-1.21 (m, 2H), 1.19-1.11 (m, 1H), 1.03 (s, 9H).

^{13}C NMR ($CDCl_3$, 500 MHz) δ 135.6 (x4), 134.2 (x2), 129.5 (x2), 127.6 (x4), 119.2, 107.1, 87.1, 74.6, 73.3, 66.8, 39.6, 38.5, 34.5, 33.1, 27.7, 27.2, 26.9 (x3), 23.3, 22.8, 20.5, 19.3, 17.5.

IR (neat) 3506, 3071, 2944, 2860, 1105 cm^{-1}.

EI HRMS calcd for $C_{33}H_{46}O_4Si$ (M^+) 534.31654, obsd 534.32466.

3.59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NAME Imo_341
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date 20021104
Time 14.50
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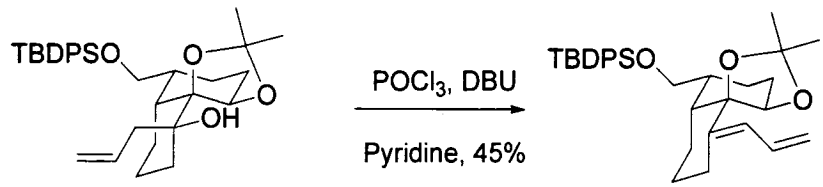
SOLVENT CDCl3
AQ 4.6530805 sec
FIDRES 0.107456 Hz
DW 71.0 usec
RG 8192
NUCLEUS 1H
HL1 0 dB
D1 0.0100000 sec
P1 5.6 usec
DE 66.8 usec
SFO1 500.1381707 MHz
SWH 7042.25 Hz
TD 65536
NS 16
DS 0
F1 - Processing parameters
SI 32768
WC2 EF
SF 500.1354311 MHz
WDW EM
SSB 0
LB 0.00 Hz
GB 0
1D NMR plot parameters
CX 22.00 cm
F1P 8.500 ppm
F1 4251.15 Hz
F2P -0.500 ppm
F2 -250.07 Hz
PPMCM 0.40909 ppm/
HZCM 204.60086 Hz/
ppm
Integral



3.59 **3.60**

(10-Allylidene-2,2-dimethyl-octahydro-naphtho[1,8a-d][1,3]dioxol-6-ylmethoxy)-tert-butyl-diphenyl-silane (3.60)

Alcohol **3.59** (0.028 g, 0.045 mmol) was dissolved in pyridine (0.5 mL) and DBU (0.1 mL) and cooled to 0°C. $POCl_3$ (0.1 mL, 1 mmol) was added and heated in a sealed tube to 100°C for 3 hours. Dichloromethane and water were added. The aqueous layer was extracted 3 times with dichloromethane (3 X 20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (10% EtOAc/hexanes) to afford 12 mg of **3.60** (45% yield) as a colourless oil.

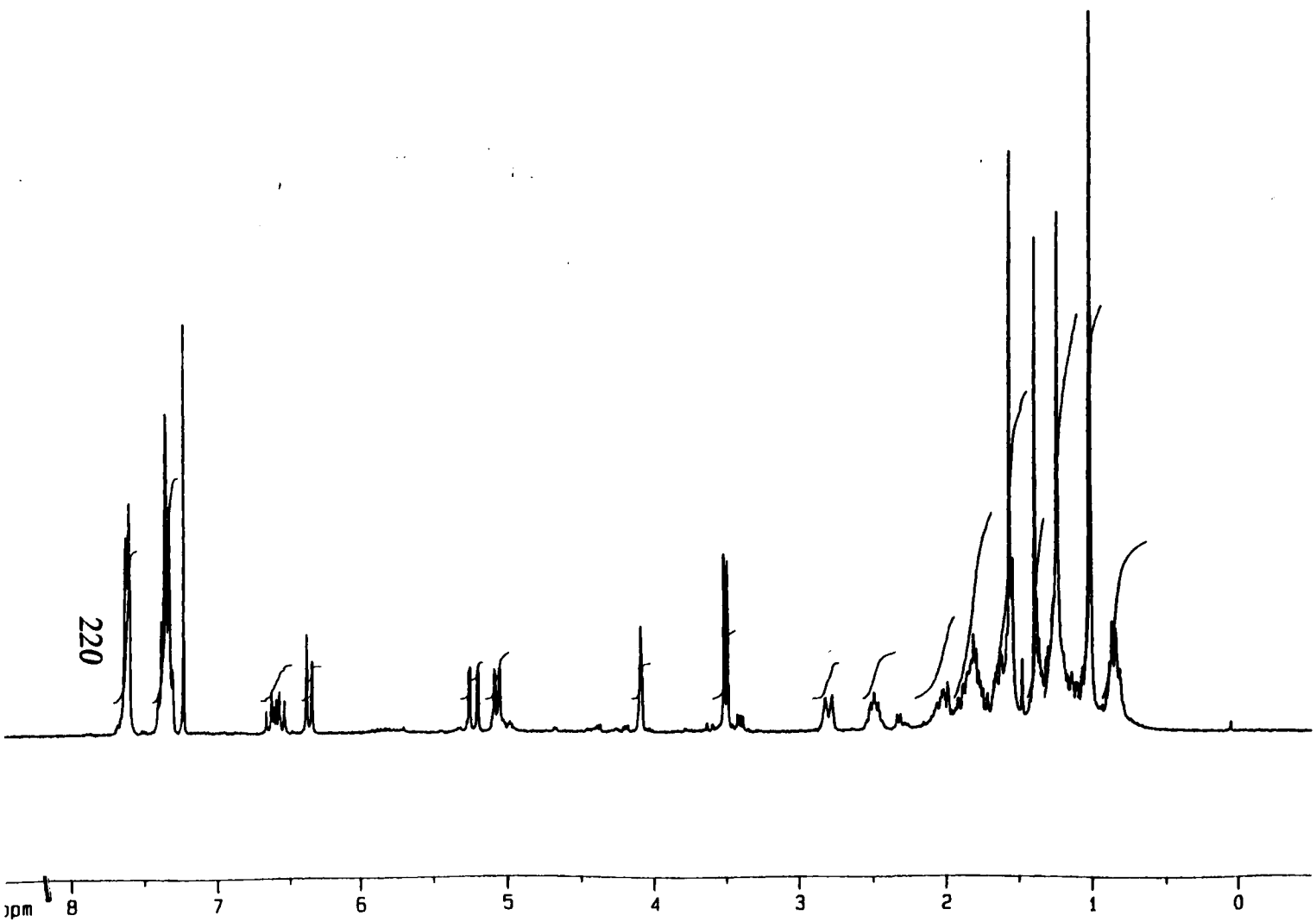
Data for **3.60**

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.70-7.61 (m, 4H), 7.42-7.31 (m, 6H), 6.67-6.55 (m, 1H), 6.37 (d, 11.2 Hz, 1H), 5.23 (dd, J= 1.6, 16.5 Hz, 1H), 5.07 (dd, J= 2.0, 10.1 Hz, 1H), 4.10-4.08 (m, 1H), 3.5 (d, J= 7.4 Hz, 2H), 2.80 (d, J= 13.4 Hz, 1H), 2.54-2.44 (m, 1H), 2.10-1.96 (m, 2H), 1.93-1.70 (m, 4H), 1.66-1.58 (m, 2H), 1.39 (s, 3H), 1.23 (s, 3H), 1.01 (s, 9H), 0.89-0.81 (m, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 145.8, 135.5 (x4), 134.1 (x2), 132.1, 129.5 (x2), 127.6 (x4), 121.3, 116.8, 107.3, 84.4, 77.8, 66.5, 42.5, 33.1, 29.7, 27.0, 26.9 (x3), 26.8, 26.1, 24.0, 22.7, 19.3, 17.1.

IR (neat) 2930, 2857, 1112 cm^{-1}.

EI HRMS calcd for $C_{33}H_{44}O_3Si$ (M^+) 516.30597, obsd 516.30314.



3.60

Current Data Parameters
NAME lmo_346
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
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Time 10.32
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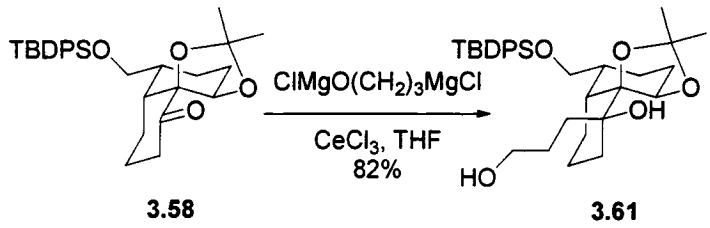
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 322.5
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

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

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

1D NMR plot parameters
CX 20.00 cm
CY 30.00 cm
F1P 8.500 ppm
F1 2551.10 Hz
F2P -0.500 ppm
F2 -150.06 Hz
PPMCM 0.45000 ppm/cm
HZCM 135.05850 Hz/cm



3.58 **3.61**

6-(tert-Butyl-diphenyl-silanyloxymethyl)-10-(3-hydroxy-propyl)-2,2-dimethyl-octahydro-naphtho[1,8a-d][1,3]dioxol-10-ol (3.61).

A suspension of $CeCl_3$ (0.328 g, 1.33 mmol) in dry THF (0.6 mL)was stirred at 0°C for 2 h. Ketone **3.58** (0.225 g, 0.44 mmol) was dissolved in THF (8 mL) and cannulated into the $CeCl_3$ suspension and stirred for 15 h at room temperature. The solution was cooled to –78 °C and $ClMgO(CH_2)_3MgCl$ 0.34 M (8 mL, 2.66 mmol) was added dropwise. Saturated $NH_4Cl_{(aq)}$ and a few drops of glacial acetic acid were added. The aqueous layer was extracted 3 times with diethylether (3 X 50 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash silica column chromatography (80% EtOAc/hexanes) to afford 41 mg of starting material **3.58** (18%) and 200 mg of **3.61** (82% yield) as a colourless oil .

Data for **3.61**

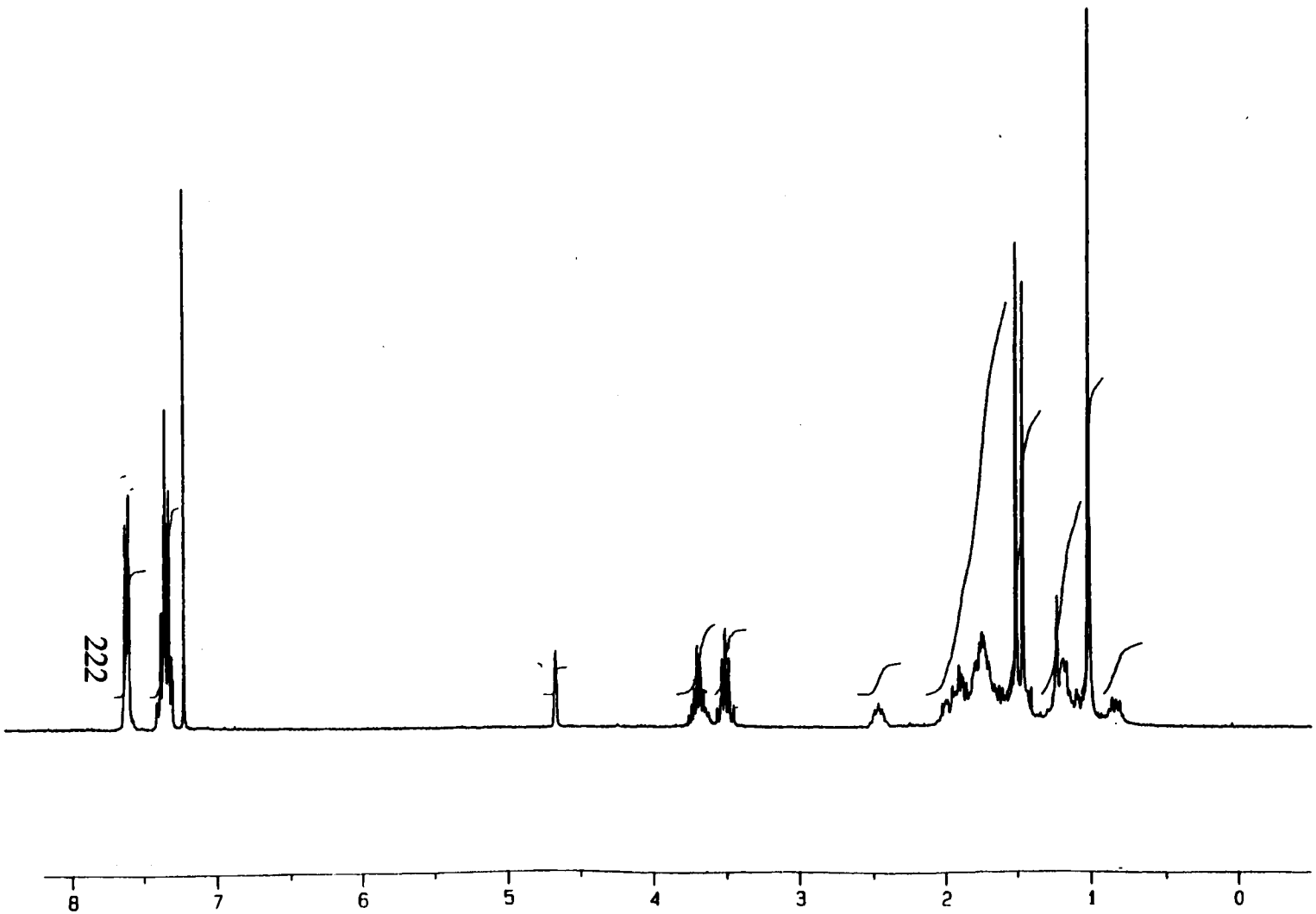
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.64-7.59 (m, 4H), 7.43-7.31 (m, 6H), 4.69-4.67 (m, 1H), 3.76-3.63 (m, 2H), 3.57-3.46 (m, 2H), 2.49-2.44 (m, 1H), 2.03-1.56 (m, 11H), 1.51 (s, 3H), 1.47 (s, 3H), 1.25-1.10 (m, 6H), 1.02 (s, 9H).

^{13}C NMR ($CDCl_3$, 125 MHz) δ 135.5 (x4), 134.1, 134.0, 129.5 (x2), 127.6 (x4), 107.0, 87.6, 75.0, 73.3, 66.8, 63.5, 38.5, 33.0, 32.9, 30.9, 27.7, 27.4, 26.9, 25.4, 23.4, 22.8, 20.8, 19.3, 17.5.

IR (neat) 3399, 2943, 2862, 1099, 1050 cm^{-1}.

EI HRMS calcd for $C_{33}H_{48}O_5Si$ (M^+) 552.32710, obsd 552.3249.

3.61



Current Data Parameters

NAME	lmo_3558
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20021119
Time	13.35
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	456.1
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

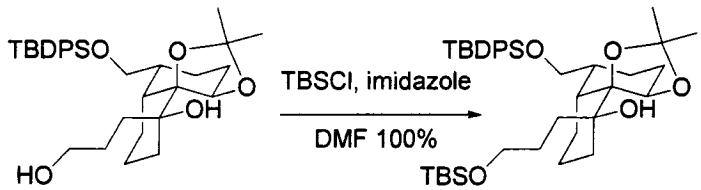
NUC1	1H
P1	9.75 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

F2 - Processing parameters

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

1D NMR plot parameters

CX	20.00 cm
CY	30.00 cm
F1P	8.500 ppm
F1	2551.10 Hz
F2P	-0.500 ppm
F2	-150.06 Hz
PPMCM	0.45000 ppm/cm
HZCM	135.05850 Hz/cm



3.61 **3.62**

10-[3-(tert-Butyl-dimethyl-silanyloxy)-propyl]-6-(tert-butyl-diphenyl-silanyloxymethyl)2,2-dimethyl-octahydro-naphtho[1,8a-d][1,3]dioxol-10-ol (3.62).

A solution of alcohol **3.61** (1.03g, 1.9 mmol), tert-Butyldimethylsilyl chloride (1.5 g, 10 mmol) and imidazole (1.5 g, 22 mmol) in DMF (25 mL) was stirred at room temperature overnight. The reaction was quenched by adding saturated $NH_4Cl_{(aq)}$. The aqueous layer was extracted 3 times with a mixture of 1:1 diethyl ether : hexanes (3 X 100 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash silica column chromatography (20% EtOAc/hexanes) to afford 1.3 g of **3.62** (100% yield) as a colorless oil.

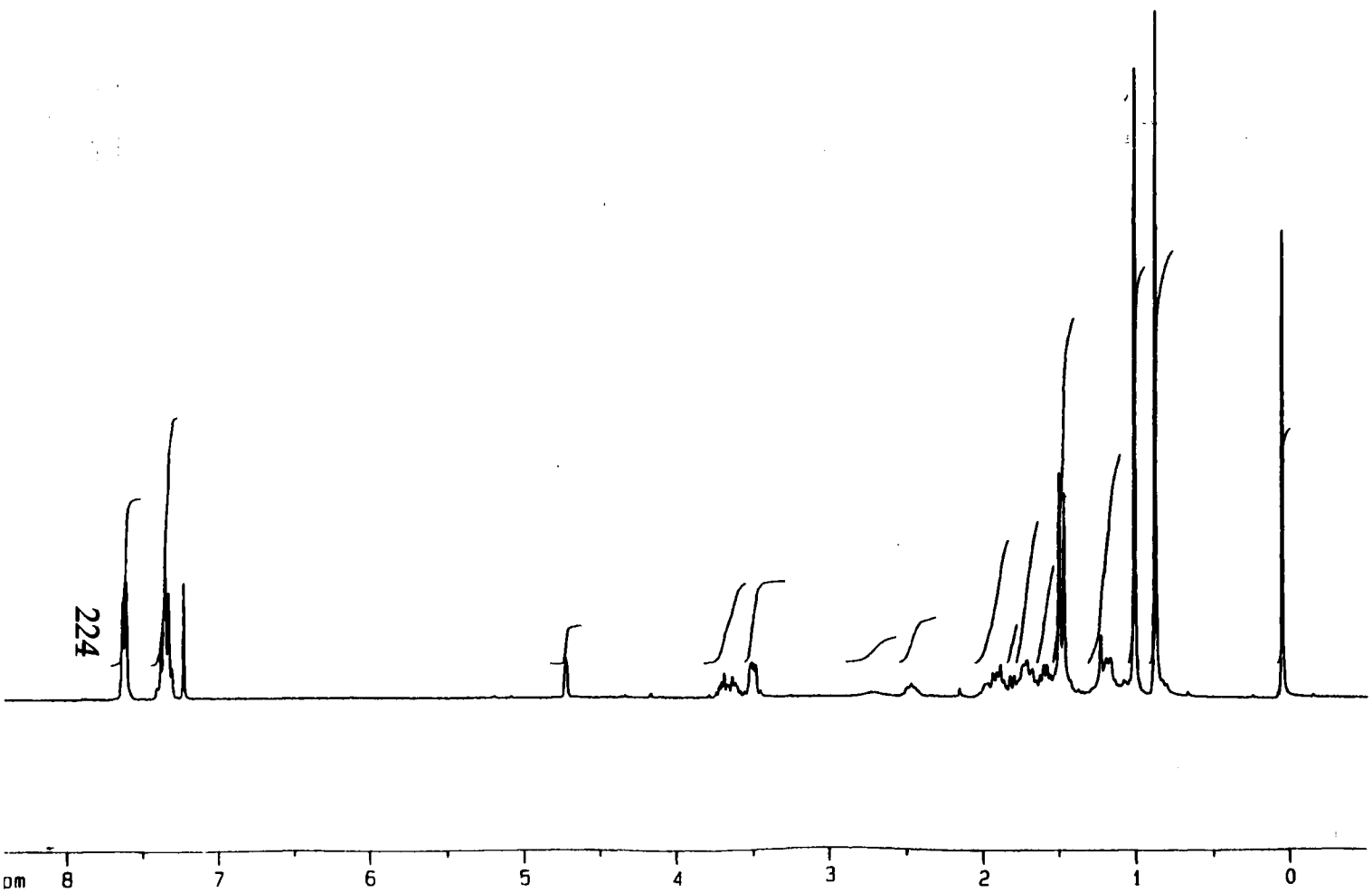
Data for **3.62**

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.63 (d, J= 7.1 Hz, 4H), 7.41-7.32 (m, 6H), 4.73 (s, 1H), 3.74-3.59 (m, 2H), 3.56-3.46 (m, 2H), 2.74-2.68 (m, 1H), 2.49-2.42 (m, 1H), 1.97-1.85 (m, 3H), 1.82-1.80 (m, 1H), 1.76-1.65 (m, 4H), 1.62-1.56 (m, 3H), 1.50-1.43 (m, 2H), 1.50 (s, 3H), 1.47 (s, 3H), 1.38-1.17 (m, 6H), 1.01 (s, 9H), 0.88 (s, 9H), 0.05 (s, 6H).

^{13}C NMR ($CDCl_3$, 75 MHz) δ 135.6 (x4), 134.1 (x2), 129.5 (x2), 127.6 (x4), 106.8, 87.5, 74.4, 73.2, 66.8, 63.8, 38.6, 33.3, 30.9, 27.7, 27.4, 26.9 (x3), 26.0 (x3), 25.4, 23.3, 22.8, 20.8, 19.3, 18.3, 17.5, -5.3 (x2).

IR (neat) 3417, 2930, 2864, 1257, 1099 cm^{-1}.

EI HRMS calcd for $C_{39}H_{62}O_5Si_2$ (M^+) 666.41358, obsd 666.4597.



3.62

Current Data Parameters
NAME lmo_363
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20021127
Time 18.07
INSTRUM av300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 406.4
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

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

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

1D NMR plot parameters
CX 20.00 cm
CY 10.00 cm
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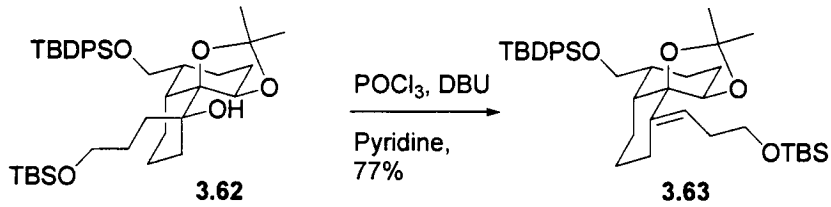
F1 2551.10 Hz
F2P -0.500 ppm
F2 -150.06 Hz
PPMCM 0.45000 ppm/cm
HZCM 135.05850 Hz/cm



10-[3-(tert-Butyl-dimethyl-silanyloxy)-propylidene]-6-(tert-butyl-diphenyl-silanyloxymethyl)-2,2-dimethyl-octahydro-naphtho[1,8a-d][1,3]dioxole (3.63).

A solution of the alcohol **3.62** (20 mg, 0.03 mmol) in DBU (0.1 mL) and pyridine (0.5 mL) was stirred at room temperature. $POCl_3$ (0.1 mL) was added and stirred for 45 min. The reaction was quenched by adding saturated $NH_4Cl_{(aq)}$. The aqueous layer was extracted 3 times with dichloromethane (3 X 15 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash silica column chromatography (20% EtOAc/hexanes) to afford 15 mg of **3.63** (77% yield) as colorless oil.

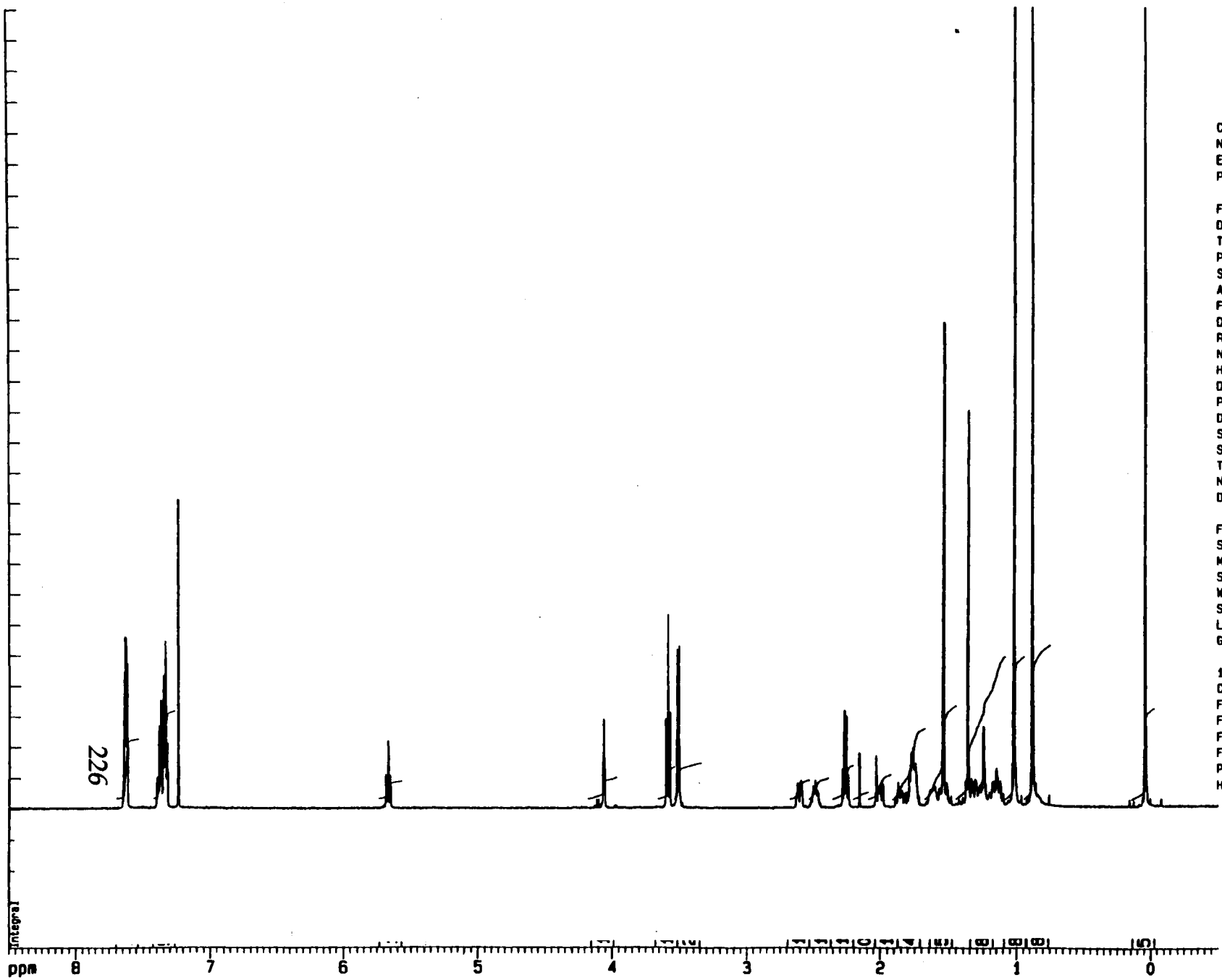
Data for **3.63**

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.65-7.62 (m, 4H), 7.41-7.32 (m, 6H), 5.67 (t, J= 7.4 Hz, 1H), 4.06 (t, J= 2.6 Hz, 1H), 3.58 (t, J= 7.3 Hz, 2H), 3.51 (d, J= 7.4 Hz, 2H), 2.61-2.59 (m, 1H), 2.52-2.45 (m, 1H), 2.25 (q, J= 7.3 Hz, 2H), 2.01-1.98 (m, 1H), 1.89-1.80 (m, 1H), 1.78-1.72 (m, 3H), 1.66-1.57 (m, 1H), 1.54 (s, 3H), 1.36 (s, 3H), 1.33-1.06 (m, 4H), 1.01 (s, 9H), 0.88 (s, 9H), 0.04 (s, 6H).

^{13}C NMR ($CDCl_3$, 125 MHz) δ 144.1, 135.6 (x4), 134.2 (x2), 129.4 (x3), 127.5 (x4), 116.6, 107.1, 84.6, 78.1, 66.7, 63.2, 42.5, 33.4, 31.0, 27.0 (x3), 26.9 (x4), 26.4, 26.0, 24.3, 22.9, 19.3, 18.3, 17.4, -5.2, -5.3.

IR (neat) 2931, 2857, 1106 cm^{-1}.

EI HRMS calcd for $C_{35}H_{51}O_4Si_2$ (M^+ -*t*Bu) 591.33259, obsd 591.35122.



Current Data Parameters
NAME lmo_370
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
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Time 2.58
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SOLVENT CDCl3
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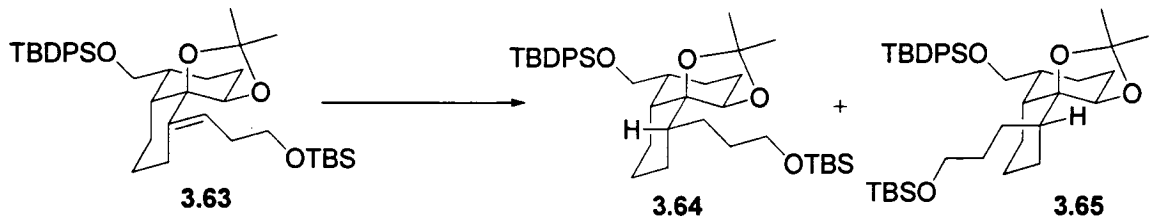
FIDRES 0.107456 Hz
DW 71.0 usec
RG 512
NUCLEUS 1H
HL1 0 dB
D1 0.0100000 sec
P1 5.6 usec
DE 88.8 usec
SFO1 500.1381707 MHz
SWH 7042.25 Hz
TD 65536
NS 16
DS 0

F1 - Processing parameters
SI 32768
WC2 QF
SF 500.1354311 MHz
WDW EM
SSB 0
LB 0.00 Hz
GB 0

1D NMR plot parameters
CX 22.00 cm
F1P 8.500 ppm
F1 4251.15 Hz
F2P -0.500 ppm
F2 -250.07 Hz
PPMCM 0.40909 ppm/
HZCM 204.60086 Hz/

C.U.C



10-[3-(tert-Butyl-dimethyl-silanyloxy)-propyl]-6-(tert-butyl-diphenyl-silanyloxymethyl)-2,2-dimethyl-octahydro-naphtho[1,8a-d][1,3]dioxole (3.64).

In a glove box, a solution of catalyst **3.66** (0.001 g, 0.0014 mmol) in methanol (1 mL) and benzene (1 mL) was added to the olefin **3.63** (0.014 g, 0.022 mmol). Triethylamine (0.0091 mL) was added and the solution was pressurized to 1350 psi with H_2. The reaction mixture in the autoclave was stirred and heated for 5 days at 80 °C. The reaction was concentrated. The crude product was purified by flash silica column chromatography (10% EtOAc/hexanes) to afford 0.013 g of **3.64** (93% yield) as a colorless oil.

Data for **3.64**

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.66-7.62 (m, 4H), 7.42-7.31 (m, 6H), 4.20-4.19 (m, 1H), 3.61 (d, J= 7 Hz, 2H), 3.50 (d, J= 7 Hz, 2H), 2.69-2.60 (m, 1H), 2.03-1.92 (m, 2H), 1.81-1.58 (m, 8H), 1.56 (s, 3H), 1.50-1.45 (m, 2H), 1.43 (s, 3H), 1.23 (s, 2H), 1.18-1.06 (m, 2H), 1.01 (s, 9H), 0.87 (s, 9H), 0.02 (s, 6H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 135.6 (x2), 134.1 (x2), 129.5 (x2), 127.6 (x4), 106.6, 85.8, 73.5, 66.4, 63.7, 46.4, 41.9, 33.2, 31.7, 28.4, 28.2, 28.0, 26.8 (x3), 26.0 (x3), 25.6, 25.3, 24.4, 22.9, 19.3, 18.3, 17.6, -5.3 (x2).

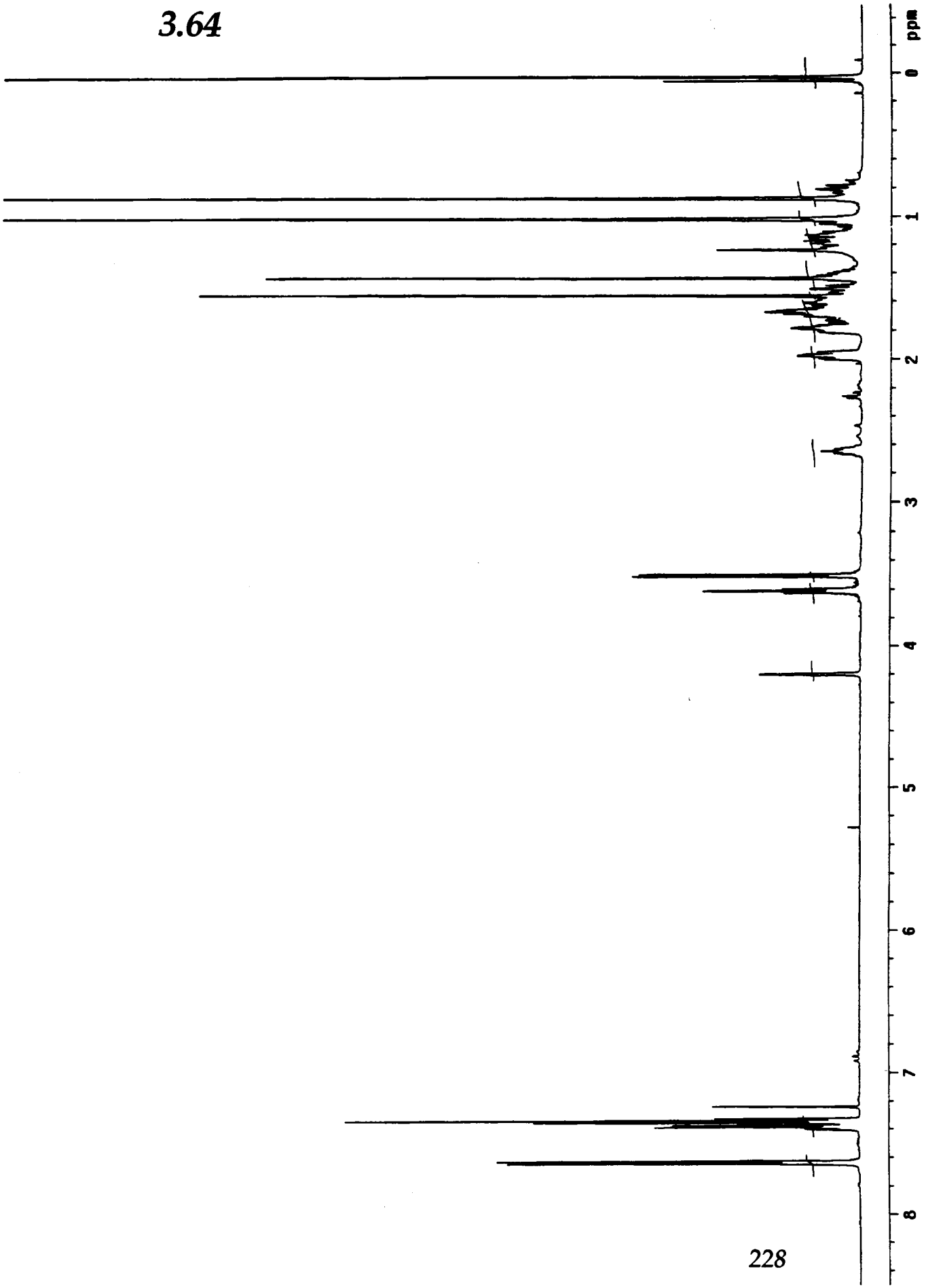
IR (neat) 2929, 2857, 1110 cm-1.

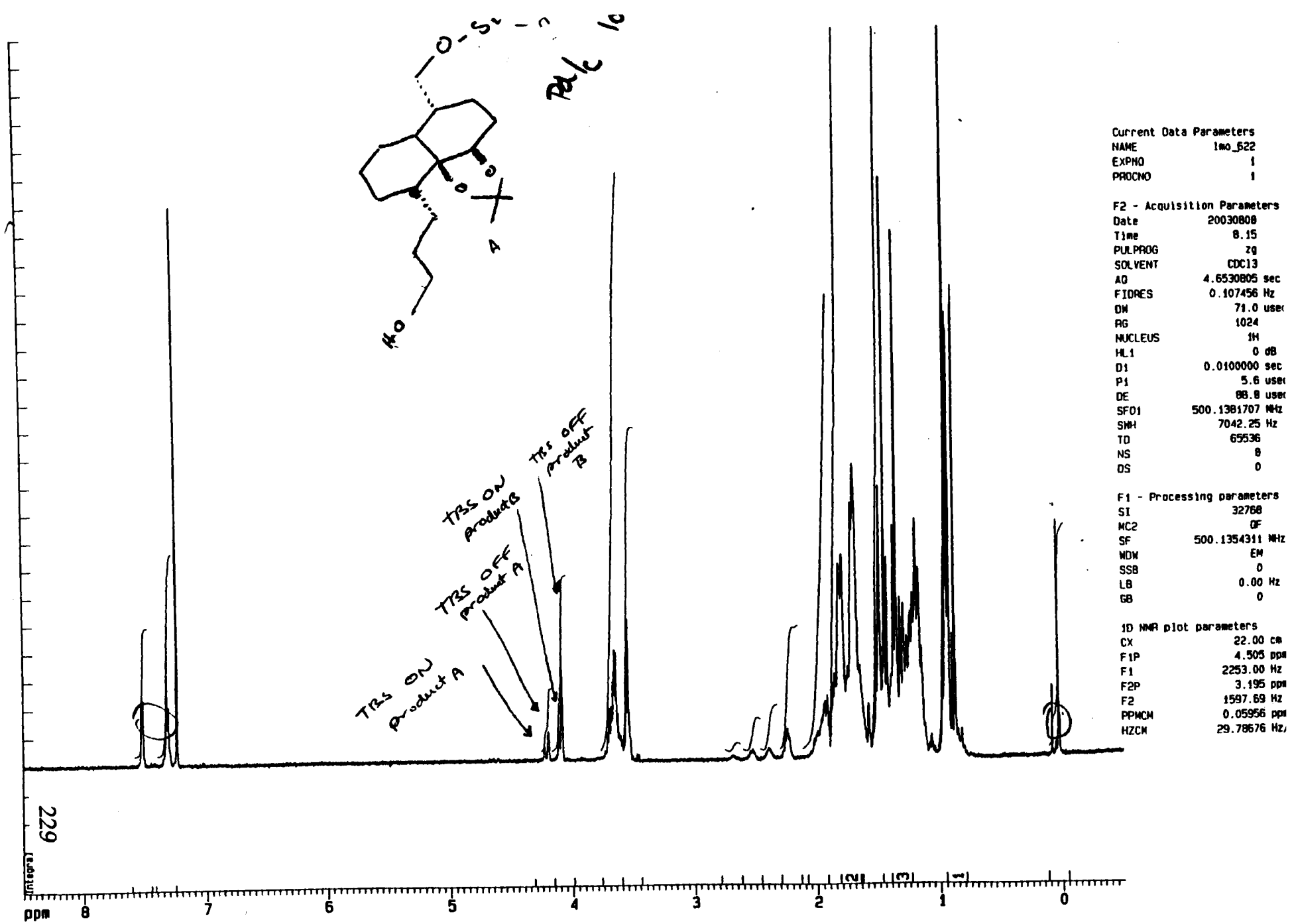
EI HRMS calcd for $C_{35}H_{51}O_4Si_2$ (M^+) 650.41866, obsd 650.41375.

10-[3-(tert-Butyl-dimethyl-silanyloxy)-propyl]-6-(tert-butyl-diphenyl-silanyloxymethyl)-2,2-dimethyl-octahydro-naphtho[1,8a-d][1,3]dioxole (3.65).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.64-7.62 (m, 4H), 7.44-7.32 (m, 6H), 4.08-4.05 (m, 1H), 3.70-3.55 (m, 2H), 3.55-3.50 (m, 2H), 2.30-2.20 (m, 1H), 2.05-1.90 (m, 2H), 1.88-1.60 (m, 10H), 1.55-1.20 (m, 11H), 1.02 (s, 9H).

3.64





Current Data Parameters

NAME	lmo_622
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

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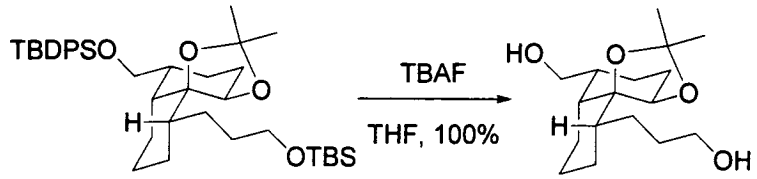
Time	8.15
PULPROG	zg
SOLVENT	CDCl3
AQ	4.6530805 sec
FIDRES	0.107456 Hz
DW	71.0 usec
RG	1024
NUCLEUS	1H
HL1	0 dB
D1	0.0100000 sec
P1	5.6 usec
DE	88.8 usec
SFO1	500.1381707 MHz
SWH	7042.25 Hz
TD	65536
NS	8
DS	0

F1 - Processing parameters

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

1D NMR plot parameters

CX	22.00 cm
F1P	4.505 ppm
F1	2253.00 Hz
F2P	3.195 ppm
F2	1597.69 Hz
PPMCM	0.05956 ppm
HZCM	29.78676 Hz/



3.64 **3.70**

3-(6-Hydroxymethyl-2,2-dimethyl-octahydro-naphtho[1,8a-d][1,3]dioxol-10-yl)-propan-1-ol (3.70).

To a solution of protected alcohols **3.64** (130 mg, 0.2 mmol) in THF (2 mL) was added TBAF (1 mL of a 1M solution in THF, 0.8 mmol). The reaction was stirred at room temperature for 72 h. The solution was concentrated and purified by flash silica column chromatography (5% MeOH/EtOAc) to afford 60 mg of **3.70** (100% yield) as a colourless oil.

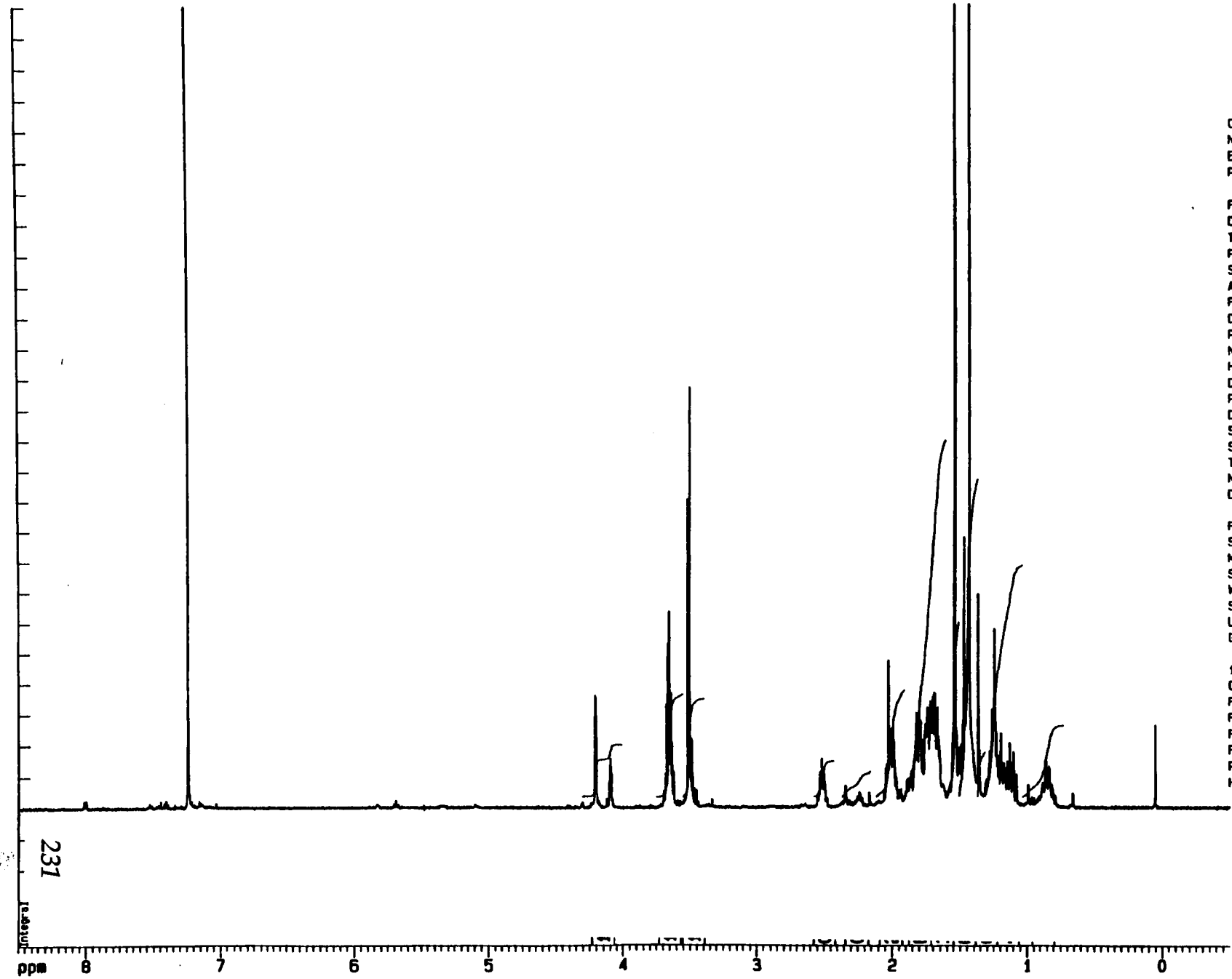
Data for **3.70**

^{1}H NMR (500 MHz, $CDCl_3$): δ 4.21-4.08 (m, 1H), 3.69-3.61 (m, 2H), 3.50 (d, J= 7.5 Hz, 2H), 2.54-2.47 (m, 1H), 2.34-2.21 (m, 1H), 2.05-1.95 (m, 2H), 1.89-1.62 (m, 7H), 1.53 (s, 3H), 1.52-1.43 (m, 3H), 1.43 (s, 3H), 1.30-1.07 (m, 5H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 106.7, 85.8, 73.4, 65.9, 63.1, 46.1, 41.9, 33.5, 31.3, 28.4 (x2), 28.1, 25.4, 25.2, 24.5, 22.9, 17.8.

IR (neat) 3377, 2933, 2866, 1033 cm^{-1}.

EI HRMS calcd for $C_{17}H_{30}O_4$ (M^+) 298.21441, obsd 298.21567.



Current Data Parameters

NAME	lmo_504
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date	20030404
Time	5.45
PULPROG	zg
SOLVENT	CDCl3
AQ	4.6530805 sec
FIDRES	0.107456 Hz
DW	71.0 usec
RG	1024
NUCLEUS	1H
HL1	0 dB
D1	0.0100000 sec
P1	5.6 usec
DE	88.8 usec
SFO1	500.1381707 MHz
SWH	7042.25 Hz
TD	65536
NS	16
DS	0

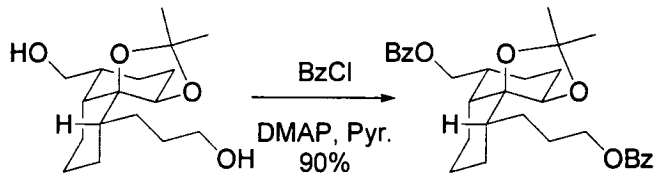
F1 - Processing parameters

SI	32768
WC2	QF
SF	500.1354313 MHz
WDW	EM
SSB	0
LB	0.00 Hz
GB	0

1D NMR plot parameters

CX	22.00 cm
F1P	8.500 ppm
F1	4251.15 Hz
F2P	-0.500 ppm
F2	-250.07 Hz
PPMCM	0.40909 ppm/
HZCM	204.60086 Hz/c

5.10



3.70 **3.71**

Bis-benzoic acid 3-(6-Hydroxymethyl-2,2-dimethyl-octahydro-naphtho[1,8a-d][1,3]dioxol-10-yl)-propan-1-ol (3.71)

A solution of diol **3.70** (29mg, 0.097 mmol), benzoyle chloride (0.034 mL, 0.29 mmol), pyridine (0.14 mL, 1.75 mmol) and one crystal of dimethylaminopyridine in dichloromethane (1 ml) was stirred at room temperature overnight. The reaction was quenched by adding saturated NH_4Cl_{aq}. The aqueous layer was extracted 3 times with dichloromethane (3 X 15 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (10% EtOAc/hexanes) to afford 44 mg of **3.71** (90% yield) as a white crystals Mp 142.4-143.8°C.

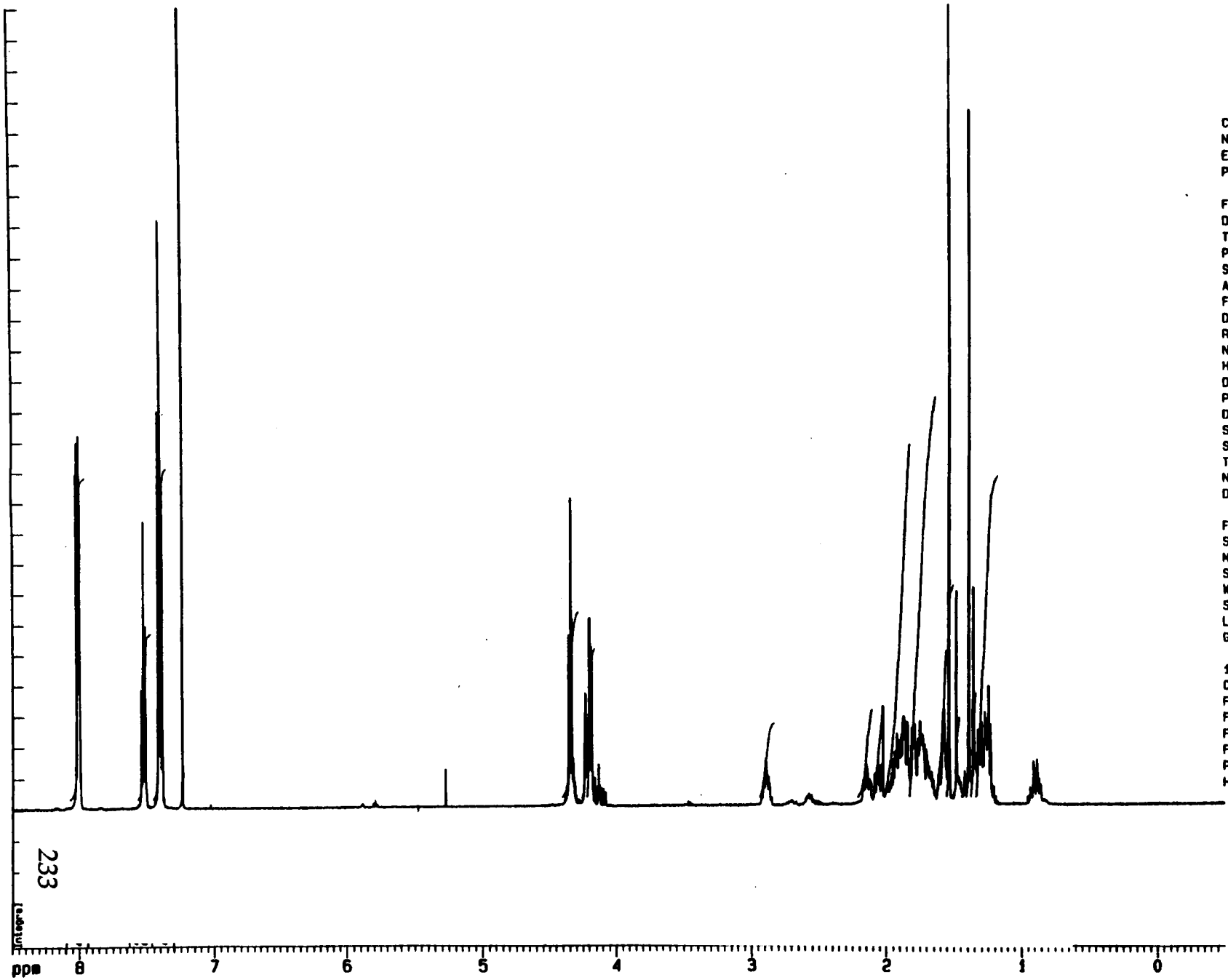
Data for **3.71**

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.03-7.99 (m, 4H), 7.55-7.50 (m, 2H), 7.42-7.38 (m, 4H), 4.34 (t, J= 6.5 Hz, 2H), 4.23-4.22 (m, 1H), 4.20-4.18 (m, 2H), 2.91-2.84 (m, 1H), 2.17-2.11 (m, 1H), 2.09-2.03 (m, 1H), 1.87-1.85 (m, 4H), 1.84-1.61 (m, 4H), 1.60-1.55 (m, 2H), 1.53 (s, 3H), 1.38 (s, 3H), 1.35 (s, 1H), 1.34-1.22 (m, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 166.6 (x2), 132.8 (x2), 130.4 (x2), 129.6 (x2), 129.5 (x2), 128.3 (x4), 106.8, 85.5, 73.3, 67.3, 65.2, 46.2, 42.4, 30.2, 28.3, 28.2, 28.0, 27.7, 25.9, 25.2, 24.5, 22.7, 17.7.

IR (neat) 2936, 2868, 1719,1274 cm^{-1}.

EI HRMS calcd for $C_{30}H_{35}O_6$ (M^+-Me) 491.24336, obsd 491.24346.



Current Data Parameters
NAME lmo_427
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
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Time 23.17
PULPROG zg
SOLVENT CDCl3
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FIDRES 0.107456 Hz
DW 71.0 usec
RG 512
NUCLEUS 1H
PL1 0 dB
D1 0.0100000 sec
P1 5.6 usec
DE 88.8 usec
SFO1 500.1381707 MHz
SWH 7042.25 Hz
TD 65536
NS 16
DS 0

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

1D NMR plot parameters
CX 22.00 cm
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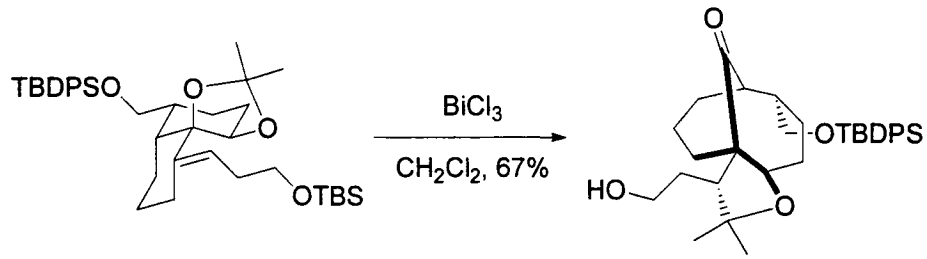
F1 4111.50 Hz
F2P 6.717 ppm
F2 3359.50 Hz
PPMCM 0.06834 ppm/
HZCM 34.18153 Hz/c



3.63 **3.72**

8-(tert-Butyl-diphenyl-silanyloxymethyl)-2-(2-hydroxy-ethyl)-3,3-dimethyl-4-oxa-tricyclo[7.3.1.01,5]tridecan-13-one (3.72)

To a solution of alkene **3.63** (0.046 g, 0.07 mmol) in dicloromethane (2 mL) was added $BiCl_3$ (0.010 g, 0.03 mmol). The reaction stirred for 3 hours. The reaction was quenched by adding water. The aqueous layer was extracted 3 times with dichloromethane (3 X 15 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (40% EtOAc/hexanes) to afford 25 mg of **3.72** (67% yield) as a colourless oil.

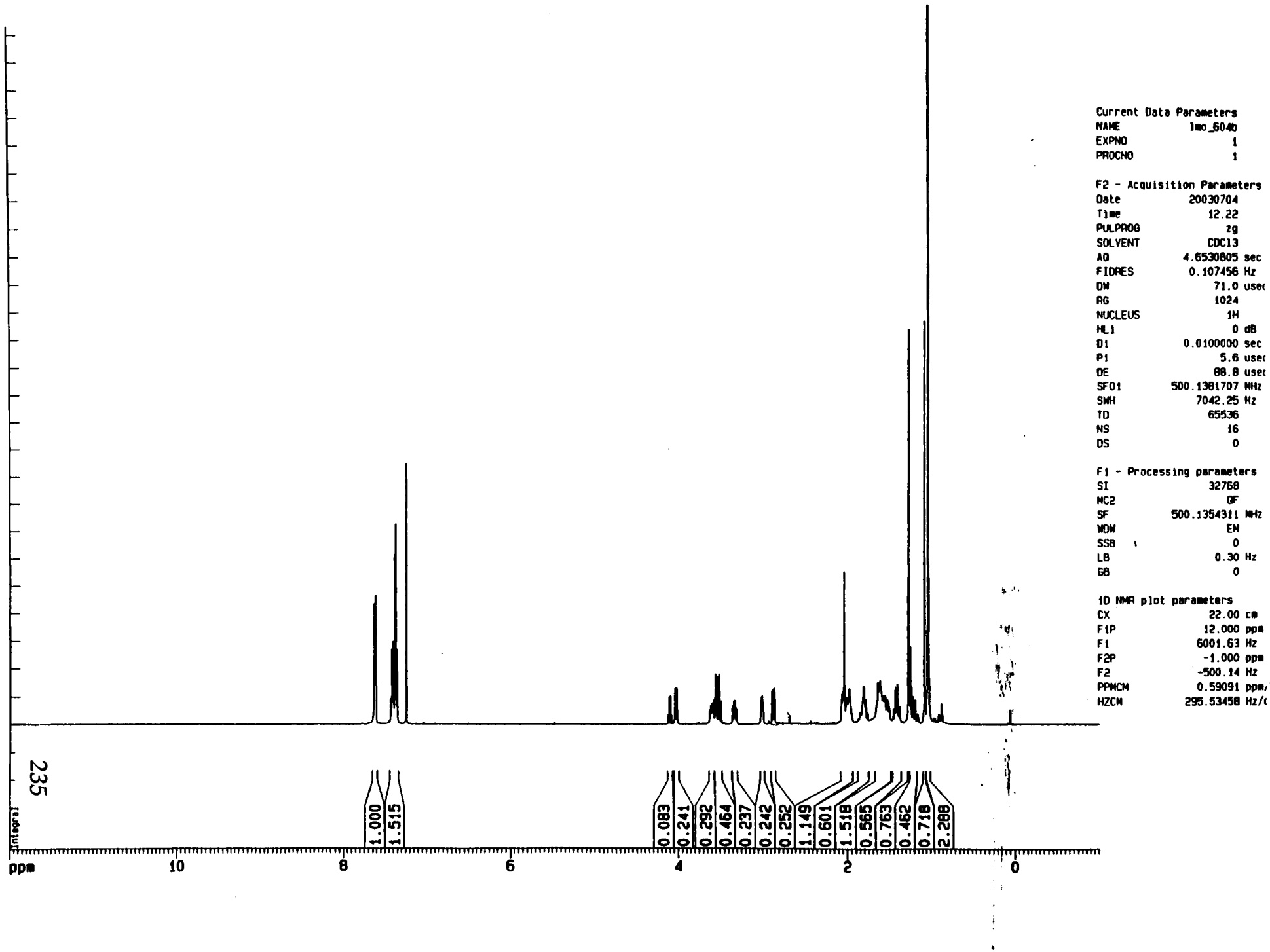
Data for **3.72**

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.63-7.61 (m, 4H), 7.45-7.31 (m, 6H), 4.02 (dd, J= 11, 4 Hz, 1H), 3.62-3.57 (m, 1H), 3.56-3.48 (m, 2H), 3.32 (td, 11, 4 Hz, 1H), 3.00-2.99 (m, 1H), 2.86 (dd, J= 12, 3 Hz, 1H), 2.05-1.93 (m, 3H), 1.86-1.75 (m, 2H), 1.66-1.49 (m, 5H), 1.45-1.37 (m, 2H), 1.26 (s, 3H), 1.25-1.15 (m, 2H), 1.07 (s, 3H), 1.02 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 216.3, 135.6 (x2), 135.5 (x2), 133.5, 133.4, 129.7 (x2), 127.7 (x4), 84.4, 82.2, 65.6, 61.3, 60.4, 49.4, 46.3, 45.5, 33.7 (x2), 29.2, 28.8, 26.8 (x3), 24.4, 24.1, 22.2, 21.0, 19.2.

IR (neat) 3460, 2930, 2856, 1691, 1106 cm^{-1}

EI HRMS calcd for $C_{29}H_{37}O_4Si$ (M^+ - tBu) 477.24611, obsd 477.2412.


Current Data Parameters
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EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date 20030704
Time 12.22
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SOLVENT CDCl3
AQ 4.6530805 sec
FIDRES 0.107456 Hz
DW 71.0 usec
RG 1024
NUCLEUS 1H
HL1 0 dB
D1 0.0100000 sec
P1 5.6 usec
DE 88.8 usec
SFO1 500.1381707 MHz
SWH 7042.25 Hz
TD 65536
NS 16
DS 0
F1 - Processing parameters
SI 32768
WC2 QF
SF 500.1354311 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
1D NMR plot parameters
CX 22.00 cm
F1P 12.000 ppm
F1 6001.63 Hz
F2P -1.000 ppm
F2 -500.14 Hz
PPMCM 0.59091 ppm/
HZCM 295.53458 Hz/
235
Integral
1.000
1.515
0.083
0.241
0.292
0.464
0.237
0.242
0.252
1.149
0.601
1.518
0.565
0.763
0.462
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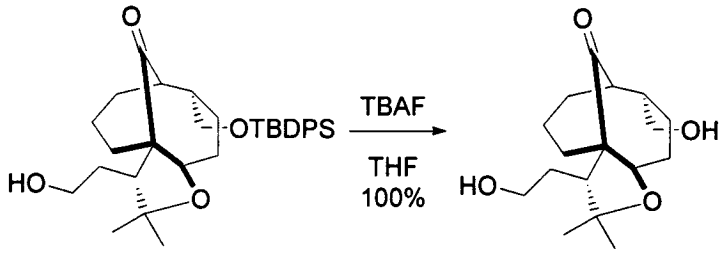
2.288
ppm
10
8
6
4
2
0



3.72 **3.73**

2-(2-Hydroxy-ethyl)-8-hydroxymethyl-3,3-dimethyl-4-oxa-tricyclo[7.3.1.01,5]tri-decan-13-one (3.73)

A solution of the silyl protected alcohol **3.72** (0.025 g, 0.05 mmol) in THF (1 mL) was stirred at 0°C. TBAF 1 M solution (0.5 mL, 0.5 mmol) was added and the reaction was stirred for 1 hour. The solvent was evaporated. The crude product was purified by flash column chromatography (100% EtOAc) to afford 17 mg of **3.73** (100% yield) as a colorless oil.

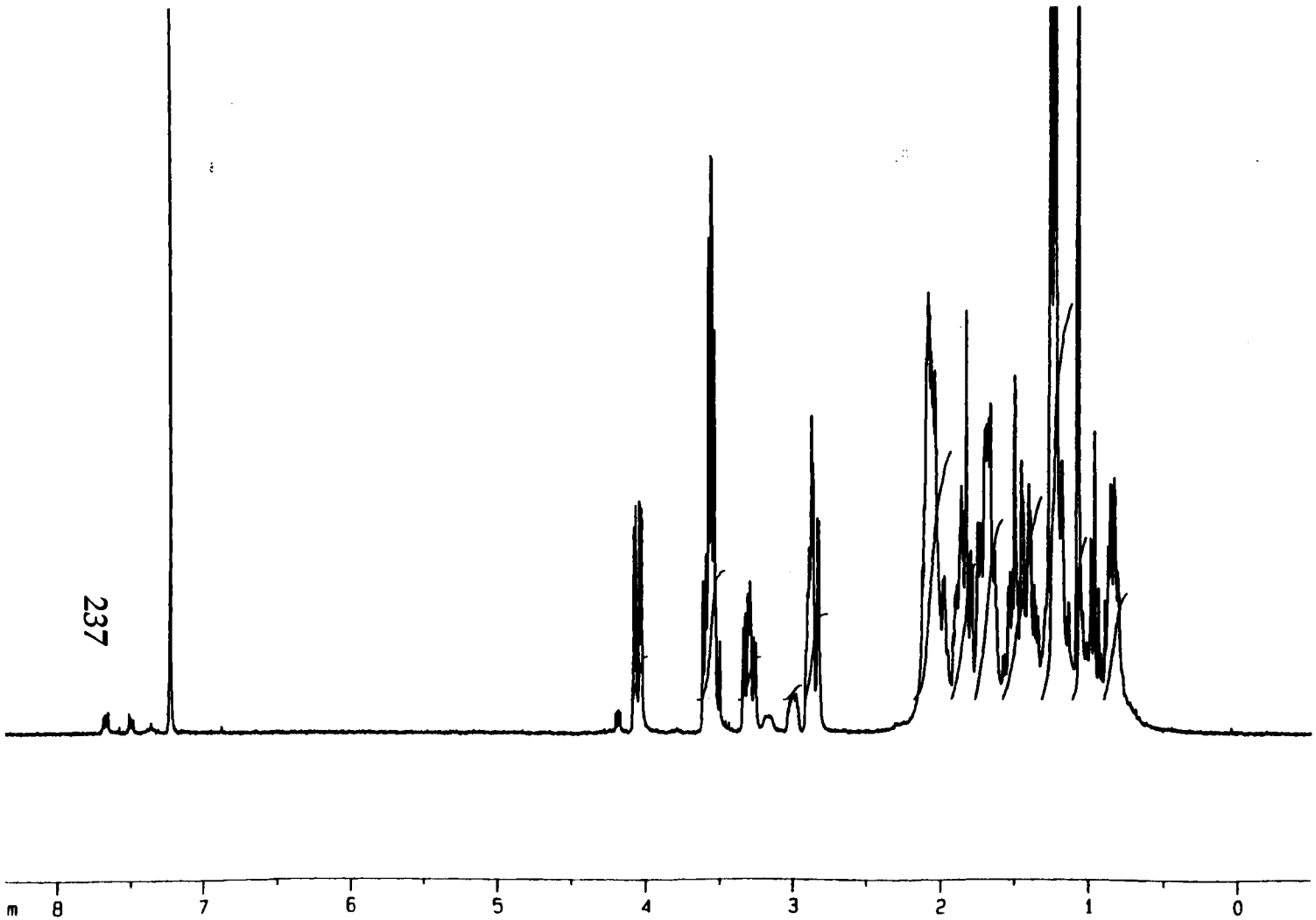
Data for **3.73**

^{1}H NMR (300 MHz, $CDCl_3$): δ 4.06 (dd, J= 11 Hz, 1H), 3.62-3.50 (m, 3H), 3.35-3.26 (m, 1H), 2.89-2.82 (m, 2H), 2.12-1.95 (m, 5H), 1.93-1.78 (m, 2H), 1.75-1.63 (m, 4H), 1.56-1.29 (m, 4H), 1.26 (s, 3H), 1.07 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 216.3, 84.3, 82.2, 64.9, 61.2, 60.3, 49.3, 46.7, 45.5, 33.7, 33.6, 29.15, 28.7, 24.3, 23.9, 22.1, 20.9.

IR (neat) 3409, 2930, 2856, 1695, 1055, 1031 cm^{-1}.

EI HRMS calcd for $C_{17}H_{28}O_4$ (M^+) 296.19876, obsd 296.20077.



3.73

Current Data Parameters

NAME	lmo_616-1
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

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Time	13.13
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PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	256
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

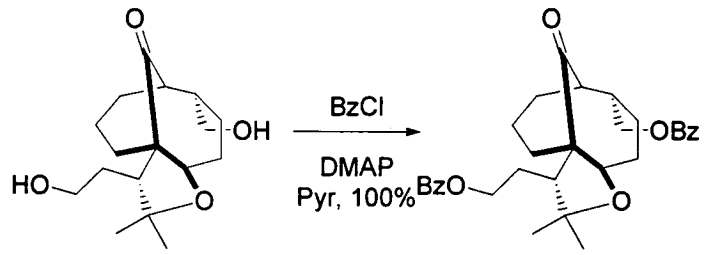
NUC1	1H
P1	10.50 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

F2 - Processing parameters

SI	65536
SF	300.1299999 MHz
WDW	EM
SSB	0
LB	0.10 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	20.00 cm
CY	40.00 cm
F1P	8.500 ppm
F1	2551.10 Hz
F2P	-0.500 ppm
F2	-150.06 Hz
PPMCM	0.45000 ppm/cm
HZCM	135.05850 Hz/cm



3.73 **3.74**

Bis-benzoic acid 2-(2-Hydroxy-ethyl)-8-hydroxymethyl-3,3-dimethyl-4-oxa-tricyclo[7.3.1.01,5]tri-decan-13-one (3.74)

A solution of alcohol **3.73** (0.017 g, 0.05 mmol), pyridine (0.015 mL, 0.18 mmol) and DMAP (0.0014 g, 0.01 mmol) in dicloromethane (3 mL) and toluene (3 mL) was stirred at room temperature. Benzoyl chloride (0.020 mL, 0.18 mmol) was added and the reaction was stirred for 15 hours. The reaction was quenched by adding saturated NH_4Cl_{aq}. The aqueous layer was extracted 3 times with dichloromethane (3 X 20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (30% EtOAc/hexanes) to afford 15 mg of **3.74** (100% yield) as white crystals with Mp 131.7-132.3 °C.

Data for **3.74**

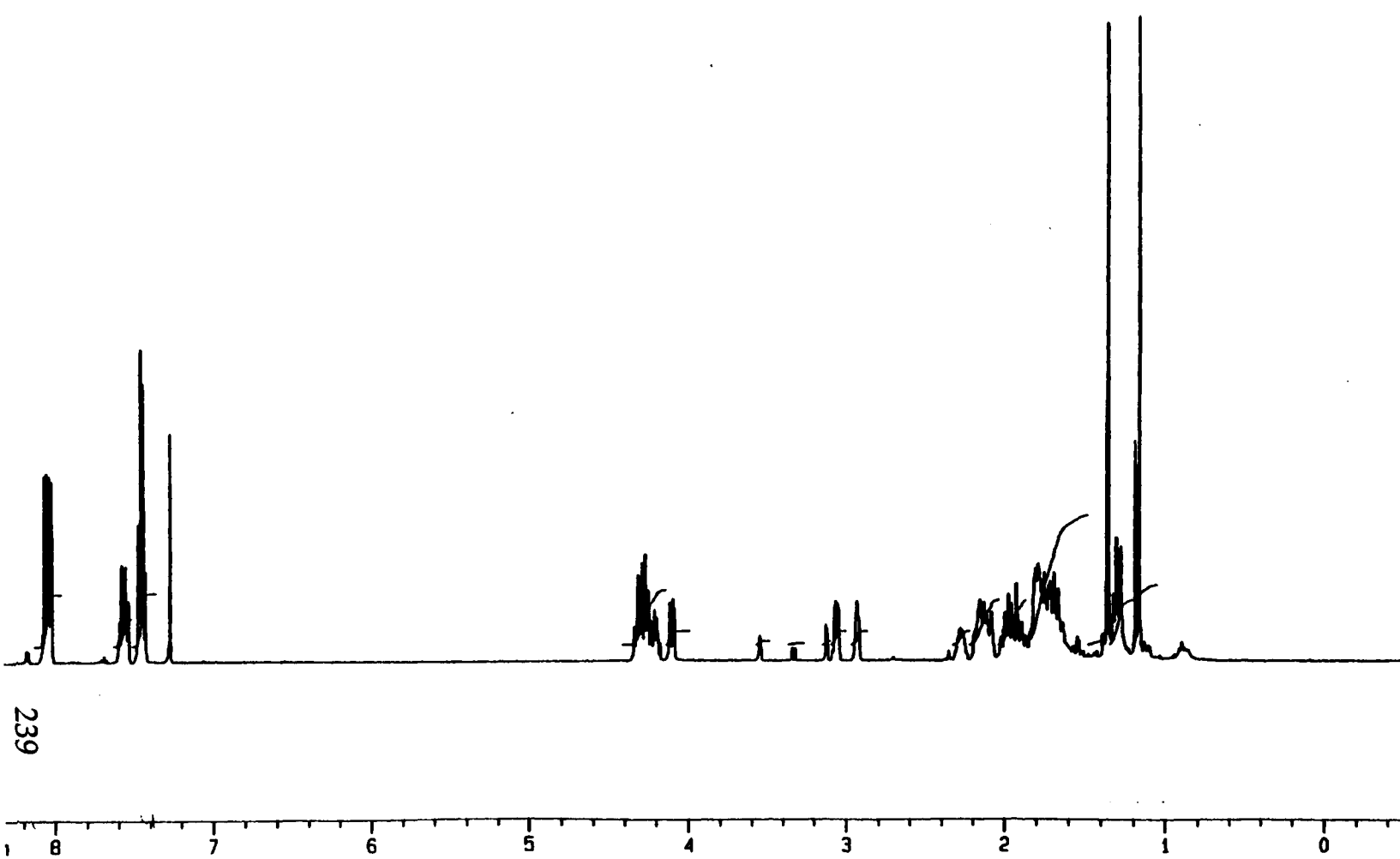
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.06 (dd, J= 15, 8 Hz, 4H), 7.60-7.53 (m, 2H), 7.45 (q, J= 8 Hz, 4H), 4.34-4.17 (m, 4H), 4.10 (dd, J= 11, 4 Hz, 1H), 3.05 (dd, J= 10, 5 Hz, 1H), 2.92-2.91 (m, 1H), 2.35-2.23 (m, 1H), 2.19-2.08 (m, 2H), 2.02-1.85 (m, 2H), 1.83-1.60 (m, 6H), 1.35 (s, 3H), 1.31-1.28 (m, 2H), 1.15 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 211.9, 166.5, 166.3, 133.1, 132.9, 130.3, 129.9, 129.6 (x4), 128.4 (x4), 83.8, 82.2, 66.2, 64.0, 61.3, 49.3, 47.0, 43.1, 33.4, 33.2, 29.2, 25.7, 24.7, 24.2, 21.3, 20.8.

IR (neat) 2933, 2865, 1719, 1690, 1453, 1272, 1108 cm^{-1}.

EI HRMS calcd for $C_{31}H_{36}O_6$ (M^+) 504.25119, obsd 504.25035.

3.74



239

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FIDRES 0.113533 Hz
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TE 300.0 K
D1 0.01000000 sec

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PL1 3.00 dB
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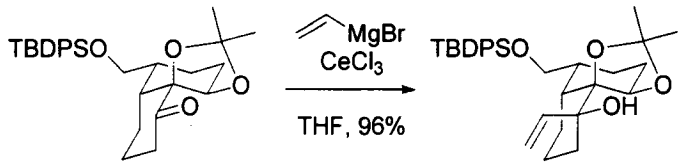


3.58 **3.77**

6-(tert-Butyl-diphenyl-silanyloxymethyl)-2,2-dimethyl-10-vinyl-octahydro-naphtho[1,8a-d][1,3]dioxol-10-ol (3.77).

A suspension of $CeCl_3$ (0.044 g, 0.18 mmol) in dry THF (0.6 mL) was stirred at 0 °C for 2 h. Ketone **3.58** (0.03 g, 0.06 mmol) was dissolved in THF (0.2 mL) and cannulated into the $CeCl_3$ suspension and stirred for 15 h at room temperature. The solution was cooled to -78°C and vinylmagnesium bromide 0.9 M (0.2 mL, 0.18 mmol) was added dropwise. The reaction was stirred for 30 min at –78 °C. Saturated $NH_4Cl_{(aq)}$ was added. The aqueous layer was extracted 3 times with dichloromethane (3 X 20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash silica column chromatography (20% EtOAc/hexanes) to afford 30 mg of **3.77** (96% yield) as a colourless oil.

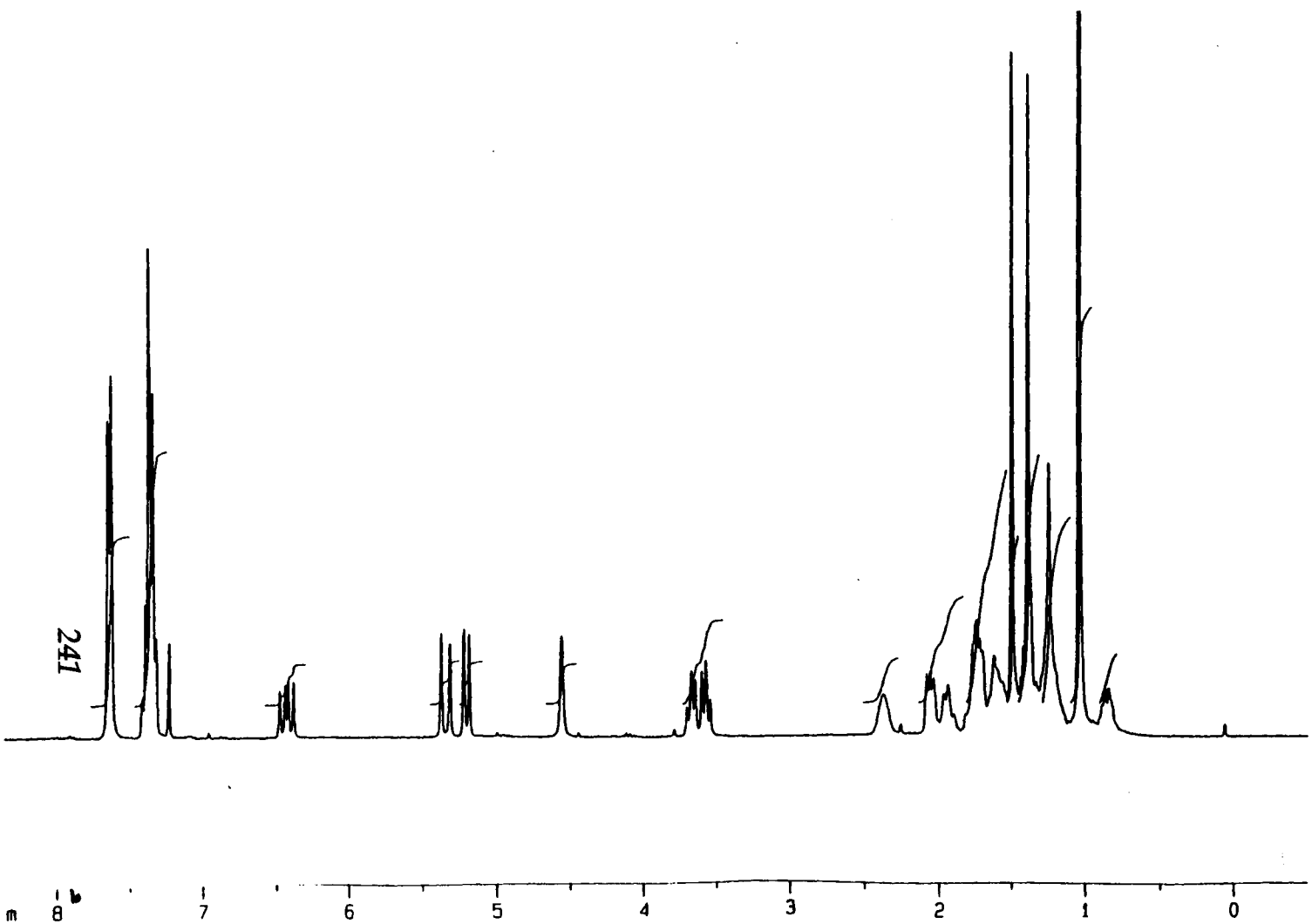
Data for **3.77**

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.66-7.64 (m, 4H), 7.42-7.33 (m, 6H), 6.44 (dd, J= 10.8, 17.3 Hz, 1H), 5.35 (d, J= 17.4 Hz, 1H), 5.21 (d, 10.9 Hz, 1H), 4.56 (s, 1H), 3.79-3.55 (m, 2H), 2.37 (s, 1H), 2.08-2.03 (m, 1H), 1.96-1.89 (m, 1H), 1.81-1.56 (m, 5H), 1.49 (s, 3H), 1.38 (s, 3H), 1.33-1.1 (m, 4H), 1.03 (s, 9H), 0.94-0.84 (m, 1H).

^{13}C NMR ($CDCl_3$, 75 MHz) δ 143.7, 135.6 (x4), 134.1 (x2), 129.5 (x2), 127.6 (x4), 113.1, 107.1, 75.5, 73.6, 65.8, 38.8, 37.4, 27.9, 27.3, 26.9 (x3), 23.3, 23.2, 20.5, 19.3, 18.1.

IR (neat) 3464, 2928, 2852, 1109, 1041 cm^{-1}.

EI HRMS calcd for $C_{32}H_{44}O_4Si$ (M^+) 520.30089, obsd 520.30007.



3.77

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FIDRES             0.165407 Hz
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RG                     161.3
DW                    98.400 usec
DE                      6.00 usec
TE                     300.0 K
D1                1.00000000 sec

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PL1                    -3.00 dB
SFO1           300.1319477 MHz

F2 - Processing parameters
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SF             300.1299999 MHz
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GB                         0
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1D NMR plot parameters
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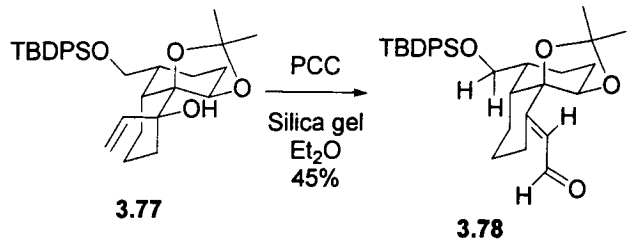


3.77 **3.78**

[6-(tert-Butyl-diphenyl-silanyloxymethyl)-2,2-dimethyl-octahydro-naphtho[1,8a-d][1,3]dioxol-10-ylidene]-acetaldehyde (3.78)

The alcohol **3.77** (0.673 g, 1.29 mmol) was dissolved in dichloromethane (34 mL). and silica gel (1.7 g) was added, followed by pyridinium chlorochromate (0.333 g, 1.55 mmol). The reaction was stirred for 48 hours at room temperature. The solvent was evaporated. The crude product was purified by flash column chromatography (15% EtOAc/hexanes to 30% EtOAc/hexanes) to afford 300 mg of **3.78** (45% yield) as white crystals Mp 137.2-138.1 °C.

Data for **3.78**

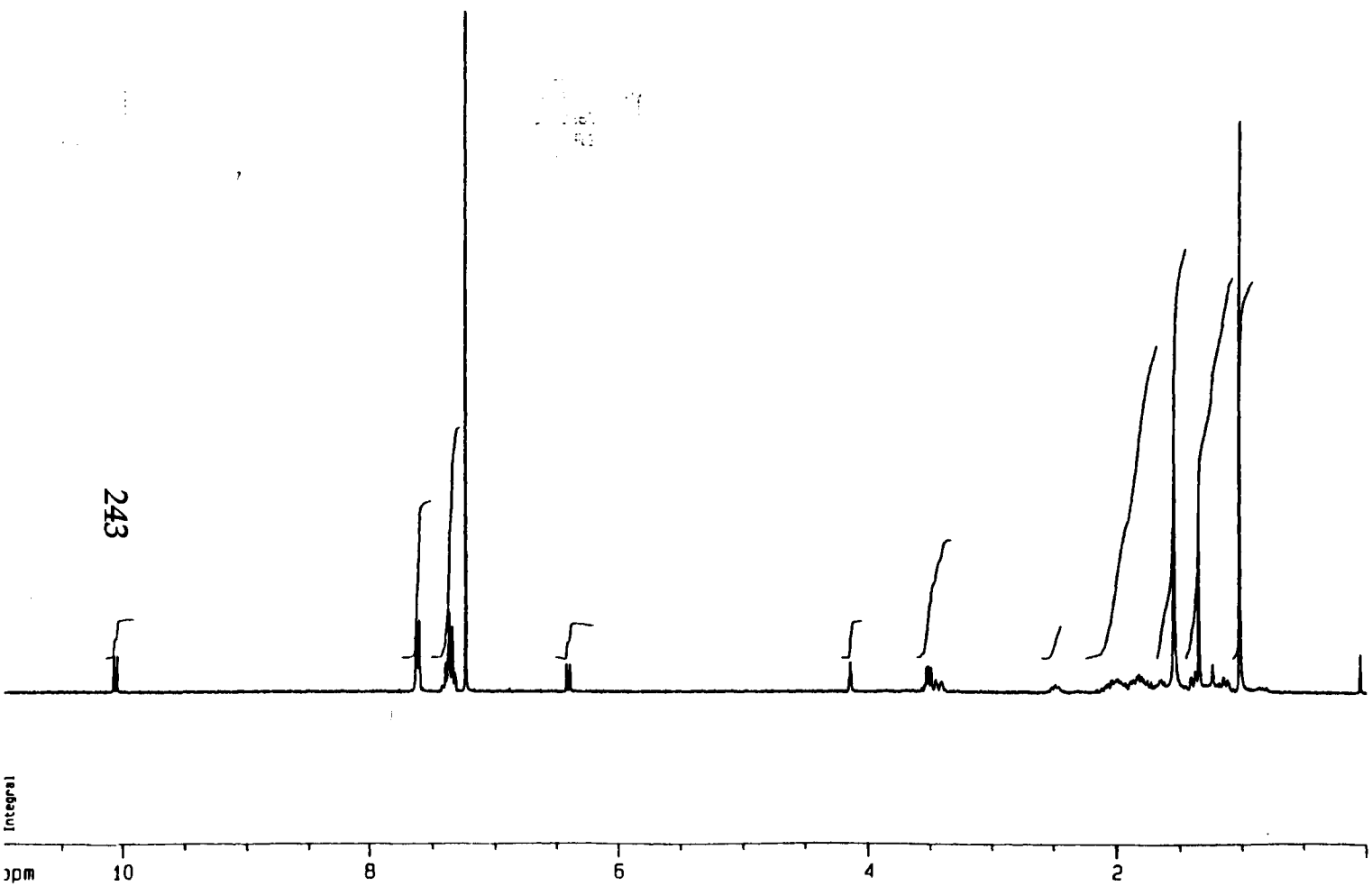
^{1}H NMR (300 MHz, $CDCl_3$): δ 10.07 (d, J= 8 Hz, 1H), 7.65-7.62 (m, 4H), 7.42-7.32 (m, 6H), 6.42 (d, J= 8 Hz, 1H), 4.15-4.09 (m, 1H), 3.52 (dd, J= 7, 4 Hz, 2H), 3.46-3.41 (m, 1H), 2.53-2.47 (m, 1H), 2.10-1.92 (m, 3H), 1.90-1.68 (m, 3H), 1.66-1.64 (m, 1H), 1.54 (s, 3H), 1.45-1.37 (m, 2H), 1.35 (s, 3H), 1.29-1.10 (m, 1H), 1.02 (s, 9H).

^{13}C NMR (300 MHz, $CDCl_3$) δ 190.5, 168.9, 135.5 (x4), 133.9 (x2), 129.6 (x2), 127.6 (x4), 122.9, 108.1, 84.2, 76.2, 66.0, 43.1, 32.7, 27.7, 27.6, 26.8 (x3), 26.7, 25.9, 23.0, 22.0, 19.3, 16.7.

IR (neat) 3066, 2861, 1671, 1112, 1082 cm^{-1}.

EI HRMS calcd for $C_{28}H_{33}O_4Si$ (M^+-tBu) 461.21481, obsd 461.21439.

3.78



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PROCNO	1

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FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	912.3
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

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PL1	-3.00 dB
SFO1	300.1319477 MHz

F2 - Processing parameters

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1D NMR plot parameters

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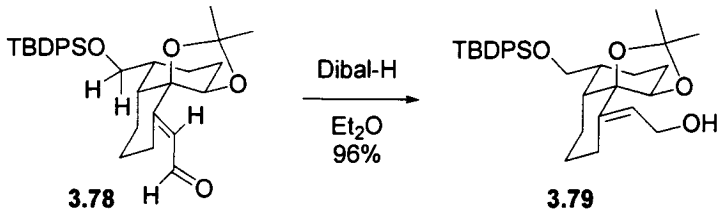


2-[6-(tert-Butyl-diphenyl-silanyloxymethyl)-2,2-dimethyl-octahydro-naphtho[1,8a-d][1,3]dioxol-10-ylidene]-ethanol (3.79)

A solution of enone **3.78** (0.031 g, 0.060 mmol)in diethylether (2 mL) was stirred at 0 °C. Dibal-H 1.5M in hexanes (0.050 mL, 0.071 mmol) was added and the reaction was stirred for 20 minutes. The reaction was quenched by adding sodium tartrate solution 1M and stirred for 15 hours. The aqueous layer was extracted 3 times with ethylacetate (3 X 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (20% EtOAc/hexanes) to afford 30 mg of **3.79** (96% yield) as a colourless oil.

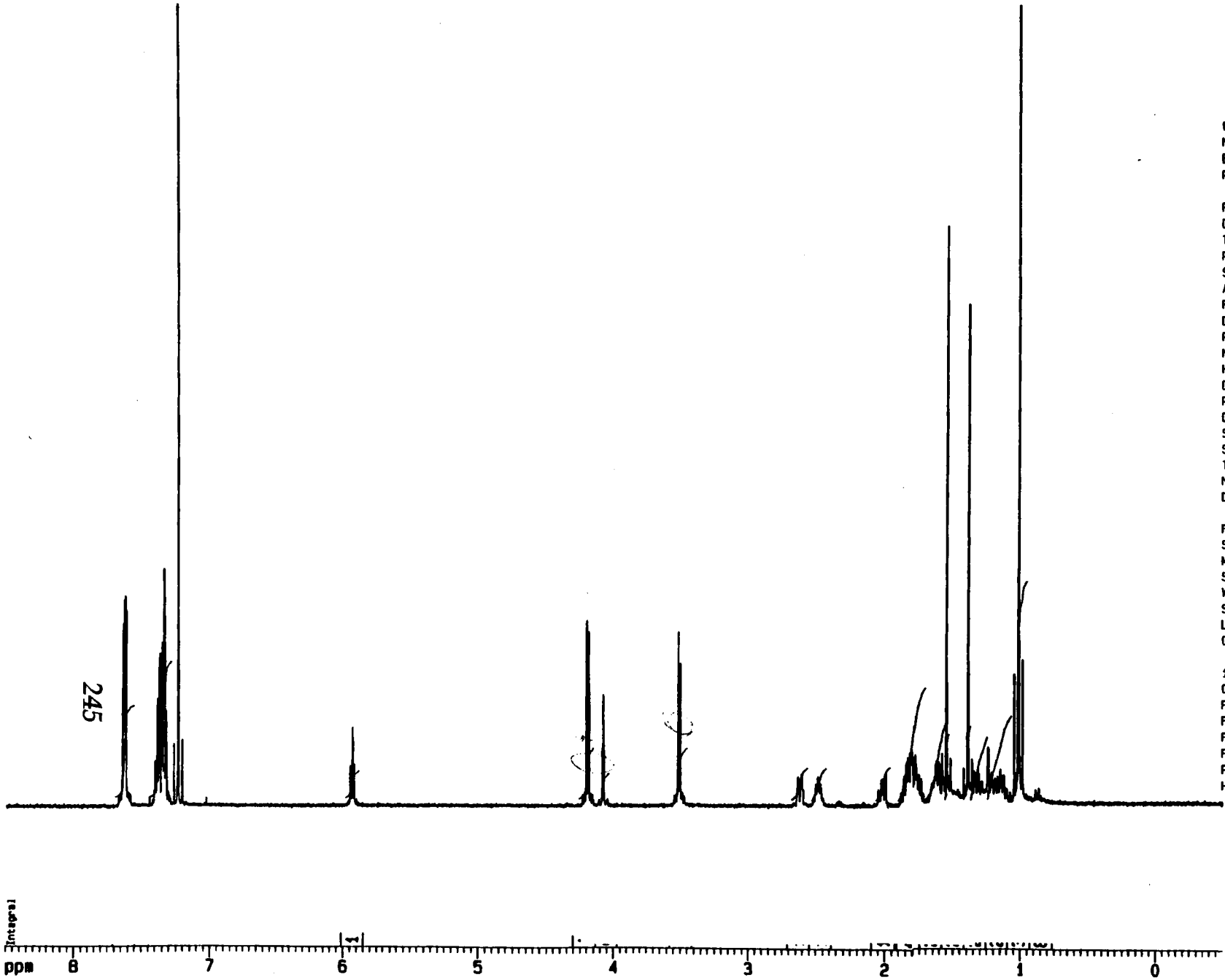
Data for **3.79**

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.66-7.59 (m, 4H), 7.41-7.30 (m, 6H), 5.93 (t, J= 7 Hz, 1H), 4.19 (d, J= 7 Hz, 2H), 4.08 (t, J= 3 Hz, 1H), 3.50 (d, J= 8 Hz, 2H), 2.63-2.60 (m, 1H), 2.50-2.46 (m, 1H), 2.04-1.99 (m, 1H), 1.88-1.72 (m, 3H), 1.65-1.59 (m, 2H), 1.55 (s, 3H), 1.39 (s, 3H), 1.34-1.28 (m, 2H), 1.23-1.08 (m, 3H), 1.01 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 146.6, 135.6 (x4), 134.1, 129.5 (x2), 127.6 (x4), 119.8, 107.3, 84.2, 77.7, 66.5, 58.8, 42.7, 33.3, 27.2, 27.0 (x4), 26.4, 24.1, 22.7, 19.3, 17.2.

IR (neat) 3398, 2932, 2858, 1112, 1083 cm^{-1}.

EI HRMS calcd for $C_{32}H_{42}O_3Si$ (M^+-H_2O) 502.29032, obsd 502.2936.



3.79

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PROCNO 1

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TD 65536
NS 16
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F1 - Processing parameters
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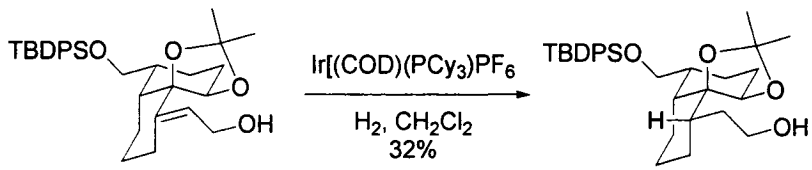


3.79 **3.80**

2-[6-(tert-Butyl-diphenyl-silanyloxymethyl)-2,2-dimethyl-octahydro-naphtho[1,8a-d][1,3]dioxol-10-yl]-ethanol (3.80)

A solution of Crabtree's catalyst (0.033 g, 0.04 mmol) in dichloromethane (2 mL) was stirred at room temperature.. Allylic alcohol **3.79** (0.265 g, 0.5 mmol) in dichloromethane (2 mL) was canulated in the Crabtree's catalyst solution. The solution was degazed with H_2 for 3 minutes and the solution was stirred for 15 hours under 1 atmosphere of H_2. The solvent was evaporated. The crude product was purified by flash column chromatography (20% EtOAc/hexanes) to afford 86 mg of **3.80** (32% yield) as a yellow oil.

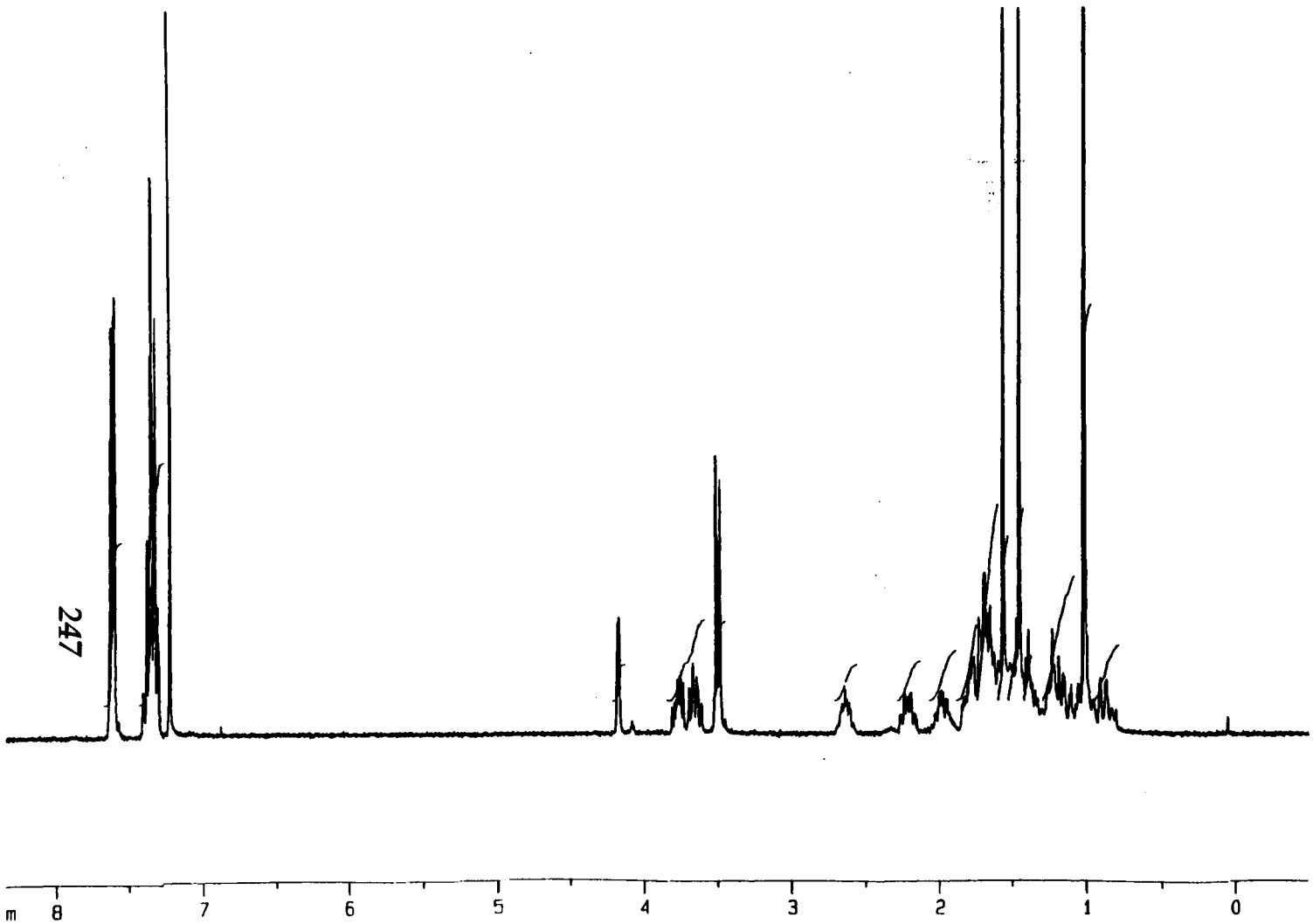
Data for **3.80**

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.65-7.59 (m, 4H), 7.42-7.31 (m, 6H), 4.18-4.17 (m, 1H), 3.81-3.73 (m, 1H), 3.69-3.61 (m, 1H), 3.50 (d, J= 8 Hz, 2H), 2.67-2.59 (m, 1H), 2.27-2.15 (m, 1H), 2.05-1.90 (m, 1H), 1.84-1.76 (m, 2H), 1.72-1.59 (m, 5H), 1.56 (s, 3H), 1.51-1.47 (m, 2H), 1.45-1.37 (m, 1H), 1.45 (s, 3H), 1.26-1.10 (m, 3H), 1.01 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 135.6 (x4), 134.1, 134.0, 129.5 (x2), 127.6 (x4), 106.7, 85.5, 73.2, 66.3, 62.0, 42.9, 41.8, 33.2, 32.7, 28.7, 28.6, 28.2, 26.8 (x3), 25.2, 24.3, 22.9, 19.3, 17.5.

IR (neat) 3418, 2939, 2868, 1101, 1046 cm^{-1}.

EI HRMS calcd for $C_{32}H_{46}O_4Si$ (M^+) 522.31624, obsd 522.31518.



3.80

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FIDRES 0.165407 Hz
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TE 300.0 K
D1 1.00000000 sec

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1D NMR plot parameters
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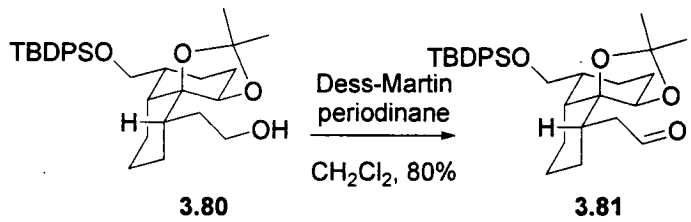


3.80 **3.81**

[6-(tert-Butyl-diphenyl-silanyloxymethyl)-2,2-dimethyl-octahydro-naphtho[1,8a-d][1,3]dioxol-10-yl]-acetaldehyde (3.81)

Alcohol **3.80** (0.005 g, 0.01 mmol) was dissolved in CH_2Cl_2 (1 mL) and Dess-Martin periodate (5 mg, 0.012 mmol) was added. The reaction was stirred for 3 hours at room temperature. A solution of $NaHCO_{3sat}$ was added, followed by $Na_2S_2O_{3sat}$ and stirred for 20 minutes. The aqueous layer was extracted 3 times with dichloromethane (3 X 20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (20% EtOAc/hexanes) to afford 4 mg of **3.81**% yield) as a colourless oil.

Data for **3.81**

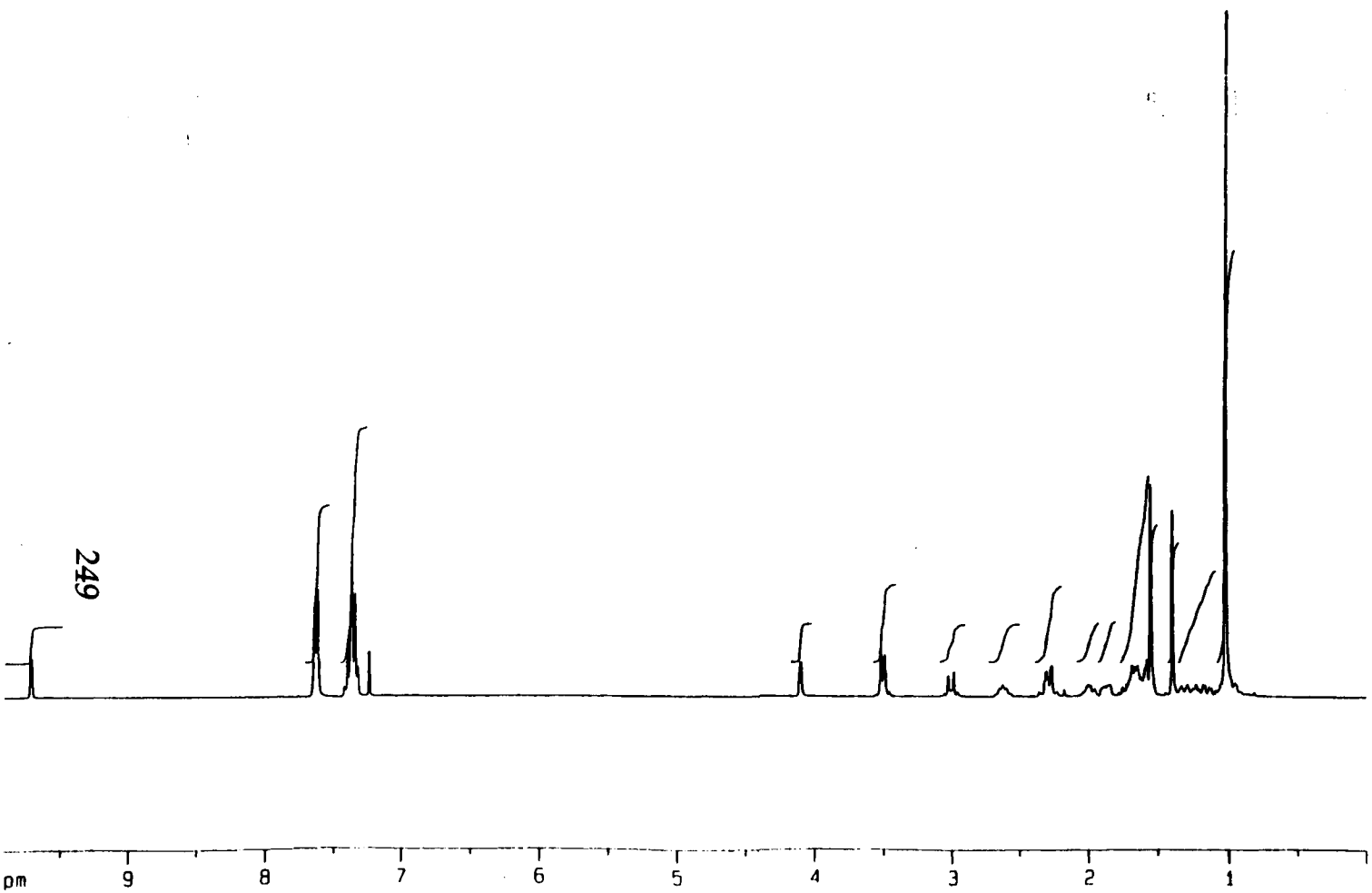
^{1}H NMR (300 MHz, $CDCl_3$): δ 9.72 (d, J= 3 Hz, 1H), 7.64 (d, J= 8 Hz, 4H), 7.43-7.33 (m, 6H), 4.10 (s, 1H), 3.52-3.49 (m, 2H), 3.03-2.96 (m, 1H), 2.65-2.60 (m, 1H), 2.36-2.27 (m, 2H), 2.02-1.96 (m, 1H), 1.89-1.85 (m, 1H), 1.75-1.59 (m, 6H), 1.56 (s, 3H), 1.40 (s, 3H), 1.34-1.06 (m, 2H), 1.02-0.96 (m, 1H), 1.02 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$): 202.9, 135.5 (x4), 134.0, 133.9, 129.5 (x2), 127.6 (x4), 106.8, 84.5, 73.8, 66.0, 45.1, 41.7, 40.7, 33.1, 29.4, 28.4, 28.0, 26.8 (x3), 25.0, 24.1, 22.8, 19.3, 17.3.

IR (neat) 2933, 2859, 1726, 1112, 1036 cm^{-1}.

EI HRMS calcd for $C_{31}H_{41}O_4Si$ (M^+ -Me) 505.27741, obsd 505.2825.

3.81

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FIDRES           0.165407 Hz
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RG                      128
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DE                  6.00 usec
TE                 300.0 K
D1              1.00000000 sec

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F2 - Processing parameters
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1D NMR plot parameters
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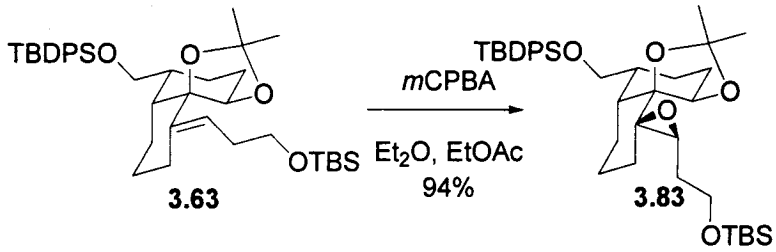


10-[3-(tert-Butyl-dimethyl-silanyloxy)-propylidene]-6-(tert-butyl-diphenyl-silanyloxymethyl)-2,2-dimethyl-octahydro-naphtho[1,8a-d][1,3]dioxole oxide (3.83)

A solution of olephin **3.63** (0.054 g, 0.083 mmol) in diethylether (1.5 mL) and ethylacetate (1.5 mL) was stirred at room temperature. 3-chloroperbenzoic acid (0.066 g, 0.029 mmol) was added and stirred for 4 hours. The reaction was quenched by adding sodium sulfite. The aqueous layer was extracted 3 times with diethylether (3 X 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (30% EtOAc/hexanes) to afford 52 mg of **3.83** (94% yield) as a colourless oil.

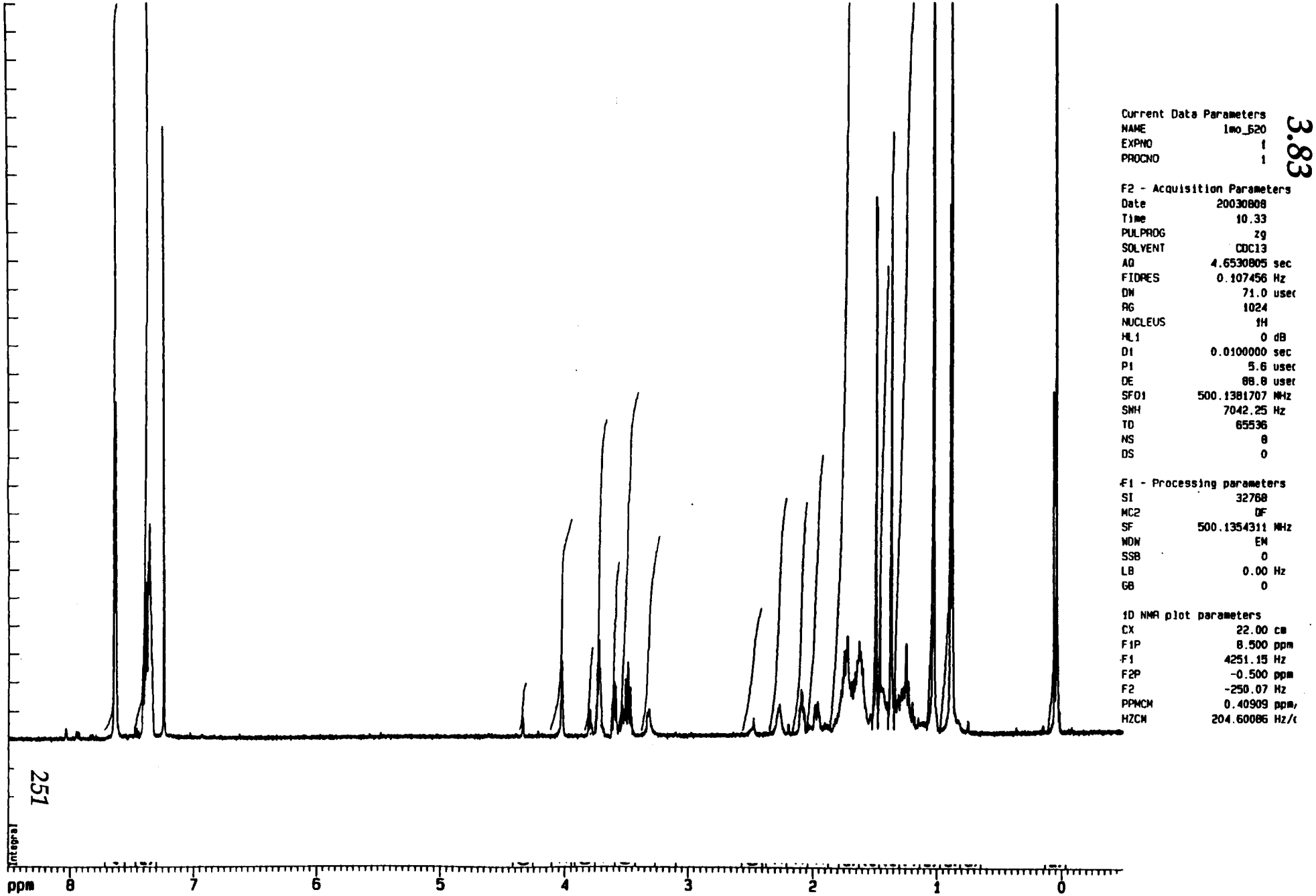
Data for **3.83**

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.64-7.62 (m, 4H), 7.41-7.33 (m, 6H), 4.02 (s, 1H), 3.73-3.70 (m, 2H), 3.61-3.58 (m, 1H), 3.50-3.46 (m, 1H), 3.33-3.31 (m, 1H), 2.33-2.26 (m, 1H), 2.10-2.07 (m, 1H), 2.02-1.94 (m, 1H), 1.77-1.59 (m, 10H), 1.48 (s, 3H), 1.45-1.39 (m, 2H), 1.36 (s, 3H), 1.33-1.21 (m, 5H), 1.02 (s, 9H), 0.87 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 135.6 (x4), 134.0 (x2), 129.6, 129.5, 127.7 (x2), 127.6 (x2), 107.2, 82.0, 75.4, 60.9, 60.4, 58.9, 57.8, 41.4, 40.5, 32.6, 31.0, 27.9, 26.9 (x3), 26.7, 26.6, 25.9 (x3), 22.8, 22.0, 19.3, 18.3, -5.4 (x2).

IR (neat) 2930, 2860, 1467, 1253, 1106 cm^{-1}.

EI HRMS calcd for $C_{38}H_{57}O_5Si_2$ (M^+ -Me) 649.37445, obsd 649.3961.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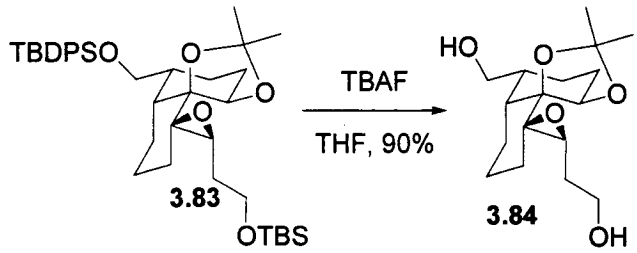


3-(6-Hydroxymethyl-2,2-dimethyl-octahydro-naphtho[1,8a-d][1,3]dioxol-10-ylidene)-propan-1-ol oxide (3.84)

A solution of bis silyl protected alcohol **3.83** (0.052 g, 0.078 mmol) in THF (2 mL) was stirred at room temperature. TBAF 1 M solution (0.234 mL, 0.234 mmol) was added and stirred for 5 hours. The solvent was evaporated. The crude product was purified by flash column chromatography (96% EtOAc, 3% MeOH, 1% Et_3N) to afford 22 mg of **3.84** (90% yield) as a colourless oil.

Data for **3.84**

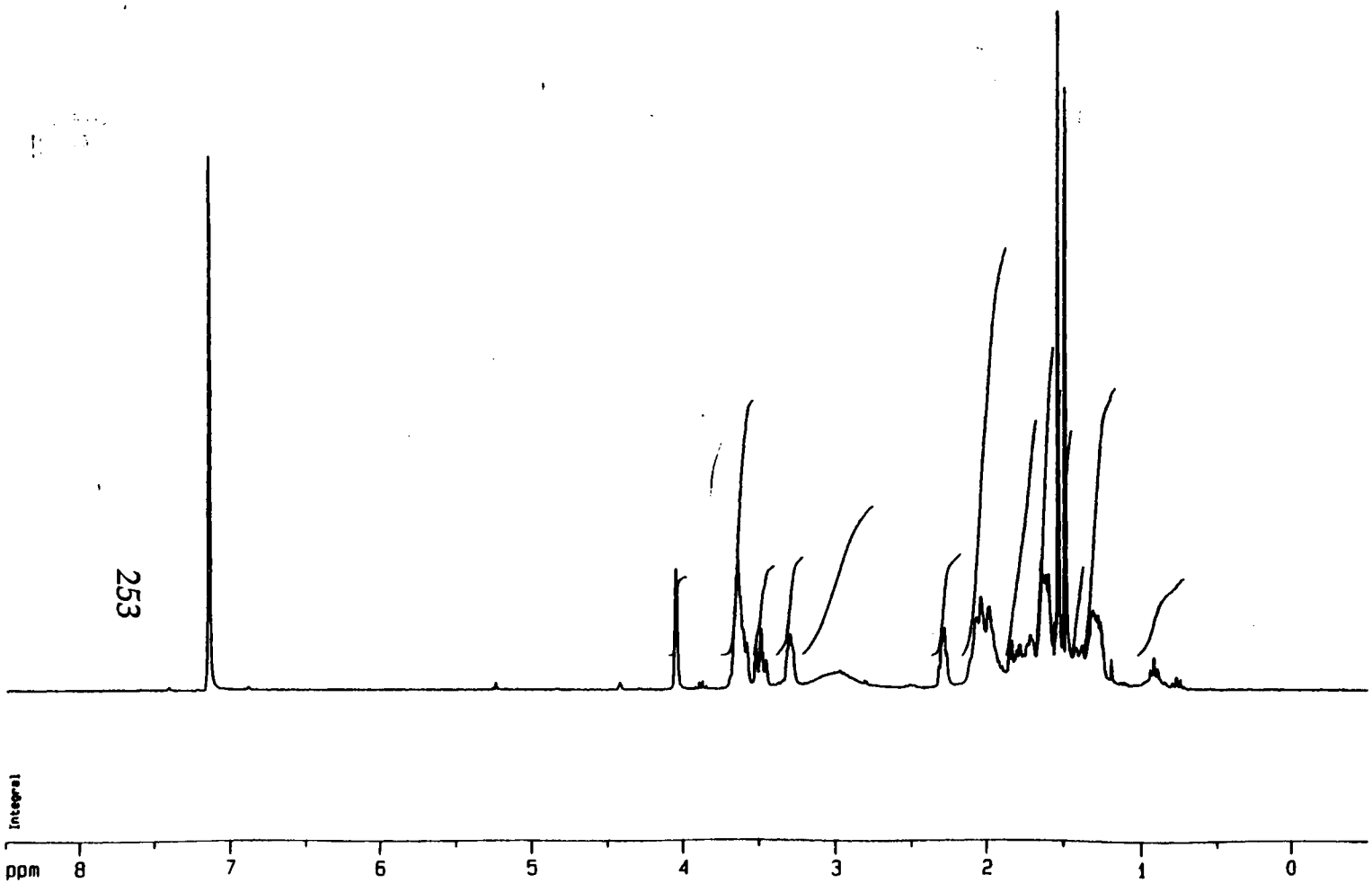
^{1}H NMR (300 MHz, C_6D_6): δ 4.05 (s, 1H), 3.64-3.58 (m, 3H), 3.52 (t, J= 10 Hz, 1H), 3.34-3.30 (m, 1H), 3.16-2.79 (m, 2H), 2.31-2.26 (m, 1H), 2.07-1.75 (m, 4H), 1.73-1.71 (m, 3H), 1.64-1.55 (m, 3H), 1.53 (s, 3H), 1.48 (s, 3H), 1.42-1.26 (m, 3H).

^{13}C NMR (75 MHz, C_6D_6) δ 107.1, 82.2, 72.3, 63.4, 62.1, 90.0, 59.7, 42.1, 40.4, 31.0, 28.5, 26.9, 26.8, 25.5, 23.6, 23.1, 20.6.

IR (neat) 3404, 2929, 2865, 1455, 1384, 1108 cm^{-1}.

EI HRMS calcd for $C_{17}H_{28}O_5$ (M^+) 312.19367, obsd 312.19365.

3.84



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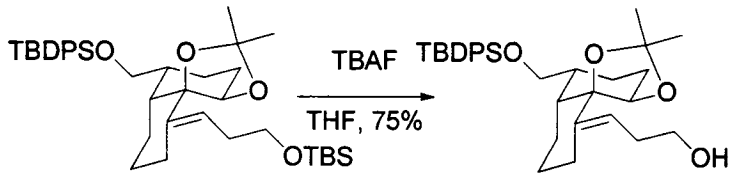


3.63 **3.92**

3-[6-(tert-Butyl-diphenyl-silanyloxymethyl)-2,2-dimethyl-octahydro-naphtho[1,8a-d][1,3]dioxol-10-ylidene]-propan-1-ol (3.92)

A solution of bis silyl protected alcohol **3.63** (0.018 g, 0.03 mmol) in THF (1 mL) was stirred at room temperature. TBAF 1 M solution (0.028 mL, 0.028 mmol) was added stirred for 15 hours. The solvent was evaporated. The crude product was purified by flash column chromatography (50% EtOAc/Hexanes to 100% EtOAc) to afford 12 mg of **3.92** (75% yield) as a colourless oil.

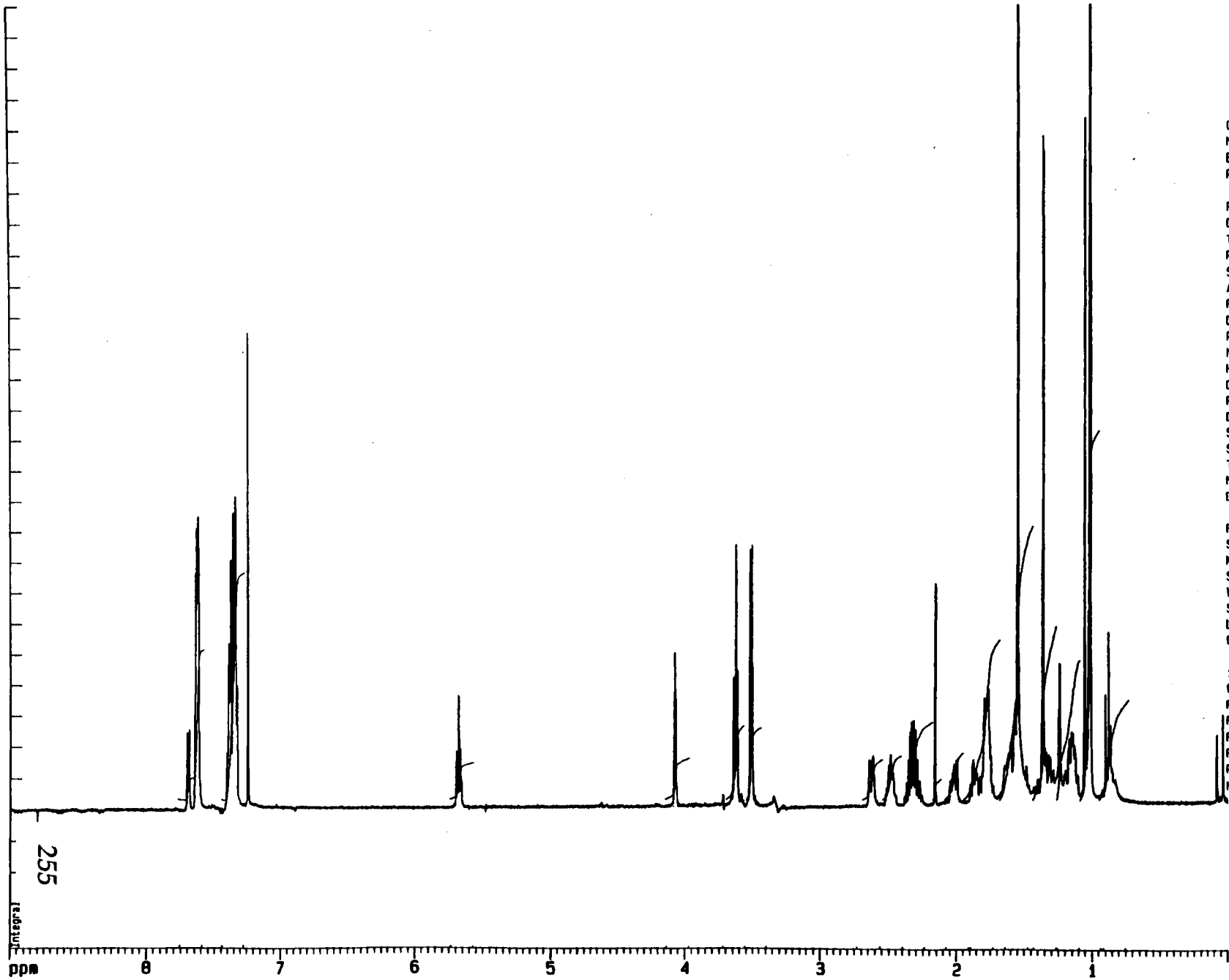
Data for **3.92**

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.71-7.62 (m, 4H), 7.41-7.33 (m, 6H), 5.68 (t, J= 7 Hz, 1H), 4.07 (s, 1H), 3.62 (t, J= 7 Hz, 2H), 3.50 (d, J= 7 Hz, 2H), 2.64-2.61 (m, 1H), 2.51-2.47 (m, 1H), 2.36-2.27 (m, 2H), 2.03-1.99 (m, 1H), 1.89-1.80 (m, 1H), 1.79-1.72 (m, 3H), 1.67-1.57 (m, 2H), 1.55 (s, 3H), 1.36 (s, 3H), 1.34-1.32 (m, 1H), 1.20-1.12 (m, 3H), 1.01 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 145.7, 135.6 (x4), 134.1 (x2), 129.5 (x2), 127.6 (x4), 116.1, 107.2, 84.6, 78.1, 66.6, 62.6, 42.5, 33.4, 30.6, 27.0, 26.9 (x3), 26.6, 26.3, 24.2, 22.8, 19.3, 17.3.

IR (neat) 3428, 2932, 2858, 1643, 1112 cm^{-1}.

EI HRMS calcd for $C_{33}H_{46}O_4Si$ (M^+) 534.31654, obsd 534.30013.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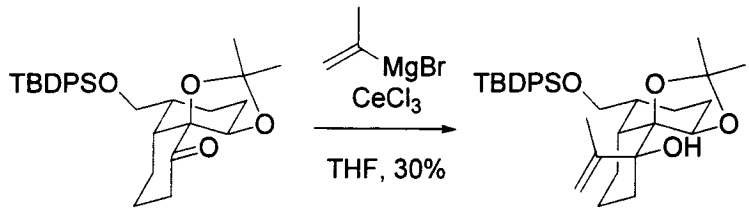


3.58 **3.99**

6-(tert-Butyl-diphenyl-silanyloxymethyl)-10-isopropenyl-2,2-dimethyl-octahydro-naphtho[1,8a-d][1,3]dioxol-10-ol (3.99)

To a suspension of anhydrous $CeCl_3$ (0.074 g, 0.3 mmol) in dry THF (1 mL) at 0°C for 2 hours was canulated ketone **3.58** (0.05 g, 0.1 mmol) in THF (1 mL). The reaction was stirred for 15 hours at room temperature. The solution was cooled to -78°C and vinylmagnesium bromide 0.9 M (0.6 mL, 0.3 mmol) was added dropwise. The reaction was stirred for 30 minutes at -78°C. The reaction was quenched by addind saturated NH_4Cl_{aq}. The aqueous layer was extracted 3 times with dichloromethane (3 X 30 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (20% EtOAc/hexanes) to afford 24 mg of **3.99** (30% yield) as colourless oil.

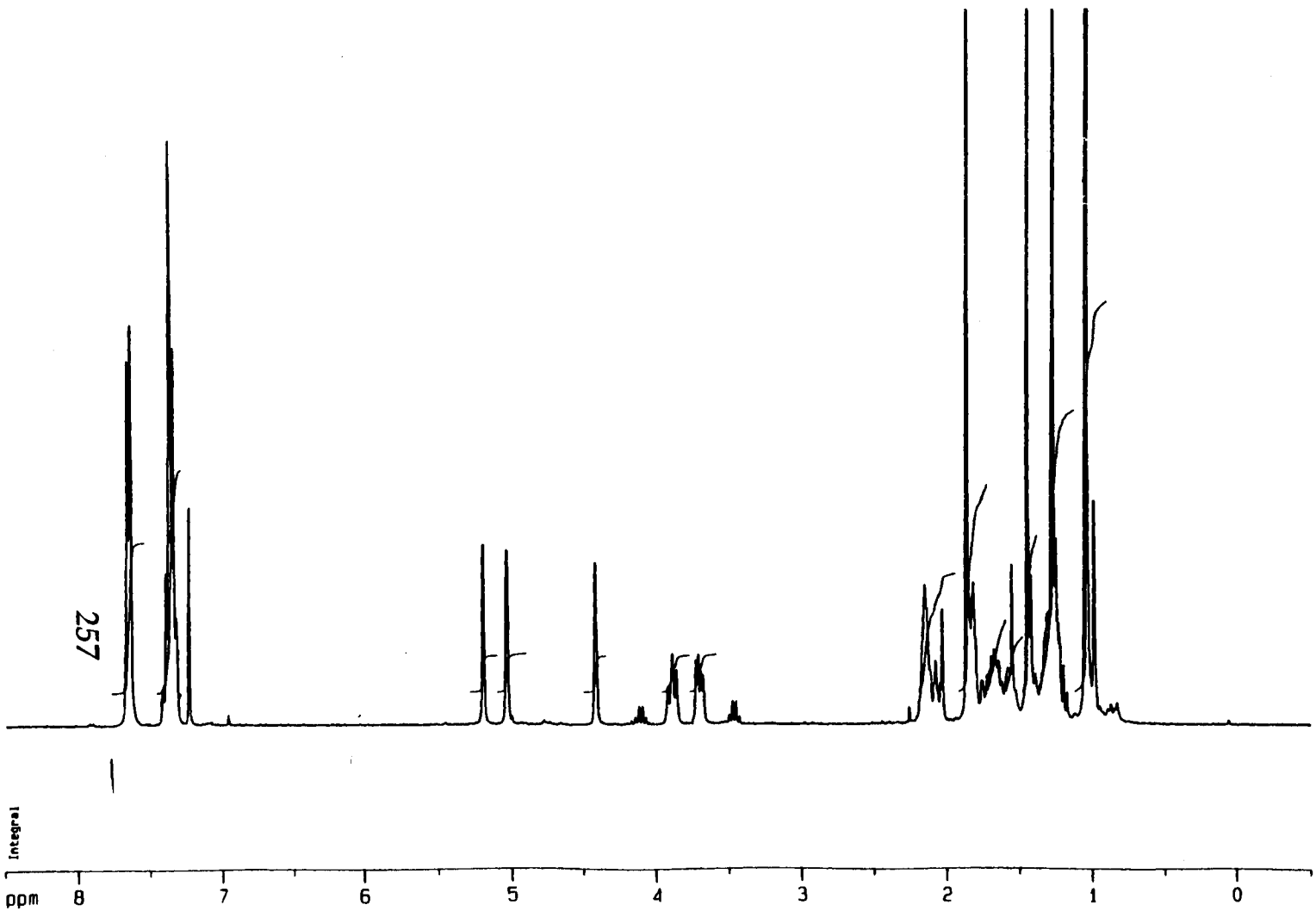
Data for **3.99**

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.65 (d, J= 7 Hz, 4H), 7.41-7.33 (m, 6H), 5.12 (d, J= 49 Hz, 2H), 4.42 (s, 1H), 3.89 (t, J= 10 Hz, 1H), 3.70 (dd, J= 10, 5 Hz, 1H), 2.15-2.02 (m, 3H), 1.86 (s, 3H), 1.82-1.81 (m, 2H), 1.76-1.62 (m, 2H), 1.57-1.55 (m, 2H), 1.44 (s, 3H), 1.42 (s, 1H), 1.32-1.19 (m, 3H), 1.27 (s, 3H), 1.03 (s, 9H).

^{13}C NMR (75 MHz, $CDCl_3$): 151.4, 136.0 (x4), 134.8 (x2), 129.8 (x2), 127.9 (x4), 114.5, 107.3, 83.7, 77.2, 74.6, 64.7, 40.4, 34.3 (x2), 28.9, 27.3 (x3), 27.0, 23.7, 23.3, 22.7, 19.6, 19.5, 19.4.

IR (neat) 3462, 2956, 2857, 1112, 1035 cm^{-1}.

EI HRMS calcd for $C_{33}H_{46}O_4Si$ (M^+) 534.31654, obsd 534.31665.



3.99

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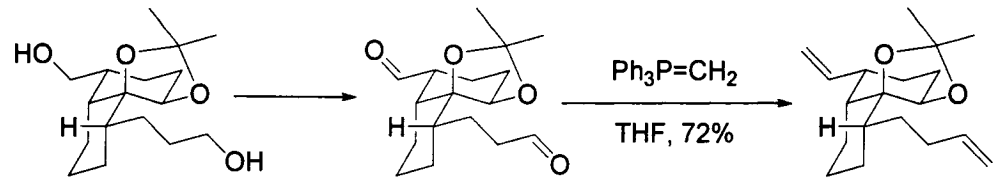


3.70 **3.101** **3.102**

10-But-3-enyl-2,2-dimethyl-6-vinyl-octahydro-naphtho[1,8a-d][1,3]dioxole (3.102).

A catalytic amount of TPAP (1 crystal) and NMO (14 mg, 0.12 mmol) were added to a solution of diol **3.70** in acetonitrile (1 mL) over 4 Å molecular sieves (50 mg). The reaction was stirred for 20 min. The mixture was filtered through a silica gel pad (5% methanol 95% ethylacetate). The solvent was evaporated and the crude dialdehyde 45 was used immediately to avoid decomposition. Methyltriphenylphosphonium iodide (0.057 g, 0.14 mmol) was dissolved in THF (1 mL) and cooled to 0 °C. KHMDS (10.43 M in toluene ,0.325 mL, 0.14 mmol) was added and the solution turned yellow. Dialdehyde **45** (0.010 g, 0.03 mmol) in THF (1 mL) was cannulated into the ylide solution. The reaction was stirred at 0 °C for 30 min. The reaction was quenched by adding saturated $NH_4Cl_{(aq)}$. The aqueous layer was extracted 3 times with diethylether (3 X 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash silica column chromatography (10% EtOAc/hexanes) to afford 7 mg of **3.102** (72% yield) as a colorless oil.

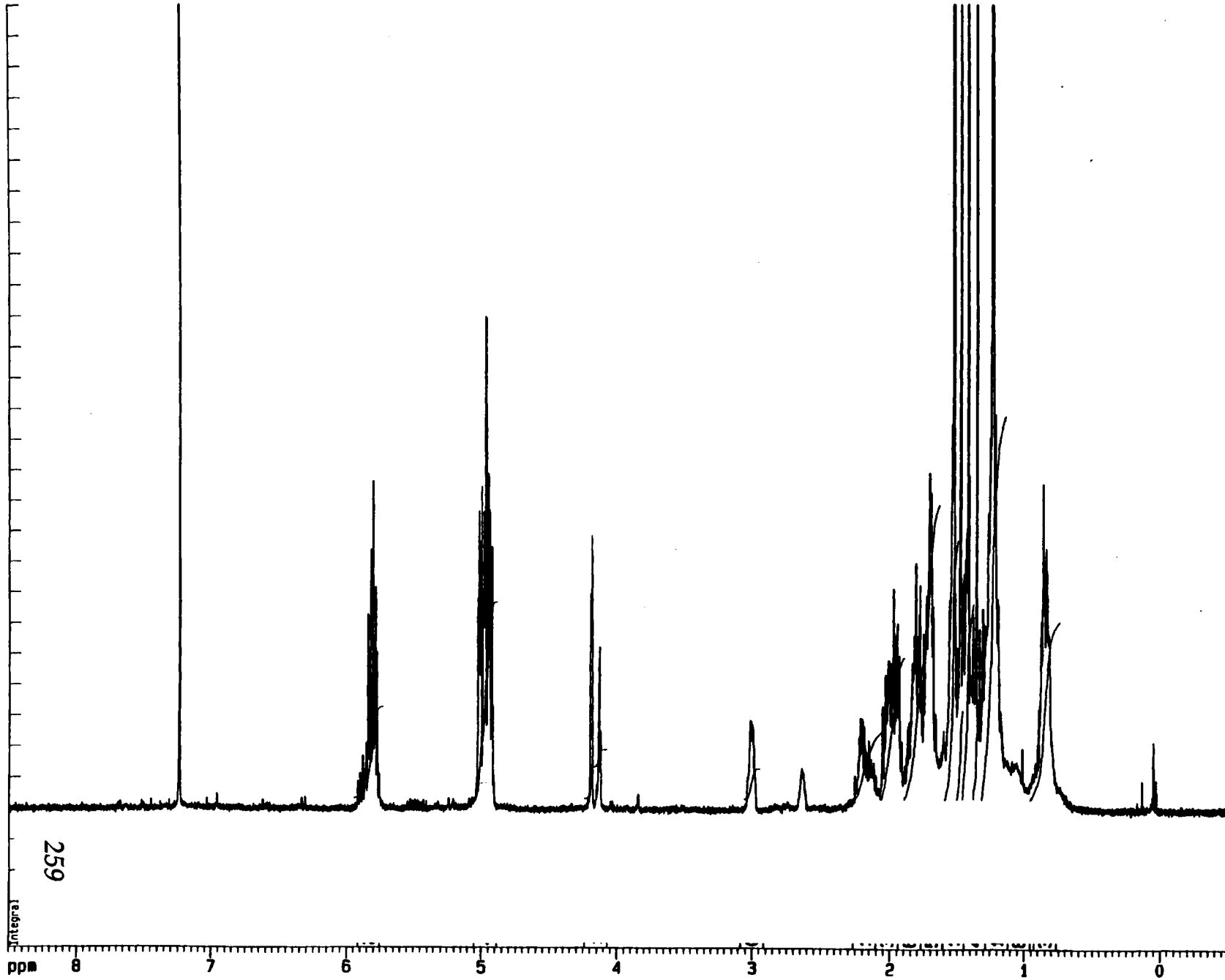
Data for **3.102**

^{1}H NMR (500 MHz, $CDCl_3$): δ 5.88-5.75 (m, 2H), 5.03-4.92 (m, 4H), 4.19 (s, 1H), 3.01-2.99 (m, 1H), 2.25-2.10 (m, 1H), 2.04-1.89 (m, 3H), 1.88-1.65 (m, 6H), 1.53 (s, 3H), 1.42 (s, 3H), 1.37-1.23 (m, 6H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 143.1, 138.8, 114.4, 113.3, 106.6, 85.9, 73.6, 46.6, 45.5, 35.0, 32.3, 29.7, 28.5, 28.4, 28.2, 28.0, 25.0, 23.2, 19.3.

IR (neat) 2930, 2859, 1247, 1036 cm^{-1}.

EI HRMS calcd for $C_{19}H_{30}O_2$ (M^+) 290.22458, obsd 290.22256.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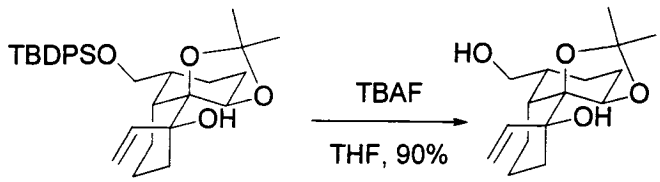


3.77 **3.106**

6-Hydroxymethyl-2,2-dimethyl-10-vinyl-octahydro-naphtho[1,8a-d][1,3]dioxol-10-ol (3.106).

Compound **3.77** (0.033 g, 0.063 mmol) was dissolved in THF (0.5 mL). TBAF (0.089 mL of a 1 M solution in THF, 0.089 mmol) was added. The reaction was stirred for 15 h, then concentrated in vacuo. The crude product was purified by flash silica column chromatography (80% EtOAc/hexanes) to afford 16 mg of **3.106** (90% yield) as a white solid. mp 119.9-123.9 °C.

Data for **3.106**

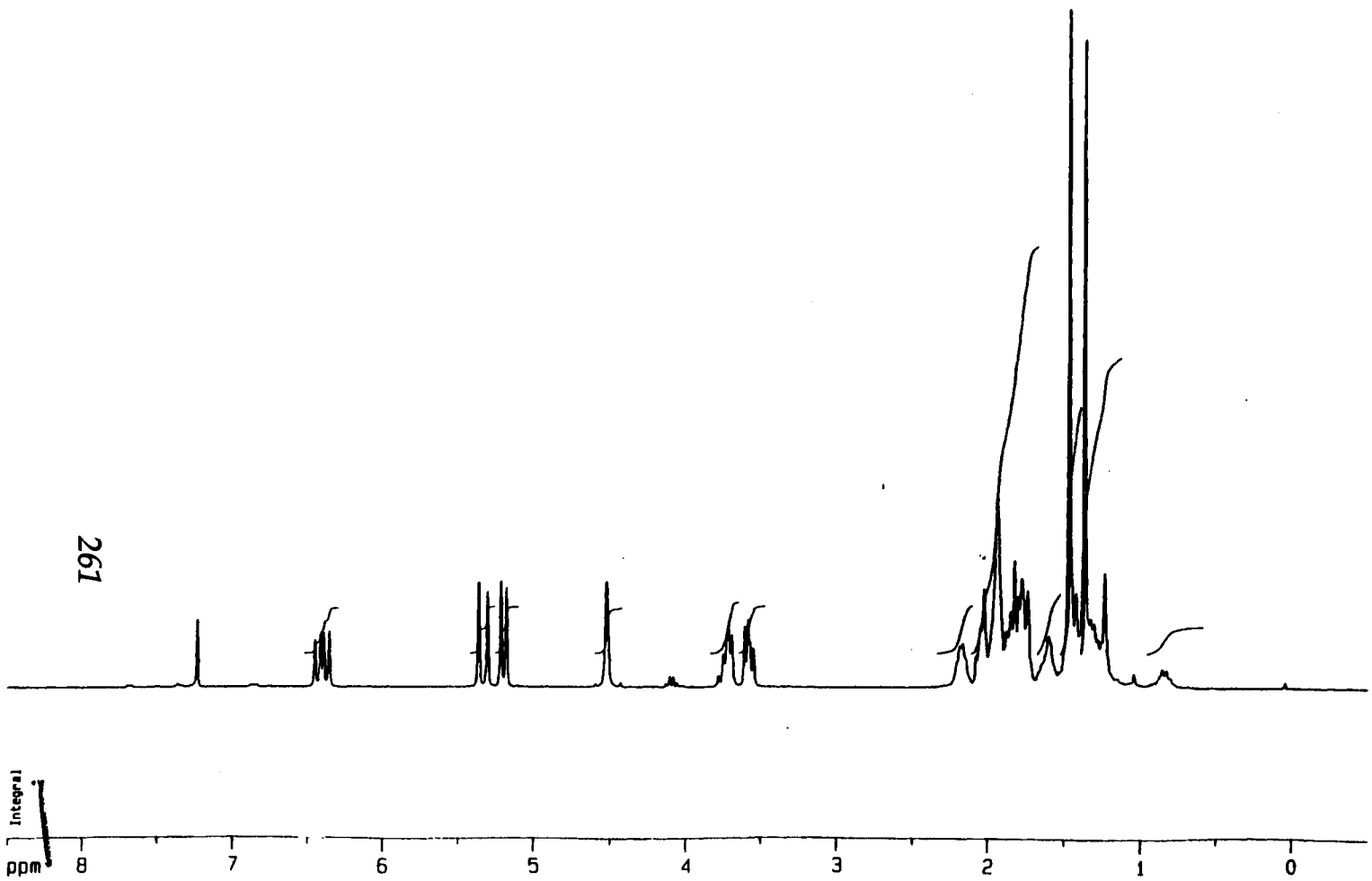
^{1}H NMR (300 MHz, $CDCl_3$): δ 6.40 (dd, J= 11.0, 17.3 Hz, 1H), 5.33 (d, J= 17.2 Hz, 1H), 5.20 (d, J= 10.9 Hz, 1H), 4.52 (s, 1H), 3.78-3.54 (m, 2H), 2.18-2.16 (m, 1H), 2.07-1.67 (m, 8H), 1.60-1.53 (m, 1H), 1.46 (s, 3H), 1.36 (s, 3H), 1.32-1.14 (m, 4H).

^{13}C NMR ($CDCl_3$, 75 MHz) δ 143.5, 113.2, 107.2, 75.4, 73.7, 64.9, 38.7, 37.3, 29.7, 28.1, 27.2, 23.6 (x2), 20.0, 18.9.

IR (neat) 3427, 2930, 2869, 1250, 1207, 1044, 1011 cm^{-1}.

EI HRMS calcd for C15H23O4 (M^+ -Me) 267.15964, obsd 267.1389.

3.106



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TE 300.0 K
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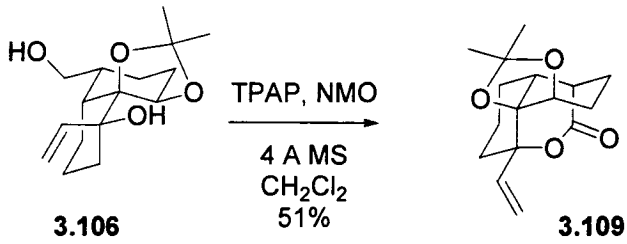


3.106 **3.109**

Lactone (27).

Molecular sieves 4 Å (0.05 g) were flame-dried under vacuum. Diol **3.106** (0.01 g, 0.035 mmol) was dissolved in dichloromethane (0.5 mL) and cannulated into the flask containing the sieves. NMO (0.017 g, 0.142 mmol) was added, followed by TPAP (1 grain). The reaction was stirred for 20 min and the crude product was purified by flash silica column chromatography (20% EtOAc/hexanes) to afford 5 mg of **3.109** (51% yield) as a colourless oil.

Data for **3.109**

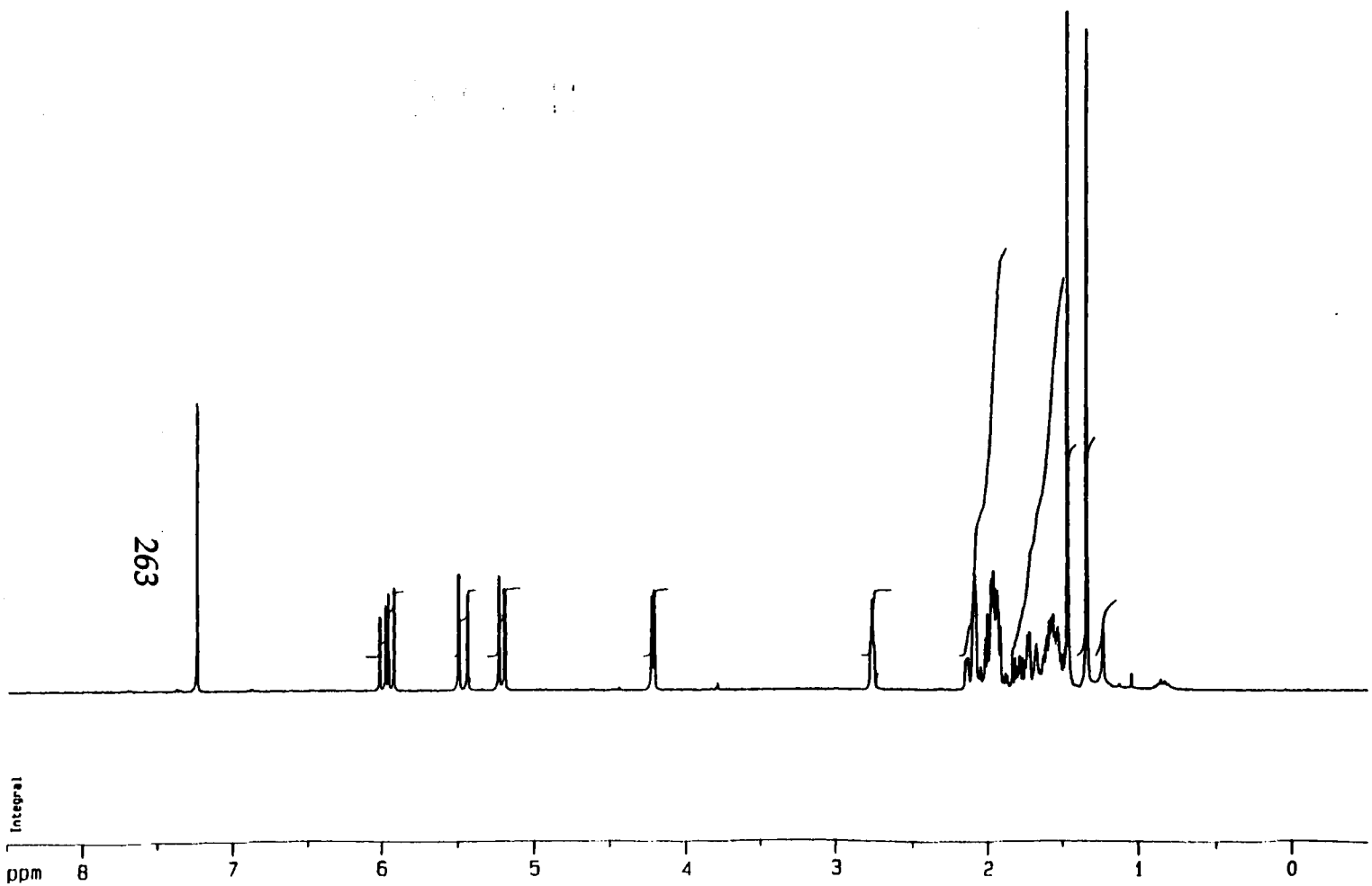
^{1}H NMR (300 MHz, $CDCl_3$): δ 5.97 (dd, J= 11.2, 17.5 Hz, 1H), 5.47 (dd, J= 1.4, 7.5 Hz, 1H), 5.21 (dd, J= 1.4, 11.2 Hz, 1H), 4.21 (d, J= 5.1 Hz, 1H), 2.76 (s, 1H), 2.14-2.09 (m, 2H), 2.06-1.87 (m, 4H), 1.83-1.77 (m, 1H), 1.75-1.60 (m, 1H), 1.59-1.50 (m, 3H), 1.46 (s, 3H), 1.34 (s, 3H) .

^{13}C NMR (75 MHz, $CDCl_3$) δ 174.1, 135.8, 114.9, 107.9, 83.3, 77.2, 74.7, 44.6, 37.4, 34.0, 28.6, 28.3, 26.3, 24.7, 23.4, 16.7.

IR (neat) 2935, 1741, 1092 cm^{-1}.

EI HRMS calcd for $C_{16}H_{22}O_4$ (M+) 278.15181, obsd 278.15268.

3.109



Current Data Parameters

NAME	1mo_344
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20021107
Time	10.30
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	512
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

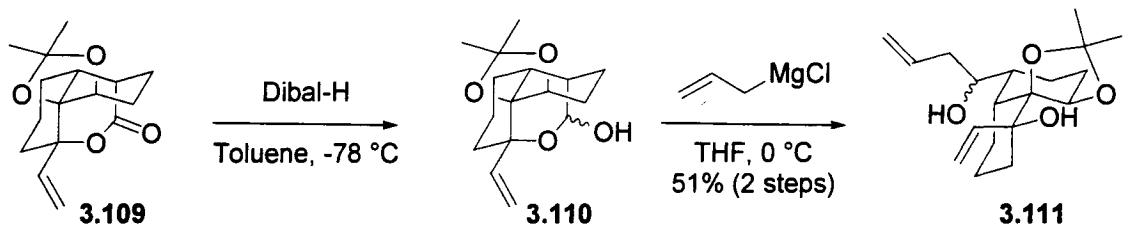
NUC1	1H
P1	9.75 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

F2 - Processing parameters

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

1D NMR plot parameters

CX	20.00 cm
CY	10.00 cm
F1P	8.500 ppm
F1	2551.10 Hz
F2P	-0.500 ppm
F2	-150.06 Hz
PPMCM	0.45000 ppm/cm
HZCM	135.05850 Hz/cm



3.109 **3.110** **3.111**

6-(1-Hydroxy-but-3-enyl)-2,2-dimethyl-10-vinyl-octahydro-naphtho[1,8a-d][1,3]dioxol-10-ol (3.111)

Lactone **3.109** (0.19g, 0.68 mmol) was dissolved in toluene (7 mL) at –78 °C. Dibal-H (0.45 mL, 0.68 mmol) was added dropwise and the reaction was stirred for 30 min. The reaction was quenched by adding sodium tartrate 1M. The aqueous layer was extracted 3 times with diethylether (3 X 30 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (20% EtOAc/hexanes) to afford 192 mg of lactol **3.110**. A solution of lactol **3.110** (192 mg, 0.69 mmol) in THF (7 mL) was cooled to 0°C. A solution of allylmagnesium chloride 2M was added (1.7 ml, 3.4 mmol) and stirred for 4 hours. The reaction was quenched by adding saturated NH_4Cl_{aq}. The aqueous layer was extracted 3 times with diethylether (3 X 30 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (30% EtOAc/hexanes) to afford 113 mg of **3.111** (51% yield) as a colourless oil.

Data for **3.111**

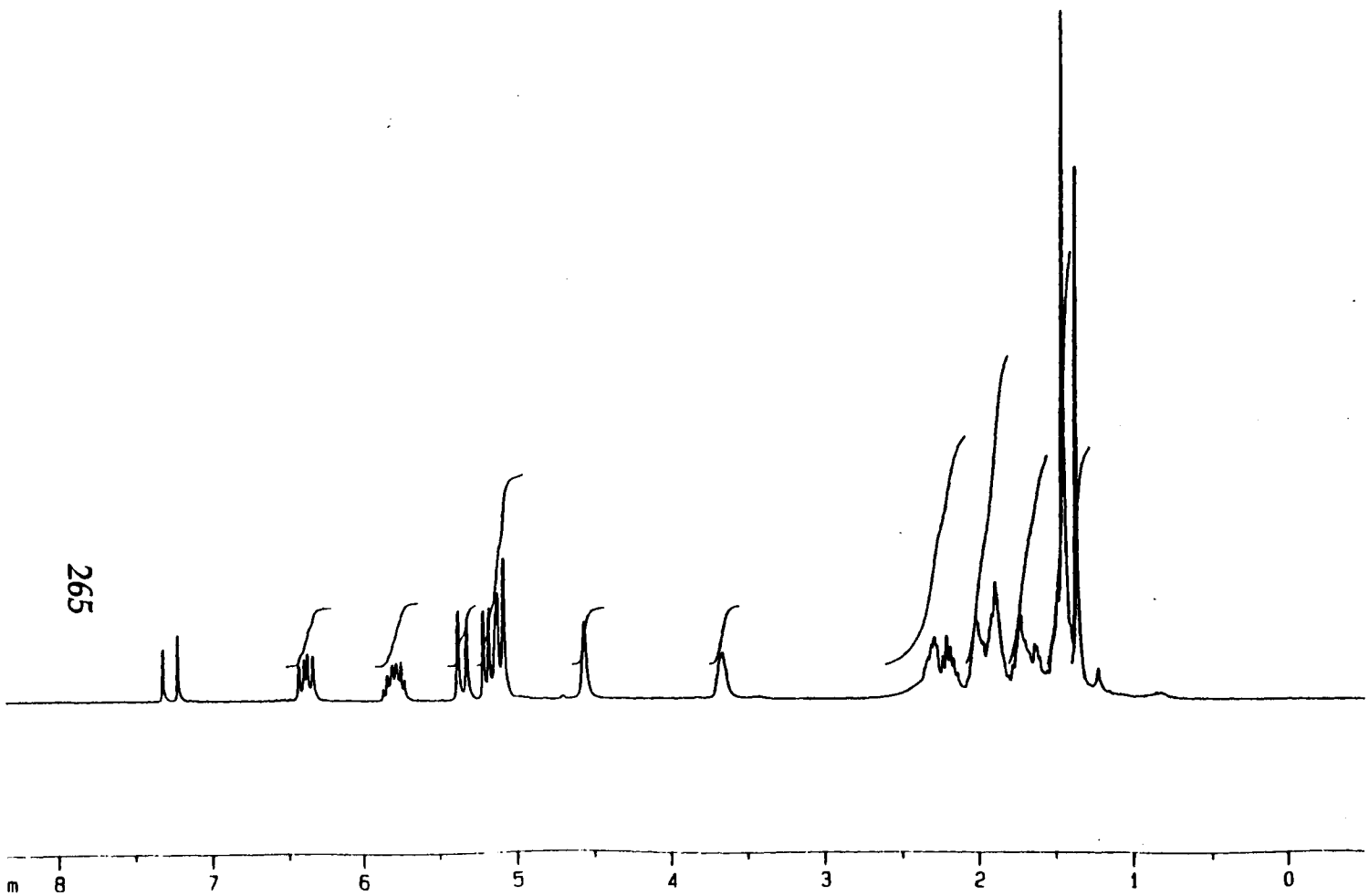
^{1}H NMR (300 MHz, $CDCl_3$): δ 6.39 (dd, J= 17.2, 10.8 Hz, 1H), 5.88-5.73 (m, 1H), 5.36 (d, J= 17.4 Hz, 1H), 5.21 (d, J= 10.8 Hz, 1H), 5.15-5.09 (m, 2H), 4.57 (s, 1H), 3.67 (s, 1H), 2.33-2.14 (m, 4H), 2.02-1.80 (m, 5H), 1.77-1.55 (m, 3H), 1.52-1.48 (m, 4H), 1.45 (s, 3H), 1.37 (s, 3H).

^{13}C NMR ($CDCl_3$, 75 MHz) δ 143.2, 134.7, 118.5, 113.5, 107.2. 75.5, 73.4, 73.1, 40.1, 39.9, 37.1, 28.0, 27.2, 24.0, 23.7, 20.3, 17.6.

IR (neat) 3274, 2932, 1378, 1367, 1251, 1211 cm^{-1}.

EI HRMS calcd for $C_{19}H_{30}O_4$ (M+) 322.21441, obsd 322.21252.

3.111



Current Data Parameters

NAME	lmo_535-2
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

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Time	11.14
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	161.3
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

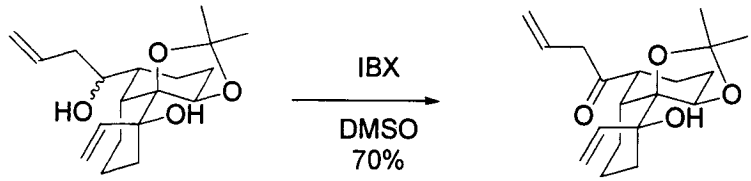
NUC1	1H
P1	10.50 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

F2 - Processing parameters

SI	65536
SF	300.1300002 MHz
WDW	EM
SSB	0
LB	0.10 Hz
GB	0
PC	1.00

1D NMR plot parameters

CX	20.00 cm
CY	10.00 cm
F1P	8.500 ppm
F1	2551.10 Hz
F2P	-0.500 ppm
F2	-150.06 Hz
PPMCM	0.45000 ppm/cm
HZCM	135.05850 Hz/cm



3.111 **3.112**

1-(10-Hydroxy-2,2-dimethyl-10-vinyl-octahydro-naphtho[1,8a-d][1,3]dioxol-6-yl)-but-3-en-1-one (3.112)

Alcohol **3.111** (31 mg, 0.1 mmol) was dissolved in DMSO (1 mL) and IBX (84 mg, 0.3 mmol) was added and stirred overnight. $NaHCO_{3sat.}$ (5 mL) was added and the aqueous layer was extracted 3 times diethylether (3 X 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (10% EtOAc/hexanes) to afford 22 mg of **3.112** (70% yield) as a colorless oil.

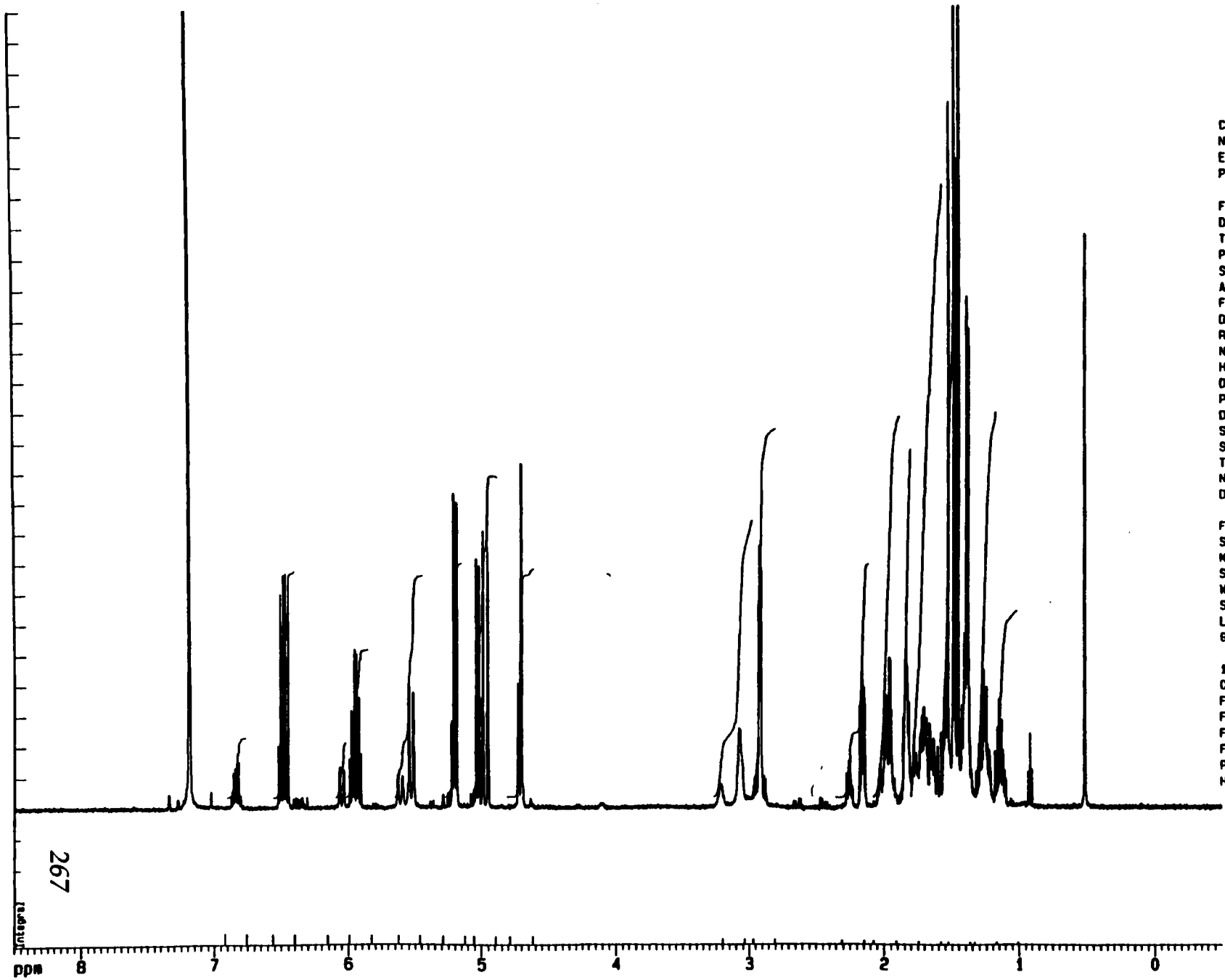
Data for **3.112**

^{1}H NMR (500 MHz, C_6D_6): δ 6.51-6.44 (m, 1H), 5.97-5.90 (m, 1H), 5.52 (d, J= 17.2 Hz, 1H), 5.18 (dd, J= 10.9, 1.8 Hz, 1H), 5.01 (dq, 10.2, 1.4 Hz, 1H), 4.96 (dq, 17.1, 1.6 Hz, 1H), 4.69 (t, J= 2.9 Hz, 1H), 3.06-3.05 (m, 1H), 2.92-2.89 (m, 2H), 2.17-2.13 (m, 1H), 1.99-1.93 (m, 2H), 1.84-1.80 (m, 2H), 1.72-1.56 (m, 3H), 1.53-1.48 (m, 1H), 1.47 (s, 3H), 1.44 (s, 3H), 1.30-1.21 (m, 2H), 1.17-1.10 (m, 1H).

^{13}C NMR (C_6D_6, 125 MHz) 210.5, 143.5, 131.5, 118.1, 113.4, 107.5, 85.0, 74.9, 74.2, 73.8, 46.7, 40.3, 37.5, 28.4, 27.1, 24.8, 23.5, 20.1.

IR (neat) 3491, 2935, 1705, 1043 cm^{-1}.

EI HRMS calcd for $C_{19}H_{28}O_4$ (M+) 320.19876, obsd 320.19706.



3.112

Current Data Parameters
NAME lmo_545
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date 20030506
Time 3.23
PULPROG zg
SOLVENT CDCl3
AQ 4.6530805 sec
FIORES 0.107456 Hz
DW 71.0 usec
RG 1024
NUCLEUS 1H
HL1 0 dB
D1 0.0100000 sec
P1 5.6 usec
DE 88.8 usec
SFO1 500.1381707 MHz
SWH 7042.25 Hz
TD 65536
NS 16
DS 0

F1 - Processing parameters
SI 32768
WC2 QF
SF 500.1354311 MHz
WDW EM
SSB 0
LB 0.00 Hz
GB 0

1D NMR plot parameters
CX 22.00 cm
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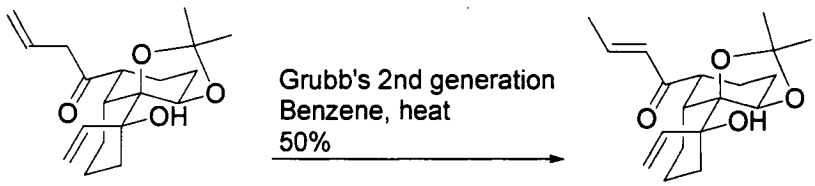
F1 4251.15 Hz
F2P -0.500 ppm
F2 -250.07 Hz
PPMCM 0.40909 ppm/
HZCM 204.60086 Hz/



3.112 **3.113**

1-(10-Hydroxy-2,2-dimethyl-10-vinyl-octahydro-naphtho[1,8a-d][1,3]dioxol-6-yl)-but-2-en-1-one (3.113)

Product **3.112** (2 mg, 0.006 mmol) was dissolved in distilled benzene (2 mL). The solution was degassed by bubbling argon for 5 minutes. Grubbs second generation catalyst (1 mg, 0.001 mmol) was added and heated to reflux for 4 hours. The reaction went to dryness. Benzene (1 mL) was added and purified by flash column chromatography (10% EtOAc/hexanes) to afford 1 mg of **3.113** (50% yield) as a colourless oil.

Data for **3.113**

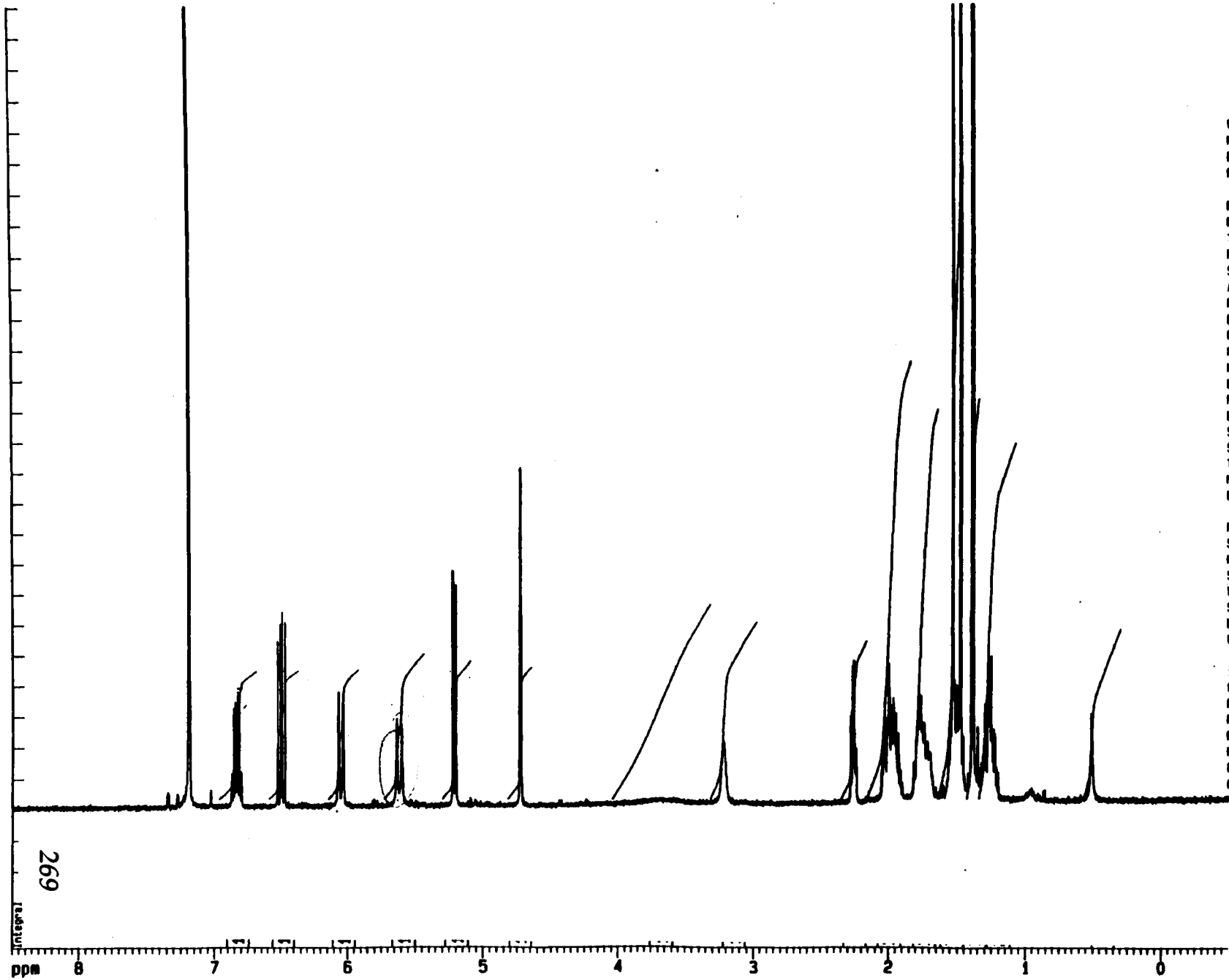
^{1}H NMR (500 MHz, C_6D_6): δ 6.83 (dt, J= 22.4, 7.0 Hz, 1H), 6.50 (ddd, J= 17.2, 10.8, 0.5 Hz, 1H), 6.05 (dd, J= 15.6, 1.6 Hz, 1H), 5.61 (d, J= 17.0 Hz, 1H), 5.20 (dd, J= 10.8, 2.0 Hz, 1H), 4.72 (t, J= 2.7 Hz, 1H), 3.21 (s, 1H), 2.25 (td, 8.1, 4.6 Hz, 1H), 2.04-1.89 (m, 3H), 1.81-1.59 (m, 3H), 1.52 (s, 3H), 1.51-1.48 (m, 2H), 1.47 (s, 3H), 1.37 (d, J= 6.9 Hz, 3H), 1.36-1.19 (m, 3H).

^{13}C NMR (C_6D_6, 125 MHz) 201.8, 143.4, 142.3, 130.9, 113.1, 107.3, 84.5, 74.5, 73.9, 46.0, 40.3, 37.3, 28.3, 27.0, 24.9, 23.5, 19.7, 17.5.

IR (neat) 3495, 3334, 2933, 1689, 1628, 1209, 1044 cm^{-1}.

EI HRMS calcd for $C_{19}H_{28}O_4$ (M+) 320.19876, obsd 320.19738.

3.113



Current Data Parameters
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EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date 20030504
Time 4.29
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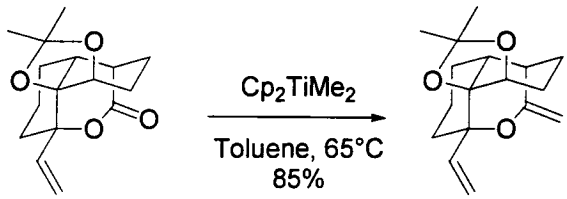
SOLVENT CDCl3
AQ 4.6530805 sec
FIDRES 0.107456 Hz
DW 71.0 usec
RG 1024
NUCLEUS 1H
ML1 - 0 dB
D1 0.0100000 sec
P1 5.6 usec
DE 88.8 usec
SFO1 500.1381707 MHz
SWH 7042.25 Hz
TD 65536
NS 8
DS 0

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

1D NMR plot parameters
CX 22.00 cm
F1P 8.500 ppm
F1 4251.15 Hz
F2P -0.500 ppm
F2 -250.07 Hz
PPMCM 0.40909 ppm/
HZCM 204.60088 Hz/



3.109 **3.115**

Enol ether (3.115).

A solution of ester **3.109** (519 mg, 1.8 mmol) in a 0.11M solution of Petasis' reagent (Cp_2TiMe_2) in toluene (50 mL,5.4 mmol) was heated at 80 °C for 15 h. The solution was concentrated and purified by flash chromatography twice (5% EtOAc/ 94% hexanes/ 1% Et_3N) to afford 420 mg of **3.115** (85% yield) as a yellow oil .

Data for **3.115**

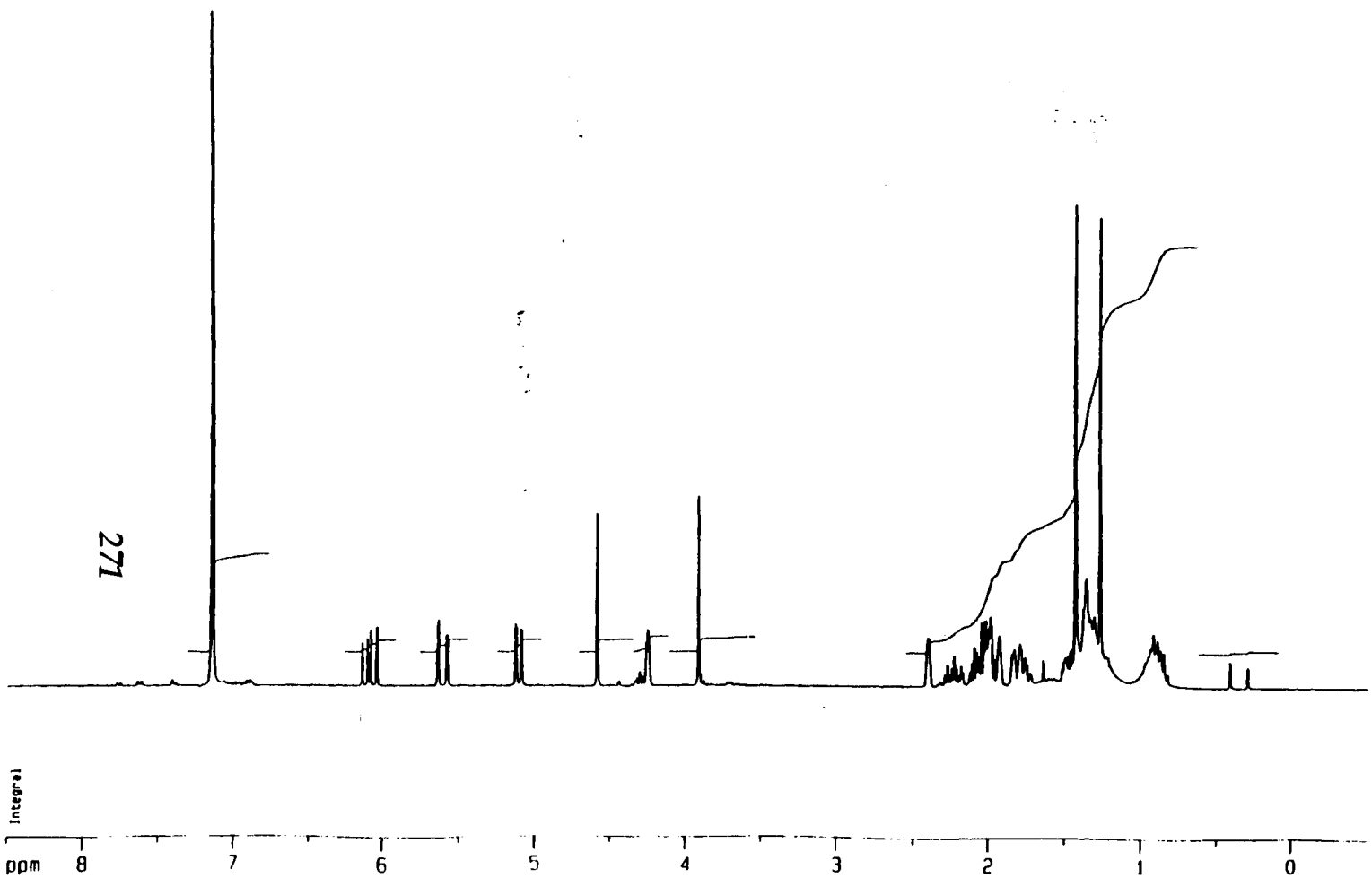
^{1}H NMR (500 MHz, C_6D_6): δ 6.12 (dd, J= 17.4, 11.1 Hz, 1H), 5.63 (dd, J= 17.4, 2.1 Hz, 1H), 5.14 (s, 1H), 4.61 (s, 1H), 4.29-4.28 (m, 1H), 3.95 (s, 1H), 2.45-2.44 (m, 1H), 2.28 (qt, 13.8, 4.7 Hz, 1H), 2.14-1.99 (m, 4H), 1.97 (s, 1H), 1.87-1.79 (m, 2H), 1.55-1.49 (m, 1H), 1.46 (d, J= 0.6 Hz, 3H), 1.45-1.32 (m, 2H), 1.30 (d, J= 0.4 Hz, 3H).

^{13}C NMR (125 MHz, C_6D_6) δ 163.4, 139.0, 113.5, 107.2, 87.2, 78.4, 78.0, 75.4, 42.7, 37.5, 35.4, 32.6, 28.8, 26.3, 25.5, 23.6, 17.7.

IR (neat) 2930, 1245, 1090 cm^{-1}

EI HRMS calcd for $C_{17}H_{24}O_3$ (M^+) 276.17255, obsd 276.17433.

3.115



Current Data Parameters
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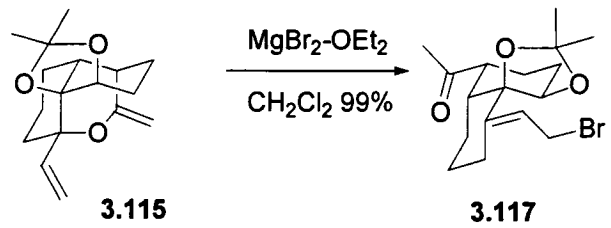
EXPNO 3
PROCNO 1

F2 - Acquisition Parameters
Date_ 20030224
Time 18.00
INSTRUM av300
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 322.5
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

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

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

1D NMR plot parameters
CX 20.00 cm
CY 10.00 cm
F1P 8.500 ppm
F1 2551.10 Hz
F2P -0.500 ppm
F2 -150.06 Hz
PPMCM 0.45000 ppm/cm
HZCM 135.05850 Hz/cm



3.115 **3.117**

1-[10-(3-Bromo-propylidene)-2,2-dimethyl-octahydro-naphtho[1,8a-d][1,3]dioxol-6-yl]-ethanone (3.117).

To a solution of **3.115** (9 mg, 0.03 mmol) in toluene (1 ml) was added $MgBr_2 \bullet OEt_2$ and stirred at room temperature for 15 h. The reaction was quenched by adding water. The aqueous layer was extracted 3 times with diethylether (3 X 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash silica column chromatography (10% EtOAc/hexanes) to afford 11 mg of **3.117** (99% yield) as a colorless oil.

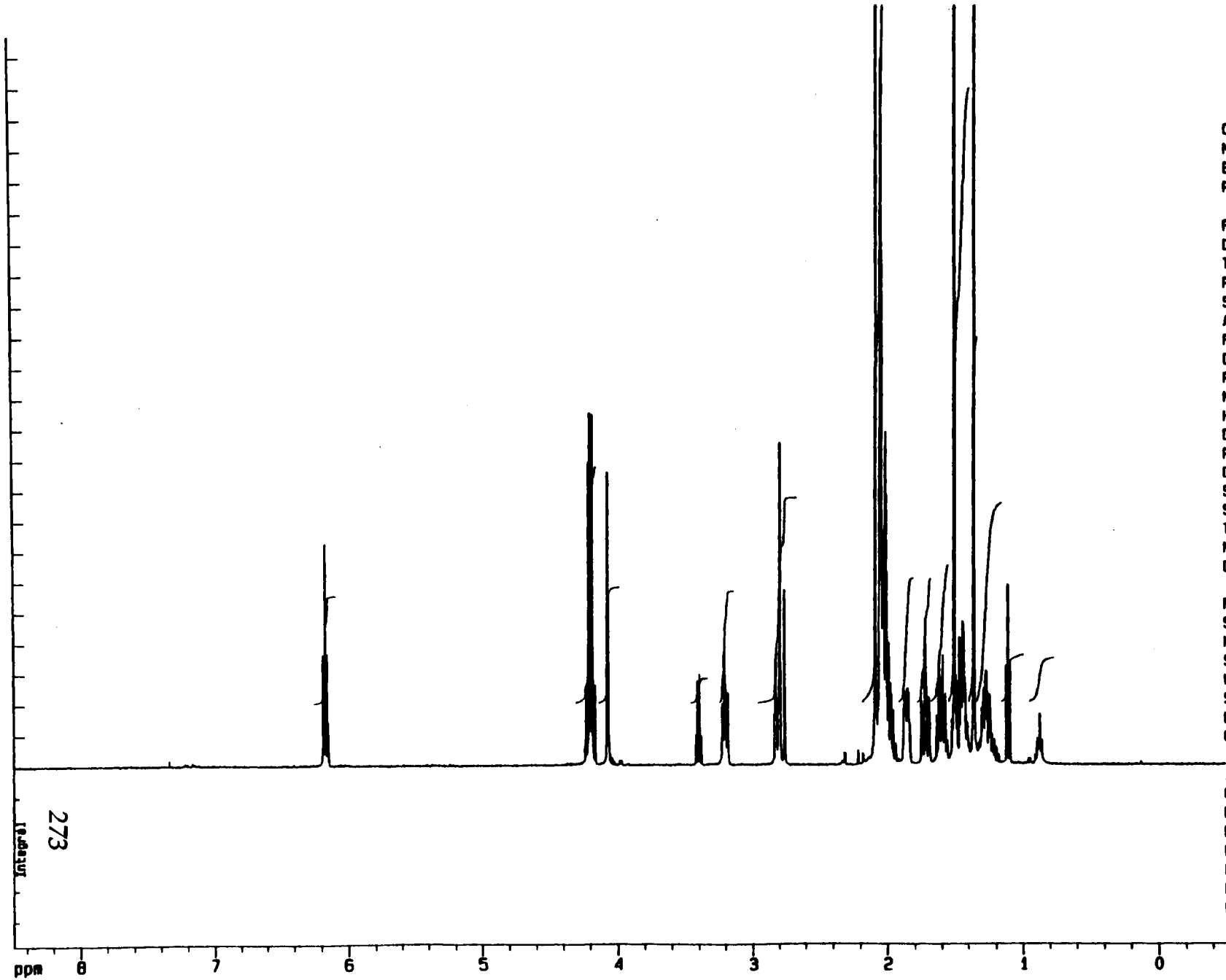
Data for **3.117**

^{1}H NMR (500 MHz, C_6D_6): δ 6.21 (t, J= 8.7 Hz, 1H), 3.77 (t, J= 2.7 Hz, 1H), 3.75-3.67 (m, 2H), 3.18-3.14 (m, 1H), 2.31-2.27 (m, 1H), 2.18 (dt, J= 14.3, 9.9 Hz, 1H), 2.01-1.97 (m, 1H), 1.93-1.88 (m, 1H), 1.74 (s, 3H), 1.73-1.66 (m, 1H), 1.47 (s, 3H), 1.46-1.41 (m, 2H), 1.29 (s, 3H), 1.28-1.23 (m, 1H), 1.16-1.06 (m, 3H).

^{13}C NMR (125 MHz, C_6D_6) δ 208.8, 148.9, 117.4, 107.4, 84.2, 77.0, 45.0, 43.6, 27.4, 27.4, 26.9, 26.3, 26.6, 25.6, 22.3, 13.7, 24.6.

IR (neat) 2988, 2934, 1707, 1207, 1056 cm^{-1}.

EI HRMS calcd for $C_{17}H_{24}O_3$ (M^+ -HBr) 276.17255, obsd 276.17233.



Current Data Parameters	
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PROCNO	1
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PULPROG	zg
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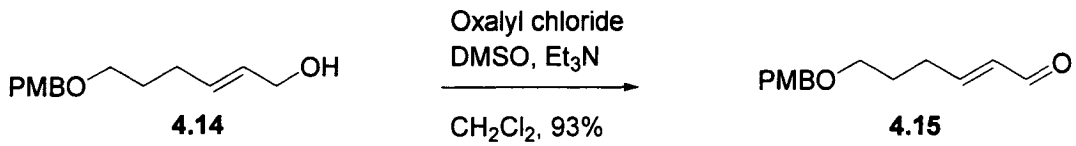
AQ	4.6530762
FIDRES	0.107456
DW	71.0
RG	1024
NUCLEUS	1H
HL1	0
D1	0.0100000
P1	5.6
DE	88.8
SFO1	500.1405972
SWH	7042.25
TD	65536
NS	16
DS	0
F1 - Processing paramet	
SI	32768
MC2	QF
SF	500.1380244
WDW	EM
SSB	0
LB	0.30
GB	0
1D NMR plot parameters	
CX	22.00
F1P	8.500
F1	4251.17
F2P	-0.500
F2	-250.07
PPMCM	0.40909
HZCM	204.60193



6-(4-Methoxy-benzyloxy)-hex-2-enal (4.15)

A solution of oxalyl chloride (0.63 mL, 7.2 mmol) in dichloromethane (50 mL) was cooled to -78°C. Methylsulfoxide (1.02 mL, 14.4 mmol) was added dropwise, forming a lot of gas. The solution was stirred 20 minutes. Alcohol **4.14** (1.33 g, 5.99 mmol) was dissolved in dichloromethane (10 mL), canulated in the swern reagent solution and stirred for 90 minutes at -78°C. Triethylamine (4.2 mL, 30 mmol) was added and was warmed to room temperature while stirred for 20 minutes. Saturated NH_4Cl_{sat} was added. The aqueous layer was extracted 3 times with dichloromethane (3 X 100 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (20% EtOAc/hexanes) to afford 968 mg of **4.15** (93% yield) as light yellow oil.

Data for **4.15**

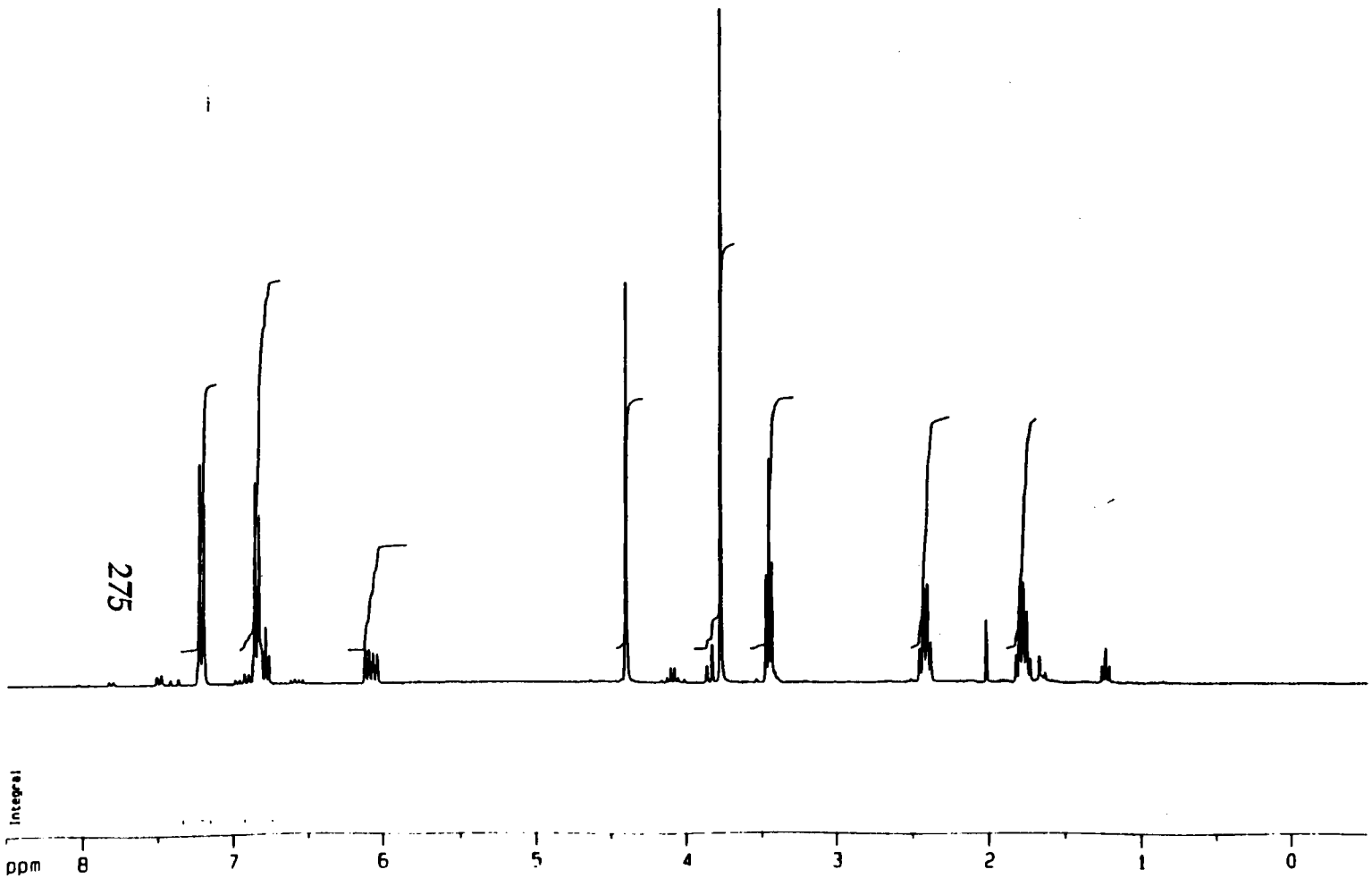
^{1}H NMR (300 MHz, $CDCl_3$): δ 9.46 (d, J= 8 Hz, 1H), 7.23 (d, J= 8 Hz, 2H), 6.86 (d, J= 9 Hz, 2H), 6.80 (t, J= 7 Hz, 1H), 6.08 (ddd, J= 16, 8, 1 Hz, 1H), 4.41 (s, 2H), 3.78 (s, 3H), 3.46 (t, J= 6 Hz, 2H), 2.42 (q, J= 8 Hz, 2H), 1.78 (quint, J= 6 Hz, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) 194.1, 159.2, 158.3, 133.1, 130.3, 129.3 (x2), 113.8 (x2), 72.7, 68.7, 55.2, 29.6, 27.9.

IR (neat) 2937, 2857, 2838, 2736, 1688, 1612, 1513, 1248, 1100 cm^{-1}.

EI HRMS calcd for $C_{14}H_{18}O_3$ (M^+) 234.12560, obsd 234.12515.

4.15



Current Data Parameters
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EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
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Time 16.23
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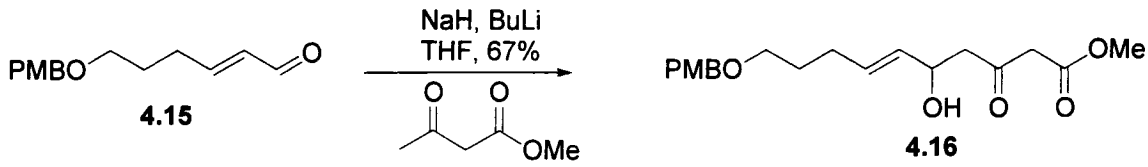
PROBHD 5 mm QNP 1H/1
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 181
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

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

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

1D NMR plot parameters
CX 20.00 cm
CY 10.00 cm
F1P 8.500 ppm
F1 2551.10 Hz
F2P -0.500 ppm
F2 -150.06 Hz
PPMCM 0.45000 ppm/cm
HZCM 135.05850 Hz/cm



5-Hydroxy-10-(4-methoxy-benzyloxy)-3-oxo-dec-6-enoic acid methyl ester (4.16).

Methyl acetoacetate (1.01 mL, 9.36 mmol) was dissolved in THF (40 mL) and cooled to 0 °C. Sodium hydride 60 % in mineral oil (0.56 g, 14.04 mmol) was added and stirred for 20 min. n-butyllithium (2.31 M in hexane, 4.5 mL, 10.3 mmol) was added and stirred for 20 min and then cooled to –78 °C. Alcohol **4.15** (1.03g, 4.68 mmol) was dissolved in THF (7 mL) and cannulated into the anion solution and the resultant mixture was stirred at –78 °C for 20 min. Saturated $NH_4Cl_{(aq)}$ was added. The aqueous layer was extracted 3 times with diethylether (3 X 100 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash silica column chromatography (30% EtOAc/hexanes) to afford 1.09 g of **4.16** (67% yield) as a light yellow oil.

Data for **4.16**

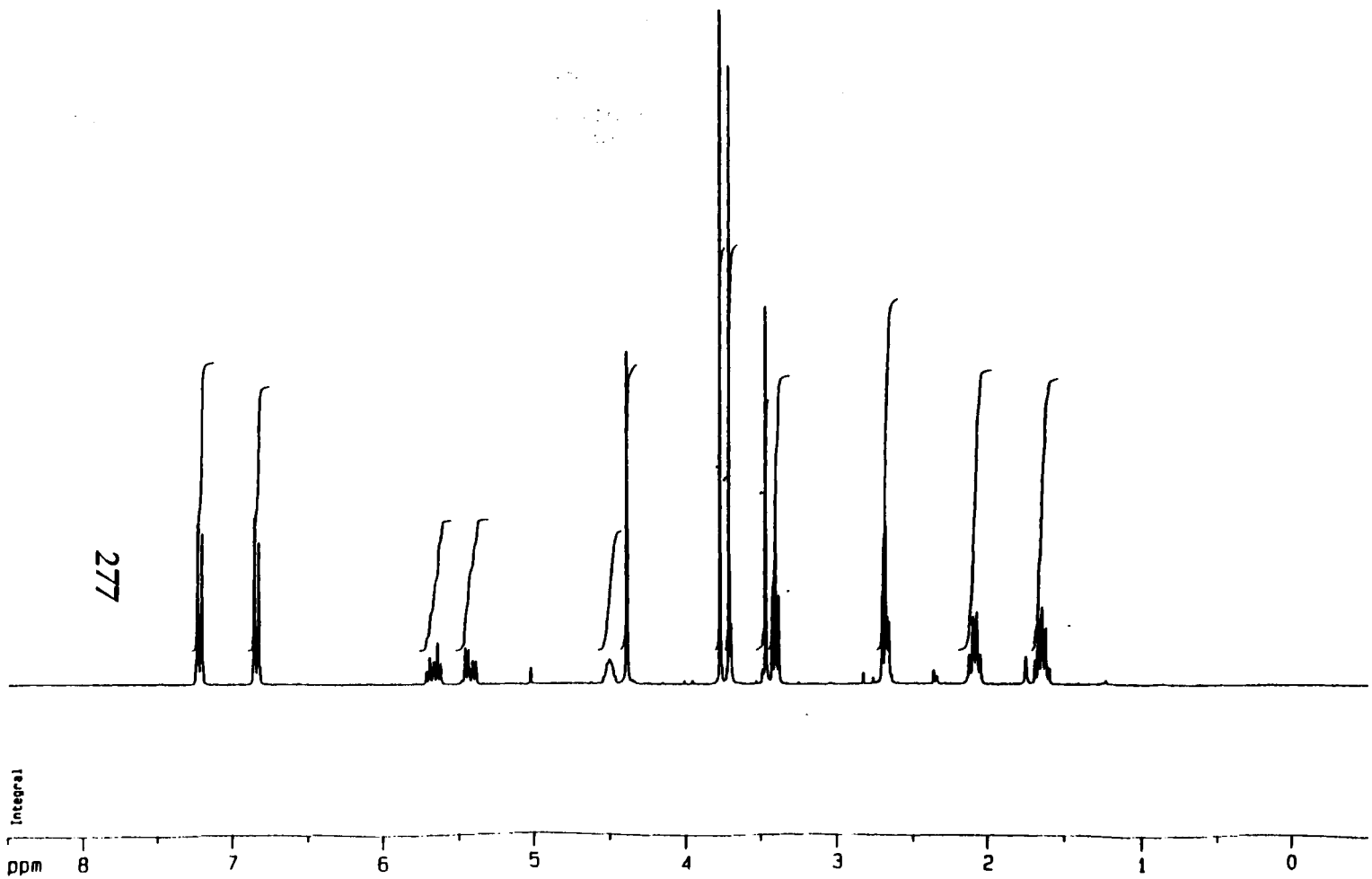
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.22 (d, J= 8 Hz, 2H), 6.85 (d, J= 8 Hz, 2H), 5.67 (dt, J= 15, 7 Hz, 1H), 5.43 (dd, J= 15, 6 Hz, 1H), 4.54-4.47 (m, 1H), 4.39 (s, 2H), 3.77 (s, 3H), 3.71 (s, 3H), 3.47 (s, 2H), 3.40 (t, J= 2 Hz, 2H), 2.70-2.66 (m, 3H), 2.08 (q, J= 7 Hz, 2H), 1.64 (quint, J= 2 Hz 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 202.7, 167.3, 159.0, 131.9 (x2), 130.8 (x2), 130.5, 129.2, 113.7, 72.5, 69.1, 68.3, 55.2, 52.4, 51.2, 49.6, 29.0, 28.7.

IR (neat) 3408, 2940, 2853, 1745, 1710, 1513, 1247 cm^{-1}.

EI HRMS calcd for $C_{19}H_{24}O_5$ (M^+ -H_2O) 332.16238, obsd 332.1583.

4.16



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PROCNO 1

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PULPROG zg30
TD 30720
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NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 128
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

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

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

1D NMR plot parameters
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CY 10.00 cm
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F2 -150.06 Hz
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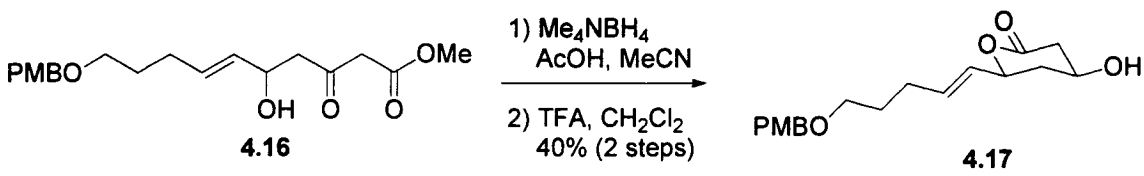
HZCM 135.05850 Hz/cm



5-Hydroxy-10-(4-methoxy-benzyloxy)-3-oxo-dec-6-enoic acid methyl ester (4.17).
Acetonitrile (13 mL) and acetic acid (13 mL) were mixed at 0 °C. Tetramethylammonium borohydride (1.1 g, 12.5 mmol) was added and stirred for 20 min. The mixture was frozen in a bath at –78 °C and a solution of ketone **4.16** (1.09 g, 3.1 mmol) in acetonitrile (5 mL) was cannulated into the flask. The reaction was kept in the freezer for 15 h at –25 °C. The reaction was quenched by adding sodium potassium tartrate 0.5 M (40 mL) and warmed to room temperature. The organic layer was washed with $NaHCO_{3sat}$ The aqueous layer was extracted 3 times with dichloromethane (3 X 60 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was dissolved in dichloromethane (26 mL) and treated directly with trifluoroacitic acid (0.047 mL, 0.63 mmol). The reaction was stirred for 15 h at room temperature. The reaction was stopped by adding Na_2CO_3 until a neutral pH was obtained. The reaction was filtered and concentrated. The crude product was purified by flash silica column chromatography (70% EtOAc) to afford 442 mg (40%) of starting material and 407 mg of **4.17** (40% yield) as a light yellow oil.

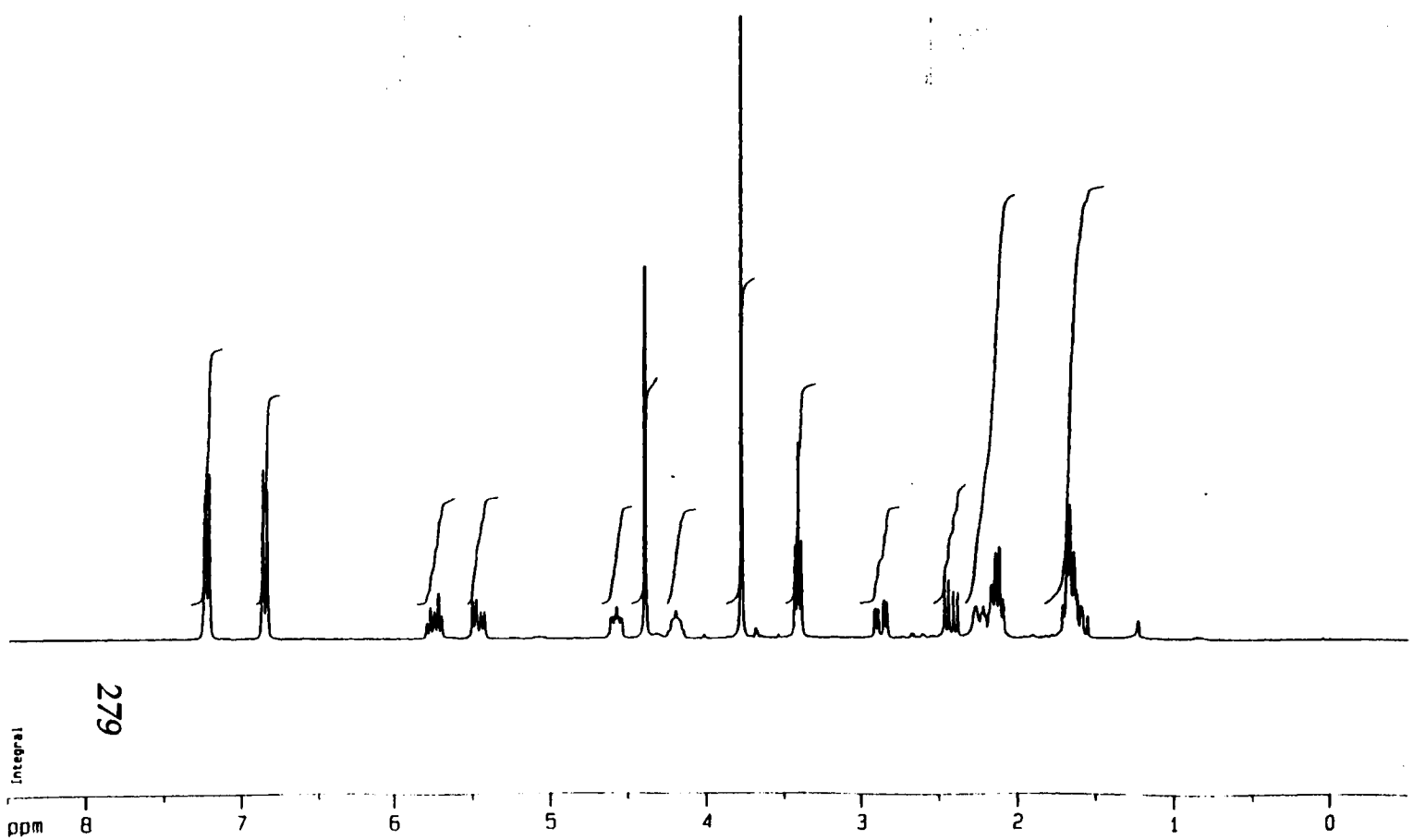
Data for **4.17**

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.25-7.22 (m, 2H), 6.85 (d, J= 9 Hz, 2H), 5.75 (dt, J= 15, 7 Hz, 1H), 5.46 (dd, J= 15, 7 Hz, 1H), 4.61-4.54 (m, 1H), 4.40 (s, 2H), 4.25-4.20 (m, 1H), 3.78 (s, 3H), 3.41 (t, J= 6 Hz, 2H), 2.87 (ddd, J= 17, 6, 1 Hz, 1H), 2.42 (dd, J= 17, 8 Hz, 1H), 2.27-2.09 (m, 4H), 1.71-1.55 (m, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 170.2, 159.1, 134.5, 130.5, 129.3 (x2), 127.6, 113.8 (x2), 77.6, 72.5, 69.0, 63.8, 55.3, 39.4, 38.3, 28.7 (x2).

IR (neat) 3427, 2933, 2860, 1732, 1512, 1245 cm^{-1}

EI HRMS calcd for $C_{14}H_{24}O_5$ (M^+) 320.16238, obsd 320.16072.



Current Data Parameters
NAME lmo026
EXPNO 1
PROCNO 1

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TD	30720	
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NS	16	
DS	0	
SWH	5081.301	Hz
FIDRES	0.165407	Hz
AQ	3.0228980	sec
RG	256	
DW	98.400	usec
DE	6.00	usec
TE	300.0	K
D1	1.00000000	sec

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

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PL1	-3.00	dB
SFO1	300.1319477	MHz

F2 - Processing parameters

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WDW	EM	
SSB	0	
LB	0.10	Hz
GB	0	
PC	1.00	

1D NMR plot parameters

CX	20.00	cm
CY	10.00	cm
F1P	8.500	ppm
F1	2551.11	Hz
F2P	-0.500	ppm
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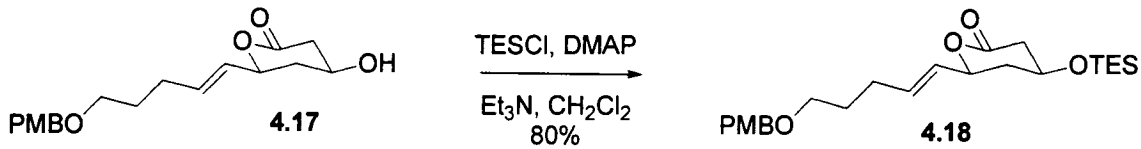
PPMCM	0.45000	ppm/cm
HZCM	135.05852	Hz/cm

4.17



6-[5-(4-Methoxy-benzyloxy)-pent-1-enyl]-4-triethylsilanyloxy-tetrahydropyran-2-one (4.18).

Alcohol **4.17** (0.407 g, 1.27 mmol) was dissolved in THF (13 mL). Triethylamine (1.1 mL, 7.63 mmol) and dimethylaminopyridine (0.014 g, 0.11 mmol) were added, followed by triethylsilyl chloride (0.064 mL, 3.81 mmol). The reaction was stirred for 30 min. Saturated $NH_4Cl_{(aq)}$ was added. The aqueous layer was extracted 3 times with diethylether (3 X 50 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash silica column chromatography (15% EtOAc/hexanes) to afford 442 mg of **4.18** (80% yield) as a colourless oil.

Data for **4.18**

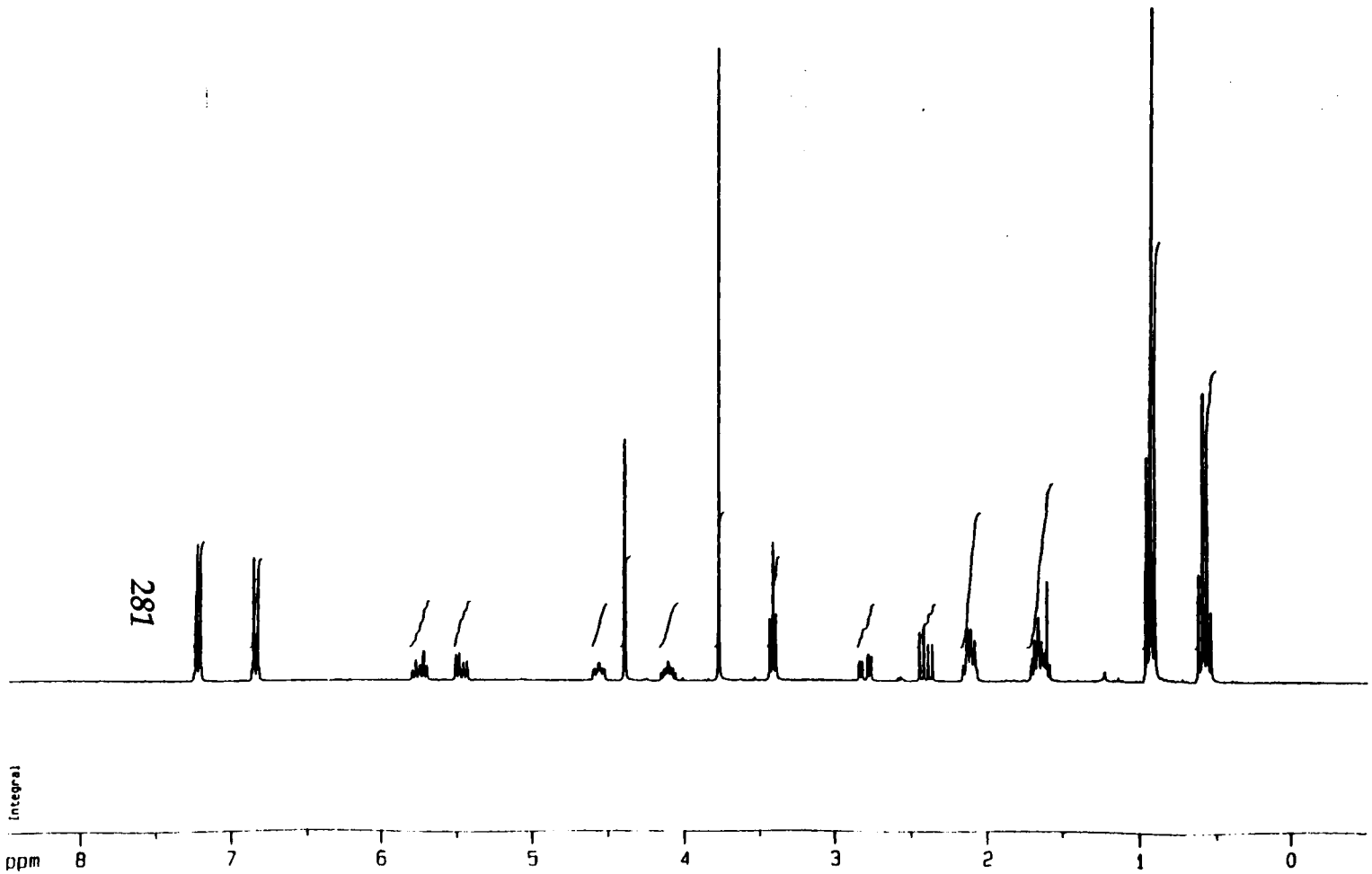
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.26-7.21 (m, 2H), 6.88-6.83 (m, 2H), 5.75 (dt, J= 15, 6 Hz, 1H), 5.52-5.44 (m, 1H), 4.60-4.53 (m, 1H), 4.40 (s, 2H), 4.16-4.07 (m, 1H), 3.78 (s, 3H), 3.42 (t, J= 6 Hz, 2H), 2.80 (ddd, J= 17, 6, 2 Hz, 1H), 2.40 (dd, J= 17, 8 Hz, 1H), 2.16-2.07 (m, 3H), 1.71-1.62 (m, 3H), 0.93 (t, J= 8 Hz, 9H), 0.50 (q, J= 8 Hz, 6H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 170.3, 159.1, 134.4, 130.5, 129.2 x2, 127.8, 113.7 (x2), 77.7, 72.5, 69.1, 64.3, 55.3, 40.3, 39.1, 28.8, 28.7, 6.7 (x3), 4.7 (x3).

IR (neat) 2954, 2876, 1741, 1513, 1247, 1096 cm^{-1}.

EI HRMS calcd for $C_{22}H_{33}O_5Si$ (M^+ -Et) 405.20973, obsd 405.20812.

4.18



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PROCNO	1

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TD	30720
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SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	181
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

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

F2 - Processing parameters

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

1D NMR plot parameters

CX	20.00 cm
CY	10.00 cm
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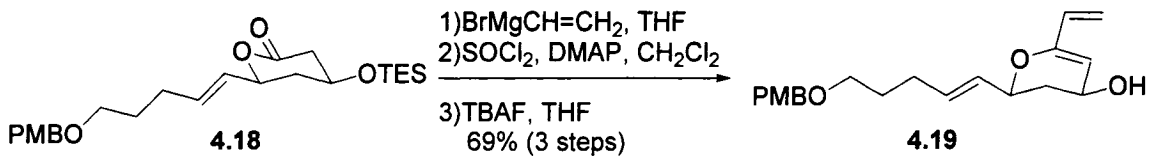
F1	2551.10 Hz
F2P	-0.500 ppm
F2	-150.06 Hz
PPMCM	0.45000 ppm/cm
HZCM	135.05850 Hz/cm



2-[5-(4-Methoxy-benzyloxy)-pent-1-enyl]-6-vinyl-3,4-dihydro-2H-pyran-4-ol (4.19).

The lactone **4.18** (0.745 g, 1.72 mmol) was dissolved in THF (17 mL) and cooled to –78 °C. Vinylmagnesium bromide, 0.9 M in THF, (5.72 mL, 5.15 mmol) was added and the reaction was stirred for 30 min. The reaction was quenched by adding saturated $NH_4Cl_{(aq)}$. The aqueous layer was extracted 3 times with diethylether (3 X 50 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was used directly to avoid decomposition. The lactol intermediate was dissolved in dichloromethane (17 mL) and cooled to 0 °C. 2,6-Dimethylaminopyridine (0.63 g, 5.16 mmol) was added, followed by thionyl chloride (0.125 mL, 1.72 mmol) and the reaction was stirred for 30 min. The reaction was quenched by adding $NaHCO_{3sat}$. The aqueous layer was extracted 3 times with dichloromethane (3 X 50 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was used directly to avoid decomposition. The diene was dissolved in THF (17 mL) and tetrabutylammonium fluoride 1 M, in THF, (1.9 mL, 1.89 mmol) was added. The reaction turned dark brown and the solvent was evaporated after 30 min. The crude product was purified by flash silica column chromatography (50% EtOAc/hexanes) to afford 392 mg of **4.19** (69% yield) as a colourless oil.

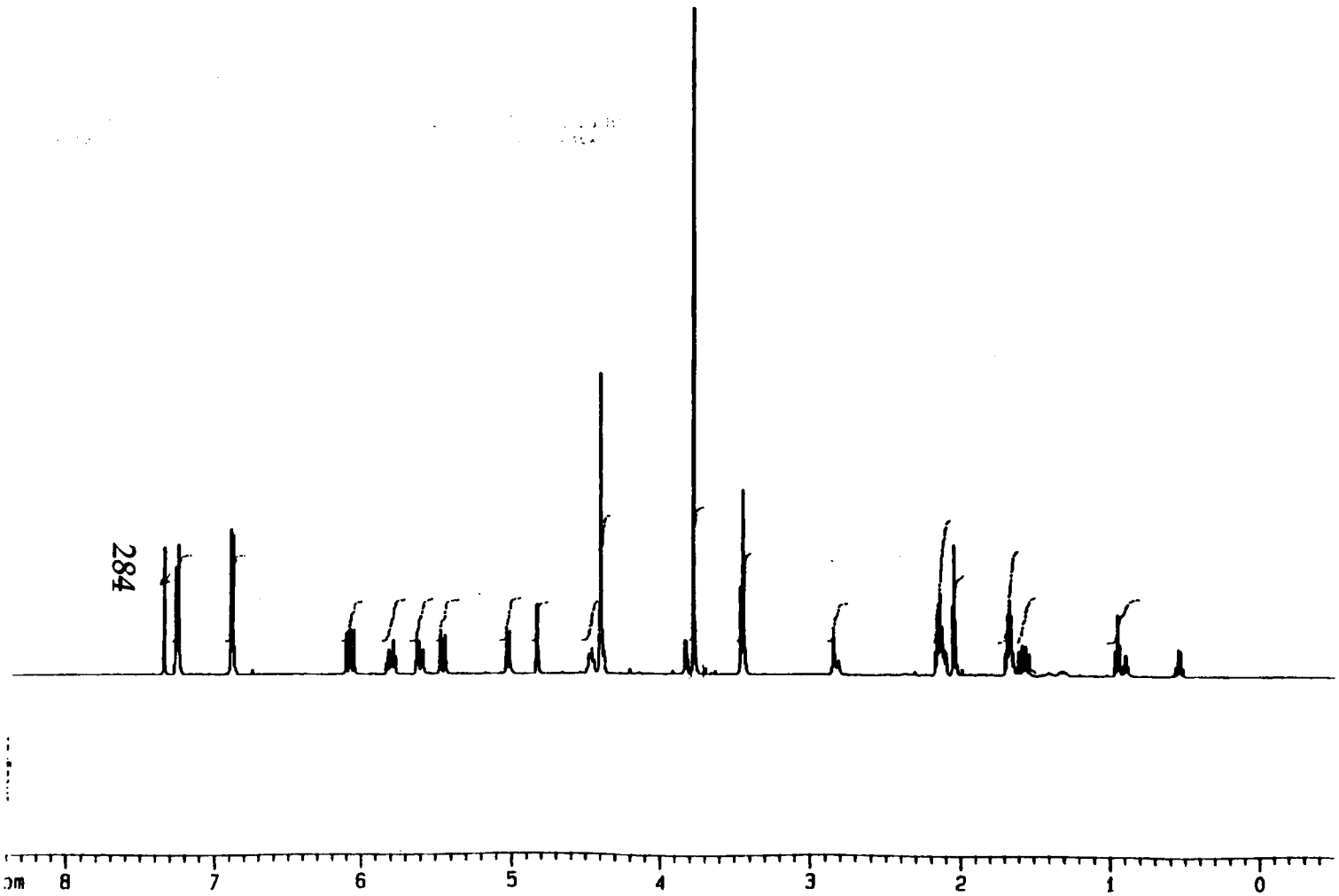
Data for **4.19**

^{1}H NMR (500 MHz, acetone-d_6): δ 7.26 (d, J= 9 Hz, 2H), 6.89 (d, J= 9 Hz, 2H), 6.08 (dd, J= 17, 11 Hz, 1H), 5.84-5.78 (m, 1H), 5.61 (ddt, J= 15, 6, 1 Hz, 1H), 5.46 (dd, J= 17, 2 Hz, 1H), 5.03 (dd, J= 11, 2 Hz, 1H), 4.84 (s, 1H), 4.48- (m, 1H), 4.41-4.38 (m, 1H), 4.41 (s, 2H), 3.78 (s, 3H), 3.45 (t, J= 6 Hz, 2H), 2.12-2.10 (m, 2H), 2.11 (quint, J= 4 Hz, 2H), 1.67 (quint, J= 6 Hz, 2H), 1.61-1.53 (m, 1H).

^{13}C NMR (125 MHz, acetone-d_6) δ 160.6, 152.0, 134.0, 133.2 (x2), 132.5, 131.5, 130.4 (x2), 114.9, 114.3, 109.4, 76.7, 73.4, 70.2, 64.2, 56.0, 39.6, 30.5, 30.1.

IR (neat) 3420, 2941, 2857, 1614, 1599, 1515 cm^{-1}.

EI HRMS indeterminable.



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PROCNO	1

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TE	300.0 K
D1	0.01000000 sec

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

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F2 - Processing parameters

SI	65536
SF	500.1300102 MHz
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1D NMR plot parameters

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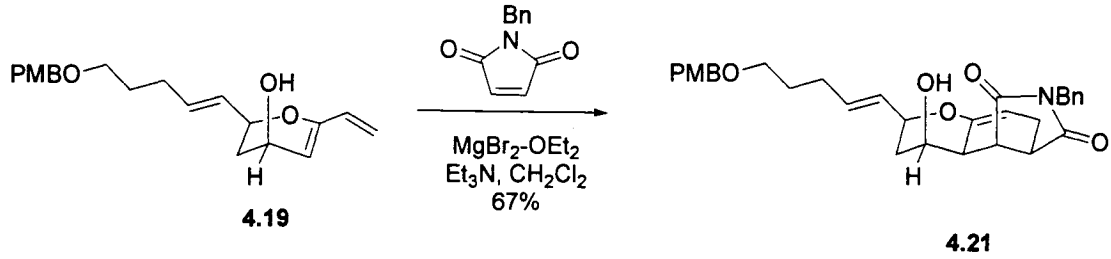
HZCM	225.05849 Hz/cm



2-Benzyl-9-hydroxy-7-[5-(4-methoxy-benzyloxy)-pent-1-enyl]-3a,7,8,9,9a,9b-hexahydro-4H-pyrano[3,2-e]isoindole-1,3-dione (4.21).

To a suspension of $MgBr_2 \cdot Et_2O$ (0.568 g, 1.1 mmol) in dichloromethane (4 mL) was added triethylamine (0.46 mL, 3.3 mmol) and the mixture stirred for 20 min at room temperature. The alcohol **4.19** (0.361 g, 1.1 mmol) and benzylmaleimide (2.1 g, 11 mmol) in dichloromethane (4 mL) were cannulated into the magnesium solution and stirred for 30 min. The reaction was quenched by adding saturated $NH_4Cl_{(aq)}$. The aqueous layer was extracted 3 times with dichloromethane (3 X 30 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash silica column chromatography (40% EtOAc/hexanes) to afford 383 mg of **4.21** (67% yield) as a yellow oil.

Data for **4.21**

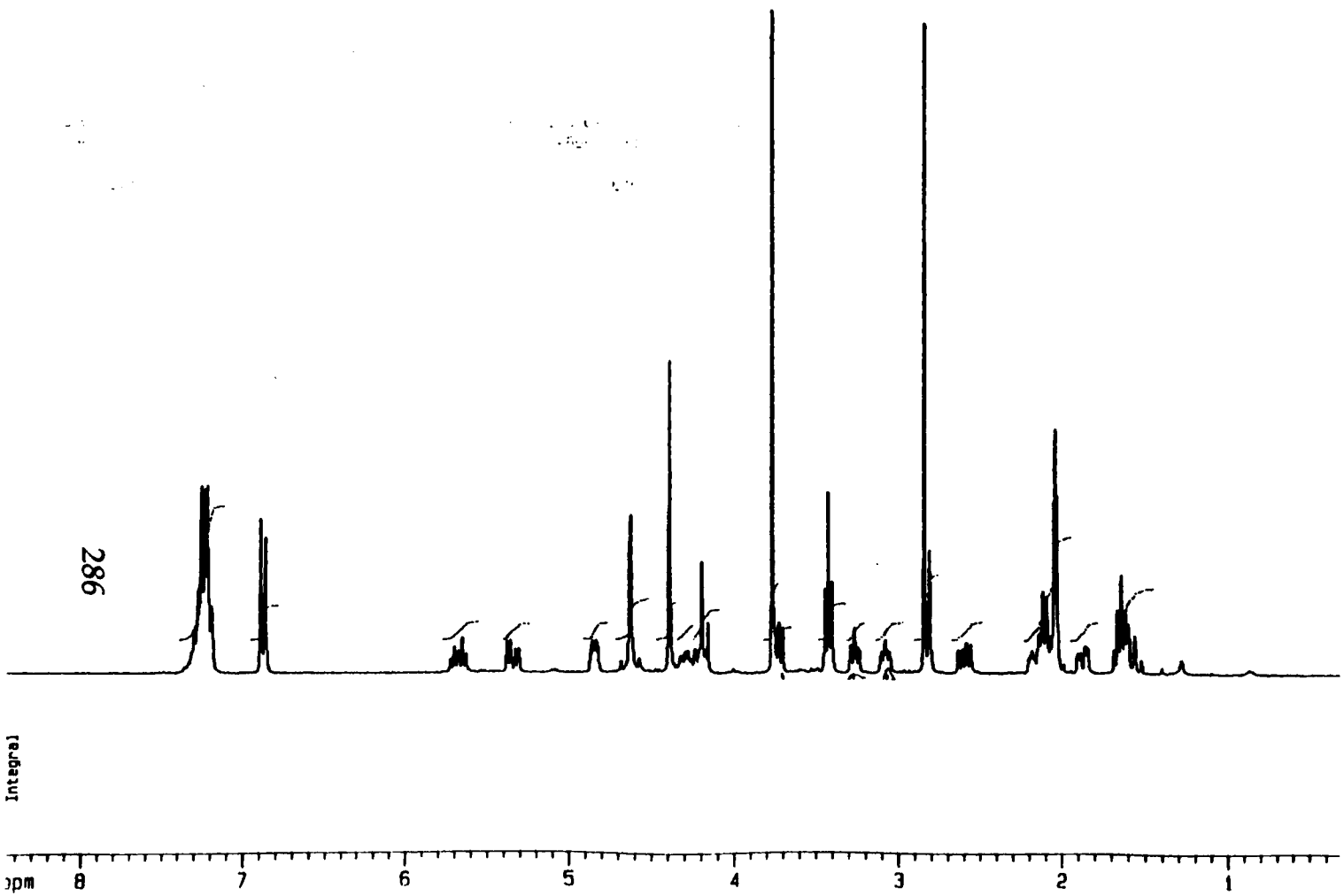
^{1}H NMR (500 MHz, acetone-d_6): δ 7.36-7.23 (m, 7H), 6.90 (d, J= 6 Hz, 2H), 5.70 (dt, J= 15, 7 Hz, 1H), 5.37 (dd, J= 15, 6 Hz, 1H), 4.88-4.85 (m, 1H), 4.67 (d, J_{AB}= 15 Hz, 1H), 4.63 (d, J_{AB}= 15 Hz, 1H), 4.42 (s, 2H), 4.36-4.29 (m, 1H), 4.25-4.20 (m, 1H), 3.79 (s, 3H), 3.75 (dd, J= 9, 6 Hz, 1H), 3.45 (t, J= 6 Hz, 2H), 3.31-3.27 (m, 1H), 3.12-3.09 (m, 1H), 2.61 (ddd, J= 15, 8, 2 Hz, 1H), 2.21-2.16 (m, 2H), 2.12 (q, J= 7 Hz, 2H), 1.94-1.88 (m, 1H), 1.66 (quint, J= 7 Hz, 2H), 1.63-1.57 (m, 1H).

^{13}C NMR (125 MHz, acetone-d_6) δ 181.7, 180.1, 160.0, 154.2, 136.7, 132.4, 131.9, 131.0 (x2), 129.8 (x2), 129.2 (x2), 128.0 (x3), 114.3, 97.0, 76.4, 72.7, 69.6, 66.1, 66.0, 55.4, 42.7, 42.5, 42.3, 39.2, 38.6, 29.4, 23.9.

IR (neat) 3665, 2924, 2853, 1688 cm^{-1}.

EI HRMS calcd for $C_{31}H_{33}NO_5$ (M^+ -H_2O) 499.23587, obsd 499.23767.

4.21

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PROCNO                  1

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TD                  30720
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DS                      0
SWH              5081.301 Hz
FIDRES           0.165407 Hz
AQ               3.0228980 sec
RG                    256
DW                 98.400 usec
DE                  6.00 usec
TE                 300.0 K
D1              1.00000000 sec

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P1                  10.50 usec
PL1                 -3.00 dB
SFO1          300.1319477 MHz

F2 - Processing parameters
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SF            300.1300000 MHz
WDW                    EM
SSB                     0
LB                   0.10 Hz
GB                      0
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1D NMR plot parameters
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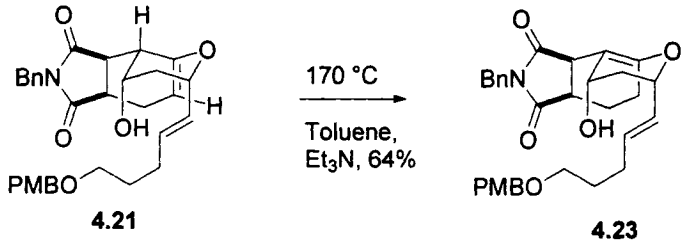


4.21 **4.23**

2-Benzyl-9-hydroxy-7-[5-(4-methoxy-benzyloxy)-pent-1-enyl]-3a,5,7,8,9,9b-hexahydro-4H-pyrano[3,2-e]isoindole-1,3-dione (4.23).

A solution of alcohol **4.21** (0.014 g, 0.03 mmol) and triethylamine (0.01 mL) in toluene (3 mL) was degassed with argon. The mixture was heated to 160 °C for 15 h in a wax bath. The reaction was cooled and concentrated. The crude product was purified by flash silica column chromatography (60% EtOAc/hexanes) to afford 9 g of **4.23** (64% yield) as a colourless oil.

Data for **4.23**

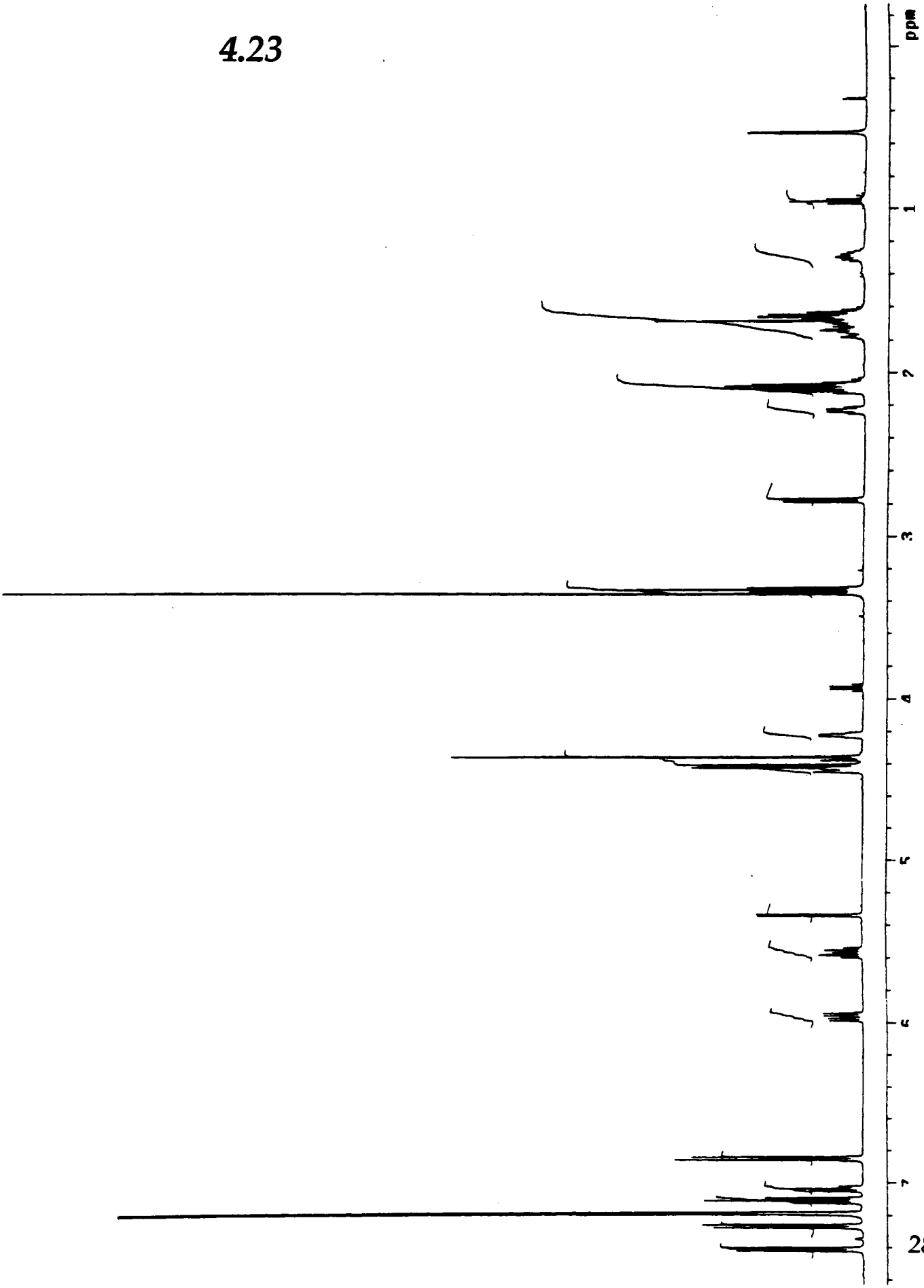
^{1}H NMR (500 MHz, C_6D_6): δ 7.46 (d, J= 7 Hz, 2H), 7.32 (d, J= 9 Hz, 2H), 7.16 (t, J= 7 Hz, 2H), 7.09 (d, J= 7 Hz, 1H), 6.90 (d, J= 9 Hz, 2H), 6.01 (dd, J= 15, 7 Hz, 1H), 5.62 (dd, J= 15, 7 Hz, 1H), 5.39 (d, J= 4 Hz, 1H), 4.50-4.43 (m, 3H), 4.41 (s, 2H), 4.28-4.27 (m, 1H), 3.40 (s, 3H), 3.38 (t, J= 6 Hz, 2H), 2.82 (d, J= 9 Hz, 1H), 2.29-2.26 (m, 1H), 2.17-2.11 (m, 3H), 1.83-1.66 (m, 6H), 1.36-1.31 (m, 1H).

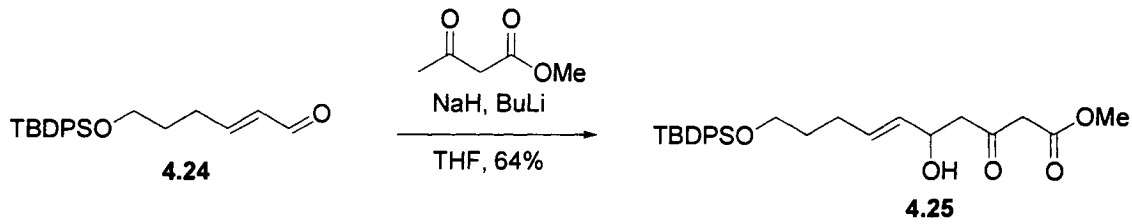
^{13}C NMR (125 MHz, C_6D_6) δ 180.5, 178.1, 159.6, 152.2, 136.3, 132.12, 131.5, 129.9 (x2), 129.3 (x2), 129.1 (x2), 128.9 (x2), 114.0, 101.1, 75.7, 72.7, 69.3, 64.4, 29.1, 25.5, 23.9.

IR (neat) 3418, 2932, 2854, 1690 cm^{-1}.

EI HRMS calcd for $C_{31}H_{33}NO_5$ (M^+ -H_2O) 499.23587, obsd 499.2335.

4.23





10-(tert-Butyl-diphenyl-silanyloxy)-5-hydroxy-3-oxo-dec-6-enoic acid methyl ester (4.25).

Methyl acetoacetate (14.5 mL, 136.5 mmol) was dissolved in THF (200 mL) and cooled to 0 °C. Sodium hydride 60 % in mineral oil (8.2 g, 204.6 mmol) was added and stirred for 20 min. n-Butyllithium (2.5 M, 60 mL, 150 mmol) was added and stirred for 20 min and then cooled to –78 °C. Aldehyde **4.24** (24 g, 68.2 mmol) was dissolved in THF (30 mL) and cannulated into the anion solution. The resulting mixture was stirred at –78 °C for 20 min. Saturated $NH_4Cl_{(aq)}$ was added. The aqueous layer was extracted 3 times with diethylether (3 X 200 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash silica column chromatography (20% EtOAc/hexanes) to afford 20.7 g of **4.25** (64% yield) as a light yellow oil.

Data for **4.25**

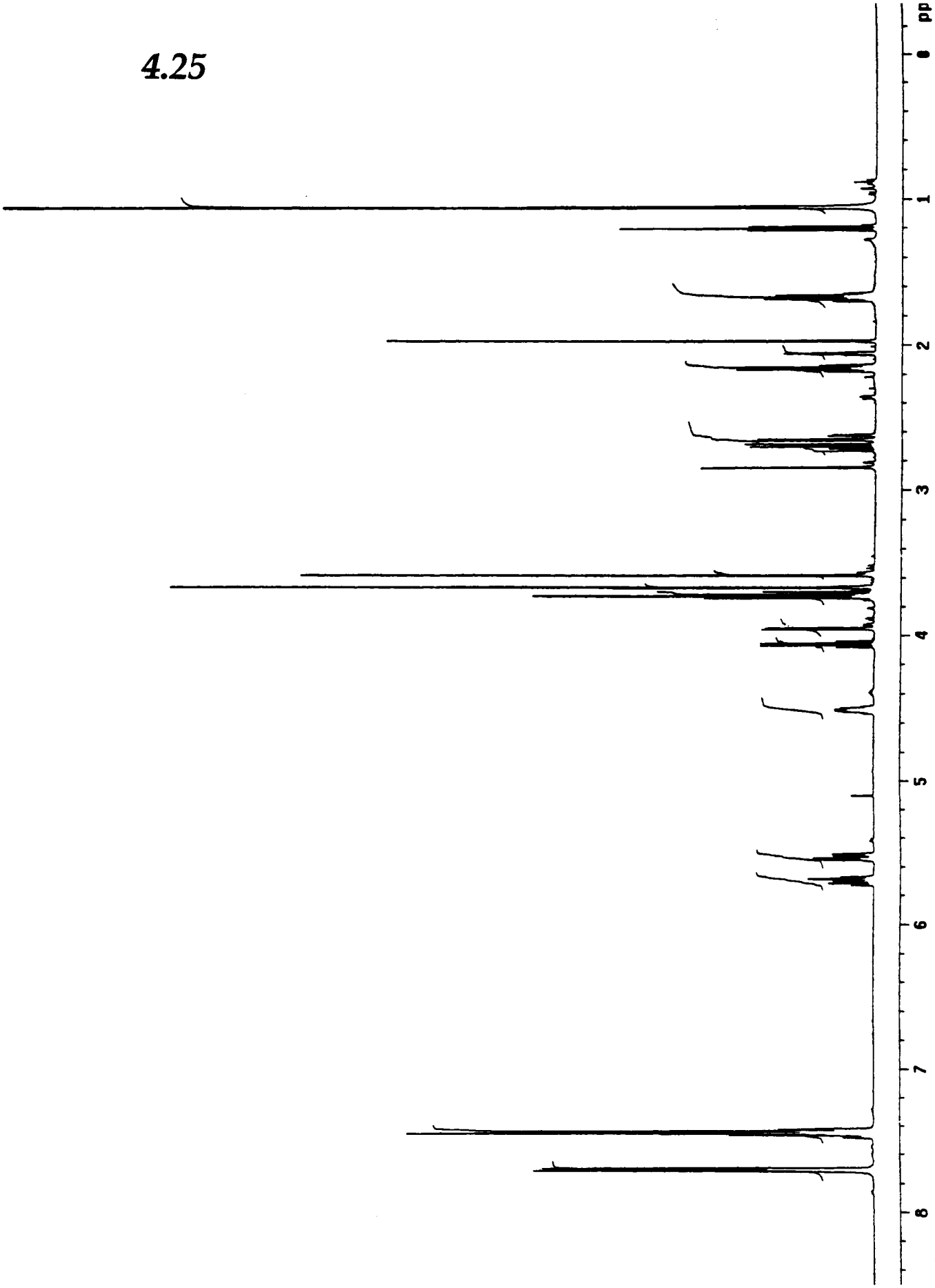
^{1}H NMR (500 MHz, acetone-d_6): δ 7.70 (dd, J= 8, 2 Hz, 4H), 7.48-7.42 (m, 6H), 5.70 (dt, J= 15, 7 Hz, 1H), 5.53 (dd, J= 15, 6 Hz, 1H), 4.52-4.50 (m, 1H), 3.95 (d, J= 4 Hz, 1H), 3.72 (t, J= 6 Hz, 2H), 3.66 (s, 3H), 3.58 (s, 2H), 2.84-2.65 (m, 2H), 2.15 (q, J= 7 Hz, 2H), 1.67 (quint, J= 7 Hz, 2H), 1.06 (s, 9H).

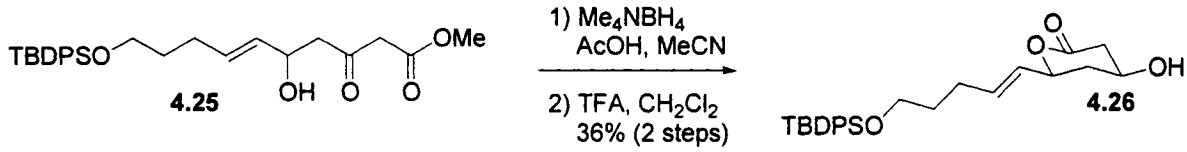
^{13}C NMR (125 MHz, acetone-d_6) δ 202.5, 168.4, 136.3 (x4), 134.8 (x2), 133.9, 130.8, 130.6 (x2), 128.7 (x4), 69.1, 63.9, 52.2, 51.2, 50.3, 32.9, 29.1, 27.3 (x3), 19.8.

IR (neat) 3448, 2932, 2857, 1748, 1716, 1428, 1111 cm^{-1}.

EI HRMS calcd for $C_{23}H_{27}O_5Si$ (M^+ -*t*Bu) 411.16278, obsd 411.16135.

4.25





6-[5-(tert-Butyl-diphenyl-silanyloxy)-pent-1-enyl]-4-hydroxy-tetrahydro-pyran-2-one (4.26).

Acetonitrile (17 mL) and acetic acid (17 mL) were mixed at 0 °C. Tetramethylammonium borohydride (1.7 g, 19.3 mmol) was added and stirred for 20 min. The mixture was frozen in a bath at –78 °C and a solution of ketone **4.25** (2.26 g, 4.82 mmol) in acetonitrile (5 mL) was cannulated into the flask. The reaction was kept in the freezer for 15 h at –25 °C. The reaction was quenched by adding sodium potassium tartrate 0.5 M (60 mL) and warmed to room temperature. The organic layer was washed with $NaHCO_{3sat.}$ The aqueous layer was extracted 3 times with dichloromethane (3 X 100 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was dissolved in dichloromethane (26 mL) and treated directly with trifluoroacitic acid (0.065 mL, 0.84 mmol). The reaction was stirred for 15 h at room temperature. The reaction was stopped by adding Na_2CO_3 until a neutral pH was obtained. The reaction was filtered and concentrated. The crude product was purified by flash silica column chromatography (25% EtOAc/hexanes to 35% EtOAc/hexanes) to afford 767 mg (34%)of starting material and 759 mg of **4.26** (36% yield) as a yellow oil.

Data for **4.26**

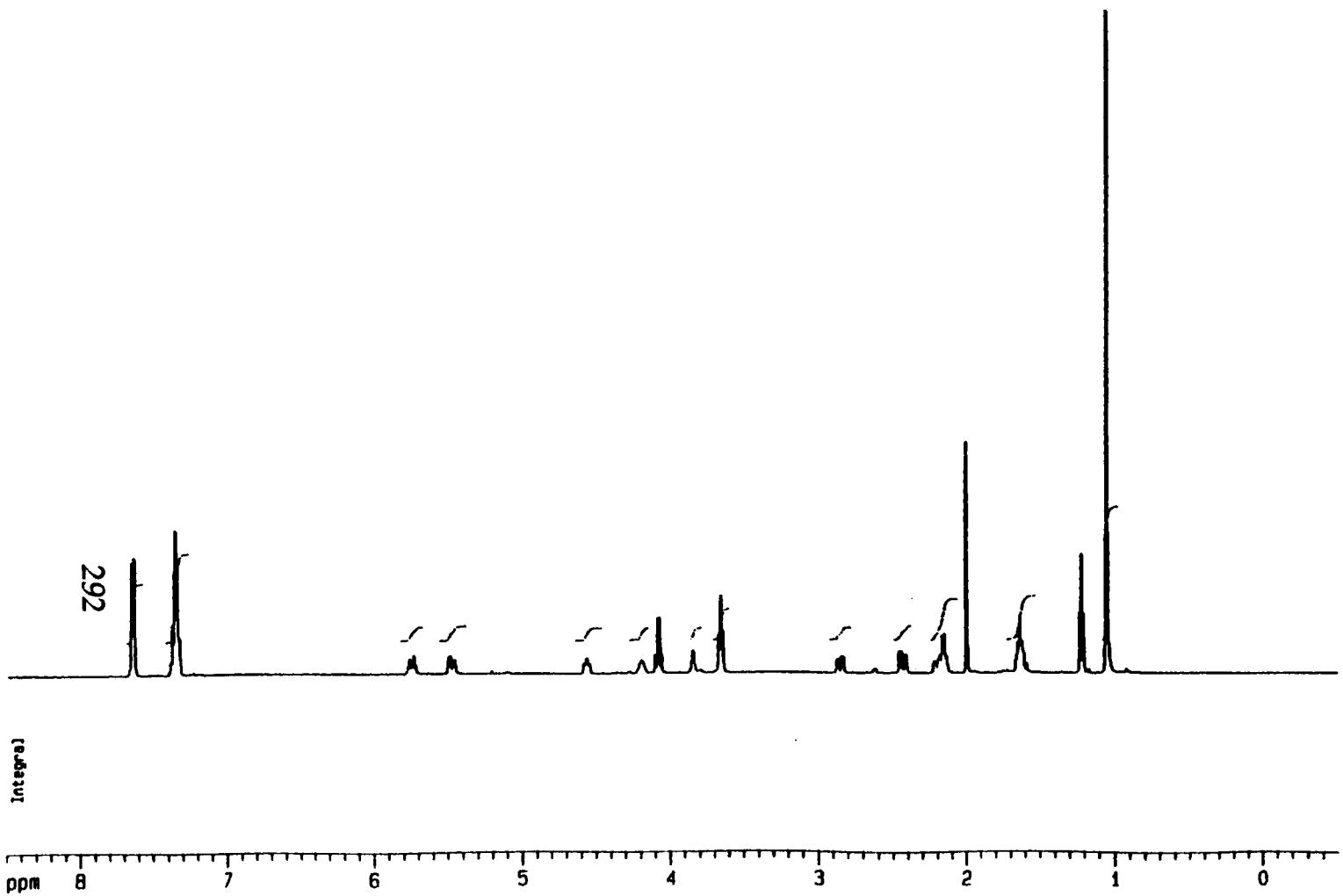
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.66-7.64 (m, 4H), 7.40-7.34 (m, 6H), 5.75 (dt, J= 15, 6 Hz, 1H), 5.47 (dd, J= 15, 7 Hz, 1H), 4.58-4.54 (m, 1H), 4.19 (br s, 1H), 3.84 (s, 1H), 3.65 (t, J= 6 Hz, 2H), 2.84 (dd, J= 17, 5 Hz, 1H), 2.43 (dd, J= 17, 8 Hz, 1H), 2.22-2.13 (m, 3H), 1.63-1.59 (m, 3H), 1.04 (s, 9H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 171.2, 135.4 (x4), 134.6, 133.7 (x2), 129.5, 127.6 (x4), 127.4, 77.9, 63.3, 62.9, 39.3, 38.0, 31.5, 28.3, 26.8 (x3), 19.1.

IR (neat) 3420, 3071, 2931, 2858, 1733, 1428, 1242, 969 cm^{-1}.

EI HRMS calcd for $C_{10}H_{14}O_3$ (M^+ -*t*BDPSOH) 182.0943, obsd 182.0506.

4.26



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F2 - Processing parameters

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1D NMR plot parameters

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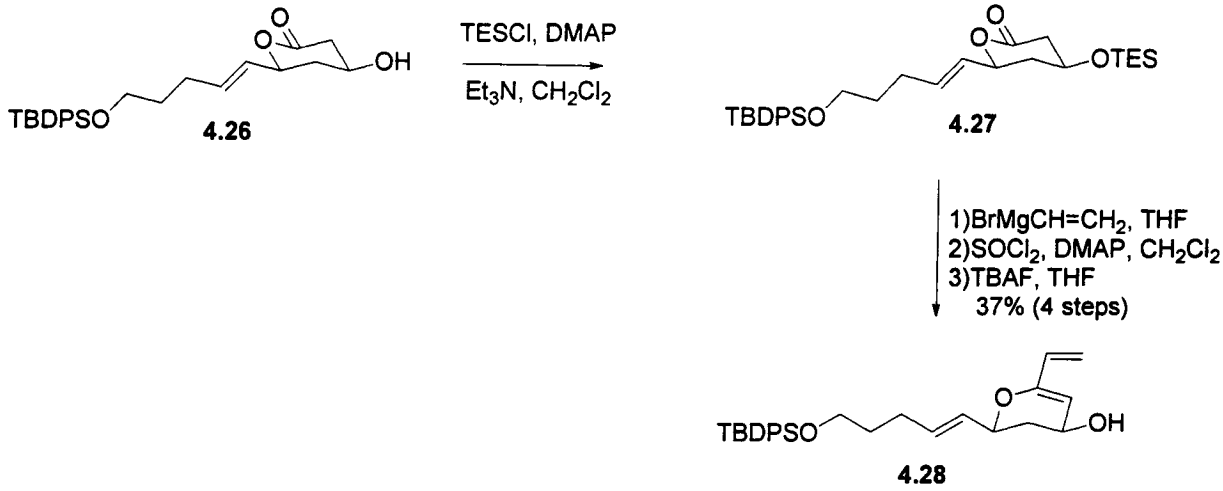


2-[5-(tert-Butyl-diphenyl-silanyloxy)-pent-1-enyl]-6-vinyl-3,4-dihydro-2H-pyran-4-ol (4.28).

The lactone **4.26** (2.04 g, 4.65 mmol) was dissolved in dichloromethane (47 mL). Triethylamine (3.9 mL, 27.9 mmol) and dimethylaminopyridine (0.051 g, 0.42 mmol) were added, followed by triethylsilyl chloride (2.3 mL, 14 mmol). The reaction was stirred for 30 min. Saturated $NH_4Cl_{(aq)}$ was added. The aqueous layer was extracted 3 times with dichloromethane (3 X 50 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash silica column chromatography (10% EtOAc/hexanes) to afford a colorless oil which dissolved in THF (41 mL) and cooled to –78 °C. Vinylmagnesium bromide, 0.9 M in THF (13.6 mL, 12.2 mmol) was added and the reaction was stirred for 30 min. The reaction was quenched by adding saturated $NH_4Cl_{(aq)}$. The aqueous layer was extracted 3 times with diethylether (3 X 50 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was used directly to avoid decomposition. The lactol intermediate was dissolved in dichloromethane (41 mL) and cooled to 0 °C. Dimethylaminopyridine (1.5 g, 12.3 mmol) was added, followed by thionyl chloride (0.3 mL, 4.1 mmol) and the reaction was stirred for 30 min. The reaction was quenched by adding $NaHCO_{3sat}$. The aqueous layer was extracted 3 times with dichloromethane (3 X 50 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was used directly to avoid decomposition. The diene was

dissolved in THF (40 mL), cooled to –78 °C and tetrabutylammonium fluoride, 1 M in THF (4 mL, 4 mmol) was added. The reaction turned dark brown and the solvent was evaporated after 30 min. The crude product was purified by flash silica column chromatography (30% EtOAc/hexanes) to afford 777 mg of **4.28** (37% yield) as a colourless oil.

Data for **4.28**

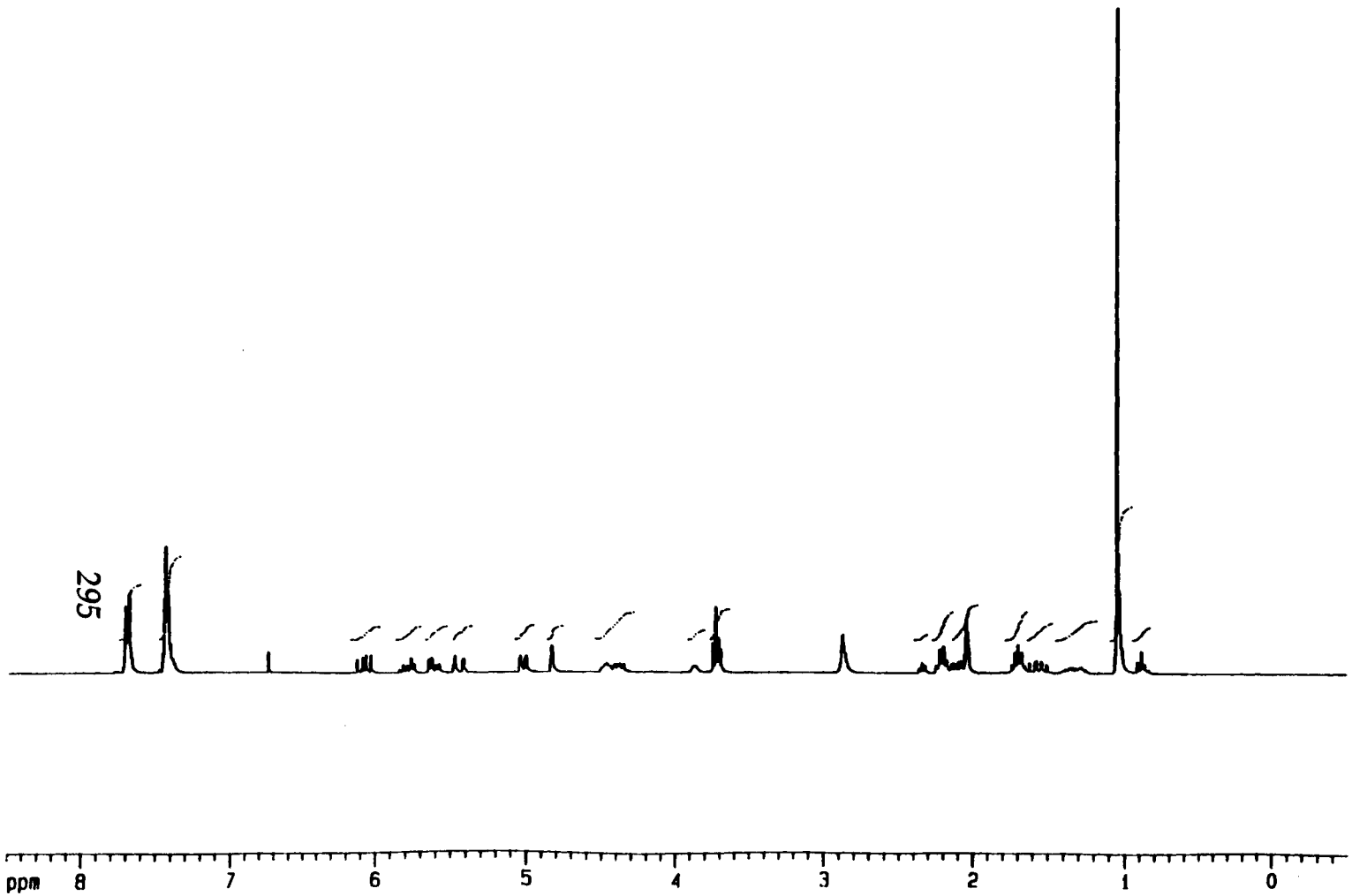
^{1}H NMR (300 MHz, acetone-d_6): δ 7.80-7.69 (m, 4H), 7.49-7.34 (m, 6H), 6.09 (dd, J= 17, 11 Hz, 1H), 5.85-5.76 (m, 1H), 5.63 (ddd, J= 15, 6, 1 Hz, 1H), 5.47 (dd, J= 17, 2 Hz, 1H), 5.03 (dd, J= 11, 2 Hz, 1H), 4.84 (s, 1H), 4.52-4.42 (m, 1H), 4.38 (dd, J= 6, 5 Hz, 1H), 3.87 (d, J= 6 Hz, 1H), 3.74 (t, J= 6 Hz, 2H), 2.22 (q, J= 7 Hz, 1H), 2.11 (ddt, J= 13, 6, 2 Hz, 1H), 2.06-2.04 (m, 1H), 1.70 (quint, J= 6 Hz, 2H), 1.63-1.52 (m, 1H), 1.05 (s, 9H).

^{13}C NMR (75 MHz, acetone-d_6) δ 152.0, 136.8 (x4), 135.1 (x2), 133.9, 133.1, 131.4, 131.1 (x2), 129.1 (x4), 114.3, 109.4, 76.6, 64.3, 64.2, 39.6, 33.1, 29.6, 27.7 (x3), 20.2.

IR (neat) 3345, 2955, 2930, 2857, 1111 cm^{-1}.

EI HRMS calcd for $C_{28}H_{34}O_2$ (M^+ -H_2O) 430.23281, obsd 430.23637.

4.28

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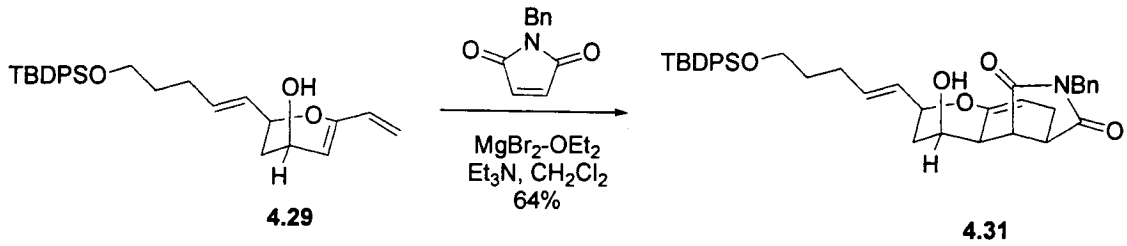


2-Benzyl-7-[5-(tert-butyl-diphenyl-silanyloxy)-pent-1-enyl]-9-hydroxy-3a,7,8,9,9a,9b-hexahydro-4H-pyrano[3,2-e]isoindole-1,3-dione (4.31).

To a suspension of $MgBr_2 \cdot Et_2O$ (0.041 g, 0.16 mmol) in dichloromethane (1 mL) was added triethylamine (0.033 mL, 0.23 mmol) and the mixture stirred for 20 min at room temperature. The alcohol **4.29** (0.035 g, 0.08 mmol) and benzylmaleimide (0.150 g, 0.8 mmol) in dichloromethane (1 mL) were cannulated into the magnesium solution and stirred for 30 min. The reaction was done, so quenched by adding saturated $NH_4Cl_{(aq)}$. The aqueous layer was extracted 3 times with dichloromethane (3 X 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash silica column chromatography (40% EtOAc/hexanes) to afford 33 mg of **4.31** (64% yield) as a yellow oil.

Data for **4.31**

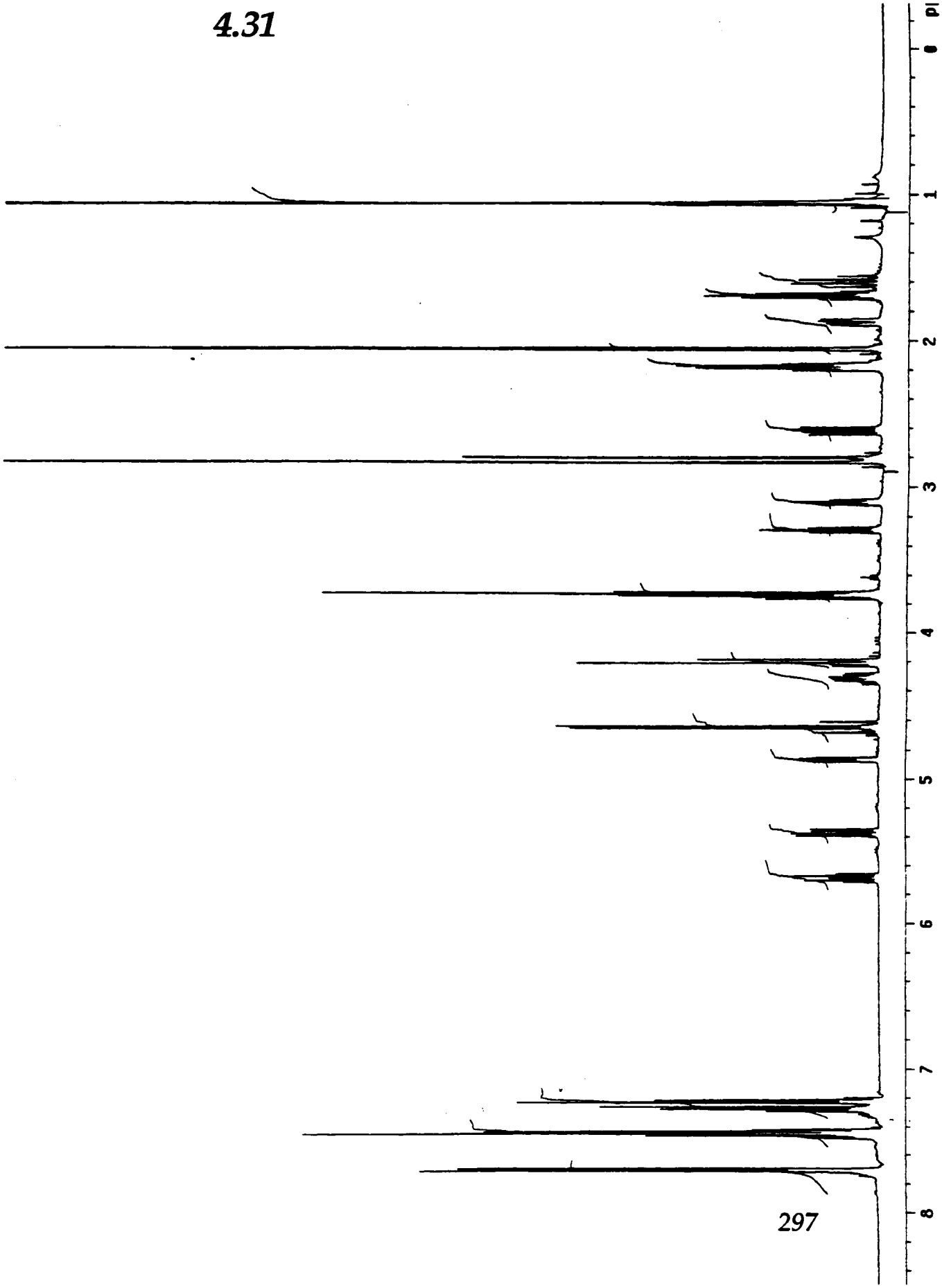
^{1}H NMR (500 MHz, acetone-d_6): δ 7.70 (dd, J= 8, 2 Hz, 4H), 7.47-7.42 (m, 6H), 7.29-7.22 (m, 5H), 5.68 (dtd, 15, 7, 1 Hz, 1H), 5.36 (ddq, 16, 7, 1 Hz, 1H), 4.88-4.85 (m, 1H), 4.66 (d, J_{AB}= 15 Hz, 1H), 4.62 (d, J_{AB}= 15 Hz, 1H), 4.35-4.28 (m, 1H), 4.21 (dd, J= 11, 7 Hz, 1H), 4.19 (d, J= 11 Hz, 1H), 3.76-3.73 (m, 1H), 3.73 (t, J= 6 Hz, 2H), 3.30-3.27 (m, 1H), 3.10 (tq, 7, 2 Hz, 1H), 2.61 (ddd, J= 15, 8, 2 Hz, 1H), 2.17 (q, J= 7 Hz, 2H), 1.86 (ddd, J= 13, 5, 2 Hz, 1H), 1.68 (quint, J= 7 Hz, 2H), 1.61 (q, J= 12 Hz, 2H), 1.06 (s, 9H).

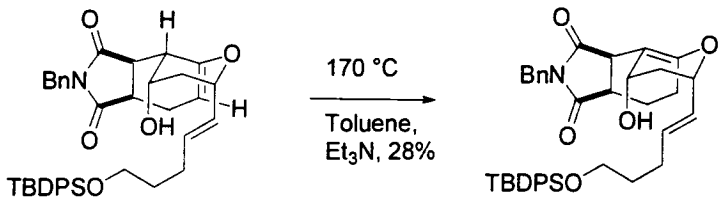
^{13}C NMR (125 MHz, acetone-d_6) δ 181.2, 179.5, 153.7, 136.2, 135.6 (x4), 134.0 (x2), 131.9, 130.4, 129.9 (x2), 128.6 (x2), 128.0 (x4), 127.5, 127.4 (x2), 96.4, 75.9, 65.6, 63.2, 42.2, 42.0, 41.8, 38.7, 38.1, 32.0, 28.4, 26.6 (x3), 23.3, 19.1.

IR (neat) 3426, 2936, 2859, 1689, 1436, 1347, 1103 cm^{-1}.

EI HRMS calcd for $C_{39}H_{43}NO_4Si$ ($M^+ - H_2O$) 617.29614, obsd 617.29546.

4.31





4.31 **4.33**

2-Benzyl-7-[5-(tert-butyl-diphenyl-silanyloxy)-pent-1-enyl]-9-hydroxy-3a,5,7,8,9,9b-hexahydro-4H-pyrano[3,2-e]isoindole-1,3-dione (4.33).

A solution of alcohol **4.31** (0.033 g, 0.05 mmol) and triethylamine (0.01 mL) in toluene (3 mL) was degassed with argon. The mixture was heated to 160 °C for 15 h in a wax bath. The reaction was cooled and concentrated. The crude product was purified by flash silica column chromatography (20% EtOAc/hexanes to 30% EtOAc/hexanes) to afford 7 mg of starting material **4.31** (21%) and 9 g of **4.33** (28% yield) as a colourless oil.

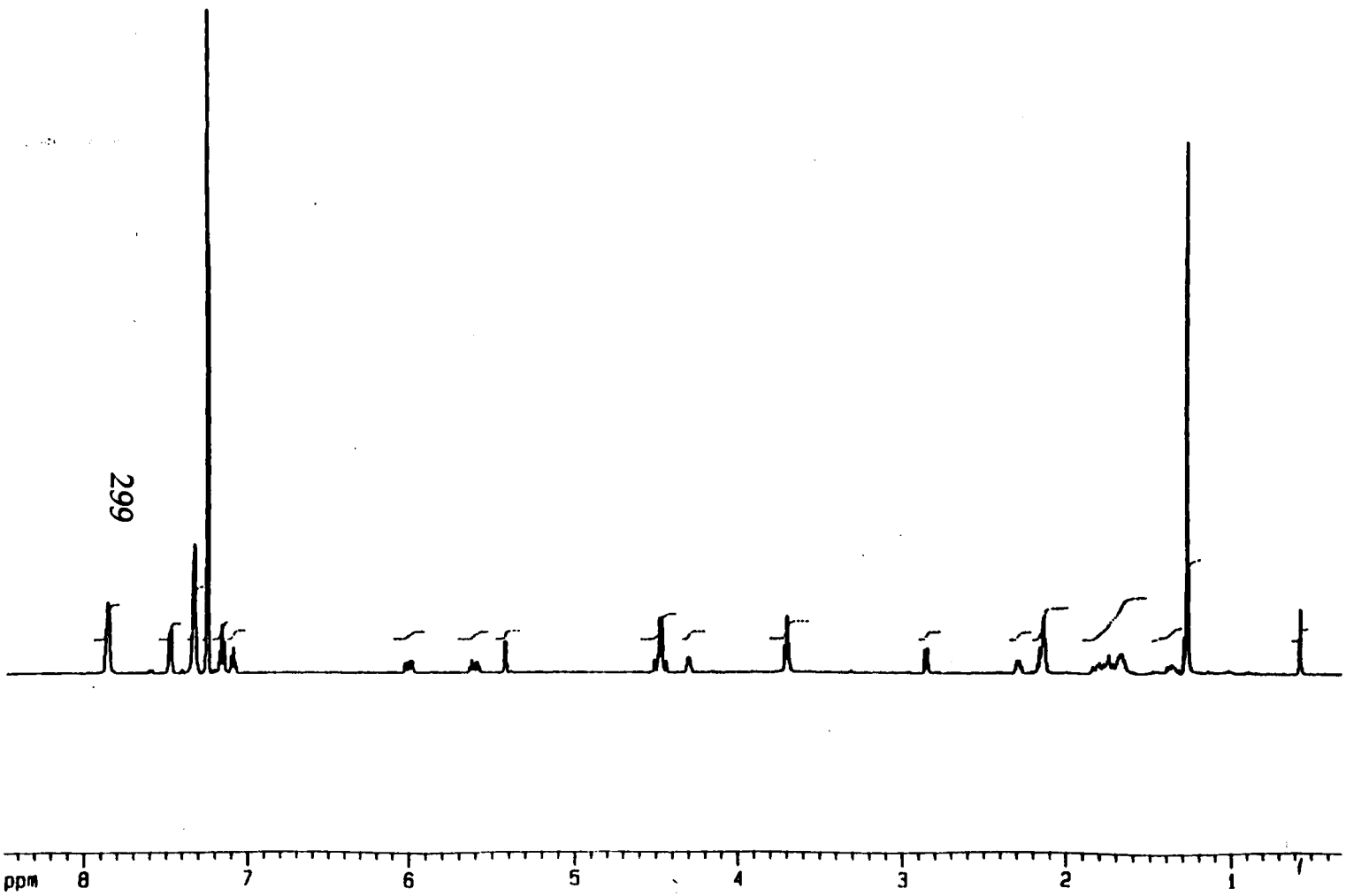
Data for **4.33**

^{1}H NMR (500 MHz, C_6D_6): δ 7.88-7.86 (m, 4H), 7.48 (d, J= 7 Hz, 2H), 7.34 (s, 6H), 7.17 (t, J= 7 Hz, 2H), 7.10 (t, J= 7 Hz, 1H), 6.01 (dd, J= 15, 7 Hz, 1H), 5.61 (dt, J= 15, 8 Hz, 1H), 5.42 (d, J= 4 Hz, 1H), 4.50 (d, J_{AB}= 14 Hz, 1H), 4.45 (d, J_{AB}= 14 Hz, 1H), 4.30 (d, J= 4 Hz, 1H), 3.70 (t, J= 6 Hz, 2H), 2.85 (d, J= 8 Hz, 1H), 2.30-2.27 (m, 1H), 2.17-2.13 (m, 4H), 1.84-1.63 (m, 5H), 1.39-1.35 (m, 2H), 1.27 (s, 9H).

^{13}C NMR (125 MHz, C_6D_6) δ 180.2, 177.8, 151.9, 136.0, 135.7 (x4), 134.0 (x2), 132.0, 129.6 (x2), 129.5, 128.8 (x2), 128.6 (x4), 127.9, 127.7, 98.9, 75.5, 64.2, 63.1, 43.3, 42.3, 39.7, 37.1, 32.0, 28.4, 26.8 (x3), 25.2, 23.7, 19.1.

IR (neat) 3420, 2931, 2857, 1691, 1428, 1399, 1110 cm^{-1}.

EI HRMS calcd for $C_{39}H_{43}NO_4Si$ (M^+ -H_2O) 617.29614, obsd 617.29653.



4.33

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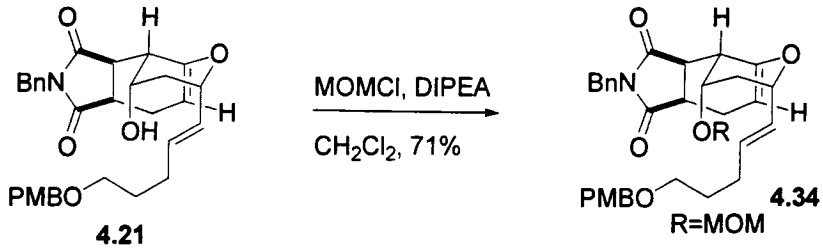


2-Benzyl-7-[5-(4-methoxy-benzyloxy)-pent-1-enyl]-9-methoxymethoxy-3a,7,8,9,9a,9b-hexahydro-4H-pyrano[3,2-e]isoindole-1,3-dione (4.34).

Alcohol **4.21** (0.02 g, 0.03 mmol) was dissolved in dichloromethane (2 mL). Diisopropylethylamine (0.052 mL, 0.3 mmol) was added, followed by MOMCl (0.005 mL, 0.06 mmol). The reaction was heated to reflux for 5 h. The reaction was cooled to room temperature and quenched by adding $NaHCO_{3sat.}$ The aqueous layer was extracted 3 times with dichloromethane (3 X 15 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (30% EtOAc/hexanes) to afford 12 mg of **4.34** (71% yield) as a colourless oil.

Data for **4.34**

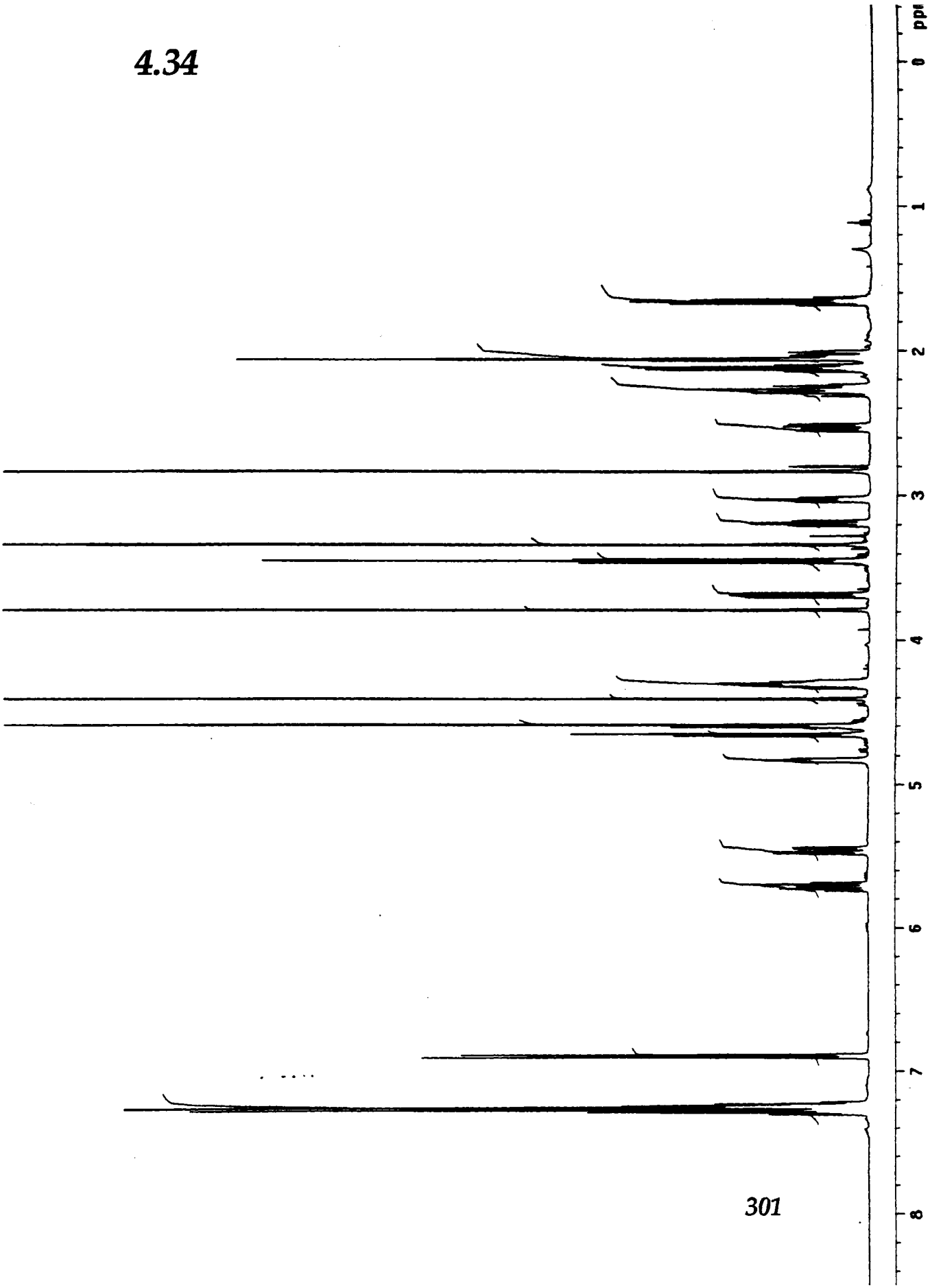
^{1}H NMR (500 MHz, acetone-d_6): δ 7.30-7.22 (m, 7H), 6.90 (d, J= 9 Hz, 2H), 5.71 (td, 15, 7 Hz, 1H), 5.46 (dd, J= 15, 7 Hz, 1H), 4.84-4.82 (m, 1H), 4.66 (d, J= 7 Hz, 1H), 4.60-4.59 (m, 3H), 4.41 (s, 2H), 4.33-4.28 (m, 2H), 3.78 (s, 3H), 3.68 (dd, J= 9, 6 Hz, 1H), 3.44 (t, J= 6 Hz, 2H), 3.33 (s, 3H), 3.18 (dt, J= 8, 2 Hz, 1H), 3.04-3.01 (m, 1H), 2.52 (ddd, J= 9, 7, 2 Hz, 1H), 2.31-2.23 (m, 2H), 2.12 (q, J= 7 Hz, 2H), 2.04-2.00 (m, 1H), 1.65 (quint, J= 6 Hz, 2H).

^{13}C NMR (125 MHz, acetone-d_6) δ 179.2, 177.4, 159.3, 153.2, 136.7, 131.7, 131.4, 130.5 (x2), 129.1 (x2), 128.4 (x2), 127.5 (x2), 127.2, 113.6, 96.2, 95.8, 75.7, 72.1, 71.8, 68.0, 54.9, 54.7, 41.7, 41.2, 41.1. 36.2, 35.1, 29.1, 28.7, 23.4.

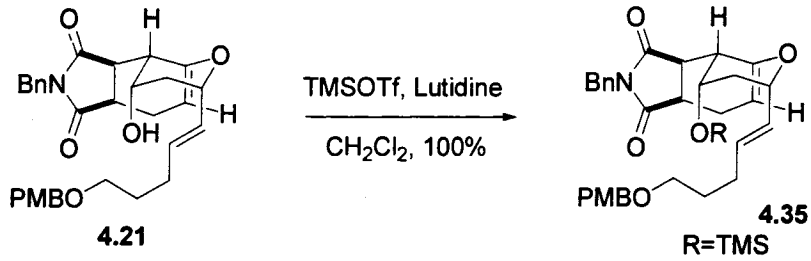
IR (neat) 2938, 2852, 1699, 1506 cm^{-1}.

EI HRMS indeterminable.

4.34



301



4.21 **4.35**

2-Benzyl-7-[5-(4-methoxy-benzyloxy)-pent-1-enyl]-9-trimethylsilanyloxy-3a,7,8,9,9a,9b-hexahydro-4H-pyrano[3,2-e]isoindole-1,3-dione (4.35).

Alcohol **4.21** (0.02 g, 0.04 mmol) was dissolved in dichloromethane (1 mL) then cooled to 0 °C. Lutidine (0.045 mL, 0.39 mmol) was added followed by trimethylsilyltriflate (0.014 mL, 0.77 mmol) and the reaction was stirred for 30 min. The reaction was quenched by adding $NHCO_{3sat}$. The aqueous layer was extracted 3 times with dichloromethane (3 X 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (50% EtOAc/hexanes) to afford 24 mg of **4.35** (quant yield) as a colourless oil.

Data for **4.35**

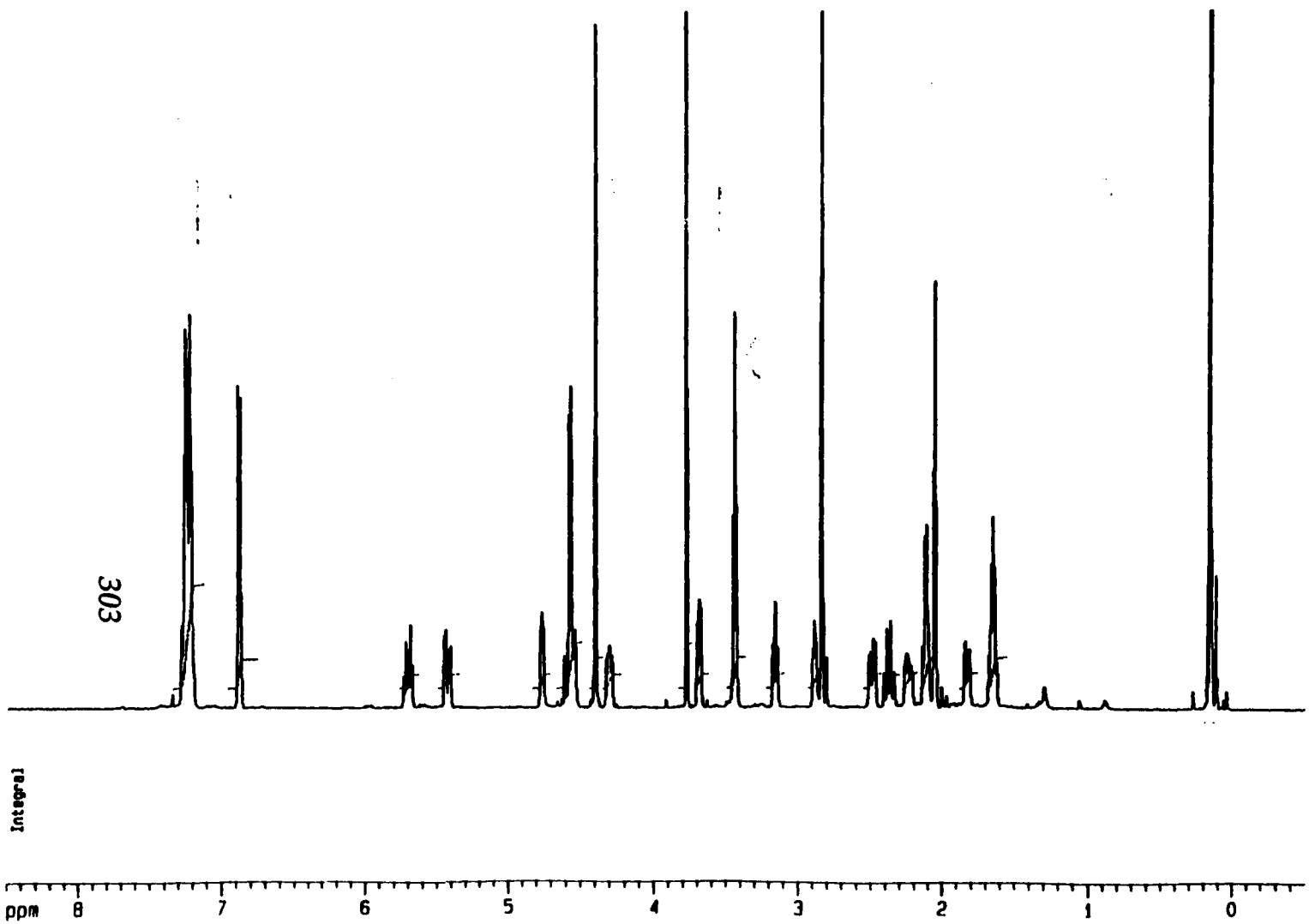
^{1}H NMR (500 MHz, acetone-d_6): δ 7.29-7.21 (m, 7H), 6.89 (d, J= 9 Hz, 2H), 5.71 (dt, J= 15, 8 Hz, 1H), 5.43 (dd, J= 15, 7 Hz, 1H), 4.78-4.76 (m, 1H), 4.61-4.55 (m, 3H), 4.40 (s, 2H), 4.32-4.29 (m, 1H), 3.78 (s, 3H), 3.69 (dd, J= 9, 5 Hz, 1H), 3.44 (t, J= 6 Hz, 2H), 3.16 (td, 9, 2 Hz, 1H), 2.90-2.87 (m, 1H), 2.48 (ddd, J= 15, 7, 2 Hz, 1H), 2.36 (q, J= 13 Hz, 1H), 2.26-2.22 (m, 1H), 2.11 (q, J= 8 Hz, 2H), 1.85-1.81 (m, 1H), 1.65 (quint, J= 7 Hz, 2H), 0.16 (s, 9H).

^{13}C NMR (125 MHz, acetone-d_6) δ 180.1, 178.1, 160.2, 155.0, 137.5, 132.5, 132.0, 131.3, 130.0 (x2), 129.2 (x2), 128.3 (x2), 128.1, 114.5(x2), 96.3, 76.9, 72.9, 69.9, 67.5, 55.6, 42.5, 42.4, 42.2, 39.1, 38.5, 30.0, 25.1, 0.4 (x3).

IR (neat) 2946, 2855, 1704, 1250, 1097 cm^{-1}.

EI HRMS calcd for $C_{34}H_{43}NO_6Si$ (M^+) 589.28597, obsd 589.28510.

4.35



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EXPNO 1
PROCNO 1

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SOLVENT Acetone
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SWH 7440.476 Hz
FIDRES 0.113533 Hz
AQ 4.4040694 sec
RG 80.63
DW 67.200 usec
DE 6.00 usec
TE 300.0 K
D1 0.01000000 sec

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P1 9.50 usec
PL1 3.00 dB
SFO1 500.1327766 MHz

F2 - Processing parameters
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LB 0.00 Hz
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1D NMR plot parameters
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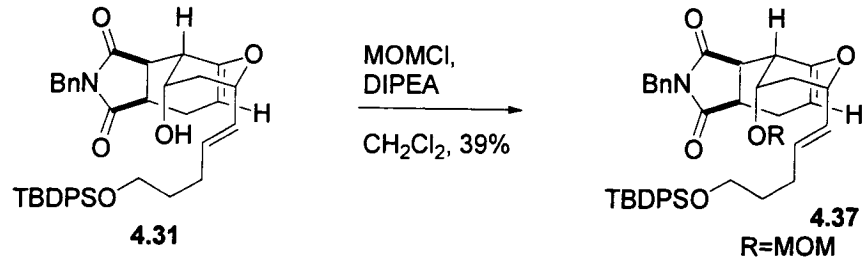
F2 -250.06 Hz
PPMCM 0.45000 ppm/cm
HZCM 225.05849 Hz/cm



2-Benzyl-7-[5-(tert-butyl-diphenyl-silanyloxy)-pent-1-enyl]-9-methoxymethoxy-3a,7,8,9,9a,9b-hexahydro-4H-pyrano[3,2-e]isoindole-1,3-dione (4.37)

Alcohol **4.31** (0.1 g, 0.16 mmol) was dissolved in dichloromethane (2 mL). Diisopropylethylamine (0.560 mL, 3.2 mmol) was added, followed by MOMCl (0.14 mL, 1.88 mmol). The reaction was heated to reflux for 7 h. The reaction was cooled to room temperature and quenched by adding $NaHCO_{3sat}$. The aqueous layer was extracted 3 times with dichloromethane (3 X 15 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (30% EtOAc/hexanes) to afford 42 mg of **4.37** (39% yield) as a colourless oil.

Data for **4.37**

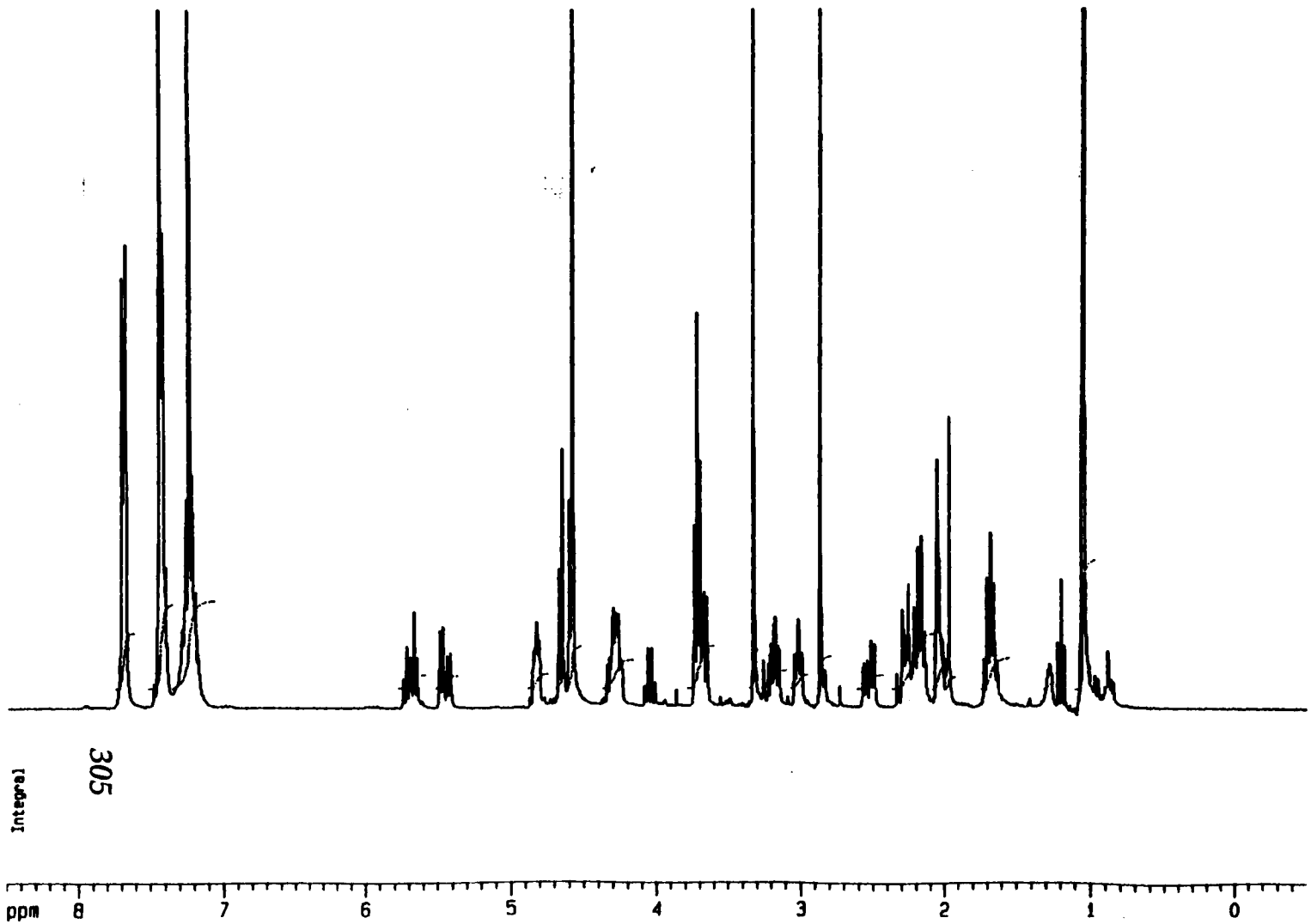
^{1}H NMR (300 MHz, acetone-d_6): δ 7.72-7.69 (m, 4H), 7.46-7.41 (m, 6H), 7.30-7.18 (m, 5H), 5.70 (dt, J= 16, 7 Hz, 1H), 5.45 (dd, J= 15, 7 Hz, 1H), 4.85-4.81 (m, 1H), 4.66 (d, J_{AB}= 7 Hz, 1H), 4.59 (d, J_{AB}= 7 Hz, 1H), 4.58 (s, 2H), 4.35-4.25 (m, 2H), 3.72 (t, J= 6 Hz, 2H), 3.67 (dd, J= 9, 6 Hz, 1H), 3.33 (s, 3H), 3.25-3.15 (m, 1H), 3.01 (t, J= 7 Hz, 1H), 2.52 (ddd, J= 16, 7, 2 Hz, 1H), 2.33-2.23 (m, 2H), 2.17 (q, J= 9 Hz, 2H), 2.02-1.96 (m, 1H), 1.68 (quint, J= 8 Hz, 2H), 1.05 (s, 9H).

^{13}C NMR (75 MHz, acetone-d_6) δ 180.1, 178.2, 154.1, 137.5, 136.3 (x4), 134.7 (x2), 132.6, 131.4, 130.7 (x2), 129.2 (x2), 128.7 (x4), 128.4 (x2), 128.1, 97.0, 96.7, 76.1, 72.6, 63.9, 55.7, 42.5, 42.1, 42.0, 37.1, 35.9, 32.7, 29.1, 27.3 (x3), 24.3, 19.8.

IR (neat) 3069, 2932, 2857, 1703, 1398, 1110 cm^{-1}.

EI HRMS indeterminable.

4.37



Current Data Parameters
NAME lmo_993
EXPNO 1
PROCNO 1

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Time 16.07
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PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 114
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

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

F2 - Processing parameters
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SF 300.1299968 MHz
WDW EM
SSB 0
LB 0.10 Hz
GB 0
PC 1.00

1D NMR plot parameters
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CY 60.00 cm
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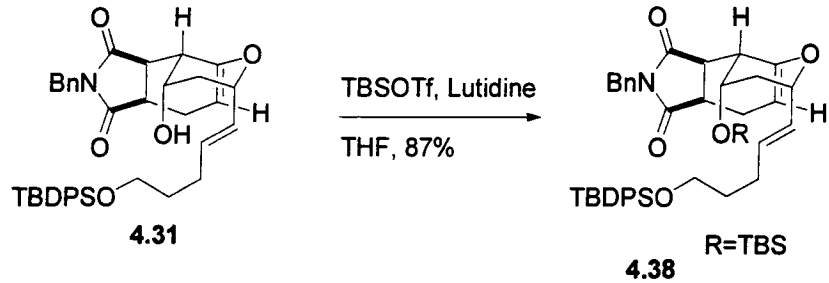
F2P -0.500 ppm
F2 -150.06 Hz
PPMCM 0.45000 ppm/cm
HZCM 135.05850 Hz/cm



4.31 **4.38**

2-Benzyl-9-(tert-butyl-dimethyl-silanyloxy)-7-[5-(tert-butyl-diphenyl-silanyloxy)-pent-1-enyl]-3 a,7,8,9,9a,9b-hexahydro-4H-pyrano[3,2-e]isoindole-1,3-dione (4.38)

To a solution of alcohol **4.31** (0.892 g, 1.405 mmol) in THF (14 mL) was added lutidine (0.49 mL, 4.2 mmol) then cooled to 0 °C. *t*-Butyldimethylsilyltriflate (0.39 mL, 1.69 mmol) was added and the reaction was stirred for 30 min. The reaction was quenched by adding $NaHCO_{3sat.}$ The aqueous layer was extracted 3 times with diethylether (3 X 30 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (15% EtOAc/hexanes) to afford 917 mg of **4.38** (87% yield) as a colourless oil.

Data for **4.38**

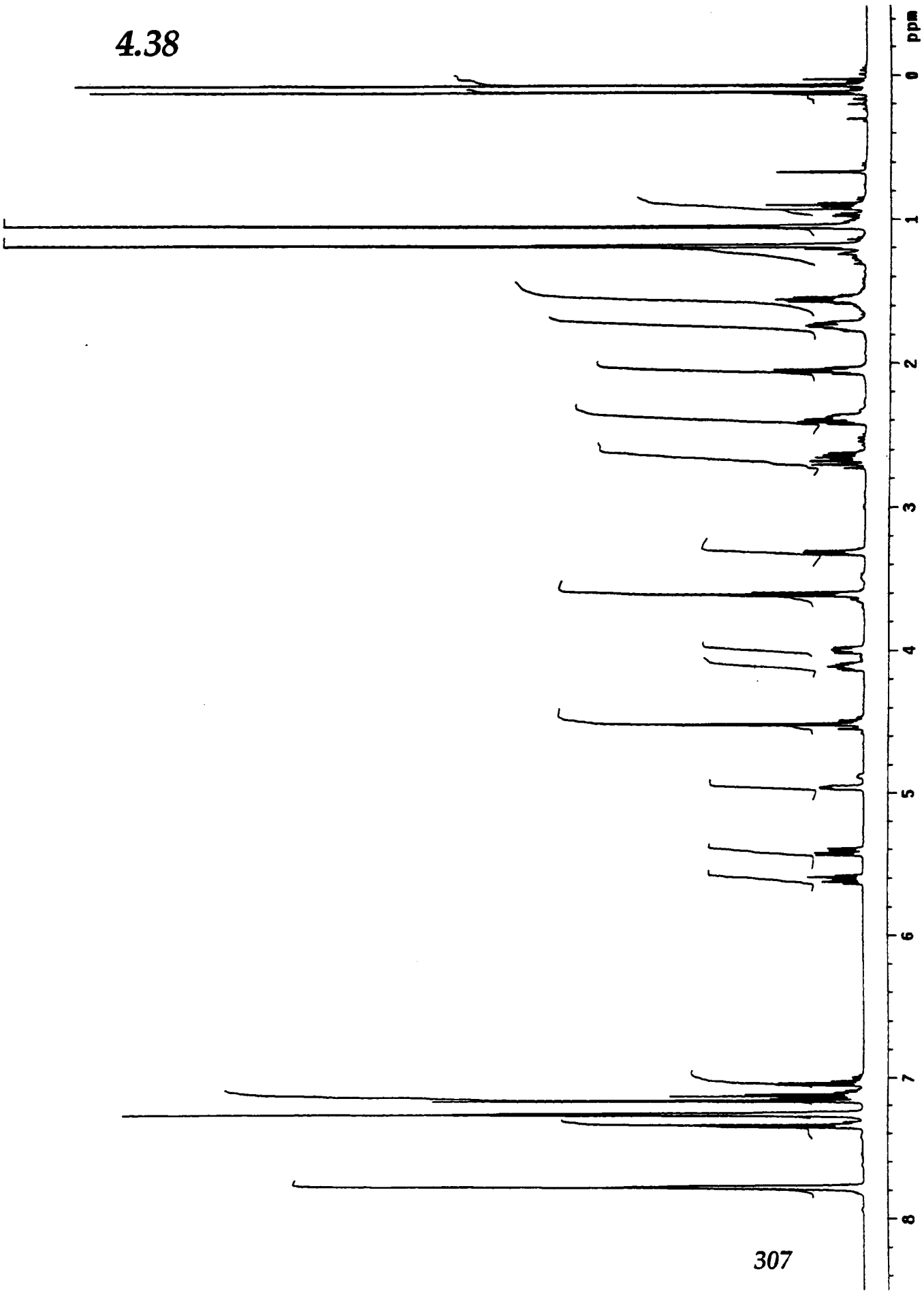
^{1}H NMR (500 MHz, C_6D_6): δ 7.81-7.77 (m, 4H), 7.35 (d, J= 7 Hz, 2H), 7.28-7.25 (m, 6H), 7.17 (t, J= 7 Hz, 2H), 7.04 (t, J= 7 Hz, 1H), 5.60 (dt, J= 15, 7 Hz, 1H), 5.41 (dd, J= 15, 7 Hz, 1H), 4.97-4.95 (m, 1H), 4.53 (d, J_{AB}= 14 Hz, 1H), 4.49 (d, J_{AB}= 14 Hz, 1H), 4.14-4.08 (m, 1H), 3.99 (dd, J= 11, 7 Hz, 1H), 3.61 (t, J= 6 Hz, 2H), 3.11 (dd, J= 9, 5 Hz, 1H), 2.69 (q, J= 12 Hz, 1H), 2.64 (ddd, J= 15, 8, 1 Hz, 1H), 2.40 (q, J= 9 Hz, 1H), 2.38-2.36 (m, 1H), 2.06 (q, J= 7 Hz, 2H), 1.77-1.71 (m, 2H), 1.55 (quint, J= 7 Hz, 2H), 1.19 (s, 9H), 1.05 (s, 9H), 0.75 (s, 3H), 0.12 (s, 3H).

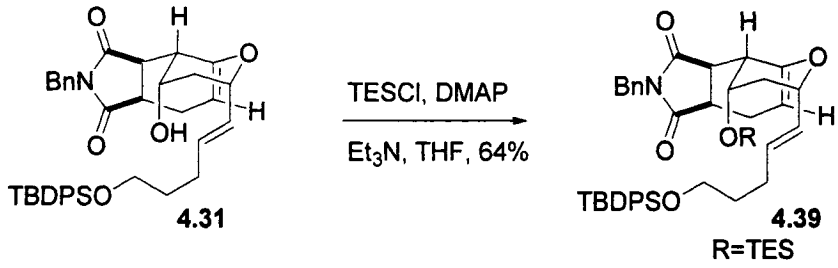
^{13}C NMR (125 MHz, C_6D_6) δ 179.0, 177.0, 154.3, 137.1, 136.3 (x4), 134.7, 132.8 (x2), 130.7, 130.3 (x2), 129.1 (x4), 129.0, 128.7 (x2), 128.0 (x2), 96.3, 76.9, 67.7, 63.9, 42.7, 42.3, 42.0, 39.2, 38.1, 32.5, 29.1, 27.5 (x3), 26.4 (x3), 25.2, 19.8, 14.7, -3.6, -4.2.

IR (neat) 2930, 2856, 1705, 1111 cm^{-1}.

MS ESI calcd for $C_{45}H_{59}NNaO_5Si_2$ (M^+ Na) 772.4, obsd. 772.6.

4.38





2-Benzyl-7-[5-(tert-butyl-diphenyl-silanyloxy)-pent-1-enyl]-9-triethylsilanyloxy-3a,7,8,9,9a,9b-hexahydro-4H-pyrano[3,2-e]isoindole-1,3-dione (4.39).

Alcohol **4.31** (0.033 g, 0.05 mmol) was dissolved in THF (1 mL). Triethylamine (0.042 mL, 0.3 mmol) and dimethylaminopyridine (0.001 g, 0.0045 mmol) were added, followed by triethylsilyl chloride (0.026 mL, 0.155 mmol). The reaction was stirred for 30 min. Saturated $NH_4Cl_{(aq)}$ was added. The aqueous layer was extracted 3 times with diethylether (3 X 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (10% EtOAc/hexanes) to afford 24 mg of **4.39** (64% yield) as a colourless oil.

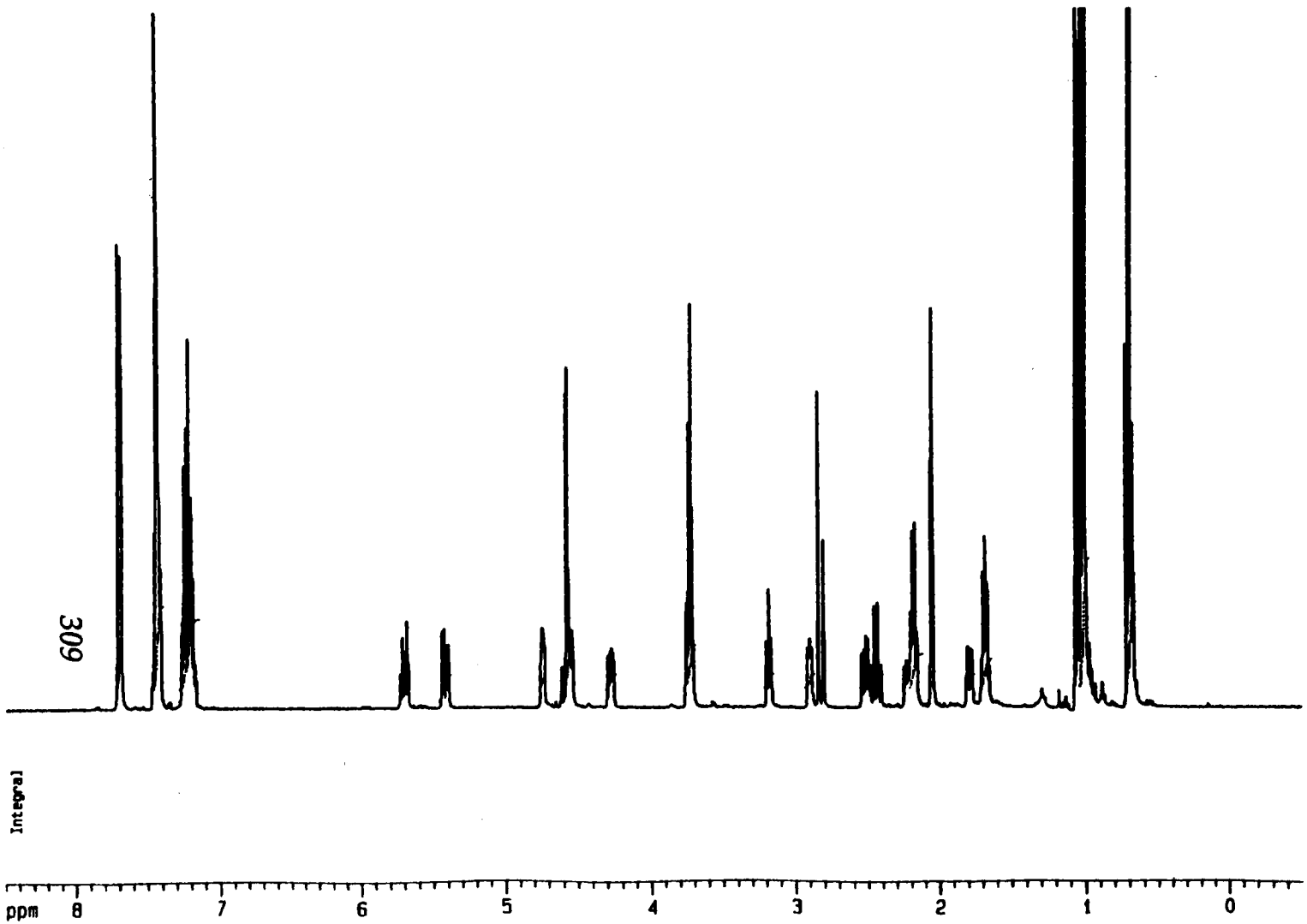
Data for **4.39**

1H NMR (500 MHz, acetone-d_6): δ 7.71 (dd, J= 7, 2 Hz, 4H), 7.48-7.42 (m, 6H), 7.27-7.18 (m, 5H), 5.71 (dt, J= 14, 6 Hz, 1H), 5.42 (dd, J= 15, 6 Hz, 1H), 4.76-4.73 (m, 1H), 4.61-4.53 (m, 3H), 4.28 (dd, J= 11, 6 Hz, 1H), 3.76-3.75 (m, 1H), 3.72 (t, J= 6 Hz, 2H), 3.20-3.16 (m, 1H), 2.91-2.80 (m, 1H), 2.51 (ddd, J= 15, 8, 1 Hz, 1H), 2.44 (q, J= 12 Hz, 1H), 1.81-1.77 (m, 1H), 1.68 (quint, J= 6 Hz, 2H), 1.05-1.00 (m, 3H), 1.05 (s, 9H), 1.00 (t, J= 8 Hz, 9H), 0.68 (q, J= 8 Hz, 6H).

13C NMR (125 MHz, acetone-d_6) δ 180.6, 178.4, 155.7, 138.0, 136.8 x4, 135.2 x2, 133.0, 131.8, 131.1, 129.7 (x2), 129.2 (x2), 128.7 (x4), 128.5 (x2), 96.2, 77.4, 68.0, 64.4, 43.2, 43.0, 42.9, 39.8, 38.9, 33.2, 29.6, 27.8 (x3), 25.8, 20.3, 7.8 (x3), 6.1 (x3).

IR (neat) 2954, 2874, 1705, 1112 cm^{-1}.

4.39



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PROCNO 1

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TD 65536
SOLVENT Acetone
NS 16
DS 0
SWH 7440.476 Hz
FIDRES 0.113533 Hz
AQ 4.4040694 sec
RG 90.51
DW 67.200 usec
DE 6.00 usec
TE 300.0 K
D1 0.01000000 sec

======== CHANNEL f1 ========
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P1 14.00 usec
PL1 0.00 dB
SFO1 500.1327786 MHz

F2 - Processing parameters
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SF 500.1300101 MHz
WDW EM
SSB 0
LB 0.00 Hz
GB 0
PC 1.00

1D NMR plot parameters
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CY 60.00 cm
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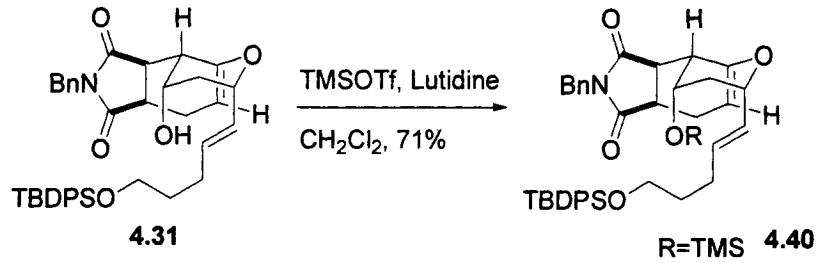
F1 4251.10 Hz
F2P -0.500 ppm
F2 -250.06 Hz
PPMCM 0.45000 ppm/cm
HZCM 225.05849 Hz/cm



4.31 **4.40**

2-Benzyl-7-[5-(tert-butyl-diphenyl-silanyloxy)-pent-1-enyl]-9-trimethylsilanyloxy-3a,7,8,9,9a,9b-hexahydro-4H-pyrano[3,2-e]isoindole-1,3-dione (4.40).

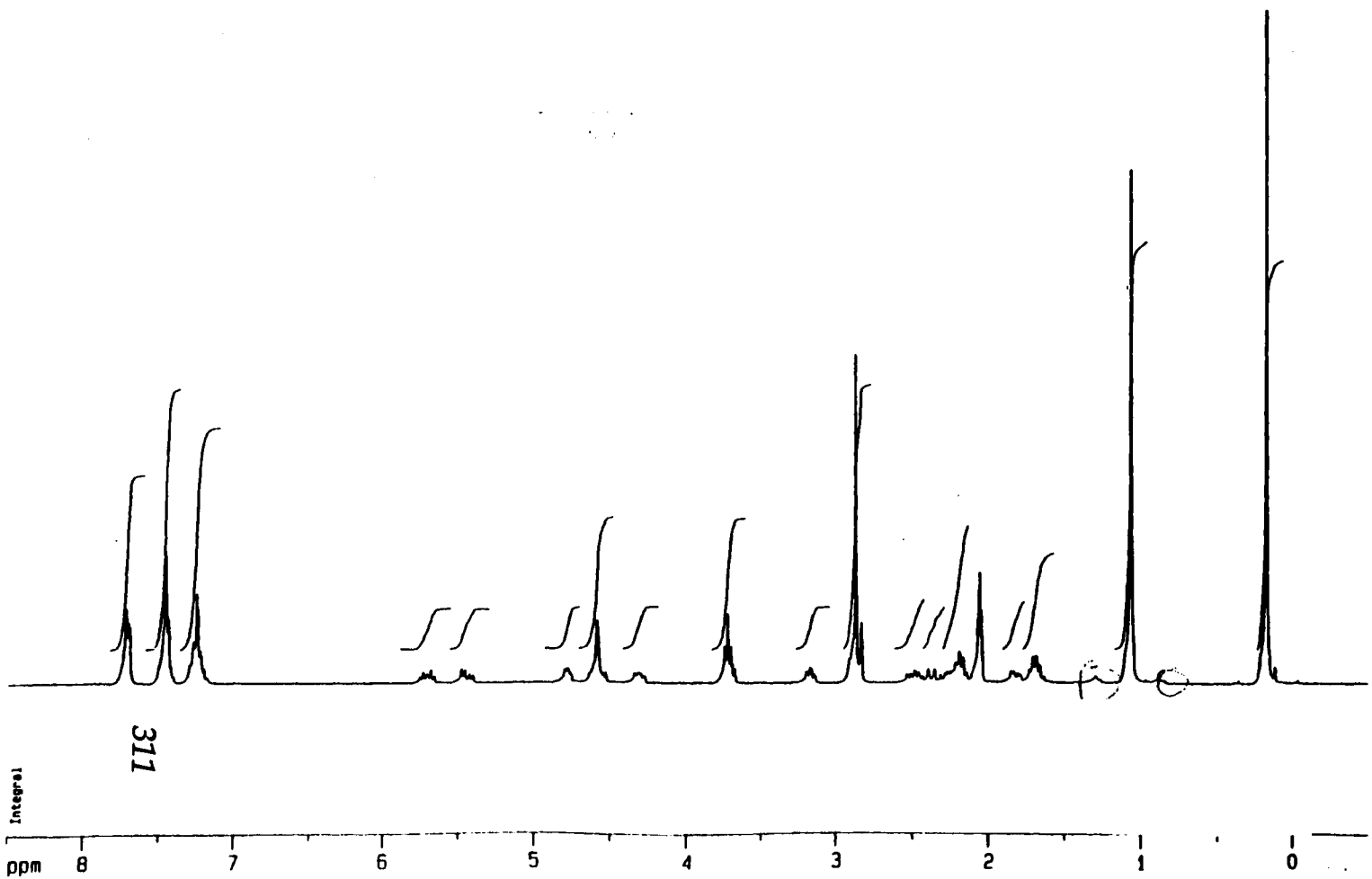
Alcohol **4.31** (0.015 g, 0.03 mmol) was dissolved in dichloromethane (1 mL) then cooled at 0°C. Lutidine (0.036 mL, 0.3 mmol) was added followed by trimethylsilyltriflate (0.011 mL, 0.06 mmol) and the reaction was stirred for 30 min. The reaction was quenched by adding $NaHCO_{3sat}$. The aqueous layer was extracted 3 times with dichloromethane (3 X 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (15% EtOAc/hexanes) to afford 15 mg of **4.40** (71% yield) as a colourless oil.

Data for **4.40**

^{1}H NMR (300 MHz, acetone-d_6): δ 7.72-7.69 (m, 4H), 7.46-7.41 (m, 6H), 7.29-7.20 (m, 5H), 5.70 (dt, J= 15, 7 Hz, 1H), 5.44 (dd, J= 15, 7 Hz, 1H), 4.79-4.76 (m, 1H), 4.63-4.52 (m, 3H), 4.30 (dd, J= 9, 7 Hz, 1H), 3.72 (t, J= 6 Hz, 2H), 3.69-3.67 (m, 1H), 3.24-3.13 (m, 1H), 2.91-2.90 (m, 1H), 2.49 (ddd, J= 15, 7, 2 Hz, 1H), 2.37 (q, J= 11 Hz, 1H), 2.28-2.14 (m, 4H), 1.81 (ddd, J= 13, 5, 2 Hz, 1H), 1.68 (quint, J= 7 Hz, 1H), 1.05 (s, 9H), 0.16 (s, 9H).

^{13}C NMR (75 MHz, acetone-d_6) δ 180.1, 178.5, 155.4, 137.9, 136.8 (x4), 135.1 (x2), 132.9, 131.8, 131.0 (x2), 129.6 (x2), 129.1 (x4), 128.7 (x2), 128.4, 96.7, 77.3, 67.9, 64.3, 42.9, 42.8, 42.6, 39.5, 38.9, 33.1, 29.6, 27.7 (x3), 25.5, 20.2, 0.8 (x3).

IR (neat) 2936, 2857, 1704, 1397, 1111 cm^{-1}.



4.40

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PROCNO 1

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SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 287.4
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

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

F2 - Processing parameters
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SF 300.1299965 MHz
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SSB 0
LB 0.10 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 20.00 cm
CY 10.00 cm
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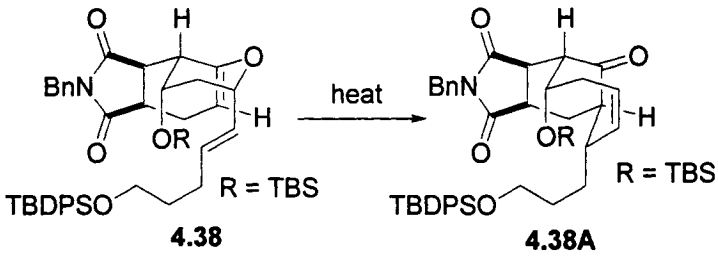
F1 2551.10 Hz
F2P -0.500 ppm
F2 -150.06 Hz
PPMCM 0.45000 ppm/cm
HZCM 135.05850 Hz/cm



4-Benzyl-13-(tert-butyl-dimethyl-silanyloxy)-9-[3-(tert-butyl-diphenyl-silanyloxy)-propyl]-4-aza-tricyclo[6.5.1.02,6]tetradec-10-ene-3,5,14-trione (4.38A)

A solution of alcohol **4.38** (0.01 g, 0.013 mmol) and triethylamine (0.05 mL) in acetonitrile (14 mL) was degassed with argon. The mixture was heated gradually, using microwaves, to 170 °C for 5 min and maintained at 170 °C for 60 min. The reaction was cooled and concentrated. The crude product was purified by flash silica column chromatography (5 % EtOAc/hexanes) to afford 3 mg of **4.38A** (30%) as a colourless oil.

Data for **4.38A**

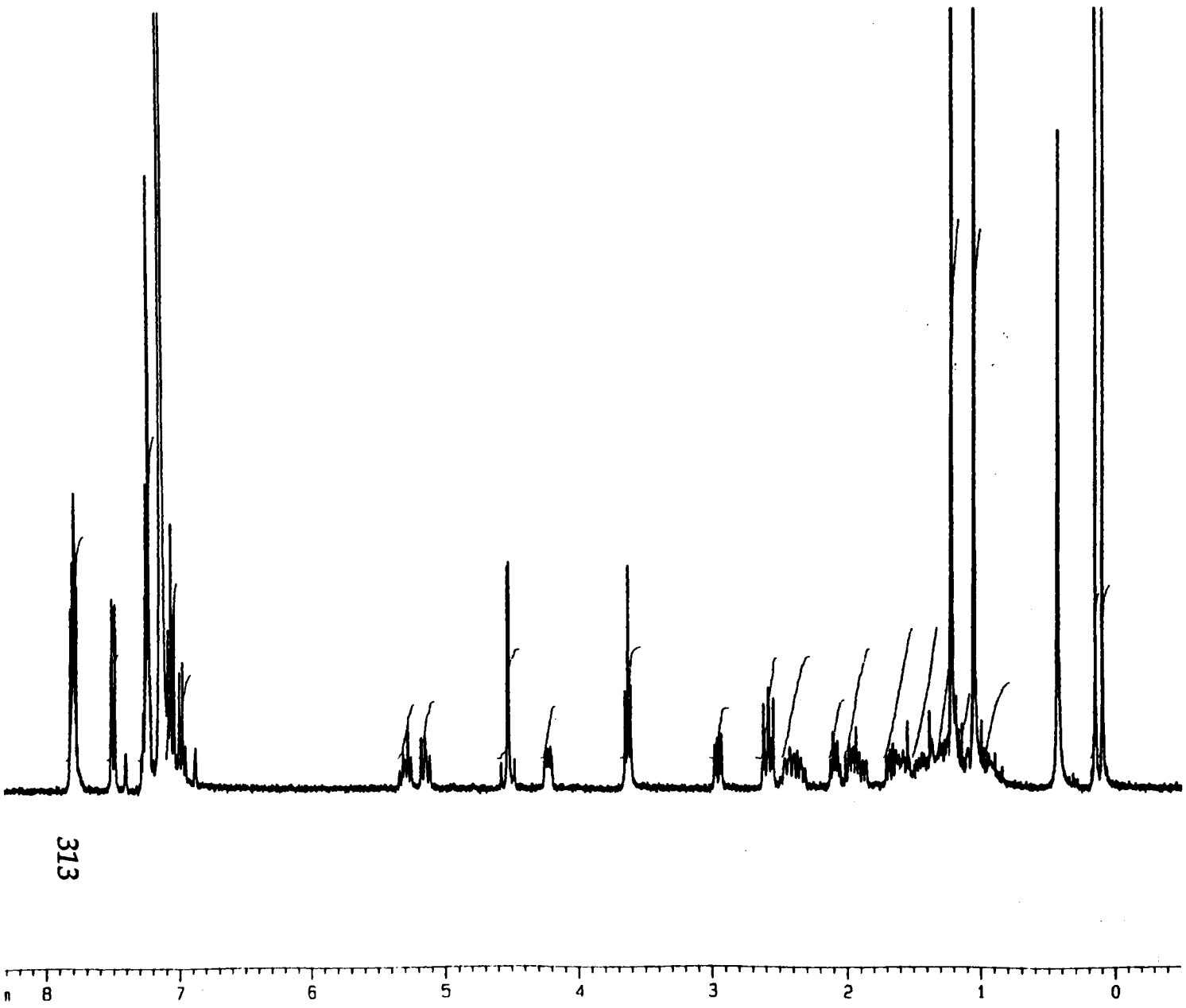
^{1}H NMR (300 MHz, C_6D_6): δ 7.84-7.80 (m, 4H), 7.52 (dd, J= 8, 1 Hz, 2H), 7.31-7.23 (m, 5H), 7.11-7.06 (m, 3H), 7.02-6.97 (m, 1H), 5.35-5.26 (m, 1H), 5.16 (dd, J= 11, 9 Hz, 1H), 4.56 (d, J_{AB}= 13 Hz, 1H), 4.50 (d, J_{AB}= 13 Hz, 1H), 4.25-4.21 (m, 1H), 3.63 (t, J= 6 Hz, 1H), 2.95 (dd, J= 11, 5 Hz, 1H), 2.63-2.55 (m, 2H), 2.52-2.32 (m, 2H), 2.09 (dt, J= 10, 6 Hz, 1H), 2.01-1.85 (m, 2H), 1.70-1.53 (m, 2H), 1.50-1.21 (m, 2H), 1.22 (s, 9H), 1.19-1.09 (m, 1H), 1.05 (s, 9H), 1.01-0.84 (m, 1H), 0.15 (s, 3H), 0.09 (s, 3H).

^{13}C NMR (75 MHz, C_6D_6) δ 210.2, 178.4, 175.3, 136.7, 136.5, 136.4 (x4), 134.8 (x2), 130.4, 130.3 (x4), 129.2 (x2), 128.5 (x4), 127.3, 72.1, 64.7, 55.2, 54.1, 43.3, 41.0, 37.7, 37.0, 35.1, 31.0, 30.1, 27.5, 27.0, 26.6 (x3), 19.9, 18.8, -4.2, -4.5.

IR (neat) 2926, 2954, 1707, 1110 cm^{-1}.

MS ESI calcd for $C_{45}H_{59}NNaO_5Si_2$ (M^+ Na) 772.4, obsd.772.6.

4.38A



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PROCNO	1

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FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	512
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

NUC1	1H
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PL1	-3.00 dB
SFO1	300.1319477 MHz

F2 - Processing parameters

SI	65536
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SSB	0
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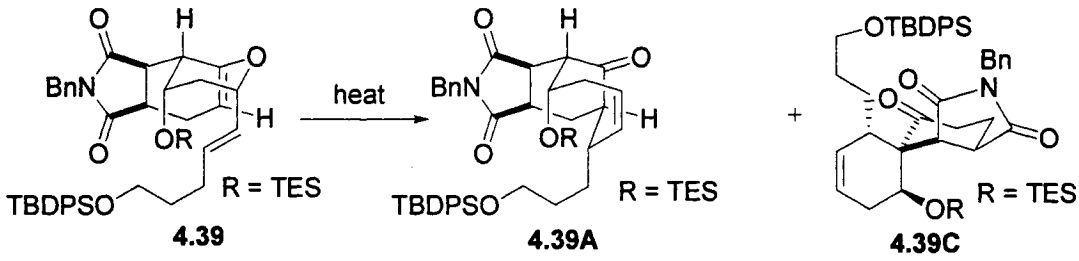
GB	0
PC	1.00

1D NMR plot parameters

CX	20.00 cm
CY	100.00 cm
F1P	8.500 ppm
F1	2551.10 Hz
F2P	-0.500 ppm
F2	-150.06 Hz
PPMCM	0.45000 ppm/cm
HZCM	135.05850 Hz/cm



A solution of alcohol **4.39** (0.06 g, 0.08 mmol) and triethylamine (0.03 mL) in toluene (14 mL) was degassed with argon. The mixture was heated at 170°C for 15 h in a wax bath. The reaction was cooled and concentrated. The crude product was purified by flash silica column chromatography (15% EtOAc/hexanes) to afford 24 mg of **4.39A** (40%) as a colourless oil and 9 mg of **4.39C** (15%) as white crystals mp = 158.5-158.9 °C.

4-Benzyl-9-[3-(tert-butyl-diphenyl-silanyloxy)-propyl]-13-triethylsilanyloxy-4-aza-tricyclo[6.5.1.02,6]tetradec-10-ene-3,5,14-trione (4.39A).

^{1}H NMR (500 MHz, C_6D_6): δ 7.82-7.79 (m, 4H), 7.52 (d, J= 7 Hz, 2H), 7.32-7.23 (m, 6H), 7.10 (t, J= 8 Hz, 2H), 7.02 (t, J= 7 Hz, 1H), 5.30-5.25 (m, 1H), 5.23-5.19 (m, 1H), 4.60 (s, 2H), 4.38-4.36 (m, 1H), 3.64 (t, J= 6 Hz, 2H), 2.88 (dd, J= 11, 5 Hz, 1H), 2.67-2.61 (m, 1H), 2.58-2.52 (m, 1H), 2.51 (t, J= 10 Hz, 1H), 2.33 (dt, J= 17, 7 Hz, 1H), 2.10 (q, J= 7 Hz, 1H), 2.02 (q, J= 160-150 Hz, 3H), 1.60-1.50 (m, 1H), 1.40-1.35 (m, 1H), 1.23-1.15 (m, 2H), 1.21 (s, 9H), 1.02 (t, J= 8 Hz, 9H), 0.65-0.62 (m, 6H) .

^{13}C NMR (125 MHz, C_6D_6) δ 211.1, 178.2, 175.8, 136.9, 136.4 (x4), 135.6, 134.8 (x2), 130.3 (x2), 130.2, 129.2 (x2), 128.7 (x2), 128.5 (x4), 127.1, 69.1, 64.7, 54.6, 53.0, 43.1, 41.6, 40.0, 36.0, 35.6, 31.4, 31.1, 29.1, 27.5 (x3), 19.9, 7.7 (x3), 5.6 (x3).

IR (neat) 2953, 2876, 1706, 1110, 1089 cm^{-1}.

Spiro 4.39C

^{1}H NMR (500 MHz, C_6D_6): δ 7.80 (t, J= 8 Hz, 4H), 7.54 (d, J= 7 Hz, 2H), 7.34 (t, J= 7 Hz, 2H), 7.32-7.27 (m, 4H), 7.11 (t, J= 7 Hz, 2H), 7.04 (t, J= 8 Hz, 1H), 5.36-5.34 (m, 1H), 4.92-4.90 (m, 1H), 4.87 (dd, J= 10, 8 Hz, 1H), 4.58 (d, J_{AB}= 13 Hz, 1H), 4.50 (d, J_{AB}= 13 Hz, 1H),

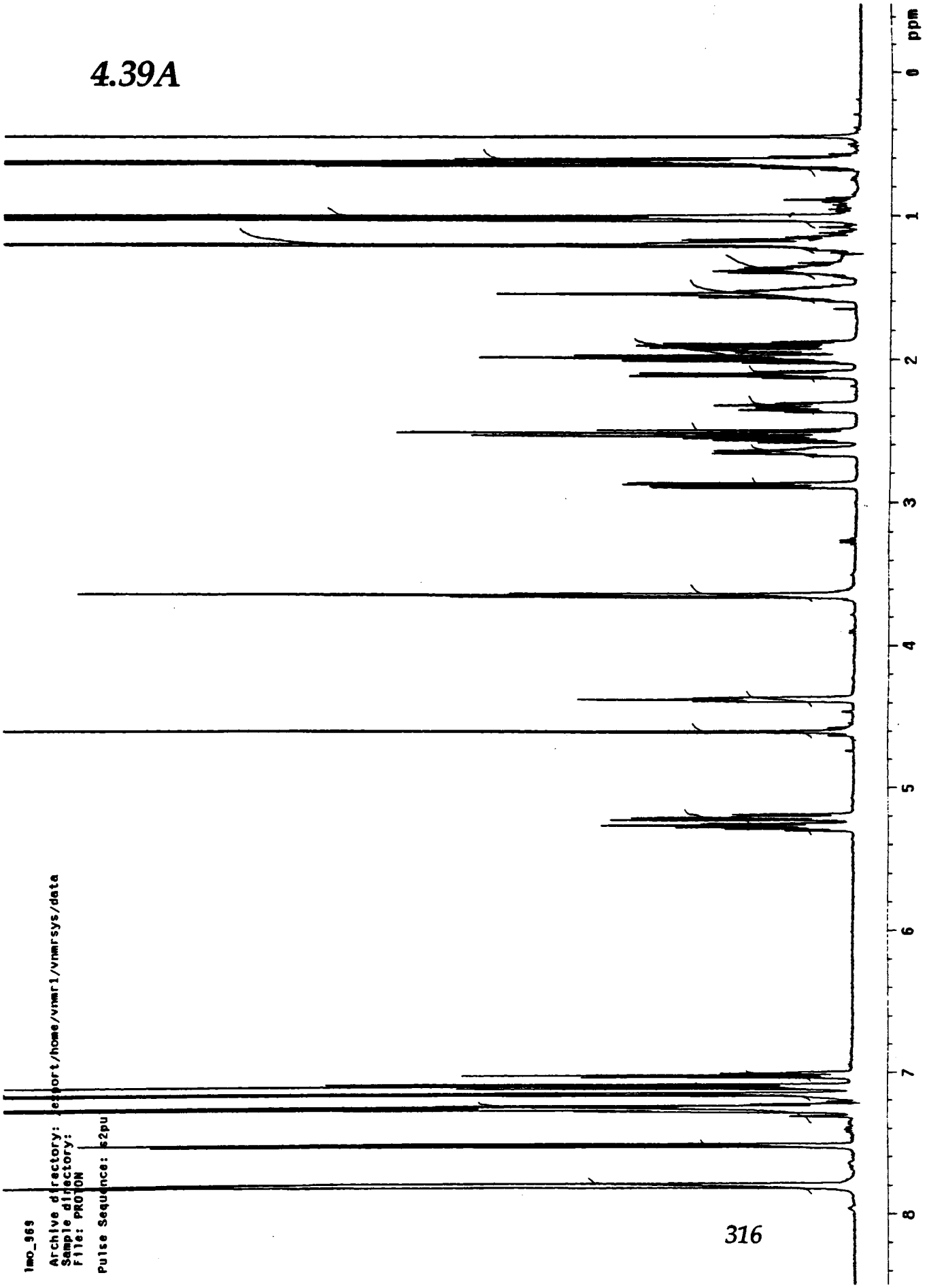
3.56-3.49 (m, 2H), 3.44 (d, J= 9 Hz, 1H), 2.93 (dd, J= 16, 10 Hz, 1H), 2.33-2.24 (m, 3H), 2.15 (dt, J= 17, 4 Hz, 1H), 1.96-1.85 (m, 2H), 1.9 (s, 9H), 1.82-1.75 (m, 1H), 1.53-1.45 (m, 1H), 1.44-1.37 (m, 1H), 1.26-1.13 (m, 2H), 1.08 (t, J= 8 Hz, 9H), 0.71 (sept, J=8 Hz, 6H).

^{13}C NMR (125 MHz, C_6D_6) δ 208.1, 178.4, 176.6, 137.3, 136.4 (x4), 134.6 (x2), 130.3 (x2), 130.2 (x2), 129.1 (x2), 128.7 (x4), 128.4, 126.7, 126.6, 67.5, 63.9, 58.2, 42.9, 41.9, 40.6, 39.3, 38.4, 33.2, 30.9, 30.7,27.5 (x3), 19.9, 19.8, 7.7 (x3), 5.8 (x3).

IR (neat) 2954, 1707, 1095 cm^{-1}

MS ESI calcd for $C_{45}H_{59}NNaO_5Si_2$ (M^+ Na) 772.4, found 772.1.

4.39A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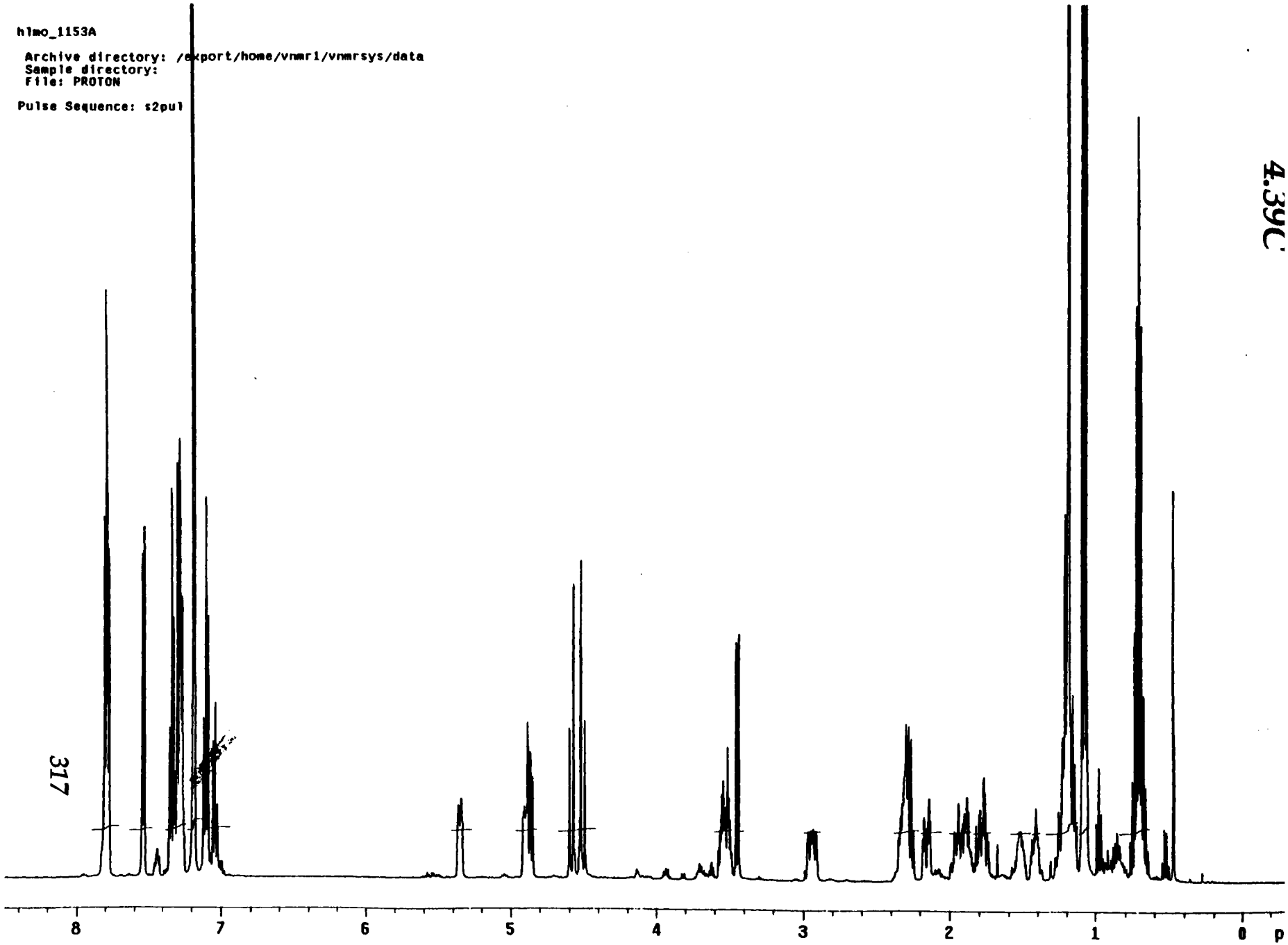
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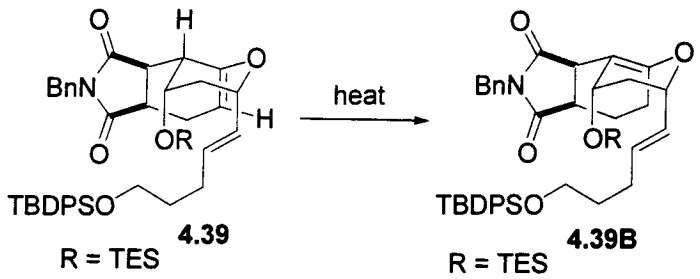


A solution of alcohol **4.39** (0.010 g, 0.013 mmol) and triethylamine (0.01 mL) in THF (4 mL) was degassed with argon. The mixture was heated to 170 °C for 15 h in a wax bath. The reaction was cooled and concentrated. The crude product was purified by flash silica column chromatography (10% EtOAc/hexanes) to afford 9 g of **4.39B** (90% yield) as a colourless oil.

Data for **4.39B**

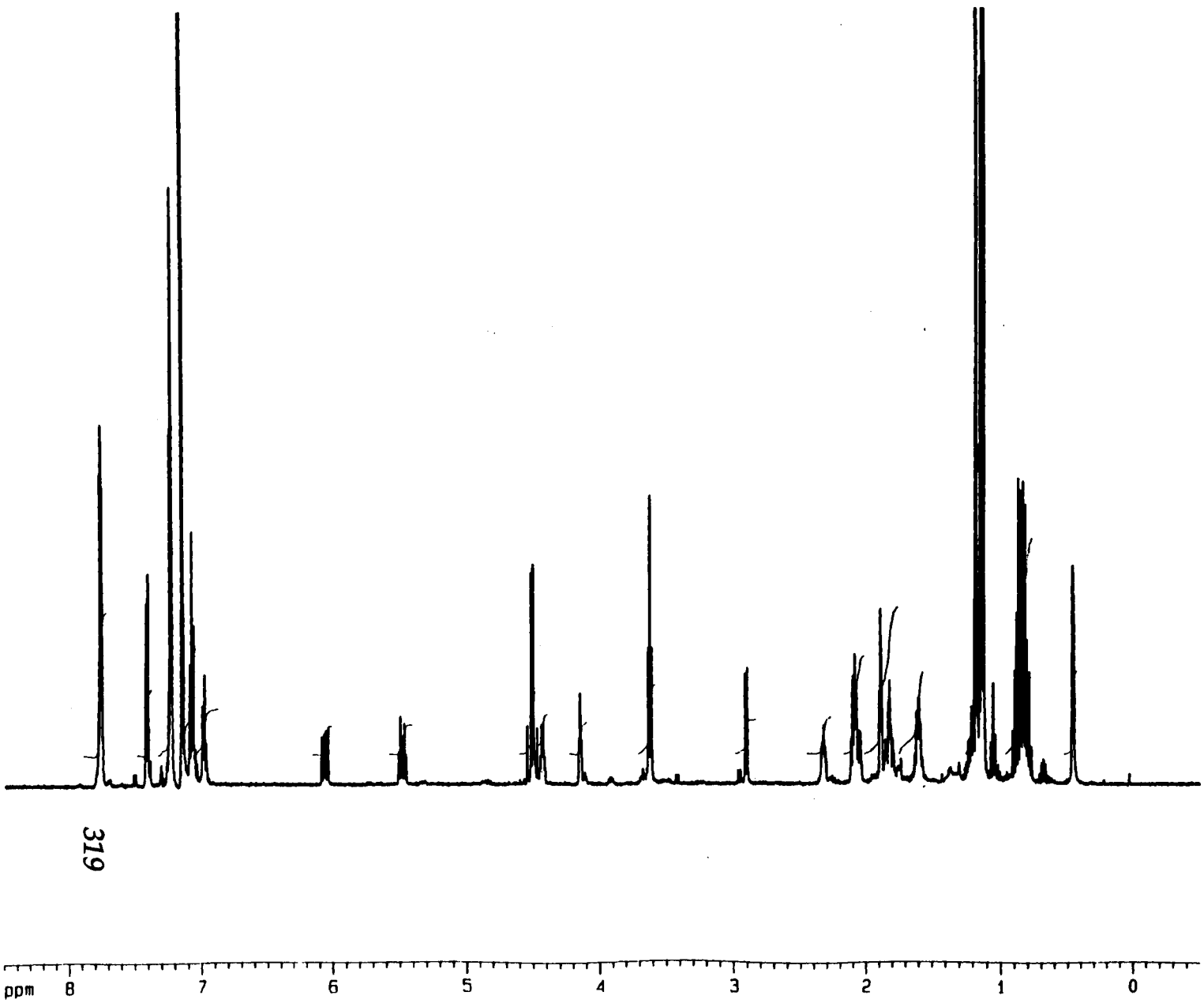
^{1}H NMR (500 MHz, C_6D_6): δ 7.80-7.75 (m, 4H), 7.42 (d, J= 7 Hz, 2H), 7.25-7.25 (m, 6H), 7.09 (t, J= 8 Hz, 2H), 7.06-6.98 (m, 1H), 6.06 (dd, J= 15, 8 Hz, 1H), 5.49 (dt, J= 15, 8 Hz, 1H), 4.52 (d, J_{AB}= 14 Hz, 1H), 4.48 (d, J_{AB}= 14 Hz, 1H), 4.45-4.42 (m, 1H), 4.15-4.14 (m, 1H), 3.62 (t, J= 6 Hz, 2H), 2.90 (d, J= 8 Hz, 1H), 2.34-2.30 (m, 1H), 2.11-2.04 (m, 3H), 1.89 (t, J= 5 Hz, 2H), 1.86-1.79 (m, 3H), 1.63-1.57 (m, 2H), 1.18 (s, 9H), 1.13 (t, J= 23 Hz, 9H), 0.89-0.80 (m, 6H).

^{13}C NMR (125 MHz, C_6D_6) δ 178.1, 176.0, 152.6, 137.5, 136.4 (x4), 134.7 (x2), 132.6, 130.3 (x3), 129.2 (x2), 129.1 (x2), 128.4 (x4), 128.2, 102.4, 75.9, 65.6, 64.1, 44.9, 42.6, 41.1, 38.3, 32.8, 29.4, 27.5 (x3), 25.8, 23.5, 19.8, 7.9 (x3), 6.0 (x3).

IR (neat) 2944, 2875, 1710 cm^{-1}.

MS ESI calcd for $C_{45}H_{59}NNaO_5Si_2$ (M^+ Na) 772.4, obsd. 773.4.

4.39B



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PROCNO 1

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SOLVENT Acetone
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SWH 7440.476 Hz
FIDRES 0.113533 Hz
AQ 4.4040694 sec
RG 203.2
DW 67.200 usec
DE 6.00 usec
TE 300.0 K
D1 0.01000000 sec

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

F2 - Processing parameters
SI 65536
SF 500.1300181 MHz
WDW EM
SSB 0
LB 0.00 Hz
GB 0
PC 1.00

1D NMR plot parameters
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CY 50.00 cm
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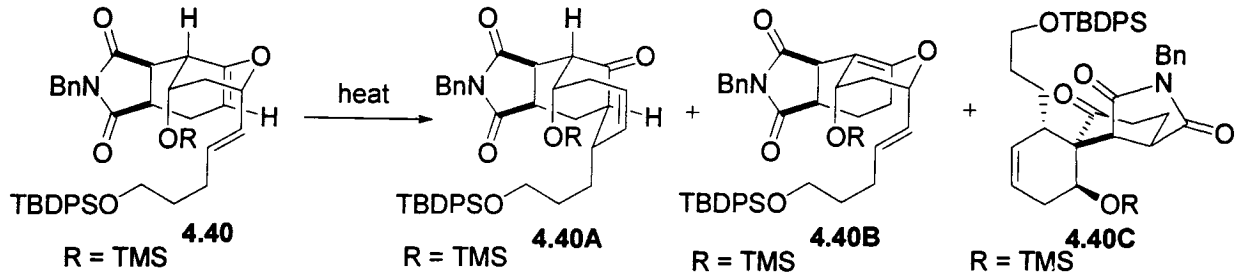
F2P -0.500 ppm
F2 -250.06 Hz
PPMCM 0.45000 ppm/cm
HZCM 225.05849 Hz/cm



A solution of alcohol **4.40** (0.03 g, 0.04 mmol) and triethylamine (0.03 mL) in toluene (20 mL) was degassed with argon. The mixture was heated to 170 °C for 15 h in a wax bath. The reaction was cooled and concentrated. The crude product was purified by flash silica column chromatography (25% EtOAc/hexanes) to afford 50 mg of **4.40A** (42% yield) as a light yellow oil and 13 mg of **4.40C** (30%) as a yellow oil.

4-Benzyl-9-[3-(tert-butyl-diphenyl-silanyloxy)-propyl]-13-trimethylsilanyloxy-4-aza-tricyclo[6.5.1.02,6]tetradec-10-ene-3,5,14-trione (4.40A).

^{1}H NMR (500 MHz, C_6D_6): δ 7.88-7.86 (m, 4H), 7.58 (d, J= 7 Hz, 2H), 7.37-7.36 (m, 6H), 7.23 (t, J= 8 Hz, 2H), 7.15 (t, J= 7 Hz, 1H), 5.37-5.33 (m, 1H), 5.30-5.26 (m, 1H), 4.72 (d, J= 4 Hz, 1H), 4.68 (d, J= 4 Hz, 1H), 4.51-4.49 (m, 1H), 3.73-3.69 (m, 2H), 2.87-2.84 (m, 2H), 2.61-2.54 (m, 2H), 2.30-2.16 (m, 3H), 2.07 (dd, 18, 5 Hz, 1H), 1.69-1.53 (m, 3H), 1.41-1.31 (m, 1H), 1.26 (s, 9H), 1.01 (dt, J= 33, 7 Hz, 1H), 0.12 (s, 9H).

^{13}C NMR (125 MHz, C_6D_6) δ 212.3, 178.2, 176.4, 137.1, 136.3 (x4), 134.7 (x2), 134.6, 130.3 (x2), 129.9 (x2), 129.2 (x2), 128.7, 128.4 (x4), 126.5, 67.0, 64.5, 54.1, 51.4, 43.0, 42.5, 42.1, 37.0, 35.1, 31.9, 31.8, 31.1, 27.5 (x3), 19.8, 0.5 (x3).

IR (neat) 3070, 2933, 2858, 1706, 1395, 1110 cm^{-1}.

Spiro (4.40C).

1H NMR (300 MHz, C_6D_6): δ 7.82-7.74 (m, 4H), 7.53 (d, J= 7 Hz, 2H), 7.36-7.26 (m, 6H), 7.13-7.01 (m, 3H), 5.36-5.32 (m, 1H), 4.98-4.93 (m, 1H), 4.82 (dd, J= 10, 7 Hz, 1H), 4.58 (d, J= 14 Hz, 1H), 4.50 (d, J= 14 Hz, 1H), 3.57-3.47 (m, 2H), 3.38 (d, J= 9 Hz, 1H), 2.87-

2.78 (m, 1H), 2.42-2.21 (m, 3H), 2.16-2.03 (m, 2H), 2.02-1.84 (m, 2H), 1.81-1.67 (m, 1H), 1.62-1.34 (m, 3H), 1.19 (s, 9H), 0.21 (s, 9H).

^{13}C NMR (75 MHz,C_6D_6) δ 208.3, 178.5, 176.7, 137.3, 136.4 (x4), 134.6 (x2), 130.3 (x4), 130.1 (x2), 129.2, 129.1 (x4), 126.9, 126.4, 67.9, 64.0, 58.0, 42.9, 42.0, 40.6, 40.6, 39.2, 38.4, 33.2, 30.8, 30.7, 27.5 (x3), 20.3, 19.8, 0.9 (x3).

IR (neat) 2959, 2858, 1703, 1110 cm^{-1}.

MS EI calcd for $C_{38}H_{44}NO_5Si_2$ (M^+ -*t*Bu) 650.27580, found 650.27348.

A solution of alcohol **4.40** (0.033 g, 0.05 mmol) and triethylamine (0.05 mL) in toluene (14 mL) was degassed with argon. The mixture was heated gradually to 170 °C for 5 min and maintained at 170 °C for 30 min. The reaction was cooled and concentrated. The crude product was purified by flash silica column chromatography (20 % EtOAc/hexanes EtOAc/hexanes) to afford 21 mg of **4.40A** (65%) as a light yellow oil and 5 g of **4.40B** (14% yield) as a colorless oil.

2-Benzyl-7-[5-(tert-butyl-diphenyl-silanyloxy)-pent-1-enyl]-9-trimethylsilanyloxy-3a,5,7,8,9,9b-hexahydro-4H-pyrano[3,2-e]isoindole-1,3-dione (4.40B).

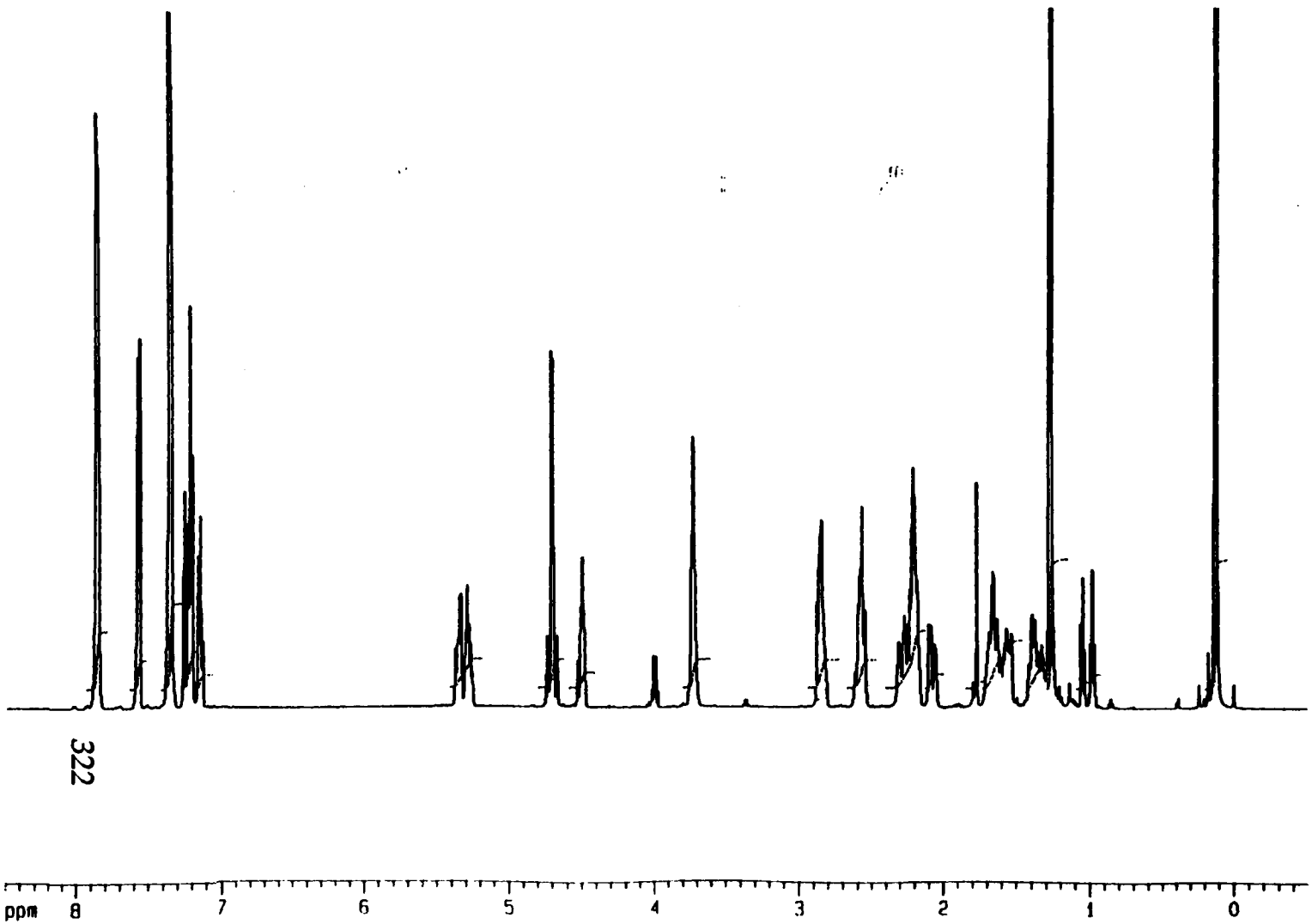
1H NMR (500 MHz, C_6D_6): δ 7.83-7.79 (m, 4H), 7.44 (d, J= 7 Hz, 2H), 7.28-7.26 (m, 6H), 7.13 (t, J= 7 Hz, 2H), 7.03 (t, J= 7 Hz, 1H), 6.14 (dd, J= 15,9 Hz, 1H), 5.47 (dt, J= 14,6 Hz, 1H), 4.55 (d, J_{AB}= 14 Hz, 1H), 4.49 (d, J_{AB}= 14 Hz, 1H), 4.48-4.47 (m, 1H), 4.14 (t, J= 3 Hz, 1H), 3.65 (t, J= 6 Hz, 2H), 2.81 (d, J= 8 Hz, 1H), 2.31-2.27 (m, 1H), 2.09 (q, J= 7 Hz, 2H), 2.02-1.95 (m, 1H), 1.82-1.75 (m, 4H), 1.68-1.61 (m, 3H), 1.20 (s, 9H), 0.35 (s, 9H).

^{13}C NMR (125 MHz, C_6D_6) δ 177.2, 175.5, 151.5, 136.7, 135.6 (x4), 134.0 (x2), 131.3, 130.1, 129.6 (x2), 128.4 (x2), 128.3 (x2), 128.2, 127.9 (x4), 101.3, 75.0, 64.5, 64.1, 44.6, 41.7, 40.4, 36.9, 32.1, 28.5, 26.7 (x3), 24.9, 21.3, 19.1, 0.4 (x3).

IR (neat) 2931, 2857, 1709, 1110 cm^{-1}.

EI HRMS calcd for $C_{38}H_{44}NO_5Si$ (M^+ -*t*Bu) 650.27580, obsd 650.27368.

4.40A



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TE	300.0 K
D1	0.01000000 sec

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

NUC1	1H
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PL1	3.00 dB
SFO1	500.1327766 MHz

F2 - Processing parameters

SI	65536
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1D NMR plot parameters

CX	20.00 cm
CY	60.00 cm
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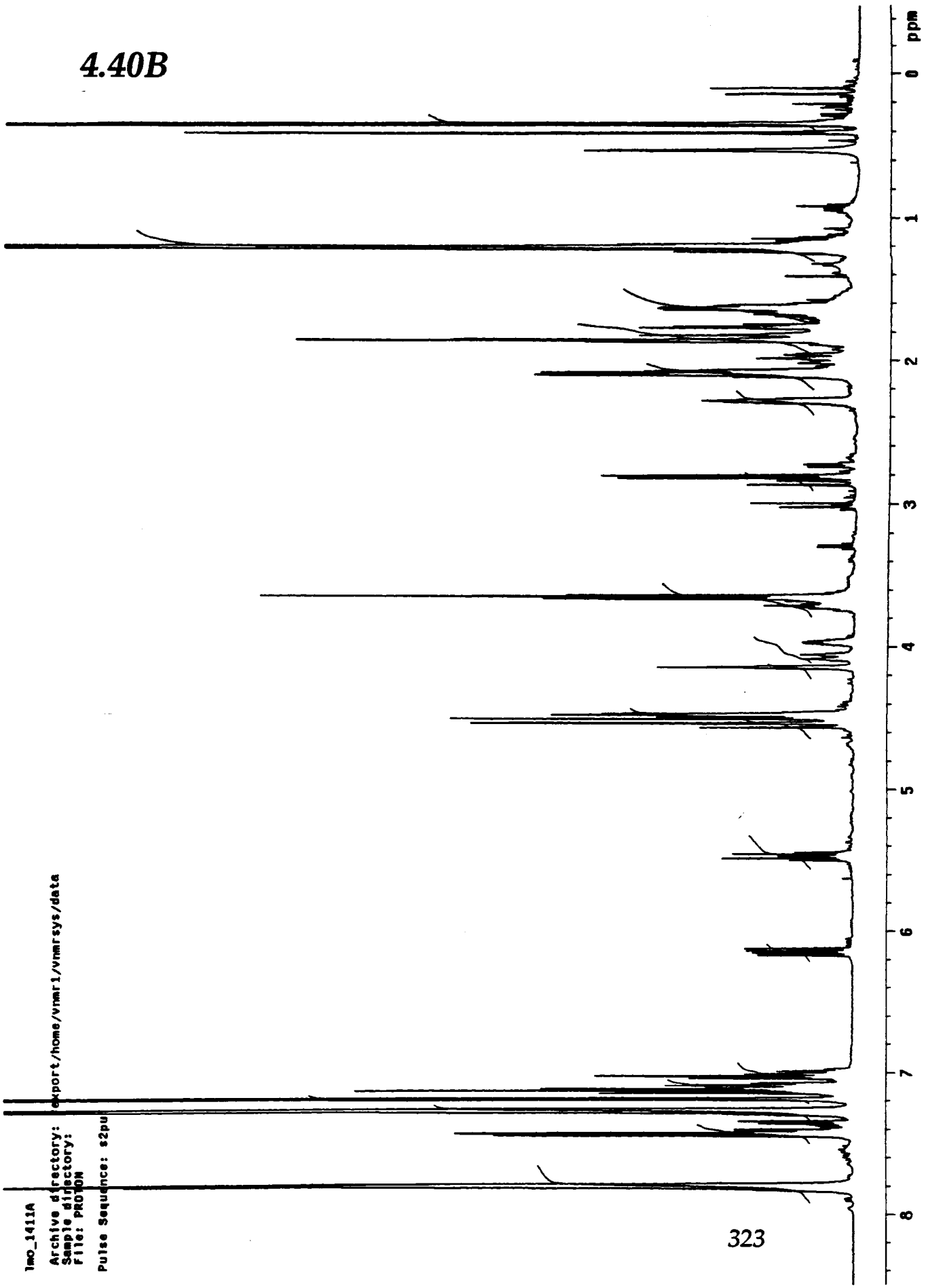
F2	-250.06 Hz
PPMCM	0.45000 ppm/cm
HZCM	225.05849 Hz/cm

4.40B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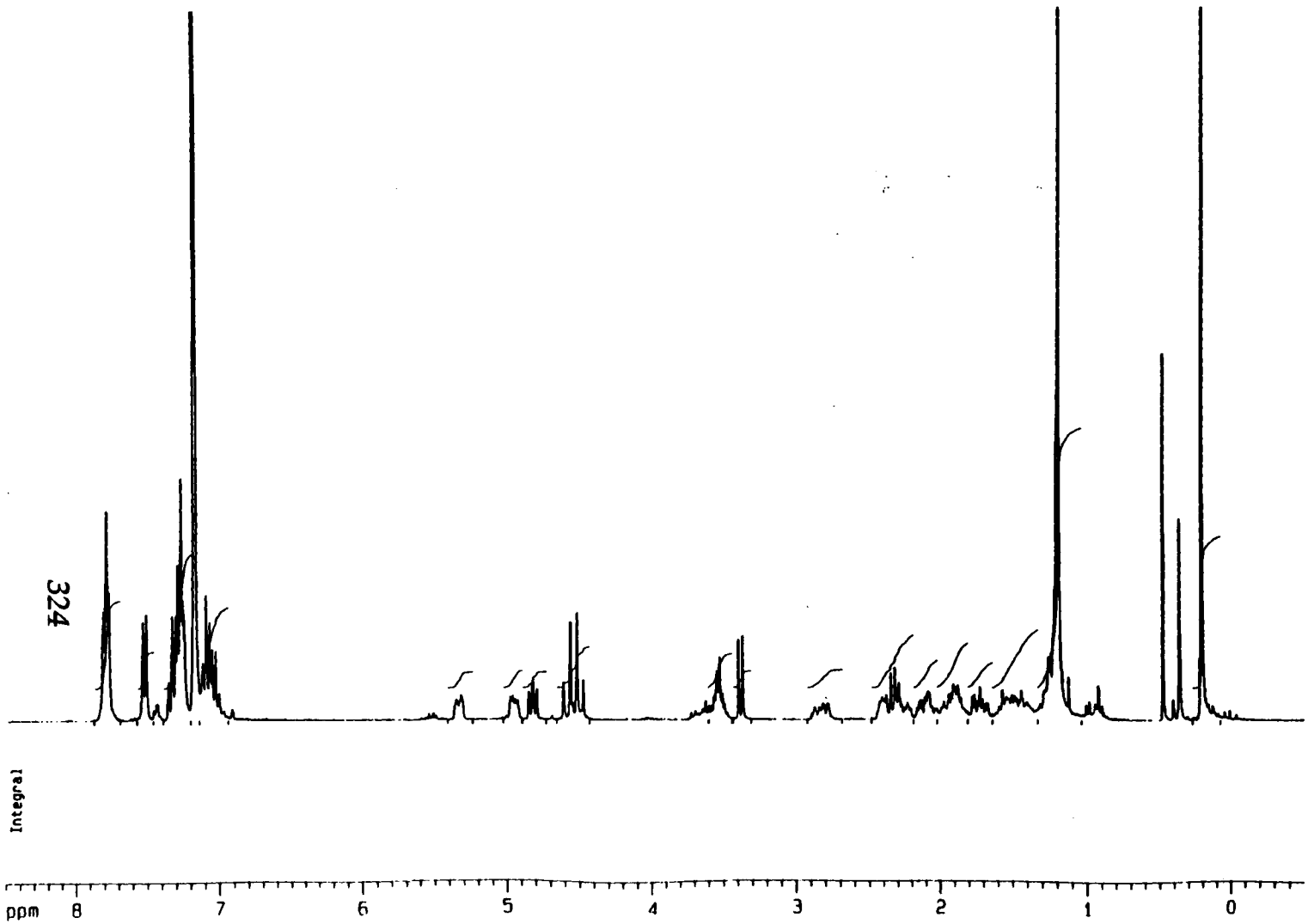
4.40C



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RG	287.4
DW	98.400 usec
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TE	300.0 K
D1	1.00000000 sec

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

NUC1	1H
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PL1	-3.00 dB
SFO1	300.1319477 MHz

F2 - Processing parameters

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SF	300.1300000 MHz
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1D NMR plot parameters

CX	20.00 cm
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F2P	-0.500 ppm
F2	-150.06 Hz
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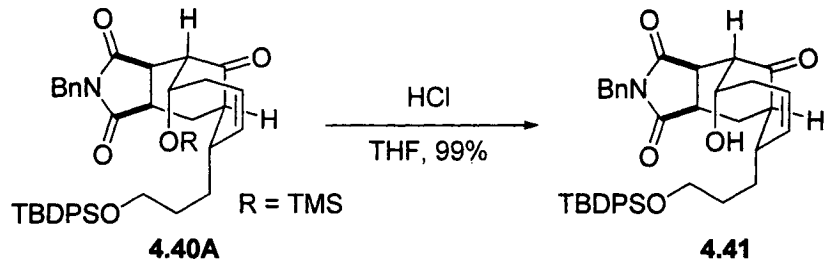
HZCM	135.05850 Hz/cm



4.40A **4.41**

4-Benzyl-9-[3-(tert-butyl-diphenyl-silanyloxy)-propyl]-13-hydroxy-4-aza-tricyclo[6.5.1.02,6]tetradec-10-ene-3,5,14-trione (4.41). Compound **4.40A** (0.039 g, 0.06 mmol) was dissolved in THF (1 mL). 2N HCl (0.1 mL) was added and stirred for 30 min at room temperature. The reaction was quenched by adding $NaHCO_{3sat}$. The aqueous layer was extracted 3 times with diethylether (3 X 15 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash silica column chromatography (40% EtOAc/hexanes) to afford 15 mg of **4.41** (99% yield) as white crystals mp = 133.3-134.4 °C.

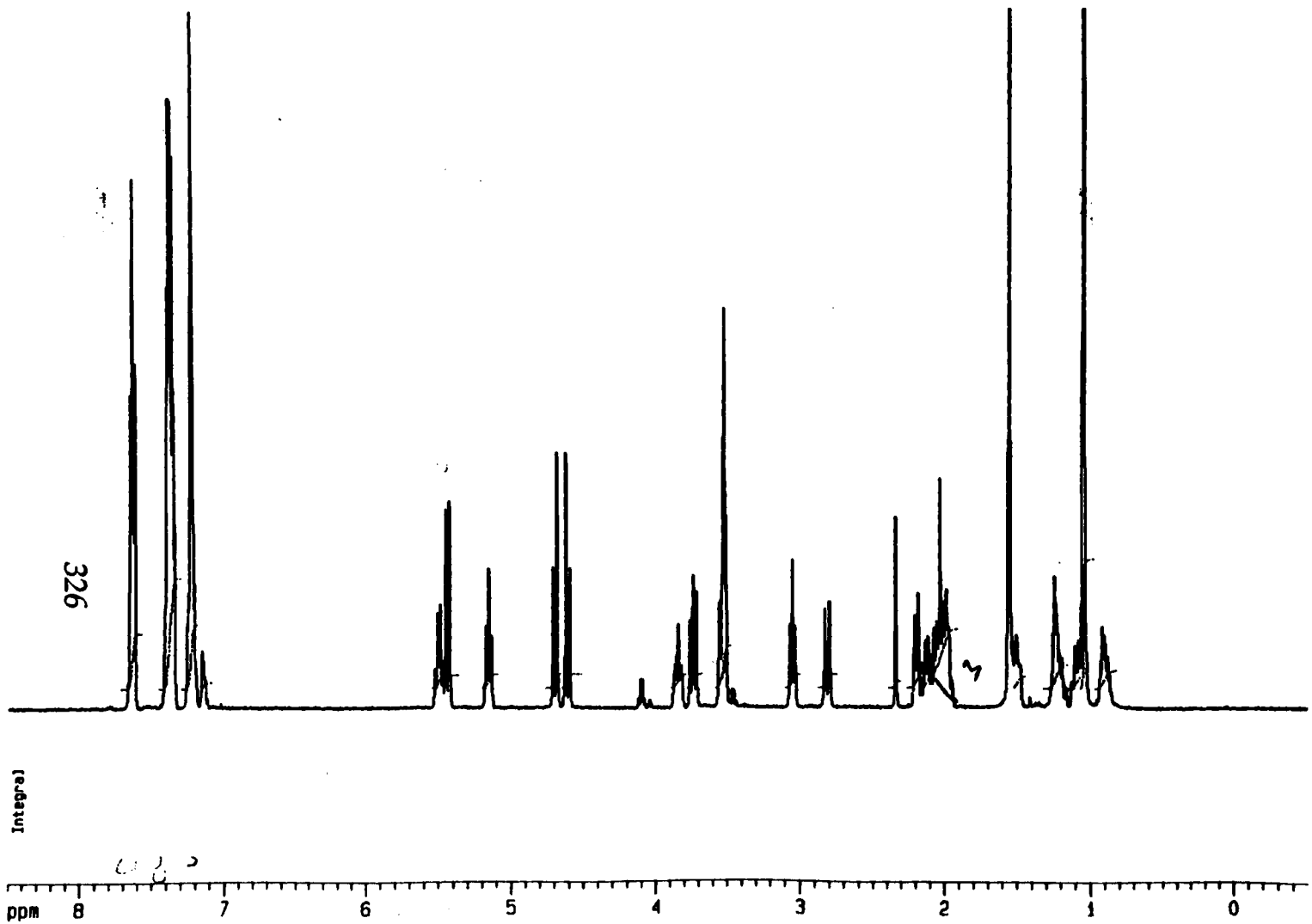
Data of **4.41**

1H NMR (500 MHz, $CDCl_3$): δ 7.66-7.62 (m, 4H), 7.42-7.35 (m, 8H), 7.26-7.22 (m, 3H), 5.49 (q, J= 9 Hz, 1H), 5.44 (t, J= 13 Hz, 1H), 5.16 (t, J= 9 Hz, 1H), 4.69 (d, J= 14 Hz, 1H), 4.60 (d, J= 14 Hz, 1H), 3.87-3.81 (m, 1H), 3.74 (dd, J= 12, 11 Hz, 1H), 3.56-3.51 (m, 3H), 3.05 (t, J= 10 Hz, 1H), 2.80 (d, J= 14 Hz, 1H), 2.20-2.18 (m, 1H), 2.15-1.95 (m, 3H), 1.52-1.48 (m, 1H), 1.27-1.16 (m, 2H), 1.12-1.08 (m, 1H), 1.04 (s, 9H), 0.94-0.85 (m, 1H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 209.4, 181.0, 178.5, 136.6, 135.4 (x4), 134.2, 133.8 (x2), 129.5 (x2), 129.4 (x2), 128.7 (x2), 128.4, 127.5 (x4), 126.7, 73.7, 63.5, 54.6, 54.0, 43.4, 39.5, 35.7, 34.3, 33.4, 29.4, 27.6, 26.7 (x3), 23.9, 19.0.

IR (neat) 3430, 2920, 2857, 1685, 1428, 1402, 1110 cm^{-1}.

EI HRMS calcd for $C_{35}H_{36}NO_5Si$ (M^+ -*t*Bu) 578.23628, obsd 578.23824.



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AQ	4.4040694 sec
RG	203.2
DW	67.200 usec
DE	6.00 usec
TE	300.0 K
D1	0.01000000 sec

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

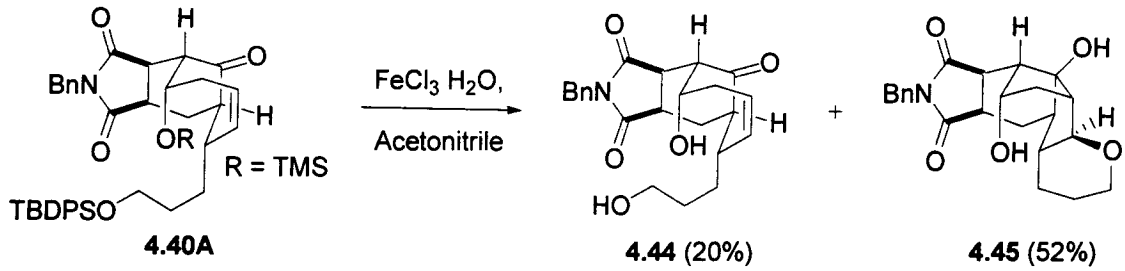
NUC1	1H
P1	10.50 usec
PL1	3.00 dB
SFO1	500.1327766 MHz

F2 - Processing parameters

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

1D NMR plot parameters

CX	20.00 cm
CY	60.00 cm
F1P	8.500 ppm
F1	4251.10 Hz
F2P	-0.500 ppm
F2	-250.06 Hz
PPMCM	0.45000 ppm/cm
HZCM	225.05849 Hz/cm



4.40A **4.44** (20%) **4.45** (52%)

Compound **4.40A** (0.287 g, 0.4 mmol) was dissolved in acetonitrile (10 mL). $FeCl_3 \bullet H_2O$ (0.109 g, 0.4 mmol) was added and stirred for 24 hours at room temperature. The reaction was purified directly by flash column chromatography (100% EtOAc) to afford 32 mg of **1017** (20% yield) and 90 mg of **1063B** (52%) as colorless oil.

4-Benzyl-13-hydroxy-9-(3-hydroxy-propyl)-4-aza-tricyclo[6.5.1.02,6]tetradec-10-ene-3,5,14-trione (4.44)

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.47-7.46 (m, 2H), 7.33-7.27 (m, 3H), 5.55 (q, J= 8 Hz, 1H), 5.45 (d, J= 9 Hz, 1H), 5.19 (t, J= 10 Hz, 1H), 4.88 (d, J= 14 Hz, 1H), 4.72 (d, J= 14 Hz, 1H), 3.87 (tq, 13, 3 Hz, 1H), 3.78 (dd, J= 12, 10 Hz, 1H), 3.57 (dd, J= 13, 4 Hz, 1H), 3.50-3.41 (m, 2H), 3.08 (t, J= 10 Hz, 1H), 2.86 (dd, J= 15, 2 Hz, 1H), 2.30-2.21 (m, 2H), 2.15-2.10 (m, 2H), 2.08-2.00 (m, 1H), 1.64-1.58 (m, 1H), 1.40-1.21 (m, 2H), 1.10-1.03 (m, 1H), 0.82-0.75 (m, 1H).

^{13}C NMR (500 MHz, $CDCl_3$) 209.3, 181.2, 179.2, 136.7, 134.5, 129.6 x2, 128.9 x2, 128.6, 127.1, 73.8, 62.3, 54.9, 54.1, 43.7, 39.6, 35.9, 34.2, 33.6, 29.6, 27.6, 23.9.

IR (neat) 3413, 2937 2876, 1682, 1403, 1050 cm^{-1}.

EI HRMS calcd for $C_{23}H_{27}NO_5$ (M^+) 397.18892, obsd 397.18989.

Data for **4.45**

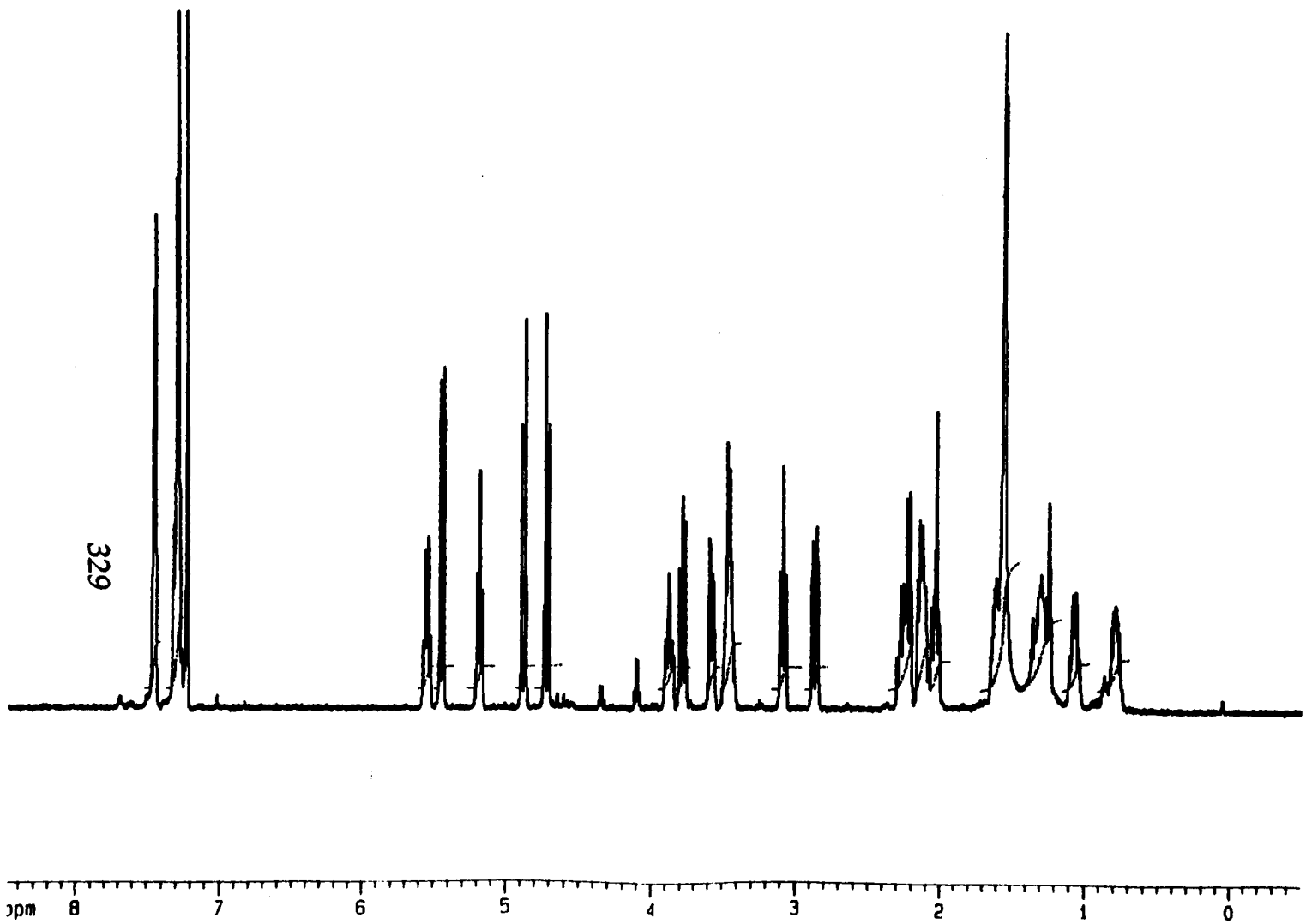
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.43-7.15 (m, 5H), 4.60-4.54 (m, 2H), 4.44-4.43 (m, 1H), 3.94-3.92 (m, 1H), 3.88 (dd, 8, 4 Hz, 1H), 3.44 (td, 12, 3 Hz, 1H), 3.10 (t, J= 10 Hz, 1H), 2.82-2.76 (m, 1H), 2.60 (dd, J= 10, 7 Hz, 1H), 2.46 (br s, 1H), 2.37-2.31 (m, 1H), 2.20-2.11

(m, 3H), 1.97-1.94 (m, 1H), 1.72 (q, J= 13 Hz, 1H), 1.59 (dd, J= 16, 6 Hz, 1H), 1.49-1.43 (m, 4H), 1.28-1.25 (m, 1H).

^{13}C NMR (500 MHz, $CDCl_3$) δ 180.1, 171.2, 135.7, 128.4 (x2), 128.0 (x2), 127.5, 87.1, 81.8, 70.2, 69.0, 52.2, 48.9, 45.9, 45.7, 41.8, 37.7, 37.0, 34.1, 28.3, 26.8, 25.8.

IR (neat) 3430, 2934, 2853, 1692, 1402 cm^{-1}.

EI HRMS calcd for $C_{23}H_{27}NO_5$ (M^+) 397.18892, obsd 397.18840.



4.44

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D1                0.01000000 sec

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PL1                    3.00 dB
SFO1             500.1327766 MHz

F2 - Processing parameters
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1D NMR plot parameters
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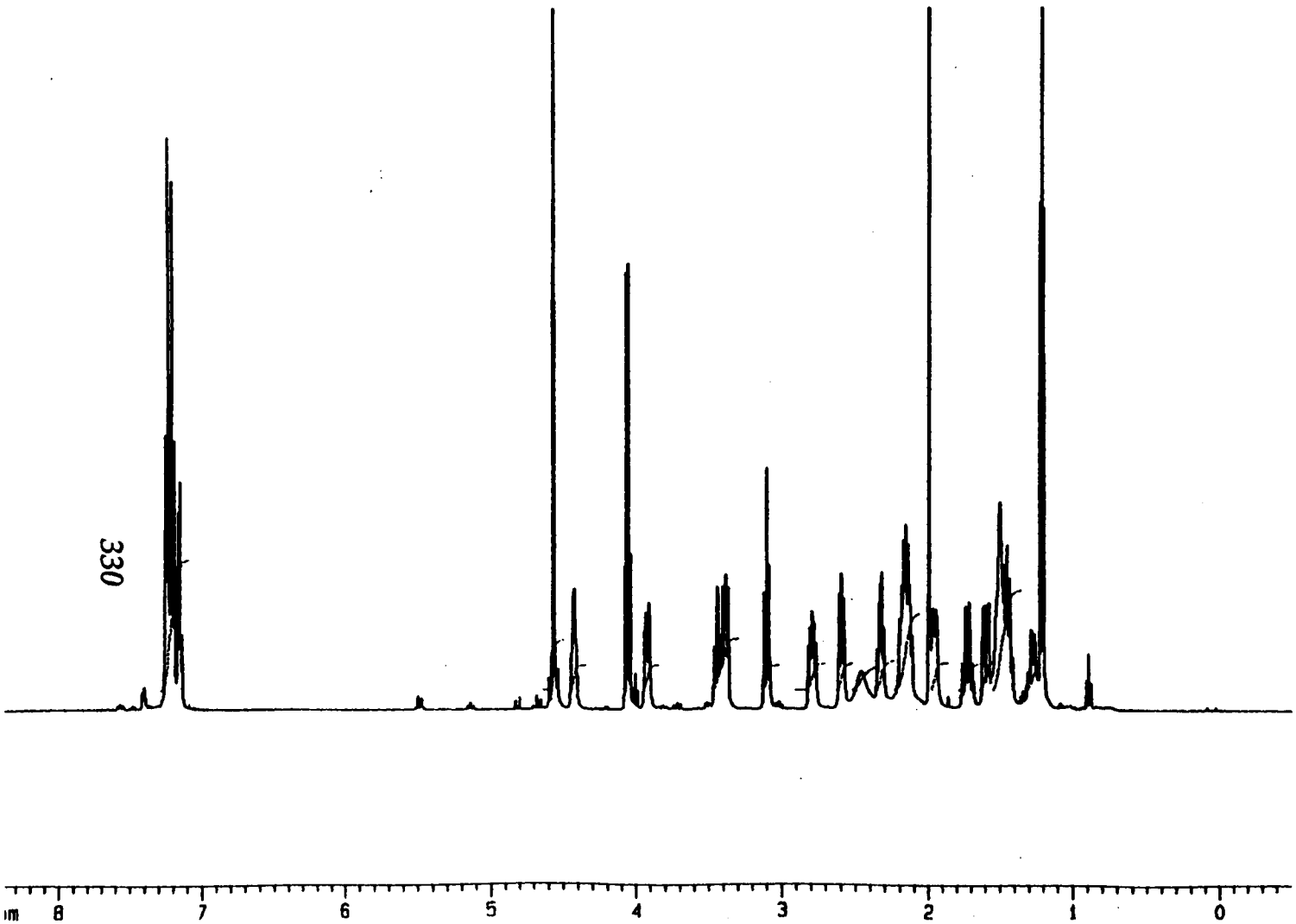
4.45



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FIDRES 0.113533 Hz
AQ 4.4040694 sec
RG 64
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TE 300.0 K
D1 0.01000000 sec

======== CHANNEL f1 ========
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P1 14.00 usec
PL1 0.00 dB
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1D NMR plot parameters
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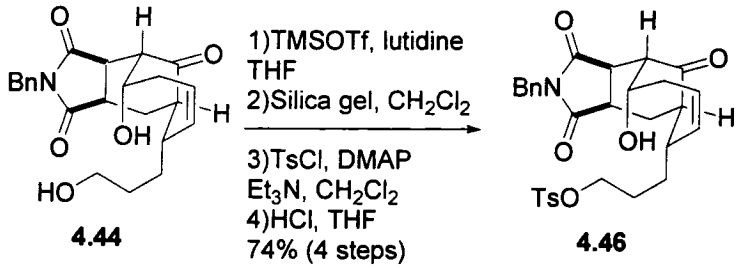


4.44 **4.46**

Toluene-4-sulfonic acid 3-(4-benzyl-13-hydroxy-3,5,14-trioxo-4-aza-tricyclo[6.5.1.02,6]tetradec-10-en-9-yl)-propyl ester (4.46)

Alcohol **4.44** (0.131 g, 0.33 mmol) was dissolved in THF (6 mL). Lutidine (0.3 mL, 2.5 mmol) was added and the mixture was cooled in an ice bath before the addition of trimethylsilyl trifluoromethanesulfonate (0.3 mL, 1.7 mmol). The reaction was completed after 10 minutes and stopped by adding $NaHCO_{3\ sat}$ (10 mL). The aqueous layer was extracted 3 times with ethylacetate (3 X 30 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was treated for 15 hours in dichloromethane (3 mL) and silica gel (2g). The product was filtered with 30 mL of ethylacetate and the solvent evaporated. The crude product was purified by flash column chromatography (50% EtOAc/hexanes). The resulting primary alcohol was dissolved in dichloromethane (2 mL). Triethylamine (0.17 mL, 1.2 mmol) and dimethylaminopyridine (1 cristal) were added, followed by *p*-toluenesulfonyl chloride(0.08 g, 0.4 mmol). The reaction was stirred at room temperature for 15 hours and stopped by adding HCl 1M (10 mL). The aqueous layer was extracted 3 times with dichloromethane (3 X 30 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (40% EtOAc/hexanes) to afford 135 mg of **4.46** (74% yield) as a yellow oil.

Data for **4.46**

^{1}H NMR (500 MHz, acetone-d_6): δ 7.84 (d, J= 8 Hz, 2H), 7.51 (d, J= 8 Hz, 2H), 7.45 (dd, J= 8, 2 Hz, 2H), 7.33-7.28 (m, 3H), 5.47 (dt, J= 11, 8 Hz, 1H), 5.40 (d, J= 13 Hz, 1H), 5.10-

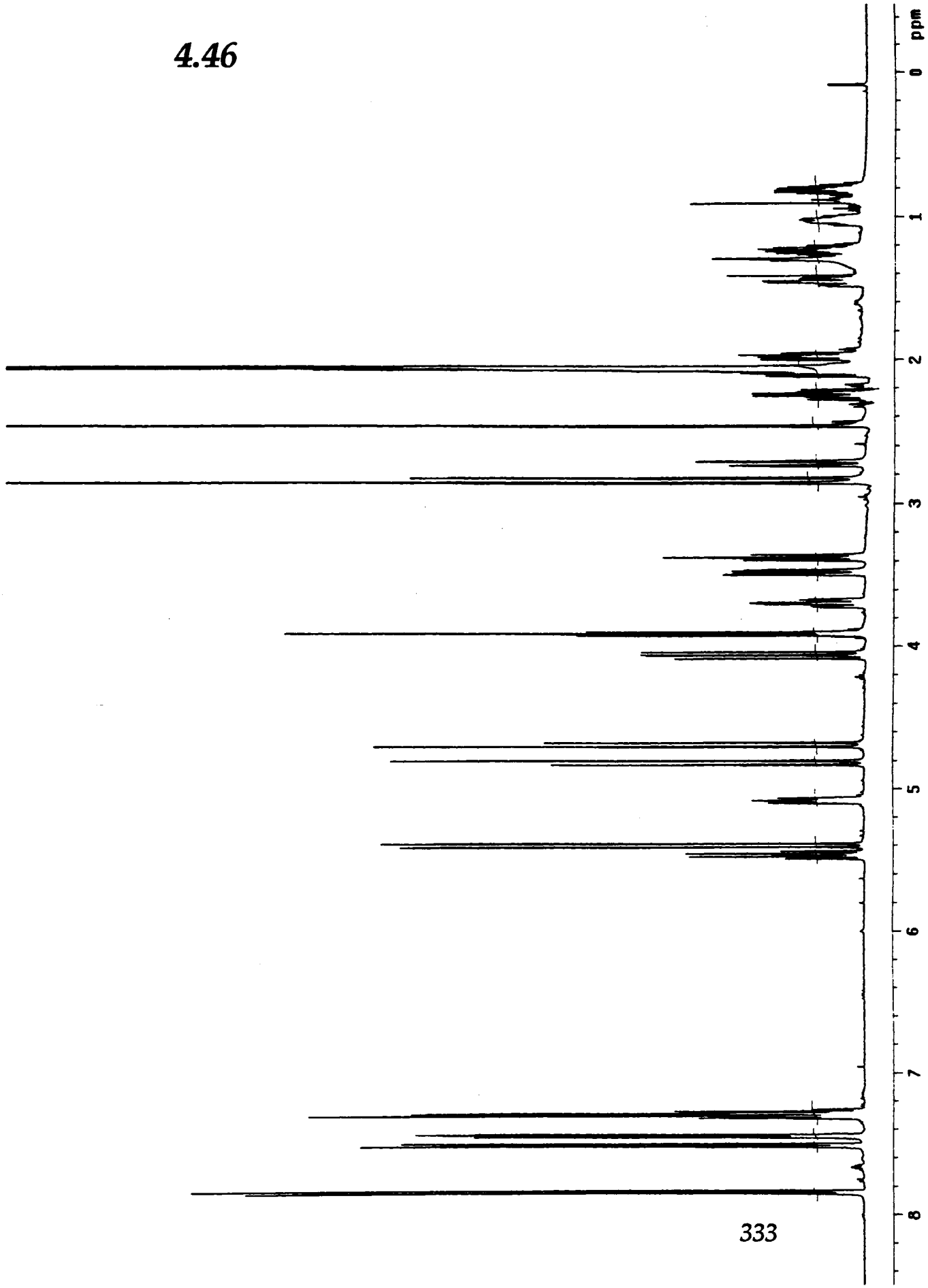
5.07 (m, 1H), 4.81 (d, J_{AB}= 14 Hz, 1H), 4.68 (d, J_{AB}= 14 Hz, 1H), 4.06 (dd, J= 13, 10 Hz, 1H), 3.91 (t, J= 6 Hz, 2H), 3.69 (tdd, J= 8, 5, 2 Hz, 1H), 3.47 (dd, J= 13, 5 Hz, 1H), 3.37 (t, J= 8 Hz, 1H), 2.72 (d, J= 14 Hz, 1H), 2.46 (s, 3H), 2.28-2.12 (m, 1H), 2.09-2.07 (m, 1H), 2.00-1.95 (m, 1H), 1.47-1.41 (m, 1H), 1.31-1.19 (m, 2H), 1.06-1.01 (m, 1H), 0.90-0.78 (m, 2H).

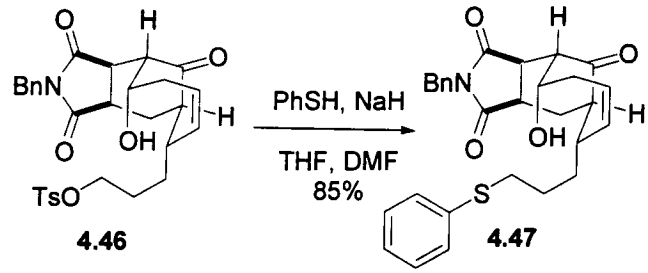
^{13}C NMR (125 MHz, acetone-d_6) δ 207.3, 180.9, 178.3, 143.6, 134.9, 134.1, 132.2, 128.7x2, 128.1x2, 127.4x2, 126.8, 126.5x2, 125.8, 71.9, 69.3, 53.3, 52.9, 41.8, 38.5, 34.6, 33.3, 32.4, 26.0, 24.7, 22.5, 19.3.

IR (neat) 3416, 2925, 1684, 1175 cm^{-1}.

EI HRMS calcd for $C_{30}H_{33}NO_7S$ (M^+) 551.19777, obsd 551.19777.

4.46





4.46 **4.47**

4-Benzyl-13-hydroxy-9-(3-phenylsulfanyl-propyl)-4-aza-tricyclo[6.5.1.02,6]tetradec-10-ene-3,5,14-trione (4.47)

Thiphenol (0.07 mL, 0.65 mmol) was dissolved in THF (0.8 mL) and NaH (0.015 g, 0.32 mmol) was added. This thiolate was stirred for 20 minutes before being canulated into the tosylate **4.46** (0.045 g, 0.08 mmol) solution in DMF (0.2 mL). The reaction was stirred at room temperature for 4 hours and stopped by adding $NaHCO_{3\ sat}$ (4 mL). The aqueous layer was extracted 3 times with diethylether (3 X 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (30% EtOAc/hexanes) to afford 38 mg of **4.47** (85% yield) as a yellow oil.

Data for **4.47**

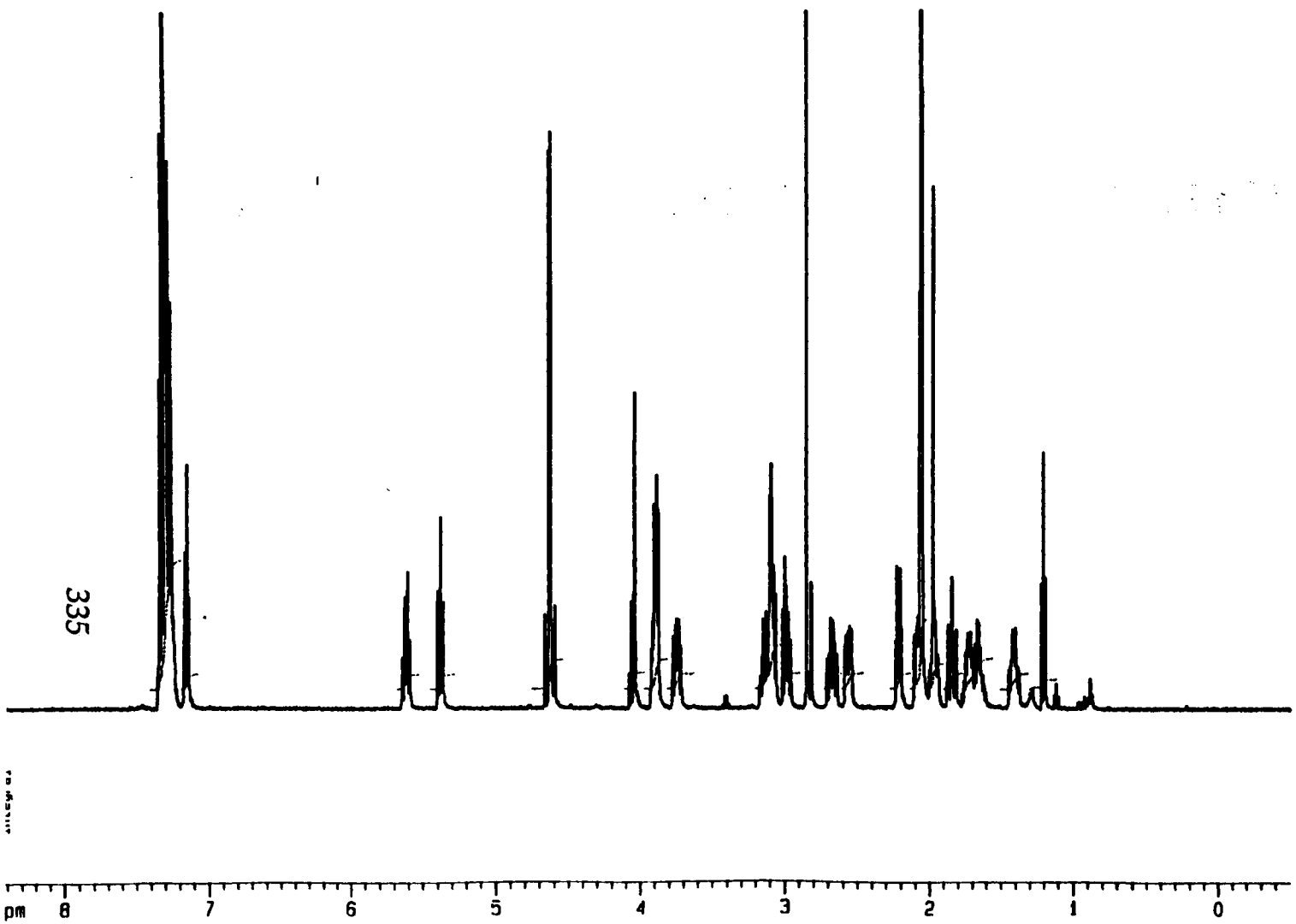
^{1}H NMR (500 MHz, acetone-d_6): δ 7.36-7.26 (m, 9H), 7.24-7.14 (m, 1H), 5.62 (q, J= 9 Hz, 1H), 5.39 (t, J= 10 Hz, 1H), 4.65 (d, J_{AB}= 15 Hz, 1H), 4.61 (d, J_{AB}= 15 Hz, 1H), 4.04 (d, J= 3 Hz, 1H), 3.92-3.88 (m, 2H), 3.77-3.72 (m, 1H), 3.17 (q, J= 2 Hz, 1H), 3.15-3.06 (m, 2H), 3.01-2.96 (m, 1H), 2.67 (q, J= 12 Hz, 1H), 2.56 (ddd, J= 14, 7, 3 Hz, 1H), 2.22 (dt, J= 11, 3 Hz, 1H), 2.11-2.08 (m, 1H), 1.98-1.94 (m, 1H), 1.87-1.81 (m, 1H), 1.77-1.62 (m, 2H), 1.45-1.37 (m, 1H).

^{13}C NMR (125 MHz, acetone-d_6) δ 209.0, 181.7, 180.1, 138.9, 138.3, 137.9, 130.4x2, 130.0x2, 129.9x2, 129.5x2, 129.0, 128.9, 127.0, 71.4, 56.3, 53.8, 43.6, 39.5, 36.7, 34.3, 33.8, 32.3, 30.9, 28.2, 27.5.

IR (neat) 3453, 2929, 1696 cm^{-1}.

EI HRMS calcd for $C_{29}H_{31}NO_4S$ (M^+) 489.19738, obsd 489.19566.

4.47



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F2 - Processing parameters	
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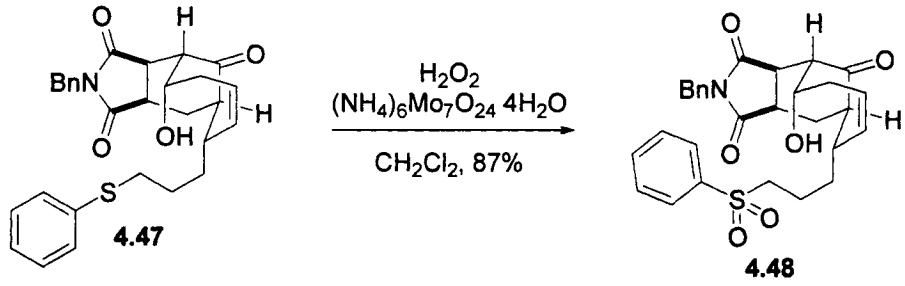
HZCM	225.05849 Hz/cm



9-(3-Benzenesulfonyl-propyl)-4-benzyl-13-hydroxy-4-aza-tricyclo[6.5.1.02,6]tetradec-10-ene-3,5,14-trione (4.48)

Thiol **4.47** (0.026g, 0.046 mmol) was dissolved in ethanol 99% (1 mL) and dichloromethane (5 drops). $(NH_4)_6Mo_7O_{24}{\cdot}4H_2O$ (0.014 g, 0.01 mmo) was added, followed by hydrogen peroxide 30% (0.02 mL, 0.18 mmol). The reaction was stirred at room temperature for 15 hours. The reaction was stopped by evaporating the ethanol and adding water (5 mL). The aqueous layer was extracted 3 times with dichloromethane (3 X 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (60% EtOAc/hexanes) to afford 24 mg of **4.48** (87% yield) as white crystals Mp = 96.9-97.7 °C.

Data for **4.48**

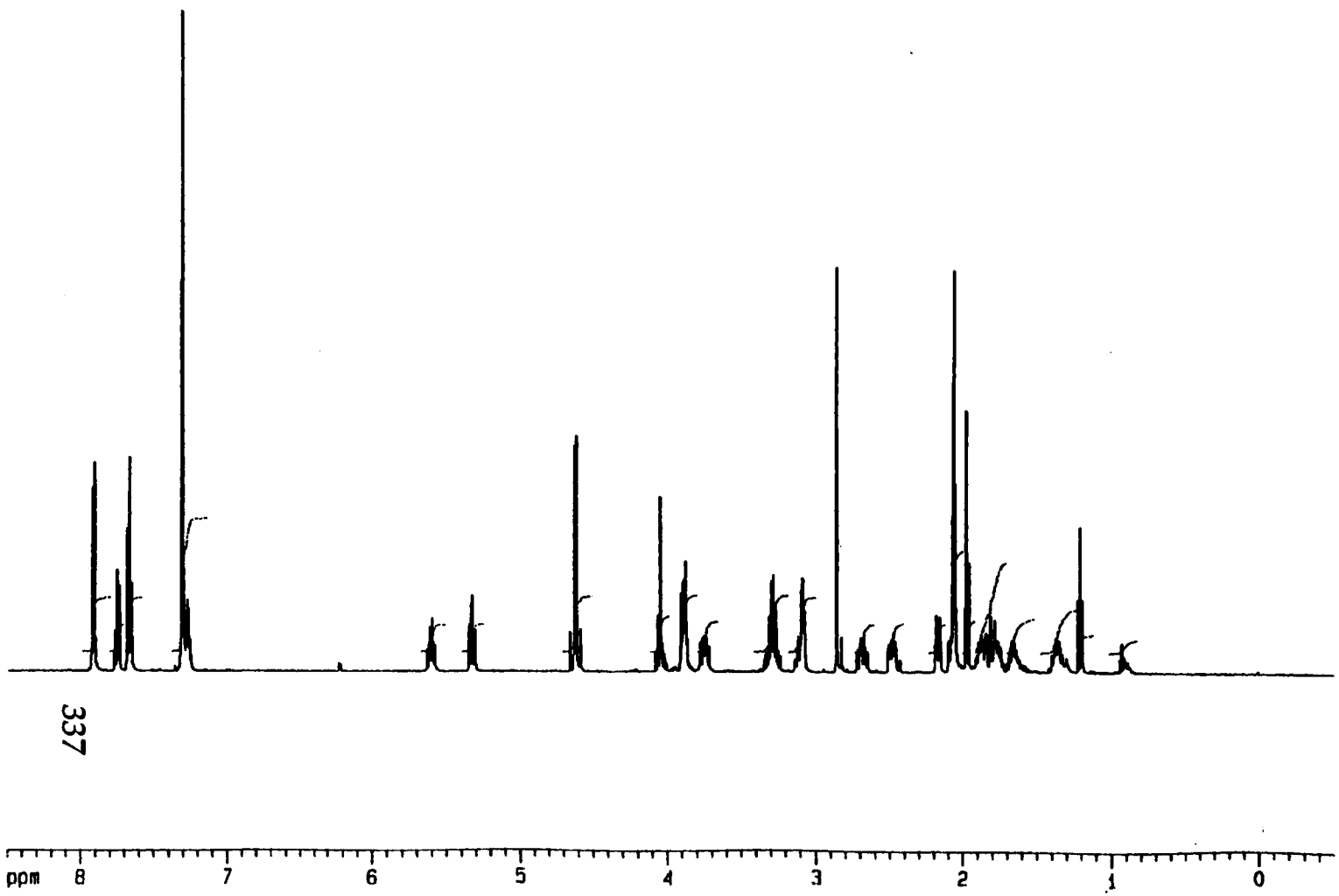
^{1}H NMR (500 MHz, $CDCL_3$): δ 7.92 (dd, J= 8, 1 Hz, 2H), 7.76 (t, J= 7 Hz, 1H), 7.68 (t, J= 8 Hz, 2H), 7.32-7.31 (m, 4H), 7.30-7.25 (m, 1H), 5.61 (q, J= 9 Hz, 1H), 5.33 (t, J= 10 Hz, 1H), 4.65 (d, J_{AB}= 15 Hz, 1H), 4.61 (d, J_{AB}= 15 Hz, 1H), 4.05 (d, J= 3 Hz, 1H), 3.89 (dd, J= 9, 5 Hz, 2H), 3.78-3.72 (m, 1H), 3.32-3.24 (m, 2H), 3.12-3.08 (m, 2H), 2.72-2.65 (m, 1H), 2.48 (ddd, J= 15, 7, 3 Hz, 1H), 2.17 (dt, J= 7, 3 Hz, 1H), 2.09-2.07 (m, 1H), 1.94-1.73 (m, 3H), 1.59-1.57 (m, 1H), 1.40-1.30 (m, 1H).

^{13}C NMR (500 MHz, $CDCl_3$) δ 208.8, 181.7, 180.1, 141.3, 138.3, 137.8, 135.0, 130.8x2, 129.9x2, 129.4x2, 129.3x2, 129.2, 129.0, 71.4, 56.4, 56.2, 53.7, 43.5, 39.5, 36.6, 34.4, 33.3, 30.9, 27.3, 22.2.

IR (neat) 3462, 2927, 1696, 1401, 1305, 1147 cm^{-1}.

EI HRMS calcd for $C_{29}H_{31}NO_6S$ (M^+) 521.18721, obsd 521.18943.

4.48



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RG	203.2
DW	67.200 usec
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TE	300.0 K
D1	0.01000000 sec

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F2 - Processing parameters

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1D NMR plot parameters

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F2	-250.06 Hz
PPMCM	0.45000 ppm/cm
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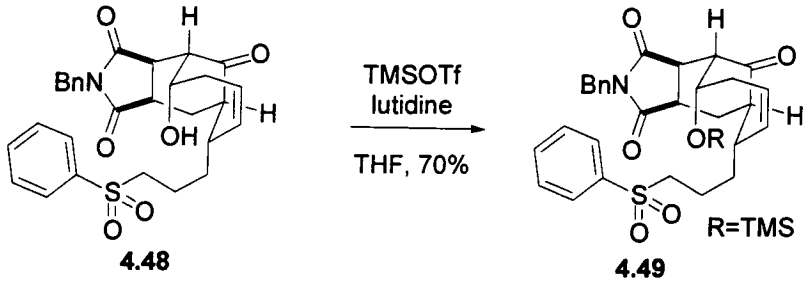


4.48 **4.49**

Alcohol **4.48** (0.024g, 0.05 mmol) was dissolved in THF (1 mL). Lutidine (0.02 mL, 0.18 mmol) was added and the mixture was cooled in an ice bath before the addition of trimethylsilyl trifluoromethanesulfonate (0.016 mL, 0.09 mmol). The reaction was completed after 10 minutes and quenched by adding $NaHCO_{3\ sat}$ (10 mL). The aqueous layer was extracted 3 times with ethylacetate (3 X 30 mL). The crude product was purified by flash column chromatography (30% EtOAc/hexanes) to afford 10 mg of **4.49** (70% yield) of a white solid Mp173.6-175.0°C.

Data for **4.49**

^{1}H NMR (500 MHz, acetone-d_6): δ 7.94-7.92 (m, 2H), 7.76 (tt, J= 7, 2Hz, 1H), 7.67 (t, J= 7 Hz, 2H), 7.38-7.25 (m, 5H), 5.41-5.36 (m, 1H), 5.31-5.27 (m, 1H), 4.70 (d, J_{AB}= 15 Hz, 1H), 4.62 (d, J_{AB}= 15 Hz, 1H), 4.54 (td, J= 6, 2 Hz, 1H), 3.58 (t, J= 10 Hz, 1H), 3.24 (t, J= 7 Hz, 2H), 3.04-2.95 (m, 2H), 2.89-2.87 (m, 1H), 2.61-2.47 (m, 2H), 2.40-2.34 (m, 1H), 2.33-2.27 (m, 1H), 2.22 (q, J= 8 Hz, 1H), 1.77-1.65 (m, 2H), 1.62-1.55 (m, 1H), 1.47-1.40 (m, 1H), 0.10 (s, 9H).

^{13}C NMR (500 MHz, acetone-d_6) δ 213.8, 179.6, 177.7, 141.2, 137.7, 135.0, 134.4, 130.7 (x2), 129.8 (x2), 129.8 (x2), 129. 3(x2), 129.0, 128.2, 67.7, 56.7, 54.7, 51.9, 43.4, 43.1, 43.0, 37.6, 35.9, 34.7, 31.9, 22.8, 0.8 (x3).

IR (neat) 2927, 1704, 1396, 1150, 1087 cm^{-1}.

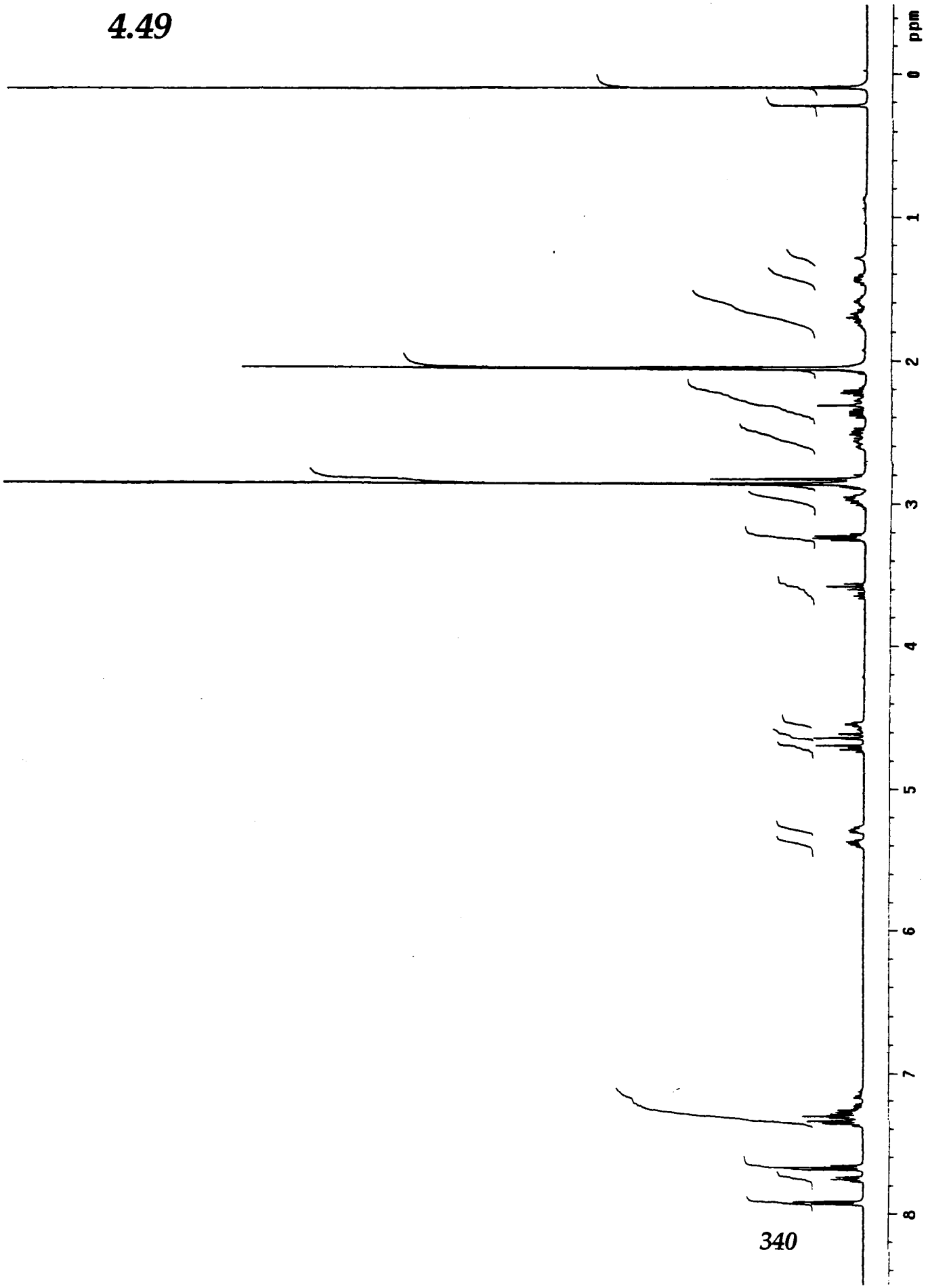
EI HRMS indeterminable.

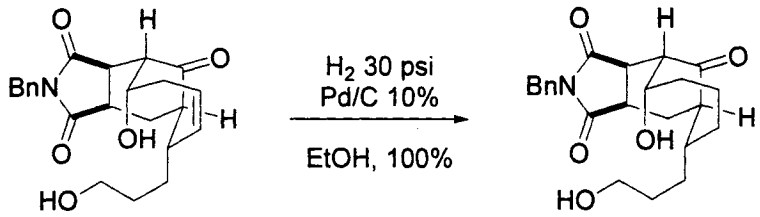
Data for the atropisomer obsd.

^{1}H NMR (500 MHz, acetone-d_6): δ 4.72 (d, J_{AB}= 14Hz, 1H), 4.63 (d, J_{AB}= 14 Hz, 1H), 3.65 (t, J= 10 Hz, 1H), 0.22 (d, J= 1 Hz, 9H).

^{13}C NMR (500 MHz, acetone-d_6) δ 213.1, 179.5, 177.6, 137.6, 134.8, 130.3, 129.5, 128.0, 69.1, 54.6, 52.4, 42.7, 42.1, 37.8, 34.5, 31.2, 22.6, -2.4, -2.5.

4.49





4.44 **4.51**

4-Benzyl-13-hydroxy-9-(3-hydroxy-propyl)-4-aza-tricyclo[6.5.1.02,6]tetradecane-3,5,14-trione (4.51)

Compound **4.44** (0.05g, 0.13 mmol) was dissolved in ethanol 99% (20 mL) and added to palladium on charcoal 10% (20 mg) in an autoclave. The reaction has been pressurized with hydrogen at 30 psi and heated at 40°C for 15 hours. The reaction was stopped by removing the left over pressure and filtered on celite pad with dichloromethane. The solvent was evaporated and the crude material was purified by flash column chromatography (100% EtOAc) to afford 50 mg of **4.51** (quant yield) as a colourless oil.

Data for **4.51**

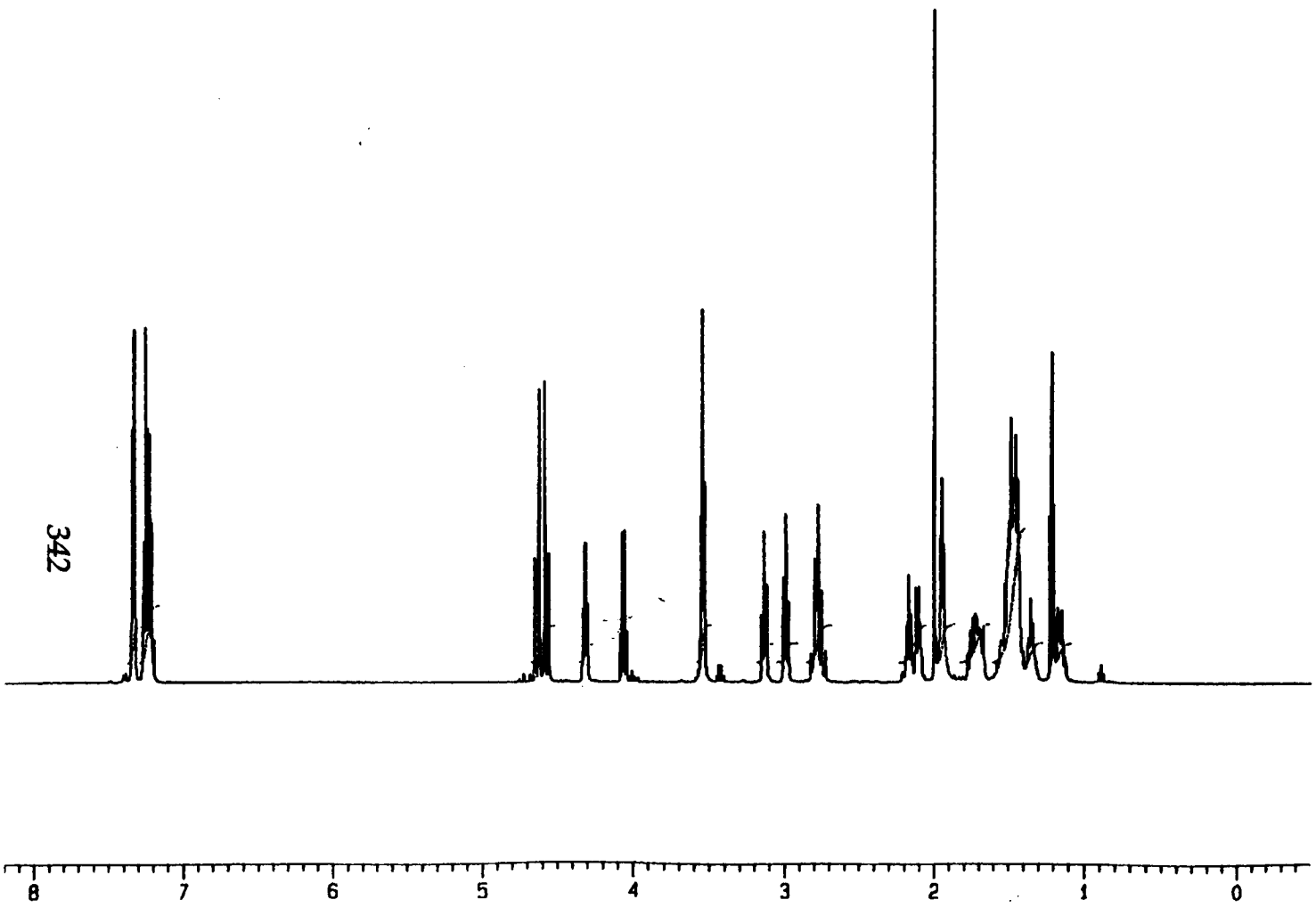
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.35 (d, J= 7 Hz, 2H), 7.28-7.21 (m, 3H), 4.64 (d, J_{AB}= 14 Hz, 1H), 4.57 (d, J_{AB}= 14 Hz, 1H), 4.32 (t, J= 7 Hz, 1H), 3.55 (t, J= 6 Hz, 2H), 3.14 (t, J= 9 Hz, 1H), 2.99 (t, J= 8 Hz, 1H), 2.80-2.73 (m, 2H), 2.18-2.14 (m, 1H), 2.12-2.09 (m, 1H), 1.94 (br s, 2H), 1.77-1.67 (m, 2H), 1.58-1.40 (m, 7H), 1.37-1.30 (m, 1H), 1.17-1.12 (m, 1H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 216.8, 178.8, 177.8, 135.5, 128.8 (x2), 128.5 (x2), 127.8, 68.4, t62.7, 52.8, 47.8, 44.2, 42.4, 40.3, 38.0, 34.0, 32.9, 31.8, 30.2, 30.1, 18.9.

IR (neat) 3449, 2935, 1694, 1402, 1177 cm^{-1}.

EI HRMS calcd for $C_{23}H_{29}NO_5$ (M^+) 397, 18892, obsd 397.1912.

4.51



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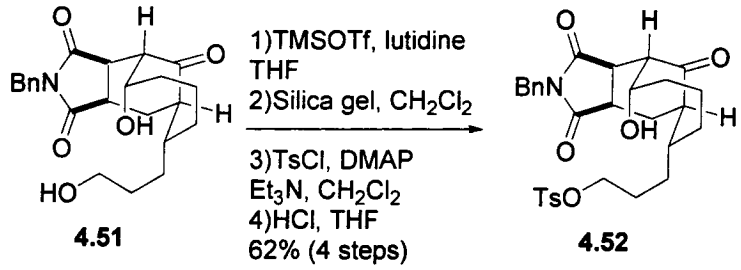


4.51 **4.52**

Toluene-4-sulfonic acid 3-(4-benzyl-13-hydroxy-3,5,14-trioxo-4-aza-tricyclo[6.5.1.02,6]tetradec-9-yl)-propyl ester (4.52)

Alcohol **4.51** (0.067 g, 0.17 mmol) was dissolved in THF (3 mL). Lutidine (0.135 mL, 1.15 mmol) was added and the mixture was cooled in an ice bath before the addition of trimethylsilyl trifluoromethanesulfonate (0.15 mL, 0.83 mmol). The reaction was completed after 10 minutes and stopped by adding $NaHCO_{3\ sat}$ (10 mL). The aqueous layer was extracted 3 times with ethylacetate (3 X 30 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was treated for 15 hours in dichloromethane (3 mL) and silica gel (2g). The product was filtered with 30 mL of ethylacetate and concentrated. The crude product was purified by flash column chromatography (50% EtOAc/hexanes). The resulting primary alcohol was dissolved in dichloromethane (2 mL). Triethylamine (0.13 mL, 1 mmol) and dimethylaminopyridine (1 cristal) were added, followed by *p*-toluenesulfonyl chloride(0.062 g, 0.32 mmol). The reaction was stirred at room temperature for 15 hours and stopped by adding HCl 1M (10 mL). The aqueous layer was extracted 3 times with dichloromethane (3 X 30 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (40% EtOAc/hexanes) to afford 75 mg of tosylate. The resulting compound was dissolved in THF (1 mL) and a solution of 1M HCl (0.1 mL) was added and stirred for 15 hours at room temperature. The reaction was quenched by adding $NaHCO_{3\ sat}$ (5 mL). The aqueous layer was extracted 3 times with ethylacetate (3 X 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column

chromatography (80% EtOAc/hexanes) to afford 58 mg of **4.52** (62% yield) as a colourless oil.

Data for **4.52**

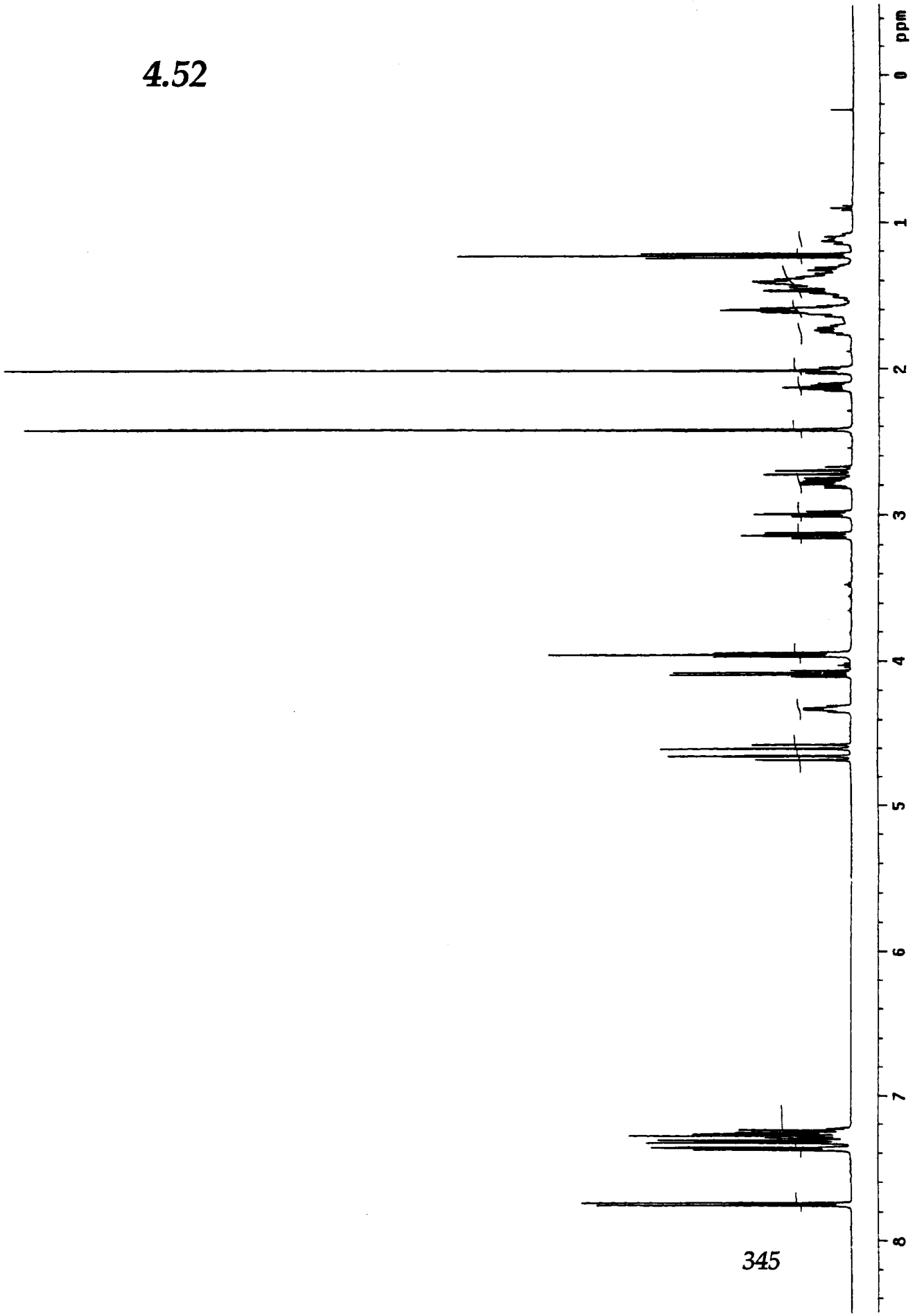
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.75 (d, J= 8 Hz, 2H), 7.38-7.36 (m, 2H), 7.33-7.23 (m, 5H), 4.66 (d, J_{AB}= 14 Hz, 1H), 4.58 (d, J_{AB}= 14 Hz, 1H), 4.32 (q, J= 7 Hz, 1H), 3.95 (t, J= 6 Hz, 2H), 3.14 (t, J= 9 Hz, 1H), 2.99 (t, J= 8 Hz, 1H), 2.82-2.76 (m, 1H), 2.71 (q, J= 12 Hz, 1H), 2.42 (s, 3H), 2.13 (quint, J= 6 Hz, 1H), 2.03-2.00 (m, 1H), 1.76-1.70 (m, 1H), 1.64-1.57 (m, 3H), 1.51-1.31 (m, 7H), 1.15-1.08 (m, 1H).

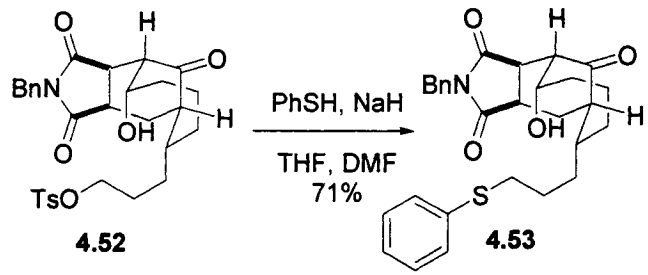
^{13}C NMR (125 MHz, $CDCl_3$) δ 216.3, 178.5, 177.6, 144.7, 135.5, 132.9, 129.8 (x2), 128.9 (x2), 128.6 (x2), 127.9, 127.8 (x2), 70.4, 68.5, 52.7, 47.5, 43.7, 42.5, 40.3, 37.9, 33.4, 32.9, 31.5, 30.0, 26.4, 21.6, 18.8.

IR (neat) 3503, 3064, 2935, 1770, 1699 cm^{-1}.

EI HRMS calcd for $C_{30}H_{33}NO_6S$ (M^+ -H_2O) 535.20286, obsd 535.2079.

4.52





4.52 **4.53**

9-(3-Benzenesulfonyl-propyl)-4-benzyl-13-hydroxy-4-aza-tricyclo[6.5.1.02,6]tetradecane-3,5,14-trione (4.53)

Thiphenol (0.09 mL, 0.84 mmol) was dissolved in THF (1 mL) and NaH (0.017 g, 0.42 mmol) was added. This thiolate was stirred for 20 minutes and canulated into the tosylate **4.52** (0.058 g, 0.1 mmol) solution in DMF (0.2 mL). The reaction was stirred at room temperature for 4 hours and quenched by adding $NaHCO_{3\ sat}$ (4 mL). The aqueous layer was extracted 3 times with diethylether (3 X 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (30% EtOAc/hexanes) to afford 38 mg of **4.53** (71% yield) as a yellow oil.

Data for **4.53**

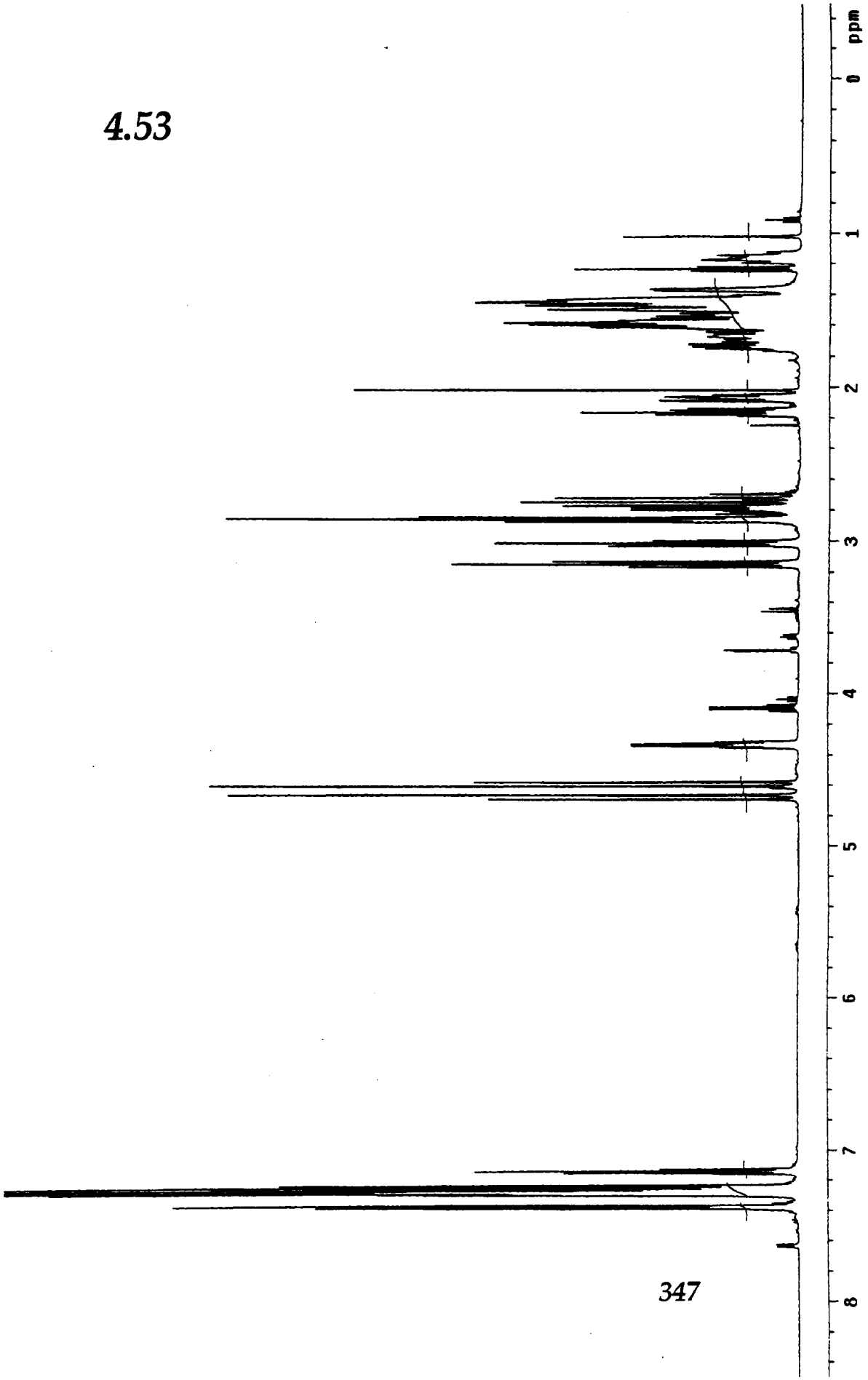
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38 (d, J= 7 Hz, 2H), 7.31-7.24 (m, 7H), 7.14 (tt, J= 7, 2 Hz, 1H), 4.68 (d, J_{AB}= 14 Hz, 1H), 4.58 (d, J_{AB}= 14 Hz, 1H), 4.33 (q, J= 8 Hz, 1H), 3.15 (t, J= 9 Hz, 1H), 3.01 (t, J= 9 Hz, 1H), 2.86 (t, J= 7 Hz, 2H), 2.82-2.69 (m, 2H), 2.19-2.14 (m, 1H), 2.06 (dd, J= 12, 8 Hz, 1H), 1.75-1.62 (m, 2H), 1.61-1.53 (m, 4H), 1.52-1.41 (m, 4H), 1.37-1.36 (m, 1H), 1.19-1.12 (m, 1H).

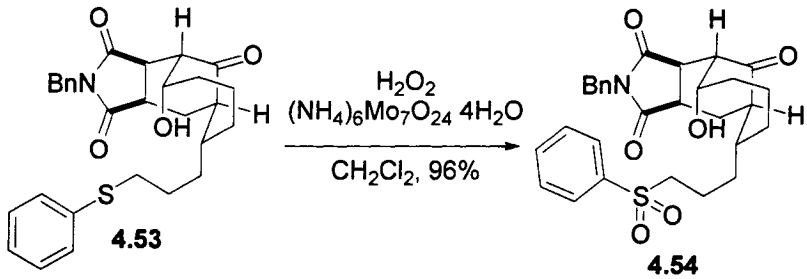
^{13}C NMR (125 MHz, $CDCl_3$) δ 216.4, 178.6, 177.7, 136.5, 135.5, 129.0 (x2), 128.9 (x2), 128.8 (x2), 128.6 (x2), 127.9, 125.8, 68.7, 52.8, 47.8, 44.0, 42.5, 40.3, 38.0, 36.9, 33.5, 32.9, 31.7, 30.0, 26.7, 18.9.

IR (neat) 3447, 2931, 1699, 1400, 1175 cm^{-1}.

EI HRMS calcd for $C_{29}H_{33}NO_4S$ (M^+) 491.21303, obsd 491.21199.

4.53





9-(3-Benzenesulfonyl-propyl)-4-benzyl-13-hydroxy-4-aza-tricyclo[6.5.1.02,6]tetradecane-3,5,14-trione (4.54)

Thiol **4.53** (0.04g, 0.082 mmol) was dissolved in ethanol 99% (1 mL) and dichloromethane (5 drops). $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$ (0.025 g, 0.02 mmo) was added, followed by hydrogen peroxide 30% (0.035 mL, 0.31 mmol). The reaction was stirred at room temperature for 15 hours than stopped by evaporating the ethanol and adding water (5 mL). The aqueous layer was extracted 3 times with dichloromethane (3 X 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (60% EtOAc/hexanes) to afford 42 mg of **4.54** (96% yield) as yellow oil.

Data for **4.54**

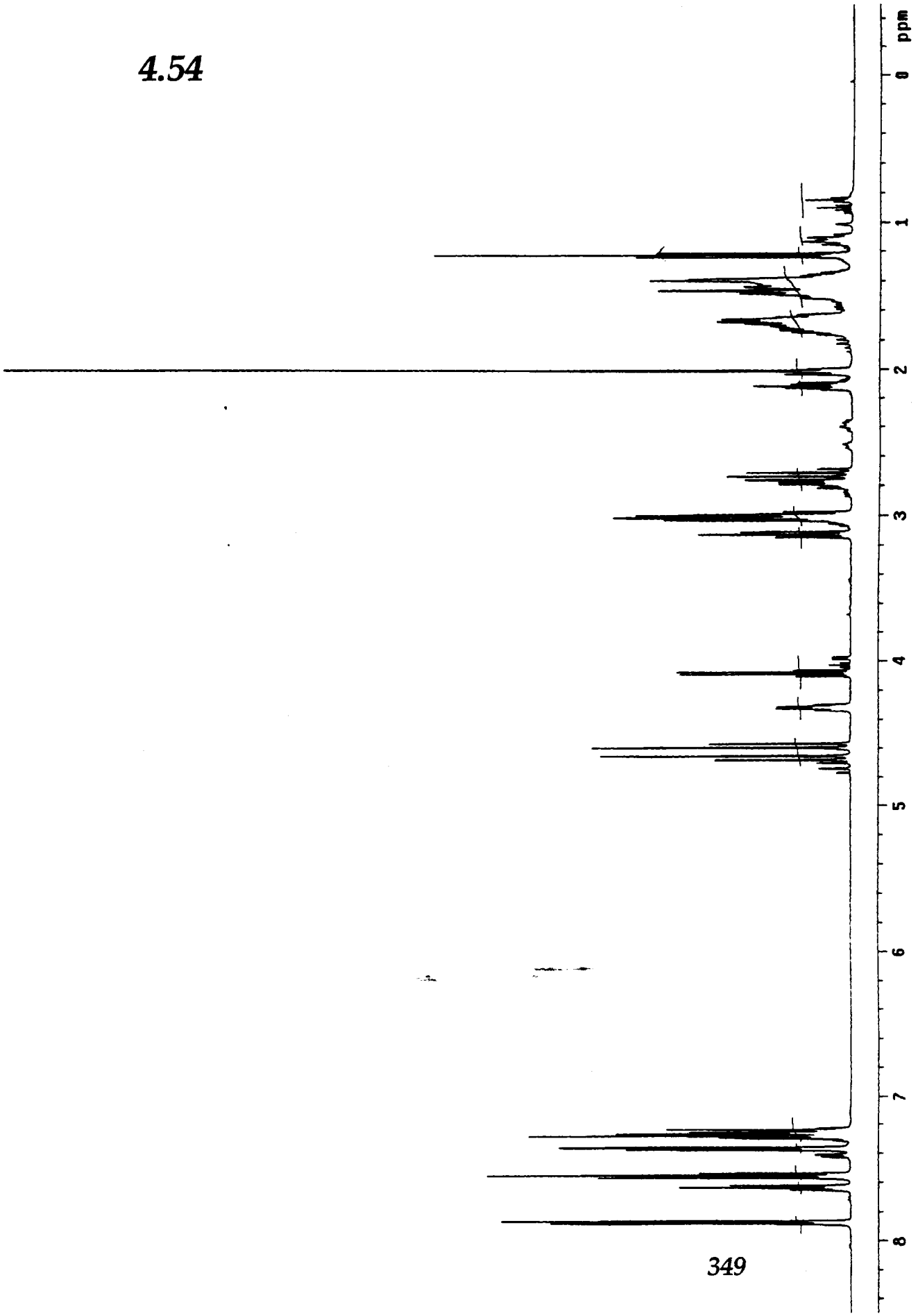
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.87 (d, J= 7 Hz, 2H), 7.64 (tt, J=7, 1 Hz, 1H), 7.55 (t, J= 8 Hz, 2H), 7.37 (d, J= 7 Hz, 2H), 7.30-7.24 (m, 3H), 4.66 (d, J_{AB}= 11 Hz, 1H), 4.58 (d, J_{AB}= 14 Hz, 1H), 4.31 (q, J= 7 Hz, 1H), 3.13 (t, J= 9 Hz, 1H), 3.03-2.98 (m, 3H), 2.79-2.71 (m, 2H), 2.13-2.09 (m, 1H), 1.75-1.63 (m, 5H), 1.52-1.37 (m, 7H), 1.24-1.21 (m, 1H).

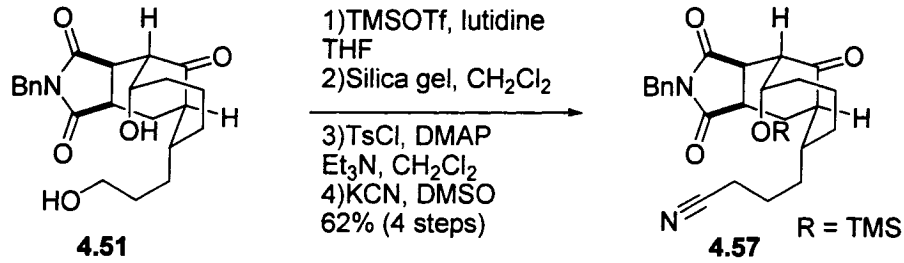
^{13}C NMR (125 MHz, $CDCl_3$) δ 216.2, 178.5, 177.5, 139.0, 135.5, 133.7, 129.3 (x2), 128.8 (x2), 128.5 (x2), 127.9 (x2), 127.8, 68.4, 56.1, 52.6, 47.4, 43.7, 42.4,40.2, 37.8,36.2,32.9, 31.3, 29.8, 20.2, 18.5.

IR (neat) 3482, 2935, 1698, 1403, 1305, 1148 cm^{-1}.

EI HRMS calcd for $C_{29}H_{33}NO_6S$ (M^+) 523.20286, obsd 523.20465.

4.54





4.51 **4.57**

4-(4-Benzyl-3,5,14-trioxo-13-trimethylsilanyloxy-4-aza-tricyclo[6.5.1.02,6]tetradec-9-yl)-butyronitrile (4.57)

Alcohol **4.51** (0.050 g, 2.5 mmol) was dissolved in THF (3 mL). Lutidine (0.135 mL, 1.15 mmol) was added and the mixture was cooled in an ice bath before the addition of trimethylsilyl trifluoromethanesulfonate (0.15 mL, 0.83 mmol). The reaction was completed after 10 minutes and stopped by adding $NaHCO_{3\ sat}$ (10 mL). The aqueous layer was extracted 3 times with ethylacetate (3 X 30 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was treated for 15 hours in dichloromethane (3 mL) and silica gel (2g). The product was filtered with 30 mL of ethylacetate and concentrated. The crude product was purified by flash column chromatography (50% EtOAc/hexanes). The resulting primary alcohol was dissolved in dichloromethane (1 mL). Triethylamine (0.08 mL, 0.56 mmol) and dimethylaminopyridine (1 cristal) were added, followed by *p*-toluenesulfonyl chloride(0.036 g, 0.19 mmol). The reaction was stirred at room temperature for 15 hours and quenched by adding saturated $NH_4Cl_{\ sat}$ (10 mL). The aqueous layer was extracted 3 times with dichloromethane (3 X 30 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (35% EtOAc/hexanes) to afford 53 mg of tosylate. The resulting compound was dissolved in DMSO (0.5 mL) and potassium cyanide (0.0014 g, 0.02 mmol) was added and stirred for 2 hours at room temperature. The reaction was quenched by adding $NaHCO_{3\ sat}$ (5 mL). The aqueous layer was extracted 3 times with diethylether (3 X 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (50% EtOAc/hexanes) to afford 29 mg of **4.57** (71% yield) as a colourless oil.

Data for **4.57**

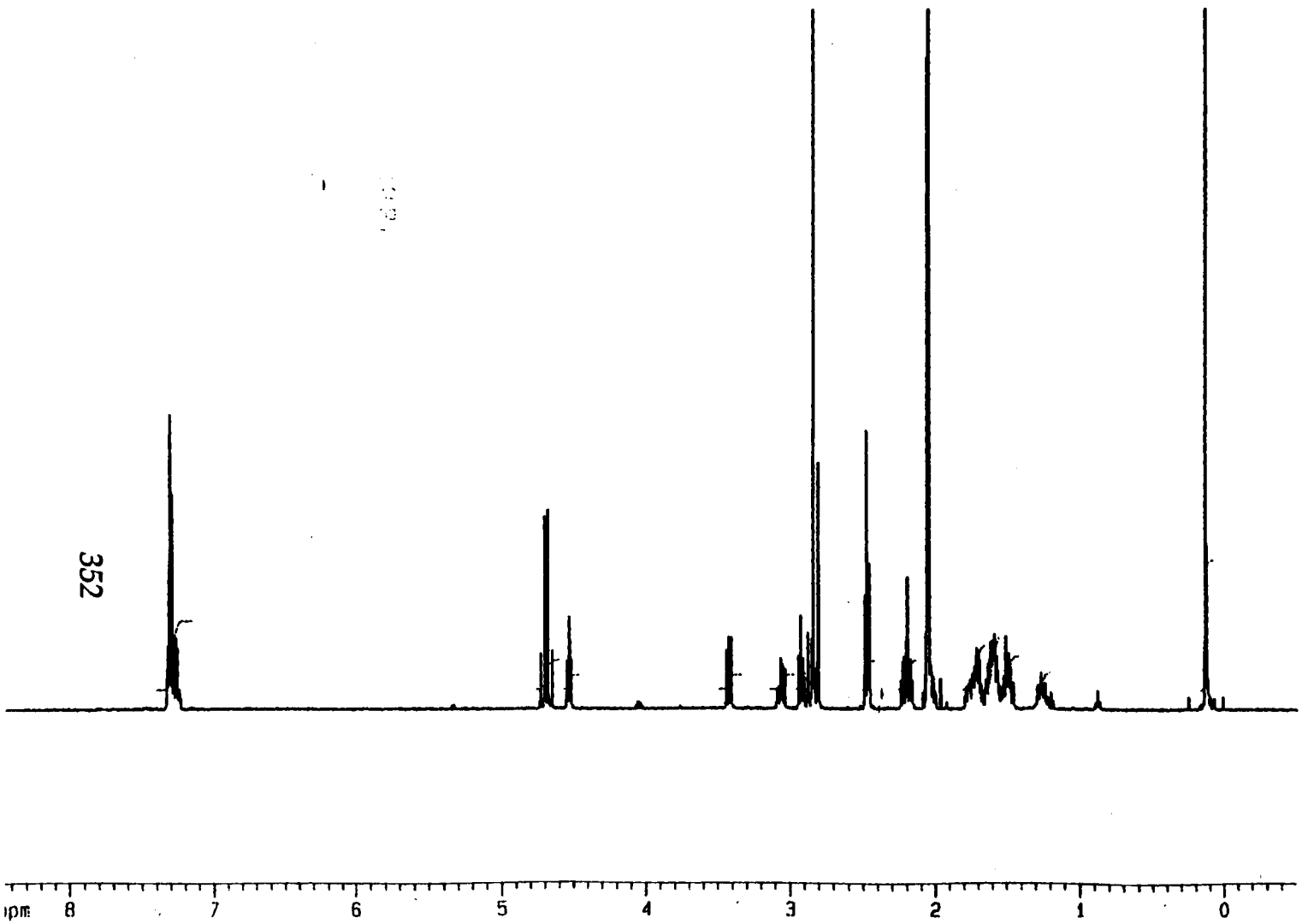
^{1}H NMR (500 MHz, acetone-d_6): δ 7.34-7.25 (m, 5H), 4.72 (d, J_{AB}= 14 Hz, 1H), 4.67 (d, J_{AB}= 14 Hz, 1H), 4.54 (t, J= 7 Hz, 1H), 3.43 (dd, J= 10, 6 Hz, 1H), 3.09-3.03 (m, 1H), 2.93 (t, J= 8 Hz, 1H), 2.86 (q, J= 12 Hz, 1H), 2.47 (t, J= 7 Hz, 2H), 2.24-2.16 (m, 2H), 2.03-1.96 (m, 1H), 1.77-1.64 (m, 3H), 1.63-1.54 (m, 4H), 1.53-1.46 (m, 2H), 1.29-1.24 (m, 1H), 0.13 (s, 9H).

^{13}C NMR (125 MHz, acetone-d_6) δ 217.0, 179.5, 178.2, 138.0, 129.9 (x2), 129.5 (x2), 129.0, 121.2, 70.7, 55.8, 48.9, 45.6, 43.3, 41.2, 39.4, 38.9, 33.5, 33.4, 30.9, 24.4, 20.9, 17.8, 1.0 (x3).

IR (neat) 2944. 2246, 1700, 1396 cm^{-1}.

EI HRMS calcd for $C_{27}H_{36}N_2O_4Si$ (M^+) 480.24444, obsd 480.24381.

4.57



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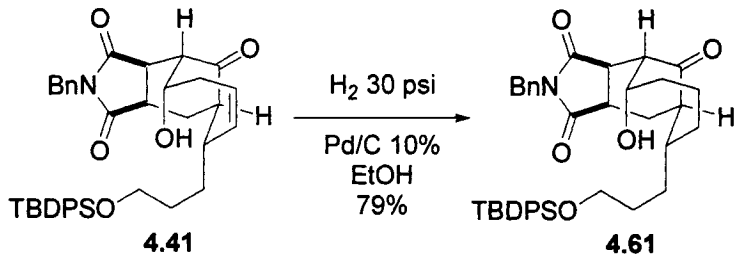


4-Benzyl-9-[3-(tert-butyl-diphenyl-silanyloxy)-propyl]-13-hydroxy-4-aza-tricyclo[6.5.1.02,6]tetradecane-3,5,14-trione (4.61)

Compound **4.41** (0.024g, 0.047 mmol) was dissolved in ethanol 99% (4 mL) and added to palladium on charcoal 10% (10 mg) in an autoclave. The reaction has been pressurized with hydrogen at 30 psi and heated at 40°C for 15 hours. The reaction was stopped by removing the left over pressure and filtered on celite pad with dichloromethane. The solvent was evaporated and the crude material has been purified by flash column chromatography (40% EtOAc/hexanes) to afford 19 mg of **4.61** (79% yield) as a yellow powder Mp = 59.0-59.9 °C.

Data of **4.61**

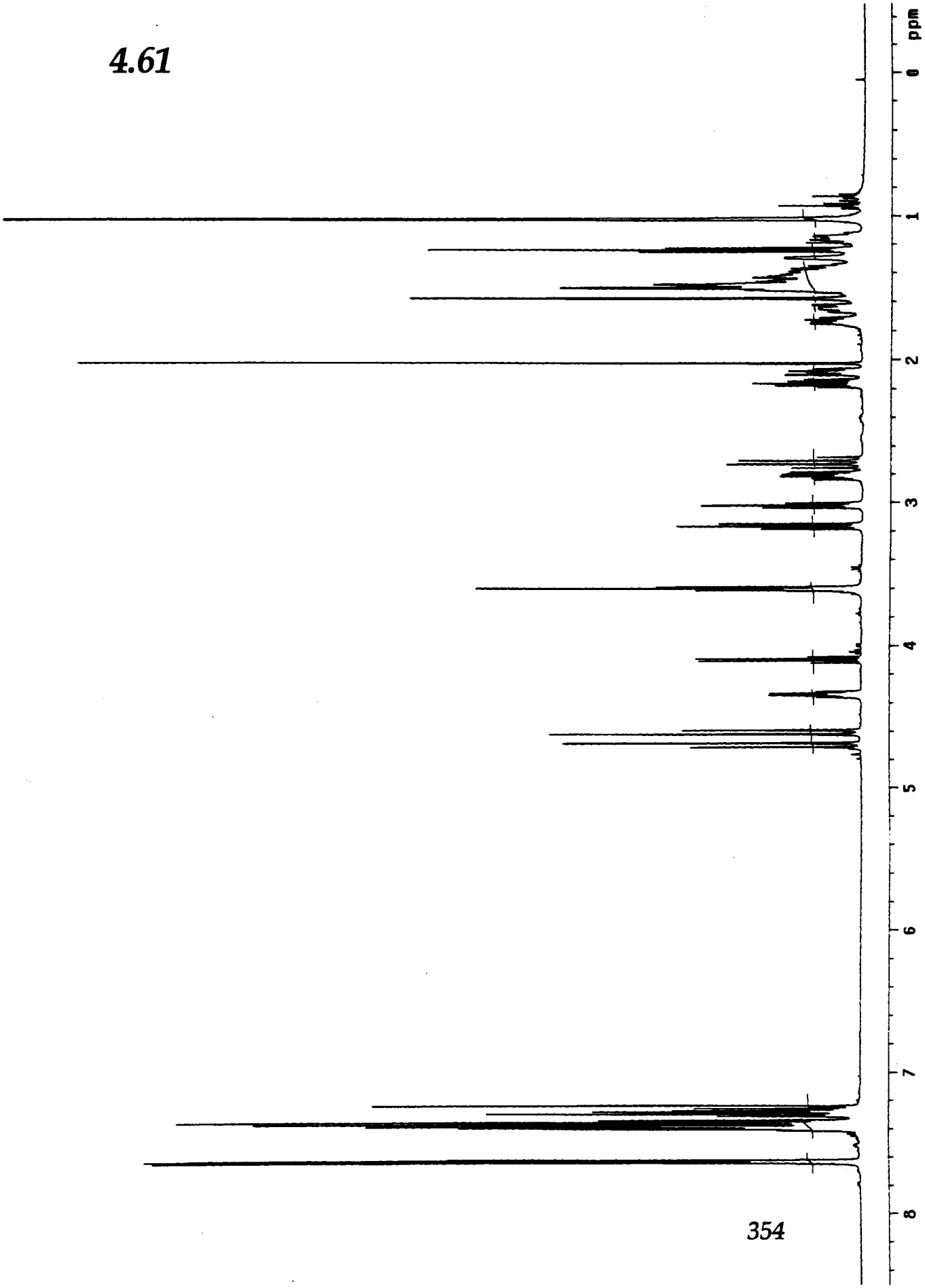
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.63 (dd, J= 8, 1 Hz, 4H), 7.41-7.30 (m, 8H), 7.29-7.24 (m, 3H), 4.70 (d, J_{AB}= 14 Hz, 1H), 4.61 (d, J_{AB}= 14 Hz, 1H), 4.34 (q, J= 7 Hz, 1H), 3.60 (t, J= 6 Hz, 2H), 3.17 (t, J= 9 Hz, 1H), 3.02 (t, J= 8 Hz, 1H), 2.84-2.78 (m, 1H), 2.71 (q, J= 13 Hz, 1H), 2.16 (quint, J=6 Hz, 1H), 2.10-2.06 (m, 1H), 1.75-1.71 (m, 1H), 1.67-1.62 (m, 1H), 1.55-1.32 (m, 8H), 1.30-1.29 (m, 1H), 1.20-1.12 (m, 1H), 1.02 (s, 9H).

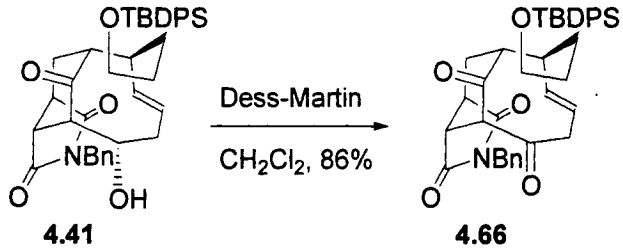
^{13}C NMR (125 MHz,$CDCl_3$) δ 216.5, 178.7, 177.8, 135.5 (x4), 133.9 (x2), 129.5 (x2), 129.0 (x2), 128.6 (x2), 128.0, 127.7, 127.6 (x4), 68.7, 63.8, 52.9, 47.8, 44.2, 42.5, 40.3, 38.0, 34.0, 33.0, 31.9, 30.2, 30.0, 26.8x3, 19.2, 19.1.

IR (neat) 2975, 2861, 1697 cm^{-1}.

EI HRMS calcd for $C_{35}H_{38}NO_5Si$ (M^+-*t*Bu) 580.25193, obsd 580.24432.

4.61





4.41 **4.66**

4-Benzyl-9-[3-(tert-butyl-diphenyl-silanyloxy)-propyl]-4-aza-tricyclo[6.5.1.02,6]tetradec-10-ene-3,5,13,14-tetraone (4.66)

Alcohol **4.41** (0.028 g, 0.045 mmol) was dissolved in CH_2Cl_2 (1 mL) and Dess-Martin periodate (31 mg, 0.072 mmol) was added and stirred for 25 minutes at room temperature. A solution of $NaHCO_{3sat}$ (10 mL) was added, followed by $Na_2S_2O_{3sat}$ (10 mL) and stirred for 20 minutes. The aqueous layer was extracted 3 times with dichloromethane (3 X 20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (30% EtOAc/hexanes) to afford 24 mg of **4.66** (86% yield) as colourless oil.

Data for **4.66**

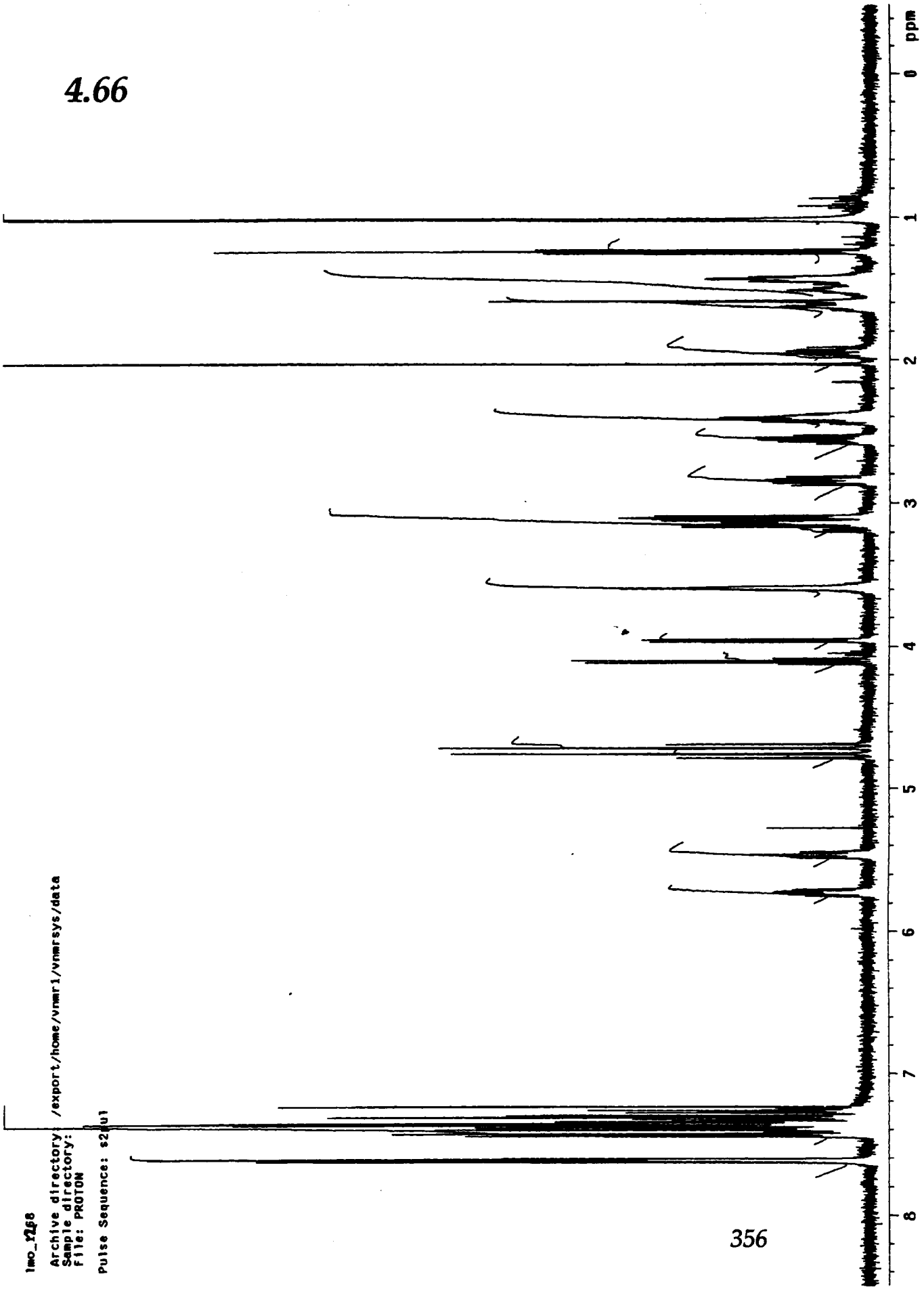
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.63-7.61 (m, 4H), 7.45-7.25 (m, 11H), 5.75-5.70 (m, 1H), 5.46 (t, J= 9 Hz, 1H), 4.77 (d, J_{AB} = 14 Hz, 1H), 4.70 (d, J_{AB} = 14 Hz, 1H), 3.96 (d, J= 8 Hz, 1H), 3.59-3.58 (m, 2H), 3.19-3.12 (m, 2H), 3.10 (dd, J= 10, 7 Hz, 1H), 2.84 (ddd, J= 13, 10, 7 Hz, 1H), 2.59-2.53 (m, 1H), 2.45-2.38 (m, 2H), 1.98-1.91 (m, 1H), 1.63-1.61 (m, 2H), 1.51-1.42 (m, 2H), 1.02 (s, 9H).

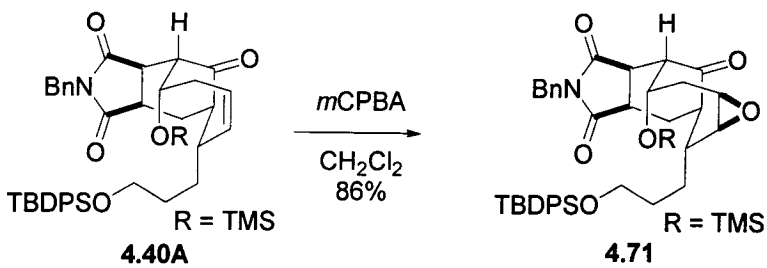
^{13}C NMR (125 MHz, $CDCl_3$): δ 207.0, 203.8, 177.2, 176.0, 137.1, 135.5 (x2), 135.4 (x2),133.7 (x2), 129.6 (x2), 128.8 (x4), 128.6 (x2), 127.9, 127.6 (x4), 124.4, 63.2, 62.4, 52.1, 44.4, 43.3, 42.9, 42.1, 36.1, 31.3, 30.3, 26.8 (x3), 19.2.

IR (neat) 2931, 2858, 1731, 1703, 1428, 1111 cm^{-1}.

EI HRMS calcd for $C_{35}H_{34}NO_5Si$ (M^+-*t*Bu) 576.22063, obsd 576.22196.

4.66


lmo_1268
Archive directory: /export/home/vnmr1/vnmrsys/data
Sample directory:
File: PROTON
Pulse Sequence: s2pul
0
1
2
3
4
5
6
7
8
ppm



4-Benzyl-9-[3-(tert-butyl-diphenyl-silanyloxy)-propyl]-13-trimethylsilanyloxy-4-aza-tricyclo[6.5.1.02,6]tetradec-10-ene-3,5,14-trione oxide (4.71)

Alkene **4.40A** (0.011g, 0.014mmol) was dissolved in dichloromethane (1 mL). *m*-chloroperoxybenzoic acid (0.003 g, 0.015 mmol) was added and stirred for 15 hours at room temperature. The reaction was quenched by adding $Na_2S_2O_{3sat}$ (5 mL) and stirred for 20 minutes. The aqueous layer was extracted 3 times with dichloromethane (3 X 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (30% EtOAc/hexanes) to afford 24 mg of **4.71** (86% yield) as a colourless oil.

Data for **4.71**

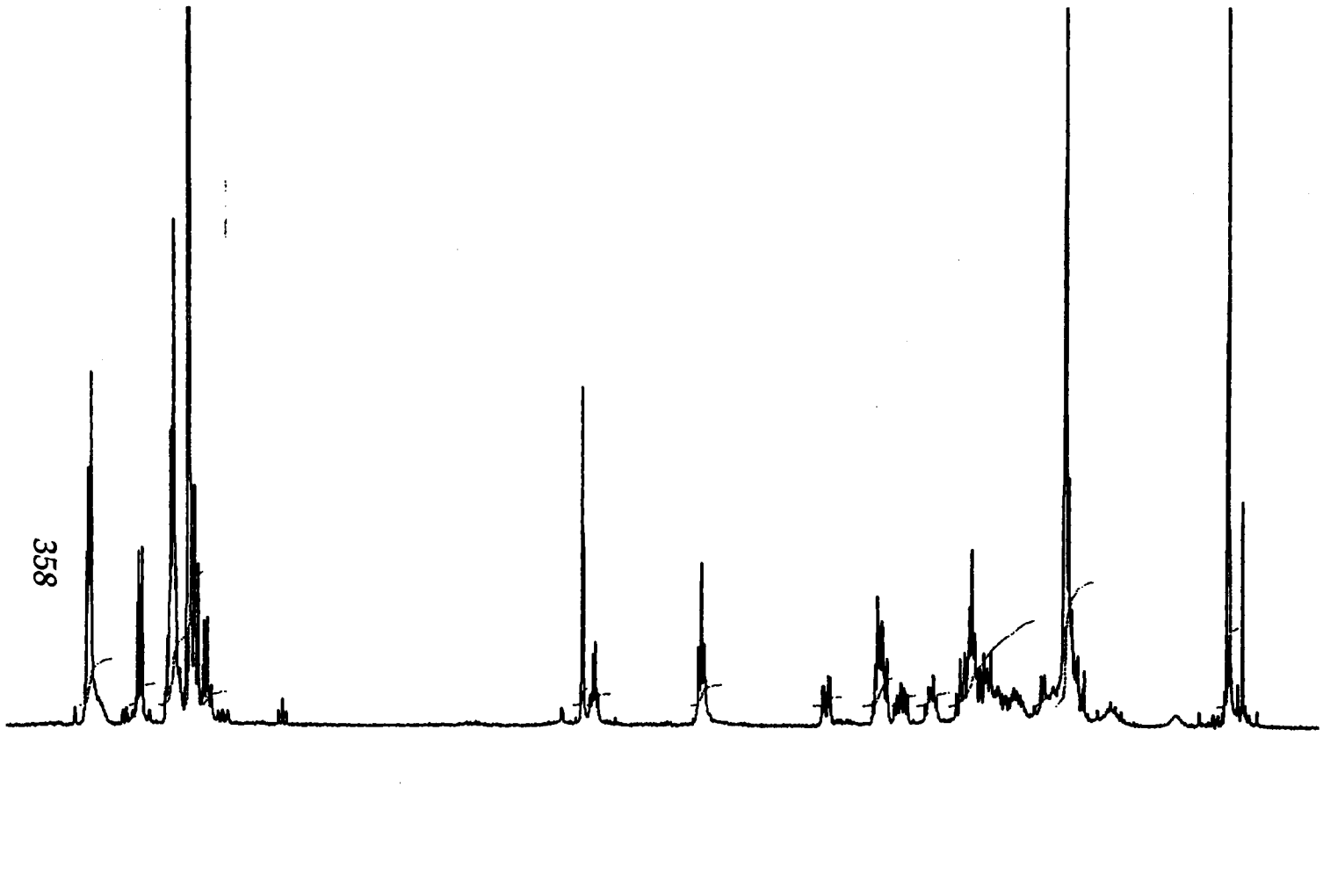
^{1}H NMR (300 MHz, C_6D_6): δ 7.84-7.70 (m, 4H), 7.47 (d, J= 7 Hz, 2H), 7.29-7.24 (m, 6H), 7.13-7.08 (m, 2H), 7.03 (dt, J= 7, 1 Hz, 1H), 4.47 (s, 2H), 4.39 (q, J= 5 Hz, 1H), 3.67 (t, J= 6 Hz, 2H), 2.82 (dd, J= 10, 4 Hz, 1H), 2.51-2.41 (m, 1H), 2.36-2.28 (m, 1H), 2.15-2.02 (m, 1H), 1.95-1.89 (m, 1H), 1.84 (t, J= 5 Hz, 2H), 1.80-1.51 (m, 5H), 1.37-1.32 (m, 1H), 1.21 (s, 9H), 1.18-1.17 (m, 2H), 0.11 (s, 9H).

^{13}C NMR (75 MHz, C_6D_6): δ 211.2, 178.0, 175.4, 136.6, 136.4(x4), 134.8 (x2), 130.3 (x2), 130.0 (x2), 129.3 (x2), 128.7, 128.5 (x4), 70.1, 64.6, 60.7, 53.9, 52.4, 51.0, 43.2, 40.9, 39.9, 36.8, 35.3, 30.7, 30.5, 28.4, 27.5 (x3), 19.9, 0.62 (x3).

IR (neat) 2953, 2931, 2857, 1706, 1395, 1252, 1111 cm^{-1}.

EI HRMS calcd for $C_{38}H_{44}NO_6Si_2$ (M^+-*t*Bu) 666.27072, obsd 666.27048.

4.71



Current Data Parameters

NAME	lmo_1284
EXPNO	3
PROCNO	1

F2 - Acquisition Parameters

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Time	20.54
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	C6D6
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	322.5
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

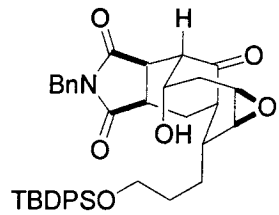
NUC1	1H
P1	10.50 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

F2 - Processing parameters

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

1D NMR plot parameters

CX	20.00 cm
CY	60.00 cm
F1P	8.500 ppm
F1	2551.10 Hz
F2P	-0.500 ppm
F2	-150.06 Hz
PPMCM	0.45000 ppm/cm
HZCM	135.05850 Hz/cm



4.72

4-Benzyl-9-[3-(tert-butyl-diphenyl-silanyloxy)-propyl]-13-hydroxy-4-aza-tricyclo[6.5.1.02,6]tetradec-10-ene-3,5,14-trione oxide(4.72)

Alkene **4.40A** (0.075 g, 0.11mmol) was dissolved in dichloromethane (1 mL). *m*-chloroperoxybenzoic acid (0.037 g, 0.21 mmol) was added and stirred for 15 hours at room temperature. The reaction was quenched by adding $Na_2S_2O_{3sat}$ (5 mL) and stirred for 20 minutes. The aqueous layer was extracted 3 times with dichloromethane (3 X 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was dissolved in THF (1 mL) and HCl 1 M (0.1 mL) was added. The reaction was completed after 15 minutes and quenched by adding $NaHCO_{3\ sat}$ (10 mL). The aqueous layer was extracted 3 times with diethylether (3 X 20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (50% EtOAc/hexanes) to afford 52 mg of **4.72** (quant yield) as colorless oil.

Data for **4.72**

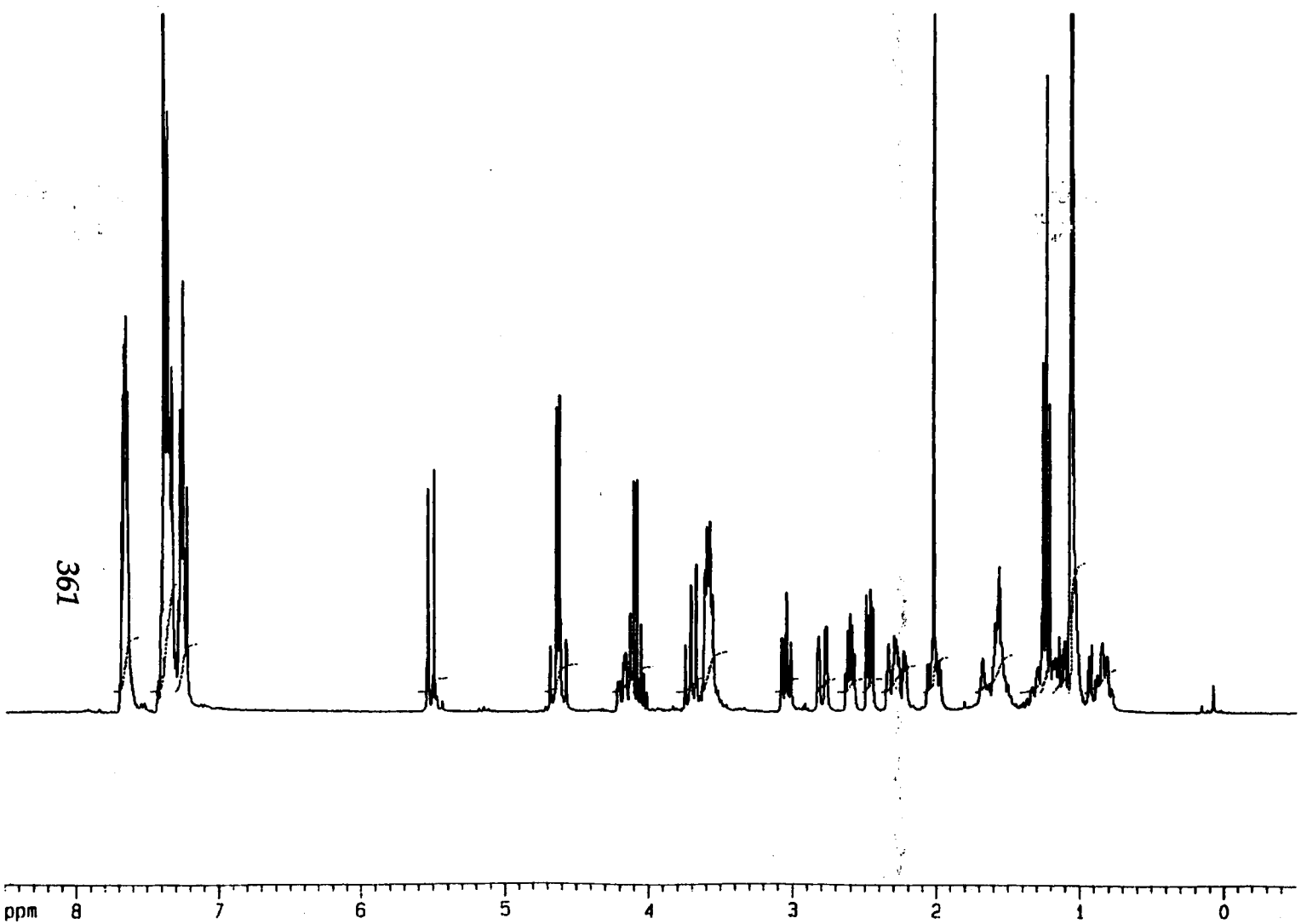
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.70-7.62 (m, 4H), 7.41-7.34 (m, 8H), 7.30-7.26 (m, 3H), 5.53 (d, J= 13 Hz, 1H), 4.66 (d, JAB= 14 Hz, 1H), 4.60 (d, JAB= 14 Hz, 1H), 4.17 (tdd, J= 13, 5, 2 Hz, 1H), 3.71 (dd, J= 13, 10 Hz, 1H), 3.61-3.56 (m, 3H), 3.05 (t, J= 10 Hz, 1H), 2.80 (d, J= 14 Hz, 1H), 2.60 (quint, J= 5 Hz, 1H), 2.47 (dd, J= 10, 5 Hz, 1H), 2.34-2.22 (m, 2H), 2.07-1.97 (m, 1H), 1.68-1.50 (m, 2H), 1.37-1.29 (m, 1H), 1.19-1.10 (m, 1H), 1.06 (s, 9H), 0.94-0.81 (m, 2H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 209.3, 180.8, 178.2, 135.5 (x4), 134.0, 133.9, 133.8, 129.5 (x2), 129.4 (x2), 128.9 (x2), 128.6, 127.6 (x4), 72.2, 63.7, 58.5, 53.3, 51.4, 50.5, 43.6, 38.9, 35.7, 35.5, 34.1, 28.4, 27.1, 26.8 (x3), 23.3,19.2.

IR (neat) 3427, 2932, 2858, 1687, 1110 cm^{-1}.

EI HRMS calcd for $C_{35}H_{36}NO_6Si$ (M^+-*t*Bu) 594.23119, obsd 594.22928.

4.72



Current Data Parameters

NAME	lmo_1292
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20050301
Time	17.41
INSTRUM	av300
PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	101.6
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

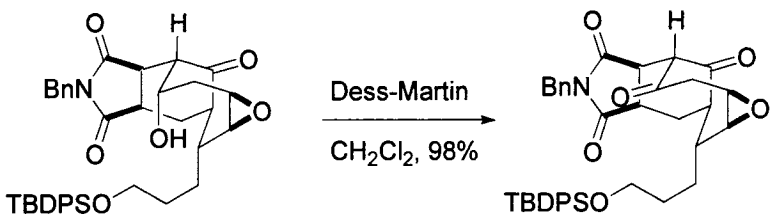
NUC1	1H
P1	10.50 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

F2 - Processing parameters

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

1D NMR plot parameters

CX	20.00 cm
CY	60.00 cm
F1P	8.500 ppm
F1	2551.10 Hz
F2P	-0.500 ppm
F2	-150.06 Hz
PPMCM	0.45000 ppm/cm
HZCM	135.05850 Hz/cm



4.72 **4.73**

4-Benzyl-9-[3-(tert-butyl-diphenyl-silanyloxy)-propyl]-4-aza-tricyclo[6.5.1.02,6]tetradec-10-ene-3,5,13,14-tetraone oxide (4.73)

Alcohol **4.72** (0.040 g, 0.063 mmol) was dissolved in CH_2Cl_2 (1 mL) and Dess-Martin periodate (43 mg, 0.1 mmol) was added and stirred for 25 minutes at room temperature. A solution of $NaHCO_{3sat}$ (10 mL) was added, followed by $Na_2S_2O_{3sat}$ (10 mL) and stirred for 20 minutes. The aqueous layer was extracted 3 times with dichloromethane (3 X 20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (40% EtOAc/hexanes) to afford 40 mg of **4.73** (98% yield) as white solid Mp = 54.8-57.6°C.

Data for **4.73**

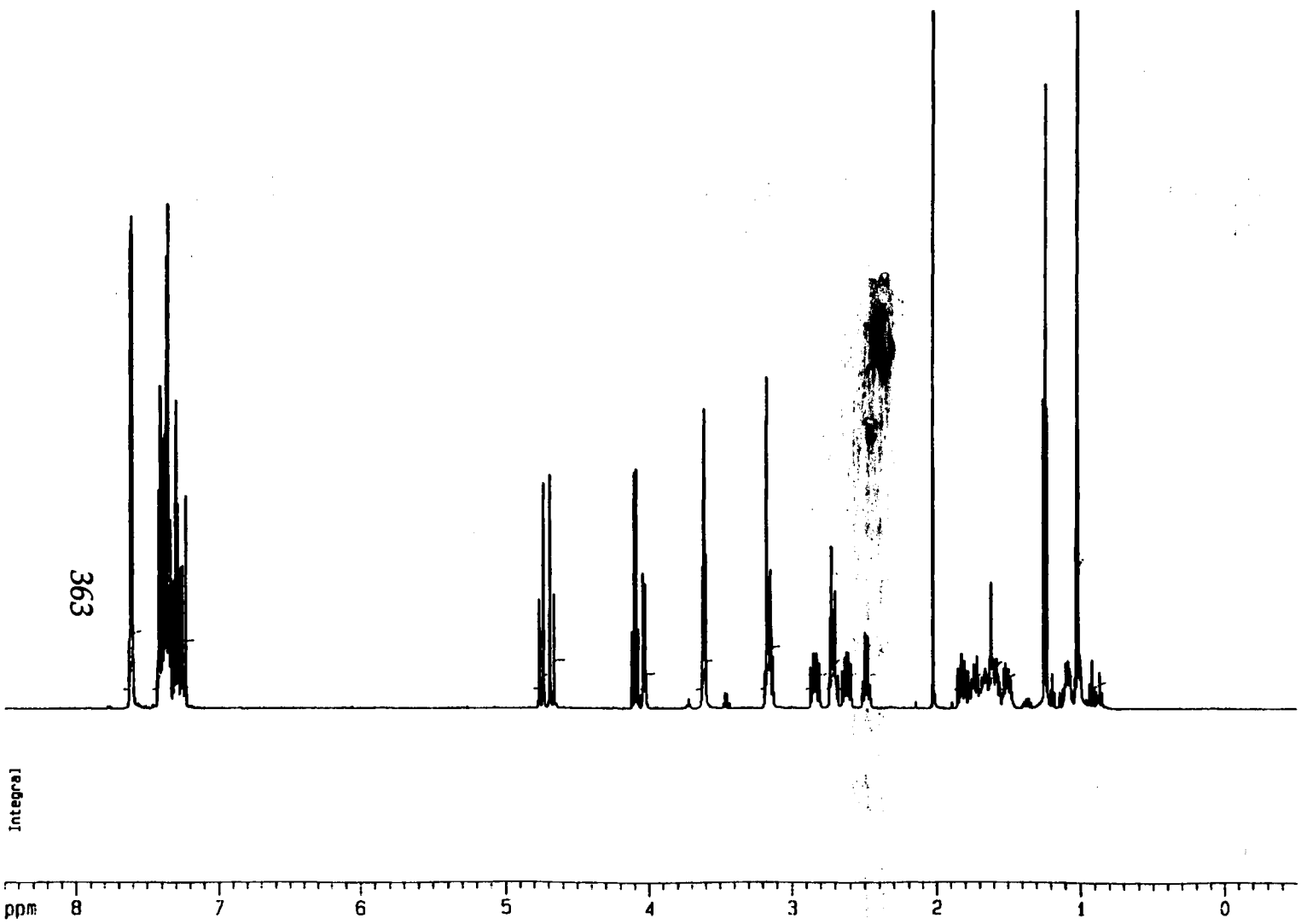
^{1}H NMR (500 MHz, acetone-d_6): δ 7.61 (dd, J= 6, 1 Hz, 4H), 7.43-7.36 (m, 8H), 7.35-7.24 (m, 3H), 4.75 (d, JAB= 14 Hz, 1H), 4.67 (d, JAB= 14 Hz, 1H), 4.03 (dd, J= 7, 1 Hz, 1H), 3.61 (t, J= 6 Hz, 2H), 3.19-3.13 (m, 3H), 2.87-2.81 (m, 1H), 2.74-2.68 (m, 2H), 2.65-2.59 (m, 1H), 2.48 (dq, J= 8, 1 Hz, 1H), 1.85-1.80 (m, 1H), 1.78-1.71 (m, 1H), 1.70-1.64 (m, 1H), 1.61-1.56 (m, 1H), 1.54-1.47 (m, 1H), 1.25-1.06 (m, 1H), 1.01 (s, 9H).

^{13}C NMR (125 MHz, acetone-d_6.) δ 205.0, 200.7, 176.7, 175.6, 135.5 (x4), 135.3, 133.7 (x2), 129.6 (x2), 128.7 (x2), 128.6 (x2), 127.9, 127.6 (x4), 63.2, 62.0, 59.5, 51.2, 50.3, 45.3, 44.3, 42.9, 42.0, 36.0, 31.6, 31.4, 29.8, 26.8 (x3), 19.0.

IR (neat) 2931, 2857, 1703, 1398, 1111 cm^{-1}.

EI HRMS calcd for $C_{35}H_{34}NO_6Si$ (M^+-*t*Bu) 592.21554, obsd 592.21694.

4.73



Current Data Parameters

NAME	lmo_1294
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

Date_	20050302
Time	16.41
INSTRUM	AV500MB
PROBHD	5 mm TBO BB/1H
PULPROG	zg30
TD	65536
SOLVENT	Acetone
NS	16
DS	0
SWH	7440.476 Hz
FIDRES	0.113533 Hz
AQ	4.4040694 sec
RG	114
DW	67.200 usec
DE	6.00 usec
TE	300.0 K
D1	0.01000000 sec

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

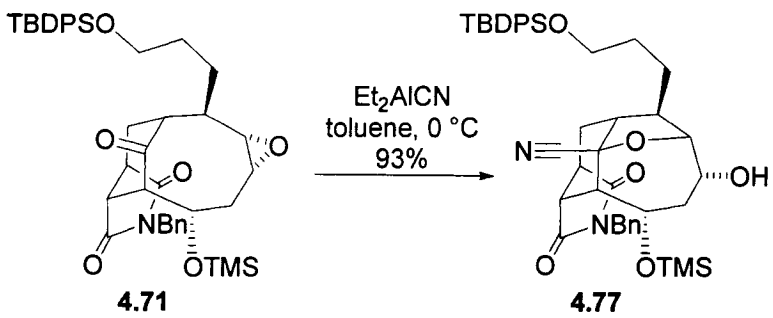
NUC1	1H
P1	14.00 usec
PL1	0.00 dB
SFO1	500.1327766 MHz

F2 - Processing parameters

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

1D NMR plot parameters

CX	20.00 cm
CY	60.00 cm
F1P	8.500 ppm
F1	4251.10 Hz
F2P	-0.500 ppm
F2	-250.06 Hz
PPMCM	0.45000 ppm/cm
HZCM	225.05849 Hz/cm



Epoxyde **4.71** (0.01 g, 0.014 mmol) was dissolved in toluene (1 mL) and cooled to 0°C. Et_2AlCN 1M (0.055 mL, 0.055 mmol) was added. The reaction was completed after 2 hours and quenched by adding $NaHCO_{3\ sat}$ (10 mL). The aqueous layer was extracted 3 times with diethylether (3 X 20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (50% EtOAc/hexanes) to afford 9 mg of **4.77** (93% yield) as colorless oil.

Data for **4.77**

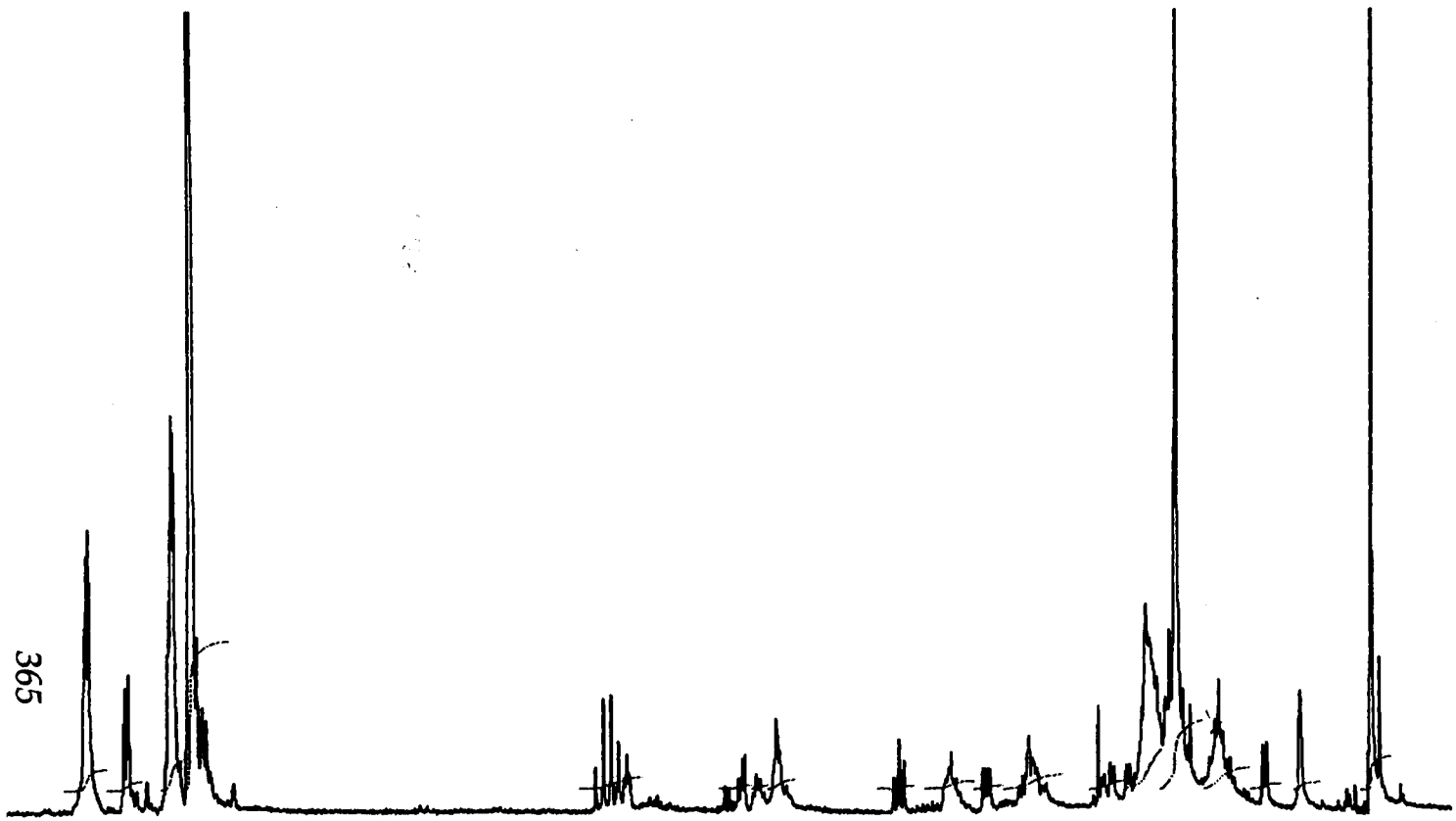
^{1}H NMR (300 MHz, C_6D_6): δ 7.79-7.76 (m, 2H), 7.55-7.53 (m, 1H), 7.28-7.25 (m, 2H), 4.65 (d, J_{AB}= 14 Hz, 1H), 4.56 (d, J_{AB}= 14 Hz, 1H), 4.50-4.47 (m, 1H), 3.79 (dd, J= 9, 4 Hz, 1H), 3.69 (q, J= 7 Hz, 1H), 3.59-3.51 (m, 2H), 2.85 (t, J= 9 Hz, 1H), 2.57-2.48 (m, 2H), 2.31 (dd, J= 9, 5 Hz, 1H), 2.12-1.95 (m, 4H), 1.61-1.50 (m, 2H), 1.46-1.21 (m, 8H), 1.19-1.09 (m, 6H), 1.17 (s, 9H), (-0.01, s, 9H).

^{13}C NMR (75 MHz, C_6D_6): δ 210.1, 177.2, 175.3, 136.2, 135.7 (x4), 134.1 (x2), 129.8 (x2), 129.6 (x2), 128.7 (x4), 128.7 (x2), 121.0, 86.7, 82.0, 70.9, 66.9, 63.8, 47.9, 45.9, 45.5, 42.6, 39.8, 38.2, 36.9, 33.1, 31.2, 27.7, 26.9 (x3), 19.2, 0.4 (x3).

IR (neat) 3507, 2928, 2859, 1704, 1112 cm^{-1}.

EI HRMS calcd for $C_{35}H_{34}N_2O_6Si_2$ (M^+-*t*Bu) 693.28162, obsd 693.28476.

4.77



365

8 7 6 5 4 3 2 1 0

Current Data Parameters
NAME lmo_1288nospot
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters

Date_	20050302
Time	11.43
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PROBHD	5 mm QNP 1H/1
PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	362
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

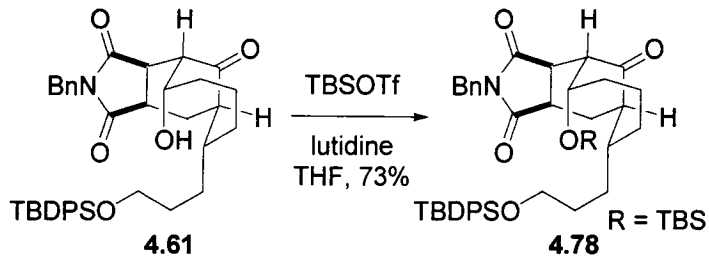
NUC1	1H
P1	10.50 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

F2 - Processing parameters

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

1D NMR plot parameters

CX	20.00 cm
CY	60.00 cm
F1P	8.500 ppm
F1	2551.10 Hz
F2P	-0.500 ppm
F2	-150.06 Hz
PPMCM	0.45000 ppm/cm
HZCM	135.05850 Hz/cm



4.61 **4.78**

4-Benzyl-13-(tert-butyl-dimethyl-silanyloxy)-9-[3-(tert-butyl-diphenyl-silanyloxy)-propyl]-4-aza-tricyclo[6.5.1.02,6]tetradecane-3,5,14-trione (4.78)

To a solution of alcohol **4.61** (0.106 g, 0.166 mmol) in THF (2 mL) was added lutidine (0.1 mL, 0.83 mmol) then cooled to 0 °C. *t*-Butyldimethylsilyltriflate (0.076 mL, 0.33 mmol) was added and the reaction was stirred for 30 min. The reaction was quenched by adding $NaHCO_{3sat.}$ The aqueous layer was extracted 3 times with diethylether (3 X 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (20% EtOAc/hexanes) to afford 91 mg **4.78** (73% yield) as a colourless oil.

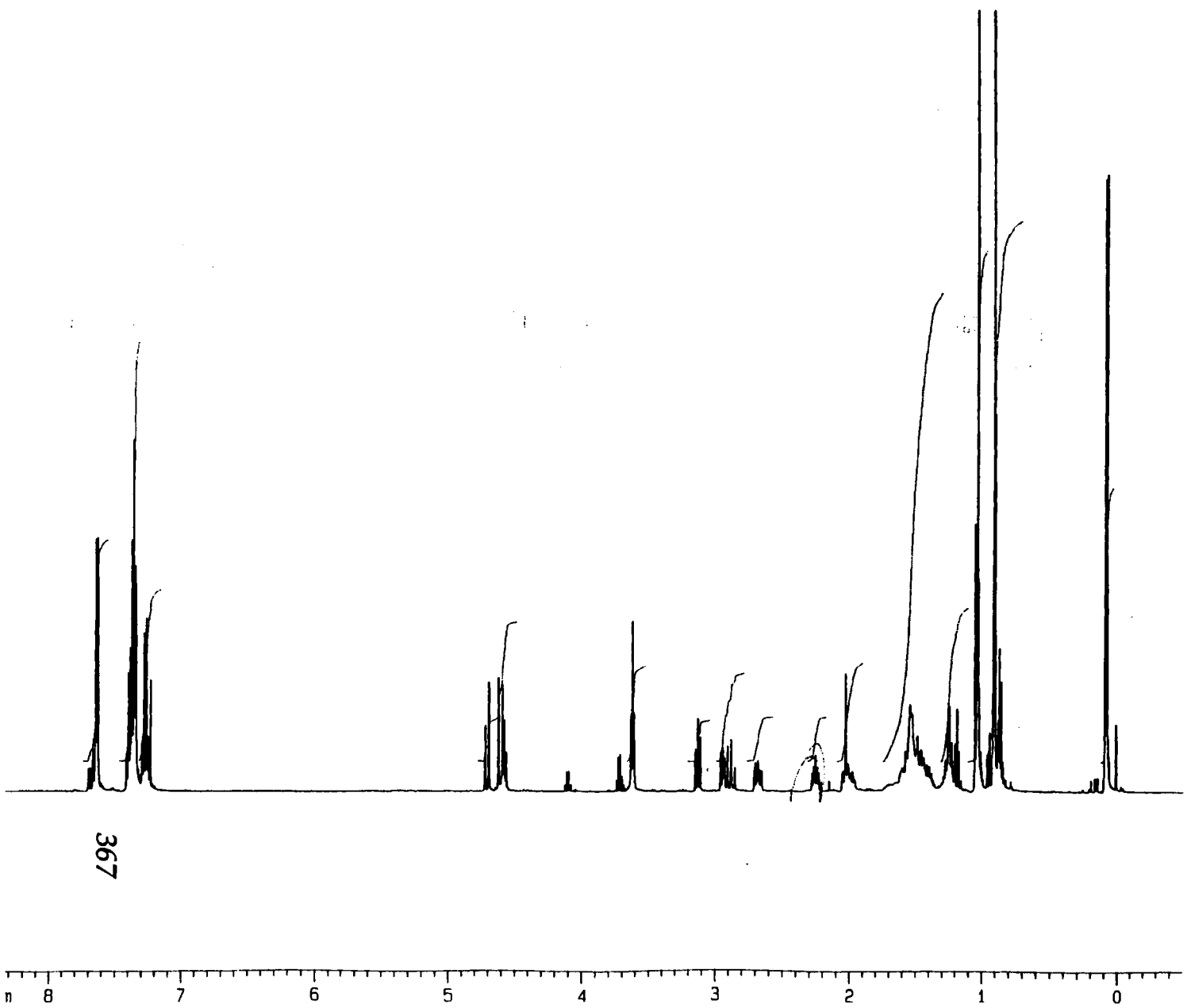
Data for **4.78**

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.66-7.64 (m, 4H), 7.41-7.35 (m, 8H), 7.29-7.27 (m, 3H), 4.71 (d, J_{AB}= 14 Hz, 1H), 4.62 (d, J_{AB}= 14 Hz, 1H), 4.58 (t, J= 7 Hz, 1H), 3.63 (t, J= 6 Hz, 2H), 3.14 (dd, J= 9, 9 Hz, 1H), 2.95 (dd, J= 8, 8 Hz, 1H), 2.90 (q, J= 13 Hz, 1H), 2.71-2.65 (m, 1H), 2.28-2.23 (m, 1H), 2.05-1.96 (m, 2H), 1.61-1.38 (m, 8H), 1.28-1.22 (m, 2H), 1.04 (s, 9H), 0.91 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 216.6, 177.7, 175.9, 135.7, 135.5 (x4), 133.9 (x2), 129.5 (x2), 128.9 (x2), 128.6 (x2), 128.0, 127.6 (x4), 68.8, 63.8, 55.0, 49.1, 45.0, 42.5, 40.2, 38.4, 35.1, 31.8 (x2), 31.5, 30.7, 30.1, 26.8 (x3), 26.5 (x3), 19.1, 18.3, -2.8, -4.8.

IR (neat) 2931, 2857, 1706, 1110 cm^{-1}.

MS ESI calcd for $C_{45}H_{61}NNaO_5Si_2$ (M^+ +Na) 774.4, obsd 774.6.



4.78

Current Data Parameters
NAME 1mo_1445
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20050705
Time 17.06
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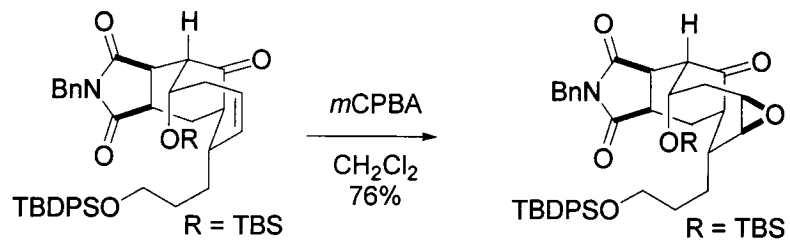
PROBHD 5 mm TBO BB/1H
PULPROG zg30
TD 65536
SOLVENT Acetone
NS 16
DS 0
SWH 7440.476 Hz
FIDRES 0.113533 Hz
AQ 4.4040694 sec
RG 45.25
DW 67.200 usec
DE 6.00 usec
TE 300.0 K
D1 0.01000000 sec

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

F2 - Processing parameters
SI 65536
SF 500.1300044 MHz
WDW EM
SSB 0
LB 0.00 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 20.00 cm
CY 40.00 cm
F1P 8.500 ppm
F1 4251.10 Hz
F2P -0.500 ppm
F2 -250.06 Hz
PPMCM 0.45000 ppm/cm
HZCM 225.05849 Hz/cm



4.38A **4.83**

4-Benzyl-13-(tert-butyl-dimethyl-silanyloxy)-9-[3-(tert-butyl-diphenyl-silanyloxy)-propyl]-4-aza-tricyclo[6.5.1.02,6]tetradec-10-ene-3,5,14-trione oxide (4.83)

To a solution of alkene **4.38A** (0.148 g, 0.20 mmol) in dichloromethane (2 mL) was added 3-chloroperbenzoic acid (0.068 g, 0.40 mmol). The solution was stirred for 15 hours. The reaction was quenched by adding a solution of sodium sulfite. The aqueous layer was extracted 3 times with dichloromethane (3 X 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (10% EtOAc/hexanes to 20% EtOAc/hexanes) to afford 115 mg of **4.83** (76% yield) as a white powder, mp = 41.5-43.0 °C.

Data for **4.83**

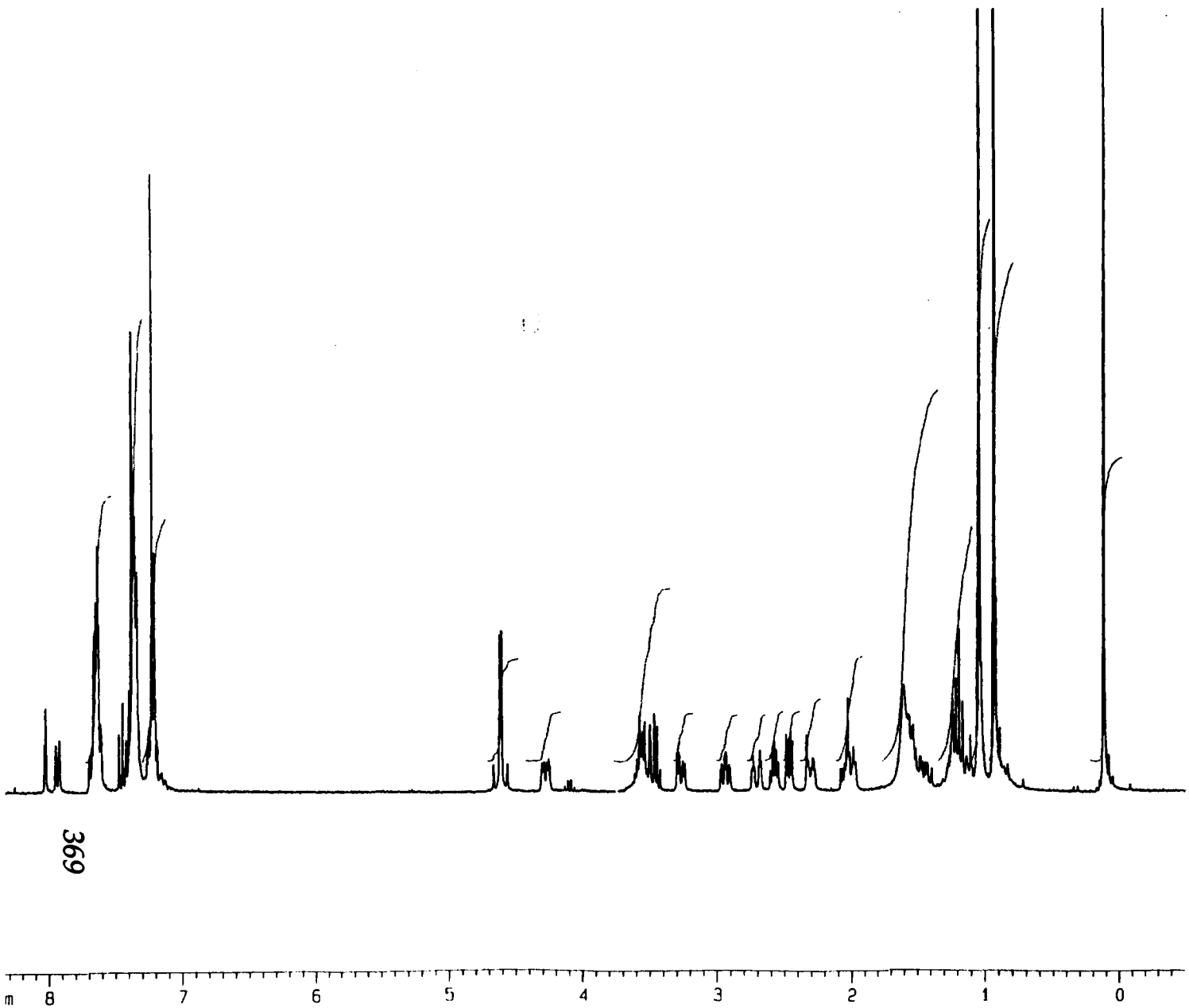
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.69-7.61 (m, 4H), 7.41-7.35 (m, 8H), 7.27-7.20 (m, 3H), 4.65 (d, J_{AB}= 14 Hz, 1H), 4.59 (d, J_{AB}= 14 Hz, 1H), 4.27 (ddd, J= 12, 5, 2 Hz, 1H), 3.58-3.45 (m, 3H), 3.27 (dd, J= 12, 5 Hz, 1H), 2.97-2.91 (m, 1H), 2.73-2.67 (m, 1H), 2.58 (quint, J= 5 Hz, 1H), 2.46 (dd, J= 9, 4 Hz, 1H), 2.34-2.29 (m, 1H), 2.05-1.97 (m, 2H), 1.56-1.42 (m, 3H), 1.24-1.17 (m, 3H), 1.05 (s, 9H), 0.93 (s, 9H), 0.12 (s, 6H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 211.1, 178.1, 174.4, 135.6 (x4), 135.0, 133.9 (x2), 129.6 (x2), 129.4 (x2), 128.7 (x2), 128.1 127.6 (x4), 72.0, 63.9, 58.7, 54.1, 51.7, 50.6, 42.9, 39.6, 36.2, 35.4, 35.2, 28.7, 27.6, 26.9 (x3), 25.7 (x3), 24.4, 19.2, 18.0, (-4.7), (-5.1).

IR (neat) 2935, 2856, 1708, 1109 cm^{-1}.

MS ESI calcd for $C_{45}H_{60}NO_6Si_2$ (M^++H) 766.4, obsd. 766.8.

4.83



Current Data Parameters

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EXPNO	2
PROCNO	1

F2 - Acquisition Parameters

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PULPROG	zg30
TD	30720
SOLVENT	CDCl3
NS	16
DS	0
SWH	5081.301 Hz
FIDRES	0.165407 Hz
AQ	3.0228980 sec
RG	362
DW	98.400 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec

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

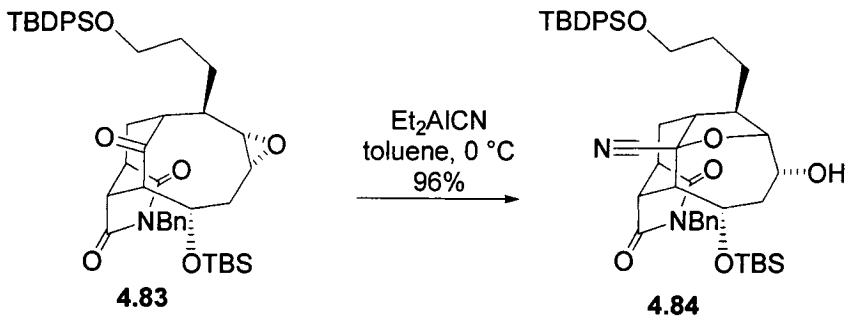
NUC1	1H
P1	10.50 usec
PL1	-3.00 dB
SFO1	300.1319477 MHz

F2 - Processing parameters

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

1D NMR plot parameters

CX	20.00 cm
CY	40.00 cm
F1P	8.500 ppm
F1	2551.10 Hz
F2P	-0.500 ppm
F2	-150.06 Hz
PPMCM	0.45000 ppm/cm
HZCM	135.05850 Hz/cm



To a solution of **4.83** (0.018 g, 0.027mmol) in toluene (1 mL) at 0°C was added diethylaluminumcyanide (0.108 mL, 0.108 mmol). The reaction was warmed to 25°C and stirred for 10 min. The reaction was quenched by adding $NaHCO_{3sat}$. The aqueous layer was extracted 3 times with diethylether (3 X 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (30% EtOAc/hexanes) to afford 18 mg of **4.84** (96% yield) as white powder, mp = 93.9-95.1 °C.

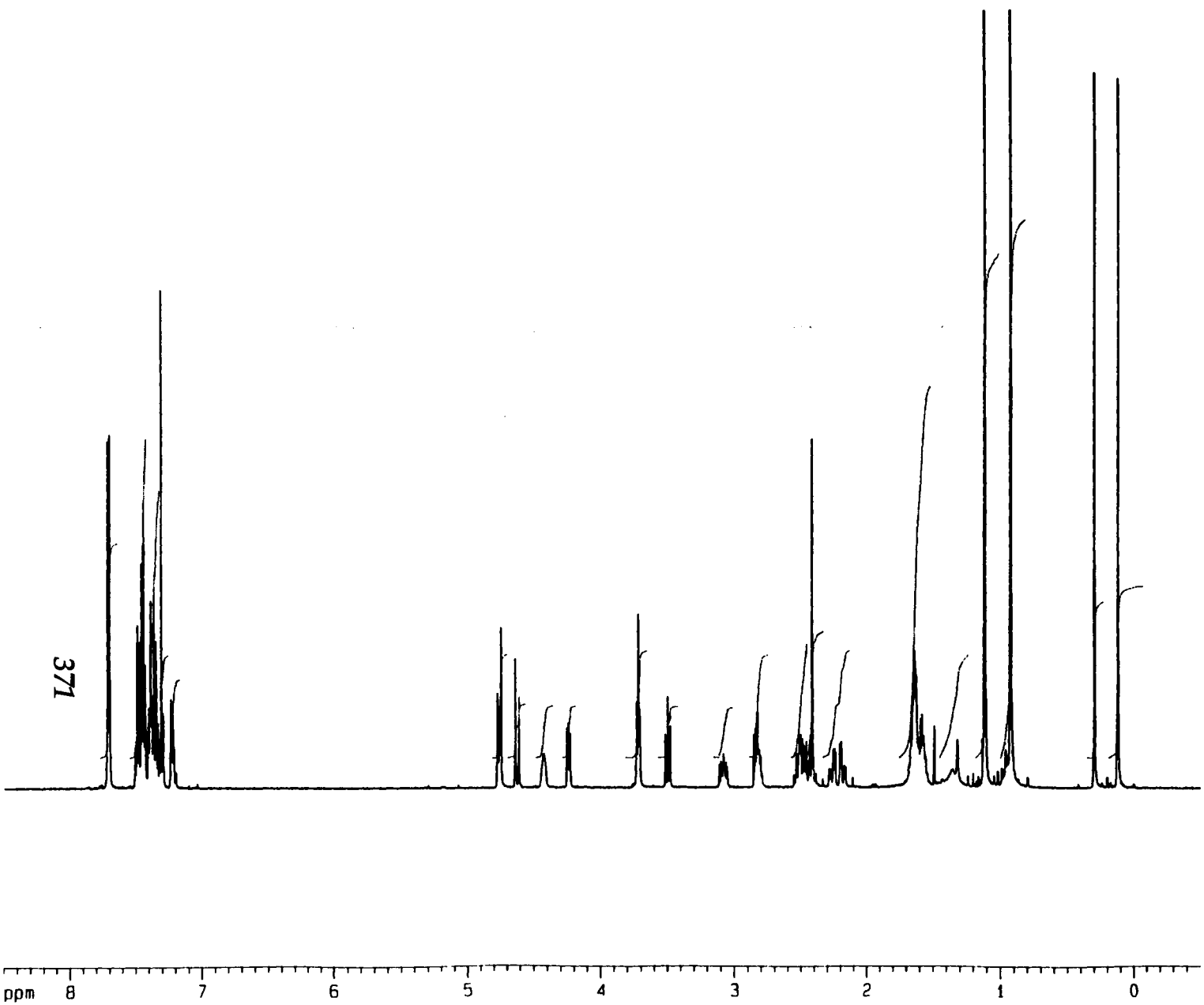
Data for **4.84**

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.74-7.71 (m, 4H), 7.51-7.45 (m, 6H), 7.44-7.33 (m, 4H), 7.24-7.22 (m, 1H), 4.77-4.76 (m, 1H), 4.77 (d, J_{AB}= 14 Hz, 1H), 4.62 (d, J_{AB}= 14 Hz, 1H), 4.44-4.43 (m, 1H), 4.24 (dd, J= 8, 4 Hz, 1H), 3.72 (t, J= 6 Hz, 2H), 3.50 (dd, J= 9, 9 Hz, 1H), 3.11-3.05 (m, 1H), 2.85-2.79 (m, 1H), 2.84 (dd, J= 9, 5 Hz, 1H), 2.53-2.43 (m, 2H), 2.41 (s, 2H), 2.29-2.16 (m, 2H), 1.65-1.63 (m, 4H), 1.11 (s, 9H), 0.92 (s, 9H), 0.30 (s, 3H), 0.12 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$) δ 177.4, 175.2, 135.6 (x4), 135.3, 133.9 (x2), 129.6 (x2), 129.0, 128.7 (x2), 128.2 (x2), 128.1, 127.7 (x2), 125,3, 120.9, 87.0, 82.6, 71.6, 68.0, 63.7, 48.4, 46.0, 45.6, 42.5, 40.4, 37.6, 37.2, 33.2, 31.3, 27.3, 26.9 (x3), 26.3 (x3), 19.2, 18.1, -1.4, -5.0.

IR (neat) 3531, 2930, 2857, 1704, 1396, 1111 cm^{-1}.

MS ESI calcd for $C_{46}H_{60}N_2NaO_6Si_2$ (M^+ +Na) 815.4, obsd. 815.4.



4.84

371

Current Data Parameters

NAME	lmo_1459
EXPNO	1
PROCNO	1

F2 - Acquisition Parameters

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PULPROG	zg30
TD	65536
SOLVENT	Acetone
NS	16
DS	0
SWH	7440.476 Hz
FIDRES	0.113533 Hz
AQ	4.4040694 sec
RG	203.2
DW	67.200 usec
DE	6.00 usec
TE	300.0 K
D1	0.01000000 sec

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

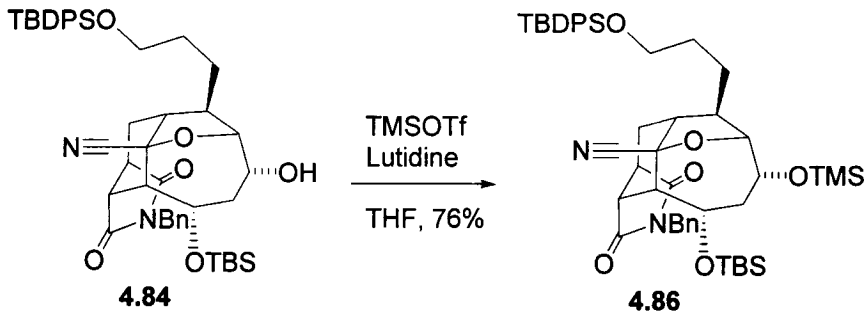
NUC1	1H
P1	14.00 usec
PL1	0.00 dB
SFO1	500.1327766 MHz

F2 - Processing parameters

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

1D NMR plot parameters

CX	20.00 cm
CY	40.00 cm
F1P	8.500 ppm
F1	4251.10 Hz
F2P	-0.500 ppm
F2	-250.06 Hz
PPMCM	0.45000 ppm/cm
HZCM	225.05849 Hz/cm



4.84 **4.86**

Alcohol **4.84** (0.006 g, 0.008 mmol) was dissolved in THF (1 mL) then cooled to 0°C. Lutidine (0.030 mL, 0.24 mmol) was added followed by trimethylsilyltriflate (0.014 mL, 0.075 mmol) and the reaction was stirred for 30 min. The reaction was quenched by adding $NaHCO_{3sat.}$ The aqueous layer was extracted 3 times with diethylether (3 X 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (10% EtOAc/hexanes) to afford 5 mg of **4.86** (76% yield) as a colourless oil.

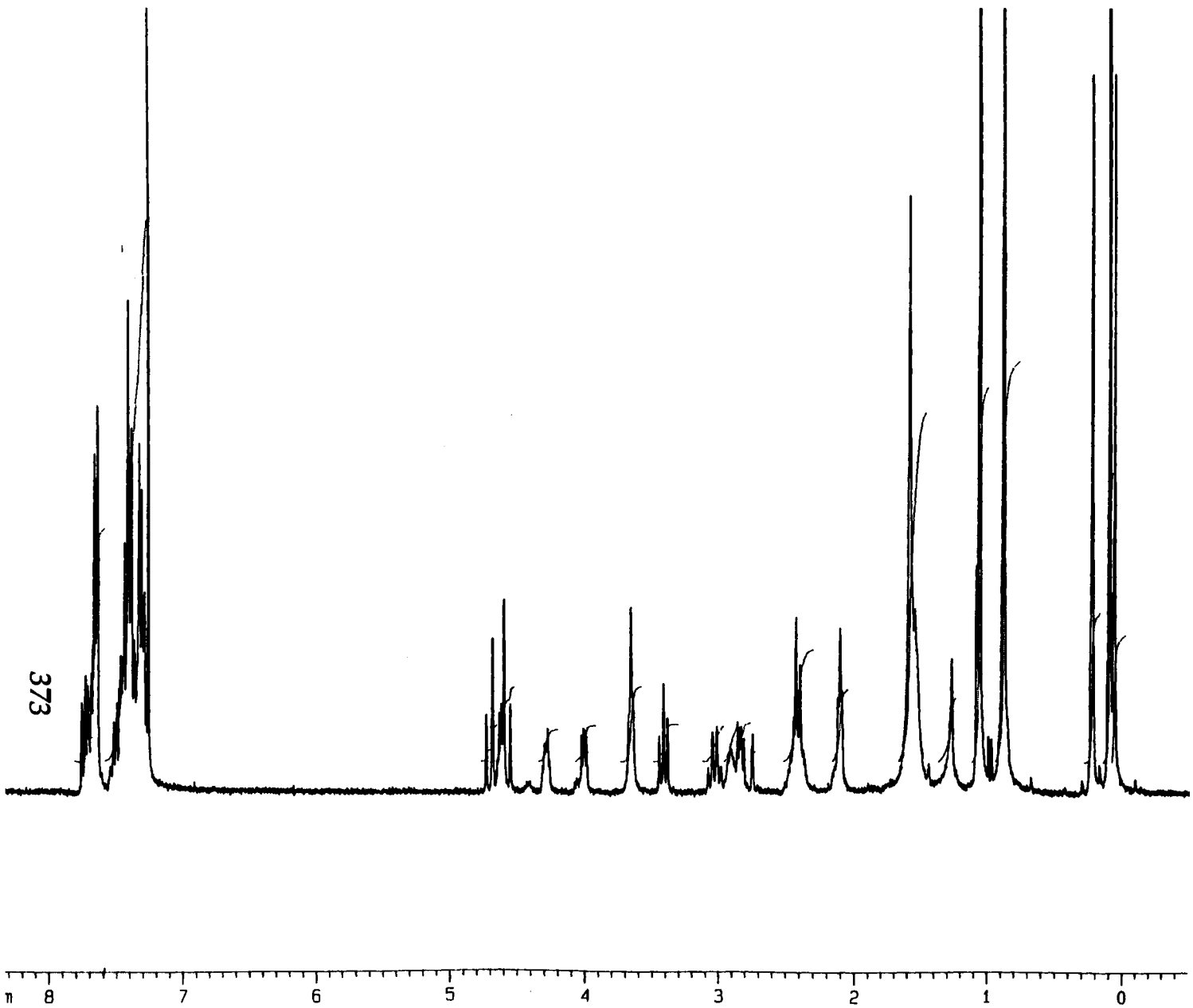
Data for **4.86**

^{1}H NMR (300 MHz, $CDCl_3$): δ 7.77-7.66 (m, 6H), 7.56-7.29 (m, 9H), 4.71 (d, J_{AB}= 14 Hz, 1H), 4.63 (d, J= 4 Hz, 1H), 4.58 (d, J_{AB}= 14 Hz, 1H), 4.32-4.27 (m, 1H), 4.01 (dd, J= 7, 4 Hz, 1H), 3.67 (s, 2H), 3.42 (t, J= 9 Hz, 1H), 3.03 (q, J= 10 Hz, 1H), 2.92-2.88 (m, 1H), 2.83 (dd, J= 9, 5 Hz, 1H), 2.47-2.36 (m, 4H), 2.11 (t, J= 4 Hz, 2H), 1.55 (s, 1H), 1.27 (s, 2H), 1.06 (s, 9H), 0.89 (s, 9H), 0.23 (s, 3H), 0.10 (s, 9H), 0.06 (s, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 177.5, 175.3, 135.5 (x4), 133.8, 132.3, 132.2, 131.5 (x2), 129.6 (x2), 128.7 (x2), 128.6, 128.4, 128.1, 127.7 (x2), 121.0, 87.5, 82.1, 77.2, 71.2, 67.3, 63.9, 48.2, 46.3, 45.5, 42.5, 40.4, 38.6, 37.1, 33.3, 31.2, 26.9 (x3), 26.4 (x3), 19.2, 18.2, -0.2 (x3), -1.7, -4.9.

IR (neat) 2954, 2930, 2857, 1710, 1111 cm^{-1}.

MS ESI calcd for $C_{49}H_{68}N_2NaO_6Si_3$ (M^+ Na) 887.4, obsd. 887.4.



4.86

Current Data Parameters
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EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
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Time 8.47
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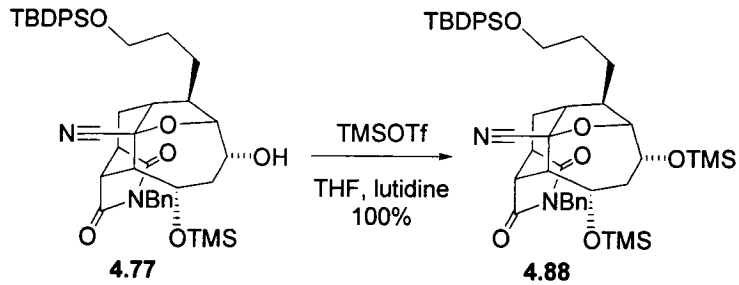
PULPROG zg30
TD 30720
SOLVENT CDCl3
NS 16
DS 0
SWH 5081.301 Hz
FIDRES 0.165407 Hz
AQ 3.0228980 sec
RG 512
DW 98.400 usec
DE 6.00 usec
TE 300.0 K
D1 1.00000000 sec

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

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

1D NMR plot parameters
CX 20.00 cm
CY 40.00 cm
F1P 8.500 ppm
F1 2551.10 Hz
F2P -0.500 ppm
F2 -150.06 Hz
PPMCM 0.45000 ppm/cm
HZCM 135.05850 Hz/cm



4.77 **4.88**

Alcohol **4.77** (0.053 g, 0.07 mmol) was dissolved in THF (1 mL). Lutidine (0.030 mL, 0.26 mmol) was added and the mixture was cooled to 0°C before the addition of trimethylsilyl trifluoromethanesulfonate (0.024 mL, 0.13 mmol). The reaction was completed after 10 minutes and quenched by adding $NaHCO_{3\ sat}$ (10 mL). The aqueous layer was extracted 3 times with diethylether (3 X 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash silica column chromatography (10% EtOAc/hexanes) to afford 60 mg of **4.88** (100% yield) as a colourless oil.

Data for **4.88**

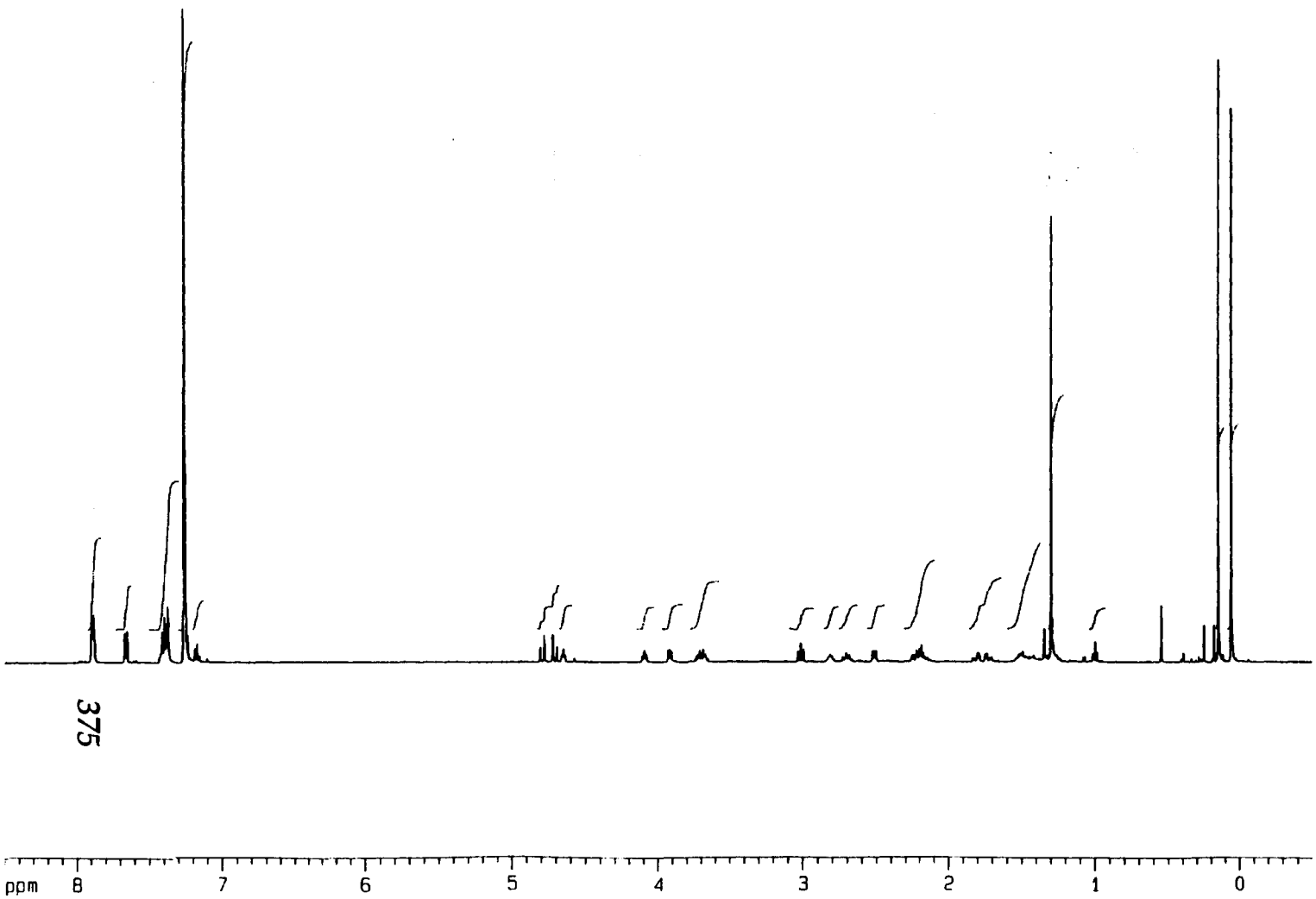
^{1}H NMR (500 MHz, C_6D_6): δ 7.99-7.88 (m, 4H), 7.67-7.66 (m, 2H), 7.43-7.35 (m, 6H), 7.26-7.24 (m, 2H), 7.19-7.16 (m, 1H), 4.79 (d, J_{AB}= 14 Hz, 1H), 4.70 (d, J_{AB}= 14 Hz, 1H), 4.64 (t, J= 5 Hz, 1H), 3.91 (dd, J= 7, 5 Hz, 1H), 3.73-3.66 (m, 2H), 3.01 (t, J= 9 Hz, 1H), 2.82-2.78 (m, 1H), 2.72-2.66 (m, 1H), 2.50 (dd, J= 9, 5 Hz, 1H), 2.25-2.13 (m, 3H), 1.83-1.70 (m, 2H), 1.54-1.41 (m, 4H), 1.33-1.26 (m, 1H), 1.29 (s, 9H), 0.15 (s, 9H), 0.06 (s, 9H).

^{13}C NMR (125 MHz, C_6D_6) δ 177.9, 176.0, 136.9, 136.3 (x4), 134.6 (x2), 130.4 (x4), 130.2 (x2), 129.3 (x2), 128.8, 128.5 (x2), 121.8, 87.8, 82.5, 72.5, 67.2, 64.6, 48.6, 46.7, 46.4, 43.3, 40.7, 39.3, 37.5, 34.1, 32.0, 28.2, 27.5 (x3), 19.8, 1.12 (x3), 0.05 (x3).

IR (neat) 2953, 2857, 1706, 1113 cm^{-1}.

MS ESI calcd for $C_{46}H_{62}N_2NaO_6Si_3$ (M^+ Na) 845.4, obsd. 845.5.

1H NMR



4.88

Current Data Parameters	
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EXPNO	1
PROCNO	1

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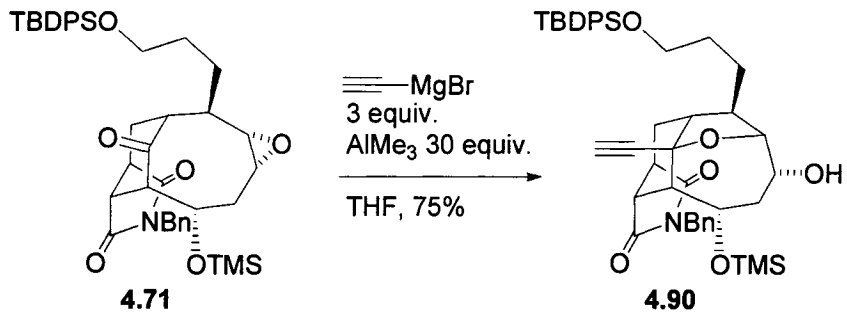
PULPROG	zg30
TD	65536
SOLVENT	Acetone
NS	16
DS	0
SWH	7440.476 Hz
FIDRES	0.113533 Hz
AQ	4.4040694 sec
RG	203.2
DW	67.200 usec
DE	6.00 usec
TE	300.0 K
D1	0.01000000 sec

======== CHANNEL f1 ========	
NUC1	1H
P1	13.50 usec
PL1	0.00 dB
SFO1	500.1327766 MHz

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

1D NMR plot parameters	
CX	20.00 cm
CY	10.00 cm
F1P	8.500 ppm
F1	4251.10 Hz
F2P	-0.500 ppm
F2	-250.06 Hz
PPMCM	0.45000 ppm/cm
HZCM	225.05849 Hz/cm



To a solution of epoxyde **4.71** (0.326 g, 0.45mmol) in toluene (5 mL) at –78°C was added trimethylaluminum neat (1.3 mL, 13.5 mmol). Ethynylmagnesium bromide 0.5 M (2.7 mL, 1.35 mmol) was added dropwise and the reaction was warmed to room temperature and stirred for 15 hours. The reaction was quenched by adding 20 mL of diethylether and adding a of sodium tartrate dropwise. The aqueous layer was extracted 3 times with diethylether (3 X 50 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography (30% EtOAc/hexanes) to afford 254 mg of **4.90** (75% yield) colourless oil.

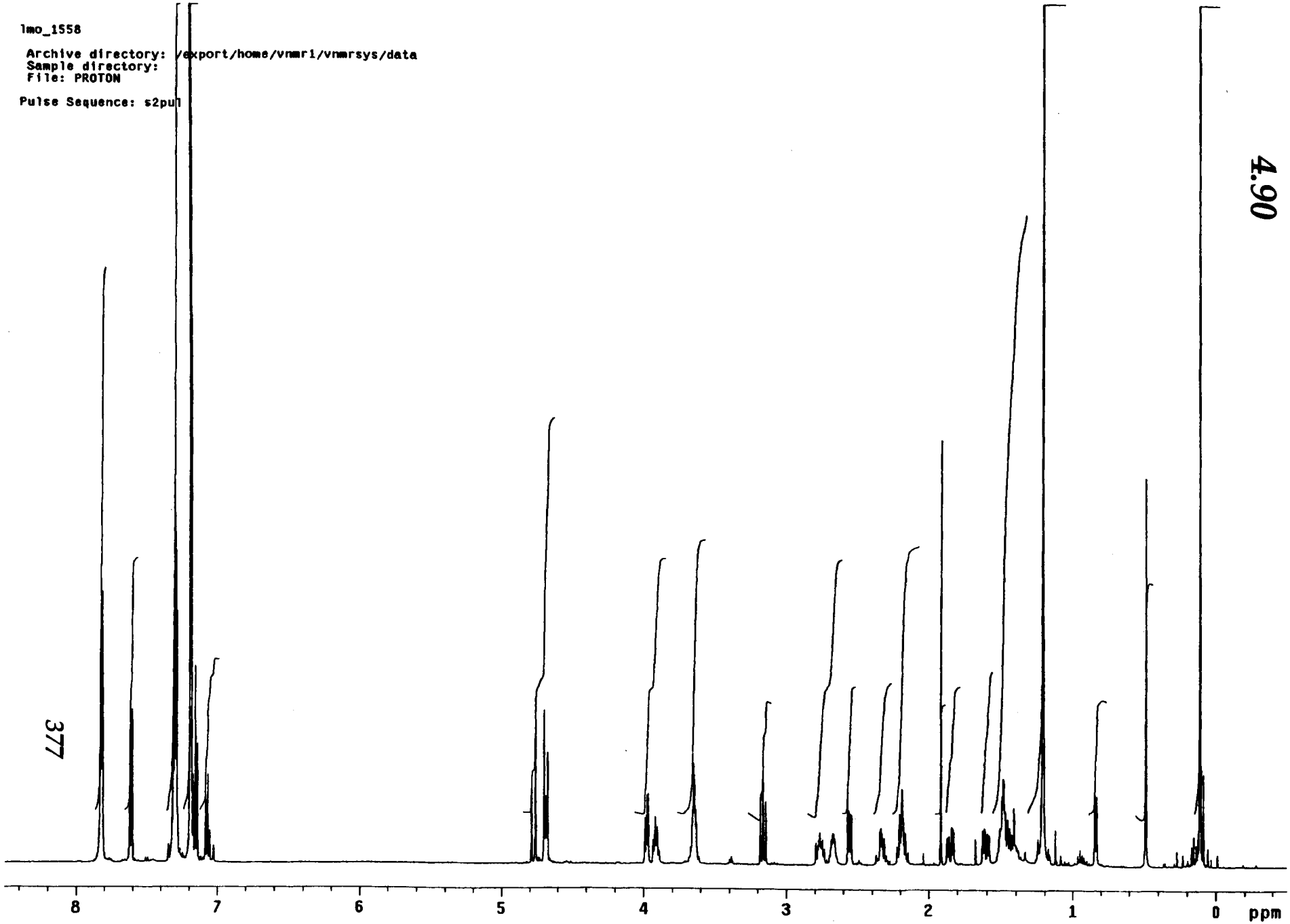
Data for **4.90**

^{1}H NMR (500 MHz, C_6D_6): δ 7.83-7.81 (m, 4H), 7.61 (d, J= 7 Hz, 2H), 7.32-7.28 (m, 6H), 7.16 (t, J= 8 Hz, 2H), 7.07 (tt, J= 7, 2 Hz, 1H), 4.77 (d, J_{AB}= 14 Hz, 1H), 4.69 (s, 1H), 4.68 (d, J_{AB}= 14 Hz, 1H), 3.97 (dd, J= 8, 5 Hz, 1H), 3.91 (q, J= 7 Hz, 1H), 3.67-3.62 (m, 2H), 3.16 (t, J= 9 Hz, 1H), 2.79-2.75 (m, 1H), 2.68-2.66 (m, 1H), 2.55 (dd, J= 9, 5 Hz, 1H), 2.34-2.31 (m, 1H), 2.22-2.15 (m, 2H), 1.92 (s, 1H), 1.85 (ddd, J= 16, 6, 1 Hz, 1H), 1.60 (ddd, J= 16, 7, 1 Hz, 1H), 1.51-1.38 (m, 4H), 1.21 (s, 9H), 0.83 (d, J= 7 Hz, 1H), 0.11 (s, 9H).

^{13}C NMR (125 MHz, C_6D_6) δ 178.9, 177.2, 137.3, 136.4 (x4), 134.8 (x2), 130.3, 130.1 (x2), 129.3 (x2), 128.5 (x2), 128.3 (x4), 87.5, 86.7, 83.3, 72.5, 72.2, 68.2, 64.6, 49.9, 48.2, 47.2, 433.1, 41.7, 39.2, 38.1, 34.3, 32.0, 29.1, 27.5 (x3), 19.8, 1.2 (x3).

IR (neat) 3496, 2930, 2857, 1701, 1094 cm^{-1}.

MS ESI calcd for $C_{44}H_{55}NNaO_6Si_2$ (M^+ Na) 772.4, found 772.5.


lmo_1558
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File: PROTON
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4.90
377
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7
6
5
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3
2
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0
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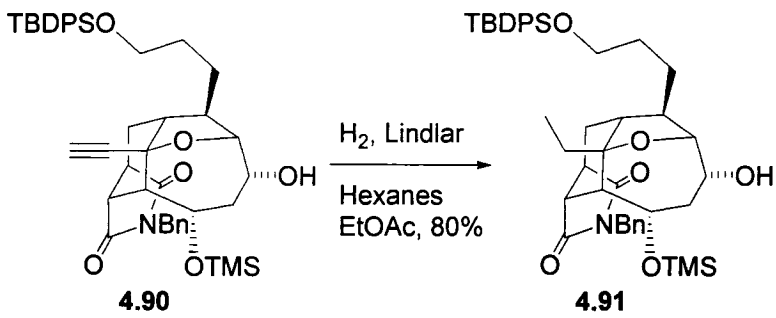


Alkyne **4.90** (0.010 g, 0.013 mmol) was dissolved in distilled hexanes (1.6 mL) and ethylacetate (0.4 mL). Lindlar's catalyst (8 mg) was added and the flask was purged with H_2 for two min. The reaction was stirred for 15 hours, filtered trough a celite pad and rinced with dichloromethane. The solvent was evaporated. The crude product was purified by flash column chromatography (20% EtOAc/hexanes) to afford 8 mg of **4.91** (80% yield) colourless oil.

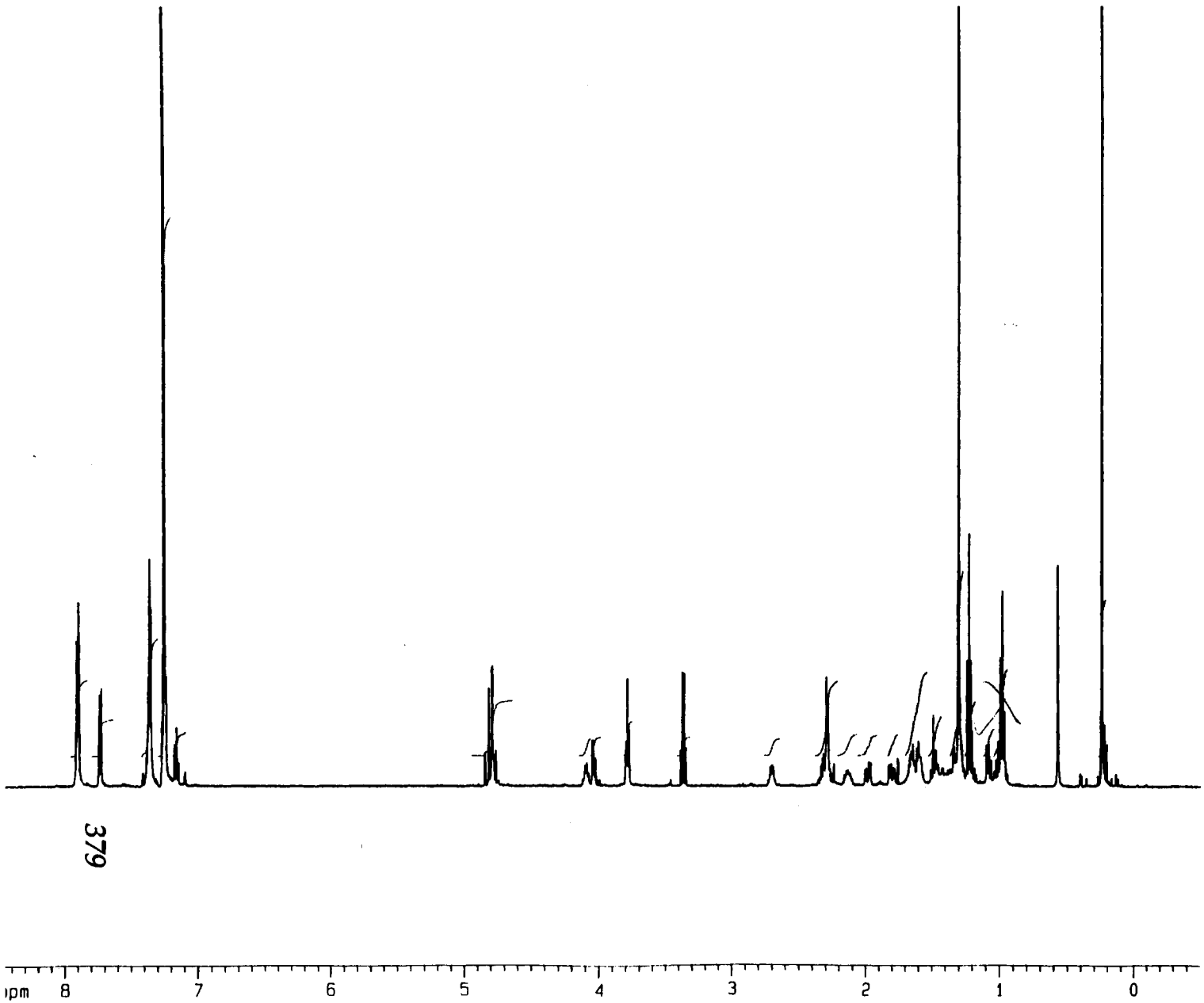
Data for **4.91**

^{1}H NMR (500 MHz, C_6D_6): δ 7.92-7.88 (m, 4H), 7.74 (d, J= 7 Hz, 2H), 7.39-7.36 (m, 6H), 7.28-7.25 (m, 2H), 7.18-7.16 (m, 1H), 4.83 (d, J_{AB}= 14 Hz, 1H), 4.80 (s, 1H), 4.78 (d, J_{AB}= 14 Hz, 1H), 4.09 (q, J= 6 Hz, 1H), 4.04 (dd, J= 8, 4 Hz, 1H), 3.79 (t, J= 6 Hz, 2H), 2.71-2.69 (m, 1H), 2.35-2.24 (m, 4H), 2.16-2.10 (m, 1H), 1.99 (dd, J= 6, 1 Hz, 1H), 1.79 (ddd, J= 15, 7, 2 Hz, 1H), 1.67-1.58 (m, 5H), 1.48 (q, J= 8 Hz, 2H), 1.38-1.32 (m, 1H), 1.30 (s, 9H), 1.22 (t, J= 7 Hz, 3H), 0.24 (s, 9H).

^{13}C NMR (125 MHz, C_6D_6) δ 179.1, 177.4, 137.5, 136.4 (x4), 134.9 (x2), 130.3 (x5), 129.3 (x4), 128.5(x2), 88.5, 86.1, 72.6, 69.3, 64.7, 48.1, 47.4, 44.8, 43.1, 41.1, 39.5, 37.9, 35.2, 34.7, 32.2, 29.1, 27.5 (x3), 19.9, 8.8, 1.3 (x3).

IR (neat) 3473, 2931, 2857, 1699, 1111 cm^{-1}.

MS ESI calcd for $C_{44}H_{59}NNaO_6Si_2$ (M^+ Na) 776.4, obsd. 776.5.



4.91

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Current Data Parameters
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EXPNO                        1
PROCNO                       1

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PULPROG                  zg30
TD                      65536
SOLVENT                  C6D6
NS                         16
DS                          0
SWH                7440.476 Hz
FIDRES             0.113533 Hz
AQ                 4.4040694 sec
RG                       203.2
DW                    67.200 usec
DE                     6.00 usec
TE                     300.0 K
D1                0.01000000 sec

======== CHANNEL f1 ========
NUC1                        1H
P1                     13.50 usec
PL1                     0.00 dB
SFO1           500.1327766 MHz

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

1D NMR plot parameters
CX                     20.00 cm
CY                     40.00 cm
F1P                    8.500 ppm
F1                   4251.10 Hz
F2P                   -0.500 ppm
F2                   -250.06 Hz
PPMCM                 0.45000 ppm/cm
HZCM                225.05849 Hz/cm
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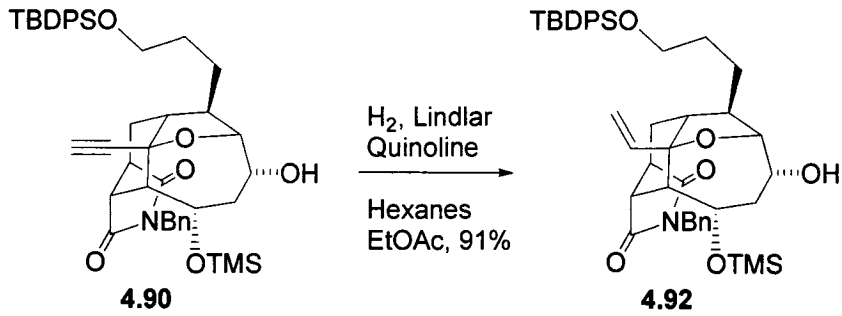


Alkyne **4.90** (0.041 g, 0.055 mmol) was dissolved in benzene (2 mL). Lindlar's catalyst (6 mg) and quinoline (0.01 mL) were added and the flask was purged with H_2 for two min. The reaction was stirred for 15 hours, filtered trough a celite pad and rinced with dichloromethane. The solvent was evaporated. The crude product was purified by flash column chromatography (20% EtOAc/hexanes to 30% EtOAc/hexanes) to afford 67 mg of **4.92** (91% yield) colourless oil.

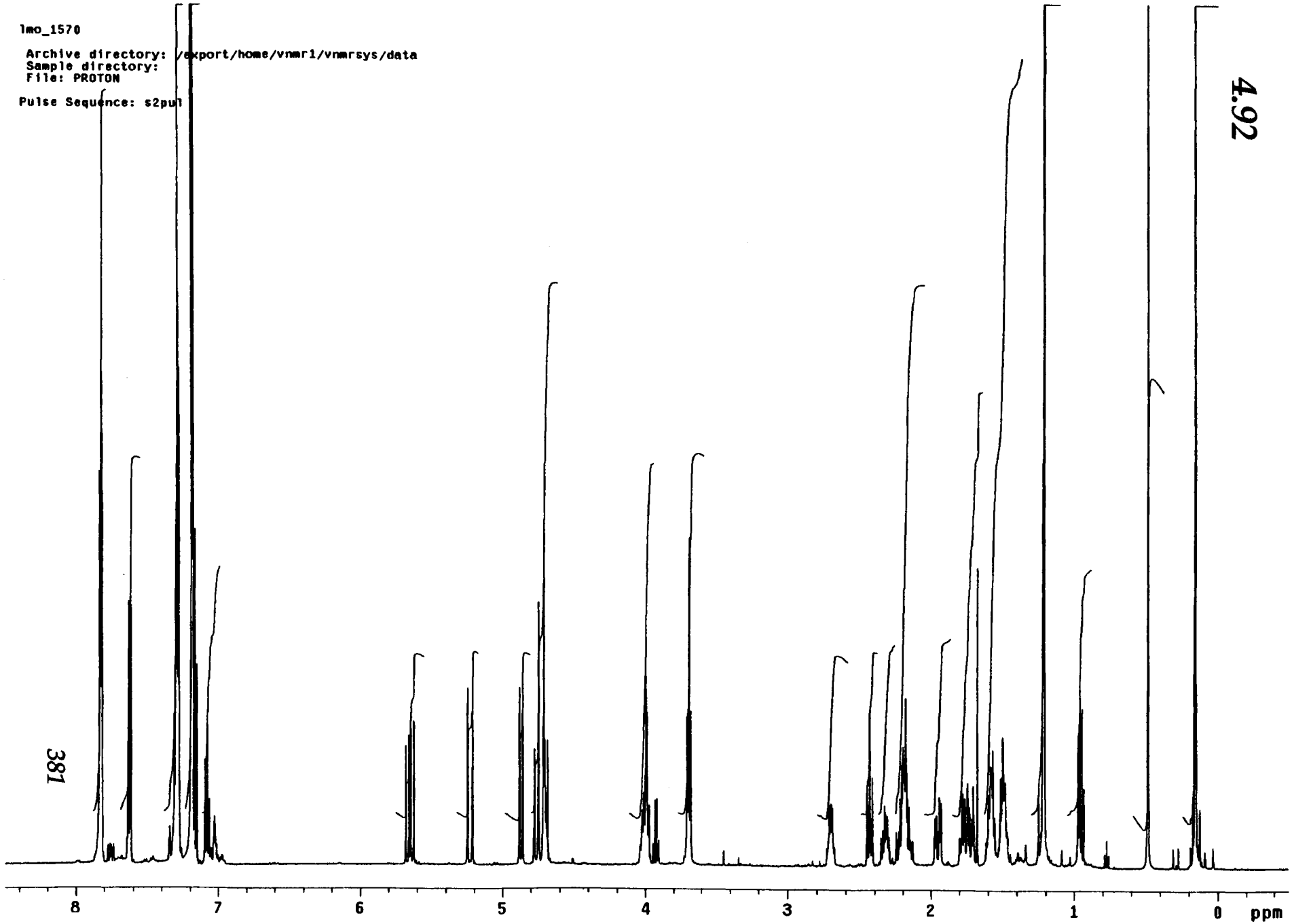
Data for **4.92**

^{1}H NMR (500 MHz, C_6D_6): δ 7.84-7.82 (m, 4H), 7.64 (d, J= 7 Hz, 2H), 7.32-7.28 (m, 6H), 7.17 (t, J= 7 Hz, 2H), 7.08 (t, J= 7 Hz, 1H), 5.65 (dd, J= 17, 10 Hz, 1H), 5.22 (dd, J= 17, 1 Hz, 1H), 4.87 (dd, J= 10, 1 Hz, 1H), 4.76 (d, J_{AB}= 14 Hz, 1H), 4.71-4.69 (m, 1H), 4.70 (d, J_{AB}= 14 Hz, 1H), 4.04-3.98 (m, 2H), 3.69 (t, J= 6 Hz, 2H), 2.72-2.68 (m, 1H), 2.43 (t, J= 9 Hz, 1H), 2.35-2.29 (m, 1H), 2.24-2.13 (m, 4H), 1.95 (ddd, J= 16, 6, 1 Hz, 1H), 1.80-1.70 (m, 3H), 1.61-1.55 (m, 2H), 1.53-1.47 (m, 1H), 1.22 (s, 9H), 0.16 (s, 9H).

^{13}C NMR (125 MHz, C_6D_6) δ 179.0, 177.3, 143.9, 137.4, 136.4 (x4), 134.9 (x2), 130.3 (x3), 130.1 (x2), 129.3 (x2), 128.3 (x4), 113.7, 88.4, 85.9, 72.5, 69.0, 64.7, 48.1, 47.9, 45.9, 43.1, 41.2, 39.5, 38.1, 34.6, 32.2, 29.0, 27.5 (x3), 19.8, 1.2 (x3).

IR (neat) 3502, 2930, 2857, 1700, 1111, 1088 cm^{-1}.

MS ESI calcd for $C_{44}H_{57}NNaO_6Si_2$ (M^+ Na) 774.4, obsd. 774.5.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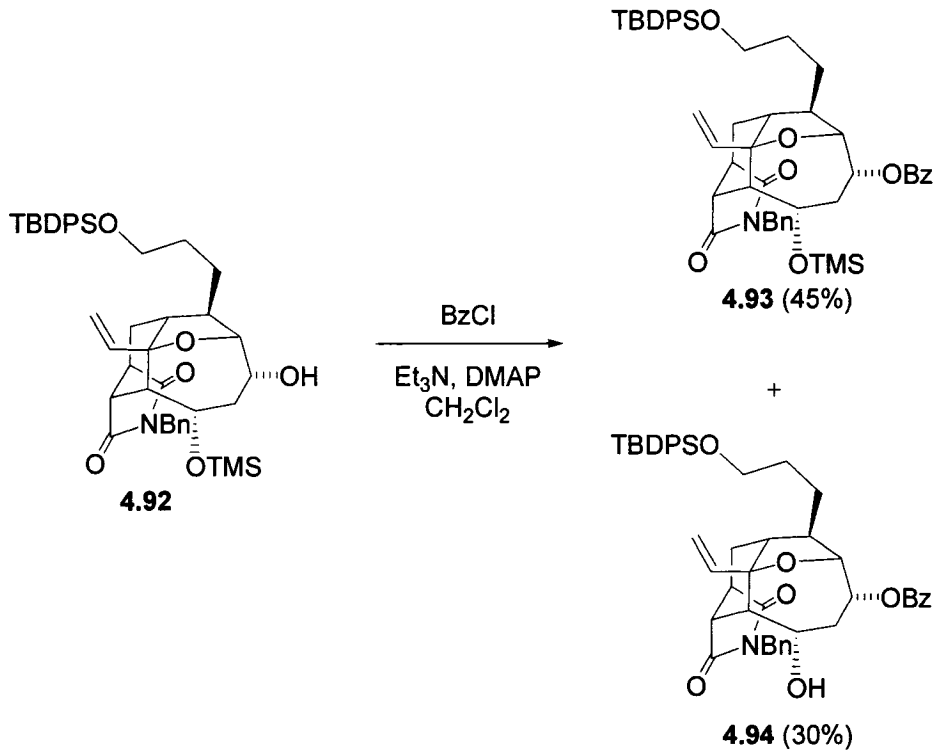


Alcohol **4.92** (0.045 g, 0.06 mmol) was dissolved in dichloromethane (1 mL). Triethylamine (0.25 mL, 1.8 mmol), DMAP (1 crystal) and benzoyl chloride (0.07 mL, 0.6 mmol) were added and stirred for 15 h. The reaction was quenched by adding $NaHCO_{3sat}$. The aqueous layer was extracted 3 times with dichloromethane (3 X 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash silica column chromatography (20% EtOAc/hexanes) to afford 23 mg of **4.93** (45% yield) as a white solid, mp = 62.0-63.6 °C and 14 mg of **4.94** (30%) as a white solid, mp = 78.3-80.6 °C.

Data for **4.93**

^{1}H NMR (500 MHz, C_6D_6): δ 8.13 (dd, J= 8, 1 Hz, 2H), 7.79-7.77 (m, 4H), 7.61 (d, J= 7 Hz, 2H), 7.30-7.26 (m, 6H), 7.18-7.15 (m, 2H), 7.11-7.03 (m, 4H), 5.74 (dt, J= 8, 4 Hz, 1H), 5.65 (dd, J= 17, 11 Hz, 1H), 5.23 (dd, J= 17, 1 Hz, 1H), 4.88 (dd, J= 11, 1 Hz, 1H), 4.75 (d, J_{AB}= 14 Hz, 1H), 4.68 (d, J_{AB}= 14 Hz, 1H), 4.64 (q, J= 4 Hz, 1H), 4.13 (dd, J= 8, 4 Hz, 1H),

3.65-3.59 (m, 2H), 2.92-2.87 (m, 1H), 2.46 (dd, J= 9, 9 Hz, 1H), 2.38-2.32 (m, 2H), 2.30-2.25 (m, 1H), 2.18 (dd, J= 5, 4 Hz, 2H), 2.16-2.12 (m, 1H), 1.80 (q, J= 9 Hz, 1H), 1.59-1.45 (m, 3H), 1.41-1.34 (m, 1H), 1.15 (s, 9H), 0.05 (s, 9H).

^{13}C NMR (125 MHz, C_6D_6) δ 178.9, 177.1, 166.4, 143.6, 137.4, 136.3 (x4), 134.7 (x2), 133.3, 131.5, 130.4 (x2), 130.3 (x2), 130.1 (x2), 129.3 (x2), 128.9 (x4), 128.5 (x3), 113.9, 88.8, 83.6, 74.8, 68.5, 64.8, 49.4, 48.3, 45.7, 43.1, 41.2, 37.9, 36.7, 34.5, 32.1, 29.0, 27.5 (x3), 19.8, 1.1 (x3).

IR (neat) 2930, 2859, 1702, 1110 cm^{-1}.

MS ESI calcd for $C_{51}H_{61}NNaO_7Si_2$ (M^+ Na) 878.4, obsd. 878.4.

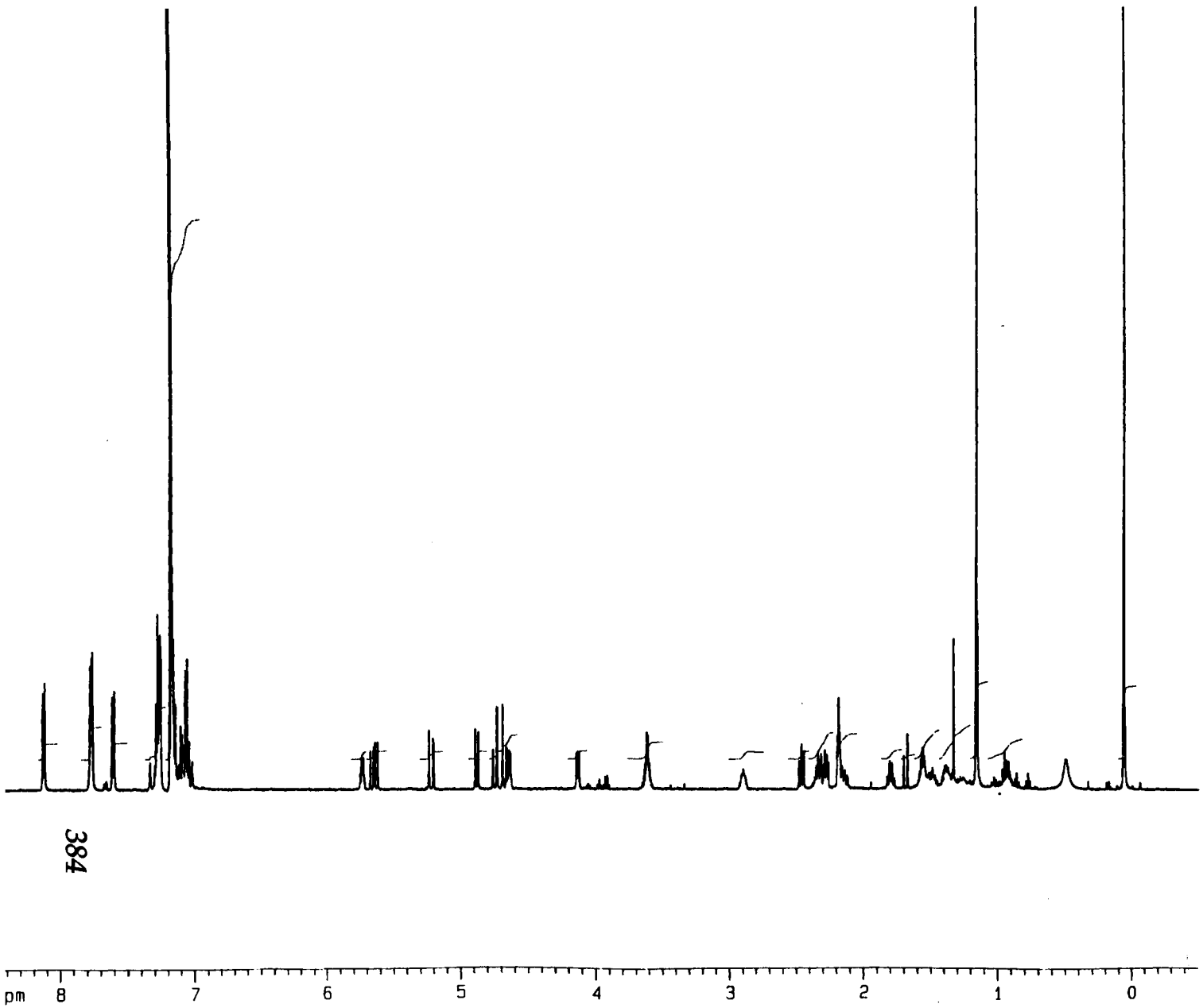
Data for **4.94**

^{1}H NMR (500 MHz, C_6D_6): δ 8.16 (d, J= 7 Hz, 4H), 8.06 (d, J= 7 Hz, 2H), 7.74-7.71 (m, 4H), 7.62 (d, J= 7 Hz, 1H), 7.28-7.26 (m, 4H), 7.18-7.15 (m, 4H), 7.12-7.05 (m, 4H), 7.02 (t, J= 7 Hz, 2H), 5.69 (dd, J= 17, 11 Hz, 1H), 5.64-5.61 (m, 1H), 5.22 (dd, J= 17, 1 Hz, 1H), 4.92 (dd, J= 11,1 Hz, 1H), 4.75 (d, J_{AB}= 14 Hz, 1H), 4.69 (d, J_{AB}= 14 Hz, 1H), 4.44 (t, J= 5 Hz, 1H), 4.32 (d, J= 8, 4 Hz, 1H), 3.46-3.44 (m, 2H), 2.79-2.78 (m, 1H), 2.35 (t, J= 9 Hz, 1H), 2.33-2.22 (m, 3H), 2.12-2.05 (m, 2H), 1.76 (q, J= 7 Hz, 1H), 1.52 (ddd, J= 16, 7, 1 Hz, 1H), 1.11 (s, 9H).

^{13}C NMR (125 MHz, C_6D_6) δ 179.3, 177.9, 165.8, 143.6, 137.5, 136.3 (x4), 134.7, 133.9 (x2), 133.3, 130.8 (x2), 130.2 (x2), 130.1 (x2), 129.7, 129.2, 129.0, 128.9 (x4), 128.7 (x2), 113.6, 89.2, 83.4, 74.8, 67.0, 64.5, 49.5, 45.9, 45.7, 42.7, 40.8, 38.2, 35.9, 34.3, 31.9, 29.7, 27.4 (x3) 19.7.

IR (neat) 3477, 3077, 2932, 2860, 1695, 1276, 1112 cm^{-1}.

MS ESI calcd for $C_{48}H_{54}NO_7Si$ (M^+ H) 783.4, obsd. 784.5.



4.93

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PROCNO 1

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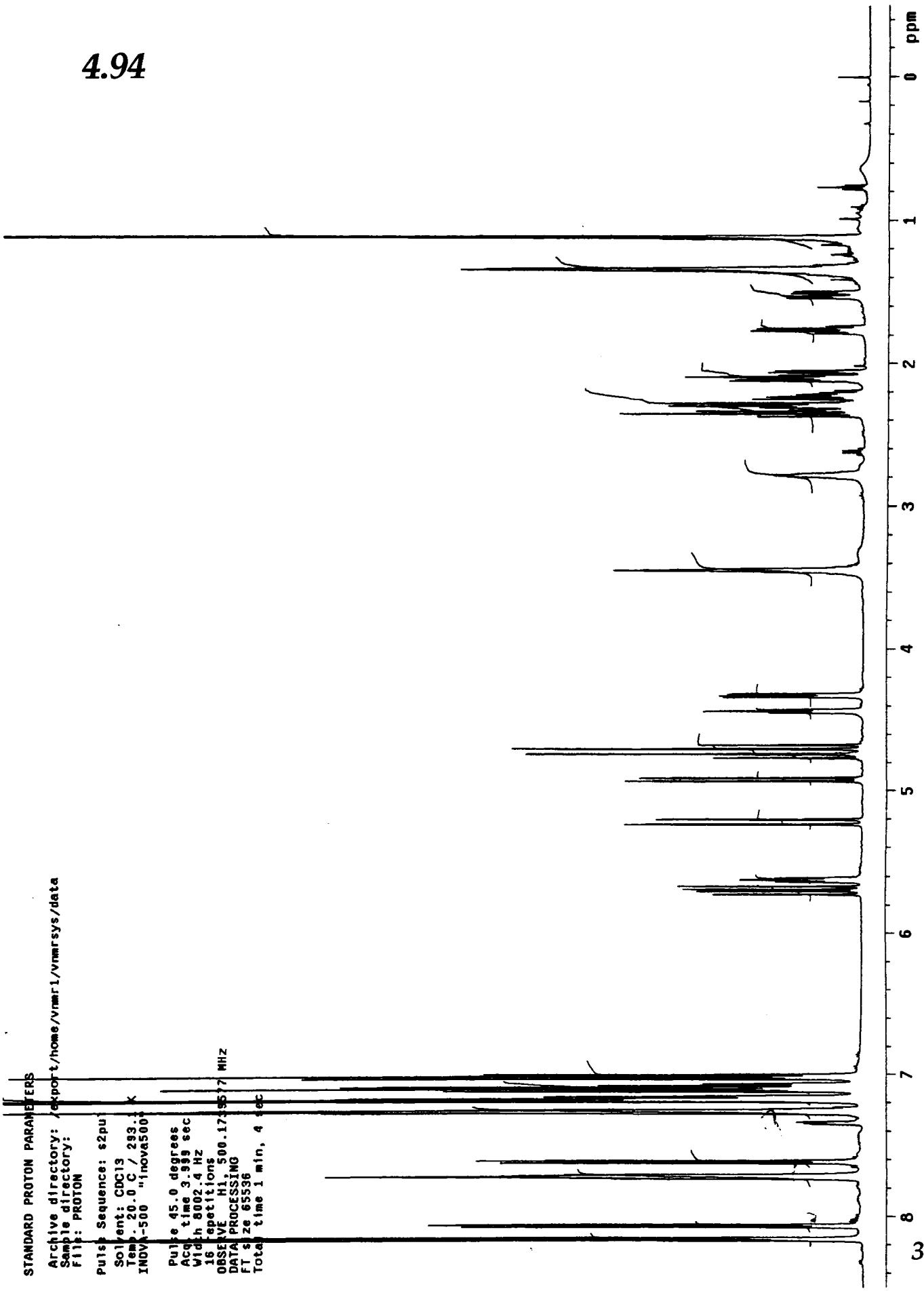
4.94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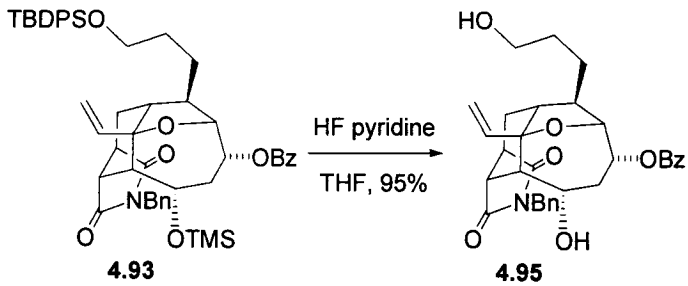


4.93 **4.95**

Compound **4.93** (0.023 g, 0.027 mmol) was dissolved in THF (2 mL). HF·Pyridine (5 drops) was added and the reaction was stirred for 15 hours at room temperature. The reaction was quenched by adding $NaHCO_{3sat.}$ The aqueous layer was extracted 3 times with diethylether (3 X 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash silica column chromatography (50% EtOAc/hexanes) to afford 14 mg of **4.95** (95% yield) as a colourless oil.

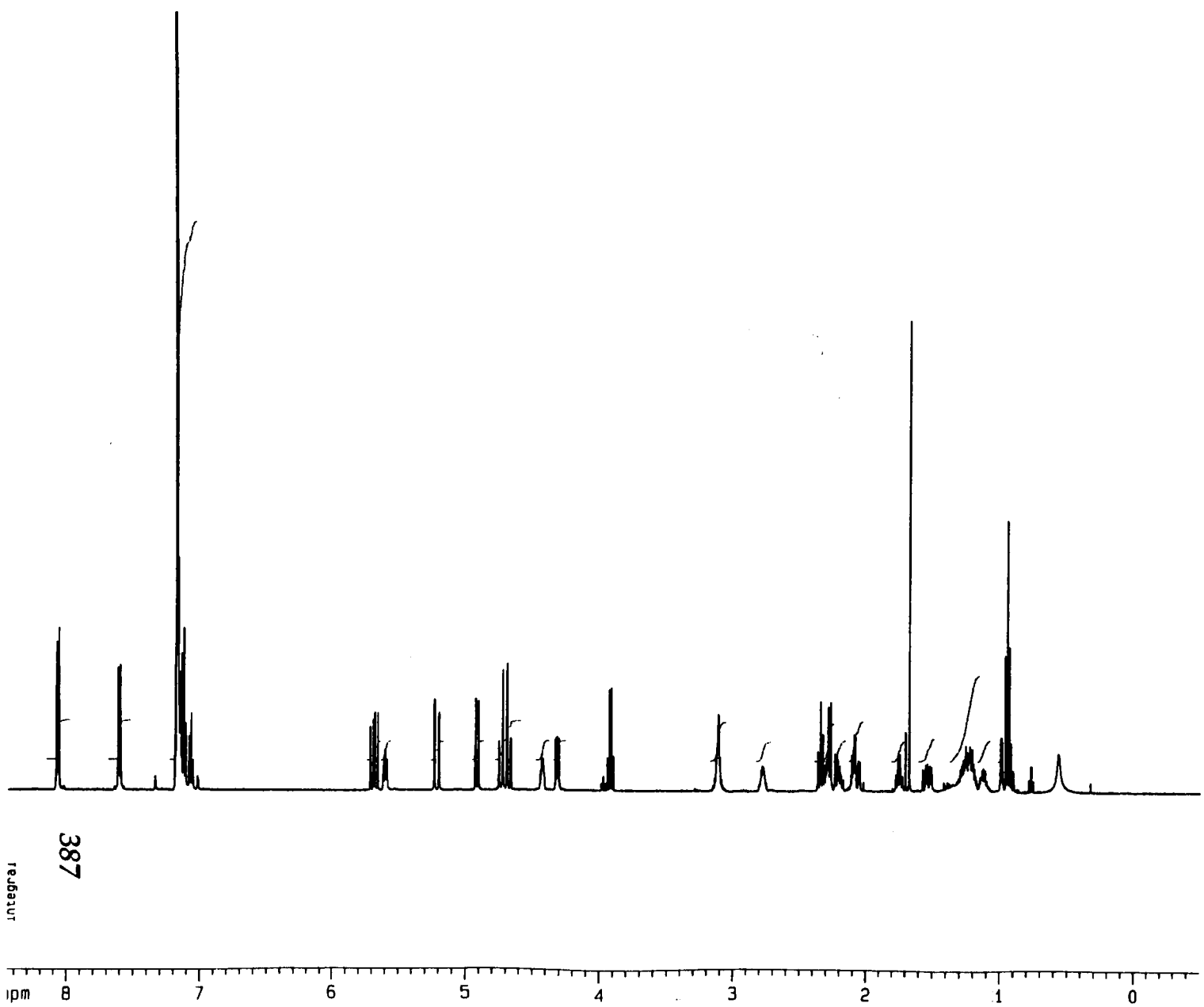
Data for **4.95**

^{1}H NMR (500 MHz, C_6D_6): δ 8.08 (dt, J= 8, 1 Hz, 2H), 7.61 (d, J= 7 Hz, 2H), 7.18-7.11 (m, 5H), 7.08 (tt, J= 7, 1 Hz, 1H), 5.69 (dd, J= 17, 11 Hz, 1H), 5.62-5.59 (m, 1H), 5.22 (dd, J= 17, 1 Hz, 1H), 4.92 (dd, J= 11, 1 Hz, 1H), 4.74 (d, J_{AB}= 14 Hz, 1H), 4.68 (d, J_{AB}= 14 Hz, 1H), 4.44-4.42 (m, 1H), 4.31 (dd, J= 8, 4 Hz, 1H), 3.14-3.08 (m, 2H), 2.79-2.75 (m, 1H), 2.34 (t, J= 9 Hz, 1H), 2.31-2.27 (m, 1H), 2.28 (d, J= 9 Hz, 1H), 2.23-2.17 (m, 1H), 2.11-2.05 (m, 2H), 1.75 (q, J= 9 Hz, 1H), 1.52 (dd, J= 16, 2 Hz, 1H), 1.32-1.17 (m, 4H), 1.14-1.09 (m, 1H), 0.99 (d, J= 3 Hz, 1H).

^{13}C NMR (125 MHz, C_6D_6) δ179.3, 177.7, 165.8, 143.6, 137.5, 133.5, 131.4, 130.2 (x2), 129.7 (x2), 129.2 (x2), 129.0 (x2), 113.6, 89.3, 83.3, 75.0, 67.1, 62.8, 49.1, 45.9, 45.8, 42.7, 40.8, 38.2, 35.9, 34.3, 31.9, 29.7.

IR (neat) 3489, 2927, 1693, 1277, 1069 cm^{-1}.

EI HRMS calcd for $C_{32}H_{35}NO_7$ (M^+) 545.24135, found 545.23971.



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PROCNO	1

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D1	0.01000000 sec

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

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PL1	0.00 dB
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F2 - Processing parameters

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1D NMR plot parameters

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CY	40.00 cm
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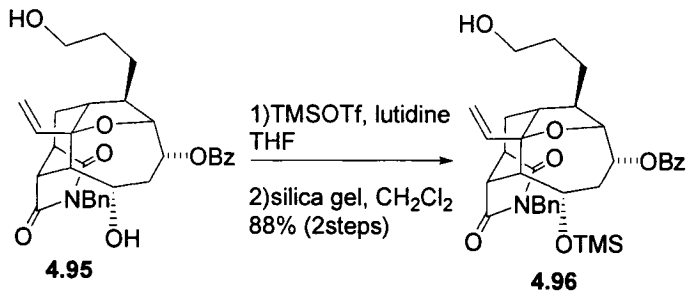
F2	-250.06 Hz
PPMCM	0.45000 ppm/cm
HZCM	225.05849 Hz/cm



Diol **4.95** (0.114 g, 0.2 mmol) was dissolved in THF (2 mL). Lutidine (0.096 mL, 0.87 mmol) was added and the mixture was cooled to 0°C before the addition of trimethylsilyl trifluoromethanesulfonate (0.076 mL, 0.41 mmol). The reaction was completed after 10 minutes and quenched by adding $NaHCO_{3\ sat}$ (10 mL). The aqueous layer was extracted 3 times with diethylether (3 X 10 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was stirred for 15 hours in dichloromethane (3 mL) and silica gel (2g). The product was filtrated with 30 mL of ethylacetate and the solvent was evaporated. The crude product was purified by flash column chromatography (50 % EtOAc /50 % hexanes) to afford 109 mg of **4.96** (88% yield) as a colourless oil.

Data for **4.96**

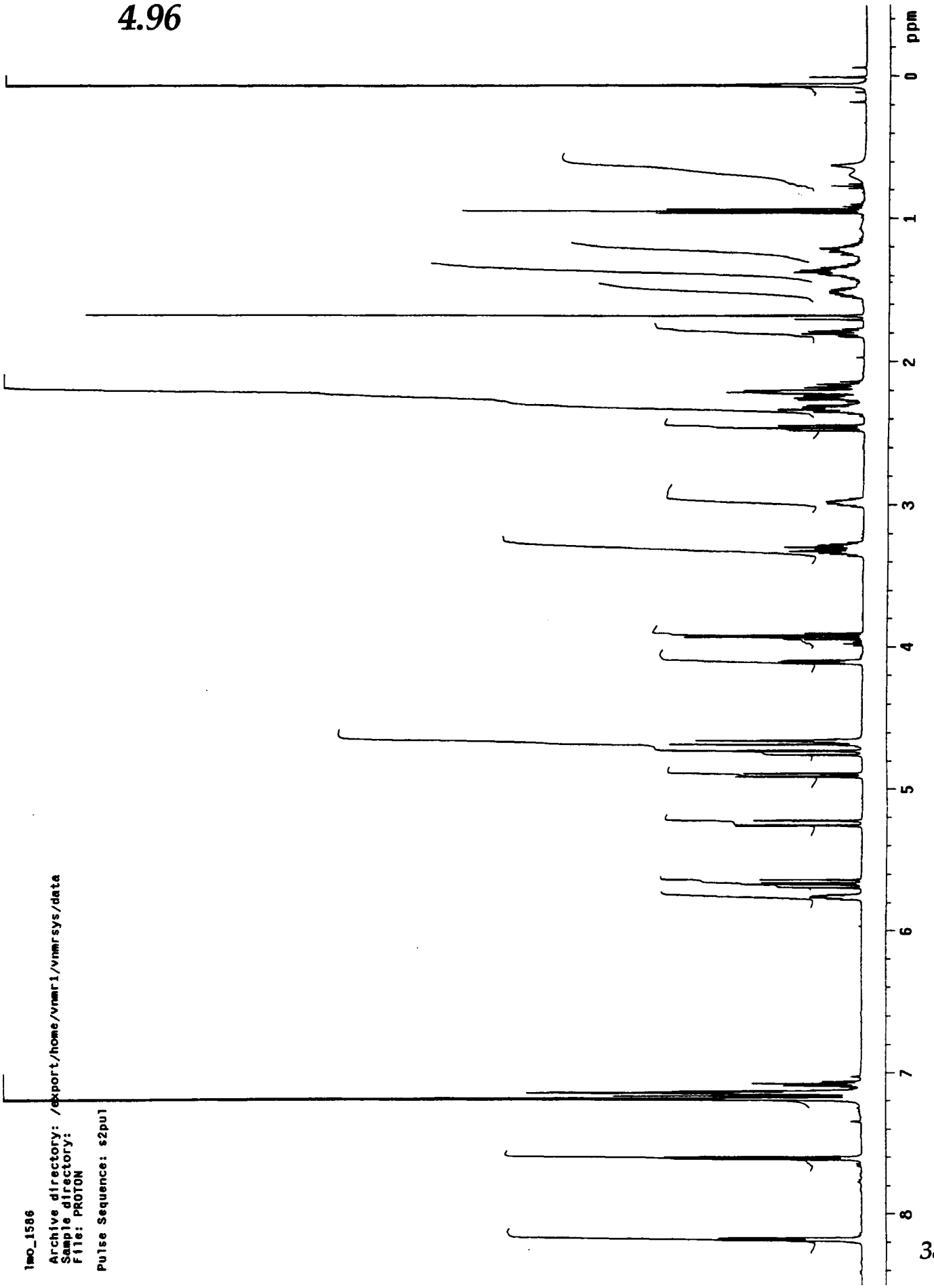
^{1}H NMR (500 MHz, C_6D_6): δ 8.20-8.17 (m, 2H), 7.61 (d, J= 7 Hz, 2H), 7.17-7.11 (m, 5H), 7.08 (t, J= 7 Hz, 1H), 5.78-5.74 (m, 1H), 5.66 (dd, J= 17, 11 Hz, 1H), 5.24 (dd, J= 17, 1 Hz, 1H), 4.90 (dd, J= 11, 1 Hz, 1H), 4.71 (d, J_{AB}= 14 Hz, 1H), 4.67-4.65 (m, 1H), 4.67 (d, J_{AB}= 14 Hz, 1H), 4.10 (dd, J= 7, 4 Hz, 1H), 3.36-3.26 (m, 2H), 3.01-2.96 (m, 1H), 2.46 (dd, J= 9, 9 Hz, 1H), 2.36-2.29 (m, 2H), 2.27-2.13 (m, 4H), 1.79 (q, J= 9 Hz, 1H), 1.55-1.48 (m, 1H), 1.42-1.31 (m, 3H), 1.26-1.18 (m, 1H), 0.06 (s, 9H).

^{13}C NMR (125 MHz, C_6D_6) δ 179.0, 177.1, 166.5, 143.5, 137.3, 133.4, 131.5, 130.5, 130.1 (x2), 129.3 (x2), 129.0 (x2), 128.7 (x2), 114.1, 88.9, 83.7, 74.9, 68.5, 62.7, 49.3, 48.3, 45.6, 43.1, 41.2, 37.9, 36.7, 34.4, 32.1, 29.1, 1.12 (x3).

IR (neat) 3453, 2942, 1699, 1274, 1069 cm^{-1}.

EI HRMS calcd for $C_{35}H_{43}NO_7Si$ (M^+) 617.28088, obsd. 617.28019.

4.96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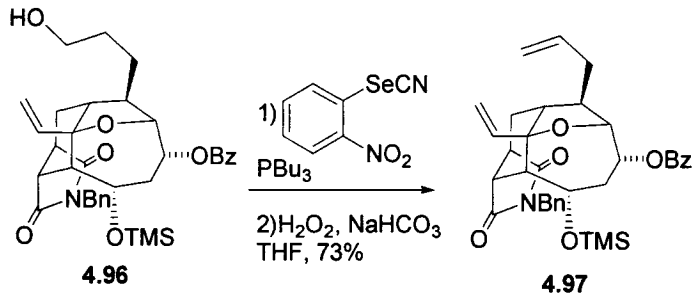


Alcohol **4.96** (0.109 g, 0.18 mmol) and 2-nitrophenylselenocyanate (0.2 g, 0.88 mmol) were loaded in a Shlenk tube. In a glove box, THF (2 mL) and tri-*n*-butylphosphine (0.22 mL, 0.88 mmol) were added. The reaction was stirred for 15 hours at room temperature. $NaHCO_3$ (0.074 g, 0.88 mmol) and H_2O_2 30% (0.2 mL, 1.77 mmol) were added and the reaction was stirred for 24 hours. The reaction was quenched by adding $NaHCO_{3sat.}$ The aqueous layer was extracted 3 times with diethylether (3 X 15 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash silica column chromatography (20% EtOAc/hexanes) to afford 77 mg of **4.97** (73% yield) as a colourless oil.

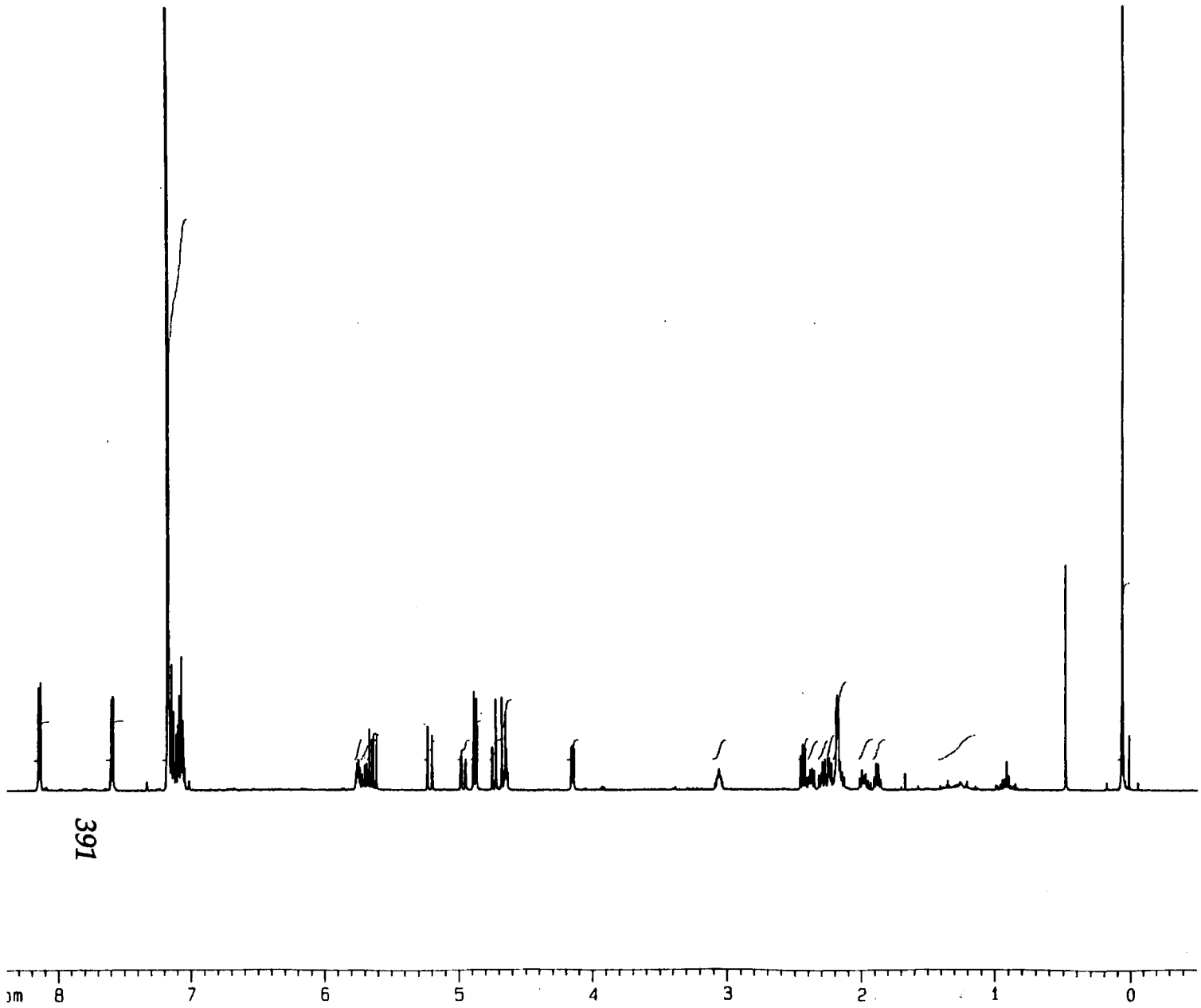
Data for **4.97**

^{1}H NMR (500 MHz, C_6D_6): δ 8.16 (dd, J= 8, 2 Hz, 2H), 7.60 (d, J= 7 Hz, 2H), 7.17-7.07 (m, 6H), 5.76 (dt, J= 7, 5 Hz, 1H), 5.70 (dd, J= 10, 7 Hz, 1H), 5.64 (dd, J= 17, 11 Hz, 1H), 5.22 (dd, J= 17, 1 Hz, 1H), 4.97 (dd, J= 17, 2 Hz, 1H), 4.88 (d, J= 10 Hz, 1H), 4.88 (dd, J= 11, 1 Hz, 1H), 4.74 (d, J_{AB}= 14 Hz, 1H), 4.66 (d, J_{AB}= 14 Hz, 1H), 4.65 (q, J= 5 Hz, 1H), 4.15 (dd, J= 7, 4 Hz, 1H), 3.09-3.04 (m, 1H), 2.44 (dd, J= 9, 9 Hz, 1H), 2.41-2.35 (m, 1H), 2.32-2.27 (m, 1H), 2.25-2.21 (m, 1H), 2.19-2.13 (m, 2H), 2.18 (dd, J= 5, 4 Hz, 2H), 2.01-1.93 (m, 1H), 1.88 (q, J= 9 Hz, 1H), 0.06 (s, 9H).

^{13}C NMR (125 MHz, C_6D_6) δ 179.0, 177.0, 166.3, 143.4, 137.4, 137.3, 133.4, 131.5, 130.4 (x2), 130.1 (x2), 129.3 (x2), 128.9 (x2), 116.9, 114.1, 88.8, 82.7, 74.8, 68.5, 49.5, 48.3, 44.9, 43.1, 42.0, 41.2, 37.9, 36.6, 28.9, 1.1 (x3).

IR (neat) 2948, 2913, 1701, 1109, 1070 cm^{-1}.

EI HRMS calcd for $C_{35}H_{41}NO_6Si$ (M^+) 599.27032, obsd. 599.27319.



4.97

Current Data Parameters

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PROCNO	1

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

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F2 - Processing parameters

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1D NMR plot parameters

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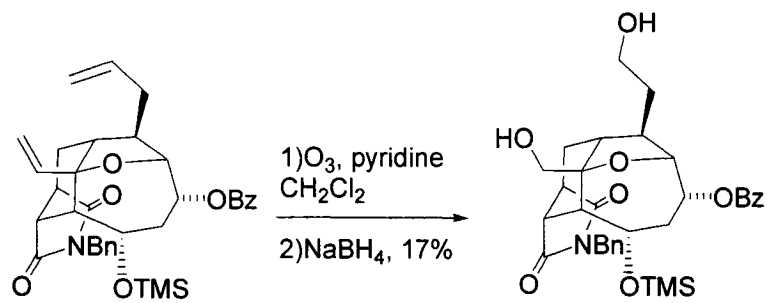
F1	4251.10 Hz
F2P	-0.500 ppm
F2	-250.06 Hz
PPMCM	0.45000 ppm/cm
HZCM	225.05849 Hz/cm



4.97 **4.100**

To a solution of diene **4.97** (0.053 g, 0.088 mmol)) in dichloromethane (4 mL) at –78°C was bubbled with ozone for 35 minutes, until a blue colour persisted. MeOH (1mL) and sodium borohydride (one little spatula) was added. The reaction was quenched by adding $NaHCO_{3sat.}$ The aqueous layer was extracted 3 times with ethylacetate (3 X 20 mL). The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was evaporated. The crude product was purified by flash silica column chromatography (80% EtOAc/hexanes) to afford 9 mg of **4.100** (17% yield) as a colourless oil.

Data for **4.100**

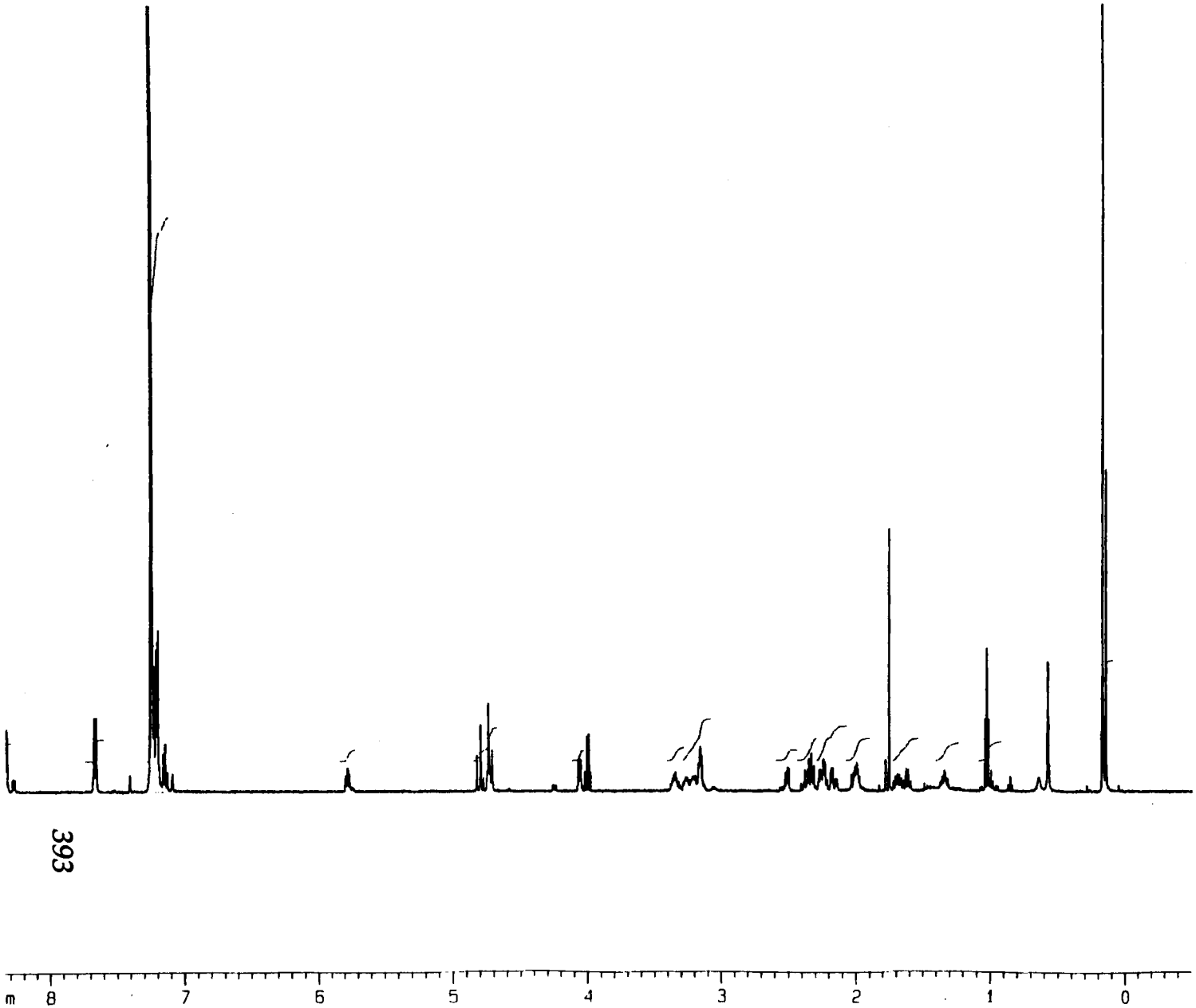
^{1}H NMR (500 MHz, C_6D_6): δ 8.36-8.34 (m, 2H), 7.68 (d, J= 7 Hz, 2H), 7.24-7.21 (m, 5H), 7.16 (tt, J= 8, 1 Hz, 1H), 5.79 (td, J= 8, 1 Hz, 1H), 4.81 (d, J_{AB}= 14 Hz, 1H), 4.76-4.71 (m, 1H), 4.73 (d, J_{AB}= 14 Hz, 1H), 4.06 (dd, J= 8, 4 Hz, 1H), 3.38-3.32 (m, 1H), 3.29-3.13 (m, 4H), 2.51 (dd, J= 8, 5 Hz, 1H), 2.38-2.31 (m, 2H), 2.27-2.23 (m, 2H), 2.16 (ddd, J= 16, 7, 2 Hz, 1H), 2.04-1.97 (m, 2H), 1.71-1.66 (m, 1H), 1.62 (q, J= 9 Hz, 1H), 1.37-1.30 (m, 2H), 0.17 (s, 9H).

^{13}C NMR (125 MHz, C_6D_6) δ 178.9, 176.9, 166.6, 137.3, 133.4, 131.5, 130.7 (x2), 130.2 (x2), 129.3 (x2), 129.0 (x2), 128.9, 89.8, 84.1, 74.4, 69.4, 68.4, 61.1, 45.8, 43.3, 43.1, 42.7, 40.7, 40.1, 37.5, 36.7, 36.7, 28.6, 1.1 (x3).

IR (neat) 2952, 1721, 1703, 1274, 1070 cm^{-1}.

EI HRMS calcd for $C_{33}H_{37}NO_8Si$ (M^+) 603.22885, obsd. 603.23434.

4.100



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PL1	0.00 dB
SFO1	500.1327766 MHz

F2 - Processing parameters	
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SF	500.1300049 MHz
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GB	0
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1D NMR plot parameters	
CX	20.00 cm
CY	50.00 cm
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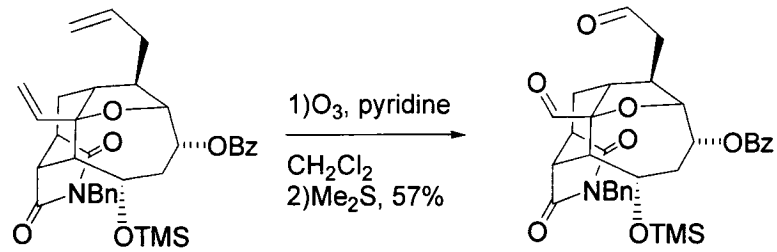
F2P	-0.500 ppm
F2	-250.06 Hz
PPMCM	0.45000 ppm/cm
HZCM	225.05849 Hz/cm



4.97 **4.101**

To a solution of diene **4.97** (0.019 g, 0.317 mmol)) in dichloromethane (2 mL) at –78°C was bubbled with ozone for 25 minutes, until a blue colour persisted. Dimethyl sulfide (1 mL) was added and the solvent was evaporated. The crude product was purified by flash silica column chromatography (30% EtOAc/hexanes to 50% EtOAc/hexanes) to afford 11 mg of **4.101** (57% yield) as a yellow solid, mp = 178-179 °C.

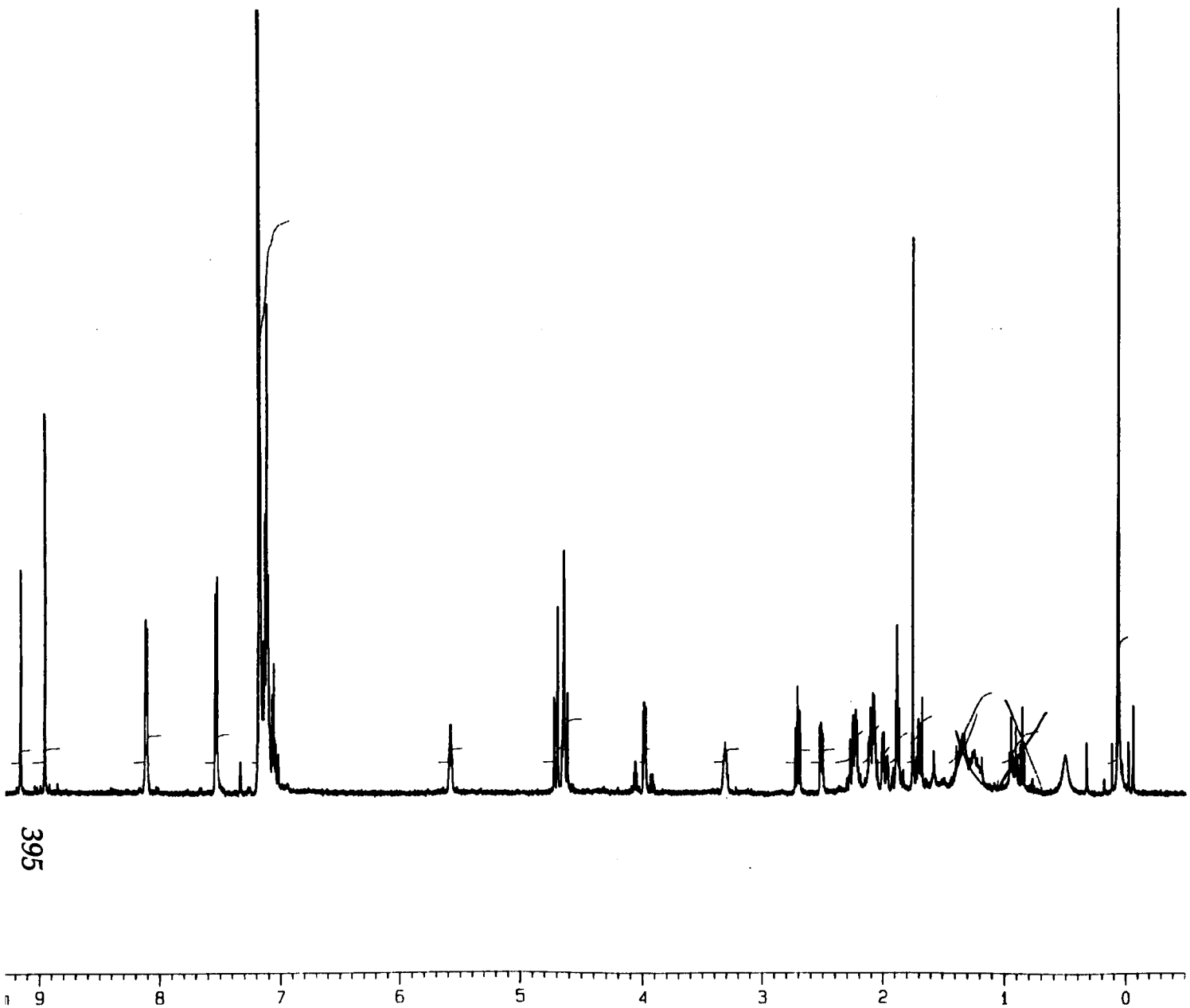
Data for **4.101**

^{1}H NMR (500 MHz, C_6D_6): δ 9.20 (s, 1H), 9.00 (s, 1H), 8.13-8.11 (m, 2H), 7.54 (d, J= 7 Hz, 2H), 7.15-7.03 (m, 6H), 5.58 (td, J= 7, 3 Hz, 1H), 4.71 (d, J_{AB}= 14 Hz, 1H), 4.66-4.64 (m, 1H), 4.63 (d, J_{AB}= 14 Hz, 1H), 3.98 (dd, J= 8, 4 Hz, 1H), 3.34-3.29 (m, 1H), 2.71 (dd, J= 9, 9 Hz, 1H), 2.51 (dd, J= 9, 5 Hz, 1H), 2.27-2.22 (m, 2H), 2.12-2.06 (m, 2H), 1.98 (ddd, J= 16, 7, 2 Hz, 1H), 1.89-1.87 (m, 2H), 1.72-1.67 (m, 1H), 0.06 (s, 9H); **^{13}C NMR** (125 MHz, C_6D_6) δ 199.2, 197.5, 178.2, 176.4, 166.3, 137.1, 133.6, 131.0, 130.4 (x2), 130.0 (x2), 129.3 (x2), 129.0 (x2), 128.6, 90.9, 84.3, 74.0, 67.9, 50.3, 43.1, 43.0 (x2), 41.2, 39.8, 37.7, 36.6, 27.8, 1.0 (x3).

IR (neat) 2952, 1721, 1703, 1274, 1070 cm^{-1}.

EI HRMS calcd for $C_{33}H_{37}NO_8Si$ (M^+) 603.22885, obsd. 603.23434.

4.101



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PROCNO	1

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TD	65536
SOLVENT	Acetone
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DS	0
SWH	7440.476 Hz
FIDRES	0.113533 Hz
AQ	4.4040694 sec
RG	203.2
DW	67.200 usec
DE	6.00 usec
TE	300.0 K
D1	0.01000000 sec

======== CHANNEL f1 ========	
NUC1	1H
P1	13.50 usec
PL1	0.00 dB
SFO1	500.1327766 MHz

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

1D NMR plot parameters	
CX	20.00 cm
CY	100.00 cm
F1P	9.500 ppm
F1	4751.23 Hz
F2P	-0.500 ppm
F2	-250.07 Hz
PPMCM	0.50000 ppm/cm
HZCM	250.06500 Hz/cm

Glossary of Abbreviations

18-C-6	18-Crown-6
Ac	acetate
AcOH	acetic acid
BBN	borabicylco[3.3.1]nonane
BHT	2,6-Di-*tert*-butyl-4-methylphenol
Bn	benzyl
BuLi	*n*-butyllitiuhm
Bz	benzoate
cat.	catalyst or catalytic
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCM	dichloromethane
Dibal-H	diisobutylaluminumhydride
DIPEA	Diisopropylethylamine
DMAP	4-Dimethylaminopyridine
DME	1,2-dimethoxymethane
DMF	dimethylformamide
DMS	dimethylsulfide
DMSO	dimethylsulfoxide
dr	diastereomeric ratio
equiv	equivalents
EI	electron impact
ESI	electrospray ionization
Et	ethyl

EtOAc	ethylacetate
Fg	functional group
HDDA	hydroxy-directed Diels-Alder
HMPA	hexamethylphosphoramide
HRMS	high resolution mass spectrum
IBX	iodoxybenzoic acid
KHMDS	potassium bis(trimethylsilyl)amide
LDA	lithiumdiisopropylamide
LiHMDS	lithium bis(trimethylsilyl)amide
m-CPBA	3-chloroperoxybenzoic acid
Me	methyl
MOM	methoxymethyl
mp	melting point
MS	molecular sieves
NMO	*N*-methylmorpholine
NMR	nuclear magnetic resonance
NOE	nuclear Overhauser effect
NOESY	nuclear Overhauser effect spectroscopy
OTf	trifluoromethylsulfonate
OTs	toluenesulfonate
PCC	pyridiniumchlorochromate
PG	protecting group
Ph	phenyl
Piv	Pivaloate
PMB	4-methoxybenzyl
ppm	parts per million
PPTS	pyridinium *p*-toluenesulfonate
PTSA	para-toluenesulfonic acid
py	pyridine
TBAF	tetrabutylammonium fluoride
TBDPS	*tert*-butyldiphenyl silyl

TBHP	*tert*-butyl hydroperoxide
TBS	*tert*-butyldimethyl silyl
TES	triethyl silyl
t-BuLi	*tert*-butyllithium
TFA	trifluoro acetic anhydride
THF	tetrahydrofuran
TIPS	triisopropyl silyl
TMS	trimethyl silyl
Tol	toluene
TPAP	tetrapropylammonium perruthenate
RCM	ring closing metathesis

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