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Prins-Pinacol Synthesis of a Variety of Highly Functionalized Bicyclo (4.n.1) alkanones

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Prins-Pinacol Synthesis of a Variety of Highly Functionalized Bicyclo[4.*n*.1]alkanones

by

Roch M. A. Lavigne

B.Sc. (Honours), University of Ottawa, 2004

Thesis submitted to the Faculty of Graduate & Postdoctoral Studies
In partial fulfillment of the requirements for the
M. Sc. degree in chemistry

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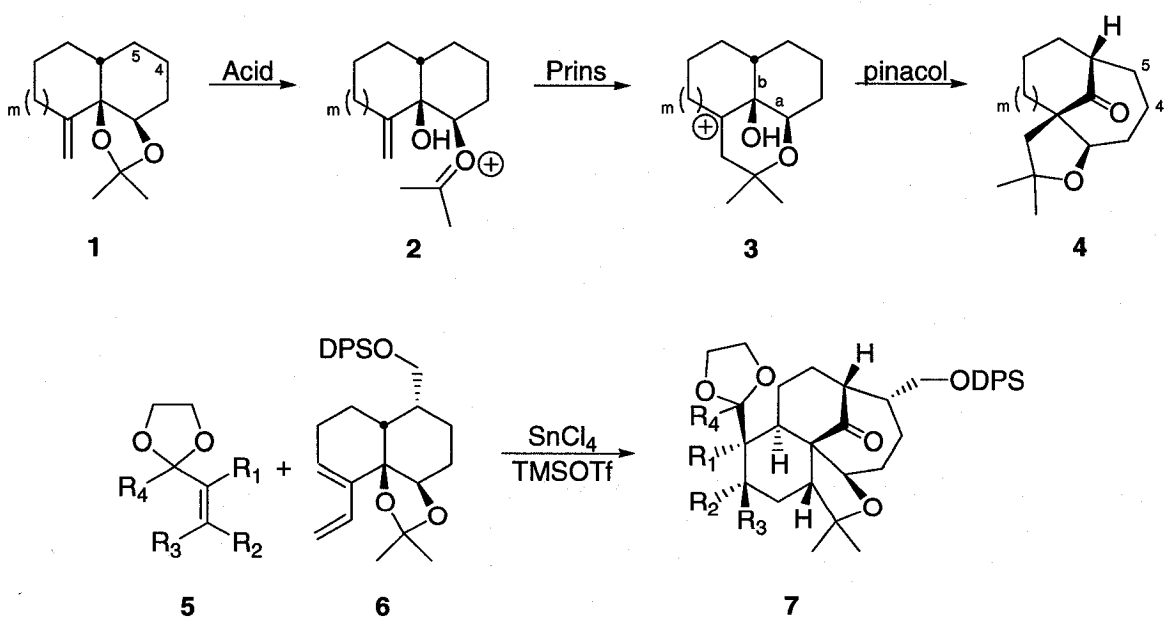
Dédié à mes parents,

pour qui je suis.

Abstract

Bridged ring cores possessing quaternary carbon centers adjacent to a bridged ketone constitute challenging structures in synthesis. Therefore, this thesis explores the development of the first Prins-pinacol synthesis of *cis*-fused bicyclo[4,*n*,1]alkanones. Subjection of the *cis*-fused bicyclic substrate **1** to acidic conditions gives the corresponding oxocarbenium ion **2** which is set to undergo a Prins cyclization. A pinacol rearrangement follows where bond *a* selectively migrates to give rise to the bicyclic ketone **4**. The reaction conditions were optimized for the rearrangement of bicyclo[4.4.0]decanes and the effect of different diol protecting groups was explored, as well as the effect of substitution at the C4 and the C5 position. The rearrangement of bicyclo[5.4.0]undecane and bicyclo[5.3.0]decanes was also investigated in order to achieve the formation of bicyclic ketones with various ring sizes. Finally, the Prins-pinacol rearrangement was coupled with an ionic Diels-Alder reaction in order to achieve the rapid synthesis of highly functionalized polycyclic bridgehead ketones.



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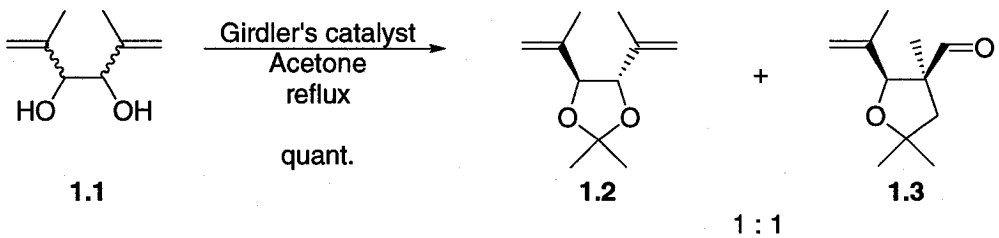
1

Introduction

History of the Prins-Pinacol Rearrangement

Organic chemistry is one of the fields where humans ability to use the information gathered from observations is eloquent and astonishing. The evolution of the Prins-pinacol rearrangement is a good example of this capacity. A lot of progress has been made since the first observed Prins-pinacol rearrangement by Mousset in 1969 (Scheme 1.1).[1] In the process of optimizing the protection of a mixture of *meso* + *dl* glycols (**1.1**) with an acetonide group, Mousset and co-workers obtained a mixture of protected diol (**1.2**) and the structural isomer (**1.3**) bearing an aldehyde functionality.



Scheme 1.1 – First Observed Prins-Pinacol Reaction

In a latter publication,[2] Mousset rationalized the formation of this compound by claiming that the tetrahydrofuran **1.3** arises from a cationic cyclization followed by an oxygen aided ring contraction, as shown in Figure 1.1. First, the acetonide is formed on both the *meso* and the racemic diols. If we look now at the *meso* compound, since this is the one leading to the rearrangement product, Girdler's catalyst (Al_2O_3, 4 SiO_2, H_2O + xH_2O) exhibits some Lewis acid

behavior and complexes one of the dioxolane oxygens (**1.4**). Opening of the acetonide leads to the formation of the oxocarbenium ion **1.5**, which can be represented by the two structures in equilibrium **1.6** and **1.7**. Conformer **1.7** should be greatly favored in the equilibrium since it bears no axial substituents compared to 3 axial substituents in conformer **1.6**. The excellent electrophile generated, the oxocarbenium ion, leads to a cationic cyclization generating a carbenium ion at C5. The β-hydroxy carbenium ion **1.9** can then undergo a ring contraction, aided by the lone pair on the exocyclic oxygen. This provokes the migration of the C3-C4 bond, which is close to being periplanar to the empty p orbital of the carbenium ion, providing the rearranged racemic product **1.3**. The alignment is not perfect due to the sp^2 hybridization of the carbenium ion, giving an approximate 30° dihedral angle between the C3-C4 σ bond and the vacant p orbital, but the alignment is good enough to allow the Wagner - Meerwein

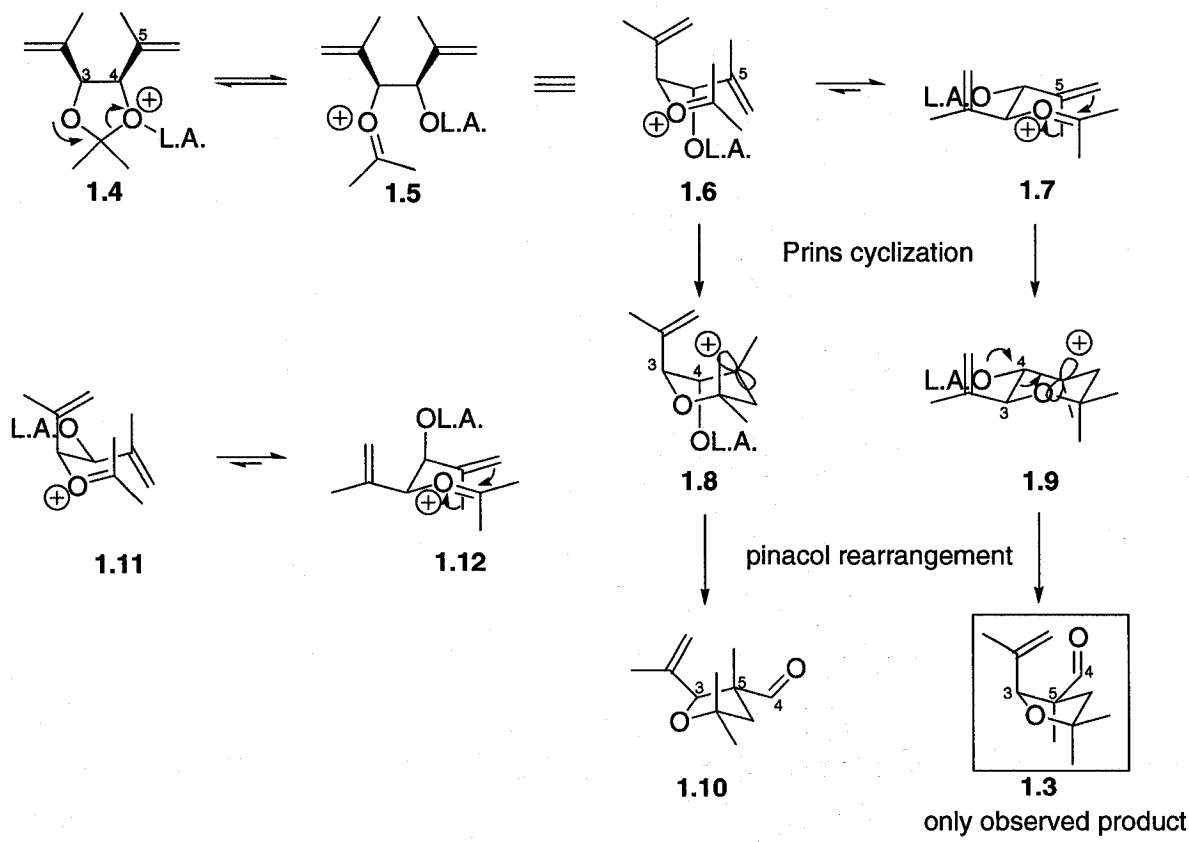
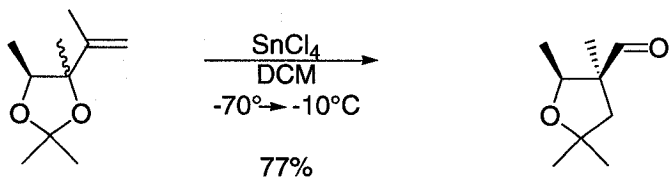


Figure 1.1 – First Proposed Mechanism for Prins-Pinacol Product

reorganization.[3] Rearranged compound **1.10** is not obtained, presumably due to severe 1,3-diaxial interactions created in the transition state of the cationic cyclization. Rearrangement of the of the protected racemic diol does not occur, again due to 1,3-diaxial interactions in both **1.11** and **1.12**. Therefore, the exocyclic oxygen attacks the oxocarbenium ion to give back the protected racemic diol. With this first example of the Prins-pinacol reaction, one can appreciate the power of the stereoselectivity of this reaction.

It was 6 years later that Overman's group published a similar transformation, calling it the Prins-pinacol rearrangement (Scheme 1.2).[4] The Prins reaction is defined as an electrophilic addition of an acid-activated carbonyl to a nucleophilic alkene. Even if it was Kriewtz who published the first examples of this reaction in 1899,[5] it was Prins, in 1917, that carried out the first comprehensive study of the reaction between formaldehyde and ethylenic hydrocarbons in the presence of sulfuric acid.[6] As depicted in Figure 1.2, four products may arise from the Prins reaction, depending on the nature of the olefin and the reaction conditions.[7] As shown in Figure 1.2, the alkene **1.15** first attacks the oxonium ion **1.16** to give the intermediate **1.17**. The carbenium ion intermediate can then lose a proton to afford an allylic alcohol (**1.18**), or alternatively it can react with water, hydrogen chloride or another equivalent of carbonyl compound to afford the 1,3-diol **1.19**, the β-chloroalcohol **1.19** and the carbenium ion **1.21** respectively. The intermediate **1.21** can then undergoes cyclization to yield the *m*-dioxane **1.22**.[8]



1.13 **1.14**

Scheme 1.2 – Overman's First Example of Prins-Pinacol Reaction

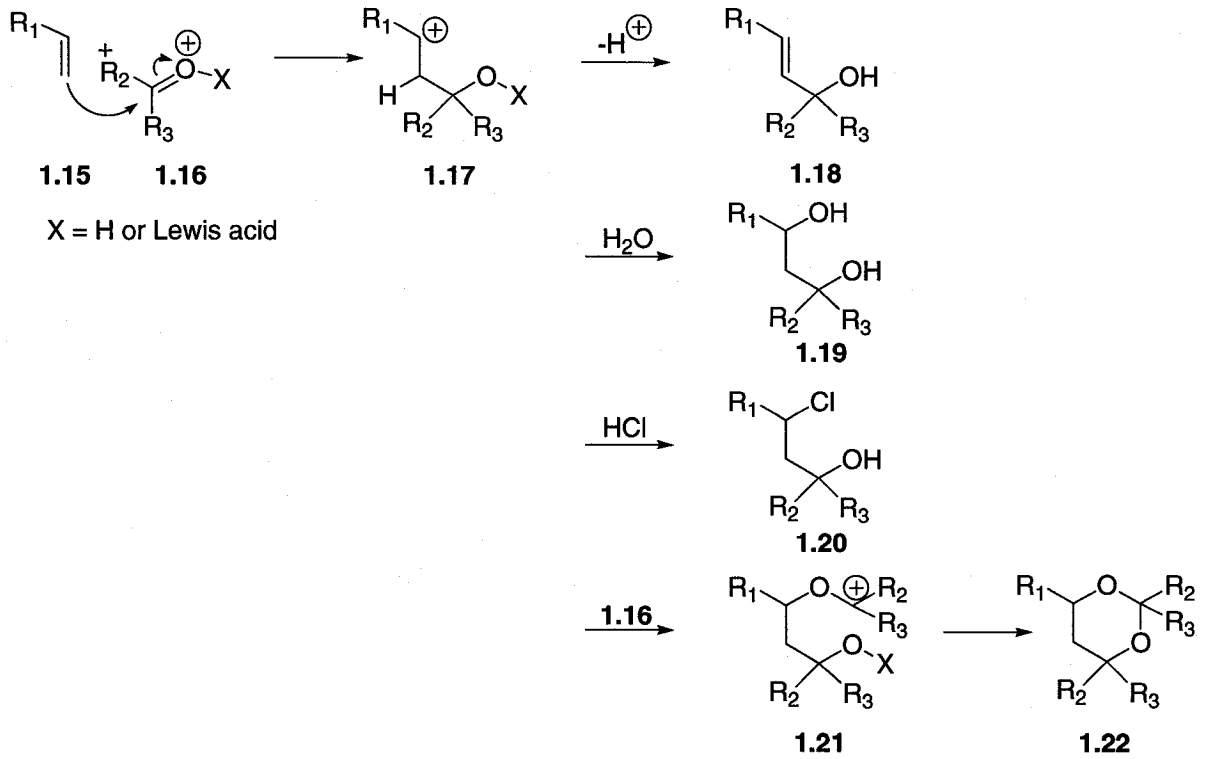
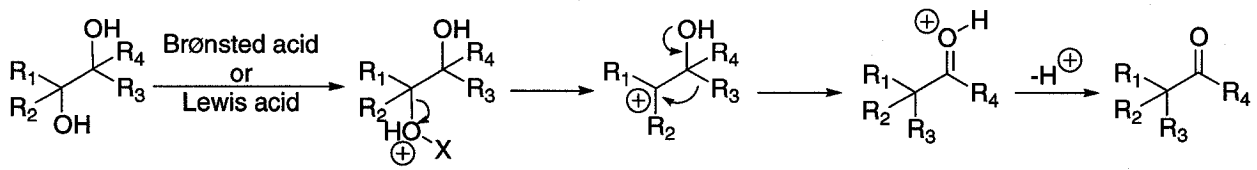


Figure 1.2 – Main Products Obtained from the Prins Reaction

For its part, the pinacol rearrangement was first described by Fittig[9] and was called so since it was first observed by treating the compound called pinacol (**1.23**) with sulphuric acid to obtain pinacone (**1.24**), or methyl *tert*-butyl ketone (Figure 1.3). As Shown in Figure 1.4, the mechanism of the reaction is a 1,2-hydride or alkyl shift via a carbocation (**1.27**).[10] The hydroxyl group that leaves is the one that will give rise to the more stable carbenium ion.[11] The identity of the migrating group is determined by different factors, such the ability of the non-migrating group to stabilize the partial positive charge created at the transition state,[12] the capacity of the migrating group to render anchimeric assistance,[13] its migratory aptitude (usually aryl>alkyl),[14] or the alignment of the migrating bond with the empty p orbital of the carbenium ion in rigid systems.[15] In most cases, mixtures are produced where the preferential migrating group depends on the reaction conditions and the factors stated above.[16] The pinacol rearrangement was originally defined as the rearrangement of 1,2-diols, but now includes all 1,2-migrations of an hydride or an alkyl group geminal to an alcohol to give the corresponding aldehyde or ketone, all having intermediates similar to **1.27** in common.[17]

1.23 **1.24**

Figure 1.3 – The Original Pinacol Rearrangement



1.25 **1.26** **1.27** **1.28** **1.29**

X = H or Lewis acid

Figure 1.4 – Pinacol Rearrangement Mechanism

Since its first disclosure in 1987, Larry E. Overman, from the University of California, published over 30 reports concerning the Prins-pinacol rearrangement. Overman is mainly responsible for the understanding of the stereoselectivity of this reaction and he has strategically used the pinacol-terminated Prins cyclization in synthesis. Overman's group has also completed the first total synthesis of more than 12 natural compounds using this methodology.[18]

Mechanism and Stereoselectivity in the Prins-Pinacol Reaction

The first thing to take in consideration in a Prins-pinacol rearrangement involving an acetal or a ketal is that the acid-promoted opening can occur in two ways to provide the oxocarbenium ions **1.31** and **1.34**. Since the overlap between alkene and the empty p orbital (or π^*) in **1.32** is poor, this intermediate is less likely to undergo a Prins cyclization and the regeneration of the dioxolane is favorable. This cyclization is also a disfavored 5-endo-trig process according to Baldwin's rules.[19] Therefore it is the productive intermediate **1.35** that will undergo a cationic rearrangement to give the 3-acyltetrahydrofuran **1.40**. Three mechanisms can

be proposed for this transformation, as depicted in Figure 1.5.[20] The first mechanism which leads to two discrete intermediates (**1.36** and **1.37**), seems unlikely since it provides no obvious rationale for the high stereoselectivity observed in these rearrangements and no fragmentation byproduct was ever observed. On the other hand, the two bottom scenarios, the oxonia-Cope-aldol and the Prins-pinacol reactions, are able to explain the stereochemistry and determining which one occurs is not an easy task.

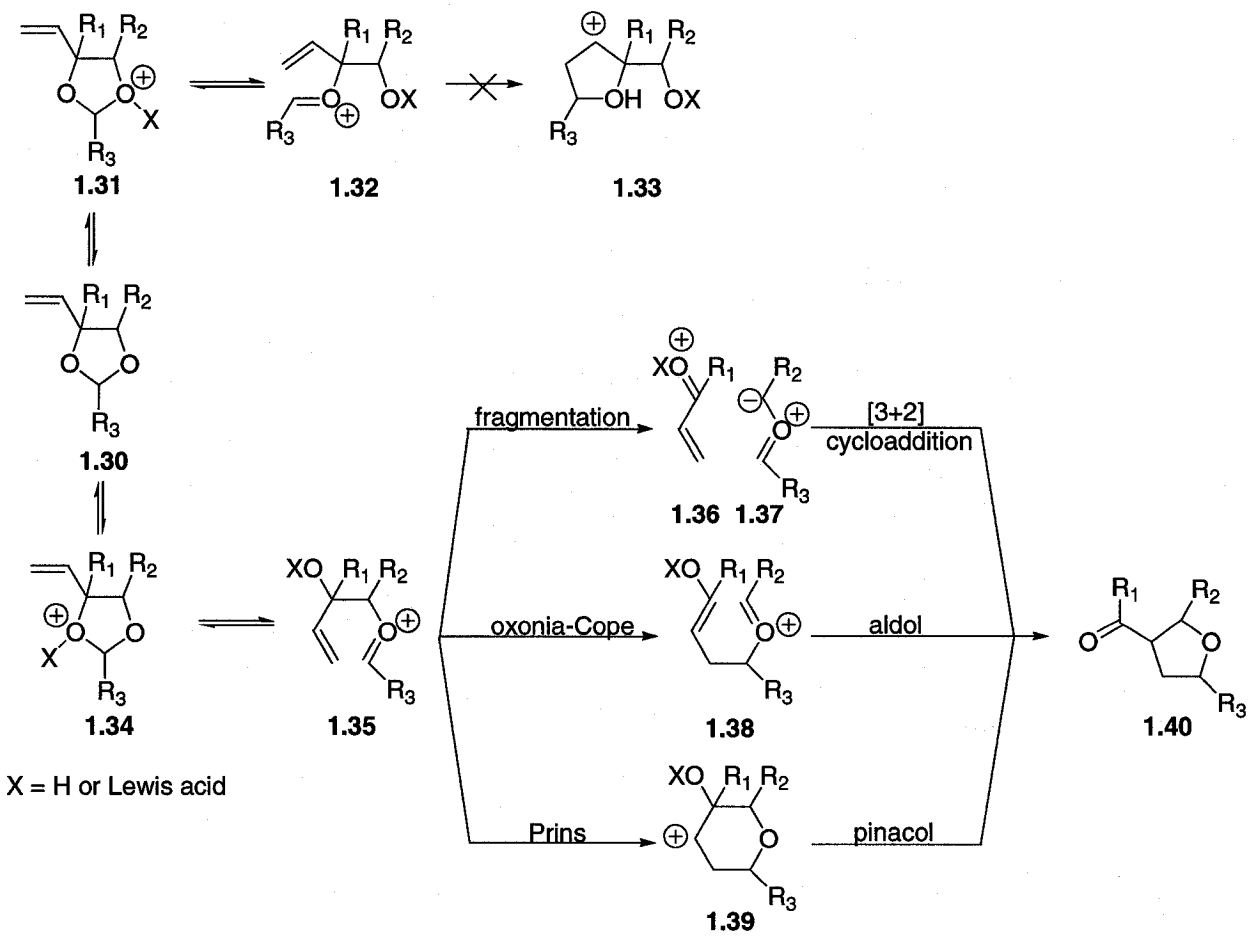


Figure 1.5 – Three Proposed Mechanisms for the Rearrangement

Good evidence that this transformation goes through a Prins-pinacol process was already given by Overman in his first publication (Figure 1.6),[4] where he performed the reaction with an enantioenriched starting material (**1.41**). A [3,3] sigmatropic rearrangement of the oxocarbenium ion **1.42** provides **1.45**. Since the C-C bond rotation in the oxocarbenium ion **1.45** should be a lower energy process than the aldol cyclization,[21] one should observe a rapid equilibrium

between **1.44** and **1.45**, which will lead to a racemic mixture of the 3-acyltetrahydrofuran **1.48**. A Prins cyclization of **1.42** will give rise to the cationic intermediate **1.46**, which is then poised to undergo a Prins cyclization to furnish only (-)-**1.48**. Since no apparent lost of enantiomeric purity was observed in the course of this reaction, it is now accepted that this transformation follows the Prins-pinacol pathway.[22]

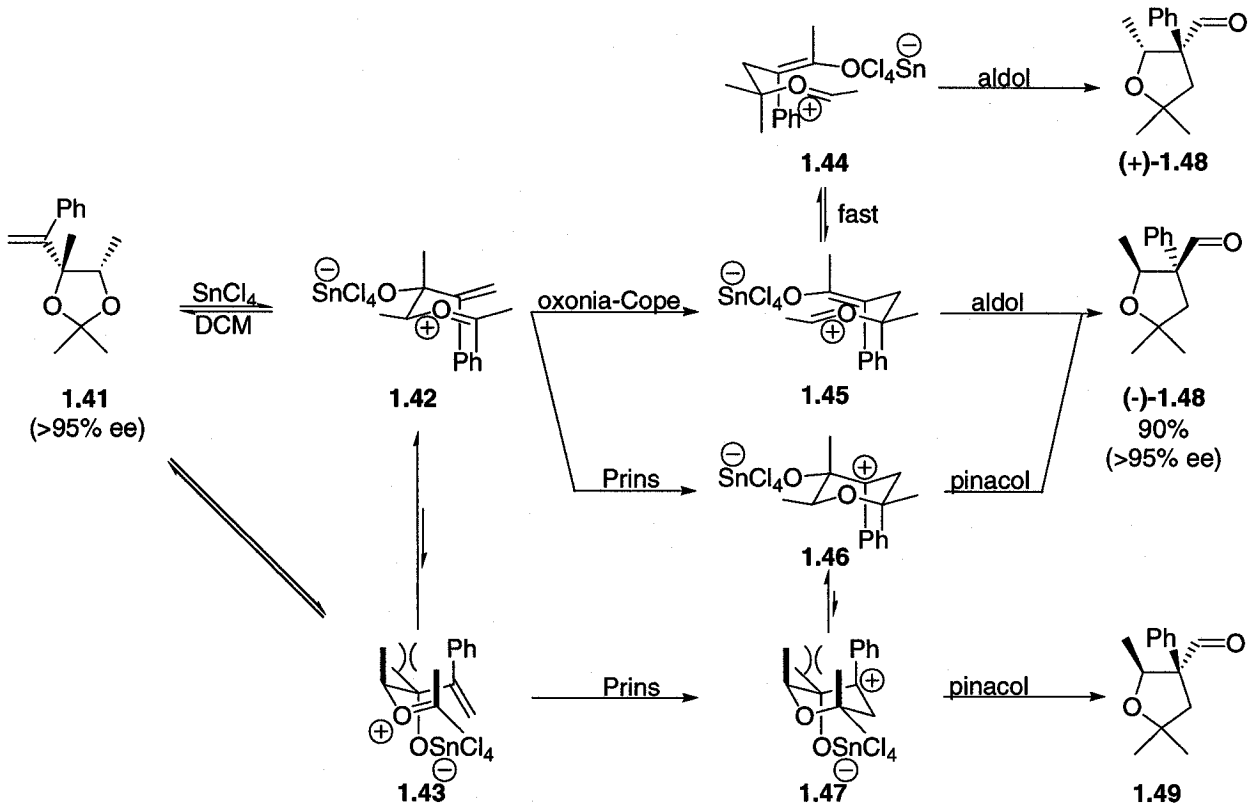
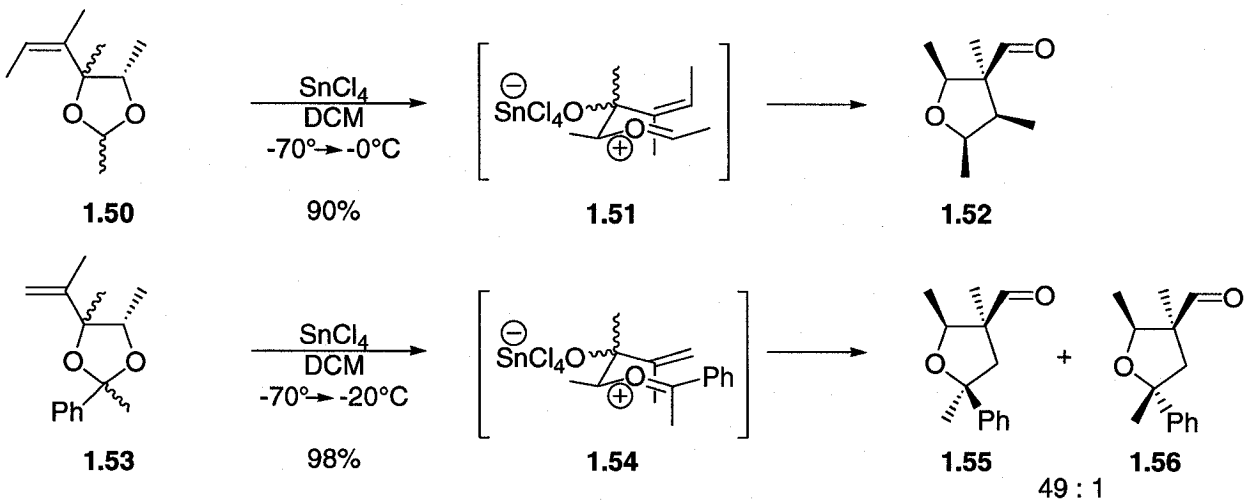


Figure 1.6 – Prins-Pinacol vs. Oxonia-Cope-Aldol Mechanisms

It is also demonstrated in Figure 1.6 that steric effects play an important role in the stereochemical outcome of the Prins-pinacol reaction. The 1,3-diaxial interactions in both **1.43** and **1.47** prevent the formation of **1.49**, since it was not observed under these reaction conditions. This implies that the pinacol rearrangement is faster than a conformational change of the hydropyranyl cation **1.46**.[23]

In the case where the starting material bears an acetal functionality, the more thermodynamically stable *E* oxonium ion is formed and inversion to the *Z* oxonium does not occur since the process is too high in energy (Scheme 1.3).[24] The substituent will take a

pseudoequatorial position in the Prins cyclization which explains the observed stereochemistry (**1.52**).[4] Hanaki *et al.* have also shown that the larger substituent of a ketal will take the pseudoequatorial position in the Prins cyclization step, leading to the formation of **1.55**.[25]



Scheme 1.3 – Effects of Oxocarbenium Ion Geometry on Product Stereochemistry

A very interesting study, done by Cohen *et al.*,[26] clearly shows that the stereoselectivity in the Prins-pinacol rearrangement is governed by both steric and stereoelectronic effects (Figure 1.7). By comparing the reaction outcome of both *syn* and *anti* diols, they access the importance of substitution at R_1 and R_2. For the *syn* diol series (**1.57**), both steric and stereoelectronic effects work in concert to favor the formation of **1.67**. For the *anti* diol series, when R_2 is small (entry 1, Table 1.1), the preferred chair conformation is **1.60** where the homoallylic methyl is in a pseudoequatorial position. The Newman projection **1.59** shows that having the homoallylic methyl in a pseudoequatorial position is not ideal, since an unfavorable $\sigma^*_{C\text{-}O}$ overlap with the alkene $\pi_{C\text{-}C}$ occurs, which decreases the nucleophilicity of the alkene. Nevertheless, the Prins cyclization product **1.64** is stabilized since $\sigma_{C\text{-}R_2}$ has hyperconjugative interactions with the vacant p orbital. This is why substrates having a less nucleophilic alkene component, like a terminal olefin for example, are believed to have a later transition state than a 1,1-disubstituted alkene in the Prins cyclization step.[27] In the pathway leading to product **1.68**, there are some favorable interactions between $\sigma_{C\text{-}R_2}$ and the alkene $\pi^*_{C\text{-}C}$ which increases the nucleophilicity,

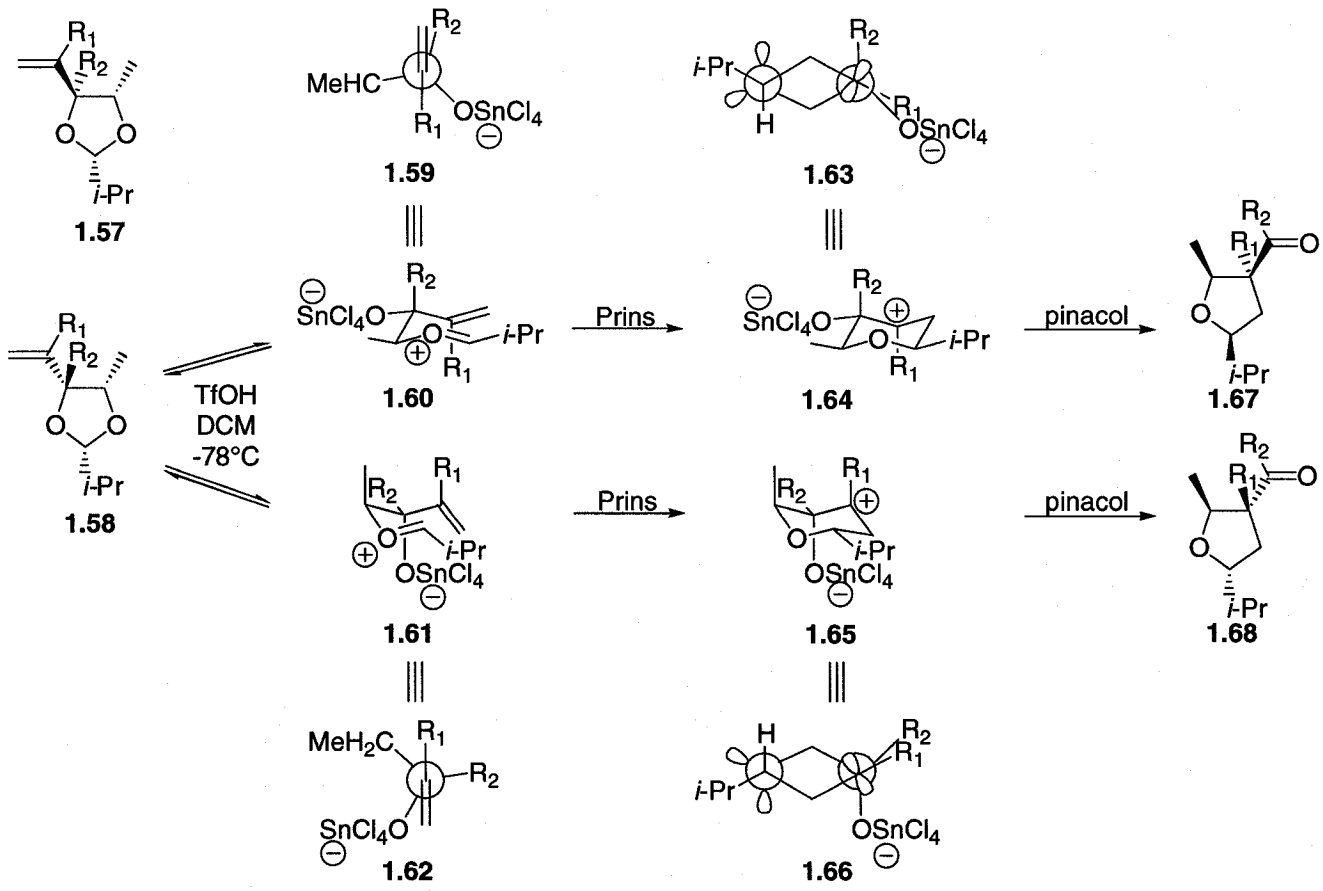


Figure 1.7 – Steric and Stereoelectronic Effects Responsible for the Stereoselectivity in the Prins-Pinacol Reaction

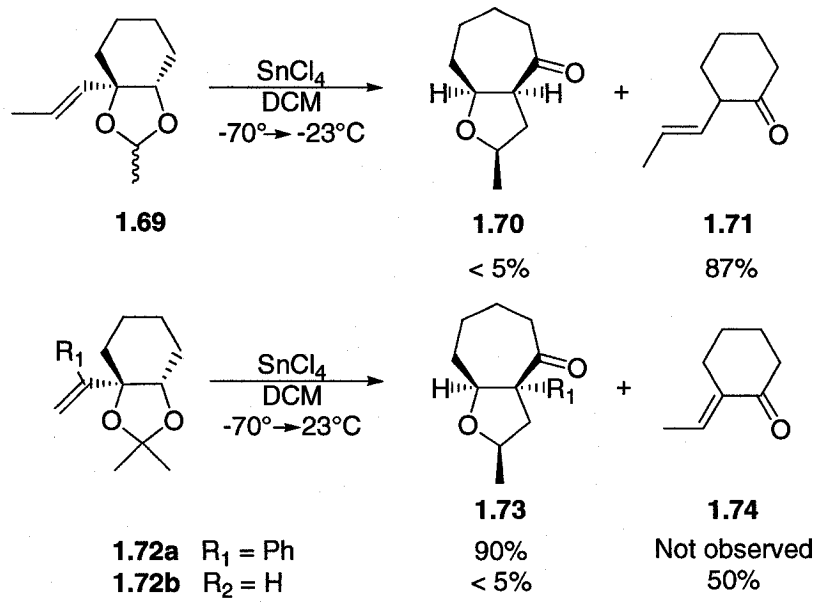
Table 1.1 – Rearrangements of Anti Acetals

entry	acetal	substitution	% conversion	**1.67** : **1.68**
1	**1.58a**	R_1 = H, R_2 = Me	97	95 : 5
2	**1.58b**	R_1 = Me, R_2 = Me	96	14 : 86
3	**1.58c**	R_1 = H, R_2 = *i*-Pr	90	7 : 93

and the overlap between the $\sigma^*_{C\text{-}O}$ and the alkene $\pi_{C\text{-}C}$ is attenuated. Unlike the Prins cyclization product **1.64**, **1.65** has a destabilizing interaction between the $\sigma_{C\text{-}O}$ and the vacant p orbital. Therefore, the Prins cyclization of **1.61** is believed to occur with an early transition state. This

explains why a more nucleophilic alkene (**1.58b**), which has an earlier transition state than a terminal alkene (**1.58a**), will favor the formation of the 3-acyltetrahydrofuran **1.68**. When R_2 gets bigger than a methyl (entry 3), it prefers to be in the pseudoequatorial position to avoid steric interactions, which favors the formation of **1.68**.

One limitation of the Prins-pinacol reaction arises when the vinyl moiety is not biased toward the addition of an electrophile, like the 1,2-disubstituted olefin in **1.69** for instance (Scheme 1.4). This results in the formation of the enone **1.71** as the major product. A similar byproduct was observed when a ketal was reacted with a less nucleophilic terminal vinyl moiety (**1.72b**), probably due to steric hindrance with the methyls.[3]

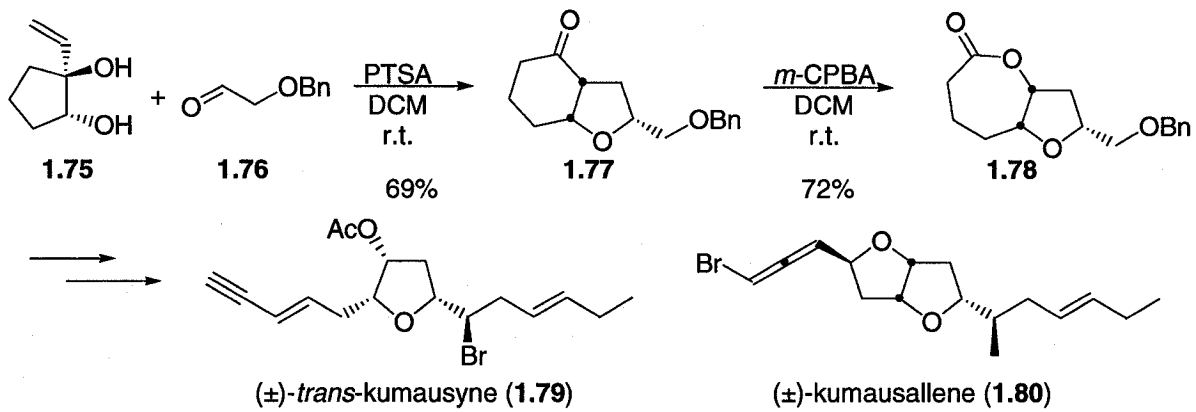


Scheme 1.4 – Limitations of the Prins-Pinacol Reaction

Prins-Pinacol Reaction in Synthesis

As mentioned earlier, it is Overman who has really taken full advantage of the stereoselectivity in the Prins-pinacol rearrangement by applying it to total synthesis. It was mainly used in synthesis to generate 3-acyltetrahydrofurans, starting from allylic acetals, or with allylic diols to do the so-called Prins-pinacol condensation, where the acetal is first formed from

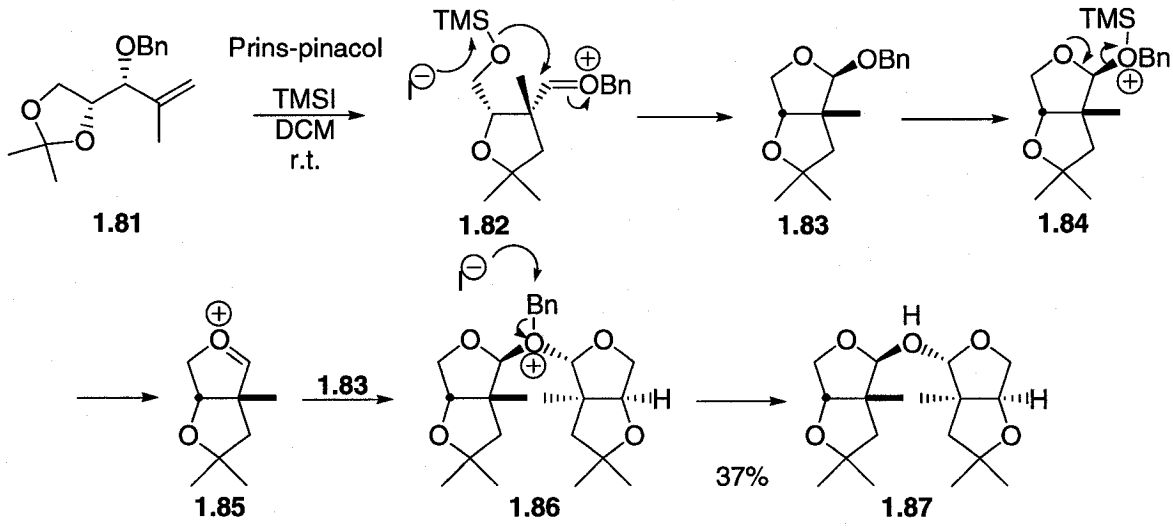
the starting materials.[28] Tetrahydrofurans are generated when the Prins cyclization is 6-endo-trig and the allylic alcohol is endocyclic. Mousset[1] was the first to generate a 3-acyltetrahydrofuran from a Prins-pinacol condensation but it is it is Overman, in 1991, that first used this methodology in synthesis to prepare (±)-*trans*-kumausyne (**1.79**, Scheme 1.5).[29] Starting with a simple allylic diol (**1.75**) and an aldehyde (**1.76**), the Prins-pinacol condensation followed by a Baeyer-Villiger oxidation afforded the correct atom connectivity and stereochemistry of all the substituents on the tetrahydrofuran of *trans*-kumausyne. Two years later, he used the same methodology in the synthesis of (±)-kumausallene (**1.80**).[30]



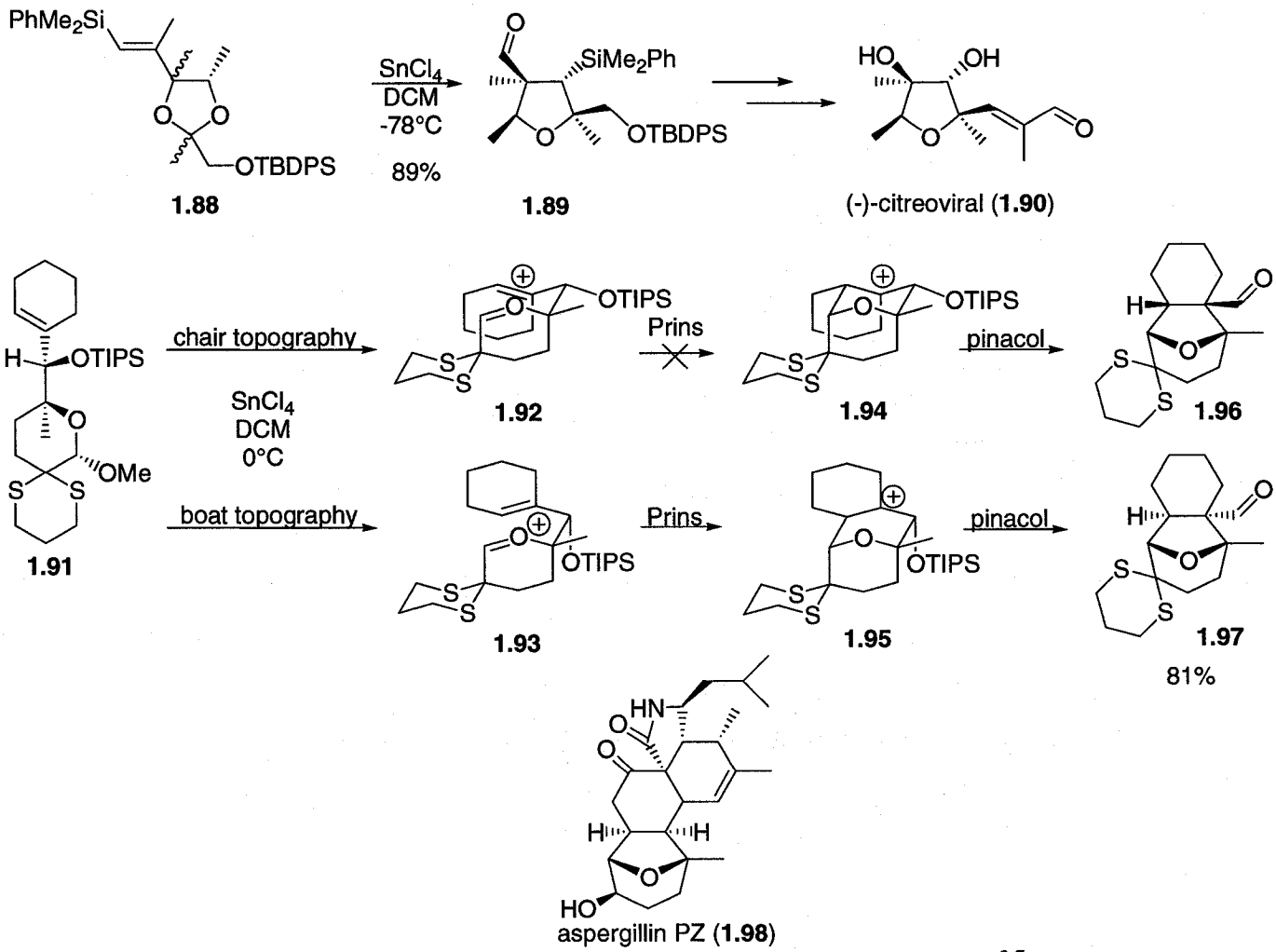
Scheme 1.5 – Synthesis of (±)-trans-Kumausyne and (±)-Kumausallene

In 1993, an interesting tetrahydrofuran synthesis was achieved by Muzler *et al.* where he used 4-ene-1,2,3-triols to generate bis(furanoside) derivatives (Scheme 1.6).[31] The protected allylic triol **1.81** was treated with trimethylsilyl iodide to first afford the Prins-pinacol product **1.82**, followed by cyclization and dimerization to afford the glycoside **1.87**.

As shown in Scheme 1.7, the Prins-pinacol reaction was also used to generate the tetrahydrofuran ring of (-)-citreoviral (**1.90**)[25] and 12-oxotricyclo[6.3.1.$0^{2,7}$]dodecane (**1.97**).[32] What is interesting in the latter is the use of a 1,3-dithiane in order to exploit unfavorable steric interactions between the two cofacially oriented six-membered rings to disfavor the chair transition structure during the Prins cyclization. The reaction proceeds through a boat topography to provide the stereoisomeric *trans*-oxatricyclic product **1.97**, which can be found in natural compounds such the fungal metabolite aspergillin PZ (**1.98**).[33]

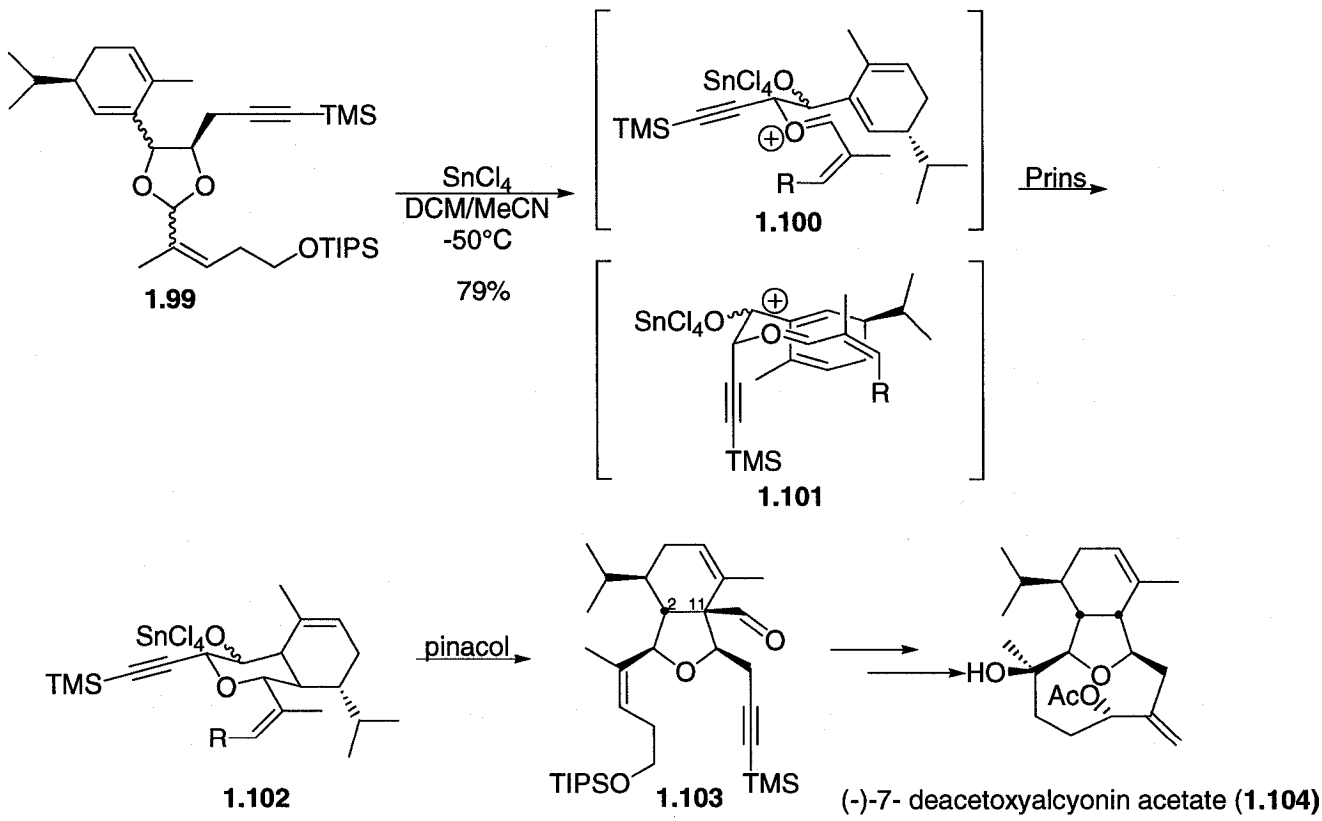


Scheme 1.6 – Synthesis of a Bis(furanoside) Derivative



Scheme 1.7 – Synthesis of (-)-Citreoviral and a 12-Oxotricyclo[6.3.1.$0^{2,7}$]dodecane

The Prins-pinacol generated tetrahydrofuran methodology was used for the total synthesis of 7 natural compounds in the C2, C11-cyclized cembranoid diterpene family of natural products. Scheme 1.8 shows how the Prins-pinacol reaction was used in the synthesis of the eunicillin diterpene (-)-7-deacetoxyalcyonin acetate (**1.104**).[34] The transition structure **1.100**, bearing the propargyl group in a pseudoequatorial position and having the oxocarbenium ion approaching the diene from the opposite face of the isopropyl substituents was greatly favored, allowing outstanding stereoselection in this reaction.[35] What is also interesting about this transformation is that no stereomutation of the conjugated oxocarbenium ion in **1.100** was observed. As shown in Scheme 1.9, the Overman group used the same methodology in the total synthesis of severals briarellin diterpenes, such as briarellin E (**1.105**) and briarellin F (**1.106**),[36] and for the synthesis of cladiellin diterpenes, such as 6-acetoxycladiell-7(16), 11-dien-3-ol (**1.107**), cladiell-11-ene-3,6,7-triol (**1.108**), sclerophytin A (**1.109**) and sclerophytin B (**1.110**).[37]



Scheme 1.8 – Synthesis of (-)-7-Deacetoxyalcyonin Acetate

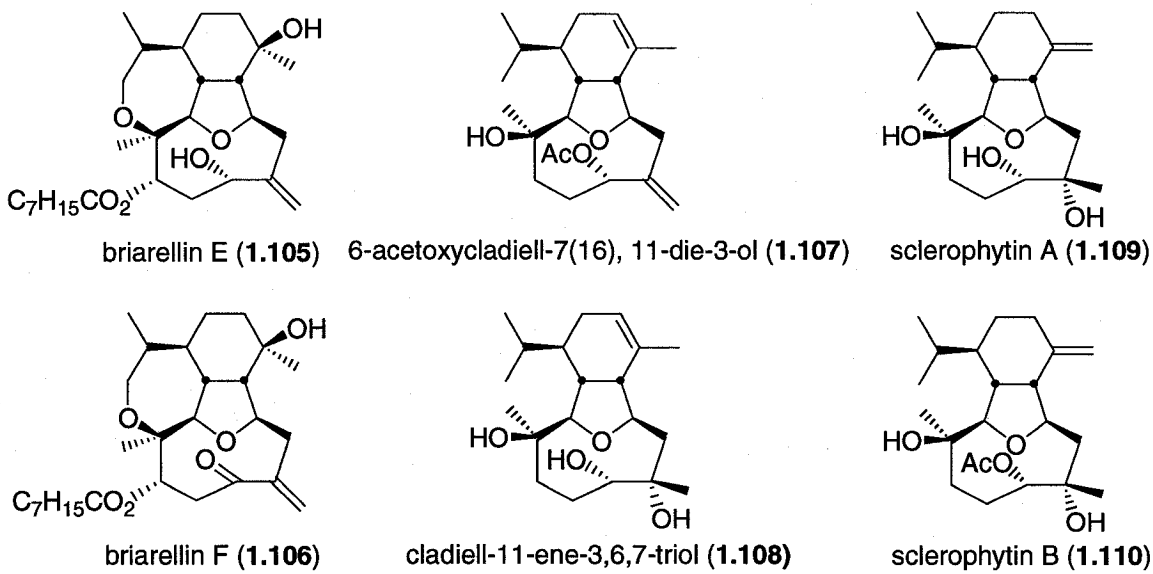
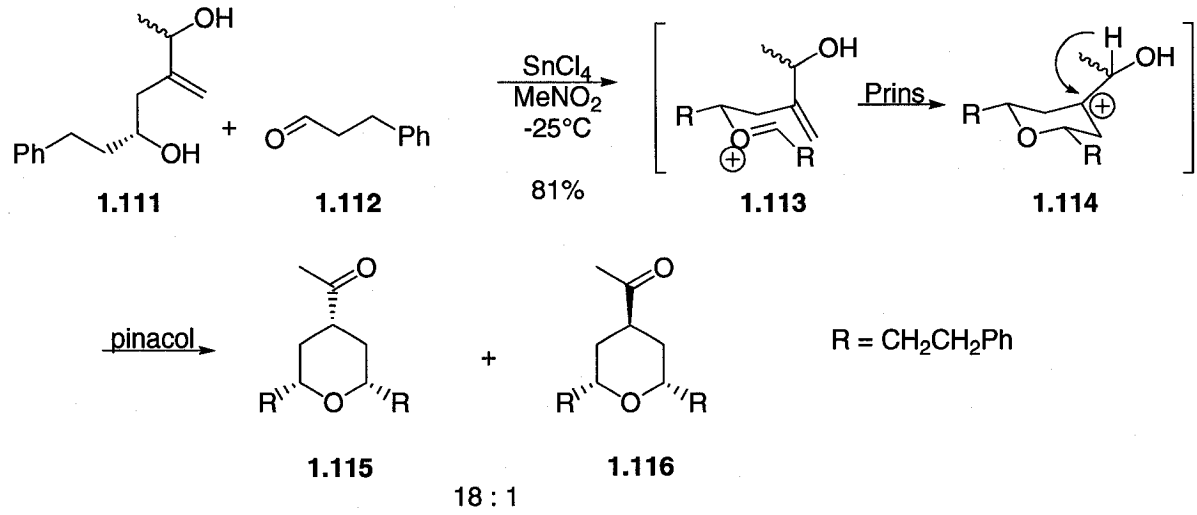


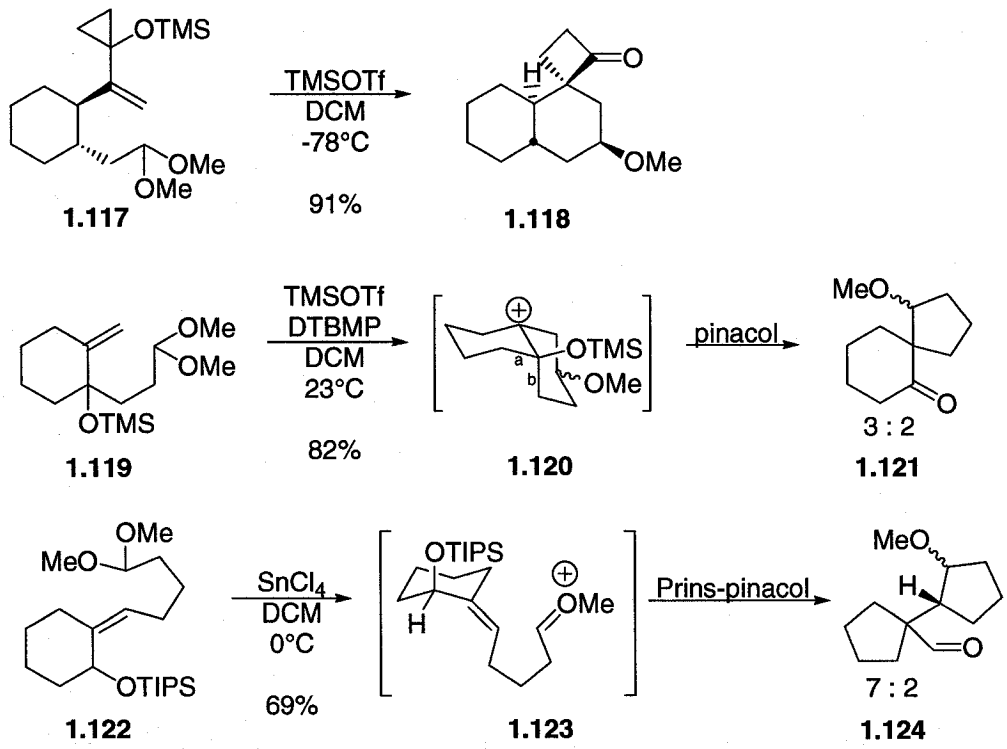
Figure 1.8 – Briarellin and Cladiellin Diterpenes Synthesized by the Overman Group

Scaffolds other than tetrahydrofurans can be obtained from the Prins-pinacol cyclization. As mentioned earlier, tetrahydrofurans are generated when the Prins reaction is 6-endo-trig cyclization and the allylic alcohol is endocyclic. When the Prins cyclization is a 6-endo-trig and the allylic alcohol is exocyclic, Oveman demonstrated that trisubstituted tetrahydropyrans can be obtained with high stereocontrol.[38] First, the productive oxocarbenium ion is generated from the homoallylic alcohol (**1.111**), then the Prins cyclization occurs with the more stabe *E* oxonium ion and with the alkyl chain in a pseudoequatorial position (**1.113**). The reaction is terminated by a pinacol shift, occurring with preferential axial hydride delivery to give **1.115**.

When the Prins cyclization is a 5, 6, 7 or 8-exo-trig cyclization, the Prins-pinacol rearrangement can generate a variety of carbocyclic rings systems (Scheme 1.10). One of the first examples was observed in 1988 by Trost when he generated spirocyclobutanone compounds such as **1.118**.[39] Overman also published many Prins-pinacol spiroannulations.[23] By treating **1.119** with TMSOTf and 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP), a mixture of methoxy epimers of the spirocycle **1.121** was observed. It is only the bond *b* that migrates since it's the one that has better overlap with the vacant p orbital. The same principles were used in the synthesis of attached rings.[27a, 40] Conformer **1.123** is favored since it minimizes 1,3-allylic strain and the resulting vacant p orbital is well aligned for ring contraction and not for hydride migration.



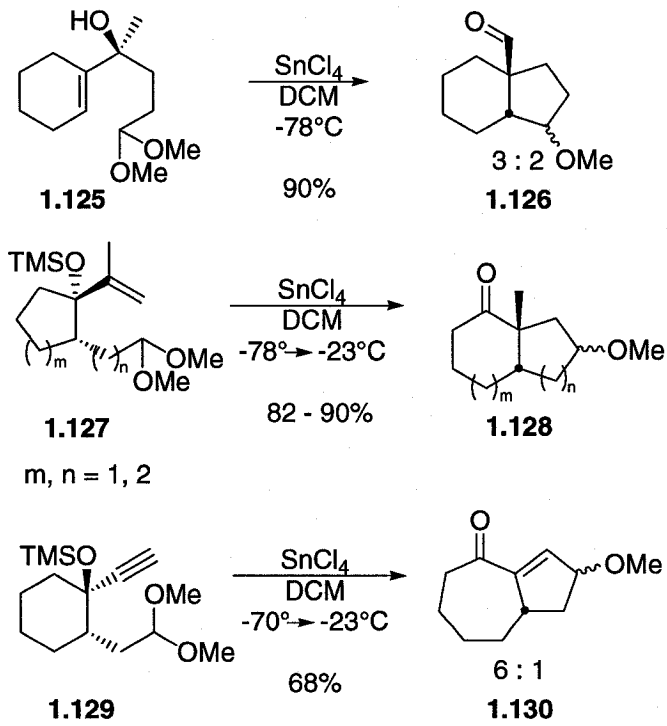
Scheme 1.9 – Synthesis of Trisubstituted Tetrahydropyrans



Scheme 1.10 – Prins-Pinacol Synthesis of Carbocyclic Ring Systems

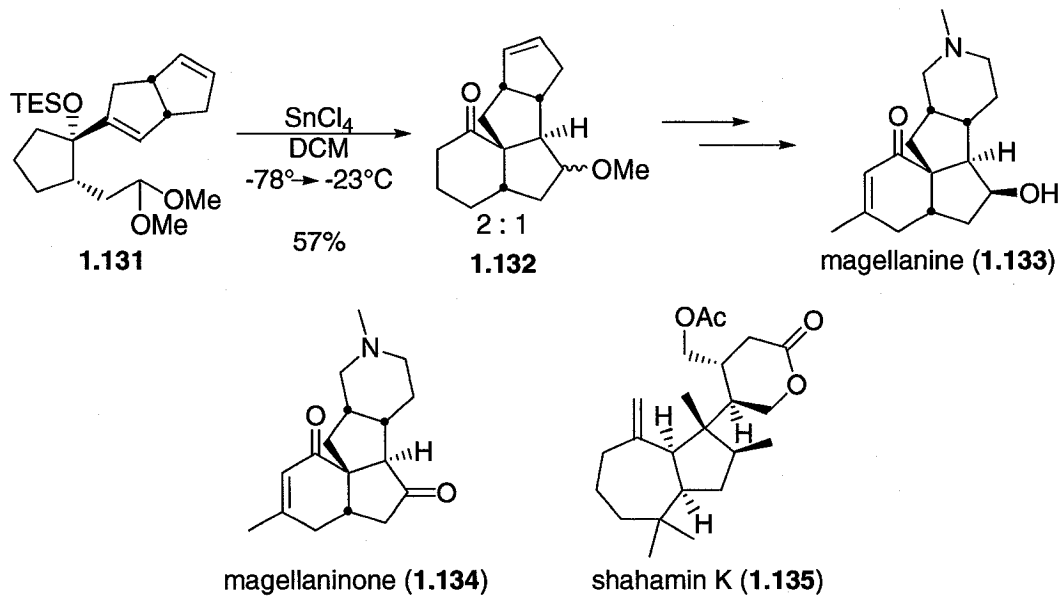
Finally, the Prins-pinacol reaction applied to the synthesis of carbocyclic ring systems was used to make *cis*-fused bicyclic compounds (Scheme 1.11). Even though the first example

was published by Sworin in 1988[41] where he generated the hydroindene **1.126**, it was Overman that developed the bulk of the methodology to generate a variety of *cis*-fused bicyclic cores (**1.128**).[42] The use of an alkyne instead of an alkene affords the cyclopentene annulated product **1.130**.[43] Overman's group applied this methodology in the synthesis of magellanine (**1.133**), magellaninone (**1.134**)[44] and shahamin K (**1.135**),[45] generating the polycyclic structures with the stereochemistry corresponding to the cores of these molecules (Scheme 1.12).

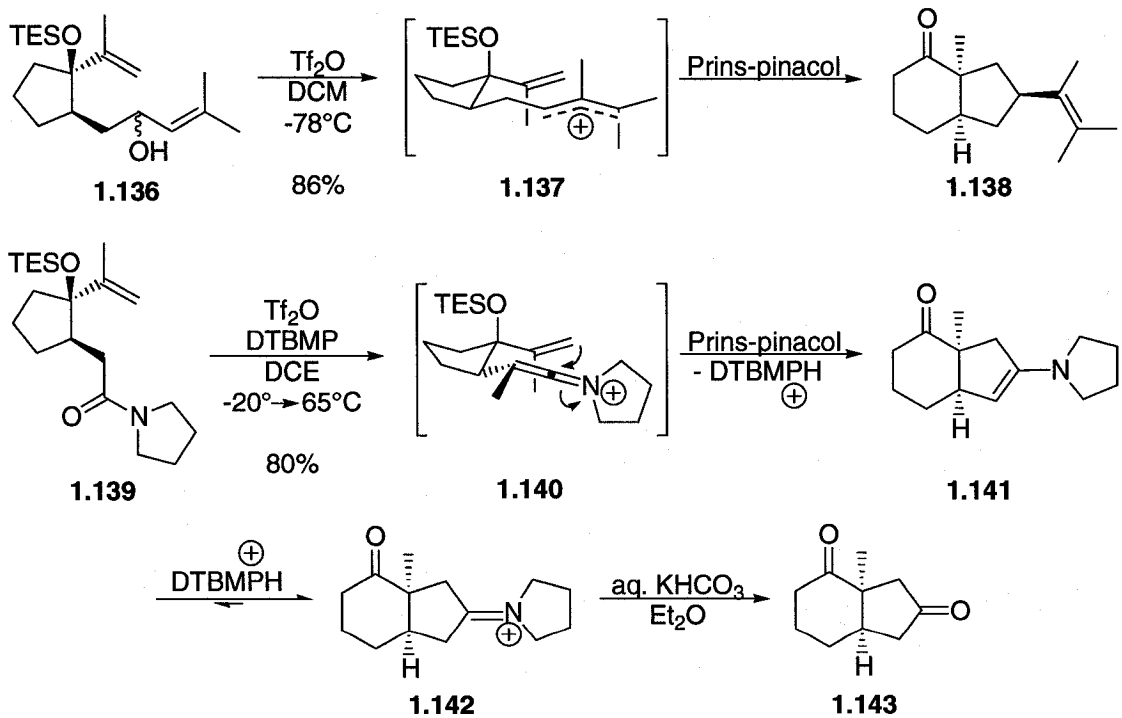


Scheme 1.11 – Prins-Pinacol Synthesis of Cis-fused Bicyclic Systems

These *cis*-fused bicyclic structures can also be obtained using allyl carbenium and keteniminium ions as cyclization initiators.[46] The allyl cation **1.137** can be obtained by treating the allylic alcohol **1.136** with triflic anhydride. Having the vinyl group in a pseudoequatorial position during the Prins cyclization explains the stereochemistry of the vinylic group in **1.138**. The keteniminum ion **1.140** is formed by treating the amide **1.139** with triflic anhydride and a base. The enamine resulting from the Prins-pinacol rearrangement is protonated under the reaction conditions by the pyridinium triflate salt to give the iminium salt **1.142** which is then hydrolyzed to give the diketone product **1.143**.

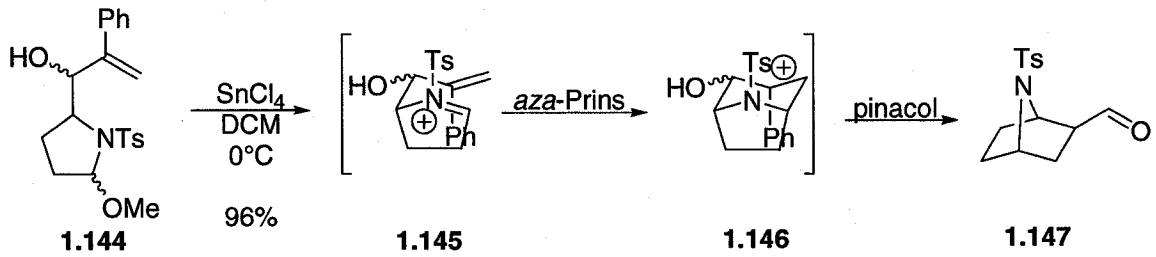


Scheme 1.12 – Synthesis of Magellanine, Magellaninone and Shahamin K



Scheme 1.13 – Allyl Carbenium and Keteniminium Ions as Cyclization Initiators

A 7-azabicyclo[2.2.1]heptane skeleton can also be obtained using an *aza*-Prins-pinacol reaction.[47] Armstrong demonstrated that homoallylic *N*-tosylpyrrolidines such as **1.144**, can undergo an *aza*-Prins cyclization followed by a pinacol rearrangement to give the [2.2.1]azabicycle **1.147**.



1.144 **1.145** **1.146** **1.147**

Scheme 1.14 – Mechanism of the aza*-Prins-Pinacol Reaction*

As it was just pointed out, the Prins-pinacol rearrangement represents an attractive and efficient strategy for the rational diastereoselective formation of carbon-carbon bonds. Many cores have been synthesized using this methodology. This report, to the best of my knowledge, illustrates the first example of the synthesis of *cis*-fused bicyclo[*m.n.*1]alkanones using the Prins-pinacol rearrangement.

About Bicyclo[m.n.1]alkanones

Cis-fused bicyclo[*m.n.*1]alkanone cores can be found in various complex, biologically active compounds such the structurally related bicyclo[3.3.1]nonanones garsubellin A (**1.148**),[48] papuaforin A (**1.149**),[49] and nemorosone (**1.150**).[50] Other ring sizes are also found in nature, such the bicyclo[4.3.1]decanone welwitindolinone C (**1.151**),[51] the bicyclo[4.4.1]undecanone isoingenol (**1.152**)[52] and the bicyclo[5.3.1]undecanone penostatin F (**1.153**).[53] The rapid synthesis of these highly funtionalized *cis*-fused bicarbocyclic cores represents a formidable synthetic challenge.[54] Methods that allow the construction of various bicyclic bridgehead ketones with flexibility in one or both of the ring sizes would be a great advancement, since this flexibility is rare.[55, 56] Methods that allow this flexibility would be a tremendous discovery, and

were impossible before a publication by our group which contains some of the results presented in this report.[57]

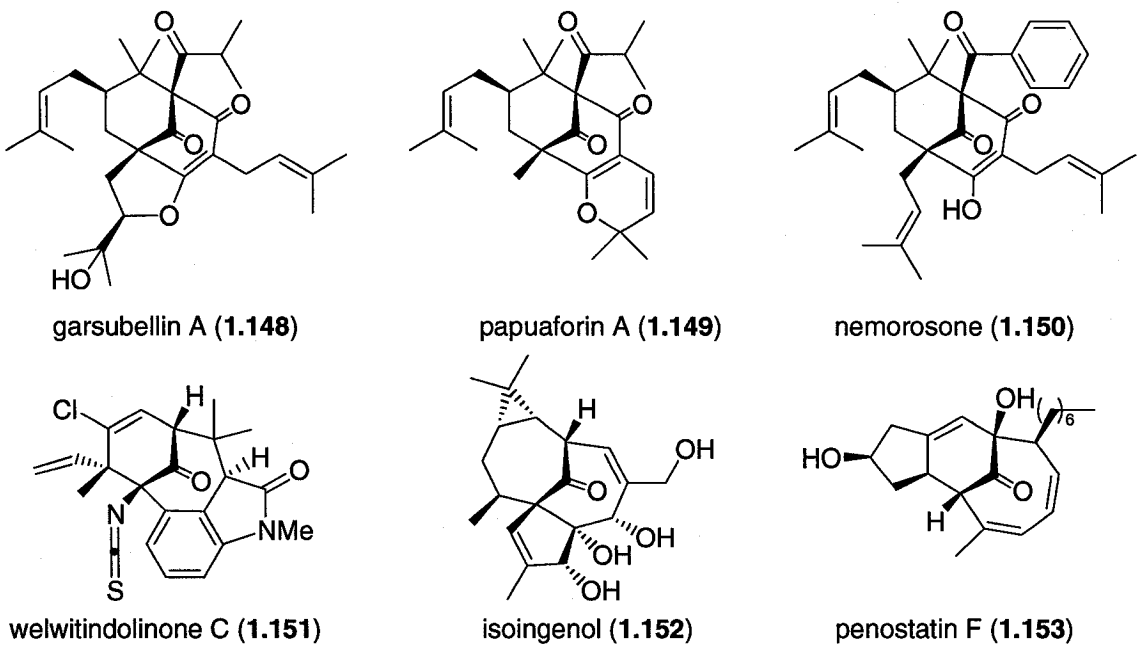
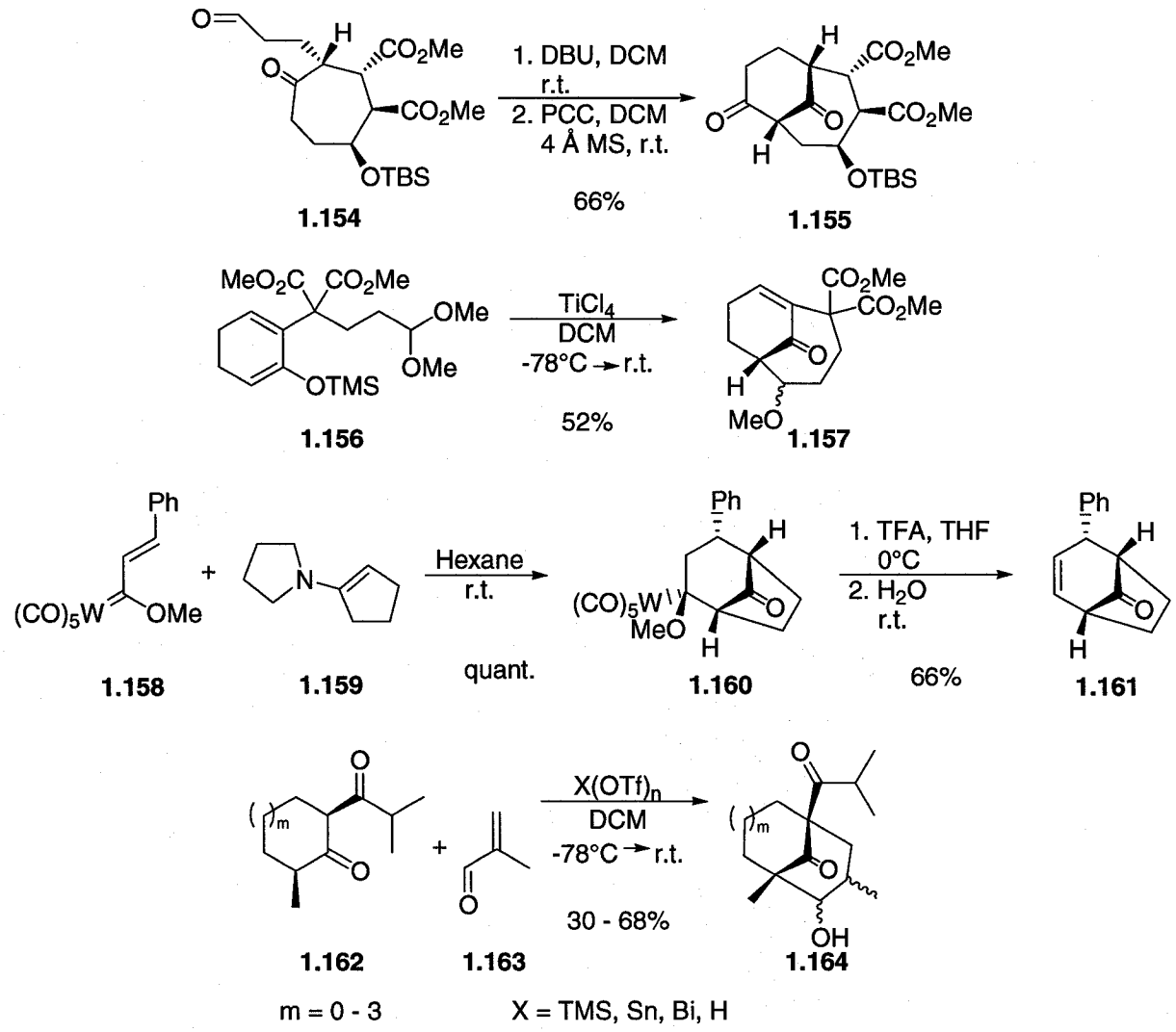


Figure 1.9 – Compounds Having a Cis-fused Bicyclo[m.n.1]alkanone Core

Since many *cis*-fused bicyclo[*m.n.*1]alkanone cores represent attractive synthetic targets for chemists, a lot of strategies have been developed to generate them. The most obvious method of bond formation α to a ketone is via an aldol reaction. Scheme 1.15 shows Ohmori's efforts towards a synthesis of phomoidride B, where he performed an intramolecular aldol followed by an oxidation to obtain the diketone **1.155**.[58] Armstrong *et al.* used the Mukaiyama variation of the aldol reaction to cyclize via titanium tetrachloride activation of the acetal **1.156** to afford the cores of both CP 225,917 and CP 263,114.[59] Methodologies using an emamine are also well documented. Below is an example where the enamine **1.159** was treated with the tungsten complex **1.158** to first give quantitative precipitation of **1.160**, which was then treated with trifluoroacetic acid and hydrolyzed to give the corresponding [3.2.1] bicyclic framework (**1.161**).[60] A more attractive and general method was proposed by Nicolaou in 2005 where he could access a variety of bicyclo[*m*,3,1]alkanones (**1.164**) starting with simple cycloalkanones (**1.162**) and α,β-unsaturated aldehydes (**1.163**).[56] This interesting reaction sequence starts with enolization of the carbon between the two carbonyl groups, followed by an intermolecular

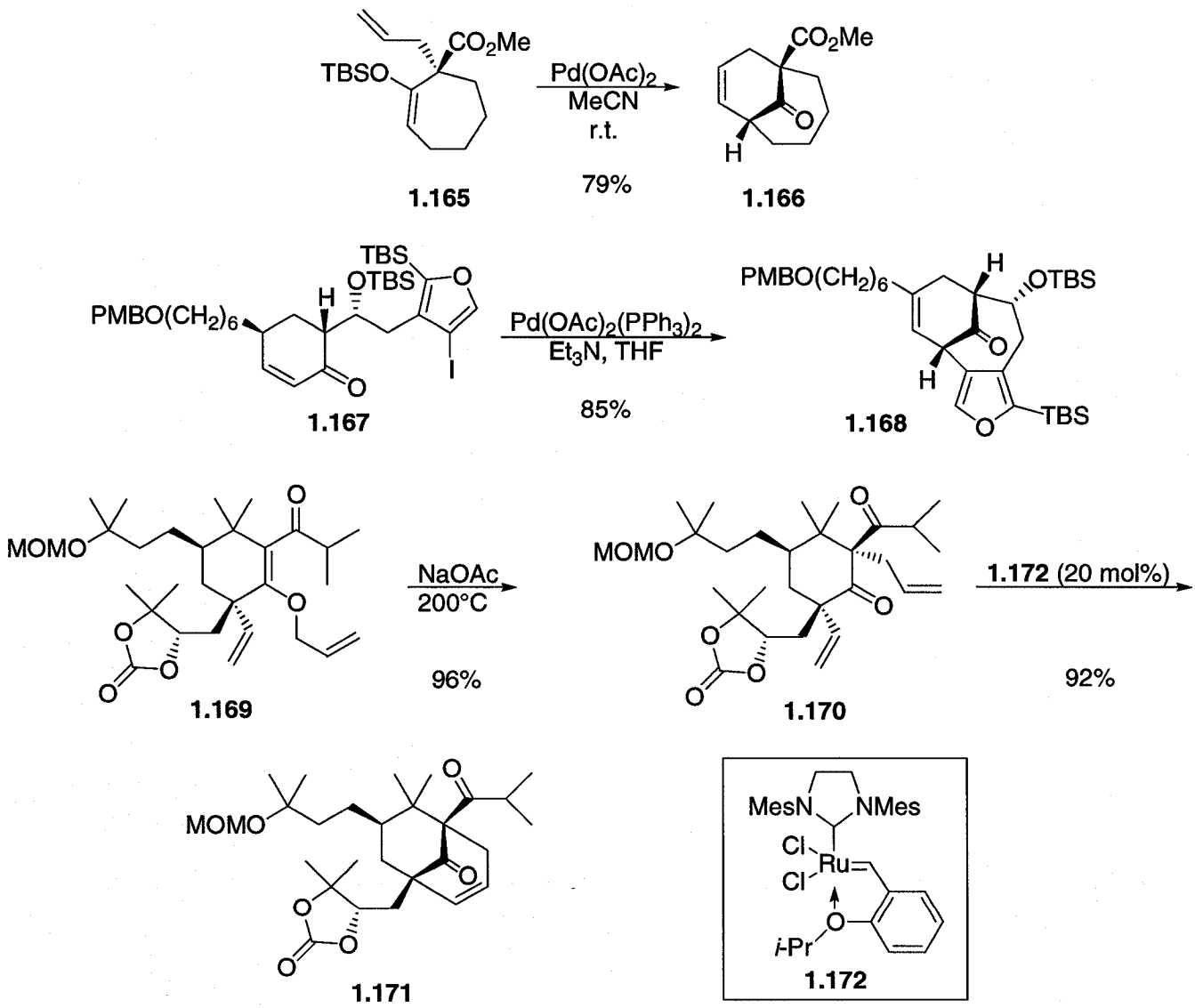
Michael addition on **1.163**, ending with an intramolecular aldol reaction. Although only modest yields were obtained, this methodology allows for the formation of two carbon-carbon bonds along with two quaternary carbon centers adjacent to a bridged ketone. They obtained a mixture of two diastereoisomers in all the reaction but since they were destroying these two chiral centers for the synthesis of perforatumone, the stereochemistry was not determined.



Scheme 1.15 – Construction of Bicyclo[m.n.1]alkanones Using the Aldol Reaction

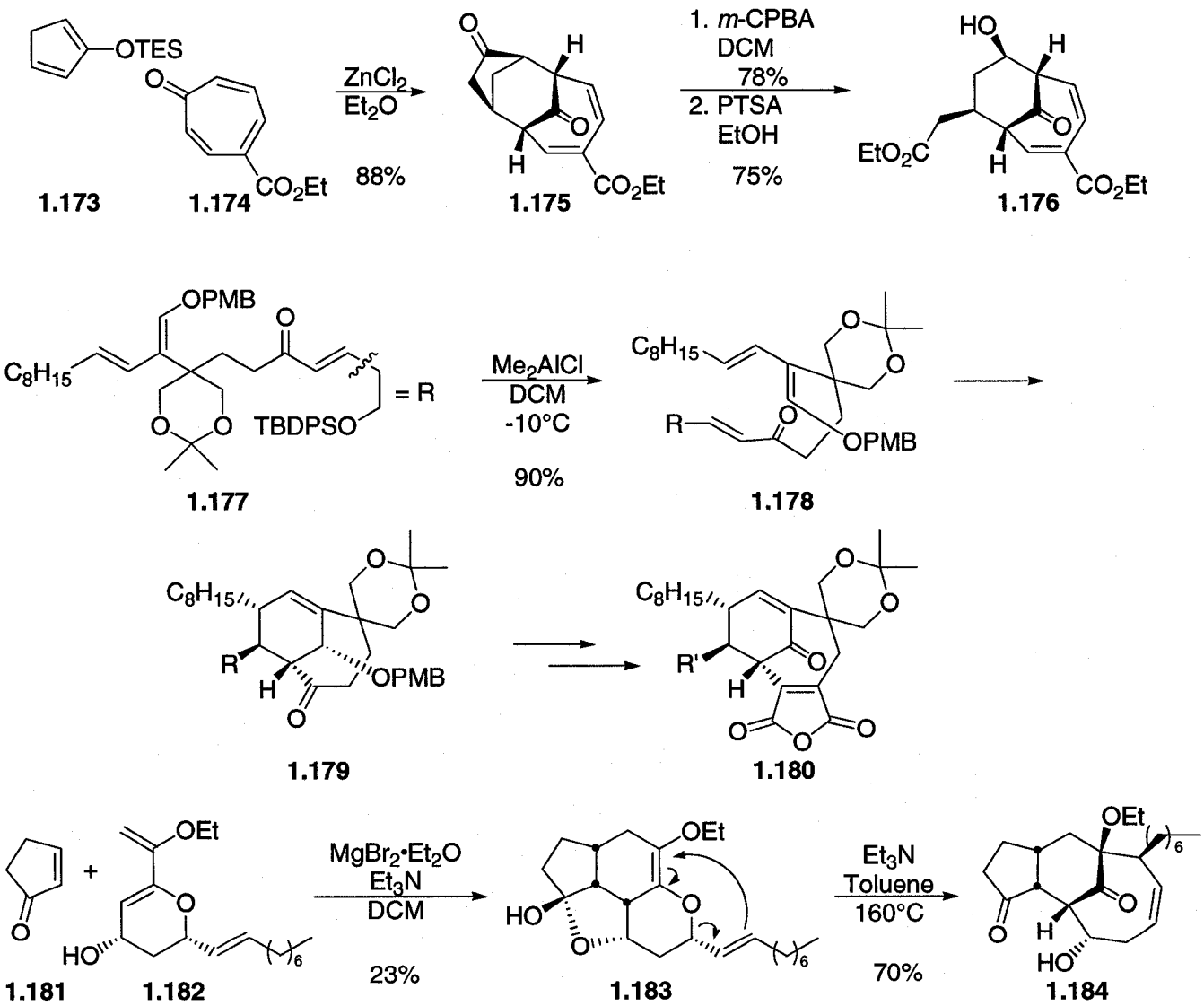
Palladium chemistry was also used in the synthesis of these bicyclic molecules (Scheme 1.16). Palladium (II) mediated cycloalkenylation was performed on the silyl enol ether (**1.165**) to furnish the bicycloalkenone (**1.166**).[61] Unfortunately, stochiometric amounts of palladium were

required and its application to other ring sizes was inefficient. An intramolecular Heck reaction was used in the synthesis CP 225,917 and CP 263,114 and it proved to be very efficient.[62] Recently, Shibasaki published an elegant synthesis of garsubellin A where he generates the bicyclo[3.3.1]nonanone core with ring closing metathesis.[63] The second quaternary carbon center adjacent to the bridgehead ketone is generated via a stereoselective Claisen rearrangement on the less hindered side of **1.169**. Then, the ring closing metathesis using the Hoveyda-Grubbs catalyst (**1.171**)[64] gave (**1.170**) in good yields.



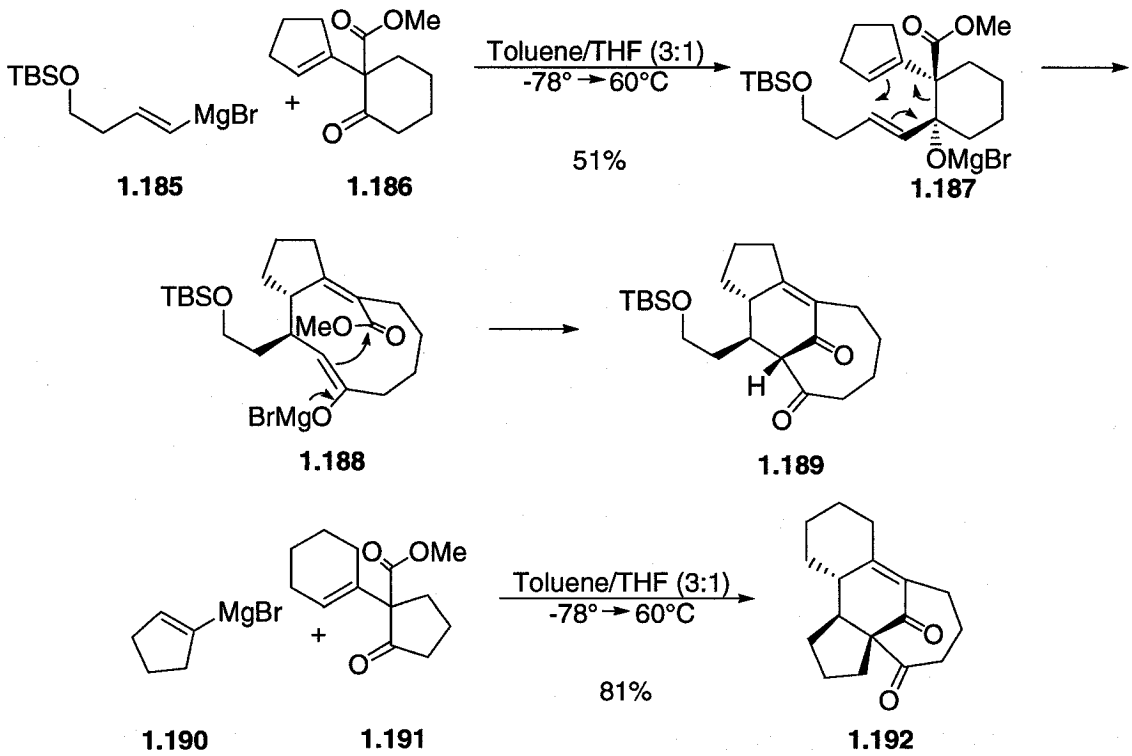
Scheme 1.16 – Construction of Bicyclo[m.n.1]alkanones Using Organometallics Chemistry

Cis-fused bicarbocycles can also be generated with cycloadditions (Scheme 1.17). Gleason uses an interesting strategy were he performs a Lewis acid catalyzed tropone (**1.174**) cycloaddition with 2-triethylsilyloxy-cyclopentadiene (**1.173**) to obtain the [6+4] cycloadduct (**1.175**).[65] Then, a highly site selective Baeyer-Villiger oxidation followed by hydrolysis of the lactone gave the bicyclic ketone **1.176**. Nicolaou made a clever use of the well known Diels-Alder reaction in order to generate the core of CP molecules.[66] Submitting **1.177** to a catalytic amount of dimethylaluminium chloride, gives a Lewis acid-catalyzed type II intramolecular



Scheme 1.17 – Use of Cycloadditions in the Synthesis of Bicylic Bridgehead Ketones

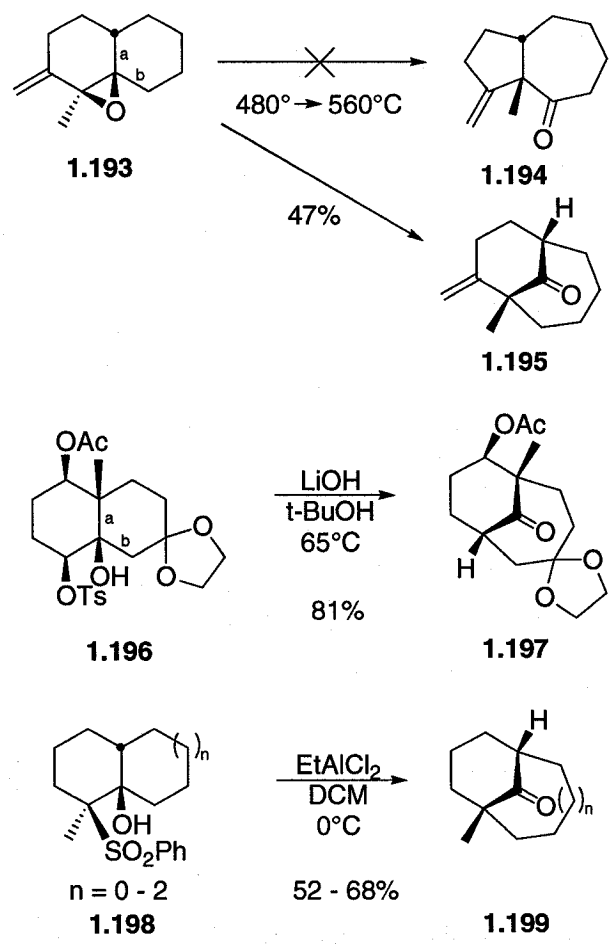
Diels-Alder reaction to give the *endo* product **1.178** that was later transformed into a bicyclic ketone by deprotection of the PMB group and oxidation of the alcohol. Our group also made a clever use of the Diels-Alder and the Claisen reaction in the synthesis of the core of penostatin F (**1.153**).[67] The diastereoselective hydroxy-directed Diels-Alder reaction between cyclopentenone **1.181** and the diene **1.182** gave **1.183**, and a subsequent Claisen rearrangement afforded the bicyclo[5.3.1]undecanone core of penostatin F. [3,3]-sigmatropic rearrangements were also used by Shair *et al.*, in the synthesis of a variety of bicyclo[*m*.3.1]polycyclic alkanones (Scheme 1.18).[55] This rapid assembly of bridged ring structures uses a clever tandem alkylation / anionic oxy-Cope / transannular Dieckmann-like cyclization sequence, and starts with quite a simple substrate (**1.186**). This methodology generates 3 contiguous chiral centers and can be applied to other ring sizes as demonstrated by the synthesis of **1.192**.



Scheme 1.18 – Shair's Synthesis of Bicyclo[m.3.1]alkenone Skeletons

Pinacolic rearrangement was also used in the generation of bicyclo[*m.n.*1]alkanones (Scheme 1.19). It was first observed by Kretchmer in 1971 when he did a pyrolysis of the

epoxide **1.193**.[68] Instead of the expected hydroazulene **1.194**, he observed the formation of bridgehead ketone **1.195**. Heathcock's group also observed the formation on a bicyclo[4.3.1]decanone when they were trying to generate hydroazulenes.[69] Solvolysis of tosylate **1.196** with lithium hydroxide gives the rearranged keto acetate **1.197** in good yields. In both Kretchmer's and Heathcock's example, the bicyclic ketones were obtained due to the better overlap of the empty p orbital, or the σ* of the leaving group, with bond *b* compared to bond *a*. Trost also did a similar rearrangement with different ring sizes using the organosulfones such as **1.198** to generate the bridge bicycles **1.199** in modest yields.

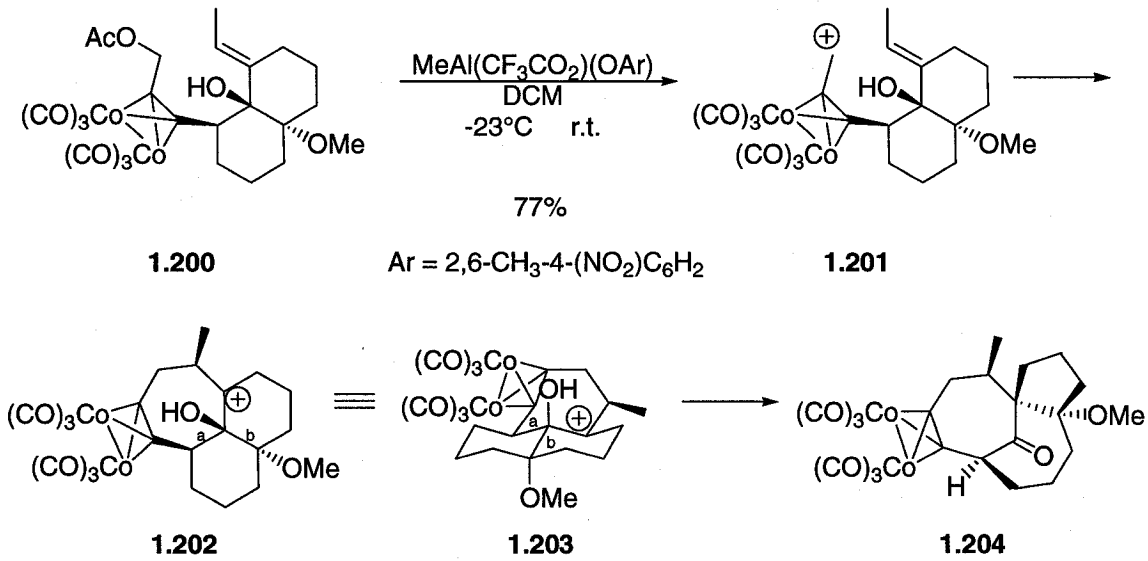


Scheme 1.19 – Bicyclo[m.3.1]alkanone Cores Obtained via a Pinacol Rearrangement

Finally, the Prins-pinacol reaction was used by Kuwajima to provide access to *trans*-fused bicyclic systems. Adding a Lewis acid to **1.200** provides the dicobalt hexacarbonyl

propargyl cation **1.201** which leads to an intramolecular electrophilic addition on the ethylidene moiety, followed by a pinacol rearrangement where bond *b* migrates to give **1.204**.[70]

In the present report, the first use of the Prins-pinacol reaction in order to generates *cis*-fused bicyclic systems varying the two ring sizes will be outlined. It will also be shown that the Prins-pinacol rearrangement can be done in tandem with the Diels-Alder reaction in order to generate high complexity with an excellent level of stereocontrol in a single step.



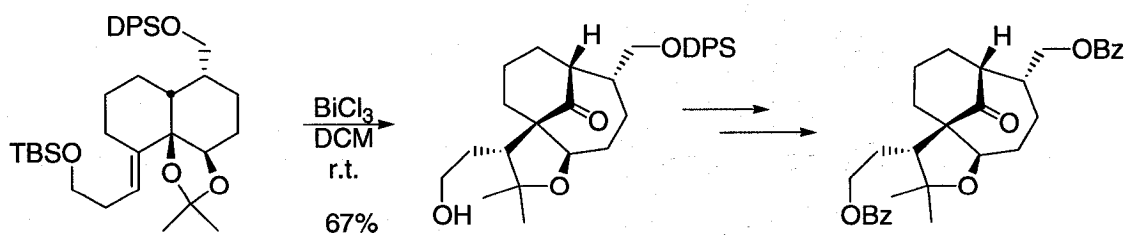
Scheme 1.20 – A Trans-fused Bicyclo[4.4.1]undecanone Core Obtained via a Prins-Pinacol Rearrangement

2

Development of the Prins-Pinacol Rearrangement to Generate Bicyclo[4.3.1]decanones

The Project's Origin

Like the first Prins-pinacol rearrangement observed by Mousset in 1969,[1] the first *cis*-fused bicyclic ketone obtained via a pinacol-terminated Prins cyclization was an unexpected result. Louis Morency, from our group, obtained the bicyclo[4.3.1]decanone **2.2** when he was attempting to deprotect the acetonide of **2.1** using bismuth trichloride in his work toward the synthesis of vinigrol (Scheme 2.1).[71] He confirms all the stereocenters by derivatization of **2.2** in **2.3** in order to get an X-ray crystallographic structure (Figure 2.1).



2.1 **2.2** **2.3**

Scheme 2.1 – First Observed Prins-Pinacol Rearrangement in our Laboratories

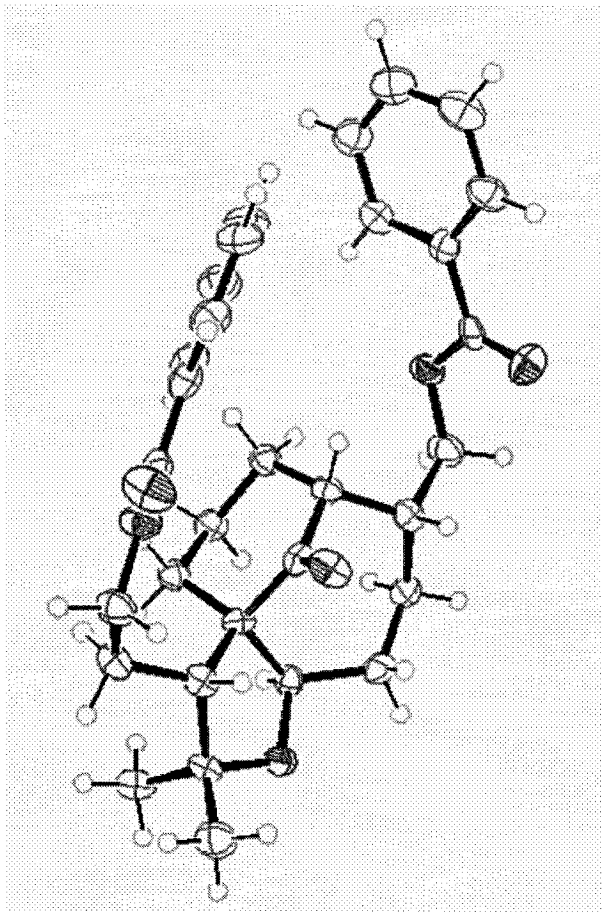


Figure 2.1 – X-Ray Crystallographic Structure of **2.3**

We rationalized that this rearranged product is results from a Prins-pinacol rearrangement. The previous mechanistic studies performed by Overman[20, 22] allowed us to define the reaction sequence, as depicted in Figure 2.2. First, the *cis*-decalin can adopt two conformations, **2.4** and **2.6**, where **2.4** should be the more stable conformer since **2.6** experiences severe *syn*-pentane interactions between C1-C10 and C5-C14. Each of these conformers can have two different ketal openings, **2.5** and **2.8** for **2.4**, **2.7** and **2.9** for **2.6**. The oxocarbenium ions **2.5** and **2.7** cannot undergo a Prins cyclization due to poor orbital overlap, therefore regeneration of the acetonide will be the favored process. The oxocarbenium ions **2.8** and **2.9** are in equilibrium where, again, **2.8** should be the more stable conformer since **2.9** experiences two severe *syn*-pentane interactions. Only **2.8** can undergo a Prins cyclization since **2.9** cannot have the alkene and the oxocarbenium ion in proximity since C2-O bond and C1-C10 bond are pointing in opposite directions. Unlike Mousset's system,[1] where the olefin is on a free chain,

the olefin is now found on a ring that will have to undergo a conformational change in order to get good overlap with the oxocarbenium ion. By using a simple molecular model, one can draw the conclusion that ring B needs to be in a twist-boat conformation (**2.11**) in order to have the alkene in close proximity with the oxocarbenium ion, and the ring will stay locked in this conformation in intermediate **2.12** to accommodate the sp^2 hybridization of C10. The carbenium

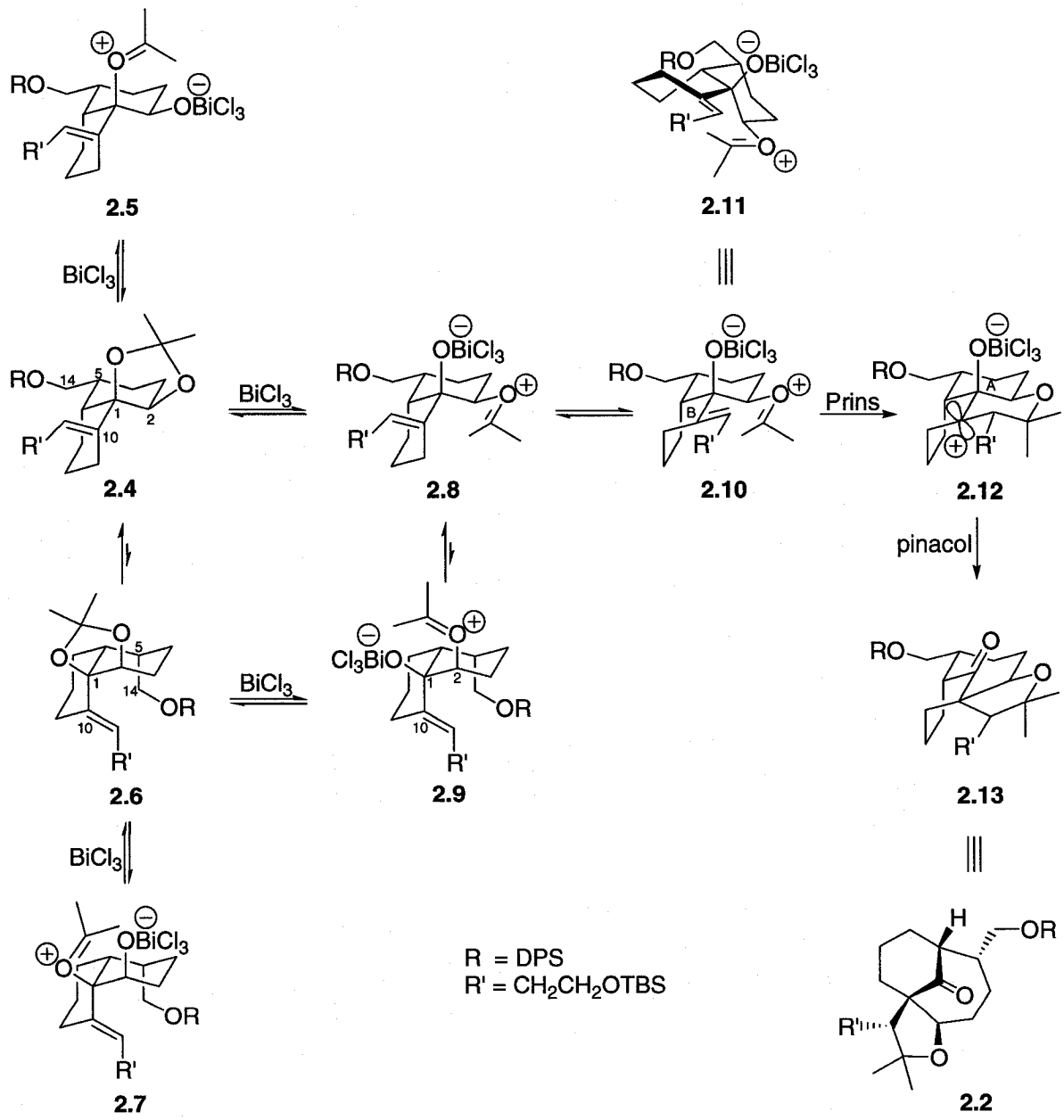
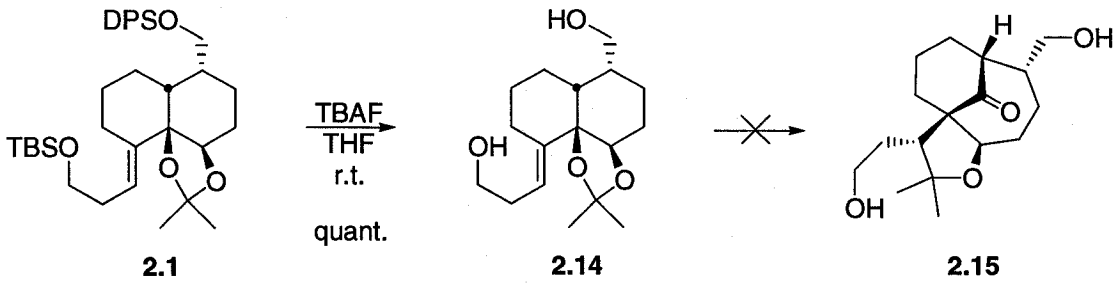


Figure 2.2 – Rationale of the Formation of ***2.2***

ion **2.12** cannot undergo ring inversion due to the trans relationship between ring A and the newly formed tetrahydropyran ring. **2.12** is then poised to undergoes a pinacol rearrangement where it is the C1-C2 bond that migrates since it is the bond that has the better alignment with the vacant p-orbital (30° angle difference). The tetrahydrofuran **2.13** is formed, which can be represented in 2D by **2.2**. Early investigation of the reaction showed an incompatibility of this system in presence of free alcohols. The diol **2.14** only leads to degradation when submitted to the Prins-pinacol conditions.



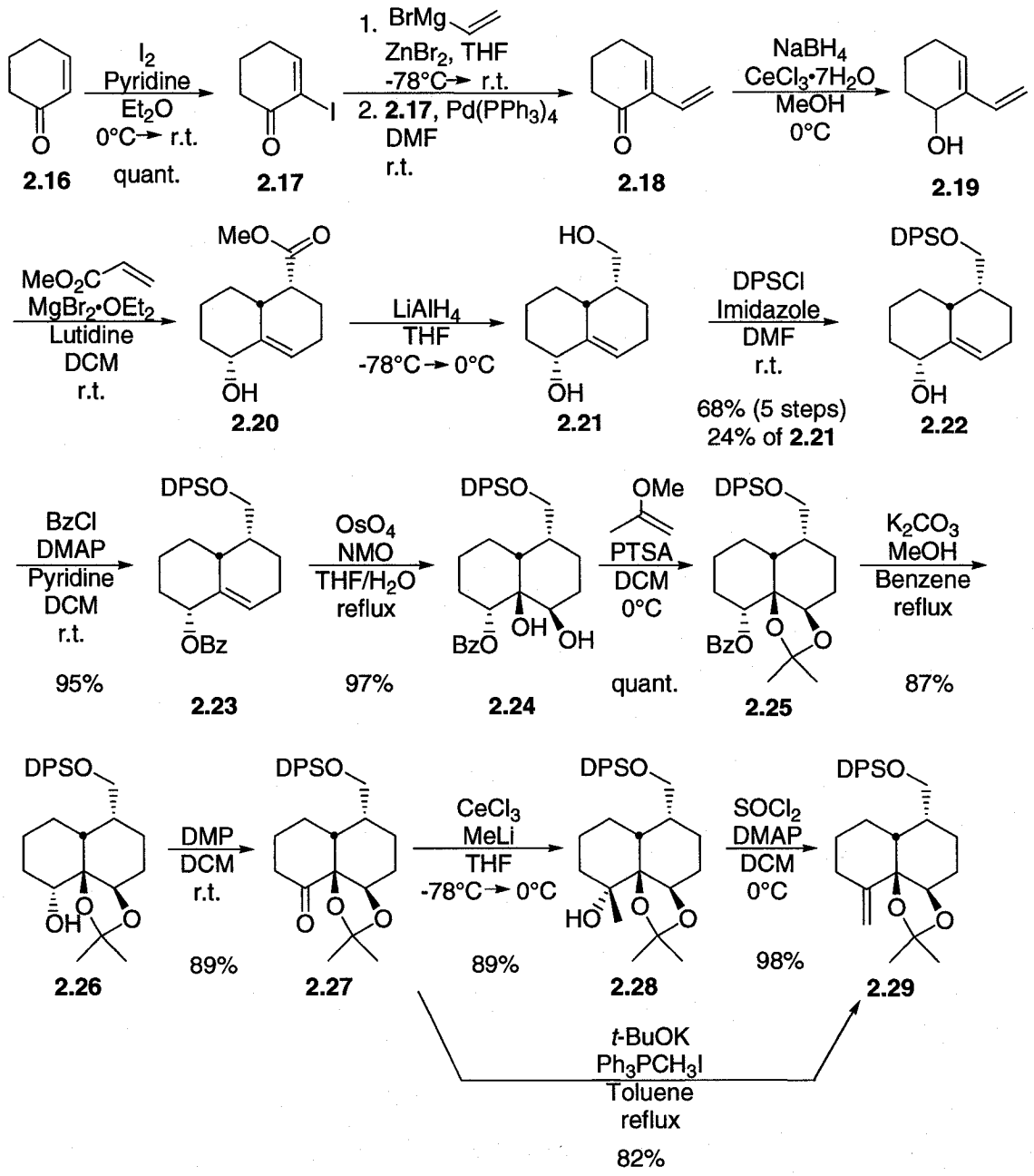
2.1 **2.14** **2.15**

Scheme 2.2 – Attempted Prins-Pinacol Rearrangement on a Substrate with Free Alcohols

Optimization of the Reaction Conditions

The project first started with some investigations by Justine Chan, a summer student. Her first goal was to generate a more general substrate having a disubstituted double bond in order to scan a variety of Lewis acids and to determine the influence of olefin substitution. She started working with the ketone **2.27**, which can be obtained in 11 steps with an overall yield of 49%. Scheme 2.3 shows the sequence, developed by Louis Morency,[71] where the iodoenone **2.17** is first obtained from cyclohexenone. A Negishi coupling, followed by a Luche reduction generates the hydroxy-directed Diels-Alder precursor, which upon treatement with methyl acrylate and magnesium bromide etherate, gives **2.20** as the only observed stereoisomer.[72] The ester moiety was then reduced, the primary alcohol was selectively protected with a *tert*-butyldiphenylsilyl group and the secondary alcohol was protected as the benzoate ester. A dihydroxylation of **2.23**, followed by an acetonide protection, a debenzoylation and an oxidation with Dess-Martin periodinane afforded the ketone **2.27** in reproducible yields. Finally, Justine

generated the Prins-pinacol precursor through a sequence of methylation and elimination but it was later found that a Wittig olefination can directly afford the alkene **2.29**.

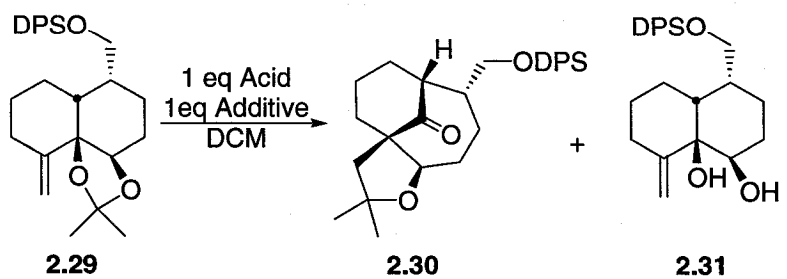


Scheme 2.3 – Generation of the Prins-Pinacol Precursor for Optimization Studies

My first goal in this project was to scan a variety of Lewis acids to perform the Prins-pinacol rearrangement. The reactions in Table 2.1 were performed in dichloromethane since it was the solvent used almost exclusively in the Prins-pinacol conditions reported in the literature.

Entry 2 shows that removing the alkyl chain on the olefin was beneficial since higher yields were obtained using the same reaction conditions. This improvement in yield is probably due to diminished steric interactions during the Prins cyclization. This increase in yield was also observed in other systems.[4a, 20a] Three Lewis acids lead to some deprotection of the diols (entries 1, 11 and 12). The majority of the Lewis acids that were tried gave the rearranged product in poor to good yields, tin tetrachloride being the most efficient. Silver salts were used as an additive since Satoh's group found that a mixture of tin tetrachloride and silver trifluoroacetic acid was improving their yields by 100% when they tried to open a ketal.[73] In our case, adding silver salts didn't have any significant benefit (entries 15–17). Adding a diol (entry 14) for coordination with the tin didn't improve the yield. To assess the possible influence of water in the reaction, molecular sieves were used to remove any traces, but no significant change was observed (entry 19). Switching to toluene as a solvent didn't make any significant difference. Overman found that in some cases, the presence of a proton scavenger improved the yields by preventing protic degradation pathways.[23, 42b] To our surprise, the addition of 2,6-di-*tert*-butyl-4-methylpyridine (DTBMP)[74] completely shut down the reaction (entries 18 and 24). This seems to indicate that that it is a Brønsted acid that is catalyzing the reaction. Overman's group also observed that in some cases, both tin tetrachloride and sulfonic acids can catalyze the Prins-pinacol reaction, but he never determined if it was a protic acid present in the tin tetrachloride that was promoting the rearrangement.[3, 26, 38, 42d] Brønsted acids were then assessed. HCl, the protic acid that is suspected to be present in the tin tetrachloride, gave some conversion, which confirms that a Brønsted acid can catalyze the Prins-pinacol rearrangement of **2.29** (entry 25). The low yield is probably due to the presence of water in the reaction mixture. Among the other Brønsted acids that were tried, it was methanesulfonic acid that proved to be the best, having a yield close to the one obtained with tin tetrachloride.

Table 2.1 – Optimization of the Reaction Conditions

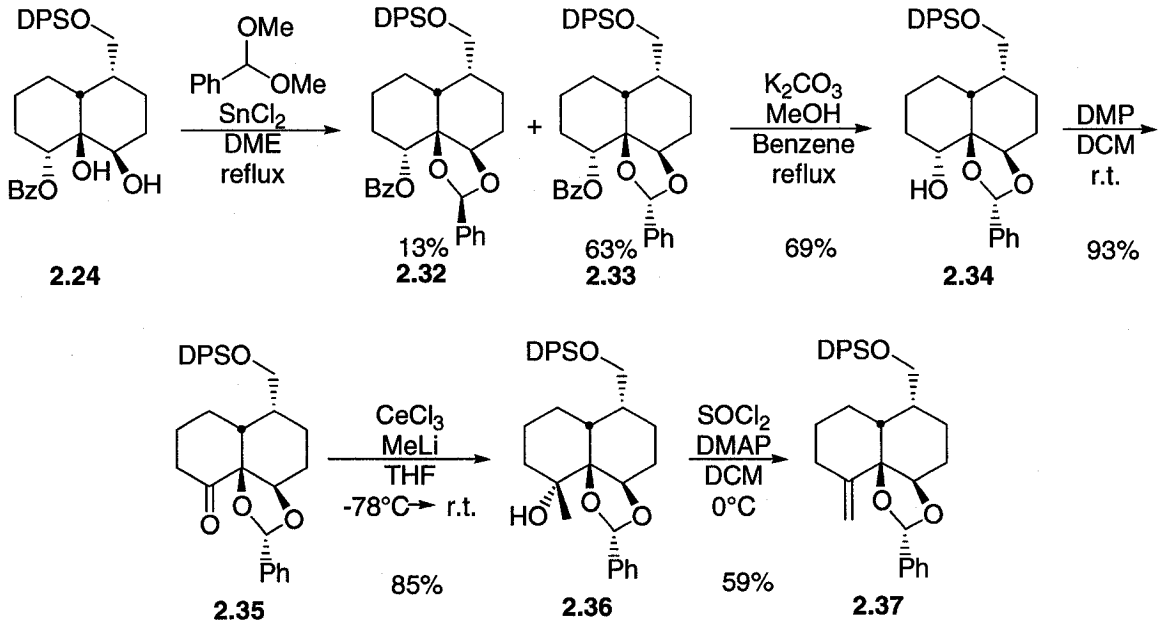


2.29 **2.30** **2.31**

Entry	Acid	Additive	Temperature (°C)	Isolated Yield of **2.30** (%)	Isolated Yield of **2.31** (%)
1	BF_3-OEt_2		r.t.	37	63
2	$BiCl_3$		r.t.	85	
3	$Bi(OTf)_3$		r.t.	61	
4	$CeCl_3$		r.t.	no reaction	
5	$Cu(OTf)_2$		r.t	78	
6	$GaCl_3$		-78	75	
7	$InCl_3$		r.t.	no reaction	
8	Me_2AlCl		r.t.	73	
9	$MeAlCl_2$		r.t.	42	
10	$MgBr_2$-OEt_2		r.t.	no reaction	
11	$MgBr_2$-OEt_2	AgOTf	r.t.	50	36
12	$SnCl_2$		r.t.	40	43
13	$SnCl_4$		-78	86	
14	$SnCl_4$	2,2'-biphenol	-78	63	
15	$SnCl_4$	$AgOCl_4$	r.t.	88	
16	$SnCl_4$	AgOTf	-78	87	
17	$SnCl_4$	AgOTfa	-78	89	
18	$SnCl_4$	DTBMP	r.t.	no reaction	
19	$SnCl_4$	MS 4 Å	-78	71	
20	$SnCl_4$ in toluene		-78	81	
21	$PdCl_2(PhCN)_2$		r.t.	no reaction	
22	$TiCl_4$		0	39	
23	TMSOTf		-78	62	
24	TMSOTf	DTBMP	r.t.	no reaction	
25	HCl		r.t.	48	26
26	$MeSO_3H$		r.t.	70	
27	PTSA		r.t.	no reaction	
28	TfOH in MeCN		-20	25	

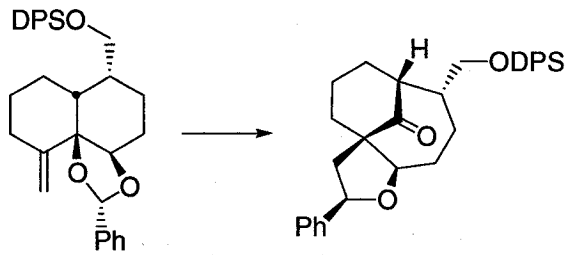
The Diol Protecting Group Effect on the Rearrangement

It was also known from the literature that a less substituted protecting group, such an acetal, can improve or decrease the efficiency of the Prins-pinacol rearrangement compared to a ketal.[4b] There are also some examples were a benzylidene acetal improved the yield of the rearrangement.[4a, 57] Other protecting groups than acetonide were then explored, starting by using the benzylidenic group (Scheme 2.4). The benzylidene acetal formation was performed in 63%, using tin dichloride in dimethoxyethane to afford **2.33**,[75] and 13% of the other epimer **2.32**[75] was isolated separately.[76] The Prins-pinacol precursor **2.37** was obtained through the same sequence as with the acetonide derivative in modest to good yields. The benzylidene acetal initially seemed to make the Prins-pinacol rearrangement more facile since some formation of **2.38** [75, 77] was observed upon standing in deuterated chloroform (5% conversion after 3 hours at room temperature). Despite this promising observation, the yields obtained for the Prins-pinacol rearrangement of **2.37** were a bit lower than with the acetonide, as depicted in Table 2.2. Interestingly enough, now it is in toluene that the reaction is more efficient and the yield obtained with triflic acid is greatly increased compared to the acetonide analogue. It was also demonstrated for the first time that the Prins-pinacol rearrangement can occur with catalytic amounts of Brønsted acid. A reaction, run in presence of a hindered base (DTBMP) gave no reaction, which demonstrates, again that a protic acid is required for the transformation. The benzylidene acetal seems to facilitate the oxocarbenium formation by producing less steric interactions, which should aids the Prins reaction to occur but it seems that it also help other decomposition pathways. The advantage of using a benzylidene group is that the benzylic C-O bond in **2.38** can be cleaved by hydrogenolysis or oxidative cleavage of a benzyl ether with dimethyldioxirane.



Scheme 2.4 – Generation of the Prins-Pinacol Precursor with a Benzylidene Acetal as a Protecting Group

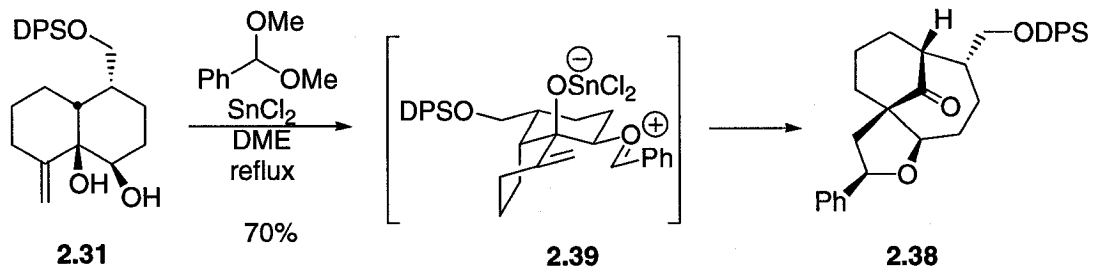
Table 2.2 – Prins-Pinacol Rearrangement of **2.37**



Entry	Acid	Equivalents of Acid	Solvent	Temperature (°C)	Yield (%)
1	$SnCl_4$	1	DCM	-78	77
2	$SnCl_4$	1	Toluene	-78	80
3	TfOH	0.05	MeCN	0	74

Direct protection of **2.31** failed since it provided directly the Prins-pinacol product **2.38**. This reaction confirms that a Prins-pinacol condensation can be performed with our type of substrates. The stereochemistry of the benzylic carbon comes from the Prins cyclization

occuring through intermediate **2.39**, which has the more stable E oxocarbenium ion, placing the phenyl in a pseudoequatorial position. All the Prins-pinacol products are easily recognized since protons H_1 and H_6 are deshielded by a diamagnetic anisotropy effect of the bridged head carbonyl. Therefore, H_1 appears as a doublet or a triplet around 3 ppm and H_2 generally appears around 1.5 ppm (Figure 2.3). This is very helpful for the determination of the stereochemistry, as it is shown in Figure 2.4.



2.31 **2.39** **2.38**

Scheme 2.5 – Prins-Pinacol Condensation

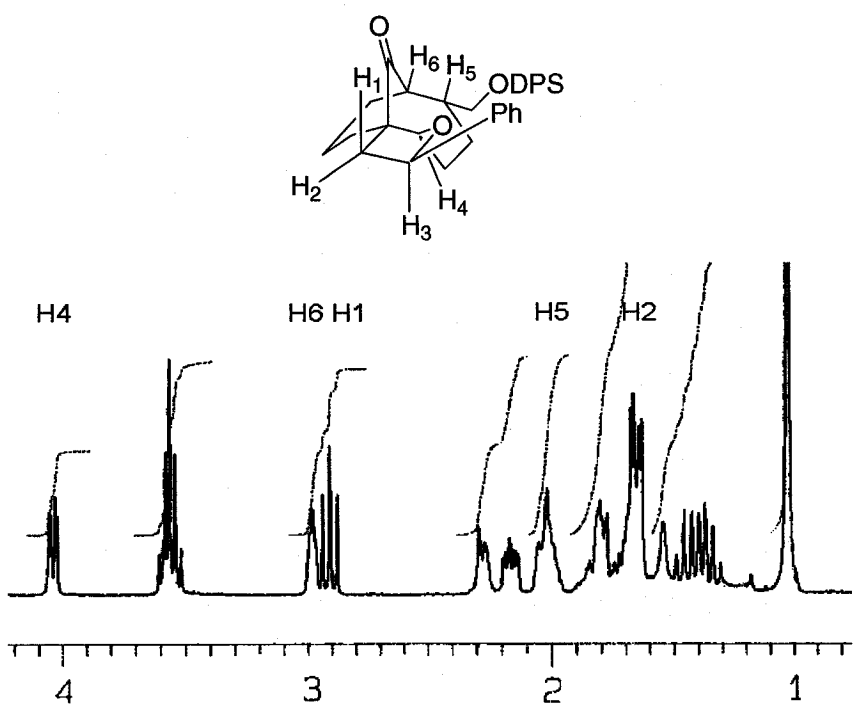


Figure 2.3 – Diamagnetic Anisotropic Effect on H_1

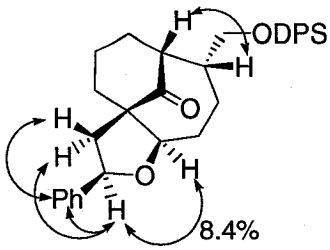
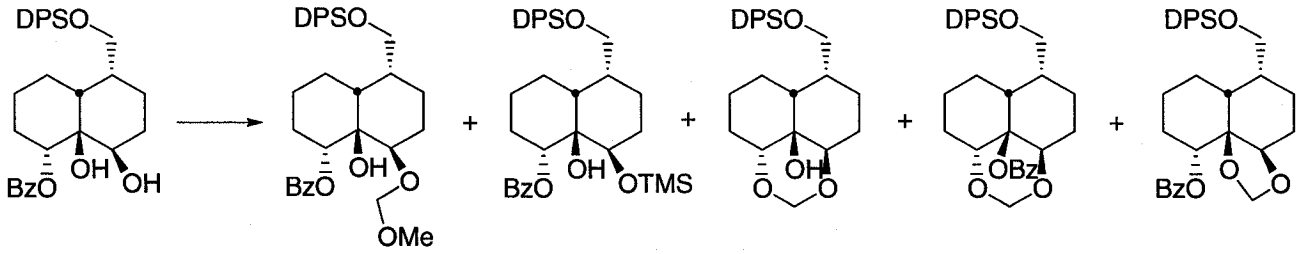


Figure 2.4 – Structure Elucidation of **2.38** *by 2D NMR*[77] *and NOE Experiments*

Another interesting protecting group to install would be a methylidene since it's going to provide a methylene group at the C12 position instead of a *gem*-dimethyl or a phenyl group (Scheme 2.6). Only one example of such a transformation was found in the literature, and their results seem to indicate that this transformation was possible.[22] The formation of the methylene acetal was found to be more difficult than expected. The presence of the benzoyl protecting group prevents the use of any basic conditions (entries 1 and 2[78]), since it cleaves the ester and forms the thermodynamic favored methylene acetal **2.42**. The use of *para*-toluene sulfonic acid seems to give a MOM protection of the secondary alcohol (**2.40**, entry 3), and the use of trimethylsilyl triflate in presence of a hindered base[79] seems to give the TMS protected product **2.41** (entry 4), although these compounds were not fully characterized. The use of trimethylsilyl triflate alone or with lithium bromide (entries 5 and 6) affords the desired product **2.44** in low yields. The best conditions found for this transformation are the ones used for the formation of the benzylidene acetal, which is the use of tin dichloride in refluxing dimethoxyethane, to afford product **2.44** in modest yields (entry 7). Interestingly enough, migration of the benzoyl group affords **2.43** along with **2.44**.[77]

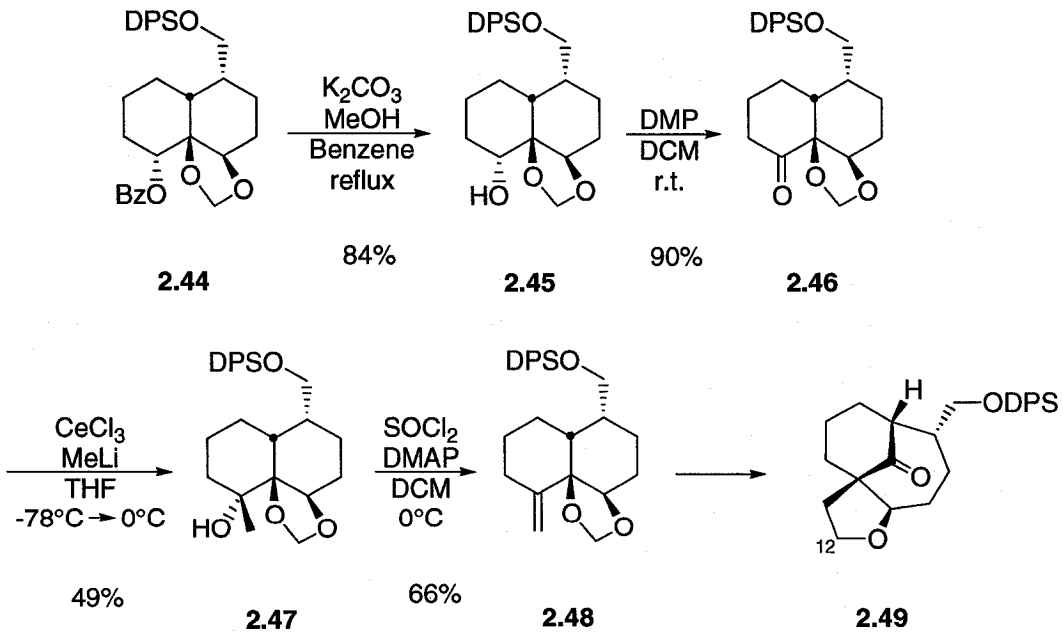
The same sequence than the one use for the acetonide derivative was followed in order to get to the Prins-pinacol precursor. Unfortunately, the rearrangement of **2.48** was found to occur only with low yields in the presence of tin tetrachloride, and it decomposed in presence of triflic acid. This is probably due to the fact that the acetal opening is too high energy of a process since no stabilization of the positive charge of the oxocarbenium ion is present. In the case of the acetonide, hyperconjugation from the two methyls was stabilizing the positive charge but the methylene acetal cannot provide this stabilization. Therefore, harsher conditions are required in order to provoke the acetal opening which is required for the Prins cyclization to occur, and this leads to decomposition of **2.48**.

Table 2.3 – Methylene Acetal Formation



2.24 **2.40** **2.41** **2.42** **2.43** **2.44**

Entry	Methylene Source	Acid / Base	Additive	Solvent	Temperature (°C)	Product	Yield (%)
1	CH_2I_2	NaH		DMF	0 → r.t.	**2.42**	28
2	CH_2Br_2	KOH		CH_2Br_2	r.t.	**2.42**	12
3	$CH_2(OMe)_2$	PTSA	LiBr	DCM	r.t.	**2.40**	11
4	$CH_2(OMe)_2$	TMSOTf	DTBMP	DCM	-78 → r.t.	**2.41**	80
5	$CH_2(OMe)_2$	TMSOTf		DCM	-78 → r.t.	**2.44**	5
6	$CH_2(OMe)_2$	TMSOTf	LiBr	DCM	-78 → r.t.	**2.44**	17
7	$CH_2(OMe)_2$	$SnCl_2$		DME	reflux	**2.44**	51
						2.43	20



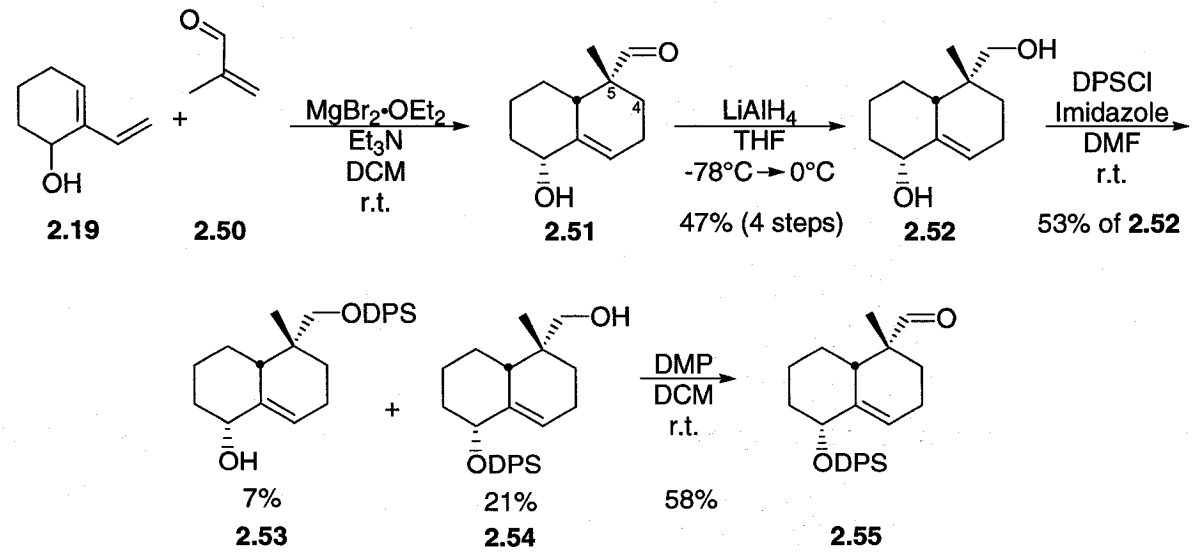
Scheme 2.6 – Generation of the Prins-Pinacol Precursor with a Methylene Acetal as a Protecting Group

Table 2.4 – Prins-Pinacol Rearrangement of ***2.48***

Entry	Acid	Equivalents of Acid	Solvent	Temperature (°C)	Yield (%)
1	$SnCl_4$	5	DCM	-78 → r.t	19
2	$SnCl_4$	2	Toluene	-78 → r.t	26
3	TfOH	1	MeCN	0	decomp.

The Effect of Substitution at C5

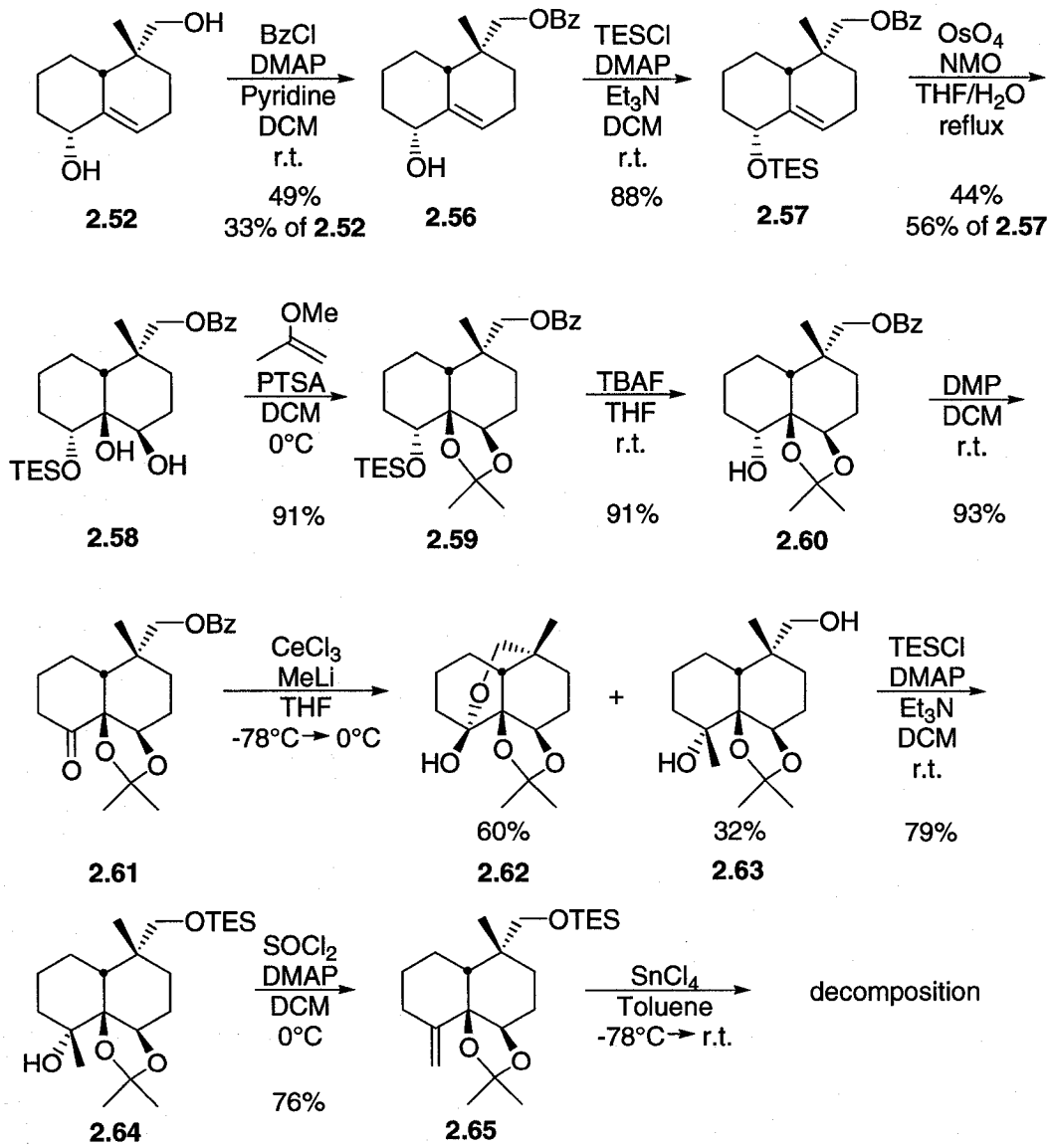
To show the versatility of this synthetic sequence, more functionalities were added at the C4 and C5 positions. Since the stereochemistry of these carbons arises from the hydroxy-directed Diels-Alder reaction, it is now possible to generate new stereocenters at these positions and examine their effect on the Prins-pinacol reaction. We first start with methacrolein as a dienophile since it generates a quaternary carbon center at the C5 position (**2.51**, Scheme 2.7). The Diels-Alder product was rapidly reduced since it tends to decompose by a hemiacetal formation with the aldehyde and the secondary alcohol. Protection of the primary alcohol with a



Scheme 2.7 – First Approach for the Synthesis of the Methacrolein Derived Prins-Pinacol Precursor

big silyl group affords a mixture of protected alcohols. The new methyl at C5 caused enough steric hindrance to prevent the primary alcohol from being protected selectively. Identification of the protected alcohols was performed by a chemical test in which **2.54** was oxidized to give the characteristic aldehyde peak.

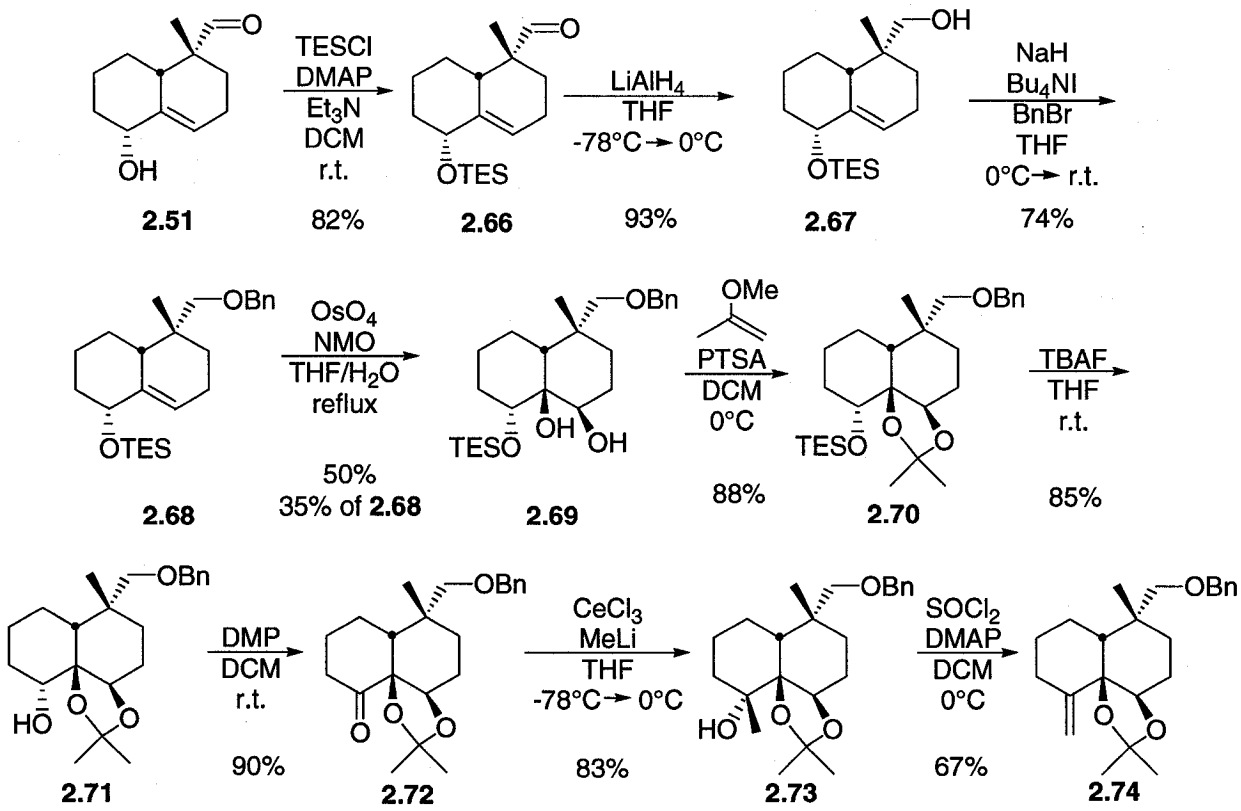
It was later found that a benzoyl group could selectively protect the primary alcohol to give **2.56** (Scheme 2.8). The secondary alcohol was then protected and the usual sequence was



Scheme 2.8 – Second Approach for the Synthesis of the Methacrolein Derived Prins-Pinacol Precursor

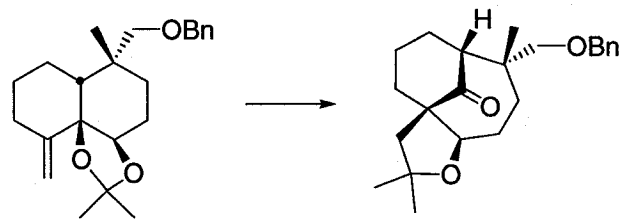
followed in order to get to the ketone **2.61**. Even though Morency already performed such an alkylation without touching the benzyl protecting group in a similar system,[71] when treating the ketone **2.61** with methyl lithium, competitive alkylation of the benzyl ester was observed which leads to the hemiketal **2.62** and the diol **2.63**. The hemiketal **2.62** results from the alkylation of the ester first whereas **2.63** results from the alkylation of the ketone first. Having little material in my possession, protection of the primary alcohol of **2.63** was performed, followed by an elimination to give the methacrolein derived Prins-pinacol precursor **2.65**. Unfortunately, when treated with tin tetrachloride in toluene, compound **2.65** only gave decomposition products.

Intrigued by this result, more Prins-pinacol precursor was required. A third route was then developed in order to prevent the problem that was occurring due to the use of a benzoyl protecting group (Scheme 2.9). The alcohol of **2.51** was first protected with a triethylsilyl protecting group and following reduction, the primary alcohol (**2.67**) was protected with a robust benzyl group.[80] The Prins-pinacol precursor **2.74** was obtained through the same sequence and again, only decomposition products were obtained using tin tetrachloride. To our surprise, the Prins-pinacol rearrangement occurs in presence of triflic acid, affording the bicyclic ketone **2.75**.[77] This example seems to demonstrate that the Prins-pinacol reactions are very substrate dependant. But how can a methyl make such a difference? If we look at the reaction intermediates in Figure 2.5, **2.76** should still be the more populated conformer. There are no obvious reasons why triflic acid would be better to help the ketal opening of **2.77** compared to tin tetrachloride. Another explanation would be to assume that the reaction goes via conformer **2.76**. Since the lone pairs on the oxygen that lead to the productive oxocarbenium ion **2.78** are well shielded by the acetonide, the alkene and the methyl at C-5, only a proton which bears a small counter anion can interact with the lone pair, assuming that only protic acids can promote this reaction in our systems. A chloride anion is smaller than a triflate anion but it is not impossible that the actual counter anion is tin pentachloride, which is much bigger than a triflate anion.[81] If the triflate anion is smaller, the proton is able reach the oxygen lone pair and the rearrangement becomes possible. The low yields obtained are probably due to opening of the ketal to give the non-productive oxocarbenium ion **2.79** and side-reactions through this intermediate are responsible for the observed degradation.



Scheme 2.9 – Third Approach for the Synthesis of the Methacrolein Derived Prins-Pinacol Precursor

Table 2.5 – Prins-Pinacol Rearrangement of **2.74**



2.74 **2.75**

Entry	Acid	Equivalents of Acid	Solvent	Temperature (°C)	Yield (%)
1	$SnCl_4$	1	DCM	-78 → 0	decomp.
2	$SnCl_4$	1	Toluene	-78 → r.t	decomp.
3	TfOH	2	MeCN	-40 → 0	63

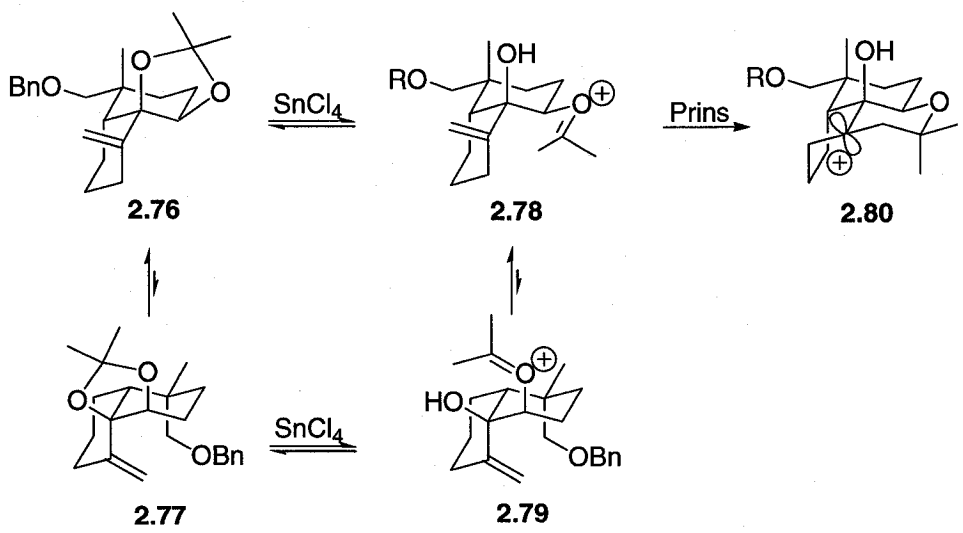
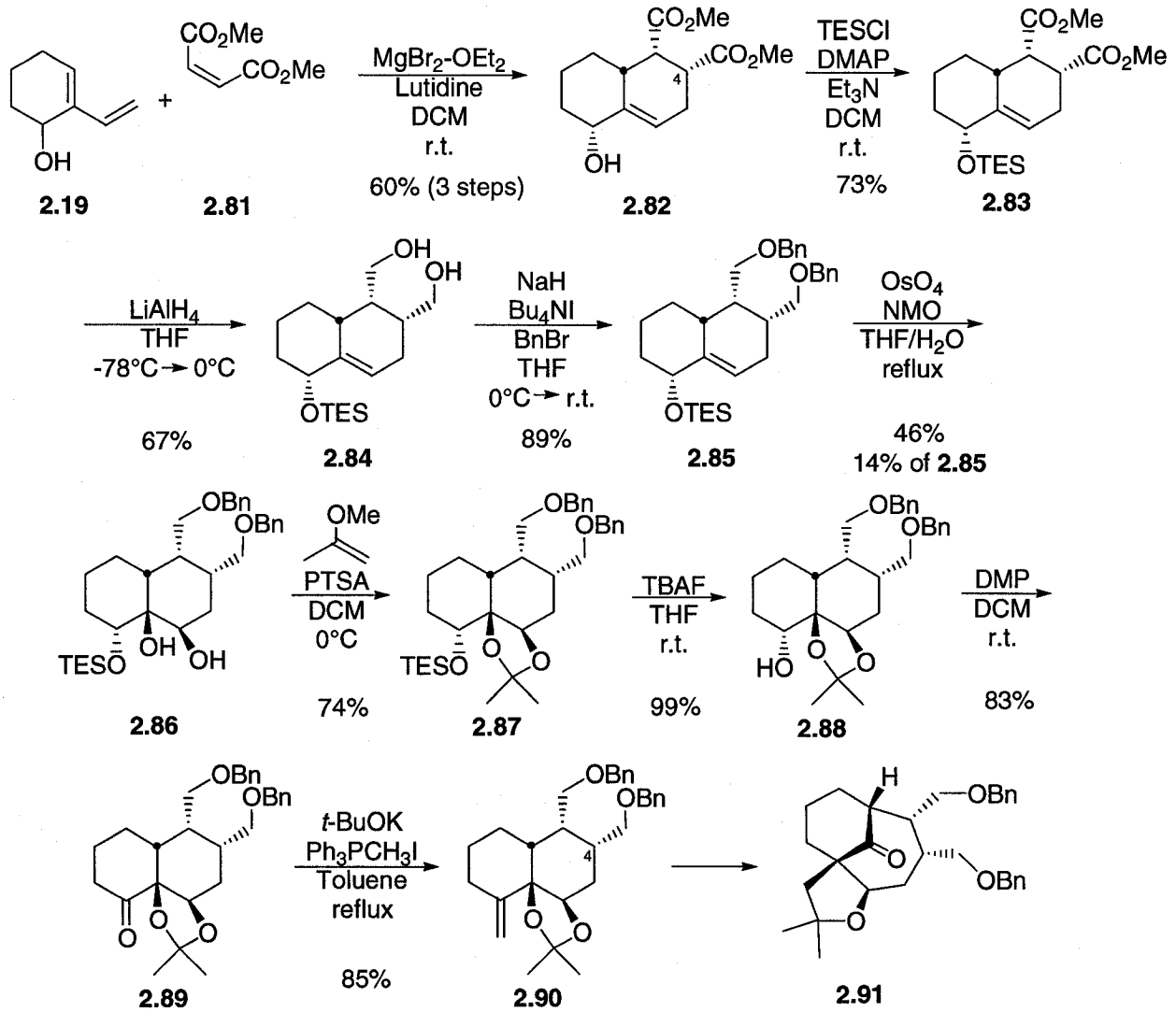


Figure 2.5 – Opening of the Ketal in the Methacrolein Derived Prins-Pinacol Precursor

The Effect of Substitution at C4

The effect of a stereocenter at the C4 position was investigated by installing the C4 stereocentre using a hydroxy-directed Diels-Alder reaction with dimethyl maleate as the dienophile (Scheme 2.10). The same sequence as used for the previous systems was followed to afford the Prins-pinacol precursor **2.90**[77] in good yields, except for the dihydroxylation which always seems to be problematic. Performing the Prins-pinacol rearrangement using 3 different set of conditions gave **2.91**[77] in similar yields as those obtained with the substrate with no substituent at C4. As demonstrated in Figure 2.6, the slightly lower yields and the higher temperature required can explained by the fact that **2.92** is less favored in the equilibrium with **2.93** since now it experience one *syn*-pentane interaction and **2.95** can potentially lead to degradation pathways. Another explanation can be that the 1,3-diaxial interaction in **2.94** can rise the energy of the transition state during the pinacol rearrangement since as the bond C1-C2 migrates, bond *a* and bond *b* get much closer in space.



Scheme 2.10 – Synthesis of the Dimethyl Maleate Derived Prins-Pinacol Precursor

*Table 2.6 – Prins-Pinacol Rearrangement of **2.90***

Entry	Acid	Equivalents of Acid	Solvent	Temperature (°C)	Yield (%)
1	$SnCl_4$	2	DCM	-78 → -20	81
2	$SnCl_4$	2	Toluene	-78 → -20	62
3	TfOH	1	MeCN	-40	58

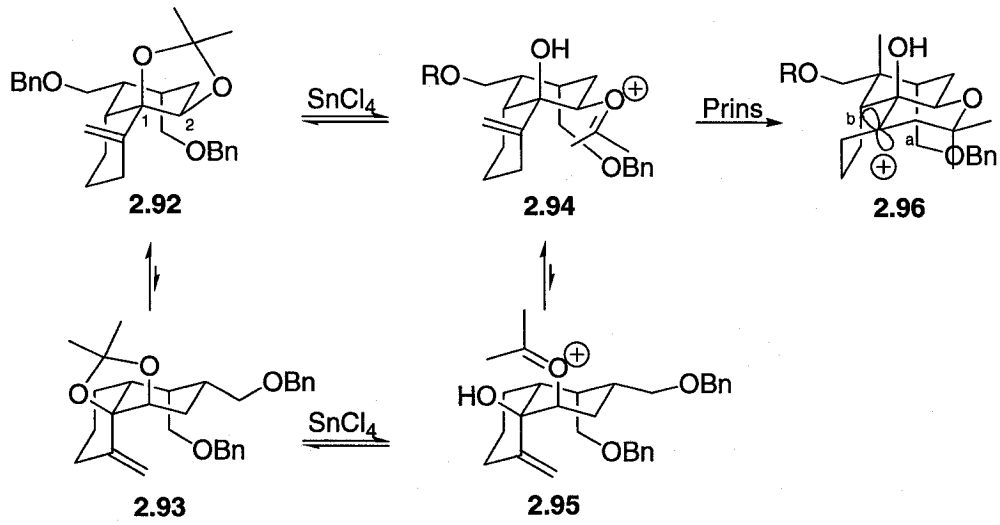
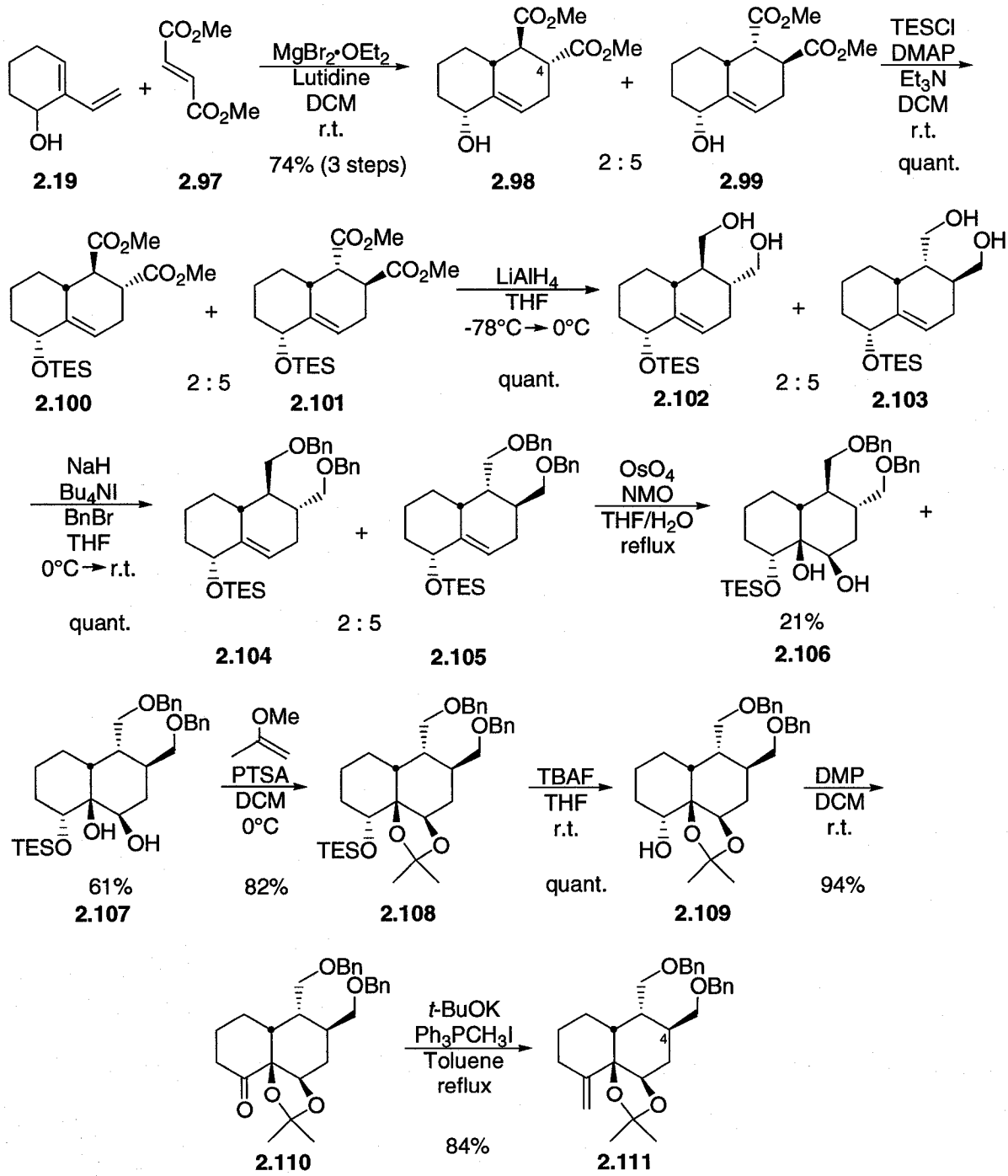


Figure 2.6 – Effect of the C4 Substituent on the Prins Cyclization

To assess the importance of the equilibrium between **2.92** and **2.93**, a match and mismatch comparison needed to be done. This could be done by preparing a dimethyl fumarate derived Prins-pinacol precursor (Scheme 2.11). A mixture of 2 : 5 between the *exo* and *endo* products was obtained from the hydroxyl-directed Diels-Alder reaction. This inseparable mixture of **2.98** and **2.99** was then submitted to the usual conditions and the two diastereoisomers were separated by flash chromatography after the dihydroxylation. The diastereoisomer **2.107** was then further modified to generate the Prins-pinacol precursor **2.111**[77] and submitting this compound to tin tetrachloride and triflic acid afforded the bicyclic ketone **2.112**[77] in yields comparable to those obtained from **2.90**. We can now conclude that the efficiency of the Prins-pinacol reaction is more dependent on the substitution at C5 rather then the substitution at C4.

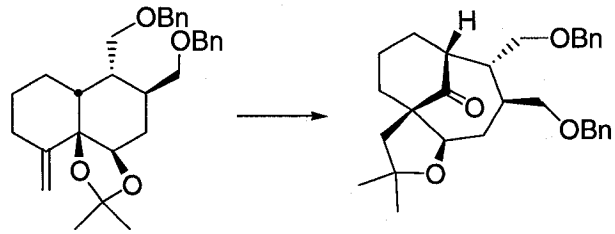
The other diastereoisomer (**2.106**) was also used for the generation of a Prins-pinacol precursor (**2.116**, Scheme 2.12).[77] To our surprise, the Prins-pinacol rearrangement product was obtained in better yields than its diastereoisomer **2.111**, although higher temperatures were required. This result was surprising since we would expect the equilibrium to favor conformers **2.119** and **2.121** over **2.118** and **2.120** since now two *syn*-pentane interactions are found in conformers **2.118** and **2.120**, and none are found in conformers **2.119** and **2.121** (Figure 2.7). Only conformer **2.120** can lead to the product, therefore these results seem to be a proof that the equilibrium between those conformers does exist. The higher temperature required for the transformation is probably due to the fact that higher temperatures increase the population of

conformer **2.120** which accelerates the reaction. We postulate that the higher yields obtained can be a result of the presence of an oxygen (O1) in proximity to one side of the acetonide in



Scheme 2.11 – Synthesis of the Dimethyl Fumarate Derived Prins-Pinacol Precursors

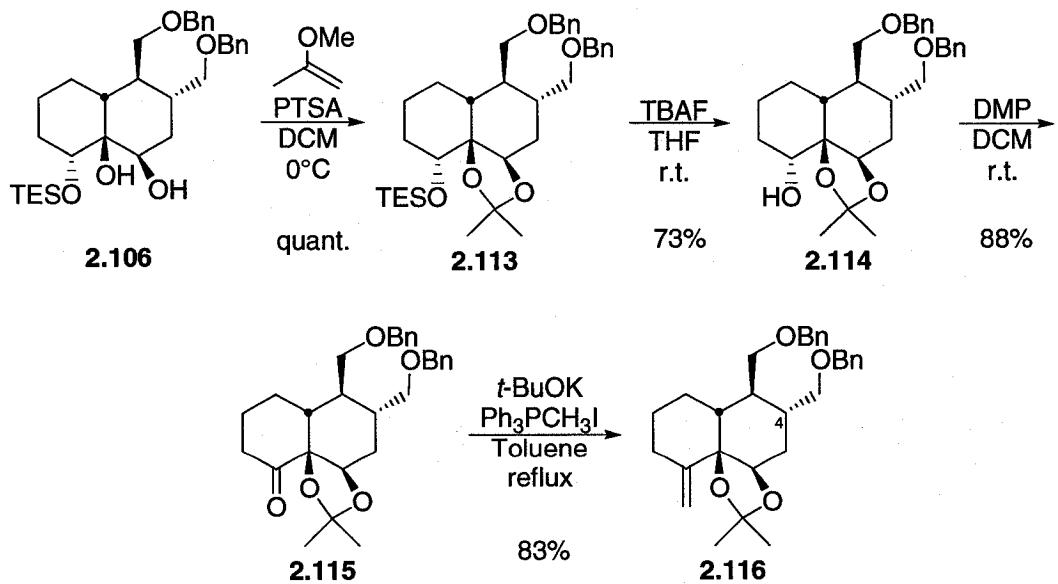
Table 2.7 – Prins-Pinacol Rearrangement of ***2.111***



2.111 **2.112**

Entry	Acid	Equivalents of Acid	Solvent	Temperature (°C)	Yield (%)
1	$SnCl_4$	2	DCM	-78 → -20	85
2	$SnCl_4$	2	Toluene	-78 → -20	67
3	TfOH	1	MeCN	-40	71

conformer **2.118**. This oxygen can bring the Lewis or Brønsted acid in close proximity to favors the opening of the ketal to give the productive conformer **2.120**. The production of **2.123** is minimized and all the degradation pathways from this intermediate are therefore avoided.

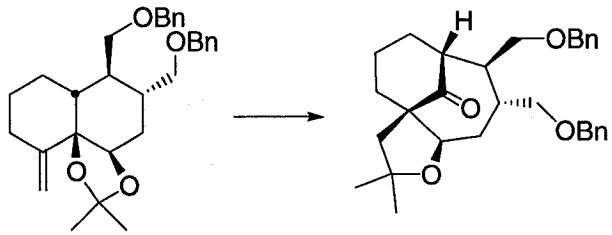


2.106 **2.113** **2.114**

2.115 **2.116**

Scheme 2.12 – Synthesis of the Second Dimethyl Fumarate Derived Prins-Pinacol Precursor

Table 2.8 – Prins-Pinacol Rearrangement of ***2.116***



2.117 **2.118**

Entry	Acid	Equivalents of Acid	Solvent	Temperature (°C)	Yield (%)
1	$SnCl_4$	2	DCM	-78 → r.t.	90
2	$SnCl_4$	2	Toluene	-78 → r.t.	91
3	TfOH	1.5	MeCN	-40 → r.t.	60

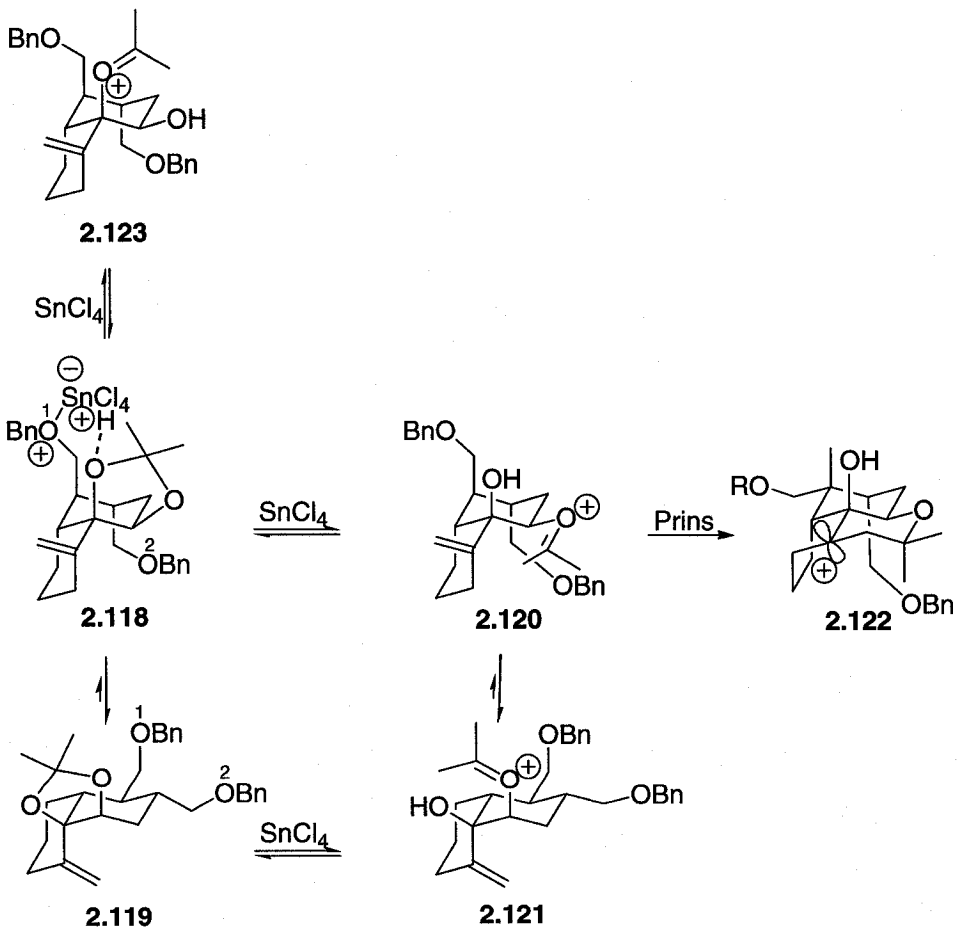


Figure 2.7 – Reactive Intermediates of ***2.116***

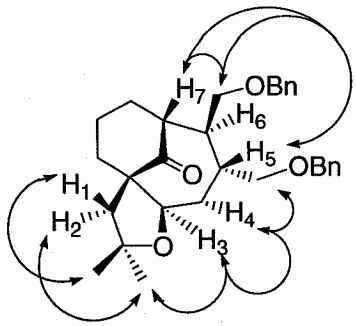
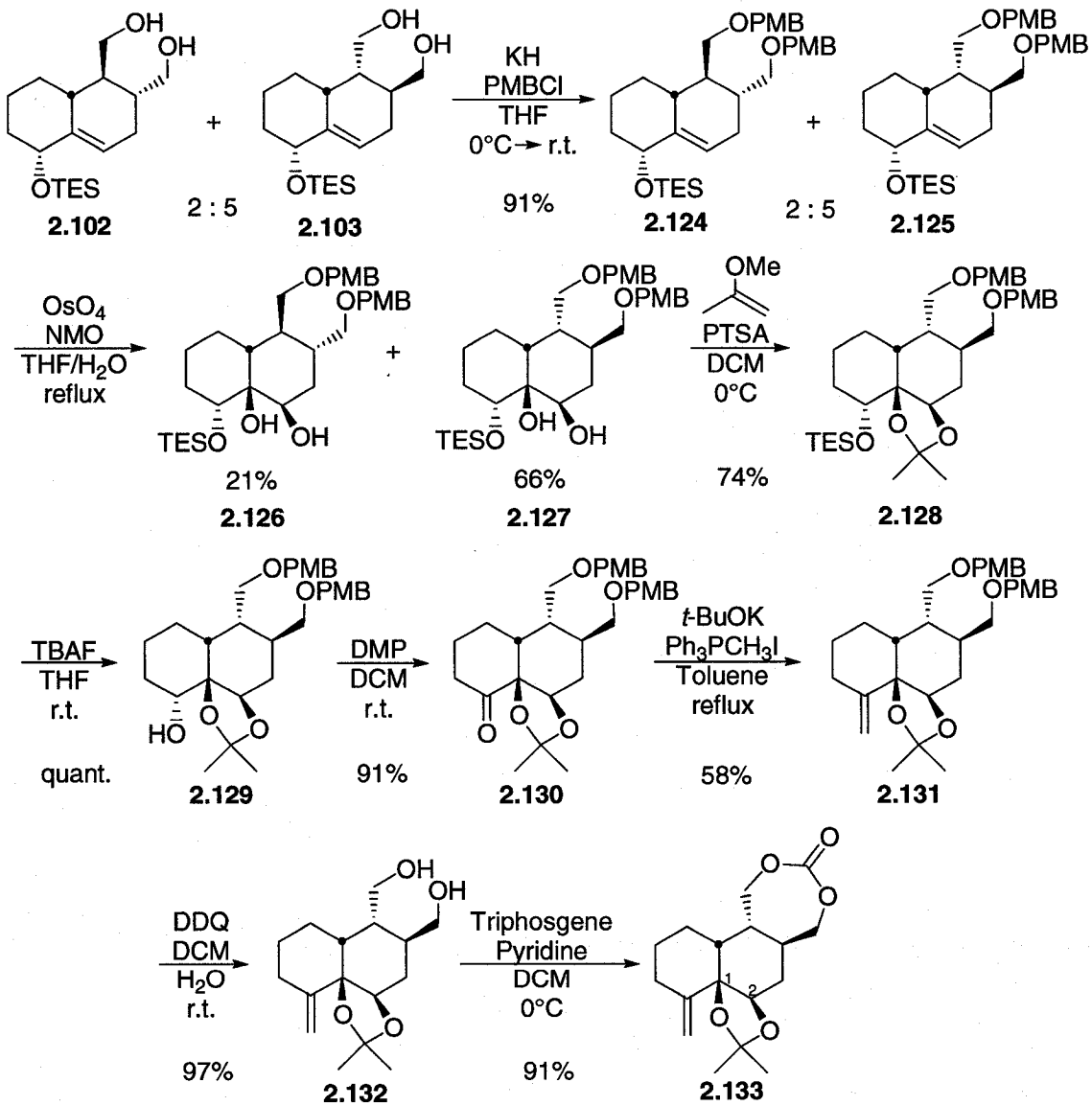


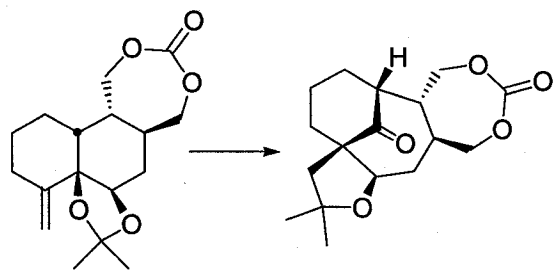
Figure 2.8 – Structure Elucidation of ***2.117*** *by 2D NMR Experiments*[77]



Scheme 2.13 – Synthesis of Conformationally Locked Prins-Pinacol Precursors

A way to definitively demonstrate that the equilibrium between the conformers exists would be to join the two side chains to form a rigid *trans*-fused bicyclic molecule. Seeing the potential problem of deprotecting of the benzyl groups, a PMB group was used for the protection of the primary alcohols of **2.101** and **2.102** (Scheme 2.13). Again, the same sequence was followed to obtain the alkene **2.131**, which was deprotected with DDQ and treated with triphosgene in order to obtain the cyclic carbonate **2.133**. Treating this molecule under Prins-pinacol conditions gave the rearranged compound **2.134** in yields comparable to those obtained in the non-cyclic side chains. This seems to indicate that the equilibrium wasn't affecting the efficiency of the Prins-pinacol rearrangement.

Table 2.9 – Prins-Pinacol Rearrangement of ***2.133***



2.133 **2.134**

Entry	Acid	Equivalents of Acid	Solvent	Temperature (°C)	Yield (%)
1	$SnCl_4$	2	DCM	-78 → -20	74
2	$SnCl_4$	3	Toluene	-78 → 0	54
3	TfOH	1	MeCN	-40	66

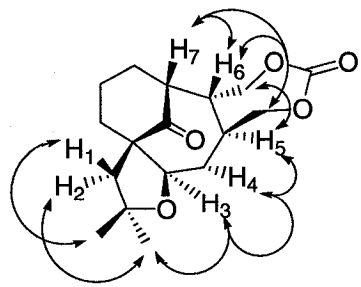
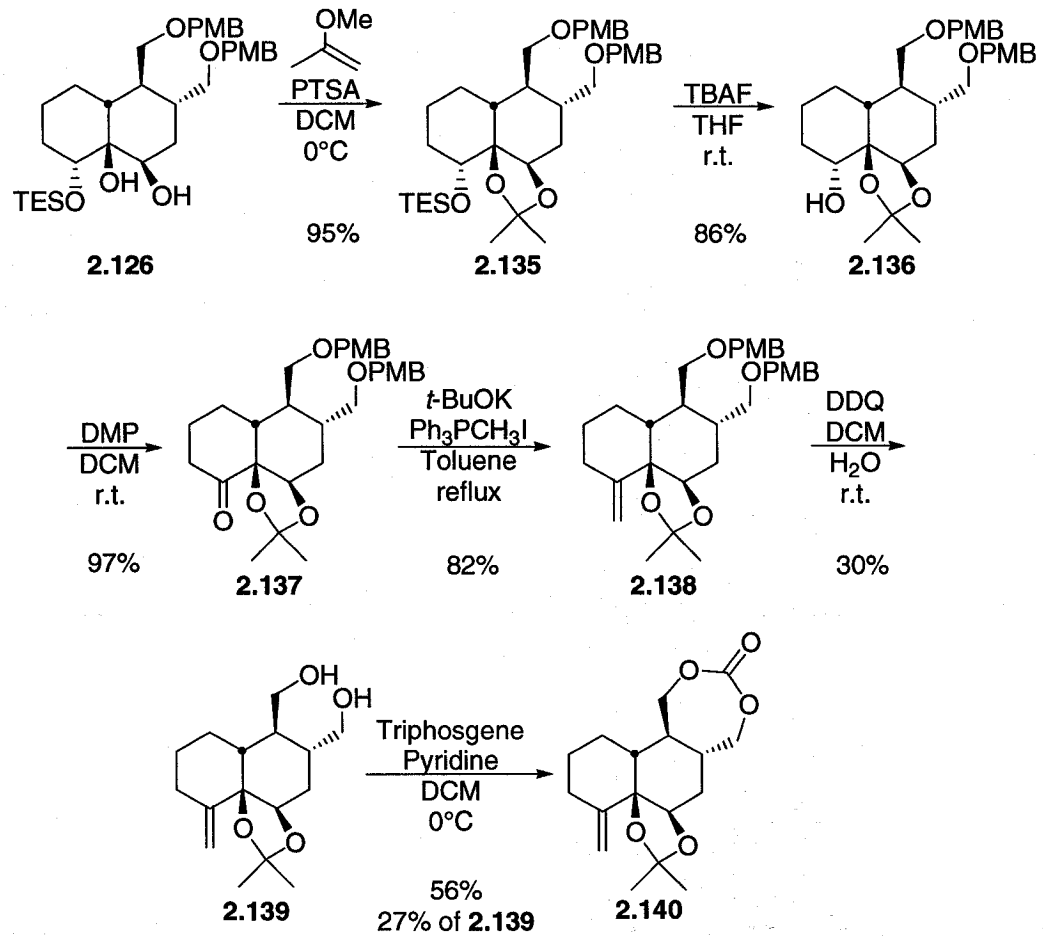


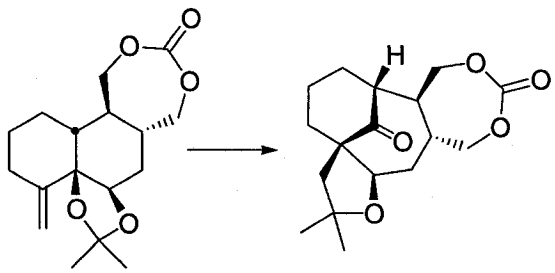
Figure 2.9 – Structure Elucidation of ***2.134*** *by 2D NMR Experiments*[77]

The same experiments were performed with the other diastereoisomer (Scheme 2.14). When **2.140** was treated with tin tetrachloride in dichloromethane, no reaction was observed. The same results were observed in toluene and with triflic acid so they were left to react for a longer time which eventually led to decomposition. These results suggest that **2.143** needs to pass through intermediate **2.144** in order for the Prins-cyclization to occur. This also confirms that **2.119** is in equilibrium with **2.118** or **2.121** is in equilibrium with **2.120** since **2.116** was able to undergo the Prins-pinacol rearrangement.



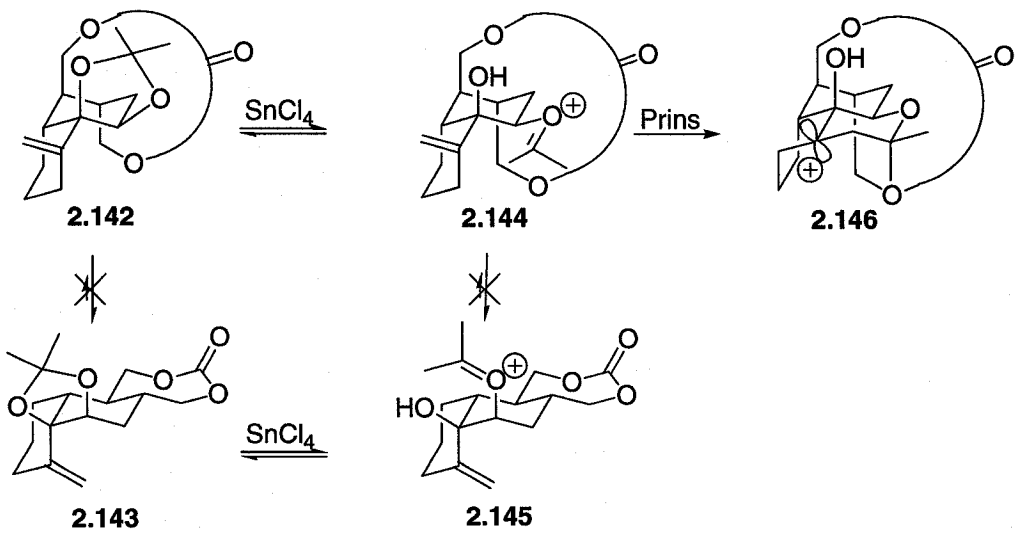
Scheme 2.14 – Synthesis of the Second Conformationally Locked Prins-Pinacol Precursor

Table 2.10 – Prins-Pinacol Rearrangement of ***2.140***



2.140 **2.141**

Entry	Acid	Equivalents of Acid	Solvent	Temperature (°C)	Yield (%)
1	$SnCl_4$	2	DCM	-78 → r.t.	no reaction
2	$SnCl_4$	2	Toluene	-78 → r.t.	decomp.
3	TfOH	2	MeCN	-40 → r.t.	decomp.



2.142 **2.144** **2.146**

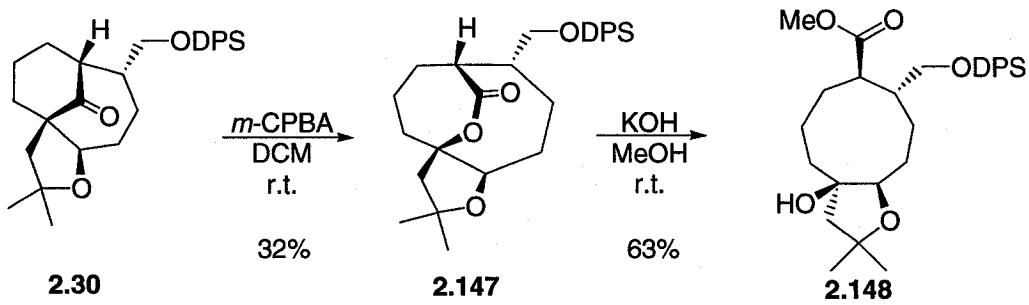
2.143 **2.145**

Figure 2.10 – Unreactive and Conformationally Locked ***2.140***

Conclusion

For the first time, a variety of *cis*-fused bicyclic bridgehead ketones were generated using a Brønsted acid mediated Prins-pinacol rearrangement. This high yielding and versatile synthetic

route was used to generate a variety of bicyclo[4.3.1]decanones where the stereocenters are generated using a hydroxyl-directed Diels-Alder reaction and a Prins-pinacol rearrangement. Benzylidene acetals seem to facilitate the reaction but they do not increase the yields whereas methylene acetals decrease significantly the yields. Substitution at the C4 position seems to have no effect on the efficiency of the reaction whereas substitution at the C5 position seems to cause some steric problems or force the molecule to undergo a conformational change in order to allow the Prins cyclization to occur. The stereocenters generated with this methodology can be used for the generation of functionalized 9-membered rings, as shown in Scheme 2.15.[82] The bicyclic bridgehead ketone **2.30** is first treated with 3-chloroperoxybenzoic acid, followed by a transesterification to afford the functionalized 9-membered ring **2.148**, which the relative stereochemistry was elucidated with COSY, NOESY and HMQC NMR experiments (Figure 2.11).



Scheme 2.15 – Synthesis of Functionalized 9-Membered Rings

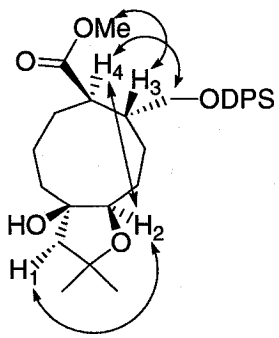


*Figure 2.11 – Structure Elucidation of **2.148** by 2D NMR Experiments*[77]

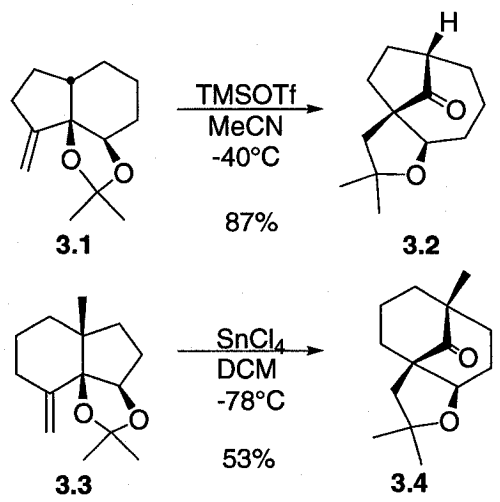
3

Generation of Bicyclic Ketones of Various Ring Sizes

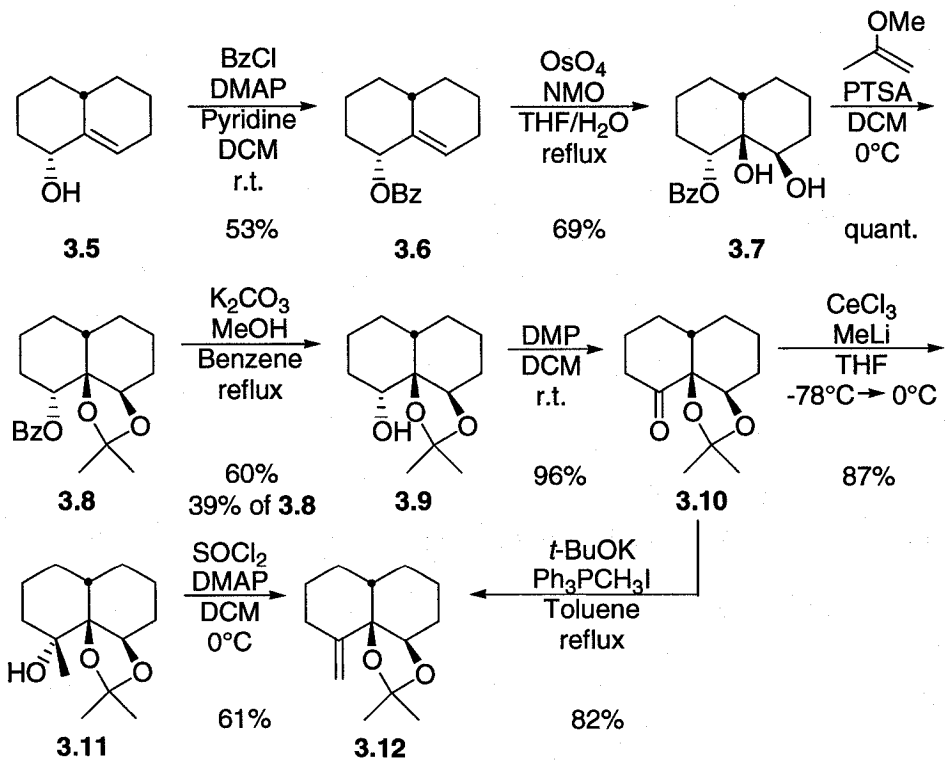
Bicyclo[4.3.1]decanones

As mentioned earlier, general methods to generate bicyclic ketones varying the two ring sizes were inexistent before our laboratory developed the Prins-pinacol synthesis of these molecules. Scheme 3.1 shows examples by Mélina Girardin and Maxime Riou from our laboratory who developed the synthesis of bicyclo[4.2.1]nonanones (**3.2**) and bicyclo[3.3.1]nonanones (**3.4**) respectively in fair to good yields.[57] En route to generating a substrate that can be compared to their substrates and to assess the importance of the C5 substituent, an unfunctionalized decalin was generated (Scheme 3.2). The allylic alcohol **3.5**, which can be obtained from literature procedures in four steps from cyclohexenone,[83] is first protected with a benzoyl protecting group. The same synthetic route as before was used to obtain compound **3.12**, which was treated with a variety of Prins-pinacol rearrangement conditions in order to generate the bicyclic ketone **3.13**.[77] Table 3.1 shows that a general yield decrease was observed compared to C5 substituted analogue (**2.29**), which is an intriguing result. The absence of the C5 substituent puts the two conformers **3.14** and **3.15** in equilibrium since they experience relatively the same steric interactions (Figure 3.1). Conformer **3.15** should even be favored since it diminishes the steric interactions between the alkene and the methyl. Experiments with the second dimethyl fumarate Prins-pinacol precursor **2.116** seems to tell us that this equilibrium was

not a problem for the Prins-pinacol reaction. The Prins-pinacol rearrangement of **3.12** seems to demonstrate that this equilibrium is responsible for the lower yields obtained, probably by degradation of intermediates **3.15** and **3.17**, and that the good yields obtained in the case of **2.116** can be attributed to the ability of the side chain to bring a Lewis or a Brønsted acid in proximity to the correct oxygen of the acetal.

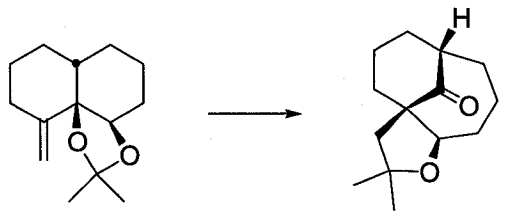


Scheme 3.1 – Synthesis of Bicyclo[m.n.1]nonanones from our Group



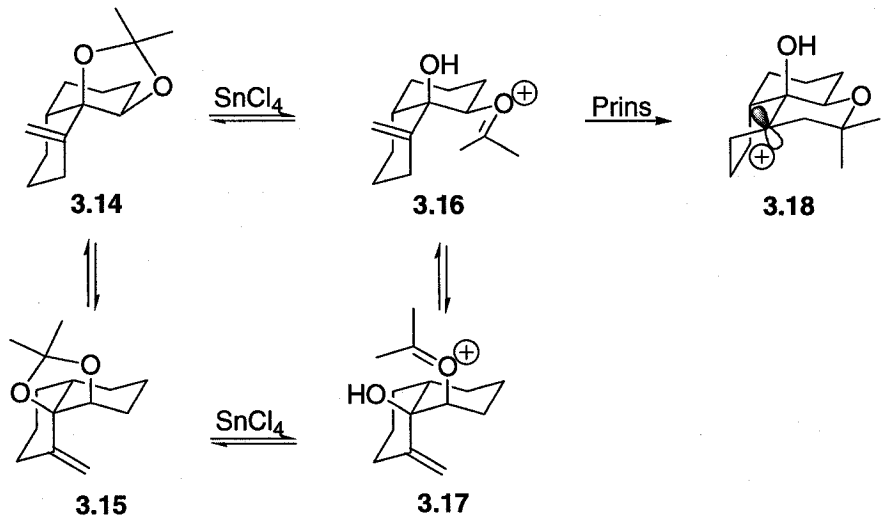
Scheme 3.2 – Synthesis of the Unfunctionalized Prins-Pinacol Precursor

Table 3.1 – Prins-Pinacol Rearrangement of ***3.12***



3.12 **3.13**

Entry	Acid	Equivalents of Acid	Solvent	Temperature (°C)	Yield (%)
1	$BiCl_3$	1	DCM	r.t.	34
2	$SnCl_4$	1	DCM	-78	61
3	$SnCl_4$	1	Toluene	-78	62
4	$SnCl_4$	2	PhCl	-78 → r.t.	37
5	$MeSO_3H$	2	DCM	-78 → r.t.	67
6	TfOH	1	MeCN	-40 → -20	49



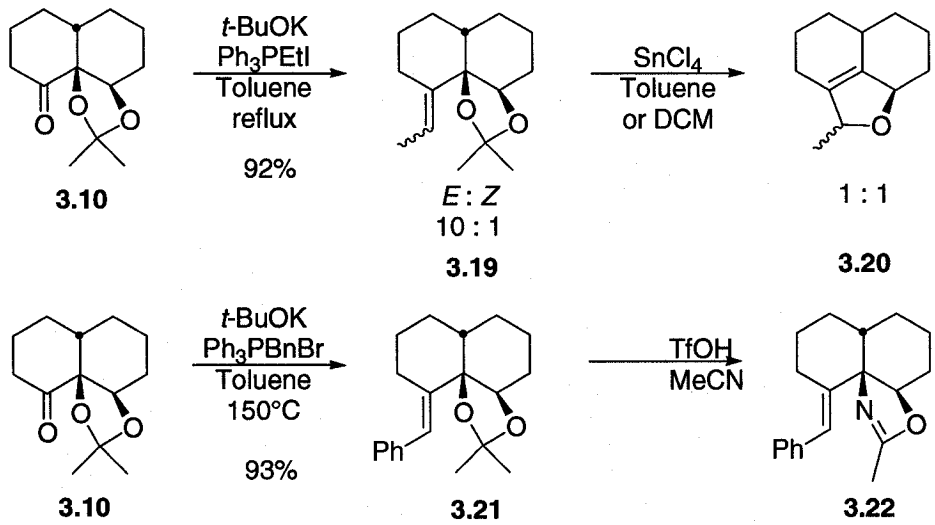
3.14 **3.16** **3.18**

3.15 **3.17**

Figure 3.1 – Reactive Intermediates for the Prins Cyclization of ***3.12***

To assess the influence of the steric and electronic properties of the alkene on the Prins-pinacol rearrangement, compounds **3.19**[77] and **3.21**[77] were generated (Scheme 3.3). In both cases, the Prins cyclization does not occur and other cationic reactions occur. In fact, Overman already observed that when C11 and C12 are highly substituted, allyl cation formation became

competitive with the Prins cyclization, affording unwanted byproducts.[4, 20a] Both compounds **3.19** and **3.21** generate allyl cation **3.26** by the elimination of acetone since steric effects lower the Prins cyclization rate (Figure 3.2). In tin tetrachloride, when R is a methyl, the dihydrofuran **3.20**[77] is formed, and when R is a phenyl decomposition was observed with trace amounts of what could be dihydrofuran formation. In triflic acid, when R is a phenyl, acetonitrile is incorporated to generate the dihydrooxazole **3.22**.[77]



Scheme 3.3 – Synthesis of Prins-Pinacol Precursors with Substituted Alkenes

*Table 3.2 – Prins-Pinacol Rearrangement of **3.19** and **3.21***

Entry	R	Acid	Equivalents of Acid	Solvent	Temperature (°C)	Product	Yield (%)
1	Me	$SnCl_4$	2	DCM	-78	**3.20**	90
2	Me	$SnCl_4$	2	Toluene	-78 → -40	**3.20**	38
3	Me	TfOH	1	MeCN	-40 → -20		decomp.
4	Ph	$SnCl_4$	2	DCM	-78		decomp.
5	Ph	$SnCl_4$	2	Toluene	-78 → -40		decomp.
6	Ph	TfOH	1	MeCN	-40 → -20	**3.22**	65

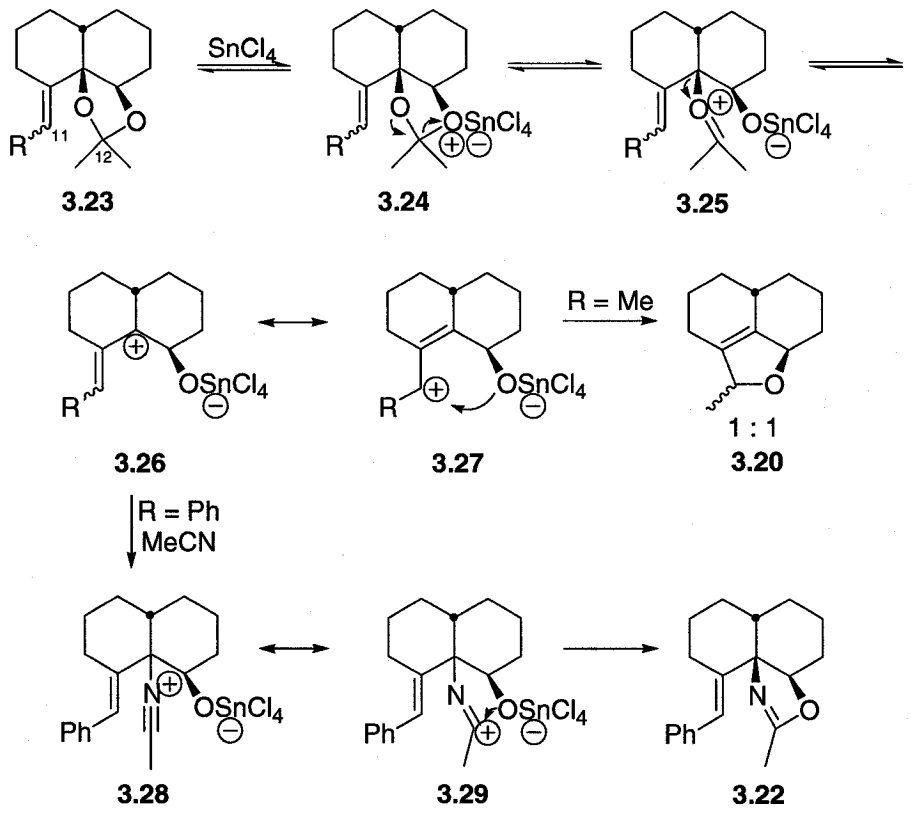


Figure 3.2 – Mechanism of the Formation of ***3.20*** *and* ***3.22***

This reactivity was somewhat surprising since the first Prins-pinacol observed by Morency had an alkyl chain on the alkene, and no other product than the Prins-pinacol product was observed (Scheme 2.1). This led to the hypothesis that the side chain at C5 was helping the reaction by preventing allyl cation formation. In fact, when we look to the orbital alignment, we can understand why preventing the formation of **3.15** and **3.31** is beneficial since in the case of **3.31**, the π system is well aligned (30° difference) with the σ* of the C-O bond that is cleaved when the allyl cation is formed (Figure 3.3). In contrast, the π system in **3.30** is orthogonal with the σ* of the C-O bond which prevents allyl cation formation. This seems to be a good explanation as to why better yields were obtain in the Prins-pinacol precursors that were biased to stay in conformation **3.14**, which prevents the loss of acetone and subsequent decomposition pathways.

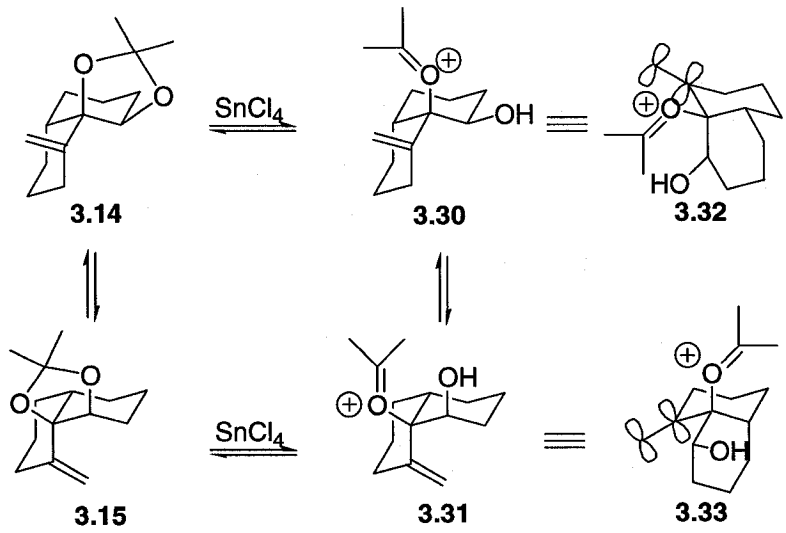


Figure 3.3 – Alignment of the Orbitals for the Allyl Cation Formation

Regioisomeric Bicyclo[4.3.1]decanones

In the previous sub-chapter, bicyclo[4.3.1]decanones was generated from bicyclo[4.4.0]decane cores. We were wondering if bicyclo[4.3.1]decanones could be generated from bicyclo[5.3.0]decane cores, which would install the tetrahydrofuran ring on the 6 membered

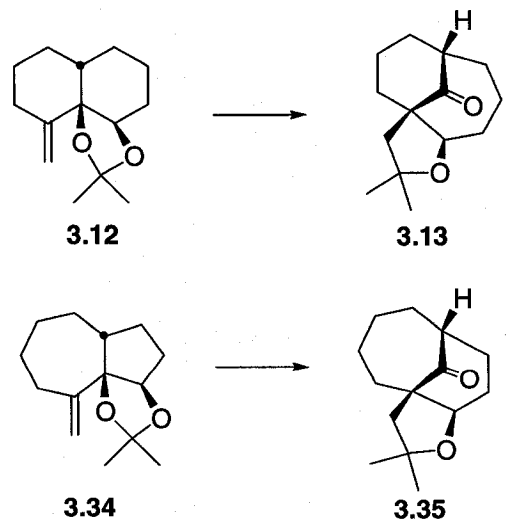
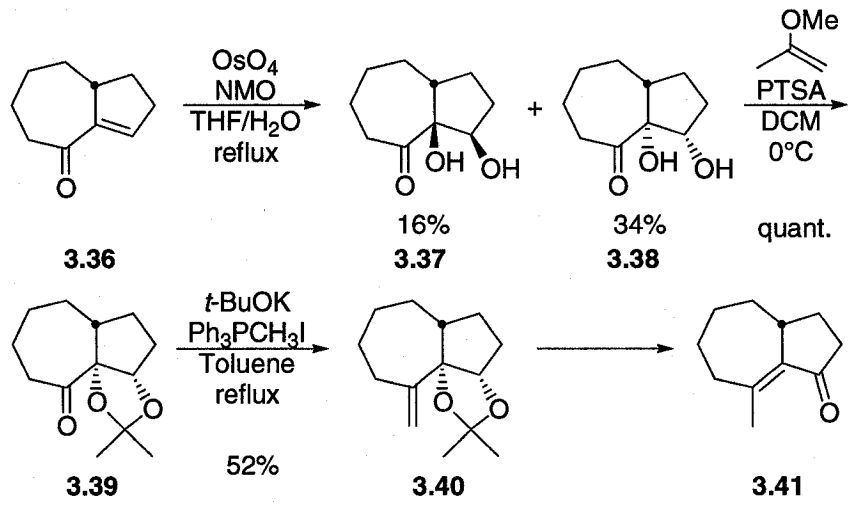


Figure 3.4 – Comparison Between the Two Bicyclo[4.3.1]decanone Formations

ring instead of installing the tetrahydrofuran ring on the 7 membered ring (Figure 3.4). To this end, we submitted **3.36**, which can be obtained from literature procedures,[83c] to the dihydroxylation conditions to obtain mixture of diastereoisomers in low yields (Scheme 3.4). Thinking that the major diastereoisomer **3.38** was the *cis*-fused bicyclo[5.3.0]decanone, it was then used to pursue the synthesis of the Prins-pinacol precursor **3.40**. 2D NMR experiments could not have been useful in this case to determine the stereochemistry since the proton at the ring junction was always overlapping with several methylene protons. When **3.40** was treated under Prins-pinacol rearrangement conditions, only the volatile compound **3.41** was observed. Similar byproducts were observed by Overman and he rationalized the formation of those byproducts through the lost of acetone followed by a 1,2-hydride shift and isomerization to generate the conjugated enone **3.49** (Figure 3.5).[4, 20a] Although Prins cyclizations are possible



*Scheme 3.4 – Synthesis of the Trans-Fused Prins-Pinacol Precursor **3.40***

*Table 3.3 – Attempted Prins-Pinacol Rearrangement of **3.40***

Entry	Acid	Equivalents of Acid	Solvent	Temperature (°C)	Yield of **3.41** (%)
1	$SnCl_4$	2.5	Toluene	-78	18
2	TfOH	2	MeCN	-40 → 0	70

with *trans*-fused bicyclic systems, fragmentation occurred because the 5-membered ring puts the oxocarbenium ion at a greater distance from the alkene and the 2 methyls of the oxocarbenium ion cause a lot of steric hinderance.

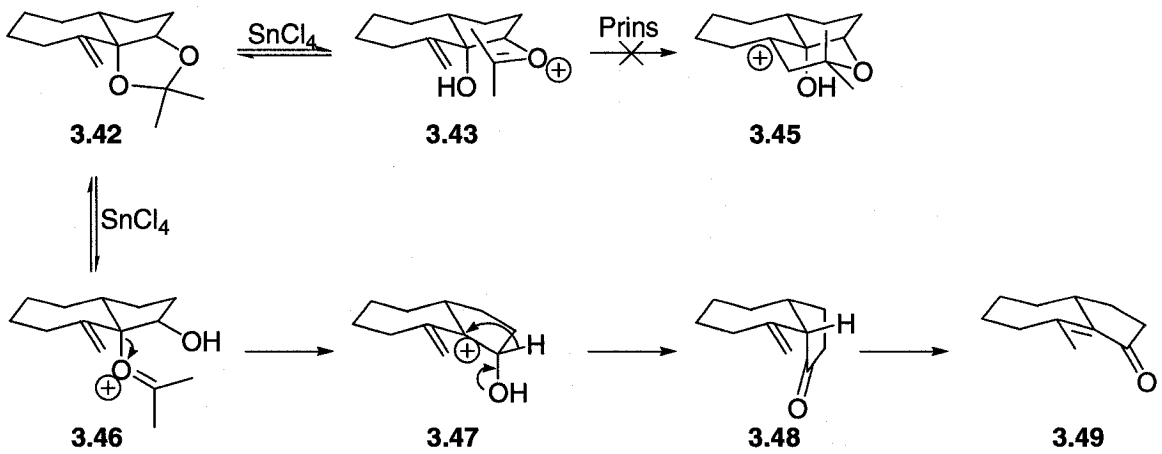
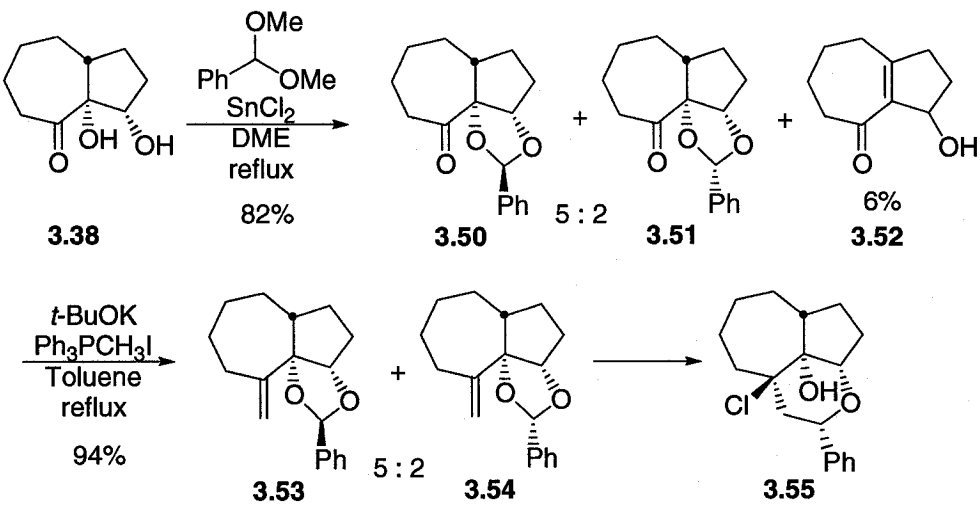


Figure 3.5 – Rationale for the Generation of ***3.31***

Still not knowing that **3.38** was the *trans*-fused bicyclic system, it was then treated with benzaldehyde dimethyl acetal to afford a mixture of benzylidene acetals (**3.50** and **3.51**).[77] The elimination product **3.52** was isolated separately (Scheme 3.5). After **3.53** and **3.54**[77] were generated by a Wittig olefination, they were submitted to the Prins-pinacol rearrangement conditions and the chloroalcohol product **3.55** was isolated. All the stereochemistry was determined by 2D experiments[77] except for the carbon bearing the chloride. The stereochemistry was later confirmed when an X-ray crystallographic structure was obtained (Figure 3.6). The formation of this compound is the result of a Prins cyclization where the carbenium ion is trapped by a chloride anion present from the tin tetrachloride (Figure 3.7). Here, the phenyl was causing less steric hindrance around the oxocarbenium ion (**3.57**) compared to **3.43** which allows the Prins cyclization to occur preferentially over the fragmentation. The stereochemistry of the benzylic carbon came from the fact that the phenyl would rather to be in a pseudoequatorial position in the transition state of the Prins cyclization. If a pinacol rearrangement would have occurred, it would have been the *b* bond that would have migrated, since it's better aligned with the vacant p orbital and the rate of pinacol rearrangements are known to be greater than the rate of conformational change in Prins-pinacol rearrangements.[23, 27a] The pinacol rearrangement does

not occur because it generates a very strained *trans*-fused bicyclo[4.3.1]decanone (**3.60**). The addition of a chloride anion is preferred. This was already observed by Overman when he tried to perform a Prins-pinacol rearrangement in the presence of tin tetrachloride.[38] One thing that this chloride anion confirmed is that under these reaction conditions, the Prins cyclization can occur, and gives additional evidence that these reactions go through a Prins-pinacol tandem reaction and not an oxonia-Cope-aldol sequence.



*Scheme 3.5 – Synthesis of the trans-Fused Prins-Pinacol Precursors **3.53** and **3.54***

*Table 3.4 – Prins-Pinacol Rearrangement of **3.53** and **5.54***

Entry	Acid	Equivalents of Acid	Solvent	Temperature (°C)	Yield of **3.55** (%)
1	$SnCl_4$	2.5	DCM	-78 → -40	71
2	$SnCl_4$	2.5	Toluene	78 → -20	63
3	TfOH	2	MeCN	-40 → 0	decomp.

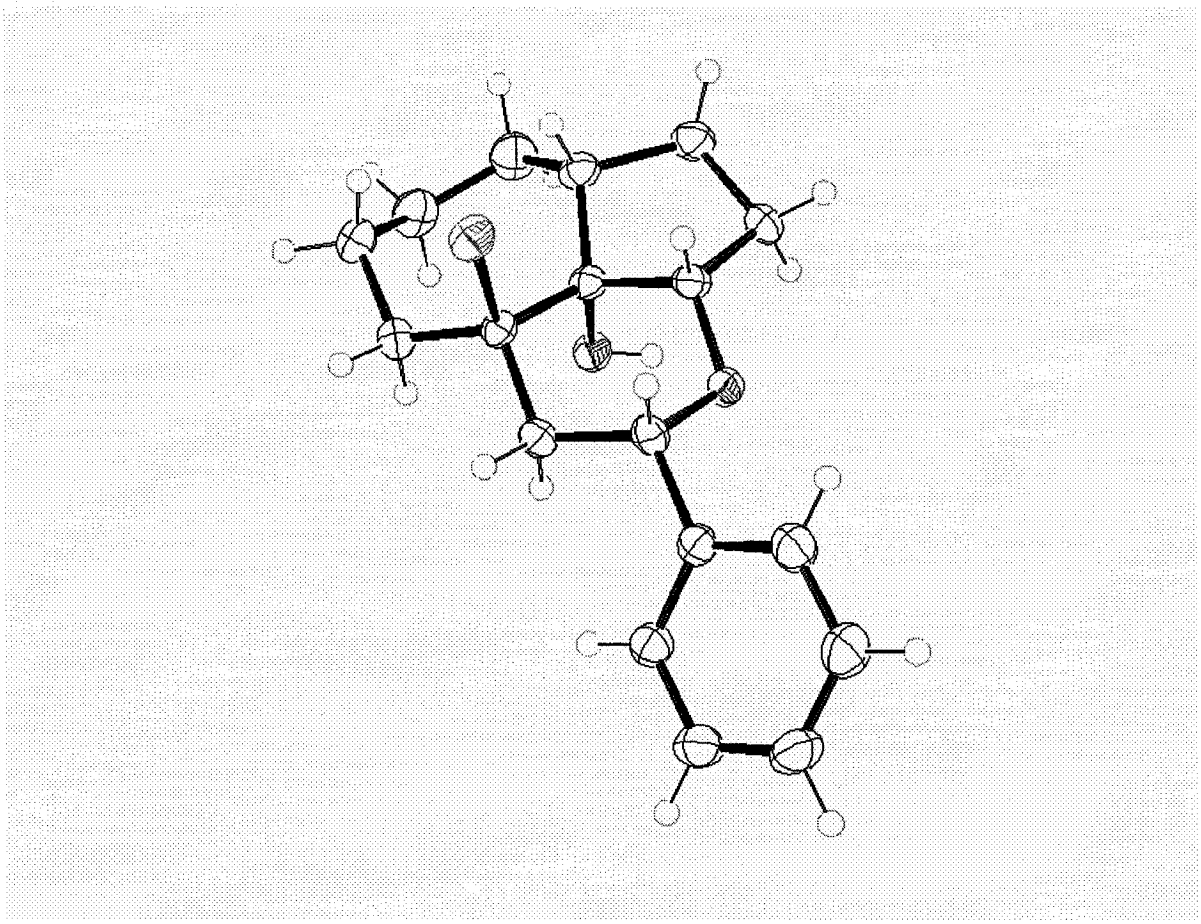


Figure3.6 – X-Ray Crystallographic Structure of ***3.55***

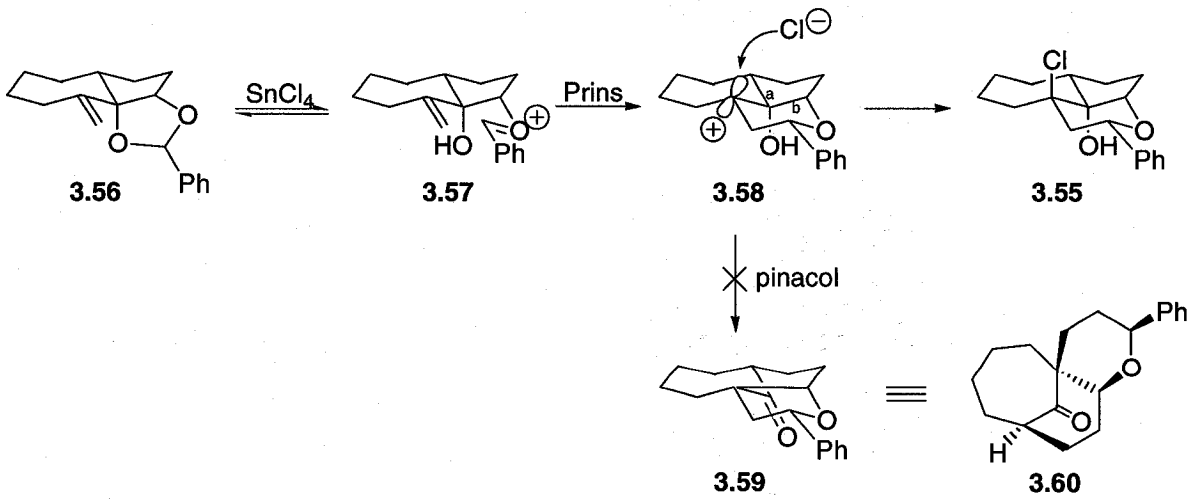
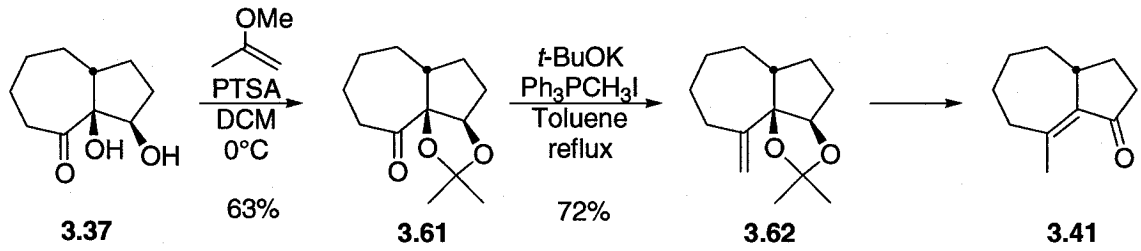


Figure 3.7 – Rationale for the Generation of ***3.55***

The stereochemistry of **3.55** confirmed that **3.38** was the *trans*-fused bicyclic system, therefore Scheme 3.6 shows how the diol **3.37** was used to generate the Prins-pinacol precursor **3.62**.[77] Again the fragmentation product **3.41** was observed, probably due to the steric hindrance of the methyls and the distant oxocarbenium ion.

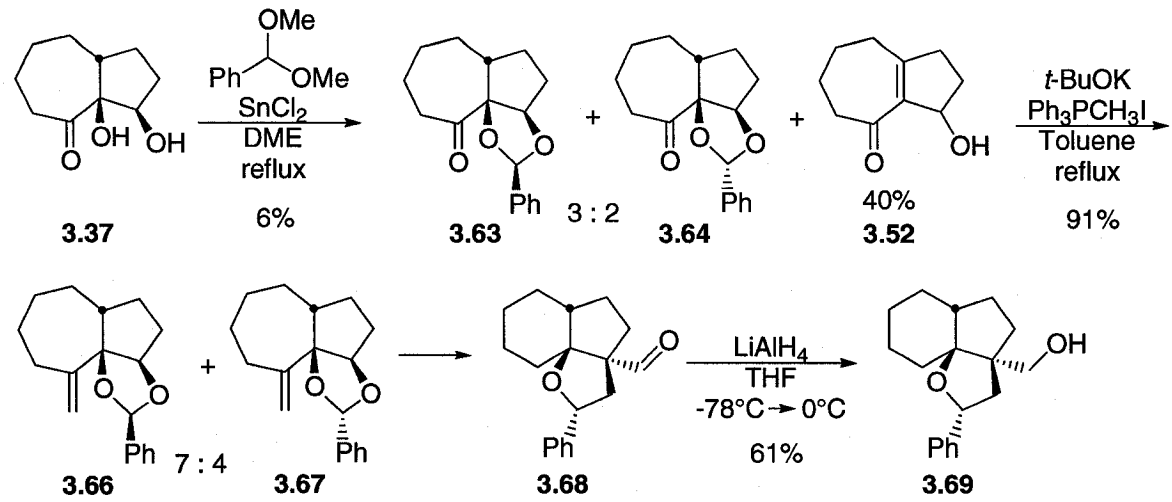


*Scheme 3.6 – Synthesis of the Cis-fused Prins-Pinacol Precursor **3.62***

*Table 3.5 – Attempted Prins-Pinacol Rearrangement of **3.62***

Entry	Acid	Equivalents of Acid	Solvent	Temperature (°C)	Yield of **3.41** (%)
1	$SnCl_4$	2	DCM	-78 → r.t.	decomp.
2	$SnCl_4$	1	Toluene	-78	9
3	TfOH	1	MeCN	-40	71

Since the benzylidene acetal was the solution for the *trans*-fused analogue, it was definitely worth a try with the *cis*-fused bicyclic diol. The Prins-pinacol rearrangement precursor **3.67** was generated in the same fashion but when treated under 3 different acidic conditions, an unusual aldehyde product was observed (dr > 25:1). Doubting my NMR structure elucidation skills, the aldehyde was reduced to the primary alcohol **3.69** in order to obtain an X-ray crystallographic structure (Figure 3.7) and to confirm if this was indeed the correct structure.



*Scheme 3.7 – Synthesis of the Cis-fused Prins-Pinacol Precursors **3.66** and **3.67***

*Table 3.6 – Attempted Prins-Pinacol Rearrangement of **3.66** and **3.67***

Entry	Acid	Equivalents of Acid	Solvent	Temperature (°C)	Yield of **3.68** (%)
1	$SnCl_4$	1	DCM	-78	80
2	$SnCl_4$	2	Toluene	-78 → -20	29
3	TfOH	1	MeCN	-40 → r.t.	40

Proposing a mechanism to explain this transformation was not a trivial task. The mechanism needs to have 2 ring contractions, and the tetrahydrofuran generated shows reversed regiochemistry than that of what we usually see in the Prins-pinacol products. The regiochemistry of the tetrahydrofuran tells us that the opened benzylidene acetal intermediate that will lead to the product is not intermediate **3.70**, but the intermediate **3.71** (Figure 3.9). **3.71** then undergoes a Prins cyclization where the alkene can attack the oxocarbenium ion from the bottom (**3.71**) or from the top (**3.76**), depending on the conformation of the seven membered ring. Only the conformers that put the phenyl in a pseudoequatorial position were took into consideration. Although this cyclization is a disfavored 5-endo-trig process according to Baldwin's rules,[19] it is known that oxocarbenium ions do not respect these rules; 1,3-dioxolane

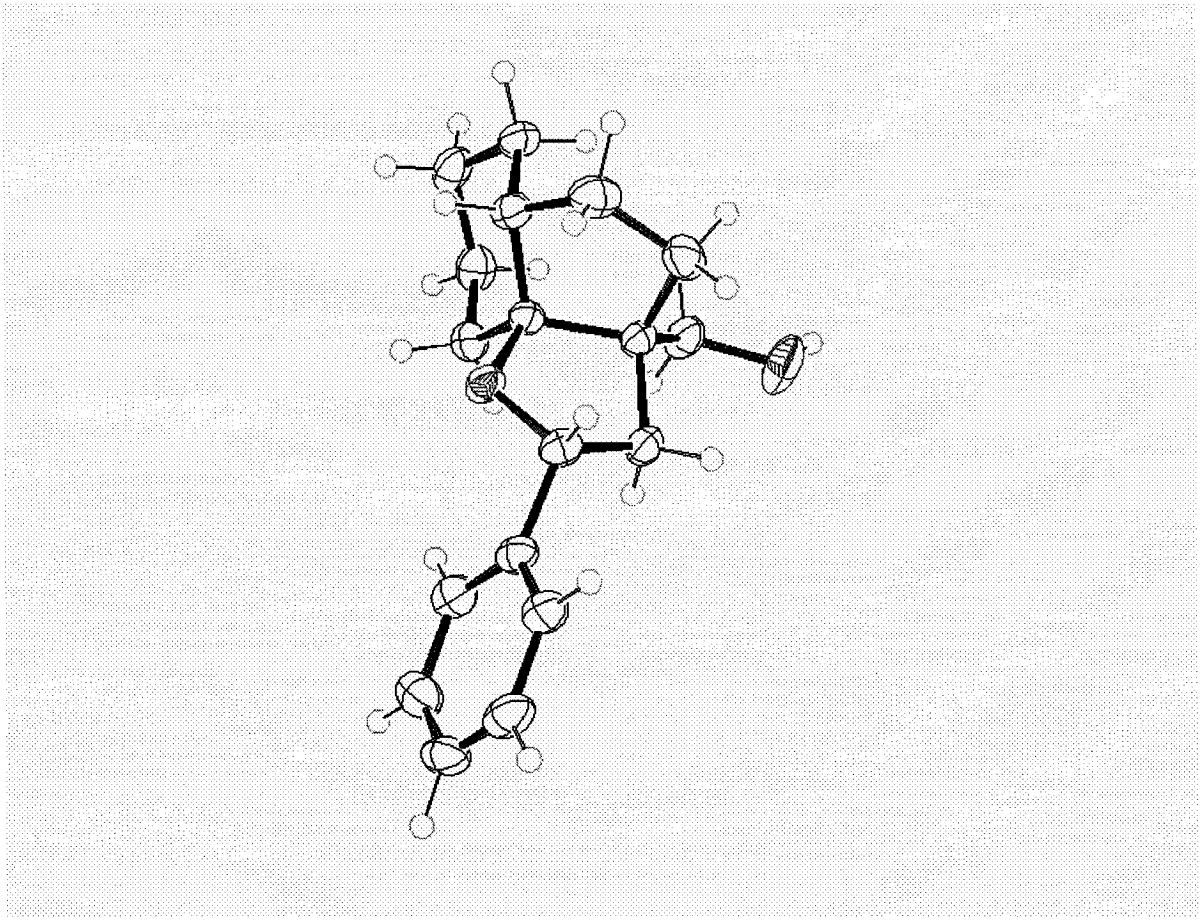


Figure3.8 – X-Ray Crystallographic Structure of ***3.69***

formation from a ketone and ethylene glycol being a representative example. Oxocarbenium ion **3.76** can be represented by the carbocation **3.77** where the alignment of the orbitals (the π orbital of the alkene and the empty p orbital of the carbocation) is better. The Prins cyclization is followed by a pinacol rearrangement where bond *a*, which is in close proximity and aligned periplanar with the empty p orbital, migrates with the help of the lone pair of the tetrahydrofuran oxygen. The cyclic oxocarbenium ions **3.74** and **3.80** have now 4 bridgehead bonds that can migrate. Migration of the bridgehead bond c leads to the product but there is no obvious reasons why this bond would preferably migrate over the others. That is why we proposed that the 6 membered ring is in a boat-like conformation, therefore, bond b is well aligned with the σ^* of bond c, which is well aligned with the π^* of the oxocarbenium ion. This Wagner-Meerwein-type rearrangement is initiated by the lone pair on the oxygen of the alcohol, therefore the whole reaction sequence is called a Prins-pinacol-pinacol rearrangement. The

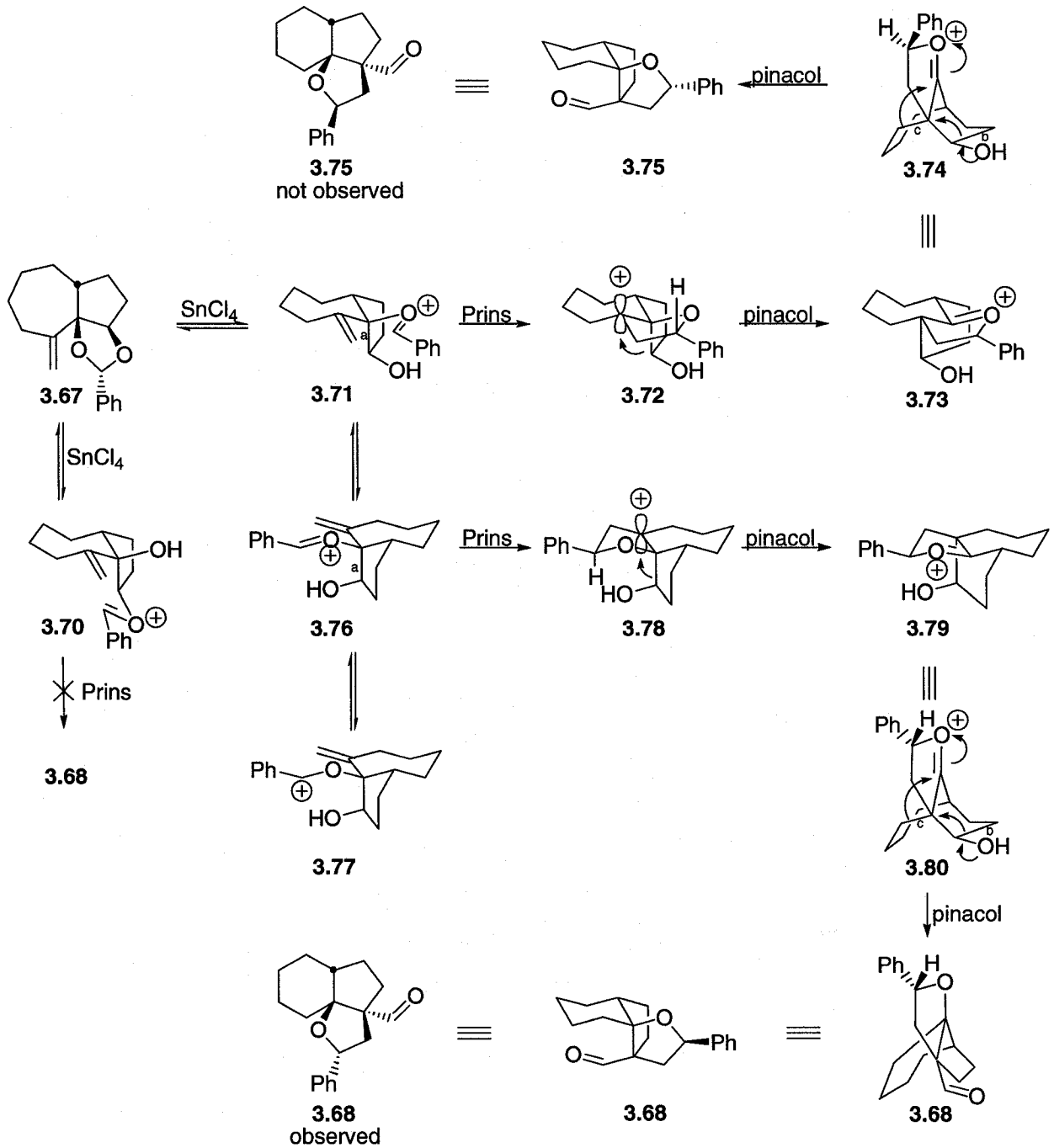
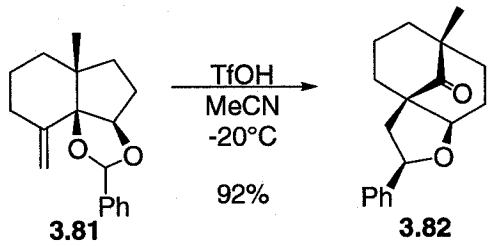


Figure 3.9 – Rationale for the Generation of ***3.68****, a Prins-Pinacol-Pinacol Rearrangement*

stereochemistry of the phenyl tells us that the alkene is attacking the oxocarbenium ion from the top. We do not have any rational for this observation but it must have something to do with the favored conformation of this molecule. The reason why it would undergo an unusual 5-endo-trig

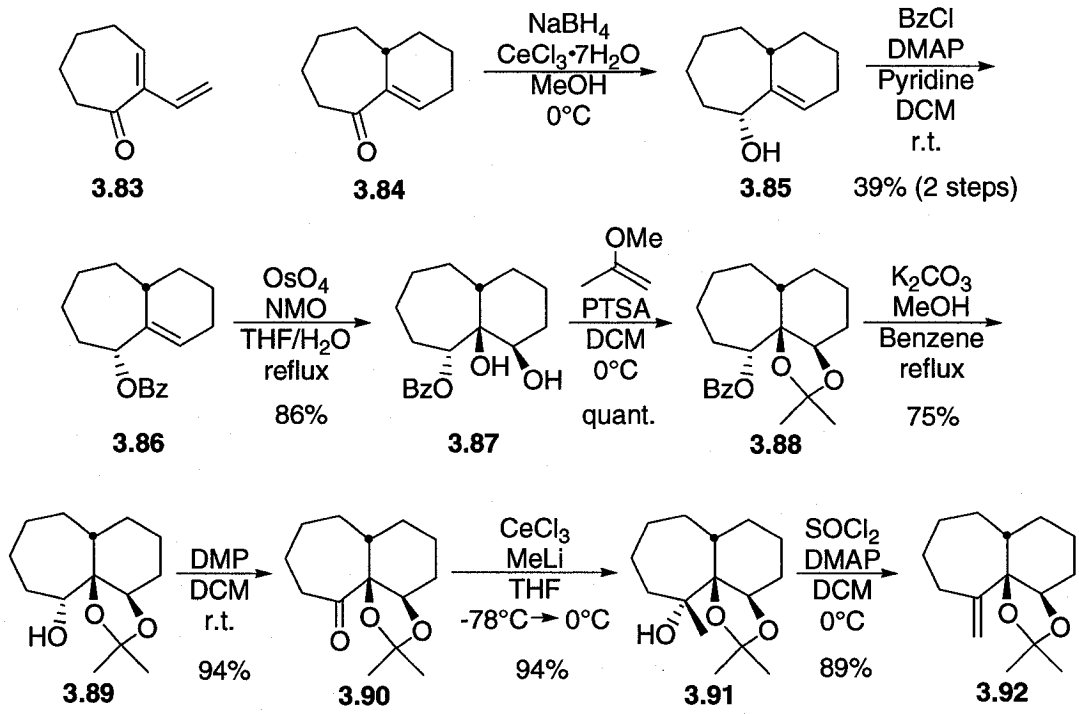
Prins cyclization is still unclear and is the first example in the Prins-pinacol rearrangement literature. Overman already observed 5 membered Prins cyclization but in all cases, it was a 5-exo-trig cyclization.[40, 42d, 43] The formation of the aldehyde **3.68** shows how a subtle change in the Prins-pinacol precursor can have a large effect on the product formed since Maxime Riou from our laboratory obtained almost exclusively the Prins-pinacol product **3.82** when he treat a similar substrate, having a 6-membered ring instead of a 7-membered ring, to similar conditions (Scheme 3.8). In summary, bicyclo[4.3.1]decanones could not be generated from bicyclo[5.3.0]decane cores but two intriguing byproducts were obtained and allowed to understand better the Prins-pinacol rearrangement.



Scheme 3.8 – Similar Prins-Pinacol Reaction Performed by Maxime Riou

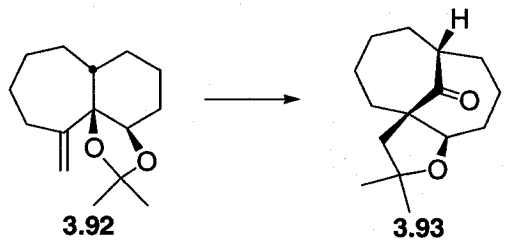
Bicyclo[4.4.1]undecanones

With the goal of generating bicyclic ketones of various ring sizes in mind, the synthesis of a *cis*-fused bicyclo[5.4.0]undecane was initiated. Attempts to use diene **3.83** for the hydroxy-directed Diels-Alder reaction failed because of its difficult isolation due to its volatility.[84] The conjugated enone **3.84**, which can be obtained in 3 steps from literature procedures, was used in place of **3.83** for the generation of the Prins-pinacol precursor **3.92**. It should be noted that dihydroxylation of **3.84** and Wittig olefination of the ketone **3.90** lead to decomposition. The Prins-pinacol rearrangement gave the bicyclic ketone **3.93**[77] in moderate yields and it requires high temperatures and many equivalents of acid (Table 3.7).



Scheme 3.9 – Synthesis of the Prins-Pinacol Precursor ***3.92***

Table 3.7 – Prins-Pinacol Rearrangement of ***3.92***



Entry	Acid	Equivalents of Acid	Solvent	Temperature (°C)	Yield (%)
1	$SnCl_4$	5.5	DCM	-78 → r.t.	34
2	$SnCl_4$	3	Toluene	-78 → r.t.	56
3	TfOH	3	MeCN	-40 → r.t.	decomp.
4	$MeSO_3H$	11	DCM	-78 → r.t.	28

The low yields can be explained in a similar fashion as for substrate **3.12**. The equilibrium between **3.94** and **3.95** is again the problem. **3.95** is slightly favored since there are

no steric interactions between the alkene and the methyls. A simple molecular model analysis showed that 5 of the 6 possible chair conformers of the 7 membered ring of **3.95** has the π system of the olefin aligned with the σ* orbital of the adjacent C-O bond, which can lead to fragmentation and decomposition. In contrast, only 1 of the 6 possible chair conformers of the 7 membered ring of **3.94** has the olefin aligned for the fragmentation or for the Prins cyclization (**3.98**). Therefore, it is reasonable to assume that substitution that favors conformer **3.94**, and a benzylidene acetal to reduce the sterics for the Prins cyclization would greatly improve the yield of the rearrangement of **3.92**.

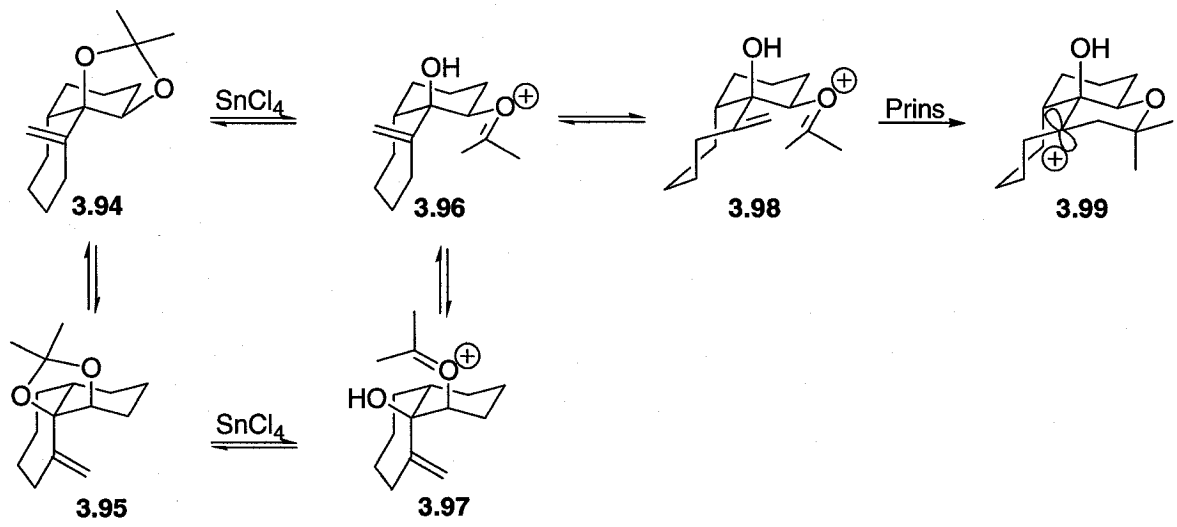
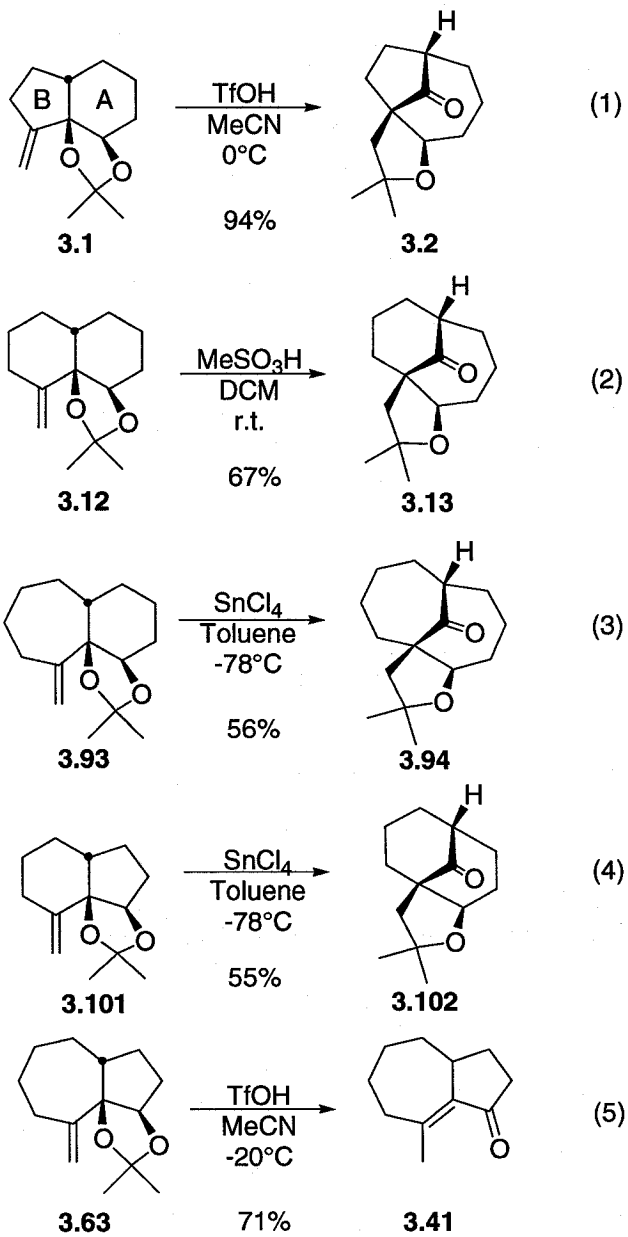


*Figure 3.10 – Rationale for the Low Yields Obtained in the Generation of **3.93***

Conclusion

The Prins-pinacol synthesis of a variety of bicyclic ketones with different ring sizes proved to be possible, albeit with limitations. The results of the present report, in combination with those of Mélina Girardin (Equation 1) and Maxime Riou (Equation 4), allowed us to draw some interesting conclusions. It was demonstrated that better yields were obtained when the A ring is a 6 membered ring since a 5 membered ring increased the distance between the alkene and the productive oxocarbenium ion. 5 membered B rings are favored, even though the alkene–oxocarbenium ion distance is increased. This is because the 5 membered ring locks the

alkene in the position required for the Prins cyclization. The 6 membered B ring needs to take a twist-boat conformation in order to achieve the Prins cyclization and the 7 membered B ring has many possible conformations which only few of them position the alkene in a way that the Prins cyclization is possible. When the two worst cases are combined (5 membered A ring and 7 membered B ring), only the fragmentation products are observed. Nevertheless, substitution on the A ring that favors the productive conformer and benzylidene acetals that cause less steric interactions during the Prins cyclization proved to be good solutions to increase the Prins-pinacol rearrangement efficiency in those systems.

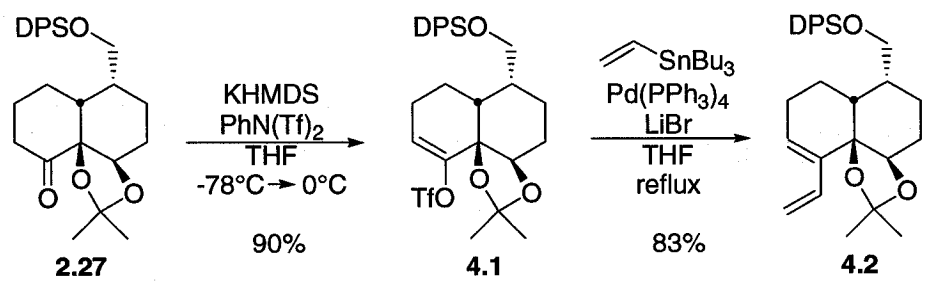


4

Prins-Pinacol Rearrangement Combined with the Diels-Alder Reaction

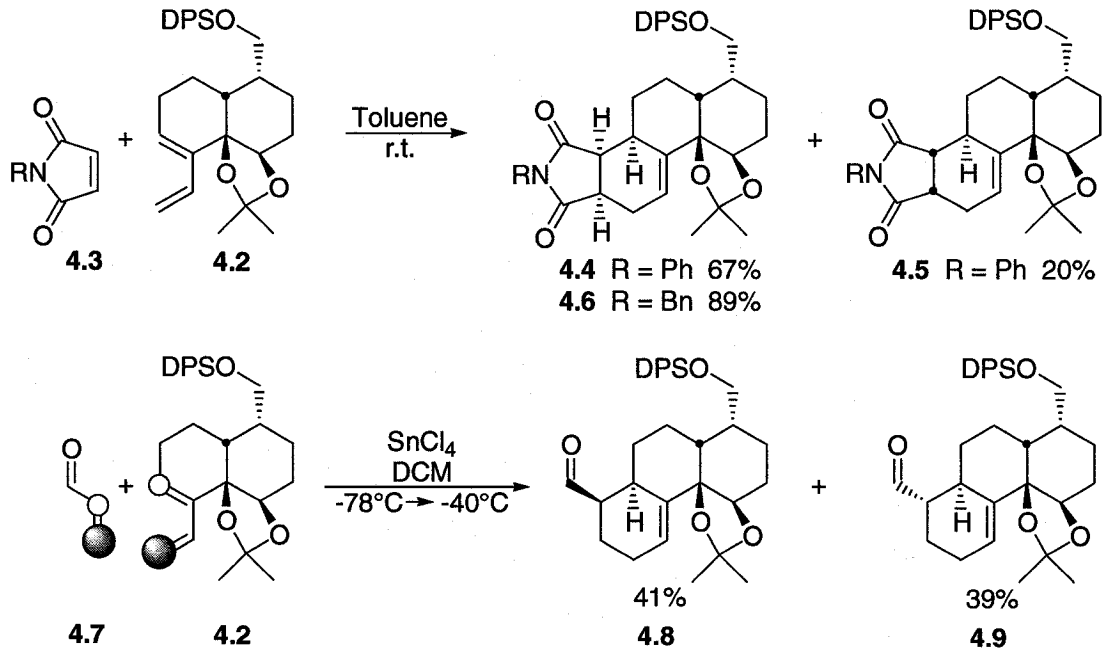
Diels-Alder Preparation of the C Ring

Having developed Prins-pinacol rearrangement conditions for the generation of bicyclo[4.3.1]decanones, we were wondering if we could generate more complexity in our molecules, such as adding an extra ring for example. A common way to generate 6-membered rings is through the Diels-Alder reaction. Performing a Diels-Alder using **4.2** as the diene is attractive since it is generating an alkene that can be used in the Prins-pinacol rearrangement. As shown in Scheme 4.1, Justine Chan, a summer student, developed an efficient route to obtain **4.2** from the ketone **2.27** using a Stille coupling.[85] Ketone **2.27** was used for those experiments since we knew that the side chain at C-5 was allowing us to get better yields from the Prins-pinacol rearrangement.



*Scheme 4.1 – Generation of Diene **4.2***

We first attempted the Diels-Alder reaction with maleimides since they are known to be efficient dienophiles. With *N*-phenylmaleimide, both *endo* (**4.4**) and *exo* (**4.5**) products were isolated whereas with *N*-benzylmaleimide, only the *endo* product **4.6** was observed (Scheme 4.2 and Figure 4.1). This result can be rationalized by the side chain rigidity of the dienophile. The aromatic ring of the benzyl can be positioned away from the diene substituents to reduce steric interactions whereas the phenyl has severe steric interactions when approaching the diene. The steric repulsions are therefore in competition with the beneficial secondary orbital interactions and a mixture of products is obtained. For both maleimides, high facial selectivity was obtained due to the cup shape of the *cis*-decalin.



Scheme 4.2 – Diels-Alder Reaction with Maleimides and Acrolein

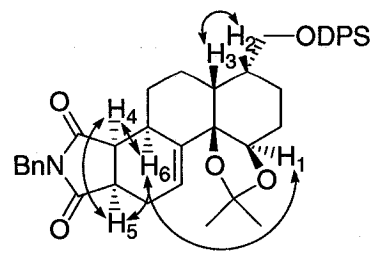
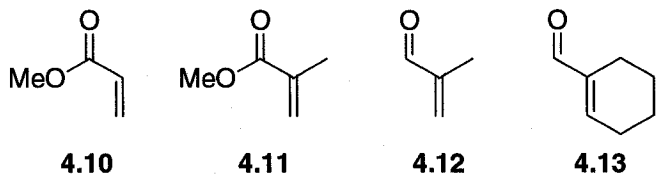


Figure 4.1 – Structure Elucidation of ***4.6*** *by 2D NMR Experiments*[77]

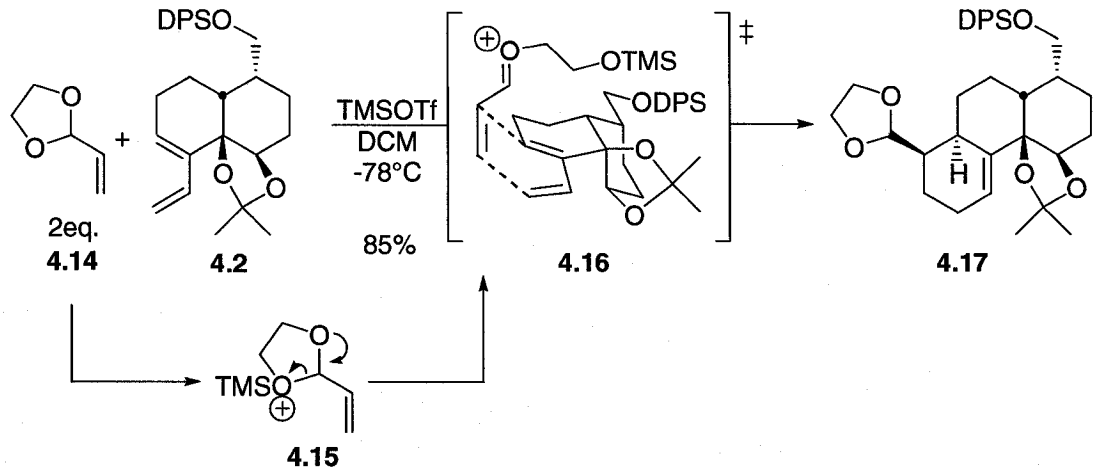
The Diels-Alder reaction with only acrolein does not provide any products but when the reaction was performed in the presence of a Lewis acid, two epimers **4.8** and **4.9** were obtained (Scheme 4.2). Lewis acids are well known to assist the Diels-Alder reaction since the oxonium ion that is formed lowers the energy of the LUMO of the dienophile, therefore better interactions occur with the HOMO of the diene and this favors the reaction. Again, the reaction occurs with high facial selectivity and a mixture of *endo* and *exo* product are obtained, which mean that steric interactions are again in competition with secondary orbital interactions. This Diels-Alder reaction also occurred with high regioselectivity and this can be explained by the size of the frontier molecular orbital coefficients, where both large and small coefficients are preferably matched together.[86] These energically favored interactions arise from the third term of the Klopman-Salem equation, which reflects the interaction of all filled orbitals with all unfilled orbitals of correct symmetry.[87] All other Diels-Alder reactions that were tried with the dienophiles in Figure 4.2 failed, even with the use of a variety of Lewis acids as additives.



4.10 **4.11** **4.12** **4.13**

Figure 4.2 – Unsuccessful Dienophiles for the Diels-Alder Reaction with ***4.2***

A well known method to improve the Diels-Alder reaction is to use Gassman-type activated dienophiles.[88] Treating diene **4.2** with acrolein ethylene acetal in the presence of trimethylsilyl trifate gives the corresponding cycloadduct **4.17** in high yield and high selectivity (Scheme 4.3). During this ionic Diels-Alder, a real oxonium ion is generated which decreases the energy of the LUMO of the dienophile and facilitates the reaction. The reaction can therefore occur at lower temperatures and better *endo*/*exo* selectivity can be obtained. The regiochemistry is still governed by the size of the frontier molecular orbital coefficients, and the regiochemistry obtained in **4.17** is consistent with that observed in the literature.[89] Deprotection of the acetal gives the **4.8**, which confirms its stereochemistry.



Scheme 4.3 – Diels-Alder Reaction with a Gassman-Type Activated Dienophile

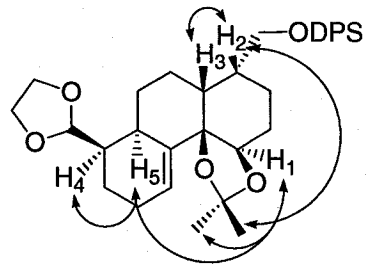
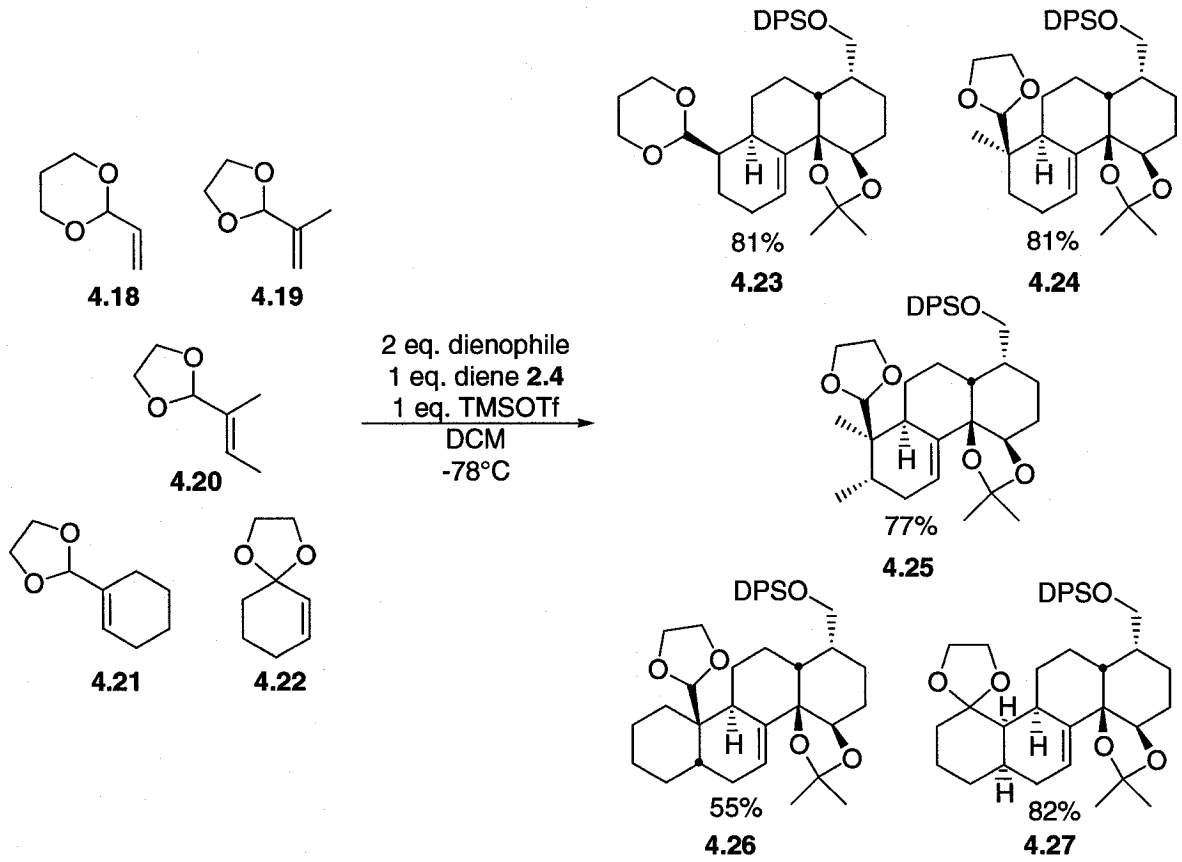


Figure 4.3 – Structure Elucidation of ***4.17*** *by 2D NMR Experiments*[77]

Five other Gassman type activated dienophiles (**4.18-4.22**) were generated according to literature procedures.[90] All five dienophiles generate the corresponding cycloadduct (**4.23-4.27**) with excellent facial-, regio- and stereoselectivity in fair to good yields (Scheme 4.4). Although 2D experiments were not performed on all these molecules, all *endo* products possess similar proton spectra that are easily distinguished from the proton spectra of the *exo* products, in particular by the chemical shift of the olefinic proton. Furthermore, crystalline analogues were obtained by Mélina Girardin and Maxime Riou from our group where the X-ray crystallographic structures shows that the *endo* product and this regiochemistry were always obtained with the Gassman-type activated dienophiles. The nature of the acetal (dioxolane versus dioxane) does not seem to have an effect on the ionic Diels-Alder efficacy (**4.23**). There are no obvious steric arguments why the generation of **4.26** occurred in lower yields, therefore it is possible that the

purity of the dienophile is responsible for the observed yield. However, the Diels-Alder reaction and the ionic Diels-Alder reaction proved to be very efficient to generate Prins-pinacol precursors that had one or two extra rings and new stereocenters.



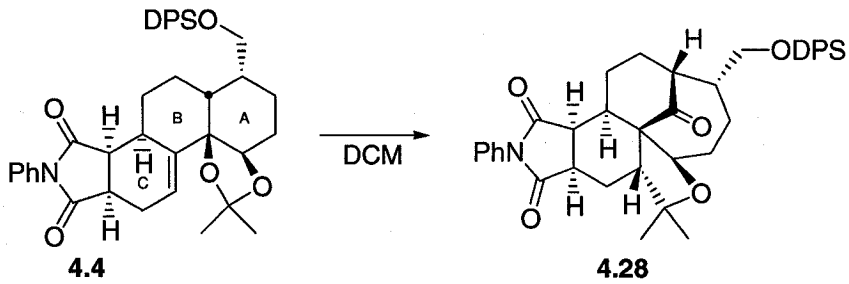
Scheme 4.4 – Ionic Diels-Alder Generation of Five Prins-Pinacol Precursors

Prins-Pinacol Rearrangement of the Diels-Alder Products

Having in our possession a variety of tri- and tetracyclic Prins-pinacol precursors, we were ready to assess how the rigidity of these molecules would affect the Prins-pinacol rearrangement. We first performed the Prins-pinacol reaction on the *N*-phenylmaleimide substrate. We initially observed that the rigidity brought on by the C ring makes the rearrangement impossible with bismuth trichloride (Table 4.1). Fortunately, we observed some rearranged product in the presence of trimethylsilyl triflate and tin tetrachloride but the yields

were lower than the substrate with the terminal alkene (**2.29**). As shown in Figure 4.4, this is probably due to difficulty in getting to conformer **4.30** since a conformational change of the C ring is required to reach the reactive conformer. This transformation is pretty impressive since **4.28** is a very complex pentacyclic molecule bearing a quaternary center and 8 other stereocenters. The relative stereochemistry of **4.28** was verified with 2D NMR experiments which also confirm the stereochemistry of the Prins-pinacol precursor **4.4** (Figure 4.5).

*Table 4.1 – Prins-Pinacol Rearrangement of **4.4***



Entry	Acid	Equivalents of Acid	Temperature (°C)	Yield (%)
1	$BiCl_3$	1	r.t.	no reaction
2	$SnCl_4$	4	-78	62
3	TMSOTf	7	-78	37

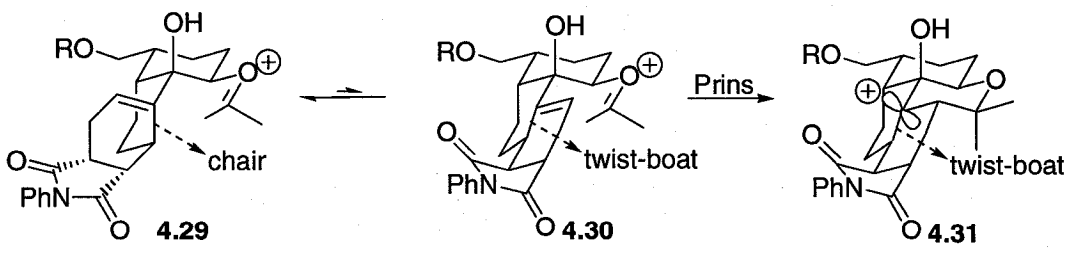


*Figure 4.4 – Rationale for the Low Yields Obtained in the Generation of **4.28***

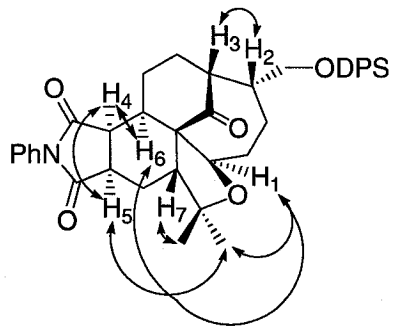
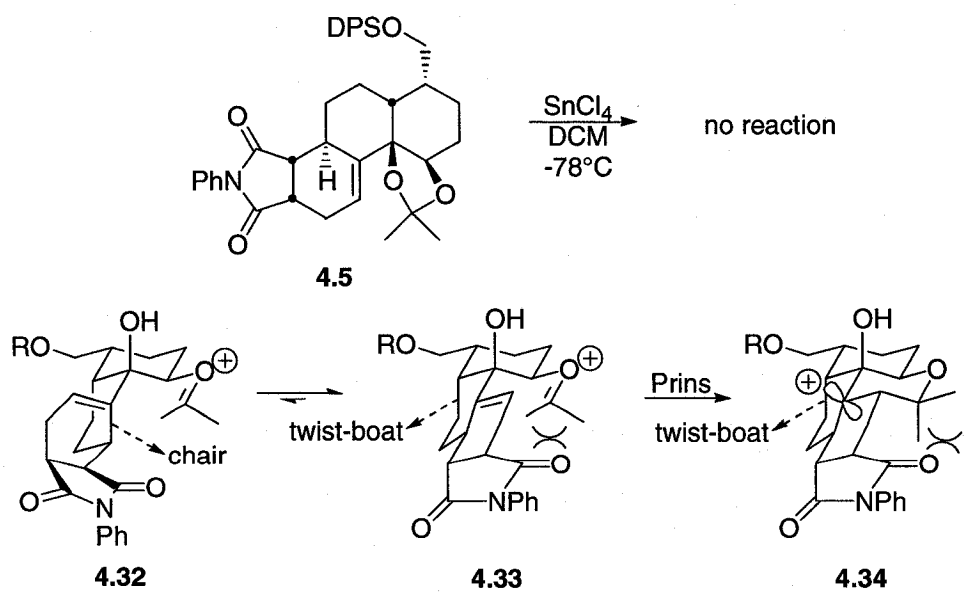


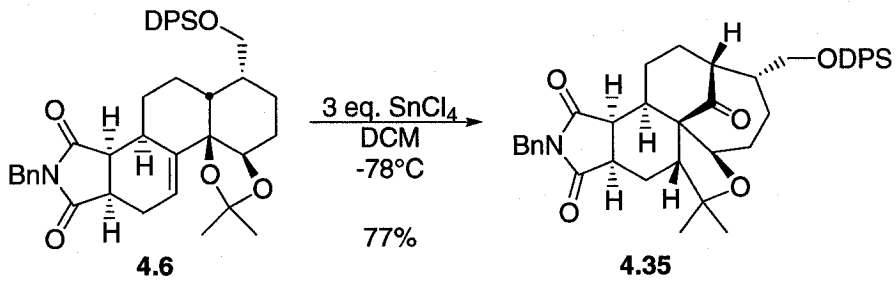
Figure 4.5 – Structure Elucidation of ***4.28*** *by 2D NMR Experiements*[77]

The Prins-pinacol rearrangement was also tried with the *exo* Diels-Alder product **4.5**. Unfortunately, when treated under the same conditions as **4.4**, no Prins-pinacol product was obtained and only the starting material was recovered. When the reaction was heated, only decomposition was observed. Scheme 4.5 shows that the problem is probably the steric interactions between the methyl and the maleimide moiety in conformer **4.33** which leads to the Prins cyclization. If the Prins cyclization does occur, the distance between the methyl and the maleimide is decreased during the pinacol rearrangement. The pinacol rearrangement does not occur because of those steric interactions and decomposition of the intermediate **4.34** is therefore obtained.



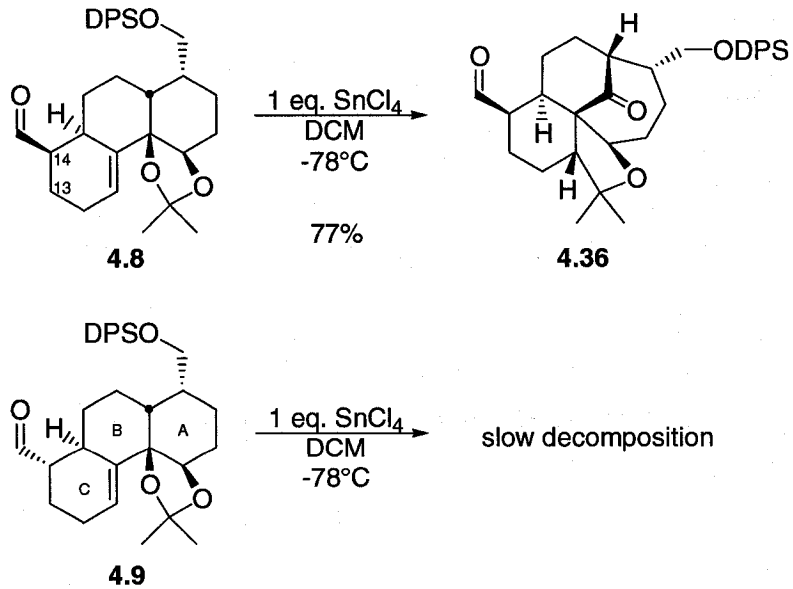
Scheme 4.5 – Rationale for the Unreactivity of ***4.5***

The rearrangement was also performed with the *N*-benzyl maleimide Diels-Alder product and the results obtained were similar than those obtained with **4.4** (Scheme 4.6). The reason why **4.35**[77] is formed in better yields can be that the benzyl side-chain allows the aromatic ring to be far from the alcohol so the conformation **4.30** is a bit more favored than for **4.4**.



Scheme 4.6 – Prins-Pinacol Rearrangement of the N-Benzyl Maleimide Diels-Alder Product

The acrolein Diels-Alder products were also submitted to tin tetrachloride rearrangement conditions and only **4.8** rearranged to give **4.36** (Scheme 4.7), in yields comparable to those obtained for the rearrangement of the maleimides *endo* Diels-Alder products (**4.4** and **4.6**). The absence of rearrangement for **4.9** seems to tell us that steric interactions between the substituents

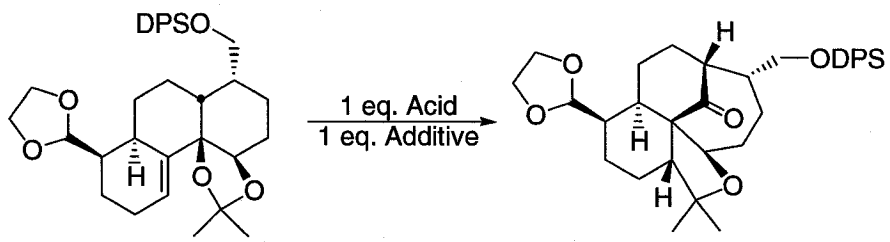


Scheme 4.7 – Prins-Pinacol Rearrangement of the Acrolein Diels-Alder Products

at C13 and the methyl of the acetonide would not be the problem for the Prins cyclization to occur. It seems that the stereochemistry at C14 is more important and probably affects the conformation of the C ring which allows the Prins cyclization.

The Prins-pinacol rearrangement conditions were applied to the vinyl dioxolane ionic Diels-Alder product in order to obtain the tetracyclic bridgehead ketone **4.37**.[77] As shown in Table 4.2, only tin tetrachloride works for this transformation which shows how the rigidity of ring C is still making the Prins cyclization difficult. To our surprise, when silver triflate was added to the reaction mixture, the rearranged product **4.37** was obtained in better yield than the substrate with the terminal alkene (**2.29**). Figure 4.6 shows a potential explanation for the good yield obtained, where the decomposition is believed to came from **4.40**, due to the alignment of the π system of the alkene and the σ^* of the C-O bond. The extra ring C prevents the formation of **4.40** since the stereochemistry at C9 forces the C ring to be in a boat conformation and this

*Table 4.2 – Prins-Pinacol Rearrangement of **4.17***



4.17 **4.37**

Entry	Acid	Additive	Solvent	Temperature (°C)	Yield (%)
1		AgOTf	DCM	-78 → r.t.	decomp.
2	$BiCl_3$		DCM	r.t.	decomp.
3	$BiCl_3$		Toluene	r.t.	decomp.
4	$GaCl_3$		DCM	-78	no reaction
5	PTSA		DCM	-78 → r.t.	no reaction
6	$SnCl_4$		MeCN	-78 → r.t	decomp.
7	$SnCl_4$		DCM	-78	77
8	$SnCl_4$	AgOTf	DCM	-78	91
9	$SnCl_4$	$Ag(OCCF_3)$	DCM	-78	71

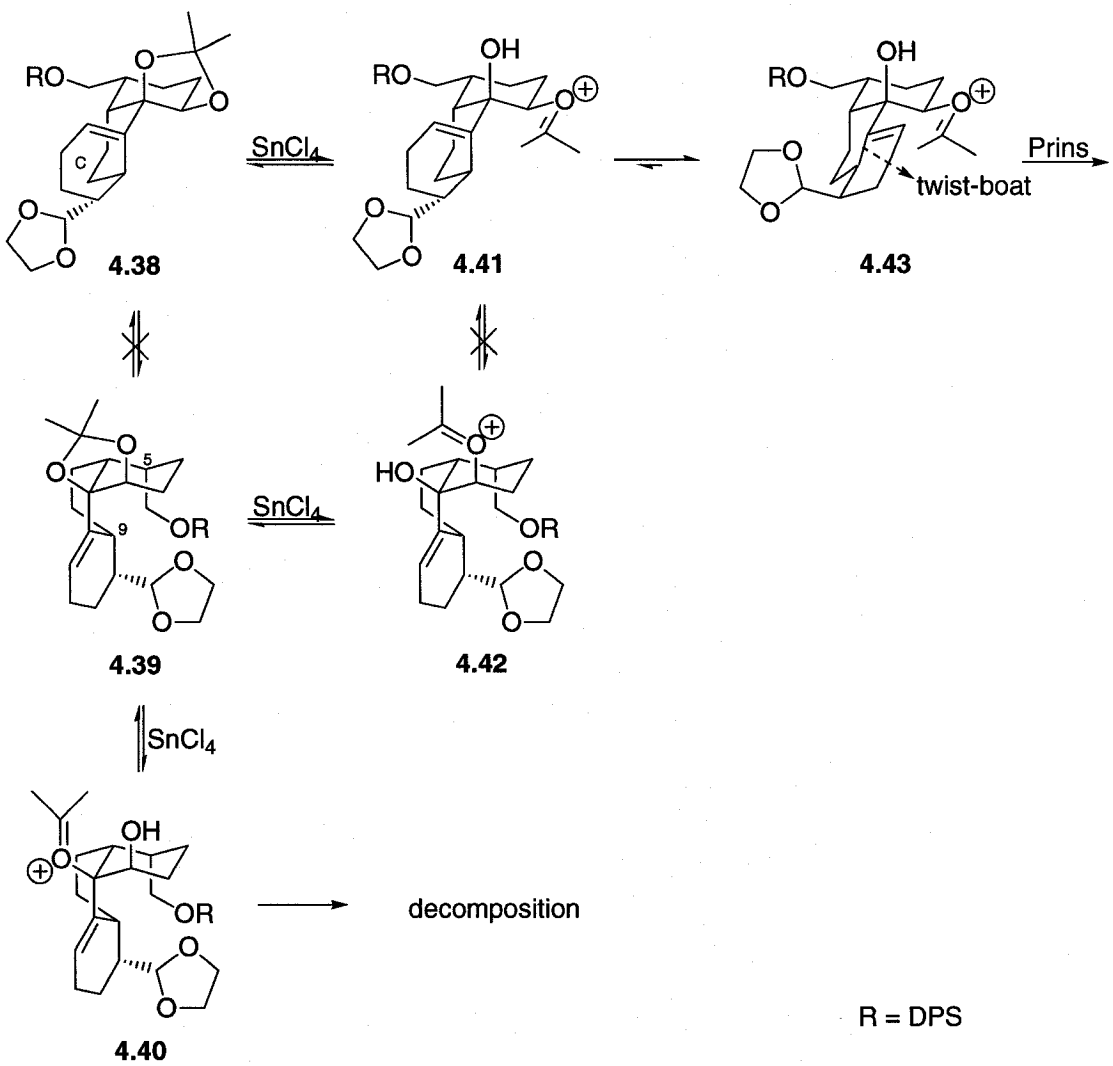


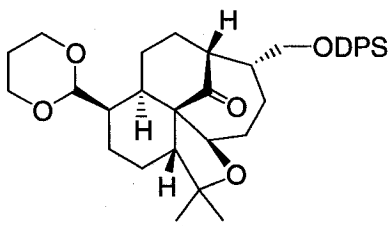
Figure 4.6 – Rationale for the Good Yields Obtained in the Generation of ***4.37***

causes severe interactions with the side-chain at C5. The Prins-pinacol reaction can therefore occur in good yields even if the alkene is more rigid.

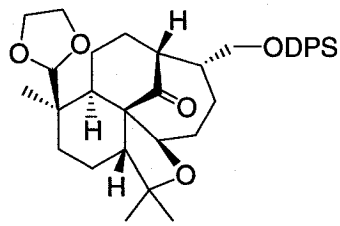
The five other ionic Diels-Alder products were submitted to tin tetrachloride conditions and the Prins-pinacol rearrangement was observed in all the cases (Table 4.3). All tricyclic Prins-pinacol precursors (**4.23**-**4.25**) rearranged in excellent yields, probably for the same reasons mentioned earlier for the rearrangement of **4.17**. The presence of the methyls in **4.24** and **4.25** seems to have a beneficial effect on the rearrangement but the reason is unclear. We postulate that they might play a role in the conformation of the alkene in order to favor the Prins cyclization. The tetracyclic Prins-pinacol precursors **4.26** and **4.27** both rearranged in low yields,

even though they have opposite stereochemistry at C and D ring junction. These results seem to indicate that the change in conformation of the alkene in order to achieve the Prins cyclization is now very difficult due to this extra ring, thus the reaction is slower and decomposition occurs. Hydrolysis of the ketal occurs during the rearrangement of **4.27** and only the ketone **4.48** is isolated. Nevertheless, the Prins-pinacol rearrangement of the Diels-Alder products shows how versatile this rearrangement is since a variety of highly functionalized bicyclic ketones were generated in a short period of time.

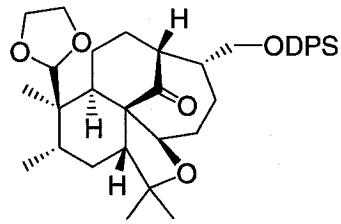
Table 4.3 – Prins-Pinacol Rearrangement of the Ionic Diels-Alder Products



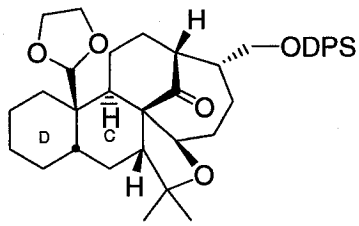
4.44



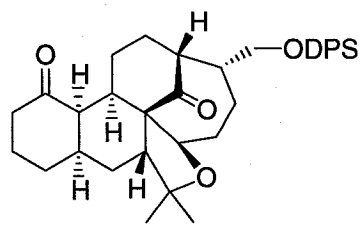
4.45



4.46



4.47



4.48

Entry	Alkene	Equivalents of $SnCl_4$[a]	Product	Yield (%)
1	**4.23**	2	**4.44**	84
2	**4.24**	2	**4.45**	98
3	**4.25**	2	**4.46**	93
4	**4.26**	1	**4.47**	21
5	**4.27**	1	**4.48**	12

[a] All reactions were performed in DCM at -78°C

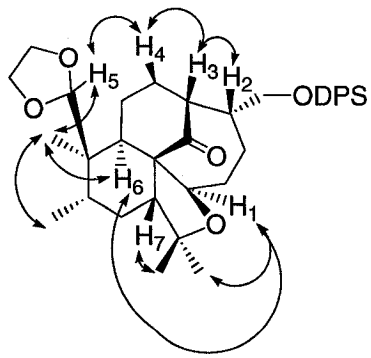
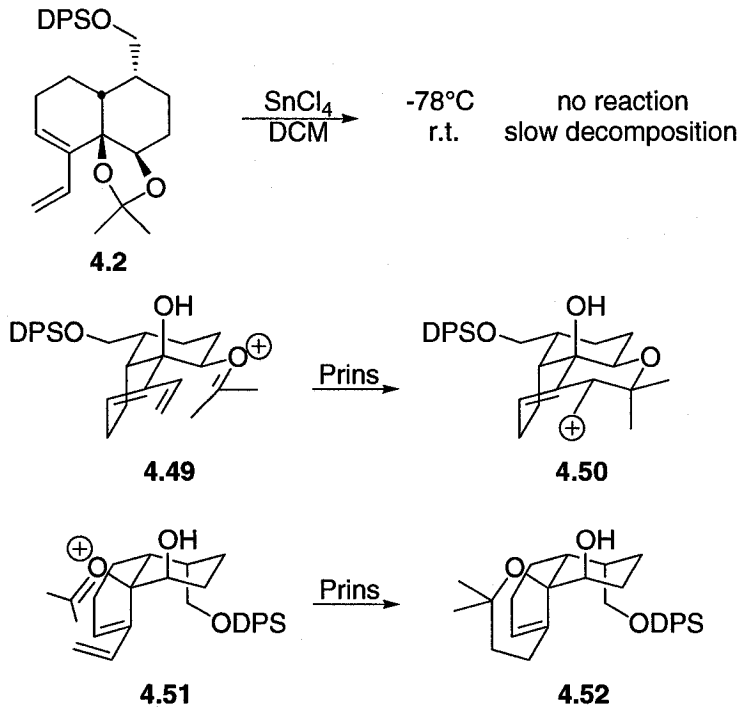


Figure 4.7 – Structure Elucidation of ***4.46*** *by 2D NMR Experiments*[77]

Tandem Ionic Diels-Alder / Prins-Pinacol Reaction

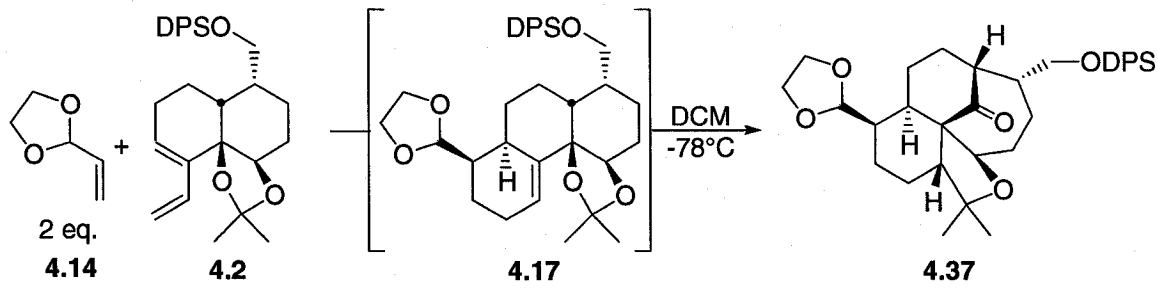
Tandem reactions are very attractive since they allow, in most cases, the diastereoselective formation of multiple carbon-carbon bonds in one pot, eliminating the need to isolate and purify intermediates.[91] Since both the ionic Diels-Alder reaction and the Prins-pinacol rearrangement are initiated by the opening of an acetal or a ketal, we hypothesized that these reactions can be performed in one pot, allowing us to access molecules with high complexity in one step. To do so, we first submitted the diene **4.2** to Prins-pinacol rearrangement conditions to make sure that it cannot undergo the Prins cyclization (Scheme 4.8). In the presence of tin tetrachloride at -78°C, only starting material was observed. This is not surprising even though two intermediates can potentially lead to a Prins cyclization since the cationic ring closure will break the conjugation of the diene and an unfavorable primary (**4.49** → **4.50**) or secondary cation (**4.51** → **4.52**) will be generated. Slow decomposition was observed at room temperature therefore it is preferable to keep the reaction temperature at -78°C for the tandem reaction.



Scheme 4.8 – Attempt to Perform a Prins-Pinacol Rearrangement with the Diene ***4.2***

In an effort to find an acid that will perform both the ionic Diels-Alder reaction and the Prins-pinacol rearrangement, we scoped a variety of Lewis and Brønsted acids (Table 4.4). All conditions that did not include tin tetrachloride or trimethylsilyl triflate gave no Diels-Alder products or Prins-pinacol products. Tin tetrachloride seems promising for the tandem reaction, affording the rearranged product in 54% yield. Addition of silver triflate does not increase the yield whereas the addition of TMSOTf dramatically increased the yields to 87%. Although the production of a super acid from tin tetrachloride and trimethylsilyl triflate is not impossible,[92] we think instead that each Lewis acid promotes one specific reaction. This hypothesis is consistent with the results obtained in entries 9 and 10 where the TMSOTf can only perform the Diels-Alder reaction and the Brønsted acid in $SnCl_4$ is required for the Prins-pinacol rearrangement to occur since the presence of a hindered base only gave rise to the Diels-Alder product.

Table 4.4 – Tandem Ionic Diels-Alder / Prins-Pinacol Rearrangement with ***4.14***



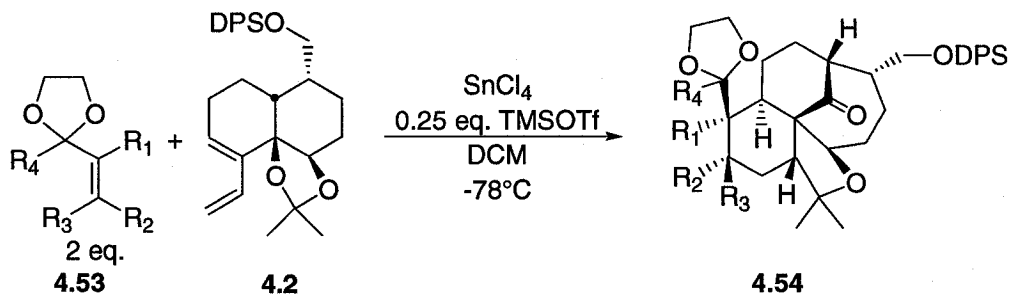
Entry	Acid	Equivalents of Acid	Additive	Equivalents of Additive	Product	Yield (%)
1			AgOTf	1	no reaction	
2	$Bi(OTf)_3$	1			no reaction	
3	$GaCl_3$	1			no reaction	
4	PTSA	1			no reaction	
5	$SnCl_4$	1.25			**4.37**	48
6	$SnCl_4$	2			**4.37**	54
7	$SnCl_4$	2	AgOTf	1	**4.37**	43
8	$SnCl_4$	1	TMSOTf	1	**4.37**	87
9			TMSOTf	1	**4.17**	85
10	$SnCl_4$	1	TMSOTf DTBMP	1 2	**4.17**	76

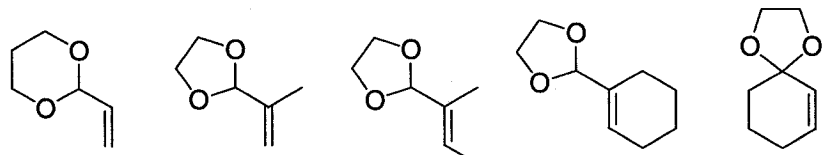
The optimum ratio of tin tetrachloride to trimethylsilyl triflate was then determined to be 4 to 1, giving a 96% yield for this transformation (Table 4.5). The yield is higher than the overall yield of these reactions performed stepwise and this is probably due to the fact that this combination of acids is ideal to promote each reaction very quickly, preventing the degradation to occur. It is really spectacular how the relatively simple *cis*-decalin **4.2** can be transformed into the highly functionalized tetracyclic bridgehead ketone **4.37** in excellent yields. Three stereocenters and one quaternary center are formed during this reaction, which is another demonstration of the power of tandem reactions. Unfortunately, the results shown in Table 4.5 were collected within three weeks and when the tandem ionic Diels-Alder / Prins-pinacol

Table 4.5 – Optimization of the Tandem Reaction with ***4.14***

Entry	Equivalents of $SnCl_4$	Equivalents of TMSOTf	Yield of **4.37** (%)
1	0.50	1.00	58
2	1.00	2.00	67
3	1.00	1.00	87
4	1.00	0.25	96
5	1.00	0.05	48

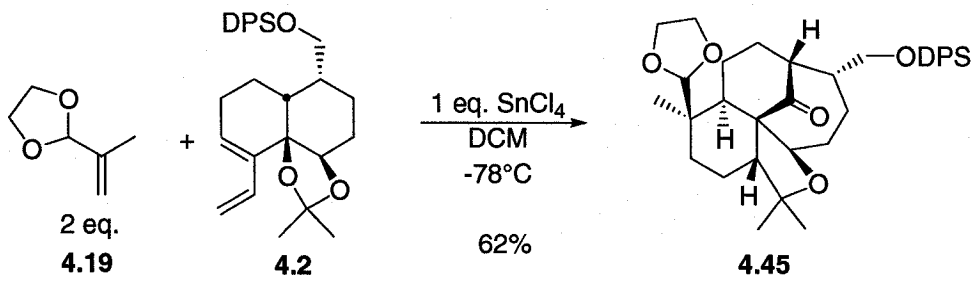
Table 4.6 – Tandem Reactions with a Variety of Gassman-Type Activated Dienophiles





Entry	Dienophile	Equivalents of $SnCl_4$[a]	Product	Yield (%)
1	**4.18**	2	**4.44**	69
2	**4.19**	3	**4.45**	44
3	**4.20**	3	**4.46**	44
4	**4.21**	3	**4.47**	10
5	**4.22**	3	**4.27**	58

rearrangement was performed with a new bottle of tin tetrachloride, a decrease in yield of up to 20% was observed. This means that optimization is required every time the bottle of tin tetrachloride is changed since the quantity of Brønsted acid in $SnCl_4$ varies from one bottle to another. Nevertheless, the conditions of entry 4 were used for the tandem ionic Diels-Alder / Prins-pinacol rearrangement of other Gassman-type activated dienophiles and the results are shown in Table 4.6. Modest yields were obtained with acyclic dienophiles whereas low yields were obtained with **4.21** and only the Diels-Alder Product was isolated with **4.22**. The later result is not surprising since the Prins-pinacol rearrangement of **4.27** was occurring only with 12 % yields. These results are unoptimized yields and higher yields can probably be obtained since the tandem reaction with **4.19** was found to occur in better yields when trimethylsilyl triflate wasn't added to the solution (Scheme 4.9).



*Scheme 4.9 – Tandem Ionic Diels-Alder / Prins-Pinacol Rearrangement with **4.19***

Conclusion

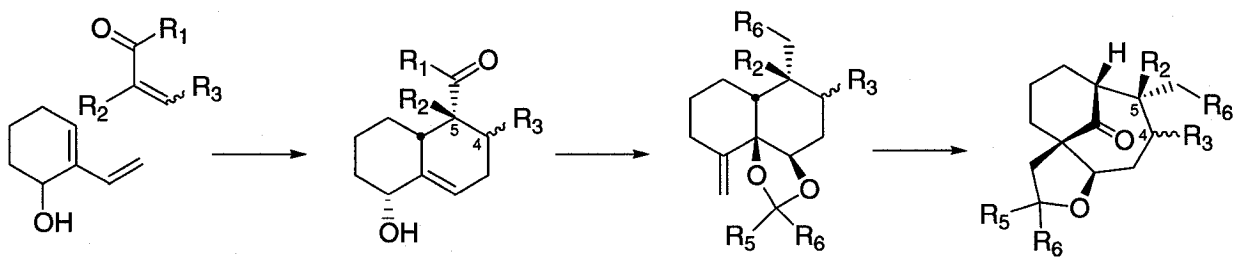
The ionic Diels-Alder reaction followed by the Prins-pinacol rearrangement proved to be very efficient for the formation of four or five stereocenters, where one is a quaternary carbon center next to the newly formed bridgehead ketone. Gassman-type activated dienophiles proved to be very efficient and allow us to perform these two reactions in tandem. The Prins-pinacol rearrangement's efficacy seems to be highly dependant on the capacity of the alkene to undergo the Prins cyclization. To the best of our knowledge, this is the first example of a tandem Diels-Alder / Prins-pinacol reaction and it is the first methodology that generates such highly functionalized bicyclic ketones so selectively and rapidly.

5

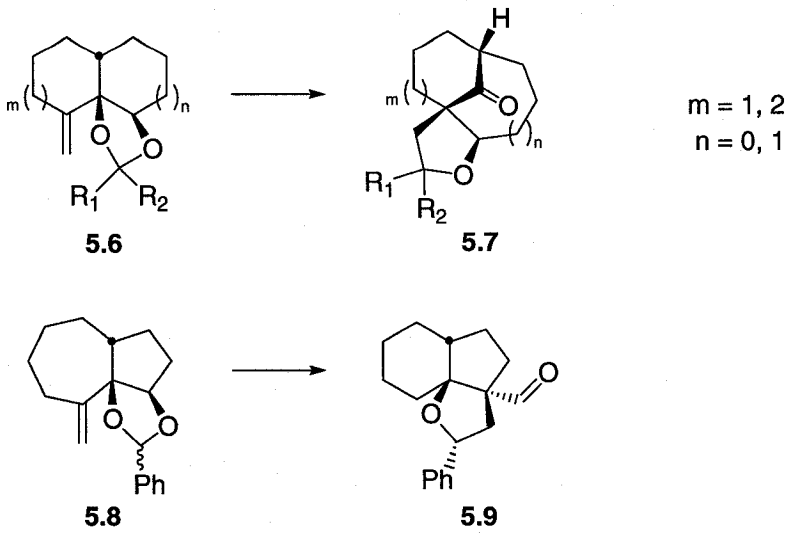
General Conclusion

Summary

The first Brønsted acid mediated Prins-pinacol synthesis of *cis*-fused bicyclic bridgehead ketones was presented. The rearrangement precursors were obtained through a high yielding and versatile synthetic route where the stereocenters were generated from hydroxyl-directed Diels-Alder reactions. Benzylidene acetals and substitution at the C5 position seems to be a reliable solution to increase the rearrangement efficiency. The importance of the conformation of the Prins-pinacol precursor was assessed by analyzing the effects of substitution at C4 and C5 and by generating conformationally rigid substrates.

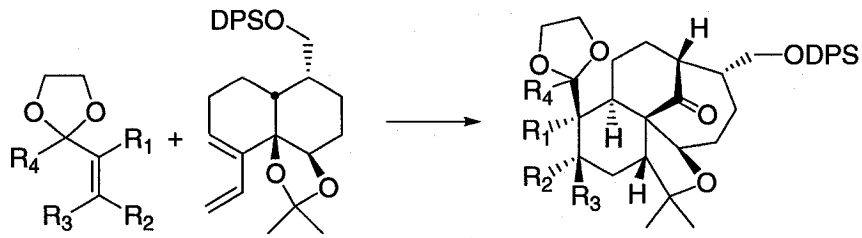


Generation of Prins-pinacol precursors with various ring sizes allowed for the development of the first methodology that can generate bicyclo[*m.n.*1]alkanones with various ring sizes. Ring sizes that favor the Prins cyclization are those that gave the more efficient rearrangement. In the systems were the Prins cyclization was difficult, fragmentation or other cationic reactions were occurring. As a result, many byproducts were isolated, such the aldehyde **5.9**, which results in what would be the first Prins-pinacol-pinacol rearrangement ever observed.



5.6 **5.7** **5.8** **5.9**

Ionic Diels-Alder reactions using Gassman-type activated dienophiles were used to generate polycyclic Prins-pinacol precursors and new stereocenters. This reaction can also be performed in tandem in order to achieve high complexity in one step. This is the first example of a tandem Diels-Alder / Prins-pinacol rearrangement and its capacity to generate bicyclo[4.3.1]decanones is astonishing.

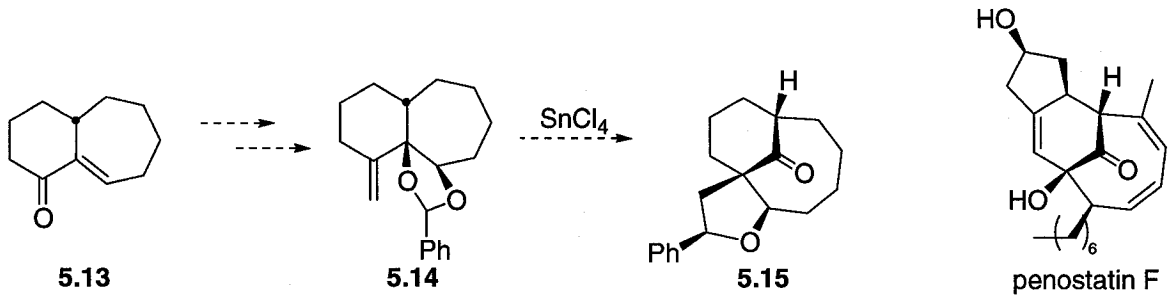


5.10 **5.11** **5.12**

Outlook

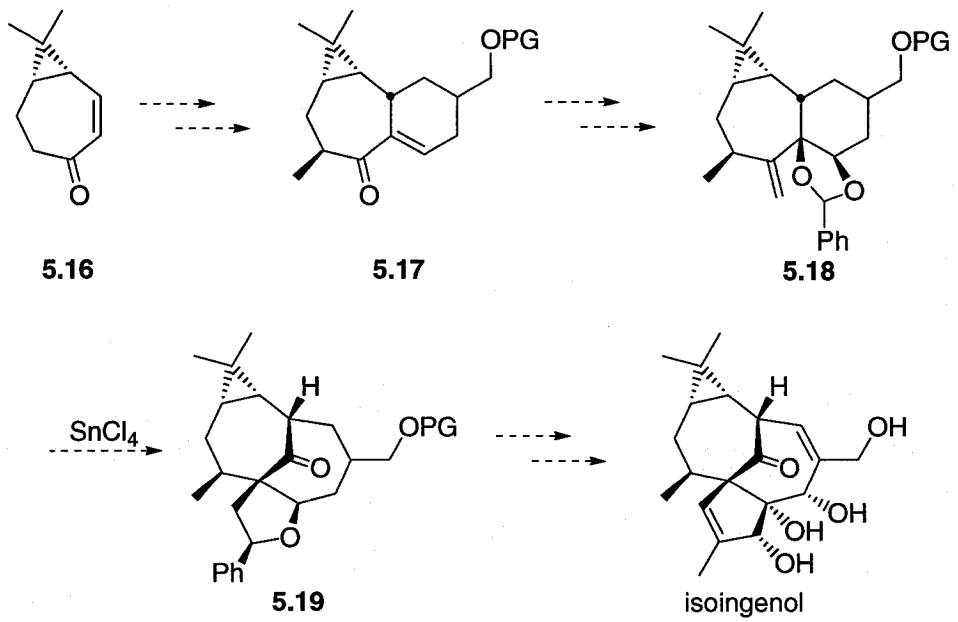
Even though numerous bicyclo[4.3.1]decanones have been synthesized during this study, no known natural compounds possess this skeleton. However, this methodology can be applied to the synthesis of other ring sized systems. For example, the bicyclo[5.4.0]undecane **5.13**, which can be obtained from literature procedures,[93] can be submitted to the same reaction sequence as the one mentioned in this work to obtain the Prins-pinacol precursor **5.14**. The Prins-pinacol

rearrangement of **5.14** should give bicyclo[5.3.1]undecanone **5.15**, which corresponds to the core of biologically active penostatin F.



5.13 **5.14** **5.15** penostatin F

We can also use our methodology to develop the highly functionalized bicyclo[4.4.1]undecanone core, which can eventually lead to the synthesis of isoingenol. The bicyclo[5.1.0]octenone **5.16**, which can be obtained from literature procedures,[94] can be used to generate the bicyclic enone **5.17** with the same chemistry that was used in chapter 3. This intermediate can then provide the Prins-pinacol precursor **5.18**, which upon treatment with tin tetrachloride, may provide the core of isoingenol. Further chemical modifications would complete the first synthesis of isoingenol.



5.16 **5.17** **5.18**

5.19 isoingenol

Claims to Original Research

1. Explored the first synthesis of *cis*-fused bicyclo[4.3.1]decanones via a Prins-pinacol rearrangement and rationalized the effect of the substituents and the protecting groups.
2. Successfully elaborated, with my fellow colleagues, the first methodology that allows the generation of a variety of *cis*-fused bicyclic bridgehead ketones with different ring sizes.
3. Developed the first tandem Diels-Alder / Prins-pinacol reaction in order to generate highly functionalized polycyclic bridgehead ketones.

Publication From This Work

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." *Org. Lett.* **2005**, *7*, 5921.

Poster Presentations

Lavigne, R. M. A.; L., Barriault, L. "Construction of Bicyclic[4.*n*.1]ketones using a Prins-Pinacol Rearrangement"

1. April 2005, Symposium International de Synthèse Organique de l'Université de Montréal (SISOUM), Université de Montréal, Québec, Canada.
2. June 2005, Ottawa-Carleton Chemical Institute Symposium (OCCI Day), University of Ottawa, Ontario, Canada.
3. June 2005, Organic Synthesis Day, University of Ottawa, Ontario, Canada.
4. November 2005, Québec-Ontario Minisymposium in Synthetic and BioOrganic Chemistry (QOMSBOC), St-Adèle, Québec, Canada.

6

Experimental

General Experimental

All reactions were performed under an argon atmosphere in flame-dried glassware equipped with a magnetic stirbar and a rubber septum unless otherwise indicated. Solvents used were freshly distilled prior to use: ether, 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.

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, *para*-anisaldehyde 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 400 MHz, Bruker Avance 500 MHz or Varian INOVA 500 MHz spectrometers in the specified deuterated solvent. IR spectra were recorded on a Bomen Michaelson 100 FT-IR spectrometer. HRMS spectra were obtained using a Kratos Analytical Concept spectrometer, and melting points were recorded using a Gallenkamp P1106G Melting Point Apparatus.

General Procedures

Procedure A : Methylation with Cerium Chloride

Dry $CeCl_3$ (3 eq.) is stirred in THF (0.5 M) for 2 hours at 0°C. The ketone (1 eq.) is subsequently canulated in the solution with THF (0.25 M) and the reaction mixture is stirred overnight. Methyllithium (6 eq.) is then added dropwise in the solution at -78°C and the reaction is warmed to room temperature until TLC revealed no starting material. The reaction is quenched with NH_4Cl (sat. aq.), extracted with diethyl ether, dried over $MgSO_4$, filtered and concentrated *in vacuo*.

Procedure B : Elimination with Thionyl Chloride

Thionyl chloride (2 eq.) is added dropwise to a solution of alcohol (1 eq.) and 4-dimethylaminopyridine (6 eq.) in CH_2Cl_2 (0.1 M) at 0°C and the reaction is warmed to room temperature until TLC revealed no starting material. The reaction is quenched with $NaHCO_3$ (sat. aq.), extracted with CH_2Cl_2, dried over $MgSO_4$, filtered and concentrated *in vacuo*.

Procedure C : General Prins-Pinacol Rearrangement

Lewis acid or Brønsted acid (1 eq.) is added to a solution of the Prins-pinacol precursor (1 eq.) in CH_2Cl_2 (0.5 M) at the specified temperature. When the TLC revealed no starting material, the reaction is quenched dropwise with triethylamine until the solution becomes colorless, and $NaHCO_3$ (aq. sat.), extracted with CH_2Cl_2, dried over $MgSO_4$, filtered and concentrated *in vacuo*.

Procedure D : Formation of a Benzylidene Acetal or a Methylidene Acetal

The acetal (1.2 eq.), followed by tin dichloride (0.01 eq.), are added to a solution of diol (1 eq.) in 1,2-dimethoxyethane (12 mL) at room temperature and the reaction is refluxed until TLC revealed no starting material. The reaction is quenched with $NaHCO_3$ (aq. sat.), extracted with CH_2Cl_2, dried over $MgSO_4$, filtered and concentrated *in vacuo*.

Procedure E : Deprotection of a Benzoate

Potassium carbonate (7 eq.) is added to a solution of the benzoate (1 eq.) in methanol (0.1 M) and benzene (0.1 M) at room temperature and the reaction is stirred at reflux until TLC revealed no starting material. The reaction is filtered through a celite pad and concentrated *in vacuo*.

Procedure F : Dess-Martin Periodinane Oxidation

Dess-Martin periodinane (1.2 eq.) is added to a solution of alcohol (1 eq.) in CH_2Cl_2 (0.1 M) at room temperature and the reaction is stirred at this temperature until TLC revealed no starting material. The reaction is quenched with sodium sulfite (sat. aq.) and the resulting mixture is stirred 2 hours before being extracted with CH_2Cl_2, dried over $MgSO_4$, filtered and concentrated *in vacuo*.

Procedure G : Hydroxy-Directed Diels-Alder

Triethylamine or lutidine (3 eq.), followed by the diene (1 eq.), are added to a solution of magnesium bromide etherate (2 eq.) in CH_2Cl_2 (0.1 M) at room temperature and the reaction is allowed to stir for 20 minutes. The dienophile (2.2 eq.) is then added and the reaction is stirred at this temperature until TLC revealed no starting material. The reaction is quenched with NH_4Cl, extracted with CH_2Cl_2, dried over $MgSO_4$, filtered and concentrated *in vacuo*.

Procedure H : Reduction with Lithium Aluminium Hydride

Lithium aluminum hydride (1.5 eq.- 4.0 eq.) is added to a solution of aldehyde or ester (1 eq.) in THF (0.1 M) at -78°C and the reaction is warmed at 0°C until TLC revealed no starting material. The reaction is slowly quenched with water, a solution of KOH 0.1 M, water and a solution sodium tartrate 0.5 M. The reaction mixture is allowed to stir for 4 hours at room temperature. The product is then extracted with diethyl ether, dried over $MgSO_4$, filtered and concentrated *in vacuo*.

Procedure I : Benzoate Protection of an Alcohol

4-Dimethylaminopyridine (0.05 eq.), followed by benzoyl chloride (1.15 eq.) are added to a solution of the alcohol (1 eq.) in pyridine (3 eq.) and CH_2Cl_2 (0.1 M) at room temperature and

the reaction is stirred at this temperature until TLC revealed no starting material. The reaction is quenched with NH_4Cl (sat. aq.), extracted with CH_2Cl_2, dried over $MgSO_4$, filtered and concentrated *in vacuo*.

Procedure J : TES Protection of an Alcohol

4-Dimethylaminopyridine (0.1 eq.), followed by triethylsilyl chloride (1.5 eq.) are added to a solution of the alcohol (1 eq.) in triethylamine (3 eq.) and THF (0.1 M) at room temperature and the reaction is stirred at this temperature until TLC revealed no starting material. The reaction is quenched with NH_4Cl (sat. aq.), extracted with diethyl ether, dried over $MgSO_4$, filtered and concentrated *in vacuo*.

Procedure K : Dihydroxylation with Osmium Tetraoxide

4-Methylmorpholine N-oxide (2 eq.), followed by a solution of osmium tetraoxide 4% in water (0.05 eq.) are added to a solution of the alkene (1 eq.) in water (0.5 M) and THF (0.1 M) at room temperature and the reaction is refluxed until TLC revealed no starting material. The reaction is quenched with sodium sulfite (sat. aq.) and the solution is stirred for 20 additional minutes before being extracted with EtOAc. The organic layers are combined and washed with brine, then dried over $MgSO_4$, filtered and concentrated *in vacuo*.

Procedure L : Acetonide Formation from a Diol

PTSA (0.01 eq.) is added to a solution of the diol (1 eq.) and 2-methoxypropene (3 eq.) in CH_2Cl_2 (0.1 M) at 0°C and the reaction is stirred at this temperature until TLC revealed no starting material. The reaction is quenched with $NaHCO_3$ (sat. aq.), extracted with CH_2Cl_2, dried over $MgSO_4$, filtered and concentrated *in vacuo*.

Procedure M : Benzyl Protection of an Alcohol

The alcohol (1 eq.) is canulated with THF (0.2 M) into a flask containing NaH (1.15 eq.) at 0°C and the reaction mixture is allowed to stir for 10 minutes. Tetrabutylammonium iodide (0.1 eq.) is subsequently added as a solution in THF (0.2 M), followed by benzyl bromide (1.1 eq.) and the reaction is warmed to room temperature until TLC revealed no starting material.

The reaction is quenched with $NaHCO_3$ (sat. aq.), extracted with diethyl ether, dried over $MgSO_4$, filtered and concentrated *in vacuo*.

Procedure N : Wittig Olefination

Potassium *tert*-butoxide (3 eq.) is added to the corresponding phosphonium salt (3 eq.) in toluene (0.5 M) at room temperature and the reaction mixture is allowed to stir for 20 minutes. The ketone (1 eq.) is canulated with toluene (0.25 M) and the reaction is refluxed until TLC revealed no starting material. The reaction is quenched with NH_4Cl (sat. aq.), extracted with diethyl ether, dried over $MgSO_4$, filtered and concentrated *in vacuo*.

Procedure O : Diels-Alder with Gassman-Type Activated Dienophiles

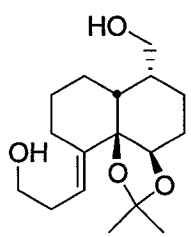
Trimethylsilyl triflate (1 eq.) is added to a solution of diene (1 eq.) and dienophile (2 eq.) in CH_2Cl_2 (0.05 M) at -78°C. The reaction mixture is stirred at -78°C until TLC revealed no starting material. The reaction is quenched with triethylamine and $NaHCO_3$ (aq. sat.), extracted with CH_2Cl_2 , dried over $MgSO_4$, filtered and concentrated *in vacuo*.

Procedure P : Tandem Diels-Alder/Prins-Pinacol Reaction

Trimethylsilyl triflate (0.25 eq.) is added to a solution of the diene **4.2** (1 eq.) and the dienophile (2 eq.) in CH_2Cl_2 (0.05 M) at -78°C. Tin tetrachloride (1-3 eq.) is then added to the solution and the reaction is stirred at -78°C until TLC revealed no starting material. The reaction is quenched with triethylamine until the solution becomes colorless, and $NaHCO_3$ (aq. sat.), extracted with CH_2Cl_2, dried over $MgSO_4$, filtrated and concentrated *in vacuo*.

Experimental Procedures and Characterization

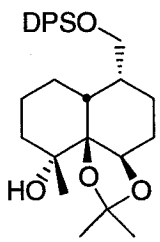
3-(6-Hydroxymethyl-2,2-dimethyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-ylidene)-propan-1-ol (2.14)



Tetrabutylammonium fluoride (0.25 mL, 0.25 mmol) was added to the protected diol **2.1**[71] (40 mg, 62 μmol) in THF (1 mL) at room temperature and the reaction

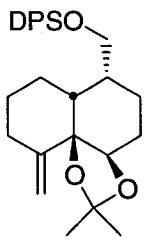
was stirred at room temperature overnight. The reaction mixture was concentrated *in vacuo* and purified by silica gel flash chromatography with 45:40:10:5 CH_2Cl_2:EtOAc:acetone:AcOH to give **2.14** as a yellow oil (18 mg, 62 μmol, quant.), with a Rf = 0.11 (50% EtOAc/hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.68 (dd, J = 7.4, 7.3 Hz, 1H), 4.08 (s, 1H), 3.63 (dd, J = 7.4, 7.4 Hz, 2H), 3.51 (dt, J = 14.7, 7.4, 2H), 2.65 (d, J = 11.9 Hz, 2H), 2.39-2.26 (m, 3H), 2.07-2.01 (m, 1H), 1.93-1.75 (m, 3H), 1.73-1.67 (m, 2H), 1.59-1.48 (m, 4H), 1.53 (s, 3H), 1.35 (s, 3H), 1.24-1.12 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.4 (C_4), 116.3 (CH), 107.3 (C_4), 84.5 (C_4), 77.8 (CH), 65.7(CH_2), 62.6 (CH_2), 42.2 (CH), 33.4 (CH), 30.6 (CH_2), 27.0 (CH_3), 27.0 (CH_2), 26.9 (CH_2), 26.2 (CH_3), 23.9 (CH_2), 22.7 (CH_2), 17.2 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3266 (br), 2929 (s), 2855 (m), 1449 (m), 1253 (m), 1169 (m), 1054 (s); HRMS (EI) *m/z* (M^+) calcd 296.19876, found 296.19929.

6-(*tert*-Butyl-diphenyl-silanyloxymethyl)-2,2,10-trimethyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-ol (2.28)



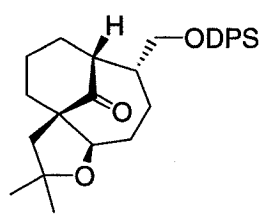
Procedure A: $CeCl_3$ (207 mg, 0.841 mmol), THF (1.7 + 1.1 mL), ketone **2.27** (138 mg, 0.280 mmol), methyllithium (1.05 mL, 1.68 mmol), warmed to room temperature for 50 minutes. Flash chromatography with 15% EtOAc/hexanes gave **2.28** as a pale yellow oil (127 mg, 0.250 mmol, 89%), with a Rf = 0.42 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (dd, J = 6.3, 1.3 Hz, 4H), 7.41-7.34 (m, 6H), 4.67 (s, 1H), 3.58-3.49 (m, 2H), 2.50-2.47 (m, 1H), 2.01-1.96 (m, 1H), 1.92-1.88 (m, 1H), 1.80-1.68 (m, 2H), 1.58-1.54 (m, 3H), 1.52 (s, 3H), 1.48 (s, 3H), 1.40-1.35 (m, 2H), 1.33 (s,3H), 1.17-1.07 (m, 2H), 1.03 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.6 (CH), 134.2 (C_4), 129.5 (CH), 127.6 (CH), 106.9 (C_4), 87.0 (C_4), 73.8 (C_4), 73.1 (CH), 66.7 (CH_2), 38.7 (CH), 37.7 (CH_2), 33.2 (CH), 27.7 (CH_3), 27.4 (CH_3), 26.9 (CH_3), 25.0 (CH_3), 23.3 (CH_2), 22.9 (CH_2), 21.3 (CH_2), 19.3 (C_4), 17.4 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3487 (br), 3071 (w), 2932 (s), 2859(s), 1589 (w), 1471 (m), 1428 (m), 1378 (m), 1364 (m), 1253 (m), 1207 (m), 1184 (m), 1111 (s), 1056 (s), 1023 (m), 1000 (m); HRMS (EI) *m/z* (M^+) calcd 508.30089, found 508.30197.

tert-Butyl-(2,2-dimethyl-10-methylene-octahydro-naphtho[1,8a-*d*][1,3]dioxol-6-ylmethoxy)-diphenylsilane (2.29)



Procedure B: Thionyl chloride (40 μL, 0.56 mmol), alcohol **2.28** (143 mg, 0.282 mmol), 4-dimethylaminopyridine (206 mg, 1.69 mmol), CH_2Cl_2 (2.8 mL), stirred for 30 minutes. Flash chromatography with 10% EtOAc/hexanes gave **2.29** as a yellow oil (136 mg, 0.277 mmol, 98%), with a Rf = 0.83 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66-7.62 (m, 4H), 7.41-7.34 (m, 6H), 5.14 (d, J = 2.4 Hz, 1H), 4.77 (s, 1H), 4.10-4.09 (m, 1H), 3.59-3.48 (m, 2H), 2.53-2.47 (m, 1H), 2.35 (d, J = 12.9 Hz, 1H), 2.08-1.99 (m, 2H), 1.88-1.71 (m, 4H), 1.65-1.62 (m, 1H), 1.55 (t, J = 13.7 Hz, 1H), 1.55 (s, 3H), 1.39 (s, 3H), 1.35-1.23 (m, 1H), 1.16-1.10 (m, 1H), 1.01 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.7 (C_4), 135.6 (CH), 134.1 (C_4), 129.5 (CH), 127.6 (CH), 107.3 (CH_2), 84.3 (C_4), 77.8 (CH), 66.6 (CH_2), 42.2 (CH), 34.4(CH_2), 28.2 (CH), 27.4 (CH_2), 27.0 (CH_3), 26.9 (CH_3), 26.3 (CH_3), 24.3 (CH_2), 22.5 (CH_2), 19.3 (C_4), 17.3 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3080 (w), 3068 (w), 3001 (w), 2933 (s), 2873 (m), 2859(m), 1491 (m), 1428 (m), 1392 (m), 1250 (m), 1232 (m), 1108 (s), 1062 (s); HRMS (EI) *m/z* (M^+) calcd 490.29032, found 490.29006.

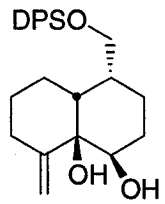
8-(_tert_-Butyl-diphenyl-silanyloxymethyl)-3,3-dimethyl-4-oxa-tricyclo[7.3.1.0^{1,5}]tridecan-13-one (2.30)



Procedure C: Bismuth trichloride (18 mg, 43 μmol), Prins-pinacol precursor **2.29** (21 mg, 43 μmol), CH_2Cl_2 (1.0 mL), at room temperature, stirred for 3 hours. Flash chromatography with 10% EtOAc/hexanes gave **2.30** as a colorless oil (15 mg, 31 μmol, 85%), with a Rf = 0.67 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63-7.61 (m, 4H), 7.43-7.35 (m, 6H), 4.08 (dd, J = 11.4, 4.2 Hz, 1H), 3.58-3.50 (m, 2H), 2.58-2.54 (m, 2H), 2.29-2.27 (m, 1H), 2.08-1.96 (m, 3H), 1.85-1.57 (m, 5H), 1.41 (dd, J = 26.7, 12.79 Hz, 1H), 1.29 (s, 3H), 1.25 (s, 3H), 1.34-1.20 (m, 2H), 1.02 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 213.3 (C_4), 135.5 (CH), 134.8(C_4), 129.7(CH), 127.7(CH), 85.5 (CH), 80.6 (C_4), 65.8 (CH_2), 60.7 (C_4), 49.3 (CH), 47.2(CH_2), 46.0 (CH), 40.8 (CH_2), 33.8 (CH_2), 29.7 (CH_3), 27.6 (CH_3), 26.8 (CH_3), 24.7 (CH_2), 24.5 (CH_2), 21.4 (CH_2), 19.3 (C_4); IR (CH_2Cl_2, cm^{-1}) 3073 (w), 3054 (w), 2930 (s), 2858 (m),

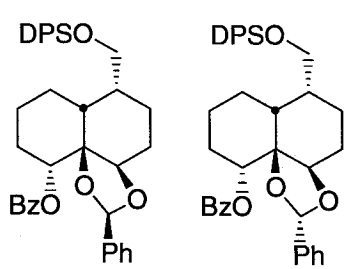
1698 (s), 1653 (m), 1559 (w), 1540 (w), 1507 (w), 1472 (m), 1457 (m), 1428 (m), 1362 (w), 1272 (w), 1112 (s), 1087 (m), 1043 (m); HRMS (EI) *m/z* (M^+) calcd 490.29032, found 433.21990.

4-(*tert*-Butyl-diphenyl-silanyloxymethyl)-8-methylene-octahydro-naphthalene-1,8a-diol (2.31)



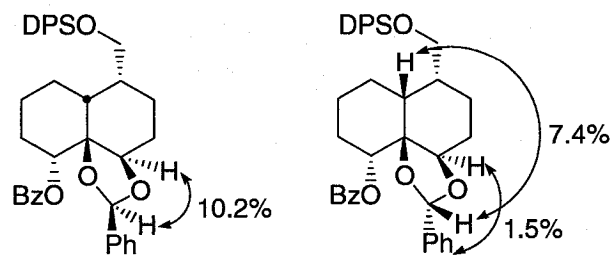
Tin dichloride (18 mg, 43 μmol) was added to a solution of **2.29** (21 mg, 43 μmol) in CH_2Cl_2 (0.7 mL) at room temperature and the reaction was stirred overnight. The reaction was quenched with $NaHCO_3$ (aq. sat.), extracted with CH_2Cl_2, dried over $MgSO_4$, filtered and concentrated *in vacuo*. Flash chromatography with 10-30 % EtOAc/hexanes gave **2.30** (7.0 mg, 14 μmol, 40%) and **2.31** as a white solid (6.5 mg, 0.15 mmol, 43%, 83 % overall yield), with a Rf = 0.28 (25% EtOAc/hexanes). ^1H NMR (300 MHz, $CDCl_3$) δ 7.64-7.61 (m, 4H), 7.40-7.32 (m, 6H), 5.11 (d, J = 2.4 Hz, 1H), 4.97 (s, 1H), 3.90 (dd, J = 11.4, 5.2 Hz), 3.50-3.43 (m, 2H), 2.40-2.34 (m, 2H), 2.02-1.81 (m, 3H), 1.67-1.49 (m, 5H), 1.36-1.17 (m, 4H), 1.01 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.7 (C_4), 136.0 (CH), 134.6 (C_4), 129.9 (CH), 127.0 (CH), 109.9 (CH_2), 77.6 (C_4), 68.5 (CH), 66.4 (CH_2), 45.6 (CH), 36.9(CH), 33.9 (CH_2), 28.8 (CH_2), 27.4 (CH_2), 27.2 (CH_3), 22.8 (CH_2), 22.8 (CH_2), 19.6 (C_4); IR (CH_2Cl_2, cm^{-1}) 3447 (br), 3071 (w), 3052 (w), 2931 (s), 2858 (s), 1734 (w), 1645 (w), 1589 (w), 1472 (m), 1460 (m), 1447 (w), 1428 (s), 1390 (m), 1361 (w), 1306(w), 1264 (w), 1112 (s), 1072 (s), 1046 (m); HRMS (EI) *m/z* (M^+-*t*Bu) calcd 393.18860, found 393.1822. Melting point: 82.2-83.1 °C.

Benzoic acid 6-(*tert*-butyl-diphenyl-silanyloxymethyl)-2-phenyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-yl ester (2.32 and 2.33)

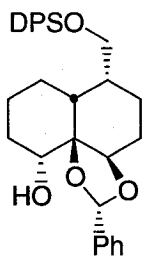


Procedure D: Benzaldehyde dimethyl acetal (0.21 mL, 1.4 mmol), tin dichloride (2.2 mg, 12 μmol), diol **2.24**[71] (66 mg, 1.2 mmol), 1,2-dimethoxyethane (12 mL), refluxed for 8 hours. Flash chromatography with 10-15% Et_2O/hexanes gave **2.32** as a pale

yellow oil (0.100 mg, 0.15 mmol, 13%), and **2.33** as white foam (480 mg, 0.74 mmol, 63%, 76% overall yield), with a respective Rf = 0.56 and 0.47 (25% EtOAc/hexanes). **2.32** ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.23 (d, J = 7.7 Hz, 2H), 7.69-7.18 (m, 18H), 6.06 (s, 1H), 5.30 (dd, J = 12.3, 5.3 Hz, 1H), 4.49 (dd, J = 10.5, 4.4 Hz, 1H), 3.61-3.33 (m, 3H), 2.42 (dd, J = 13.7, 10.1 Hz, 1H), 2.20-1.84 (m, 4H), 1.76-1.41 (m, 3H), 1.38-1.22 (m, 3H), 1.03 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.8 (C_4), 138.9 (C_4), 136.0 (CH), 135.9 (CH), 134.2 (C_4), 134.0 (C_4), 133.2 (CH), 132.4 (C_4), 130.2 (CH), 130.0 (CH), 129.9 (CH), 129.5 (CH), 128.8 (CH), 128.0 (CH), 128.0 (CH), 127.0 (CH), 95.5 (CH), 81.3 (C_4), 73.8 (CH), 72.8 (CH), 66.1 (CH_2), 38.3 (CH), 37.4 (CH), 27.2 (CH_3), 27.1 (CH_2), 26.4 (CH_2), 23.5 (CH_2), 22.9 (CH_2), 22.3 (CH_2), 19.6 (C_4); IR (CH_2Cl_2, cm^{-1}) 3071 (m), 3051 (m), 2952 (s), 2932 (s), 2858 (s), 1964 (w), 1901 (w), 1824 (w), 1711 (s), 1600 (w), 1588 (w), 1450 (m), 1427 (m), 1376 (w), 1315 (m), 1288 (s), 1265 (s), 1111 (s), 1087 (m), 1025 (m); HRMS (EI) *m/z* (M^+-H) calcd 645.30363, found 645.30081. NOE experiments were performed in order to obtain the correlation illustrated below. **2.33** ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82-7.73 (m, 6H), 7.50-7.26 (m, 11H), 6.98-6.88 (m, 3H), 6.20 (s, 1H), 5,29 (dd, J = 12.1, 4.4 Hz, 1H), 4.86 (t, J = 4.3 Hz, 1H), 3.75-3.60 (m, 2H), 2.54-2.43 (m, 1H), 2.34 (dt, J = 12.8, 4.2 Hz, 1H), 2.20-2.01 (m, 3H), 1.92-1.69 (m, 3H), 1.62-1.45 (m, 1H), 1.44-1.15 (m, 3H), 1.14 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.2 (C_4), 139.7 (C_4), 136.1 (CH), 134.3 (C_4), 132.8 (CH), 130.7 (C_4), 130.1 (CH), 130.1 (CH), 128.8 (CH), 128.4 (CH), 128.2 (CH), 128.1 (CH), 126.0 (CH), 103.7 (CH), 85.2 (C_4), 77.8 (CH), 73.7 (CH), 66.6 (CH_2), 41.3 (CH), 34.0 (CH), 30.9 (CH_2) , 27.4 (CH_3), 25.4 (CH_2), 24.6 (CH_2), 23.2 (CH_2), 19.8 (C_4), 19.0 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3069 (w), 2934 (s), 2892 (m), 2859 (s), 1960 (w), 1900 (w), 1717 (s), 1602 (w), 1587 (w), 1470 (w), 1462 (w), 1427 (m), 1389 (w), 1360 (w), 1316 (w), 1275 (s), 1112 (s), 1070 (m), 1027 (m), 1009 (w); HRMS (EI) *m/z* (M^+) calcd 646.31145, found 646.31335. NOE experiments were performed in order to obtain the correlations illustrated below:

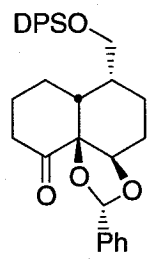


6-(*tert*-Butyl-diphenyl-silanyloxymethyl)-2-phenyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-ol (2.34)



Procedure E: Potassium carbonate (60 mg, 0.45 mmol), benzoate **2.33** (40 mg, 62 μmol), methanol (0.62 mL), benzene (0.62 mL), refluxed overnight. Flash chromatography with 15% EtOAc/hexanes gave **2.34** as a pale yellow oil (23 mg, 42 μmol, 69%), with a Rf = 0.61 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76-7.68 (m, 4H), 7.59-7.56 (m, 2H), 7.50-7.37 (m, 9H), 6.20 (s, 1H), 4.64 (t, J = 4.7 Hz, 1H), 3.73-3.58 (m, 3H), 2.44-2.32 (m, 1H), 2.14 (dt, J = 13.0, 4.5 Hz, 1H), 2.04-1.94 (m, 3H), 1.85-1.69 (m, 2H), 1.67-1.57 (m, 1H), 1.41-1.14 (m, 4H), 1.14 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.8 (C_4), 136.1 (CH), 134.3 (C_4), 130.1 (CH), 129.4 (CH), 129.2 (CH), 128.1 (CH), 126.2 (CH), 102.6 (CH), 87.2 (C_4), 76.3 (CH), 73.2 (CH), 66.7 (CH_2), 40.4 (CH), 34.4 (CH), 31.9 (CH_2), 27.4 (CH_3), 25.3 (CH_2), 24.6 (CH_2), 23.2 (CH_2), 19.7 (C_4), 19.2 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3486 (br), 3069 (w), 3048 (w), 2932 (s), 2893 (m), 2859 (s), 1958 (w), 1892 (w), 1738 (m), 1588 (w), 1470 (m), 1462 (m), 1451 (m), 1427 (m), 1389 (m), 1360 (w), 1220 (w), 1105 (s), 1067 (m), 1027 (m); HRMS (EI) *m/z* (M^+) calcd 542.28524, found 542.28501.

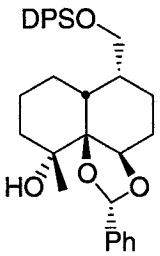
6-(*tert*-Butyl-diphenyl-silanyloxymethyl)-2-phenyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-one (2.35)



Procedure F: Dess-Martin periodinane (0.224 g, 0.528 mmol), alcohol **2.34** (0.239 g, 0.440 mmol), CH_2Cl_2 (4.4 mL), stirred for 20 minutes. Flash chromatography with 15% EtOAc/hexanes gave **2.35** as a white foam (0.222 g, 0.410 mmol, 93%), with a Rf = 0.53 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75-7.64 (m, 6H), 7.53-7.39 (m, 9H), 6.24 (s, 1H), 4.61 (t, J = 7.6 Hz, 1H), 3.72-3.56 (m, 2H), 2.68-2.44 (m, 3H), 2.35-2.13 (m, 2H), 2.11-2.03 (m, 1H), 1.89-1.55 (m, 2H), 1.61-1.38 (m, 4H), 1.14 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.3 (C_4), 138.2 (C_4), 136.1 (CH), 134.1 (C_4), 130.2 (CH), 129.4 (CH), 128.5 (CH), 128.2 (CH), 127.5 (CH), 102.9 (CH), 88.9 (C_4), 75.6 (CH), 65.7 (CH_2), 42.9 (CH), 40.9 (CH_2), 36.8 (CH), 27.8 (CH_3), 26.0 (CH_2), 25.7 (CH_2), 23.9

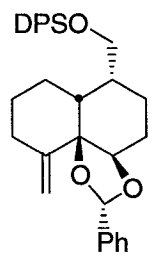
(CH_2), 20.3 (CH_2), 19.7 (C_4); IR (CH_2Cl_2, cm^{-1}) 3070 (w), 3048 (w), 2954 (s), 2932 (s), 2859 (s), 1960 (w), 1890 (w), 1825 (w), 1727 (s), 1588 (w), 1472 (w), 1460 (w), 1449 (w), 1428 (m), 1389 (w), 1361 (w), 1312 (w), 1265 (w), 1224 (w), 1187 (w), 1111 (s), 1090 (s), 1067 (m), 1027 (w); HRMS (EI) *m/z* (M^+-*t*Bu) calcd 483.19916, found 483.20053.

6-(*tert*-Butyl-diphenyl-silanyloxymethyl)-10-methyl-2-phenyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-ol (2.36)



Procedure A: $CeCl_3$ (267 mg, 1.08 mmol), THF (2.2 mL + 1.4 mL), ketone **2.35** (195 mg, 0.361 mmol), methyllithium (1.6 M solution in THF, 1.35 mL, 2.16 mmol), stirred for 1 hour. Flash chromatography with 15% EtOAc/hexanes gave **2.36** as a pale yellow oil (165 mg, 0.296 mmol, 85%), with a Rf = 0.67 (25% EtOAc/hexanes). ^1H NMR (300 MHz, $CDCl_3$) δ 7.74 (d, J = 6.9 Hz, 4H), 7.60 (d, J = 7.3 Hz, 2H), 7.52-7.37 (m, 9H), 6.19 (s, 1H), 4.78 (t, J = 4.7 Hz, 1H), 3.72-3.57 (m, 2H), 2.46-2.34 (m, 1H), 2.28 (dt, J = 12.8, 4.6 Hz, 1H), 2.15-1.95 (m, 2H), 1.88-1.70 (m, 3H), 1.69-1.56 (m, 2H), 1.48-1.32 (m, 2H), 1.39 (s, 3H), 1.31-0.98 (m, 1H), 1.14 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.0 (C_4), 136.1 (CH), 134.3 (C_4), 130.1 (CH), 129.3 (CH), 129.1 (CH), 128.1 (CH), 126.3 (CH), 102.9 (CH), 88.5 (C_4), 75.1 (C_4), 74.5 (CH), 66.9 (CH_2), 38.6 (CH), 37.9 (CH_2), 34.3 (CH), 27.4 (CH_3), 25.6 (CH_2), 24.2 (CH_2), 24.2 (CH_3), 21.9 (CH_2), 19.8 (C_4), 18.9 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3465 (br), 3069 (w), 3048 (w), 2932 (s), 2891 (m), 2859 (s), 1959 (w), 1890 (w), 1824 (w), 1738 (w), 1588 (w), 1471 (m), 1450 (w), 1427 (m), 1389 (w), 1373 (w), 1264 (w), 1224 (w), 1112 (s), 1069 (s), 1034 (m); HRMS (EI) *m/z* (M^+) calcd 556.30039, found 556.30300.

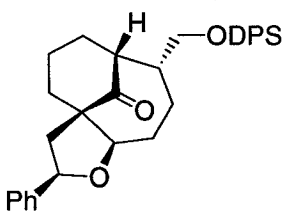
***tert*-Butyl-(10-methylene-2-phenyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-6-ylmethoxy)-diphenyl-silane (2.37)**



Procedure B: Thionyl chloride (44 μL, 0.61 mmol), alcohol **2.36** (170 mg, 0.305 mmol), 4-dimethylaminopyridine (223 mg, 1.83 mmol), CH_2Cl_2 (3.1 mL), stirred for 15 minutes. Flash chromatography with 2.5-3.5% EtOAc/hexanes gave **2.37** as

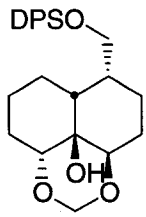
a white foam (97.3 mg, 0.181 mmol, 59%), with a Rf = 0.47 (5% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76-7.69 (m, 4H), 7.62-7.55 (m, 2H), 7.52-7.35 (m, 9H), 6.28 (s, 1H), 4.70 (s, 1H), 4.66 (d, J = 1.8 Hz, 1H), 4.45 (t, J = 6.8 Hz, 1H), 3.63 (d, J = 7.5 Hz, 2H), 2.46-2.33 (m, 2H), 2.27-1.99 (m, 3H), 1.95-1.64 (m, 4H), 1.52-1.28 (m, 3H), 1.12 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.9 (C_4), 139.7 (C_4), 136.1 (CH), 134.3 (C_4), 130.1 (CH), 128.9 (CH), 128.5 (CH), 128.1 (CH), 126.8 (CH), 110.7 (CH_2), 101.9 (CH), 86.0 (C_4), 76.9 (CH), 66.3 (CH_2), 42.7 (CH), 36.8 (CH), 35.7(CH_2), 27.6 (CH_2), 27.4 (CH_3), 25.6 (CH_2), 25.2 (CH_2), 20.3 (CH_2), 19.7 (C_4); IR (CH_2Cl_2, cm^{-1}) 3134 (w), 3069 (m), 3048 (w), 2932 (s), 2892 (m), 2858(s), 1959 (w), 1890 (w), 1825 (w), 1739 (m), 1648 (w), 1588 (w), 1471 (m), 1462 (m), 1447 (m), 1427 (m), 1389 (m), 1240 (m), 1111 (s), 1069 (s), 1028 (w), 1007 (w); HRMS (EI) *m/z* (M^+-*t*Bu) calcd 481.21990, found 481.22138.

8-(*tert*-Butyl-diphenyl-silanyloxymethyl)-3-phenyl-4-oxa-tricyclo[7.3.1.0^{1,5}]tridecan-13-one (2.38)



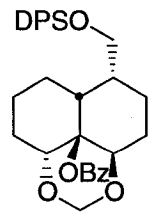
Procedure C: Tin tetrachloride (1.0 M solution in CH_2Cl_2, 12 μL, 12 μmol), Prins-pinacol precursor **2.37** (6.6 mg, 12 μmol), CH_2Cl_2 (0.24 mL), at -78°C, stirred for 15 minutes. Flash chromatography with 5.0-7.5% EtOAc/hexanes gave **2.38** as a colorless oil (5.3 mg, 9.8 μmol, 80%), with a Rf = 0.59 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65-7.59 (m, 4H), 7.44-7.23 (m, 11H), 4.79 (dd, J = 11.7, 4.3 Hz, 1H), 4.04 (dd, J = 11.0, 3.9 Hz, 1H), 3.59-3.50 (m, 2H), 3.03-2.94 (m, 1H), 2.91 (t, J = 12.5 Hz, 1H), 2.34-2.26 (m, 1H), 2.25-2.14 (m, 1H), 2.12-1.98 (m, 2H), 1.93-1.27 (m, 8H), 1.03 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.9 (C_4), 140.9 (C_4), 135.9 (CH), 133.8(C_4), 130.1 (CH), 128.7 (CH), 128.2 (CH), 128.1 (CH), 126.7 (CH), 86.7 (CH), 80.0 (C_4), 66.2 (CH_2), 59.7 (C_4), 49.6 (CH), 46.2 (CH), 44.1 (CH_2), 39.0 (CH_2), 32.9 (CH_2), 27.2 (CH_3), 24.9 (CH_2), 24.9 (CH_2), 20.7 (CH_2), 19.6 (C_4); IR (CH_2Cl_2, cm^{-1}) 3069 (m), 3048 (w), 3030 (w), 2998 (w), 2928 (s), 2857 (s), 1960 (w), 1890 (w), 1823 (w), 1737 (m), 1697 (s), 1667 (w), 1589 (w), 1455 (m), 1428 (m), 1388 (m), 1361 (m), 1281 (w), 1265 (w), 1185 (w), 1112 (s), 1085 (m), 1055 (m), 1021 (w); HRMS (EI) *m/z* (M^+-*t*Bu) calcd 481.21990, found 481.22018. COSY, NOESY, HMQC and NOE experiments were performed in order to obtain the correlations in Figure 2.4.

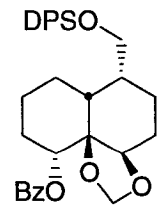
6-(*tert*-Butyl-diphenyl-silanyloxymethyl)-octahydro-naphtho[1,8-*de*][1,3]dioxin-9b-ol (2.42)



Sodium hydride (9.0 mg, 0.22 mmol) was added to a solution of **2.24**[71] (21 mg, 37 μmol) in DMF (0.37 mL) at 0°C and the reaction was allowed to stir for 10 minutes. Diiodomethane (3.0 μL, 40 μmol) was added at 0°C and the reaction was warmed to room temperature overnight. The reaction was quenched with NH_4Cl (aq. sat.), extracted with diethyl ether, dried over $MgSO_4$, filtered and concentrated *in vacuo*. Flash chromatography with 20% EtOAc/hexanes gave **2.42** as a pale yellow oil (4.8 mg, 10 μmol, 28%), with a Rf = 0.44 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68-7.63 (m, 4H), 4.47-7.36 (m, 6H), 5.11 (d, J = 6.4 Hz, 1H), 4.83 (d, J = 6.4 Hz, 1H), 4.01 (dd, J = 11.5, 4.8 Hz, 1H), 3.74 (dd, J = 12.6, 5.4 Hz, 1H), 3.52-3.43 (m, 2H), 2.49-2.38 (m, 1H), 2.22 (ddd, J = 25.8, 13.2, 3.9 Hz, 1H), 1.94-1.49 (m, 7H), 1.45-1.08 (m, 4H), 1.05 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.0 (CH), 134.2 (C_4), 130.0 (CH), 128.0 (CH), 88.3 (CH_2), 80.7 (CH), 74.1 (CH), 69.9 (C_4), 66.3 (CH_2), 42.3 (CH), 36.7 (CH), 27.2 (CH_3), 26.4 (CH_2), 24.9 (CH_2), 23.7 (CH_2), 22.7 (CH_2), 21.9 (CH_2), 19.7 (C_4); IR (CH_2Cl_2, cm^{-1}) 3574 (m), 3465 (br), 3072 (m), 3050 (m), 2937 (s), 2859 (s), 2775 (w), 1961 (w), 1892 (w), 1825 (w), 1737 (m), 1589 (w), 1471 (m), 1460 (m), 1450 (m), 1428 (m), 1388 (m), 1265 (w), 1161 (m), 1113 (s), 1080 (s), 1022 (s); HRMS (EI) *m/z* (M^+-*t*Bu-H_2O) calcd 379.17295, found 379.17101.

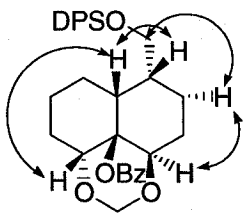
Benzoic acid 6-(*tert*-butyl-diphenyl-silanyloxymethyl)-octahydro-naphtho[1,8-*de*][1,3]dioxin-9b-yl ester (2.43) and Benzoic acid 6-(*tert*-butyl-diphenyl-silanyloxymethyl)-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-yl ester (2.44)



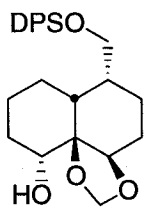


Procedure D: Dimethoxymethane (0.42 mL, 4.8 mmol), tin dichloride (0.23 mg, 1.2 mmol), diol **2.24**[71] (66 mg, 1.2 mmol), 1,2-dimethoxyethane (12 mL), refluxed overnight. Flash chromatography with 8-25% EtOAc/hexanes gave **2.43** as a white foam (137 mg, 0.241 mmol, 20%), and **2.44** as a sticky colorless oil (0.35 mg, 0.61 mmol, 51%, 71 % overall yield), with a respective Rf = 0.62 and 0.77 (25% EtOAc/hexanes). **2.43** ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.22-8.17 (m, 2H), 7.66-7.18 (m, 13H), 5.25 (d, J = 6.4 Hz, 1H), 5.20 (dd, J = 12.3, 5.5 Hz, 1H), 4.88 (d, J = 6.4 Hz, 1H), 4.23 (dd, J =

11.6, 4.8 Hz, 1H), 3.58-3.41 (m, 2H), 3.31 (dt, J = 13.0, 4.5 Hz, 1H), 2.29 (ddd, J = 25.3, 12.7, 3.5 Hz, 1H), 2.17-1.83 (m, 5H), 1.69-1.48 (m, 3H), 1.36-1.18 (m, 2H), 1.04 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.0 (C_4), 135.9 (CH), 134.2 (C_4), 133.2 (CH), 132.3 (C_4), 130.3 (CH), 130.0 (CH), 128.8 (CH), 128.0 (CH), 87.5 (CH_2), 82.2 (C_4), 72.6 (CH), 72.6 (CH), 66.1 (CH_2), 38.3 (CH), 37.4 (CH), 27.2 (CH_3), 27.0 (CH_2), 25.6 (CH_2), 23.4 (CH_2), 22.8 (CH_2), 22.3 (CH_2), 19.6 (C_4); IR (CH_2Cl_2, cm^{-1}) 3070 (m), 3052 (m), 2952 (s), 2859 (s), 2778 (w), 1964 (w), 1892 (w), 1824 (w), 1737 (s), 1712 (s), 1601 (w), 1586 (w), 1471 (s), 1450 (s), 1374 (m), 1287 (s), 1188 (m), 1163 (s), 1083 (s), 1036 (s), 1019 (s); HRMS (EI) *m/z* (M^+-*t*Bu-H_2CO) calcd 483.19916, found 483.19681. COSY, NOESY, HMQC, HMBC and TOCSY experiments were performed in order to obtain the correlations illustrated below. **2.44** ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.17-8.10 (m, 2H), 7.80-7.68 (m, 4H), 7.60 (tt, J = 7.4, 1.3 Hz, 1H), 7.53-7.38 (m, 8H), 5.32 (dd, J = 12.4, 4.3 Hz, 1H), 5.14 (s, 1H), 4.96 (s, 1H), 4.71 (s, 1H), 3.68-3.53 (m, 2H), 2.57-2.42 (m, 1H), 2.21-1.08 (m, 11H), 1.13 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.0 (C_4), 136.1 (CH), 134.3 (C_4), 133.5 (CH), 130.9 (C_4), 130.1 (CH), 130.1 (CH), 128.9 (CH), 128.1 (CH), 95.2 (CH_2), 82.6 (C_4), 79.7 (CH), 73.2 (CH), 66.6 (CH_2), 40.1 (CH), 32.7 (CH), 30.0 (CH_2), 27.4 (CH_3), 24.0 (CH_2), 23.5 (CH_2), 23.2 (CH_2), 19.8 (C_4), 18.3 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3070 (m), 3051 (m), 2937 (s), 2857 (s), 2764 (w), 1964 (w), 1905 (w), 1824 (w), 1727 (s), 1601 (w), 1471 (m), 1428 (m), 1315 (m), 1263 (m), 1085 (m), 1025 (m); HRMS (EI) *m/z* (M^+-*t*Bu) calcd 513.20973, found 513.20824.



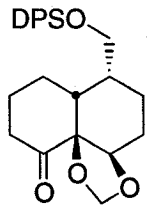
6-(*tert*-Butyl-diphenyl-silanyloxymethyl)-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-ol (2.45)



Procedure E: Potassium carbonate (0.48 g, 3.5 mmol), benzoate **2.44** (0.28 g, 0.48 mmol), methanol (4.8 mL), benzene (4.8 mL), refluxed overnight. Flash chromatography with 25-33% EtOAc/hexanes gave **2.45** as a pale yellow oil (0.19 g, 41 mmol, 84%), with a Rf = 0.28 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz,

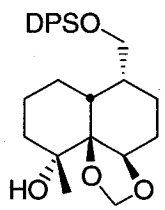
$CDCl_3$) δ 7.72-7.64 (m, 4H), 7.49-7.33 (m, 6H), 5.14 (d, J = 4.4 Hz, 1H), 4.45 (t, J = 4.7 Hz, 1H), 3.79 (dd, J = 11.7, 4.2 Hz, 1H), 3.61-3.47 (m, 2H), 2.49-2.26 (m, 2H), 2.06-1.82 (m, 4H), 1.79-1.47 (m, 3H), 1.41-1.01 (m, 5H), 1.08 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.0 (CH), 134.3 (C_4), 130.0 (CH), 128.0 (CH), 94.9 (CH_2), 84.5 (C_4), 78.0 (CH), 72.1 (CH), 66.6 (CH_2), 39.8 (CH), 33.8 (CH), 32.9 (CH_2), 27.3 (CH_3), 24.4 (CH_2), 23.8 (CH_2), 23.5 (CH_2), 19.7 (C_4), 19.0 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3462 (br), 3070 (w), 3048 (w), 2931 (s), 2891 (m), 2859 (s), 2764 (w), 1962 (w), 1894 (w), 1827 (w), 1588 (w), 1470 (m), 1427 (m), 1389 (w), 1111 (s), 1094 (s), 1009 (m); HRMS (EI) *m/z* (M^+-*t*Bu) calcd 409.18351, found 409.18329.

6-(*tert*-Butyl-diphenyl-silanyloxymethyl)-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-one (2.46)



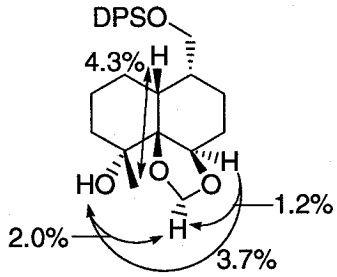
Procedure F: Dess-Martin periodinane (0.205 g, 0.483 mmol), alcohol **2.45** (0.188 g, 0.403 mmol), CH_2Cl_2 (4.0 mL), stirred for 15 minutes. Flash chromatography with 20% EtOAc/hexanes gave **2.46** as a colorless oil (0.169 g, 0.364 mmol, 90%), with a Rf = 0.44 (25% EtOAc/hexanes). ^1H NMR (300 MHz, $CDCl_3$) δ 7.71-7.64 (m, 4H), 7.49-7.37 (m, 6H), 5.28 (d, J = 1.3 Hz, 1H), 5.20 (d, J = 1.5 Hz, 1H), 4.26 (t, J = 6.7 Hz, 1H), 3.65-3.46 (m, 2H), 2.60-2.41 (m, 3H), 2.34-2.22 (m, 1H), 2.13-1.93 (m, 2H), 1.81-1.42 (m, 5H), 1.36-1.22 (m, 1H), 1.07 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.3 (C_4), 136.0 (CH), 134.0 (C_4), 130.1 (CH), 128.1 (CH), 94.4 (CH_2), 88.0 (C_4), 74.2 (CH), 65.8 (CH_2), 42.3 (CH), 40.5 (CH_2), 35.8 (CH), 27.3 (CH_3), 25.9 (CH_2), 25.8 (CH_2), 23.6 (CH_2), 20.2 (CH_2), 19.7 (C_4); IR (CH_2Cl_2, cm^{-1}) 3071 (m), 3050 (m), 3011 (m), 2999 (m), 2932 (s), 2864 (s), 2763 (w), 1961 (w), 1893 (w), 1827 (w), 1723 (s), 1589 (w), 1472 (s), 1428 (s), 1390 (m), 1247 (m), 1190 (m), 1100 (s), 1006 (m); HRMS (EI) *m/z* (M^+-*t*Bu) calcd 407.16786, found 407.16746.

6-(*tert*-Butyl-diphenyl-silanyloxymethyl)-10-methyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-ol (2.47)

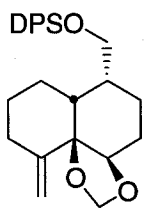


Procedure A: $CeCl_3$ (269 mg, 1.09 mmol), THF (2.2 mL + 1.4 mL), ketone **2.46** (169 mg, 0.364 mmol), methyllithium (1.6 M solution in THF, 1.36 mL, 2.18

mmol), stirred for 1 hour. Flash chromatography with 33% EtOAc/hexanes gave **2.47** as a pale yellow oil (86 mg, 0.18 mmol, 49%), with a Rf = 0.21 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72-7.59 (m, 4H), 7.48-7.31 (m, 6H), 5.13 (s, 1H), 4.58 (t, J = 5.2 Hz, 1H), 3.61-3.44 (m, 2H), 2.64-2.30 (br, 1H), 2.36-2.23 (m, 1H), 2.17 (dt, J = 13.0, 4.4 Hz, 1H), 2.00-1.84 (m, 1H), 1.83-1.22 (m, 7H), 1.37 (s, 3H), 1.20-1.05 (m, 2H), 1.08 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 136.0 (CH), 134.3 (C_4), 130.0 (CH), 128.0 (CH), 94.7 (CH_2), 86.1 (C_4), 76.7 (C_4), 73.4 (CH), 66.6 (CH_2), 39.2 (CH_2), 38.0 (CH), 34.3 (CH), 27.3 (CH_3), 25.2 (CH_2), 23.6 (CH_2), 23.6 (CH_3), 22.3 (CH_2), 19.7 (C_4), 18.9 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3483 (br), 3070 (w), 3048 (w), 2931 (s), 2859 (s), 2764 (w), 1961 (w), 1891 (w), 1824 (w), 1589 (w), 1470 (m), 1427 (m), 1389 (w), 1331 (w), 1266 (w), 1159 (w), 1111 (s), 1036 (w), 1019 (m); HRMS (EI) *m/z* (M^+-*t*Bu) calcd 423.19916, found 423.19948. NOE experiments were performed in order to obtain the correlations illustrated below:



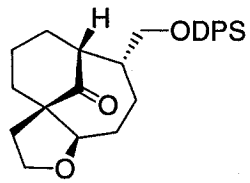
tert-Butyl-(10-methylene-octahydro-naphtho[1,8a-*d*][1,3]dioxol-6-ylmethoxy)-diphenyl-silane (2.48)



Procedure B: Thionyl chloride (21 μL, 0.29 mmol), alcohol **2.47** (69 mg, 0.14 mmol), 4-dimethylaminopyridine (0.11 g, 0.87 mmol), CH_2Cl_2 (1.4 mL), stirred for 15 minutes. Flash chromatography with 3.0-3.5% EtOAc/hexanes gave **2.48** as a colorless oil (44 mg, 95 μmol, 66%), with a Rf = 0.51 (5% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71-7.63 (m, 4H), 7.34-7.47 (m, 6H), 5.23 (s, 1H), 5.14 (s, 1H), 5.01 (s, 1H), 4.85 (s, 1H), 4.12 (t, J = 5.7 Hz, 1H), 3.59-3.48 (m, 2H), 2.43 (dd, J = 12.9, 2.7 Hz, 1H), 2.43-2.29 (m, 1H), 2.22-2.13 (m, 1H), 2.06-1.46 (m, 6H), 1.41-1.18 (m, 3H), 1.07 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.6 (C_4), 136.0 (CH), 134.2 (C_4), 130.0 (CH), 128.0 (CH), 108.0 (CH_2), 93.2 (CH_2), 84.6 (C_4), 75.9 (CH), 66.4 (CH_2), 42.0 (CH), 35.6 (CH), 35.1 (CH_2),

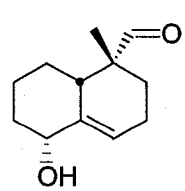
27.7 (CH_2), 27.3 (CH_3), 25.3 (CH_2), 24.6 (CH_2), 20.1 (CH_2), 19.7 (C_4); IR (CH_2Cl_2, cm^{-1}) 3135 (w), 3070 (m), 3048 (m), 2946 (s), 2857 (s), 2757 (m), 1960 (w), 1890 (w), 1823 (w), 1724 (m), 1647 (m), 1589 (m), 1471 (m), 1428 (m), 1390 (m), 1361 (w), 1265 (m), 1189 (m), 1084 (m), 1007 (m); HRMS (EI) *m/z* (M^+-*t*Bu) calcd 405.18860, found 405.18693.

8-(*tert*-Butyl-diphenyl-silanyloxymethyl)-4-oxa-tricyclo[7.3.1.0^{1,5}]tridecan-13-one (2.49)



Procedure C: Tin tetrachloride (1.0 M solution in CH_2Cl_2, 56 μL, 56 μmol), Prins-pinacol precursor **2.48** (13 mg, 28 μmol), toluene (0.56 mL), from -78°C to room temperature, stirred for 2 hours and 30 minutes. Flash chromatography with 10-15% EtOAc/hexanes gave **2.49** as a colorless oil (3.4 mg, 7.3 μmol, 26%), with a Rf = 0.36 (15% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70-7.62 (m, 4H), 7.48-7.36 (m, 6H), 3.99-3.85 (m, 2H), 3.72-3.66 (m, 1H), 3.64-3.51 (m, 2H), 3.01-2.85 (m, 2H), 2.13-1.96 (m, 3H), 1.83-1.18 (m, 9H), 1.06 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.5 (C_4), 136.0 (CH), 133.8 (C_4), 130.1 (CH), 128.1 (CH), 86.6 (CH), 67.5 (CH_2), 66.2 (CH_2), 59.4 (C_4), 49.7 (CH), 46.2 (CH), 39.1 (CH_2), 36.6 (CH_2), 32.7 (CH_2), 27.2 (CH_3), 25.1 (CH_2), 25.0 (CH_2), 21.3 (CH_2), 19.6 (C_4); IR (CH_2Cl_2, cm^{-1}) 3071 (m), 3051 (m), 3014 (w), 2930 (s), 2862 (s), 1960 (w), 1891 (w), 1825 (w), 1695 (s), 1589 (w), 1471 (m), 1428 (m), 1389 (w), 1265 (m), 1111 (m), 1085 (m), 1030 (w), 1007 (w); HRMS (EI) *m/z* (M^+-*t*Bu) calcd 405.18860, found 405.18982.

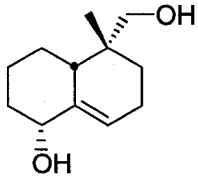
5-Hydroxy-1-methyl-1,2,3,5,6,7,8,8a-octahydro-naphthalene-1-carbaldehyde (2.51)



Procedure G: Triethylamine (5.65 mL, 40.5 mmol), diene **2.19**[71] (1.68 g, 13.5 mmol), magnesium bromide etherate (6.98 g, 27.0 mmol), CH_2Cl_2 (135 mL), methacrolein (2.45 mL, 29.7 mmol), stirred for 1 hour. Flash chromatography with 25-33% EtOAc/hexanes gave **2.51** as a pale yellow oil (1.09 g, 5.61 mmol, 42% over 3 steps), with a Rf = 0.25 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.52 (s, 1H), 5.61 (s, 1H), 3.83 (d, J = 12.0 Hz, 1H), 3.18 (s, 1H), 2.09-1.87 (m, 3H), 1.81-1.46 (m, 4H), 1.42-1.26 (m 2H), 1.17-0.95 (m, 2H), 0.94 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.5

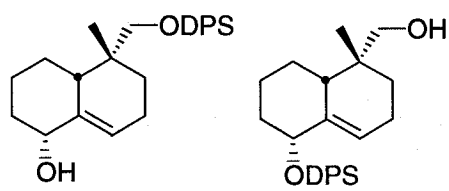
(CH), 141.5 (C_4), 114.9 (CH), 72.9 (CH), 47.3 (C_4), 43.9 (CH), 38.0 (CH_2), 30.2 (CH_2), 25.9 (CH_2), 24.5 (CH_2), 21.4 (CH_2), 19.9 (CH_3); IR (CH_2Cl_2, cm^{-1}) 3420 (br), 3054 (w), 2926 (s), 2870 (s), 2720 (w), 1725 (s), 1681 (s), 1613 (s), 1513 (w), 1455 (m), 1374 (w), 1268 (w), 1183 (w), 1075 (w); HRMS (EI) *m/z* (M^+) calcd 194.13068, found 194.12820.

5-Hydroxymethyl-5-methyl-1,2,3,4,4a,5,6,7-octahydro-naphthalen-1-ol (2.52)



Procedure H: Lithium aluminum hydride (189 mg, 5.37 mmol), aldehyde **2.51** (682 mg, 3.51 mmol), THF (35 mL), warmed at 0°C for 20 minutes, water (2 x 1 mL), solution of KOH 0.1 M (1 mL), solution of sodium tartrate 0.5 M (9 mL). Flash chromatography with 50% EtOAc/hexanes gave **2.52** as a white foam (320 mg, 1.63 mmol, 47% over 4 steps), with a Rf = 0.19 (20% EtOAc/hexanes). ^1H NMR (300 MHz, $CDCl_3$) δ 5.52 (s, 1H), 3.69 (dt, J = 8.6, 2.2 Hz, 1H), 3.22 (d, J = 10.3 Hz, 1H), 3.05 (d, J = 10.3 Hz, 1H), 1.94-1.84 (m, 3H), 1.78-1.66 (m, 2H), 1.49 (d, J = 11.8 Hz, 1H), 1.41-1.18 (m 2H), 1.11-0.97 (m, 2H), 0.94-0.83 (m, 1H), 0.83 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.7 (C_4), 113.9 (CH), 72.6 (CH), 68.6 (CH_2), 44.9 (CH), 39.0 (CH_2), 36.2 (C_4), 29.4 (CH_2), 28.1 (CH_2), 25.0 (CH_2), 22.7 (CH_3), 21.9 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3419 (br), 2950 (m), 2928 (s), 2860 (m), 2101 (br), 1642 (s), 1444 (w), 1352 (w), 1281 (w), 1111 (m), 1060 (m), 1021 (m); HRMS (EI) *m/z* (M^+-H_2O) calcd 178.13577, found 178.13558.

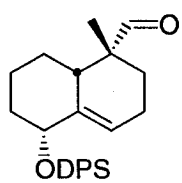
5-(*tert*-Butyl-diphenyl-silanyloxymethyl)-5-methyl-1,2,3,4,4a,5,6,7-octahydro-naphthalen-1-ol (2.53) and [5-(*tert*-Butyl-diphenyl-silanyloxy)-1-methyl-1,2,3,5,6,7,8,8a-octahydro-naphthalen-1-yl]-methanol (2.54)



Imidazole (466 mg, 6.84 mmol), then TBDPSCl (0.81 mL, 3.1 mmol) were added to a solution of **2.52** (400 mg, 2.04 mmol) in DMF (35 mL) at room temperature and the reaction was stirred at this temperature for 7 hours. The resulting mixture was then concentrated *in vacuo* and a purification by silica gel flash chromatography with 20% EtOAce/hexanes gave **2.52** (210 mg, 1.07 mmol, 53%), **2.54** as a white foam (128 mg, 0.294 mmol, 14%) and a mixture of **2.53** and **2.54**, (128 mg, 0.294 mmol, 14%, 81% overall yield) with a respective Rf = 0.64 and 0.63 (25% EtOAc/hexanes). **2.53** ^1H

NMR (300 MHz, $CDCl_3$) δ 7.72-7.59 (m, 4H), 7.44-7.26 (m, 6H), 5.57 (s, 1H), 4.00-3.91 (m, 1H), 3.44 (d, J = 9.6 Hz, 1H), 3.32 (d, J = 9.7 Hz, 1H), 2.15-1.99 (m, 3H), 1.85-1.74 (m, 2H), 1.72-1.62 (m, 1H), 1.53 (br, 1H), 1.47-0.97 (m, 4H), 1.06 (s, 9H), 1.00 (s, 3H), 0.95-0.85 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.7 (C_4), 136,1 (CH), 134.2 (C_4), 129.9 (CH), 127.8 (CH), 113.8 (CH), 73.8 (CH), 70.9 (CH_2), 44.9 (CH), 38.8 (CH_2), 36.8 (C_4), 29.4 (CH_2), 27.6 (CH_2), 27.3 (CH_3), 24.8 (CH_2), 22.6 (CH_3), 22.0 (CH_2), 19.8 (C_4); **2.54** ^1H NMR (300 MHz, $CDCl_3$) δ 7.71-7.63 (m, 4H), 7.43-7.29 (m, 6H), 5.86 (s, 1H), 3.98-3.89 (m, 1H), 3.43 (d, J = 10.7 Hz, 1H), 3.27 (d, J = 10.7 Hz, 1H), 2.08-2.01 (m, 2H), 1.86-1.75 (m, 1H), 1.71-1.61 (m, 2H), 1.46-0.97 (m, 7H), 1.09 (s, 9H), 0.84 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.1 (C_4), 136,2 (CH), 136.1 (CH), 135.1 (C_4), 134.7 (C_4), 129.9 (CH), 129.8 (CH), 128.0 (CH), 127.8 (CH), 115.2 (CH), 75.4 (CH), 70.6 (CH_2), 44.9 (CH), 39.0 (CH_2), 36.2 (C_4), 29.6 (CH_2), 27.5 (CH_3), 27.4 (CH_2), 24.8 (CH_2), 22.0 (CH_2), 21.5 (CH_3), 19.8 (C_4); IR (CH_2Cl_2, cm^{-1}) 3464 (br), 3071 (w), 3049 (w), 2928 (s), 2855 (s), 1959 (w), 1890 (w), 1824 (w), 1771 (w), 1737 (w), 1650 (m), 1589 (m), 1472 (s), 1461 (m), 1445 (m), 1427 (s), 1389 (m), 1360 (m), 1265 (m), 1190 (w), 1113 (s), 1090 (m), 1078 (m), 1006 (w); HRMS (EI) *m/z* (M^+-*t*Bu) calcd 377.19368, found 377.19277.

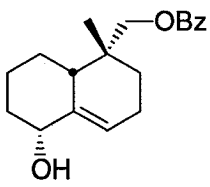
5-(*tert*-Butyl-diphenyl-silanyloxy)-1-methyl-1,2,3,5,6,7,8,8a-octahydro-naphthalene-1-carbaldehyde (2.55)



Procedure F: Dess-Martin periodinane (80 mg, 0.19 mmol), alcohol **2.54** (68 mg, 0.16 mmol), CH_2Cl_2 (1.6 mL), stirred for 20 minutes. Flash chromatography with 10-15 EtOAc/hexanes gave **2.55** as a pale yellow oil (39 mg, 90 μmol, 58%), with a Rf = 0.79 (25% EtOAc/hexanes). ^1H NMR (300 MHz, $CDCl_3$) δ 9.58 (s, 1H), 7.76-7.63 (m, 4H), 7.48-7.30 (m, 6H), 5.94 (s, 1H), 3.99 (d, J = 9.5 Hz, 1H), 2.28-2.14 (m, 1H), 2.13-1.96 (m, 1H), 1.90-1.63 (m, 4H), 1.58-1.40 (m, 2H), 1.37-1.16 (m, 3H), 1.13 (s, 9H), 0.99 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 207.4 (CH), 141.2 (C_4), 136,2 (CH), 136.1 (CH), 134.9 (C_4), 134.5 (C_4), 130.0 (CH), 129.9 (CH), 127.9 (CH), 127.9 (CH), 115.8 (CH), 75.0 (CH), 47.3 (C_4), 44.1 (CH), 38.7 (CH_2), 30.7 (CH_2), 27.5 (CH_3), 24.9 (CH_2), 24.6 (CH_2), 21.4 (CH_2), 19.7 (C_4), 19.6 (CH_3); IR (CH_2Cl_2, cm^{-1}) 3434 (w), 3134 (w), 3071 (m), 3048 (m), 2998 (w), 2930 (s), 2856 (s), 2769 (w), 2707 (m), 2304 (w), 2255 (w), 1960 (w), 1899 (w), 1823 (w), 1731 (s), 1589 (w), 1487 (w), 1462 (m), 1446 (m), 1427 (m), 1390 (w), 1372 (w), 1361 (w), 1343

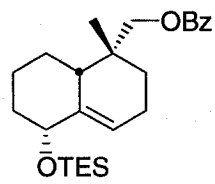
(w), 1265 (w), 1112 (m), 1073 (m), 1037 (w); HRMS (EI) *m/z* (M^+-*t*Bu) calcd 375.17803, found 375.17934.

Benzoic acid 5-hydroxy-1-methyl-1,2,3,5,6,7,8,8a-octahydro-naphthalen-1-ylmethyl ester (2.56)



Procedure I: 4-Dimethylaminopyridine (24 mg, 0.20 mmol), benzoyl chloride (0.53 mL, 4.6 mmol), diol **2.52** (779 mg, 3.97 mmol), pyridine (0.96 mL, 12 mmol), CH_2Cl_2 (40 mL), stirred overnight. Flash chromatography with 25%, then 50% EtOAc/hexanes gave **2.52** (262 mg, 1.33 mmol, 33%) and **2.56** as a white foam (570 mg, 1.90 mmol, 49%, 82% overall yield), with a Rf = 0.27 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04 (d, J = 7.0 Hz, 2H), 7.57 (dt, J = 7.5, 13 Hz, 1H), 7.46 (t, J = 7.7 Hz, 2H), 5.68 (s, 1H), 4.14 (d, J = 13.4 Hz, 1H), 4.10 (d, J = 13.4 Hz, 1H), 3.99 (d, J = 8.6 Hz, 1H), 2.20-2.05 (m, 4H), 1.83-1.75 (m, 3H), 1.61-1.38 (m, 2H), 1.36-1.06 (m, 3H), 1.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.1 (C_4), 143.0 (C_4), 133.4 (CH), 130.8 (C_4), 130.0 (CH), 128.8 (CH), 114.3 (CH), 73.6 (CH), 71.8 (CH_2), 45.4 (CH), 38.5 (CH_2), 35.3 (C_4), 29.5 (CH_2), 28.1 (CH_2), 24.8 (CH_2), 22.8 (CH_3), 21.7 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3409 (br), 3057 (w), 2930 (s), 2856 (m), 1718 (s), 1601 (w), 1584 (w), 1450 (m), 1386 (w), 1370 (w), 1314 (m), 1275 (s), 1175 (w), 1116 (s), 1069 (m), 1026 (w); HRMS (EI) *m/z* (M^+-BzOH-H_2O) calcd 160.12520, found 160.12460.

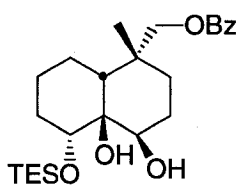
Benzoic acid 1-methyl-5-triethylsilanyloxy-1,2,3,5,6,7,8,8a-octahydro-naphthalen-1-ylmethyl ester (2.57)



Procedure J: 4-Dimethylaminopyridine (23 mg, 0.19 mmol), triethylsilyl chloride (0.48 mL, 2.9 mmol), alcohol **2.56** (570 mg, 1.90 mmol), triethylamine (0.79 mL, 5.7 mmol), THF (19 mL), stirred for 2 hours and 20 minutes. Flash chromatography with 2.5-5.0% EtOAc/hexanes gave **2.57** as a pale yellow oil (690 mg, 1.66 mmol, 88%) with a Rf = 0.81 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (d, J = 7.2 Hz, 2H), 7.58 (t, J = 7.4, 1H), 7.47 (t, J = 7.3 Hz, 2H), 5.75 (s, 1H), 4.14 (d, J = 11.0 Hz, 1H), 4.10 (d, J = 11.0 Hz, 1H), 3.95 (d, J = 8.2 Hz, 1H), 2.14-2.06 (m, 2H), 2.06-1.98 (m, 1H), 1.86-1.72 (m, 3H), 1.60-1.25 (m, 4H), 1.22-1.06 (m, 1H), 1.07

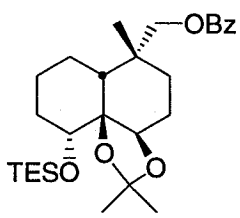
(s, 3H), 0.99 (t, J = 8.0 Hz, 9H), 0.63 (q, J = 7.9 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.0 (C_4), 142.4 (C_4), 133.3 (CH), 130.9 (C_4), 129.9 (CH), 128.8 (CH), 115.0 (CH), 74.1 (CH), 71.9 (CH_2), 45.6 (CH), 39.2 (CH_2), 35.3 (C_4), 29.5 (CH_2), 28.0 (CH_2), 25.0 (CH_2), 22.7 (CH_3), 21.8 (CH_2), 7.4 (CH_3), 5.3 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3063 (w), 3038 (w), 2952 (s), 2934 (s), 2914 (s), 2875 (s), 2857 (m), 1721 (s), 1602 (w), 1451 (m), 1414(w), 1385 (w), 1314 (w), 1273 (s), 1175 (w), 1121 (s), 1094 (m), 1070 (w), 1026 (w); HRMS (EI) *m/z* (M^+) calcd 414.25902, found 414.25701.

Benzoic acid 4,4a-dihydroxy-1-methyl-5-triethylsilanyloxy-decahydro-naphthalen-1-ylmethyl ester (2.58)



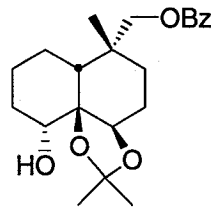
Procedure K: 4-Methylmorpholine N-oxide (390 mg, 3.33 mmol), solution of osmium tetraoxide 4% in water (0.53 mL, 83 μmol), **2.57** (690 mg, 1.66 mmol), water (5.5 mL), THF (17 mL), refluxed for 18 hours. Flash chromatography with 10-15% EtOAc/hexanes gave **2.57** (393 mg, 0.948 mmol, 56%) and **2.58** as a white foam (198 mg, 0.441 mmol, 44%, quantitative overall yield), with a Rf = 0.22 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 (d, J = 7.2 Hz, 2H), 7.58 (t, J = 7.4, 1H), 7.46 (t, J = 7.8 Hz, 2H), 4.56 (s, 1H), 4.26 (dd, J = 11.2, 5.0 Hz, 1H), 4.09 (d, J = 10.9 Hz, 1H), 3.85 (d, J = 10.9 Hz, 1H), 3.76 (dd, J = 12.1, 4.2 Hz, 1H), 3.22 (s, 1H), 2.02-1.88 (m, 1H), 1.88-1.55 (m, 7H), 1.53-1.46 (m, 1H), 1.50 (s, 3H), 1.33-1.22 (m, 2H), 0.99 (t, J = 7.8 Hz, 9H), 0.67 (q, J = 7.9 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.0 (C_4), 133.4 (CH), 130.7 (C_4), 130.0 (CH), 128.8 (CH), 84.0 (CH), 74.8 (C_4), 74.1 (CH_2), 69.5 (CH), 46.7 (CH), 37.4 (C_4), 32.4 (CH_2), 28.4 (CH_2), 25.7 (CH_2), 25.6 (CH_3), 25.1 (CH_2), 24.0 (CH_2), 7.2 (CH_3), 5.2 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3459 (br), 2952 (s), 2875 (m), 1720 (s), 1603 (w), 1450 (s), 1420 (m), 1393 (w), 1313 (w), 1273 (s), 1176 (w), 1150 (w), 1099 (s), 1089 (m), 1063 (m), 1039 (m), 1023 (m); HRMS (EI) *m/z* (M^+) calcd 448.26450, found 448.26520.

Benzoic acid 2,2,6-trimethyl-10-triethylsilanyloxy-octahydro-naphtho[1,8a-*d*][1,3]dioxol-6-ylmethyl ester (2.59)



Procedure L: PTSA (8.4 mg, 44 μmol), diol **2.58** (198 mg, 0.441 mmol), 2-methoxypropene (0.13 mL, 1.3 mmol), CH_2Cl_2 (4.4 mL), stirred for 15 minutes. Flash chromatography with 2.5-5.0% EtOAc/hexanes gave **2.59** as a pale yellow oil (197 mg, 0.403 mmol, 91%), with a Rf = 0.79 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (d, J = 7.1 Hz, 2H), 7.57 (t, J = 7.2, 1H), 7.46 (t, J = 7.7 Hz, 2H), 4.94 (d, J = 11.1Hz, 1H), 4.35 (d, J = 11.2, 1H), 4.02 (s, 1H), 3.70 (s, 1H), 2.06-1.86 (m, 3H), 1.83-1.53 (m, 7H), 1.49 (s, 3H), 1.45-1.38 (m, 1H), 1.35 (s, 3H), 1.11 (s, 3H), 0.99 (t, J = 7.8 Hz, 9H), 0.68 (q, J = 8.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.8 (C_4), 133.0 (CH), 131.3 (C_4), 129.9 (CH), 128.7 (CH), 107.8 (C_4), 80.9 (C_4), 79.4 (CH), 74.6 (CH), 68.2 (CH_2), 47.9 (CH), 39.3 (C_4), 31.1 (CH_2), 29.4 (CH_2), 29.0 (CH_3), 27.8 (CH_3), 27.4 (CH_3), 24.3 (CH_2), 21.2 (CH_2), 18.1(CH_2), 7.3 (CH_3), 5.3 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3091 (w), 3066 (w), 3034 (w), 2954 (s), 2936 (s), 2876 (s), 2733 (w), 1721 (s), 1602 (w), 1585 (w), 1451 (m), 1414 (w), 1378 (m), 1366 (m), 1339 (w), 1313 (w), 1274 (s), 1250 (m), 1214 (m), 1187 (w), 1171 (w), 1115 (m), 1069 (m), 1054 (m), 1019 (m), 1007 (m); HRMS (EI) *m/z* (M^+) calcd 488.29580, found 488.29593.

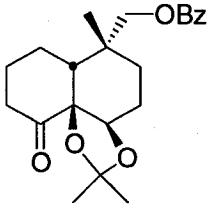
Benzoic acid 10-hydroxy-2,2,6-trimethyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-6-ylmethyl ester (2.60)



Tetrabutyl ammonium fluoride 1.0 M in THF (0.61 mL, 0.61 mmol) was added to a solution of **2.59** (197 mg, 0.403 mmol) in THF (4.4 mL) at room temperature and the reaction was stirred at this temperature for 50 minutes. The reaction was concentrated *in vacuo* and flash chromatography with 25% EtOAc/hexanes gave **2.60** as a pale yellow oil (138 mg, 0.368 mmol, 91%), with a Rf = 0.48 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04 (d, J = 7.1 Hz, 2H), 7.56 (t, J = 7.2, 1H), 7.44 (t, J = 7.7 Hz, 2H), 5.16 (d, J = 11.1Hz, 1H), 4.30 (d, J = 11.0, 1H), 4.14 (s, 1H), 3.74 (s, 1H), 2.27 (s, 1H), 2.08 (tt, J = 14.6, 3.2 Hz, 1H), 1.95-1.83 (m, 4H), 1.79-1.56 (m, 5H), 1.50 (s, 3H), 1.44-1.38 (m, 1H), 1.35 (s, 3H), 1.15 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.3 (C_4), 133.2 (CH), 131.0 (C_4), 129.9 (CH), 128.8 (CH), 107.9 (C_4), 80.3 (C_4), 79.4 (CH), 73.2 (CH),

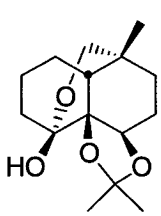
68.4 (CH_2), 47.8 (CH), 39.3 (C_4), 31.5 (CH_2), 29.3 (CH_2), 29.0 (CH_3), 27.8 (CH_3), 27.3 (CH_3), 24.1 (CH_2), 21.1 (CH_2), 18.0(CH_2); IR (CH_2Cl_2, cm^{-1}) 3457 (br), 2956 (m), 2924 (s), 2853 (m), 1778 (w), 1720 (s), 1461 (s), 1377 (m), 1313 (w), 1275 (m), 1251 (w), 1214 (w), 1115 (w), 1070 (w), 1050 (w), 1013 (w); HRMS (EI) *m/z* (M^+) calcd 374.20933, found 374.21060.

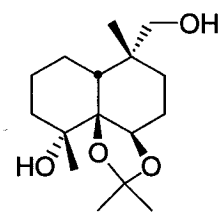
Benzoic acid 2,2,6-trimethyl-10-oxo-octahydro-naphtho[1,8a-*d*][1,3]dioxol-6-ylmethyl ester (2.61)



Procedure F: Dess-Martin periodinane (194 mg, 0.458 mmol), alcohol **2.60** (138 mg, 0.382 mmol), CH_2Cl_2 (4 mL), stirred for 4 minutes. Flash chromatography with 15-20% EtOAc/hexanes gave **2.61** as a pale yellow oil that solidified upon storage in the fridge (133 mg, 0.357 mmol, 93%), with a Rf = 0.64 (25% EtOAc/hexanes). ^1H NMR (300 MHz, $CDCl_3$) δ 8.00 (d, J = 7.2 Hz, 2H), 7.56 (t, J = 7.3, 1H), 7.44 (t, J = 7.8 Hz, 2H), 4.64 (t, J = 3.2 Hz, 1H), 4.20 (d, J = 10.9, 1H), 4.01 (d, J = 10.9 Hz, 1H), 2.20 (td, J = 13.0, 6.7Hz, 1H), 2.33 (dt, J = 13.4, 4.4 Hz, 1H), 2.25-2.04 (m, 3H), 2.02-1.80 (m, 4H), 1.74 (dt, J = 13.8, 3.7 Hz, 1H), 1.58-1.47 (m, 1H), 1.52 (s, 3H), 1.29 (s, 3H), 1.10 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.9 (C_4), 166.6 (C_4), 133.4 (CH), 130.5 (C_4), 129.9 (CH), 128.8 (CH), 108.5 (C_4), 83.1 (C_4), 72.2 (CH), 66.4 (CH_2), 52.7 (CH), 39.6 (CH_2), 39.1 (C_4), 30.3 (CH_2), 29.1 (CH_3), 26.6 (CH_3), 26.5 (CH_3), 25.5 (CH_2), 22.8 (CH_2), 20.8 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3420 (w), 3063 (w), 2983 (m), 2940 (s), 2879 (m), 1968 (w), 1907 (w), 1825 (w), 1721 (s), 1602 (m), 1584 (m), 1451 (s), 1381 (m), 1370 (m), 1314 (m), 1217 (m), 1176 (m), 1140 (w), 1113 (m), 1069 (m), 1055 (m), 1026 (w), 1013 (w); HRMS (EI) *m/z* (M^+) calcd 372.19368, found 372.19412.

Hemiketal form of 6-hydroxymethyl-2,2,6-trimethyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-one (2.62) and 6-Hydroxymethyl-2,2,6,10-tetramethyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-ol (2.63)

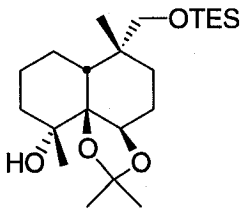




Procedure A: $CeCl_3$ (262 mg, 1.06 mmol), THF (2.1 mL + 1.4 mL), ketone **2.61** (132 mg, 0.354 mmol), methyllithium 1.6 M in diethyl ether (1.30 mL, 2.12 mmol), warmed to

room temperature for 15 minutes. Flash chromatography with 20%, then 40-50% EtOAc/hexanes gave **2.62** as a white solid (57 mg, 0.21 mmol, 60%) and **2.63** as a colorless oil (32 mg, 0.11 mmol, 32%), with a respective Rf = 0.54 and 0.33 (50% EtOAc/hexanes). **2.62** ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.54 (d, J = 5.4 Hz, 1H), 4.13 (dd, J = 12.0, 2.3 Hz, 1H), 3.64 (d, J = 12.0 Hz, 1H), 2.70 (s, 1H), 2.31-2.17 (m, 1H), 2.06 (dd, J = 14.8, 6.1 Hz, 1H), 2.01-1.77 (m, 6H), 1.70-1.58 (m, 2H), 1.49 (s, 3H), 1.41 (s, 3H), 1.41-1.35 (m, 1H), 0.86 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 107.8 (C_4), 95.3 (C_4), 81.3 (C_4), 75.0 (CH_2), 72.9 (CH), 44.3 (CH), 38.6 (CH_2), 38.1 (C_4), 36.1 (CH_2), 29.4 (CH_3), 26.9 (CH_3), 24.4 (CH_2), 23.5 (CH_3), 20.8 (CH_2), 20.0 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3424 (br), 2987 (m), 2928 (s), 2879 (m), 1718 (w), 1493 (w), 1458 (m), 1442 (w), 1381 (m), 1366 (m), 1349 (w), 1315 (w), 1248 (m), 1217 (s), 1190 (w), 1138 (m), 1118 (w), 1060 (s), 1028 (m); HRMS (EI) *m/z* (M^+) calcd 253.14398, found 253.14233. **2.63** ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.39 (t, J = 4.1 Hz, 1H), 3.83 (d, J = 11.3 Hz, 1H), 3.29 (d, J = 11.3 Hz, 1H), 2.21-2.11 (m, 1H), 1.92-1.84 (m, 2H), 1.92-1.50 (m, 7H), 1.48 (s, 3H), 1.49-1.37 (m, 1H), 1.39 (s, 3H), 1.29 (s, 3H), 0.88 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 108.5 (C_4), 83.8 (C_4), 78.0 (CH), 72.5 (C_4), 68.8 (CH_2), 46.6 (CH), 39.4 (C_4), 38.6 (CH_2), 30.4 (CH_3), 30.3 (CH_2), 29.5 (CH_3), 27.8 (CH_3), 27.1 (CH_3), 26.0 (CH_2), 21.4 (CH_2), 18.6 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3226 (br), 2930 (s), 2875 (m), 1455 (m), 1378 (s), 1367 (m), 1249 (s), 1211 (s), 1188 (w), 1158 (w), 1106 (w), 1061 (m), 1031 (s), 1012 (m); HRMS (EI) *m/z* (M^+) calcd 284.19876, found 284.19797.

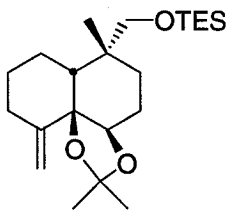
2,2,6,10-Tetramethyl-6-triethylsilanyloxymethyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-ol (2.64)



Procedure J: 4-Dimethylaminopyridine (1.2 mg, 10 μmol), triethylsilyl chloride (26 μL, 0.15 mmol), diol **2.63** (29 mg, 0.10 mmol), triethylamine (42 μL, 0.31 mmol), THF (1 mL), stirred for 4 hours. Flash chromatography with 5-8% EtOAc/hexanes gave **2.64** as a pale yellow oil (32 mg, 80 μmol, 79%) with a Rf = 0.77 (50% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.44-4.38 (m, 2H), 3.86 (d, J = 10.5 Hz, 1H), 3.27 (d, J = 10.5 Hz, 1H), 2.18-2.07 (m, 1H), 1.94 (t, J = 4.1 Hz, 1H), 1.89-1.79 (m, 1H), 1.73-1.38 (m, 8H), 1.47 (s, 3H), 1.39 (s, 3H), 1.25 (s, 3H), 0.98 (t, J = 7.7 Hz, 9H), 0.90 (s, 3H), 0.66 (q, J = 8.3 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 108.6 (C_4), 84.5 (C_4), 76.3 (CH), 71.3 (C_4), 68.8 (CH_2), 46.6 (CH), 39.4 (C_4), 38.5 (CH_2), 30.2

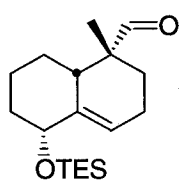
(CH_3), 29.9 (CH_2), 29.6 (CH_3), 27.9 (CH_3), 26.8 (CH_3), 25.9 (CH_2), 21.6 (CH_2), 18.5 (CH_2), 7.1 (CH_3), 4.3 (CH_2) ; IR (CH_2Cl_2, cm^{-1}) 3613 (w), 3466 (br), 3393 (br), 2955 (s), 2876 (s), 2805 (w), 2733 (w), 1726 (w), 1457 (s), 1414 (m), 1378 (s), 1367 (m), 1289 (w), 1249 (s), 1212 (s), 1192 (w), 1158 (w), 1121 (w), 1060 (m), 1031 (m), 1012 (m); HRMS (EI) *m/z* (M^+) calcd 398.28524, found 398.28447.

Triethyl-(2,2,6-trimethyl-10-methylene-octahydro-naphtho[1,8a-*d*][1,3]dioxol-6-ylmethoxy)-silane (2.65)



Procedure B: Thionyl chloride (12 μL, 0.16 mmol), alcohol **2.64** (32 mg, 79 μmol), 4-dimethylaminopyridine (58 mg, 0.47 mmol), CH_2Cl_2 (0.8 mL), stirred for 15 minutes. Flash chromatography with 2.5-5.0% EtOAc/hexanes gave **2.65** as a colorless oil (23 mg, 60 μmol, 76%), with a Rf = 0.86 (25% EtOAc/hexanes). ^1H NMR (300 MHz, $CDCl_3$) δ 4.86 (s, 1H), 4.76 (s, 1H), 4.44 (s, 1H), 3.83 (d, J = 9.6 Hz, 1H), 3.25 (d, J = 9.7 Hz, 1H), 2.46 (td, J = 13.2, 5.0 Hz, 1H), 2.19 (d, J = 12.6 Hz, 1H), 2.02-1.57 (m, 8H), 1.51 (s, 3H), 1.39-1.22 (m, 1H), 1.32 (s, 3H), 0.97 (s, 3H), 0.95 (t, J = 7.8 Hz, 9H), 0.55 (q, J = 7.9 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.0 (C_4), 107.3 (CH_2), 106.9 (C_4), 81.4 (C_4), 74.8 (CH), 64.7 (CH_2), 49.5 (CH), 41.0 (C_4), 34.4 (CH_2), 29.2 (CH_2), 29.1 (CH_3), 27.5 (CH_3), 26.9 (CH_3), 26.6 (CH_2), 23.2 (CH_2), 21.3 (CH_2), 7.2 (CH_3), 4.8 (CH_2) ; IR (CH_2Cl_2, cm^{-1}) 3081 (w), 2986 (w), 2951 (s), 2936 (s), 2875 (m), 1645 (w), 1459 (m), 1443 (m), 1416 (w), 1378 (m), 1367 (m), 1247 (m), 1213 (m), 1188 (w), 1163 (w), 1139 (w), 1083 (s), 1056 (w), 1045 (w), 1008 (s); HRMS (EI) *m/z* (M^+) calcd 380.27467, found 380.27680.

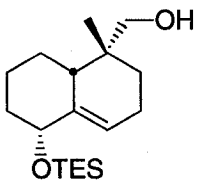
1-Methyl-5-triethylsilanyloxy-1,2,3,5,6,7,8,8a-octahydro-naphthalene-1-carbaldehyde (2.66)



Procedure J: 4-Dimethylaminopyridine (6.9 mg, 0.56 mmol), triethylsilyl chloride (1.13 mL, 6.73 mmol), alcohol **2.51** (1.09 g, 5.61 mmol), triethylamine (2.35 mL, 16.8 mmol), THF (56 mL), stirred for 30 minutes. Flash chromatography with 2.5-5% EtOAc/hexanes gave **2.66** as a pale yellow oil (1.41

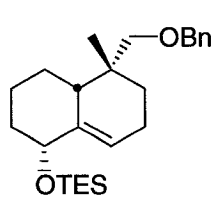
g, 4.58 mmol, 82%) with a Rf = 0.84 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.50 (s, 1H), 5.64 (s, 1H), 3.81 (d, J = 10.0 Hz, 1H), 2.11-1.80 (m, 3H), 1.79-1.56 (m, 3H), 1.54-1.44 (m, 1H), 1.38-1.08 (m, 3H), 1.05-0.91 (m, 1H), 0.94 (s, 3H), 0.84 (t, J = 8.0 Hz, 9H), 0.49 (q, J = 8.4 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.8 (CH), 140.1 (C_4), 114.4 (CH), 72.5 (CH), 46.2 (C_4), 43.1 (CH), 37.9 (CH_2), 29.3 (CH_2), 24.8 (CH_2), 23.6 (CH_2), 20.3 (CH_2), 18.7 (CH_3), 6.1 (CH_3), 4.1 (CH_2); IR (CH_2Cl_2, cm^{-1}) 2952 (s), 2936 (s), 2876 (s), 2858 (m), 2688 (w), 1727 (s), 1459 (m), 1413 (w), 1376 (w), 1343 (w), 1250 (w), 1239 (w), 1123 (s), 1090 (s), 1009 (m); HRMS (EI) *m/z* (M^+) calcd 308.21716, found 308.21568.

(1-Methyl-5-triethylsilanyloxy-1,2,3,5,6,7,8,8a-octahydro-naphthalen-1-yl)-methanol (2.67)



Procedure H: Lithium aluminum hydride (162 mg, 4.51 mmol), aldehyde **2.66** (928 mg, 3.01 mmol), THF (30 mL), warmed at 0°C for 30 minutes, water (2 x 1 mL), solution of KOH 0.1 M (1 mL), solution of sodium tartrate 0.5 M (9 mL). Flash chromatography with 15% EtOAc/hexanes gave **2.67** as a colorless oil (0.87 g, 2.8 mmol, 93%), with a Rf = 0.58 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.65 (s, 1H), 3.86 (d, J = 8.2 Hz, 1H), 3.43 (d, J = 10.6 Hz, 1H), 3.28 (d, J = 10.6 Hz, 1H), 2.20 (br, 1H), 2.06-1.88 (m, 3H), 1.83-1.71 (m, 2H), 1.56 (d, J = 12.0 Hz, 1H), 1.48-1.17 (m, 3H), 1.14-0.97 (m, 2H), 0.92 (s, 3H), 0.93 (t, J = 7.8 Hz, 9H), 0.58 (q, J = 8.0 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.8 (C_4), 114.9 (CH), 74.2 (CH), 70.2 (CH_2), 45.1 (CH), 39.3 (CH_2), 36.2 (C_4), 29.3 (CH_2), 27.8 (CH_2), 25.0 (CH_2), 21.9 (CH_2), 21.8 (CH_3), 7.3 (CH_3), 5.2 (CH_2); IR (CH_2Cl_2, cm^{-1}) 2952 (s), 2936 (s), 2876 (s), 2858 (m), 2688 (w), 1727 (s), 1459 (m), 1413 (w), 1376 (w), 1343 (w), 1250 (w), 1239 (w), 1123 (s), 1090 (s), 1009 (m); HRMS (EI) *m/z* (M^+) calcd 308.21716, found 308.21568.

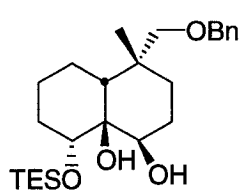
(5-Benzyloxymethyl-5-methyl-1,2,3,4,4a,5,6,7-octahydro-naphthalen-1-yloxy)-triethyl-silane (2.68)



Procedure M: Alcohol **2.67** (0.800 g, 2.58 mmol), THF (2 x 1.3 mL), NaH 60% dispersion in mineral oil (1.18 g, 2.96 mmol), tetrabutylammonium

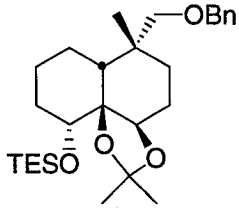
iodide (95 mg, 0.26 mmol), benzyl bromide (0.34 mL, 2.8 mmol), stirred for 2 days. Flash chromatography with 1.0-3.5% EtOAc/hexanes gave **2.68** as a colorless oil (0.76 g, 1.9 mmol, 74%), with a Rf = 0.90 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46-7.30 (m, 5H), 5.78 (s, 1H), 4.57 (s, 2H), 4.01 (d, J = 10.4 Hz, 1H), 3.35 (d, J = 8.7 Hz, 1H), 3.21 (d, J = 8.7 Hz, 1H), 2.18-2.02 (m, 3H), 1.91-1.72 (m, 3H), 1.61-0.98 (m, 5H), 1.11 (s, 3H), 1.07 (t, J = 7.9 Hz, 9H), 0.71 (q, J = 7.9 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.1 (C_4), 139.4 (C_4), 128.7 (CH), 127.8 (CH), 127.8 (CH), 114.9 (CH), 78.1 (CH_2), 74.3 (CH), 73.7 (CH_2), 45.4 (CH), 39.5 (CH_2), 35.9 (C_4), 29.5 (CH_2), 28.5 (CH_2), 25.1 (CH_2), 22.8 (CH_3), 21.9 (CH_2), 7.4 (CH_3), 5.4 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3089 (w), 3064 (w), 3031 (w), 2952 (s), 2933 (s), 2913 (s), 2875 (s), 2856 (s), 1497 (w), 1455 (m), 1413 (w), 1373 (w), 1239 (w), 1124 (s), 1092 (s), 1017 (m); HRMS (EI) *m/z* (M^+) calcd 400.27976, found 400.28108.

4-Benzyloxymethyl-4-methyl-8-triethylsilanyloxy-octahydro-naphthalene-1,8a-diol (2.69)



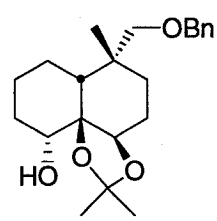
Procedure K: 4-Methylmorpholine N-oxide (0.44 g, 3.8 mmol), solution of osmium tetraoxide 4% in water (0.60 mL, 95 μmol), **2.68** (0.76 g, 1.9 mmol), water (4 mL), THF (19 mL), refluxed overnight. Flash chromatography with 2.5-15% EtOAc/hexanes gave **2.68** (0.27 g, 0.67 mmol, 35%) and **2.69** as a white foam (0.41 g, 0.94 mmol, 50%, 85% overall yield), with a Rf = 0.67 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38-7.25 (m, 5H), 4.53 (s, 1H), 4.46 (s, 2H), 4.21 (dd, J = 11.3, 5.0 Hz, 1H), 3.73 (dd, J = 12.0, 4.4 Hz, 1H), 3.24 (d, J = 8.8 Hz, 1H), 3.11 (s, 1H), 2.89 (d, J = 8.7 Hz, 1H), 2.01-1.47 (m, 7H), 1.44 (s, 3H), 1.43-1.05 (m, 4H), 0.99 (t, J = 7.6 Hz, 9H), 0.66 (q, J = 8.0 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.2 (C_4), 128.6 (CH), 127.7 (CH), 127.7 (CH), 84.0 (CH), 80.5 (CH_2), 74.8 (C_4), 73.5 (CH_2), 69.8 (CH), 46.4 (CH), 38.0 (C_4), 32.6 (CH_2), 28.7 (CH_2), 26.0 (CH_3), 25.8 (CH_2), 24.9 (CH_2), 24.1 (CH_2), 7.2 (CH_3), 5.7 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3560 (m), 3469 (br), 3088 (w), 3064 (w), 3029 (w), 2951 (s), 2913 (s), 2876 (s), 1947 (w), 1867 (w), 1808 (w), 1496 (w), 1454 (m), 1413 (m), 1382 (w), 1240 (w), 1100 (m), 1042 (m), 1008 (m); HRMS (EI) *m/z* (M^+) calcd 434.28524, found 434.28563.

(6-Benzyloxymethyl-2,2,6-trimethyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-yloxy)-triethyl-silane (2.70)



Procedure L: PTSA (1.8 mg, 9.4 μmol), diol **2.69** (0.41 g, 0.94 mmol), 2-methoxypropene (0.27 mL, 2.8 mmol), CH_2Cl_2 (9.4 mL), stirred for 15 minutes. Flash chromatography with 2-4% EtOAc/hexanes gave **2.70** as a pale yellow oil (392 mg, 0.826 mmol, 88%), with a Rf = 0.91 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40-7.24 (m, 5H), 4.54 (d, J = 12.2 Hz, 1H), 4.48 (d, J = 12.2 Hz, 1H), 4.15 (d, J = 9.0 Hz, 1H), 4.00 (t, J = 2.8 Hz, 1H), 3.67 (t, J = 2.5 Hz, 1H), 3.34 (d, J = 8.9 Hz, 1H), 1.96-1.52 (m, 8H), 1.48 (s, 3H), 1.48-1.27 (m, 3H), 1.35 (s, 3H), 1.09 (s, 3H), 1.01 (t, J = 8.1 Hz, 9H), 0.64 (q, J = 8.0 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.0 (C_4), 128.6 (CH), 127.5 (CH), 127.3 (CH), 107.7 (C_4), 81.1 (C_4), 79.5 (CH), 74.7 (CH), 73.5 (CH_2), 73.4 (CH_2), 48.1 (CH), 40.1 (C_4), 31.6 (CH_2), 29.0 (CH_3), 28.8 (CH_2), 28.0 (CH_3), 27.4 (CH_3), 24.4 (CH_2), 21.2 (CH_2), 18.2 (CH_2), 7.4 (CH_3), 5.4 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3089 (w), 3064 (w), 3030 (w), 2954 (s), 2877 (s), 1496 (w), 1454 (m), 1376 (m), 1251 (m), 1214 (m), 1170 (w), 1100 (m), 1054 (m), 1017 (m), 1006 (m); HRMS (EI) *m/z* (M^+) calcd 474.31654, found 474.31585.

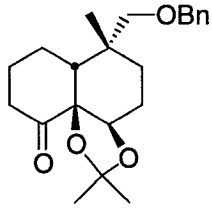
6-Benzyloxymethyl-2,2,6-trimethyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-ol (2.71)



Tetrabutyl ammonium fluoride 1.0 M in THF (1.24 mL, 1.24 mmol) was added to a solution of **2.70** (392 mg, 0.826 mmol) in THF (8.3 mL) at room temperature and the reaction was stirred at this temperature for 30 minutes. The reaction was concentrated *in vacuo* and flash chromatography with 15-20% EtOAc/hexanes gave **2.71** as a pale yellow oil (252 mg, 0.700 mmol, 85%), with a Rf = 0.53 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41-7.27 (m, 5H), 4.58 (d, J = 12.1 Hz, 1H), 4.46 (d, J = 12.1 Hz, 1H), 4.19 (t, J = 3.4 Hz, 1H), 4.30-3.98 (br, 1H), 3.75 (d, J = 9.5 Hz, 1H), 3.58 (s, 1H), 3.21 (d, J = 9.5 Hz, 1H), 2.25-2.11 (m, 1H), 1.97-1.52 (m, 8H), 1.47 (s, 3H), 1.34 (s, 3H), 1.42-1.23 (m, 2H), 0.94 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.7 (C_4), 128.8 (CH), 128.4 (CH), 128.3 (CH), 107.9 (C_4), 80.9 (C_4), 79.0 (CH), 76.1 (CH_2), 74.0 (CH_2), 73.1 (CH), 46.0 (CH), 39.0 (C_4), 31.4 (CH_2), 31.0 (CH_2), 29.8 (CH_3), 29.1 (CH_3),

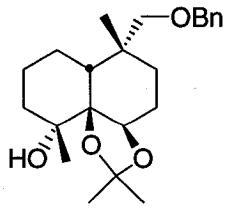
27.4 (CH_3), 25.2 (CH_2), 21.2 (CH_2), 17.3 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3456 (br), 3090 (w), 3064 (w), 3030 (w), 2982 (s), 2934 (s), 2870 (s), 1739 (w), 1496 (w), 1454 (m), 1377 (m), 1251 (m), 1213 (m), 1092 (m), 1048 (m), 1011 (m); HRMS (EI) *m/z* (M^+) calcd 360.23006, found 360.23051.

6-Benzyloxymethyl-2,2,6-trimethyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-one (2.72)



Procedure F: Dess-Martin periodinane (356 mg, 0.840 mmol), alcohol **2.71** (252 mg, 0.700 mmol), CH_2Cl_2 (7 mL), stirred for 50 minutes. Flash chromatography with 7.5-10% EtOAc/hexanes gave **2.72** as a pale yellow oil (226 mg, 0.630 mmol, 90%), with a Rf = 0.40 (10% EtOAc/hexanes). ^1H NMR (300 MHz, $CDCl_3$) δ 7.40-7.24 (m, 5H), 4.75 (t, J = 3.5 Hz, 1H), 4.43 (d, J = 12.2 Hz, 1H), 4.28 (d, J = 12.2 Hz, 1H), 3.21 (d, J = 9.0 Hz, 1H), 3.14 (d, J = 9.0 Hz, 1H), 2.76 (ddd, J = 14.6, 11.4, 6.5 Hz, 1H), 2.28 (dt, J = 14.8, 4.3 Hz, 1H), 2.15-1.41 (m, 9H), 1.50 (s, 3H), 1.29 (s, 3H), 0.98 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.6 (C_4), 138.3 (C_4), 128.7 (CH), 128.3 (CH), 128.0 (CH), 108.3 (C_4), 82.9 (C_4), 74.4 (CH_2), 73.1 (CH_2), 72.3 (CH), 51.5 (CH), 39.4 (CH_2), 39.3 (C_4), 32.5 (CH_2), 29.1 (CH_3), 26.6 (CH_3), 26.6 (CH_3), 24.0 (CH_2), 23.4 (CH_2), 20.8 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3089 (w), 3064 (w), 3031 (w), 2985 (m), 2937 (s), 2877 (m), 1718 (s), 1454 (m), 1379 (m), 1254 (m), 1216 (m), 1096 (m), 1054 (m), 1007 (m); HRMS (EI) *m/z* (M^+) calcd 358.21441, found 358.21481.

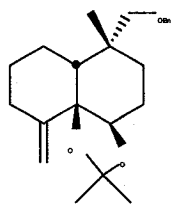
6-Benzyloxymethyl-2,2,6,10-tetramethyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-ol (2.73)



Procedure A: $CeCl_3$ (466 mg, 1.89 mmol), THF (3.8 mL + 2.5 mL), ketone **2.72** (226 mg, 0.630 mmol), methyllithium 1.6 M in diethyl ether (2.36 mL, 3.78 mmol), warmed to room temperature for 15 minutes. Flash chromatography with 15-17% EtOAc/hexanes gave **2.73** as a colorless oil (196 mg, 0.523 mmol, 83%), with a Rf = 0.26 (15% EtOAc/hexanes). ^1H NMR (300 MHz, $CDCl_3$) δ 7.40-7.26 (m, 5H), 4.54-4.45 (br, 1H), 4.65 (d, J = 12.5 Hz, 1H), 4.44 (d, J = 12.6 Hz, 1H), 4.43 (d, J = 4.9 Hz, 1H), 3.65 (d, J = 9.6 Hz, 1H), 3.16 (d, J = 9.6 Hz,

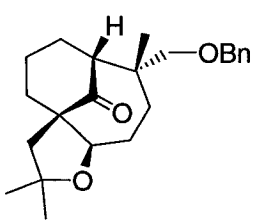
1H), 2.24-2.09 (m, 1H), 1.94-1.83 (m, 2H), 1.76-1.31 (m, 8H), 1.47 (s, 3H), 1.39 (s, 3H), 1.27 (s, 3H), 0.91 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.5 (C_4), 128.9 (CH), 128.4 (CH), 128.3 (CH), 108.3 (C_4), 83.9 (C_4), 76.1 (CH_2), 75.8 (CH), 73.7 (CH_2), 71.5 (C_4), 46.9 (CH), 39.0 (C_4), 38.7 (CH_2), 30.6 (CH_2), 30.4 (CH_3), 29.5 (CH_3), 27.8 (CH_3),), 26.9 (CH_3), 25.8 (CH_2), 21.5 (CH_2), 18.7 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3389 (br), 3089 (w), 3064 (w), 3030 (w), 2987 (m), 2934 (s), 2868 (m), 1453 (m), 1378 (m), 1249 (m), 1212 (m), 1100 (w), 1061 (m), 1031 (m), 1015 (m); HRMS (EI) *m/z* (M^+) calcd 374.24571, found 374.24609.

6-Benzyloxymethyl-2,2,6-trimethyl-10-methylene-octahydro-naphtho[1,8a-*d*][1,3]dioxole (2.74)



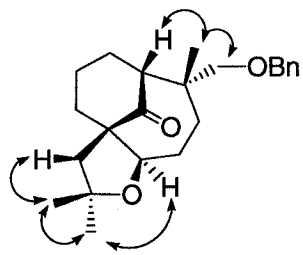
Procedure B: Thionyl chloride (76 μL, 1.1 mmol), alcohol **2.73** (196 mg, 0.523 mmol), 4-dimethylaminopyridine (383 mg, 3.14 mmol), CH_2Cl_2 (5.2 mL), stirred for 15 minutes. Flash chromatography with 4-8% EtOAc/hexanes gave **2.74** as a pale yellow oil (125 mg, 350 μmol, 67%), with a Rf = 0.49 (10% EtOAc/hexanes). ^1H NMR (300 MHz, $CDCl_3$) δ 7.40-7.26 (m, 5H), 4.76 (s, 1H), 4.58 (s, 1H), 4.55 (d, J = 12.3 Hz, 1H), 4.37 (d, J = 12.0 Hz, 1H), 4.37 (s, 1H), 3.68 (d, J = 8.9 Hz, 1H), 3.14 (d, J = 8.9 Hz, 1H), 2.46 (td, J = 13.1, 4.9 Hz, 1H), 2.17 (d, J = 12.6 Hz, 1H), 1.99-1.60 (m, 7H), 1.51 (s, 3H), 1.48-1.22 (m, 2H), 1.32 (s, 3H), 1.07 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.5 (C_4), 139.4 (C_4), 128.6 (CH), 128.0 (CH), 127.8 (CH), 107.7 (CH_2), 106.9 (C_4), 81.3 (C_4), 74.6 (CH), 73.6 (CH_2), 72.5 (CH_2), 49.9 (CH), 40.1 (C_4), 34.3 (CH_2), 30.0 (CH_2), 29.1 (CH_3), 27.5 (CH_3), 27.4 (CH_3), 26.4 (CH_2), 23.2 (CH_2), 21.4 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3080 (w), 3065 (w), 3029 (w), 2984 (m), 2938 (s), 2868 (m), 1946 (w), 1874 (w), 1807 (w), 1646 (w), 1455 (m), 1378 (m), 1249 (m), 1213 (m), 1090 (m), 1057 (m), 1009 (s); HRMS (EI) *m/z* (M^+) calcd 356.23514, found 356.23631.

8-Benzyloxymethyl-3,3,8-trimethyl-4-oxa-tricyclo[7.3.1.$0^{1,5}$]tridecan-13-one (2.75)

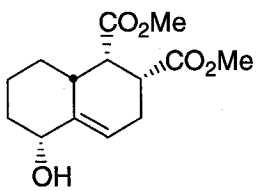


Procedure C: Triflic acid (100 μL, 112 μmol), Prins-pinacol precursor **2.74** (20 mg, 56 μmol), MeCN (1.1 mL), from -40°C to 0°C, stirred for 2 hours

and 30 minutes. Flash chromatography with 12.5% EtOAc/hexanes gave **2.75** as a colorless oil (13 mg, 34 μmol, 63%), with a Rf = 0.41 (15% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35-7.24 (m, 5H), 4.47 (s, 2H), 4.09 (dd, J = 11.3, 4.0 Hz, 1H), 3.35 (d, J = 9.0 Hz, 1H), 3.09 (d, J = 9.0 Hz, 1H), 2.93 (d, J = 13.1 Hz, 1H), 2.54 (dd, J = 6.8, 3.5 Hz, 1H), 2.31-2.24 (m, 1H), 2.12-2.04 (m, 1H), 1.86-1.55 (m, 5H), 1.54-1.30 (m, 4H), 1.28 (s, 3H), 1.24 (s, 3H), 1.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.5 (C_4), 138.5 (C_4), 128.3 (CH), 127.5 (CH), 127.3 (CH), 86.7 (CH), 80.4 (C_4), 77.9 (CH_2), 73.2 (CH_2), 61.4 (C_4), 55.1 (CH), 47.6 (CH_2), 42.2 (CH_2), 39.9 (C_4), 31.3 (CH_2), 30.0 (CH_3), 29.2 (CH_2), 28.0 (CH_3), 27.0 (CH_2), 24.2 (CH_3), 20.8 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3088 (w), 3063 (w), 3030 (w), 2968 (s), 2934 (s), 2859 (s), 1694 (s), 1453 (m), 1379 (m), 1364 (m), 1272 (m), 1182 (w), 1148 (w), 1100 (s), 1046 (s); HRMS (EI) *m/z* (M^+) calcd 356.23514, found 356.23861. COSY, NOES and HMQC experiments were performed in order to obtain the correlations illustrated below:



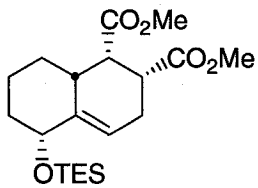
5-Hydroxy-1,2,3,5,6,7,8,8a-octahydro-naphthalene-1,2-dicarboxylic acid dimethyl ester (2.82)



Procedure G: Lutidine (3.83 mL, 32.9 mmol), diene **2.19**[71] (1.36 g, 11.0 mmol), magnesium bromide etherate (5.66 g, 21.9 mmol), CH_2Cl_2 (110 mL), dimethyl maleate (3.02 mL, 24.1 mmol), stirred for 30 minutes. Flash chromatography with 40-50% EtOAc/hexanes gave **2.82** as a pale yellow oil (1.76 g, 5.61 mmol, 60% over 3 steps), with a Rf = 0.61 (80% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.72 (d, J = 3.8 Hz, 1H), 3.81-3.72 (m 1H), 3.32-2.96 (br, 1H), 3.52 (s, 3H), 3.48 (s, 3H), 3.04 (dd, J = 6.7, 2.9 Hz, 1H), 2.70-2.48 (m, 2H), 2.33-2.02 (m, 2H), 1.94-1.83 (m, 1H), 1.72-1.58 (m, 2H), 1.34-1.01 (m, 2H), 0.84 (qd, 12.3, 3.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.6 (C_4), 173.1 (C_4), 139.4 (C_4), 115.9 (CH), 71.9 (CH), 52.1 (CH_3), 51.4

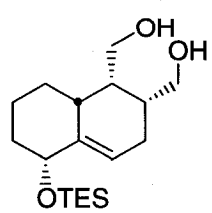
(CH_3), 44.4 (CH), 41.4 (CH), 38.0 (CH), 36.2 (CH_2), 29.9 (CH_2), 24.8 (CH_2), 23.7 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3504 (br), 2996 (w), 2948 (s), 2858 (m), 1735 (s), 1619 (w), 1437 (m), 1387 (w), 1365 (w), 1276 (m), 1199 (s), 1164 (s), 1106 (w), 1073 (w), 1028 (m); HRMS (EI) *m/z* (M^+-H_2O) calcd 250.12051, found 250.12133.

5-Triethylsilanyloxy-1,2,3,5,6,7,8,8a-octahydro-naphthalene-1,2-dicarboxylic acid dimethyl ester (2.83)



Procedure J: 4-Dimethylaminopyridine (80 mg, 0.66 mmol), triethylsilyl chloride (1.32 mL, 7.88 mmol), alcohol **2.82** (1.76 g, 6.56 mmol), triethylamine (2.74 mL, 19.7 mmol), THF (66 mL), stirred for 30 minutes. Flash chromatography with 10% EtOAc/hexanes gave **2.83** as a colorless oil (1.82 g, 4.76 mmol, 73%), with a Rf = 0.82 (40% EtOAc/hexanes). ^1H NMR (300 MHz, $CDCl_3$) δ 5.86 (d, J = 3.3 Hz, 1H), 3.94-3.84 (m 1H), 3.65 (s, 3H), 3.62 (s, 3H), 3.17 (dd, J = 6.6, 2.7 Hz, 1H), 2.83-2.68 (m, 2H), 2.40-2.22 (m, 2H), 1.97-1.70 (m, 3H), 1.41-1.13 (m, 2H), 1.03-0.87 (m, 1H), 0.94 (t, 7.9 Hz, 9H), 0.58 (q, J = 8.1Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.7 (C_4), 173.1 (C_4), 139.1 (C_4), 116.5 (CH), 72.9 (CH), 52.2 (CH_3), 51.5 (CH_3), 44.6 (CH), 41.5 (CH), 38.1 (CH), 37.0 (CH_2), 30.1 (CH_2), 25.0 (CH_2), 23.9 (CH_2), 7.3 (CH_3), 5.3 (CH_2); IR (CH_2Cl_2, cm^{-1}) 2950 (s), 2937 (s), 2875 (m), 1738 (s), 1435 (m), 1376 (w), 1276 (w), 1240 (w), 1196 (m), 1160 (m), 1117 (m), 1081 (w), 1017 (w); HRMS (EI) *m/z* (M^+) calcd 382.21755, found 382.21732.

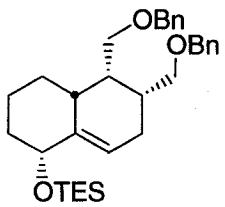
(2-Hydroxymethyl-5-triethylsilanyloxy-1,2,3,5,6,7,8,8a-octahydro-naphthalen-1-yl)-methanol (2.84)



Procedure H: Lithium aluminum hydride (94 mg, 2.6 mmol), diester **2.83** (0.25 g, 0.65 mmol), THF (6.5 mL), warmed at 0°C for 30 minutes, water (2 x 1 mL), solution of KOH 0.1 M (1 mL), solution of sodium tartrate 0.5 M (9 mL). Flash chromatography with 90% EtOAc/hexanes gave **2.84** as a pale yellow oil (142 mg, 0.435 mmol, 67%), with a Rf = 0.28 (100% EtOAc). ^1H NMR (300 MHz, acetone-d_6)

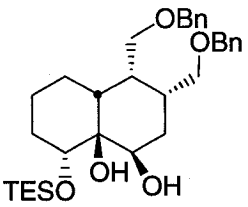
δ 5.75-5.66 (m, 1H), 4.07-3.97 (m 1H), 3.74-3.48 (m, 6H), 2.28-2.13 (m, 2H), 2.13-1.89 (m, 4H), 1.82-1.67 (m, 2H), 1.39 (qt, J = 13.2, 3.2 Hz, 1H), 1.34-1.15 (m, 1H), 1.06 (qd, J = 12.9, 4.2 Hz, 1H), 0.98 (t, 7.7 Hz, 9H), 0.63 (q, J = 8.0 Hz, 6H); ^{13}C NMR (75 MHz, acetone-d_6) δ 142.0 (C_4), 115.0 (CH), 73.5 (CH), 62.8 (CH_2), 61.1 (CH_2), 42.2 (CH), 39.3 (CH), 39.3 (CH), 38.2 (CH_2), 29.7 (CH_2), 26.7 (CH_2), 24.5 (CH_2), 6.8 (CH_3), 5.0 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3353 (br), 2935 (s), 2876 (m), 2732 (s), 1667 (w), 1457 (m), 1414 (m), 1378 (m), 1239 (m), 1143 (m), 1113 (m), 1087 (s), 1017 (s); HRMS (EI) *m/z* (M^+) calcd 326.22772, found 326.22950.

(5,6-Bis-benzyloxymethyl-1,2,3,4,4a,5,6,7-octahydro-naphthalen-1-yloxy)-triethyl-silane (2.85)



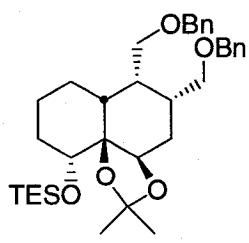
Procedure M: Diol **2.84** (0.142 g, 0.435 mmol), THF (2 x 2.2 mL), NaH 60% dispersion in mineral oil (40 mg, 1.0 mmol), tetrabutylammonium iodide (32 mg, 87 μmol), benzyl bromide (0.12 mL, 0.96 mmol), stirred overnight. Flash chromatography with 3-6% EtOAc/hexanes gave **2.85** as a colorless oil (0.197 g, 0.389 mmol, 89%), with a Rf = 0.92 (50% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.26 (m, 10H), 5.75 (s, 1H), 4.52-4.45 (m, 4H), 4.02-3.95 (m, 1H), 3.61-3.44 (m, 4H), 2.36-2.29 (m, 1H), 2.28-2.14 (m, 3H), 2.14-2.01 (m, 1H), 1.99-1.93 (m, 1H), 1.84-1.76 (m, 1H), 1.72-1.64 (m, 1H), 1.43-1.25 (m, 2H), 1.12-1.01 (m, 1H), 1.01 (t, 7.8 Hz, 9H), 0.66 (q, J = 8.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.2 (C_4), 138.8 (C_4), 138.8 (C_4), 128.5 (CH), 128.4 (CH), 127.8 (CH), 127.7 (CH), 127.6 (CH), 127.5 (CH), 115.2 (CH), 73.2 (CH_2), 73.1 (CH), 73.1 (CH_2), 72.1 (CH_2), 69.7 (CH_2), 39.2 (CH), 39.0 (CH), 37.7 (CH_2), 36.5 (CH), 29.4 (CH_2), 27.1 (CH_2), 24.4 (CH_2), 7.0 (CH_3), 5.0 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3088 (w), 3062 (w), 3029 (w), 2934 (s), 2914 (s), 2875 (s), 2855 (s), 1947 (w), 1868 (w), 1806 (w), 1605 (w), 1496 (w), 1454 (m), 1414 (w), 1364 (w), 1239 (w), 1150 (w), 1112 (s), 1101 (s), 1090 (s), 1027 (w) 1015 (m); HRMS (EI) *m/z* (M^+) calcd 506.32162, found 506.32131.

3,4-Bis-benzyloxymethyl-8-triethylsilanyloxy-octahydro-naphthalene-1,8a-diol (2.86)



Procedure K: 4-Methylmorpholine N-oxide (91 mg, 0.77 mmol), solution of osmium tetraoxide 4% in water (0.12 mL, 19 μmol), **2.85** (0.197 g, 0.389 mmol), water (0.8 mL), THF (3.9 mL), refluxed for 12 days. Flash chromatography with 15% EtOAc/hexanes gave **2.85** (27 mg, 54 μmol, 14%) and **2.86** as a white foam (97.0 mg, 0.179 mmol, 46%, 60% overall yield), with a Rf = 0.31 (15% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.23 (m, 10H), 4.61 (s, 1H), 4.51-4.43 (m, 4H), 4.29 (dd, J = 11.5, 4.9 Hz, 1H), 3.71 (dd, J = 12.2, 4.5 Hz, 1H), 3.46-3.34 (m, 4H), 3.02 (s, 1H), 2.73-2.67 (m, 1H), 2.33-2.24 (m, 1H), 2.03 (ddd, J = 13.3, 4.8, 1.6 Hz, 1H), 1.88-1.71 (m, 3H), 1.70-1.63 (m, 1H), 1.56 (qd, J = 13.4, 3.4 Hz, 1H), 1.38 (d, J = 13.4 Hz, 1H), 1.19 (qt, J = 13.4, 3.5 Hz, 1H), 0.96 (t, J = 7.8 Hz, 9H), 0.63 (q, J = 8.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7 (C_4), 138.6 (C_4), 128.4 (CH), 128.3 (CH), 127.6 (CH), 127.5 (CH), 127.5 (CH), 127.5 (CH), 83.2 (CH), 73.4 (C_4), 73.0 (CH_2), 72.9 (CH_2), 70.8 (CH_2), 70.2 (CH_2), 66.2 (CH), 42.7 (CH), 35.6 (CH), 35.0 (CH), 32.4 (CH_2), 31.2 (CH_2), 25.2 (CH_2), 24.0 (CH_2), 6.8 (CH_3), 4.9 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3565 (w), 3461 (br), 3087 (w), 3063 (w), 3028 (w), 2951 (s), 2936 (s), 2913 (s), 2876 (s), 2804 (w), 1950 (w), 1867 (w), 1808 (w), 1495 (w), 1453 (m), 1413 (w), 1366 (w), 1239 (w), 1091 (s), 1010 (m); HRMS (EI) *m/z* (M^+) calcd 540.32710, found 540.32393.

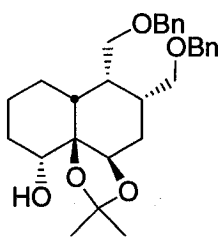
(5,6-Bis-benzyloxymethyl-2,2-dimethyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-yloxy)-triethyl-silane (2.87)



Procedure L: PTSA (0.34 mg, 1.8 μmol), diol **2.86** (97.0 mg, 0.179 mmol), 2-methoxypropene (52 μL, 0.54 mmol), CH_2Cl_2 (1.8 mL), stirred for 30 minutes. Flash chromatography with 5.0-7.5% EtOAc/hexanes gave **2.87** as a pale yellow oil (77.0 mg, 0.133 mmol, 74%), with a Rf = 0.72 (15% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.21 (m, 10H), 4.51-4.38 (m, 4H), 4.11 (s, 1H), 3.80-3.68 (m, 1H), 3.65-3.61 (m, 1H), 3.61-3.54 (m, 2H), 3.40-3.34 (m, 1H), 2.42-2.20 (m, 2H), 2.10 (d, J = 14.5 Hz, 1H), 2.00 (s, 1H), 1.84-1.46 (m, 6H), 1.45 (s, 3H), 1.36 (s, 3H), 1.37-1.26 (m, 1H), 0.96 (t, J = 7.8 Hz, 9H), 0.62 (q, J = 8.0 Hz, 6H); ^{13}C

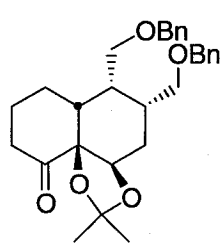
NMR (100 MHz, $CDCl_3$) δ 139.0 (C_4), 138.9 (C_4), 128.3 (CH), 128.2 (CH), 128.1 (CH), 127.6 (CH), 127.4 (CH), 127.3 (CH), 107.3 (C_4), 74.3 (C_4), 74.3 (CH), 73.3 (CH_2), 72.9 (CH_2), 72.7 (CH_2), 69.3 (CH_2), 66.2 (CH), 41.1 (CH), 35.6 (CH), 35.0 (CH), 31.2 (CH_2), 30.7 (CH_2), 28.4 (CH_3), 27.9 (CH_2), 27.0 (CH_3), 25.6 (CH_2), 7.0 (CH_3), 5.0 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3087 (w), 3063 (w), 3030 (w), 2952 (s), 2934 (s), 2912 (s), 2876 (s), 2798 (w), 1947 (w), 1868 (w), 1806 (w), 1496 (w), 1454 (m), 1413 (w), 1378 (m), 1251 (m), 1212 (m), 1176 (w), 1112 (s), 1095 (s), 1066 (s), 1035 (s), 1003 (m); HRMS (EI) *m/z* (M^+-HOBn) calcd 472.30089, found 472.29997.

5,6-Bis-benzyloxymethyl-2,2-dimethyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-ol (2.88)



Tetrabutyl ammonium fluoride 1.0 M in THF (0.19 mL, 0.19 mmol) was added to a solution of **2.87** (74.0 mg, 0.127 mmol) in THF (1.3 mL) at room temperature and the reaction was stirred at this temperature for 40 minutes. The reaction was concentrated *in vacuo* and flash chromatography with 33% EtOAc/hexanes gave **2.88** as a pale yellow oil (59.0 mg, 0.126 mmol, 99%), with a Rf = 0.60 (40% EtOAc/hexanes). ^1H NMR (400 MHz, $CDCl_3$) δ 7.36-7.22 (m, 10H), 4.48 (d, J = 11.8 Hz, 1H), 5.42-4.63 (br, 1H), 4.35-4.23 (m, 4H), 3.61 (dd, J = 10.4, 3.1 Hz, 1H), 3.59-3.49 (m, 2H), 3.40-3.21 (m, 2H), 2.47-2.36 (m, 1H), 2.21-1.94 (m, 1H), 1.94-1.52 (m, 6H), 1.52-1.25 (m, 3H), 1.43 (s, 3H), 1.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4 (C_4), 136.8 (C_4), 128.7 (CH), 128.5 (CH), 128.4 (CH), 128.2 (CH), 127.8 (CH), 127.6 (CH), 107.5 (C_4), 79.9 (CH), 74.3 (C_4), 73.5 (CH_2), 73.0 (CH_2), 72.1 (CH_2), 69.3 (CH_2), 66.2 (CH), 41.1 (CH), 31.1 (CH), 30.7 (CH_2), 28.7 (CH_3), 28.7 (CH_3), 28.5 (CH_2), 26.9 (CH_2), 25.6 (CH_2), 25.3 (CH); IR (CH_2Cl_2, cm^{-1}) 3390 (br), 3088 (w), 3062 (w), 3030 (w), 2983 (s), 2930 (s), 2865 (s), 2797 (w), 1951 (w), 1874 (w), 1811 (w), 1495 (m), 1453 (s), 1366 (s), 1251 (m), 1212 (m), 1160 (w), 1088 (s), 1073 (s), 1027 (s); HRMS (EI) *m/z* (M^+) calcd 466.27193, found 466.27029.

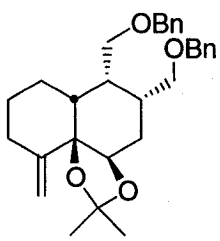
5,6-Bis-benzyloxymethyl-2,2-dimethyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-one (2.89)



Procedure F: Dess-Martin periodinane (64 mg, 0.15 mmol), alcohol **2.88** (59.0 mg, 0.126 mmol), CH_2Cl_2 (1.3 mL), stirred for 30 minutes. Flash

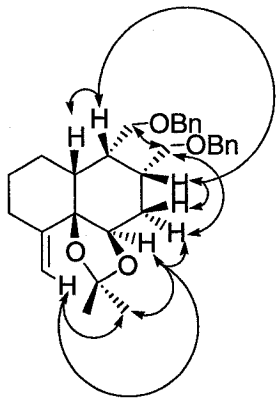
chromatography with 15% EtOAc/hexanes gave **2.89** as a pale yellow oil (48.5 mg, 0.104 mmol, 83%), with a Rf = 0.78 (40% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33-7.19 (m, 10H), 4.72 (s, 1H), 4.41-4.32 (m, 3H), 4.15 (d, J = 12.1 Hz, 1H), 3.38-3.28 (m, 3H), 3.23 (t, J = 9.2 Hz, 1H), 2.66 (ddd, J = 14.5, 10.9, 6.5 Hz, 1H), 2.37-2.23 (m, 3H), 2.22-2.04 (m, 2H), 1.93-1.72 (m, 4H), 1.66-1.58 (m, 1H), 1.46 (s, 3H), 1.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.8 (C_4), 138.4 (C_4), 137.6 (C_4), 128.4 (CH), 128.3 (CH), 127.7 (CH), 127.6 (CH), 127.6 (CH), 127.6 (CH), 108.2 (C_4), 82.7 (C_4), 73.0 (CH_2), 72.3 (CH_2), 72.1 (CH), 72.1 (CH_2), 66.3 (CH_2), 45.0 (CH), 39.5 (CH), 39.4 (CH_2), 34.3 (CH), 28.5 (CH_3), 27.0 (CH_2), 26.1 (CH_3), 25.0 (CH_2), 23.4 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3088 (w), 3065 (w), 3030 (w), 2985 (m), 2917 (s), 2857 (s), 2799 (w), 1951 (w), 1874 (w), 1811 (w), 1720 (s), 1496 (w), 1454 (m), 1367 (m), 1255 (m), 1217 (m), 1161 (m), 1097 (s), 1066 (s), 1027 (s), 1016 (s); HRMS (EI) *m/z* (M^+) calcd 464.25628, found 464.25736.

5,6-Bis-benzyloxymethyl-2,2-dimethyl-10-methylene-octahydro-naphtho[1,8a-*d*][1,3]dioxole (2.90)

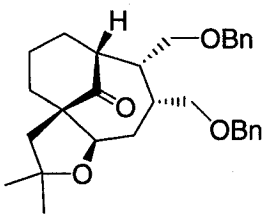


Procedure N: Potassium *tert*-butoxide 1.0 M solution in THF (0.31 mL, 0.13 mmol), methyltriphenylphosphonium iodide (126 mg, 0.313 mmol), toluene (0.6 + 0.4 mL), ketone **2.89** (48.5 mg, 0.104 mmol), refluxed for 1 hour. Flash chromatography with 10% EtOAc/hexanes gave **2.90** as a pale yellow oil (41.0 mg, 88.6 μmol, 85%), with a Rf = 0.61 (15% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.22 (m, 10H), 4.95 (s, 1H), 4.78 (s, 1H), 4.46 (d, J = 12.0 Hz, 1H), 4.39 (d, J = 12.0 Hz, 1H), 4.39 (s, 2H), 4.27 (s, 1H), 3.54 (dd, J = 9.2, 5.6 Hz, 1H), 3.53-3.42 (m, 3H), 2.63-2.36 (m, 3H), 2.17 (dq, J = 15.0, 2.8 Hz, 1H), 2.04-1.56 (m, 6H), 1.51 (s, 3H), 1.48-1.33 (m, 1H), 1.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.7 (C_4), 138.8 (C_4), 138.6 (C_4), 128.3 (CH), 128.3 (CH), 127.7 (CH), 127.5 (CH), 127.5 (CH), 127.4 (CH), 107.4 (CH_2), 107.2 (C_4), 83.1 (C_4), 76.4 (CH), 72.9 (CH_2), 72.7 (CH_2), 72.6 (CH_2), 69.1 (CH_2), 44.1 (CH), 44.0 (CH), 34.4 (CH_2), 34.2 (CH_2), 27.8 (CH_2), 27.7 (CH), 26.8 (CH_3), 26.8 (CH_3), 26.4 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3087 (w), 3068 (w), 3029 (w), 2987 (m), 2931 (s), 2857 (s), 2795 (w), 1951 (w), 1871 (w), 1809 (w), 1646 (w), 1496 (w), 1453 (s), 1366 (s), 1252 (m), 1210 (s), 1181 (m), 1098 (s), 1070 (s), 1027 (m); HRMS (EI) *m/z* (M^+) calcd 462.27701, found 462.27954. COSY,

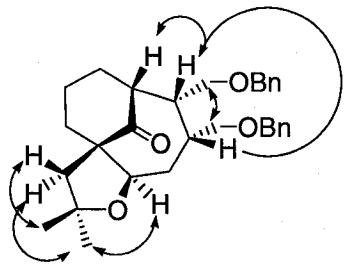
NOESY and HMQC experiments were performed in order to obtain the correlations illustrated below:



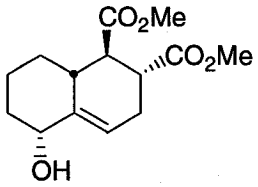
7,8-Bis-benzyloxymethyl-3,3-dimethyl-4-oxa-tricyclo[7.3.1.0^{1,5}]tridecan-13-one (2.91)

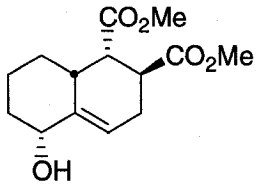


Procedure C: Tin tetrachloride 1.0 M in CH_2Cl_2 (28 μL, 28 μmol), Prins-pinacol precursor **2.90** (13.0 mg, 28.1 μmol), CH_2Cl_2 (0.56 mL), from -78°C to -20°C, stirred for 2 hours and 30 minutes. Flash chromatography with 15-20% EtOAc/hexanes gave **2.91** as a colorless oil (10.5 mg, 22.7 μmol, 81%), with a Rf = 0.34 (20% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.22 (m, 10H), 4.45-4.33 (m, 4H), 3.91 (s, 1H), 3.58 (d, J = 6.1 Hz, 2H), 3.39-3.30 (m, 2H), 3.09-3.03 (m, 1H), 2.83 (d, J = 12.8 Hz, 1H), 2.55-2.46 (m, 1H), 2.20-2.08 (m, 3H), 1.98-1.89 (m, 1H), 1.87-1.64 (m, 4H), 1.47-1.36 (m, 1H), 1.35-1.23 (m, 1H), 1.30 (s, 3H), 1.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 213.2 (C_4), 138.4 (C_4), 138.4 (C_4), 128.3 (CH), 128.3 (CH), 127.8 (CH), 127.6 (CH), 127.6 (CH), 127.5 (CH), 82.7 (CH), 78.6 (C_4), 73.0 (CH_2), 72.6 (CH_2), 72.6 (CH_2), 68.4 (CH_2), 61.0 (C_4), 49.6 (CH), 48.4 (CH_2), 39.0 (CH_2), 37.1 (CH), 32.2 (CH), 31.4 (CH_2), 29.7 (CH_3), 29.5 (CH_3), 27.3 (CH_2), 21.0 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3088 (w), 3062 (w), 3029 (w), 2964 (m), 2926 (s), 2856 (s), 1951 (w), 1870 (w), 1811 (w), 1694 (s), 1496 (w), 1453 (m), 1363 (m), 1246 (w), 1086 (s), 1026 (m); HRMS (EI) *m/z* (M^+-Bn) calcd 371.22224, found 371.22544. COSY, NOESY and HMQC experiments were performed in order to obtain the correlations illustrated below:



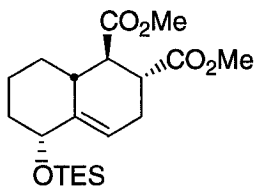
5-Hydroxy-1,2,3,5,6,7,8,8a-octahydro-naphthalene-1,2-dicarboxylic acid dimethyl ester (2.98 and 2.99)

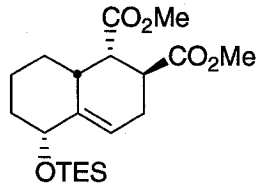




Procedure G: Lutidine (1.27 mL, 10.9 mmol), diene **2.19**[71] (0.45 g, 3.6 mmol), magnesium bromide etherate (1.87 g, 7.26 mmol), CH_2Cl_2 (36 mL), dimethyl fumarate (1.15 g, 7.99 mmol), stirred for 2 days. Flash chromatography with 40-50% EtOAc/hexanes gave a 2 : 5 mixture of **2.98** and **2.99**, which is a yellow oil (0.72 g, 2.7 mmol, 74% over 3 steps), with a Rf = 0.62 (80% EtOAc/hexanes). **2.98** ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.68 (d, J = 4.8 Hz, 1H), 3.91-3.74 (m 1H), 3.57 (s, 3H), 3.53 (s, 3H), 3.49-3.36 (br, 1H), 2.70 (dd, J = 11.7, 5.2 Hz, 1H), 2.39-1.59 (m, 6H), 1.48-0.78 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.9 (C_4), 175.3 (C_4), 141.5 (C_4), 114.6 (CH), 71.6 (CH), 52.2 (CH_3), 52.2 (CH_3), 49.9 (CH), 42.3 (CH), 39.9 (CH), 36.3 (CH_2), 33.2 (CH_2), 28.0 (CH_2), 23.4 (CH_2); **2.99** ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.54 (d, J = 4.8 Hz, 1H), 3.91-3.74 (m 1H), 3.55 (s, 3H), 3.55 (s, 3H), 3.49-3.36 (br, 1H), 2.89 (dd, J = 12.1, 6.3 Hz, 1H), 2.62-2.56 (m, 1H), 2.39-1.59 (m, 5H), 1.48-0.78 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.5 (C_4), 174.3 (C_4), 143.5 (C_4), 113.0 (CH), 72.5 (CH), 52.2 (CH_3), 52.0 (CH_3), 45.7 (CH), 38.5 (CH), 38.4 (CH), 37.9 (CH_2), 30.3 (CH_2), 28.9 (CH_2), 24.3 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3471 (br), 2998 (w), 2934 (s), 2856 (s), 1738 (s), 1440 (m), 1344 (m), 1315 (m), 1261 (m), 1197 (m), 1160 (m), 1135 (m), 1102 (w), 1077 (m), 1026 (m), 1001 (w); HRMS (EI) *m/z* (M^+-H_2O) calcd 250.12051, found 250.11896.

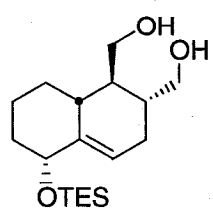
5-Triethylsilanyloxy-1,2,3,5,6,7,8,8a-octahydro-naphthalene-1,2-dicarboxylic acid dimethyl ester (2.100 and 2.101)

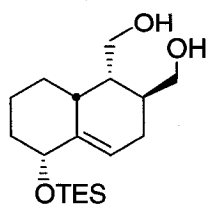




Procedure J: 4-Dimethylaminopyridine (16.5 mg, 0.135 mmol), triethylsilyl chloride (0.27 mL, 1.6 mmol), alcohols **2.98** and **2.99** (2 : 5 ratio, 0.361 g, 1.35 mmol), triethylamine (0.56 mL, 4.0 mmol), THF (13 mL), stirred for 1 hour. Flash chromatography with 10% EtOAc/hexanes gave a 2 : 5 mixture of **2.100** and **2.101**, which is a colorless oil (0.52 g, 1.4 mmol, quant.), with a Rf = 0.76 (40% EtOAc/hexanes). **2.100** ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.70 (d, J = 4.9 Hz, 1H), 3.90-3.76 (m 1H), 3.57 (s, 3H), 3.53 (s, 3H), 2.76-2.57 (m, 1H), 2.42-2.17 (m, 2H), 2.17-1.76 (m, 4H), 1.76-1.54 (m, 1H), 1.43-0.91 (m, 3H), 0.83 (t, 7.9 Hz, 9H), 0.48 (q, J = 8.0Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.8 (C_4), 175.0 (C_4), 140.9 (C_4), 115.2 (CH), 72.4 (CH), 52.0 (CH_3), 50.0 (CH_3), 42.4 (CH), 40.0 (CH), 38.6 (CH), 37.1 (CH_2), 33.2 (CH_2), 28.0 (CH_2), 23.4 (CH_2), 7.1 (CH_3), 5.1 (CH_2); **2.101** ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.56 (d, J = 4.7 Hz, 1H), 3.90-3.76 (m 1H), 3.55 (s, 6H), 2.91 (dd, J = 12.1, 6.2 Hz, 1H), 2.66 (qd, J = 12.2, 5.2 Hz, 1H), 2.42-2.17 (m, 2H), 2.17-1.76 (m, 2H), 1.76-1.54 (m, 1H), 1.43-0.91 (m, 4H), 0.83 (t, 7.9 Hz, 9H), 0.48 (q, J = 8.0Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.3 (C_4), 174.1 (C_4), 142.8 (C_4), 113.6 (CH), 73.2 (CH), 51.9 (CH_3), 51.7 (CH_3), 45.8 (CH), 38.9 (CH_2), 38.6 (CH), 38.3 (CH), 30.3 (CH_2), 28.9 (CH_2), 24.4 (CH_2), 7.1 (CH_3), 5.1 (CH_2); IR (CH_2Cl_2, cm^{-1}) 2951 (s), 2936 (s), 2875 (m), 1740 (s), 1458 (w), 1436 (m), 1378 (w), 1314 (w), 1260 (m), 1196 (m), 1159 (m), 1138 (m), 1109 (m), 1086 (m), 1005 (m); HRMS (EI) *m/z* (M^+) calcd 382.21755, found 382.21619.

(2-Hydroxymethyl-5-triethylsilanyloxy-1,2,3,5,6,7,8,8a-octahydro-naphthalen-1-yl)-methanol (2.102 and 2.103)

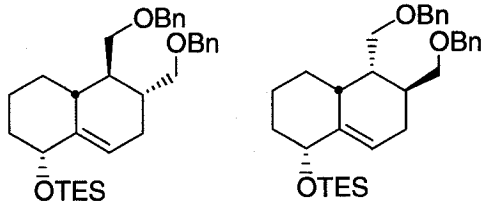




Procedure H: Lithium aluminum hydride (0.49 g, 14 mmol), diesters **2.100** and **2.101** (2 : 5 ratio, 1.3 g, 3.4 mol), THF (34 mL), warmed at 0°C for 30 minutes, water (2 x 2 mL), solution of KOH 0.1 M (2 mL), solution of sodium tartrate 0.5 M (15 mL). Flash chromatography with 90% EtOAc/hexanes gave a 2 : 5

mixture of **2.102** and **2.103**, which is a pale yellow oil (1.1 g, 3.4 mmol, quant.), with a Rf = 0.59 (100% EtOAc/hexanes). **2.102** ^{1}H NMR (300 MHz, acetone-d_6) δ 5.79 (s, 1H), 4.14-3.87 (m, 1H), 3.85-3.46 (m, 4H), 3.11-2.88 (br, 2H), 2.16-1.87 (m, 3H), 1.86-1.58 (m, 5H), 1.57-1.35 (m, 1H), 1.32-0.73 (m, 2H), 0.98 (t, 7.7 Hz, 9H), 0.63 (q, J = 8.0 Hz, 6H); ^{13}C NMR (75 MHz, acetone-d_6) δ 142.3 (C_4), 116.0 (CH), 73.2 (CH), 65.3 (CH_2), 62.1 (CH_2), 46.6 (CH), 38.7 (CH), 38.3 (CH), 38.1 (CH_2), 33.8 (CH_2), 28.2 (CH_2), 24.1 (CH_2), 6.8 (CH_3), 5.0 (CH_2); **2.103** ^{1}H NMR (300 MHz, acetone-d_6) δ 5.66 (s, 1H), 4.14-3.87 (m, 3H), 3.85-3.46 (m, 4H), 2.16-1.87 (m, 5H), 1.86-1.58 (m, 3H), 1.57-1.35 (m, 1H), 1.32-0.73 (m, 2H), 0.98 (t, 7.7 Hz, 9H), 0.63 (q, J = 8.0 Hz, 6H); ^{13}C NMR (75 MHz, acetone-d_6) δ 144.1 (C_4), 114.6 (CH), 73.6 (CH), 64.9 (CH_2), 63.4 (CH_2), 42.5 (CH), 40.6 (CH), 39.5 (CH_2), 36.3 (CH), 29.4 (CH_2), 28.7 (CH_2), 24.8 (CH_2), 6.8 (CH_3), 5.0 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3381 (br), 2874 (s), 2732 (w), 1679 (w), 1458 (s), 1414 (s), 1379 (m), 1239 (m), 1143 (m), 1103 (s), 1082 (s), 1007 (s); HRMS (EI) *m/z* (M^+) calcd 326.22772, found 326.22718.

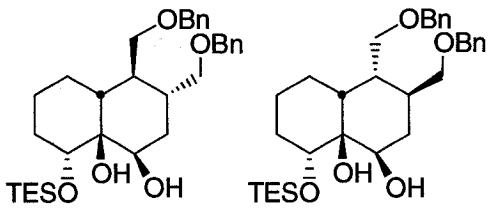
(5,6-Bis-benzyloxymethyl-1,2,3,4,4a,5,6,7-octahydro-naphthalen-1-yloxy)-triethyl-silane (2.104 and 2.105)



Procedure M: Diols **2.102** and **2.103** (2 : 5 ratio, 1.11 g, 3.40 mmol), THF (2 x 17 mL), NaH 60% dispersion in mineral oil (156 mg, 3.91 mmol), tetrabutylammonium iodide (126 mg, 340 μmol), benzyl bromide (0.44 mL, 3.7 mmol), stirred 2 days. Flash chromatography with 3-20% EtOAc/hexanes gave a 2 : 5 mixture of **2.104** and **2.105**, which is a colorless oil (1.72 g, 3.40 mmol, quant.), with a Rf = 0.91 (50% EtOAc/hexanes). **2.104** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.25 (m, 10H), 5.80 (d, J = 3.7 Hz, 1H), 4.51-4.41 (m, 4H), 3.92 (d, J = 11.0 Hz, 1H), 3.54-3.46 (m, 1H), 3.46-3.39 (m, 3H), 2.23-2.11 (m, 1H), 2.09-1.62 (m, 7H), 1.52-1.22 (m, 2H), 1.13-1.00 (m, 1H), 0.97 (t, 7.8 Hz, 9H), 0.61 (q, J = 7.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.3 (C_4), 138.8 (C_4), 138.7 (C_4), 128.5 (CH), 128.3 (CH), 127.8 (CH), 127.7 (CH), 127.5 (CH), 127.4 (CH), 115.7 (CH), 73.3 (CH), 73.1 (CH_2), 73.1 (CH_2), 72.9 (CH_2), 69.5 (CH_2), 42.7 (CH), 38.4 (CH), 37.6 (CH_2), 33.3 (CH_2), 28.1 (CH_2), 24.0 (CH_2), 7.0 (CH_3), 4.9 (CH_2); **2.105** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.25 (m, 10H), 5.67 (d, J = 3.6 Hz, 1H), 4.51-4.41 (m, 4H),

3.97 (d, J = 10.5 Hz, 1H), 3.58 (dd, J = 9.6, 5.6 Hz, 1H), 3.54-3.46 (m, 1H), 3.46-3.39 (m, 1H), 3.35 (dd, J = 9.2, 5.4 Hz, 1H), 2.23-2.11 (m, 2H), 2.09-1.62 (m, 5H), 1.52-1.22 (m, 3H), 1.13-1.00 (m, 1H), 0.97 (t, 7.8 Hz, 9H), 0.61 (q, J = 7.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.1 (C_4), 138.7 (C_4), 138.7 (C_4), 128.4 (CH), 128.4 (CH), 127.7 (CH), 127.6 (CH), 127.5 (CH), 127.5 (CH), 114.4 (CH), 73.3 (CH), 73.2 (CH_2), 73.1 (CH_2), 73.1 (CH_2), 70.5 (CH_2), 39.6 (CH), 38.9 (CH_2), 38.8 (CH), 33.3 (CH), 29.1 (CH_2), 28.2 (CH_2), 24.6 (CH_2), 7.0 (CH_3), 4.9 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3087 (w), 3063 (w), 3029 (w), 2933 (s), 2910 (s), 2855 (s), 1947 (w), 1869 (w), 1806 (w), 1604 (w), 1496 (w), 1454 (s), 1363 (m), 1239 (w), 1102 (s), 1015 (m); HRMS (EI) *m/z* (M^+) calcd 506.32162, found 506.32029.

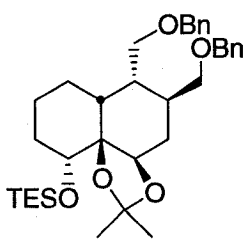
3,4-Bis-benzyloxymethyl-8-triethylsilanyloxy-octahydro-naphthalene-1,8a-diol (2.106 and 2.107)



Procedure K: 4-Methylmorpholine N-oxide (0.65 g, 5.6 mmol), solution of osmium tetraoxide 4% in water (0.89 mL, 0.14 mmol), alkenes **2.104** and **2.105** (2 : 5 ratio, 1.45 g, 2.80 mmol), water (5 mL), THF (28 mL), refluxed 2 days. Flash chromatography with 4-15% EtOAc/hexanes gave **2.106** as a colorless oil (320 mg, 592 μmol, 21%) and **2.107** as a pale yellow oil (888 mg, 1.64 mmol, 61%, 82% overall yield), with a respective Rf = 0.38 and 0.41 (15% EtOAc/hexanes). **2.106** ^1H NMR (300 MHz, $CDCl_3$) δ 7.41-7.25 (m, 10H), 4.60-4.44 (m, 4H), 4.30 (t, J = 6.6 Hz, 1H), 4.22-4.14 (br, 1H), 3.76-3.66 (m, 2H), 3.60 (dd, J = 9.0, 6.1 Hz, !H), 3.50 (d, J = 6.8 Hz, 2H), 3.34-3.27 (br, 1H), 2.38-2.23 (m, 1H), 1.97-1.20 (m, 10H), 1.01 (t, J = 7.9 Hz, 9H), 0.67 (q, J = 8.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.2 (C_4), 139.0 (C_4), 128.7 (CH), 128.7 (CH), 128.0 (CH), 127.9 (CH), 127.9 (CH), 127.8 (CH), 83.0 (CH), 75.6 (CH_2), 74.9 (CH_2), 74.2 (C_4), 73.3 (CH_2), 73.1 (CH_2), 66.3 (CH), 43.5 (CH), 41.6 (CH), 34.1 (CH), 32.7 (CH_2), 32.3 (CH_2), 29.5 (CH_2), 24.1 (CH_2), 7.2 (CH_3), 5.2 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3462 (br), 3087 (w), 3063 (w), 3029 (w), 2936 (s), 2875 (s), 2793 (w), 1947 (w), 1871 (w), 1807 (w), 1496 (m), 1453 (s), 1412 (m), 1362 (m), 1240 (m), 1090 (s), 1075 (s), 1028 (m), 1007 (m); HRMS (EI) *m/z* (M^+) calcd 540.32710, found 540.32380. **2.107** ^1H NMR (300 MHz, $CDCl_3$) δ 7.39-7.26 (m, 10H), 4.54-4.32 (m, 6H), 4.79 (dd, J = 11.8, 4.6 Hz, 1H), 3.56-3.47 (m, 2H), 3.40-3.26 (m, 2H), 3.19-3.08 (br, 1H), 2.46-2.34

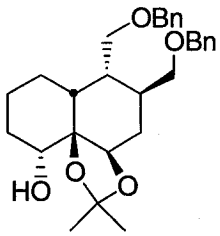
(m, 1H), 2.05-1.74 (m, 5H), 1.74-1.47 (m, 3H), 1.47-1.12 (m, 2H), 1.02 (t, J = 8.0 Hz, 9H), 0.69 (q, J = 8.0 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.1 (C_4), 139.0 (C_4), 128.7 (CH), 128.7 (CH), 128.0 (CH), 127.9 (CH), 127.9 (CH), 127.8 (CH), 83.2 (CH), 73.9 (CH_2), 73.5 (CH_2), 73.2 (CH_2), 71.3 (CH_2), 71.3 (C_4), 68.5 (CH), 44.1 (CH), 36.8 (CH), 33.8 (CH), 33.8 (CH_2), 32.9 (CH_2), 24.2 (CH_2), 22.7 (CH_2), 7.2 (CH_3), 5.2 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3563 (m), 3466 (br), 3087 (w), 3063 (w), 3029 (w), 2938 (s), 2875 (s), 2794 (w), 1949 (w), 1871 (w), 1811 (w), 1496 (m), 1453 (s), 1414 (m), 1363 (m), 1300 (w), 1241 (w), 1085 (s), 1065 (s), 1028 (m), 1007 (m); HRMS (EI) *m/z* (M^+) calcd 540.32710, found 540.32240.

(5,6-Bis-benzyloxymethyl-2,2-dimethyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-yloxy)-triethyl-silane (2.108)



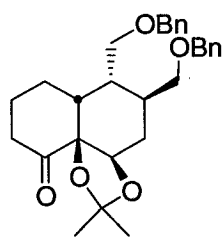
Procedure L: PTSA (1.1 mg, 5.9 μmol), diol **2.107** (320 mg, 0.592 mmol), 2-methoxypropene (0.17 mL, 1.8 mmol), CH_2Cl_2 (5.9 mL), stirred for 30 minutes. Flash chromatography with 5.0-7.5% EtOAc/hexanes gave **2.108** as a pale yellow oil (284 mg, 0.489 mmol, 82%), with a Rf = 0.65 (15% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41-7.26 (m, 10H), 4.66-4.38 (m, 5H), 3.87-3.58 (m, 4H), 3.45 (t, J = 9.3 Hz, 1H), 2.38-2.16 (m, 2H), 1.96-1.61 (m, 6H), 1.52 (s, 3H), 1.49 (s, 3H), 1.41-1.09 (m, 3H), 1.03 (t, J = 7.8 Hz, 9H), 0.69 (q, J = 8.1 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.2 (C_4), 139.2 (C_4), 128.7 (CH), 128.7 (CH), 128.0 (CH), 128.0 (CH), 127.8 (CH), 127.8 (CH), 107.5 (C_4), 85.6 (C_4), 76.9 (CH_2), 76.2 (CH), 73.5 (CH_2), 73.0 (CH_2), 72.5 (CH), 72.2 (CH_2), 41.3 (CH), 34.8 (CH), 33.1 (CH_2), 32.5 (CH), 28.2 (CH_3), 27.7 (CH_3), 26.4 (CH_2), 24.3 (CH_2), 23.0 (CH_2), 7.5 (CH_3), 5.7 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3087 (w), 3063 (w), 3029 (w), 2951 (s), 2937 (s), 2874 (s), 2798 (w), 1947 (w), 1868 (w), 1806 (w), 1496 (w), 1453 (m), 1365 (m), 1252 (m), 1210 (m), 1098 (s), 1053 (m), 1012 (m); HRMS (EI) *m/z* (M^+) calcd 580.35840, found 580.35604.

5,6-Bis-benzyloxymethyl-2,2-dimethyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-ol (2.109)



Tetrabutyl ammonium fluoride 1.0 M in THF (0.69 mL, 0.69 mmol) was added to a solution of **2.108** (266 mg, 0.458 mmol) in THF (4.6 mL) at room temperature and the reaction was stirred at this temperature for 30 minutes. The reaction was concentrated *in vacuo* and flash chromatography with 33-40% EtOAc/hexanes gave **2.109** as a colorless sticky oil (0.213 g, 0.458 mmol, quant.), with a Rf = 0.44 (40% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40-7.26 (m, 10H), 4.56 (d, J = 14.2 Hz, 3H), 4.44 (t, J = 12.0 Hz, 2H), 3.80-3.57 (m, 4H), 3.42 (t, J = 9.3 Hz, 1H), 2.33-2.17 (m, 3H), 1.94-1.61 (m, 6H), 1.52 (s, 3H), 1.50 (s, 3H), 1.44-1.08 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.1 (C_4), 139.0 (C_4), 128.7 (CH), 128.7 (CH), 128.0 (CH), 128.0 (CH), 127.9 (CH), 127.9 (CH), 107.3 (C_4), 86.0 (C_4), 76.8 (CH_2), 75.2 (CH), 73.5 (CH_2), 73.1 (CH_2), 72.4 (CH), 72.1 (CH_2), 40.8 (CH), 34.5 (CH), 32.4 (CH), 31.6 (CH_2), 28.2 (CH_3), 27.5 (CH_3), 26.4 (CH_2), 24.4 (CH_2), 23.3 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3460 (br), 3087 (w), 3063 (w), 3030 (m), 2985 (m), 2934 (s), 2860 (s), 2795 (w), 1950 (w), 1873 (w), 1810 (w), 1586 (w), 1496 (m), 1453 (s), 1366 (m), 1252 (m), 1208 (m), 1086 (m), 1046 (m), 1013 (w); HRMS (EI) *m/z* (M^+) calcd 466.27193, found 466.27076.

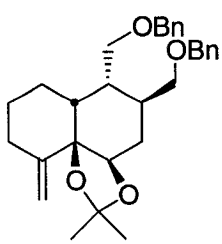
5,6-Bis-benzyloxymethyl-2,2-dimethyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-one (2.110)



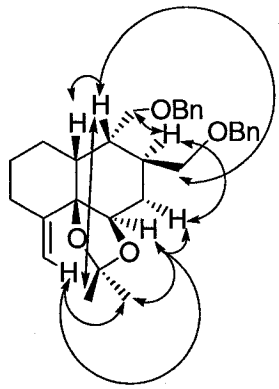
Procedure F: Dess-Martin periodinane (233 mg, 0.550 mmol), alcohol **2.109** (213 mg, 0.458 mmol), CH_2Cl_2 (4.6 mL), stirred for 30 minutes. Flash chromatography with 25-33% EtOAc/hexanes gave **2.110** as a colorless oil (201 mg, 0.433 mmol, 94%), with a Rf = 0.41 (33% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41-7.26 (m, 10H), 4.62-4.36 (m, 4H), 4.23 (s, 1H), 3.72-3.64 (m, 2H), 3.57 (t, J = 8.7 Hz, 1H), 3.45 (t, J = 9.1 Hz, 1H), 2.60 (d, J = 13.2 Hz, 1H), 2.34-1.95 (m, 6H), 1.95-1.78 (m, 2H), 1.72-1.32 (m, 2H), 1.52 (s, 3H), 1.38 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.6 (C_4), 134.4 (C_4), 134.2 (C_4), 124.2 (CH), 124.2 (CH), 123.5 (CH), 123.5 (CH), 123.4 (CH), 123.4 (CH), 105.1 (C_4), 82.8 (C_4), 71.7 (CH_2), 70.3 (CH), 69.0 (CH_2), 68.5 (CH_2), 67.4 (CH_2), 39.1 (CH), 36.8 (CH_2), 29.8 (CH), 27.1 (CH), 22.7 (CH_3), 21.0 (CH_3), 20.9 (CH_2), 20.4 (CH_2), 19.7 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3087 (w), 3062 (w), 3030 (w),

2989 (m), 2937 (s), 2863 (s), 2795 (w), 1952 (w), 1873 (w), 1810 (w), 1723 (s), 1496 (m), 1454 (m), 1380 (m), 1264 (m), 1210 (w), 1074 (w), 1017 (w); HRMS (EI) *m/z* (M^+) calcd 464.25628, found 464.25574.

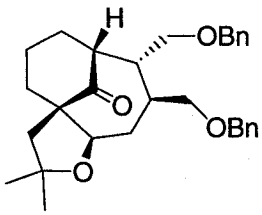
5,6-Bis-benzyloxymethyl-2,2-dimethyl-10-methylene-octahydro-naphtho[1,8a-*d*][1,3]dioxole (2.111)



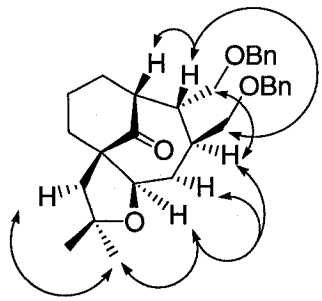
Procedure N: Potassium *tert*-butoxide 1.0 M solution in THF (0.24 mL, 0.24 mmol), methyltriphenylphosphonium iodide (98 mg, 0.24 mmol), toluene (0.5 + 0.3 mL), ketone **2.110** (37.5 mg, 80.7 μmol), refluxed for 4 hours and 30 minutes. Flash chromatography with 8-10% EtOAc/hexanes gave **2.111** as a pale yellow oil (31.4 mg, 67.9 μmol, 84%), with a Rf = 0.82 (33% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50-7.14 (m, 10H), 5.51 (d, J = 2.6 Hz, 1H), 4.92 (d, J = 1.9 Hz, 1H), 4.58-4.43 (m, 3H), 4.38 (d, J = 12.2 Hz, 1H), 4.14 (s, 1H), 3.94-3.81 (m, 2H), 3.70 (dd, J = 9.4, 5.2 Hz, 1H), 3.42 (t, J = 9.2 Hz, 1H), 2.61-2.49 (m, 1H), 2.41 (dd, J = 15.1, 2.8 Hz, 1H), 2.31-2.21 (m, 2H), 1.95-1.62 (m, 5H), 1.60 (s, 3H), 1.44 (s, 3H), 1.43-1.12 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.5 (C_4), 139.8 (C_4), 139.5 (C_4), 128.7 (CH), 128.5 (CH), 128.2 (CH), 128.0 (CH), 127.9 (CH), 127.7 (CH), 107.8 (CH_2), 107.6 (C_4), 84.5 (C_4), 78.5 (CH), 76.9 (CH_2), 73.3 (CH_2), 73.1 (CH_2), 72.7 (CH_2), 43.1 (CH), 35.0 (CH), 34.6 (CH_2), 32.0 (CH), 28.0 (CH_2), 27.4 (CH_3), 26.5 (CH_3), 26.1 (CH_2), 25.0 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3088 (w), 3063 (w), 3029 (w), 2988 (m), 2935 (s), 2858 (s), 2793 (w), 1949 (w), 1871 (w), 1809 (w), 1647 (m), 1496 (m), 1453 (s), 1378 (s), 1264 (m), 1208 (s), 1179 (m), 1100 (s), 1066 (s), 1027 (m); HRMS (EI) *m/z* (M^+) calcd 462.27701, found 462.27387. COSY, NOESY and HMQC experiments were performed in order to obtain the correlations illustrated below:



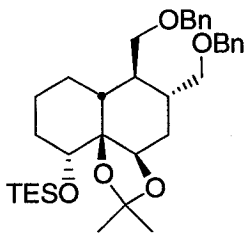
7,8-Bis-benzyloxymethyl-3,3-dimethyl-4-oxa-tricyclo[7.3.1.0^{1,5}]tridecan-13-one (2.112)



Procedure C: Tin tetrachloride 1.0 M in CH_2Cl_2 (65 μL, 65 μmol), Prins-pinacol precursor **2.111** (15.0 mg, 32.5 μmol), CH_2Cl_2 (0.66 mL), from -78°C to -20°C, stirred for 4 hours. Flash chromatography with 20% EtOAc/hexanes gave **2.112** as a colorless oil (12.8 mg, 27.7 μmol, 85%), with a Rf = 0.57 (33% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.21 (m, 10H), 4.47-4.29 (m, 4H), 4.16 (dd, J = 11.7, 3.7 Hz, 1H), 3.47 (dd, J = 9.6, 3.6 Hz, 1H), 3.44-3.35 (m, 2H), 3.22 (dd, J = 9.1, 5.4 Hz, 1H), 2.92 (d, J = 13.0 Hz, 1H), 2.92-2.86 (m, 1H), 2.37-2.25 (m, 1H), 2.19 (dd, J = 14.3, 3.7 Hz, 1H), 2.14-1.97 (m, 3H), 1.86-1.49 (m, 4H), 1.33 (d, J = 13.0 Hz, 1H), 1.35-1.23 (m, 1H), 1.28 (s, 3H), 1.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 213.5 (C_4), 138.3 (C_4), 138.3 (C_4), 128.4 (CH), 128.3 (CH), 127.7 (CH), 127.6 (CH), 127.6 (CH), 127.5 (CH), 84.8 (CH), 80.7 (C_4), 73.7 (CH_2), 73.2 (CH_2), 72.9 (CH_2), 70.8 (CH_2), 60.5 (C_4), 50.7 (CH), 46.9 (CH_2), 45.0 (CH), 40.8 (CH_2), 39.5 (CH_2), 36.1 (CH), 30.0 (CH_3), 27.9 (CH_3), 25.3 (CH_2), 21.3 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3088 (w), 3063 (w), 3029 (w), 2967 (s), 2933 (s), 2858 (s), 2794 (w), 1951 (w), 1874 (w), 1810 (w), 1696 (s), 1496 (w), 1453 (m), 1363 (m), 1266 (w), 1170 (w), 1113 (s), 1094 (s), 1027 (m); HRMS (EI) *m/z* (M^+-Bn) calcd 371.22224, found 371.20044. COSY, NOESY and HMQC experiments were performed in order to obtain the correlations illustrated below:

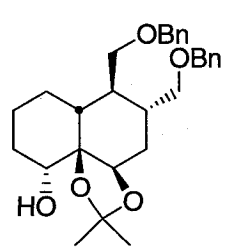


(5,6-Bis-benzyloxymethyl-2,2-dimethyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-yloxy)-triethyl-silane (2.113)



Procedure L: PTSA (0.5 mg, 3 μmol), diol **2.106** (138 mg, 0.255 mmol), 2-methoxypropene (73 μL, 0.77 mmol), CH_2Cl_2 (2.6 mL), stirred for 30 minutes. Flash chromatography with 5.0-7.5% EtOAc/hexanes gave **2.113** as a pale yellow oil (148 mg, 0.255 mmol, quant.), with a Rf = 0.53 (15% EtOAc/hexanes). ^{1}H NMR (300 MHz, C_6D_6) δ 7.45-7.14 (m, 10H), 4.48-4.25 (m, 5H), 4,00 (s, 1H), 3.64-3.38 (m, 4H), 2.64-2.48 (m, 4H), 2.47-2.34 (m, 1H), 2.22-2.04 (m, 3H), 1.91-1.69 (m, 2H), 1.64 (s, 3H), 1.52-1.32 (m, 1H), 1.49 (s, 3H), 1.04 (t, J = 7.8 Hz, 9H), 0.65 (q, J = 8.1 Hz, 6H); ^{13}C NMR (75 MHz, C_6D_6) δ 139.6 (C_4), 139.6 (C_4), 128.6 (CH), 128.6 (CH), 128.2 (CH), 128.1 (CH), 127.8 (CH), 127.7 (CH), 107.4 (C_4), 81.0 (C_4), 80.2 (CH), 75.8 (CH), 73.5 (CH_2), 73.4 (CH_2), 73.0 (CH_2), 67.5 (CH_2), 40.4 (CH), 36.9 (CH), 34.8 (CH), 32.5 (CH_2), 32.4 (CH_2), 29.2 (CH_3), 27.4 (CH_3), 22.9 (CH_2), 16.1 (CH_2), 7.4 (CH_3), 5.5 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3087 (w), 3064 (w), 3030 (w), 2935 (s), 2875 (s), 2792 (w), 1946 (w), 1873 (w), 1807 (w), 1496 (w), 1454 (m), 1365 (m), 1238 (m), 1215 (m), 1113 (s), 1083 (s), 1048 (s), 1027 (s); HRMS (EI) *m/z* (M^+) calcd 580.35840, found 580.35685.

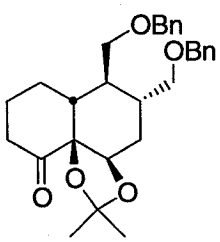
5,6-Bis-benzyloxymethyl-2,2-dimethyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-ol (2.114)



Tetrabutyl ammonium fluoride 1.0 M in THF (0.38 mL, 0.38 mmol) was added to a solution of **2.113** (148 mg, 0.255 mmol) in THF (2.6 mL) at room temperature and the reaction was stirred at this temperature for 1 hour and 15

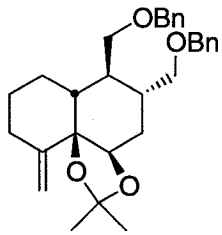
minutes. The reaction was concentrated *in vacuo* and flash chromatography with 20-33% EtOAc/hexanes gave **2.114** as a colorless oil (94.1 mg, 0.202 mmol, 73%), with a Rf = 0.51 (33% EtOAc/hexanes). ^{1}H NMR (300 MHz, C_6D_6) δ 7.40-7.15 (m, 10H), 4.43-4.27 (m, 4H), 4.21 (s, 1H), 3.64-3.43 (m, 5H), 2.64-2.34 (m, 5H), 2.13-1.96 (m, 3H), 1.75-1.59 (m, 1H), 1.62 (s, 3H), 1.53-1.29 (m, 2H), 1.45 (s, 3H), 0.98-0.91 (m, 1H); ^{13}C NMR (75 MHz, C_6D_6) δ 139.7 (C_4), 139.6 (C_4), 128.7 (CH), 128.7 (CH), 128.1 (CH), 127.9 (CH), 127.8 (CH), 127.7 (CH), 107.6 (C_4), 80.5 (C_4), 80.0 (CH), 74.4 (CH), 73.4 (CH_2), 73.2 (CH_2), 73.2 (CH_2), 67.7 (CH_2), 40.2 (CH), 37.2 (CH), 34.7 (CH), 32.6 (CH_2), 32.4 (CH_2), 29.2 (CH_3), 27.4 (CH_3), 22.9 (CH_2), 15.8 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3471 (br), 3087 (w), 3063 (w), 3029 (m), 2982 (m), 2932 (s), 2864 (s), 2792 (w), 1950 (w), 1876 (w), 1809 (w), 1496 (m), 1454 (s), 1366 (m), 1247 (m), 1215 (m), 1110 (m), 1053 (m), 1026 (s); HRMS (EI) *m/z* (M^+) calcd 466.27193, found 466.27284.

5,6-Bis-benzyloxymethyl-2,2-dimethyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-one (2.115)

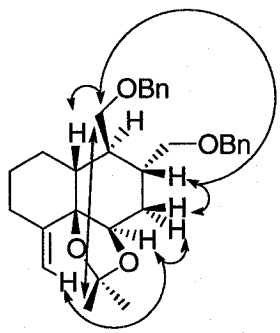


Procedure F: Dess-Martin periodinane (94 mg, 0.22 mmol), alcohol **2.14** (86 mg, 0.18 mmol), CH_2Cl_2 (1.8 mL), stirred for 45 minutes. Flash chromatography with 10-20% EtOAc/hexanes gave **2.15** as a colorless oil (75 mg, 0.16 mmol, 88%), with a Rf = 0.59 (33% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40-7.26 (m, 10H), 4.62 (s, 1H), 4.45 (d, J = 12.3 Hz, 2H), 4.39 (d, J = 12.3 Hz, 2H), 3.47-3.26 (m, 4H), 2.79 (td, J = 13.2, 6.4 Hz, 1H), 2.36 (t, J = 13.4 Hz, 2H), 2.21-1.59 (m, 7H), 1.52 (s, 3H), 1.34-1.17 (m, 1H), 1.31 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.0 (C_4), 139.0 (C_4), 138.9 (C_4), 128.7 (CH), 128.7 (CH), 128.0 (CH), 128.0 (CH), 128.0 (CH), 127.9 (CH), 108.8 (C_4), 84.9 (C_4), 73.6 (CH_2), 73.4 (CH_2), 72.7 (CH), 72.4 (CH_2), 67.6 (CH_2), 43.9 (CH), 40.7 (CH_2), 36.6 (CH), 34.5 (CH), 30.0 (CH_2), 29.1 (CH_3), 26.7 (CH_3), 23.2 (CH_2), 22.3 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3087 (w), 3062 (w), 3029 (w), 2985 (m), 2936 (s), 2866 (s), 2793 (w), 1952 (w), 1874 (w), 1809 (w), 1716 (s), 1496 (m), 1454 (s), 1368 (m), 1248 (m), 1216 (m), 1162 (m), 1117 (m), 1093 (m), 1051 (m), 1026 (m); HRMS (EI) *m/z* (M^+) calcd 464.25628, found 464.25595.

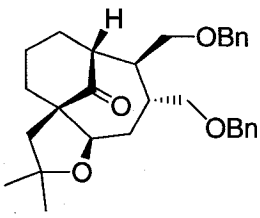
5,6-Bis-benzyloxymethyl-2,2-dimethyl-10-methylene-octahydro-naphtho[1,8a-*d*][1,3]dioxole (2.116)



Procedure N: Potassium *tert*-butoxide 1.0 M solution in THF (0.46 mL, 0.46 mmol), methyltriphenylphosphonium iodide (188 mg, 0.188 mmol), toluene (1.0 + 0.6 mL), ketone **2.115** (72.0 mg, 155 mmol), refluxed for 1 hour. Flash chromatography with 10% EtOAc/hexanes gave **2.116** as a pale yellow oil (59.2 mg, 0.128 mmol, 83%), with a Rf = 0.61 (15% EtOAc/hexanes). ^{1}H NMR (300 MHz, C_6D_6) δ 7.37-7.15 (m, 10H), 4.94 (s, 1H), 4.77 (s, !H), 4.54 (1H), 4.38 (d, J = 12.3 Hz, 2H), 4.34 (d, J = 12.3 Hz, 1H), 4.27 (d, J = 12.3 Hz, 1H), 3.52-3.39 (m, 3H), 3.32 (dd, J = 9.4, 2.6 Hz, 1H), 2.74 (td, J = 12.7, 4.4 Hz, 1H), 2.66-2.41 (m, 3H), 2.33 (tt, J = 14.0, 4.2 Hz, 1H), 2.21 (d, J = 12.7 Hz, 1H), 2.13-1.91 (m, 2H), 1.65 (s, 3H), 1.48 (s, 3H), 1.35 (qt, J = 13.7, 3.5 Hz, 1H); ^{13}C NMR (75 MHz, C_6D_6) δ 147.7 (C_4), 139.5 (C_4), 139.4 (C_4), 128.7 (CH), 128.7 (CH), 128.1 (CH), 128.0 (CH), 127.9 (CH), 127.8 (CH), 109.5 (CH_2), 107.0 (C_4), 82.8 (C_4), 75.3 (CH), 73.5 (CH_2), 73.3 (CH_2), 72.5 (CH_2), 67.2 (CH_2), 42.4 (CH), 37.6 (CH), 35.6 (CH), 35.5 (CH_2), 31.1 (CH_2), 29.4 (CH_3), 27.6 (CH_3), 23.8 (CH_2), 23.2 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3086 (w), 3063 (w), 3029 (w), 2985 (m), 2933 (s), 2859 (s), 2791 (w), 1950 (w), 1874 (w), 1809 (w), 1645 (m), 1496 (m), 1454 (s), 1366 (m), 1246 (m), 1215 (m), 1164 (m), 1113 (s), 1094 (m), 1047 (m), 1019 (m); HRMS (EI) *m/z* (M^+) calcd 462.27701, found 462.27752. COSY, NOESY and HMQC experiments were performed in order to obtain the correlations illustrated below:

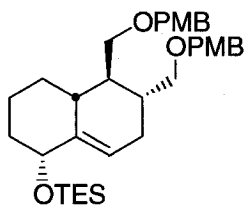


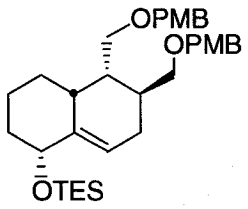
7,8-Bis-benzyloxymethyl-3,3-dimethyl-4-oxa-tricyclo[7.3.1.0^{1,5}]tridecan-13-one (2.117)



Procedure C: Tin tetrachloride 1.0 M in CH_2Cl_2 (60 μL, 60 μmol), Prins-pinacol precursor **2.116** (14.0 mg, 30.2 μmol), toluene (0.60 mL), from -78°C to room temperature for 1 hour and 45 minutes. Flash chromatography with 15-20% EtOAc/hexanes gave **2.117** as a colorless oil (12.7 mg, 27.5 μmol, 91%), with a Rf = 0.47 (33% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.24 (m, 10H), 4.50 (d, J = 12.4 Hz, 1H), 4.44 (d, J = 12.2 Hz, 1H), 4.37 (s, 2H), 3.98 (s, 1H), 3.46 (td, J = 9.1, 3.4 Hz, 2H), 3.40-3.33 (m, 1H), 3.30 (dd, J = 9.3, 2.3 Hz, 1H), 2.95 (s, 1H), 2.74 (d, J = 12.8 Hz, 1H), 2.29-2.13 (m, 2H), 2.01-1.49 (m, 8H), 1.37 (s, 3H), 1.26 (s, 3H), 1.26 (d, J = 11.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 213.2 (C_4), 138.5 (C_4), 138.5 (C_4), 128.3 (CH), 128.3 (CH), 127.8 (CH), 127.6 (CH), 127.6 (CH), 127.5 (CH), 82.0 (CH), 77.9 (C_4), 73.7 (CH_2), 73.1 (CH_2), 73.1 (CH_2), 72.5 (CH_2), 60.7 (C_4), 52.4 (CH), 48.5 (CH_2), 42.9 (CH), 38.0 (CH_2), 37.9 (CH_2), 33.4 (CH_2), 32.7 (CH), 29.7 (CH_3), 28.7 (CH_3), 19.3 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3087 (w), 3063 (w), 3029 (w), 2959 (m), 2928 (s), 2854 (s), 2790 (w), 1948 (w), 1870 (w), 1811 (w), 1696 (s), 1453 (m), 1363 (m), 1095 (s), 1027 (w), 1014 (w); HRMS (EI) *m/z* (M^+) calcd 462.27701, found 462.27630. COSY, NOESY and HMQC experiments were performed in order to obtain the correlations illustrated in Figure 2.8.

[5,6-Bis-(4-methoxy-benzyloxymethyl)-1,2,3,4,4a,5,6,7-octahydro-naphthalen-1-yloxy]-triethyl-silane (2.124 and 2.125)

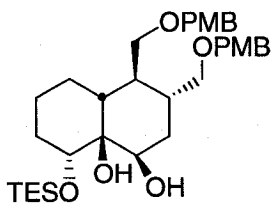


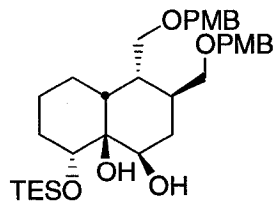


2.102 and **2.103** (2 : 5 ratio, 985 mg, 3.02 mmol) was canulated with THF (15 mL) to KH (30 wt % dispersion in mineral oil, 2.02 g, 15.1 mmol) in THF (15 mL) at 0°C and the reaction mixture was allowed to stir for 10 minutes. *Para*-methoxybenzyl chloride (1.63 mL, 12.1 mmol) was added to the solution at 0°C and the reaction is warmed to room temperature overnight. The reaction is quenched with NH_4Cl (sat. aq.), extracted with diethyl ether, dried over $MgSO_4$, filtrated and concentrated *in vacuo*. Flash chromatography with 10-15% EtOAc/hexanes gave a 2 : 5 mixture of **2.124** and **2.125**, which is a colorless oil (1.55 g, 2.73 mmol, 91%), with a Rf = 0.64 (20%

EtOAc/hexanes). **2.124** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24-7.18 (m, 4H), 6.86-6.82 (m, 4H), 5.74 (d, J = 3.5 Hz, 1H), 4.42-4.31 (m, 4H), 3.86 (d, J = 8.2 Hz, 1H), 3.79 (s, 3H), 3.78 (s, 3H), 3.44 (dd, J = 9.1, 3.9 Hz, 1H), 3.44-3.31 (m, 3H), 2.18-2.03 (m, 2H), 2.00-1.66 (m, 5H), 1.64-1.55 (m, 1H), 1.44-1.16 (m, 2H), 0.93 (t, 7.8 Hz, 9H), 0.82 (qd, J = 12.1, 3.4 Hz, 1H), 0.57 (q, J = 8.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1 (C_4), 159.0 (C_4), 141.2 (C_4), 130.9 (C_4), 130.8 (C_4), 129.2 (CH), 129.2 (CH), 114.3 (CH), 113.7 (CH), 113.7 (CH), 72.8 (CH), 72.7 (CH_2), 72.7 (CH_2), 72.6 (CH_2), 69.4 (CH_2), 55.3 (CH_3), 55.3 (CH_3), 42.6 (CH), 38.4 (CH), 37.6 (CH_2), 35.0 (CH), 33.2 (CH_2), 28.0 (CH_2), 23.9 (CH_2), 7.0 (CH_3), 4.9 (CH_2); **2.125** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24-7.18 (m, 4H), 6.86-6.82 (m, 4H), 5.62 (d, J = 3.8 Hz, 1H), 4.42-4.31 (m, 4H), 3.92 (d, J = 10.6 Hz, 1H), 3.79 (s, 3H), 3.78 (s, 3H), 3.50 (dd, J = 9.3, 6.0 Hz, 1H), 3.44-3.31 (m, 2H), 3.27 (dd, J = 9.2, 5.5 Hz, 1H), 2.18-2.03 (m, 1H), 2.00-1.66 (m, 6H), 1.64-1.55 (m, 1H), 1.44-1.16 (m, 2H), 1.01 (qd, J = 12.5, 3.6 Hz, 1H), 0.93 (t, 7.8 Hz, 9H), 0.57 (q, J = 8.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1 (C_4), 159.1 (C_4), 143.1 (C_4), 130.8 (C_4), 180.8 (C_4), 129.2 (CH), 129.2 (CH), 114.3 (CH), 113.7 (CH), 113.7 (CH), 73.2 (CH), 72.9 (CH_2), 72.7 (CH_2), 72.7 (CH_2), 70.2 (CH_2), 55.3 (CH_3), 55.3 (CH_3), 39.6 (CH), 38.8 (CH_2), 38.7 (CH), 33.2 (CH), 29.0 (CH_2), 28.1 (CH_2), 24.6 (CH_2), 7.0 (CH_3), 4.9 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3102 (w), 3063 (w), 3033 (w), 2998 (m), 2873 (s), 2063 (w), 1880 (w), 1728 (w), 1613 (s), 1586 (m), 1514 (s), 1463 (m), 1362 (m), 1302 (m), 1252 (m), 1085 (m), 1037 (m); HRMS (EI) *m/z* (M^+-PMB) calcd 445.27741, found 445.27849.

3,4-Bis-(4-methoxy-benzyloxymethyl)-8-triethylsilanyloxy-octahydro-naphthalene-1,8a-diol (2.126 and 2.127)

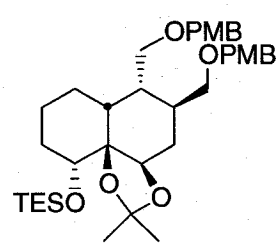




Procedure K: 4-Methylmorpholine N-oxide (0.64 g, 5.5 mmol), solution of osmium tetraoxide 4% in water (0.86 mL, 0.14 mmol), **2.124** and **2.125** (2 : 5 ratio, 1.55 g, 2.73 mmol), water (5.4 mL), THF (27 mL), refluxed 2 days. Flash chromatography with 20-40% EtOAc/hexanes gave **2.126** as a colorless oil (346 mg, 576 μmol, 21%) and **2.127** as a pale yellow oil (1.09 g, 1.81 mmol, 66%, 87% overall yield), with a respective Rf = 0.27 and 0.45 (25% EtOAc/hexanes). **2.126** ^{1}H NMR (400 MHz, C_6D_6) δ 7.36-7.30 (m, 4H), 6.89-6.84 (m, 4H), 4.51 (d, J = 11.8 Hz, 1H), 4.47 (d, J =

11.8 Hz, 1H), 4.42 (s, 2H), 4.32 (t, J = 5.8 Hz, 1H), 3.86 (dd, J = 9.0, 6.3 Hz, !H), 3.82-3.72 (m, 3H), 3.61-3.57 (br, 1H), 3.54-3.45 (m, 2H), 3.38 (s, 3H), 3.37 (s, 3H), 2.39-2.30 (m, 1H), 2.25 (dt, J = 14.3, 5.5 Hz, 1H), 2.13-1.93 (m, 3H), 1.77-1.70 (m, 1H), 1.54-1.37 (m, 3H), 1.31-1.09 (m, 2H), 0.99 (t, J = 8.0 Hz, 9H), 0.58 (q, J = 8.1 Hz, 6H); ^{13}C NMR (100 MHz, C_6D_6) δ 159.4 (C_4), 159.4 (C_4), 131.4 (C_4), 131.2 (C_4), 129.2 (CH), 129.1 (CH), 113.8 (CH), 113.8 (CH), 82.0 (CH), 74.9 (CH_2), 74.2 (CH_2), 73.9 (C_4), 72.7 (CH_2), 72.4 (CH_2), 66.3 (CH), 54.5 (CH_3), 54.5 (CH_3), 42.8 (CH), 41.4 (CH), 33.7 (CH), 32.3 (CH_2), 31.4 (CH_2), 30.7 (CH_2), 23.2 (CH_2), 6.8 (CH_3), 4.9 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3451 (br), 3030 (w), 2936 (s), 2874 (s), 1612 (m), 1586 (w), 1513 (s), 1463 (m), 1301 (m), 1247 (s), 1173 (w), 1086 (m), 1035 (m); HRMS (EI) *m/z* (M^+-PMB) calcd 479.28289, found 479.30270. **2.127** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21-7.15 (m, 4H), 6.86-6.80 (m, 4H), 4.44-4.24 (m, 6H), 3.78 (s, 3H), 3.77 (s, 3H), 3.71 (dd, J = 12.0, 4.6 Hz, 1H), 3.44-3.38 (m, 2H), 3.26-3.15 (m, 2H), 3.06-2.98 (br, 1H), 2.28-2.22 (m, 1H), 1.93 (dt, J = 12.5, 3.9 Hz, 1H), 1.84 (dt, J = 13.1, 4.0 Hz, 1H), 1.81-1.67 (m, 3H), 1.59 (qd, J = 13.2, 3.6 Hz, 1H), 0.96 (t, J = 7.8 Hz, 9H), 0.62 (q, J = 8.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1 (C_4), 159.0 (C_4), 130.8 (C_4), 130.7 (C_4), 129.1 (CH), 129.1 (CH), 113.7 (CH), 113.7 (CH), 82.7 (CH), 73.2 (CH_2), 73.1 (C_4), 72.7 (CH_2), 72.4 (CH_2), 70.5 (CH_2), 68.1 (CH), 55.3 (CH_3), 55.3 (CH_3), 43.6 (CH), 36.4 (CH), 33.4 (CH), 33.4 (CH_2), 32.5 (CH_2), 23.8 (CH_2), 22.3 (CH_2), 6.8 (CH_3), 4.8 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3456 (br), 3030 (w), 2936 (s), 2874 (s), 1612 (m), 1586 (w), 1513 (s), 1463 (m), 1301 (m), 1247 (s), 1173 (m), 1085 (m), 1035 (m); HRMS (EI) *m/z* (M^+-PMB) calcd 479.28289, found 479.28490.

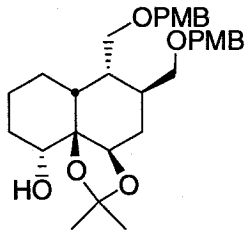
[5,6-Bis-(4-methoxy-benzyloxymethyl)-2,2-dimethyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-yloxy]-triethyl-silane (2.128)



Procedure L: PTSA (3.4 mg, 18 μmol), diol **2.127** (1.09 g, 1.81 mmol), 2-methoxypropene (0.52 mL, 5.4 mmol), CH_2Cl_2 (18 mL), stirred for 1 hour. Flash chromatography with 10% EtOAc/hexanes gave **2.128** as a pale yellow oil (864 mg, 1.35 mmol, 74%), with a Rf = 0.50 (20% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24-7.19 (m, 4H), 6.86-6.82 (m, 4H), 4.53 (s, 1H), 4.45 (d, J = 1.7 Hz, 1H), 4.42 (s, 1H), 4.32 (dd, J= 16.5, 11.8, 2H), 3.78 (s, 3H), 3.77 (s, 3H), 3.74 (dd, J = 11.4, 3.7 Hz, 1H), 3.64 (dd, J = 8.6, 5.1 Hz, 1H),

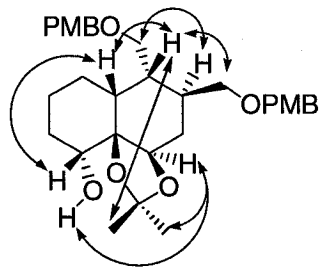
3.59-3.52 (m, 2H), 3.33 (t, J = 9.4 Hz, 1H), 2.27-2.17 (m, 1H), 2.13 (dd, J = 14.9, 3.1 Hz, 1H), 1.85-1.52 (m, 6H), 1.44 (s, 3H), 1.41 (s, 3H), 1.34-1.02 (m, 3H), 0.95 (t, J = 7.8 Hz, 9H), 0.62 (q, J = 8.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0 (C_4), 159.0 (C_4), 130.9 (C_4), 130.9 (C_4), 129.2 (CH), 129.1 (CH), 113.7 (CH), 113.7 (CH), 107.1 (C_4), 85.2 (C_4), 76.2 (CH_2), 75.9 (CH), 72.7 (CH_2), 72.3 (CH_2), 72.2 (CH), 71.4 (CH_2), 55.3 (CH_3), 55.3 (CH_3), 40.8 (CH), 34.3 (CH), 32.7 (CH_2), 32.1 (CH), 27.7 (CH_3), 27.3 (CH_3), 26.0 (CH_2), 23.8 (CH_2), 22.5 (CH_2), 7.0 (CH_3), 5.2 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3065 (w), 2952 (s), 2936 (s), 2874 (s), 2063 (w), 1613 (s), 1586 (m), 1513 (s), 1464 (m), 1365 (m), 1301 (m), 1248 (s), 1209 (m), 1177 (m), 1096 (s), 1048 (s), 1011 (m); HRMS (EI) *m/z* (M^+) calcd 640.37953, found 640.37711.

5,6-Bis-(4-methoxy-benzyloxymethyl)-2,2-dimethyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-ol (2.129)

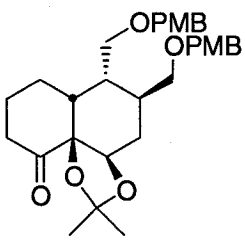


Tetrabutyl ammonium fluoride 1.0 M in THF (2.02 mL, 2.02 mmol) was added to a solution of **2.128** (864 mg, 1.35 mmol) in THF (14 mL) at room temperature and the reaction was stirred at this temperature for 40 minutes. The reaction was concentrated *in vacuo* and flash chromatography with 45% EtOAc/hexanes gave **2.129** as a colorless sticky oil (711 mg, 1.35 mmol, quant.), with a Rf = 0.42 (50% EtOAc/hexanes). ^1H NMR (400 MHz, C_6D_6) δ 7.35-7.27 (m, 4H), 6.91-6.83 (m, 4H), 4.72 (t, J = 2.6 Hz, 1H), 4.52 (d, J = 11.6 Hz, 1H), 4.49 (d, J = 11.7 Hz, 1H), 4.45 (d, J = 11.6 Hz, 1H), 4.37 (d, J = 11.7 Hz, 1H), 3.76 (dd, J = 8.6, 5.5 Hz, 1H), 3.83 (t, J = 8.6 Hz, 1H), 3.76 (dd, J = 9.5, 5.1 Hz, 1H), 3.71 (dd, J = 11.7, 3.5 Hz, 1H), 3.41 (t, J = 9.3 Hz, 1H), 3.40 (s, 3H), 3.38 (s, 3H), 2.61-2.54 (m, 1H), 2.37 (dd, J = 15.7, 3.2 Hz, 1H), 2.17-2.06 (m, 2H), 1.91-1.81 (m, 1H), 1.74-1.57 (m, 3H), 1.60 (s, 3H), 1.57 (s, 3H), 1.53-1.46 (m, 1H), 1.19-1.06 (m, 2H), 1.05-0.93 (m, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 159.4 (C_4), 159.4 (C_4), 131.4 (C_4), 131.1 (C_4), 129.2 (CH), 129.1 (CH), 113.8 (CH), 113.8 (CH), 106.8 (C_4), 85.5 (C_4), 76.4 (CH_2), 74.7 (CH), 72.7 (CH_2), 72.5 (CH_2), 72.1 (CH), 71.8 (CH_2), 54.6 (CH_3), 54.6 (CH_3), 40.8 (CH), 34.6 (CH), 32.4 (CH), 31.9 (CH_2), 27.9 (CH_3), 27.0 (CH_3), 26.1 (CH_2), 24.1 (CH_2), 23.0 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3463 (br), 3036 (m), 2991 (s), 2934 (s), 2859 (s), 2795 (w), 2060 (w), 1883 (w), 1736 (w), 1613 (s), 1586 (w), 1513 (s), 1464 (m), 1365 (m), 1249 (s), 1175 (m), 1085 (s), 1038 (m); HRMS (EI) *m/z* (M^+-Me) calcd 511.26958, found 511.26862. COSY,

NOESY and HMQC experiments were performed in order to obtain the correlations illustrated below:

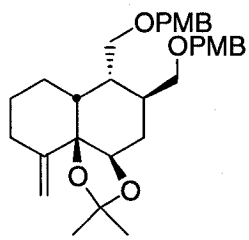


5,6-Bis-(4-methoxy-benzyloxymethyl)-2,2-dimethyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-one (2.130)



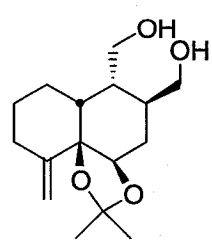
Procedure F: Dess-Martin periodinane (689 mg, 1.62 mmol), alcohol **2.129** (700 mg, 1.33 mmol), CH_2Cl_2 (13 mL), stirred for 40 minutes. Flash chromatography with 35% EtOAc/hexanes gave **2.130** as a colorless oil (638 mg, 1.22 mmol, 91%), with a Rf = 0.42 (40% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22-7.14 (m, 4H), 6.83-6.78 (m, 4H), 4.41 (d, J = 11.4 Hz, 1H), 4.40 (d, J = 11.6 Hz, 1H), 4.34 (d, J = 11.4 Hz, 1H), 4.25 (d, J = 11.6 Hz, 1H), 4.13 (t, J = 2.6 Hz, 1H), 3.73 (s, 3H), 3.72 (s, 3H), 3.59-3.53 (m, 2H), 3.45 (t, J = 8.7 Hz, 1H), 3.33 (t, J = 9.5 Hz, 1H), 2.49 (d, J = 12.6 Hz, 1H), 2.22-1.72 (m, 2H), 1.54 (qt, J = 13.1, 3.2 Hz, 1H), 1.44 (s, 3H), 1.39 (qd, J = 12.9, 3.6 Hz, 1H), 1.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.4 (C_4), 159.1 (C_4), 159.1 (C_4), 130.7 (C_4), 130.5 (C_4), 129.2 (CH), 129.2 (CH), 113.7 (CH), 113.7 (CH), 109.1 (C_4), 86.9 (C_4), 75.5 (CH_2), 74.5 (CH), 72.7 (CH_2), 72.2 (CH_2), 71.1 (CH_2), 55.2 (CH_3), 55.2 (CH_3), 43.1 (CH), 40.8 (CH_2), 34.0 (CH), 31.3 (CH), 26.9 (CH_3), 25.2 (CH_3), 25.0 (CH_2), 24.5 (CH_2), 23.8 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3061 (w), 3034 (w), 2993 (m), 2937 (s), 2863 (s), 2795 (w), 2060 (w), 1883 (w), 1723 (s), 1613 (m), 1586 (m), 1514 (m), 1464 (w), 1380 (m), 1245 (m), 1209 (m), 1173 (m), 1085 (m), 1034 (m); HRMS (EI) *m/z* (M^+-PMB) calcd 403.21207, found 403.21924.

5,6-Bis-benzyloxymethyl-2,2-dimethyl-10-methylene-octahydro-naphtho[1,8a-*d*][1,3]dioxole (2.131)



Procedure N: Potassium *tert*-butoxide 1.0 M solution in THF (3.6 mL, 3.6 mmol), methyltriphenylphosphonium iodide (1.46 g, 3.60 mmol), toluene (7.5 + 4.5 mL), ketone **2.130** (630 mg, 1.20 mmol), stirred at room temperature for 45 minutes. Flash chromatography with 15-20% EtOAc/hexanes gave **2.131** as a colorless oil (366 mg, 0.700 mmol, 58%), with a Rf = 0.56 (33% EtOAc/hexanes). ^{1}H NMR (400 MHz, C_6D_6) δ 7.35-7.31 (m, 2H), 7.27-7.24 (m, 2H), 6.91-6.86 (m, 2H), 6.85-6.81 (m, 2H), 5.45 (d, J = 2.7 Hz, 1H), 4.87 (d, J = 1.9 Hz, 1H), 4.51 (d, J = 11.6 Hz, 1H), 4.46 (d, J = 10.8 Hz, 2H), 4.34 (d, J = 11.7 Hz, 1H), 4.11 (t, J = 2.2 Hz, 1H), 3.90 (dd, J = 8.5, 5.3 Hz, 1H), 3.82 (t, J = 8.5 Hz, 1H), 3.70 (dd, J = 9.4, 5.2 Hz, 1H), 3.43-3.39 (m, 1H), 3.40 (s, 3H), 3.38 (s, 3H), 2.57-2.49 (m, 1H), 2.38 (dd, J = 15.2, 2.9 Hz, 1H), 2.27-2.19 (m, 2H), 1.91-1.74 (m, 2H), 1.73-1.62 (m, 3H), 1.57 (s, 3H), 1.40 (s, 3H), 1.28 (qt, J = 12.9, 3.9 Hz, 1H), 1.17 (qd, J = 13.0, 4.2 Hz, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 159.4 (C_4), 159.4 (C_4), 153.1 (C_4), 131.4 (C_4), 131.1 (C_4), 129.2 (CH), 129.1 (CH), 113.8 (CH), 113.8 (CH), 107.4 (C_4), 107.2 (CH_2), 84.2 (C_4), 78.2 (CH), 74.3 (CH_2), 72.7 (CH_2), 72.4 (CH_2), 71.9 (CH_2), 54.6 (CH_3), 54.5 (CH_3), 42.6 (CH), 34.7 (CH), 34.2 (CH_2), 31.6 (CH), 27.7 (CH_2), 27.0 (CH_3), 26.1 (CH_3), 25.7 (CH_2), 24.6 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3101 (w), 3034 (w), 2990 (m), 2935 (s), 2858 (s), 2793 (w), 2063 (w), 1882 (w), 1647 (w), 1613 (m), 1586 (m), 1513 (s), 1464 (m), 1378 (m), 1301 (m), 1248 (s), 1208 (m), 1177 (m), 1099 (m), 1067 (m), 1036 (m); HRMS (EI) *m/z* (M^+-PMB) calcd 401.23280, found 401.23543.

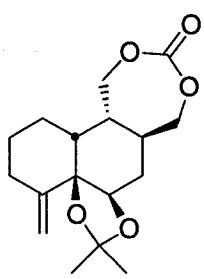
(5-Hydroxymethyl-2,2-dimethyl-10-methylene-octahydro-naphtho[1,8a-*d*][1,3]dioxol-6-yl)-methanol (2.132)



DDQ (294 mg, 1.29 mmol) was added to a solution of **2.131** (338 mg, 0.647 mmol) in CH_2Cl_2 (6.5 mL) and water (0.65 mL) at room temperature and the reaction was stirred at this temperature for 1 hour and 30 minutes. The reaction was quenched with sodium sulfite (aq. sat.), extracted with CH_2Cl_2, dried over $MgSO_4$, filtered and concentrated *in vacuo*. Flash chromatography

with 100% EtOAc/hexanes gave **2.132** as a pale yellow oil (178 mg, 0.630 mmol, 97%), with a Rf = 0.19 (80% EtOAc/hexanes). ^{1}H NMR (400 MHz, C_6D_6) δ 5.38 (d, J = 2.5 Hz, 1H), 5.11-4.83 (br, 2H), 4.85 (d, J = 1.9 Hz, 1H), 3.97 (t, J = 2.4 Hz, 1H), 3.95 (dd, J = 10.6, 6.6 Hz, 1H), 3.88 (dd, J = 10.5, 4.3 Hz, 1H), 3.80 (dd, J = 10.6, 6.9 Hz, 1H), 3.63 (dd, J = 10.9, 6.0 Hz, 1H), 2.49-2.42 (m, 1H), 2.22 (d, J = 12.8 Hz, 1H), 2.06-1.98 (m, 1H), 1.91 (ddd, J = 15.9, 9.7, 2.1 Hz, 1H), 1.82 (dd, J = 15.7, 2.5 Hz, 1H), 1.77-1.60 (m, 4H), 1.65 (s, 3H), 1.37 (s, 3H), 1.26 (qt, J = 13.6, 3.5 Hz, 1H), 1.16 (qd, J = 13.7, 3.2 Hz, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 152.7 (C_4), 107.6 (CH_2), 107.6 (C_4), 84.4 (C_4), 77.1 (CH), 68.4 (CH_2), 66.1 (CH_2), 43.8 (CH), 37.7 (CH), 35.3 (CH), 34.1 (CH_2), 28.0 (CH_2), 27.7 (CH_2), 26.7 (CH_3), 26.2 (CH_3), 24.7 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3394 (br), 3102 (w), 2985 (m), 2933 (s), 2864 (m), 1645 (w), 1448 (w), 1369 (m), 1246 (m), 1217 (m), 1045 (m), 1020 (m); HRMS (EI) *m/z* (M^+) calcd 282.18311, found 282.18170. Melting point : 94.3-96.2 °C.

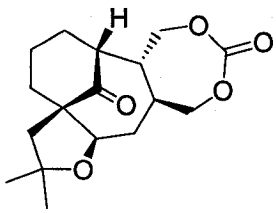
Carbonate protected (5-Hydroxymethyl-2,2-dimethyl-10-methylene-octahydro-naphtho[1,8a-*d*][1,3]dioxol-6-yl)-methanol (2.133)



Triphosgene (32 mg, 0.11 mmol) was added to CH_2Cl_2 (0.8 mL) followed by pyridine (49 μL) and the solution was cooled down to 0°C. **2.132** (19.0 mg, 67.2 μmol) was canulated with CH_2Cl_2 (0.5 mL) to the solution and the reaction was stirred at 0°C for 30 minutes. The reaction was quenched with $NaHCO_3$ (aq. sat.), extracted with CH_2Cl_2, dried over Na_2SO_4, filtered and concentrated *in vacuo*. Flash chromatography with 30% EtOAc/hexanes gave **2.133** as a pale yellow oil (18.9 mg, 61.3 μmol, 91%), with a Rf = 0.78 (80% EtOAc/hexanes). ^{1}H NMR (400 MHz, C_6D_6) δ 5.38 (d, J = 2.5 Hz, 1H), 4.84 (s, 1H), 3.90 (t, J = 10.7 Hz, 1H), 3.74 (t, J = 2.9 Hz, 1H), 3.68 (dd, J = 11.5, 2.7 Hz, 1H), 3.61 (dd, J = 11.5, 2.2 Hz, 1H), 3.44 (t, J = 10.3 Hz, 1H), 2.42 (tt, J = 10.6, 2.2 Hz, 1H), 2.19-2.14 (m, 1H), 1.53 (qt, J = 10.9, 2.2 Hz, 1H), 1.47-1.37 (m, 4H), 1.43 (s, 3H), 1.28 (s, 3H), 1.16 (dt, J = 15.8, 2.3 Hz, 1H), 1.09-0.96 (m, 1H), 0.87-0.68 (m, 2H); ^{13}C NMR (100 MHz, C_6D_6) δ 154.0 (C_4), 151.4 (C_4), 108.7 (CH_2), 107.4 (C_4), 84.4 (C_4), 77.0 (CH), 76.2 (CH_2), 74.7 (CH_2), 44.4 (CH), 39.5 (CH), 34.7 (CH), 34.3 (CH_2), 27.1 (CH_2), 27.0 (CH_3), 25.9 (CH_3), 25.7 (CH_2), 24.9 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3102 (w), 2988 (m), 2939 (s), 2898 (m), 2864 (m), 1756 (s), 1647 (w), 1464 (w), 1379 (m), 1264 (m), 1229 (m),

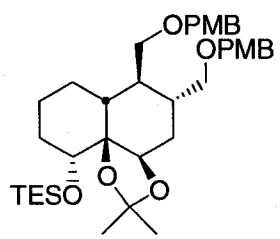
1184 (s), 1084 (m), 1061 (m); HRMS (EI) *m/z* (M^+) calcd 308.16238, found 308.16427. Melting point : 160.5-162.3 °C.

Carbonate protected 7,8-Bis-hydroxymethyl-3,3-dimethyl-4-oxa-tricyclo[7.3.1.$0^{1,5}$]tridecan-13-one (2.134)



Procedure C: Tin tetrachloride 1.0 M in CH_2Cl_2 (62 μL, 62 μmol), Prins-pinacol precursor **2.133** (9.5 mg, 31 μmol), toluene (0.62 mL), from -78°C to -20°C for 1 hour and 45 minutes. Flash chromatography with 45% EtOAc/hexanes gave **2.134** as a white solid (7.1 mg, 23 μmol, 74%), with a Rf = 0.24 (40% EtOAc/hexanes). ^1H NMR (400 MHz, C_6D_6) δ 3.68 (dd, J = 11.4, 4.2 Hz, 1H), 3.43-3.19 (m, 4H), 2.98 (t, J = 10.6 Hz, 1H), 2.30 (s, 1H), 1.85 (d, J = 14.1 Hz, 1H), 1.59-1.31 (m, 3H), 1.40 (s, 3H), 1.31-0.93 (m, 6H), 1.21 (s, 3H), 0.87-0.74 (m, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 208.3 (C_4), 153.6 (C_4), 83.4 (CH), 80.4 (C_4), 74.1 (CH_2), 72.4 (CH_2), 60.3 (C_4), 50.2 (CH), 47.5 (CH), 47.3 (CH_2), 40.0 (CH_2), 36.5 (CH), 36.2 (CH_2), 29.5 (CH_3), 27.2 (CH_3), 25.1 (CH_2), 20.8 (CH_2); IR (CH_2Cl_2, cm^{-1}) 2973 (s), 2942 (s), 2872 (m), 1769 (s), 1699 (s), 1464 (m), 1376 (m), 1268 (m), 1209 (m), 1181 (s), 1088 (s), 1043 (m); HRMS (EI) *m/z* (M^+) calcd 308.16238, found 308.16433. Melting point : 177.4 – 179.8°C. COSY, NOESY and HMQC experiments were performed in order to obtain the correlations illustrated in Figure 2.9.

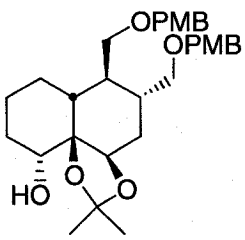
[5,6-Bis-(4-methoxy-benzyloxymethyl)-2,2-dimethyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-yloxy]-triethyl-silane (2.135)



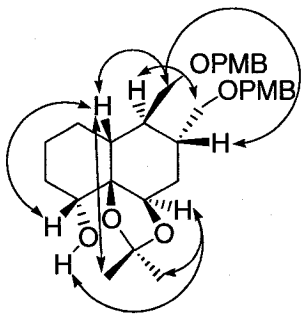
Procedure L: PTSA (1.1 mg, 5.8 μmol), diol **2.127** (0.346 g, 0.576 mmol), 2-methoxypropene (0.165 mL, 1.73 mmol), CH_2Cl_2 (5.8 mL), stirred for 40 minutes. Flash chromatography with 10-15% EtOAc/hexanes gave **2.135** as a pale yellow oil (349 mg, 0.544 mmol, 95%), with a Rf = 0.77 (25% EtOAc/hexanes). ^1H NMR (400 MHz, $CDCl_3$) δ 7.22-7.18 (m, 4H), 6.86-6.82 (m, 4H), 4.36 (d, J = 11.8 Hz, 2H), 4.27 (t, J= 10.5, 2H), 3.97 (s, 1H), 3.78 (s, 6H), 3.71 (s, 1H), 3.42 (dd, J = 9.9, 1.9 Hz, 1H), 3.35-3.30 (m, 3H), 2.19-

2.00 (m, 4H), 1.94 (dd, J = 11.8, 2.5 Hz, 1H), 1.79-1.47 (m, 5H), 1.46 (s, 3H), 1.32 (s, 3H), 1.30-1.20 (m, 1H), 0.91 (t, J = 8.1 Hz, 9H), 0.56 (q, J = 8.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0 (C_4), 159.0 (C_4), 131.2 (C_4), 131.1 (C_4), 129.2 (CH), 129.0 (CH), 113.6 (CH), 113.5 (CH), 106.9 (C_4), 80.6 (C_4), 79.5 (CH), 75.0 (CH), 72.6 (CH_2), 72.5 (CH_2), 72.2 (CH_2), 66.8 (CH_2), 55.2 (CH_3), 55.2 (CH_3), 39.6 (CH), 36.3 (CH), 33.9 (CH), 31.7 (CH_2), 31.7 (CH_2), 28.7 (CH_3), 27.0 (CH_3), 22.2 (CH_2), 15.3 (CH_2), 7.0 (CH_3), 5.0 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3064 (w), 3034 (w), 2934 (s), 2874 (s), 2792 (w), 2063 (w), 1881 (w), 1613 (s), 1586 (m), 1514 (s), 1455 (m), 1415 (w), 1366 (m), 1302 (m), 1247 (m), 1172 (m), 1113 (m), 1083 (s), 1039 (s); HRMS (EI) *m/z* (M^+) calcd 640.37953, found 640.37855.

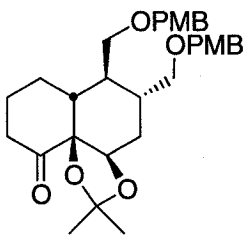
5,6-Bis-(4-methoxy-benzyloxymethyl)-2,2-dimethyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-ol (2.136)



Tetrabutyl ammonium fluoride 1.0 M in THF (0.82 mL, 0.82 mmol) was added to a solution of **2.135** (349 mg, 0.545 mmol) in THF (5.5 mL) at room temperature and the reaction was stirred at this temperature for 40 minutes. The reaction was concentrated *in vacuo* and flash chromatography with 33% EtOAc/hexanes gave **2.136** as a colorless sticky oil (248 mg, 0.471 mmol, 86%), with a Rf = 0.37 (33% EtOAc/hexanes). ^{1}H NMR (400 MHz, C_6D_6) δ 7.28-7.21 (m, 4H), 6.87-6.83 (m, 4H), 4.39 (dd, J = 11.8, 5.6 Hz, 2H), 4.32 (t, J = 12.0 Hz, 2H), 4.19 (s, 1H), 3.63-3.49 (m, 4H), 3.46 (dd, J = 9.2, 2.9 Hz, 1H), 3.39 (s, 3H), 3.38 (s, 3H), 2.59-2.50 (m, 2H), 2.46-2.36 (m, 3H), 2.10-1.99 (m, 3H), 1.72-1.58 (m, 1H), 1.58 (s, 3H), 1.52-1.29 (m, 2H), 1.41 (s, 3H), 1.11-1.03 (br, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 159.4 (C_4), 159.4 (C_4), 131.3 (C_4), 131.2 (C_4), 129.3 (CH), 129.2 (CH), 113.8 (CH), 113.8 (CH), 107.2 (C_4), 80.2 (C_4), 79.6 (CH), 74.0 (CH), 72.6 (CH_2), 72.5 (CH_2), 72.5 (CH_2), 67.0 (CH_2), 54.5 (CH_3), 54.5 (CH_3), 39.9 (CH), 36.8 (CH), 34.3 (CH), 32.2 (CH_2), 32.1 (CH_2), 28.8 (CH_3), 27.0 (CH_3), 22.5 (CH_2), 15.5 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3473 (br), 3031 (w), 2982 (m), 2934 (s), 2864 (s), 2060 (w), 1884 (w), 1736 (w), 1612 (m), 1586 (w), 1513 (s), 1463 (m), 1366 (m), 1302 (w), 1248 (s), 1173 (m), 1098 (m), 1029 (s); HRMS (EI) *m/z* (M^+-Me) calcd 511.26958, found 511.27074. COSY, NOESY and HMQC experiments were performed in order to obtain the correlations illustrated below:

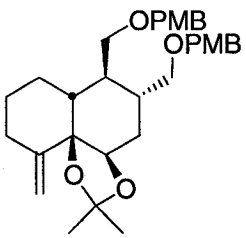


5,6-Bis-(4-methoxy-benzyloxymethyl)-2,2-dimethyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-one (2.137)



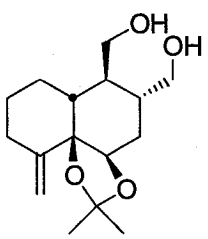
Procedure F: Dess-Martin periodinane (239 mg, 0.563 mmol), alcohol **2.136** (247 mg, 0.469 mmol), CH_2Cl_2 (4.7 mL), stirred for 40 minutes. Flash chromatography with 40% EtOAc/hexanes gave **2.137** as a colorless oil (238 mg, 0.454 mmol, 97%), with a Rf = 0.79 (40% EtOAc/hexanes). ^1H NMR (400 MHz, $CDCl_3$) δ 7.19-7.15 (m, 4H), 6.86-6.81 (m, 4H), 4.56 (t, J = 4.1 Hz, 1H), 4.32 (dd, J = 11.8, 2.4 Hz, 2H), 4.27 (dd, J = 11.8, 2.4 Hz, 2H), 3.77 (s, 3H), 3.76 (s, 3H), 3.34-3.26 (m, 3H), 3.22 (dd, J = 9.4, 3.5 Hz, 1H), 2.74 (td, J = 13.2, 6.4 Hz, 1H), 2.29 (t, J = 13.6 Hz, 2H), 2.14-1.96 (m, 3H), 1.95-1.81 (m, 2H), 1.72 (d, J = 14.4 Hz, 1H), 1.58 (qt, J = 13.5, 3.3 Hz, 1H), 1.48 (s, 3H), 1.26 (s, 3H), 1.20-1.11 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.5 (C_4), 159.2 (C_4), 159.1 (C_4), 130.7 (C_4), 130.6 (C_4), 129.2 (CH), 129.2 (CH), 113.7 (CH), 113.7 (CH), 108.3 (C_4), 84.5 (C_4), 72.8 (CH_2), 72.6 (CH_2), 72.2 (CH), 71.7 (CH_2), 66.9 (CH_2), 55.2 (CH_3), 55.2 (CH_3), 43.5 (CH), 40.3 (CH_2), 36.2 (CH), 34.1 (CH), 29.7 (CH_2), 28.7 (CH_3), 26.7 (CH_3), 22.8 (CH_2), 22.0 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3033 (w), 2986 (m), 2936 (s), 2864 (s), 2792 (w), 2060 (w), 1885 (w), 1715 (s), 1613 (s), 1586 (m), 1514 (s), 1463 (m), 1369 (m), 1302 (m), 1247 (m), 1172 (m), 1086 (m), 1034 (m); HRMS (EI) *m/z* (M^+-PMB) calcd 403.21207, found 403.21434.

5,6-Bis-(4-methoxy-benzyloxymethyl)-2,2-dimethyl-10-methylene-octahydro-naphtho[1,8a-*d*][1,3]dioxole (2.138)



Procedure N: Potassium *tert*-butoxide 1.0 M solution in THF (1.3 mL, 1.3 mmol), methyltriphenylphosphonium iodide (0.54 g, 1.3 mmol), toluene (3.0 + 1.5 mL), ketone **2.137** (235 mg, 0.448 mmol), stirred at room temperature for 45 minutes. Flash chromatography with 15-20% EtOAc/hexanes gave **2.138** as a colorless oil (193 mg, 0.369 mmol, 82%), with a Rf = 0.61 (33% EtOAc/hexanes). ^{1}H NMR (400 MHz, C_6D_6) δ 7.25-7.20 (m, 4H), 6.87-6.82 (m, 4H), 4.89 (s, 1H), 4.73 (s, 1H), 4.50 (s, 1H), 4.35 (d, J = 11.8 Hz, 2H), 4.27 (dd, J = 15.4, 11.9 Hz, 2H), 3.48-3.38 (m, 3H), 3.39 (s, 3H), 3.39 (s, 3H), 3.30 (dd, J = 9.3, 2.9 Hz, 1H), 2.68 (td, J = 12.9, 4.3 Hz, 1H), 2.56 (d, J + 12.0 Hz, 1H), 2.54-2.39 (m, 2H), 2.27 (tt, J = 14.1, 4.2 Hz, 1H), 2.17 (d, J = 12.6 Hz, 1H), 2.04 (ddd, J = 14.7, 12.9, 4.1 Hz, 1H), 2.01 (d, J = 4.2 Hz, 1H), 1.65-1.54 (m, 2H), 1.59 (s, 3H), 1.42 (s, 3H), 1.33 (qt, J = 13.5, 3.4 Hz, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 159.5 (C_4), 159.4 (C_4), 147.4 (C_4), 131.1 (C_4), 131.0 (C_4), 129.3 (CH), 129.2 (CH), 113.8 (CH), 113.8 (CH), 109.1 (CH_2), 106.6 (C_4), 82.5 (C_4), 75.0 (CH), 72.8 (CH_2), 72.6 (CH_2), 71.7 (CH_2), 66.4 (CH_2), 54.6 (CH_3), 54.6 (CH_3), 42.0 (CH), 37.2 (CH), 35.2 (CH), 35.1 (CH_2), 30.8 (CH_2), 29.0 (CH_3), 27.1 (CH_3), 23.5 (CH_2), 22.8 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3080 (w), 3033 (w), 2986 (s), 2932 (s), 2857 (s), 2791 (w), 2061 (w), 1883 (w), 1738 (w), 1645 (m), 1613 (s), 1586 (m), 1513 (s), 1455 (s), 1366 (m), 1301 (m), 1215 (s), 1172 (m), 1086 (s), 1036 (s); HRMS (EI) *m/z* (M^+-PMB) calcd 401.23280, found 401.23072.

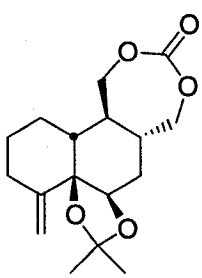
(5-Hydroxymethyl-2,2-dimethyl-10-methylene-octahydro-naphtho[1,8a-*d*][1,3]dioxol-6-yl)-methanol (2.139)



DDQ (168 mg, 0.738 mmol) was added to a solution of **2.138** (193 mg, 0.369 mmol) in CH_2Cl_2 (3.7 mL) and water (0.37 mL) at room temperature and the reaction was stirred at this temperature for 5 hours. The reaction was quenched with sodium sulfite (aq. sat.), extracted with CH_2Cl_2, dried over $MgSO_4$, filtered and concentrated *in vacuo*. Flash chromatography with 100% EtOAc/hexanes gave **2.139** as a white solid (31.3 mg, 0.111 mmol, 30%), with a Rf = 0.24 (80%

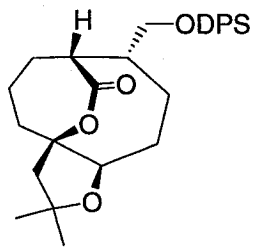
EtOAc/hexanes). ^{1}H NMR (400 MHz, C_6D_6) δ 4.88 (s, 1H), 4.64 (s, 1H), 4.40 (s, 1H), 3.73 (dd, J = 11.2, 2.3 Hz, 1H), 3.52 (dd, J = 11.2, 3.6 Hz, 1H), 3.42 (dd, J = 10.4, 2.8 Hz, 1H), 3.32 (dd, J = 10.4, 5.2 Hz, 1H), 2.65 (td, J = 12.9, 4.2 Hz, 1H), 2.28 (d, J = 11.0 Hz, 1H), 2.21-1.98 (m, 6H), 1.87 (d, J = 14.4 Hz, 1H), 1.58-1.47 (m, 2H), 1.59 (s, 3H), 1.41 (s, 3H), 1.30-1.18 (m, 2H); ^{13}C NMR (100 MHz, C_6D_6) δ 147.4 (C_4), 109.0 (CH_2), 106.6 (C_4), 82.4 (C_4), 74.8 (CH), 65.8 (CH_2), 60.1 (CH_2), 41.9 (CH), 40.3 (CH), 38.3 (CH), 35.0 (CH_2), 30.4 (CH_2), 28.9 (CH_3), 27.1 (CH_3), 23.1 (CH_2), 22.5 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3370 (br), 3103 (w), 2990 (m), 2936 (s), 2873 (m), 1814 (w), 1723 (w), 1648 (w), 1449 (m), 1380 (m), 1265 (m), 1208 (m), 1177 (w), 1063 (s), 1044 (m), 1021 (m); HRMS (EI) *m/z* (M^+) calcd 282.18311, found 282.18239. Melting point : 142.7-144.3 °C.

Carbonate protected (5-Hydroxymethyl-2,2-dimethyl-10-methylene-octahydro-naphtho[1,8a-*d*][1,3]dioxol-6-yl)-methanol (2.140)



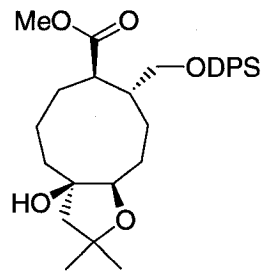
Triphosgene (17 mg, 57 μmol) was added to CH_2Cl_2 (0.4 mL) and pyridine (32 μL) and the solution was cooled down to 0°C. **2.139** (10.0 mg, 35.4 μmol) was canulated with CH_2Cl_2 (0.3 mL) to the solution and the reaction was stirred at 0°C for 45 minutes. The reaction was quenched with $NaHCO_3$ (aq. sat.), extracted with CH_2Cl_2, dried over Na_2SO_4, filtered and concentrated *in vacuo*. Flash chromatography with 30%, then 100% EtOAc/hexanes gave **2.139** (2.7 mg, 9.6 μmol, 27%), and **2.140** as a pale yellow oil (6.1 mg, 20 μmol, 56%, 83% overall yield), with a Rf = 0.90 (80% EtOAc/hexanes). ^{1}H NMR (400 MHz, C_6D_6) δ 4.78 (s, 1H), 4.38 (s, 1H), 4.15 (d, J = 2.5 Hz, 1H), 3.77 (dd, J = 12.2, 3.5 Hz, 1H), 3.34 (dd, J = 12.1, 3.0 Hz, 1H), 3.19 (dd, J = 12.0, 10.6 Hz, 1H), 3.07 (t, J = 11.5 Hz, 1H), 2.45 (tdt, J = 13.0, 4.8, 1.5 Hz, 1H), 2.03 (d, J = 12.8 Hz, 1H), 1.80 (tt, J = 14.4, 4.1 Hz, 1H), 1.74-1.63 (m, 1H), 1.58-1.52 (m, 2H), 1.47 (s, 3H), 1.34 (s, 3H), 1.31-1.16 (m, 2H), 1.06 (d, J = 14.5 Hz, 1H), 1.04-0.87 (m, 1H), 0.73 (ddd, J = 14.7, 13.1, 4.2 Hz, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 154.2 (C_4), 146.1 (C_4), 109.6 (CH_2), 106.8 (C_4), 81.2 (C_4), 73.7 (CH), 72.6 (CH_2), 70.8 (CH_2), 41.4 (CH), 39.2 (CH), 38.9 (CH), 34.5 (CH_2), 28.7 (CH_3), 27.8 (CH_2), 26.9 (CH_3), 22.2 (CH_2), 21.3 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3085 (w), 2986 (m), 2934 (s), 2861 (w), 1769 (s), 1646 (w), 1461 (w), 1370 (m), 1248 (m), 1183 (s), 1096 (m), 1082 (s), 1050 (m), 1017 (w); HRMS (EI) *m/z* (M^+) calcd 308.16238, found 308.16045.

8-(*tert*-Butyl-diphenyl-silanyloxymethyl)-3,3-dimethyl-4,13-dioxa-tricyclo [7.3.2.0^{1,5}]tetradecan-14-one (2.147)



m-CPBA (23.0 mg, 104 μmol) was added to a solution of **2.30** (41.0 mg, 83.5 μmol) in CH_2Cl_2 (0.8 mL) at room temperature and the reaction was stirred at this temperature for 1 day. More *m*-CPBA (23.0 mg, 104 μmol) was added at room temperature and the reaction was stirred for one more day. A third potion of *m*-CPBA (23.0 mg, 104 μmol) was added at room temperature and the reaction was stirred for four more days. The reaction was quenched with sodium sulfite (sat. aq.), extracted with CH_2Cl_2, the organic layers were combined and washed two times with $NaHCO_3$ (aq. sat.) and once with brine. The resulting solution was dried over $MgSO_4$, filtered and concentrated *in vacuo*. Flash chromatography with 15-20 % EtOAc/hexanes gave **2.147** as a pale yellow oil (14 mg, 27 μmol, 32%), with a Rf = 0.49 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65-7.58 (m, 4H), 7.44-7.33 (m, 6H), 4.00 (dd, J = 10.7, 3.1 Hz, 1H), 3.58 (dd, J = 10.3, 5.4 Hz, 1H), 2.53-2.44 (m, 2H), 2.48 (d, J = 13.5 Hz, 1H), 2.37-2.23 (m, 1H), 2.22-2.04 (m, 3H), 1.93-1.54 (m, 6H), 1.51-1.38 (m, 1H), 1.34 (s, 3H), 1.19 (s, 3H), 1.26-1.21 (m, 1H), 1.02 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 178.4 (C_4), 135.9 (CH), 133.6 (C_4), 130.1 (CH), 128.1 (CH), 93.2 (C_4), 86.7 (CH), 78.1 (C_4), 66.5 (CH_2), 58.7 (CH_2), 46.7 (CH), 45.2 (CH), 41.7 (CH_2), 29.1 (CH_2), 29.1 (CH_3), 27.2 (CH_3), 27.2 (CH_3), 25.8 (CH_2), 24.4 (CH_2), 23.7 (CH_2), 19.6 (C_4); IR (CH_2Cl_2, cm^{-1}) 3071 (w), 3052 (w), 2966 (m), 2931 (s), 2858 (m), 1964 (w), 1894 (w), 1823 (w), 1708 (s), 1589 (w), 1471 (w), 1449 (w), 1428 (m), 1362 (w), 1289 (w), 1271 (w), 1196 (m), 1140 (m), 1111 (s), 1080 (m), 1044 (m); HRMS (EI) *m/z* (M^+-*t*Bu) calcd 449.21481, found 449.21333.

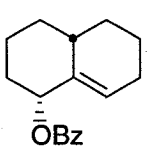
8-(*tert*-Butyl-diphenyl-silanyloxymethyl)-3a-hydroxy-2,2-dimethyl-decahydro-cyclonona[*b*]furan-7-carboxylic acid methyl ester (2.148)



Potassium hydroxide (0.12 g, excess) was added to a solution of **2.147** (11.5 mg, 22.6 μmol) in methanol (0.44 mL) at room temperature and the reaction was stirred at this temperature for 15 minutes. The reaction was quenched with NH_4Cl (sat. aq.), extracted with CH_2Cl_2, dried over $MgSO_4$, filtered and concentrated *in vacuo*. Flash chromatography with 20 %

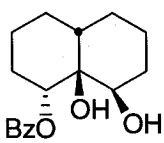
EtOAc/hexanes gave **2.148** as a pale yellow oil (7.7 mg, 15 μmol, 63%), with a Rf = 0.42 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66-7.60 (m, 4H), 7.47-7.34 (m, 6H), 3.92-2.41 (m, 1H), 3.56-3.45 (m, 2H), 3.52 (s,3H), 2.48-2.41 (m, 1H), 2.21-2.25 (m, 14H), 1.35 (s, 3H), 1.25 (s, 3H), 1.05 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.1 (C_4), 136.0 (CH), 134.0 (C_4), 130.0 (CH), 128.0 (CH), 84.3 (CH), 81.9 (C_4), 76.5 (C_4), 67.1 (CH_2), 55.6 (CH_2), 51.8 (CH_3), 46.1 (CH), 43.6 (CH), 35.5 (CH_2), 30.7 (CH_3), 30.5 (CH_2), 29.1 (CH_3), 28.2 (CH_2), 27.2 (CH_3), 26.7 (CH_2), 19.7 (CH_2), 19.7 (C_4); IR (CH_2Cl_2, cm^{-1}) 4393 (br), 3071 (w), 3049 (w), 2959 (s), 2930 (s), 2857 (s), 1960 (w), 1892 (w), 1733 (s), 1594 (w), 1473 (m), 1447 (w), 1428 (m), 1378 (w), 1363 (w), 1265 (w), 1192 (w), 1112 (s), 1084 (m), 1023 (m); HRMS (EI) *m/z* (M^+-*t*Bu) calcd 481.24103, found 481.24276. COSY, NOESY and HMQC experiments were performed in order to obtain the correlations illustrated in Figure 2.11.

Benzoic acid 1,2,3,4,4a,5,6,7-octahydro-naphthalen-1-yl ester (3.6)



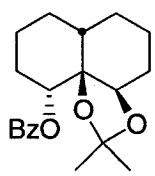
Procedure I: 4-Dimethylaminopyridine (15 mg, 0.12 mmol), benzoyl chloride (0.32 mL, 2.8 mmol), alcohol **3.5**[83] (370 mg, 2.43 mmol), pyridine (0.59 mL, 7.3 mmol), CH_2Cl_2 (10 mL), stirred for 4 hours. Flash chromatography with 3% EtOAc/hexanes gave **3.6** as a colorless oil (330 mg, 1.29 mmol, 53%), with a Rf = 0.85 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.04-8.01 (m, 2H), 7.42 (tt, J = 7.2, 1.3 Hz, 1H), 7.32 (tt, J = 7.1, 1.1 Hz, 2H), 5.56 (s, 1H), 5.32-5.28 (m, 1H), 2.33-2.11 (m, 2H), 2.07-1.95 (m, 1H), 1.90-1.79 (m 2H), 1.76-1.70 (m, 1H), 1.64-1.56 (m, 1H), 1.55-1.39 (m, 3H), 1.37-1.22 (m, 1H), 1.13 (ddd, J = 26.7, 12.6, 3.9 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.6 (C_4), 138.6 (C_4), 133.1 (CH), 130.9 (C_4), 129.9 (CH), 128.6 (CH), 117.2 (CH), 75.6 (CH), 36.9 (CH), 34.8 (CH_2), 33.9 (CH_2), 30.8 (CH_2), 25.5 (CH_2), 24.0 (CH_2), 21.3 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3060 (w), 3032 (w), 2929 (s), 2857 (s), 1723 (s), 1669 (w), 1602 (m), 1584 (m), 1450 (s), 1314 (s), 1275 (s), 1176 (m), 1116 (s), 1070 (m), 1026 (m); HRMS (EI) *m/z* (M^+) calcd 256.14633, found 256.14479.

Benzoic acid 8,8a-dihydroxy-decahydro-naphthalen-1-yl ester (3.7)



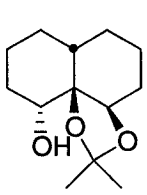
Procedure K: 4-Methylmorpholine N-oxide (2.82 g, 24.2 mmol), solution of osmium tetraoxide 4% in water (3.83 mL, 0.603 mmol), alkene **3.6** (3.09 g, 12.1 mmol), water (24 mL), THF (120 mL), refluxed for 18 hours. Flash chromatography with 20-25% EtOAc/hexanes gave **3.7** as a white solid (2.41 g, 8.30 mmol, 69%), with a Rf = 0.32 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92-7.89 (m,2H), 7.53 (td, J = 7.5, 1.3 Hz, 1H), 7.39 (t, J = 7.8 Hz, 2H), 5.05 (dd, J = 11.7, 4.2 Hz, 1H), 4.30 (dd, J = 10.3, 5.0 Hz, 1H), 2.94 (br, 2H), 2.09-2.04 (m, 1H), 1.99-1.71 (m, 4H), 1.69-1.36 (m, 7H), 1.26 (d, J = 12.6, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.2 (C_4), 133.6 (CH), 130.4 (C_4), 129.7 (CH), 129.0 (CH), 84.0 (CH), 73.9 (C_4), 68.6 (CH), 42.6 (CH), 30.1 (CH_2), 29.4 (CH_2), 27.8 (CH_2), 25.9 (CH_2), 23.9 (CH_2), 19.4 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3409 (br), 3194 (br), 2943 (s), 2923 (s), 2867 (m), 2847 (m), 1708 (s), 1449 (m), 1413 (w), 1313 (w), 1277 (m), 1250 (w), 1117 (m), 1066 (m); HRMS (EI) *m/z* (M^+) calcd 272.14124, found 272.14090. Melting point : 143.2-143.9°C.

Benzoic acid 2,2-dimethyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-yl ester (3.8)



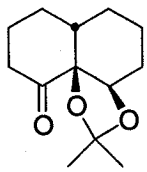
Procedure L: PTSA (16 mg, 83 μmol), diol **3.7** (2.41 g, 8.30 mmol), 2-methoxypropene (2.38 mL, 24.9 mmol), CH_2Cl_2 (83 mL), stirred for 10 minutes. Flash chromatography with 5-10% EtOAc/hexanes gave **3.8** as a colorless oil (2.74 g, 8.30 mmol, quant.), with a Rf = 0.68 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95-7.92 (m, 2H), 7.43 (t, J = 7.2 Hz, 1H), 7.33 (t, J = 7.7 Hz, 2H), 5.08 (s, 1H), 3.85 (s, 1H), 1.89-1.75 (m, 6H), 1.70-1.51 (m, 4H), 1.38-1.24 (m, 3H), 1.37 (s, 3H), 1.25 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.6 (C_4), 133.3 (CH), 130.5 (C_4), 129.9 (CH), 128.9 (CH), 107.8 (C_4), 78.9 (C_4), 78.4 (CH), 76.2 (CH), 39.1 (CH), 28.8 (CH_3), 28.6 (CH_2), 28.2 (CH_2), 27.8 (CH_2), 27.7 (CH_2), 27.0 (CH_3), 21.3 (CH_2), 16.2 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3063 (m), 3034 (w), 2984 (s), 2932 (s), 2865 (s), 1715 (s), 1602 (m), 1584 (m), 1450 (s), 1379 (s), 1368 (s), 1327 (m), 1266 (m), 1217 (m), 1179 (m), 1129 (m), 1069 (m), 1049 (m); HRMS (EI) *m/z* (M^+) calcd 330.18311, found 330.18126.

2,2-Dimethyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-ol (3.9)



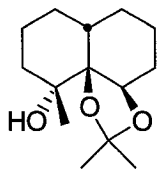
Procedure E: Potassium carbonate (8.3 g, excess), benzoate **3.8** (2.74 g, 8.30 mmol), methanol (40 mL), benzene (10 mL), refluxed for 18 hours. Flash chromatography with 10%, then 20% EtOAc/hexanes gave **3.8** (1.07 g, 3.24 mmol, 39%) and **3.9** as a colorless oil (1.12 g, 4.95 mmol, 60%, 99% overall yield), with a Rf = 0.48 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.91 (t, J = 2.2 Hz, 1H), 3.58 (s, 1H), 2.06 (s, 1H), 1.97-1.80 (m, 2H), 1.75-1.43 (m, 8H), 1.33 (s, 3H), 1.28-1.17 (m, 3H), 1.20 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 107.3 (C_4), 79.8 (C_4), 79.4 (CH), 74.1 (CH), 39.1 (CH), 31.9 (CH_2), 28.8 (CH_3), 28.3 (CH_2), 28.0 (CH_2), 27.9 (CH_2), 27.2 (CH_3), 21.5 (CH_2), 15.4 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3465 (br), 2984 (m), 2932 (s), 2865 (m), 1644 (m), 1447 (m), 1379 (m), 1368 (m), 1247 (m), 1216 (m), 1179 (m), 1125 (w), 1033 (s); HRMS (EI) *m/z* (M^+) calcd 226.15689, found 226.15756.

2,2-Dimethyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-one (3.10)



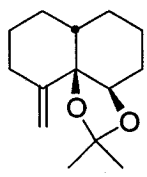
Procedure F: Dess-Martin periodinane (2.52 g, 5.94 mmol), alcohol **3.9** (1.12 g, 4.95 mmol), CH_2Cl_2 (50 mL), stirred for 15 minutes. Flash chromatography with 5% EtOAc/hexanes gave **3.10** as a white solid (1.07g, 4.77 mmol, 96%), with a Rf = 0.77 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.18 (t, J = 2.6 Hz, 1H), 2.46 (td, J = 13.5, 6.1 Hz, 1H), 2.05-1.91 (m, 3H), 1.80 (d, J = 14.5 Hz, 1H), 1.72-1.62 (m, 1H), 1.55-1.36 (m, 2H), 1.24 (s, 3H), 1.31-1.11 (m, 4H), 1.03 (s, 3H), 0.93-0.82 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.9 (C_4), 108.1 (C_4), 83.7 (C_4), 72.7 (CH), 43.3 (CH), 40.6 (CH_2), 28.9 (CH_3), 26.8 (CH_2), 26.7 (CH_2), 26.5 (CH_2), 26.5 (CH_3), 23.4 (CH_2), 21.2 (CH_2); IR (CH_2Cl_2, cm^{-1}) 2986 (m), 2935 (s), 2866 (m), 1719 (s), 1644 (m), 1446 (m), 1430 (w), 1310 (w), 1248 (w), 1217 (m), 1175 (m), 1047 (m); HRMS (EI) *m/z* (M^+) calcd 224.14125, found 224.14010. Melting point : 57.2-58.1°C.

2,2,10-Trimethyl-octahydro-naphtho[1,8a-*d*][1,3]dioxol-10-ol (3.11)



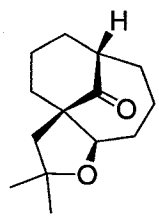
Procedure A: $CeCl_3$ (906 mg, 3.68 mmol), THF (10 + 2 mL), ketone **3.10** (275 mg, 1.23 mmol), methyllithium 1.6 M in diethyl ether (4.60 mL, 7.36 mmol), warmed to room temperature for 25 minutes. Flash chromatography with 15-20% EtOAc/hexanes gave **3.11** as a white solid (257 mg, 1.07 mmol, 87%), with a Rf = 0.62 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.24 (s, 1H), 1.98 (d, J = 12.6 Hz, 1H), 1.91-1.68 (m, 4H), 1.65-1.37 (m, 5H), 1.39 (s, 3H), 1.31-1.16 (m, 3H), 1.27 (s, 3H), 1.22 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 107.1 (C_4), 81.8 (C_4), 75.1 (CH), 73.6 (C_4), 39.6 (CH), 39.6 (CH_2), 29.3 (CH_2), 29.2 (CH_3), 28.3 (CH_2), 28.2 (CH_2), 27.3 (CH_3), 27.3 (CH_3), 21.3 (CH_2), 17.1 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3481 (br), 2989 (m), 2932 (s), 2863 (m), 1455 (m), 1379 (m), 1367 (s), 1246 (s), 1214 (s), 1175 (m), 1124 (w), 1038 (s), 1019 (s); HRMS (EI) *m/z* (M^+) calcd 240.17255, found 240.17034. Melting point : 104.9-105.7°C.

2,2-Dimethyl-10-methylene-octahydro-naphtho[1,8a-*d*][1,3]dioxole (3.12)

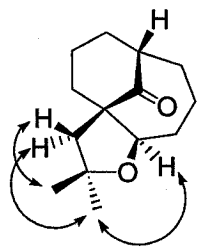


Procedure B: Thionyl chloride (0.15 mL, 2.1 mmol), alcohol **3.11** (251 mg, 1.04 mmol), 4-dimethylaminopyridine (764 mg, 6.27 mmol), CH_2Cl_2 (10.4 mL), warmed at room temperature for 15 minutes. Flash chromatography with 2.5-5.0% EtOAc/hexanes gave **3.12** as a colorless oil that solidify upon storage in the fridge (141 mg, 0.637 mmol, 61%), with a Rf = 0.88 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.91 (s, 1H), 4.69 (s, 1H), 4.28-4.26 (m, 1H), 2.32 (tdt, J = 12.8, 3.0, 1.2 Hz, 1H), 2.18-1.92 (m, 4H), 1.74-1.50 (m, 4H), 1.48 (s, 3H), 1.30 (s, 3H), 1.44-1.21 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.1 (C_4), 109.8 (CH_2), 106.8 (C_4), 82.3 (C_4), 75.1 (CH), 41.2 (CH), 35.2 (CH_2), 29.2 (CH_3), 28.1 (CH_2), 27.9 (CH_2), 27.6 (CH_3), 27.1 (CH_2), 23.7 (CH_2), 22.3 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3082 (w), 2986 (m), 2932 (s), 2863 (m), 1646 (w), 1445 (m), 1379 (m), 1366 (m), 1246 (s), 1215 (s), 1179 (m), 1163 (w), 1131 (m), 1040 (s), 1005 (w); HRMS (EI) *m/z* (M^+) calcd 222.16198, found 222.16124.

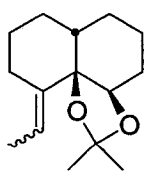
3,3-Dimethyl-4-oxa-tricyclo[7.3.1.0^{1,5}]tridecan-13-one (3.13)



Procedure C: Methane sulfonic acid (6.4 μL, 98 μmol), Prins-pinacol precursor **3.12** (11 mg, 49 μmol), CH_2Cl_2 (1.0 mL), at -78°C and the reaction was warmed to room temperature overnight. Flash chromatography with 15% EtOAc/hexanes gave **3.13** as a colorless oil (7.4 mg, 33 μmol, 67%), with a Rf = 0.68 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.03 (dd, J = 9.8, 4.3 Hz, 1H), 2.92 (d, J = 12.8 Hz, 1H), 2.76-2.70 (m, 1H), 2.22-2.16 (m, 1H), 2.11-1.99 (m, 1H), 1.95-1.59 (m, 9H), 1.48-1.34 (m, 1H), 1.30 (s, 3H), 1.25 (s, 3H), 1.27-1.23 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.4 (C_4), 84.4 (CH), 80.4 (C_4), 61.5 (C_4), 48.5 (CH), 48.0 (CH_2), 40.7 (CH_2), 35.5 (CH_2), 34.9 (CH_2), 33.0 (CH_2), 29.6 (CH_3), 28.0 (CH_3), 22.1 (CH_2), 21.4 (CH_2); IR (CH_2Cl_2, cm^{-1}) 2969 (m), 2929 (s), 2855 (m), 1701 (s), 1453 (m), 1379 (m), 1362 (m), 1268 (m), 1268 (m), 1246 (m), 1169 (m), 1142 (w), 1059 (w), 1046 (m); HRMS (EI) *m/z* (M^+) calcd 222.16198, found 222.16098. COSY, NOESY and HMQC experiments were performed in order to obtain the correlations illustrated below:

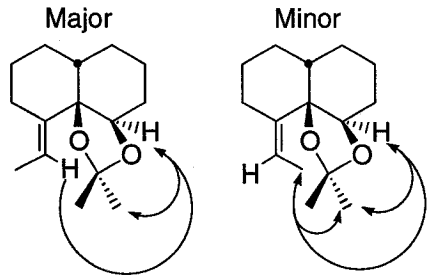


10-Ethylidene-2,2-dimethyl-octahydro-naphtho[1,8a-*d*][1,3]dioxole (3.19)

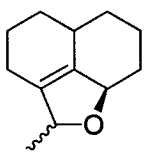


Procedure N: Potassium *tert*-butoxide 1.0 M solution in THF (2.01 mL, 2.01 mmol), ethyltriphenylphosphonium iodide (0.840 g, 2.01 mmol), toluene (5 + 2 mL), ketone **3.10** (150 mg, 0.669 mmol), refluxed for 45 minutes. Flash chromatography with 4-5% EtOAc/hexanes gave **3.19** as a colorless oil (146 mg, 0.616 mmol, 92%), which is a 10 : 1 mixture of *E* : *Z* isomers, with a Rf = 0.61 (33% EtOAc/hexanes). ***E*-3.19** ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.25 (q, J = 6.6 Hz, 1H), 4.23 (t, J = 2.5 Hz, 1H), 2.52 (d, J = 13.2 Hz, 1H), 2.10-1.77 (m, 4H), 1.77-1.64 (m, 1H), 1.61 (dd, J = 6.7, 1.3 Hz, 3H), 1.62-1.49 (m, 3H), 1.48 (s, 3H), 1.37-1.18 (m, 4H), 1.30 (s, 3H); ^{13}C NMR (100

MHz, $CDCl_3$) δ 137.4 (C_4), 117.8 (CH), 106.0 (C_4), 83.2 (C_4), 74.7 (CH), 41.0 (CH), 28.9 (CH_3), 28.0 (CH_2), 27.8 (CH_2), 27.4 (CH_3), 26.9 (CH_2), 26.4 (CH_2), 22.6 (CH_2), 22.1 (CH_2), 13.0 (CH_3); **Z-3.19** ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.39 (qd, J = 7.6, 1.1 Hz, 1H), 4.61 (t, J = 3.1 Hz, 1H), 2.32 (d, J = 11.5 Hz, 1H), 2.10-1.77 (m, 4H), 1.74 (dd, J = 7.6, 1.7 Hz, 3H) 1.77-1.64 (m, 1H), 1.62-1.49 (m, 3H), 1.48 (s, 3H), 1.37-1.18 (m, 4H), 1.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.4 (C_4), 120.6 (CH), 106.1 (C_4), 85.0 (C_4), 74.8 (CH), 40.4 (CH), 38.1 (CH_2), 28.9 (CH_3), 28.3 (CH_2), 27.7 (CH_2), 27.3 (CH_3), 26.2 (CH_2), 22.4 (CH_2), 21.4 (CH_2), 14.9 (CH_3); IR (CH_2Cl_2, cm^{-1}) 3062 (w), 2983 (m), 2930 (s), 2860 (m), 1729 (w), 1444 (m), 1376 (m), 1245 (s), 1214 (s), 1179 (m), 1130 (m), 1038 (s), 1000 (m); HRMS (EI) *m/z* (M^+) calcd 236.17763, found 236.17700. COSY, NOESY and HMQC experiments were performed in order to obtain the correlations illustrated below:

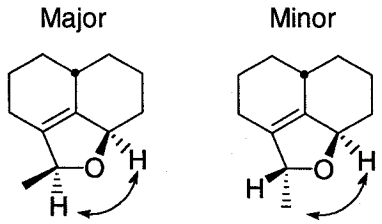


2-Methyl-3,4,5,5a,6,7,8,8a-octahydro-2*H*-naphtho[1,8-*bc*]furan (3.20)

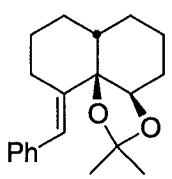


Procedure C: Tin tetrachloride (14.4 μL, 144 μmol), Prins-pinacol precursor **3.19** (10 : 1 ratio of *E* : *Z* isomers, 17.0 mg, 71.9 μmol), CH_2Cl_2 (1.4 mL), at -78°C, stirred for 1 hour and 30 minutes. Flash chromatography with 15% EtOAc/hexanes gave **3.20** as a colorless oil (11.6 mg, 65.1 μmol, 90%), which is a 6 : 5 mixture of diastereoisomers, with a Rf = 0.25 (15% EtOAc/hexanes). **Major isomer of 3.20** ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.30 (t, J = 2.4 Hz, 1H), 5.23-5.14 (m, 1H), 2.63-2.47 (m, 1H), 2.38-0.74 (m, 12H), 1.57 (d, J = 6.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.2 (C_4), 134.2 (C_4), 57.4 (CH), 55.5 (CH), 35.5 (CH_2), 34.2 (CH_2), 32.2 (CH), 29.9 (CH_2), 24.1 (CH_2), 23.1 (CH_3), 20.1 (CH_2), 20.0 (CH_2); **Minor isomer of 3.20** ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.37 (t, J = 2.4 Hz, 1H), 5.23-5.14 (m, 1H), 2.63-2.47 (m, 1H), 2.38-0.74 (m, 12H), 1.55 (d, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.8 (C_4), 133.9 (C_4), 56.7 (CH), 55.0 (CH), 35.6 (CH_2), 34.5

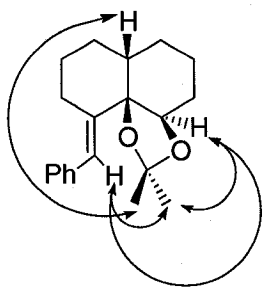
(CH_2), 32.7 (CH), 30.7 (CH_2), 24.4 (CH_2), 23.4 (CH_3), 20.8 (CH_2), 19.7 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3061 (w), 2923 (s), 2850 (m), 1725 (w), 1454 (m), 1377 (w), 1271 (w), 1099 (m), 1072 (m), 1025 (w); HRMS (EI) *m/z* (M^+) calcd 178.13576, found 178.13360. COSY, NOESY and HMQC experiments were performed in order to obtain the correlations illustrated below:



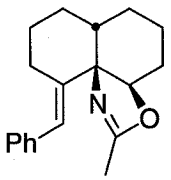
10-Benzylidene-2,2-dimethyl-octahydro-naphtho[1,8a-*d*][1,3]dioxole (3.21)



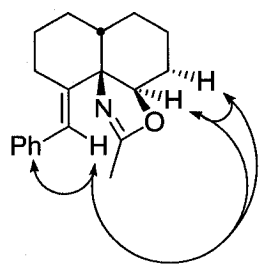
Procedure N: Potassium *tert*-butoxide 1.0 M solution in THF (0.80 mL, 0.80 mmol), benzyltriphenylphosphonium bromide (0.35 g, 0.80 mmol), toluene (2.0 + 0.7 mL), ketone **3.10** (60 mg, 0.27 mmol), refluxed for 2 days. Flash chromatography with 4-5% EtOAc/hexanes gave **3.21** as a colorless oil (74 mg, 0.25 mmol, 93%), with a Rf = 0.39 (33% EtOAc/hexanes). ^1H NMR (300 MHz, $CDCl_3$) δ 7.41-7.31 (m, 2H), 7.30-7.20 (m, 3H), 6.43 (s, 1H), 4.45 (dd, J = 3.3, 2.2 Hz, 1H), 2.79 (d, J = 13.3 Hz, 1H), 2.21-2.04 (m, 4H), 1.89-1.76 (m, 1H), 1.76-1.54 (m, 3H), 1.58 (s, 3H), 1.54-1.32 (m, 4H), 1.42 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.8 (C_4), 138.0 (C_4), 129.4 (CH), 128.5 (CH), 126.9 (CH), 124.1 (CH), 106.7 (C_4), 83.5 (C_4), 75.2 (CH), 42.0 (CH), 29.3 (CH_3), 28.3 (CH_2), 28.2 (CH_2), 27.9 (CH_2), 27.7 (CH_3), 27.3 (CH_2), 23.7 (CH_2), 22.4 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3103 (w), 3080 (w), 3056 (w), 3023 (w), 2984 (s), 2931 (s), 2861 (s), 1945 (w), 1884 (w), 1807 (w), 1650 (w), 1599 (w), 1494 (m), 1445 (m), 1366 (m), 1243 (s), 1215 (s), 1177 (s), 1128 (m), 1071 (w), 1038 (s); HRMS (EI) *m/z* (M^+) calcd 298.19323, found 298.19096. COSY, NOESY and HMQC experiments were performed in order to obtain the correlations illustrated below:



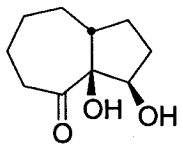
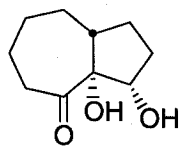
10-Benzylidene-2-methyl-4,5,6,6a,7,8,9,10-octahydro-3a*H*-3-oxa-1-aza-cyclopenta[*d*]naphthalene (3.22)



Procedure C: Triflic acid (19 μL, 0.22 mmol), Prins-pinacol precursor **3.21** (51.0 mg, 0.216 mmol), MeCN (2.2 mL), from -40°C to -20°C, stirred for 1 hour. Flash chromatography with 7.5-10% EtOAc/hexanes gave **3.22** as a colorless oil (39.2 mg, 0.139 mmol, 65%), with a Rf = 0.23 (15% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.26 (m, 2H), 7.21-7.15 (m, 3H), 6.25 (s, 1H), 4.54 (t, J = 3.4 Hz, 1H), 2.59 (ddd, J = 13.9, 7.9, 5.6 Hz, 1H), 2.44-2.36 (m, 1H), 2.09 (d, J = 15.2 Hz, 1H), 2.01 (s, 3H), 2.01-1.92 (m, 1H), 1.90-1.80 (m, 1H), 1.77-1.69 (m, 1H), 1.68-1.50 (m, 4H), 1.50-1.32 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8 (C_4), 142.5 (C_4), 138.1 (C_4), 129.0 (CH), 128.0 (CH), 126.2 (CH), 123.3 (CH), 81.6 (CH), 73.9 (C_4), 42.4 (CH), 29.9 (CH_2), 27.2 (CH_2), 25.5 (CH_2), 25.2 (CH_2), 24.8 (CH_2), 18.7 (CH_2), 14.6 (CH_3); IR (CH_2Cl_2, cm^{-1}) 3079 (w), 3054 (w), 3022 (m), 2926 (s), 2859 (s), 1948 (w), 1885 (w), 1808 (w), 1732 (m), 1661 (s), 1599 (m), 1494 (m), 1444 (m), 1385 (m), 1264 (m), 1239 (m), 1123 (m), 1072 (w), 1029 (m); HRMS (EI) *m/z* (M^+) calcd 281.17796, found 281.17950. COSY, NOESY and HMQC experiments were performed in order to obtain the correlations illustrated below:

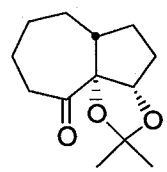


3,3a-Dihydroxy-octahydro-azulen-4-one (3.37 and 3.38)

Procedure K: 4-Methylmorpholine N-oxide (1.38 g, 11.8 mmol), solution of osmium tetraoxide 4% in water (0.94 mL, 0.15 mmol), **3.36**[83c] (0.88 g, 5.9 mmol), water (12 mL), THF (60 mL), refluxed for 4 hours. Flash chromatography with 40-45% EtOAc/hexanes gave **3.37** as a pale yellow oil (0.17 g, 0.94 mmol, 16%), and **3.38** as a white solid (0.368 g, 2.00 mmol, 34%), with a respective Rf = 0.42 and 0.52 (50% EtOAc/hexanes). **3.37** ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.35-3.94 (br, 1H), 4.27 (dd, J = 10.9, 6.6 Hz, 1H), 2.88-2.18 (br, 1H), 2.87-2.73 (m, 1H), 2.50-2.39 (m, 1H), 2.50-2.39 (m, 1H), 2.18-2.01 (m, 2H), 1.95-1.46 (m, 7H), 1.46-1.17 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.5 (C_4), 86.2 (C_4), 74.4 (CH), 47.8 (CH), 38.7 (CH_2), 32.7 (CH_2), 31.4 (CH_2), 27.0 (CH_2), 26.7 (CH_2), 26.2 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3500 (br), 2919 (s), 2860 (s), 2681 (w), 1746 (m), 1694 (s), 1454 (m), 1403 (m), 1323 (m), 1173 (w), 1063 (m), 1013 (m); HRMS (EI) *m/z* (M^+) calcd 184.10995, found 184.10864. **3.38** ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.57 (t, J = 8.4 Hz, 1H), 3.72-3.49 (br, 1H), 3.58-3.22 (br, 1H), 2.75 (dt, J = 16.9, 3.6 Hz, 1H), 2.32 (ddd, J = 16.9, 11.7, 5.4 Hz, 1H), 2.13-1.44 (m, 10H), 1.18-1.02 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 215.7 (C_4), 86.6 (C_4), 75.0 (CH), 44.8 (CH), 42.8 (CH_2), 30.5 (CH_2), 28.7 (CH_2), 28.1 (CH_2), 27.9 (CH_2), 23.1 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3435 (s), 3256 (br), 2927 (s), 2915 (s), 2862 (m), 2847 (m), 1694 (s), 1445 (w), 1375 (w), 1271 (m), 1190 (w), 1102 (m), 1085 (m), 1036 (w); HRMS (EI) *m/z* (M^+) calcd 184.10995, found 184.11071. Melting point : 83.5–84.4°C.

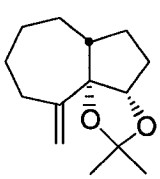
2,2-Dimethyl-octahydro-1,3-dioxa-cyclopenta[*c*]azulen-10-one (3.39)



Procedure L: PTSA (1.8 mg, 9.2 μmol), diol **3.38** (170 mg, 0.923 mmol), 2-methoxypropene (0.27 mL, 2.8 mmol), CH_2Cl_2 (9.2 mL), stirred for 15 minutes. Flash chromatography with 4-6% EtOAc/hexanes gave **3.39** as a pale yellow oil (207 mg, 0.923 mmol, quant.), with a Rf = 0.87 (50% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.98 (d, J = 4.9 Hz, 1H), 2.74 (dt, J = 17.5, 3.5 Hz, 1H), 2.41 (ddd, J = 17.4, 11.8, 5.5 Hz, 1H), 2.16 (qd, J = 12.0, 5.3 Hz, 1H), 1.96-1.83 (m, 1H), 1.82-1.29 (m, 8H), 1.47 (s, 3H), 1.25-1.06 (m, 1H), 1.19 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.6 (C_4), 109.7

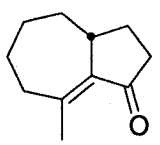
(C_4), 97.0 (C_4), 83.0 (CH), 49.6 (CH), 42.6 (CH_2), 32.9 (CH_2), 30.9 (CH_2), 28.5 (CH_2), 28.0 (CH_2), 26.6 (CH_3), 25.3 (CH_3), 22.7 (CH_2); IR (CH_2Cl_2, cm^{-1}) 2931 (s), 2855 (s), 1704 (s), 1455 (m), 1372 (m), 1264 (w), 1210 (m), 1155 (m), 1075 (w), 1035 (m), 1015 (m); HRMS (EI) *m/z* (M^+) calcd 224.14125, found 224.13983.

2,2-Dimethyl-10-methylene-octahydro-1,3-dioxa-cyclopenta[*c*]azulene (3.40)



Procedure N: Potassium *tert*-butoxide 1.0 M solution in THF (0.32 mL, 0.32 mmol), methyltriphenylphosphonium iodide (0.13 g, 0.32 mmol), toluene (0.7 + 0.4 mL), ketone **3.39** (24 mg, 0.11 mmol), refluxed for 2 hours and 30 minutes. Flash chromatography with 3.5-4% EtOAc/hexanes gave **3.40** as a colorless oil (12 mg, 54 μmol, 52%), with a Rf = 0.50 (5% EtOAc/hexanes). ^1H NMR (300 MHz, $CDCl_3$) δ 4.80 (s, 2H), 4.72 (s, 1H), 2.66-2.53 (m, 1H), 2.29 (ddd, J = 14.8, 9.2, 5.5 Hz, 1H), 1.92-1.20 (m, 11H), 1.44 (s, 3H), 1.29 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.5 (C_4), 108.7 (C_4), 107.0 (CH_2), 94.0 (C_4), 85.8 (CH), 54.8 (CH), 36.0 (CH_2), 33.6 (CH_2), 31.4 (CH_2), 28.9 (CH_2), 27.1 (CH_3), 26.6 (CH_2), 26.3 (CH_2), 25.6 (CH_3); IR (CH_2Cl_2, cm^{-1}) 3076 (w), 2985 (m), 2927 (s), 2850 (m), 1633 (w), 1437 (m), 1380 (m), 1260 (m), 1210 (m), 1184 (m), 1163 (w), 1095 (m), 1043 (m), 1028 (m); HRMS (EI) *m/z* (M^+) calcd 222.16198, found 222.16104.

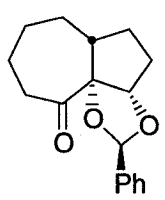
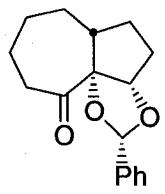
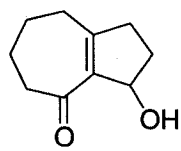
8-Methyl-3,3a,4,5,6,7-hexahydro-2*H*-azulen-1-one (3.41)



Procedure C: Triflic acid (13.2 μL, 148 μmol), Prins-pinacol precursor **3.40** (16.5 mg, 74.2 μmol), MeCN (1.5 mL), from -40°C to 0°C, stirred for 2 hours and 45 minutes. Flash chromatography with 8-10% EtOAc/hexanes gave **3.41** as a colorless oil (8.6 mg, 52 μmol, 70%), with a Rf = 0.51 (15% EtOAc/hexanes). ^1H NMR (400 MHz, $CDCl_3$) δ 2.86 (dd, J = 16.2, 7.7 Hz, 1H), 2.38-2.14 (m, 4H), 2.23 (d, J = 2.3 Hz, 3H), 2.11-2.02 (m, 1H), 1.93-1.85 (m, 1H), 1.80-1.67 (m, 2H), 1.63-1.52 (m, 1H), 1.44-1.26 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.2 (C_4), 155.2 (C_4), 137.1 (C_4), 42.0 (CH), 39.6 (CH_2), 39.2 (CH_2), 34.7 (CH_2), 30.4 (CH_2), 27.7 (CH_2), 24.9 (CH_2), 21.7 (CH_3); IR (CH_2Cl_2, cm^{-1}) 3010

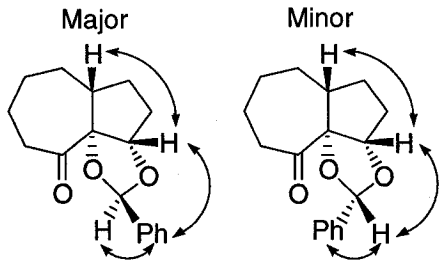
(w), 2920 (s), 2850 (s), 1704 (s), 1623 (s), 1446 (m), 1368 (w), 1273 (m), 1241 (m), 1183 (m), 1073 (w), 1010 (w); HRMS (EI) *m/z* (M^+) calcd 164.12012, found 164.12286.

2-Phenyl-octahydro-1,3-dioxa-cyclopenta[*c*]azulen-10-one (3.50 and 3.51) and 3-hydroxy-2,3,5,6,7,8-hexahydro-1*H*-azulen-4-one (3.52)

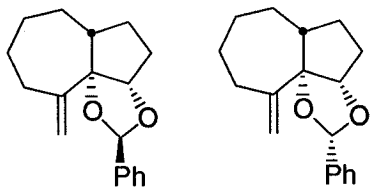




Procedure D: Benzaldehyde dimethyl acetal (0.19 mL, 1.1 mmol), tin dichloride (2.0 mg, 11 μmol), diol **3.38** (195 mg, 1.06 mmol), 1,2-dimethoxyethane (11 mL), refluxed overnight. Flash chromatography with 5% EtOAc/hexanes gave a 5 : 2 mixture of **3.50** and **3.51,** which is a pale yellow oil (0.236 g, 0.867 mmol, 82%), and byproduct **3.52** as a white solid (11.2 mg, 67.4 μmol, 6%, overall yield of 88%), with a respective Rf = 0.75 and 0.66 (25% EtOAc/hexanes). **3.50** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.27 (m, 5H), 6.20 (s, 1H), 5.21 (d, J = 6.4 Hz, 1H), 2.50-2.42 (m, 1H), 2.29-2.07 (m, 2H), 2.00-1.87 (m, 2H), 1.86-1.52 (m, 7H), 1.18-1.06 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.7 (C_4), 138.8 (C_4), 129.0 (CH), 128.4 (CH), 126.2 (CH), 105.4 (CH), 97.8 (C_4), 84.0 (CH), 49.2 (CH), 41.8 (CH_2), 32.5 (CH_2), 32.5 (CH_2), 29.0 (CH_2), 27.3 (CH_2), 22.3 (CH_2); **3.51** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53-7.49 (m, 2H), 7.41-7.27 (m, 3H), 5.55 (s, 1H), 5.08 (d, J = 5.3 Hz, 1H), 2.76 (dt, J = 17.7, 4.2 Hz, 1H), 2.51-2.41 (m, 1H), 2.21-2.07 (m, 1H), 2.00-1.87 (m, 2H), 1.86-1.52 (m, 7H), 1.29-1.18 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.9 (C_4), 136.4 (C_4), 129.7 (CH), 128.4 (CH), 126.9 (CH), 103.1 (CH), 96.3 (C_4), 83.4 (CH), 48.4 (CH), 42.5 (CH_2), 32.0 (CH_2), 31.0 (CH_2), 28.2 (CH_2), 28.2 (CH_2), 22.5 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3087 (w), 3063 (w), 3033 (w), 2928 (s), 2854 (s), 2762 (w), 1958 (w), 1896 (w), 1813 (w), 1704 (s), 1493 (w), 1453 (m), 1402 (m), 1348 (w), 1290 (w), 1208 (m), 1102 (m), 1004 (m); HRMS (EI) *m/z* (M^+) calcd 272.14124, found 272.14023. COSY, NOESY and HMQC experiments were performed in order to obtain the correlations illustrated below. **3.52** ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.09 (s, 1H), 3.02 (d, J = 16.9 Hz, 1H), 2.50 (dt, J = 17.0, 4.4 Hz, 1H), 2.41-2.28 (m, 2H), 2.03-1.94 (m, 1H), 1.91-1.73 (m, 4H), 1.61-1.49 (m, 1H), 1.44-1.24 (m, 2H), 1.12 (qd, J = 12.2, 3.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 194.5 (C_4), 141.9 (C_4), 135.7 (C_4), 36.7 (CH), 34.8 (CH_2), 34.7 (CH_2), 28.8 (CH_2), 26.2 (CH_2), 25.6 (CH_2), 25.2 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3367 (br), 2921 (s), 2855 (m), 2826 (w), 1707 (w), 1668 (s), 1638 (m), 1447

(w), 1412 (m), 1387 (m), 1320 (w), 1215 (m), 1179 (s), 1160 (m), 1110 (m), 1086 (w), 1016 (w); HRMS (EI) *m/z* (M^+) calcd 166.09938, found 166.09809. Melting Point : 89.8-91.2°C.

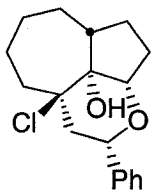


10-Methylene-2-phenyl-octahydro-1,3-dioxa-cyclopenta[*c*]azulene (3.53 and 3.54)

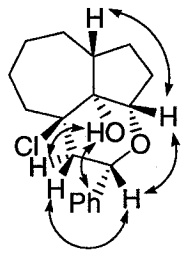


Procedure N: Potassium *tert*-butoxide 1.0 M solution in THF (1.38 mL, 1.38 mmol), methyltriphenylphosphonium iodide (0.557 g, 1.38 mmol), toluene (3.0 + 1.6 mL), ketone **3.50** and **3.51** (5 : 2 ratio, 125 mg, 0.459 mmol), refluxed for 30 minutes. Flash chromatography with 2.5-4% EtOAc/hexanes gave **3.53** and **3.54** as a colorless oil (117 mg, 0.433 mmol, 94%), with a Rf = 0.40 (5% EtOAc/hexanes). **3.53** ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51-7.43 (m, 2H), 7.42-7.31 (m, 3H), 6.13 (s, 1H), 5.01-4.94 (m, 1H), 4.99 (s, 1H), 4.85 (s, 1H), 2.59 (dt, J = 14.9, 4.4 Hz, 1H), 2.35-2.21 (m, 1H), 2.06-1.54 (m, 10H), 1.47-1.29 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.5 (C_4), 139.7 (C_4), 129.3 (CH), 128.6 (CH), 127.1 (CH), 110.2 (CH_2), 106.0 (CH), 95.0 (C_4), 87.6 (CH), 52.4 (CH), 36.4 (CH_2), 33.9 (CH_2), 33.2 (CH_2), 29.6 (CH_2), 27.8 (CH_2), 26.8 (CH_2); **3.54** ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63-7.56 (m, 2H), 7.46-7.33 (m, 3H), 5.68 (s, 1H), 5.07-5.03 (m, 2H), 4.89 (d, J = 5.1 Hz, 1H), 2.68 (dt, J = 15.5, 4.8 Hz, 1H), 2.46-2.37 (m, 1H), 2.08-1.59 (m, 10H), 1.47-1.29 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.3 (C_4), 137.8 (C_4), 129.8 (CH), 128.7 (CH), 127.5 (CH), 111.5 (CH_2), 102.0 (CH), 93.9 (C_4), 86.3 (CH), 51.5 (CH), 36.7 (CH_2), 32.8 (CH_2), 31.8 (CH_2), 28.8 (CH_2), 28.6 (CH_2), 26.5 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3070 (w), 3034 (w), 2928 (s), 2852 (s), 2757 (w), 1951 (w), 1885 (w), 1808 (w), 1633 (m), 1456 (m), 1397 (m), 1220 (m), 1090 (s), 1064 (m), 1026 (m); HRMS (EI) *m/z* (M^+) calcd 270.16198, found 270.16087.

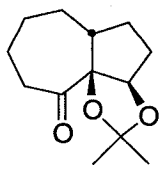
5a-Chloro-4-phenyl-decahydro-3-oxa-benzo[*cd*]azulen-9b-ol (3.55)



Procedure C: Tin tetrachloride (130 μL, 130 μmol), Prins-pinacol precursor **3.53** and **3.54** (5 : 2 ratio, 14.0 mg, 51.7 μmol), CH_2Cl_2 (1.0 mL), from -78°C to -40°C, stirred for 4 hours and 30 minutes. Flash chromatography with 7.5% EtOAc/hexanes gave **3.55** as a colorless oil (11.2 mg, 36.5 μmol, 71%), with a Rf = 0.47 (10% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37-7.25 (m, 5H), 4.93 (dd, J = 11.3, 2.8 Hz, 1H), 4.34-4.26 (m, 1H), 2.46-2.36 (m, 1H), 2.34-2.26 (br, 1H), 2.15 (dd, J = 14.9, 11.2 Hz, 1H), 2.13-2.04 (m, 1H), 2.00 (dd, J = 14.9, 2.9 Hz, 1H), 1.95-1.61 (m, 9H), 1.60-1.50 (m, 1H), 1.46-1.36 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.8 (C_4), 128.6 (CH), 127.9 (CH), 126.0 (CH), 79.9 (CH), 78.8 (C_4), 77.2 (CH), 76.9 (C_4), 44.6 (CH_2), 42.3 (CH_2), 36.1 (CH), 29.2 (CH_2), 27.3 (CH_2), 25.9 (CH_2), 25.7 (CH_2), 22.7 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3540 (br), 3090 (w), 3064 (w), 3032 (w), 2926 (s), 2861 (s), 1947 (w), 1880 (w), 1806 (w), 1726 (w), 1606 (w), 1497 (m), 1449 (m), 1340 (m), 1267 (m), 1111 (s), 1087 (m), 1030 (s); HRMS (EI) *m/z* (M^+-H_2O-Cl) calcd 253.15924, found 253.15119. A X-ray crystallographic structure was obtained and is shown in Figure 3.6. COSY, NOESY and HMQC experiments were performed in order to obtain the correlations illustrated below:



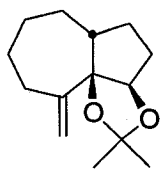
2,2-Dimethyl-octahydro-1,3-dioxa-cyclopenta[*c*]azulen-10-one (3.61)



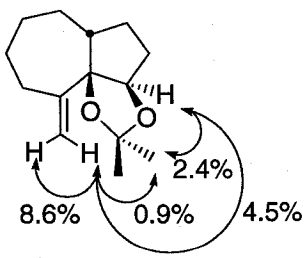
Procedure L: PTSA (1.3 mg, 1.6 μmol), diol **3.37** (30.0 mg, 0.163 mmol), 2-methoxypropene (47 μL, 0.49 mmol), CH_2Cl_2 (1.6 mL), stirred for 20 minutes. Flash chromatography with 4-5% EtOAc/hexanes gave **3.61** as a pale yellow oil (23.0 mg, 0.103 mmol, 63%), with a Rf = 0.74 (25% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.04 (t, J = 3.8 Hz, 1H), 2.96 (ddd, J = 12.3, 11.3, 4.0 Hz, 1H), 2.36-2.29 (m, 1H), 2.24-2.13 (m, 1H), 2.09-2.01 (m, 1H), 2.00-1.91 (m, 1H), 1.88-1.71 (m, 3H), 1.65-1.58

(m, 1H), 1.52-1.33 (m, 3H), 1.45 (s, 3H), 1.15 (s, 3H), 1.09-0.98 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.3 (C_4), 111.1 (C_4), 97.7 (C_4), 81.2 (CH), 48.2 (CH), 40.0 (CH_2), 32.5 (CH_2), 31.8 (CH_2), 31.6 (CH_2), 28.6 (CH_2), 27.8 (CH_2), 27.2 (CH_3), 25.3 (CH_3); IR (CH_2Cl_2, cm^{-1}) 2988 (m), 2935 (s), 2859 (m), 1712 (s), 1453 (m), 1373 (m), 1328 (w), 1262 (m), 1211 (m), 1151 (m), 1072 (m), 1041 (s); HRMS (EI) *m/z* (M^+-Me) calcd 209.11777, found 209.11832.

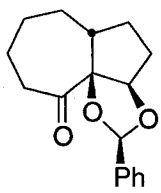
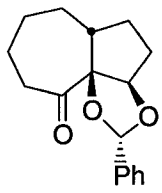
2,2-Dimethyl-10-methylene-octahydro-1,3-dioxa-cyclopenta[*c*]azulene (3.62)



Procedure N: Potassium *tert*-butoxide 1.0 M solution in THF (0.61 mL, 0.61 mmol), methyltriphenylphosphonium iodide (0.248 g, 0.612 mmol), toluene (1.2 + 0.8 mL), ketone **3.61** (45.8 mg, 0.204 mmol), refluxed for 1 hour. Flash chromatography with 5% EtOAc/hexanes gave **3.62** as a colorless oil (32.8 mg, 0.148 mmol, 72%), with a Rf = 0.53 (5% EtOAc/hexanes). ^1H NMR (300 MHz, $CDCl_3$) δ 5.04 (s, 1H), 4.94 (s, 1H), 4.75 (t, J = 4.0 Hz, 1H), 2.40 (ddd, J = 1298, 10.5, 3.9 Hz, 1H), 2.24-2.09 (m, 3H), 1.90-1.17 (m, 9H), 1.47 (s, 3H), 1.29 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.2 (C_4), 110.6 (C_4), 110.4 (CH_2), 96.6 (C_4), 84.3 (CH), 51.2 (CH), 33.8 (CH_2), 32.4 (CH_2), 32.3 (CH_2), 32.2 (CH_2), 32.2 (CH_2), 28.5 (CH_3), 28.2 (CH_2), 26.5 (CH_3); IR (CH_2Cl_2, cm^{-1}) 3079 (w), 2986 (m), 2926 (s), 2854 (m), 1636 (w), 1455 (m), 1370 (m), 1258 (m), 1210 (s), 1156 (w), 1052 (m), 1029 (s); HRMS (EI) *m/z* (M^+) calcd 222.16198, found 222.16052. COSY, NOESY, HMQC and NOE experiments were performed in order to obtain the correlations illustrated below:

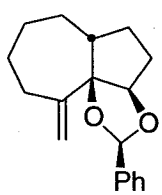
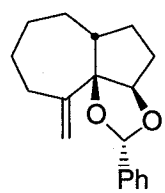


2-Phenyl-octahydro-1,3-dioxa-cyclopenta[*c*]azulen-10-one (3.63 and 3.64)

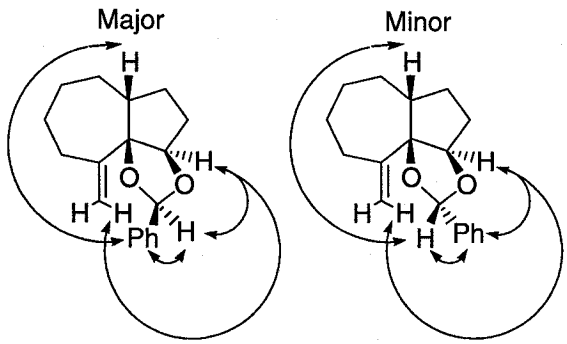
Procedure D: Benzaldehyde dimethyl acetal (0.25 mL, 1.6 mmol), tin dichloride (1.5 mg, 8.1 μmol), diol **3.37** (150 mg, 0.814 mmol), 1,2-dimethoxyethane (8.1 mL), refluxed for 2 days. Flash chromatography with 7.5% EtOAc/hexanes gave a 3 : 2 mixture of **3.63** and **3.64**, which is a pale yellow oil (13.0 mg, 47.7 μmol, 6%), and byproduct **3.52** (54.0 mg, 0.325 mmol, 40%, overall yield of 46%), with a respective Rf = 0.47 and 0.66 (25% EtOAc/hexanes). **3.63** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51-7.44 (m, 2H), 7.40-7.30 (m, 3H), 5.98 (s, 1H), 4.03 (s, 1H), 2.63-2.39 (m, 2H), 2.28-1.13 (m, 1H), 2.05-1.95 (m, 1H), 1.94-1.33 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.9 (C_4), 136.9 (C_4), 129.5 (CH), 128.4 (CH), 126.8 (CH), 102.8 (CH), 86.0 (C_4), 83.3 (CH), 38.7 (CH), 36.7 (CH_2), 35.0 (CH_2), 28.3 (CH_2), 25.7 (CH_2), 24.2 (CH_2), 23.0 (CH_2); **3.64** ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51-7.44 (m, 2H), 7.40-7.30 (m, 3H), 6.03 (s, 1H), 4.07 (s, 1H), 2.63-2.39 (m, 2H), 2.28-2.13 (m, 1H), 2.05-1.95 (m, 1H), 1.94-1.33 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.0 (C_4), 138.4 (C_4), 129.1 (CH), 128.3 (CH), 126.4 (CH), 103.4 (CH), 86.6 (C_4), 83.5 (CH), 36.8 (CH), 33.2 (CH_2), 32.6 (CH_2), 28.2 (CH_2), 25.7 (CH_2), 23.5 (CH_2), 22.3 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3092 (w), 3065 (w), 3036 (w), 2932 (s), 2861 (m), 1963 (w), 1892 (w), 1721 (s), 1451 (m), 1400 (w), 1313 (w), 1220 (w), 1090 (s), 1067 (s), 1026 (m); HRMS (EI) *m/z* (M^+) calcd 272.14124, found 272.14111.

10-Methylene-2-phenyl-octahydro-1,3-dioxa-cyclopenta[*c*]azulene (3.66 and 3.67)

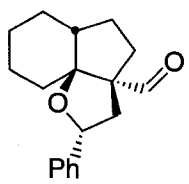



Procedure N: Potassium *tert*-butoxide 1.0 M solution in THF (0.25 mL, 0.25 mmol), methyltriphenylphosphonium iodide (0.102 g, 0.253 mmol), toluene (0.6 + 0.25 mL), ketone **3.63** and **3.64** (3 : 2 ratio, 23.0 mg, 84.4 μmol), refluxed for 20 minutes. Flash chromatography with 2.5-4% EtOAc/hexanes gave a 7 : 4 mixture of **3.66** and **3.67**, which is a colorless oil (20.6 mg, 76.2 μmol, 91%), with a Rf = 0.84 (20% EtOAc/hexanes). **3.66** ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55-7.50 (m, 2H), 7.40-7.29 (m, 3H), 6.00 (s, 1H), 5.14 (t, J = 1.7 Hz, 1H), 5.09 (t, J = 1.9 Hz, 1H), 4.01 (s, 1H), 2.43-2.32 (m, 1H), 2.29-2.23 (m, 1H), 1.99-1.81 (m, 2H), 1.73-1.24 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.5 (C_4), 138.9 (C_4), 128.9 (CH),

128.3 (CH), 126.5 (CH), 117.1 (CH_2), 103.0 (CH), 86.8 (CH), 82.0 (C_4), 39.0 (CH), 30.5 (CH_2), 29.9 (CH_2), 28.5 (CH_2), 27.6 (CH_2), 23.0 (CH_2), 21.2 (CH_2); **3.67** ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50-7.45 (m, 2H), 7.40-7.29 (m, 3H), 6.14 (s, 1H), 5.05-5.01 (m, 2H), 3.91 (s, 1H), 2.43-2.32 (m, 1H), 2.29-1.23 (m, 1H), 2.14-2.06 (m, 1H), 1.99-1.81 (m, 1H), 1.73-1.24 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.7 (C_4), 140.2 (C_4), 128.8 (CH), 128.3 (CH), 126.4 (CH), 116.4 (CH_2), 102.3 (CH), 84.4 (CH), 83.4 (C_4), 35.2 (CH), 30.6 (CH_2), 29.1 (CH_2), 28.7 (CH_2), 27.6 (CH_2), 23.0 (CH_2), 20.9 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3073 (w), 3033 (w), 2986 (w), 2930 (s), 2860 (m), 1951 (w), 1885 (w), 1808 (w), 1450 (m), 1392 (w), 1291 (w), 1217 (m), 1161 (w), 1084 (s), 1065 (s), 1027 (m); HRMS (EI) *m/z* (M^+) calcd 270.16198, found 270.16162. COSY, NOESY and HMQC experiments were performed in order to obtain the correlations illustrated below:

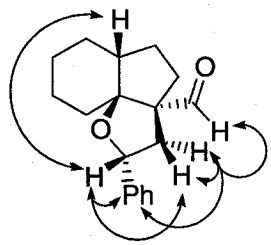


2-Phenyl-octahydro-1-oxa-cyclopenta[*c*]indene-3a-carbaldehyde (3.68)

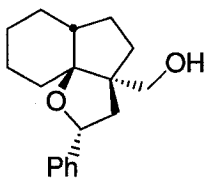


Procedure C: Tin tetrachloride (24 μL, 24 μmol), Prins-pinacol precursor **3.66** and **3.67** (7 : 4 ratio, 6.5 mg, 24 μmol), CH_2Cl_2 (0.5 mL), at -78°C, stirred for 1 hour and 30 minutes. Flash chromatography with 4-6% EtOAc/hexanes gave **3.68** as a colorless oil (5.2 mg, 19 μmol, 80%), with a Rf = 0.55 (15% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.68 (s, 1H), 7.39-7.30 (m, 4H), 7.29-7.24 (m, 1H), 5.06 (dd, J = 11.0, 4.9 Hz, 1H), 2.85-2.73 (m, 1H), 2.43 (t, J = 11.5 Hz, 1H), 2.16-2.07 (m, 3H), 2.01 (dd, J = 12.4, 5.0 Hz, 1H), 1.84 (ddd, J = 14.2, 12.7, 5.0 Hz, 1H), 1.69 (d, J = 14.0 Hz, 1H), 1.63-1.48 (m, 5H), 1.29-1.16 (m, 1H), 1.15-0.99 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.0 (C_4), 141.8 (C_4), 128.5 (CH), 127.8 (CH), 125.9 (CH), 97.9 (C_4), 81.4 (CH), 65.1 (C_4), 48.3 (CH), 46.3 (CH_2), 32.2 (CH_2), 30.4 (CH_2), 30.0 (CH_2), 28.7 (CH_2), 24.1 (CH_2), 23.9 (CH_2); ^{1}H NMR (400 MHz, C_6D_6) δ 9.40 (s, 1H), 7.44-7.37 (m, 2H), 7.32-7.26 (m, 2H), 7.22-7.17 (m,

1H), 4.95 (dd, J = 10.9, 5.0 Hz, 1H), 2.83-2.72 (m, 1H), 2.23 (t, J = 11.8 Hz, 1H), 2.07-1.98 (m, 1H), 1.96-1.86 (m, 2H), 1.83-1.72 (m, 1H), 1.64 (dd, J = 12.4, 5.1 Hz, 1H), 1.56-1.46 (m, 1H), 1.45-1.31 (m, 3H), 1.24 (ddd, J = 14.1, 8.9, 2.7 Hz, 1H), 1.16-0.94 (m, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 201.7 (C_4), 142.7 (C_4), 128.3 (CH), 127.4 (CH), 125.9 (CH), 97.3 (C_4), 81.0 (CH), 64.8 (C_4), 48.1 (CH), 46.1 (CH_2), 32.1 (CH_2), 30.3 (CH_2), 29.8 (CH_2), 28.4 (CH_2), 24.0 (CH_2), 23.8 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3087 (w), 3063 (w), 3031 (w), 2932 (s), 2858 (m), 2818 (w), 2715 (w), 1949 (w), 1885 (w), 1806 (w), 1717 (s), 1494 (w), 1452 (m), 1147 (w), 1076 (w), 1062 (s), 1015 (w); HRMS (EI) *m/z* (M^+) calcd 270.16198, found 270.16294. COSY, NOESY, HMQC and HMBC experiments were performed in order to obtain the correlations illustrated below:



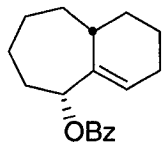
(2-Phenyl-octahydro-1-oxa-cyclopenta[c]inden-3a-yl)-methanol (3.69)



Procedure H: Lithium aluminum hydride (0.90 mg, 25 μmol), aldehyde **3.68** (4.5 mg, 17 μmol), THF (0.4 mL), warmed at 0°C for 40 minutes, water (2 x 1 drop), solution of KOH 0.1 M (1 drop), solution of sodium tartrate 0.5 M (1 mL). **3.69** was obtained as a pale yellow oil (2.8 mg, 10.3 μmol, 61%), with a Rf = 0.38 (15% EtOAc/hexanes), and the crude was clean enough for characterization. ^1H NMR (300 MHz, $CDCl_3$) δ 7.40-7.22 (m, 5H), 4.96 (dd, J = 10.8, 5.3 Hz, 1H), 3.82 (d, J = 10.2 Hz, 1H), 3.73 (d, J = 10.2 Hz, 1H), 2.29 (dd, J = 12.2, 5.3 Hz, 1H), 2.19-1.92 (m, 5H), 1.86-1.20 (m, 10H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.8 (C_4), 128.2 (CH), 127.1 (CH), 125.7 (CH), 93.3 (C_4), 79.2 (CH), 69.6 (CH_2), 56.8 (C_4), 48.7 (CH), 34.8 (CH_2), 31.8 (CH_2), 29.9 (CH_2), 29.6 (CH_2), 28.5 (CH_2), 23.6 (CH_2), 23.1 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3422 (br), 3088 (w), 3063 (w), 3030 (w), 2928 (s), 2870 (s), 2870 (s), 2856 (s), 1949 (w), 1877 (w), 1807 (w), 1495 (w), 1451

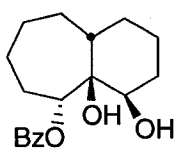
(m), 1265 (w), 1077 (w), 1059 (m), 1010 (w); HRMS (EI) *m/z* (M^+) calcd 272.17763, found 272.17825. A X-ray crystallographic structure was obtained and is shown in Figure 3.8.

Benzoic acid 2,3,5,6,7,8,9,9a-octahydro-1*H*-benzocyclohepten-5-yl ester (3.86)



Procedure I: 4-Dimethylaminopyridine (3.0 mg, 24 μmol), benzoyl chloride (0.130 mL, 1.12 mmol), alcohol **3.85**[83c] (81 mg, 0.49 mmol), pyridine (0.12 mL, 1.5 mmol), CH_2Cl_2 (5 mL), stirred overnight. Flash chromatography with 4.0-5.0% EtOAc/hexanes gave **3.86** as a white foam (52 mg, 0.19 mmol, 39% over 2 steps), with a Rf = 0.80 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.07-8.02 (m, 2H), 7.53 (tt, J = 7.4, 1.3 Hz, 1H), 7.42 (t, J = 7.6, 2H), 5.84 (s, 1H), 5.45 (d, J = 9.3 Hz, 1H), 2.38-2.29 (m, 1H), 2.07-1.96 (m, 3H), 1.88-1.36 (m 11H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.0 (C_4), 141.8 (C_4), 133.1 (CH), 131.3 (C_4), 129.9 (CH), 128.7 (CH), 123.7 (CH), 76.7 (CH), 37.0 (CH), 35.2 (CH_2), 34.6 (CH_2), 31.5 (CH_2), 26.3 (CH_2), 25.7 (CH_2), 25.6 (CH_2), 21.3 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3088 (w), 3061 (w), 3033 (w), 3009 (w), 2927 (s), 2856 (m), 1713 (s), 1601 (s), 1584 (s), 1451 (s), 1314 (m), 1273 (m), 1174 (m), 1113 (m), 1069 (m), 1029 (m); HRMS (EI) *m/z* (M^+) calcd 270.16198, found 270.16339.

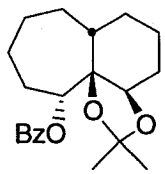
Benzoic acid 4,4a-dihydroxy-decahydro-benzocyclohepten-5-yl ester (3.87)



Procedure K: 4-Methylmorpholine N-oxide (39 mg, 0.33 mmol), solution of osmium tetraoxide 4% in water (53 μL, 8.3 μmol), alkene **3.86** (45 mg, 0.17 mmol), water (0.3 mL), THF (1.7 mL), refluxed for 15 hours. Flash chromatography with 25-30% EtOAc/hexanes gave **3.87** as a white foam (44 mg, 0.14 mmol, 86%), with a Rf = 0.22 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06-8.00 (m,2H), 7.58 (t, J = 7.1, 1H), 7.46 (t, J = 7.7 Hz, 2H), 5.25 (dd, J = 7.0, 1.6 Hz, 1H), 4.08 (dd, J = 14.0, 7.0 Hz, 1H), 2.58 (br, 2H), 2.12-1.22 (m, 15H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.7 (C_4), 133.7 (CH), 130.4 (C_4), 130.1 (CH), 129.0 (CH), 78.7 (CH), 76.8 (C_4), 68.9 (CH), 44.4 (CH), 30.9 (CH_2), 30.3 (CH_2), 30.1 (CH_2), 29.7 (CH_2), 25.9 (CH_2), 22.3 (CH_2), 20.2 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3462 (br), 3067 (w), 2936 (s), 2862 (m), 1964 (w), 1912 (w), 1714 (s), 1601 (w),

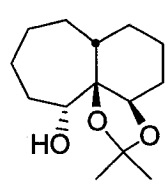
1578 (w), 1493 (w), 1449 (m), 1401 (w), 1372 (w), 1344 (w), 1314 (m), 1278 (s), 1207 (w), 1176 (w), 1113 (m), 1070 (m), 1026 (m); HRMS (EI) *m/z* (M^+) calcd 304.16746, found 304.16582.

Benzoic acid 2,2-dimethyl-decahydro-1,3-dioxa-cyclohepta[*d*]inden-11-yl ester (3.88)



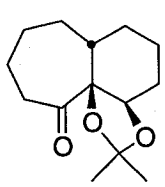
Procedure L: PTSA (0.30 mg, 1.4 μmol), diol **3.87** (43 mg, 0.14 mmol), 2-methoxypropene (41 μL, 0.42 mmol), CH_2Cl_2 (1.4 mL), stirred for 10 minutes. Flash chromatography with 5% EtOAc/hexanes gave **3.88** as a pale yellow oil (49 mg, 0.14 mmol, quant.), with a Rf = 0.73 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06-8.02 (m, 2H), 7.57 (tt, J = 7.3, 2.2 Hz, 1H), 7.46 (t, J = 7.7 Hz, 2H), 5.31 (d, J = 6.0 Hz, 1H), 4.11 (t, J = 2.8 Hz, 1H), 2.18-1.94 (m, 5H), 1.83-1.44 (m, 10H), 1.48 (s, 3H), 1.35 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.0 (C_4), 133.5 (CH), 130.4 (C_4), 130.0 (CH), 129.0 (CH), 107.6 (C_4), 83.3 (C_4), 81.2 (CH), 80.4 (CH), 43.8 (CH), 30.8 (CH_2), 30.0 (CH_2), 28.8 (CH_3), 27.7 (CH_2), 27.5 (CH_2), 27.3 (CH_3), 23.7 (CH_2), 23.2 (CH_2), 19.9 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3069 (w), 2984 (w), 2933 (s), 2863 (m), 1719 (s), 1451 (m), 1378 (w), 1367 (m), 1269 (s), 1250 (m), 1216 (m), 1177 (m), 1109 (m), 1068 (m), 1038 (m), 1026 (w); HRMS (EI) *m/z* (M^+) calcd 344.19876, found 344.19962.

2,2-Dimethyl-decahydro-1,3-dioxa-cyclohepta[*d*]inden-11-ol (3.89)



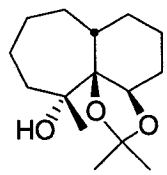
Procedure E: Potassium carbonate (1 g, excess), **3.88** (0.358 g, 1.02 mmol), methanol (5 mL), benzene (2 mL), refluxed for 18 hours. Flash chromatography with 5%, then 10-15% EtOAc/hexanes gave **3.89** as a pale yellow oil (0.184g, 0.766 mmol, 75%), with a Rf = 0.70 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.22 (t, J = 2.9 Hz, 1H), 3.94 (d, J = 6.8 Hz, 1H), 2.17-1.33 (m, 15H), 1.49 (s, 3H), 1.34 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 106.9 (C_4), 84.8 (C_4), 79.4 (CH), 74.3 (CH), 43.1 (CH), 30.4 (CH_2), 30.4 (CH_2), 30.4 (CH_2), 28.9 (CH_3), 28.2 (CH_2), 27.6 (CH_3), 24.1 (CH_2), 23.0 (CH_2), 20.2 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3480 (br), 2983 (m), 2931 (s), 2863 (s), 2691 (w), 1719 (w), 1616 (w), 1481 (w), 1455 (m), 1378 (m), 1368 (m), 1248 (m), 1214 (m), 1180 (m), 1135 (m), 1073 (w), 1037 (m), 1014 (m); HRMS (EI) *m/z* (M^+) calcd 240.17255, found 240.17354.

2,2-Dimethyl-octahydro-1,3-dioxa-cyclohepta[*d*]inden-11-one (3.90)



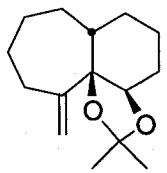
Procedure F: Dess-Martin periodinane (389 mg, 0.919 mmol), alcohol **3.89** (184 mg, 0.766 mmol), CH_2Cl_2 (8 mL), stirred for 15 minutes. Flash chromatography with 10-15% EtOAc/hexanes gave **3.90** as a white foam (176 mg, 0.739 mmol, 94%), with a Rf = 0.73 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.13 (t, J = 3.6 Hz, 1H), 3.27 (td, J = 11.2, 7.2 Hz, 1H), 2.22-2.16 (m, 1H), 2.13-1.74 (m, 6H), 1.67-1.39 (m, 5H), 1.53 (s, 3H), 1.34 (s, 3H), 1.18-0.96 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.9 (C_4), 108.1 (C_4), 89.1 (C_4), 75.2 (CH), 40.5 (CH), 39.2 (CH_2), 34.2 (CH_2), 29.4 (CH_2), 28.9 (CH_3), 27.8 (CH_2), 26.7 (CH_3), 26.6 (CH_2), 23.4 (CH_2), 19.9 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3051 (w), 2930 (s), 2855 (m), 1704 (s), 1455 (s), 1380 (m), 1368 (m), 1320 (w), 1250 (m), 1218 (m), 1179 (m), 1061 (m), 1046 (s), 1014 (w); HRMS (EI) *m/z* (M^+) calcd 238.15689, found 238.15476.

2,2,11-Trimethyl-decahydro-1,3-dioxa-cyclohepta[*d*]inden-11-ol (3.91)



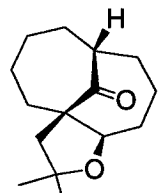
Procedure A: $CeCl_3$ (546 mg, 2.22 mmol), THF (6.0 + 1.4 mL), ketone **3.90** (176 mg, 0.739 mmol), methyllithium 1.6 M in diethyl ether (2.77 mL, 4.43 mmol), warmed to room temperature for 15 minutes. Flash chromatography with 10-15% EtOAc/hexanes gave **3.91** as a colorless oil (177 mg, 0.696 mmol, 94%), with a Rf = 0.72 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.31 (t, J = 2.9 Hz, 1H), 2.12-1.83 (m, 5H), 1.54-1.73 (m, 11H), 1.44 (s, 3H), 1.31 (s, 3H), 1.29 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 106.9 (C_4), 86.0 (C_4), 78.3 (C_4), 76.7 (CH), 43.3 (CH), 38.4 (CH_2), 29.9 (CH_3), 29.2 (CH_3), 29.2 (CH_2), 28.0 (CH_2), 28.0 (CH_2), 27.6 (CH_3), 21.9 (CH_2), 21.7 (CH_2), 21.5 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3467 (br), 2984 (w), 2926 (s), 2856 (m), 1593 (w), 1453 (m), 1377 (m), 1364 (m), 1247 (m), 1208 (m), 1182 (w), 1139 (w), 1113 (w), 1090 (w), 1037 (s), 1012 (m); HRMS (EI) *m/z* (M^+) calcd 254.18820, found 254.18679.

2,2-Dimethyl-11-methylene-decahydro-1,3-dioxa-cyclohepta[*d*]indene (3.92)

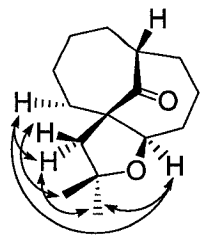


Procedure B: Thionyl chloride (0.10 mL, 1.4 mmol), alcohol **3.91** (177 mg, 0.696 mmol), 4-dimethylaminopyridine (510 mg, 4.18 mmol), CH_2Cl_2 (7.0 mL), warmed at room temperature for 15 minutes. Flash chromatography with 2.5% EtOAc/hexanes gave **3.92** as a colorless oil (146 mg, 0.618 mmol, 89%), with a Rf = 0.91 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.91 (s, 1H), 4.90 (s, 1H), 4.04 (t, J = 2.6 Hz, 1H), 2.61-2.52 (m, 1H), 2.18-2.05 (m, 2H), 1.93-1.28 (m, 10H), 1.50 (s, 3H), 1.34 (s, 3H), 1.28-1.12 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.6 (C_4), 111.3 (CH_2), 106.6 (C_4), 86.5 (C_4), 79.8 (CH), 44.7 (CH), 34.2 (CH_2), 32.4 (CH_2), 31.8 (CH_2), 29.6 (CH_2), 29.0 (CH_3), 28.7 (CH_2), 27.2 (CH_3), 23.4 (CH_2), 20.6 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3085 (w), 2984 (m), 2931 (s), 2863 (m), 1633 (m), 1450 (m), 1377 (m), 1247 (s), 1215 (s), 1180 (m), 1152 (w), 1127 (w), 1078 (w) 1035 (s); HRMS (EI) *m/z* (M^+) calcd 236.17763, found 236.17500.

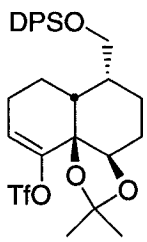
3,3-Dimethyl-4-oxa-tricyclo[7.4.1.0^{1,5}]tetradecan-14-one (3.93)



Procedure C: Tin tetrachloride solution 1.0 M in CH_2Cl_2 (0.156 mL, 0.156 mmol), Prins-pinacol precursor **3.92** (12 mg, 52 μmol), toluene (1.0 mL), at -78°C, stirred for 30 minutes. Flash chromatography with a gradient from 5-10% EtOAc/hexanes gave **3.93** as a colorless oil (6.9 mg, 29 μmol, 56%), with a Rf = 0.53 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.32 (dd, J = 11.3, 1.7 Hz, 1H), 2.83-2.73 (m, 1H), 2.53 (d, J = 13.5 Hz, 1H), 2.21-2.14 (m, 1H), 1.94-1.43 (m, 13H), 1.38-1.27 (m, 1H), 1.31 (s, 3H), 1.30 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 217.0 (C_4), 81.3 (CH), 79.4 (C_4), 66.0 (C_4), 54.7 (CH), 48.0 (CH_2), 38.5 (CH_2), 36.3 (CH_2), 32.6 (CH_3), 31.5 (CH_2), 30.3 (CH_3), 28.4 (CH_2), 27.2 (CH_2), 26.6 (CH_2), 21.9 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3362 (w), 2928 (s), 2856 (m), 2671 (w), 1740 (w), 1690 (s), 1457 (m), 1380 (m), 1366 (m), 1287 (m), 1225 (w), 1188 (w), 1161 (w), 1134 (w), 1119 (w), 1108 (w), 1054 (m), 1026 (w); HRMS (EI) *m/z* (M^+) calcd 236.17763, found 236.17801. COSY, NOESY and HMQC experiments were performed in order to obtain the correlations illustrated below:

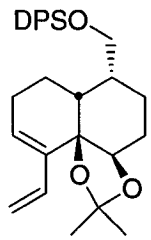


Trifluoro-methanesulfonic acid 6-(*tert*-butyl-diphenyl-silanyloxymethyl)-2,2-dimethyl-4,5,6,6a,7,8-hexahydro-3a*H*-naphtho[1,8a-*d*][1,3]dioxol-10-yl ester (4.1)



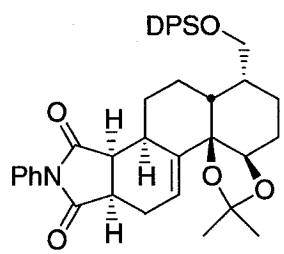
Ketone **2.27**[71] (1.26 g, 2.56 mmol) was canulated with THF (3.0 mL) to a solution of potassium bis(trimethylsilyl)amide (0.92g, 4.6 mmol) in THF (20 mL) at -78°C and the reaction mixture was allowed to stir for 20 minutes. *N*-phenyltrifluromethane sulfonimide (1.83 g, 5.12 mmol) was cumulated in the solution with THF (3.0 mL) at -78°C and the reaction was stirred at this temperature for 15 minutes, then warmed at room temperature for 4 hours. The reaction was concentrated *in vacuo* and a purification by silica gel flash chromatography with 25% benzene/hexanes gave **4.1** as a colorless oil, (1.43 g, 2.29 mmol, 90%), with a Rf = 0.80 (20% EtOAc/hexanes). ^{1}H NMR (300 MHz, C_6D_6) δ 7.64-7.55 (m, 4H), 7.42-7.32 (m, 6H), 6.14 (t, J = 4.2 Hz, 1H), 4.30 (s, 1H), 3.58 (dd, J = 5.9, 10.1, 1H), 3.49 (t, J = 8.7 Hz, 1H), 2.58-2.56 (m, 1H), 2.17 (m, 1H), 2.06-2.02 (m, 1H), 1.75-1.61 (m, 4H), 1.54 (s, 3H), 1.44 (s, 3H), 1.31-1.17 (m, 2H), 1.14-1.09 (m, 1H), 1.02 (s, 9H); ^{13}C NMR (75 MHz, C_6D_6) δ 148.2 (C_4), 136.3 (CH), 134.6 (C_4), 130.4 (CH), 128.5 (CH), 124.1 (CH), 109.3 (C_4), 81.5 (C_4), 75.0 (CH), 66.3 (CH_2), 42.5 (CH), 33.6 (CH), 28.3 (CH_3), 27.4 (CH_3), 26.7 (CH_3), 23.6 (CH_2), 21.0 (CH_2), 20.0 (CH_2), 19.9 (C_4), 18.1 (CH_2), the CF_3 is missing; IR (CH_2Cl_2, cm^{-1}) 3071 (m), 2937 (s), 2859 (s), 1675 (w), 1590 (w), 1473 (m), 1417 (s), 1144 (m), 1046 (m), 1028 (m); HRMS (EI) *m/z* (M^+-*t*Bu) calcd 567.14845, found 567.14829.

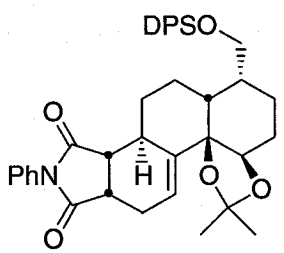
tert-Butyl-(2,2-dimethyl-10-vinyl-4,5,6,6a,7,8-hexahydro-3a*H*-naphtho[1,8a-*d*][1,3]dioxol-6-ylmethoxy)-diphenyl-silane (4.2)



Lithium chloride (58 mg, 1.4 mmol) was added at room temperature, in a sealed tube, to tetrakis triphenylphosphine palladium (5.3 mg, 4.5 μmol), vinyl tributyltin (0.16 mL, 0.46 mmol) and the vinyl triflate **4.1** (287 mg, 0.460 mmol) in THF (4.6 mL). The reaction mixture was then heated to 90°C for 2 days. The reaction was diluted in hexanes (15 mL), washed with water (15 mL), aq. NH_4OH (15 mL), water (15 mL) and brine (15 mL). The organic phase was dried over $MgSO_4$, filtered and concentrated *in vacuo*. Flash chromatography with 0.5% EtOAc/benzene gave **4.2** as a pale yellow oil, (0.191 g, 0.380 mmol, 83%), with a Rf = 0.67 (3% EtOAc/benzene). ^1H NMR (300 MHz, acetone-d_6) δ 7.64-7.58 (m, 4H), 7.42-7.32 (m, 6H), 6.52 (dd, J = 10.1, 16.0 Hz, 1H), 6.07 (t, J = 3.7 Hz, 1H), 5.19 (dd, J = 17.0, 2.1 Hz, 1H), 5.00 (dd, J = 10.6, 2.2 Hz, 1H), 4.16 (s, 1H), 3.54 (d, J = 7.5 Hz, 2H), 2.71-2.61 (m, 1H), 2.12-1.87 (m, 3H), 1.85-1.78 (m, 1H), 1.76-1.59 (m, 3H), 1.53 (s, 3H), 1.43 (s, 3H), 1.40-1.18 (m, 2H), 1.01 (s, 9H); ^{13}C NMR (75 MHz, acetone-d_6) δ 140.2 (C_4), 139.0 (CH), 136.7 (CH), 135.1 (C_4), 131.8 (CH), 131.1 (CH), 129.6 (CH), 115.8 (CH_2), 82.5 (C_4), 77.4 (CH), 66.3 (CH_2), 41.5 (CH), 36.1 (CH), 29.0 (CH_3), 28.1 (CH_3), 27.7 (CH_3), 25.8 (CH_2), 22.2 (CH_2), 21.0 (CH_2), 19.4 (C_4); IR (CH_2Cl_2, cm^{-1}) 3071 (w), 2933 (s), 2858 (s), 1739 (w), 1472 (m), 1461 (m), 1428 (s), 1378 (m), 1365 (m), 1247 (s), 1212 (m), 1189 (w), 1177 (w), 1136 (w), 1113 (s), 1037 (m); HRMS (EI) *m/z* (M^+) calcd 502.29032, found 502.29021.

***N*-phenylmaleimide cycloadduct with *tert*-butyl-(2,2-dimethyl-10-vinyl-4,5,6,6a,7,8-hexahydro-3a*H*-naphtho[1,8a-*d*][1,3]dioxol-6-ylmethoxy)-diphenyl-silane (4.4 and 4.5)**

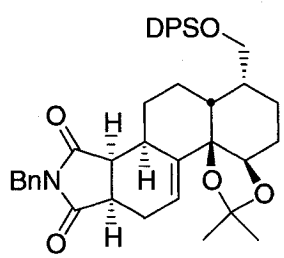




N-phenylmaleimide (20 mg, 0.12 mmol) was canulated with toluene (0.3 mL) to a solution of the diene **4.2** (39 mg, 77 μmol) in toluene (0.5 mL) at room temperature. The reaction mixture was then stirred for 3 days. The reaction was concentrated *in vacuo* and purified by silica gel flash chromatography with 20% EtOAc/hexanes

to give **4.4** as a yellow oil (10 mg, 15 μmol, 20%), and **4.5** as a yellow oil, (35 mg, 52 μmol, 67%, 87% overall yield), with a respective Rf = 0.24 and 0.16 (25% EtOAc/hexanes). **4.4** ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62-7.58 (m, 4H), 7.46-7.31 (m, 9H), 7.12 (d, J = 6.9 Hz, 2H), 5.80 (s, 1H), 3.98 (s, 1H), 3.50 (d, J = 7.6 Hz, 2H), 3.21 (dt, J = 11.9, 5.9 Hz, 2H), 2.76-2.65 (m, 2H), 2.33-2.25 (m, 2H), 2.12-2.10 (m, 1H), 1.88-1.22 (m, 8H), 1.48 (s, 3H), 1.32 (s, 3H), 1.01 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 184.2 (C_4), 179.0 (C_4), 143.2 (C_4), 135.9 (CH), 134.2 (C_4), 132.2 (C_4), 129.9 (CH), 129.6 (CH), 128.9 (CH), 128.0 (CH), 126.7 (CH), 119.1 (CH), 107.0 (C_4), 83.2 (C_4), 77.6 (CH), 64.2 (CH_2), 43.0 (CH), 40.2 (CH), 38.6 (CH), 35.9 (CH), 32.2 (CH), 30.3 (CH_2), 28.2 (CH_3), 27.4 (CH_3), 27.3 (CH_3), 26.0 (CH_2), 23.3 (CH_2), 22.6 (CH_2), 19.7 (C_4), 18.5 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3483 (w), 3070 (m), 3049 (m), 2933 (s), 2858 (s), 1960 (w), 1897 (w), 1775 (w), 1717 (s), 1598 (m), 1502 (m), 1472 (w), 1457 (w), 1428 (m), 1380 (s), 1264 (m), 1248 (m), 1209 (m), 1147 (m), 1112 (s), 1063 (m), 1025 (w); HRMS (EI) *m/z* (M^+-*t*Bu) calcd 618.26757 found 618.2498. **4.5** ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63-7.60 (m, 4H), 7.48-7.31 (m, 10H), 7.27-7.26 (m, 1H), 5.93 (t, J = 3.7 Hz, 1H), 4.14 (s, 1H), 3.45 (dt, J = 5.7, 7.1 Hz, 2H), 3.23-3.19 (m, 2H), 2.76-2.75 (m, 1H), 2.42-2.37 (m, 3H), 2.12-1.98 (m, 1H), 1.81-1.49 (m, 5H), 1.52 (s, 3H), 1.31 (s, 3H), 1.26-1.18 (m, 3H), 1.01 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 179.2 (C_4), 178.1 (C_4), 142.8 (C_4), 135.9 (CH), 134.3 (C_4), 132.1 (C_4), 129.9 (CH), 129.5 (CH), 128.9 (CH), 128.0 (CH), 126.7 (CH), 116.2 (CH), 107.6 (C_4), 84.2 (C_4), 76.7 (CH), 65.2 (CH_2), 42.6 (CH), 42.3 (CH), 37.3 (CH), 35.4(CH), 34.0 (CH), 29.2 (CH_2), 27.4 (CH_3), 27.3 (CH_3), 26.3 (CH_3), 24.0 (CH_2), 23.2 (CH_2), 20.8 (CH_2), 19.7 (C_4), 17.5 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3488 (w), 3050 (m), 2987 (m), 2933 (s), 2858 (s), 1964 (w), 1891 (w), 1782 (m), 1716 (s), 1598 (m), 1500 (s), 1472 (m), 1463 (m), 1428 (m), 1380 (s), 1265 (m), 1199 (m), 1111 (s), 1049 (s), 1030 (m); HRMS (EI) *m/z* (M^+-*t*Bu) calcd 618.26757, found 618.24686.

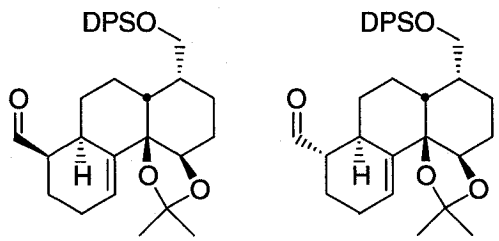
_N_-benzylmaleimide cycloadduct with _tert_-butyl-(2,2-dimethyl-10-vinyl-4,5,6,6a,7,8-hexahydro-3a_H_-naphtho[1,8a-_d_][1,3]dioxol-6-ylmethoxy)-diphenyl-silane (4.6)



N-benzylmaleimide (18 mg, 96 μmol) was canulated with toluene (0.3 mL) to a solution of the diene **4.2** (32 mg, 64 μmol) in toluene (0.3 mL) at room temperature. The reaction mixture was then stirred for 1 day.

The reaction was concentrated *in vacuo* and purified by silica gel flash chromatography with 20% EtOAc/hexanes to give **4.6** as a yellow oil, (39 mg, 57 μmol, 89%), with a Rf = 0.67 (50% EtOAc/hexanes). ^{1}H NMR (300 MHz, acetone-d_6) δ 7.61-7.58 (m, 4H), 7.41-7.32 (m, 8H), 7.28-7.21 (m, 3H), 5.86 (t, J = 3.7 Hz, 1H), 4.60 (q, J = 14.0 Hz, 2H), 4.09 (s, 1H), 3.43 (dt, J = 5.7, 7.1 Hz, 2H), 3.04 (t, J = 8.7 Hz, 1H), 2.97 (td, J = 10.0, 3.8 Hz, 1H), 2.61 (d, J = 18.5 Hz, 1H), 2.44-2.34 (m, 2H), 2.29-2.25 (m, 1H), 2.03-1.98 (m, 1H), 1.79-1.67 (m, 3H), 1.49 (s, 3H), 1.45-1.37 (m, 1H), 1.28 (s, 3H), 1.25-1.12 (m, 4H), 1.00 (s, 9H); ^{13}C NMR (75 MHz, acetone-d_6) δ 179.6 (C_4), 178.3 (C_4), 142.8 (C_4), 135.7 (CH), 133.9 (C_4), 129.5 (CH), 129.0 (CH), 128.6 (C_4), 128.5 (CH), 127.9 (CH), 127.6 (CH), 115.5 (CH), 107.1 (C_4), 83.9 (C_4), 76.2 (CH), 65.8 (CH_2), 42.6 (CH), 42.2 (CH_2), 41.7 (CH), 36.8 (CH), 34.9(CH), 33.4 (CH), 31.6 (CH_2), 26.9 (CH_3), 26.8 (CH_3), 25.7 (CH_3), 23.7 (CH_2), 22.9 (CH_2), 20.5 (CH_2), 19.3 (C_4), 17.1 (CH_2)); IR (CH_2Cl_2, cm^{-1}) 2933 (s), 2858 (m), 1705 (s), 1428 (m), 1395 (m), 1111 (s), 1051 (m); HRMS (EI) *m/z* (M^+-*t*Bu) calcd 632.28322, found 632.28130. COSY, NOESY and HMQC experiments were performed in order to obtain the correlations illustrated in Figure 4.1.

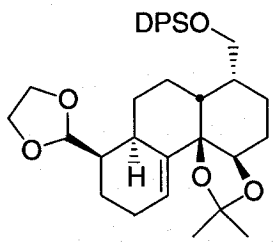
Acrolein cycloadduct with *tert*-butyl-(2,2-dimethyl-10-vinyl-4,5,6,6a,7,8-hexahydro-3a*H*-naphtho[1,8a-*d*][1,3]dioxol-6-ylmethoxy)-diphenyl-silane (4.8 and 4.9)



Tin tetrachloride (10 μL, 10 μmol) was added to a solution of **4.2** (26 mg, 52 μmol) and acrolein (7.0 μL, 0.10 mmol) in CH_2Cl_2 (0.5 mL) at -78°C and the reaction was stirred at this temperature for 4 hours and 30 minutes. The reaction was quenched with $NaHCO_3$ (aq. sat.), extracted with CH_2Cl_2 , dried over $MgSO_4$, filtered and concentrated *in vacuo*. Flash chromatography with 15-30% EtOAc/hexanes gave **4.8** as a yellow oil, (11.3 mg, 20.2 μmol, 39%), and **4.9** as a yellow oil (12.1 mg, 21.7 μmol, 41%, 80% overall yield), with a respective Rf = 0.56 and 0.45 (25% EtOAc/hexanes). **4.8** ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.67 (s, 1H), 7.61-7.56 (m, 4H), 7.41-7.33 (m, 6H), 5.23 (d, J = 3.8 Hz, 1H), 4.19 (s 1H), 3.57-3.54 (m, 2H), 2.98-2.92 (m, 1H), 2.56-2.47 (m, 1H), 2.21-1.84 (m, 6H), 1.81-1.55 (m, 5H), 1.45 (s, 3H), 1.42-1.32 (m, 3H), 1.27 (s, 3H), 1.27-1.25 (m, 1H), 1.02 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 204.9

(CH), 141.1 (C_4), 135.9 (CH), 134.3 (C_4), 130.0 (CH), 128.0 (CH), 119.7 (CH), 106.6 (C_4), 82.0 (C_4), 74.6 (CH), 62.0 (CH_2), 50.8 (CH), 42.9 (CH), 34.2 (CH), 29.0 (CH), 28.6 (CH_2), 27.6 (CH_3), 27.3 (CH_3), 27.2 (CH_3), 25.9 (CH_2), 24.3 (CH_2), 22.5 (CH_2), 21.5 (CH_2), 19.7 (C_4), 16.9 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3076 (w), 3052 (w), 2988 (w), 2932 (s), 2894 (m), 2858 (m), 2704 (w), 1963 (w), 1896 (w), 1819 (w), 1725 (s), 1590 (w), 1475 (w), 1450 (w), 1429 (m), 1376 (m), 1366 (m), 1246 (m), 1208 (m), 1183 (w), 1158 (w), 1112 (s), 1074 (s), 1050 (s), 1025 (m); HRMS (EI) *m/z* (M^+-*t*Bu) calcd 501.24611 found 501.24549. **4.9** ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.76 (s, 1H), 7.64-7.60 (m, 4H), 7.39-7.30 (m, 6H), 5.93 (d, J = 4.6 Hz, 1H), 4.12 (s 1H), 3.50-3.47 (m, 2H), 2.41-2.33 (m, 1H), 2.30-2.19 (dt, J = 16.9, 4.6 Hz, 1H), 2.14-2.00 (m, 2H), 1.94-1.54 (m, 7H), 1.54 (s, 3H), 1.44-1.23 (m, 2H), 1.37 (s, 3H), 1.16-1.04 (m, 1H), 1.01 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.3 (CH), 143.4 (C_4), 135.9 (CH), 134.4 (C_4), 129.9 (CH), 128.0 (CH), 118.2 (CH), 107.6 (C_4), 84.8 (C_4), 78.2 (CH), 67.0 (CH_2), 51.1 (CH), 42.5 (CH), 35.9 (CH), 33.0 (CH), 28.9 (CH_2), 27.2 (CH_3), 27.2 (CH_3), 26.4 (CH_3), 24.4 (CH_2), 23.8 (CH_2), 23.2 (CH_2), 19.7 (C_4), 17.7 (CH_2),17.2 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3077 (w), 3049 (w), 2990 (m), 2933 (s), 2897 (m), 2859 (s), 2712 (w), 1959 (w), 1889 (w), 1823 (w), 1725 (s), 1587 (w), 1472 (m), 1428 (m), 1379 (m), 1265 (m), 1241 (m), 1212 (m), 1181 (m), 1111 (s), 1042 (m); HRMS (EI) *m/z* (M^+-*t*Bu) calcd 501.24611, found 501.24547.

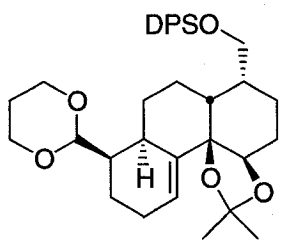
2-vinyl-[1,3]dioxolane cycloadduct with *tert*-butyl-(2,2-dimethyl-10-vinyl-4,5,6,6a,7,8-hexahydro-3a*H*-naphtho[1,8a-*d*][1,3]dioxol-6-ylmethoxy)-diphenyl-silane (4.17)



Procedure O: Trimethylsilyl triflate (14 *u*L, 76 μmol), diene **4.2** (38.0 mg, 75.6 μmol), 2-vinyl-[1,3]dioxolane (15 *u*L, 0.15 mmol), CH_2Cl_2 (1.6 mL), stirred for 2 hours. Flash chromatography with 15-25% EtOAc/hexanes gave **4.17** as a yellow oil (38.6 mg, 64.1 μmol, 85%), with a Rf = 0.53 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.69-7.61 (m, 4H), 7.52-7.31 (m, 6H), 5.89 (d, J = 4.4 Hz, 1H), 4.71 (d, J = 7.2 Hz, 1H), 4.21-4.08 (m, 1H), 3.99-2.90 (m, 2H), 3.88-3.81 (m, 2H), 3.49 (d, J = 7.3 Hz, 2H), 2.53-2.43 (m, 1H), 2.21-1.65 (m, 12H), 1.53 (s, 3H), 1.48-1.19 (m, 2H), 1.36 (s, 3H), 1.14-1.03 (m, 1H), 1.01 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.2 (C_4), 135.9 (CH), 134.5 (C_4), 129.8 (CH), 127.9 (CH), 117.7 (CH), 107.3 (C_4), 106.4 (CH), 84.9 (C_4), 78.2 (CH), 67.3 (CH_2), 65.2 (CH_2), 65.1 (CH_2), 42.7 (CH),

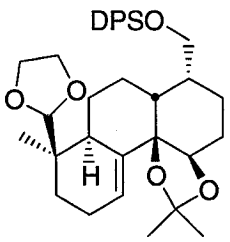
42.4 (CH), 36.6 (CH), 33.1(CH), 27.8 (CH_2), 27.3 (CH_3), 27.2 (CH_3), 26.5 (CH_3), 25.0 (CH_2), 23.9 (CH_2), 23.3 (CH_2), 19.7 (C_4), 19.6 (CH_2), 17.5 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3071 (w), 3051 (w), 2987 (m), 2932 (s), 2867 (s), 1726 (w), 1589 (w), 1472 (m), 1428 (m), 1379 (m), 1266 (m), 1212 (m), 1180 (m), 1111(s), 1072 (m), 1040 (m); HRMS (EI) *m/z* (M^+) calcd 602.34275, found 602.34172. COSY, NOESY and HMQC experiments were performed in order to obtain the correlations illustrated in Figure 4.3.

2-vinyl-[1,3]-dioxane cycloadduct with *tert*-butyl-(2,2-dimethyl-10-vinyl-4,5,6,6a,7,8-hexahydro-3a*H*-naphtho[1,8a-*d*][1,3]dioxol-6-ylmethoxy)-diphenyl-silane (4.23)



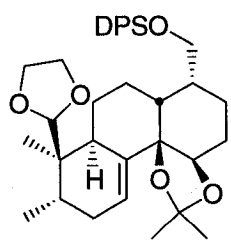
Procedure O: Trimethylsilyl triflate (10 *u*L, 54 μmol), diene **4.2** (27.0 mg, 53.7 μmol), 2-vinyl-[1,3]-dioxane (9.0 *u*L, 81 μmol), CH_2Cl_2 (1.1 mL), stirred for 1 hour. Flash chromatography with 15-20% EtOAc/hexanes gave **4.23** as a yellow oil, (26.7 mg, 43.3 μmol, 81%), with a Rf = 0.57 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65-7.58 (m, 4H), 7.41-7.31 (m, 6H), 5.87 (d, J = 3.8 Hz, 1H), 4.34 (d, J = 7.9 Hz, 1H), 4.12-4.06 (m, 3H), 3.71 (dt, J = 12.3, 12.6 Hz, 2H), 3.49 (d, J = 7.4 Hz, 2H), 2.51-2.45 (m, 1H), 2.13-1.55 (m, 14H), 1.53 (s, 3H), 1.43-1.02 (m, 3H), 1.35 (s, 3H), 1.01 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.2 (C_4), 135.9 (CH), 134.5 (C_4), 129.8 (CH), 127.9 (CH), 117.3 (CH), 107.3 (C_4), 104.0 (CH), 84.9 (C_4), 78.1 (CH), 67.0 (CH_2), 53.4 (CH_2), 53.5 (CH_2), 42.8 (CH), 42.7 (CH), 35.7 (CH), 33.1(CH), 27.6 (CH_2), 27.3 (CH_3), 27.2 (CH_3), 26.5 (CH_3), 25.2 (CH_2), 23.9 (CH_2), 23.2 (CH_2), 22.7 (CH_2), 19.7 (C_4), 19.4 (CH_2), 17.5 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3134 (w), 3071 (w), 3050 (m), 2926 (s), 2856 (s), 2733 (m), 2657 (w), 1960 (w), 1890 (w), 1824 (w), 1738 (m), 1665 (w), 1589 (m), 1486 (m), 1471 (s), 1428 (m), 1379 (m), 1335 (w), 1292 (m), 1265 (m), 1241 (m), 1212 (m), 1181 (m), 1104 (m), 1041 (m), 1005 (m); HRMS (EI) *m/z* (M^+-*t*Bu) calcd 559.28798, found 559.29343.

2-isopropenyl-[1,3]-dioxolane cycloadduct with *tert*-butyl-(2,2-dimethyl-10-vinyl-4,5,6,6a,7,8-hexahydro-3a*H*-naphtho[1,8a-*d*][1,3]dioxol-6-ylmethoxy)-diphenyl-silane (4.24)



Procedure O: Trimethylsilyl triflate (7.0 *u*L, 40 μmol), diene **4.2** (20.0 mg, 39.8 μmol), 2-isopropenyl-[1,3]-dioxolane (9.0 mg, 80 μmol), CH_2Cl_2 (0.8 mL), stirred for 3 hours. Flash chromatography with 10-15% EtOAc/hexanes gave **4.24** as a yellow oil, (19.9 mg, 32.2 μmol, 81%), with a Rf = 0.66 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64-7.61 (m, 4H), 7.41-7.31 (m, 6H), 5.85 (s, 1H), 4.64 (s, 1H), 4.02 (s, 1H), 3.93-3.81 (m, 4H), 3.49 (d, J = 7.4 Hz, 2H), 2.52-2.42 (m, 1H), 2.10-1.84 (m, 4H), 1.82-1.64 (m, 3H), 1.63-0.92 (m, 7H), 1.53 (s, 3H), 1.34 (s, 3H), 1.01 (s, 9H), 0.83 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.4 (C_4), 135.9 (CH), 134.5 (C_4), 129.8 (CH), 127.9 (CH), 116.2 (CH), 108.7 (C_4), 107.3 (CH), 84.8 (C_4), 77.8 (CH), 67.3 (CH_2), 65.7 (CH_2), 65.4 (CH_2), 43.1 (CH), 42.9 (CH), 38.2 (C_4), 33.1 (CH), 28.9 (CH_2), 27.2 (CH_3), 27.2 (CH_3), 26.4 (CH_3), 25.2 (CH_2), 24.0 (CH_2), 23.4 (CH_2), 21.5 (CH_2), 19.7 (C_4), 17.4 (CH_2), 16.4 (CH_3); IR (CH_2Cl_2, cm^{-1}) 3071 (w), 3050 (w), 2985 (m), 2932 (s), 2865 (s), 1740 (m), 1589 (w), 1472 (m), 1464 (m), 1428 (m), 1378 (m), 1362 (w), 1346 (w), 1264 (m), 1212 (m), 1204 (m), 1183 (m), 1150 (m), 1131(w), 1104 (s), 1078 (m), 1048 (m), 1028 (w); HRMS (EI) *m/z* (M^+-*t*Bu) calcd 559.28798, found 559.28884.

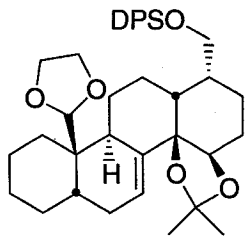
2-(1-methyl-propenyl)-[1,3]-dioxolane cycloadduct with *tert*-butyl-(2,2-dimethyl-10-vinyl-4,5,6,6a,7,8-hexahydro-3a*H*-naphtho[1,8a-*d*][1,3]dioxol-6-ylmethoxy)-diphenyl-silane (4.25)



Procedure O: Trimethylsilyl triflate (8.0 *u*L, 43 μmol), diene **4.2** (21.5 mg, 42.8 μmol), 2-(1-methyl-propenyl)-[1,3]-dioxolane (11 mg, 86 μmol), CH_2Cl_2 (0.9 mL), stirred for 2 hours. Flash chromatography with 3-10% EtOAc/hexanes gave **4.25** as a colorless oil (20.9 mg, 33.2 μmol, 77%), with a Rf = 0.71 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65-7.61 (m, 4H), 7.39-7.31 (m, 6H), 5.76 (d, J = 3.7 Hz, 1H), 4.65 (s, 1H), 4.03 (s, 1H), 3.95-3.81 (m, 3H), 3.78-3.74 (m, 1H), 3.49 (d, J = 7.4 Hz, 2H), 2.52-2.41(m, 1H), 2.09-1.83 (m, 5H), 1.81-1.55 (m, 5H), 1.53 (s, 3H), 1.34 (s, 3H), 1.33-1.04 (m, 3H), 1.01 (s, 9H), 0.89 (d, J = 6.5 Hz, 3H), 0.75 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.9 (C_4), 135.9 (CH), 134.5 (C_4), 129.8 (CH), 127.9

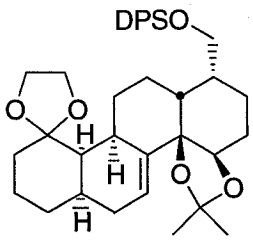
(CH), 116.2 (CH), 109.3 (CH), 107.2 (C_4), 84.8 (C_4), 77.6 (CH), 67.4 (CH_2), 65.5 (CH_2), 64.4 (CH_2), 45.5 (CH), 43.0 (CH), 40.8 (C_4), 33.1 (CH), 31.9 (CH_2), 29.2 (CH_2), 29.1 (CH), 27.2 (CH_3), 27.2 (CH_3), 26.4 (CH_3), 24.2 (CH_2), 23.4 (CH_2), 19.7 (C_4), 17.5(CH_2), 17.1 (CH_3), 12.9 (CH_3); IR (CH_2Cl_2, cm^{-1}) 3133 (w), 3071 (m), 3050 (m), 2985 (s), 2932 (s), 2870 (s), 2771 (w), 2742 (w), 2709 (w), 1960 (w), 1890 (w), 1822 (w), 1775 (w), 1726 (w), 1678 (w), 1589 (w), 1472 (s), 1464 (s), 1428 (s), 1380 (s), 1362 (m), 1332 (w), 1264 (s), 1213 (s), 1204 (s), 1184 (s), 1148 (s), 1132(s), 1085 (s), 1043 (s), 1023 (s); HRMS (EI) *m/z* (M^+– *t*Bu) calcd 573.30363, found 573.30383.

2-cyclohex-1-enyl-[1,3]-dioxolane cycloadduct with *tert*-butyl-(2,2-dimethyl-10-vinyl-4,5,6,6a,7,8-hexahydro-3a*H*-naphtho[1,8a-*d*][1,3]dioxol-6-ylmethoxy)-diphenyl-silane (4.26)



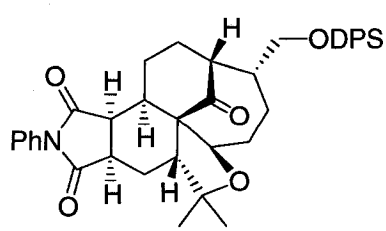
Procedure O: Trimethylsilyl triflate (10 *u*L, 54 μmol), diene **4.2** (27.0 mg, 53.7 μmol), 2-cyclohex-1-enyl-[1,3]-dioxolane (17 mg, 107 μmol), CH_2Cl_2 (1.0 mL), stirred for 2 hours. Flash chromatography with 3-5% EtOAc/hexanes gave **4.26** as a pale yellow oil (19.4 mg, 30.0 μmol, 55%), with a Rf = 0.78 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65-7.61 (m, 4H), 7.42-7.31 (m, 6H), 6.07 (d, J = 5.4 Hz, 1H), 4.82 (s, 1H), 3.97 (s, 1H), 3.89-3.72 (m, 4H), 3.51 (d, J = 7.3 Hz, 2H), 2.54-2.40 (m, 2H), 2.15-1.55 (m, 12H), 1.57 (s, 3H), 1.42 (s, 3H), 1.30-1.11 (m, 8H), 1.01 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.5 (C_4), 135.9 (CH), 134.5 (C_4), 129.8 (CH), 127.9 (CH), 118.8 (CH), 107.8 (C_4), 106.3 (CH), 85.3 (C_4), 81.0 (CH), 66.8 (CH_2), 65.3 (CH_2), 64.5 (CH_2), 41.8 (CH), 41.7 (C_4), 33.3 (CH), 29.4 (CH_2), 29.3 (CH_2), 28.5 (CH_2), 27.7 (CH), 27.5 (CH_2), 27.3 (CH_3), 27.3 (CH_3), 27.2 (CH), 27.2 (CH_3), 26.2 (CH_2), 24.0 (CH_2), 23.0 (CH_2), 21.9 (CH_2), 19.7 (C_4), 17.5(CH_2); IR (CH_2Cl_2, cm^{-1}) 3071 (w), 3048 (w), 2930 (s), 2859 (s), 1959 (w), 1893 (w), 1823 (w), 1739 (s), 1700 (s), 1585 (w), 1471 (s), 1428 (s), 1383 (m), 1364 (m), 1256 (m), 1241 (m), 1186 (w), 1112(s), 1029 (m); HRMS (EI) *m/z* (M^+) calcd 656.38970, found 656.39963.

1,4-dioxa-spiro[4.5]dec-6-ene cycloadduct with *tert*-butyl-(2,2-dimethyl-10-vinyl-4,5,6,6a,7,8-hexahydro-3a*H*-naphtho[1,8a-*d*][1,3]dioxol-6-ylmethoxy)-diphenyl-silane (4.27)



Procedure O: Trimethylsilyl triflate (8.3 *u*L, 46 *μ*mol), diene **4.2** (23.0 mg, 45.7 *μ*mol), 1,4-dioxa-spiro[4.5]dec-6-ene (13 mg, 91 *μ*mol), CH_2Cl_2 (0.9 mL), stirred for 1 hour and 15 minutes. Flash chromatography with 5-10% EtOAc/hexanes gave **4.27** as a white foam (24.0 mg, 37.3 *μ*mol, 82%), with a Rf = 0.67 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65-7.62 (m, 4H), 7.40-7.32 (m, 6H), 5.92 (dd, J = 5.0, 2.5 Hz, 1H), 4.03 (dd, J = 2.4, 2.5 Hz, 1H), 3.96-3.87 (m, 4H), 3.50 (d, J = 7.3 Hz, 2H), 2.53-2.46 (m, 1H), 2.38 (dd, J = 18.3, 7.8 Hz, 1H), 2.16-2.11 (m, 1H), 2.06-1.96 (m, 4H), 1.93-1.85 (m, 1H), 1.80-1.63 (m, 6H), 1.58-1.47 (m, 1H), 1.55 (s, 3H), 1.38 (s, 3H), 1.44-1.37 (m, 1H), 1.33-1.24 (m, 4H), 1.14-1.03 (m, 1H), 1.01 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.4 (C_4), 135.4 (CH), 134.0 (C_4), 129.3 (CH), 127.4 (CH), 116.1 (CH), 110.9 (C_4), 106.9 (C_4), 84.6 (C_4), 78.3 (CH), 66.7 (CH_2), 64.5 (CH_2), 63.6 (CH_2), 44.0 (CH), 41.7 (CH), 35.2 (CH), 33.2 (CH_2), 32.6 (CH), 32.4 (CH_2), 31.9 (CH), 30.6 (CH_2), 29.5 (CH_2), 26.9 (CH_3), 26.7 (CH_3), 26.2 (CH_3), 24.3 (CH_2), 23.2 (CH_2), 22.9 (CH_2), 19.2 (C_4), 16.9 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3143 (w), 3074 (m), 3050 (m), 2934 (s), 2738 (w), 2705 (w), 1960 (w), 1890 (w), 1825 (w), 1743 (w), 1669 (w), 1589 (w), 1477 (s), 1428 (s), 1379 (s), 1361 (s), 1330 (w), 1299 (m), 1263 (s), 1213 (s), 1174 (s), 1113 (s), 1017 (s); HRMS (EI) *m/z* (M^+–*t*Bu) calcd 585.30363, found 585.30226.

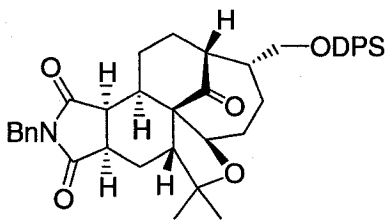
12-*N*-phenylmaleimide-8-(*tert*-butyl-diphenyl-silanyloxymethyl)-2-methylene-3,3-dimethyl-4-oxa-tricyclo[7.3.1.0^{1,5}]tridecan-13-one (4.28)



Procedure C: Tin tetrachloride (0.1 M solution in CH_2Cl_2, 80 *μ*L, 80 *μ*mol), Prins-pinacol precursor **4.4** (13.5 mg, 20.0 *μ*mol), CH_2Cl_2 (0.4 mL), at -78°C, stirred for 7 hours. Flash chromatography with 40-50% EtOAc/hexanes gave **4.28** as a yellow oil, (8.4 mg, 12 *μ*mol, 62%), with a Rf = 0.36 (50% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62-7.59 (m, 4H), 7.49-7.32 (m, 9H), 7.25-7.22 (m, 2H), 4.14 (dd, J = 4.4-11.4 Hz, 1H), 3.50 (d, J = 7.2 Hz, 2H), 3.22 (dtt, J = 6.8, 3.0, 3.3

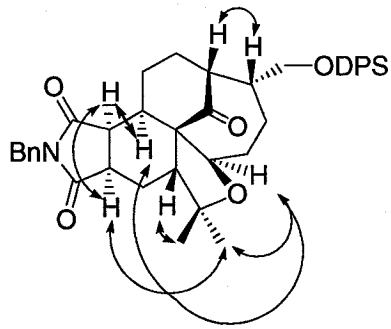
Hz, 1H), 3.07 (dd, J, 4.9, 9.8 Hz, 1H), 2.99-2.95 (m, 1H), 2.92 (dd, J = 13.1, 5.0 Hz, 1H), 2.73-2.62 (m, 1H), 2.58-2.55 (m, 1H), 2.22-1.09 (m, 3H), 1.97-1.24 (m, 7H), 1.20 (s, 3H), 1.19 (s, 3H), 1.01 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.3 (C_4), 179.0 (C_4), 175.5 (C_4), 135.9 (CH), 133.8 (C_4), 132.3 (C_4), 130.1 (CH), 129.6 (CH), 129.2 (CH), 128.1 (CH), 127.1 (CH), 86.4 (CH), 84.2 (C_4), 66.3(CH_2), 63.9 (C_4), 49.7 (CH), 47.9 (CH), 43.9 (CH), 43.5 (CH), 42.2 (CH), 39.8 (CH), 36.3 (CH_2), 30.4 (CH_3), 27.2 (CH_3), 25.2 (CH_2), 25.1 (CH_3), 23.7 (CH_2), 22.4 (CH_2), 21.0 (CH_2), 19.6 (C_4); IR (CH_2Cl_2, cm^{-1}) 3467 (w), 3070 (m), 3050 (m), 2930 (s), 2859 (s), 1962 (w), 1887 (w), 1774 (m), 1711 (s), 1598 (m), 1500 (m), 1472 (m), 1461 (m), 1428 (m), 1386 (s), 1333 (w), 1303 (w), 1266 (m), 1191 (s), 1112 (s), 1072 (m), 1054 (m), 1040 (m), 1014 (w); HRMS (EI) *m/z* (M^+-*t*Bu) calcd 618.26757, found 618.26932. COSY, NOESY and HMQC experiments were performed in order to obtain the correlations illustrated in Figure 4.5.

12-*N*-benzylmaleimide-8-(*tert*-butyl-diphenyl-silanyloxymethyl)-2-methylene-3,3-dimethyl-4-oxa-tricyclo[7.3.1.0^{1,5}]tridecan-13-one (4.35)

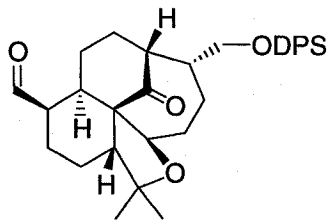


Procedure C: Tin tetrachloride (0.1 M solution in CH_2Cl_2, 65 μL, 65 μmol), Prins-pinacol precursor **4.6** (15 mg, 22 μmol), CH_2Cl_2 (0.4 mL), at -78°C, stirred 1 hour and 30 minutes. Flash chromatography with 40% EtOAc/hexanes gave **4.35** as a yellow oil, (12 mg, 17 μmol, 77%), with a Rf = 0.47 (50% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68-7.67 (m, 4H), 7.63-7.26 (m, 11H), 4.63 (d, J = 13.9 Hz, 1H), 4.49 (d, J = 14.1 Hz, 1H), 4.06-4.02 (m, 1H), 3.50 (d, J = 7.2 Hz, 2H), 3.01-2.87 (m, 3H), 2.73 (dd, J = 11.5, 4.9 Hz, 1H), 2.56-2.42 (m, 2H), 2.15-2.11 (m, 1H), 2.02-1.87 (m, 2H), 1.82-1.59 (m, 5H), 1.42-1.21 (m, 2H), 1.18 (s, 3H), 1.16 (s, 3H), 1.02 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.6 (C_4), 179.6 (C_4), 177.9 (C_4), 135.9 (CH), 133.8 (C_4), 130.0 (CH), 129.3 (C_4), 129.1 (CH), 128.9 (CH), 128.2 (CH), 128.0 (CH), 85.6 (CH), 84.0 (C_4), 77.4 (C_4), 66.1 (CH_2), 49.1 (CH), 47.2 (CH), 43.8 (CH), 43.0 (CH), 42.7 (CH_2), 41.4 (CH), 39.0 (CH), 35.5 (CH_2), 30.0 (CH_3), 26.9 (CH_3), 24.8 (CH_2), 24.7 (CH_3), 23.2 (CH_2), 21.7 (CH_2), 21.1 (CH_2), 19.3 (C_4); IR (CH_2Cl_2, cm^{-1}) 3454 (w), 3069 (w), 2930 (s), 2859 (m), 1772 (w), 1702 (s), 1471 (m), 1428 (s), 1398 (s), 1350 (m), 1266 (w), 1180 (m), 1112 (s), 1071 (s); HRMS (EI) *m/z* (M^+-

*t*Bu) calcd 632.28322, found 632.28380. COSY, NOESY and HMQC experiments were performed in order to obtain the correlations illustrated below:

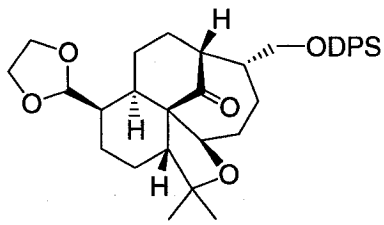


12-acrolein-8-(*tert*-butyl-diphenyl-silanyloxymethyl)-2-methylene-3,3-dimethyl-4-oxa-tricyclo[7.3.1.0^{1,5}]tridecan-13-one (4.36)

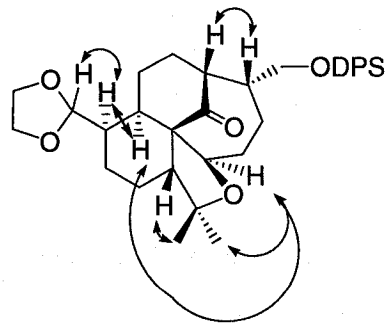


Procedure C: Tin tetrachloride (0.1 M solution in CH_2Cl_2, 20 μL, 20 μmol), Prins-pinacol precursor **4.8** (11.3 mg, 20.2 μmol), CH_2Cl_2 (0.4 mL), at -78°C, stirred for 1 hour. Flash chromatography with 25% EtOAc/hexanes gave **4.36** as a pale yellow oil (8.7 mg, 16 μmol, 77%), with a Rf = 0.36 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.77 (d, J = 3.4 Hz, 1H), 7.63-7.59 (m, 4H), 7.41-7.32 (m, 6H), 4.02 (dd, J = 11.2, 4.1 Hz, 1H), 3.53-3.49 (m, 2H), 3.05 (d, J = 6.7 Hz, 1H), 2.98-2.97 (m, 1H), 2.62 (t, J = 3.9 Hz, 1H), 2.55-2.45 (m, 1H), 2.17-1.98 (m, 2H), 1.93-1.76 (m, 3H), 1.69-1.55 (m, 4H), 1.52-1.16 (m, 5H), 1.28 (s, 3H), 1.22 (s, 3H), 1.01 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 212.9 (C_4), 205.3 (CH), 135.9 (CH), 133.8 (C_4), 130.1 (CH), 128.1 (CH), 86.3 (CH), 83.6 (C_4), 66.2 (CH_2), 60.7 (C_4), 52.8 (CH), 48.6 (CH), 47.1 (CH), 44.0 (CH), 43.7 (CH), 34.1 (CH_2), 30.3 (CH_3), 27.2 (CH_3), 26.3 (CH_2), 25.0 (CH_3), 24.7 (CH_2), 24.1 (CH_2), 21.1 (CH_2), 19.6 (C_4), 18.9 (CH_2); IR (CH_2Cl_2, cm^{-1}) 3375 (br), 3075 (w), 3047 (w), 2930 (s), 2859 (s), 1960 (w), 1894 (w), 1824 (w), 1730 (s), 1698 (s), 1589 (w), 1471 (s), 1463 (s), 1428 (s), 1386 (m), 1363 (m), 1167 (m), 1111 (s), 1028 (w), 1009 (w); HRMS (EI) *m/z* (M^+-*t*Bu) calcd 501.24611, found 501.24798.

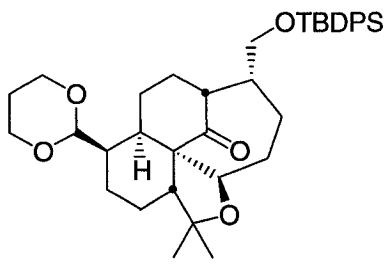
12-(2-vinyl-[1,3]-dioxolane)-8-(*tert*-butyl-diphenyl-silanyloxymethyl)-2-methylene-3,3-dimethyl-4-oxa-tricyclo[7.3.1.0^{1,5}]tridecan-13-one (4.37)



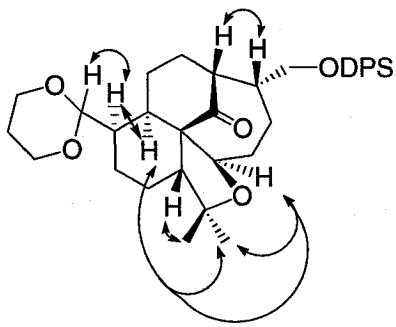
Procedure P: Trimethylsilyl triflate (1.0 *u*L, 5.1 *μ*mol), diene **4.2** (10.4 mg, 20.7 *μ*mol), 2-vinyl-[1,3]-dioxolane (4.1 *u*L, 41 *μ*mol), CH_2Cl_2 (0.4 mL), tin tetrachloride (1.0 M solution in CH_2Cl_2, 21 *μ*L, 21 *μ*mol), stirred for 30 minutes. Flash chromatography with 20-25% EtOAc/hexanes gave **4.37** as a white foam (12 mg, 20 *μ*mol, 96%), with a Rf = 0.43 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63-7.61 (m, 4H), 7.44-7.34 (m, 6H), 4.70 (d, J = 6.2 Hz, 1H), 4.02 (dd, J = 11.1, 3.4 Hz, 1H), 3.91 (td, J = 10.0, 3.3 Hz, 2H), 3.83-3.73 (m, 2H), 3.46 (dt, J = 3.1, 9.4 Hz, 2H), 2.87 (d, J = 9.1 Hz, 2H), 2.56-2.53 (m, 1H), 2.11-1.97 (m, 2H), 1.94-1.82 (m, 3H), 1.78-1.64 (m, 3H), 1.57-1.22 (m, 6H), 1.22 (s, 3H), 1.19 (s, 3H), 1.02 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 215.7 (C_4), 135.9 (CH), 133.9 (C_4), 130.0 (CH), 128.1 (CH), 105.4 (CH), 87.6 (CH), 83.5 (C_4), 66.1(CH_2), 65.1 (CH_2), 64.8 (CH_2), 61.6 (C_4), 49.8 (CH), 46.6 (CH), 44.5 (CH), 44.2 (CH), 42.3 (CH), 35.0 (CH_2), 30.8 (CH_3), 27.2 (CH_3), 25.6 (CH_3), 24.7 (CH_2), 24.0 (CH_2), 20.6 (CH_2), 20.4 (CH_2), 20.2 (CH_2), 19.6 (C_4); IR (CH_2Cl_2, cm^{-1}) 3071 (w), 3048 (w), 2930 (s), 2859 (s), 1959 (w), 1893 (w), 1823 (w), 1739 (s), 1700 (s), 1585 (w), 1471 (s), 1428 (s), 1383 (m), 1364 (m), 1256 (m), 1241 (m), 1186 (w), 1112 (s), 1029 (m); HRMS (EI) *m/z* (M^+-*t*Bu) calcd 545.27233, found 545.27419. COSY, NOESY and HMQC experiments were performed in order to obtain the correlations illustrated below:



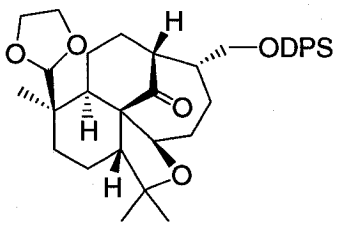
12-(2-vinyl-[1,3]-dioxane)-8-(*tert*-butyl-diphenyl-silanyloxymethyl)-2-methylene-3,3-dimethyl-4-oxa-tricyclo[7.3.1.0^{1,5}]tridecan-13-one (4.44)



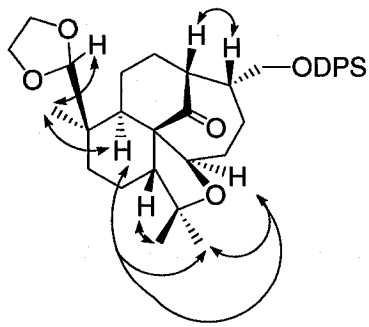
Procedure P: Trimethylsilyl triflate (1.8 *u*L, 10 *μ*mol), diene **4.2** (20.5 mg, 40.8 *μ*mol), 2-vinyl-[1,3]-dioxane (9.0 *u*L, 82 *μ*mol), CH_2Cl_2 (0.8 mL), tin tetrachloride (1.0 M solution in CH_2Cl_2, 82 *μ*L, 82 *μ*mol), stirred for 4 hours. Flash chromatography with 20% EtOAc/hexanes gave **4.44** as a pale yellow oil (17.4 mg, 28.3 *μ*mol, 69%), with a Rf = 0.38 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64-7.61 (m, 4H), 7.41-7.34 (m, 6H), 4.50 (d, J = 5.4 Hz, 1H), 4.06 (ddd, J = 18.0, 18.0, 4.9 Hz, 3H), 3.94 (dd, J = 10.5, 3.9 Hz, 1H), 3.67 (t, J = 9.9 Hz, 1H), 3.58-3.44 (m, 3H), 2.93 (d, J = 8.3 Hz, 1H), 2.86 (dd, J = 10.5, 6.6 Hz, 1H), 2.43 (dd, J = 5.9, 5.9 Hz, 1H), 2.08-1.83 (m, 6H), 1.74 (dd, J = 6.4, 6.4 Hz, 2H), 1.61-1.37 (m, 4H), 1.33-1.13 (m, 4H), 1.23 (s, 3H), 1.20 (s, 3H), 1.02 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.1 (C_4), 135.9 (CH), 134,0 (C_4), 130.0 (CH), 128.1 (CH), 103.3 (CH), 87.5 (CH), 83.7 (C_4), 67.0 (CH_2), 66.25.1 (CH_2), 66.1 (CH_2), 60.9 (C_4), 48.3 (CH), 47.0 (CH), 44.3 (CH), 43.8 (CH), 43.0 (CH), 34.6 (CH_2), 30.4 (CH_3), 27.2 (CH_3), 26.0 (CH_2), 25.3 (CH_3), 25.1 (CH_2), 24.1 (CH_2), 21.2 (CH_2), 20.8 (CH_2), 20.3 (CH_2), 19.6 (C_4); IR (CH_2Cl_2, cm^{-1}) 3072 (w), 3048 (w), 2959 (s), 2932 (s), 2857 (s), 2734 (w), 2382 (m), 2355 (m), 1959 (w), 1894 (w), 1823 (w), 1690 (s), 1587 (w), 1468 (s), 1427 (s), 1379 (m), 1362 (m), 1263 (m), 1167 (m), 1143 (s), 1109 (s), 1096 (s), 1044 (m), 1024 (m), 1003 (m); HRMS (EI) *m/z* (M^+) calcd 616.35840, found 616.35676. COSY, NOESY and HMQC experiments were performed in order to obtain the correlations illustrated below:



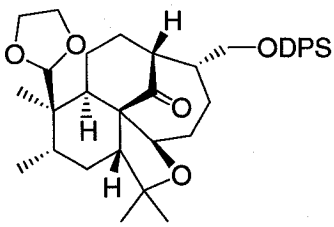
12-(2-isopropenyl-[1,3]-dioxolane)-8-(*tert*-butyl-diphenyl-silanyloxymethyl)-2-methylene-3,3-dimethyl-4-oxa-tricyclo[7.3.1.0^{1,5}]tridecan-13-one (4.45)



Procedure P: Trimethylsilyl triflate (1.2 *u*L, 6.7 μmol), diene **4.2** (13.5 mg, 26.8 μmol), 2-isopropenyl-[1,3]-dioxolane (6.1 mg, 54 μmol), CH_2Cl_2 (0.6 mL), tin tetrachloride (1.0 M solution in CH_2Cl_2, 80 μL, 80 μmol), stirred for 3 hours. Flash chromatography with 10-25% EtOAc/hexanes gave **4.45** as a pale yellow oil (7.3 mg, 12 μmol, 44%), with a Rf = 0.55 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64-7.61 (m, 4H), 7.41-7.33 (m, 6H), 4.67 (s, 1H), 3.95 (dd, J = 10.8, 4.2 Hz, 1H), 3.86-3.76 (m, 3H), 3.63-3.58 (m, 1H), 3.52 (dt, J = 12.6, 6.6 Hz, 2H), 3.05 (d, J = 5.2 Hz, 1H), 2.88-2.84 (m, 1H), 2.08-1.67 (m, 8H), 1.63-1.53 (m, 2H), 1.42-1.15 (m, 4H), 1.26 (s, 3H), 1.21 (s, 3H), 1.01 (s, 9H), 0.98 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 212.3 (C_4), 135.9 (CH), 134.0 (C_4), 130.0 (CH), 128.0 (CH), 107.5 (CH), 87.2 (CH), 83.9 (C_4), 66.4(CH_2), 65.0 (CH_2), 64.2 (CH_2), 61.8 (C_4), 51.2 (CH), 47.7 (CH), 47.3 (CH), 44.5 (CH), 39.7 (C_4), 34.5 (CH_2), 31.2 (CH_2), 30.3 (CH_3), 27.2 (CH_3), 26.0 (CH_3), 25.4 (CH_3), 24.5 (CH_2), 21.1 (CH_2), 20.8 (CH_2), 19.6 (CH_2), 19.6 (C_4); IR (CH_2Cl_2, cm^{-1}) 3135 (w), 3070 (m), 3050 (m), 2931 (s), 2860 (s), 2707 (w), 1960 (w), 1893 (w), 1825 (w), 1694 (s), 1589 (m), 1472 (s), 1428 (s), 1384 (m), 1362 (m), 1330 (w), 1267 (m), 1228 (m), 1206 (w), 1167 (w), 1104 (s), 1035 (m), 1005 (m); HRMS (EI) *m/z* (M^+– *t*Bu) calcd 559.28798, found 559.28987. COSY, NOESY and HMQC experiments were performed in order to obtain the correlations illustrated below:

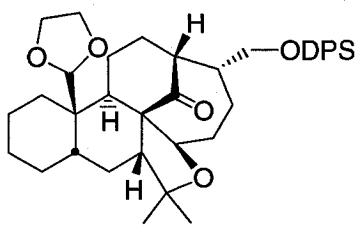


12-(2-(1-methyl-propenyl)-[1,3]-dioxolane)-8-(*tert*-butyl-diphenyl-silanyloxymethyl)-2-methylene-3,3-dimethyl-4-oxa-tricyclo[7.3.1.0^{1,5}]tridecan-13-one (4.46)



Procedure P: Trimethylsilyl triflate (1.8 *u*L, 9.5 μmol), diene **4.2** (19.0 mg, 37.8 μmol), 2-(1-methyl-propenyl)-[1,3]-dioxolane (10 mg, 76 μmol), CH_2Cl_2 (0.8 mL), tin tetrachloride (1.0 M solution in CH_2Cl_2, 0.11 mL, 0.11 mmol), stirred for 5 hours and 30 minutes. Flash chromatography with 5-10% EtOAc/hexanes gave **4.46** as a white foam (10.6 mg, 16.8 μmol, 44%), with a Rf = 0.65 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64-7.61 (m, 4H), 7.44-7.33 (m, 6H), 4.64 (s, 1H), 3.97 (dd, J = 11.8, 3.9 Hz, 1H), 3.90 (dt, J = 12.2, 6.1 Hz, 1H), 3.75 (ddd, J = 14.5, 5.3, 7.3 Hz, 2H), 3.63 (dt, J = 14.1, 7.1 Hz, 1H), 3.55-3.44 (m, 2H), 2.97 (dd, J = 13.2, 5.8 Hz, 2H), 2.07-1.88 (m, 4H), 1.84-1.81 (m, 1H), 1.76-1.42 (m, 5H), 1.29-1.12 (m, 3H), 1.24 (s, 3H), 1.14 (s, 3H), 1.01 (s, 9H), 0.95 (s, 3H), 0.93 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.2 (C_4), 135.9 (CH), 134.0 (C_4), 130.0 (CH), 128.0 (CH), 109.1 (CH), 88.9 (CH), 84.3 (C_4), 66.1(CH_2), 65.1 (CH_2), 64.8 (C_4), 64.6 (CH_2), 50.6 (CH), 49.1 (CH), 47.9 (CH), 47.7 (CH), 41.8 (C_4), 36.2 (CH_2), 31.0 (CH_3), 30.4 (CH), 29.8 (CH_2), 27.2 (CH_3), 25.5 (CH_3), 24.4 (CH_2), 21.5 (CH_2), 21.4 (CH_2), 20.0 (CH_3), 19.6 (C_4), 19.5 (CH_3); IR (CH_2Cl_2, cm^{-1}) 3074 (w), 3049 (w), 2931 (s), 2858 (s), 2705 (w), 1961 (w), 1896 (w), 1826 (w), 1697 (s), 1589 (w), 1471 (s), 1428 (s), 1381 (m), 1364 (m), 1328 (w), 1266 (m), 1248 (w), 1206 (w), 1189 (w), 1106 (s), 1064 (m), 1035 (m), 1006 (m); HRMS (EI) *m/z* (M^+– *t*Bu) calcd 573.30363, found 573.30289. COSY, NOESY and HMQC experiments were performed in order to obtain the correlations illustrated in Figure 4.7.

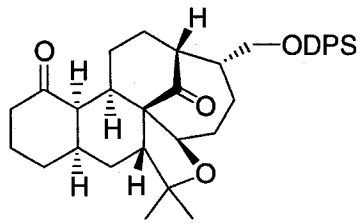
12-(2-cyclohex-1-enyl-[1,3]-dioxolane)-8-(*tert*-butyl-diphenyl-silanyloxymethyl)-2-methylene-3,3-dimethyl-4-oxa-tricyclo[7.3.1.0^{1,5}]tridecan-13-one (4.47)



Procedure C: Tin tetrachloride (1.0 M solution in CH_2Cl_2, 30 μL, 30 μmol), Prins-pinacol precursor **4.26** (19.4 mg, 29.5 μmol), CH_2Cl_2 (0.6 mL), at -78°C, stirred for 2 hours. Flash chromatography with 5-25% EtOAc/hexanes gave **4.47** as a pale yellow oil (4.0 mg, 6.1 μmol, 21%), with a Rf = 0.53 (25%

EtOAc/hexanes). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63-7.62 (m, 4H), 7.41-7.35 (m, 6H), 4.66 (s, 1H), 3.98 (dd, J = 10.8, 3.8 Hz, 1H), 3.85 (dd, J = 6.0, 5.2 Hz, 1H), 3.82 (dd, J = 6.0, 7.0 Hz, 1H), 3.73 (dd, J = 5.6, 5.6 Hz, 1H), 3.60 (dd, J = 6.7, 6.7 Hz, 1H), 3.54-3.46 (m, 2H), 2.98-2.92 (m, 2H), 2.02-1.94 (m, 3H), 1.92-1.83 (m, 3H), 1.83-1.65 (m, 2H), 1.58-1.44 (m, 8H), 1.34-1.12 (m, 5H), 1.26 (s, 3H), 1.15 (s, 3H), 1.01 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 213.0 (C_4), 135.7 (CH), 133.8 (C_4), 129.8 (CH), 127.8 (CH), 109.0 (CH), 88.9 (CH), 84.2 (C_4), 65.9 (CH_2), 64.7 (C_4), 64.4 (CH_2), 63.9 (CH_2), 50.8 (CH), 49.4 (C_4), 47.7 (CH), 47.5 (CH), 40.9 (C_4), 36.1 (CH_2), 33.1 (CH_2), 31.7 (CH), 30,8 (CH_3), 29.9 (CH_2), 28.5 (CH_2), 27.0 (CH_3), 25.4 (CH_3), 24.2 (CH_2), 21.3 (CH_2), 21.0 (CH_2), 20.8 (CH_2), 20.5 (CH_2), 19.4 (C_4); IR (CH_2Cl_2, cm^{-1}) 3135 (w), 3071 (w), 3050 (w), 2928 (s), 2858 (s), 2709 (w), 1959 (w), 1891 (w), 1824 (w), 1723 (w), 1696 (s), 1590 (w), 1471 (s), 1463 (s), 1428 (s), 1363 (m), 1328 (w), 1266 (m), 1205 (w), 1133 (m), 1112 (s), 1031 (m), 1010 (w); HRMS (EI) *m/z* (M^+) calcd 656.38970, found 656.38816.

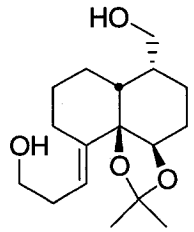
12-(2-cyclohexen-1-one)-8-(*tert*-butyl-diphenyl-silanyloxymethyl)-2-methylene-3,3-dimethyl-4-oxa-tricyclo[7.3.1.0^{1,5}]tridecan-13-one (4.48)



Procedure C: Tin tetrachloride (1.0 M solution in CH_2Cl_2, 36 μL, 36 μmol), Prins-pinacol precursor **4.27** (23.0 mg, 35.7 μmol), CH_2Cl_2 (0.7 mL), at -78°C, stirred for 3 hours and 30 minutes. Flash chromatography with 15-25% EtOAc/hexanes gave **4.48** as a pale yellow oil (2.5 mg, 4.2 μmol, 12%), with a Rf = 0.32 (25% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66-7.62 (m, 4H), 7.43-7.33 (m, 6H), 3.95 (dd, J = 10.9, 3.2 Hz, 1H), 3.52 (d, J = 7.0, 2H), 3.18-3.11 (m, 1H), 3.11 (d, J = 7.4 Hz, 1H), 2.80 (t, J = 3.8Hz, 1H), 2.45 (d, J = 13.9Hz, 1H), 2.38-1.95 (m, 7H), 1.90-1.87 (m, 3H), 1.82-1.74 (m, 2H), 1.65-1.50 (m, 2H), 1.51-1.30 (m, 4H), 1.25 (s, 3H), 1.17 (s, 3H), 1.02 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.9(C_4), 209.9 (C_4), 136.0 (CH), 134.1 (C_4), 129.9 (CH), 128.0 (CH), 86.5 (CH), 83.6 (C_4), 66.8 (CH_2), 59.2 (C_4), 56.2 (CH), 48.4 (CH), 47.3 (CH), 44.3 (CH), 44.2 (CH), 43.5 (CH_2), 40.0 (CH), 32.3 (CH_2), 31.1 (CH_2), 30.4 (CH_3), 27.2 (CH_3), 26.7 (CH_2), 25.3 (CH_3), 24.7 (CH_2), 24.6 (CH_2), 24.5 (CH_2), 21.8 (CH_2), 19.6 (C_4); IR (CH_2Cl_2, cm^{-1}) 3073 (w), 3050 (m), 2929 (s), 2857 (m), 1713 (s), 1693 (m), 1463 (m), 1428 (m), 1384 (w), 1264 (m), 1169 (m),

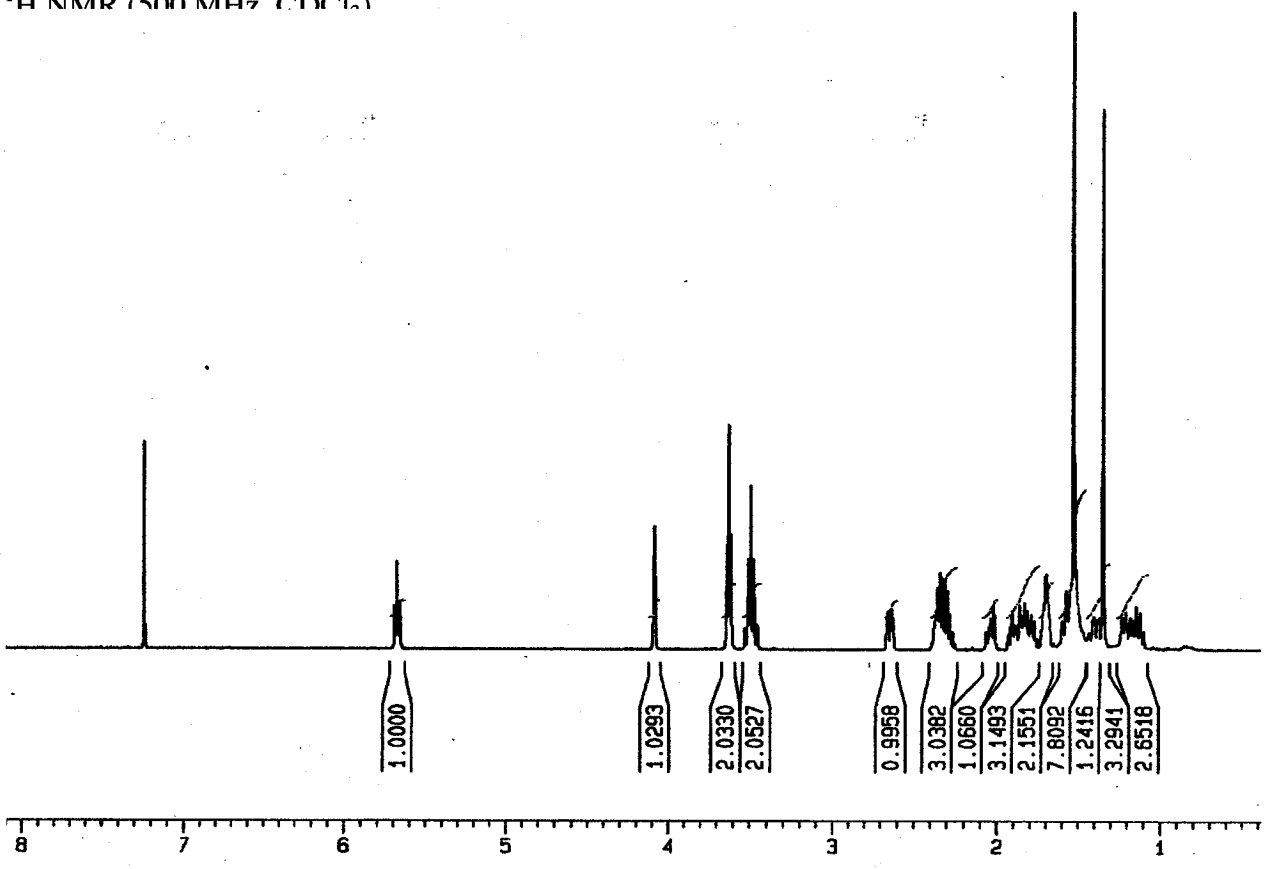
1111 (s), 1188 (m), 1047 (w), 1009 (w); HRMS (EI) *m/z* (M^+– *t*Bu) calcd 541.27741, found 541.27799.

Spectra

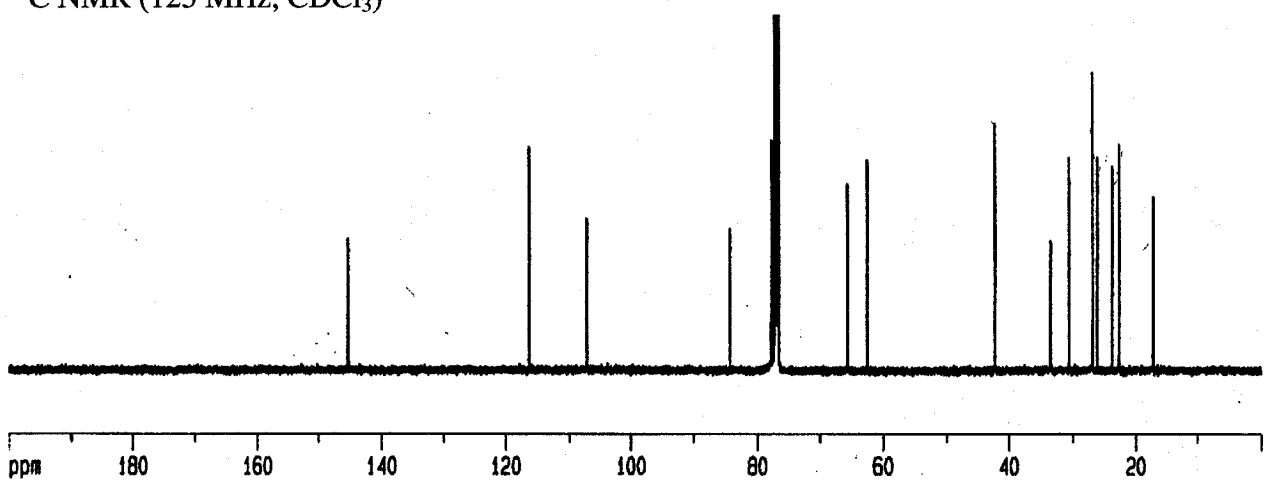


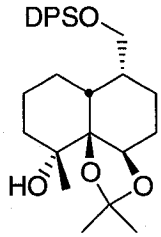
2.14

^{1}H NMR (500 MHz, $CDCl_3$)



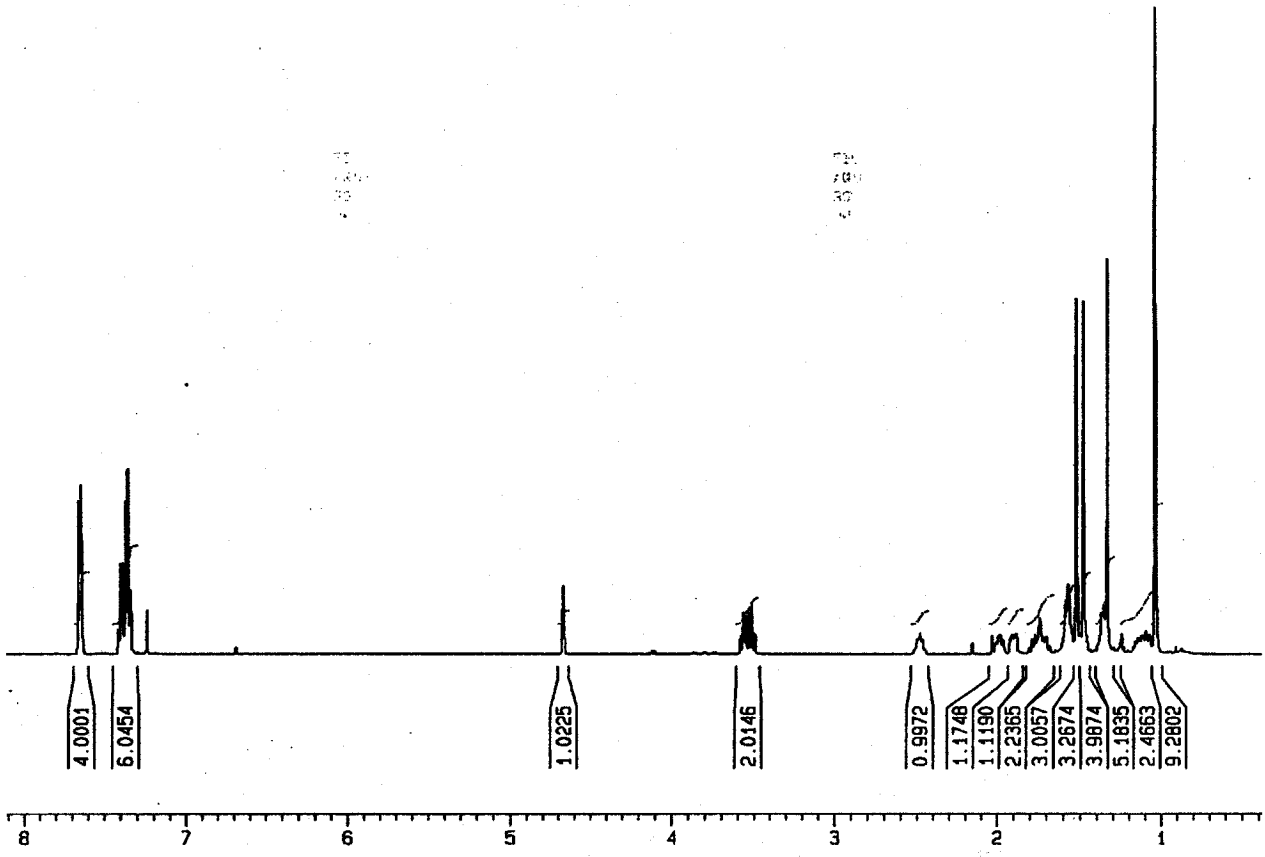
^{13}C NMR (125 MHz, $CDCl_3$)



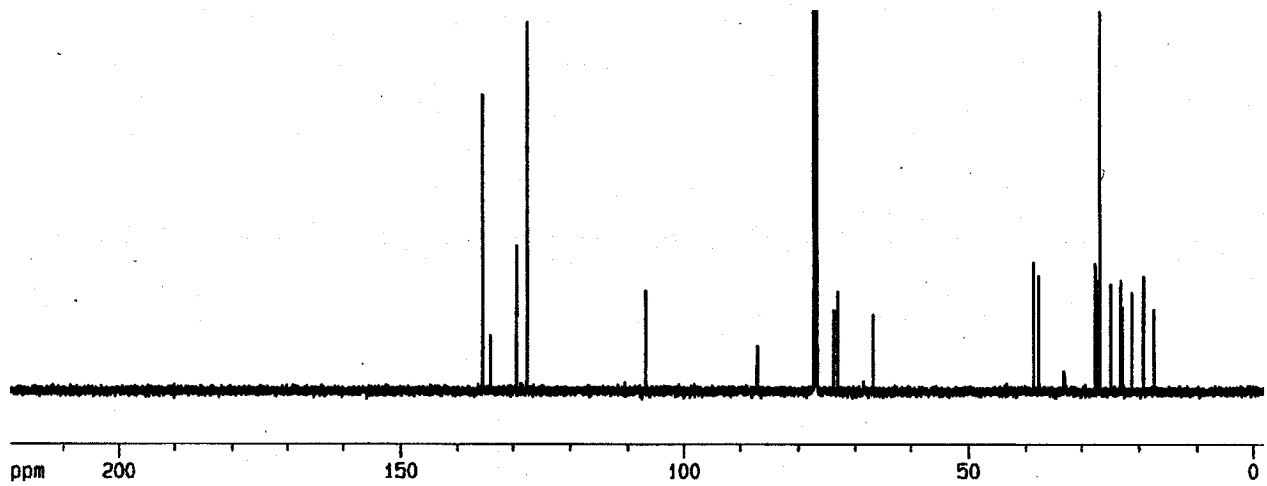


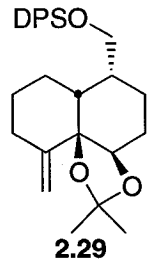
2.28

^{1}H NMR (500 MHz, $CDCl_3$)



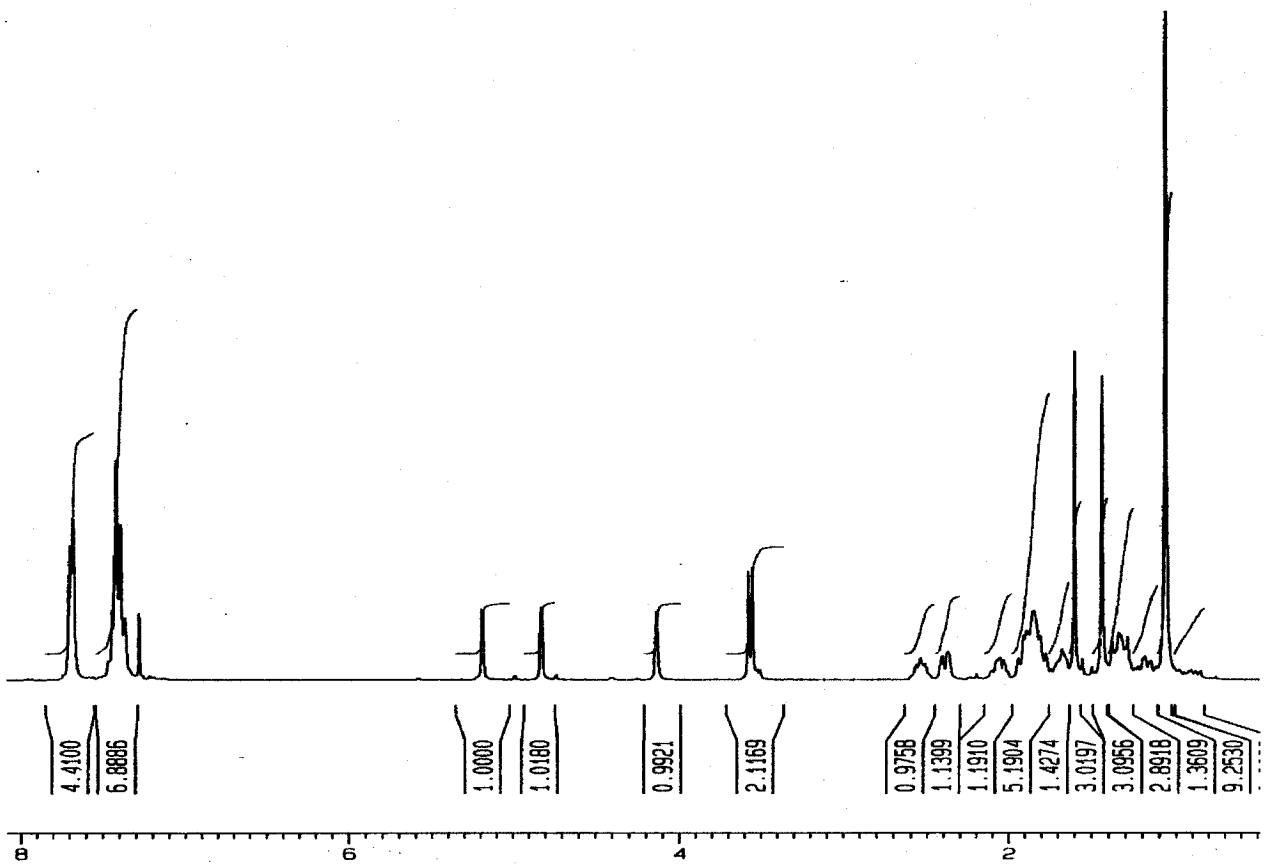
^{13}C NMR (125 MHz, $CDCl_3$)



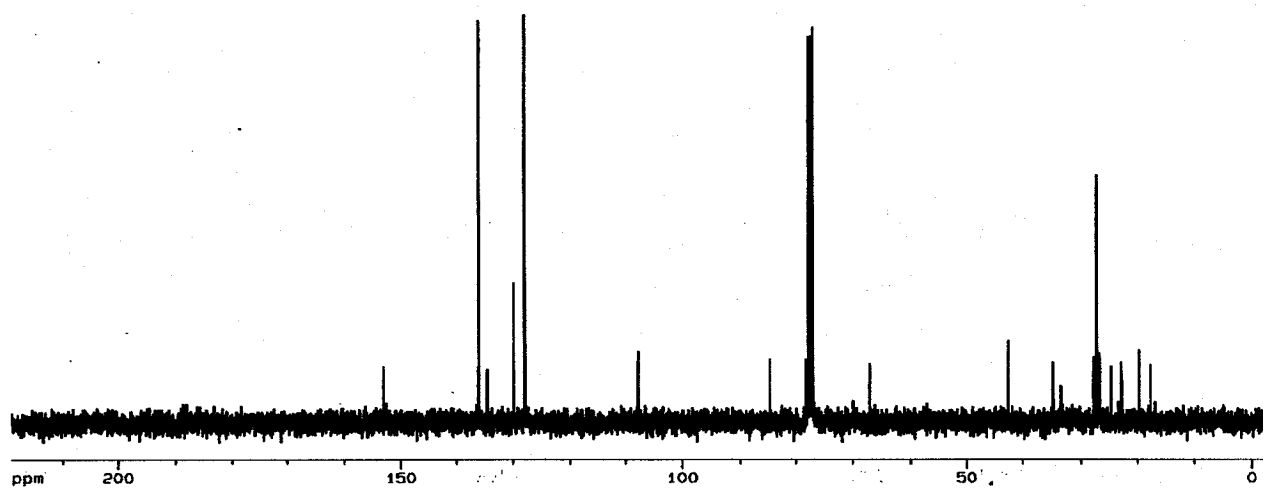


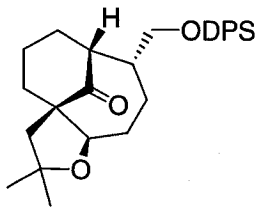
2.29

^{1}H NMR (300 MHz, $CDCl_3$)



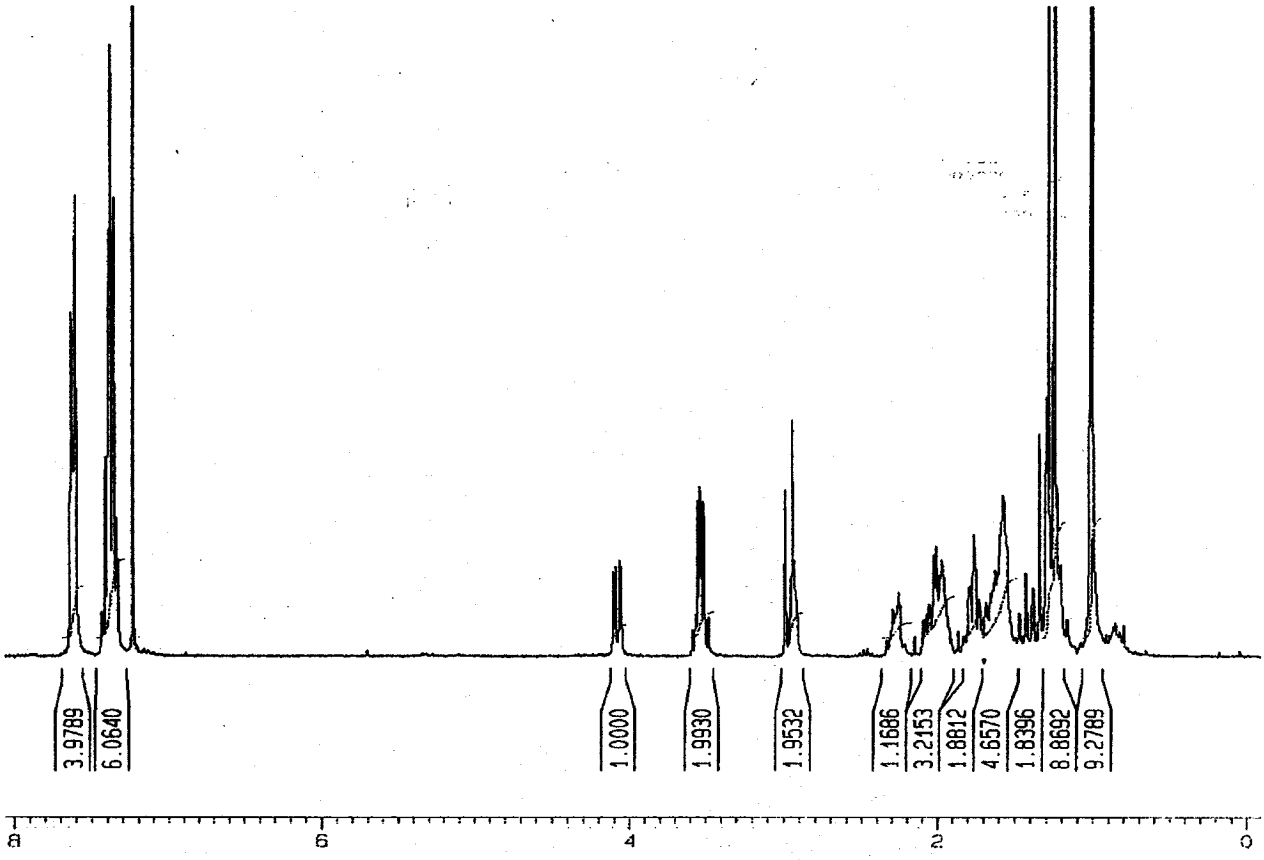
^{13}C NMR (75 MHz, $CDCl_3$)



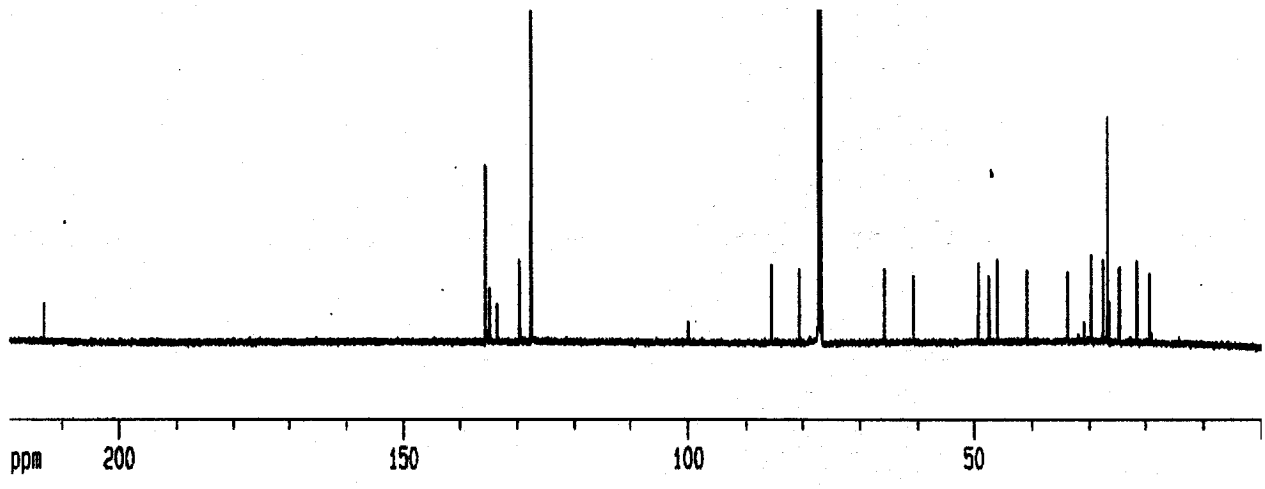


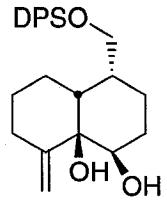
2.30

^{1}H NMR (300 MHz, $CDCl_3$)



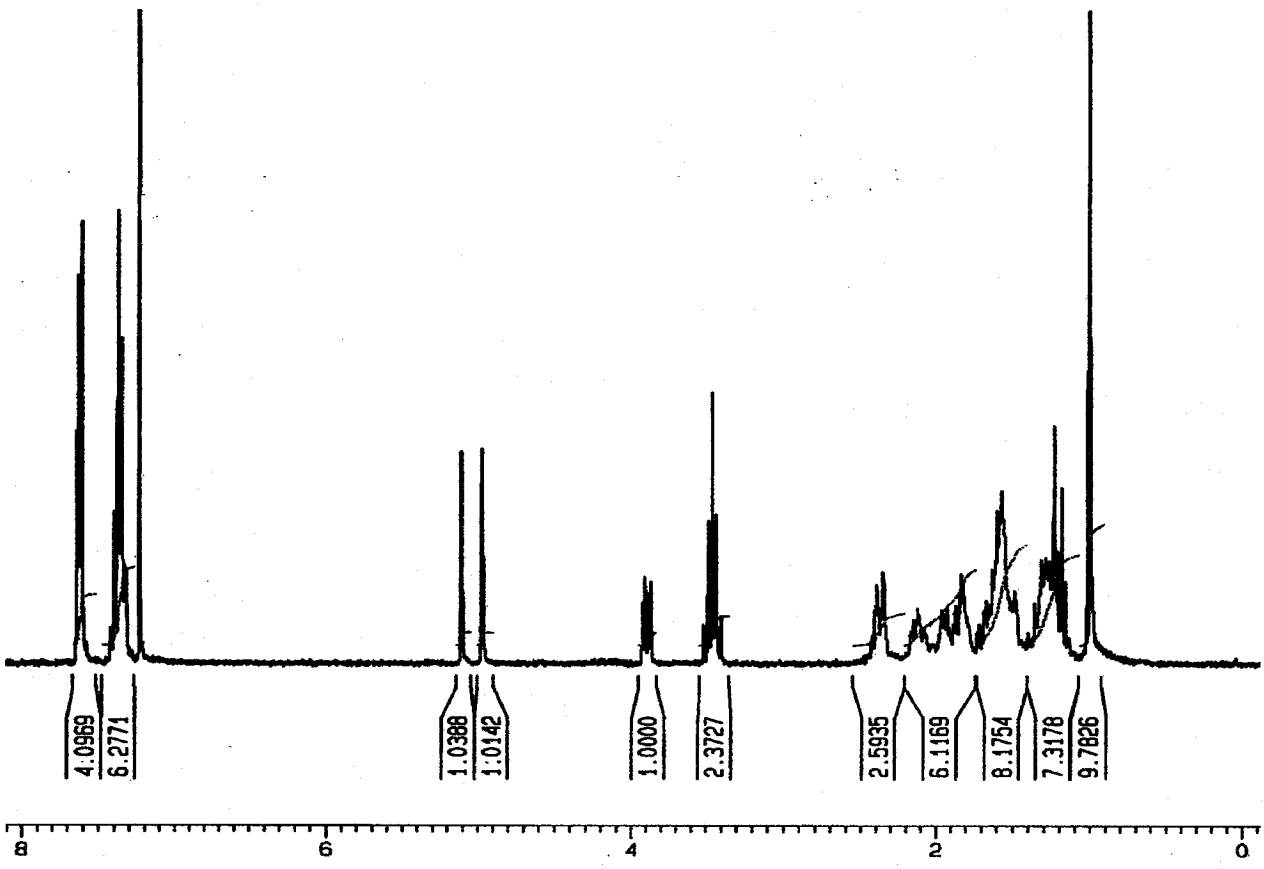
^{13}C NMR (125 MHz, $CDCl_3$)



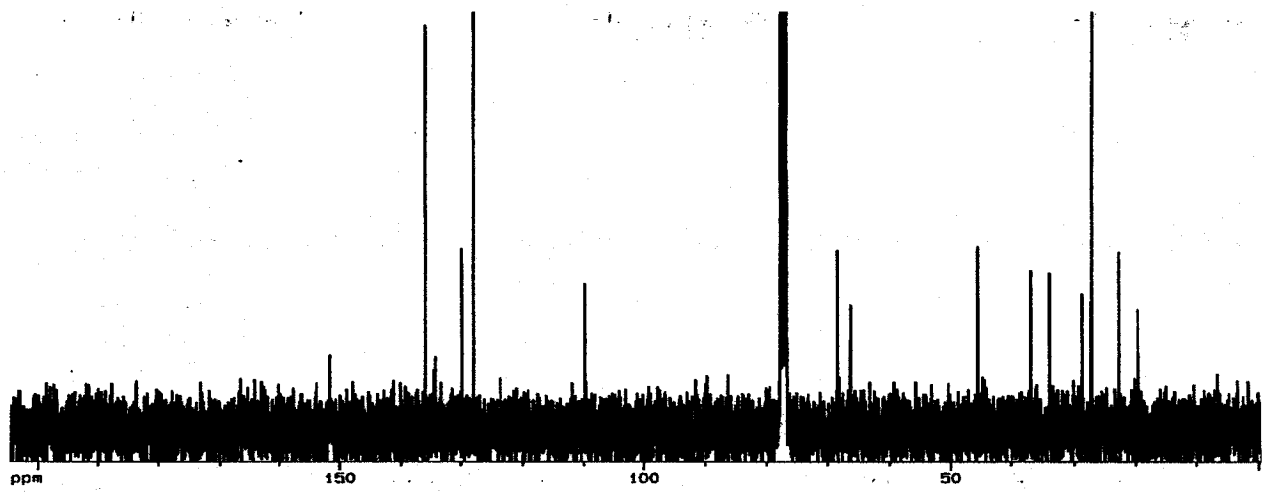


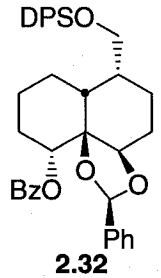
2.31

^{1}H NMR (300 MHz, $CDCl_3$)



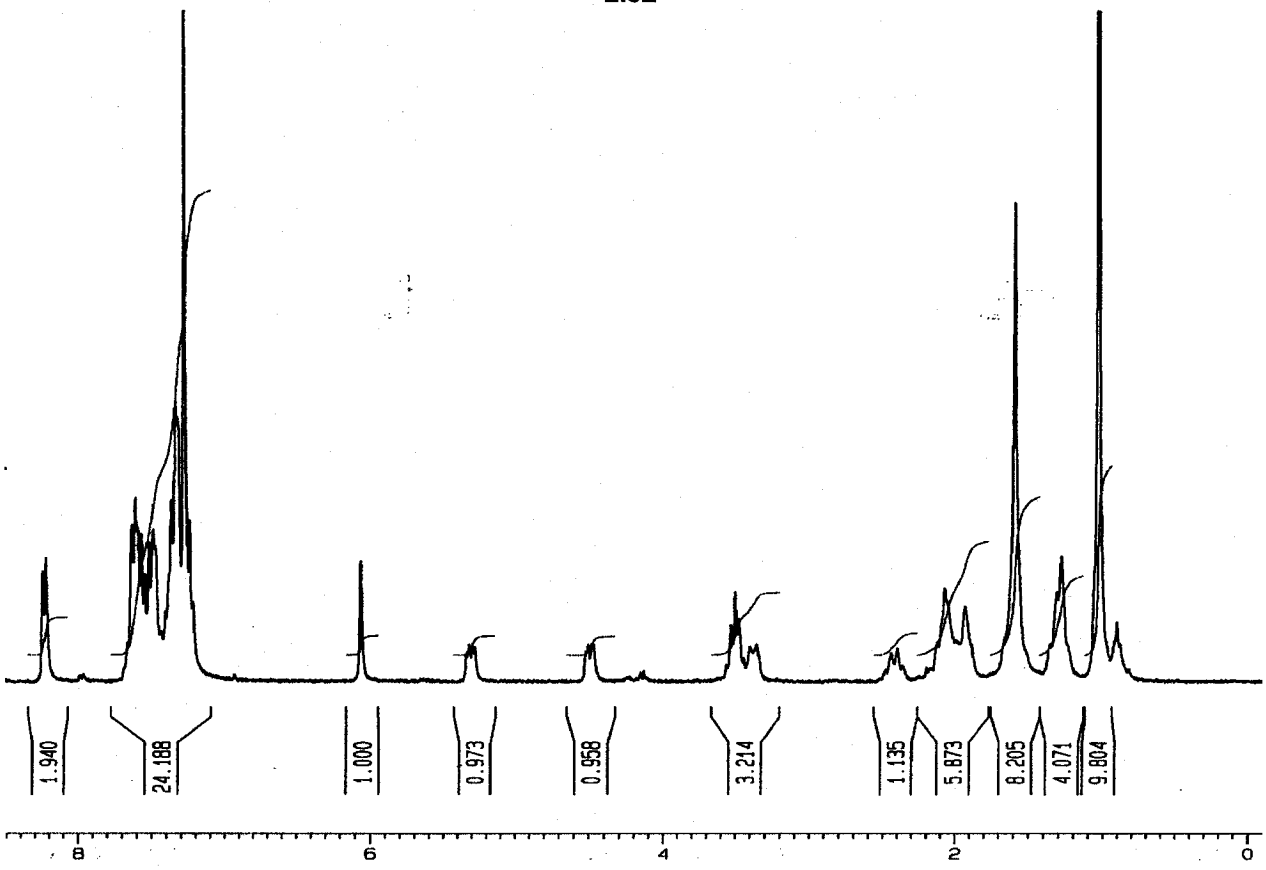
^{13}C NMR (75 MHz, $CDCl_3$)



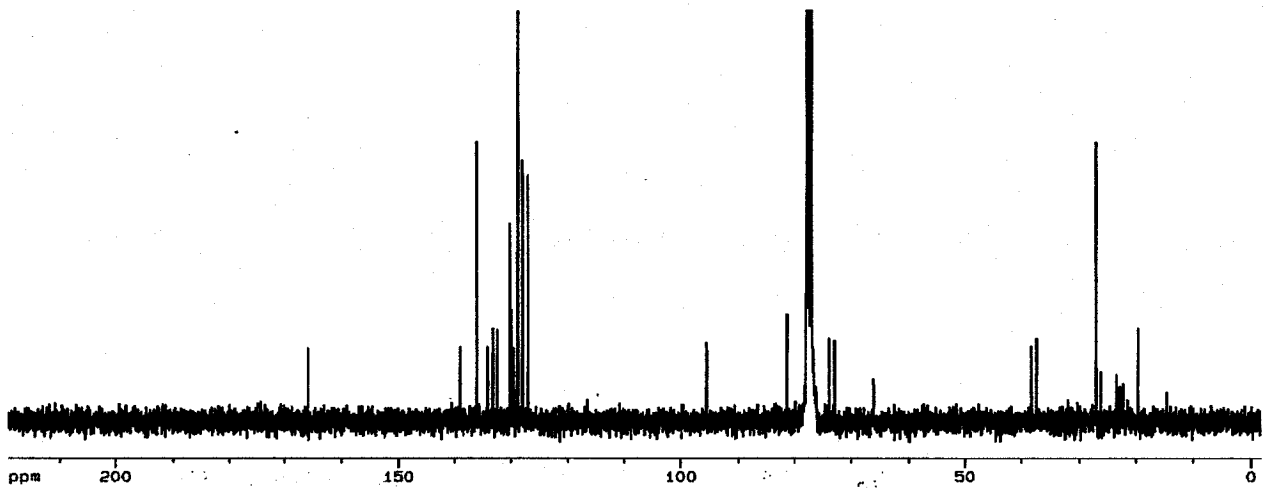


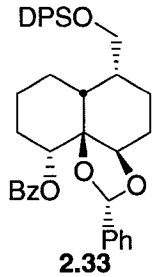
2.32

^{1}H NMR (300 MHz, $CDCl_3$)



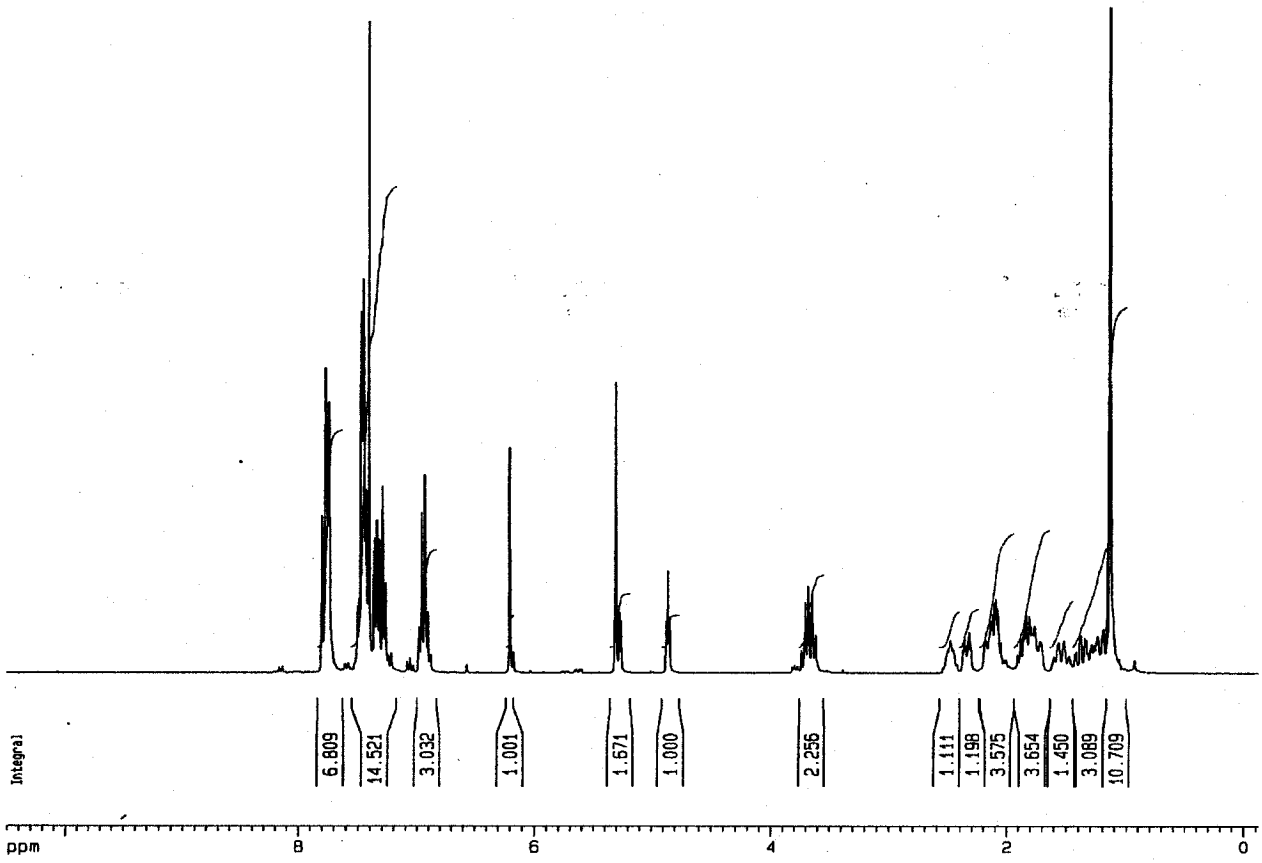
^{13}C NMR (75 MHz, $CDCl_3$)



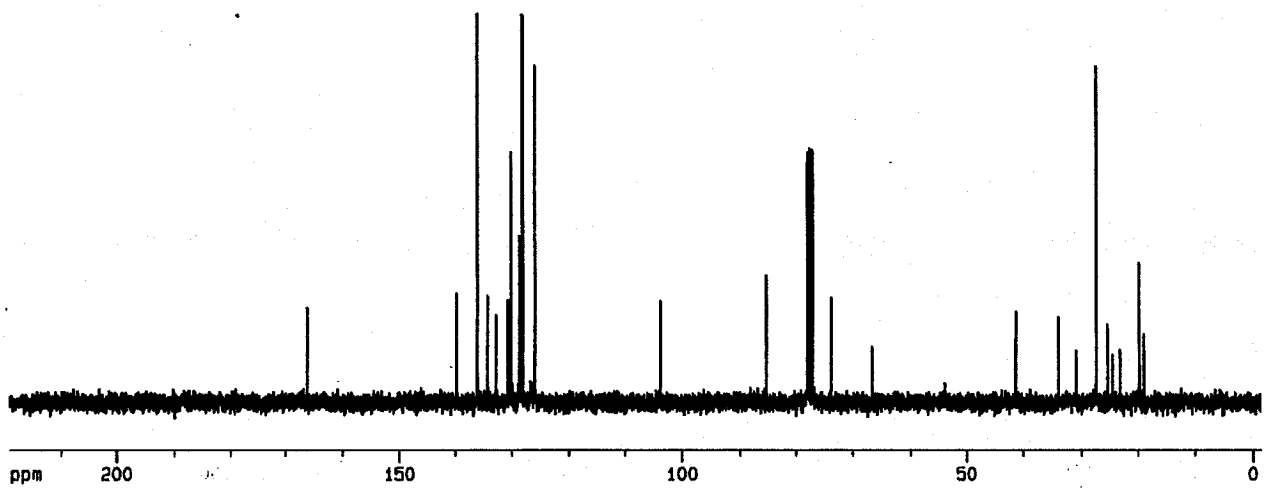


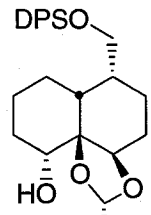
2.33

^{1}H NMR (300 MHz, $CDCl_3$)



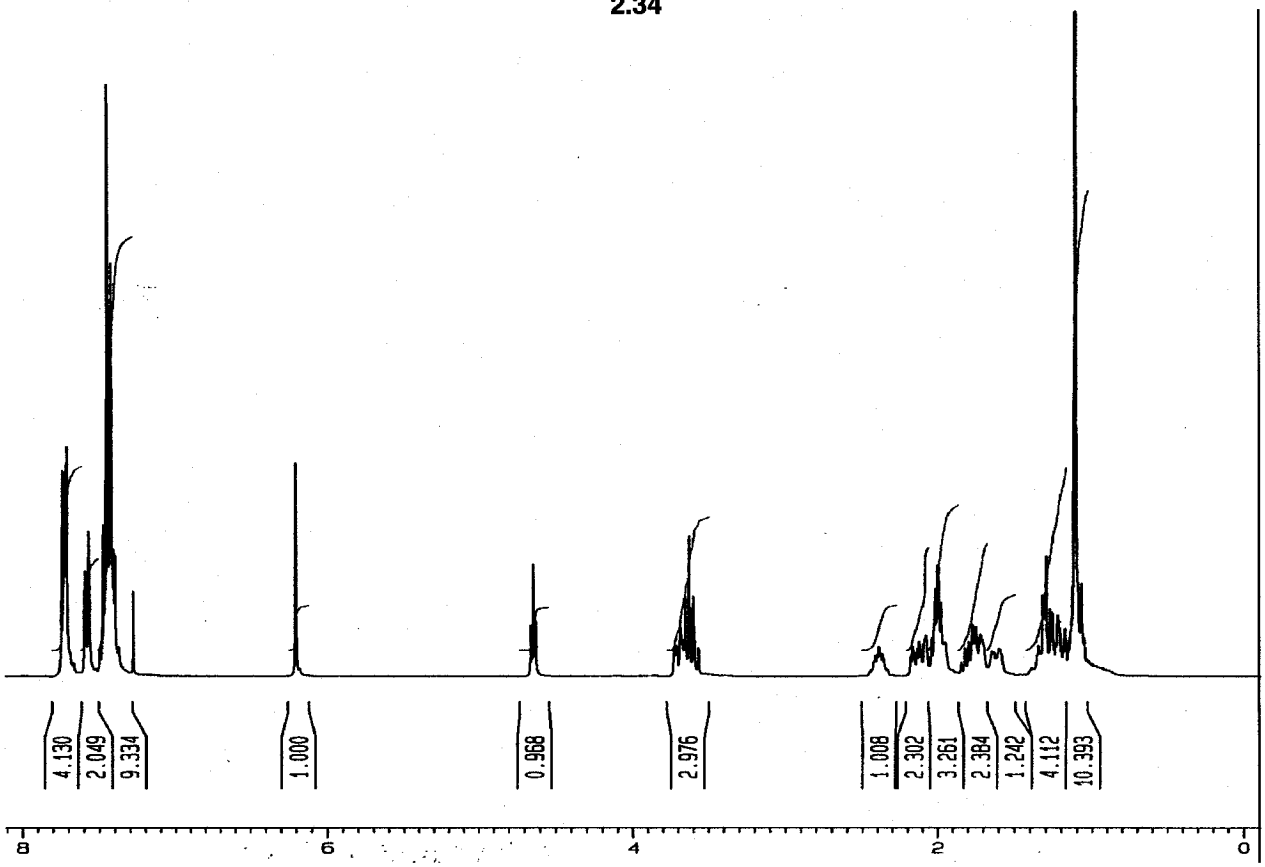
^{13}C NMR (75 MHz, $CDCl_3$)



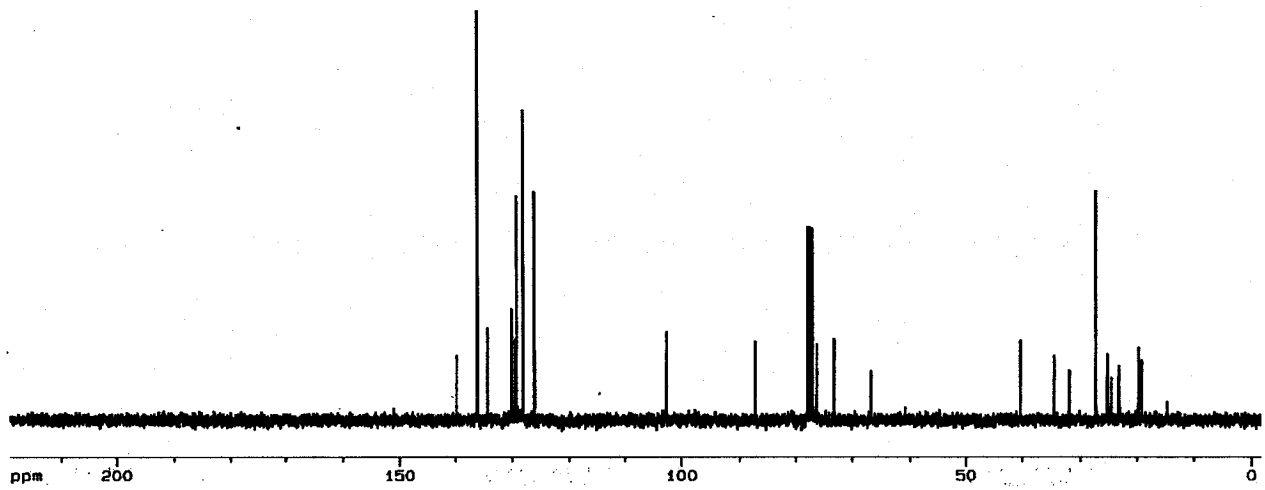


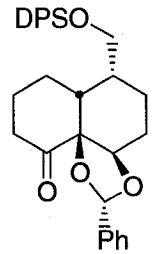
2.34

^{1}H NMR (300 MHz, $CDCl_3$)



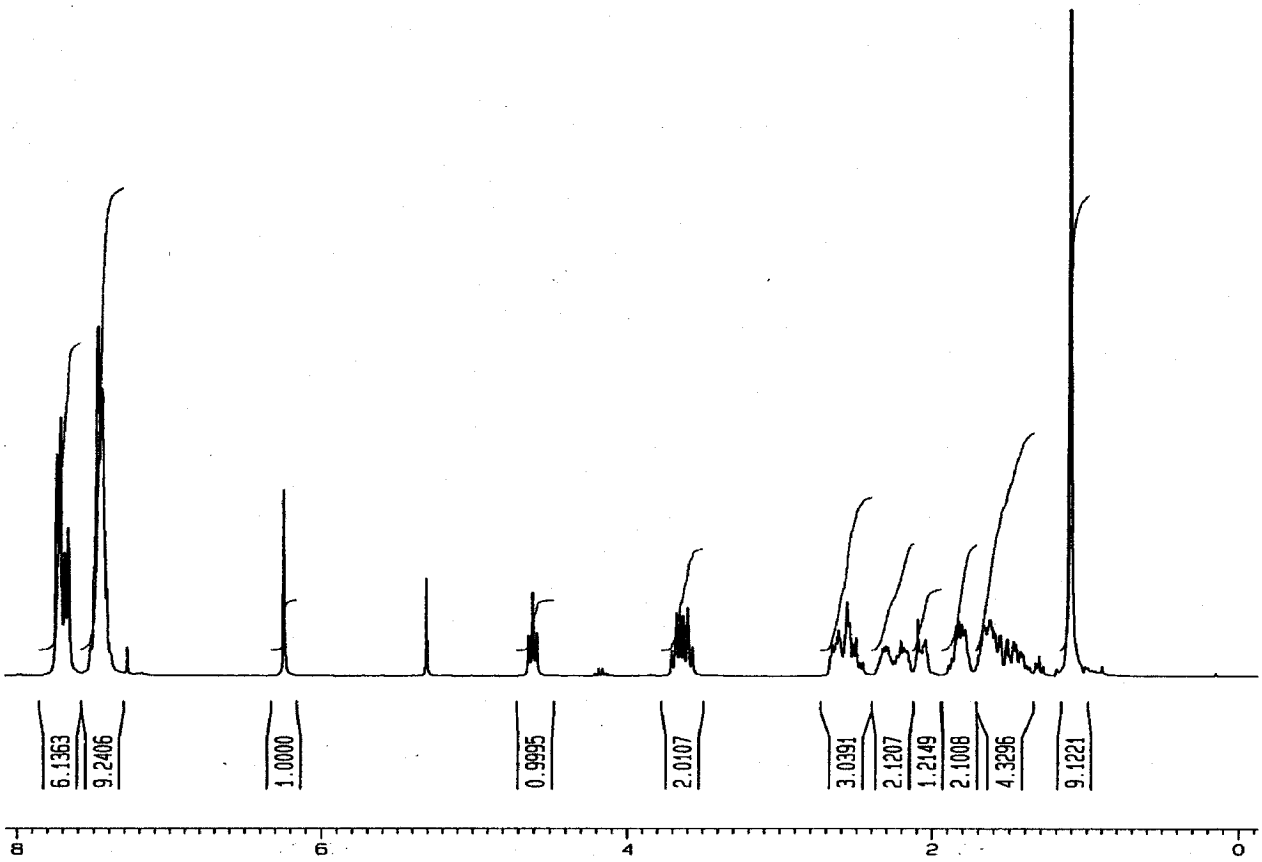
^{13}C NMR (75 MHz, $CDCl_3$)



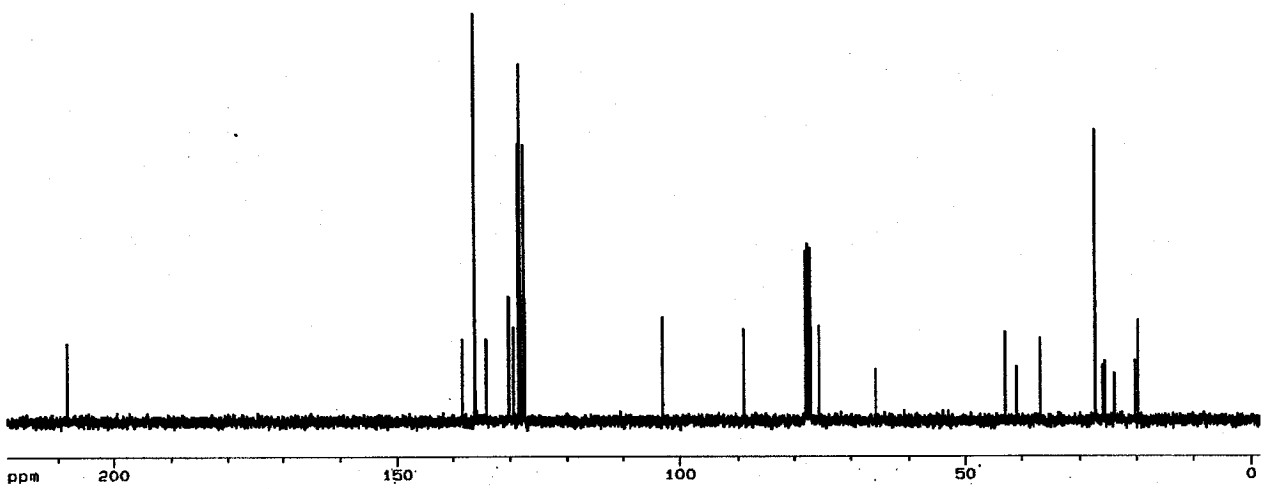


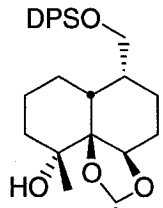
2.35

^{1}H NMR (300 MHz, $CDCl_3$)



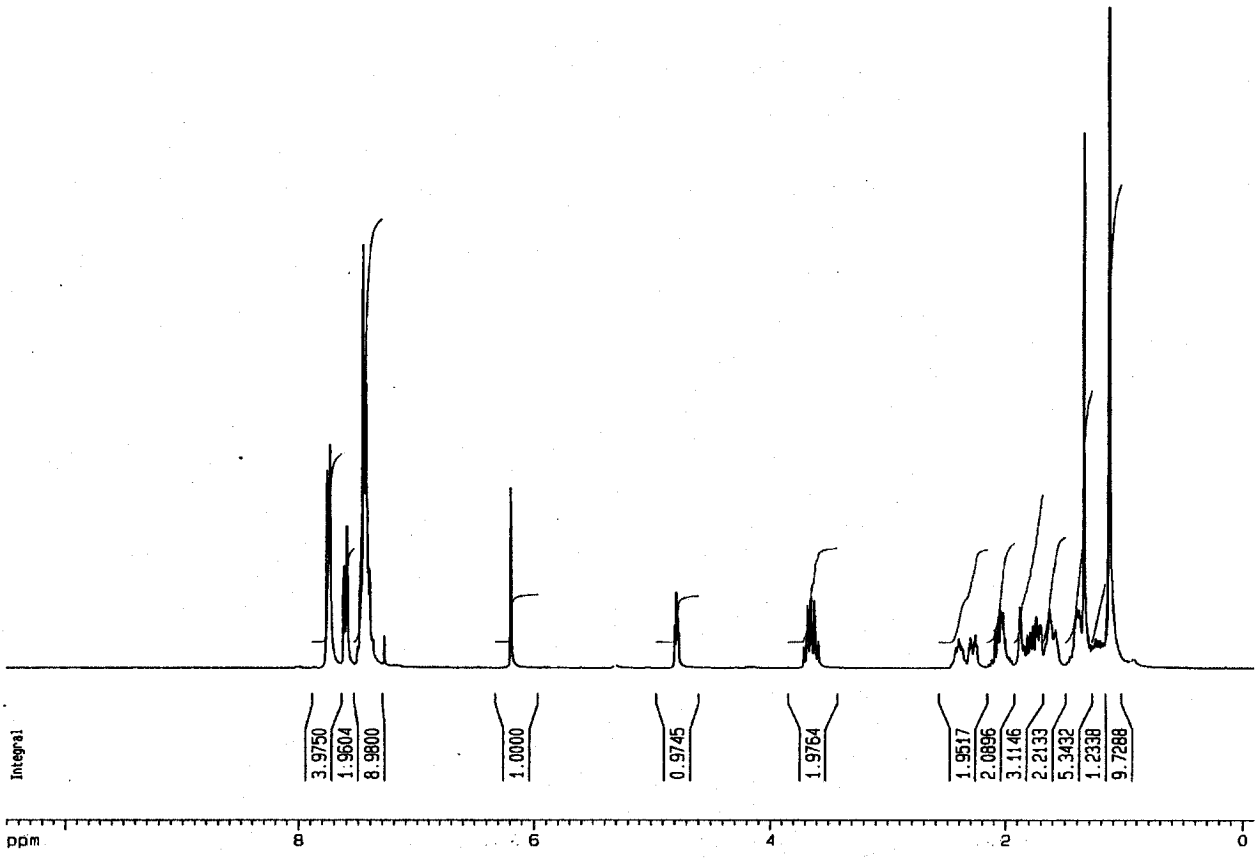
^{13}C NMR (75 MHz, $CDCl_3$)



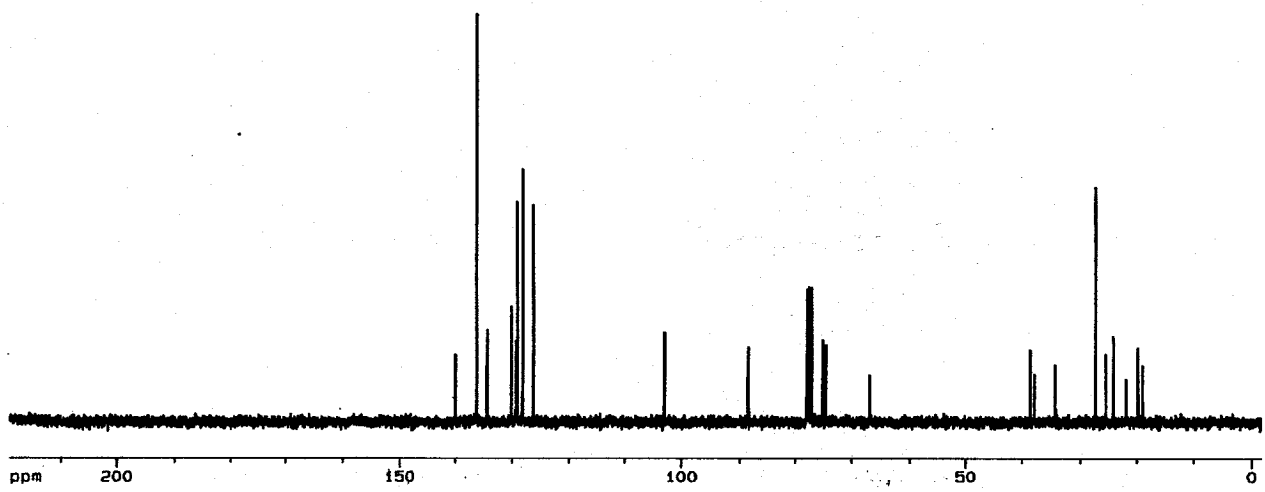


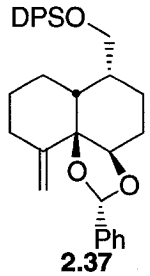
2.36

^{1}H NMR (300 MHz, $CDCl_3$)



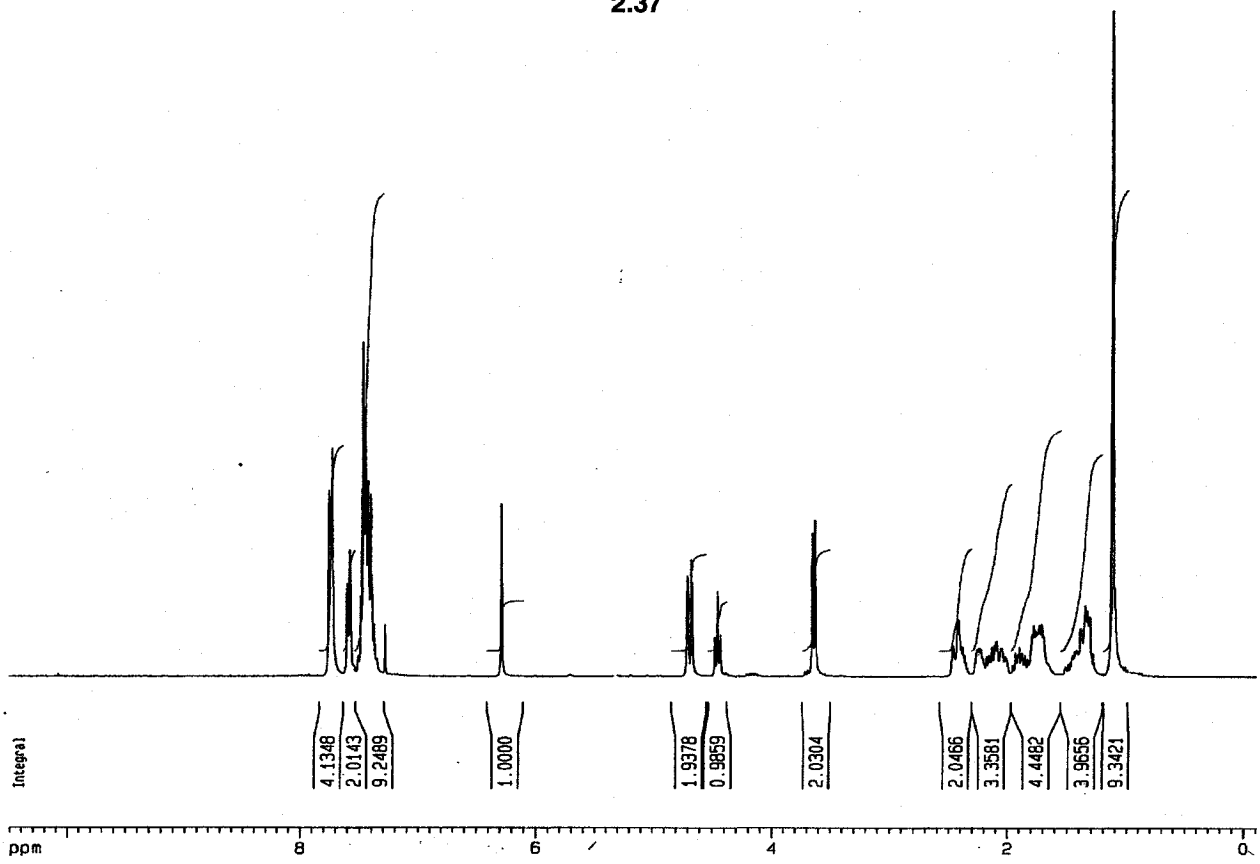
^{13}C NMR (75 MHz, $CDCl_3$)



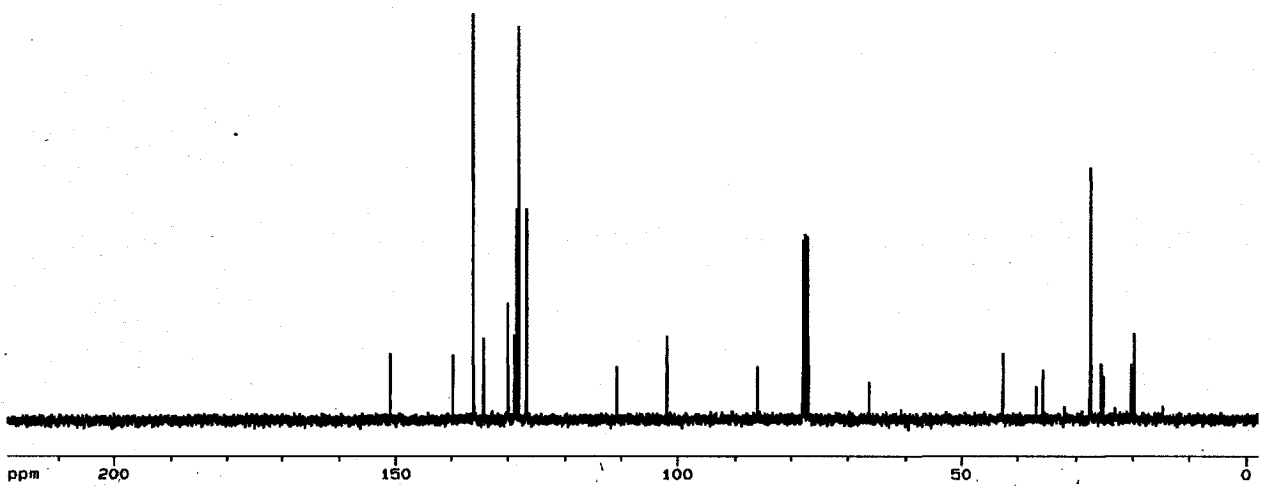


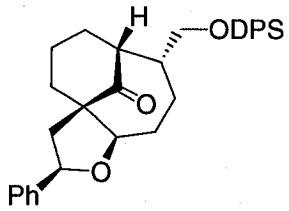
2.37

^{1}H NMR (300 MHz, $CDCl_3$)



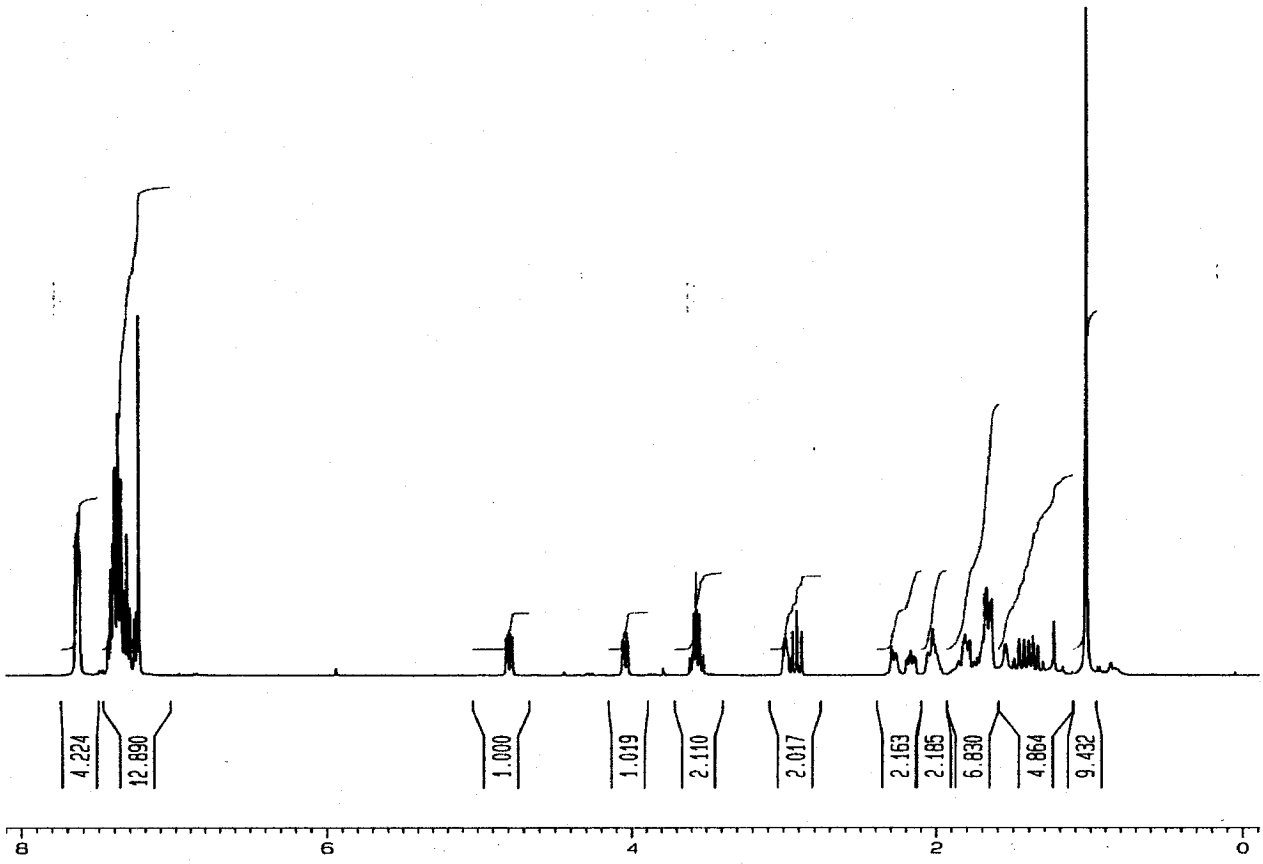
^{13}C NMR (75 MHz, $CDCl_3$)



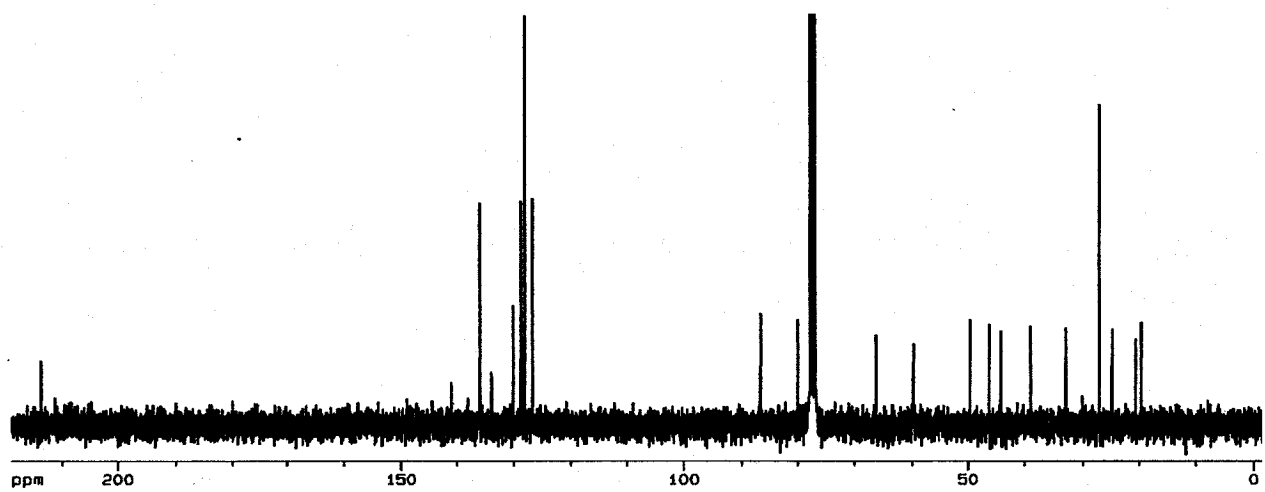


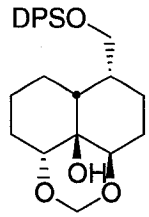
2.38

^{1}H NMR (300 MHz, $CDCl_3$)



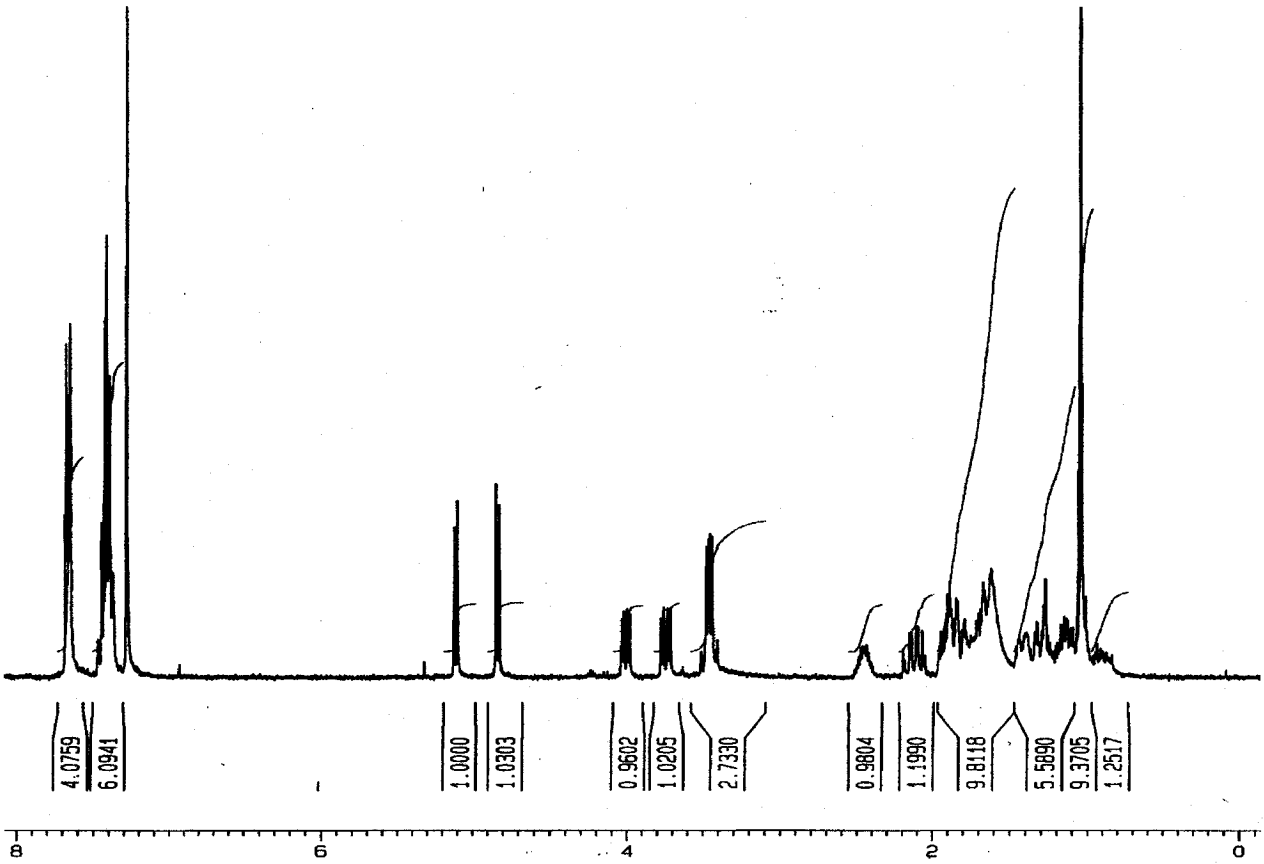
^{13}C NMR (75 MHz, $CDCl_3$)



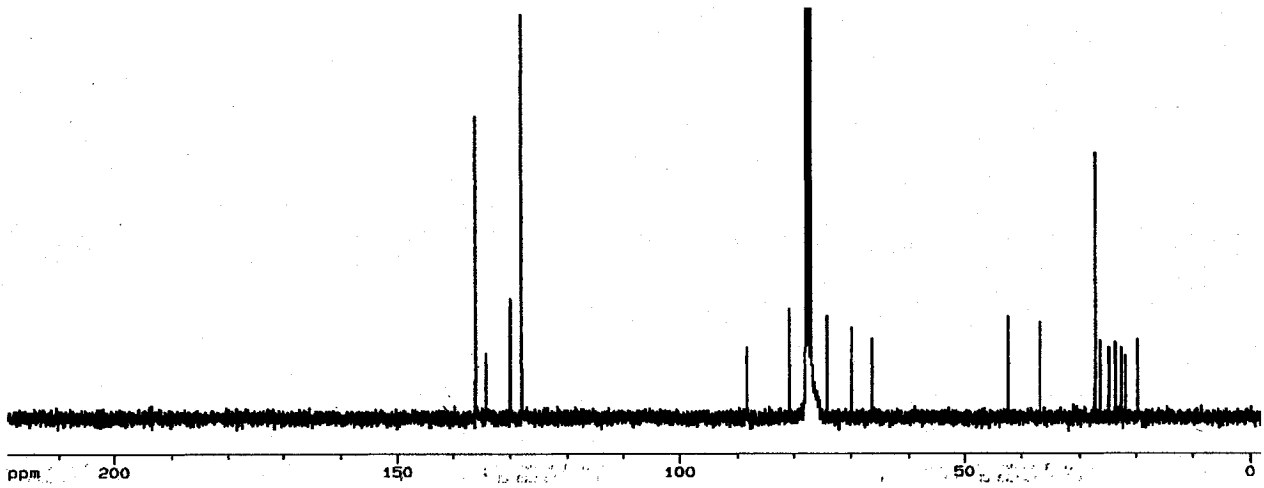


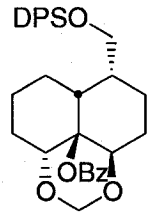
2.42

^{1}H NMR (300 MHz, $CDCl_3$)



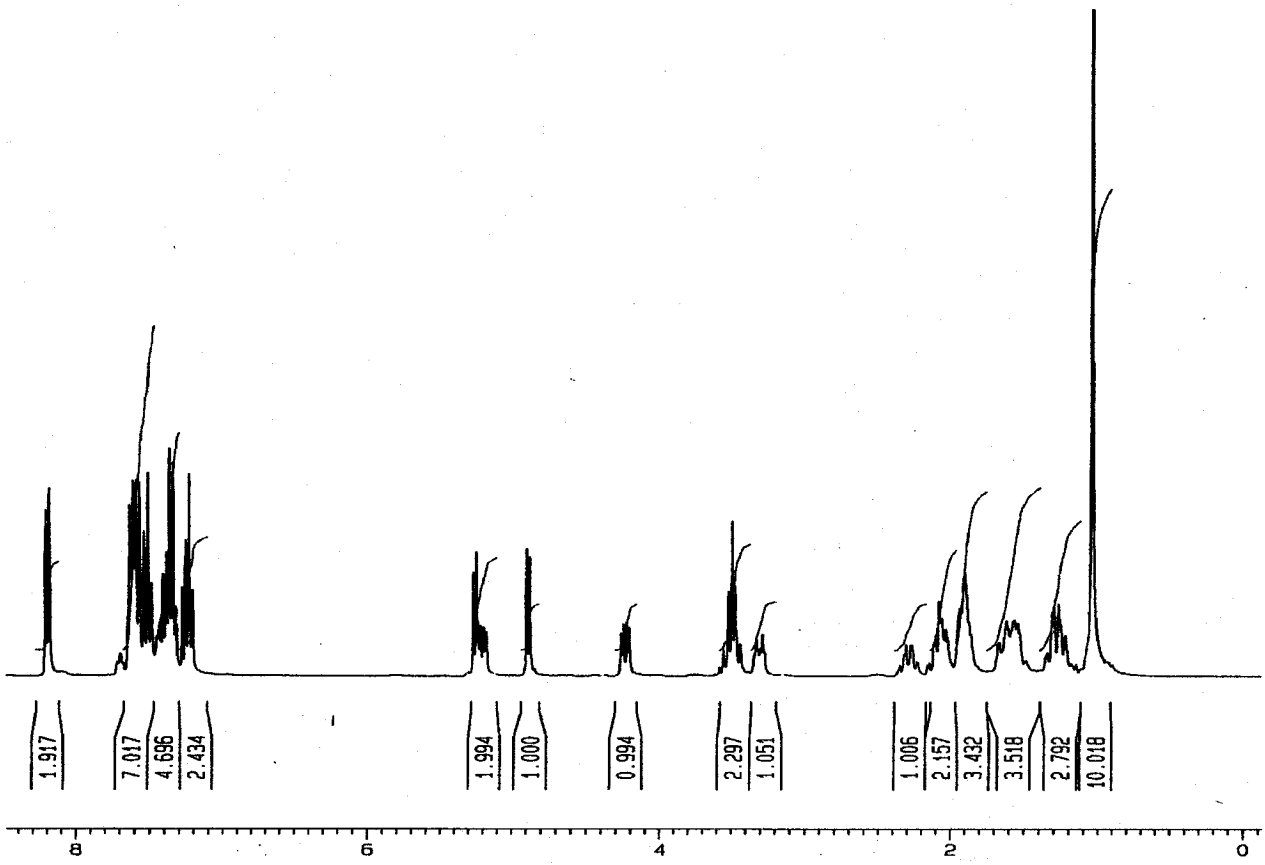
^{13}C NMR (75 MHz, $CDCl_3$)



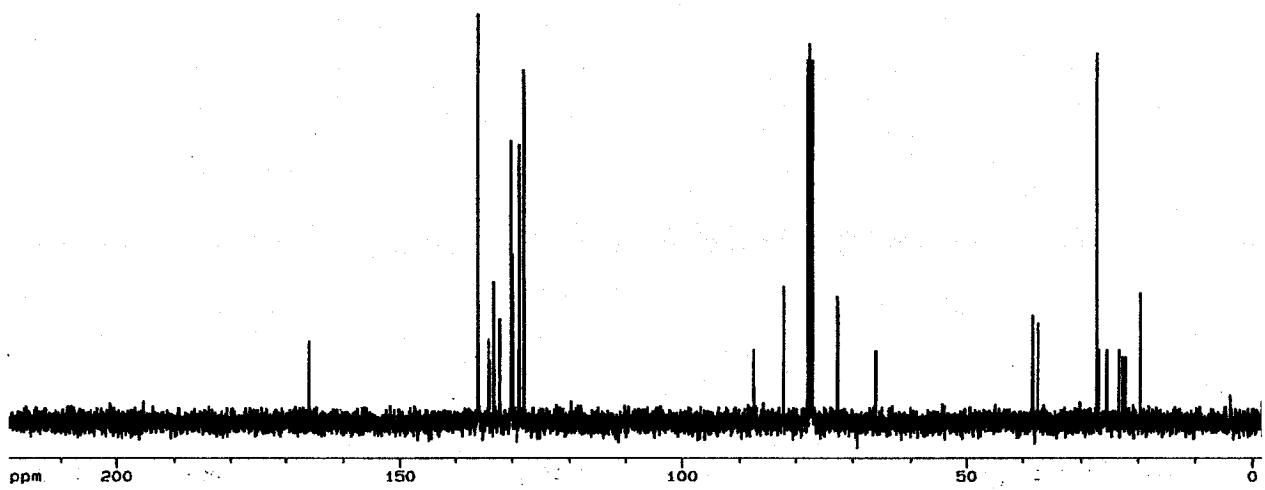


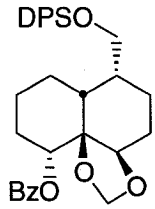
2.43

^{1}H NMR (300 MHz, $CDCl_3$)



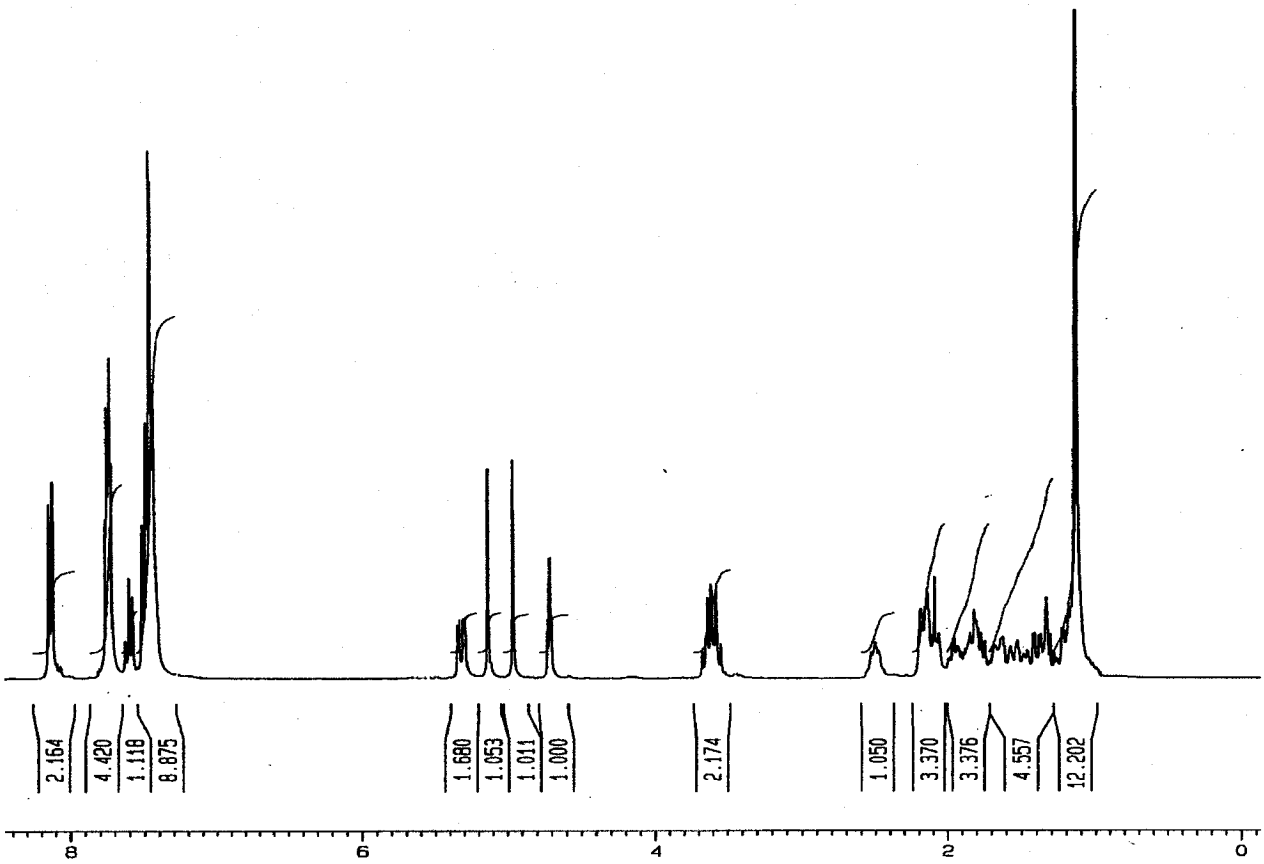
^{13}C NMR (75 MHz, $CDCl_3$)



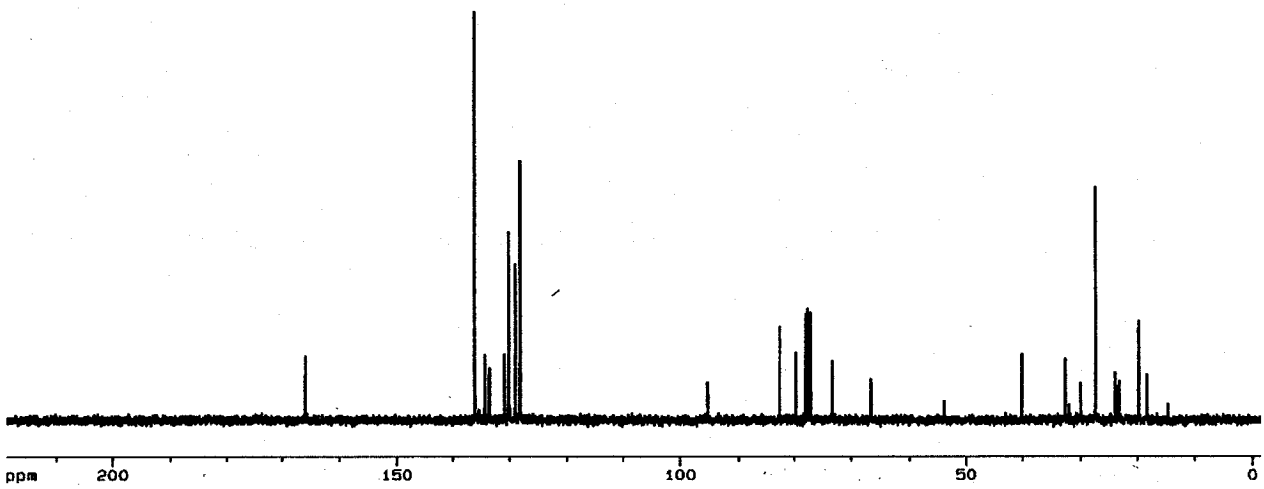


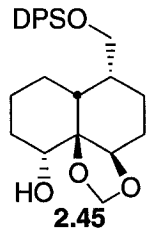
2.44

^{1}H NMR (300 MHz, $CDCl_3$)



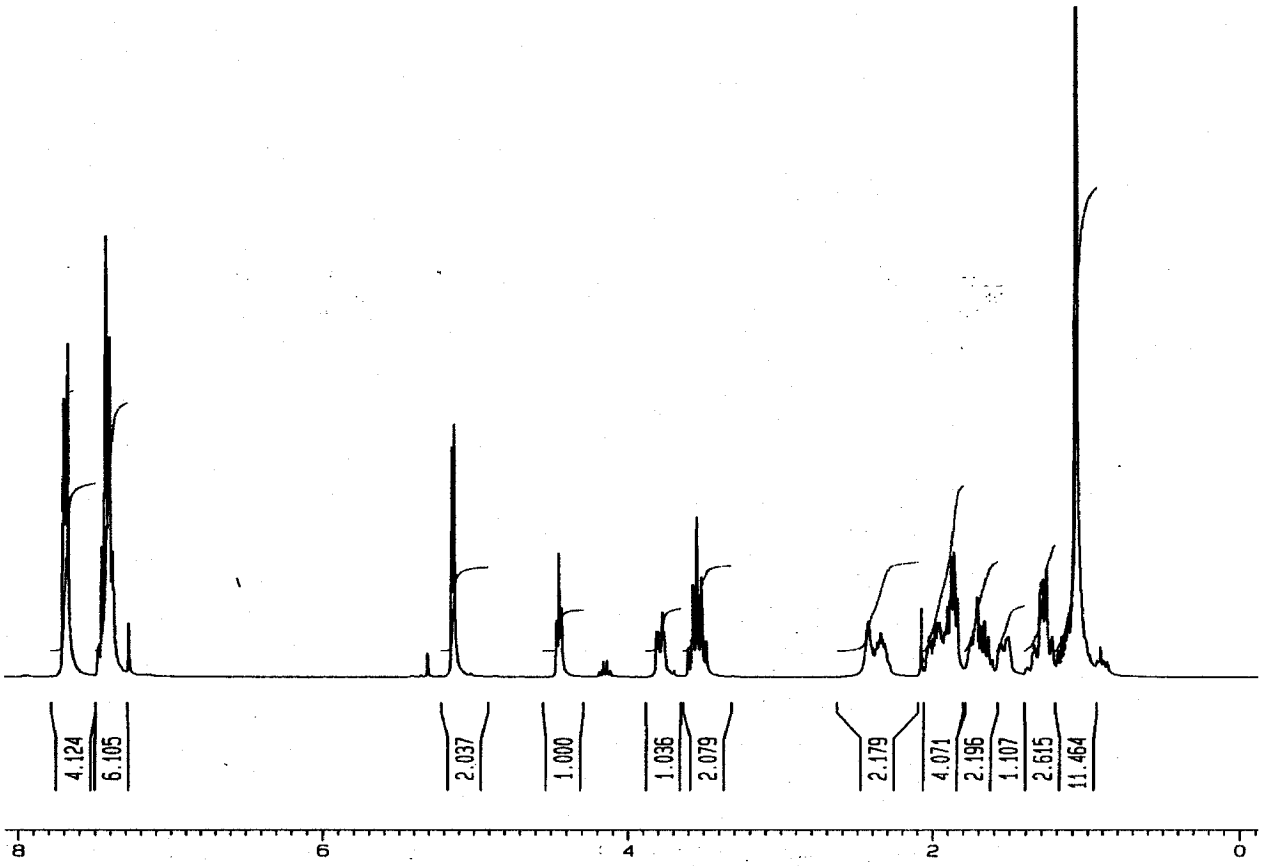
^{13}C NMR (75 MHz, $CDCl_3$)



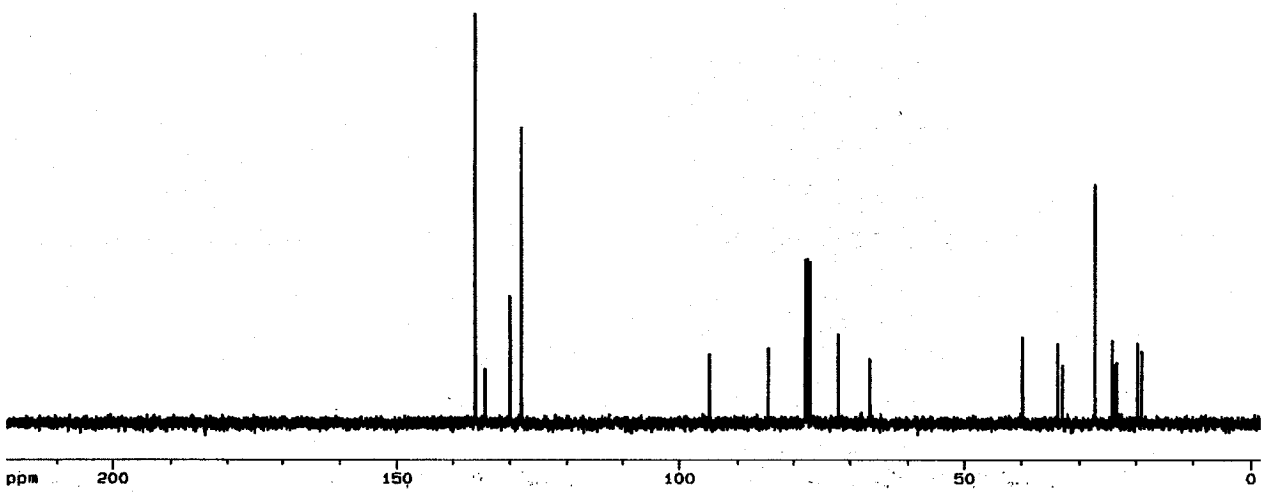


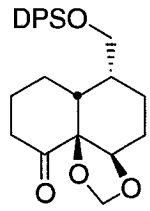
2.45

^{1}H NMR (300 MHz, $CDCl_3$)



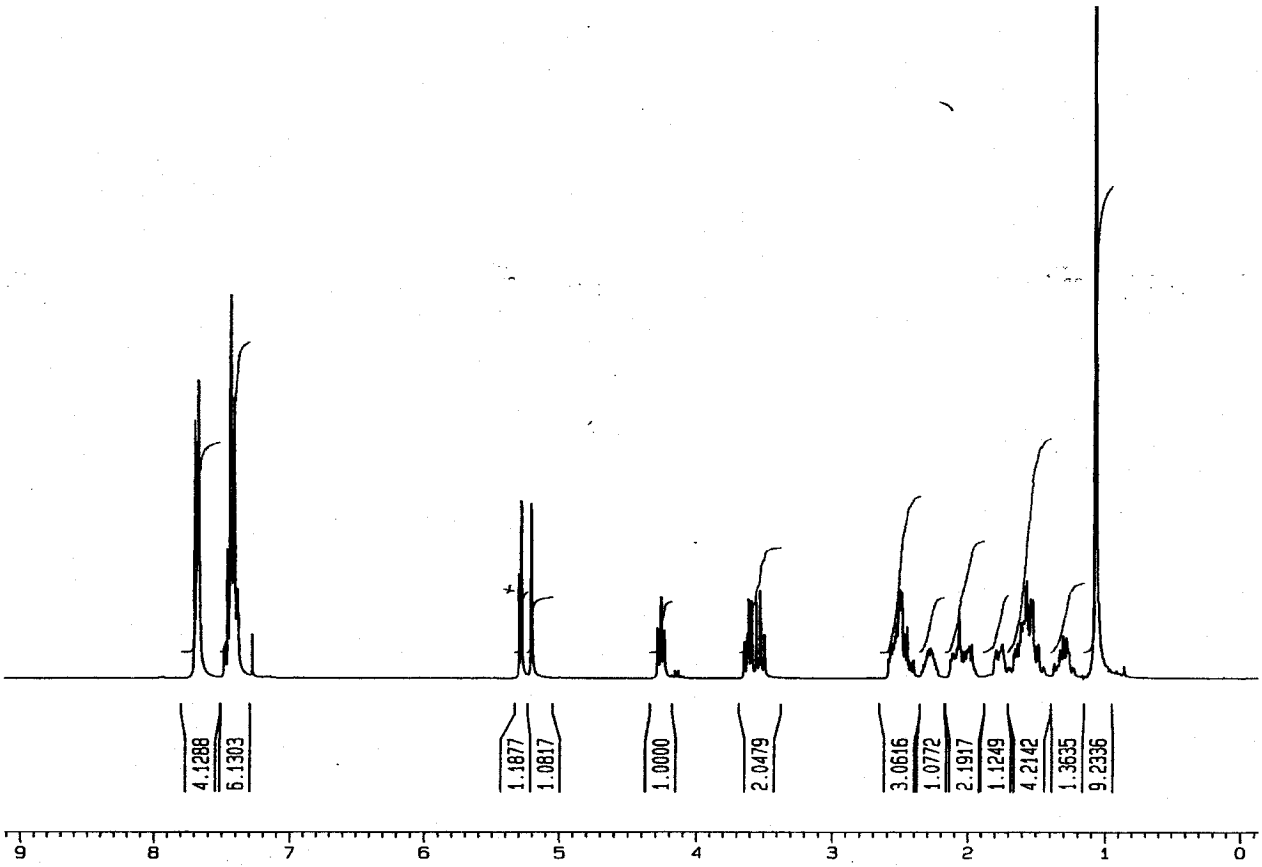
^{13}C NMR (75 MHz, $CDCl_3$)



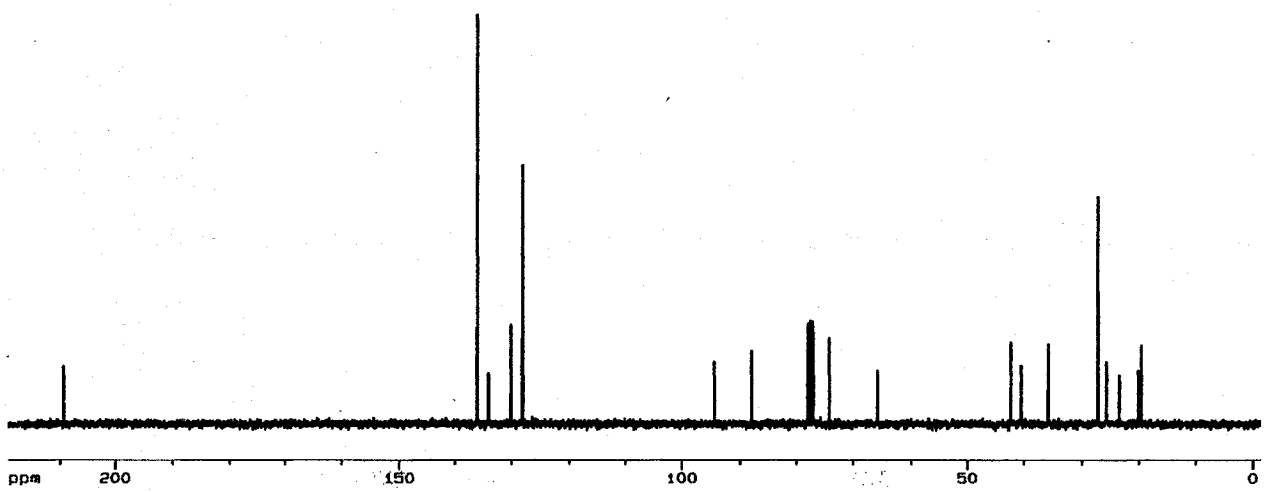


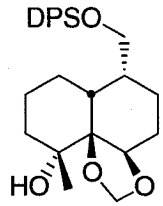
2.46

^{1}H NMR (300 MHz, $CDCl_3$)



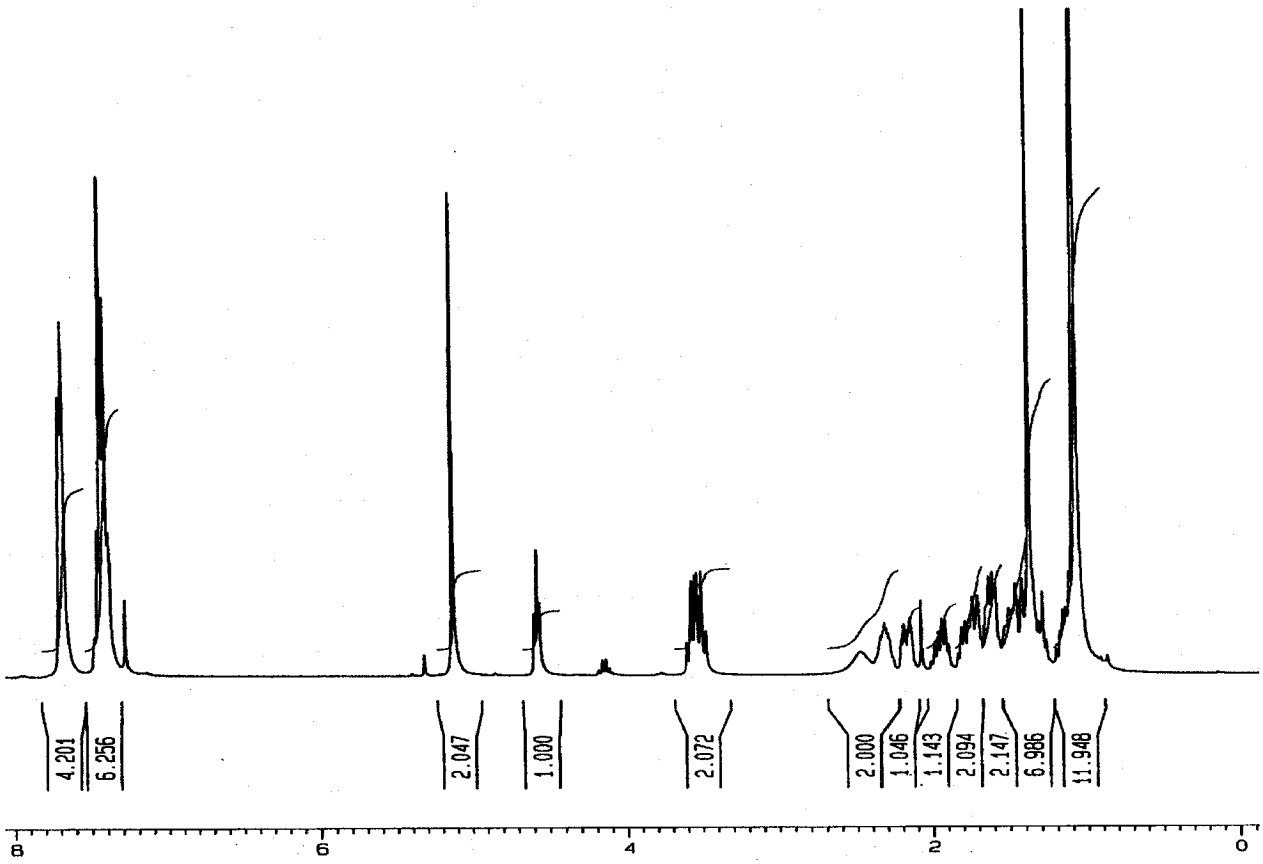
^{13}C NMR (75 MHz, $CDCl_3$)



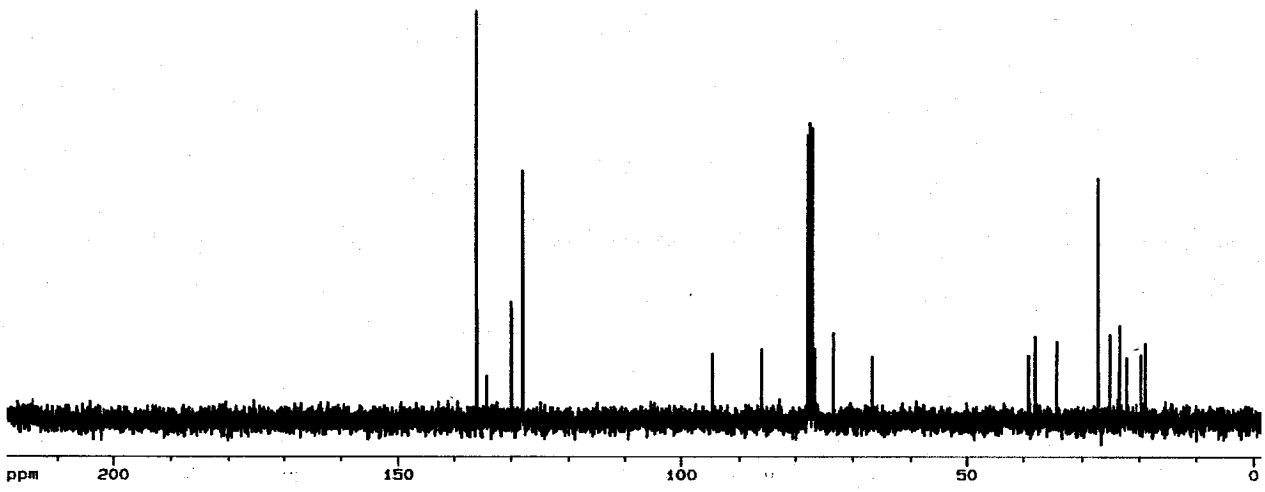


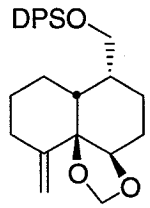
2.47

^{1}H NMR (300 MHz, $CDCl_3$)



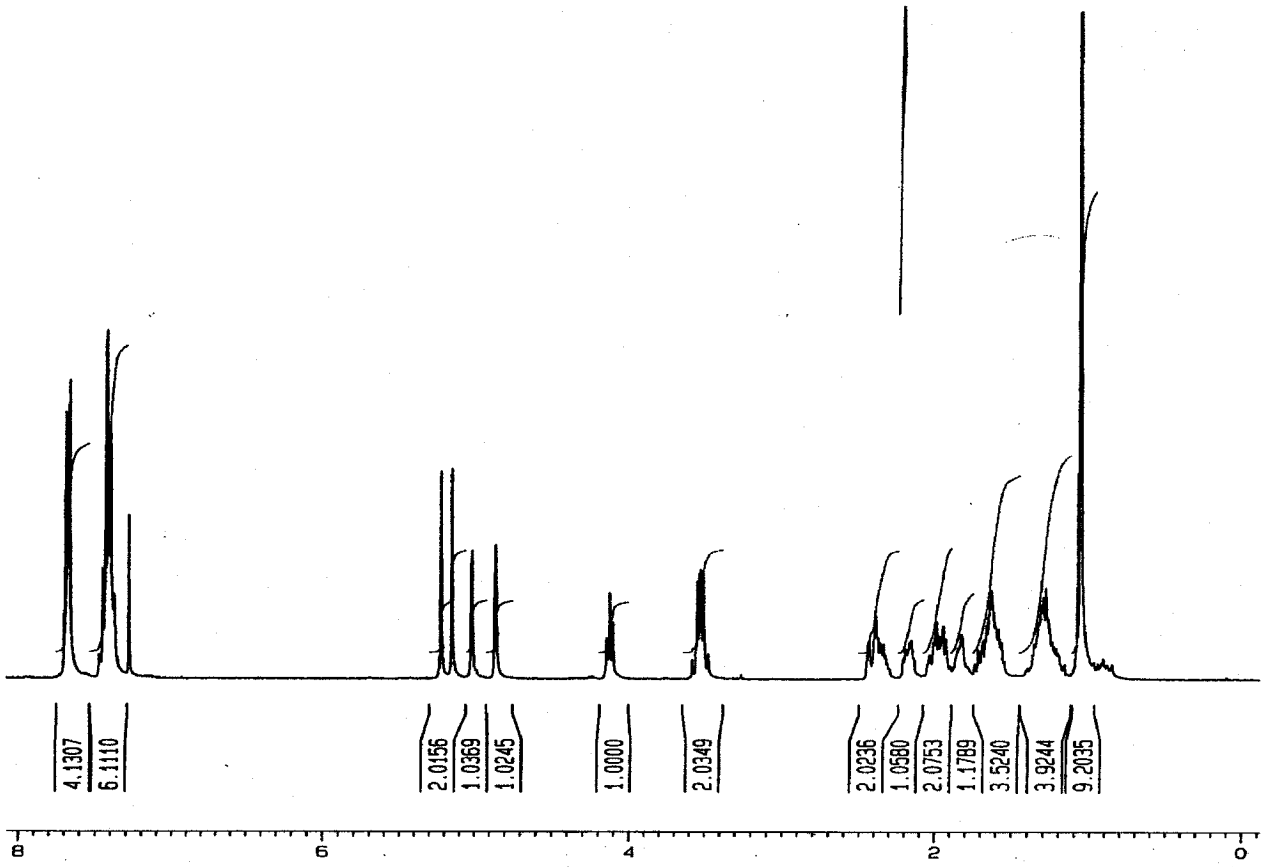
^{13}C NMR (75 MHz, $CDCl_3$)



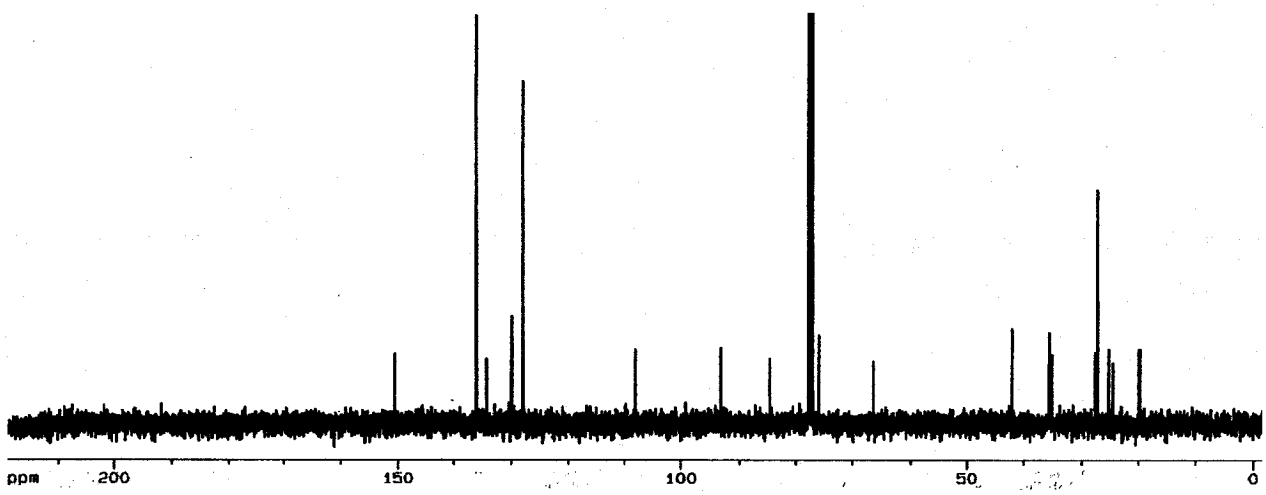


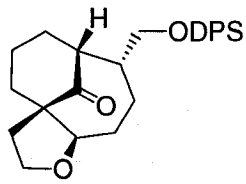
2.48

^{1}H NMR (300 MHz, $CDCl_3$)



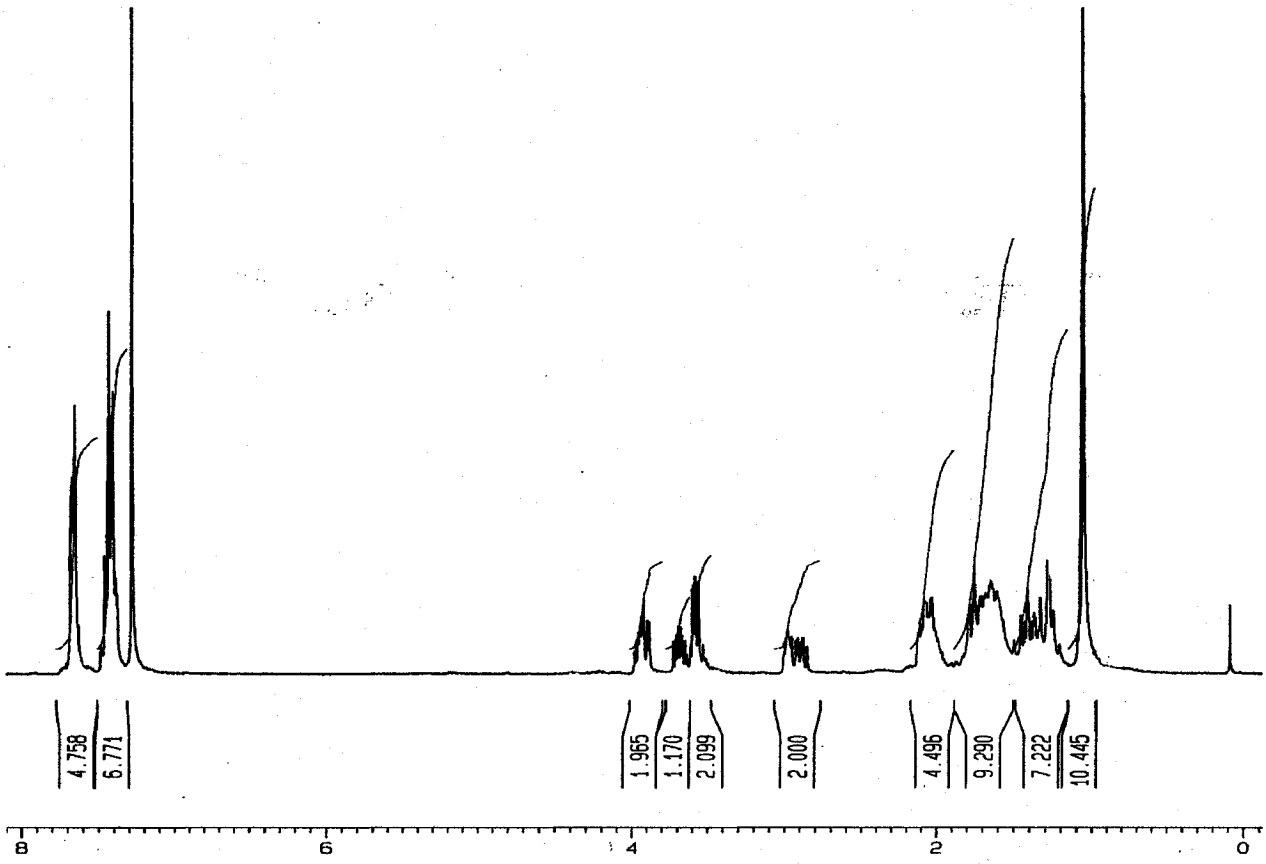
^{13}C NMR (75 MHz, $CDCl_3$)



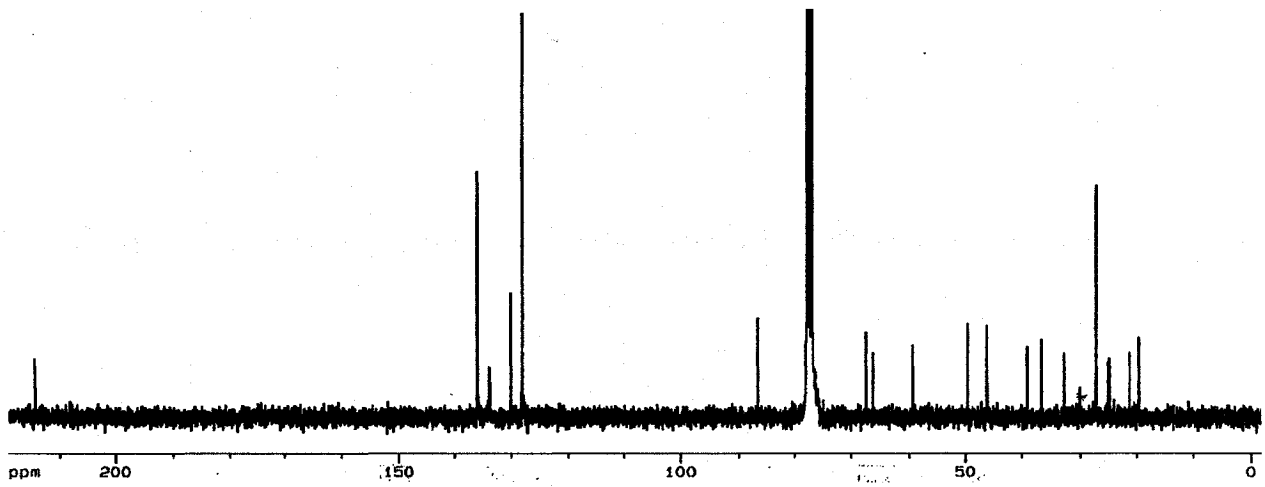


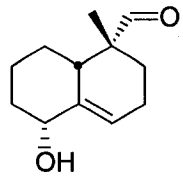
2.49

^{1}H NMR (300 MHz, $CDCl_3$)



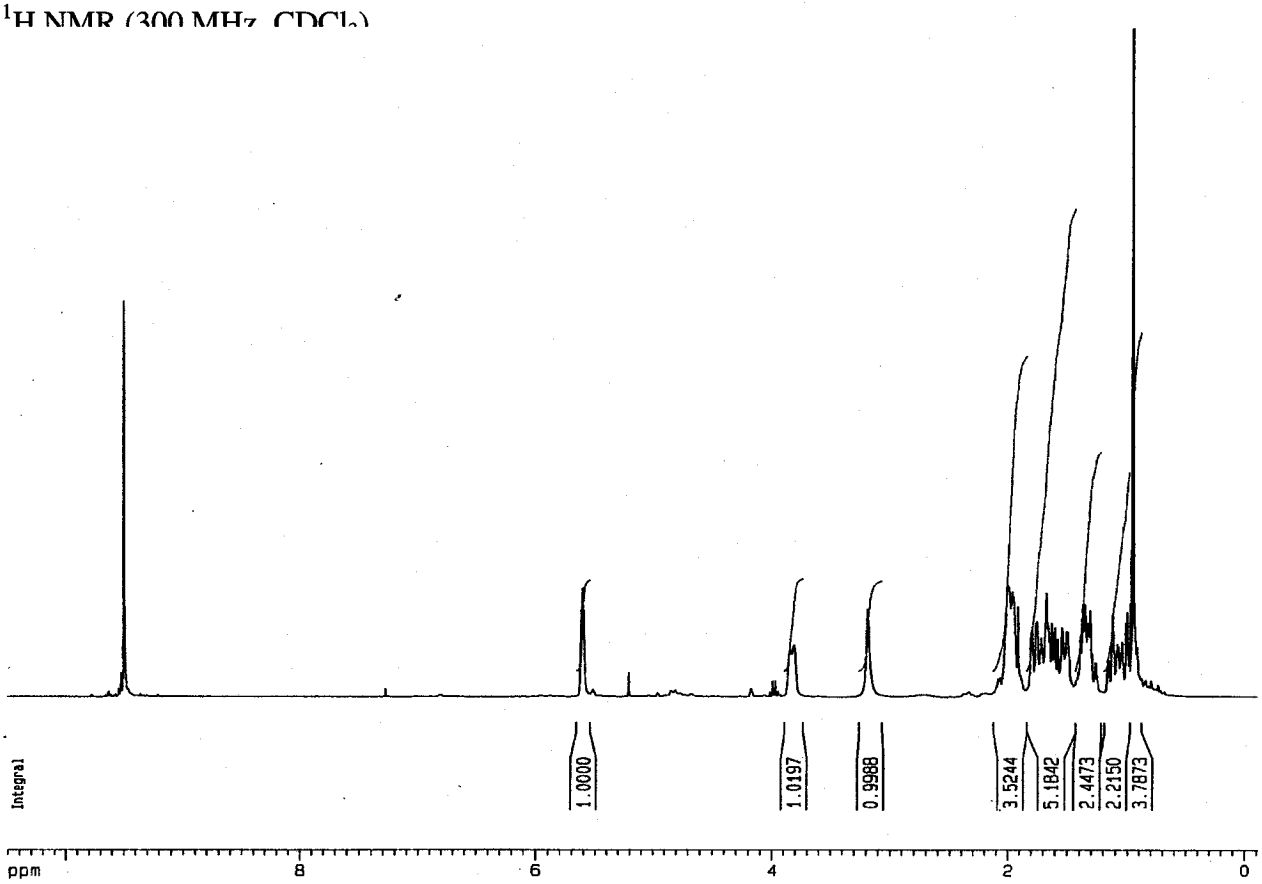
^{13}C NMR (75 MHz, $CDCl_3$)



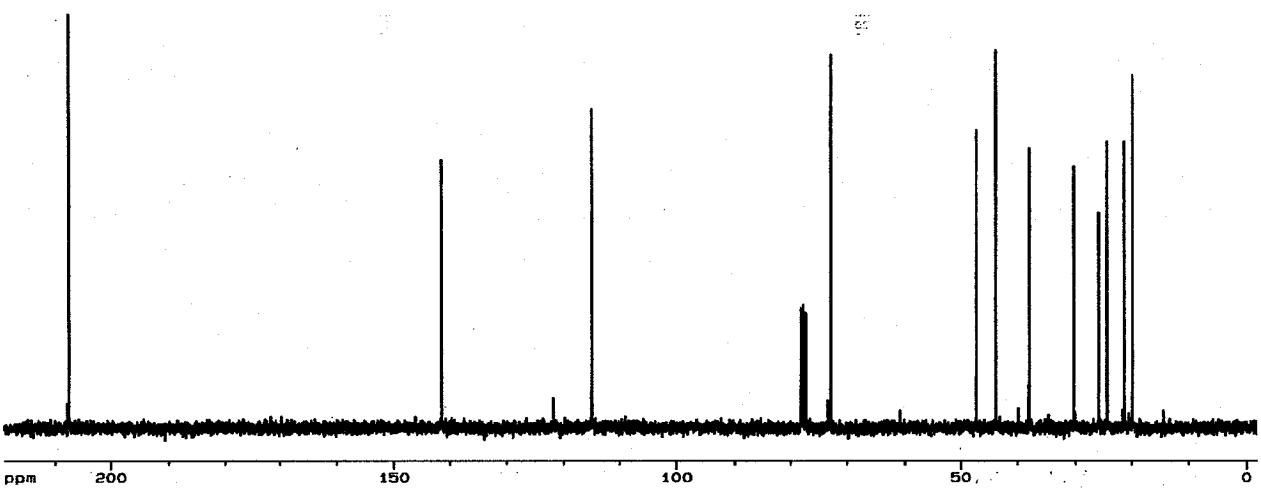


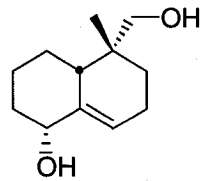
2.51

^{1}H NMR (300 MHz, $CDCl_3$)



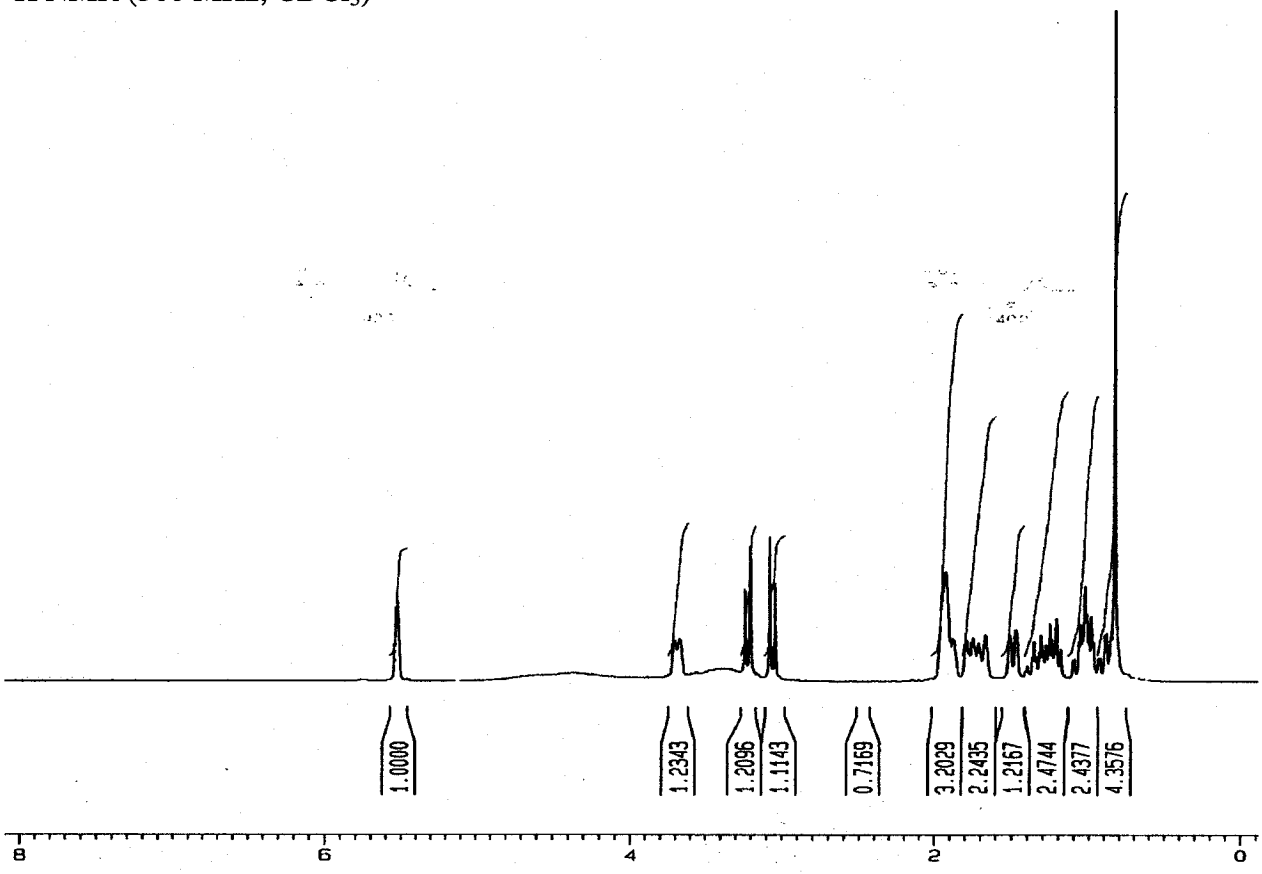
^{13}C NMR (75 MHz, $CDCl_3$)



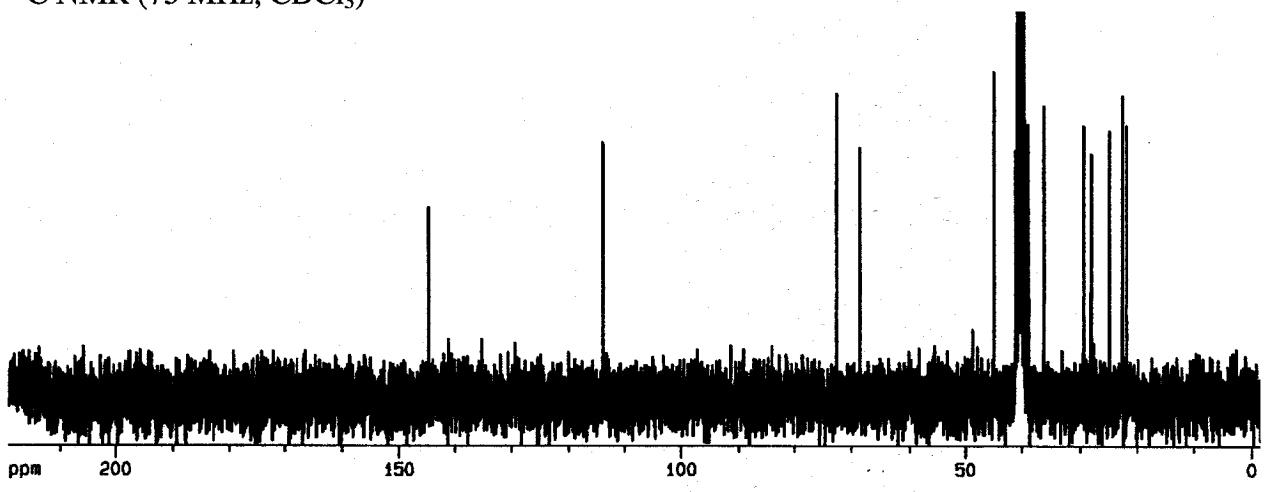


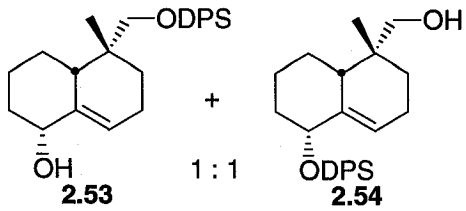
2.52

^{1}H NMR (300 MHz, $CDCl_3$)

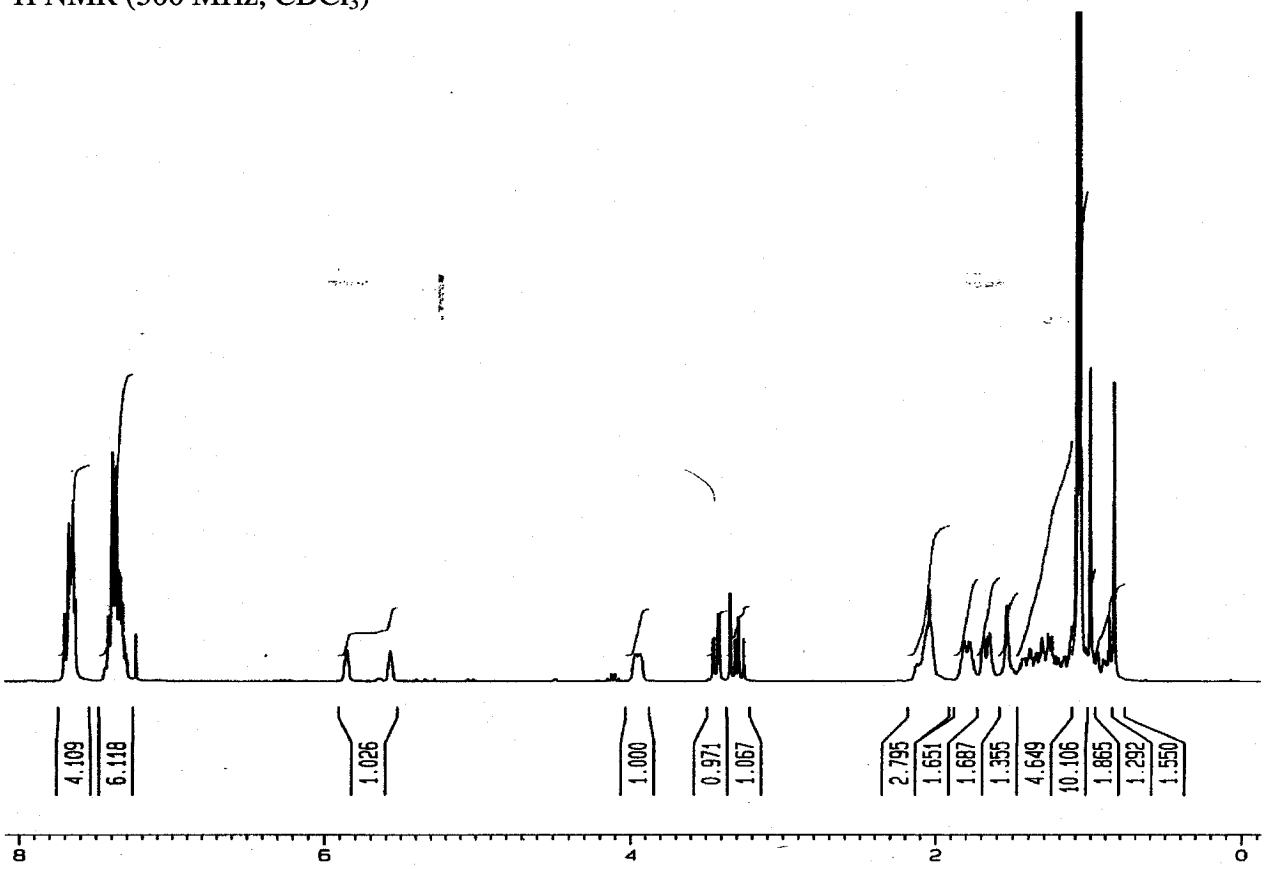


^{13}C NMR (75 MHz, $CDCl_3$)

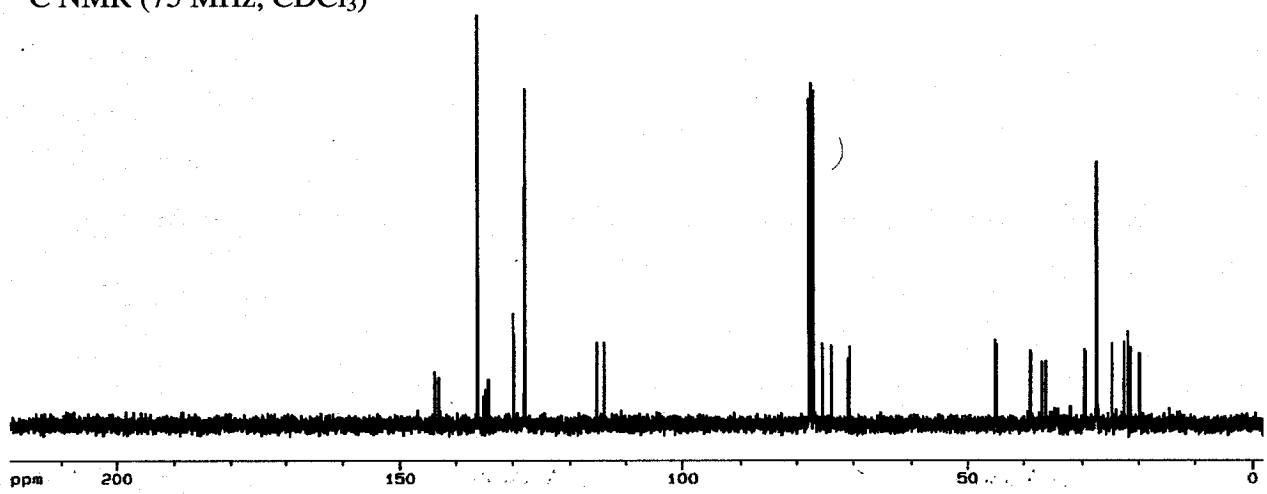


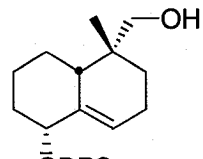


^{1}H NMR (300 MHz, $CDCl_3$)



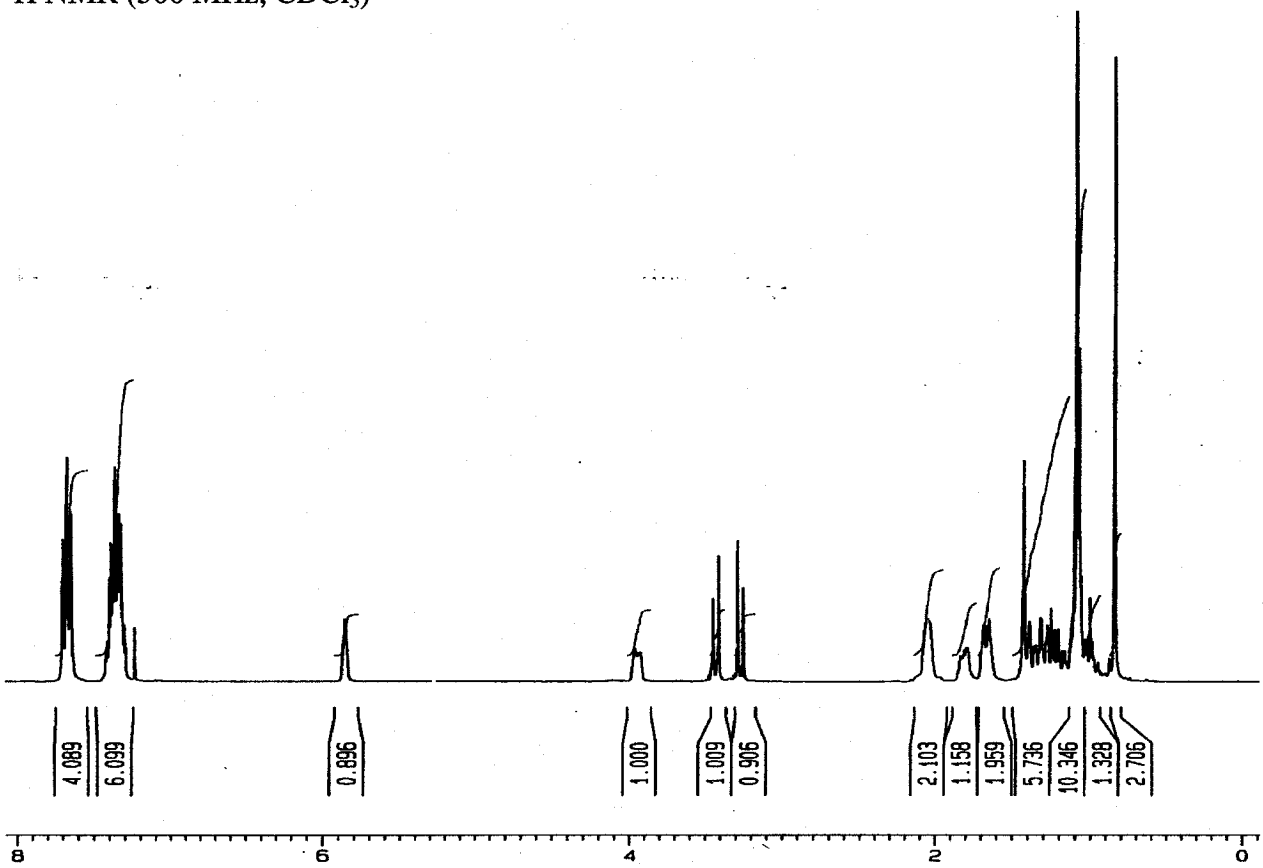
^{13}C NMR (75 MHz, $CDCl_3$)



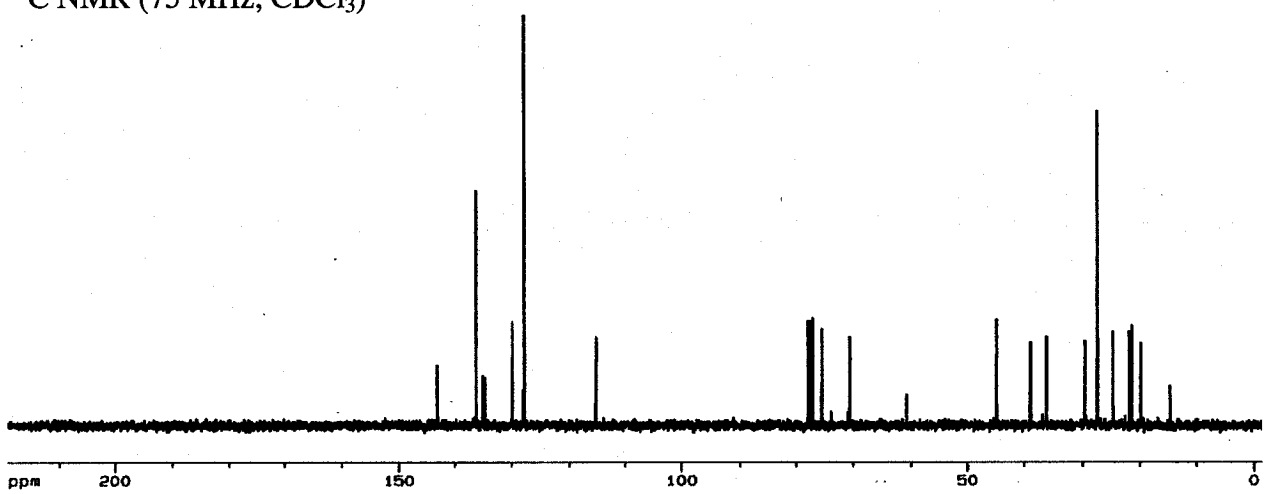


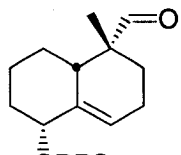
2.54

^{1}H NMR (300 MHz, $CDCl_3$)



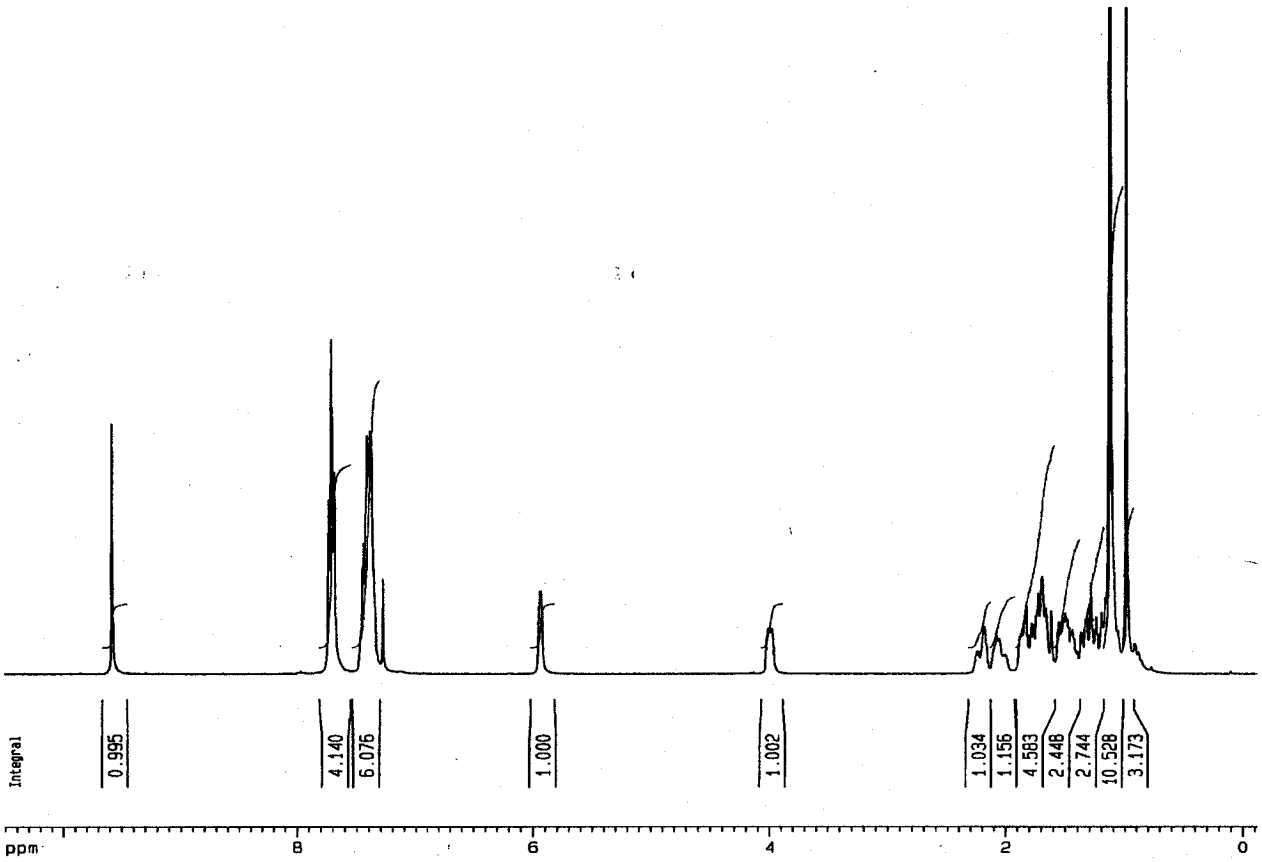
^{13}C NMR (75 MHz, $CDCl_3$)



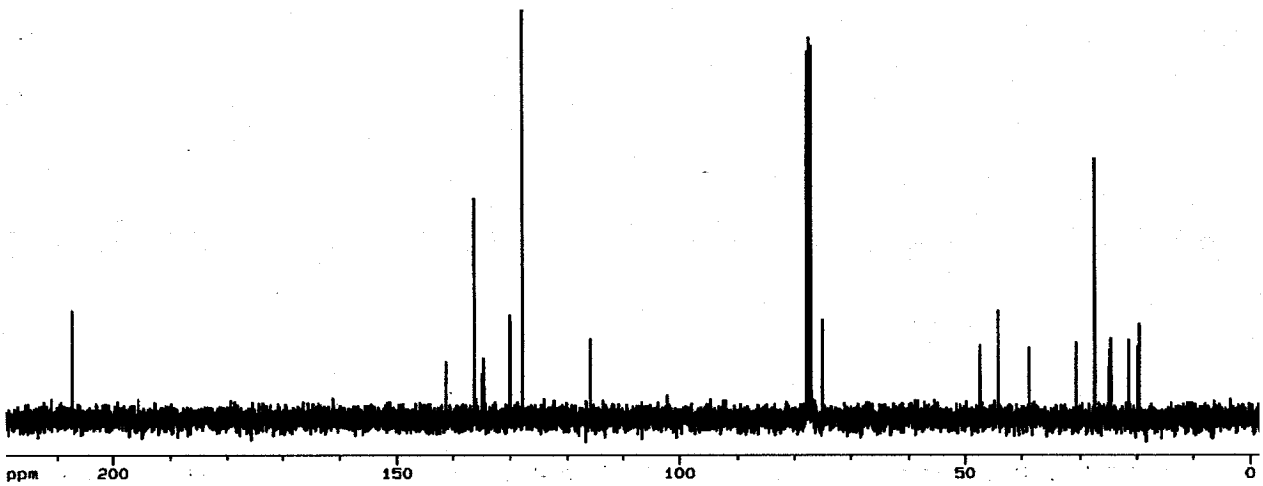


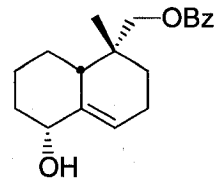
2.55

^{1}H NMR (300 MHz, $CDCl_3$)



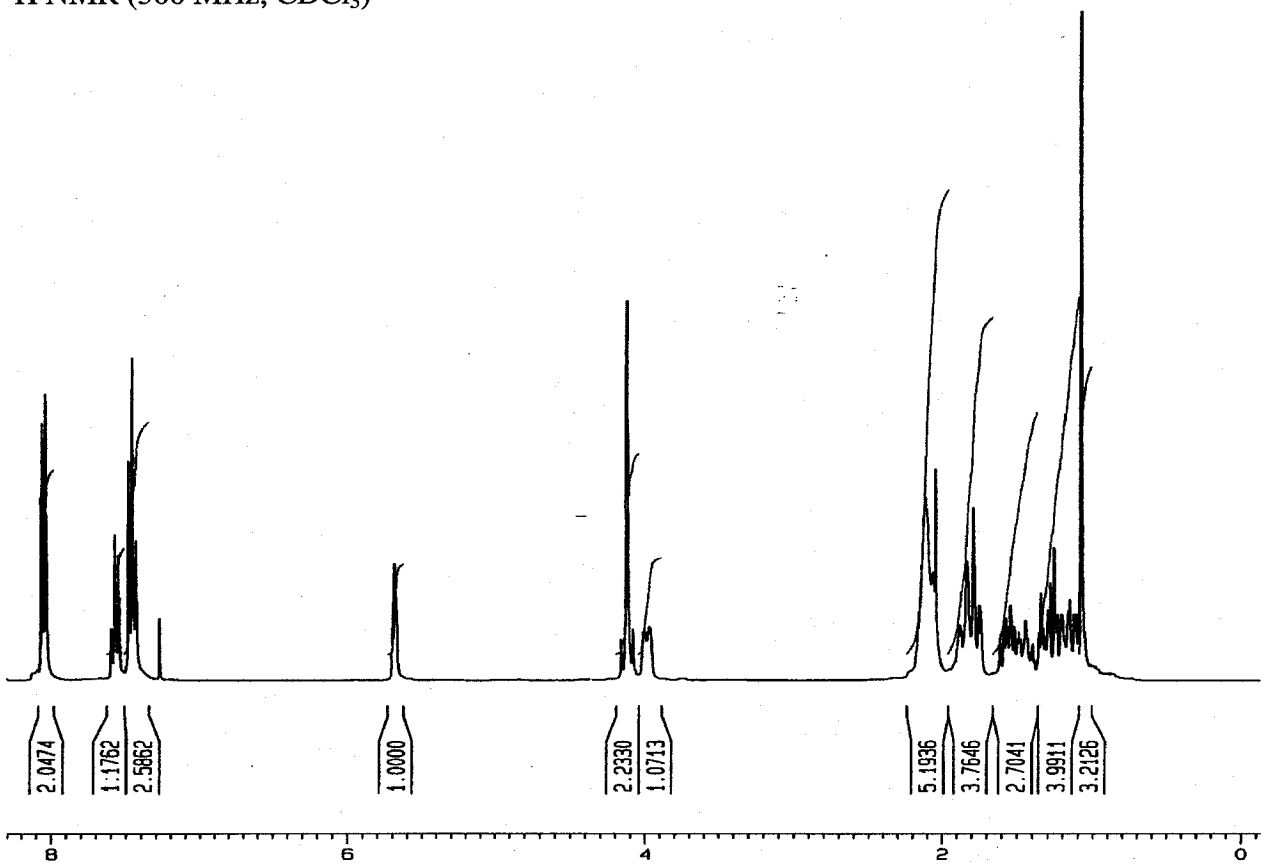
^{13}C NMR (75 MHz, $CDCl_3$)



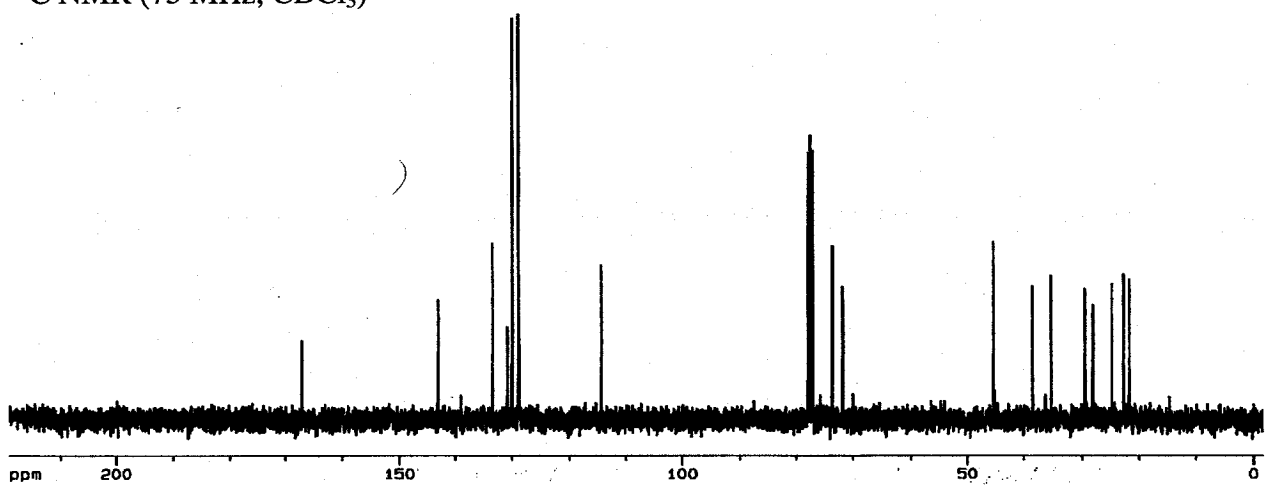


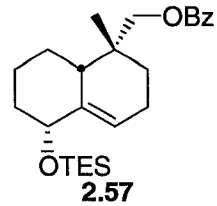
2.56

^{1}H NMR (300 MHz, $CDCl_3$)



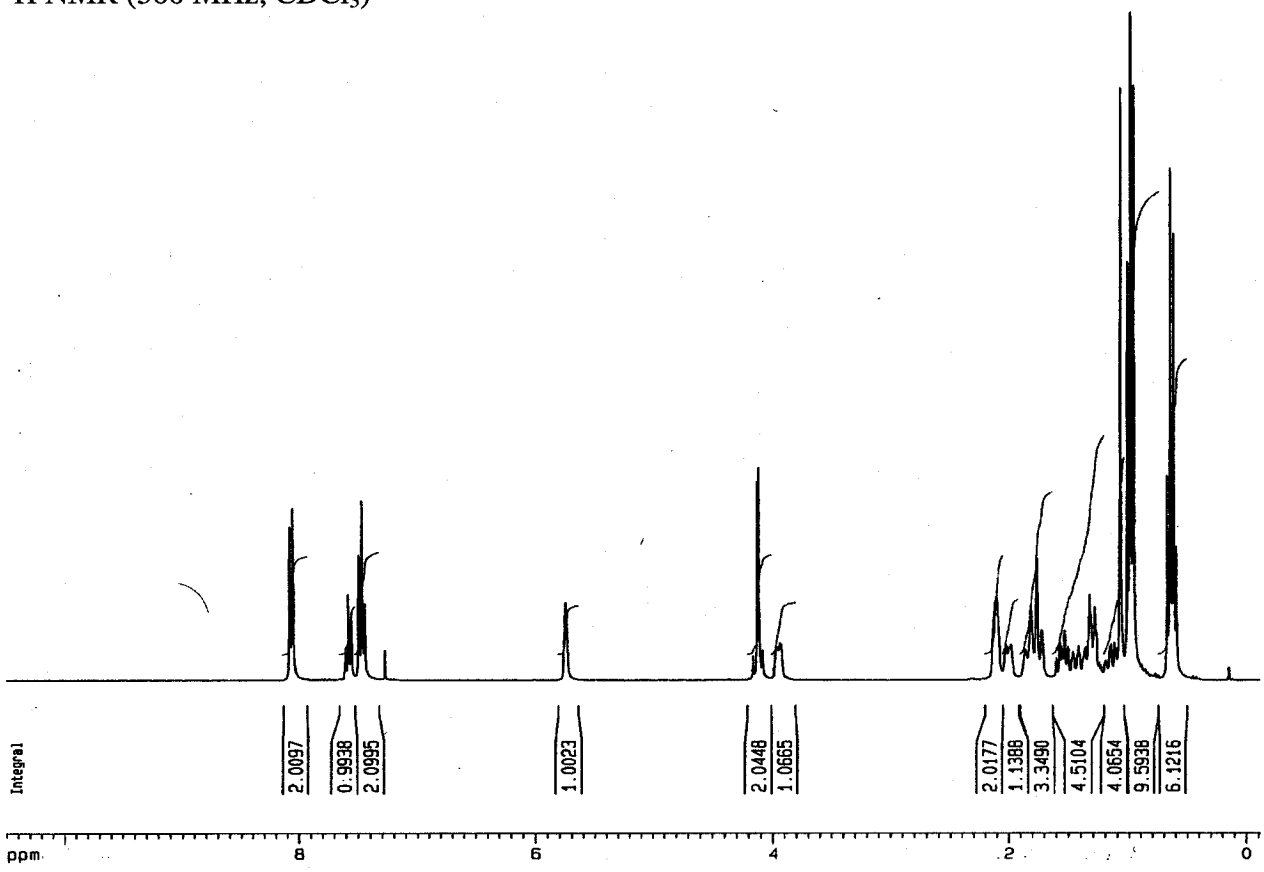
^{13}C NMR (75 MHz, $CDCl_3$)



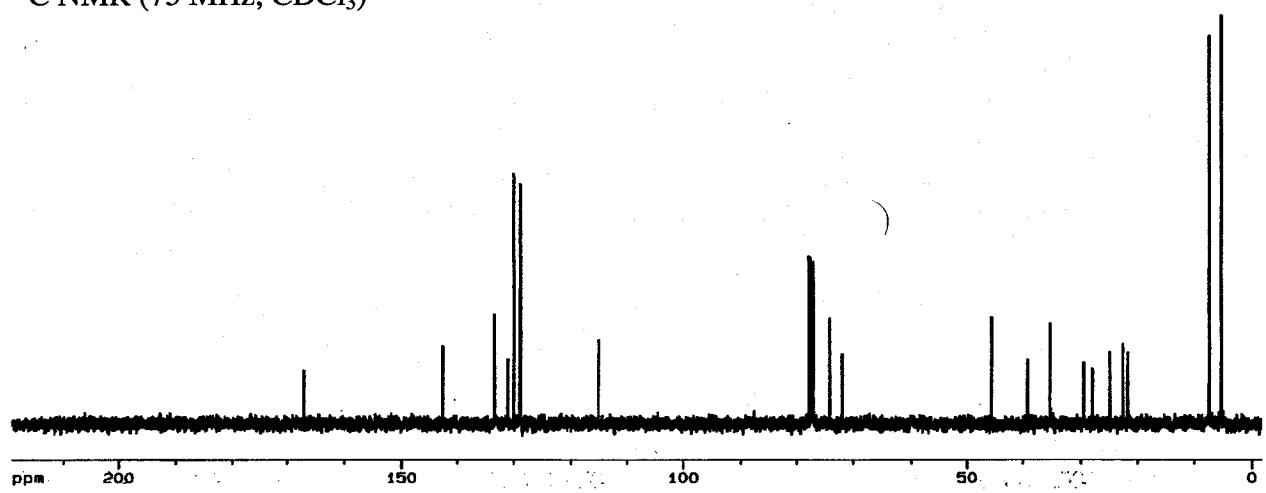


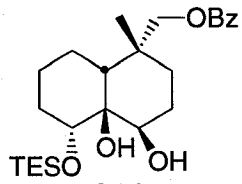
2.57

^{1}H NMR (300 MHz, $CDCl_3$)



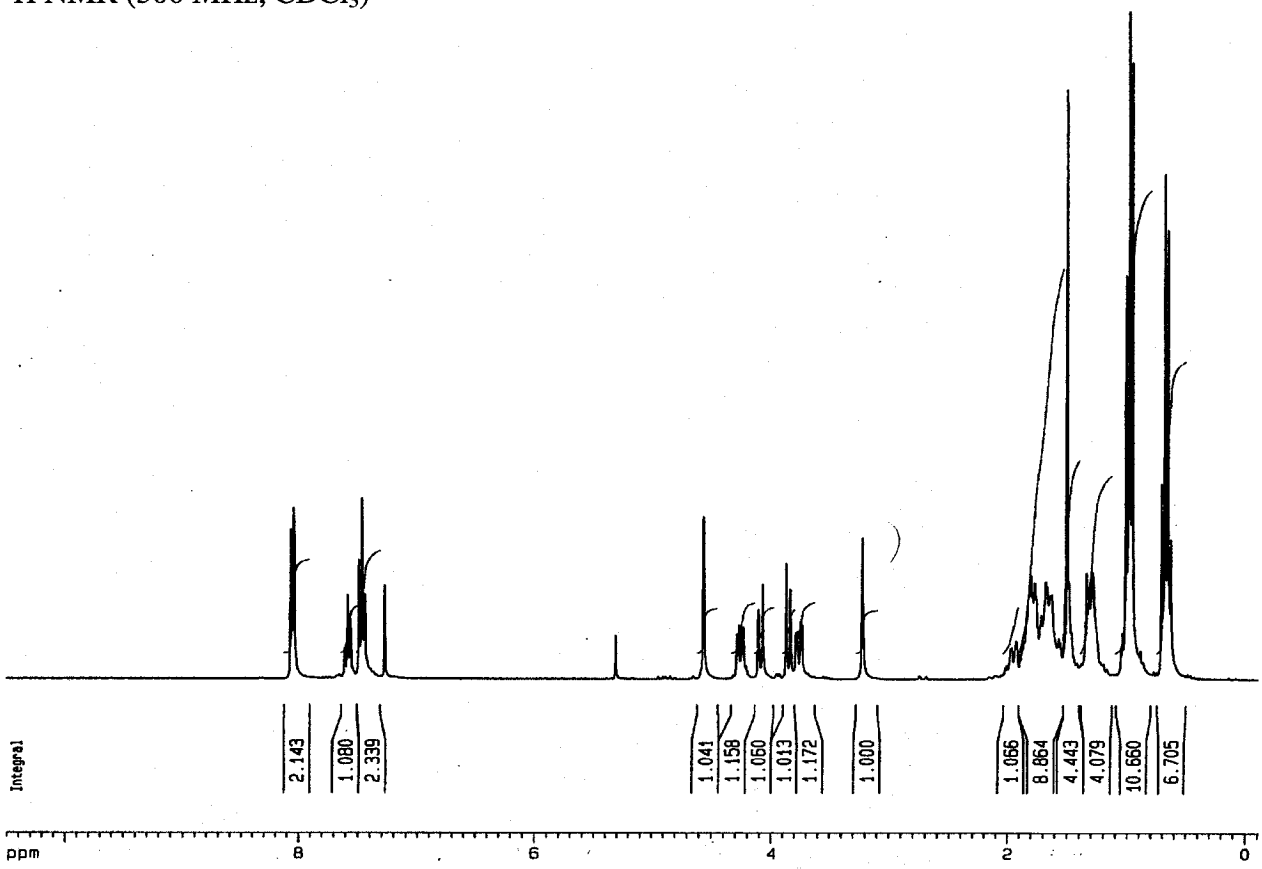
^{13}C NMR (75 MHz, $CDCl_3$)



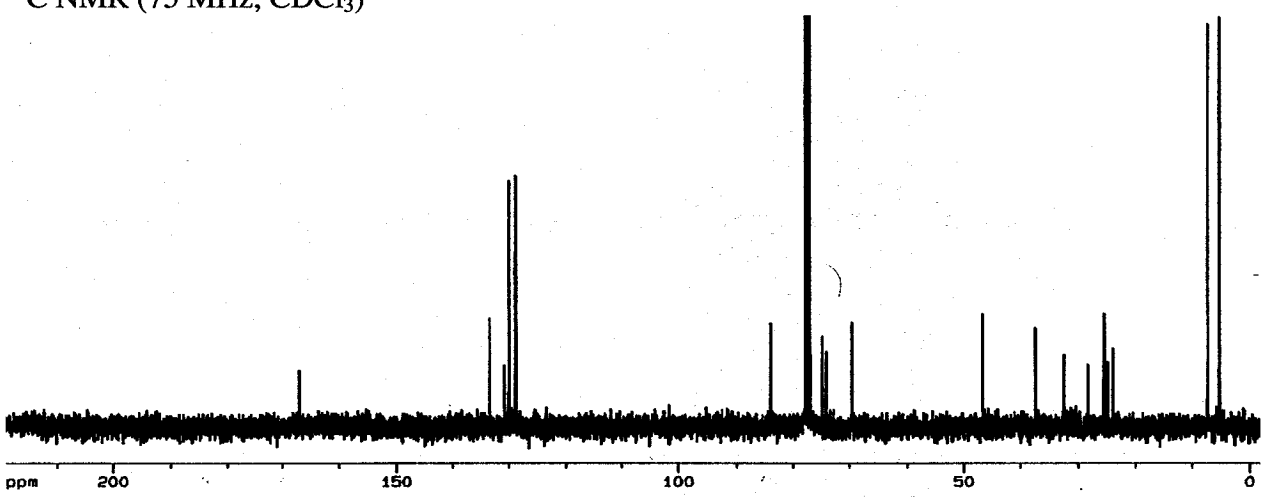


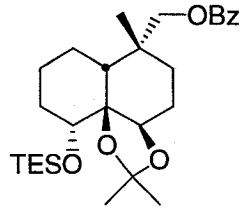
2.58

^{1}H NMR (300 MHz, $CDCl_3$)



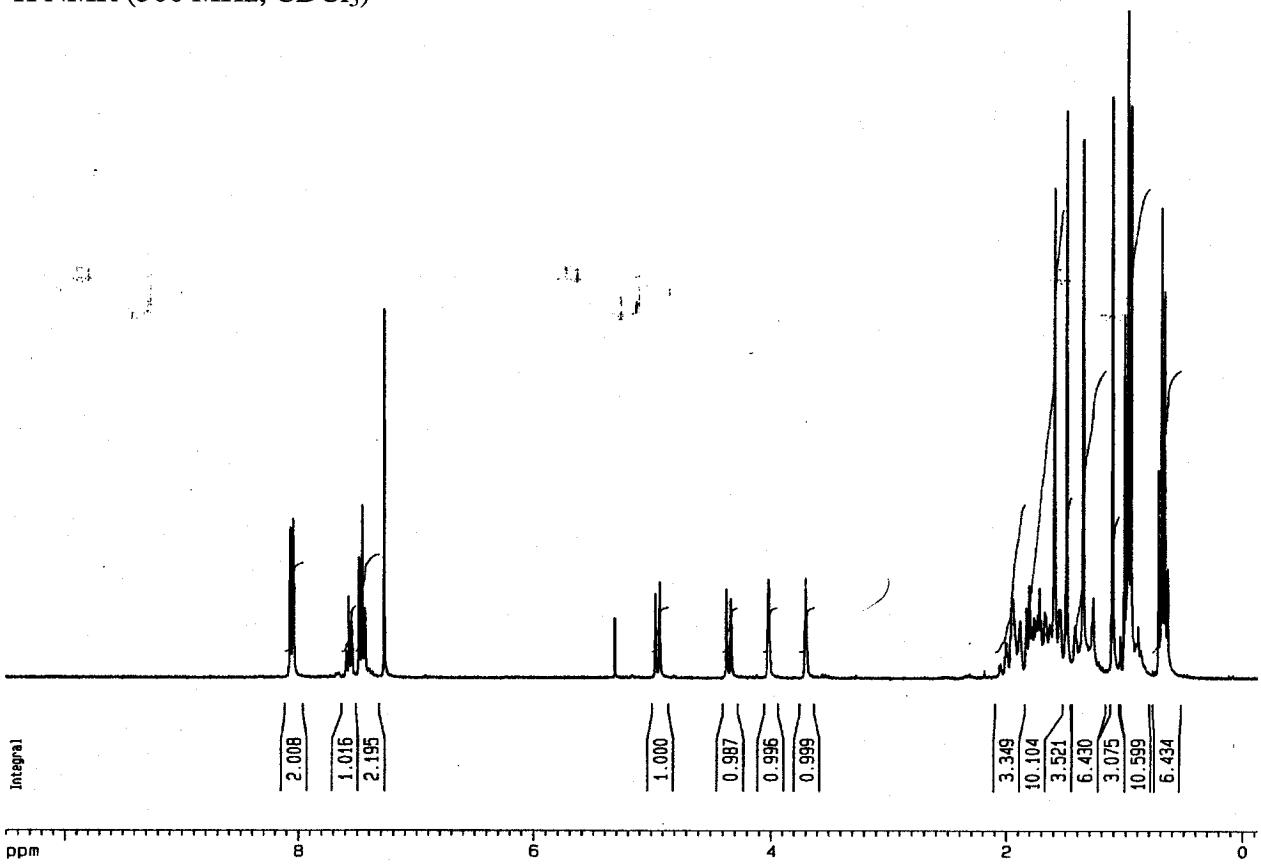
^{13}C NMR (75 MHz, $CDCl_3$)



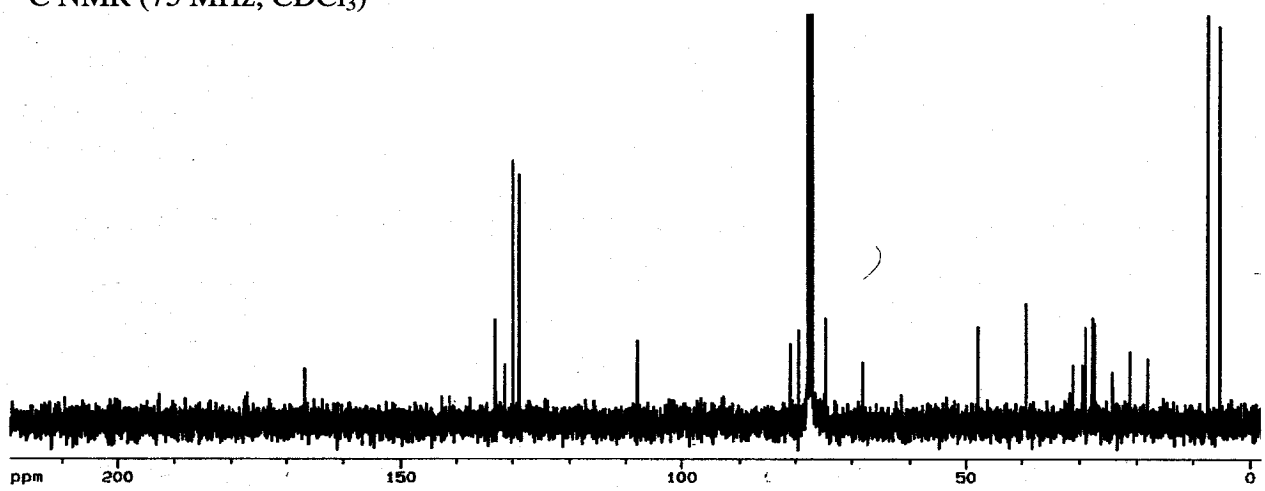


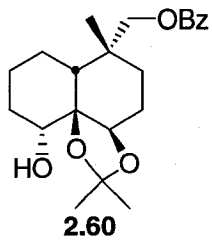
2.59

^{1}H NMR (300 MHz, $CDCl_3$)



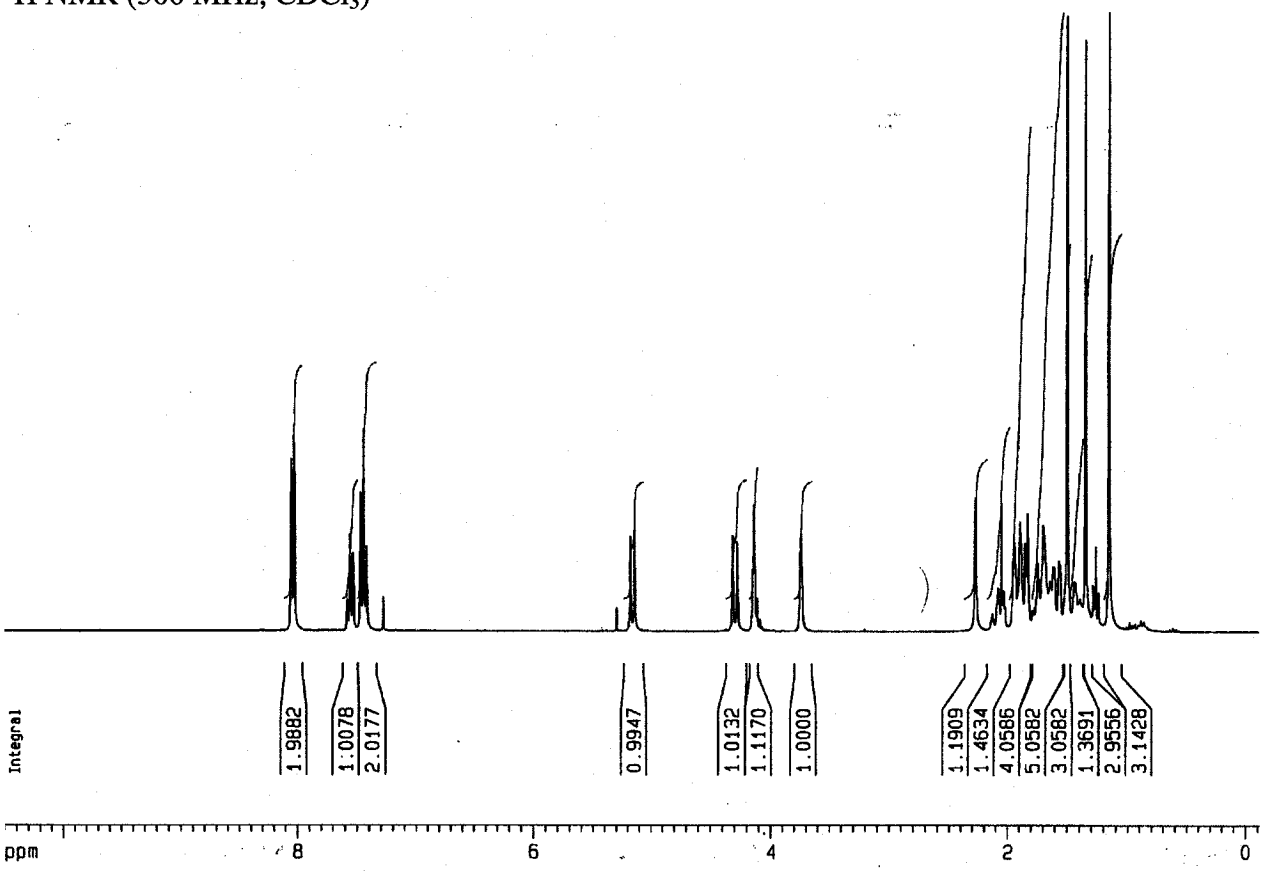
^{13}C NMR (75 MHz, $CDCl_3$)



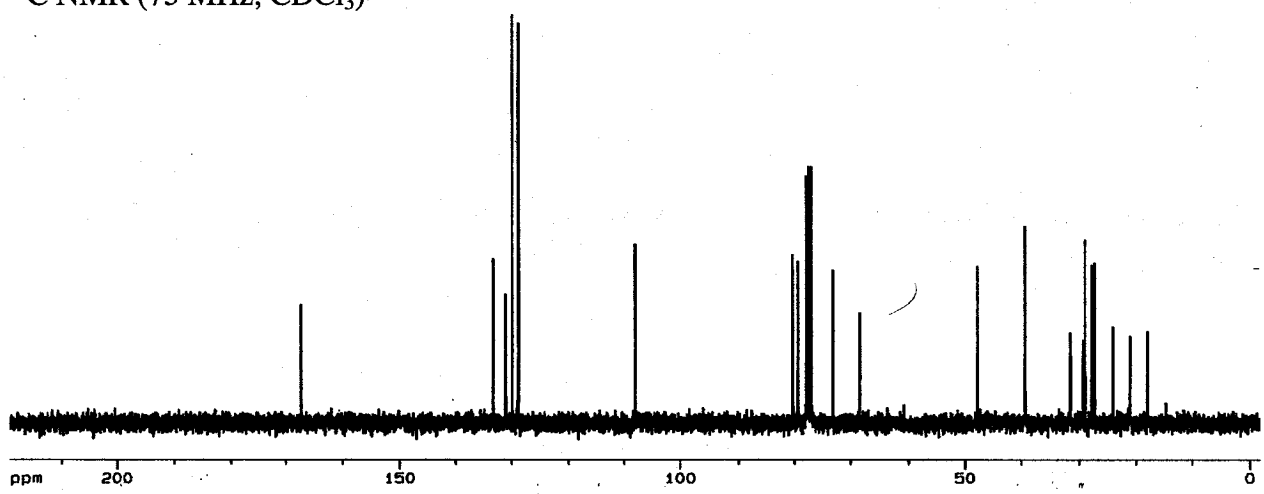


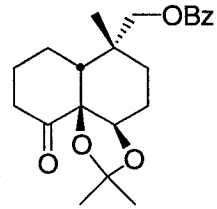
2.60

^{1}H NMR (300 MHz, $CDCl_3$)



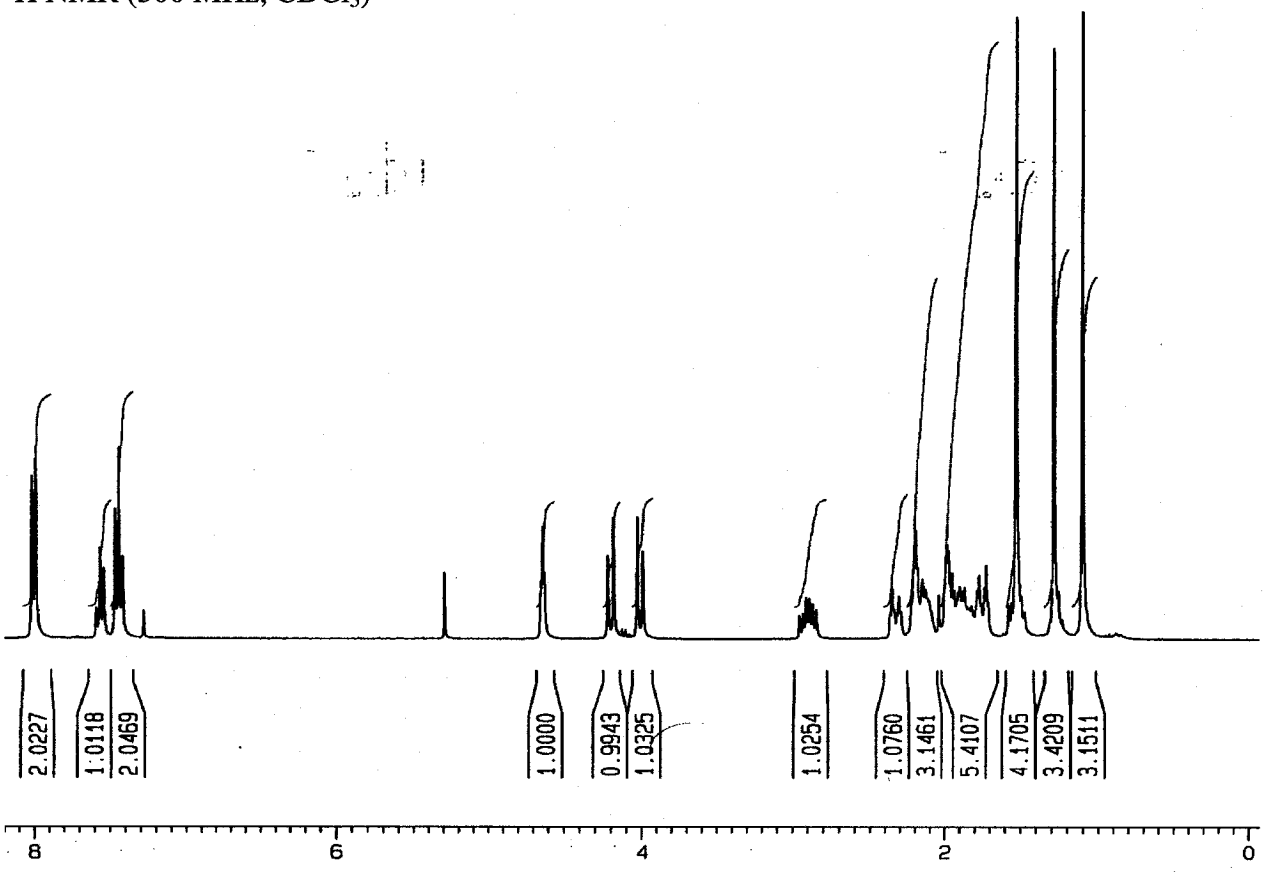
^{13}C NMR (75 MHz, $CDCl_3$)



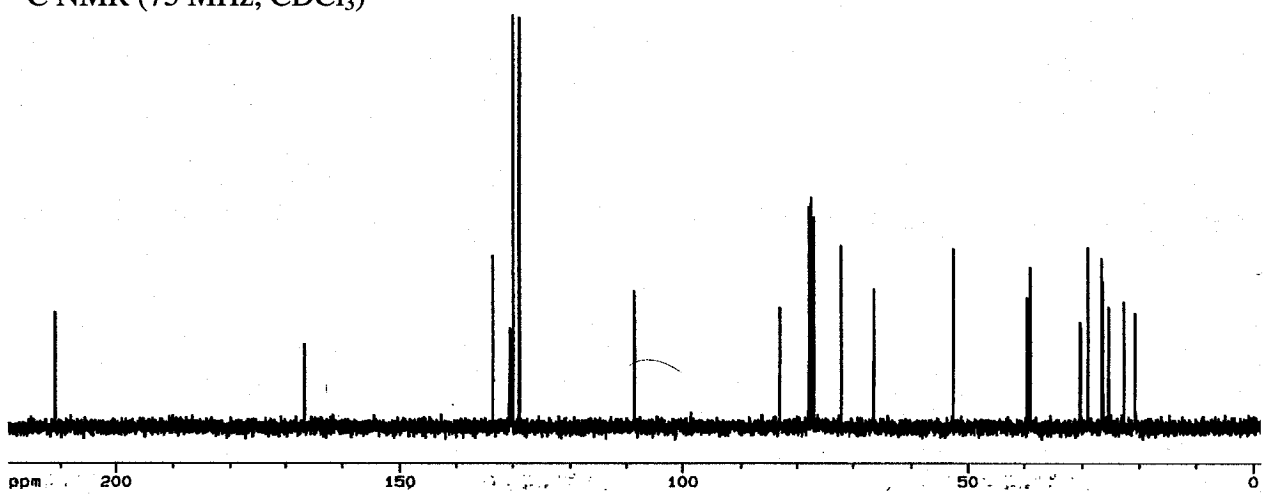


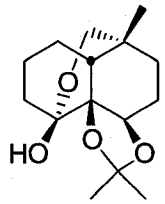
2.61

^{1}H NMR (300 MHz, $CDCl_3$)



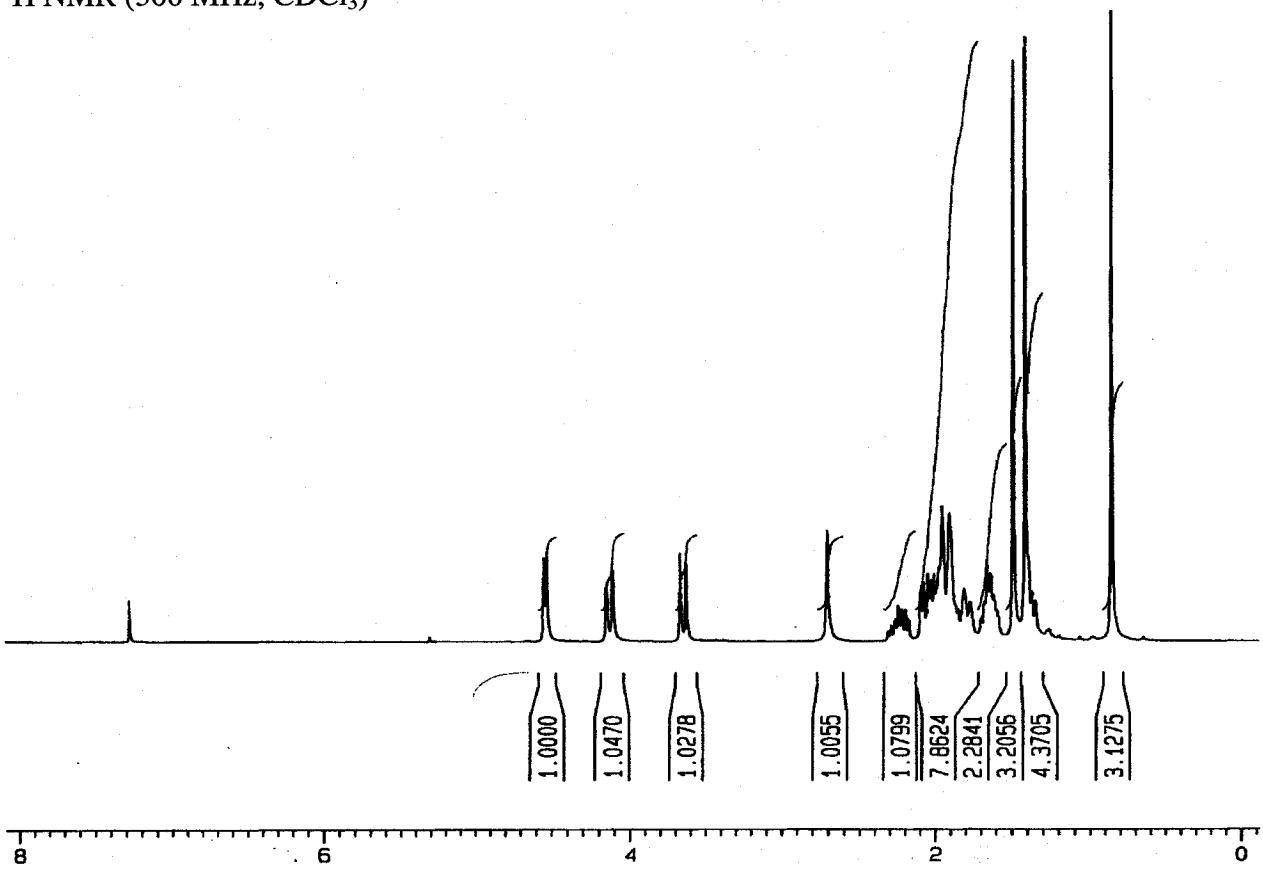
^{13}C NMR (75 MHz, $CDCl_3$)



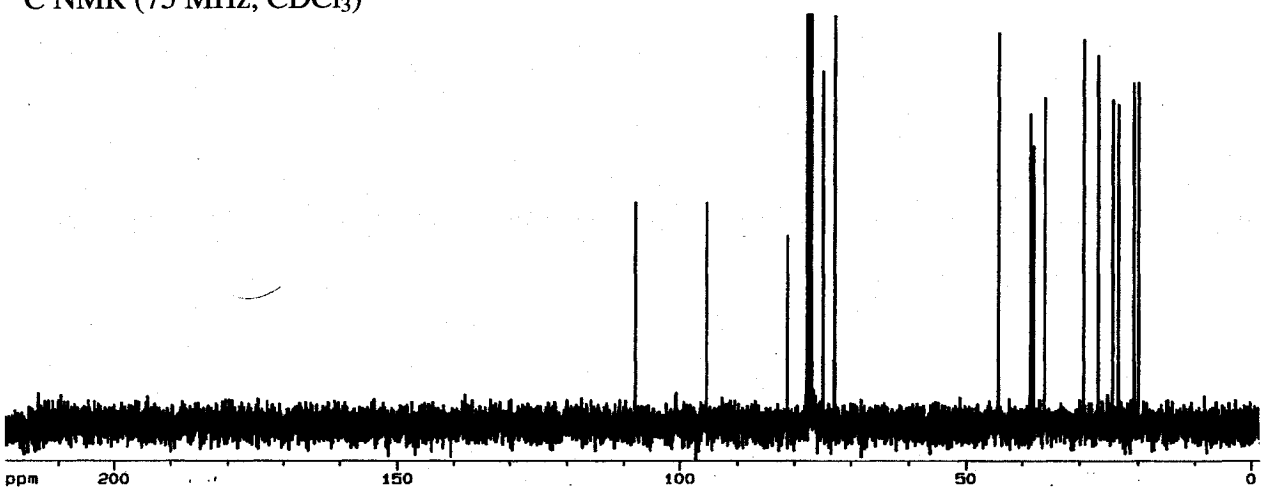


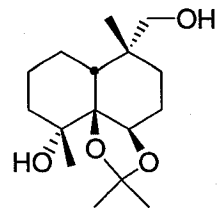
2.62

^{1}H NMR (300 MHz, $CDCl_3$)



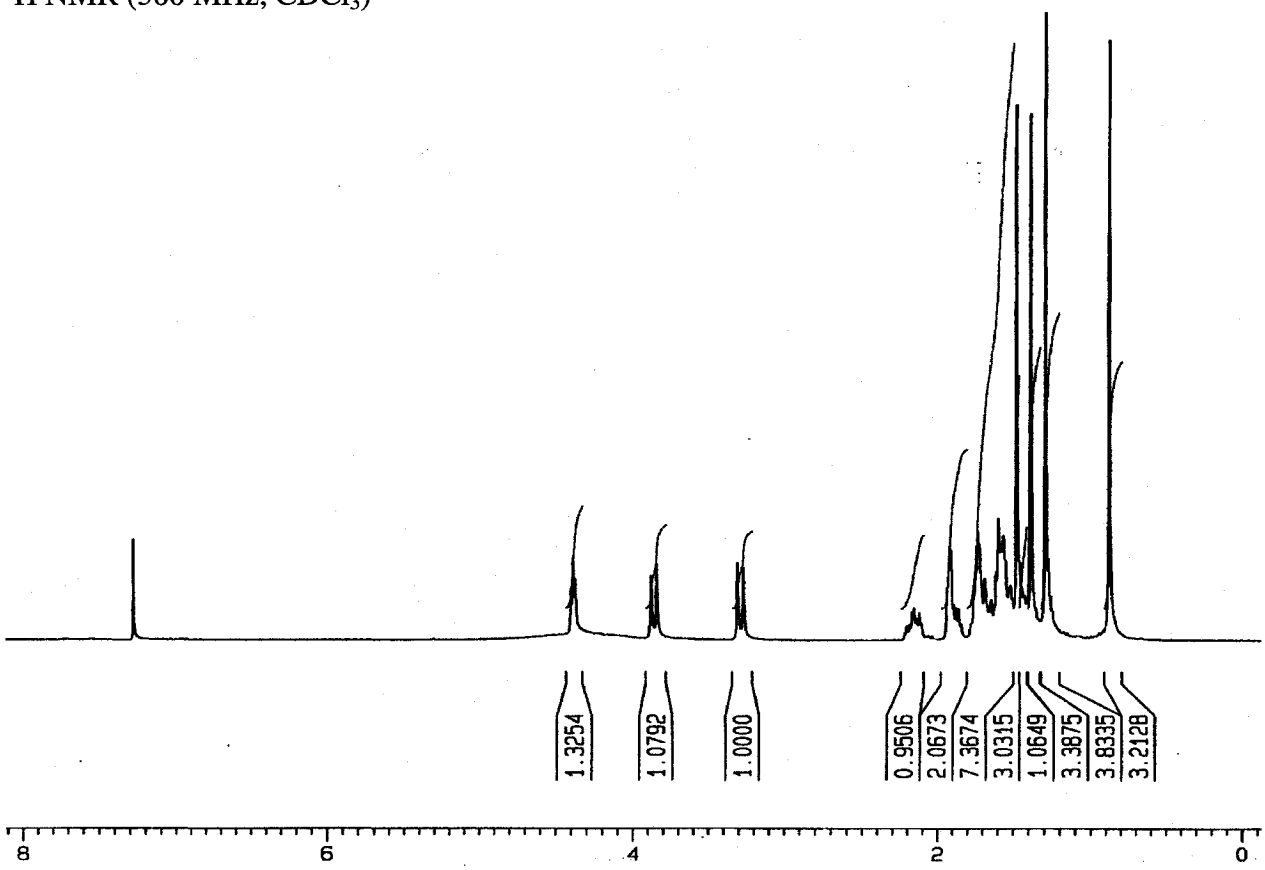
^{13}C NMR (75 MHz, $CDCl_3$)



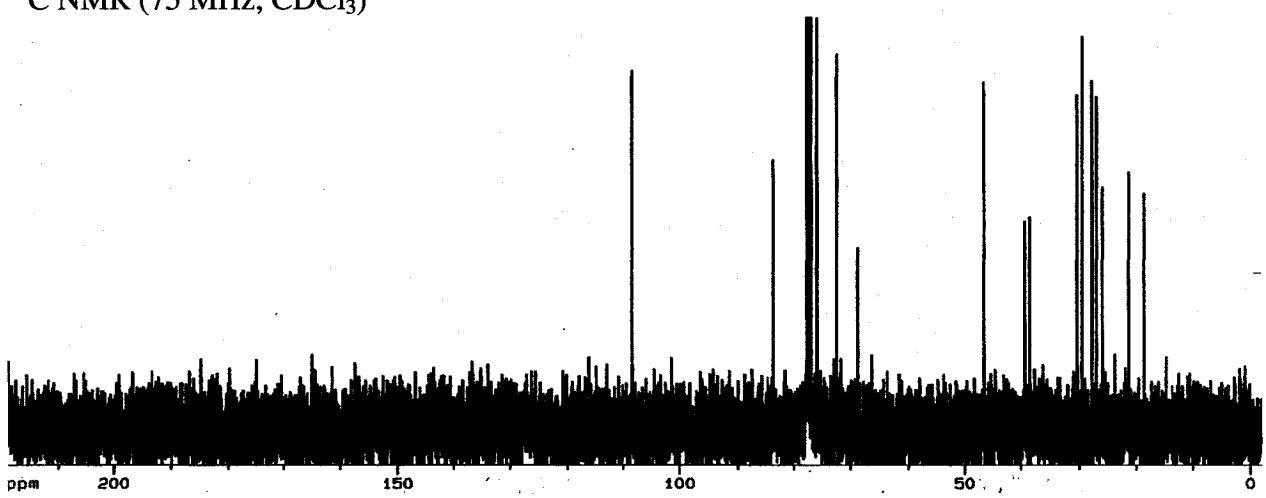


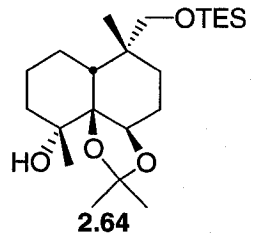
2.63

^{1}H NMR (300 MHz, $CDCl_3$)



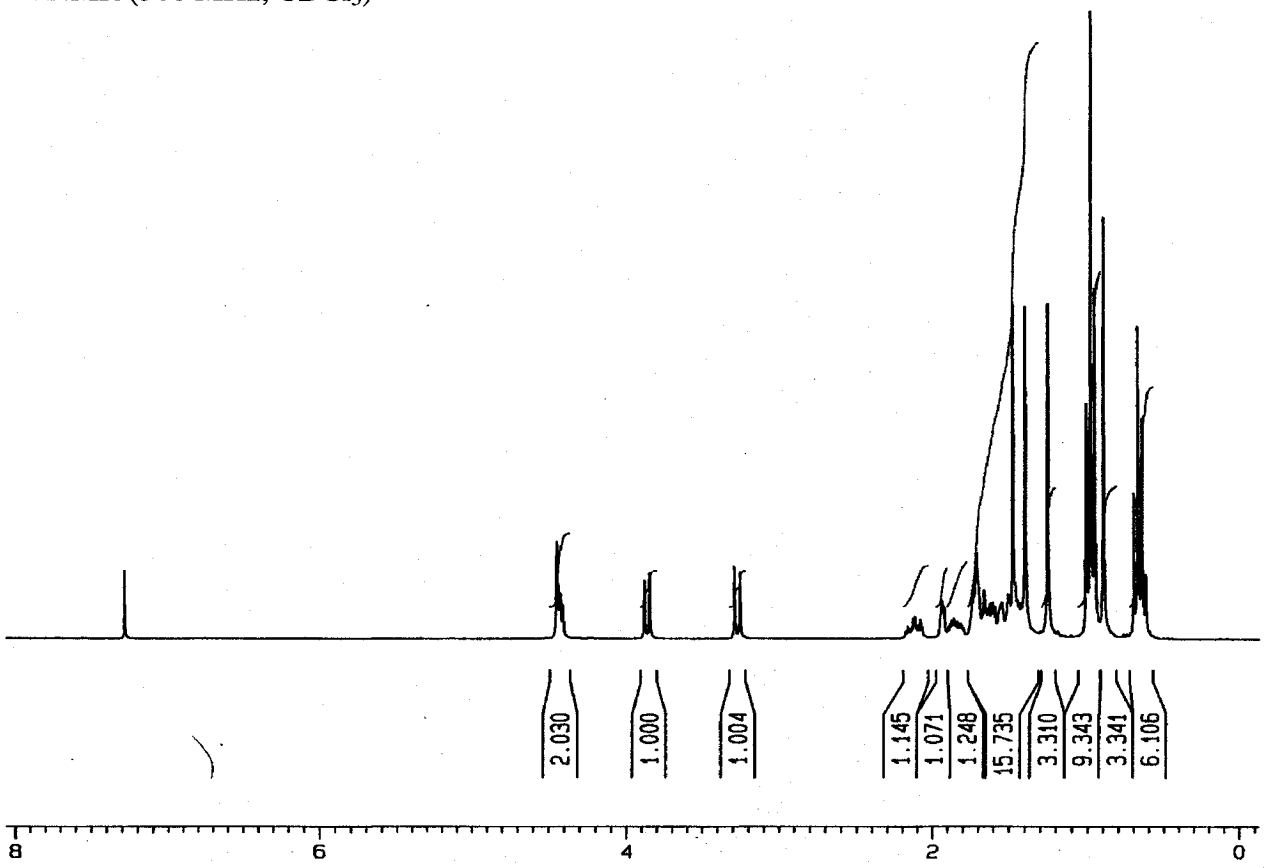
^{13}C NMR (75 MHz, $CDCl_3$)



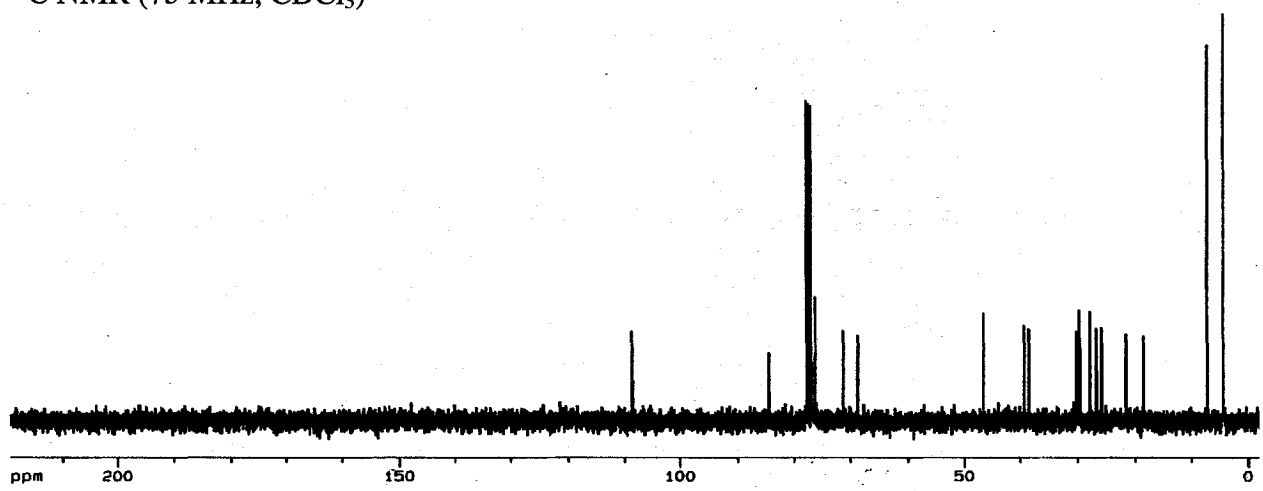


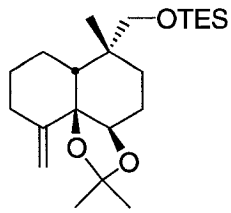
2.64

^{1}H NMR (300 MHz, $CDCl_3$)



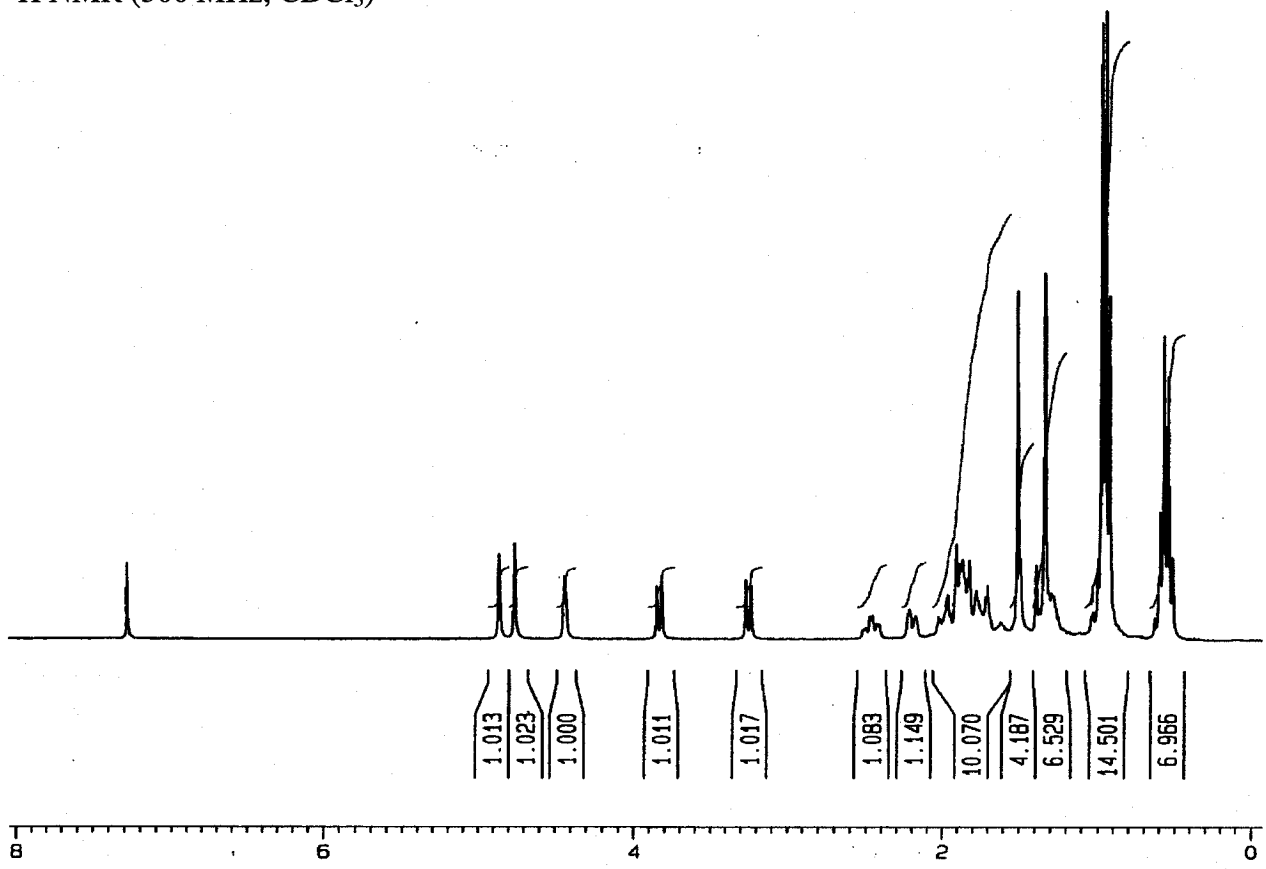
^{13}C NMR (75 MHz, $CDCl_3$)



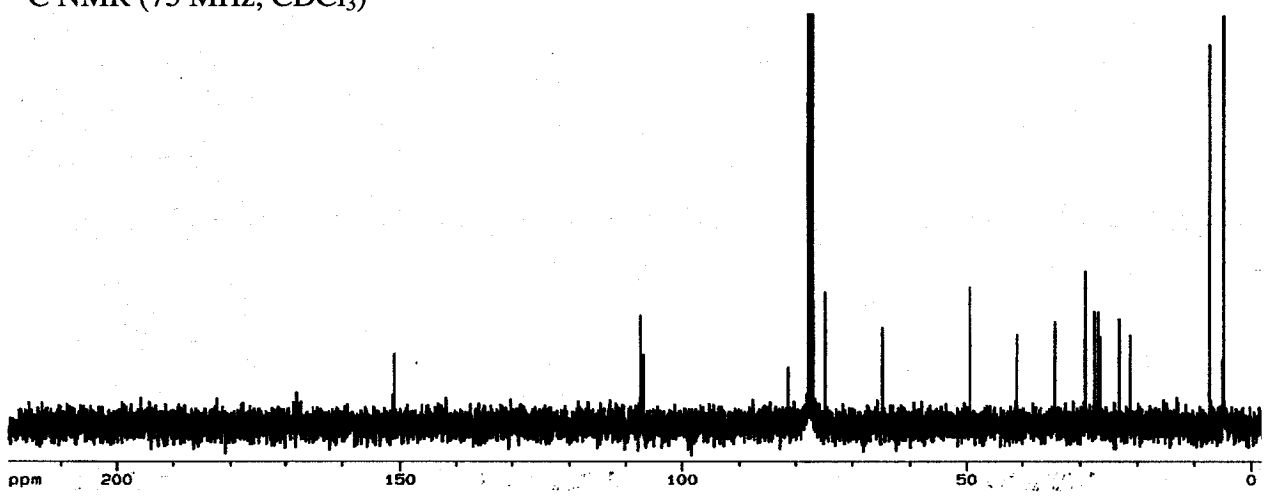


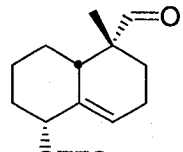
2.65

^{1}H NMR (300 MHz, $CDCl_3$)



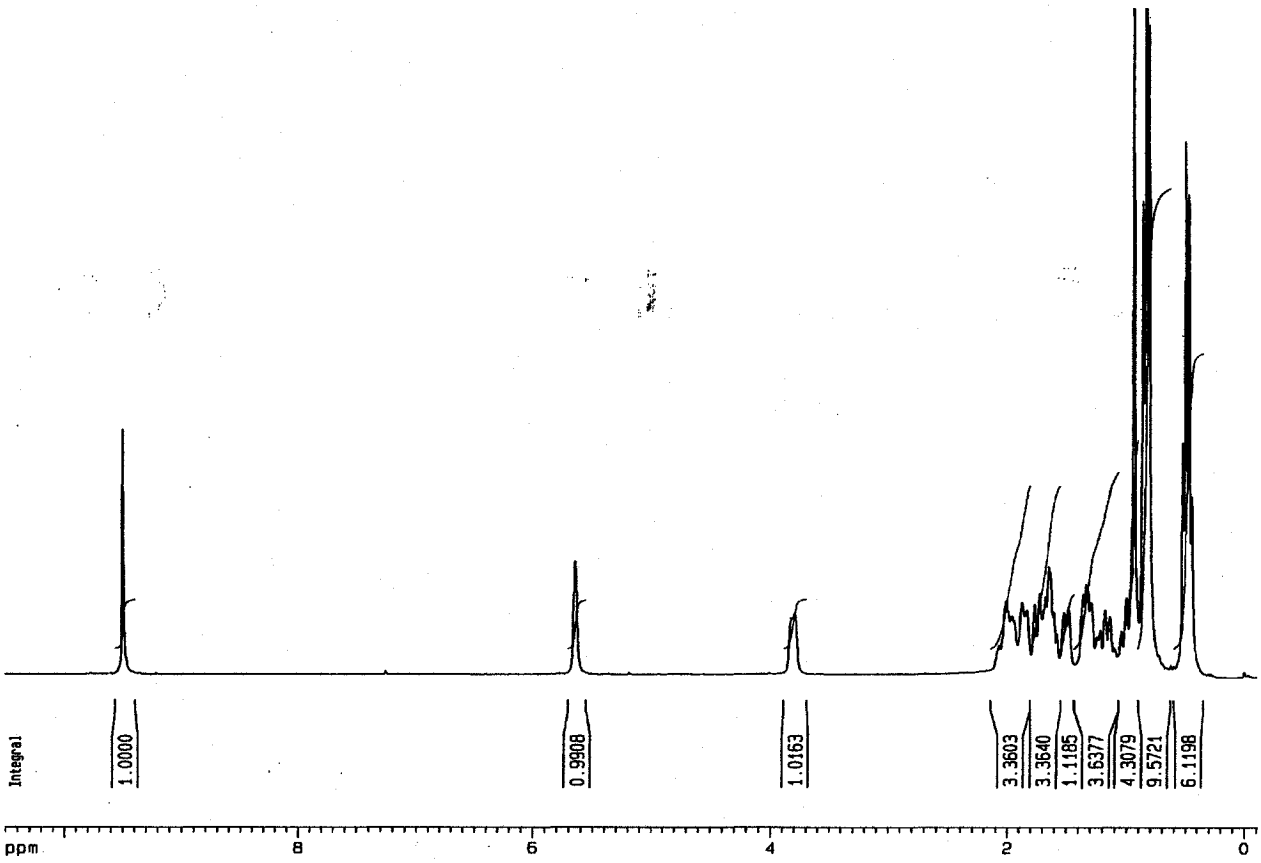
^{13}C NMR (75 MHz, $CDCl_3$)



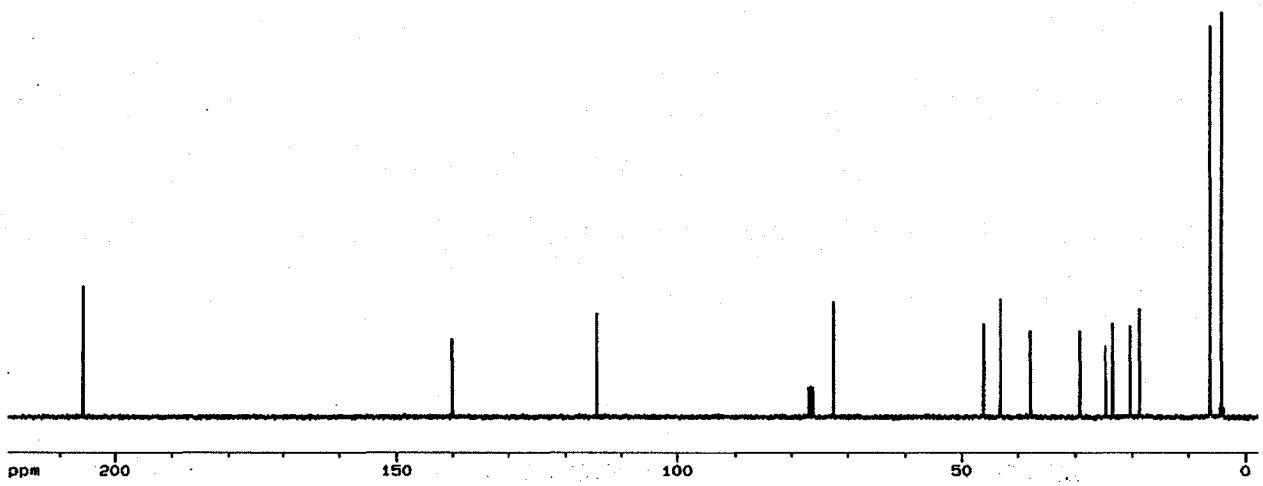


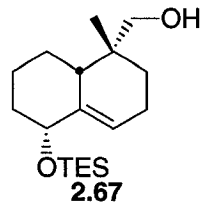
2.66

^{1}H NMR (300 MHz, $CDCl_3$)



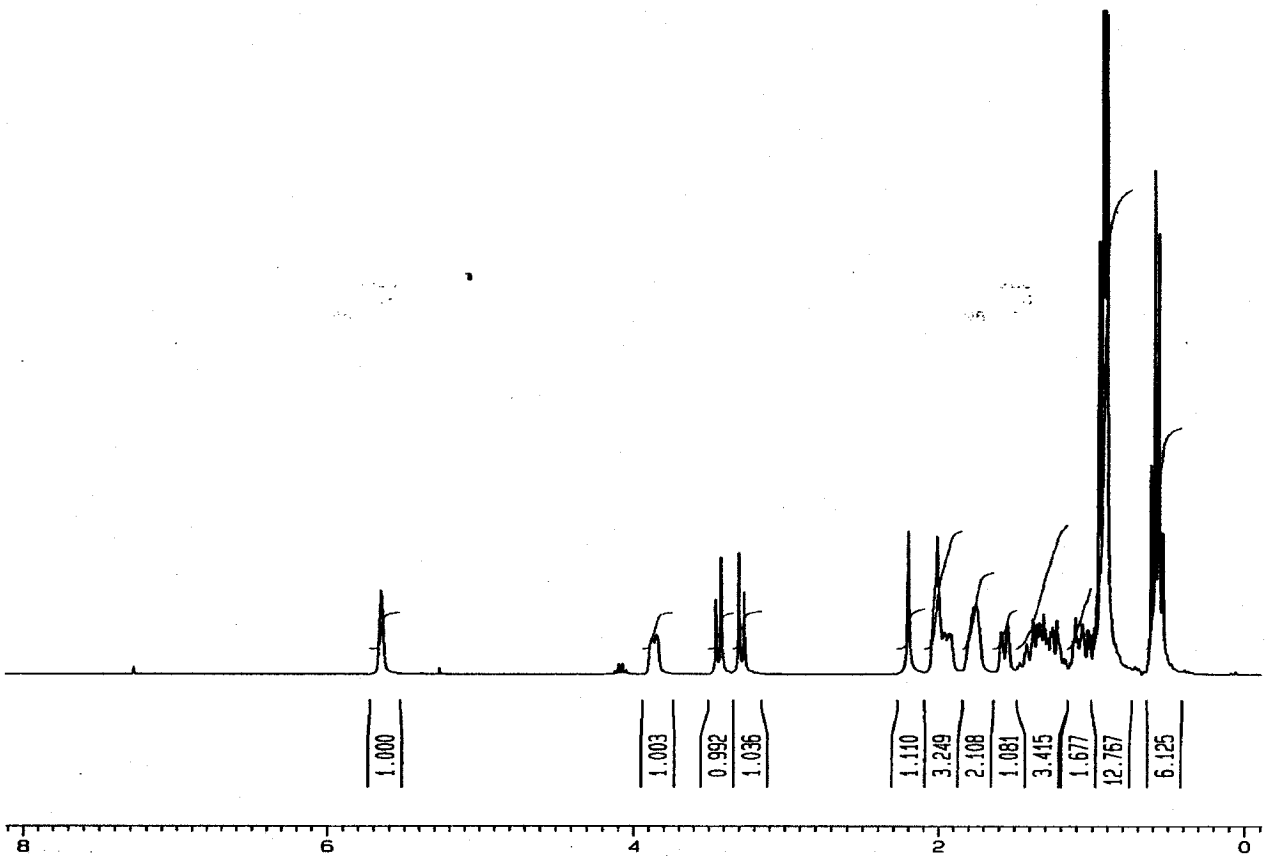
^{13}C NMR (75 MHz, $CDCl_3$)



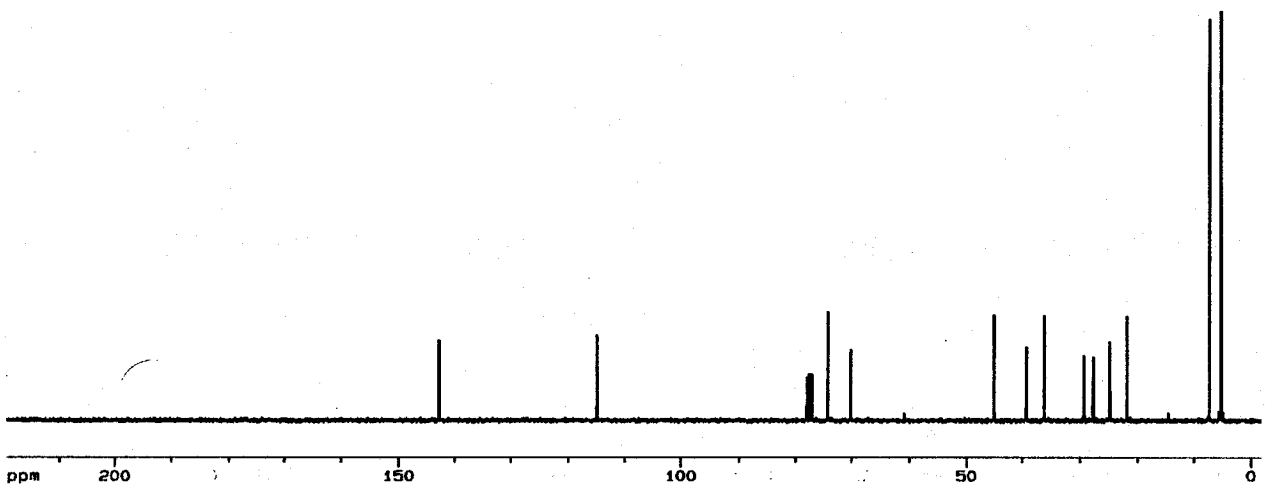


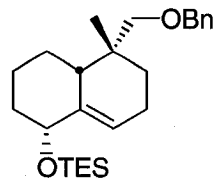
2.67

^{1}H NMR (300 MHz, $CDCl_3$)



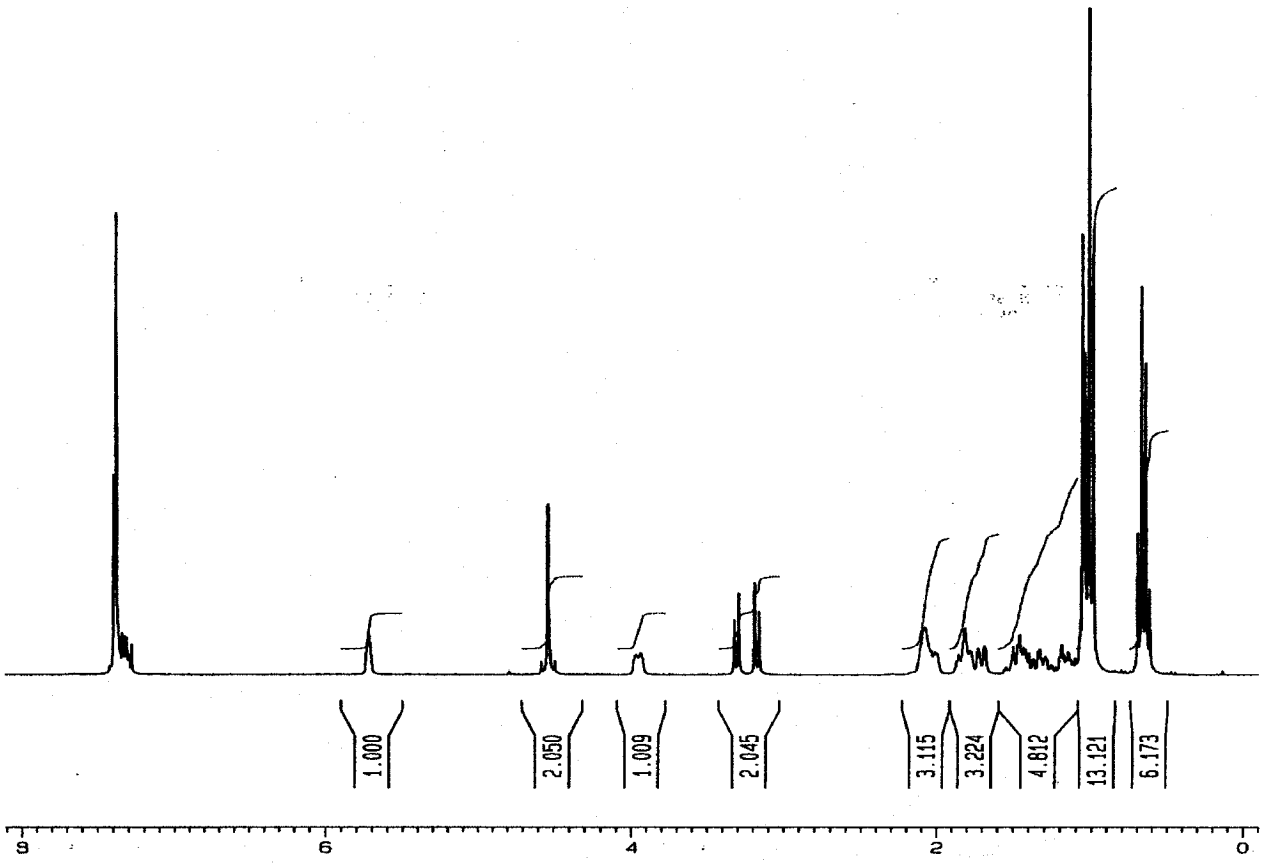
^{13}C NMR (75 MHz, $CDCl_3$)



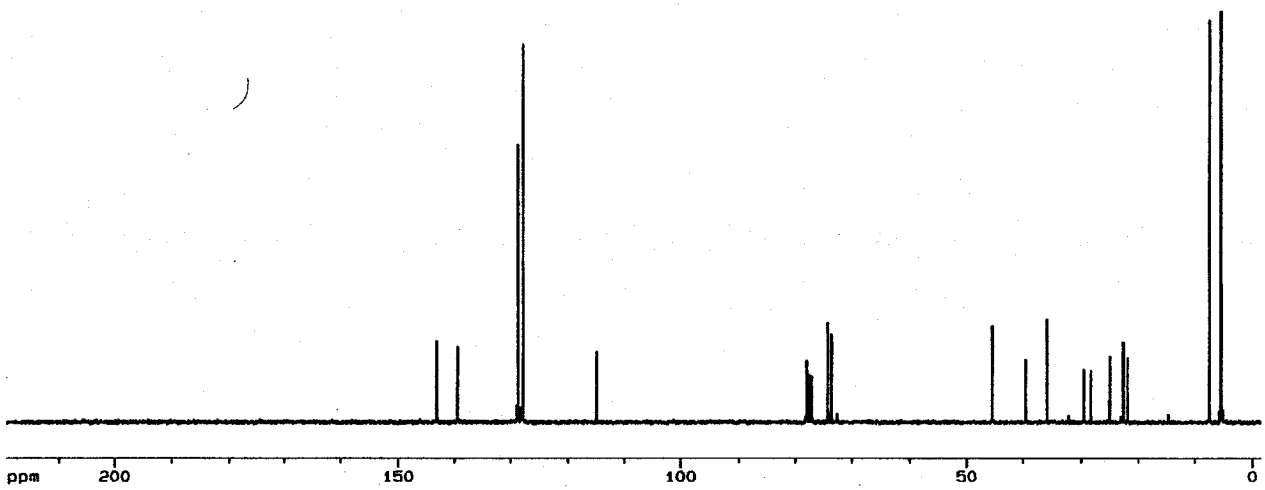


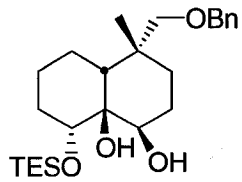
2.68

^{1}H NMR (300 MHz, $CDCl_3$)



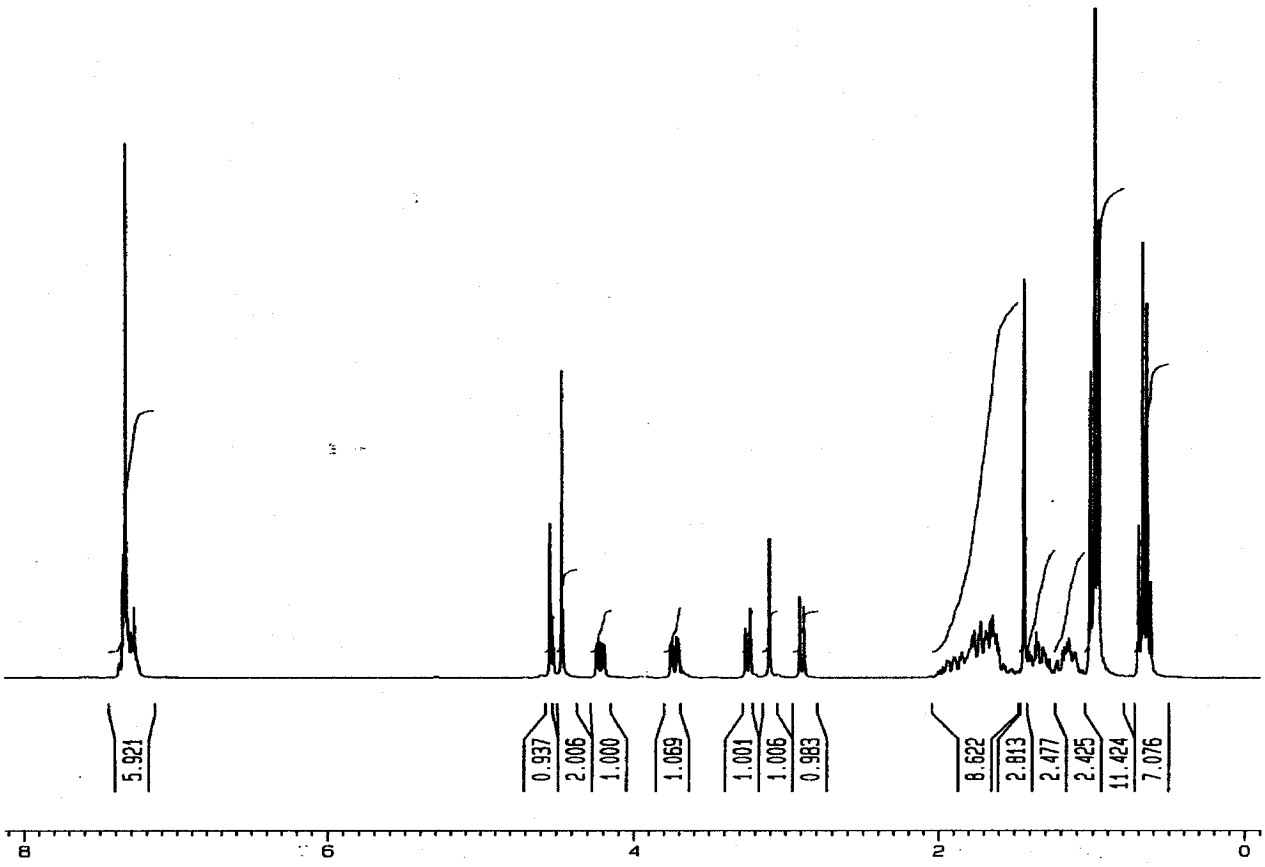
^{13}C NMR (75 MHz, $CDCl_3$)



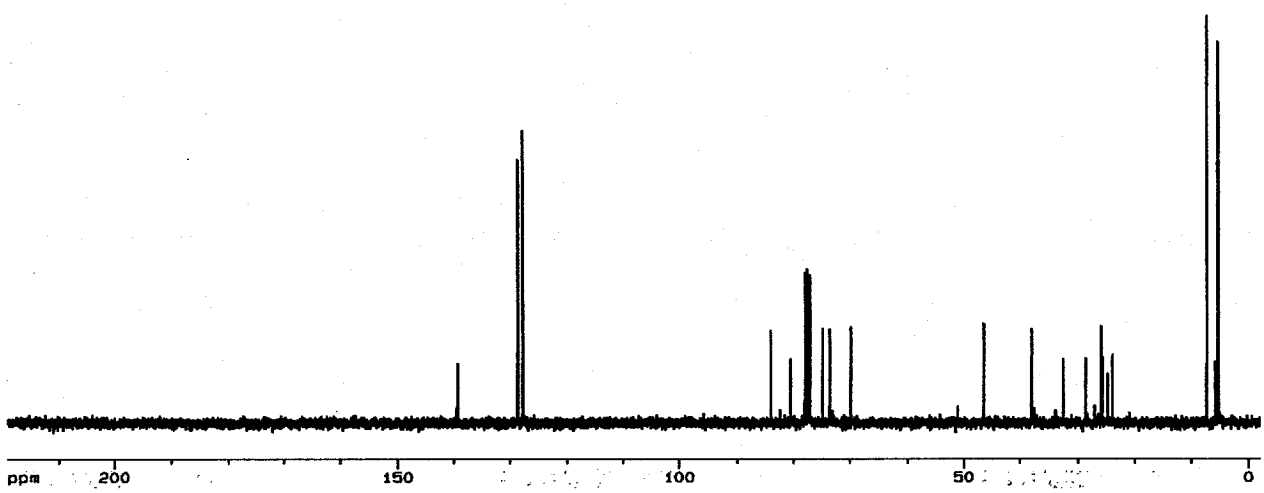


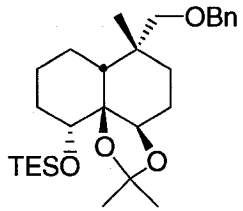
2.69

^{1}H NMR (300 MHz, $CDCl_3$)



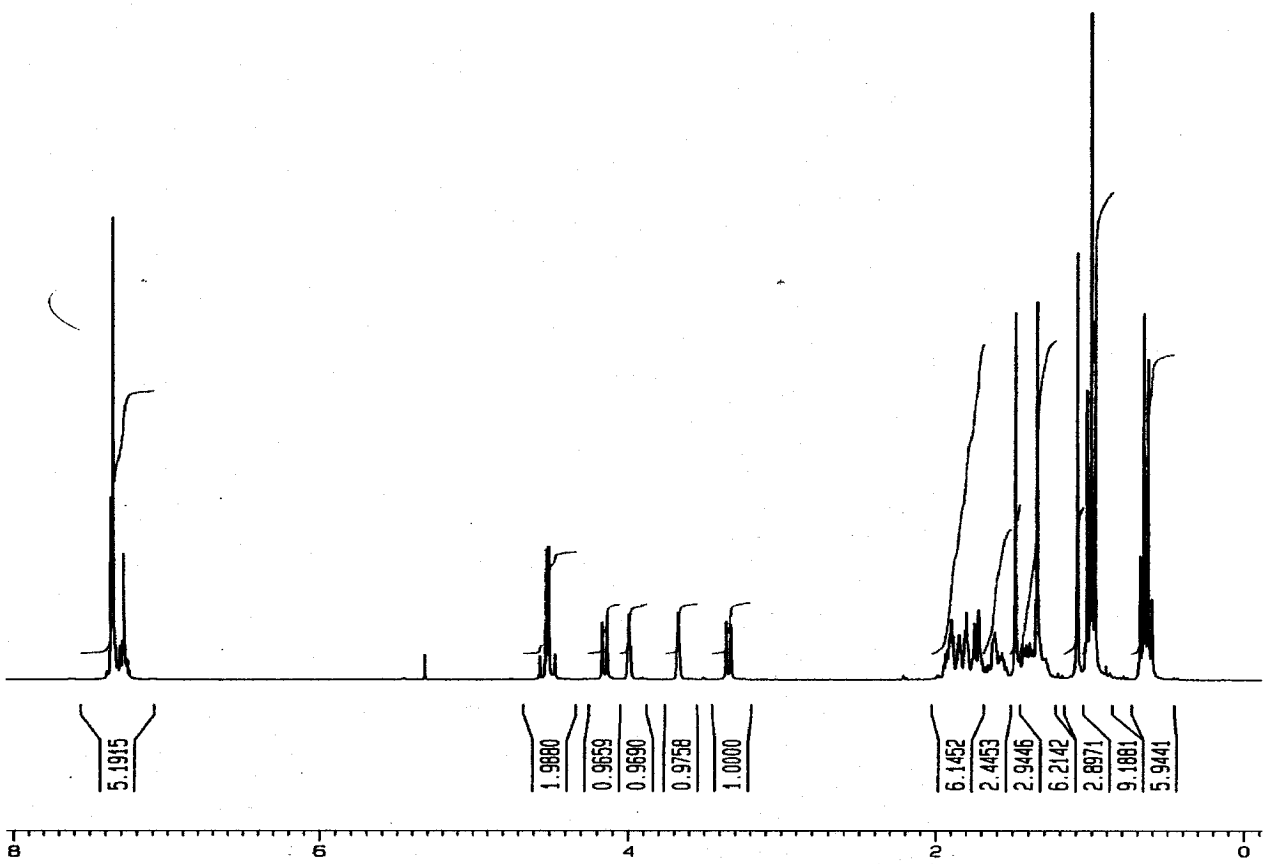
^{13}C NMR (75 MHz, $CDCl_3$)



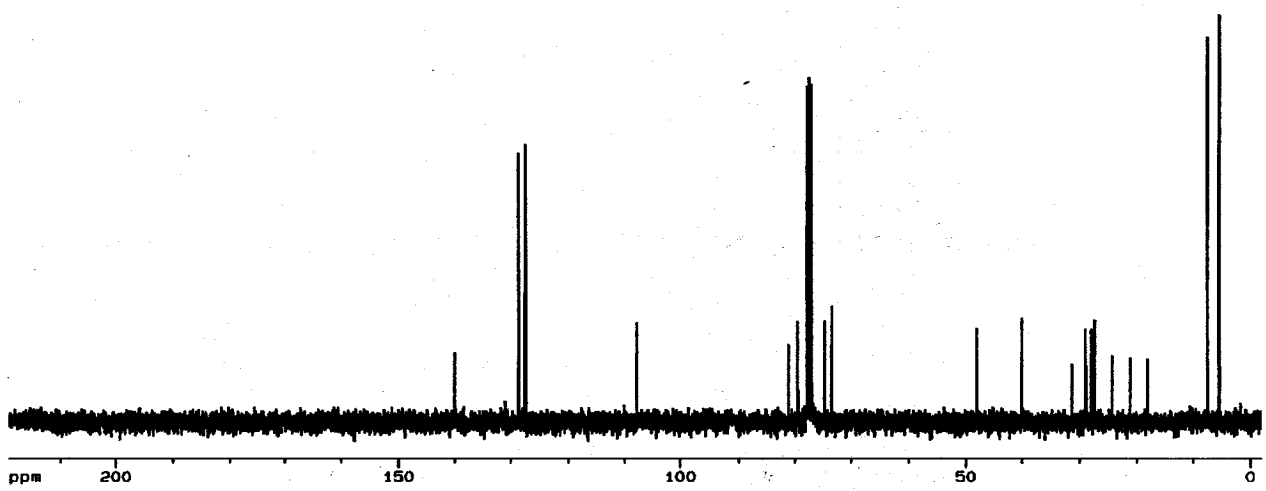


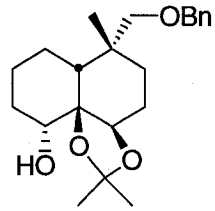
2.70

^{1}H NMR (300 MHz, $CDCl_3$)



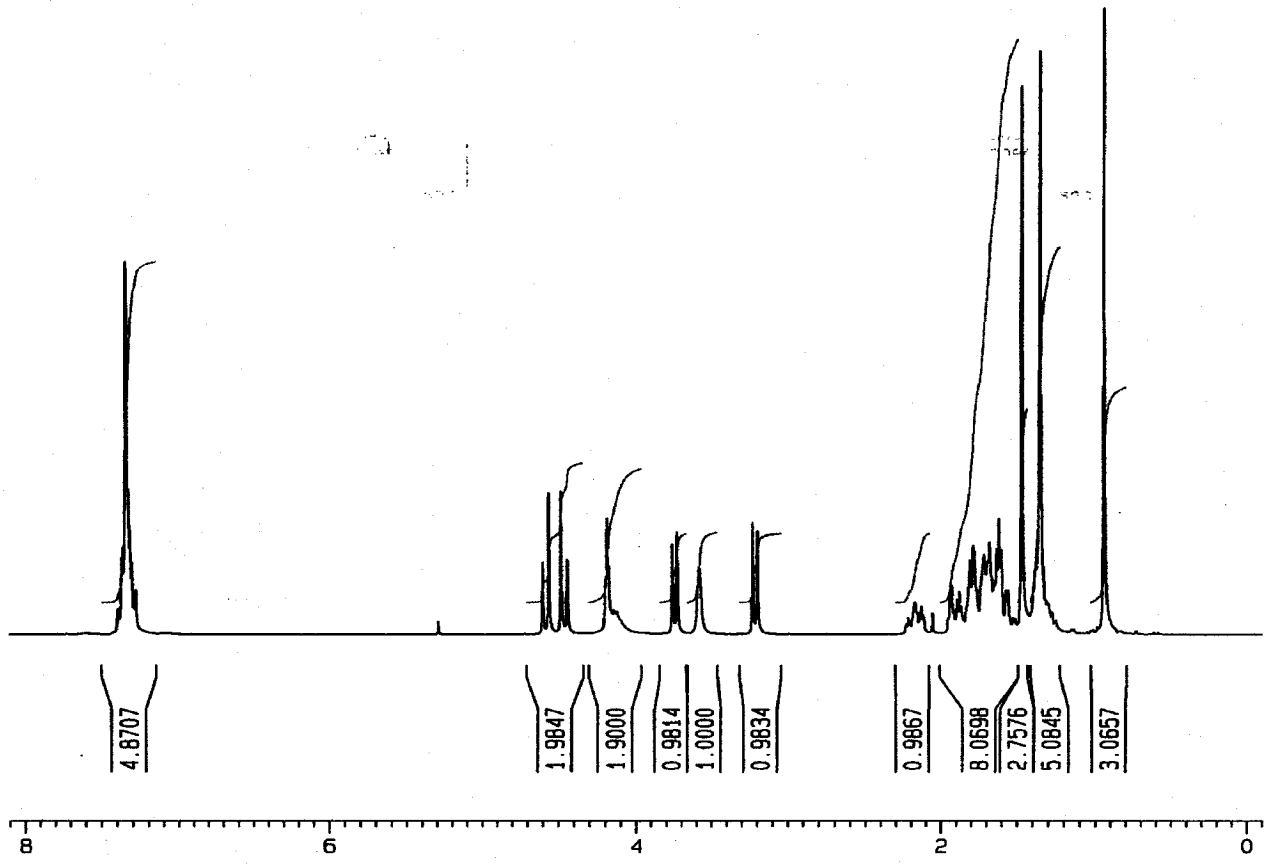
^{13}C NMR (75 MHz, $CDCl_3$)



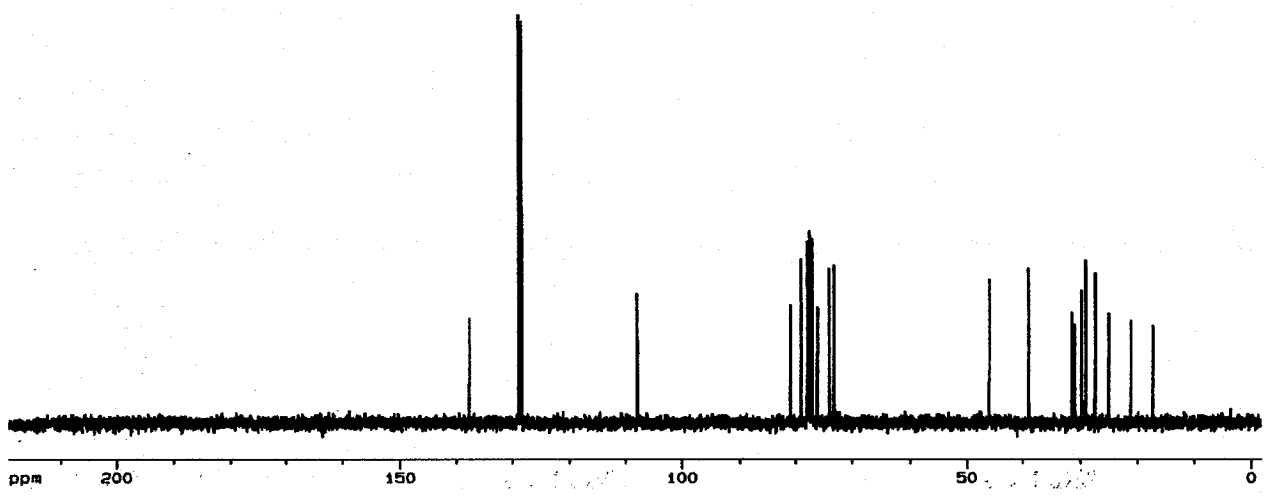


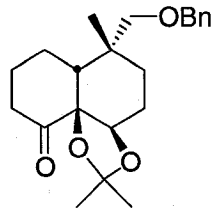
2.71

^{1}H NMR (300 MHz, $CDCl_3$)



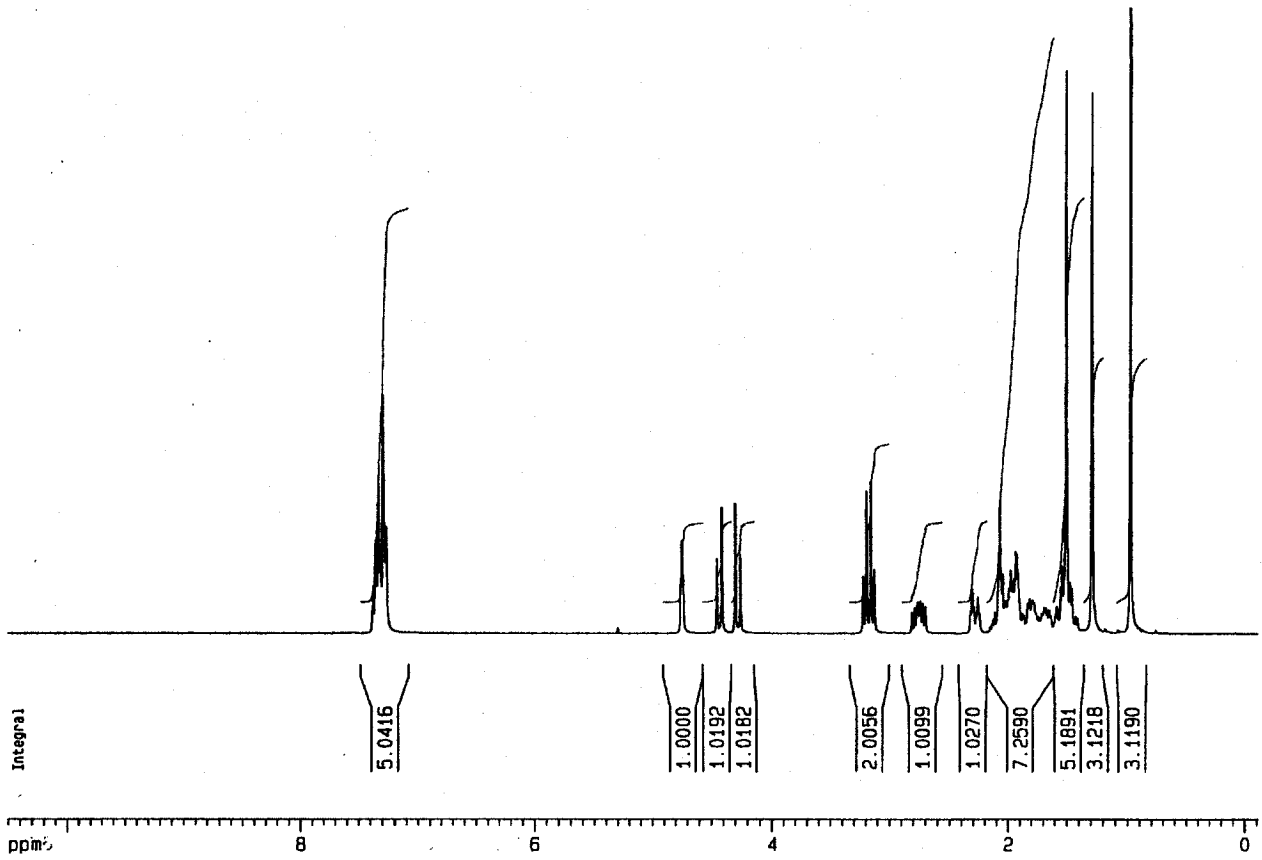
^{13}C NMR (75 MHz, $CDCl_3$)



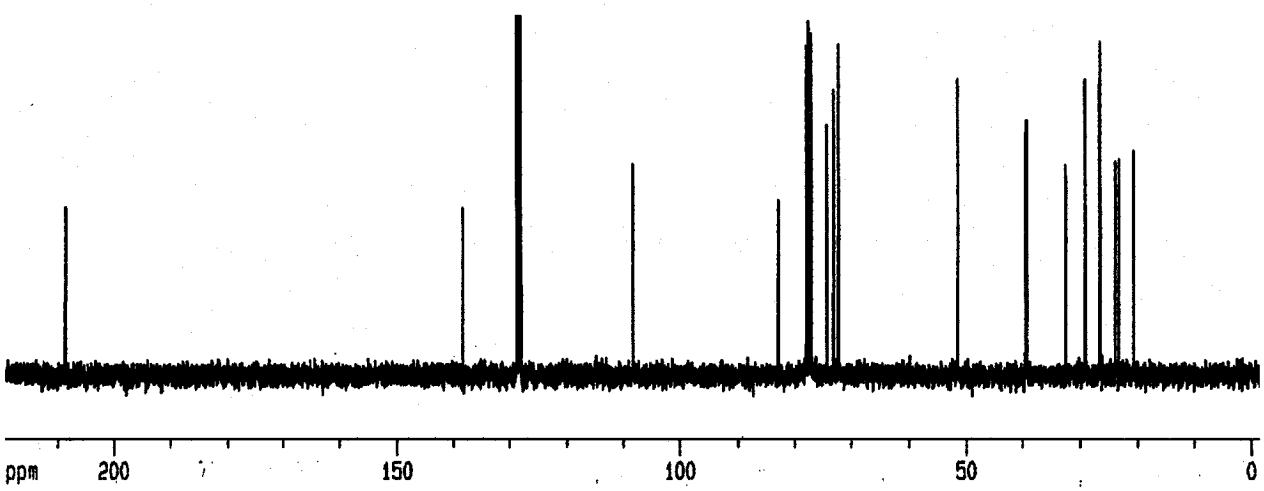


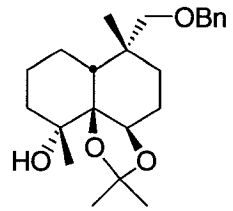
2.72

^{1}H NMR (300 MHz, $CDCl_3$)



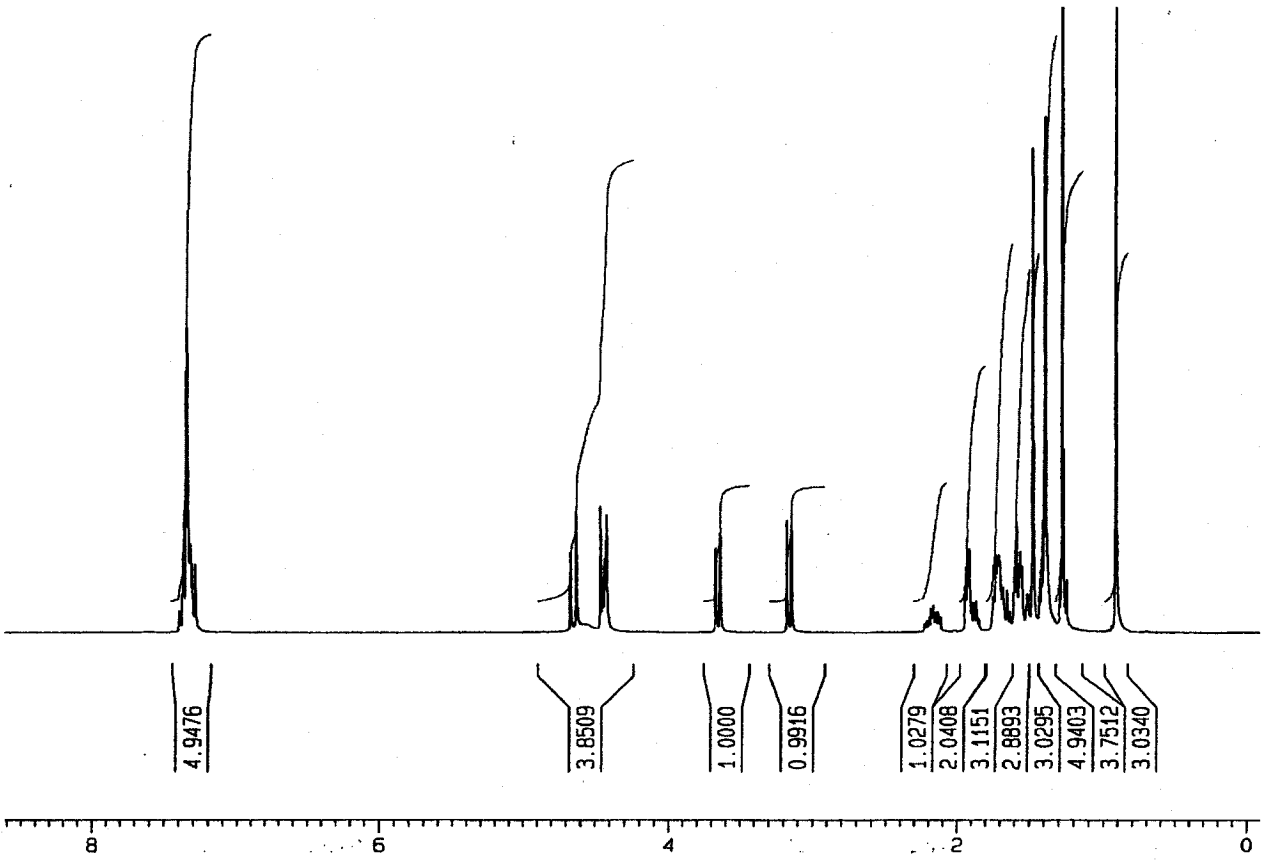
^{13}C NMR (75 MHz, $CDCl_3$)



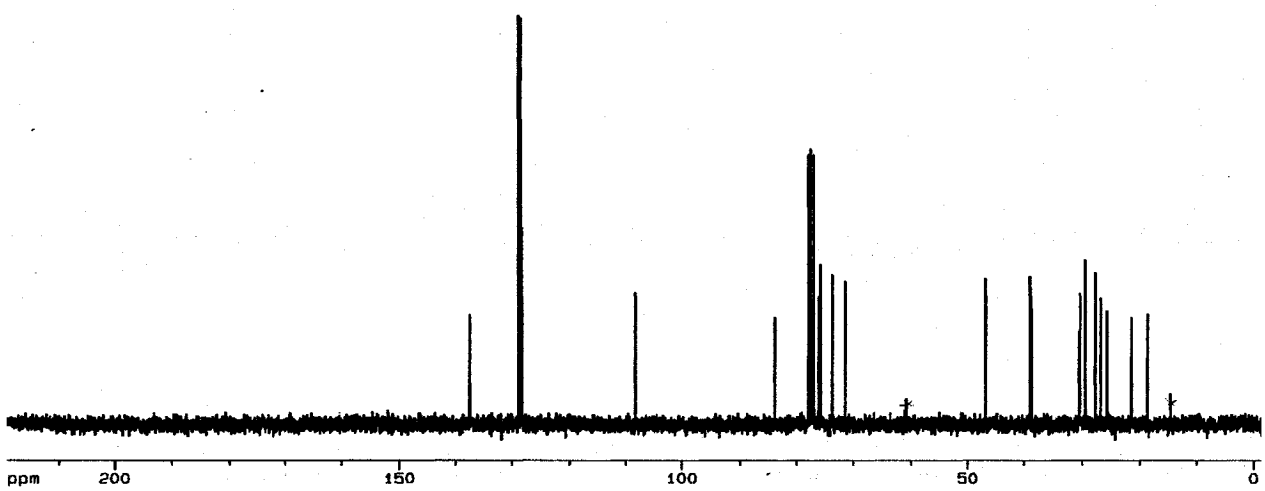


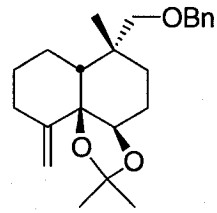
2.73

^{1}H NMR (300 MHz, $CDCl_3$)



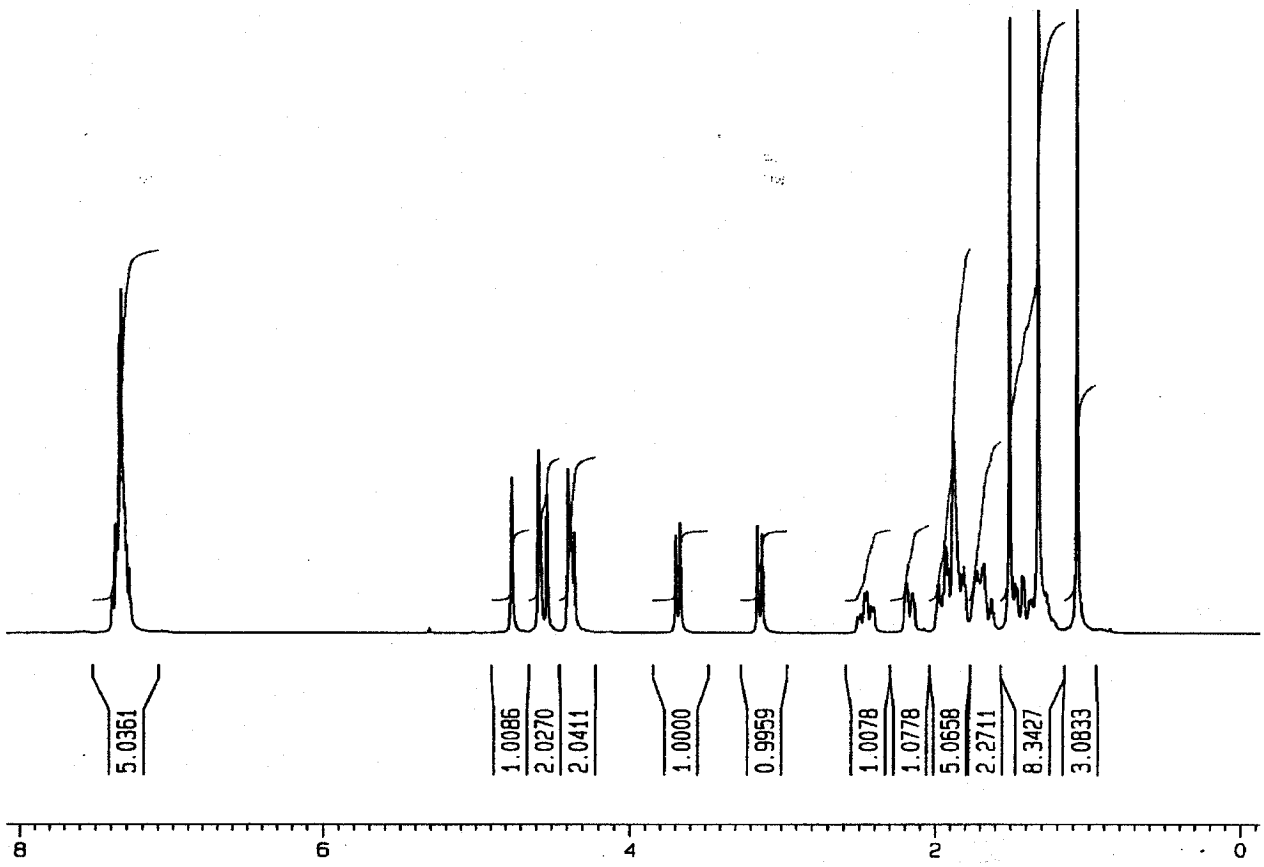
^{13}C NMR (75 MHz, $CDCl_3$)



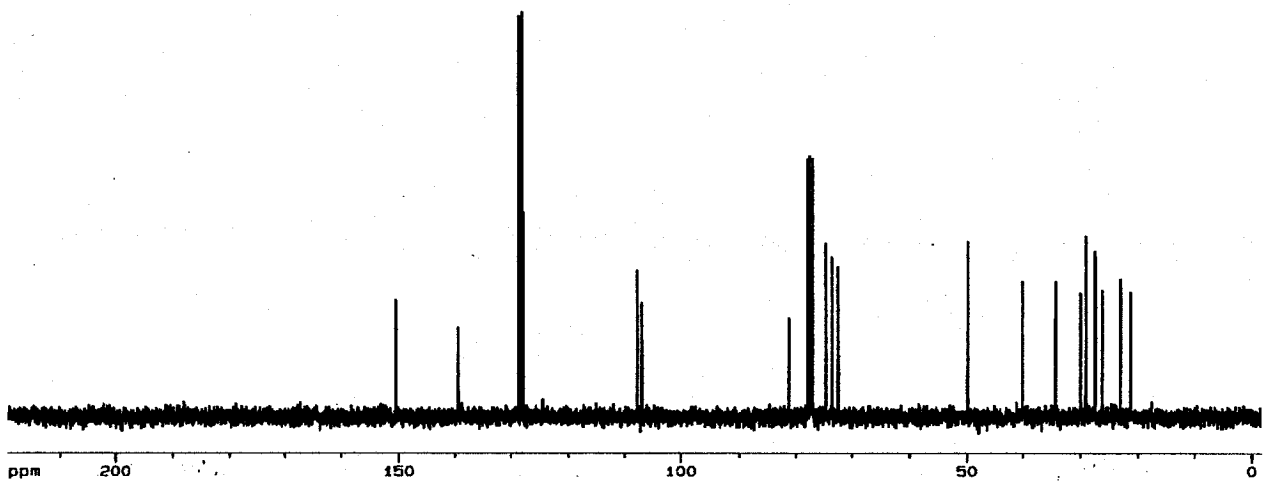


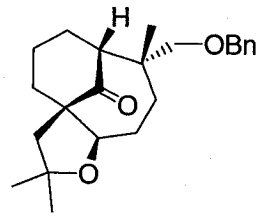
2.74

^{1}H NMR (300 MHz, $CDCl_3$)



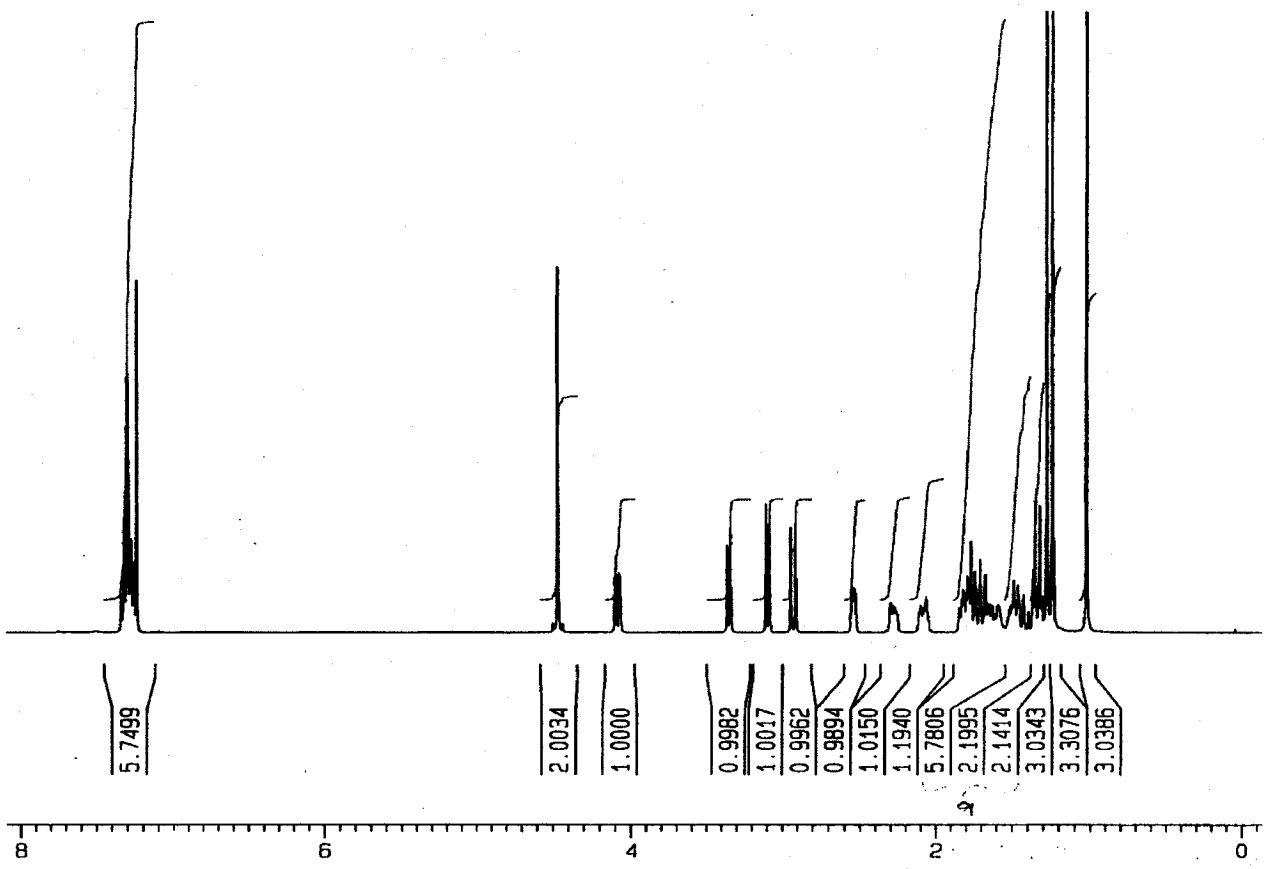
^{13}C NMR (75 MHz, $CDCl_3$)



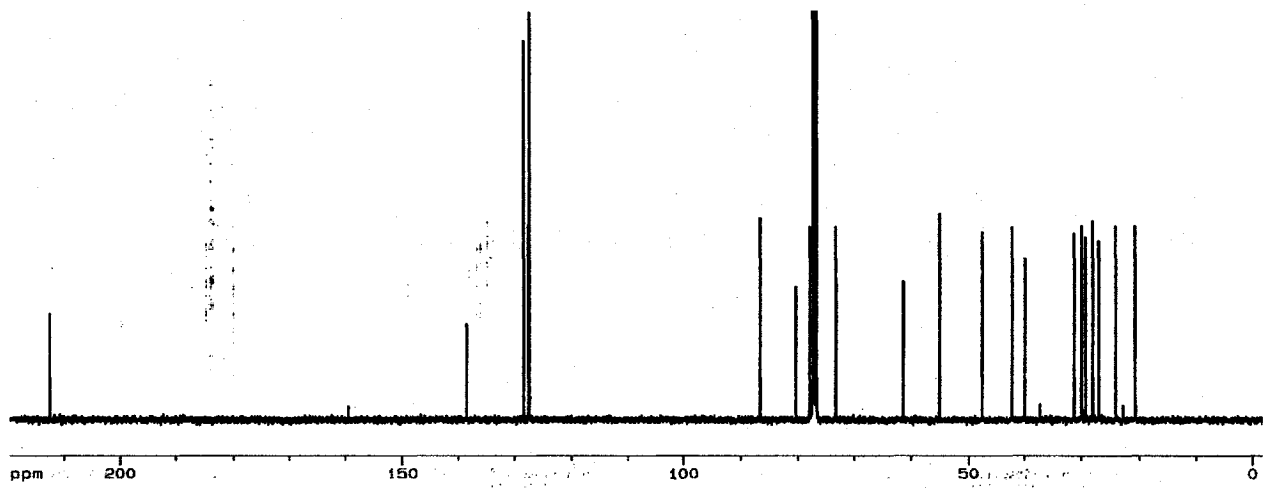


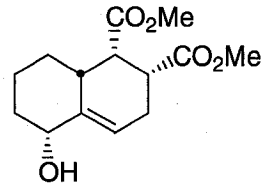
2.75

^{1}H NMR (400 MHz, $CDCl_3$)



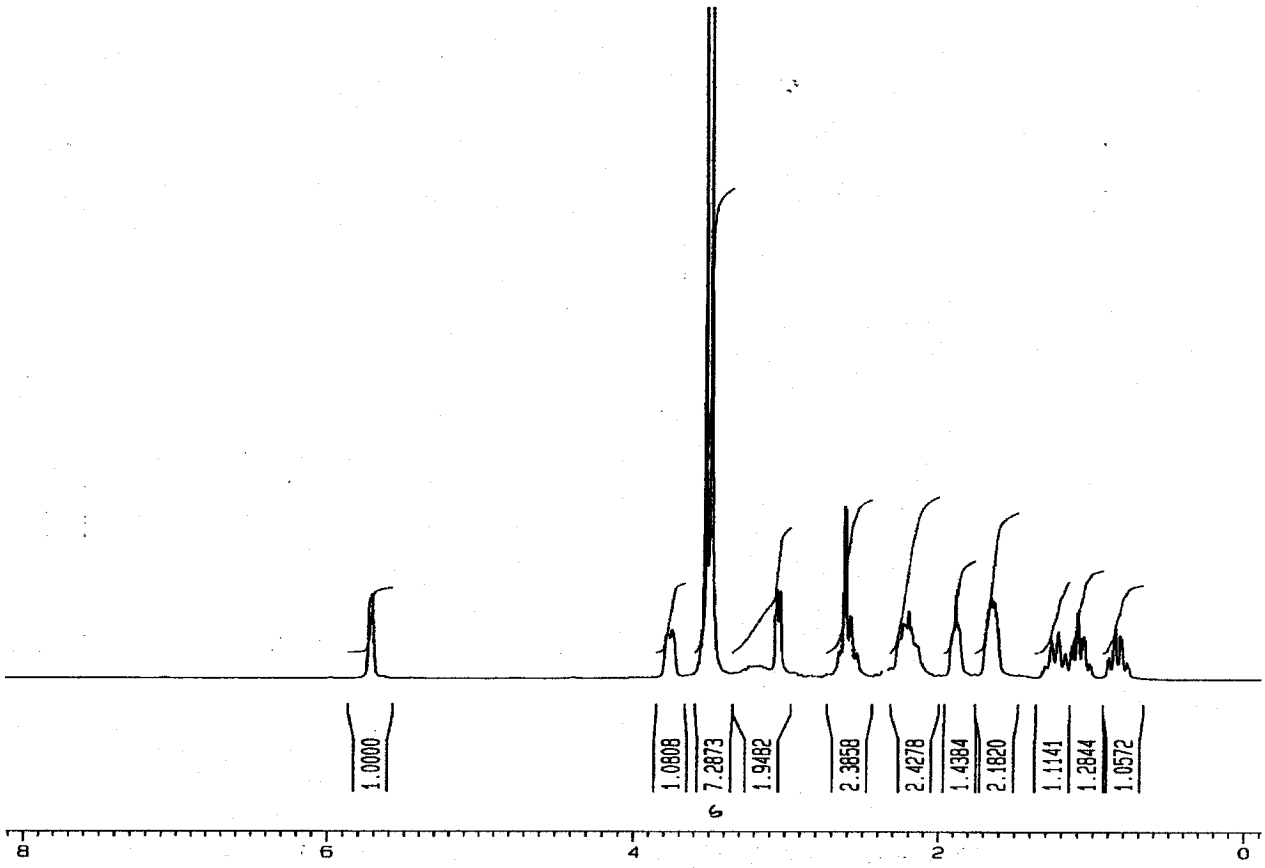
^{13}C NMR (100 MHz, $CDCl_3$)



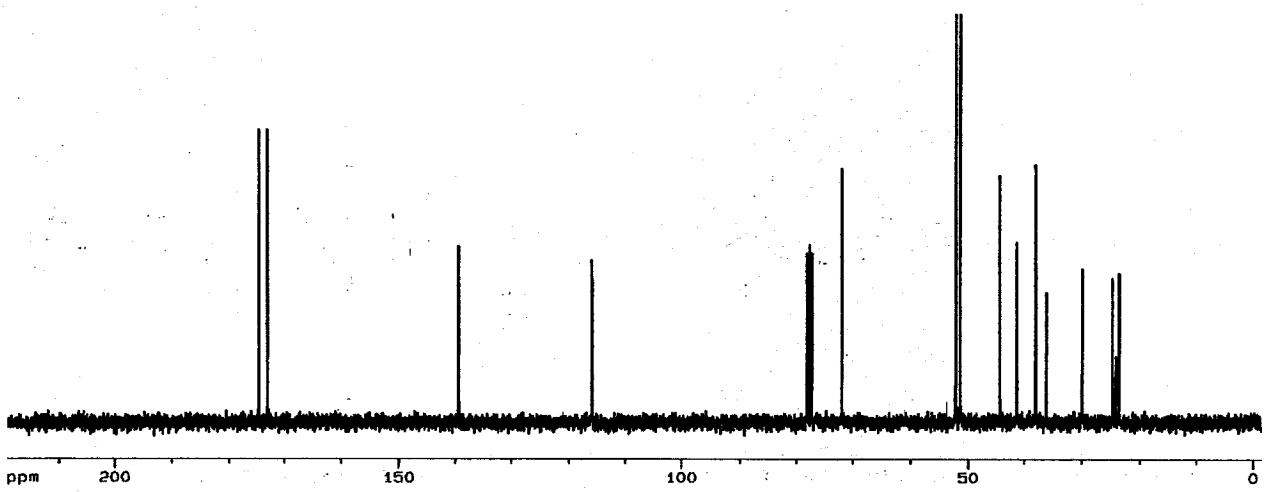


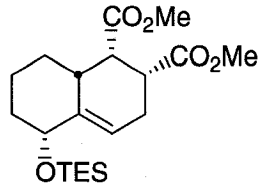
2.82

^{1}H NMR (300 MHz, $CDCl_3$)



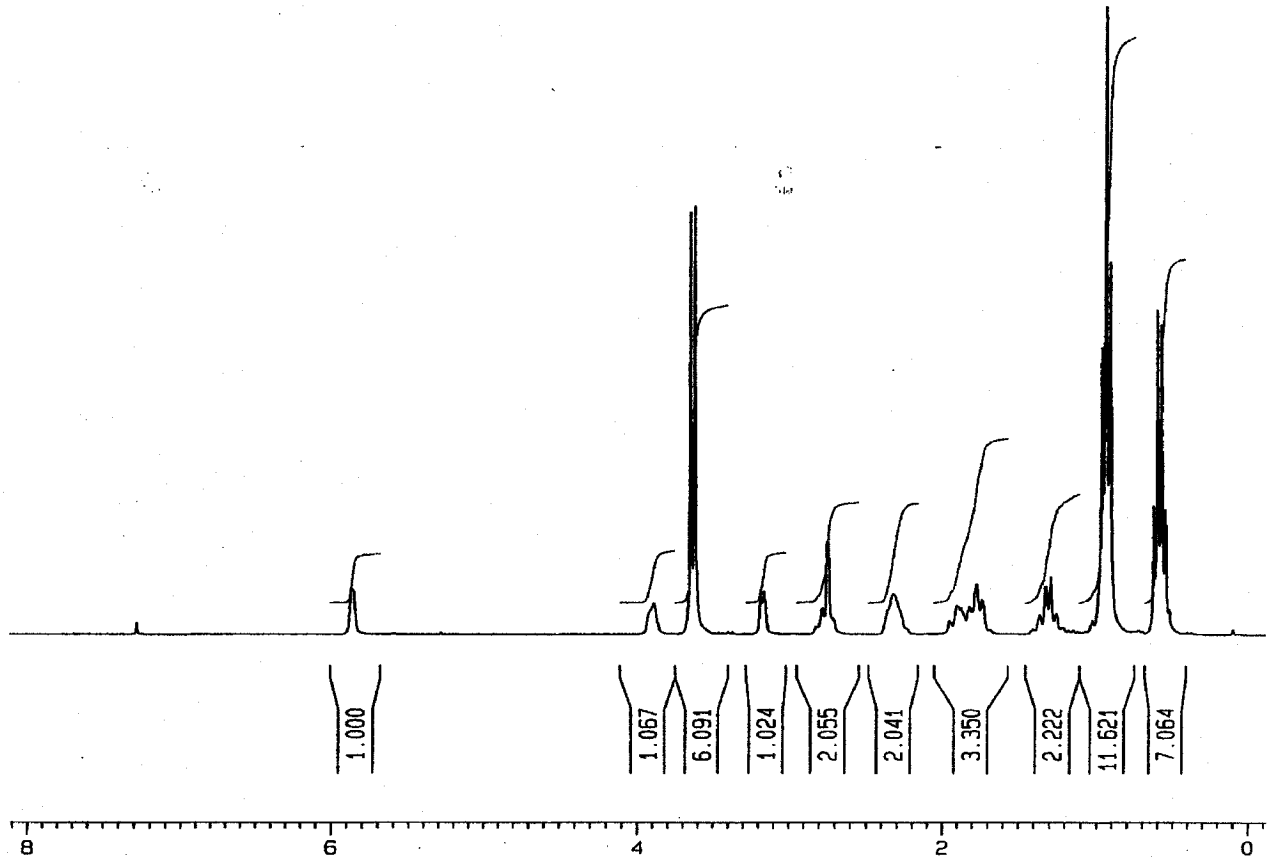
^{13}C NMR (75 MHz, $CDCl_3$)



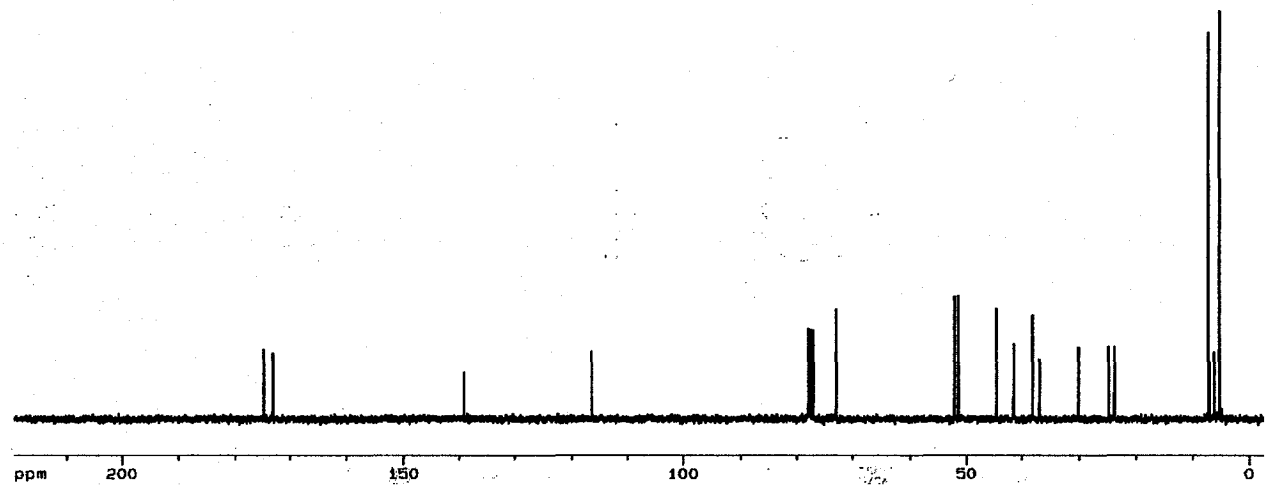


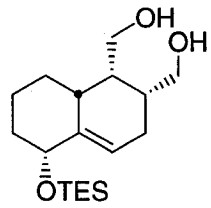
2.83

^{1}H NMR (300 MHz, $CDCl_3$)



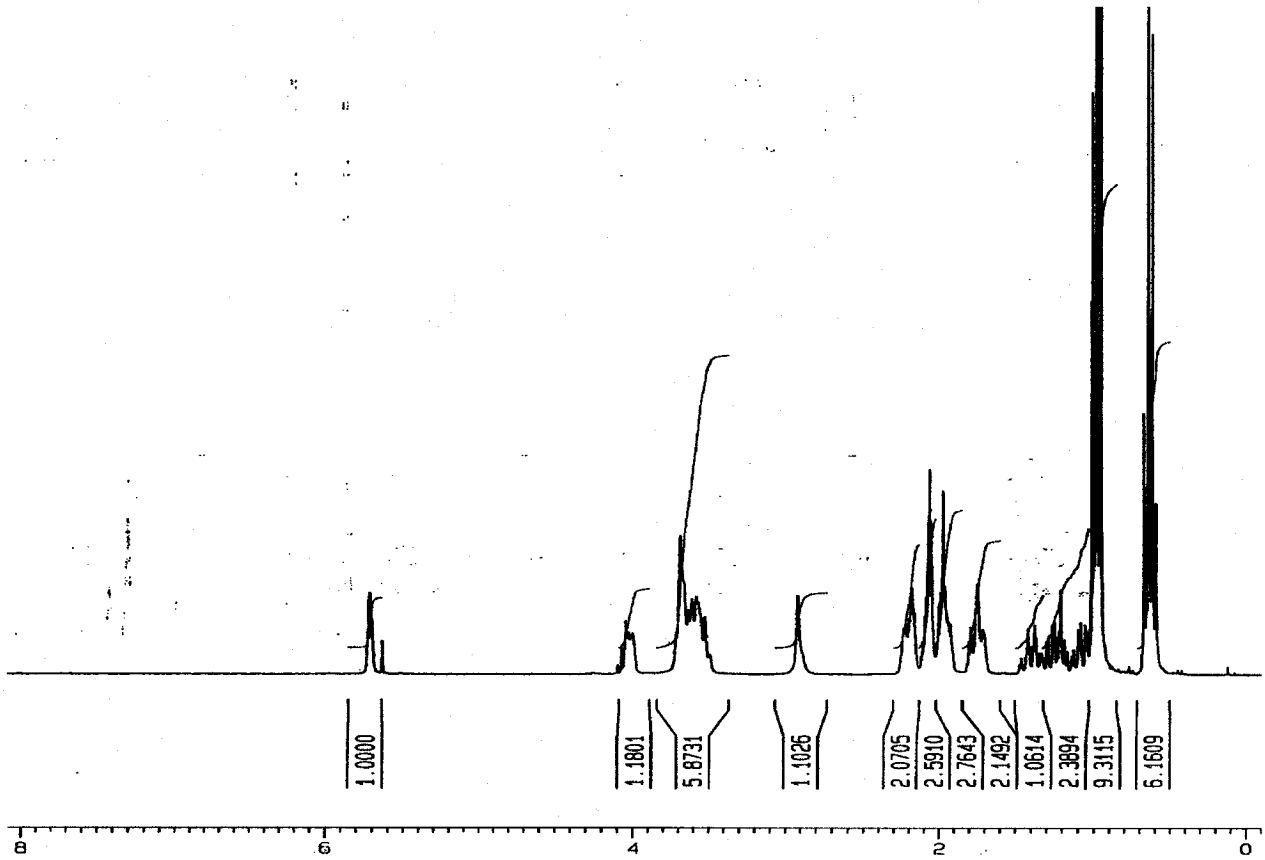
^{13}C NMR (75 MHz, $CDCl_3$)



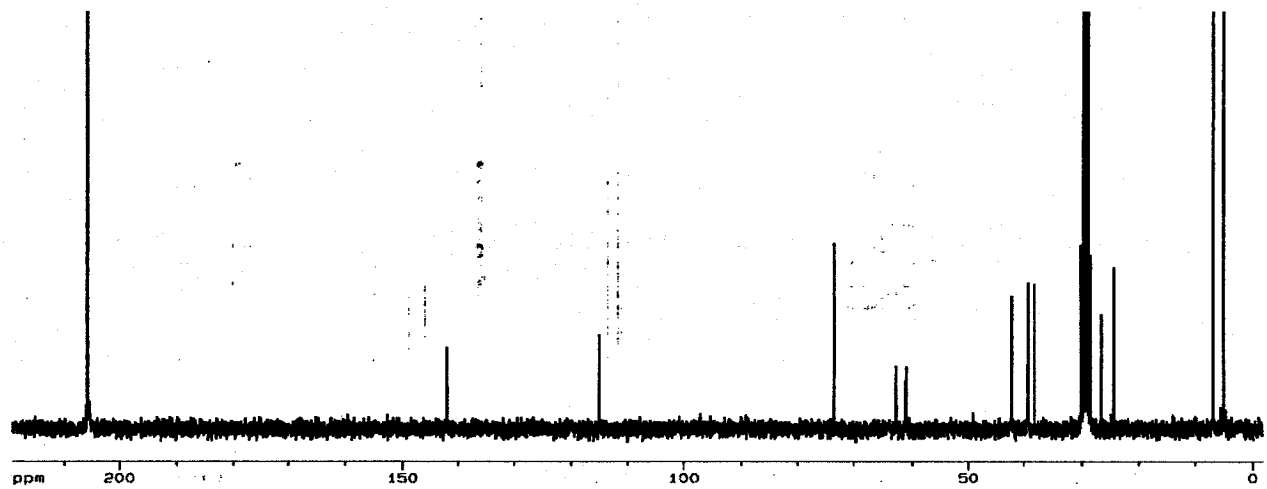


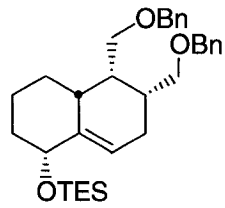
2.84

^{1}H NMR (300 MHz, acetone-d_6)



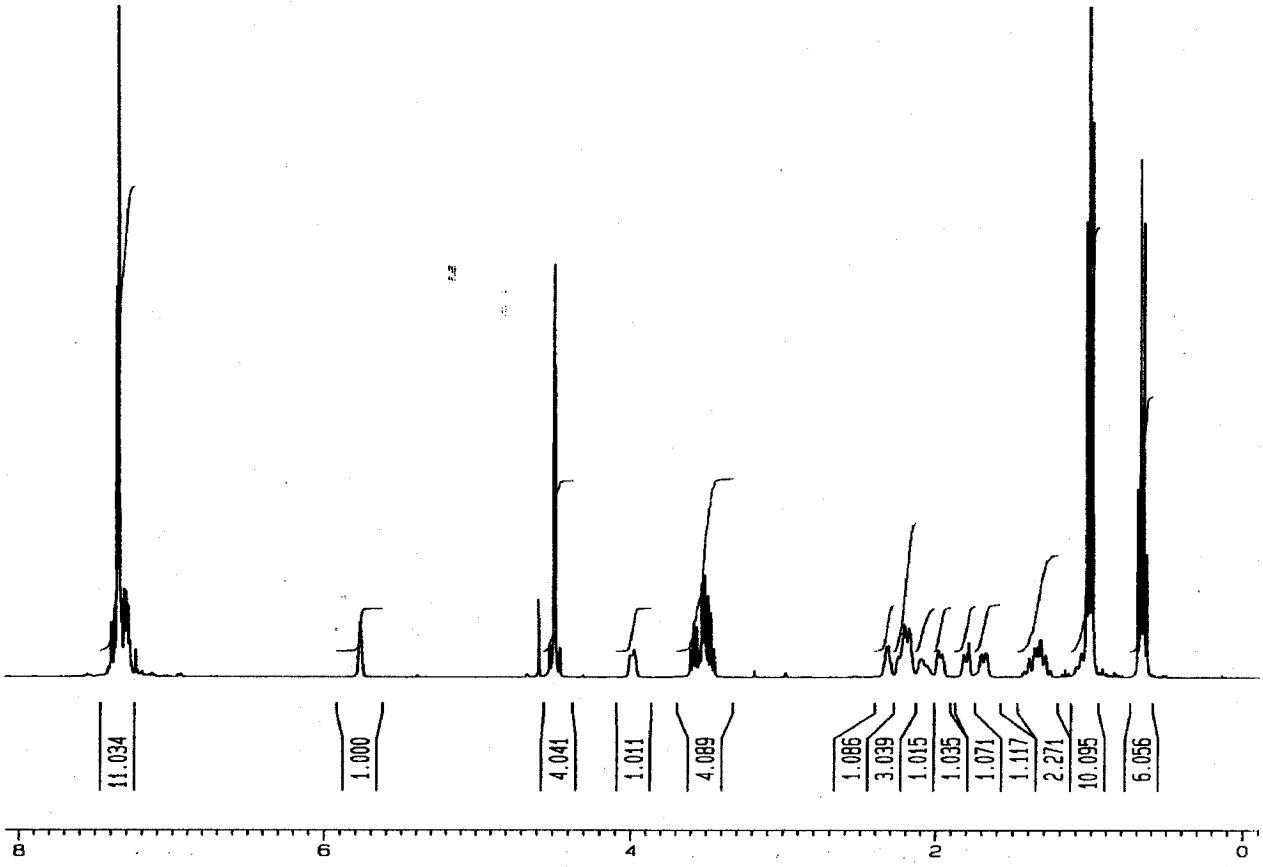
^{13}C NMR (75 MHz, acetone-d_6)



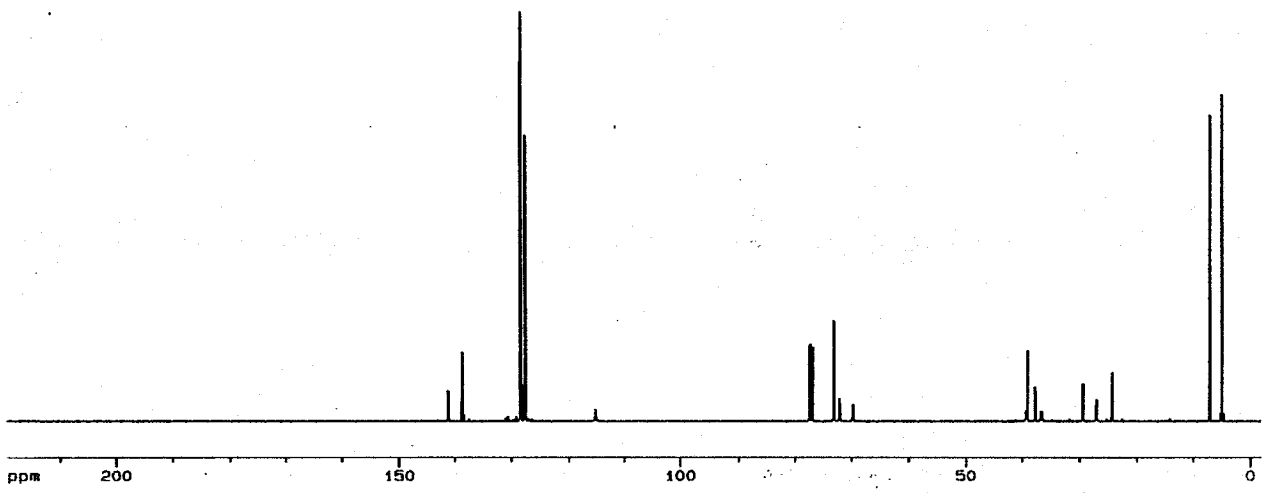


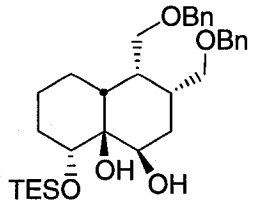
2.85

^{1}H NMR (400 MHz, $CDCl_3$)



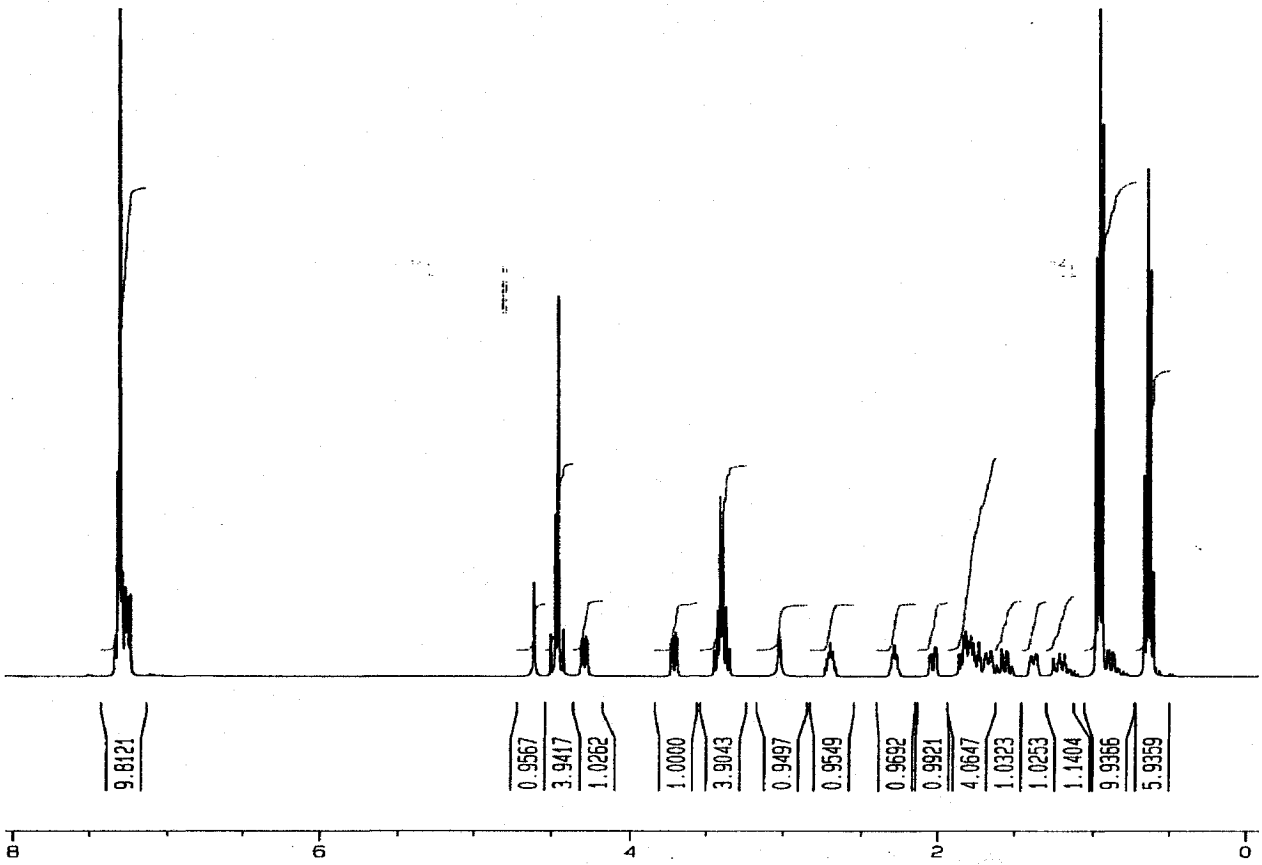
^{13}C NMR (100 MHz, $CDCl_3$)



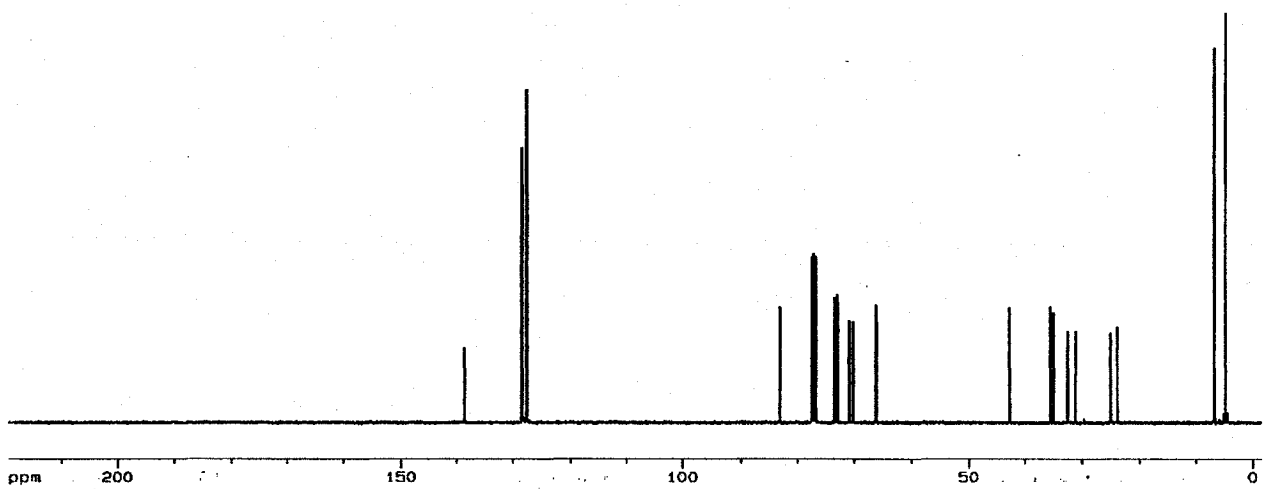


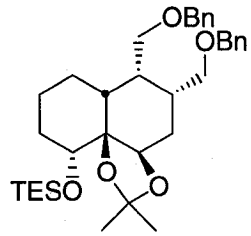
2.86

^{1}H NMR (400 MHz, $CDCl_3$)



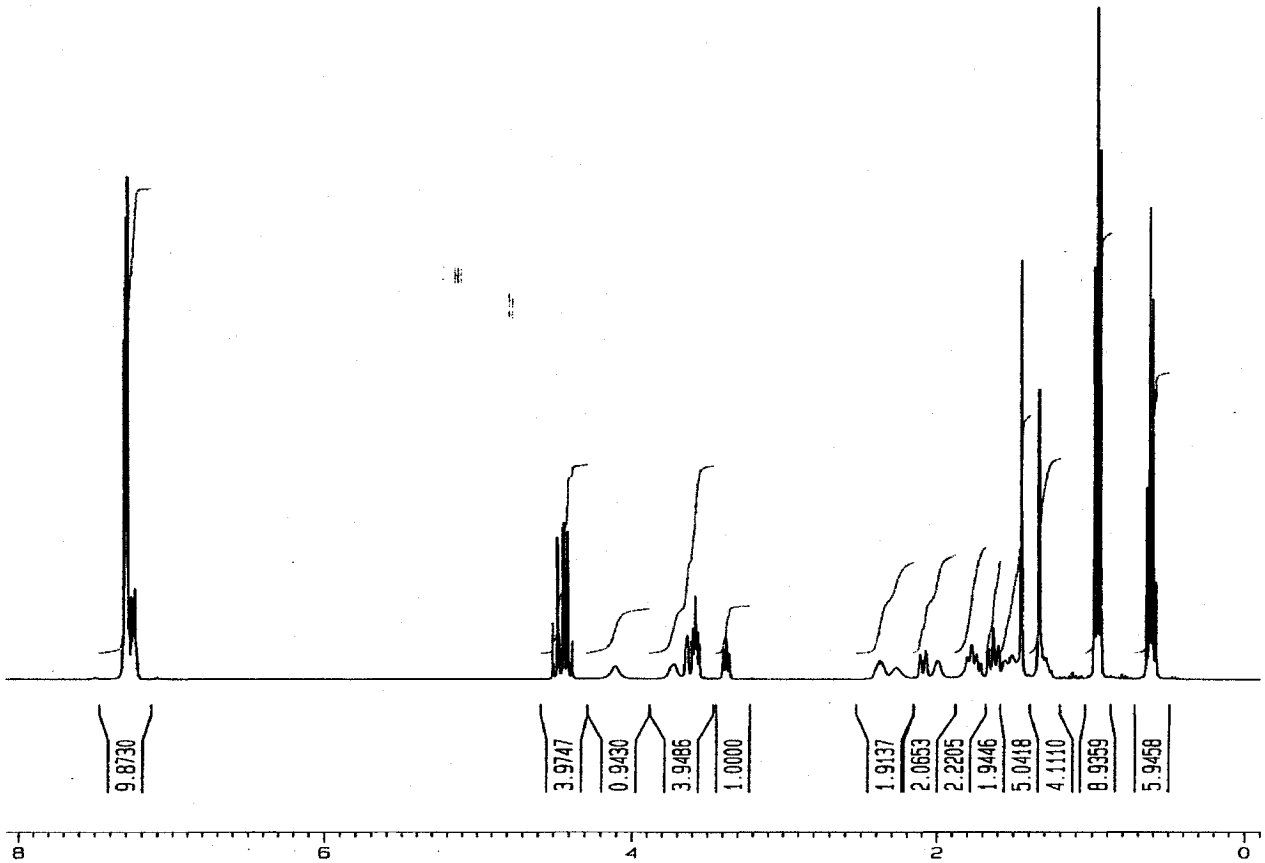
^{13}C NMR (100 MHz, $CDCl_3$)



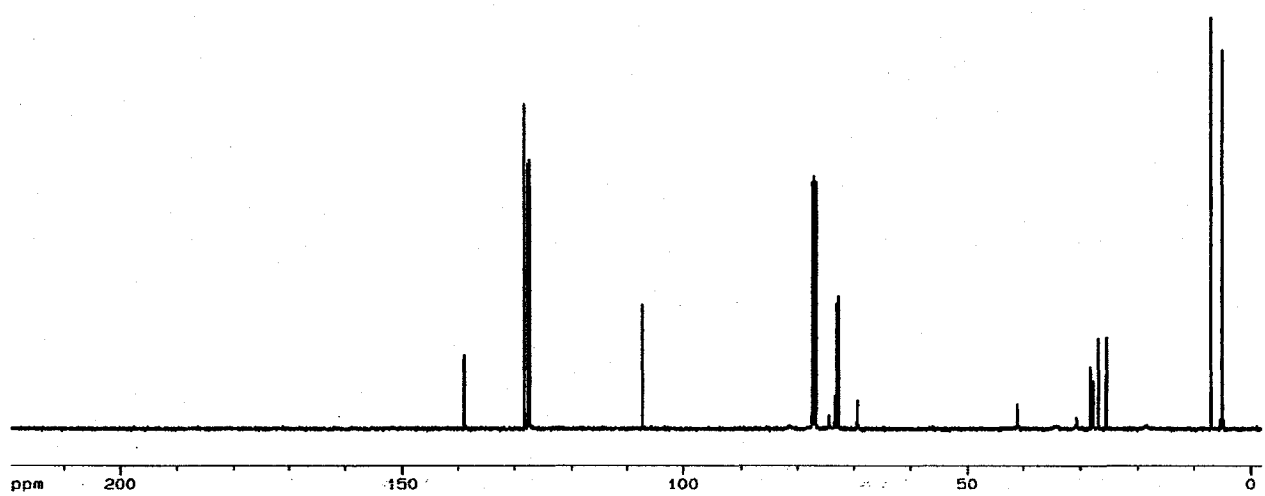


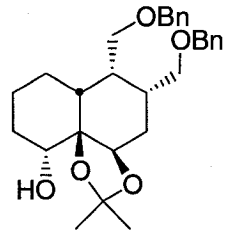
2.87

^{1}H NMR (400 MHz, $CDCl_3$)



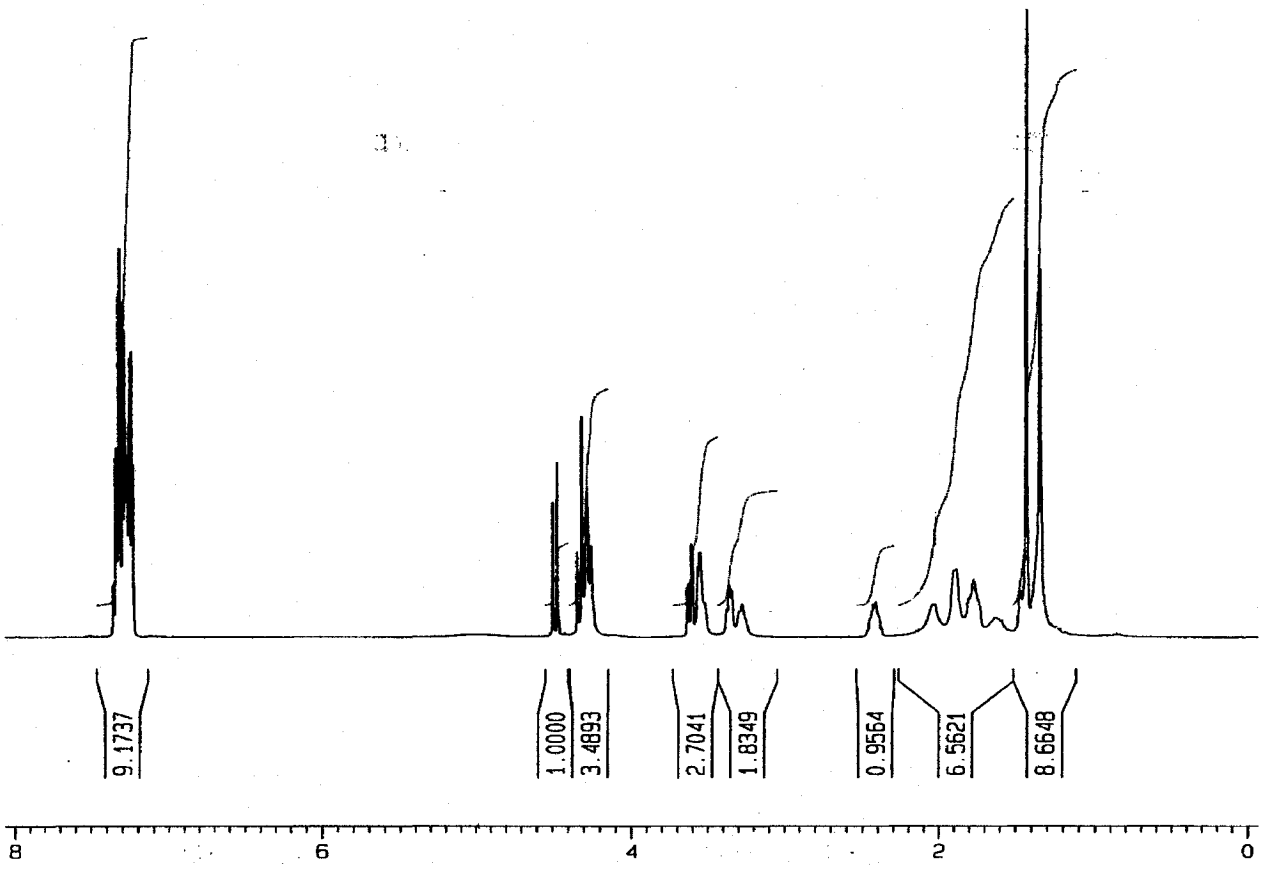
^{13}C NMR (100 MHz, $CDCl_3$)



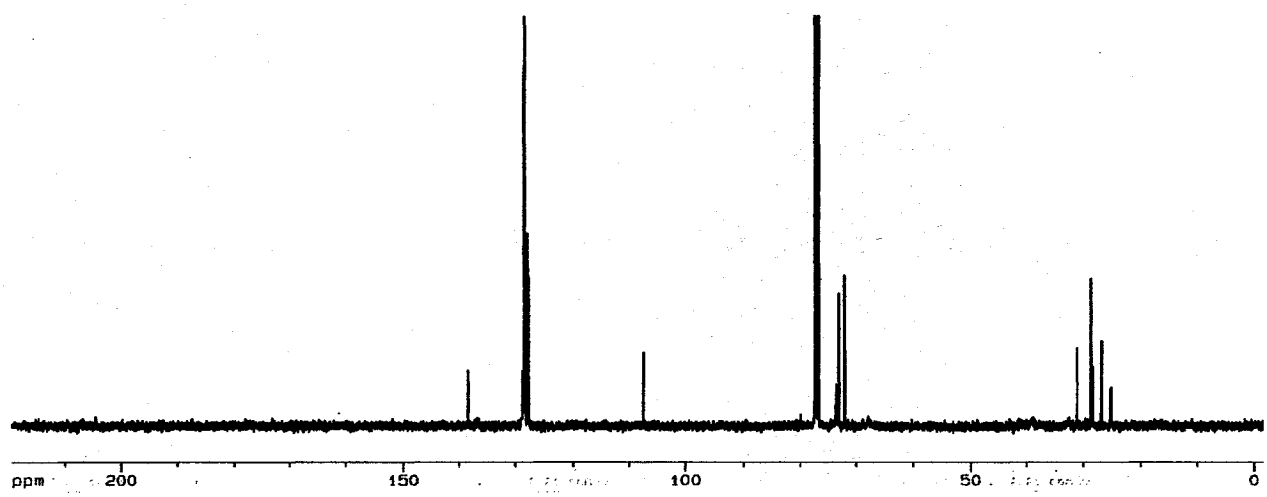


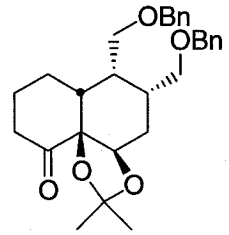
2.88

^{1}H NMR (400 MHz, $CDCl_3$)



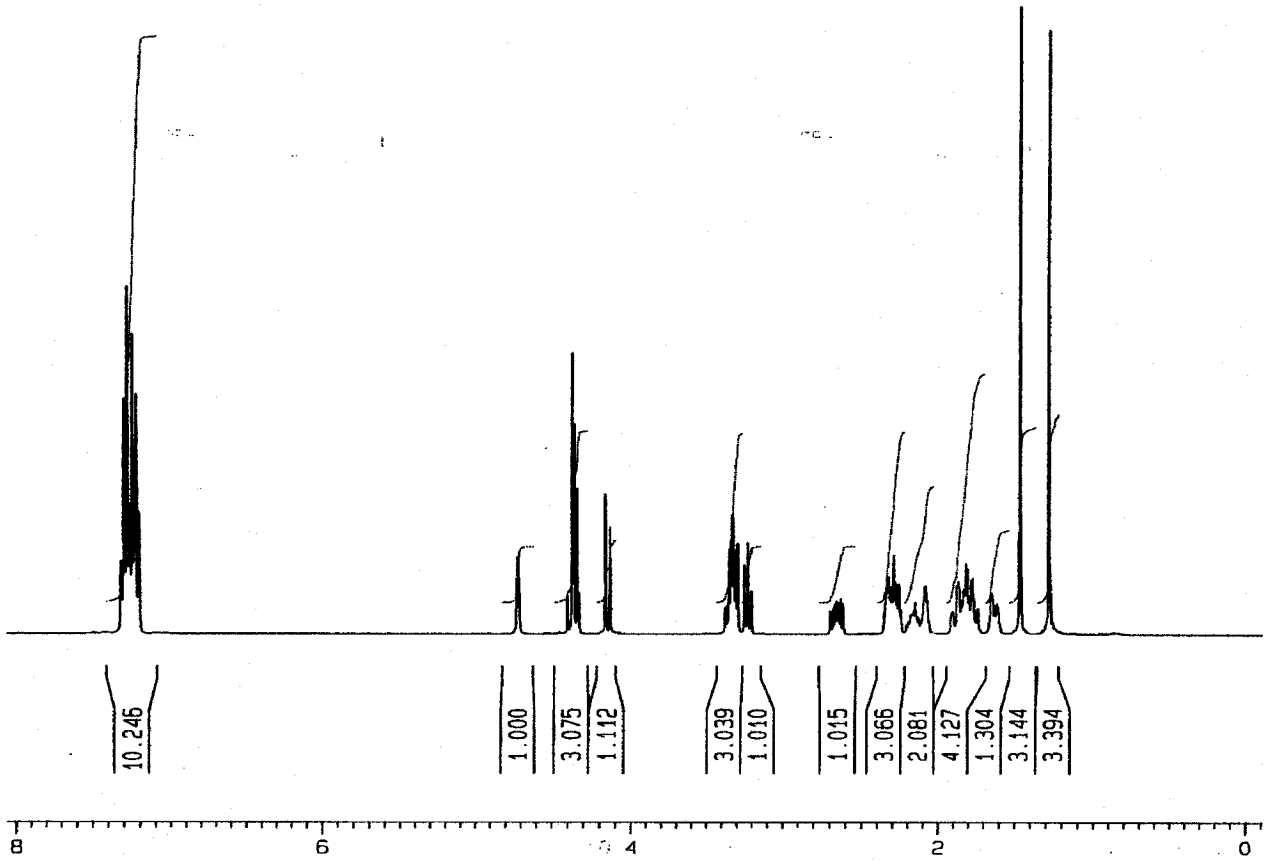
^{13}C NMR (100 MHz, $CDCl_3$)



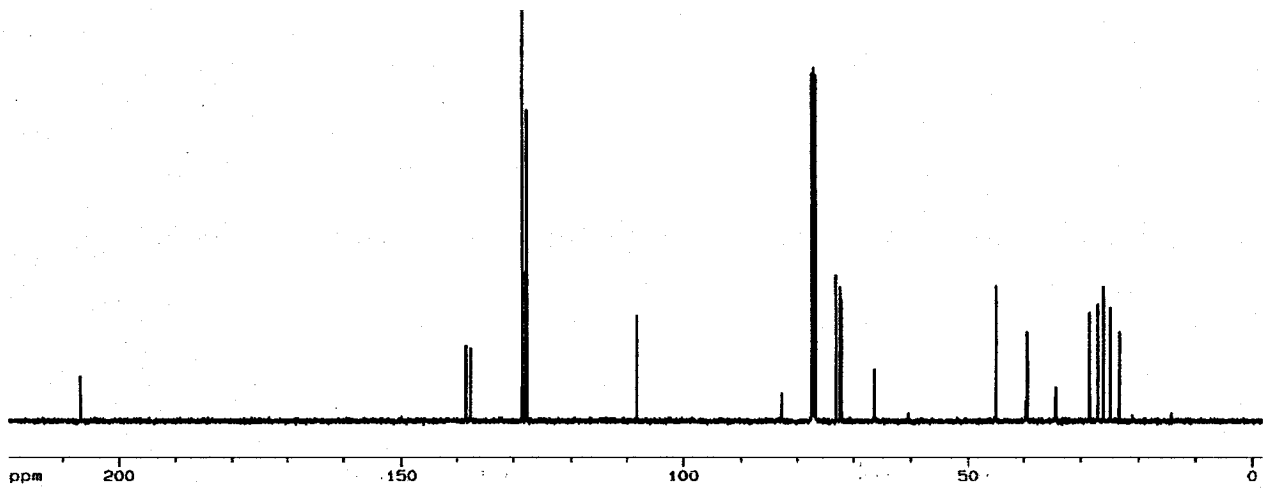


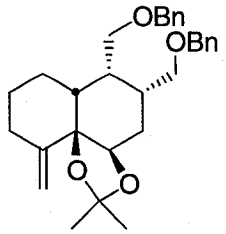
2.89

^{1}H NMR (400 MHz, $CDCl_3$)



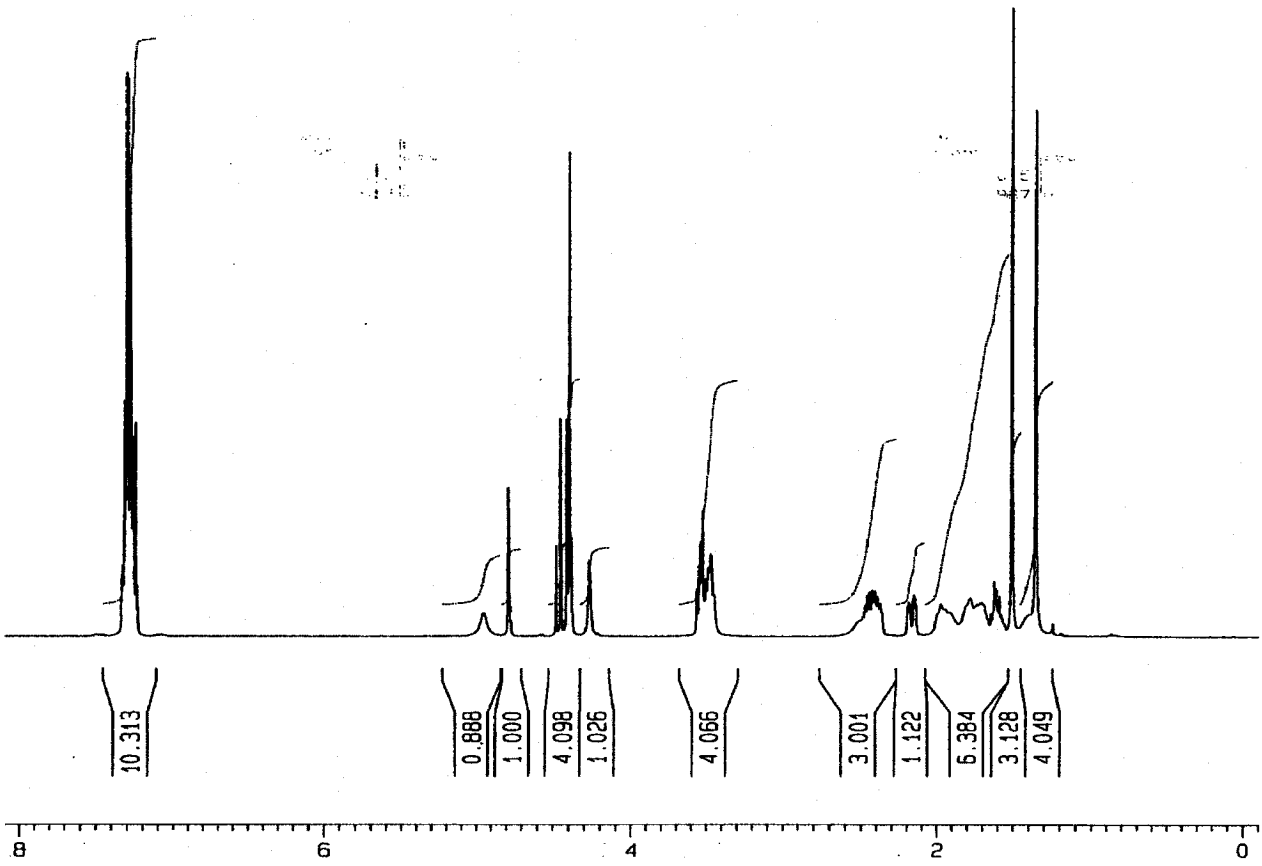
^{13}C NMR (100 MHz, $CDCl_3$)



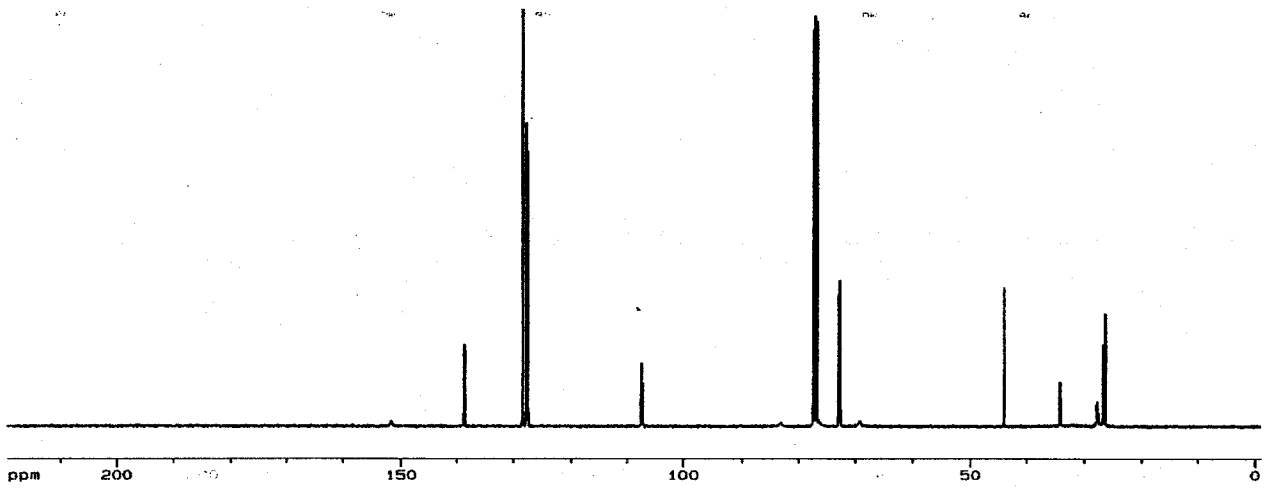


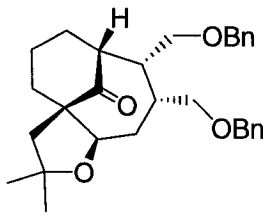
2.90

^{1}H NMR (400 MHz, $CDCl_3$)



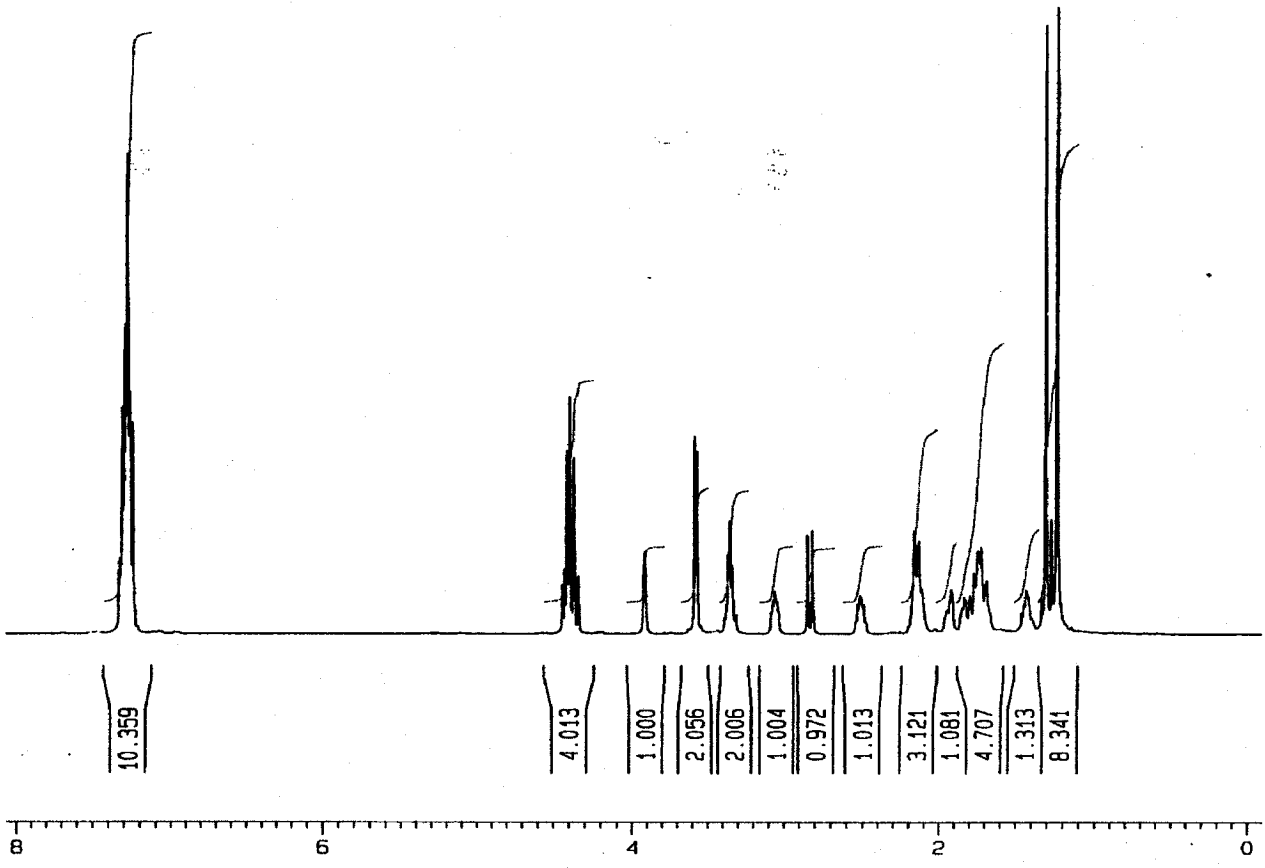
^{13}C NMR (100 MHz, $CDCl_3$)



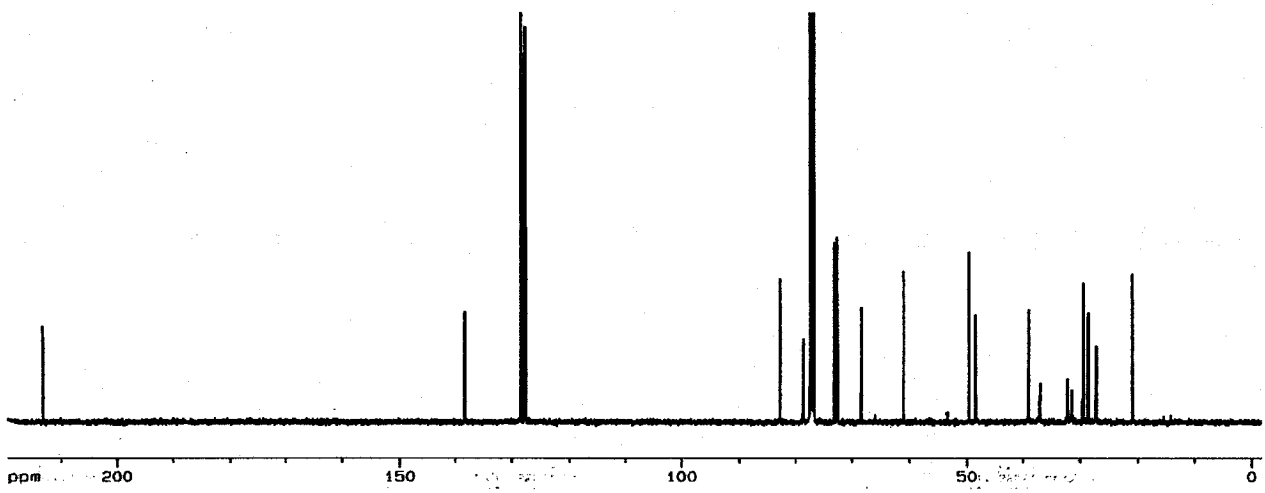


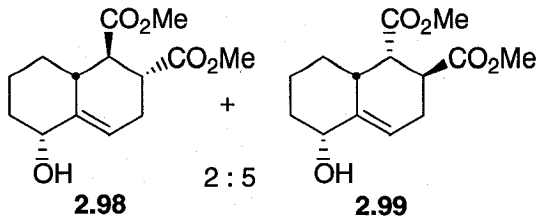
2.91

^{1}H NMR (400 MHz, $CDCl_3$)



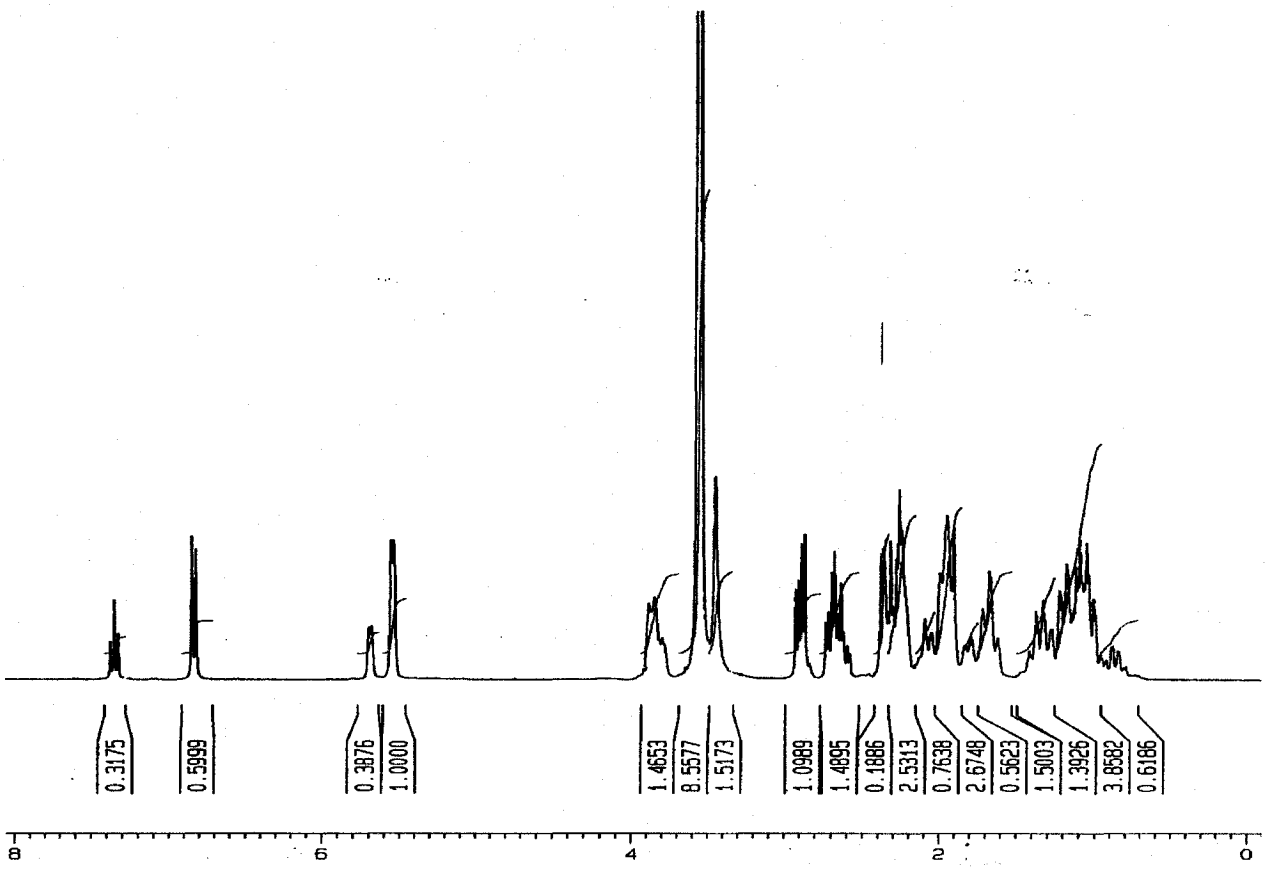
^{13}C NMR (100 MHz, $CDCl_3$)



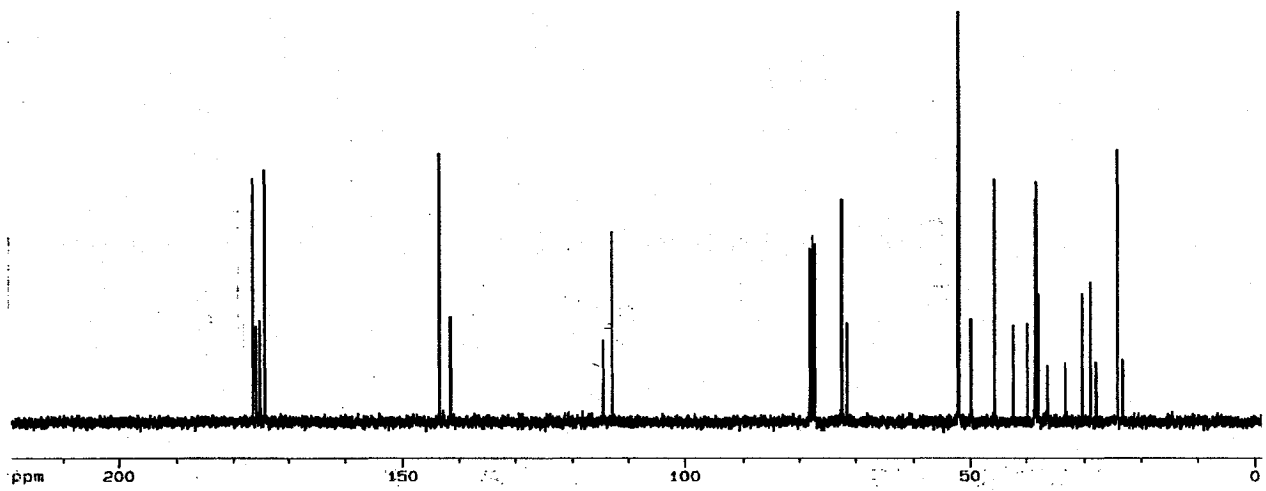


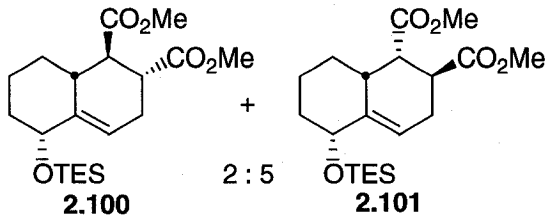
2.98 **2.99**

^{1}H NMR (300 MHz, $CDCl_3$)

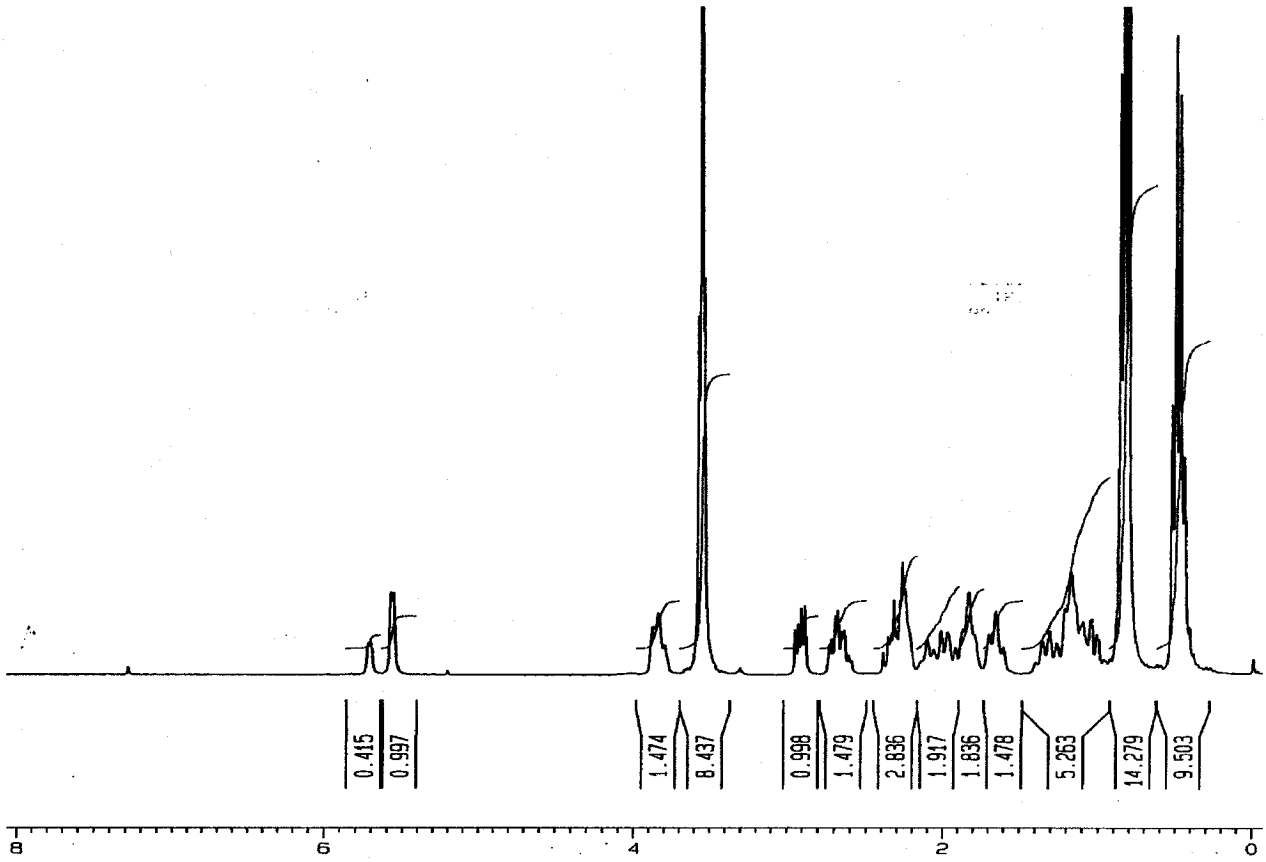


^{13}C NMR (75 MHz, $CDCl_3$)

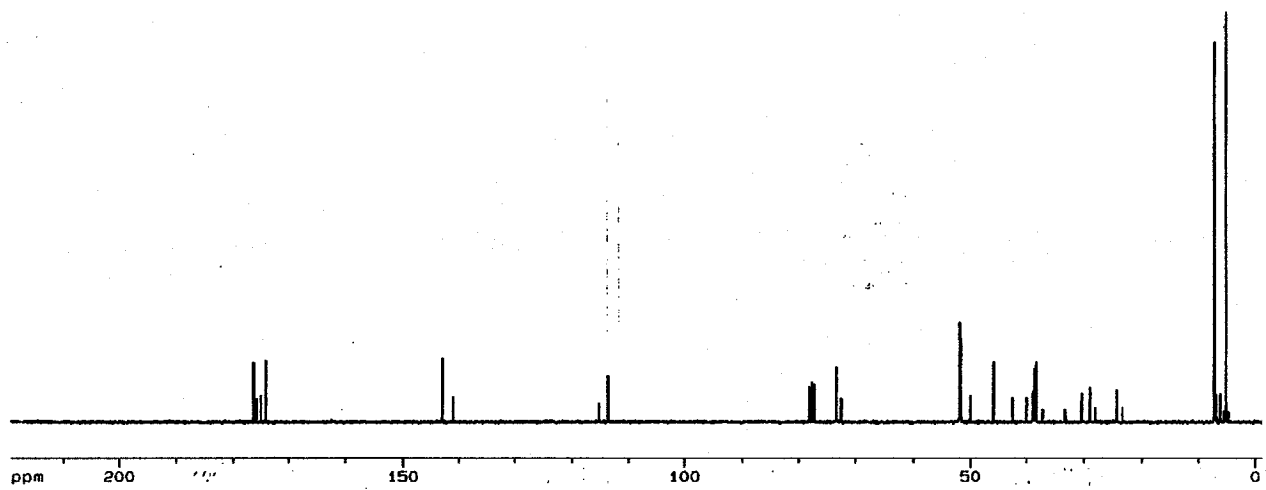


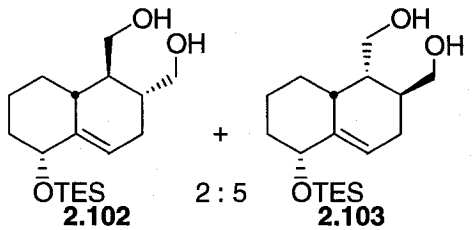


^{1}H NMR (300 MHz, $CDCl_3$)

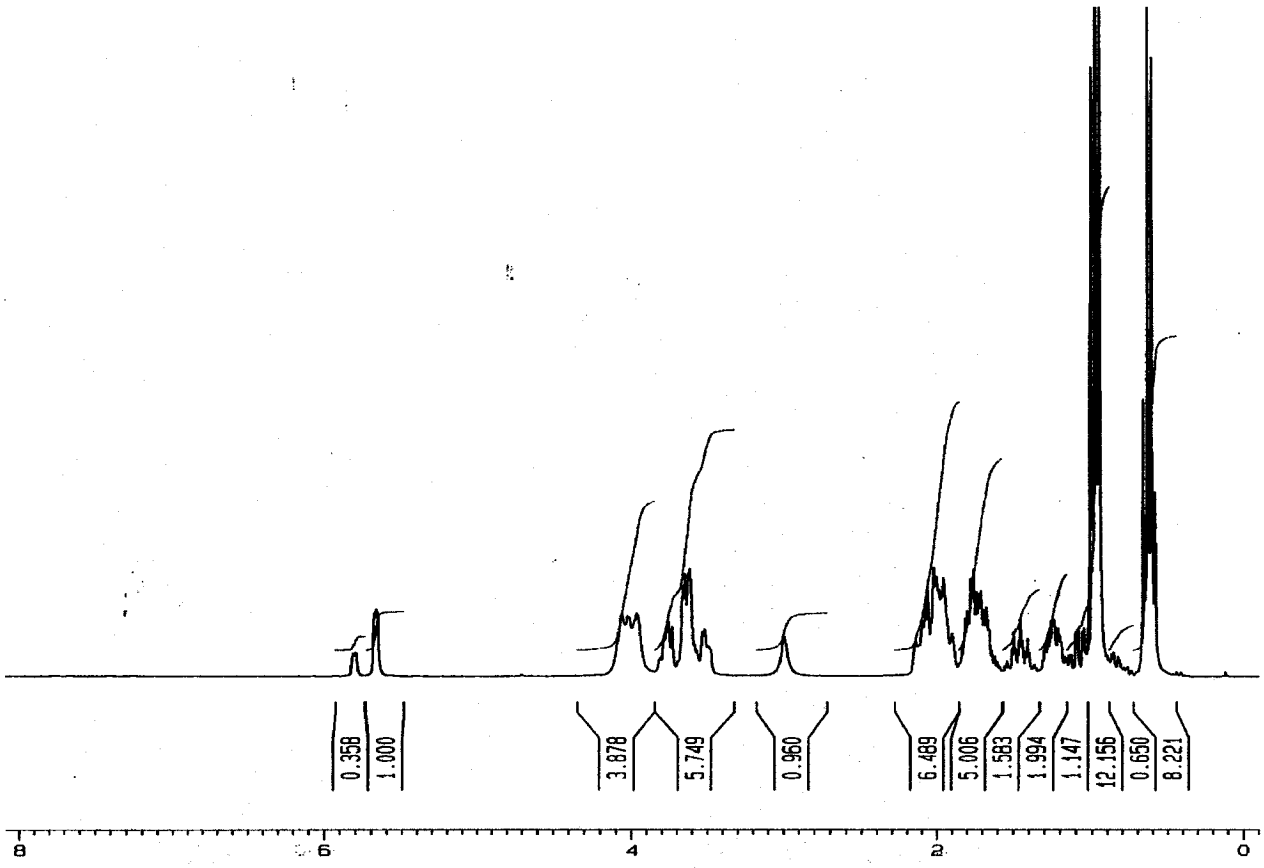


^{13}C NMR (75 MHz, $CDCl_3$)

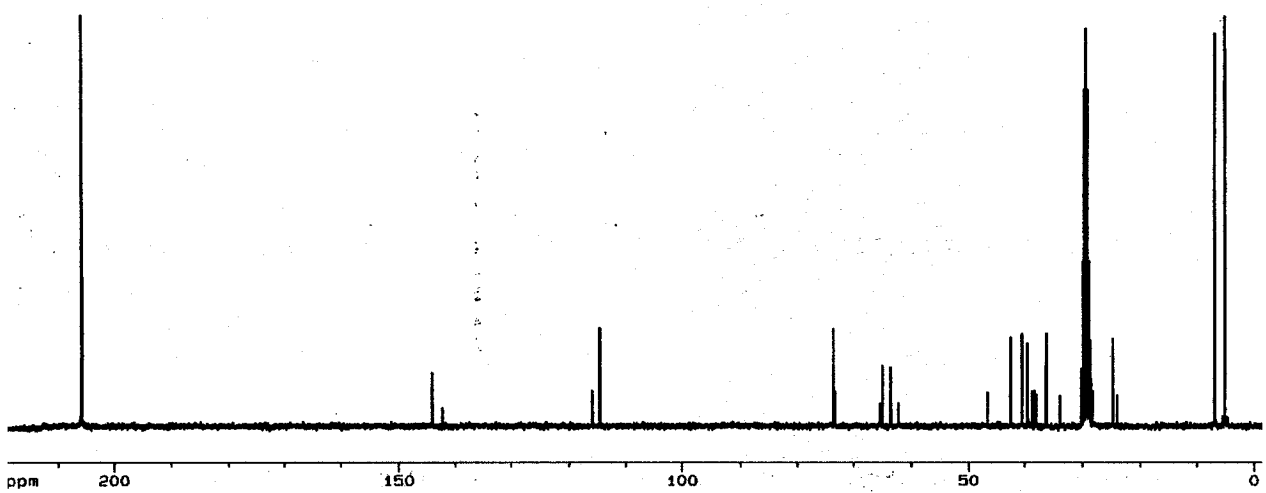


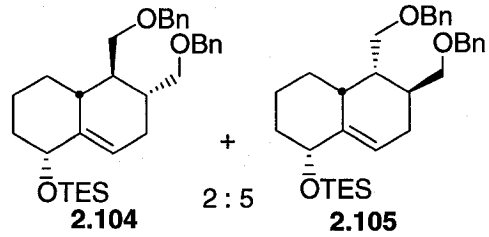


^{1}H NMR (300 MHz, acetone-d_6)

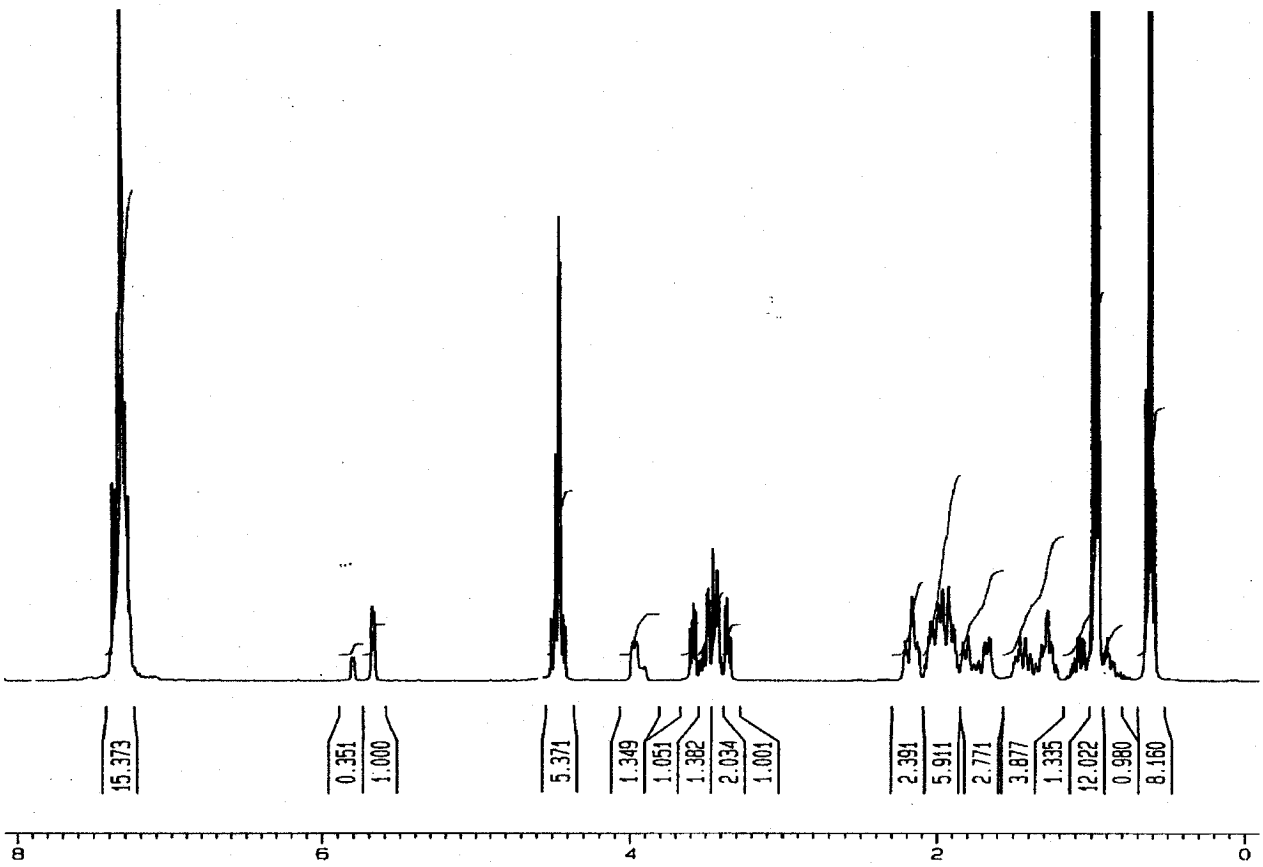


^{13}C NMR (75 MHz, acetone-d_6)

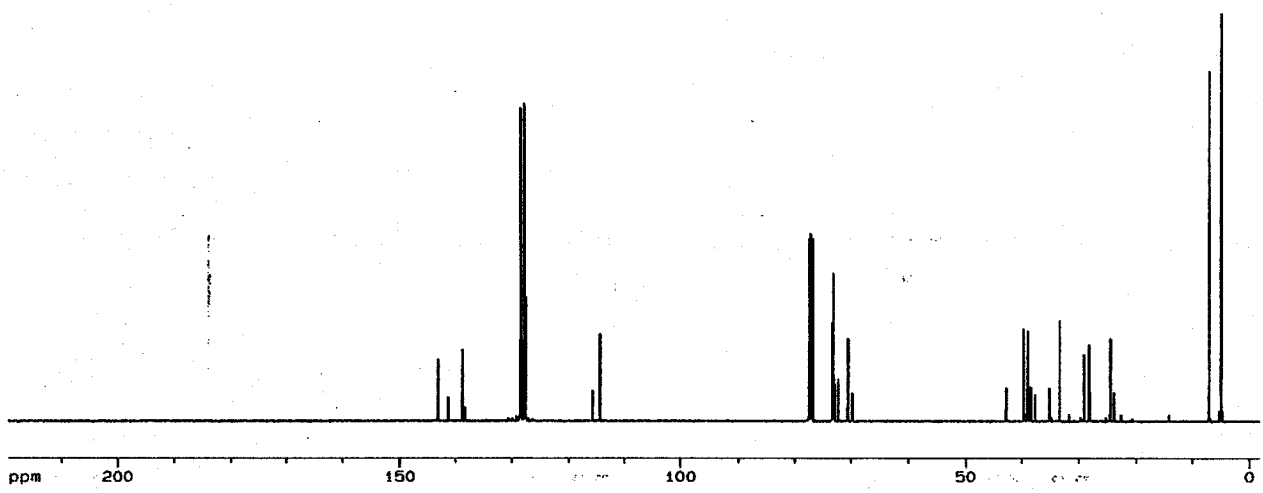


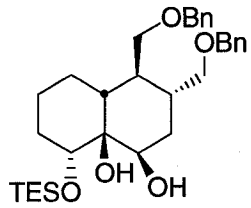


^{1}H NMR (400 MHz, $CDCl_3$)



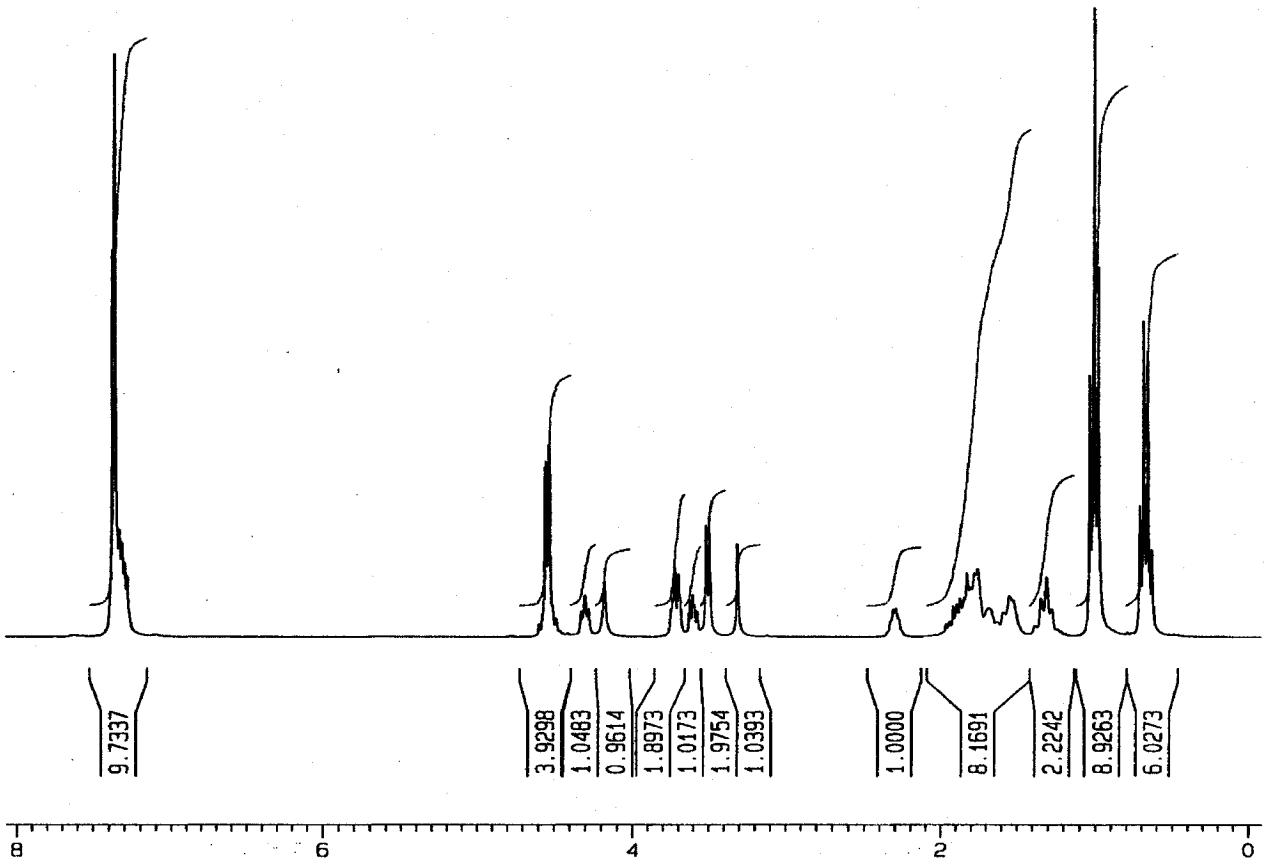
^{13}C NMR (100 MHz, $CDCl_3$)



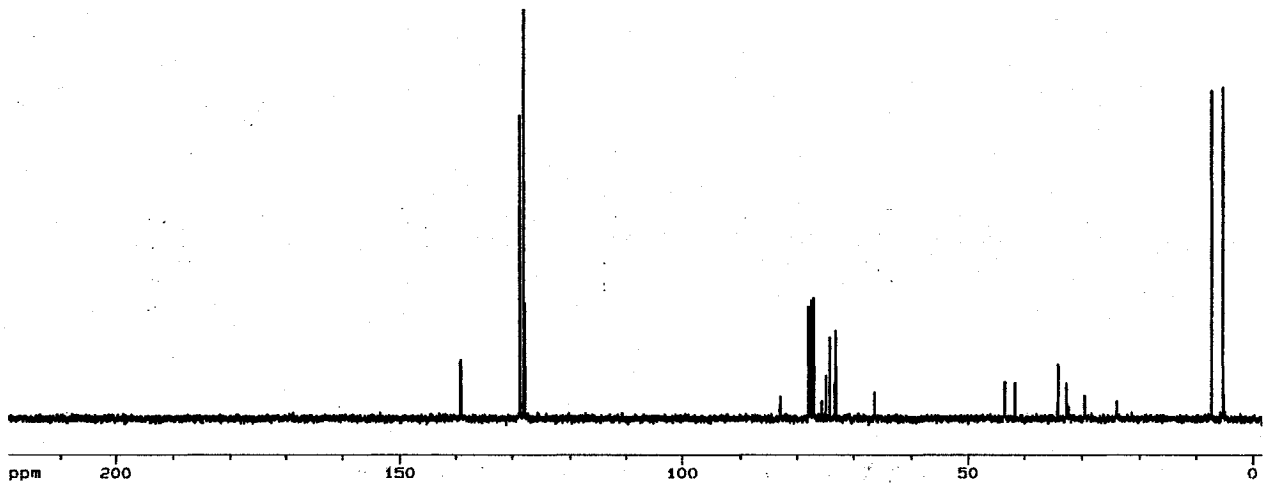


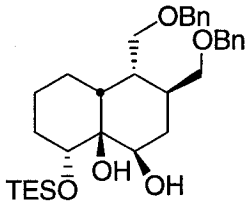
2.106

^{1}H NMR (300 MHz, $CDCl_3$)



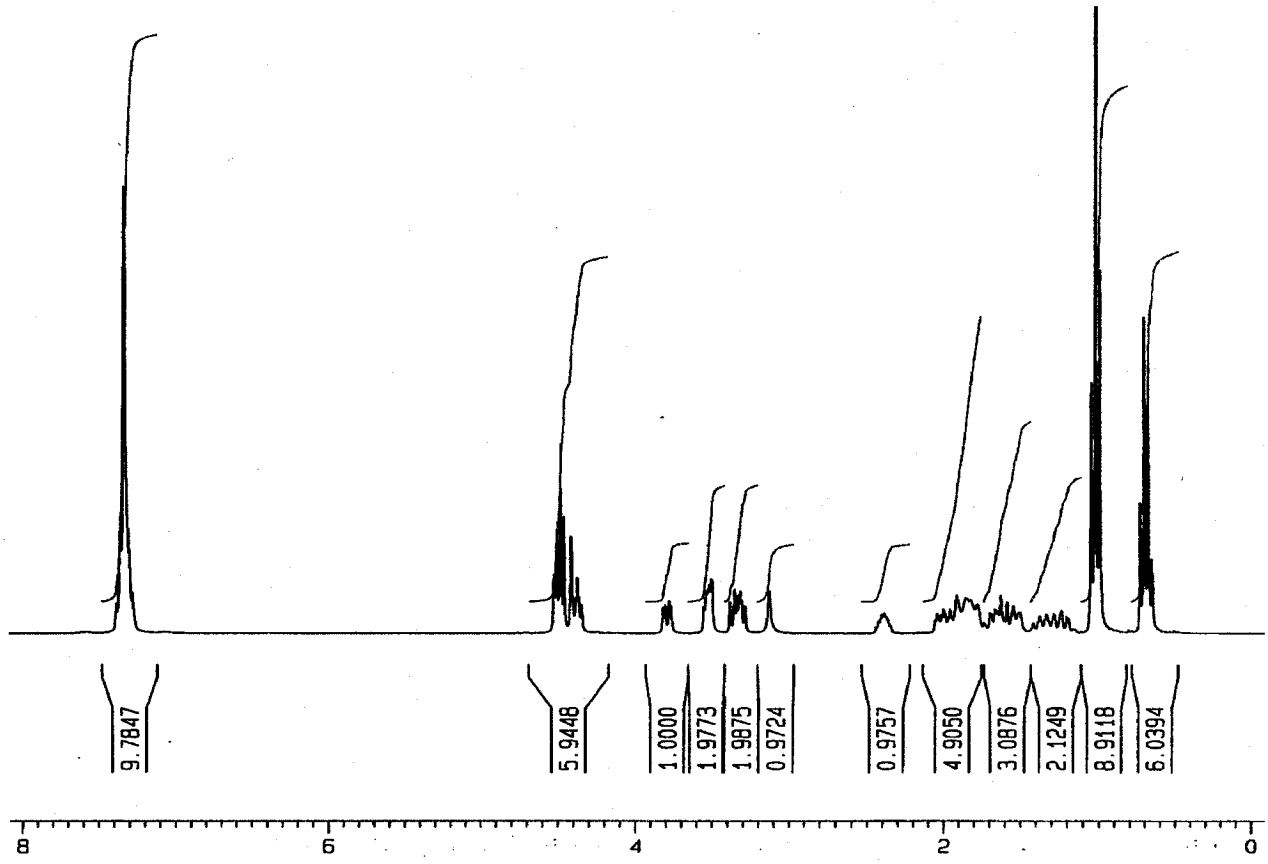
^{13}C NMR (75 MHz, $CDCl_3$)



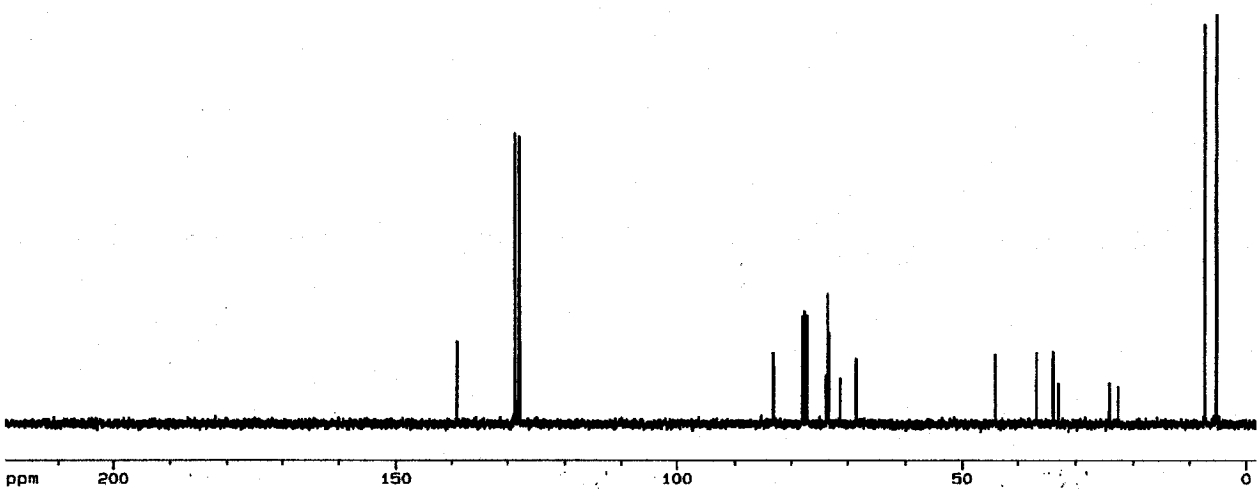


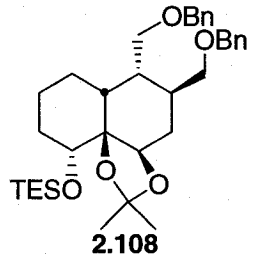
2.107

^{1}H NMR (300 MHz, $CDCl_3$)



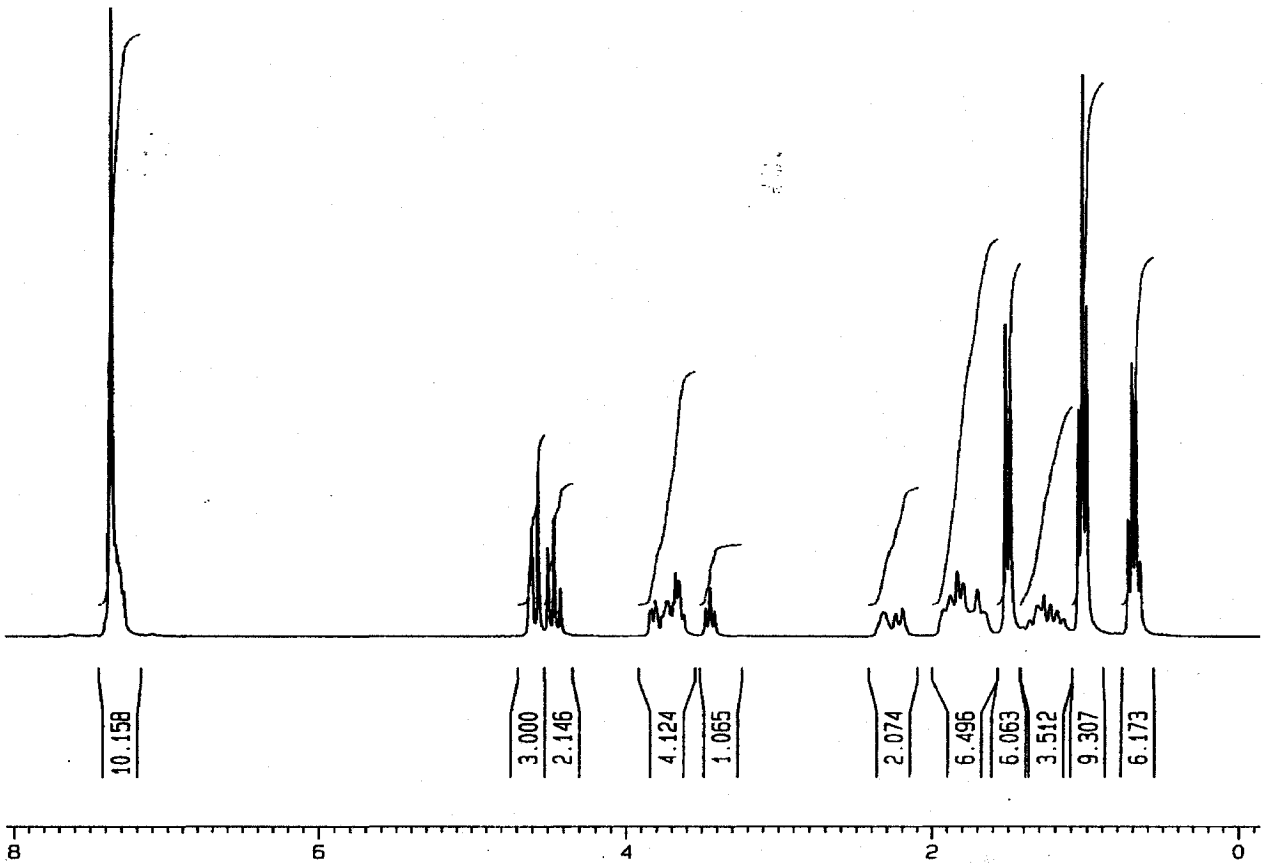
^{13}C NMR (75 MHz, $CDCl_3$)



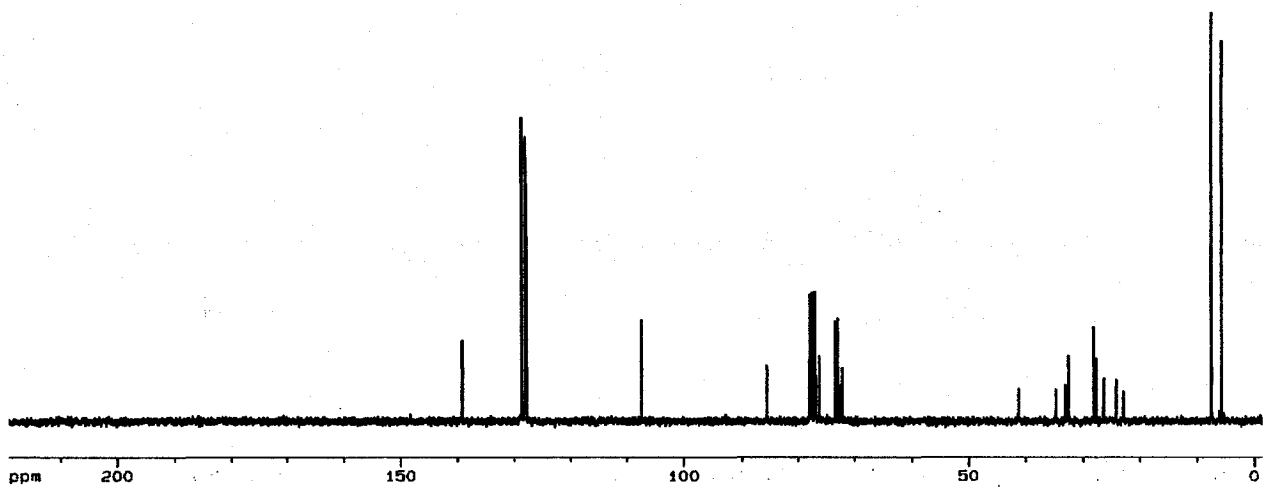


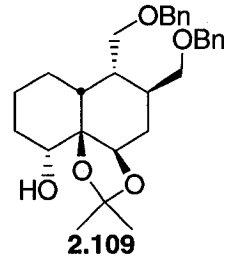
2.108

^{1}H NMR (300 MHz, $CDCl_3$)



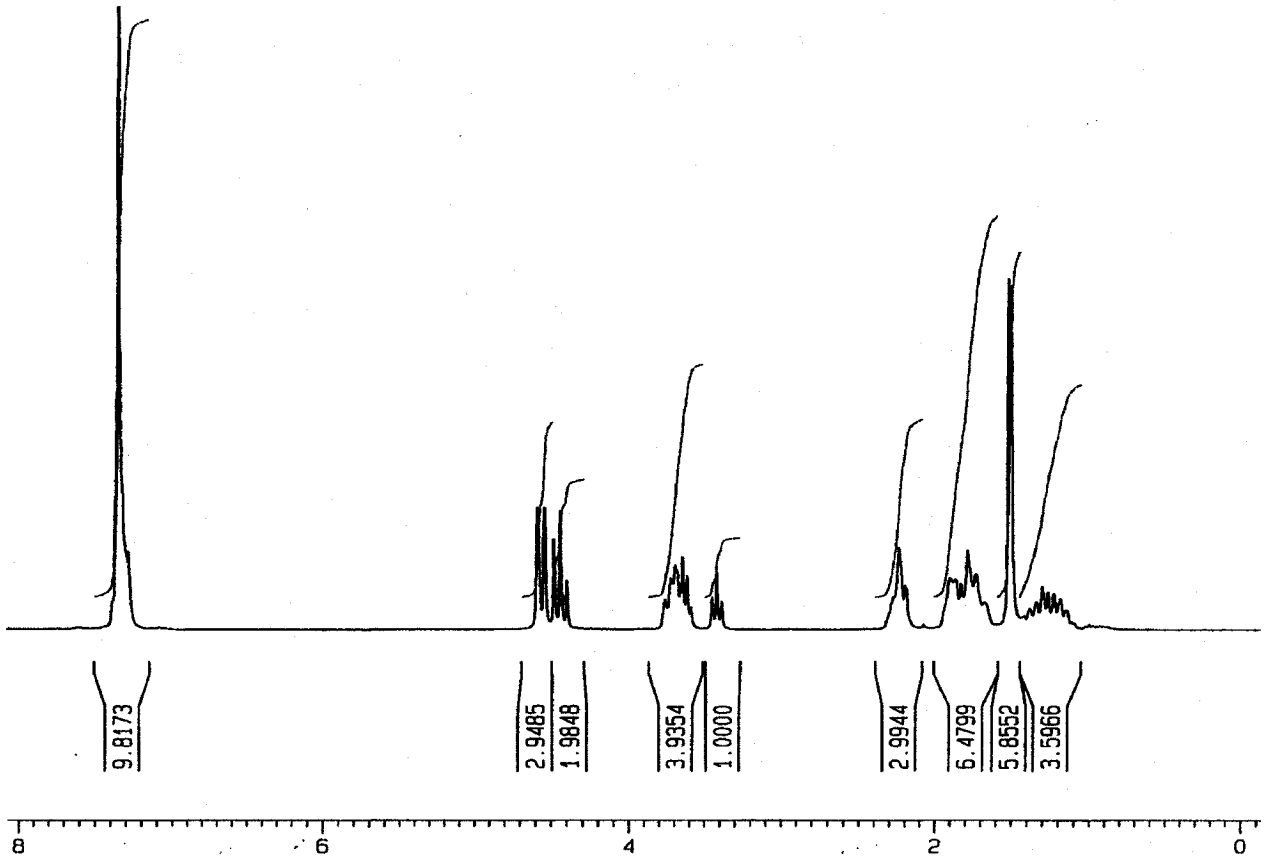
^{13}C NMR (75 MHz, $CDCl_3$)



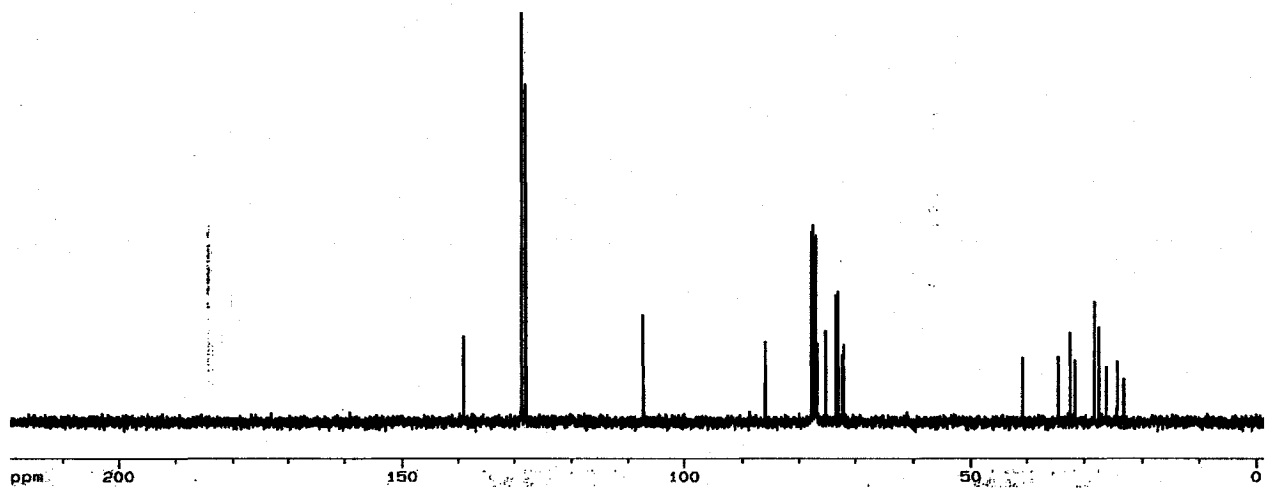


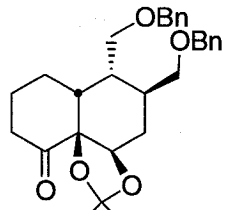
2.109

^{1}H NMR (300 MHz, $CDCl_3$)



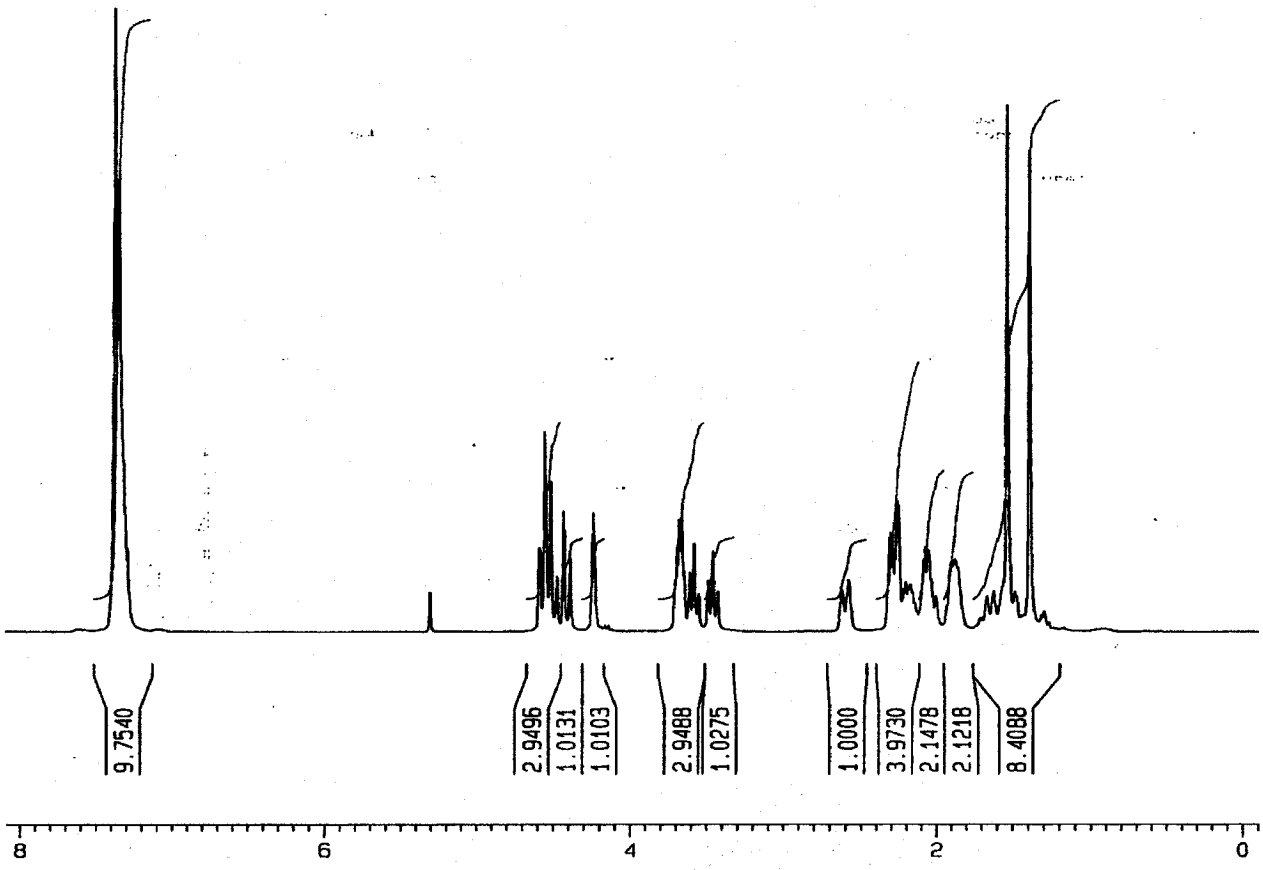
^{13}C NMR (75 MHz, $CDCl_3$)



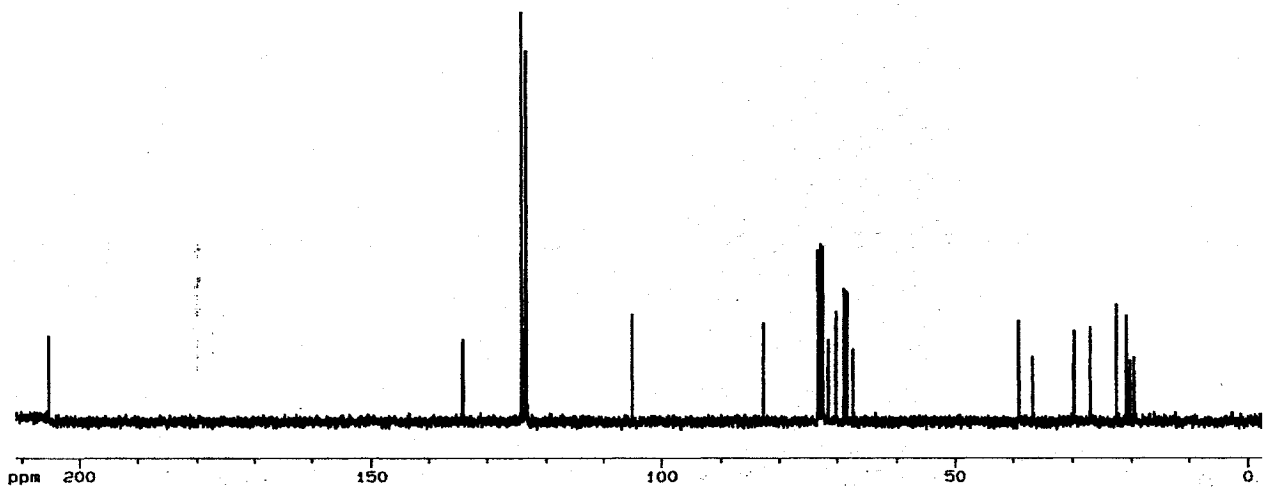


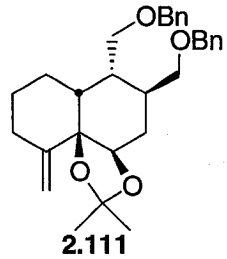
2.110

^{1}H NMR (300 MHz, $CDCl_3$)



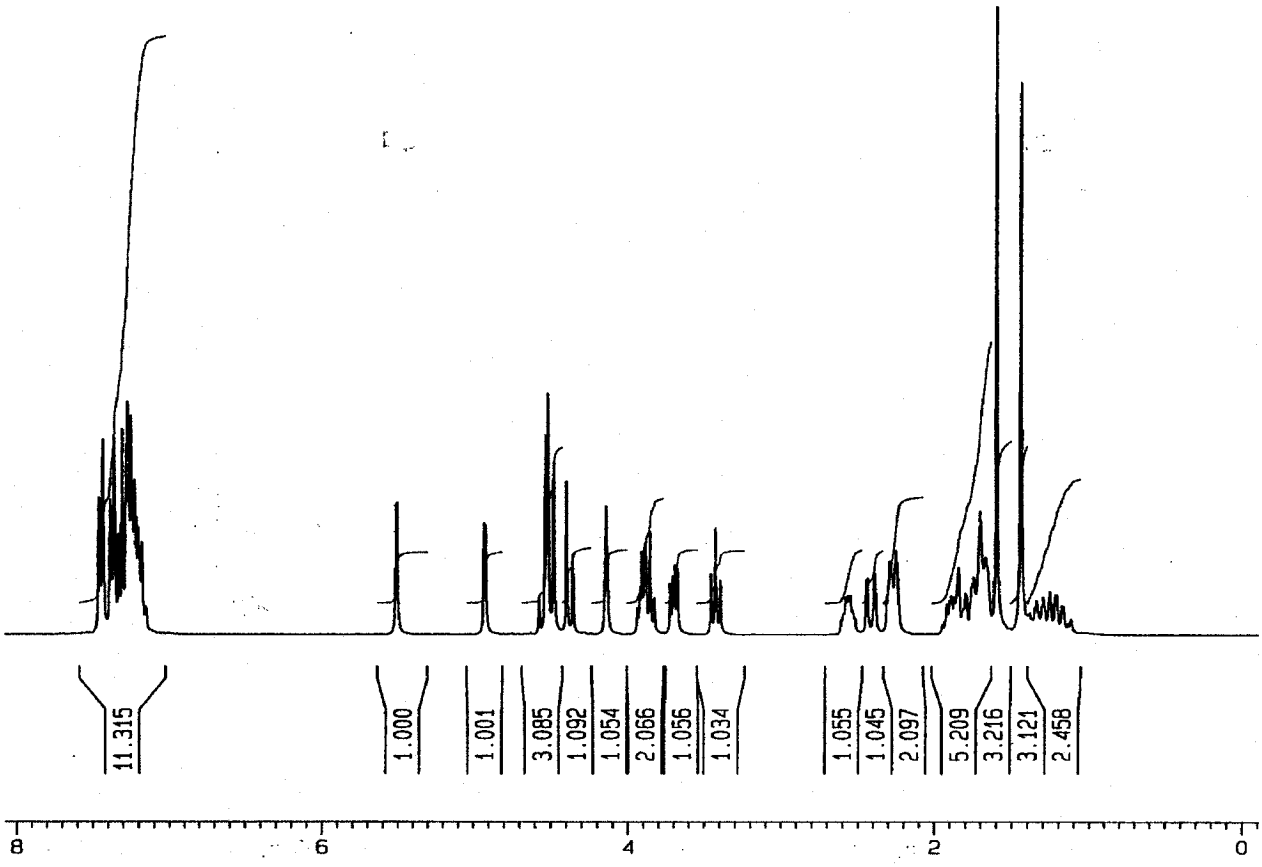
^{13}C NMR (75 MHz, $CDCl_3$)



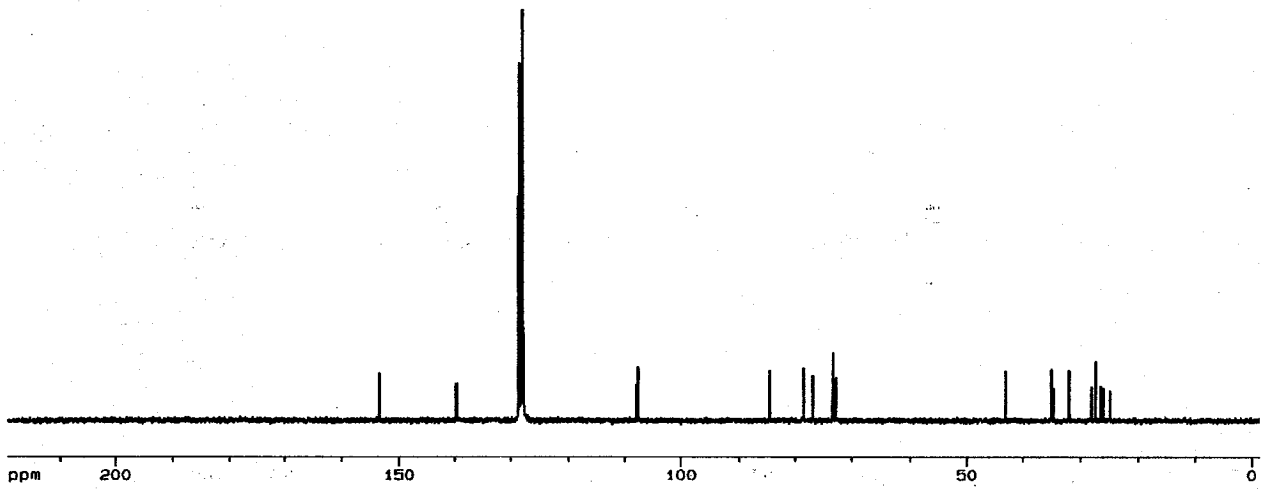


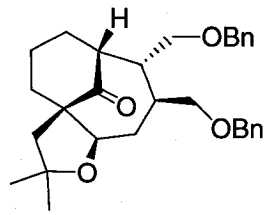
2.111

^{1}H NMR (300 MHz, $CDCl_3$)



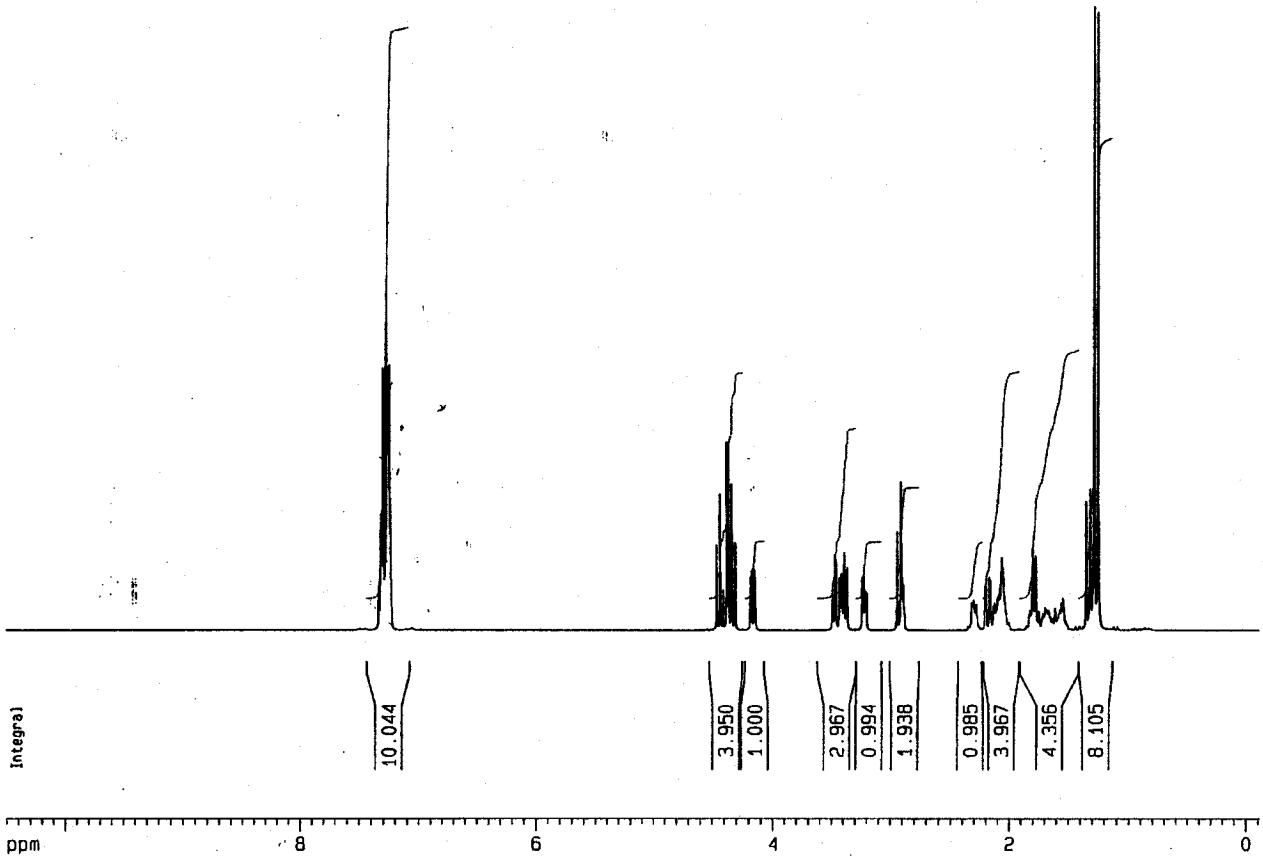
^{13}C NMR (75 MHz, $CDCl_3$)



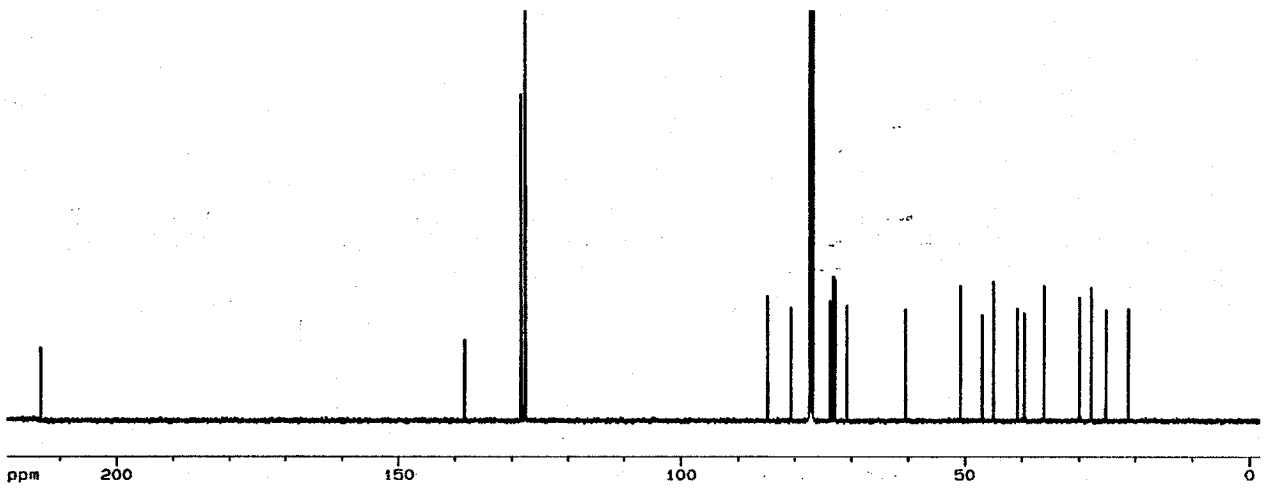


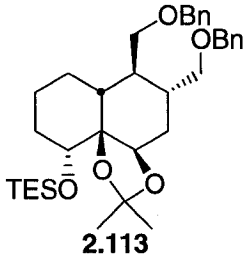
2.112

^{1}H NMR (400 MHz, $CDCl_3$)



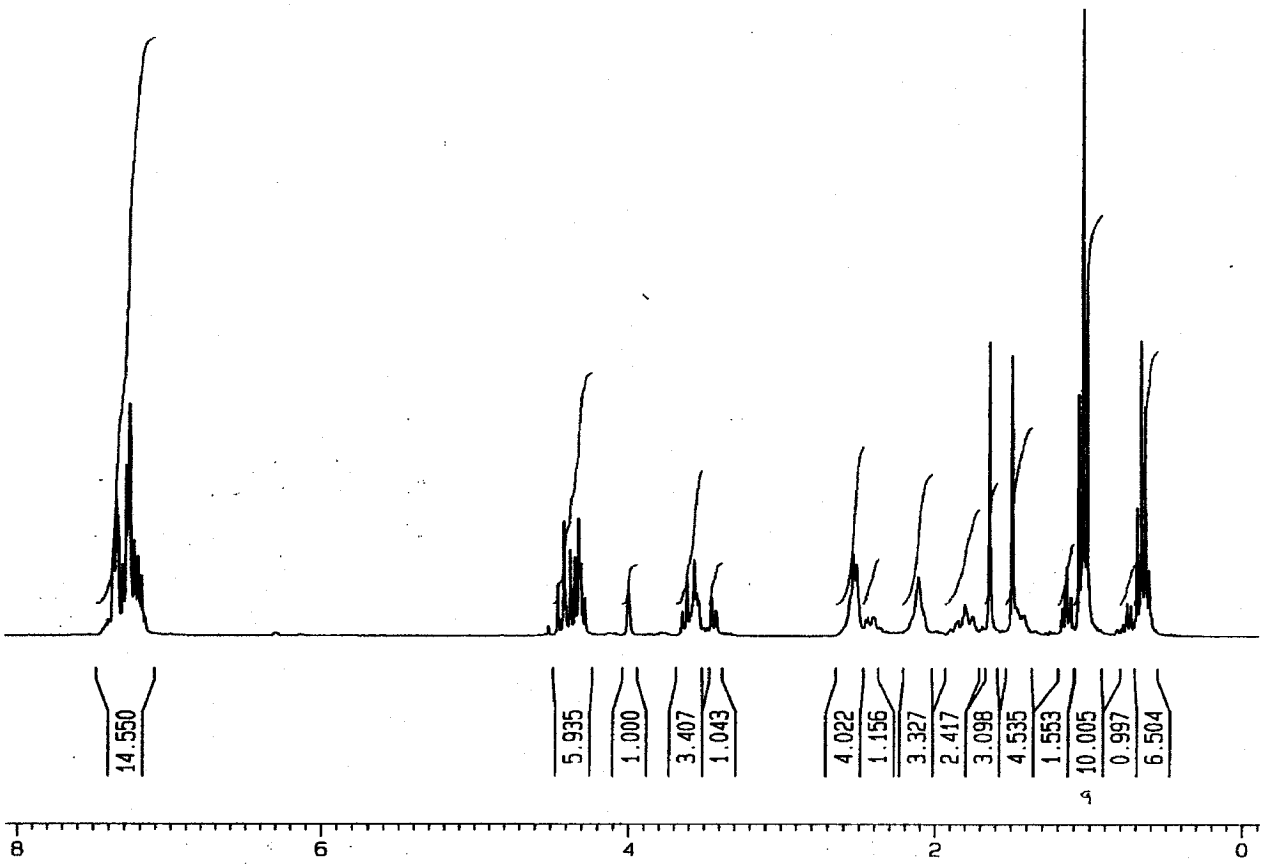
^{13}C NMR (100 MHz, $CDCl_3$)



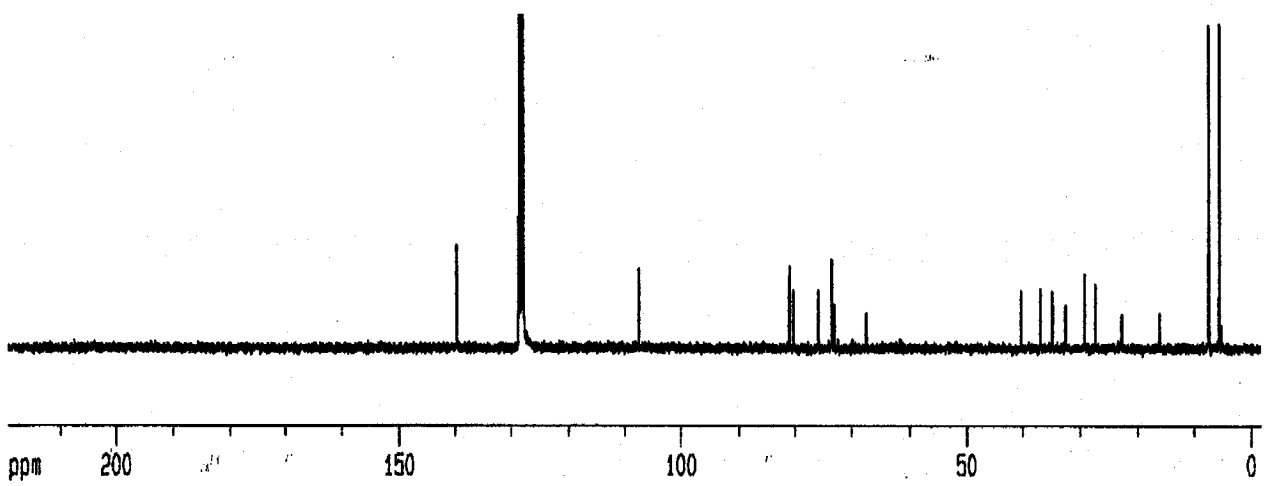


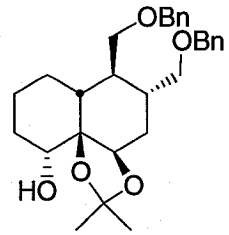
2.113

^{1}H NMR (300 MHz, C_6D_6)



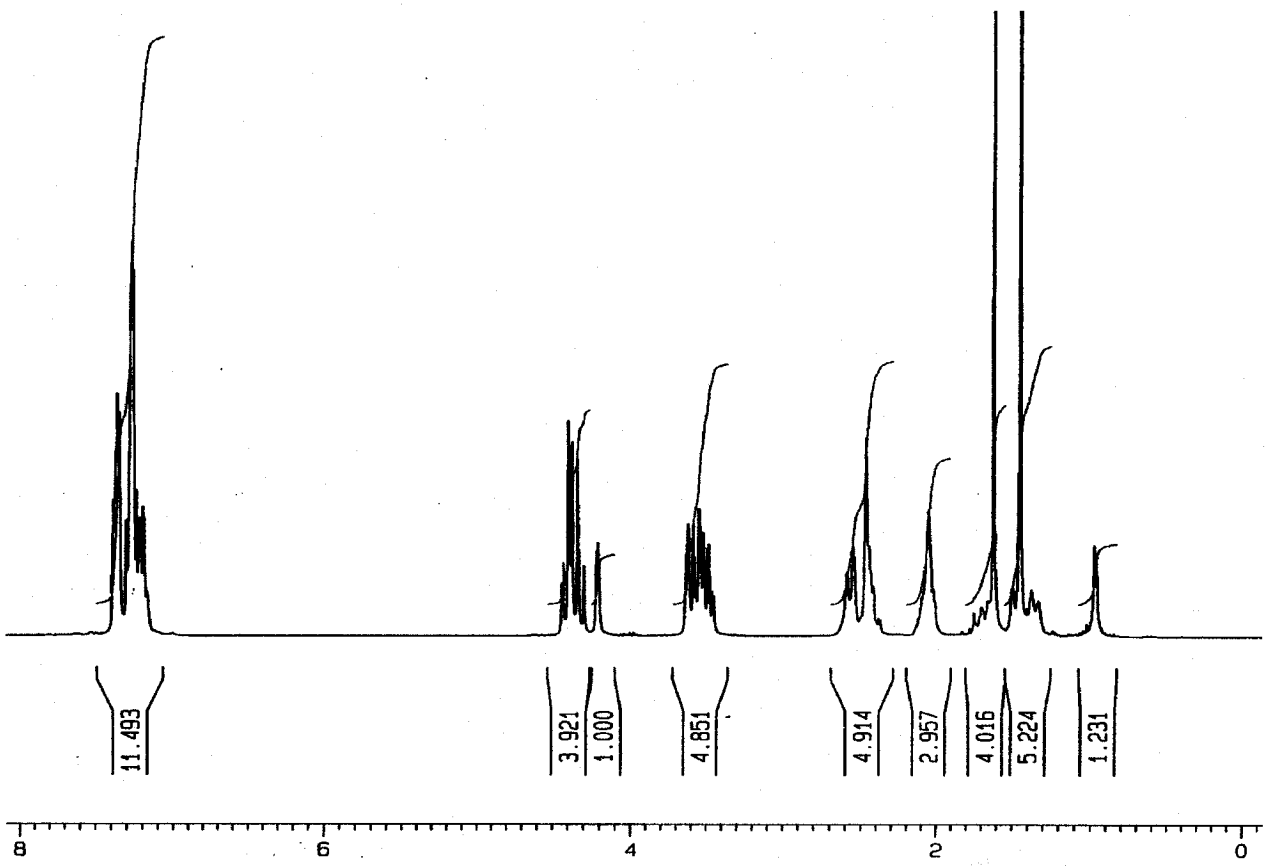
^{13}C NMR (75 MHz, C_6D_6)



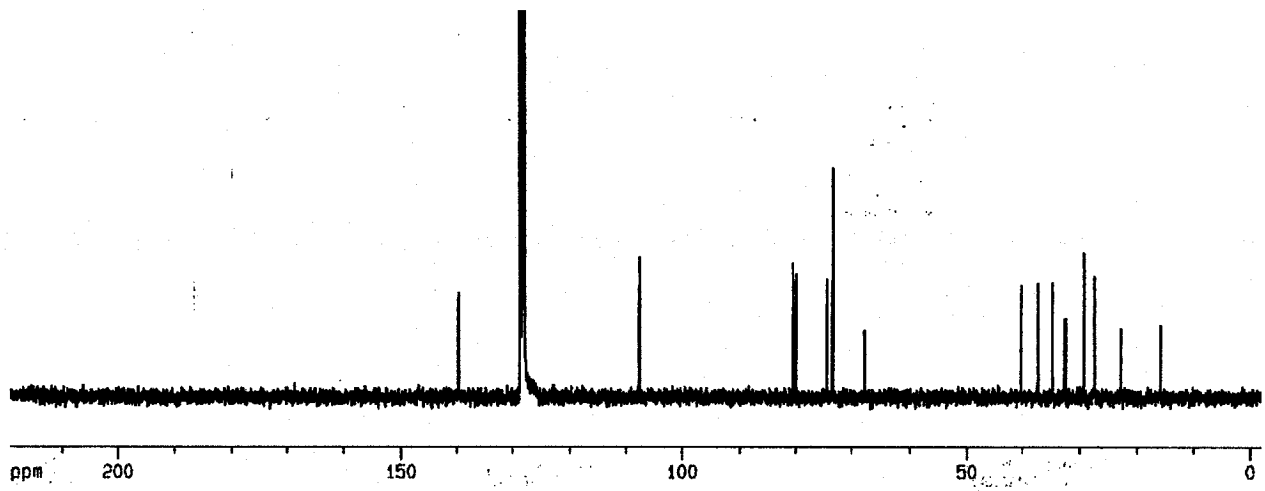


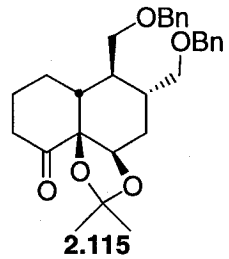
2.114

^{1}H NMR (300 MHz, C_6D_6)



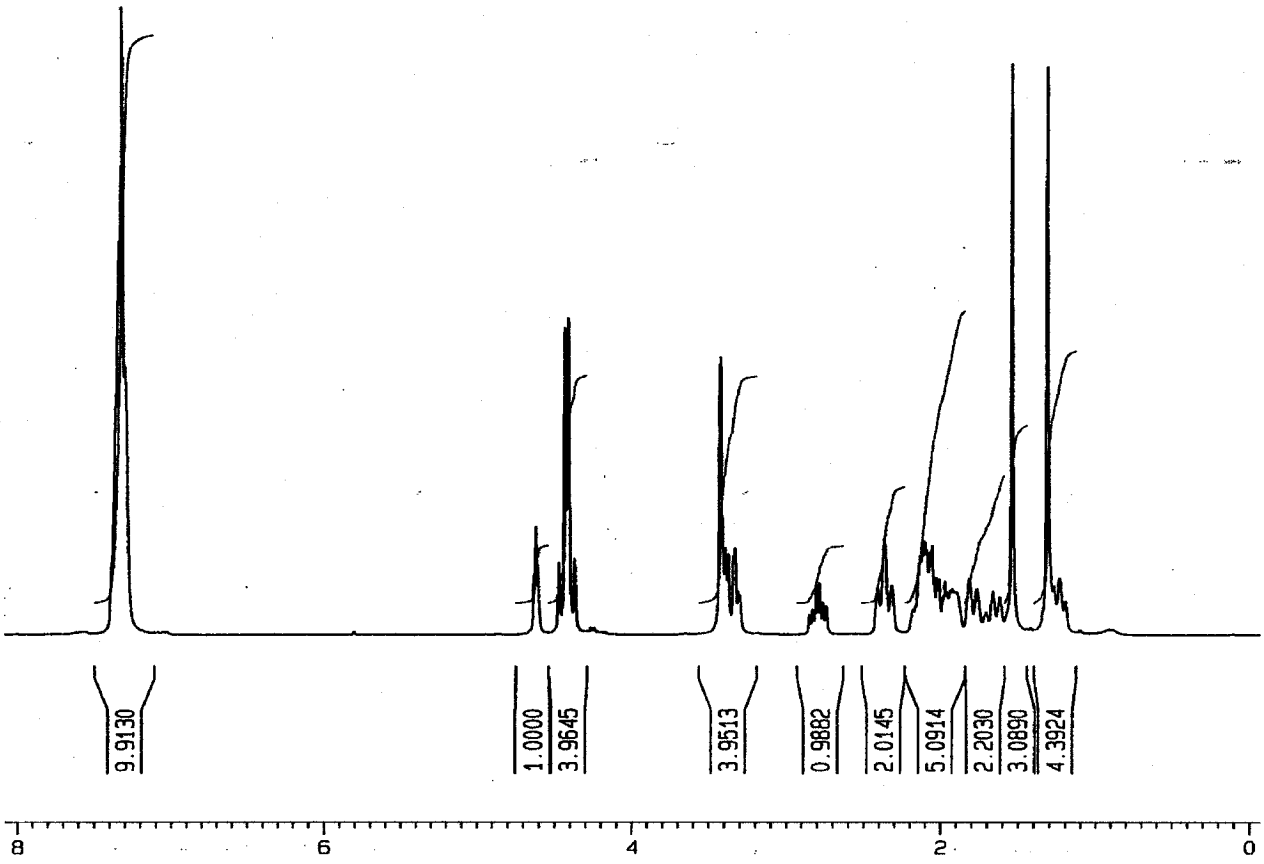
^{13}C NMR (75 MHz, C_6D_6)



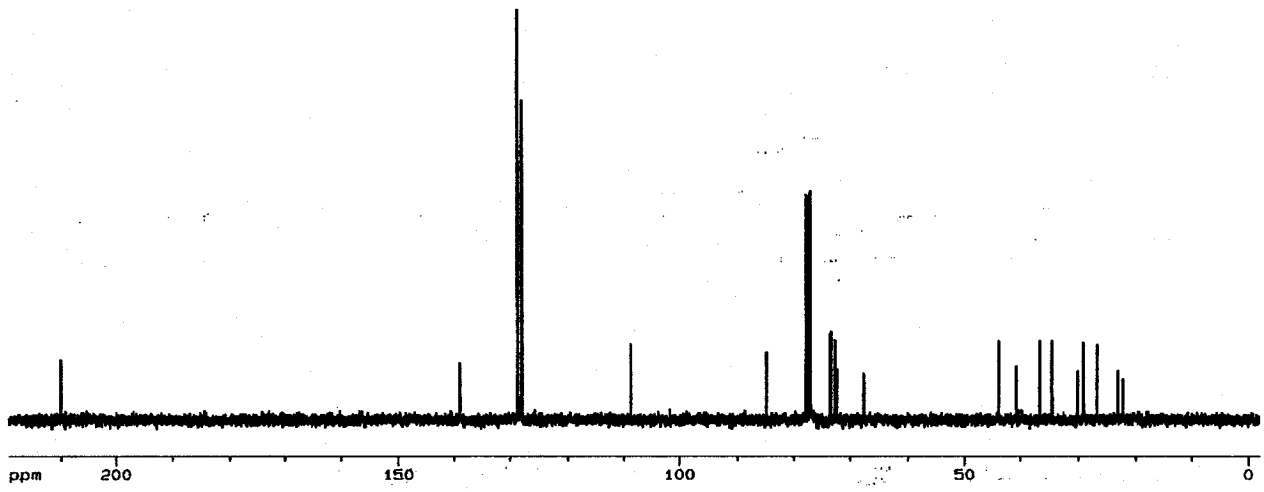


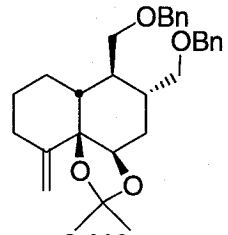
2.115

^{1}H NMR (300 MHz, $CDCl_3$)



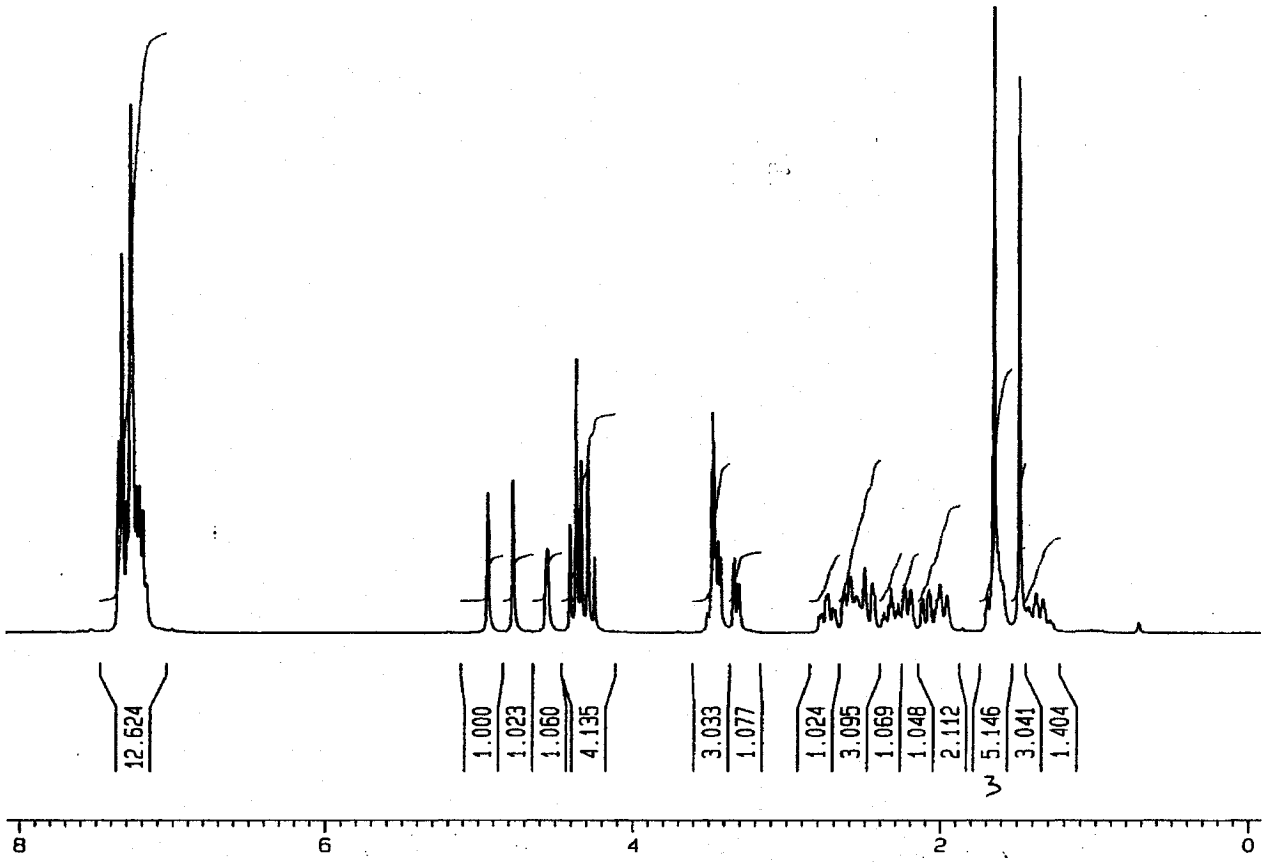
^{13}C NMR (75 MHz, $CDCl_3$)



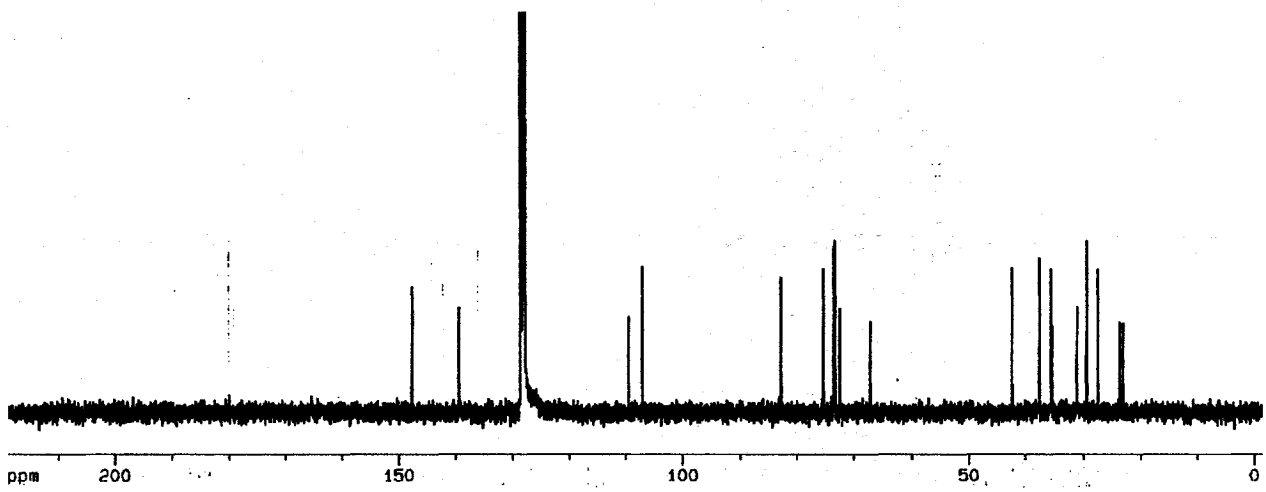


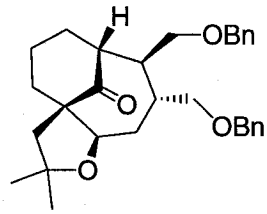
2.116

^{1}H NMR (300 MHz, C_6D_6)



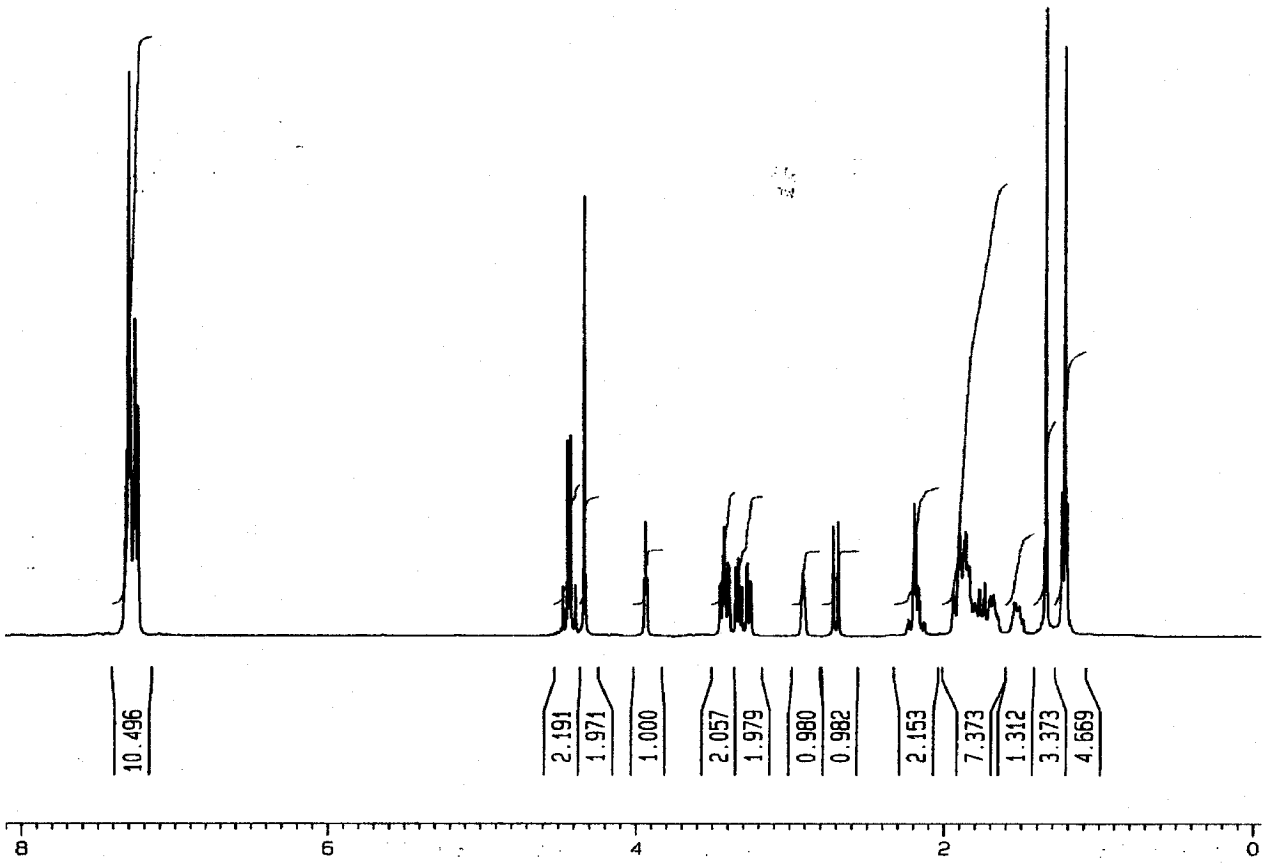
^{13}C NMR (75 MHz, C_6D_6)



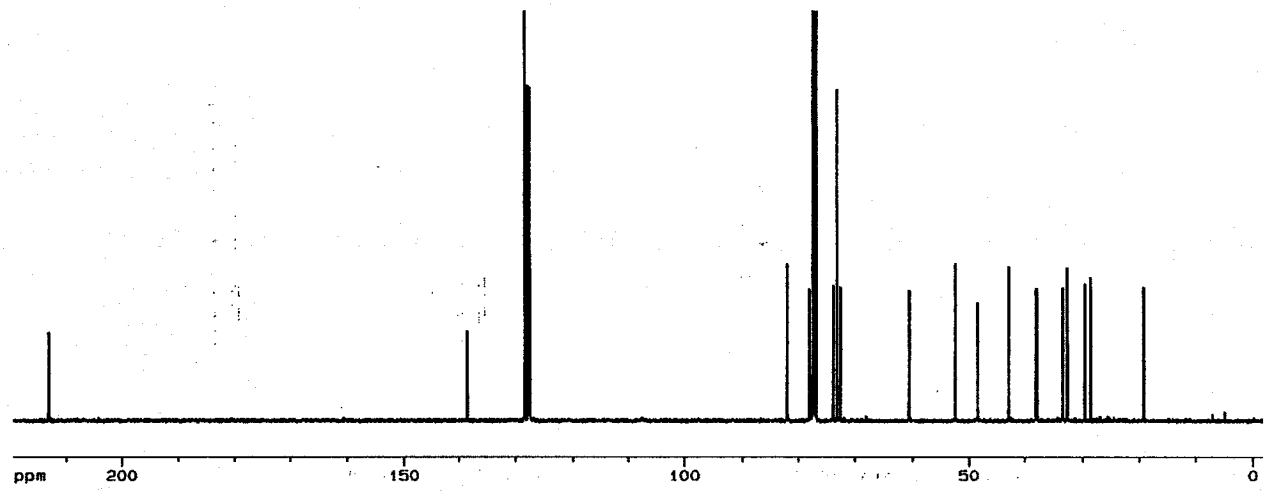


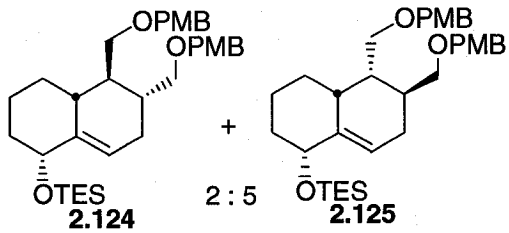
2.117

^{1}H NMR (400 MHz, $CDCl_3$)

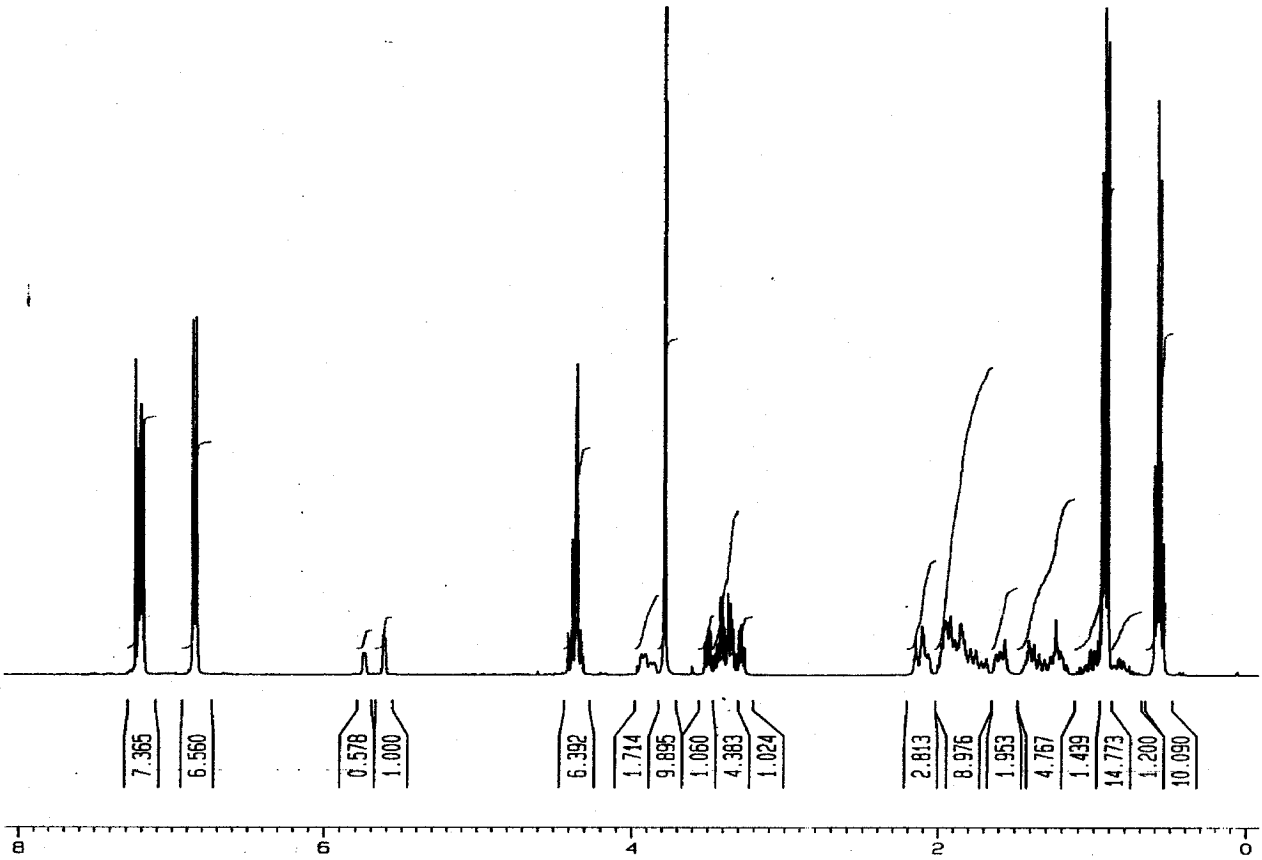


^{13}C NMR (100 MHz, $CDCl_3$)

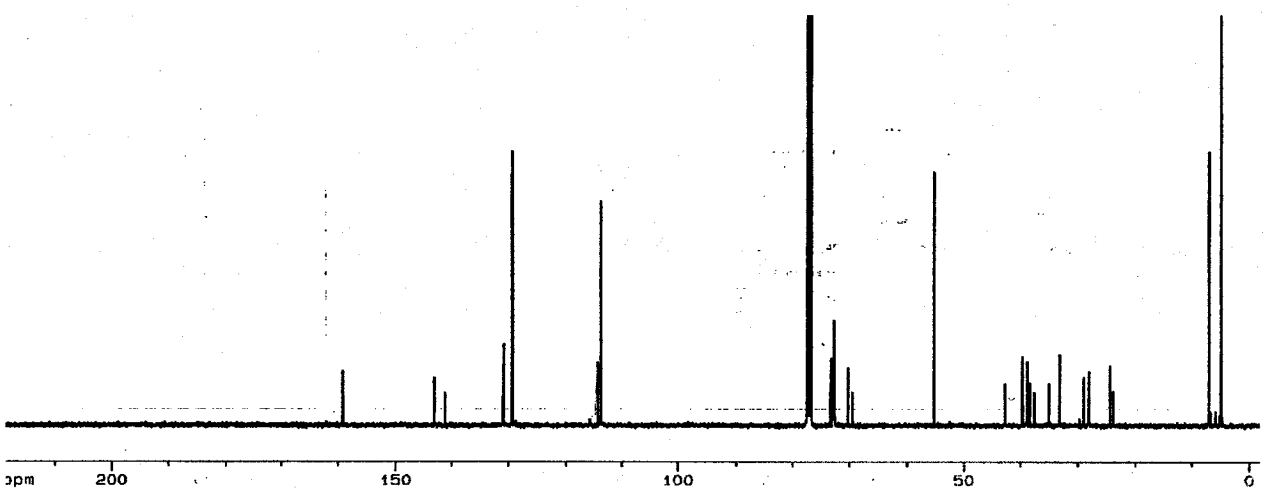


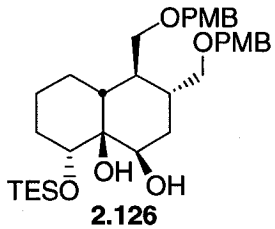


^{1}H NMR (400 MHz, $CDCl_3$)



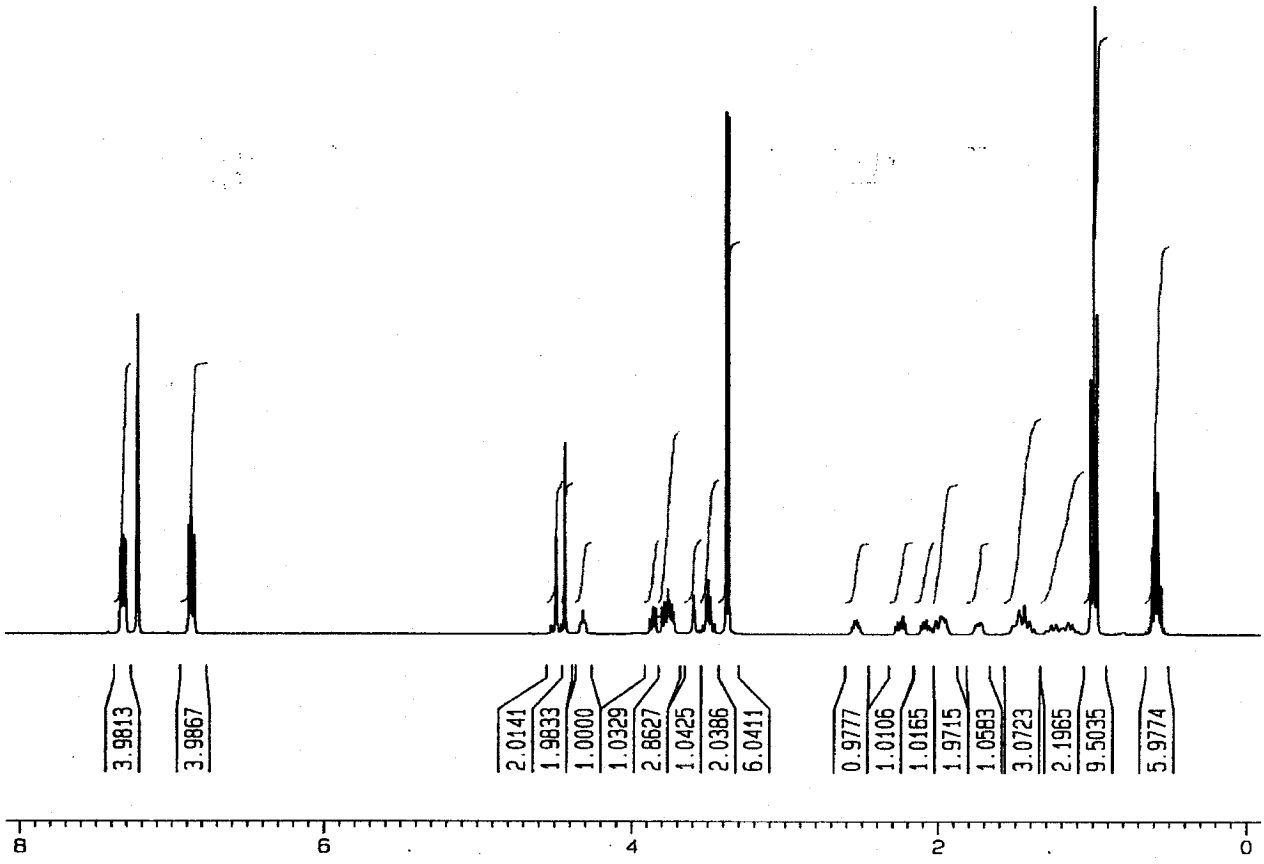
^{13}C NMR (100 MHz, $CDCl_3$)



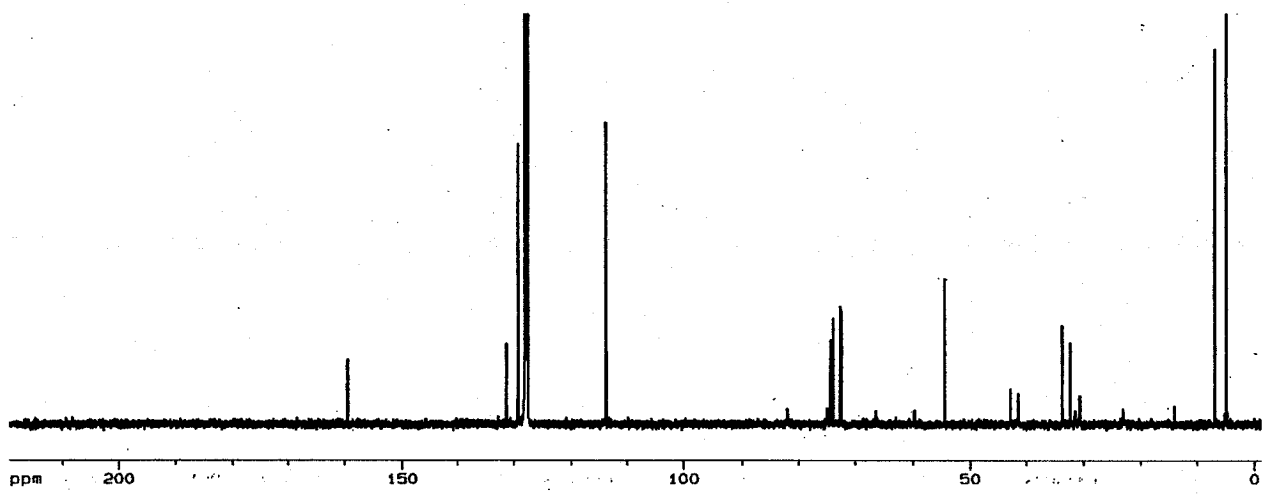


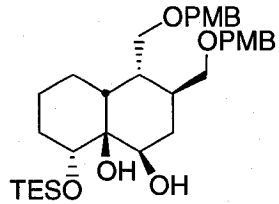
2.126

^{1}H NMR (400 MHz, C_6D_6)



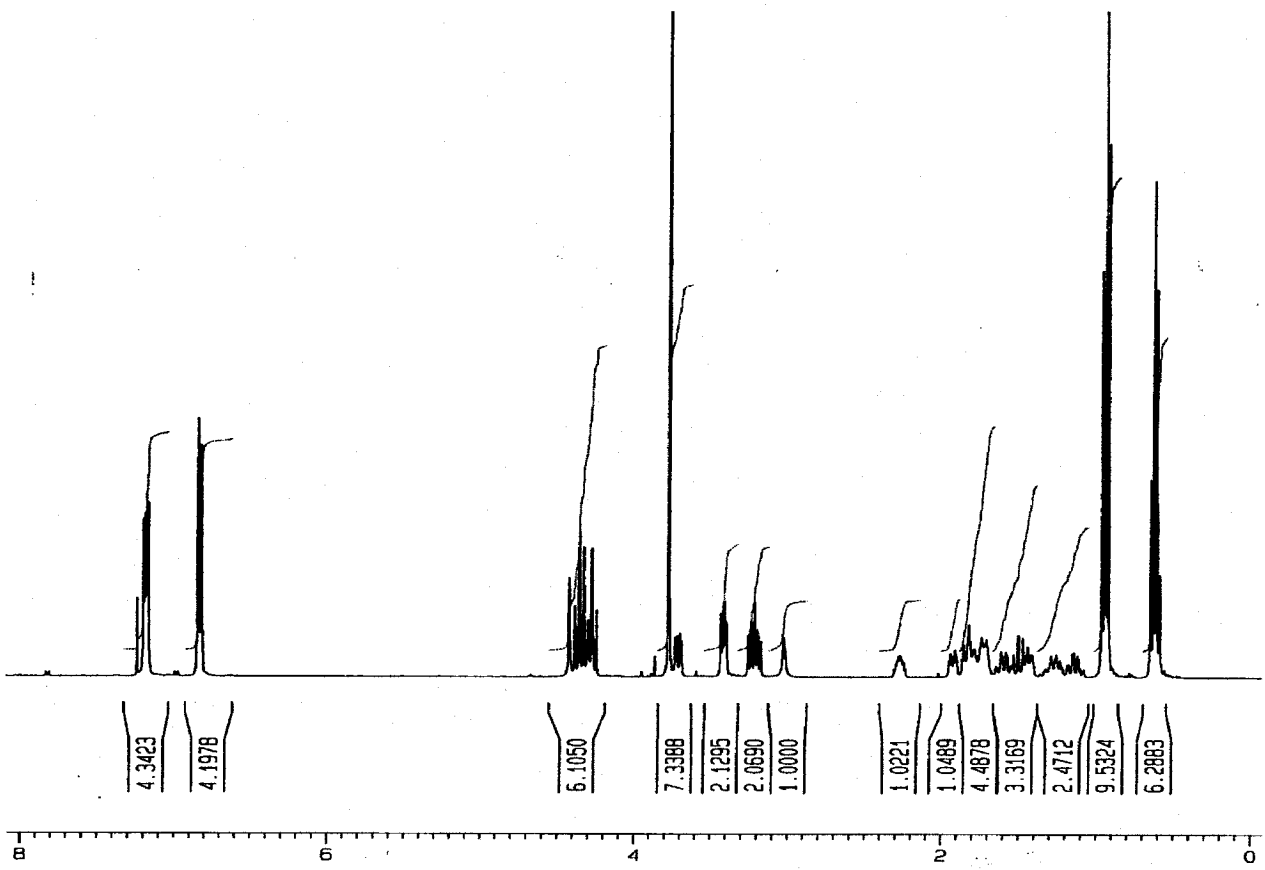
^{13}C NMR (100 MHz, C_6D_6)



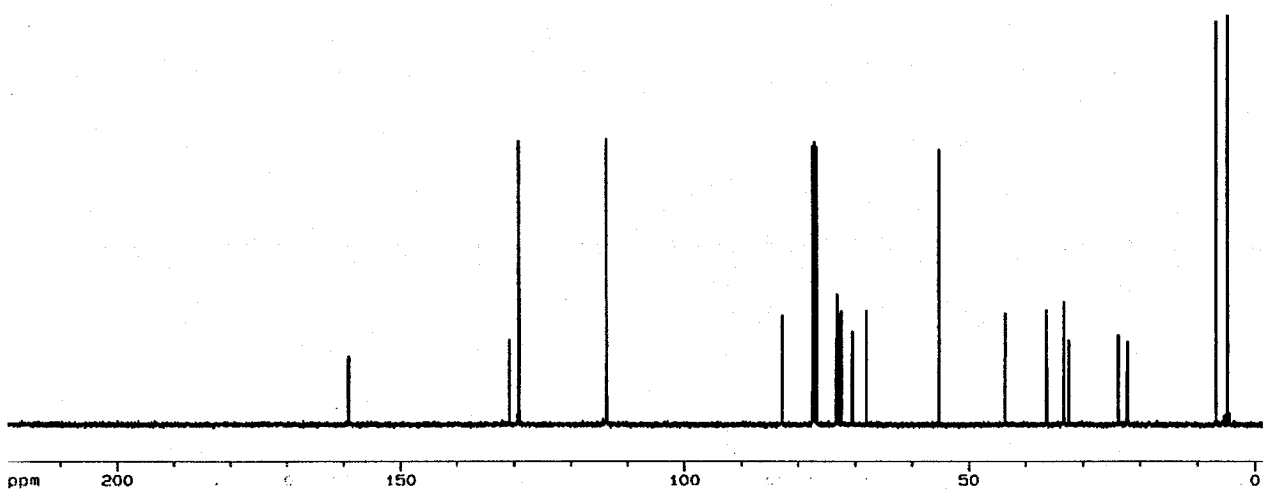


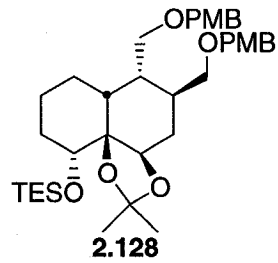
2.127

^{1}H NMR (400 MHz, $CDCl_3$



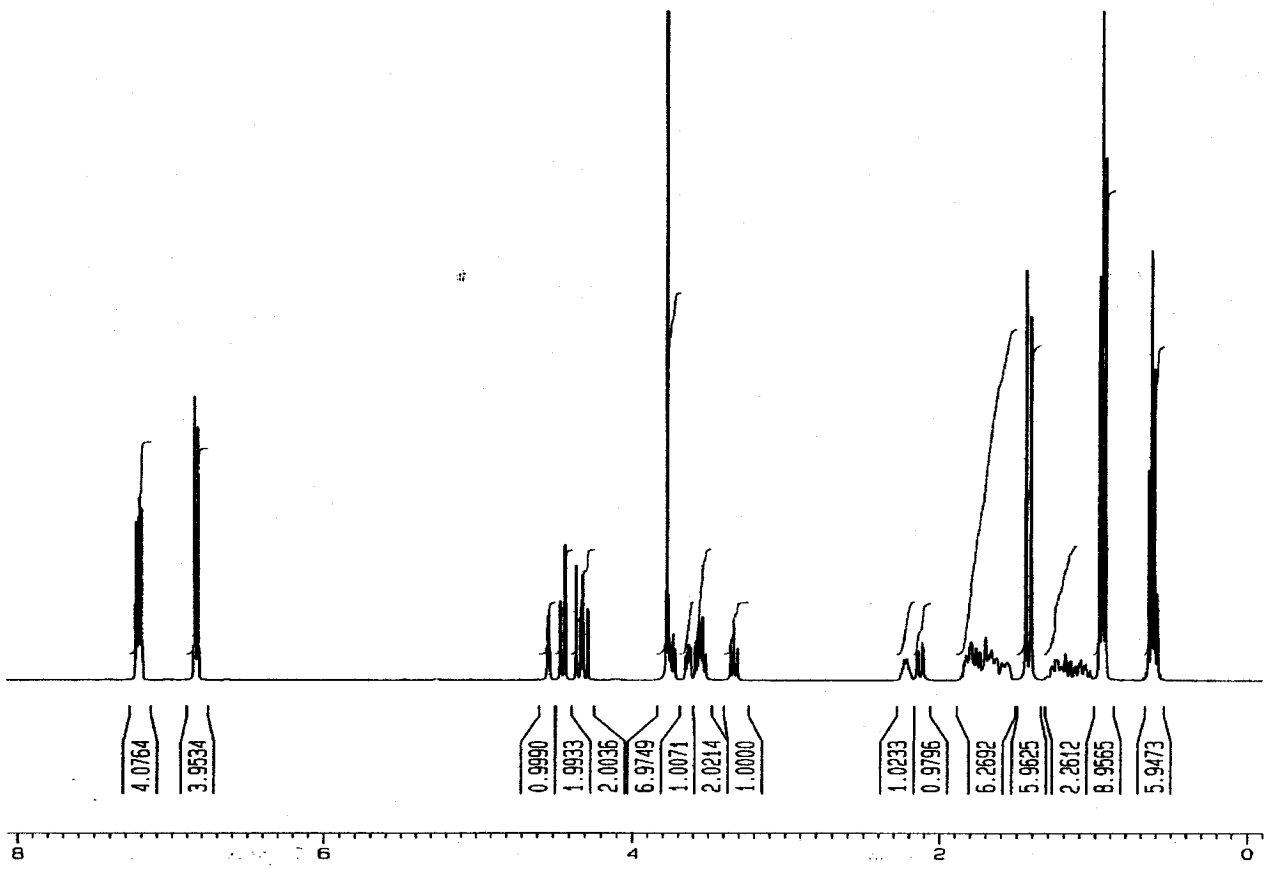
^{13}C NMR (100 MHz, $CDCl_3$)



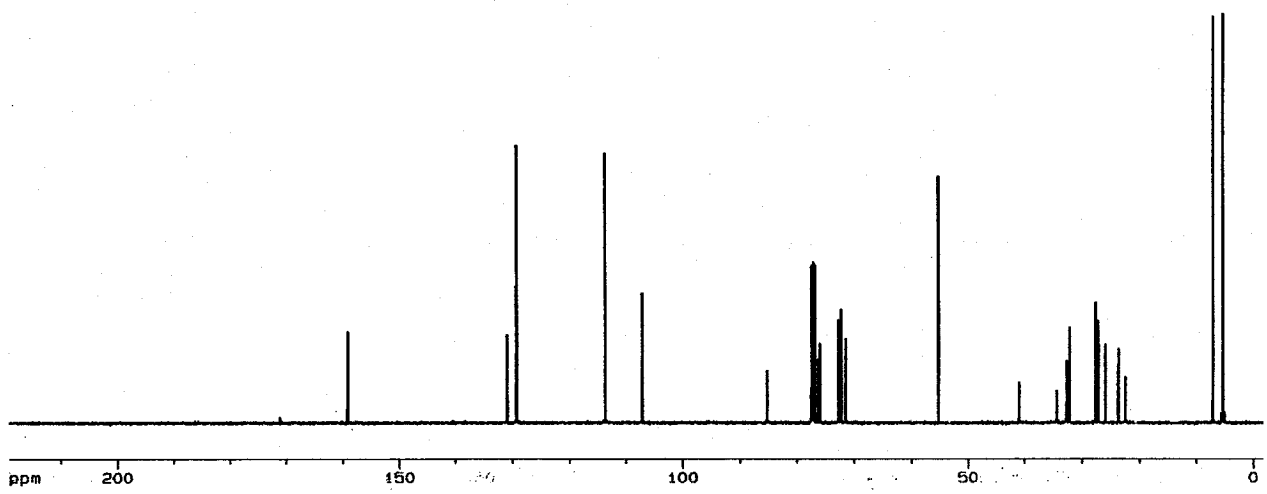


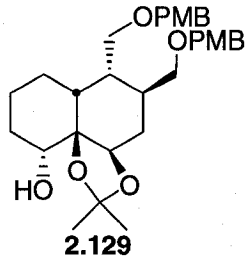
2.128

^{1}H NMR (400 MHz, $CDCl_3$)



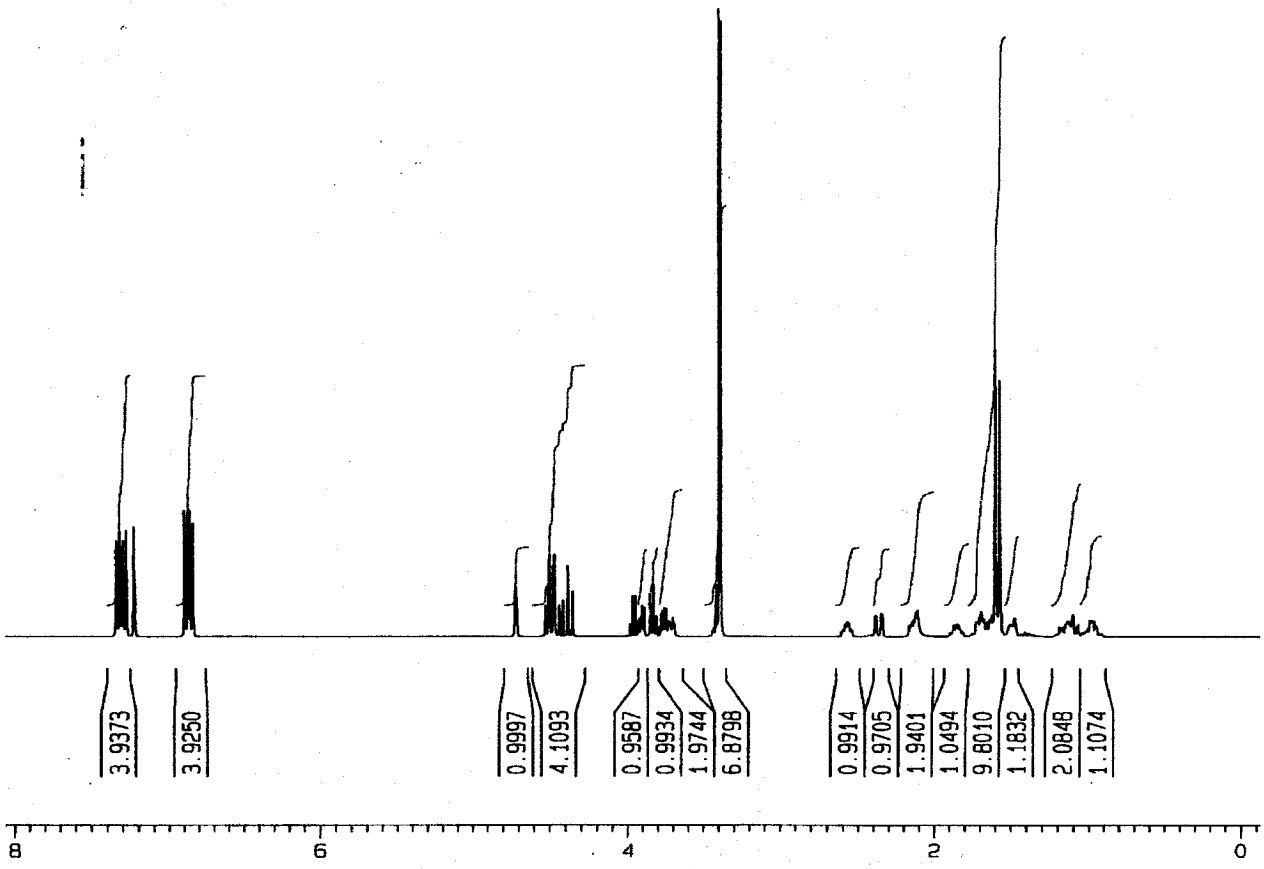
^{13}C NMR (100 MHz, $CDCl_3$)



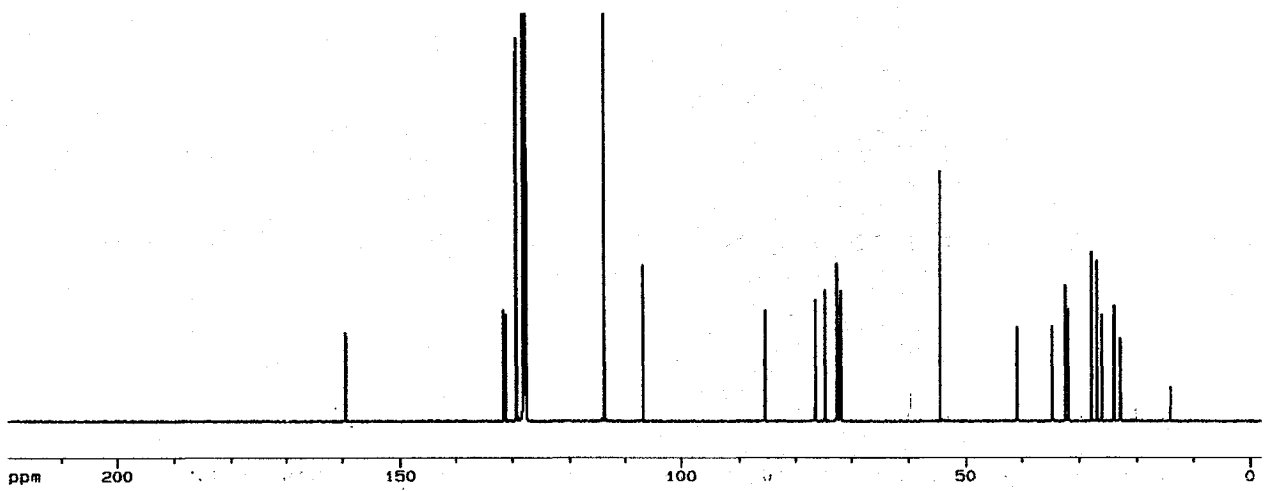


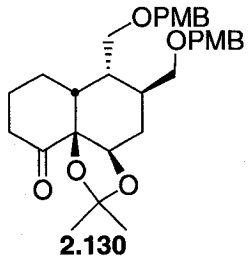
2.129

^{1}H NMR (400 MHz, C_6D_6)



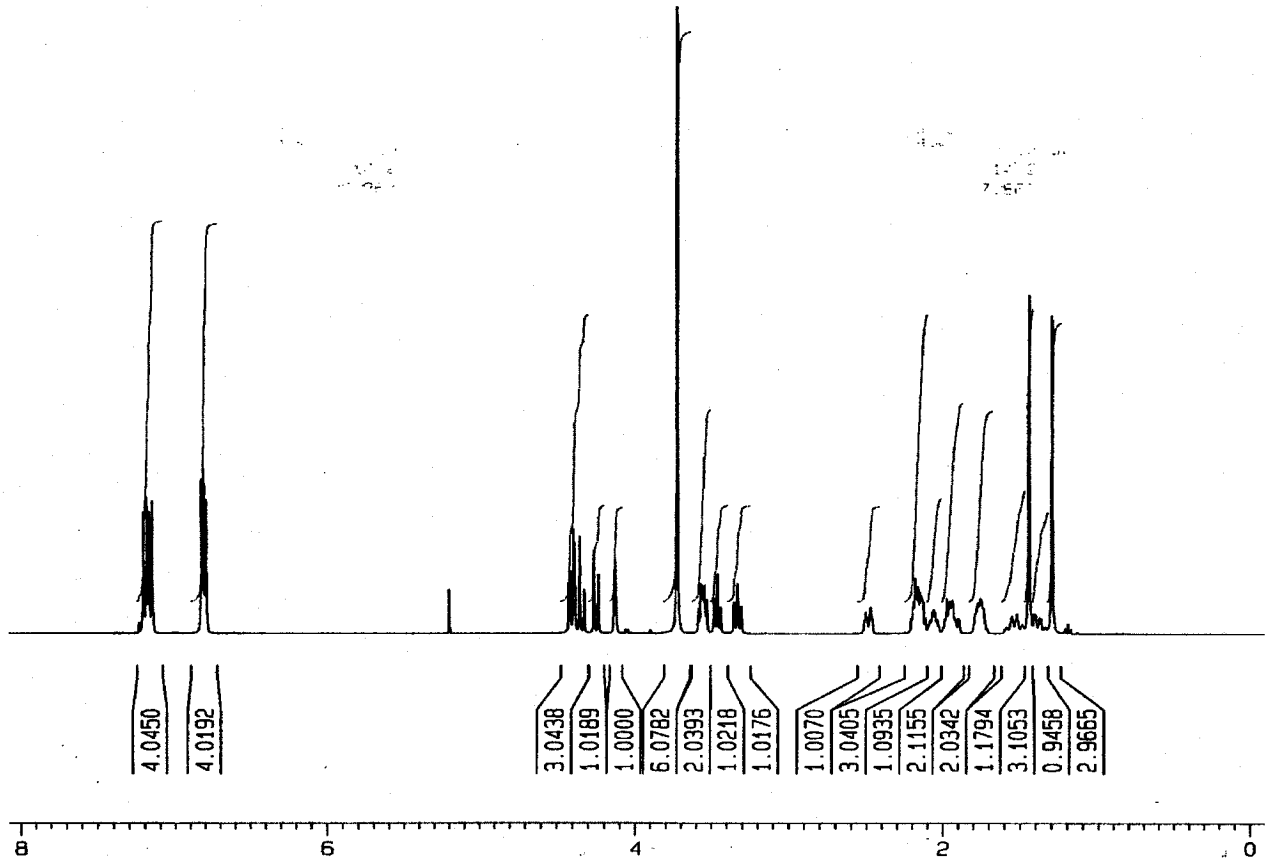
^{13}C NMR (100 MHz, C_6D_6)



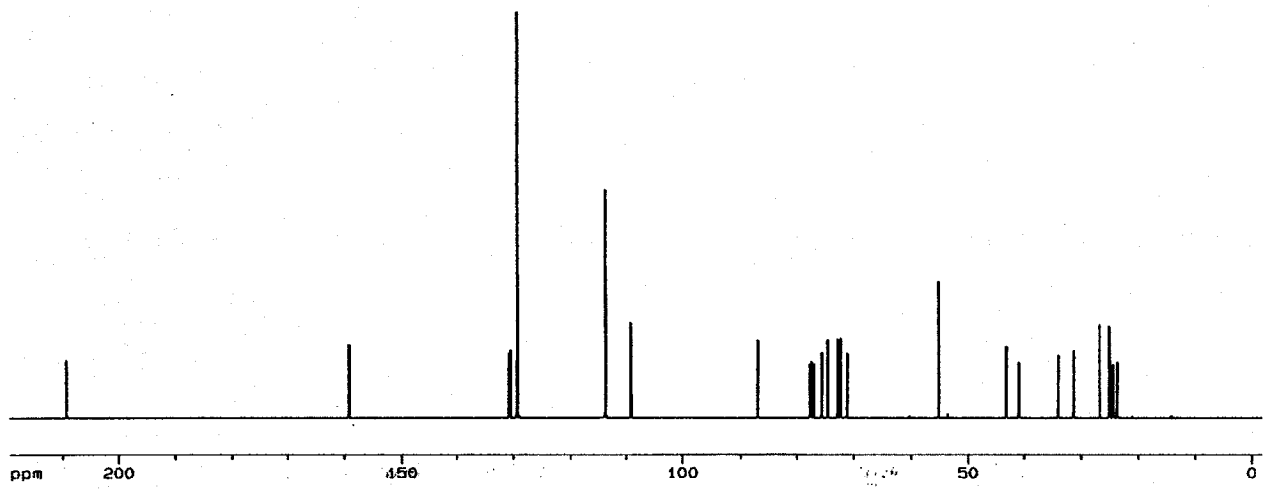


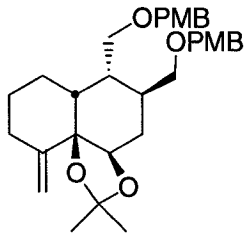
2.130

^{1}H NMR (400 MHz, $CDCl_3$)



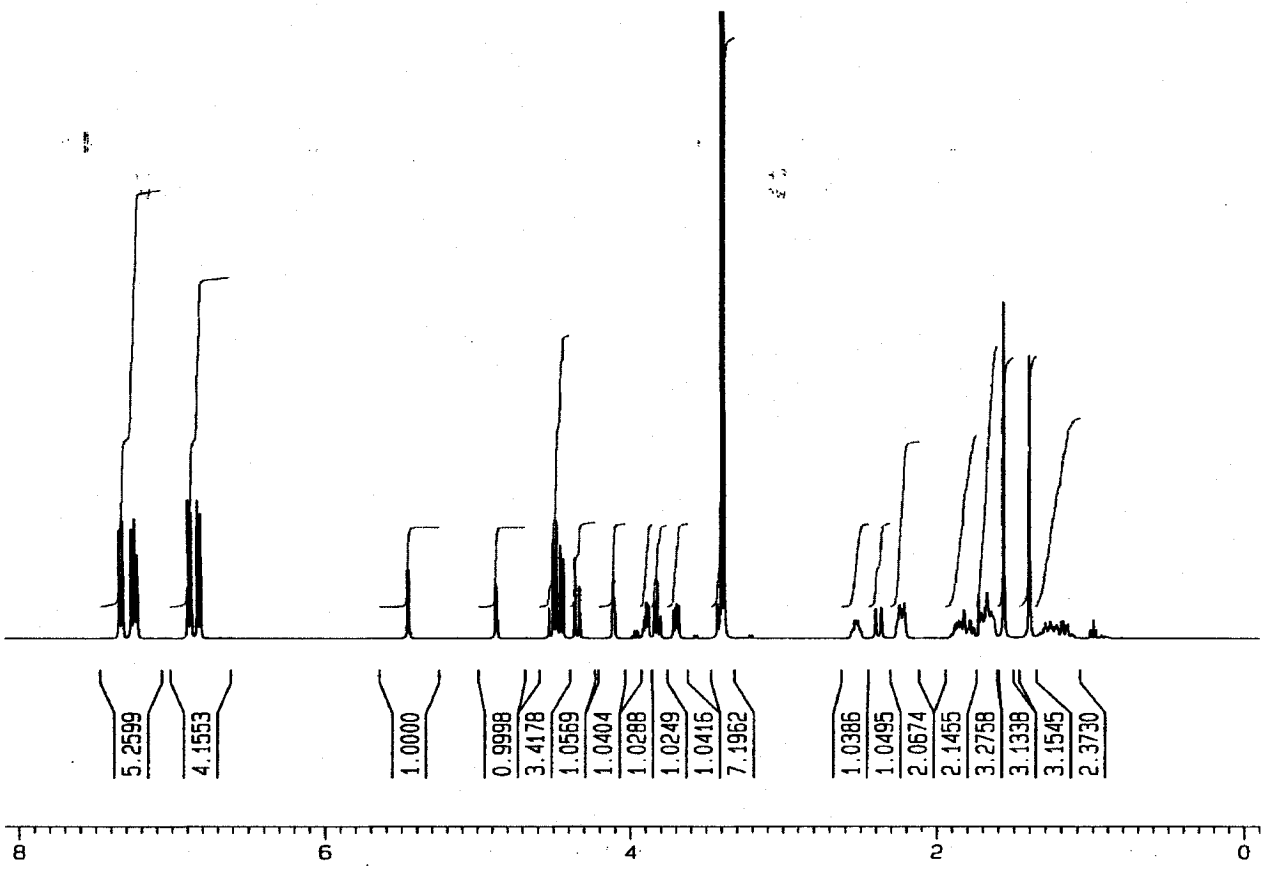
^{13}C NMR (100 MHz, $CDCl_3$)



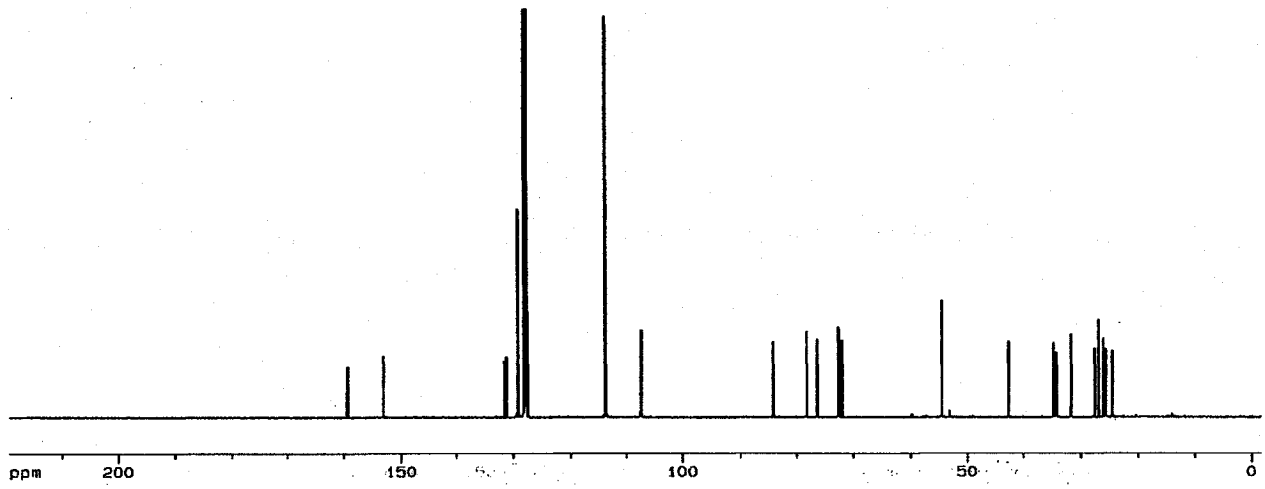


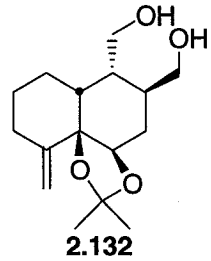
2.131

^{1}H NMR (400 MHz, C_6D_6)



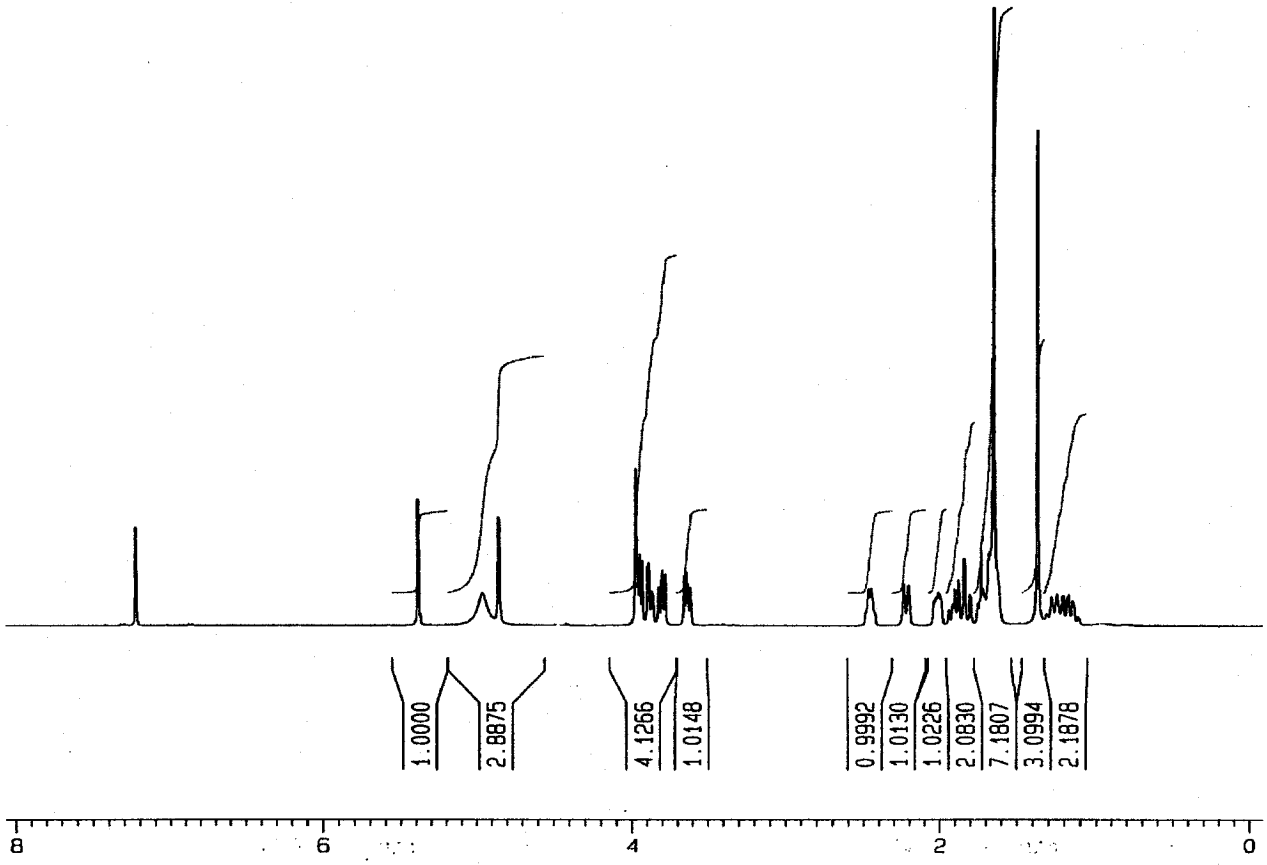
^{13}C NMR (100 MHz, C_6D_6)



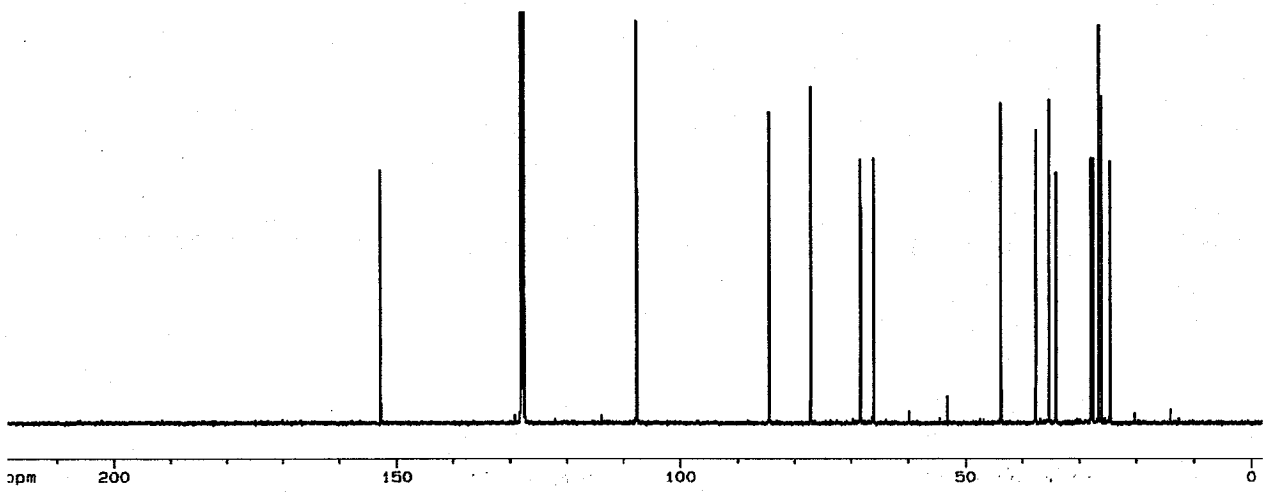


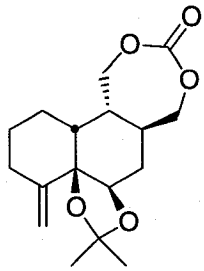
2.132

^{1}H NMR (400 MHz, C_6D_6)



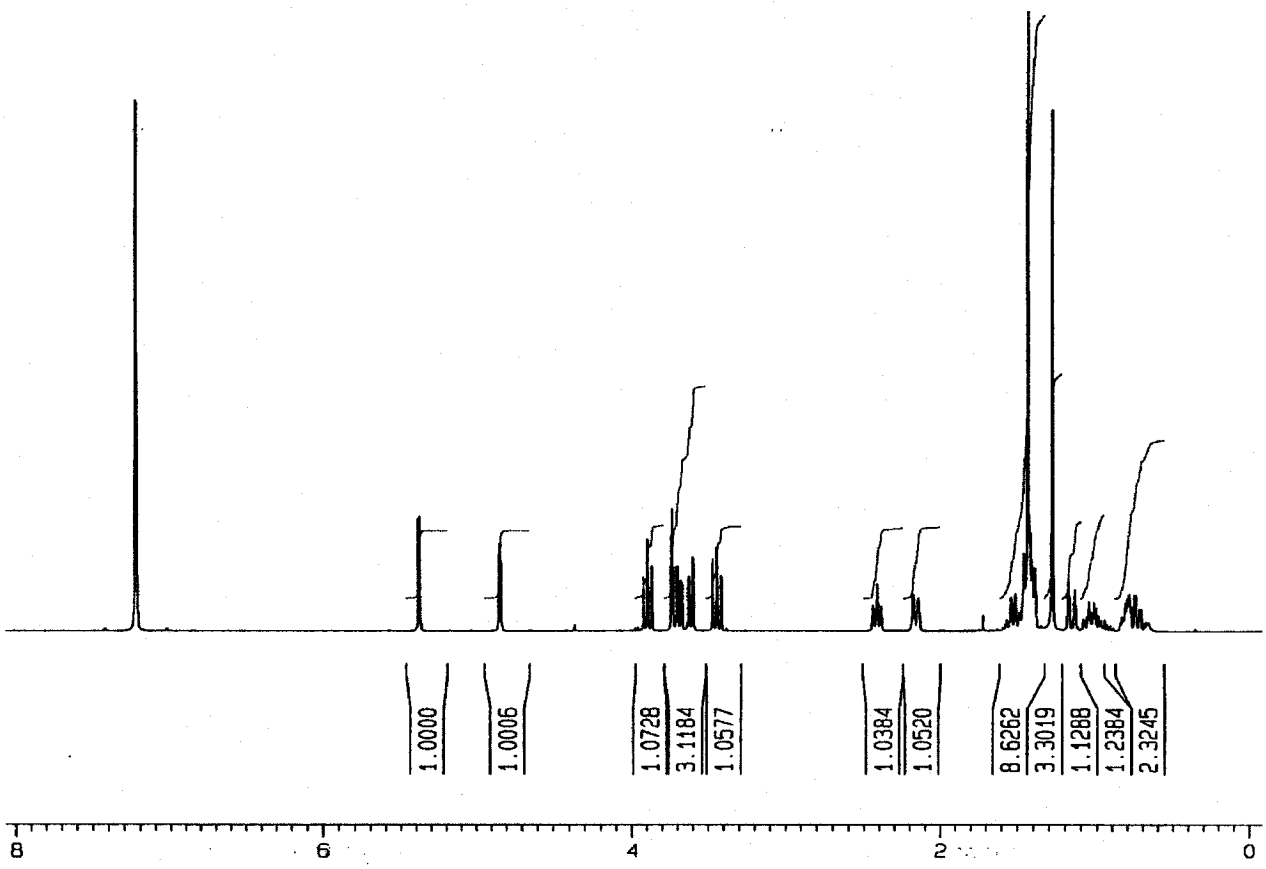
^{13}C NMR (100 MHz, C_6D_6)



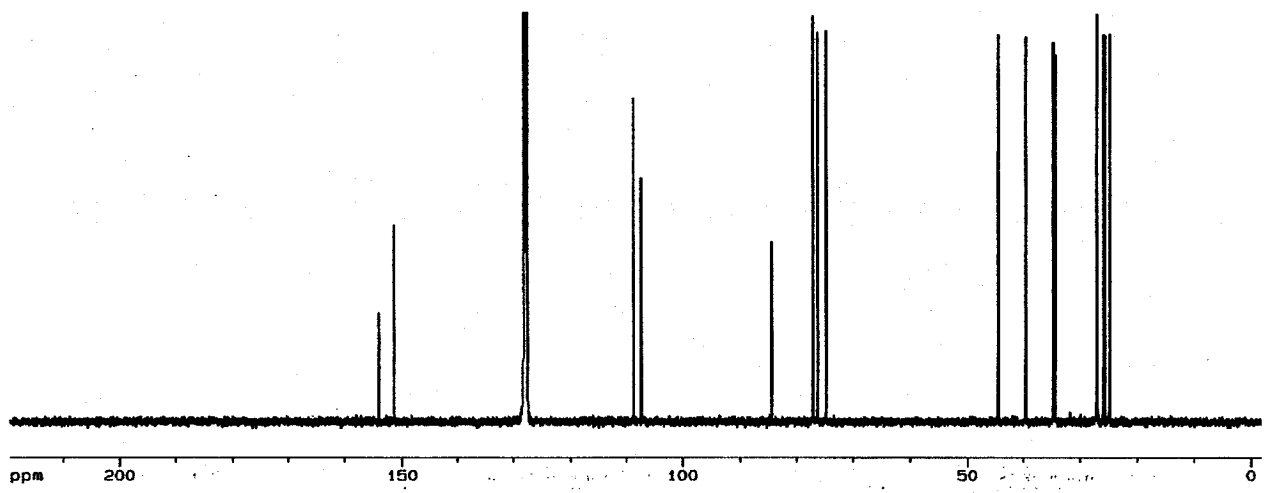


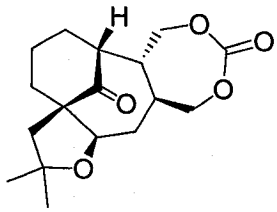
2.133

^{1}H NMR (400 MHz, C_6D_6)



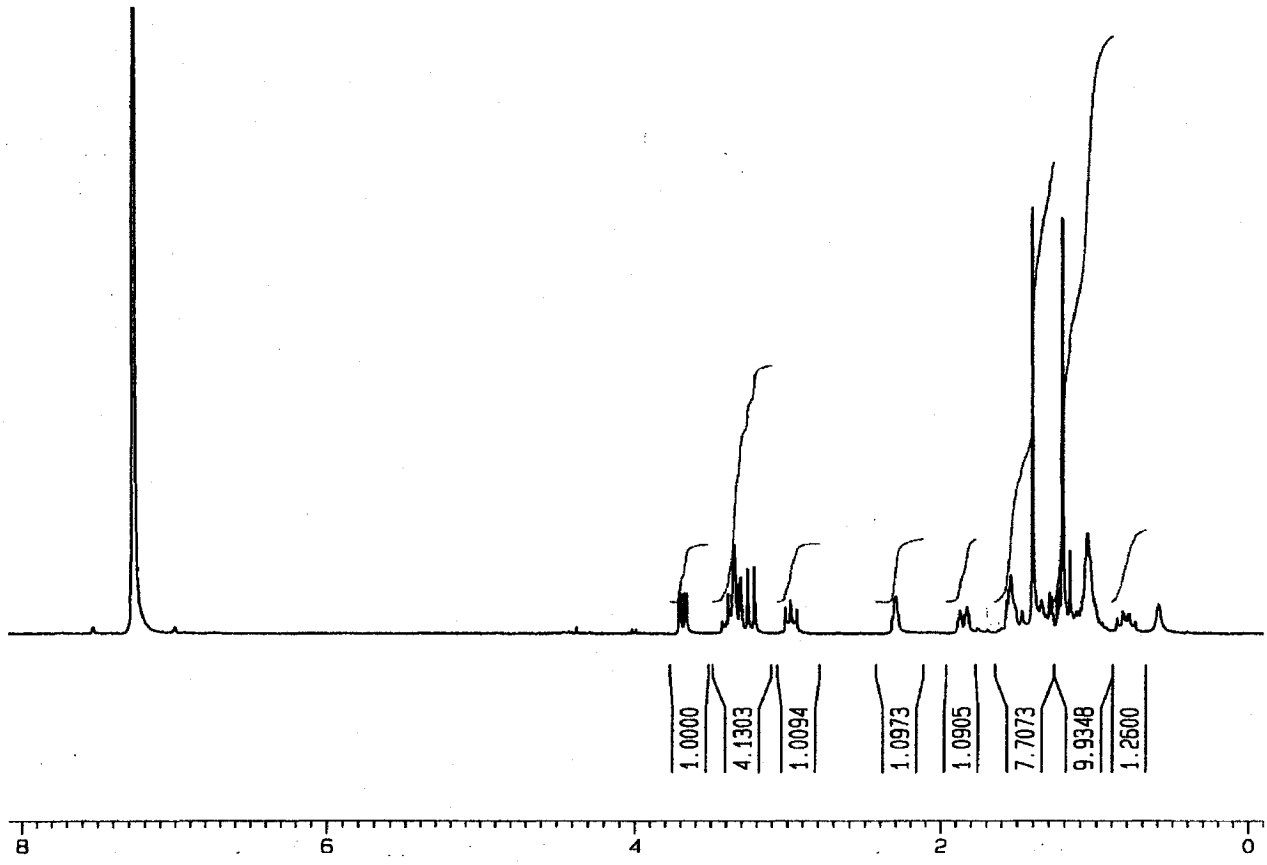
^{13}C NMR (100 MHz, C_6D_6)



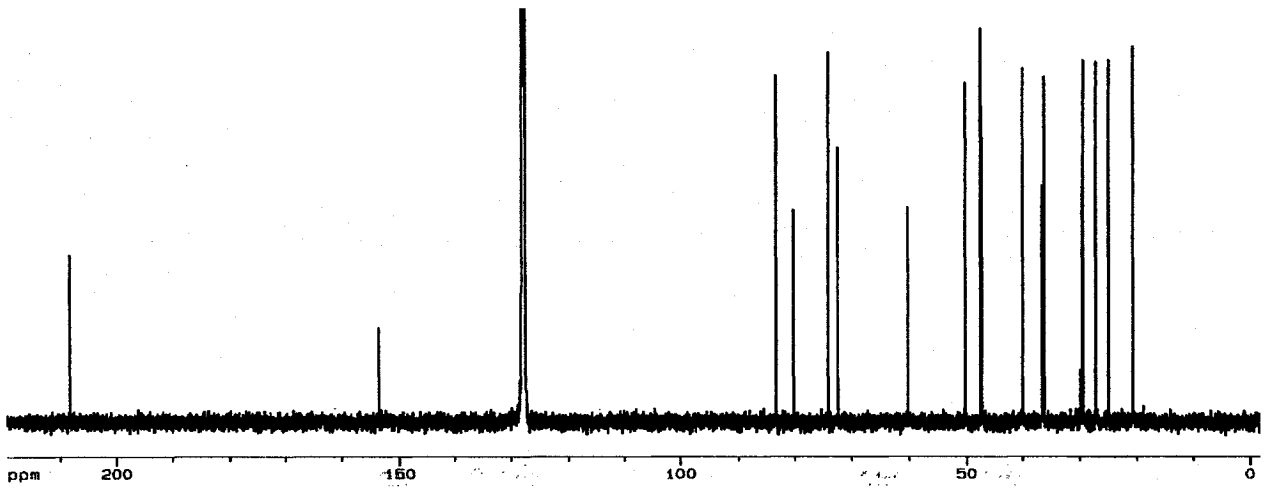


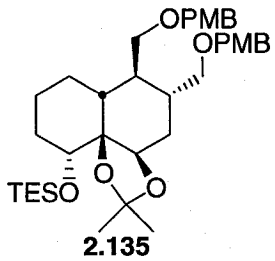
2.134

^{1}H NMR (400 MHz, C_6D_6)



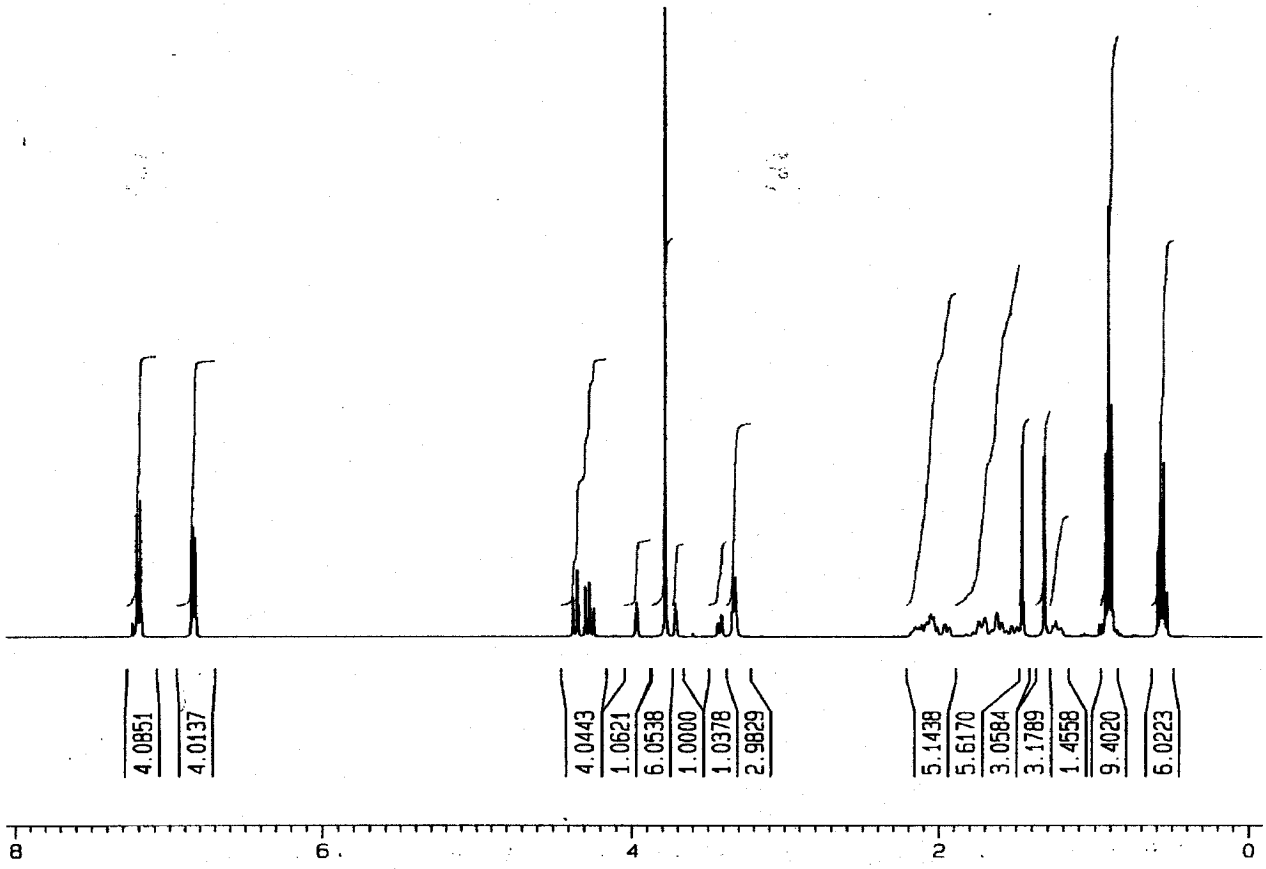
^{13}C NMR (100 MHz, C_6D_6)



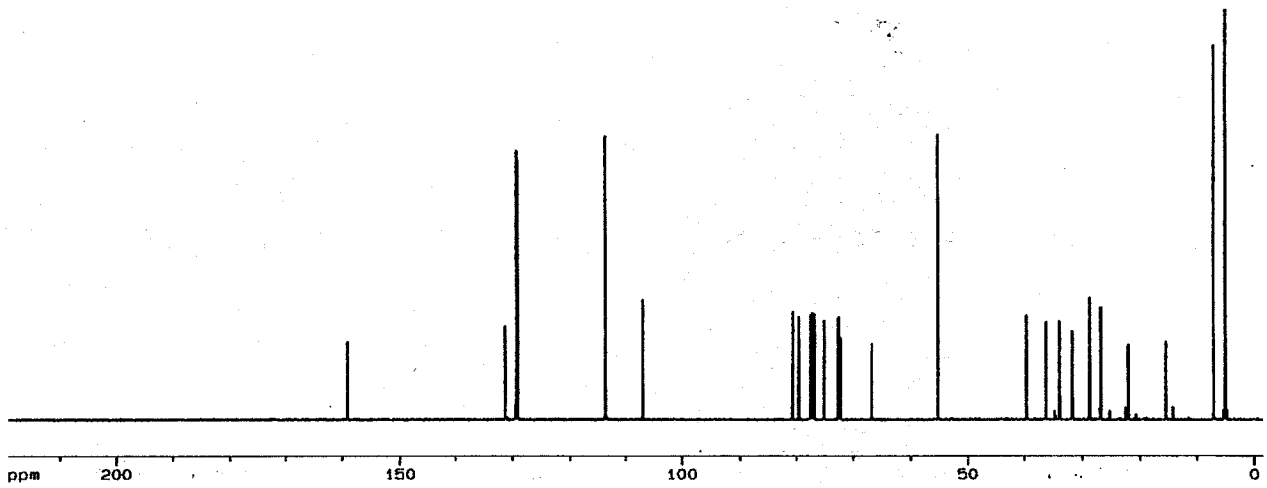


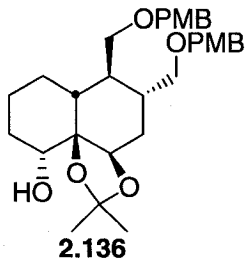
2.135

^{1}H NMR (400 MHz, $CDCl_3$)



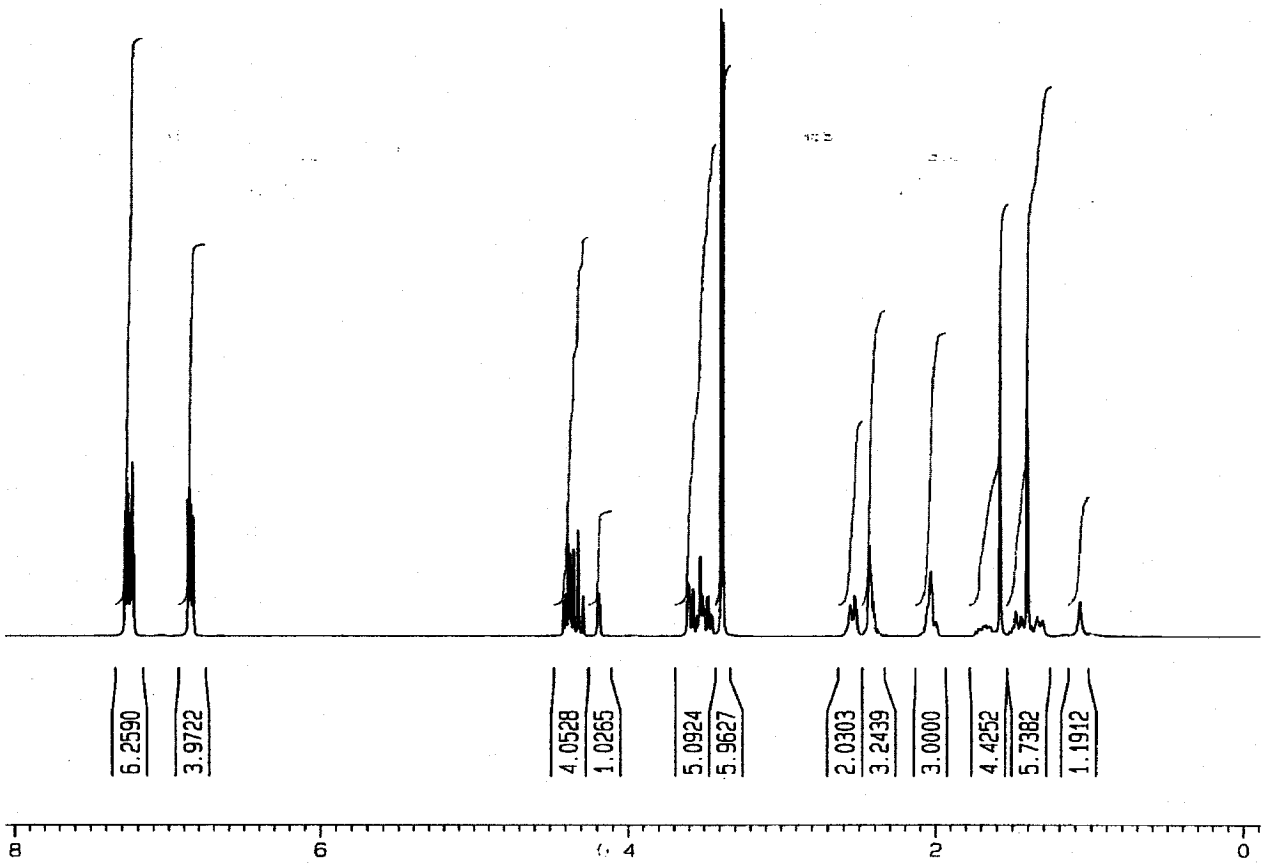
^{13}C NMR (100 MHz, $CDCl_3$)



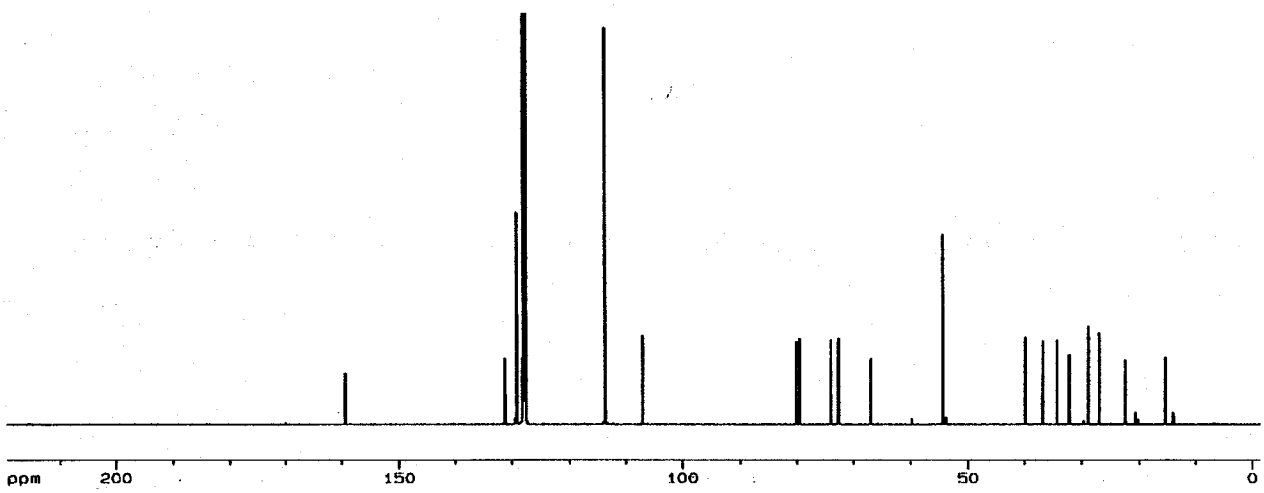


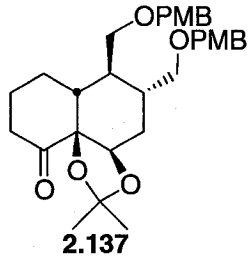
2.136

^{1}H NMR (400 MHz, C_6D_6)



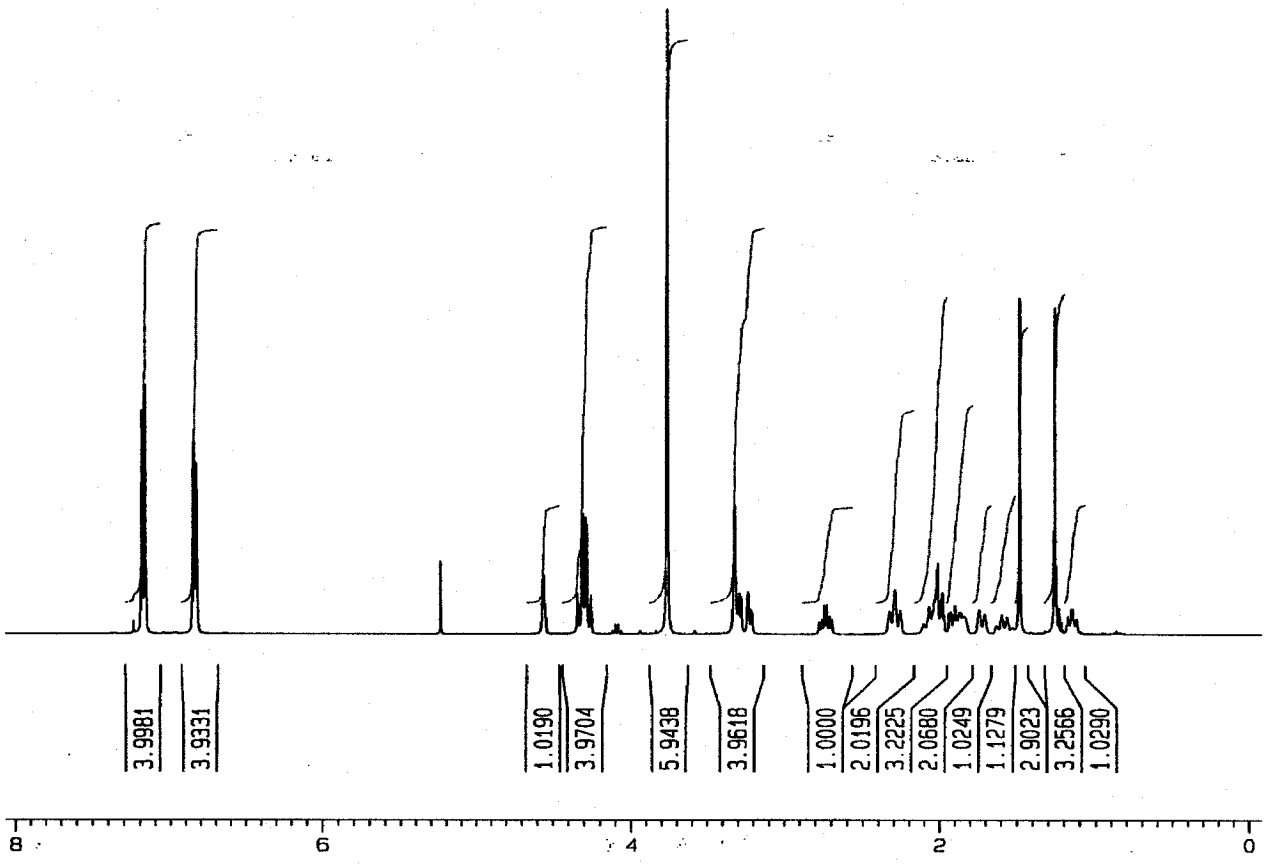
^{13}C NMR (100 MHz, C_6D_6)



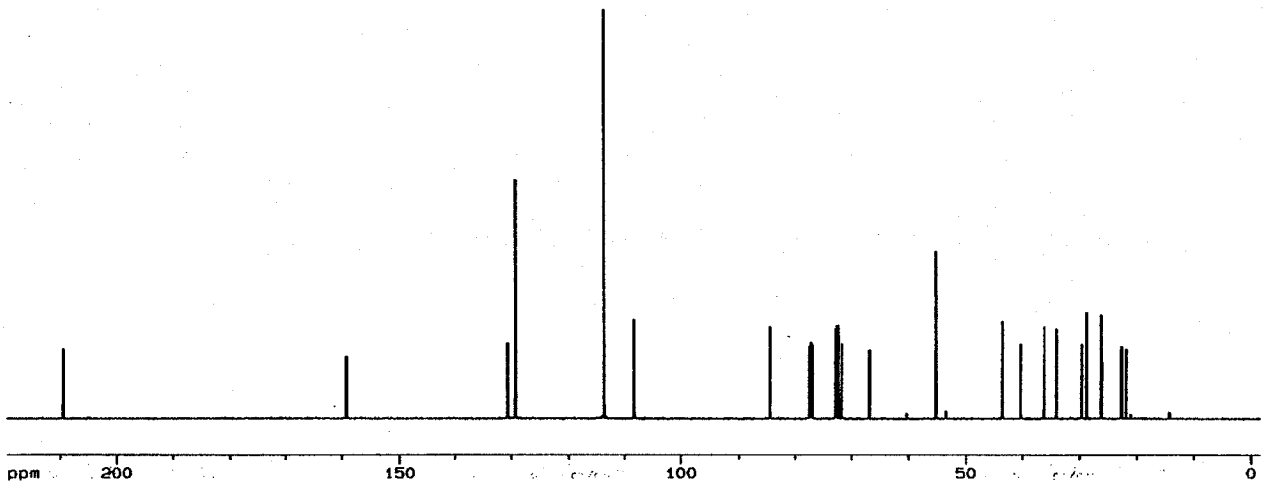


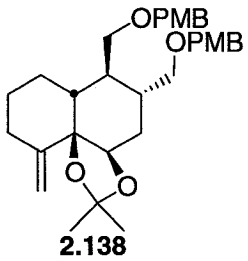
2.137

^{1}H NMR (400 MHz, $CDCl_3$)



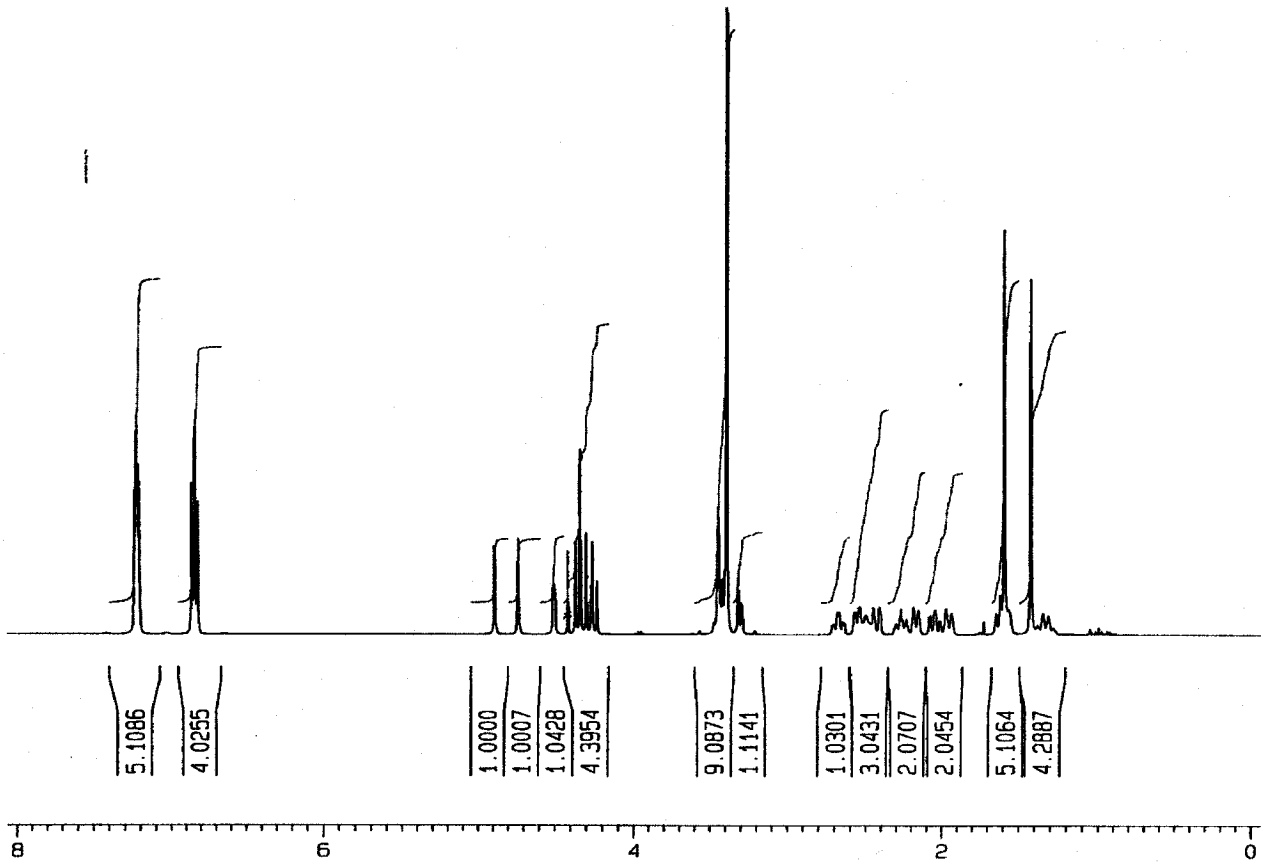
^{13}C NMR (100 MHz, $CDCl_3$)



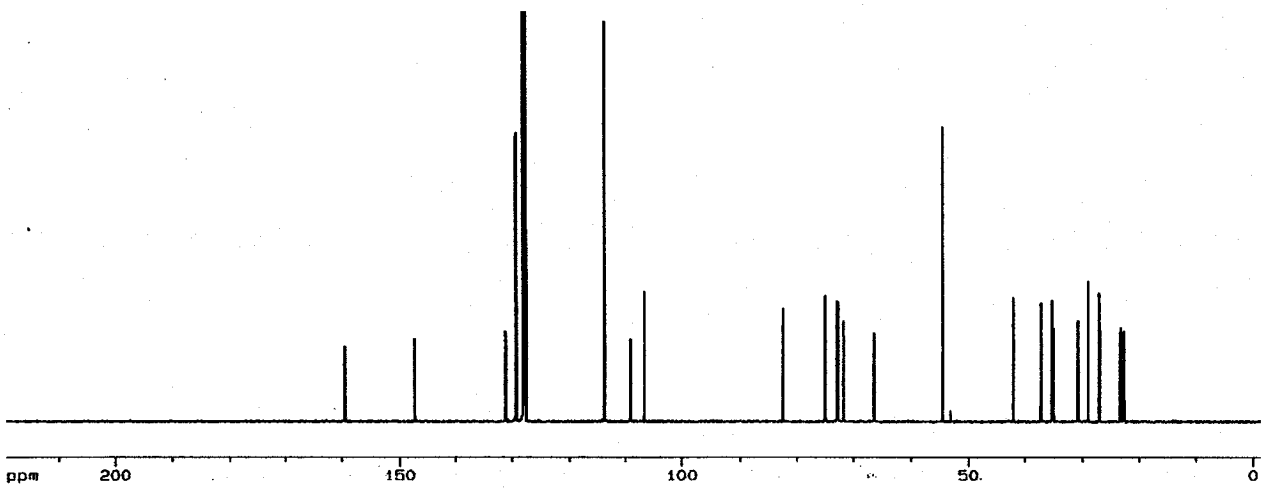


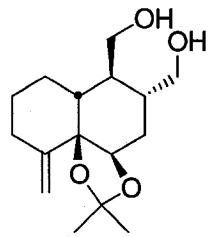
2.138

^{1}H NMR (400 MHz, C_6D_6)



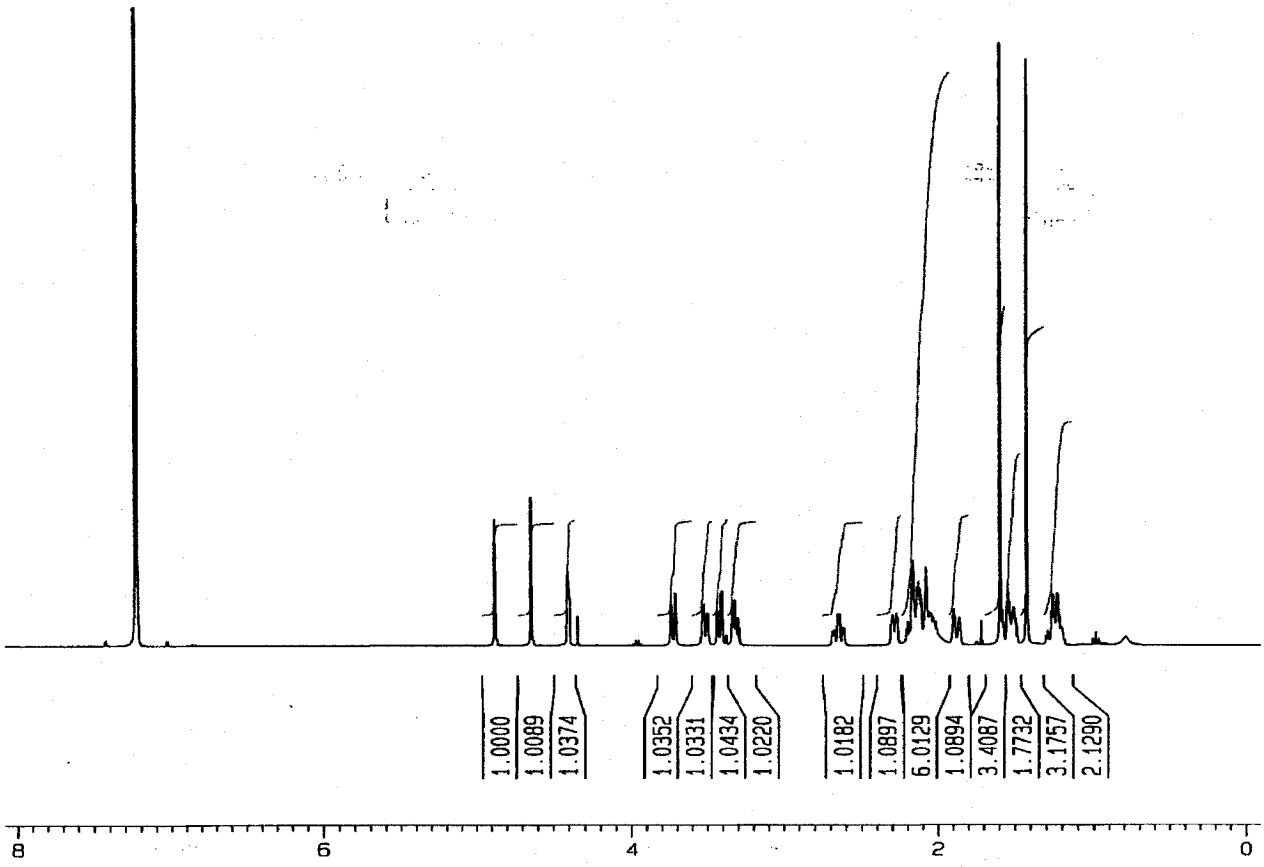
^{13}C NMR (100 MHz, C_6D_6)



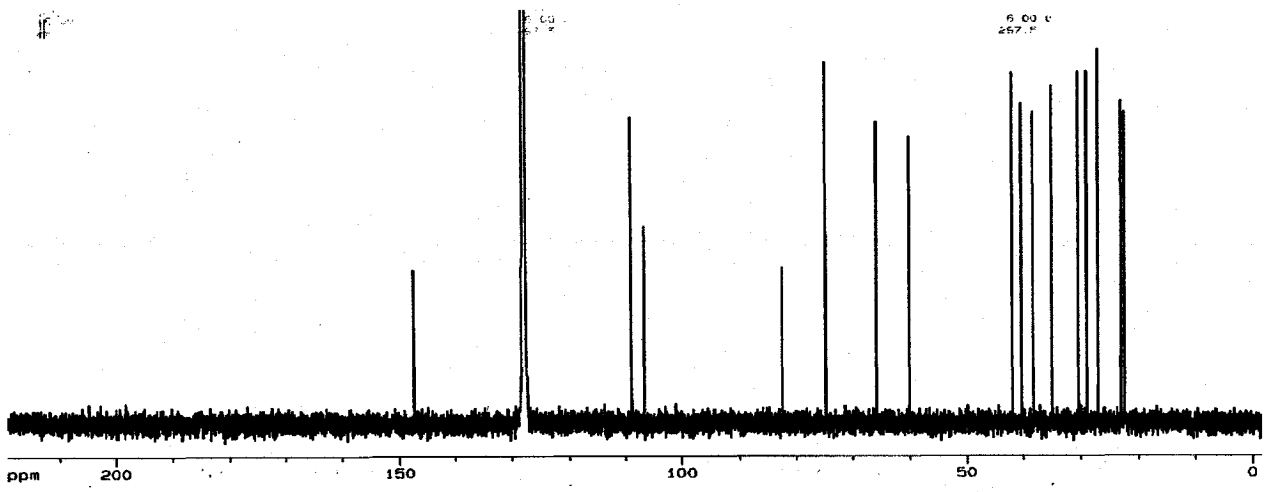


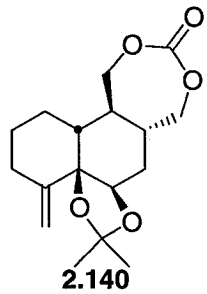
2.139

^{1}H NMR (400 MHz, C_6D_6)

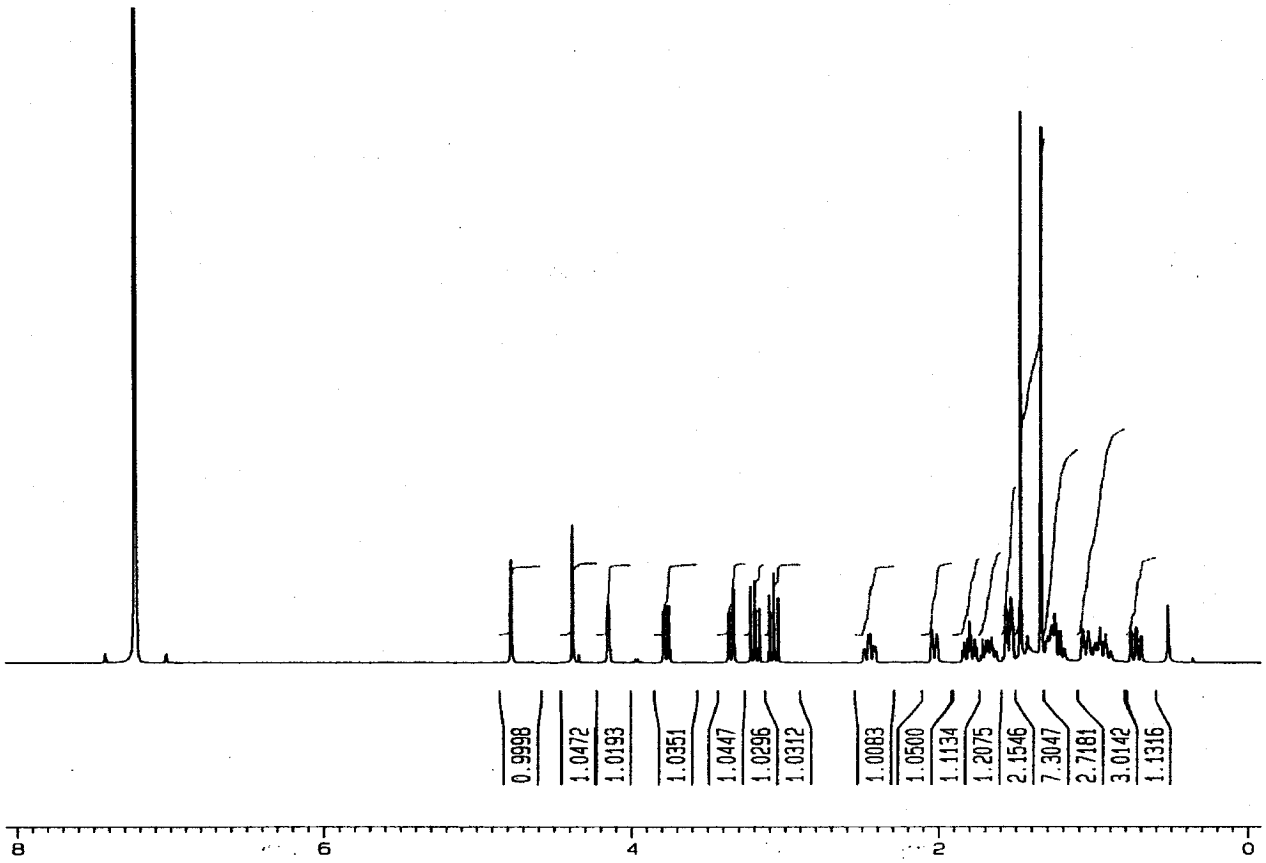


^{13}C NMR (100 MHz, C_6D_6)

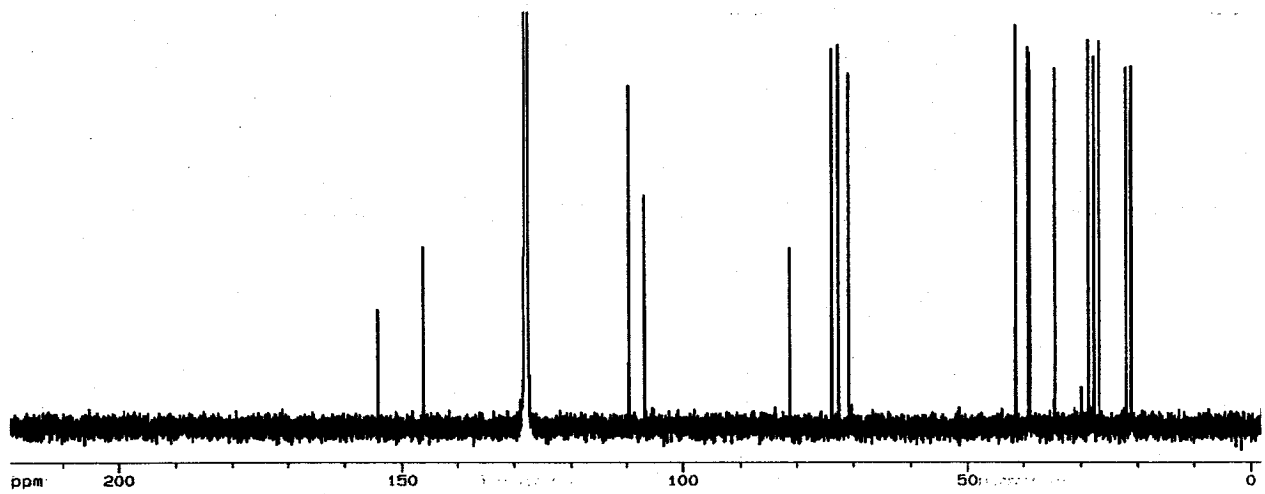


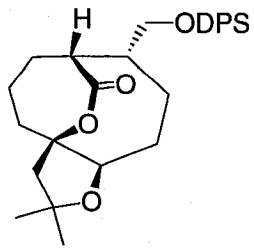


^{1}H NMR (400 MHz, C_6D_6)



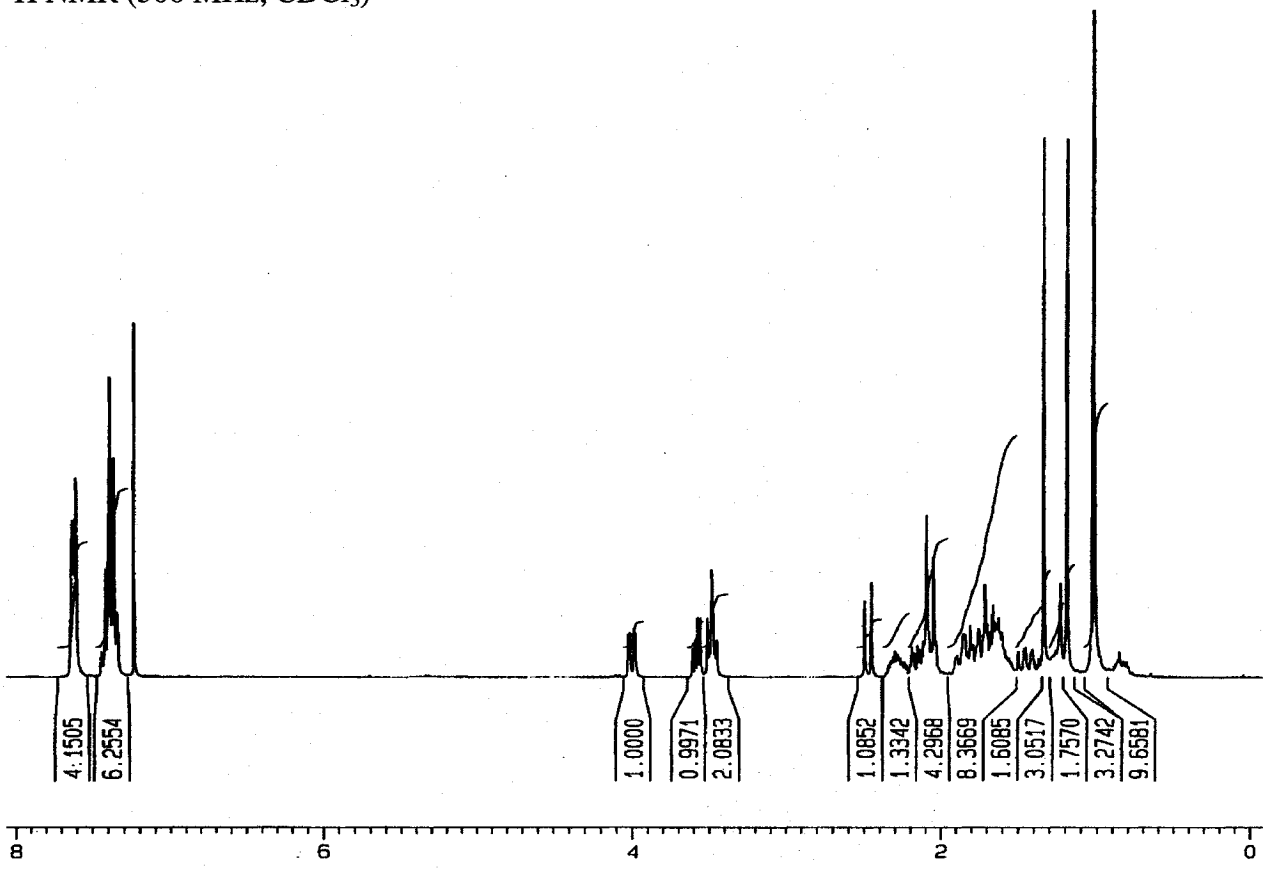
^{13}C NMR (100 MHz, C_6D_6)



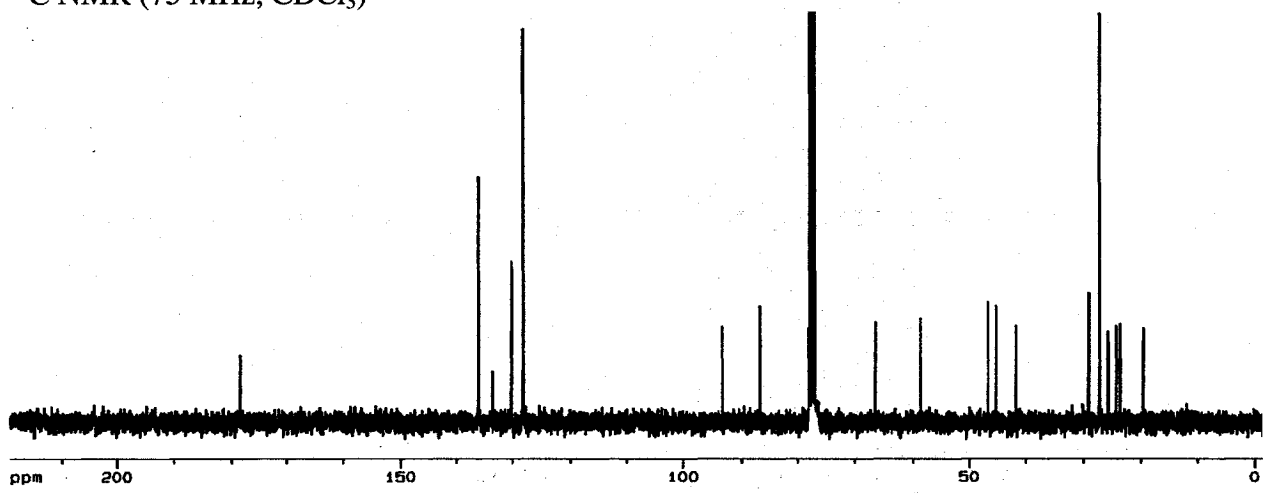


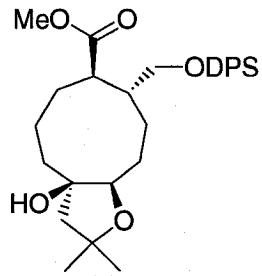
2.147

^{1}H NMR (300 MHz, $CDCl_3$)



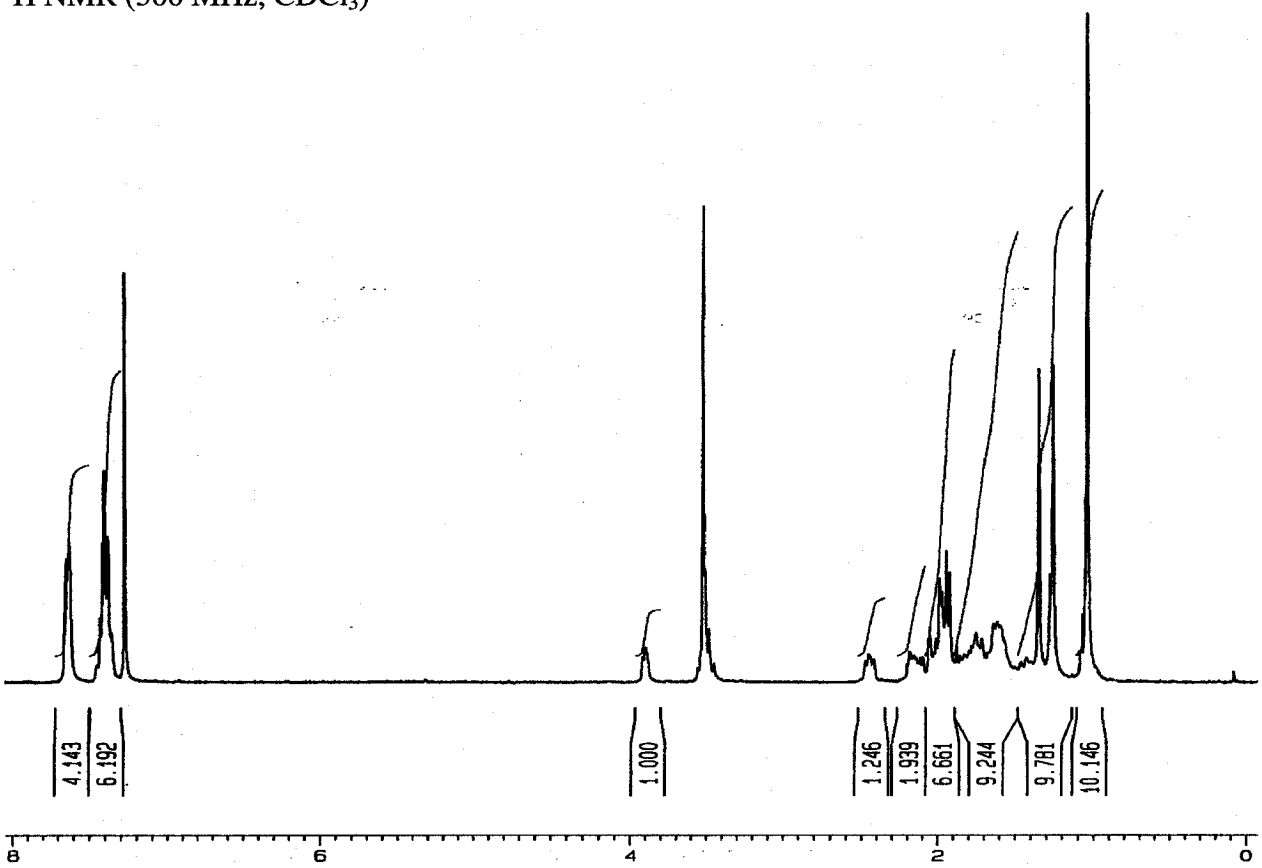
^{13}C NMR (75 MHz, $CDCl_3$)



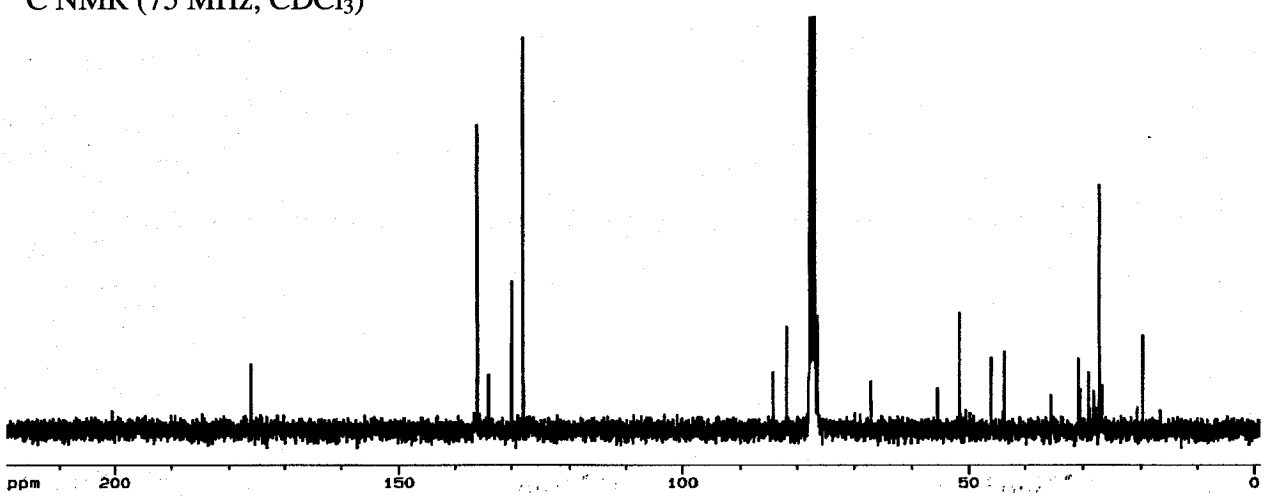


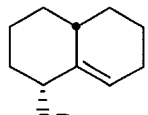
2.148

^{1}H NMR (300 MHz, $CDCl_3$)



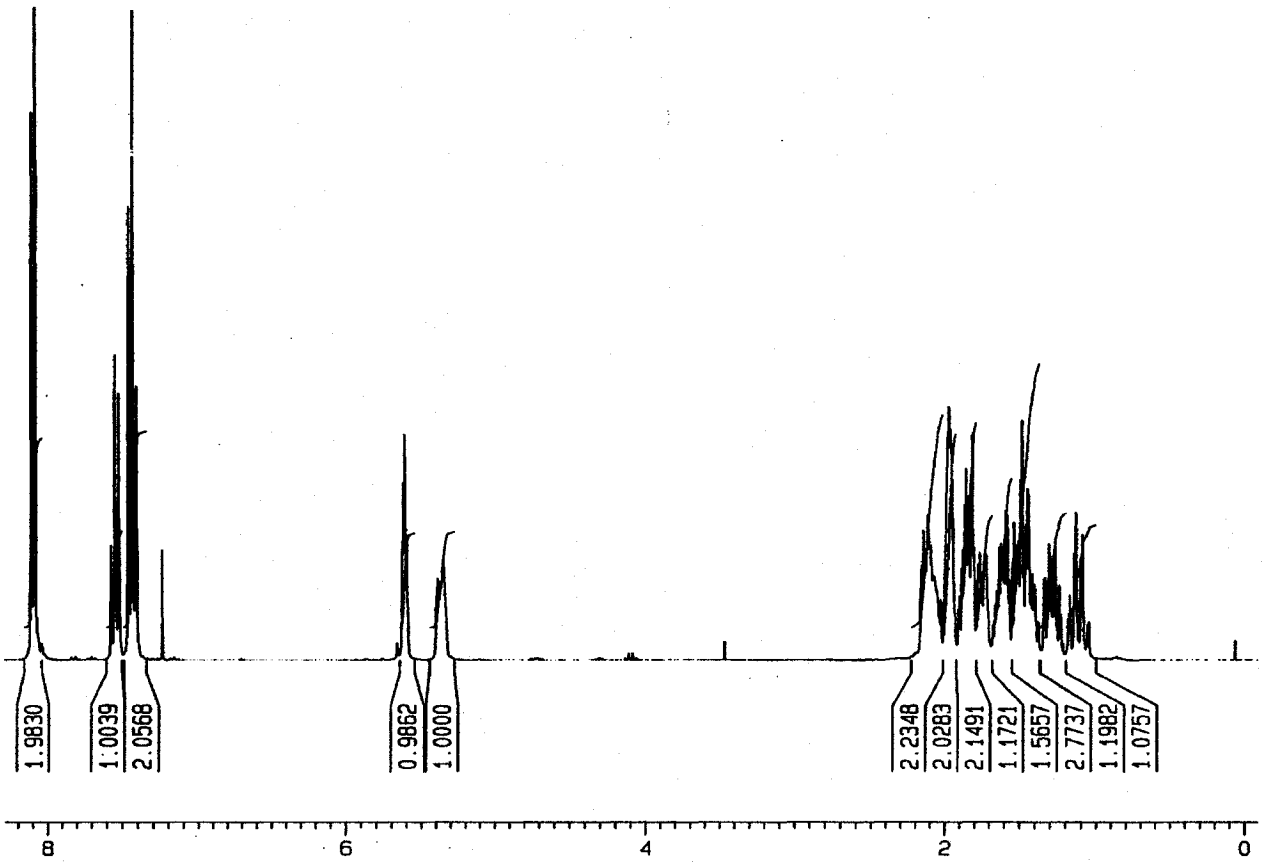
^{13}C NMR (75 MHz, $CDCl_3$)



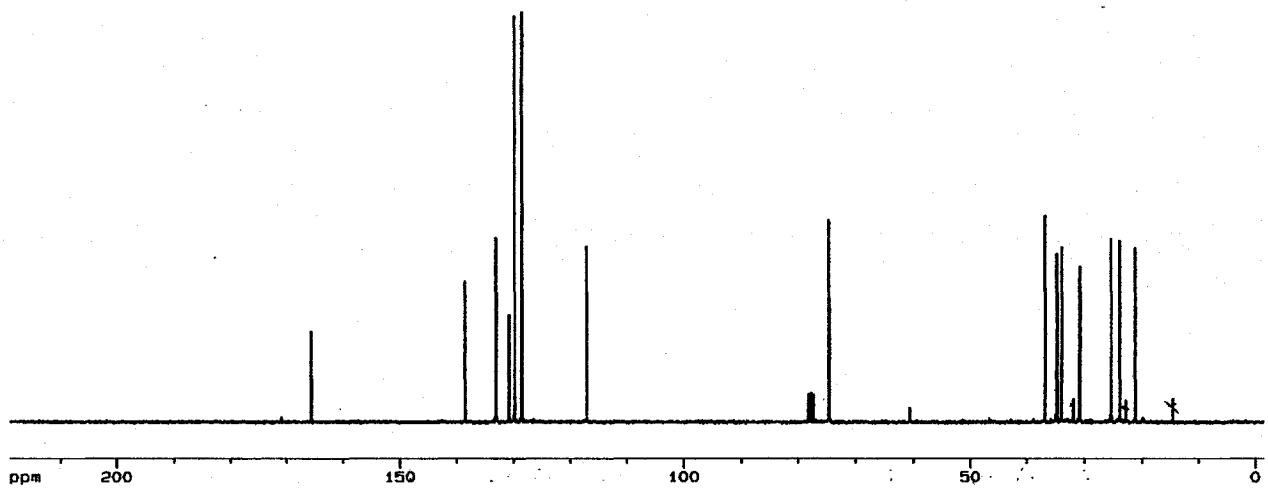


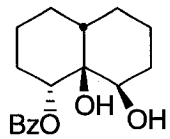
3.6

^{1}H NMR (300 MHz, $CDCl_3$)



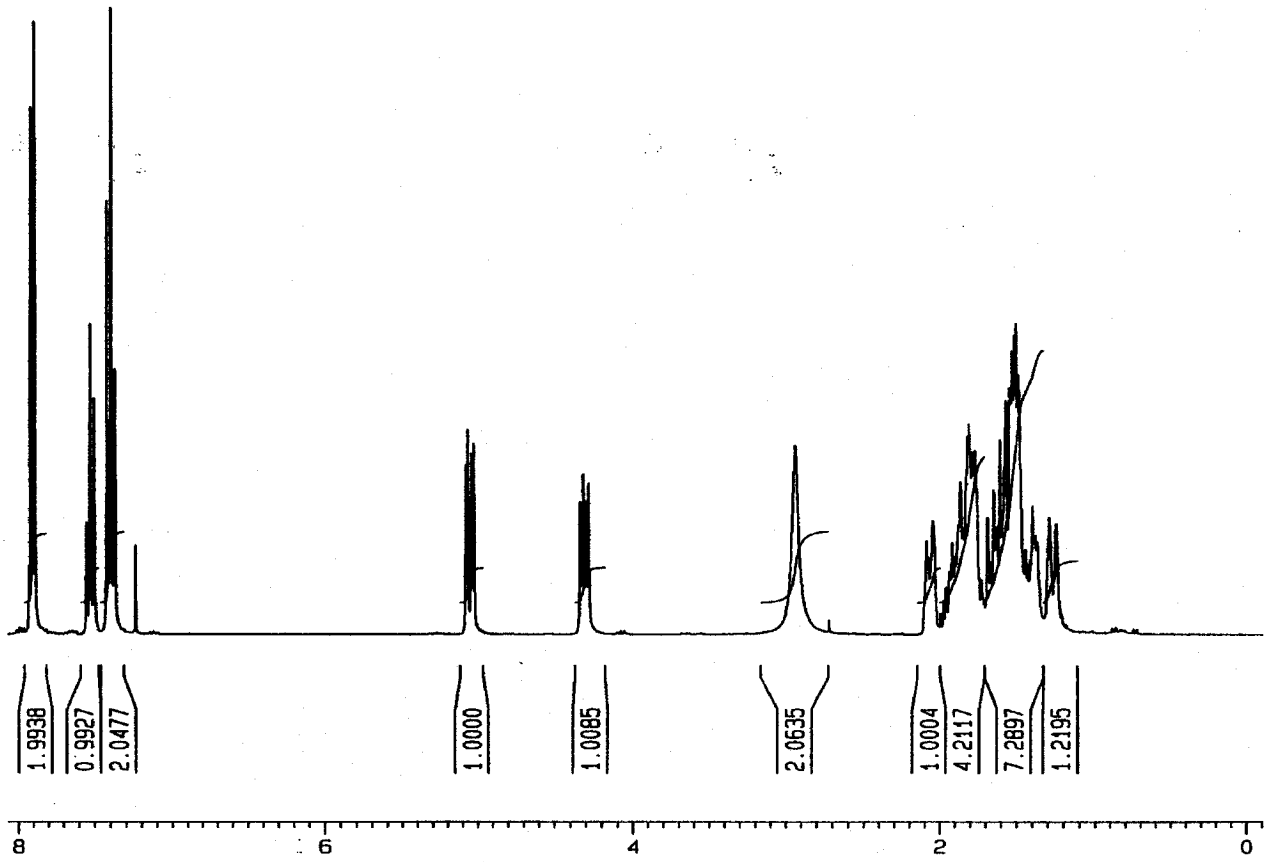
^{13}C NMR (75 MHz, $CDCl_3$)



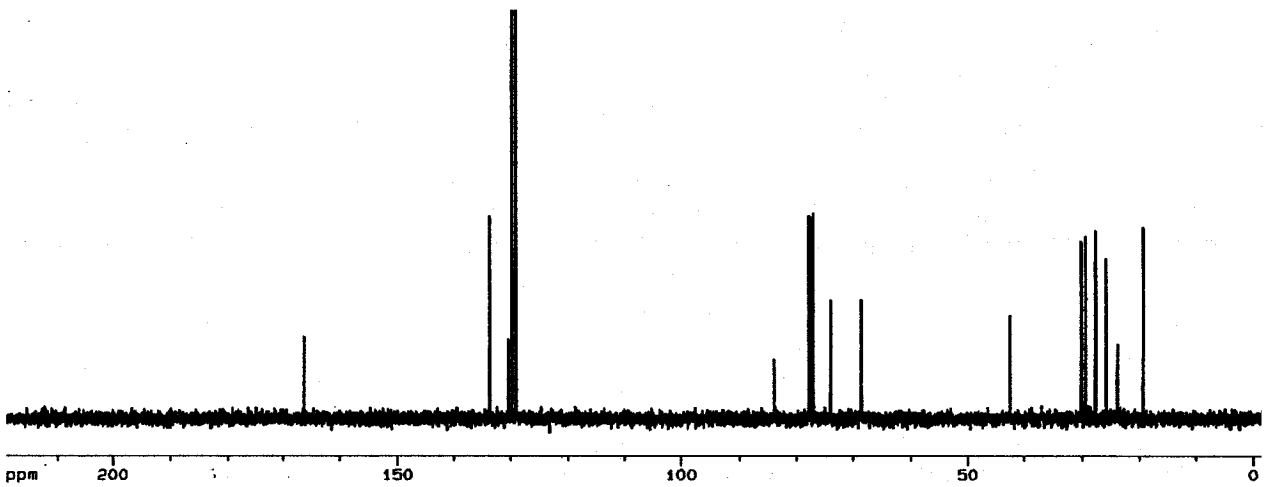


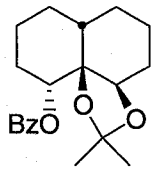
3.7

^{1}H NMR (300 MHz, $CDCl_3$)



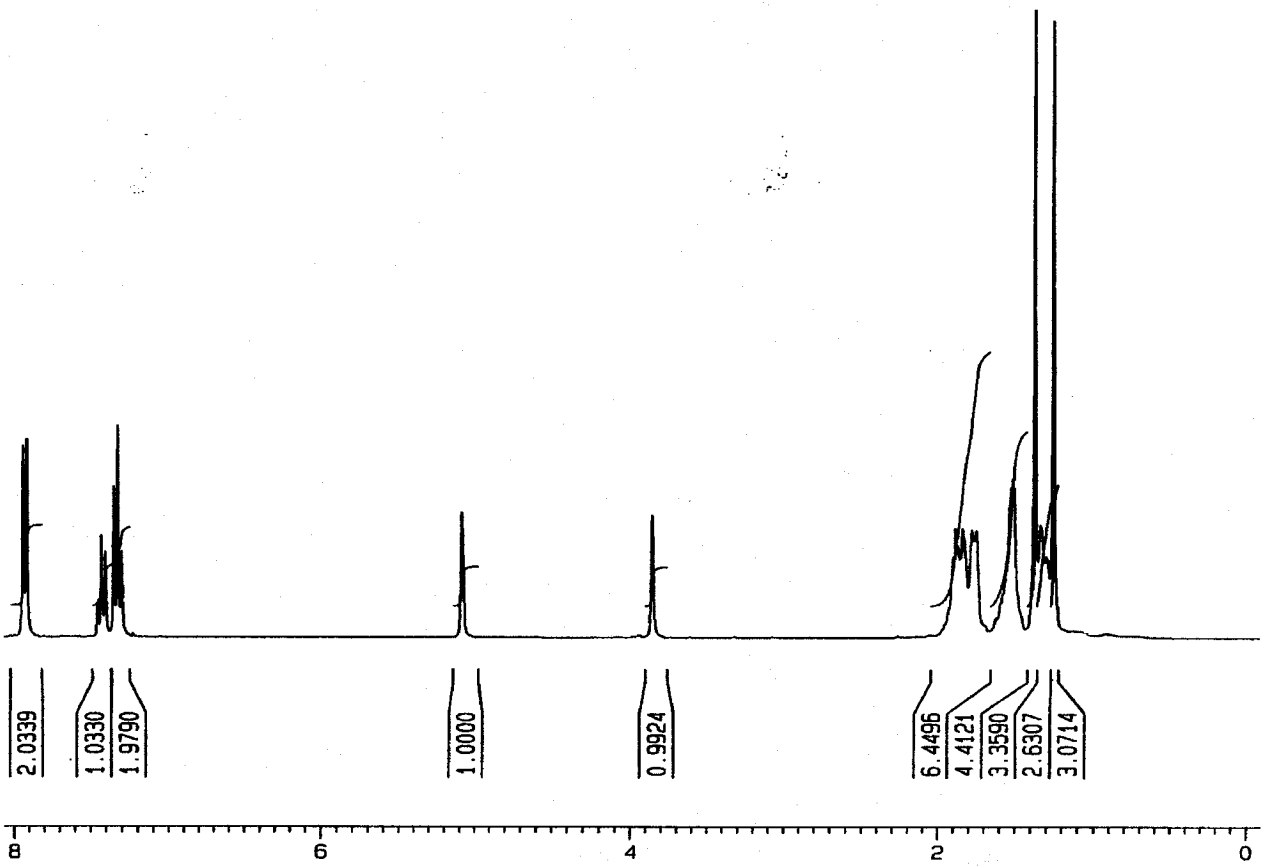
^{13}C NMR (75 MHz, $CDCl_3$)



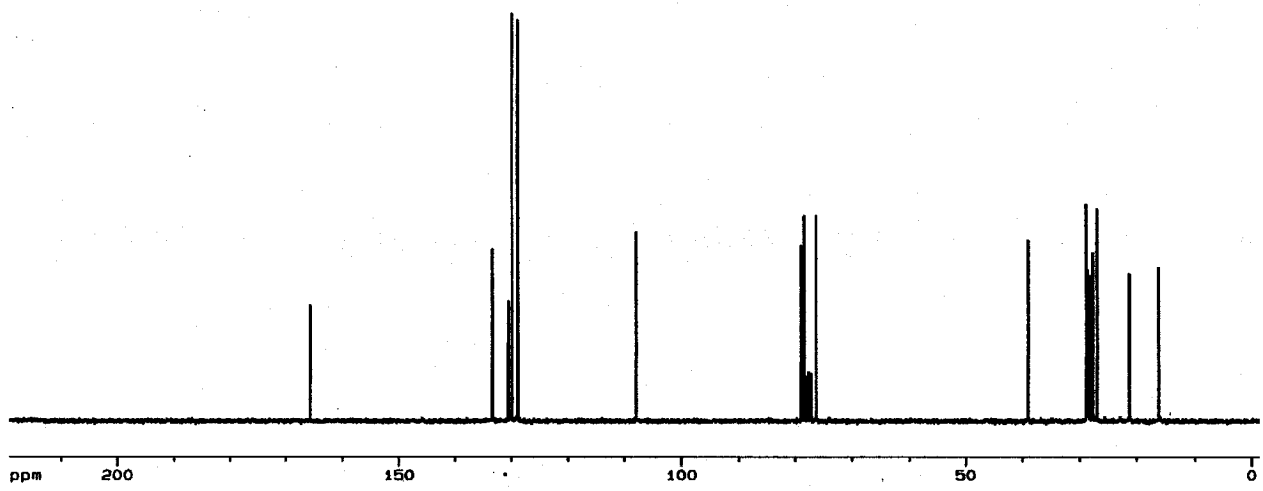


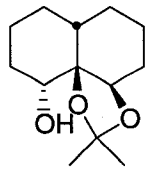
3.8

^{1}H NMR (300 MHz, $CDCl_3$)



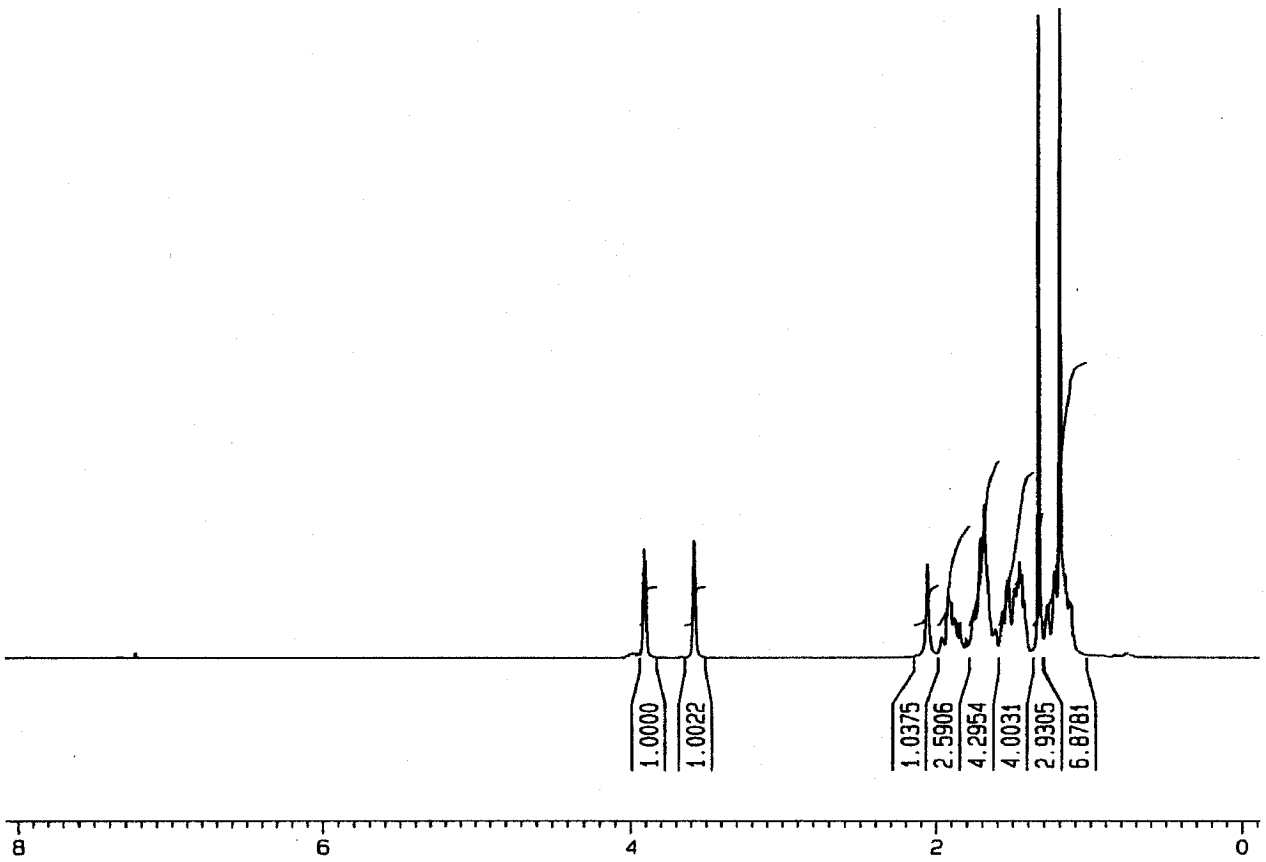
^{13}C NMR (75 MHz, $CDCl_3$)



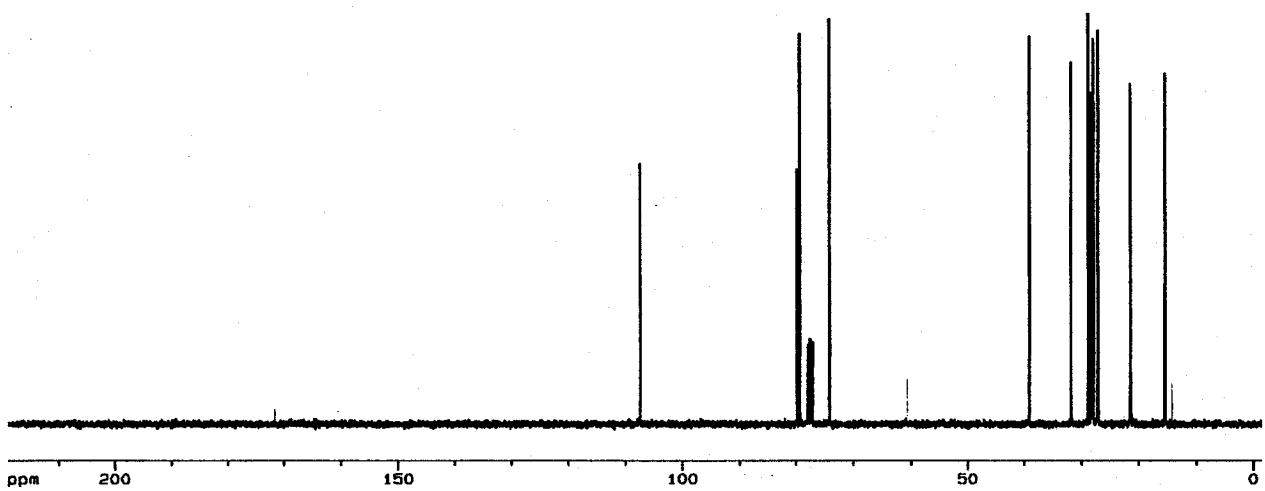


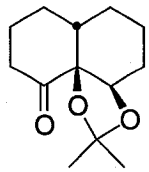
3.9

^{1}H NMR (300 MHz, $CDCl_3$)



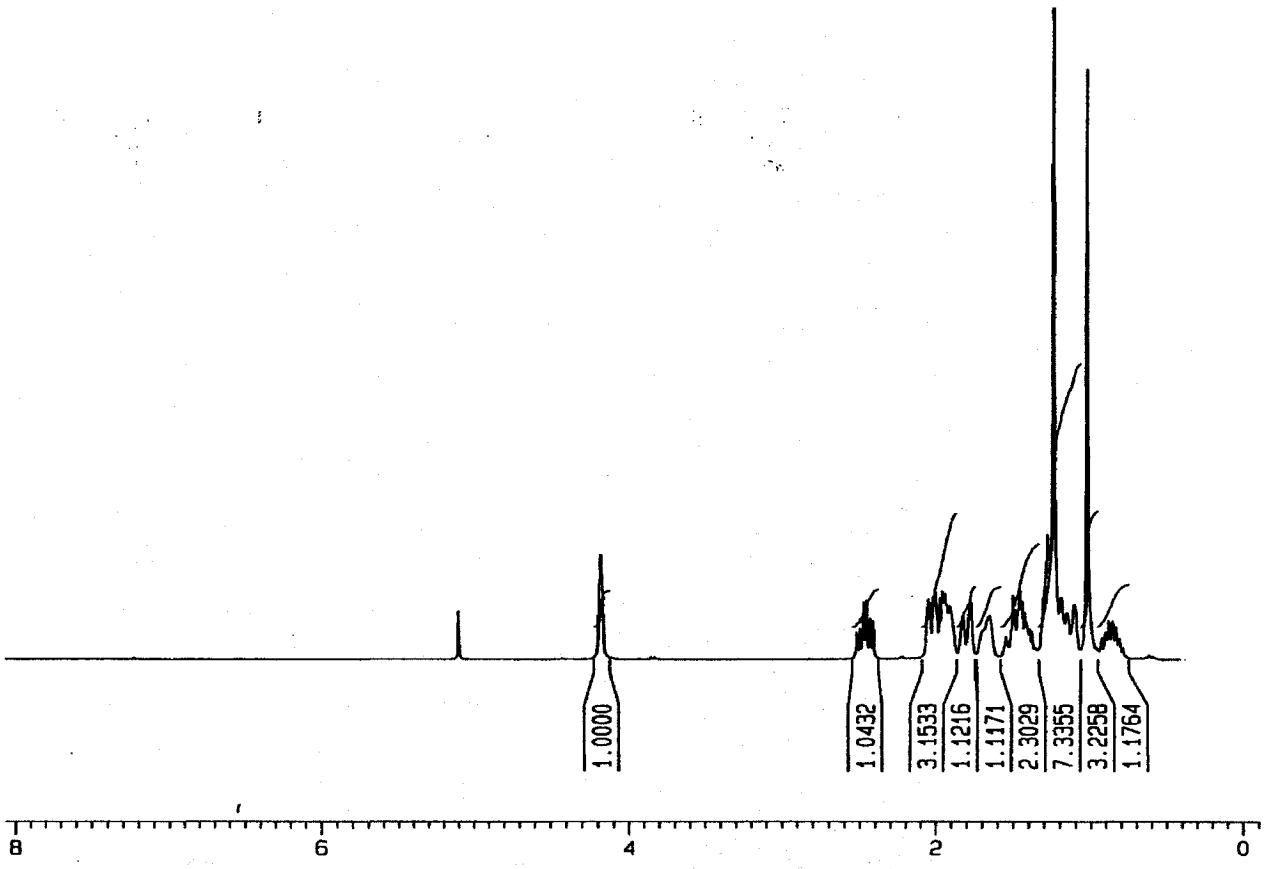
^{13}C NMR (75 MHz, $CDCl_3$)



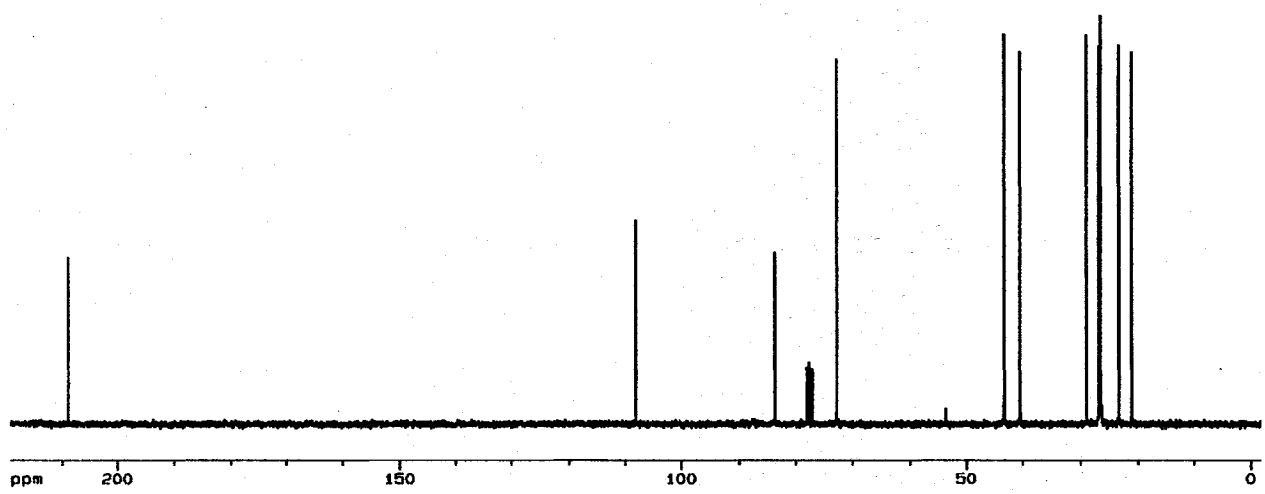


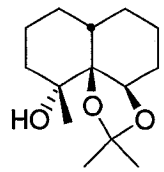
3.10

^{1}H NMR (300 MHz, $CDCl_3$)



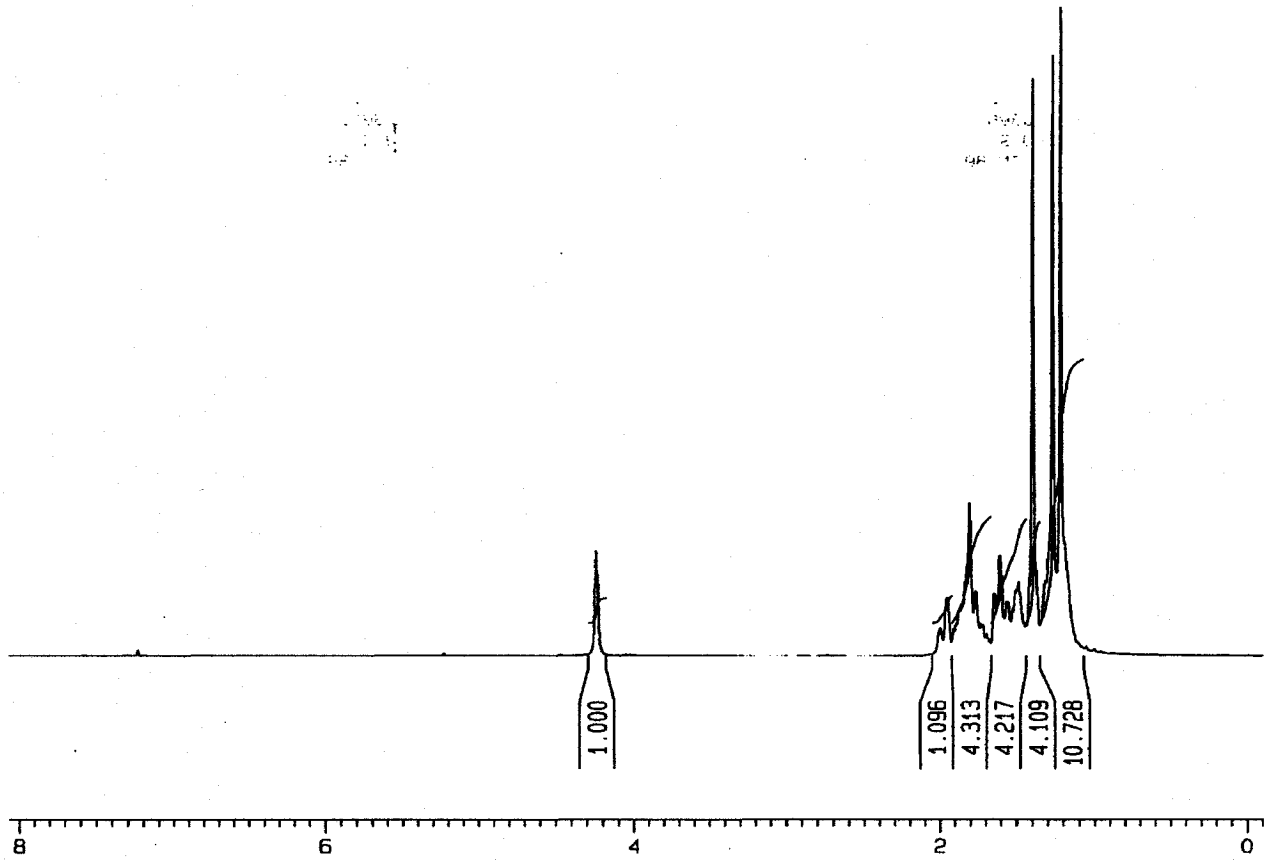
^{13}C NMR (75 MHz, $CDCl_3$)



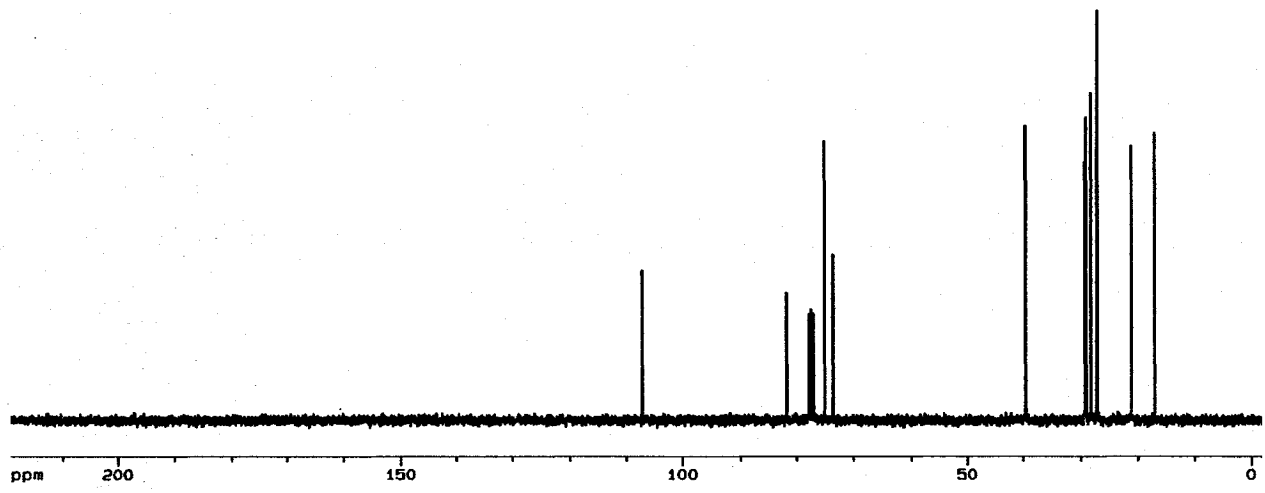


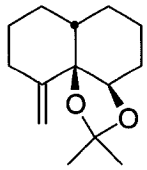
3.11

^{1}H NMR (300 MHz, $CDCl_3$)



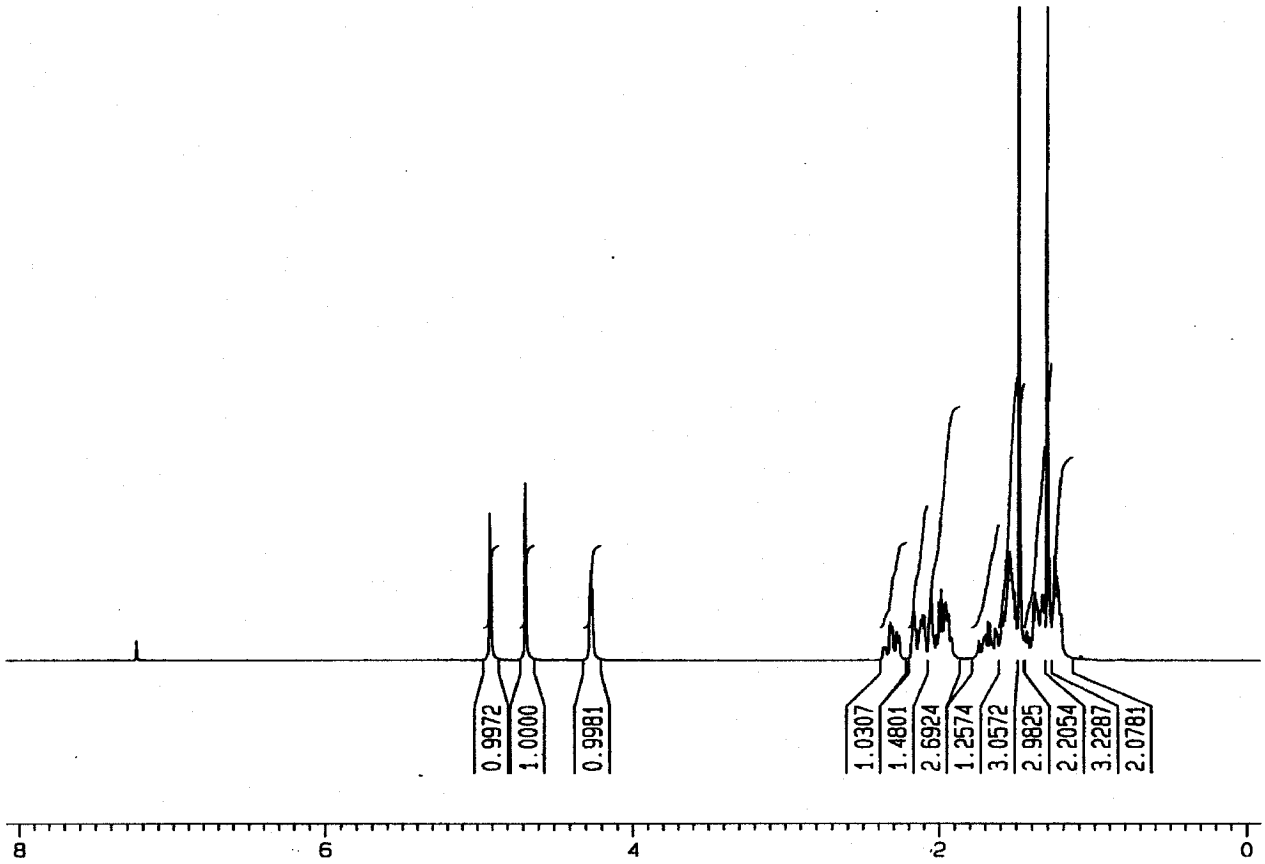
^{13}C NMR (75 MHz, $CDCl_3$)



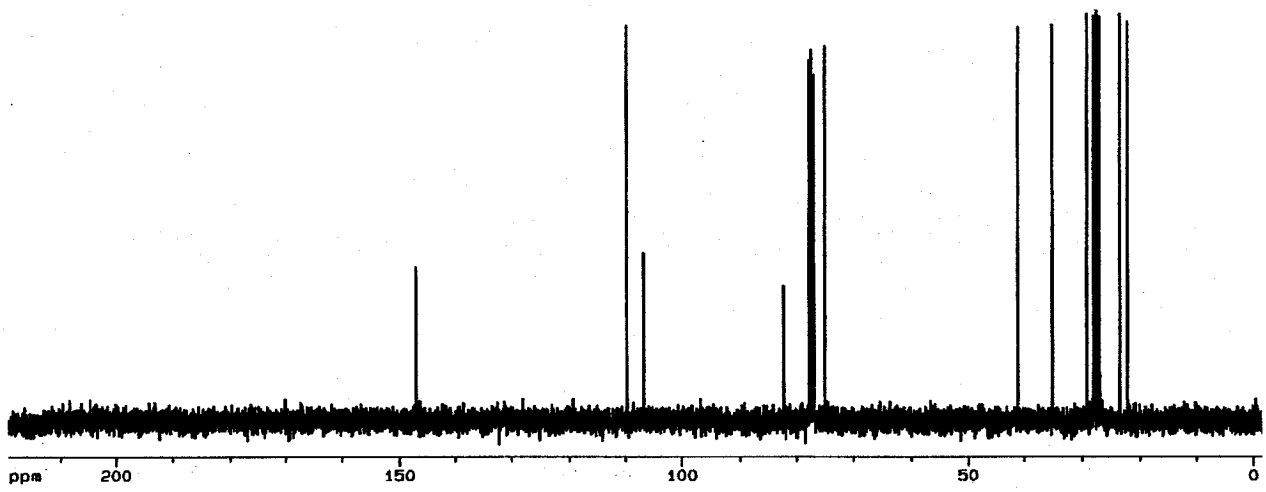


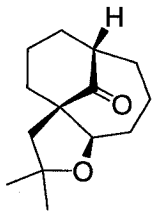
3.12

^{1}H NMR (300 MHz, $CDCl_3$)



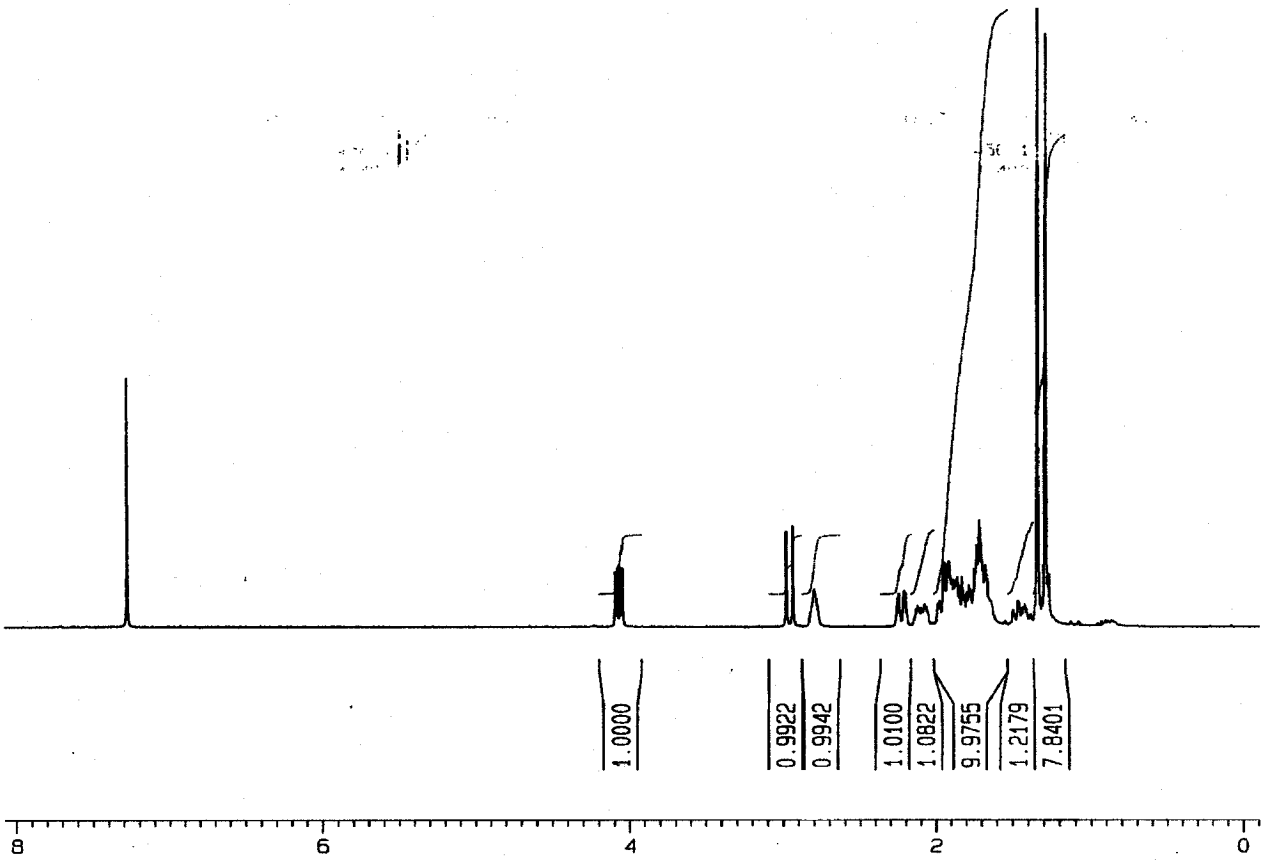
^{13}C NMR (75 MHz, $CDCl_3$)



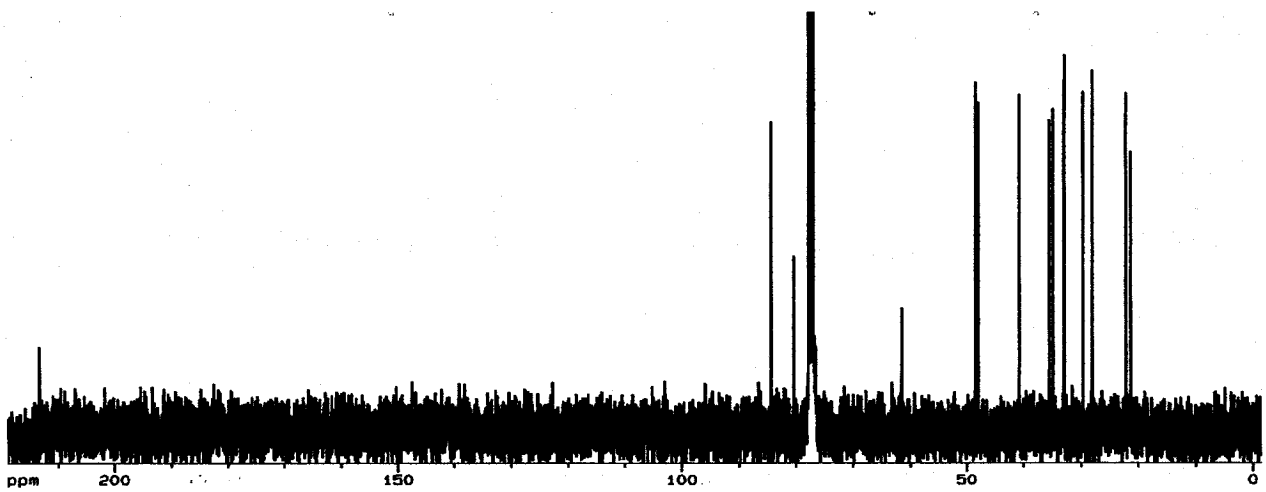


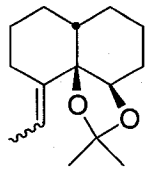
3.13

^{1}H NMR (300 MHz, $CDCl_3$)



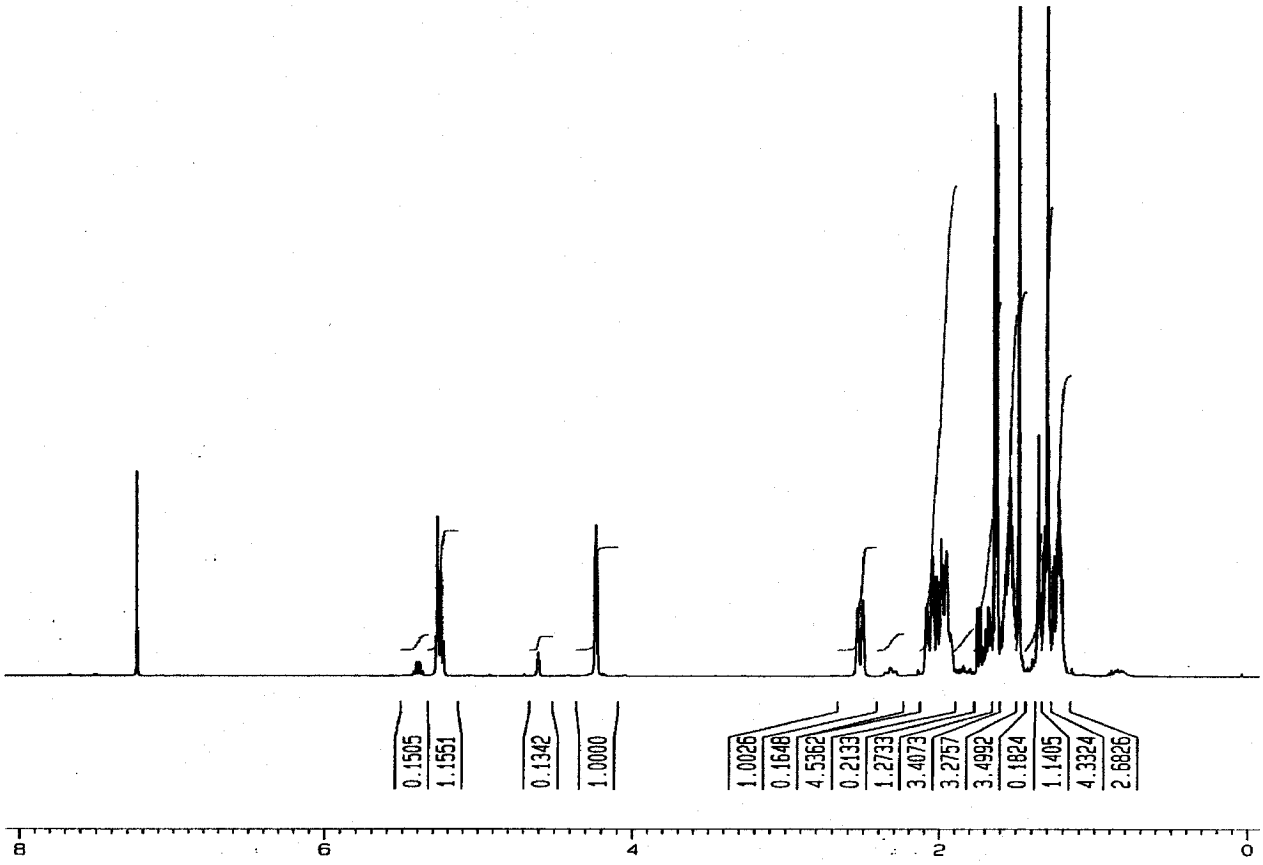
^{13}C NMR (75 MHz, $CDCl_3$)



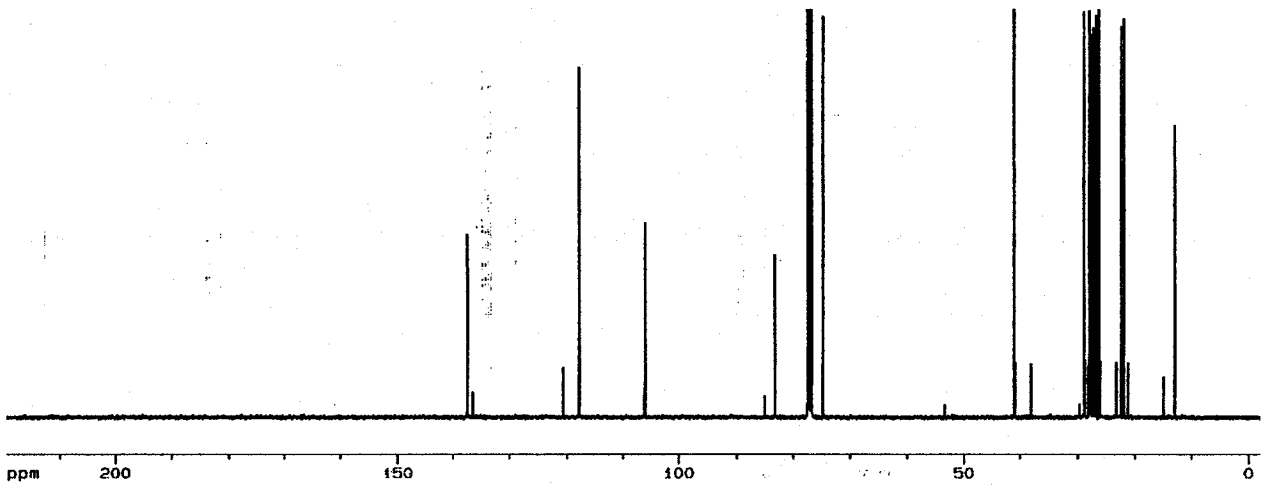


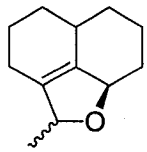
3.19

^{1}H NMR (400 MHz, $CDCl_3$)



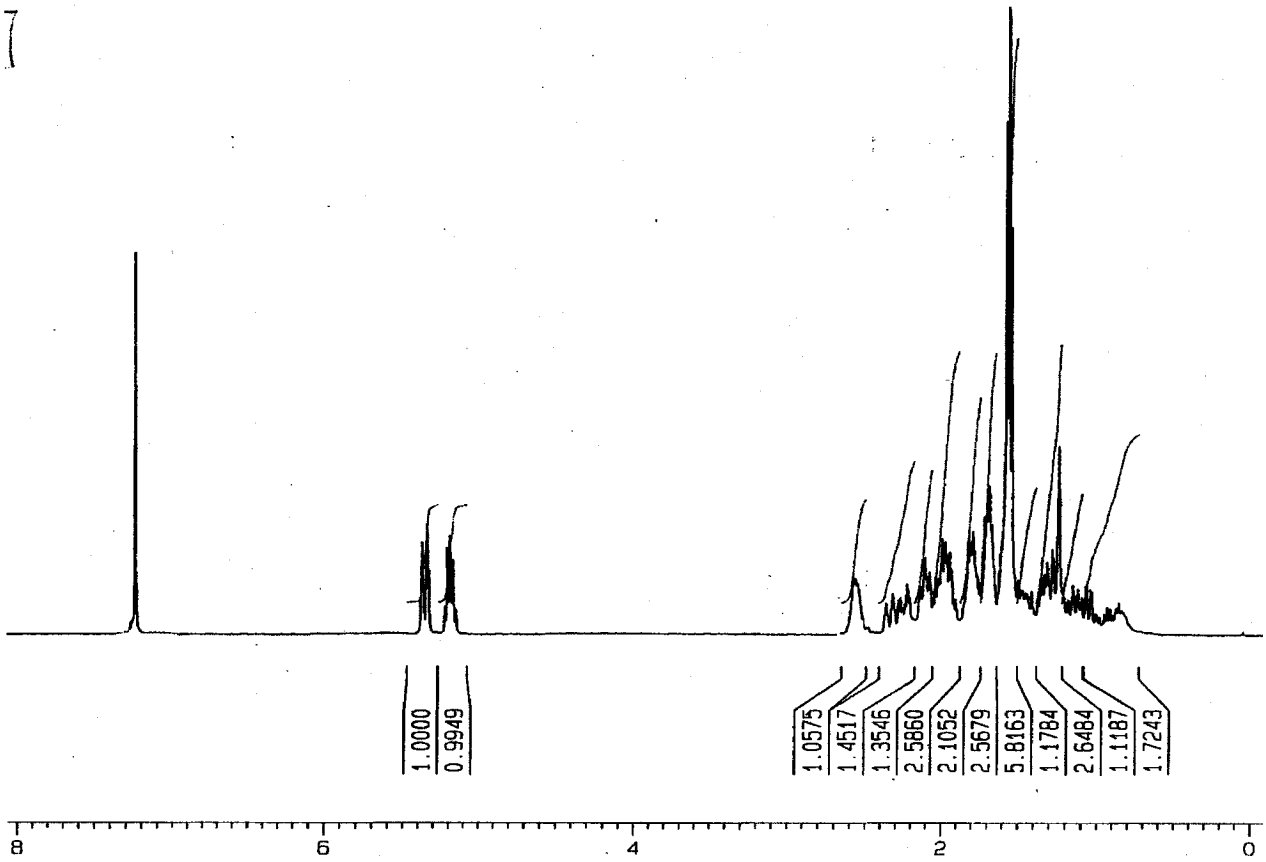
^{13}C NMR (100 MHz, $CDCl_3$)



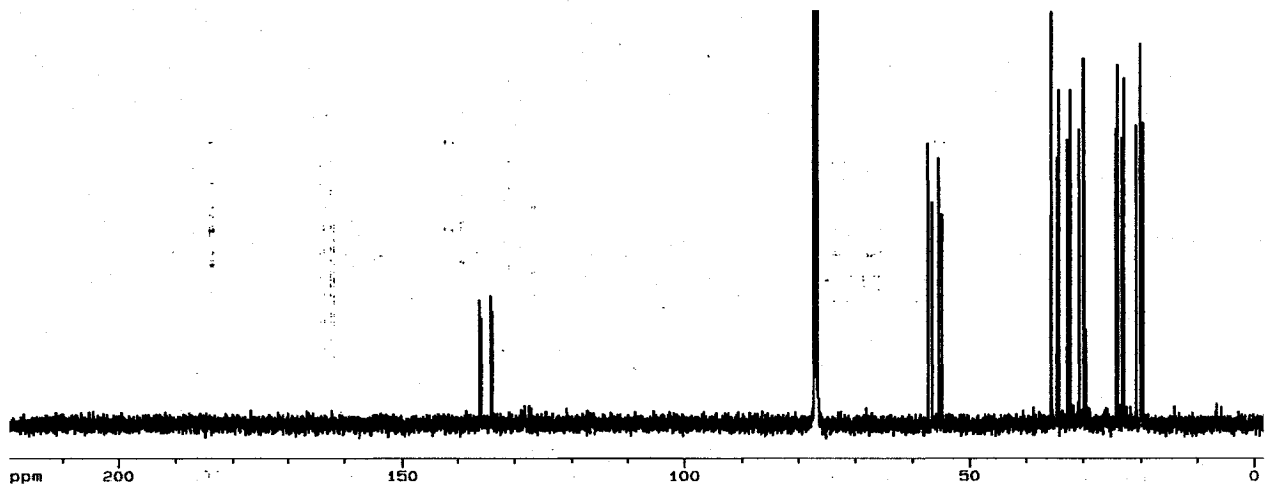


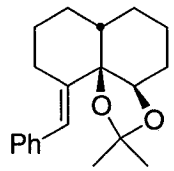
3.20

^{1}H NMR (400 MHz, $CDCl_3$)



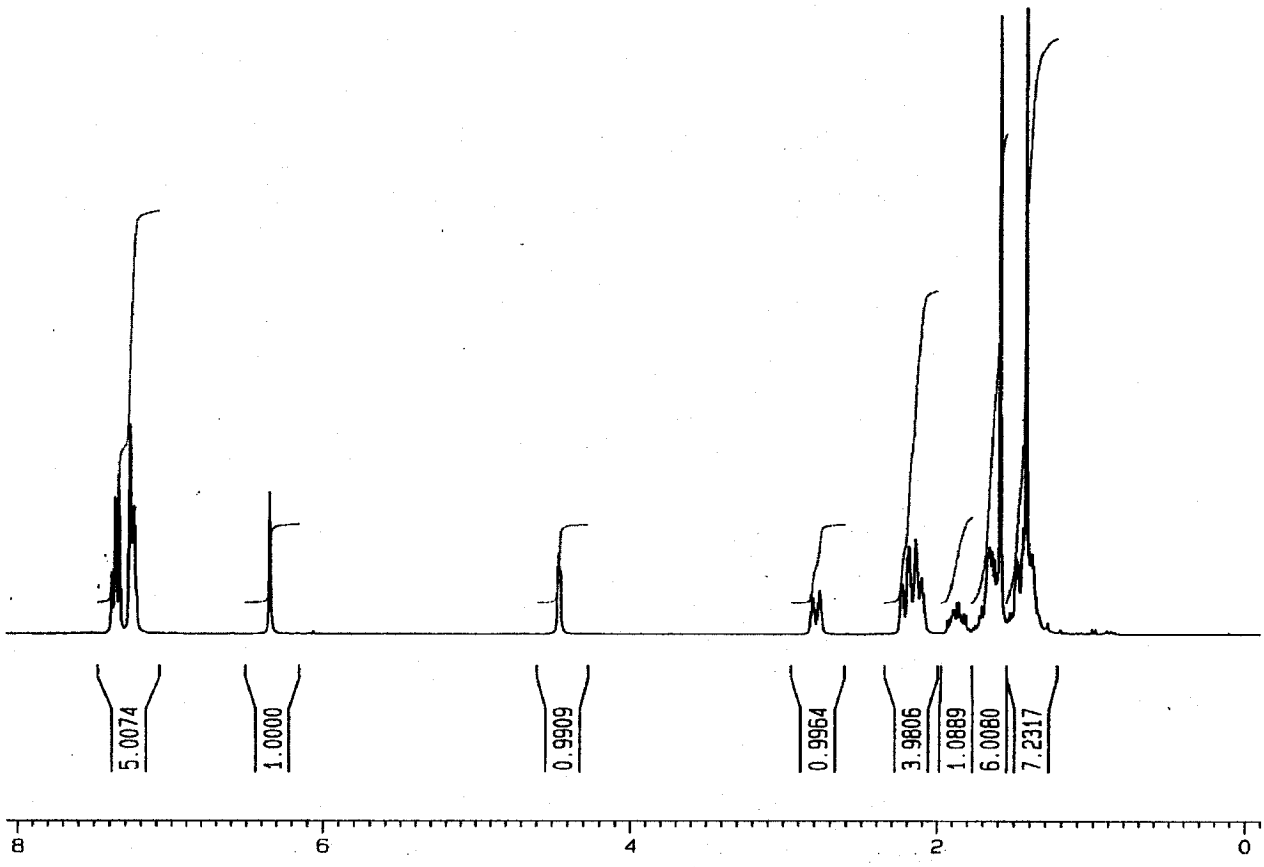
^{13}C NMR (100 MHz, $CDCl_3$)



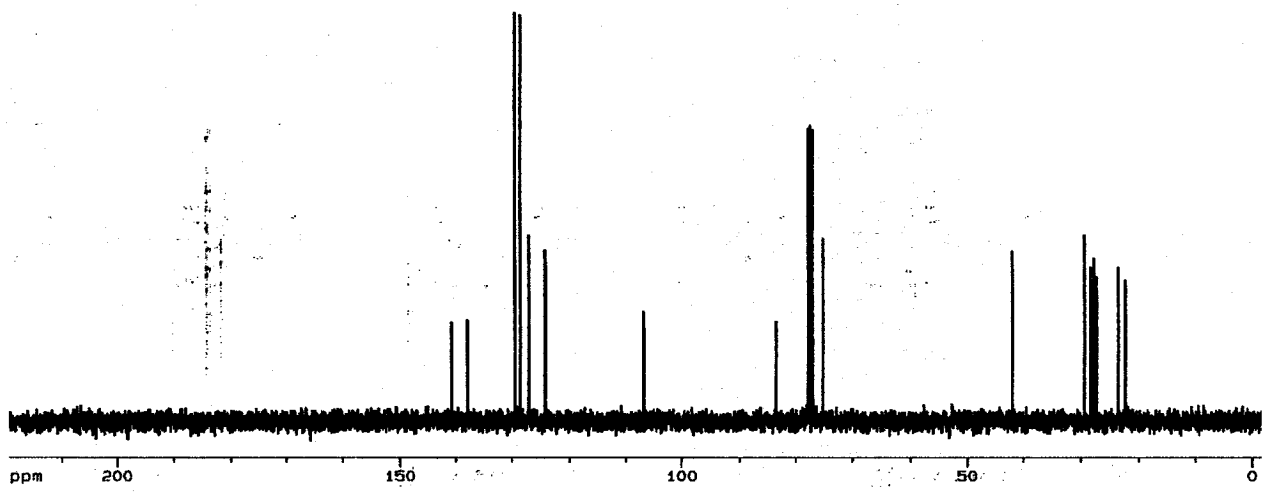


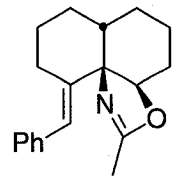
3.21

^{1}H NMR (300 MHz, $CDCl_3$)



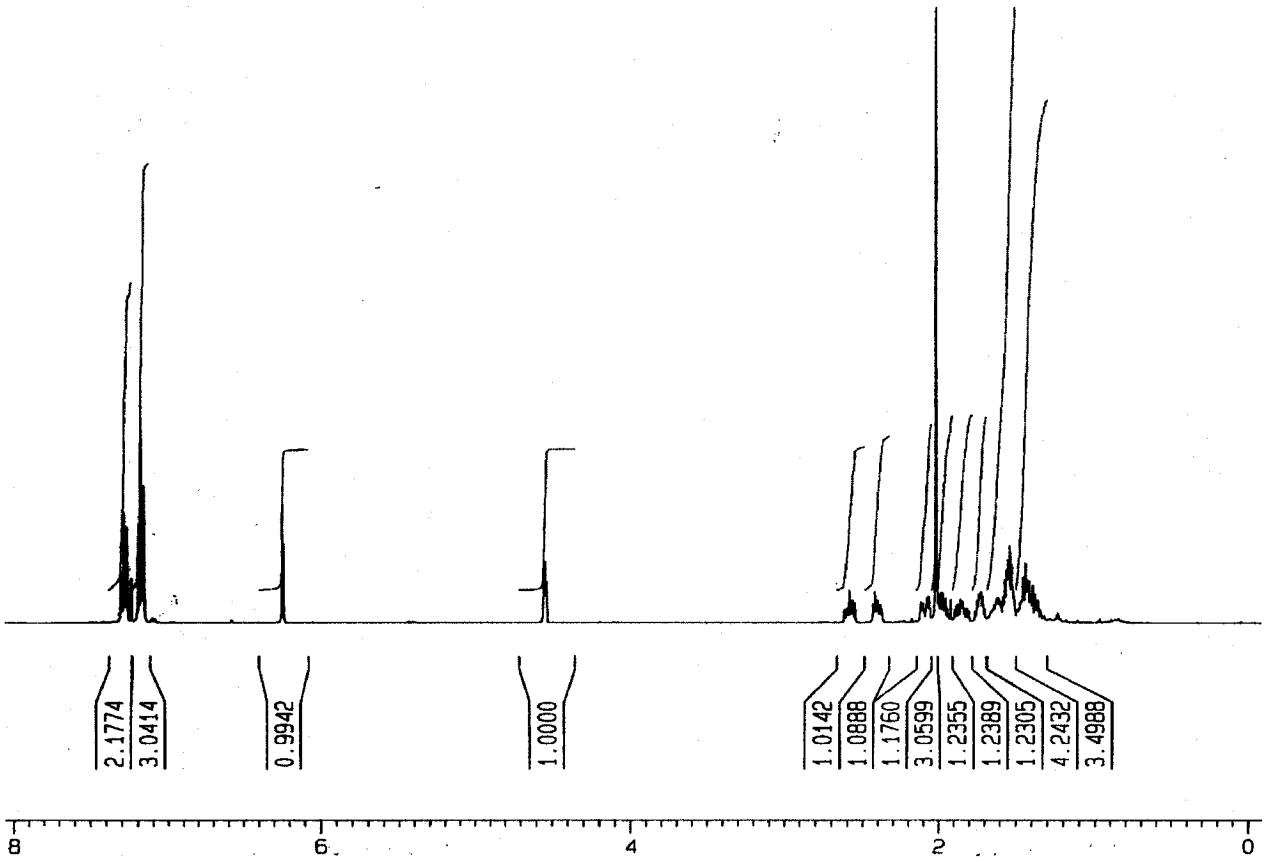
^{13}C NMR (75 MHz, $CDCl_3$)



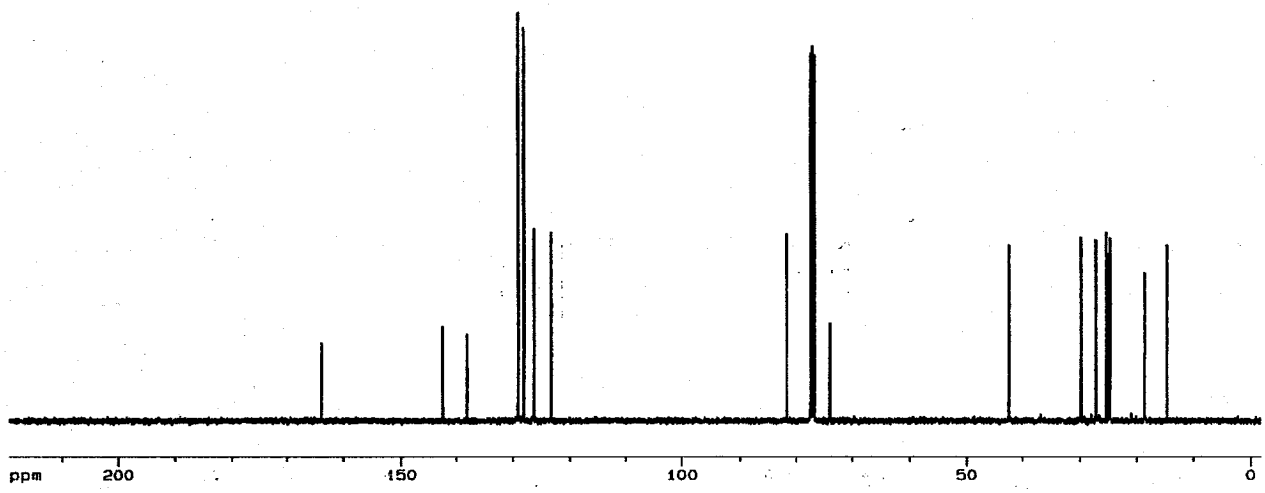


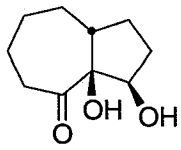
3.22

^{1}H NMR (400 MHz, $CDCl_3$)



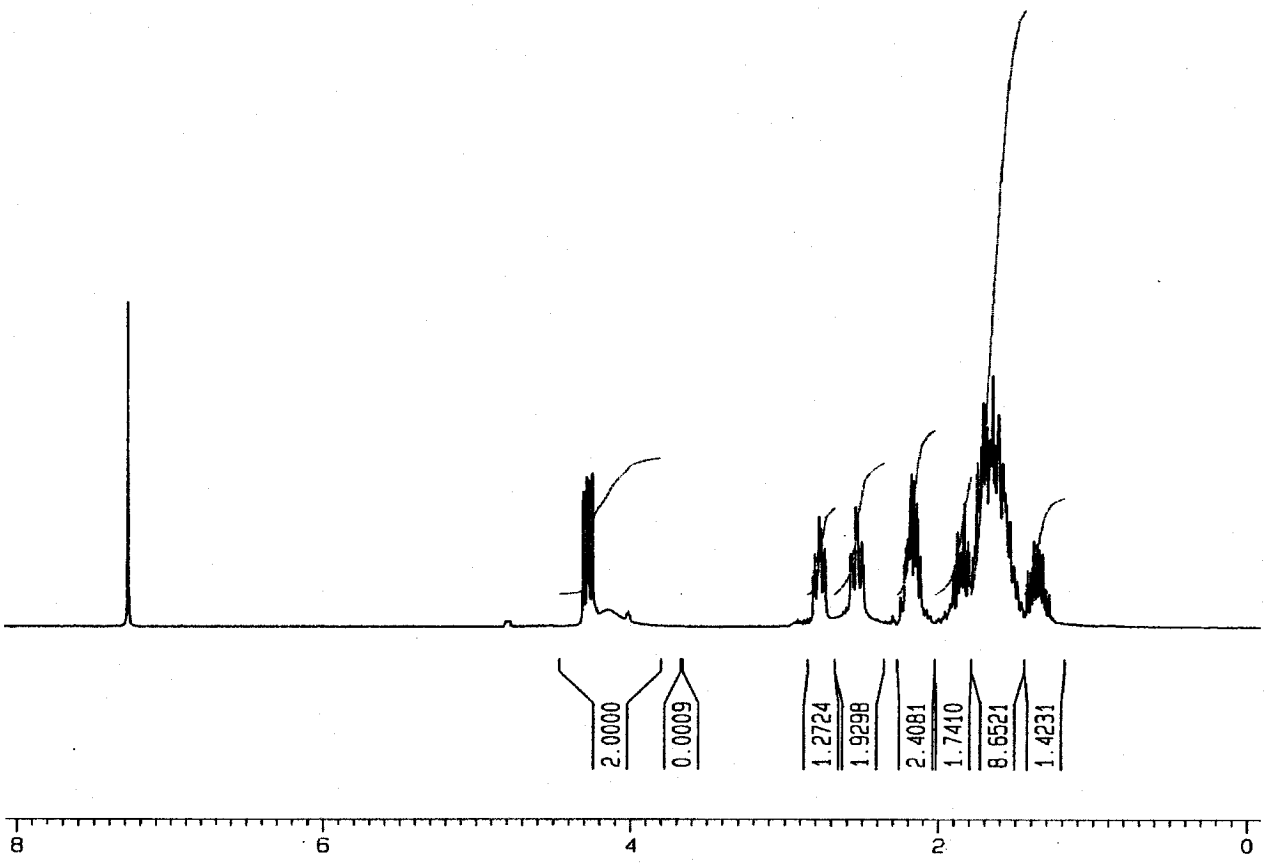
^{13}C NMR (100 MHz, $CDCl_3$)



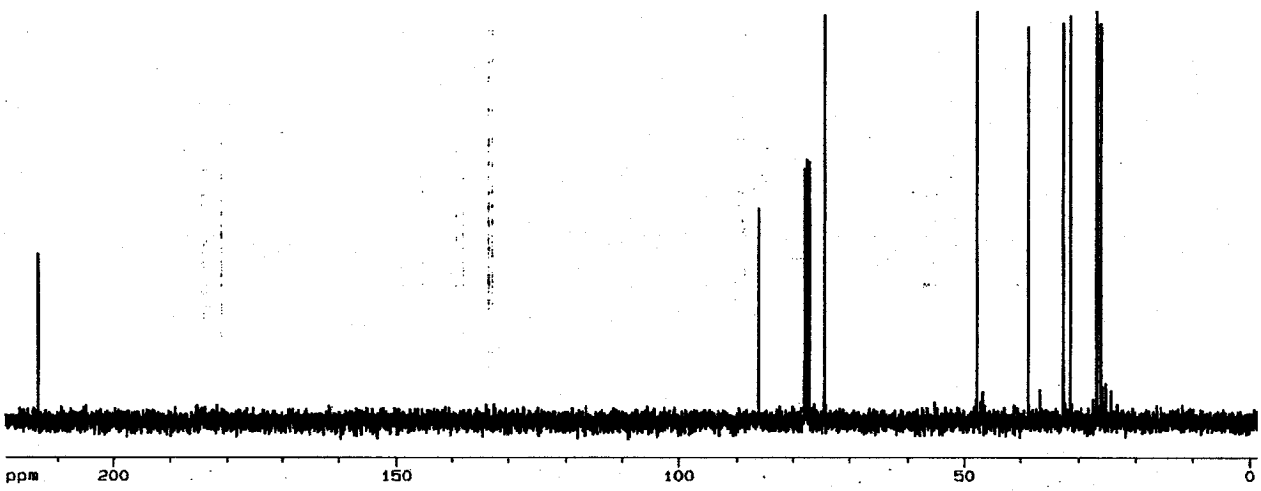


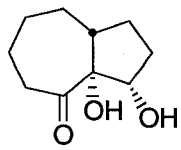
3.37

^{1}H NMR (300 MHz, $CDCl_3$)



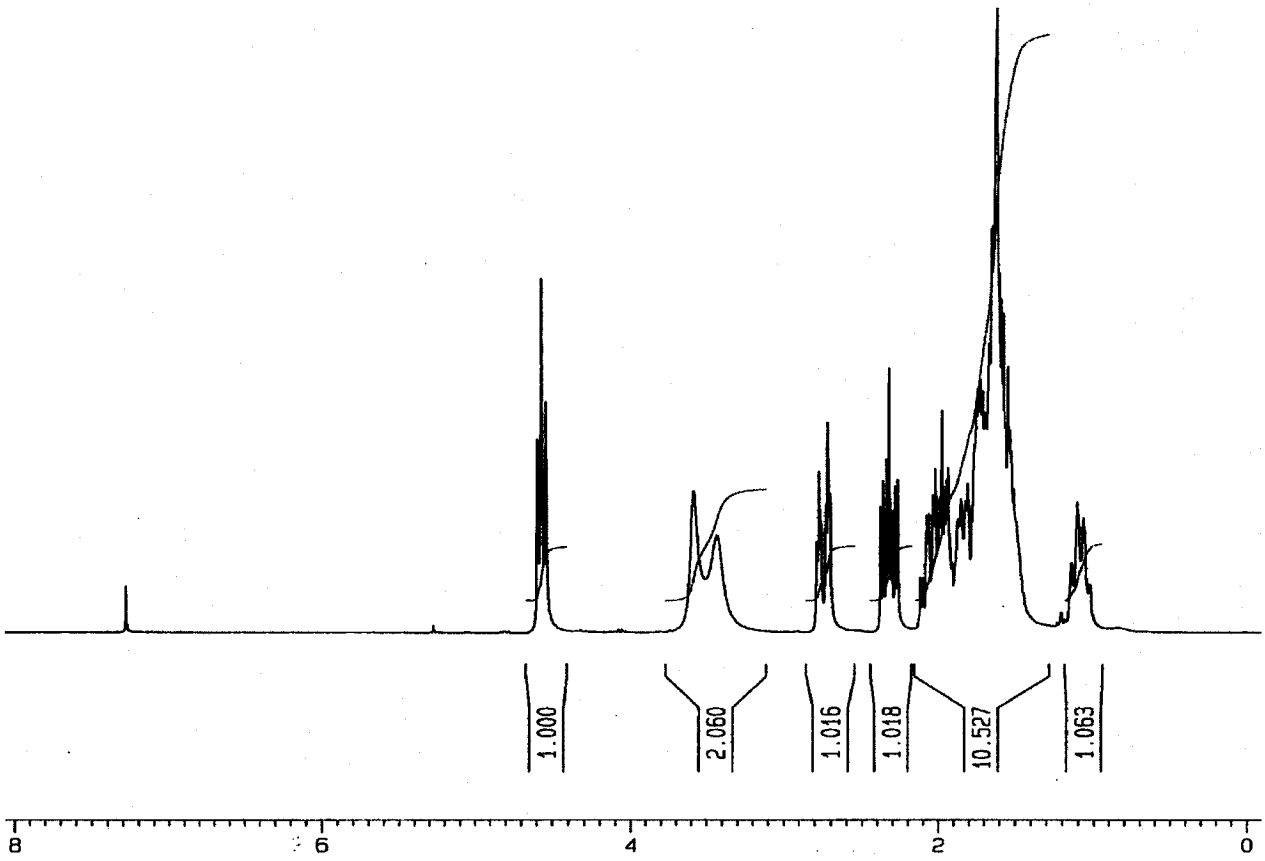
^{13}C NMR (75 MHz, $CDCl_3$)



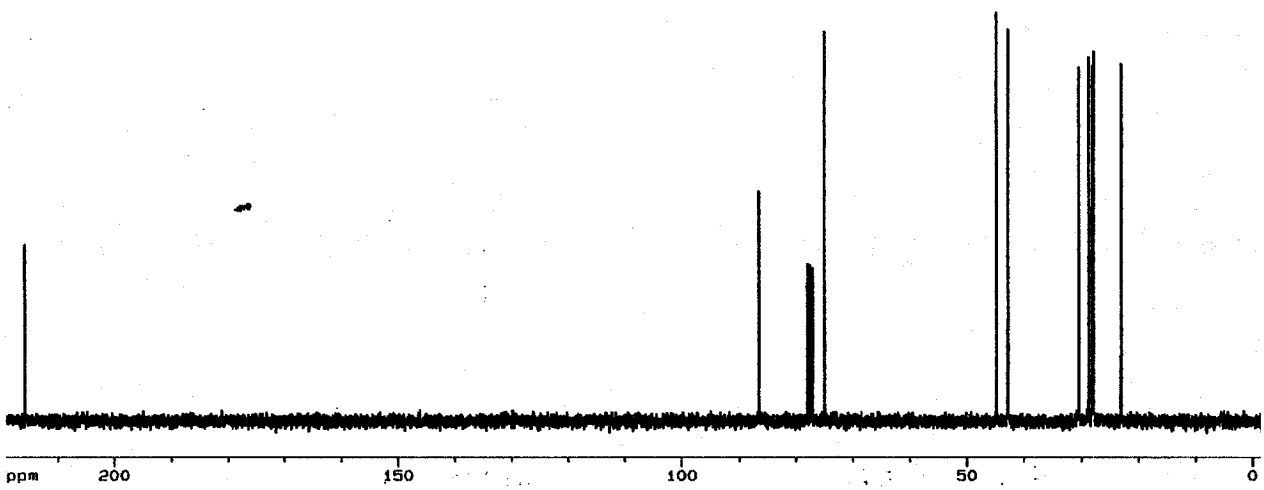


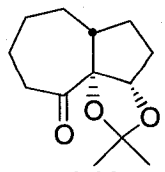
3.38

^{1}H NMR (300 MHz, $CDCl_3$)



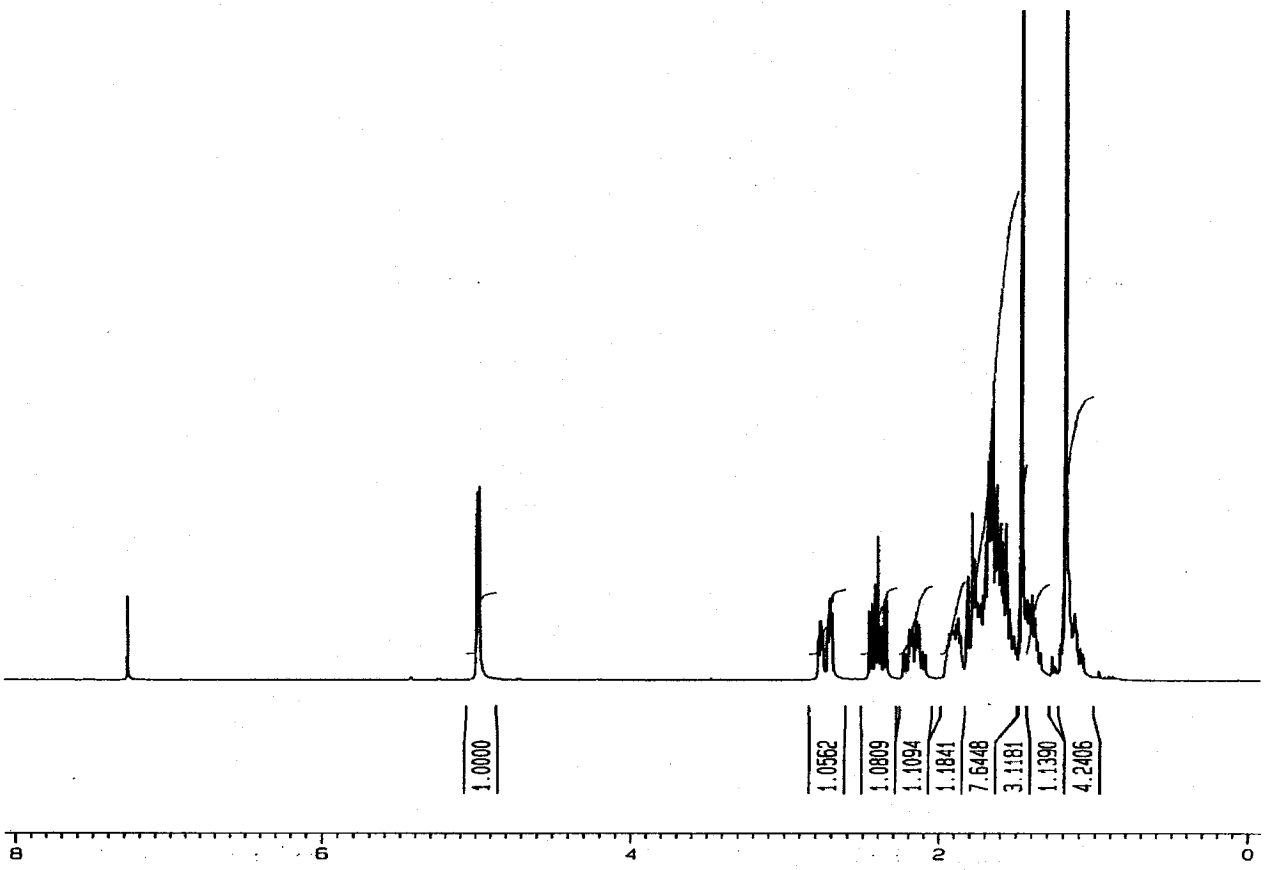
^{13}C NMR (75 MHz, $CDCl_3$)



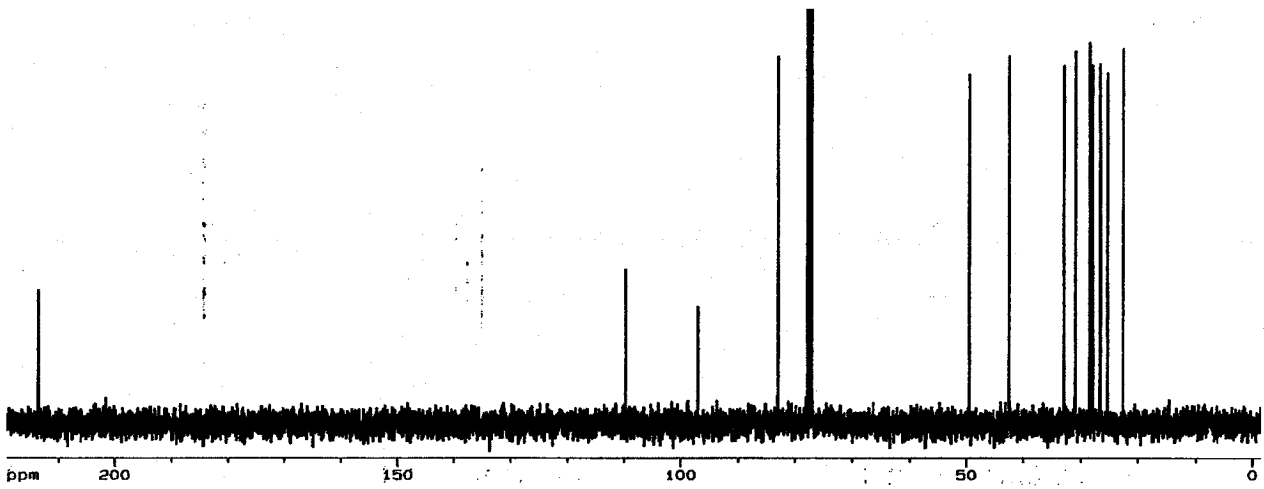


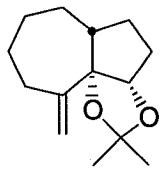
3.39

^{1}H NMR (300 MHz, $CDCl_3$)



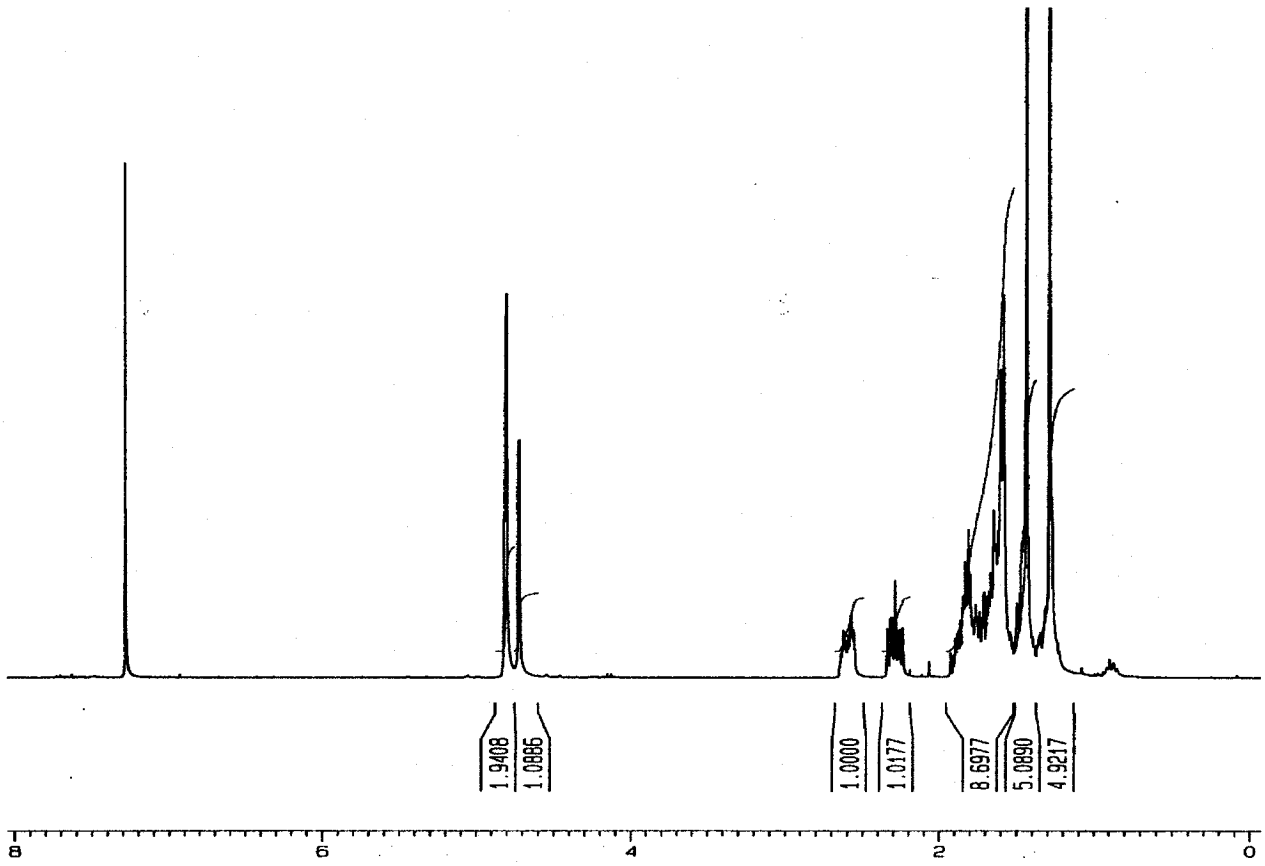
^{13}C NMR (75 MHz, $CDCl_3$)



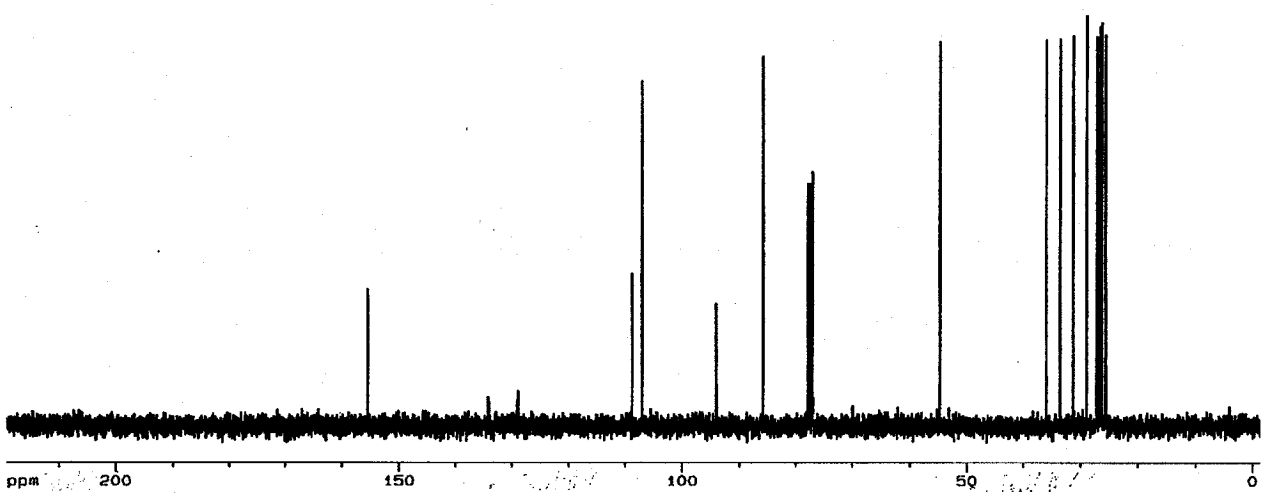


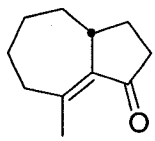
3.40

^{1}H NMR (300 MHz, $CDCl_3$)



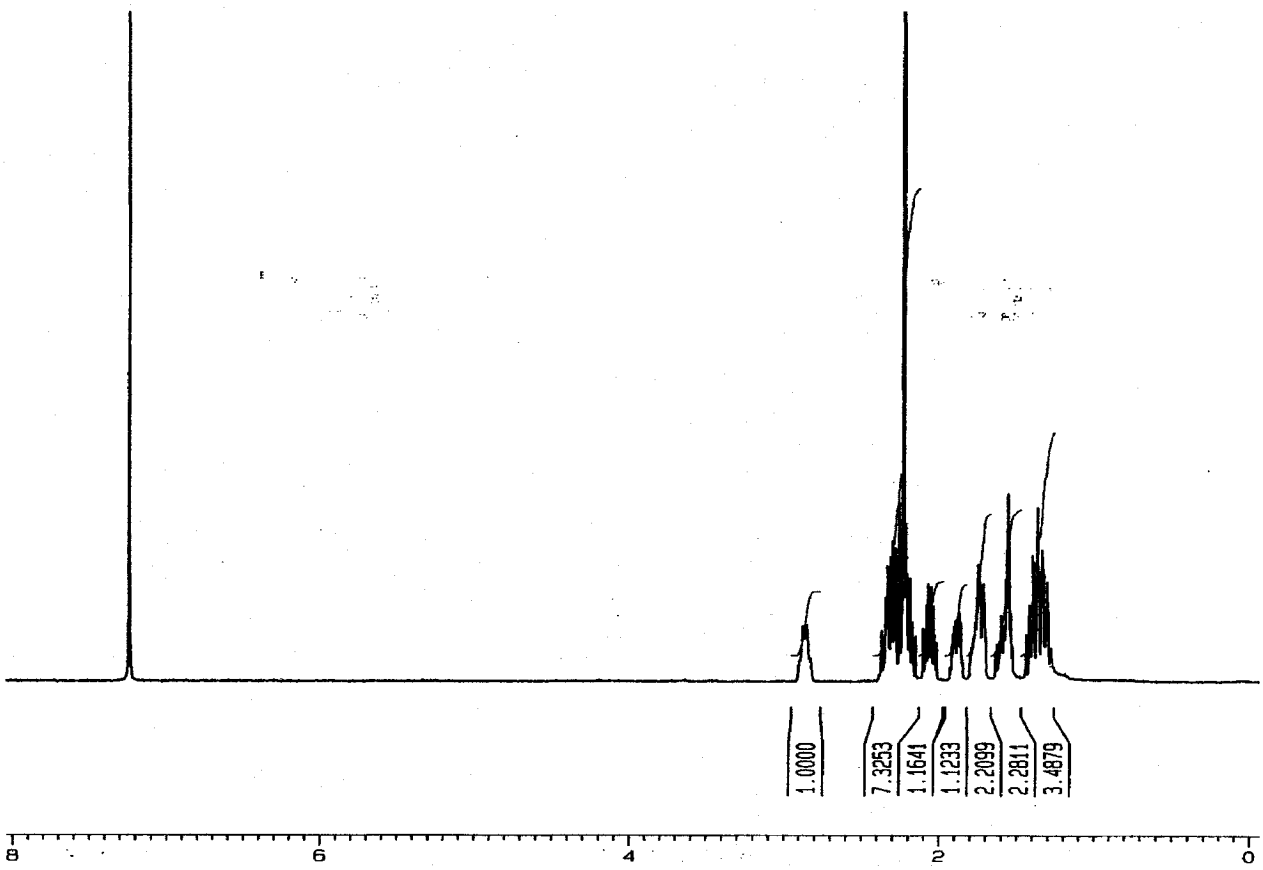
^{13}C NMR (75 MHz, $CDCl_3$)



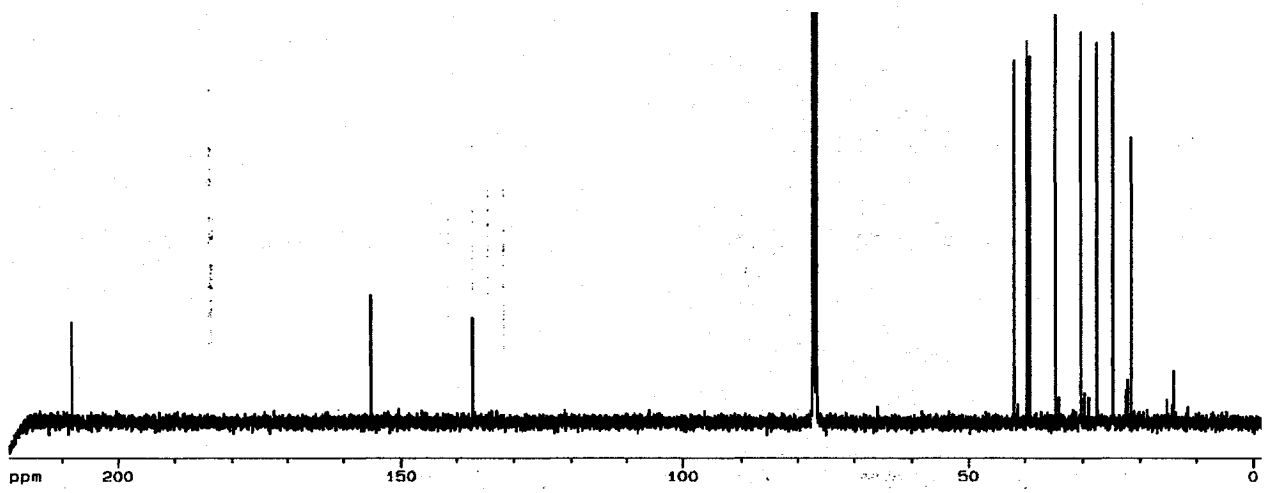


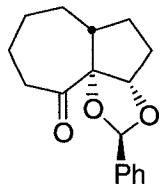
3.41

^{1}H NMR (400 MHz, $CDCl_3$)



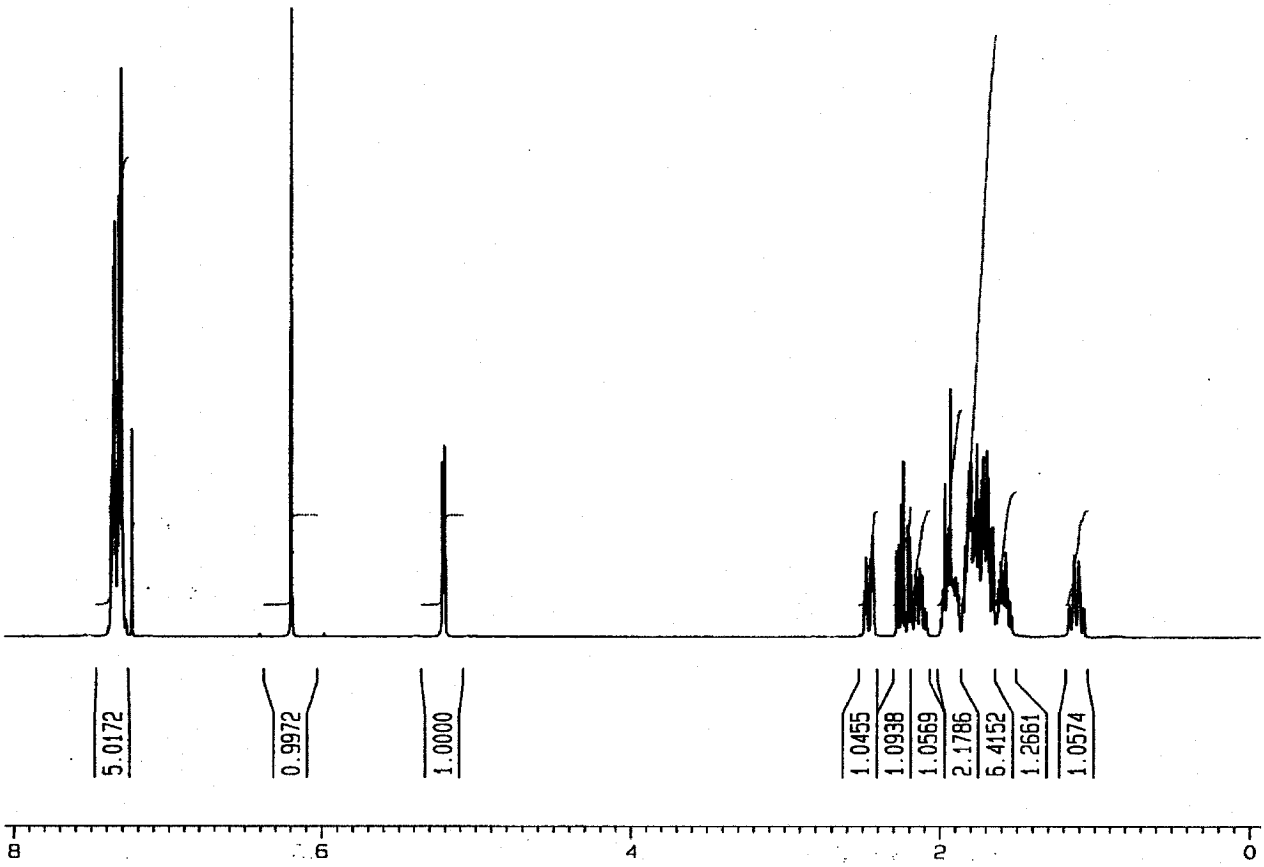
^{13}C NMR (100 MHz, $CDCl_3$)



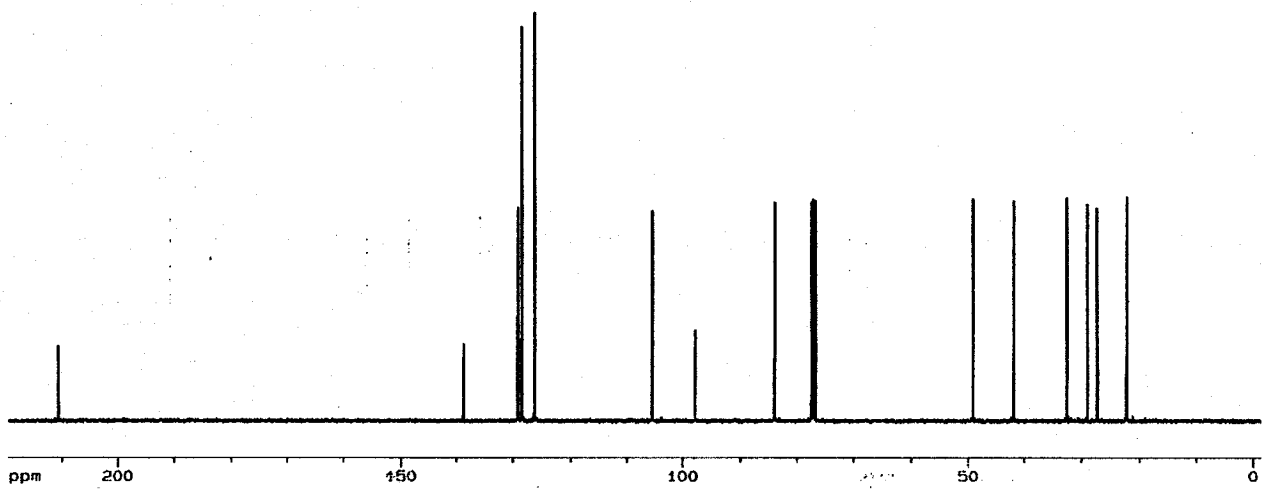


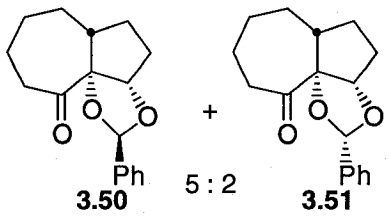
3.50

^{1}H NMR (400 MHz, $CDCl_3$)

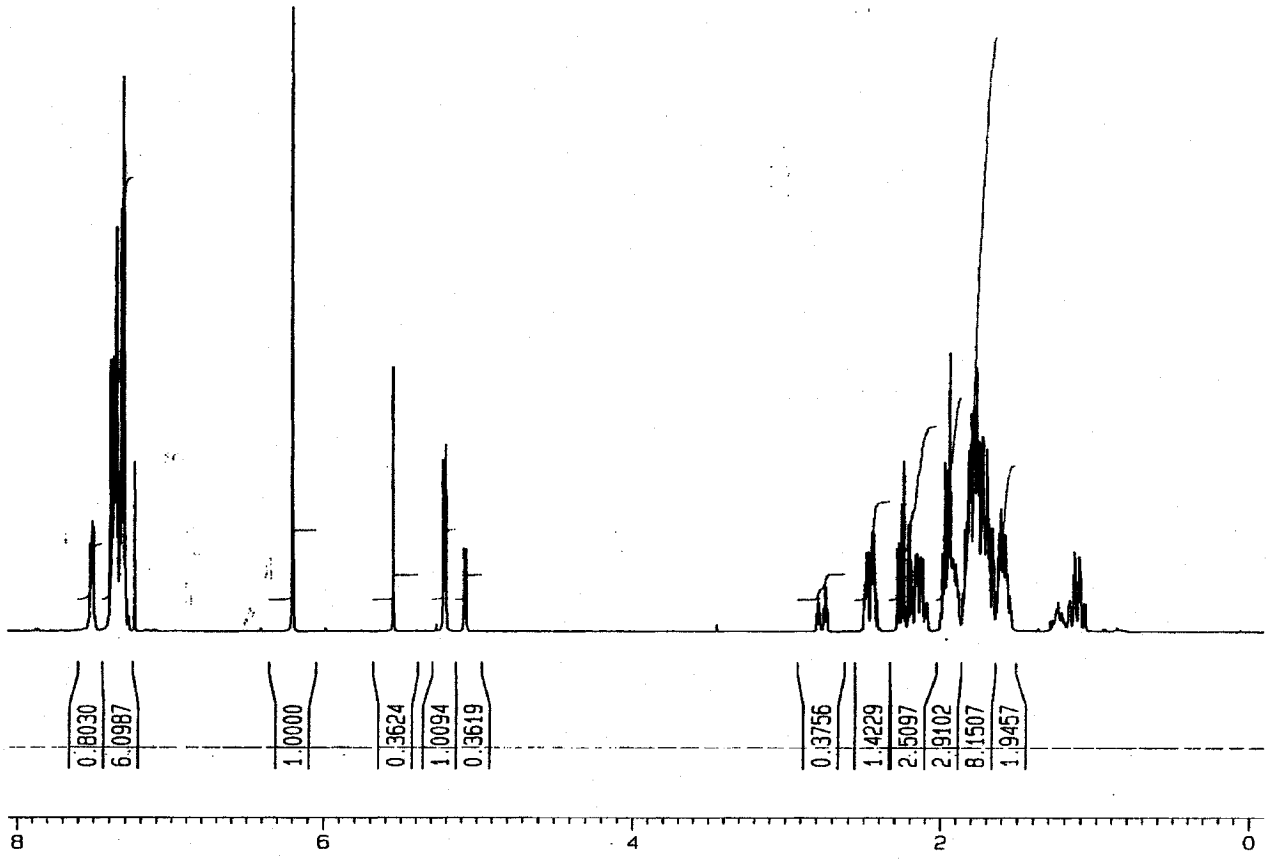


^{13}C NMR (100 MHz, $CDCl_3$)

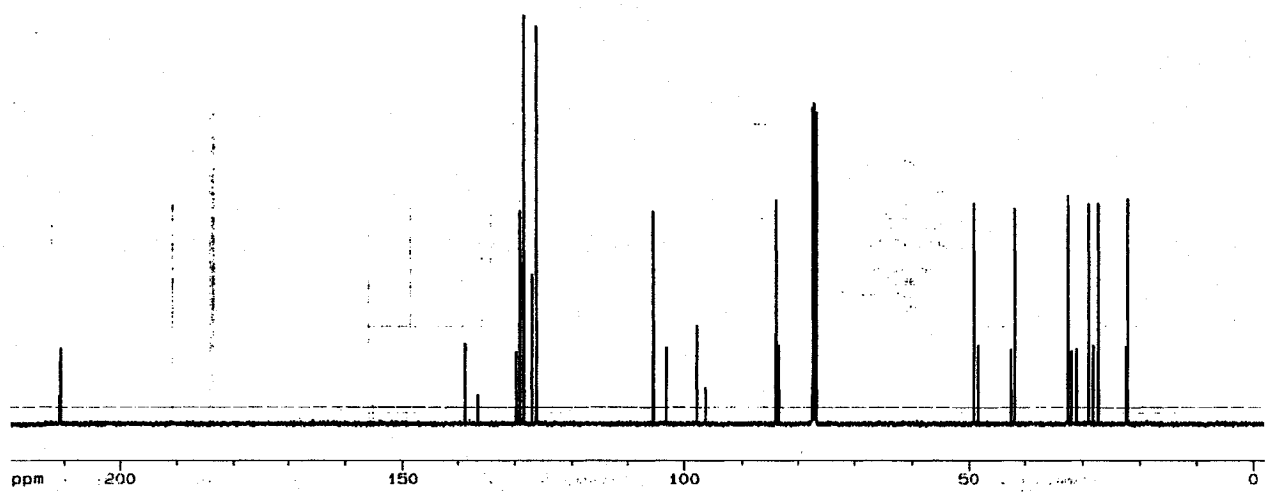


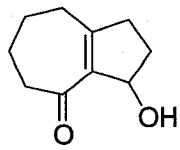


^{1}H NMR (400 MHz, $CDCl_3$)



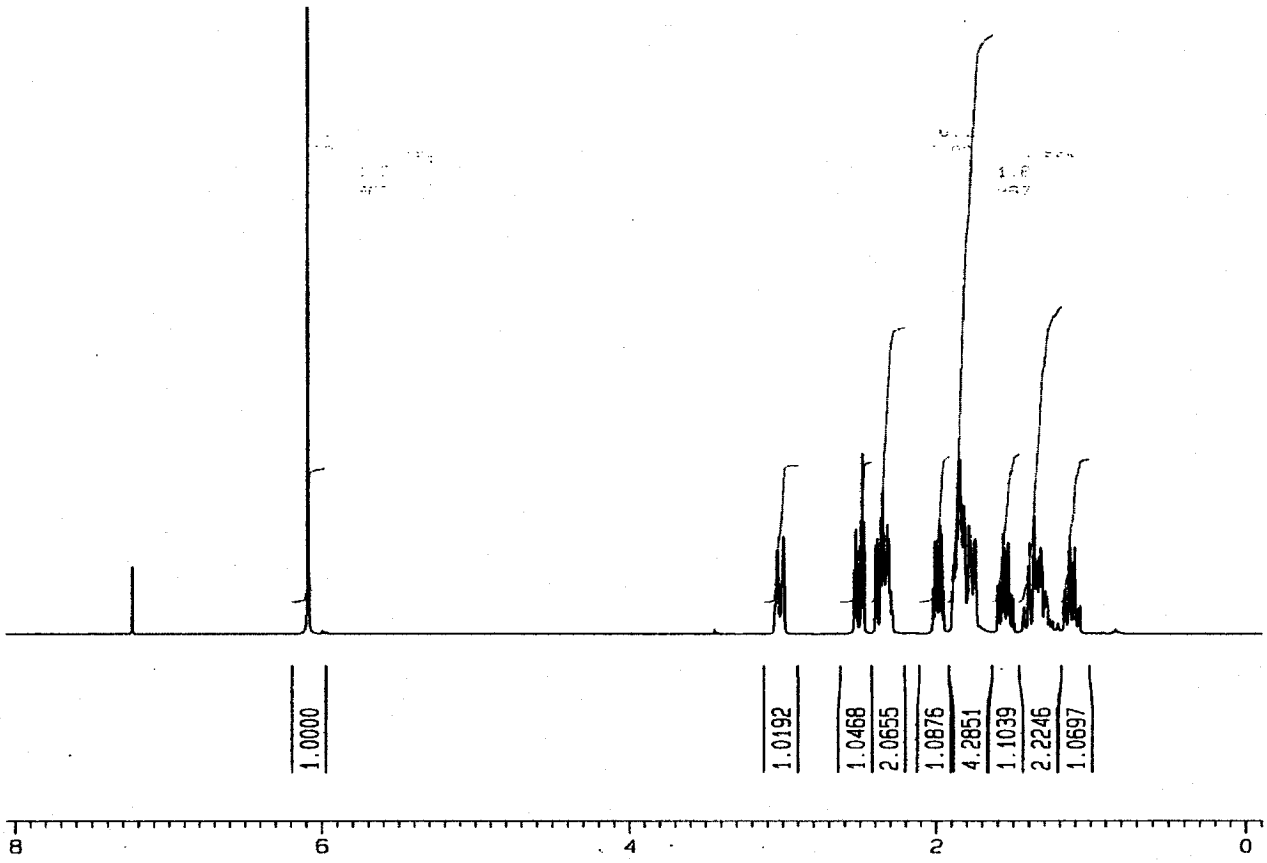
^{13}C NMR (100 MHz, $CDCl_3$)



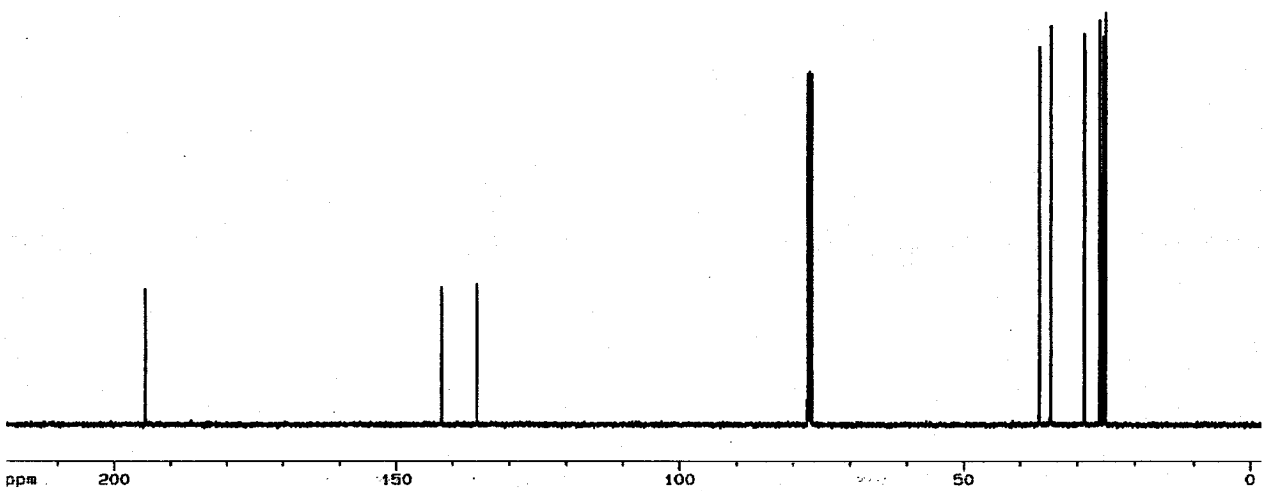


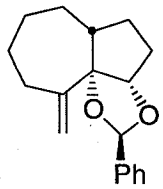
3.52

^{1}H NMR (400 MHz, $CDCl_3$)



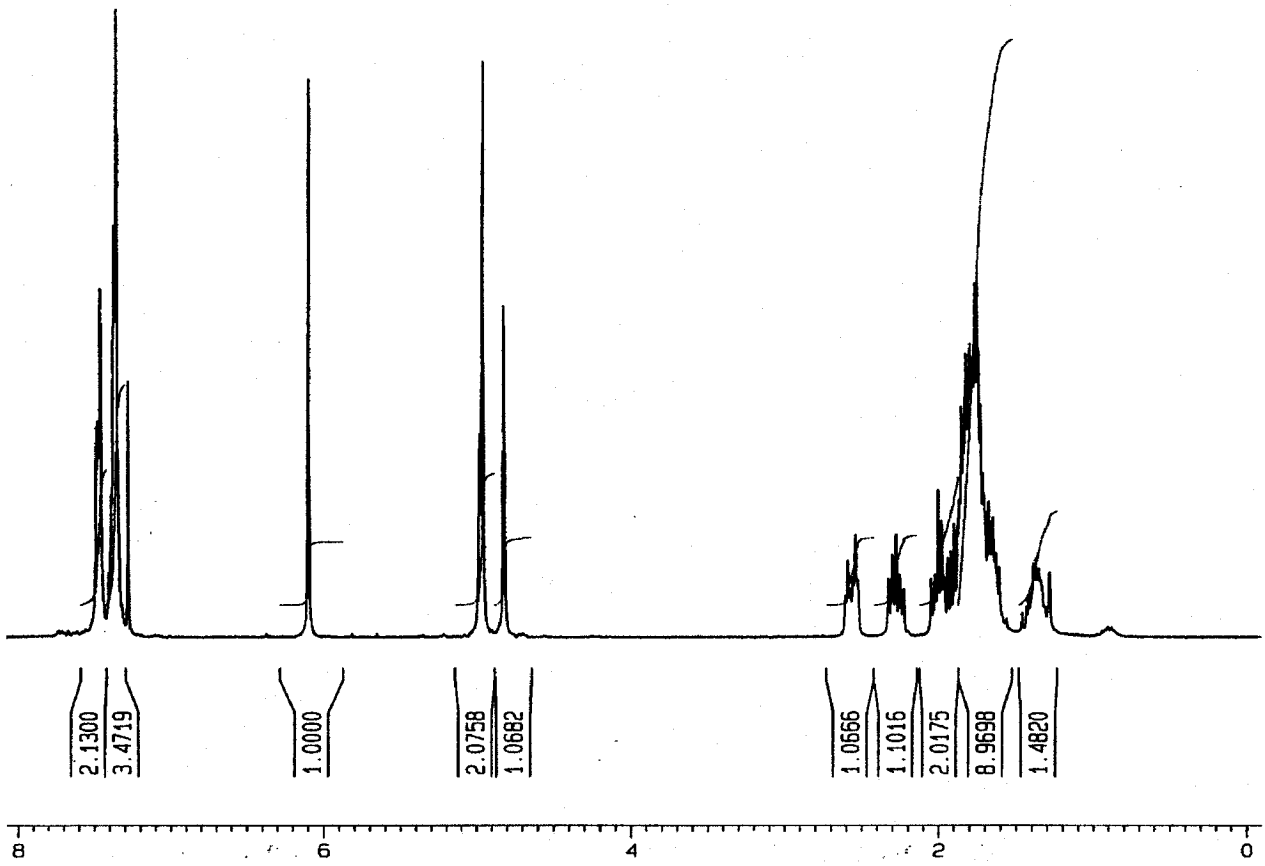
^{13}C NMR (100 MHz, $CDCl_3$)



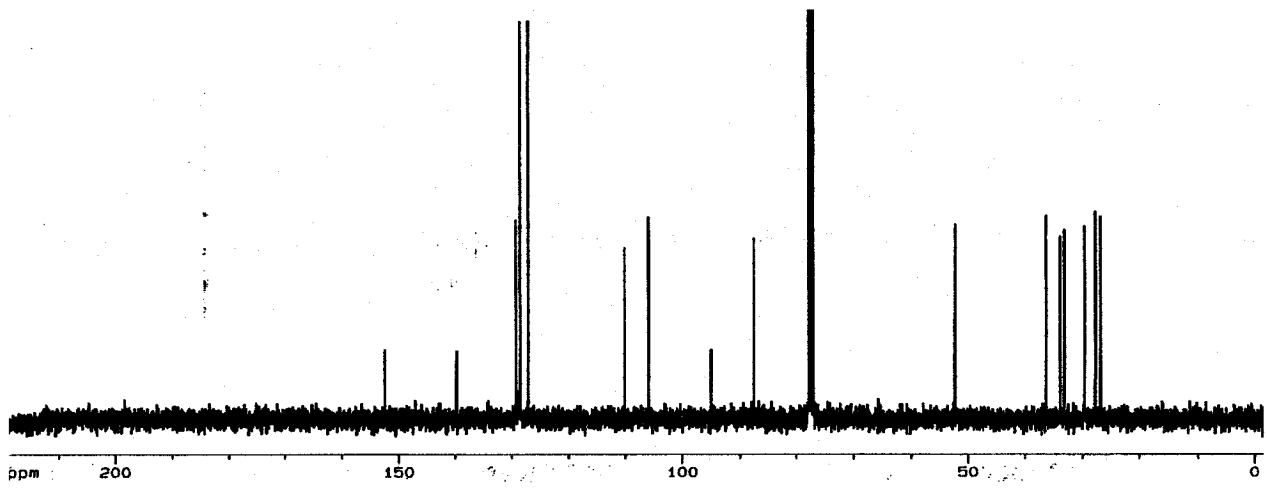


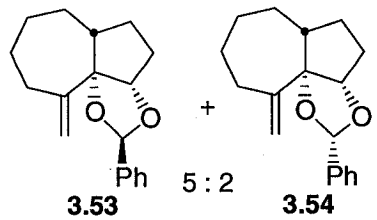
3.53

^{1}H NMR (300 MHz, $CDCl_3$)



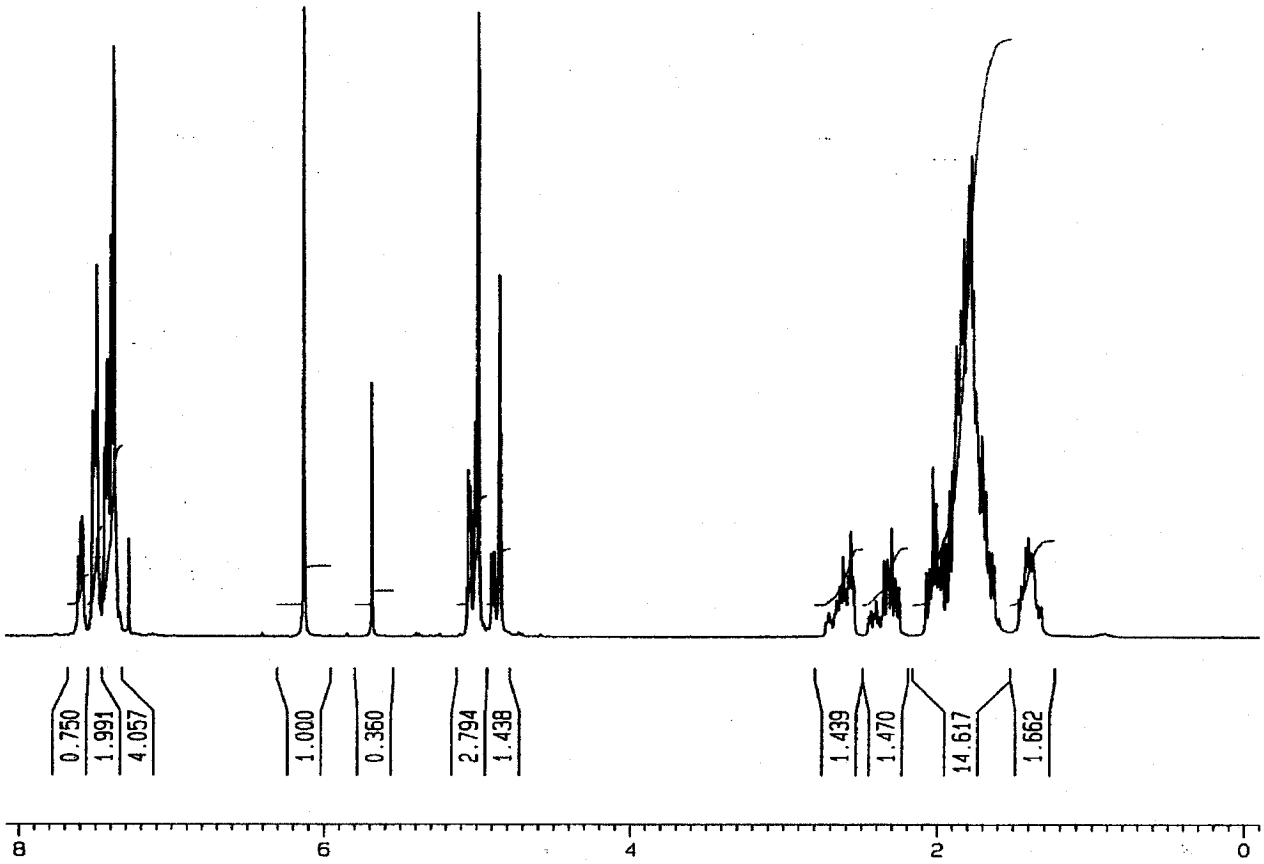
^{13}C NMR (75 MHz, $CDCl_3$)



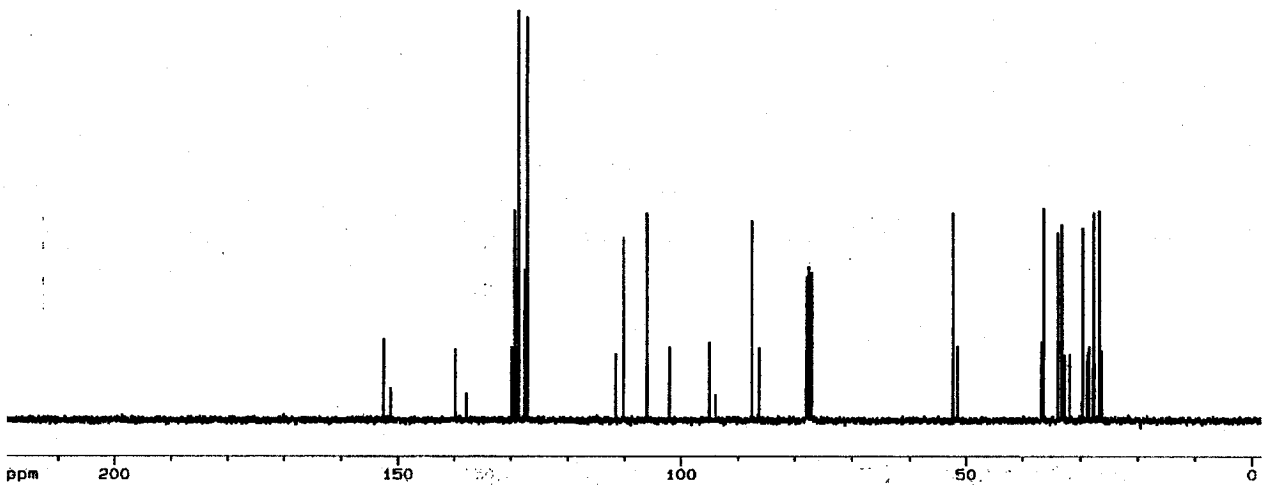


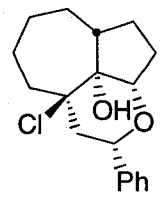
3.53 **3.54**

^{1}H NMR (300 MHz, $CDCl_3$)



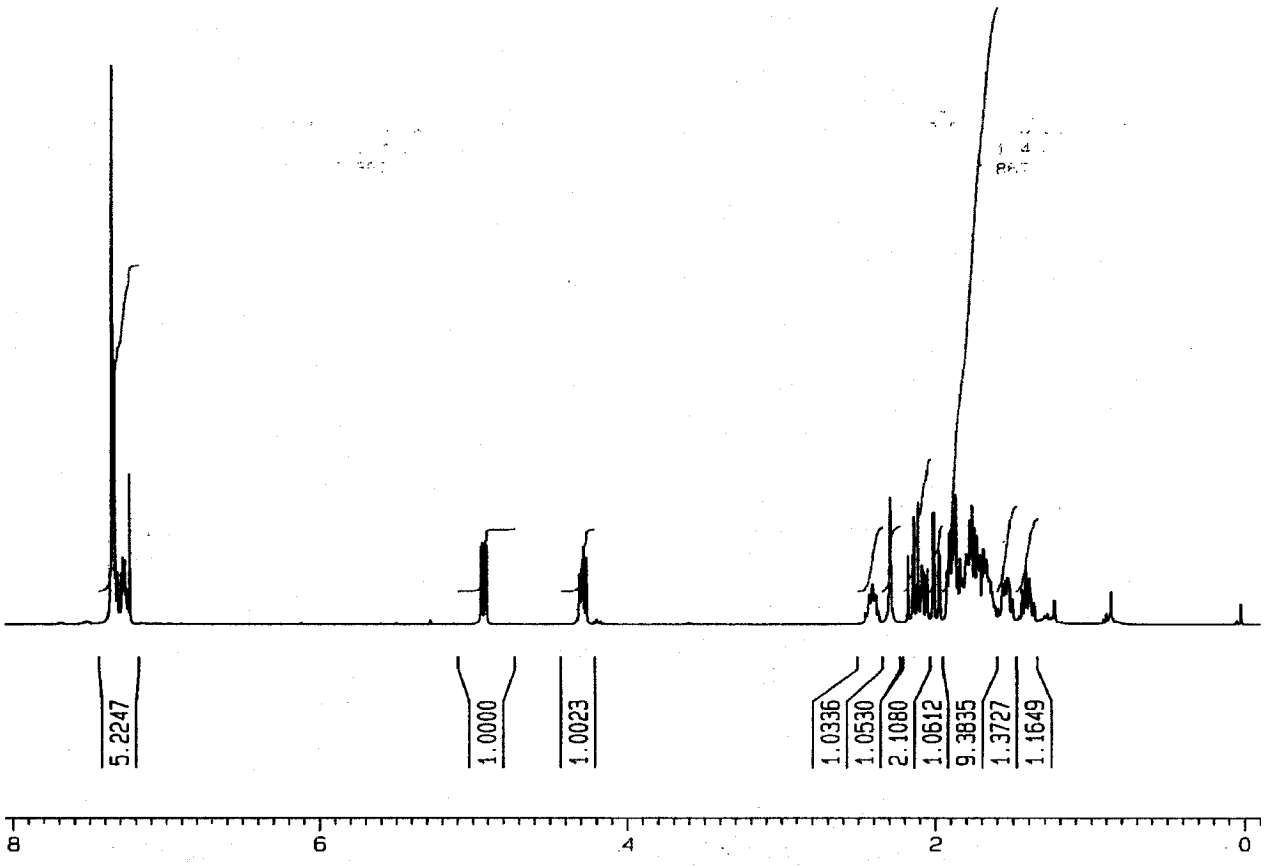
^{13}C NMR (75 MHz, $CDCl_3$)



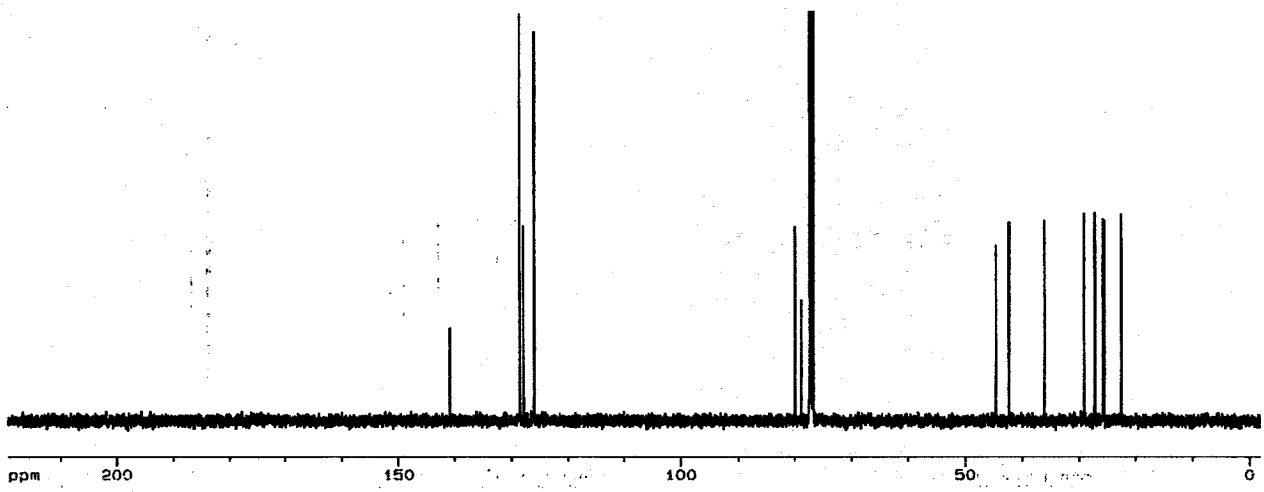


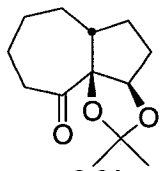
3.55

^{1}H NMR (400 MHz, $CDCl_3$)



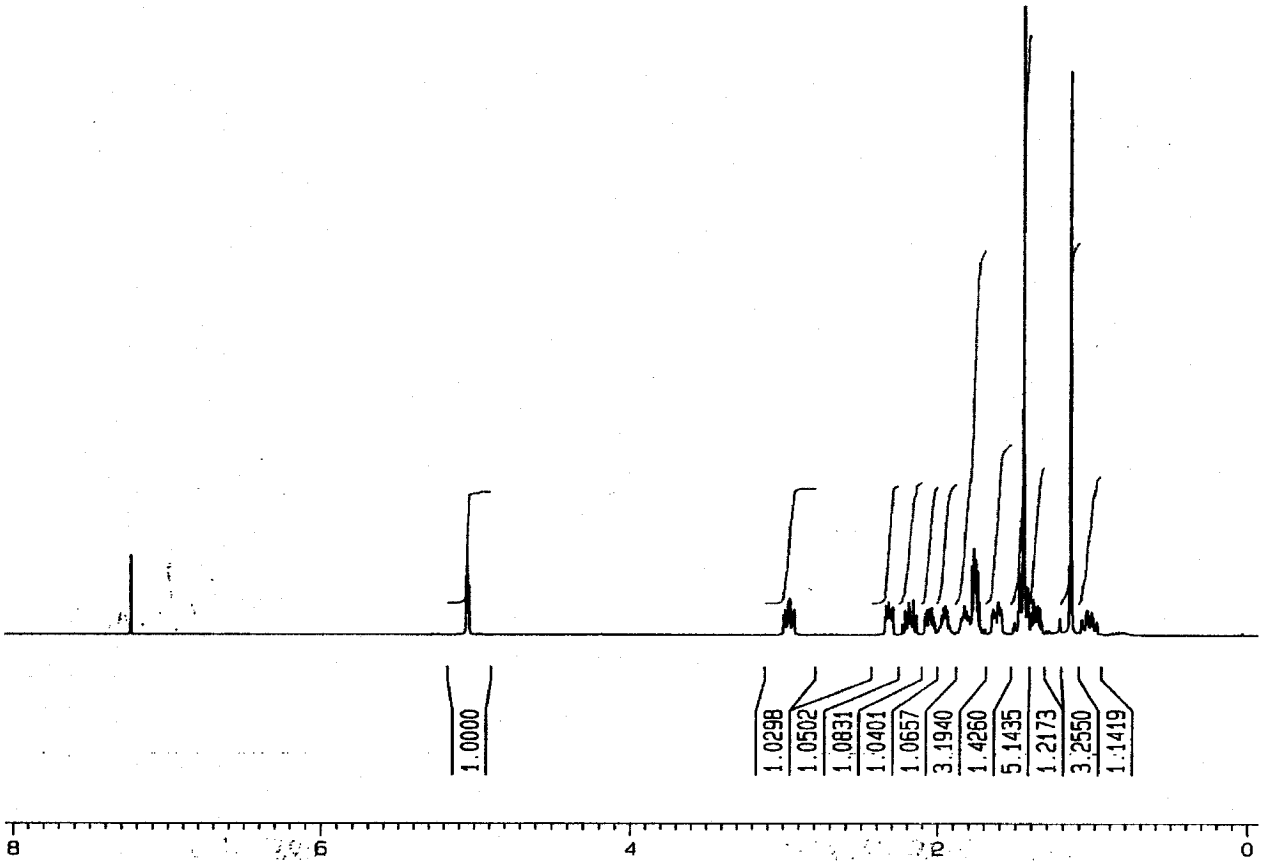
^{13}C NMR (100 MHz, $CDCl_3$)



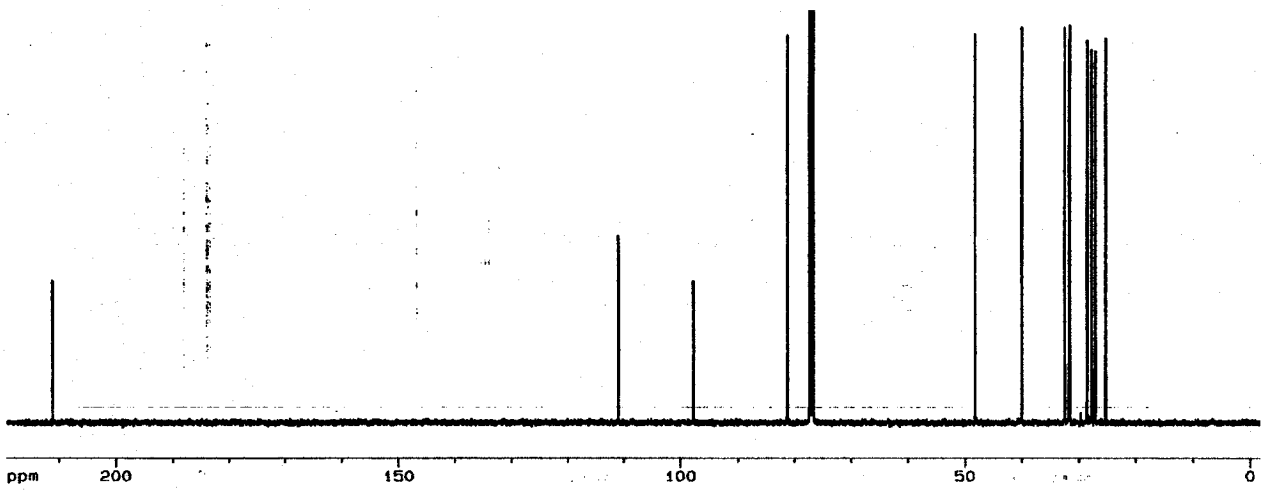


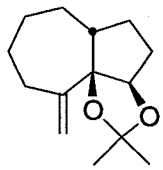
3.61

^{1}H NMR (400 MHz, $CDCl_3$)



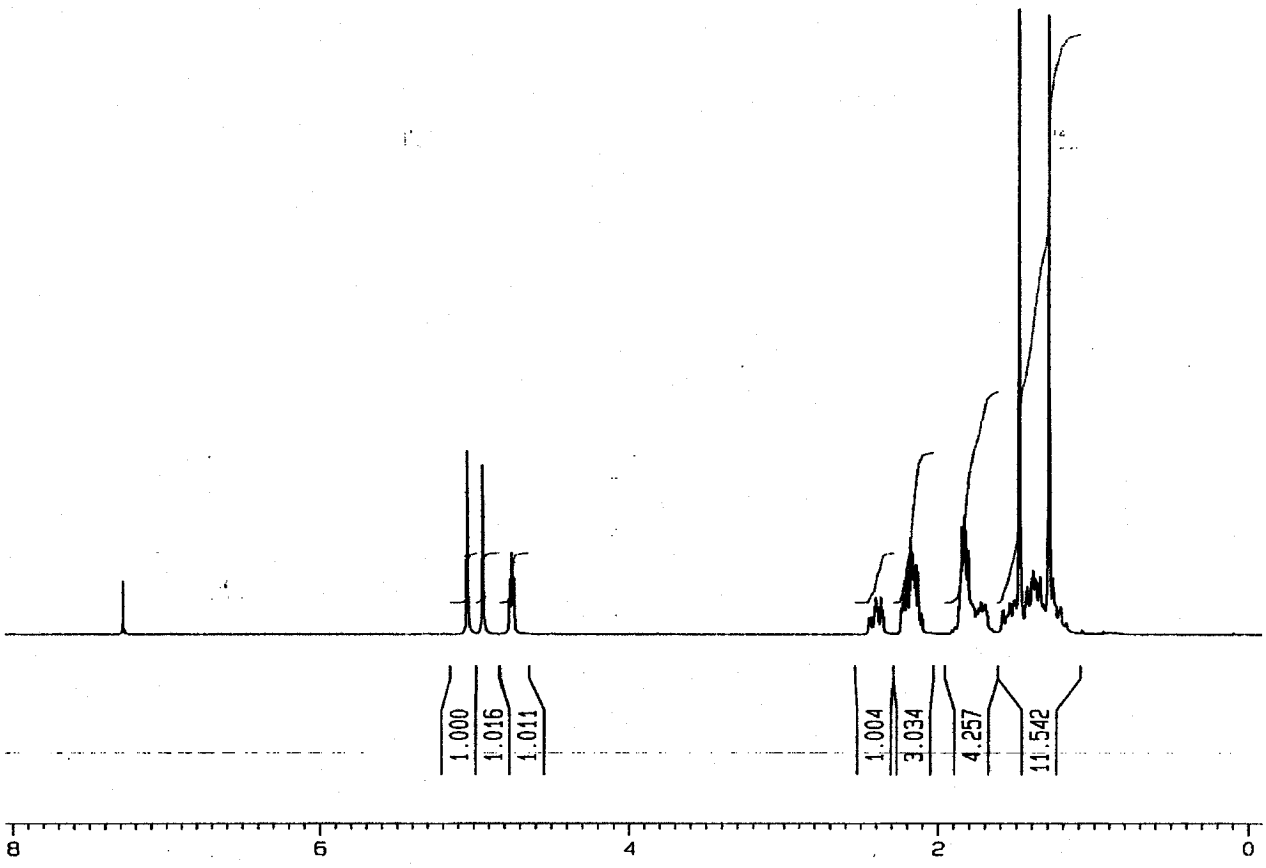
^{13}C NMR (100 MHz, $CDCl_3$)



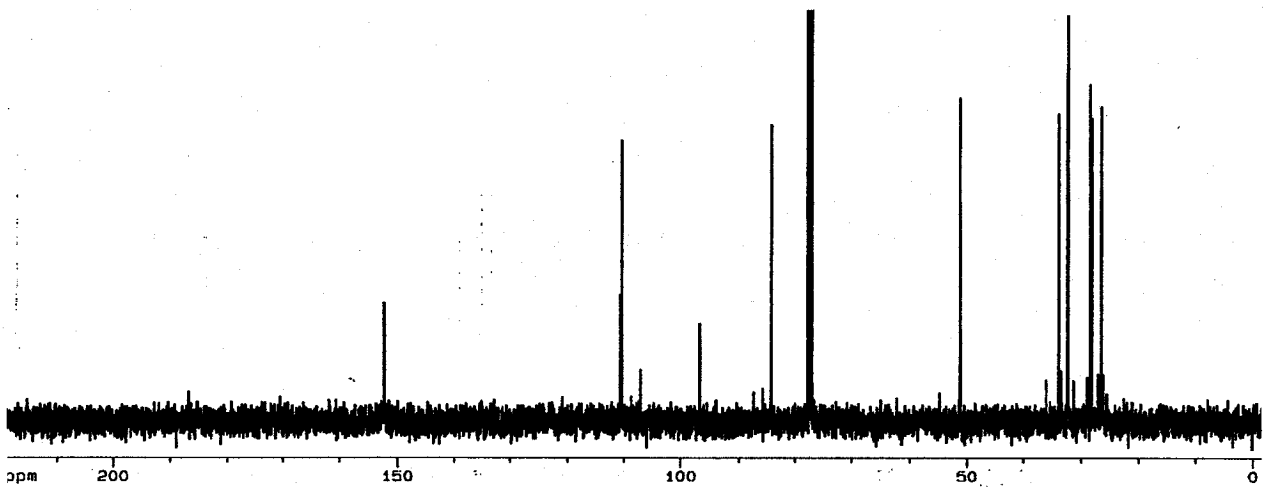


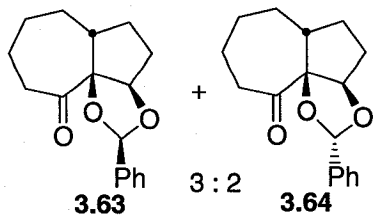
3.62

^{1}H NMR (300 MHz, $CDCl_3$)



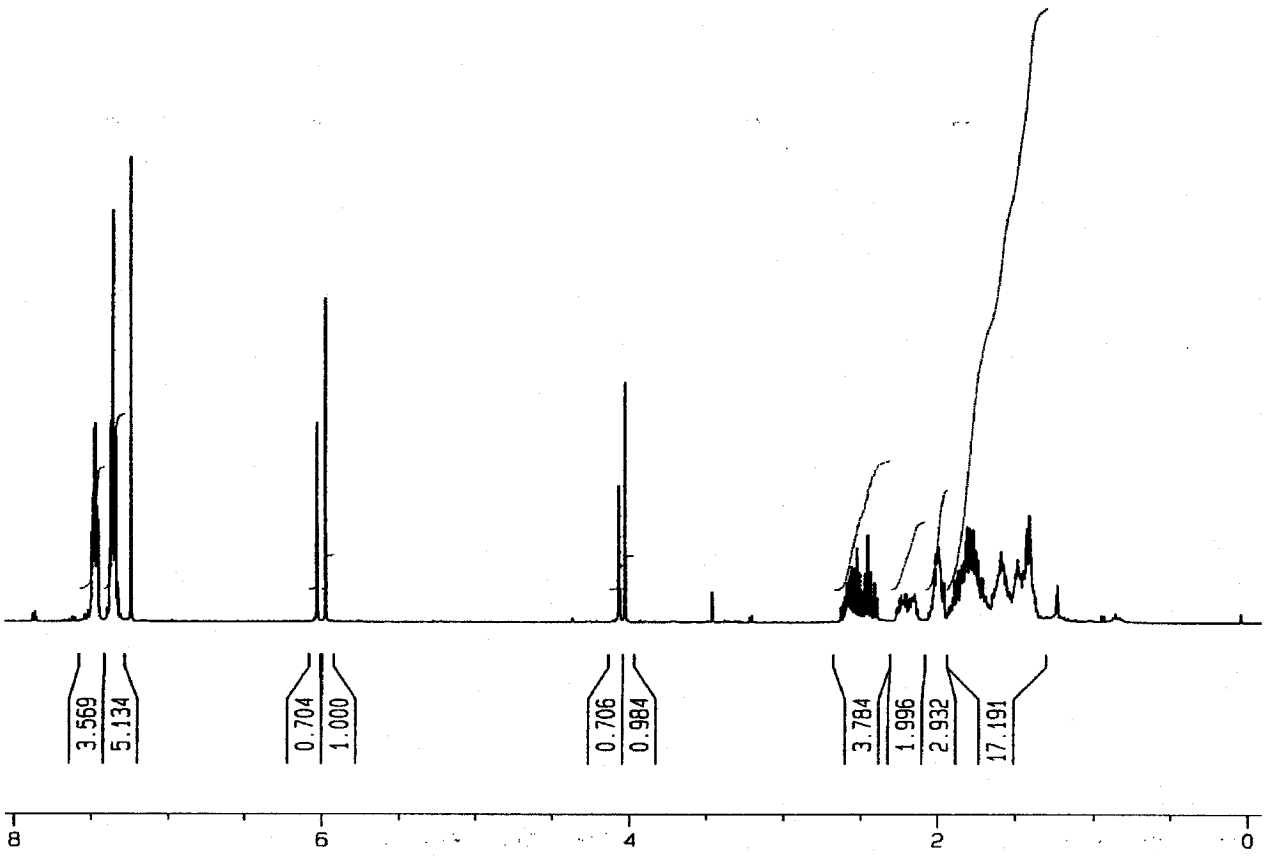
^{13}C NMR (75 MHz, $CDCl_3$)



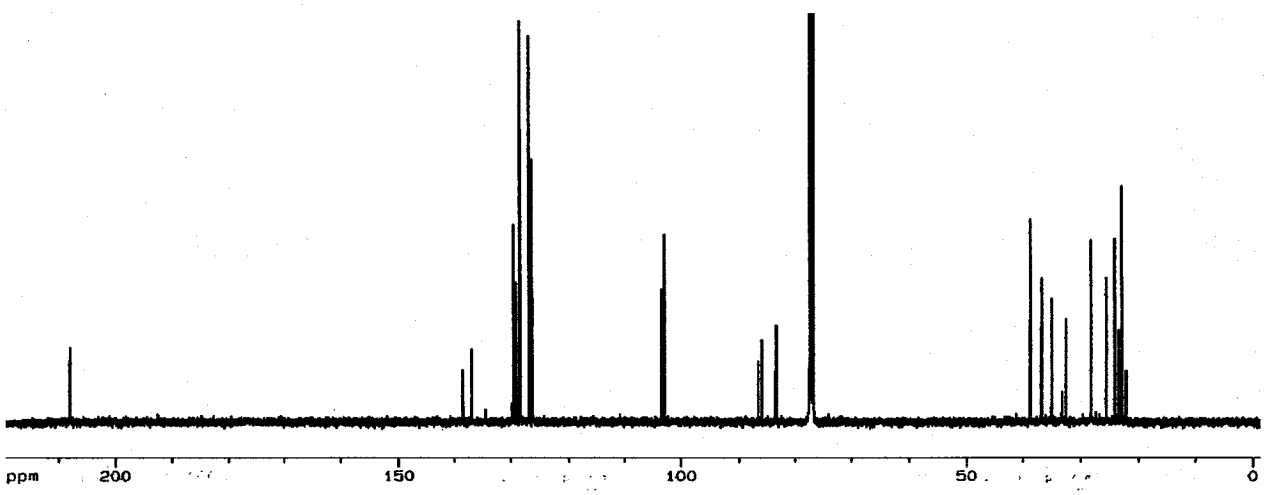


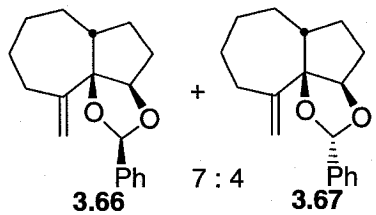
3.63 **3.64**

^{1}H NMR (400 MHz, $CDCl_3$)



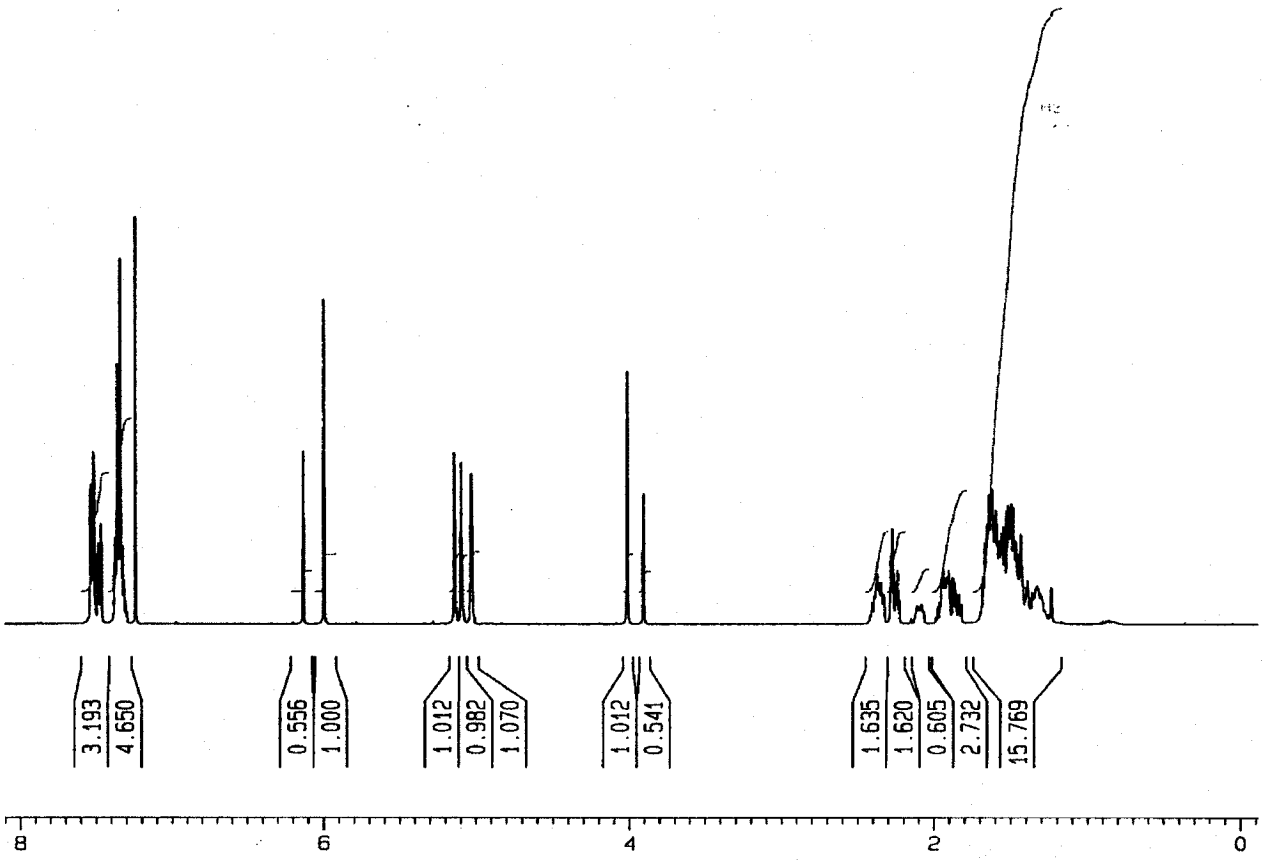
^{13}C NMR (100 MHz, $CDCl_3$)



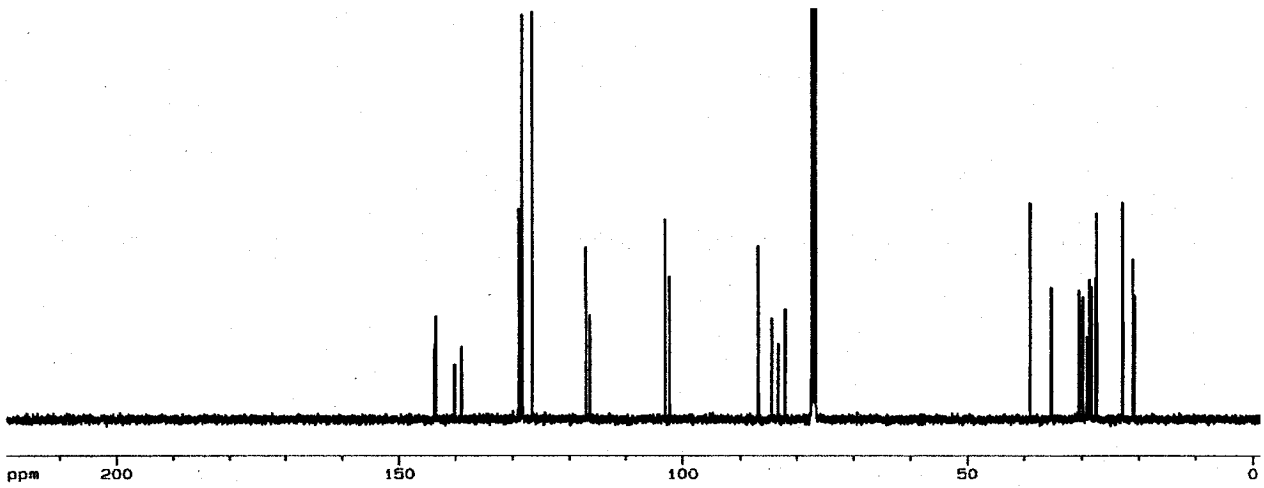


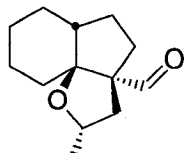
3.66 **3.67**

^{1}H NMR (300 MHz, $CDCl_3$)



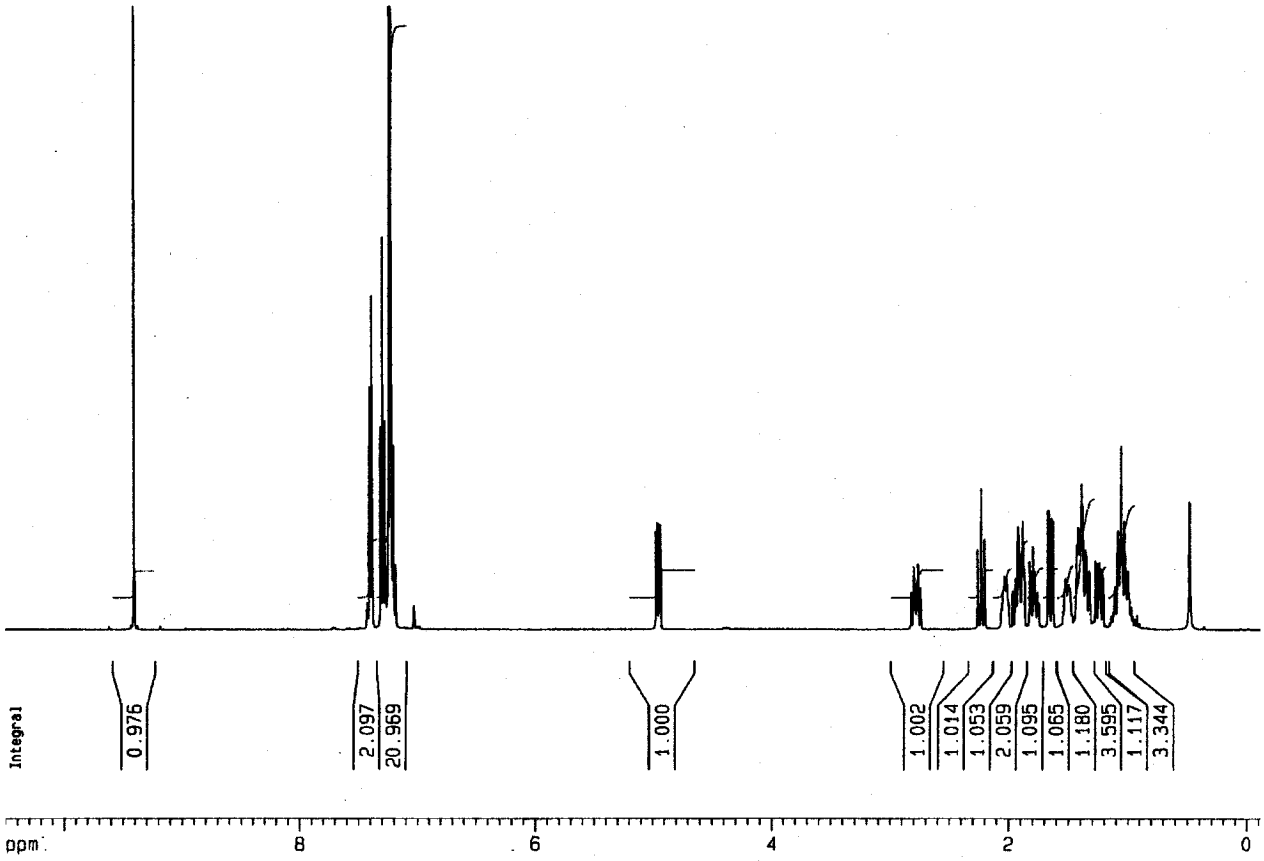
^{13}C NMR (75 MHz, $CDCl_3$)



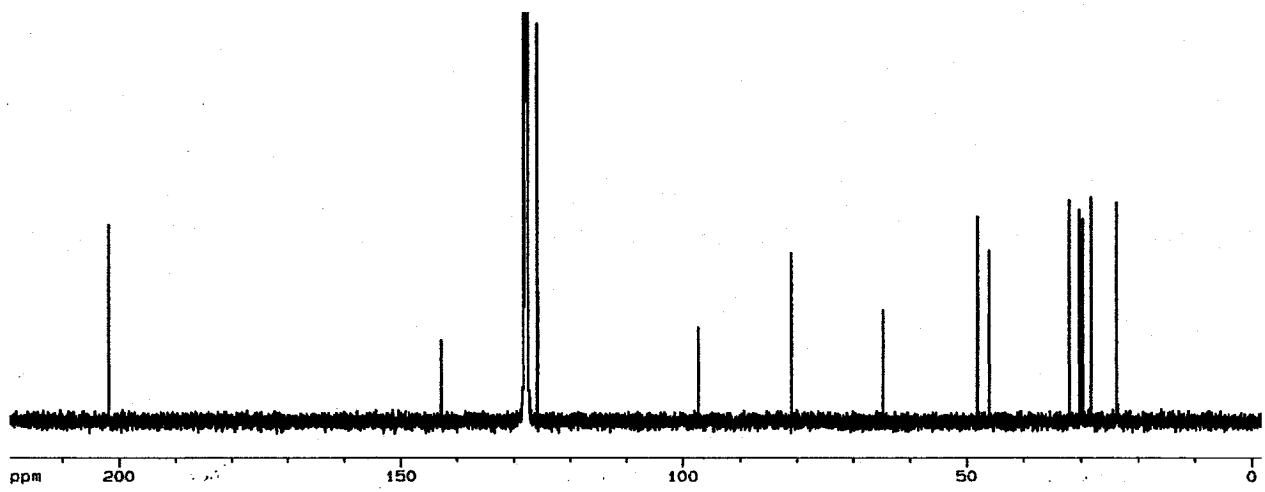


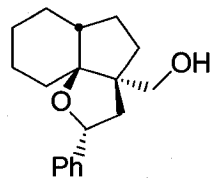
3.68

^{1}H NMR (400 MHz, C_6D_6)



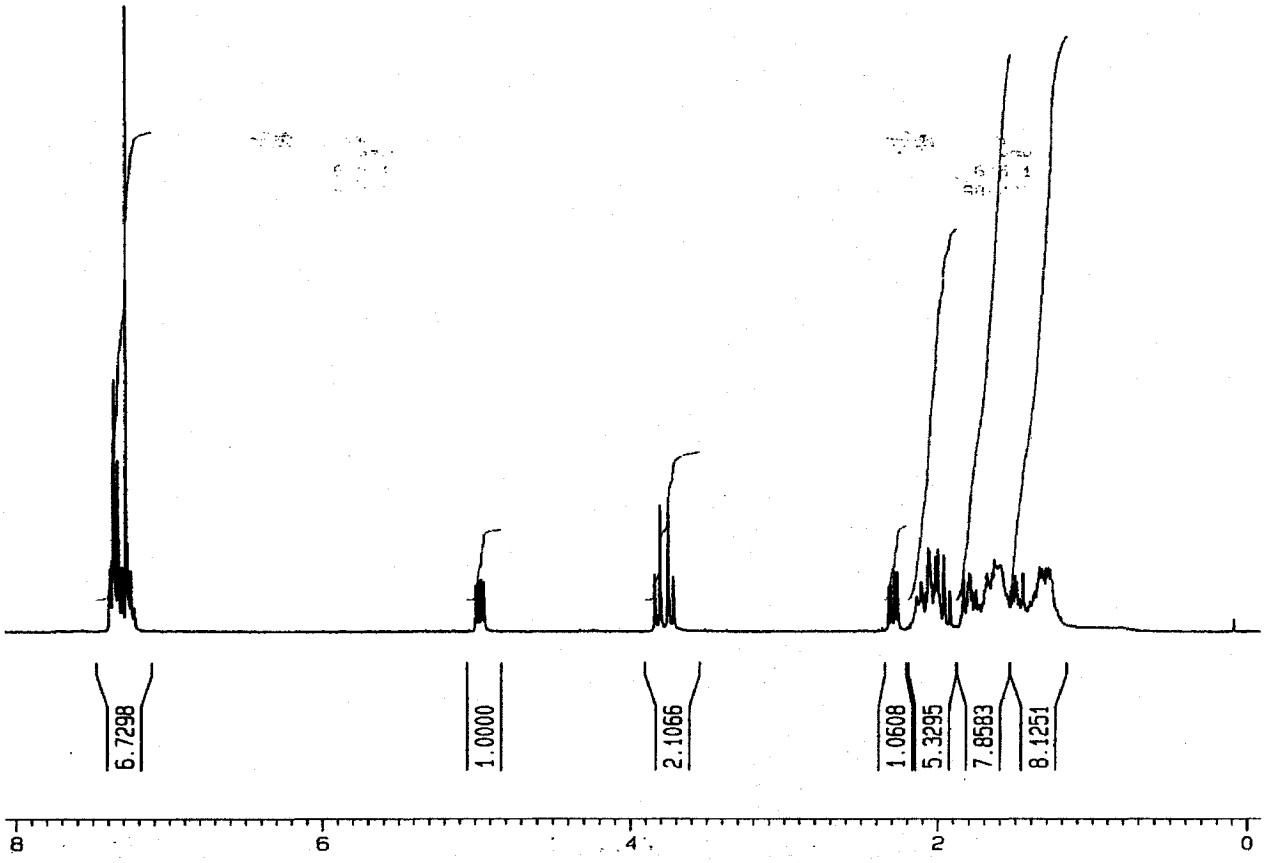
^{13}C NMR (100 MHz, C_6D_6)



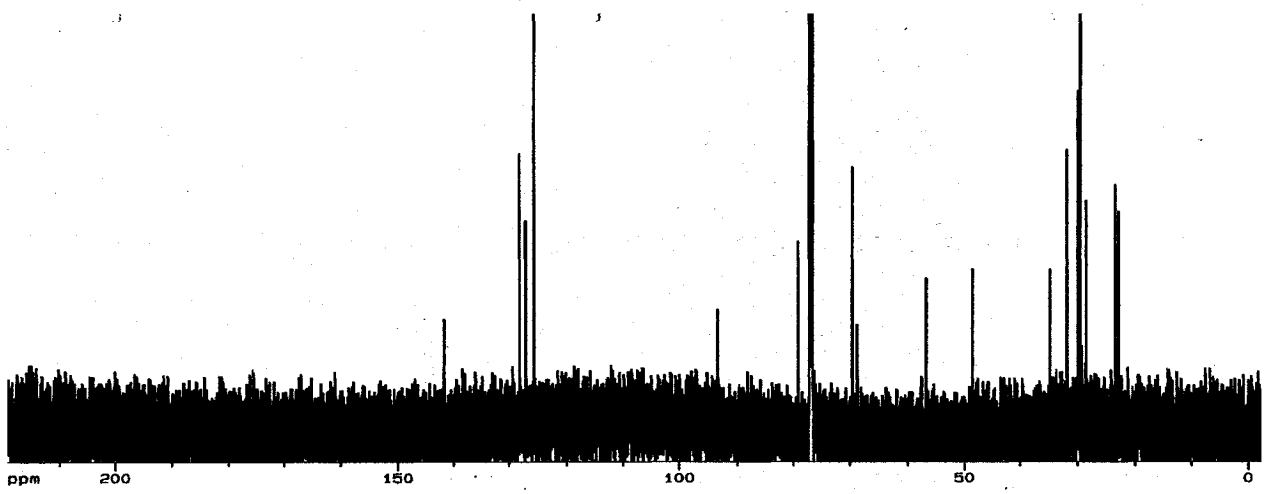


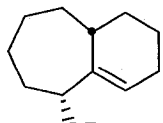
3.69

^{1}H NMR (300 MHz, $CDCl_3$)



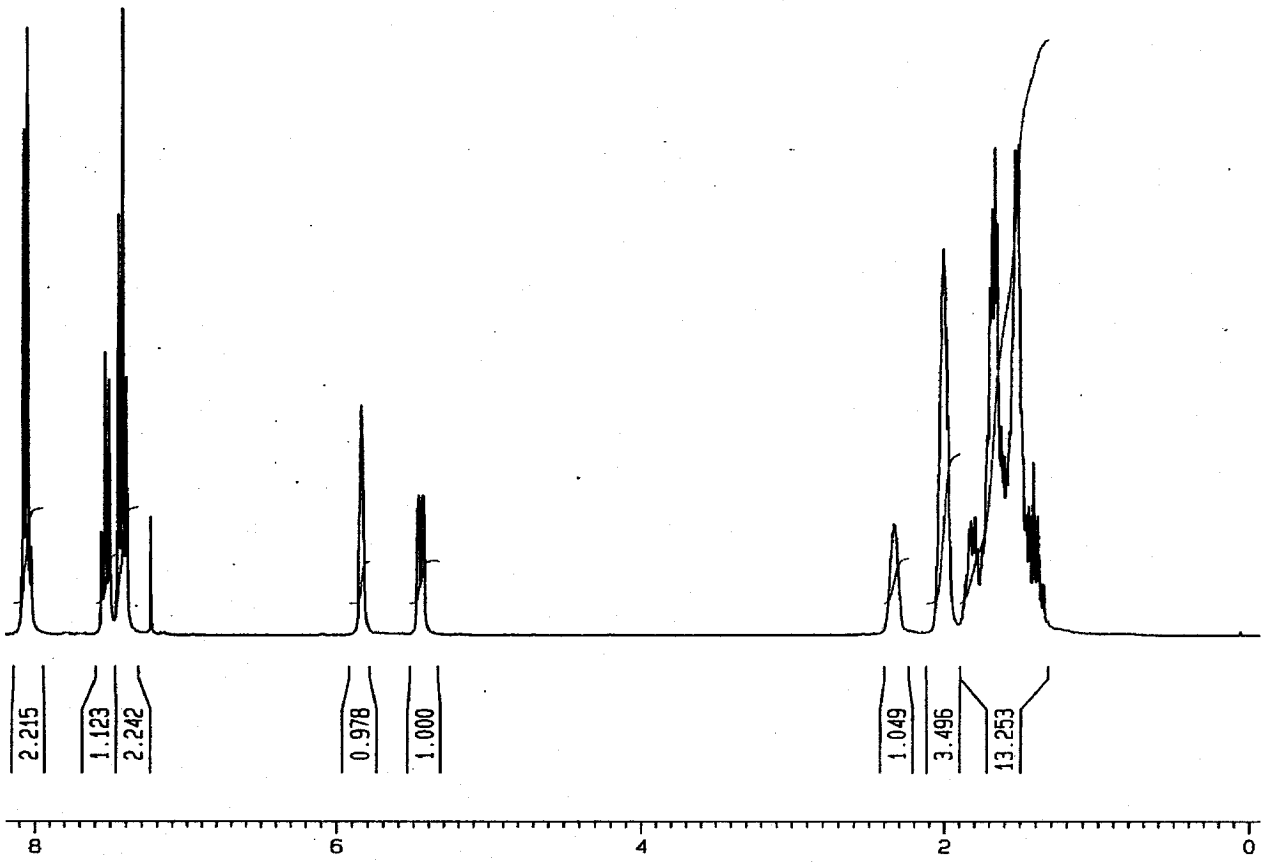
^{13}C NMR (125 MHz, $CDCl_3$)



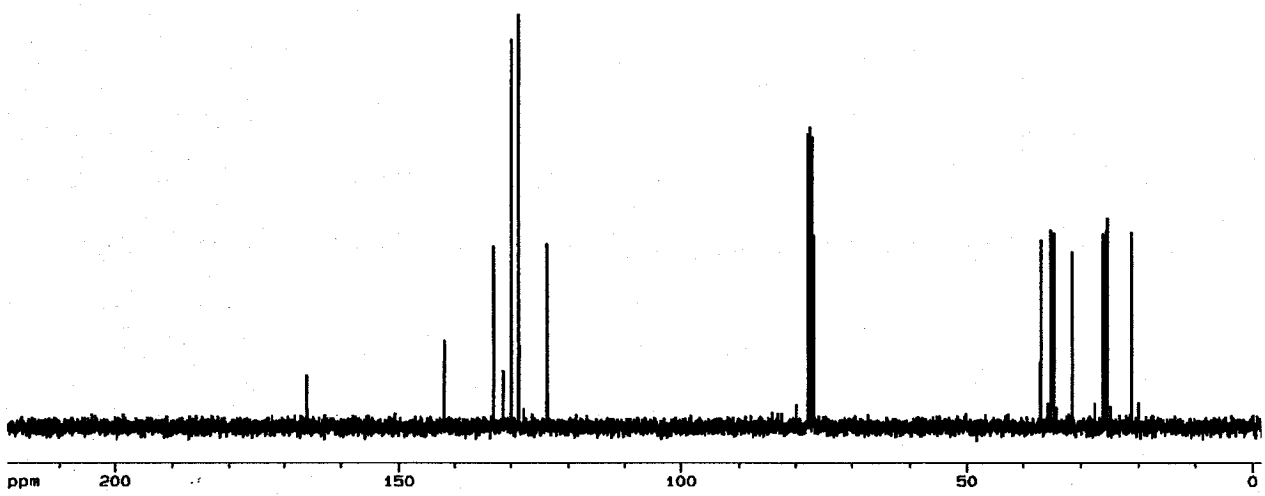


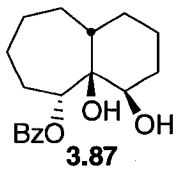
3.86

^{1}H NMR (300 MHz, $CDCl_3$)



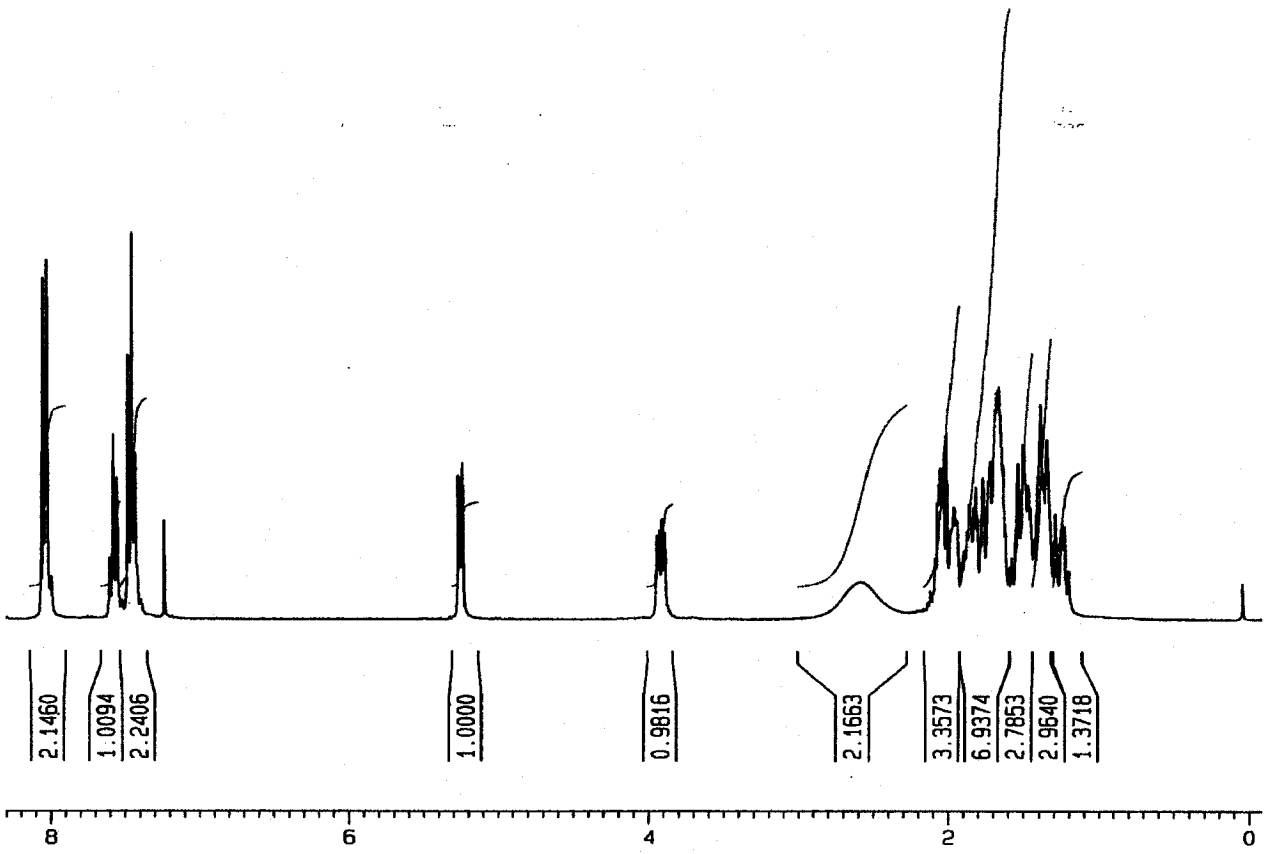
^{13}C NMR (75 MHz, $CDCl_3$)



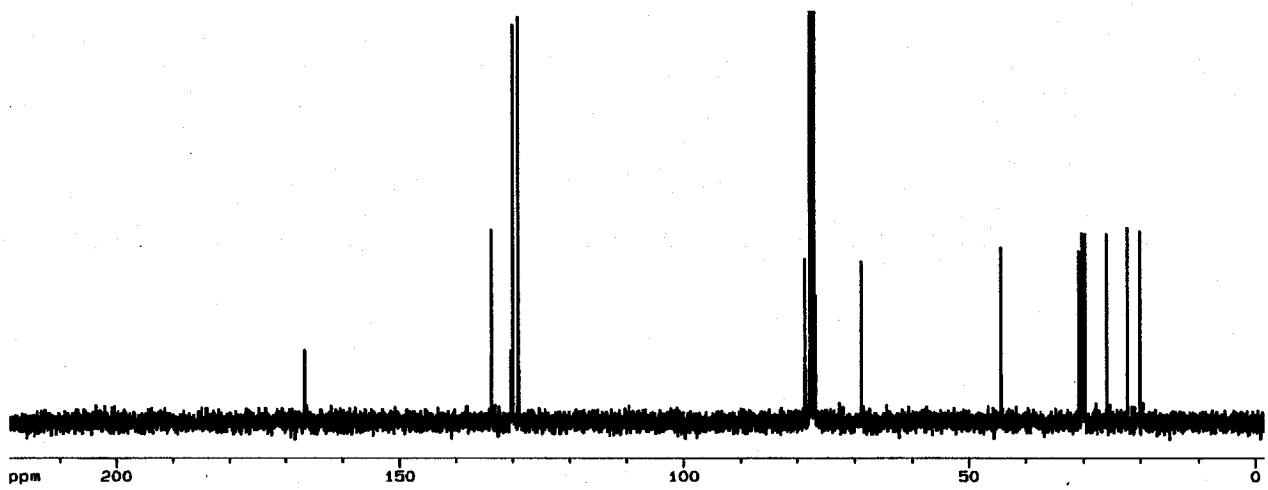


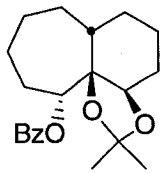
3.87

^{1}H NMR (300 MHz, $CDCl_3$)



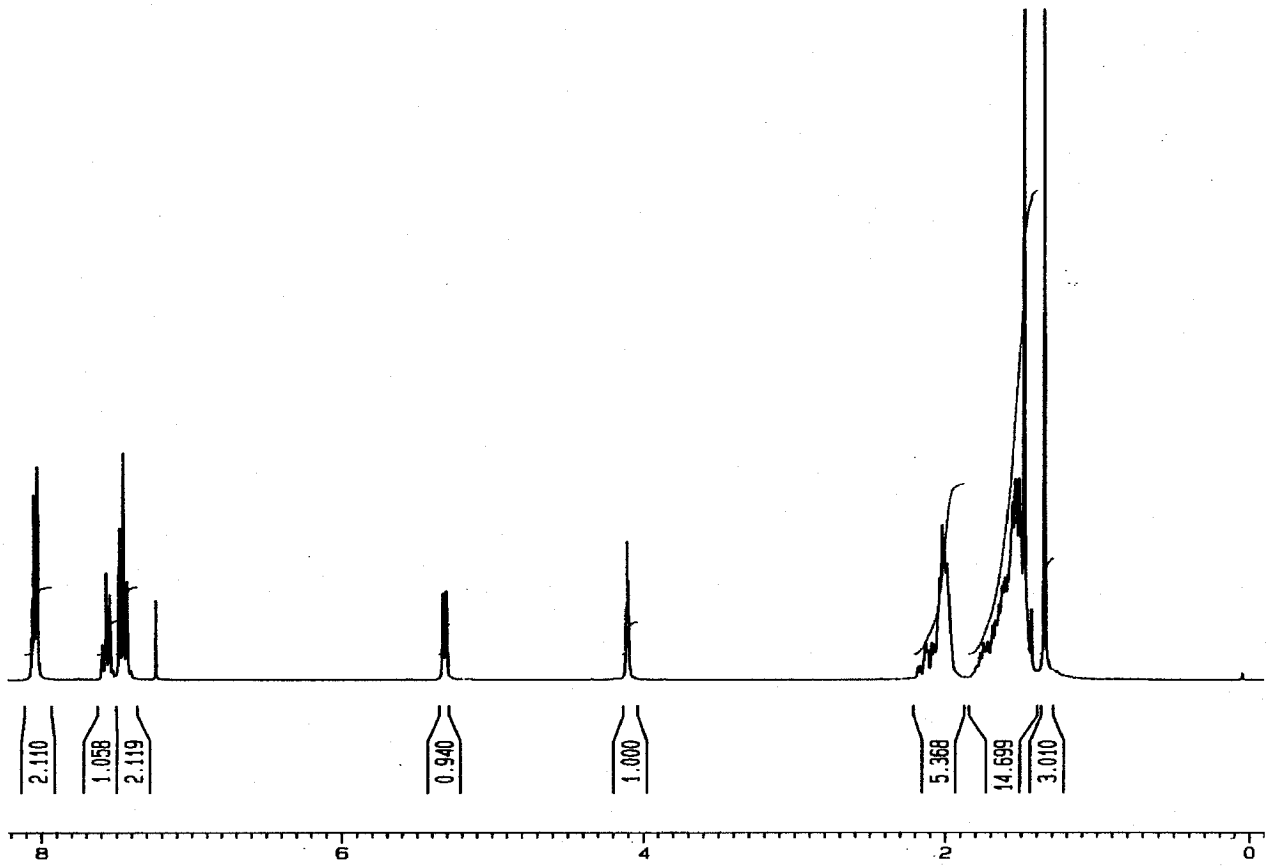
^{13}C NMR (75 MHz, $CDCl_3$)



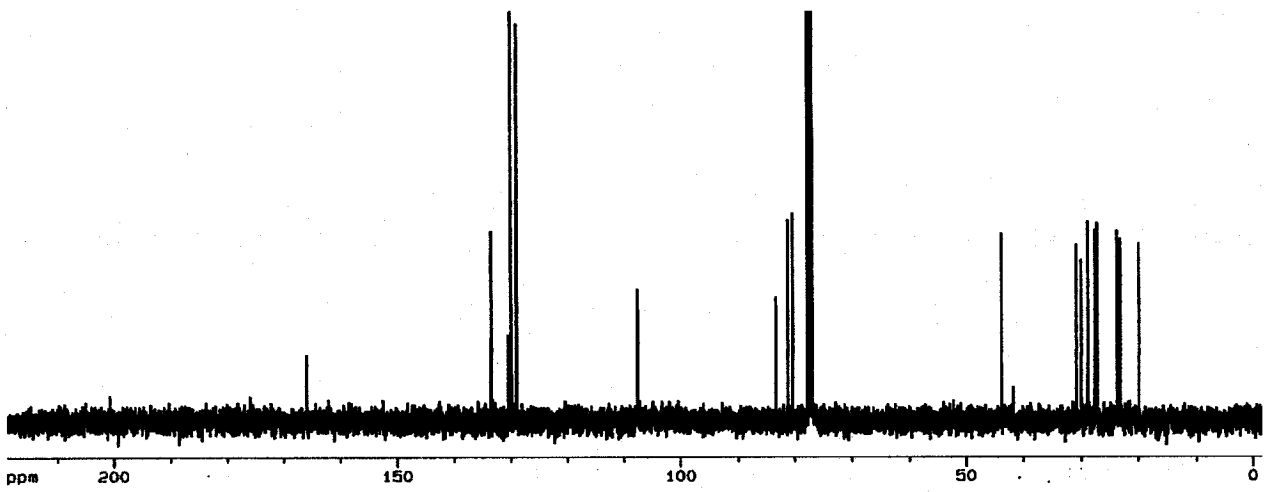


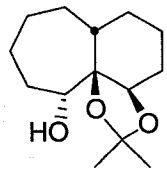
3.88

^{1}H NMR (300 MHz, $CDCl_3$)



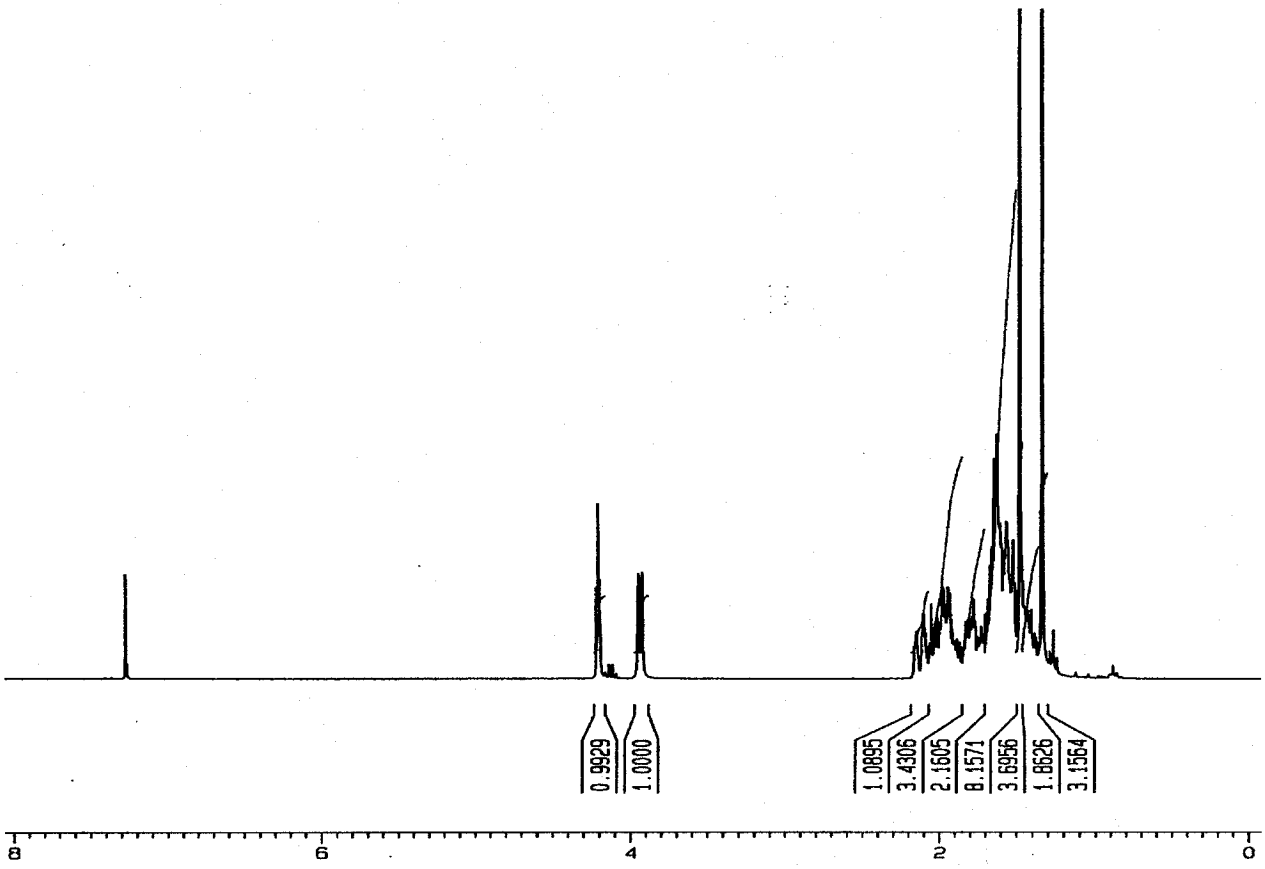
^{13}C NMR (75 MHz, $CDCl_3$)



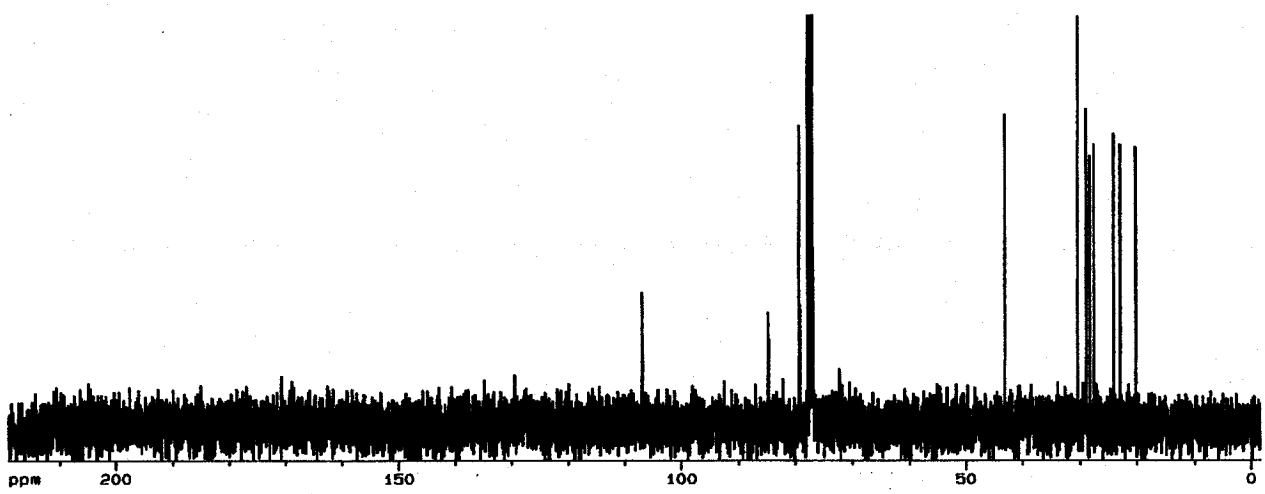


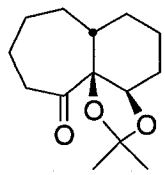
3.89

^{1}H NMR (300 MHz, $CDCl_3$)



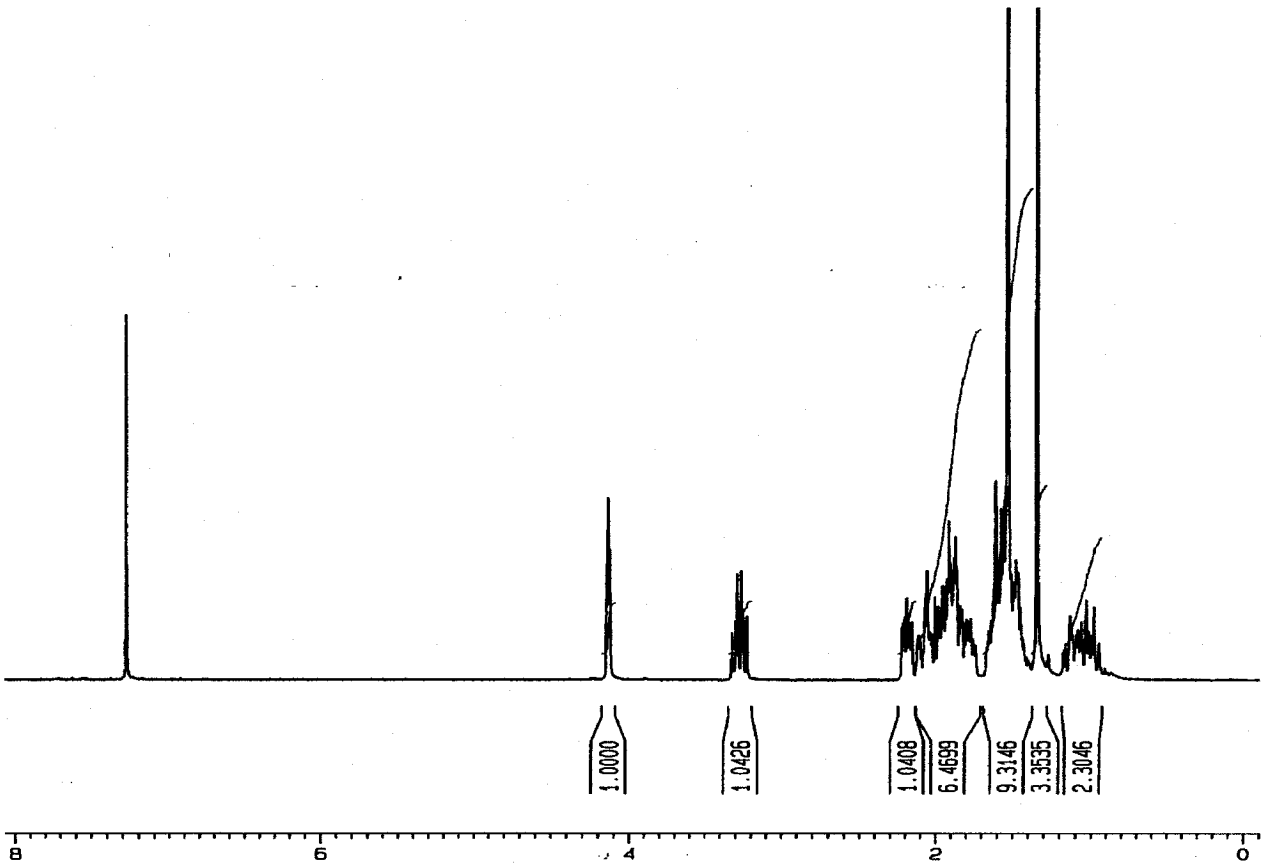
^{13}C NMR (75 MHz, $CDCl_3$)



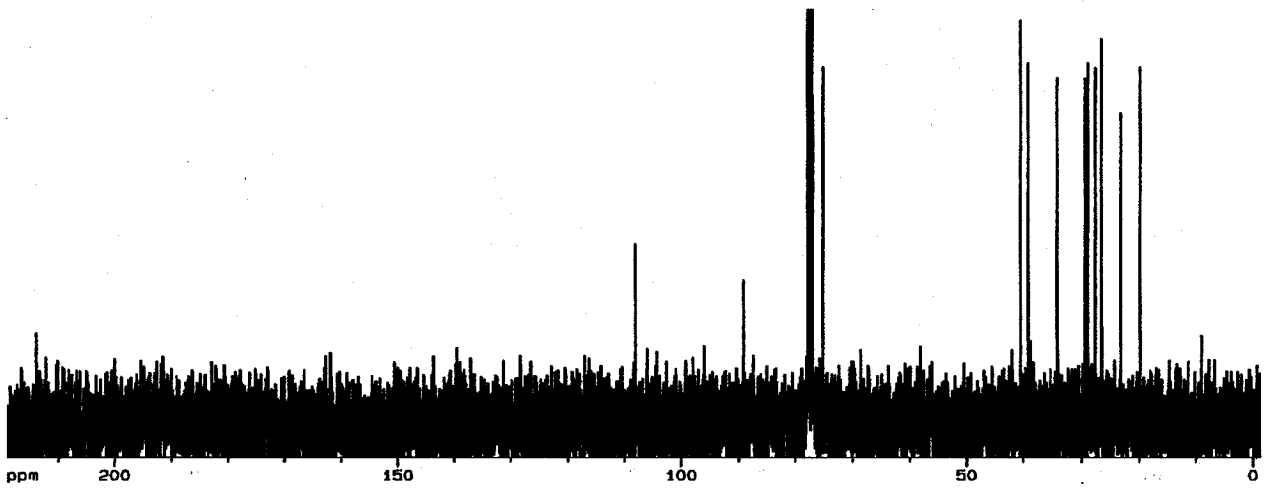


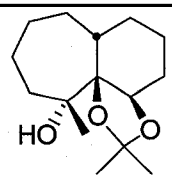
3.90

^{1}H NMR (300 MHz, $CDCl_3$)



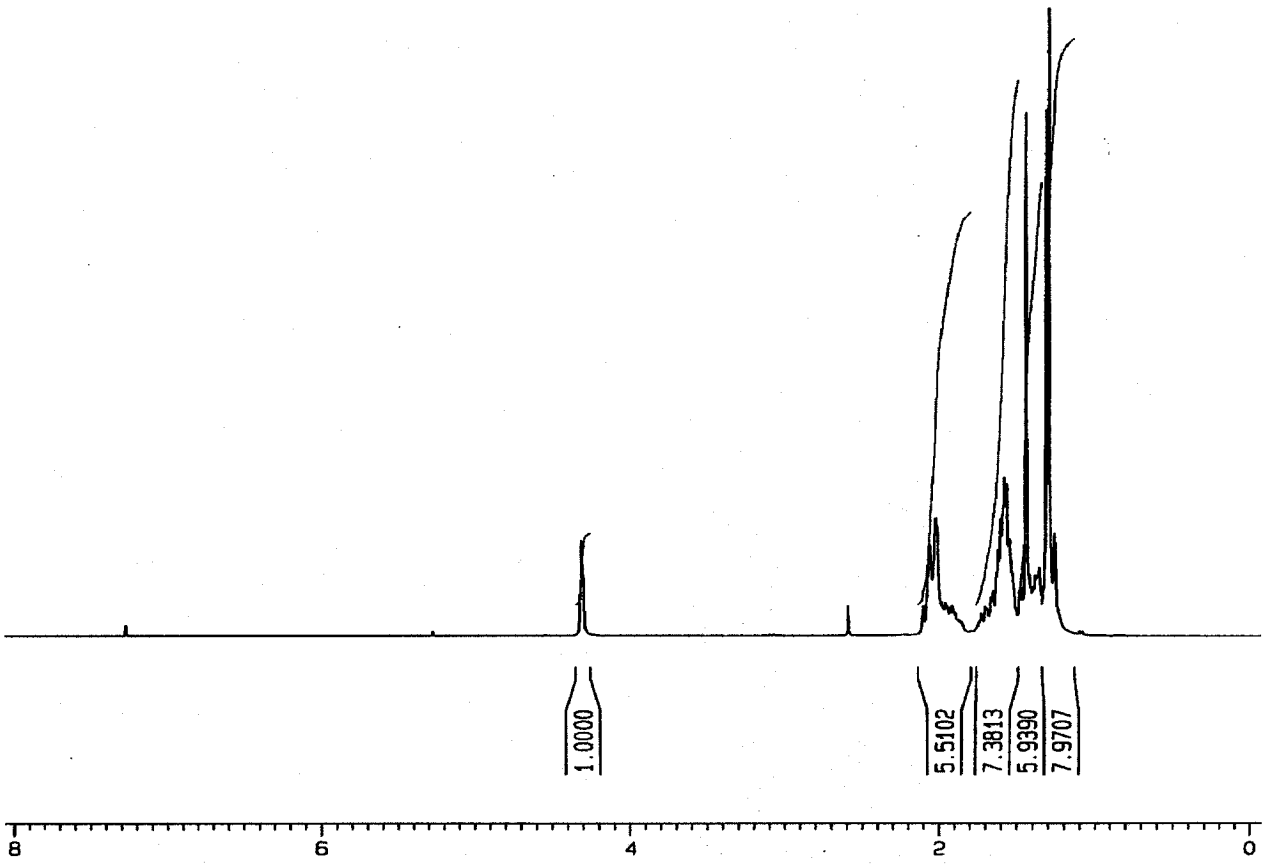
^{13}C NMR (75 MHz, $CDCl_3$)



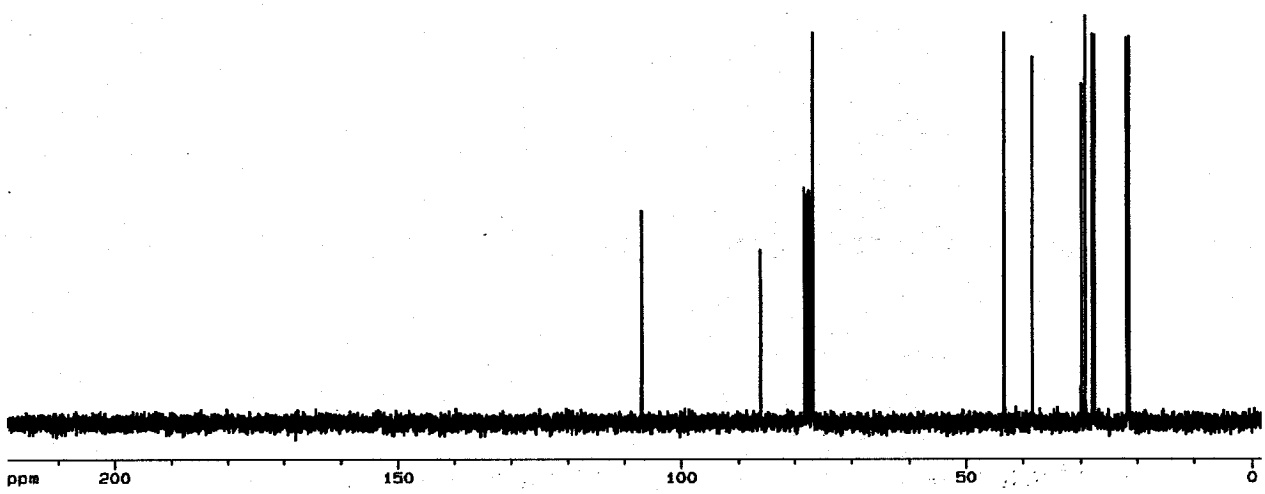


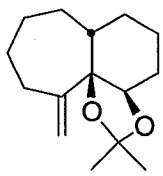
3.91

^{1}H NMR (300 MHz, $CDCl_3$)



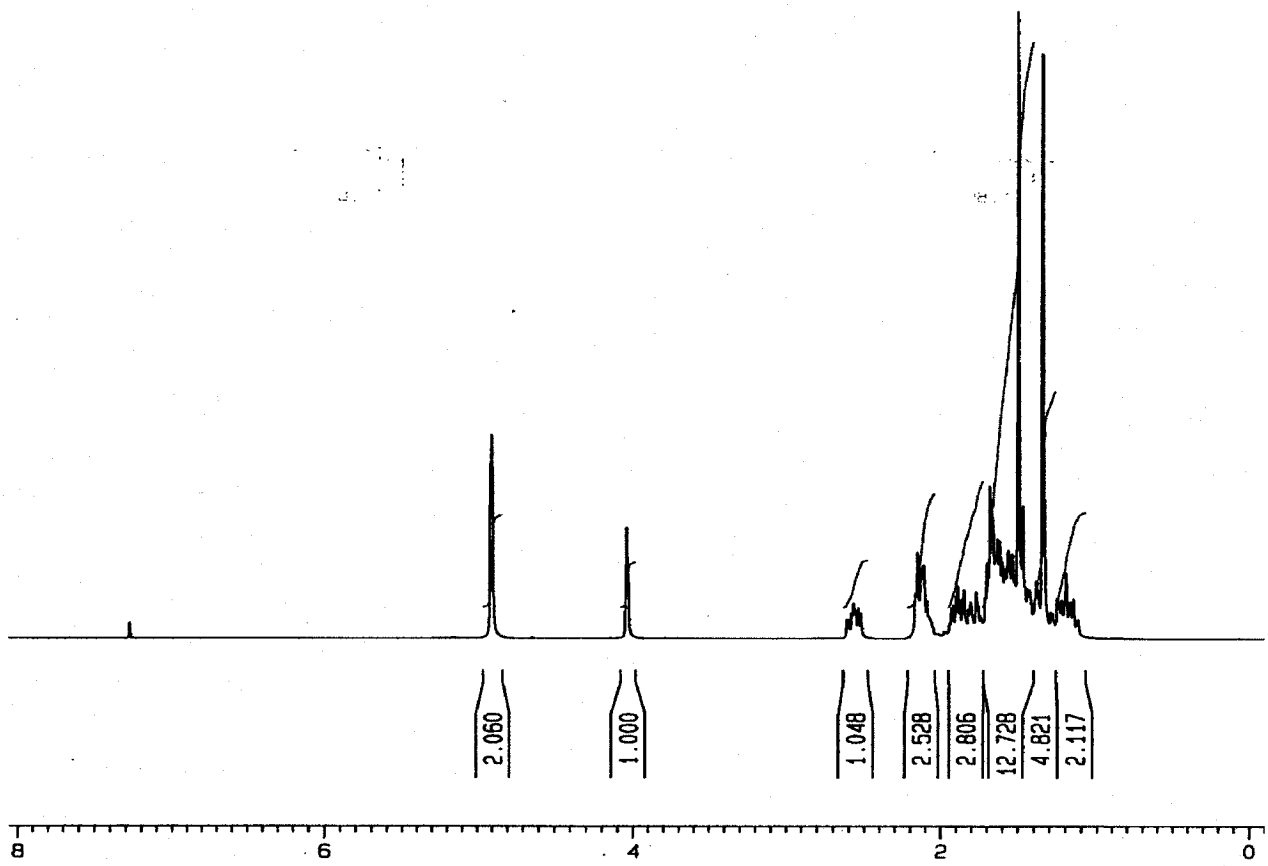
^{13}C NMR (75 MHz, $CDCl_3$)



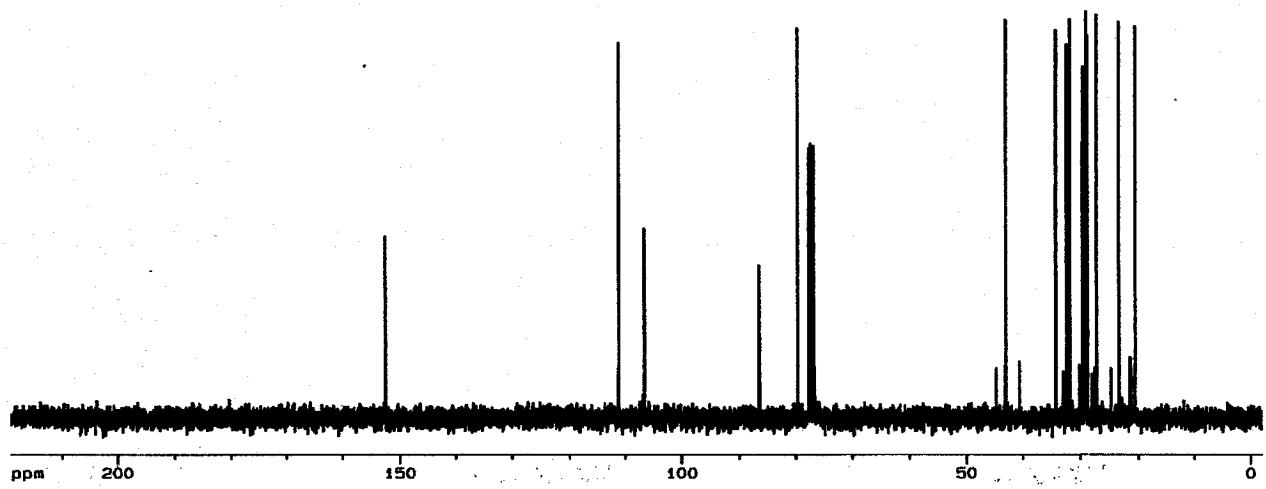


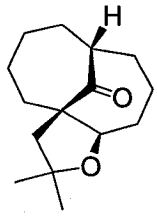
3.92

^{1}H NMR (300 MHz, $CDCl_3$)



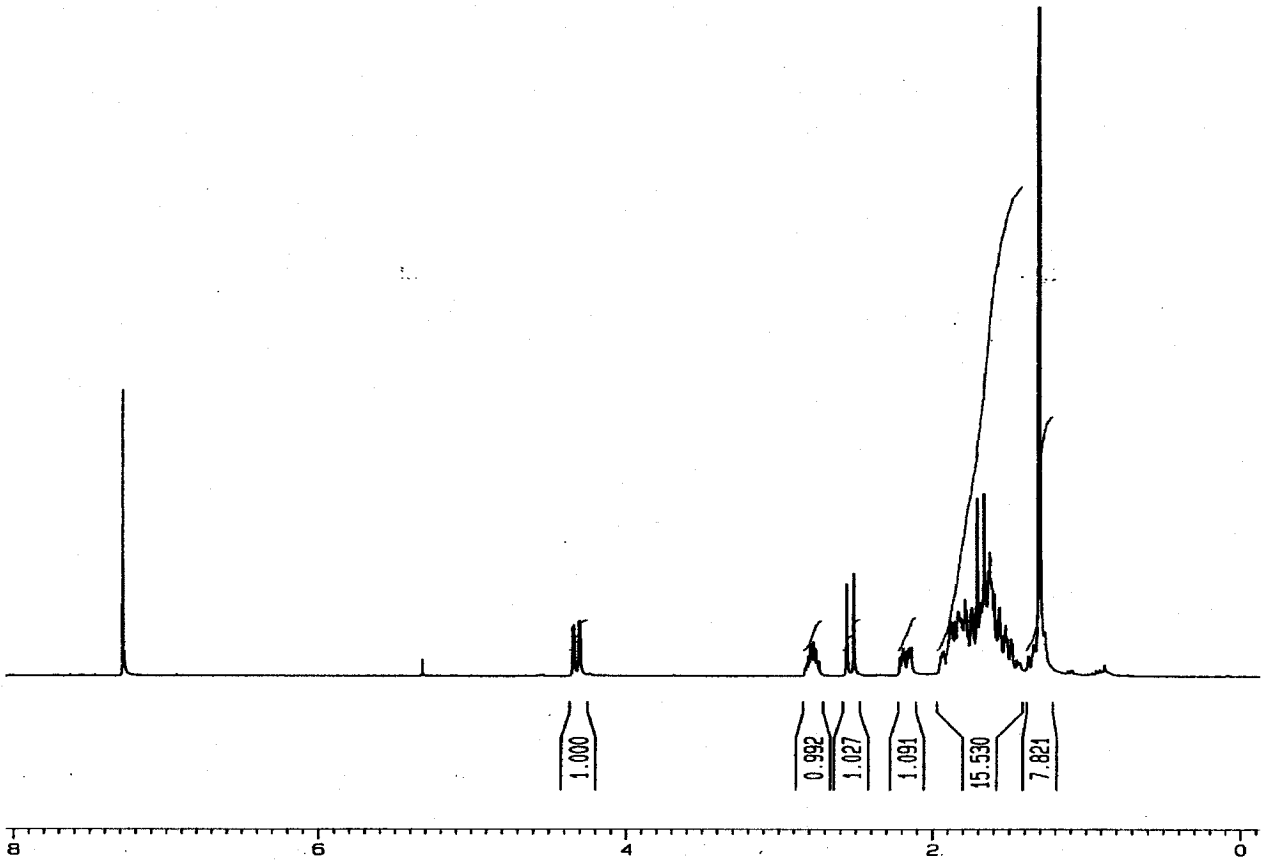
^{13}C NMR (75 MHz, $CDCl_3$)



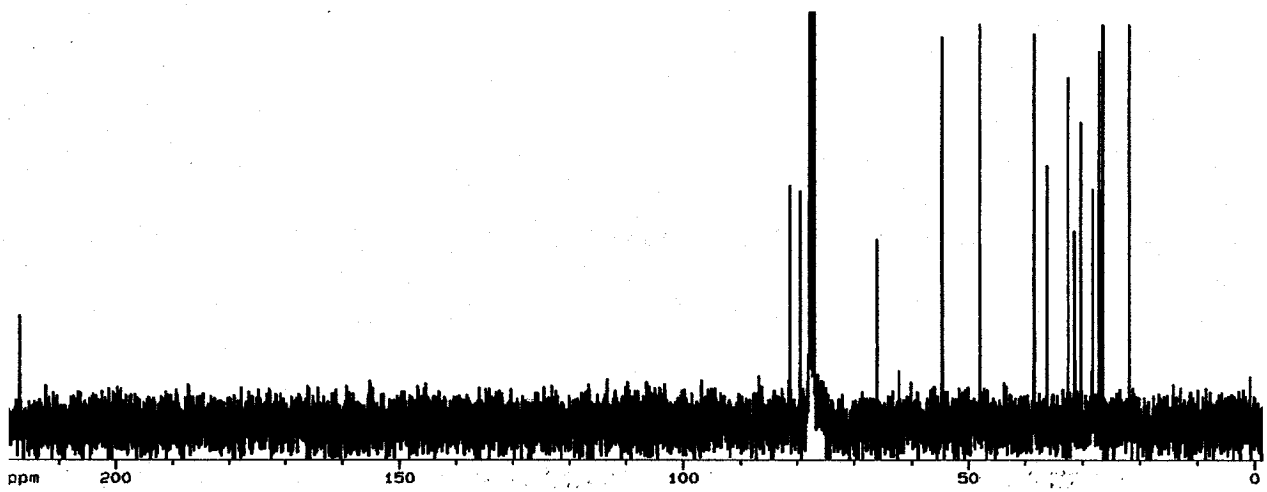


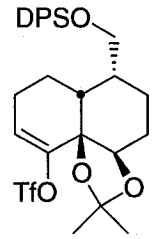
3.93

^{1}H NMR (300 MHz, $CDCl_3$)



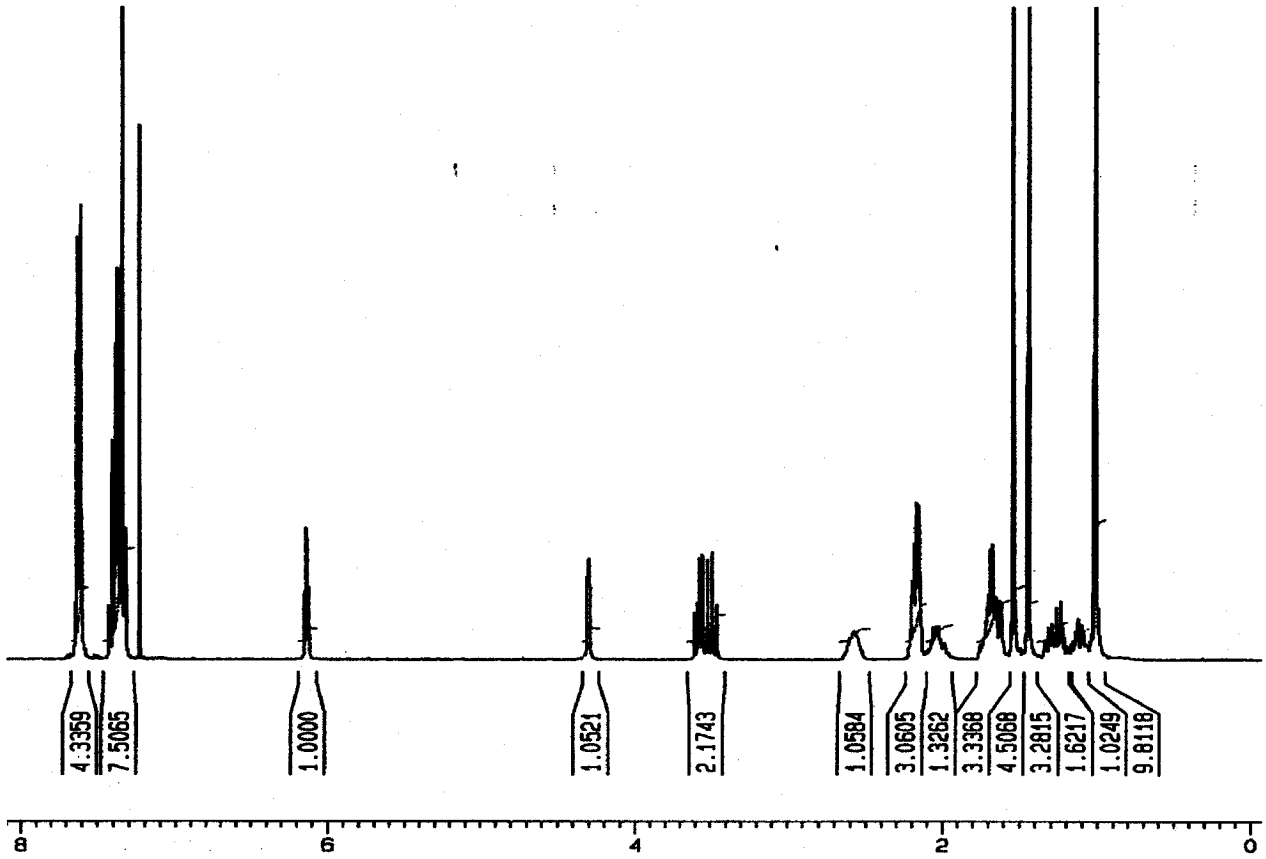
^{13}C NMR (75 MHz, $CDCl_3$)



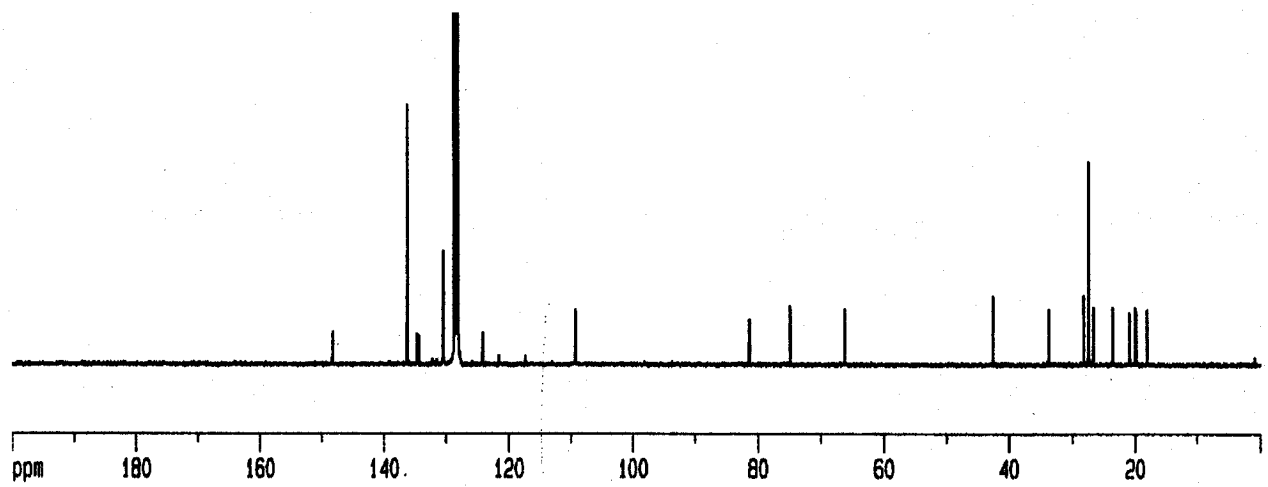


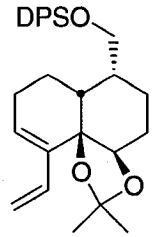
4.1

^{1}H NMR (300 MHz, C_6D_6)



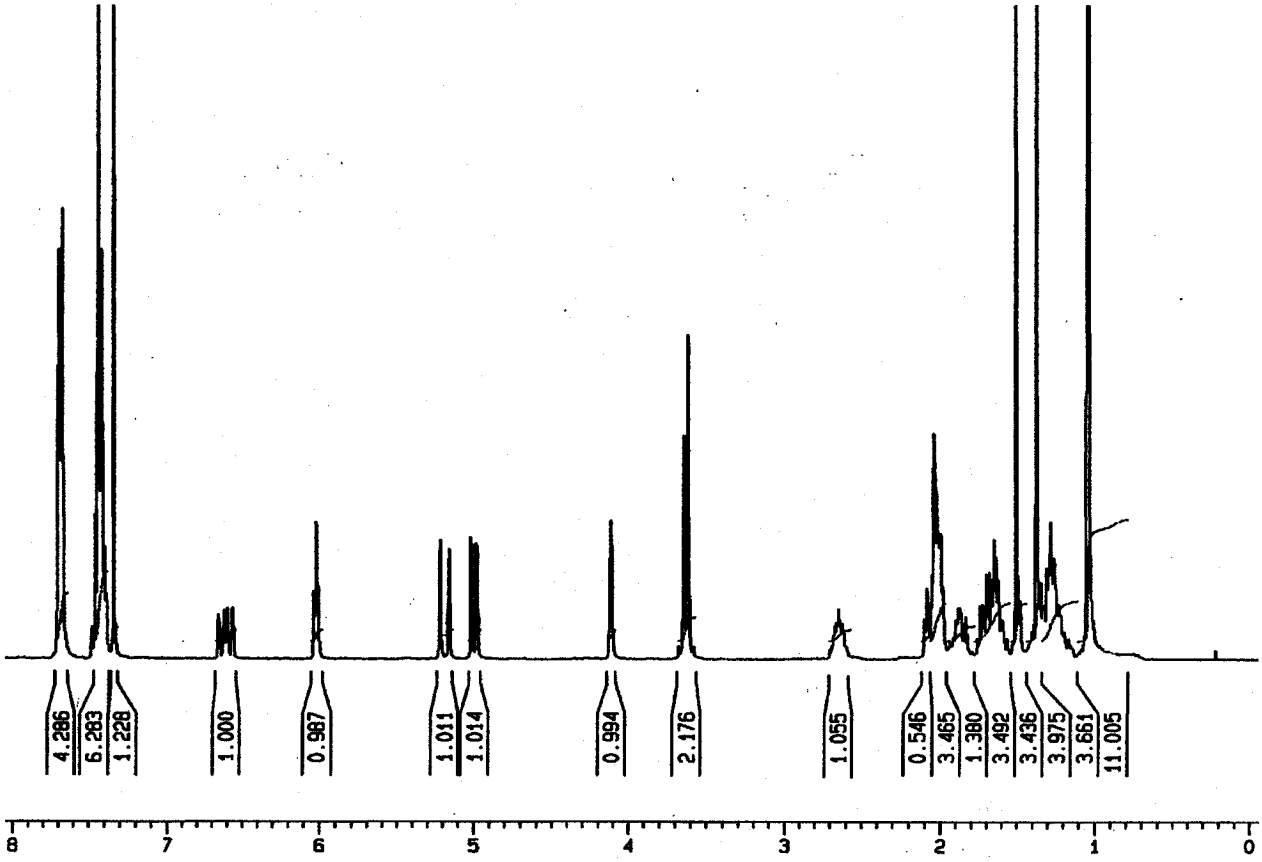
^{13}C NMR (75 MHz, C_6D_6)



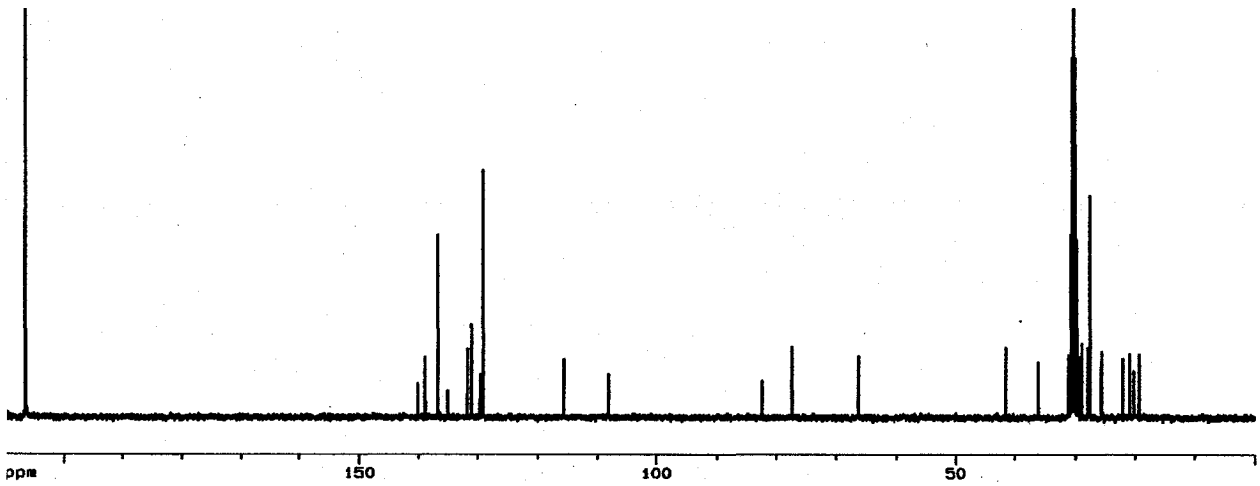


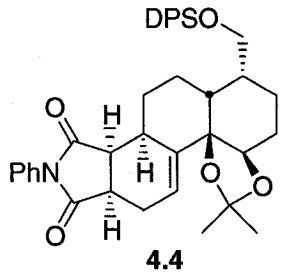
4.2

^{1}H NMR (300 MHz, acetone-d_6)



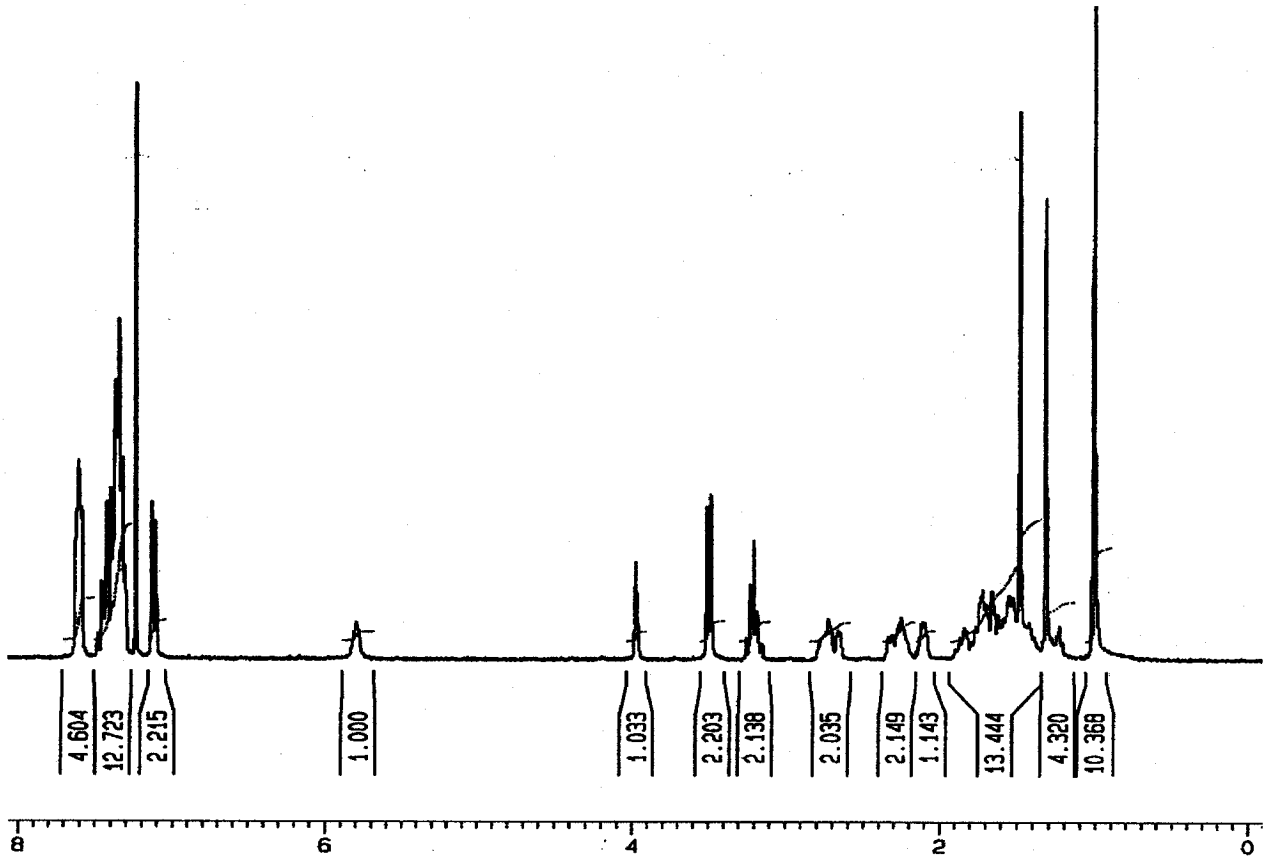
^{13}C NMR (75 MHz, acetone-d_6)



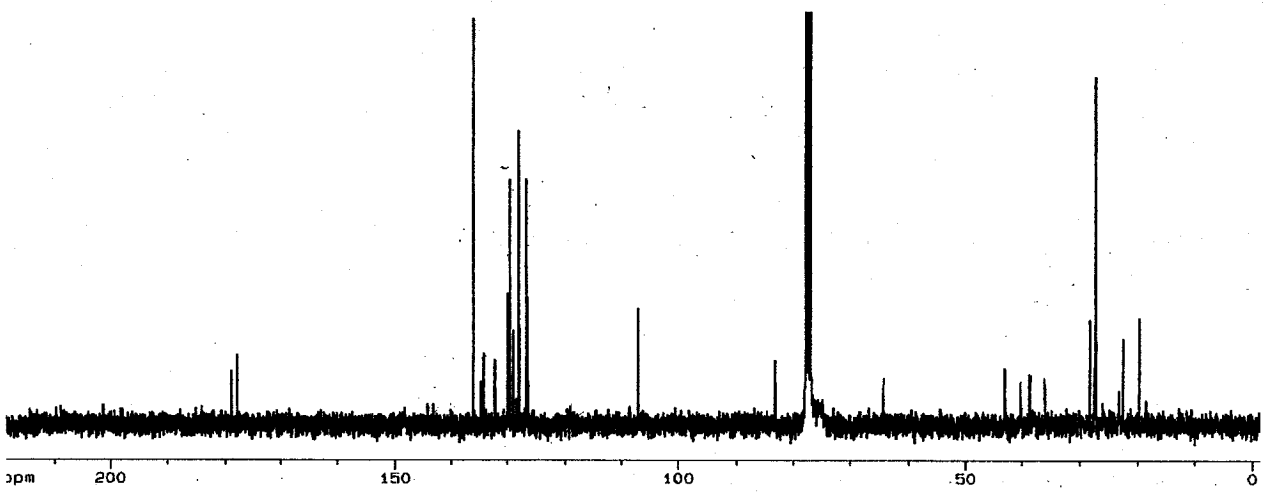


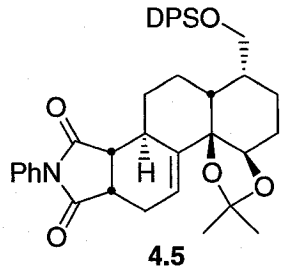
4.4

^{1}H NMR (300 MHz, $CDCl_3$)



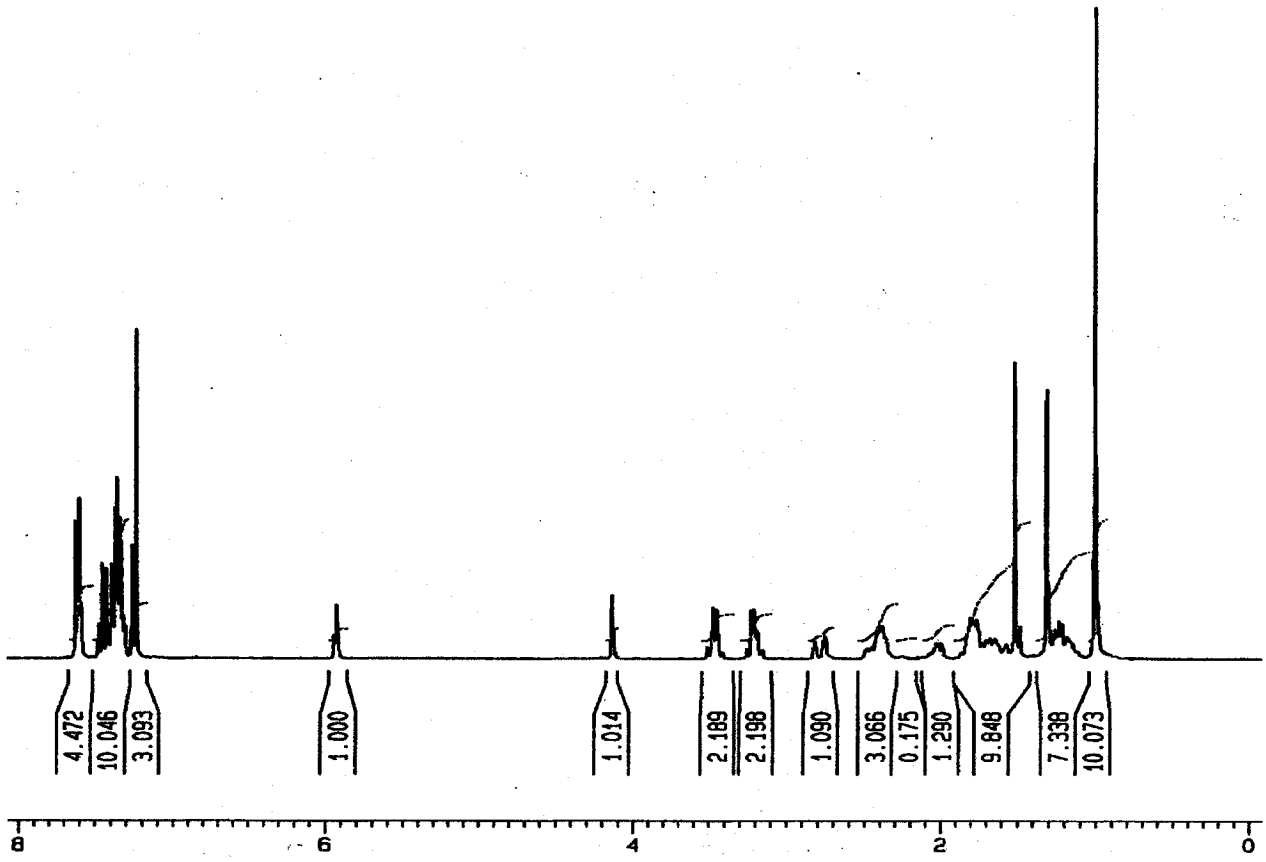
^{13}C NMR (75 MHz, $CDCl_3$)



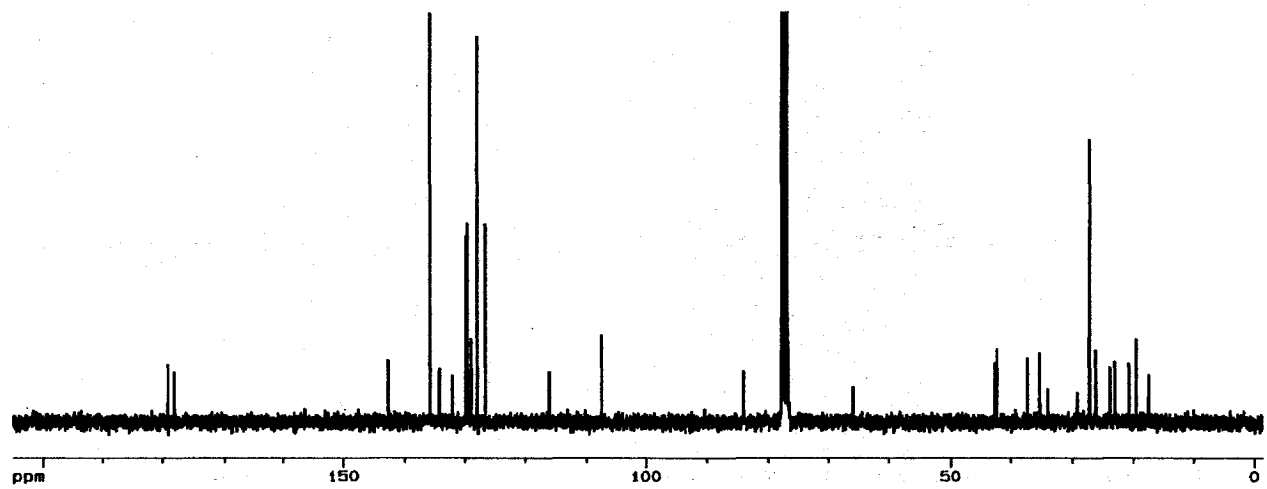


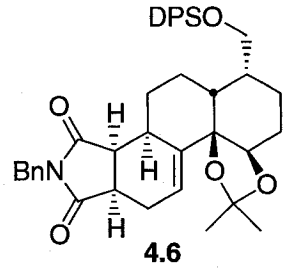
4.5

^{1}H NMR (300 MHz, $CDCl_3$)



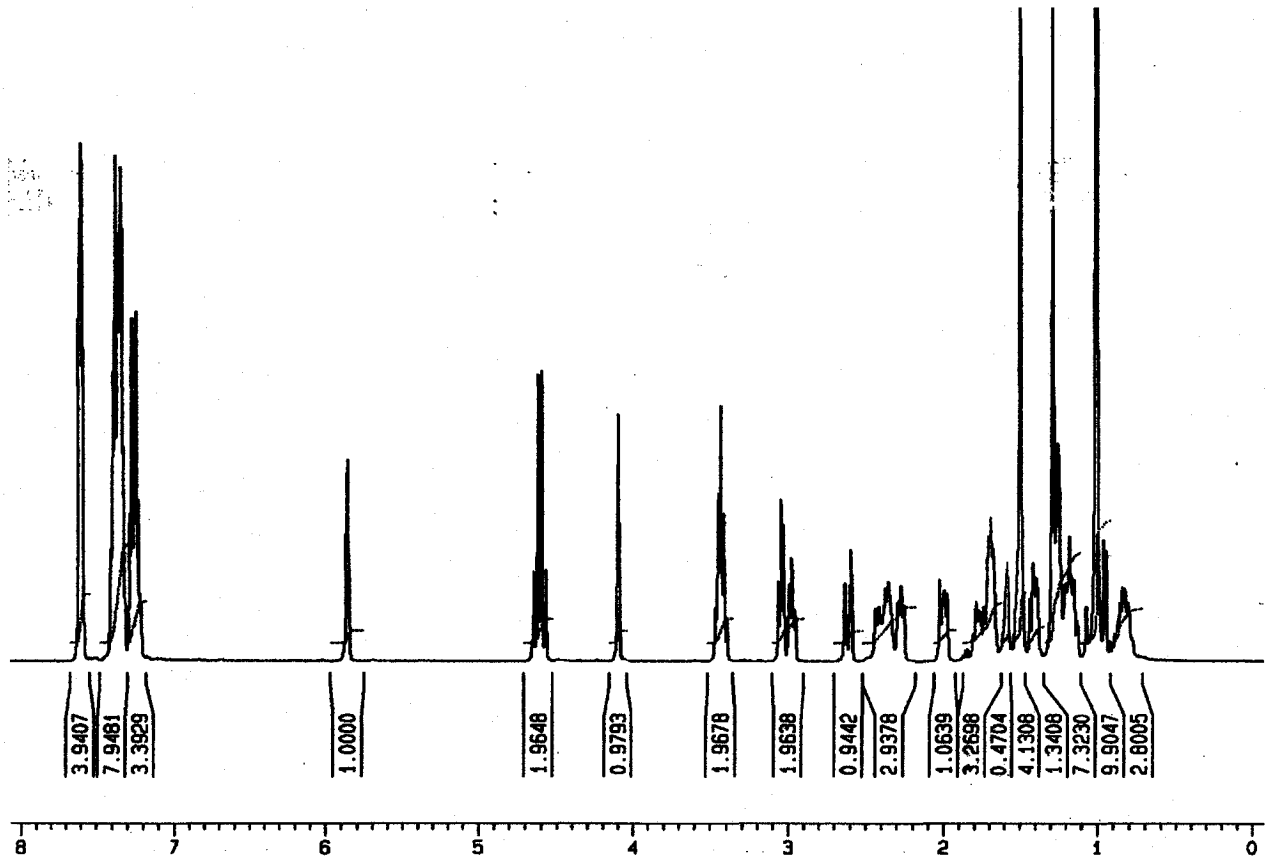
^{13}C NMR (75 MHz, $CDCl_3$)



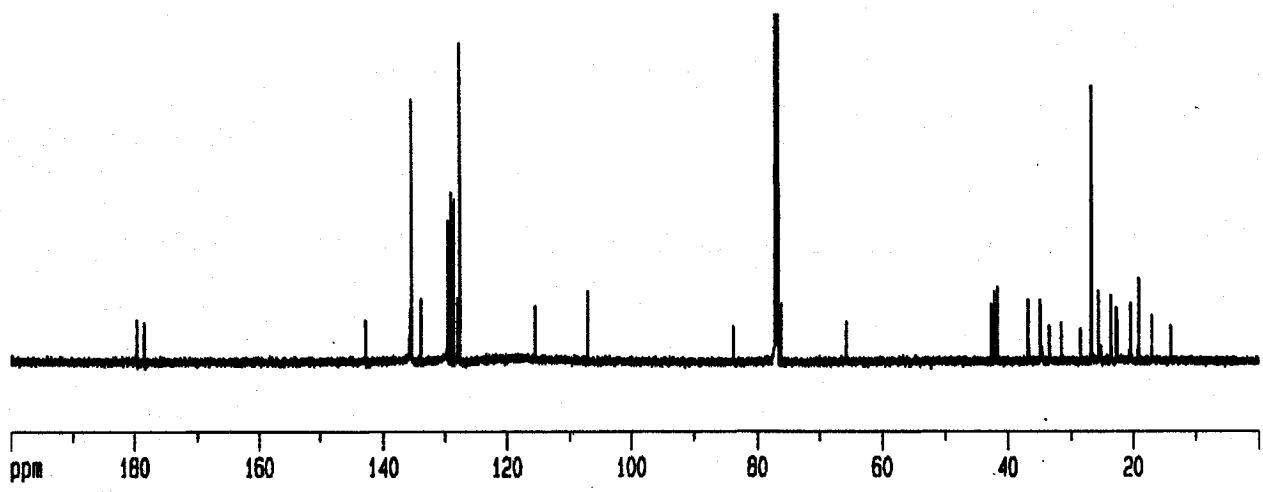


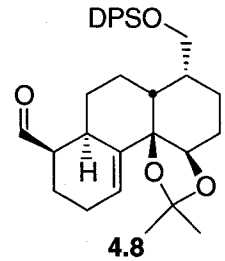
4.6

^{1}H NMR (300 MHz, acetone-d_6)



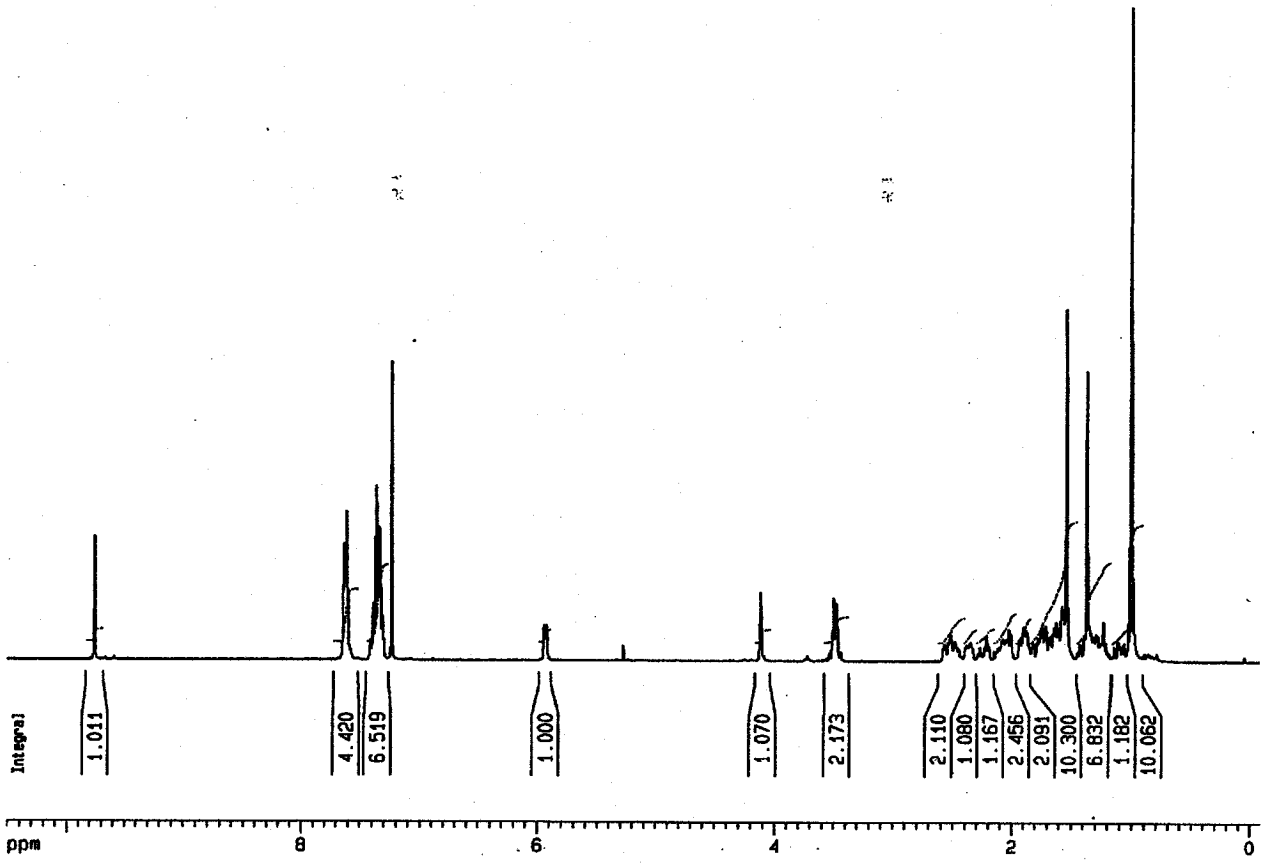
^{13}C NMR (75 MHz, acetone-d_6)



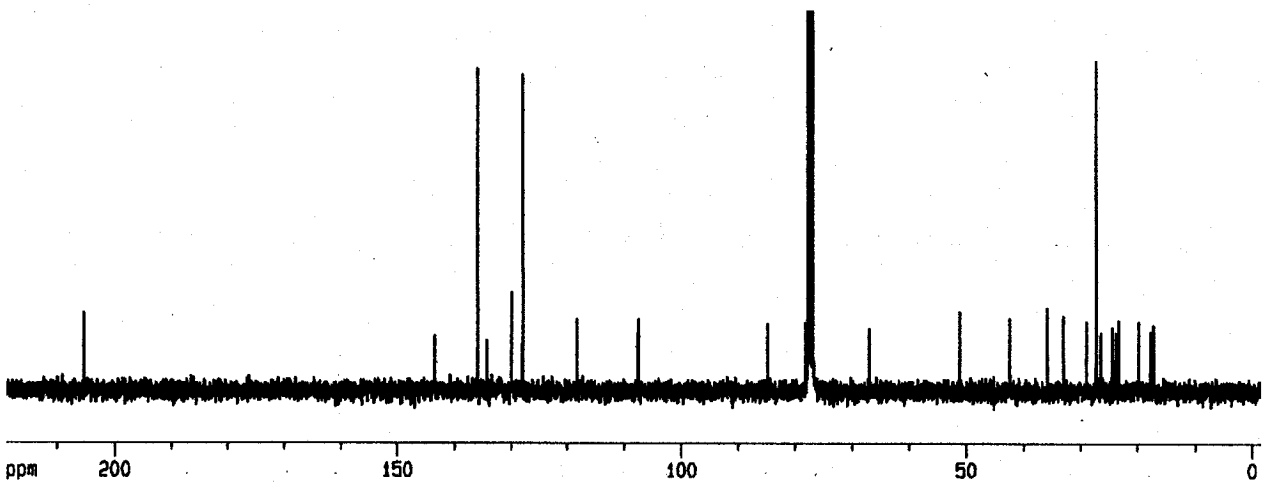


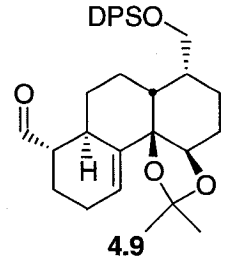
4.8

^{1}H NMR (300 MHz, $CDCl_3$)



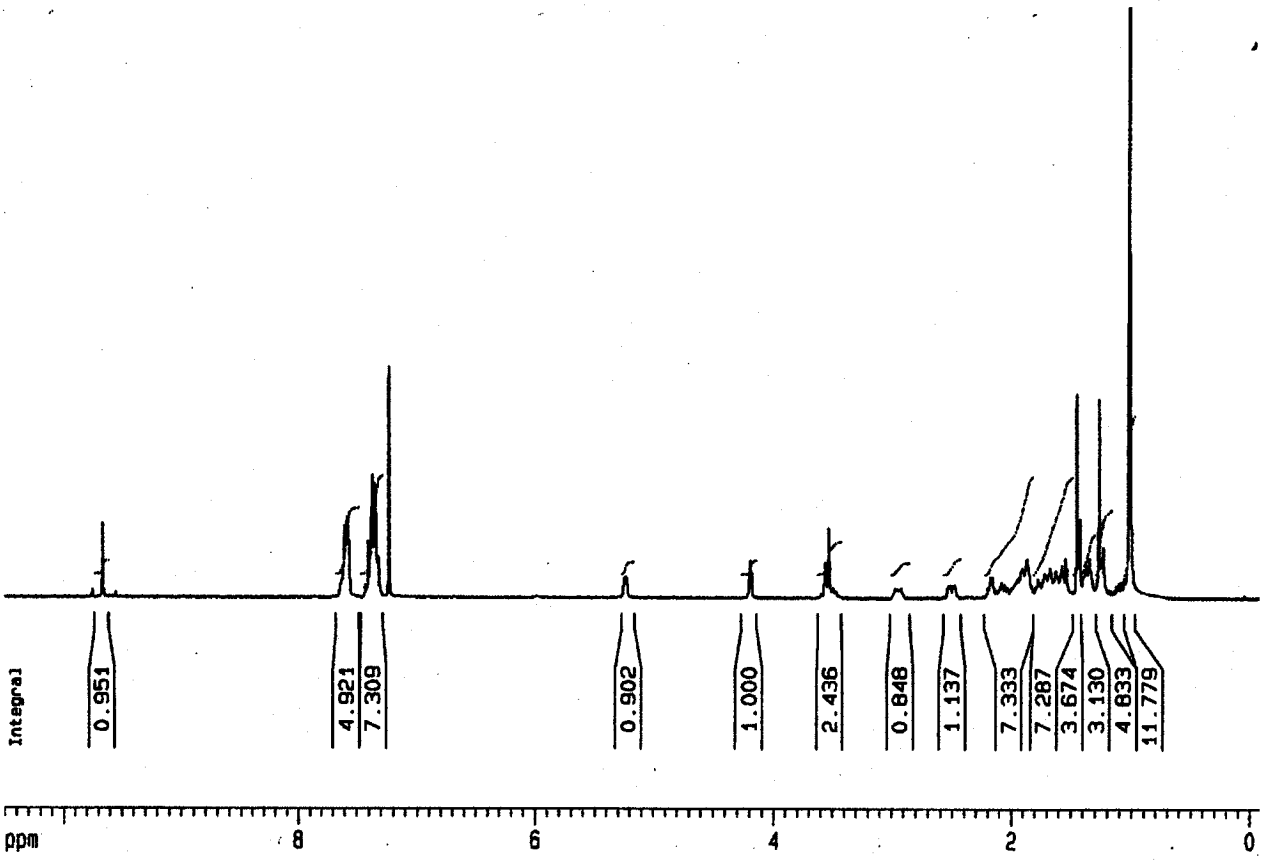
^{13}C NMR (75 MHz, $CDCl_3$)



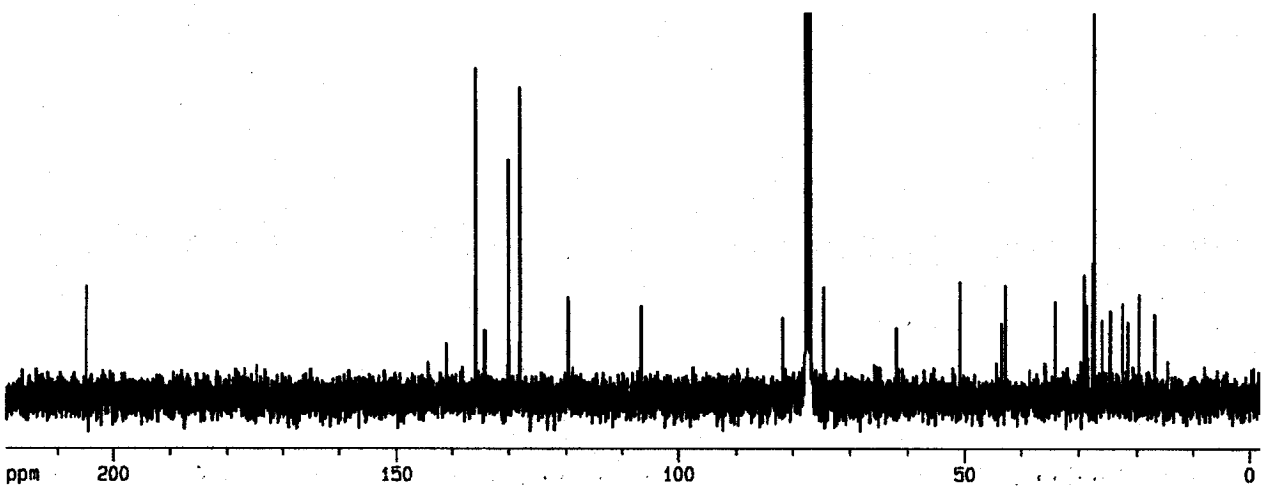


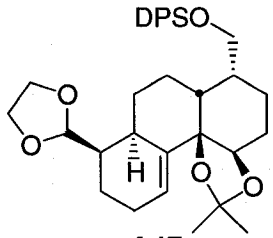
4.9

^{1}H NMR (300 MHz, $CDCl_3$)



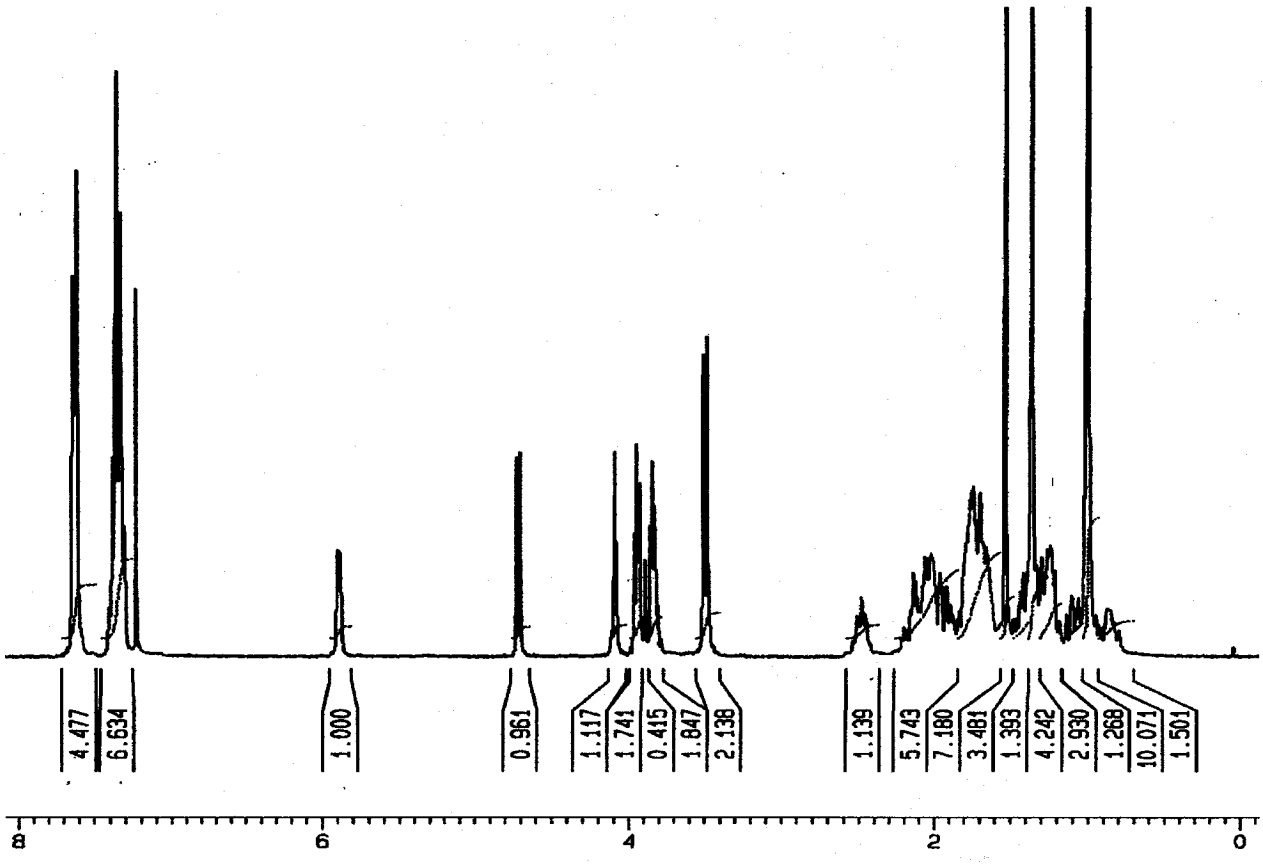
^{13}C NMR (75 MHz, $CDCl_3$)



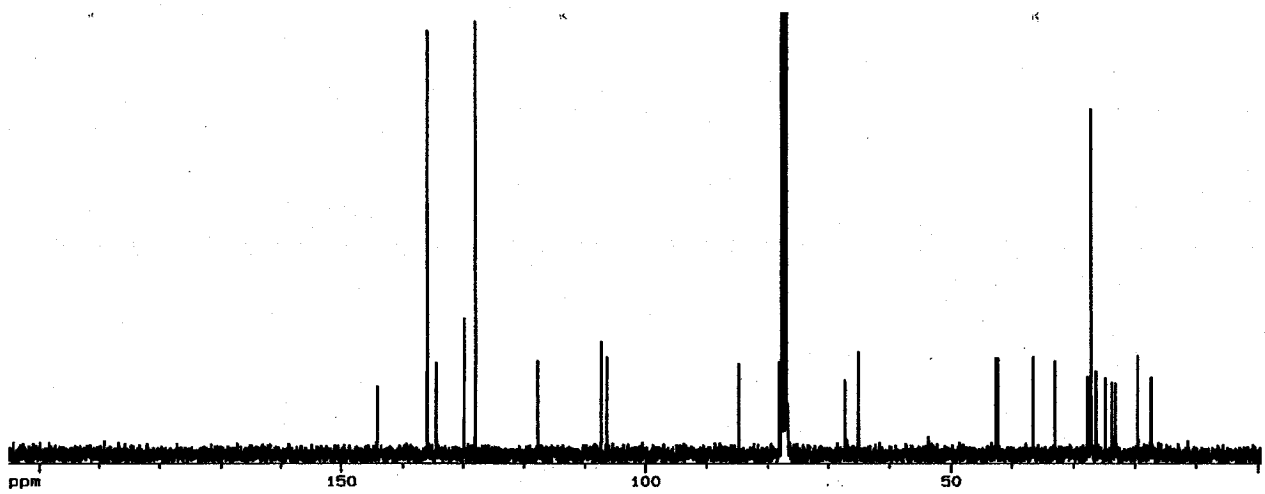


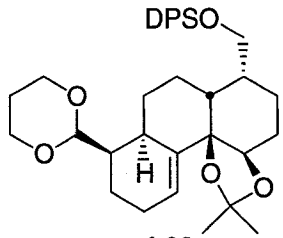
4.17

^{1}H NMR (300 MHz, $CDCl_3$)



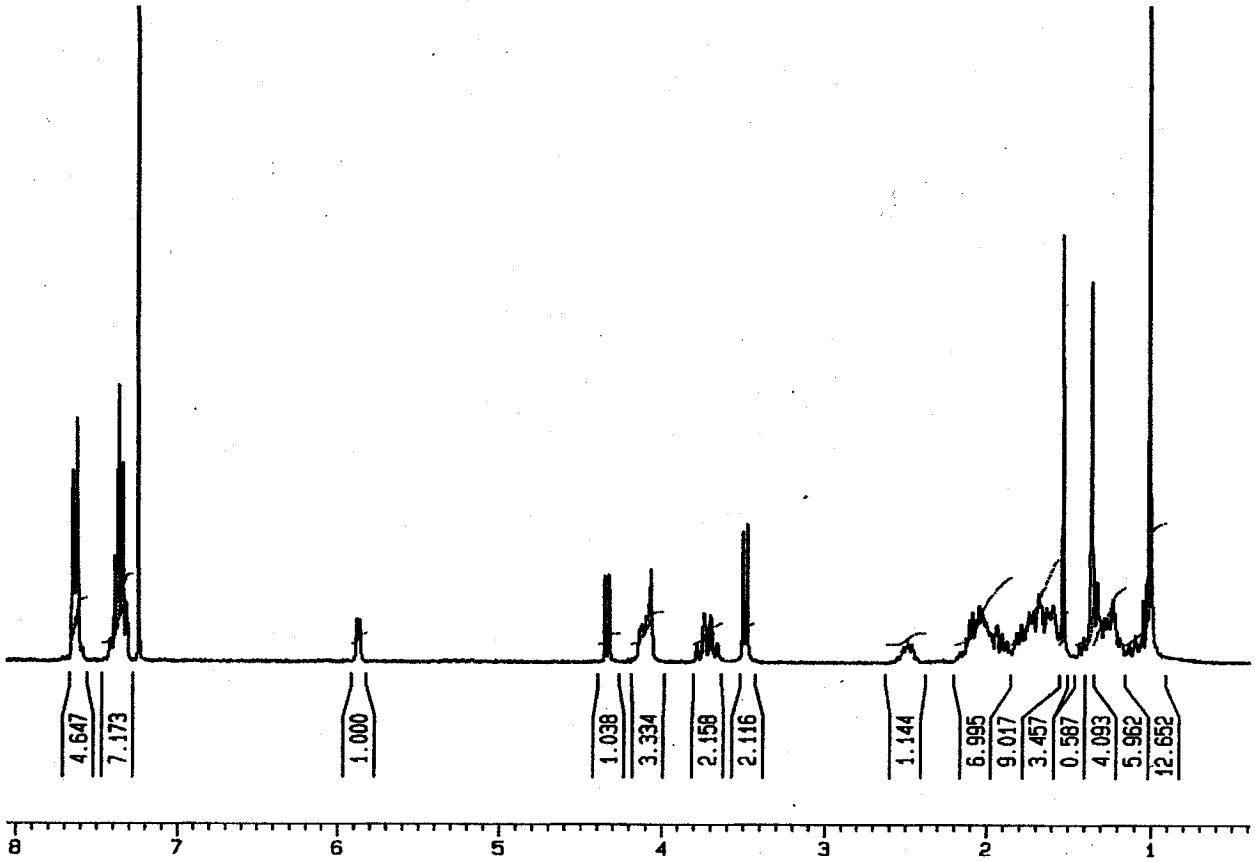
^{13}C NMR (75 MHz, $CDCl_3$)





4.23

^{1}H NMR (300 MHz, $CDCl_3$)



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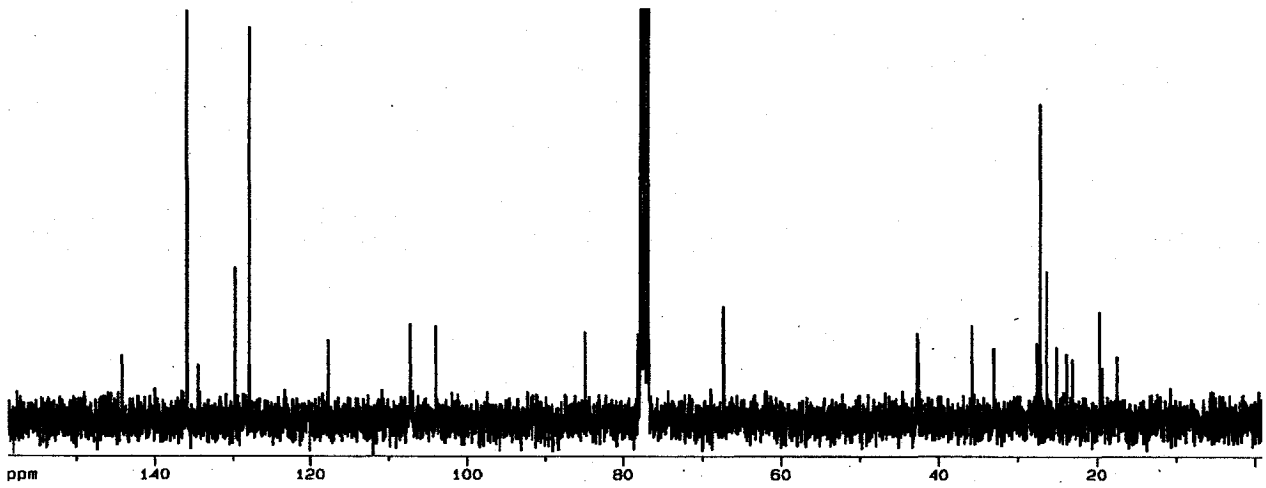
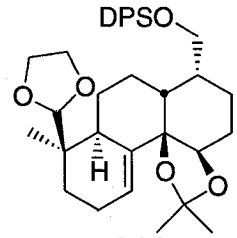
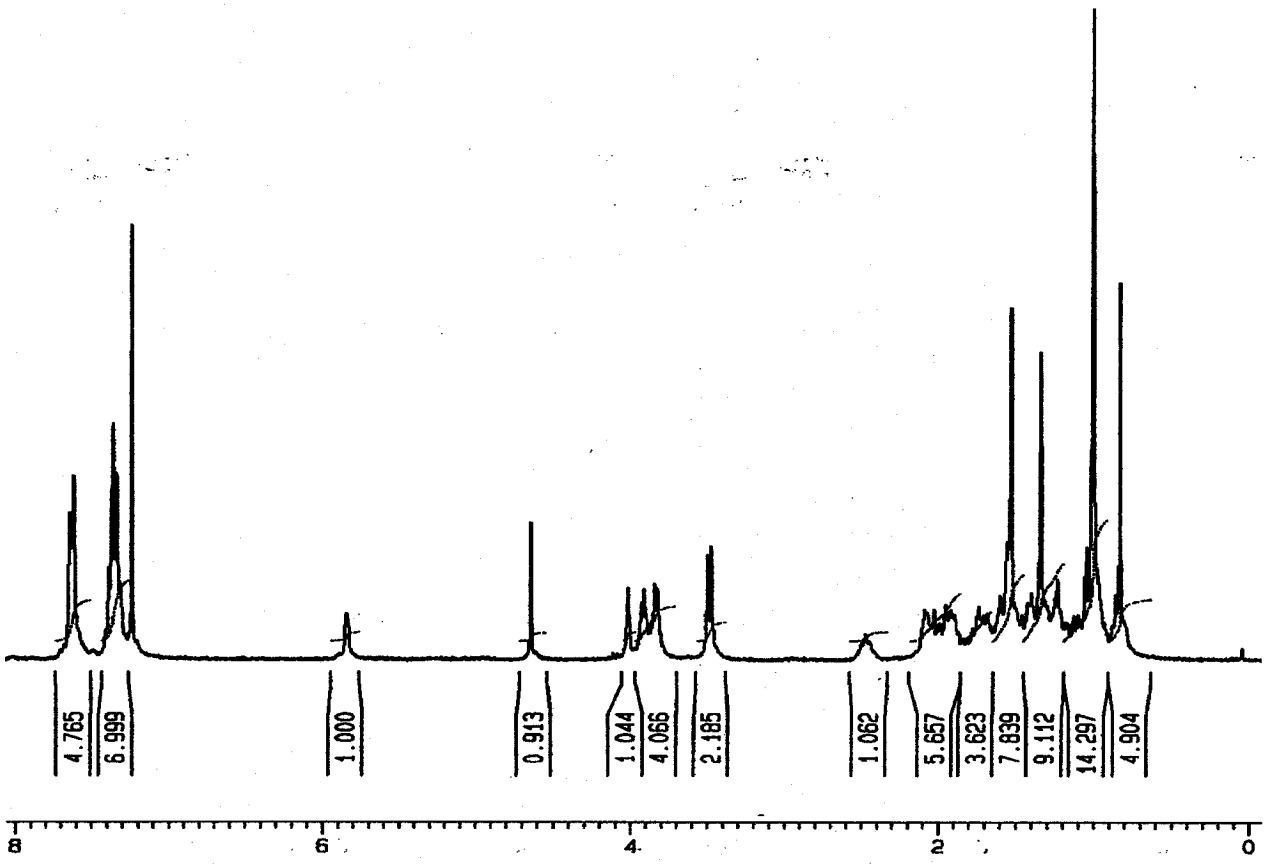




4.24

^{1}H NMR (300 MHz, $CDCl_3$)



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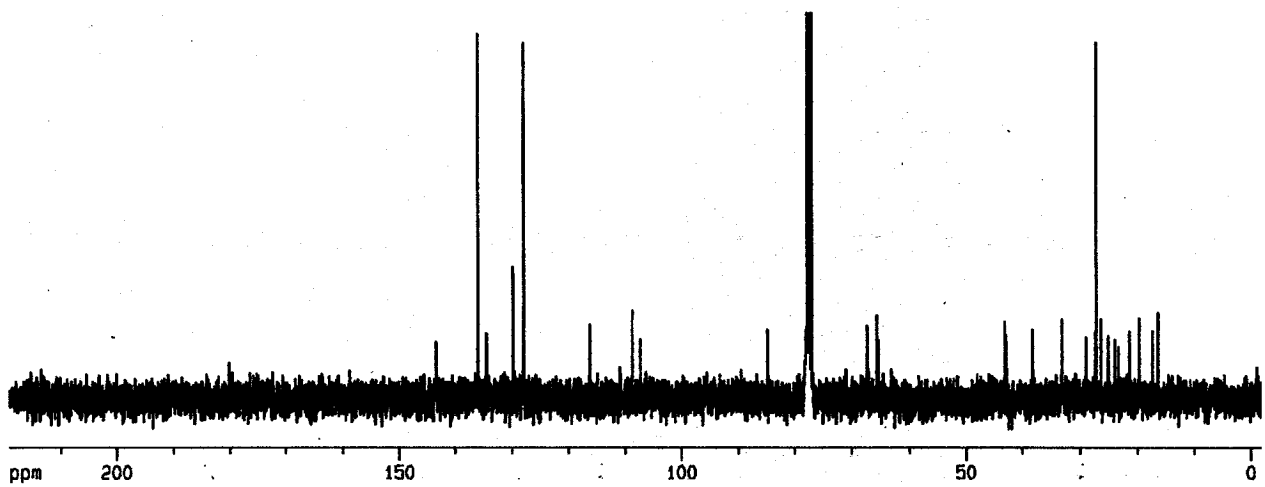
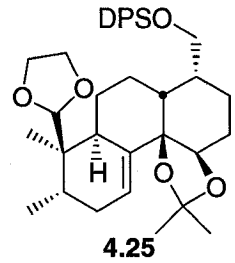
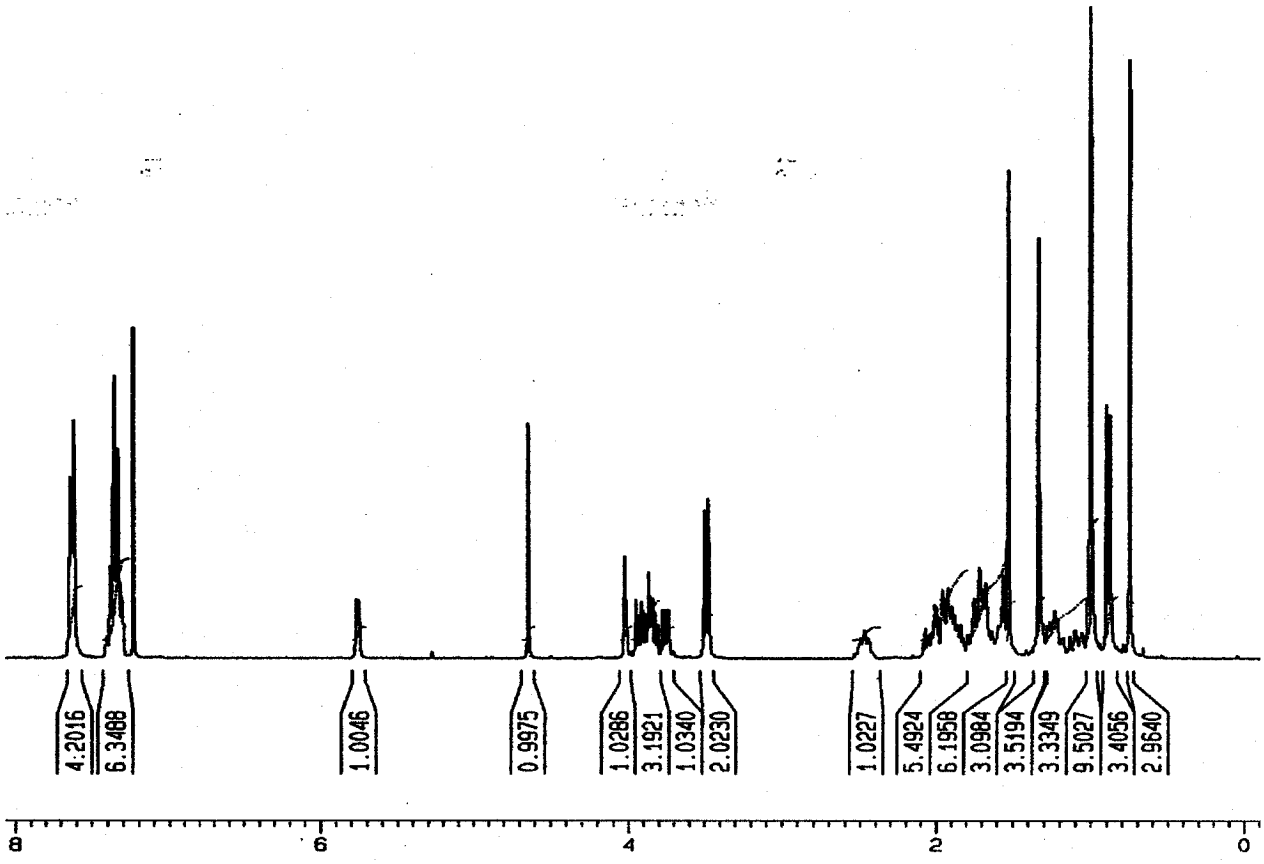


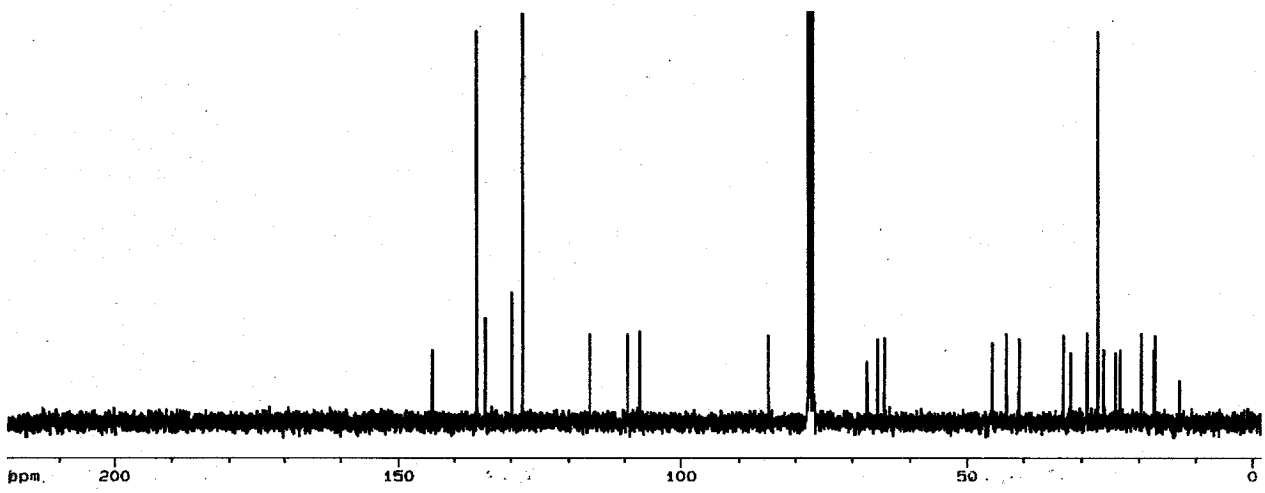


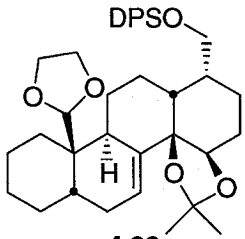
4.25

^{1}H NMR (300 MHz, $CDCl_3$)



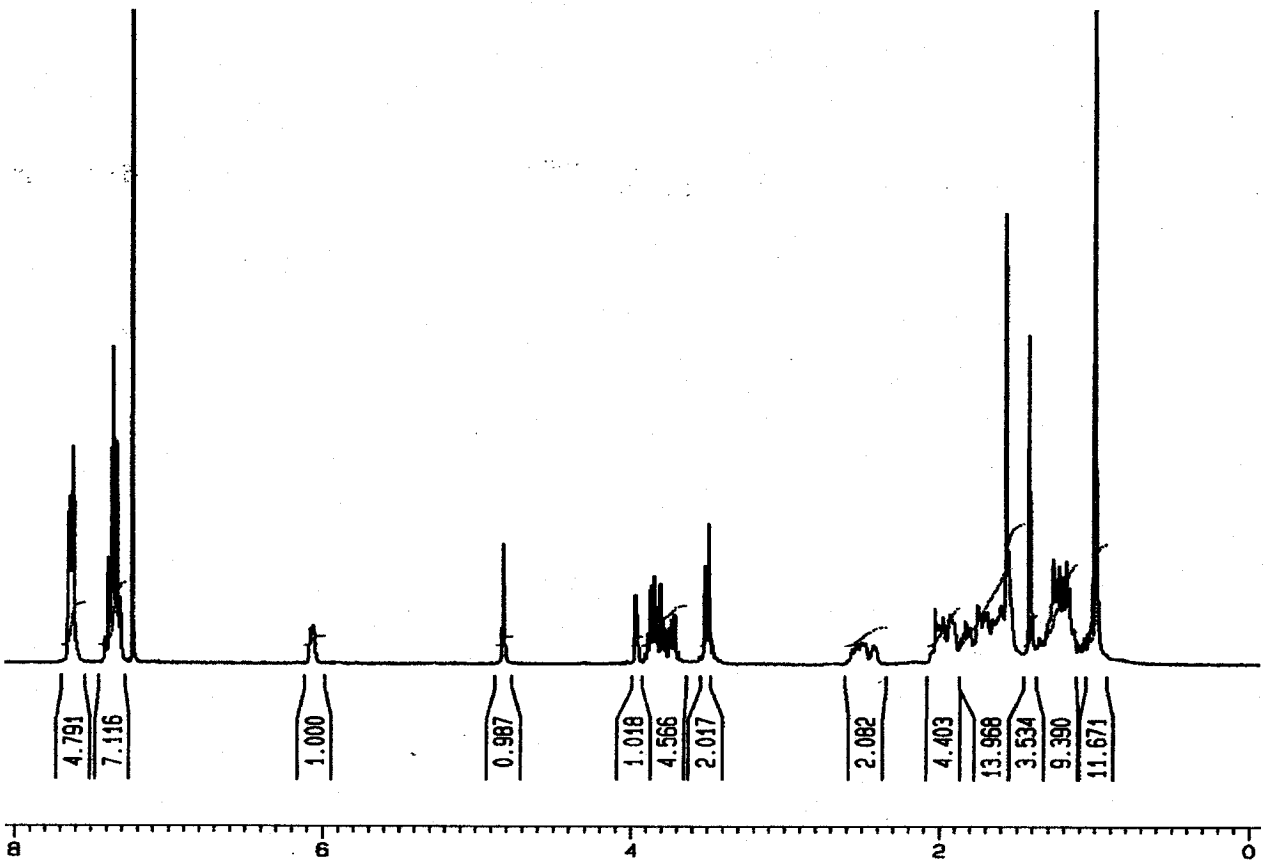
^{13}C NMR (75 MHz, $CDCl_3$)





4.26

^{1}H NMR (300 MHz, $CDCl_3$)



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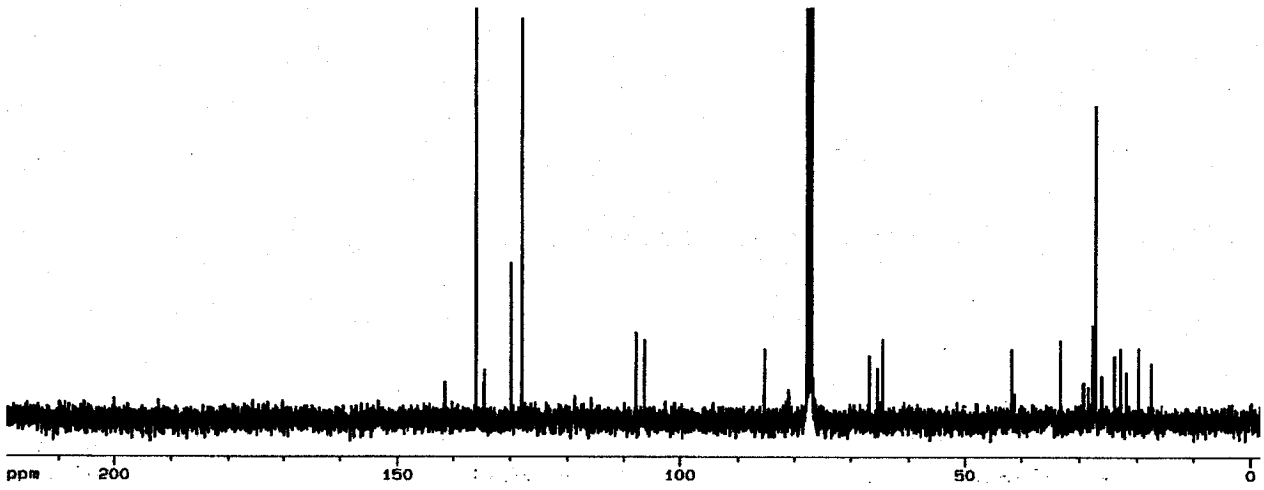
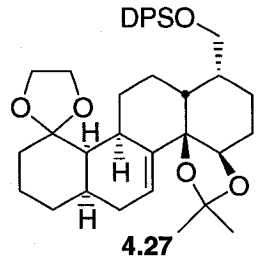
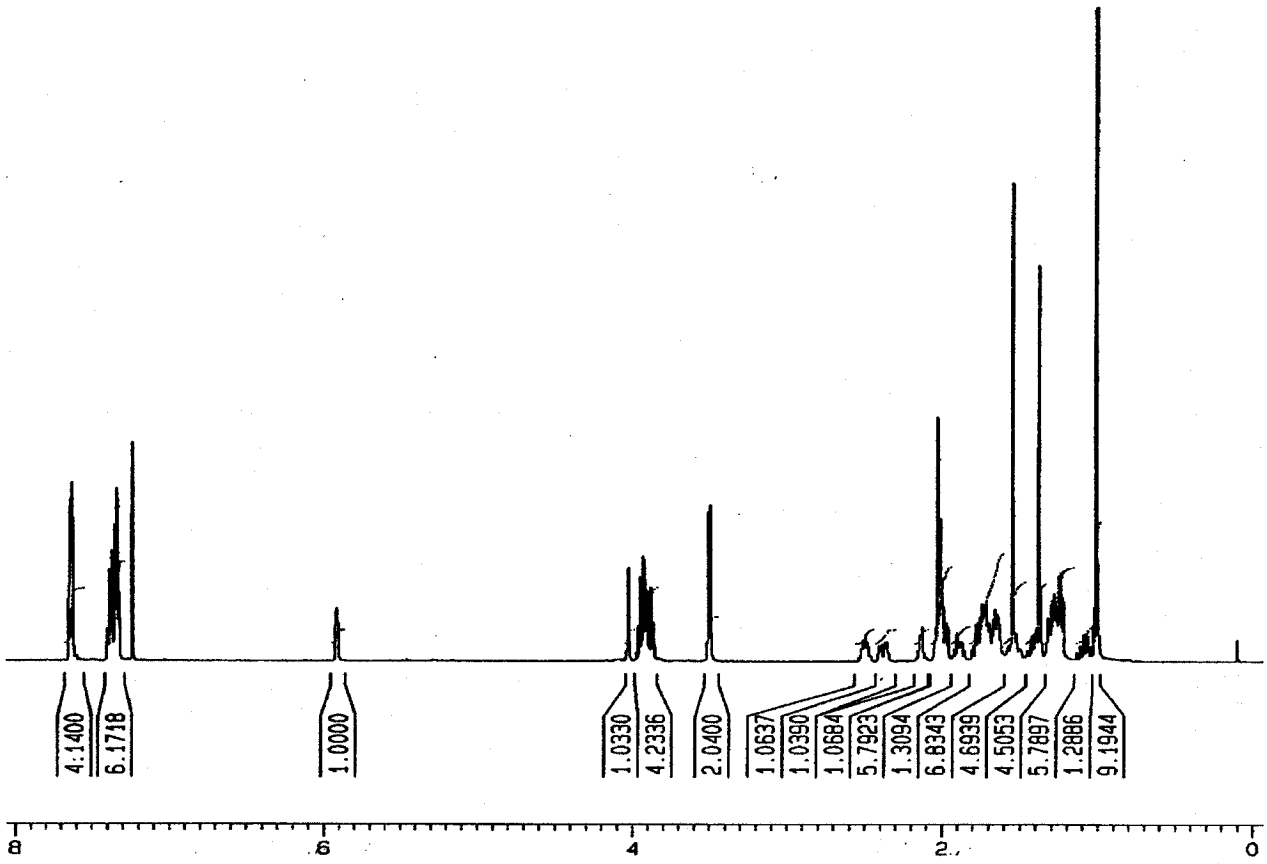


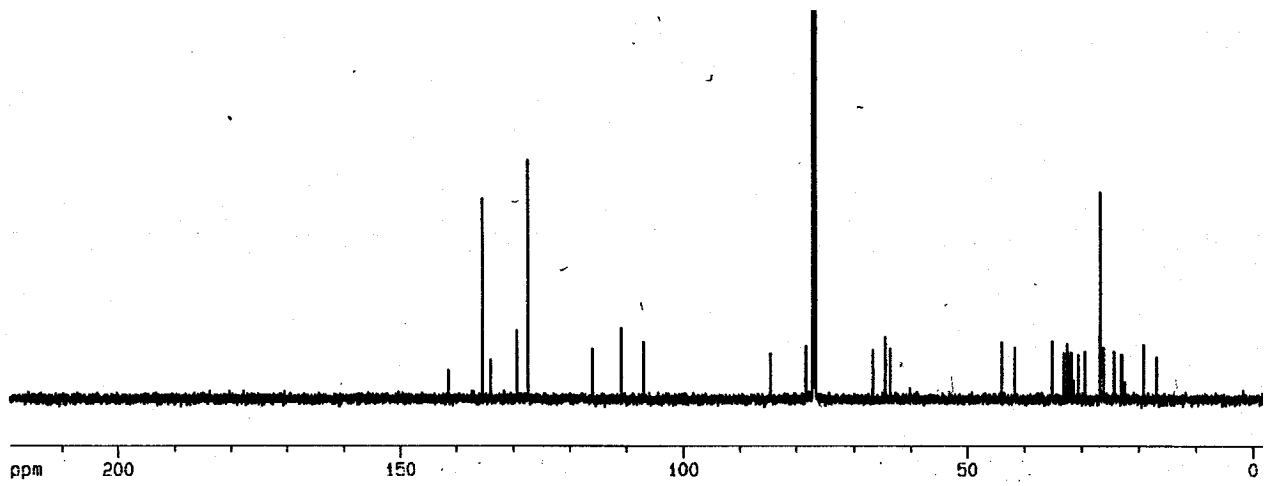


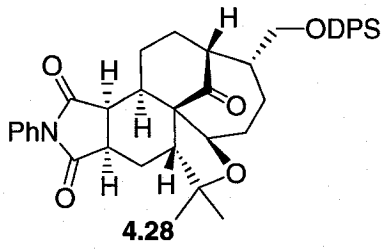
4.27

^{1}H NMR (300 MHz, $CDCl_3$)



^{13}C NMR (75 MHz, $CDCl_3$)

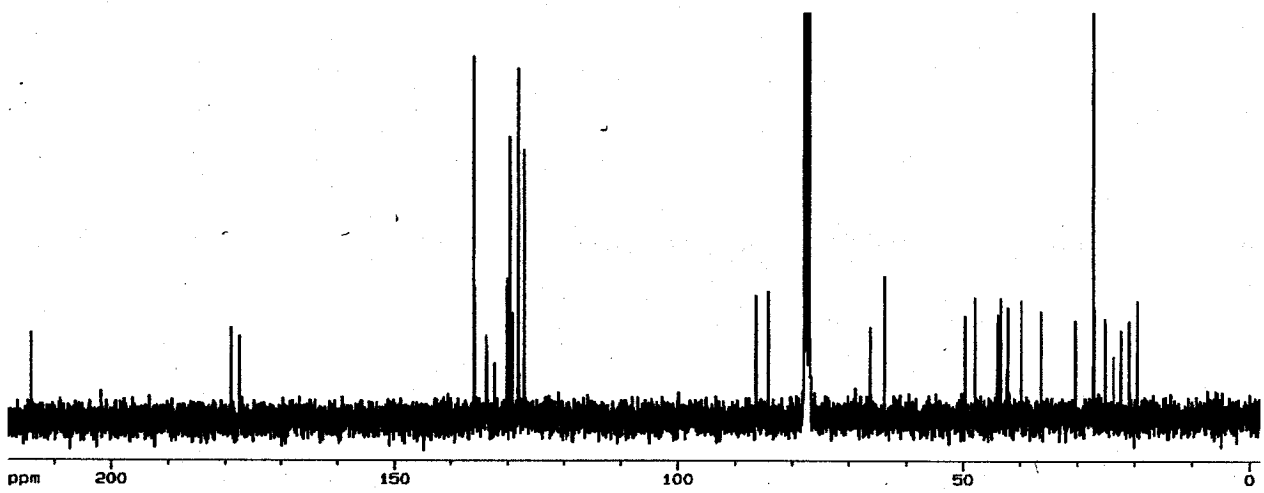


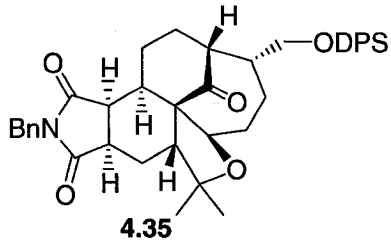


4.28

^{1}H NMR (300 MHz, $CDCl_3$)

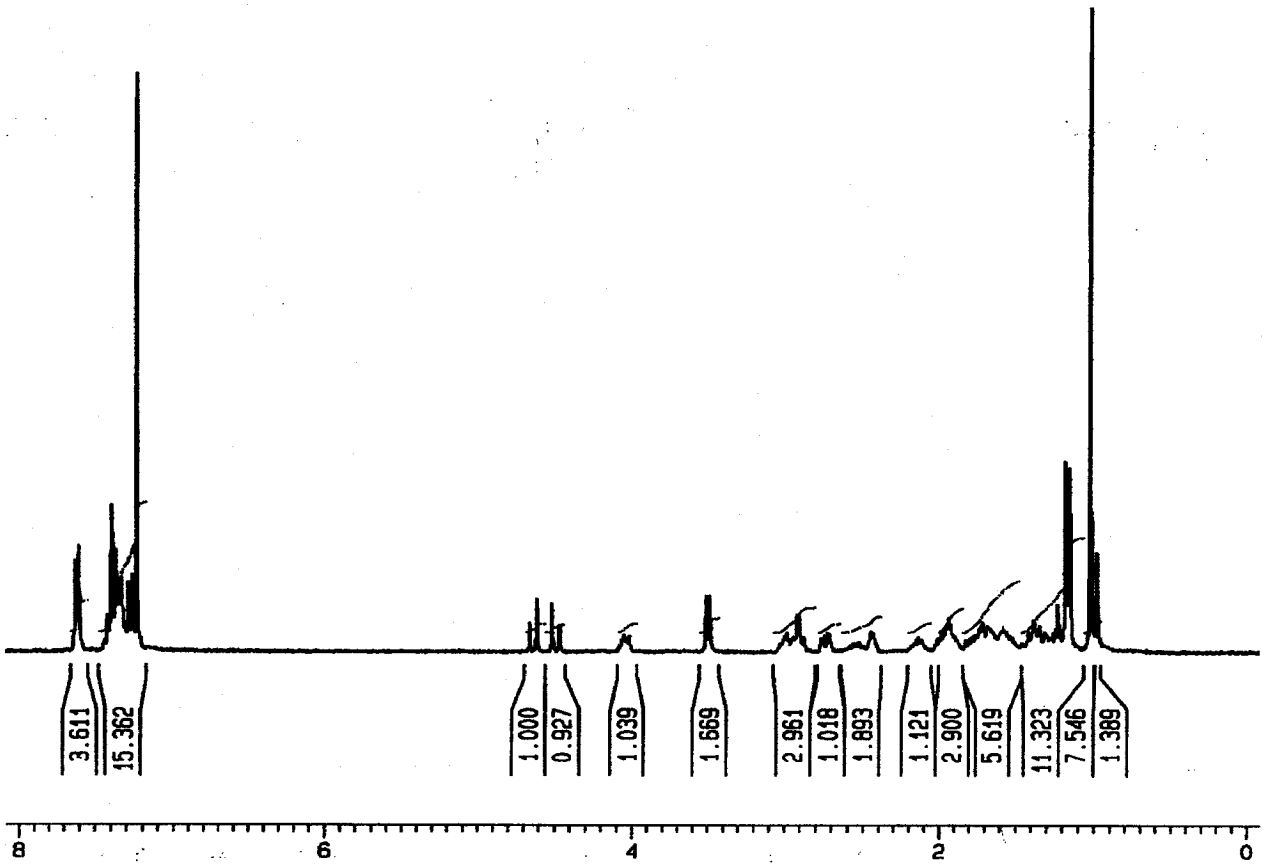
^{13}C NMR (75 MHz, $CDCl_3$)



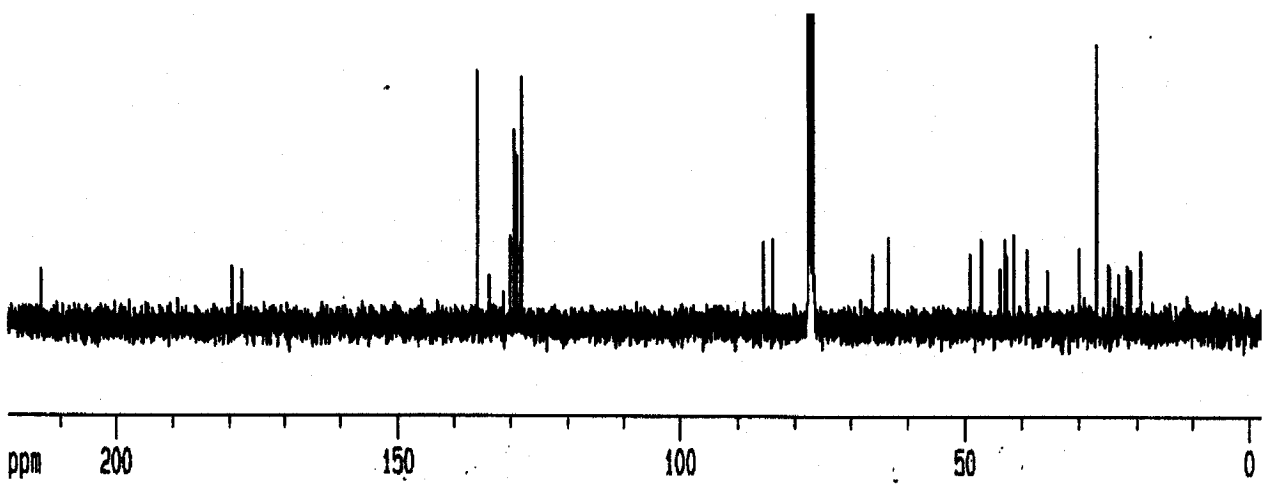


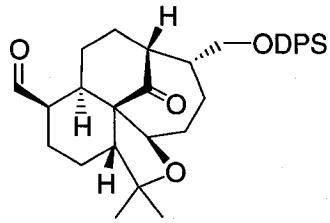
4.35

^{1}H NMR (300 MHz, $CDCl_3$)



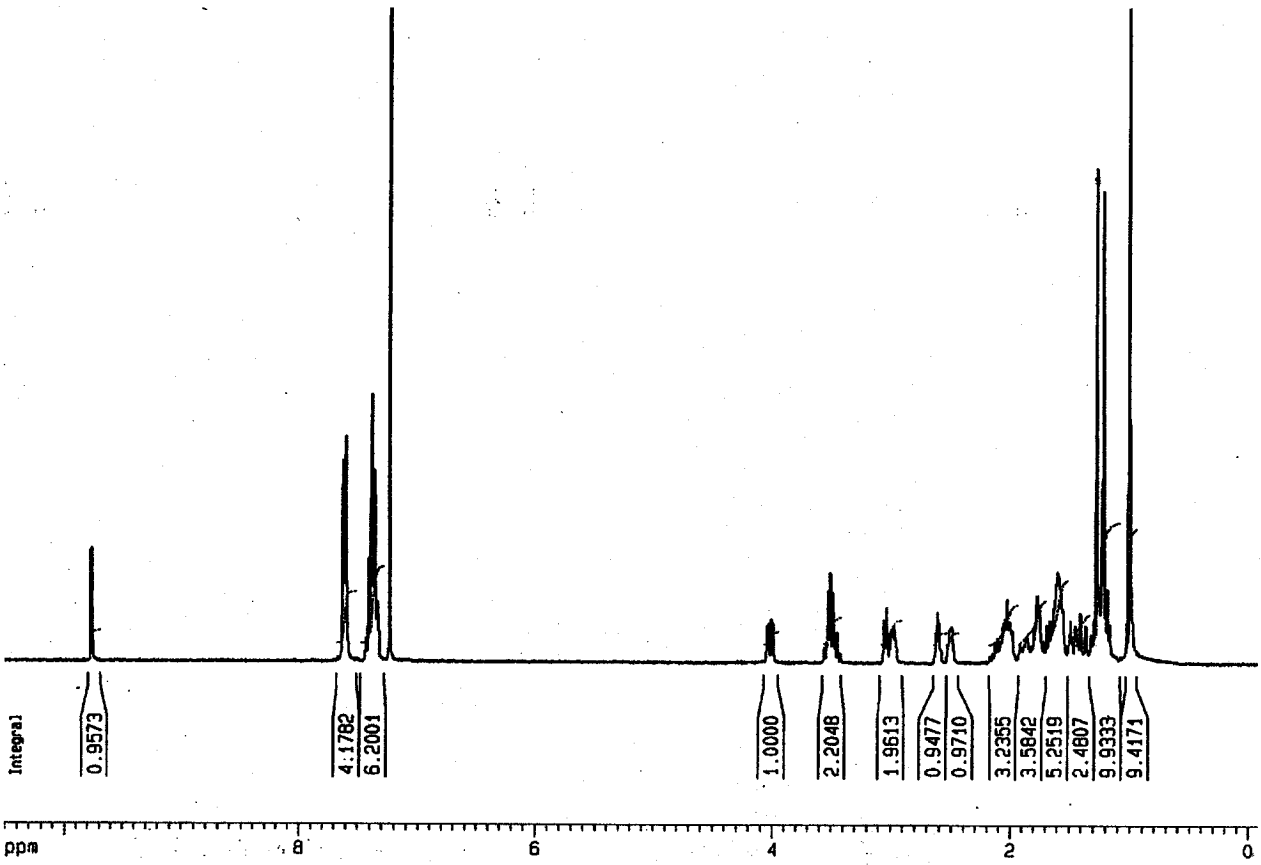
^{13}C NMR (75 MHz, $CDCl_3$)



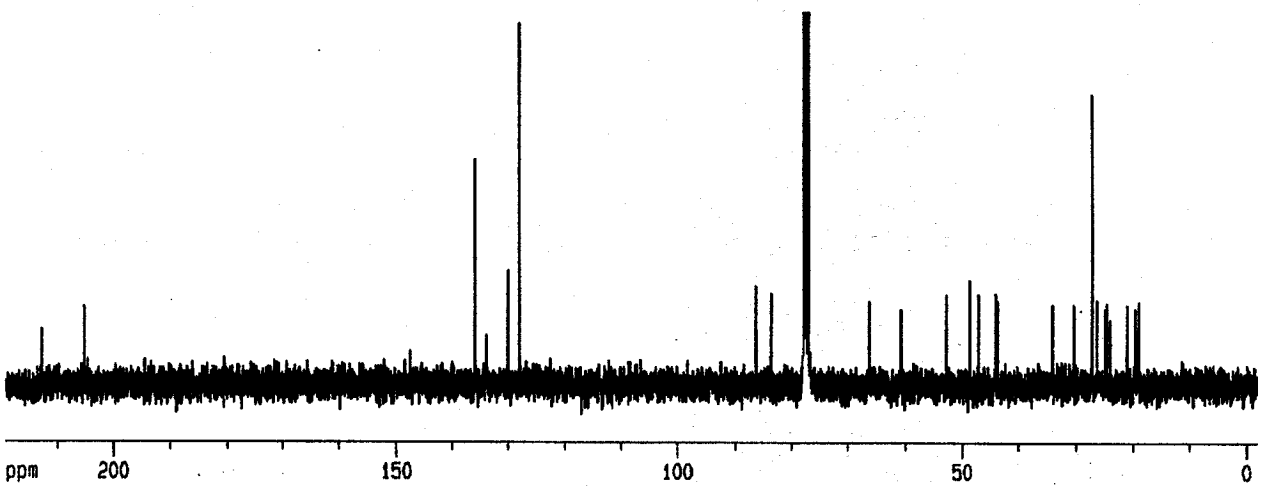


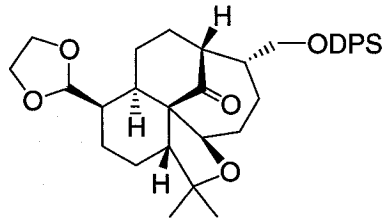
4.36

^{1}H NMR (300 MHz, $CDCl_3$)



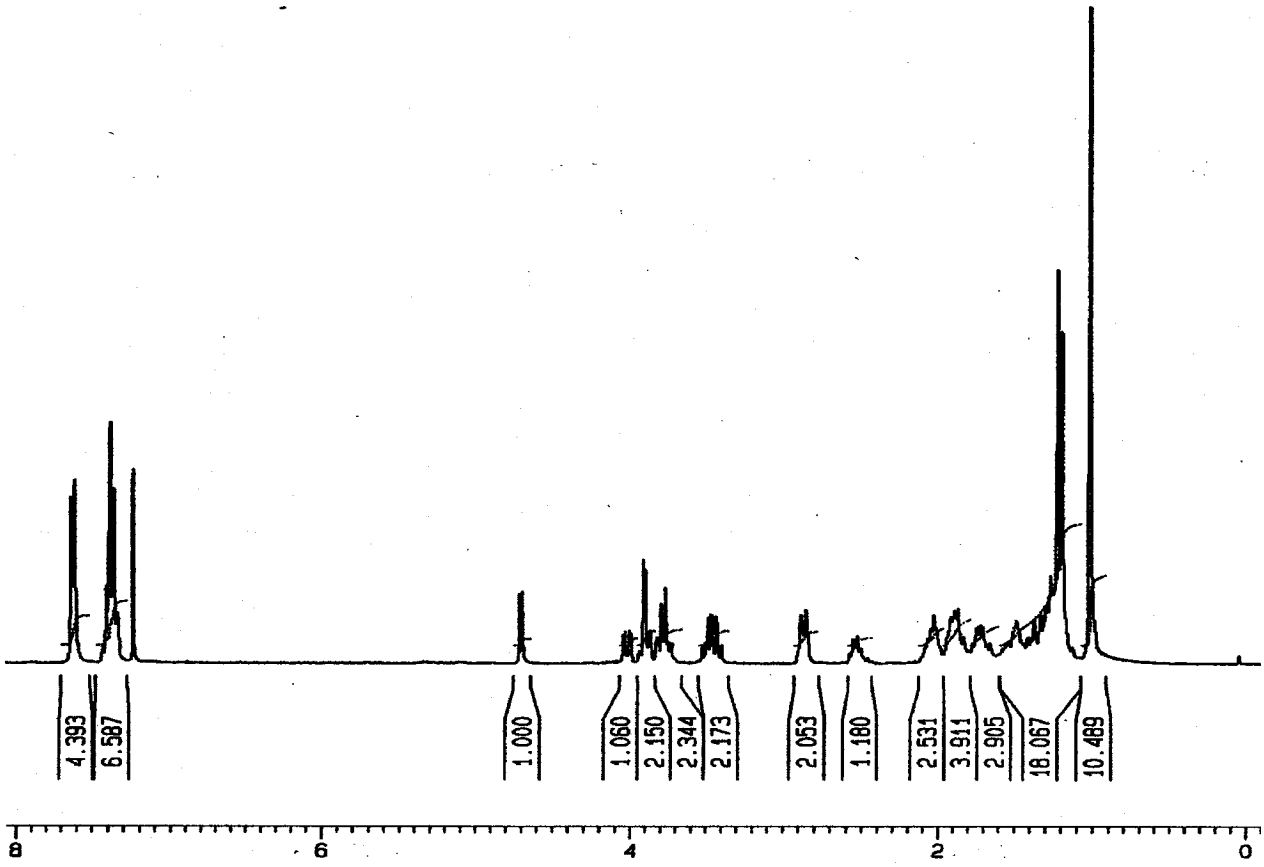
^{13}C NMR (75 MHz, $CDCl_3$)



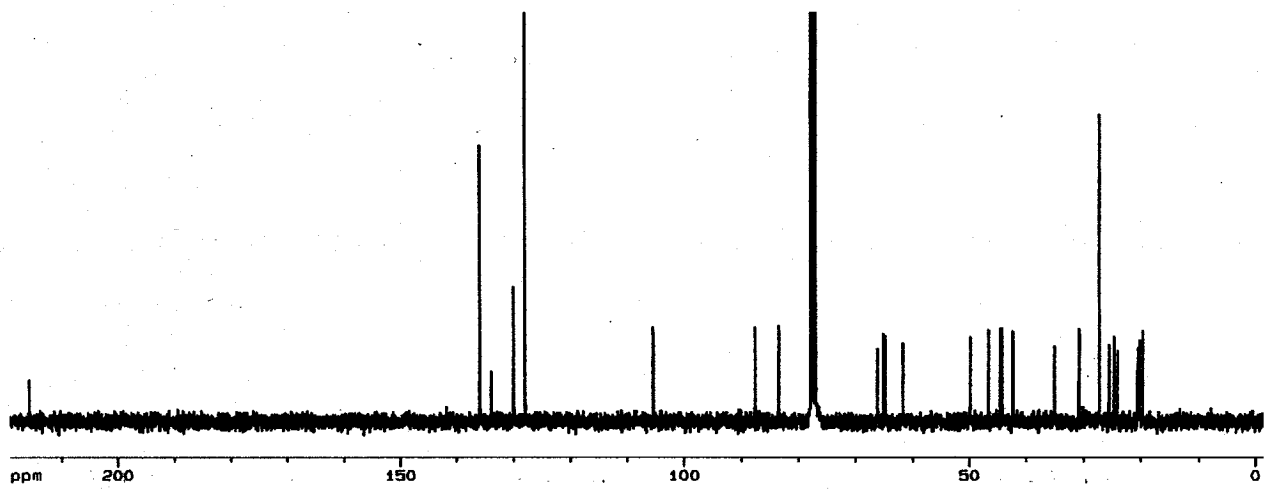


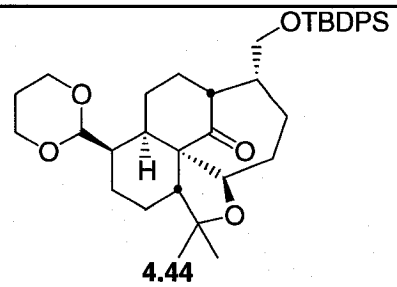
4.37

^{1}H NMR (300 MHz, $CDCl_3$)



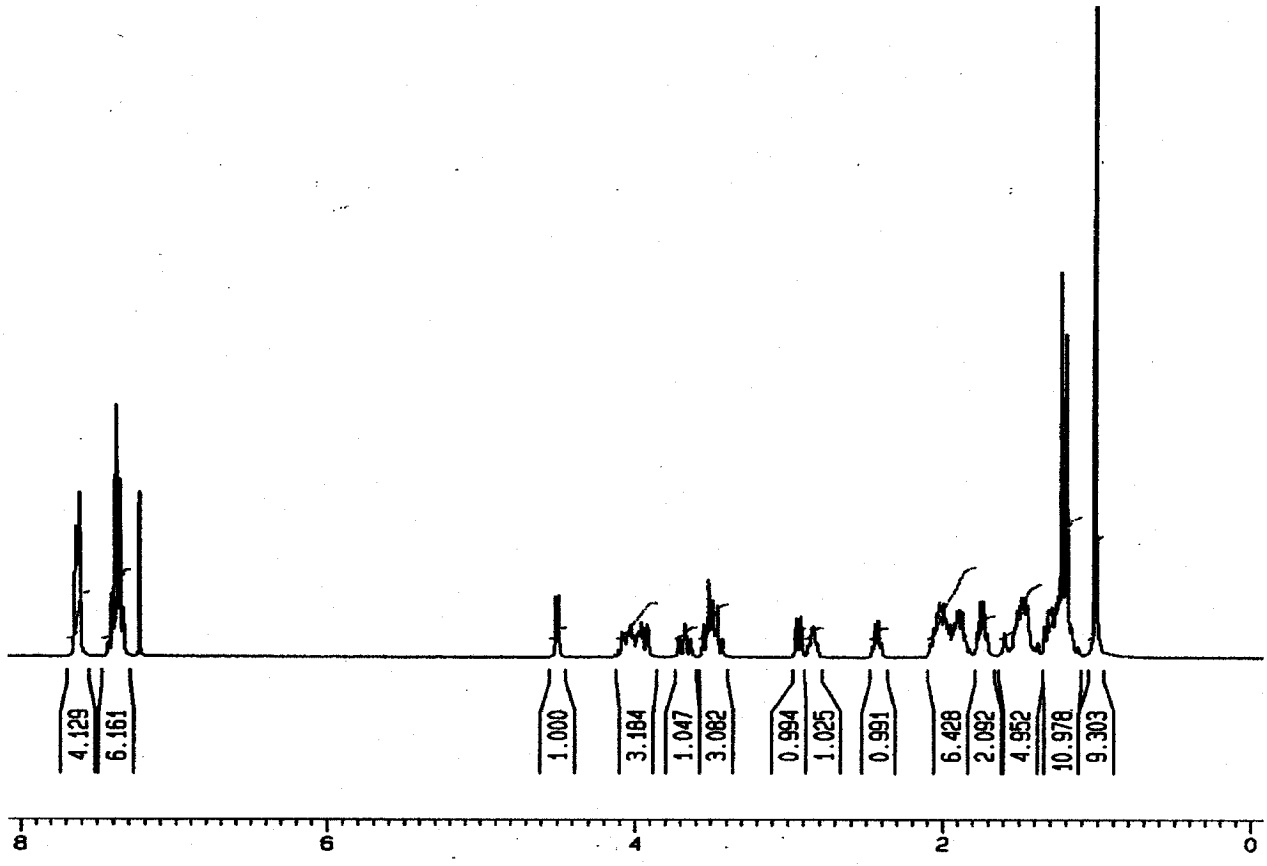
^{13}C NMR (75 MHz, $CDCl_3$)



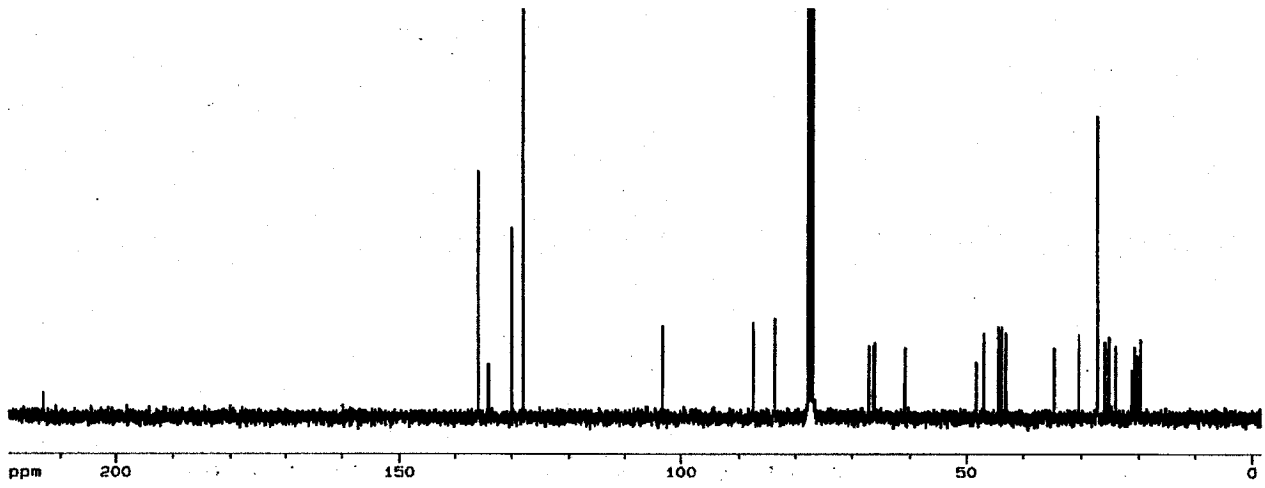


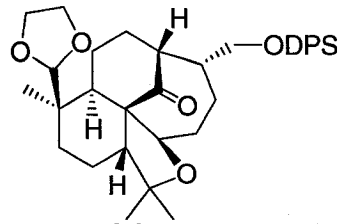
4.44

^{1}H NMR (300 MHz, $CDCl_3$)



^{13}C NMR (75 MHz, $CDCl_3$)





4.45

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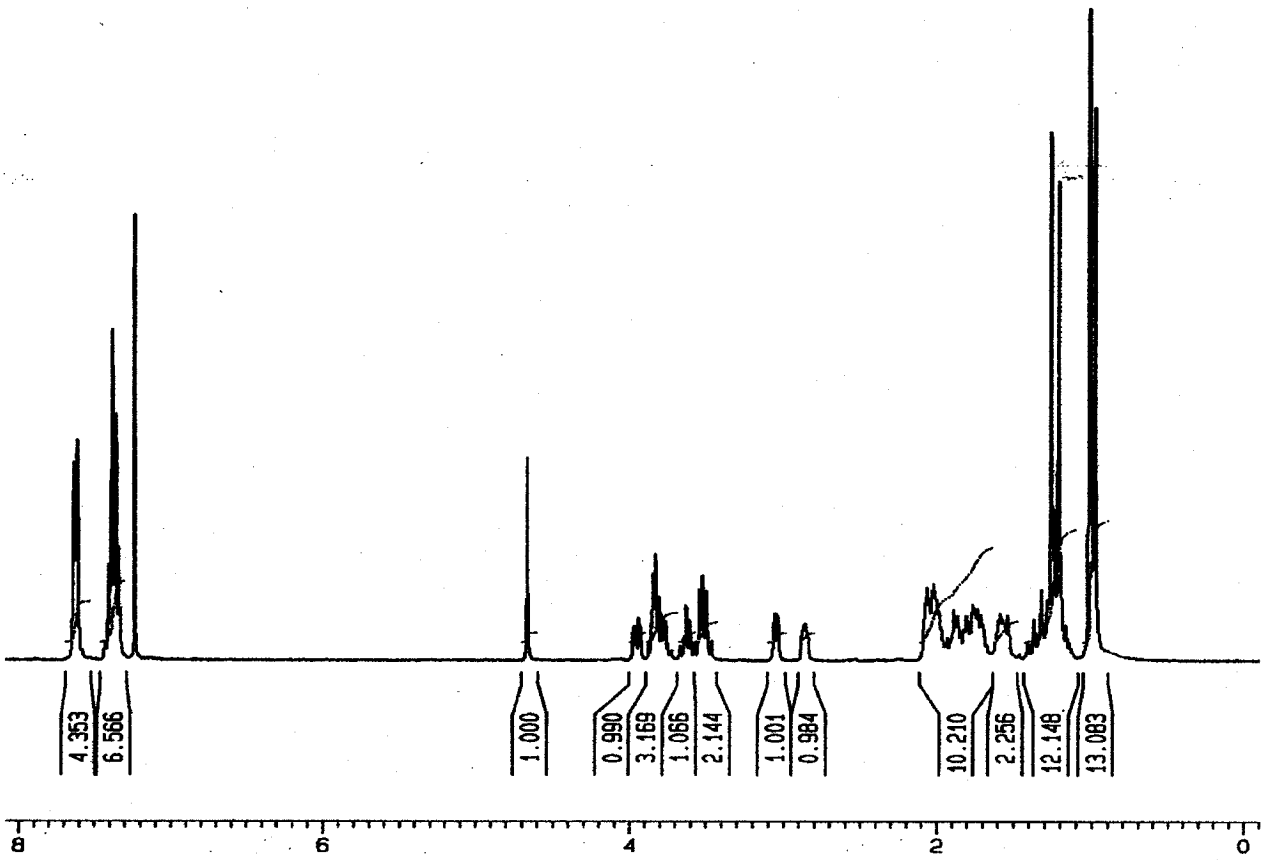
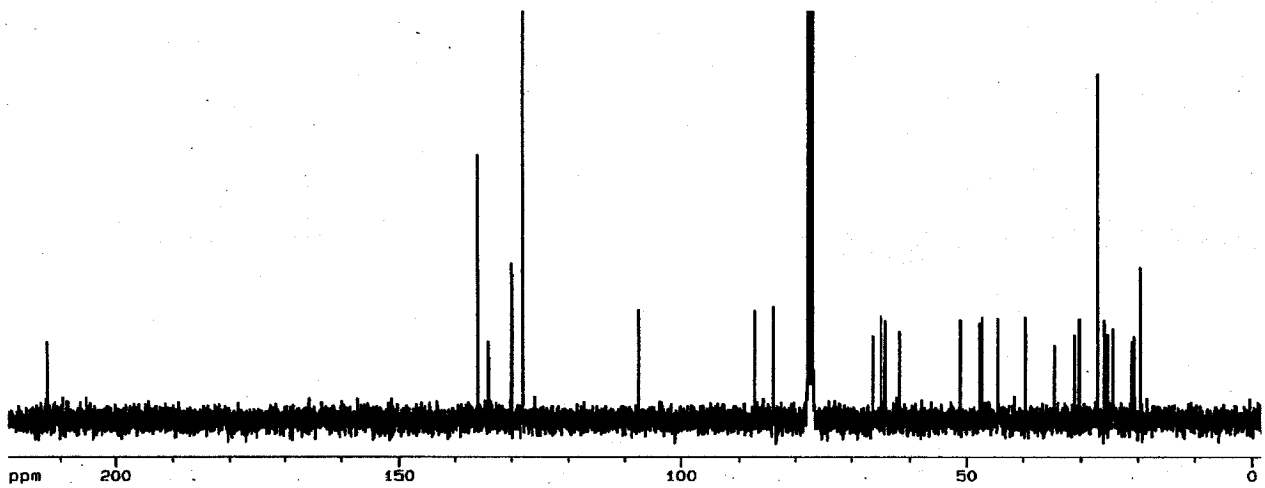
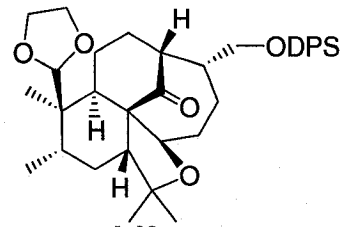


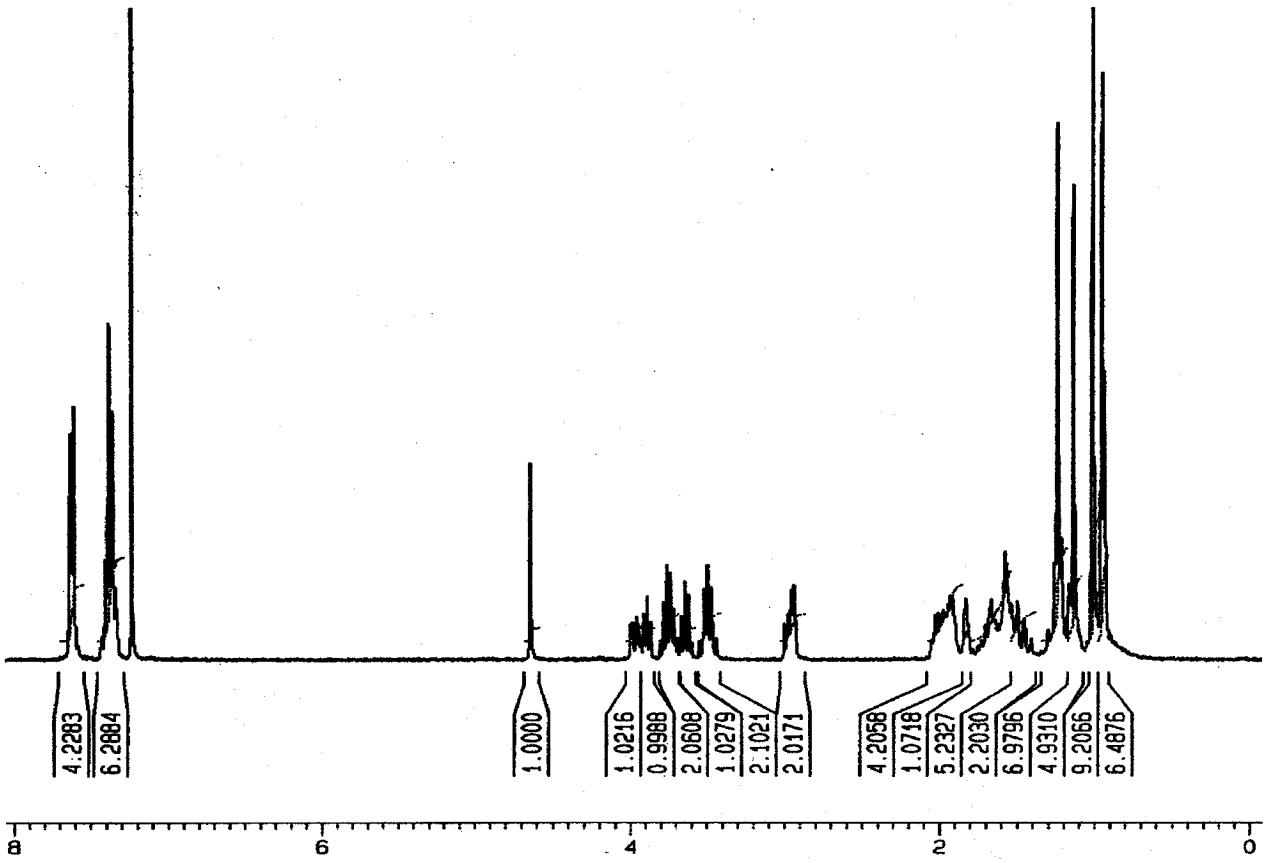
^{13}C NMR (75 MHz, $CDCl_3$)



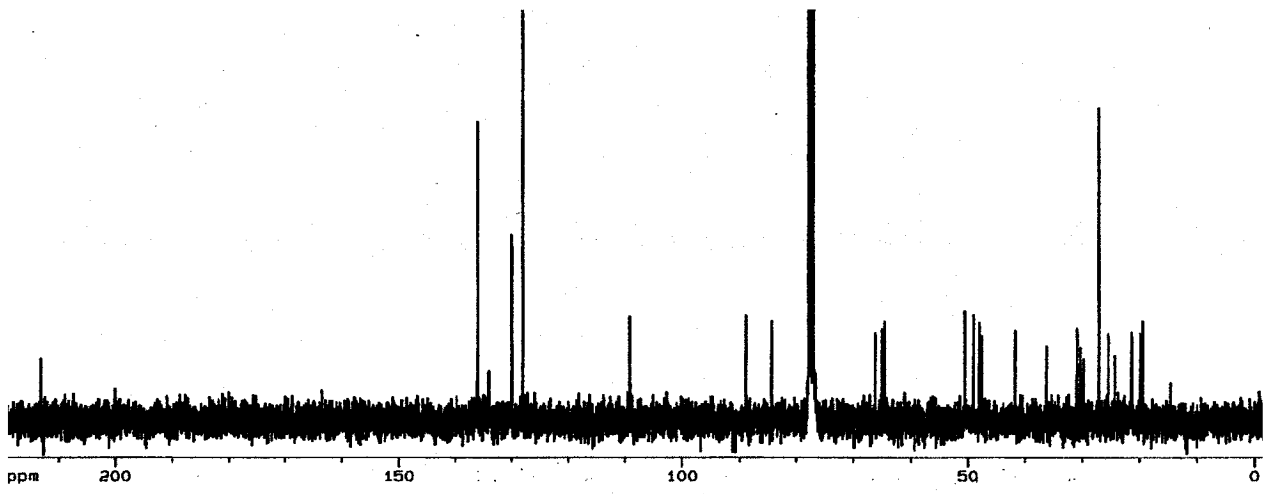


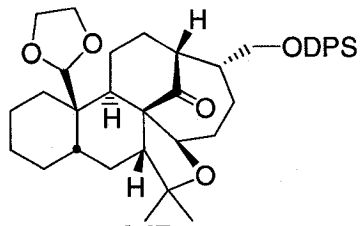
4.46

^{1}H NMR (300 MHz, $CDCl_3$)



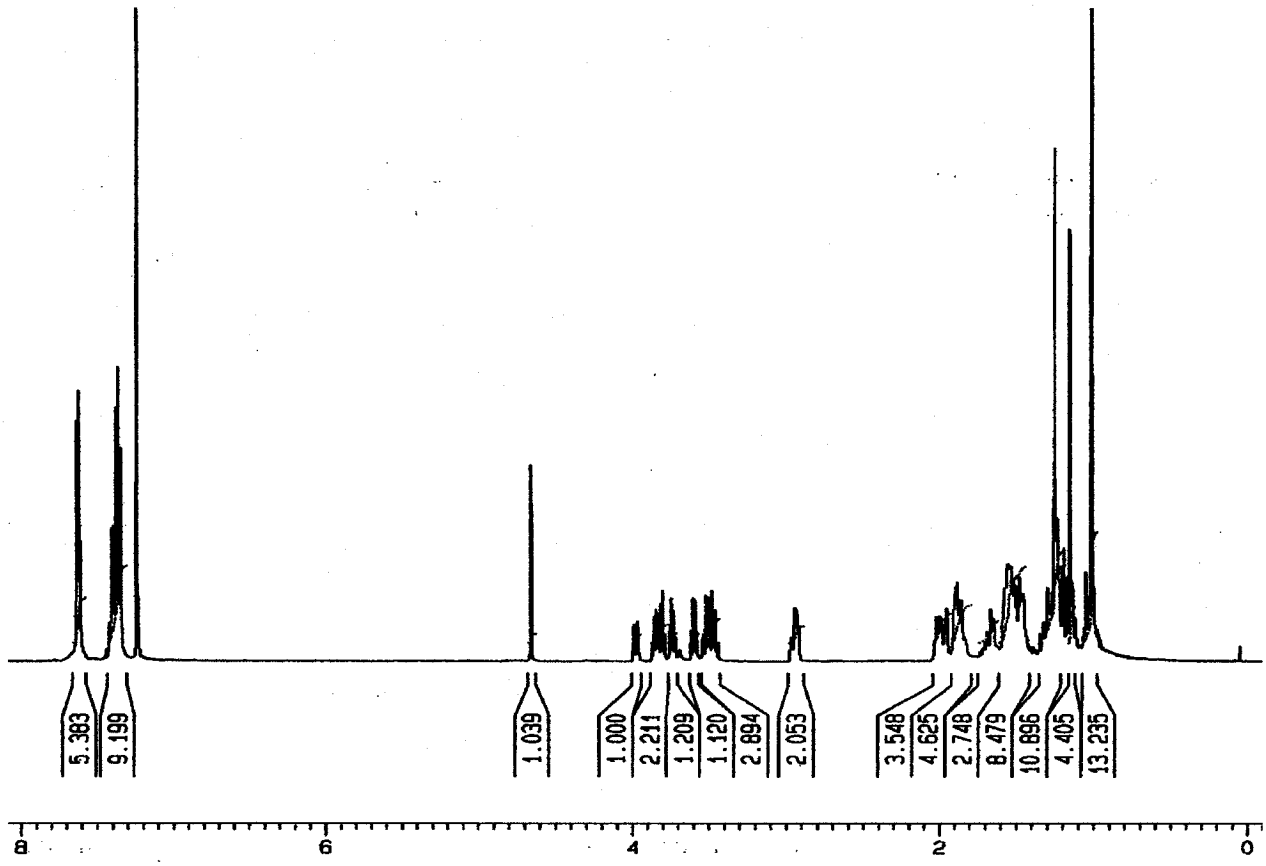
^{13}C NMR (75 MHz, $CDCl_3$)



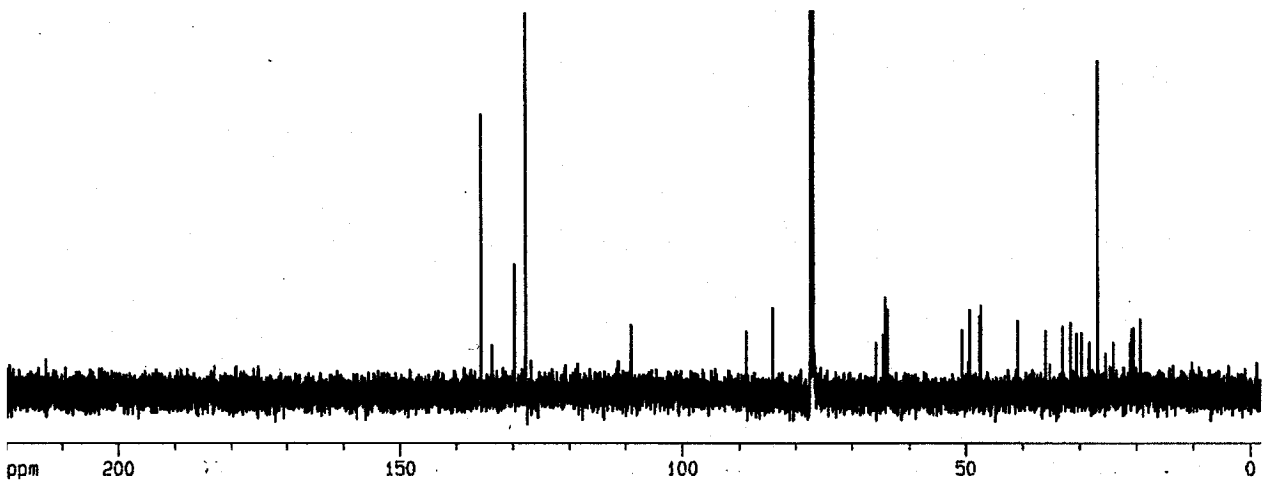


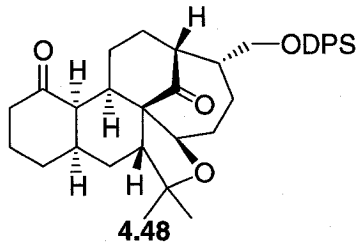
4.47

^{1}H NMR (500 MHz, $CDCl_3$)



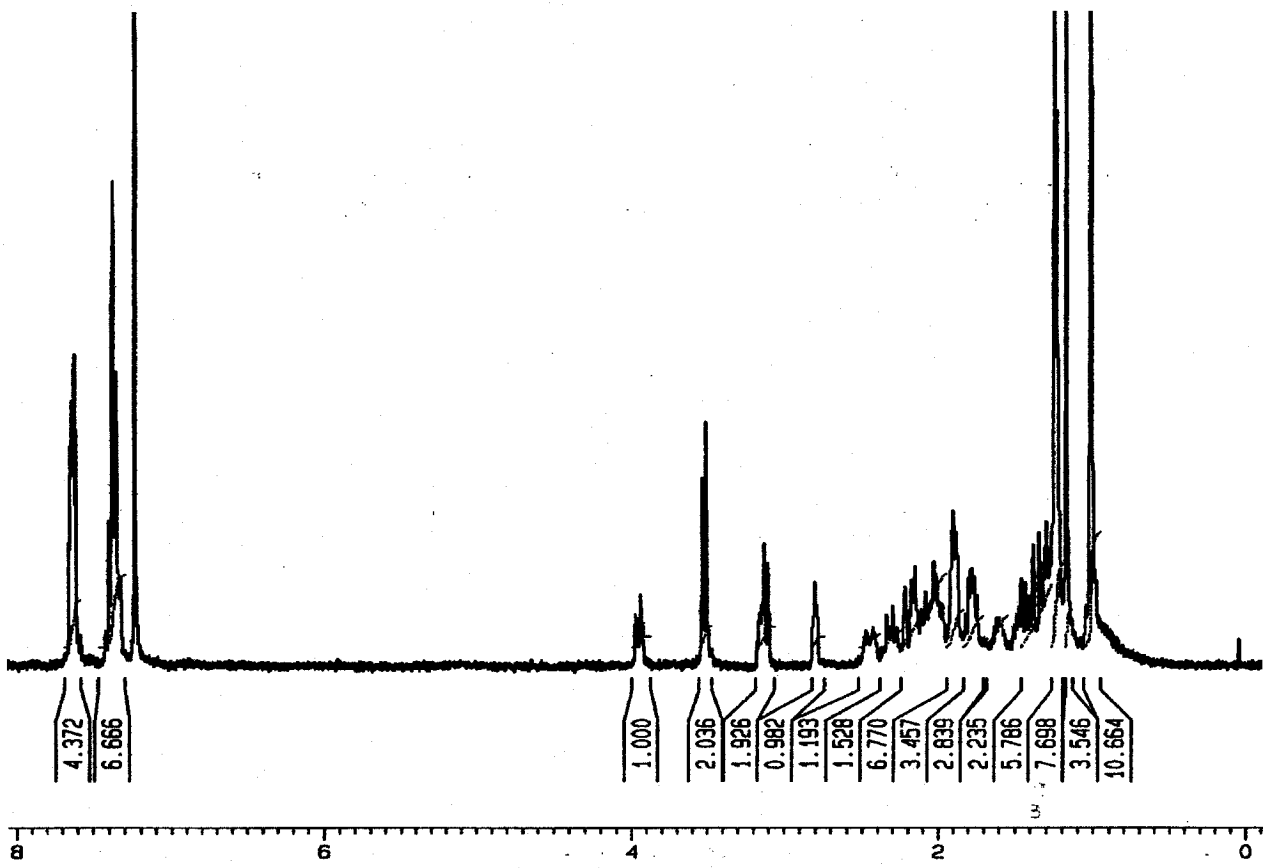
^{13}C NMR (125 MHz, $CDCl_3$)



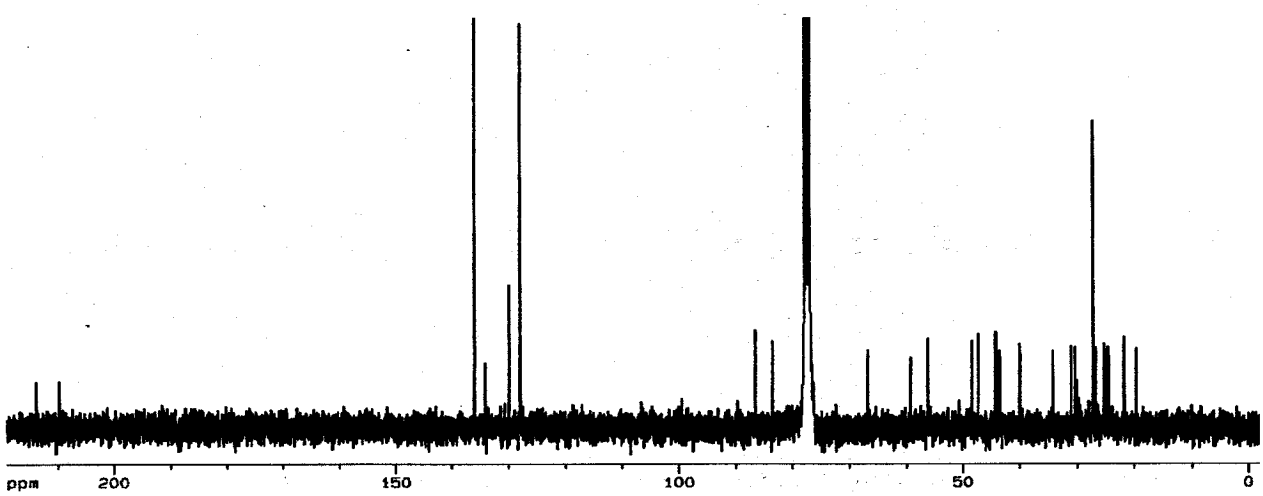


4.48

^{1}H NMR (300 MHz, $CDCl_3$)



^{13}C NMR (75 MHz, $CDCl_3$)



Glossary and Abbreviations

±	racemic
Ac	acetate
aq.	aqueous
Bn	benzyl
br	broad
Bz	benzoyl
COSY	correlation spectroscopy
d	doublet
DBU	1,8-diazobicyclo[5.4.0]undec-7-ene
DCE	1,2-dichloroethane
DCM	dichloromethane
DDQ	2,3-dichloro-5,6-dicyano-*p*-benzoquinone
decomp.	decomposition
DMAP	4-dimethylaminopyridine
DME	1,2-dimethoxyethane
DMF	*N*,*N*-dimethylformamide
DMP	Dess-Martin periodinane
DTBMP	2,6-di-*tert*-butyl-4-methylpyridine
DPS	*tert*-butyldiphenylsilyl
EI	electron ionization
eq.	equivalents
Et	ethyl
Et_2O	diethyl ether
Et_3N	triethylamine
EtOAc	ethyl acetate

HMBC	heteronuclear multiple bond correlations
HRMS	high resolution mass spectrometry
i-Pr	isopropyl
IR	infrared
J	coupling constant
KHMDS	potassium hexamethyldisilazane
m	multiplet or medium
M^+	molecular ion
m-CPBA	3-chloroperoxybenzoic acid
Me	methyl
Mes	2,4,6-trimethyl phenyl
MOM	methoxymethyl ether
MS	molecular sieves
NMO	*N*-methylmorpholine *N*-oxide
NMR	nuclear magnetic resonance
NOE	nuclear Overhauser effect
NOESY	nuclear Overhauser effect spectroscopy
PA	*para*-anisaldehyde
PCC	pyridinium chlorochromate
PG	protecting group
Ph	phenyl
PMB	*para*-methoxybenzyl
ppm	parts per million
PTSA	*para*-toluene sulphonic acid
q	quartet
quant.	quantitative yield
Rf	retention factor
r.t.	room temperature
s	singlet or strong
t	triplet
TBAF	tetrabutylammonium fluoride

TBS	*tert*-butyldimethylsilyl
t-Bu	*tert*-butyl
TES	triethylsilyl
Tf	trifluoromethylsulfone
Tfa	trifluoroacetate
THF	tetrahydrofuran
TIPS	triisopropylsilyl
TLC	thin layer chromatography
TMS	trimethylsilyl
TOCSY	totally correlated spectroscopy
w	weak

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