Synthetic Study on (+)-Obtusenyne

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ABBREVIATIONS

Ac	acetyl
AcOH	acetic acid
AIBN	2,2'-azobisisobutyronitrile
aq	aqueous
Ar	aryl
Bn	benzyl
Bu	butyl
CSA	camphorsulfonic acid
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCE	dichloroethane
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DEAD	diethyl azodicaboxylate
DIBAL	diisobutylaluminum hydride
DMAP	*N*,*N*-dimethylaminopyridine
DMF	dimethylformamide
DMSO	dimethylsulfoxide
EDCI	*N*-Ethyl-*N*-(3-dimethylaminopropyl)carbodiimide hydrochloride
Et	ethyl
Fod	tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedionate)
hfa	hexafluoroacetylacetonate
HMPA	hexamethylphosphoric triamide
HMPT	hexamethylphosphorous triamide
i-Pr	isopropyl
KHMDS	potassium hexamethyldisilazide
L.A.	Lewis acid
LAH	lithium aluminum hydride

Mc	monochloromethanesulfonyl (monochlart)
MCPBA	*m*-chloroperoxybenzoic acid
Me	methyl
MEM	2-methoxyethoxymethyl
^{2}MPM	*m*-methoxybenzyl
^{4}MPM	*p*-methoxybenzyl
MS	molecular sieves
Ms	methanesulfonyl (mesylate)
NaHMDS	sodium hexametyldisilazide
NMR	nuclear magnetic resonance
NOE	nuclear Overhauser effect
oct	octyl
Ph	phenyl
PPTS	pyridinium *p*-toluenesulfonate
Py	pyridine
Red-Al	sodium bis(2-methoxyethoxy)aluminum hydride
SET	single electron transfer
t-Bu	*tert*-butyl
TBAF	tetrabutylammonium fluoride
TBDPS	*tert*-butyldiphenulsilyl
TBHP	*tert*-butylhydroperoxide
TBS	*tert*-butyldimethylsilyl
TCDI	thiocarbonyldiimidazole
TEA	triethylamine
Tf	trifluoromethanesulfonyl
THF	tetrahydrofuran
TLC	thin layer chromatography
TMS	trimethylsilyl

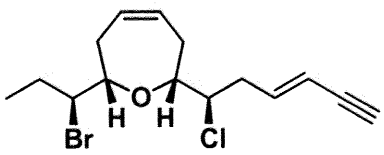
Ts	*p*-toluenesulfonyl (tosyl)

Chapter 1

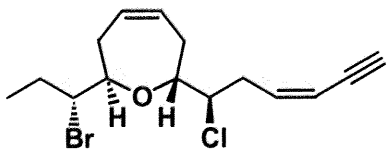
Introduction

1.1 Prologue

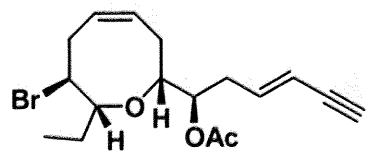
Recently, the advancement of analytical ability on NMR instrument and the development of new strategies for measurement bring a rapid progress in a field of natural compound chemistry. From this point of view, the structure determination for a small amount of sample has been achieved and great amounts of intriguing compounds have been discovered from nature by now. Above all, marine organic substrates are expected to have interesting structures and unique biological activities. Thus, marine natural products which have not been familiar yet have a possibility as a new medicine and an opportunity as a lead compound having newly action mechanism for various diseases. Additionally, ciguatoxins[1] which is the principal causative toxins for ciguatera seafood poisoning, brevetoxins[2] which is produced by the red tide organism, yessotoxin[3] which is shellfish biotoxin and so on, the representative toxic polycyclic ether compounds also have been discovered from worldwide sea. Since these compounds have extremely strong toxicity and unique ladder structure as a common part, which involve medium-sized ring as a part of the assemblage, they are attracting numerous attention from science community. Because of these issues, the research of various marine products has been conducted enthusiastically all over the world.



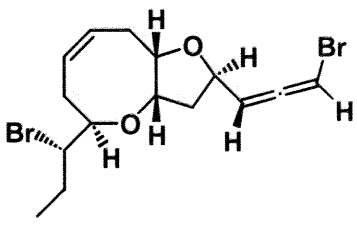
(+)-isolaurepinnacin (1)



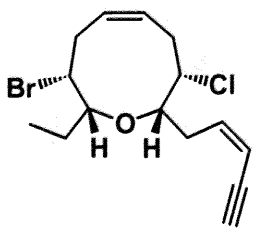
(+)-rogioloxepane (2)



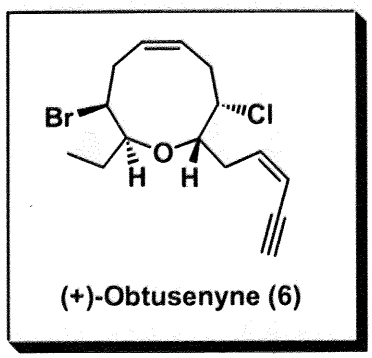
(+)-laurencin (3)



(+)-laurallene (4)



(-)-12,13-*epi*-Obtusenyne (5)



(+)-Obtusenyne (6)

Fig.1 Medium-sized Oxacyclics from Marine Sources

Among many marine sources, the *Laurencia* red algae, in particular, have produced a large number of metabolites containing medium-sized ring ether acetogenins[4]. Representative compounds are illustrated in Fig.1. These compounds have harogen substituents, *cis* or *trans*-enyne moiety and α,α'-alkyl side chain as common structures. Since their biological activities have not fully known yet and quantity of the samples from nature is a little, the supply by organic synthetic methodology is demanded. The efficient construction of medium-sized ring ether and stereocontrol at the α,α'-alkyl position are a key point in total synthesis of these compounds. Therefore, these are paid attention by many chemists and the synthetic studies utilizing various strategies are carried out.

Since the assemblage of medium ring ether is disadvantage in the terms of entropy due to the long distance between reaction points as well as transannular repulsion, its construction needs especial protocol. At present a large number of the total synthesis of compounds involving medium-sized ring ether have been achieved by utilizing various strategies[5]. At any case, stereoselective and effective methodologies have been devised to assemble medium-sized ring ether.

1.2 Biogenetic Synthesis of Medium-sized Oxacyclics

The biogenetic pathway of acetogenin family is proposed as the following scheme[6] (fig.2). Namely, all the medium-sized oxacycles isolated from red algae are derived from laurediol, common intermediate in biosynthetic chemistry (Fig.2). Laurediols have two asymmetric centers in its structure and moreover, various geometric isomers exist. Cyclization on their compounds proceeds though enzymatic bromoetheration-mechanism promoted by bromoperoxydase (BPO) via various cyclization-forms. For example, (+)-*cis*-dihydrorhodophytin (**4**) and (+)-obtusenyne (**6**) are obtained from (6R, 7S)-laurediol via 8-*exo* mode cyclization and 9-*endo* mode cyclization, respectively. Since laurediol have various isomers and BPO also have some sorts, so that a large number of natural products are generated in the end.

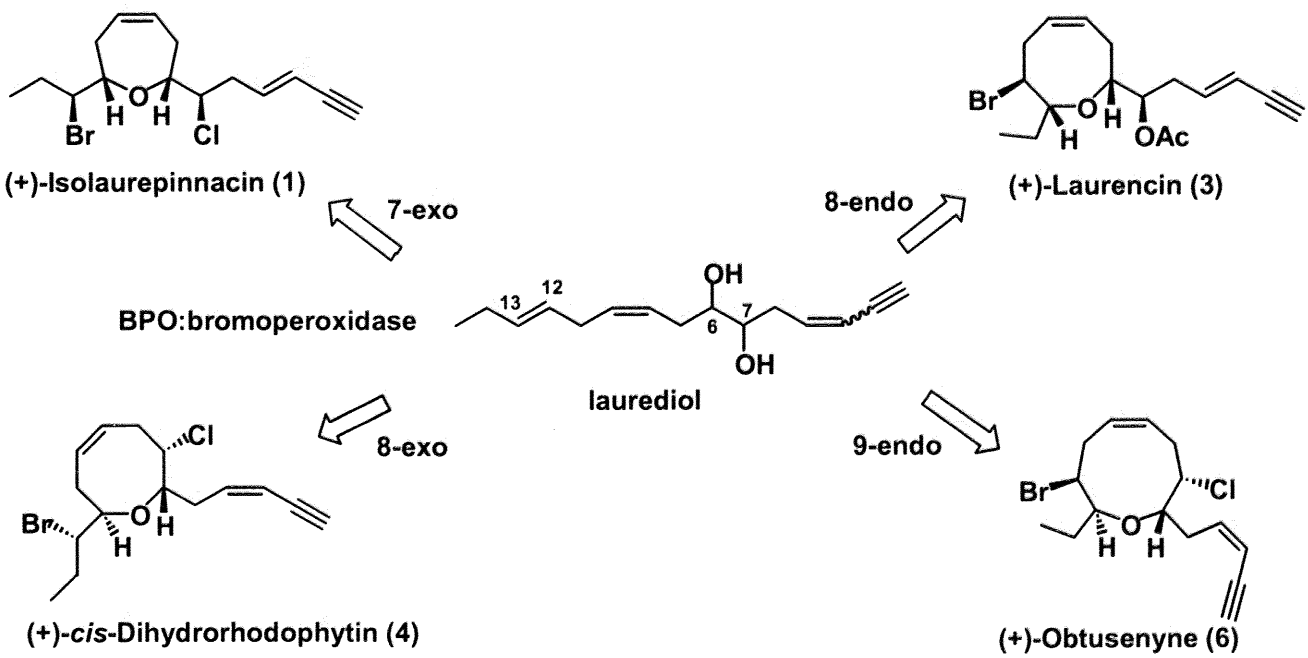


Fig.2 Biogenetic Synthesis of Medium-sized Oxacyclics

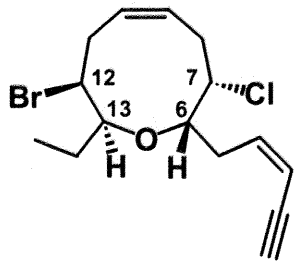
In the field of bioorganic chemistry, medium-sized oxacyclics are easily formed, however, it is quite difficult in the field of organic synthetic chemistry as above mentioned. In addition, quantitative and selective synthesis is impossible on biomimetic pathway, even though the assemblage of natural product can be easily formed. Therefore, the approach using organic synthesis is required to supply large quantities of natural product. Herein, the author reports on the total synthesis of (+)-obtusenyne.

Chapter 2

Examples of the Total Synthesis of (+)-Obtusenyne

2.1 Introduction of (+)-Obtusenyne

(+)-Obtusenyne which belongs to nonterpenoid was isolated from red alga *laurencia obtusa* by King's group[1] in the Agean Sea and Fenical's group[2] at Positano, Italy independently. The structure and absolute configuration were identified by a combination of single X-ray crystallography and spectroscopic analysis[1]. The structural features are unusual nine-membered ring ether with substituents in *trans*-orientation, a (*Z*)-enyne terminus and bromo (C12) and chloro (C7) substituents. Because the construction of nine-membered ring ether is the most difficult in medium-sized ethereal ring and moreover, transannular repulsion of oxonene skeleton that substituents at α and α' position are in *trans*-orientation is much more than that in *cis*-orientation. Therefore, the accomplishment of (+)-obtusenyne would be one of the most formidable subject in natural products possessing medium-sized cyclic ether of single-ring system. Motivated by the challenging structure of (+)-obtusenyne, many organic chemists launch the synthesis.



(+)-Obtusenyne (6)

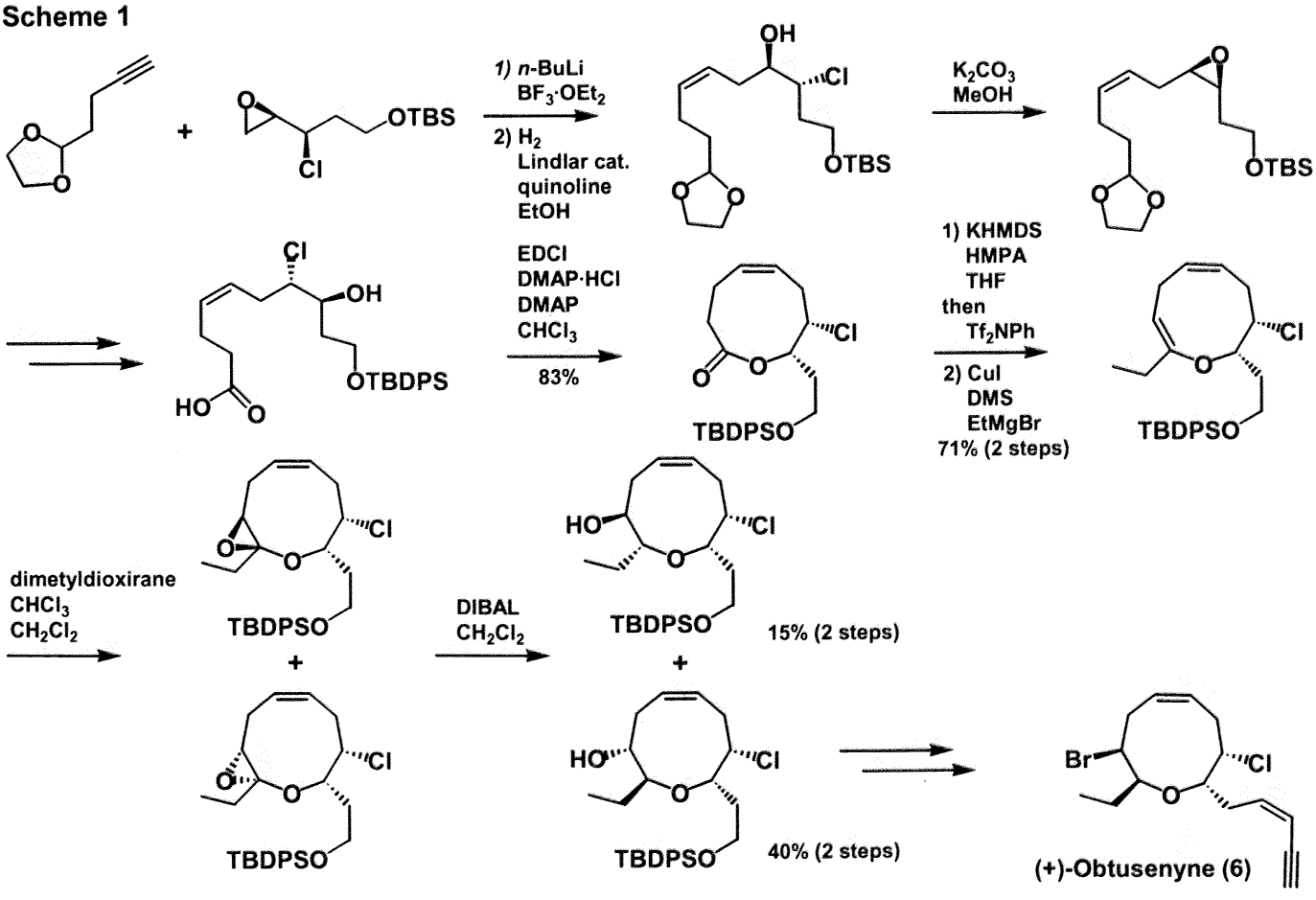
The first total synthesis of (+)-obtusenyne was reported by Murai's group[3] in 1999. Then, the second synthesis using olefin methathesis reaction by Crimmins' group[4] and recently, the synthesis involving Claisen rearrangement and intramolecular hydrosilation as key steps by Holmes' group[5] were accomplished.

The abstracts about their synthesis are outlined below.

2.2.1 First Total Synthesis of (+)-Obtusenyne by Murai's group [3]

His group developed a new synthetic methodology using lactones in order to construct medium-sized ethers. The synthesis was begun from coupling reaction of acetylene and epoxide by Yamaguchi's method [6]. To prepare the acyclic precursor, the partial reduction of triple bond, conversion into epoxide and subsequent multiple steps were conducted. With the carboxylic acid in hand, the intramolecular lactonization [7] was carried out and the expected nine-membered lactone was afforded in high yield. Incidentally, it is reported that the formation of a nine-membered lactone is easier than that of a nine-membered ether. The alkylation of enol triflate derived from the corresponding lactones with diethyl cuprate led to cyclic dienyl ether, whose epoxidation with diethyldioxirane afforded two epoxides as diastereomeric mixture. The mixture was reduced with DIBAL in CH_2Cl_2 to give alcohols (40% and 19%, respectively, based on the consumption of dienyl ether).

Scheme 1



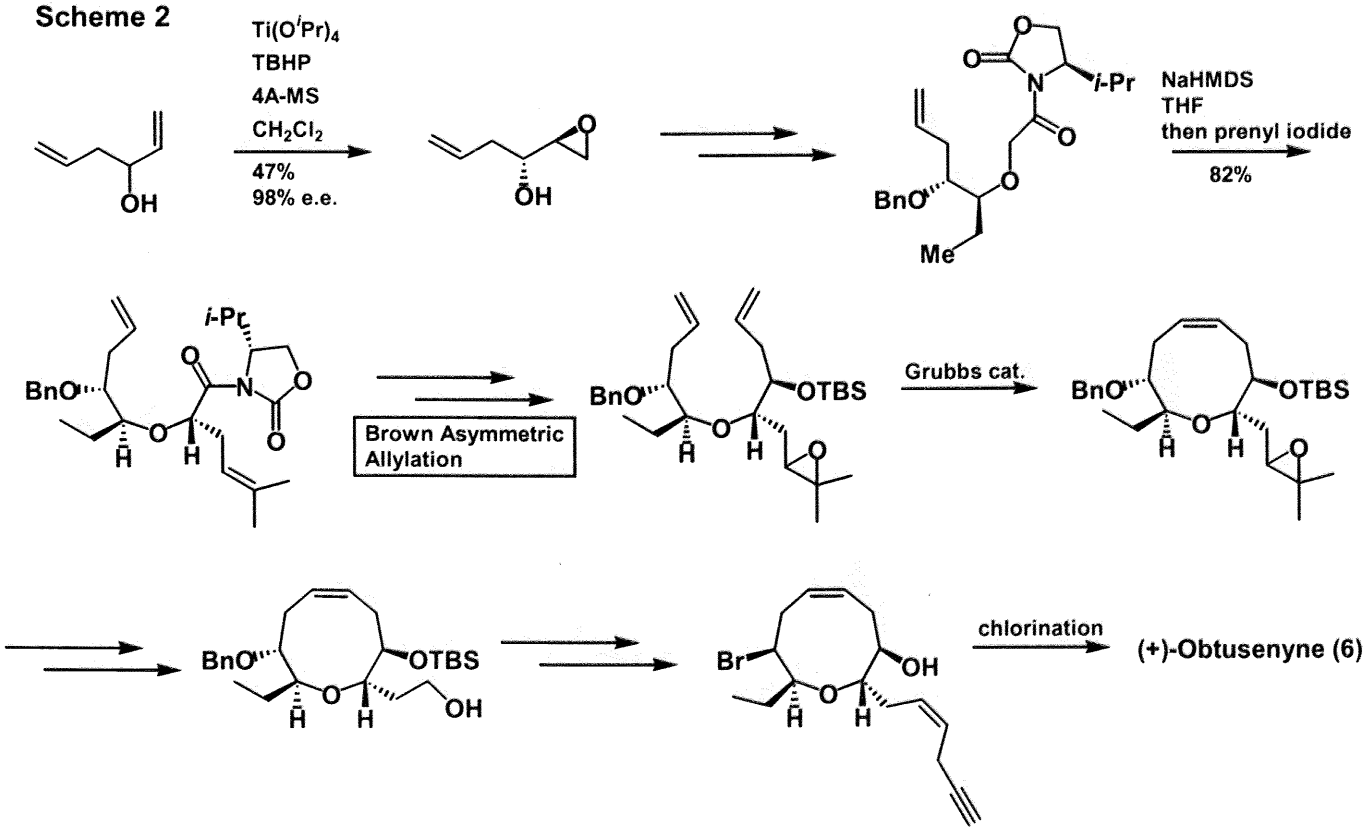
Stereochemistry of the obtained cyclic ether was assigned by NOE experiment so that it was confirmed that the major isomer had the *trans* relationship between the α- and α'-position. The major product was then converted into (+)-obtusenyne via several steps.

By utilizing this enol ether, the total synthesis of (+)-obtusenyne was briefly accomplished. Although the approach was superior in terms of effective and brief synthesis of medium-sized oxacyclics, difficulty of the stereocontrol on the α- and α'-positions was inevitable due to introduction of the stereocenters via the enol ethers.

2.2.2 Second Total Synthesis using RCM (Ring-Closing-Metathesis) Reaction by Crimmins' group [4]

In 2003, total synthesis of (+)-obtusenyne using ring-closing metathesis reaction[8] was reported by Crimmins' group. 1,5-Hexadien-3-ol, the starting material was exposed to a standard Sharpless kinetic resolution[9] and then the furnished epoxide was lead to oxazolidinone[10] compound via several steps. Subsequently, Evans asymmetric aldol reaction was undertaken to introduce prenyl group, which was the side chain part of (+)-obtusenyne. Thus, the equipment for the construction of α,α'-*trans* cyclic substrate that the relationship between the prenyl group and Ethyl group is *trans*-orientation was prepared. After the transformation of oxazolidinone derivative to alcohol, Brown asymmetric allylation[11] yielded the diene product in exclusive stereoselectivity. To accomplish the α,α'-*trans* oxonene skeleton, the ring-closing metathesis reaction using Grubbs' first generation catalyst[8] was applied on the TBS-ether substrate of the former diene. As a result, the reaction effectively proceeded, furnishing the desired cyclic compound.

Scheme 2

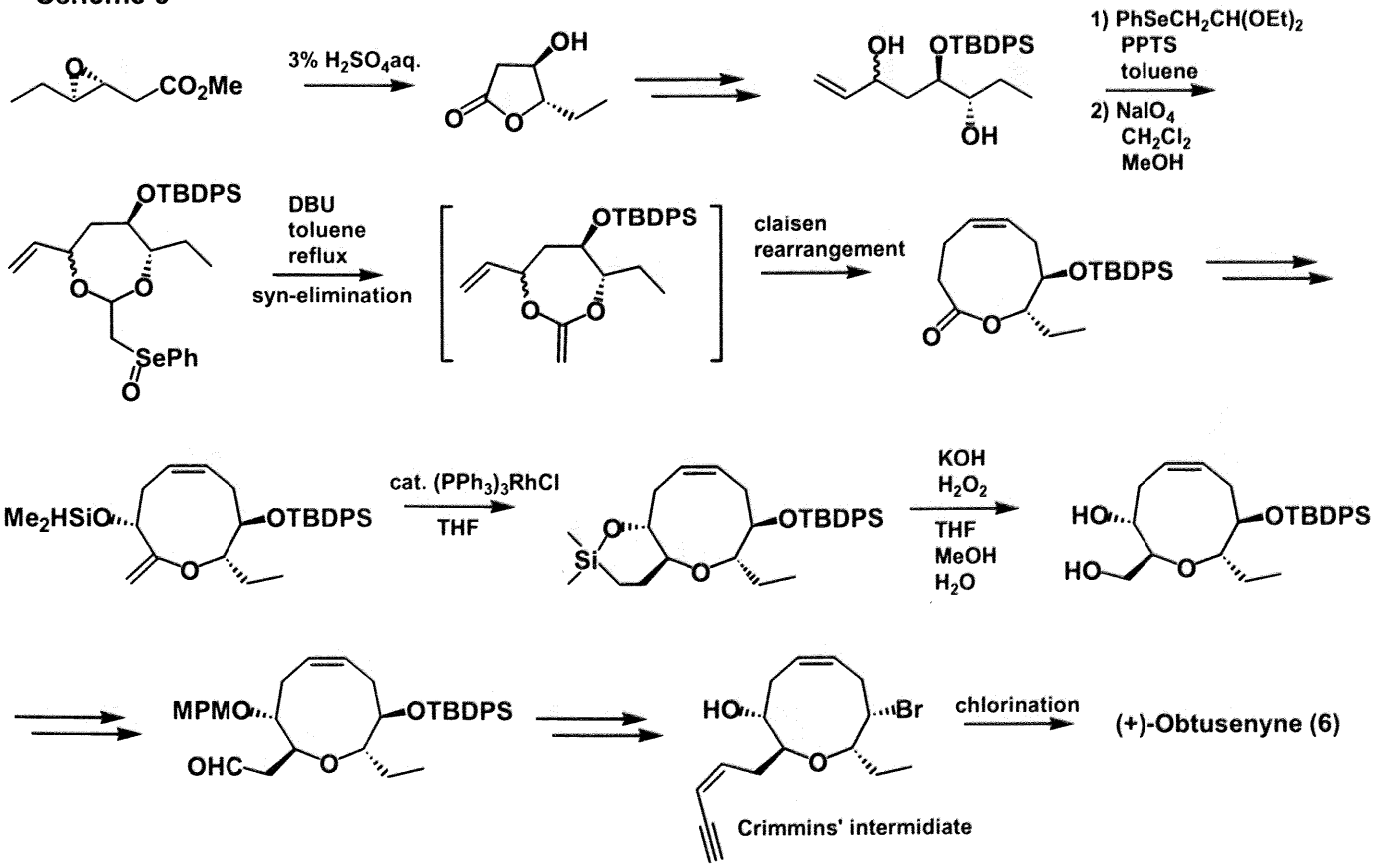


Installment of *cis*-enyne moiety followed by bromination furnished pre-obtusenyne substrate, whose chlorination at later stage achieved the total synthesis of (+)-obtusenyne. This approach is very simple and efficient in the case of the synthesis of medium-sized ring natural product, as well as (+)-obtusenyne. However, this strategy needs several asymmetric reactions utilizing chiral auxiliaries, so that the strategic limitation exists. Although there are a few disadvantages, it is considered that the methodology utilizing the RCM reaction is very powerful tool for the construction of medium-sized rings. It is utilized in total synthesis of various natural compounds these days.

2.2.3 More recently Total Synthesis using Claisen Rearrangement as a Key Reaction by Holmes' group [5]

More recently, a new synthetic strategy of (+)-obtusenyne was reported by Holmes' group. They applied Claisen rearrangement as a key reaction in constructing nine-membered ring, the backbone of (+)-obtusenyne. The synthetic approach involved an intramolecular hydrosilation as another key step. The synthesis was commenced on the conversion of methyl *trans*-3,4-epoxyhexanoate into γ-lactone. The chiral non-racemic epoxide, the starting material was derived from kinetic resolution of racemic methyl *trans*-3,4-epoxyhexanoate with a pig liver esterase[12]. Exposure of the chiral epoxide to 3% aq. H_2SO_4 afforded furanolactone derivative, which was changed into diol via multi step sequence. Treatment under the condition of $PhSeCH_2CH(OEt)_2$/PPTS in toluene at reflux and subsequent oxidation of selenide with $NaIO_4$ afforded the seven-membered cyclic acetal. The *syn*-elimination of selenoxide with DBU in toluene at reflux generated vinyl acetal intermediate, which yielded the nine-membered cyclic lactone smoothly through Claisen rearrangement.

Scheme 3



Likewise, this compound could be obtained from a lactonization methodology as like the previous approach by Murai's group, but this strategy is quite valuable in the term of the newly constructive methodology for medium-sized cyclic ether or lactone. To introduce α-hydroxy group and *exo*-methylene, the hydroxylation with Davis oxazolidine[13] and the terminal olefination using Tebbe reagent[14] were carried out. The hydroxy group of the resulting vinyl ether was protected as its dimethylsilylether, which was submitted to next intramolecular hydrosilation sequence, a major attraction. The hydrosilation proceeded with $(PPh_3)_3RhCl$ in THF, yielding α,α'-*trans* nine-membered cyclic ether, followed by Tamao oxidation provided the desired diol in good yield. Then, the regioselective protection of the secondary alcohol and transformation into the corresponding aldehyde via cyanide/reduction sequence were conducted and then the following introduction of *cis*-enyne moiety furnished the Crimmins' intermediate. Finally, the total synthesis of (+)-obtusenyne was achieved by the chlorination[15] under the same condition as Crimmins'. In summary, they have developed an efficient and diastereoselective synthesis of (+)-obtusenyne, which further demonstrated the utility of the Claisen rearrangement/intramolecular hydrosilation approach to these strained medium-ring system.

2.3 Stereoselective Construction of Eight- and Nine-membered Cyclic Ethers with α,α'-*cis*- and α,α'-*trans*-Orientation

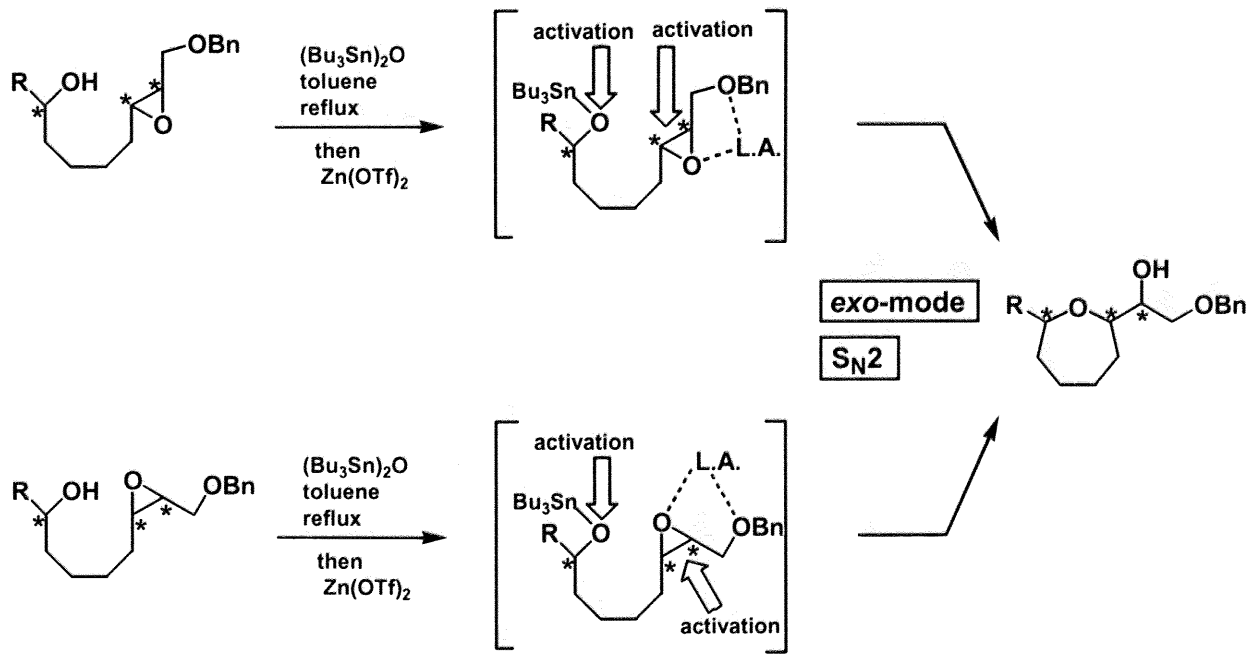
The method for synthesis of marine metabolites required efficiency and flexibility on assembling medium-sized cyclic ethers of all sizes as well as introduction of the stereochemistry at α,α'-positions. As discussed in the previous sections, notable methods have been developed and applied to synthesis of marine metabolite. However, a crucial problem incurred in controlling the stereochemistry at the α,α'-positions has not been overcome entirely. Several methods have been developed for the stereoselective construction of the α,α'-*cis*-orientation system. In contrast, there have been few reports on the synthesis of α,α'-*trans*-orientation system. Therefore, the author investigated development of the new methodology for the stereoselective construction of α,α'-*cis*- and α,α'-*trans*-medium-sized cyclic ethers at the outset of my research program.

Access via cyclization of hydroxy epoxides is one of the reliable candidates to attain the purpose. In fact, this approach is being used often for the synthesis of tetrahydropyran, tetrahydrofuran and other related systems.[16] In these cases, the reactions are generally carried out either by the activation of an epoxide under acid catalysis or a hydroxyl group by a base. In the case of epoxy substrates, the nucleophilic attack by the hydroxyl group is expected to provide the products corresponding those afforded by the S_N2 reaction and *exo* mode process.[17] However, depending on the substituent adjacent to the epoxide and the geometry of the epoxide, the reaction gave products derived from a competing *endo* mode process.[18,19] In contrast, very few applications[18)a,c-e,19)a,d] of these methodologies towards the synthesis of medium-sized cyclic ethers have been pursued mainly due to the problems described in the previous sections.

In an effort to overcome the limitation of an approach via cyclization of hydroxy epoxides, our group has been developed the new method towards the stereospecific construction of α,α'-*cis*- and α,α'-*trans*- seven-membered cyclic ethers by using of a $(Bu_3Sn)_2O/Zn(OTf)_2$

system. This method has a potential advantage in that stereochemistry at the α- and α'-positions could be controlled stereospecifically since the reaction proceeds via an S_N2 process and *exo* mode selectivity regardless of the configuration. This reaction system was ingeniously designed based on the following considerations. Activation of both groups, namely the hydroxyl moiety via formation of tin ether and the epoxide group by coordination with a suitable Lewis acid, would cause an increase in the cyclization reactivity and result in the efficient formation of medium-sized cyclic ethers. The presence of an oxygenated substituent adjacent to the epoxide is expected to enhance the substrate reactivity and the *exo* mode selectivity through coordination of the Lewis acid with the epoxide to form a rigid five-membered chelate structure (Scheme 4).[20]

Scheme 4

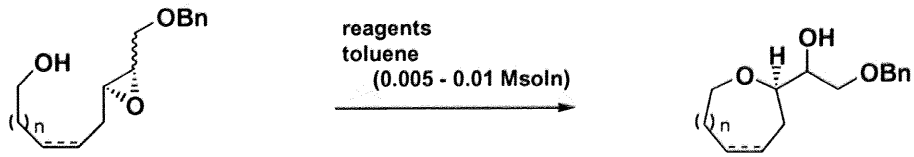


In order to establish the method as a general approach towards medium-sized cyclic ethers, an extension to synthesis of eight- and nine-membered cyclic ether systems that are abundantly found in *Laurencia* metabolites was required.

At the outset, model compound **7b** was subjected to the $(Bu_3Sn)_2O/Zn(OTf)_2$ conditions[21] employed for the formation of seven-membered cyclic ethers in an effort to examine the capability for the formation of eight-membered cyclic ethers (Table 1). Reaction was quite

sluggish and a large excess of $Zn(OTf)_2$ (3.3 equiv.) was required to complete the reaction, and the corresponding cyclic ether **8b** was obtained in 51% yield (entry 2). The unsatisfactory result led me to survey suitable Lewis acids for use in combination with $(Bu_3Sn)_2O$ for the reaction. As the result, it was proved that $Eu(fod)_3$ and $Pr(fod)_3$ were superior Lewis acids[22] for this purpose to afford **8b** in 79% and 77% yields, respectively (entries 3 and 4). Moreover, it was revealed that use of $Eu(fod)_3$ in itself exhibited higher activity to promote the cyclization.[23] The reaction proceeded cleanly and its yield improved up to 85% (entry 5). An attempt at using a catalytic amount of $Eu(fod)_3$ in this reaction resulted in drastic decrease in the reaction rate (entry 6). This result showed that a stoichiometric amount of $Eu(fod)_3$, though it was not essential for the reaction to proceed, was required to obtain the practical reaction rate. The improved method could be applied to *cis*-epoxide **7c**, and the corresponding cyclic product **8c** was obtained selectively in high yield regardless of the geometry of the epoxy group (entry 7).

Scheme 5



7a : n=1, *trans*-epoxide
7b : n=2, *trans*-epoxide
7c : n=2, *cis*-epoxide
7d : n=3, *trans*-epoxide
7e : n=3, Δ^4, *trans*-epoxide
7f : n=3, Δ^4, *cis*-epoxide

8a : β-OH
8b : β-OH
8c : α-OH
8d : β-OH
8e : β-OH
8f : α-OH

Table 1. Cyclization of Hydroxy Epoxides Leading to Eight- and Nine-membered Cyclic Ethers

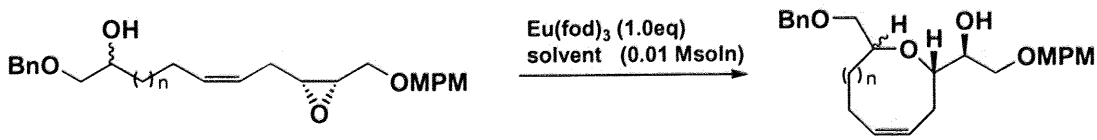
entry	substrate	reagents(eq)	temp(°C)	time(h)	product	yield (%)
1	**7a**	$(Bu_3Sn)_2O$ (0.6)/$Zn(OTf)_2$ (0.4)	90	12	**8a**	99[b]
2	**7b**	$(Bu_3Sn)_2O$ (1.0)/$Zn(OTf)_2$ (3.3)[b]	90	68	**8b**	29
3	**7b**	$(Bu_3Sn)_2O$ (0.6)/$Eu(fod)_3$ (2.0)	90-120	38+81	**8b**	79
4	**7b**	$(Bu_3Sn)_2O$ (0.6)/$Pr(fod)_3$ (2.0)	90-120	17+103	**8b**	77
5	**7b**	$Eu(fod)_3$ (1.1)	130	50	**8b**	85
6	**7b**	$Eu(fod)_3$ (0.2)	130	50	**8b**	35(**81b**, 55)
7[a]	**7c**	$Eu(fod)_3$ (1.0)	140	116	**8c**	79
8	**7d**	$Eu(fod)_3$ (1.0)	110	24	**8d**	–(**81d**, 96)
9	**7e**	$Eu(fod)_3$ (1.0)	100	99	**8e**	82
10	**7f**	$Eu(fod)_3$ (1.0)	100	64	**8f**	86

[a]with creation of tin ether. [b]ref. 40a.

Similarly, successful results were obtained in formation of nine-membered cyclic ethers under identical reaction conditions. Although the presence of a *cis*-double bond in acyclic precursors was essential, the reaction of **7e** and **7f** proceeded smoothly to afford the corresponding products **8e** (82%) and **8f** (86%), respectively (entries 9 and 10). It should be noted that the excellent yields in the formation of eight- and nine-membered cyclic ethers were comparable to that of the ring-closing metathesis method[8] popularly employed for the synthesis of these systems.

The excellent results of the preliminary experiments led me to proceed with the stereospecific cyclization protocol leading to the α,α'-*cis*- and α,α'-*trans*-cyclic ethers. The *cis*-double bond in the substrates proved necessary for cyclization to occur in all cases. Model compound **9a** having a *cis*-epoxide group was reacted under identical conditions. As expected, the corresponding eight- membered cyclic ether **10a** possessing alkyl substituents at the α- and α'-positions with *cis*-orientation was obtained in 97% yield, arising from cyclization via the selective S_N2 process and *exo* mode (Table 2, entry 1). Similarly, cyclization of the isomer **9b** leading to the α,α'-*trans*-derivative proceeded stereospecifically to afford the corresponding product **10b** in 76% yield (entry 2). Furthermore, the present method was applicable to the stereospecific synthesis of α,α'-*cis*- and α,α'-*trans*-nine-membered cyclic ethers. The substrates **9c** and **9d** having the *cis*-epoxide afforded the corresponding cyclic ethers **10c** and **10d**, respectively, without any decrease in chemical yields (entries 3 and 4). It was noteworthy that no regio- and stereoisomeric products were detected in all reactions.

Scheme 6



9a–d **10a–d**

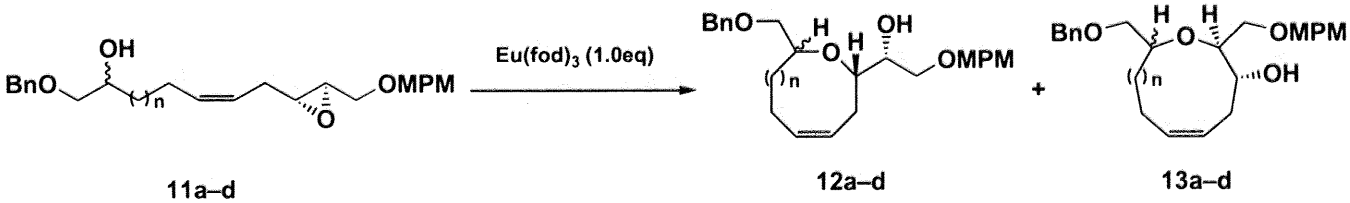
Table 2. Cyclization of Hydroxy *cis*-Epoxides Leading to α,ω-*cis*- and α,ω-*trans*-Cyclic Ethers

entry	substrate	solv.	temp. (°C)	time (h)	product [a]	yield (%)
1	**9a** : n=1, α-OH	toluene	100	44	**10a** : α,α'-*cis*	97
2	**9b** : n=1, β-OH	xylenes	120	55	**10b** : α,α'-*trans*	76
3	**9c** : n=2, α-OH	toluene	110	95	**10c** : α,α'-*cis*	87
4	**9d** : n=2, β-OH	toluene	110	74	**10d** : α,α'-*trans*	85

[a]Relative stereochemistry at α,ω-positions was determined by NOE experiments.

Interestingly, it was found that the relative configuration generated at the α,α'-positions had an influence on the regioselectivity in the cyclization from the results employing a series of *trans*-epoxide substrates (Table 3). While compound **11a** gave the α,α'-*cis*-orientated cyclic ether **12a** exclusively via an 8-*exo* mode (entry 1), the reaction of its isomer **11b** resulted in competitive 9-*endo* cyclization to afford α,α'-*cis*-oriented **13b** accompanied with α,α'-*trans*-oriented **12b** via 8-*exo* cyclization (entry 2). Similarly, competitive 10-*endo* cyclization was observed in the reaction of **11d** in contrast to the exclusive 9-*exo* cyclization of the isomer **11c**. These results suggested that cyclization in all cases proceeded via the S_N2 process and *exo* mode except the substrates such as **11b** and **11d** which led to the α,α'-*trans*-orientation via *exo* mode, and, on the other hand, α,α'-*cis*-orientation via *endo* mode. The exceptional *endo* cyclization was a minor problem in view of the stereospecific synthesis of α,α'-*cis*- and α,ω-*trans*-cyclic ethers, since all stereoisomers with regard to these positions could be stereospecifially derived from the corresponding substrates possessing the *cis*-epoxide group via the convincing S_N2 and *exo* cyclization.

Scheme 7



11a–d **12a–d** **13a–d**

Table 3. Cyclization of Hydroxy *trans*-Epoxides Leading to α,ω-*cis*- and α,ω-*trans*-Cyclic Ethers

entry	substrate	solv. (Msoln)	temp. (°C)	time(h)	products[b] (%yield)	
1[a]	**11a** : n=1, α-OH	toluene (0.01)	100	51	**12a** : α,α'-*cis* (84)	**13a** : α,ω-*trans* (-)[c]
2	**11b** : n=1, β-OH	toluene (0.005)	110	70	**12b** : α,α'-*trans* (61)	**13b** : α,ω-*cis* (23)
3	**11c** : n=2, α-OH	xylenes (0.01)	120	94	**12c** : α,α'-*cis* (64)	**13c** : α,ω-*trans* (-)[c]
4	**11d** : n=2, β-OH	xylenes (0.01)	120	94	**12d** : α,α'-*trans* (35)	**13d** : α,ω-*cis* (8)

[a]With creation of tin ether.
[b]Relative stereochemistry at α,ω-positions was determined by NOE experiments.
[c]Not detected.

As described above, the author have developed a highly efficient methodology for the stereospecific construction of eight- and nine-membered cyclic ether systems possessing alkyl

substituents at the α,α'-positions with *cis*- and *trans*-orientation by cyclization of hydroxy epoxides promoted by $Eu(fod)_3$. In fact, cyclic ethers synthesized in this paper inherited the requisite carbon skeleton for the synthesis of a variety of *Laurencia* metabolites. Therefore, the present method provides an extremely useful tool for the synthetic study of these natural products.

Chapter 3

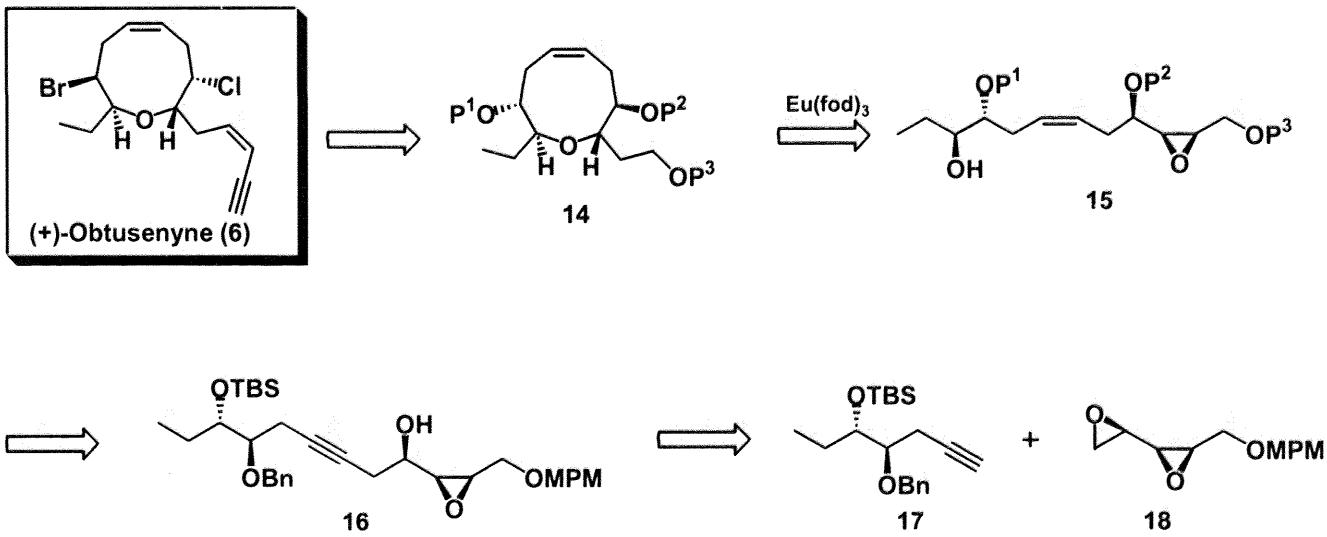
Background on the Construction of Oxonene Skeleton of (+)-Obtusenyne

3.1 Synthetic Strategy towards (+)-Obtusenyne

Retro-synthetic analysis based on our developed methodology[1] is depicted in scheme 1. The total synthesis of (+)-obtusenyne would be accomplished through halogenation and installment of the *cis*-enyne moiety on **14**. On our developed methodology, the acyclic precursor **15** was thought as the most efficient intermediate to obtain the oxonene **14**. However, the construction of nine-membered ring via *exo*-mode cyclization with a type like this substrate had no precedent.

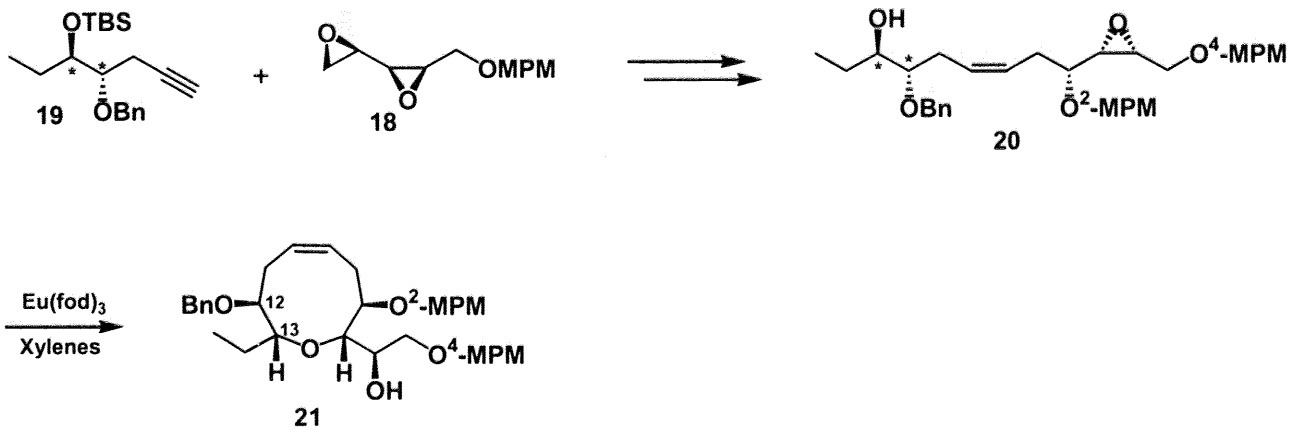
Therefore, we had to conduct a survey on this cyclization. Acyclic precursor **7** for the cyclization will be derived from coupling of acetylene **17** and diepoxide **18**. By the application of directive acyclic precursor toward oxonene **14**, concise synthesis of (+)-obtusenyne was expected.

Scheme 8



In this time, since we had the acetylene fragment **19** and the epoxy fragment **18** in hand, we planed to synthesize **20** and examine its cyclization. Although the stereochemistry at C12 and C13 on the resultant oxonene will be differ from that of (+)-obtusenyne, the cyclization on this type will be proved to be unfruitful if this reaction do not proceed smoothly that thermodynamically more favorable α,α'-*cis* nine-membered ring would be formed.

Scheme 9



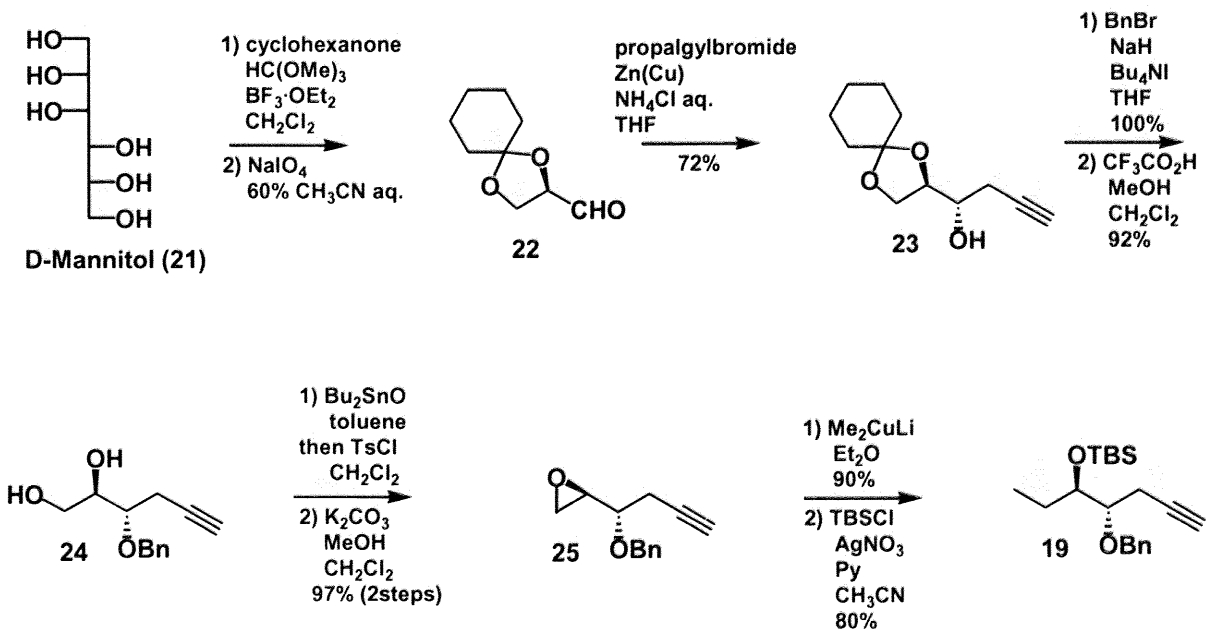
3.2.1 Synthesis of the Acetylene Fragment

The synthesis of the acetylene fragment **19** was illustrated in Scheme 2. Stereocenter of the acetylene fragment **19** was introduced by utilizing the asymmetric center of D-mannitol. As a first step, aldehyde **22** was prepared by regioselective cyclohexylidene protection followed by the oxidative cleavage of 1,2-diol with $NaIO_4$. Addition of propalgyl moiety using propalgylbromide and $Zn(Cu)^2$ afforded Ferkin-Anh type product **23** mainly, as inseparable diastereomeric products (anti : syn = ca. 5 : 1). After conversion to the benzyl ether, exposure to 80% aq. AcOH gave diol **24**, whose resioselective tosylation via cyclic tin ether and then basic treatment provided terminal epoxide **25**.

Finally, the acetylene fragment **19** was accomplished by addition of methyl group with Me_2CuLi, followed by the protection as its TBS ether. The diastereomeric by-product on the installment of propalgyl moiety was able to separate in last step.

Therefore, the acetylene fragment **19** was afforded as a single isomer.

Scheme 10



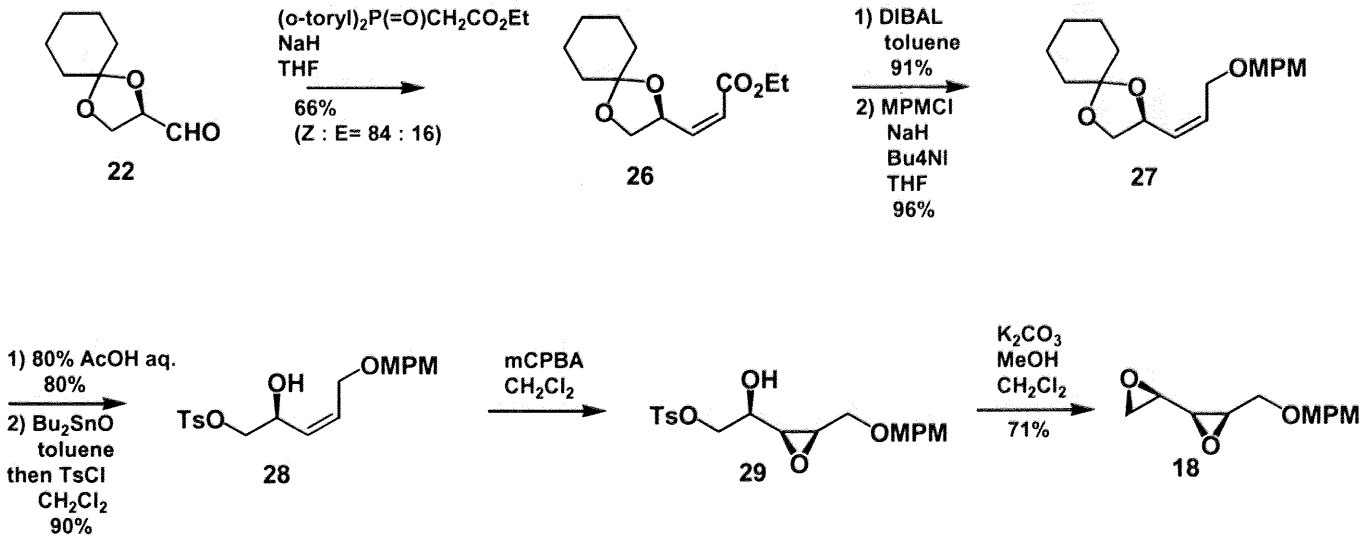
3.2.2 Synthesis of the Diepoxy Fragment 18

The diepoxy fragment **18** was possible to derive from the intermediate **22** on above presented the synthesis of the acetylene fragment **19**. Horner-Emmons reaction of **22** with (*Z*)-selective phosphate reagent[3] provided the expected (*Z*)-alkene **26** prior to (*E*)-alkene (*Z* : *E* =84 : 16).

MPM ether **27** was afforded by LAH reduction of the ester group on **26** followed by protection as its MPM ether. The cyclohexylidene group of the obtained **27** was deprotected with 80% aq. AcOH and then resioselective tosylation via cyclic tin ether gave alcohol **28**.

Epoxidation of **28** with MCPBA proceeded stereoselectively due to the neighboring effect of the hydroxy group[4], affording β-epoxide **29** as a main product. Treatment of **29** with K_2CO_3 in $MeOH/CH_2Cl_2$ accomplished the synthesis of the diepoxy fragment **18** in 71% yield.

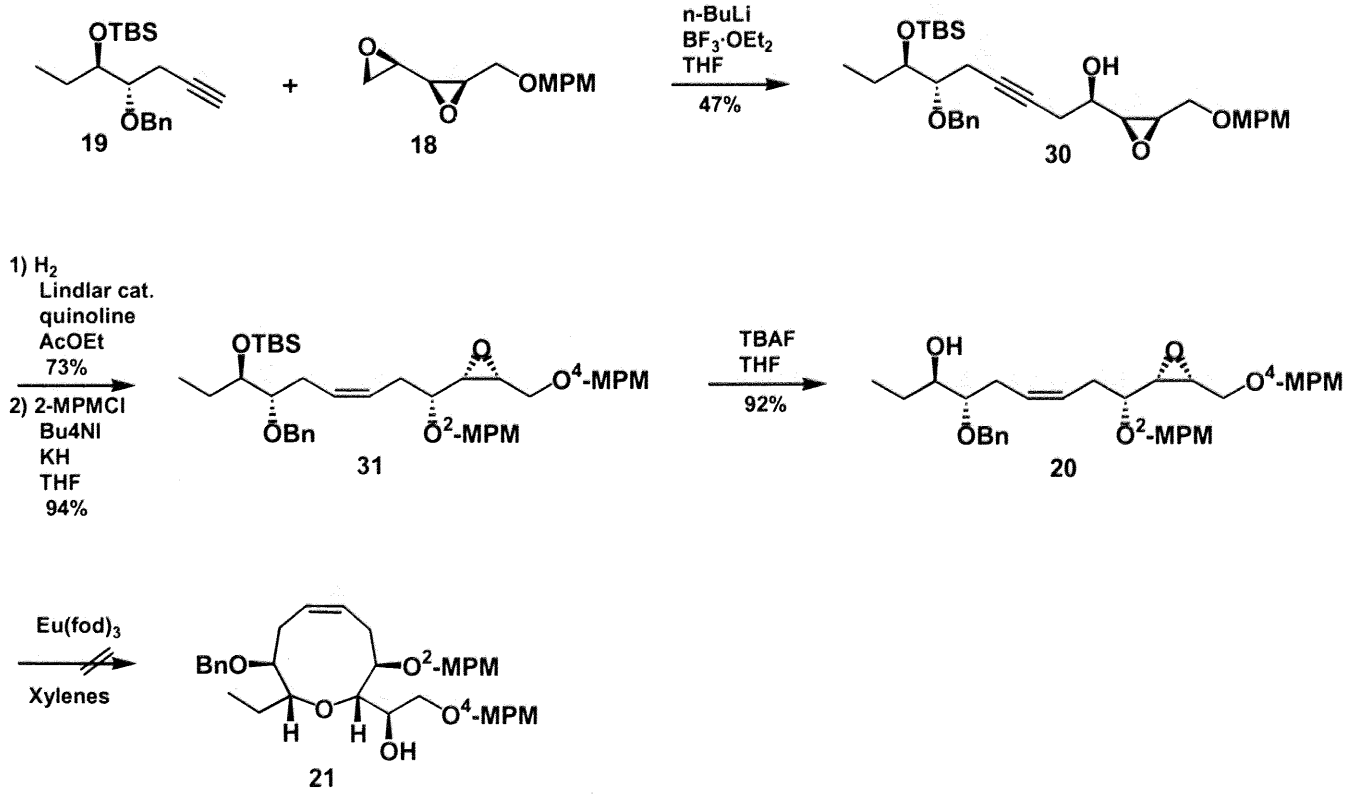
Scheme 11



3.2.3 Synthesis of the Acyclic Precursor and Examination of Cyclization

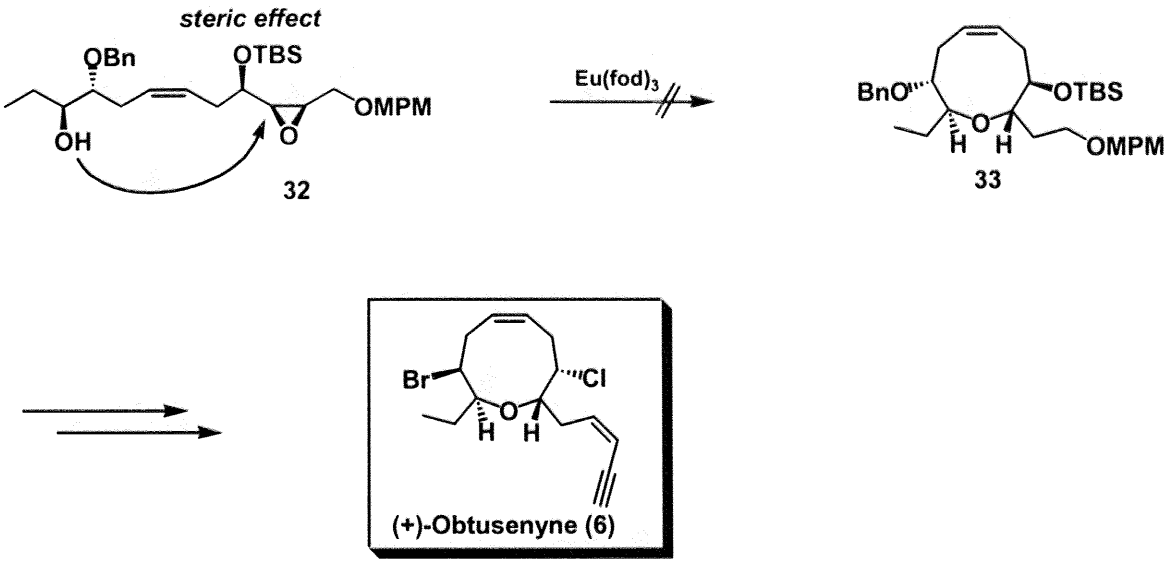
After coupling reaction of acetylene **19** and epoxide **18** under Yamaguchi's condition[5], hydrogenation of the triple bond with Lindlar catalyst and protection as its 2-MPM ether of the secondary alcohol afforded **31**. Exposure of **31** to TBAF/THF completed the synthesis of acyclic precursor for the cyclization promoted by $Eu(fod)_3$. While the formation of seven or eight-membered ring on a similar type substrates succeeded, this reaction which provides nine-membered ring resulted in a failure finally. It was too sluggish to afford the expected product so that ten-membered ring, a side product which was derived from *endo*-cyclization was a main product. This result should have been caused to the existence of two ethereal oxygen atoms around the epoxide part that each of them were able to have chelation with $Eu(fod)_3$.

Scheme 12



According to this consideration, the 2-MPM group would need to be changed to sterically larger protecting group like TBS group to mask the lone pair electron of the oxygen atom at the C2 position.

Scheme 13



Thus, the improvement [for instance 2-MPM→TBS] based on this hypothesis was executed. In this time, acyclic precursor **32** for the cyclization promoted by $Eu(fod)_3$ which had a right stereochemistry to achieve the synthesis of (+)-obtusenyne was synthesized and it was used in an examination. However, the reaction would not proceed again because of increasing of the steric hindrance by TBS group. Additionally, it is obvious that less hindered protecting groups like TES or TMS can not tolerate in this acidic reaction. Moreover, even though we could find out the suitable protecting group for this substrate, it is skeptical whether the desired reaction will proceed or not. Therefore, this synthetic route was abandoned.

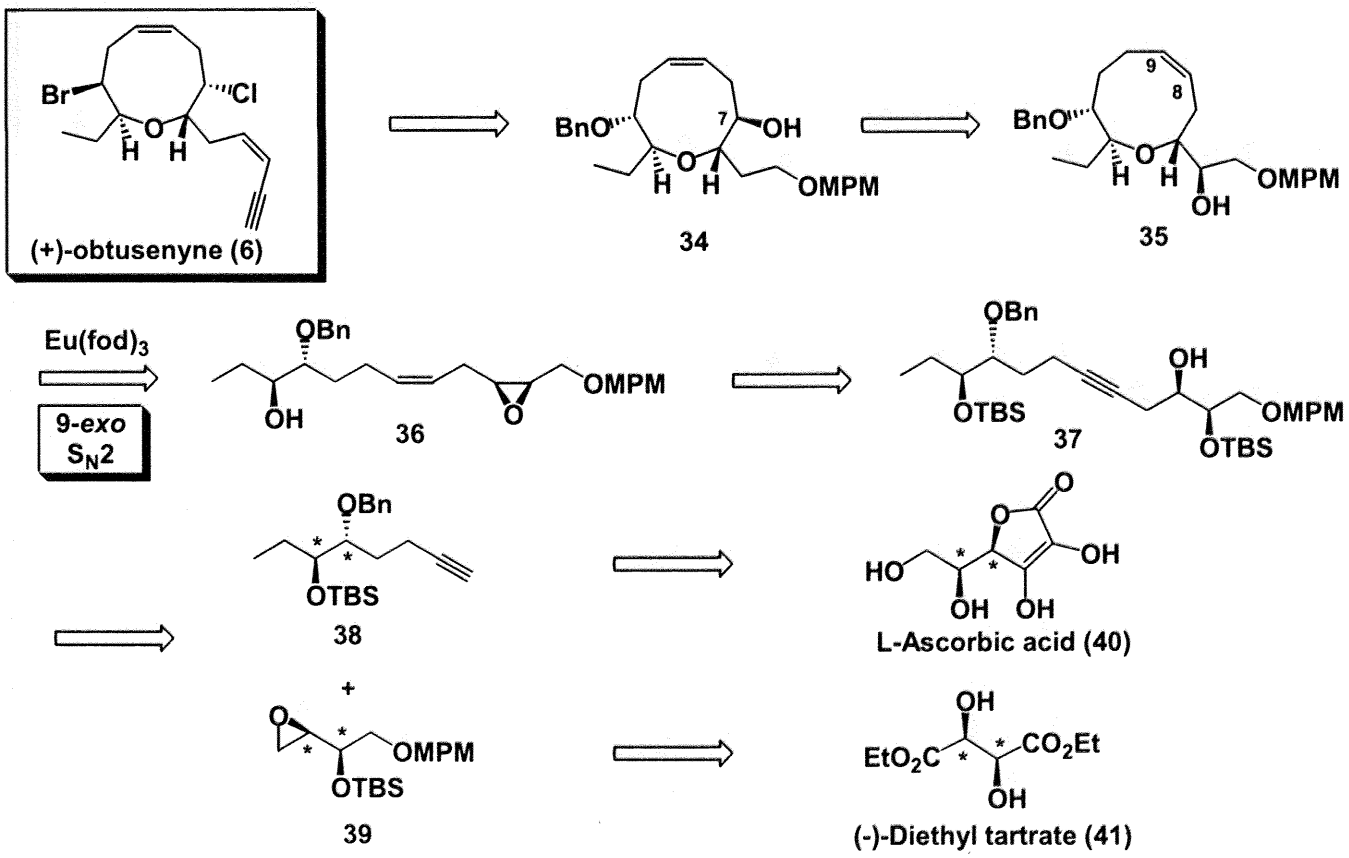
Because it was obvious that the protected hydroxy group adjecent to epoxide interrupted progress of the reaction, we elected new synthetic plan that the C7-OH was introduced afterward (Chapter 4).

Chapter 4

Second approach to (+)-Obtusenyne

4.1 New Retro-synthetic Analysis of (+)-Obtusenyne

New retro-synthetic analysis is shown in Scheme 14. Hydroxy epoxide **36** was selected as the precursor for cyclization. The cyclization of this compound would lead to nine-membered cyclic ether **35** stereo-specifically via 9-*exo* and S_N2 mechanism. Introduction of the C7-OH would be achieved by utilizing the C8, 9 double bond on the prepared oxonene **35**. But in the term of its stereochemistry, the selectivity was unclear at this stage. We expected that stereoselective conversion may be accomplished due to unique characteristic of the nine-membered ring skeleton. Finally, the total synthesis of (+)-obtusenyne would be achieved by the installment of *cis*-enyne moiety and two halogen substituents. On the other hand, hydroxy epoxide **36**, acyclic precursor will be lead through coupling of acetylene **38** and epoxide **39** derived from L-ascorbic acid (**40**) and (-)-diethyl tartrate (**41**), respectively.

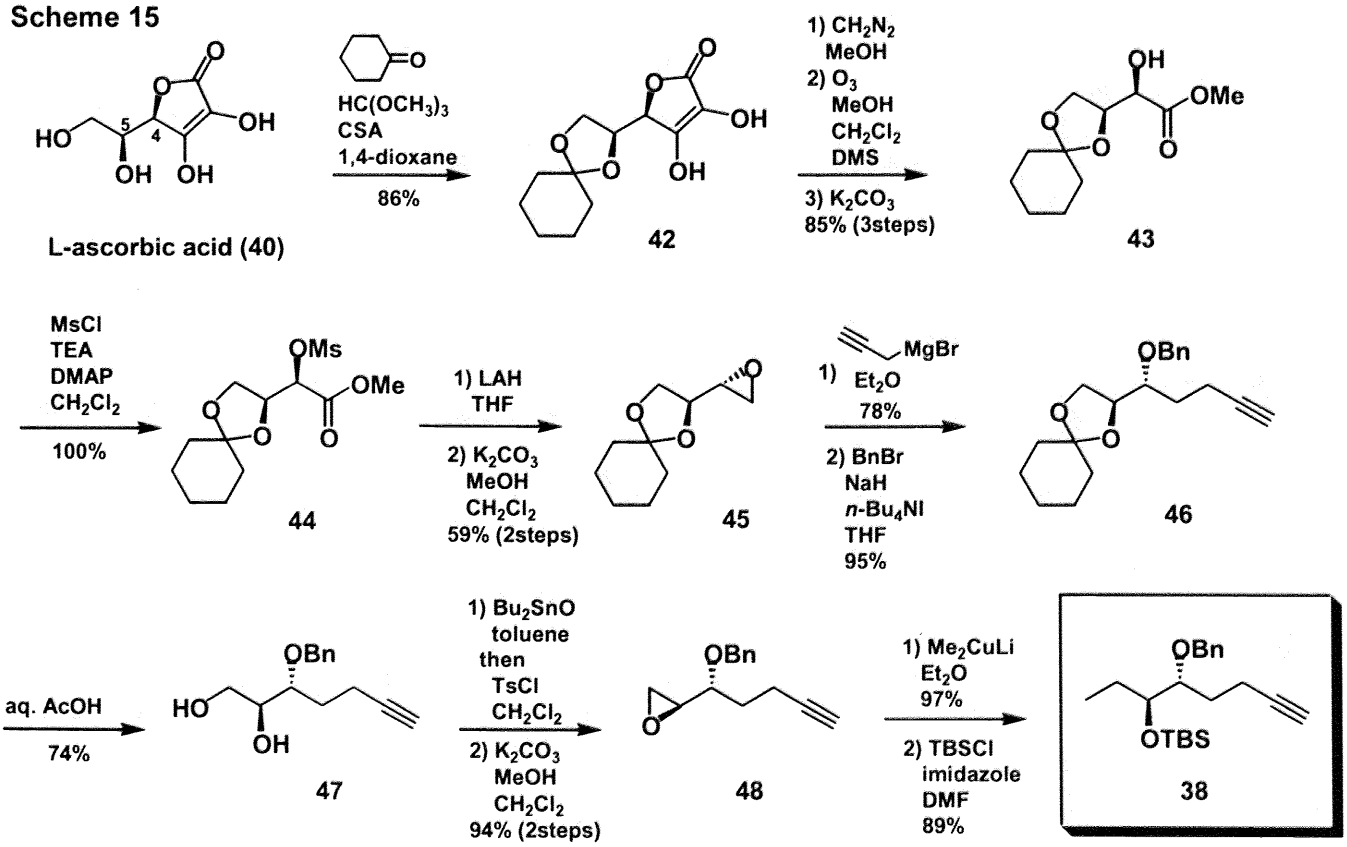


Scheme 14 Retro-synthetic Analysis

4.2.1 Synthesis of the Acetylene Fragment 38

Acetylene **38** was synthesized as depicted in Scheme 15. We chose readily available L-ascorbic acid as the starting material. Exposure of L-ascorbic acid **40** to cyclohexanone/$HC(OMe)_3$/CSA in 1,4-dioxane furnished cyclohexylidene acetal derivative **42**, which converted into ester **43** though Me-protection of the intact acidic hydroxy group and then ozonolysis (Me_2S), followed by removal of the generated oxalyl group with K_2CO_3/MeOH in 85% yield. After mesylation of **43**, LAH reduction of the ester group and treatment with K_2CO_3/MeOH/CH_2Cl_2 afforded terminal epoxide **45**. In this time, the reaction proceeded via S_N2 mechanism yielding stereo-inverted product. The reaction of **45** with propalgyl grignard provided the corresponding alcohol, which was subjected to next benzyl protection. Deprotection of the cyclohexylidene group of **46** with 80% aq. AcOH and then regioselective tosylation via cyclic tin ether followed by treatment with K_2CO_3/MeOH/CH_2Cl_2 gave epoxyacetylene **48**. Finally, addition of Me group by Me_2CuLi and then conversion into its TBS ether completed the stereoselective synthesis of **38**. The total yield from L-ascorbic acid (**40**) to **38**was 19.2% in 14 steps.

Scheme 15

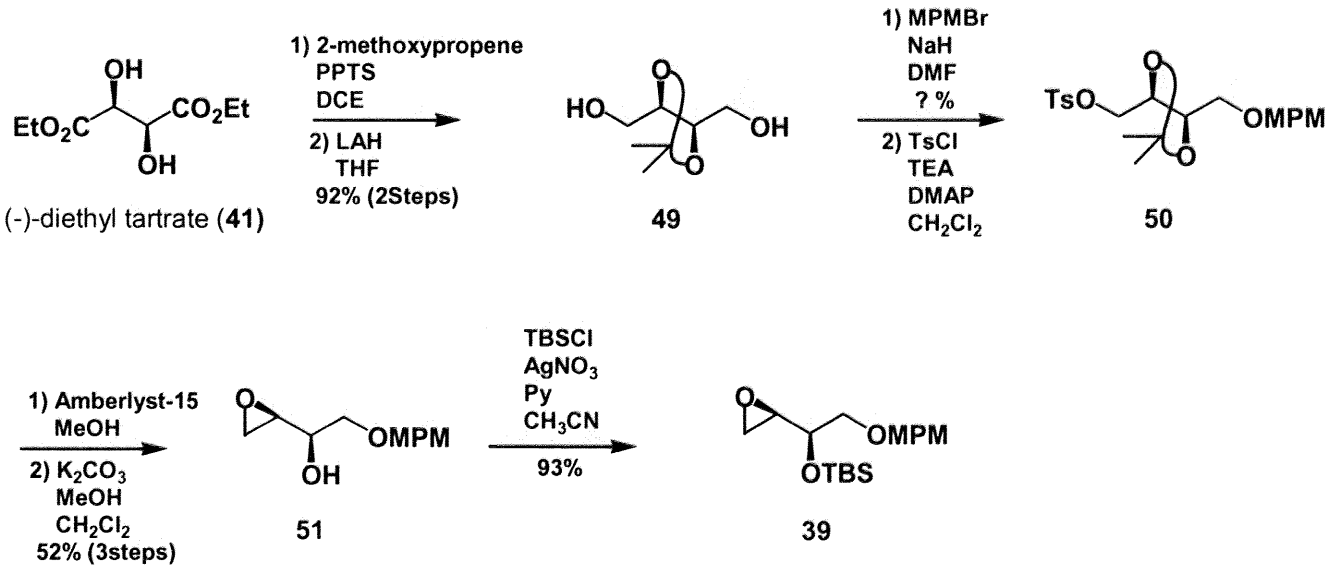


4.2.2 Synthesis of the Epoxy Fragment 39

The synthesis of the epoxy fragment **39** was commenced with transformation of (-)-diethyl tartrate **41** into diol **49**, namely acetonide protection of the 1,2-diol and LAH reduction of the ethylester part afforded **49** (Scheme 16). After the prepared diol was mono-protected by MPM group, another hydroxy group was changed to *p*-toluenesulfonyl derivative. Treatment of Amberlyst-15/MeOH gave 1,2-diol, whose treatment with K_2CO_3 in $MeOH/CH_2Cl_2$ provided hydroxy epoxide **51** stereo-retentively in moderate yield. Finally, the synthesis of the epoxy fragment **39** was accomplished by TBS protection of the remained hydroxy group under the condition of $TBSCl/AgNO_3$/pyridine in CH_3CN.

Other conditions like TBSCl/imdazole/DMF or $TBSOTf/2,6\text{-lutidine}/CH_2Cl_2$ did not satisfactorily provide **39,** or produced side products.

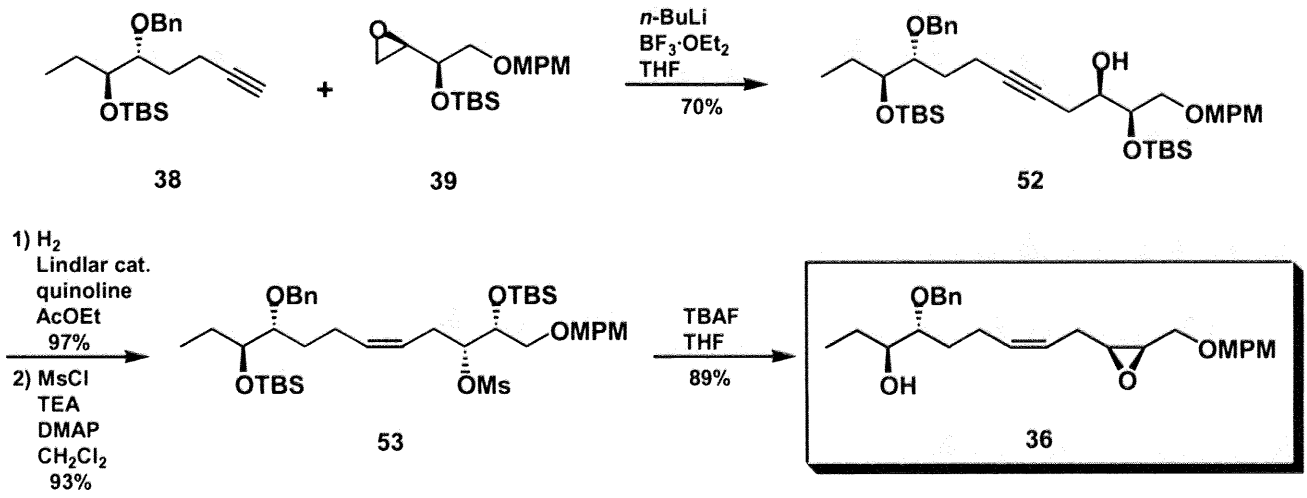
Scheme 16



4.2.3 Synthesis of Acyclic Precursor and Construction of Oxonene Skeleton

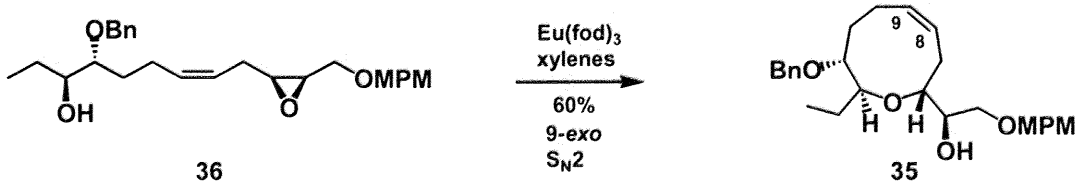
Thus, the prepared **38** and **39** were subjected to coupling reaction under Yamaguchi's condition[1]. The reaction proceeded smoothly at −78°C providing **52** in 70% yield. Conversion of triple bond on **52** to *cis*-olefin substrate with Lindlar catalyst and introduction of the methanesulfonyl group gave *Z*-olefin **53**. Subsequently, exposure of **53** to TBAF/THF induced deprotection of the TBS group and simultaneous epoxide formation, providing **36**, which was the desired acyclic precursor.

Scheme 17



Cyclization promoted by $Eu(fod)_3$, which is the key reaction in this synthetic strategy was examined to obtain nine-membered ring skeleton(Scheme 18). The cyclization was carried out under the condition of stoichiometric $Eu(fod)_3$ in 0.01M xylenes at 110°C for 70h. Consequently, the oxonene skeleton was successfully achieved in 60% yield. In this time, trace amount of 10-*endo* mode derivative and dimer of the starting material were obtained, respectively. Thus, an efficient construction of α,α'-*trans*-nine-membered ring was easily and briefly accomplished in comparison with other methodologies. Stereochemistry of **35** was determined by NOE analysis after epoxidation of the C8, 9 double bond.

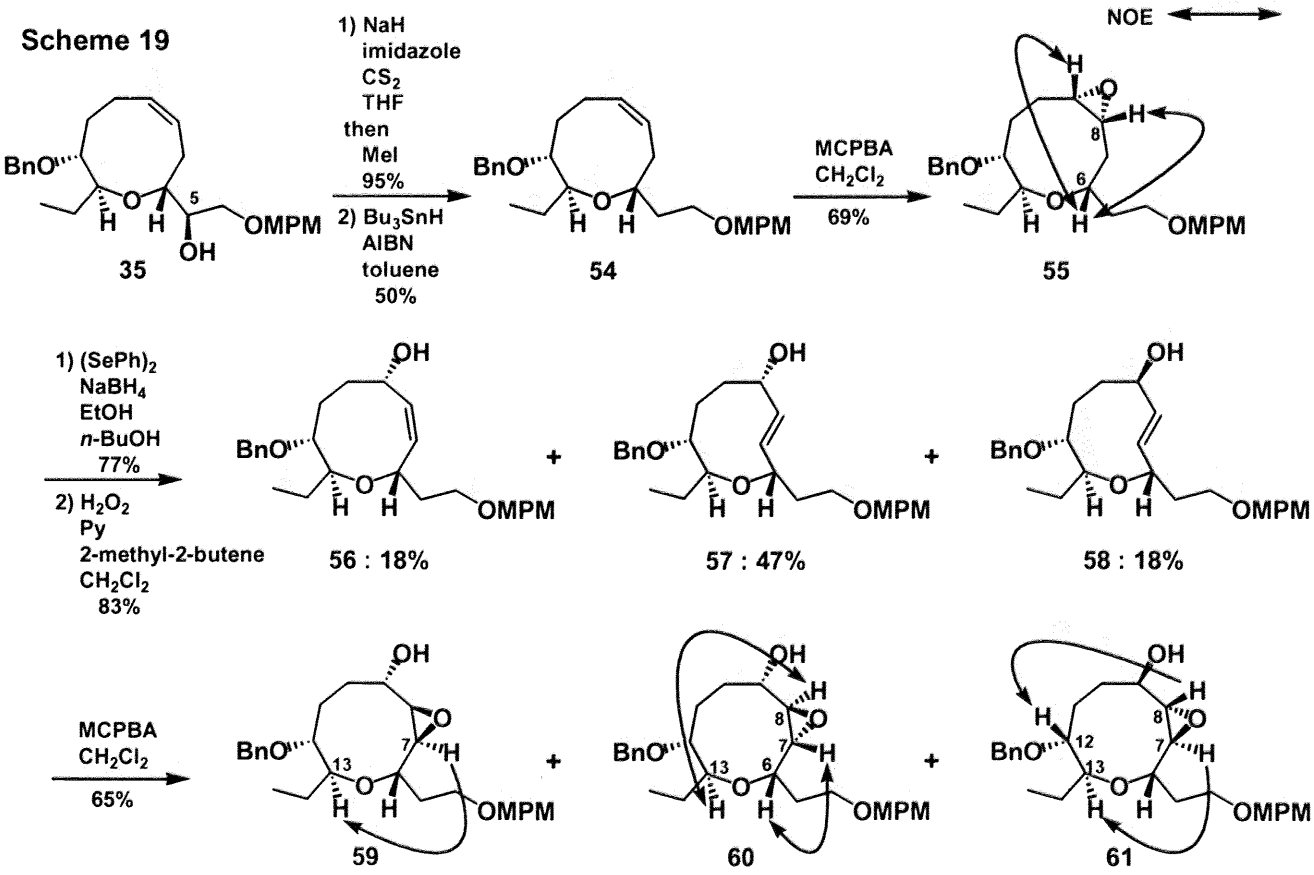
Scheme 18



4.3.1 Introduction of Hydroxyl group on the Substrate that the C5-OH was removed

With the desired nine-membered ring in hand, stereoselective introduction of oxygenated group on the oxonene ring was investigated. At first, we attempt removal of the unnecessary C5-OH group. To remove the C5-OH, alcohol **35** was converted to xantate derivative and then radical reduction with *n*-Bu_3SnH/AIBN in toluene at 100°C gave the desired reductive product **54** in moderate yield. The obtained product was submitted to epoxidation with MCPBA. Conformation analysis of **54** (which is mostly similar to **35)** by MM2 calculation suggested that the subsequent epoxidation proceeds from the convex α-site (see Scheme 20). As expected, the epoxidation proceeded stereoselectively from α-site, convex face and α-epoxide **55** was obtained as a single isomer. It was impossible to anticipate the regioselectivity on next epoxy-opening reaction by phenyl selenide anion, even though conformation of the substrate and diaxial opening of epoxide were considered.

Scheme 19

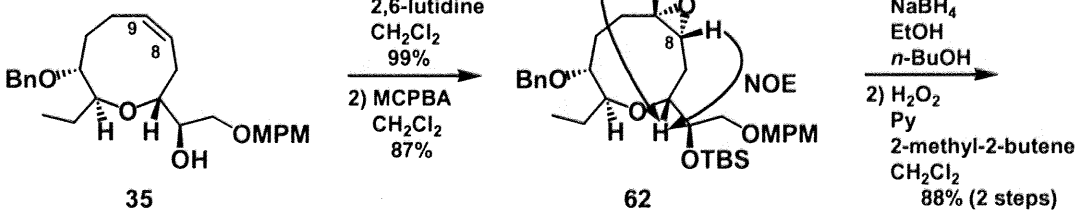


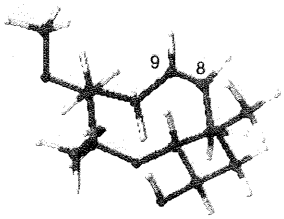
Fortunately, the reaction occurred at the C8 position, followed by H_2O_2 treatment afforded allylalcohols. Conformation of nine-membered ring is quite flexible and furthermore, the reaction at high temperature (140°C) that the nature of nine-membered ring would be more remarkable, would be helpful to its regioselectivity. But, in fact, a detail about this sequence has not well known yet. Although allylalcohols were obtained like this, *trans*-isomer was prior to *cis*-isomer in their geometry. The cause of this result also is not clear yet, but sigmatropic elimination may hardly proceed due to a ring-strain, which is distinctive of nine-membered ring. Next *anti*-selective epoxidation with MCPBA because of an affection of C9-OH^2 afforded the corresponding epoxides, respectively. Stereochemistry of the obtained epoxides was confirmed by NOE experiment. Consequently, conversion of **35** into epoxide **59** was unsuccessful. Because a possibility was considered that the existence of C5-OH affects the conformation, our next attempt was examination on the substrate that C5-OH of **35** was protected by TBS group.

4.3.2 Introduction of Oxygenated Group on Oxonene Skeleton

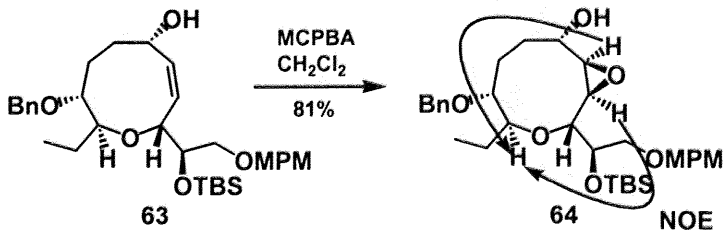
The C5-OH of **35** was protected under the condition of TBSOTf/2,6-lutidine in CH_2Cl_2. Epoxydation of the obtained substrate with MCPBA provided α-epoxide because the reaction proceeded from α-site, convex face (see below figure) as the previous case. Next opening reaction of epoxide by PhSe was similar to the former result, namely nucleophile attacked at the C8 position. Subsequent treatment with hydrogenperoxide gave *cis*-allylalcohol **63** in 88% yield. In this time, few (*E*)-olefins was observed. *Anti*-selective epoxidation of **63** with MCPBA was affected by the neighboring hydroxy group[2] and β-epoxide was provided in 81% yield along with a trace amount of α-epoxide. Stereochemistry of both epoxides **62** and **64** were determined by NOE study. According to this result, it was clear that the existence of the C5-OH was essential for conversion of **35** into **64**. When protecting group of the C5-OH was MEM, an excellent result alike was obtained, but the yield on TBS-protected substrate was the best result.

Scheme 20





Conformation analysis of 35

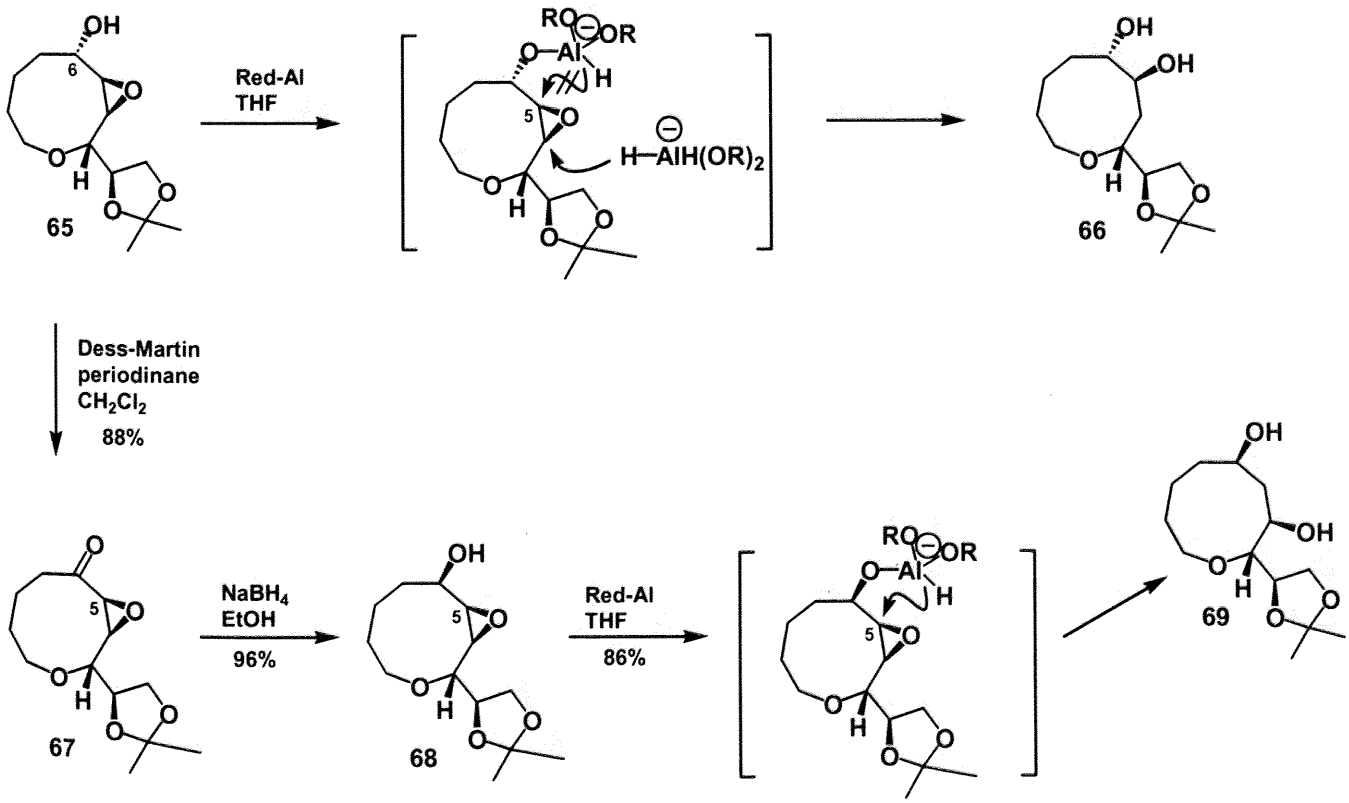


4.3.3 Regioselective Epoxy Opening reaction on Model Substrate

Regioselective opening of epoxide was examined to approach skeleton of (+)-obtusenyne. Hydroxy epoxide **65** that the relationship of stereochemistry between the C6-OH and the epoxide was *trans*-fashion, led to undesired 1,2-diol under the condition of Red-Al/THF. At first, this reaction generates an ate complex from hydroxyl group and Red-Al. Although the intramolecular hydride transfer from the ate complex was expected, intermolecular hydride attack was prior because of thermodynamically disadvantage 5,9-cis fused transition state (As a premise, hydride attack occurs on α face, backside of the epoxide). Thus, stereo-inversion of hydroxyl group was planned to introduce thermodynamically favor 5,9-trans fused transition state. According to this anticipation, inversion of the C6-OH was carried out through Dess-Martin oxidation, followed by $NaBH_4$ reduction. As expected, the reaction of the resulting **68** with Red-Al/THF provided the desired 1,3-diol in 86% yield. Consequently, *trans*-relationship between the epoxide and hydroxy group would be important issue for achievement of the regioselective epoxy-opening.

Following conversion on actual substrate was carried out based on this obtained knowledge.

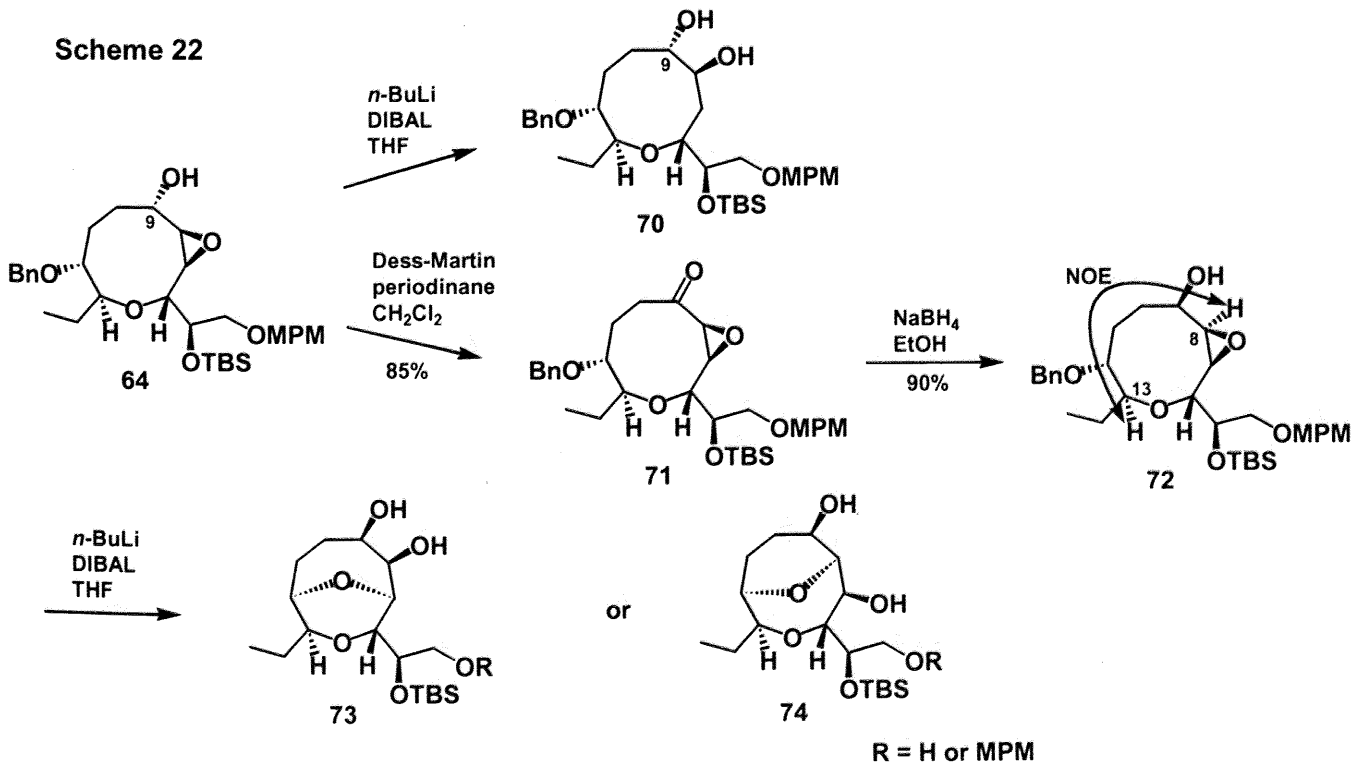
Scheme 21



4.3.4 Reflection on the Actual Substrate

Reaction of Red-Al with **64** which has trans-relationship between the C9-OH and the epoxide gave the undesired 1,2-diol as a former case. Although the reaction proceeds via intermolecular hydride attack not intramolecular hydride transfer when more reactive and bulky ate complex[3] prepared from DIBAL and *n*-BuLi, was used as a hydride-supplying agent instead of Red-Al, the resultant product also was 1,2-diol. Thus, the C9-OH of **64** was inverted by oxidation/reduction protocol as before. Stereochemistry of the obtained alcohol was assigned by NMR experiment and it was proved that β-alcohol was produced stereoselectively. However, in the case of this substrate, the desired 1,3-diol was not produced at all and consequently, the observed products were only bicycle **73** and **74** (same result was obtained again when Red-Al was used as a hydride agent). The driving force of this side reaction will be Lewis acidity of trivalent aluminum. Anyway, it is considered that more or less change of the conformation should have caused this result, rational experiments for the proof have not been carried out. Transannular reaction like this has been often observed on the synthesis of medium-sized ring. Synthetic plan in order to prevent the transannular reaction is essential for achievement of natural products possessing medium-sized ring. Thus, we had to investigate another strategy.

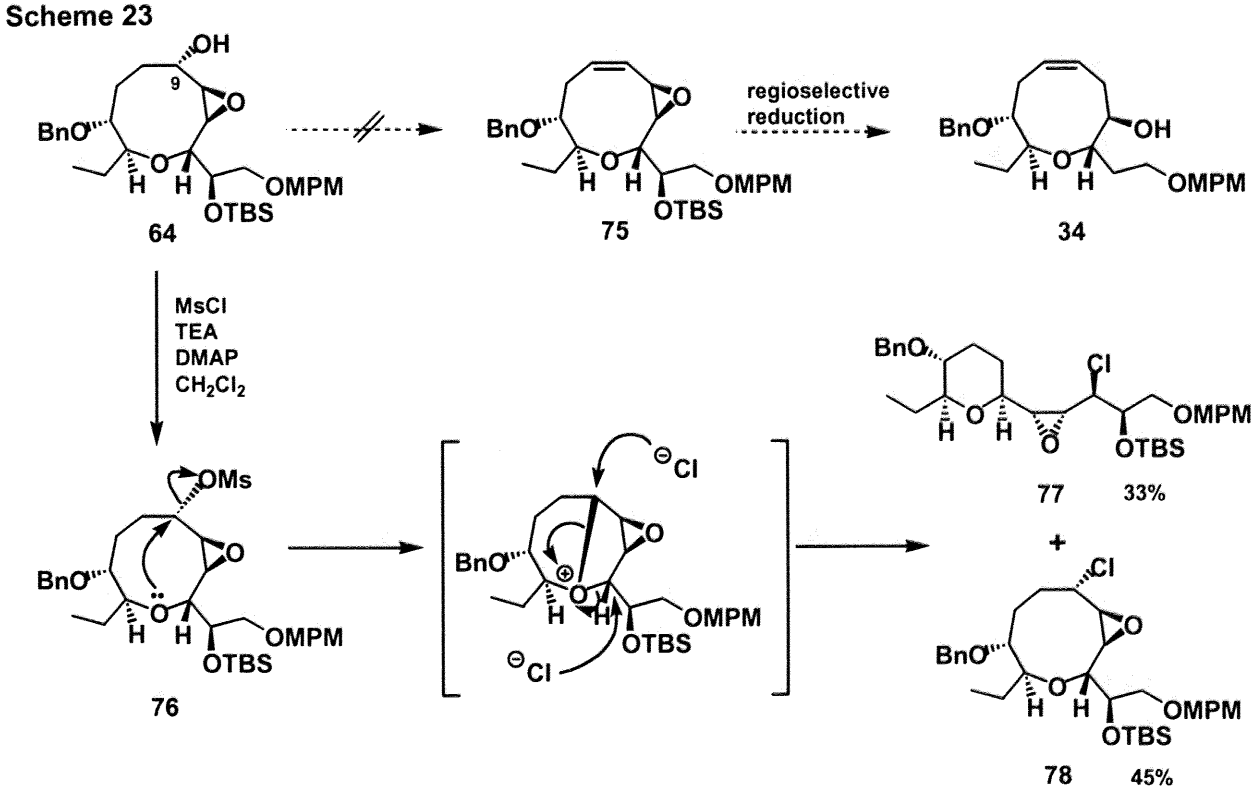
Scheme 22



4.3.5 Conversion to Allylepoxide 75

Our next plan was transformation of hydroxyepoxide **64** into homoallylalcohol **34** via allylepoxide **75**. It was expected that regioselective epoxy-opening would proceed at allyl position because of the distribution by π-electron of double bond and disappearance of the hindered hydroxy group. At first, **64** was subjected to mesylation under the basic condition. Unexpectedly, the corresponding mesylate **76** was not obtained at all. As a result, **77** and **78** were observed in 33% and 45% yield, respectively in stead of mesylate **76**. Probably, after the normal mesylation, the intramolecular ethereal oxygen atom attacked mesylate to generate oxonium intermediate followed by addition of the resultant chlorine anion on mesylation would lead to these compounds.

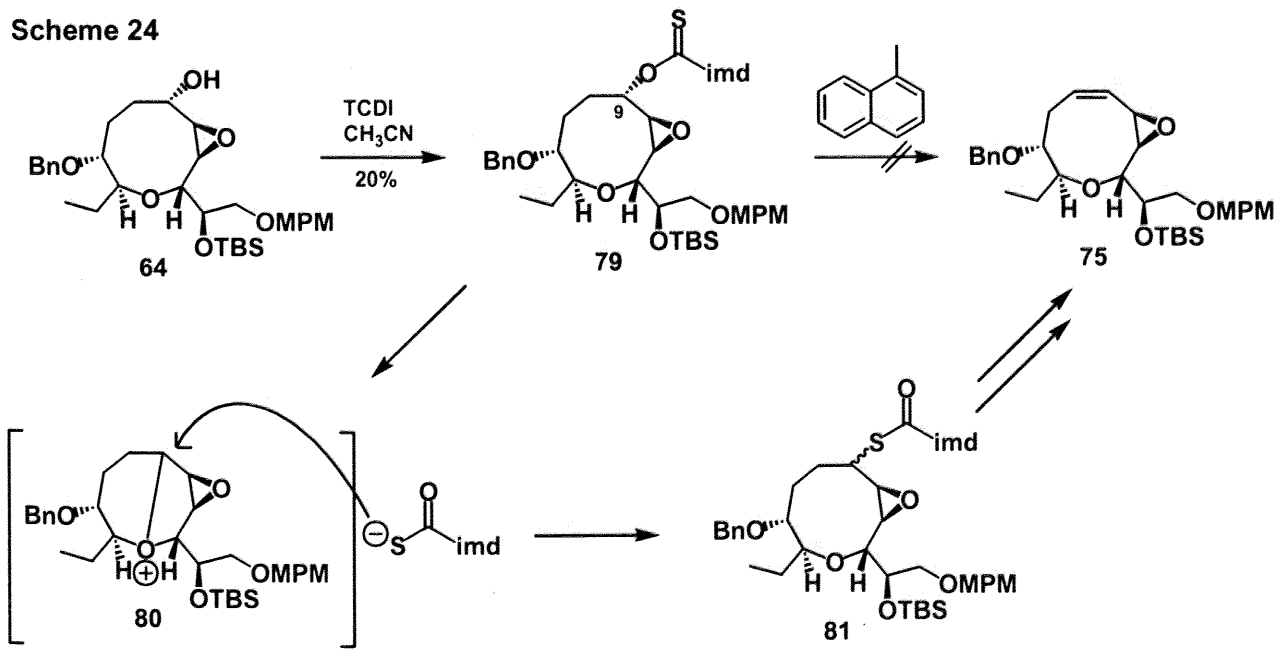
Scheme 23



Thus, our next attempt was the protocol using chugaev reaction[4]. Since introduction of leaving group on the C9-OH of substrate **64** was impossible, elimination without leaving group was demanded. To achieve this task, alcohol **64** was converted to imidate **79**. Although the yield was poor, next thermolysis-elimination step was attempted by using the obtained product. Imidate **79** was heated to 145°C in 1-methyl-naphthalene, so that the starting material disappeared on TLC plate after 1h. Unexpectedly, the desired product was not obtained at all, but thioester **81** was afforded instead. This reaction mechanism was also considered as above mesylation step. Namely, intramolecular ethereal oxygen attacked C9 carbon yielding oxonium intermediate due to high reaction temperature and then oxycarbonylimidazole thiol anion generated in the reaction would attack the oxonium intermediate.

Nevertheless, the resulting thioester **81** might be converted into allylepoxide **75** via *syn*-elimination of sulfoxide. According to this anticipation, the compound was followed by treatment with K_2CO_3 in MeOH to obtain thiol and then thio-methylation with MeI, but only unidentified product was afforded. As a result, this synthetic route was unfruitful too.

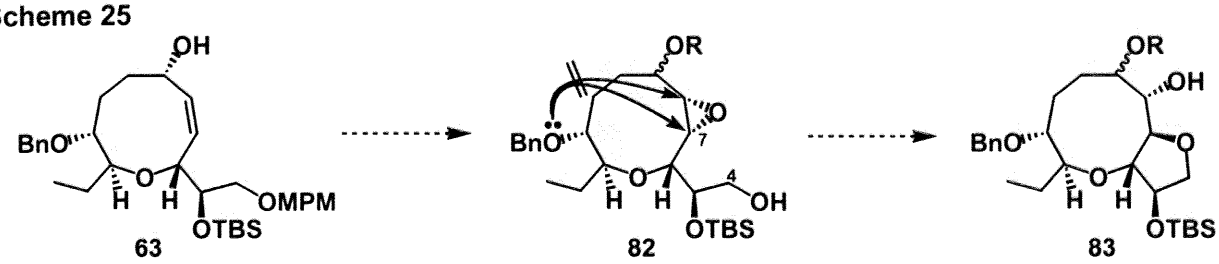
Scheme 24



4.3.6 Introduction of α-epoxide

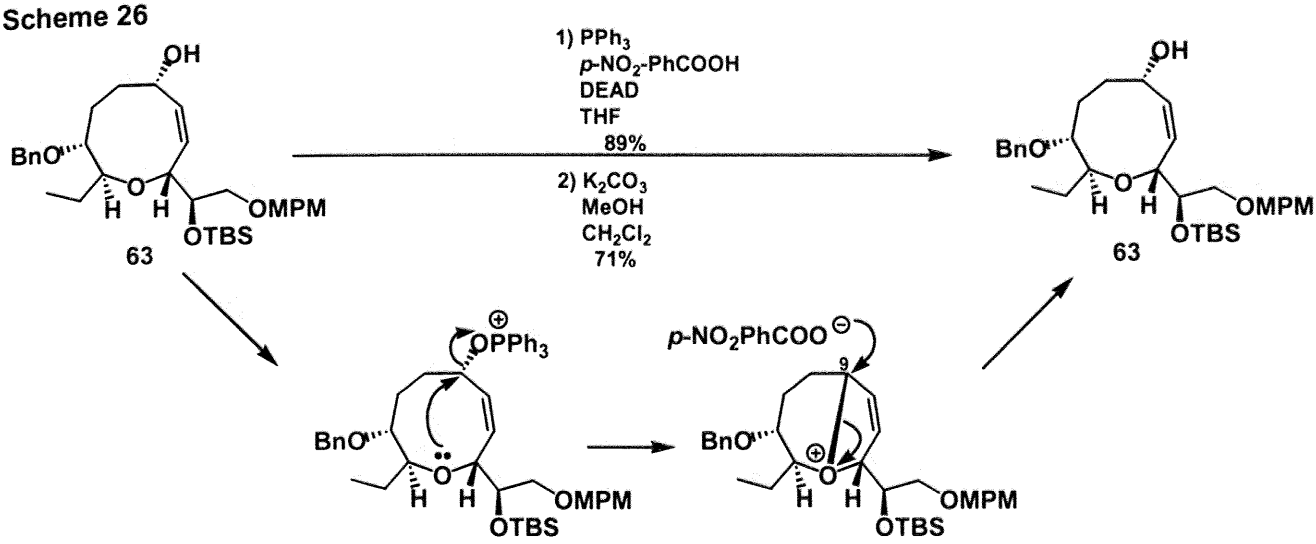
According to above result, it was obvious that conversion of epoxyalcohol **64** into allylepoxide **75** was unrealizable. Therefore, we planned to examine with the substrate introduced α-epoxide. In the substrate introduced α-epoxide, since the relative stereochemistry between the C12-BnO and epoxide is *syn*-relationship, it is expected that the previously presented transannular reaction should not proceed. Subsequently, the resulting α-epoxide would be changed into 5,9-*trans*-fused compound, namely the introduction of regio- and stereoselective hydroxy group would be accomplished (Scheme 25).

Scheme 25



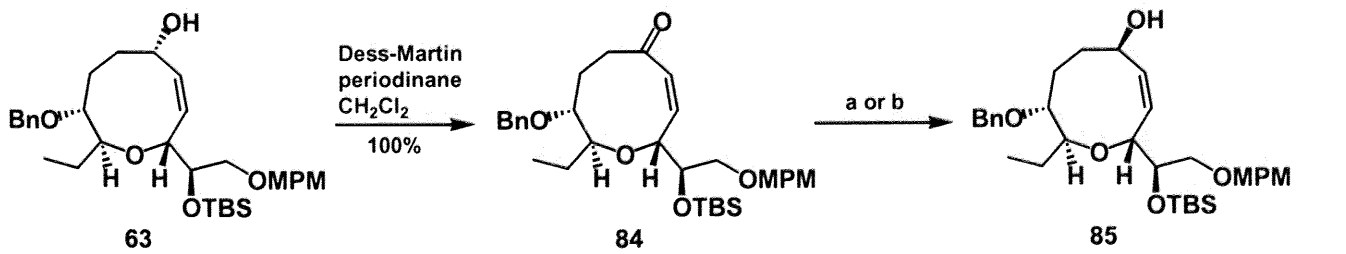
At first, inversion of the C9-OH was undertaken to obtain α-epoxide. This transformation was carried out why epoxidation of allylalcohol on medium-sized ring with MCPBA proceeds *anti*-selectively via affection between hydroxy group and MCPBA[2]. To invert the stereochemistry at C9 position, Mitsunobu reaction[5] was applied, however, starting material **63** was predominantly obtained instead of the desired stereo-inverted product. It was thought that above described transannular reaction between the ethereal oxygen and the C9 position proceeded, generating the oxonium intermediate and then C9-attack by the carboxylate and then removal of the acyl group with K_2CO_3/MeOH gave the starting material **63** (Scheme 26).

Scheme 26



The inversion using Mitsunobu reaction was unfruitful, so that the strategy through oxidation-reduction was attempted. Oxydation of **63** with Dess-Martin periodinane[6] gave ketone **84** in quantitative yield, which was submitted to next reduction with hydride metal reagents. Exposure to $NaBH_4/CeCl_3 \cdot 7H_2O/EtOH$[7] afforded β-alcohol in poor selectivity (α:β=45:55). In contrast with this result, the following reduction with DIBAL provided undesired α-alcohol as a major product. As a result, the strategy through oxidation-reduction process met with failure either.

Scheme 27



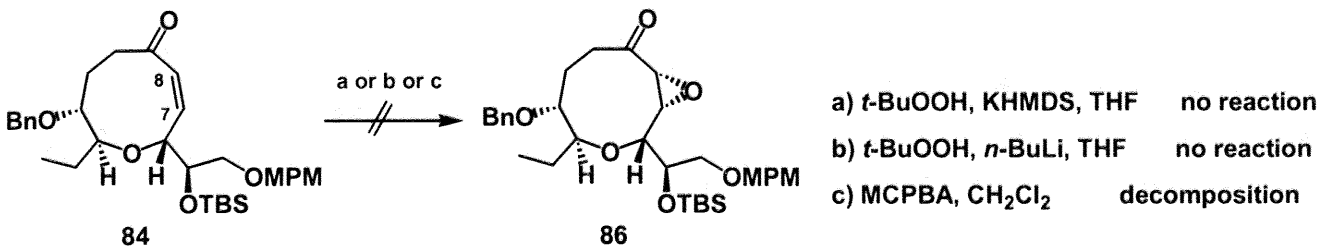
a) $NaBH_4$, $CeCl_3$, MeOH , 48:45%, 63:55%

b) DIBAL, toluene, 48:74%, 63:26%

Since inversion of the C9-OH did not successfully occur, we examined directive epoxidation on ketone **84**. Epoxidation under the basic condition of *t*-BuOOH/KHMDS in THF resulted in recovery of the starting material. Although the base was altered from KHMDS to *n*-BuLi, likewise the desired epoxide was not obtained.

Probably, π-electrons between the C7, 8 double bond and the carbonyl group of ketone did not conjugate, so that epoxidation under a basic condition did not yield the corresponding epoxide at all. In that case, epoxidation under an ordinary condition might afford the desired epoxide. According to this hypothesis, the reaction with MCPBA was examined, but the reactive substrate decomposed.

Scheme 28



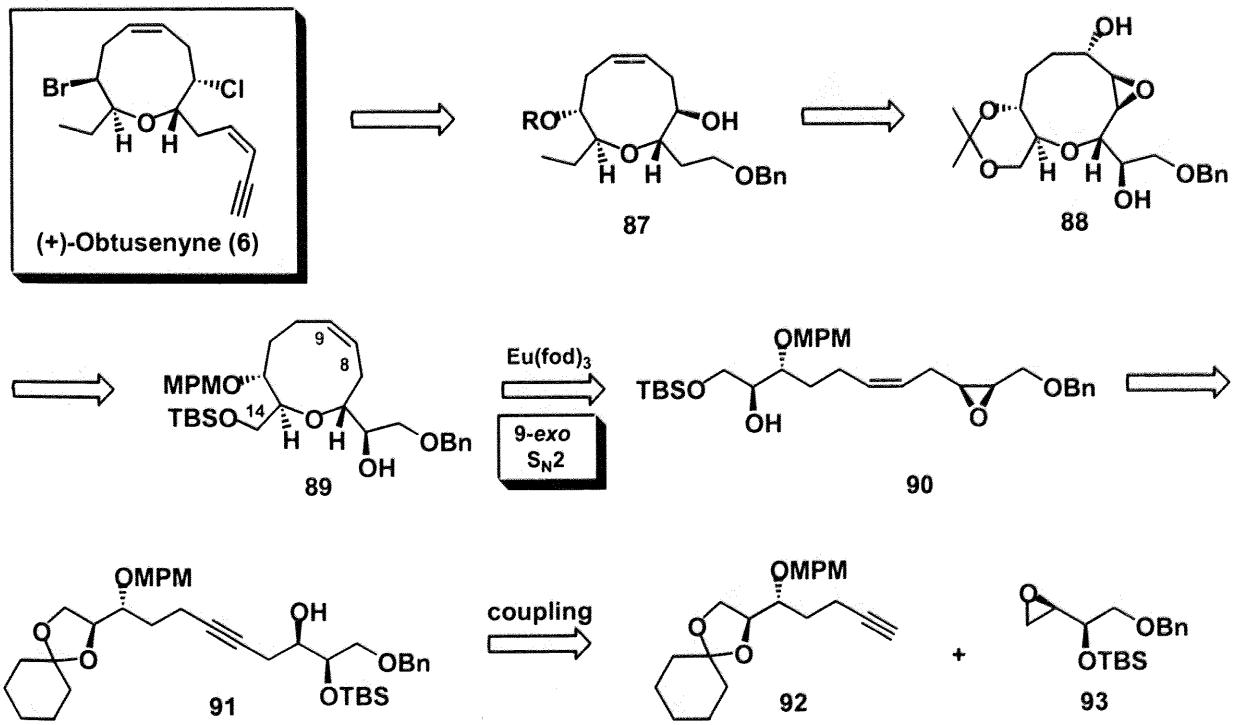
As a consequence, various attempts on the subject of introduction of the β-hydroxy group at the C7 position were unsuccessful. These failures forced us to devise an alternative synthetic plan. To prevent a transannular reaction from ethereal oxygen atom is the most important task for the new plan.

Chapter 5

Achievement of the Total Synthesis of (+)-Obtusenyne

5.1 Third Synthetic Strategy towards (+)-Obtusenyne

We envisaged that the structure introduced a fused-ring system was efficient for prevention of the previously observed transannular reaction. This was the idea inspired by the Tachibana' s synthesis of ciguatoxin[1], because the knowledge had been reported that the corresponding product was obtained quantitatively when the same sequence was conducted on nine-membered ether possessing a fused structure . To obtain the *trans*-fused acetonide **88**, the cyclic compound **89** that oxygen functional group was introduced at the C14 position on the former substrate was needed. The required **89** would be achieved from the cyclization of acyclic precursor **90** promoted by $Eu(fod)_3$. Compound **90** would be provided via few steps involving the coupling reaction of acetylene **92** and epoxide **93**. Acetylene **92** will be readily derived from the replacement of protection group [Bn → MPM] of intermediate **45** in the previous synthesis of acetylene. Epoxide **93** will be afforded by the same procedure as the former epoxide synthesis.

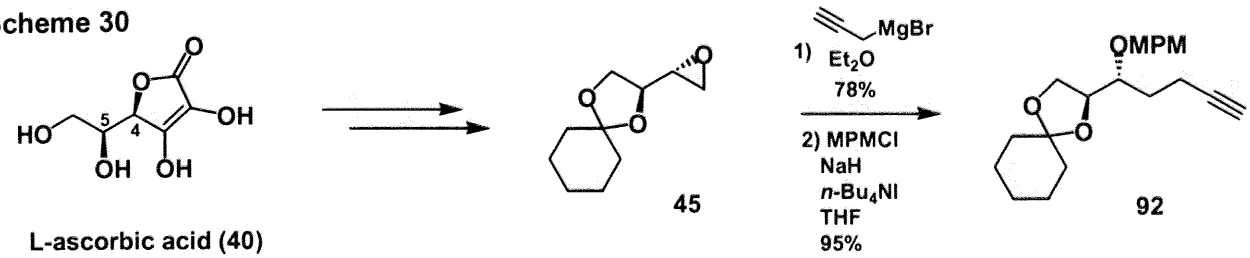


Scheme 29 New Synthetic Strategy

5.2.1 Synthesis of the Acetylene Fragment 92

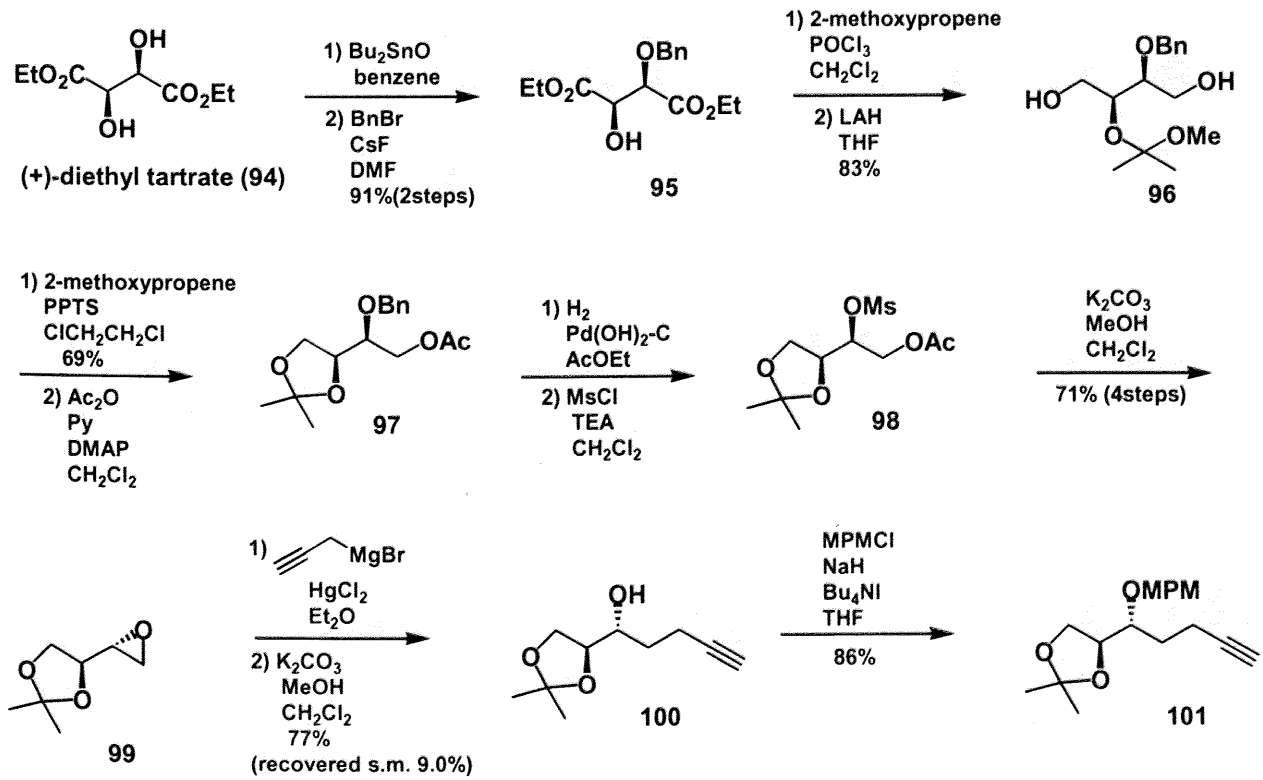
Acetylene **92** was obtained from an intermediate in the previous acetylene synthesis, namely it was furnished by addition of propalgyl group to the previously common intermediate **45** (section 4.2.1) and then protection as its MPM ether. However, the synthetic route involved methylesteration with hazardous CH_2N_2 and comparatively troublesome ozonolysis. Therefore, we decided to devise an alternative route without these operations.

Scheme 30



To avoid the ozonolysis process and the preparation and the using of CH_2N_2, (+)-diethyl tartrate was chosen as the starting material. By the way, the protecting group of diol part on the acetylene fragment **92** was altered from cyclohexylidene to acetonide.

Scheme 31

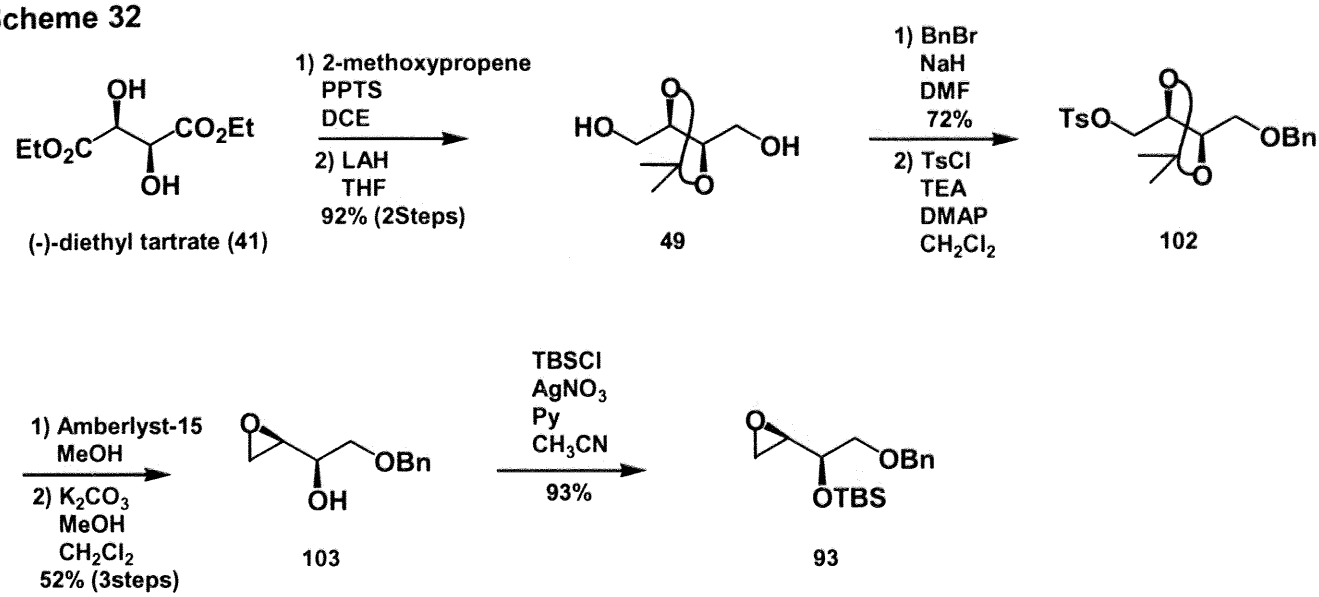


After mono-protection by benzyl group utilizing a cyclic tin ether[2], introduction of ketal moiety to the intact hydroxy group with $POCl_3$/2-methoxypropene and subsequent LAH reduction gave diol **96**. Acidic treatment of **96** afforded kinetically and thermodynamically favorable five-membered ring acetonide as a main product, whose the remaining hydroxy group was protected by acetyl group. Then, the obtained **97** was converted into epoxide **99** with inversion of the configuration via the following sequence: (1) deprotection of benzyl group, (2) mesylation of the resulting hydroxy group, (3) treatment with K_2CO_3 in $MeOH/CH_2Cl_2$. All steps proceeded in good yields. Addition of 3-propynylmagnesium bromide (77%) followed by protection of the resulting hydroxy group as its MPM ether afforded acetylene **101**. Consequently, the number of synthetic step decreased from 14 to 12 and the total yield was improved from 19.2% to 24.5%.

5.2.2 Synthesis of the Epoxy Fragment 93

Synthesis of epoxide **93** could be accomplished by the previous synthetic strategy (section 4.2.2). Difference from the former epoxy fragment is only a protecting group, i.e., from MPM group to benzyl group. As a matter of course, the synthesis of epoxy fragment **93** was completed without any problems.

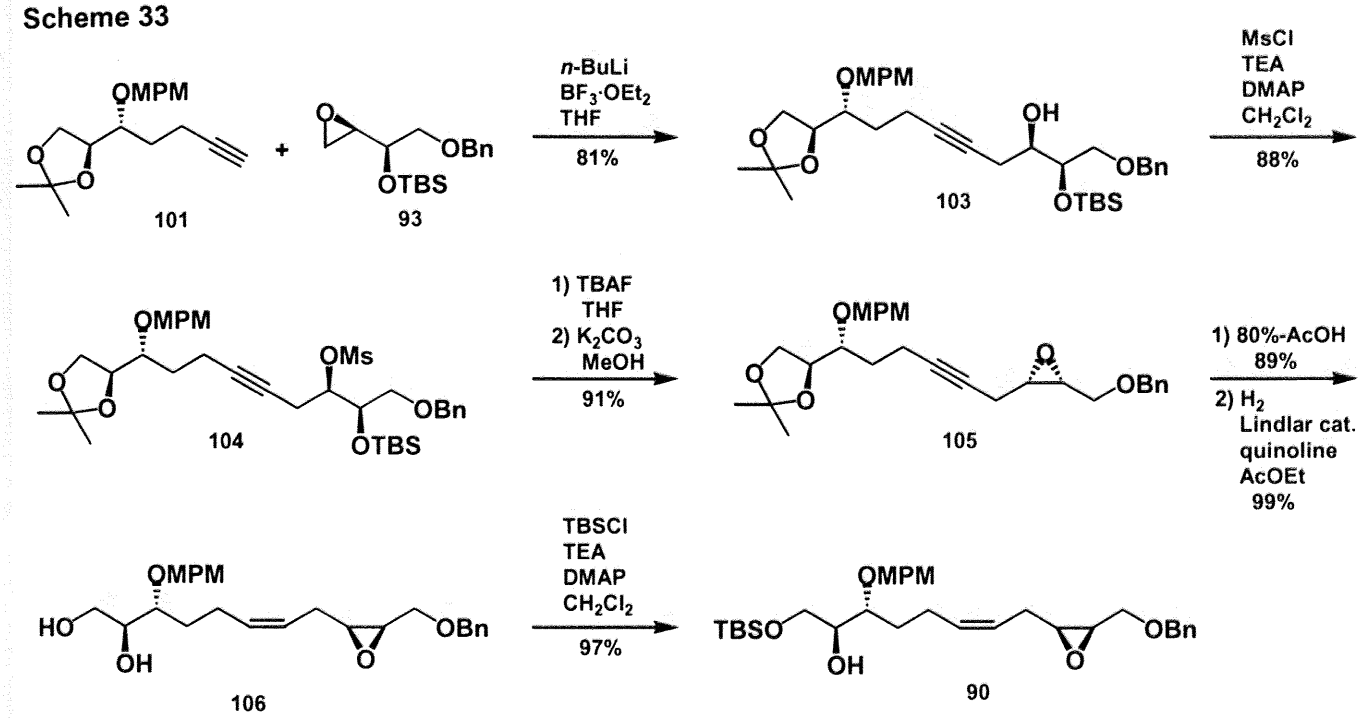
Scheme 32



5.2.3 Synthesis of Acyclic precursor and Cyclization

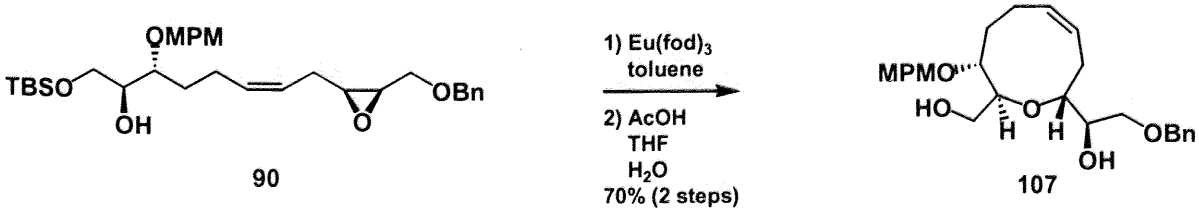
Coupling reaction of acetylene **101** and epoxide **93** was achieved under Yamaguchi's condition[3] as before. By using the similar strategy to precedent, epoxy acetylene **105** was furnished. Subsequently, deprotection of the acetonide and hydrogenation by Lindlar catalyst gave diol **106**. Acyclic precursor **90** for cyclization was completed by TBS protection of the primary hydroxy group.

Scheme 33



Although the stereospecific cyclization of **90** proceeded smoothly, since a partial deprotection of the TBS group was observed on TLC plate, its crude product was subjected to next acid treatment with AcOH/H_2O/THF to remove the TBS group. Thus, diol **107** was obtained in 70% yield via two steps. This observed yield is good result for assemblage of nine-membered ring.

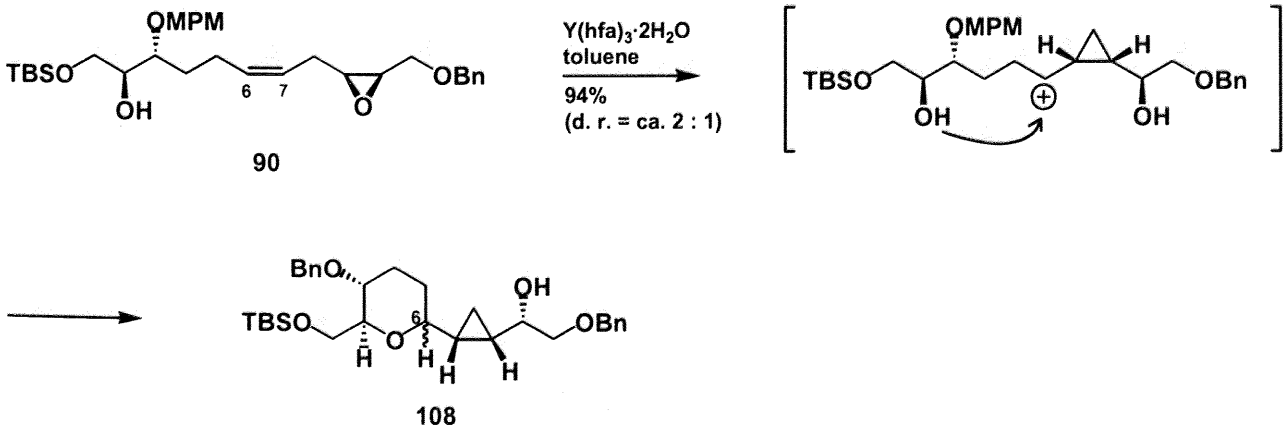
Scheme 34



In contrast to this result, cyclization of **90** promoted by $Y(hfa)_3 \cdot 2H_2O$ afforded two cyclopropane derivatives as its diastereomer at C6. This reaction mechanism was considered that the C7 double bond attacked to epoxide via *exo*-mode and then the generated cation at the C6 position was trapped with hydroxy group, forming tetrahydropyran ring. The diastereomeric ratio on the observed products was approximately 2:1. Difference of the reactivity on this reaction would be caused by stronger Lewis acidity of $Y(hfa)_3 \cdot 2H_2O$. Although the reaction of **90** with $Eu(fod)_3$ was quite sluggish, in the case of the reaction promoted by $Y(hfa)_3 \cdot 2H_2O$, the reaction time was dramatically short (100h → 1h). Since formation of the nine-membered ring usually did not occur smoothly even though more reactive Lewis acid was used, only side reaction was activated and consequently, the cyclopropane products **108** would be obtained prior to **107**.

If this reaction could proceed via a concerted process, an improvement of the diastereoselectivity is able to be expected so that it should be applied to the synthesis of natural products involving cyclopropane in its structure. In the point of view, this reaction is very attractive and it is worth further investigation. Our laboratory is investigating about this reaction and further details would be reported someday.

Scheme 35

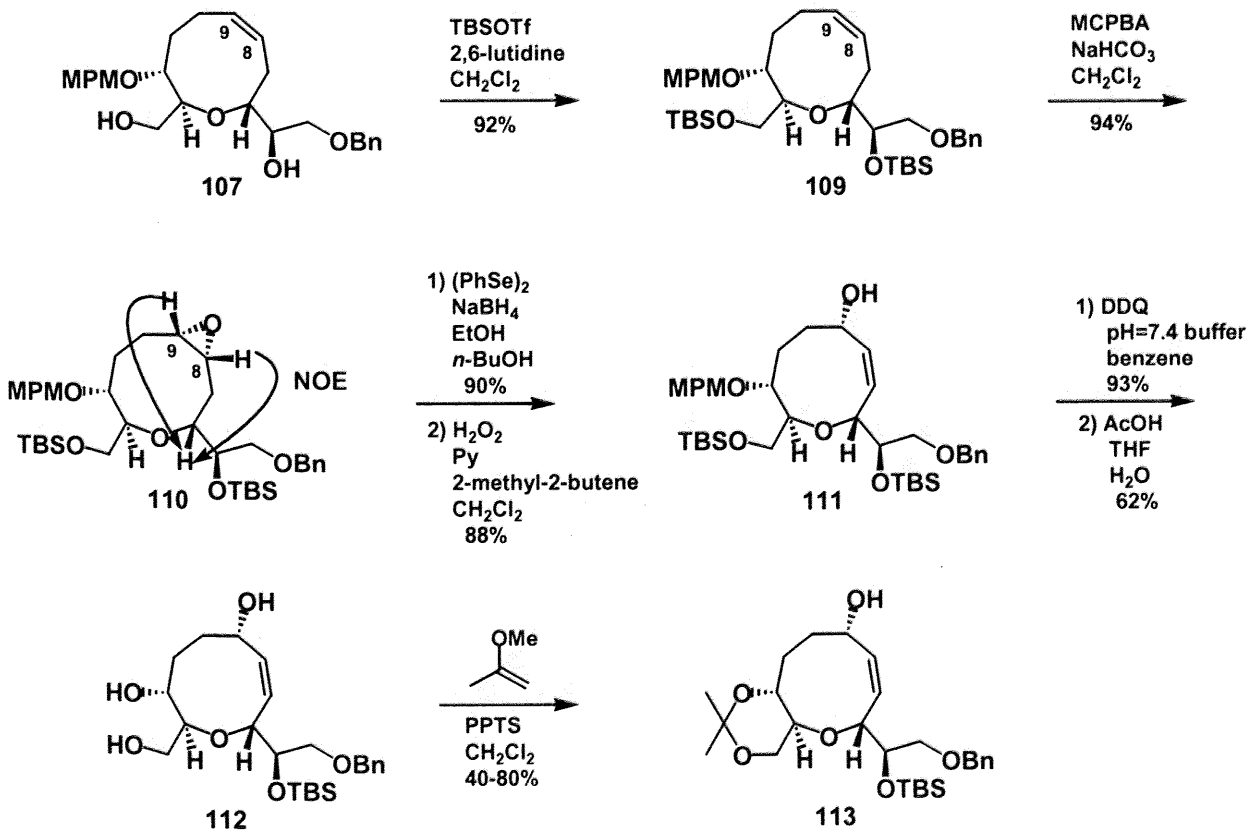


5.3 Introduction of Oxygenated group on Nine-membered Ring

Next, stereoselective introduction of oxygenated group on the oxonene ring by utilization of the C8, 9 double bond was examined. The two hydroxy groups resulting from cyclization were protected as its TBS ether and then epoxidation with MCPBA on convex face afforded α-epoxide **110**. The obtained α-epoxide was changed into allylalcohol **111** by the former procedure. As following conversion, deprotection of the MPM group and regioselective cleavage of the primary TBS ether under acidic condition followed by formation of the acetonide using a basic condition was carried out. However, the reproducibility was poor on the acetonide-formation process so that **113** was produced in 40-81% yield.

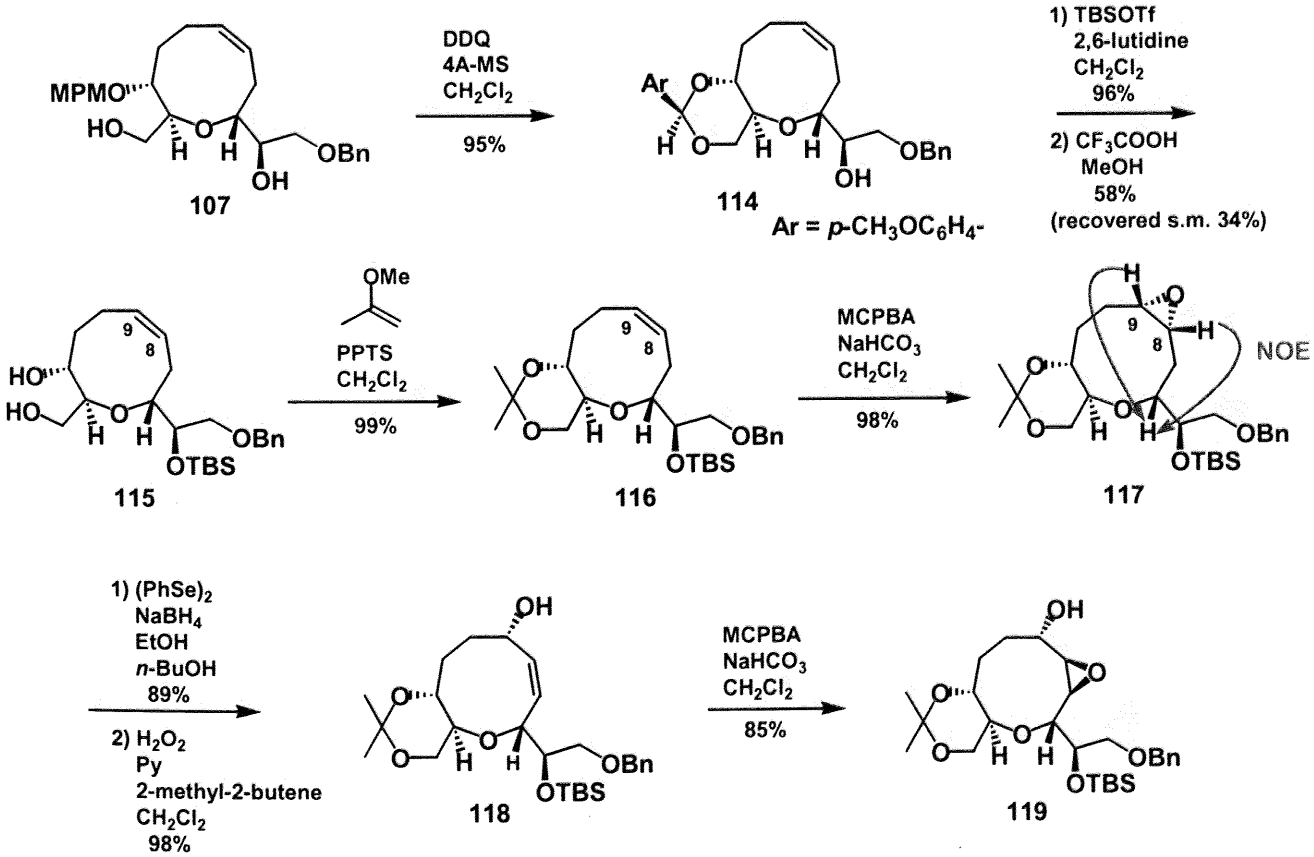
Since some products derived from the free allylalcohol were observed on TLC plate, this reaction was interrupted presumably by side reaction contributed to the free allylic hydroxy group. In addition to this result, triol was not feasible for a synthetic intermediate because of its hydrophilicity. Therefore, new route was applied that triol was not involved as an intermediate.

Scheme 36



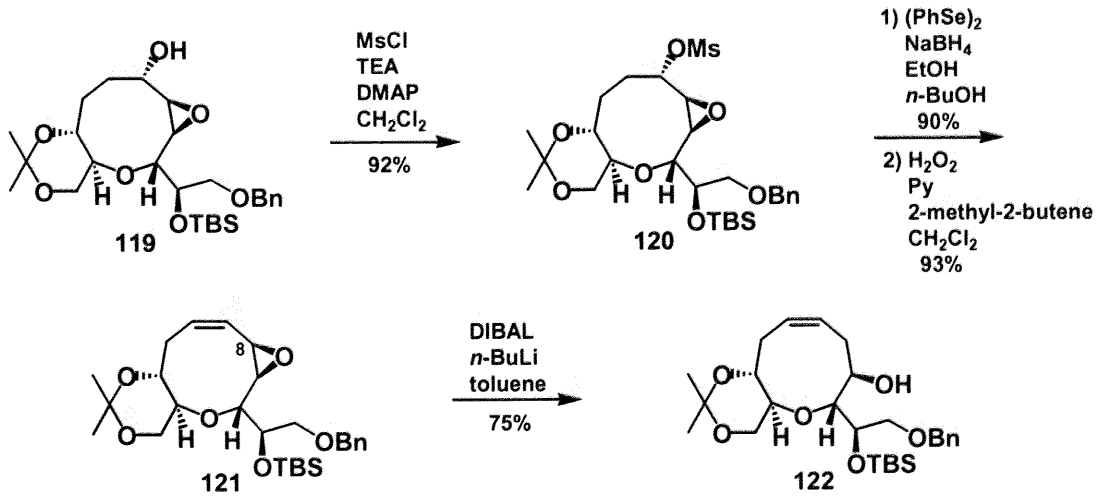
Diol **107** which was obtained by cyclization was converted into anisilidene **114** under the condition of DDQ/4A-MS/CH_2Cl_2 in 95% yield. The remaining secondary hydroxy group of **114** was protected as its TBS ether followed by exposure to CF_3COOH/MeOH afforded diol **115**. Protection of the diol part on **115** with acetonide was completed in quantitative yield and following stereoselective introduction of oxygenated group on oxonene **116** by utilization of the C8, 9 double bond was examined. Expectedly, its transformation proceeded as before, namely epoxydation of **116** with MCPBA gave α-epoxide and subsequent PhSe-addition/oxidation by peroxide afforded allylalcohol **118**, which was changed into β-epoxy alcohol **119** exclusively via affection between the neighboring C9-OH and MCPBA[4]. The prepared **119** was subjected to next examination step for conversion into allylepoxide.

Scheme 37



Then the mesylation of **119** was examined under the condition of MsCl/TEA/DMAP in CH_2Cl_2. In the case of this substrate, transannular reaction was not occurred at all and the expected mesylate **120** was afforded quantitatively. It was obvious that the trans-fused structure by the acetonide moiety played an important role in this reaction. Although a slight conformational change was predicted, experiments using computational analysis for the confirmation have not been conducted yet. Substitution of PhSe and then *syn*-elimination using selenoxide gave the expected allylepoxide **121**. Resioselective epoxide-opening at the C8 position of the obtained **121** was achieved by the ate complex prepared from DIBAL and *n*-BuLi[5], affording homoallylalcohol **122** in 75% yield. In the case of using superhydride, the reaction did not proceed at all. As a result, highly reactive and hinder hydride agent like Red-Al, $[(i\text{-Bu})_2Al(n\text{-Bu})]^-Li^+$ and so on, was required in this reaction. Thus, the construction of oxonene skeleton possessing the required stereochemistry was completed.

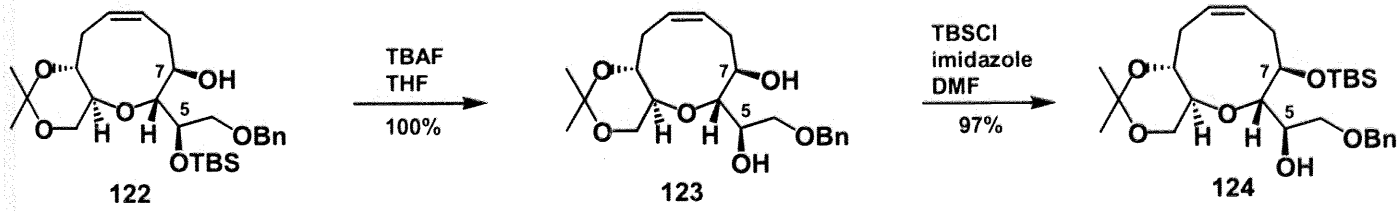
Scheme 38



5.4 Removal of the C5-OH

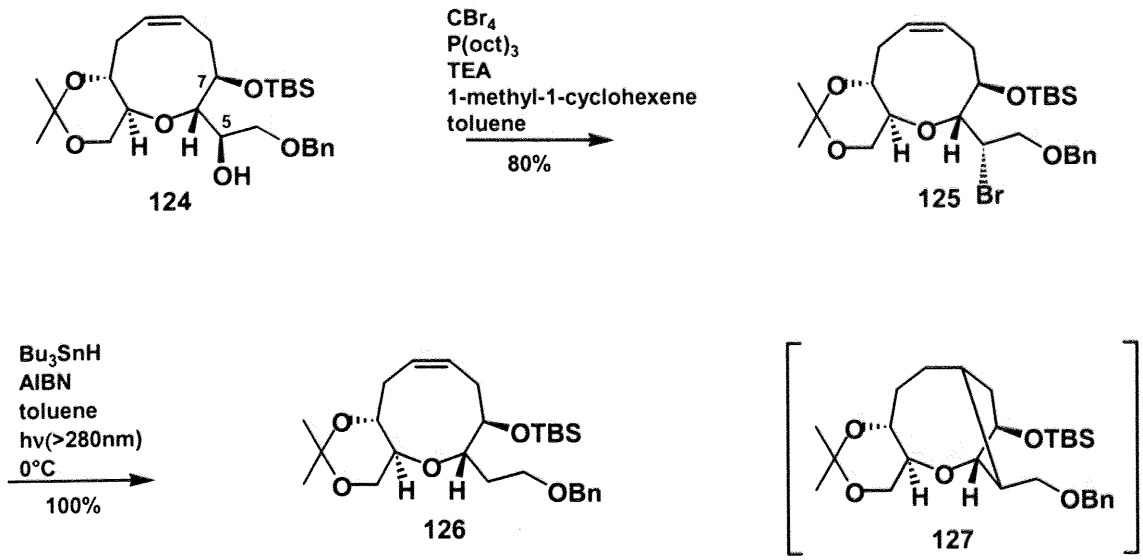
Our next attempt was removal of the C5-OH. To achieve this task, the hydroxy group at C7 was protected as its acetate, which was subjected to next desilylation under various conditions. Disappointedly, the reaction with HF·Py/Py/THF, TBAF/AcOH/THF, $KF{\cdot}2H_2O$/pH=6.7 buffer/CH_3CN and so on, resulted in recovery of the starting material in any cases, while basic condition like TBAF/THF provided diol **123**. It was obvious that the steric hindrance at C5 increased due to introduction of protecting group at the C7-OH. In addition, conversion via silyl migration from the C5-OTBS to the C7-OH using NaH or KH did not give a satisfied result (**122**:**124** = 2:3-3:2). Serendipitously, transformation of **122** into diol **123** followed by TBS-protection under the condition of TBSCl/imidazole/DMF was found out to afford only the desired alcohol **124**. This result would be obtained because of the difference of steric hindrance between C5 and C7 and the nature that introduction of protecting group at C7-OH increased the steric hindrance at the C5 position.

Scheme 39



Next bromination was carried out by stepwise protocol at first. Specifically, bromide **125** was provided by the conversion into trifluoromethanesulfonate derivative under the condition of Tf_2O/pyridine/DMAP/CH_2Cl_2, followed by bromide S_N2 replacement with *n*-Bu_4NBr/toluene at 50°C. This protocol was applied because it was anticipated that the C5-OH had a major steric hindrance. Though, the yield was moderate and the result could not be improved. We estimated that this unsatisfied result was caused by highly reactive the triflic group.

Scheme 40



124 125 126 127

Although it was anticipated that the reaction was not occurred due to the steric hindrance at the C5 position, we examined the directive bromination using $CBr_4/P(oct)_3$[6].

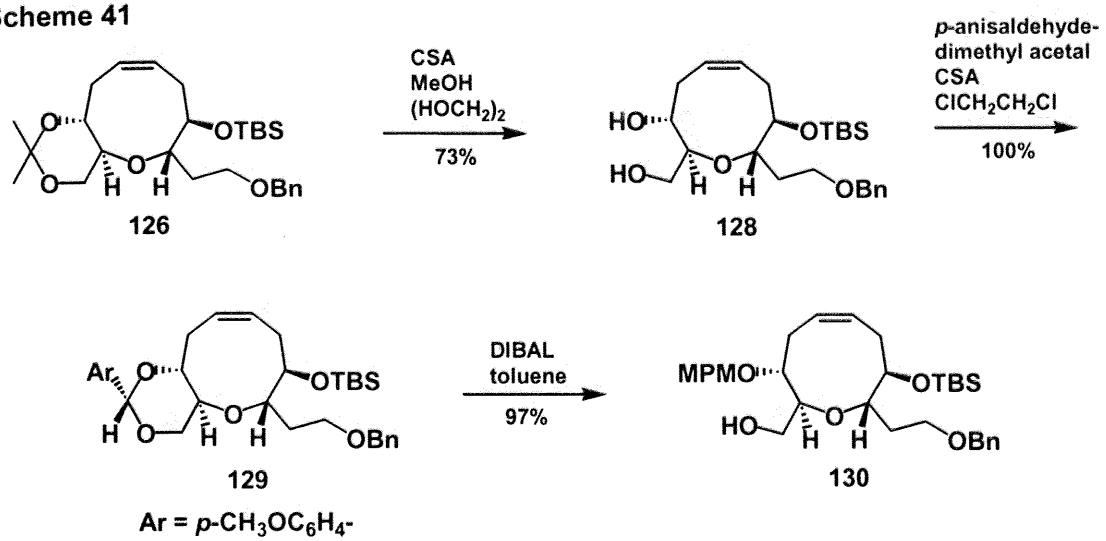
To our delight, this reaction proceeded very well. According to this result, the problem of bromination of the hydroxy group at the C5 position was overcome.

Next removal of bromine substituent was accomplished by photo-irradiation in the presence of *n*-Bu_3SnH/AIBN in toluene at 0°C[7] in excellent yield. The most important issue on this reaction was reaction temperature. Indeed, a basic condition, like *n*-Bu_3SnH/AIBN/toluene at 100°C gave by-product **127**, which was formed through olefin insertion of radical arising from the removal of bromide substituent. In the case of another condition of *n*-Bu_3SnH/BEt_3/toluene at 0°C, unidentified by-product was produced probably due to Lewis acidity of BEt_3. As a result, the strategy using photo-irradiation was the best methodology on removal of the bromine substituent.

5.5.1 Installment of C1 moiety

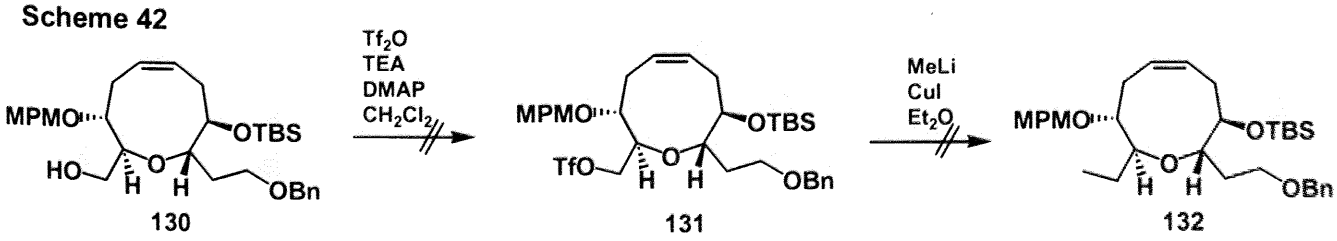
Next, to examine C1 homologation, alcohol **130** was furnished by a standard transformation. The acetonide group of **126** was deprotected with CSA/MeOH/$(HOCH_2)_2$. The resulting diol was changed into anisylidene **129** and the following regioselective anisylidene opening with DIBAL provided alcohol **130**.

Scheme 41



The methodology developed by Kotsuki[8] was applied to introduce C1 unit to alcohol **130**. Specifically, this strategy is efficient for a substitution reaction that hydroxy group is at β-position of cyclic ether and it consists of following sequence (1) introduction of trifluoromethanesulfonyl group (2) substitution by R_2CuLi. Substitution at this position requires rather reactive triflic group as the leaving group and highly reactive R_2CuLi as a nucleophile due to electro-withdrawing effect of ethereal oxygen atom. However, the triflate derivative generated from **130** was very unstable and immediately decomposed. Although the generation of triflate derivative could not be unambiguously confirmed on TLC plate, following treatment by Me_2CuLi was carried out for confirmation. Consequently, the desired product introduced the C1 unit was not obtained at all. Therefore, experiment on model substrate for the replacement of Me group was examined.

Scheme 42



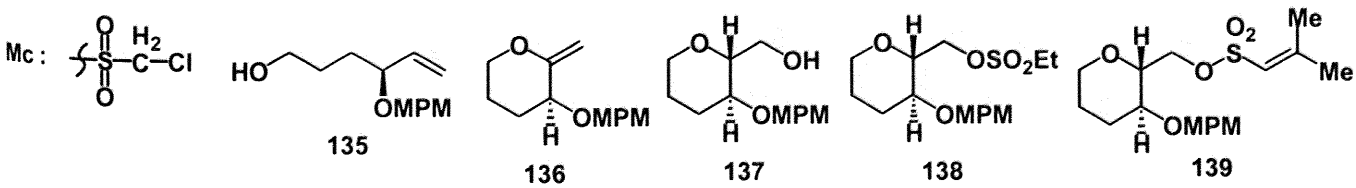
5.5.2 Examination of C1 Homologation on Model Substrates

When bromide and iodide were used as the leaving group, terminal olefin and ring opening product were afforded via single electron transfer mechanism, respectively. Since the knowledge had already been reported that substitution in this position did not proceed in using *p*-toluenesulfonate (tosyl) or methanesulfonate (mesyl) as the leaving group, next attempting leaving groups were monochlate[9] and tresyl[10] group which were more reactive than tosyl and mesyl group. Monochlate group was utilized as useful leaving group in ring-expanding reaction and S_N2 substitution reaction by CsOAc, nevertheless alkylation on the type like this model substrate had not been reported. We were expected that this leaving group had moderate reactivity between triflic group and mesyl group. However, reaction on monochlate derivative with Me_2CuLi or $Me_2CuCNLi_2$[11] yielded ethylsulfonate substrate **138** that methyl group displaced chlorine substituent and alcohol **137** which was furnished by desulfonation via single electron transfer mechanism. Thus the tresyl group was applied as the next leaving group. It has trifluoromethyl moiety instead of chlorine substituent, which is less capacity of single electron transfer so that by-products via SET mechanism were not obtained at all, but only the undesired product **139** was afforded through elimination-addition process.

Table 4

133 134

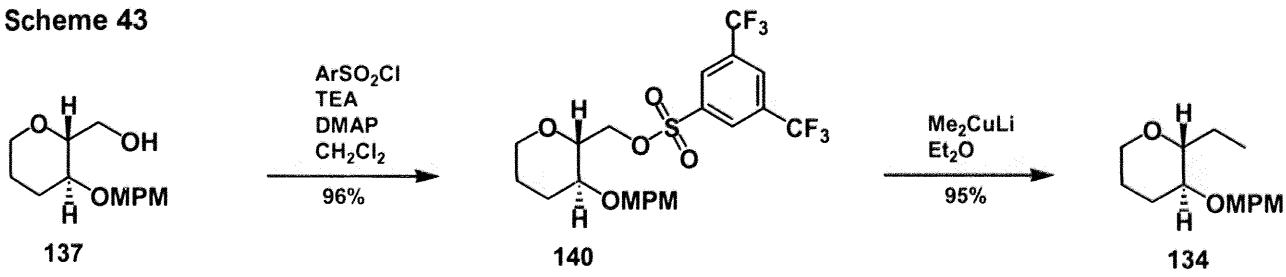
entry	x	reagent (eq.)	solvent	temp. (°C)	product	yield (%)
1	I	$Me_2Cu(CN)Li_2$(4.0)	THF	-78 ~ -50	35	97
2	Br	$Me_2Cu(CN)Li_2$(3.0)	THF	-78 ~ r.t.	36	87
3	OMc	$Me_2Cu(CN)Li_2$(4.0)	THF	-78 ~ 0	31	76
4	OMc	Me_2CuLi(2.0)	Et_2O	-78 ~ 0	31, 32	51, 37



135 136 137 138 139

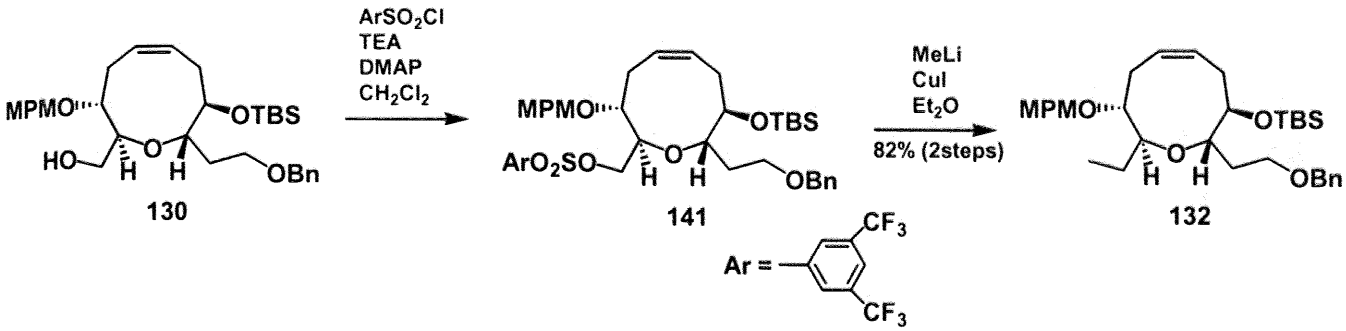
In both cases, the existence of the methylene part adjacent to sulfonyl moiety was probably problematic. To solve this problem, benzenesulfonate derivative was applied as the leaving group. Thus, 3,5-bis(trifluoromethyl)benzenesulfonyl[12] group that trifluoromethyl substituent was introduced to activate the reactivity was applied as the next leaving group. Sulfonate **140** derived from alcohol **137** could be isolated steadily by silica gel column. Incidentally, triflate derivative derived from this substrate was unstable and could not be isolated. Subsequently, treatment of sulfonate **140** with Me_2CuLi provided the desired product **134** in excellent yield. This newly found leaving group has a moderate reactivity and stability. Example of substitution utilizing this leaving group have not been reported yet and further application to broad alkylation is expected. Alkylation reactions on various substrates using various alkyl cuprates have been studying in our laboratory now.

Scheme 43



5.5.3 Achievement of Installment of C1 Moiety

Scheme 44

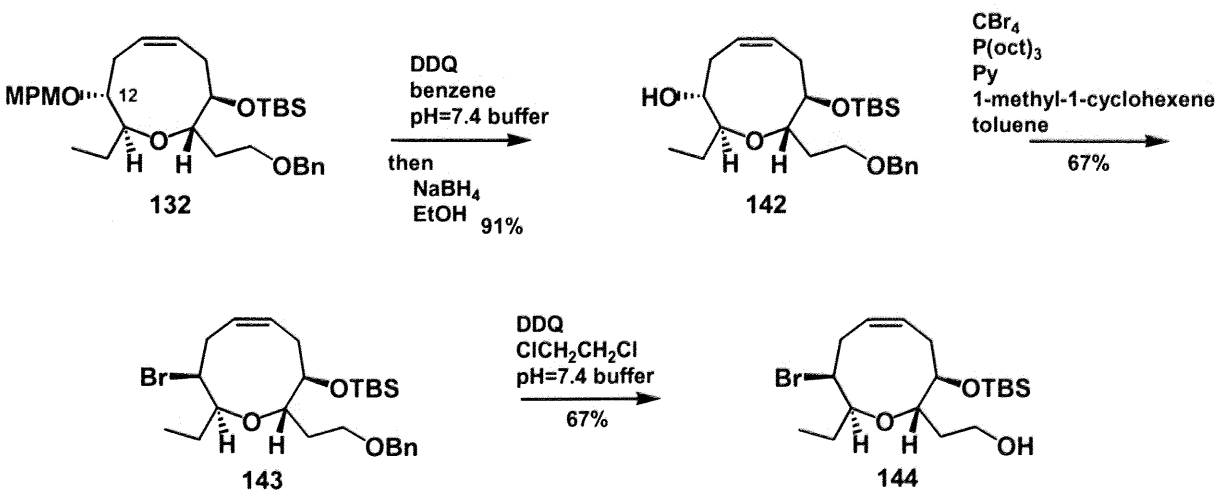


The above developed methodology was also efficient in the case of the actual substrate. The reaction with 3,5-bis(trifluoromethyl)benezenesulfonyl chloride/TEA/DMAP in CH_2Cl_2 yielded sulfonate **141** smoothly. In the case of this substrate, the sulfonate was a little unstable and therefore, the crude product was subjected to next alkylation step without purification. As the precedent, exposure to Me_2CuLi afforded alkylated product **132** in 82% yield. This strategy would be the powerful tool in order to introduce alkyl group to this position on cyclic ether.

5.6 The Total Synthesis of (+)-Obtusenyne

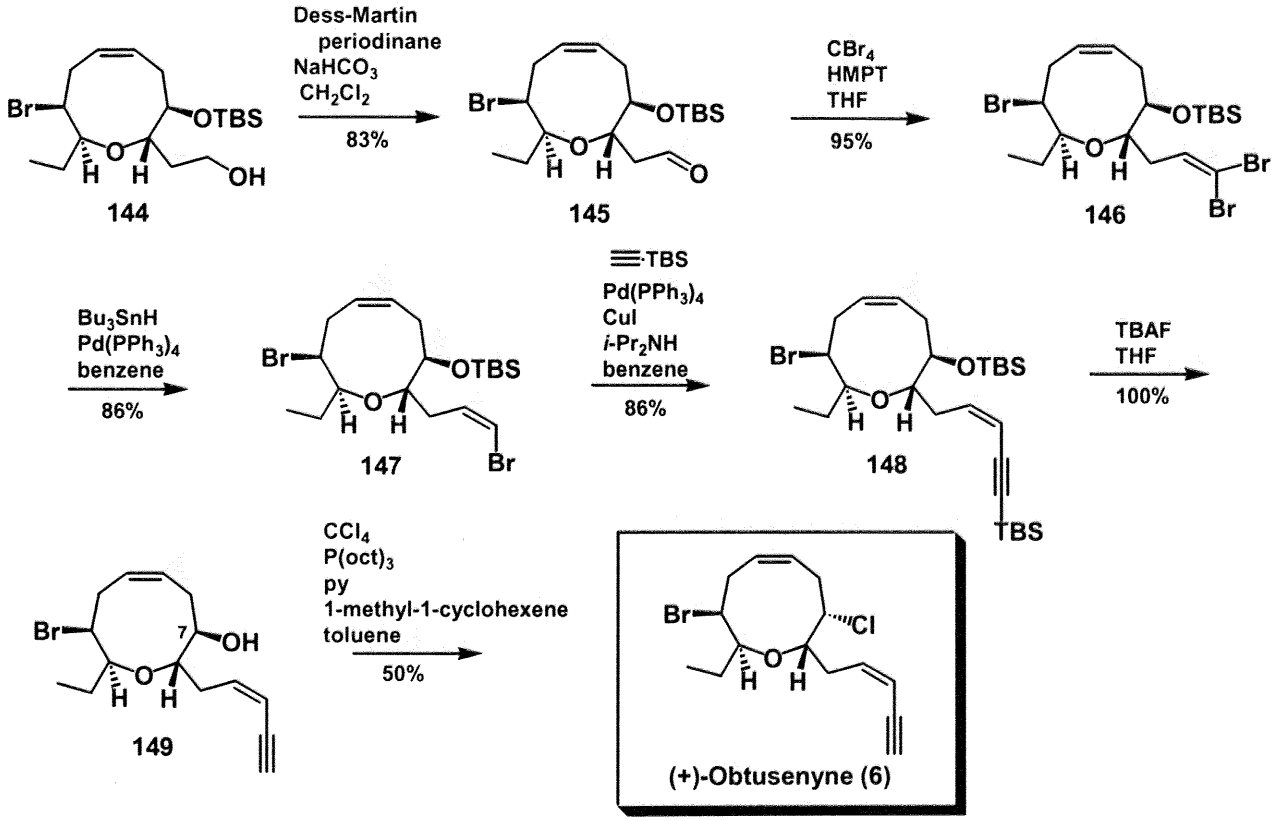
Next task was introduction of the bromine substituent at the C12 position. Treatment with DDQ in the mixed solution of benzene/pH=7.4 buffer was carried out to remove only MPM group and following $NaBH_4$ reduction of anisaldehyde (inseparable by-product on DDQ treatment) gave alcohol **142** as a pure product. Conversion of **142** to bromide **143** was achieved by treatment with $CBr_4/P(oct)_3$/pyridine/1-methyl-1-cyclohexene/toluene[6] in moderate yield. Because the knowledge had been reported in the total synthesis of (-)-12,13-epi-obtusenyne[1] that 5,9-*cis*-fused product was afforded via nucleophilic attack from benzyl ethereal oxygen if chlorination was executed before installment of enyne moiety, transformation from the obtained **144** to (+)-obtusenyne had to submit following order (1) installment of enyne moiety (2) chlorination at later stage. Thus next operation was deprotection of the benzyl group, which was completed under the condition of DDQ/DCE/pH=7.4 buffer at 50°C, providing alcohol **144**. Submission to $BCl_3 \cdot SMe_2/CH_2Cl_2$[13] or $PhSTMS/ZnX_2$(X=Br or Cl)/CH_2Cl_2[14] resulted in a poor yield due to simultaneous deprotection of the TBS group.

Scheme 45



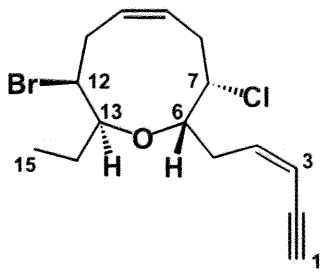
To install *cis*-enyne moiety, alcohol **144** was oxidized with Dess-Martin periodinane[15] and the resulting aldehyde was converted into dibromoolefin **146** by corey-fuchs procedure[16]. (*Z*)-Bromoolefin **147** was afforded through Pd-mediated reduction of **146** by Uenishi method[17], whose Sonogashira coupling[18] with TBS acetylene furnished **148** having *cis*-enyne moiety. Exposure of **148** to TBAF in THF gave alcohol **149**, a common intermediate in Crimmins' synthesis[19]. Finally, chlorination under the same condition as Crimmins' accomplished the total synthesis of (+)-obtusenyne.

Scheme 46



The specific data of the synthetic product showed a good accordance with natural product's data[20]. In conclusion, we achieved the total synthesis of (+)-obtusenyne using the original medium-sized ring cyclization promoted by $Eu(fod)_3$. It is expected that this accomplishment is as not only a new strategy for an approach to (+)-obtusenyne, but a platform of the synthesis for various natural products involving medium-sized rings.

^{13}C NMR of (+)-Obtusenyne



(+)-Obtusenyne (6)

Synthetic : $[\alpha]^{21.6}_{D}$ = +145.2°($CDCl_3$)

Natural : $[\alpha]^{21.6}_{D}$ = +155° ($CDCl_3$)

	Synthetic (125MHz, $CDCl_3$)	Natural (75MHz, $CDCl_3$)[1)]
C_4	141.0 (d)	140.9
C_{10}	130.6 (d)	130.7
C_9	128.3 (d)	128.9
C_3	111.0 (d)	110.0
C_1	83.0 (d)	83.0
C_2	80.3 (s)	80.3
C_6	n.d.[2)] (d)	77.9
C_{13}	n.d.[2)] (d)	75.4
C_7	63.6 (d)	63.6
C_{12}	56.9 (d)	56.8
C_5	35.6 (t)	35.6
C_8	32.7 (t)	32.1
C_{11}	31.6 (t)	31.6
C_{14}	29.0 (t)	29.0
C_{15}	10.3 (q)	10.4

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2) Not detectable

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EXPERIMENTAL SECTION

General Information

Unless otherwise noted, all reactions were conducted in oven-dried glassware with magnetic stirring under an atmosphere of dry nitrogen, and were monitored by thin layer chromatography (TLC). Solvents used for extraction and flash chromatography were HPLC grade. Preparative thin layer chromatography was performed on Merck silica gel 60-F_{254} plates (20 cm x 20 cm) of the indicated thickness. Flash column chromatography was performed on Merck silica gel 60 (230-400 mesh) or Kanto florisil 75-150 μm (100-200 mesh).

When necessary, reaction solvents and reagents were distilled under inert atmosphere (or reduced pressure). Tetrahydrofuran (THF) and diethyl ether (Et_2O) were distilled from sodium benzophenone ketyl prior to use. Dichloromethane (CH_2Cl_2) and benzene were distilled from calcium hydride prior to use. Toluene, xylenes, acetonitrile (CH_3CN), 1,2-dichloroethane (DCE), acetic anhydride (Ac_2O), pyridine, triethylamine (Et_3N), and diisopropylamine (*i*-Pr_2NH) were distilled from calcium hydride and stored over 4Å molecular sieves under a nitrogen atmosphere. 2,2-Dimethoxypropane was distilled from sodium metal and stored under a nitrogen atmosphere. Hexamethylphosphoramide (HMPA) and 2,6- lutidine were distilled under reduced pressure from calcium hydride and stored over 4Å molecular sieves under a nitrogen atmosphere. Boron trifluoride diethyl etherate ($Et_2O{\cdot}BF_3$) was distilled under reduced pressure from calcium hydride prior to use. Anhydrous *N,N*-dimethylformamide (DMF) and dimethyl sulfoxide (DMSO) were purchased from Wako Pure Chemical Industries. Methanol, ethanol, acetone, 1-methyl-1-cyclohexene, diethyl L-tartrate and titanium(IV) isopropoxide were distilled without the addition of a drying agent. pH 6.7 Phosphate buffer was prepared by mixing 1/30 M Na_2HPO_4 and 1/30 M KH_2PO_4 solution with a 1:1 ratio, and also pH 7.4 one was an 84:16 mixture of 1/15 M Na_2HPO_4 and 1/15 M KH_2PO_4 solution. All other reagents were purchased and used as received.

Melting points were determined with a Yanaco MP-S3 melting point apparatus. Specific rotations were measured at 15 - 25 °C on a Horiba SEPA-2000 spectrophotometer using sodium lamp (589 nm, D line), and reported as follows: $[\alpha]^{temp.}{}_{D}$ (c = g/100 mL, solvent). Infrared spectra were taken on a Hitachi 270-30 or a Shimazu FT/IR-4200 spectrophotometer. ^{1}H NMR spectra were recorded on a Varian Gemini 500 plus (500MHz), 200 plus (200MHz) and JEOL 270 plus (270MHz) spectrometer. Chemical shifts are reported in ppm from the solvent resonance as the internal standard [deuterochloroform: 7.26 ppm, deuterobenzene: 7.15 ppm or 0.00ppm (TMS)]. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), and integration. ^{13}C NMR spectra were recorded on Varian Gemini 500 plus (125MHz) spectrometers with complete proton decoupling. Chemical shifts are reported in ppm from the solvent resonance as the internal standard (deuterochloroform: 77.0 ppm). DEPT experiment was used to assign signals in particular cases. Two dimensional ^{1}H and ^{13}C NMR (COSY, HMQC, and HMBC) experiments were recorded on a Varian Gemini 500 plus (500MHz) spectrometer. As indicated in the text, stereochemistry was assigned using NOE difference spectroscopy and HMBC experiment. Mass spectra were obtained on a JEOL GC-mate. High performance liquid chromatography (HPLC) was carried out on a Hitachi L-6250 instrument with a silica gel packed column.

Chapter 3

Cyclohexylidene acetal

To a mixture of D-mannitol (45.0g, 247.3mmol), cyclohexanone (79.1ml, 717.1mmol) and $HC(OMe)_3$ (16.6ml, 148.4mmol) in DMSO (98.9ml) was added $BF_3 \cdot OEt_2$ (2.43ml, 19.78mmol) at room temperature. The mixture was stirred for 20h at room temperature under nitrogen. Then sat. $NaHCO_3$ was added to quench $BF_3 \cdot OEt_2$ at 0°C and the stirring was continued for 30min at room temperature. The resultant products were extracted with Et_2O and the organic layer was washed with H_2O and sat. brine. The aqueous layer was extracted once with Et_2O. The organic extracts were dried with Na_2SO_4 and concentrated *in vacuo*. The obtained crystal was purified by recrystallization with hexane:Et_2O=2:1 (washed with hexane:Et_2O=4:1) followed by silica gel column [EtOAc:hexane (1:10)] afforded cyclohexyridene acetal (50.86g, 148.5mmol) as a crystal: ^{1}H-NMR (200MHz, $CDCl_3$) δ 4.21 (ddd, J=6.8, 6.2, 5.4Hz, 2H), 4.12 (dd, J=8.2, 6.2Hz, 2H), 3.89 (dd, J=8.2, 5.4Hz, 2H), 3.75 (ddd, J=6.8, 6.8, 2.0Hz, 2H), 2.65 (d, J=2.0Hz, 1H), 2.65 (d, J=2.0Hz, 1H), 1.78-1.19 (m, 20H)

Aldehyde **22**

$NaIO_4$ (3.20g, 14.98mmol) was added portion-wise to a stirred mixture of the former product (2.56g, 7.49mmol) in CH_3CN (45.0ml)/H_2O (30.0ml) at 0°C. The mixture was stirred for 30min at room temperature under nitrogen. Then the resulting mixture was filtered through a pad of silica gel by the aid of EtOAc and the obtained organic layer was washed with H_2O and sat. brine. The aqueous layer was extracted once with EtOAc and the combined layers were dried with Na_2SO_4. Removal of the solvent *in vacuo* gave an oil, which was subjected to next addition of propalgyl substituent.

Alcohol **23**

To a solution of the crude aldehyde **22** (2.55g, 14.98mmol) and propargyl bromide

(3.49ml, 44.94mmol) in THF (75.0ml) was added a mixture of Zn(Cu) (11.63g, 89.88mmol) and NH_4Cl (2.40g, 44.94mmol) in H_2O (15.0ml) at 0°C. The mixture was stirred for 1h at room temperature under nitrogen. Filtration through a pad of Celite by the aid of CH_2Cl_2 gave a clear solution, which was washed with 5% HCl, sat. $NaHCO_3$ and sat. brine. The aqueous layer was extracted once with CH_2Cl_2 and the combined organic layer was dried with Na_2SO_4. Evaporation of the solvent provided an oil, which was purified by silica gel column [EtOAc:hexane (2:5 to 1:2)] to give **23** (2.27g, 10.78mmol) as an oil: ^{1}H-NMR (200MHz, $CDCl_3$) δ 4.24-3.90 (m, 3H), 3.88-3.66 (m, 1H), 2.54 (ddd, J=17.1, 5.4, 2.7Hz, 1H), 2.58 (ddd, J=17.1, 6.4, 2.7Hz, 1H), 2.18 (d, J=4.6Hz, 1H), 2.07 (dd, J=2.7, 2.7Hz, 1H), 1.68-1.50 (m, 8H), 1.48-1.32 (m, 2H)

Benzyl ether

NaH (646.8mg, 16.17mmol) was added to prepare an anion to a solution of **23** (2.27g, 10.78mmol) in THF (36.0ml) at 0°C and then *n*-Bu_4NI (796.2mg, 2.156mmol) and BnBr (1.92ml, 16.17mmol) were added at room temperature. The mixture was stirred for 1h at room temperature under nitrogen. The reaction was quenched with sat. NH_4Cl and diluted with EtOAc. The organic layer was washed with sat. NH_4Cl and sat. brine and dried with Na_2SO_4. Removal of the solvent left an oil, which was purified by silica gel column [EtOAc:hexane (1:6)] to give benzyl ether (3.24g, 11.77mmol) as an oil: ^{1}H-NMR (200MHz, $CDCl_3$) δ 7.38-7.28 (m, 5H), 4.85 (d, J=11.9Hz, 1H), 4.56 (d, J=11.9Hz, 1H), 4.24 (ddd, J=6.3, 6.3, 5.3Hz, 1H), 2.52 (d, J=2.0Hz, 1H), 1.72-1.48 (m, 8H), 1.50-1.30 (m, 2H)

Diol **24**

To a solution of benzyl ether (303.2mg, 1.059mmol) in MeOH (5.3ml)/CH_2Cl_2 (530.0μl) was added CF_3CO_2H (24.5ml, 0.318mmol) at room temperature and the mixture was stirred for 1h45min. Because the reaction was quite sluggish, the mixture was heated at 40°C for 22h. Subsequently, 530.0μl more of H_2O was further added and the stirring was continued

for 7h30min at 40°C. Since a few amount of the starting material was observed on TLC plate, moreover, 530.0μl more of H_2O was added again and the reaction was finished after 2h. CF_3CO_2H was quenched with K_2CO_3 (229.9mg, 1.589mmol) and the resulting salt was filtered through a pad of Celite by the aid of CH_2Cl_2. Evaporation of the solvent *in vacuo* gave an oil, which was purified by silica gel column [EtOAc:hexane (1:10 to 2:3)] to afford **24** (201.2mg, 0.976mmol) as an oil: ^{1}H-NMR (200MHz, $CDCl_3$) δ 7.41-7.29 (m, 5H), 4.86 (d, J=11.5Hz, 1H), 4.52 (d, J=11.5Hz, 1H), 4.27 (dd, J=4.3, 2.0Hz, 1H), 3.98-3.71 (m, 3H), 2.71(d, J=6.3Hz, 1H), 2.60 (d, J=2.0Hz, 1H), 2.09 (dd, J=7.9, 4.3Hz, 1H)

Tosylate

In a 300ml flask attached a Dean-Stark trap (4A-MS), equipped with a reflux condenser is placed **24** (1.79g, 8.14mmol), toluene (81.0ml) and Bu_2SnO (3.04g, 12.21mmol). The flask was heated to 140°C and the water which distilled out of the mixture with the refluxing toluene is removed at intervals. Refluxing is continued until no more water separates (about 2h). The toluene was then distilled under reduced pressure, and the residual crystal was dissolved in CH_2Cl_2 (81.0ml). To the suspension was added TsCl (1.71g, 8.95mmol) and the mixture was stirred for 3h at room temperature under nitrogen. Removal of the solvent provide a mixture of yellow oil and white crystal, which was purified by silica gel column [EtOAc:hexane (3:5 to 4:5) contained 1% TEA] to afford tosylate (3.05g, 8.14mmol). The obtained product was assigned as a mixture of tosylate and the desired product in next step, epoxide **25** by NMR analysis. Thus, these mixed products were subjected to next base treatment without further purification.

Epoxide **25**

K_2CO_3 (1.69g, 12.2mmol) was added to a solution of tosylate (3.05g, 8.14mmol) in MeOH (20.0ml)/CH_2Cl_2 (20.0ml) at room temperature and the mixture was stirred for 4h under nitrogen. The reaction was quenched with sat. NH_4Cl and the organic layer was washed with sat. NH_4Cl and sat. brine and dried with Na_2SO_4. Removal of the solvent gave

an oil, which was purified by silica gel column [EtOAc:hexane (1:6)] to provide **25** (1.60g, 7.89mmol) as an oil: ^{1}H-NMR (200MHz, $CDCl_3$) δ 7.40-7.29 (m, 5H), 4.82 (d, J=12.0Hz, 1H), 4.68 (d, J=12.0Hz, 1H), 3.52-3.3.43 (m, 1H), 3.14 (ddd, J=5.6, 4.0, 2.6Hz, 1H), 2.81(dd, J=5.1, 4.0Hz, 1H), 2.75 (dd, J=5.1, 2.6Hz, 1H), 2.58 (dt, J=2.6, 2.6Hz, 1H), 2.07 (t, J=2.6Hz, 1H)

Alcohol

The flask containing CuI (1.63g, 8.13mmol) was heated to dry under high vacuum and after cooling, Et_2O (54.0ml) was added to the flask. To the mixture was added dropwise MeLi (16.6ml, 18.97mmol) at − 30°C and the mixture was stirred to prepare cuprate for 5min. Then a solution of **25** (1.10g, 5.42mmol) in Et_2O (9.0ml), which was azeotroped twice with toluene was added to a colorless clear solution of cuprate at − 78°C and the reaction mixture was stirred for 1h30min under nitrogen. In this time, the reaction temperature was rose from − 78 to − 15°C gradually. The reaction was quenched with sat. NH_4Cl and diluted with EtOAc. The organic phase was washed with sat. NH_4Cl, H_2O and sat. brine and dried with Na_2SO_4. Removal of the solvent *in vacuo* left an oil, which was purified by silica gel column [EtOAc:hexane (1:5 to 1:3)] to furnish alcohol (1.06g, 4.85mmol) as an oil: ^{1}H-NMR (200MHz, $CDCl_3$) δ 7.41-7.29 (m, 5H), 4.75 (d, J=11.5Hz, 1H), 4.60 (d, J=11.5Hz, 1H), 3.75 (dt, J=4.2, 4.0Hz, 1H), 3.56 (ddd, J=5.6, 5.6, 4.2Hz, 1H), 2.56 (dt, J=4.0, 2.6Hz, 1H), 2.20 (t, J=2.6Hz, 1H), 1.70-1.35 (m, 2H), 0.99 (dd, J=7.3, 7.3Hz, 3H)

Silyl ether **19**

To a solution of alcohol (1.50g, 6.88mmol) in CH_3CN (46.0ml) were added pyridine (1.11ml, 13.8mmol), TBSCl (1.56g, 10.3mmol) and $AgNO_3$ (1.75g, 10.3mmol) at room temperature and the mixture was stirred for 3h under nitrogen. Then 213.6mg (1.38mmol) more of TBSCl and 235.8mg (1.38mmol) more of $AgNO_3$ were further added and the stirring was continued for additional 1h. The reaction was quenched with sat. brine and the

mixture was filtered through a pad of Celite by the aid of EtOAc. The filtrate was washed with sat. NH_4Cl, H_2O and sat. brine and dried with Na_2SO_4. Removal of the solvent *in vacuo* gave an oil, which was purified by silica gel column [benzene:hexane (1:6 to 1:5 to 1:3 to 1:2)] to provide **19** (1.58g, 4.75mmol):^{1}H-NMR (200MHz, $CDCl_3$) δ 7.42-7.20 (m, 5H), 4.72 (d, J=11.5Hz, 1H), 4.68 (d, J=11.5Hz, 1H), 3.82 (dt, J=5.4, 5.3Hz, 1H), 3.52 (ddd, J=5.4, 5.3, 5.3Hz, 1H), 2.55 (dt, J=5.3, 2.7Hz, 1H), 2.00 (t, J=2.7Hz, 1H), 1.65 (dtd, J=14.1, 7.2, 5.3Hz, 1H), 1.52 (dtd, J=14.1, 7.2, 5.3Hz, 1H), 0.96 (s, 9H), 0.87 (t, J=7.2, 3H), 0.09 (s, 3H), 0.07 (s, 3H)

(*Z*)-Olefin **26**

To a solution of $(o\text{-toryl})_2P(=O)CH_2CO_2Et$ (6.27g, 18.0mmol) in THF (60.0ml) was added NaH (660.0mg, 16.5mmol) at 0°C and the mixture was stirred to prepare an anion for 10min at room temperature. Then a solution of **22** (2.55g, 15.0mmol) in THF (9.0ml) was added by reverse-addition to the former mixture at − 78°C. The reaction mixture was stirred under nitrogen and the reaction temperature was rose to 0°C gradually over 3h. The reaction was quenched with sat. NH_4Cl and the organic layer was washed with H_2O and sat. brine. The aqueous layer was extracted three times with EtOAc and the combined organic phase was dried with Na_2SO_4. Concentration *in vacuo* left an oil, which was purified by silica gel column [EtOAc:hexane (1:15 to 1:10 to 1:5)] to afford **26** (2.37g, 9.86mmol) as an oil: ^{1}H-NMR (200MHz, $CDCl_3$) δ 6.38 (dd, J=11.6, 6.7Hz, 1H), 5.85 (dd, J=11.6, 1.7Hz, 1H), 5.50 (dddd, J=6.9, 6.7, 6.7, 1.7Hz, 1H), 4.37 (dd, J=8.2, 6.9Hz, 1H), 3.71 (s, 3H), 3.62 (dd, J=8.2, 6.7Hz, 1H), 1.73-1.32 (m, 10H)

Allyl alcohol

DIBAL (26.0ml, 24.7mmol) was added to a solution of **26** (2.37g, 9.87mmol) in toluene (49.4ml) at − 78°C. The mixture was stirred under nitrogen and the reaction temperature was rose to − 30°C gradually over 1h45min. The reaction was quenched with EtOAc at − 30°C and after 30min, sat. Rochell salt was added to be formed a chelation with

aluminum at − 15°C. After 2h, the mixture was diluted with EtOAc and washed with sat. brine. The aqueous layer was extracted once with EtOAc and the combined organic layer was dried with Na_2SO_4. Evaporation of the solvent *in vacuo* gave an oil, which was purified by silica gel column [EtOAc:hexane (4:5)] to furnish allyl alcohol (1.77g, 8.94mmol) as an oil: ^{1}H-NMR (200MHz, $CDCl_3$) δ 5.84 (dddd, J=11.2, 7.2, 7.0, 1.2Hz, 1H), 5.57 (dddd, J=11.2, 7.7, 1.4, 1.3Hz, 1H), 4.86 (dddd, J=8.0, 7.7, 6.2, 1.2Hz, 1H), 4.39-4.14 (m, 2H), 4.09 (dd, J=8.0, 6.2Hz, 1H), 3.56 (dd, J=8.0, 8.0Hz, 1H), 1.82-1.31 (m, 11H)

p-Methoxy benzyl ether **27**

To a solution of allyl alcohol (1.77g, 8.94mmol) in THF (29.8ml) were added NaH (500.8mg, 12.5mmol), *n*-Bu_4NI (330.1mg, 0.894mmol) and MPMCl (1.45ml, 10.7mmol) at 0°C and the mixture was stirred for 21h at room temperature under nitrogen. The reaction was quenched with sat. NH_4Cl and the organic layer was washed with sat. NH_4Cl and sat. brine and dried with Na_2SO_4. Concentration of the solution *in vacuo* gave an oil, which was purified by silica gel column [EtOAc:hexane (1:15 to 1:10 to 1:5 to 1:2)] to provide **27** (2.72g, 8.54mmol) as an oil: ^{1}H-NMR (200MHz, $CDCl_3$) δ 7.26 (d, J=8.7Hz, 2H), 6.88 (d, J=8.7Hz, 2H), 5.78 (dtd, J=11.2, 6.1, 1.0Hz, 1H), 5.62 (ddt, J=11.2, 8.1, 1.3Hz, 1H), 4.78 (dddd, J=8.1, 7.9, 6.2, 1.0Hz, 1H), 4.47 (d, J=11.5Hz, 1H), 4.42 (d, J=11.5Hz, 1H), 4.08 (dd, J=6.1, 1.3Hz, 1H), 4.03 (dd, J=8.1, 6.2Hz, 1H), 3.81 (s, 3H), 3.52 (dd, J=8.1, 7.9Hz, 1H), 1.66-1.30 (m, 10H)

Diol

A solution of **27** (202.3mg, 0.635mmol) in 80% aqueous AcOH (1.27ml) was stirred for 1h at 60°C under nitrogen before removing the solvent. The residual oil was purified by silica gel column [EtOAc:hexane (5:2 to 3:1 to 5:1 to 1:0) to afford diol (121.2mg, 0.509mmol) as an oil: ^{1}H-NMR (200MHz, $CDCl_3$) δ 7.26 (d, J=8.7Hz, 2H), 6.89 (d, J=8.7Hz, 2H), 5.77 (dddd, J=11.4, 6.3, 6.0, 1.0Hz, 1H), 5.62 (dddd, J=11.4, 7.7, 1.3, 1.3Hz,

1H), 4.48 (dddd, J=7.7, 7.1, 4.3, 1.0Hz, 1H), 4.12 (ddd, J=12.3, 6.3, 1.3Hz, 1H), 4.04 (ddd, J=12.3, 6.0, 1.3Hz, 1H), 3.80 (s, 3H), 3.56 (dd, J=11.1, 4.3Hz, 1H), 3.50 (dd, J=11.1, 7.1Hz, 1H)

Tosylate **28**

A solution of diol (121.2mg, 0.509mmol) and Bu_2SnO (190.2mg, 0.764mmol) in toluene (5.1mmol) was heated with Dean-Stark (4A-MS) trap for 2h at 140°C and then toluene was removed *in vacuo*. The obtained white crystal was dissolved in CH_2Cl_2 and TsCl (106.7mg, 0.560mmol) was added to the solution. After 1h, the mixture was evaporated *in vacuo*, furnishing an oil, which was purified by silica gel column [EtOAc:hexane (1:2 to 1:1)] to give **28** (179.0mg, 0.456mmol) as an oil: ^{1}H-NMR (200MHz, $CDCl_3$) δ 7.77 (d, J=8.2Hz, 2H), 7.32 (d, J=8.2Hz, 2H), 7.23 (d, J=8.7Hz, 2H), 6.87 (d, J=8.7Hz, 2H), 5.74 (dddd, J=11.4, 6.2, 6.0, 1.1Hz, 1H), 5.49 (dddd, J=11.4, 7.8, 1.5, 1.4Hz, 1H), 4.70-4.53 (m, 1H), 4.04 (ddd, J=12.9, 6.2, 1.5Hz, 1H), 3.99 (ddd, J=12.9, 6.0, 1.4Hz, 1H), 3.96 (dd, J=10.1, 4.3Hz, 1H), 3.91 (dd, J=10.1, 6.9Hz, 1H), 3.80 (s, 3H)

Epoxide **29**

MCPBA (118.0mg, 0.547mmol) was added to a solution of **28** (179.0mg, 0.456mmol) in CH_2Cl_2 (4.6ml) at − 10°C and the mixture was stirred for 2h under nitrogen. Since the reaction was quite sluggish, the reaction temperature was rose to 0°C and the stirring was continued. After 2h, the reaction temperature was rose to room temperature and the mixture was stirred for 25h. Moreover, 49.2mg (0.228mmol) more of MCPBA was added to complete the reaction and the stirring was continued for additional 16h. Excess MCPBA was quenched with aqueous $NaHSO_3$ (76.6mg, 0.638mmol) and the organic phase was washed with 0.5N-NaOH, sat. $NaHCO_3$ and sat. brine. The aqueous layer was extracted once with EtOAc and the combined layer was dried with Na_2SO_4. Removal of the solvent gave an oil, which was subjected to next base treatment.

Diepoxide **18**

To a solution of the crude oil (based on the assumption that yield was 100% in the former step) in MeOH (2.3ml)/CH_2Cl_2 (2.3ml) was added K_2CO_3 (94.5mg, 0.684mmol) at 0°C. The mixture was stirred for 3h30min at room temperature under nitrogen. Then the mixture was diluted with CH_2Cl_2 (2.3ml) and filtered through a pad of Celite by the aid of CH_2Cl_2. Removal of the solvent *in vacuo* left an oil, which was purified by silica gel column [EtOAc:hexane (1:2)] to afford **18** (76.9mg, 0.325mmol) as an oil: ^{1}H-NMR (200MHz, $CDCl_3$) δ 7.24 (d, J=8.7Hz, 2H), 6.85 (d, J=8.7Hz, 2H), 4.54 (d, J=11.5Hz, 1H), 4.45 (d, J=11.5Hz, 1H), 3.81 (s, 3H), 3.74 (dd, J=11.4, 4.4Hz, 1H), 3.65 (dd, J=11.4, 5.9Hz, 1H), 3.25 (ddd, J=5.9, 4.4, 4.4Hz, 1H), 2.88 (ddd, J=5.9, 4.1, 2.6Hz, 1H), 2.78 (dd, J=5.9, 4.4Hz, 1H), 2.79 (dd, J=5.0, 4.1Hz, 1H), 2.68 (dd, J=5.0, 2.6Hz, 1H)

Coupling compound

Acetylene **19** (108.3mg, 0.326mmol) was azeotroped twice with toluene and dissolved to THF (2.0ml). To the solution was added *n*-BuLi (238.8μl, 0.358mmol) at − 78°C and the mixture was stirred to prepare acetylide for 30min under nitrogen. As a following preparation, $BF_3{\cdot}OEt_2$ (80.1μl, 0.651mmol) was added at − 78°C and the mixture was stirred for 30min before the injection of diepoxide **18**. Then a solution of diepoxide [76.9mg, 0.326mmol (azeotroped twice with toluene)] in THF (1.3ml) was added at − 78°C and the stirring was continued for additional 1h. The reaction was quenched with pH=7.4 phosphate buffer and the mixture was stirred to fully decompose $BF_3{\cdot}OEt_2$. After 2h, the mixture was diluted with EtOAc and the organic layer was washed three times with sat. $NaHCO_3$ and once with sat. brine. The combined organic layer was dried with Na_2SO_4 and concentrated *in vacuo*. The residual oil was purified by silica gel column [EtOAc:hexane (1:20 to 1:5 to 1:3) to give **30** (87.9mg, 0.155mmol) as an oil: ^{1}H-NMR (200MHz, $CDCl_3$) δ 7.38-7.21 (m, 5H), 7.26 (d, J=8.8Hz, 2H), 6.80 (d, J=8.8Hz, 2H), 4.68 (d, J=12.2Hz, 1H), 4.60 (d, J=11.4Hz, 1H), 4.54 (d, J=12.2Hz, 1H), 4.44 (d, J=11.4Hz, 1H), 3.80 (s, 3H), 3.79-3.42 (m, 5H), 3.25 (ddd, J=6.6, 4.4, 4.4Hz, 1H), 3.08 (dd, J=7.1, 4.4Hz, 1H),

2.53-2.43 (m, 4H), 1.75-1.45 (m, 2H), 2.78 (dd, J=5.9, 4.4Hz, 1H), 2.79 (dd, J=5.0, 4.1Hz, 1H), 2.68 (dd, J=5.0, 2.6Hz, 1H), 0.90 (t, J=7.3Hz, 3H), 0.89 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H)

(*Z*)-Olefin

To a stirred solution of **30** (77.8mg, 0.102mmol) in EtOAc (2.4ml) containing quinoline (13.3μl, same weight as Lindlar cat.) was added Lindlar cat. (57.8mg, same weight as s.m.). The flask was purged with triple balloon of hydrogen, and then stirred under a hydrogen balloon at ambient temperature. After 2h, 57.8mg more of Lindlar cat. was added and the stirring was continued for 2h under the same condition. Because the starting material was still observed on TLC plate, 57.8mg more of Lindlar cat. was further added and the mixture was stirred for 1h before being purged with air to evaporate all of the hydrogen. Then, the mixture was filtered through a pad of Celite by the aid of EtOAc, and filtrate was washed with 0.5N HCl, sat. $NaHCO_3$ and sat. brine. Adsorption of H_2O with Na_2SO_4 followed by evaporation of the solvent gave an oil, which was purified by silica gel column [EtOAc:hexane (1:3 to 2:5)] to provide (*Z*)-olefin (64.0mg, 0.112mmol) as an oil: ^{1}H-NMR (200MHz, $CDCl_3$) δ 7.38-7.21 (m, 5H), 7.26 (d, J=8.8Hz, 2H), 6.80 (d, J=8.8Hz, 2H), 5.60 (ddd, J=11.2, 7.4, 6.8Hz, 1H), 5.45 (ddd, J=11.2, 8.0, 6.8Hz, 1H), 4.67 (d, J=11.8Hz, 1H), 4.56 (d, J=11.4Hz, 1H), 4.50 (d, J=11.8Hz, 1H), 4.45 (d, J=11.4Hz, 1H), 3.81 (s, 3H), 3.76-3.63 (m, 1H), 3.67 (dd, J=11.2, 4.2Hz, 1H), 3.54 (dd, J=11.2, 6.4Hz, 1H), 3.57-3.33 (m, 2H), 3.25 (ddd, J=6.4, 4.4, 4.2Hz, 1H), 2.99 (dd, J=7.5, 4.4Hz, 1H), 2.51-2.15 (m, 4H), 1.70-1.40 (m, 2H), 0.92 (s, 9H), 0.91 (t, J=7.3Hz, 3H), 0.08 (s, 3H), 0.06 (s, 3H)

m-Methoxy benzyl ether **31**

As a pre-treatment, a 30ml flask was heated to remove moisture under high vacuum. To the vessel were added KH (30.1mg, 0.336mmol), THF (1.0ml) and a solution of (*Z*)-olefin (64.0mg, 0.112mmol) in THF (1.0ml) at 0°C, which was azeotroped once with toluene. After stirring for 10min at room temperature under nitrogen, *n*-Bu_4NI (8.1mg, 0.022mmol)

and 2-MPMCl (28.1μl, 0.202mmol) were added and the reaction was begun. The mixture was stirred for 4h at room temperature under nitrogen and then a small portion of KH (ca. 5.0mg) was added to complete the reaction. After 40min, the reaction was quenched with sat. NH_4Cl and EtOH and diluted with EtOAc. The organic phase was washed with sat. NH_4Cl, H_2O and sat. brine and dried with Na_2SO_4. Removal of the solvent *in vacuo* left an oil, which was purified by silica gel column [EtOAc:hexane (1:5 to 1:1)] to provide **31** (72.7mg, 0.105mmol) as an oil: ^{1}H-NMR (200MHz, $CDCl_3$) δ 7.42 (d, J=7.4Hz, 1H), 7.35-7.19 (m, 5H), 7.26 (d, J=8.8Hz, 2H), 7.25 (dd, J=8.4, 7.7Hz, 1H), 6.93 (dd, J=7.7, 7.4Hz, 1H), 6.86 (d, J=8.8Hz, 2H), 6.85 (d, J=8.4Hz, 1H), 5.67-5.38 (m, 2H), 4.86 (d, J=12.5Hz, 1H), 4.63 (d, J=11.6Hz, 1H), 4.61 (d, J=12.5Hz, 1H), 4.55 (d, J=11.4Hz, 1H), 4.49 (d, J=11.6Hz, 1H), 4.44 (d, J=11.4Hz, 1H), 3.81 (s, 3H), 3.79 (s, 3H), 3.74-3.61 (m, 1H), 3.68 (dd, J=11.3, 3.4Hz, 1H), 3.50-3.23 (m, 2H), 3.43 (dd, J=11.3, 6.7Hz, 1H), 3.16 (ddd, J=6.7, 4.5, 3.4Hz, 1H), 3.08 (dd, J=8.1, 4.5Hz, 1H), 2.42-2.23 (m, 4H), 1.70-1.38 (m, 2H), 0.91 (s, 9H), 0.90 (t, J=7.3Hz, 3H), 0.04 (s, 6H)

Acyclic precursor **20**

To a solution of **31** (72.7mg, 0.105mmol) in THF (1.0ml) was added TBAF (126.2μl, 0.126mmol) at 0°C and the mixture was stirred for 27h30min at room temperature under nitrogen. In order to promote the reaction, the reaction temperature was rose to 45°C and the stirring was continued for 3h30min. The reaction was quenched with sat. NH_4Cl and diluted with EtOAc. The organic layer was washed with sat. brine and dried with Na_2SO_4. Concentration of the solution *in vacuo* gave an oil, which was purified by silica gel column [EtOAc:hexane (1:3 to 1:2 to 1:1)] to afford **20** (55.6mg, 0.0964mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.39 (d, J=7.3Hz, 1H), 7.36-7.26 (m, 5H), 7.25 (d, J=8.8Hz, 2H), 7.25 (dd, J=8.3, 7.6Hz, 1H), 6.92 (dd, J=7.6, 7.3Hz, 1H), 6.86 (d, J=8.8Hz, 2H), 6.85 (d, J=8.3Hz, 1H), 5.62 (ddd, J=10.7, 8.5, 6.6Hz, 1H), 5.49 (ddd, J=10.7, 8.2, 6.5Hz, 1H), 4.86 (d, J=12.5Hz, 1H), 4.64 (d, J=12.5Hz, 1H), 4.58 (d, J=11.5Hz, 1H), 4.55 (d, J=11.5Hz, 1H), 4.49 (d, J=11.5Hz, 1H), 4.45 (d, J=11.5Hz, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 3.63 (dd, J=11.2,

4.2Hz, 1H), 3.52 (ddd, J=8.8, 5.6, 3.7Hz, 1H), 3.49 (dd, J=11.2, 6.6Hz, 1H), 3.35 (ddd, J=5.9, 5.6, 4.6Hz, 1H), 3.34 (ddd, J=8.3, 8.1, 4.4Hz, 1H), 3.16 (ddd, J=6.6, 4.5, 4.2Hz, 1H), 3.09 (dd, J=8.1, 4.5Hz, 1H), 2.53-2.44 (m, 2H), 2.30-2.20 (m, 2H), 1.51 (dqd, J=14.0, 7.3, 3.7Hz, 1H), 1.38 (dqd, J=14.0, 8.8, 7.3Hz, 1H), 0.88 (t, J=7.3Hz, 3H)

Chapter 4

Cyclohexylidene acetal **42**

Cyclohexanone (9.5ml, 86.8mmol), $HC(OMe)_3$ (1.9ml, 17.3mmol) and CSA (671.3mg, 2.9mmol) were added to a solution of L-ascorbic acid (5.1g, 28.9mmol) in 1,4-dioxane (28.9ml) and the reaction mixture were stirred at room temperature under nitrogen. After 21h, the mixture was evaporated *in vacuo* to give a crystal, which was followed by next recrystallization with benzene. Filtration through a glass filter with a filter paper and washed with benzene afforded a pure white crystal (6.8g, 26.7mmol), which was submitted to next Me-protection.

Methylether

CH_2N_2 in Et_2O (ca.220ml) was added to a solution of **42** (6.8g, 26.7mmol) in MeOH (26.7ml) until the colorless solution turned to a yellow solution at 0°C. The resulting yellow solution was evaporated *in vacuo* and viscous yellow oil was obtained. To purify the resultant product, filtration through a pad of silica gel by the aid of EtOAc:hexane = 1:1 was carried out, followed by removal of the solvent *in vacuo* gave an oil. The crude oil (6.8g, 23.9mmol) was exposed to next ozonolysis.

α-hydroxyl ester **43**

To a solution of the former product (6.79g, 23.9mmol) in CH_2Cl_2 (12.0ml)/MeOH (12.0ml) was poured ozone at − 78°C and the ozone bubbling was continued for 7h. During the reaction, the yellow solution turned to a blue solution gradually. As the following

reductive treatment, Me_2S (16.0ml, 21.7mmol) was added to the reaction mixture at − 78°C and immediately rose to room temperature. The reaction mixture was stirred for 4h and then K_2CO_3 (9.90g, 71.64mmol) was added to removal the oxalyl group. After stirring for 1h, the mixture was diluted with EtOAc and washed with H_2O and sat. brine. The organic layer was dried with Na_2SO_4 followed by removal of the solvent gave an oil, which was purified by silica gel column [EtOAc:hexane (1:2)] to afford **43** (4.5g, 19.5mmol) as an oil: ^{1}H-NMR (200MHz, $CDCl_3$) δ 4.40 (ddd, J=6.8, 6.6, 2.7Hz, 1H), 4.13 (br-d, J=2.7Hz, 1H), 4.09 (dd, J=8.3, 6.6Hz, 1H), 4.01 (dd, J=8.3, 6.8Hz, 1H), 3.83 (s, 3H), 1.70-1.30 (m, 10H)

Mesylate **44**

MsCl (3.03ml, 39.1mmol) and TEA (10.9ml, 78.2mmol) were added to a solution of **43** (4.5g, 19.5mmol) in CH_2Cl_2 (97.5ml) at 0°C and the mixture was stirred at room temperature under nitrogen. After 1h, the reaction was quenched with sat. $NaHCO_3$ and diluted with EtOAc. The organic layer was washed with sat. $NaHCO_3$ and sat. brine and then dried with Na_2SO_4. Evaporation of the solvent *in vacuo* left an oil, which was purified by silica gel column [EtOAc:hexane (1:2) to obtain **44** (5.25g, 17.0mmol) as a yellow crystal: ^{1}H-NMR (200MHz, $CDCl_3$) δ 5.01 (d, J=5.4Hz, 1H), 4.54 (ddd, J=6.6, 5.7, 5.4Hz, 1H), 4.15(dd, J=9.1, 6.6Hz, 1H), 4.02 (dd, J=9.1, 5.7Hz, 1H), 3.85 (s, 3H), 3.21 (s, 3H), 1.76-1.31 (m, 10H)

Alcohol

To a solution of **44** (5.25g, 17.0mmol) in THF (85.1ml) was added LAH (1.40g, 34.1mmol) and the mixture was stirred at 0°C under nitrogen. After 30min, the mixture was diluted with wet Et_2O and quenched with H_2O (9.0ml) at 0°C. After stirring for 1h30min, the reaction mixture was filtrated through a pad of Celite by the aid of MeOH. Subsequently, further filtration through a pad of silica gel by the aid of MeOH was carried out and removal of the solvent *in vacuo* afforded alcohol (4.77g, 17.0mmol). The obtained product was followed by next epoxidation step.

Epoxide **45**

To a solution of alcohol (4.8g, 17.0mmol) in CH_2Cl_2 (42.5ml)/MeOH (42.5ml) was added K_2CO_3 (3.53g, 25.5mmol) at 0°C and the mixture was stirred at room temperature under nitrogen. After 8h, the mixture was filtrated through a pad of silica gel by the aid of CH_2Cl_2. Removal of the solvent *in vacuo* gave an oil, which was purified by silica gel [EtOAc:hexane (1:3-2:1)] to provide **45** (1.78g, 9.66mmol) as an oil: ^{1}H-NMR (200MHz, $CDCl_3$) δ 4.11 (dd, J=8.1, 6.0Hz, 1H), 3.93 (dd, J=8.1, 5.4Hz, 1H), 3.85 (ddd, J=6.2, 6.0, 5.4Hz, 1H), 3.01 (ddd, J=6.2, 4.0, 2.6Hz, 1H), 2.85 (dd, J=4.9, 4.0Hz, 1H), 2.67 (dd, J=4.9, 2.6Hz, 1H), 1.70-1.30 (m, 10H)

Acetylene

To a mixture of heated and pumped up (i.e., evacuated under high vacuum) magnesium (469.7mg, 19.3mmol) and $HgCl_2$ (26.2mg, 0.97mmol) in Et_2O (10.0ml) was added propalgyl bromide (1.45ml, 19.3mmol) dropwise at room temperature to prepare propalgyl Grignard. After 30min from last injection of propalgyl bromide, Et_2O (56.6ml) was added to the mixture, which was cooled down to − 50°C. Then, a solution of epoxide **45** (1.78g, 9.66mmol) in Et_2O was added and the reaction was begun. The reaction mixture was stirred for 30min at − 50°C and then allowed to naturally warm up to − 20°C. After 1h40min, the reaction was quenched with sat. NH_4Cl at − 20°C and the mixture was diluted with EtOAc. The organic layer was washed three times with sat. NH_4Cl and once with sat. brine and then dried with Na_2SO_4. Removal of the solvent *in vacuo* gave an oil, which was submitted to next base treatment.

Epoxide **45**

K_2CO_3 (534.1mg, 3.87mmol) was added to a solution of crude oil [1.93mmol (based on the assumption that bromohydrine generated about 20%)] in MeOH (9.7ml)/CH_2Cl_2 (9.7ml) at room temperature. After stirring for 1h at room temperature under nitrogen, the mixture was diluted with EtOAc and filtered through a pad of Celite by the aid of CH_2Cl_2.

Evaporation of the solvent gave an oil, which was purified by silica gel column [EtOAc:hexane (1:3-1:2)] to give acetylene (1.64g, 7.31mmol) and epoxide **45** (448.5mg, 2.43mmol): ^{1}H-NMR (200MHz, $CDCl_3$) δ 4.10-3.80 (m, J=8.1, 6.0Hz, 4H), 2.39 (td, J=7.0, 2.6Hz, 2H), 2.14 (d, J=3.4Hz, 1H), 1.99 (t, J=2.6Hz, 1H), 1.83-1.43 (m, 12H)

Benzyl ether **46**

BnBr (1.23ml, 10.2mmol), NaH (470.8mg, 11.8mmol) and *n*-Bu_4NI (290.0mg, 0.785mmol) were added to a solution of acetylene (1.76g, 7.85mmol) in THF (78.5ml) at 0°C and the mixture was stirred at room temperature under nitrogen. After 20h, 94.2mg (2.35mmol) more of NaH and 280.0μl (2.35mmol) more of BnBr were added to the mixture and the stirring was continued for additional 4h30min. The reaction was quenched with sat. NH_4Cl at 0°C and diluted with EtOAc. The organic layer was washed with sat. NH_4Cl and sat. brine and dried with Na_2SO_4. Evaporation of the solvent *in vacuo* left an oil, which was purified by silica gel column [EtOAc:hexane (1:15)] to give **46** (1.85g, 5.88mmol) as an oil: ^{1}H-NMR (200MHz, $CDCl_3$) δ 7.32-7.22 (m, 5H), 4.69 (d, J=11.2Hz, 1H), 4.62 (d, J=11.2Hz, 1H), 4.01 (ddd, J=6.3, 6.2, 5.2Hz, 1H), 3.95 (dd, J=7.6, 6.2Hz, 1H), 3.87 (dd, J=7.6, 6.3Hz, 1H), 3.70 (ddd, J=7.4, 5.2, 4.3Hz, 1H), 2.46 (ddt, J=7.5, 7.0, 2.6Hz, 1H), 1.96 (t, J=2.6Hz, 1H), 1.87-1.58 (m, 2H), 1.58-1.23 (m, 10H)

Diol **47**

A solution of **46** (1.85g, 5.88mmol) in 80% aqueous AcOH (11.8ml) was stirred for 2h at 50°C under nitrogen and then the stirring was continued for additional 5h at 60°C. Since the reaction did not complete, 10.0ml more of 80% aqueous AcOH was added to the mixture whose the stirring was continued for 2h at 50°C. The reaction was quenched with 2N-NaOH (155ml) at 0°C and the organic products were extracted with CH_2Cl_2. The organic extracts were dried with Na_2SO_4 and evaporated *in vacuo*. The residual oil was purified by silica gel column [EtOAc:hexane (1:5-2:1-3:1)] to afford **47** (1.02g, 4.35mmol) as an oil: ^{1}H-NMR (200MHz, $CDCl_3$) δ 7.39-7.29 (m, 5H), 4.63 (s, 2H), 3.88-3.65 (m, 4H),

2.35 (ddd, J=6.6, 6.1, 2.7Hz, 2H), 1.99 (t, J=2.7Hz, 1H), 1.97-1.66 (m, 2H)

Tosylate

A solution of **47** (1.02g, 4.35mmol) and Bu_2SnO (1.63g, 6.53mmol) in toluene (43.5mmol) was heated with Dean-Stark (4A-MS) trap for 2h at 140°C and then toluene was removed *in vacuo*. The obtained yellow crystal was dissolved in CH_2Cl_2 and TsCl (912.8mg, 4.79mmol) was added to the solution. After 1h, the reaction was quenched with sat. $NaHCO_3$ and the resultant products were extracted with EtOAc. The organic extracts were washed with sat. $NaHCO_3$ and sat. brine and filtrated through a pad of Celite by the aid of EtOAc. Removal of the solvent gave an oil, which was submitted to next epoxidation.

Epoxide **48**

K_2CO_3 (1.20g, 8.71mmol) was added to a solution of the crude oil (1.69g, 1.93mmol) in MeOH (21.8ml)/CH_2Cl_2 (21.8ml) at room temperature. After stirring for 4h, the mixture was diluted with EtOAc and filtered through a pad of silica gel by the aid of EtOAc:hexane = 1:2. Evaporation of the solvent gave an oil, which was purified by silica gel column [EtOAc:hexane (1:6)] to give **48** (882.4mg, 4.08mmol) as an oil: ^{1}H-NMR (200MHz, $CDCl_3$) δ 7.39-7.26 (m, 5H), 4.69 (d, J=11.4Hz, 1H), 4.52 (d, J=11.4Hz, 1H), 3.46 (ddd, J=8.3, 5.3, 4.4Hz, 1H), 2.96 (ddd, J=5.3, 3.9, 2.7Hz, 1H), 2.79 (dd, J=5.3, 3.9Hz, 1H), 2.74 (dd, J=5.3, 2.7Hz, 1H), 2.38 (td, J=7.6, 2.7Hz, 2H), 1.95 (t, J=2.7Hz, 1H), 2.00-1.74 (m, 2H)

Alcohol

To a mixture of heated and pumped up (i.e., evacuated under high vacuum) CuI (1.09g, 5.72mmol) in Et_2O (38.0ml), was added MeLi (11.7ml, 13.3mmol) at − 30°C and the mixture was stirred for 15min in order to prepare Me_2CuLi. Then, the mixture was cooled down to − 78°C and a solution of **48** [azeotroped twice with toluene (824.0mg, 3.81mmol)]

in Et_2O (5.0ml) was added. After injection of the starting material at − 78°C, the reaction was allowed to naturally warm up to 0°C over 2h and quenched with sat. NH_4Cl. The mixture was stirred to be formed a cupper complex until the yellow solution turned to a blue solution. The organic phase was washed three times with sat. NH_4Cl and once with sat. brine and then dried with Na_2SO_4. Removal of the solvent *in vacuo* gave an oil, which was purified by silica gel column [EtOAc:hexane (1:5-1:2)] to obtain alcohol (857.0mg, 3.69mmol) as an oil: ^{1}H-NMR (200MHz, $CDCl_3$) δ 7.40-7.27 (m, 5H), 4.64 (d, J=11.2Hz, 1H), 4.56 (d, J=11.2Hz, 1H), 3.81 (ddd, J=7.7, 5.6, 3.4Hz, 1H), 3.57 (td, J=9.1, 3.4Hz, 1H), 2.39 (ddd, J=5.7, 2.7, 1.7Hz, 1H), 2.32 (ddd, J=5.7, 3.4, 2.7Hz, 1H), 1.96 (t, J=2.7Hz, 1H), 2.03-1.58 (m, 2H), 1.58-1.40 (m, 2H), 1.00 (t, J=7.3Hz, 3H)

Silyl ether **38**

TBSCl (800.7mg, 5.15mmol) and imidazole (701.9mg, 10.3mmol) were added to a solution of the former product (797.9mg, 3.44mmol) in DMF (11.3ml) and the mixture was stirred at room temperature under nitrogen. After 18h, 227.4mg (4.81mmol) more of imidazole and 373.6mg (2.40mmol) more of TBSCl were added and the stirring was continued for additional 4h. The reaction was quenched with sat. NH_4Cl and diluted with EtOAc. The organic layer was washed with sat. NH_4Cl and sat. brine and dried with Na_2SO_4. Evaporation of the solvent *in vacuo* left an oil, which was purified by silica gel column [EtOAc:hexane (1:20-1:3)] to give **38** (1.13g, 3.26mmol) as an oil: ^{1}H-NMR (200MHz, $CDCl_3$) δ 7.39-7.26 (m, 5H), 4.73 (d, J=11.4Hz, 1H), 4.49 (d, J=11.4Hz, 1H), 3.70 (ddd, J=7.0, 4.8, 3.0Hz, 1H), 3.53 (ddd, J=8.3, 3.8, 3.0Hz, 1H), 2.31 (ddd, J=6.0, 2.7, 1.3Hz, 2H), 1.94 (t, J=2.7Hz, 1H), 2.03-1.40 (m, 4H), 0.92 (t, J=7.3Hz, 3H), 0.90 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H)

Coupled compound **52**

Acetylene **38** (1.14g, 3.27mmol) and epoxide **39** (851.5mg, 2.52mmol) were azeotroped twice with toluene *in vacuo* and dissolved in THF (32.7ml). To the solution was added

n-BuLi (2.20ml, 3.52mmol) at − 78°C and an anion preparation was carried out for 30min. Then, $BF_3 \cdot OEt_2$ (828.8ml, 6.54mmol) was added and the stirring was continued for 2h. The mixture was quenched with sat. $NaHCO_3$ and stirred for 1h to neutralize $BF_3 \cdot OEt_2$. The resultant product was extracted with EtOAc and washed with sat. $NaHCO_3$ and sat. brine and dried with Na_2SO_4. Removal of the solvent gave an oil, which was purified by silica gel column [EtOAc:hexane (1:7)] to afford **52** (1.21g, 1.77mmol) as an oil: ^{1}H-NMR (200MHz, $CDCl_3$) δ 7.39-7.18 (m, 5H), 7.24 (d, J=8.8Hz, 2H), 6.86 (d, J=8.8Hz, 2H), 4.71 (d, J=11.4Hz, 1H), 4.47 (d, J=11.4Hz, 1H), 4.44 (s, 2H), 3.99 (ddd, J=6.0, 5.7, 2.0Hz, 1H), 3.80 (s, 3H), 3.80-3.63 (m, 1H), 3.58-3.44 (m, 1H), 3.52 (dd, J=9.6, 6.0Hz, 1H), 3.44 (dd, J=9.6, 5.7Hz, 1H), 2.40-2.20 (m, 4H), 1.80-1.35 (m, 4H), 0.91 (t, J=7.5Hz, 3H), 0.90 (s, 9H), 0.88 (s, 9H), 0.10 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H), 0.05 (s, 3H)

Olefin

To a solution of **52** (1.21g, 1.77mmol) in EtOAc (17.7ml) were added quinoline (276.7μl, 1/4 weight % of s.m.) and Lindlar catalyst (1.21g, equal amount to starting material). The flask was purged with triple balloon of hydrogen, and then stirred under a hydrogen balloon at ambient temperature. Every 30min, 1.21g (equal weight amount to starting material) more of Lindlar catalyst was added three times and then the mixture was filtrated through a pad of Celite by the aid of EtOAc. The organic layer was washed with 0.5N-HCl, sat. $NaHCO_3$ and sat. brine and dried with Na_2SO_4. Combined organic layer was evaporated *in vacuo* and the residual oil was purified by silica gel column [EtOAc:hexane (1:5)] to provide olefin (1.18g, 1.72mmol) as an oil: ^{1}H-NMR (200MHz, $CDCl_3$) δ 7.37-7.23 (m, 5H), 7.23 (d, J=8.8Hz, 2H), 6.87 (d, J=8.8Hz, 2H), 5.51-5.41 (m, 2H), 4.72 (d, J=11.6Hz, 1H), 4.45 (d, J=11.6Hz, 1H), 3.80 (s, 2H), 3.80-3.30 (m, 6H), 3.28-2.02 (m, 4H), 1.70-1.39 (m, 4H), 0.91 (t, J=7.5Hz, 3H), 0.90 (s, 9H), 0.88 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H), 0.05 (s, 3H), 0.05 (s, 3H)

Mesylate **53**

To a solution of olefin (1.18g, 1.71mmol) in CH_2Cl_2 (17.1ml) were added TEA (955.0μl, 6.85mmol), MsCl (265.1μl, 3.42mmol) and DMAP (20.9mg, 0.17mmol) at room temperature and the mixture was stirred for 50min under nitrogen. Then sat. $NaHCO_3$ (10.0ml) was added to quench MsCl and the stirring was continued for 1h. The mixture was diluted with EtOAc and washed with sat. $NaHCO_3$ and sat. brine. Removal of the solvent left an oil, which was purified by silica gel column [EtOAc:hexane (1:5-1:4)] to give **53** (1.22g, 1.59mmol) as an oil: ^{1}H-NMR (200MHz, $CDCl_3$) δ 7.36-7.20 (m, 5H), 7.25 (d, J=8.6Hz, 2H), 6.86 (d, J=8.6Hz, 2H), 5.60-5.30 (m, 2H), 4.73 (d, J=11.4Hz, 1H), 4.68 (td, J=6.8, 3.8Hz, 1H), 4.46 (d, J=11.3Hz, 1H), 4.41 (d, J=11.4Hz, 1H), 4.38 (d, J=11.3Hz, 1H), 3.97 (dd, J=5.7, 5.5, 3.8Hz, 2H), 3.79 (s, 3H), 3.72-3.29 (m, 3H), 3.55 (dd, J=9.6, 5.5,Hz, 1H), 3.42 (dd, J=9.6, 5.7,Hz, 1H), 2.94 (s, 3H), 2.50 (br-dd, J=7.3, 6.8Hz, 2H), 2.24-2.03 (m, 1.70-1.39, 2H), 1.70-1.48 (m, 4H), 0.91 (t, J=7.5Hz, 3H), 0.90 (s, 9H), 0.88 (s, 9H), 0.07 (s, 6H), 0.05 (s, 6H)

Acyclic precursor **36**

To a solution of **53** (1.22g, 1.59mmol) in THF (15.9ml) was added TBAF (4.77ml, 4.77mmol) at 0°C and the mixture was stirred at room temperature under nitrogen. After 9h, the reaction temperature was rose to 40°C and the stirring was continued for 73h. The reaction was quenched with sat.NH_4Cl and diluted with EtOAc. The organic layer was washed with sat. NH_4Cl and sat. brine and dried with Na_2SO_4. Evaporation of the solvent *in vacuo* gave an oil, which was purified by silica gel column [EtOAc:hexane (1:2-2:3)] to afford **36** (623.9mg, 1.42mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.37-7.25 (m, 5H), 7.27 (d, J=8.8Hz, 2H), 6.88 (d, J=8.8Hz, 2H), 5.55-5.48 (m, 1H), 5.47-5.40 (m, 1H), 4.61 (d, J=11.5Hz, 1H), 4.54 (d, J=11.5Hz, 1H), 4.52 (d, J=11.5Hz, 1H), 4.44 (d, J=11.5Hz, 1H), 3.80 (s, 3H), 3.78-3.73 (m, 1H), 3.66 (dd, J=11.0, 4.4Hz, 1H), 3.53 (dd, J=11.0, 6.4Hz, 1H), 3.36 (ddd, J=9.0, 3.7, 3.4Hz, 1H), 3.18 (ddd, J=6.4, 4.4, 4.4Hz, 1H), 2.98 (ddd, J=6.6, 6.1, 4.4Hz, 1H), 2.36-2.27 (m, 1H), 2.26-2.16 (m, 2H), 2.13-2.04 (m, 1H), 1.69 (dddd,

J=18.4, 14.3, 9.0, 5.1Hz, 1H), 1.70-1.48 (m, 3H), 0.99 (t, J=7.3Hz, 3H)

Cyclic ether **35**

To a solution of **36** (518.3mg, 1.18mmol) in xylenes (11.3ml) was added $Eu(fod)_3$ (1.22g, 1.18mmol) and the mixture was stirred at 120°C under nitrogen. After 57h, 366mg (0.35mmol) more of $Eu(fod)_3$ was added and the stirring was continued for additional 15h. Evaporation of the solvent *in vacuo* left an oil, which was purified by silica gel column [EtOAc:hexane (1:2)] to obtain **35** (264.9mg, 0.60mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.35-7.24 (m, 5H), 7.26 (d, J=8.6Hz, 2H), 6.89 (d, J=8.6Hz, 2H), 5.65 (ddd, J=10.7, 7.6, 7.6Hz, 1H), 5.62 (ddd, J=10.7, 5.4, 4.6Hz, 1H), 4.52 (d, J=11.6Hz, 1H), 4.51 (d, J=11.5Hz, 1H), 4.49 (d, J=11.5Hz, 1H), 4.41 (d, J=11.6Hz, 1H), 3.87 (ddd, J=8.1, 5.0, 2.9Hz, 1H), 3.81 (s, 3H), 3.72 (dd, J=9.6, 2.9Hz, 1H), 3.59 (br-dd, J=8.1, 5.0Hz, 1H), 3.56 (ddd, J=9.0, 9.0, 2.7Hz, 1H), 3.46 (dd, J=9.6, 8.1Hz, 1H), 3.35 (ddd, J=10.0, 9.0, 2.7Hz, 1H), 2.76 (dddd, J=12.9, 12.5, 10.4, 4.2Hz, 1H), 2.24-2.11 (m, 2H), 2.02-1.85 (m, 3H), 1.67 (dddd, J=15.0, 10.0, 4.2, 3.9Hz, 1H), 1.52-1.42 (m, 3H), 0.98 (t, J=7.3Hz, 3H)

Xantate

To a solution of cyclic ether **35** (57.0mg, 0.129mmol) in THF (1.3ml) were added imidazole (0.9mg, 0.0129mmol), CS_2 (78.6μl, 1.29mmol) and NaH (15.5mg, 0.388mmol) at 0°C and the mixture was stirred for 30min at 0°C under nitrogen. The reaction temperature was rose to room temperature in order to promote reaction and the stirring was continued for 1h before MeI (82.8μl, 1.29mmol) was added. After 40min from injection of MeI, the reaction was quenched with sat. NH_4Cl and diluted with EtOAc. The organic layer was washed with sat. NH_4Cl and sat. brine and dried with Na_2SO_4. Removal of the solvent left an oil, which was purified by silica gel column [EtOAc:hexane (1:5)] to give xantate (65.3mg, 0.123mmol) as an oil: ^{1}H-NMR (200MHz, $CDCl_3$) δ 7.39-7.20 (m, 5H), 7.25 (d, J=8.8Hz, 2H), 6.87 (d, J=8.8Hz, 2H), 5.86 (ddd, J=8.2, 5.0, 2.2Hz, 1H), 5.70-5.50 (m, 2H), 4.52 (d, J=11.8Hz, 1H), 4.49 (d, J=11.2Hz, 1H), 4.46 (d, J=11.8Hz, 1H), 4.39 (d, J=11.2Hz,

1H), 3.97 (dd, J=11.4, 2.2Hz, 1H), 3.85-3.71 (m, 1H), 3.80 (s, 3H), 3.79 (dd, J=11.4, 8.3Hz, 1H), 3.55 (ddd, J=9.8, 9.6, 9.2Hz, 1H), 3.23 (ddd, J=9.8, 9.6, 2.2Hz, 1H), 2.95-2.65 (m, 1H), 2.58 (s, 3H), 2.34-1.57 (m, 5H), 1.05 (dd, J=7.0Hz, 3H)

Deoxygenated compound **54**

To a solution of xantate (65.3mg, 0.123mmol) in toluene (1.2ml) were added Bu_3SnH (40.9µl, 0.148mmol) and AIBN (2.0mg, 0.0123mmol) at room temperature and immediately, the reaction temperature was rose to 100°C. After stirring for 2h, 17.1µl (0.0615mmol) more of Bu_3SnH was added and the stirring was continued for additional 2h at 100°C. The reaction mixture was concentrated *in vacuo* to afford an oil, which was purified by silica gel column [EtOAc:hexane (1:10) contained with 1%TEA] to afford **54** (35.4mg, 0.0833mmol) as an oil: ^{1}H-NMR (200MHz, $CDCl_3$) δ 7.36-7.27 (m, 5H), 7.25 (d, J=8.8Hz, 2H), 6.87 (d, J=8.8Hz, 2H), 5.73-5.50 (m, 2H), 4.54 (d, J=11.3Hz, 1H), 4.47 (d, J=12.1Hz, 1H), 4.40 (d, J=12.1Hz, 1H), 4.39 (d, J=11.3Hz, 1H), 3.80-3.44 (m, 4H), 3.80 (s, 3H), 3.38 (ddd, J=8.9, 8.7, 2.9Hz, 1H), 2.84-2.62 (m, 1H), 2.48-2.28 (m, 1H), 2.04-1.44 (m, 6H), 0.89 (dd, J=7.4, 7.2Hz, 1H)

Epoxide **55**

To a solution of **54** (26.1mg, 0.0615mmol) in CH_2Cl_2 (1.2ml) was added MCPBA (14.8mg, 0.0922mmol) at 0°C and the mixture was stirred under nitrogen. After 1h, 9.8mg (0.0615mmol) more of MCPBA was added, furthermore 4.9mg (0.0307mmol) more of MCPBA was added again after 1h. After stirring for 7h at 0°C, the reaction temperature was rose to room temperature and the stirring was continued for 2h. Since a small amount of starting material was observed on TLC, 4.9mg (0,0307mmol) more of MCPBA was further added. After 1h, aqueous $NaHSO_3$ (28.8mg, 0.184mmol) was added to decompose the excess MCPBA and the mixture was diluted with EtOAc. The organic layer was washed with 1N-NaOH, sat. $NaHCO_3$ and sat. brine and dried with Na_2SO_4. Removal of the solvent gave an oil, which was purified by silica gel column [EtOAc:hexane (1:3-1:2)] to obtain **55**

(18.5mg, 0.0420mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.36-7.23 (m, 5H), 7.25 (d, J=8.5Hz, 2H), 6.88 (d, J=8.5Hz, 2H), 4.57 (d, J=11.5Hz, 1H), 4.46 (d, J=11.7Hz, 1H), 4.41 (d, J=11.5Hz, 1H), 4.40 (d, J=11.7Hz, 1H), 4.01 (dd, J=12.3, 6.8, 6.6Hz, 1H), 3.80 (s, 3H), 3.58-3.46 (m, 4H), 2.98 (ddd, J=6.8, 4.2, 2.8Hz, 1H), 2.96 (ddd, J=8.1, 4.2,3.9Hz, 1H), 2.03-1.92 (m, 4H), 1.76-1.62 (m, 5H), 1.49-1.38 (m, 1H), 0.89 (t, J=7.3Hz, 3H)

Allylalcohol **56**

A mixture of $(PhSe)_2$ (19.7mg, 0.0630mmol) and $NaBH_4$ (5.2mg, 0.126mmol) in EtOH (degas 2h) (600μl) was stirred for 5min under nitrogen to provide $Na^+[PhSeB(OEt)_3]^-$ as a yellow solution. Then it was added to a solution of **55** (18.5mg, 0.0420mmol) in *n*-BuOH (degas 2h) (840μl) at room temperature. After stirring at 140°C for 9h under nitrogen, the mixture was diluted with EtOAc and washed with sat. NH_4Cl and sat. brine. Adsorption of H_2O with Na_2SO_4 followed by evaporation of the solvent left an oil, which was purified by silica gel column [EtOAc:hexane (1:10-1:2)] to give selenide compound (19.2mg, 0.0321mmol) as an oil. This compound was immediately subjected to next *syn*-elimination step.

To a solution of selenide compound (19.2mg, 0.0321mmol) in CH_2Cl_2 (1.5ml) were added pyridine (5.2μl, 0.0643mmol), 2-methyl-2-butene (34.0μl, 0.321mmol) and H_2O_2 (7.1μl, 0.0643mmol) and the mixture was stirred at room temperature for 2h under nitrogen. The mixture was quenched with sat. $NaHCO_3$ and diluted with EtOAc. The organic layer was washed with sat. $NaHCO_3$ and sat. brine and dried with Na_2SO_4. Removal of the solvent *in vacuo* gave an oil, which was purified by silica gel column [EtOAc:hexane (1:2)] to afford **56** (11.8mg, 0.0268mmol) as an oil. The obtained product was a mixture of geometric isomers. These compounds were submitted to next epoxidation with MCPBA.

Allylepoxide **59**

To a solution of **56** (11.8mg, 0.0268mmol) in CH_2Cl_2 (1.0ml) was added MCPBA (11.5mg, 0.0536mmol) at 0°C and the mixture was stirred at 0°C under nitrogen. To complete the reaction, after every 2h, 2.88g (0.0134mmol) more of MCPBA was added twice. After 17h from last addition, excess MCPBA was quenched with aqueous $NaHSO_3$ (16.7mg, 0.160mmol) and the mixture was diluted with EtOAc. The organic layer was washed with 1N-NaOH, sat. $NaHCO_3$ and sat. brine and dried with Na_2SO_4. Removal of the solvent *in vacuo* provided an oil. The residual oil was purified by silica gel column [EtOAc:hexane (3:2)] to give *cis*-epoxyalcohol **59** (1.4mg, 3.07μmol), *trans*-epoxyalcohol **60** (3.3mg, 7.23μmol) and C7-epimer of **61** (0.8mg, 1.75μmol): data for *cis*-epoxide **59** ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.38-7.24 (m, 5H), 7.26 (d, J=8.6Hz, 2H), 6.88 (d, J=8.6Hz, 2H), 4.64 (d, J=11.2Hz, 1H), 4.45 (d, J=11.5Hz, 1H), 4.44 (s, 2H), 3.81 (s, 3H), 3.69-3.59 (m, 2H), 3.58-3.51 (m, 1H), 3.45-3.39 (m, 1H), 3.30-3.29 (m, 1H), 3.03 (dd, J=9.3, 4.4Hz, 1H), 2.90 (dd, J=8.3, 4.4Hz, 1H), 2.32-2.23 (m, 1H), 2.07-1.82 (m, 5H), 1.76-1.69 (m, 1H), 1.45-1.35 (m, 1H), 1.00 (t, J=7.3Hz, 3H)

data for *trans*-epoxide **60** ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.36-7.27 (m, 5H), 7.25 (d, J=8.5Hz, 2H), 6.89 (d, J=8.5Hz, 2H), 4.56 (d, J=11.5Hz, 1H), 4.48-4.43 (m, 1H), 4.43 (d, J=11.5Hz, 1H), 4.42 (d, J=11.5Hz, 1H), 4.37 (d, J=11.5Hz, 1H), 3.80 (s, 3H), 3.69 (dt, J=9.0, 4.2Hz, 1H), 3.53 (t, J=6.6Hz, 2H), 3.45 (ddd, J=9.3, 5.4, 1.7Hz, 1H), 3.34 (br-dd, J=8.5, 7.8Hz, 1H), 3.14 (dd, J=4.6, 2.7Hz, 1H), 3.03 (dd, J=8.5, 4.6Hz, 1H), 2.20-2.12 (m, 1H), 1.89-1.79 (m, 3H), 1.69-1.60 (m, 1H), 1.61 (dt, J=13.1, 6.6Hz, 2H), 1.49 (dtd, J=14.3, 7.5, 4.4Hz, 1H), 0.85 (t, J=7.3Hz, 3H)

data for C7-epimer of **61** ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.38-7.24 (m, 5H), 7.27 (d, J=9.0Hz, 2H), 6.89 (d, J=9.0Hz, 2H), 4.62 (d, J=11.4Hz, 1H), 4.52 (d, J=11.4Hz, 1H), 4.45 (d, J=11.7Hz, 1H), 4.44 (d, J=11.7Hz, 1H), 4.22-4.18 (m, 1H), 3.81 (s, 3H), 3.69-3.59 (m, 2H), 3.55-3.50 (m, 1H), 3.50-3.45 (m, 1H), 3.30-3.26 (m, 1H), 3.15 (dd, J=8.6, 2.4Hz, 1H), 2.92-2.89 (m, 1H), 2.42-2.34 (m, 1H), 2.16-2.09 (m, 1H), 2.07-1.76 (m, 1H), 1.60-1.46 (m, 2H), 1.01 (t, J=7.3Hz, 3H)

TBS ether

To a solution of cyclic ether **35** (41.2mg, 0.0935mmol) in CH_2Cl_2 (0.94ml) were added 2,6-lutidine (43.6ml,0.374mmol) and TBSOTf (32.9ml, 0.140mmol) at 0°C and the mixture was stirred for 30min under nitrogen. The reaction was quenched with H_2O and diluted with EtOAc. The mixture was washed with sat. $NaHCO_3$ and sat. brine and dried with Na_2SO_4. Evaporation of the solution *in vacuo* gave an oil, which was purified by silica gel column [EtOAc:hexane (1:10)] to afford TBS ether (51.1mg, 0.0921mmol) as an oil: ^{1}H-NMR (200MHz, $CDCl_3$) δ 7.36-7.27 (m, 5H), 7.25 (d, J=8.8Hz, 2H), 6.86 (d, J=8.8Hz, 2H), 5.71-5.49 (m, 2H), 4.54 (d, J=11.4Hz, 1H), 4.46 (s, 2H), 4.40 (d, J=11.4Hz, 1H), 3.88-3.79 (m, 1H), 3.80 (s, 3H), 3.75 (dd, J=9.8, 1.9Hz, 1H), 3.50 (ddd, J=9.5, 9.5, 2.6Hz, 1H), 3.34 (dd, J=9.8, 8.3Hz, 1H), 3.34-3.20 (m, 2H), 2.92-2.68 (m, 1H), 2.36-2.20 (m, 1H), 2.10-1.80 (m, 4H), 1.74-1.55 (m, 5H), 1.47-1.18 (m, 2H), 1.01 (dd, J=7.3, 7.3Hz, 3H), 0.89 (s, 9H), 0.06 (s, 3H), 0.03 (s, 3H)

Epoxide **62**

To a solution of TBS ether (51.1mg, 0.0921mmol) in CH_2Cl_2 (0.92ml) was added MCPBA (29.8mg, 0.138mmol) at 0°C and the mixture was stirred under nitrogen. After 4h, aqueous $NaHSO_3$ (43.0mg, 0.414mmol) was added to decompose excess MCPBA and the mixture was diluted with EtOAc. The organic layer was washed with 1N-NaOH, sat. $NaHCO_3$ and sat. brine and dried with Na_2SO_4. Removal of the solvent gave an oil, which was purified by silica gel column [EtOAc:hexane (1:5-1:2)] to obtain **62** (45.5mg, 0.0797mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.37-7.26 (m, 5H), 7.24 (d, J=8.3Hz, 2H), 6.86 (d, J=8.3Hz, 2H), 4.60 (d, J=7.7Hz, 1H), 4.49 (d, J=7.7Hz, 1H), 4.44 (s, 2H), 3.84-3.79 (m, 1H), 3.80 (s, 3H), 3.66 (dd, J=9.8, 3.1Hz, 1H), 3.58-3.51 (m, 2H), 3.44 (ddd, J=9.2, 9.2, 1.7Hz, 1H), 3.31 (dd, J=9.8, 8.3Hz, 1H), 2.88 (ddd, J=9.0, 5.1, 4.4Hz, 1H), 2.86 (ddd, J=12.0, 2.9, 2.9Hz, 1H), 2.36 (dd, J=14.3, 5.1Hz, 1H), 2.07-1.94 (m, 3H), 1.81-1.73 (m, 1H), 1.70-1.61 (m, 4H), 1.49-1.39 (m, 5H), 1.36-1.27 (m, 2H), 0.97 (dd, J=7.3, 7.3Hz, 3H), 0.89 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H)

Allylalcohol **63**

A mixture of $(PhSe)_2$ (37.3mg, 0.120mmol) and $NaBH_4$ (9.8mg, 0.239mmol) in EtOH (degas 2h) (250μl) was stirred for 5min under nitrogen to prepare $Na^+[PhSeB(OEt)_3]^-$ as a yellow solution. Then it was added to a solution of **62** (45.5mg, 0.0797mmol) in *n*-BuOH (degas 2h) (780μl). After stirring at 140°C for 8h under nitrogen, additional PhSe-anion (1.2eq) was added. Moreover, equal amount of PhSe-anion (1.2eq) was added after 1h from the former addition. The reaction was continued for 4h and the mixture was washed with sat. NH_4Cl and sat. brine. Adsorption of H_2O with Na_2SO_4 followed by evaporation of the solvent left an oil, which was purified by silica gel column [EtOAc:hexane (1:3)] to give selenide compound (55.3mg, 0.0760mmol) as an oil. This compound was immediately subjected to next *syn*-elimination step.

To a solution of selenide compound (55.3mg, 0.0760mmol) in CH_2Cl_2 (1.5ml) were added pyridine (12.3μl, 0.152mmol), 2-methyl-2-butene (83.7μl, 0.760mmol) and H_2O_2 (13.5μl, 0.152mmol) and the mixture was stirred at room temperature for 2h under nitrogen. The reaction was quenched with sat. $NaHCO_3$ and diluted with EtOAc. The mixture was washed with sat. $NaHCO_3$ and sat. brine and dried with Na_2SO_4. Concentration of *in vacuo* gave an oil, which was purified by silica gel column [EtOAc:hexane (1:3-1:2)] to afford **63** (38.3mg, 0.0671mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.37-7.27 (m, 5H), 7.26 (d, J=8.8Hz, 2H), 6.86 (d, J=8.8Hz, 2H), 5.78 (dd, J=11.2, 8.8Hz, 1H), 5.51 (ddd, J=11.2, 8.8, 1.2Hz, 1H), 4.58-4.53 (m, 1H), 4.55 (d, J=11.2Hz, 1H), 4.49 (d, J=11.7Hz, 1H), 4.46 (d, J=11.7Hz, 1H), 4.35 (d, J=11.2Hz, 1H), 4.33 (dd, J=8.8, 4.9Hz, 1H), 3.86 (ddd, J=5.4, 4.9, 4.3Hz, 1H), 3.81 (s, 3H), 3.62 (dd, J=9.8, 4.3Hz, 1H), 3.49 (ddd, J=9.0, 8.8, 2.9, 1H), 3.46 (dd, J=9.8, 5.4Hz, 1H), 3.35 (ddd, J=9.0, 5.4, 1.3Hz, 1H), 2.27-2.19 (m, 1H), 1.96-1.86 (m, 2H), 1.82-1.71 (m, 2H), 1.49-1.40 (m, 1H), 0.93 (dd, J=7.3, 7.1Hz, 3H), 0.89 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H)

Epoxyalcohol **64**

To a solution of **63** (147.0mg, 0.258mmol) in CH_2Cl_2 (2.6ml) was added MCPBA (66.7mg, 0.386mmol) at 0°C and the mixture was stirred at 0°C under nitrogen. After 20h, 22.2mg (0.129mmol) more of MCPBA was added and the stirring was continued for 24h. Excess MCPBA was quenched with aqueous $NaHSO_3$ (160.8mg, 1.16mmol) and the mixture was diluted with EtOAc. The organic layer was washed with 1N-NaOH, sat. $NaHCO_3$ and sat. brine and dried with Na_2SO_4. Removal of the solvent *in vacuo* gave an oil. The residual oil was purified by silica gel column [EtOAc:hexane (3:5)] to give epoxyalcohol **64** (122.6mg, 0.209mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.37-7.27 (m, 5H), 7.23 (d, J=8.8Hz, 2H), 6.86 (d, J=8.8Hz, 2H), 4.56 (d, J=11.3Hz, 1H), 4.46 (d, J=11.7Hz, 1H), 4.42 (d, J=11.7Hz, 1H), 4.39 (d, J=11.3Hz, 1H), 3.95 (ddd, J=6.6, 6.1, 2.5Hz, 1H), 3.80 (s, 3H), 3.67 (dd, J=9.3, 6.3Hz, 1H), 3.63 (ddd, J=8.5, 8.3, 2.9Hz, 1H), 3.57 (dddd, J=10.7, 7.8, 2.7, 2.7Hz, 1H), 3.48 (dd, J=9.5, 2.5Hz, 1H), 3.46 (dd, J=9.3, 6.1Hz, 1H), 3.27 (ddd, J=8.3, 5.1, 2.2Hz, 1H), 3.20 (dd, J=9.5, 4.4Hz, 1H), 3.06 (dd, J=7.8, 4.4Hz, 1H), 2.27-2.19 (m, 1H), 2.10-2.00 (m, 1H), 1.95-1.86 (m, 1H), 1.76-1.68 (m, 1H), 1.65-1.56 (m, 1H), 1.43-1.33 (m, 1H), 0.93 (dd, J=7.6, 7.3Hz, 3H), 0.88 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H)

Epoxy ketone **71**

To a solution of **64** (6.0mg, 10.2μmol) in CH_2Cl_2 (0.34ml) was added Dess-Martin periodinane (6.5mg, 15.3μmol) at room temperature and the mixture was stirred under nitrogen. After 1h, 6.5mg (15.3μmol) more of Dess-Martin periodinane was added and then it was further added twice at every 2h. After 1h from the last addition of reagent, the reaction was quenched with sat. $NaHCO_3$ and diluted with EtOAc. Subsequently, the mixture was washed with sat. $NaHCO_3$ and sat. brine and dried with Na_2SO_4. Removal of the solvent gave an oil, which was purified by silica gel column [EtOAc:hexane (1:3)] to afford **71** (5.5mg, 9.41μmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.40-7.25 (m, 5H), 7.23 (d, J=8.7Hz, 2H), 6.85 (d, J=8.7Hz, 2H), 4.56 (d, J=11.4Hz, 1H), 4.43 (s, 2H), 4.40 (d, J=11.4Hz, 1H), 3.96 (ddd, J=6.2, 5.7 4.0Hz, 1H), 3.82-3.64 (m, 2H), 3.90 (ddd, J=5.1, 4.9,

4.6Hz, 1H), 3.79 (s, 3H), 3.75-3.68 (m, 2H), 3.65 (ddd, J=6.6, 5.6, 5.1Hz, 1H), 3.58 (dd, J=11.0, 3.9Hz, 1H), 3.57 (dd, J=11.0, 5.4Hz, 1H), 3.49 (t, J=4.6Hz, 2H), 3.49-3.43 (m, 2H), 3.41-3.34 (m, 1H), 3.36 (s, 3H), 2.73-2.66 (m, 1H), 2.41-2.33 (m, 1H), 2.15-2.08 (m, 1H), 2.03-1.95 (m, 1H), 1.74-1.66 (m, 2H), 0.86 (dd, J=7.6, 7.3Hz, 3H)

C7-epimer **72**

To a solution of **71** (5.5mg, 9.41μmol) in EtOH (314μl) was added $NaBH_4$ (0.8mg, 18.8μmol) at 0°C and the mixture was stirred for 45min under nitrogen. The reaction was quenched with sat. NH_4Cl and diluted with EtOAc. The organic layer was washed with sat. NH_4Cl and sat. brine and dried with Na_2SO_4. Evaporation of the solvent left an oil, which was purified by silica gel column [EtOAc:hexane (1:2)] to give **72** (3.1mg, 5.28μmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.37-7.27 (m, 5H), 7.25 (d, J=8.8Hz, 2H), 6.86 (d, J=8.8Hz, 2H), 4.57 (d, J=11.2Hz, 1H), 4.47 (d, J=11.7Hz, 1H), 4.50-4.45 (m, 1H), 4.43 (d, J=11.7Hz, 1H), 4.38 (d, J=11.2Hz, 1H), 4.19-4.14 (m, 1H), 3.93 (ddd, J=6.1, 5.9, 2.7Hz, 1H), 3.68 (dd, J=9.5, 5.6Hz, 1H), 3.60-3.54 (m, 1H), 3.50 (dd, J=9.5, 6.1Hz, 1H), 3.49 (s, 3H), 3.36-3.31 (m, 1H), 3.13-3.09 (m, 2H), 2.12-1.99 (m, 4H), 1.99-1.90 (m, 1H), 1.37-1.27 (m, 1H), 0.98 (dd, J=7.4, 7.3Hz, 3H), 0.88 (s, 9H), 0.07 (s, 6H)

Chapter 5

Alcohol **95**

In a flask attached a dean stark (4A-MS) trap, equipped with a reflux condenser is placed (+)-diethyltartrate (15.1g, 73.0mmol), Bu_2SnO (20,0g, 80.3mmol) and benzene (73.0ml). The flask was heated at 110°C and the water which distilled out of the mixture with the refluxing benzene was removed at intervals. Refluxing was continued until no more water separates (about 2h). The benzene was then distilled under reduced pressure, and the residual crystal was dissolved in DMF (73.0ml). To the suspension were added BnBr (11.3ml, 94.95mmol) and CsF (17.2g, 109.6mmol). After stirring for 2h under nitrogen, the

reaction was quenched with sat. $NaHCO_3$ and the heterogeneous mixture was stirred to fully decompose BnBr for 12h. The resultant product was extracted with EtOAc and filtrated through a pad of Celite by the aid of EtOAc. The combined organic layer was washed with sat. $NaHCO_3$ and sat. brine and dried with Na_2SO_4. Evaporation *in vacuo* left an oil, which was purified by silica gel column [EtOAc:hexane (1:2) contained with 1%TEA] to afford **95** (19.7g, 66.5mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ7.38-7.24 (m, 5H), 4.86 (d, J=11.9Hz, 1H), 4.58 (dd, J=8.9, 2.3Hz, 1H), 4.42 (d, J=11.9Hz, 1H), 4.36-4.20 (m, 2H), 4.32 (d, J=2.3Hz, 1H), 4.22 (qd, J=10.9, 7.2Hz, 1H), 4.06 (qd, J=10.9, 7.2Hz, 1H), 3.10 (d, J=8.9Hz, 1H), 3.73 (dd, J=11.2, 4.3Hz, 1H), 1.33 (dd, J=7.2, 7.2Hz, 3H), 1.17 (dd, J=7.2, 7.2Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.1, 169.3, 136.7, 128.4, 128.2, 128.1, 78.2, 72.9, 72.3, 62.0, 61.0, 14.2, 14.0 (2 unresolved); FTIR (neat) ν_{max} 3504, 2984, 2940, 2907, 1748, 1499, 1467, 1454, 1393, 1370, 1263, 1200, 1142, 1101, 1024, 911, 860, 747, 700 cm^{-1}; $[\alpha]^{20}_D$ +82.8° (C 1.54, $CDCl_3$); HRMS (EI, M^+) calculated for $C_{15}H_{20}O_6$:296.1260, found 296.1258

Ketal

$POCl_3$ (637.3μl, 6.84mmol) was added to a solution of alcohol (20.3g, 68.4mmol) and isopropenylmethylether (32.7ml, 341.5mmol) in CH_2Cl_2 (68.4ml) at 0 °C under nitrogen and the mixture was stirred at room temperature. After 1h, 6.5ml (68.4mmol) more of isopropenylmethylether and 318.7μl (3.42mmol) more of $POCl_3$ were added to complete the reaction and the stirring was continued for 34 min. The mixture was quenched with TEA (14.3ml, 102.6mmol) and evaporated *in vacuo*. The crude adduct was submitted to following reduction without purification.

Diol **96**

$LiAlH_4$ (5.2g, 136.7mmol) was added to a solution of the crude ketal (68.4mmol) in THF (68.4ml) at 0°C under nitrogen, and the mixture was stirred for 34 min at room temperature. Then Et_2O (30.0ml) and H_2O (48.0ml) were added to decompose excess $LiAlH_4$ and the

heterogeneous mixture was filtered through a pad of Celite by the aid of THF. Evaporation of the solvent gave an oil, which was purified by a silica gel column. Elution with EtOAc:hexane (7:1) gave diol **96** (11.4g, 40.0mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ7.39-7.29 (m, 5H), 4.66 (s, 2H), 4.07 (ddd, J=4.5, 4.4, 4.4Hz, 1H), 3.81 (dd, J=11.9, 4.6Hz, 1H), 3.73 (dd, J=11.9, 4.9Hz, 1H), 3.72 (d, J=4.4Hz, 2H), 3.59 (ddd, J=4.9, 4.6, 4.5Hz, 1H), 3.26 (s, 3H), 1.39 (s, 3H), 1.37 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.9, 128.5, 128.0, 127.9, 101.4, 79.3, 72.3, 71.7, 62.2, 60.7, 49.7, 25.1, 24.6 (2 unresolved); FTIR (neat) ν_{max} 3453, 2990, 2944, 2907, 1497, 1466, 1456, 1381, 1260, 1206, 1184, 1148, 1104, 1076, 1053, 899, 855, 822, 741, 698 cm^{-1}; $[\alpha]^{20}_D$ − 18.8° (C 1.00, acetone); HRMS (EI, M^+) calculated for $C_{15}H_{24}O_5$:284.1624, found 284.1625

Acetonide

A solution of **96** (11.4g, 40.0mmol), isopropenylmethylether (3.83ml, 40.0mmol) and PPTS (1.08g, 4.0mmol) in CH_2Cl_2 (40.0ml) was stirred at room temperature under nitrogen. After stirring for 1h, H_2O (400μl) was added to the mixture and the stirring was continued for an additional 1h. The resultant mixture was added slowly to a 300ml beaker with sat. $NaHCO_3$ (40.0ml) and extracted with EtOAc. The organic layer was washed with sat. $NaHCO_3$ and sat. brine and dried with Na_2SO_4. Evaporation of the solvent gave an oil, which was purified on silica gel column [EtOAc:hexane (4:5-3:1)] to give five-membered acetonide (6.58g, 26.1mmol) and six-membered acetonide (1.64g, 6.50mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.40-7.27 (m, 5H), 4.77 (d, J=11.9Hz, 1H), 4.71 (d, J=11.9Hz, 1H), 4.35-4.27 (m, 1H), 4.01 (dd, J=8.6, 6.6Hz, 1H), 3.82 (dd, J=8.6, 7.3Hz, 1H), 3.76-3.68 (m, 1H), 3.60 (ddd, J=8.4, 5.2, 5.2Hz, 1H), 3.58 (ddd, J=8.4, 5.9, 5.9Hz, 1H), 2.13 (dd, J=5.9, 5.2Hz, 1H), 1.44 (s, 3H), 1.37 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.2, 128.4, 127.8, 109.4, 7923, 76.6, 72.7, 65.5, 61.7, 26.4, 25.3 (2 unresolved); FTIR (neat) ν_{max} 3455, 2990, 2938, 2888, 1497, 1455, 1381, 1373, 1258, 1213, 1157, 1074, 1030, 961, 916, 855, 741, 698 cm^{-1}; $[\alpha]^{20}_D$ − 22.3° (C 2.35, $CDCl_3$); HRMS (EI, M^+) calculated for $C_{14}H_{20}O_4$:252.1361, found 252.1362

Acetate **97**

A solution of five-membered acetonide (6.58g, 26.1mmol), Ac_2O (3.21ml, 33.9mmol), pyridine (5.48ml, 67.8mmol) and DMAP (318.6mg, 2.61mmol) in CH_2Cl_2 (32.6ml) was stirred for 39 min at room temperature under nitrogen. The reaction was quenched with MeOH (8.36ml, 260.8mmol) and the resultant products were extracted with EtOAc. The organic extracts were washed with 0.5N HCl, sat. $NaHCO_3$ and sat. brine and dried with Na_2SO_4. Evaporation of the solvent left an oil, which was subjected to the next hydrogenation: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.38-7.28 (m, 5H), 4.74 (d, J=11.9Hz, 1H), 4.70 (d, J=11.9Hz, 1H), 4.25 (dd, J=12.5, 6.7Hz, 1H), 4.24-4.16 (m, 1H), 4.16 (dd, J=12.5, 1H), 4.00 (dd, J=8.2, 6.9Hz, 1H), 3.81 (dd, J=8.2, 6.9Hz, 1H), 3.66 (ddd, J=6.7, 6.7, 5.6Hz, 1H), 2.05 (s, 3H), 1.43 (s, 3H), 1.37 (s, 3H); ^{13}C NMR: 170.7 (s), 138.0 (s), 128.3 (d), 127.9 (d), 127.7 (d), 109.5(s), 76.8 (d), 75.9 (d), 72.9 (t), 65.5 (t), 63.6 (t), 26.3 (q), 25.3 (q), 20.9 (q); IR (neat) ν_{max} 3028, 2996, 2972, 2880, 1760, 1744, 1466, 1450, 1370, 1312, 1256, 1172, 1094, 940, 848 cm^{-1}; $[\alpha]^{20}_D$ $-8.29°$ (C 1.000, $CDCl_3$); HRMS (EI, M^+) calculated for $C_{15}H_{19}O_5$ ($-CH_3$):279.1235, found 279.1232

Alcohol

$Pd(OH)_2$-C (753.0mg, 1/10 weight% of s.m.) was added to a solution of crude adduct (7.53g, 25.6mmol) in EtOH (51.1ml) and the mixture was stirred at room temperature under hydrogen. After 3h, an equal amount of $Pd(OH)_2$-C (753.0mg, 1/10 weight% of s.m.) was added and the stirring was continued for 6h. The mixture was filtered through a pad of Celite by the aid of EtOAc. Evaporation of the solvent gave an oil, which was subjected to the next mesylation.

Mesylate **98**

MsCl (2.57ml, 33.3mmol) was added to a solution of crude alcohol (5.22g, 25.6mmol) and TEA (9.27ml, 66.5mmol) in CH_2Cl_2 (51.1ml) at 0°C and the mixture was stirred for 40min at room temperature under nitrogen. After quenching with MeOH (8.20ml,

255.8mmol), the mixture was extracted with EtOAc and the organic layer was washed with sat. $NaHCO_3$ and sat. brine. The aqueous layer was extracted once with EtOAc and the combined layer was dried with Na_2SO_4. Evaporation of the solvent left an oil, which was subjected to the next epoxydation.

Epoxide **99**

To a solution of crude mesylate (7.22g, 25.6mmol) in MeOH (120.1ml) was added K_2CO_3 (10.6g, 76.7mmol) at room temperature. After stirring for 15 min under nitrogen, CH_2Cl_2 (17.1ml) was added and the stirring was continued for additional 2h. The mixture was diluted with EtOAc and washed with sat. NH_4Cl and sat.brine. The aqueous layer was extracted once with EtOAc and the obtained organic extracts were dried with Na_2SO_4. Removal of the solvent *in vacuo* left an oil, which was purified by silica gel column [EtOAc:hexane (1:3)] to give **99** (2.12g, 14.7mmol): ^{1}H-NMR (500MHz, $CDCl_3$) δ 4.12 (dd, J=8.3, 6.0Hz, 1H), 3.93 (dd, J=8.3, 6.0Hz, 1H), 3.86 (ddd, J=6.0, 6.0, 6.0Hz, 1H), 3.02 (ddd, J=6.0, 4.9, 2.3Hz, 1H), 2.85 (dd, J=5.0, 4.9Hz, 1H), 2.67 (dd, J=5.0, 2.3Hz, 1H), 1.46 (s, 3H), 1.37 (s, 3H); ^{13}C NMR: 109.7 (s), 76.2 (d), 66.8 (t), 52.0 (d), 45.6 (t), 26.5 (q), 25.2 (q); IR (neat) ν_{max} 2992, 2944, 2880, 1460, 1374, 1254, 1176, 1052, 956, 896, 840 cm^{-1}; $[\alpha]^{20}_D$ $-6.48°$ (C 1.003, $CDCl_3$); HRMS (EI, M^+) calculated for $C_7H_{11}O_3$ ($-$H):143.0714, found 143.0708

Acetylene **100**

To the mixture of magnesium (715mg, 29.4mmol) pre-treated by heating under decompression and $HgCl_2$ (39.9mg, 0.01eq) in Et_2O (20.0ml) was added a solution of propalgylbromide (2.21ml, 29.4mmol) in Et_2O (23.5ml) and the mixture was stirred at room temperature under nitrogen. After 30min, Et_2O (20.0ml) was added at room temperature and the solution of the prepared propalgyl Grignard was cooled down to $-50°C$. Then, a solution of epoxide (2.12g, 14.7mmol) in Et_2O (10.0ml) was added at $-50°C$ and the mixture was rose to $-20°C$ over 1h50min before the reaction was quenched

with sat. NH_4Cl at $-20°C$. The mixture was diluted with EtOAc and washed with sat. NH_4Cl and sat. brine. The aqueous layer was extracted once with EtOAc. The obtained organic extracts were dried with Na_2SO_4. Removal of the solvent gave an oil, which contained desired acetylene and undesired bromohydrine. The residual oil was subjected to the next reformation of epoxide.

Epoxide **99**

K_2CO_3 (812.7mg, 5.88mmol) was added to a solution of crude oil [2.94mmol (based on the assumption that bromohydrine generated 20%)] in MeOH (14.7ml)/CH_2Cl_2 (14.7ml) at room temperature. After stirring for 1h, the mixture was diluted with EtOAc and filtered through a pad of Celite by the aid of CH_2Cl_2. Evaporation of the solvent gave an oil, which was purified by silica gel column [EtOAc:hexane (1:2)] to give acetylene **100** (2.34g, 12.7mmol) and epoxide **99** (320.6mg, 2.22mmol): ^{1}H-NMR (500MHz, $CDCl_3$) δ 4.16-3.85 (m, 4H), 2.43-2.35 (m, 2H), 2.12 (d, J=3.6Hz, 1H), 1.99 (t, J=3.0Hz, 1H), 1.80-1.66 (m, 1H), 1.43 (s, 3H), 1.37 (s, 3H); ^{13}C NMR: 109.1 (s), 83.7 (d), 78.4 (d), 69.9 (d), 69.0 (s), 64.8 (t), 31.2 (t), 26.5 (q), 25.2 (q), 15.0 (t); IR (neat) ν_{max} 3468, 3300, 2992, 2948, 2120, 1436, 1374, 1212, 1158, 1052, 962, 922, 848 cm^{-1}; $[\alpha]^{20}_D - 2.79°$ (C 1.003, $CDCl_3$); HRMS (EI, M^+) calculated for $C_9H_{13}O_3$ ($-CH_3$):169.0865, found 169.0865

MPM ether **101**

MPMCl (2.24ml, 16.5ml), NaH (831.3mg, 19.1mmol) and *n*-Bu_4NI (469.0mg, 1.27mmol) were added to a solution of acetylene **100** (2.34g, 12.7mmol) in THF (42.4ml) at 0°C and the mixture was stirred at room temperature for 12h under nitrogen. Then sat. $NaHCO_3$ was added to decompose excess MPMCl and the stirring was continued for 6h. The mixture was diluted with EtOAc and washed with sat. $NaHCO_3$ and sat. brine. Adsorption of H_2O with Na_2SO_4 followed by evaporation of the solvent gave an oil, which was purified by silica gel column [EtOAc:hexane (0:1-1:4)] to give **101** (3.34g, 11.0 mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.26 (d, J=8.6Hz, 2H), 6.88 (d, J=8.6Hz, 2H), 4.62 (d, J=10.9Hz, 1H),

4.55 (d, J=10.9Hz, 1H), 4.12-4.05 (m, 1H), 4.02 (dd, J=7.6, 6.3Hz, 1H), 3.86 (dd, J=7.6, 6.3Hz, 1H), 3.81 (s, 3H), 3.68 (ddd, J=7.9, 4.3, 4.3Hz, 1H), 2.33 (ddd, J=7.6, 7.6, 2.6Hz, 2H), 1.97 (t, J=2.6Hz, 1H), 1.89-1.66 (m, 2H), 1.44 (s, 3H), 1.36 (s, 3H); ^{13}C NMR: 159.3 (s), 130.5 (s), 129.5 (d), 113.8 (d), 109,1 (s), 84.1 (d), 77.8 (d), 77.3 (d), 72.9 (t), 68.7 (s), 66.3 (t), 55.3 (q), 30.2 (t), 26.6 (q), 25.3 (q) , 14.4 (t); IR (neat) ν_{max} 3300, 2996, 2940, 2120, 1614, 1588, 1460, 1372, 1304, 1250, 1156, 1064, 846 cm^{-1}; $[\alpha]^{20}_{D}$ +16.71° (C 1.023, $CDCl_3$); HRMS (EI, M^+) calculated for $C_{18}H_{24}O_4$:304.1676, found 304.1674

Coupled compound **103**

To THF (20.3ml) solution of epoxide **93** (2.83g, 9.17mmol) and acetyrene **101** (4.19g, 13.8mmol), which was each azeotroped once with toluene was added *n*-BuLi (9.23ml, 14.7mmol) at − 78°C and stirred for 30 min under nitrogen. Then $BF_3{\cdot}OEt_2$ (2.91ml, 22.9mmol) was added to the mixture at − 78°C and the stirring was continued for additional 1h. After quenching with sat. $NaHCO_3$, the mixture was diluted with EtOAc and washed with sat. $NaHCO_3$ and sat. brine. The aqueous layer was extracted once with EtOAc. The obtained organic layer was dried with Na_2SO_4. Removal of the solvent left an oil, which was purified by silica gel column [EtOAc:hexane (1:4-1:3)] to provide **103** (4.50g, 2.93mmol) as an oil. In addition, epoxide (308.1mg, 0.999mmol) and acetylene (784.5mg, 7.34mmol) were recovered, respectively. The desired product was subjected to the next mesylation: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.40-7.30 (m, 5H), 7.27 (d, J=8.6Hz, 2H), 6.89 (d, J=8.6Hz, 2H), 4.62 (d, J=10.9Hz, 1H), 4.56 (d, J=10.9Hz, 1H), 4.55 (m, 2H), 4.19-4.10 (m, 1H), 4.09 (dd, J=6.6, 5.2Hz, 1H), 4.02 (ddd, J=6.3, 6.3, 2.0Hz, 1H), 3.87 (dd, J=7.6, 6.6Hz, 1H), 3.82 (s, 3H), 3.80-3.74 (m, 1H), 3.71-3.64 (m, 1H), 3.59 (dd, J=9.5, 7.2Hz, 1H), 3.49 (dd, J=9.5, 5.6Hz, 1H), 2.47 (d, J=8.5Hz, 1H), 2.44-2.30 (m, 4H), 1.88-1.74 (m, 2H), 1.45 (s, 3H), 1.38 (s, 3H), 0.92 (s, 9H), 0.14 (s, 3H), 0.11 (s, 3H); ^{13}C NMR: 159.2 (s), 138.0 (s), 130.5 (s), 129.5 (d), 128.4 (d), 127.7 (d), 113.8 (d), 109.1 (s), 81.7 (s), 77.8 (d), 77.5 (d), 76.9 (s), 73.4 (t), 72.8 (t), 71.9 (t), 71.6 (d), 70.9 (d), 66.2 (t), 55.3 (q), 30.7 (t), 26.6 (q), 25.9 (q), 25.3 (q), 24.3 (t), 18.1 (s), 14.8 (t), − 4.3 (q), − 4.9 (q); IR (neat) ν_{max}

3516, 2944, 2080, 1614, 1588, 1514, 1456, 1374, 1302, 1254, 1158, 1096, 840 cm^{-1}; $[\alpha]^{20}_D$ +10.22° (C 1.076, $CDCl_3$); HRMS (EI, M^+) calculated for $C_{34}H_{49}O_7Si$ (– CH_3):143.0714, found 143.0708

Mesylate **104**

A solution of alcohol (1.80g, 2.93mmol), MsCl (340.1µl, 4.41mmol), TEA (1.23ml, 8.81mmol) and DMAP (35.9mg, 0.293mmol) in CH_2Cl_2 (14.7ml) was stirred for 15min at 0°C under nitrogen. The mixture was diluted with EtOAc and washed with sat. $NaHCO_3$ and sat. brine. Adsorption of H_2O with Na_2SO_4 followed by evaporation of the solvent gave an oil, which was purified by silica gel column [EtOAc:hexane (1:4-1:3)] to afford **104** (1.95g, 2.82mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.40-7.30 (m, 5H), 7.18 (d, J=8.6Hz, 2H), 6.80 (d, J=8.6Hz, 2H), 4.71 (ddd, J=6.9, 6.9, 3.0Hz, 1H), 4.53 (d, J=10.9Hz, 1H), 4.48 (d, J=10.9Hz, 1H), 4.44 (d, J=10.9Hz, 1H), 4.42 (d, J=10.9Hz, 1H), 4.08 (ddd, J=5.9, 5.9, 3.0Hz, 1H), 4.04-3.94 (m, 1H), 3.94 (dd, J=7.6, 6.2Hz, 1H), 3.77 (dd, J=7.6, 5.9Hz, 1H), 3.73 (s, 3H), 3.58-3.48 (m, 1H), 3.50 (dd, J=9.6, 5.9Hz, 1H), 3.43 (dd, J=9.6, 5.9Hz, 1H), 2.95 (s, 3H), 2.73-2.54 (m, 2H), 1.75-1.55 (m, 2H), 1.36 (s, 3H), 1.28 (s, 3H), 0.82 (s, 9H), 0.04 (s, 3H), 0.00 (s, 3H); ^{13}C NMR: 159.2 (s), 137.7 (s), 130.4 (s), 129.5 (d), 128.4 (d), 127.8 (d), 127.7 (d), 113.8 (d), 109.1 (s), 82.7 (s), 80.5 (d), 77.6 (d), 77.4 (d), 75.2 (s), 73.5 (t), 72.7 (t), 70.5 (d), 70.5 (t), 66.3 (t), 55.2 (q), 38.4 (q), 30.4 (t), 26.5 (q), 25.8 (q), 25.3 (q), 21.4 (t), 18.1 (s), 14.6 (t), – 4.5 (q), – 4.9 (q); IR (neat) ν_{max} 2952, 2072, 1614, 1588, 1514, 1460, 1372, 1336, 1304, 1174, 1300-800, 1260, 1158, 1098 cm^{-1}; $[\alpha]^{20}_D$ +17.47° (C 1.030, $CDCl_3$); HRMS (EI, M^+) calculated for $C_{36}H_{54}O_9SiS$:690.3262, found 690.3257

Epoxide **105**

To a solution of mesylate (6.35g, 9.19mmol) in THF (61.3ml) was added TBAF (13.8ml, 13.8mmol) and the mixture was stirred at room temperature under nitrogen. After stirring for 1h, MeOH (61.3ml) and K_2CO_3 (2.54g, 18.4mmol) were added and the reaction was

continued for 3h40min under nitrogen. The mixture was diluted with EtOAc and washed with sat. NH_4Cl and sat. brine. Removal of the solvent gave an oil, which was purified by silica gel column [EtOAc:hexane (1:20-2:5-3:1)] to afford **105** (3.41g, 7.01mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.40-7.28 (m, 5H), 7.25 (d, J=8.6Hz, 2H), 6.87 (d, J=8.6Hz, 2H), 4.63 (d, J=11.9Hz, 1H), 4.61 (d, J=10.9Hz, 1H), 4.54 (d, J=10.9Hz, 1H), 4.53 (d, J=10.9Hz, 1H), 4.07 (ddd, J=6.3, 6.3, 5.6Hz, 1H), 4.00 (dd, J=7.6, 6.3Hz, 1H), 3.85 (dd, J=7.6, 6.3Hz, 1H), 3.80 (s, 3H), 3.75 (dd, J=11.5, 4.0Hz, 1H), 3.64 (ddd, J=7.6, 5.6, 4.0Hz, 1H), 3.56 (dd, J=11.5, 6.3Hz, 1H), 3.23 (ddd, J=6.3, 4.0, 4.0Hz, 1H), 3.17 (ddd, J=6.9, 6.0, 4.0Hz, 1H), 2.61-2.50 (m, 1H), 2.38-2.20 (m, 3H), 1.80-1.62 (m, 2H), 1.43 (s, 3H), 1.35 (s, 3H); ^{13}C NMR: 159.2 (s), 137.8 (s), 130.5 (s), 129.5 (d), 128.4 (d), 127.8 (d), 127.7 (d), 113.8 (d), 109.1 (s), 82.2 (s), 77.8 (d), 77.4 (d), 75.1 (s), 73.3 (t), 72.8 (t), 67.8 (t), 66.2 (t), 55.3 (q), 55.2 (d), 54.4 (d), 30.6 (t), 26.6 (q), 25.3 (q), 19.1 (t), 14.7 (t); IR (neat) ν_{max} 2932, 2060, 1616, 1588, 1514, 1458, 1374, 1302, 1252, 1066, 918, 844 cm^{-1}; $[\alpha]^{20}_D$ +43.39° (C 1.030, $CDCl_3$); HRMS (EI, M^+) calculated for $C_{29}H_{36}O_6$:480.2517, found 480.2512

Diol

A solution of epoxide **105** (3.41g, 7.01mmol) in 80% aqueous AcOH (70.1ml) was stirred for 7h at room temperature under nitrogen. The mixture was added to aqueous $NaHCO_3$ (98.8g 84.1mmol) and the stirring was continued to quench the reaction. After 15h, the mixture was diluted with EtOAc and washed with 0.5N NaOH and sat. brine. Adsorption of H_2O with Na_2SO_4 followed by evaporation of the solvent gave an oil, which was purified by silica gel column [EtOAc:hexane (1:1-3:1)] to provide diol (2.80g, 6.36mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.38-7.27 (m, 5H), 7.25 (d, J=8.6Hz, 2H), 6.88 (d, J=8.6Hz, 2H), 4.63 (d, J=11.9Hz, 1H), 4.55 (d, J=11.9Hz, 1H), 4.54 (d, J=10.9Hz, 1H), 4.53 (d, J=10.9Hz, 1H), 3.80 (s, 3H), 3.80-3.63 (m, 4H), 3.73 (dd, J=11.2, 4.3Hz, 1H), 3.58 (dd, J=11.2, 6.3, 1H), 3.17 (ddd, J=6.3, 4.3, 4.3Hz, 1H), 2.60-2.47 (m, 2H), 2.36-2.22 (m, 2H), 1.88-1.60 (m, 2H); ^{13}C NMR: 159.4 (s), 137.7 (s), 130.2 (s), 129.6 (d), 128.5 (d), 127.8 (d), 127.8 (d), 113.9 (d), 82.2 (s), 79.1 (d), 75.4 (s), 73.3 (t), 72.6 (t), 72.5 (d), 67.8 (t), 63.4 (t),

55.3 (q), 55.2 (d), 54.4 (d), 29.5 (t), 19.1 (t), 14.8 (t); IR (neat) ν_{max} 3440, 2936, 2064, 1614, 1588, 1512, 1456, 1302, 1252, 822 cm^{-1}; $[\alpha]^{20}_D$ +37.57° (C 1.030, $CDCl_3$); HRMS (EI, M^+) calculated for $C_{26}H_{32}O_6$:440.2198, found 440.2199

Olefin **106**

To a stirred solution of diol (2.33g, 5.29mmol) in EtOAc (52.9ml) containing quinoline (266.5μl, same weight as Lindlar cat.) was added Lindlar cat. (291.3mg, 1/8 weight% of s.m.). The flask was purged with triple balloon of hydrogen, and then stirred under a hydrogen balloon at ambient temperature for 1h before being purged with air to evaporate all of the hydrogen. Then, the mixture was filtered through a pad of Celite by the aid of EtOAc, and filtrate was washed with 0.5N HCl, sat. $NaHCO_3$ and sat. brine. Adsorption of H_2O with Na_2SO_4 followed by evaporation of the solvent gave an oil, which was purified by silica gel column [EtOAc:hexane (4:1)] to provide **106** (2.31g, 5.22mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.37-7.27 (m, 5H), 7.25 (d, J=8.6Hz, 2H), 6.88 (d, J=8.6Hz, 2H), 5.59-5.40 (m, 2H), 4.52 (d, J=11.9Hz, 1H), 4.53 (d, J=11.9Hz, 1H), 4.53 (d, J=11.2Hz, 1H), 4.49 (d, J=11.2Hz, 1H), 3.79 (s, 3H), 3.77-3.64 (m, 3H), 3.71 (dd, J=11.0, 4.3Hz, 1H), 3.57 (dd, J=11.0, 6.3Hz, 1H), 3.68-3.50 (m, 1H), 3.21 (ddd, J=6.3, 4.6, 4.3Hz, 1H), 3.00 (ddd, J=6.6, 5.9, 4.3Hz, 1H), 2.40-2.01 (m, 4H), 1.78-1.48 (m, 2H); ^{13}C NMR: 159.4 (s), 137.8 (s), 132.0 (d), 130.2 (s), 129.5 (d), 128.4 (d), 127.8 (d), 124.5 (d), 113.9 (d), 80.1 (d), 73.3 (t), 72.4 (d), 72.3 (t), 68.1 (t), 63.4 (t), 55.5 (d), 55.3 (q), 55.2 (d), 30.2 (t), 26.4 (t), 23.2 (t); IR (neat) ν_{max} 3456, 2940, 2900, 1654, 1612, 1588, 1512, 1454, 1304, 1250, 1174, 1034, 822 cm^{-1}; $[\alpha]^{20}_D$ − 10.69° (C 1.010, $CDCl_3$); HRMS (EI, M^+) calculated for $C_{26}H_{33}O_6$(− H): 441.2272, found 441.2277

Acyclic precursor **90**

TBSCl (1.18g, 7.83mmol) and DMAP (63.8mg, 0.522mmol) were added to a solution of **106** (2.31g, 5.22mmol) and TEA (2.18ml, 15.7mmol) in CH_2Cl_2 (52.2ml) at 0°C under nitrogen. After stirring for 22h, the mixture was diluted with EtOAc and washed with sat.

$NaHCO_3$ and sat. brine. Removal of the solvent left an oil, which was purified by silica gel column [EtOAc:hexane (1:10-1:3)] to give **90** (2.81g, 5.05mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.39-7.26 (m, 5H), 7.25 (d, J=8.6Hz, 2H), 6.87 (d, J=8.6Hz, 2H), 5.60-5.46 (m, 2H), 4.62 (d, J=11.9Hz, 1H), 4.50 (d, J=11.9Hz, 1H), 4.49 (s, 2H), 3.79 (s, 3H), 3.76-3.63 (m, 3H), 3.71 (dd, J=11.2, 4.3Hz, 1H), 3.56 (dd, J=11.2, 6.3Hz, 1H), 3.50-3.41 (m, 1H), 3.20 (ddd, J=6.3, 4.3, 4.3Hz, 1H), 3.00 (ddd, J=6.6, 6.3, 4.3Hz, 1H), 2.45-2.28 (m, 1H), 2.28-2.05 (m, 3H), 1.72-1.61 (m, 2H), 0.91 (s, 9H), 0.08 (s, 6H); ^{13}C NMR: 159.3 (s), 137.9 (s), 132.5 (d), 130.6 (s), 129.4 (d), 128.4 (d), 127.8 (d), 127.7 (d), 124.0 (d), 113.8 (d), 78.4 (d), 73.3 (t), 72.7 (d), 72.0 (t), 68.2 (t), 63.9 (t), 55.5 (d), 55.3 (q), 55.2 (d), 30.0 (t), 26.5 (t), 25.9 (q), 23.0 (t), 18.3 (s), − 5.4 (q); IR (neat) ν_{max} 3552, 2928, 1650, 1614, 1588, 1514, 1464, 1392, 1302, 1246, 1174, 904, 832 cm^{-1}; $[\alpha]^{20}_D$ − 5.01° (C 1.096, $CDCl_3$); HRMS (EI, M^+) calculated for $C_{28}H_{39}O_6Si(-C_4H_9)$: 499.2521, found 499.2516

Cyclic compound **107**

$Eu(fod)_3$ (3.55g, 3.39mmol) was added to a solution of **90** (1.89g, 3.39mmol) in toluene (339.0ml) at room temperature and the reaction was carried out at 120°C under nitrogen. After stirring for 108h, (710.0mg, 0.679mmol) more of $Eu(fod)_3$ was added and the stirring was continued for 72h under nitrogen. The mixture was concentrated *in vacuo*, leaving an oil, which was subjected to the next desilylation.

To a solution of the crude oil in THF (6.79ml)/H_2O (6.79ml) was added AcOH (20.4 ml) (namely, AcOH:THF:H_2O = 3:1:1, total 0.1Msoln.) and the mixture was stirred at room temperature for 8h under nitrogen. The reaction was quenched with 4N NaOH (89.0ml) and the resultant products were extracted with EtOAc. The organic extracts were washed with 1N NaOH, sat. $NaHCO_3$ and sat. brine and dried with Na_2SO_4. Evaporated of the solvent gave an oil, which was purified by silica gel column [EtOAc:hexane (1:3-2:1 contained with 1%TEA)] to provide **107** (1.05g, 2.36mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.38-7.28 (m, 5H), 7.26 (d, J=8.6Hz, 2H), 6.89 (d, J=8.6Hz, 2H), 5.65 (ddd, J=10.8, 10.6,

5.0Hz, 1H), 5.57 (ddd, J=10.6, 8.3, 8.0Hz, 1H), 4.59 (d, J=11.0Hz, 1H), 4.55 (d, J=11.5Hz, 1H), 4.48 (d, J=11.5Hz, 1H), 4.33 (d, J=11.6Hz, 1H), 3.93 (ddd, J=7.6, 7.6, 3.7Hz, 1H), 3.92-3.86 (m, 1H), 3.80 (s, 3H), 3.76 (ddd, J=7.2, 6.6, 3.2Hz, 1H), 3.75-3.68 (m, 1H), 3.65 (dd, J=9.8, 3.2Hz, 1H), 3.50 (ddd, J=10.3, 7.6, 2.7Hz, 1H), 3.47 (dd, J=9.8, 6.6Hz, 1H), 2.69 (dddd, J=14.7, 12.5, 12.4, 5.0Hz, 1H), 2.39 (ddd, J=14.7, 8.5, 8.3Hz, 1H), 2.07-2.00 (m, 1H), 1.99-1.89 (m, 2H), 1.78-1.70 (m, 1H); ^{13}C NMR: 159.2 (s), 137.7 (s), 132.4 (d), 130.3 (s), 129.4 (d), 128.4 (d), 127.8 (d), 127.7 (d), 126.3 (d), 113.8 (d), 80.1 (d), 77.5 (d), 76.2 (d), 73.5 (t), 73.0 (d), 71.5 (t), 71.2 (t), 62.0 (t), 55.2 (q), 30.8 (t), 28.9 (t), 23.3 (t); IR (neat) ν_{max} 3532, 2896, 1612, 1588, 1510, 1454, 1304, 1172, 1062, 820 cm^{-1}; $[\alpha]^{20}_{D}$ – 7.47° (C 1.003, $CDCl_3$); HRMS (EI, M^+) calculated for $C_{26}H_{33}O_6$(– H): 441.2272, found 441.2277

Anisylidene **114**

To a solution of **107** (1.53g, 3.46mmol) in CH_2Cl_2 (34.6ml) was added the crushed 4A-MS (1.73g) which was dehydrated by heating under high decompression and the mixture was stirred at room temperature under nitrogen. After 1h, DDQ (890.9mg, 3.80mmol) was added to the mixture and the stirring was continued for 2h at 0°C under nitrogen. The reaction mixture was extracted with EtOAc and the combined organic extracts were washed sat. $NaHCO_3$ three times, H_2O and sat. brine. Removal of the solvent left an oil, which was purified by silica gel column [EtOAc:hexane (4:5 contained with 1%TEA)] to give **114** (1.41g, 3.20mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.40-7.29 (m, 7H), 6.76 (d, J=9.0Hz, 2H), 5.75-5.67 (m, 2H), 5.33 (s, 1H), 4.59 (d, J=11.7Hz, 1H), 4.56 (d, J=11.7Hz, 1H), 4.16 (dd, J=10.5, 4.6Hz, 1H), 3.90-3.76 (m, 3H), 3.79 (s, 3H), 3.71-3.64 (m, 3H), 3.50 (ddd, J=8.3, 8.3, 2.0Hz, 1H), 2.83 (dddd, J=18.3, 10.8, 6.8, 5.9Hz, 1H), 2.21 (ddd, J=14.2, 8.8, 5.4Hz, 1H), 2.17-2.11 (m, 1H), 2.10-2.04 (m, 1H), 2.24-2.10 (m, 1H), 1.93-1.82 (m, 2H); ^{13}C NMR: 160.0 (s), 137.7 (s), 132.5 (d), 130.3 (s), 128.5 (d), 127.9 (d), 127.8 (d), 127.0 (d), 113.6 (d), 100.7 (d), 76.2 (d), 75.5 (d), 73.6 (t), 73.5 (d), 73.2 (d), 70.2 (t), 67.5 (t), 55.3 (q), 33.6 (t), 28.5 (t), 24.4 (t); IR (neat) ν_{max} 3460, 2924,

1616, 1590, 1512, 1448, 1392, 1306, 1256, 1172, 1102, 826 cm^{-1}; $[\alpha]^{20}_D$ +46.82° (C 1.023, $CDCl_3$); HRMS (EI, M^+) calculated for $C_{26}H_{32}O_6$:440.2196 found 440.2199

TBS ether

TBSOTf (882.1μl, 3.84mmol) was added to a solution of **114** (1.41g, 3.20mmol) and 2,6-lutidine (894.7μl, 7.68mmol) in CH_2Cl_2 (32.0ml) at 0°C and the mixture was stirred for 30min under nitrogen. The reaction mixture was diluted with EtOAc and washed with sat. $NaHCO_3$ and sat. brine. The organic layer was concentrated *in vacuo* leaving an oil, which was purified by silica gel column [EtOAc:hexane (1:6 contained with 1%TEA)] to give TBS ether (1.67g, 3.02mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.39 (d, J=8.8Hz, 2H), 7.36-7.32 (m, 5H), 6.87 (d, J=8.8Hz, 2H), 5.73-5.65 (m, 2H), 5.33 (s, 1H), 4.54 (d, J=12.2Hz, 1H), 4.52 (d, J=12.2Hz, 1H), 4.22-4.16 (m, 1H), 3.85-3.75 (m, 3H), 3.79 (s, 3H), 3.72 (dd, J=9.8, 2.2Hz, 1H), 3.64 (ddd, J=7.3, 4.9, 2.2Hz, 1H), 3.46 (ddd, J=4.9, 4.9, 4.9Hz, 1H), 3.37 (dd, J=9.8, 7.3Hz, 1H), 2.87-2.78 (m, 1H), 2.30-2.24 (m, 1H), 2.11-2.08 (m, 1H), 2.07-2.01 (m, 1H), 1.91-1.80 (m, 2H), 0.90 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H); ^{13}C NMR: 160.0 (s), 138.5 (s), 132.3 (d), 130.3 (s), 128.2 (d), 127.8 (d), 127.5 (d), 127.4 (d), 113.6 (d), 100.8 (d), 77.1 (d), 76.2 (d), 75.0 (d), 73.4 (t), 73.1 (d), 71.1 (t), 67.6 (t), 55.3 (q), 33.6 (t), 27.0 (t), 25.8 (q), 24.4 (t), 18.0 (s), − 4.3(q), − 4.7 (q); IR (neat) ν_{max} 3016, 2932, 1618, 1590, 1516, 1458, 1394, 1362, 1304, 1244, 1172, 1130, 916, 836 cm^{-1}; $[\alpha]^{20}_D$ +42.04° (C 1.056, $CDCl_3$); HRMS (EI, M^+) calculated for $C_{32}H_{45}O_6Si(-H)$: 553.2985, found 553.2991

Diol **115**

TFA (62.9μl, 0.816mmol) was added to a solution of TBS ether (2.26g, 4.08mmol) in MeOH (40.8ml) and the stirring was run at room temperature under nitrogen. After 30min, the mixture was diluted with EtOAc and washed with sat. $NaHCO_3$ and sat. brine. Removal of the solvent gave an oil, which was purified by silica gel column. Elution with EtOAc:hexane (1:8) gave s.m. (628.0mg, 0.278mmol) as an oil, and further elution with EtOAc:hexane (2:3) afforded diol **115** (1.03g, 2.36mmol) as an oil: ^{1}H-NMR (500MHz,

$CDCl_3$) δ 7.37-7.27 (5H, m, C_{13-18}-H), 5.67-5.59 (m, 2H), 4.55 (d, J=12.2Hz, 1H), 4.52 (d, J=12.2Hz, 1H), 3.91 (dd, J=11.7, 4.2Hz, 1H), 3.86-3.80 (m, 2H), 3.80-3.71 (m, 3H), 3.68 (dd, J=9.8, 4.9Hz, 1H), 3.41 (dd, J=9.8, 5.9Hz, 1H), 2.73 (dddd, J=18.3, 13.2, 5.4, 5.4Hz, 1H), 2.43-2.36 (m, 1H), 2.08-2.03 (m, 1H), 2.03-1.96 (m, 1H), 1.85-1.77 (m, 1H), 1.76-1.69 (m, 1H), 0.89 (s, 9H), 0.09 (s, 3H), 0.07 (s, 3H); ^{13}C NMR: 138.2 (s), 131.7 (d), 128.3 (d), 127.6 (d), 127.5 (d), 127.4 (d), 79.7 (d), 76.5 (d), 74.5 (d), 73.3 (t), 71.4 (t), 70.5 (d), 63.0 (t), 36.1 (t), 27.6 (t), 25.8 (q), 23.9 (t), 18.1 (s), − 4.5 (q), − 4.9 (q); IR (neat) ν_{max} 3428, 3020, 2860, 1650, 1456, 1360, 1334, 1252, 1020, 914, 834 cm^{-1}; $[\alpha]^{20}_D$ +9.87° (C 1.063, $CDCl_3$); HRMS (EI, M^+) calculated for $C_{20}H_{31}O_5Si(-C_4H_9)$:379.1941, found 379.1935

Acetonide **116**

To a solution of **115** (1.03g, 2.36mmol), 2-methoxypropane (0.57ml, 5.91mmol) in CH_2Cl_2 (23.6ml) was added PPTS (63.7mg, 0.24mmol) at room temperature and the mixture was stirred under nitrogen. After 30min, the mixture was diluted with EtOAc and washed with sat. $NaHCO_3$ and sat. brine. Removal of the solvent gave an oil, which was purified by silica gel column [EtOAc:hexane (1:10)] to provide **116** (1.11g, 2.33mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.36-7.26 (m, 5H), 5.71-5.60 (m, 2H), 4.53 (d, J=12.2Hz, 1H), 4.51 (d, J=12.2Hz, 1H), 3.84 (ddd, J=9.5, 9.5, 3.9Hz, 1H), 3.80 (dd, J=11.2, 6.1Hz, 1H), 3.78 (dd, J=11.2, 5.1Hz, 1H), 3.76-3.65 (m, 1H), 3.72 (dd, J=9.8, 2.7Hz, 1H), 3.69-3.65 (m, 1H), 3.55-3.51 (m, 1H), 3.38 (dd, J=9.8, 7.6Hz, 1H), 2.80-2.70 (m, 1H), 2.24-2.13 (m, 2H), 2.05-1.99 (m, 1H), 1.75-1.63 (m, 2H), 1.41 (s, 3H), 1.34 (s, 3H), 0.90 (s, 9H), 0.09 (s, 6H); ^{13}C NMR: 138.5 (s), 132.1 (d), 128.3 (d), 127.7 (d), 127.5 (d), 127.4 (d), 98.4 (s), 77.2 (d), 75.2 (d), 74.3 (d), 73.4 (t), 71.2 (t), 68.4 (d), 61.5 (t), 33.8 (t), 28.1 (q), 27.2 (t), 25.8 (q), 24.2 (t), 20.3 (q), 18.0 (s), − 4.4 (q), − 4.8 (q); IR (neat) ν_{max} 2860, 1654, 1498, 1462, 1380, 1330, 1266, 1090, 924, 836 cm^{-1}; $[\alpha]^{20}_D$ +37.08° (C 1.030, $CDCl_3$); HRMS (EI, M^+) calculated for $C_{26}H_{41}O_5Si(-CH_3)$: 461.2723, found 461.2720

Epoxide **117**

MCPBA (753.4mg, 3.49mmol) was added to the mixture of **116** (1.11g, 2.33mmol), $NaHCO_3$ (1.96g, 23.3mmol) in CH_2Cl_2 (23.3ml) and the mixture was stirred at 0°C under nitrogen. After stirring for 2h, 251.1mg (1.16mmol) more of MCPBA was added and stirring was continued for 3h. The excess MCPBA was decomposed by aqueous $NaHSO_3$ (1.45g, 14.0mmol) and the generated MCBA was quenched by sat. $NaHCO_3$. The mixture was extracted with EtOAc and the combined extracts were washed with 1N NaOH, sat. $NaHCO_3$ and sat. brine. After removal of the solvent, the residue was purified by silica gel column [EtOAc:hexane (1:4)] to afford **117** (1.09g, 2.21mmol) as a crystal:^{1}H-NMR (500MHz, $CDCl_3$) δ 7.36-7.26 (m, 5H), 4.53 (d, J=12.0Hz, 1H), 4.50 (d, J=12.0Hz, 1H), 3.95 (ddd, J=10.5, 8.0, 4.2Hz, 1H), 3.85 (dd, J=11.2, 5.1Hz, 1H), 3.87-3.82 (m, 1H), 3.78 (dd, J=11.2, 7.3Hz, 1H), 3.70-3.60 (m, 3H), 3.36 (dd, J=10.7, 8.1Hz, 1H), 3.04 (ddd, J=9.0, 4.2, 4.2Hz, 1H), 2.98 (ddd, J=12.2, 4.2, 4.2Hz, 1H), 2.32-2.26 (m, 1H), 2.15-2.09 (m, 1H), 1.89 (dddd, J=13.4, 13.4, 4.2, 4.2Hz, 1H), 1.75 (dddd, J=13.4, 8.0, 4.2, 4.2,Hz, 1H), 1.68-1.58 (m, 1H), 1.50-1.44 (m, 1H), 1.44 (s, 3H), 1.35 (s, 3H), 0.89 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H); ^{13}C NMR: 138.2 (s), 128.3 (d), 127.6 (d), 127.5 (d), 98.6 (s), 75.0 (d), 73.4 (t), 73.0 (d), 72.7 (d), 71.0 (t), 68.8 (d), 61.9 (t), 56.4 (d), 55.6 (d), 31.3 (t), 29.0 (t), 27.9 (q), 25.8 (q), 22.7 (t), 20.7 (q), 18.0 (s), − 4.4 (q), − 5.0 (q); IR (neat, KBr) ν_{max} 3076, 2936, 1498, 1462, 1372, 1328, 1308, 1260, 1152, 996, 944, 908, 834 cm^{-1}; $[\alpha]^{20}_D$ +12.48° (C 1.129, $CDCl_3$); m.p. 89.5°C; HRMS (EI, M^+) calculated for $C_{26}H_{41}O_6Si(-CH_3)$: 477.2672, found 477.2668

Allylalcohol **118**

A mixture of $(PhSe)_2$ (1.03g, 3.31mmol) and $NaBH_4$ (272.1mg, 6.62mmol) in EtOH (degas 2h) (8.0ml) was stirred to provide $Na^+[PhSeB(OEt)_3]^-$ as a yellow solution. Then it was added to a solution of **117** (1.09g, 2.21mmol) in *n*-BuOH (degas 2h) (22.1ml). After stirring at 140°C for 8h under nitrogen, the mixture was diluted with EtOAc and washed with sat. NH_4Cl and sat. brine. Evaporation of the solvent left an oil, which was purified by

silica gel column [EtOAc:hexane (0:1-1:3)] to give selenide derivative (1.25g, 1.95mmol) as an oil. This compound was immediately subjected to next *syn*-elimination step.

To a solution of selenide derivative (1.25g, 1.95mmol), Pyridine (315.8μl, 3.91mmol) and 2-methyl-2-butene (2.07ml, 19.5mmol) in CH_2Cl_2 (19.5ml) was added H_2O_2 (348.1μl, 3.91mmol) and the mixture was stirred at room temperature for 2h under nitrogen. The reaction was quenched with sat. $NaHCO_3$ and diluted with EtOAc. The mixture was washed with sat. $NaHCO_3$ and sat. brine and dried with Na_2SO_4. Removal of the solvent *in vacuo* gave an oil, which was purified by silica gel column [EtOAc:hexane (1:20-1:2)] to afford **118** (950.0mg, 1.93mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.39-7.26 (m, 5H), 5.74 (dd, J=10.6, 4.3Hz, 1H), 5.70 (ddd, J=10.6, 8.9, 1.7Hz, 1H), 5.00-4.87 (m, 1H), 4.58-4.54 (m, 1H), 4.53 (d, J=11.9Hz, 1H), 4.50 (d, J=11.9Hz, 1H), 3.94 (dd, J=12.2, 5.3Hz, 1H), 3.80 (ddd, J=7.1, 5.3, 2.0Hz, 1H), 3.69 (ddd, J=7.9, 7.6, 5.3Hz, 1H), 3.62 (dd, J=9.2, 7.1Hz, 1H), 3.55 (dd, J=12.2, 7.6Hz, 1H), 3.42 (dd, J=9.2, 5.3Hz, 1H), 2.20-1.04 (m, 1H), 1.87-1.60 (m, 3H), 1.41 (s, 3H), 1.31 (s, 3H), 0.89 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H); ^{13}C NMR: 140.0(d), 138.0(s), 128.4(d), 128.3(d), 127.7 (d), 127.6 (d), 98.0 (s), 75.2 (d), 73.6 (d), 73.4 (d), 73.4 (t), 72.8 (d), 71.1 (t), 68.4 (d), 63.9 (t), 34.1 (t), 32.7 (t), 27.8 (q), 25.8 (q), 20.0 (q), 18.1 (s), − 4.2 (q), − 5.1 (q); IR (neat) ν_{max} 3436, 2900, 1656, 1648, 1456, 1370, 1032, 840 cm^{-1}; $[\alpha]^{20}_D$ +19.09° (C 1.063, $CDCl_3$); HRMS (EI, M^+) calculated for $C_{26}H_{41}O_6Si(-CH_3)$: 477.2672, found 477.2668

Epoxy alcohol **119**

MCPBA (623.9mg, 2.89mmol) was added to the mixture of **118** (950.0mg, 1.93mmol) and $NaHCO_3$ (1.62g, 19.3mmol) in CH_2Cl_2 (19.3ml) and the stirring was run at room temperature under nitrogen. After 21h, 623.9mg (2.89mmol) more of MCPBA was added and the stirring was continued for 2h. Excess MCPBA was decomposed with aqueous $NaHSO_3$ and the generated MCBA was quenched with sat. $NaHCO_3$. The mixture was diluted with EtOAc and washed with 1N NaOH, sat. $NaHCO_3$ and sat. brine. Removal of

the solvent gave an oil, which was purified by silica gel column [EtOAc:hexane (3:5-3:1)] to afford **119** (650.6mg, 1.28mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.38-7.26 (m, 5H), 4.51 (s, 2H), 4.20-3.90 (m, 2H), 3.69-3.50 (m, 5H), 3.57 (dd, J=9.2, 7.6Hz, 1H), 3.43 (dd, J=9.2, 5.6Hz, 1H), 3.37 (dd, J=7.6, 4.3Hz, 1H), 3.14 (dd, J=8.9, 4.3Hz, 1H), 2.06-1.67 (m, 4H), 1.40 (s, 3H), 1.34 (s, 3H), 0.90 (s, 9H), 0.10 (s, 3H), 0.08 (s, 3H); ^{13}C NMR: 137.9 (s), 128.3 (d), 127.7 (d), 98.2 (s), 75.5 (d), 73.3 (t), 73.1 (d), 72.8 (d), 72.3 (d), 70.9 (d), 70.2 (t), 63.6 (t), 60.6 (d), 55.3 (d), 31.1 (t), 30.1 (t), 28.4 (q), 25.8 (q), 19.4 (q), 18.1 (s), -4.3 (q), - 5.1 (q); IR (neat) ν_{max} 3480, 2940, 1464, 1372, 1256, 1200, 1104, 832 cm^{-1}; $[\alpha]^{20}_D$ +10.49° (C 1.188, $CDCl_3$); HRMS (EI, M^+) calculated for $C_{27}H_{44}O_7Si(-CH_3)$: 508.2856, found 508.2862

Mesylate **120**

A solution of **119** (650.6mg, 1.28mmol), MsCl (148.5μl, 1.92mmol), TEA (534.7μl, 3.83mmol) and DMAP (15.6mg, 0.128mmol) in CH_2Cl_2 (12.8ml) was stirred at 0°C under nitrogen. After stirring for 30min, 49.5μl (0.639mmol) more of MsCl and 178.2μl (1.28mmol) more of TEA were added and the stirring was continued for additional 30min. The mixture was diluted with EtOAc and washed with sat. $NaHCO_3$ and sat. brine. Adsorption of H_2O with Na_2SO_4 followed by evaporation of the solvent gave an oil, which was purified by silica gel column [EtOAc:hexane (1:3-2:3)] to provide **120** (580.3mg, 0.989mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.40-7.24 (m, 5H), 4.71 (ddd, J=9.9, 9.5, 5.6Hz, 1H), 4.52 (d, J=12.0Hz, 1H), 4.50 (d, J=12.0Hz, 1H), 4.00 (dd, J=7.6, 5.6Hz, 1H), 3.97 (dd, J=11.0, 4.9Hz, 1H), 3.70 (dd, J=7.6, 2.0Hz, 1H), 3.60-3.48 (m, 4H), 3.46 (dd, J=9.3, 5.6Hz, 1H), 3.45 (dd, J=7.6, 4.4Hz, 1H), 3.32 (dd, J=9.5, 4.4Hz, 1H), 3.10 (s, 3H), 2.31-2.22 (m, 1H), 2.18-2.10 (m, 1H), 1.94-1.85 (m, 1H), 1.85-1.77 (m, 1H), 1.41 (s, 3H), 1.33 (s, 3H), 0.90 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H); ^{13}C NMR: 137.8 (s), 128.4 (d), 127.8 (d), 127.7 (d), 98.1 (s), 82.5 (d), 76.1 (d), 73.3 (t), 73.2 (d), 72.7 (d), 72.4 (d), 70.1 (t), 63.5 (t), 57.1 (d), 55.3 (d), 38.8 (q), 31.1 (t), 29.7 (t), 28.5 (q), 25.8 (q), 19.2 (q), 18.1 (s), - 4.2 (q), - 5.2 (q); IR (neat) ν_{max} 2944, 1500, 1458, 1362, 1340, 1316, 1254, 1174, 1096, 1022,

936, 892, 834, 1300-800 cm^{-1}; $[\alpha]^{20}_D$ +26.73° (C 1.096, $CDCl_3$); HRMS (EI, M^+) calculated for $C_{27}H_{43}O_9SiS(-CH_3)$: 571.2397, found 571.2391

Allylepoxide **121**

To a solution of **120** (580.3mg, 0.989mmol) in *n*-BuOH (degas 2h) (9.9ml) was added an ethanol solution of $Na^+[PhSeB(OEt)_3]^-$ at room temperature under nitrogen, which was prepared by reduction of $(PhSe)_2$ (463.0mg, 1.48mmol) with $NaBH_4$ (122.0mg, 2.97mmol) in EtOH (3.0ml). After injection of the PhSe anion, the reaction temperature was immediately rose to 80°C. After stirring for 2h, the mixture was diluted with EtOAc and washed with sat. NH_4Cl and sat. brine. Removal of the solvent left an oil, which was purified by silica gel column [EtOAc:hexane (1:30-1:7)] to give selenide derivative (573.7mg, 0.886mmol) as an oil.

To a solution of selenide derivative (573.7mg, 0.886mmol), Pyridine (143.3µl, 1.77mmol) and 2-methyl-2-butene (938.2µl, 8.86mmol) in CH_2Cl_2 (8.9ml) was added H_2O_2 (157.9µl, 1.77mmol) and the mixture was stirred at room temperature for 2h under nitrogen. The reaction was quenched with sat. $NaHCO_3$ and diluted with EtOAc. The mixture was washed with sat. $NaHCO_3$ and sat. brine, followed by concentration *in vacuo* gave an oil. The residue was purified by silica gel column [EtOAc:hexane (1:30-1:7)] to afford **121** (437.1mg, mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.35-7.26 (m, 5H), 5.85 (dddd, J=10.5, 10.5, 6.8, 1.9Hz, 1H), 5.71 (dd, J=10.5, 2.2Hz, 1H), 4.48 (s, 2H), 4.11 (dd, J=11.2, 5.4Hz, 1H), 3.95-3.91 (m, 2H), 3.65 (ddd, J=9.3, 9.0, 5.4Hz, 1H), 3.54 (ddd, J=11.0, 9.0, 2.4Hz, 1H), 3.52 (dd, J=9.5, 6.8Hz, 1H), 3.49 (dd, J=11.2, 9.3Hz, 1H), 3.40 (dd, J=7.6, 3.9Hz, 1H), 3.39 (dd, J=9.5, 5.9Hz, 1H), 3.37 (dd, J=7.6, 1.2Hz, 1H), 2.64 (ddd, J=12.9, 11.0, 10.5Hz, 1H), 2.24 (dddd, J=12.9, 6.8, 2.4, 1.9Hz, 1H), 1.44 (s, 3H), 1.36 (s, 3H), 0.92 (s, 9H), 0.11 (s, 3H), 0.07 (s, 3H); ^{13}C NMR: 138.0 (s), 129.7 (d), 128.2 (d), 127.6 (d), 127.5 (d), 126.1 (d), 98.1 (s), 78.8 (d), 73.9 (d), 73.4 (d), 73.1 (t), 71.2 (d), 70.8 (t), 63.8 (t), 54.1 (d), 54.0 (d), 36.0 (t), 28.7 (q), 25.9 (q), 19.1 (q), 18.2 (s), −4.1 (q), −5.1 (q); IR

(neat) ν_{max} 3040, 2876, 1652, 1498, 1456, 1368, 1310, 1254, 1162, 1046, 964, 920, 880, 828 cm^{-1}; $[\alpha]^{20}_D$ − 18.72° (C 1.036, $CDCl_3$); HRMS (EI, M^+) calculated for $C_{27}H_{42}O_6Si(-CH_3)$: 490.2750, found 490.2751

Homoallylalcohol **122**

To toluene (6.9ml) solution of **121** (434.6mg, 0.886mmol) which was azeotroped once with toluene was added a toluene solution of $Li^+[AlH(i\text{-}Bu)_2 \cdot n\text{-}Bu]^-$, which was prepared from DIBAL (2.83ml, 2.66mmol) and *n*-BuLi (1.66ml, 2.66mmol) in toluene (2.0ml) at 0°C under nitrogen. After stirring for 1h at room temperature, the reaction was quenched with sat. Rochelle salt and the mixture was stirred for additional 1h30min. Then, the organic phase was washed with H_2O and sat. brine and dried with Na_2SO_4. Removal of the solvent gave an oil, which was purified by silica gel column [EtOAc:hexane (1:4-1:3)] to afford **122** (314.5mg, mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.36-7.27 (m, 5H), 5.82 (ddd, J=10.5, 8.8, 8.5Hz, 1H), 5.73 (ddd, J=10.5, 9.3, 8.5Hz, 1H), 4.53 (d, J=12.0Hz, 1H), 4.50 (d, J=12.0Hz, 1H), 4.11-4.04 (m, 2H), 3.90 (dd, J=8.3, 6.8Hz, 1H), 3.80 (ddd, J=9.5, 4.9, 2.4Hz, 1H), 3.65 (dd, J=9.8, 4.6Hz, 1H), 3.6 (dd, J=10.3, 10.3Hz, 1H), 3.51-3.42 (m, 3H), 2.65-2.50 (m, 2H), 2.37-2.24 (m, 2H), 1.44 (s, 3H), 1.34 (s, 3H), 0.90 (s, 9H), 0.13 (s, 3H), 0.09 (s, 3H); ^{13}C NMR: 138.2 (s), 128.4 (d), 128.3 (d), 127.6 (d), 127.6 (d), 127.0 (d), 98.5 (s), 78.6 (d), 73.5 (d), 73.4 (t), 71.9 (d), 71.4 (t), 69.1 (d), 64.6 (t), 33.1 (t), 29.8 (t), 28.9 (q), 25.9 (q), 19.1 (q), 18.1 (s), − 4.4 (q), − 5.1 (q); IR (neat) ν_{max} 3496, 2932, 1652, 1456, 1380, 1334, 1308, 1256, 1220, 1200, 1162, 1110, 900, 828 cm^{-1}; $[\alpha]^{20}_D$ +0.60° (C 0.990, $CDCl_3$); HRMS (EI, M^+) calculated for $C_{27}H_{44}O_6Si(-CH_3)$: 477.2672, found 477.2668

Diol **123**

TBAF (1.24ml, 1.24mmol) was added to a solution of **122** (407.8mg, 0.828mmol) in THF (8.3ml) at 0°C and the mixture was stirred at room temperature under nitrogen. After 30min, the mixture was diluted with EtOAc and washed with sat. NH_4Cl and sat. brine. Adsorption of H_2O with Na_2SO_4 followed by evaporation of the solvent left an oil, which was purified

by silica gel column [EtOAc:hexane (5:4)] to give **123** (288.8mg, 0.763mmol) as an oil; ^{1}H-NMR (500MHz, $CDCl_3$) δ : 7.40-7.30 (m, 5H), 5.90-5.64 (m, 2H), 4.57 (s, 2H), 4.09-3.96 (m, 3H), 3.79 (ddd, J=8.9, 4.6, 3.0Hz, 1H), 3.68-3.44 (m, 5H), 2.72-2.54 (m, 2H), 2.38-2.18 (m, 2H), 1.45 (s, C3H), 1.33 (s, 3H); ^{13}C NMR: 137.6 (s), 128.6 (d), 128.5 (d), 128.0 (d), 127.9 (d), 126.9 (d), 98.5 (s), 80.1 (d), 73.6 (t), 71.5 (t), 71.3 (d), 71.1 (d), 70.6 (d), 68.8 (d), 64.5 (t), 33.4 (t), 29.4 (t), 28.9 (q), 19.1 (q); IR (neat) ν_{max} 3436, 2936, 1648, 1456, 1378, 1334, 1306, 1258, 1228, 1168, 1112, 834 cm^{-1}; $[\alpha]^{20}_D$ +7.86° (C 0.521, $CDCl_3$); HRMS (EI, M^+) calculated for $C_{14}H_{21}O_5(-C_7H_9O)$: 261.1389, found 269.1388

TBS ether **124**

To a solution of **123** (288.8mg, 0.763mmol) in DMF (7.6ml) were added imidazole (311.8mg, 4.58mmol) and TBSCl (345.0mg, 2.29mmol) and the mixture was stirred at room temperature for 10h under nitrogen. The reaction mixture was diluted with EtOAc and washed with sat. $NaHCO_3$ and sat. brine. Removal of the solvent gave an oil, which was purified by silica gel column [EtOAc:hexane (1:20-1:5)] to provide **124** (364.5mg, 0.740mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.38-7.28 (m, 5H), 5.89 (ddd, J=10.5, 10.5, 7.3Hz, 1H), 5.61 (ddd, J=10.5, 10.5, 6.6Hz, 1H), 4.57 (d, J=12.0Hz, 1H), 4.54 (d, J=12.0Hz, 1H), 4.38 (dd, J=15.6, 10.3Hz, 1H), 4.16-4.03 (m, 1H), 4.09 (d, J=9.3Hz, 1H), 3.72-3.67 (m, 1H), 3.53-3.42 (m, 4H), 3.37 (d, J=9.3Hz, 1H), 2.85-2.50 (m, 2H), 2.08 (ddd, J=14.2, 14.2, 7.3Hz, 1H), 2.03 (ddd, J=6.6, 6.6, 3.7Hz, 1H), 1.42 (s, 3H), 1.37 (s, 3H), 0.89 (s, 9H), 0.07 (s, 6H); ^{13}C NMR: 138.0 (s), 129.2 (d), 128.5 (d), 127.9 (d), 127.8 (d), 126.2 (d), 98.1 (s), 82.2 (d), 73.4 (t), 72.3 (d), 71.6 (t), 68.9 (d), 68.6 (d), 68.5 (d), 64.7 (t), 34.8 (t), 28.9 (q), 28.5 (t), 25.8 (q), 19.0 (q), 17.9 (s), − 4.3 (q), − 5.0 (q); IR (neat) ν_{max} 3452, 2952, 1658, 1608, 1452, 1384, 1330, 1302, 1258, 1222, 1168, 1108, 832 cm^{-1}; $[\alpha]^{20}_D$ − 19.91° (C 0.462, $CDCl_3$); HRMS (EI, M^+) calculated for $C_{27}H_{44}O_6$ Si: 492.2907, found 492.2907

Bromide **125**

To toluene (7.4ml) solution of alcohol (364.5mg, 0.74mmol) which was azeotroped once with toluene were added $P(oct)_3$ (494.9µl, 1.11mmol), CBr_4 (368.0mg, 1.11mmol), TEA (309.3µl, 2.22mmol) and 1-methyl-1cyclohexene (1.75ml, 14.8mmol). The mixture was stirred at 90°C for 2h under nitrogen. Then, 0.99ml (2.22mmol) more of $P(oct)_3$, 736.0mg (2.22mmol) of CBr_4 and 0.62ml (4.44mmol) more of TEA were added and the reaction was continued under above condition. After 2h, 0.99ml (2.22mmol) more of $P(oct)_3$, 736.0mg (2.22mmol) of CBr_4 and 0.62ml (4.44mmol) more of TEA were further added and the stirring was continued for additional 1h. The mixture was filtered through Silica gel with EtOAc:hexane (1:3) and washed with sat. $NaHCO_3$ and sat. brine. Removal of the solvent gave an oil, which was purified by silica gel column [EtOAc:hexane (1:10)] to afford **125** (328.9mg, 0.59mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.38-7.28 (m, 5H), 5.85 (ddd, J=9.9, 8.6, 8.6Hz, 1H), 5.70 (ddd, J=9.9, 9.9, 6.6Hz, 1H), 4.56 (d, J=12.2Hz, 1H), 4.54 (d, J=12.2Hz, 1H), 4.41 (dd, J=7.3, 7.3Hz, 1H), 4.17-4.07 (m, 1H), 4.00-3.93 (m, 1H), 3.90-3.78 (m, 4H), 3.68 (dd, J=10.6, 7.2Hz, 1H), 3.62 (dd, J=10.6, 5.3Hz, 1H), 2.70-2.59 (m, 1H), 2.55-2.43 (m, 1H), 2.30-2.19 (m, 2H), 1.40 (s, 3H), 1.35 (s, 3H), 0.89 (s, 9H), 0.07 (s, 6H); ^{13}C NMR: 137.9 (s), 128.4 (d), 128.0 (d), 127.8 (d), 127.8 (d), 127.6 (d), 98.6 (s), 77.8 (d), 75.9 (d), 73.4 (t), 72.8 (d), 72.0 (t), 70.6 (d), 64.7 (t), 56.0 (d), 32.3 (t), 31.3 (t), 28.9 (q), 26.0 (q), 19.2 (q), 18.1 (s), −4.1 (q), −4.3 (q); IR (neat) ν_{max} 2924, 1652, 1460, 1376, 1336, 1306, 1254, 1220, 1160, 968, 838 cm^{-1}; $[\alpha]^{20}_D$ −71.71° (C 0.442, $CDCl_3$); HRMS (EI, M^+) calculated for $C_{27}H_{43}O_5SiBr$: 554.2063, found 554.2063

Reductive product **126**

A solution of **125** (328.9mg, 0.592mol), Bu_3SnH (238.8ml, 0.888mmol) and AIBN (9.7mg, 0.059mmol) in toluene (5.9ml) was irradiated with a 500W Hg-Xe lamp (>280nm). The mixture was stirred at 0°C for 30min under nitrogen. Evaporation of the solvent left an oil, which was purified by silica gel column [EtOAc:hexane (0:1-1:10 contained with 1% TEA)] to give **126** (282.5mg, 0.592mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ

7.38-7.28 (m, 5H), 5.81 (ddd, J=10.5, 10.5, 8.6Hz, 1H), 5.62 (ddd, J=10.5, 10.5, 7.1Hz, 1H), 4.52 (d, J=12.2Hz, 1H), 4.48 (d, J=12.2Hz, 1H), 3.83 (dd, J=10.7, 4.6Hz, 1H), 3.77 (ddd, J=9.0, 3.2, 3.2Hz, 1H), 3.65 (dd, J=10.7, 10.7Hz, C1), 3.60 (dd, J=8.8, 6.6Hz, 1H), 3.55-3.47 (m, 3H), 3.34 (ddd, J=10.7, 10.7, 4.6Hz, 1H), 2.83-2.73 (m, 2H), 2.17-2.07 (m, 3H), 1.41 (s, 3H), 1.35 (s, 3H), 1.00-0.80 (m, 1H), 0.89 (s, 9H), 0.07 (s, 6H); ^{13}C NMR: 138.6 (s), 129.2 (d), 128.3 (d), 127.6 (d), 127.4 (d), 126.1 (d), 98.5 (s), 79.1 (d), 73.4 (d), 72.8 (t), 71.6 (d), 68.1 (d), 67.1 (t), 65.2 (t), 33.8 (t), 33.1 (t), 29.1 (q), 28.7 (t), 25.8 (q), 18.8 (q), 17.9 (s), − 4.2 (q), − 4.7 (q); IR (neat) ν_{max} 2932, 1652, 1456, 1378, 1308, 1256, 1198, 1088, 1004, 970, 900, 834 cm^{-1}; $[\alpha]^{20}_D$ − 38.07° (C 0.436, $CDCl_3$); HRMS (EI, M^+) calculated for $C_{21}H_{29}O_4$(− $C_6H_{15}OSi$): 345.2066, found 345.2074

Diol **128**

CSA (13.8mg, 0.0593mmol) was added to a solution of **126** (282.5mg, 0.593mmol) and $(HOCH_2)_2$ (1.65ml, 29.6mmol) in MeOH (5.9ml) and the mixture was stirred at room temperature for 30min under nitrogen. The reaction was quenched with sat. $NaHCO_3$ and diluted with EtOAc. The organic layer was washed with sat. $NaHCO_3$ and sat. brine and dried with Na_2SO_4. Evaporation *in vacuo* gave an oil, which was purified by silica gel column [EtOAc:hexane (1:1)] to afford **128** (187.8mg, 0.43mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.38-7.28 (m, 5H), 5.74 (ddd, J=10.7, 10.7, 8.3Hz, 1H), 5.70 (ddd, J=10.7, 10.7, 7.8Hz, 1H), 4.55 (d, J=11.9Hz, 1H), 4.53 (d, J=11.9Hz, 1H), 3.87-3.77 (m, 1H), 3.83 (dd, J=12.0, 4.2Hz, 1H), 3.79 (dd, J=12.0, 3.9Hz, 1H), 3.64 (ddd, J=9.3, 7.1, 5.1Hz, 1H), 3.61-3.55 (m, 2H), 3.52 (ddd, J=9.3, 7.2, 3.2Hz, 1H), 3.40 (ddd, J=8.5, 8.5, 3.9Hz, 1H), 2.60-2.53 (m, 2H), 2.46-2.40 (m, 1H), 2.38-2.33 (m, 1H), 2.11-2.04 (m, 1H), 1.87 (dddd, J=14.2, 12.2, 6.6, 5.6Hz, 1H), 0.87 (s, 9H), 0.10 (s, 3H), 0.02 (s, 3H); ^{13}C NMR: 138.0 (s), 128.4 (d), 128.3 (d), 127.9 (d), 127.7 (d), 126.7 (d), 78.4 (d), 77.4 (d), 73.2 (t), 72.4 (d), 70.0 (d), 67.6 (t), 63.1 (t), 33.3 (t), 31.9 (t), 31.6 (t), 25.8 (q), 17.9 (s), − 4.2 (q), − 4.8 (q); IR (neat) ν_{max} 3436, 3024, 2944, 1654, 1454, 1362, 1304, 1254, 1094, 942, 832 cm^{-1}; $[\alpha]^{20}_D$ − 37.02° (C 0.343, $CDCl_3$); HRMS (EI, M^+) calculated for

$C_{18}H_{24}O_4$(− $C_6H_{16}OSi$): 304.1674, found 304.1671

Anisylidene **129**

To a solution of **128** (187.8mg, 0.430mmol) in CH_2Cl_2 (4.3ml) were added *p*-anisaldehydedimethylacetal (95.2μl, 0.559mmol) and CSA (9.99mg, 0.043mmol) and the mixture was stirred at room temperature for 30min under nitrogen. The mixture was added to a 50ml beaker with sat. $NaHCO_3$ to neutralize CSA and diluted with EtOAc. The mixture was washed with sat. $NaHCO_3$ and sat. brine and dried with Na_2SO_4. Evaporation *in vacuo* left an oil, which was purified by silica gel column [EtOAc:hexane (1:8)] to provide **129** (235.6mg, 0.425mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.40-7.27 (m, 5H), 7.37 (d, J=8.9Hz, 2H), 6.87 (d, J=8.9Hz, 2H), 5.84 (ddd, J=10.2, 10.2, 7.3Hz, 1H), 5.69 (ddd, J=10.2, 10.2, 6.9Hz, 1H), 5.35 (s, 1H), 4.54 (d, J=11.9Hz, 1H), 4.50 (d, J=11.9Hz, 1H), 4.24 (dd, J=10.2, 4.3Hz, 1H), 3.80 (s, 3H), 3.73-3.47 (m, 7H), 2.91-2.75 (m, 2H), 2.36-2.25 (m, 1H), 2.24-2.10 (m, 1H), 1.72-1.58 (m, 2H), 0.91 (s, 9H), 0.14 (s, 3H), 0.08 (s, 3H); ^{13}C NMR: 160.1 (s), 138.6 (s), 130.4 (s), 129.3 (d), 128.3 (d), 127.6 (d), 127.5 (d), 127.4 (d), 126.2 (d), 113.7 (d), 101.4 (d), 79.7 (d), 79.1 (d), 73.3 (d), 72.9 (t), 71.6 (t), 67.1 (t), 55.3 (q), 33.8 (t), 33.1 (t), 28.7 (t), 25.8 (q), 17.9 (s), − 4.2 (q), − 4.7 (q), C_2 not detected; IR (neat) ν_{max} 2860, 1614, 1590, 1512, 1454, 1392, 1300, 1252, 1172, 1036, 824 cm^{-1}; $[\alpha]^{20}_D$ = − 77.68° (C = 0.475, $CDCl_3$); HRMS (EI, M^+) calculated for $C_{32}H_{46}O_6Si$: 554.3063, found 554.3069

Alcohol **130**

To toluene (4.3ml) solution of **129** (235.6mg, 0.425mmol) which was azeotroped twice with toluene was added DIBAL (1.13ml, 1.062mmol) and the mixture was stirred at − 5 to − 10°C under nitrogen. After 1h, 452.0μl (1.062mmol) more of DIBAL was added and the stirring was continued for 1h. The reaction was quenched with sat. Rochell salt and diluted with EtOAc. The mixture was washed with sat. brine and dried with Na_2SO_4. Removal of the solvent *in vacuo* left an oil, which was purified by silica gel column [EtOAc:hexane

(2:5)] to give **130** (211.7mg, 0.380mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.36-7.26 (m, 5H), 7.24 (d, J=8.3Hz, 2H), 6.87 (d, J=8.3Hz, 2H), 5.76-5.59 (m, 2H), 4.59 (d, J=10.9Hz, 1H), 4.56 (d, J=12.5Hz, 1H), 4.59 (d, J=12.5Hz, 1H), 4.50 (d, J=10.9Hz, 1H), 3.80 (s, 3H), 3.79-3.46 (m, 8H), 2.63-2.42 (m, 4H), 2.10-1.84 (m, 2H), 0.86 (s, 9H), 0.09 (s, 3H), 0.00 (s, 3H); ^{13}C NMR: 159.4 (s), 138.1 (s), 130.2 (s), 129.6 (d), 128.3 (d), 127.8 (d), 127.7 (d), 127.6 (d), 127.5 (d), 114.0 (d), 77.3 (d), 76.7 (d), 73.2 (t), 72.1 (d), 71.1 (t), 67.3 (t), 62.6 (t), 55.3 (q), 32.8 (t), 31.6 (t), 27.5 (t), 25.8 (q), 17.9 (s), − 4.2 (q), − 4.9 (q), C_2 not detectable; IR (neat) ν_{max} 3476, 2928, 1610, 1588, 1456, 1364, 1302, 1250, 1174, 1030, 934, 828 cm^{-1}; $[\alpha]^{20}_D$ − 64.43° (C 0.284, $CDCl_3$); HRMS (EI, M^+) calculated for $C_{32}H_{48}O_6Si$: 556.3220, found 556.3214

Methyl substituted compound **132**

A solution of **130** (153.0mg, 0.275mmol), 3,5-bis(trifluoro)methylsulfonyl chloride (265.7mg, 0.824mmol), TEA (229.8μl, 1.649mmol), DMAP (3.4mg, 0.028mmol) in CH_2Cl_2 (2.8ml) was stirred at room temperature for 2h under nitrogen. The reaction was quenched with sat. $NaHCO_3$ and the resultant products were extracted with EtOAc. The organic extracts were washed with sat. $NaHCO_3$, H_2O (two times) and sat. brine and dried with Na_2SO_4. Concentration *in vacuo* gave an oil, which was immediately subjected to the next methyl group substitution.

The mixture of CuI (220.3mg, 1.099mmol) was placed in 50ml flask and then dehydrated by heating under high decompression. To the flask were added Et_2O (5.0ml) and MeLi (1.92ml, 2.31mmol) and the mixture was stirred to prepare Me_2CuLi for 5min at 0°C under nitrogen. Then sulfonate derivative (228.9mg, 0.275mmol) azeotroped with benzene was added to the flask and the stirring was continued for 30min at − 12°C under nitrogen. The reaction was quenched with sat. NH_4Cl and diluted with EtOAc. The mixture was washed with sat. NH_4Cl and sat. brine and the combined organic layer was evaporated *in vacuo*. The residue was purified by silica gel column [EtOAc:benzene (1:28)] to give **132**

(121.8mg, 0.224mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.34-7.26 (m, 5H), 7.24 (d, J=8.8Hz, 2H), 6.87 (d, J=8.8Hz, 2H), 5.69 (ddd, J=10.5, 8.3, 8.3Hz, 1H), 5.64 (ddd, J=10.5, 8.5, 8.5Hz, 1H), 4.58 (d, J=11.0Hz, 1H), 4.52 (d, J=12.0Hz, 1H), 4.47 (d, J=12.0Hz, 1H), 4.34 (d, J=11.0Hz, 1H), 3.80 (s, 3H), 3.63-3.57 (m, 3H), 3.45-3.39 (m, 2H), 3.38-3.33 (m, 1H), 2.58-2.52 (m, 1H), 2.48-2.39 (m, 3H), 2.05-1.98 (m, 1H), 1.93 (ddd, J=13.9, 7.6, 7.6Hz, 1H), 1.75-1.67 (m, 2H), 0.89 (dd, J=7.3, 7.3Hz, 3H), 0.88 (s, 9H), 0.09 (s, 3H), 0.03 (s, 3H); ^{13}C NMR: 159.3 (s), 138.7 (s), 130.4 (s), 129.5 (d), 128.3 (d), 127.6 (d), 127.4 (d), 113.9 (d), 78.3 (d), 76.2 (d), 73.0 (t), 72.9 (d), 71.0 (t), 67.4 (t), 55.3 (q), 32.8 (t), 32.4 (t), 27.9 (t), 25.9 (q), 24.2 (t), 17.9 (s), 9.3 (q), −4.2 (q), −4.8 (q), C_3 not detected; IR (neat) ν_{max} 2932, 1612, 1588, 1454, 1362, 1302, 1250, 1096, 938, 816 cm^{-1}; $[\alpha]^{20}_D$ − 28.22° (C 1.116, $CDCl_3$); HRMS (EI, M^+) calculated for $C_{33}H_{50}O_5Si$: 554.3427, found 554.3428

Alcohol **142**

To a suspension of **132** (119.7mg, 0.221mmol) in pH=7.4 phosphate buffer (200μl)/ benzene (2.0ml) was added DDQ (77.4mg, 0.331mmol) and the mixture was stirred at room temperature for 2h under nitrogen. The mixture was diluted with EtOAc and washed twice with sat. $NaHCO_3$ and sat. brine. Removal of the solvent gave an oil, which was subjected to the next reduction of anisaldehyde, inseparable side product.

$NaBH_4$ (3.34mg, 0.09mmol) was added to a solution of the crude oil in EtOH (2.2ml) and the mixture was stirred for 30min at 0°C under nitrogen. The mixture was diluted with EtOAc and washed with sat. NH_4Cl and sat. brine. Evaporation of the solvent gave an oil, which was purified by silica gel column [EtOAc:hexane (1:3)] to afford **142** (87.6mg, 0.202mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.29-7.18 (m, 5H), 5.72-5.64 (m, 1H), 5.64-5.56 (m, 1H), 4.45 (d, J=12.2Hz, 1H), 4.42 (d, J=12.2Hz, 1H), 3.65-3.58 (m, 1H), 3.58-3.50 (m, 2H), 3.50-3.47 (m, 1H), 3.44-3.39 (m, 1H), 3.31 (ddd, J=9.0, 4.8, 4.8Hz, 1H), 2.54-2.46 (m, 2H), 2.34-2.26 (m, 1H), 2.25-2.18 (m, 1H), 2.05-1.97 (m, 1H), 1.82-1.74 (m, 1H), 1.75-1.68 (m, 1H), 1.68-1.59 (m, 1H), 1.40 (brd-d, J=6.1Hz, 1H), 0.87 (dd, J=7.3,

7.3Hz, 3H), 0.82 (s, 9H), 0.04 (s, 3H), − 0.01 (s, 3H); ^{13}C NMR: 138.7 (s), 128.9 (d), 128.3 (d), 127.6 (d), 127.4 (d), 127.2 (d), 78.8 (d), 77.0 (d), 73.0 (d), 72.9 (t), 70.7 (d), 67.4 (t), 33.8 (t), 32.7 (t), 31.3 (t), 25.8 (q), 24.1 (t), 17.9 (s), 8.9 (q), − 4.2 (q), − 4.8 (q); IR (neat) ν_{max} 3460, 3024, 2936, 1616, 1454, 1360, 1256, 1076, 938, 828 cm^{-1}; $[\alpha]^{20}_D$ − 40.36° (C 0.488, $CDCl_3$); HRMS (EI, M^+) calculated for $C_{25}H_{42}O_4Si$: 434.2852, found 434.2849

Bromide **143**

To toluene (0.57ml) solution of alcohol (24.6mg, 0.057mmol) which was azeotroped once with toluene were added $P(oct)_3$ (75.7µl, 0.17mmol), CBr_4 (56.3mg, 0.17mmol), pyridine (27.5µl, 0.34mmol) and 1-methyl-1-cyclohexene (133.9µl, 1.132mmol). The mixture was stirred for 2h at 80°C under nitrogen. Then, 75.7µl (0.17mmol) more of $P(oct)_3$, 56.3mg (0.17mmol) of CBr_4 and 27.5µl (0.34mmol) more of pyridine were added and the stirring was continued for 1h. The mixture was diluted with EtOAc and washed with 1N HCl, sat. $NaHCO_3$ and sat. brine. Removal of the solvent gave an oil, which was purified by silica gel column [EtOAc:hexane (1:15-1:3)] to afford **143** (15.8mg, 0.0318mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.36-7.26 (m, 5H), 5.82 (ddd, J=10.5, 10.5, 7.3Hz, 1H), 5.40 (ddd, J=10.5, 10.5, 6.4Hz, 1H), 4.54 (d, J=12.2Hz, 1H), 4.50 (d, J=12.2Hz, 1H), 4.03-3.98 (m, 1H), 3.71 (ddd, J=9.3, 9.3, 3.9Hz, 1H), 3.65-3.58 (m, 2H), 3.52-3.47 (m, 1H), 3.33-3.24 (m, 2H), 3.06-2.98 (m, 1H), 2.52-2.46 (m, 1H), 2.25-2.18 (m, 3H), 2.01-1.96 (m, 1H), 1.81-1.68 (m, 3H), 0.90 (s, 9H), 0.77 (t, J=7.3Hz, 3H), 0.12 (s, 3H), 0.08 (s, 3H); ^{13}C NMR: 138.8 (s), 130.5 (d), 128.3 (d), 127.6 (d), 127.4 (d), 126.8 (d), 80.9 (d), 73.1 (d), 72.9 (t), 72.8 (d), 67.9 (t), 55.7 (d), 34.6 (t), 33.8 (t), 32.7 (t), 28.7 (t), 25.8 (q), 17.9 (s), 9.7 (q), − 4.2 (q), − 4.7 (q) ; IR (neat) ν_{max} 2964, 1620, 1452, 1360, 1306, 1254, 1086, 912, 828 cm^{-1}; $[\alpha]^{20}_D$ +35.85° (C 0.647, $CDCl_3$); HRMS (EI, M^+) calculated for $C_{25}H_{41}O_3SiBr$: 496.2008, found 496.2002

Alcohol **144**

DDQ (43.8mg, 0.187mmol) was added to a heterogeneous solution of bromide **143**

(46.6mg, 0.0937mmol) in pH=7.4 phosphate buffer (94.0μl)/dichloroethane (0.85ml) at room temperature and the mixture was stirred at 50°C under nitrogen. After 1h 30min, the reaction was quenched with sat. $NaHCO_3$ and diluted with EtOAc. The reaction mixture was washed twice with sat. $NaHCO_3$ and sat. brine. The aqueous layer was extracted once with EtOAc. The obtained organic layer was dried with Na_2SO_4. Removal of the solvent gave an oil, the residue was purified by silica gel column [EtOAc:hexane (1:10-1:4)] to provide **144** (25.5mg, 0.0626mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 5.84 (ddd, J=10.5, 10.5, 8.5Hz, 1H), 5.43 (ddd, J=10.5, 10.5, 6.3Hz, 1H), 4.04-4.00 (m, 1H), 3.89-3.83 (m, 2H), 3.76-3.69 (m, 1H), 3.57-3.51 (m, 1H), 3.36-3.31 (m, 1H), 3.31-3.23 (m, 1H), 3.03-2.95 (m, 1H), 2.55-2.48 (m, 1H), 2.11-2.01 (m, 2H), 1.92-1.80 (m, 2H), 1.80-1.69 (m, 1H), 0.90 (s, 6H), 0.81 (t, J=7.3Hz, 3H), 0.13 (s, 3H), 0.08 (s, 3H); ^{13}C NMR: 130.3 (d), 127.1 (d), 81.4 (d), 73.1 (d), 72.7 (d), 60.8 (t), 55.5 (d), 35.0 (t), 34.8 (t), 33.8 (t), 28.9 (t), 25.8 (q), 17.9 (s), 9.8 (q), − 4.2 (q), − 4.7 (q); IR (neat) ν_{max} 3428, 2956, 2896, 1640, 1626, 1454, 1362, 1296, 1250, 1164, 1088, 912, 828 cm^{-1}; $[\alpha]^{20}_D$ +36.25° (C 0.251, $CDCl_3$); HRMS (EI, M^+) calculated for $C_{14}H_{26}O_3Si^{81}Br$ (− C_4H_9): 351.0814, found 351.0817

cis-bromoolefin **147**

1) Synthesis of the aldehyde

To a solution of **144** (30.5mg, 0.0749mmol) in CH_2Cl_2 (0.75ml), were added $NaHCO_3$ (25.2mg, 0.299mmol) and Dess-Martin periodinane (63.5mg, 0.150mmol) at room temperature and the mixture was stirred for 15min under nitrogen. The reaction mixture was diluted with EtOAc and washed with sat. $NaHCO_3$ and sat. brine. Adsorption of H_2O with Na_2SO_4 followed by evaporation of the solvent left an oil, which was purified by silica gel column [EtOAc:hexane (1:5)] to give aldehyde (25.1mg, 0.0619mmol) as an oil.

2) Transformation to dibromoolefin

HMPT (69.6ml, 0.371mmol) was added to a solution of aldehyde (25.1mg, 0.0619mmol)

and CBr_4 (61.6mg, 0.186mmol) in THF (0.62ml) and the mixture was stirred at 0°C under nitrogen. After 15min, the mixture was diluted with EtOAc and washed with sat. $NaHCO_3$ and sat. brine. The organic layer was dried with Na_2SO_4 and evaporated *in vacuo*. The residual oil was purified by short silica gel column [EtOAc:hexane (1:18)] to afford dibromoolefin (33.0mg, 0.0588mmol) as an oil.

3) Introduction of *cis*-bromoolefin moiety

To a solution of dibromoolefin (33.0mg, 0.0588mmol) in benzene [degas with nitrogen for 30min (0.59ml)] were added $Pd(PPh_3)_4$ (6.8mg, 5.880mmol) and Bu_3SnH (23.7μl, 0.088mmol) and the mixture was stirred at room temperature under nitrogen. After stirring for 40min, 6.8mg (5.880mmol) more of $Pd(PPh_3)_4$ and 7.9μl (0.029mmol) more of Bu_3SnH was added to the reaction mixture and the stirring was continued for additional 10min. The mixture was diluted with EtOAc and washed with H_2O and sat. brine. Removal of the solvent gave an oil, which was purified by silica gel column [benzene:hexane (2:5) contained with 1%TEA] to provide **147** (21.0mg, 0.0435mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 6.39 (ddd, J=6.6, 6.4, 6.4Hz, 1H), 6.20 (ddd, J=6.4, 1.7, 1.7Hz, 1H), 5.83 (ddd, J=10.5, 10.5, 7.8Hz, 1H), 5.42 (ddd, J=10.5, 10.5, 6.3Hz, 1H), 4.06-3.99 (m, 1H), 3.70 (ddd, J=11.7, 8.8, 2.8Hz, 1H), 3.56-3.51 (m, 1H), 3.34-3.24 (m, 2H), 3.06-2.96 (m, 1H), 2.79 (dddd, J=16.8, 6.4, 2.8, 1.7Hz, 1H), 2.52 (ddd, J=11.1, 6.3, 5.6Hz, 1H), 2.21 (dddd, J=16.8, 11.7, 6.4, 1.7Hz, 1H), 2.06-1.99 (m, 1H), 1.83-1.70 (m, 2H), 0.91 (s, 9H), 0.79 (t, J=7.6Hz, 3H), 0.14 (s, 3H), 0.12 (s, 3H); ^{13}C NMR: 132.5 (d), 130.3 (d), 127.0 (d), 108.8 (d), 82.0 (d), 73.1 (d), 55.6 (d), 34.3 (t), 33.7 (t), 33.6 (t), 28.6 (t), 25.8 (q), 17.9 (s), 9.8 (q), − 4.2 (q), − 4.7 (q); IR (neat) ν_{max} 2948, 2936, 2888, 1622, 1458, 1360, 1306, 1256, 1082, 914, 830 cm^{-1}; $[\alpha]^{20}_D$ +40.72° (C 1.267, $CDCl_3$);

TBS acetylene **148**

To a solution of **147** (21.0mg, 0.0435mmol) in benzene [degas with nitrogen for 30min (0.5ml)] were added $Pd(PPh_3)_4$ (5.0mg, 4.354μmol), TBS-acetylene (24.4μl, 0.131mmol),

CuI (2.5mg, 0.0131mmol) and $^{i}Pr_2NH$ (18.3μl, 0.131mmol) and the mixture was stirred at room temperature under nitrogen. After 2h, same amount of reagents were added to the reaction mixture and then after 2h, same amount of reagents were further added. After stirring for 2h, the mixture was diluted with EtOAc and washed with H_2O and sat. brine. Adsorption of H_2O dried with Na_2SO_4 followed by evaporation of the solvent left an oil, which was purified by silica gel column [benzene:hexane (2:5)] to give **148** (19.5mg, 0.0360mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 6.15 (ddd, J=11.5, 7.1, 5.1Hz, 1H), 5.84 (ddd, J=10.5, 10.5, 7.6Hz, 1H), 5.61-5.56 (m, 1H), 5.43 (ddd, J=10.5, 10.5, 6.6Hz, 1H), 4.05-4.00 (m, 1H), 3.80-3.74 (m, 1H), 3.57-3.52 (m, 1H), 3.33-3.25 (m, 2H), 3.07-2.98 (m, 1H), 2.83-2.76 (m, 1H), 2.60-2.48 (m, 2H), 2.06-2.00 (m, 1H), 1.87-1.79 (m, 1H), 1.77-1.70 (m, 1H), 0.95 (s, 9H), 0.90 (s, 9H), 0.77 (dd, J=7.6, 7.6Hz, 3H), 0.13 (s, 3H), 0.12 (s, 3H), 0.09 (s, 3H); ^{13}C NMR: 142.9 (d), 130.4 (d), 127.1 (d), 110.3 (d), 102.9 (s), 97.7 (s), 82.5 (d), 73.2 (d), 55.8 (d), 34.5 (t), 34.0 (t), 33.7 (t), 28.3 (t), 26.2 (q), 25.9 (q), 17.9 (s), 16.5 (s), 9.9 (q), − 4.3 (q), − 4.4 (q), − 4.6 (q; IR (neat) ν_{max} 2932, 2912, 2864, 2144, 1456, 1360, 1310, 1250, 1078, 928, 902 cm^{-1}; $[\alpha]^{20}_{D}$ +117.87° (C 1.287, $CDCl_3$); HRMS (EI, M^+) calculated for $C_{27}H_{49}O_2Si_2Br$: 540.2454, found 540.2452

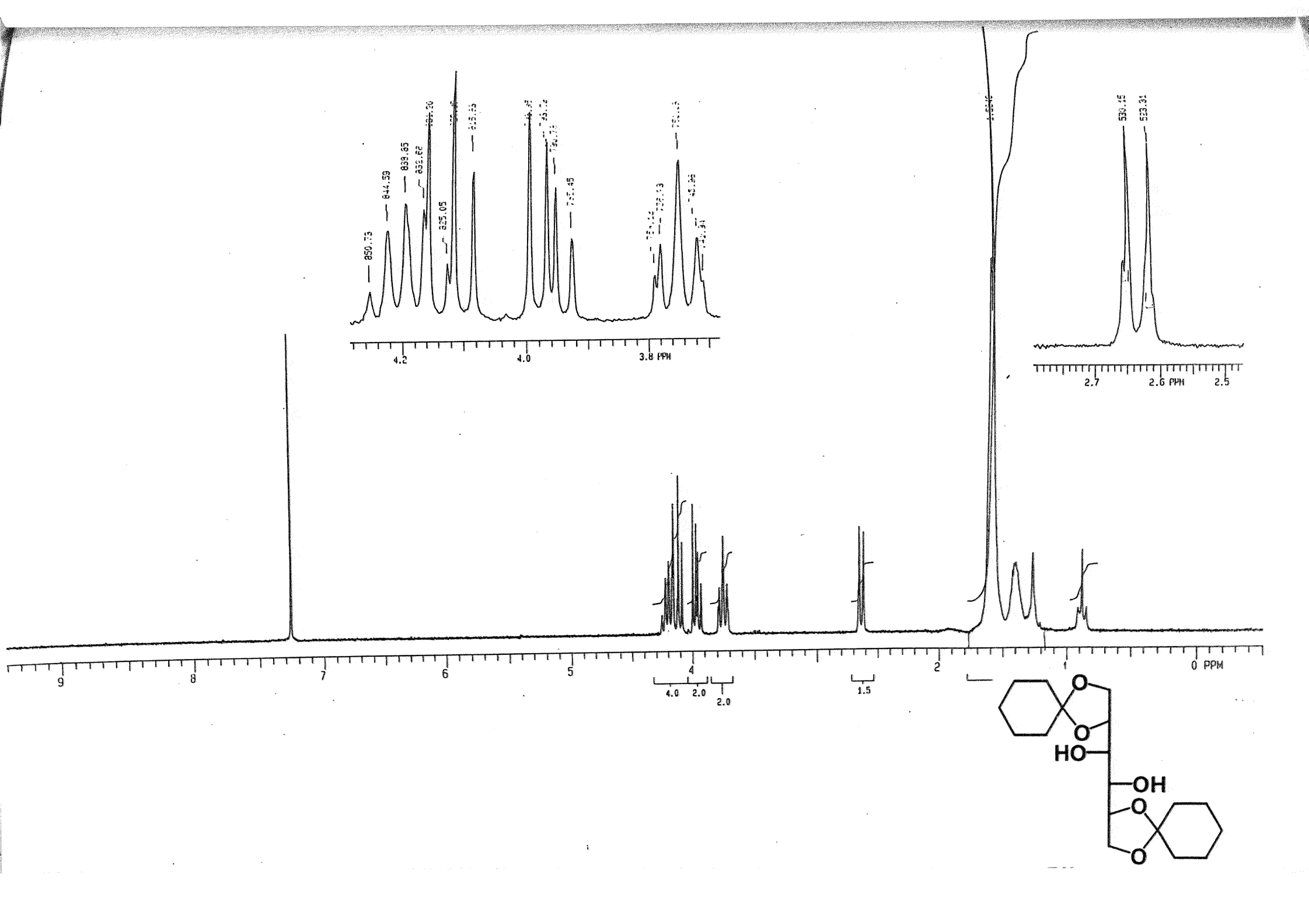
Alcohol **149**

TBAF (85.8μl, 0.0858mmol) was added to a solution of **148** (18.6mg, 0.0343mmol) in THF (0.5ml) and the mixture was stirred at 0°C under nitrogen. After stirring for 1h, 17.2μl (0.0171mmol) more of TBAF was added and the stirring was continued for additional 1h. Then 17.2μl (0.0171mmol) more of TBAF was further added. After 1h, the reaction was quenched with sat. NH_4Cl at 0°C and diluted with EtOAc. The organic layer was washed with sat. NH_4Cl and sat. brine and dried with Na_2SO_4. Removal of the solvent gave an oil, which was purified by silica gel column [EtOAc:hexane (2:5)] to provide **149** (10.5mg, 0.0335mmol) as an oil: ^{1}H-NMR (500MHz, $CDCl_3$) δ 6.24 (ddd, J=11.0, 6.8, 6.8Hz, 1H), 5.85 (ddd, J=10.3, 10.3, 7.3Hz, 1H), 5.60-5.57 (m, 1H), 5.47 (ddd, J=10.3, 10.3, 6.3Hz, 1H), 4.12-4.07 (m, 1H), 3.80 (ddd, J=9.0, 9.0, 4.4Hz, 1H), 3.67-3.61 (m, 1H), 3.39-3.34 (m,

1H), 3.26-3.17 (m, 1H), 3.15 (d, J=2.0Hz, 1H), 2.98-2.91 (m, 2H), 2.72-2.64 (m, 1H), 2.60-2.54 (m, 1H), 2.22-2.15 (m, 1H), 1.88-1.79 (m, 2H), 1.69 (d, J=5.9Hz, 1H), 0.82 (t, J=7.3Hz, 3H); ^{13}C NMR: 142.6 (d), 129.8 (d), 127.6 (d), 109.7 (d), 82.3 (s), 81.3 (d), 80.5 (s), 74.5 (d), 73.0 (d), 55.8 (d), 34.2 (t), 33.6 (t), 33.2 (t), 28.5 (t), 9.9 (q); IR (neat) ν_{max} 3292, 2976, 2940, 2888, 1704, 1616, 1426, 1358, 1292, 1202, 1042, 938, 884 cm^{-1}; $[\alpha]^{20}_{D}$ +116.18° (C 0.587, $CDCl_3$); HRMS (EI, M^+) HRMS (EI, M^+) calculated for $C_{15}H_{21}O_2Br$: 312.0724, found 312.0720

(+)-Obtusenyne (**6**)

To a solution of alcohol **149** (11.8mg, 0.0377mmol) in toluene [degassed (0.5ml)], were added $P(oct)_3$ (84.0µl, 0.188mmol), CCl_4 (0.5ml), pyridine (30.5µl, 0.377mmol) and 1-methyl-1-cyclohexene (89.1µl, 0.753mmol) at room temperature and the mixture was stirred at 80°C under nitrogen. After stirring for 1h, the mixture was diluted with EtOAc and washed with sat. $NaHCO_3$ and sat. brine. Removal of the solvent gave an oil, which was purified by silica gel column [EtOAc:hexane (1:12)] and then HPLC [EtOAc:hexane (1:6)] to afford (+)-Obtusenyne (6.2mg, 0.0187mmol) as an oil: ^{1}H-NMR (500MHz, C_6D_6, 50°C) δ 5.83 (brd-dddd, J=10.7, 7.1, 7.0, 0.9Hz, 1H), 5.46-5.36 (m, 3H), 5.60-5.57 (m, 1H), 4.11-4.03 (m, 1H), 3.82 (ddd, J=11.0, 2.9, 2.9Hz, 1H), 3.69 (ddd, J=11.0, 2.9, 2.9Hz, 1H), 3.66-3.60 (m, 1H), 2.94 (brd-dddd, J=14.5, 7.1, 7.0, 1.4Hz, 1H), 2.84 (brd-d, J=2.2Hz, 1H), 2.80 (brd-ddd, J=14.5, 7.1, 6.8Hz, 1H), 2.70-2.54 (m, 2H), 2.44 (ddd, J=12.9, 6.4, 2.9Hz, 1H), 2.32 (ddd, J=13.0, 6.5, 2.9Hz, 1H), 1.84 (qdd, J=14.2, 7.3, 6.3Hz, 1H), 1.66 (qd, J=14.2, 7.3Hz, 1H), 0.77 (dd, J=7.3, 7.3Hz, 3H); ^{13}C NMR: 141.0 (d), 130.6 (d), 128.3 (d), 111.0 (d), 83.0 (d), 80.3 (s), 63.6 (d), 56.9 (d), 35.6 (t), 32.7 (t), 31.6 (t), 29.0 (t), 10.3 (q), C_6, C_{13} not detectable; IR (neat) ν_{max} 3296, 3028, 2936, 1730, 1630, 1620, 1450, 1380, 1304, 1258, 1190, 1130, 1118, 1060, 1010, 980, 920, 840 cm^{-1}; $[\alpha]^{20}_{D}$ +145.20° (C 0.380, $CDCl_3$); HRMS (EI, M^+) calculated for $C_{15}H_{20}O^{37}ClBr$: 332.0356, found 332.0354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523.31
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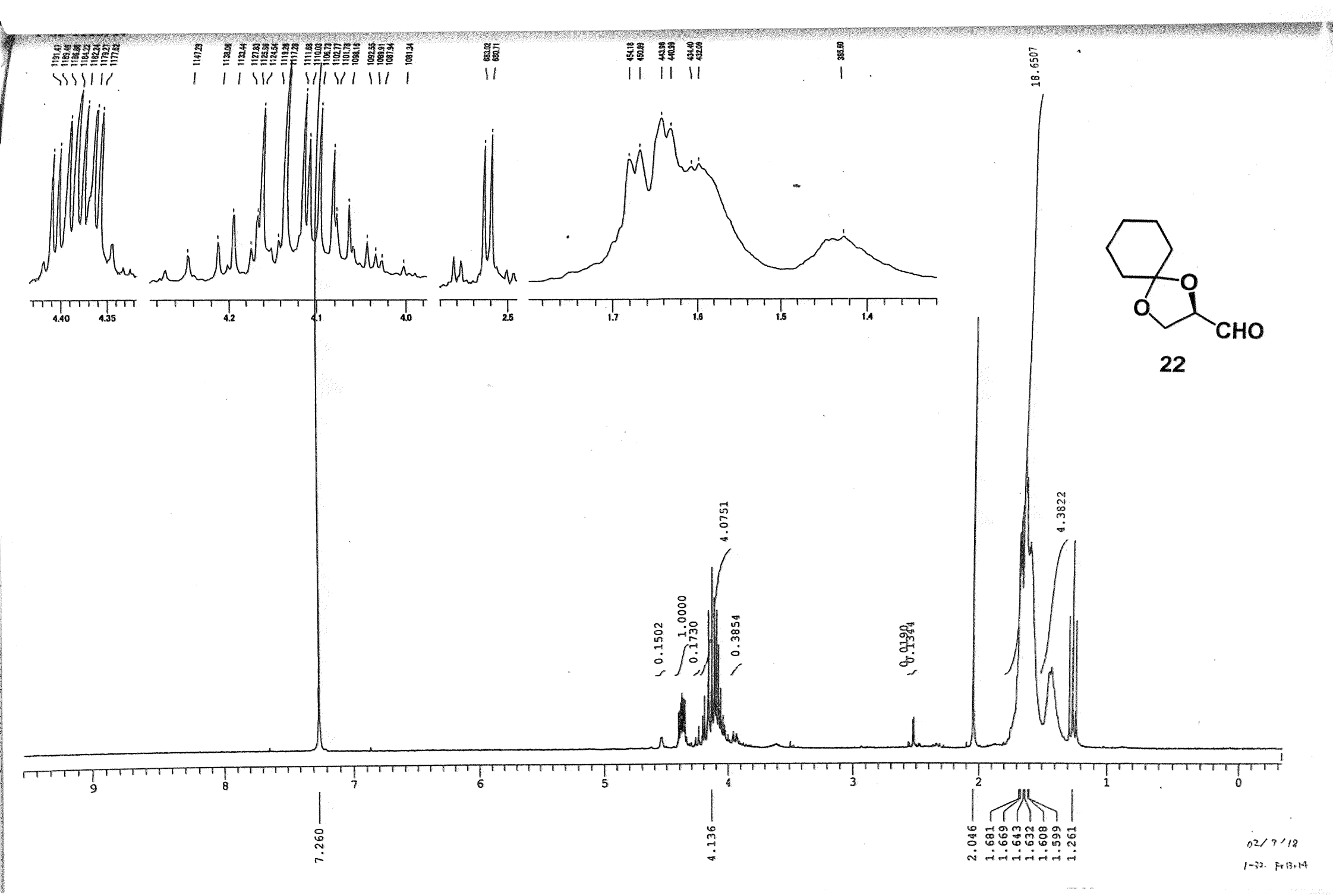
2.6 PPM
2.5
9
8
7
6
5
4
2
1
0 PPM
4.0
2.0
2.0
1.5
O
O
HO
OH
O
O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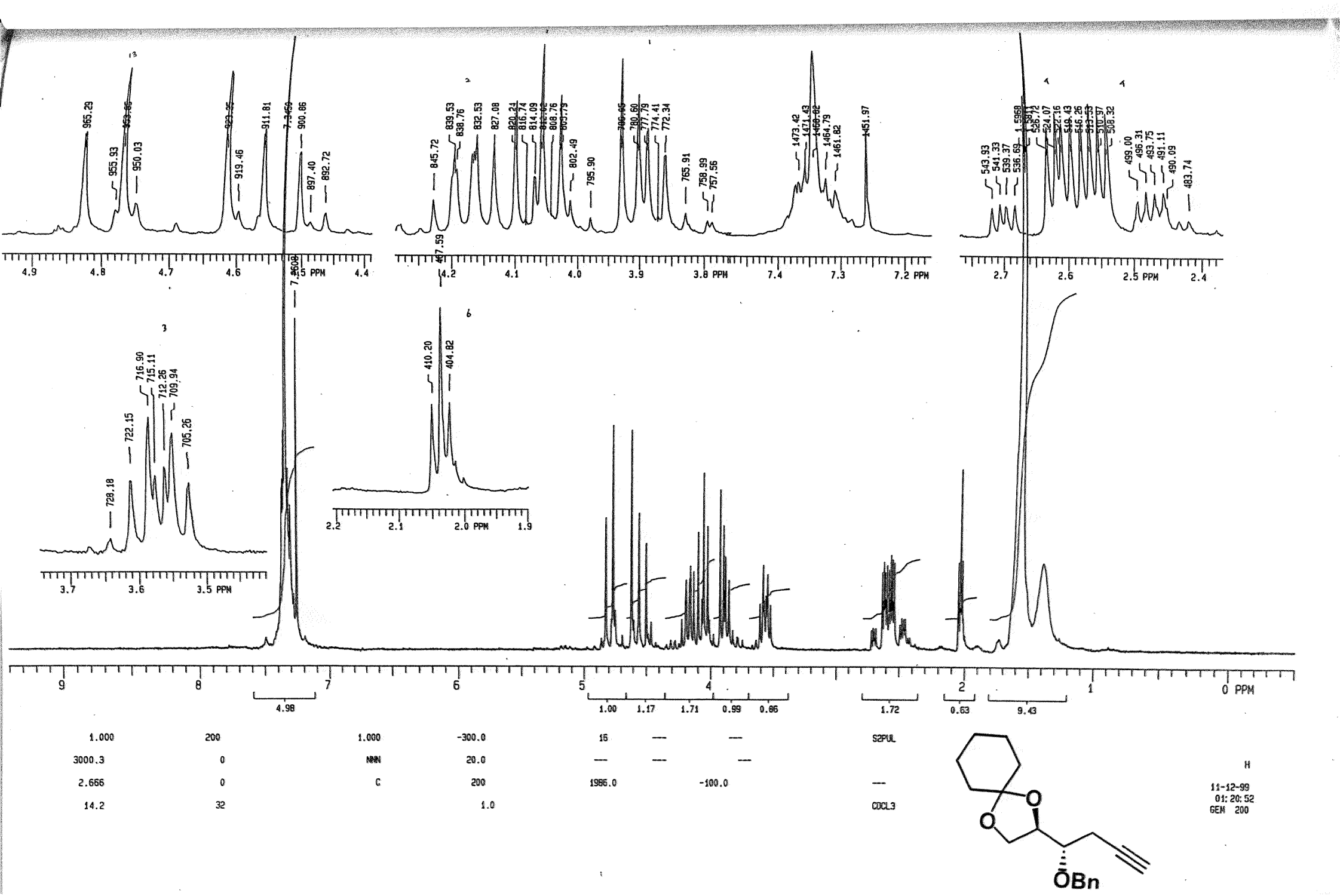
1.599
1.261
02/7/18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795.90
802.49
765.91
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757.56
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491.11
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483.74
728.18
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715.11
712.26
709.94
705.26
410.20
404.82
4.98
1.00
1.17
1.71
0.99
0.86
1.72
0.63
9.43
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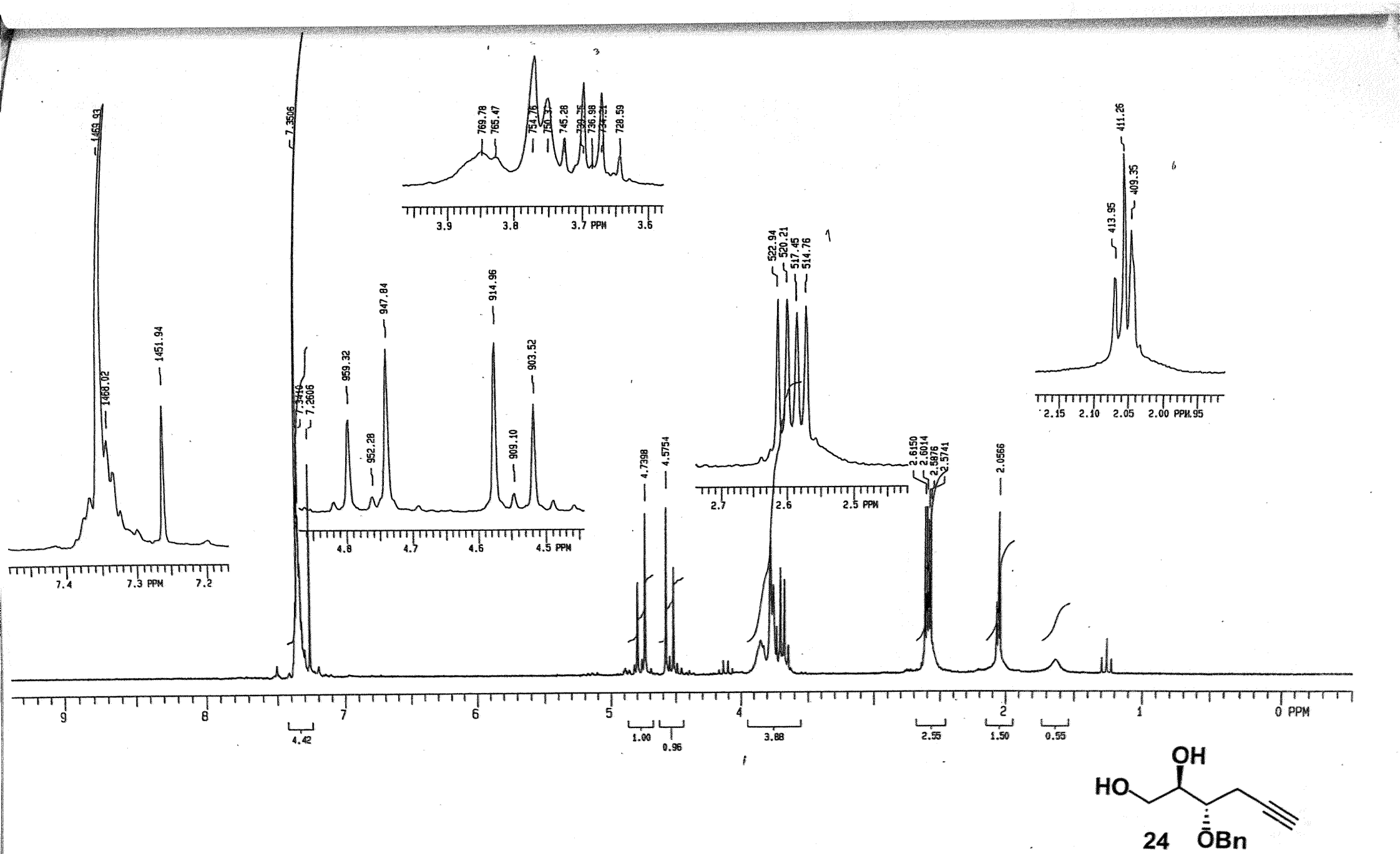
11-12-99
01:20:52
GEM 200
ÖBn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4.8
4.7
4.6
4.5 PPM
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728.59
3.9
3.8
3.7 PPM
3.6
4.7398
4.5754
522.94
520.21
517.45
514.76
2.7
2.6
2.5 PPM
2.6150
2.6014
2.5876
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2.0566
411.26
409.35
413.95
2.15
2.10
2.05
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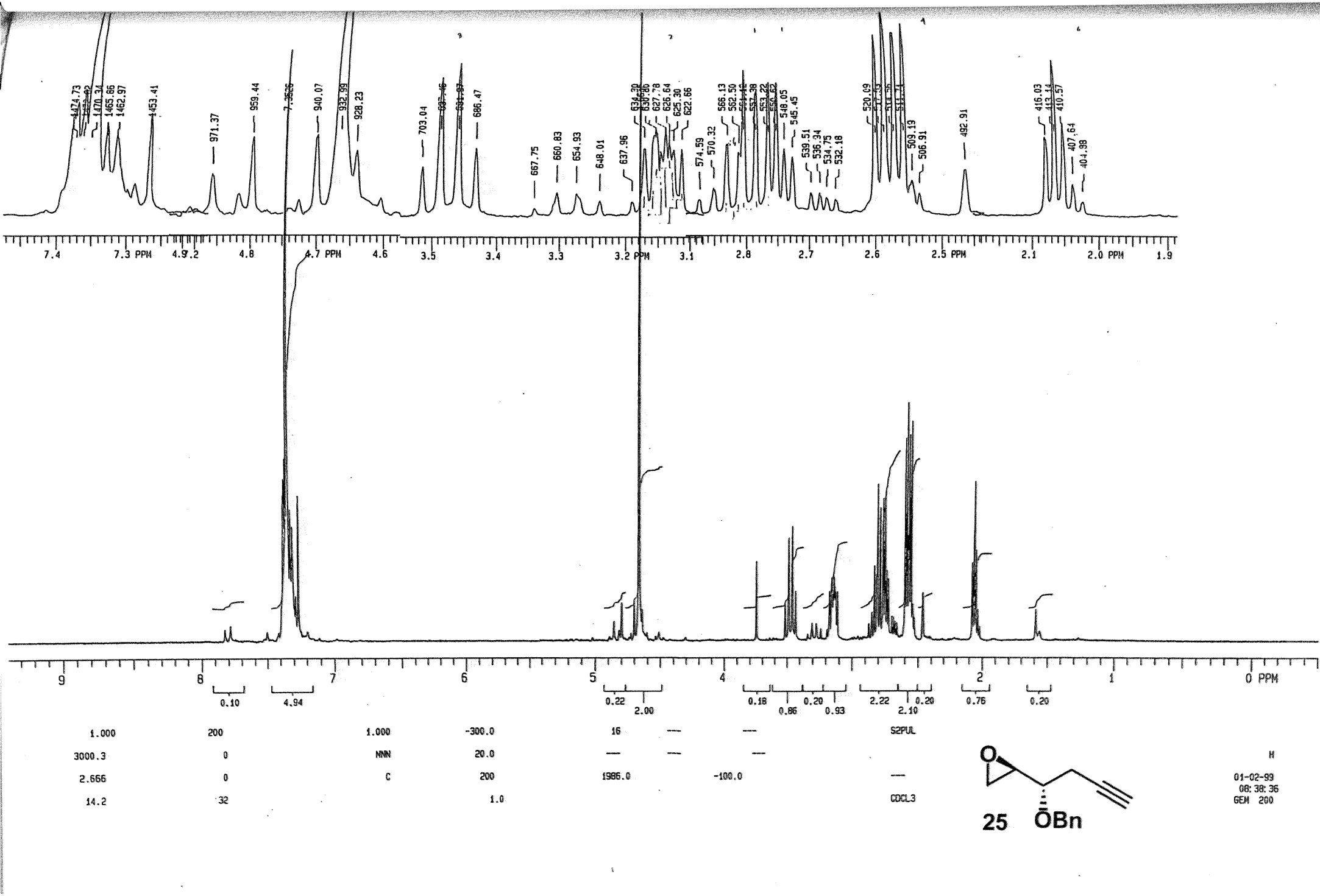
HO
24
OBn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536.34
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532.18
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416.03
413.14
410.57
407.64
404.98
7.4
7.3 PPM
4.9
4.8
4.7 PPM
4.6
3.5
3.4
3.3
3.2 PPM
3.1
2.8
2.7
2.6
2.5 PPM
2.1
2.0 PPM
1.9
9
8
7
6
5
4
2
1
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0.20
0.93
2.22
2.10
0.20
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0.20
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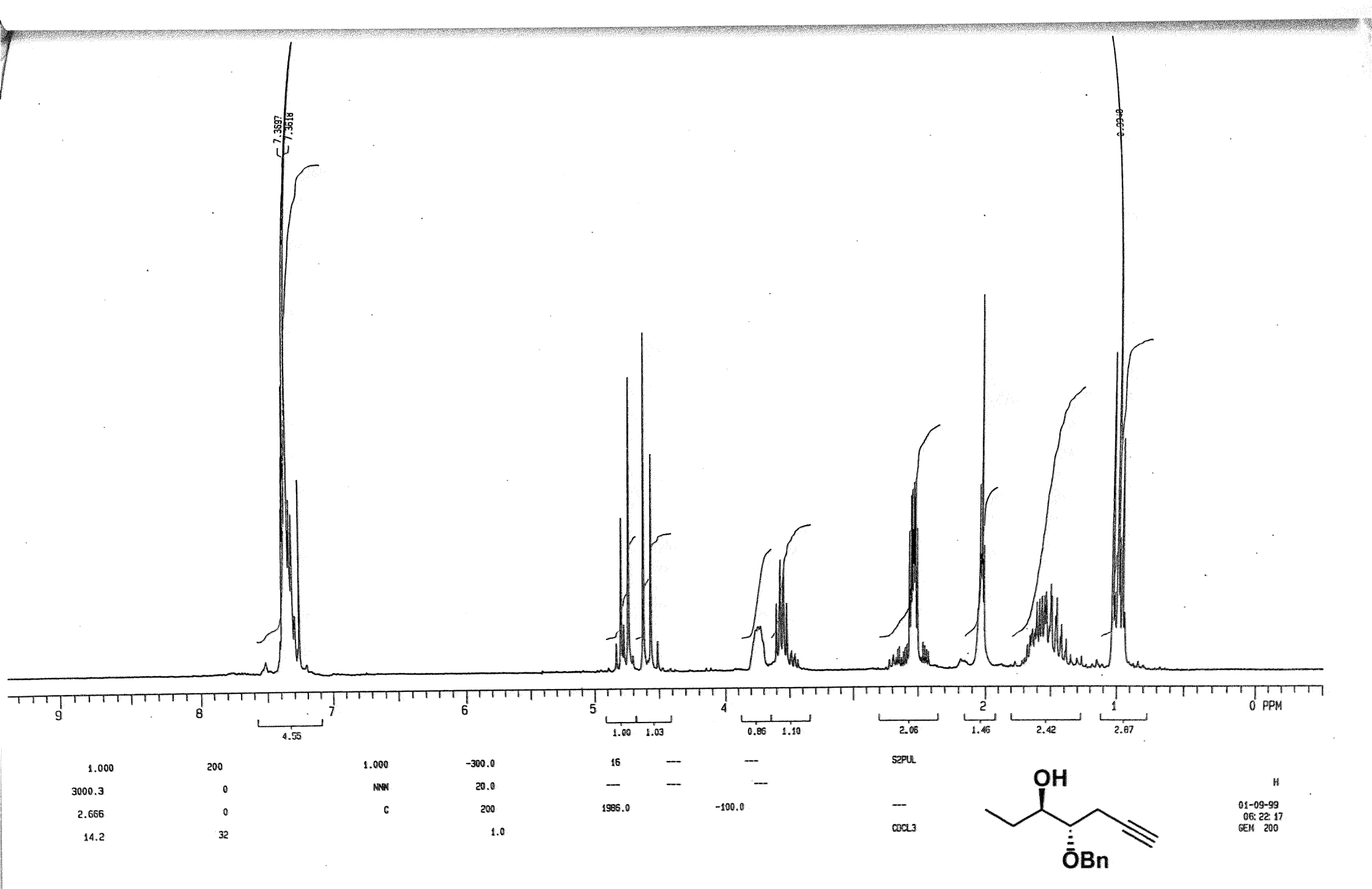
01-02-99
08:38:36
GEM 200
O
25 ÖBn



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H

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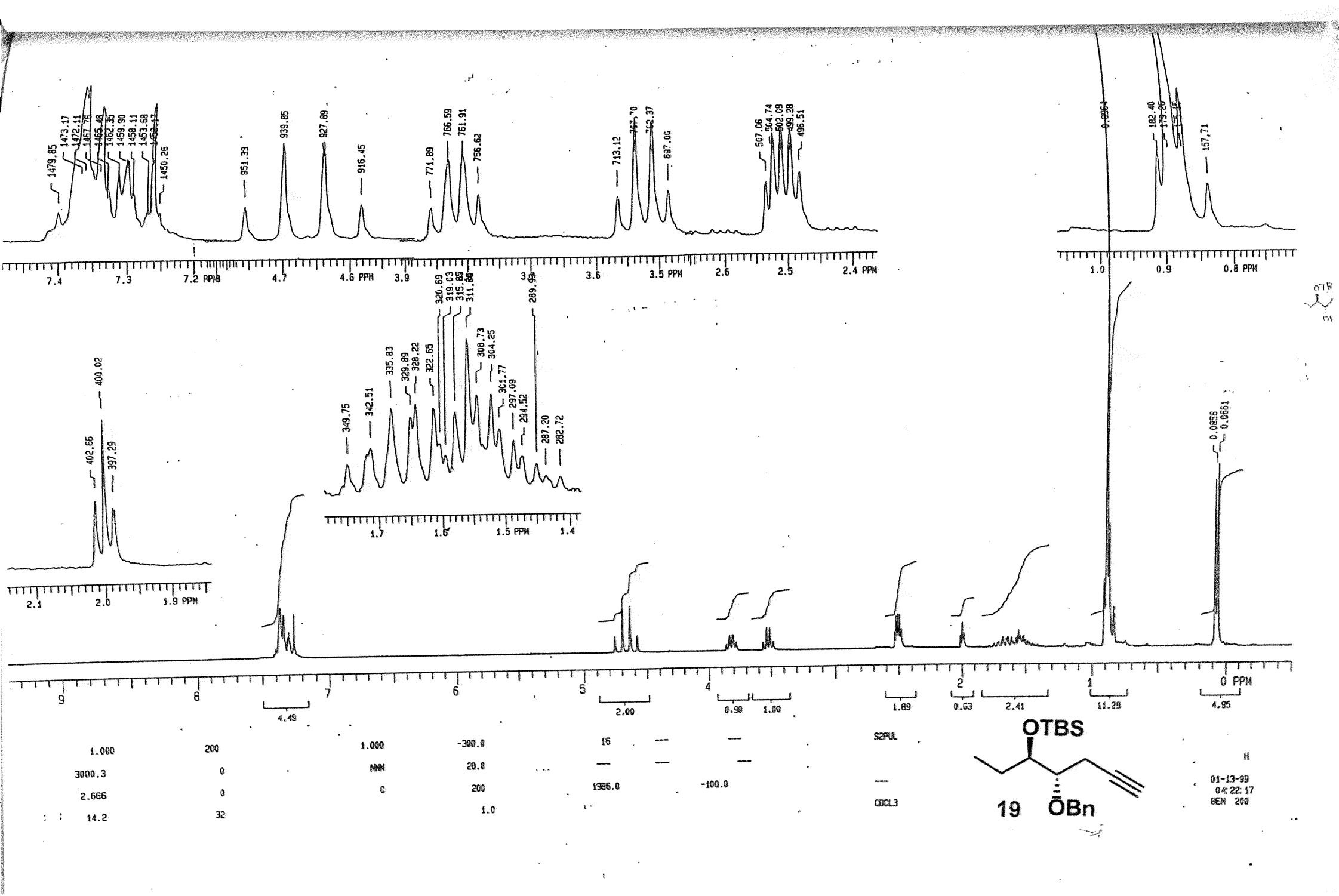
GEM 200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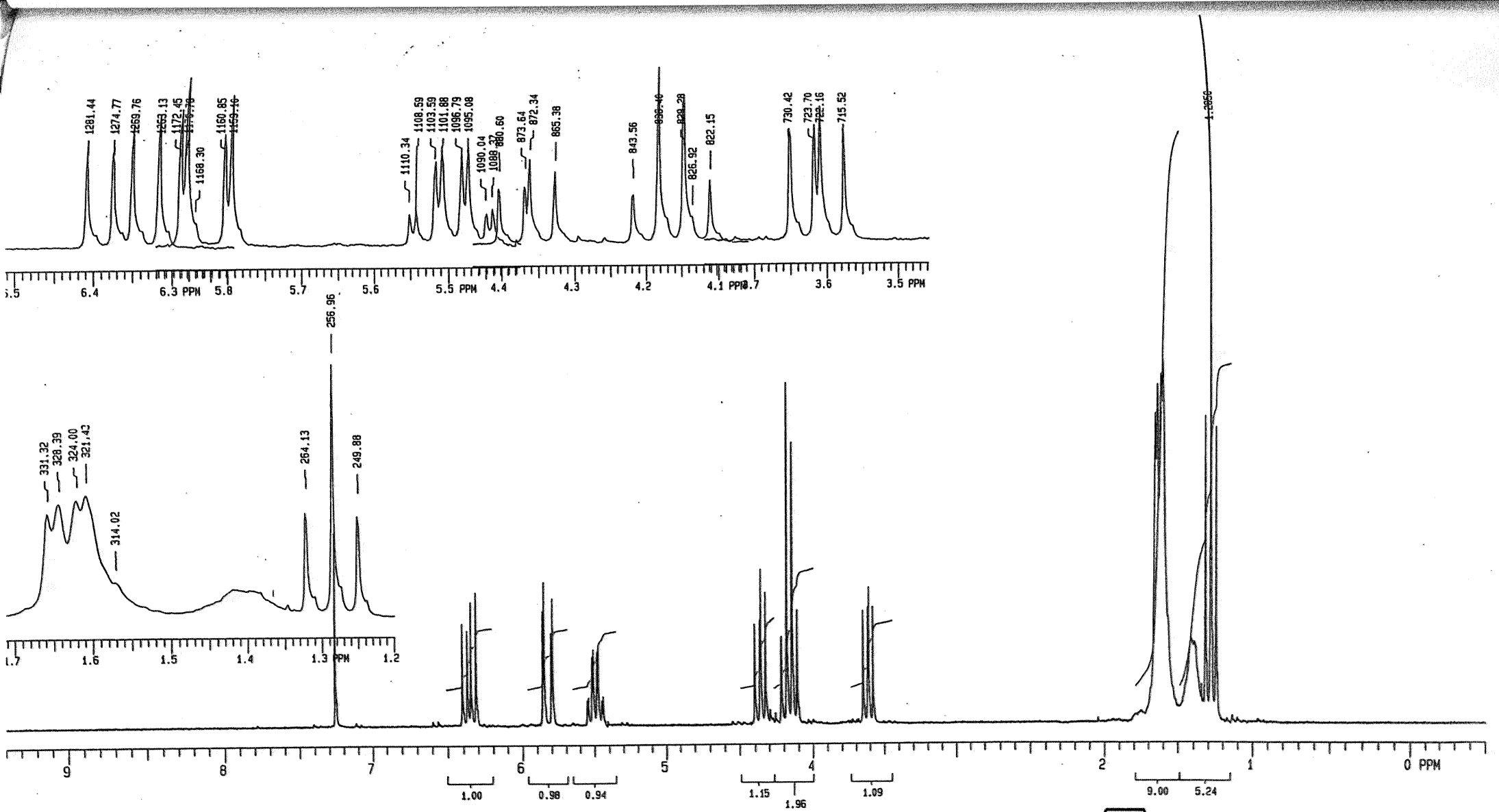
19 OBn



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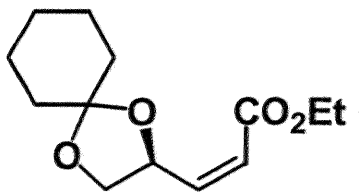

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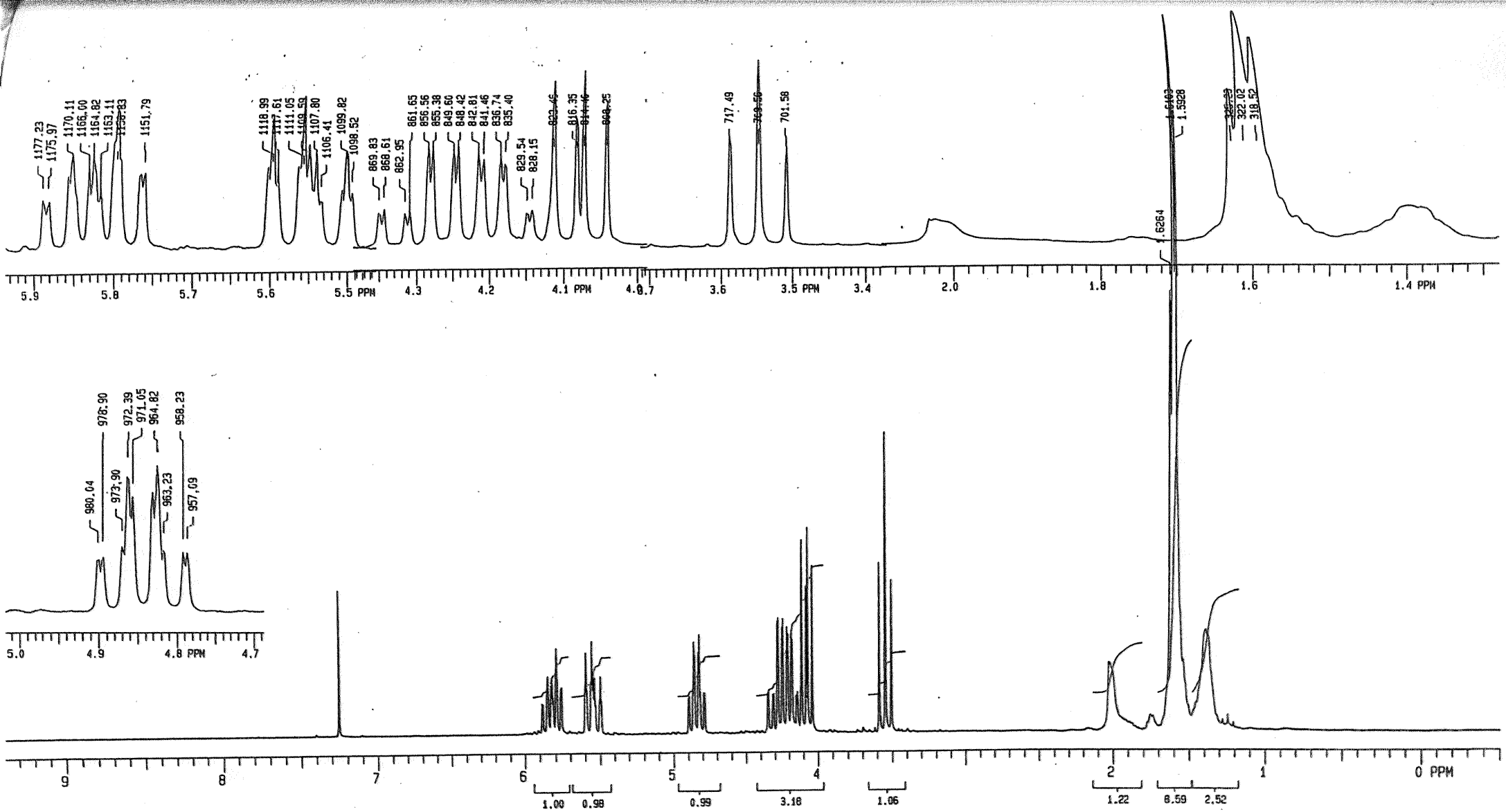

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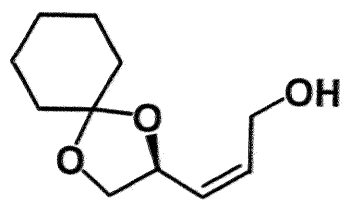

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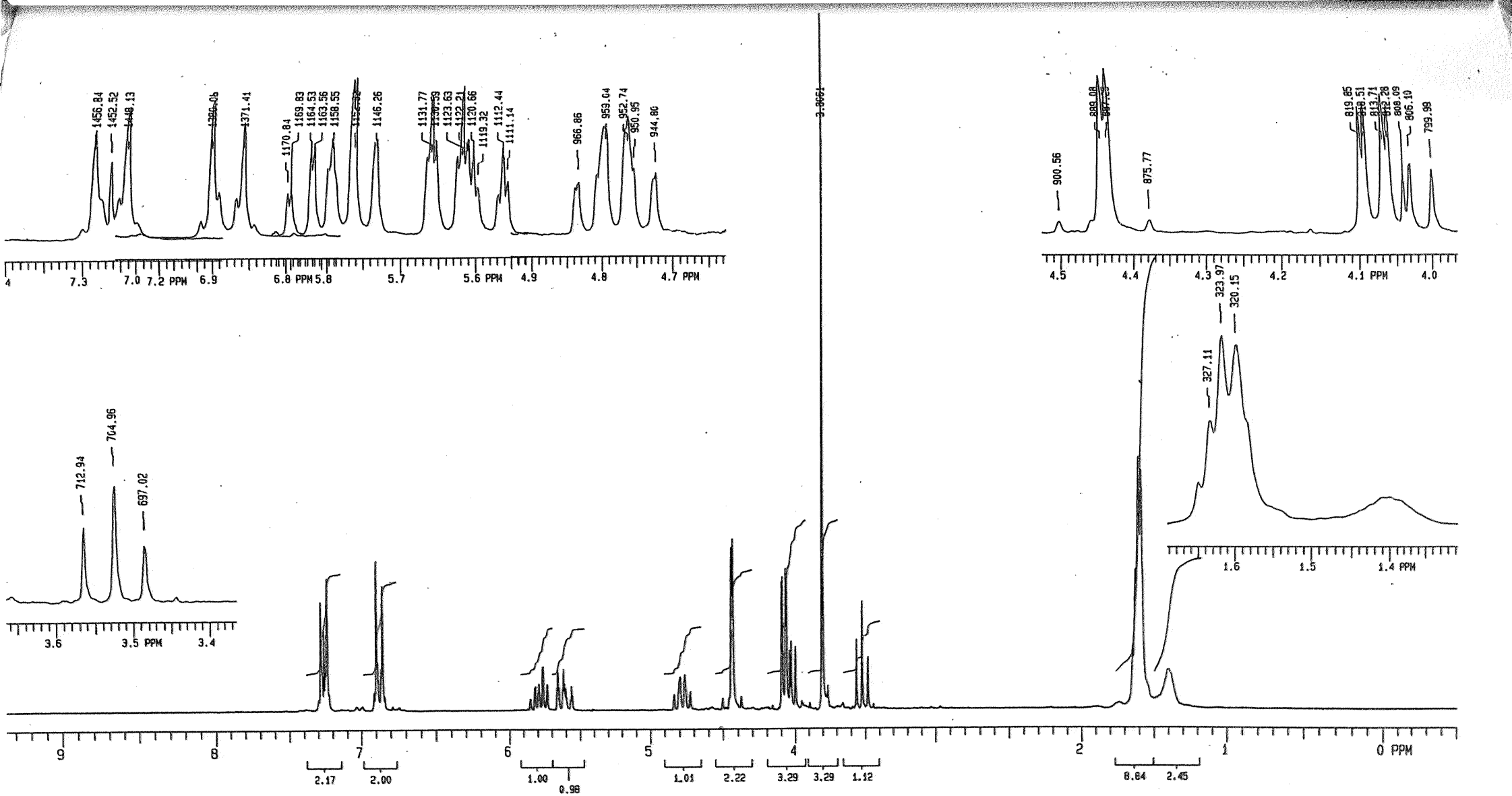

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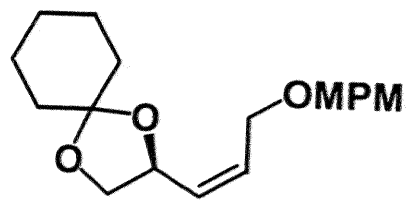
14.2	32		1.0				CDCL3



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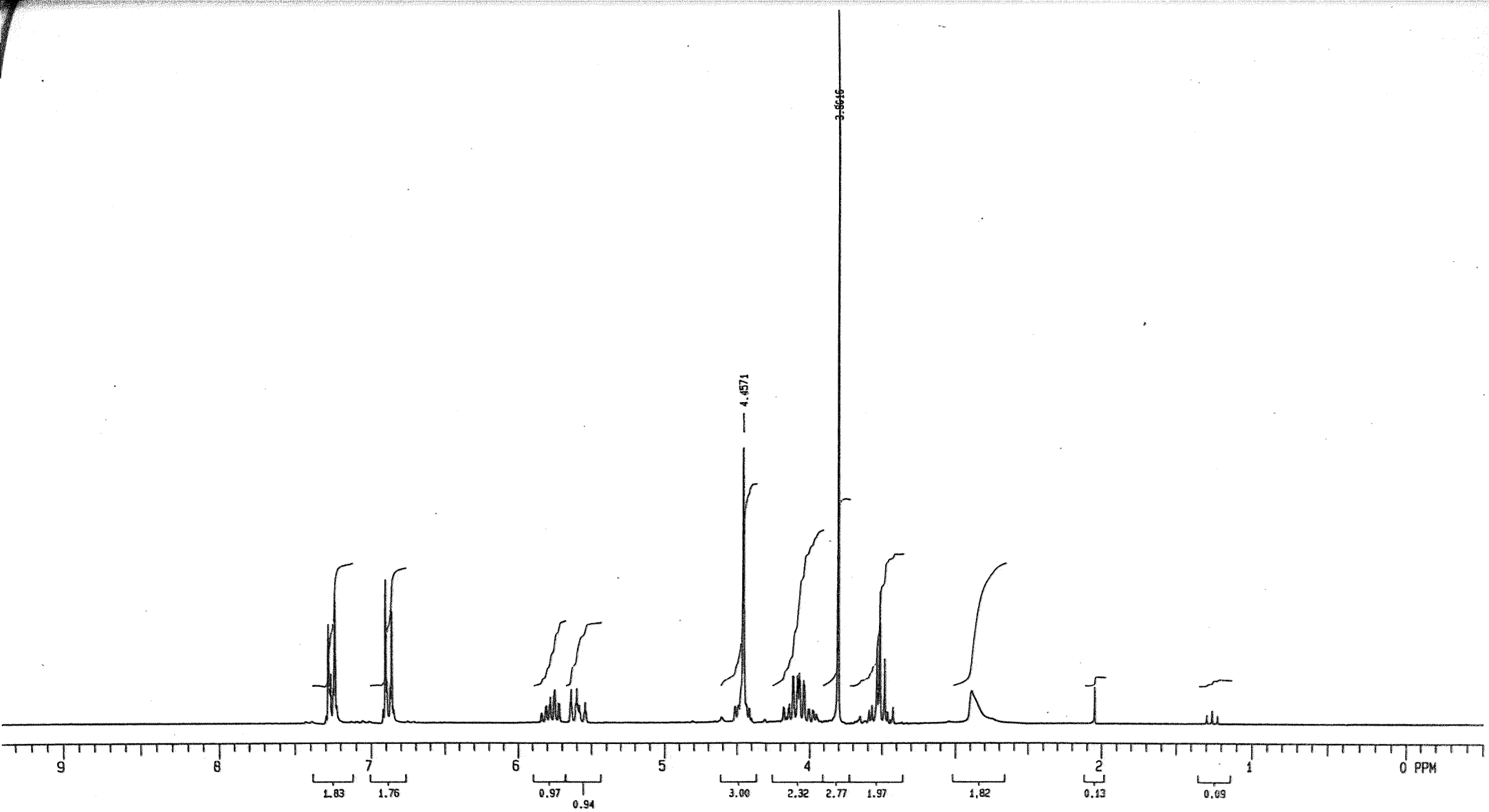
27



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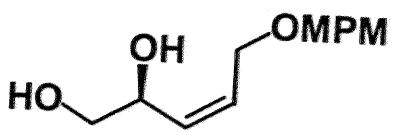
14.2	32		1.0				CDCL3



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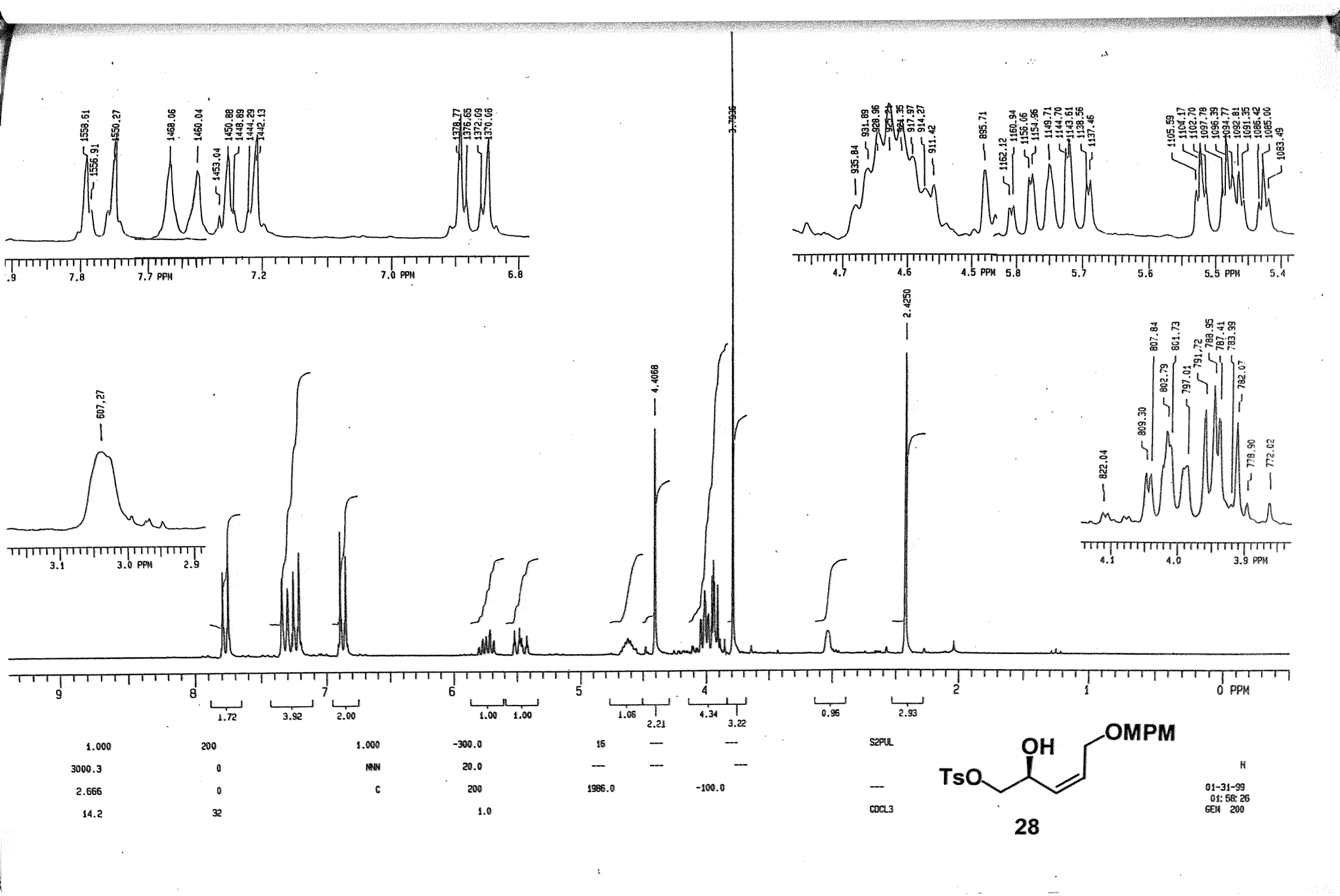
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787.41
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OMPM
OH
TsO
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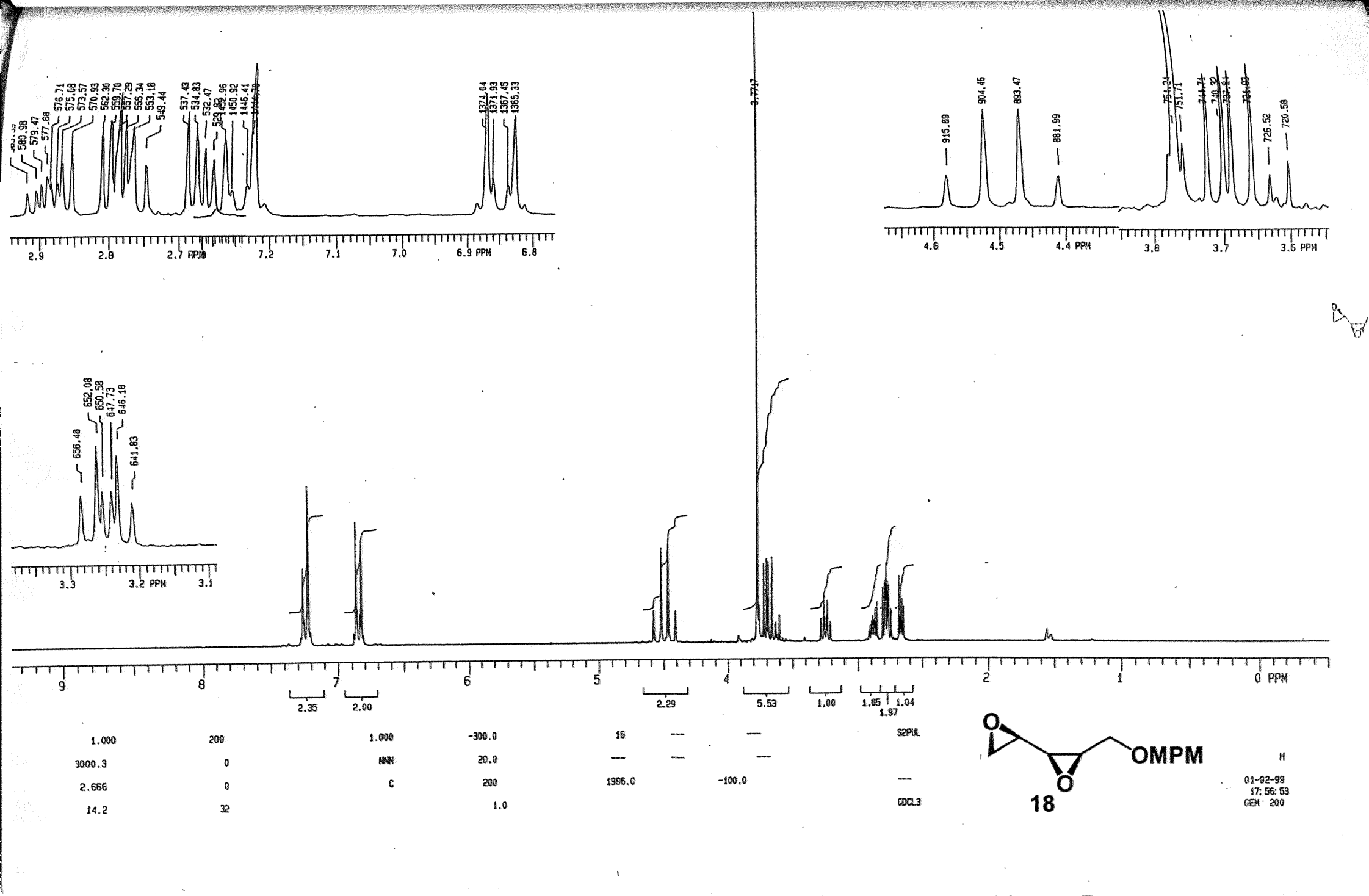
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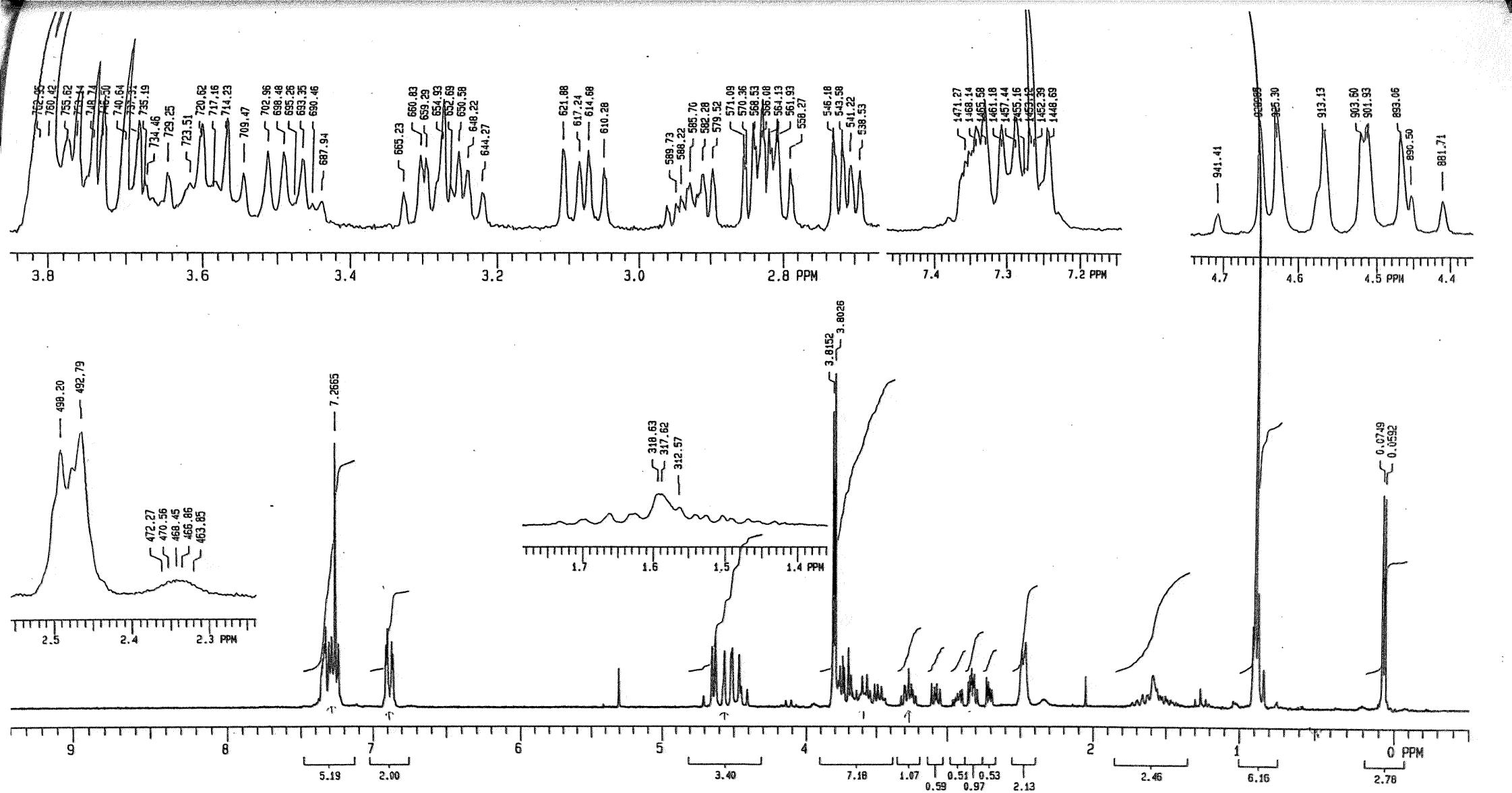
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OH
OBn
OMPM
O
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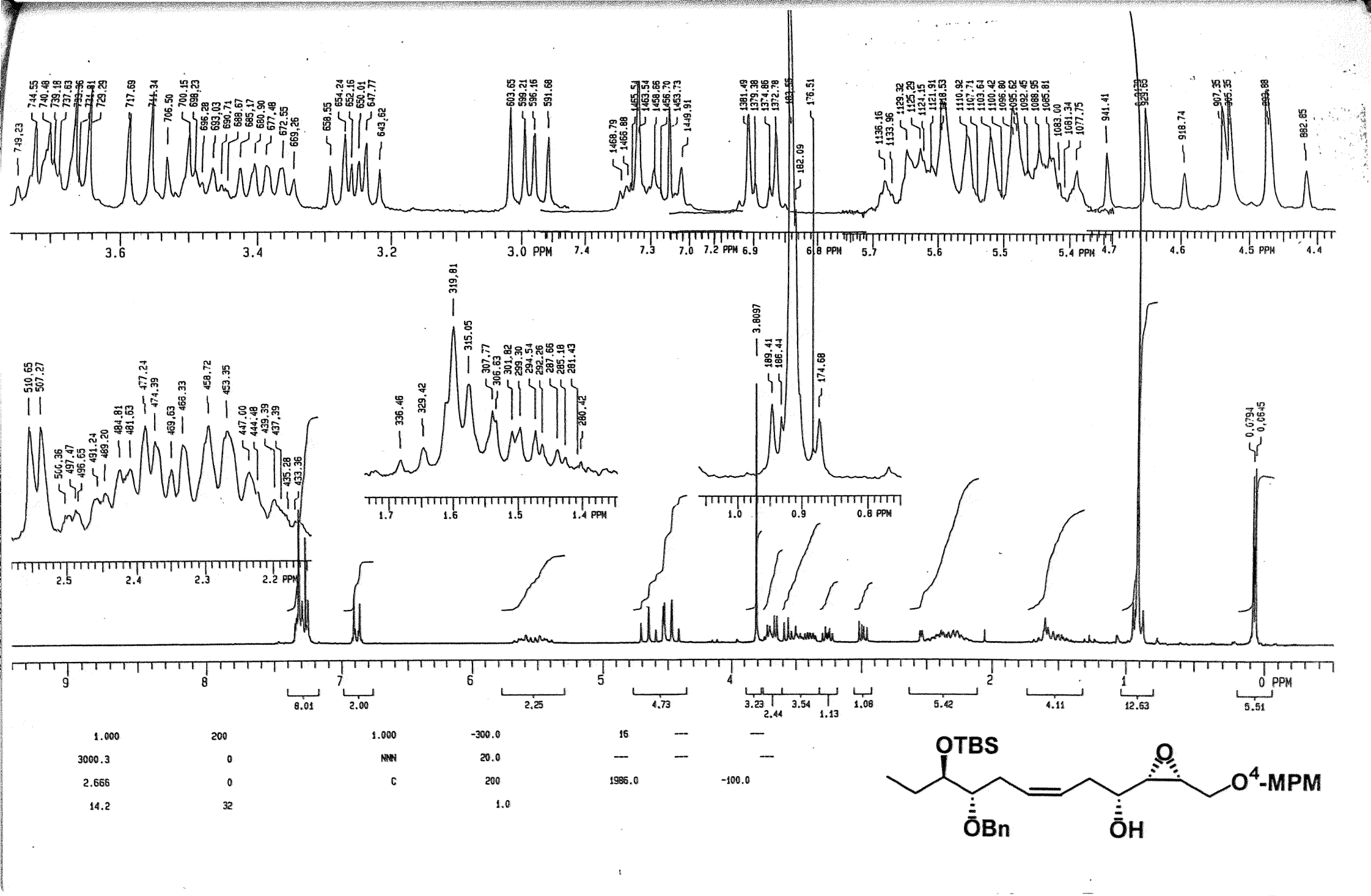
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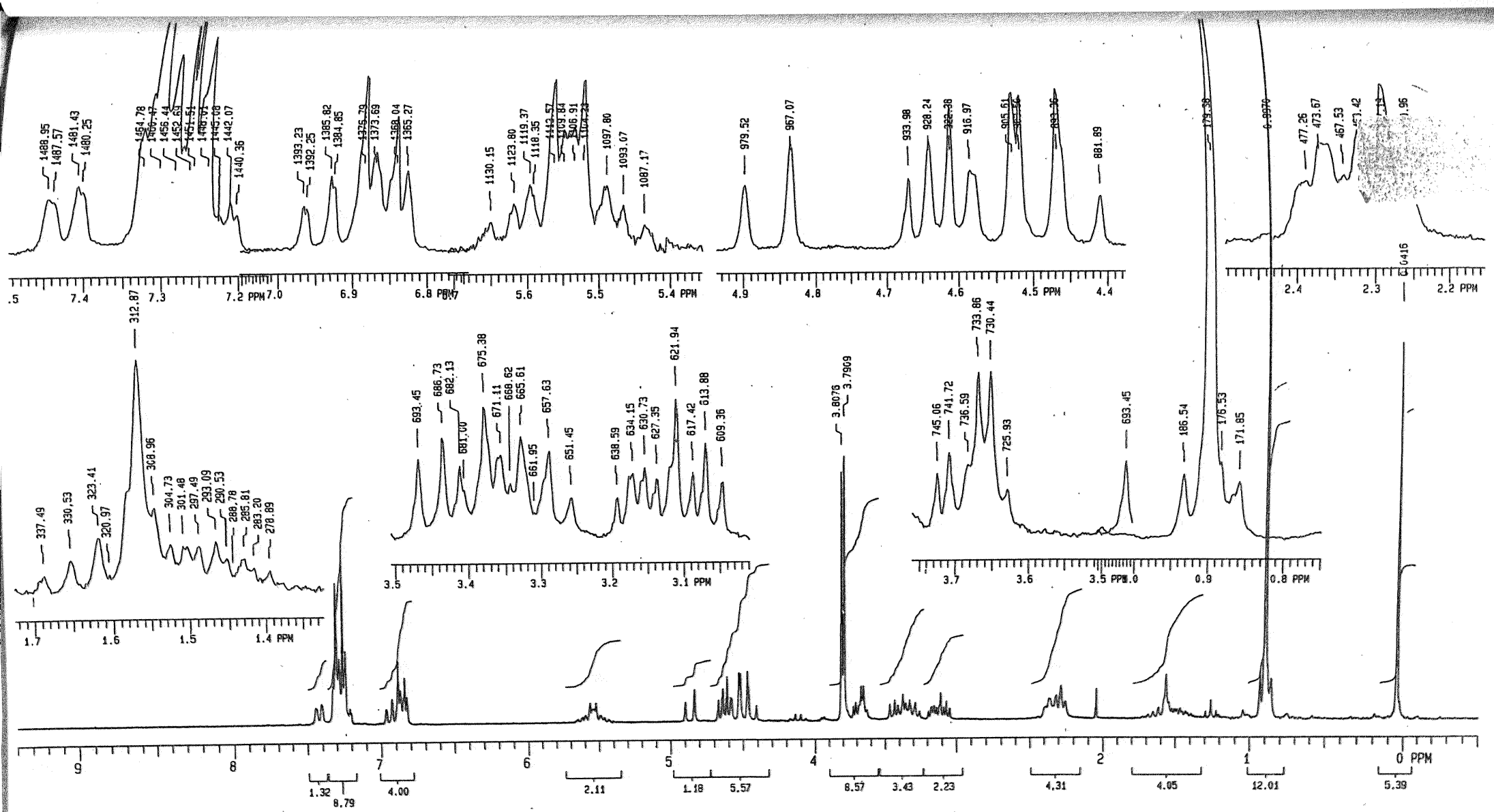

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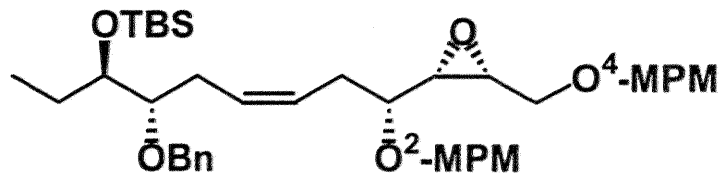

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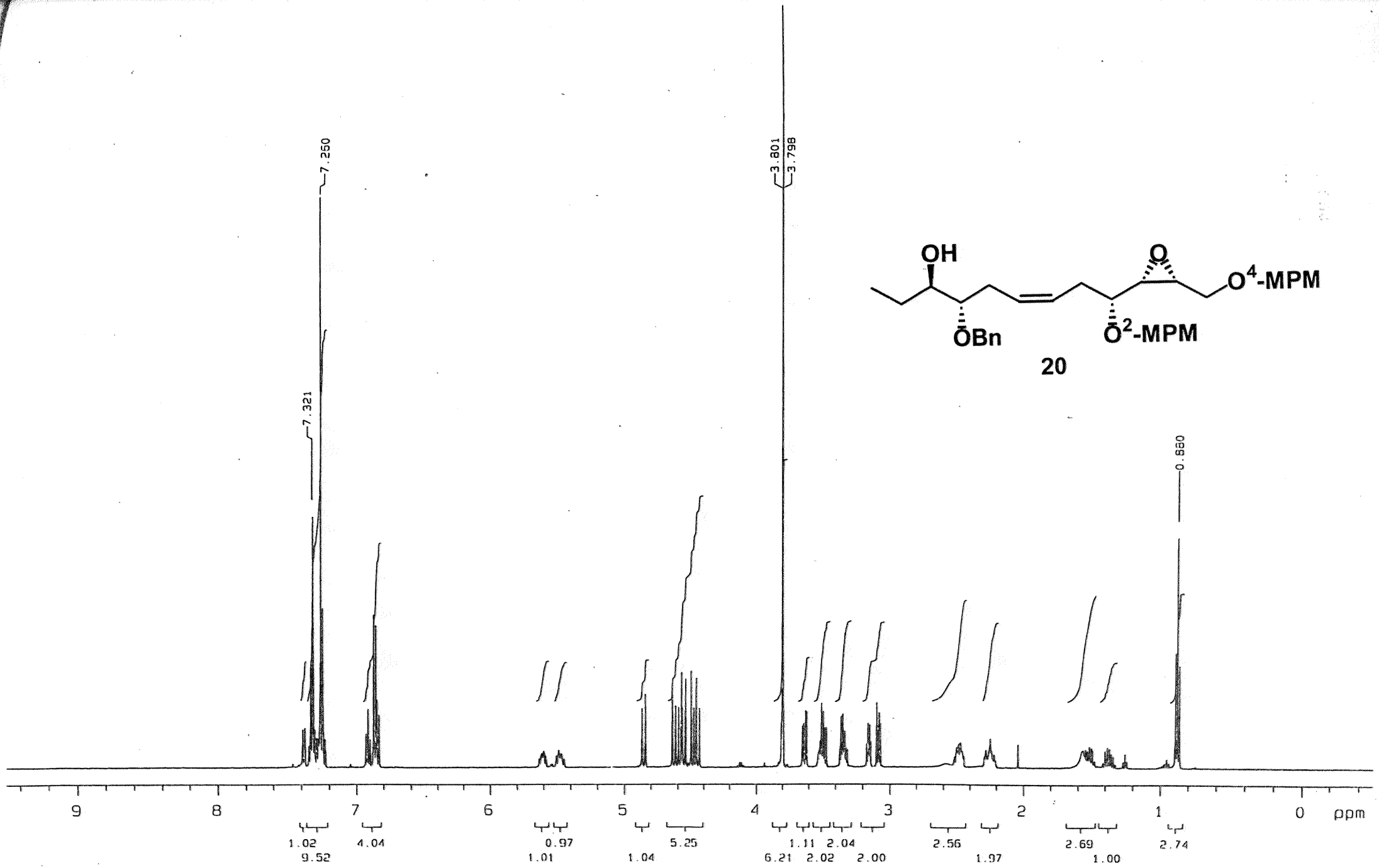
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O2-MPM
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3
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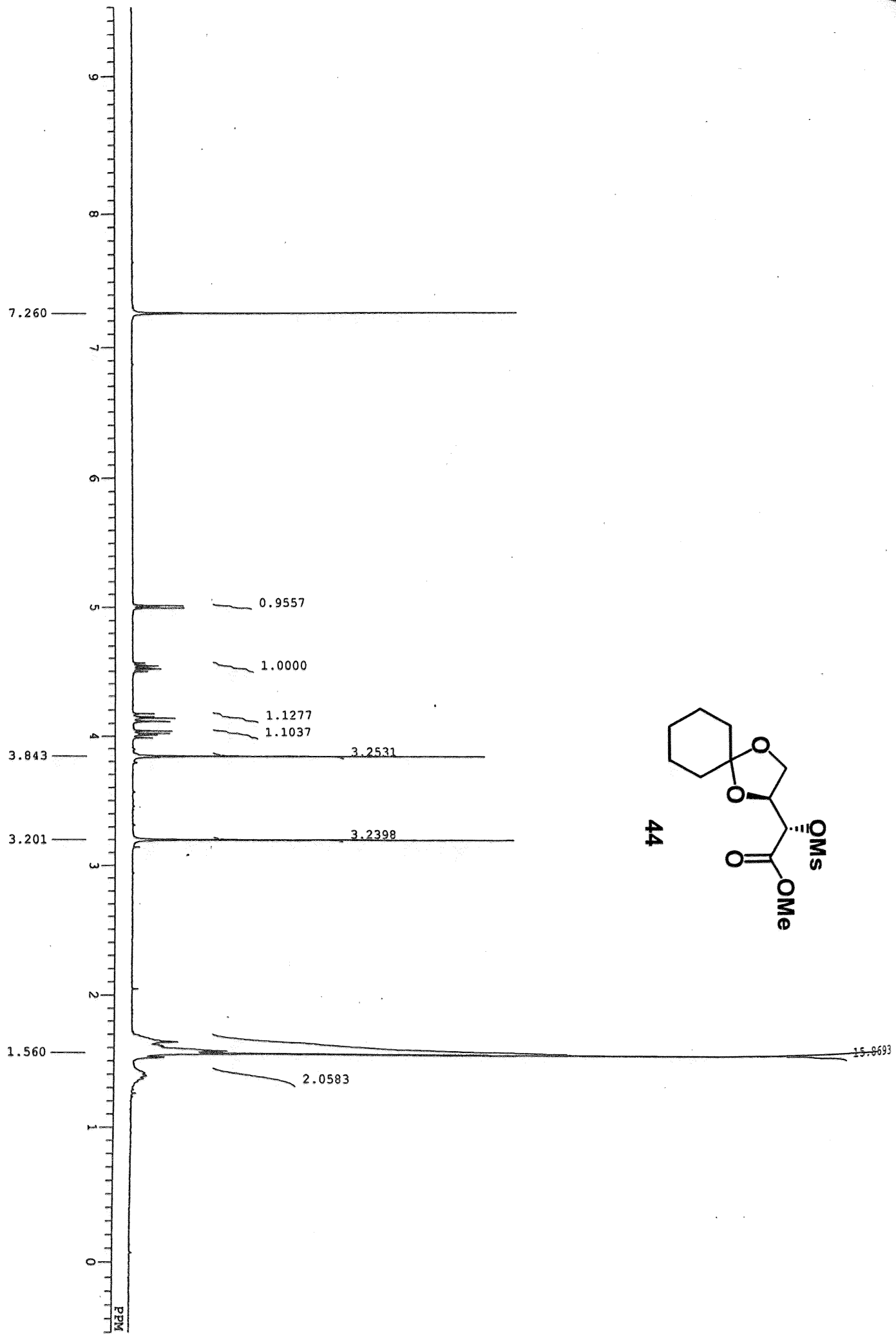
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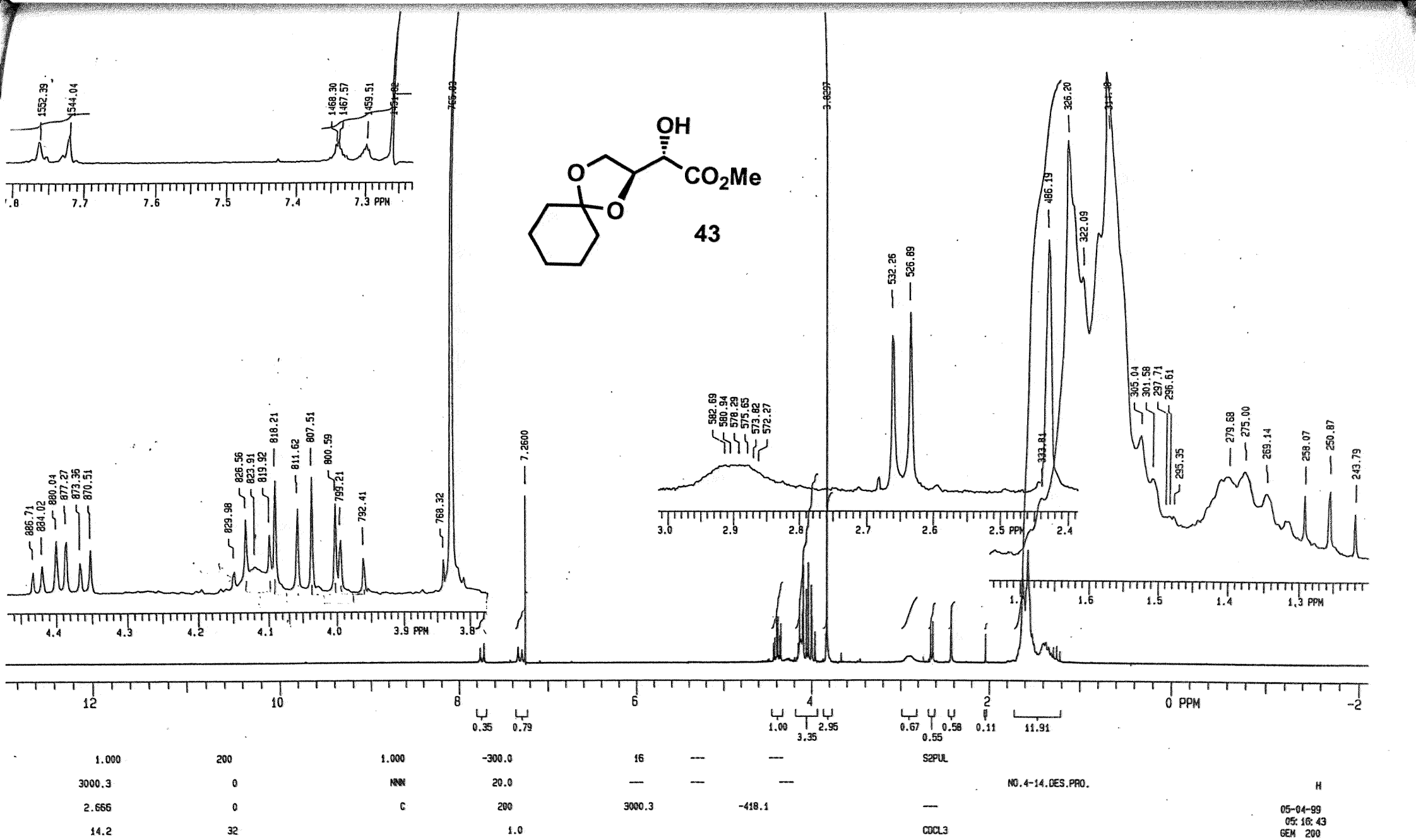
PPM
44
OMs
OMe



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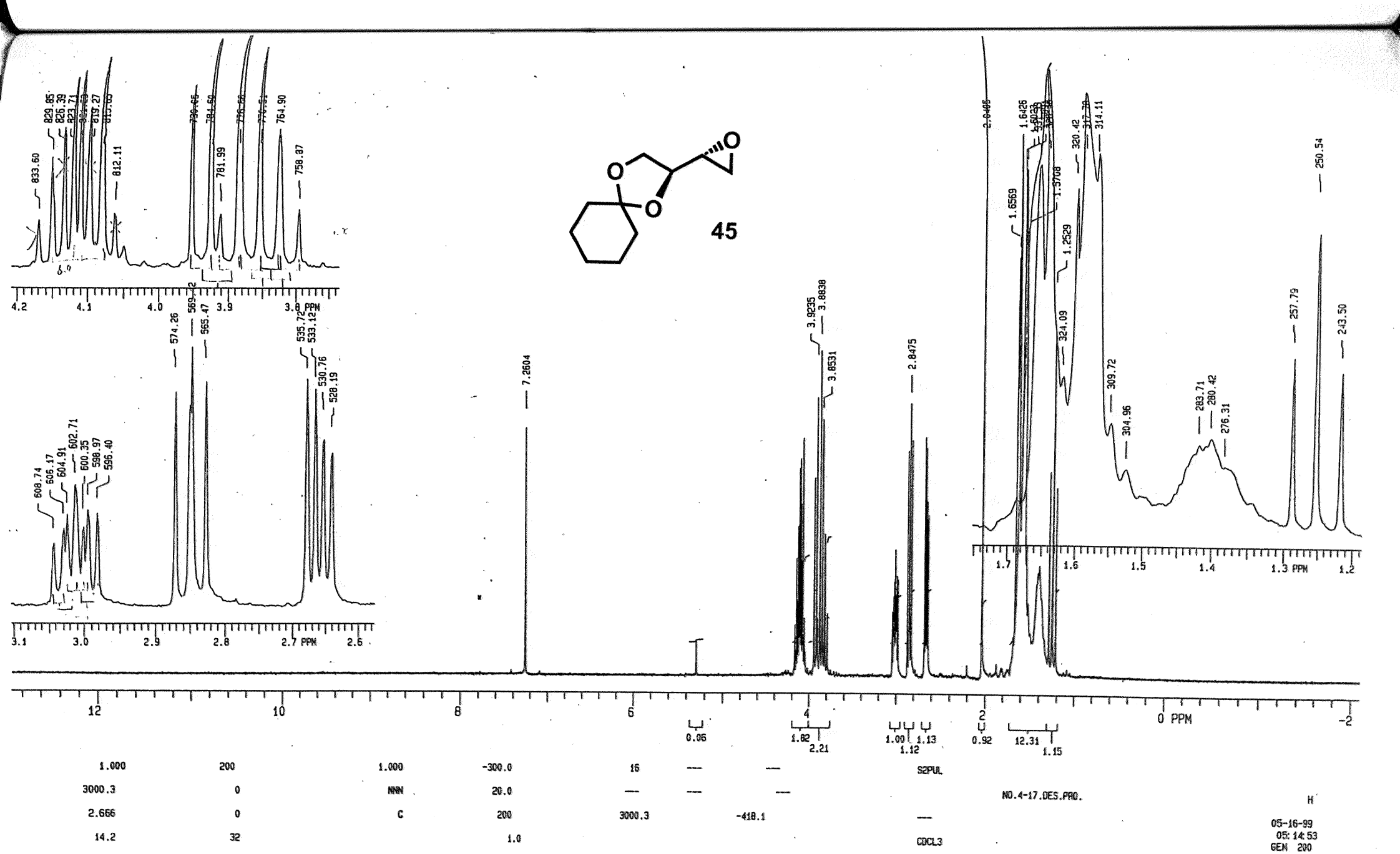
								GEM 200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276.31
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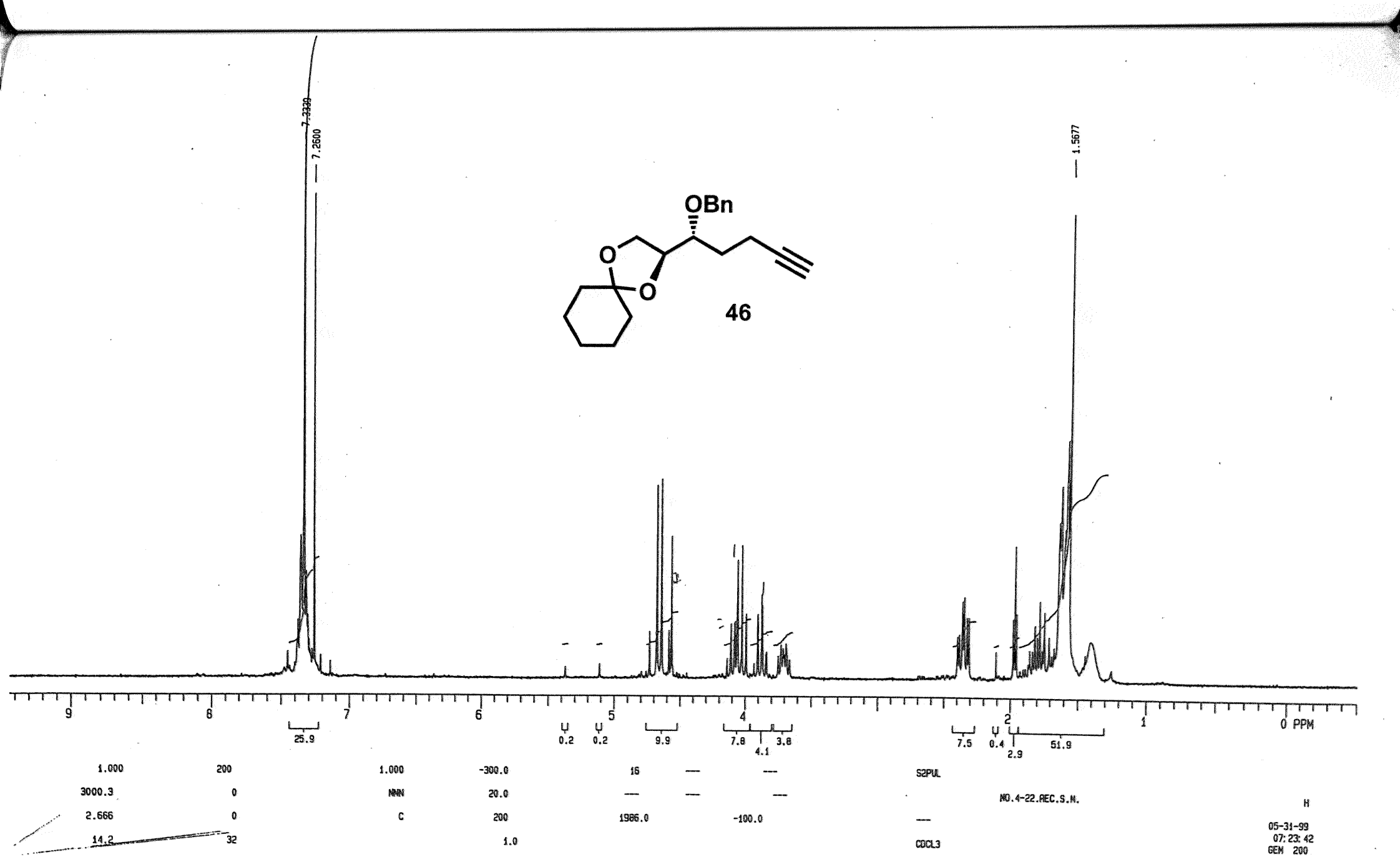
GEN 200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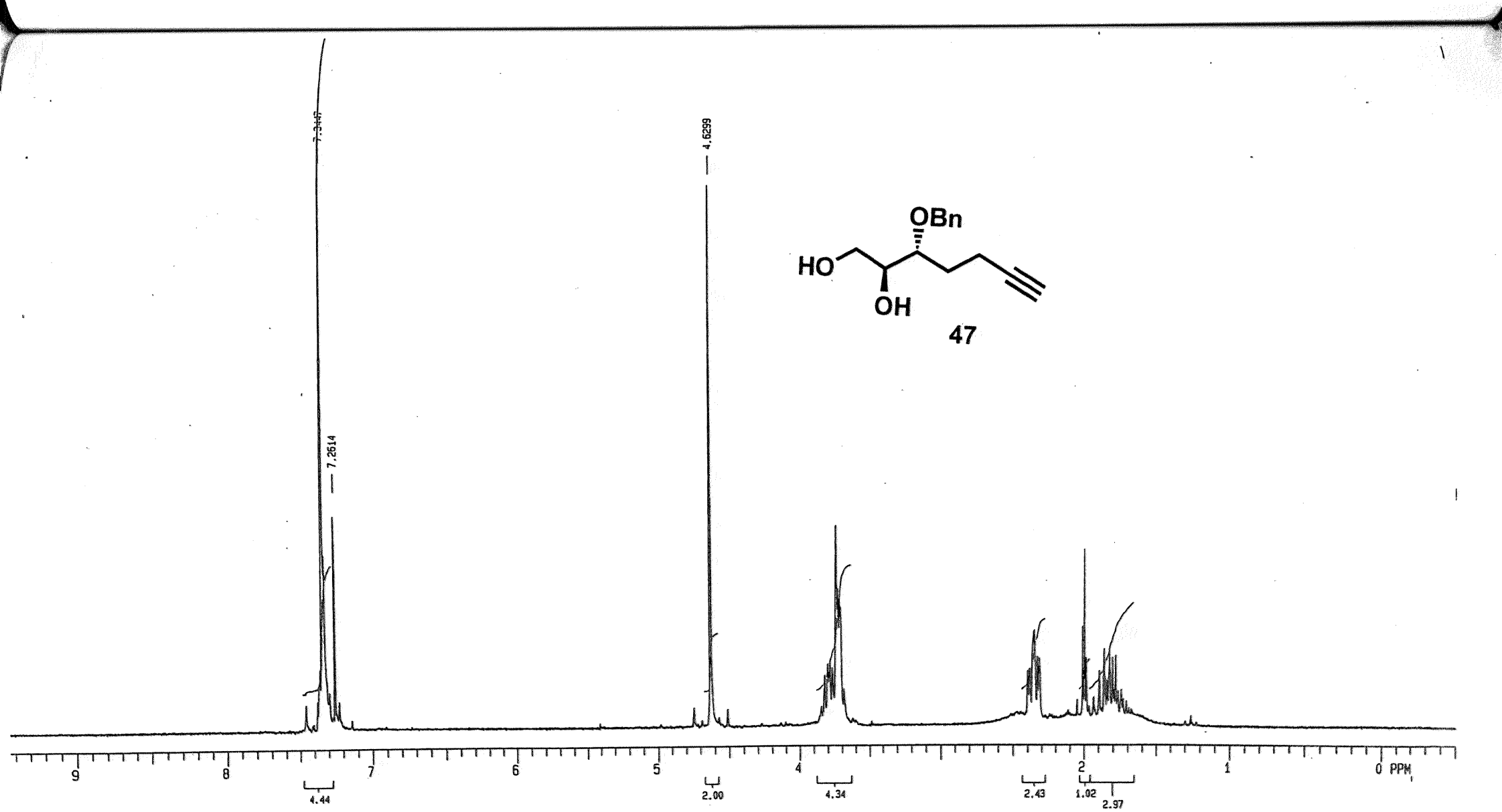
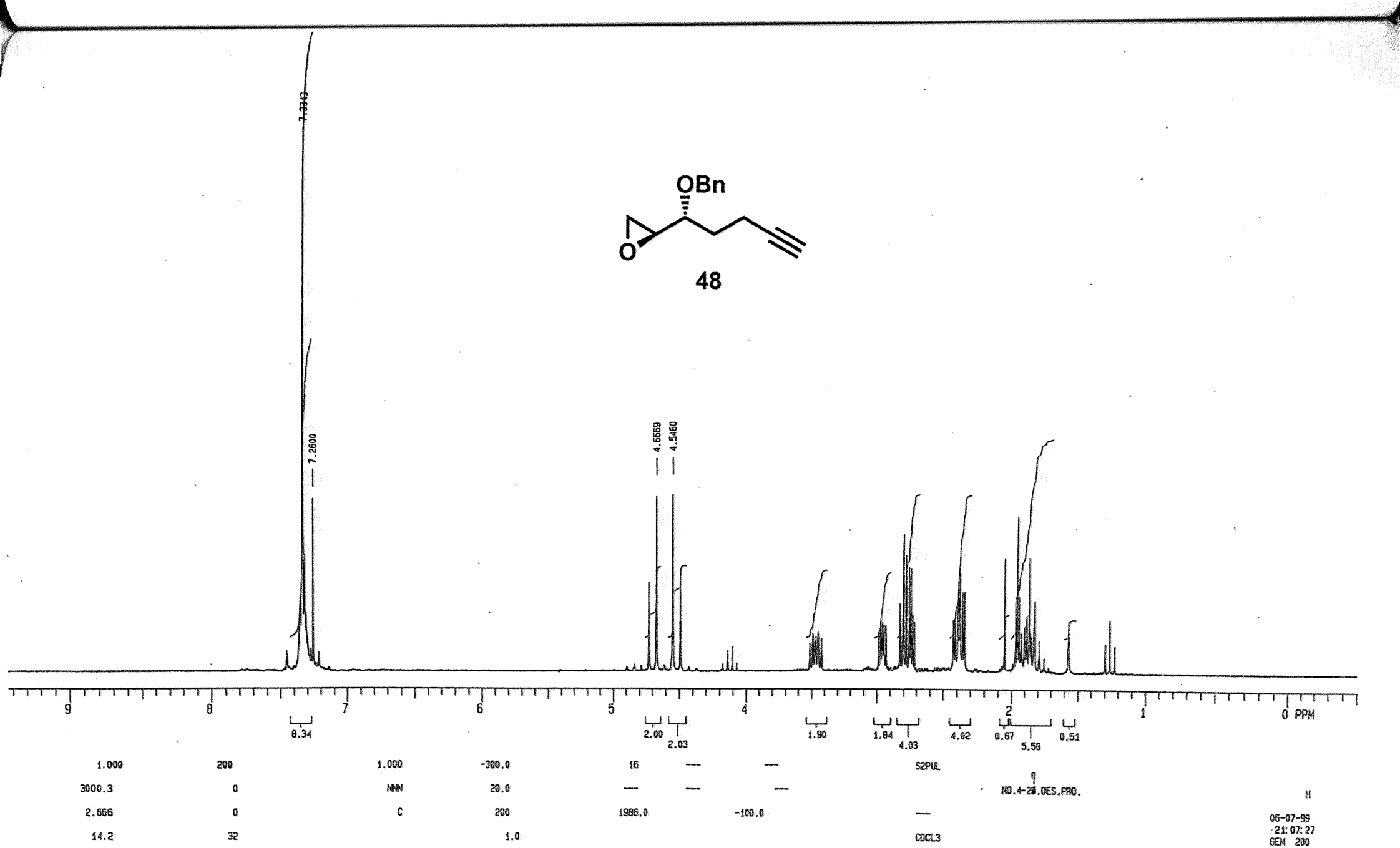
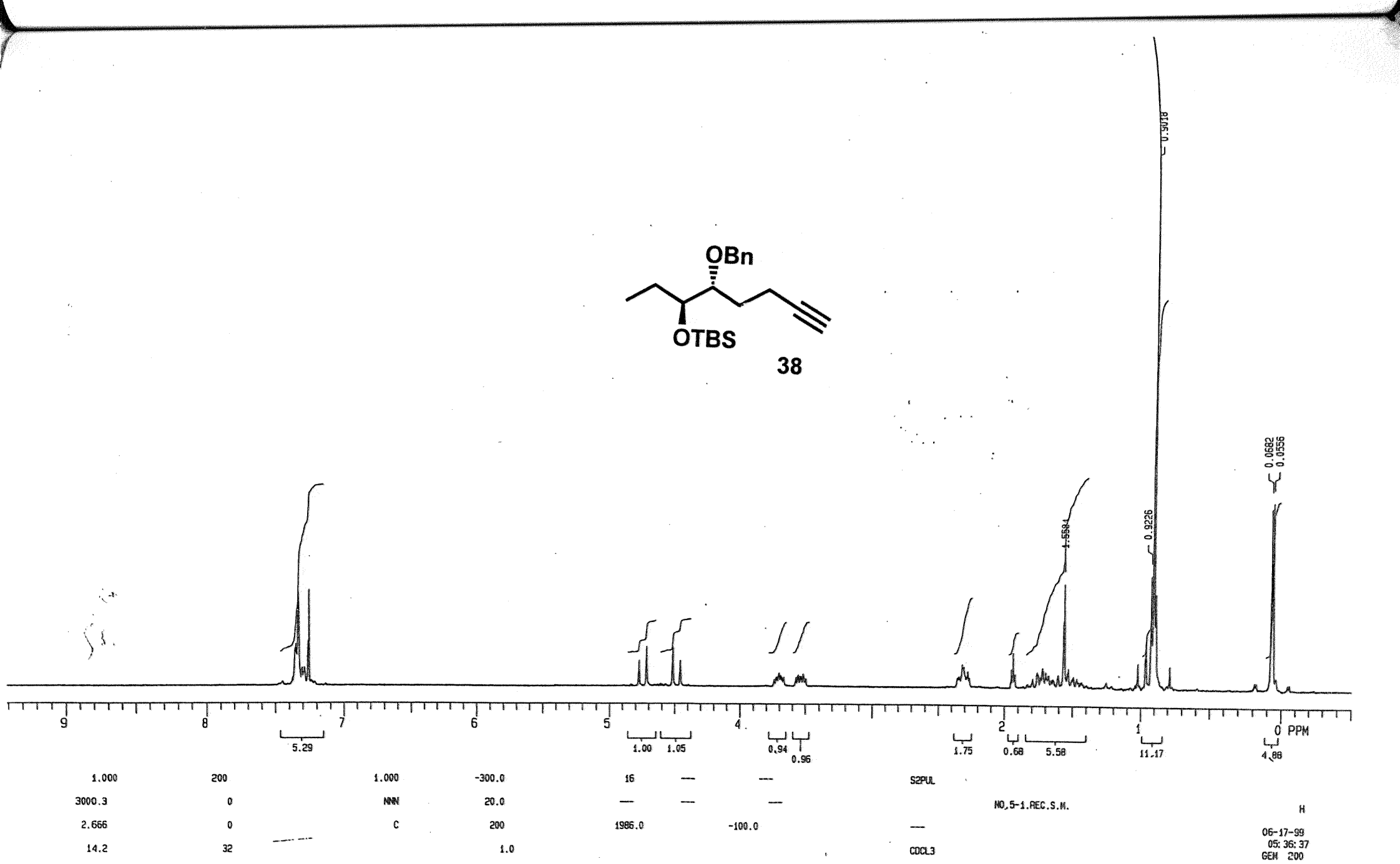
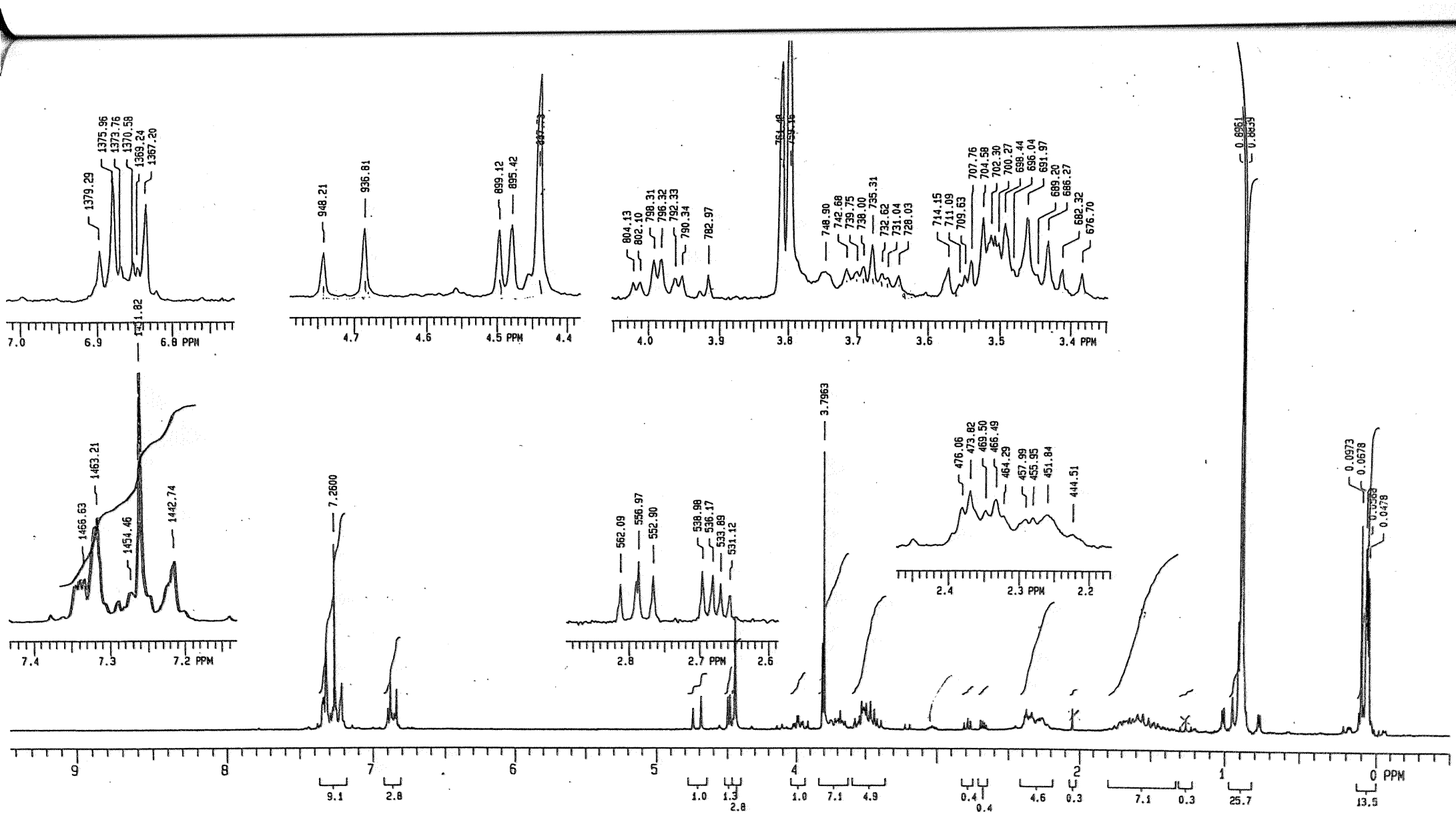
7.5
0.4
2.9
51.9
1.000
200
1.000
-300.0
16
S2PUL
3000.3
0
NNN
20.0
NO.4-22.REC.S.N.
H
2.666
0
C
200
1986.0
-100.0
CDCL3
05-31-99
07:23:42
GEM 200
14.2
32
1.0



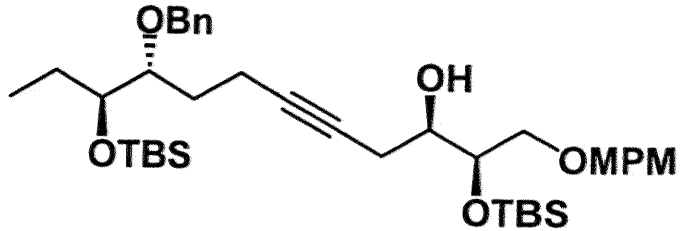
1.000	200	1.000	-300.0	16	—	—	S2PUL	
3000.3	0	NNN	20.0	—	—	—	NO.4-23.DES.PRO.	H
2.666	0	C	200	1986.0		-100.0	—	06-03-99 03:21:21
14.2	32		1.0				CDCL3	GEM 200


OBn
O
48
7.3343
7.2600
4.6669
4.5460
9
8
7
6
5
4
2
1
0 PPM
8.34
2.00
2.03
1.90
1.84
4.03
4.02
0.67
5.58
0.51
1.000 200 1.000 -300.0 16 S2PUL
3000.3 0 NNN 20.0
2.666 0 C 200 1986.0 -100.0
14.2 32 1.0 CDCL3
NO.4-28.DES.PRO.
H
06-07-99
21:07:27
GEM 200

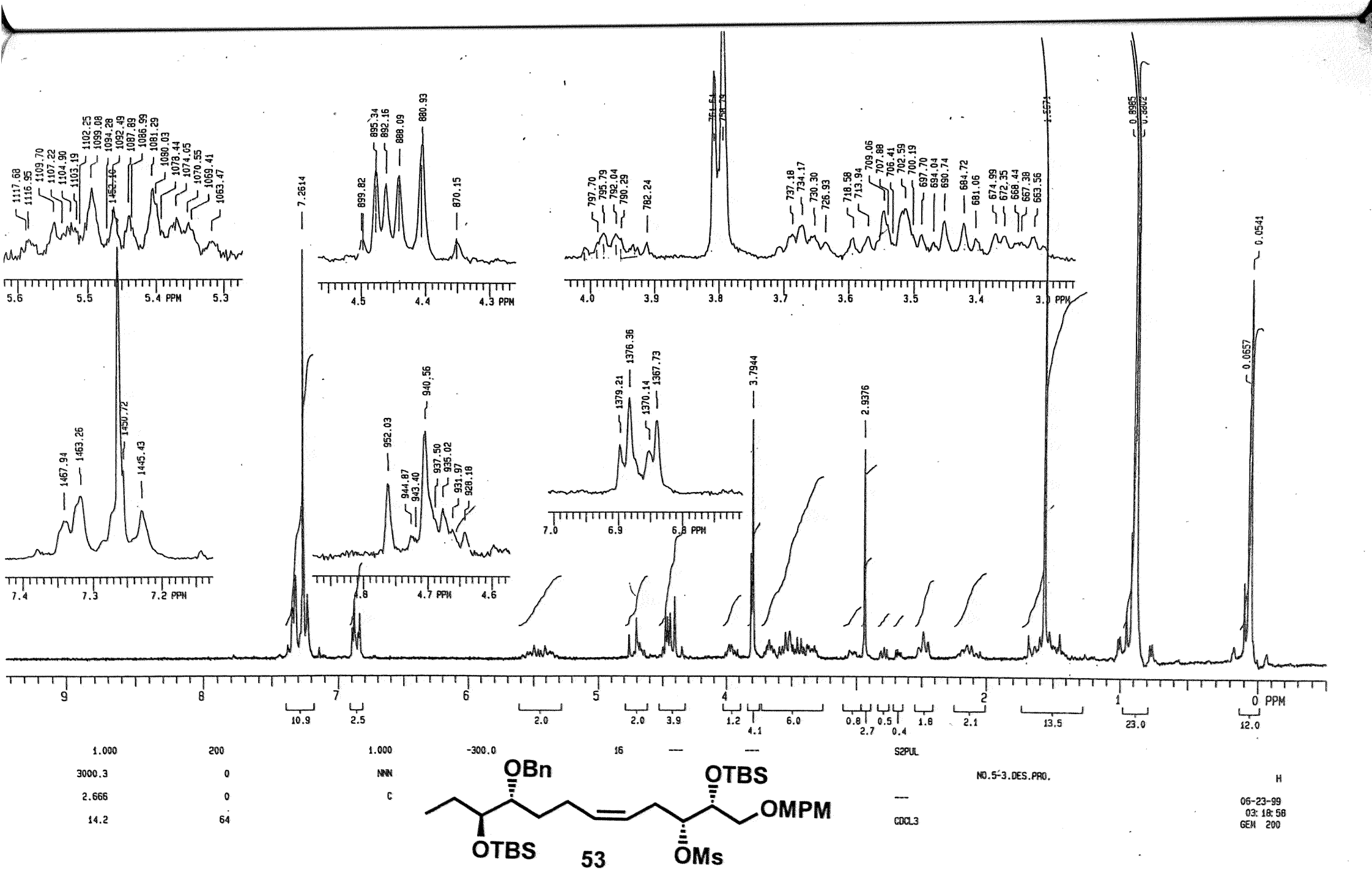

OBn
OTBS
38
0.5018
0.0682
0.0556
1.5584
0.9226
9
8
7
6
5
4
2
1
0 PPM
5.29
1.00
1.05
0.94
0.96
1.75
0.68
5.58
11.17
4.88
1.000 200 1.000 -300.0 16 — — S2PUL
3000.3 0 NNN 20.0 — — —
NO,5-1.REC.S.M.
H
2.666 0 C 200 1986.0 -100.0 —
06-17-99
05:36:37
14.2 32 1.0 CDCL3
GEM 200

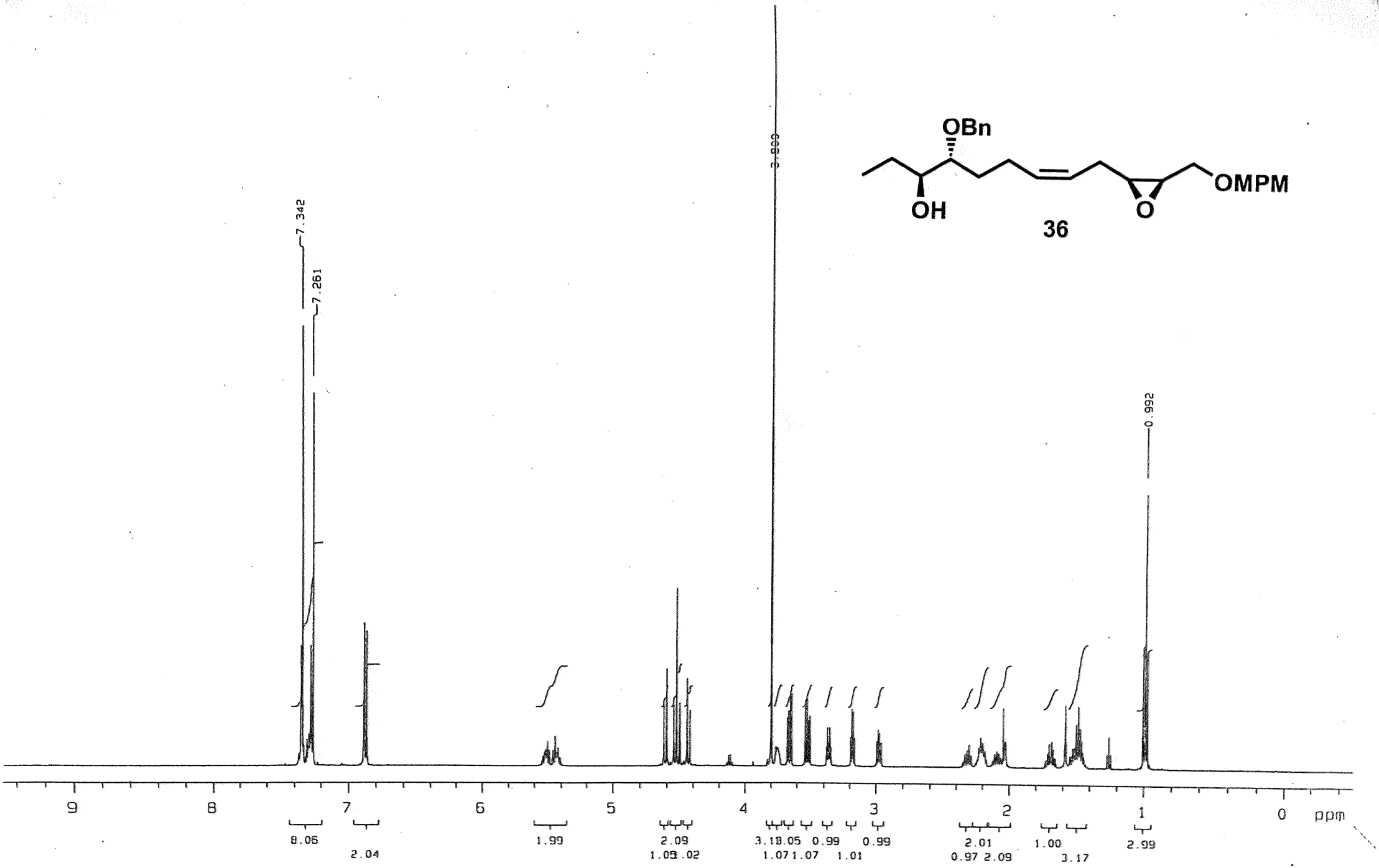


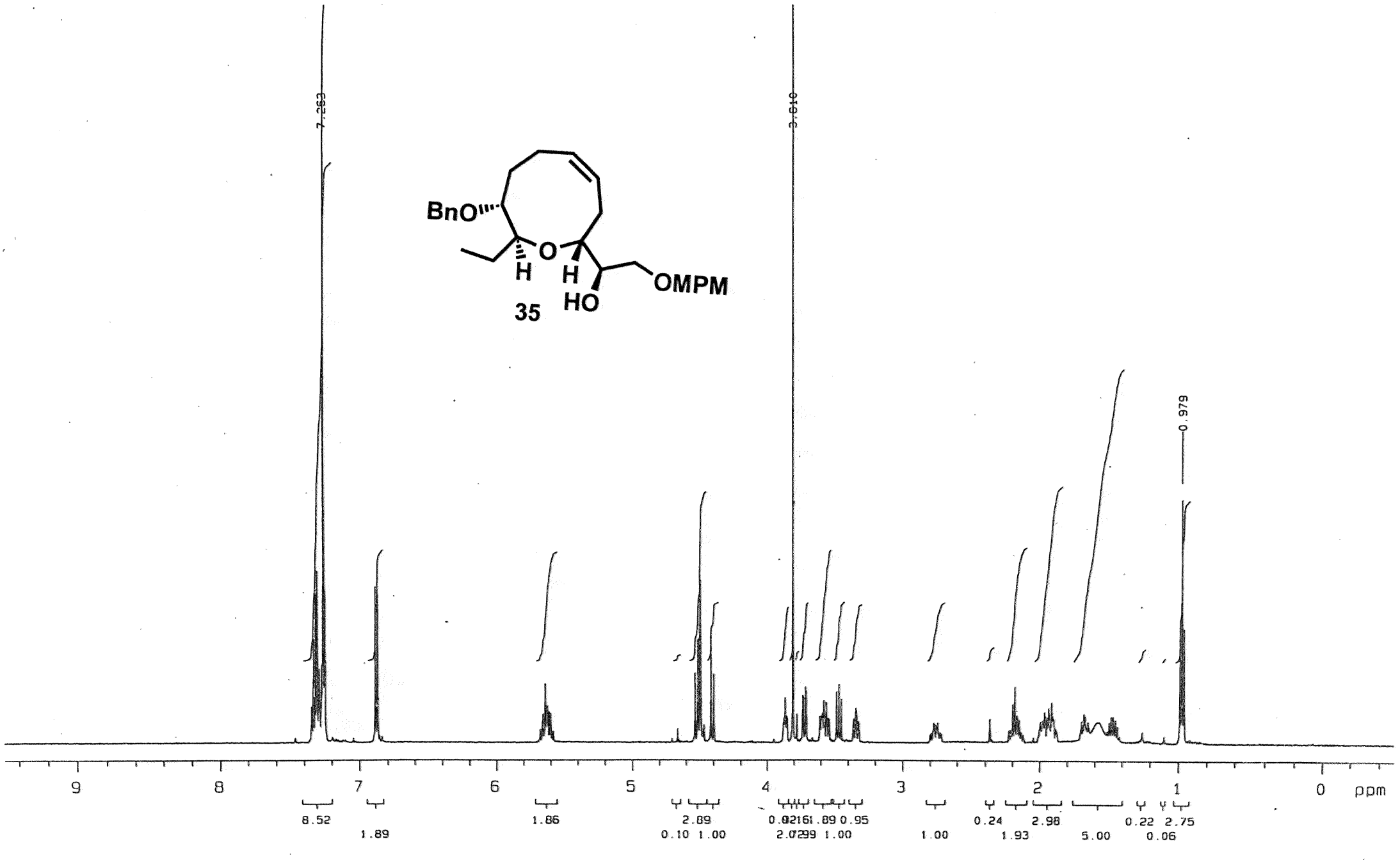
1.000	200	1.000	-300.0	16	—	—
3000.3	0	NNN	20.0	—	—	—
2.666	0	C	200	1986.0		-100.0
14.2	32		1.0			

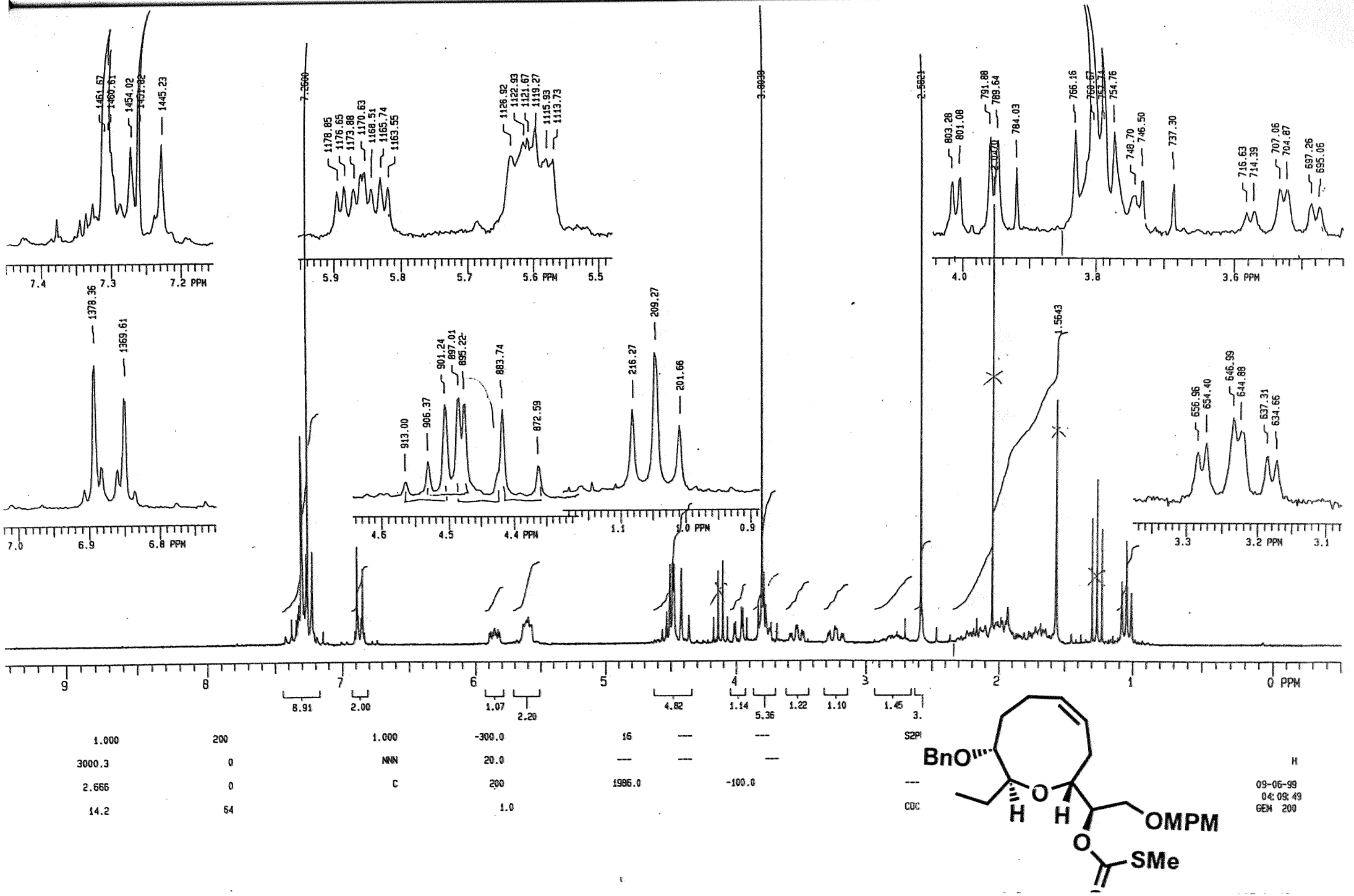


52


OBn
OTBS
OTBS
OMPM
OMs
53


OBn
OH
O
OMPM
36
7.342
7.261
3.803
0.992
9
8
7
6
5
4
3
2
1
0
ppm
8.06
2.04
1.99
2.09
1.09
1.02
3.18
1.07
3.05
1.07
0.99
1.01
0.99
2.01
0.97
2.09
1.00
3.17
2.99


7.263
3.610
0.979
BnO
O
H
H
HO
OMPM
35
9
8
7
6
5
4
3
2
1
0
ppm
8.52
1.89
1.86
2.89
0.10
1.00
0.95
1.00
0.24
1.93
2.98
5.00
0.22
2.75
0.06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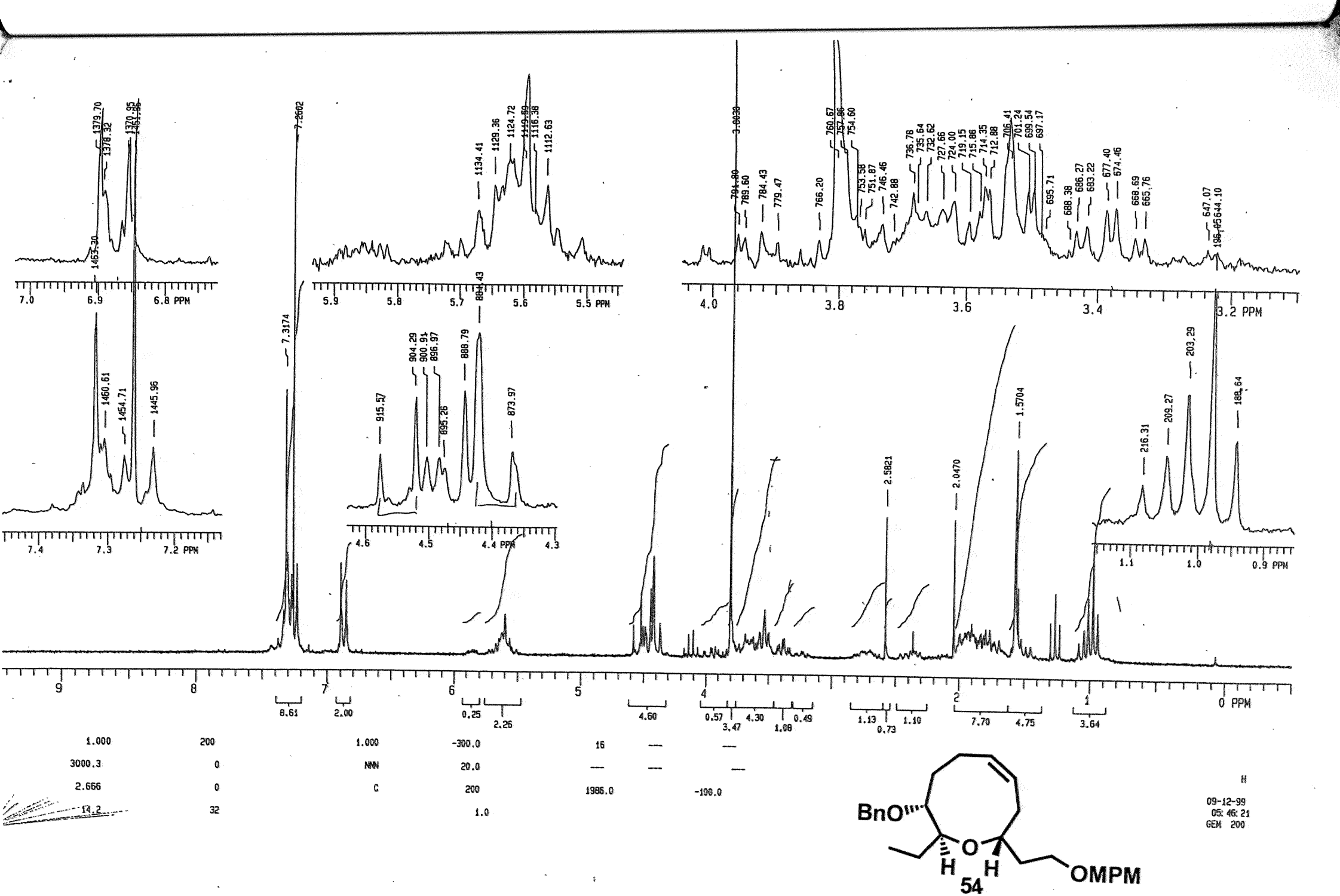
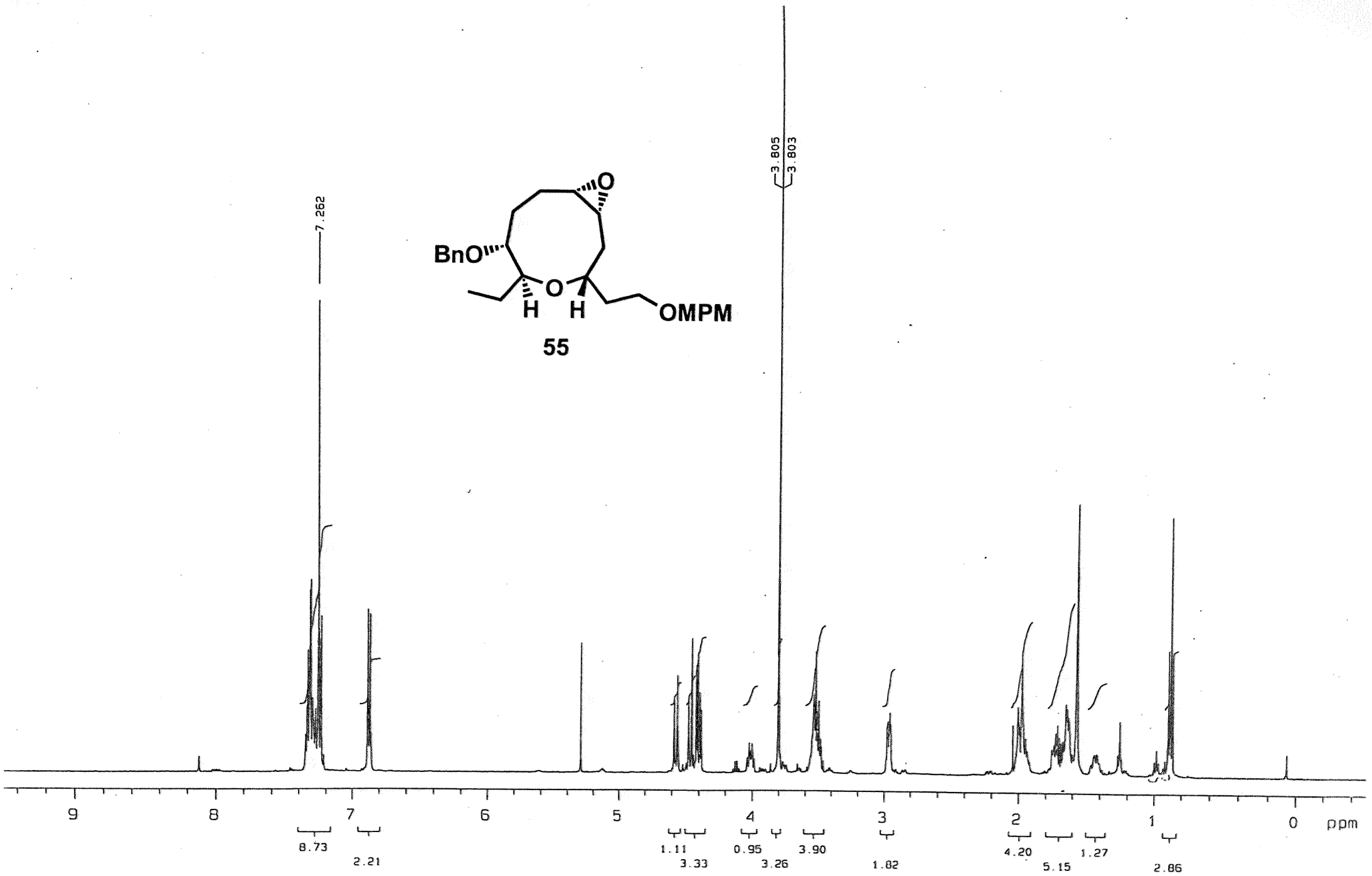
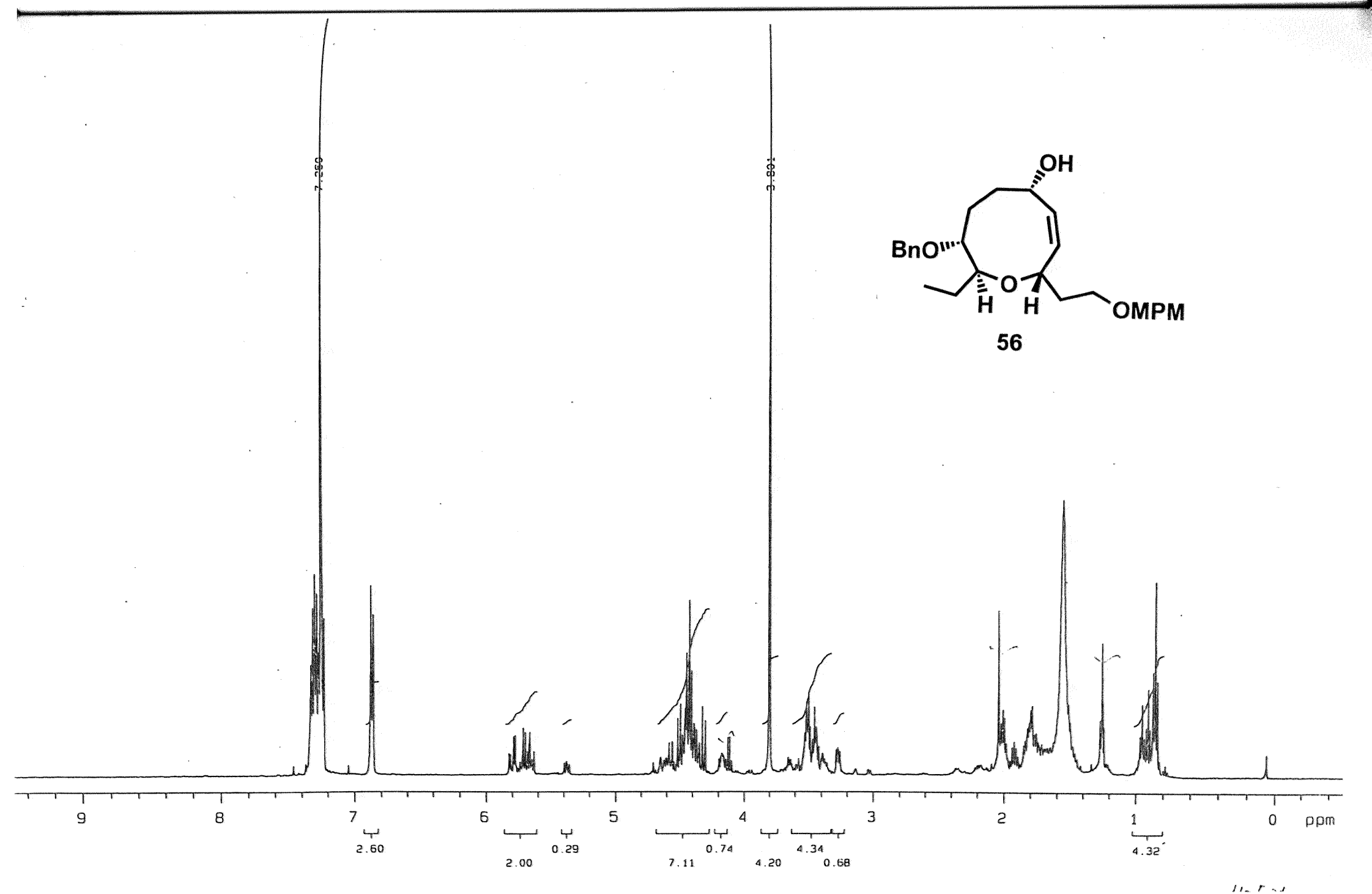
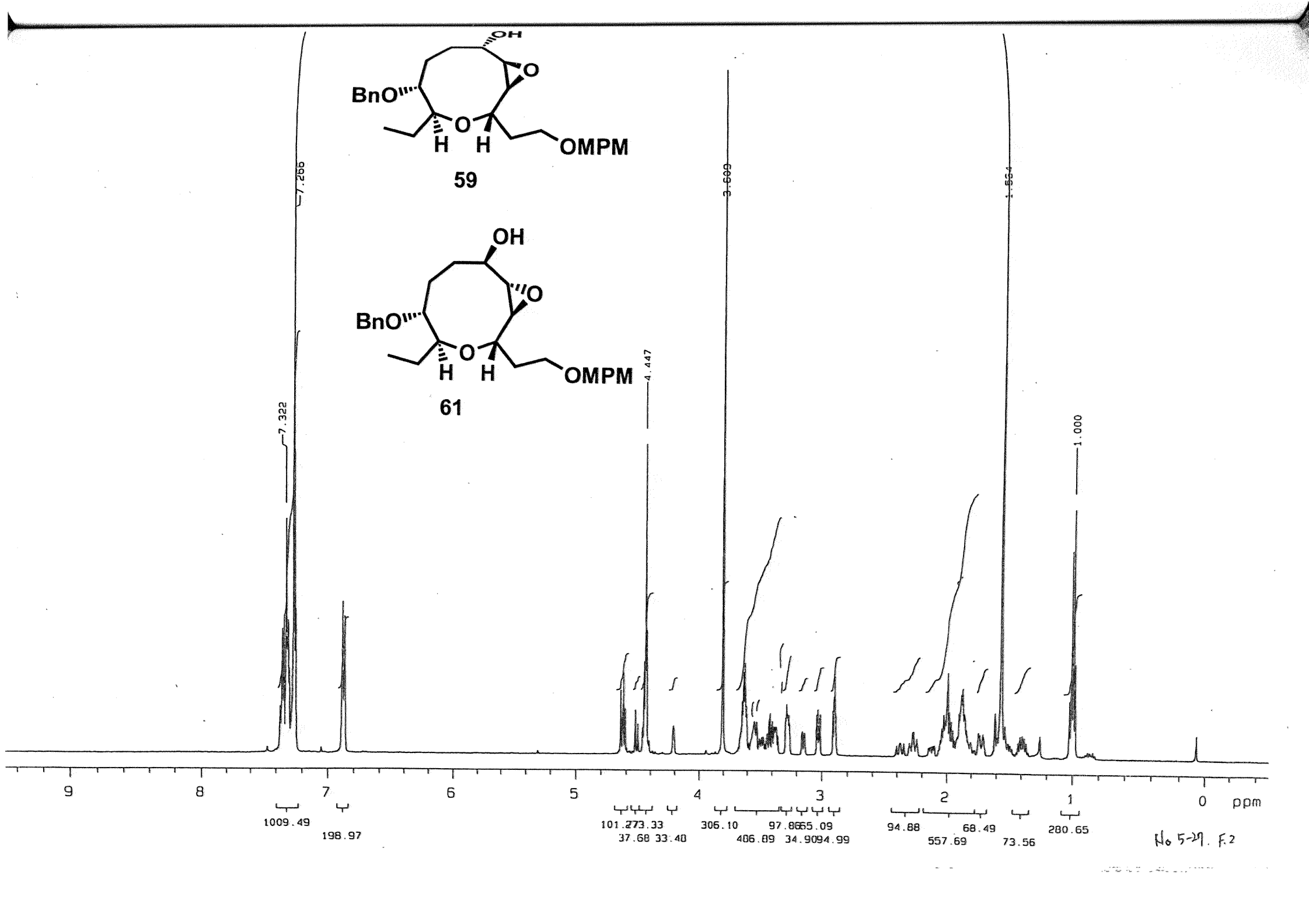
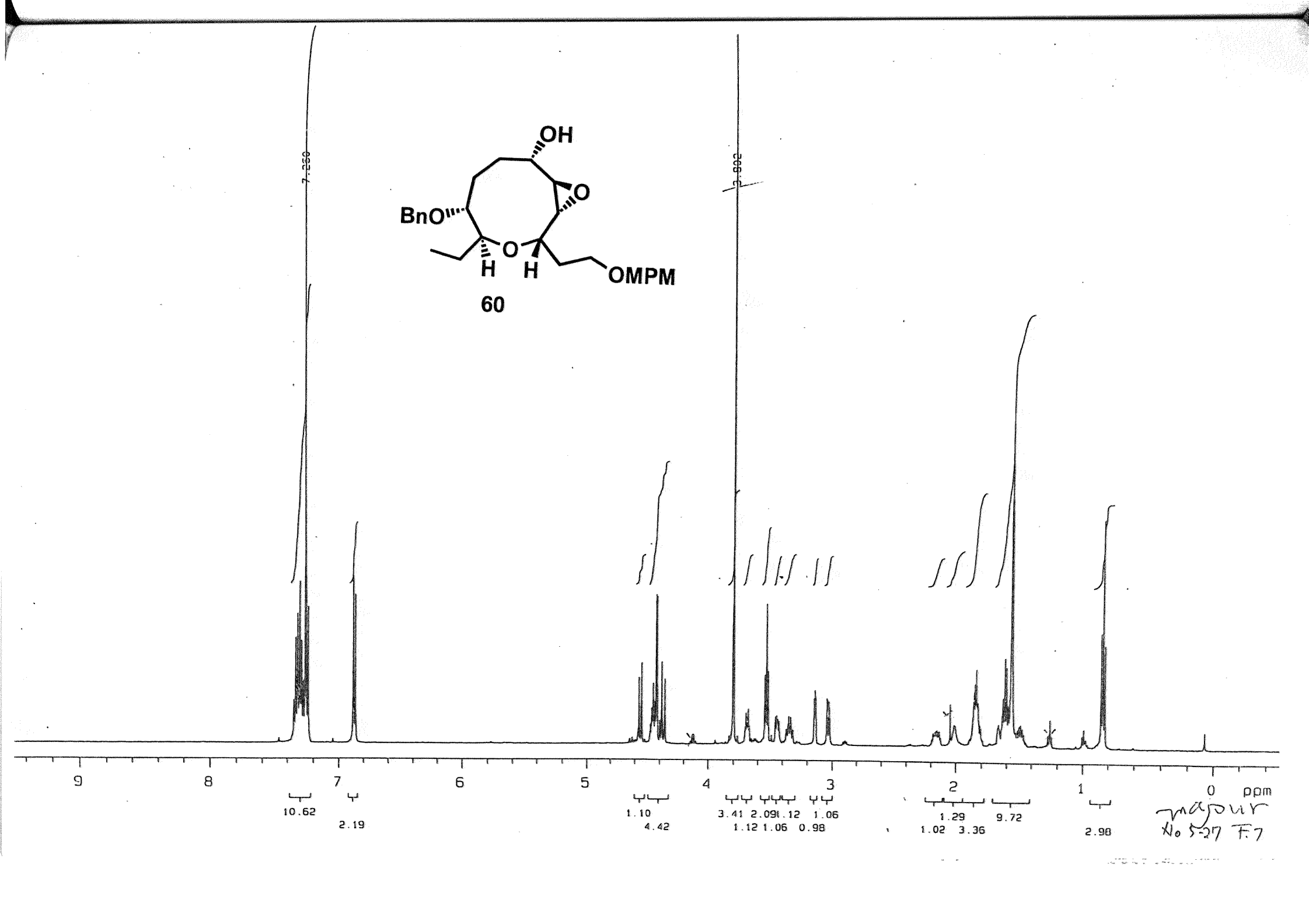
1460.61
1454.02
1445.23
7.4
7.3
7.2 PPM
7.2600
1178.85
1176.65
1173.88
1170.63
1168.51
1165.74
1163.55
1126.92
1122.93
1121.67
1119.27
1115.93
1113.73
5.9
5.8
5.7
5.6 PPM
5.5
3.8930
2.5821
803.28
801.08
791.88
789.64
784.03
766.16
760.67
754.76
748.70
745.50
737.30
716.63
714.39
707.06
704.87
697.26
695.05
4.0
3.8
3.6 PPM
1378.36
1369.61
7.0
6.9
6.8 PPM
913.00
906.37
901.24
897.01
895.22
883.74
872.59
216.27
209.27
201.66
4.6
4.5
4.4 PPM
1.1
1.0 PPM
0.9
1.5643
656.96
654.40
646.99
644.88
637.31
634.66
3.3
3.2 PPM
3.1
9
8
7
6
5
4
3
2
1
0 PPM
8.91
2.00
1.07
2.20
4.82
1.14
5.36
1.22
1.10
1.45
3.
1.000
200
1.000
-300.0
16
S2PI
3000.3
0
NNN
20.0
H
2.666
0
C
200
1986.0
-100.0
09-06-99
04:09:49
14.2
64
1.0
CDC
GEM 200
BnO
O
H
H
OMPM
O
SMe

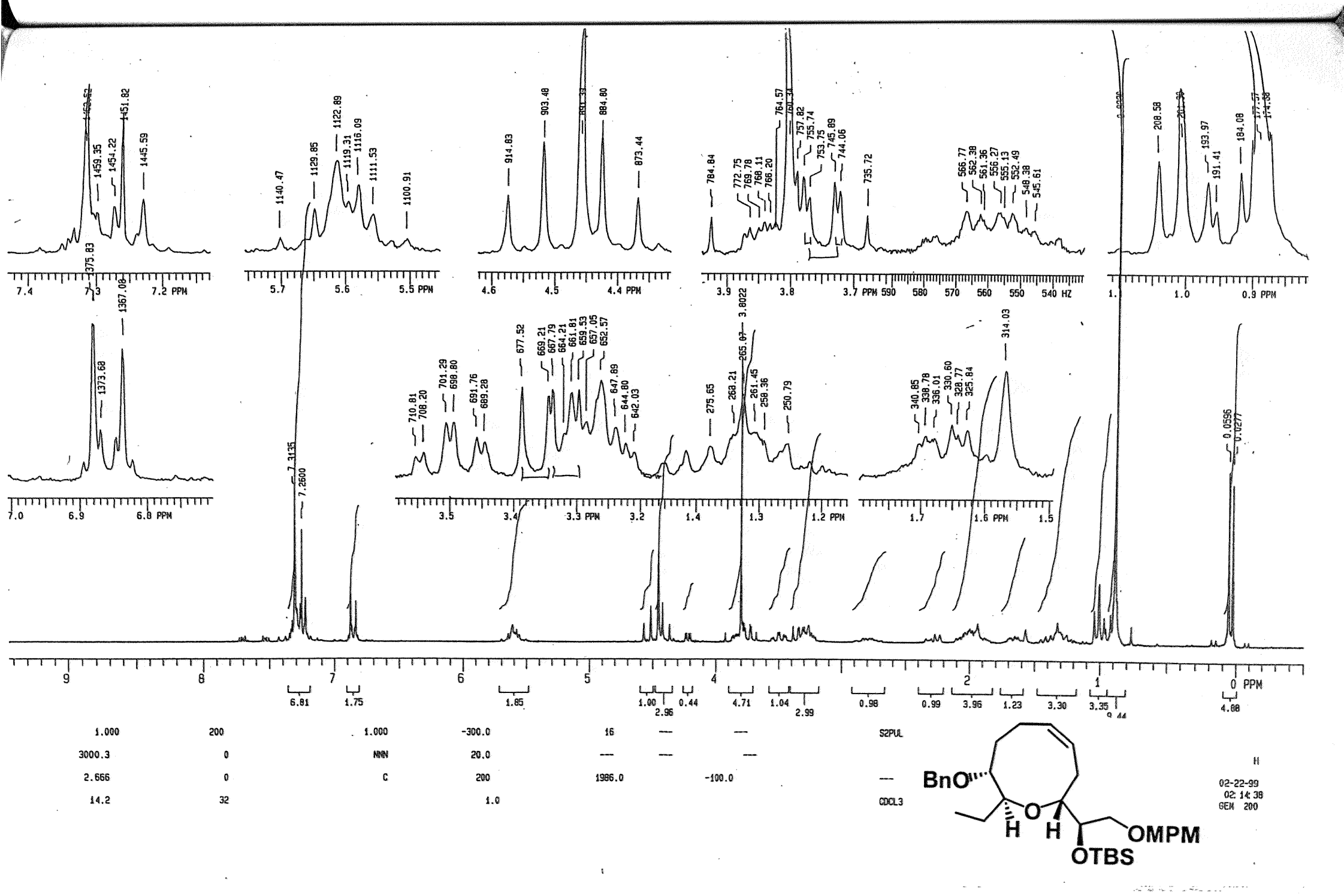

1379.70
1378.32
1370.95
1461.96
1463.30
7.2602
7.3174
1134.41
1129.36
1124.72
1119.69
1116.38
1112.63
3.8038
794.80
789.60
784.43
779.47
766.20
760.67
757.86
754.60
753.58
751.87
746.46
742.88
736.78
735.64
732.62
727.66
724.00
719.15
715.86
714.35
712.88
706.41
701.24
699.54
697.17
695.71
688.38
686.27
683.22
677.40
674.46
668.69
665.76
647.07
644.10
1460.61
1454.71
1445.96
915.57
904.29
900.91
896.97
895.26
888.79
884.43
873.97
2.5821
2.0470
1.5704
216.31
209.27
203.29
188.64
8.61
2.00
0.25
2.26
4.60
0.57
3.47
4.30
1.08
0.49
1.13
0.73
1.10
7.70
4.75
3.64
1.000
200
1.000
-300.0
16
3000.3
0
NNN
20.0
2.666
0
C
200
1986.0
-100.0
14.2
32
1.0
BnO
O
H
H
OMPM
54
H
09-12-99
05:46:21
GEM 200

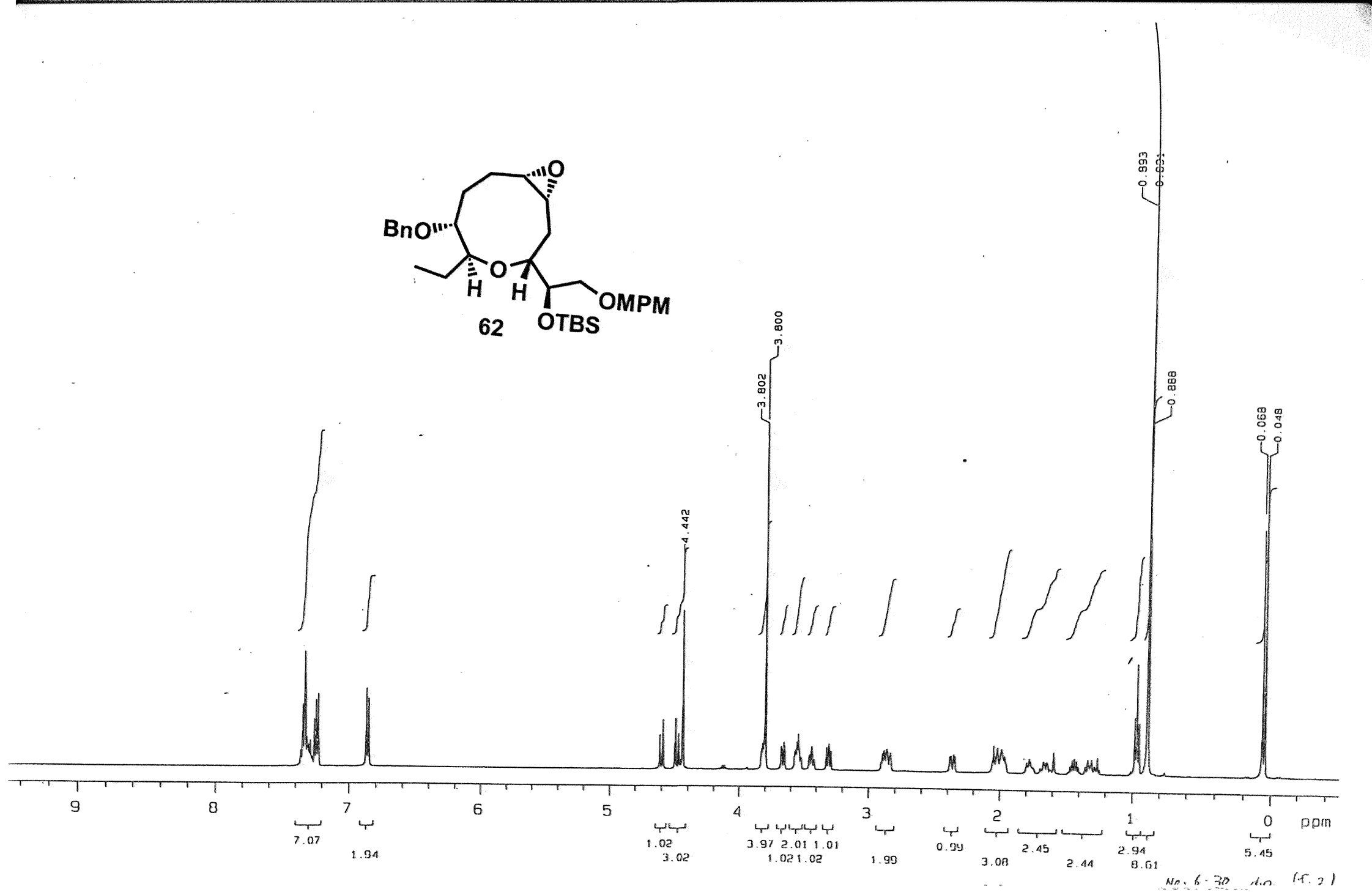

7.262
3.805
3.803
BnO
O
O
H
H
OMPM
55
9
8
7
6
5
4
3
2
1
0
ppm
8.73
2.21
1.11
3.33
0.95
3.26
3.90
1.82
4.20
5.15
1.27
2.86

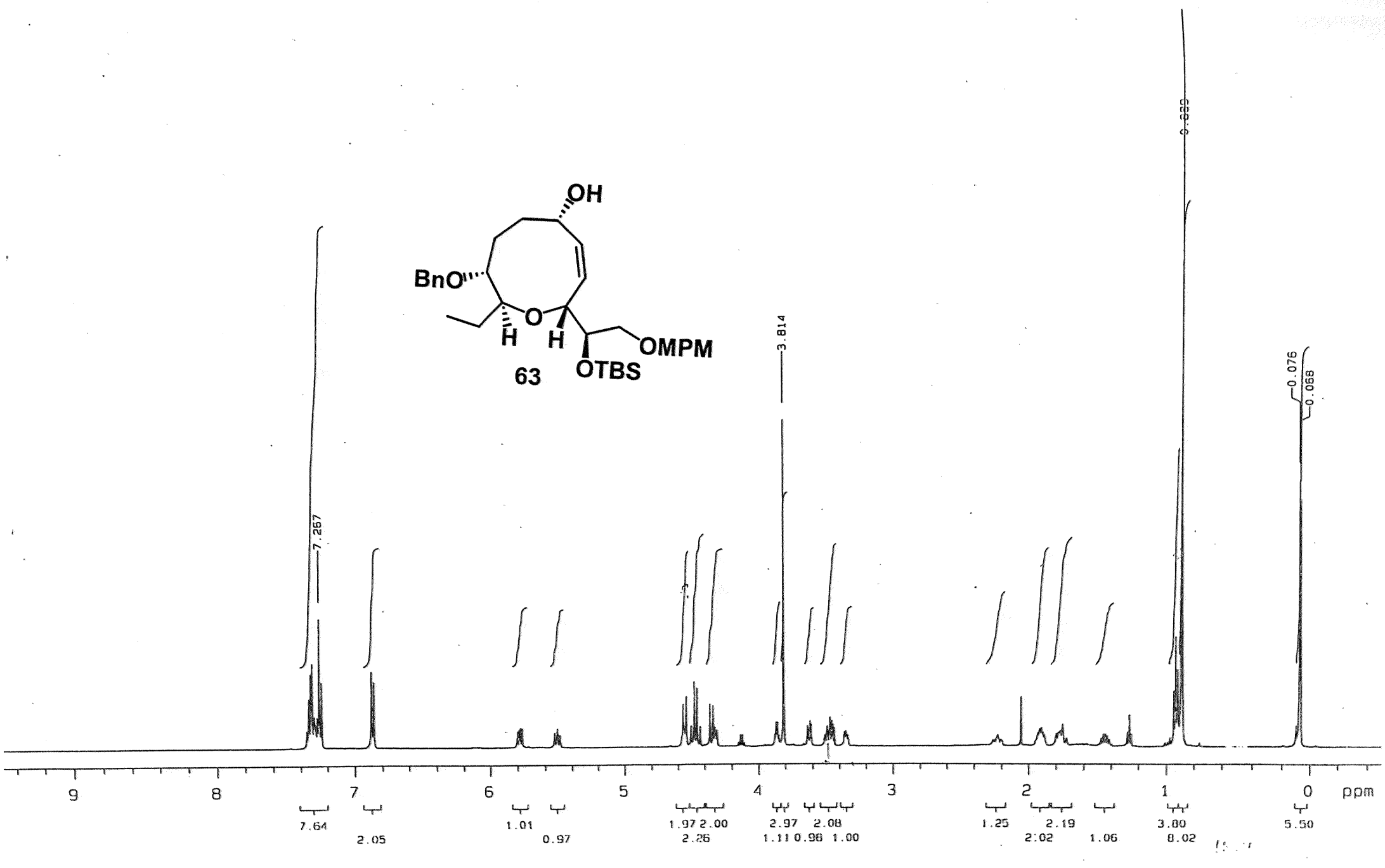

7.260
3.801
OH
BnO
O
H
H
OMPM
56
9
8
7
6
5
4
3
2
1
0
ppm
2.60
2.00
0.29
7.11
0.74
4.20
4.34
0.68
4.32

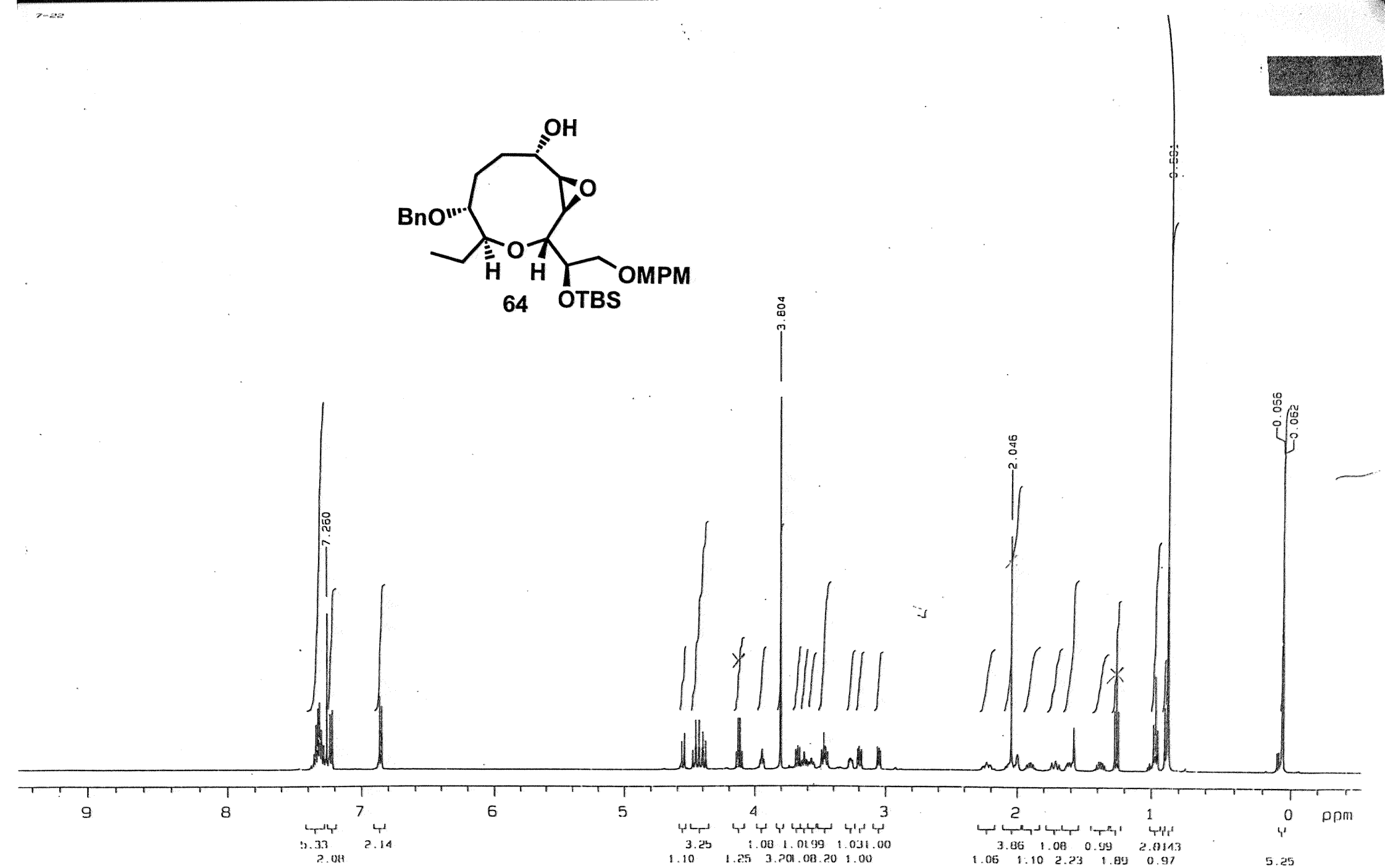

OH
O
BnO
O
H H
OMPM
59
OH
O
BnO
O
H H
OMPM
61
7.256
7.322
4.447
3.609
1.854
1.000
9
8
7
6
5
4
3
2
1
0
ppm
1009.49
198.97
101.27
73.33
37.68 33.40
306.10
97.86
65.09
406.89 34.90
94.99
94.88
68.49
557.69
73.56
280.65
No 5-29. F.2

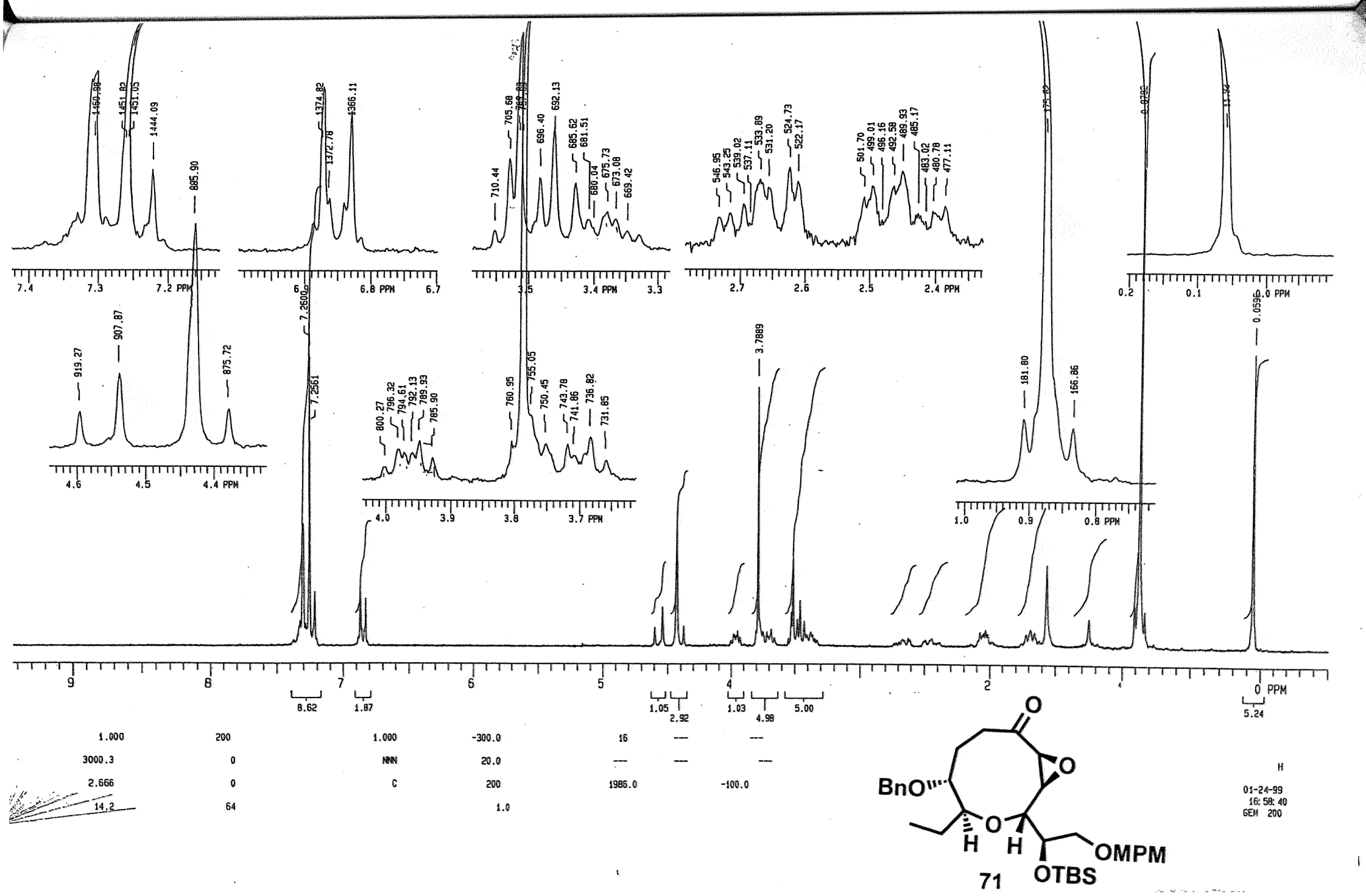

OH
BnO
O
O
H
H
OMPM
60
7.330
2.882
9
8
7
6
5
4
3
2
1
0
ppm
10.62
2.19
1.10
4.42
3.41
2.09
1.12
1.06
1.12
1.06
0.98
1.29
1.02
3.36
9.72
2.98
major
No 5-27 F.7

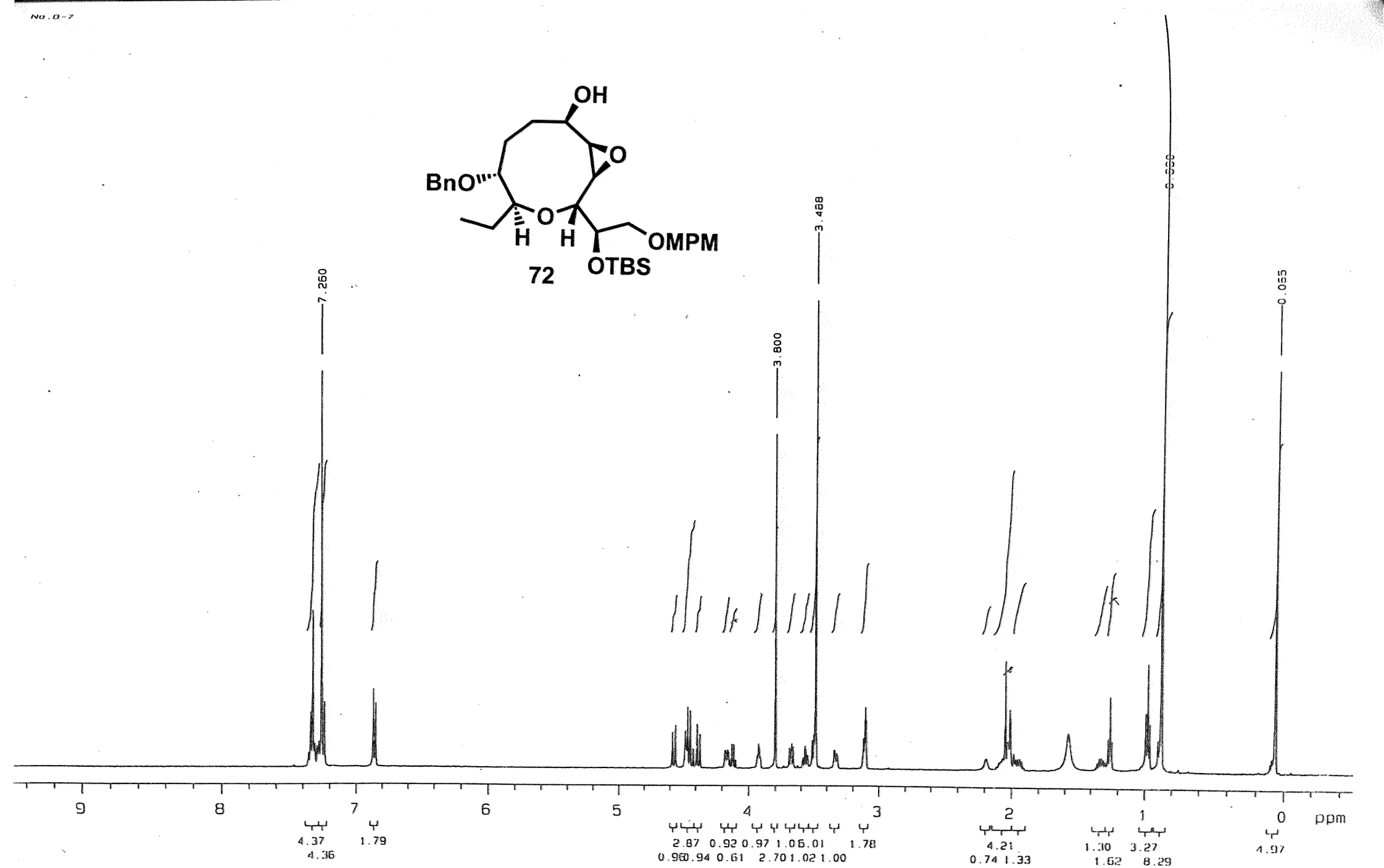

1459.35
1454.22
1451.82
1445.59
1140.47
1129.85
1122.89
1119.31
1116.09
1111.53
1100.91
914.83
903.48
884.80
873.44
784.84
772.75
769.78
768.11
766.20
764.57
757.82
755.74
753.75
745.89
744.06
735.72
566.77
562.38
561.36
556.27
555.13
552.49
548.38
545.61
208.58
193.97
191.41
184.08
1373.68
1367.08
7.3135
7.2600
710.81
708.20
701.29
698.80
691.76
689.28
677.52
669.21
667.79
664.21
661.81
659.53
657.05
652.57
647.89
644.80
642.03
275.65
268.21
265.87
261.45
258.36
250.79
3.8022
340.85
338.78
336.01
330.60
328.77
325.84
314.03
0.0596
0.0277
6.81
1.75
1.85
1.00
0.44
2.96
4.71
1.04
2.99
0.98
0.99
3.96
1.23
3.30
3.35
4.88
PPM
1.000
200
1.000
-300.0
16
S2PUL
3000.3
0
MNN
20.0
2.666
0
C
200
1986.0
-100.0
CDCL3
14.2
32
1.0
BnO
O
H
H
OMPM
OTBS
H
02-22-99
02:14:38
GEM 200

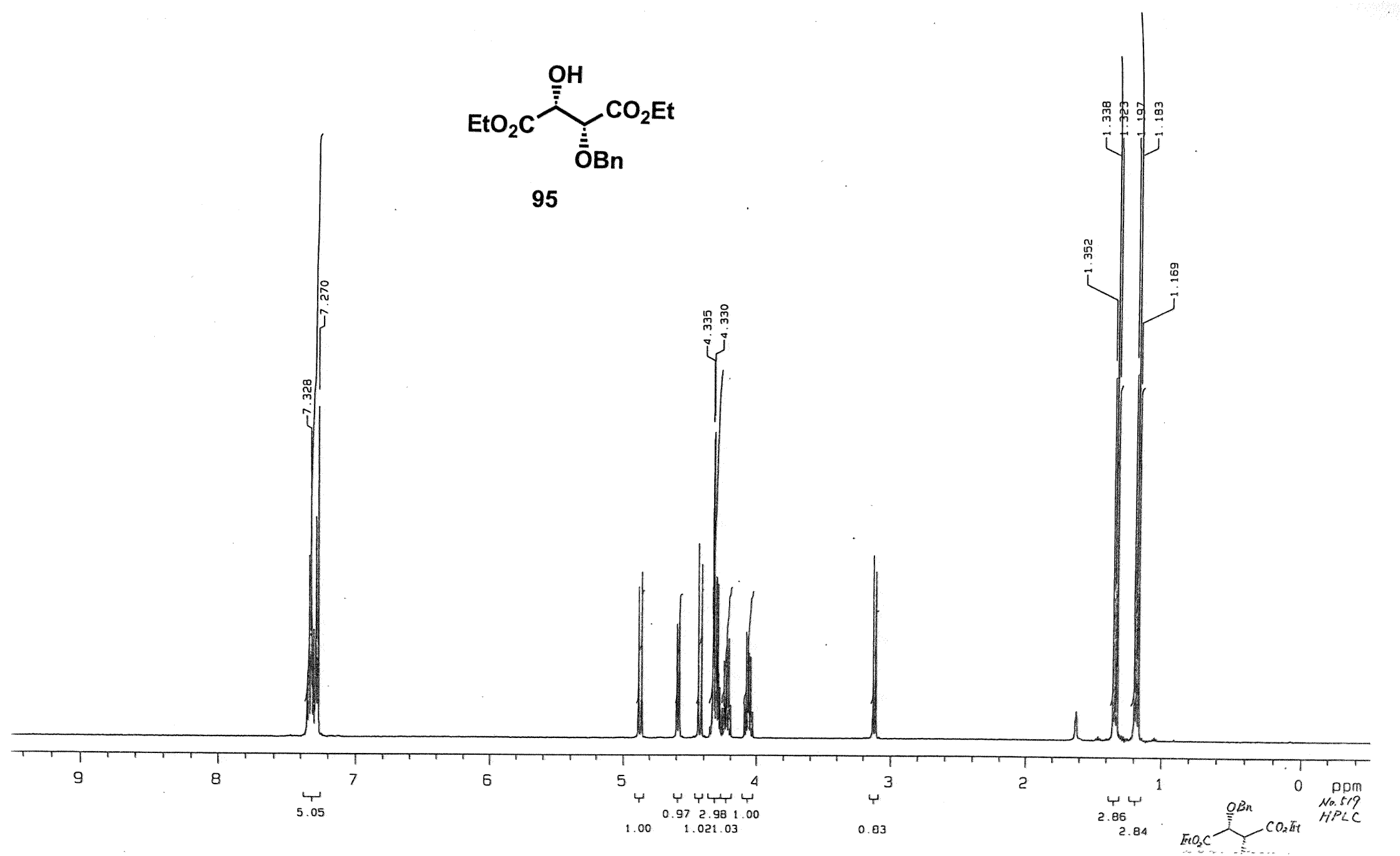

BnO
O
H
O
H
OMPM
OTBS
62
0.893
0.833
3.800
3.802
0.888
0.068
0.048
4.442
9
8
7
6
5
4
3
2
1
0
ppm
7.07
1.94
1.02
3.02
3.97
2.01
1.01
1.02
1.02
1.99
0.99
3.08
2.45
2.44
2.94
8.61
5.45

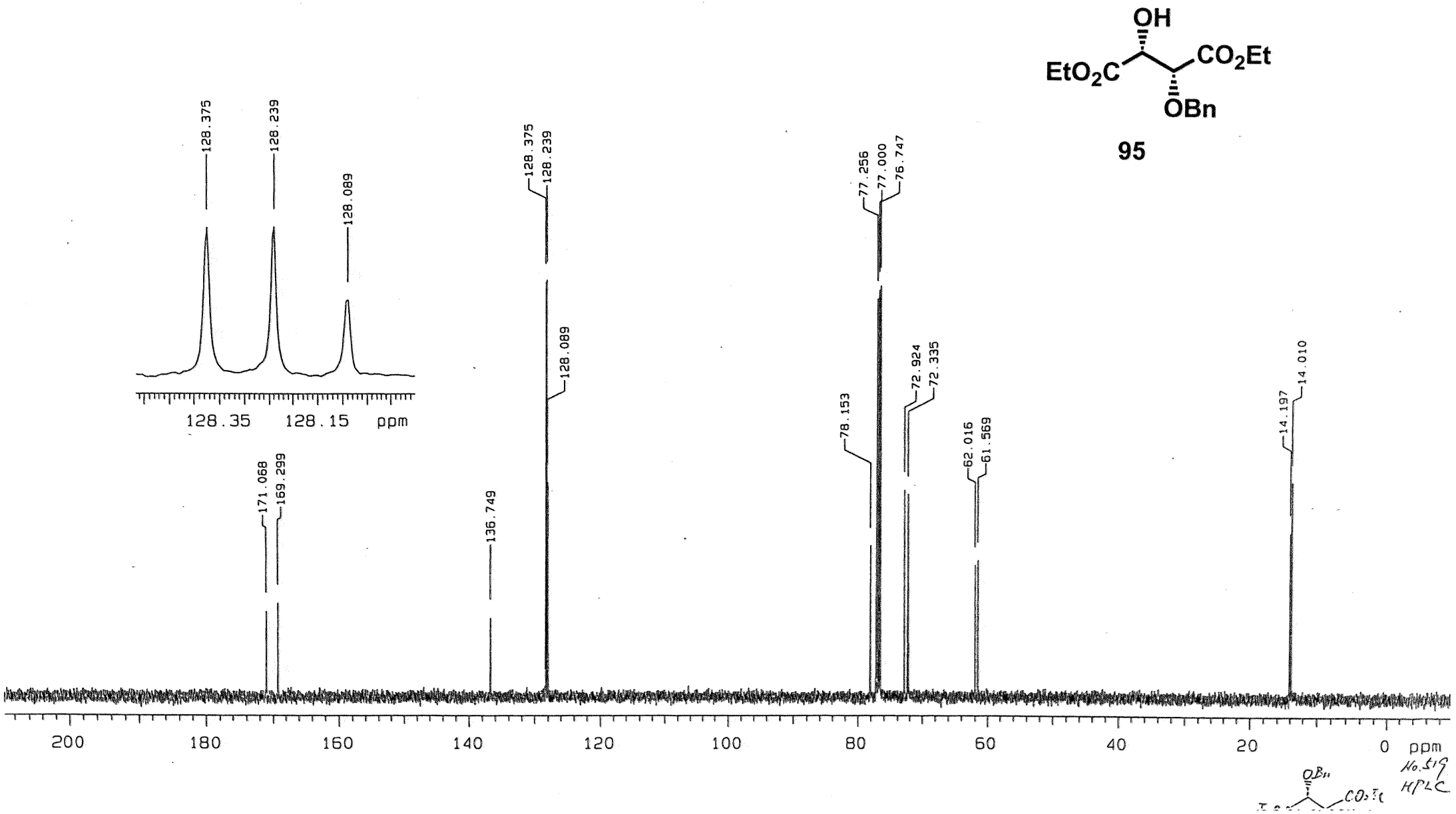

OH
BnO
O
H
H
OMPM
OTBS
63
7.267
3.814
0.889
0.076
0.068
9
8
7
6
5
4
3
2
1
0
ppm
7.64
2.05
1.01
0.97
1.97
2.00
2.26
2.97
2.08
1.11
0.98
1.00
1.25
2.19
2.02
1.06
3.80
8.02
5.50

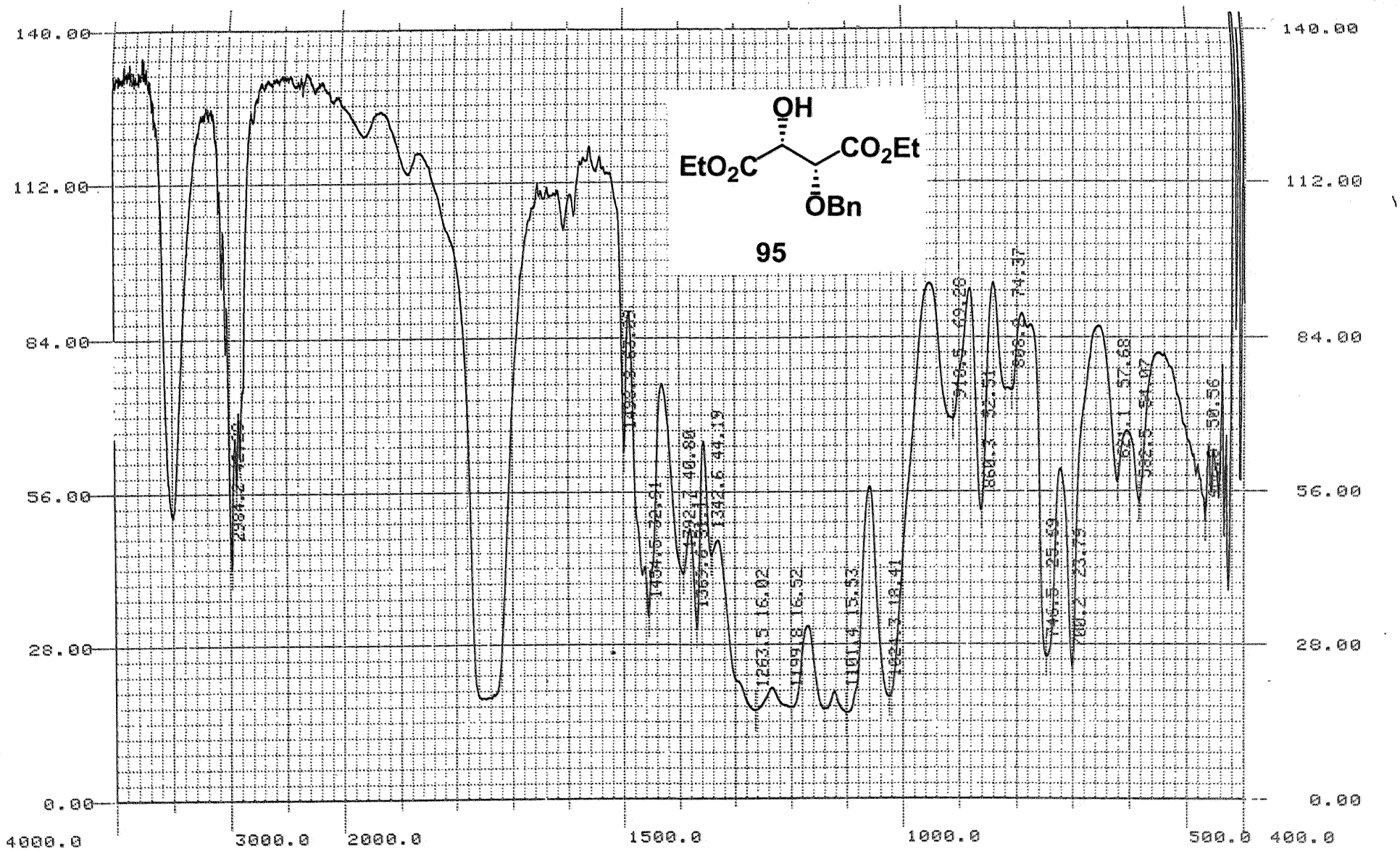

OH
O
BnO
O
H
H
OMPM
OTBS
64
7.260
3.804
2.046
0.056
0.052
9
8
7
6
5
4
3
2
1
0
ppm


1460.98
1451.82
1451.05
1444.09
885.90
919.27
907.87
875.72
1374.82
1372.78
1366.11
710.44
705.68
692.13
696.40
685.62
681.51
680.04
675.73
673.08
669.42
546.95
543.25
539.02
537.11
533.89
531.20
524.73
522.17
501.70
499.01
496.16
492.58
489.93
485.17
483.02
480.78
477.11
7.2600
7.2561
800.27
796.32
794.61
792.13
789.93
785.90
760.95
755.05
750.45
743.78
741.86
736.82
731.85
3.7889
181.80
166.86
176.82
0.0795
11.36
0.0598
9 8 7 6 5 4 2 0 PPM
8.62
1.87
1.05
2.92
1.03
4.98
5.00
5.24
1.000 200 1.000 -300.0 16
3000.3 0 NNN 20.0
2.666 0 C 200 1985.0 -100.0
14.2 64 1.0
H
01-24-99
16:58:40
GEM 200
BnO
O
O
H
O
H
OMPM
OTBS
71

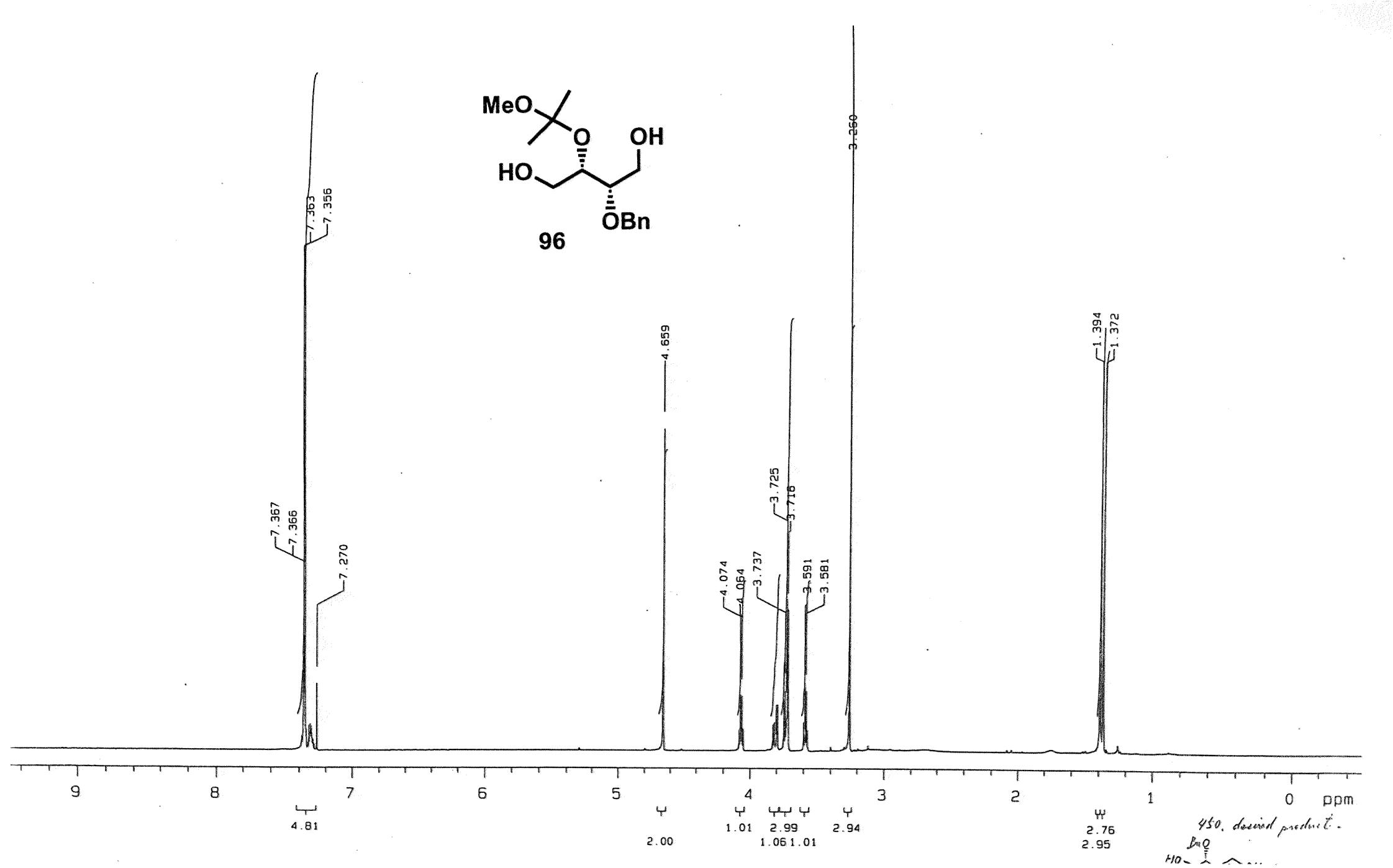

No.0-7
OH
O
BnO
O
H
H
OMPM
OTBS
72
7.260
3.800
3.488
3.350
0.055
9
8
7
6
5
4
3
2
1
0
ppm
4.37
4.36
1.79
2.87
0.96
0.92
0.94
0.97
0.61
1.06
2.70
1.01
1.02
1.78
1.00
4.21
0.74
1.33
1.30
1.62
3.27
8.29
4.97

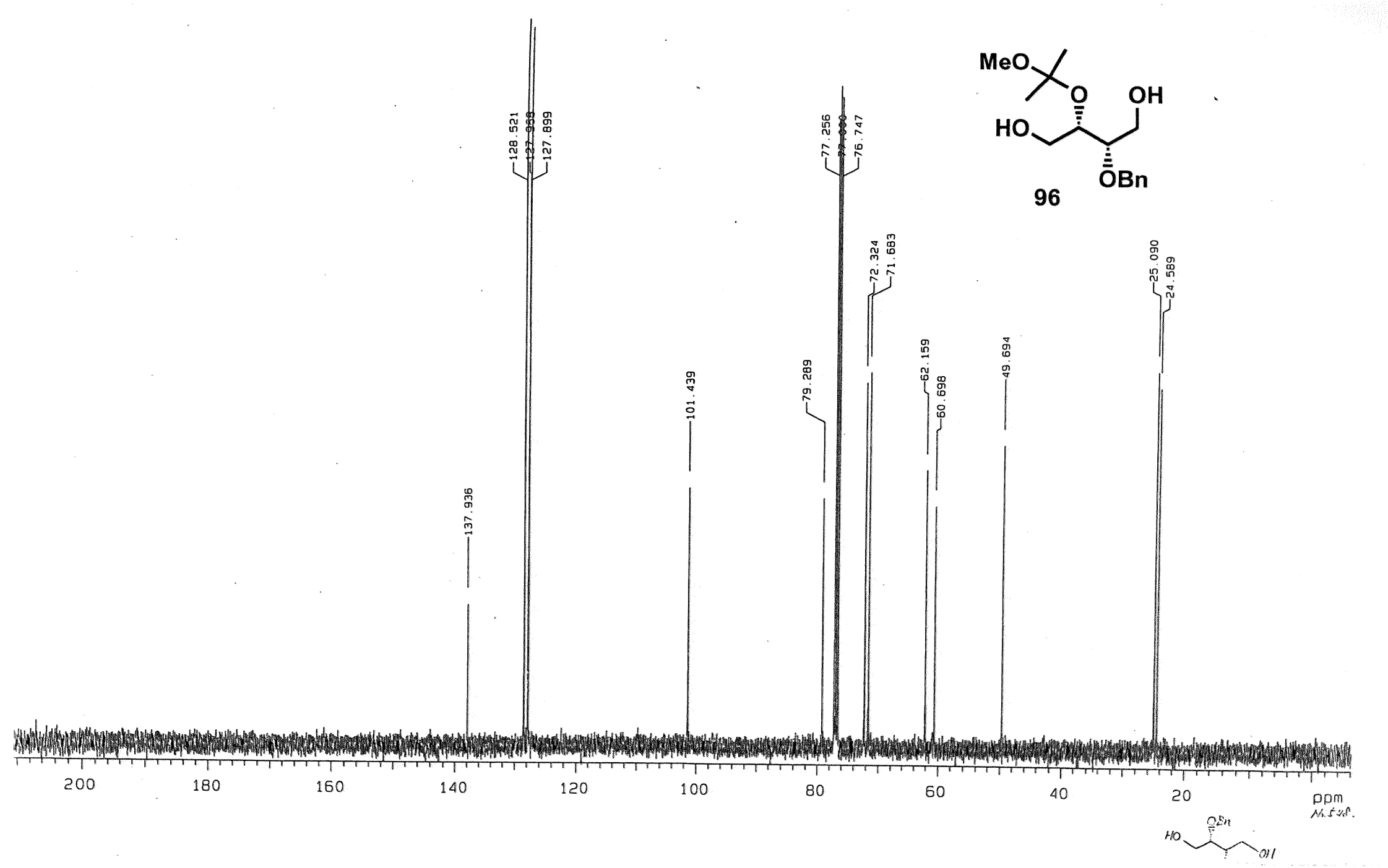

OH
EtO2C
CO2Et
OBn
95
7.328
7.270
4.335
4.330
1.352
1.338
1.323
1.197
1.183
1.169
9
8
7
6
5
4
3
2
1
0
ppm
5.05
1.00
0.97
2.98
1.00
1.02
1.03
0.83
2.86
2.84
No. 519
HPLC

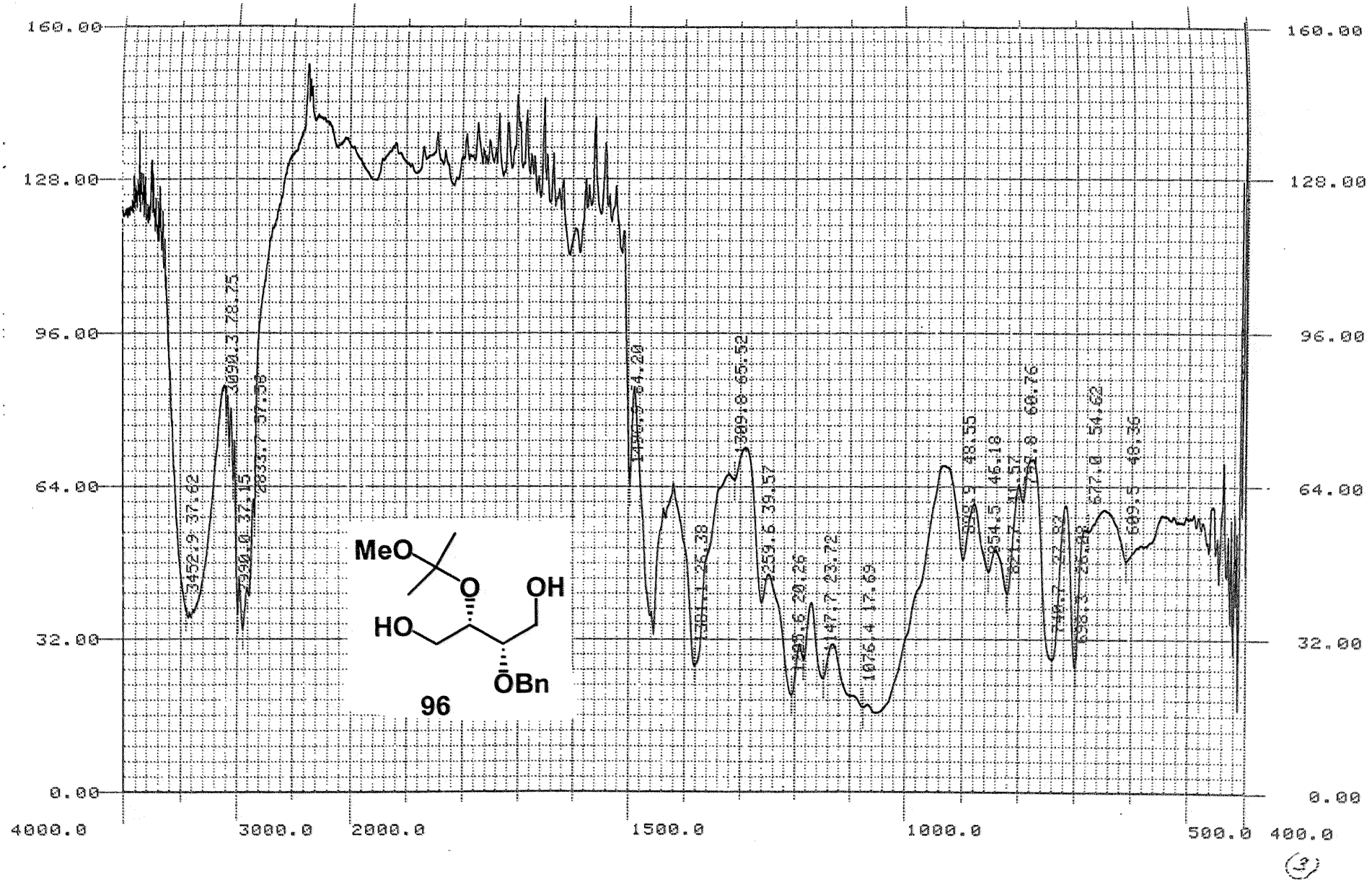

OH
EtO2C
CO2Et
OBn
95
128.375
128.239
128.089
128.35
128.15
ppm
171.068
169.299
136.749
128.375
128.239
128.089
77.256
77.000
76.747
78.153
72.924
72.335
62.016
61.569
14.197
14.010
200
180
160
140
120
100
80
60
40
20
0
ppm
No.519
HPLC



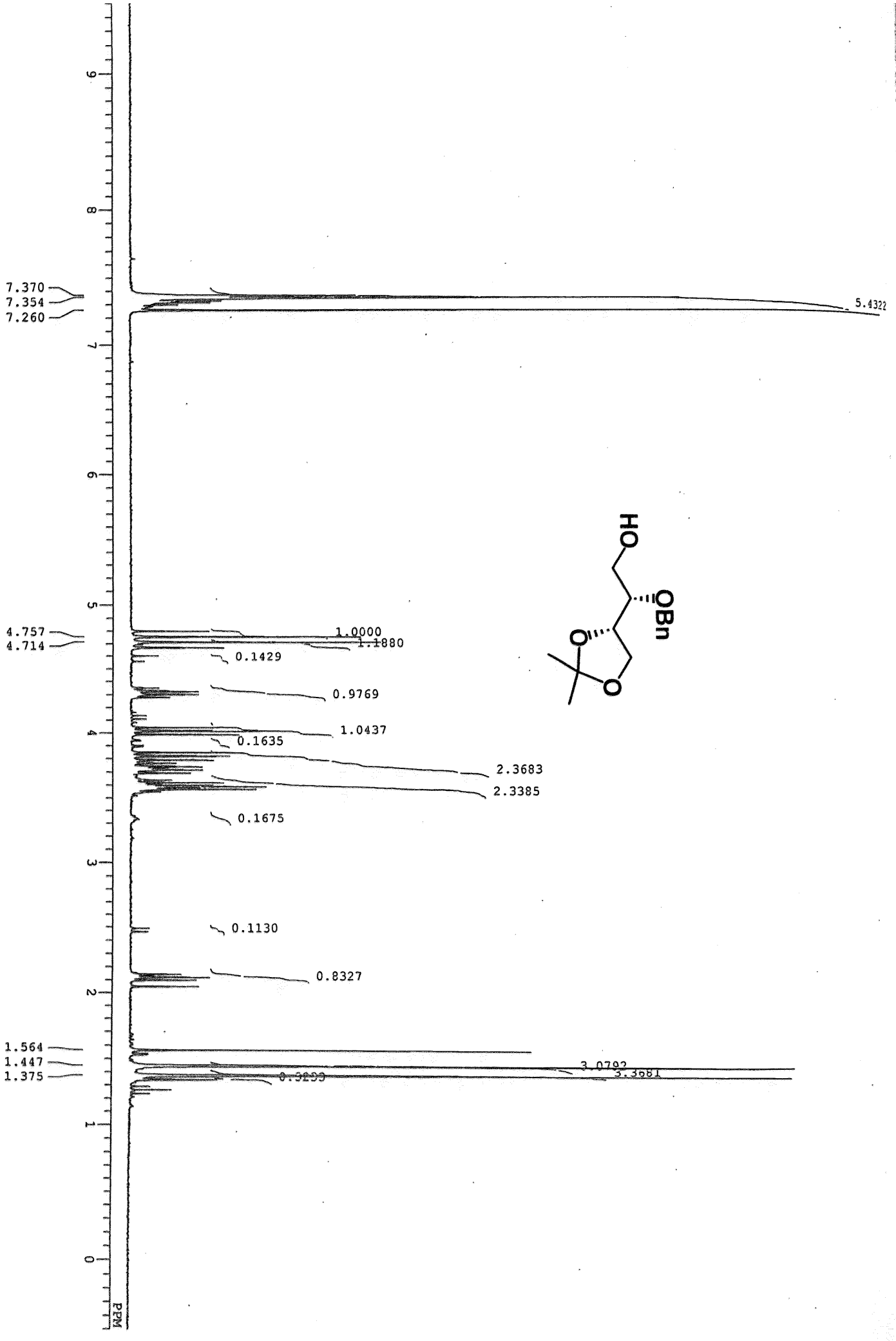
(1)

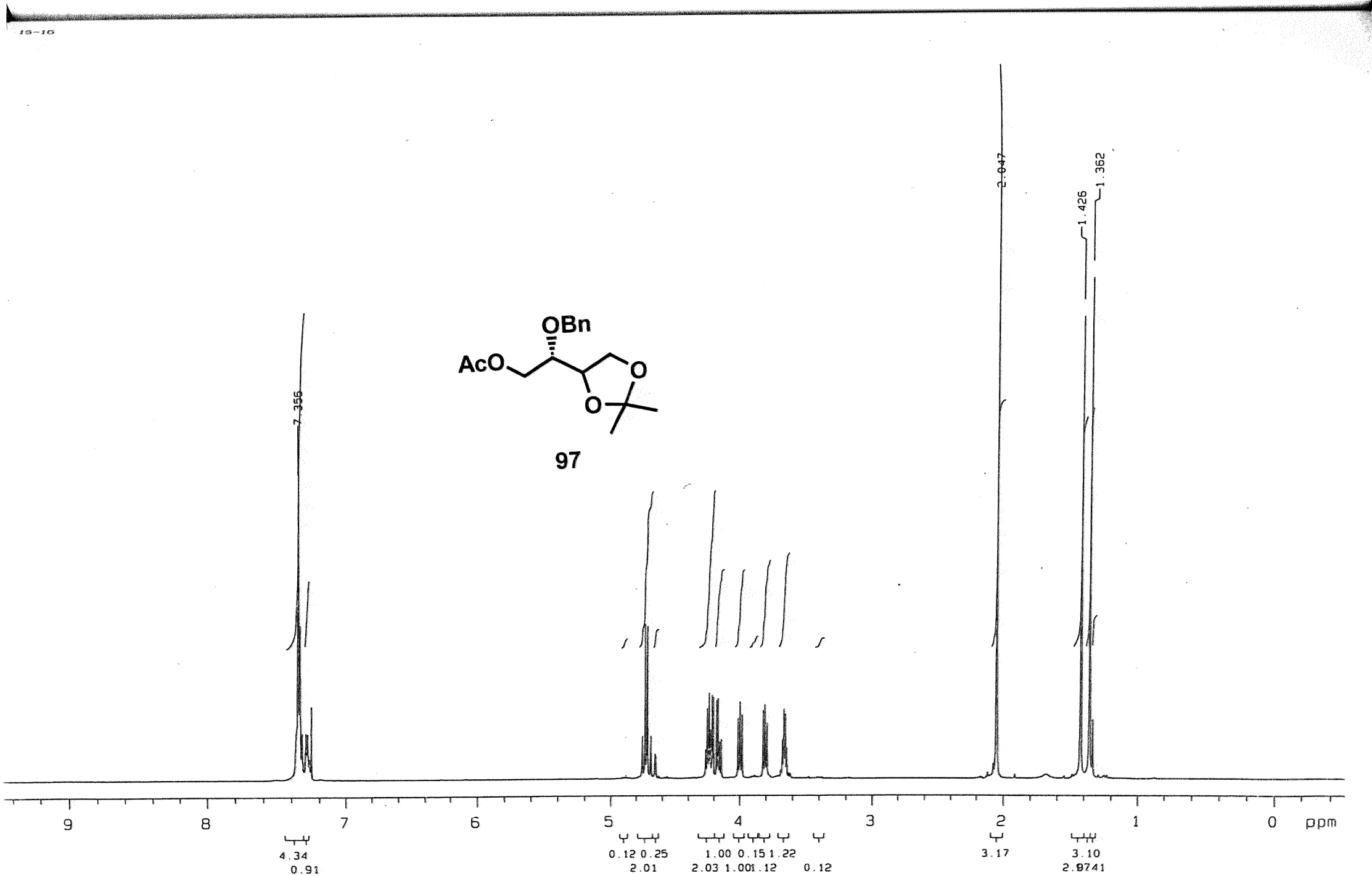

MeO
O
OH
HO
OBn
96
7.363
7.356
7.367
7.366
7.270
4.659
4.074
4.064
3.737
3.725
3.716
3.591
3.581
3.260
1.394
1.372
9
8
7
6
5
4
3
2
1
0
ppm
4.81
2.00
1.01
2.99
1.06
1.01
2.94
2.76
2.95
450. desired product.


MeO
O
OH
HO
OBn
96
128.521
127.899
77.256
76.747
72.324
71.683
62.159
60.698
49.694
25.090
24.589
137.936
101.439
79.289
200
180
160
140
120
100
80
60
40
20
ppm


160.00
128.00
96.00
64.00
32.00
0.00
4000.0
3000.0
2000.0
1500.0
1000.0
500.0
400.0
3452.9 37.62
3090.3 78.75
2990.0 37.15
2933.7 37.56
1496.2 84.20
1389.8 65.52
1359.6 39.57
1147.7 23.72
1076.4 17.69
MeO
O
OH
HO
OBn
96

(3)

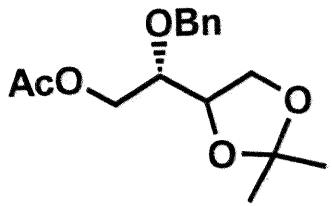

7.370
7.354
7.260
5.4322
4.757
4.714
1.0000
1.1880
0.1429
0.9769
1.0437
0.1635
2.3683
2.3385
0.1675
0.1130
0.8327
1.564
1.447
1.375
3.0792
3.3681
0.5299
OH
OBn
O
O
O
PPM


16-16
OBn
AcO
O
O
97
7.355
2.047
1.426
1.362
9
8
7
6
5
4
3
2
1
0
ppm
4.34
0.91
0.12 0.25
2.01
1.00 0.15 1.22
2.03 1.00 1.12
0.12
3.17
3.10
2.9741

16-16

exp2 s2pul

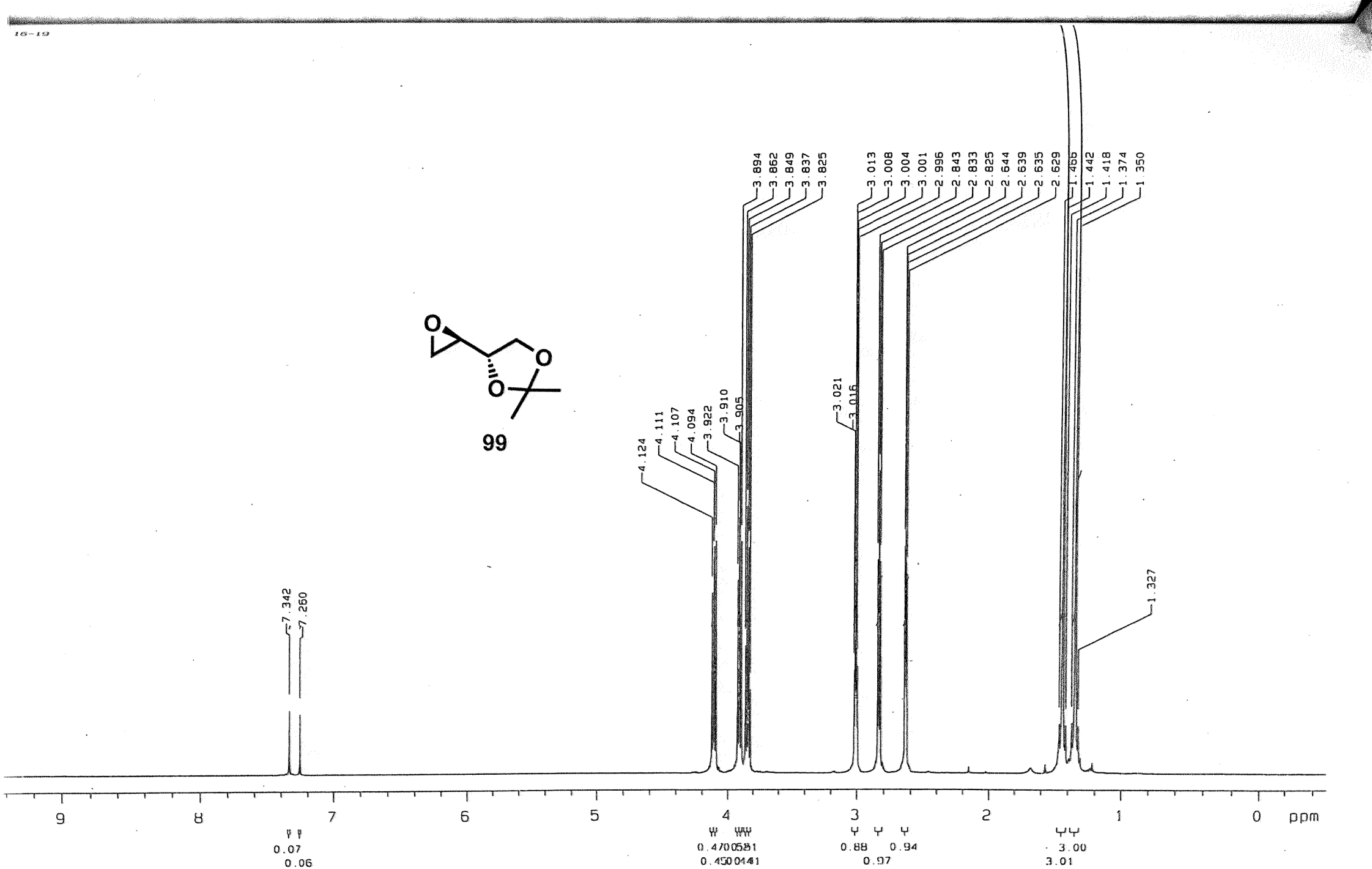
SAMPLE		DEC. & VT	
date	Nov 9 05	dfrq	499.864
solvent	CDCl3	dn	H1
file	exp	dpwr	45
ACQUISITION		dof	0
sfrq	125.704	dm	yyy
tn	C13	dmm	g
at	1.299	dmf	10000
np	78400	dseq	undefined
sw	30165.9	dres	undefined
fb	16600	homo	n
bs	16	PROCESSING	
tpwr	48	lb	1.00
pw	6.0	wtfile	
d1	0.900	proc	ft
tof	1885.5	fn	not used
nt	8000	math	f
ct	192		
alock	n	werr	react
gain	not used	wexp	c13p
FLAGS		wbs	
il	n	wnt	
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	1316.9		
wp	26047.1		
vs	21998		
sc	0		
wc	400		
hzmm	5.62		
is	500.00		
rfl	10969.0		
rfp	9679.2		
th	30		
ins	1.000		
ai cdc ph			



97

170.720
138.046
128.346
127.884
127.745
109.465
77.256
77.000
76.747
75.949
72.884
65.520
63.620
26.343
25.266
20.854

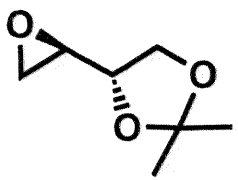
200 180 160 140 120 100 80 60 40 20 ppm


16-19
99
7.342
7.260
4.124
4.111
4.107
4.094
3.922
3.910
3.905
3.894
3.862
3.849
3.837
3.825
3.021
3.016
3.013
3.008
3.004
3.001
2.996
2.843
2.833
2.825
2.644
2.639
2.635
2.629
1.466
1.442
1.418
1.374
1.350
1.327
9
8
7
6
5
4
3
2
1
0
ppm
0.07
0.06
0.47
0.45
0.88
0.94
0.97
3.00
3.01

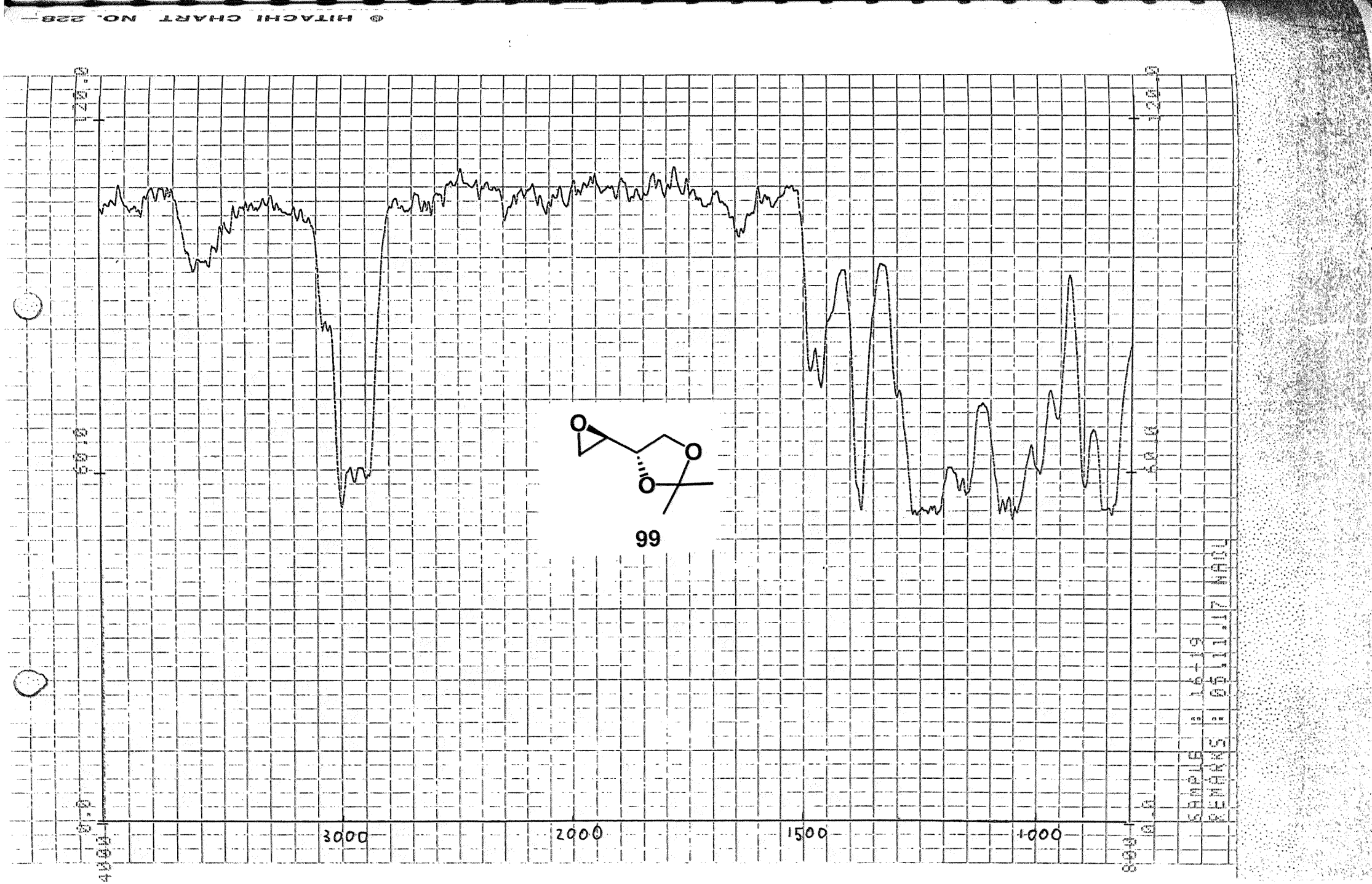
16-19

exp2 s2pul

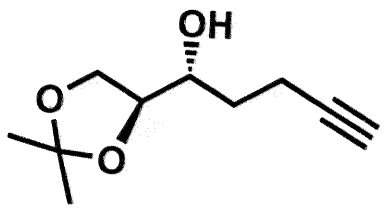
SAMPLE		DEC. & VT	
date	Nov 17 05	dfrq	499.864
solvent	CDCl3	dn	H1
file	exp	dpwr	45
ACQUISITION		dof	0
sfrq	125.704	dm	yyy
tn	C13	dmm	g
at	1.299	dmf	10000
np	78400	dseq	undefined
sw	30165.9	dres	undefined
fb	16600	homo	n
bs	16	PROCESSING	
tpwr	48	lb	0.50
pw	6.0	wtfile	
d1	0.900	proc	ft
tof	1885.5	fn	not used
nt	16000	math	f
ct	128		
alock	n	werr	react
gain	not used	wexp	c13p
FLAGS		wbs	
il	n	wnt	
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	1079.9		
wp	25597.4		
vs	8441		
sc	0		
wc	400		
hzmm	63.99		
is	500.00		
rfl	10970.4		
rfp	9679.2		
th	14		
ins	1.000		
ai cdc ph			



99


HITACHI CHART NO. 228
3000
2000
1500
1000
99

uemura 16-20

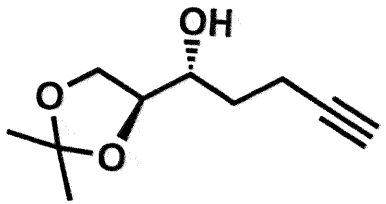


100

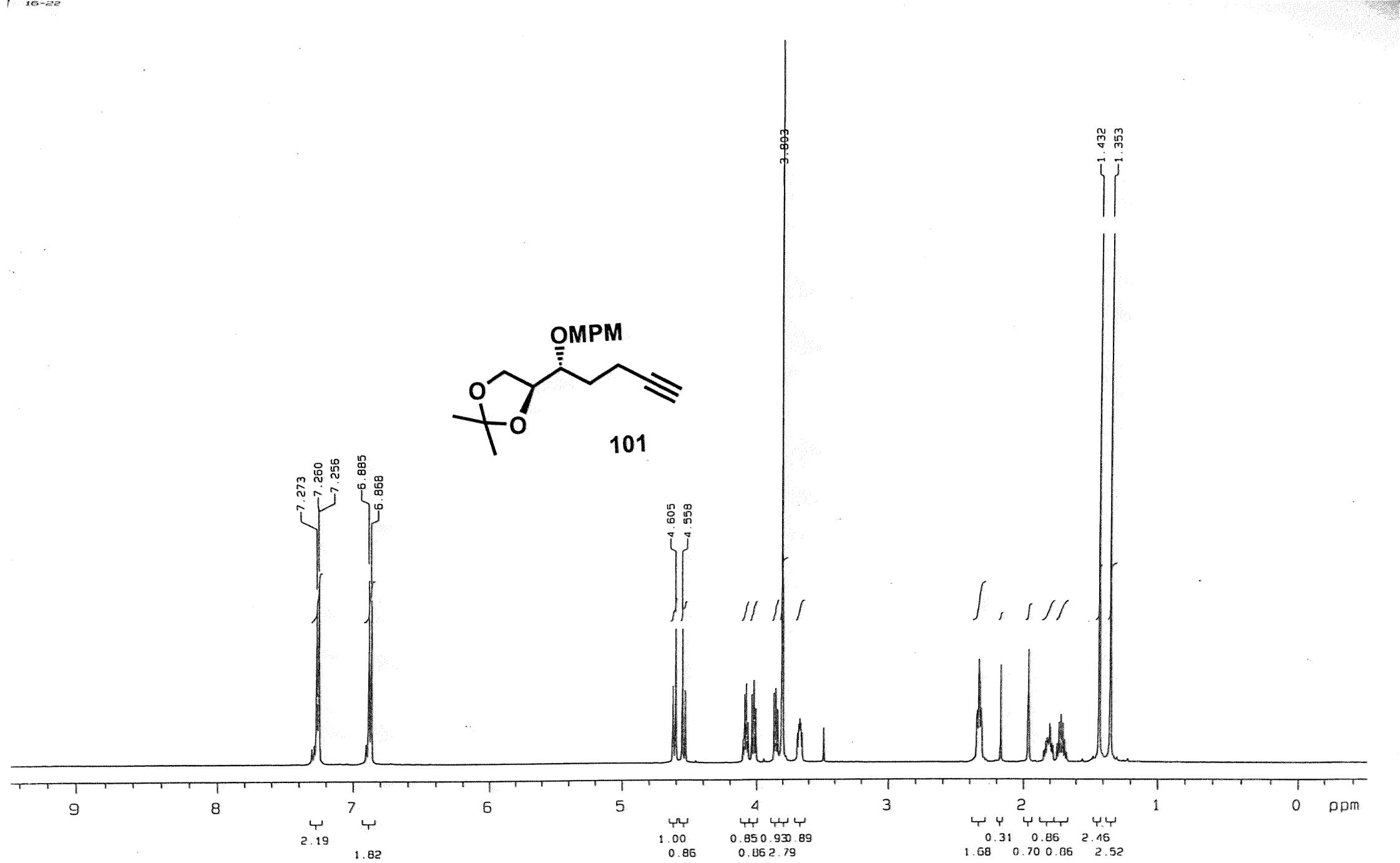
uemura 16-20

exp2 s2pul

SAMPLE		DEC. & VT	
date	Dec 1 05	dfrq	499.864
solvent	CDCl3	dn	H1
file	exp	dpwr	45
ACQUISITION		dof	0
sfrq	125.704	dm	yyy
tn	C13	dmm	g
at	1.299	dmf	10000
np	78400	dseq	undefined
sw	30165.9	dres	undefined
fb	16600	homo	n
bs	16	PROCESSING	
tpwr	48	lb	1.00
pw	6.0	wtfile	
d1	0.900	proc	ft
tof	1885.5	fn	not used
nt	16000	math	f
ct	176		
alock	n	werr	react
gain	not used	wexp	c13p
FLAGS		wbs	
il	n	wnt	
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	922.0		
wp	25596.0		
vs	30142		
sc	0		
wc	400		
hzmm	31.12		
is	500.00		
rfl	10967.6		
rfp	9679.2		
th	17		
ins	1.000		
ai cdc ph			



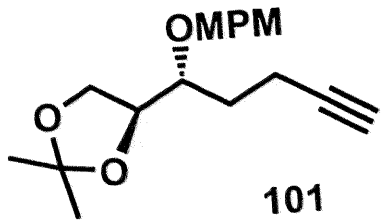
100


16-22
OMPM
O
O
101
7.273
7.260
7.256
6.885
6.868
4.605
4.558
3.803
1.432
1.353
9
8
7
6
5
4
3
2
1
0
ppm
2.19
1.82
1.00
0.86
0.85
0.86
0.93
2.79
0.89
0.31
1.68
0.86
0.70
0.86
2.46
2.52

uemura_16-22

exp2 s2pul

SAMPLE		DEC. & VT	
date	Dec 6 05	dfrq	499.864
solvent	CDCl3	dn	H1
file	exp	dpwr	45
ACQUISITION		dof	0
sfrq	125.704	dm	yyy
tn	C13	dmm	g
at	1.299	dmf	10000
np	78400	dseq	undefined
sw	30165.9	dres	undefined
fb	16600	homo	n
bs	16	**PROCESSING**	
tpwr	48	lb	1.00
pw	6.0	wtfile	
d1	0.900	proc	ft
tof	1885.5	fn	not used
nt	16000	math	f
ct	192		
alock	n	werr	react
gain	not used	wexp	c13p
FLAGS		wbs	
il	n	wnt	
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	791.7		
wp	27078.7		
vs	26946		
sc	0		
wc	400		
hzmm	3.24		
is	500.00		
rfl	10967.2		
rfp	9679.2		
th	17		
ins	1.000		
ai cdc ph			



101

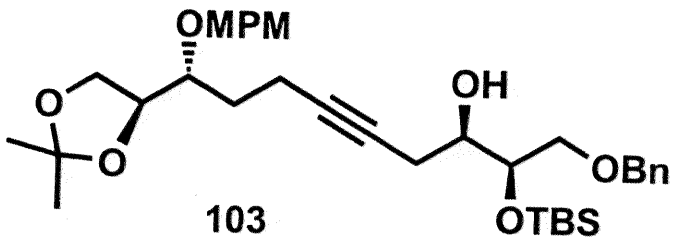
159.273
130.462
129.528
113.823
109.136
84.086
77.769
77.341
77.256
77.000
76.747
72.851
68.691
66.308
55.271
30.235
26.555
25.288
14.431

200 180 160 140 120 100 80 60 40 20 ppm

uemura 14-24

exp2 s2pul

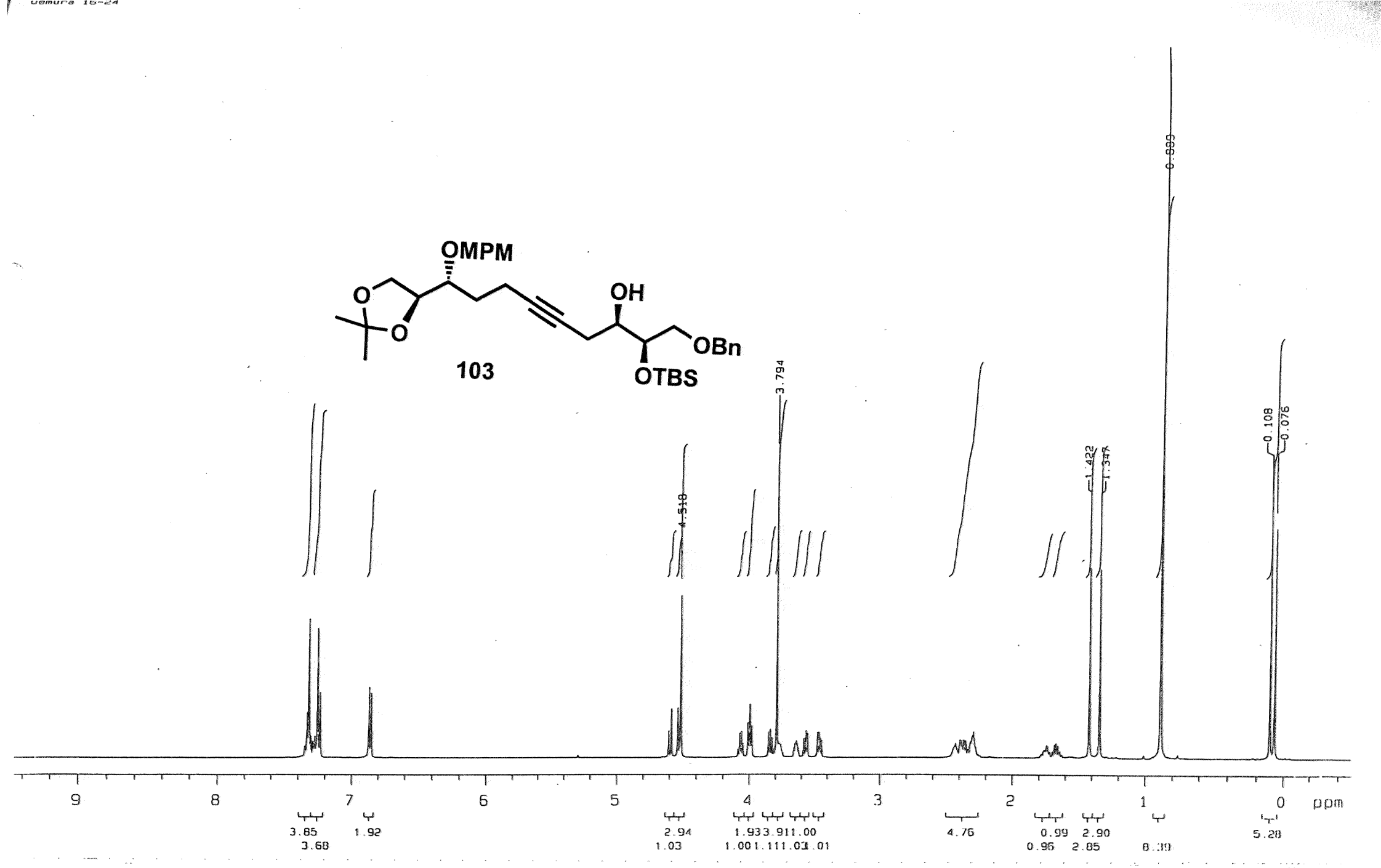
SAMPLE		DEC. & VT	
date	Dec 15 05	dfrq	499.864
solvent	CDCl3	dn	H1
file	exp	dpwr	45
ACQUISITION		dof	0
sfrq	125.704	dm	yyy
tn	C13	dmm	g
at	1.299	dmf	10000
np	78400	dseq	undefined
sw	30165.9	dres	undefined
fb	16600	homo	n
bs	16	PROCESSING	
tpwr	48	lb	1.00
pw	6.0	wtfile	
d1	0.900	proc	ft
tof	1885.5	fn	not used
nt	16000	math	f
ct	128		
alock	n	werr	react
gain	not used	wexp	c13p
FLAGS		wbs	
il	n	wnt	
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-1013.1		
wp	26887.6		
vs	13854		
sc	0		
wc	400		
hzmm	5.69		
is	500.00		
rfl	10971.3		
rfp	9679.2		
th	12		
ins	1.000		
ai cdc ph			

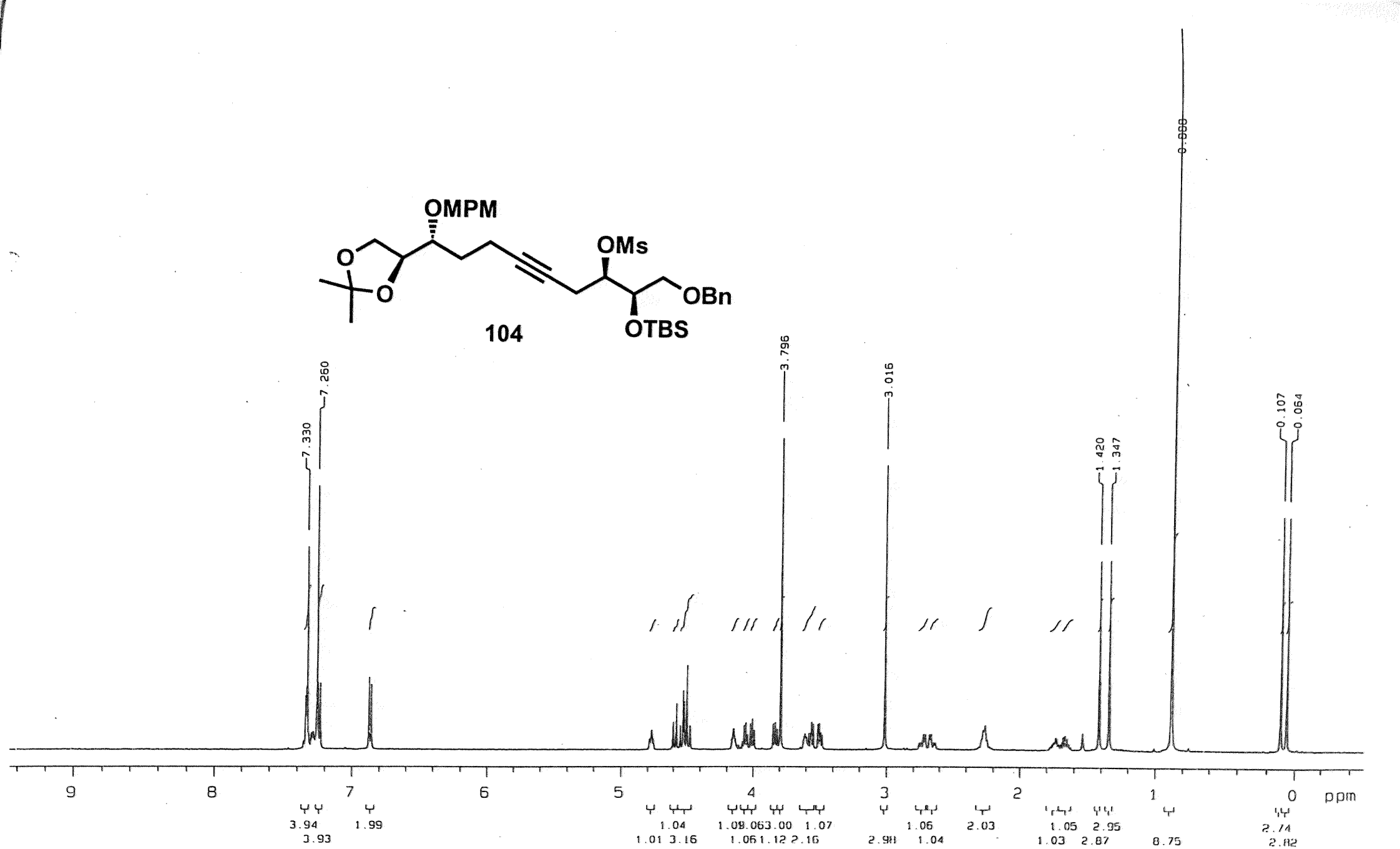


103

159.233
137.723
130.411
129.451
128.364
127.785
127.719
113.786
109.070
82.676
80.523
77.623
77.406
77.256
77.000
76.747
75.231
73.466
72.705
70.486
66.278
55.234
38.357
30.378
26.544
25.775
25.263
21.366
18.074
14.614
4.497
4.944

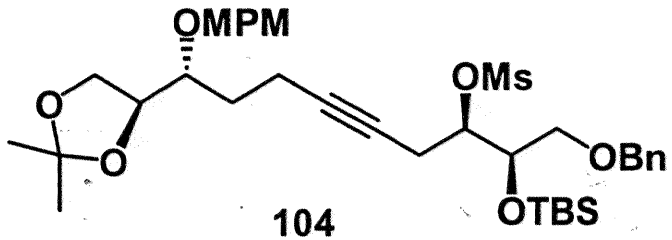
200 180 160 140 120 100 80 60 40 20 0 ppm


OMPM
OH
OBn
OTBS
103
3.794
4.518
1.422
1.347
0.889
0.108
0.076
9
8
7
6
5
4
3
2
1
0
ppm
3.85
3.68
1.92
2.94
1.03
1.93
1.00
3.91
1.11
1.00
1.03
1.01
4.76
0.99
0.96
2.90
2.85
8.39
5.28

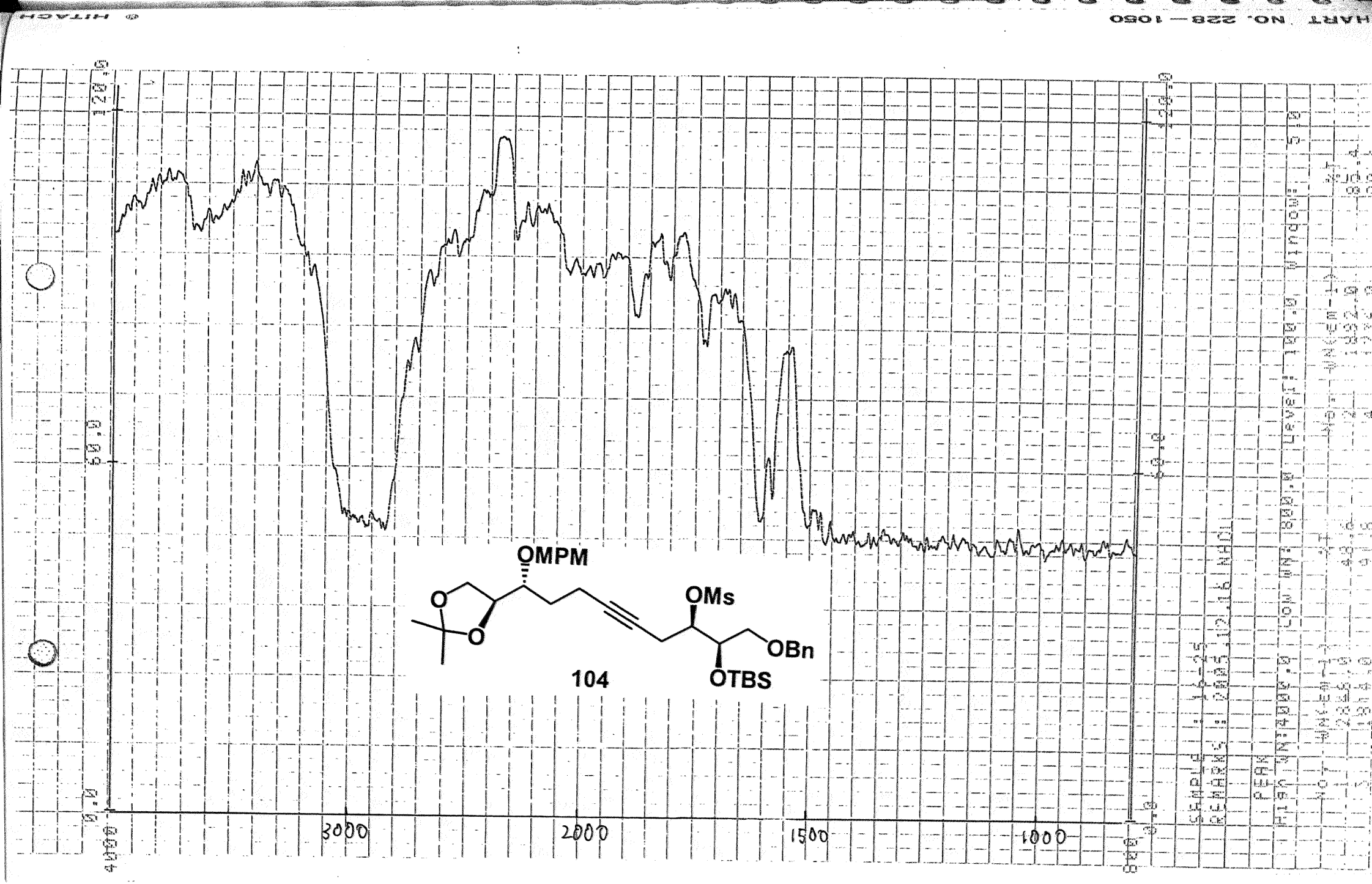

OMPM
OMs
OBn
OTBS
104
7.330
7.260
3.796
3.016
1.420
1.347
0.888
0.107
0.064
9
8
7
6
5
4
3
2
1
0
ppm
3.94
3.93
1.99
1.04
1.01
3.16
1.09
1.06
3.06
1.12
3.00
2.16
1.07
2.98
1.06
1.04
2.03
1.05
1.03
2.95
2.87
8.75
2.74
2.82

exp2 s2pul

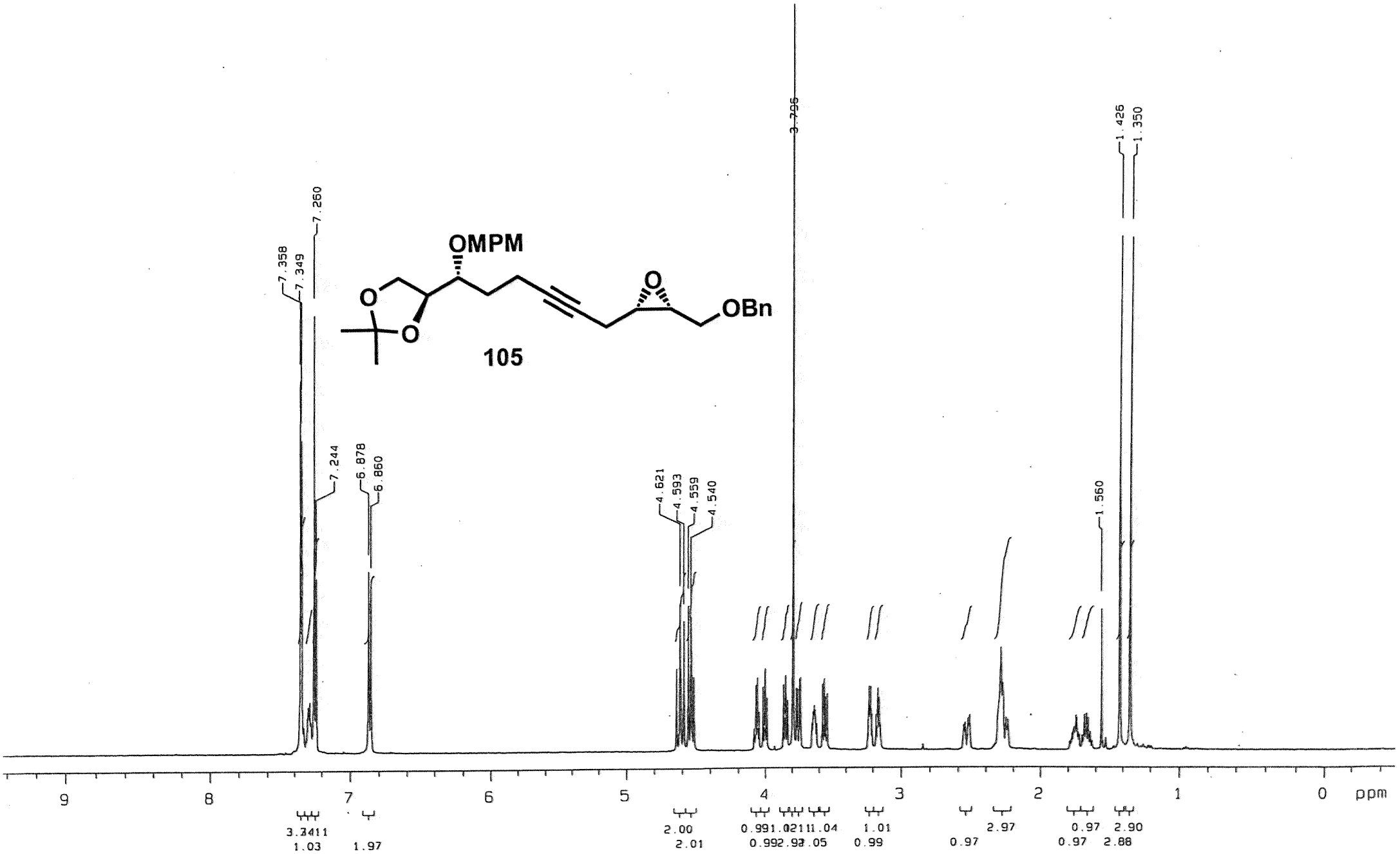
SAMPLE		DEC. & VT	
date	Dec 13 05	dfrq	499.864
solvent	CDCl3	dn	H1
file	exp	dpwr	45
ACQUISITION		dof	0
sfrq	125.704	dm	yyy
tn	C13	dmm	g
at	1.299	dmf	10000
np	78400	dseq	undefined
sw	30165.9	dres	undefined
fb	16600	homo	n
bs	16	PROCESSING	
tpwr	48	lb	0.80
pw	6.0	wtfile	
d1	0.900	proc	ft
tof	1885.5	fn	not used
nt	16000	math	f
ct	400		
alock	n	werr	react
gain	not used	wexp	c13p
FLAGS		wbs	
il	n	wnt	
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-1081.3		
wp	26464.2		
vs	28733		
sc	0		
wc	400		
hzmm	19.73		
is	500.00		
rfl	10967.6		
rfp	9679.2		
th	12		
ins	1.000		
ai cdc ph			



104


OMPM
OMs
OBn
OTBS
104
3000
2000
1500
1000

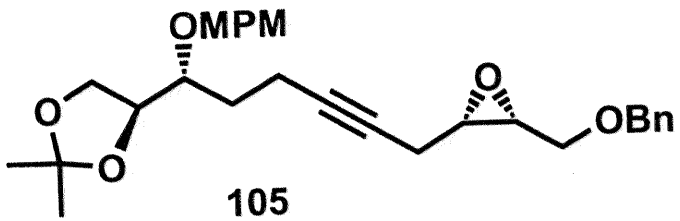
16-28


OMPM
OBn
O
O
O
105
7.358
7.349
7.260
7.244
6.878
6.860
4.621
4.593
4.559
4.540
3.795
1.560
1.426
1.350
9
8
7
6
5
4
3
2
1
0
ppm
3.3411
1.03
1.97
2.00
2.01
0.99
1.02
1.04
1.05
1.01
0.99
0.97
2.97
0.97
0.97
2.90
2.88

uemura 16-28

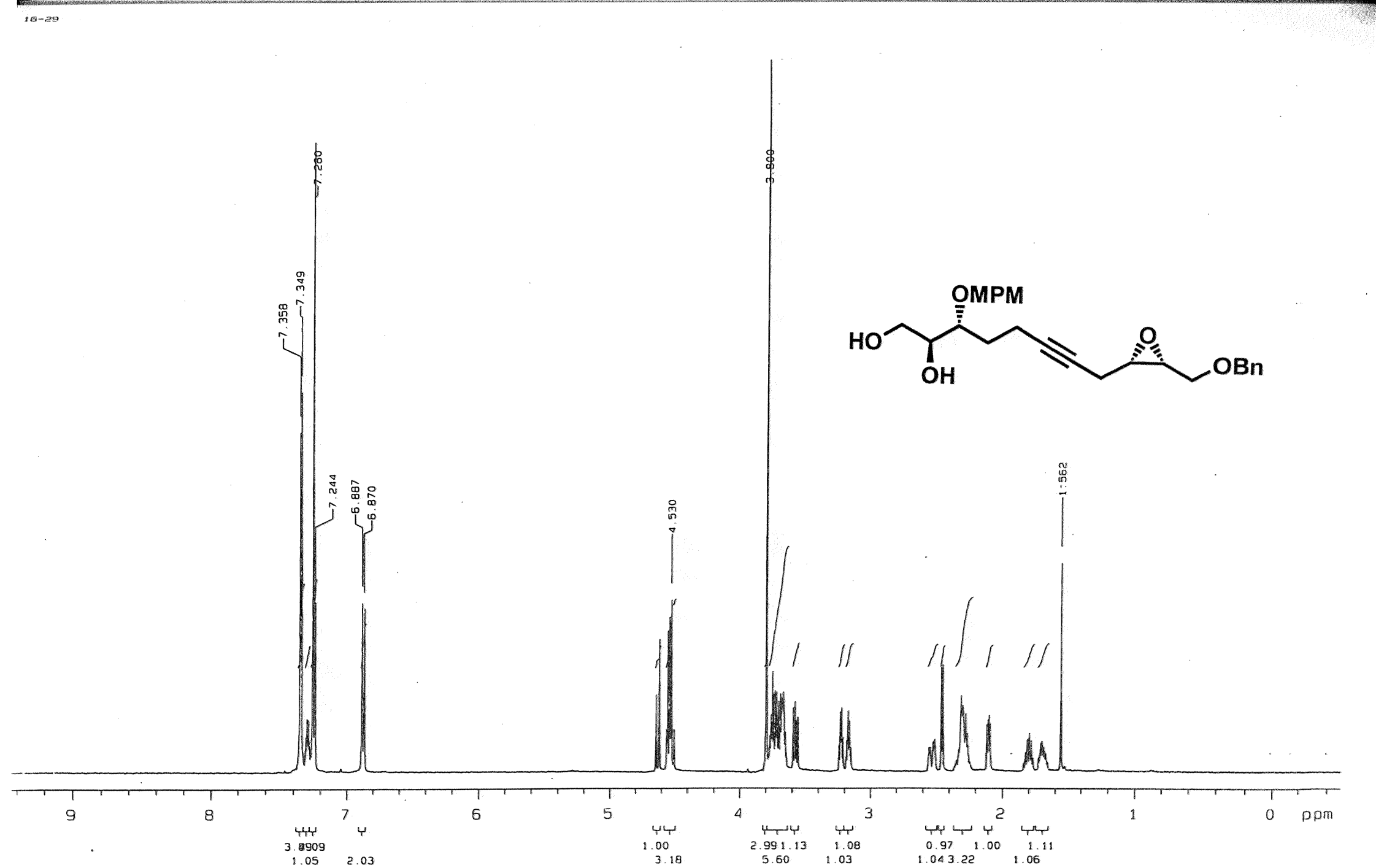
exp2 s2pul

SAMPLE		DEC. & VT	
date	Jan 10 06	dfrq	499.864
solvent	CDCl3	dn	H1
file	exp	dpwr	45
ACQUISITION		dof	0
sfrq	125.704	dm	yyy
tn	C13	dmm	g
at	1.299	dmf	10000
np	78400	dseq	undefined
sw	30165.9	dres	undefined
fb	16600	homo	n
bs	16	PROCESSING	
tpwr	48	lb	1.00
pw	6.0	wtfile	
d1	0.900	proc	ft
tof	1885.5	fn	not used
nt	16000	math	f
ct	416		
alock	n	werr	react
gain	not used	wexp	c13p
FLAGS		wbs	
il	n	wnt	
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	1257.1		
wp	26205.0		
vs	35689		
sc	0		
wc	400		
hzmm	65.51		
is	500.00		
rfl	10968.1		
rfp	9679.2		
th	12		
ins	1.000		
ai cdc ph			

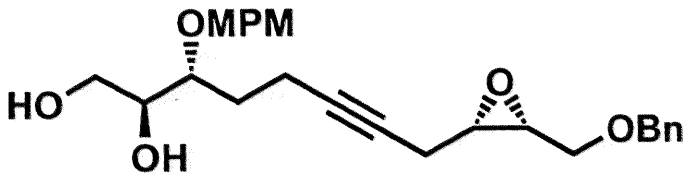


105

16-29


7.358
7.349
7.260
7.244
6.887
6.870
4.530
3.800
1.562
OMPM
HO
OH
O
OBn
9
8
7
6
5
4
3
2
1
0
ppm
3.8909
1.05
2.03
1.00
3.18
2.99
1.13
5.60
1.08
1.03
0.97
1.04
1.00
3.22
1.11
1.06

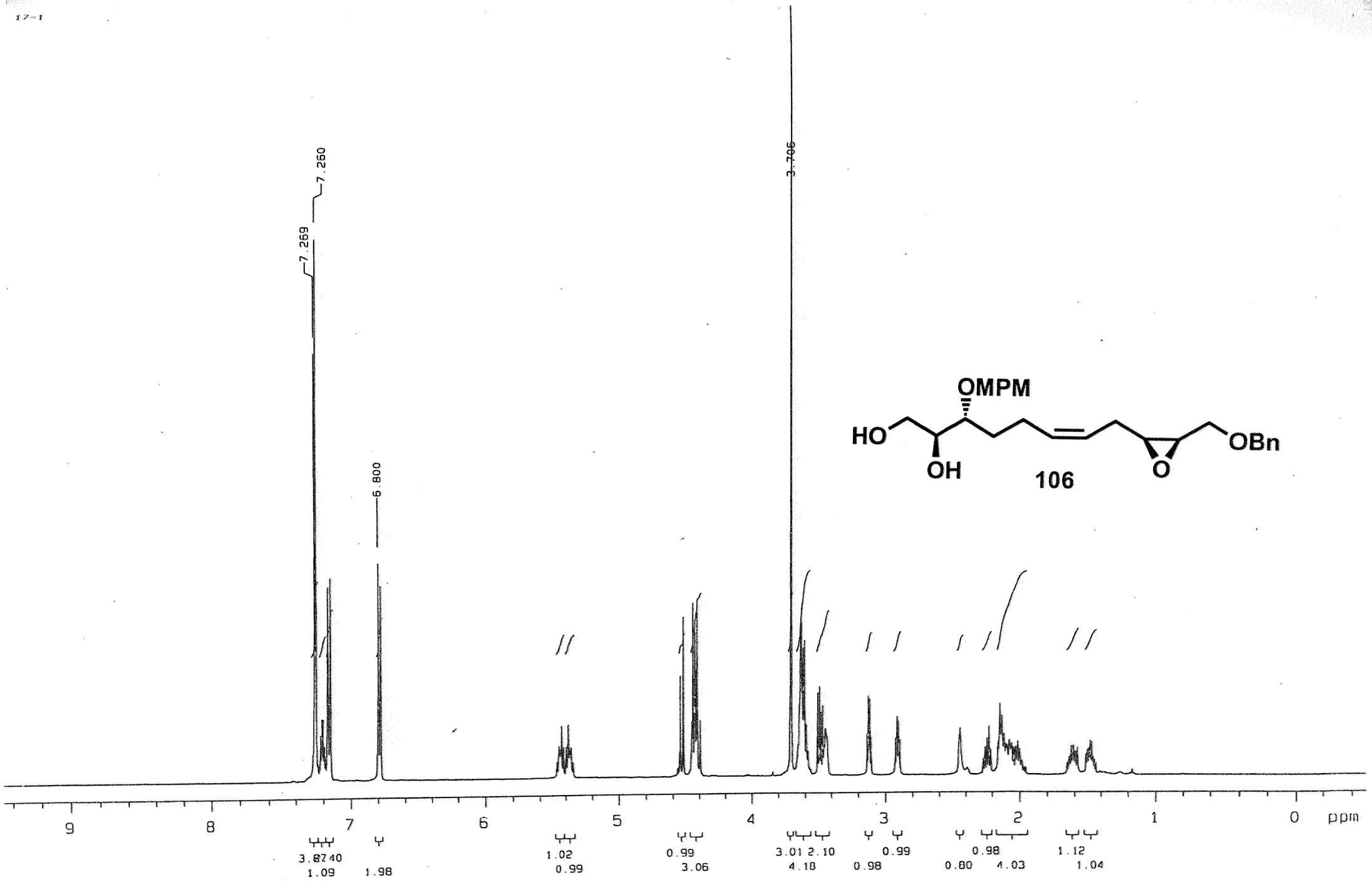
aura 0112 F4-f4-2 4.2 mg

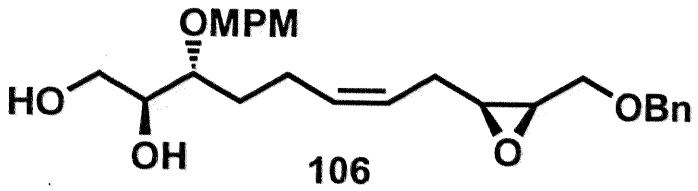


159.405
137.723
130.155
129.565
128.459
127.837
127.771
113.940
82.163
79.106
77.282
77.256
77.029
77.000
76.773
76.747
75.392
73.320
72.606
72.470
67.769
63.407
55.282
55.187
54.414
29.503
19.059
14.775

200 180 160 140 120 100 80 60 40 20 ppm

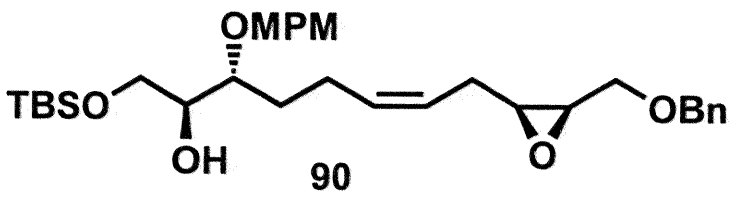
SAMPLE : 16-29
REMARKS : 2006.1.16 NAOL
OBn
OMPM
HO
OH
O
HITACHI CHART NO. 228—1050


12-1
7.260
7.269
6.800
3.706
OMPM
HO
OH
OBn
O
106
9
8
7
6
5
4
3
2
1
0
ppm
3.87 4.0
1.09
1.98
1.02
0.99
0.99
3.06
3.01 2.10
4.18
0.98
0.99
0.80
0.98
4.03
1.12
1.04


OMPM
HO
OH
106
O
OBn

129.462
128.423
127.785
127.763
113.933
77.256
77.000
76.747
73.294
72.423
72.320
68.109
63.393
55.491
55.256
55.201
30.243
26.442
23.245
80.113
124.449
132.018
130.158
137.782
159.379
200
180
160
140
120
100
80
60
40
ppm

17-2


OMPM
TBSO
OH
O
OBn

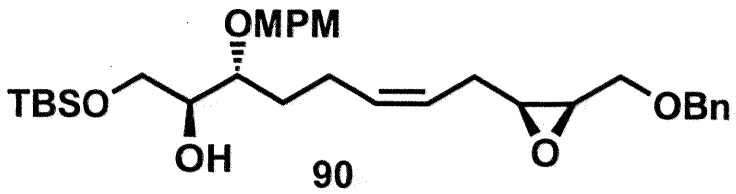
90

7.260
7.342
3.788
0.905
0.075
9
8
7
6
5
4
3
2
1
0
ppm
3.8477
1.11
2.08
1.04
1.05
1.00
3.14
3.04
4.34
1.12
1.12
1.07
1.08
0.99
1.00
2.02
1.09
1.98
8.81
5.44

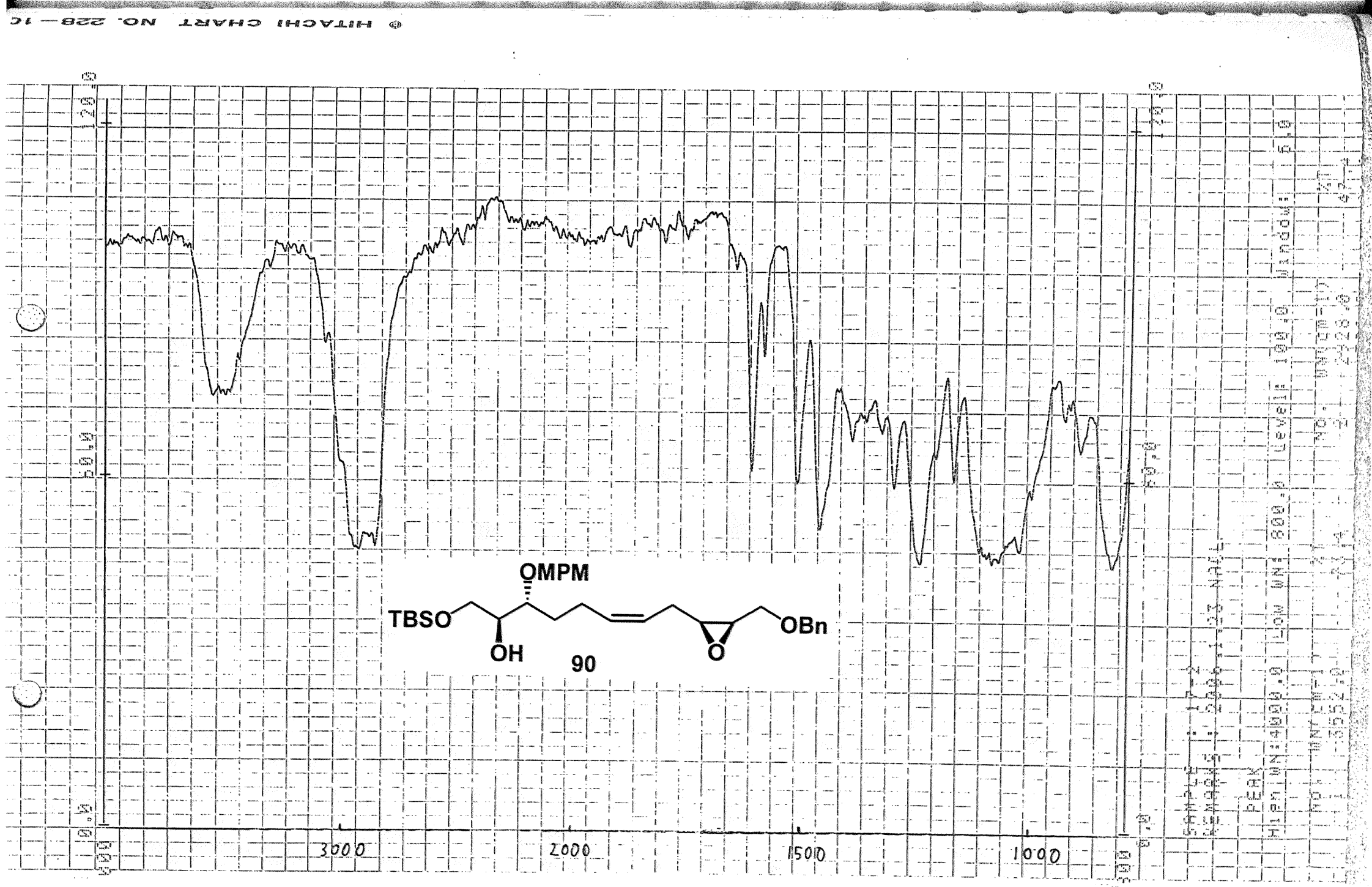
17-2

exp2 s2pul

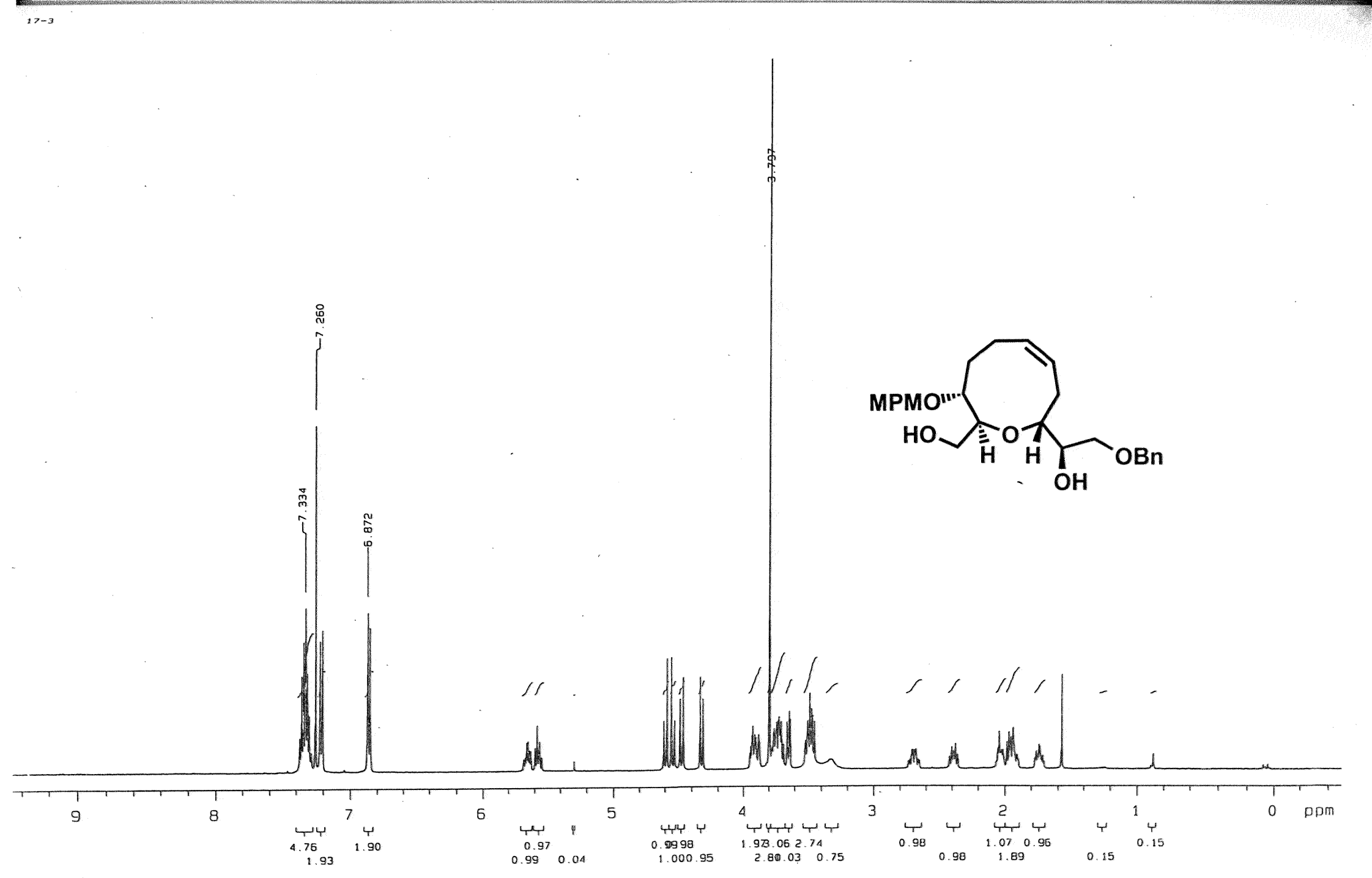
SAMPLE		DEC. & VT	
date	Jan 24 06	dfrq	499.864
solvent	CDCl3	dn	H1
file	exp	dpwr	45
ACQUISITION		dof	0
sfrq	125.704	dm	yyy
tn	C13	dmm	g
at	1.299	dmf	10000
np	78400	dseq	undefined
sw	30165.9	dres	undefined
fb	16600	homo	n
bs	16	temp	25.0
tpwr	48	PROCESSING	
pw	6.0	lb	1.00
d1	0.900	wtfile	
tof	1885.5	proc	ft
nt	16000	fn	not used
ct	400	math	f
alock	n		
gain	not used	werr	react
FLAGS		wexp	c13p
il	n	wbs	
in	n	wnt	
dp	y		
hs	nn		
DISPLAY			
sp	-1062.9		
wp	27126.5		
vs	35336		
sc	0		
wc	400		
hzmm	1.05		
is	500.00		
rfl	10966.7		
rfp	9679.2		
th	13		
ins	1.000		
ai cdc ph			



90


OMPM
TBSO
OH
O
OBn
90
3000
2000
1500
1000

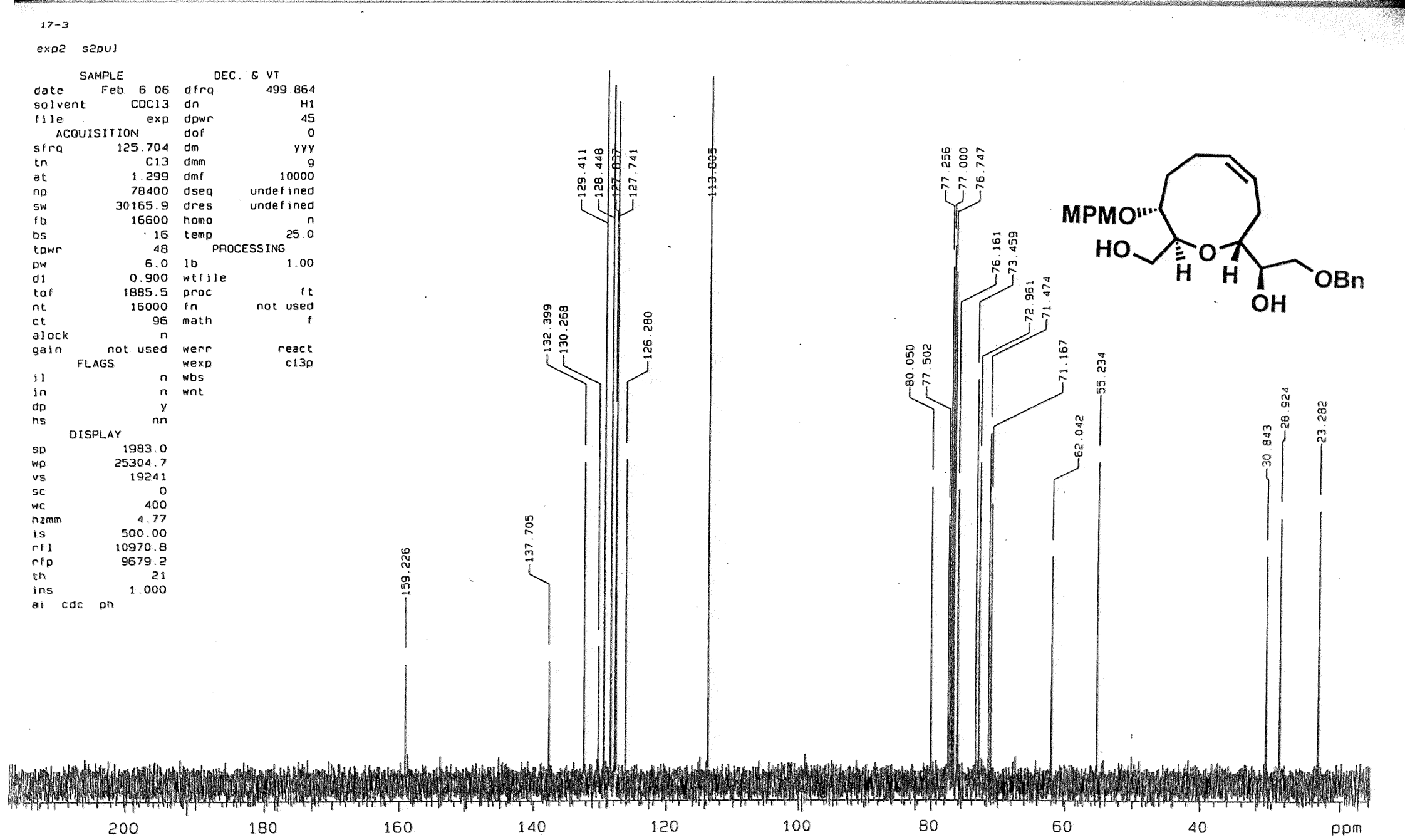
17-3


7.334
7.260
6.872
3.797
MPMO
HO
O
H
H
OBn
OH
9
8
7
6
5
4
3
2
1
0
ppm
4.76
1.93
1.90
0.97
0.99
0.04
0.99
98
1.000
.95
1.97
3.06
2.74
2.80
0.03
0.75
0.98
0.98
1.07
0.96
1.89
0.15
0.15

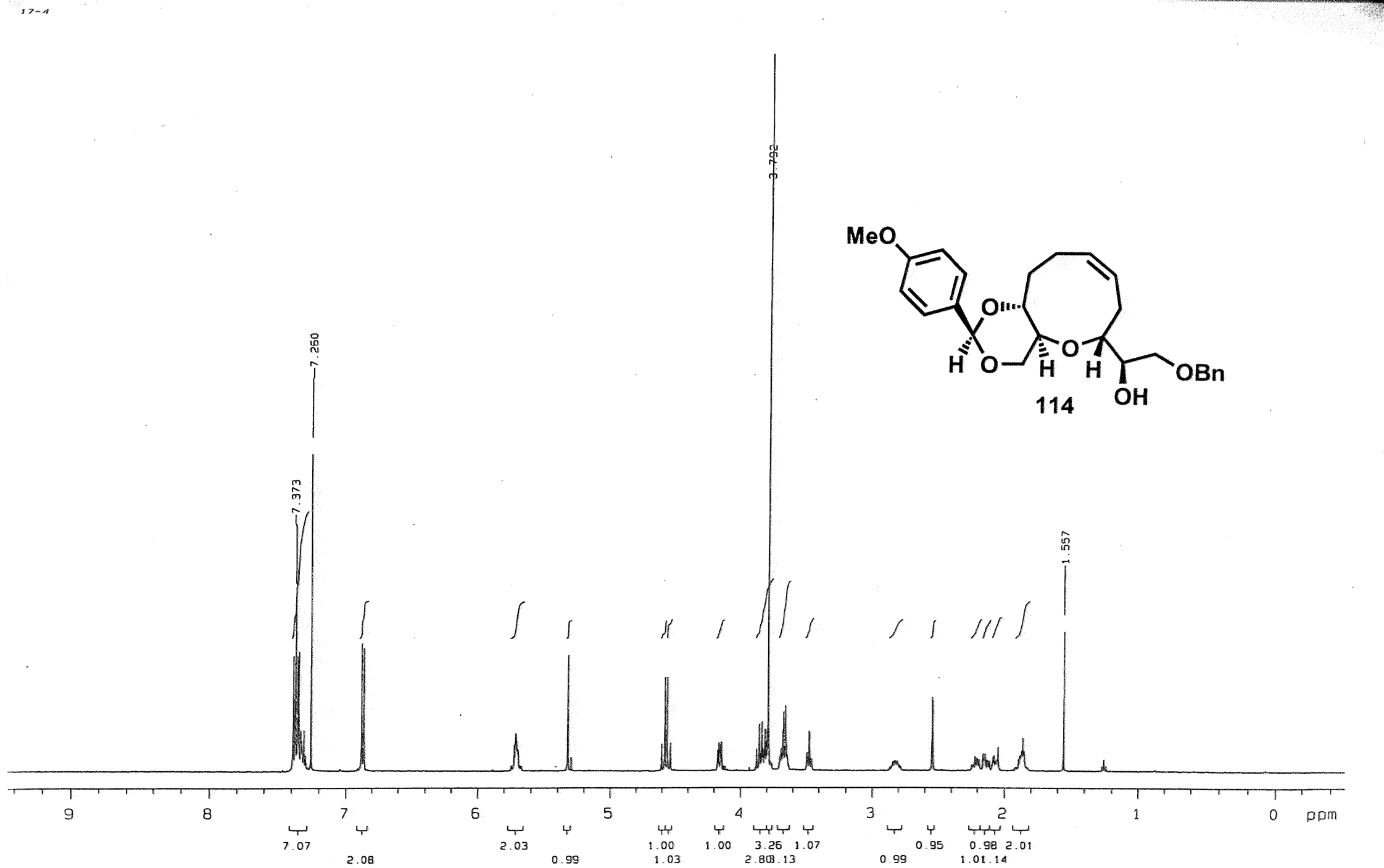
17-3

exp2 s2pul

SAMPLE		DEC. & VT	
date	Feb 6 06	dfrq	499.864
solvent	CDCl3	dn	H1
file	exp	dpwr	45
ACQUISITION		dof	0
sfrq	125.704	dm	yyy
tn	C13	dmm	g
at	1.299	dmf	10000
np	78400	dseq	undefined
sw	30165.9	dres	undefined
fb	16600	homo	n
bs	16	temp	25.0
tpwr	48	PROCESSING	
pw	6.0	lb	1.00
d1	0.900	wtfile	
tof	1885.5	proc	ft
nt	16000	fn	not used
ct	96	math	f
alock	n		
gain	not used	werr	react
FLAGS		wexp	c13p
il	n	wbs	
in	n	wnt	
dp	y		
hs	nn		
DISPLAY			
sp	1983.0		
wp	25304.7		
vs	19241		
sc	0		
wc	400		
hzmm	4.77		
is	500.00		
rfl	10970.8		
rfp	9679.2		
th	21		
ins	1.000		
ai cdc ph			



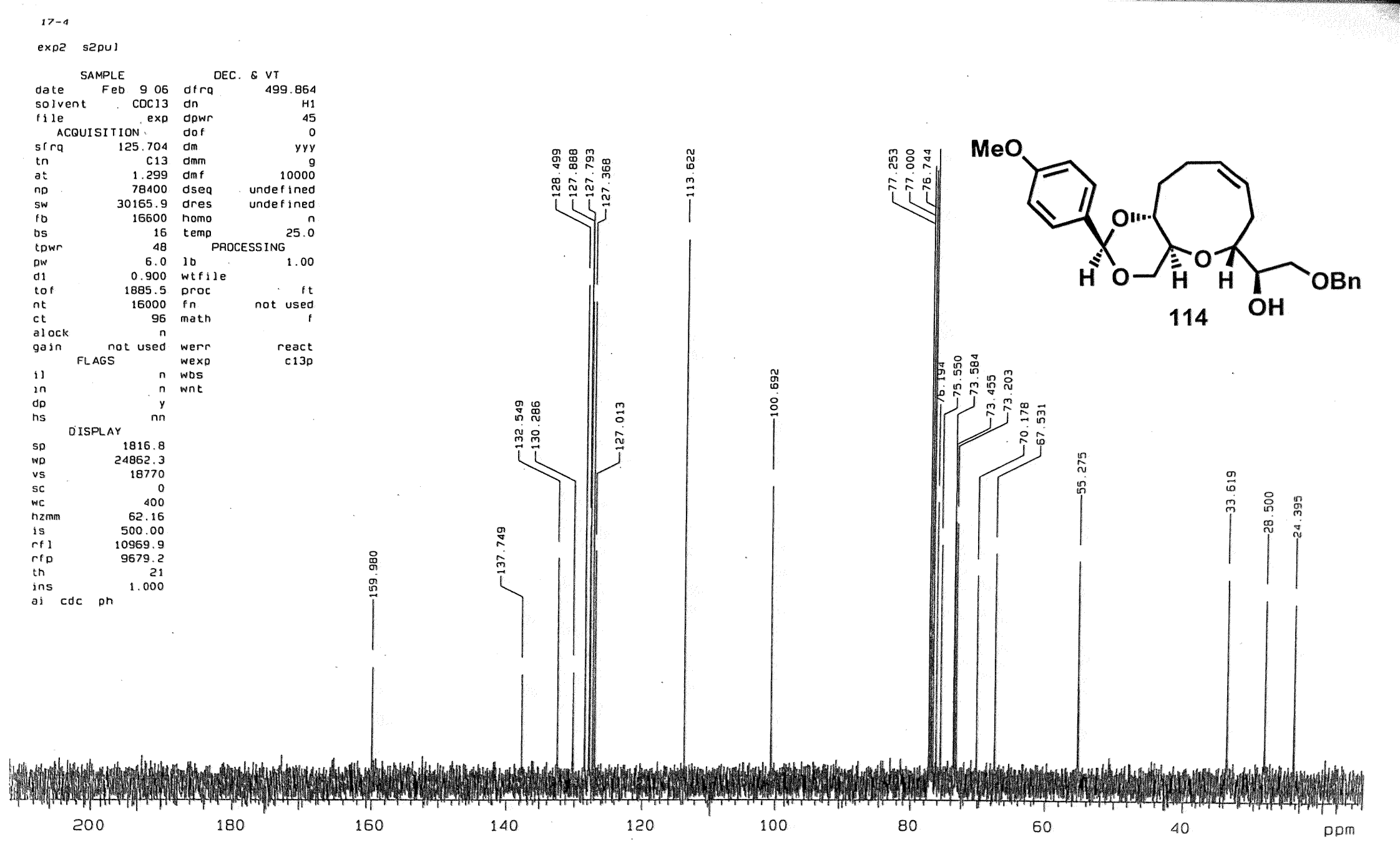
17-4

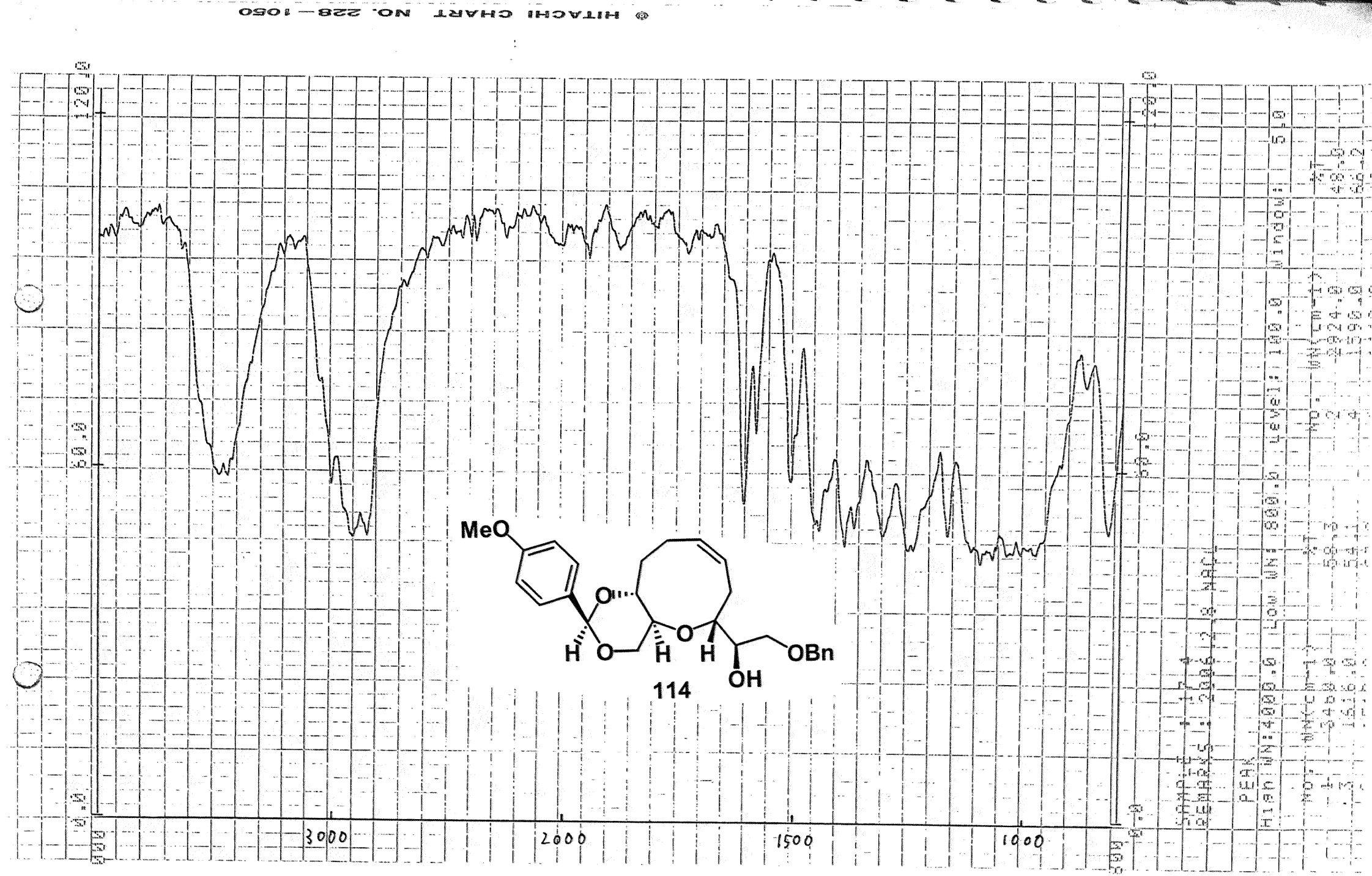

7.260
7.373
3.792
1.557
MeO
O
H
O
O
H
H
H
OBn
OH
114
9
8
7
6
5
4
3
2
1
0
ppm
7.07
2.08
2.03
0.99
1.00
1.03
1.00
3.26
1.07
0.99
0.95
0.98
2.01

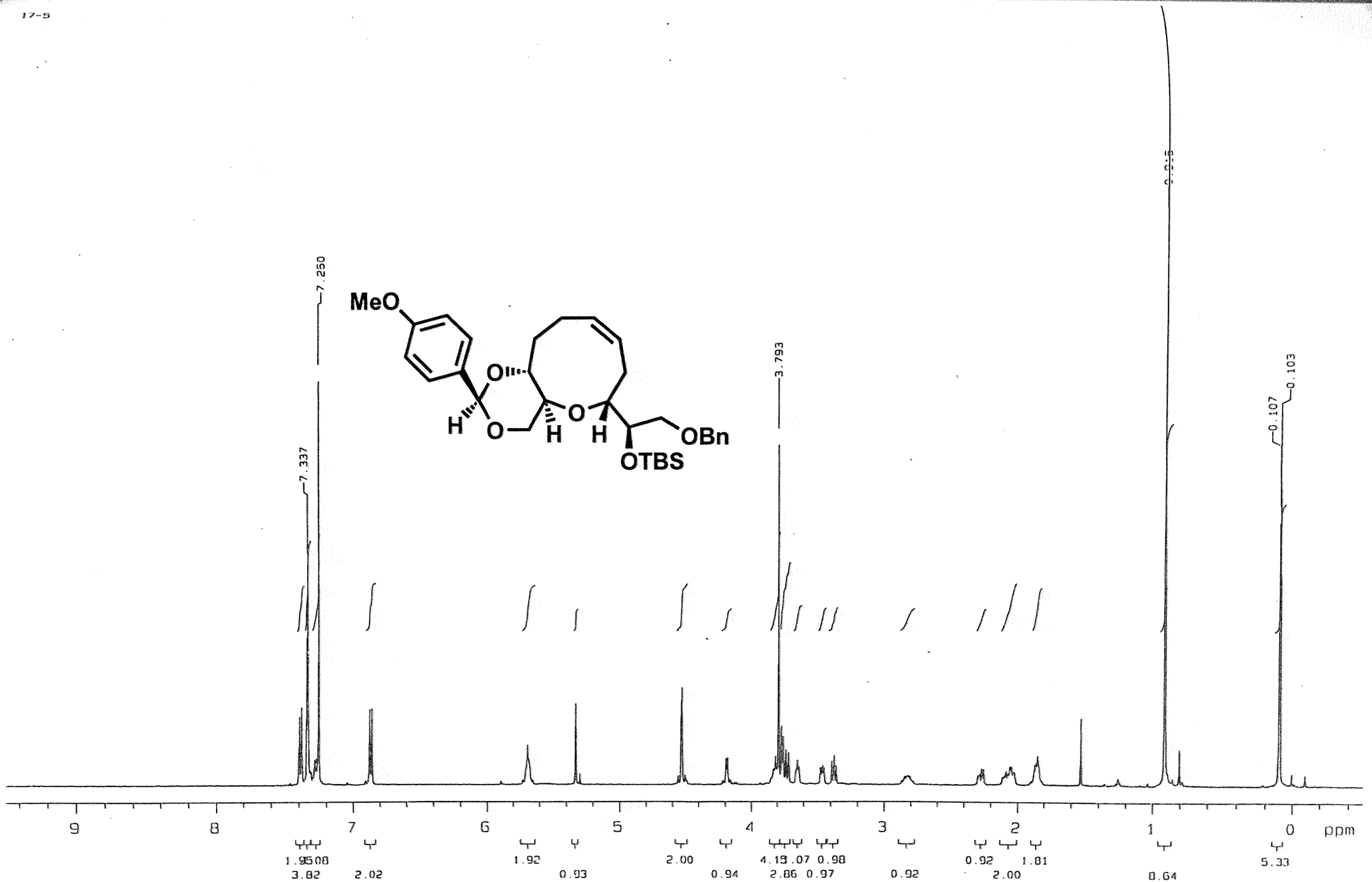
17-4

exp2 s2pul

SAMPLE		DEC. & VT	
date	Feb 9 06	dfrq	499.864
solvent	CDCl3	dn	H1
file	exp	dpwr	45
ACQUISITION		dof	0
sfrq	125.704	dm	yyy
tn	C13	dmm	g
at	1.299	dmf	10000
np	78400	dseq	undefined
sw	30165.9	dres	undefined
fb	16600	homo	n
bs	16	temp	25.0
tpwr	48	PROCESSING	
pw	6.0	lb	1.00
d1	0.900	wtfile	
tof	1885.5	proc	ft
nt	16000	fn	not used
ct	96	math	f
alock	n		
gain	not used	werr	react
FLAGS		wexp	c13p
il	n	wbs	
in	n	wnt	
dp	y		
hs	nn		
DISPLAY			
sp	1816.8		
wp	24862.3		
vs	18770		
sc	0		
wc	400		
hzmm	62.16		
is	500.00		
rfl	10969.9		
rfp	9679.2		
th	21		
ins	1.000		
ai cdc ph			



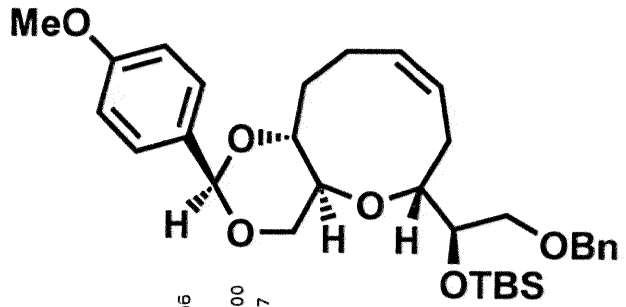

MeO
O
H
O
H
O
H
OBn
OH
114
3000
2000
1500
1000


17-5
7.260
7.337
3.793
0.107
0.103
MeO
O
O
H
O
H
O
H
OBn
OTBS
9
8
7
6
5
4
3
2
1
0
ppm
1.95 0.08
3.82
2.02
1.92
0.93
2.00
0.94
4.15 3.07 0.98
2.86 0.97
0.92
0.92 1.81
2.00
8.64
5.33

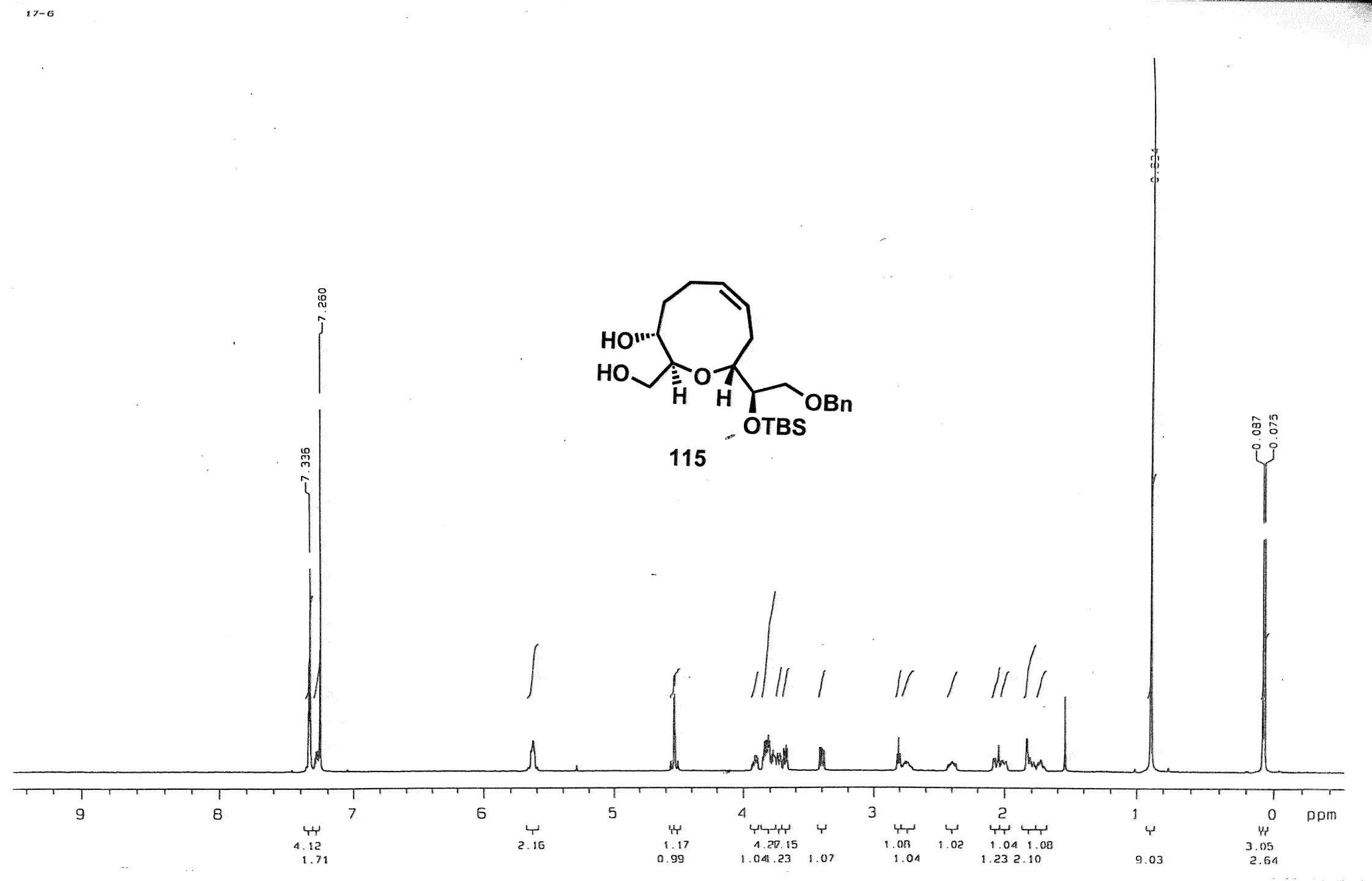
17-5

exp2 s2pul

SAMPLE		DEC. & VT	
date	Feb 14 06	dfrq	499.864
solvent	CDCl3	dn	H1
file	exp	dpwr	45
ACQUISITION		dof	0
sfrq	125.704	dm	yyy
tn	C13	dmm	g
at	1.299	dmf	10000
np	78400	dseq	undefined
sw	30165.9	dres	undefined
fb	16600	homo	n
bs	16	PROCESSING	
tpwr	48	lb	1.00
pw	6.0	wtfile	
d1	0.900	proc	ft
tof	1885.5	fn	not used
nt	6400	math	f
ct	80		
alock	n	werr	react
gain	not used	wexp	c13p
FLAGS		wbs	
il	n	wnt	
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-1292.5		
wp	30165.9		
vs	10063		
sc	0		
wc	400		
hzmm	75.41		
is	500.00		
rfl	10971.8		
rfp	9679.2		
th	17		
ins	1.000		
ai cdc ph			



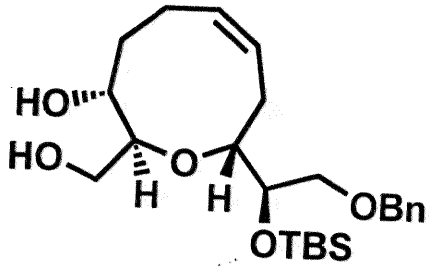
17-6


HO
HO
O
H
H
OBn
OTBS
115
7.260
7.336
0.087
0.075
9
8
7
6
5
4
3
2
1
0
ppm
4.12
1.71
2.16
1.17
0.99
4.20
1.04
7.15
1.23
1.07
1.08
1.04
1.02
1.04
2.10
1.08
9.03
3.05
2.64

17-5

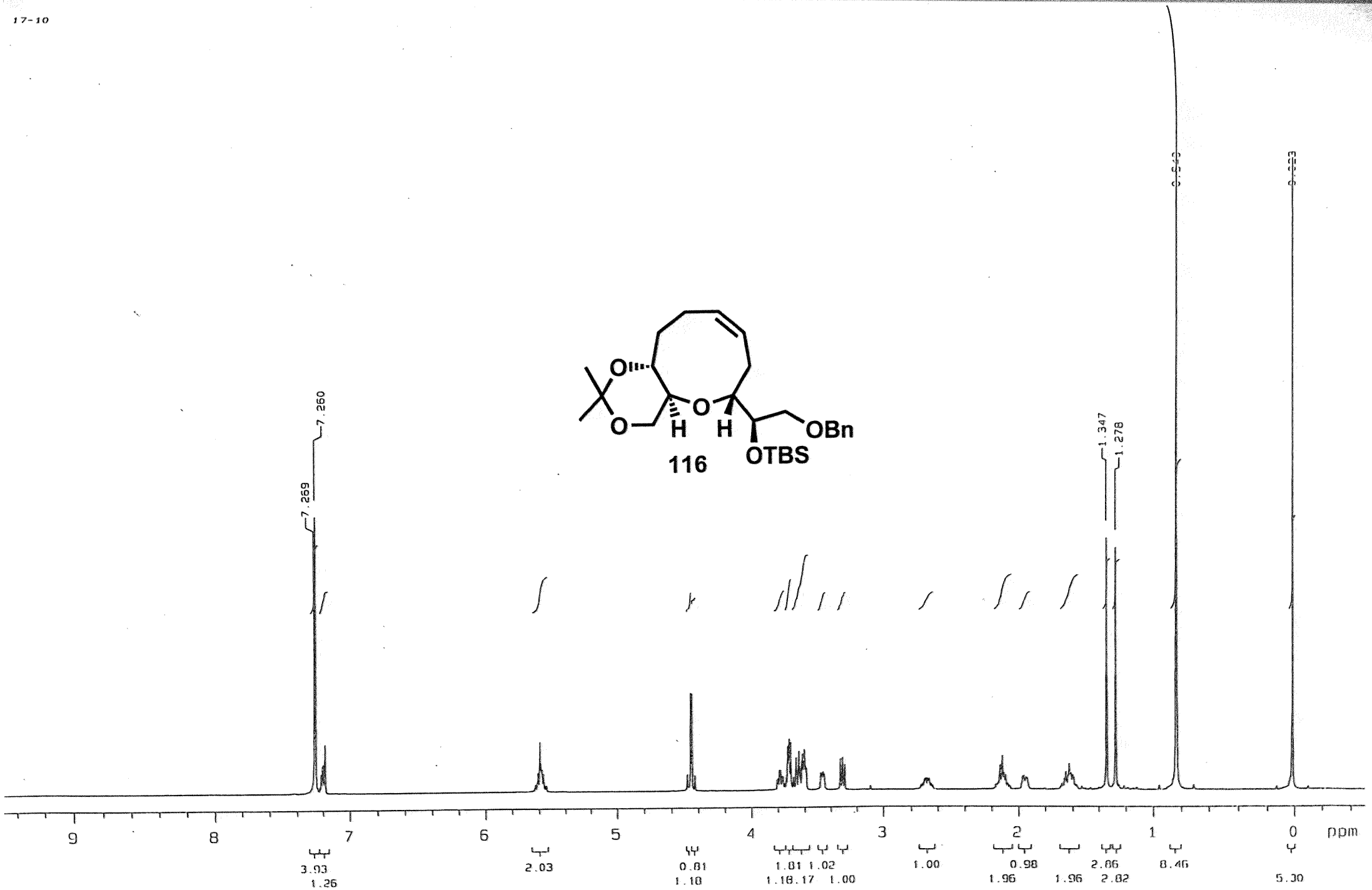
exp2 s2pul

SAMPLE		DEC. & VT	
date	Feb 27 06	dfrq	499.864
solvent	CDCl3	dn	H1
file	exp	dpwr	45
ACQUISITION		dof	0
sfrq	125.704	dm	yyy
tn	C13	dmm	g
at	1.299	dmf	10000
np	78400	dseq	undefined
sw	30165.9	dres	undefined
fb	16600	homo	n
bs	16	PROCESSING	
tpwr	48	lb	1.00
pw	6.0	wtfile	
d1	0.900	proc	ft
tof	1885.5	fn	not used
nt	6400	math	f
ct	80		
alock	n	werr	react
gain	not used	wexp	c13p
FLAGS		wbs	
il	n	wnt	
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-989.2		
wp	27542.6		
vs	8159		
sc	0		
wc	400		
hzmm	68.86		
is	500.00		
rfl	10970.8		
rfp	9679.2		
th	12		
ins	1.000		
ai cdc ph			



115

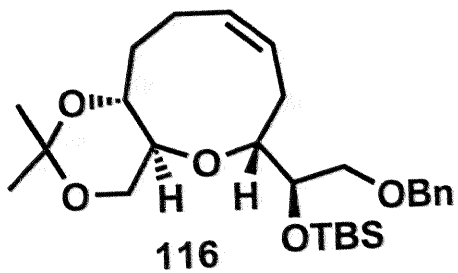
17-10


O
O
O
H
H
OBn
OTBS
116
7.269
7.260
1.347
1.278
9 8 7 6 5 4 3 2 1 0 ppm
3.93
1.26
2.03
0.81
1.18
1.81
1.18.17
1.02
1.00
1.00
0.98
1.96
1.96
2.86
2.82
8.46
5.30

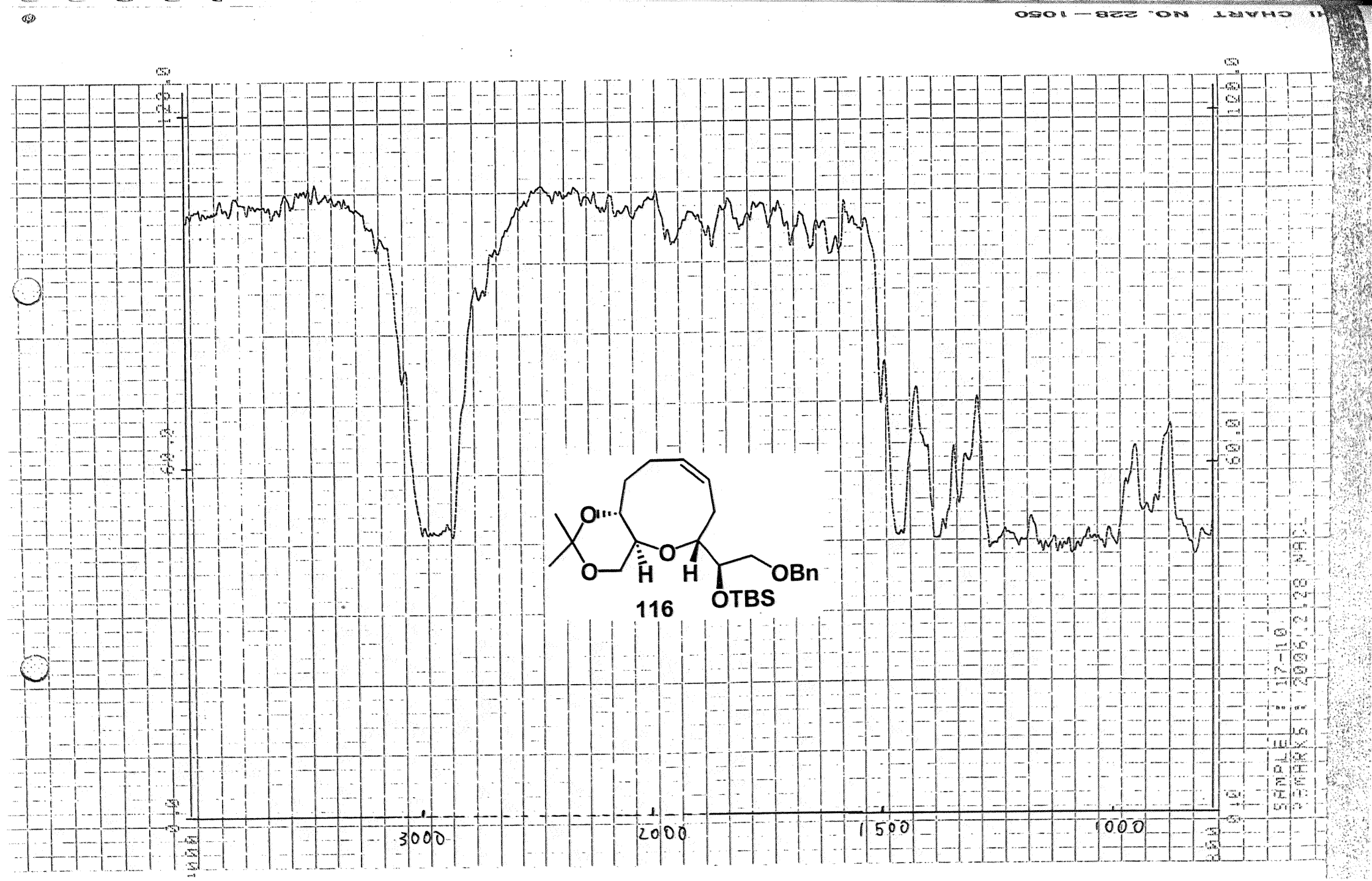
17-10

exp2 s2pul

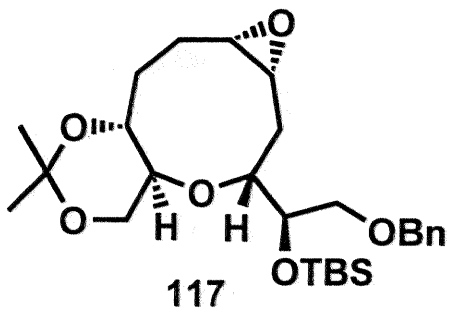
SAMPLE		DEC. & VT	
date	Mar 1 06	dfrq	499.864
solvent	CDCl3	dn	H1
file	exp	dpwr	45
ACQUISITION		dof	0
sfrq	125.704	dm	yyy
tn	C13	dmm	g
at	1.299	dmf	10000
np	78400	dseq	undefined
sw	30165.9	dres	undefined
fb	16600	homo	n
bs	16	PROCESSING	
tpwr	48	lb	1.00
pw	6.0	wtfile	
d1	0.900	proc	ft
tof	1885.5	fn	not used
nt	6400	math	f
ct	96		
alock	n	werr	react
gain	not used	wexp	c13p
FLAGS		wbs	
il	n	wnt	
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-1149.9		
wp	29189.2		
vs	14714		
sc	0		
wc	400		
hzmm	1.43		
is	500.00		
rfl	10968.1		
rfp	9679.2		
th	24		
ins	1.000		
ai cdc ph			



116


O
O
H
O
H
OBn
OTBS
116

17-11


O
O
O
O
H
H
OBn
OTBS

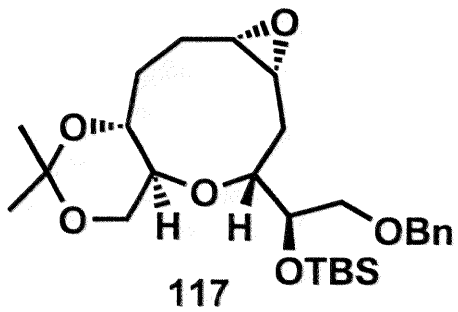
117

7.324
4.520
4.511
3.694
1.447
1.350
0.089
0.080
9
8
7
6
5
4
3
2
1
0
ppm
4.00
1.14
1.00
1.02
1.02
2.01
2.03
1.02
0.98
0.99
1.02
0.95
0.95
0.97
0.98
1.14
0.99
2.95
0.82
8.64
3.02
2.38

17-11

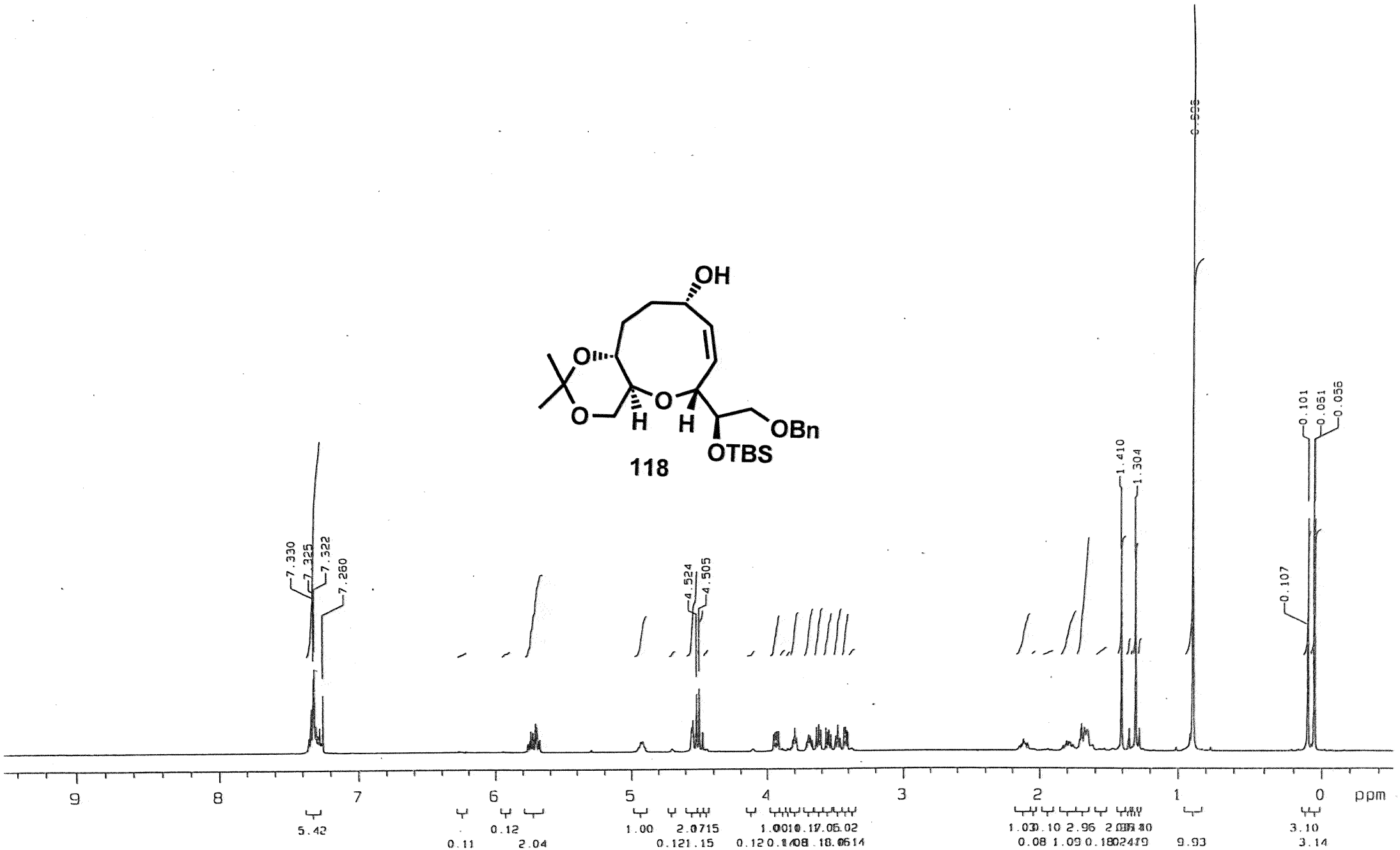
exp2 s2pul

SAMPLE		DEC. & VT	
date	Mar 6 06	dfrq	499.864
solvent	CDCl3	dn	H1
file	exp	dpwr	45
ACQUISITION		dof	0
sfrq	125.704	dm	yyy
tn	C13	dmm	g
at	1.299	dmf	10000
np	78400	dseq	undefined
sw	30165.9	dres	undefined
fb	16600	homo	n
bs	16	PROCESSING	
tpwr	48	lb	1.00
pw	6.0	wtfile	
dl	0.900	proc	ft
tof	1885.5	fn	not used
nt	32000	math	f
ct	80		
alock	n	werr	react
gain	not used	wexp	c13p
FLAGS		wbs	
il	n	wnt	
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-990.1		
wp	27615.4		
vs	10508		
sc	0		
wc	400		
hzmm	5.09		
is	500.00		
rfl	10971.3		
rfp	9679.2		
th	16		
ins	1.000		
ai cdc ph			



117

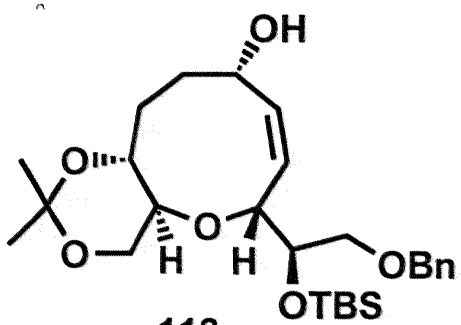
17-13


OH
O
O
O
H
H
OBn
OTBS
118
7.330
7.325
7.322
7.260
4.524
4.505
1.410
1.304
0.101
0.061
0.056
0.107
9
8
7
6
5
4
3
2
1
0
ppm

17-13

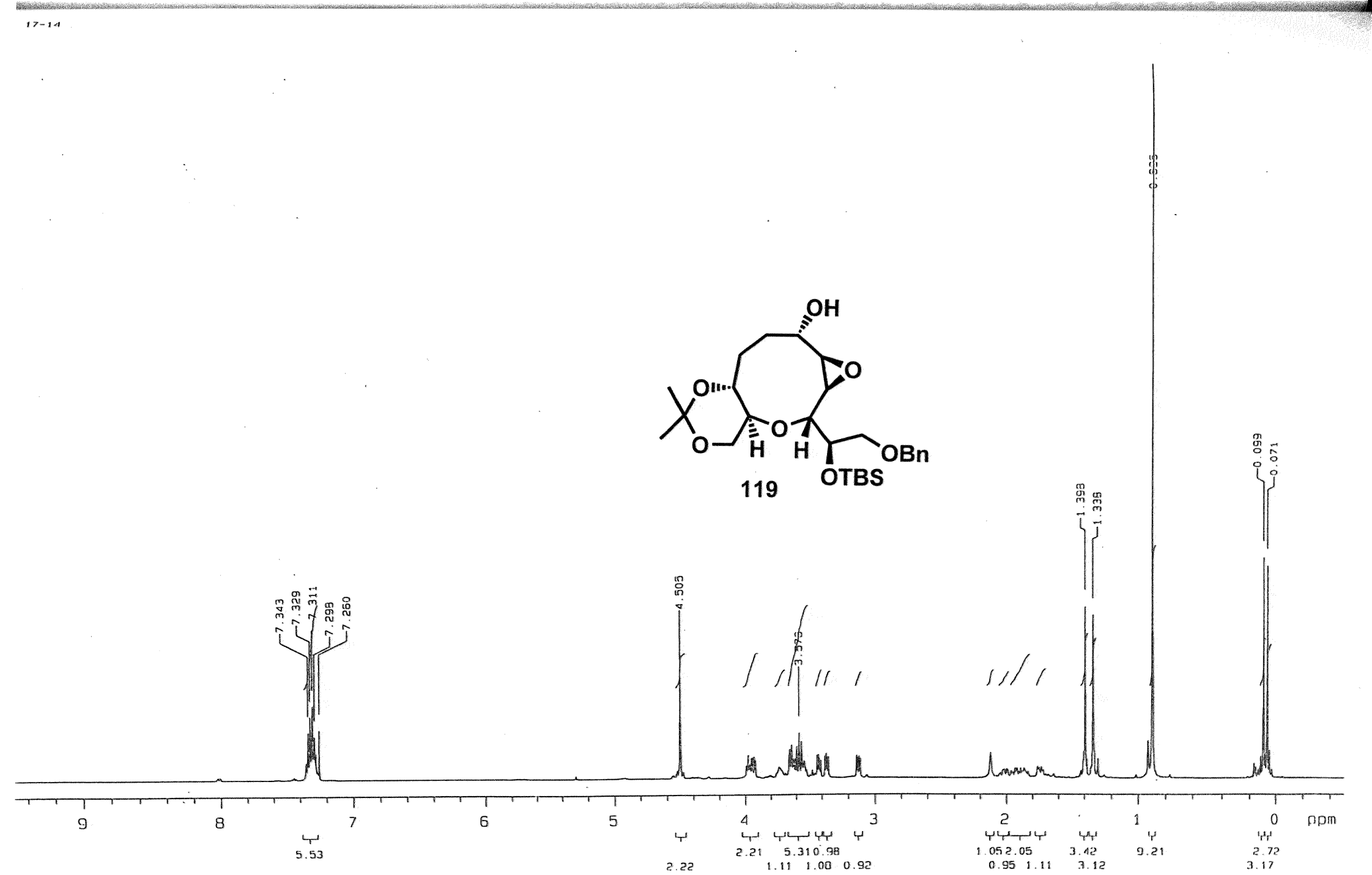
exp2 s2pul

SAMPLE		DEC. & VT	
date	Mar 10 06	dfrq	499.864
solvent	CDCl3	dn	H1
file	exp	dpwr	45
ACQUISITION		dof	0
sfrq	125.704	dm	yyy
tn	C13	dmm	g
at	1.299	dmf	10000
np	78400	dseq	undefined
sw	30165.9	dres	undefined
fb	16600	homo	n
bs	16	PROCESSING	
tpwr	48	lb	1.00
pw	6.0	wtfile	
d1	0.900	proc	ft
tof	1885.5	fn	not used
nt	32000	math	f
ct	128		
alock	n	werr	react
gain	not used	wexp	c13p
FLAGS		wbs	
il	n	wnt	
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-1052.3		
wp	27166.1		
vs	13048		
sc			
wc			
hzmm			
is	5(		
rfl	10(		
rfp	9(		
th			
ins	1		
ai cdc ph			



118

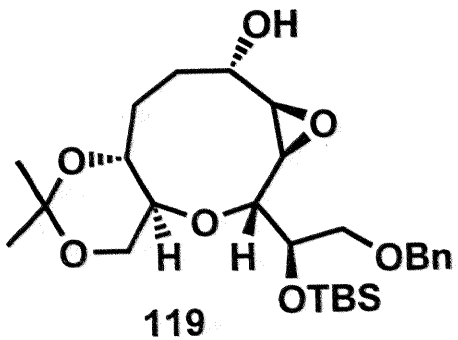
17-14


OH
O
O
O
O
H
H
OBn
OTBS
119
7.343
7.329
7.311
7.298
7.260
4.505
3.575
1.393
1.336
0.825
0.099
0.071
9
8
7
6
5
4
3
2
1
0
ppm
5.53
2.22
2.21
1.11
5.31
1.00
0.98
0.92
1.05
0.95
2.05
1.11
3.42
3.12
9.21
2.72
3.17

17-14

exp2 s2pul

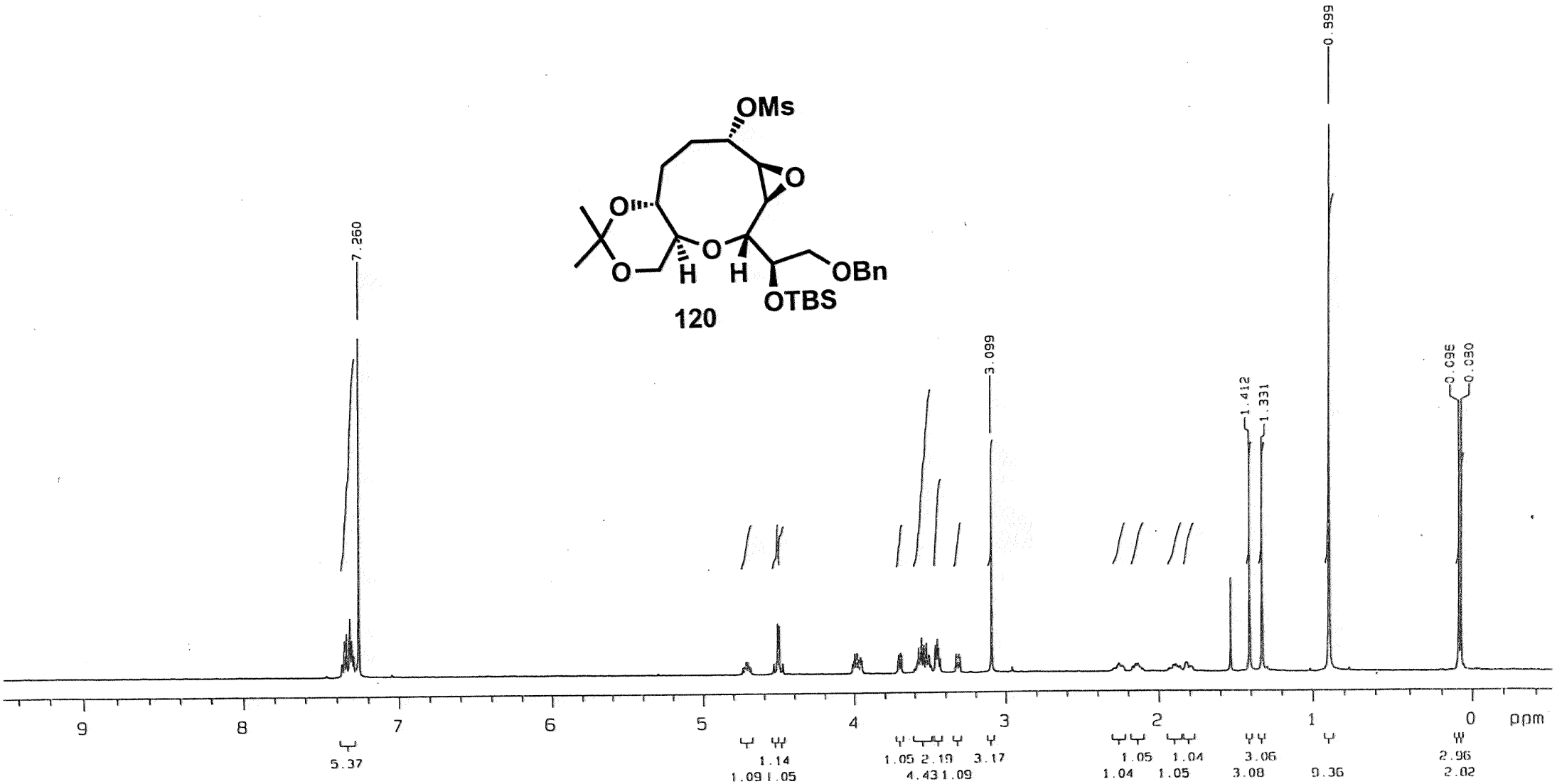
SAMPLE		DEC. & VT	
date	Mar 16 06	dfrq	499.864
solvent	CDCl3	dn	H1
file	exp	dpwr	45
ACQUISITION		dof	0
sfrq	125.704	dm	yyy
tn	C13	dmm	g
at	1.299	dmf	10000
np	78400	dseq	undefined
sw	30165.9	dres	undefined
fb	16600	homo	n
bs	16	PROCESSING	
tpwr	48	lb	1.00
pw	6.0	wtfile	
d1	0.900	proc	ft
tof	1885.5	fn	not used
nt	32000	math	f
ct	160		
alock	n	werr	react
gain	not used	wexp	c13p
FLAGS		wbs	
il	n	wnt	
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-1122.7		
wp	29063.5		
vs	21082		
sc	0		
wc	400		
hzmm	2.93		
is	500.00		
rfl	10968.5		
rfp	9679.2		
th	24		
ins	1.000		
ai cdc ph			



119

HITACHI CHART NO. 228—1050
SAMPLE : LY-14
REMARKS : 2006.3.16 MeOH
OBn
OTBS
OH
H
H
O
O
O
O
119

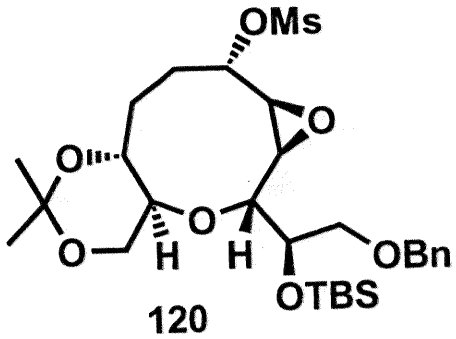
17-15


OMs
O
O
O
O
H
H
OBn
OTBS
120
7.260
3.099
1.412
1.331
0.999
0.095
0.080
9
8
7
6
5
4
3
2
1
0
ppm
5.37
1.14
1.09 1.05
1.05 2.19 3.17
4.43 1.09
1.05 1.04
1.04 1.05
3.06
3.08
9.36
2.96
2.02

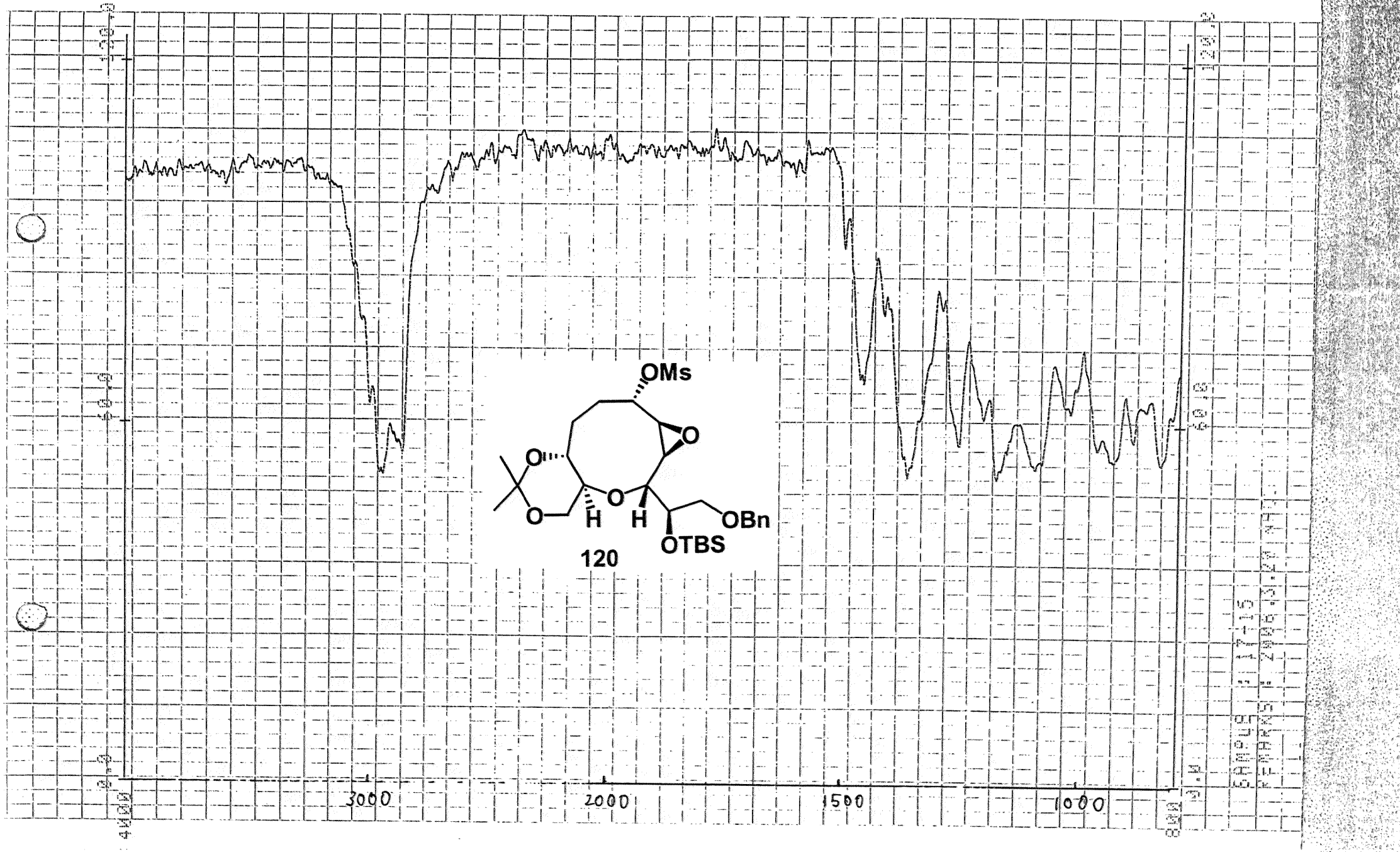
17-15

exp2 s2pul

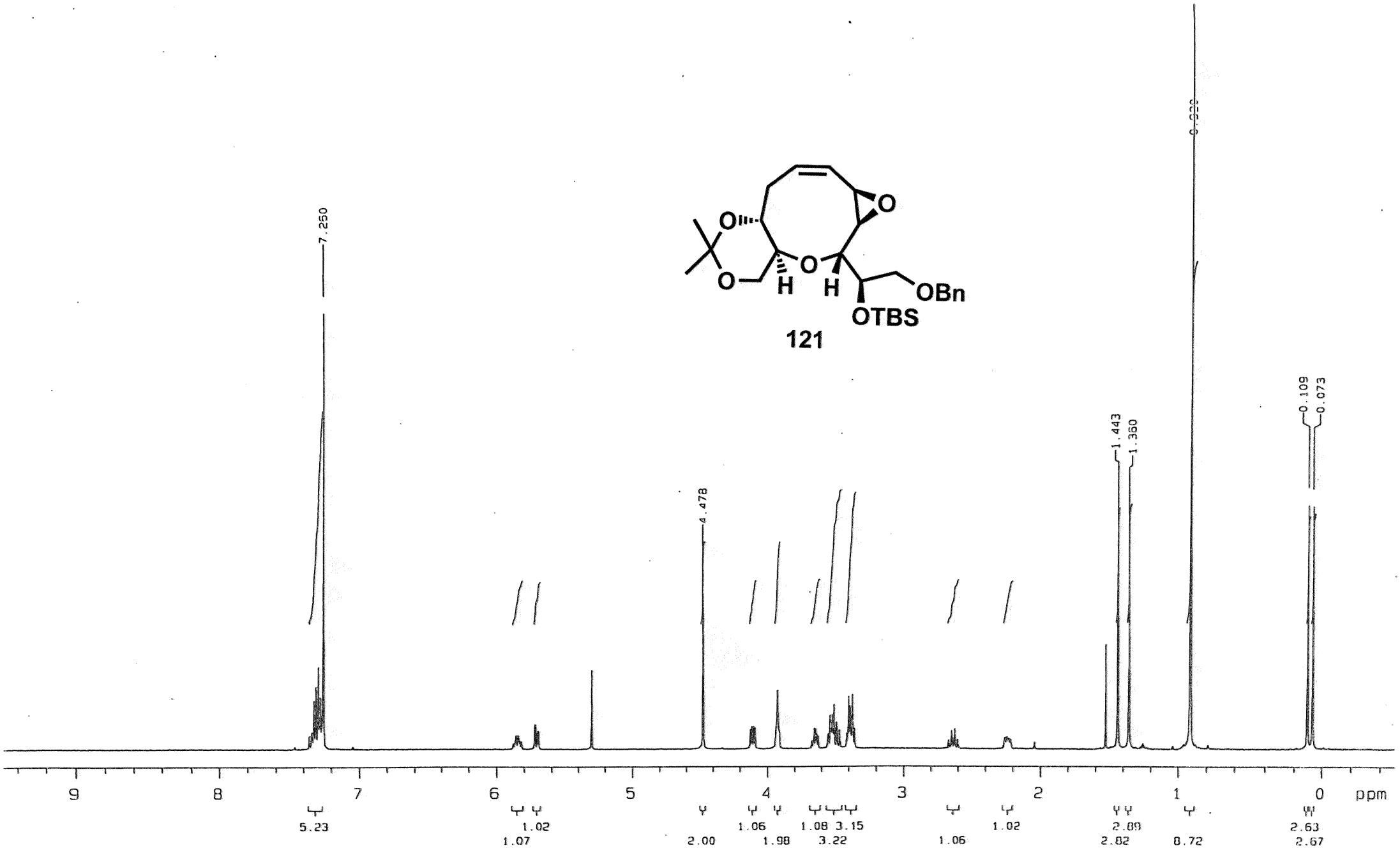
SAMPLE		DEC. & VT	
date	Mar 22 06	dfrq	499.864
solvent	CDCl3	dn	H1
file	exp	dpwr	45
ACQUISITION		dof	0
sfrq	125.704	dm	yyy
tn	C13	dmm	g
at	1.299	dmf	10000
np	78400	dseq	undefined
sw	30165.9	dres	undefined
fb	16600	homo	n
bs	16	PROCESSING	
tpwr	48	lb	1.00
pw	6.0	wtfile	
d1	0.900	proc	ft
tof	1805.5	fn	not used
nt	32000	math	f
ct	80		
alock	n	werr	react
gain	not used	wexp	c13p
FLAGS		wbs	
il	n	wnt	
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-1079.9		
wp	27159.7		
vs	10050		
sc	0		
wc	400		
hzmm	3.63		
is	500.00		
rfl	10970.8		
rfp	9679.2		
th	23		
ins	1.000		
ai cdc ph			



120


OMs
O
O
O
O
H
H
OBn
OTBS
120
3000
2000
1500
1000

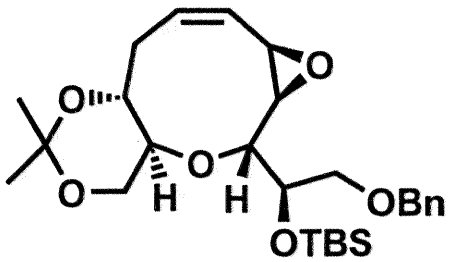
17-17


7.250
4.478
1.443
1.360
0.109
0.073
O
O
O
O
H
H
OBn
OTBS
121
9
8
7
6
5
4
3
2
1
0
ppm
5.23
1.02
1.07
2.00
1.06
1.98
1.08
3.15
3.22
1.06
1.02
2.09
2.82
8.72
2.63
2.67

17-17

exp2 s2pul

SAMPLE		DEC. & VT	
date	Mar 29 06	dfrq.	499.864
solvent	CDCl3	dn	H1
file	exp	dpwr	45
ACQUISITION		dof	0
sfrq	125.704	dm	yyy
tn	C13	dmm	g
at	1.299	dmf	10000
np	78400	dseq	undefined
sw	30165.9	dres	undefined
fb	16600	homo	n
bs	16	**PROCESSING**	
tpwr	48	lb	1.00
pw	6.0	wtfile	
dl	0.900	proc	ft
tof	1885.5	fn	not used
nt	6400	math	f
ct	80		
alock	n	werr	react
gain	not used	wexp	c13p
FLAGS		wbs	
il	n	wnt	
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-1292.1		
wp	30165.9		
vs	6448		
sc	0		
wc	400		
hzmm	75.41		
is	500.00		
rfl	10971.3		
rfp	9679.2		
th	24		
ins	1.000		
ai cdc ph			

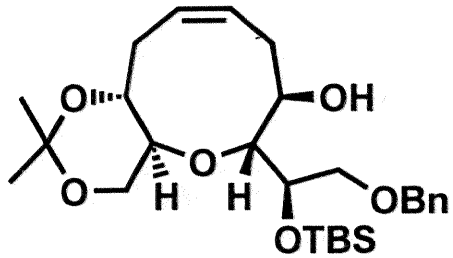


121

138.031
129.704
126.243
127.605
127.525
126.123
98.147
78.750
77.253
77.000
76.747
73.917
73.368
73.123
71.159
70.819
63.847
54.088
53.957
35.962
28.749
23.333
19.114
18.151
-4.109
-5.141

220 200 180 160 140 120 100 80 60 40 20 0 ppm

17-18


O
O
O
H
H
OH
OBn
OTBS

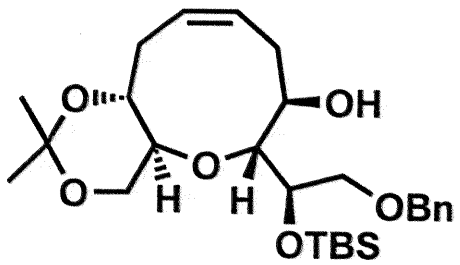
122

7.343
7.342
7.329
7.327
7.314
7.260
4.531
4.523
4.095
4.090
4.086
3.645
3.594
3.495
3.487
3.482
3.476
3.462
1.442
1.339
0.131
0.091
9 8 7 6 5 4 3 2 1 0 ppm
5.26
1.09
1.09
1.00
1.15
1.06 1.08 1.12
2.04 1.08 1.09 1.13
1.76 2.07
1.10
3.12
2.98
8.97
2.03
2.82

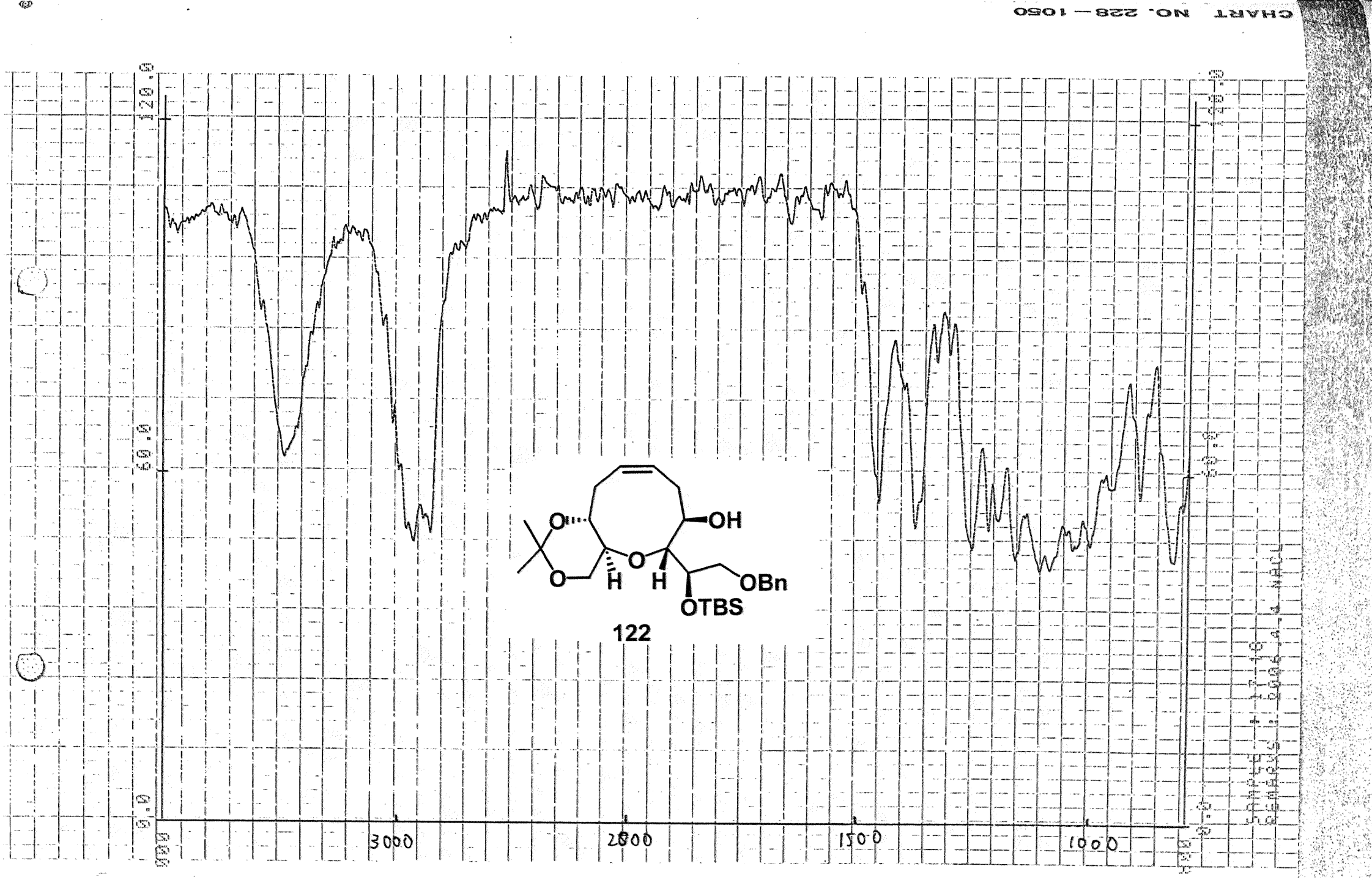
17-18 temp=40

exp2 s2pul

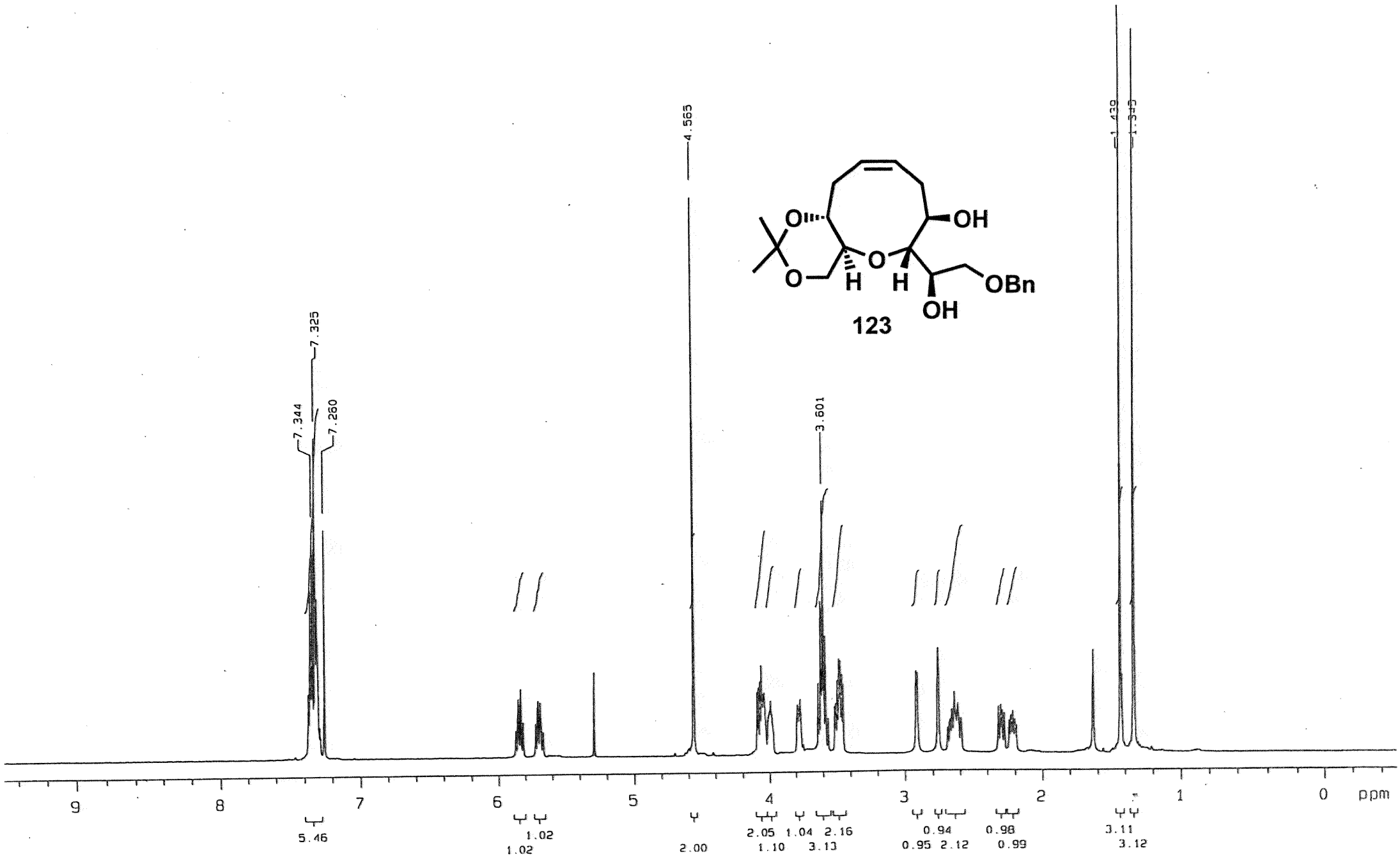
SAMPLE		DEC. & VT	
date	Apr 10 06	dfrq	499.864
solvent	CDCl3	dn	H1
file	exp	dpwr	45
ACQUISITION		dof	0
sfrq	125.704	dm	yyy
tn	C13	dmm	g
at	1.299	dmf	10000
np	78400	dseq	undefined
sw	30165.9	dres	undefined
fb	16600	homo	n
bs	16	temp	40.0
tpwr	48	PROCESSING	
pw	6.0	lb	1.00
d1	0.900	wtfile	
tof	1885.5	proc	ft
nt	16000	fn	not used
ct	272	math	f
alock	n		
gain	not used	werr	react
FLAGS		wexp	c13p
il	n	wbs	
in	n	wnt	
dp	y		
hs	nn		
DISPLAY			
sp	-970.8		
wp	27672.0		
vs	15401		
sc	0		
wc	400		
hzmm	21.60		
is	500.00		
rfl	10961.6		
rfp	9679.2		
th	9		
ins	1.000		
ai cdc ph			



122


OH
O
O
O
H
H
OBn
OTBS
122
3000
2000
1500
1000

17-22


7.344
7.325
7.260
4.565
3.601
1.439
1.345
9
8
7
6
5
4
3
2
1
0
ppm
5.46
1.02
1.02
2.00
2.05
1.10
1.04
3.13
2.16
0.95
0.94
2.12
0.98
0.99
3.11
3.12

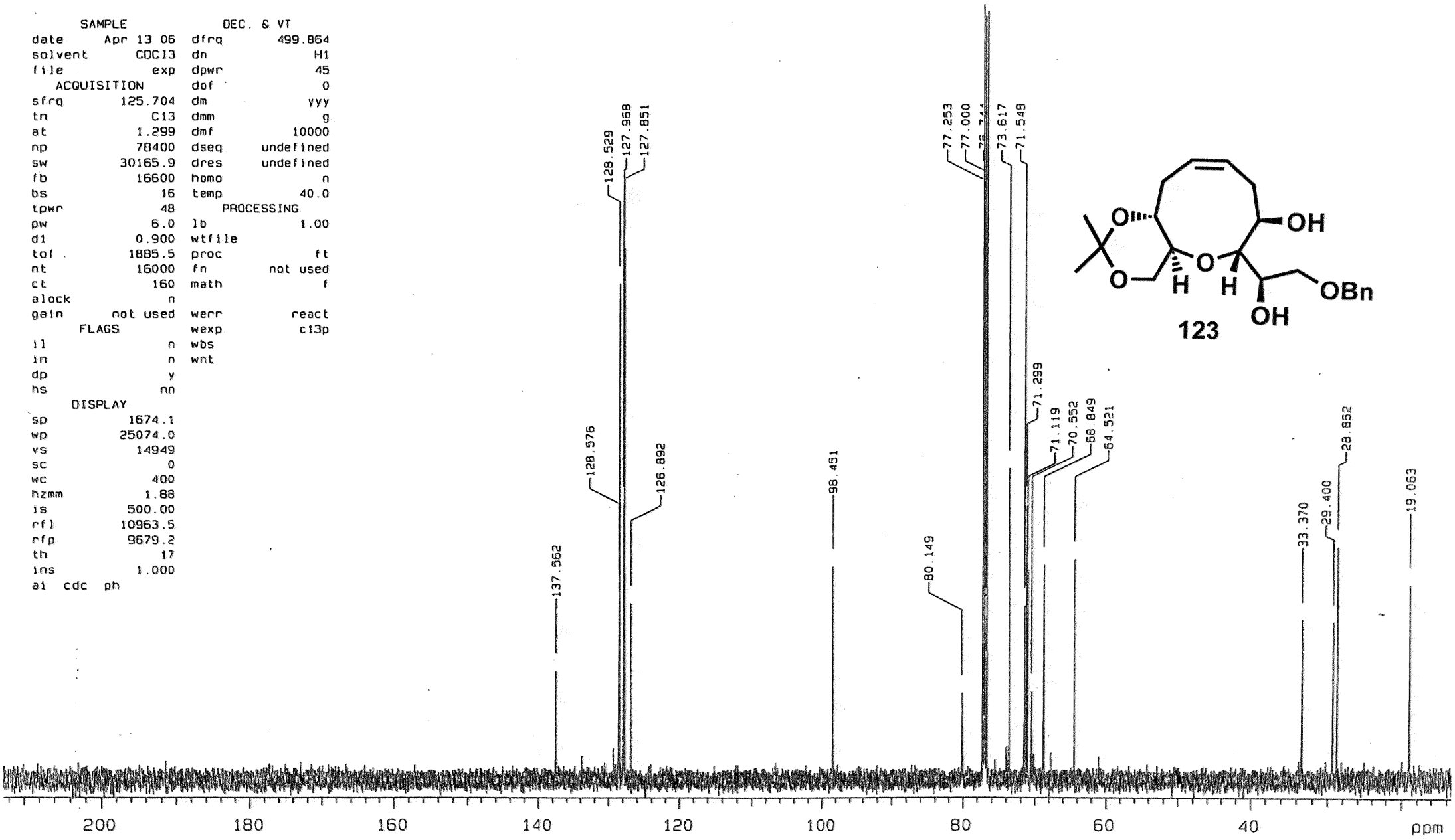
O
O
O
H
H
OH
OH
OBn

123

17-22

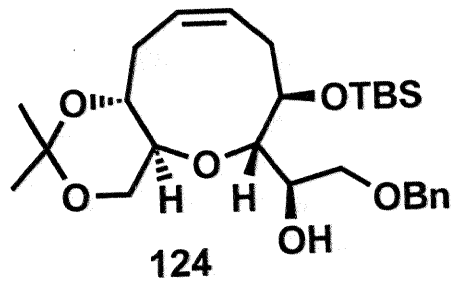
exp2 s2pul

SAMPLE		DEC. & VT	
date	Apr 13 06	dfrq	499.864
solvent	CDCl3	dn	H1
file	exp	dpwr	45
ACQUISITION		dof	0
sfrq	125.704	dm	yyy
tn	C13	dmm	g
at	1.299	dmf	10000
np	78400	dseq	undefined
sw	30165.9	dres	undefined
fb	16600	homo	n
bs	16	temp	40.0
tpwr	48	**PROCESSING**	
pw	6.0	lb	1.00
d1	0.900	wtfile	
tof	1885.5	proc	ft
nt	16000	fn	not used
ct	160	math	f
alock	n		
gain	not used	werr	react
FLAGS		wexp	c13p
il	n	wbs	
in	n	wnt	
dp	y		
hs	nn		
DISPLAY			
sp	1674.1		
wp	25074.0		
vs	14949		
sc	0		
wc	400		
hzmm	1.88		
is	500.00		
rfl	10963.5		
rfp	9679.2		
th	17		
ins	1.000		
ai cdc ph			



123

17-23


OTBS
OBn
OH
H
H
O
O
O

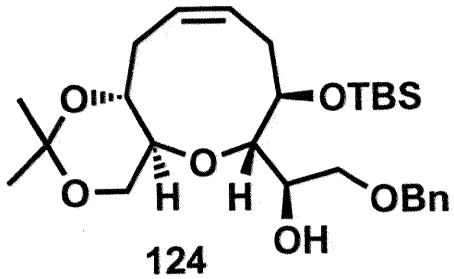
124

7.351
7.347
7.337
7.324
7.317
7.314
7.300
7.260
4.594
4.571
4.551
4.527
4.397
4.355
4.121
4.108
3.515
3.497
3.488
3.480
3.462
3.448
3.389
3.371
2.820
2.813
2.266
2.072
1.422
1.335
0.915
0.639
0.160
0.100
0.094
9
8
7
6
5
4
3
2
1
0
ppm
4.95
1.01
1.00
1.01
1.02
1.00
2.02
0.98
4.08
0.97
1.97
0.94
1.98
2.82
2.81
8.99
2.63
2.97

17-23

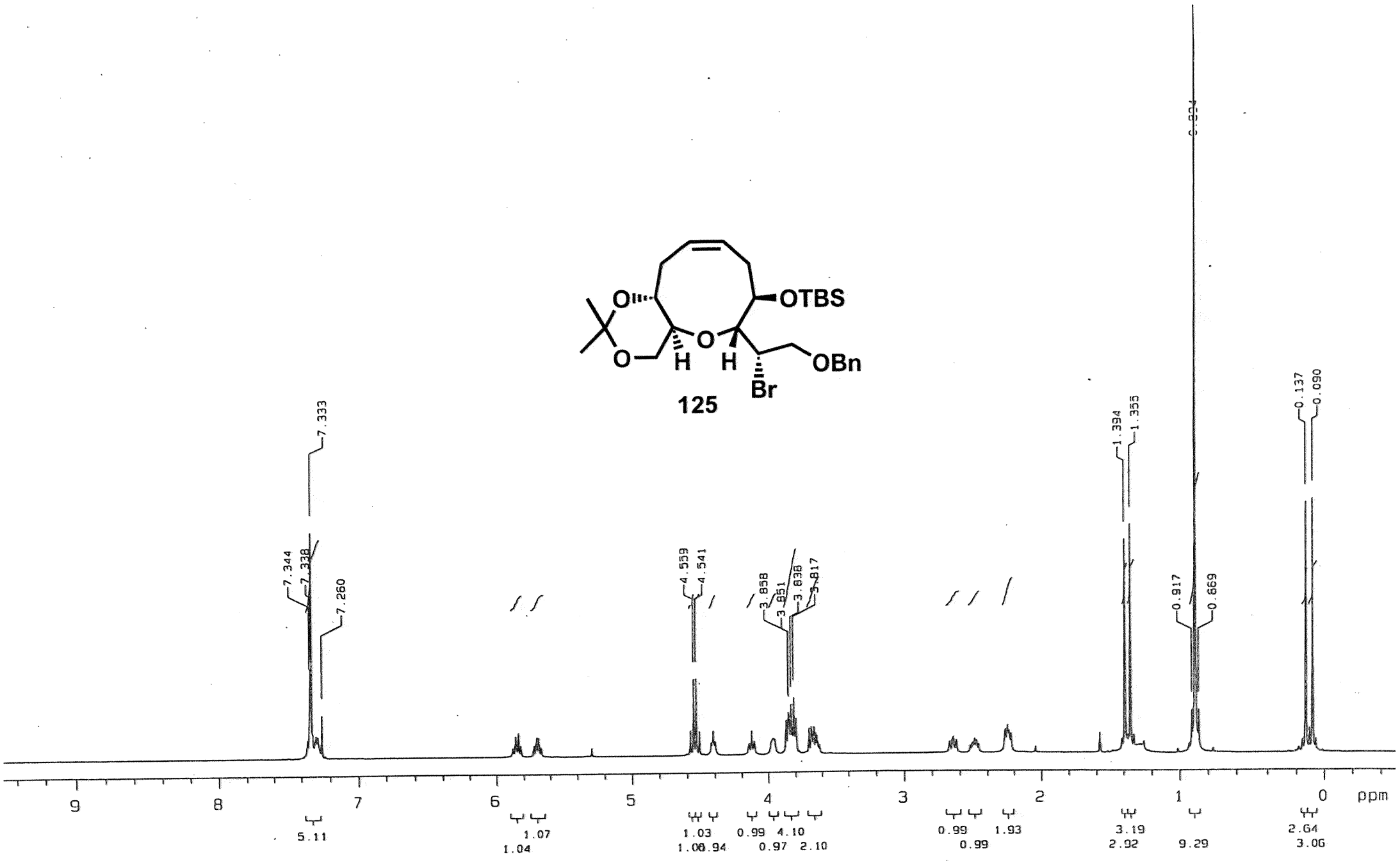
exp2 s2pul

SAMPLE		DEC. & VT	
date	Apr 18 06	dfrq	499.864
solvent	CDCl3	dn	H1
file	exp	dpwr	45
ACQUISITION		dof	0
sfrq	125.704	dm	yyy
tn	C13	dmm	g
at	1.299	dmf	10000
np	78400	dseq	undefined
sw	30165.9	dres	undefined
fb	16600	homo	n
bs	16	temp	40.0
tpwr	48	PROCESSING	
pw	6.0	lb	1.00
d1	0.900	wtfile	
tof	1885.5	proc	ft
nt	16000	fn	not used
ct	80	math	f
alock	n		
gain	not used	werr	react
FLAGS		wexp	c13p
il	n	wbs	
in	n	wnt	
dp	y		
hs	nn		
DISPLAY			
sp	-1074.4		
wp	28983.9		
vs	11968		
sc	0		
wc	400		
hzmm	72.46		
is	500.00		
rfl	10962.1		
rfp	9679.2		
th	21		
ins	1.000		
ai cdc ph			



124

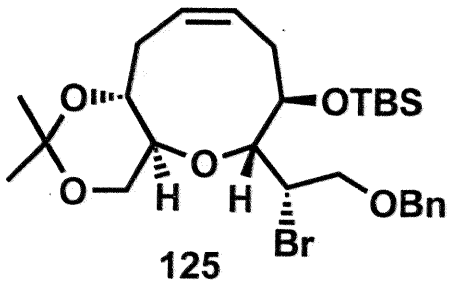
17-24


OTBS
O
O
O
H
H
OBn
Br
125
7.333
7.344
7.338
7.260
4.559
4.541
3.858
3.851
3.838
3.817
1.394
1.355
0.917
0.669
0.137
0.090
9
8
7
6
5
4
3
2
1
0
ppm
5.11
1.07
1.04
1.03
1.00
0.94
0.99
4.10
0.97
2.10
0.99
0.99
1.93
3.19
2.92
9.29
2.64
3.06

17-24

exp2 s2pul

SAMPLE		DEC. & VT	
date	Apr 21 06	dfrq	499.864
solvent	CDCl3	dn	H1
file	exp	dpwr	45
ACQUISITION		dof	0
sfrq	125.704	dm	yyy
tn	C13	dmm	g
at	1.299	dmf	10000
np	78400	dseq	undefined
sw	30165.9	dres	undefined
fb	16600	homo	n
bs	16	temp	40.0
tpwr	48	**PROCESSING**	
pw	6.0	lb	1.00
d1	0.900	wtfile	
tof	1885.5	proc	fl
nt	6400	fn	not used
ct	240	math	f
alock	n		
gain	not used	werr	react
FLAGS		wexp	c13p
il	n	wbs	
in	n	wnt	
dp	y		
hs	nn		
DISPLAY			
sp	-867.7		
wp	23654.5		
vs	16455		
sc	0		
wc	400		
hzmm	15.48		
is	500.00		
rfl	10962.1		
rfp	9679.2		
th	10		
ins	1.000		
ai cdc ph			



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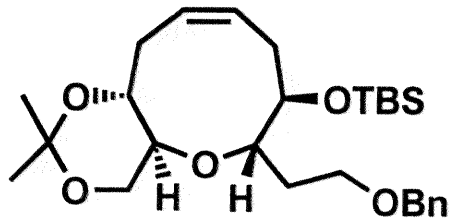
17-25


OTBS
OBn
O
O
O
H
H

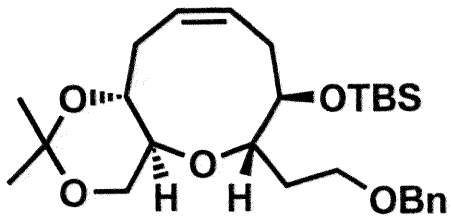
126

7.327
1.416
1.348
0.128
0.069
9
8
7
6
5
4
3
2
1
0
ppm
4.93
1.00
1.00
0.57
1.00
0.98
1.00
1.05
1.01
0.99
1.08
0.96
1.95
2.94
1.08
3.04
3.00
8.87
2.71
2.82

17-254

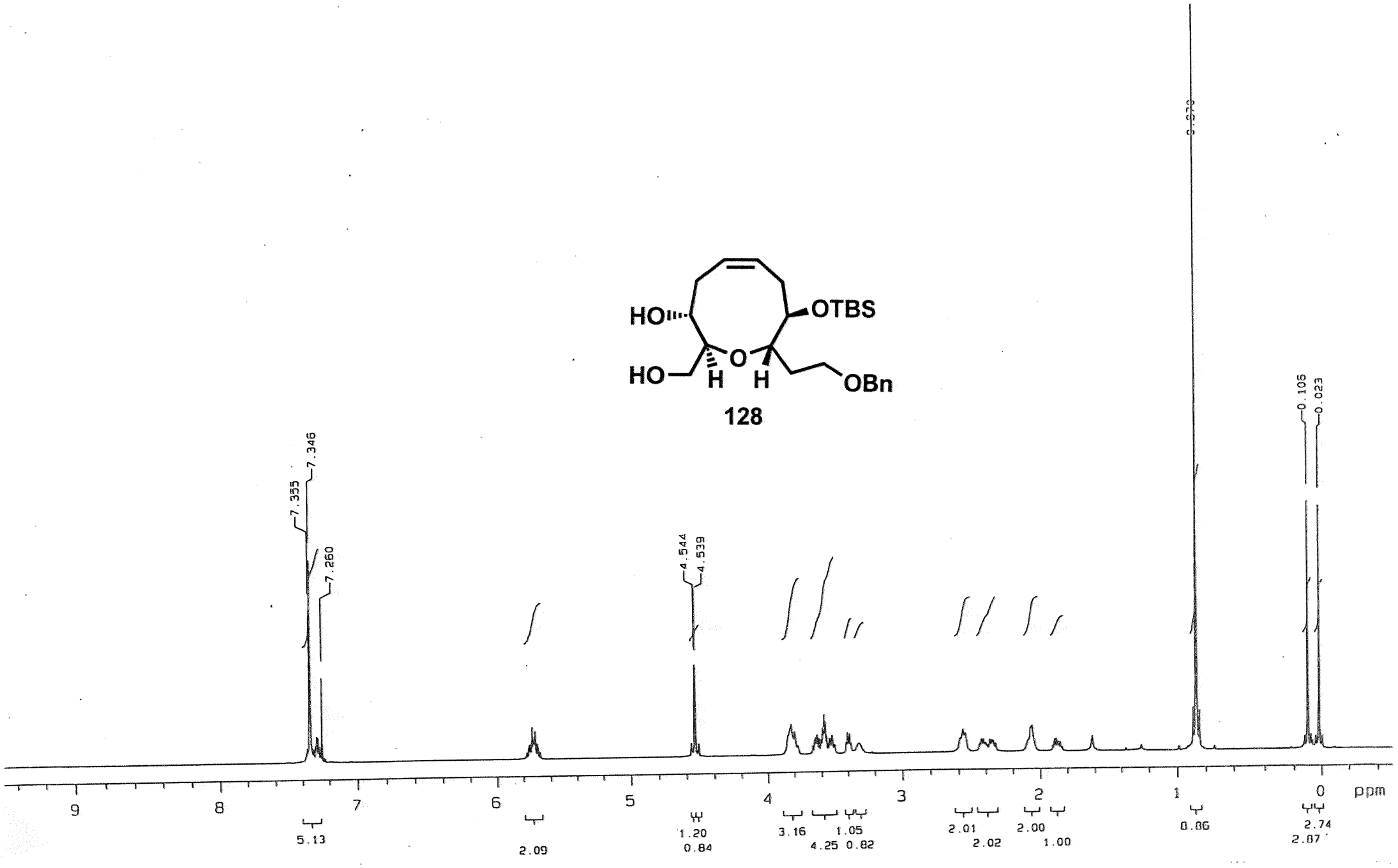
exp3 s2pul

SAMPLE		DEC. & VT	
date	Apr 27 06	dfrq	499.864
solvent	CDCl3	dn	H1
file	exp	dpwr	45
ACQUISITION		dof	0
sfrq	125.704	dm	yyy
tn	C13	dmm	g
at	1.299	dmf	10000
np	78400	dseq	undefined
sw	30165.9	dres	undefined
fb	16600	homo	n
bs	16	temp	40.0
tpwr	48	PROCESSING	
pw	6.0	lb	1.00
d1	0.900	wtfile	
tof	1885.5	proc	ft
nt	8000	fn	not used
ct	80	math	f
alock	n		
gain	not used	werr	react
FLAGS		wexp	c13p
il	n	wbs	
in	n	wnt	
dp	y		
hs	nn		
DISPLAY			
sp	-1002.6		
wp	26903.7		
vs	11764		
sc	0		
wc	400		
hzmm	67.26		
is	500.00		
rfl	10962.1		
rfp	9679.2		
th	18		
ins	1.000		
ai cdc ph			



126

17-26

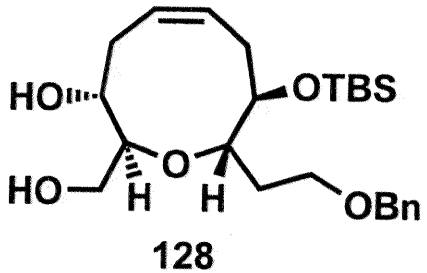

HO
OTBS
HO
O
H
H
OBn
128
7.355
7.346
7.260
4.544
4.539
0.105
0.023
9
8
7
6
5
4
3
2
1
0
ppm
5.13
2.09
1.20
0.84
3.16
1.05
4.25
0.82
2.01
2.02
2.00
1.00
8.86
2.74
2.87

17-26

exp2 s2pul

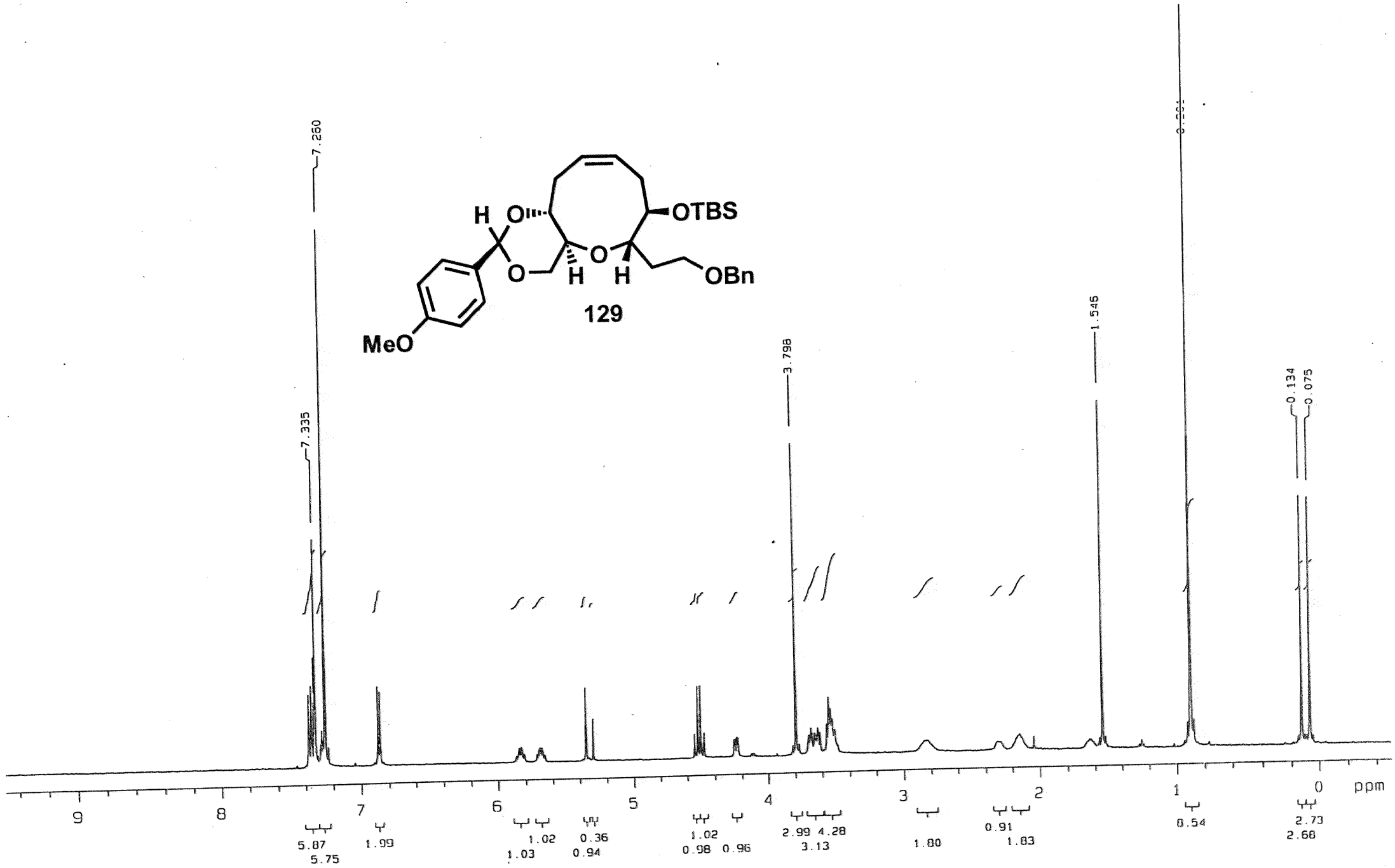
SAMPLE		DEC. & VT	
date	May 2 06	dfrq	499.864
solvent	CDCl3	dn	H1
file	exp	dpwr	45
ACQUISITION		dof	0
sfrq	125.704	dm	yyy
tn	C13	dmm	g
at	1.299	dmf	10000
np	78400	dseq	undefined
sw	30165.9	dres	undefined
fb	16600	homo	n
bs	16	temp	40.0
tpwr	48	PROCESSING	
pw	6.0	lb	0.60
d1	0.900	wtfile	
tof	1885.5	proc	ft
nt	6400	fn	not used
ct	208	math	f
alock	n		
gain	not used	werr	react
FLAGS		wexp	c13p
il	n	wbs	
in	n	wnt	
dp	y		
hs	nn		
DISPLAY			
sp	-983.7		
wp	26673.1		
vs	9418		
sc	0		
wc	400		
hzmm	6.21		
is	500.00		
rfl	10963.5		
rfp	9679.2		
th	7		
ins	1.000		

at cdc ph



128

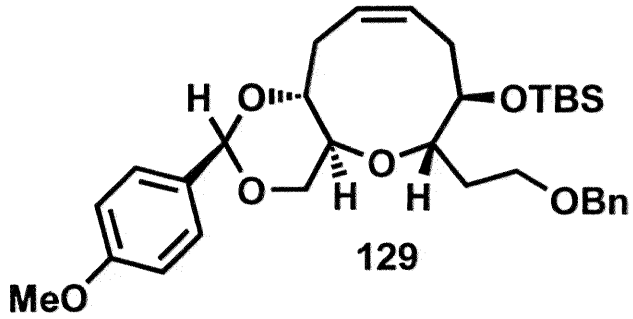
17-28


7.260
7.335
3.798
1.546
0.134
0.075
H
O
O
O
H
H
OTBS
OBn
MeO
129
9
8
7
6
5
4
3
2
1
0
ppm
5.87
5.75
1.99
1.03
1.02
0.94
0.36
1.02
0.98
0.96
2.99
3.13
4.28
1.80
0.91
1.83
0.54
2.73
2.68

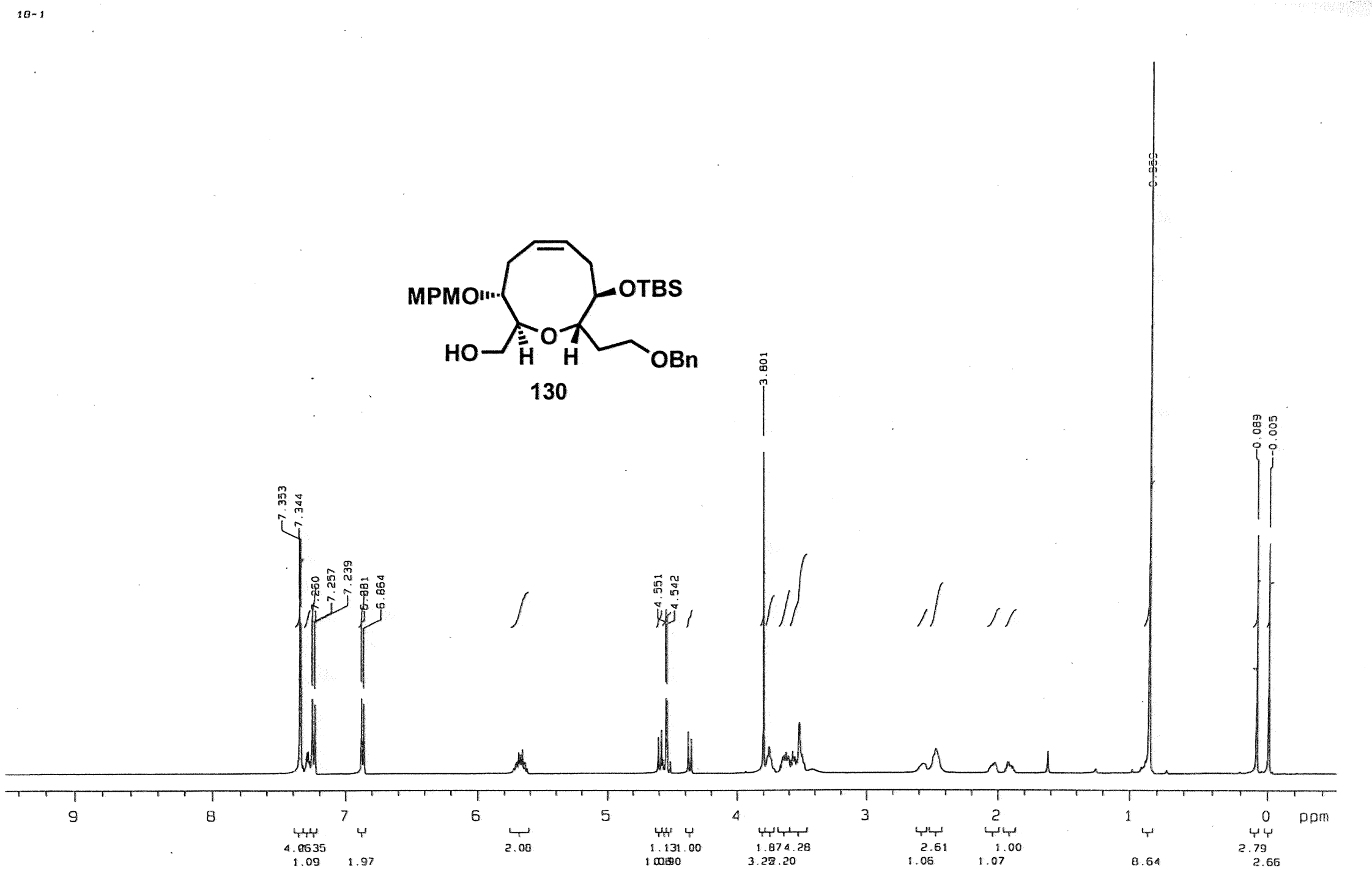
17-28

exp2 s2pul

SAMPLE		DEC. & VT	
date	May 8 06	dfrq	499.864
solvent	CDCl3	dn	H1
file	exp	dpwr	45
ACQUISITION		dof	0
sfrq	125.704	dm	yyy
tn	C13	dmm	g
at	1.299	dmf	10000
np	78400	dseq	undefined
sw	30165.9	dres	undefined
fb	16600	homo	n
bs	16	temp	40.0
tpwr	48	PROCESSING	
pw	6.0	lb	0.60
d1	0.900	wtfile	
tof	1885.5	proc	ft
nt	6400	fn	not used
ct	256	math	f
alock	n		
gain	not used	werr	react
FLAGS		wexp	c13p
il	n	wbs	
in	n	wnt	
dp	y		
hs	nn		
DISPLAY			
sp	-1016.4		
wp	26713.2		
vs	7330		
sc	0		
wc	400		
hzmm	10.68		
is	500.00		
rfl	10966.2		
rfp	9679.2		
th	4		
ins	1.000		
ai cdc ph			



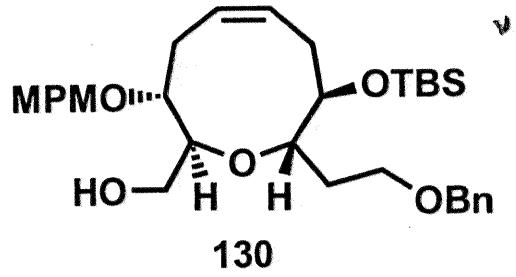
129


MPMO
OTBS
HO
H
H
O
OBn
130
7.353
7.344
7.260
7.257
7.239
6.881
6.864
4.551
4.542
3.801
0.089
-0.005
9
8
7
6
5
4
3
2
1
0
ppm
4.08
35
1.09
1.97
2.00
1.13
1.00
1.87
4.28
3.22
2.20
2.61
1.06
1.00
1.07
8.64
2.79
2.66

18-1

exp2 s2pul

SAMPLE		DEC. & VT	
date	May 12 06	dfrq	499.864
solvent	CDCl3	dn	H1
file	exp	dpwr	45
ACQUISITION		dof	0
sfrq	125.704	dm	yyy
tn	C13	dmm	g
at	1.299	dmf	10000
np	78400	dseq	undefined
sw	30165.9	dres	undefined
fb	16600	homo	n
bs	16	temp	40.0
tpwr	48	**PROCESSING**	
pw	6.0	lb	0.80
d1	0.900	wtfile	
tof	1885.5	proc	ft
nt	6400	fn	not used
ct	288	math	f
alock	n		
gain	not used	werr	react
FLAGS		wexp	c13p
il	n	wbs	
in	n	wnt	
dp	y		
hs	nn		
DISPLAY			
sp	-1020.0		
wp	26598.6		
vs	11328		
sc	0		
wc	400		
hzmm	3.15		
is	500.00		
rfl	10964.4		
rfp	9679.2		
th	5		
ins	1.000		
ai cdc ph			

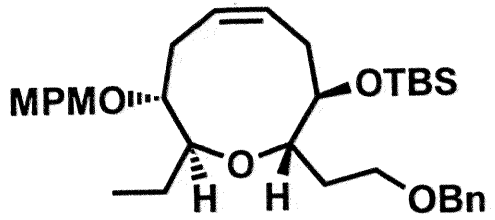


130

159.405
138.058
130.169
129.554
128.345
127.840
127.650
127.599
127.489
113.951
77.253
77.000
76.744
76.586
73.217
72.104
71.075
67.300
62.591
55.271
32.784
31.641
27.544
23.733
17.880
14.197
4.889

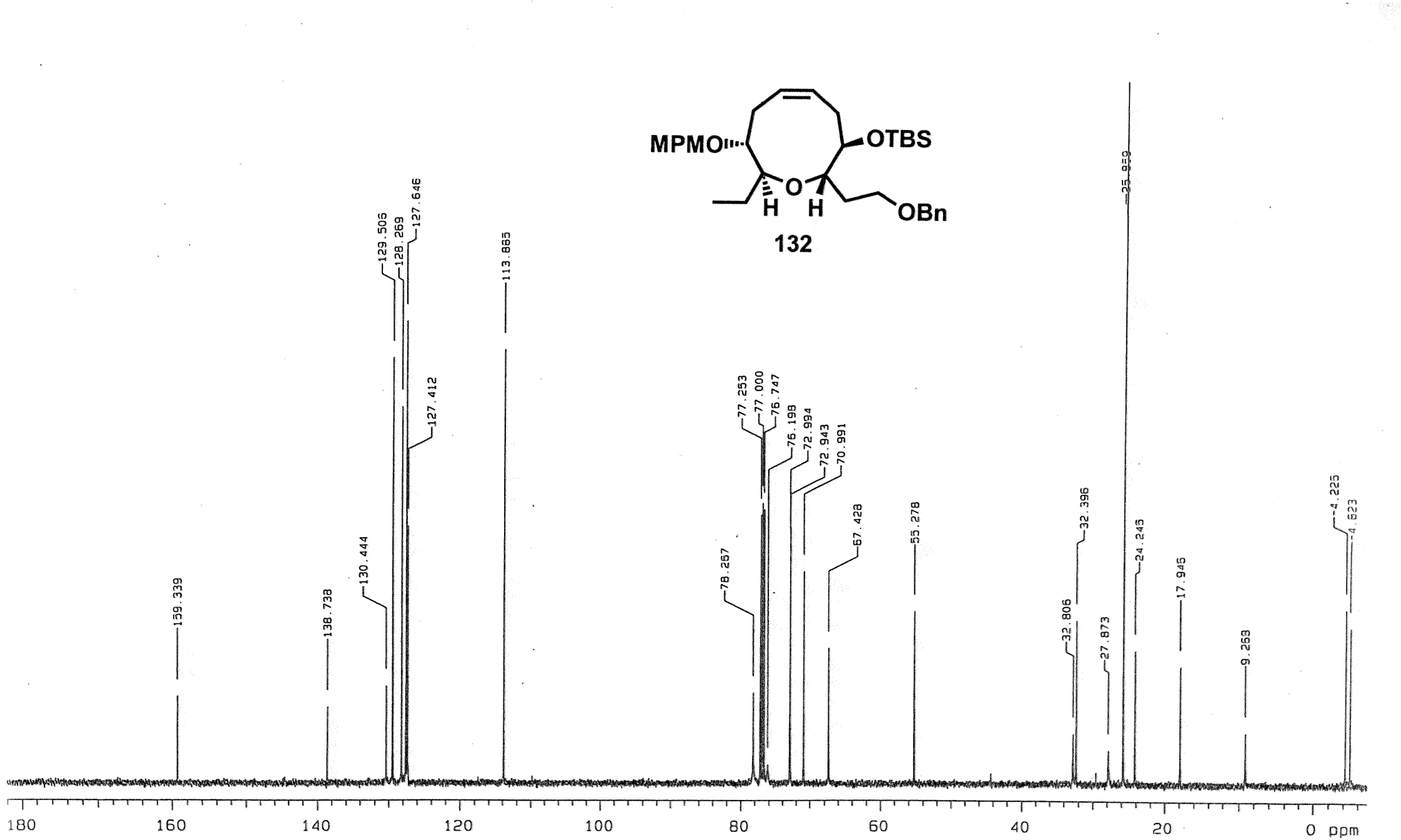
77.8 77.0 ppm

200 180 160 140 120 100 80 60 40 20 0 ppm

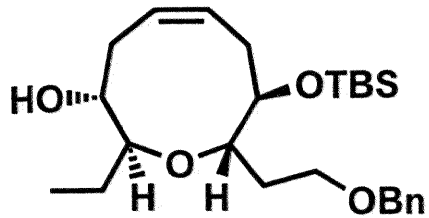

MPMO
OTBS
O
H
H
OBn

132

7.319
7.250
3.799
1.566
0.036
0.027
9 8 7 6 5 4 3 2 1 0 ppm
4.23 6.18
2.14
2.26
1.0116 1.1307
3.33 2.20 3.3001.16
1.07 2.81
1.14 2.00 1.03
12.99
3.12 3.02


MPMO
OTBS
O
H
H
OBn
132
159.339
138.738
130.444
129.506
128.269
127.646
127.412
113.885
78.267
77.253
77.000
76.747
76.198
72.994
72.943
70.991
67.428
55.278
32.806
32.396
27.873
25.959
24.245
17.945
9.268
-4.225
-4.823
180
160
140
120
100
80
60
40
20
0 ppm

18-6 d.p.


HO
OTBS
O
H
H
OBn

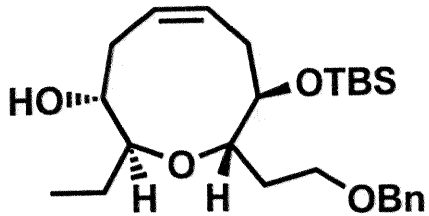
142

7.335
7.326
7.280
4.515
4.494
0.933
0.891
0.105
0.035
9
8
7
6
5
4
3
2
1
0
ppm
4.06
1.43
0.98
1.04
1.11
1.00
0.93
0.98
0.97
1.79
1.01
0.74
8.84
2.99
2.95
2.81

18-6

exp2 s2pul

SAMPLE		DEC. & VT	
date	May 29 06	dfrq	499.864
solvent	CDCl3	dn	H1
file	exp	dpwr	45
ACQUISITION		dof	0
sfrq	125.704	dm	yyy
tn	C13	dmm	g
at	1.299	dmf	10000
np	78400	dseq	undefined
sw	30165.9	dres	undefined
fb	16600	homo	n
bs	16	temp	40.0
tpwr	48	PROCESSING	
pw	6.0	lb	1.00
d1	0.900	wtfile	
tof	1885.5	proc	ft
nt	16000	fn	not used
ct	240	math	f
alock	n		
gain	not used	werr	react
FLAGS		wexp	c13p
il	n	wbs	
in	n	wnt	
dp	y		
hs	nn		
DISPLAY			
sp	-1074.4		
wp	26806.2		
vs	8336		
sc	0		
wc	400		
hzmm	0.70		
is	500.00		
rfl	10963.9		
rfp	9679.2		
th	5		
ins	1.000		
ai cdc ph			



142

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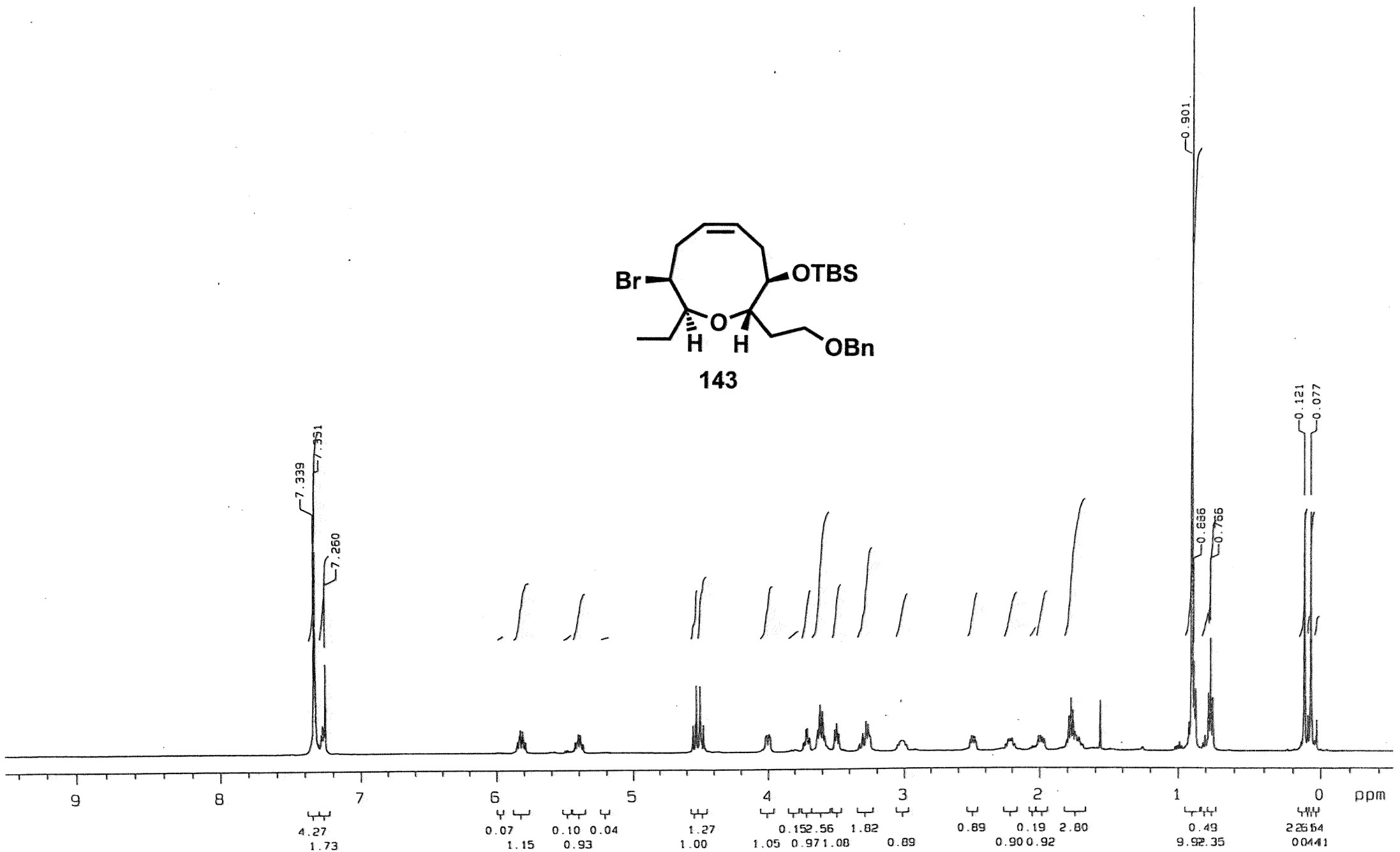
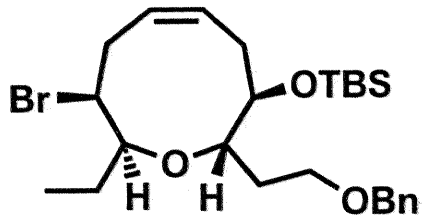

Br
OTBS
O
H
H
OBn
143
7.339
7.351
7.260
0.901
0.886
0.766
0.121
0.077
9
8
7
6
5
4
3
2
1
0
ppm
4.27
1.73
0.07
1.15
0.10
0.93
0.04
1.27
1.00
0.15
2.56
1.05
0.97
1.08
1.82
0.89
0.89
0.90
0.19
0.92
2.80
0.49
9.92
2.35
2.26
0.04
4.41

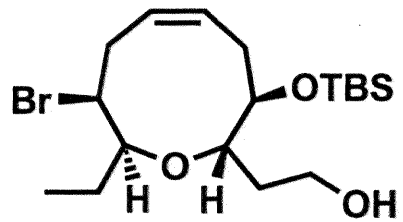
18-7

exp2 s2pul

SAMPLE		DEC. & VT	
date	Jun 2 06	dfrq	499.864
solvent	CDCl3	dn	H1
file	exp	dpwr	45
ACQUISITION		dof	0
sfrq	125.704	dm	yyy
tn	C13	dmm	g
at	1.299	dmf	10000
np	78400	dseq	undefined
sw	30165.9	dres	undefined
fb	16600	homo	n
bs	16	temp	40.0
tpwr	48	PROCESSING	
pw	6.0	lb	1.00
d1	0.900	wtfile	
tof	1885.5	proc	ft
nt	16000	fn	not used
ct	368	math	
alock	n		
gain	not used	werr	react
FLAGS		wexp	c13p
il	n	wbs	
in	n	wnt	
dp	y		
hs	nn		
DISPLAY			
sp	-1102.9		
wp	22417.2		
vs	19296		
sc	0		
wc	400		
hzmm	1.27		
is	500.00		
rfl	10961.6		
rfp	9679.2		
th	12		
ins	1.000		
ai cdc ph			



143


Br
OTBS
O
H
H
OH

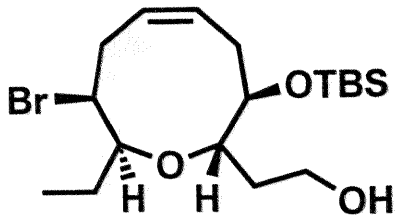
144

0.895
0.822
0.806
0.128
0.078
7.260
9
8
7
6
5
4
3
2
1
0
ppm
1.00
0.99
0.93
1.01
0.98
0.94
1.95
1.00
0.98
0.97
1.97
1.91
2.09
2.76
8.97
2.94
2.64

18-8

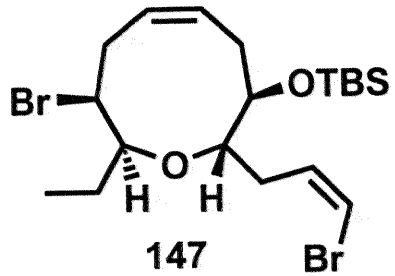
exp2 s2pul

SAMPLE		DEC. & VT	
date	Jun 7 06	dfrq	499.864
solvent	CDCl3	dn	H1
file	exp	dpwr	45
ACQUISITION		dof	0
sfrq	125.704	dm	yyy
tn	C13	dmm	g
at	1.299	dmf	10000
np	78400	dseq	undefined
sw	30165.9	dres	undefined
fb	16600	homo	n
bs	16	temp	40.0
tpwr	48	PROCESSING	
pw	6.0	lb	1.00
d1	0.900	wtfile	
tof	1885.5	proc	ft
nt	16000	fn	not used
ct	192	math	f
alock	n		
gain	not used	werr	react
FLAGS		wexp	c13p
il	n	wbs	
in	n	wnt	
dp	y		
hs	nn		
DISPLAY			
sp	-911.4		
wp	26380.8		
vs	18858		
sc	0		
wc	400		
hzmm	4.54		
is	500.00		
rfl	10961.2		
rfp	9679.2		
th	10		
ins	1.000		
ai cdc ph			



144

18-12


Br
OTBS
O
H
H
Br

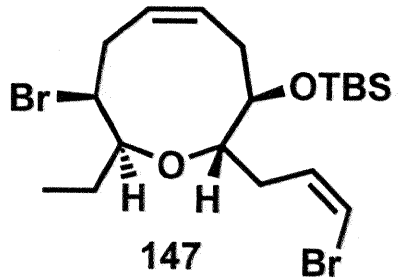
147

7.260
1.566
0.903
0.895
0.805
0.790
0.775
0.137
0.117
9
8
7
6
5
4
3
2
1
0
ppm
0.91
0.92
1.01
1.01
1.00
0.98
1.03
1.99
0.95
0.93
1.00
1.05
1.08
1.95
9.29
2.95
2.72
2.55

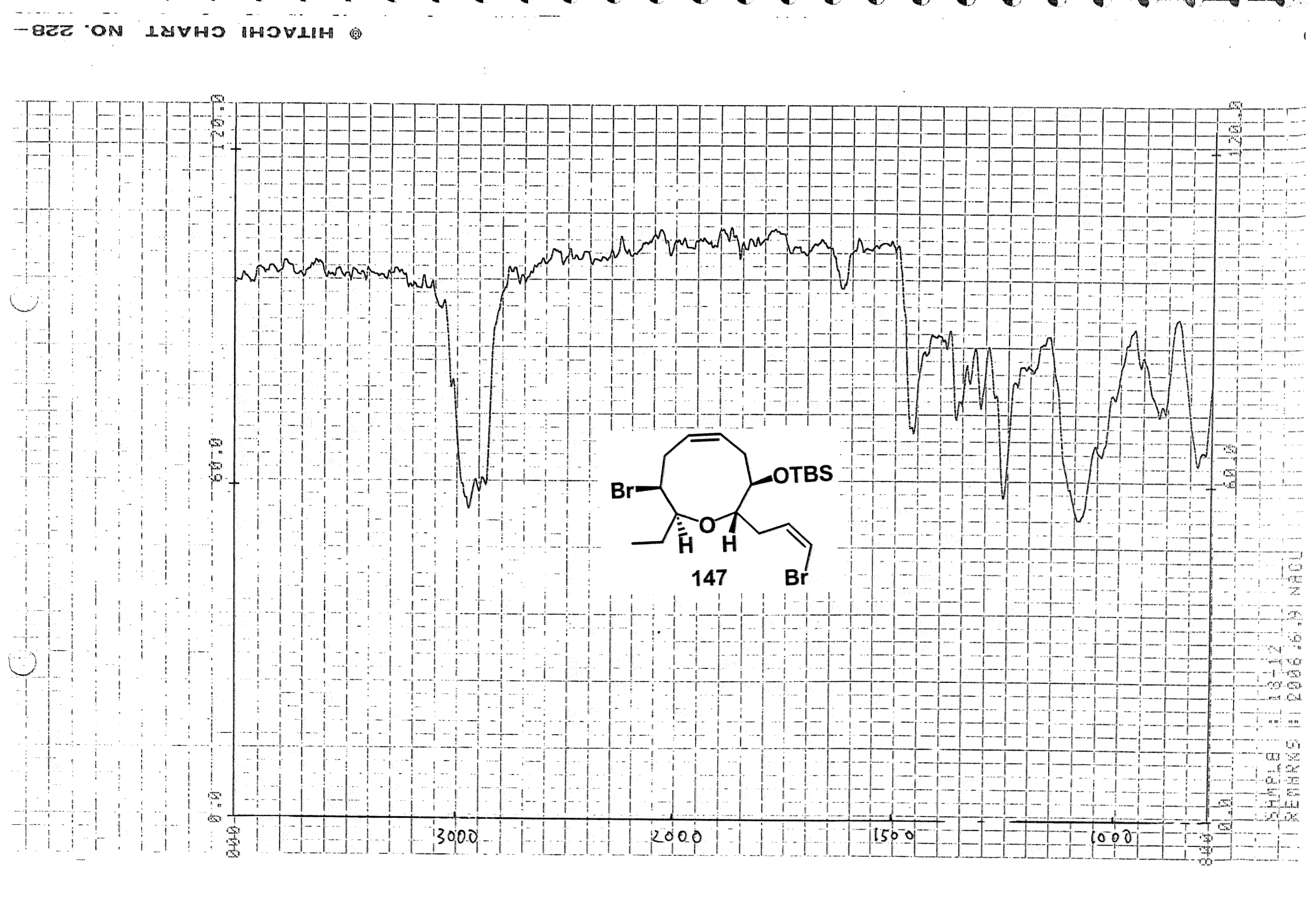
18-12

exp2 s2pul

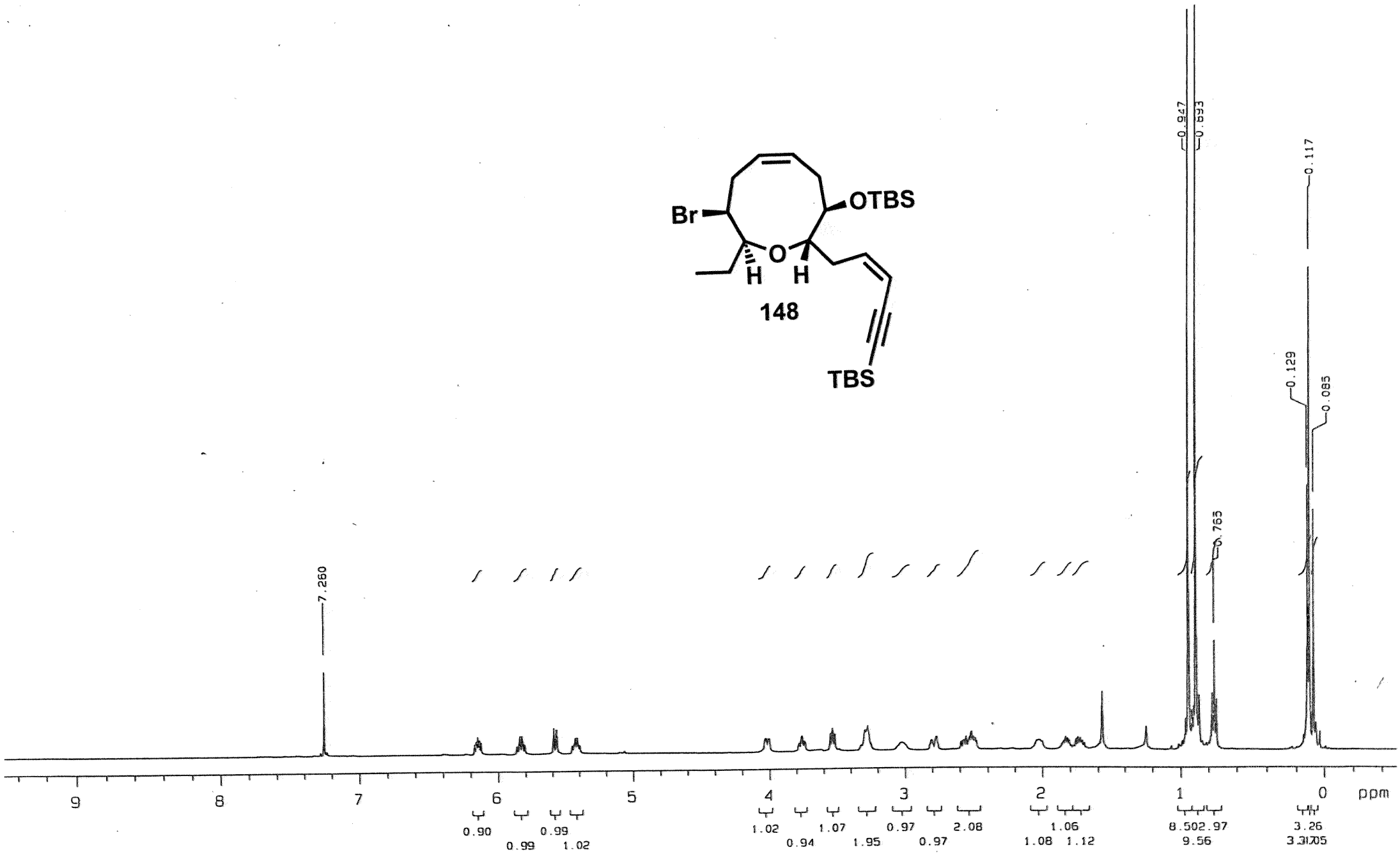
SAMPLE		DEC. & VT	
date	Jun 9 06	dfrq	499.864
solvent	CDCl3	dn	H1
file	exp	dpwr	45
ACQUISITION		dof	0
sfrq	125.704	dm	yyy
tn	C13	dmm	g
at	1.299	dmf	10000
np	78400	dseq	undefined
sw	30165.9	dres	undefined
fb	16600	homo	n
bs	16	temp	40.0
tpwr	48	PROCESSING	
pw	6.0	lb	1.00
d1	0.900	wtfile	
tof	1885.5	proc	ft
nt	16000	fn	not used
ct	1120	math	f
alock	n		
gain	not used	werr	react
FLAGS		wexp	c13p
il	n	wbs	
in	n	wnt	
dp	y		
hs	nn		
DISPLAY			
sp	-1176.1		
wp	23799.9		
vs	33511		
sc	0		
wc	400		
hzmm	8.16		
is	500.00		
rfl	10960.3		
rfp	9679.2		
th	6		
ins	1.000		
ai cdc ph			



147


OTBS
Br
O
H
H
147
Br
3000
2000
1500
1000

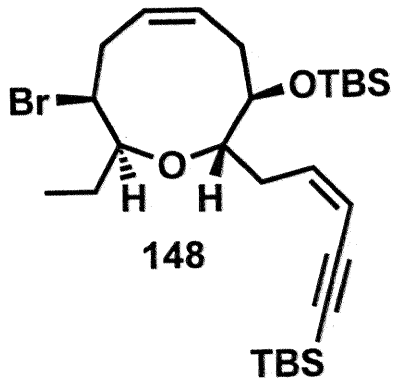
18-13


Br
OTBS
O
H
H
148
TBS
7.260
0.947
0.893
0.765
0.129
0.117
0.085
9
8
7
6
5
4
3
2
1
0
ppm
0.90
0.99
0.99
1.02
1.02
0.94
1.07
1.95
0.97
0.97
2.08
1.08
1.06
1.12
8.50
2.97
9.56
3.26
3.31
3.05

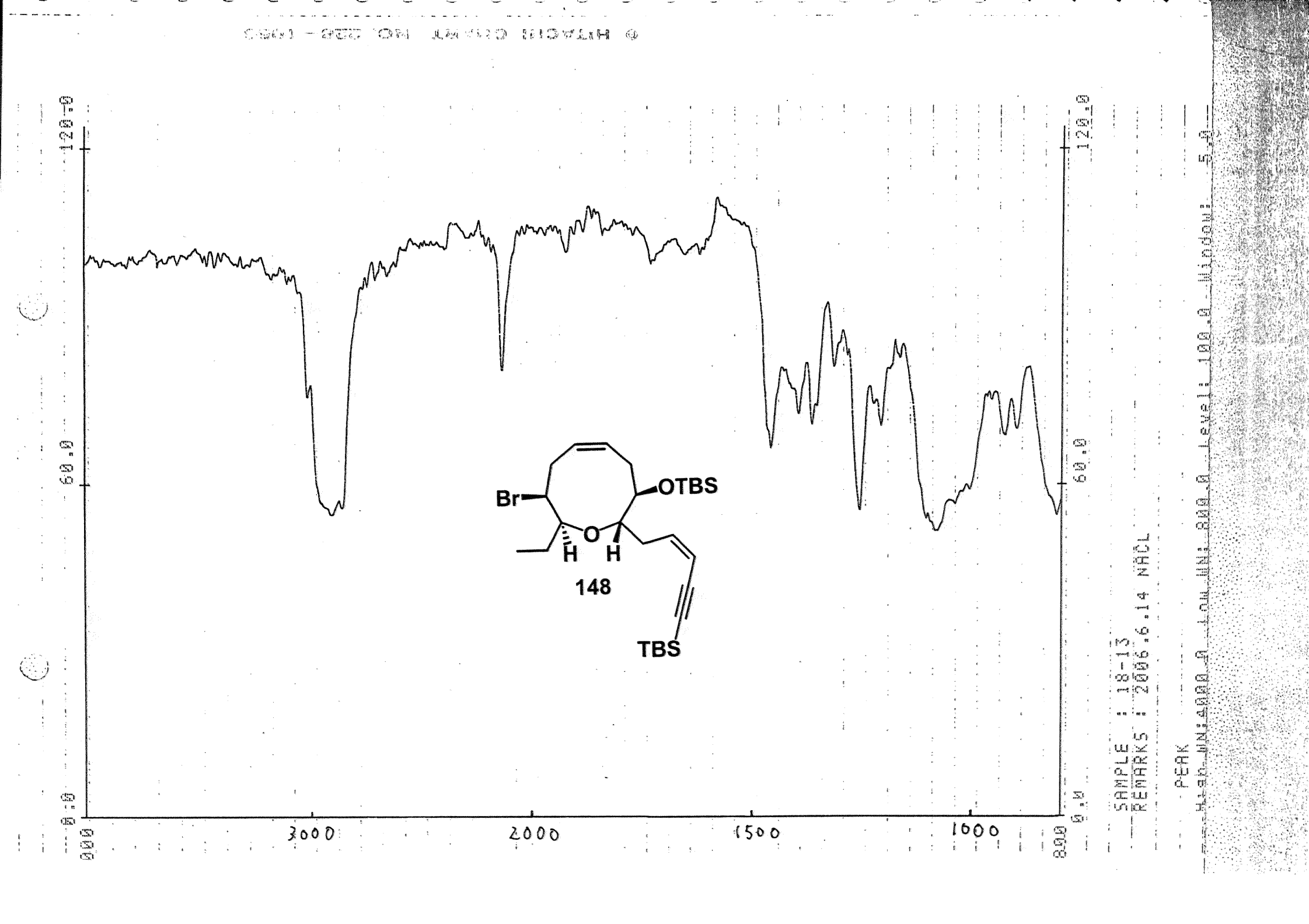
18-13

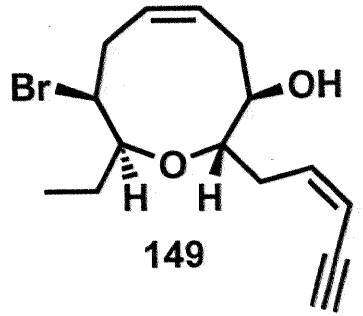
exp2 s2pul

SAMPLE		DEC. & VT	
date	Jun 14 06	dfrq	499.864
solvent	CDCl3	dn	H1
file	.exp	dpwr	45
ACQUISITION		dof	0
sfrq	125.704	dm	yyy
tn	C13	dmm	g
at	1.299	dmf	10000
np	78400	dseq	undefined
sw	30165.9	dres	undefined
fb	16600	homo	n
bs	16	temp	40.0
tpwr	48	PROCESSING	
pw	6.0	lb	1.00
d1	0.900	wtfile	
tof	1885.5	proc	ft
nt	16000	fn	not used
ct	1008	math	f
alock	n		
gain	not used	werr	react
FLAGS		wexp	c13p
il	n	wbs	
in	n	wnt	
dp	y		
hs	nn		
DISPLAY			
sp	-942.3		
wp	25115.5		
vs	32853		
sc	0		
wc	400		
hzmm	24.69		
is	500.00		
rfl	10960.3		
rfp	9679.2		
th	7		
ins	1.000		
ai cdc ph			

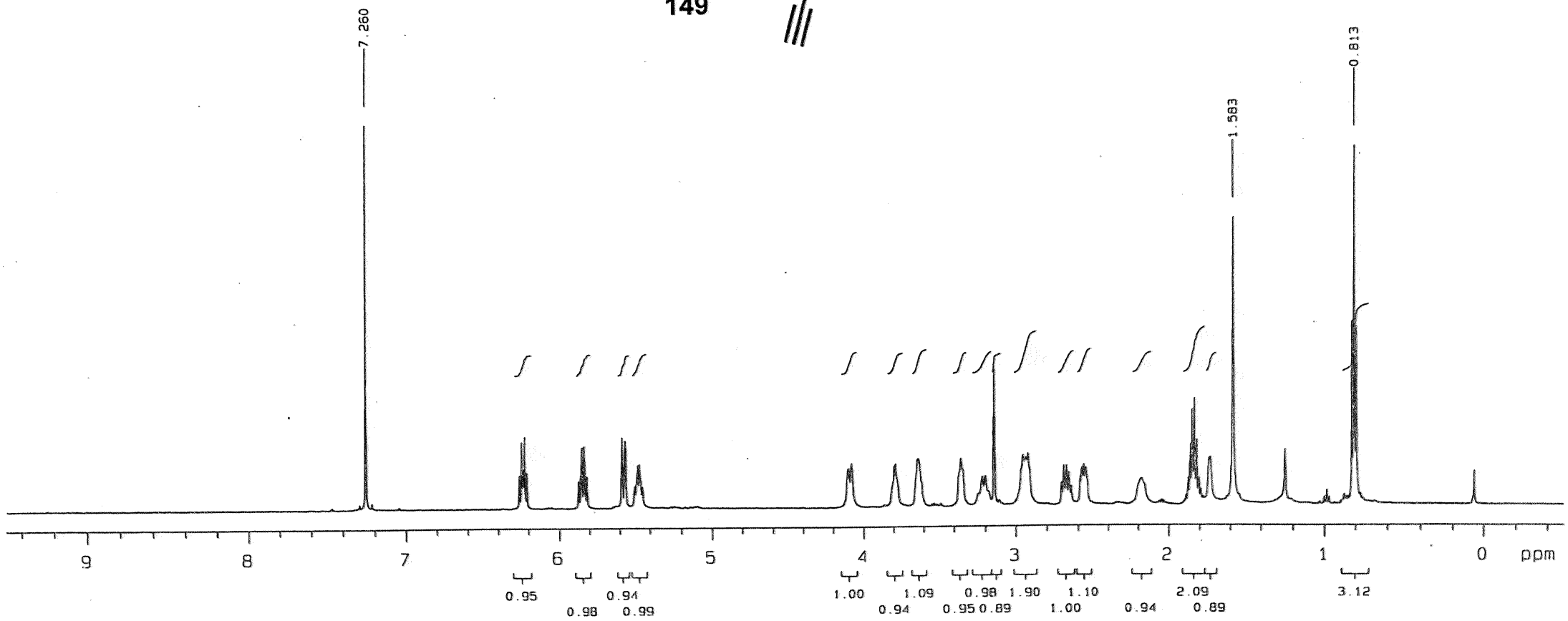


148


120.0
60.0
0.0
4000
3000
2000
1500
1000
800
SAMPLE : 18-13
REMARKS : 2006.6.14 NACL
PEAK
OTBS
Br
O
H
H
TBS
148


Br
OH
O
H
H

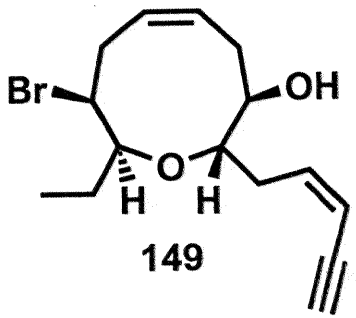
149


7.260
1.583
0.813
9
8
7
6
5
4
3
2
1
0
ppm
0.95
0.98
0.94
0.99
1.00
0.94
1.09
0.95
0.98
0.89
1.90
1.00
1.10
0.94
2.09
0.89
3.12

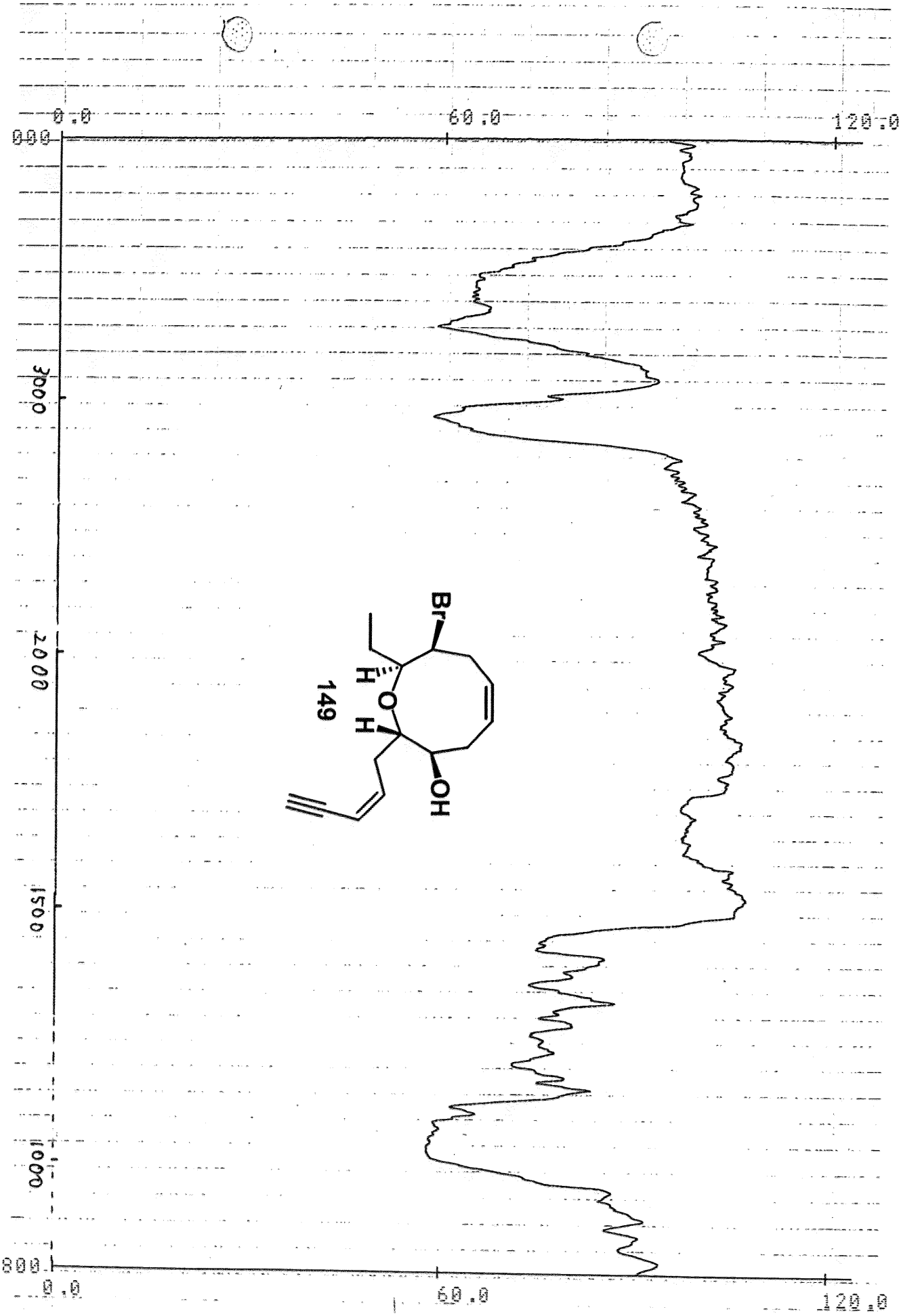
18-14

exp2 s2pul

SAMPLE		DEC. & VT	
date	Jun 16 06	dfrq	499.864
solvent	CDCl3	dn	H1
file	exp	dpwr	45
ACQUISITION		dof	0
sfrq	125.704	dm	yyy
tn	C13	dmm	g
at	1.299	dmf	10000
np	78400	dseq	undefined
sw	30165.9	dres	undefined
fb	16600	homo	n
bs	16	temp	40.0
tpwr	48	PROCESSING	
pw	6.0	lb	1.00
d1	0.900	wtfile	
tof	1885.5	proc	ft
nt	16000	fn	not used
ct	1312	math	f
alock	n		
gain	not used	werr	react
FLAGS		wexp	c13p
il	n	wbs	
in	n	wnt	
dp	y		
hs	nn		
DISPLAY			
sp	663.7		
wp	22385.4		
vs	71305		
sc	0		
wc	400		
hzmm	4.33		
is	500.00		
rfl	10960.3		
rfp	9679.2		
th	11		
ins	1.000		
ai cdc ph			



149

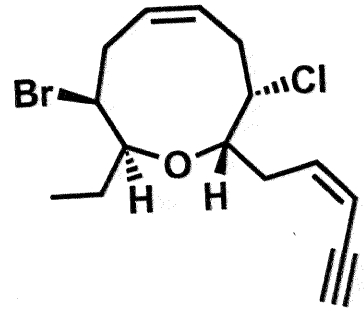


SAMPLE : 18-14
REMARKS : 2006.6.17 NACL

PEAK
High WN: 4000.0 Low WN: 800.0 Level: 100.0 Window: 5.0

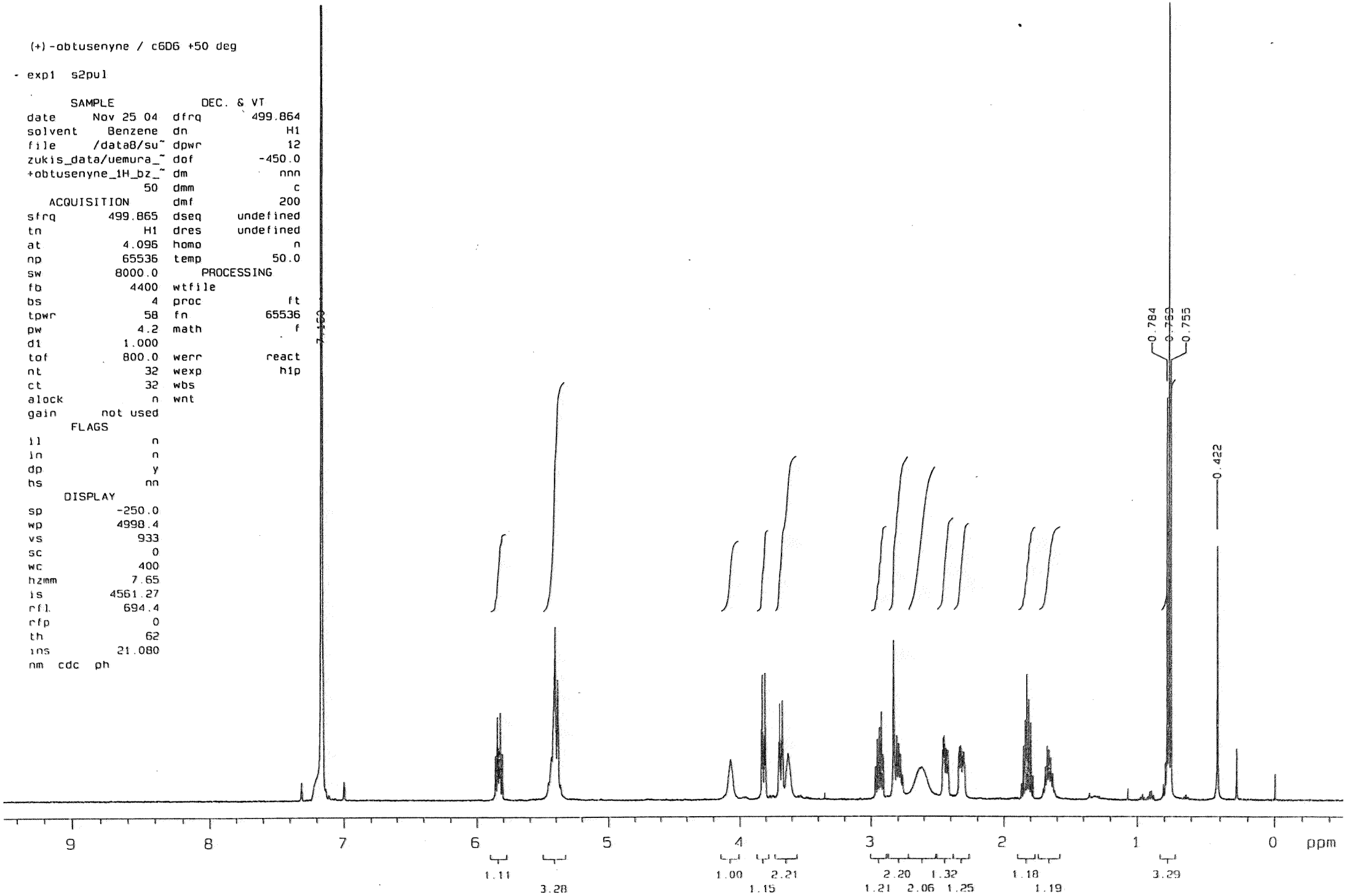
No.	WN(cm-1)	%T	No.	WN(cm-1)	%T
1	3292.0	58.8	2	2940.0	58.3

14-14 fr.2



(+)-Obtusenyne (6)

(+)-Obtusenyne

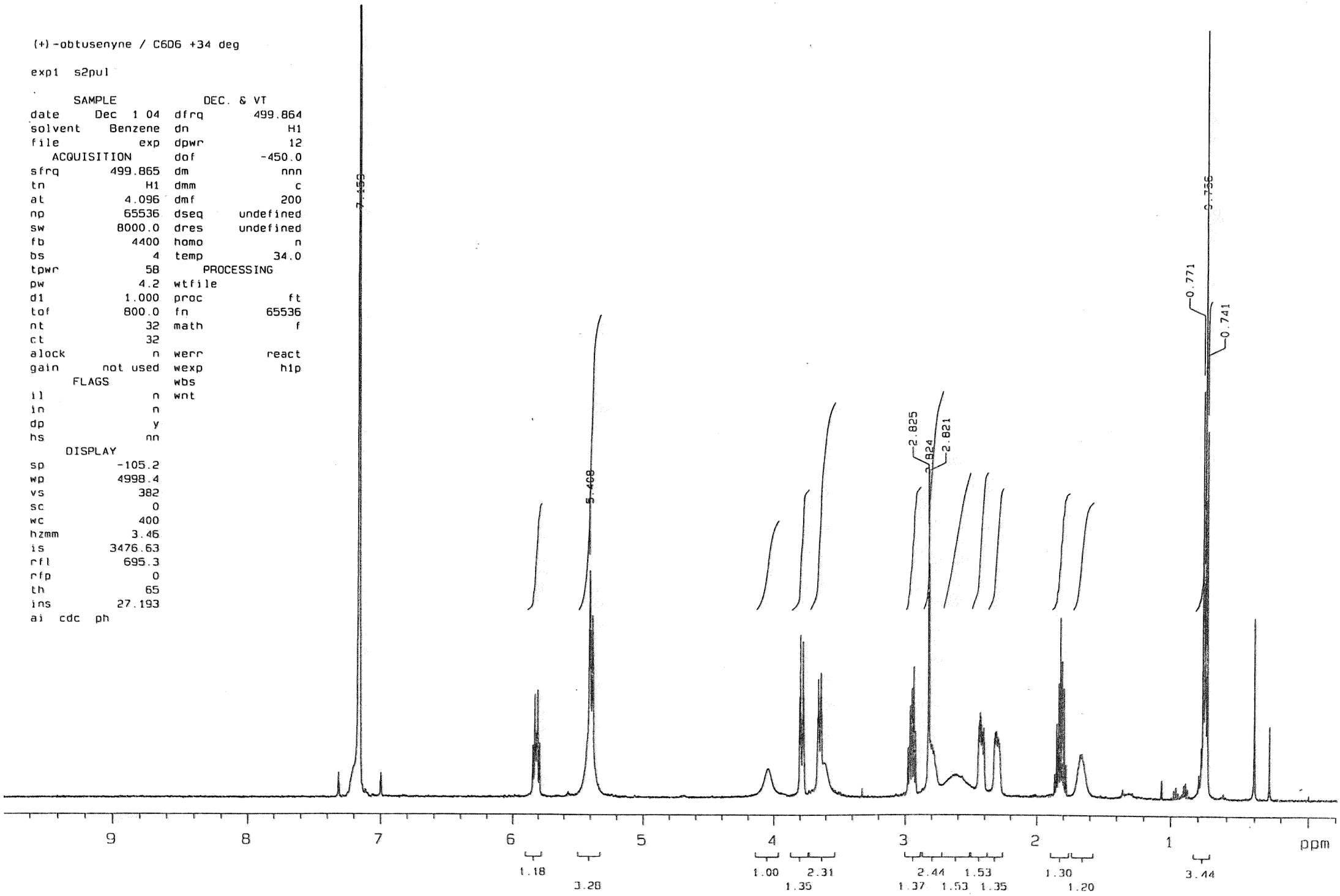

(+)-obtusenyne / c6D6 +50 deg
- exp1 s2pul
SAMPLE
date Nov 25 04
solvent Benzene
file /data8/su~
zukis_data/uemura_~
+obtusenyne_1H_bz_~
50
ACQUISITION
sfrq 499.865
tn H1
at 4.096
np 65536
sw 8000.0
fb 4400
bs 4
tpwr 58
pw 4.2
d1 1.000
tof 800.0
nt 32
ct 32
alock n
gain not used
FLAGS
il n
in n
dp y
hs nn
DISPLAY
sp -250.0
wp 4998.4
vs 933
sc 0
wc 400
hzmm 7.65
is 4561.27
rfl 694.4
rfp 0
th 62
ins 21.080
nm cdc ph
DEC. & VT
dfrq 499.864
dn H1
dpwr 12
dof -450.0
dm nnn
dmm c
dmf 200
dseq undefined
dres undefined
homo n
temp 50.0
PROCESSING
wtfile
proc ft
fn 65536
math f
werr react
wexp h1p
wbs
wnt
7.160
0.784
0.769
0.755
0.422
9
8
7
6
5
4
3
2
1
0
ppm
1.11
3.28
1.00
2.21
1.15
2.20
1.32
1.21
2.06
1.25
1.18
1.19
3.29

(+)-obtusenyne / C6D6 +34 deg

exp1 s2pul

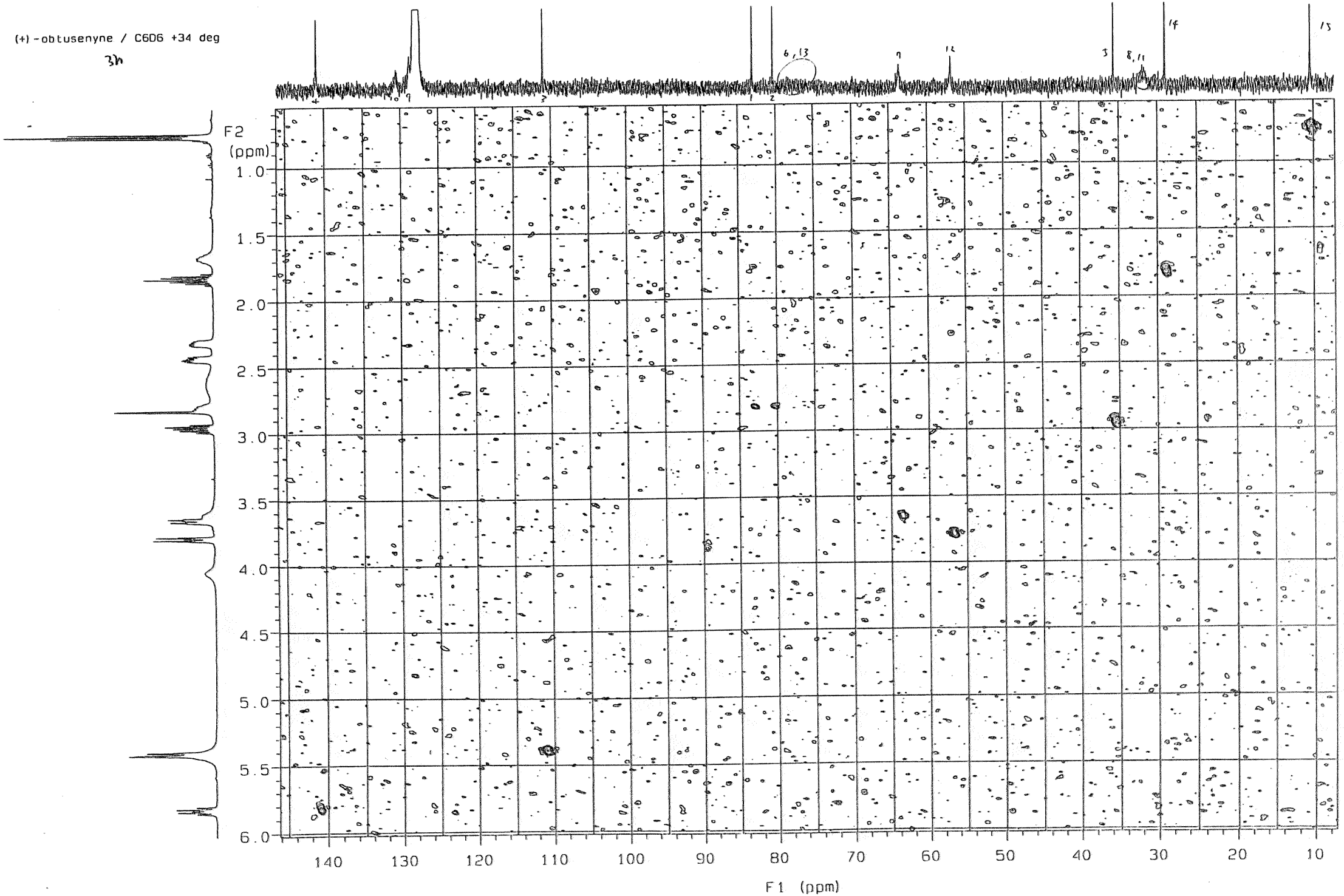
SAMPLE		DEC. & VT	
date	Dec 1 04	dfrq	499.864
solvent	Benzene	dn	H1
file	exp	dpwr	12
ACQUISITION		dof	-450.0
sfrq	499.865	dm	nnn
tn	H1	dmm	c
at	4.096	dmf	200
np	65536	dseq	undefined
sw	8000.0	dres	undefined
fb	4400	homo	n
bs	4	temp	34.0
tpwr	58	PROCESSING	
pw	4.2	wtfile	
d1	1.000	proc	ft
tof	800.0	fn	65536
nt	32	math	f
ct	32		
alock	n	werr	react
gain	not used	wexp	h1p
FLAGS		wbs	
il	n	wnt	
in	n		
dp	y		
hs	nn		
DISPLAY			
sp	-105.2		
wp	4998.4		
vs	382		
sc	0		
wc	400		
hzmm	3.46		
is	3476.63		
rfl	695.3		
rfp	0		
th	65		
ins	27.193		

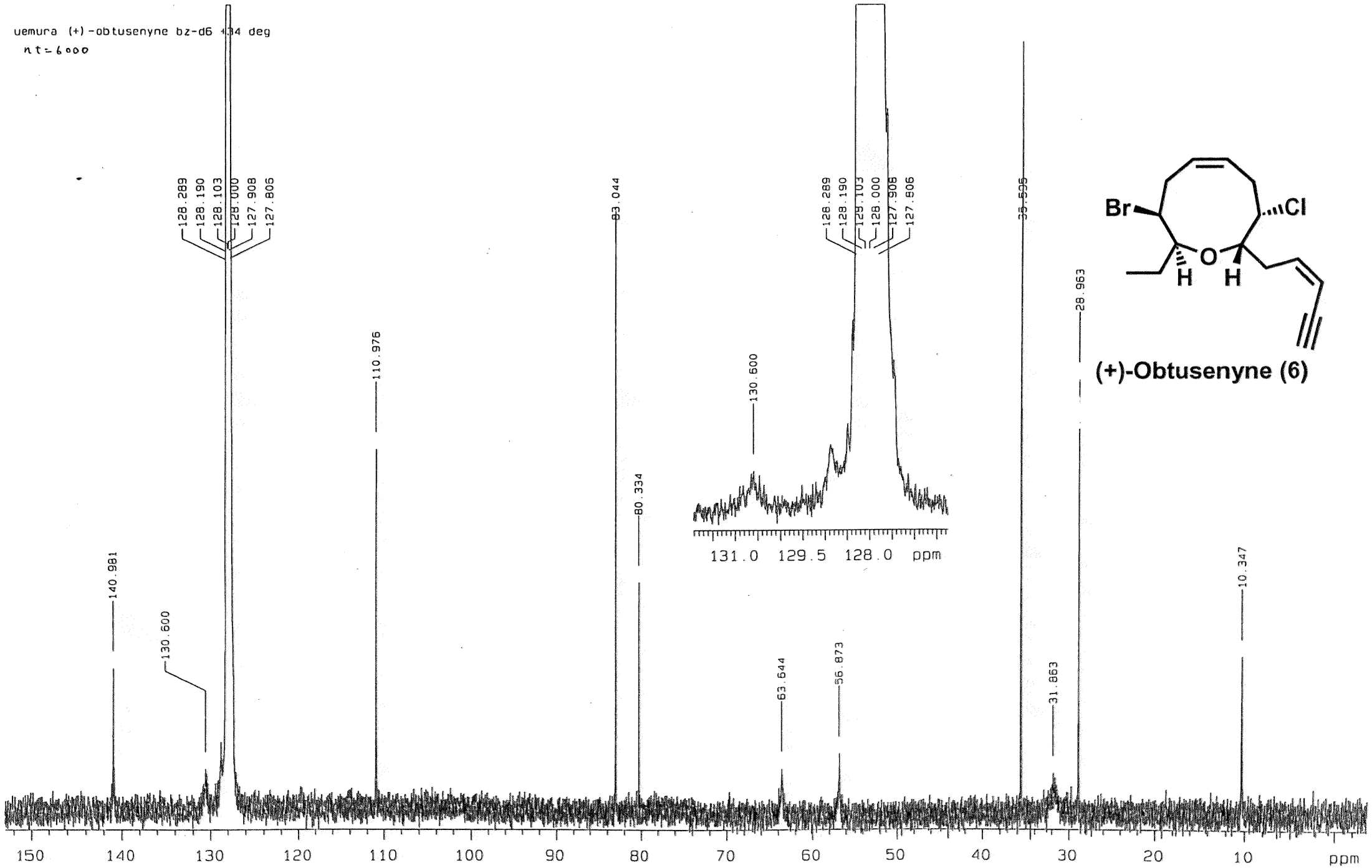
ai cdc ph



(+)-obtusenyne / C6D6 +34 deg

3h




uemura (+)-obtusenyne bz-d6 [illegible] deg
nt=6000
128.289
128.190
128.103
128.000
127.908
127.805
110.976
83.044
80.334
140.981
130.600
63.644
56.873
35.595
31.863
28.963
10.347
130.600
131.0
129.5
128.0
ppm
Br
Cl
O
H
H
(+)-Obtusenyne (6)
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

SAMPLE : OBTUSENYNE
REMARKS : 2006.6.28 NRCL
DATA
High WN:4000.0 Low WN: 800.0
WN(CM-1) %T WN(CM-1) %T
4000.0 99.6 3980.0 101.4
4000
3000
2000
1500
1000
800
0.0
60.0
120.0
Cl
Br
O
H
H
(+)-Obtusenyne (6)