Construction of Carbocycles from Carbohydrates via 1,3-Dipolar Cycloaddition

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Abstract

In this thesis, the background information on the construction of carbocycles from carbohydrates via intramolecular 1,3-dipolar cycloaddition is presented. A review regarding the syntheses of gabosine B and cocaine are also descibed.

By using intramolecular nitrile oxide-alkene cycloaddition (INOC) as the kep step to construct hydroxylated carbocycles, gabosine F was synthesized for the first time from L-arabinose. Hence, theoretically, gabosine B, which is the enantiomer of gabosine F, can also be synthesized from D-arabinose by the same synthetic strategy.

A 5-membered INOC cycloadduct **84** was employed to prepare alcohol **91**, which was transformed into several cyclopent-2-enone derivatives **94–96**.

The regioselectivity of intramolecular nitrone-alkene cycloaddition (INAC) was studied. The INAC of hept-6-enose nitrone **98**, with a 3,4-*trans*-pentylidene acetal as the only blocking group, afforded *endo*-cycloadduct **97** (cycloheptane) exclusively. This result concluded that the regiospecific outcome of this INAC reaction is due to the present of the 3,4-*trans*-pentylidene acetal blocking group.

Starting with D-ribose, INAC of nitrones **113**, **129**, and **140**, bearing an α,β-unsaturated ester as the dipolarophile was studied. The INAC *endo*-cycloadduct **141** (cycloheptane) was converted into natural cocaine sucessfully, together with cocaine analogues **162**, **169**, **170**, **173**, **175**, and **177**.

To investigate the regioselectivity in INAC of hex-5-enose with a 2,3-*trans*-pentylidene acetal blocking group, nitrones **178** and **195** were prepared from D-mannitol. *endo*-Cycloadducts (cyclohexanes) were afforded exclusively.

摘要

本文描述了以單糖爲起始原料，應用分子內 1，3-偶極環加成反應製備碳環的背景資料。另外，本文還綜述了 gabosine B 和可卡因之合成的研究進展。

以 L-阿拉伯糖作爲起始原料，通過分子內腈氧化物環加成 (INOC) 反應爲關鍵的一步，首次地合成了 gabosine F。所以理論上，利用相同的合成方法便能把 D-阿拉伯糖合成爲 gabosine F 的對映體，即是 gabosine B。

通過製備分子內腈氧化物環加成五員環化合物 **84**，製備了合成中間體 **91**，以及另外三種環戊-2-烯酮的衍生物 **94**–**96**。

爲了研究分子內硝酮環加成 (INAC) 反應的區域選擇性，製備了擁有 3，4-反式亞戊基縮醛保護的硝酮 **98**，其分子內硝酮環加成反應只生成了一種七員環內產物 **97**。這證明 3，4-反式亞戊基縮醛保護能引導生成七員環內產物。

以 D-核糖作爲起始原料，研究了以 α，β-不飽和酯作爲親偶極體的硝酮 **113**，**129** 和 **140** 之分子內硝酮環加成反應。其中以七員環內產物 **141** 能製備成天然產物可卡因，以及另外六種可卡因的類似物 **162**， **169**，**170**，**173**，**175** 和 **177**。

其後，以 D-甘露醇作爲起始原料，製備了擁有 2，3-反式亞戊基縮醛保護的硝酮 **178** 和 **195** 並研究其分子內硝酮環加成反應的區域選擇性。結果這些環加成反應只生成了六員環內產物。

Abbreviation

[α]	specific rotation	DEPT	Distortionless Enhancement by Polarization Transfer
Å	angstrom (s)		
Ac	acetyl		
Anal.	analytical	DMAP	4-dimethylaminopyridine
aq.	aqueous	DMF	dimethylformamide
atm.	atmosphere	DMSO	dimethyl sulfoxide
Boc	*t*-butyloxycarbonyl	ee	enantiomeric excess
BORSM	based on recovering starting material	EI	Electron Impact
		ESI	Electrospray Ionization
Bn	benzyl	Et	ethyl
br	broad (spectral)	Et_2O	diethyl ether
Bz	benzoyl	FAB	Fast Atom Bombardment
^{n}Bu	*n*-butyl	FT	Fourier transform
^{t}Bu	*tert*-butyl	g	gram
°C	degree Celsius	h	hour
calcd	calculated	HRMS	high-resolution mass spectrum
cat.	catalytic		
Chloramine-T	*N*-chloro-*p*-toluenesulfonamide sodium salt	Hz	hertz
		IBX	2-iodoxybenzoic acid
CI	chemical ionization	INAC	Intramolecular nitrone-alkene cycloaddition
conc.	concentrated		
COSY	Correlated Spectroscopy		
COTC	2-crotonyloxymethyl-(4*R*,5*R*,6*R*)-4,5,6-trihydroxy-2-cyclohexenone	INOC	Intramolecular nitrile oxide-alkene cycloaddition
		IR	infrared
(±)-CSA	(±)-10-camphorsulfonic acid	*J*	coupling constant (in NMR)
δ	chemical shift in parts per million downfield from tetramethylsilane (spectral)	KHMDS	potassium hexamethyldisilylamide
		L	liter(s)
δ+	delta positive charge	lit.	literature
δ−	delta negative charge	μ	micro-
d	day (s) or doublet (spectral)	M	moles per liter
		m	multiplet (spectral), milli-
DBU	1,8-Diazabicyclo[5.4.0] undec-7-ene	Me	methyl
		MHz	megahertz

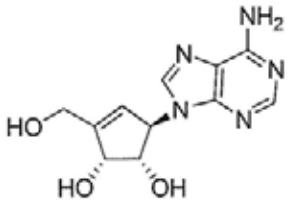
min	minute	*rac*	racemic
mp	melting point	R_f	retention factor
Ms	methanesulfonyl	rt	room temperature
MS	molecular sieves or mass spectrum	s	singlet (spectral)
		sat.	saturated
MTO	methyltrioxorhenium	S_N2	bimolecular nucleophilic substitution
m/z	mass-to-charge ratio		
n	nano	t	triplet (spectral)
NCS	*N*-chlorosuccinimide	TBAF	tetrabutylammonium fluoride
NMO	4-methylmorpholine *N*-oxide		
		TBS	*tert*-butyldimethylsilyl
NMR	nuclear magnetic resonance	Tf	trifluoromethanesufonate
		TFA	trifluoroacetic acid
NOESY	nuclear overhauser enhancement spectroscopy	THF	tetrahydrofuran
		TLC	thin layer chromatography
Nu	nucleophile	TPAP	tetra-*n*-propylammonium perruthenate
Ph	phenyl		
ppm	parts per million (in NMR)	*p*-TsOH	*p*-toluenesulfonic acid
py	pyridine	TS	transition state
q	quartet (spectral)	UHP	urea hydrogen peroxide
quin	quintet (spectral)		

Chapter 1

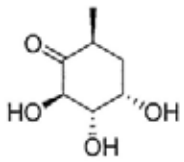
Introduction

1.1 General background

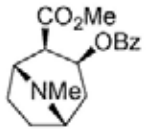
Construction of carbocycles from their acyclic precursors have drawn great attention in organic synthesis, mainly due to the majority of natural products consists of carbocycles, especially the 5-, 6-, and 7-membered carbocyclic rings. For example, natural products like (−)-neplanocin A (**1**), (+)-gabosine F (**2**), and (−)-cocaine (**3**) consist of carbocycle with a 5-, 6-, and 7-membered rings respectively (Figure 1). For these natural products, most of them are enantiopure substances. That is, the syntheses of these compounds require either asymmetric synthesis from achiral precursors or using chiral starting materials.



(–)-neplanocin A (**1**)



(+)-gabosine F (**2**)



(–)-cocaine (**3**)

Figure 1

Carbohydrates have been considered as the most versatile starting materials for natural product synthesis because it is readily available and in large quantities. More importantly, carbohydrates are enantiopure substances so the final products must be

optically pure. Thus, there is no need to worry about the presence of undesired enantiomer that may affect the bioactivity of the synthesized product. The 1,3-dipolar cycloaddition is a powerful tool for preparing carbocycles as this reaction can create new chiral centers and can form a new carbon-carbon bond.[1–4] When carbohydrates are used to prepare the chiral 1,3-dipolar to perform the cycloaddition, the cycloadducts generally contain newly formed chiral centers in high diastereoselectivity.

In this chapter, the 1,3-dipolar cycloaddition in organic synthesis and its applications to the construction of carbocycles are presented in detail.

1.2 1,3-Dipolar Cycloaddition

The 1,3-dipole is defined as a species that is represented by the zwitterionic octet structures, which contains four electrons in three parallel atomic p orbitals.[1] It can be divided into two different types: the allyl anion type and the propargyl/allenyl anion type (Figure 2).[2]

Allyl anion type 1,3-dipole

Propargyl/Allenyl anion type 1,3-dipole

Figure 2

Where atoms a and c are mainly carbon, nitrogen, oxygen and sulphur. The allyl anion type has four electrons in those three p orbitals with perpendicular to the plane of the dipole and the dipole is bent. The central atom b in allyl anion type 1,3-dipole can be nitrogen, oxygen and sulphur. The propargyl/allenyl anion type has one extra π orbital located in the plane orthogonal to the four-electrons π molecular orbital of the dipole, the extra π orbital hence will not involved in the resonance structures and will not take part in the cycloaddition reaction. The propargyl/allenyl anion type 1,3-dipole is linear and the central atom b is limited to nitrogen only.

For all of the 1,3-dipoles, 1,3-dipolar cycloaddition can take place with the dipolarophile, usually alkenes and alkynes, which involves 4 π electrons from the dipole and 2 π electrons from the dipolarophile. When the cycloaddition proceeds through the concerted mechanism, thermally allowed $[_{\pi}4_s + _{\pi}2_s]$ cycloaddition will occur in which the π orbital of dipole and the π orbital of the dipolarophile are combined suprafacially (Figure 3).[4]

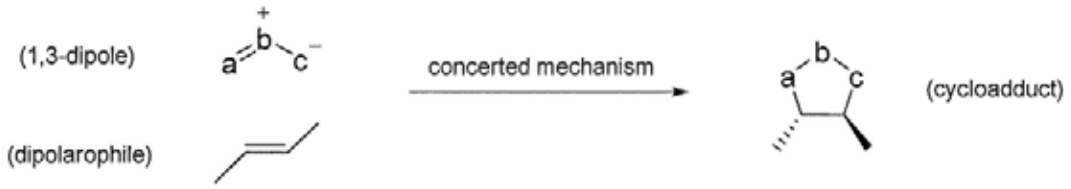


Figure 3

The result is that, a *trans*-cycloadduct will be formed as the only diastereomer when *trans*-alkene is used as the dipolarophile (Figure 3).

1.2.1 Intramolecular Nitrile Oxide-Alkene Cycloaddition (INOC)

Intramolecular nitrile oxide-alkene cycloaddition (INOC) is the 1,3-dipolar cycloaddition reaction between a nitrile oxide (1,3-dipole) and an alkene (dipolarophile) within the same molecule (Figure 4).

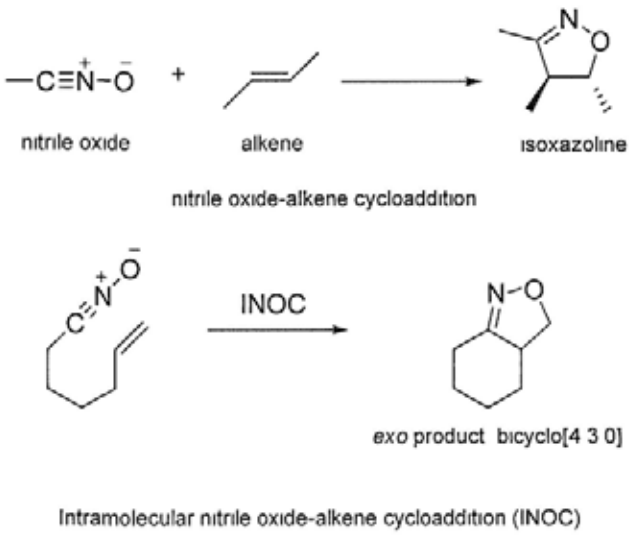
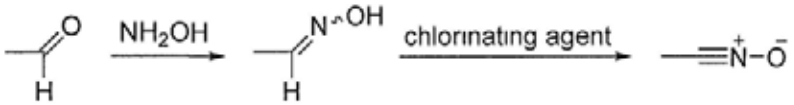


Figure 4

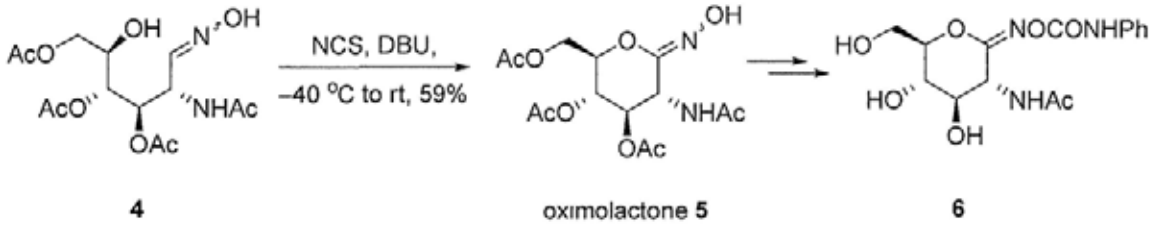
This reaction allows the formation of one carbon-carbon bond and the creation of up to two carbon stereocenters within one step. It had been used to construct many bi- and polycyclic isoxazolines. As the nitrile oxide functional group is in a linear structure, the INOC almost always proceeds to give the bicyclo[*x*.3.0] derivatives (*exo* product) for $x = 3 - 5$ (Figure 4).[2]

The nitrile oxides are commonly generated from treatment of a chlorinating agent (e.g. sodium hypochlorite, chloramine-T and *N*-chlorosuccinimide) and a weak base to an oxime,[5] which can be readily synthesized by condensation of aldehyde with hydroxylamine (Scheme 1).



Scheme 1

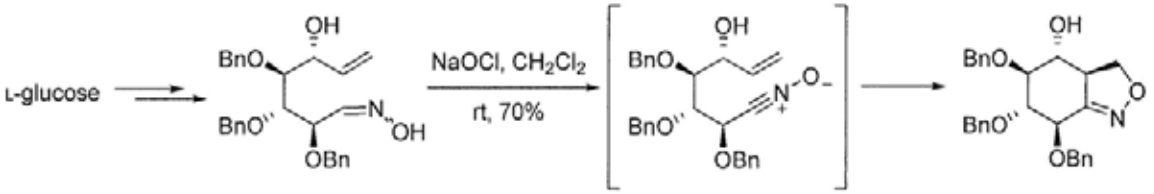
These reaction conditions for generating nitrile oxide are basic and could deprotonate the acidic proton(s) of the substrates. Since nitrile oxides derived from sugars are highly oxygenated, the presence of free hydroxyl group(s) could attack the electrophilic carbon of the nitrile oxide, forming the oximolactone as the side product. The formation of oximolactone side product was reported by Vasella and co-workers in the synthesis of phenylcarbamate **6** with oximolactone **5** as the key intermediate (Scheme 2).[6]



4 oximolactone **5** **6**

Scheme 2

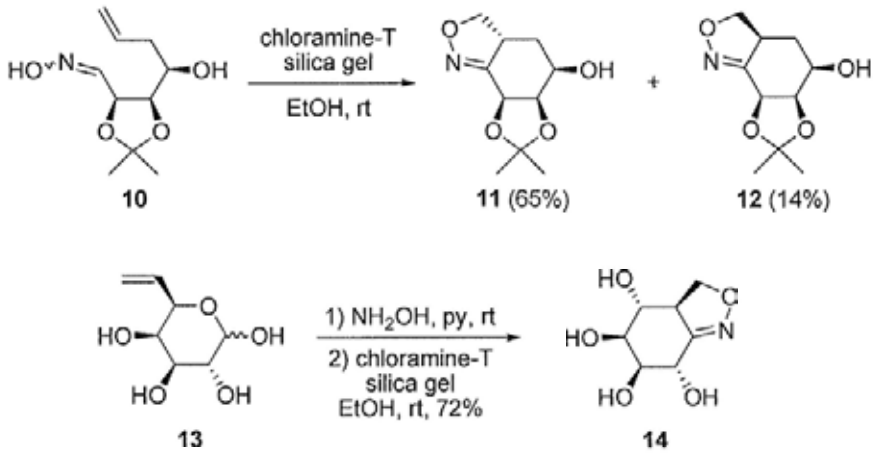
Reports on INOC reactions in the presence of free hydroxyl group(s) are rare. Tatsuta *et al*. had prepared oxime **7**, which had a free hydroxyl group in the δ position, to react with NaOCl at room temperature to generate nitrile oxide **8** which then cyclized to give isoxazoline **9** (Scheme 3).[7]



7 **8** **9**

Scheme 3

Recently, Shing *et al*. had used chloramine-T in the presence of silica gel to perform INOC reaction of many sugar derivatives with one or more hydroxyl groups (Scheme 4).[8]



Scheme 4

Adding silica gel to the reaction allows improvement of the yield of the cycloadduct(s). It was believed that the silica gel can provide a slightly acidic environment for the INOC reaction so to prevent the formation of undesired oximolactone product.[8] In the thesis, INOC reactions were carried out by this chloramine-T/silica gel methodology in order to attain maximum yield of cycloadducts.

1.2.2 Intramolecular Nitrone-Alkene Cycloaddition (INAC)

Intramolecular nitrone-alkene cycloaddition (INAC) is the 1,3-dipolar cycloaddition reaction between a nitrone (1,3-dipole) and an alkene (dipolarophile) within the same molecule (Figure 5).

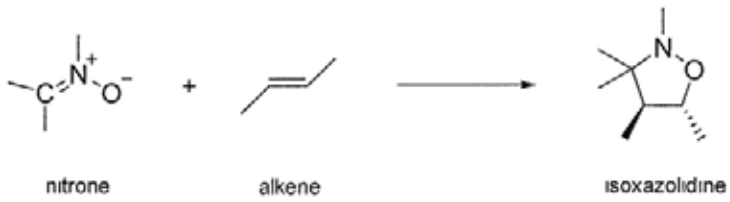
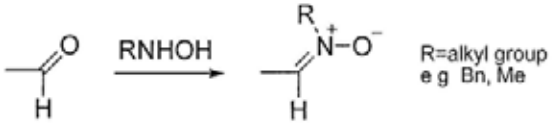


Figure 5

Throughout this reaction, formation of a carbon-carbon bond and up to three carbon stereocenters will take place. It is a powerful synthetic method for the preparation of polyhydroxylated carbocycles of different ring sizes from sugars. Also, the introduction of a nitrogen functionality to the substrate during INAC reaction allows the formation of alkaloids and related natural products from INAC cycloadducts. The nitrone can be prepared by reacting aldehyde with alkyl hydroxylamine (Scheme 5).



Scheme 5

Unlike INOC reactions, INAC reactions have two modes of cyclization, namely the *exo* or the *endo* mode, which lead to the formation of a fused or a bridged cycloadduct respectively (Figure 6).[2]

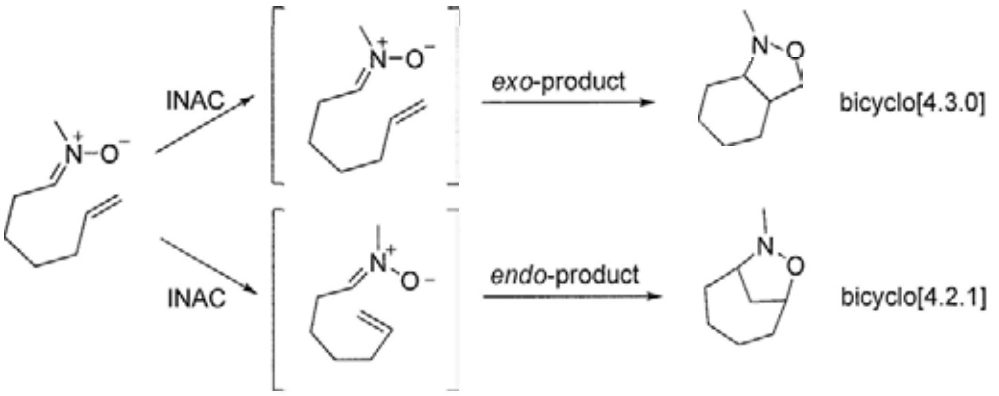
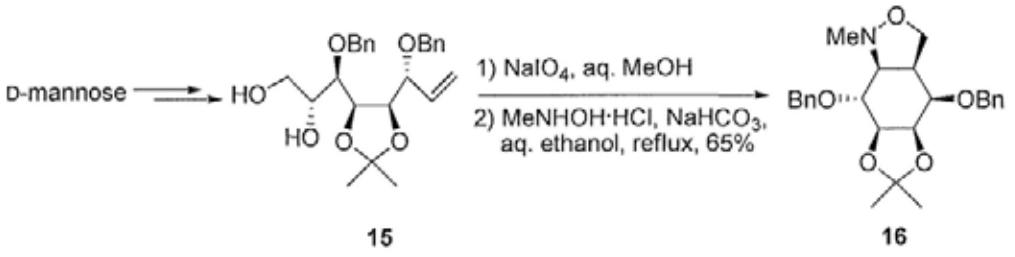


Figure 6

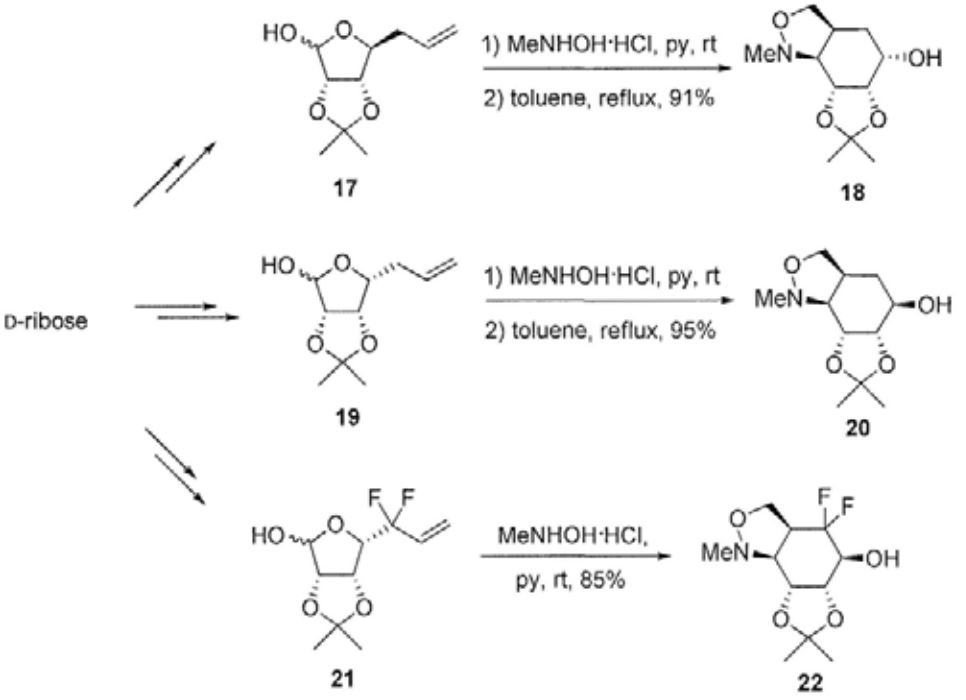
In most cases, INAC reactions lead to the formation of the *exo*-cycloadducts instead of *endo*-cycloadducts. For example, Shing and co-workers reported[9] an entry to *cis*-fused cyclohexane **16** from D-mannose through the unbranched sugar derivative **15** (Scheme 6).



15 **16**

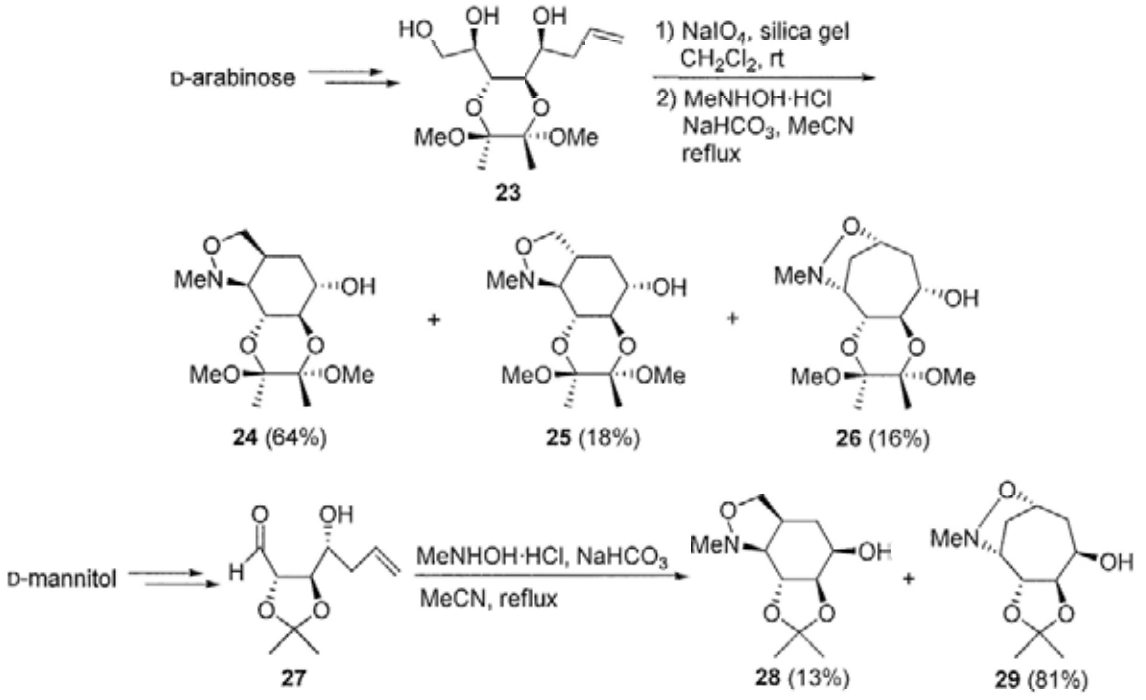
Scheme 6

Singh *et al*. had prepared three unbranched sugar derivatives **17**, **19** and **21** from D-ribose to give *cis*-fused cyclohexanes, **18**, **20** and **22**, respectively through the *exo*-mode INAC reaction (Scheme 7).[10,11]



Scheme 7

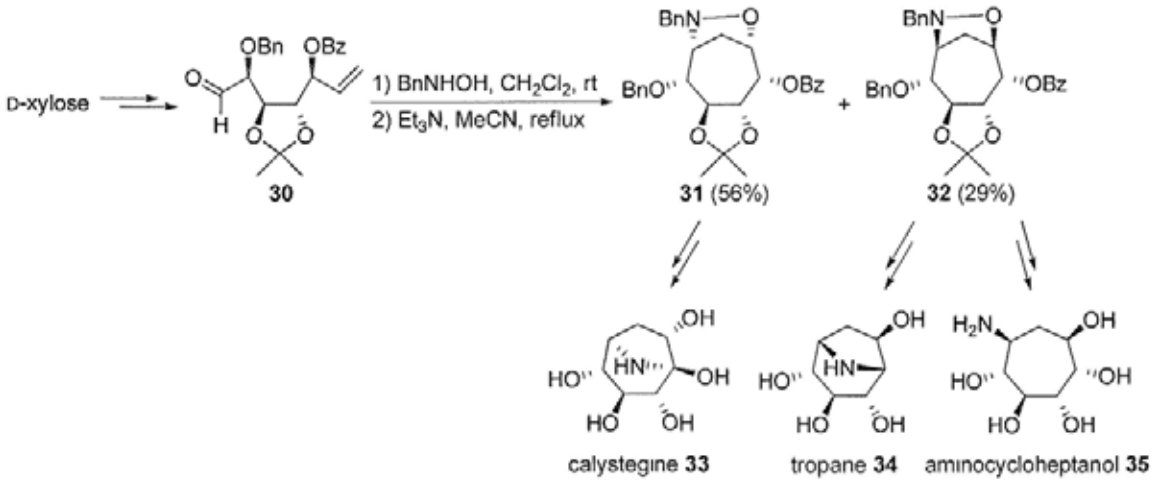
However the formation of *endo*-cycloadducts from sugar derivatives is rare[12] until 2006. Shing *et al.* had discovered the formation of *endo*-cycloadducts was enhanced when the acyclic INAC precursor contains a *trans*-blocking protecting group (Scheme 8).[13–15]



Scheme 8

It was suggested that the presence of *trans*-blocking group will impose a torsional strain that can affect the conformation of the transition states of INAC reactions hence enhance the formation of *endo*-cycloadducts. These suggestions were further supported by the theoretical analysis performed by Yamada *et al.*[13–15]

It was found that when a 3,4-*trans*-acetonide was employed, the INAC reactions of hept-6-enoses yielded *endo*-cycloadducts exclusively. The cycloadducts formed could be transformed to optically active calystegines, tropanes and aminocycloheptanols (Scheme 9).[14]



Scheme 9

In this thesis, further studies on the regioselectivity of INAC reactions of sugar derivatives and transformation of cycloadducts to some natural products or analogues with biological importance are discussed.

1.3 Applications of Carbocycles Constructed from 1,3-Dipolar Cycloadditions

1.3.1 Gabosine B and Gabosine F

Gabosines (Figure 7) belong to a family of hydroxylated cyclohexenones and cyclohexanones that have been shown to display interesting bioactivities such as antibiotic, anticancer, and DNA binding properties.[16]

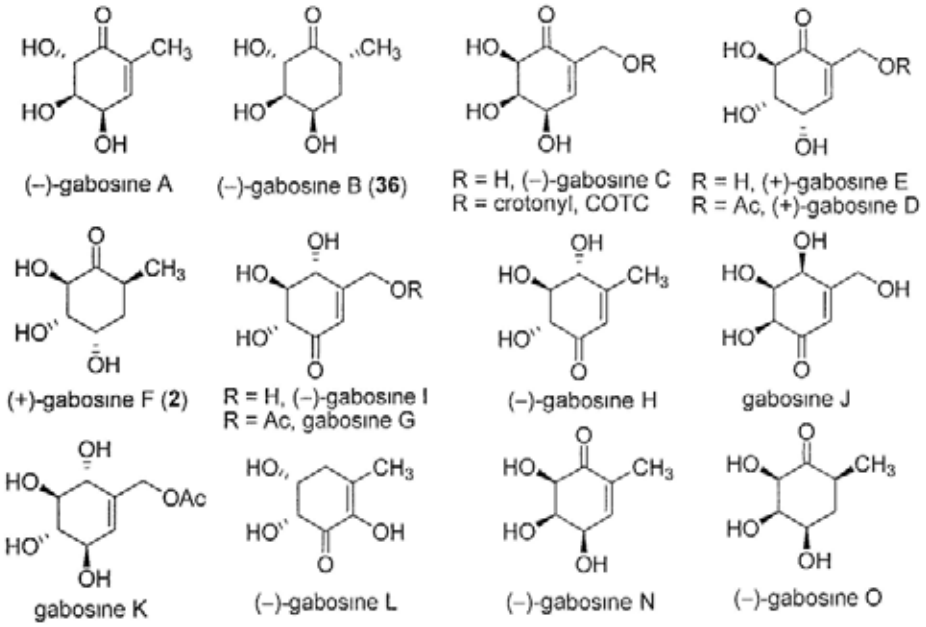
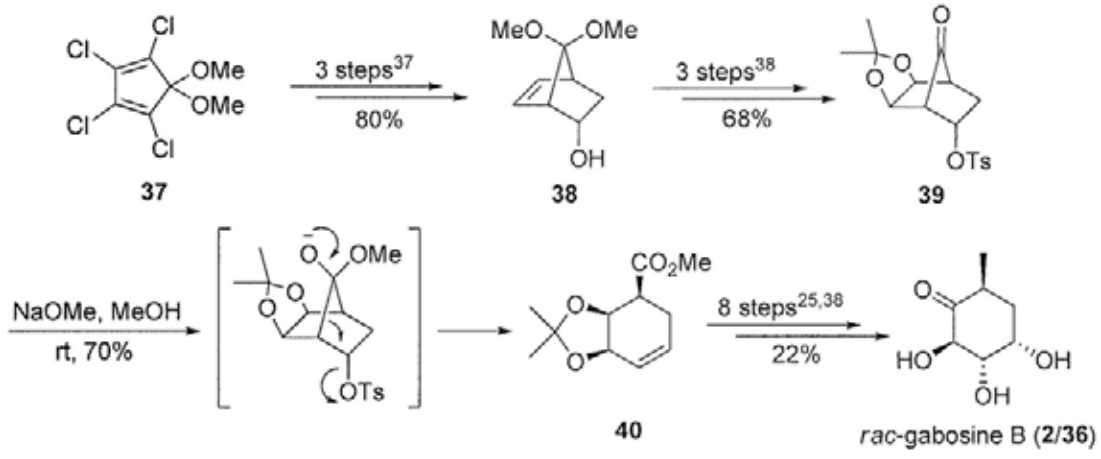


Figure 7

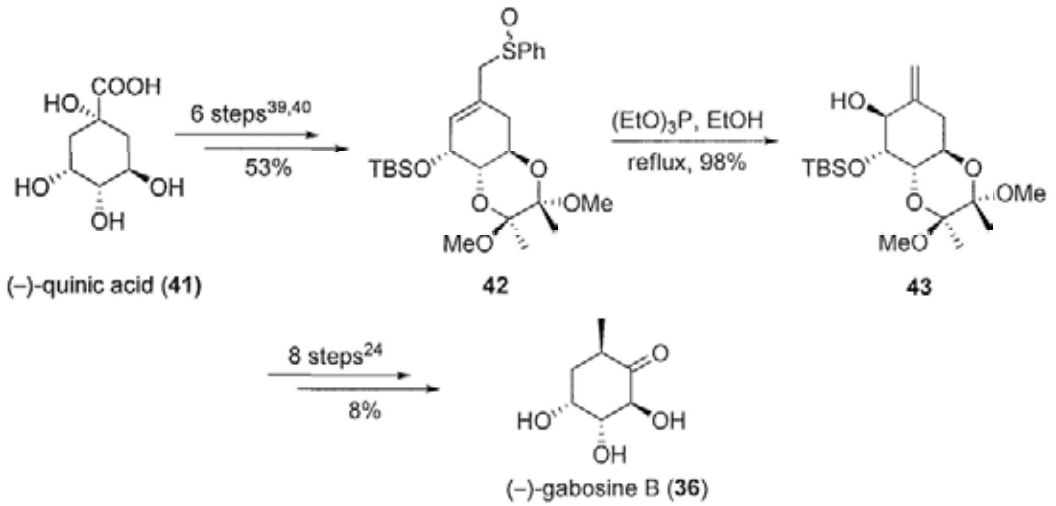
Since the first isolation of gabosine C from *Streptomyces* strains in 1974,[17] 15 other gabosines have been isolated. Within the family, gabosines B (**36**), F (**2**), and O are saturated cyclohexanones, while the others are unsaturated cyclohexenones. Because of their interesting biological activities, numerous reports on the synthesis of

gabosines (some were synthesized as the enantiomer of natural gabosines) were found.[18–36] The most recent reports include (i) the synthesis of (+)-gabosine N and (+)-gabosine O by Rao *et al.* using ring-closing metathesis as the key step for carbocyclization,[30] (ii) synthesis of (−)-gabosine E by Gallos *et al.* using INAC as the key step,[31] (iii) synthesis of (−)-gabosine A and (−)-gabosine N by Madsen and co-workers using ring-closing metathesis as the key step,[32] (iv) synthesis of (+)-gabosine A, (−)-gabosine B, (+)-gabosine D, (+)-gabosine E, (+)-gabosine F, (−)-gabosine G, (−)-gabosine I, (−)-gabosine K and (−)-gabosine O by Shing and co-workers.[33–36] (−)-Gabosine B (**36**) and (+)-gabosine F (**2**) are a pair of enantiomers which belong to the class of hydroxylated cyclohexanones (saturated carbocycle). The first synthesis of racemic gabosine B (**36**) was achieved by Mehta and Lakshminath in 15 steps with 8.4% overall yield from 5,5-dimethoxy-tetrachloro-cyclopenta-diene (**35**), giving a mixture of *rac*-gabosines B (**33**) and F (**34**), using the Grob-like 'top-to-bottom' fragmentation as the key step (Scheme 10).[25]



Scheme 10

Enantiopure gabosine B (**36**), was constructed by Shinada *et al.*, starting from (–)-quinic acid (**41**) and using a Mislow-Evans rearrangement as the key step, in 15 steps with 4.3% overall yield (Scheme 11).[24]



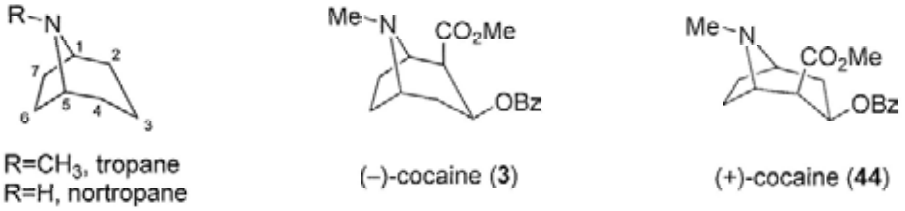
Scheme 11

However, there is still no report on the synthesis of enantiopure gabosine F (**2**). Since the products of intramolecular nitrile oxide-alkene cycloaddition (INOC) can be easily transformed into saturated carbocyclic ketone, the enantiopure (+)-gabosine F (**2**) could be synthesized from the INOC cycloadduct in a few steps. The synthesis of (+)-gabosine F (**2**) from carbohydrate via INOC reaction is described in the following chapter.

1.3.2 Cocaine and Cocaine Analogues

Natural (–)-cocaine (**3**) (Figure 8) is a tropane alkaloid component of coca leaves of *Erythroxylum Coca*.[41] It is a powerful stimulant of the central nervous system and its

neuronal reinforcing properties are due to its inhibition of dopamine reuptake.[42] However its additive properties makes cocaine abuse become one of the greatest concerns of the public today and long-term cocaine abuse can produce neurophysiological alternations in the central nervous system.[43]



R=CH_3, tropane
R=H, nortropane

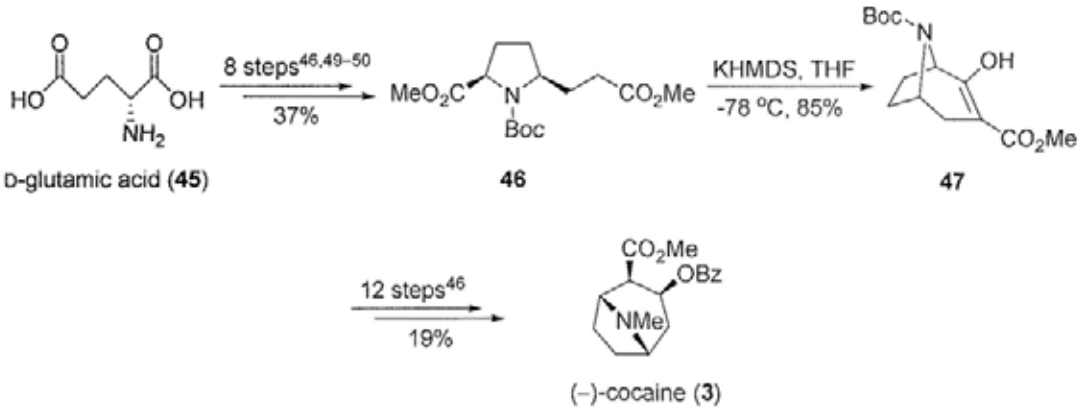
(–)-cocaine (**3**)

(+)-cocaine (**44**)

Figure 8

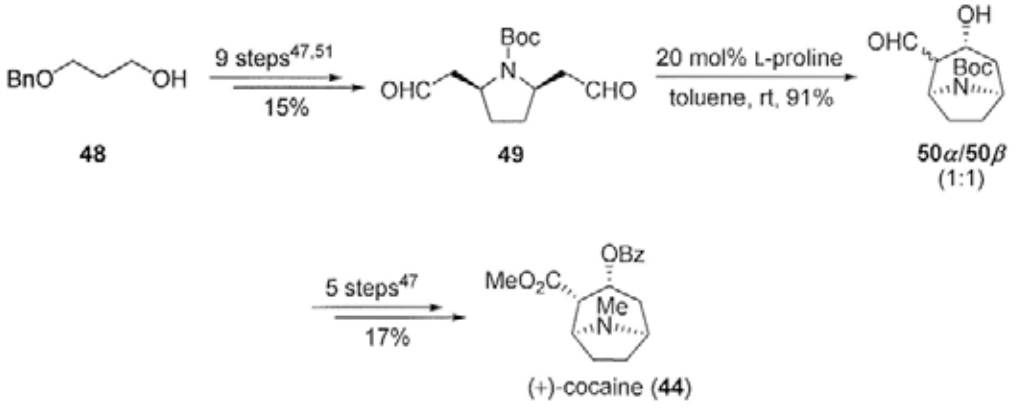
The total synthesis of cocaine has been a challenging task to numerous synthetic chemists for nearly a century, mainly due to the difficulties on building the tropane skeleton as well as to functionalize this skeleton in correct stereochemistry, especially the axial 2-carbomethoxy group which is less thermodynamically stable. The early synthesis of cocaine yield racemic mixture hence optical resolution of *rac*-cocaine was needed.[44,45] Until now only three syntheses of optically pure cocaine were reported.[46–48]

In 1998, Rapoport and co-workers had using D- and L-glutamic acid to synthesize natural (–)-cocaine (**3**) and unnatural (+)-cocaine (**44**) respectively in 21 steps with 5.9% overall yield, in which the 8-azabicyclo[3.2.1]octane framework was constructed by Dieckmann condensation (Scheme 12).[46]



Scheme 12

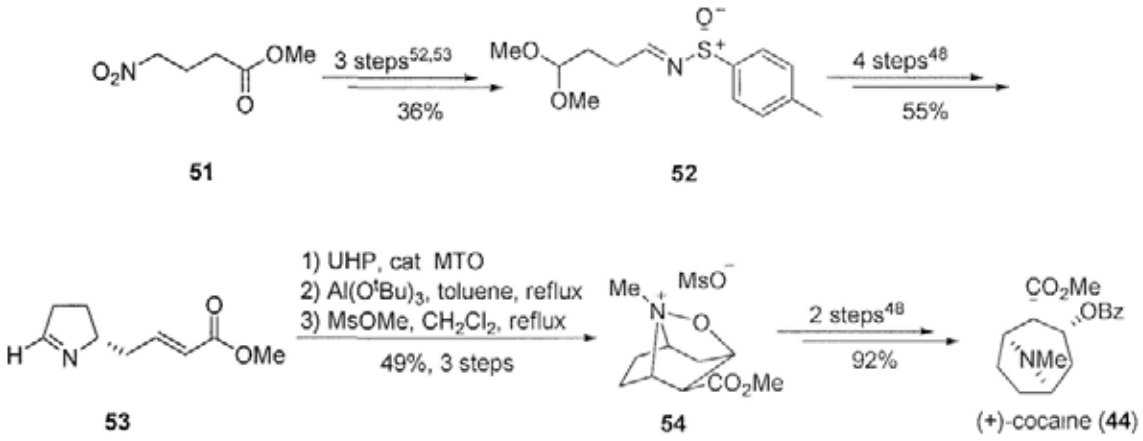
Pearson *et al.* reported an asymmetric synthesis of (+)-cocaine (**44**) using L-proline catalyzed intramolecular aldol reaction to form the tropane skeleton. However, 1:1 mixture of C-2 epimers was obtained during this key reaction. This synthesis involved 15 steps, 2.2% overall yield and 86% ee starting from commercially available 3-benzyloxy-1-propanol (**48**) (Scheme 13).[47]



Scheme 13

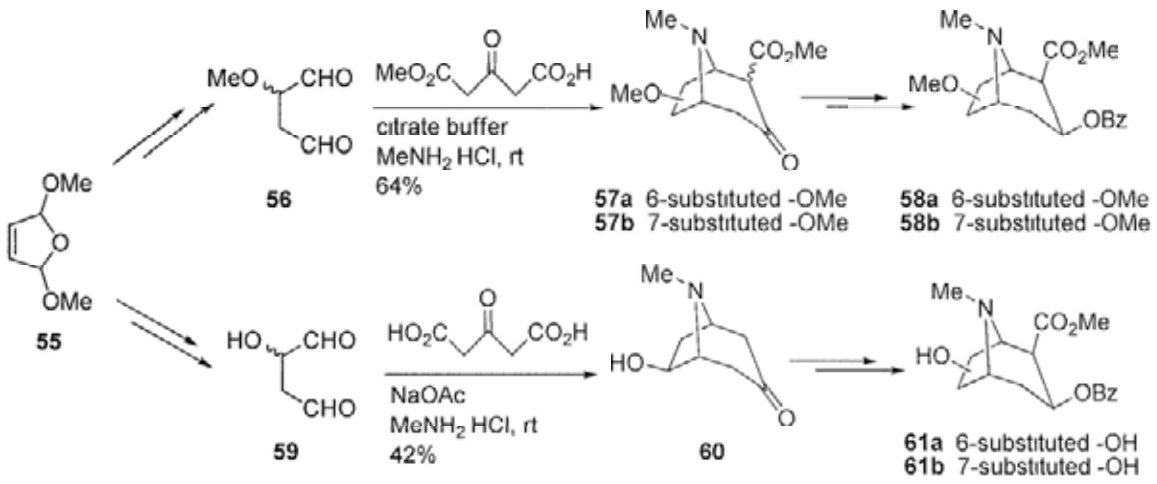
The latest asymmetric total synthesis of cocaine was reported by Davis *et al.* in 2010.[48] Starting with a chiral masked oxo sulfinimine **52** to prepare a chiral imine

intermediate **53**, the tropane skeleton was constructed in the same strategy as in Tufariello' s *rac*-cocaine synthesis, using INAC as the key step.[45] Both (–)- and (+)-cocaine could be synthesized in 12 steps and 9% overall yield from methyl 4-nitrobutanoate (**51**) (Scheme 14).



Scheme 14

Since cocaine abuse is one of the greatest concerns in the society, much effort had been used to obtain cocaine analogues for abuse treatment. Because of the difficulties on the synthesis of optically pure natural (–)-cocaine (**3**), preparation of cocaine analogues was limited and analogues were mainly derived from natural (–)-cocaine (**3**).[54–57] A few examples were based on minor modification of the reported synthetic strategies.[48,58–60] Kozikowski and co-workers had prepared racemic 6- and 7-methoxylated and hydroxylated cocaine analogues using Willstätter' s synthesis,[44] followed by optical resolution (Scheme 15).[58–60]



Scheme 15

This 7β-hydroxylated cocaine **61b** had been used by Dickerson and Janda to synthesize haptens for immunopharmacotherpy in cocaine abuse (Figure 9).[61]

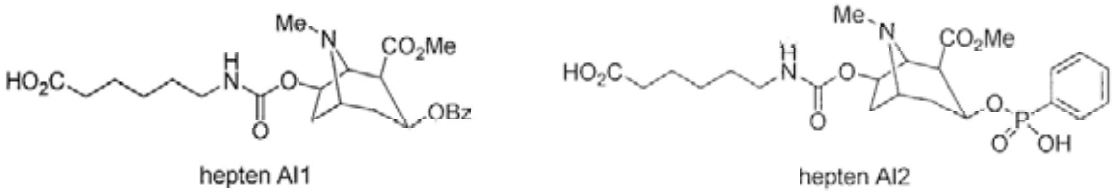
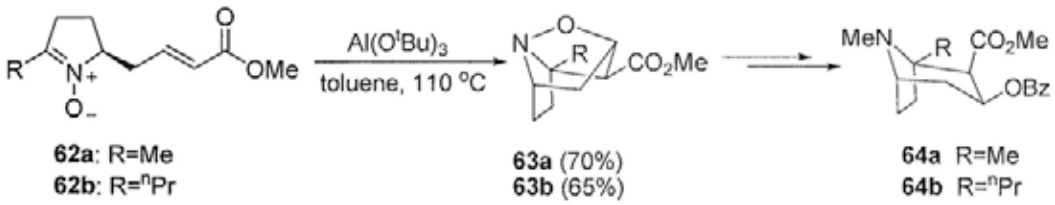


Figure 9

In 2010, Davis *et al*. prepared optically pure cocaine C-1 analogues **64a** and **64b**, starting from the chiral masked oxo sulfinimine to prepare chiral intermediates **62** and following the same strategy as Tufariello' s synthesis (Scheme 16).[48]



Scheme 16

However, there are still no therapeutically useful cocaine derivative reported hence further syntheses of cocaine analogues syntheses are needed.

The *endo*-mode INAC reaction of hept-6-enoses allows the construction of 7-membered ring carbocycles with nitrogen functionality on the carbocycles. These *endo*-cycloadducts had been shown to be transformed into optically pure tropanes.[14] In this thesis, synthetic studies on natural (–)-cocaine (**3**) and its analogues are discussed.

Chapter 2

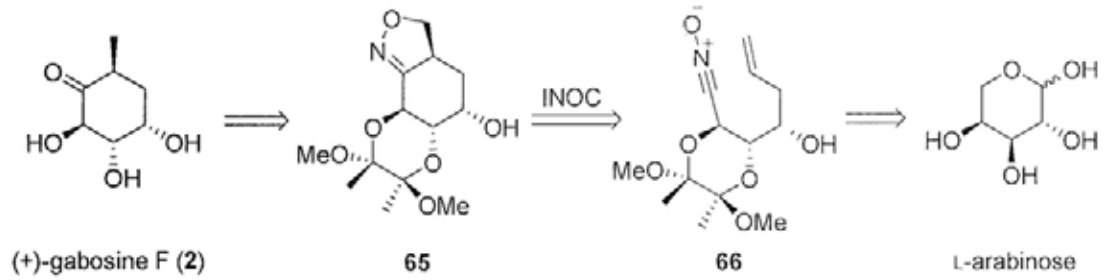
Results and Discussion

2.1 Construction of Carbocycles via Intramolecular Nitrile Oxide-Alkene Cycloaddition (INOC)

The intramolecular nitrile oxide-alkene cycloaddition (INOC) allows the formation of saturated carbocycles from sugar derivatives in good diastereoselectivity. These cycloadducts can be transformed into either natural products or their analogues with biological interests. In this section, application of INOC cycloadducts in the syntheses of gabosine F and a potentially bio-active cyclopent-2-enone is discussed.

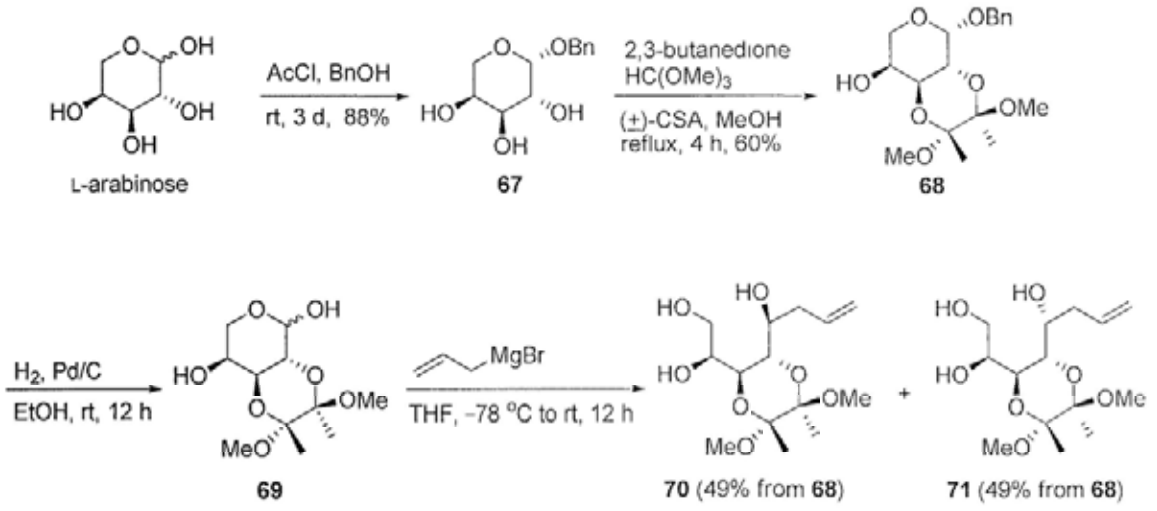
2.1.1 Synthesis of Optically Pure (+)-Gabosine F (2) from L-Arabinose

Retrosynthesis of (+)-gabosine F (**2**) shows that it could be synthesized from isoxazoline **65**, which should be prepared from L-arabinose as shown below, using INOC as the key step (Scheme 17).



Scheme 17

Starting with L-arabinose, it was subjected to Fischer glycosidation to give benzyl-β-L-arabinopyranoside (**67**)[62] by reacting with acidic benzyl alcohol (Scheme 18). Protection of the 2,3-*trans*-diol in **67** as butane 2,3-bisacetal[39] gave acetal **68**.

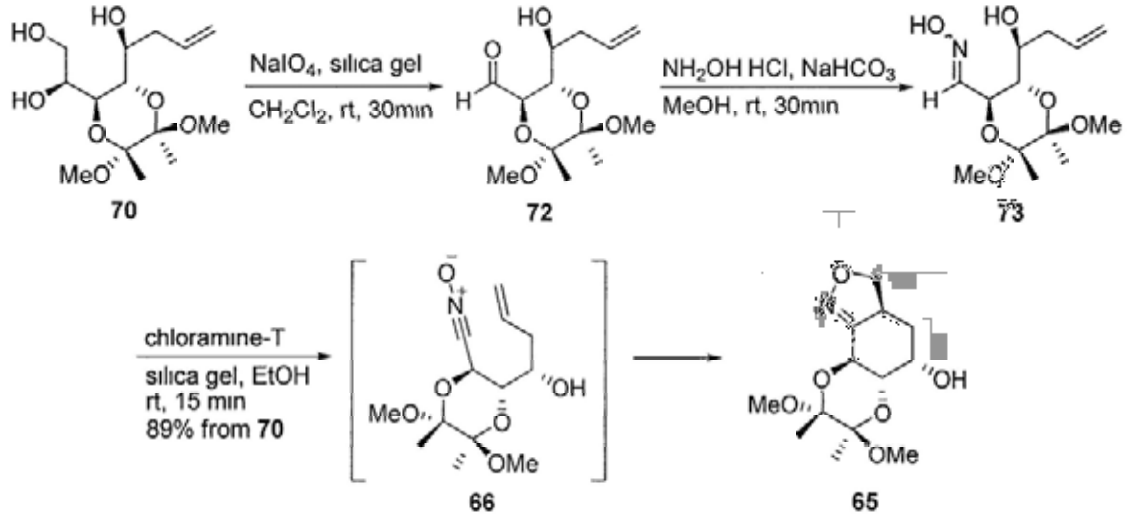


Scheme 18

The benzyl group in acetal **68** was removed by hydrogenolysis using palladium-on-charcoal as catalyst to yield lactol **69**, which was then reacted with an excess of allylmagnesium bromide to give alkenes **70** and **71** in equal amounts.[13] The poor diastereoselectivity of this allylation might be due to the inherent multi-oxygen functionalities of the *trans*-diacetal blocking group, which could offer chelation and complicate the transition state model, making no preference for either side of the addition.[13]

The alkene **70** was then transformed into the INOC cycloadduct, isoxazoline **65**, in excellent overall yield via a reaction sequence involving (i) silica-gel mediated glycol

cleavage oxidation,[63] (ii) oxination with hydroxylamine and (iii) chloramine-T/silica gel mediated INOC of oxime **73** (Scheme 19).[8]



Scheme 19

In this INOC reaction, isoxazoline **65** was obtained as the only one diastereomer. The reason of the diastereospecific outcome for this reaction can be explained by the following proposed transition states (Figure 10).

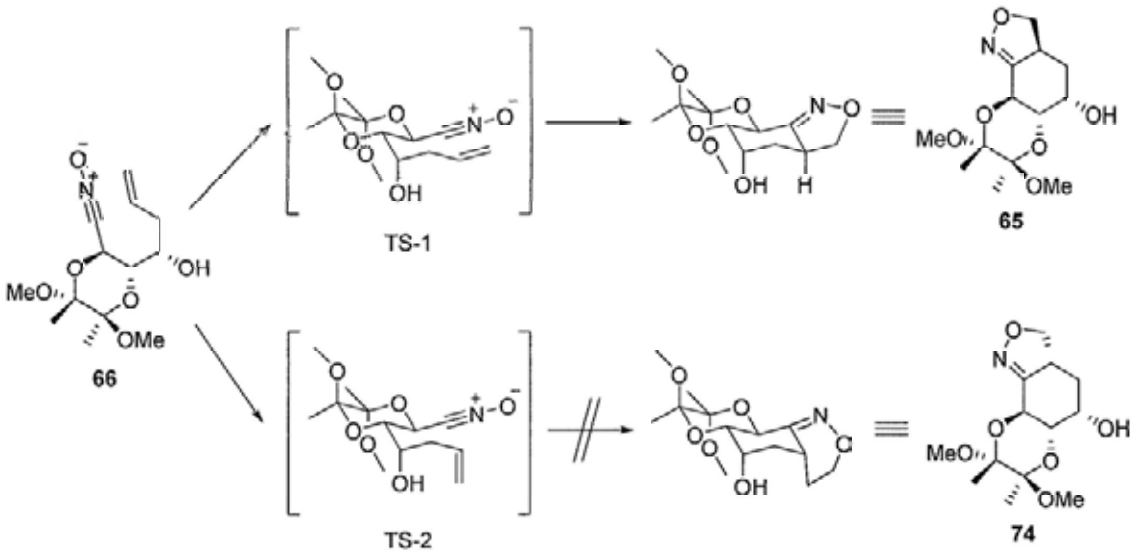
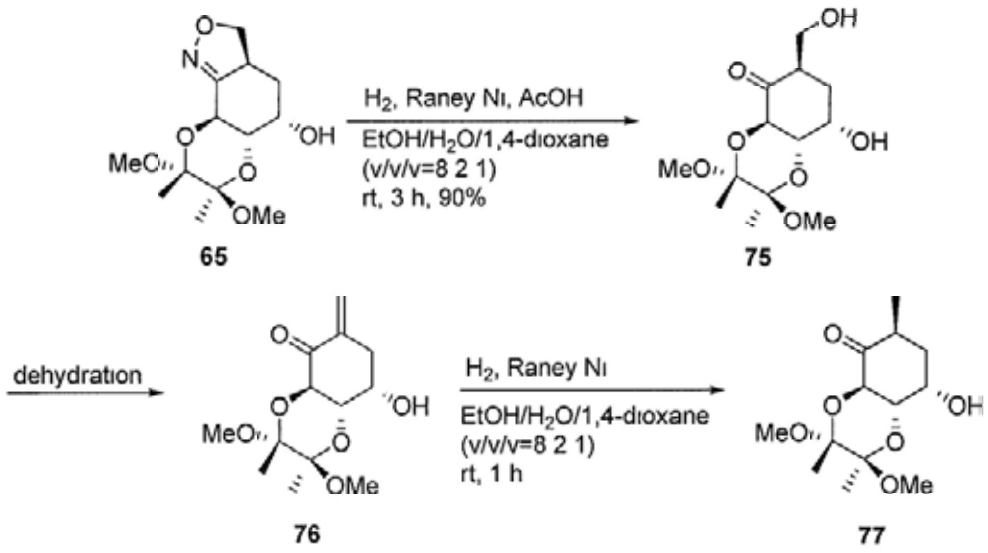


Figure 10

Due to the rigidity of the *trans*-diacetal blocking group, the acyclic carbon chain on hept-6-enose is occupying the equatorial position of the *trans*-diacetal ring, as shown in both TS-1 and TS-2. For TS-1, bonding orbitals of the nitrile oxide group and the alkene moiety are aligned in the same plane in space hence a better overlapping of orbitals leads to lower TS energy, resulting in the formation of isoxazoline **65**. On the other hand, there are no good overlapping of bonding orbitals in TS-2 and this cycloaddition pathway is not favoured, hence no isoxazoline **74** was formed.

The isoxazoline **65** obtained was subjected to Raney®-Nickel catalyzed hydrogenolysis to yield ketone **75** smoothly (Scheme 20). In order to remove the primary hydroxyl group in **75**, it was first dehydrated to give exocyclic enone **76**, which then was hydrogenated to provide the corresponding β-methyl ketone **77**.



65 75 76 77

Scheme 20

The ketone **75** was dehydrated under different conditions and the results are summarized in Table 1.

Table 1. Dehydration conditions of ketone **75**.

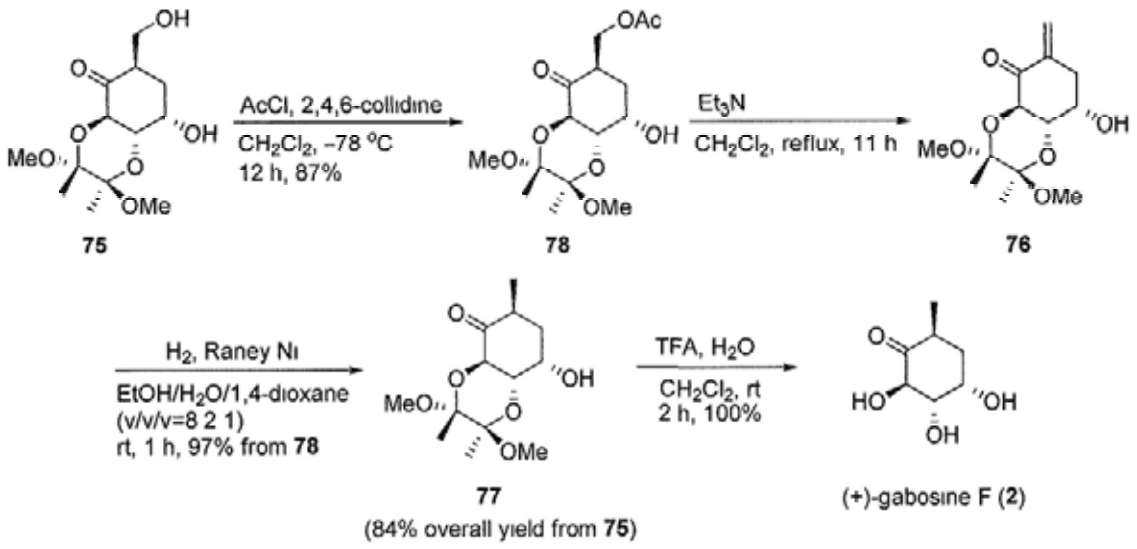
Entry	Dehydration Conditions	Yield of **77** from **75**
1	Martin's sulfurane, THF, −78 °C	No reaction
2	Martin's sulfurane, THF, rt	Decomposed
3	Burgess reagent, THF, −78 °C	No reaction
4	Burgess reagent, CH_2Cl_2, −78 °C	No reaction
5	Burgess reagent, CH_2Cl_2, rt	No reaction
6	Burgess reagent, CH_2Cl_2, reflux, 18 h	38%
7	Burgess reagent, THF, reflux, 2 h	34%
8	MsCl (1 eq.) , 2,4,6-collidine, CH_2Cl_2, −78 °C to rt, 15 h then add Et_3N, rt, 1 h	43%
9	AcCl (1 eq.), 2,6-lutidine, CH_2Cl_2, −78 °C, 18 h then add Et_3N reflux, 10 h	61%
10	AcCl (1 eq.), 2,4,6-collidine, CH_2Cl_2, −78 °C, 18 h then add Et_3N reflux, 10 h	61%

Ketone **75** was first attempted to be dehydrated by Martin's sulfurane, which is a mild dehydrating agent which can do the activation and elimination in one pot without the addition of an external base.[64] No reaction was observed with ketone **75** at −78 °C (entry 1), but at room temperature the starting material was decomposed and did not lead to ketone **75** or any product (entry 2). It was suggested that at room temperature the dehydration may have take place, but the exocyclic enone **76** formed may be unstable and destroyed by Martin's sulfurane. Another mild dehydrating agent, Burgess reagent,[65] was then used to react with ketone **75**. It had no reaction with **75** at −78 °C (entries 3 and 4). When the reaction was risen to room temperature, ketone **75** still remained inert but no decomposition was observed (entry 5). The dehydration finally

occurred when reacting under boiling CH_2Cl_2 to afford enone **76**, which was then subjected to Raney®-Nickel catalyzed hydrogenation to yield the β-methyl ketone **77**, in 38% overall yield from ketone **75** (entry 6). Changing the reaction solvent for dehydration from CH_2Cl_2 to THF gave similar yields (entry 7).

The primary alcohol of ketone **75** was also mesylated regioselectively[66] by methanesulfonyl chloride with 2,4,6-collidine as base to give the corresponding mono-mesylate (entry 8), it was observed that some of the mesylate had been converted into the enone **76** from the TLC, but the elimination was not complete. The elimination reaction was completed by adding triethylamine into the same reaction flask to afford enone **76**, and the subsequent hydrogenation yielded **77** in 43% overall yield from ketone **75**. When ketone **75** was subjected to regioselective acetylation[66] with either 2,6-lutidine or 2,4,6-collidine as base, the corresponding mono-acetate **78** was formed without enone **76** showing on TLC (entries 9 and 10). Triethylamine was then added and the reaction was heated to cause the elimination to take place. Hydrogenation of resulting enone **76** afforded β-methyl ketone **77** in 61% overall yield from ketone **75**.

The acetate **78** was recognized to be fairly stable and could be isolated in a pure form. It was isolated prior to the elimination process in order to avoid any side reaction that might affect the elimination (Scheme 21). Regioselective acetylation of ketone **75** in the same conditions as mentioned previously furnished acetate **78** in an excellent yield.

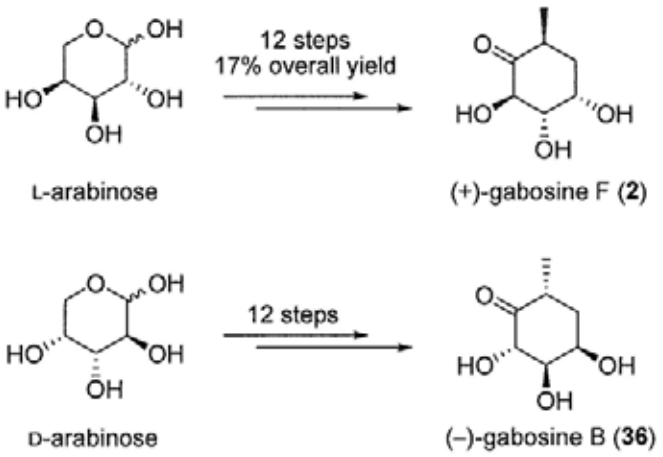


Scheme 21

The purified acetate **78** was reacted with triethylamine in CH_2Cl_2 under reflux to afforded enone **76**, followed by hydrogenation to give β-methyl ketone **77** in 97% overall yield from acetate **78**. That is, 84% overall yield from ketone **75** and these condition furnished the highest yield to form β-methyl ketone **77** from ketone **75**. It should be noted that the Raney®-Nickel catalyzed hydrogenation of enone **76** afforded β-methyl ketone **77** as the sole product. The stereospecific outcome of this reaction might be due to the "anchor effect" of the axial free α-alcohol,[67] which directed the approach of the hydrogen from the α-face, resulting in the formation of β-methyl ketone **77**.

The remaining *trans*-diacetal blocking group of β-methyl ketone **77** was hydrolyzed with trifluoroacetic acid to give the target molecule (+)-gabosine F (**2**) in a quantitative yield (Scheme 21). The specific rotation, $[\alpha]_D^{20}$ +88.4 (*c* 0.69, MeOH) {lit. $[\alpha]_D^{20}$ +94 (*c* 1.0, MeOH)}, and the NMR spectral data are in good agreement with the

literature values.[16a] The enantiopure (+)-gabosine F (**2**) was hence synthesized for the first time by using L-arabinose as the starting material, in 12 steps and 17% overall yield (Scheme 22).

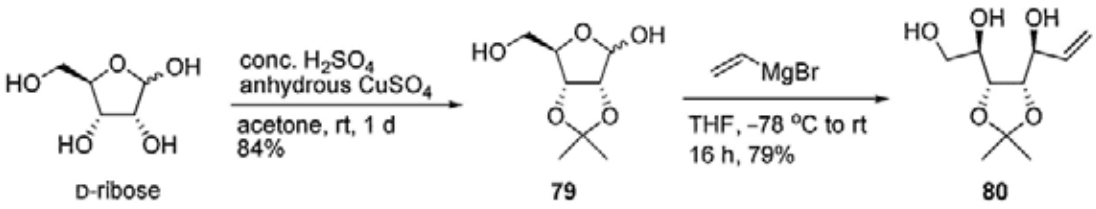


Scheme 22

Using the same synthetic strategy, (−)-gabosine B (**36**), which is the enantiomer of (+)-gabosine F (**2**), in theory can also be synthesized from D-arabinose, the enantiomer of L-arabinose (Scheme 22). This synthesis of (−)-gabosine B (**36**) is believed to be superior than the previous synthesis (15 steps, 4.3% overall yield) reported by Shinada *et al.*[24]

2.1.2 Synthesis of Cyclopent-2-enone Derivatives

In the previous section, an INOC cycloadduct had been transformed into (+)-gabosine F (**2**), which is a hydroxylated cyclohexanone. In this section, preparation of hydroxylated cyclopent-2-enone derivatives from another INOC cycloadduct is discussed.



Scheme 23

The acetonide **79**,[68] synthesized from D-ribose by isopropylidenation, was reacted with vinylmagnesium bromide to afford alkene **80** in a good yield (Scheme 23).[9] The highly stereoselectivity of vinylation was explained with the chelation controlled transition model[9] shown in Figure 11.

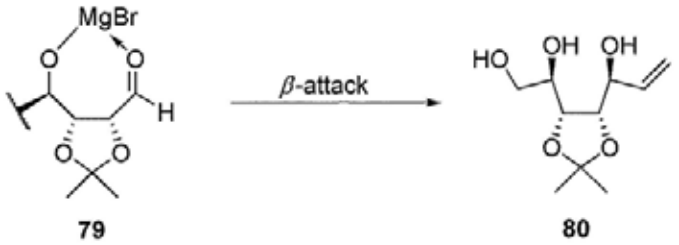
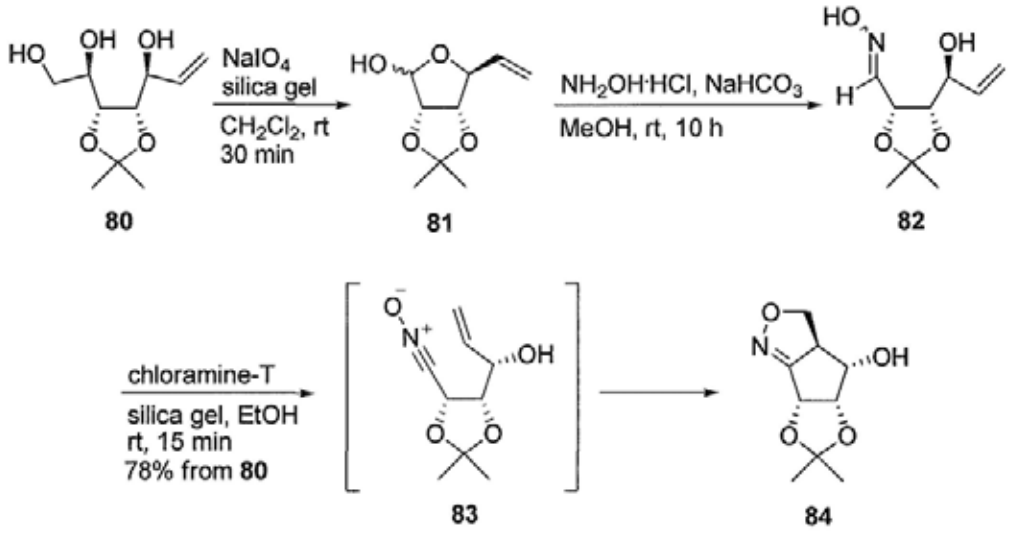


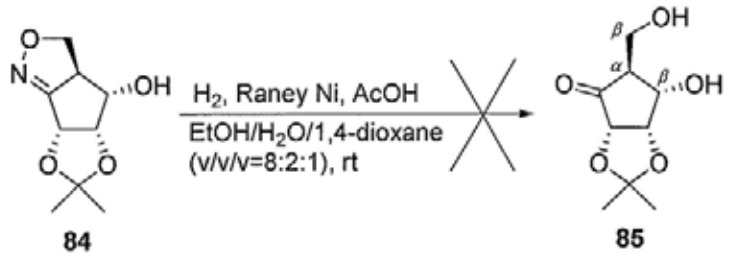
Figure 11

As the α-face of **79** is hindered by the bulky isopropylidene group, the vinylmagnesium bromide attack on the β-side, resulting in the formation of alkene **80**. The alkene **80** was then subjected to glycol cleavage oxidation to give crude lactol **81**, which was followed by oximation to afford oxime **82** (Scheme 24). The crude oxime **82** was then reacted with chloramine-T in the presence of silica gel to generate nitrile oxide **83** in situ and cyclized through INOC to form isoxazoline **84** as a single diastereomer.[8]



Scheme 24

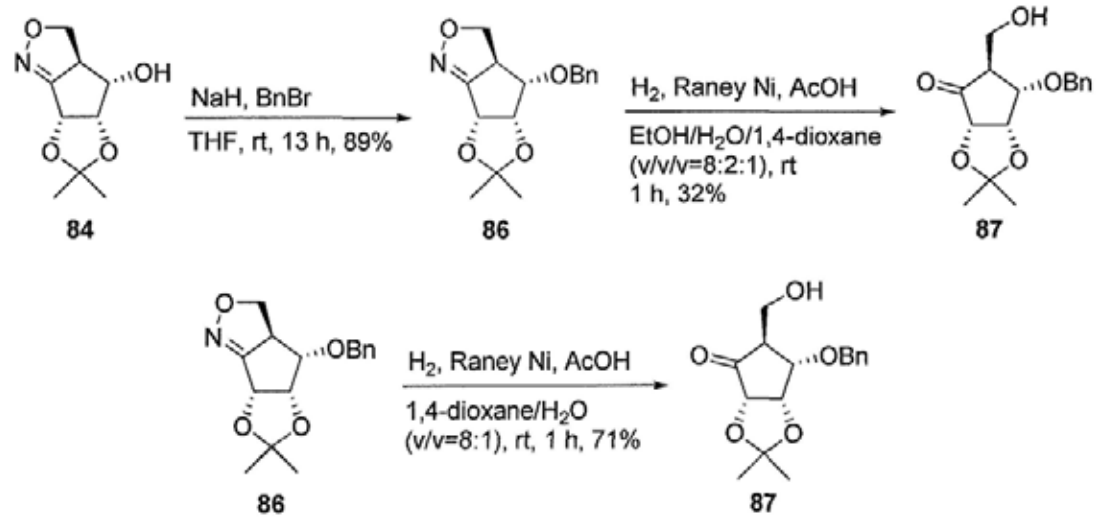
In order to convert isoxazoline **84** into the cyclopentanone moiety, the nitrogen-oxygen bond was attempted to cleave by hydrogenolysis to give β-hydroxyl ketone **85** (Scheme 25).



Scheme 25

However, Raney®-Nickel catalyzed hydrogenolysis of isoxazoline **84** did not afford β-hydroxyl ketone **85**. Surprisingly the starting material decomposed into a complex mixture of products which cannot be characterized. It was suggested that the presence of two β-hydroxyl groups in ketone **85** would allow the retro-aldol reaction to occur readily, leading the decomposition of ketone **85**.

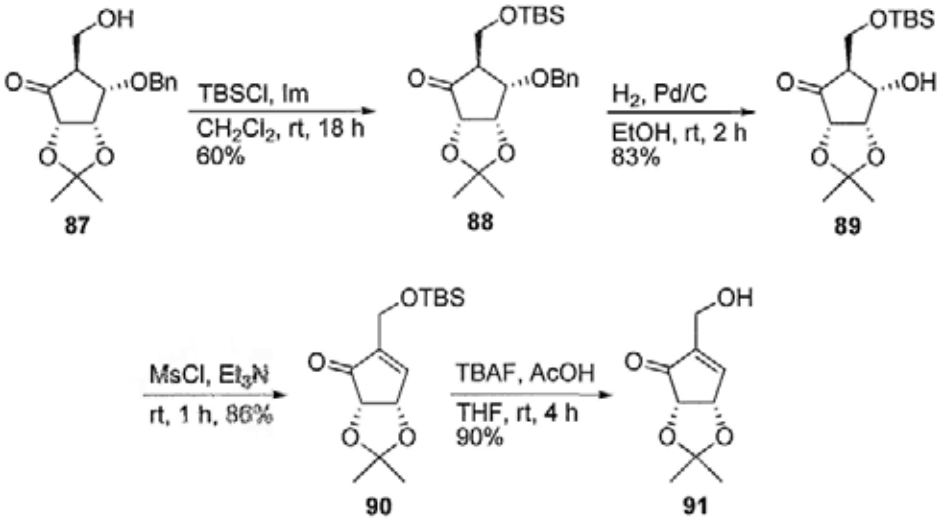
If the instability of ketone **85** was really due to the retro-aldol reaction, the stability of the cyclopentanone may be increased on reducing the number of β-hydroxyl groups. Isoxazoline **84** was therefore protected as a benzyl ether to form **86**, which was followed by hydrogenolysis in the same conditions as before to afford ketone **87** in moderate yield (Scheme 26).



Scheme 26

Changing the reaction solvent from EtOH/H_2O/dioxane (v/v/v=8:2:1) to dioxane/H_2O (v/v=8:1) improved the reaction yield of ketone **87**. Although ketone **87** is more stable than ketone **85**, ketone **87** is still not very stable and prone to decompose upon prolonged standing. Ketone **87** was hence directed quickly to the next step after purification by short column chromatography without characterization. Silylation of ketone **87** with *t*-butyldimethylsilyl chloride and imidazole in CH_2Cl_2 furnished silyl ether **88** (Scheme 27). Unlike the previous β-hydroxyl ketones, this silyl ether **88** is

stable enough to be characterized. The benzyl group in **88** was then removed by hydrogenolysis using palladium-on-charcoal as catalyst to give alcohol **89** in good yield.

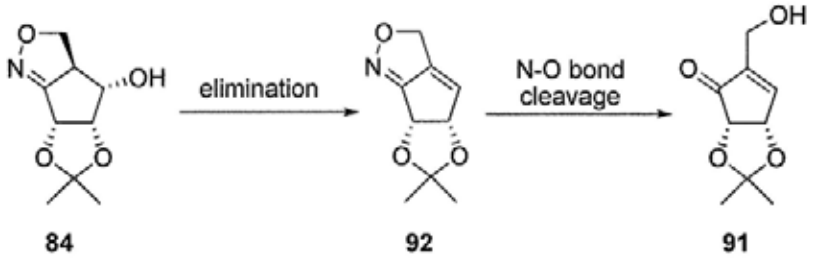


Scheme 27

In order to synthesize the target molecules, cyclopent-2-enone derivatives, the secondary hydroxyl group in silyl ether **89** had to be eliminated to give the resulting enone. Reacting silyl ether **89** with methanesulfonyl chloride and triethylamine at room temperature furnished the enone **90** directly. Alcohol **91**, was obtained easily by removing the silyl group of enone **90** with tetra-*n*-butylammonium fluoride, in an excellent yield. This alcohol **91** has a primary allylic alcohol in a cyclopent-2-enone moiety hence can be functionalized easily by replacng the allylic alcohol with different substituents. Alcohol **91** is actually the key intermediate of Khan's synthesis of (±)-neplanocin A.[69] Now, using the mentioned strategy, optically pure alcohol **91** can be synthesized from isoxazoline **84**, and this is a formal synthesis of natural (−)-neplanocin A (**1**).[69] A survey of neplanocin A syntheses from literatures showed that another approach[70] is more efficient than Khan's synthesis, but Khan's synthesis showed that the

alcohol **91** is an useful intermediate for natural product synthesis, as well as a potential anti-tumor substance.

Starting from D-ribose, the cyclopent-2-enone derivative, alcohol **91**, was synthesized through the INOC cycloadduct, isoxazoline **84**, in 11 steps and 13% overall yield. Obviously this synthetic scheme requires too many steps and is not practical. Especially one of the intermediates, ketone **87**, is not stable upon prolonged standing. In order to make the synthesis more efficient, another synthetic pathway had to be explored.

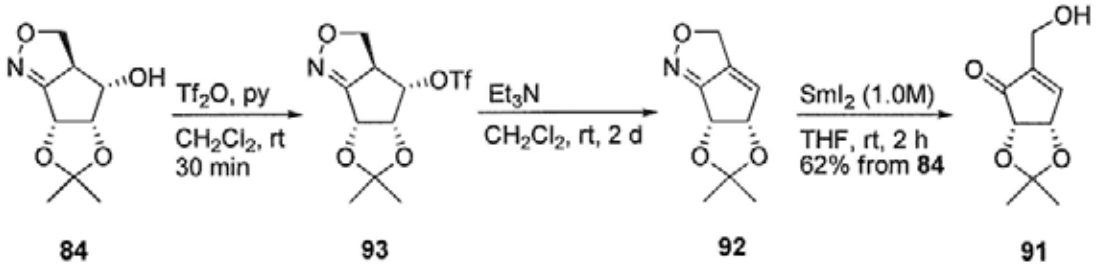


84 **92** **91**

Scheme 28

Another approach to cyclopent-2-enone **91** is to carry out elimination prior to nitrogen-oxygen bond cleavage (Scheme 28). As the intermediate **92** is already unsaturated, attempts to cleave the nitrogen-oxygen bond in **92** by hydrogenolysis would lead to hydrogenation on the alkene moiety as well. In order to obtain the alcohol **91**, the nitrogen-oxygen bond should be cleaved by another strategy. It was found that samarium(II) iodide is capable to perform nitrogen-oxygen bond cleavage,[71] without saturating the alkene moiety. Thus starting with isoxazoline **84** as in the previous synthesis, the free hydroxyl group was first activated by trifluoromethanesulfonic anhydride to afford triflate **93** (Scheme 29). Elimination of crude triflate **93** under mild conditions furnished **92** smoothly, and this was followed by the samarium(II) iodide

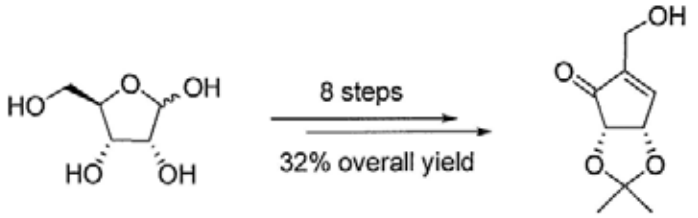
mediated N-O bond cleavage to give the alcohol **91**, in 62% overall yield from isoxazoline **84**.



84 **93** **92** **91**

Scheme 29

Using this new synthetic strategy, alcohol **91** was obtained from D-ribose in 8 steps with 32% overall yield (Scheme 30), providing an efficient approach to prepare optically pure alcohol **91**.

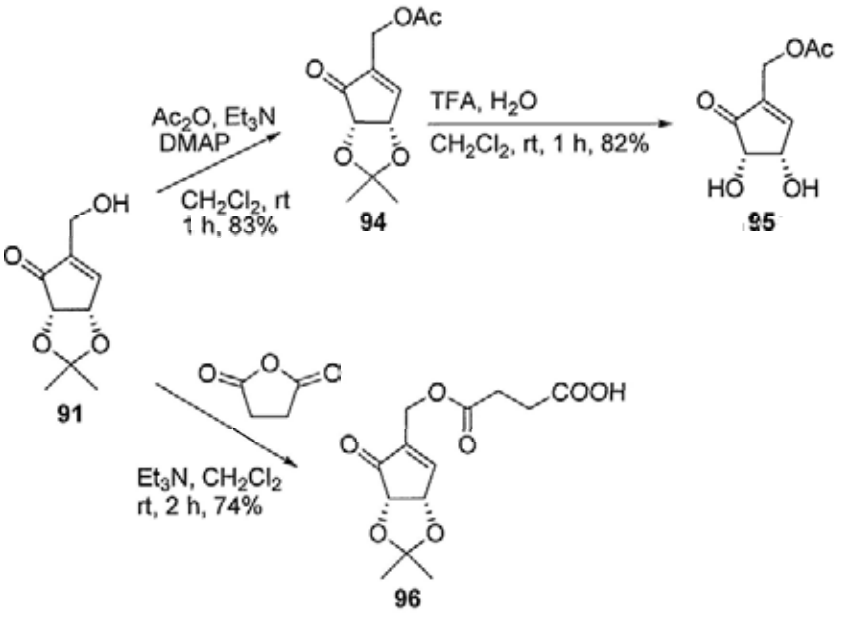


D-ribose **91**

Scheme 30

With the alcohol **91** in hand, it can be transformed into several cyclopent-2-enone derivatives (Scheme 31). The allylic alcohol of **91** was reacted with acetic anhydride to give acetate **94** in 83% yield. The isopropylidene group in acetate **94** can be removed by TFA hydrolysis, yielding diol **95**. Both acetate **94** and diol **95** can be recognized as the 5-membered ring versions of COTC[72] analogues and their anti-tumor activities would be investigated. Reacting alcohol **91** with succinic anhydride and

triethylamine, followed by acid work-up afforded carboxylic acid **96**. The carboxylic acid functionality in **96** is capable to form peptide linkage with any proteins or peptides and the bioactivity of these conjugates would be studied.



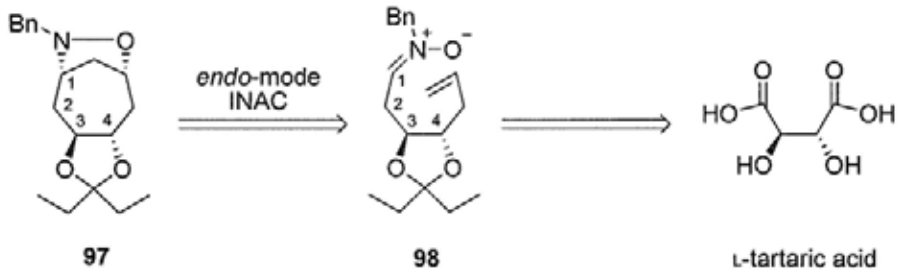
Scheme 31

2.2 Construction of Carbocycles via Intramolecular Nitrone-Alkene Cycloaddition (INAC)

As mentioned in the previous section, optically pure carbocycles were formed from carbohydrates via INOC reactions. In this section 6- and 7-membered carbocycles were prepared by INAC reactions. Also, synthetic studies towards optically pure (−)-cocaine (**3**) and its analogues from carbohydrates are discussed.

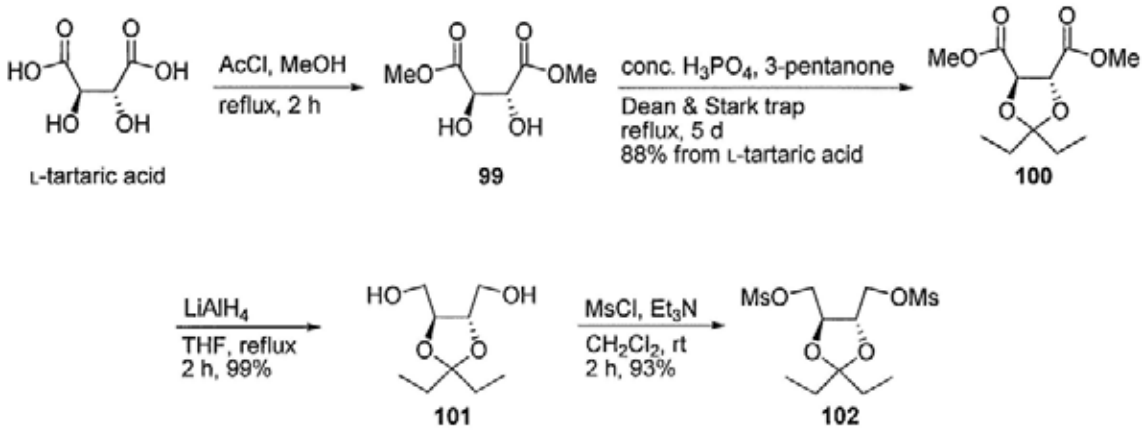
2.2.1 Studies on Regioselectivity of INAC on Hept-6-enose from L-Tartaric Acid with a 3,4-*trans*-Pentylidene Blocking Group

From the works conducted by my previous colleague, Dr. Wong Wai Fun, INAC of hept-6-enose containing 3,4-*trans*-isopropylidene blocking group furnished exclusive formation of 7-membered *endo*-cycloadducts due to the torsional strain of the blocking group.[14] In order to further support this explanation, INAC of nitrone **98**, a hept-6-enose bearing a 3,4-*trans*-pentylidene as the only blocking group, which providing the same torsional strain as 3,4-*trans*-isopropylidene moiety, was studied (Scheme 32). If the *endo*-cycloaddition is really due to the torsional strain of the *trans*-blocking group, INAC of nitrone **98** would also lead to exclusive formation of an *endo*-cycloadduct. As one of the synthetic intermediates towards nitrone **98** is volatile, using a pentylidene instead of isopropylidene as the blocking group can increase the molecular weight of this intermediate hence reduce its volatility.



Scheme 32

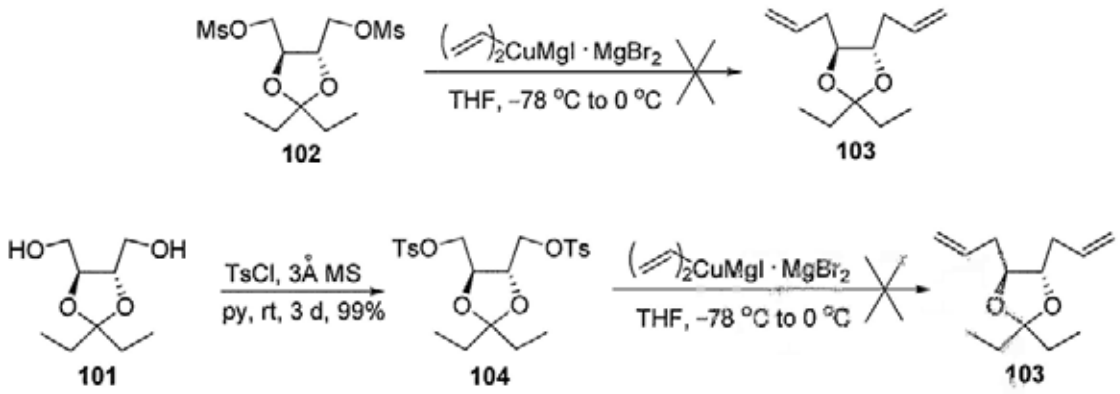
Thus starting with L-tartaric acid, it was first transformed into its methyl ester **99** through Fischer esterification[73] (Scheme 33). The 2,3-*trans*-diol of ester **99** were then protected by a pentylidene group by heating in 3-pentanone with a catalytic amount of H_3PO_4. A Dean and Stark trap allowed continuous removal of water from the reaction mixture, hence, forcing the equilibrium toward the product side, resulting in an excellent overall yield of diester **100** from L-tartaric acid.



Scheme 33

Reduction of ester **100** with $LiAlH_4$ in THF under reflux led to the formation of diol **101**, followed by activation of two hydroxyl groups by methanesulfonyl chloride to give dimesylate **102** (Scheme 33). The dimesylate **102** was attempted to carry out vinyl

substitution with cuprate,[74a] which was generated from mixing vinylmagnesium bromide with copper(I) iodide at low temperature, in order to afford the desired dialkene **103** (Scheme 34).

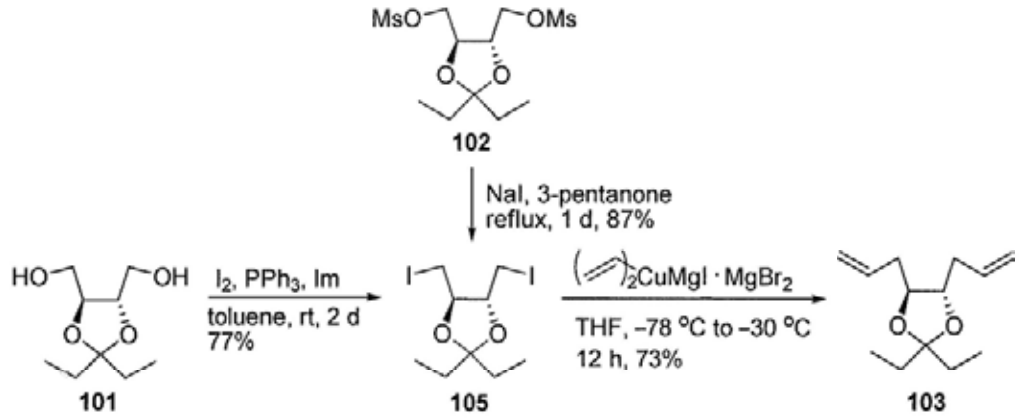


Scheme 34

However, no desired dialkene **103** was formed and the starting material decomposed into a mixture of products which could not be isolated as pure compound. The ditosylate **104**, formed by tosylation of diol **101**, showed no reaction under the same reaction conditions. Unlike dimesylate **102**, reacting divinyl cuprate with ditosylate **104** did not lead to the decomposition of the starting material. It was suggested that the methyl protons in the mesylate moiety of **102** were acidic enough to be deprotonated by the cuprate, leading to a series of undesired rearrangement reactions.

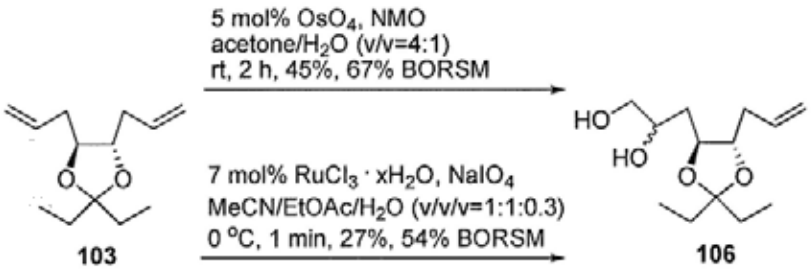
Besides activating diol **101** by sulfonate esters, transformation of **101** into the corresponding iodide **105** was also performed in order to realize the vinyl substitution (Scheme 35). Thus diiodide **105** was prepared by either (i) reacting diol **101** with iodine, triphenylphosphine and imidazole in toluene or (ii) displacement of mesylates in **102** with iodide ions. This diiodide **105** was then subjected to vinylation with the cuprate.

The dialkene **103**, which was found to be a volatile substance, was formed in good yield, especially when performing this reaction at lower temperature (−30 °C instead of 0 °C).



Scheme 35

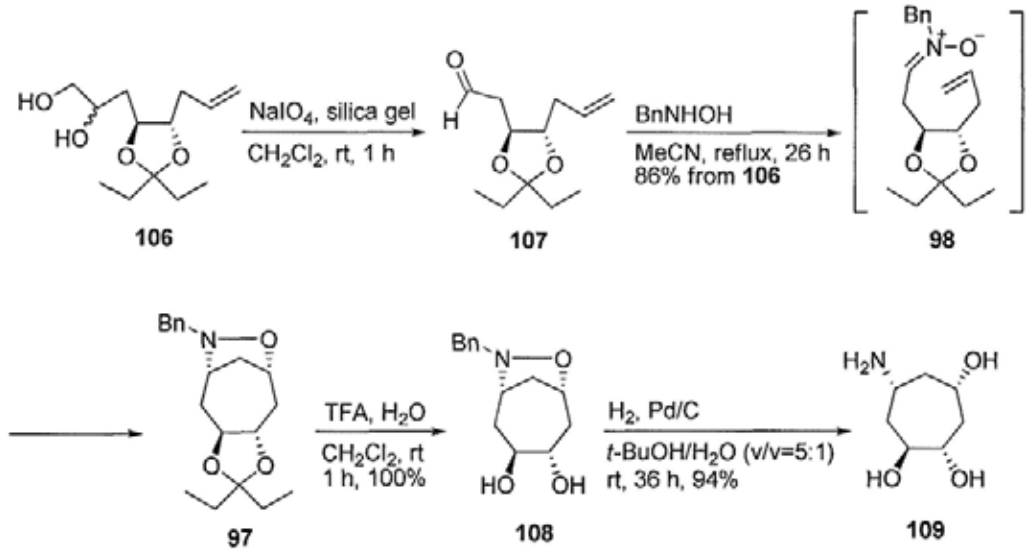
The difference in reactivity between disulfonates **102/104** and diiodide **105** probably because they were reacting under different mechanisms.[74b,c] According to literature, the reaction between alkyl iodide and cuprate reagent was not a classical S_N2 substitution.[74c] This can explain why diiodide **105** but not disulfonates **102/104** was vinylated.



Scheme 36

With the dialkene **103** in hand, one of its alkene moieties was dihydroxylated to form diol **106** (Scheme 36). Catalytic osmium tetraoxide dihydroxylation with one

equivalent of 4-methylmorpholine *N*-oxide as co-oxidant furnished diol **106** in good yield in counting the recovery of starting material. The ruthenium tetraoxide catalyzed flash dihydroxylation[75] afforded a lower yield of diol **106**, although the reaction proceeded much faster.



Scheme 37

The diol **106** was then subjected to glycol cleavage oxidation to form aldehyde **107** (Scheme 37), which was condensated with *N*-benzylhydroxylamine to form nitrone **98**. Subsequence INAC reaction by heating the reaction mixture to reflux yielded the *endo*-cycloadduct isoxazolidine **97** as the only diastereomer. The ring size of cycloadduct was confirmed by the ^{13}C DEPT NMR spectrum of isoxazolidine **97**. There are five resonances in the upfield region (δ 25−40 ppm) were assigned to be methylene group, two of which are the methylene carbons of pentylidene moiety, the other three are belonged to the cycloheptane ring. If *exo*-cycloadduct cyclohexane had been formed, only four methylene resonances in upfield region would have been found. Both the

regio- and stereochemistry of diol **108** were further confirmed by X-ray crystallographic analysis (Figure 12). Diol **108** was obtained from TFA hydrolysis of isoxazolidine **97** in quantitative yield.

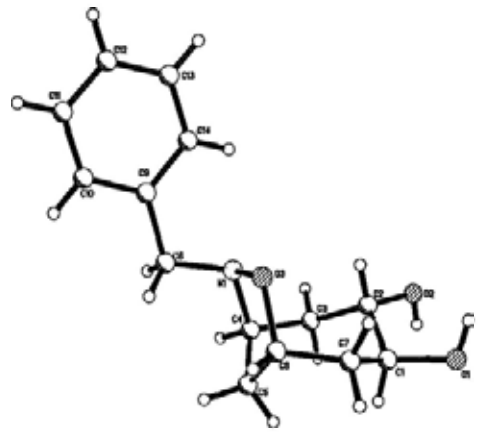


Figure 12. X-ray crystallographic structure of diol **108**.

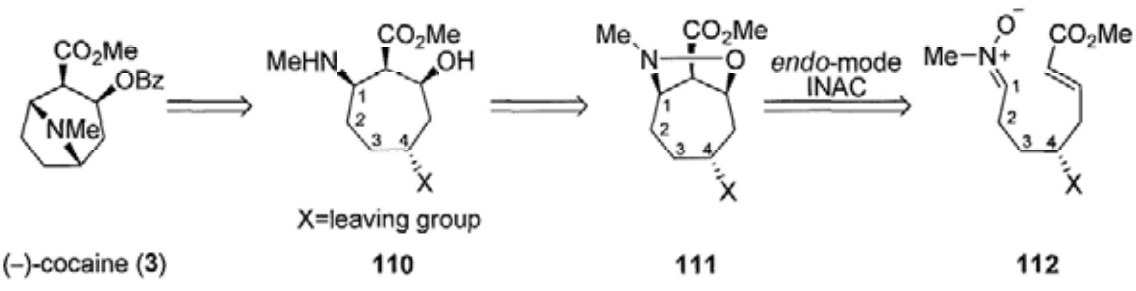
Since the INAC of nitrone **98**, which consists of 3,4-*trans*-pentylidene as the only blocking group, afforded exclusive formation of *endo*-cycloadduct, isoxazolidine **97**. It is concluded that the presence of 3,4-*trans*-pentylidene (or isopropylidene) can induce the *endo*-mode INAC reaction to perform exclusively. Thus the regioselectivity of INAC reactions can be certainly controlled by changing the blocking group of substrates.

In addition, the diol **108** was transformed into aminocycloheptanol **109**, by hydrogenolysis catalyzed by palladium-on-charcoal (Scheme 37). Both nitrogen-oxygen bond and nitrogen-benzyl moiety were cleaved, resulting in the formation of **109** in 94% yield. Thus aminocycloheptanol **109** were synthesized from L-tartaric acid in 10 steps

with 27% overall yield, thus providing a high yielding approach of aminocycloheptanol synthesis.

2.2.2 Synthetic Studies towards (−)-Cocaine (3) and (−)-Cocaine Analogues

By analyzing the structure of (−)-cocaine (**3**), it was noted that the structure of cocaine consists of a 7-membered carbocycle, with a carboxylate ester moiety connected to the carbocyclic ring (Scheme 38). The tropane skeleton might be constructed by allowing the amine group in C-1 position to attack the C-4 of **110**, obtained from hydrogenolysis of isoxazolidine **111**. The isoxazolidine **111** might be prepared by *endo*-mode INAC reaction of **112**, using an α,β-unsaturated ester as the dipolarophile.

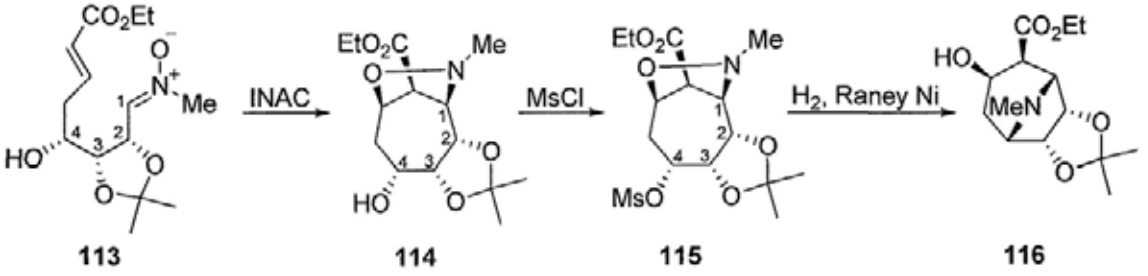


Scheme 38

In this section, approaches towards (−)-cocaine (**3**) and (−)-cocaine analogues syntheses from carbohydrate via *endo*-mode INAC reaction as the key step are discussed.

2.2.2.1 INAC of Nitrones with a 2,3-*cis*-Isopropylidene as Blocking Group and an *α,β*-Unsaturated Ester as Dipolarophile

It was attempted to use the nitrone **113**, which bearing an *α,β*-unsaturated ester moiety, to perform INAC reaction to furnish *endo*-cycloadduct **114** (Scheme 39). The C-4 free hydroxyl group of cycloadduct **114** could be activated by MsCl hence allowing the formation of a tropane skeleton in the next step. Although previous studies[13] showed that the INAC of hept-6-enose bearing 2,3-*cis*-isopropylidene would lead to an exclusive formation of 6-membered *exo*-cycloadduct, it was hoped that the presence of *α,β*-unsaturated ester moiety in nitrone **113** could induce the *endo*-mode INAC reaction, by electronic effect.



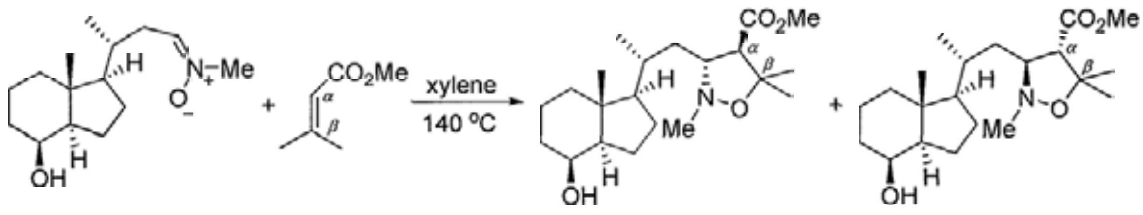
113 **114** **115** **116**

Scheme 39

Obviously, the *α,β*-unsaturated ester is an electron deficient alkene with the *β*-carbon bearing slightly positive charge (Figure 13).

Figure 13. Resonance structures of the *α,β*-unsaturated ester.

During 1,3-dipolar cycloaddition between a nitrone and the α,β-unsaturated ester, the oxygen atom of nitrone, bearing a negative charge, would attack the β-carbon of the α,β-unsaturated ester.[4] This regiochemical outcome was supported by several literature reports of intermolecular 1,3-dipolar cycloaddition between the nitrone and the α,β-unsaturated ester.[76–78] For example, Baggiolini *et al.* reported the formation of 1:1 mixture of isoxazolidine esters **118** and **119** by intermolecular nitrone-alkene cycloaddition, in which the oxygen atom of nitrone attacked the β-carbon of the methyl 3,3-dimethylacrylate (**118**) (Scheme 40).[76]

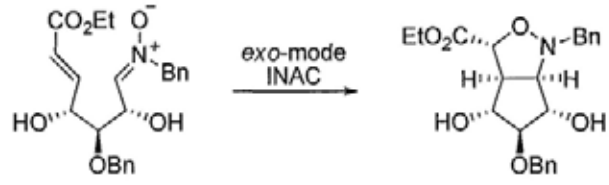


117 **118** **119** (40%) **120** (41%)

(Reported by Baggiolini *et al.*)

Scheme 40

However, it was reported that the INAC reaction of nitrone **121**, bearing an α,β-unsaturated ester as the dipolarophile, had led to the formation of an 5-membered *exo*-cycloadduct rather than a 6-membered *endo*-cycloadduct (Scheme 41).[79]



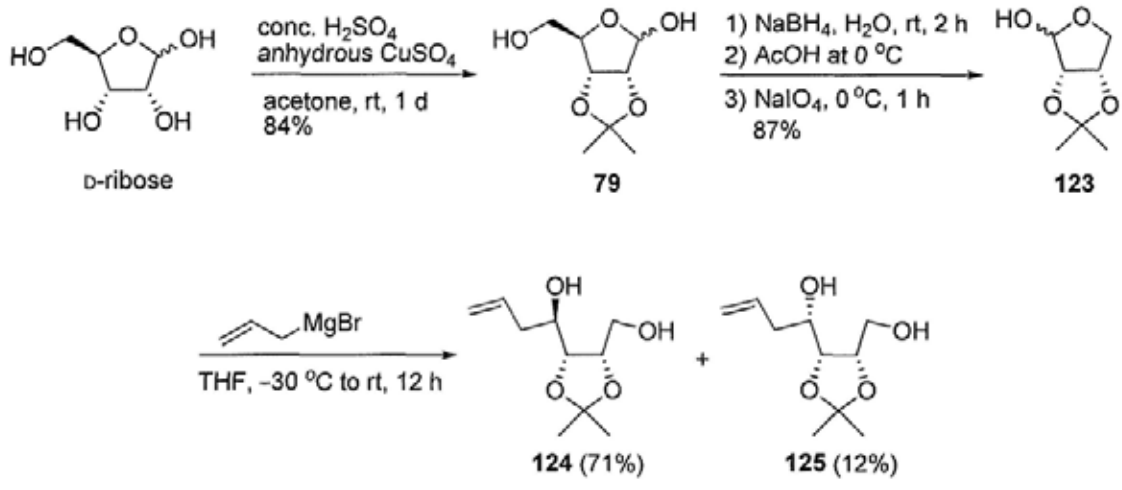
121 **122**

(Reported by Jachak *et al.*)

Scheme 41

In contrast to the nitrone **121**, the INAC of nitrone **113** involved selectivity between the formations of 6- or 7-membered cycloadducts (Scheme 39). Such regiochemical studies of INAC reaction are discussed in this thesis.

Starting from acetonide **79**, it was transformed into lactol **123** in an one pot reaction, firstly sodium borohydride reduction (Scheme 42), followed by glycol cleavage oxidation, as reported by Baxter *et al.*[80] The lactol **123** was subjected to Grignard reaction with allylmagnesium bromide, affording alkene **124** as the major product and its 4-epimer alkene **125** as the minor product.[81]



Scheme 42

The diastereoselectivity of the allylation can be explained by the chelation controlled transition model as shown in Figure 14. The α-face of **123** is blocked by the bulky isopropylidene moiety, causing the allyl group more likely to attack on the β-face of carbonyl carbon, yielding **124** as the major product.

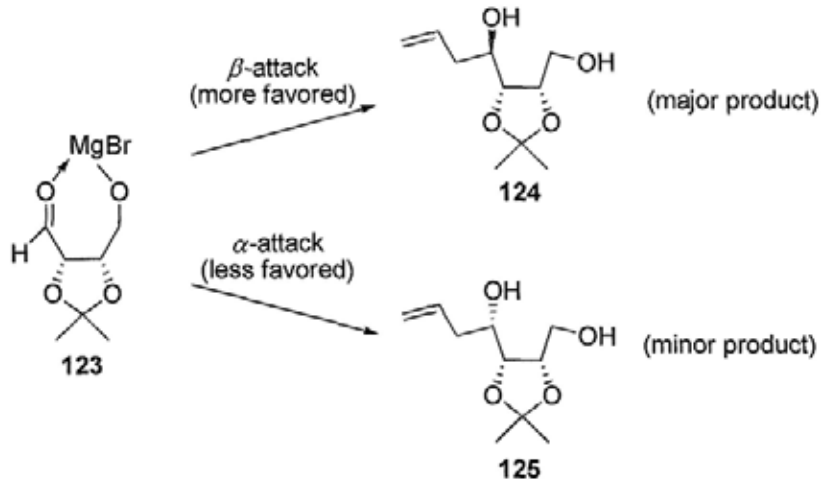
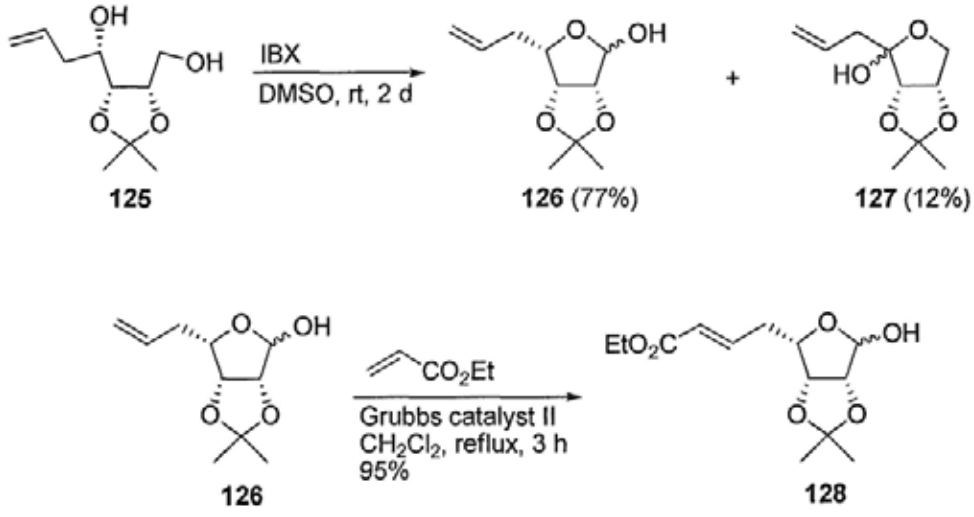


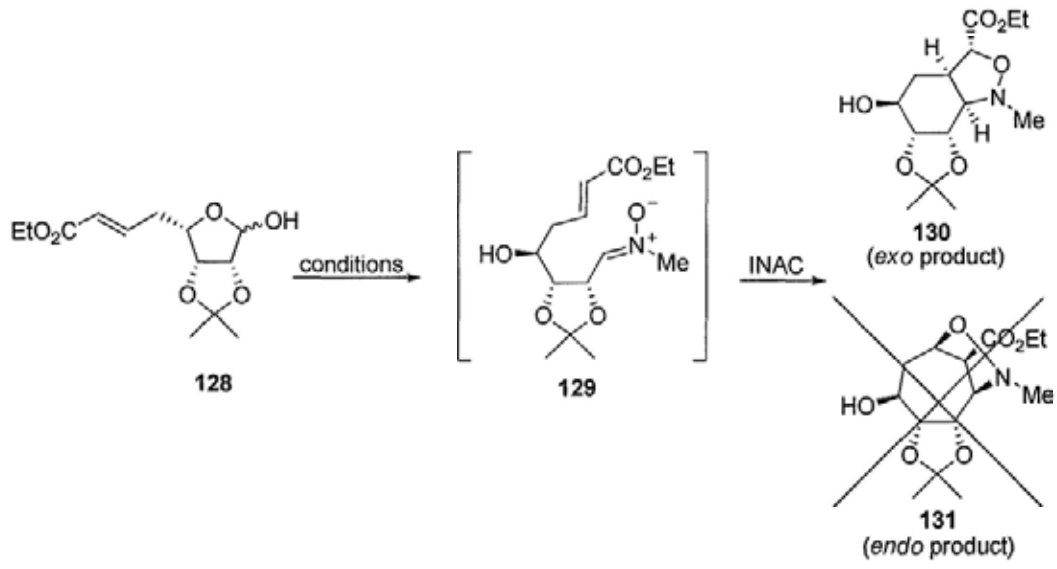
Figure 14

Firstly, the alkene **125** was used to prepare the nitrone for studying INAC reaction. It was subjected to selective oxidation of its primary alcohol by one equivalent of 2-iodoxybenzoic acid[82] in DMSO to give the desired lactol **126** in a good yield. Lactol **127**, formed by oxidizing the secondary alcohol of **125**, was isolated as the minor product (Scheme 43).



Scheme 43

The lactol **126** was then carried out cross-metathesis with ethyl acrylate, catalyzed by the second generation Grubbs catalyst,[83] to furnish α,β-unsaturated ester **128** as the only product in an excellent yield (Scheme 43). The large coupling constant (J = 15.6 Hz) of the two alkene signals (δ 5.95 and 7.00 ppm) in the ^{1}H NMR spectrum of **128** indicated that a *trans*-alkene was formed.



128 129

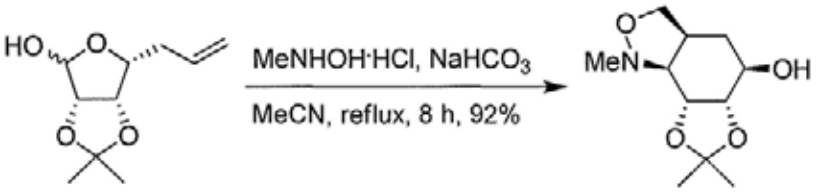
Scheme 44

With the α,β-unsaturated ester **128** in hand, it was subjected to condensation with *N*-methylhydroxylamine to give nitrone **129** in order to perform the INAC reaction (Scheme 44). Several INAC conditions were tried and the results are summarized in Table 2.

Table 2. Reaction conditions between ester **128** and *N*-methylhydroxylamine.

Entry	Conditions	Yield of **130**
1	MeNHOH·HCl, $NaHCO_3$, MeCN, rt	nil
2	MeNHOH·HCl, $NaHCO_3$, MeCN, reflux	decomposed
3	MeNHOH·HCl, py, MeCN, reflux, 17 h	41%
4	MeNHOH·HCl, py, CH_2Cl_2, reflux, 34 h	67%
5	MeNHOH·HCl, py, EtOH, reflux, 2 h	72%

When α,β-unsaturated ester **128** was reacted with *N*-methylhydroxylamine hydrochloride and sodium hydrogen carbonate, no desired INAC cycloadduct formed, with a mixture of products in which none of them could be purely isolated (entry 1). This result was in contrast to the INAC reaction of lactol **19**, the enantiomer of **126**, which was able to furnish the INAC cycloadduct in an excellent yield (Scheme 45).[13]



19 **20**

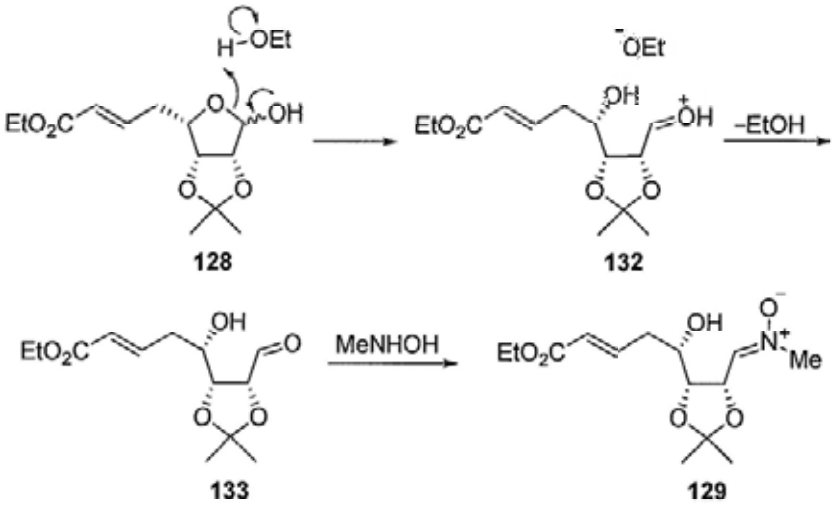
Scheme 45

The same reaction conditions were then repeated on the α,β-unsaturated ester **128** as shown in entry 2. However, decomposition of **128** occurred after prolonged heating instead of yielding any INAC cycloadduct. Actually the only difference in structure between lactol **19** and α,β-unsaturated ester **128** is the alkene moiety, with lactol **19** bearing a terminal alkene and the α,β-unsaturated ester **128** having an ethyl carboxylate substituted alkene. Thus the difference in reactivity should be due to the presence of α,β-unsaturated ester moiety in **128**, which is more likely to be attached by nucleophiles.

It was suggested that the base ($NaHCO_3$) used in the entries 1 and 2 was too basic, causing 1,4-Michael addition of *N*-methylhydroxylamine to the ester **128** hence did not afford any INAC cycloadduct.

When allowing ester **128** to react with *N*-methylhydroxylamine hydrochloride and pyridine in MeCN and heated under reflux (entry 3), the INAC *exo*-cycloadduct **130** was formed as the only product (Scheme 44). Changing the reaction solvent for INAC reaction did not encourage the formation of any desired *endo*-cycloadduct, even though some improvements of reaction yields (*exo*-cycloadduct) were observed (entries 4 and 5).

It should be noted that using EtOH as reaction solvent allowed the formation of the INAC cycloadduct **130** in much shorter time (entry 5). It is probably due to the protic nature of EtOH, which facilitated the opening of lactol **128** into its aldehyde form **133**. Aldehyde **133** then reacted with *N*-methylhydroxylamine to give nitrone **129** (Scheme 46). Whereas in aprotic solvents like CH_2Cl_2 and MeCN such the lactol ring opening to free aldehyde **133** was not facilitated, resulting in a longer reaction time (entries 3 and 4).



Scheme 46

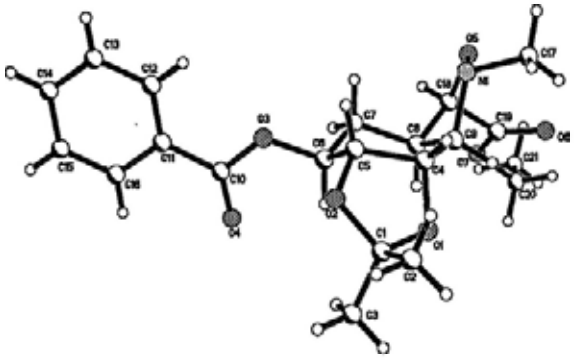
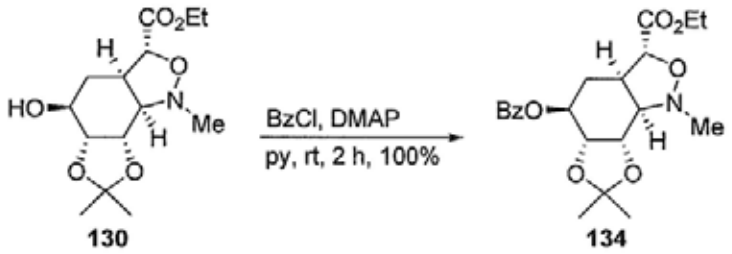


Figure 15. X-ray crystallographic structure of benzoate **134**.

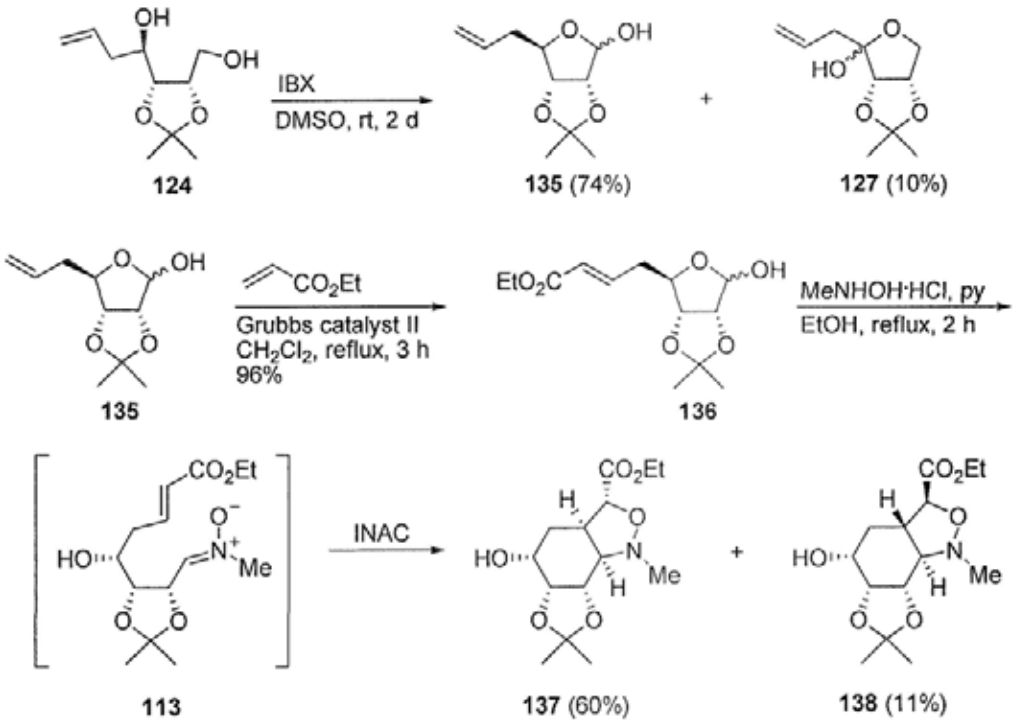
Although the ring size of this cycloadduct could not be convincingly confirmed by ^{13}C DEPT NMR, both the regio- and stereochemistry of cycloadduct **130** were assigned by X-ray crystallographic analysis of its benzoate **134** (Figure 15), formed in quantitative yield by reacting cycloadduct **130** with benzoyl chloride (Scheme 47).



Scheme 47

From the X-ray crystallographic structure of benzoate **134** (Figure 15), it clearly shows that a 6-membered *exo*-cycloadduct was formed. That is, the α,β-unsaturated ester moiety in nitrone **129** cannot direct the *endo*-mode INAC reaction, by means of electronic effect.

Then the INAC of nitrone **113**, which is the 4-epimer of nitrone **129**, was also studied (Scheme 48). Following the same strategy as described previously, alkene **124** was subjected to selective IBX oxidation, giving lactol **135** as the major product. Lactol **135** was then reacted with ethyl acrylate in the presence of second generation Grubbs catalyst to give *trans*-α,β-unsaturated ester **136** in an excellent yield. The nitrone **113** was formed by reacting the α,β-unsaturated ester **136** with *N*-methylhydroxylamine hydrochloride and pyridine under boiling EtOH, and cyclized to give two INAC *exo*-cycloadducts, isoxazolidines **137** and **138**.



Scheme 48

The regio- and stereochemistry of the minor cycloadduct **138** was confirmed by X-ray crystallography (Figure 16).

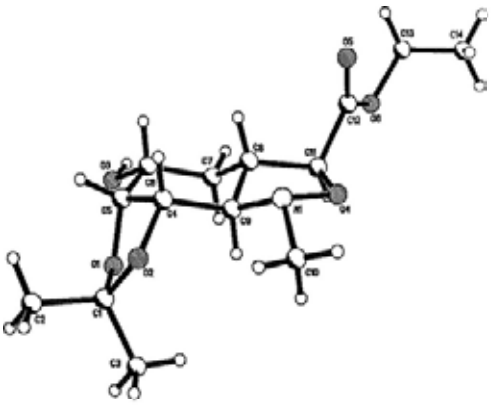
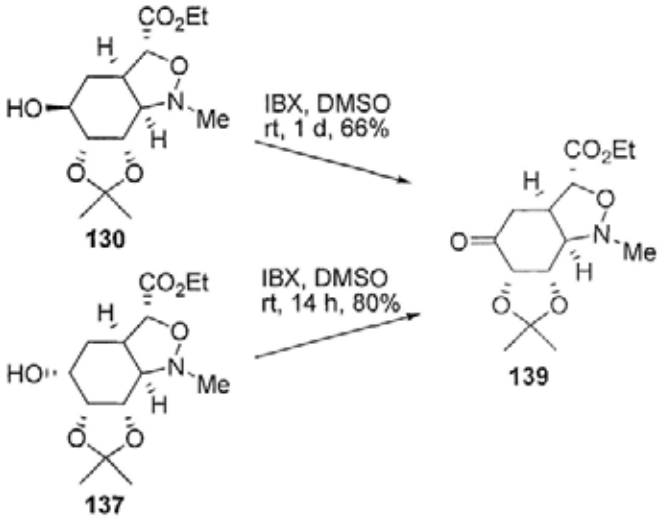


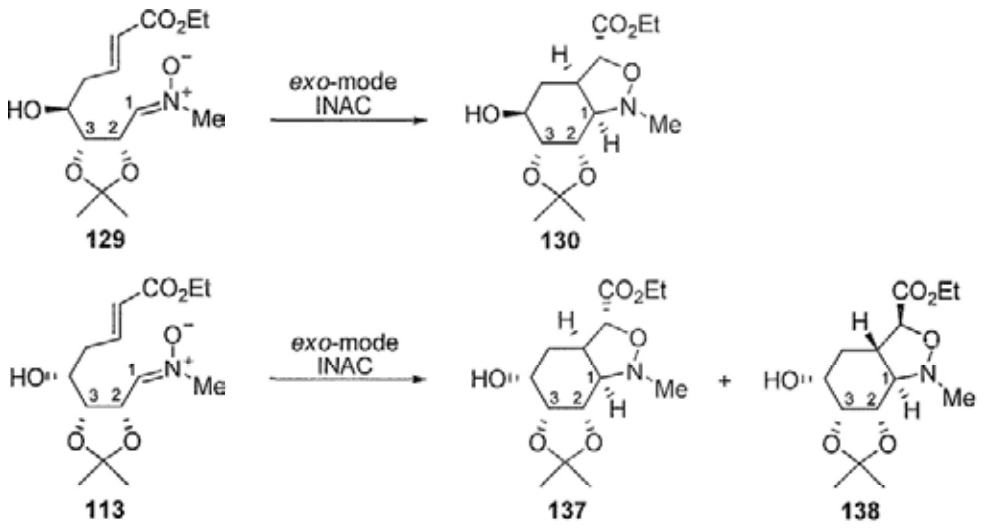
Figure 16. X-ray crystallographic structure of isoxazolidine **138**.

The ring size and stereochemistry of the other cycloadduct, isoxazolidine **137**, formed in this INAC reaction, was assigned as follows. Both isoxazolidines **130** and **137** were able to afford the identical ketone **139** by IBX oxidation (Scheme 49).



Scheme 49

To summarize this section, the INAC reactions of both nitrone **113** and **129** resulted exclusive formation of *exo*-cycloadducts (Scheme 50). No desired *endo*-cycloadduct was formed with α,β-unsaturated ester moiety as the dipolarophile in the presence of a 2,3-*cis*-isopropylidene blocking group.



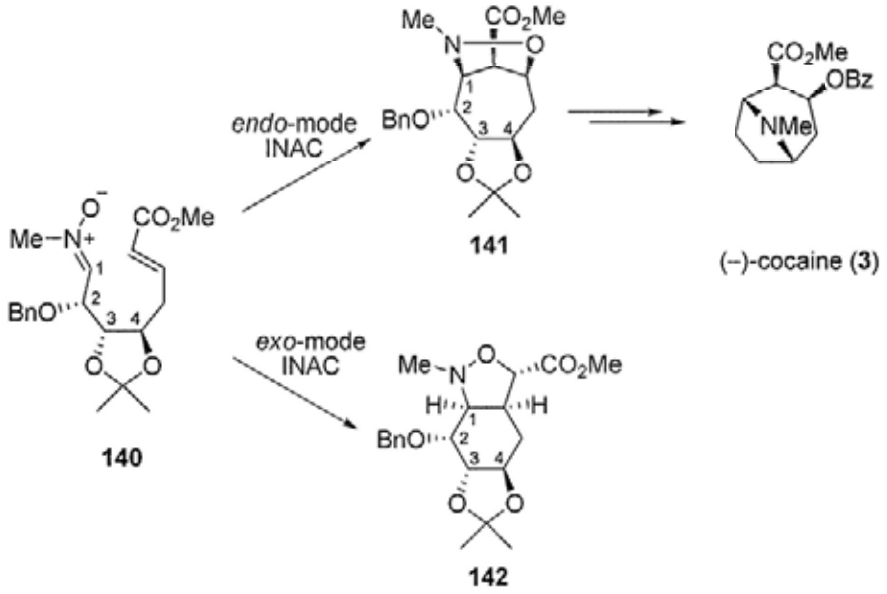
Scheme 50

Since these 6-membered carbocycles are not useful for cocaine synthesis, another synthetic strategy towards cocaine was developed and is to be discussed in the next section.

2.2.2.2 INAC of Nitrone with a 3,4-*trans*-Isopropylidene as Blocking Group and an *α,β*-Unsaturated Ester as Dipolarophile

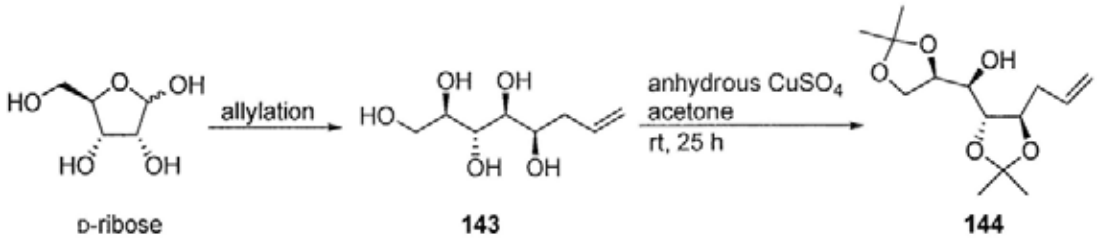
In section 2.2.1 of this thesis, it was concluded that the presence of 3,4-*trans*-pentylidene blocking group in hept-6-enoses can induce exclusive formation of INAC *endo*-cycloadducts. In section 2.2.2.1 it was discovered that using *α,β*-unsaturated ester as the dipolarophile did not cause any *endo*-cycloadduct formation during INAC of nitrone bearing a 2,3-*cis*-isopropylidene moiety. In order to obtain the desired 7-membered *endo*-cycloadduct, which is the synthetic precursor of cocaine and its

analogues, INAC of the nitrone **140**, with a 3,4-*trans*-isopropylidene moiety and an *α,β*-unsaturated ester as dipolarophile, was studied (Scheme 51).



Scheme 51

The diacetonide **144** was prepared from D-ribose through two synthetic steps, firstly aqueous allylation of D-ribose afforded alkene **143**,[84] which was followed by isopropylidenation of the crude alkene **143** (Scheme 52). The allylation conditions performed are listed in Table 3.

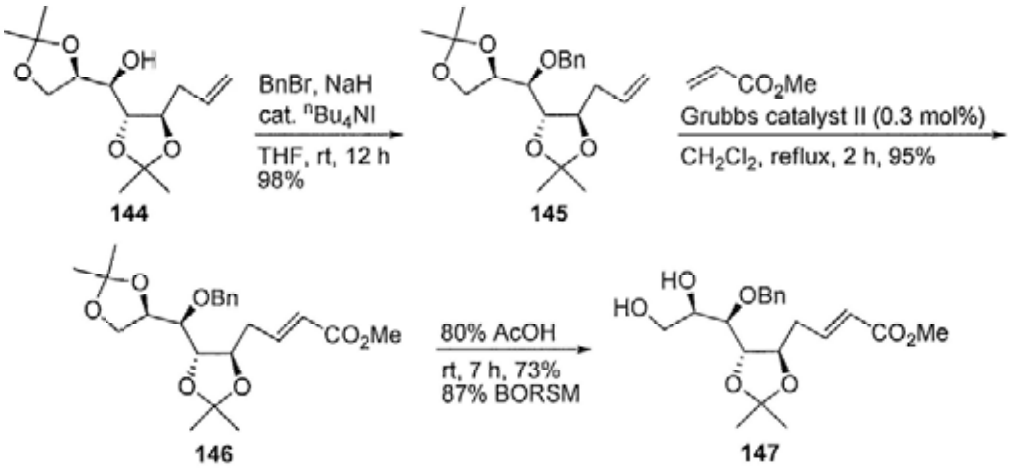


Scheme 52

Table 3. Sequential allylation and isopropylidenation of D-ribose.

Entry	Allylation Conditions	Overall Yield of **144** from D-ribose
1	In, allyl bromide, EtOH/H_2O (v/v=4:1), rt, 12 h	64%
2	Sn, allyl bromide, EtOH/H_2O (v/v=4:1), reflux, 2 h	50%

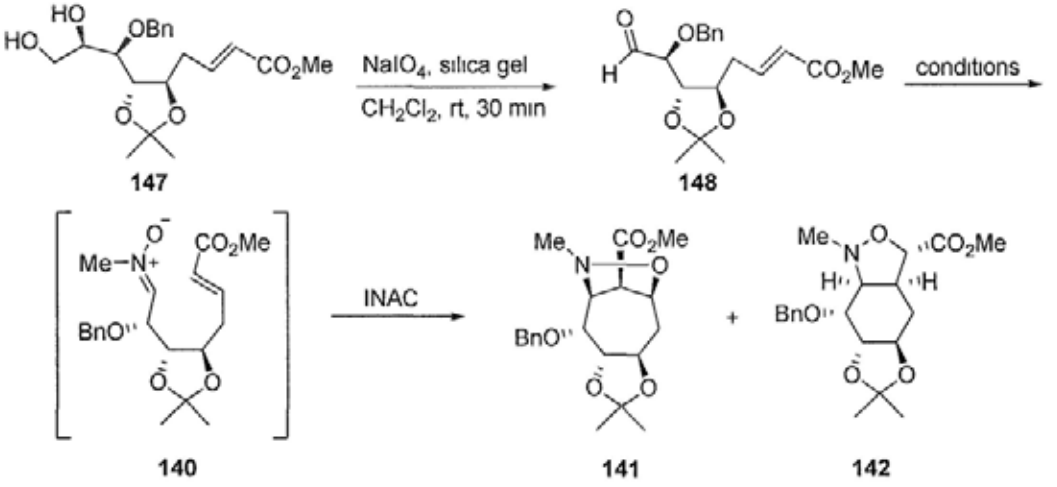
Indium metal is able to perform allylation of D-ribose smoothly at room temperature, giving alkene **143** (entry 1). Subsequence isopropylidenation furnished alkene **144** in a good overall yield from D-ribose. When indium was replaced by tin, which is a more economical reagent, no allylation occurred unless the reaction was heated, and afforded a moderate yield of **144** finally (entry 2).



Scheme 53

Benzylation of alcohol **144** with sodium hydride and benzyl bromide gave benzyl ether **145** in an excellent yield (Scheme 53).[14] Cross metathesis of benzyl ether **145** with methyl acrylate catalyzed by a trace amount (0.3 mol%) of the second generation Grubbs catalyst afforded α,β-unsaturated ester **146** in 95% yield. The large coupling constant (J = 15.7 Hz) of the two alkene signals (δ 5.86 and 5.96 ppm) in ^{1}H NMR confirmed that a *trans*-alkene was formed. The α,β-unsaturated ester **146** was then

subjected to regioselective acid hydrolysis to give 1,2-diol **147** in 87% yield based on starting material recovery.



Scheme 54

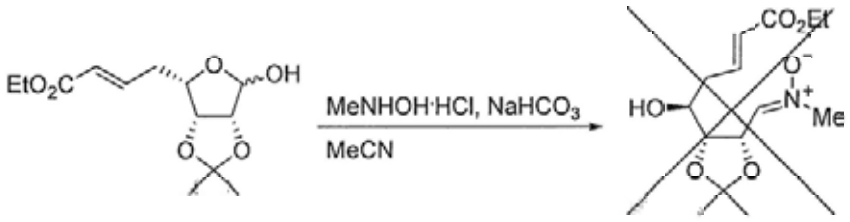
With the diol **147** in hand, silica gel mediated glycol cleavage oxidation furnished aldehyde **148** (Scheme 54). The aldehyde **148** was then subjected to several conditions to afford nitrone **140** that carried out the INAC reaction (Table 4).

Table 4. Reaction conditions between aldehyde **148** and *N*-methylhydroxylamine.

Entry	Conditions	Yield of **141**/**142** from **147**	**141**:**142** by NMR
1	MeNHOH·HCl, $NaHCO_3$, MeCN, reflux, 4 h	70%	8:1
2	MeNHOH·HCl, $NaHCO_3$, MeOH, rt to reflux	decomposed	–
3	1) MeNHOH·HCl, $NaHCO_3$, MeCN, rt, 30 min 2) MeOH, reflux, 29 h	63%	14:1
4	1) MeNHOH·HCl, $NaHCO_3$, MeCN, rt, 30 min 2) CH_2Cl_2, reflux, 72 h	62%	10:1
5	MeNHOH·HCl, $NaHCO_3$, DMF, reflux, 1 h	64%	13:1
6	MeNHOH·HCl, py, toluene, reflux, 2 h	72%	14:1
7	MeNHOH·HCl, Et_3N, toluene, reflux, 2 h	75%	15:1

When using MeCN as solvent, reaction between aldehyde **148** and *N*-methylhydroxylamine with $NaHCO_3$ as base afforded nitrone **140** as shown in the TLC (entry 1). Without isolating the nitrone, the reaction mixture was heated to reflux and furnishing an inseparable mixture of two INAC cycloadducts. The major cycloadduct was found to be a 7-membered *endo*-cycloadduct **141**, with 6-membered *exo*-cycloadduct **142** as the minor product (Scheme 54). Their ratio was determined by measuring the integration of the individual *N*-methyl group in the ^1H NMR spectrum of the mixture of cycloadducts. Although in this stage the mixture of isoxazolidines **141** and **142** could neither be separated nor their regiochemistry be characterized, these two cycloadducts were separated in the following step and their regiochemistry was confirmed, as described later.

It should be noted that the reaction conditions in entry 1 is actually identical with the INAC reaction conditions of α,β-unsaturated ester **128** as mentioned in the last section, where no nitrone **129** was formed under the conditions (Scheme 55).



128 **129**

Scheme 55

However, INAC of aldehyde **148** in such conditions did give nitrone **140** which cyclized to INAC cycloadducts **141/142** (Scheme 54). The difference in reactivity

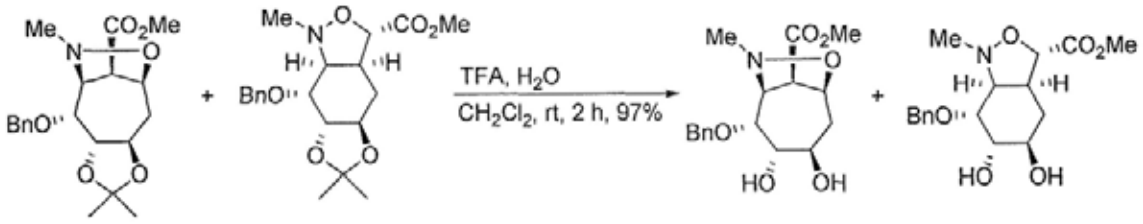
between lactol **128** and aldehyde **148** under the same reaction conditions is probably due to the **128** exists in lactol form, which makes condensation to MeNHOH more difficult hence nucleophilic MeNHOH may attack on the α,β-unsaturated ester moiety instead. On the other hand, aldehyde **148** exists as the free aldehyde form and hence it is more likely to condense with MeNHOH to give the nitrone **140**.

In order to study the solvent effect on the regioselectivity of INAC of nitrone **140**, solvents other than MeCN were used as well (entries 2–7). The reaction between aldehyde **148** and *N*-methylhydroxylamine with $NaHCO_3$ as base in MeOH did not furnish complete conversion into nitrone **140** at room temperature and decomposed upon heating (entry 2). It was suggested that the mixture of MeOH and $NaHCO_3$ produced a trace amount of the strongly basic methoxide anion that destroyed the α,β-unsaturated ester moiety, resulting in no INAC reaction.

Using the conditions as shown in entry 3 instead, INAC reaction of nitrone **140** in boiling MeOH occurred, resulting higher *endo*/*exo* ratio (**141**:**142** = 14:1) although a longer reaction time was needed and a lower reaction yield was afforded. When CH_2Cl_2 and DMF were used as INAC reaction solvents (entries 4 and 5), also higher *endo*/*exo* ratios were observed than using MeCN.

It was also found that mixing aldehyde **148** with either pyridine or triethylamine in boiling toluene also allowed the formation of INAC cycloadducts in a short reaction time with higher *endo*/*exo* selectivity (entries 6 and 7). Thus the conditions in entry 7 was considered as the most efficient approach towards the desired *endo*-cycloadduct **141**.

When this inseparable mixture of isoxazolidines **141** and **142** was subjected to hydrolysis by trifluoroacetic acid, diols **149** and **150** were formed and now they could be separated by column chromatography (Scheme 56).



141 (8 : 1) **142**

149 (86%) **150** (11%)

Scheme 56

The diol **149** was isolated and its structure was confirmed by X-ray crystallography (Figure 17), which in turns confirmed the regio- and stereochemistry of the *endo*-cycloadduct **141**.

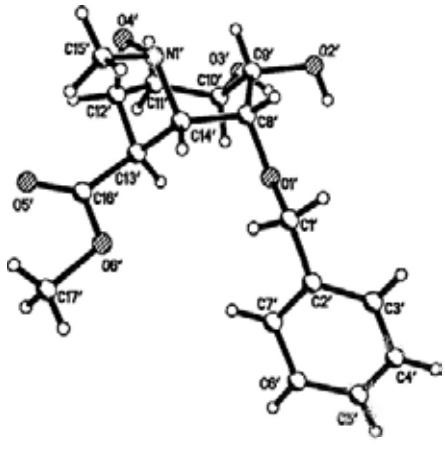


Figure 17. X-ray crystallographic structure of diol **149**.

Although diol **150** is not a solid at room temperature and pressure, it crystallized in a hydrated form hence its structure can also be confirmed (Figure 18).

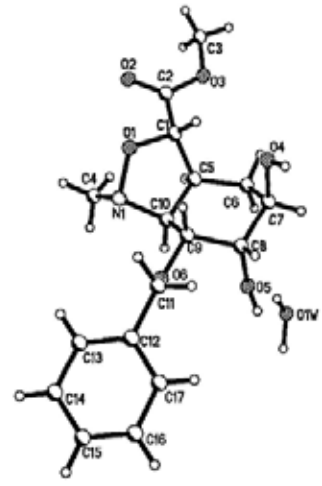
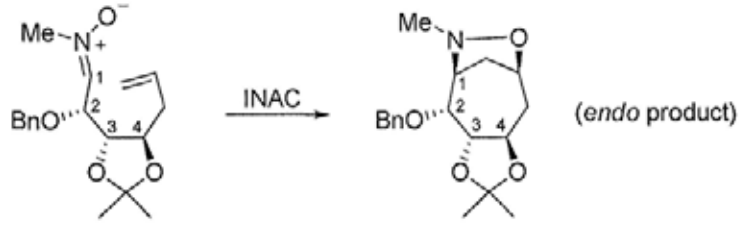


Figure 18. X-ray crystallographic structure of hydrated diol **150.**

Thus it was concluded that INAC reaction nitrone **140** gave 7-membered *endo*-cycloadduct **141** as the major product, with a small amount of 6-membered *exo*-cycloadduct **142**. This result was in contrast to the INAC reaction of nitrone **151**, which gave exclusive formation of *endo*-cycloadduct **152** (Scheme 57).[14]



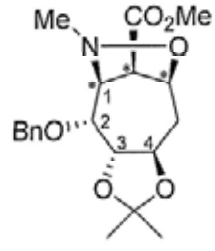
151 **152** (97%)

Scheme 57

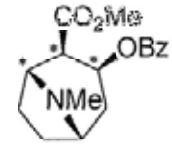
Both nitrones **140** and **151** bearing the same 3,4-*trans*-isopropylidene moiety, but nitrone **140**, with an α,β-unsaturated ester as the dipolarophile, yielded a small amount of *exo*-cycloadduct upon INAC reaction. Thus adding a carboxylate ester moiety into the terminal alkene did not induce the formation of *endo*-cycloadduct by electronic effect, but favoured more *exo*-cycloadduct formation instead. The reason may be due to the somewhat bulky carboxylate ester moiety, preventing the dipolarophile to perform *endo*-cyclization as the carboxylate ester moiety is closer to the isoxazolidine ring in *endo*-cycloadduct. The steric effect of the substituted alkene on the regioselectivity of INAC reaction was not further studied and the aim of this project, that is the synthetic studies of cocaine and its analogues, was focused again.

2.2.2.3 Transformation of Isoxazolidine 141 into (−)-Cocaine (3) and Cocaine Analogues

The INAC reaction of nitrone **140** gave preponderantly isoxazolidine **141**. Through this reaction, three new stereocenters were formed, and all of them have the correct stereochemistry when compared to the natural (−)-cocaine (**3**) (Figure 19).



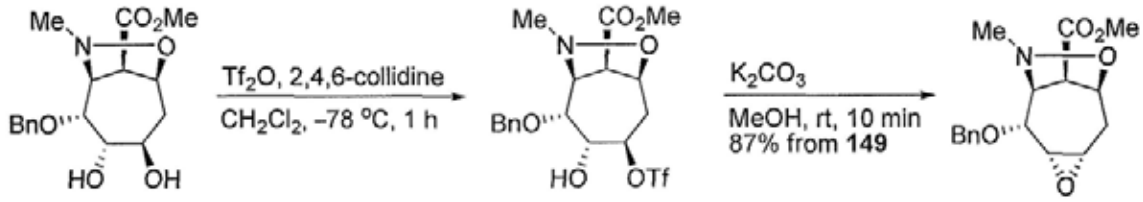
141



(−)-cocaine (**3**)

Figure 19

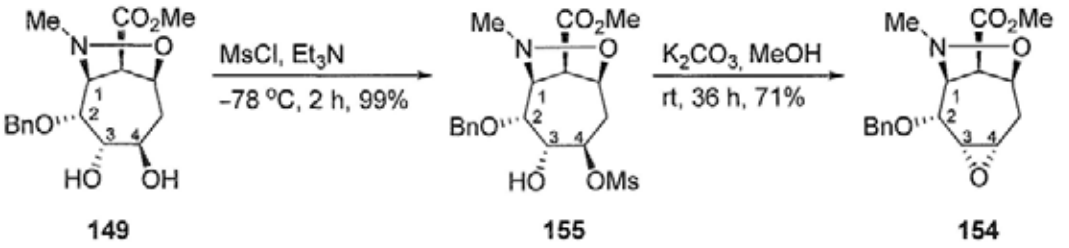
In order to construct the tropane skeleton for cocaine synthesis, the C-4 hydroxyl group in **141** would be converted into a leaving group like a sulfonate ester. Hydrogenolysis of nitrogen-oxygen bond would give an amino function that could undergo intramolecular S_N2 displacement to form the tropane skeleton. However, it was noted that the stereochemistry of C-4 hydroxyl group in **141** is *syn* to the C-1, causing the corresponding sulfonate would also be *syn* to C-1, which would make intramolecular S_N2 displacement not feasible. Thus isoxazolidine **141** should be transformed into tropane skeleton by another strategy.



149 **153** **154**

Scheme 58

The diol **149**, which was obtained from isoxazolidine **141** as described in the previous section, was converted into the corresponding monotriflate **153** by reacting with trifluoromethanesulfonic anhydride and 2,4,6-collidine under low temperature (Scheme 58). The triflate **153** isolated was found to be unstable upon prolonged standing at room temperature, hence it was subjected to the next synthetic step once formed. Reacting triflate **153** with potassium carbonate in MeOH at room temperature allowed the formation of epoxide **154** in 87% overall yield from diol **149**.

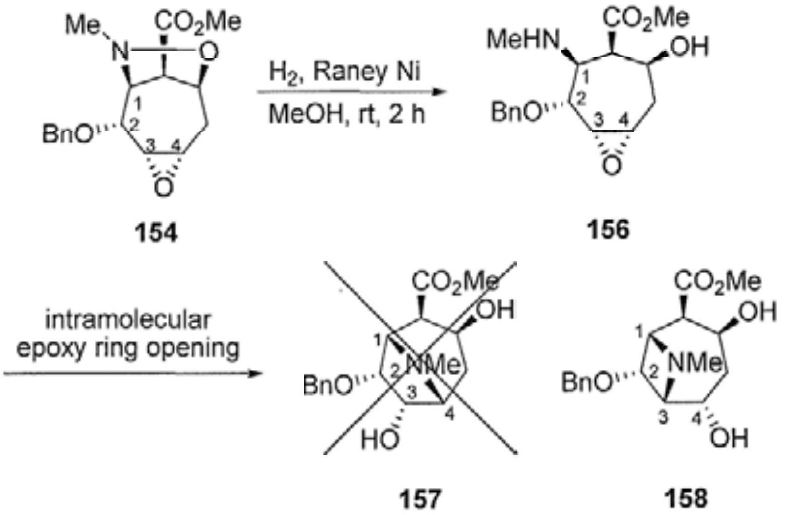


149 155 154

Scheme 59

The epoxide **154** could also be synthesized by another method (Scheme 59). Selective mesylation of diol **149** furnished mesylate **155** in an excellent yield, the mesylate **155** was then reacted with potassium carbonate in MeOH to afford the same epoxide **154**. However, the overall yield of epoxide **154** from diol **149** is lower using this strategy hence the previous triflate strategy is considered to be more efficient.

It should be noted that after converting diol **149** into the corresponding epoxide **154**, the C-4 stereochemistry was inverted, which is *anti* to the C-1 so that intramolecular S_N2 displacement to form the tropane skeleton became possible.



154 156 157 158

Scheme 60

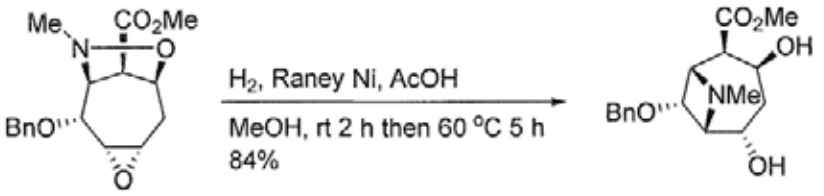
It was attempted to transform epoxide **154** into the corresponding tropane **157** by first hydrogenolysis of nitrogen-oxygen bond to obtain amine **156**, which was followed by intramolecular epoxy ring opening reaction by the amino function (Scheme 60). Thus the epoxide **154** was subjected to Raney®-Nickel hydrogenolysis to furnish amine **156**. However, when amine **156** was attempted to be characterized by ^{1}H NMR, the presence of another product was observed and the amount of this product was found to increase with time at room temperature. After 21 days at room temperature, all amine **156** was found to be consumed (Table 5, entry 1), but no desired tropane **157** was formed. Instead the diol **158**, formed by the amino function in **156** attacking on the C-3 position, was obtained. Other intramolecular epoxy ring opening conditions are shown in the Table 5 as well.

Table 5. Intramolecular epoxy ring opening conditions of amine **156**.

Entry	Conditions	Yield of **158** from **154**
1	neat, rt, 21 d	60%
2	neat, 70 °C, 29 h	88%
3	CH_2Cl_2, reflux	no reaction
4	toluene, 90 °C	no reaction
5	AcOH, MeOH, reflux, 4 h	88%

Since it was found that the neat amine **156** could be transformed into diol **158** under solvent free conditions at room temperature (entry 1), elevation of reaction temperature furnished diol **158** in 88% overall yield from epoxide **154** (entry 2). However, when amine **156** was heated in the presence of solvents like CH_2Cl_2 and toluene, no reaction resulted (entries 3 and 4), probably due to the aprotic nature of such

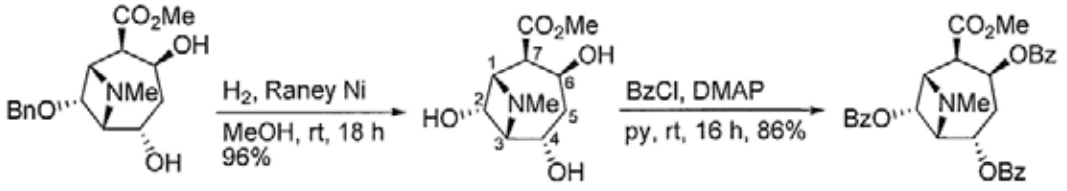
solvents that disfavoured epoxy ring opening to afford diol **158**. Thus protic solvent like MeOH was then used, in addition to a catalytic amount of acetic acid, which also gave diol **158** in 88% overall yield (entry 5).



154 **158**

Scheme 61

Actually this diol **158** could be prepared from epoxide **154** in one step. Hydrogenolysis of epoxide **154** catalyzed by Raney®-Nickel at room temperature, after all starting material epoxide **154** was consumed, the reaction mixture was heated up to 60 °C for 5 more hours to furnish diol **158** (Scheme 61). As the reaction yield is still comparable to the previous two-step synthesis (Scheme 60) hence this one-step synthesis (Scheme 61) is a more efficient approach.

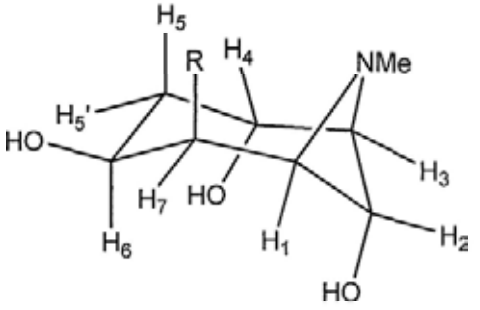


158 **159** **160**

Scheme 62

The benzyl ether **158** was then subjected to hydrogenolysis with a stoichiometric amount of Raney®-Nickel to give triol **159** (Scheme 62). If Raney®-Nickel was added in a catalytic amount, the reaction was sluggish and the starting material **158** was not

completely consumed. After analyzing the ^{1}H NMR and 2D COSY NMR spectra of triol **159**, the proton's assignment was supported by the ^{1}H-^{1}H connectivities (Figure 20). The three most downfield proton signals (δ 5.15, 4.53, and 4.10 ppm) were assigned as H_2, H_6, and H_4 respectively as the C-2, C-6, and C-4 are bonded to oxygen atoms, whereas two more upfield proton signals (δ 4.00 and 3.41 ppm) were assigned as H_1 and H_3 respectively as the C-1 and C-3 are bonded to nitrogen atoms. H_2 is correlated to both H_1 and H_3 and this evidence indicated that the triol **159** and hence diol **158** consist of a bicyclo[4.1.1] skeleton instead of a tropane skeleton.



$J_{1,2}$ = 8.4 Hz
$J_{2,3}$ = 7.6 Hz
$J_{3,4}$ = 3.0 Hz
$J_{4,5}$ = $J_{4,5'}$ = 8.4 Hz
$J_{6,7}$ = 3.4 Hz

Figure 20. Conformation of triol **159**.

The presence of such bicyclo[4.1.1] skeleton in diol **158** and triol **159** was confirmed by X-ray crystallographic analysis of tribenzoate **160** (Figure 21), which was formed by benzoylation of triol **159** (Scheme 62). It means that no tropane ring was formed by intramolecular epoxy ring opening reaction of amine **156**.

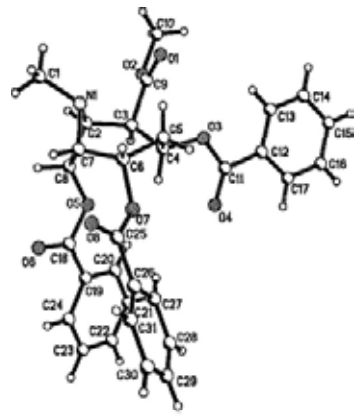
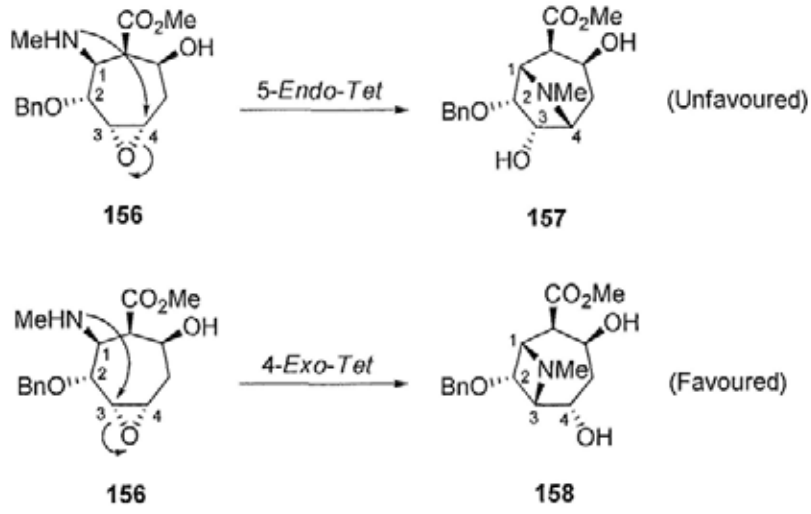


Figure 21. X-ray crystallographic structure of tribenzoate **160**.

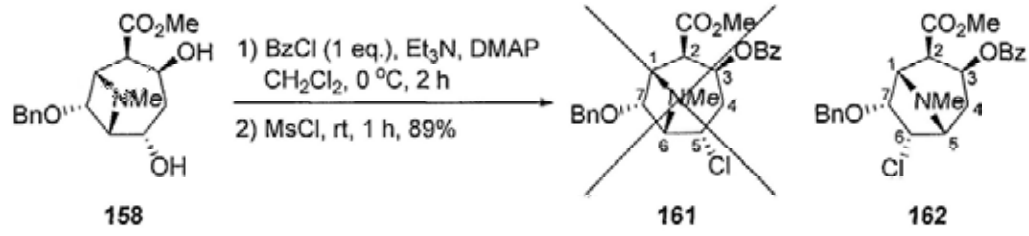
The formation of the bicyclo[4.1.1] skeleton instead of the tropane ring after intramolecular epoxy ring opening reaction of amine **156** can be explained by Baldwin's rule.[85] When amine **156** was carry out intramolecular epoxy ring opening reaction, the amino function could attack either C-3 or C-4 position of the epoxy moiety (Scheme 63).



Scheme 63

When the amino function attacked the C-4 position of the epoxy moiety, a tropane skeleton would be formed through the 5-*Endo-Tet* cyclization, which is an unfavoured process according to Baldwin's rule (Scheme 63). If the amino function attacked the C-3 position of the epoxy moiety instead, a bicyclo[4.1.1] skeleton would be formed through the 4-*Exo-Tet* cyclization, a favoured process according to Baldwin's rule, hence the diol **158** instead of tropane **157** was formed.

As the diol **158** does not consist of a tropane skeleton, it seems that the desired cocaine cannot be synthesized by this strategy. However, when diol **158** was first benzoylated with one equivalent of benzoyl chloride, followed by the addition of methanesulfonyl chloride, chloride **162** was obtained in an excellent yield (Scheme 64).



158 **161** **162**

Scheme 64

The presence of a chlorine atom in chloride **162** was confirmed by mass spectrometry, in which the intensity of $M + 2$ peak is one-third of the molecular ion (M) peak. The existence of a tropane skeleton in chloride **162** was assigned by determining the ^{1}H-^{1}H connectivities from the 2D COSY NMR (Figure 22). It should be noted that a strong correlation between H_6 and H_7 was found, which belonged to the methine proton next to chloride group and benzyloxy moiety respectively (Figure 22). If the product existed as a bicyclo[4.1.1] skeleton as shown in the chloride **161** instead (Scheme 64),

no such strong correlation between these two proton signals (between H_5 and H_7 in this case) should be found in the 2D COSY NMR. Thus the existence of tropane structure in chloride **162** was supported by the presence of correlation between these two proton signals (H_6 and H_7).

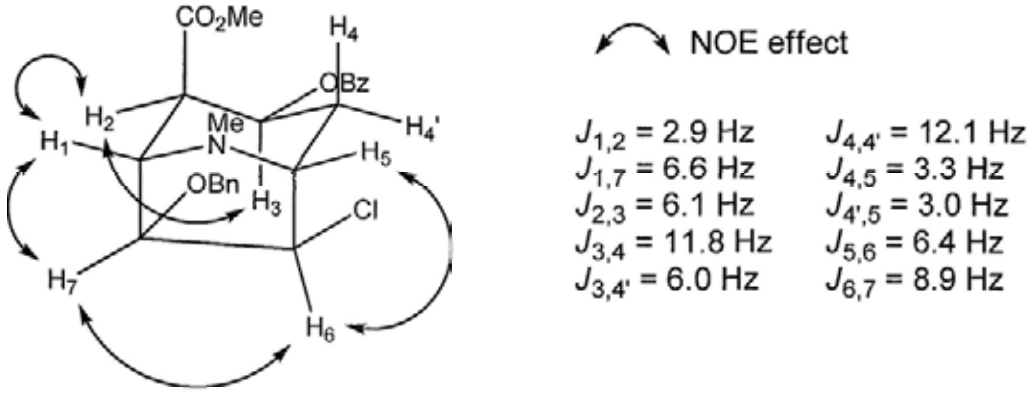
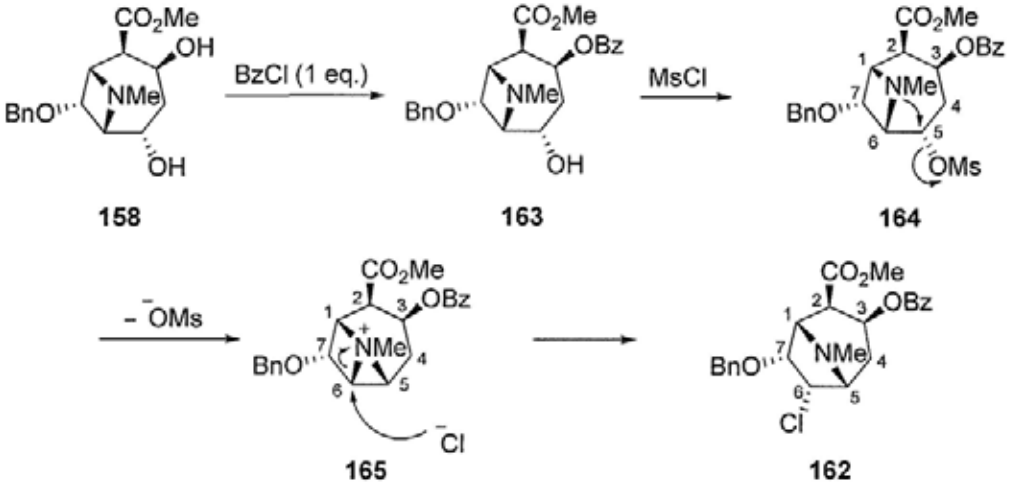


Figure 22. NOE correlations of chloride **162**.

From the 2D NOESY NMR spectrum of chloride **162**, there was NOE correlation between H_6 and H_7, showing that the chloride function is *syn* to the benzyl group in **162** (Figure 22). Since the α-stereochemistry of the benzyl group was already confirmed by X-ray crystallographic analysis of both diol **149** and benzoate **160**, the chloride function in **162** should also have the α-stereochemistry, as shown in Figure 22.

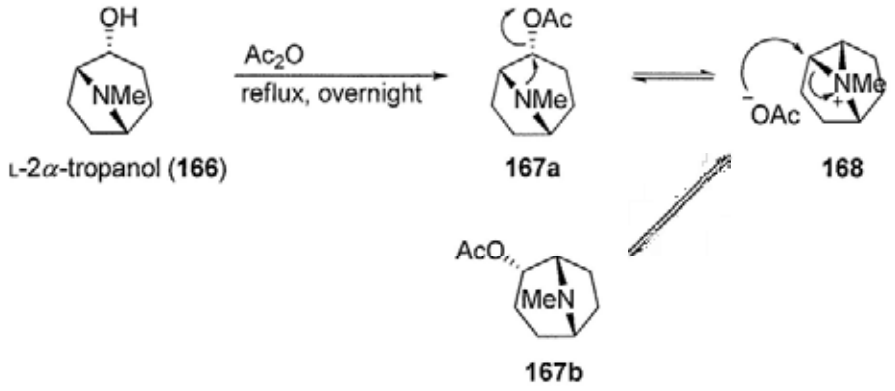
The formation of chloride **162** from diol **158** in Scheme 64 can be explained as follows. First, the regioselective esterification of diol **158** with one equivalent of benzoyl chloride afforded monobenzoate **163** (Scheme 65). Then, the addition of methanesulfonyl chloride to the reaction mixture produced mesylate **164**, in which the mesylate moiety is now *anti* to the adjacent aza-bridge. Due to this neighboring-group participation, the mesylate **164** would dissociate easily to give ammonium ion **165**.

Then the nucleophilic chloride ion attacked the α-face of C-6 position in **165** to furnish α-chloride **162**.



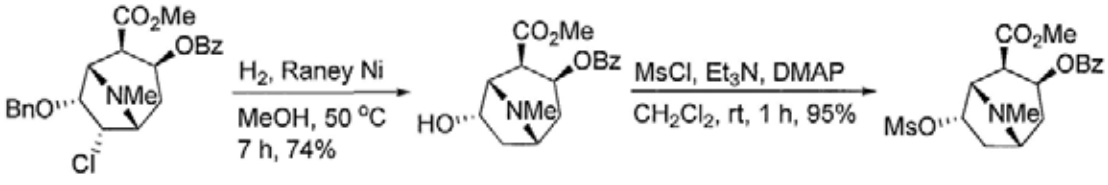
Scheme 65

The release of ring strain from bicyclo[4.1.1] skeleton to tropane ring is probably the driving force of C-6 attack instead of C-5. The formation of ammonium ion **165** is the result of neighboring-group participation, and the existence of this ammonium ion **165** was supported by a similar example reported by Archer *et al.* Racemic acetates **167a/167b** were obtained via ammonium ion **168** upon acetylation of L-2α-tropanol (**166**) under prolonged heating in acetic anhydride (Scheme 66).[86]



Scheme 66

The chloride **162** obtained is actually one of the (−)-cocaine analogue, with a chloride in C-6 position and a benzyloxy moiety in C-7 position. Thus natural (−)-cocaine (**3**) could be obtained easily by simply eliminating both the chloride and benzyloxy moieties in **162**. When chloride **162** was subjected to hydrogenolysis in the presence of a stoichiometric amount of Raney®-Nickel at 50 °C, alcohol **169** was afforded in 74% yield (Scheme 67).



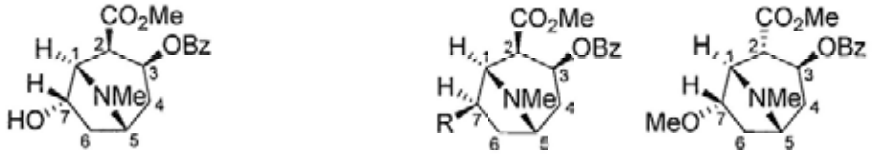
162 **169** **170**

Scheme 67

Both the benzyl group and the chloride moiety were removed during this reaction. It should be noted that if Raney®-Nickel was added in a catalytic amount, the reaction was sluggish and even the starting material chloride **162** was not be completely consumed.

This alcohol **169** is another (−)-cocaine analogue, with α-hydroxyl group in the C-7 position, which is the 7-epimer of a cocaine analogue **61b** reported by Kozikowski and co-workers[59] (Figure 23). According to Kozikowski's publication, there is no coupling between H-1 and H-7 from their ^{1}H NMR spectra when the H-7 is in the α-stereochemistry.[58,59] They also observed that there is a coupling ($J_{1,7}$ = 6.0 Hz) between

H-1 and H-7 in the ^{1}H NMR spectrum of the pseudococaine analogue **171**, in which the H-7 has the β-stereochemistry (Figure 23).[58]



169 $J_{1,7}$ = 6.4 Hz

58b: R = OMe
61b: R = OH
$J_{1,7}$ = 0 Hz

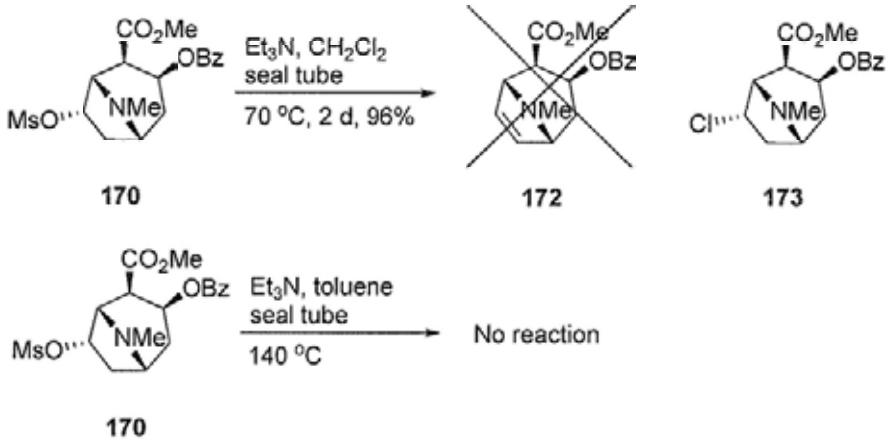
171 $J_{1,7}$ = 6.0 Hz

(Synthesized by Kozikowski *et al.*)

Figure 23

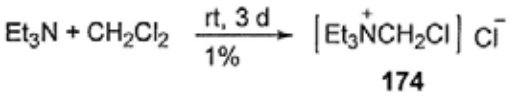
In the ^{1}H NMR spectrum of alcohol **169**, it was found that there is also a coupling ($J_{1,7}$ = 6.4 Hz) between H-1 and H-7 hence confirmed the β-stereochemistry of the H-7 (Figure 23). More importantly, the stereochemistry of H-7 in other cocaine analogues can also be assigned by analyzing their ^{1}H NMR spectra.

The alcohol **169** was then subjected to mesylation to give mesylate **170** in an excellent yield (Scheme 67). It was attempted to afford alkene **172** by performing elimination reaction on mesylate **170** (Scheme 68). However, no alkene **172** was found and chloride **173** was obtained instead when mesylate **170** was reacted with triethylamine in CH_2Cl_2 at 70 °C inside a seal tube.



Scheme 68

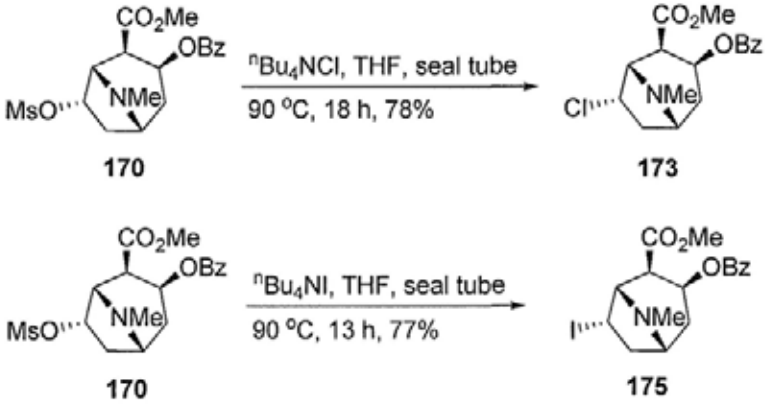
However, when the reaction solvent CH_2Cl_2 was replaced by toluene, no reaction was observed even the reaction was heated at higher temperature (Scheme 68). It seems that CH_2Cl_2 itself may be also one of the reagents in this reaction. After searching for examples from literature it was found that chloromethyltriethylammonium chloride (**174**) would be formed upon mixing triethylamine and CH_2Cl_2 at room temperature (Scheme 69).[87]



Scheme 69

Although the authors did not perform this reaction at higher temperature, they did realize the formation of **174** was inhibited at lower temperature.[87] Thus in the reaction conditions shown in Scheme 68, in which the mixture of triethylamine and CH_2Cl_2 was heated at 70 °C, more ionic salt **174** would probably be formed. As the salt **174** consists of chloride anion, this chloride anion could act as a nucleophile to displace

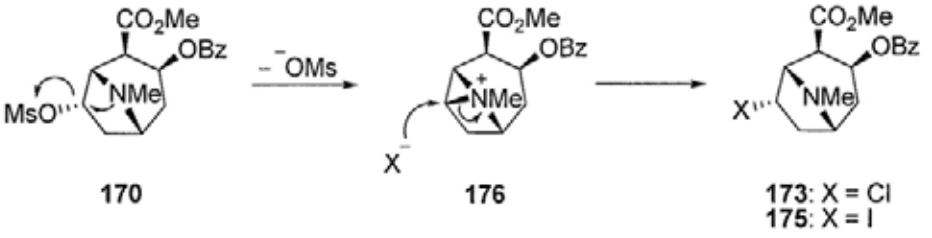
the mesylate moiety in mesylate **170** to give chloride **173**. This formation of chloride **173** from displacement of mesylate by chloride was corroborated by the formation of the same chloride **173** via reaction of mesylate **170** with tetra-*n*-butylammonium chloride (Scheme 70). It showed that the mesylate moiety in **170** was readily displaced by chloride ion.



Scheme 70

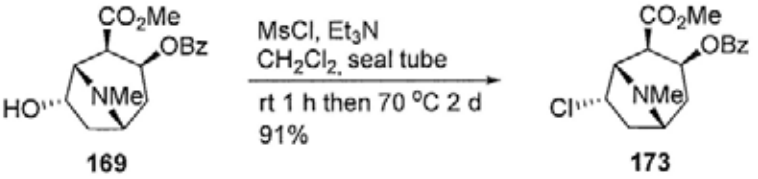
By replacing chloride ion with iodide ion, iodide **175** could be synthesized by reacting mesylate **170** with tetra-*n*-butylammonium iodide (Scheme 70). Thus two more (−)-cocaine analogues, namely 7*α*-chlorococaine (**173**) and 7*α*-iodococaine (**175**), were prepared as well. The presence of a chlorine atom in chloride **173** was confirmed by mass spectrometry, in which the intensity of the $M + 2$ peak is one-third of the molecular ion (M) peak. The presence of iodine atom in iodide was also supported by mass spectrometry. In addition, from the ^{13}C DEPT NMR spectrum of iodide **175**, there is an upfield methine carbon signal (δ 19.0 ppm), which corresponds to the iodo-substituted methine carbon at 7-position.

After analyzing the ^{1}H NMR spectra of chloride **173** and iodide **175**, it was found that both of these two cocaine analogues had coupling ($J_{1,7}$ = 6.4 Hz in chloride **173** and $J_{1,7}$ = 6.1 Hz in iodide **175**) between H-1 and H-7. According to these results, both chloride **173** and iodide **175** were found to be α-substituted. The retention of configuration upon displacement reactions of α-mesylate **170** can be explained by the neighboring-group participation of aza-bridge, which forcing the nucleophile to attack on the α-face of the ammonium ion **176** (Scheme 71).



Scheme 71

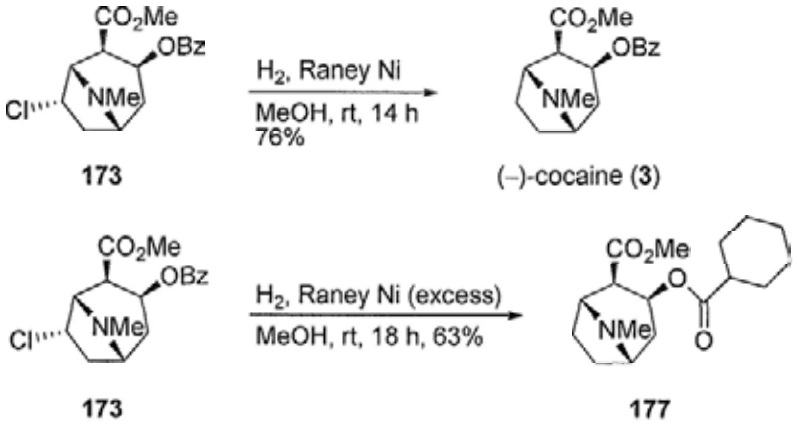
Actually the chloride **173** could be synthesized from alcohol **169** in one step, by the reaction of alcohol **169** with methanesulfonyl chloride and an excess of triethylamine in CH_2Cl_2 at room temperature, followed by heating (Scheme 72).



Scheme 72

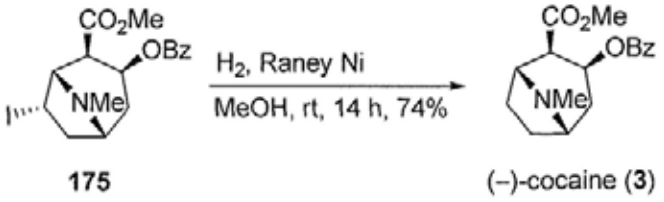
With the chloride **173** in hand, the natural product (−)-cocaine (**3**) can be obtained by simply hydrogenolysis of chloride **173**, with a stoichiometric amount of Raney®-Nickel (Scheme 73). The specific rotation, $[\alpha]_D^{20}$ −16.9 (*c* 0.18, $CHCl_3$) {lit. $[\alpha]_D^{23}$

−16.2 (*c* 1.2, $CHCl_3$)}, and all NMR spectral data of the synthesized (−)-cocaine (**3**) are in good agreement with the literature values.[46]



Scheme 73

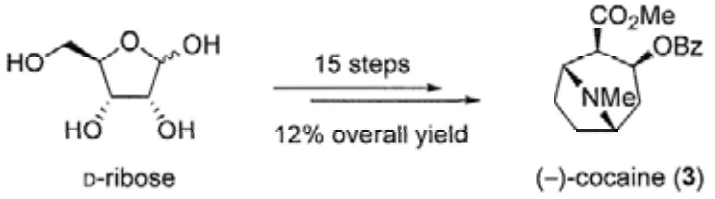
It should be noted that if the amount of Raney®-Nickel used was in highly excess, amine **177** instead of (−)-cocaine (**3**) would be obtained (Scheme 73). Beside the carbon-chlorine bond in chloride **173** was cleaved, the benzoate moiety was also fully hydrogenated as well. Surprisingly this amine **177**, with just replacing the benzoyl group in (−)-cocaine (**3**) with cyclohexanecarbonyl moiety, has not been reported in the literature hence the first synthesis of amine **177** is reported in this thesis.



Scheme 74

The iodide **175** was also transformed into the same (−)-cocaine (**3**) by Raney®-Nickel hydrogenolysis (Scheme 74).

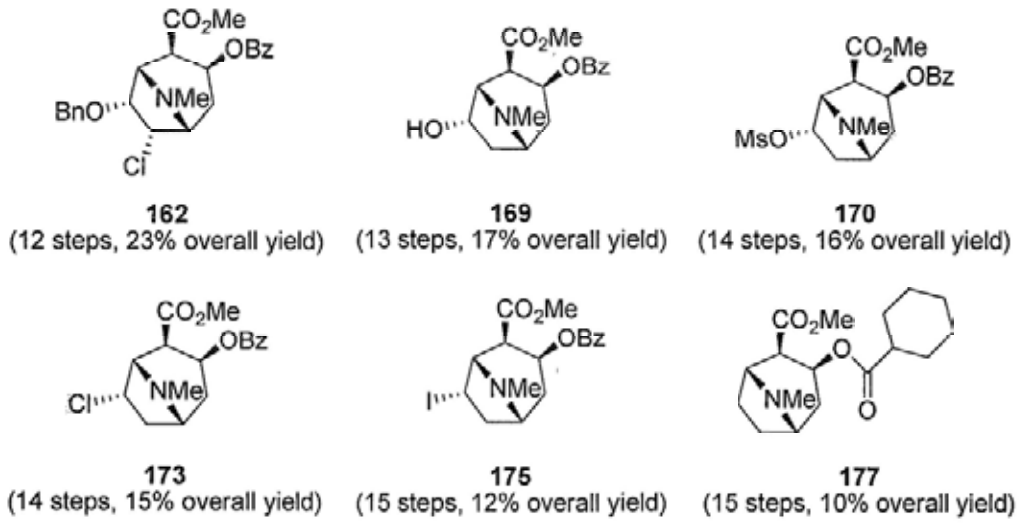
To summarize this section, the natural product (−)-cocaine (**3**) was synthesized from D-ribose via an *endo*-mode INAC reaction as the key step, with 15 steps in 12% overall yield (Scheme 75).



Scheme 75

This synthesis is more efficient than both Rapoport's[46] (21 steps, 5.9% overall yield) and Pearson's[47] (15 steps, 2.2% overall yield) cocaine syntheses. Although this new strategy required three more synthetic steps than the latest Davis' cocaine synthesis (12 steps, 9% overall yield),[48] it produced cocaine in higher overall yield. More importantly, the readily available D-ribose was used as the starting material hence this new synthetic strategy is considered to be more practical.

In addition to the natural product (−)-cocaine (**3**), six more (−)-cocaine analogues were synthesized as well (Figure 24).



162
(12 steps, 23% overall yield)

169
(13 steps, 17% overall yield)

170
(14 steps, 16% overall yield)

173
(14 steps, 15% overall yield)

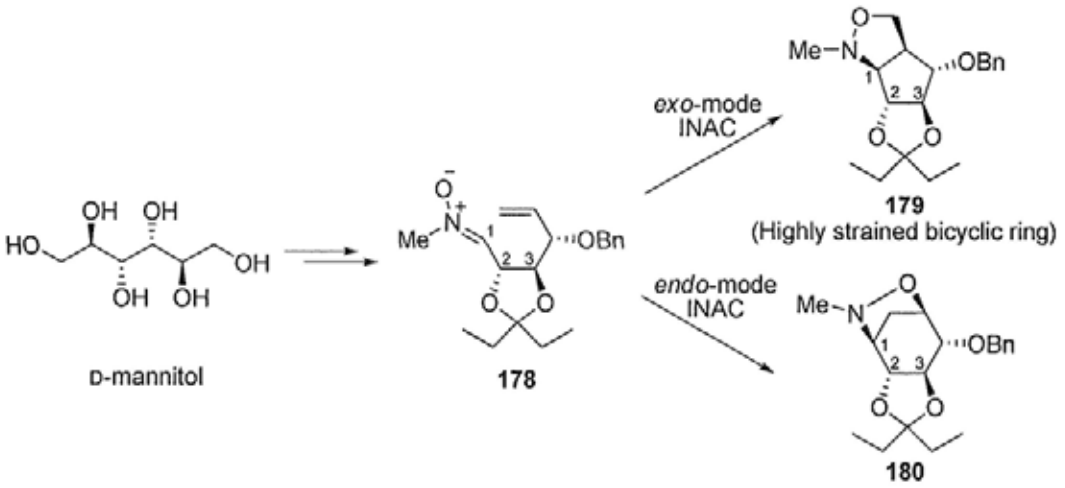
175
(15 steps, 12% overall yield)

177
(15 steps, 10% overall yield)

Figure 24

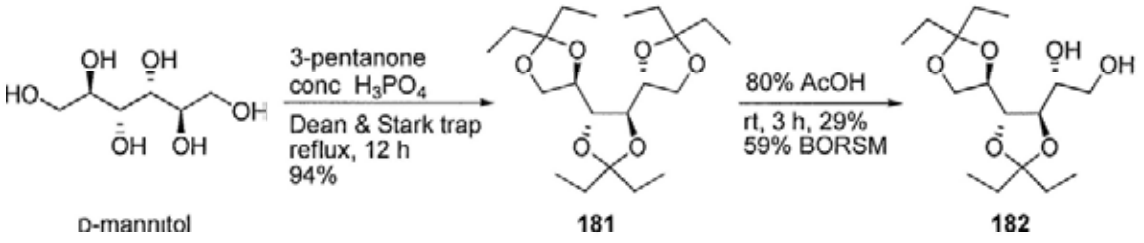
2.2.3 Studies on Regioselectivity of INAC on Hex-5-enoses from D-Mannitol with a 2,3-*trans*-Pentylidene Blocking Group

In this section, regioselectivity of INAC reactions on hex-5-enoses with a 2,3-*trans*-pentylidene moiety are studied (Scheme 76). Due to the severe torsional strain of the 5-5 *trans*-fused bicyclic ring in isoxazolidine **179**, formation of *exo*-cycloadducts from INAC of such hex-5-enoses are not expected to be observed.



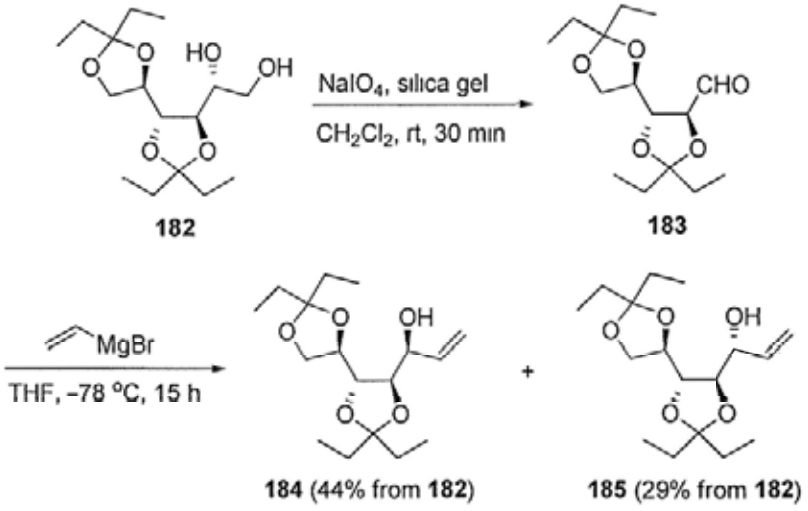
Scheme 76

Using D-mannitol as starting material, all of the hydroxyl groups were protected as pentylidene to afford **181** (Scheme 77). Using Dean and Stark trap allows continuous removal of water from the reaction mixture hence forcing the equilibrium toward the product side, resulting in an excellent yield of **181**.



Scheme 77

The 1,2-diol **182** was then formed by regioselective acid hydrolysis of **181** (Scheme 77). However, it was found that the regioselectivity of this hydrolysis is not good. Over-hydrolysis occurred if the reaction time was too long hence this reaction was stopped after 3 hours and a moderate yield of diol **182** was obtained based on the starting material recovery.



Scheme 78

With the 1,2-diol **182** in hand, it was first subjected to glycol cleavage oxidation to furnish aldehyde **183**, followed by Grignard addition with vinylmagnesium bromide to give alkenes **184** and **185** in ratio of 3:2 (Scheme 78). The configuration of the newly formed stereocenter of alkene **184** was assigned by an X-ray crystallographic analysis of the INAC cycloadduct synthesized later.

The diastereoselectivity of this vinylation can be explained by the chelation controlled transition model shown in Figure 25. As the α-face of **183** was blocked by the pentylidene group, the Grignard reagent would like to attack the β-face of **183**, the formation of alkene **184** is more favoured.

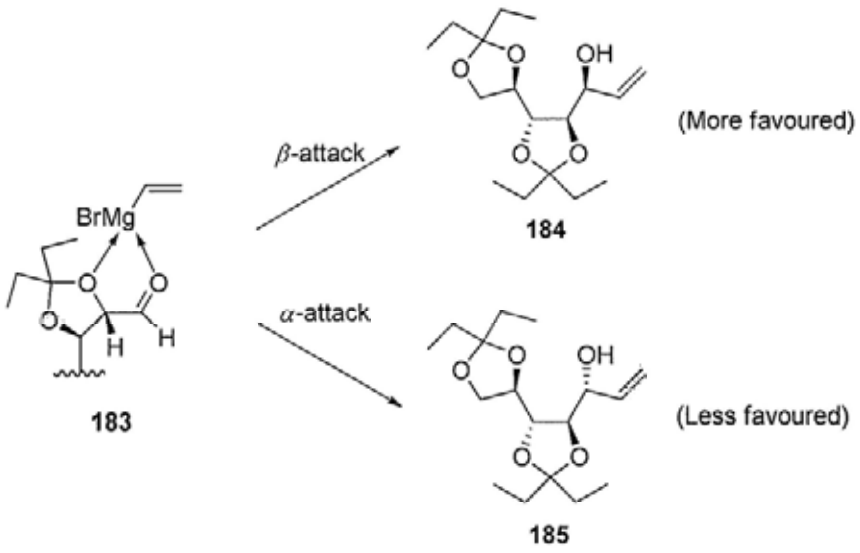
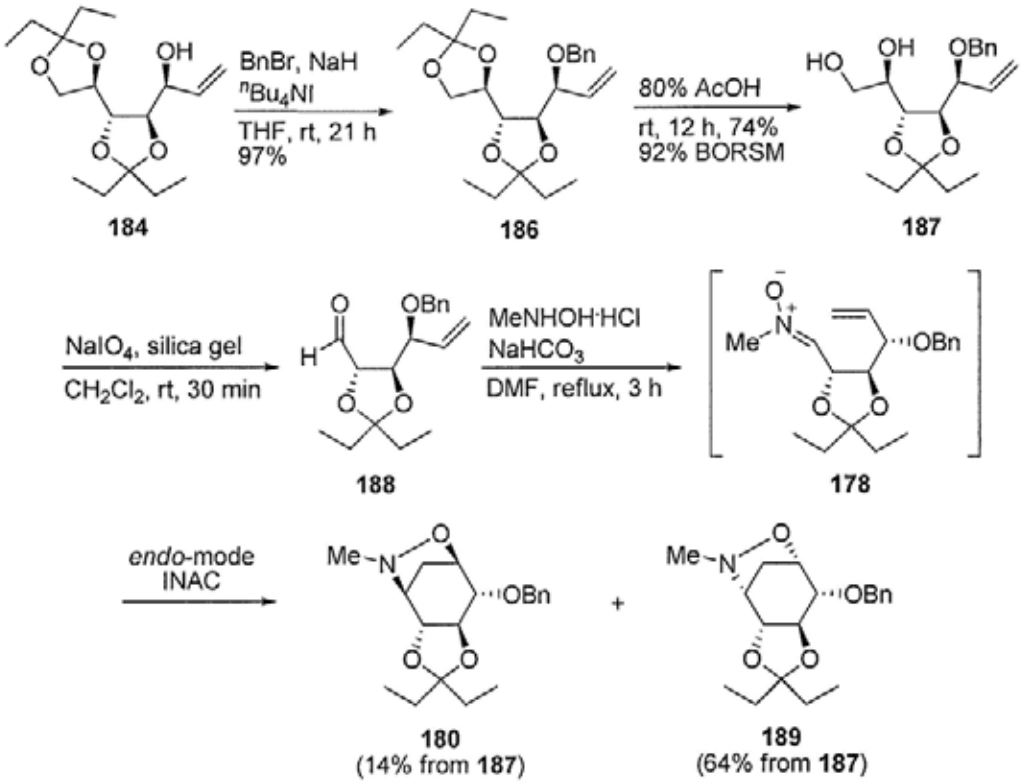


Figure 25

The alkene **184** was then transformed into the corresponding nitrone by the following synthetic sequence. First, the free hydroxyl group of alkene **184** was protected as a benzyl ether to afford compound **186**, which was followed by

regioselective acid hydrolysis of its terminal pentylidene group to give 1,2-diol **187** (Scheme 79). Glycol cleavage oxidation of diol **187** furnished aldehyde **188**. Then the nitrone **178** was prepared by reacting the aldehyde with *N*-methylhydroxylamine. Subsequent heating of the resulting mixture allowed the INAC reaction to take place, yielding two 6-membered *endo*-cycloadducts, isoxazolidines **180** and **189**.



Scheme 79

The ring size of both isoxazolidines **180** and **189** were assigned by their ^{13}C DEPT NMR spectra. For both isoxazolidines **180** and **189**, each having three resonances in the upfield region (δ 25–40 ppm) were assigned to a methylene group, two of which are the methylene carbons of pentylidene group and the remaining one is the methylene carbon in the cyclohexane ring. If a 5-membered *exo*-cycloadduct had been formed

instead, only two methylene carbon resonances have been found. The structure of the major cycloadduct **189** was confirmed by X-ray crystallography (Figure 26).

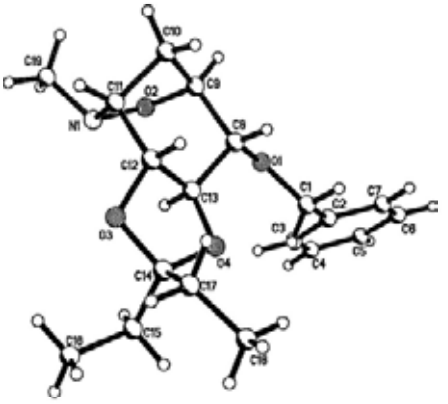


Figure 26. X-ray crystallographic structure of isoxazolidine **189**.

It shows that isoxazolidine **189** is consists of a 6-membered carbocycle with the isoxazolidine ring *cis* to the benzyloxy moiety, which in turns concluded that the isoxazolidine ring of another cycloadduct, isoxazolidine **180**, is *trans* to its benzyloxy moiety as shown in Scheme 79.

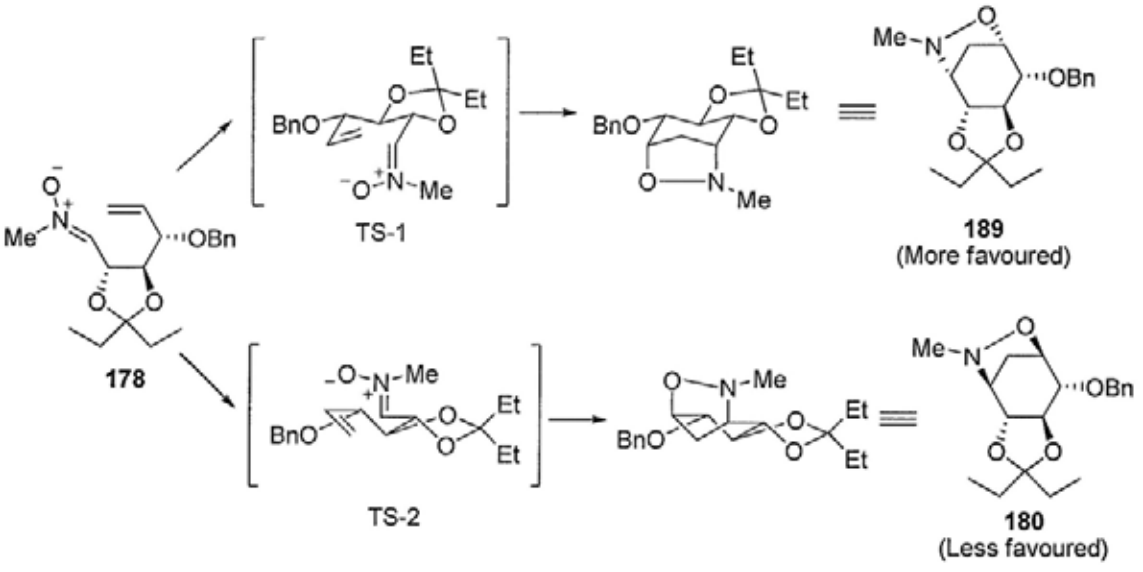
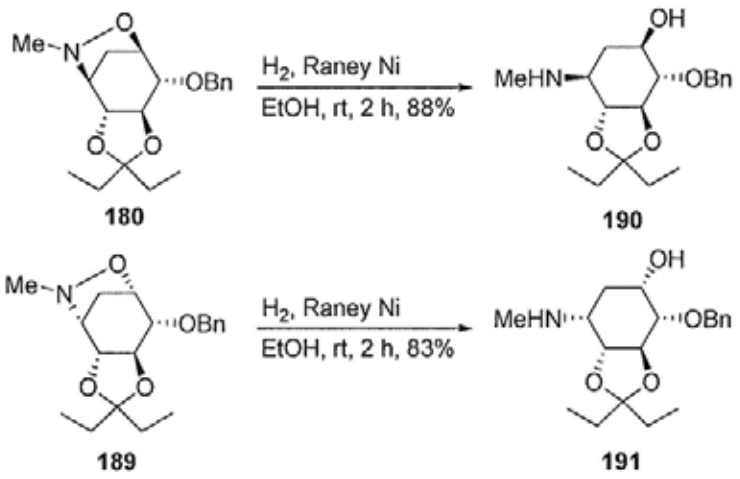


Figure 27

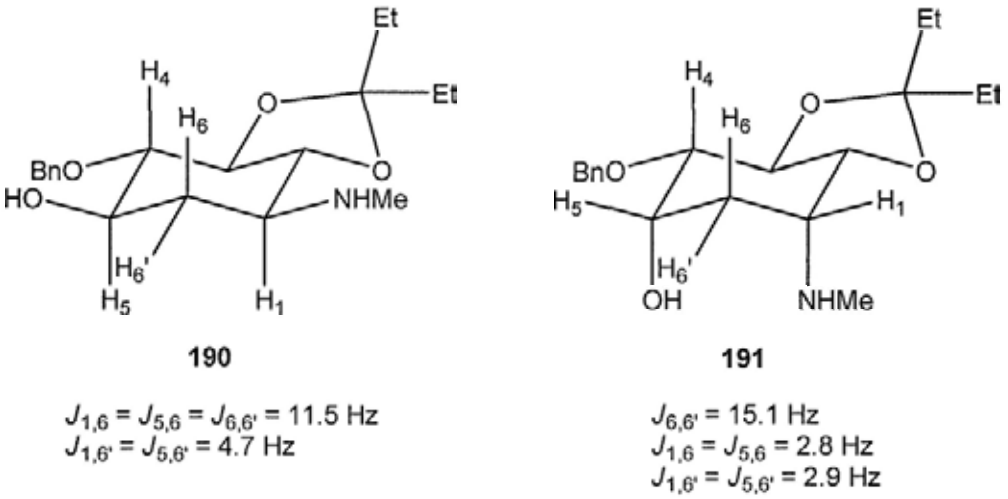
During this INAC reaction, isoxazolidine **189** rather than isoxazolidine **180** was formed as the major product. The reason of this outcome can be explained by the proposed transition states (Figure 27). In order to minimize the torsional strain of the 5-membered *trans*-pentylidene ring, this pentylidene ring would occupy the *trans*-diequatorial position as shown in both TS-1 and TS-2. For TS-1, the carbocycle was formed by adopting a chair-like conformation which led to lower TS energy, resulting in the formation of isoxazolidine **189** as the major product. On the other hand, a boat-like conformation was adopted during the formation of carbocycle in TS-2. As the TS energy is higher than that in TS-1, the isoxazolidine **180** was formed as the minor product.

The stereochemistry of the newly formed chiral centers of the INAC cycloadducts **180** and **189** was also assigned by converting them into their corresponding hydrogenolysis products. Isoxazolidine **180** and **189** were subjected to Raney®-Nickel catalyzed hydrogenolysis to afford amines **190** and **191** respectively (Scheme 80).



Scheme 80

Now the carbocyclic ring of both amines **190** and **191** are aligned in chair conformation, with the pentylidene group occupying the *trans*-diequatorial position (Figure 28). After analyzing their ^{1}H NMR spectra, it was found that the coupling patterns of methylene protons (H_6 and $H_{6'}$) in the carbocyclic ring of amines **190** are different from that of amine **191**. In amine **190**, as both H_1 and H_5 are occupying in the axial position, the $J_{1,6}$ and $J_{5,6}$ have large values (Figure 28). Thus together with the large geminal coupling of $J_{6,6'}$, the H_6 was observed as quartet (q, J = 11.5 Hz). Since the $H_{6'}$ is occupying the equatorial position, it has smaller magnitude of both $J_{1,6'}$ and $J_{5,6'}$. The $H_{6'}$ was hence observed as a doublet of triplets (dt, J = 13.0, 4.7 Hz).



190

$J_{1,6} = J_{5,6} = J_{6,6'} = 11.5$ Hz
$J_{1,6'} = J_{5,6'} = 4.7$ Hz

191

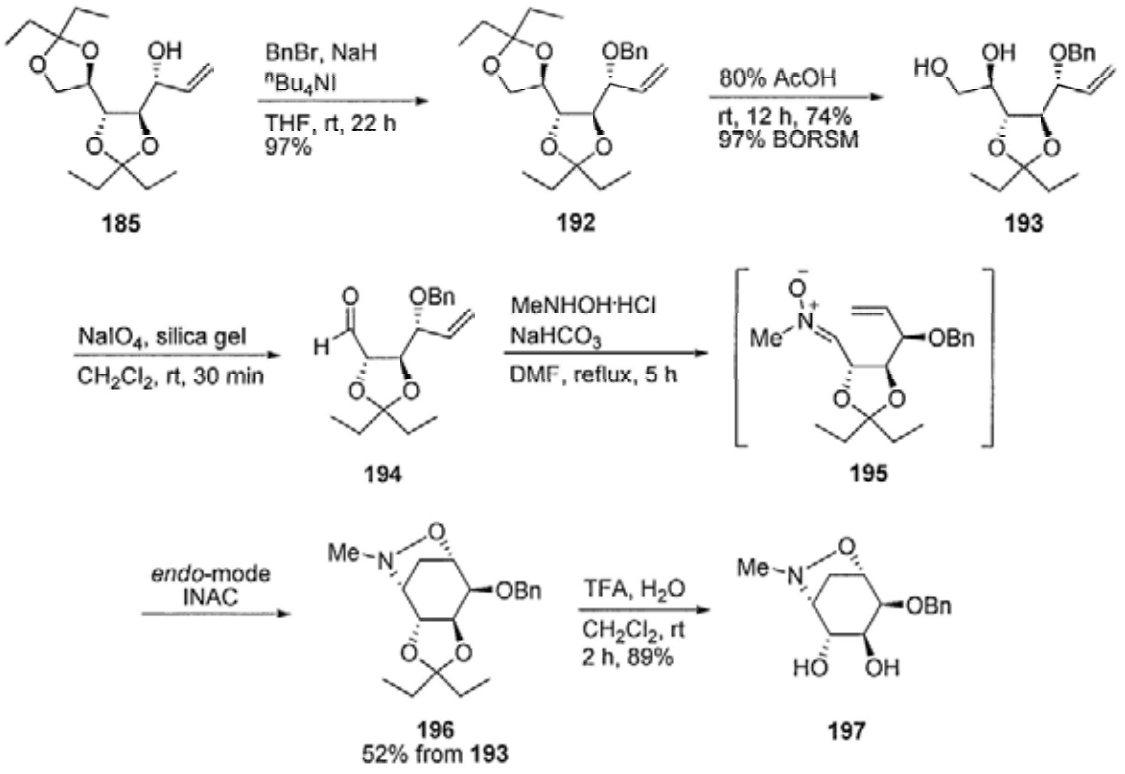
$J_{6,6'} = 15.1$ Hz
$J_{1,6} = J_{5,6} = 2.8$ Hz
$J_{1,6'} = J_{5,6'} = 2.9$ Hz

Figure 28. Conformations of **190** and **191**.

However, both H_1 and H_5 in amine **191** are occupying the equatorial position hence all of the $J_{1,6}$, $J_{5,6}$, $J_{1,6'}$, and $J_{5,6'}$ are small in magnitude (Figure 28). Both H_6 and $H_{6'}$ were observed as a doublet of triplets (dt, J = 15.1, 2.8 Hz and dt, J = 15.2, 2.9 Hz) in the ^{1}H NMR spectrum, which is different from the case in amine **190** (one quartet and one doublet of triplets). Hence by analyzing the coupling patterns of H_6 and $H_{6'}$ from

the ^{1}H NMR spectra, the stereochemistry of the amine and hydroxyl moieties can be assigned.

The alkene **185**, which is the minor product of the previous Grignard vinylation shown in Scheme 78, was also transformed into its corresponding nitrone **195** by the same synthetic strategy (Scheme 81). First, benzylation of alcohol **185** gave benzyl ether **192**, which was followed by regioselective acid hydrolysis to furnish 1,2-diol **193**. Glycol cleavage oxidation of diol **193** afforded aldehyde **194**. This aldehyde **194** was then reacted with *N*-methylhydroxylamine to yield nitrone **195**. After heating the nitrone **195**, the INAC reaction occurred and one 6-membered *endo*-cycloadduct **196** was formed in a moderate overall yield from diol **193**.



Scheme 81

The ring size of the INAC cycloadduct **196** was confirmed by its ^{13}C DEPT NMR spectrum as mentioned previously. Isoxazolidine **196** has three resonances in the upfield region (δ 25−40 ppm) which were assigned to be a methylene group, two of which are the methylene carbons of pentylidene group and the remaining one is the methylene carbon in the cyclohexane ring. Thus the formation of a 6-membered cycloadduct was confirmed.

In contrast to the INAC reaction of nitrone **178** which gave two INAC cycloadducts (Scheme 79), the INAC reaction of nitrone **195** furnished only one INAC cycloadduct. The reason can be explained by the following proposed transition states (Figure 29). In order to minimize the torsion strain of both TS-1 and TS-2, the pentylidene group is occupying *trans*-diequatorial position, and then the benzyl group should occupy the axial position. For TS-2, the carbocycle was formed by adopting a boat-like conformation which led to higher TS energy. Also, there is steric repulsion between the axial benzyl group and the nitrone moiety. These two factors make the formation of isoxazolidine **198** became highly unfavoured. Thus no isoxazolidine **198** was formed. On the other hand, there is no such steric repulsion between the benzyl group and nitrone moiety in TS-1, and the formation of carbocycle in TS-1 adopted a chair-like conformation which led to lower TS energy. Hence isoxazolidine **196** was obtained as the sole product during this INAC reaction.

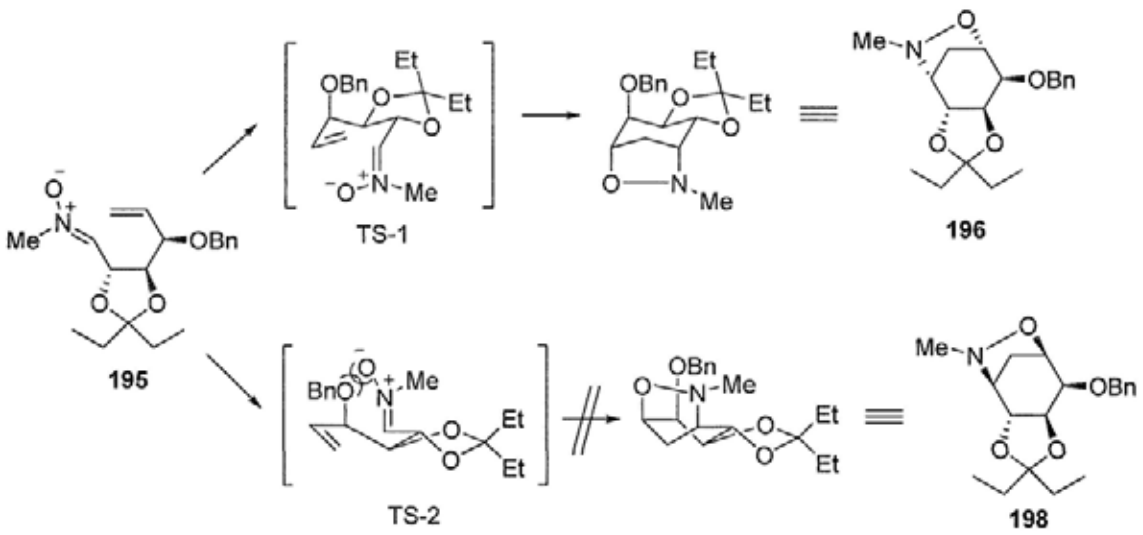
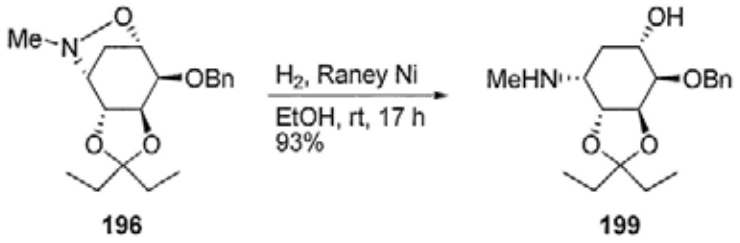


Figure 29

The pentylidene group of isoxazolidine **196** was removed by trifluoroacetic acid hydrolysis to afford diol **197** in 89% yield (Scheme 81). Although diol **197** is a solid at room temperature and pressure, it cannot be crystallized in good single crystals hence its structure cannot be confirmed by X-ray crystallography. However, the stereochemistry of this INAC cycloadduct was confirmed by the ^{1}H NMR spectrum of amine **199**, which was formed by Raney®-Nickel hydrogenolysis of isoxazolidine **196** (Scheme 82).



Scheme 82

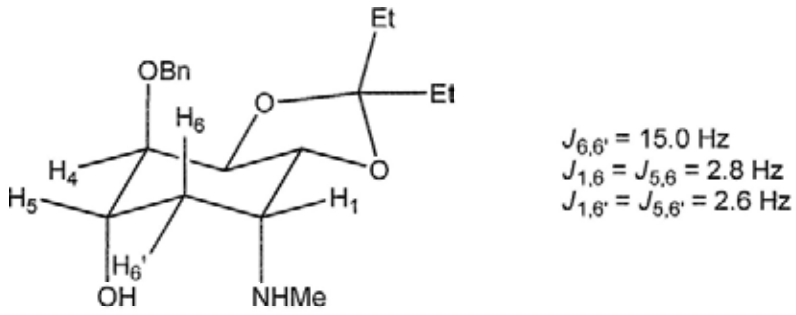


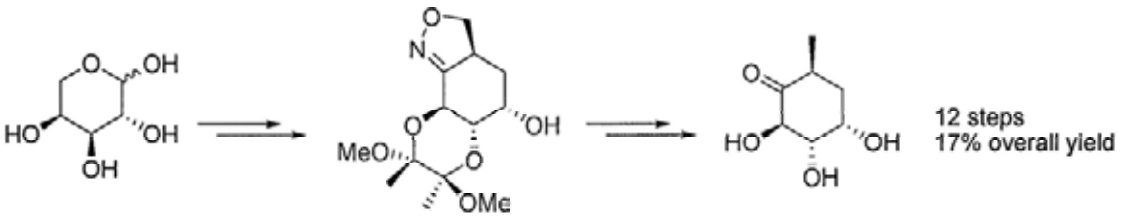
Figure 30. Conformation of amine **199**

In order to adopt the most stable conformation, the carbocycle of amine **199** is in chair conformation with a pentylidene group occupying the *trans*-diequatorial position (Figure 30). From the ^{1}H NMR spectrum of amine **199**, both H_6 and $H_{6'}$ were observed as a doublet of triplets (dt, J = 15.0, 2.8 Hz and dt, J = 15.0, 2.6 Hz). This observation is comparable to the coupling patterns of H_6 and $H_{6'}$ in amine **191** (Figure 28), in which both the amine and hydroxyl moieties are occupied in the α-position. Hence the hydroxyl and amine moieties in amine **199** should also have such α-stereochemistry as well.

Chapter 3

Conclusion

Enantiopure (+)-gabosine F (**2**) was successfully synthesized from L-arabinose via intramolecular nitrile oxide-alkene cycloaddition (INOC) as the key step, in 12 steps and 17% overall yield (Scheme 83).



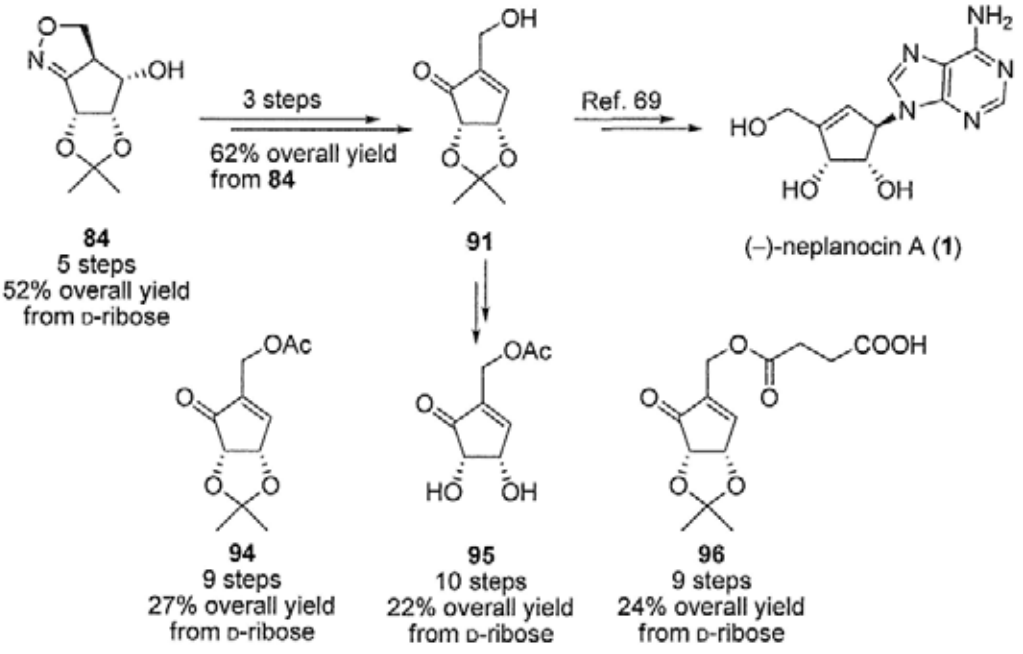
Scheme 83

Theoretically, by following the same synthetic strategy, another natural product (−)-gabosine B (**36**), which is the enantiomer of (+)-gabosine F (**2**), can also be synthesized from D-arabinose (Scheme 84).

Scheme 84

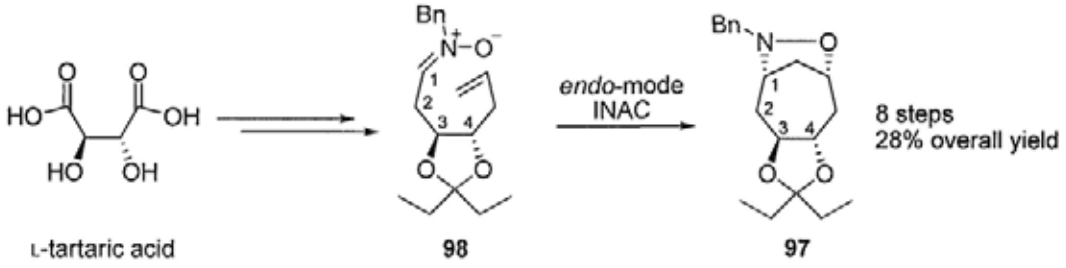
The INOC cycloadduct isoxazoline **84** was transformed into optically pure alcohol **91**, which is the key intermediate of Khan's synthesis of (±)-neplanocin A.[69]

This alcohol **91** was also converted into cyclopent-2-enone derivatives **94**–**96** (Scheme 85).



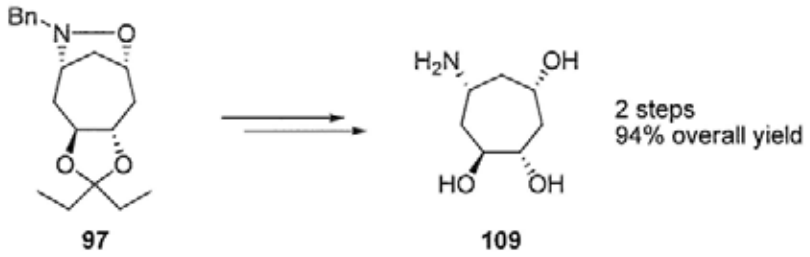
Scheme 85

In the studies on regioselectivity of INAC of hept-6-enose bearing a 3,4-*trans*-pentylidene blocking group, the INAC of nitrone **98**, which was prepared from L-tartaric acid, gave exclusive formation of *endo*-cycloadduct isoxazolidine **97** (Scheme 86). As the nitrone **98** consists of only nitrone, alkene and 3,4-*trans*-pentylidene moieties, its exclusive formation of *endo*-cycloadduct concluded that the presence of 3,4-*trans*-pentylidene group can induce the *endo*-mode INAC reaction to take place.



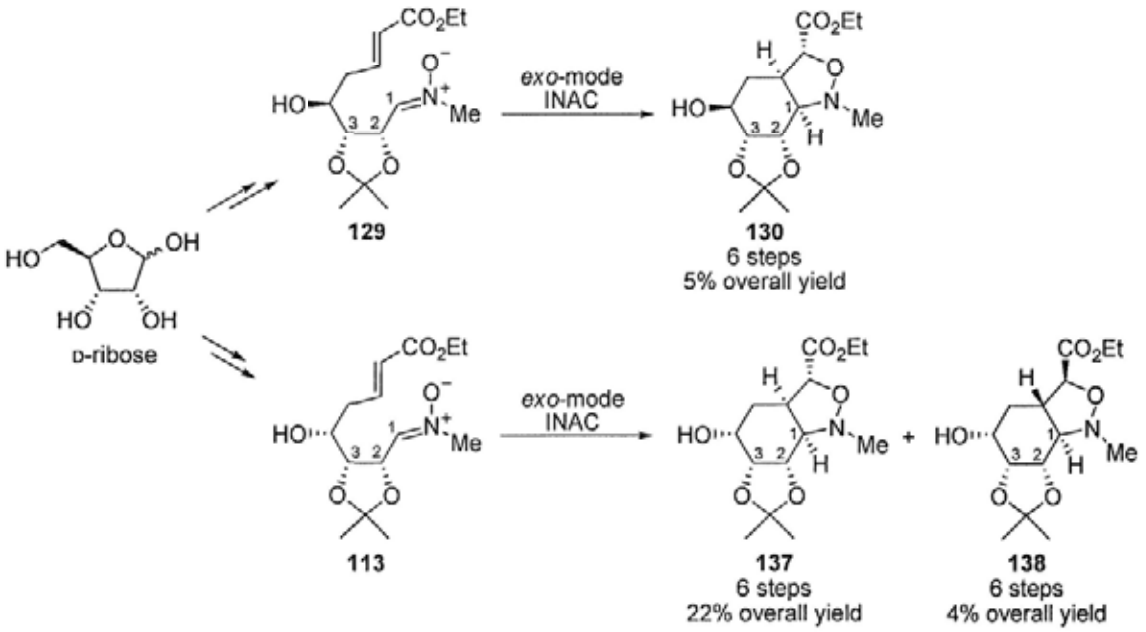
Scheme 86

The cycloadduct isoxazolidine **97** was transformed into aminocycloheptanol **109** readily (Scheme 87).



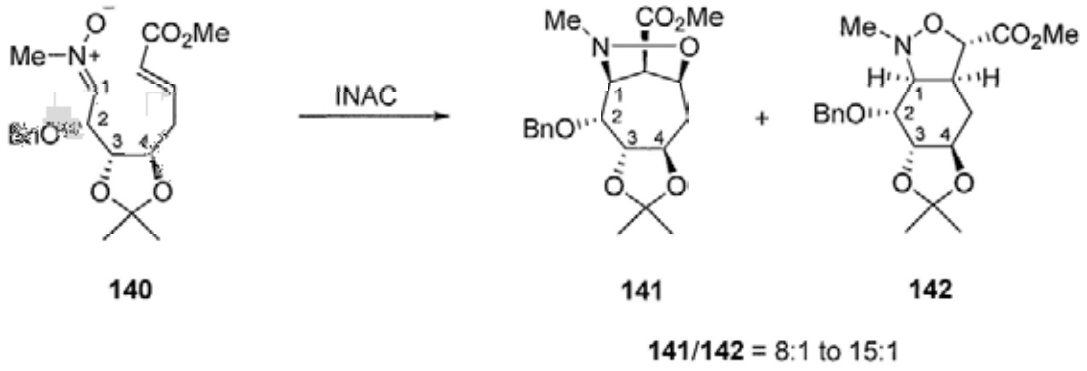
Scheme 87

In the studies of INAC reaction between nitrone moiety and α,β-unsaturated ester, exclusive formation of 6-membered *exo*-cycloadducts **130**, **137** and **138** was observed when substrates were bearing a 2,3-*cis*-isopropylidene group (nitrones **129** and **113**) (Scheme 88).



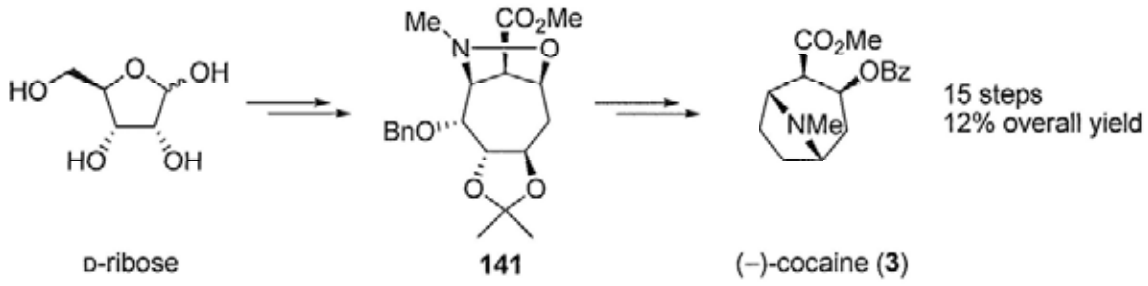
Scheme 88

When the substrate was bearing a 3,4-*trans*-isopropylidene (nitrone **140**), INAC reaction between nitrone moiety and α,β-unsaturated ester afforded 7-membered *endo*-cycloadduct **141** as the major product, with 6-membered *exo*-cycloadduct **142** formed as the minor product (Scheme 89).



Scheme 89

Through this *endo*-cycloadduct isoxazolidine **141**, natural product (−)-cocaine (**3**) was hence synthesized from D-ribose in 15 steps and 12% overall yield (Scheme 90).



Scheme 90

By using this synthetic strategy, six more (−)-cocaine analogues were obtained as well (Figure 31).

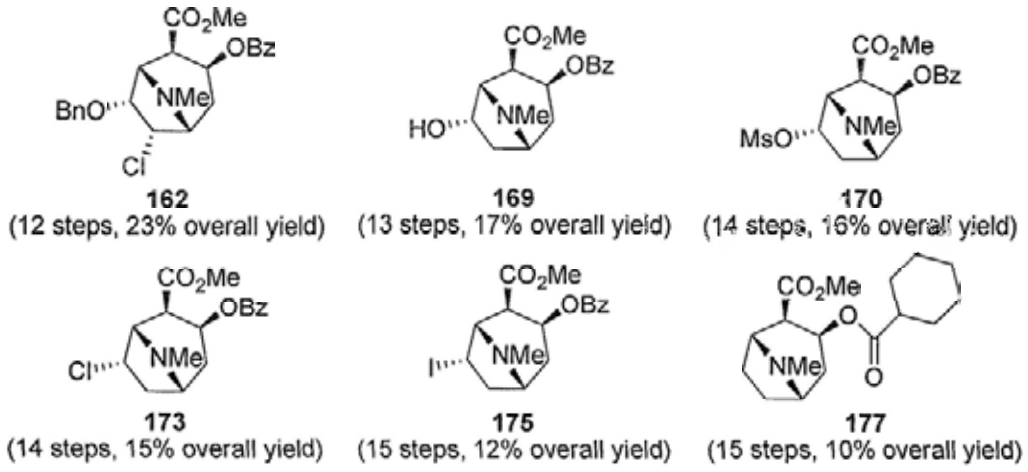
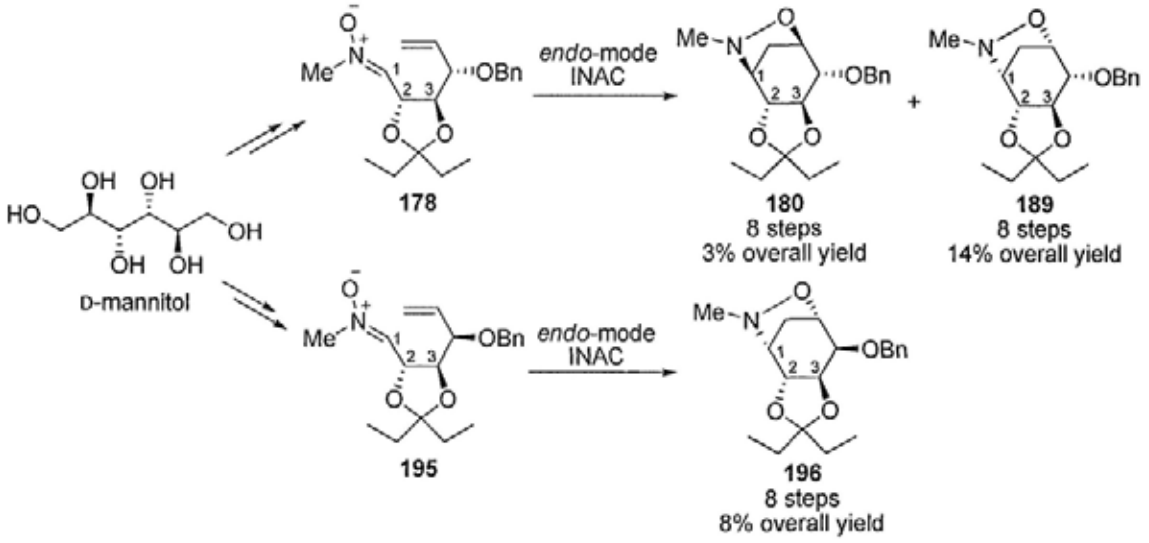


Figure 31

The regioselectivity of INAC reaction of hex-5-enoses with 2,3-*trans*-pentylidene blocking group were also studied. Exclusive formation of 6-membered *endo*-cycloadducts were observed during INAC reaction of nitrones **178** and **195**, which were accessed from D-mannitol, in 8 steps (Scheme 91).



Scheme 91

Experimental Section

Melting points were measured with a Reichert apparatus in Celsius degrees and are uncorrected. Optical rotations were obtained with a Perkin-Elmer model 341 polarimeter, operating at 589nm. Infrared (IR) spectra were recorded on a Nicolet 205 or a Perkin-Elmer 1600 FT-IR spectrophotometer as thin films on potassium bromide discs. Nuclear magnetic resonance (NMR) spectra were measured with either (i) Bruker DPX300 NMR spectrometer at 300.13 MHz (^{1}H) or at 75.47 MHz (^{13}C) or (ii) Bruker Avance III 400 NMR spectrometer at 400.19 MHz (^{1}H) or at 100.62 MHz (^{13}C) as mentioned, in $CDCl_3$ solutions, unless stated otherwise. All chemical shifts were recorded in ppm relative to tetramethylsilane ($\delta = 0.0$). Spin-spin coupling constants (*J* value) recorded in Hz were measured directly from the spectra. MS and HRMS were measured on a ThermoFinnigan MAT 95 KL at the Department of Chemistry, The Chinese University of Hong Kong, Hong Kong, China. Elemental analyses were carried out by MEDAC Ltd, Department of Chemistry, Brunel University, Uxbridge, UK. All reactions were monitored by analytical thin-layer chromatography (TLC) on Merck aluminium-precoated plates of silica gel 60 F254 with detection by spraying with 5% (w/v) dodecamolybdophosphoric acid in ethanol or 5% (w/v) ninhydrin in ethanol, and subsequent heating. E. Merck silica gel 60 (230-400 mesh) was used for flash chromatography. All reagents and solvents were general reagent grade unless otherwise stated. Pyridine was distilled from barium oxide and stored in the presence of potassium hydroxide pellets. DMF was dried by magnesium sulfate, filtered and the filtrate was then distilled under reduced pressure. Acetonitrile was freshly distilled from P_2O_5 under

nitrogen. Acetone was dried by $CaSO_4$ and filtered. THF and toluene were freshly distilled from Na/benzophenone ketyl under nitrogen. Et_2O was freshly distilled from K/benzophenone ketyl under nitrogen. Dichloromethane was freshly distilled from P_2O_5 under nitrogen. Other reagents were purchased from commercial suppliers and were used without purification.

General procedure for glycol cleavage reaction. $NaIO_4$ (3 eq.) was dissolved in a minimum amount of hot water (~80 °C) followed by the addition of silica gel (230–400 mesh, 10 × weight of diol) with vigorous swirling and shaking. The mixture was suspended in CH_2Cl_2 and then a solution of diol (1 eq.) in CH_2Cl_2 was added. After vigorous stirring at room temperature for 1 h, the mixture was filtered then concentrated under reduced pressure to give the crude aldehyde product.

Generation of allylmagnesium bromide. To a suspension of magnesium powder (3.65 g, 150 mmol) in Et_2O (10 mL) was added a catalytic amount of iodine and the mixture was stirred at room temperature for 15 min. A solution of allyl bromide (4.30 mL, 50.0 mmol) in Et_2O (50 mL) was added dropwise to the mixture at a rate to maintain a gentle reflux of the Et_2O. After the addition of the allyl bromide solution, the mixture was heated under reflux for 30 min and then cooled down for use. The concentration of the allylmagnesium bromide solution generated was around 1.5 M.

Generation of vinylmagnesium bromide. Vinyl bromide (1.34 mL, 19.0 mmol) was condensed with an acetone-dry ice cold finger and diluted with THF (20mL) at –78 °C. To a suspension of magnesium powder (1.48 g, 60.9 mmol) in THF (30 mL) was

added 1,2-dibromoethane (0.2 mL) and the vinyl bromide solution was added dropwise to the reaction mixture at a rate that a moderate reflux was maintained. After the addition had been completed, the solution was heated to reflux for 30 min and then cooled down for use. The concentration of the vinylmagnesium bromide solution generated was around 1.5 M.

Generation of BnNHOH.[88] Hydroxylamine hydrochloride (3.76 g, 54.1 mmol) and $NaHCO_3$ (6.20 g, 73.8 mmol) were added to a solution of benzaldehyde (5.0 mL, 49.2 mmol) in CH_3CN (50 mL) and the mixture was stirred at room temperature for 1 h. The reaction mixture was partitioned between Et_2O (50 mL) and water (50 mL). The aqueous layer was extracted with Et_2O (2 × 50 mL). The combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, and filtered. Concentration of the filtrate followed by flash chromatography (hexane:Et_2O, 1:2) gave benzylaldehyde oxime as a colorless oil. To a solution of benzyladehyde oxime in MeOH (24 mL) was added a trace amount of bromocresol green to give a clear yellow solution. $NaBH_3CN$ (3.55 g, 56.5 mmol) was added to the reaction mixture which turned the mixture into dark blue and 2 M HCl in MeOH was added dropwise with stirring until the color of the mixture turned yellow. The addition of 2 M HCl in MeOH was continued whenever the color of the mixture turned blue. After stirring at room temperature for 1 h, the reaction was completed indicated by the permanent yellow color of the mixture without the addition of the acid. The solvent was then removed under reduced pressure and the residue was dissolved in water (20 mL). 6 M NaOH was added to attain a pH value greater than 9. After saturation of the mixture with NaCl, the aqueous phase was

extracted with $CHCl_3$ (4 × 30 mL). The solvent was removed under reduced pressure and the residue was purified by recrystallization from hexane-CH_2Cl_2 to give benzylhydroxylamine (4.92 g, 81%) as a white solid.

General procedure for INAC reaction (Method A). *N*-Methylhydroxylamine hydrochloride (1.05 eq.) and $NaHCO_3$ (2.10 eq.) were then added to a solution of aldehyde in the selected solvent. The reaction mixture was stirred at room temperature for until the disappearance of the aldehyde as shown on TLC. It was then heated under reflux until the disappearance of the nitrone as shown on TLC. After cooling, the reaction mixture was partitioned between EtOAc and water. The aqueous layer was extracted with EtOAc for three times. The combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, and filtered. The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography to give the cycloadduct(s).

General procedure for INAC reaction (Method B). *N*-Methylhydroxylamine hydrochloride (1.05 eq.) and $NaHCO_3$ (2.10 eq.) were added to a solution of aldehyde in MeCN. The reaction mixture was stirred at room temperature for until the disappearance of the aldehyde as shown on TLC. Et_2O was added to the reaction mixture to precipitate out most of the salt. The salt was filtered off through a thin layer of silica gel and washed with EtOAc. Concentration of the filtrate gave the crude product of nitrone. The crude nitrone was then redissolved in the selected solvent and the solution was heated under reflux until the disappearance of the nitrone as shown on

TLC. The reaction mixture was then concentrated under reduced pressure and the residue was purified by flash chromatography to give the cycloadduct(s).

General procedure for INAC reaction (Method C). *N*-Methylhydroxylamine hydrochloride (1.05 eq.) and the selected base (3 eq.) were added to a solution of aldehyde/lactol in the selected solvent. The mixture was then heated under reflux. After the completion of the reaction, the mixture was filtered. The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography to yield the cycloadduct(s).

(+)-Gabosine F (2). To a stirred solution of ketone **77** (9.3 mg, 0.034 mmol) in CH_2Cl_2 (1 mL) were added deionized water (0.05 mL) and TFA (0.25 mL, 3.4 mmol) at room temperature to form a clear solution. The mixture was stirred at room temperature for 2 h. Concentration of the mixture under reduced pressure and the residue was purified by flash chromatography ($CHCl_3$:MeOH, 20:1) furnished (+)-gabosine F (**2**) (5.5 mg, 100%) as colorless crystals: mp 88–90 °C {lit.[16a] mp 82–85 °C}; $[\alpha]_D^{20}$ +88.4 (*c* 0.69, MeOH) {lit.[16a] $[\alpha]_D^{20}$ +94 (*c* 1.0, MeOH)}; R_f 0.20 ($CHCl_3$:MeOH, 9:1); IR (thin film) 3390, 2969, 2931, 1716, 1455, 1379, 1347, 1199, 1122, 1080 cm^{-1}; ^1H NMR (300 MHz, CD_3OD) δ 1.03 (3H, d, J = 6.6 Hz), 1.41 (1H, td, J = 13.8, 2.4 Hz), 2.12 (1H, ddd, J = 14.1, 6.0, 3.3 Hz), 2.86–2.99 (1H, m), 3.46 (1H, dd, J = 9.9, 3.0 Hz), 4.09 (1H, q, J = 2.7 Hz), 4.40 (1H, d, J = 10.2 Hz); ^{13}C NMR (75 MHz, CD_3OD) δ 13.7, 37.8, 38.1, 69.7, 78.1, 79.2, 211.4; MS (ESI) *m/z* (relative intensity) 183 ($[M+Na]^+$, 100), 159 ($[M–H]^+$, 55); HRMS (ESI) calcd for $C_7H_{12}O_4$ $[M+Na]^+$ 183.0628, found 183.0632.

(−)-Cocaine (3). To a solution of chloride **173** (1.9 mg, 0.006 mmol) in MeOH (0.5 mL) was added Raney®-Nickel (2 mg). The mixture was activated with an atmosphere of H_2 (balloon) by three times followed by stirring under the same H_2 atmosphere at room temperature for another 14 h. The reaction mixture was filtered and washed with MeOH. The filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography (CH_2Cl_2:MeOH, 19:1) to afford (−)-cocaine (**3**) (1.3 mg, 76%) as a white solid: mp 92–93 °C {lit.[46] mp 93−94 °C}; $[\alpha]_D^{20}$ −16.9 (*c* 0.18, $CHCl_3$) {lit.[46] $[\alpha]_D^{23}$ −16.2 (*c* 1.2, $CHCl_3$)}; R_f 0.48 (CH_2Cl_2:MeOH, 5:1); IR (thin film) 2947, 1749, 1714, 1450, 1315, 1278, 1229, 1176, 1114 cm^{-1}; ^1H NMR (400 MHz) δ 1.68−1.77 (2H, m), 1.84−1.90 (1H, m), 2.06−2.20 (2H, m), 2.23 (3H, s), 2.44 (1H, td, *J* = 11.8, 2.8 Hz), 3.02 (1H, dd, *J* = 5.2, 3.4 Hz), 3.30 (1H, s), 3.56−3.58 (1H, m), 3.71 (3H, s), 5.24 (1H, dt, *J* = 11.9, 6.0 Hz), 7.42 (2H, t, *J* = 7.8 Hz), 7.54 (1H, tt, *J* = 7.4, 1.2 Hz), 8.01−8.03 (2H, m); ^{13}C NMR (100 MHz) δ 25.6 (CH_2), 25.8 (CH_2), 35.9 (CH_2), 41.5 (CH_3), 50.6 (CH), 51.8 (CH_3), 61.9 (CH), 65.2 (CH), 67.3 (CH), 128.7 (CH), 130.1 (CH), 130.6 (C), 133.3 (CH), 166.6 (C), 171.1 (C); MS (ESI) *m/z* (relative intensity) 304 ($[M+H]^+$, 100); HRMS (ESI) calcd for $C_{17}H_{21}NO_4$ $[M+H]^+$ 304.1543, found 304.1539.

(−)-Cocaine (3) from iodide 175. To a solution of iodide **175** (4.0 mg, 0.009 mmol) in MeOH (1 mL) was added Raney Nickel (4 mg). The mixture was activated with an atmosphere of H_2 (balloon) by three times followed by stirring under the same H_2 atmosphere at room temperature for another 14 h. The reaction mixture was filtered and washed with MeOH. The filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography (CH_2Cl_2:MeOH, 19:1) to afford (−)-cocaine (**3**) (2.1 mg, 74%) as a white solid.

Isoxazoline 65. Following the glycol cleavage produce, alkene **70** (69.1 mg, 0.226 mmol) was converted into aldehyde **72** as a colorless oil. $NaHCO_3$ (38.0 mg, 0.452 mmol) and hydroxylamine hydrochloride (23.6 mg, 0.339 mmol) were added to the solution of aldehyde **72** in MeOH (3 mL). The mixture was stirred at room temperature for 30 min. Deionized water (8 mL) was added to the reaction mixture and the MeOH was removed under reduced pressure. The remaining aqueous solution was then extracted with EtOAc (3 × 10 mL) and the combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, and filtered. Concentration of the filtrate afforded crude oxime **73**. To the stirred suspension the crude oxime **73** and silica gel (230−400 mesh, 300 mg) in EtOH (10 mL) was added chloramine-T trihydrate (95.5 mg, 0.339 mmol) in small portions. After stirring at room temperature for 15 min, the silica gel was filtered. Concentration of the filtrate and the residue was purified by flash chromatography (hexane:EtOAc, 2:1 to 1:2) afforded isoxazoline **65** (57.4 mg, 89% overall yield from **70**) as a white solid: mp 232–233 °C; $[\alpha]_D^{20}$ –10.9 (*c* 1.96, $CHCl_3$); R_f 0.29 (hexane:EtOAc, 1:4); IR (thin film) 3545, 2949, 1377, 1118, 1032, 873 cm^{-1}; ^1H NMR (300 MHz) δ 1.33 (3H, s), 1.37 (3H, s), 1.53 (1H, ddd, *J* = 14.1, 11.7, 2.4 Hz), 2.32 (1H, ddd, *J* = 14.1, 6.6, 3.3 Hz), 3.22 (3H, s), 3.30 (3H, s), 3.66–3.87 (3H, m), 4.15 (1H, q, *J* = 2.7 Hz), 4.55 (1H, dd, *J* = 10.2, 7.5 Hz), 4.95 (1H, d, *J* = 9.9 Hz); ^{13}C NMR (75 MHz) δ 18.0, 35.0, 44.9, 48.4, 48.7, 64.6, 68.8, 73.9, 74.1, 100.7, 100.8, 157.2; MS (ESI) *m/z* (relative intensity) 310 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{13}H_{21}NO_6$ $[M+Na]^+$ 310.1261, found 310.1265.

Benzyl *β*-L-arabinopyranoside (67). Acetyl chloride (9.47 mL, 133 mmol) was added dropwise to BnOH (140 mL) at 0 °C over 30 min. L-Arabinose (20.6 g, 133 mmol) was then added to the reaction mixture which was stirred vigorously at room temperature for 3 d. Et_2O (700 mL) was added to precipitate the benzyl glycoside that was filtered and the crude white solid was washed with Et_2O. Recrystallization from EtOH afforded glycoside **67** (29.1 g, 88%) as white crystals: mp 171–172 °C {lit.[89] mp 167−169 °C}; $[\alpha]_D^{20}$ +217.9 (*c* 1.11, MeOH) {lit.[89] $[\alpha]_D^{20}$ −217 (*c* 0.400, H_2O)}; R_f 0.50 (CH_3Cl:MeOH, 5:1); ^1H NMR (300 MHz, CD_3OD) δ 3.60 (1H, dd, *J* = 12.6, 2.4 Hz), 3.80–3.88 (4H, m), 4.52 (1H, d, *J* = 12 Hz), 4.71 (1H, d, *J* = 11.7 Hz), 7.25–7.42 (5H, m); ^{13}C NMR (75 MHz, CD_3OD) δ 65.2, 71.2, 71.6, 71.7, 100.8, 129.6, 130.0, 130.2, 139.9; MS (ESI) *m/z* (relative intensity) 263 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{12}H_{16}O_5$ $[M+Na]^+$ 263.0890, found 263.0897.

Benzyl-2,3-*O*-[(2*R*,3*R*)-2,3-dimethoxybutan-2,3-dioxy]-*β*-L-arabinopyranoside (68). To a suspension of **67** (23.0 g, 95.9 mmol) in methanol (500 mL), 2,3-butanedione (12.6 mL, 144 mmol), trimethylorthoformate (52.5 mL, 480 mmol) and (±)-10-camphorsulfonic acid (2.23 g, 9.59 mmol) were added and the mixture was heated under reflux for 4 h. Powdered $NaHCO_3$ (3.99 g) was then added to the cooled reaction mixture and stirred for 5 h. The mixture was filtered and the filtrate was concentrated under reduced pressure. The residue was dissolved in EtOAc and the solution was washed with saturated $NaHCO_3$ solution. The organic layer was dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure and the crude residue was purified by flash chromatography (hexane:EtOAc, 1:1) to

afford product **68** (20.4 g, 60%) as a white solid: mp 143–144 °C; $[\alpha]_D^{20}$ +3.9 (*c* 1.27, $CHCl_3$); R_f 0.32 (hexane:EtOAc, 1:1); IR (thin film) 3480, 2945, 1455, 1378, 1136, 1038, 885 cm^{-1}; ^1H NMR (300 MHz) δ 1.31–1.33 (6H, 2s), 2.02 (1H, br s), 3.22 (3H, s), 3.26 (3H, s), 3.68 (1H, dd, *J* = 12.6, 1.5 Hz), 3.79 (1H, dd, *J* = 12.6, 1.5 Hz), 3.92–3.93 (1H, m), 4.11 (1H, dd, *J* = 10.5, 3 Hz), 4.16 (1H, dd, *J* = 10.5, 3 Hz), 4.65 (1H, d, *J* = 12.3 Hz), 4.73 (1H, d, *J* = 12.6 Hz), 4.95 (1H, d, *J* = 3 Hz), 7.26–7.42 (5H, m); ^{13}C NMR (75 MHz) δ 18.0, 48.1, 48.2, 63.4, 65.4, 66.1, 68.2, 69.5, 97.1, 100.3, 100.4, 127.8, 128.2, 128.5, 137.9; MS (ESI) *m/z* (relative intensity) 377 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{18}H_{26}O_7$ $[M+Na]^+$ 377.1571, found 377.1572.

Alkenes 70 and 71. To a solution of *trans*-diacetal **68** (23.2 g, 65.5 mmol) in EtOH (200 mL) was added 10% Pd-on-charcoal (696 mg, 0.655 mmol) and the mixture was stirred under an atmosphere of H_2 (balloon). After stirring at room temperature under H_2 for 12 h, the mixture was filtered and the filtrate was concentrated to give lactol **69** as a white solid. A solution of allylmagnesium bromide was generated with magnesium powder (39.8 g, 1.64 mol) and allyl bromide (85.0 mL, 982 mmol) in Et_2O (500 mL). The Et_2O solution of allylmagnesium bromide was added dropwise to a stirred solution of lactol **69** in THF (400 mL) at –78 °C under N_2 over 2 h. After stirring at –78 °C for a further 1 h and then room temperature for 12 h, the mixture was quenched with saturated NH_4Cl solution and the aqueous phase was extracted with EtOAc (2 × 500 mL). The combined organic extracts were dried over anhydrous $MgSO_4$, and filtered. The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography ($CHCl_3$:EtOAc, 1:4) to afford firstly

alkene **70** (9.89 g, 49% overall yield from **68**) as a colorless oil and secondly alkene **71** (9.77 g, 49% overall yield from **68**) as a colorless oil: Data for **70**: $[\alpha]_D^{20}$ –147.5 (*c* 2.52, $CHCl_3$); R_f 0.33 ($CHCl_3$:EtOAc, 1:3); IR (thin film) 3371, 2949, 1376, 1128, 1037 cm^{-1}; ^1H NMR (300 MHz) δ 1.26–1.27 (6H, 2s), 2.15 (1H, dt, *J* = 14.1, 8.4 Hz), 2.81 (1H, dddd, *J* = 14.1, 6.0, 2.7, 1.5 Hz), 3.01–3.34 (9H, m), 3.55 (1H, ddd, *J* = 10.8, 8.1, 2.7 Hz), 3.70–3.90 (5H, m), 5.17–5.22 (2H, m), 5.84 (1H, dddd, *J* = 17.7, 9.3, 8.4, 6.0 Hz); ^1H NMR (300 MHz, $CDCl_3$-D_2O) δ 1.26–1.27 (6H, 2s), 2.15 (1H, dt, *J* = 14.4, 9.0 Hz), 2.80 (1H, dddd, *J* = 14.1, 6.0, 2.7, 1.5 Hz), 3.25–3.26 (6H, 2s), 3.54 (1H, dd, *J* = 9.3, 8.1 Hz), 3.70–3.90 (5H, m), 5.16–5.22 (2H, m), 5.83 (1H, dddd, *J* = 17.7, 9.3, 8.4, 6.0 Hz); ^{13}C NMR (75 MHz) δ 17.7, 17.8, 37.8, 48.6, 63.8, 70.6, 70.9, 73.6, 73.9, 99.8, 99.0, 119.3, 135.0; MS (ESI) *m/z* (relative intensity) 329 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{14}H_{26}O_7$ $[M+Na]^+$ 329.1571, found 329.1575.

Data for **71:** $[\alpha]_D^{20}$ –148.9 (*c* 1.26, $CHCl_3$); R_f 0.24 ($CHCl_3$:EtOAc, 1:3); IR (thin film) 3393, 2949, 1377, 1127, 1037 cm^{-1}; ^1H NMR (300 MHz) δ 1.25–1.28 (6H, 2s), 2.32–2.51 (2H, 1ddd, *J* = 14.4, 6.9, 5.7 Hz, 1ddd, *J* = 14.4, 8.4, 7.2 Hz), 3.13 (3H, s), 3.22–3.24 (6H, 2s), 3.68 (1H, dd, *J* = 9.9, 1.8 Hz), 3.72–3.81 (3H, m), 3.92 (1H, ddd, *J* = 8.1, 5.1, 1.8 Hz), 3.99 (1H, dd, *J* = 9.9, 6.3 Hz), 5.08–5.15 (2H, m), 5.83 (1H, ddt, *J* = 17.1, 10.2, 6.9 Hz; ^1H NMR (300 MHz, $CDCl_3$-D_2O) δ 1.25–1.27 (6H, 2s), 2.30–2.51 (2H, 1ddd, *J* = 14.1, 6.6, 5.4 Hz, 1ddd, *J* = 14.4, 8.4, 7.2 Hz), 3.22–3.24 (6H, 2s), 3.67 (1H, dd, *J* = 9.9, 1.8 Hz), 3.70–3.79 (3H, m), 3.91–3.99 (2H, 1ddd, *J* = 8.1, 5.1, 1.8 Hz, 1dd, *J* = 9.9, 6.3 Hz), 5.06–5.15 (2H, m), 5.83 (1H, ddt, *J* = 17.1, 10.2, 6.9 Hz); ^{13}C NMR (75 MHz) δ 17.8, 17.9, 37.9, 48.8, 48.5, 63.7, 69.7, 70.4, 71.5, 72.2, 99.0, 99.2, 117.9, 135.5; MS (ESI) *m/z* (relative intensity) 329 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{14}H_{26}O_7$ $[M+Na]^+$ 329.1571, found 329.1579.

Ketone 75. To a solution of isoxazoline **65** (220 mg, 0.765 mmol) in EtOH/H_2O/1,4-dioxane (v/v/v = 8:2:1, 12 mL) were added AcOH (0.08 mL, 1.53 mmol) and Raney®-Nickel (59 mg). The mixture was activated with an atmosphere of H_2 (balloon) by three times followed by stirring under the same H_2 atmosphere at room temperature for another 3 h. The mixture was filtered and washed with EtOH. The filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography (EtOAc) to afford ketones **75** (200 mg, 90%) as a colorless oil: $[\alpha]_D^{20}$ – 89.9 (*c* 0.47, $CHCl_3$); R_f 0.21 (EtOAc); IR (thin film) 3455, 2997, 2951, 1727, 1461, 1379, 1212, 1139, 1116, 1008 cm^{-1}; ^1H NMR (300 MHz) δ 1.31 (3H, s), 1.37 (3H, s), 1.74 (1H, td, *J* = 14.1, 2.4 Hz), 2.16 (1H, ddd, *J* = 14.4, 6.3, 3.3 Hz), 2.43 (2H, br s), 2.96–3.03 (1H, m), 3.21 (3H, s), 3.24 (3H, s), 3.65 (1H, dd, *J* = 11.7, 6.0 Hz), 3.78–3.88 (2H, m), 4.22 (1H, q, *J* = 2.7 Hz), 4.82 (1H, dd, *J* = 10.8, 1.2 Hz); ^{13}C NMR (75 MHz) δ 18.0, 31.2, 45.5, 48.5, 48.8, 61.7, 67.2, 72.5, 73.8, 100.4, 100.6, 206.6; MS (ESI) *m/z* (relative intensity) 313 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{13}H_{22}O_7$ $[M+Na]^+$ 313.1256, found 313.1258.

Ketone 77. To a stirred solution of **75** (32.5 mg, 0.112 mmol) in CH_2Cl_2 (4 mL) at room temperature was added Burgess reagent (48.1 mg, 0.202 mmol). The mixture was heated to reflux for 18 h then the solvent was removed under reduced pressure to give the crude enone **76**. The crude product was redissolved in EtOH/H_2O/1,4-dioxane (v/v/v = 8:2:1, 4 mL) followed by the addition of Raney®-Nickel (10 mg). The mixture was activated with an atmosphere of H_2 (balloon) by three times followed by stirring under the same H_2 atmosphere at room temperature for another 1 h. The mixture was

filtered and washed with EtOH. The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography (hexane:Et_2O, 1:2) to yield **77** (11.7 mg, 38% overall yield from **75**) as colorless crystals: mp 190 °C; $[\alpha]_D^{20}$ –81.0 (*c* 0.62, $CHCl_3$); R_f 0.17 (hexane:Et_2O, 1:2); IR (thin film) 3516, 2926, 1731, 1455, 1379, 1206, 1138, 1036 cm^{-1}; ^1H NMR (300 MHz) δ 1.05 (3H, d, *J* = 6.6 Hz), 1.31 (3H, s), 1.37 (3H, s), 1.44 (1H, td, *J* = 13.8, 2.4 Hz), 1.76 (1H, br s), 2.23 (1H, ddd, *J* = 14.4, 6.0, 3.0 Hz), 2.83–2.96 (1H, m), 3.20 (3H, s), 3.23 (3H, s), 3.78 (1H, dd, *J* = 10.8, 2.7 Hz), 4.15 (1H, q, *J* = 2.7 Hz), 4.78 (1H, d, *J* = 10.8 Hz); ^{13}C NMR (75 MHz) δ 13.7, 18.0, 18.1, 37.0, 38.2, 48.4, 48.7, 67.5, 72.5, 73.9, 100.3, 100.6, 205.3; MS (ESI) *m/z* (relative intensity) 297 ($[M+Na]^+$, 100); HRMS (ESI): calcd for $C_{13}H_{22}O_6$ $[M+Na]^+$ 297.1309, found 297.1314.

Ketone 77 by mesylation of 75. To a stirred solution of **75** (13.8 mg, 0.048 mmol) and 2,4,6-collidine (0.02 mL, 0.152 mmol) in CH_2Cl_2 (1 mL) at –78 °C was added methanesulfonyl chloride (0.006 mL, 0.076 mmol). The mixture was stirred at –78 °C for 1 h and then room temperature for 12 h to afford a mixture of mesylate and enone **76**. Et_3N (0.01 mL, 0.072 mmol) was added to the reaction mixture and stirred at room temperature for 1 h to allow the complete elimination of mesylate to enone **76**. The reaction mixture was quenched by saturated $NaHCO_3$ solution. The aqueous phase was extracted with EtOAc (2 × 15 mL) and the combined organic extracts were washed with 1 M hydrochloric acid then saturated $NaHCO_3$ solution. The organic phase was then dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure to give crude enone **76**. The crude product was redissolved in EtOH/H_2O/1,4-dioxane (v/v/v = 8:2:1, 1 mL) and Raney®-Nickel (4 mg) was added to

the solution. The mixture was activated with an atmosphere of H_2 (balloon) by three times followed by stirring under the same H_2 atmosphere at room temperature for another 1 h. The mixture was filtered and washed with EtOH. The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography (hexane:Et_2O, 1:2) to yield **77** (5.6 mg, 43% overall yield from **75**) as colorless crystals.

Ketone 77 by acetylation of 75. To a stirred solution of **75** (14.0 mg, 0.048 mmol) and 2,4,6-collidine (0.015 mL, 0.116 mmol) in CH_2Cl_2 (2 mL) at –78 °C was added acetyl chloride (0.004 mL, 0.058 mmol). The mixture was stirred at –78 °C for 18 h to afford crude acetate **78**. Et_3N (0.02 mL, 0.144 mmol) was added to the reaction mixture and the mixture was heated to reflux for 10 h. The reaction mixture was quenched by saturated $NaHCO_3$ solution. The aqueous phase was extracted with EtOAc (2 × 15 mL) and the combined organic extracts were washed with 1 M hydrochloric acid then saturated $NaHCO_3$ solution. The organic phase was then dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure to give crude enone **76**. The crude product was redissolved in EtOH/H_2O/1,4-dioxane (v/v/v = 8:2:1, 2 mL) and Raney®-Nickel (4 mg) was added to the solution. The mixture was activated with an atmosphere of H_2 (balloon) by three times followed by stirring under the same H_2 atmosphere at room temperature for another 1 h. The mixture was filtered and washed with EtOH. The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography (hexane:Et_2O, 1:2) to yield **77** (8.0 mg, 61% overall yield from **75**) as colorless crystals.

Ketone 77 from acetate 78. To a stirred solution of **78** (46.7 mg, 0.141 mmol) in CH_2Cl_2 (5 mL) was added Et_3N (0.059 mL, 0.42 mmol). The mixture was heated to reflux for 11 h then the solvent was removed under reduced pressure to give the crude enone **76**. The crude product was redissolved in EtOH/H_2O/1,4-dioxane (v/v/v = 8:2:1, 5 mL) and Raney®-Nickel (10 mg) was added to the solution. The mixture was activated with an atmosphere of H_2 (balloon) by three times followed by stirring under the same H_2 atmosphere at room temperature for another 1 h. The mixture was filtered and washed with EtOH. The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography (hexane:Et_2O, 1:2) to yield ketone **77** (37.2 mg, 97% overall yield from acetate **78**) as colorless crystals.

Acetate 78. To a stirred solution of **75** (51.3 mg, 0.177 mmol) and 2,4,6-collidine (0.056 mL, 0.424 mmol) in CH_2Cl_2 (5 mL) at –78 °C was added acetyl chloride (0.015 mL, 0.212 mmol). The reaction mixture was stirred at –78 °C for 12 h then was quenched by saturated $NaHCO_3$ solution. The aqueous phase was extracted with EtOAc (2 × 25 mL) and the combined organic extracts were washed with 1 M hydrochloric acid then saturated $NaHCO_3$ solution. The organic phase was then dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography (hexane:EtOAc, 2:3) to yield acetate **78** (49.3 mg, 87%) as colorless crystals: mp 140–141 °C; $[\alpha]_D^{20}$ –67.7 (*c* 0.63, $CHCl_3$); R_f 0.19 (hexane:EtOAc, 2:3); IR (thin film) 3472, 2995, 2952, 1739, 1456, 1378, 1241, 1139, 1117, 1037 cm^{-1}; ^1H NMR (300 MHz) δ 1.32 (3H, s), 1.37 (3H, s), 1.60 (1H, td, *J* = 14.1, 2.4 Hz), 2.03 (3H, s), 2.32 (1H, ddd, *J* = 14.1, 6.0, 3.3 Hz), 3.13–3.21 (1H, m), 3.21 (3H, s), 3.25 (3H, s), 3.82 (1H, dd, *J* = 10.8, 2.4 Hz), 4.15 (1H, dd, *J* = 11.4, 5.7

Hz), 4.22 (1H, q, J = 2.4 Hz), 4.37 (1H, dd, J = 11.4, 5.4 Hz), 4.80 (1H, d, J = 10.8 Hz); ^{13}C NMR (75 MHz) δ 18.0, 21.3, 32.0, 42.7, 48.5, 48.8, 62.4, 67.1, 72.5, 73.7, 100.4, 100.7, 171.3, 202.2; MS (ESI) *m/z* (relative intensity) 355 ([M+Na]$^+$, 100), 295 (17); HRMS (ESI) calcd for $C_{15}H_{24}O_8$ [M+Na]$^+$ 355.1363, found 355.1365.

2,3-*O*-Isopropylidene-*α*,*β*-D-ribofuranose (79). Concentrated H_2SO_4 (0.19 mL, 3.59 mmol) and anhydrous $CuSO_4$ (11.0 g) were added to a suspension of D-ribose (10.8 g, 71.7 mmol) in dry acetone (350 mL). The reaction mixture was stirred at room temperature for 1 d. The mixture was neutralized with saturated $NaHCO_3$ solution and then filtered. The filtrate was partitioned between EtOAc (200 mL) and water (200 mL). The aqueous layer was extracted with EtOAc (2 × 200 mL). The combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, and filtered. Concentration of the filtrate and the residue was purified by flash chromatography (hexane:EtOAc, 1:1) gave acetonide **79** (11.5 g, 84%) as a colorless oil: $[\alpha]_D^{20}$ –23.6 (*c* 2.65, $CHCl_3$) {lit.[68] $[\alpha]_D^{20}$ –27.4 (*c* 4.17, acetone)}; R_f 0.28 (hexane:EtOAc, 1:1); IR (thin film) 3403, 2988, 2942, 1459 cm^{-1}; ^{1}H NMR (300 MHz, mixture of *α* and *β* isomer with ratio *α*:*β*=1:10) δ 1.31 (3.0H, s), 1.38 (0.3H, s), 1.47 (3.0H, s), 1.56 (0.3H, s), 3.65–3.75 (2.2H, m), 3.92 (1.0H, br s), 4.16 (0.1H, t, J = 3.3 Hz), 4.38 (1.0H, t, J = 2.7 Hz), 4.56 (1.0H, d, J = 5.7 Hz), 4.62 (0.1H, dd, J = 6.9, 4.2 Hz), 4.70 (0.1H, dd, J = 6.6, 2.4 Hz), 4.80 (1.0H, d, J = 6 Hz), 5.18 (1.0H, d, J = 4.8 Hz), 5.39–5.44 (1.1H, m); ^{13}C NMR (75 MHz) δ 24.9, 26.3, 26.5, 63.3, 63.6, 79.6, 81.3, 81.7, 81.8, 86.8, 87.7, 97.3, 102.8, 112.4, 114.3; MS (FAB) *m/z* (relative intensity) 190 ([M]$^-$, 10), 189 ([M–H]$^-$, 100), 183 (55),

127 (51), 91 (68), 71 (59); HRMS (FAB) calcd for $C_8H_{14}O_5$ $[M-H]^-$ 189.0768, found 189.0764.

Alkene 80. To the stirred solution of acetonide **79** (10.6 g, 55.6 mmol) in THF (200 mL) was added vinylmagnesium bromide solution in THF (300 mL, 342 mmol) at –78 °C. The mixture was stirred at –78 °C for 1 h and then room temperature for 16 h. The reaction mixture was quenched by saturated NH_4Cl solution. The aqueous phase was extracted with EtOAc (3 × 300 mL) and the combined organic extracts were dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography (hexane:Et_2O, 1:4) to afford alkene **80** (9.54 g, 79%) as a white solid: mp 75 °C {lit.[9] mp 74 °C}; $[\alpha]_D^{20}$ –36.9 (*c* 1.77, $CHCl_3$) {lit.[9] $[\alpha]_D^{20}$ –31 (*c* 1.8, $CHCl_3$)}; R_f 0.24 (hexane:EtOAc, 1:2); IR (thin film) 3172, 2983, 2920, 1458, 1371, 1259, 1216, 1167, 1069 cm^{-1}; ^1H NMR (400 MHz) δ 1.33 (3H, s), 1.39 (3H, s), 3.30 (3H, br s), 3.71 (1H, dd, *J* = 10.9, 5.7 Hz), 3.88–3.94 (2H, m), 4.05 (1H, dd, *J* = 9.2, 5.3 Hz), 4.14 (1H, dd, *J* = 9.3, 5.4 Hz), 4.33 (1H, dd, *J* = 9.0, 6.1 Hz), 5.29 (1H, d, *J* = 10.5 Hz), 5.40 (1H, d, *J* = 17.2 Hz), 6.03 (1H, ddd, *J* = 16.9, 10.5, 5.8 Hz); ^{13}C NMR (100 MHz) δ 25.8, 28.3, 64.8, 69.8, 71.1, 78.0, 80.3, 109.4, 117.4, 137.9; MS (ESI) *m/z* (relative intensity) 241 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{10}H_{18}O_5$ $[M+Na]^+$ 241.1046, found 241.1047.

Isoxazoline 84. Following the glycol cleavage produce, alkene **80** (4.71 g, 21.6 mmol) was converted into lactol **81** as a colorless oil. $NaHCO_3$ (7.26 g, 86.4 mmol) and hydroxylamine hydrochloride (4.50 g, 64.8 mmol) were added to the solution of lactol **81** in MeOH (40 mL). The mixture was stirred at room temperature for 10 h. Deionized

water (100 mL) was added to the reaction mixture and the MeOH was removed under reduced pressure. The remaining aqueous solution was then extracted with EtOAc (3 × 100 mL) and the combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, and filtered. Concentration of the filtrate afforded crude oxime **82**. To a stirred suspension the crude oxime **82** and silica gel (230–400 mesh, 23.6 g) in EtOH (300 mL) was added chloramine-T trihydrate (9.13 g, 32.4 mmol) in small portions. After stirring at room temperature for 15 min, the silica gel was filtered. Concentration of the filtrate and the residue was purified by flash chromatography (hexane:EtOAc, 1:1) to yield isoxazoline **84** (3.36 g, 78% overall yield from alkene **80**) as a white solid: mp 75 °C; $[\alpha]_D^{20}$ +127.7 (*c* 1.23, $CHCl_3$); R_f 0.19 (hexane:EtOAc, 1:1); IR (thin film) 3305, 2987, 2939, 1647, 1381, 1267, 1212, 1159, 1103, 1053 cm^{-1}; ^1H NMR (400 MHz) δ 1.39 (3H, s), 1.54 (3H, s), 2.54 (1H, br s), 3.74 (1H, dd, *J* = 8.7, 5.1 Hz), 3.88 (1H, q, *J* = 9.3 Hz), 4.20 (1H, t, *J* = 9.0 Hz), 4.63 (1H, dd, *J* = 10.6, 8.8 Hz), 4.85 (1H, t, *J* = 5.2 Hz), 5.02 (1H, d, *J* = 5.3 Hz); ^{13}C NMR (100 MHz) δ 24.3, 26.3, 56.9, 72.3, 74.3, 74.5, 83.3, 113.3, 161.0; MS (ESI) *m/z* (relative intensity) 222 ($[M+Na]^+$, 100), 200 ($[M+H]^+$, 42); HRMS (ESI) calcd for $C_9H_{13}NO_4$ $[M+Na]^+$ 222.0737, found 222.0740.

Benzyl ether 86. Sodium hydride (60%, 110 mg, 2.76 mmol) was suspended in dry THF (5 mL) under nitrogen at 0 °C. A solution of the **84** (183 mg, 0.920 mmol) in THF (10 mL) was added dropwise over 1 h at 0 °C, and then the mixture was stirred at 0 °C for 1 h. Benzyl bromide (0.16 mL, 1.38 mmol) was added dropwise over 15 min. The reaction mixture was stirred at room temperature for 13 h. Water was then added

slowly at 0 °C to destroy the excess of hydride, and this was followed by the addition of saturated NH_4Cl solution. The aqueous layer was extracted with Et_2O (2 × 20 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, and filtered. Concentration of the filtrate and the residue was purified by flash chromatography (hexane:Et_2O, 3:2) to afford benzyl ether **86** (237 mg, 89%) as a white solid: mp 90 °C; $[\alpha]_D^{20}$ +51.4 (*c* 2.06, $CHCl_3$); R_f 0.13 (hexane:Et_2O, 3:2); IR (thin film) 2986, 2937, 2872, 1457, 1377, 1266, 1210, 1158, 1117, 1054 cm^{-1}; ^1H NMR (400 MHz) δ 1.39 (3H, s), 1.58 (3H, s), 3.53 (1H, dd, *J* = 9.3, 4.3 Hz), 3.87 (1H, dd, *J* = 10.0, 8.6 Hz), 4.09 (1H, qd, *J* = 10.2, 0.9 Hz), 4.45 (1H, dd, *J* = 10.4, 8.5 Hz), 4.58 (1H, d, *J* = 12.4 Hz), 4.66 (1H, d, *J* = 12.4 Hz), 4.94 (1H, dd, *J* = 5.2, 0.9 Hz), 4.98 (1H, t, *J* = 5.2 Hz), 7.29−7.39 (5H, m); ^{13}C NMR (100 MHz) δ 24.3 (CH_3), 26.5 (CH_3), 54.7 (CH), 71.9 (CH), 72.5 (CH_2), 74.3 (CH_2), 79.9 (CH), 83.4 (CH), 113.3 (C), 128.3 (CH), 128.7 (CH), 129.0 (CH), 137.4 (C), 161.8 (C); MS (ESI) *m/z* (relative intensity) 312 ($[M+Na]^+$, 100), 290 ($[M+H]^+$, 70); HRMS (ESI) calcd for $C_{16}H_{19}NO_4$ $[M+Na]^+$ 312.1206, found 312.1206.

Silyl ether 88. To a solution of isoxazoline **86** (251 mg, 0.869 mmol) in 1,4-dioxane/H_2O (v/v = 8:1, 12 mL) were added AcOH (1 mL, 17.4 mmol) and Raney®-Nickel (25 mg). The mixture was activated with an atmosphere of H_2 (balloon) by three times followed by stirring under the same H_2 atmosphere at room temperature for another 2 h. The mixture was filtered and washed with EtOH. The filtrate was concentrated under reduced pressure. The residue was purified by short column chromatography (hexane:EtOAc, 3:2) to afford ketone **87** (194 mg, 76%) as a colorless oil. The ketone **87** was then immediately redissolved in CH_2Cl_2 (10 mL), followed by

the addition of imidazole (109 mg, 1.60 mmol) and TBSCl (120 mg, 0.798 mmol). The mixture was stirred at room temperature for 18 h and was then quenched by saturated $NaHCO_3$ solution. The aqueous phase was extracted with EtOAc (3 × 25 mL) and the combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, and filtered. Concentration of the filtrate followed by flash chromatography (hexane:Et_2O, 8:1) to yield silyl ether **88** (162 mg, 60%) as a colorless oil: $[\alpha]_D^{20}$ +52.9 (*c* 0.30, $CHCl_3$); R_f 0.40 (hexane:Et_2O, 2:1); IR (thin film) 2930, 2858, 1761, 1462, 1378, 1255, 1213, 1099 cm^{-1}; ^1H NMR (400 MHz) δ −0.03 (6H, s), 0.78 (9H, s), 1.39 (3H, s), 1.44 (3H, s), 2.71 (1H, dd, *J* = 9.5, 1.3 Hz), 3.69 (1H, dd, *J* = 10.0, 2.7 Hz), 4.06 (1H, dd, *J* = 10.0, 2.1 Hz), 4.12 (1H, dd, *J* = 4.6, 1.0 Hz), 4.33 (1H, dd, *J* = 9.5, 3.8 Hz), 4.71 (1H, d, *J* = 12.2 Hz), 4.78 (1H, t, *J* = 4.2 Hz), 4.84 (1H, d, *J* = 12.2 Hz), 7.29–7.42 (5H, m); ^{13}C NMR (100 MHz) δ −5.4 (CH_3), −5.3 (CH_3), 18.5 (C), 25.8 (CH_3), 26.1 (CH_3), 27.4 (CH_3), 53.4 (CH), 59.1 (CH_2), 72.1 (CH_2), 72.9 (CH), 76.1 (CH), 81.4 (CH), 113.5 (C), 128.4 (CH), 128.9 (CH), 138.1 (C), 212.5 (C); MS (ESI) *m/z* (relative intensity) 429 ($[M+Na]^+$, 100), 413 (48); HRMS (ESI) calcd for $C_{22}H_{34}O_5Si$ $[M+Na]^+$ 429.2068, found 429.2070.

Alcohol 89. To a solution of silyl ether **88** (29.9 mg, 0.074 mmol) in EtOH (3 mL) was added 10% Pd-on-charcoal (5.0 mg). The mixture was activated with an atmosphere of H_2 (balloon) by three times followed by stirring under the same H_2 atmosphere at room temperature for another 2 h. The reaction mixture was filtered and washed with EtOH. The filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography (hexane:Et_2O, 2:1) to afford alcohol **89** (19.4 mg, 83%) as a white solid: mp 69 °C; $[\alpha]_D^{20}$ +112.6 (*c* 0.16, $CHCl_3$); R_f 0.13 (hexane:Et_2O,

2:1); IR (thin film) 3474, 2936, 2854, 1744, 1461, 1427, 1254, 1109, 1071 cm^{-1}; ^1H NMR (400 MHz) δ 0.03 (3H, s), 0.05 (3H, s), 0.85 (9H, s), 1.40 (3H, s), 1.47 (3H, s), 2.62–2.66 (1H, m), 3.90 (1H, dd, J = 10.0, 3.3 Hz), 3.99 (1H, dd, J = 10.0, 4.0 Hz), 4.22 (1H, dd, J = 5.2, 1.2 Hz), 4.43 (1H, dd, J = 8.4, 4.6 Hz), 4.82 (1H, t, J = 4.9 Hz); ^{13}C NMR (100 MHz) δ −5.3 (CH_3), −5.3 (CH_3), 18.5 (C), 25.5 (CH_3), 26.2 (CH_3), 27.0 (CH_3), 55.3 (CH), 60.2 (CH_2), 69.2 (CH), 77.8 (CH), 80.9 (CH), 113.9 (C), 211.6 (C); MS (ESI) *m/z* (relative intensity) 339 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{15}H_{28}O_5Si$ $[M+Na]^+$ 339.1598, found 339.1591.

Enone 90. To a stirred solution of alcohol **89** (79.1 mg, 0.250 mmol) and triethylamine (0.10 mL, 0.750 mmol) in CH_2Cl_2 (7 mL) at 0 °C were added methanesulfonyl chloride (0.03 mL, 0.375 mmol). The reaction mixture was stirred at room temperature for 1 h and was quenched by saturated $NaHCO_3$ solution. The aqueous phase was extracted with EtOAc (3 × 20 mL) and the combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, and filtered. Concentration of the filtrate and the residue was purified by flash chromatography (hexane:Et_2O, 8:1) to yield enone **90** (64.4 mg, 86%) as a colorless oil: $[\alpha]_D^{20}$ −11.0 (*c* 0.36, $CHCl_3$); R_f 0.13 (hexane:Et_2O, 8:1); IR (thin film) 2932, 2857, 1725, 1376, 1255, 1204, 1123, 1089 cm^{-1}; ^1H NMR (400 MHz) δ 0.07–0.08 (6H, 2s), 0.91 (9H, s), 1.40–1.41 (6H, 2s), 4.36 (2H, t, J = 1.8 Hz), 4.53 (1H, d, J = 5.4 Hz), 5.22 (1H, dq, J = 5.6, 1.8 Hz), 7.43 (1H, q, J = 2.1 Hz); ^{13}C NMR (100 MHz) δ −5.2 (CH_3), −5.1 (CH_3), 18.6 (C), 26.2 (CH_3), 26.5 (CH_3), 27.9 (CH_3), 58.2 (CH_2), 77.3 (CH), 78.4 (CH), 115.8 (C), 147.7 (C), 152.9 (CH), 202.0 (C); MS (ESI) *m/z* (relative intensity) 299 ($[M+H]^+$, 100); HRMS (ESI) calcd for $C_{15}H_{26}O_4Si$ $[M+H]^+$ 299.1673, found 299.1666.

Alcohol 91. To a solution of enone **90** (33.3 mg, 0.112 mmol) in THF (3 mL) was added AcOH (0.12 mL, 2.10 mmol) a 1 M THF solution of TBAF (0.12 mL, 0.123 mmol). The reaction mixture was stirred at room temperature for 4 h and the solvent was removed under reduced pressure. Flash chromatography of the residue (hexane: EtOAc, 1:1) afforded alcohol **91** (18.4 mg, 90%) as a colorless oil: $[\alpha]_D^{20}$ +16.2 (*c* 1.54, $CHCl_3$); R_f 0.19 (hexane:EtOAc, 1:1); IR (thin film) 3428, 2990, 2933, 1720, 1380, 1206, 1101, 1061 cm^{-1}; ^1H NMR (400 MHz) δ 1.38−1.39 (6H, 2s), 2.72 (1H, br s), 4.34 (2H, s), 4.51 (1H, d, *J* = 5.5 Hz), 5.21−5.23 (1H, m), 7.44 (1H, q, *J* = 1.7 Hz); ^1H NMR (400 MHz, $CDCl_3$-D_2O) δ 1.38−1.39 (6H, 2s), 4.33 (2H, s), 4.51 (1H, d, *J* = 5.4 Hz), 5.21−5.23 (1H, m), 7.44 (1H, d, *J* = 1.3 Hz); ^{13}C NMR (100 MHz) δ 26.3 (CH_3), 27.7 (CH_3), 57.4 (CH_2), 77.3 (CH), 78.0 (CH), 115.9 (C), 146.3 (C), 153.5 (CH), 202.8 (C); MS (ESI) *m/z* (relative intensity) 207 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_9H_{12}O_4$ $[M+Na]^+$ 207.0628, found 207.0632.

Alcohol 91 by reacting 92 with SmI_2. To a stirred solution of isoxazoline **84** (49.7 mg, 0.249 mmol) and pyridine (0.044 mL, 0.549 mmol) in CH_2Cl_2 (4 mL) was added trifluoromethanesulfonic anhydride (0.046 mL, 0.274 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 30 min and was quenched by saturated $NaHCO_3$ solution. The aqueous phase was extracted with EtOAc (3 × 15 mL) and the combined organic extracts were concentrated under reduced pressure to give crude triflate **93**. The crude product was then redissolved in CH_2Cl_2 (2 mL) and triethylamine (0.17 mL, 1.25 mmol) was added. The reaction mixture was stirred at room temperature for 2 d and then was filtered. Concentration of filtrate gave crude **92**

and then 0.1 M THF solution of SmI_2 (7.4 mL, 0.750 mmol) was added. The mixture was stirred at room temperature for 2 h and then quenched by water. The aqueous phase was extracted with EtOAc (3 × 15 mL) and the combined organic extracts were concentrated under reduced pressure. The residue was purified by flash chromatography (hexane:EtOAc, 1:1) to afford alcohol **91** (28.3 mg, 62% overall yield from isoxazoline **84**) as a colorless oil.

Acetate 94. To a stirred solution of alcohol **91** (17.1 mg, 0.093 mmol) and triethylamine (0.031 mL, 0.223 mmol) in CH_2Cl_2 (2 mL) at 0 °C were added acetic anhydride (0.010 mL, 0.111 mmol) and DMAP (1.1 mg, 0.009 mmol). The reaction mixture was stirred at room temperature for 1 h and was quenched by saturated $NaHCO_3$ solution. The aqueous phase was extracted with EtOAc (3 × 15 mL) and the combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, and filtered. Concentration of the filtrate and the residue was purified by flash chromatography (hexane:Et_2O, 1:1) to yield acetate **94** (17.5 mg, 83%) as a colorless oil: $[\alpha]_D^{20}$ +6.2 (*c* 0.53, $CHCl_3$); R_f 0.22 (hexane:Et_2O, 1:1); IR (thin film) 2991, 2939, 1746, 1726, 1373, 1226, 1204, 1099, 1055 cm^{-1}; ^1H NMR (400 MHz) δ 1.39 (3H, s), 1.40 (3H, s), 2.10 (3H, s), 4.53 (1H, d, J = 5.5 Hz), 4.73−4.81 (2H, m), 5.21−5.24 (1H, m), 7.40 (1H, q, J = 1.7 Hz); ^{13}C NMR (100 MHz) δ 21.1, 26.5, 27.8, 58.1, 77.3, 77.8, 116.0, 142.3, 154.6, 170.7, 201.1; MS (ESI) *m/z* (relative intensity) 249 ($[M+Na]^+$, 88), 213 (100); HRMS (ESI) calcd for $C_{11}H_{14}O_5$ $[M+Na]^+$ 249.0733, found 249.0732.

Diol 95. To a stirred solution of acetate **94** (17.5 mg, 0.077 mmol) in CH_2Cl_2 (2 mL) were added deionized water (0.05 mL) and TFA (0.5 mL) at room temperature to

form a clear solution. The mixture was stirred at room temperature for 1 h. Concentration of the reaction mixture under reduced pressure and the residue was purified by flash chromatography (hexane:EtOAc, 1:8) furnished diol **95** (11.8 mg, 82%) as a white solid: mp 40–41 °C; $[\alpha]_D^{20}$ −24.4 (*c* 0.44, $CHCl_3$); R_f 0.21 (hexane:EtOAc, 1:8); IR (thin film) 3409, 2924, 1728, 1372, 1244, 1146, 1065 cm^{-1}; ^1H NMR (400 MHz, MeOD) δ 2.09 (3H, s), 4.11 (1H, d, *J* = 5.4 Hz), 4.73–4.77 (3H, m), 7.45 (1H, dt, *J* = 3.0, 1.5 Hz); ^{13}C NMR (100 MHz) δ 21.1 (CH_3), 58.2 (CH_2), 68.0 (CH), 72.1 (CH), 141.8 (C), 156.1 (CH), 171.0 (C), 205.2 (C); MS (ESI) *m/z* (relative intensity) 209 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_8H_{10}O_5$ $[M+Na]^+$ 209.0420, found 209.0421.

Carboxylic acid 96. To a stirred solution of alcohol **91** (11.7 mg, 0.063 mmol) and triethylamine (0.020 mL, 0.140 mmol) in CH_2Cl_2 (0.8 mL) at 0 °C were added succinic anhydride (7.0 mg, 0.070 mmol). The reaction mixture was stirred at room temperature for 30 min until the disappearance of the starting material as shown on TLC. Acetic acid (0.072 mL, 1.30 mmol) was added at room temperature and the mixture was stirred for 2 h. The reaction mixture was concentrated under reduced pressure and the residue was purified by flash chromatography ($CHCl_3$:MeOH, 40:1) to give carboxylic acid **96** (13.3 mg, 74%) as a colorless oil: $[\alpha]_D^{20}$ −2.9 (*c* 0.63, $CHCl_3$); R_f 0.31 ($CHCl_3$:MeOH, 19:1); IR (thin film) 3498, 2988, 2923, 1725, 1374, 1204, 1155, 1098, 1046 cm^{-1}; ^1H NMR (400 MHz) δ 1.39 (3H, s), 1.41 (3H, s), 2.65–2.73 (4H, m), 4.54 (1H, d, *J* = 5.5 Hz), 4.78 (1H, d, *J* = 15.1 Hz), 4.84 (1H, dt, *J* = 15.1, 1.4 Hz), 5.22–5.24 (1H, m), 7.42 (1H, q, *J* = 2.0 Hz); ^{13}C NMR (100 MHz, C_6D_6) δ 26.3 (CH_3), 27.6 (CH_3), 28.6 (CH_2), 28.8 (CH_2), 58.2 (CH_2), 77.3 (CH), 77.6 (CH), 115.2 (C), 141.8 (C), 154.1

(CH), 171.4 (C), 178.0 (C), 200.2 (C); MS (ESI) *m/z* (relative intensity) 307 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{13}H_{16}O_7$ $[M+Na]^+$ 307.0788, found 307.0787.

Isoxazolidine 97. Following the glycol cleavage produce, diol **106** (137 mg, 0.56 mmol) was converted into aldehyde **107** as a colorless oil. The crude product was then redissolved in CH_3CN (15 mL), followed by addition of *N*-benzylhydroxylamine (72.5 mg, 0.59 mmol) at room temperature. The mixture was stirred at room temperature for 30 min until the disappearance of the starting material as shown on TLC. The mixture was then heated under reflux for 26 h. After cooling, the reaction mixture was concentrated under reduced pressure and the residue was purified by flash chromatography (hexane:Et_2O, 4:1) to furnish isoxazolidine **97** (153 mg, 86% overall yield from diol **106**) as a colorless oil: $[\alpha]_D^{20}$ +116.6 (*c* 0.44, $CHCl_3$); R_f 0.18 (hexane:Et_2O, 7:2); IR (thin film) 2970, 2939, 1496, 1454, 1353, 1304, 1201, 1167, 1146, 1080 cm^{-1}; ^1H NMR (300 MHz) δ 0.90 (6H, t, J = 7.5 Hz), 1.38 (1H, ddd, J = 13.2, 11.1, 2.7 Hz), 1.63 (4H, q, J = 7.5 Hz), 1.73 (1H, ddd, J = 14.1, 10.2, 0.6 Hz), 1.94 (1H, d, J = 13.2 Hz), 2.19 (1H, ddd, J = 14.1, 6.3, 3.9 Hz), 2.30 (1H, dt, J = 12.9, 3.9 Hz), 2.52 (1H, dt, J = 13.2, 8.4 Hz), 3.51 (1H, quin, J = 3.9 Hz), 3.68–3.79 (2H, m), 4.04 (1H, d, J = 12.9 Hz), 4.18 (1H, td, J = 10.8, 4.2 Hz), 4.70 (1H, dd, J = 9.6, 3.9 Hz), 7.24–7.38 (5H, m); ^{13}C NMR (75 MHz) δ 8.5 (CH_3), 8.8 (CH_3), 30.9 (CH_2), 31.2 (CH_2), 33.4 (CH_2), 35.3 (CH_2), 37.3 (CH_2), 60.2 (CH), 63.1 (CH_2), 75.7 (CH), 76.9 (CH), 78.4 (CH), 112.2 (C), 128.0 (CH), 129.0 (CH), 129.4 (CH), 137.8 (C); MS (ESI) *m/z* (relative intensity) 340 ($[M+Na]^+$, 100), 318 ($[M+H]^+$, 76); HRMS (ESI) calcd for $C_{19}H_{27}NO_3$ $[M+Na]^+$ 340.1883, found 340.1882.

Dimethyl-2,3-*O*-(3,3-pentylidene)-L-tartrate (100). Acetyl chloride (2.61 mL, 33.3 mmol) was added dropwise to methanol (200 mL) at 0 °C. L-Tartaric acid (5.39 g, 33.3 mmol) was added and the mixture was heated to reflux for 2 h. The solvent was removed under reduced pressure to give crude **99**. It was then redissolved in 3-pentanone (50 mL). Concentrated phosphoric acid (1 mL) was added and the mixture was heated to reflux with Dean and Stark apparatus for 5 d. The mixture was cooled to room temperature, concentrated and redissolved in EtOAc (100 mL). The mixture was washed with saturated $NaHCO_3$ solution (2 × 50 mL). The combined aqueous solution was then extracted with EtOAc (2 × 50 mL) and the combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, and filtered. Concentration of the filtrate and the residue was purified by flash chromatography (hexane:Et_2O, 3:1) to give **100** (7.82 g, 88% overall yield from L-tartaric acid) as a colorless oil: $[\alpha]_D^{20}$ –17.6 (*c* 0.96, $CHCl_3$) {lit.[90] $[\alpha]_D^{25}$ –16.4 (*c* 3.35, $CHCl_3$)}; R_f 0.25 (hexane:Et_2O, 3:1); IR (thin film) 2977, 2954, 2855, 1761, 1463, 1439, 1361, 1205, 1172, 1113, 1021 cm^{-1}; ^1H NMR (300 MHz) δ 0.94 (6H, t, J = 7.5 Hz), 1.73 (4H, q, J = 7.5 Hz), 3.82 (6H, s), 4.75 (2H, s); ^{13}C NMR (75 MHz) δ 8.3, 30.0, 53.2, 77.7, 118.4, 170.4; MS (ESI) *m/z* (relative intensity) 269 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{11}H_{18}O_6$ $[M+Na]^+$ 269.1007, found 269.1105.

Diol 101. To a stirred solution of **100** (1.36 g, 5.52 mmol) in THF (40 mL) at 0 °C were added $LiAlH_4$ (0.23 g, 6.09 mmol) and the mixture was heated to reflux for 2 h. The reaction mixture was cooled to 0 °C and was quenched with water and saturated NH_4Cl solution. The aqueous phase was extracted with EtOAc (3 × 100 mL) and the

combined organic extracts were dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography (hexane:EtOAc, 1:2) to afford diol **101** (1.04 g, 99%) as a white solid: mp 43–45 °C {lit.[90] mp 43.5–45 °C}; $[\alpha]_D^{20}$ +1.6 (*c* 0.48, $CHCl_3$) {lit.[90] $[\alpha]_D^{25}$ +2.80 (*c* 5.0, $CHCl_3$)}; R_f 0.23 (hexane:EtOAc, 1:2); IR (thin film) 3396, 2974, 2940, 2883, 1464, 1201, 1173, 1084, 1055 cm^{-1}; ^1H NMR (300 MHz) δ 0.91 (6H, t, *J* = 7.5 Hz), 1.66 (4H, q, *J* = 7.5 Hz), 2.13 (2H, br s), 3.69–3.83 (4H, m), 3.96–3.98 (2H, m); ^{13}C NMR (75 MHz) δ 8.5, 30.8, 62.6, 78.7, 113.4; MS (ESI) *m/z* (relative intensity) 213 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_9H_{18}O_4$ $[M+Na]^+$ 213.1108, found 213.1113.

Dimesylate 102. To a stirred solution of diol **101** (1.28 g, 6.75 mmol) and triethylamine (5.64 mL, 40.5 mmol) in CH_2Cl_2 (100 mL) at 0 °C was added methanesulfonyl chloride (1.57 mL, 20.2 mmol). The mixture was stirred at room temperature for 2 h then was quenched by saturated $NaHCO_3$ solution. The aqueous phase was extracted with Et_2O (2 × 100 mL) and the combined organic extracts were dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography (hexane:EtOAc, 1:1) to give dimesylate **102** (2.18 g, 93%) as a colorless oil: $[\alpha]_D^{20}$ –4.4 (*c* 3.82, $CHCl_3$); R_f 0.47 (hexane:EtOAc, 1:2); IR (thin film) 2977, 2943, 1464, 1356, 1175, 1088 cm^{-1}; ^1H NMR (300 MHz) δ 0.90 (6H, t, *J* = 7.5 Hz), 1.66 (4H, q, *J* = 7.5 Hz), 3.07 (6H, s), 4.14–4.15 (2H, m), 4.35–4.36 (4H, m); ^{13}C NMR (75 MHz) δ 8.3, 30.6, 38.1, 68.3, 75.8, 115.2; MS (ESI) *m/z* (relative intensity) 369 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{11}H_{22}S_2O_8$ $[M+Na]^+$ 369.0648, found 369.0646.

Dialkene 103. The solution of vinylmagnesium bromide in THF (4.0 mL, 2.3 mmol) freshly generated was added to the solution of copper (I) iodide (49.8 mg, 0.26 mmol) in THF (2 mL) at –78 °C. The mixture was stirred at –78 °C for 30 min, followed by the adding a solution of diiodide **105** (104 mg, 0.25 mmol) in THF (2 mL). The mixture was stirred at –30 °C for 12 h. The reaction was then quenched by saturated NH_4Cl solution. The aqueous phase was extracted with Et_2O (3 × 20 mL) and the combined organic extracts were dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography (hexane:CH_2Cl_2, 3:1) to afford dialkene **103** (39.0 mg, 73%) as a colorless oil: $[\alpha]_D^{20}$ –33.6 (*c* 1.22, $CHCl_3$); R_f 0.33 (hexane:CH_2Cl_2, 3:1); IR (thin film) 2974, 2940, 1464, 1357, 1176, 1084 cm^{-1}; ^1H NMR (300 MHz) δ 0.90 (6H, t, *J* = 7.5 Hz), 1.63 (4H, q, *J* = 7.5 Hz), 2.29–2.37 (4H, m), 3.68–3.73 (2H, m), 5.07–5.11 (3H, m), 5.14–5.16 (1H, m), 5.86 (2H, ddt, *J* = 17.1, 10.2, 7.2 Hz); ^{13}C NMR (75 MHz) δ 8.5, 31.1, 37.5, 80.2, 112.3, 117.8, 134.5; MS (CI) *m/z* (relative intensity) 211 ($[M+H]^+$, 100), 181 (81), 169 (30) 125 (37); HRMS (CI) calcd for $C_{13}H_{22}O_2$ $[M+H]^+$ 211.1693, found 211.1692.

Ditosylate 104. To a mixture of 3 Å molecular sieves (0.5 g) and diol **101** (102 mg, 0.54 mmol) in pyridine (6 mL) at 0 °C was added *p*-toluenesulfonyl chloride (829 mg, 4.35 mmol) then the mixture was stirred at room temperature for 3 d. The mixture was filtered, diluted with EtOAc and washed with 0.2 M NaOH solution (2 × 10 mL). The aqueous layer was extracted with EtOAc (2 × 25 mL) and the combined organic extracts were dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated

under reduced pressure and the residue was purified by flash chromatography (hexane:Et_2O, 1:1) to afford tosylate **104** (264 mg, 99%) as a white solid: mp 86–88 °C; $[\alpha]_D^{20}$ –10.2 (*c* 1.28, $CHCl_3$); R_f 0.24 (hexane:Et_2O, 1:1); IR (thin film) 2975, 2941, 2883, 1598, 1495, 1463, 1363, 1307, 1190, 1177, 1096 cm^{-1}; ^1H NMR (300 MHz) δ 0.78 (6H, t, *J* = 7.5 Hz), 1.53 (4H, q, *J* = 7.5 Hz), 2.46 (6H, s), 3.97–3.98 (2H, m), 4.09–4.10 (4H, m), 7.36 (4H, d, *J* = 8.4 Hz), 7.78 (4H, d, *J* = 8.1 Hz); ^{13}C NMR (75 MHz) δ 8.2, 22.1, 30.5, 68.8, 75.7, 115.1, 128.5, 130.4, 132.9, 145.7; MS (ESI) *m/z* (relative intensity) 537 (100), 521 ($[M+Na]^+$, 66); HRMS (ESI) calcd for $C_{23}H_{30}S_2O_8$ $[M+Na]^+$ 521.1274, found 521.1300.

Diiodide 105 from diol 101. To a stirred solution of diol **101** (491 mg, 2.58 mmol), triphenylphosphine (2.03 g, 7.74 mmol) and imidazole (703 mg, 10.3 mmol) in toluene (50 mL) were added iodine (1.64 g, 6.45 mmol) and the mixture was stirred at room temperature for 2 d. The reaction was quenched with saturated $Na_2S_2O_3$ solution, the aqueous phase was extracted with Et_2O (2 × 50 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography (hexane:CH_2Cl_2, 5:1) to yield diiodide **105** (813 mg, 77%) as a yellowish oil: $[\alpha]_D^{20}$ –3.1 (*c* 0.55, $CHCl_3$); R_f 0.21 (hexane:CH_2Cl_2, 5:1); IR (thin film) 2972, 2938, 2880, 1463, 1354, 1271, 1203, 1169, 1107, 1068 cm^{-1}; ^1H NMR (300 MHz) δ 0.93 (6H, t, *J* = 7.5 Hz), 1.69 (4H, q, *J* = 7.5 Hz), 3.33–3.43 (4H, m), 3.74–3.81 (2H, m); ^{13}C NMR (75 MHz) δ 6.4, 8.6, 31.0, 80.7, 114.0; MS (EI) *m/z* (relative intensity) 381 ($[M-C_2H_5]^+$, 45), 57 (68), 44 (100); HRMS (EI) calcd for $C_9H_{16}I_2O_2$ $[M-C_2H_5]^+$ 380.8843, found 380.8847.

Diiodide 105 from dimesylate 102. Sodium iodide (526 mg, 3.50 mmol) were added to a solution of dimesylate **102** (304 mg, 0.88 mmol) in 3-pentanone (15 mL). The mixture was heated to reflux for 1 d. The reaction mixture was partitioned between Et_2O (20 mL) and saturated $Na_2S_2O_3$ solution (15 mL). The aqueous layer was extracted with Et_2O (2 × 20 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography (hexane:CH_2Cl_2, 5:1) to give diiodide **105** (314 mg, 87%) as a yellowish oil.

Diol 106 by OsO_4 dihydroxylation. NMO (75.9 mg, 0.65 mmol) was added to a solution of dialkene **103** (118 mg, 0.56 mmol) in acetone/H_2O (v/v = 4:1, 10 mL) with a catalytic amount of osmium tetraoxide (0.72 mL of 10 mg mL^{-1} *t*-butanol solution, 0.028 mmol) at room temperature and stirred for 2 h. The reaction mixture was then diluted with EtOAc (25 mL) and quenched with saturated $Na_2S_2O_3$ solution (15 mL). The resultant mixture was extracted with EtOAc (2 × 25 mL). The combined extracts were washed with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated and the residue was purified by flash chromatography (hexane:CH_2Cl_2, 3:1 to hexane:EtOAc, 1:1) to afford firstly starting material dialkene **103** (39.8 mg, 34%) and secondly diol **106** (61.6 mg, 45%) as a colorless oil: $[\alpha]_D^{20}$ −35.8 (*c* 0.70, $CHCl_3$); R_f 0.22 (hexane:EtOAc, 1:1); IR (thin film) 3401, 2975, 2940, 2882, 1643, 1465, 1355, 1202, 1175, 1084 cm^{-1}; ^1H NMR (300 MHz) δ 0.89 (6H, t, *J* = 7.5 Hz), 1.55−1.86 (6H, m), 2.35 (2H, t, *J* = 5.7 Hz), 2.56 (2H, br s), 3.50−3.75 (1H, m), 3.63−3.74 (2H, m), 3.83 (1H, qd, *J* = 8.7, 2.7 Hz), 3.91−3.98 (1H, m), 5.08−5.16 (2H, m), 5.77−5.91 (1H, m); ^{13}C

NMR (75 MHz) δ 8.4, 8.5, 8.6, 31.0, 31.0, 31.1, 35.8, 36.4, 37.0, 66.8, 67.2, 70.4, 71.6, 78.3, 80.3, 80.6, 81.3, 112.8, 113.3, 118.1, 118.2, 134.0, 134.1; MS (ESI) *m/z* (relative intensity) 267 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{13}H_{24}O_4$ $[M+Na]^+$ 267.1578, found 267.1571.

Diol 106 by RuO_4 dihydroxylation. $NaIO_4$ (10.8 mg, 0.050 mmol) in deionized water (0.3 mL) was added to a solution of dialkene **103** (10.6 mg, 0.050 mmol) and ruthenium trichloride (0.7 mg, 0.004 mmol) in CH_3CN/EtOAc (v/v = 1:1, 2 mL) at room temperature and stirred for 1 min. The reaction was quenched with saturated $Na_2S_2O_3$ solution (5 mL). The resultant mixture was extracted with EtOAc (3 × 10 mL). The combined extracts were washed with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated and the residue was purified by flash chromatography (hexane:CH_2Cl_2, 3:1 to hexane:EtOAc, 1:1) to afford firstly starting material dialkene **103** (5.3 mg, 50%) and secondly diol **106** (3.3 mg, 27%) as a colorless oil.

Diol 108. To a stirred solution of isoxazolidine **97** (203 mg, 0.64 mmol) in CH_2Cl_2 (15 mL) were added deionized water (0.8 mL) and TFA (3 mL) at room temperature to form a clear solution. The mixture was stirred at room temperature for 1 h. Concentration of the mixture under reduced pressure and the residue was purified by flash chromatography ($CHCl_3$:MeOH, 50:1) to yield diol **108** (162 mg, 100%) as a white solid: mp 127−128 °C; $[\alpha]_D^{20}$ +170.8 (*c* 0.50, MeOH); R_f 0.12 ($CHCl_3$:MeOH, 50:1); IR (thin film) 3355, 2922, 2853, 1495, 1453, 1314, 1077, 1028 cm^{-1}; ^1H NMR (300 MHz,

MeOD) δ 1.42 (1H, ddd, J = 13.5, 10.2, 2.7 Hz), 1.61 (1H, dd, J = 14.7, 9.3 Hz), 1.97 (1H, d, J = 12.6 Hz), 2.02–2.07 (1H, m), 2.15 (1H, ddd, J = 14.7, 6.3, 3.9 Hz), 2.52–2.62 (1H, m), 3.46–3.49 (1H, m), 3.59 (1H, td, J = 9.0, 6.3 Hz), 3.73, (1H, d, J = 12.6 Hz), 3.82 (1H, td, J = 9.9, 3.9 Hz), 3.96 (1H, d, J = 12.6 Hz), 4.63 (1H, s), 7.27–7.37 (5H, m); ^{13}C NMR (75 MHz, MeOD) δ 34.0, 40.4, 41.8, 61.0, 63.2, 71.9, 73.4, 76.7, 128.6, 129.4, 130.6, 138.4; MS (ESI) *m/z* (relative intensity) 272 ($[M+Na]^+$, 100), 250 ($[M+H]^+$, 57); HRMS (ESI) calcd for $C_{14}H_{19}NO_3$ $[M+Na]^+$ 272.1257, found 272.1259.

Amine 109. To a solution of diol **108** (17.8 mg, 0.071 mmol) in ^{t}BuOH/H_2O (v/v = 5:1, 1.5 mL) was added 10% Pd-on-charcoal (5.0 mg). The mixture was activated with an atmosphere of H_2 (balloon) by three times followed by stirring under the same H_2 atmosphere at room temperature for another 36 h. The reaction mixture was filtered and washed with EtOH. The filtrate was concentrated under reduced pressure. The residue was purified by Sephadex LH-20 (eluent: EtOH) to afford amine **109** (10.8 mg, 94%) as a colorless oil: $[\alpha]_D^{20}$ −6.1 (*c* 0.84, $CHCl_3$); R_f 0.34 ($CHCl_3$:MeOH:30% aq. NH_3, 1.2:1.8:0.5); ^{1}H NMR (400 MHz, MeOD) δ 1.47 (1H, q, J = 11.0 Hz), 1.72 (1H, dt, J = 13.6, 10.4 Hz), 1.84–1.89 (1H, m), 1.97–2.09 (2H, m), 2.16–2.20 (1H, m), 3.22–3.29 (1H, m), 3.55 (1H, ddd, J = 10.1, 7.0, 2.9 Hz), 3.75 (1H, dt, J = 7.1, 4.4 Hz), 3.84 (1H, tt, J = 10.6, 3.8 Hz); ^{13}C NMR (100 MHz, MeOD) δ 41.0 (CH_2), 43.9 (CH_2), 44.5 (CH), 46.4 (CH_2), 68.2 (CH), 73.7 (CH), 73.9 (CH); MS (ESI) *m/z* (relative intensity) 162 ($[M+H]^+$, 100), 149 (90); HRMS (ESI) calcd for $C_7H_{15}NO_3$ $[M+H]^+$ 162.1125, found 162.1127.

2,3-*O*-Isopropylidene-*α*,*β*-L-erythrose (123). To a stirred solution of acetonide **79** (11.5 g, 60.3 mmol) in deionized water (250 mL) at 0 °C was added $NaBH_4$ (3.42 g, 90.5 mmol). The mixture was stirred at 0 °C for 1 h and then at room temperature for a further 2 h. The reaction mixture was quenched by dropwise addition of AcOH (20 mL) at 0 °C. $NaIO_4$ was then added to the reaction mixture at 0 °C and stirred at 0 °C for 1 h. MeOH (500 mL) was added to precipitate out most of the salt. The salt was filtered off and washed with EtOAc. Concentration of filtrate under reduced pressure and the residue was purified by flash chromatography (hexane:Et_2O, 2:3) to yield lactol **123** (8.44 g, 87%) as a colorless oil: $[\alpha]_D^{20}$ +73.6 (*c* 1.70, $CHCl_3$) {lit.[80] $[\alpha]_D^{25}$ +72 (*c* 2.4, MeOH)}; R_f 0.38 (hexane:Et_2O, 2:3); IR (thin film) 3427, 2943, 1376, 1210, 1100, 1068 cm^{-1}; ^1H NMR (300 MHz) δ 1.32 (3H, s), 1.47 (3H, s), 2.74 (1H, d, J = 2.4 Hz), 4.00 (1H, d, J = 10.2 Hz), 4.05 (1H, dd, J = 10.5, 3.3 Hz), 4.57 (1H, d, J = 6.0 Hz), 4.82 (1H, dd, J = 6.0, 3.3 Hz), 5.42 (1H, d, J = 2.4 Hz); ^{13}C NMR (75 MHz) δ 25.1, 26.6, 72.4, 80.3, 85.5, 102.1, 112.7; MS (ESI) *m/z* (relative intensity) 183 ($[M+Na]^+$, 100), 149 (19), 143 ($[M–OH]^+$, 14); HRMS (ESI) calcd for $C_7H_{12}O_4$ $[M+Na]^+$ 183.0628, found 183.0635.

Alkenes 124 and 125. To a stirred solution of lactol **123** (15.0 g, 93.6 mmol) in dry THF (300 mL) was added a Et_2O solution of allylmagnesium bromide (89 mL, 1.03 mol) dropwise at 0 °C under N_2. After the addition, the mixture was allowed to rise to room temperature and stirred for another 12 h. The mixture was quenched with saturated NH_4Cl solution and the aqueous phase was extracted with EtOAc (3 × 500 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and filtered.

The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography (hexane:Et_2O, 2:3) to afford firstly alkene **124** (13.4 g, 71%) as a colorless oil and secondly its 4-epimer alkene **125** (4.01 g, 21%) as a colorless oil. Data for **124**: $[\alpha]_D^{20}$ –5.4 (*c* 2.14, $CHCl_3$); R_f 0.21 (hexane:Et_2O, 2:3); IR (thin film) 3386, 3078, 2982, 2927, 1641, 1381, 1219, 1166 cm^{-1}; ^1H NMR (300 MHz) δ 1.35 (3H, s), 1.41 (3H, s), 2.15 (1H, dt, *J* = 14.1, 8.4 Hz), 2.31 (3H, br s), 2.59–2.66 (1H, m), 3.73 (1H, dd, *J* = 11.4, 4.5 Hz), 3.79–3.89 (2H, m), 3.96 (1H, dd, *J* = 9.0, 5.7 Hz), 4.29 (1H, dt, *J* = 8.1, 5.4 Hz), 5.18 (1H, d, *J* = 2.4 Hz), 5.23 (1H, s), 5.81–5.95 (1H, m); ^{13}C NMR (75 MHz) δ 25.7, 28.3, 39.0, 61.1, 69.0, 77.6, 79.7, 108.8, 119.0, 134.4; MS (ESI) *m/z* (relative intensity) 225 ($[M+Na]^+$, 100), 222 (5), 185 ($[M–OH]^+$, 3); HRMS (ESI) calcd for $C_{10}H_{18}O_4$ $[M+Na]^+$ 225.1097, found 225.1105.

Data for **125**: $[\alpha]_D^{20}$ –16.4 (*c* 1.12, $CHCl_3$); R_f 0.14 (hexane:Et_2O, 2:3); IR (thin film) 3410, 3077, 2985, 2936, 1642, 1381, 1217, 1166 cm^{-1}; ^1H NMR (300 MHz) δ 1.38 (3H, s), 1.52 (3H, s), 2.00 (3H, br s), 2.29–2.45 (2H, m), 3.74–3.85 (3H, m), 4.09 (1H, dd, *J* = 6.9, 3.0 Hz), 4.20 (1H, dt, *J* = 6.9, 5.1 Hz), 5.12 (1H, s), 5.16 (1H, d, *J* = 10.8 Hz), 5.80–5.93 (1H, m); ^{13}C NMR (75 MHz) δ 25.2, 27.3, 39.4, 61.0, 68.8, 77.5, 78.5, 108.4, 118.0, 134.6; MS (ESI) *m/z* (relative intensity) 225 ($[M+Na]^+$, 100), 222 (4), 185 ($[M– OH]^+$, 2); HRMS (ESI) calcd for $C_{10}H_{18}O_4$ $[M+Na]^+$ 225.1097, found 225.1101.

Lactols 126 and 127. To a solution of alkene **125** (484 mg, 2.93 mmol) in DMSO (10 mL) was added IBX (822 mg, 2.93 mmol) and the mixture was stirred at room temperature for 2 d. The mixture was partitioned between Et_2O (50 mL) and water (25 mL). The aqueous layer was extracted with Et_2O (2 × 50 mL). The combined

organic extracts were dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography (hexane:Et_2O, 3:2) to give firstly lactol **126** (371 mg, 77%) as a colorless oil and secondly its regioisomer **127** (56.6 mg, 12%) as a white solid. Data for **126**: $[\alpha]_D^{20}$ –16.6 (*c* 2.01, $CHCl_3$); R_f 0.43 (hexane:Et_2O, 2:3); IR (thin film) 3429, 3071, 2983, 2942, 1644, 1374, 1210, 1165, 1064 cm^{-1}; ^1H NMR (300 MHz) δ 1.32 (3H, s), 1.46 (3H, s), 2,45 (2H, t, *J* = 6.9 Hz), 2.72 (1H, br s), 4.16 (1H, td, *J* = 6.9, 3.6 Hz), 4.59 (1H, d, *J* = 6.0 Hz), 4.66 (1H, dd, *J* = 6.0, 3.6 Hz), 5.07 (1H, dd, *J* = 10.2, 0.9 Hz), 5.14 (1H, dd, *J* = 17.1, 1.5 Hz), 5.40 (1H, d, *J* = 2.1 Hz), 5.80–5.94 (1H, m); ^{13}C NMR (75 MHz) δ 25.3, 26.4, 33.3, 80.0, 80.6, 86.0, 101.2, 112.8, 117.6, 134.7; MS (ESI) *m/z* (relative intensity) 223 ($[M+Na]^+$, 100), 200 ($[M]^+$, 12), 195 (12), 185 ($[M–CH_3]^+$, 15), 183 ($[M–OH]^+$, 25); HRMS (ESI) calcd for $C_{10}H_{16}O_4$ $[M+Na]^+$ 223.0941, found 223.0944.

Data for **127**: mp 38–39 °C; $[\alpha]_D^{20}$ +38.4 (*c* 2.08, $CHCl_3$); R_f 0.20 (hexane:Et_2O, 3:2); IR (thin film) 3423, 3078, 2983, 2938, 1643, 1458, 1382, 1210, 1097 cm^{-1}; ^1H NMR (300 MHz, mixture of stereomer in ratio of 1:4) δ 1.32 (3.0H, s), 1.37 (0.8H, s), 1.48 (3.0H, s), 1.56 (0.8H, s), 2.29 (0.3H, dd, *J* = 14.4, 7.8 Hz), 2.40 (1.0H, br s) 2.45 (1.3H, dd, *J* = 14.1, 8.7 Hz), 2.64 (1.0H, dd, *J* = 14.1, 6.3 Hz), 3.68 (0.3H, dd, *J* = 10.8, 4.5 Hz), 3.91–4.02 (2.3H, m), 4.33 (0.3H, d, *J* = 6.3 Hz), 4.42 (1.0H, d, *J* = 6.0 Hz), 4.76 (0.3H, ddd, *J* = 6.3, 4.5, 1.8 Hz) 4.84 (1.0H, dd, *J* = 5.7, 3.6 Hz), 5.12 (0.3H, d, *J* = 6.6 Hz), 5.17 (0.3H, s), 5.22 (1.0H, d, *J* = 8.1 Hz), 5.28 (1.0H, s), 5.85–5.99 (1.3H, m); ^{13}C NMR (75 MHz) δ 25.3, 26.6, 26.7, 40.3, 40.8, 69.2, 71.5, 80.5, 81.0, 85.4, 104.0, 106.1, 112.9, 114.3, 119.3, 121.0, 132.4, 132.7; MS (ESI) *m/z* (relative intensity) 239 (53), 223

([M+Na]$^+$, 100), 183 ([M–OH]$^+$, 92); HRMS (ESI) calcd for $C_{10}H_{16}O_4$ [M+Na]$^+$ 223.0941, found 223.0948.

Ester 128. To the solution of lactol **126** (52.0 mg, 0.26 mmol) in CH_2Cl_2 (5 mL) were added ethyl acrylate (0.11 mL, 1.04 mmol) and the 2nd generation Grubbs catalyst (4.2 mg, 0.005 mmol). The mixture was heated to reflux for 3 h. It was then concentrated under reduced pressure and the residue was purified by flash chromatography (hexane:Et_2O, 3:2) to furnish ester **128** (67.3 mg, 95%) as a colorless oil: $[\alpha]_D^{20}$ −17.5 (*c* 0.66, $CHCl_3$); R_f 0.23 (hexane:Et_2O, 1:1); IR (thin film) 3431, 2984, 2939, 1720, 1657, 1373, 1321, 1271, 1211, 1164, 1068 cm^{-1}; ^{1}H NMR (300 MHz, mixture of α and β isomer with ratio α:β = 1:5) δ 1.28 (3.6H, t, *J* = 7.2 Hz), 1.32 (3.0H, s), 1.37 (0.6H, s), 1.46 (3.0H, s), 1.53 (0.6H, s), 2.39 (1.2H, br s), 2.58–2.64 (2.2H, m), 2.99–3.10 (0.2H, m), 3.59 (0.2H, td, *J* = 6.6, 3.3 Hz), 4.13–4.22 (2.4H, m), 4.28 (1.0H, td, *J* = 6.6, 3.3 Hz), 4.51 (0.2H, dd, *J* = 6.0, 3.6 Hz), 4.60–4.62 (1.2H, m), 4.69 (1.0H, dd, *J* = 6.0, 3.6 Hz), 4.97 (0.2H, d, *J* = 3.3 Hz), 5.37 (1.0H, s), 5.86 (0.2H, dt, *J* = 11.7, 1.8 Hz), 5.95 (1.0H, dt, *J* = 15.6, 1.5 Hz), 6.36 (0.2H, dt, *J* = 11.7, 7.5 Hz), 7.00 (1.0H, dt, *J* = 15.6, 6.9 Hz); ^{13}C NMR (75 MHz) δ 14.7, 25.3, 25.5, 26.3, 26.5, 31.7, 32.0, 60.8, 74.8, 79.0, 79.2, 80.4, 80.7, 86.0, 97.1, 101.4, 113.0, 123.9, 124.2, 144.5, 145.2, 167.0; MS (ESI) *m/z* (relative intensity) 295 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{13}H_{20}O_6$ [M+Na]$^+$ 295.1152, found 295.1157.

Isoxazolidine 130. Following the INAC reaction procedure (Method C) using pyridine as base and EtOH (2 mL) as the reaction solvent and the product was purified by flash chromatography (hexane:EtOAc, 2:3), ester **128** (12.3 mg, 0.045 mmol) was

converted into isoxazolidine **130** (9.8 mg, 72%) as a colorless oil: $[\alpha]_D^{20}$ +40.0 (*c* 0.80, $CHCl_3$); R_f 0.20 (hexane:EtOAc, 2:3); IR (thin film) 3403, 2982, 2934, 1751, 1458, 1380, 1242, 1212, 1058 cm^{-1}; ^1H NMR (400 MHz) δ 1.29 (3H, t, *J* = 7.1 Hz), 1.34 (3H, s), 1.45 (3H, s), 1.74–1.81 (1H, m), 2.12 (1H, ddd, *J* = 14.2, 7.8, 3.0 Hz), 2.86 (3H, s), 2.93–2.99 (1H, m), 3.08 (1H, dd, *J* = 7.5, 2.6 Hz), 3.77–3.78 (1H, m), 4.17–4.24 (3H, m), 4.26 (1H, dd, *J* = 7.0, 2.6 Hz), 4.31 (1H, br s), 4.40 (1H, d, *J* = 4.2 Hz); ^1H NMR (400 MHz, $CDCl_3$-D_2O) δ 1.29 (3H, t, *J* = 7.1 Hz), 1.34 (3H, s), 1.46 (3H, s), 1.78 (1H, dt, *J* = 14.0, 5.6 Hz), 2.13 (1H, ddd, *J* = 14.3, 7.9, 3.0 Hz), 2.86 (3H, s), 2.93–3.00 (1H, m), 3.09 (1H, dd, *J* = 7.5, 2.6 Hz), 3.77 (1H, quin, *J* = 3.3 Hz), 4.18–4.24 (3H, m), 4.26 (1H, dd, *J* = 7.0, 2.6 Hz), 4.41 (1H, d, *J* = 4.2 Hz); ^{13}C NMR (100 MHz) δ 14.5 (CH_3), 24.6 (CH_3), 27.2 (CH_3), 29.3 (CH_2), 42.7 (CH), 44.6 (CH_3), 61.9 (CH_2), 67.2 (CH), 68.7 (CH), 72.1 (CH), 77.2 (CH), 82.8 (CH), 108.8 (C), 171.0 (C); MS (ESI) *m/z* (relative intensity) 324 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{14}H_{23}NO_6$ $[M+Na]^+$ 324.1418, found 324.1414.

Benzoate 134. To a stirred solution of isoxazolidine **130** (10.2 mg, 0.034 mmol) in pyridine (0.16 mL) at 0 °C were added benzoyl chloride (0.008 mL, 0.068 mmol) and DMAP (0.4 mg, 0.003 mmol). The mixture was stirred at room temperature for 2 d and was quenched by saturated $NaHCO_3$ solution. The aqueous phase was extracted with EtOAc (3 × 10 mL) and the combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, and filtered. Concentration of the filtrate and the residue was purified by flash chromatography (hexane:Et_2O, 3:2) to yield benzoate **134** (13.7 mg, 100%) as a white solid: mp 116 °C; $[\alpha]_D^{20}$ +62.3 (*c* 0.36, $CHCl_3$); R_f 0.16 (hexane:Et_2O, 3:2); IR (thin film) 2983, 2930, 1719, 1373, 1272, 1209, 1114, 1065, 1026 cm^{-1}; ^1H

NMR (400 MHz) δ 1.30 (3H, t, J = 7.1 Hz), 1.37 (3H, s), 1.52 (3H, s), 1.83 (1H, q, J = 12.2 Hz), 2.21 (1H, dt, J = 12.5, 4.6 Hz), 2.95 (3H, s), 3.08−3.11 (1H, m), 3.19 (1H, dd, J = 6.3, 2.2 Hz), 4.18−4.27 (4H, m), 4.38 (1H, dd, J = 7.7, 6.0 Hz), 5.16 (1H, ddd, J = 11.9, 7.9, 3.8 Hz), 7.44 (2H, t, J = 7.6 Hz), 7.56 (1H, t, J = 7.4 Hz), 8.04−8.06 (2H, m); ^{13}C NMR (100 MHz) δ 14.5, 26.2, 28.2, 29.9, 44.8, 45.6, 62.0, 67.7, 73.1, 74.3, 76.6, 81.3, 109.5, 128.7, 130.1, 130.3, 133.5, 166.4, 171.3; MS (ESI) *m/z* (relative intensity) 428 ([M+Na]$^+$, 100), 413 (33); HRMS (ESI) calcd for $C_{21}H_{27}NO_7$ [M+Na]$^+$ 428.1680, found 428.1687.

Lactols 135 and 127. To a solution of alkene **124** (949 mg, 4.69 mmol) in DMSO (30 mL) was added IBX (1.58 g, 5.16 mmol) and the mixture was stirred at room temperature for 2 d. The mixture was partitioned between Et_2O (100 mL) and water (100 mL). The aqueous layer was extracted with Et_2O (2 × 100 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography (hexane:Et_2O, 3:2) to give firstly lactol **135** (693 mg, 74%) as a colorless oil and secondly its regioisomer **127** (94.2 mg, 10.0%) as a white solid. Data for **135**: $[\alpha]_D^{20}$ –5.3 (*c* 2.53, $CHCl_3$); R_f 0.45 (hexane:Et_2O, 2:3); IR (thin film) 3434, 3079, 2984, 2941, 1642, 1438, 1375, 1211, 1075 cm^{-1}; ^{1}H NMR (300 MHz, mixture of α and β isomer with ratio α:β=1:5.6) δ 1.31 (3.00H, s), 1.38 (0.54H, s), 1.47 (3.00H, s), 1.56 (0.54H, s), 2.21–2.53 (2.36H, m), 3.08 (1.00H, d, J = 2.1 Hz), 3.91 (0.18H, d, J = 9.0 Hz), 4.11 (0.18H, td, J = 9.0, 2.7 Hz), 4.22 (1.00H, t, J = 8.1 Hz), 4.47 (0.18H, dd, J = 6.6, 2.7 Hz), 4.60 (1.00H, d, J = 6.0 Hz), 4.63 (1.00H, d, J = 6.0 Hz), 5.10 (1.18H, s),

5.14 (1.18H, d, J = 4.2 Hz), 5.26 (0.18H, dd, J = 9.3, 4.2 Hz), 5.44 (1.00H, d, J = 2.4 Hz), 5.72–5.87 (1.18H, m); ^{13}C NMR (75 MHz) δ 25.4, 26.7, 26.9, 37.5, 40.4, 79.9, 80.3, 83.5, 84.1, 86.5, 86.8, 96.3, 103.6, 112.8, 115.2, 118.2, 118.7, 133.6, 134.5; MS (ESI) *m/z* (relative intensity) 223 ([M+Na]$^+$, 100), 185 ([M–CH_3]$^+$, 7), 183 ([M–OH]$^+$, 3), 149 (3); HRMS (ESI) calcd for $C_{10}H_{16}O_4$ [M+Na]$^+$ 223.0941, found 223.0945.

Ester 136. To the solution of lactol **135** (63.1 mg, 0.32 mmol) in CH_2Cl_2 (4 mL) were added ethyl acrylate (0.14 mL, 1.26 mmol) and the 2nd generation Grubbs catalyst (2.7 mg, 0.003 mmol). The mixture was heated to reflux for 2 h. It was then concentrated under reduced pressure and the residue was purified by flash chromatography (hexane:Et_2O, 2:1) to afford ester **136** (82.3 mg, 96%) as a colorless oil: $[\alpha]_D^{20}$ +20.9 (*c* 0.82, $CHCl_3$); R_f 0.15 (hexane:Et_2O, 2:1); IR (thin film) 3428, 2984, 2940, 1718, 1654, 1373, 1274, 1211, 1162, 1073 cm^{-1}; ^{1}H NMR (300 MHz, mixture of α and β isomer with ratio α:β = 1:2) δ 1.28 (4.5H, t, J = 7.2 Hz), 1.31 (3.0H, s), 1.38 (1.5H, s), 1.47 (3.0H, s), 1.56 (1.5H, s), 2.41–2.65 (3.0H, m), 4.14–4.21 (3.5H, m), 4.30 (1.0H, t, J = 7.5 Hz), 4.46 (0.5H, dd, J = 6.9, 3.0 Hz), 4.59–4.67 (2.5H, m), 5.29 (0.5H, d, J = 3.9 Hz), 5.46 (1.0H, s), 5.87–5.95 (1.5H, m), 6.85–6.99 (1.5H, m); ^{13}C NMR (75 MHz) δ 14.7, 25.5, 26.8, 26.9, 35.8, 38.8, 60.9, 79.6, 80.0, 83.6, 84.5, 86.0, 86.5, 96.3, 103.7, 113.0, 115.7, 124.3, 124.9, 143.4, 144.7, 166.5, 166.8; MS (ESI) *m/z* (relative intensity) 295 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{13}H_{20}O_6$ [M+Na]$^+$ 295.1152, found 295.1150.

Isoxazolidines 137 and 138. Following the INAC reaction procedure (Method C) using pyridine as base and EtOH (10 mL) as the reaction solvent and the product was purified by flash chromatography (hexane:EtOAc, 1:1 to 1:3), ester **136** (75.0 mg, 0.275 mmol) was converted to firstly isoxazolidine **137** (49.6 mg, 60%) as a colorless oil then secondly isoxazolidine **138** (9.1 mg, 11%) as a white solid. Data for **137**: $[\alpha]_D^{20}$ +26.4 (*c* 1.82, $CHCl_3$); R_f 0.18 (hexane:EtOAc, 1:1); IR (thin film) 3491, 2983, 2936, 1751, 1451, 1380, 1262, 1209, 1055 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 0.87 (3H, t, *J* = 7.1 Hz), 1.15 (3H, s), 1.34 (3H, s), 1.41 (1H, d, *J* = 12.8 Hz), 2.04–2.11 (1H, m), 2.35 (1H, d, *J* = 5.2 Hz), 2.63 (3H, s), 3.12–3.15 (2H, m), 3.88 (2H, q, *J* = 7.1 Hz), 3.94–3.97 (1H, m), 4.02 (1H, dd, *J* = 7.7, 3.4 Hz), 4.07 (1H, br s), 4.15 (1H, d, *J* = 6.0 Hz); ^1H NMR (400 MHz, C_6D_6-D_2O) δ 0.87 (3H, t, *J* = 7.1 Hz), 1.15 (3H, s), 1.34 (3H, s), 1.41 (1H, d, *J* = 12.6 Hz), 2.04–2.11 (1H, m), 2.63 (3H, s), 3.12 (2H, s), 3.88 (2H, q, *J* = 7.1 Hz), 3.94–3.97 (1H, m), 4.02 (1H, dd, *J* = 7.7, 3.4 Hz), 4.06–4.09 (1H, m), 4.15 (1H, d, *J* = 5.7 Hz); ^{13}C NMR (100 MHz, C_6D_6) δ 14.1 (CH_3), 24.1 (CH_3), 26.3 (CH_3), 28.9 (CH_2), 43.2 (CH), 44.7 (CH_3), 61.0 (CH_2), 64.5 (CH), 68.4 (CH), 74.3 (CH), 75.1 (CH), 82.1 (CH), 108.4 (C), 170.7 (C); MS (ESI) *m/z* (relative intensity) 324 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{14}H_{23}NO_6$ $[M+Na]^+$ 324.1418, found 324.1420.

Data for **138**: mp 123–124 °C; $[\alpha]_D^{20}$ +62.3 (*c* 0.88, $CHCl_3$); R_f 0.10 (hexane:EtOAc, 1:2); IR (thin film) 3227, 2987, 2931, 2877, 1745, 1461, 1381, 1218, 1167, 1039 cm^{-1}; ^1H NMR (400 MHz) δ 1.28 (3H, t, *J* = 7.1 Hz), 1.36 (3H, s), 1.53 (3H, s), 1.77 (1H, td, *J* = 13.2, 9.1 Hz), 2.17–2.27 (2H, m), 2.44 (1H, br s), 2.66 (1H, dd, *J* = 11.3, 8.8 Hz), 2.83 (3H, s), 4.02 (1H, quin, *J* = 4.6 Hz), 4.16 (1H, dd, *J* = 7.9, 5.7 Hz), 4.19–4.26 (3H, m), 4.32 (1H, t, *J* = 4.8 Hz); ^{13}C NMR (100 MHz) δ 14.6 (CH_3), 26.1 (CH_3), 28.2 (CH_3), 31.2 (CH_2), 46.2 (CH), 47.0 (CH_3), 61.8 (CH_2), 69.4 (CH), 73.6 (CH),

76.3 (CH), 76.7 (CH), 78.0 (CH), 110.1 (C), 117.3 (C); MS (ESI) *m/z* (relative intensity) 302 ($[M+H]^+$, 100); HRMS (ESI) calcd for $C_{14}H_{23}NO_6$ $[M+H]^+$ 302.1598, found 302.1591.

Ketone 139 from isoxazolidine 130. To the solution of isoxazolidine **130** (4.6 mg, 0.015 mmol) in DMSO (0.015 mL) was added IBX (6.4 mg, 0.023 mmol) and the mixture was stirred at room temperature for 1 d. The reaction mixture was partitioned between Et_2O (10 mL) and water (10 mL). The aqueous layer was extracted with Et_2O (3 × 10 mL). The combined extracts were washed with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated and the residue was purified by flash chromatography (hexane:Et_2O, 2:3) to afford ketone **139** (3.0 mg, 66%) as a colorless oil: $[\alpha]_D^{20}$ +30.2 (*c* 0.91, $CHCl_3$); R_f 0.20 (hexane:Et_2O, 2:3); IR (thin film) 2984, 2937, 1736, 1461, 1433, 1374, 1213, 1165, 1080, 1039 cm^{-1}; ^1H NMR (400 MHz) δ 1.26 (3H, t, *J* = 7.2 Hz), 1.35 (3H, s), 1.44 (3H, s), 2.65 (1H, dd, *J* = 13.4, 9.4 Hz), 2.74 (1H, dd, *J* = 13.4, 6.2 Hz), 2.92 (3H, s), 3.19 (1H, dtd, *J* = 9.0, 6.0, 2.7 Hz), 3.24 (1H, dd, *J* = 6.0, 1.8 Hz), 4.12–4.25 (3H, m), 4.37–4.42 (2H, m); ^{13}C NMR (100 MHz) δ 14.4 (CH_3), 25.7 (CH_3), 27.2 (CH_3), 39.1 (CH_2), 45.3 (CH_3), 47.3 (CH), 62.0 (CH_2), 66.3 (CH), 76.8 (CH), 77.2 (CH), 80.9 (CH), 110.6 (C), 170.7 (C), 205.8 (C); MS (ESI) *m/z* (relative intensity) 322 ($[M+Na]^+$, 100), 301 (40), 242 (27), 130 (20); HRMS (ESI) calcd for $C_{14}H_{21}NO_6$ $[M+Na]^+$ 322.1261, found 322.1262.

Ketone 139 from isoxazolidine 137. To the solution of isoxazolidine **137** (59.8 mg, 0.198 mmol) in DMSO (2 mL) was added IBX (83.3 mg, 0.298 mmol) and the mixture was stirred at room temperature for 14 h. The reaction mixture was partitioned

between Et_2O (20 mL) and water (20 mL). The aqueous layer was extracted with Et_2O (3 × 20 mL). The combined extracts were washed with brine, dried over $MgSO_4$, and filtered. The filtrate was concentrated and the residue was purified by flash chromatography (hexane:Et_2O, 2:3) to afford ketone **139** (47.3 mg, 80%) as a colorless oil.

Isoxazolidines 141 and 142 using MeCN as the INAC reaction solvent. Following the glycol cleavage procedure, diol **147** (6.39 g, 16.8 mmol) was converted into aldehyde **148** as a colorless oil. Following the INAC reaction procedure (Method A) using MeCN (300 mL) as the reaction solvent and the product was purified by flash chromatography (hexane:Et_2O, 3:2), aldehyde **148** was converted into an inseparable mixture of isoxazolidines **141** and **142** (4.45 g, 70% overall yield from diol **147**) as a colorless oil: R_f 0.17 (hexane:Et_2O, 3:2); ^{1}H NMR (400 MHz, mixture of **141** and **142** with ratio **141**:**142** = 8:1) δ 1.42 (6.00H, s), 1.44 (0.39H, s), 1.48 (0.39H, s), 1.73 (1.00H, d, J = 14.3, 9.1 Hz), 1.87 (0.13H, q, J = 11.8 Hz), 2.22–2.28 (1.00H, m), 2.35–2.41 (0.13H, m), 2.58 (3.00H, s), 2.82 (0.39H, s), 2.96–3.03 (0.26H, m), 3.47 (1.00H, s), 3.75 (0.39H, s), 3.78 (3.00H, s), 3.96–3.98 (0.13H, m), 4.02–4.07 (2.26H, m), 4.14–4.23 (2.13H, m), 4.62 (0.13H, d, J = 11.8 Hz), 4.72 (1.00H, d, J = 11.8 Hz), 4.90 (1.00H, d, J = 11.8 Hz), 4.94 (0.13H, d, J = 11.8 Hz), 5.18–5.19 (1.00H, m), 7.27–7.40 (5.65H, m); ^{13}C NMR (100 MHz) δ 26.9, 26.9, 27.2, 27.3, 32.4, 34.6, 45.5, 46.1, 46.9, 49.4, 52.5, 52.8, 53.6, 69.7, 71.0, 71.1, 72.1, 73.8, 73.9, 74.7, 76.5, 78.5, 80.0, 80.5, 108.2, 110.0, 127.6, 127.7, 127.9, 128.4, 128.5, 138.3, 138.7, 172.2, 172.9.

Isoxazolidines 141 and 142 using CH_2Cl_2 as the INAC reaction solvent. Following the glycol cleavage procedure, diol **147** (22.4 mg, 0.059 mmol) was converted into aldehyde **148**. Following the INAC reaction procedure (Method B) using CH_2Cl_2 (3 mL) as reaction solvent and the product was purified by flash chromatography (hexane:Et_2O, 3:2), aldehyde **148** was converted into an inseparable mixture of isoxazolidines **141** and **142** (13.8 mg, 62% overall yield from diol **147**, **141**:**142** = 10:1 by NMR) as a colorless oil.

Isoxazolidines 141 and 142 using MeOH as the INAC reaction solvent. Following the glycol cleavage procedure, diol **147** (38.2 mg, 0.100 mmol) was converted into aldehyde **148**. Following the INAC reaction procedure (Method B) using MeOH (4 mL) as the reaction solvent and the product was purified by flash chromatography (hexane:Et_2O, 3:2), aldehyde **148** was converted into an inseparable mixture of isoxazolidines **141** and **142** (23.9 mg, 63% overall yield from diol **147**, **141**:**142** = 14:1 by NMR) as a colorless oil.

Isoxazolidines 141 and 142 using DMF as the INAC reaction solvent. Following the glycol cleavage procedure, diol **147** (30.4 mg, 0.080 mmol) was converted into aldehyde **148**. Following the INAC reaction procedure (Method A) using DMF (3 mL) as the reaction solvent and the product was purified by flash chromatography (hexane:Et_2O, 3:2), aldehyde **148** was converted into an inseparable mixture of isoxazolidines **141** and **142** (19.2 mg, 64% overall yield from diol **147**, **141**:**142** = 13:1 by NMR) as a colorless oil.

Isoxazolidines 141 and 142 using toluene as the INAC reaction solvent. Following the glycol cleavage procedure, diol **147** (38.7 mg, 0.102 mmol) was converted into aldehyde **148**. Following the INAC reaction procedure (Method C) using triethylamine as base and toluene (5 mL) as the reaction solvent and the product was purified by flash chromatography (hexane:Et_2O, 3:2), aldehyde **148** was converted into an inseparable mixture of isoxazolidines **141** and **142** (28.9 mg, 75% overall yield from diol **147**, **141**:**142** = 15:1 by NMR) as a colorless oil.

Diacetonide 144. To a solution of D-ribose (1.44 g, 9.58 mmol) in EtOH (40 mL) and H_2O (10 mL) were added indium (1.21 g, 10.5 mmol) and allyl bromide (3.32 mL, 38.3 mmol). The mixture was stirred vigorously at room temperature for 12 h until the disappearance of the starting material as shown on TLC. The solvent was removed under reduced pressure and the residue was dissolved in acetone (50 mL). Anhydrous $CuSO_4$ (1.40 g) was added and the reaction mixture was stirred at room temperature for 25 h. The mixture was neutralized with saturated $NaHCO_3$ solution and then filtered. The filtrate was partitioned between Et_2O (50 mL) and water (50 mL). The aqueous layer was extracted with Et_2O (2 × 50 mL). The combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, and filtered. Concentration of the filtrate and the residue was purified by flash chromatography (hexane:Et_2O, 3:1) to give diacetonide **144** (1.66 g, 64% overall yield from D-ribose) as a colorless oil: $[\alpha]_D^{20}$ +25.0 (*c* 4.07, $CHCl_3$); R_f 0.54 (hexane:Et_2O, 1:1); IR (thin film) 3475, 2987, 2936, 1372, 1216, 1166, 1068, 849, 514 cm^{-1}; ^1H NMR (400 MHz) δ 1.36 (3H, s), 1.39 (3H, s), 1.40 (3H, s), 1.43 (3H, s), 1.68 (1H, br s), 2.30–2.38 (1H, m), 2.52–2.59 (1H, m), 3.68 (1H, dd, *J* = 7.8, 6.0

Hz), 3.87 (1H, t, J = 5.5 Hz), 3.97 (1H, dd, J = 8.2, 6.7 Hz), 4.07 (1H, dd, J = 8.2, 6.4 Hz), 4.12 (1H, td, J = 7.6, 3.6 Hz), 4.19 (1H, td, J = 6.5, 5.4 Hz), 5.10–5.18 (2H, m), 5.90 (1H, ddt, J = 17.2, 10.2, 7.0 Hz); ^{13}C NMR δ 25.5, 26.8, 27.3, 27.6, 38.0, 65.7, 71.8, 75.9, 78.1, 80.1, 109.2, 109.4, 117.8, 134.5; MS (EI) *m/z* (relative intensity) 257 ([M–OCH_3]$^+$, 46), 101 (79), 84 (69), 83 (61), 59 (55), 49 (64), 44 (92), 43 (100); HRMS (EI) calcd for $C_{14}H_{24}O_5$ [M–OCH_3]$^+$ 257.1384, found 257.1385.

Diacetonide 144 by tin allylation. To a solution of D-ribose (5.29 g, 35.2 mmol) in EtOH/H_2O (v/v = 4:1, 150 mL) were added tin (4.60 g, 38.7 mmol) and allyl bromide (12.2 mL, 0.14 mol). The mixture was heated to reflux for 2 h until the disappearance of the starting material as shown on TLC. The solvent was removed under reduced pressure and the residue was dissolved in acetone (50 mL). The reaction mixture was stirred at room temperature for 25 h. The mixture was neutralized with saturated $NaHCO_3$ solution and was partitioned between Et_2O (200 mL) and water (200 mL). The aqueous layer was extracted with Et_2O (2 × 200 mL). The combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, and filtered. Concentration of the filtrate and the residue was purified by flash chromatography (hexane:Et_2O, 3:1) to yield diacetonide **144** (4.77 g, 50% overall yield from D-ribose) as a colorless oil.

6-*O*-Benzyl-1,2,3-trideoxy-4,5:7,8-di-*O*-isopropylidene-D-*altro*-oct-1-enitol (145). Sodium hydride (60%, 217 mg, 5.43 mmol) was suspended in dry THF (10 mL) under nitrogen at 0 °C. A solution of the diacetonide **144** (604 mg, 2.22 mmol) in THF (30 mL) was added dropwise over 1 h at 0 °C, and then the mixture was stirred at 0 °C for 1 h. Benzyl bromide (0.32 mL, 2.71 mmol) was added dropwise over 15 min and

tetra-*n*-butylammomium iodide (83.6 mg, 0.23 mmol) was added. The reaction mixture was stirred at room temperature for 12 h. Water was then added slowly at 0 °C to destroy the excess of hydride, and followed by the addition of saturated NH_4Cl solution. The aqueous layer was extracted with Et_2O (2 × 30 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, and filtered. Concentration of the filtrate and the residue was purified by flash chromatography (hexane:Et_2O, 10:1) to furnish benzyl ether **145** (786 mg, 98%) as a colorless oil: $[\alpha]_D^{20}$ +23.6 (*c* 1.08, $CHCl_3$) {lit.[14] $[\alpha]_D^{20}$ +28.0 (*c* 2.71, $CHCl_3$)}; R_f 0.55 (hexane:Et_2O, 2:1); IR (thin film) 2986, 2935, 1372, 1215, 1072, 849, 699 cm^{-1}; ^1H NMR (400 MHz) δ 1.36 (3H, s), 1.38 (6H, s), 1.44 (3H, s), 2.24–2.32 (1H, m), 2.40–2.47 (1H, m), 3.72–3.79 (2H, m), 3.94 (1H, dd, *J* = 8.0, 7.2 Hz), 4.01–4.08 (2H, m), 4.27 (1H, td, *J* = 6.8, 4.6 Hz), 4.74 (1H, d, *J* = 11.4 Hz), 4.79 (1H, d, *J* = 11.4 Hz), 5.06–5.10 (2H, m), 5.76–5.88 (1H, m), 7.28–7.37 (5H, m); ^{13}C NMR (100 MHz) δ 25.6, 26.8, 27.3, 27.5, 38.4, 66.1, 74.9, 76.2, 78.0, 78.9, 80.4, 109.2, 109.3, 117.7, 128.2, 128.5, 128.8, 134.5, 138.4; MS (ESI) *m/z* (relative intensity) 385 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{21}H_{30}O_5$ $[M+Na]^+$ 385.1985, found 385.1986.

Ester 146. To the solution of benzyl ether **145** (8.98 g, 24.8 mmol) in CH_2Cl_2 (250 mL) were added methyl acrylate (4.46 mL, 49.6 mmol) and the 2nd generation Grubbs catalyst (63.0 mg, 0.074 mmol). The mixture was heated to reflux for 2 h. It was then concentrated under reduced pressure and the residue was purified by flash chromatography (hexane:Et_2O, 4:1) to yield ester **146** (9.87 g, 95%) as a white solid: mp 56–57 °C; $[\alpha]_D^{20}$ +31.9 (*c* 0.52, $CHCl_3$); R_f 0.12 (hexane:Et_2O, 4:1); IR (thin film) 2985, 2936, 2890, 1725, 1660, 1454, 1435, 1371, 1214, 1166, 1076 cm^{-1}; ^1H NMR (400 MHz)

δ 1.36 (3H, s), 1.37 (6H, s), 1.44 (3H, s), 2.33−2.41 (1H, m), 2.57 (1H, dddd, J = 15.2, 6.8, 3.2, 1.5 Hz), 3.69 (1H, dd, J = 7.8, 5.6 Hz), 3.73 (3H, s), 3.76 (1H, t, J = 5.4 Hz), 3.91 (1H, dd, J = 7.8, 7.2 Hz), 4.03−4.08 (2H, m), 4.23 (1H, td, J = 6.7, 5.1 Hz), 4.73 (1H, d, J = 11.4 Hz), 4.79 (1H, d, J = 11.4 Hz), 5.86 (1H, d, J = 15.7 Hz), 6.96 (1H, dt, J = 15.7, 7.1 Hz), 7.28−7.37 (5H, m); ^{13}C NMR (100 MHz) δ 25.5 (CH_3), 26.7 (CH_3), 27.3 (CH_3), 27.5 (CH_3), 36.7 (CH_2), 51.8 (CH_3), 66.2 (CH_2), 75.1 (CH_2), 76.2 (CH), 77.2 (CH), 79.0 (CH), 80.2 (CH), 109.5 (C), 109.6 (C) 123.6 (CH), 128.3 (CH), 128.5 (CH), 128.9 (CH), 138.3 (C), 145.1 (CH), 167.1 (C); MS (ESI) *m/z* (relative intensity) 443 ($[M+Na]^+$, 55), 435 (50), 403 (100); HRMS (ESI) calcd for $C_{23}H_{32}O_7$ $[M+Na]^+$ 443.2040, found 443.2036.

Diol 147. A solution of ester **146** (815 mg, 1.94 mmol) in 80% aqueous AcOH (50 mL) was stirred at room temperature for 7 h. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (hexane:Et_2O, 4:1 to hexane:EtOAc, 1:1) to afford firstly starting material ester **146** (131 mg, 16%) and secondly diol **147** (538 mg, 73%) as a colorless oil: $[\alpha]_D^{20}$ +16.0 (*c* 0.55, $CHCl_3$); R_f 0.12 (hexane:EtOAc, 1:1); IR (thin film) 3443, 2986, 2939, 1719, 1658, 1453, 1381, 1274, 1214, 1173, 1071 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.36 (3H, s), 1.39 (3H, s), 2.35−2.43 (2H, m), 2.60−2.67 (1H, m), 3.00 (1H, d, J = 3.3 Hz), 3.60 (1H, dd, J = 7.6, 5.4 Hz), 3.73 (3H, s), 3.79 (2H, br s), 3.84 (1H, t, J = 7.6 Hz), 3.90−3.92 (1H, m), 3.99 (1H, td, J = 7.9, 3.0 Hz), 4.60 (1H, d, J = 11.2 Hz), 4.75 (1H, d, J = 11.2 Hz), 5.85 (1H, d, J = 15.8 Hz), 6.96 (1H, dt, J = 15.7, 7.1 Hz), 7.29−7.38 (5H, m); ^{13}C NMR (100 MHz) δ 27.2 (CH_3), 27.5 (CH_3), 36.8 (CH_2), 51.9 (CH_3), 63.1 (CH_2), 72.5 (CH), 74.3 (CH_2), 78.7 (CH), 79.5 (CH), 80.7 (CH), 109.9 (C), 123.5 (CH), 128.6, (CH), 129.0 (CH), 137.6 (C), 145.2 (CH),

167.1 (C); MS (ESI) *m/z* (relative intensity) 403 ([M+Na]$^+$, 100), 368 (60); HRMS (ESI) calcd for $C_{20}H_{28}O_7$ [M+Na]$^+$ 403.1727, found 403.1729.

Diols 149 and 150. To a stirred solution of isoxazolidines **141** and **142** (337 mg, 0.89 mmol, **141**:**142** = 8:1 by NMR) in CH_2Cl_2 (20 mL) were added deionized water (0.5 mL) and TFA (3 mL) at room temperature to form a clear solution. The mixture was stirred at room temperature for 2 h. Concentration of the mixture under reduced pressure and the residue was purified by flash chromatography (hexane:EtOAc, 1:2 to 1:4) to afford firstly diol **149** (258 mg, 86%) as a white solid then secondly diol **150** (34.3 mg, 11%) as a colorless oil. Data for **149**: mp 113–114 °C; $[\alpha]_D^{20}$ −82.9 (*c* 1.88, $CHCl_3$); R_f 0.21 (hexane:EtOAc, 1:2); IR (thin film) 3386, 2950, 2892, 1735, 1436, 1333, 1216, 1070, 1019 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 1.64−1.67 (1H, m), 2.17−2.23 (1H, m), 2.59 (3H, s), 3.69 (1H, br s), 3.75 (3H, s), 3.83 (1H, br s), 3.94−3.97 (3H, m), 4.71−4.78 (2H, m), 5.00 (1H, br s), 7.29−7.31 (1H, m), 7.33−7.37 (2H, m), 7.42−7.44 (2H, m); ^{13}C NMR (100 MHz) δ 36.5, 45.8, 50.5, 52.7, 67.8, 68.2, 72.1, 72.6, 77.6, 79.0, 128.1, 128.3, 128.7, 137.6, 172.9; MS (ESI) *m/z* (relative intensity) 360 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{17}H_{23}NO_6$ [M+Na]$^+$ 360.1418, found 360.1410; Anal. Calcd for $C_{17}H_{23}NO_6$: C, 60.52; H, 6.87; N, 4.15, found: C, 60.53; H, 6.68; N, 4.14.

Data for **150**: $[\alpha]_D^{20}$ −43.6 (*c* 1.60, $CHCl_3$); R_f 0.07 (hexane:EtOAc, 1:2); IR (thin film) 3402, 2951, 2883, 1749, 1455, 1436, 1357, 1210, 1077 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.77 (1H, q, *J* = 11.1 Hz), 2.13 (1H, dt, *J* = 12.9, 5.0 Hz), 2.42 (2H, br s), 2.81 (3H, s), 2.90−2.96 (1H, m), 3.05 (1H, s), 3.69−3.74 (5H, m), 3.84−3.90 (1H, m), 4.28 (1H, s), 4.60 (1H, d, *J* = 11.7 Hz), 4.68 (1H, d, *J* = 11.7 Hz), 7.30−7.38 (5H, m); ^{1}H NMR (400 MHz, $CDCl_3$-D_2O) δ 1.72 (1H, q, *J* = 11.2 Hz), 2.08 (1H, dt, *J* = 13.0, 5.2 Hz), 2.76 (3H,

s), 2.87–2.92 (1H, m), 2.99 (1H, s), 3.68–3.72 (5H, m), 3.83–3.89 (1H, m), 4.24 (1H, s), 4.60–4.66 (2H, m), 7.27–7.35 (5H, m); ^{13}C NMR (100 MHz) δ 33.0 (CH_2), 45.3 (CH), 45.8 (CH_3), 52.7 (CH_3), 68.4 (CH), 69.2 (CH), 73.3 (CH), 73.7 (CH_2), 76.8 (CH), 80.6 (CH), 128.2 (CH), 128.4 (CH), 128.9 (CH), 138.0 (C), 172.7 (C); MS (ESI) *m/z* (relative intensity) 338 ($[M+H]^+$, 100); HRMS (ESI) calcd for $C_{17}H_{23}NO_6$ $[M+H]^+$ 338.1598, found 338.1607.

Epoxide 154. To a stirred solution of diol **149** (136 mg, 0.40 mmol) and 2,4,6-collidine (0.12 mL, 0.89 mmol) in CH_2Cl_2 (8 mL) was added trifluoromethanesulfonic anhydride (0.07 mL, 0.44 mmol) at −78 °C. The reaction mixture was stirred at −78 °C for 1 h and was quenched by saturated $NaHCO_3$ solution. The aqueous phase was extracted with EtOAc (3 × 20 mL) and the combined organic extracts were washed with 1 M hydrochloric acid then saturated $NaHCO_3$ solution. The organic phase was then concentrated under reduced pressure to give crude triflate **153**. The crude product was then redissolved in MeOH (8 mL) and potassium carbonate (83.5 mg, 0.60 mmol) was added. The mixture was stirred at room temperature for 10 min. Deionized water (20 mL) was added to the reaction mixture and the MeOH was removed under reduced pressure. The remaining aqueous solution was then extracted with EtOAc (3 × 20 mL) and the combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, and filtered. Concentration of the filtrate and the residue was purified by flash chromatography (hexane:EtOAc, 3:2) to yield epoxide **154** (112 mg, 87% overall yield from diol **149**) as a colorless oil: $[\alpha]_D^{20}$ +18.6 (*c* 0.95, $CHCl_3$); R_f 0.21 (hexane:EtOAc, 3:2); IR (thin film) 2954, 1734, 1436, 1242, 1204, 1072, 1052 cm^{-1}; ^{1}H NMR (400 MHz)

δ 2.30 (1H, d, J = 16.0 Hz), 2.55 (1H, dd, J = 16.8, 4.9 Hz), 2.67 (3H, s), 3.34 (2H, d, J = 3.4 Hz), 3.69 (1H, d, J = 3.4 Hz), 3.71 (3H, s), 3.92 (1H, t, J = 3.6 Hz), 3.96 (1H, s), 4.68 (1H, d, J = 3.8 Hz), 4.74 (1H, d, J = 12.0 Hz), 4.80 (1H, d, J = 12.0 Hz), 7.29–7.42 (5H, m); ^{13}C NMR (100 MHz) δ 33.4 (CH_2), 46.4 (CH_3), 49.6 (CH), 52.8 (CH_3), 57.9 (CH), 58.7 (CH), 68.7 (CH), 71.7 (CH_2), 75.4 (CH), 77.7 (CH), 128.3 (CH), 128.3 (CH), 128.8 (CH), 138.0 (C), 173.1 (C); MS (ESI) *m/z* (relative intensity) 320 ($[M+H]^+$, 100); HRMS (ESI) calcd for $C_{17}H_{21}NO_5$ $[M+H]^+$ 320.1492, found 320.1493.

Epoxide 154 from mesylate 155. To a stirred solution of mesylate **155** (23.4 mg, 0.056 mmol) in MeOH (1.5 mL) were added potassium carbonate (11.7 mg, 0.084 mmol). The reaction mixture was stirred at room temperature for 36 h and deionized water (10 mL) was added to the reaction mixture and the MeOH was removed under reduced pressure. The remaining aqueous solution was then extracted with EtOAc (3 × 10 mL) and the combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, and filtered. Concentration of the filtrate and the residue was purified by flash chromatography (hexane:EtOAc, 3:2) to yield epoxide **154** (12.7 mg, 71%) as a colorless oil.

Mesylate 155. To a stirred solution of diol **149** (54.9 mg, 0.163 mmol) and triethylamine (0.05 mL, 0.358 mmol) in CH_2Cl_2 (1.5 mL) at −78 °C were added methanesulfonyl chloride (0.017 mL, 0.179 mmol) and DMAP (2.0 mg, 0.016 mmol). The reaction mixture was stirred at −78 °C for 2 h and was quenched by saturated $NaHCO_3$ solution. The aqueous phase was extracted with EtOAc (3 × 20 mL) and the

combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, and filtered. Concentration of the filtrate and the residue was purified by flash chromatography (hexane:EtOAc, 1:1) to yield mesylate **155** (66.8 mg, 99%) as a colorless oil: $[\alpha]_D^{20}$ −104.0 (*c* 0.90, $CHCl_3$); R_f 0.17 (hexane:EtOAc, 1:1); IR (thin film) 3537, 2951, 1734, 1438, 1348, 1222, 1172, 1080 cm^{-1}; ^1H NMR (400 MHz) δ 1.98 (1H, ddd, *J* = 14.7, 9.6, 1.7 Hz), 2.38 (1H, ddd, *J* = 14.8, 7.1, 4.4 Hz), 2.55 (3H, s), 2.78 (1H, d, *J* = 7.5 Hz), 3.02 (3H, s), 3.36 (1H, s), 3.76 (3H, s), 3.96–4.00 (2H, m), 4.13 (1H, t, *J* = 8.0 Hz), 4.73 (1H, d, *J* = 11.6 Hz), 4.78 (1H, d, *J* = 11.6 Hz), 4.89 (1H, td, *J* = 9.8, 7.2 Hz), 5.06–5.07 (1H, m), 7.30–7.37 (5H, m); ^1H NMR (400 MHz, $CDCl_3$-D_2O) δ 1.97 (1H, ddd, *J* = 14.6, 9.6, 1.6 Hz), 2.38 (1H, ddd, *J* = 14.7, 7.1, 4.4 Hz), 2.54 (3H, s), 3.02 (3H, s), 3.37 (1H, s), 3.76 (3H, s), 3.96–4.00 (2H, m), 4.12 (1H, dd, *J* = 10.3, 1.8 Hz), 4.73 (1H, d, *J* = 11.6 Hz), 4.78 (1H, d, *J* = 11.6 Hz), 4.88 (1H, td, *J* = 9.8, 7.2 Hz), 5.06–5.07 (1H, m), 7.28–7.37 (5H, m); ^{13}C NMR (100 MHz) δ 38.3 (CH_2), 38.5 (CH_3), 46.9 (CH_3), 49.3 (CH), 53.2 (CH_3), 67.9 (CH), 70.7 (CH), 73.8 (CH_2), 75.4 (CH), 78.0 (CH), 79.6 (CH), 128.1 (CH), 128.4 (CH), 128.9 (CH), 137.9 (C), 172.6 (C); MS (ESI) *m/z* (relative intensity) 416 ($[M+H]^+$, 100); HRMS (ESI) calcd for $C_{18}H_{25}NO_8S$ $[M+H]^+$ 416.1374, found 416.1378.

Diol 158. To a solution of epoxide **154** (616 mg, 1.93 mmol) in MeOH (20 mL) was added Raney®-Nickel (60 mg). The mixture was activated with an atmosphere of H_2 (balloon) by three times followed by stirring under the same H_2 atmosphere at room temperature for another 2 h. The mixture was filtered and washed with MeOH. The filtrate was concentrated under reduced pressure to give crude amine **156**. The crude

product was redissolved in MeOH (50 mL) and was added AcOH (0.01 mL, 0.19 mmol). The mixture was heated to reflux for 4 h. Concentration of the reaction mixture under reduced pressure and the residue was purified by flash chromatography ($CHCl_3$:MeOH, 80:1) to afford diol **158** (543 mg, 88% overall yield from epoxide **154**) as a colorless oil: $[\alpha]_D^{20}$ +9.4 (*c* 0.95, $CHCl_3$); R_f 0.23 ($CHCl_3$:MeOH, 30:1); IR (thin film) 3403, 2948, 1734, 1457, 1436, 1270, 1173, 1119, 1060, 1015 cm^{-1}; ^1H NMR (400 MHz) δ 1.68 (2H, br s), 2.24 (1H, ddd, *J* = 13.5, 10.2, 1.4 Hz), 2.63−2.70 (4H, m), 2.74 (1H, d, *J* = 3.5 Hz), 3.53−3.56 (1H, m), 3.73 (3H, s), 4.06 (1H, ddd, *J* = 8.0, 2.9, 1.1 Hz), 4.21 (1H, br s), 4.44 (1H, d, *J* = 11.6 Hz), 4.54−4.57 (2H, m), 4.89 (1H, t, *J* = 7.8 Hz), 7.27−7.38 (5H, m); ^1H NMR (400 MHz, $CDCl_3$-D_2O) δ 2.23 (1H, dd, *J* = 12.4, 10.3 Hz), 2.63−2.69 (4H, m), 2.74 (1H, d, *J* = 3.5 Hz), 3.53−3.56 (1H, m), 3.73 (3H, s), 4.06 (1H, dd, *J* = 8.0, 1.8 Hz), 4.19 (1H, ddd, *J* = 10.0, 6.7, 3.2 Hz), 4.44 (1H, d, *J* = 11.6 Hz), 4.52−4.57 (2H, m), 4.89 (1H, t, *J* = 7.8 Hz), 7.27−7.38 (5H, m); ^{13}C NMR (100 MHz) δ 40.8 (CH_2), 44.2 (CH_3), 48.0 (CH), 52.4 (CH_3), 69.4 (CH), 70.4 (CH), 70.8 (CH), 72.4 (CH_2), 73.2 (CH), 128.0 (CH), 128.4 (CH), 128.9 (CH), 137.6 (C), 173.8 (C); MS (ESI) *m/z* (relative intensity) 322 ($[M+H]^+$, 100); HRMS (ESI) calcd for $C_{17}H_{23}NO_5$ $[M+H]^+$ 322.1649, found 322.1652.

Diol 158 by heating the neat amine 156. To a solution of epoxide **154** (69.2 mg, 0.217 mmol) in MeOH (5 mL) was added Raney®-Nickel (8 mg). The mixture was activated with an atmosphere of H_2 (balloon) by three times followed by stirring under the same H_2 atmosphere at room temperature for another 2 h. The mixture was filtered and washed with MeOH. The filtrate was evaporated to dryness under reduced pressure

to give crude amine **156**. The neat crude product was heated at 70 °C for 29 h. The resulting residue was purified by flash chromatography ($CHCl_3$:MeOH, 80:1) to afford diol **158** (61.2 mg, 88% overall yield from epoxide **154**) as a colorless oil.

Diol 158 from epoxide 154 in one step reaction. To a solution of epoxide **154** (24.1 mg, 0.076 mmol) in MeOH (5 mL) was added AcOH (0.4 μL, 0.008 mmol) and Raney®-Nickel (3 mg). The mixture was activated with an atmosphere of H_2 (balloon) by three times followed by stirring under the same H_2 atmosphere at room temperature for 2 h. The H_2 balloon was removed and then the mixture was heated to 60 °C for another 5 h. The reaction mixture was filtered and washed with MeOH. Concentration of filtrate under reduced pressure and the residue was purified by flash chromatography ($CHCl_3$:MeOH, 80:1) to yield diol **158** (20.3 mg, 84%) as a colorless oil.

Triol 159. To a solution of diol **158** (5.8 mg, 0.018 mmol) in MeOH (1 mL) was added Raney®-Nickel (15 mg). The mixture was activated with an atmosphere of H_2 (balloon) by three times followed by stirring under the same H_2 atmosphere at room temperature for another 18 h. The mixture was filtered and washed with MeOH. The filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography ($CHCl_3$:MeOH, 8:1) to afford triol **159** (4.0 mg, 96%) as a colorless oil: $[\alpha]_D^{20}$ +12.2 (*c* 0.60, $CHCl_3$); R_f 0.27 ($CHCl_3$:MeOH, 8:1); IR (thin film) 3380, 2943, 1733, 1437, 1269, 1175, 1058 cm^{-1}; ^1H NMR (400 MHz, MeOD) δ 2.46 (2H, dd, *J* = 8.5, 3.4 Hz), 2.65 (3H, s), 2.94 (1H, d, *J* = 3.4 Hz), 3.41 (1H, dt, *J* = 7.6, 3.0 Hz), 3.73 (3H,

s), 4.00 (1H, dd, J = 8.4, 1.5 Hz), 4.10 (1H, td, J = 8.4, 3.1 Hz), 4.53 (1H, m), 5.15 (1H, t, J = 8.0 Hz); ^{13}C NMR (100 MHz, MeOD) δ 40.4 (CH_2), 44.1 (CH_3), 48.5 (CH), 52.5 (CH_3), 64.1 (CH), 71.1 (CH), 71.5 (CH), 71.9 (CH), 75.2 (CH), 175.2 (C); MS (ESI) *m/z* (relative intensity) 232 ($[M+H]^+$, 100); HRMS (ESI) calcd for $C_{10}H_{17}NO_5$ $[M+H]^+$ 232.1179, found 232.1181.

Tribenzoate 160. To a stirred solution of triol **159** (18.4 mg, 0.080 mmol) in pyridine (0.7 mL) at 0 °C were added benzoyl chloride (0.032 mL, 0.279 mmol) and DMAP (1.0 mg, 0.008 mmol). The reaction mixture was stirred at room temperature for 16 h. Toluene (3 mL) was added and the mixture was then filtered. Concentration of the filtrate and the residue was purified by flash chromatography (hexane:Et_2O, 3:2) to yield tribenzoate **160** (37.0 mg, 86%) as a white solid: mp 151−152 °C; $[\alpha]_D^{20}$ −87.7 (*c* 2.00, $CHCl_3$); R_f 0.18 (hexane:Et_2O, 3:2); IR (thin film) 2946, 1720, 1450, 1273, 1109 cm^{-1}; ^{1}H NMR (400 MHz) δ 2.38 (1H, d, J = 12.1 Hz), 2.85 (3H, s), 3.38 (1H, br s), 3.47 (1H, s), 3.65 (3H, s), 4.04 (1H, s), 4.14 (1H, d, J = 7.3 Hz), 5.59 (1H, q, J = 5.2 Hz), 6.15 (1H, t, J = 7.9 Hz), 6.38 (1H, br s), 7.12 (2H, t, J = 7.3 Hz), 7.38 (1H, t, J = 7.3 Hz), 7.42−7.47 (4H, m), 7.54−7.62 (2H, m), 7.74 (2H, d, J = 7.9 Hz), 8.07 (4H, d, J = 7.7 Hz); ^{13}C NMR (100 MHz, C_6D_6) δ 33.9 (CH_2), 43.9 (CH_3), 47.9 (CH), 51.2 (CH_3), 65.5 (CH), 68.7 (CH), 69.1 (CH), 69.4 (CH), 72.0 (CH), 128.2 (CH), 128.6 (CH), 128.8 (CH), 130.0 (CH), 130.2 (CH), 130.4 (CH), 130.6 (C), 131.1 (C), 132.6 (CH), 133.0 (CH), 133.3 (CH), 165.3 (C), 165.6 (C), 166.0 (C), 170.1 (C); MS (ESI) *m/z* (relative intensity) 544 ($[M+H]^+$, 100); HRMS (ESI) calcd for $C_{31}H_{29}NO_8$ $[M+H]^+$ 544.1966, found 544.1969.

Chloride 162. To a stirred solution of diol **158** (345 mg, 1.07 mmol) and triethylamine (0.60 mL, 4.30 mmol) in CH_2Cl_2 (11 mL) at 0 °C were added benzoyl chloride (0.14 mL, 1.18 mmol) and DMAP (13.1 mg, 0.11 mmol). The reaction mixture was stirred at 0 °C for 2 h and then was added methanesulfonyl chloride (0.16 mL, 1.61 mmol) at 0 °C. The mixture was stirred at room temperature for another 1 h and was quenched by saturated $NaHCO_3$ solution. The aqueous phase was extracted with EtOAc (3 × 25 mL) and the combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, and filtered. Concentration of the filtrate and the residue was purified by flash chromatography (hexane:Et_2O, 2:3) to furnish chloride **162** (424 mg, 89%) as a colorless oil: $[\alpha]_D^{20}$ +43.5 (*c* 1.02, $CHCl_3$); R_f 0.19 (hexane:Et_2O, 2:3); IR (thin film) 3029, 2948, 2901, 1748, 1717, 1452, 1314, 1279, 1175, 1116, 1027 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 1.87 (3H, s), 2.43 (1H, ddd, *J* = 12.2, 6.0, 3.0 Hz), 2.68 (1H, td, *J* = 12.1, 3.3 Hz), 2.84–2.86 (1H, m), 3.36 (3H, s), 3.49 (1H, ddd, *J* = 6.5, 2.9, 1.2 Hz), 3.68 (1H, dd, *J* = 6.1, 2.9 Hz), 3.87 (1H, dd, *J* = 8.9, 6.6 Hz), 4.09 (1H, dd, *J* = 8.9, 6.4 Hz), 4.30 (1H, d, *J* = 12.2 Hz), 4.80 (1H, d, *J* = 12.2 Hz), 6.19 (1H, dt, *J* = 11.8, 6.2 Hz), 7.01–7.14 (4H, m), 7.28 (2H, t, *J* = 7.9 Hz), 7.52 (2H, d, *J* = 7.7 Hz), 8.27–8.30 (2H, m); ^{13}C NMR (100 MHz) δ 29.9 (CH_2), 40.8 (CH_3), 44.6 (CH), 51.8 (CH_3), 57.3 (CH), 64.2 (CH), 65.8 (CH), 66.4 (CH), 73.7 (CH_2), 74.9 (CH), 127.5 (CH), 127.9 (CH), 128.6 (CH), 128.8 (CH), 130.0 (CH), 130.9 (C), 133.0 (CH), 138.1 (C), 166.0 (C), 171.9 (C); MS (ESI) *m/z* (relative intensity) 444 ($[M+H]^+$, 100), 413 (30), 301 (27); HRMS (ESI) calcd for $C_{24}H_{26}ClNO_5$ $[M+H]^+$ 444.1572, found 444.1580.

Alcohol 169. To a solution of chloride **162** (39.2 mg, 0.088 mmol) in MeOH (4 mL) was added Raney®-Nickel (70 mg). The mixture was activated with an atmosphere

of H_2 (balloon) by three times followed by stirring under the same H_2 atmosphere at 50 °C for another 7 h. The reaction mixture was filtered and washed with MeOH. The filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography ($CHCl_3$:MeOH, 15:1) to afford alcohol **169** (20.9 mg, 74%) as a colorless oil: $[\alpha]_D^{20}$ −23.3 (*c* 1.05, $CHCl_3$); R_f 0.12 ($CHCl_3$:MeOH, 15:1); IR (thin film) 3411, 2950, 2805, 1743, 1717, 1602, 1584, 1451, 1316, 1281, 1177, 1118, 1071 cm^{-1}; ^1H NMR (400 MHz) δ 1.63 (1H, dd, *J* = 14.0, 3.6 Hz), 1.84 (1H, br s), 1.97 (1H, ddd, *J* = 11.1, 5.6, 3.3 Hz), 2.34 (3H, s), 2.49 (1H, td, *J* = 11.8, 2.8 Hz), 2.65 (1H, ddd, *J* = 13.8, 10.5, 7.5 Hz), 3.24−3.26 (1H, m), 3.43 (1H, dd, *J* = 6.1, 2.8 Hz), 3.53−3.55 (1H, m), 3.71 (3H, s), 4.89 (1H, ddd, *J* = 10.2, 6.4, 3.6 Hz), 5.71 (1H, dt, *J* = 11.8, 6.2 Hz), 7.41 (2H, t, *J* = 7.8 Hz), 7.53 (1H, tt, *J* = 7.4, 1.3 Hz), 8.02−8.05 (2H, m); ^{13}C NMR (100 MHz) δ 34.8 (CH_2), 35.7 (CH_2), 41.1 (CH_3), 45.1 (CH), 51.9 (CH_3), 60.7 (CH), 67.3 (CH), 67.8 (CH), 71.5 (CH), 128.7 (CH), 130.1 (CH), 130.9 (C), 133.2 (CH), 166.5 (C), 172.3 (C); MS (ESI) *m/z* (relative intensity) 320 ($[M+H]^+$, 100); HRMS (ESI) calcd for $C_{17}H_{21}NO_5$ $[M+H]^+$ 320.1492, found 320.1487.

Mesylate 170. To a stirred solution of alcohol **169** (22.2 mg, 0.70 mmol) and triethylamine (0.023 mL, 0.167 mmol) in CH_2Cl_2 (0.7 mL) at 0 °C were added methanesulfonyl chloride (0.008 mL, 0.083 mmol) and DMAP (0.8 mg, 0.007 mmol). The reaction mixture was stirred at room temperature for 1 h and was quenched by saturated $NaHCO_3$ solution. The aqueous phase was extracted with EtOAc (3 × 15 mL) and the combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, and filtered. Concentration of the filtrate and the residue was purified by flash chromatography (hexane:EtOAc, 2:3) to yield mesylate **170** (26.3 mg, 95%) as a

colorless oil: $[\alpha]_D^{20}$ −14.1 (*c* 1.32, $CHCl_3$); R_f 0.22 (hexane:EtOAc, 2:3); IR (thin film) 2952, 1748, 1717, 1451, 1359, 1281, 1232, 1179, 1116, 1071 cm^{-1}; ^1H NMR (400 MHz) δ 1.89–2.00 (2H, m), 2.35 (3H, s), 2.57 (1H, td, *J* = 11.9, 3.0 Hz), 2.77 (1H, ddd, *J* = 14.8, 10.7, 7.3 Hz), 3.20 (3H, s), 3.32–3.34 (1H, m), 3.39 (1H, dd, *J* = 5.8, 2.9 Hz), 3.71 (3H, s), 3.81 (1H, d, *J* = 5.4 Hz), 5.47–5.53 (2H, m), 7.42 (2H, t, *J* = 7.8 Hz), 7.55 (1H, t, *J* = 7.4 Hz), 8.02 (2H, d, *J* = 7.2 Hz); ^{13}C NMR (100 MHz) δ 32.7 (CH_2), 34.7 (CH_2), 38.8 (CH_3), 41.3 (CH_3), 45.2 (CH), 52.0 (CH_3), 60.4 (CH), 66.4 (CH), 66.5 (CH), 77.5 (CH), 128.7 (CH), 130.0 (CH), 130.5 (C), 133.4 (CH), 166.5 (C), 170.7 (C); MS (ESI) *m/z* (relative intensity) 398 ($[M+H]^+$, 100); HRMS (ESI) calcd for $C_{18}H_{23}SNO_7$ $[M+H]^+$ 398.1268, found 398.1267.

Chloride 173. To a solution of mesylate **170** (16.9 mg, 0.043 mmol) in CH_2Cl_2 (0.4 mL) in a seal tube was added triethylamine (0.03 mL, 0.21 mmol). The solution was degassed and heated at 70 °C for 2 d. The reaction mixture was concentrated under reduced pressure and the residue was purified by flash chromatography (hexane:Et_2O, 2:3) to give chloride **173** (13.8 mg, 96%) as a colorless oil: $[\alpha]_D^{20}$ −39.4 (*c* 0.69, $CHCl_3$); R_f 0.21 (hexane:Et_2O, 2:3); IR (thin film) 2950, 2805, 1750, 1717, 1602, 1451, 1345, 1315, 1280, 1176, 1116 cm^{-1}; ^1H NMR (400 MHz) δ 1.88 (1H, dd, *J* = 14.4, 4.9 Hz), 1.96–2.01 (1H, m), 2.35 (3H, s), 2.48 (1H, td, *J* = 11.8, 2.8 Hz), 2.86 (1H, ddd, *J* = 14.6, 11.4, 7.4 Hz), 3.30–3.31 (1H, m), 3.53 (1H, dd, *J* = 5.9, 2.9 Hz), 3.68–3.70 (1H, m), 3.73 (3H, s), 4.66 (1H, ddd, *J* = 11.3, 6.4, 5.0 Hz), 5.61 (1H, dt, *J* = 12.0, 6.2 Hz), 7.42 (2H, t, *J* = 7.8 Hz), 7.54 (1H, tt, *J* = 7.4, 1.3 Hz), 8.02–8.05 (2H, m); ^{13}C NMR (100 MHz) δ 35.1 (CH_2), 36.4 (CH_2), 41.3 (CH_3), 46.2 (CH), 52.0 (CH_3), 55.4 (CH), 61.0 (CH), 66.4 (CH), 68.6 (CH), 128.7 (CH), 130.1 (CH), 130.6 (C), 133.3 (CH), 166.3 (C),

171.2 (C); MS (ESI) *m/z* (relative intensity) 338 ($[M+H]^+$, 100); HRMS (ESI) calcd for $C_{17}H_{20}ClNO_4$ $[M+H]^+$ 338.1154, found 338.1163.

Chloride 173 from alcohol 169 in one step reaction. To a solution of alcohol **169** (7.2 mg, 0.023 mmol) in CH_2Cl_2 (0.2 mL) in a seal tube at 0 °C was added triethylamine (0.03 mL, 0.184 mmol) and methanesulfonyl chloride (0.002 mL, 0.025 mmol). The reaction mixture was stirred at room temperature for 1 h and was then degassed and heated at 70 °C for 2 d. The reaction mixture was quenched by saturated $NaHCO_3$ solution. The aqueous phase was extracted with EtOAc (3 × 15 mL) and the combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$, and filtered. Concentration of the filtrate and the residue was purified by flash chromatography (hexane:Et_2O, 2:3) to furnish chloride **173** (6.9 mg, 91%) as a colorless oil.

Chloride 173 by reacting mesylate 170 with $^nBu_4NCl$. To a solution of mesylate **170** (3.9 mg, 0.010 mmol) in THF (0.09 mL) in a seal tube was added tetra-*n*-butylammomium chloride (3.3 mg, 0.012 mmol). The solution was degassed and heated at 90 °C for 18 h. The reaction mixture was then filtered and the filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography (hexane:Et_2O, 2:3) to yield chloride **173** (2.6 mg, 78%) as a colorless oil.

Iodide 175. To a solution of mesylate **170** (5.5 mg, 0.014 mmol) in THF (0.14 mL) in a seal tube was added tetra-*n*-butylammomium iodide (6.1 mg, 0.017 mmol). The solution was degassed and heated at 90 °C for 13 h. The reaction mixture was then

filtered and the filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography (hexane:Et_2O, 1:1) to yield iodide **175** (4.6 mg, 77%) as a colorless oil: $[\alpha]_D^{20}$ −48.7 (*c* 0.43, $CHCl_3$); R_f 0.16 (hexane:Et_2O, 1:1); IR (thin film) 2947, 2854, 1748, 1718, 1451, 1277, 1171, 1116, 1026 cm^{-1}; ^1H NMR (400 MHz) δ 1.91−2.00 (2H, m), 2.30 (3H, s), 2.35 (1H, td, *J* = 11.8, 2.8 Hz), 2.82 (1H, ddd, *J* = 14.3, 11.7, 7.2 Hz), 3.26−3.28 (1H, m), 3.57 (1H, dd, *J* = 5.8, 3.0 Hz), 3.65−3.66 (1H, m), 3.73 (3H, s), 4.53 (1H, dt, *J* = 11.9, 6.1 Hz), 5.50 (1H, dt, *J* = 12.0, 6.1 Hz), 7.42 (2H, t, *J* = 7.6 Hz), 7.54 (1H, t, *J* = 7.4 Hz), 8.03−8.05 (2H, m); ^{13}C NMR (100 MHz) δ 19.0 (CH), 35.6 (CH_2), 38.2 (CH_2), 41.4 (CH_3), 49.9 (CH), 52.0 (CH_3), 61.8 (CH), 66.3 (CH), 69.7 (CH), 128.7 (CH), 130.1 (CH), 130.6 (C), 133.3 (CH), 166.3 (C), 171.2 (C); MS (ESI) *m/z* (relative intensity) 430 ($[M+H]^+$, 100); HRMS (ESI) calcd for $C_{17}H_{20}INO_4$ $[M+H]^+$ 430.0510, found 430.0505.

Amine 177. To a solution of chloride **173** (4.7 mg, 0.014 mmol) in MeOH (1 mL) was added Raney®-Nickel (20 mg). The mixture was activated with an atmosphere of H_2 (balloon) by three times followed by stirring under the same H_2 atmosphere at room temperature for another 18 h. The reaction mixture was filtered and washed with MeOH. The filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography (CH_2Cl_2:MeOH, 19:1) to afford amine **177** (2.7 mg, 63%) as a colorless oil: $[\alpha]_D^{20}$ −53.6 (*c* 0.15, $CHCl_3$); R_f 0.43 (CH_2Cl_2:MeOH, 5:1); IR (thin film) 2932, 2854, 1750, 1727, 1449, 1248, 1174, 1140, 1045 cm^{-1}; ^1H NMR (400 MHz) δ 1.17−1.31 (4H, m), 1.34−1.43 (2H, m), 1.59−1.71 (5H, m), 1.83−1.85 (2H, m), 2.00−2.13 (2H, m), 2.19 (3H, s), 2.23−2.33 (2H, m), 2.92 (1H, dd, *J* = 5.5, 3.4 Hz), 3.24 (1H, s), 3.48−3.49 (1H, m), 3.70 (3H, s), 4.95 (1H, dt, *J* = 11.9, 6.0 Hz); ^{13}C NMR (100

MHz) δ 25.5 (CH_2), 25.7 (CH_2), 25.8 (CH_2), 25.8 (CH_2), 26.1 (CH_2), 29.1 (CH_2), 29.3 (CH_2), 35.7 (CH_2), 41.5 (CH_3), 43.4 (CH), 50.4 (CH), 51.7 (CH_3), 61.9 (CH), 65.1 (CH), 66.4 (CH), 171.2 (C), 176.4 (C); MS (ESI) *m/z* (relative intensity) 310 ($[M+H]^+$, 100); HRMS (ESI) calcd for $C_{17}H_{27}NO_4$ $[M+H]^+$ 310.2013, found 310.2014.

1,2:3,4:5,6-Tri-*O*-pentylidene-D-mannitol (181). To a solution of D-mannitol (1.01 g, 5.57 mmol) in 3-pentanone (50 mL) was added concentrated phosphoric acid (0.5 mL). The mixture was heated to reflux with Dean and Stark apparatus for 12 h. It was then cooled down to room temperature and $NaHCO_3$ (3 g) was added. The solution was then filtered, concentration of the filtrate and the residue was purified by flash chromatography (hexane:Et_2O, 12:1) to give **181** (2.02 g, 94%) as a colorless oil: $[\alpha]_D^{20}$ +21.3 (*c* 1.99, $CHCl_3$); R_f 0.21 (hexane:Et_2O, 12:1); IR (thin film) 2974, 2942, 2883, 1464, 1357, 1201, 1174, 1085, 1059 cm^{-1}; ^1H NMR (400 MHz) δ 0.84–0.91 (18H, m), 1.57–1.67 (12H, m), 3.87–3.95 (4H, m), 4.06 (1H, dd, J = 8.0, 6.6 Hz), 4.15–4.19 (2H, m); ^{13}C NMR (100 MHz) δ 8.3, 8.5, 8.6, 29.4, 29.8, 30.5, 67.2, 77.0, 80.1, 113.7, 113.8; MS (ESI) *m/z* (relative intensity) 409 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{21}H_{38}O_6$ $[M+Na]^+$ 409.2561, found 409.2566.

1,2:3,4-Di-*O*-pentylidene-D-mannitol (182). A solution of **181** (11.7 g, 30.3 mmol) in 80% aqueous AcOH (160 mL) was stirred at room temperature for 3 h. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (hexane:Et_2O, 12:1 to hexane:EtOAc, 3:1) to afford firstly starting material **181** (5.93 g, 51%) and secondly diol **182** (2.79 g, 29%) as a colorless oil: $[\alpha]_D^{20}$ +14.9 (*c* 0.86, $CHCl_3$); R_f 0.14 (hexane:EtOAc, 3:1); IR (thin film) 3437, 2973, 2940,

2882, 1464, 1201, 1174, 1130, 1084, 1058 cm^{-1}; ^1H NMR (400 MHz) δ 0.84–0.93 (12H, m), 1.56–1.71 (8H, m), 2.43 (1H, t, J = 6.9 Hz), 3.68–3.89 (6H, m), 3.94 (1H, dd, J = 8.4, 6.5 Hz), 4.02 (1H, dt, J = 8.8, 6.4 Hz), 4.25 (1H, dd, J = 8.4, 6.1 Hz); ^1H NMR (400 MHz, $CDCl_3$-D_2O) δ 0.84–0.93 (12H, m), 1.57–1.71 (8H, m), 3.68–3.82 (4H, m), 3.87 (1H, t, J = 7.7 Hz), 3.92–3.97 (1H, m), 4.00–4.05 (1H, m), 4.23–4.27 (1H, m); ^{13}C NMR (100 MHz) δ 8.3, 8.4, 8.5, 29.1, 29.6, 30.5, 30.6, 64.5, 69.2, 72.6, 76.8, 81.9, 82.0, 113.7, 114.9; MS (ESI) *m/z* (relative intensity) 341 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{16}H_{30}O_6$ $[M+Na]^+$ 341.1935, found 341.1930.

Alkenes 184 and 185. Following the glycol cleavage produce, diol **182** (3.34 g, 10.5 mmol) was converted into aldehyde **183** as a colorless oil. The crude product was redissolved in THF (40 mL) and was cooled to −78 °C. A solution of vinylmagnesium bromide in THF (90 mL, 31.5 mmol) freshly generated was added at –78 °C. The mixture was stirred at –78 °C for 15 h and was then quenched by saturated NH_4Cl solution. The aqueous phase was extracted with EtOAc (3 × 100 mL) and the combined organic extracts were dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure and the residue was purified by flash chromatography (hexane:Et_2O, 8:1) to afford firstly alkene **184** (1.45 g, 44% overall yield from diol **182**) as a colorless oil and secondly alkene **185** (0.97 g, 29% overall yield from diol **182**) as a colorless oil. Data for **184**: $[\alpha]_D^{20}$ −18.0 (*c* 0.91, $CHCl_3$); R_f 0.35 (hexane:Et_2O, 4:1); IR (thin film) 3481, 2973, 2941, 2883, 1464, 1357, 1272, 1174, 1082, 1059 cm^{-1}; ^1H NMR (400 MHz) δ 0.85–0.90 (12H, m), 1.57–1.65 (8H, m), 2.86 (1H, d, J = 9.8 Hz), 3.80 (1H, t, J = 8.2 Hz), 3.89 (1H, dd, J = 8.1, 6.6 Hz), 3.98–4.03 (2H, m), 4.18 (1H, dd, J = 8.1, 6.4 Hz), 4.35–4.37 (1H, m), 5.23 (1H, d, J = 10.6 Hz),

5.38 (1H, d, J = 17.3 Hz), 6.01 (1H, ddd, J = 17.0, 10.6, 4.6 Hz); ^{1}H NMR (400 MHz, $CHCl_3$-D_2O) δ 0.84–0.90 (12H, m), 1.57–1.65 (8H, m), 3.80 (1H, t, J = 8.2 Hz), 3.88 (1H, dd, J = 8.2, 6.6 Hz), 3.98–4.03 (2H, m), 4.18 (1H, dd, J = 8.1, 6.3 Hz), 4.35 (1H, s), 5.23 (1H, dd, J = 10.6, 1.5 Hz), 5.37 (1H, dd, J = 17.3, 1.5 Hz), 6.01 (1H, ddd, J = 17.0, 10.6, 4.6 Hz); ^{13}C NMR (100 MHz) δ 8.4, 8.4, 8.4, 8.5, 29.1, 29.8, 30.5, 30.5, 69.1, 71.1, 77.3, 78.0, 83.3, 113.4, 114.4, 116.1, 137.8; MS (ESI) *m/z* (relative intensity) 337 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{17}H_{30}O_5$ [M+Na]$^+$ 337.1985, found 337.1992.

Data for **185**: $[\alpha]_D^{20}$ +31.0 (*c* 0.45, $CHCl_3$); R_f 0.28 (hexane:Et_2O, 4:1); IR (thin film) 3473, 2973, 2940, 2882, 1464, 1357, 1200, 1174, 1084, 1059 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.84–0.93 (12H, m), 1.57–1.70 (8H, m), 3.51 (1H, d, J = 2.3 Hz), 3.71 (1H, t, J = 8.0 Hz), 3.79 (1H, t, J = 7.0 Hz), 3.94 (1H, dd, J = 8.4, 6.6 Hz), 4.04 (1H, dt, J = 8.4, 6.4 Hz), 4.15 (1H, t, J = 5.9 Hz), 4.23 (1H, dd, J = 8.4, 6.2 Hz), 5.25 (1H, dt, J = 10.5, 1.4 Hz), 5.40 (1H, dt, J = 17.3, 1.5 Hz), 6.03 (1H, ddd, J = 16.8, 10.5, 5.8 Hz); ^{1}H NMR (400 MHz, $CHCl_3$-D_2O) δ 0.84–0.93 (12H, m), 1.57–1.71 (8H, m), 3.71 (1H, t, J = 8.0 Hz), 3.79 (1H, t, J = 7.0 Hz), 3.94 (1H, dd, J = 8.4, 6.6 Hz), 4.04 (1H, dt, J = 8.4, 6.4 Hz), 4.12–4.16 (1H, m), 4.23 (1H, dd, J = 8.4, 6.2 Hz), 5.25 (1H, dt, J = 10.5, 1.4 Hz), 5.40 (1H, dt, J = 17.2, 1.6 Hz), 6.03 (1H, ddd, J = 17.1, 10.5, 5.8 Hz); ^{13}C NMR (100 MHz) δ 8.3, 8.4, 8.5, 29.1, 29.7, 30.6, 30.6, 69.1, 73.8, 76.9, 81.7, 84.2, 113.6, 114.7, 116.9, 137.3; MS (ESI) *m/z* (relative intensity) 337 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{17}H_{30}O_5$ [M+Na]$^+$ 337.1985, found 337.1989.

Benzyl ether 186. Sodium hydride (60%, 140 mg, 3.49 mmol) was suspended in dry THF (10 mL) under nitrogen at 0 °C. A solution of the alkene **184** (457 mg, 1.45 mmol) in THF (10 mL) was added dropwise over 1 h at 0 °C, and then the mixture was

stirred at 0 °C for 1 h. Benzyl bromide (0.21 mL, 1.75 mmol) was added dropwise over 15 min and tetra-*n*-butylammomium iodide (53.7 mg, 0.15 mmol) was added. The reaction mixture was stirred at room temperature for 21 h. Water was then added slowly at 0 °C to destroy the excess of hydride, and this was followed by the addition of saturated NH_4Cl solution. The aqueous layer was extracted with Et_2O (2 × 20 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, and filtered. Concentration of the filtrate and the residue was purified by flash chromatography (hexane:Et_2O, 20:1) to give benzyl ether **186** (570 mg, 97%) as a colorless oil: $[\alpha]_D^{20}$ +40.5 (*c* 0.96, $CHCl_3$); R_f 0.24 (hexane:Et_2O, 19:1); IR (thin film) 2973, 2940, 2881, 1457, 1201, 1173, 1123, 1083, 1059 cm^{-1}; ^1H NMR (400 MHz) δ 0.84–0.89 (12H, m), 1.52–1.68 (8H, m), 3.88 (1H, dd, *J* = 7.2, 5.4 Hz), 3.92–3.98 (2H, m), 4.04–4.13 (3H, m), 4.37 (1H, d, *J* = 12.0 Hz), 4.67 (1H, d, *J* = 12.0 Hz), 5.31–5.34 (1H, m), 5.36 (1H, s), 5.94 (1H, ddd, *J* = 16.7, 10.9, 7.9 Hz), 7.24–7.35 (5H, m); ^{13}C NMR (100 MHz) δ 8.3, 8.5, 8.6, 29.3, 30.0, 30.4, 30.5, 68.3, 70.7, 77.6, 77.8, 80.5, 83.1, 113.8, 119.4, 127.0, 127.8, 128.6, 136.0, 138.8; MS (ESI) *m/z* (relative intensity) 427 ($[M+Na]^+$, 100), 413 (38); HRMS (ESI) calcd for $C_{24}H_{36}O_5$ $[M+Na]^+$ 427.2455, found 427.2450.

Diol 187. A solution of benzyl ether **186** (327 mg, 0.81 mmol) in 80% aqueous AcOH (15 mL) was stirred at room temperature for 12 h. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (hexane:Et_2O, 19:1 to hexane:EtOAc, 2:1) to afford firstly starting material benzyl ether **186** (62.7 mg, 19%) and secondly diol **187** (203 mg, 74%) as a colorless oil: $[\alpha]_D^{20}$ +14.8 (*c* 0.95, $CHCl_3$); R_f 0.19 (hexane:EtOAc, 2:1); IR (thin film) 3427, 2973, 2938, 2880,

1456, 1203, 1121, 1085, 1059 cm^{-1}; ^1H NMR (400 MHz) δ 0.83−0.89 (6H, m), 1.55−1.63 (4H, m), 2.32 (1H, t, *J* = 6.2 Hz), 3.62−3.66 (1H, m), 3.67−3.71 (1H, m), 3.75−3.80 (2H, m), 3.91 (1H, t, *J* = 8.0 Hz), 4.02 (1H, dd, *J* = 8.2, 4.1 Hz), 4.25 (1H, dd, *J* = 6.6, 4.2 Hz), 4.45 (1H, d, *J* = 11.6 Hz), 4.72 (1H, d, *J* = 11.6 Hz), 5.39−5.46 (2H, m), 5.90 (1H, ddd, *J* = 17.4, 10.6, 7.0 Hz), 7.30−7.38 (5H, m); ^1H NMR (400 MHz, $CHCl_3$-D_2O) δ 0.82−0.88 (6H, m), 1.55−1.63 (4H, m), 3.60−3.64 (1H, m), 3.66−3.70 (1H, m), 3.77 (1H, dd, *J* = 11.3, 3.9 Hz), 3.91 (1H, t, *J* = 8.1 Hz), 4.01 (1H, dd, *J* = 8.2, 4.2 Hz), 4.25 (1H, dd, *J* = 6.8, 4.2 Hz), 4.45 (1H, d, *J* = 11.6 Hz), 4.72 (1H, d, *J* = 11.6 Hz), 5.39−5.46 (2H, m), 5.90 (1H, ddd, *J* = 17.4, 10.6, 6.9 Hz), 7.30−7.38 (5H, m); ^{13}C NMR (100 MHz) δ 8.3, 8.3, 30.4, 30.4, 64.6, 71.8, 73.0, 77.5, 78.8, 81.8, 113.3, 120.7, 128.5, 128.6, 129.0, 133.5, 137.2; MS (ESI) *m/z* (relative intensity) 359 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{19}H_{28}O_5$ $[M+Na]^+$ 359.1829, found 359.1829.

Isoxazolidines 180 and 189. Following the glycol cleavage produce, diol **187** (30.7 mg, 0.091 mmol) was converted into aldehyde **188** as a colorless oil. Following the INAC reaction procedure (Method A) using DMF (6 mL) as the reaction solvent and the product was purified by flash chromatography (hexane:Et_2O, 2:1 to 1:1), aldehyde **188** was converted into firstly isoxazolidine **180** (4.4 mg, 14% overall yield from diol **187**) as a colorless oil and secondly isoxazolidine **189** (19.4 mg, 64% overall yield from diol **187**) as a white solid. Data for **180**: $[\alpha]_D^{20}$ −94.5 (*c* 0.75, $CHCl_3$); R_f 0.15 (hexane:Et_2O, 2:1); IR (thin film) 2972, 2941, 2882, 1461, 1199, 1176, 1119, 1072, 1057, 1003 cm^{-1}; ^1H NMR (400 MHz) δ 0.92−0.97 (6H, m), 1.65−1.76 (4H, m), 2.12 (1H, ddd, *J* = 13.0, 5.2, 4.0 Hz), 2.42 (1H, d, *J* = 13.0 Hz), 2.61 (3H, s), 3.46 (1H, d, *J* = 8.0 Hz), 3.53−3.63 (3H, m), 4.42 (1H, d, *J* = 5.6 Hz), 4.60 (1H, d, *J* = 11.6 Hz), 4.73

(1H, d, J = 11.6 Hz), 7.27–7.37 (5H, m); ^{13}C NMR (100 MHz) δ 8.6 (CH_3), 8.7 (CH_3), 26.2 (CH_2), 29.9 (CH_2), 30.2 (CH_2), 45.7 (CH_3), 60.9 (CH), 71.9 (CH_2), 77.7 (CH), 78.6 (CH), 79.3 (CH), 81.5 (CH), 116.4 (C), 128.1 (CH), 128.2 (CH), 128.8 (CH), 138.2 (C); MS (ESI) *m/z* (relative intensity) 334 ($[M+H]^+$, 100); HRMS (ESI) calcd for $C_{19}H_{27}NO_4$ $[M+H]^+$ 334.2013, found 334.2007.

Data for **189**: mp 81–82 °C; $[\alpha]_D^{20}$ +24.1 (*c* 0.45, $CHCl_3$); R_f 0.14 (hexane:Et_2O, 1:1); IR (thin film) 2969, 2941, 2881, 1455, 1127, 1084, 1061 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.92–0.99 (6H, m), 1.66–1.75 (4H, m), 1.77–1.88 (1H, m), 2.34 (1H, dt, J = 12.0, 5.8 Hz), 2.68 (3H, s), 3.28 (1H, d, J = 9.1 Hz), 3.45 (1H, d, J = 9.0 Hz), 3.57 (1H, d, J = 5.4 Hz), 4.12 (1H, t, J = 9.1 Hz), 4.51 (1H, d, J = 6.1 Hz), 4.63 (1H, d, J = 12.2 Hz), 4.82 (1H, d, J = 12.2 Hz), 7.24–7.39 (5H, m); ^{13}C NMR (100 MHz) δ 8.6 (CH_3), 8.9 (CH_3), 29.9 (CH_2), 30.0 (CH_2), 33.1 (CH_2), 47.6 (CH_3), 62.2 (CH), 71.5 (CH_2), 78.8 (CH), 79.9 (CH), 79.9 (CH), 80.0 (CH), 115.2 (C), 127.8 (CH), 128.2 (CH), 128.6 (CH), 138.7 (C); MS (ESI) *m/z* (relative intensity) 356 ($[M+Na]^+$, 100), 248 (29); HRMS (ESI) calcd for $C_{19}H_{27}NO_4$ $[M+Na]^+$ 356.1832, found 356.1833; Anal. Calcd for $C_{19}H_{27}NO_4$: C, 68.44; H, 8.16; N, 4.20, found: C, 68.73; H, 8.34; N, 4.33.

Amine 190. To a solution of isoxazolidine **180** (9.0 mg, 0.027 mmol) in EtOH (1 mL) was added Raney®-Nickel (2 mg). The mixture was activated with an atmosphere of H_2 (balloon) by three times followed by stirring under the same H_2 atmosphere at room temperature for another 2 h. The reaction mixture was filtered and washed with EtOH. The filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography (CH_2Cl_2:MeOH, 20:1) to afford amine **190** (8.0 mg, 88%) as a colorless oil: $[\alpha]_D^{20}$ −36.4 (*c* 0.20, $CHCl_3$); R_f 0.16 ($CHCl_3$:MeOH, 10:1);

IR (thin film) 3315, 2969, 2933, 2883, 1460, 1357, 1167, 1073 cm^{-1}; ^1H NMR (400 MHz) δ 0.92–0.96 (6H, m), 1.29 (1H, q, J = 11.5 Hz), 1.66–1.73 (4H, m), 2.07 (2H, br s), 2.30 (1H, dt, J = 13.0, 4.7 Hz), 2.47 (3H, s), 2.72 (1H, ddd, J = 11.0, 9.8, 4.3 Hz), 3.38 (1H, t, J = 9.2 Hz), 3.42–3.50 (2H, m), 3.63–3.69 (1H, m), 4.65 (1H, d, J = 11.5 Hz), 4.97 (1H, d, J = 11.6 Hz), 7.28–7.40 (5H, m); ^{13}C NMR (100 MHz) δ 8.6 (CH_3), 30.6 (CH_2), 30.6 (CH_2), 34.2 (CH_3), 35.8 (CH_2), 56.5 (CH), 71.5 (CH), 73.0 (CH_2), 80.8 (CH), 82.1 (CH), 82.7 (CH), 115.8 (C), 128.2 (CH), 128.5 (CH), 128.8 (CH), 138.6 (C); MS (ESI) *m/z* (relative intensity) 336 ($[M+H]^+$, 100), 250 (43), 142 (27); HRMS (ESI) calcd for $C_{19}H_{29}NO_4$ $[M+H]^+$ 336.2169, found 336.2178.

Amine 191. To a solution of isoxazolidine **189** (18.7 mg, 0.056 mmol) in EtOH (2 mL) was added Raney®-Nickel (5 mg). The mixture was activated with an atmosphere of H_2 (balloon) by three times followed by stirring under the same H_2 atmosphere at room temperature for another 2 h. The reaction mixture was filtered and washed with EtOH. The filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography (CH_2Cl_2:MeOH, 40:1) to afford amine **191** (15.6 mg, 83%) as a white solid: mp 60 °C; $[\alpha]_D^{20}$ −27.8 (*c* 0.26, $CHCl_3$); R_f 0.12 ($CHCl_3$:MeOH, 40:1); IR (thin film) 3316, 2968, 2932, 2879, 1460, 1356, 1093 cm^{-1}; ^1H NMR (400 MHz) δ 0.93–0.99 (6H, m), 1.23 (1H, dt, J = 15.1, 2.8 Hz), 1.68–1.76 (4H, m), 2.33 (1H, dt, J = 15.2, 2.9 Hz), 2.48 (3H, s), 3.22–3.23 (1H, m), 3.38–3.43 (2H, m), 4.10–4.11 (1H, m), 4.34 (1H, t, J = 9.8 Hz), 4.79 (1H, d, J = 12.5 Hz), 4.87 (1H, d, J = 12.6 Hz), 7.25–7.28 (1H, m), 7.33 (2H, t, J = 7.6 Hz), 7.42 (2H, d, J = 7.3 Hz); ^{13}C NMR (100 MHz) δ 8.5 (CH_3), 8.9 (CH_3), 30.4 (CH_2), 30.4 (CH_2), 30.5 (CH_2), 34.8 (CH_3), 56.9 (CH), 71.2 (CH), 71.5 (CH_2), 75.3 (CH), 79.4 (CH), 80.2 (CH), 114.0 (C),

127.8 (CH), 128.4 (CH), 128.6 (CH), 139.0 (C); MS (ESI) *m/z* (relative intensity) 336 ($[M+H]^+$, 100), 250 (23); HRMS (ESI) calcd for $C_{19}H_{29}NO_4$ $[M+H]^+$ 336.2169, found 336.2157.

Benzyl ether 192. Sodium hydride (60%, 26.3 mg, 0.657 mmol) was suspended in dry THF (4 mL) under nitrogen at 0 °C. A solution of the alkene **185** (93.9 mg, 0.299 mmol) in THF (4 mL) was added dropwise over 1 h at 0 °C, and then the mixture was stirred at 0 °C for 1 h. Benzyl bromide (0.039 mL, 0.329 mmol) was added dropwise over 15 min and tetra-*n*-butylammomium iodide (11.0 mg, 0.030 mmol) was added. The reaction mixture was stirred at room temperature for 22 h. Water was then added slowly at 0 °C to destroy the excess of hydride, and this was followed by the addition of saturated NH_4Cl solution. The aqueous layer was extracted with Et_2O (2 × 10 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, and filtered. Concentration of the filtrate and the residue was purified by flash chromatography (hexane:Et_2O, 20:1) to yield benzyl ether **192** (117 mg, 97%) as a colorless oil: $[\alpha]_D^{20}$ −24.0 (*c* 0.41, $CHCl_3$); R_f 0.17 (hexane:Et_2O, 20:1); IR (thin film) 2974, 2941, 2882, 1456, 1174, 1080, 1059 cm^{-1}; ^1H NMR (400 MHz) δ 0.79 (3H, t, *J* = 7.5 Hz), 0.84 (3H, t, *J* = 7.5 Hz), 0.85−0.90 (6H, m), 1.52−1.66 (8H, m), 3.72 (1H, t, *J* = 7.8 Hz), 3.84 (1H, dd, *J* = 7.6, 6.4 Hz), 3.96 (1H, dd, *J* = 8.5, 3.2 Hz), 4.03−4.13 (3H, m), 4.41 (1H, d, *J* = 12.3 Hz), 4.69 (1H, d, *J* = 12.3 Hz), 5.23 (1H, dd, *J* = 17.4, 1.3 Hz), 5.41 (1H, dd, *J* = 10.3, 1.7 Hz), 5.97 (1H, ddd, *J* = 17.4, 10.3, 8.5 Hz), 7.23−7.30 (5H, m); ^{13}C NMR (100 MHz) δ 8.4 (CH_3), 8.4 (CH_3), 8.5 (CH_3), 8.6 (CH_3), 29.3 (CH_2), 29.9 (CH_2), 30.5 (CH_2), 30.5 (CH_2), 68.4 (CH_2), 70.5 (CH_2), 77.7 (CH), 79.0 (CH), 80.7 (CH), 82.8 (CH), 113.7

(C), 114.0 (C), 121.0 (CH_2), 127.9 (CH), 128.3 (CH), 128.6 (CH), 134.7 (CH), 138.5 (C); MS (ESI) *m/z* (relative intensity) 427 ($[M+Na]^+$, 100), 413 (55), 149 (70); HRMS (ESI) calcd for $C_{24}H_{36}O_5$ $[M+Na]^+$ 427.2455, found 427.2446.

Diol 193. A solution of benzyl ether **192** (64.4 mg, 0.16 mmol) in 80% aqueous AcOH (5 mL) was stirred at room temperature for 12 h. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (hexane:Et_2O, 20:1 to hexane:EtOAc, 2:1) to afford firstly starting material benzyl ether **192** (15.2 mg, 24%) and secondly diol **193** (39.7 mg, 74%) as a colorless oil: $[\alpha]_D^{20}$ −41.9 (*c* 0.33, $CHCl_3$); R_f 0.19 (hexane:EtOAc, 2:1); IR (thin film) 3396, 2973, 2939, 2881, 1457, 1203, 1087, 1058 cm^{-1}; ^1H NMR (400 MHz) δ 0.83−0.87 (6H, m), 1.55−1.62 (4H, m), 2.28 (1H, t, *J* = 6.1 Hz), 3.61−3.65 (1H, m), 3.66−3.72 (1H, m), 3.75−3.90 (5H, m), 4.38 (1H, d, *J* = 11.4 Hz), 4.69 (1H, d, *J* = 11.3 Hz), 5.41 (1H, d, *J* = 17.3 Hz), 5.48 (1H, dd, *J* = 10.3, 1.2 Hz), 5.87 (1H, ddd, *J* = 17.2, 10.4, 7.7 Hz), 7.30−7.38 (5H, m); ^1H NMR (400 MHz, $CHCl_3$-D_2O) δ 0.82−0.87 (6H, m), 1.55−1.63 (4H, m), 3.60−3.64 (1H, m), 3.68 (1H, dd, *J* = 11.4, 4.2 Hz), 3.74−3.90 (4H, m), 4.38 (1H, d, *J* = 11.3 Hz), 4.69 (1H, d, *J* = 11.3 Hz), 5.41 (1H, d, *J* = 17.3 Hz), 5.48 (1H, d, *J* = 10.3 Hz), 5.87 (1H, ddd, *J* = 17.4, 10.3, 7.8 Hz), 7.30−7.39 (5H, m); ^{13}C NMR (100 MHz) δ 8.2 (CH_3), 8.4 (CH_3), 30.4 (CH_2), 30.6 (CH_2), 64.5 (CH_2), 70.9 (CH_2), 73.1 (CH), 81.5 (CH), 81.9 (CH), 82.3 (CH), 114.0 (C), 121.1 (CH_2), 128.7 (CH), 128.8 (CH), 129.0 (CH), 135.4 (CH), 136.9 (C); MS (ESI) *m/z* (relative intensity) 359 ($[M+Na]^+$, 100), 301 (15), 149 (33); HRMS (ESI) calcd for $C_{19}H_{28}O_5$ $[M+Na]^+$ 359.1829, found 359.1824.

Isoxazolidine 196. Following the glycol cleavage produce, diol **193** (32.0 mg, 0.095 mmol) was converted into aldehyde **194** as a colorless oil. Following the INAC reaction procedure (Method A) using DMF (5 mL) as the reaction solvent and the product was purified by flash chromatography (hexane:Et_2O, 2:1), aldehyde **194** was converted into isoxazolidine **196** (16.5 mg, 52% overall yield from diol **193**) as a colorless oil: $[\alpha]_D^{20}$ +47.1 (*c* 0.61, $CHCl_3$); R_f 0.27 (hexane:Et_2O, 3:2); IR (thin film) 2966, 2938, 2880, 1457, 1167, 1142, 1111, 1071, 1057 cm^{-1}; ^1H NMR (400 MHz) δ 0.93–0.99 (6H, m), 1.69–1.84 (4H, m), 2.18–2.23 (1H, m), 2.31 (1H, d, *J* = 12.2 Hz), 2.67 (3H, s), 3.59 (1H, d, *J* = 5.4 Hz), 3.73 (1H, d, *J* = 9.6 Hz), 4.00 (1H, dd, *J* = 9.6, 3.3 Hz), 4.10 (1H, dd, *J* = 4.7, 3.4 Hz), 4.53–4.55 (2H, m), 4.93 (1H, d, *J* = 11.7 Hz); ^{13}C NMR (100 MHz) δ 8.6 (CH_3), 8.8 (CH_3), 30.1 (CH_2), 30.2 (CH_2), 31.5 (CH_2), 47.6 (CH_3), 63.0 (CH), 73.2 (CH_2), 74.4 (CH), 77.4 (CH), 77.7 (CH), 78.4 (CH), 114.3 (C), 127.9 (CH), 127.9 (CH), 128.7 (CH), 139.0 (C); MS (ESI) *m/z* (relative intensity) 334 ($[M+H]^+$, 100); HRMS (ESI) calcd for $C_{19}H_{27}NO_4$ $[M+H]^+$ 334.2013, found 334.2005.

Diol 197. To a stirred solution of isoxazolidine **196** (26.0 mg, 0.078 mmol) in CH_2Cl_2 (3 mL) were added deionized water (0.05 mL) and TFA (0.2 mL) at room temperature to form a clear solution. The mixture was stirred at room temperature for 2 h. Concentration of the mixture under reduced pressure and the residue was purified by flash chromatography ($CHCl_3$:MeOH, 40:1) to furnish diol **197** (18.5 mg, 89%) as a white solid: mp 159 °C; $[\alpha]_D^{20}$ +20.7 (*c* 0.35, $CHCl_3$); R_f 0.25 ($CHCl_3$:MeOH, 19:1); IR (thin film) 3332, 2927, 1442, 1240, 1164, 1110, 1081, 1047 cm^{-1}; ^1H NMR (400 MHz) δ 2.13 (1H, dt, *J* = 12.2, 5.6 Hz), 2.31 (1H, d, *J* = 12.2 Hz), 2.50 (1H, d, *J* = 9.7 Hz), 2.61–2.63 (4H, m), 3.24 (1H, dd, *J* = 5.5, 2.2 Hz), 3.43 (1H, t, *J* = 7.4 Hz), 3.74–3.82

(2H, m), 4.47 (1H, t, J = 4.6 Hz), 4.56 (1H, d, J = 11.6 Hz), 4.62 (1H, d, J = 11.6 Hz), 7.30−7.38 (5H, m); ^{1}H NMR (400 MHz, $CHCl_3$-D_2O) δ 2.13 (1H, dt, J = 12.2, 5.6 Hz), 2.31 (1H, d, J = 12.2 Hz), 2.63 (3H, s), 3.24 (1H, dd, J = 5.2, 1.6 Hz), 3.43 (1H, d, J = 8.1 Hz), 3.74−3.80 (2H, m), 4.46 (1H, t, J = 4.9 Hz), 4.55 (1H, d, J = 11.6 Hz), 4.62 (1H, d, J = 11.6 Hz), 7.30−7.37 (5H, m); ^{13}C NMR (100 MHz) δ 28.9 (CH_2), 47.6 (CH_3), 66.9 (CH), 73.8 (CH_2), 74.1 (CH), 75.5 (CH), 76.7 (CH), 77.8 (CH), 128.3 (CH), 128.6 (CH), 129.0 (CH), 138.0 (C); MS (ESI) *m/z* (relative intensity) 266 ($[M+H]^+$, 100), 149 (40); HRMS (ESI) calcd for $C_{14}H_{19}NO_4$ $[M+H]^+$ 266.1387, found 266.1386.

Amine 199. To a solution of isoxazolidine **196** (8.3 mg, 0.025 mmol) in EtOH (1 mL) was added Raney®-Nickel (2 mg). The mixture was activated with an atmosphere of H_2 (balloon) by three times followed by stirring under the same H_2 atmosphere at room temperature for another 17 h. The reaction mixture was filtered and washed with EtOH. The filtrate was concentrated under reduced pressure. The residue was purified by flash chromatography (CH_2Cl_2:MeOH, 80:1) to afford amine **199** (7.8 mg, 93%) as a colorless oil: $[\alpha]_D^{20}$ +11.2 (*c* 0.32, $CHCl_3$); R_f 0.40 ($CHCl_3$:MeOH, 19:1); IR (thin film) 3314, 2968, 2931, 1459, 1359, 1131, 1095 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.97 (6H, t, J = 7.4 Hz), 1.61 (1H, dt, J = 15.0, 2.8 Hz), 1.67−1.79 (4H, m), 2.12 (1H, dt, J = 15.0, 2.6 Hz), 2.48 (3H, s), 3.31 (1H, d, J = 2.7 Hz), 3.98 (1H, d, J = 2.8 Hz), 4.08 (1H, dd, J = 10.2, 3.4 Hz), 4.19 (1H, t, J = 2.8 Hz), 4.32 (1H, dd, J = 10.2, 2.4 Hz), 4.63 (1H, d, J = 11.8 Hz), 4.91 (1H, d, J = 11.8 Hz), 7.28−7.33 (5H, m); ^{13}C NMR (100 MHz) δ 8.6 (CH_3), 8.7 (CH_3), 27.5 (CH_2), 30.5 (CH_2), 30.6 (CH_2), 34.7 (CH_3), 58.1 (CH), 72.1 (CH), 73.5 (CH_2), 74.0 (CH), 75.6 (CH), 78.0 (CH), 113.0 (C), 127.7 (CH), 127.8 (CH),

128.6 (CH), 139.2 (C); MS (ESI) *m/z* (relative intensity) 336 ($[M+H]^+$, 100), 250 (35); HRMS (ESI) calcd for $C_{19}H_{29}NO_4$ $[M+H]^+$ 336.2169, found 336.2176.

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Appendix

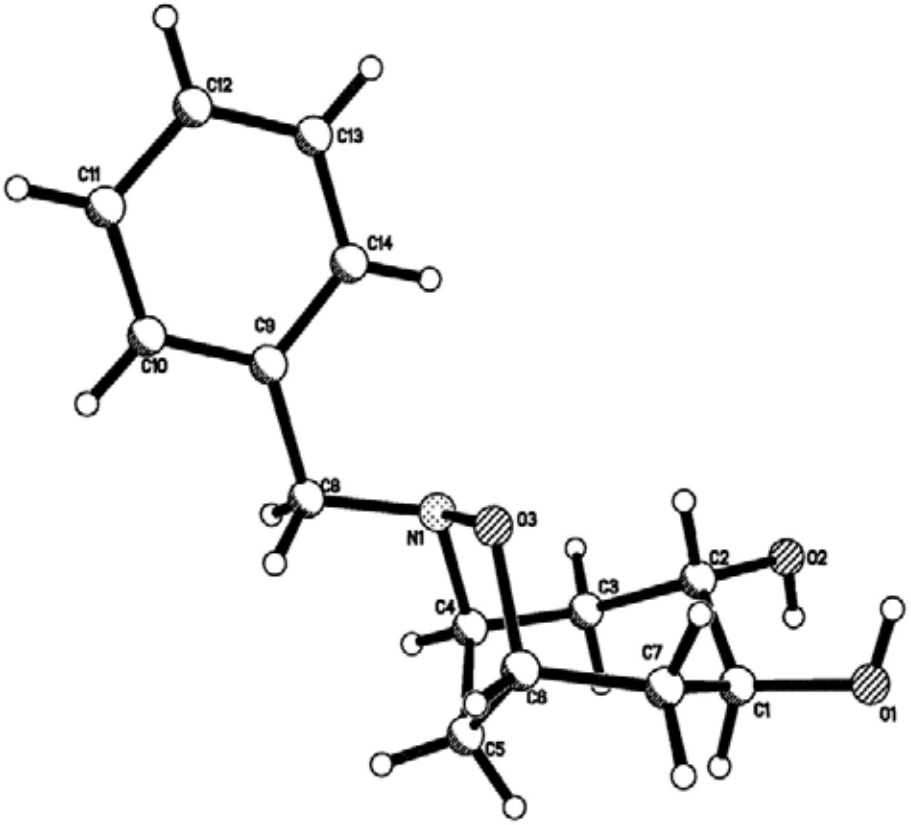
NMR spectra were measured in $CDCl_3$ solutions, unless stated otherwise.

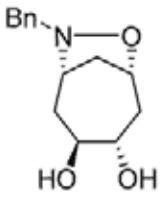
X-ray crystallographic data and structure of diol **108**

Table 1. Crystal data and structure refinement for p.

Identification code	shb32
Empirical formula	C14 H19 N O3
Formula weight	249.30
Temperature	293(2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, C2
Unit cell dimensions	a = 8.750(2) A alpha = 90 deg. b = 7.445(2) A beta = 94.372(7) deg. c = 20.096(6) A gamma = 90 deg.
Volume	1305.3(6) A^3
Z, Calculated density	4, 1.269 Mg/m^3
Absorption coefficient	0.089 mm^-1
F(000)	536
Crystal size	0.40 x 0.30 x 0.30 mm
Theta range for data collection	1.02 to 24.99 deg.
Limiting indices	-9<=h<=10, -8<=k<=8, -19<=l<=23
Reflections collected / unique	3521 / 2154 [R(int) = 0.0643]
Completeness to theta = 24.99	100.0 %
Absorption correction	SADBS
Max. and min. transmission	1.000 and 0.089585
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2154 / 1 / 164
Goodness-of-fit on F^2	1.046
Final R indices [I>2sigma(I)]	R1 = 0.0679, wR2 = 0.1657

R indices (all data)	R1 = 0.1219, wR2 = 0.2226
Absolute structure parameter	1(3)
Largest diff. peak and hole	0.308 and -0.513 e.A^-3





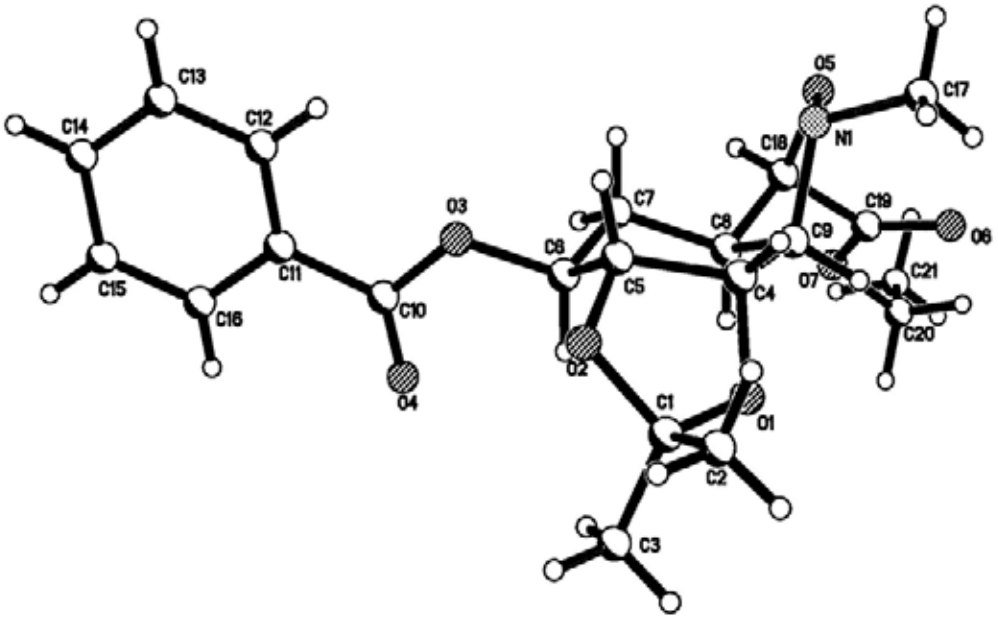
108

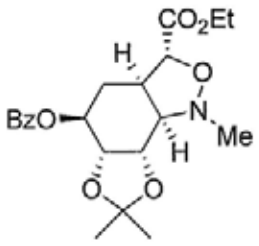
X-ray crystallographic data and structure of benzoate **134**

Table 1. Crystal data and structure refinement for p.

Identification code	skh78(cu)
Empirical formula	C21 H27 N O7
Formula weight	405.44
Temperature	296(2) K
Wavelength	1.54178 A
Crystal system, space group	Monoclinic, P2(1)
Unit cell dimensions	a = 8.7187(2) A alpha = 90 deg. b = 10.0275(2) A beta = 103.938(2) deg. c = 12.7718(3) A gamma = 90 deg.
Volume	1083.72(4) A^3
Z, Calculated density	2, 1.242 Mg/m^3
Absorption coefficient	0.776 mm^-1
F(000)	432
Crystal size	0.40 x 0.20 x 0.20 mm
Theta range for data collection	3.57 to 67.31 deg.
Limiting indices	-10<=h<=9, -7<=k<=11, -15<=l<=14
Reflections collected / unique	3660 / 2326 [R(int) = 0.0291]
Completeness to theta = 67.31	91.4 %
Absorption correction	Multiscan
Max. and min. transmission	1.0000 and 0.162000
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2326 / 1 / 263
Goodness-of-fit on F^2	1.063

Final R indices [I>2sigma(I)]	R1 = 0.0473, wR2 = 0.1449
R indices (all data)	R1 = 0.0561, wR2 = 0.1600
Absolute structure parameter	-0.3(4)
Extinction coefficient	0.0084(16)
Largest diff. peak and hole	0.193 and -0.192 e.A^-3





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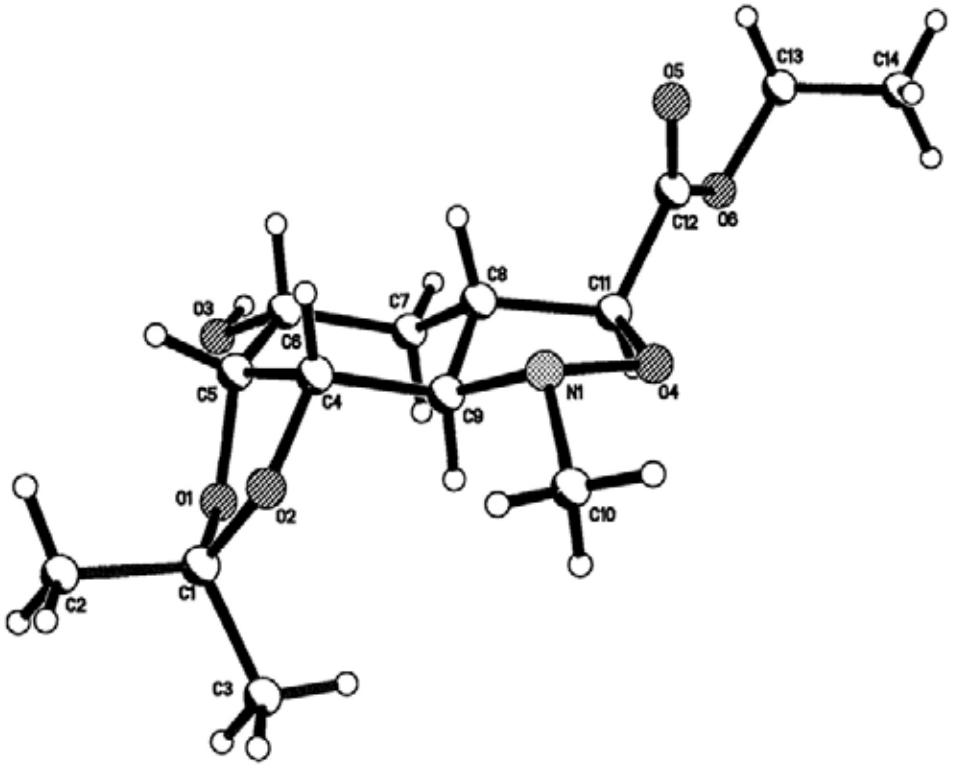
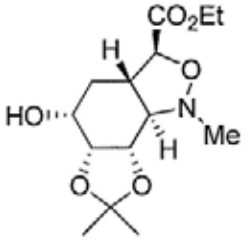
X-ray crystallographic data and structure of isoxazolidine **138**

Table 1. Crystal data and structure refinement for p.

Identification code	skh73-3
Empirical formula	C14 H23 N O6
Formula weight	301.33
Temperature	296(2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, P2(1)
Unit cell dimensions	a = 10.4120(8) A alpha = 90 deg. b = 6.8959(5) A beta = 107.878(2) deg. c = 11.3411(9) A gamma = 90 deg.
Volume	774.97(10) A^3
Z, Calculated density	2, 1.291 Mg/m^3
Absorption coefficient	0.101 mm^-1
F(000)	324
Crystal size	0.40 x 0.40 x 0.30 mm
Theta range for data collection	1.89 to 27.89 deg.
Limiting indices	-13<=h<=13, -9<=k<=9, -14<=l<=8
Reflections collected / unique	6452 / 3402 [R(int) = 0.0182]
Completeness to theta = 27.89	98.2 %
Absorption correction	Multiscan
Max. and min. transmission	1.000 and 0.826843
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3402 / 1 / 191
Goodness-of-fit on F^2	1.049

Final R indices [I>2sigma(I)]	R1 = 0.0489, wR2 = 0.1351
R indices (all data)	R1 = 0.0629, wR2 = 0.1478
Absolute structure parameter	-0.4(13)
Largest diff. peak and hole	0.279 and -0.239 e.A^-3





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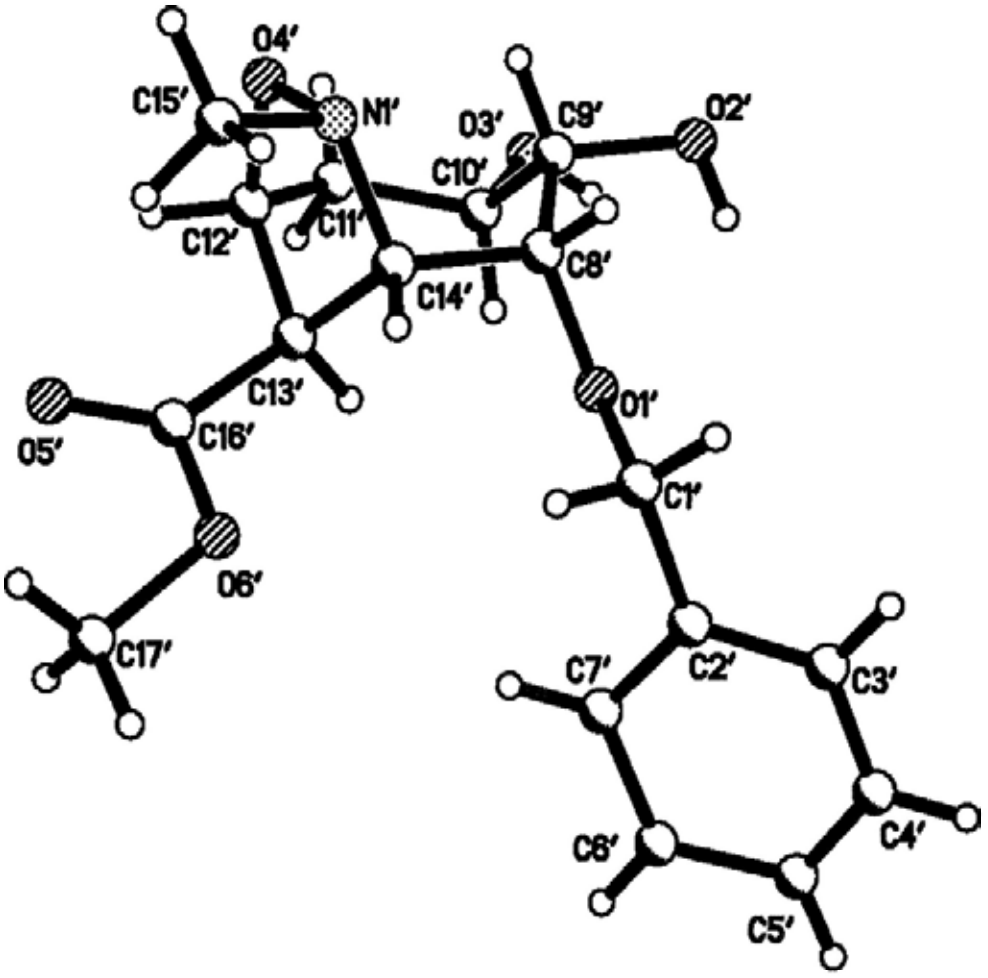
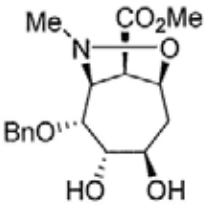
X-ray crystallographic data and structure of diol **149**

Table 1. Crystal data and structure refinement for p.

Identification code	shr11
Empirical formula	C17 H23 N O6
Formula weight	337.36
Temperature	296(2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, P2(1)
Unit cell dimensions	a = 12.322(2) A alpha = 90 deg. b = 10.019(2) A beta = 112.203(3) deg. c = 15.678(3) A gamma = 90 deg.
Volume	1791.9(6) A^3
Z, Calculated density	4, 1.251 Mg/m^3
Absorption coefficient	0.095 mm^-1
F(000)	720
Crystal size	0.40 x 0.30 x 0.20 mm
Theta range for data collection	2.47 to 25.00 deg.
Limiting indices	-13<=h<=14, -9<=k<=11, -18<=l<=17
Reflections collected / unique	11292 / 5789 [R(int) = 0.0480]
Completeness to theta = 25.00	99.4 %
Absorption correction	Multiscan
Max. and min. transmission	0.7456 and 0.5126
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5789 / 1 / 433
Goodness-of-fit on F^2	0.908

Final R indices [I>2sigma(I)]	R1 = 0.0609, wR2 = 0.1431
R indices (all data)	R1 = 0.1200, wR2 = 0.1626
Absolute structure parameter	2.3(15)
Largest diff. peak and hole	0.376 and -0.270 e.A^-3





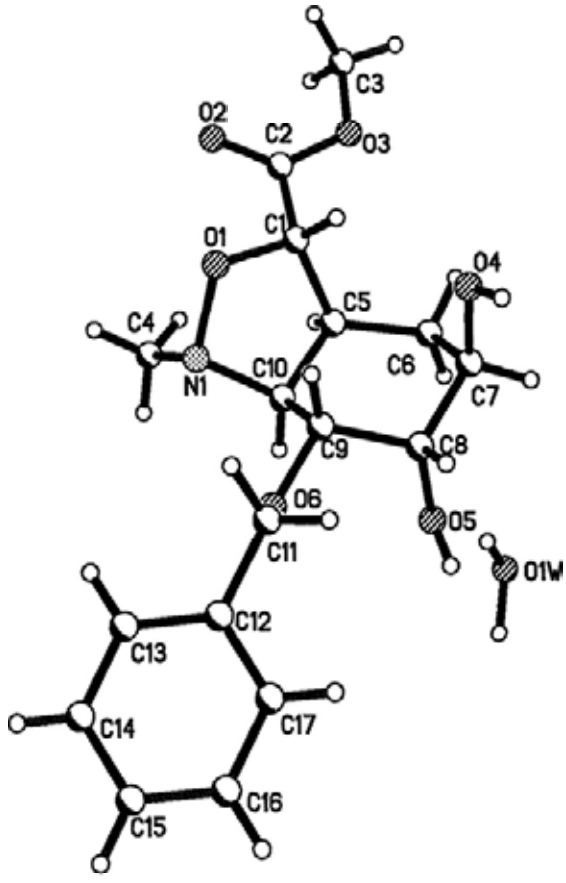
149

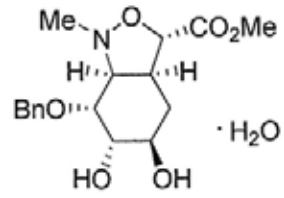
X-ray crystallographic data and structure of hydrated diol **150**

Table 1. Crystal data and structure refinement for p.

Identification code	SHR12
Empirical formula	C17 H25 N O7
Formula weight	355.38
Temperature	296(2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, P2(1)2(1)2(1)
Unit cell dimensions	a = 8.7316(8) A alpha = 90 deg. b = 11.9598(11) A beta = 90 deg. c = 16.9623(15) A gamma = 90 deg.
Volume	1771.3(3) A^3
Z, Calculated density	4, 1.333 Mg/m^3
Absorption coefficient	0.103 mm^-1
F(000)	760
Crystal size	0.40 x 0.30 x 0.20 mm
Theta range for data collection	2.08 to 25.25 deg.
Limiting indices	-10<=h<=10, -14<=k<=14, -20<=l<=20
Reflections collected / unique	15155 / 1856 [R(int) = 0.0377]
Completeness to theta = 25.25	100.0 %
Absorption correction	multi-scan
Max. and min. transmission	0.7456 and 0.6563
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1856 / 0 / 226
Goodness-of-fit on F^2	1.086

Final R indices [I>2sigma(I)]	R1 = 0.0427, wR2 = 0.1195
R indices (all data)	R1 = 0.0535, wR2 = 0.1316
Absolute structure parameter	0.6(19)
Largest diff. peak and hole	0.334 and -0.281 e.A^-3





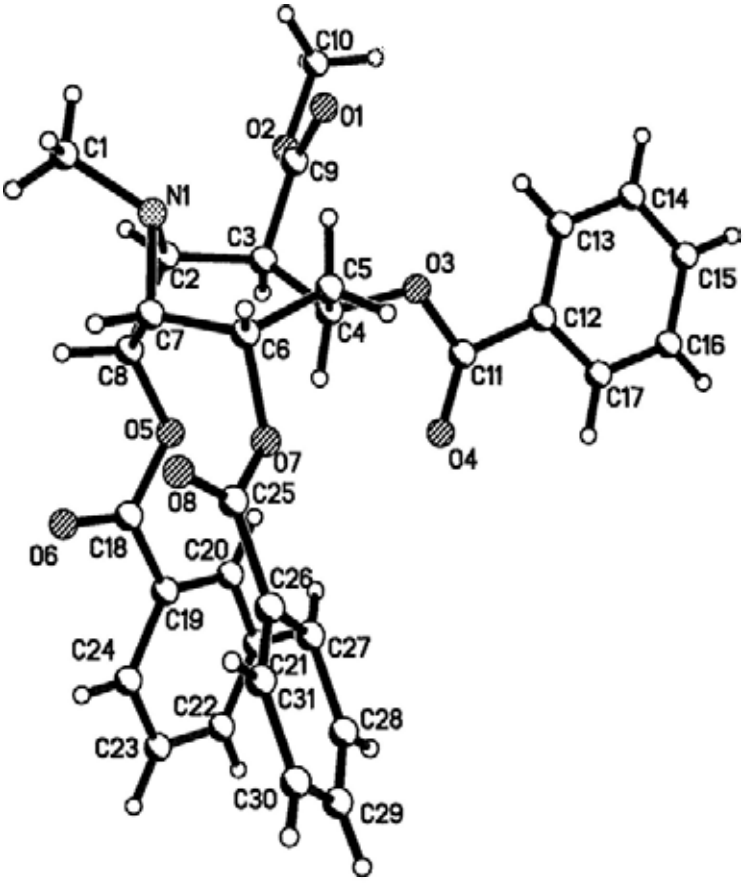
150

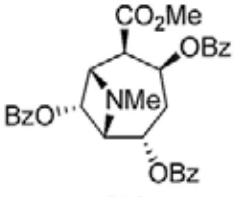
X-ray crystallographic data and structure of tribenzoate **160**

Table 1. Crystal data and structure refinement for p.

Identification code	SHR65
Empirical formula	C31 H29 N O8
Formula weight	543.55
Temperature	296(2) K
Wavelength	0.71073 A
Crystal system, space group	Orthorhombic, P2(1)2(1)2(1)
Unit cell dimensions	a = 9.897(6) A alpha = 90 deg. b = 11.401(8) A beta = 90 deg. c = 24.683(16) A gamma = 90 deg.
Volume	2785(3) A^3
Z, Calculated density	4, 1.296 Mg/m^3
Absorption coefficient	0.094 mm^-1
F(000)	1144
Crystal size	0.40 x 0.30 x 0.20 mm
Theta range for data collection	1.65 to 25.25 deg.
Limiting indices	-5<=h<=11, -13<=k<=13, -29<=l<=29
Reflections collected / unique	16943 / 5034 [R(int) = 0.1148]
Completeness to theta = 25.25	99.9 %
Absorption correction	multi-scan
Max. and min. transmission	0.7456 and 0.4761
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5034 / 0 / 361
Goodness-of-fit on F^2	0.987
Final R indices [I>2sigma(I)]	R1 = 0.0781, wR2 = 0.1676

R indices (all data)	R1 = 0.1712, wR2 = 0.2127
Absolute structure parameter	2(2)
Largest diff. peak and hole	0.399 and -0.274 e.A^-3





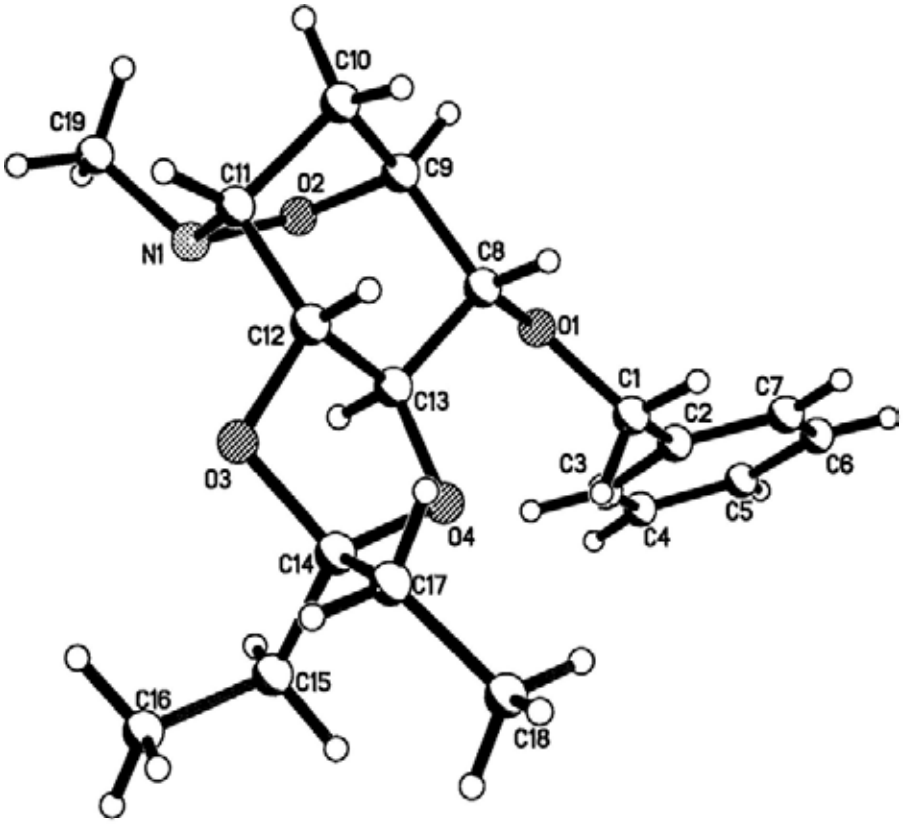
160

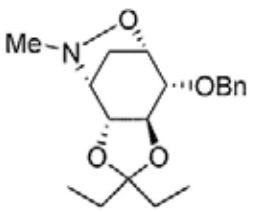
X-ray crystallographic data and structure of isoxazolidine **189**

Table 1. Crystal data and structure refinement for p.

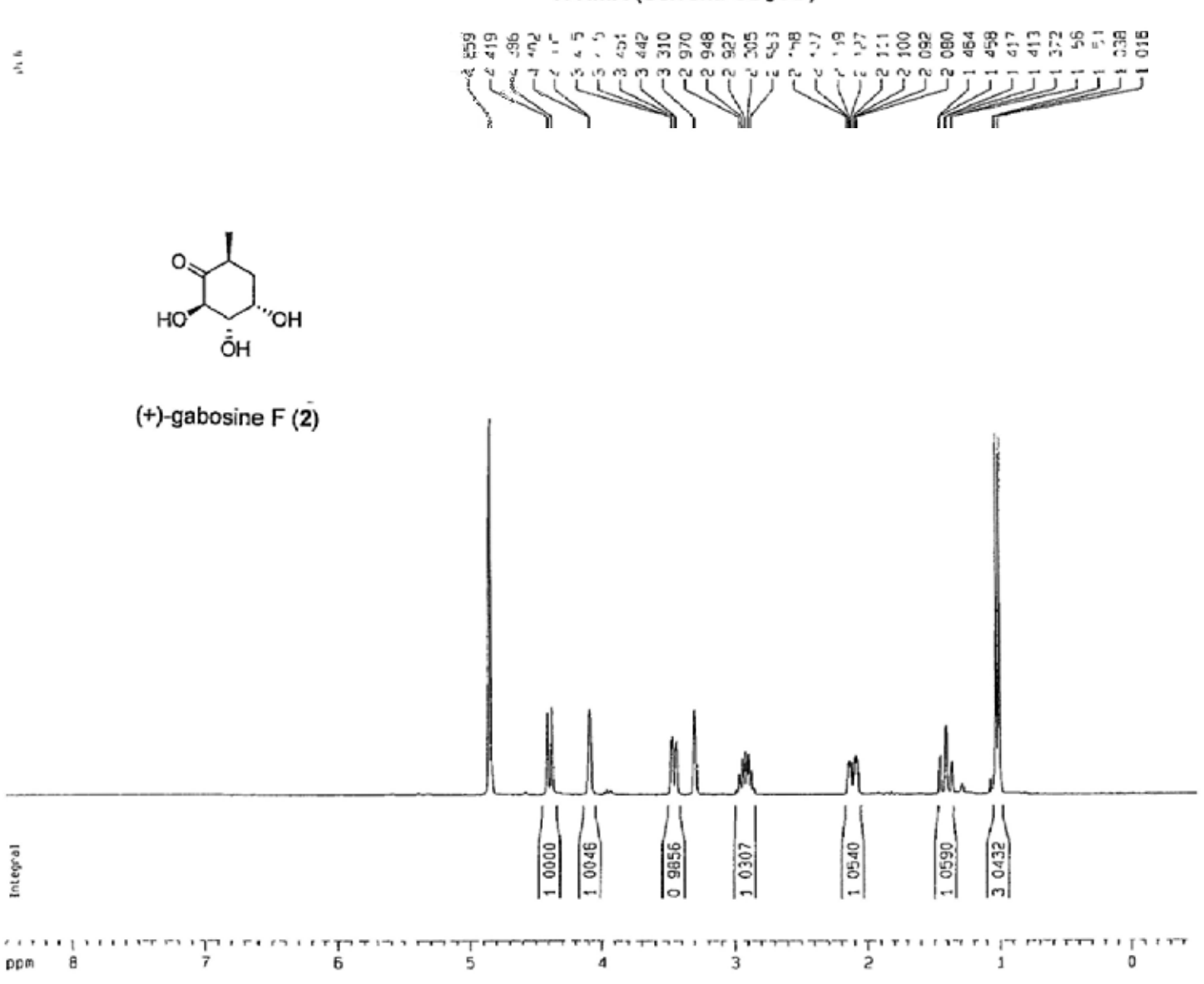
Identification code	sha37
Empirical formula	C19 H27 N O4
Formula weight	333.42
Temperature	296(2) K
Wavelength	0.71073 A
Crystal system, space group	Orthorhombic, P2(1)2(1)2(1)
Unit cell dimensions	a = 8.9665(5) A alpha = 90 deg. b = 10.5916(7) A beta = 90 deg. c = 19.6233(14) A gamma = 90 deg.
Volume	1863.6(2) A^3
Z, Calculated density	4, 1.188 Mg/m^3
Absorption coefficient	0.083 mm^-1
F(000)	720
Crystal size	0.40 x 0.30 x 0.20 mm
Theta range for data collection	2.08 to 25.25 deg.
Limiting indices	-5<=h<=10, -12<=k<=12, -23<=l<=23
Reflections collected / unique	13263 / 3375 [R(int) = 0.0487]
Completeness to theta = 25.25	100.0 %
Absorption correction	multi-scan
Max. and min. transmission	0.7456 and 0.6385
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3375 / 0 / 217
Goodness-of-fit on F^2	1.047

Final R indices [I>2sigma(I)]	R1 = 0.0435, wR2 = 0.1073
R indices (all data)	R1 = 0.0582, wR2 = 0.1213
Absolute structure parameter	0.6(13)
Largest diff. peak and hole	0.154 and -0.211 e.A^-3

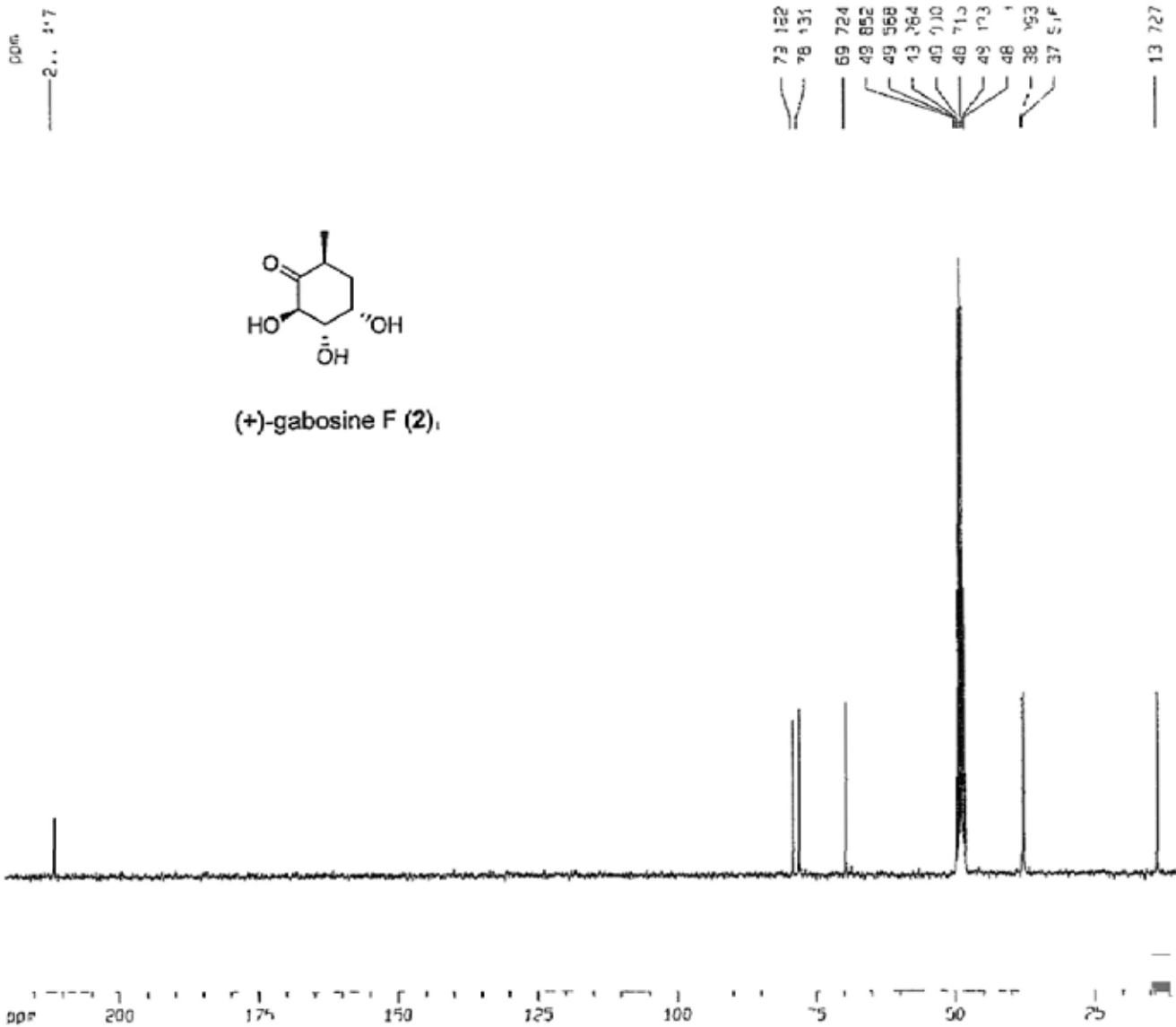




189


^{1}H NMR (Solvent: CD_3OD)
(+)-gabosine F (2)
Integral
1.0000
1.0046
0.9856
1.0307
1.0540
1.0590
3.0432
ppm 8 7 6 5 4 3 2 1 0
Current Data Parameters
NAME
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date 20071215
Time 13 36
INSTRUM spect
PROBHD 5 mm PABBO BB/
PULPROG zg30
TD 65536
SOLVENT CD3OD
NS 8
DS 0
SWH 6172.839 Hz
FIDRES 0.274439 Hz
AQ 5.3084928 sec
RG 181
DW 55.600 usec
DE 79.63 usec
TE 0.0 K
D1 1.00000000 sec
D11 0.03000000 sec
D12 0.00002000 sec
D13 0.00000400 sec
D16 0.00020000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 5.00 usec
PL1 2.00 dB
SFO1 300.1312008 MHz
F2 - Processing parameters
SI 32768
SF 300.1300046 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1D NMR plot parameters
CX 22.00 cm
CY 6.91 cm
F1P 8.500 ppm
F1 2551.10 Hz
F2P -0.500 ppm
F2 150.07 Hz
PPMCM 0.40909 ppm/cm
HZCM 122.78046 Hz/cm

^{13}C NMR (Solvent CD_3OD)



(+)-gabosine F (**2**).

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EXPNO 1
PROCNO 1

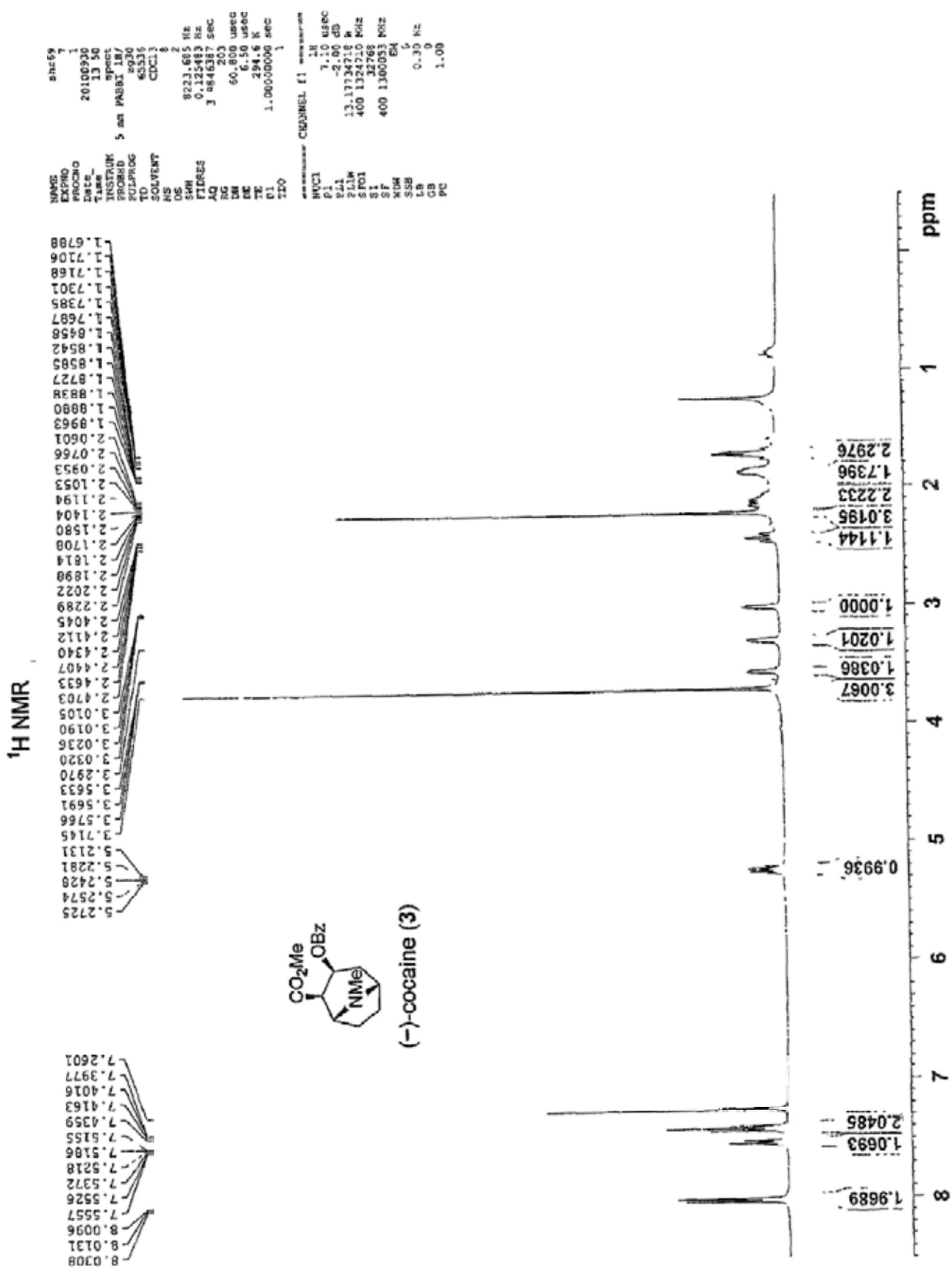
F2 Acquisition Parameters
Date 20071215
Time 13 10
INSTRUM dpx300
PROBHD 5 mm DBO PB 1H
PULPROG zgpg
TD 65536
SOLVENT CD3OD
NS 1024
DS 4
SWH 22 050 Hz
FIDRES 0 673584 Hz
AQ 1 4868267 sec
RG 8192
DW 22 650 usec
DE 6 00 usec
TE 0 0 K
D1 1 00000000 sec
D11 0 03000000 sec
TCREST 0 00000000 sec
TCWRK 0 01500000 sec

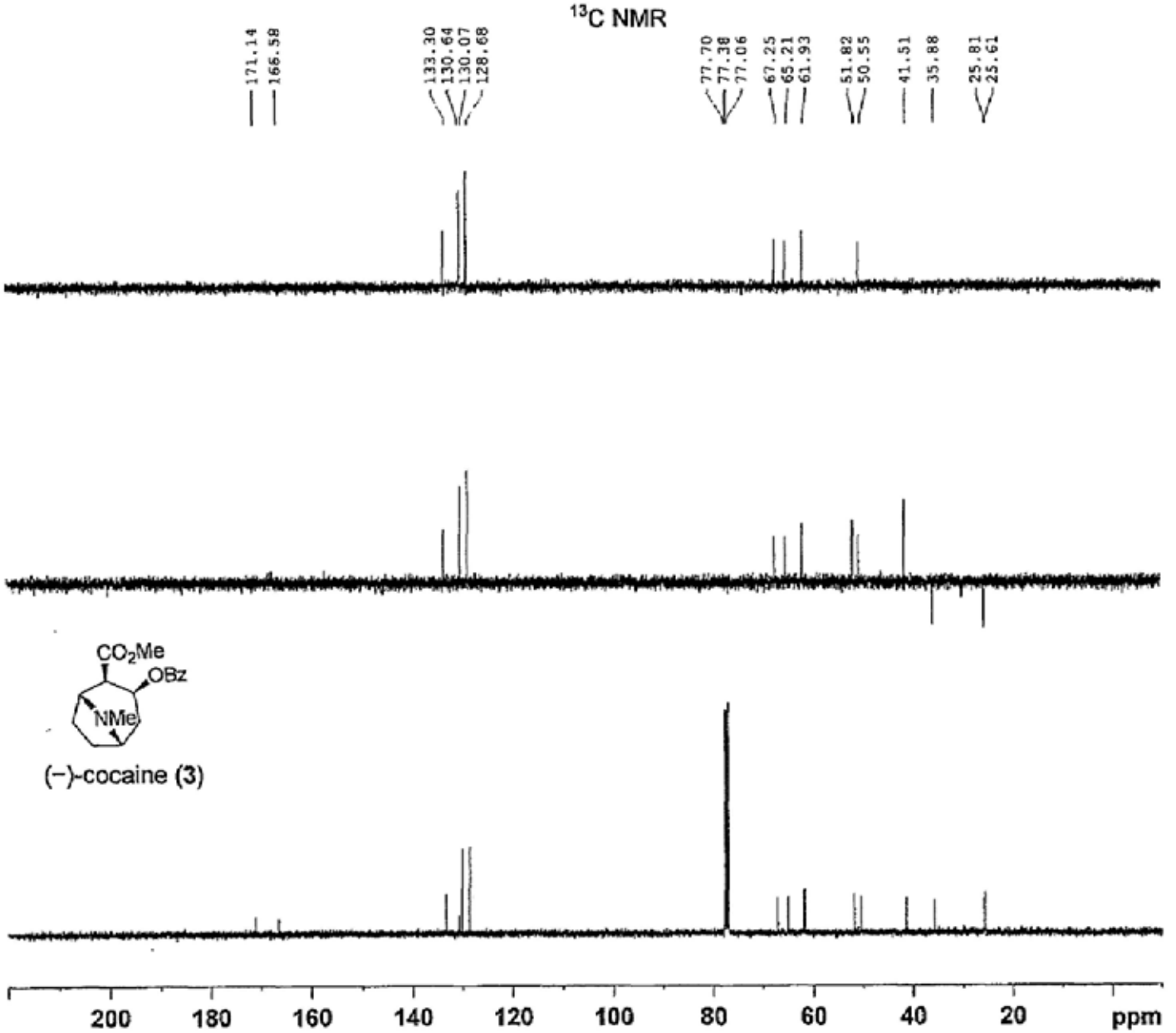
======== CHANNEL f1 ========
NUC1 13C
P1 3 00 usec
PL1 -6 00 dB
SFO1 75 4745111 MHz

======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100 00 usec
PL2 120 00 dB
PL12 19 00 dB
SFO2 300 1315007 MHz

F2 Processing parameters
SI 65536
SF 75 4675438 MHz
WDW EM
SSB 0
LB 3 00 Hz
GB 0
PC 1 40

1D NMR plot parameters
CX 23 00 cm
CY 11 30 cm
F1P 220 000 ppm
F1 16602 88 Hz
F2P -20 000 ppm
F2 -1509 35 Hz
PPMCM 10 43478 ppm/cm
HZCM 787 48846 Hz/cm


^{1}H NMR
(−)-cocaine (3)
CO2Me
OBz
NMe
ppm



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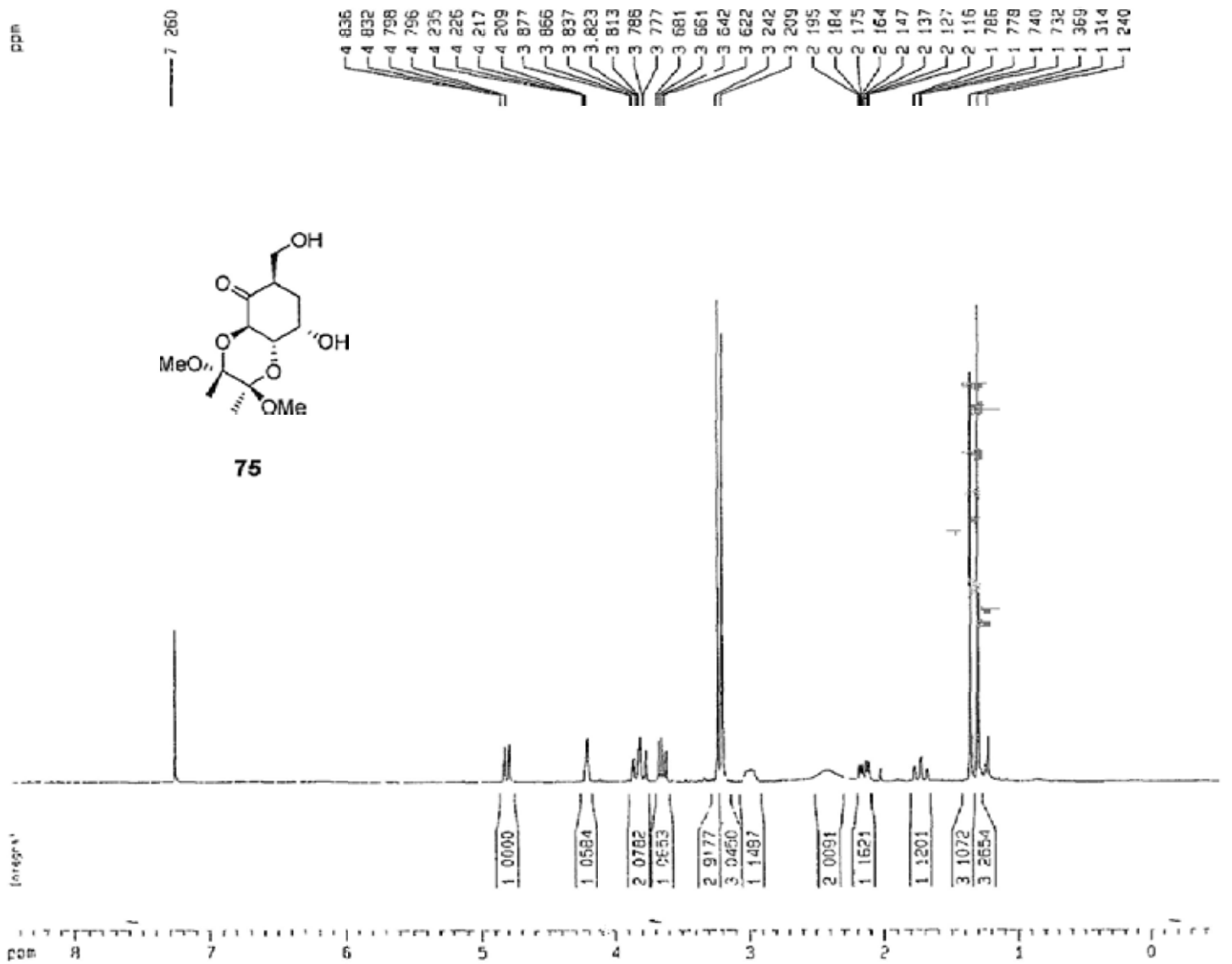
PROCNO	1
Date_	20100602
Time	12.06
INSTRUM	spect
PROBHD	5 mm PABBI 1H/
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	253
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	294.7 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
--------	CHANNEL f1 --------
NUC1	13C
P1	14.50 usec
PL1	-4.00 dB
PL1W	90.22689819 W
SFO1	100.6228298 MHz
--------	CHANNEL f2 --------
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	-2.00 dB
PL12	18.80 dB
PL13	18.80 dB
PL2W	13.17734718 W
PL12W	0.10960442 W
PL13W	0.10960442 W
SFO2	400.1316005 MHz
SI	32768
SF	100.6127339 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

^{1}H NMR



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Current Data Parameters
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PROCNO                     1

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Time                  19 56
INSTRUM             cpx300
PROBHD     5 mm BBO BB-1H
PULPROG                zg
TD                    32768
SOLVENT               CDCl3
NS                        8
DS                        0
SWH               8992 806 Hz
FIDRES            0 274439 Hz
AQ                1 8219508 sec
RG                  203 2
DW                 55 600 usec
DE                 79 43 usec
TE                  0 0 K
D1                1 00000000 sec
MCREST            0 00000000 sec
MCWRK             0 01500000 sec

======== CHANNEL f1 ========
NUC1                      1H
P1                  5 00 usec
PL1                -2 00 dB
SFO1          300 1312000 MHz

F2 - Processing parameters
SI                    32768
SF          300 1300063 MHz
WDW                      EM
SSB                       0
LB                 0 30 Hz
GB                        0
PC                     1 00

1D NMR plot parameters
CX                   22 60 cm
CY                    8 71 cm
F1P                8 500 ppm
F1                 2551 10 Hz
F2P                -0 500 ppm
F2                 -150 07 Hz
PPMCM             0 40909 ppm/cm
HZCM             122 78046 Hz/cm
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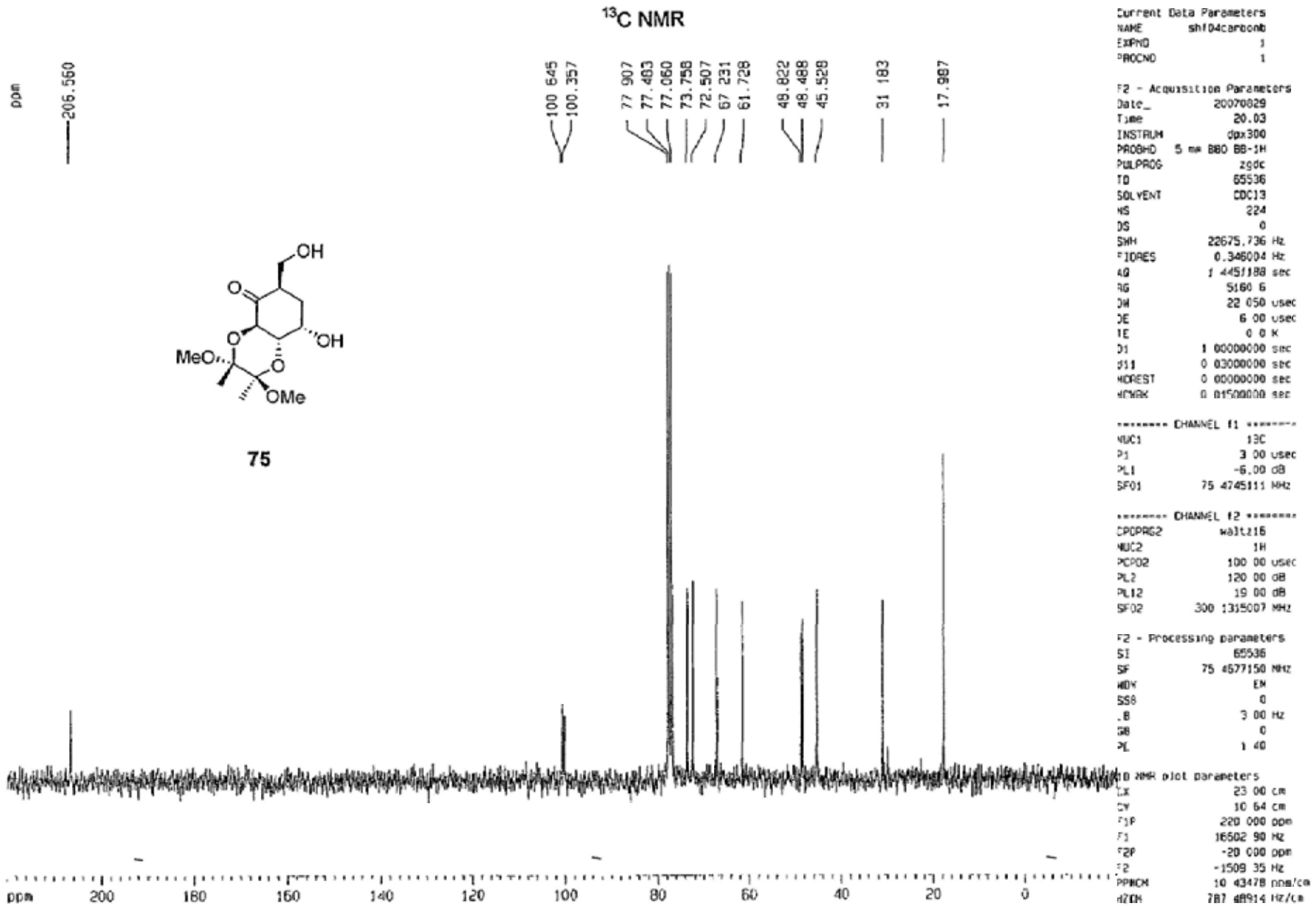
^{13}C NMR
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100.357
77.907
77.483
77.060
73.758
72.507
67.231
61.728
48.822
48.488
45.528
31.183
17.987
OH
O
O
OH
MeO
O
OMe
75
ppm
200
180
160
140
120
100
80
60
40
20
0
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EXPNO 1
PROCNO 1
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Date_ 20070829
Time 20.03
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PULPROG zgdc
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SOLVENT CDCl3
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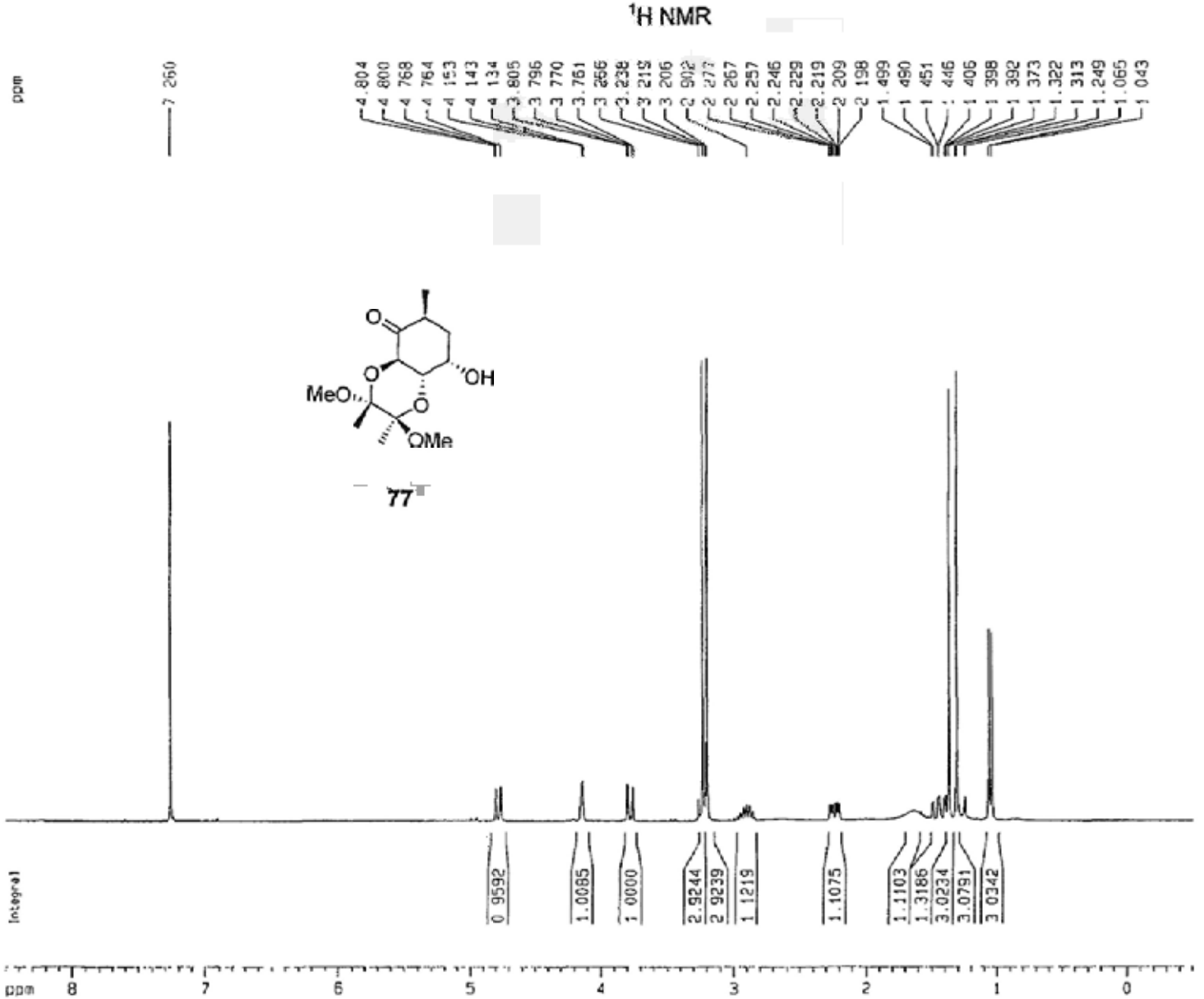
DS 0
SWH 22675.736 Hz
FIDRES 0.346004 Hz
AQ 1.4451188 sec
RG 5160.6
DW 22.050 usec
DE 6.00 usec
TE 0.0 K
D1 1.00000000 sec
D11 0.03000000 sec
MDREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 13C
P1 3.00 usec
PL1 -6.00 dB
SF01 75.4745111 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 120.00 dB
PL12 19.00 dB
SF02 300.1315007 MHz
F2 - Processing parameters
SI 65536
SF 75.4677150 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
1D NMR plot parameters
CX 23.00 cm
CY 10.64 cm
F1P 220.000 ppm
F1 16602.90 Hz
F2P -20.000 ppm
F2 -1509.35 Hz
PPMCM 10.43478 ppm/cm
HZCM 787.48914 Hz/cm



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EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
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Time 11 52
INSTRUM qux300
PROBHD 5 mm BBO BB-1H
PULPROG cd
TD 32768
SOLVENT CDCl3
NS 16
DS 0
SWH 8992.806 Hz
FIDRES 0.274439 Hz
AQ 1.8219508 sec
RG 456.1
DW 55.600 usec
DE 79.63 usec
TE 0.0 K
D1 1.00000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec

-------- CHANNEL f1 --------
NUC1 1H
P1 5.00 usec
PL1 -2.00 dB
SFO1 300.1312000 MHz

F2 - Processing parameters
SI 32768
SF 300.1300063 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 22.00 cm
CY 9.52 cm
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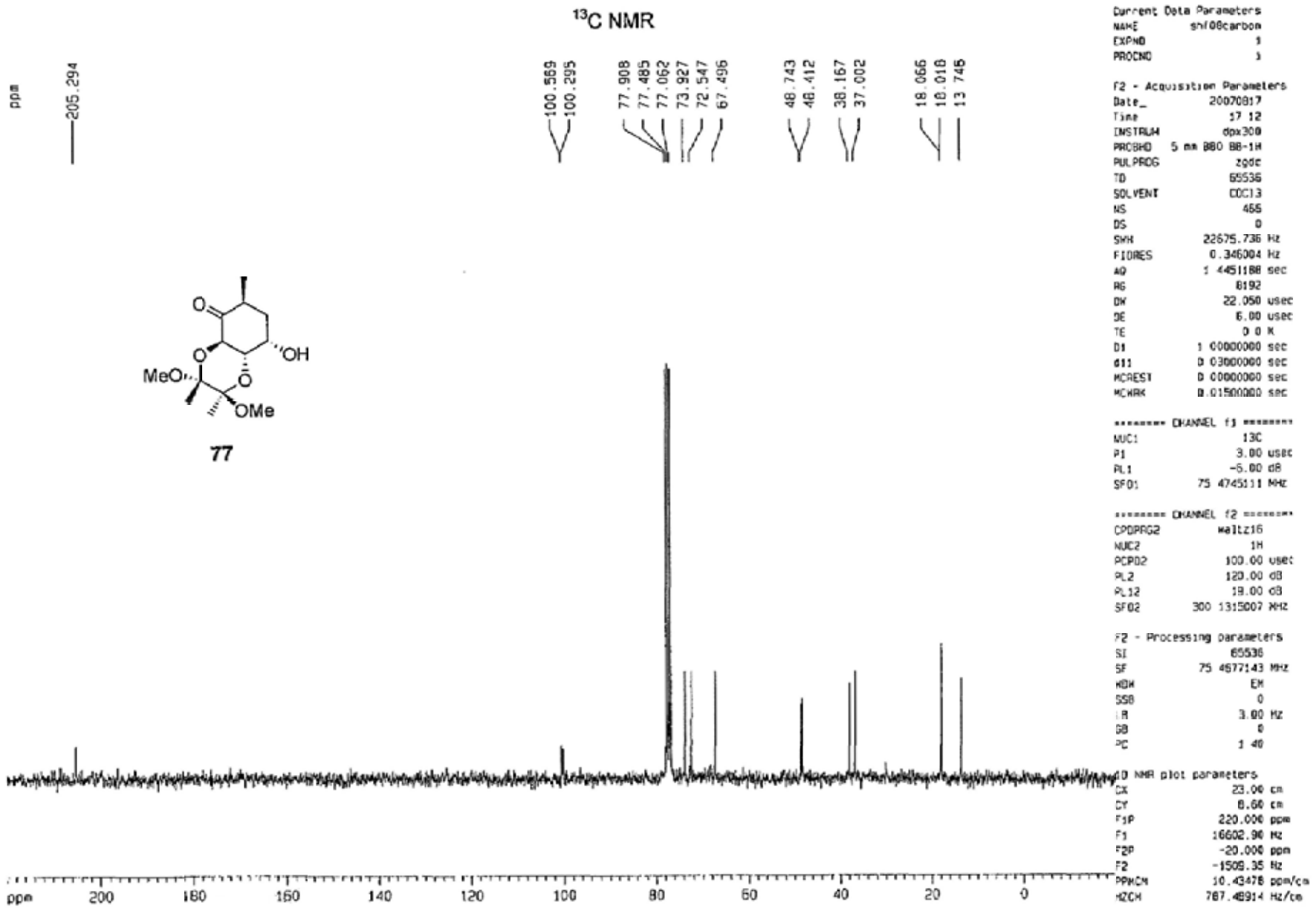
F1 2551.10 Hz
F2P -0.500 ppm
F2 -150.07 Hz
PPMCM 0.40909 ppm/cm
HZCM 122.78046 Hz/cm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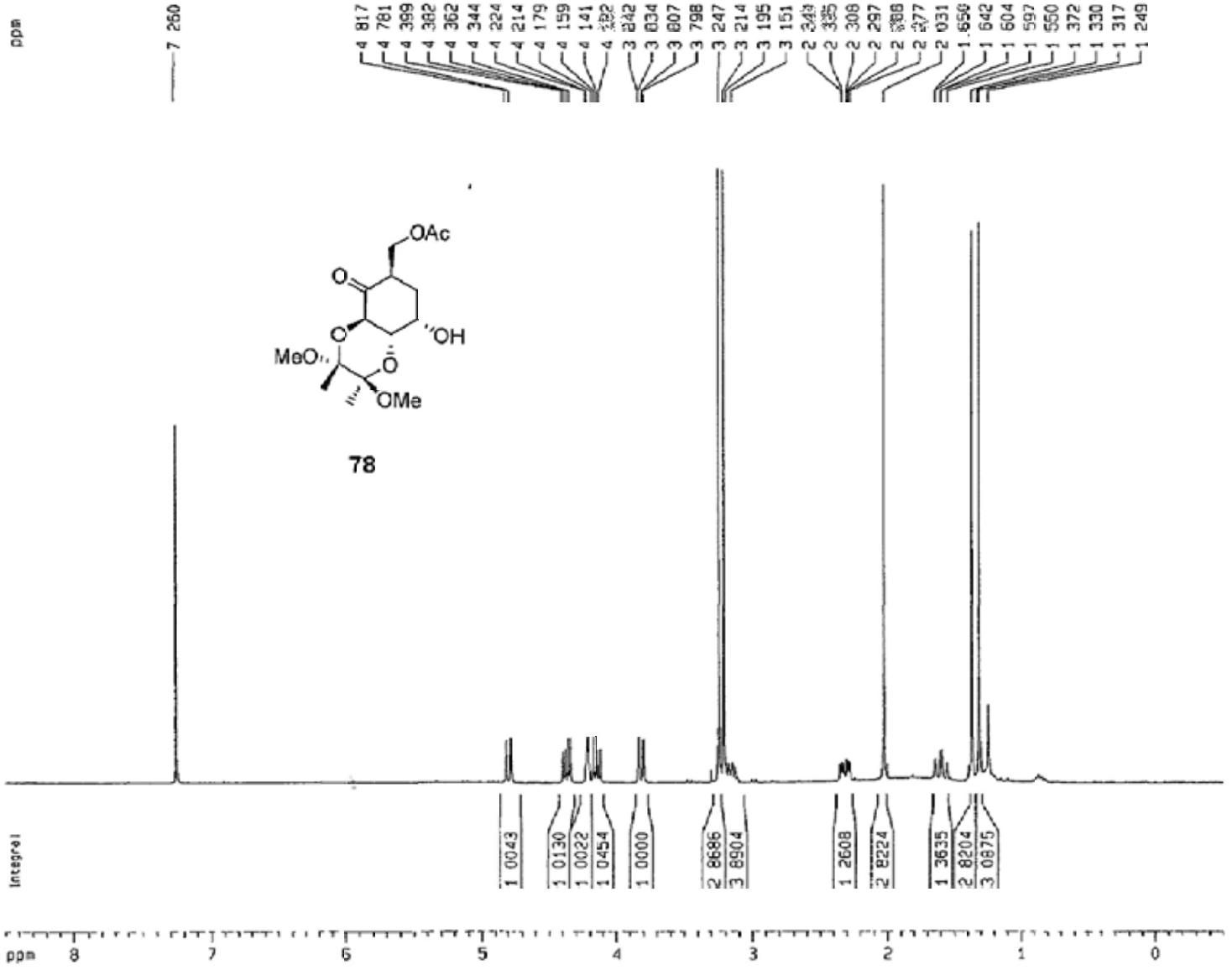
100.295
77.908
77.485
77.062
73.927
72.547
67.496
48.743
48.412
38.167
37.002
18.066
18.018
13.746
O
OH
MeO
O
O
OMe
77
ppm
200
180
160
140
120
100
80
60
40
20
0
Current Data Parameters
NAME shf06carbon
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20070817
Time 17 12
INSTRUM dpx300
PROBHD 5 mm BBO BB-1H
PULPROG zgdc
TD 65536
SOLVENT CDCl3
NS 455
DS 0
SWH 22675.736 Hz
FIDRES 0.346004 Hz
AQ 1.4451188 sec
RG 8192
DW 22.050 usec
DE 6.00 usec
TE 0.0 K
D1 1.00000000 sec
d11 0.03000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 13C
P1 3.00 usec
PL1 -6.00 dB
SFO1 75.4745111 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 120.00 dB
PL12 18.00 dB
SFO2 300.1315007 MHz
F2 - Processing parameters
SI 65536
SF 75.4577143 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
1D NMR plot parameters
CX 23.00 cm
CY 8.00 cm
F1P 220.000 ppm
F1 16602.96 Hz
F2P -20.000 ppm
F2 -1506.35 Hz
PPMCM 10.43478 ppm/cm
HZCM 787.48914 Hz/cm

^{1}H NMR

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EXPNO                      1
PROCNO                     1

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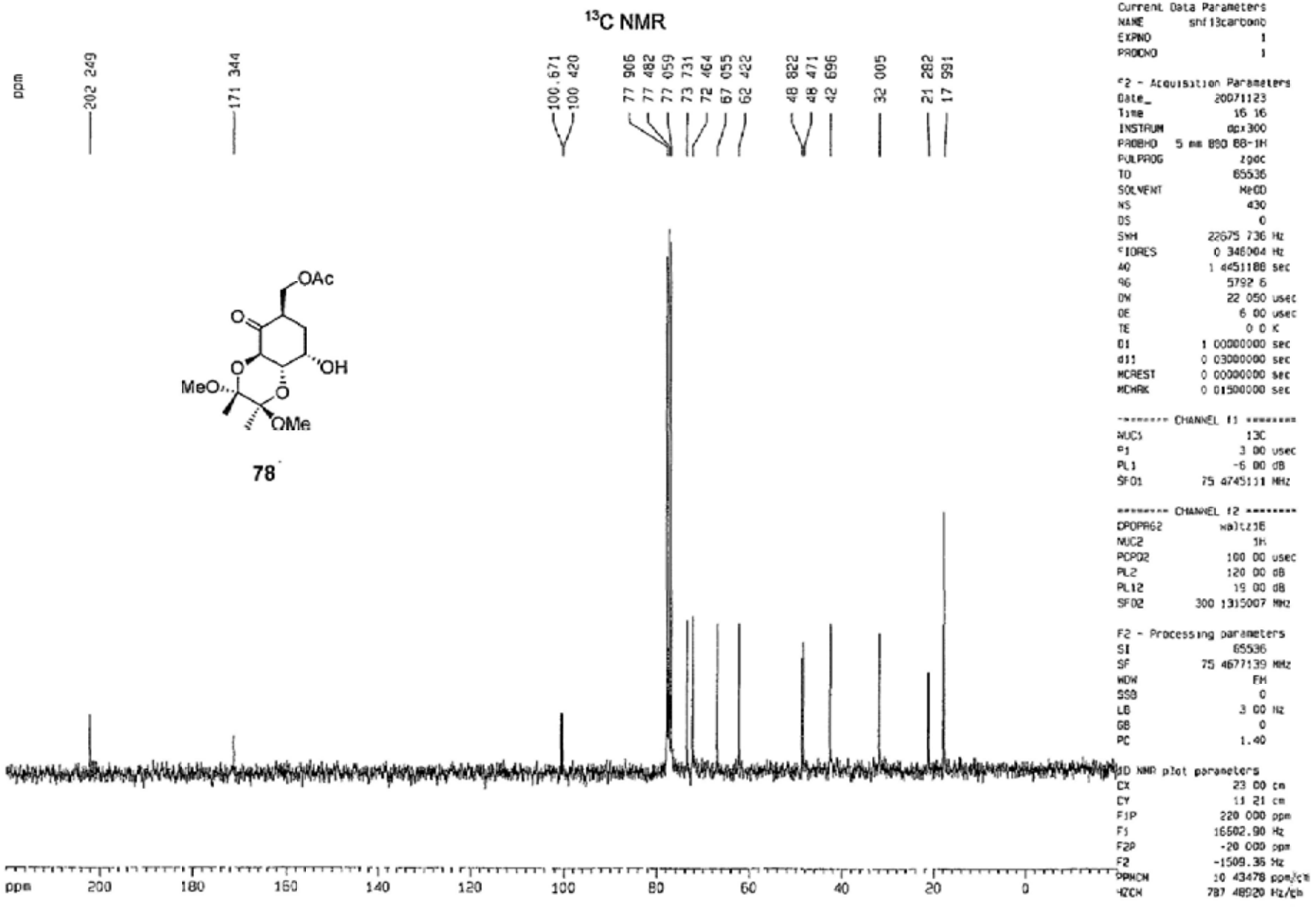
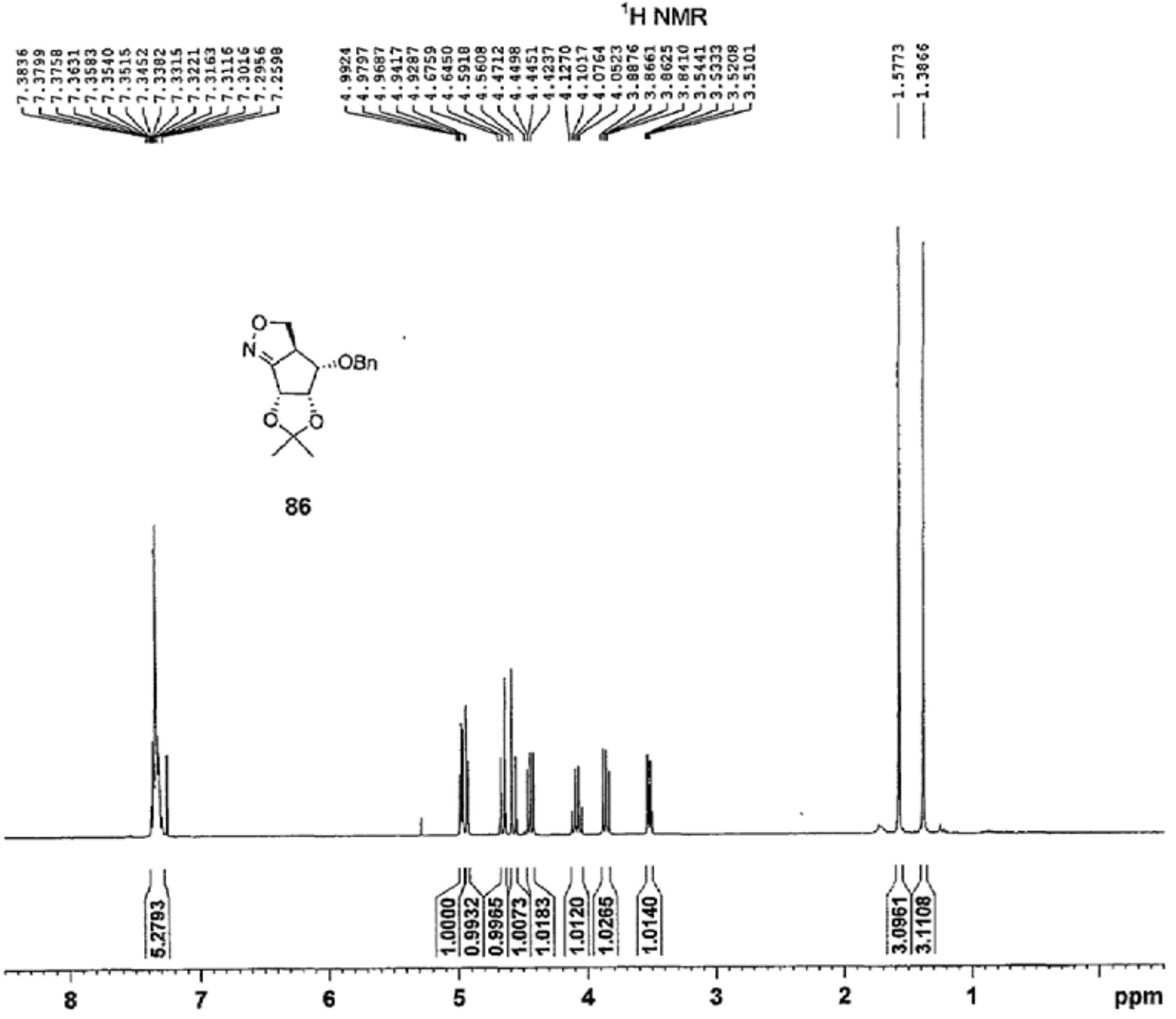
Time                   10 13
INSTRUM              dpx300
PROBHD   5 mm BBO BB-1H
PULPROG                zg
TD                     32768
SOLVENT                CDCl3
NS                        16
DS                         0
SWH                8992.806 Hz
FIDRES             0.274439 Hz
AQ                 1.8219508 sec
RG                       362
DW                  55.600 usec
DE                  79.43 usec
TE                     0.0 K
D1                 1.00000000 sec
MCREST             0.00000000 sec
MCWRK              0.01500000 sec

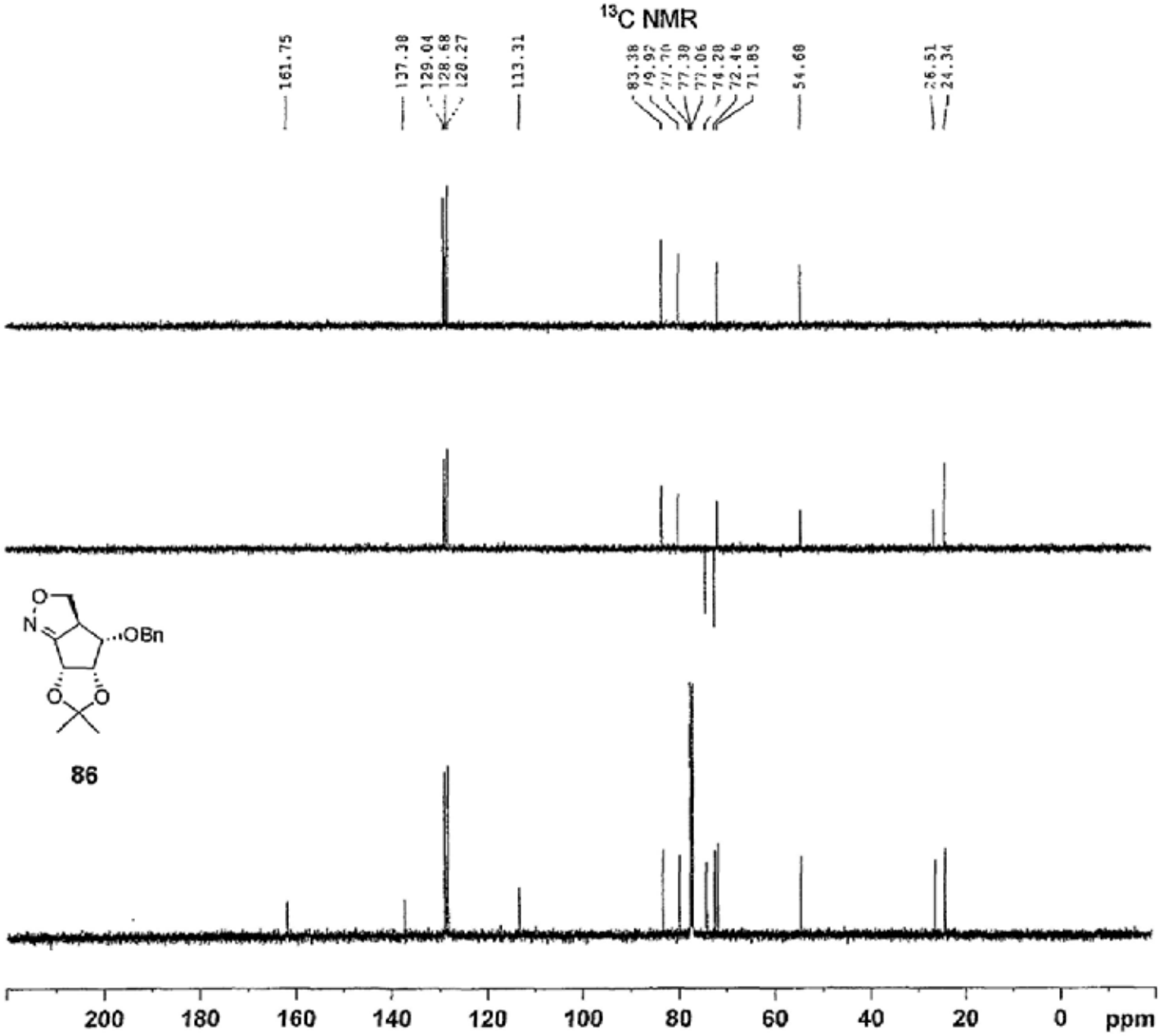
======== CHANNEL f1 ========
NUC1                       1H
P1                      5.00 usec
PL1                    -2.00 dB
SFO1              300.1312000 MHz

F2 - Processing parameters
SI                         32768
SF                300.1300063 MHz
WDW                           EM
SSB                            0
LB                      0.30 Hz
GB                             0
PC                      1.00

1D NMR plot parameters
CX                     22.00 cm
CY                     11.15 cm
F1P                    8.500 ppm
F1                   2551.10 Hz
F2P                   -0.500 ppm
F2                   -150.07 Hz
PPMCM                0.40909 ppm/cm
HZCM                 122.78046 Hz/cm
```

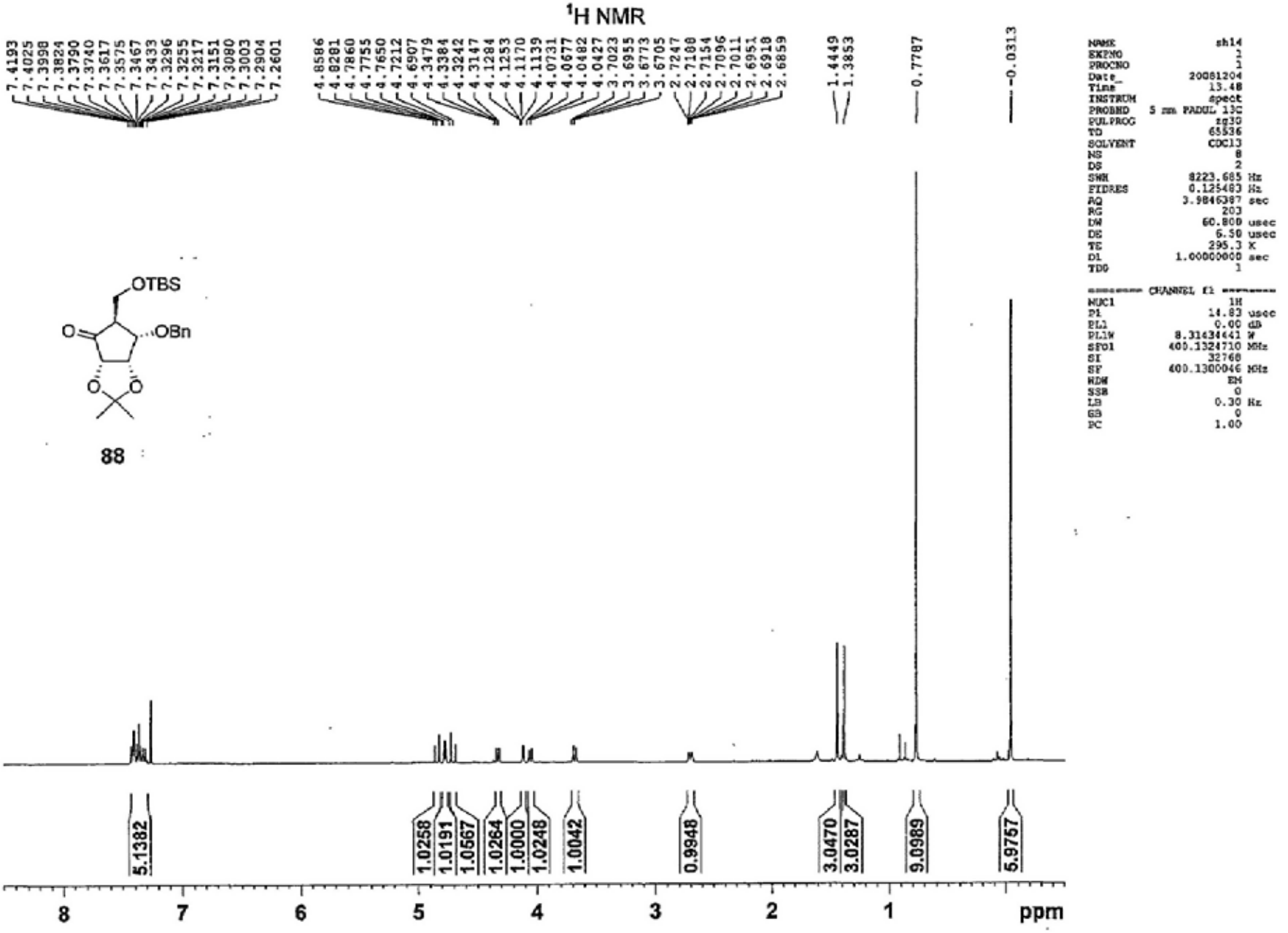

13C NMR
ppm
202 249
171 344
100 671
100 420
77 906
77 482
77 059
73 731
72 464
67 055
62 422
48 822
48 471
42 696
32 005
21 282
17 991
OAc
OH
MeO
OMe
O
78
ppm
200
180
160
140
120
100
80
60
40
20
0
Current Data Parameters
NAME shf13carbono
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20071123
Time 16 16
INSTRUM qcx300
PROBHD 5 mm BBO BB-1H
PULPROG zgpg
TD 65536
SOLVENT MeOD
NS 430
DS 0
SWH 22675 736 Hz
FIDRES 0 346004 Hz
AQ 1 4451188 sec
RG 5792 6
DW 22 050 usec
DE 6 00 usec
TE 0 0 K
D1 1 00000000 sec
D11 0 03000000 sec
MCREST 0 00000000 sec
MCWRK 0 01500000 sec
======== CHANNEL f1 ========
NUC1 13C
P1 3 00 usec
PL1 -6 00 dB
SFO1 75 4745111 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100 00 usec
PL2 120 00 dB
PL12 19 00 dB
SFO2 300 1315007 MHz
F2 - Processing parameters
SI 65536
SF 75 4677139 MHz
WDW EM
SSB 0
LB 3 00 Hz
GB 0
PC 1.40
1D NMR plot parameters
CX 23 00 cm
CY 11 21 cm
F1P 220 000 ppm
F1 16502.90 Hz
F2P -20 000 ppm
F2 -1509.35 Hz
PPMCM 10 43478 ppm/cm
HZCM 787 48920 Hz/cm

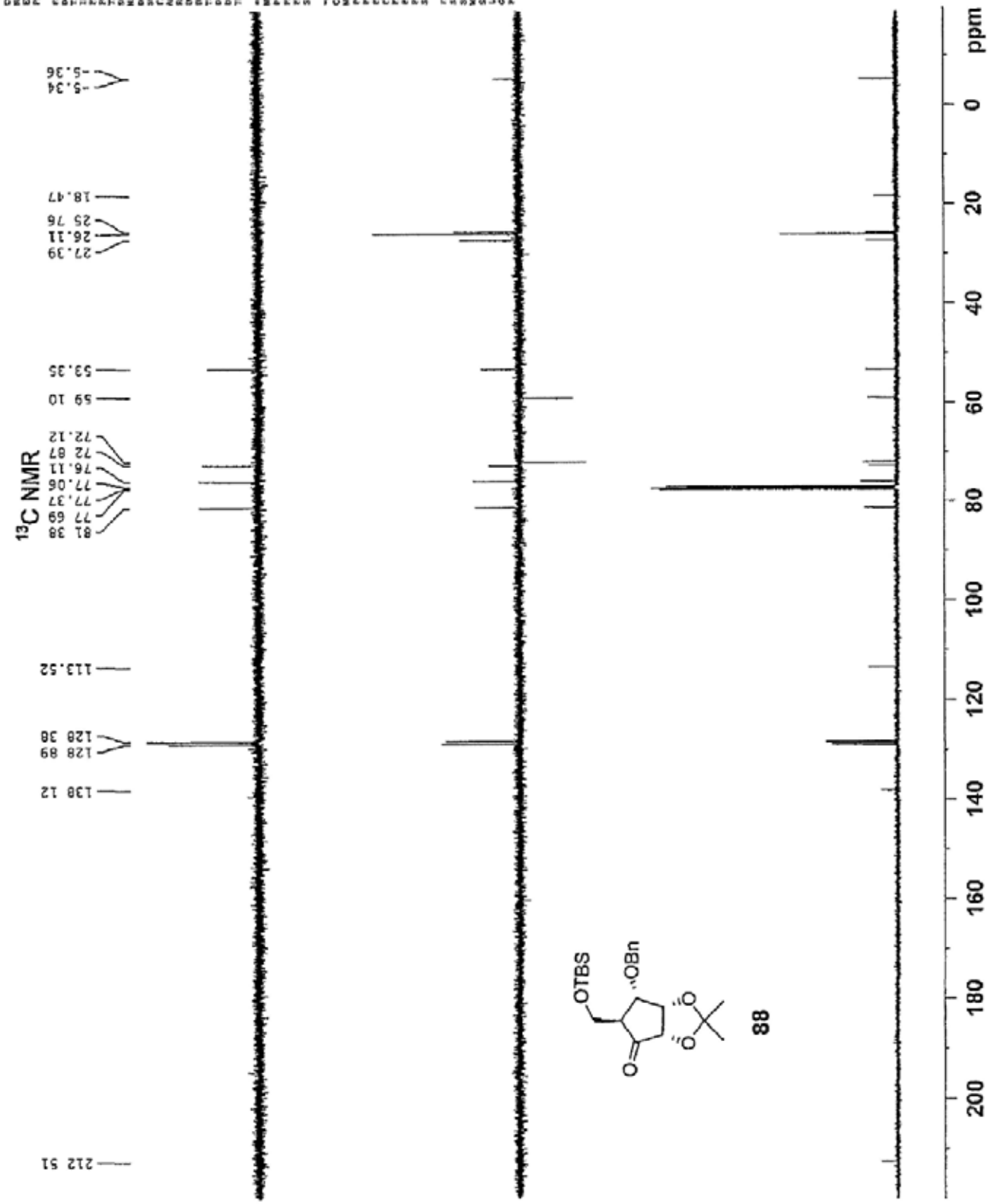

^{1}H NMR
7.3836
7.3799
7.3758
7.3631
7.3583
7.3540
7.3515
7.3452
7.3382
7.3315
7.3221
7.3163
7.3116
7.3016
7.2956
7.2598
4.9924
4.9797
4.9687
4.9417
4.9287
4.6759
4.6450
4.5918
4.5608
4.4712
4.4498
4.4451
4.4237
4.1270
4.1017
4.0764
4.0523
3.8876
3.8661
3.8625
3.8410
3.5441
3.5333
3.5208
3.5101
1.5773
1.3866
NAME sh10
EXPNO 1
PROCNO 1
Date_ 20081114
Time_ 15.48
INSTRUM spect
PROBHD 5 mm PADUL 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 4
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 101
DW 60.800 usec
DE 6.50 usec
TE 295.2 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.83 usec
PL1 0.00 dB
PL1W 8.31434441 W
SFO1 400.1324710 MHz
SI 32768
SF 400.1300045 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
O
N
OBn
O
O
86
5.2793
1.0000
0.9932
0.9965
1.0073
1.0183
1.0120
1.0265
1.0140
3.0961
3.1108
8
7
6
5
4
3
2
1
ppm

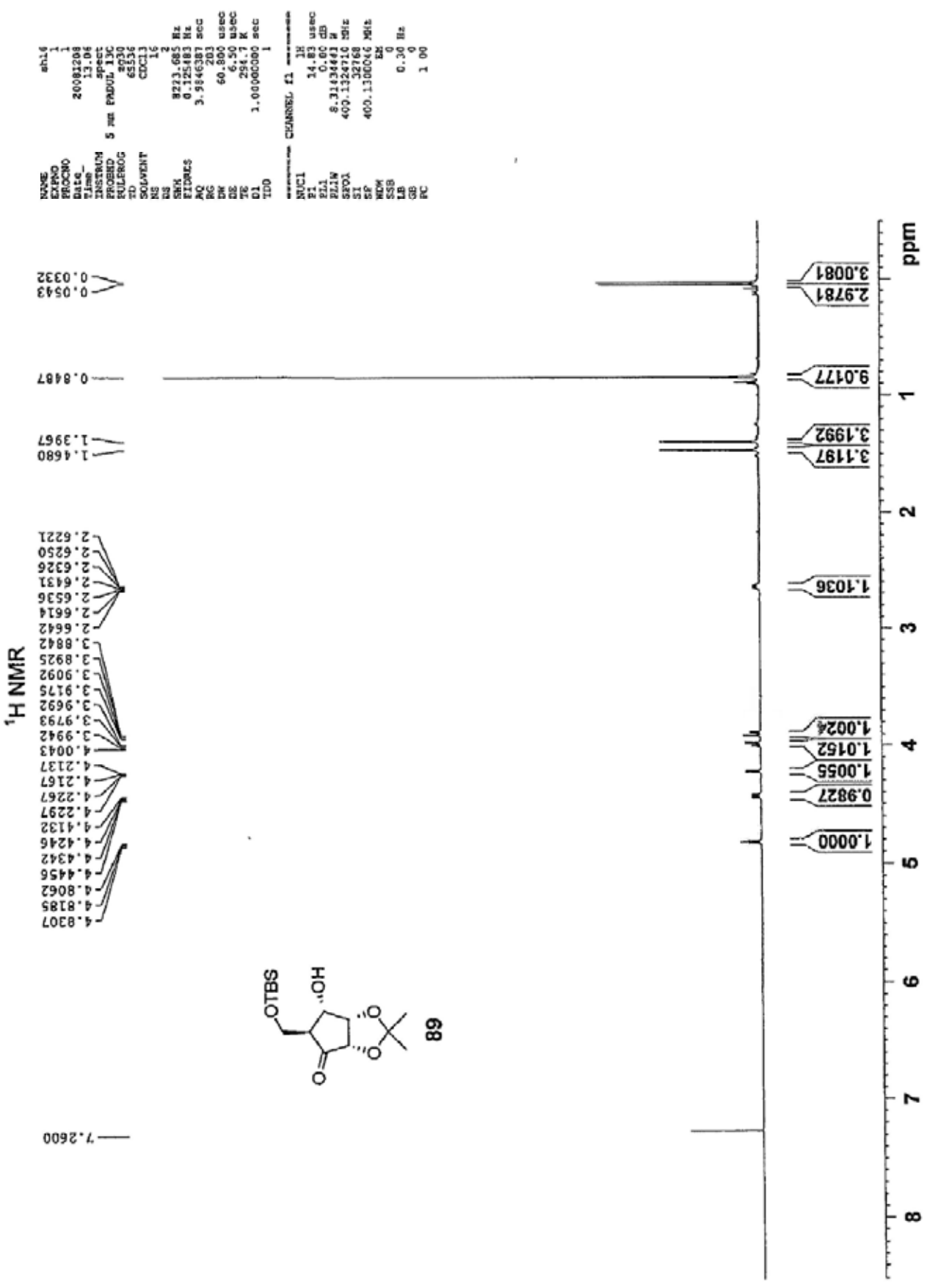


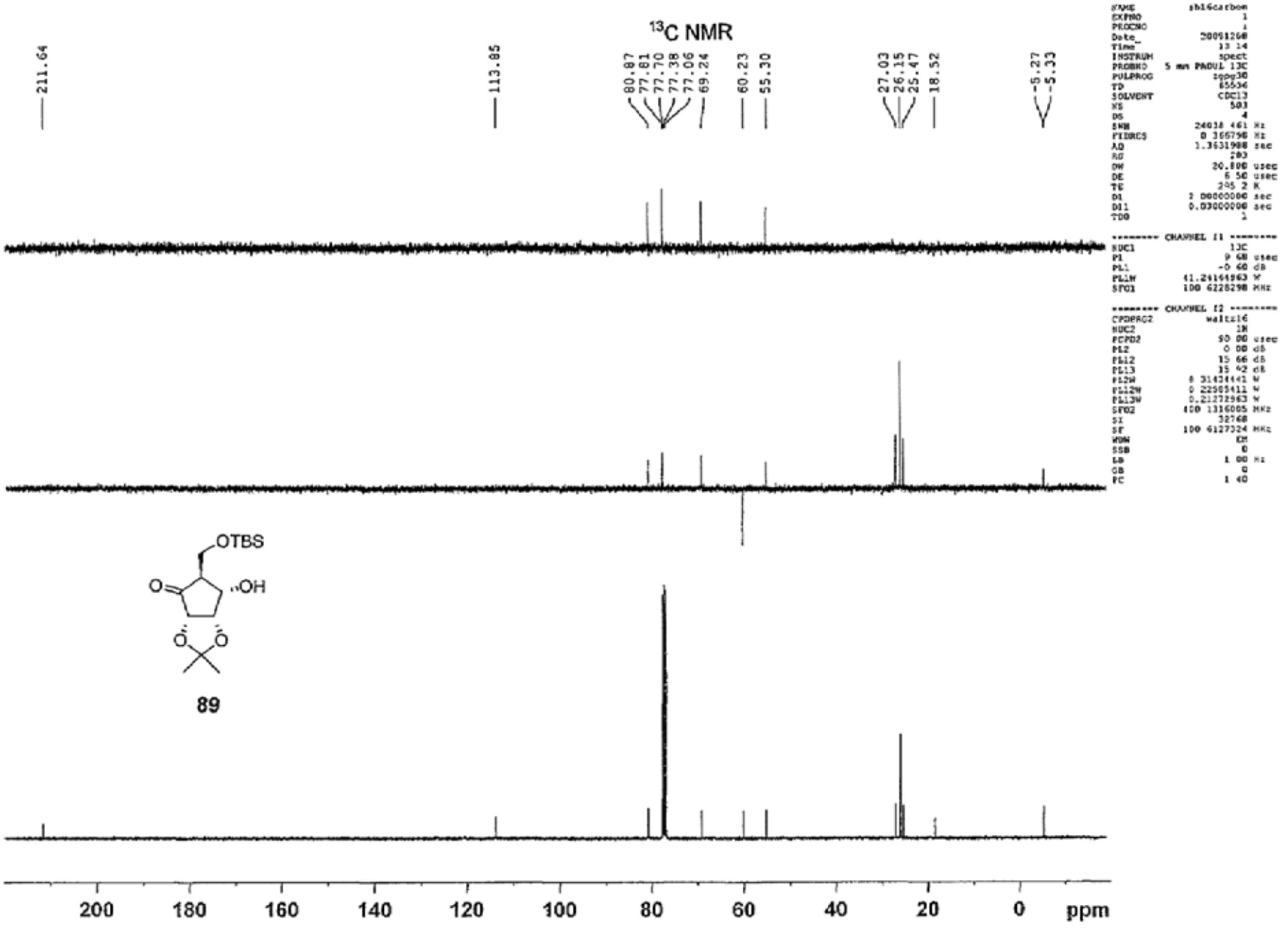
86

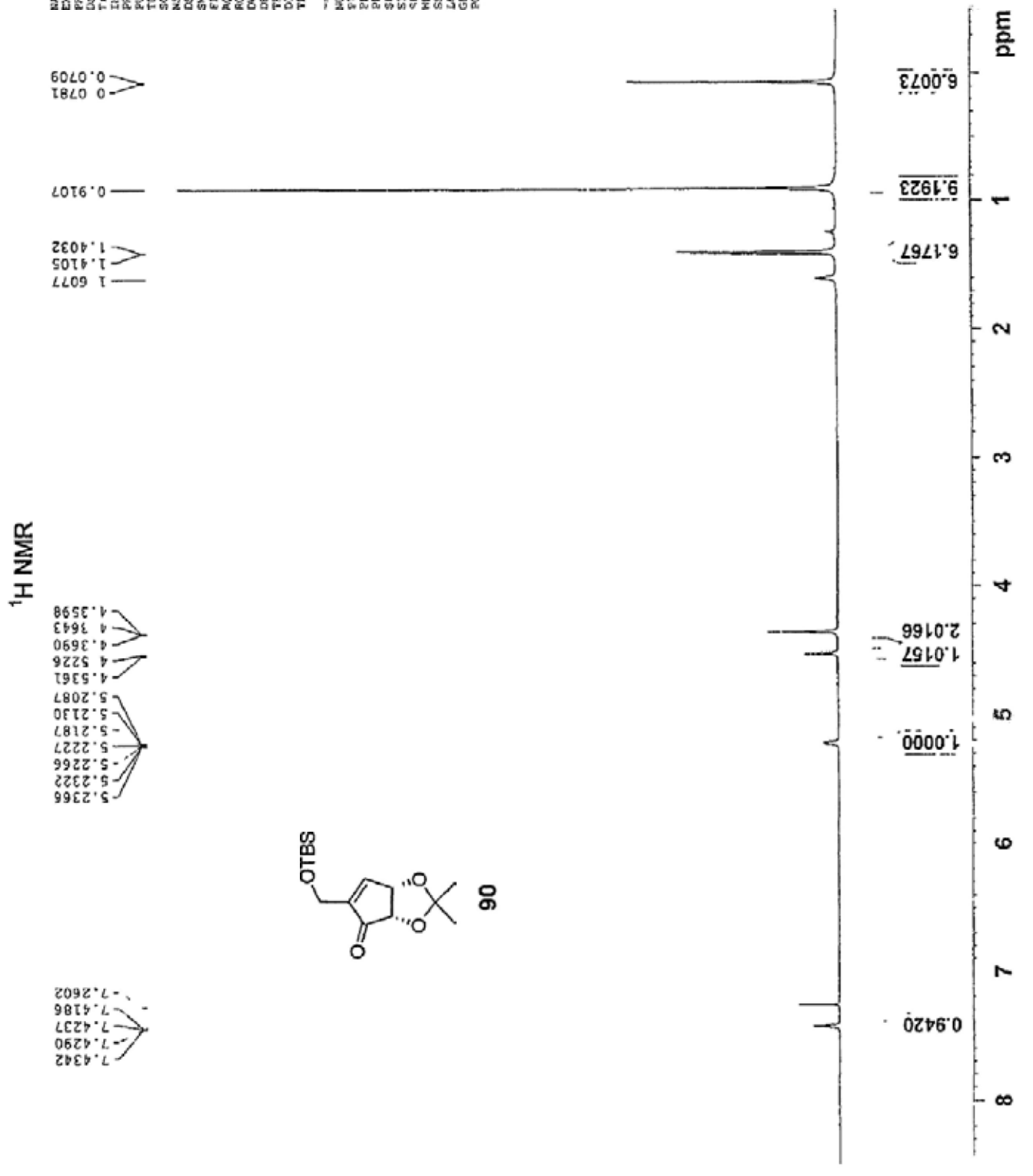
NAME	sh10carbon	
EXPNO	2	
PROCNO	1	
Date_	20100924	
Time	11.09	
INSTRUM	spect	
PROBHD	5 mm PABBI 1H/	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	125	
DS	4	
SWH	24038.461	Hz
FIDRES	0.366798	Hz
AQ	1.3631988	sec
RG	203	
DW	20.800	usec
DE	6.50	usec
TE	294.8	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	14.50	usec
PL1	-4.00	dB
PL1W	90.22689819	W
SFO1	100.6228298	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	80.00	usec
PL2	-2.00	dB
PL12	18.80	dB
PL13	18.80	dB
PL2W	13.17734718	W
PL12W	0.10960442	W
PL13W	0.10960442	W
SFO2	400.1316005	MHz
SI	32768	
SF	100.6127353	MHz
WDW	EM	
SSB	0	
LB	1.00	Hz
GB	0	
PC	1.40	

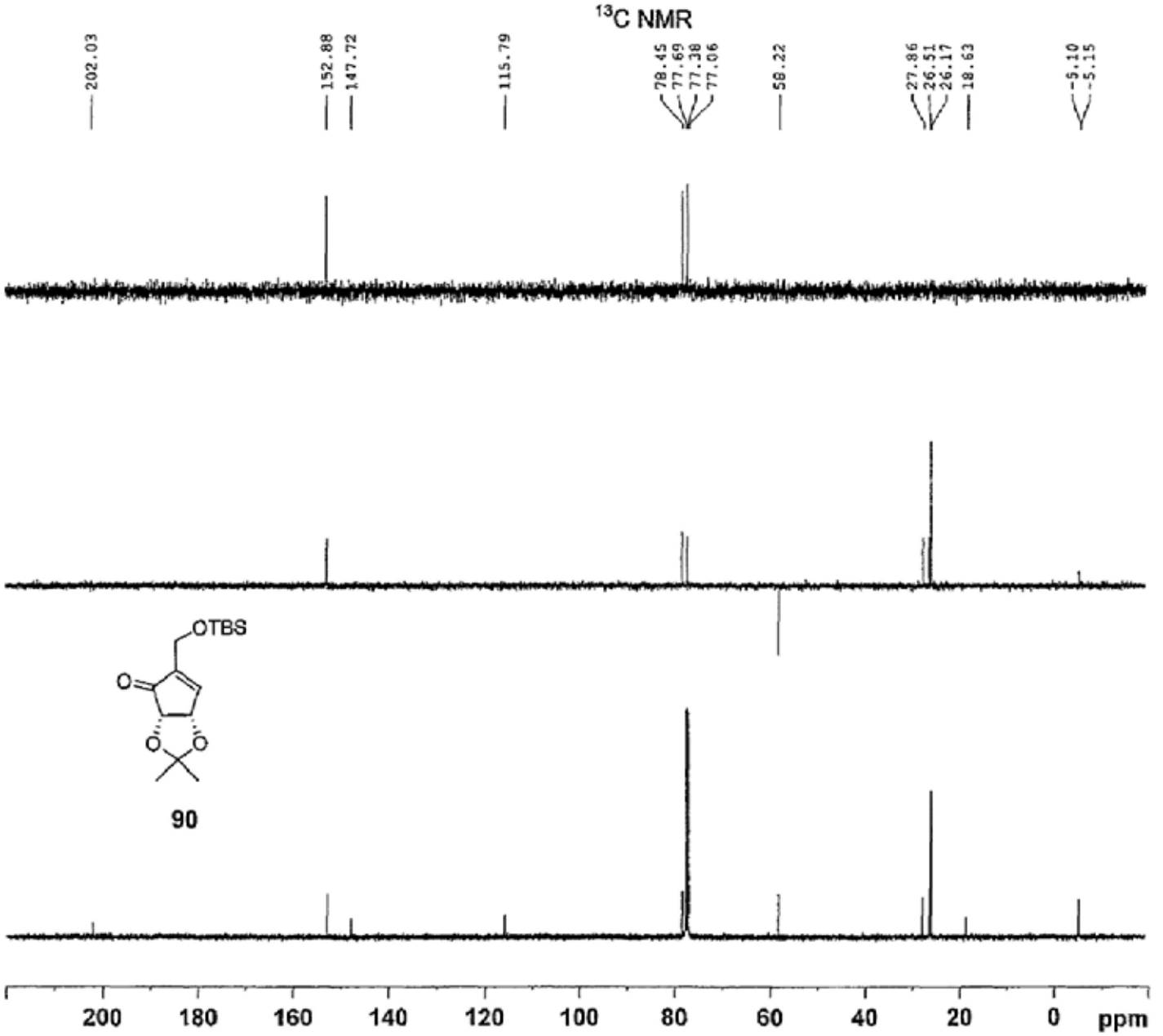

^{1}H NMR
7.4193
7.4025
7.3998
7.3824
7.3790
7.3740
7.3617
7.3575
7.3467
7.3433
7.3296
7.3255
7.3217
7.3151
7.3080
7.3003
7.2904
7.2601
4.8586
4.8281
4.7860
4.7755
4.7650
4.7212
4.6907
4.3479
4.3384
4.3242
4.3147
4.1284
4.1253
4.1170
4.1139
4.0731
4.0677
4.0482
4.0427
3.7023
3.6955
3.6773
3.6705
2.7247
2.7188
2.7154
2.7096
2.7011
2.6951
2.6918
2.6859
1.4449
1.3853
0.7787
-0.0313
OTBS
O
OBn
O
O
88
NAME sh14
EXPNO 1
PROCNO 1
Date_ 20081204
Time 13.48
INSTRUM spect
PROBHD 5 mm PADUL 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 203
DW 60.800 usec
DE 6.50 usec
TE 295.3 K
D1 1.00000000 sec
TD0 1
CHANNEL f1
NUC1 1H
P1 14.83 usec
PL1 0.00 dB
PL1W 8.31434441 W
SFO1 400.1324710 MHz
SI 32768
SF 400.1300046 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
5.1382
1.0258
1.0191
1.0567
1.0264
1.0000
1.0248
1.0042
0.9948
3.0470
3.0287
9.0989
5.9757
8
7
6
5
4
3
2
1
ppm


13C NMR
-5.36
-5.34
18.47
25.76
26.11
27.39
53.35
59.10
72.12
72.87
76.11
77.06
77.37
77.69
81.38
113.52
128.38
128.89
138.12
212.51
ppm
0
20
40
60
80
100
120
140
160
180
200
OTBS
OBn
O
O
O
88


^{1}H NMR
ppm
OTBS
OH
O
O
O
89

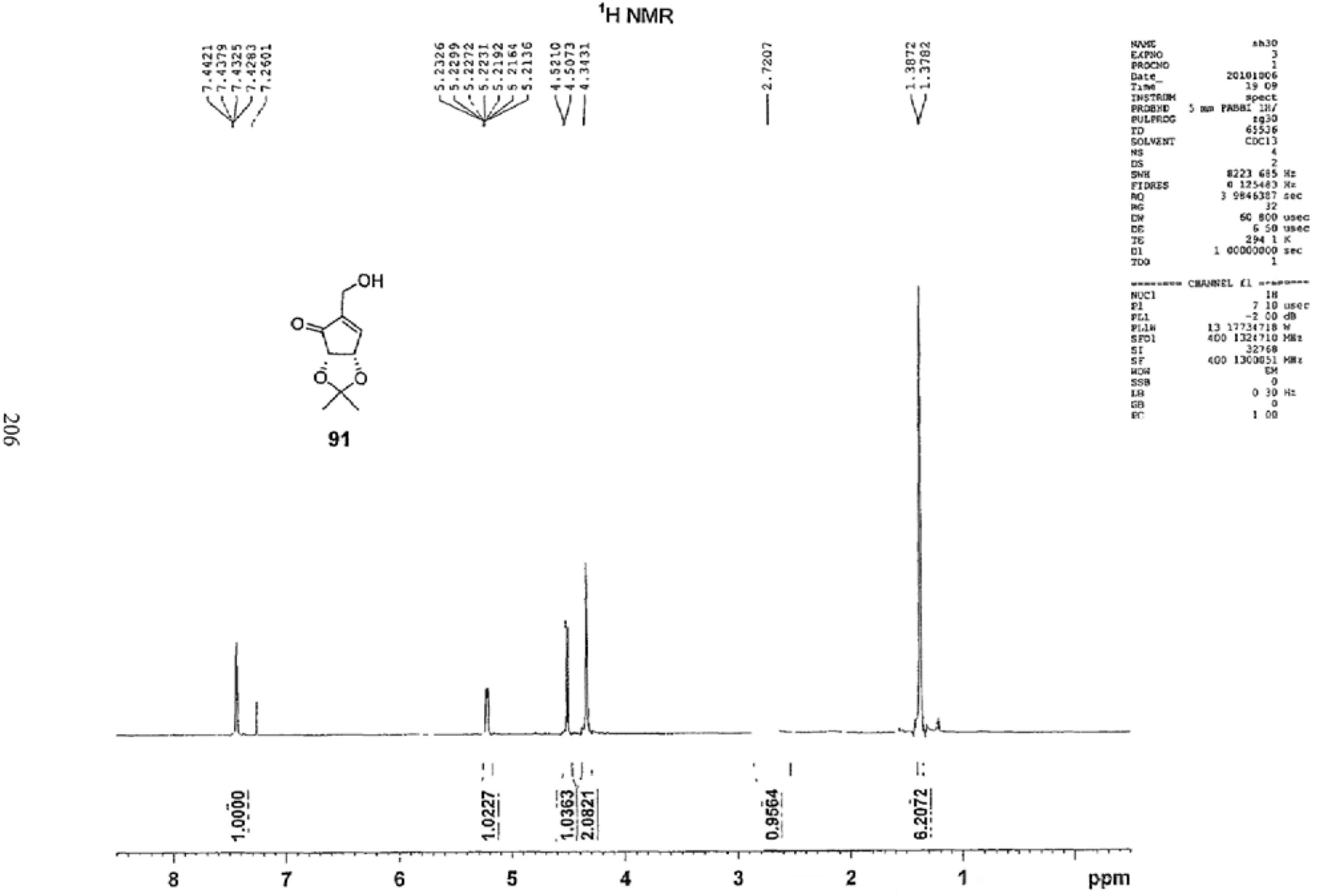

^{13}C NMR
211.64
113.85
80.87
77.81
77.70
77.38
77.06
69.24
60.23
55.30
27.03
26.15
25.47
18.52
-5.27
-5.33
OTBS
OH
O
O
O
89
200
180
160
140
120
100
80
60
40
20
0
ppm


^{1}H NMR
OTBS
90
ppm

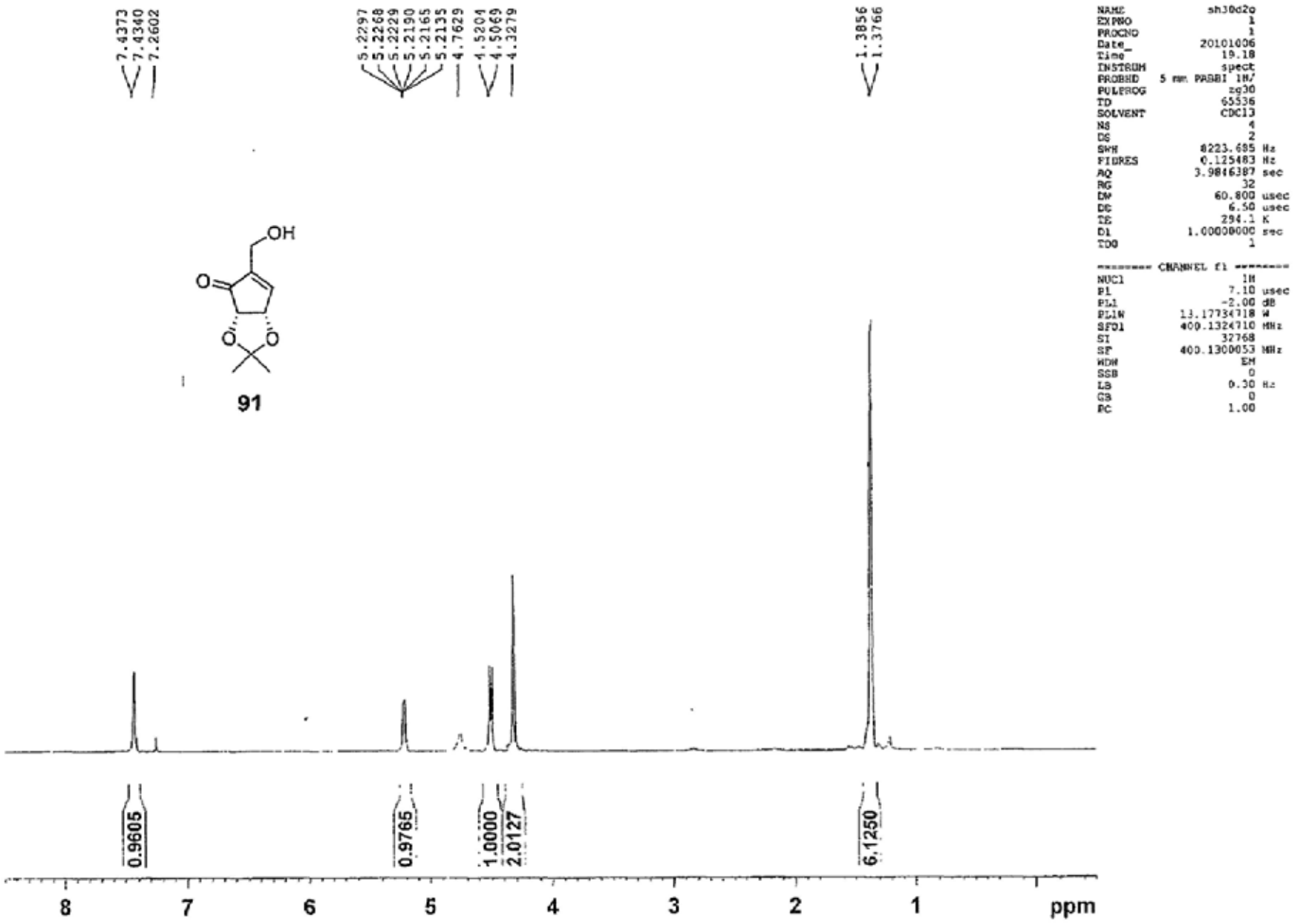


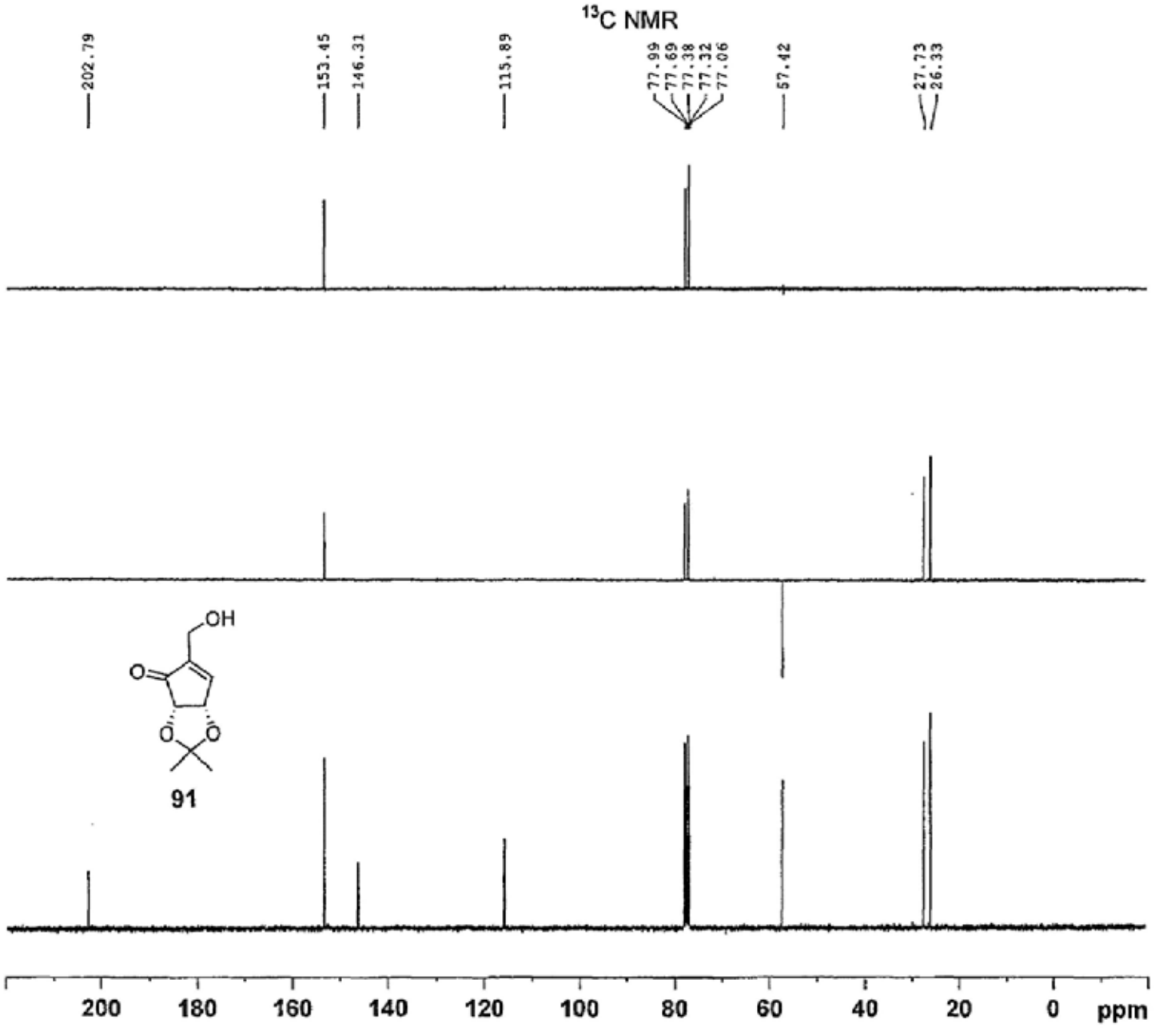
90

NAME	sh19carbon	
EXPNO	2	
PROCNO	1	
Date_	20101021	
Time	12.57	
INSTRUM	spect	
PROBHD	5 mm PADUL 13C	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	305	
DS	4	
SWH	24038.461	Hz
FIDRES	0.366798	Hz
AQ	1.3631988	sec
RG	203	
DW	20.800	usec
DE	6.50	usec
TE	295.4	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	9.68	usec
PL1	-0.60	dB
PL1W	41.24164963	W
SFO1	100.6228298	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	90.00	usec
PL2	0.00	dB
PL12	15.66	dB
PL13	15.92	dB
PL2W	8.11434441	W
PL12W	0.22585411	W
PL13W	0.21272963	W
SFO2	400.1316005	MHz
SI	32768	
SF	100.6127331	MHz
WDW	EM	
SSB	0	
LB	1.00	Hz
GB	0	
PC	1.40	

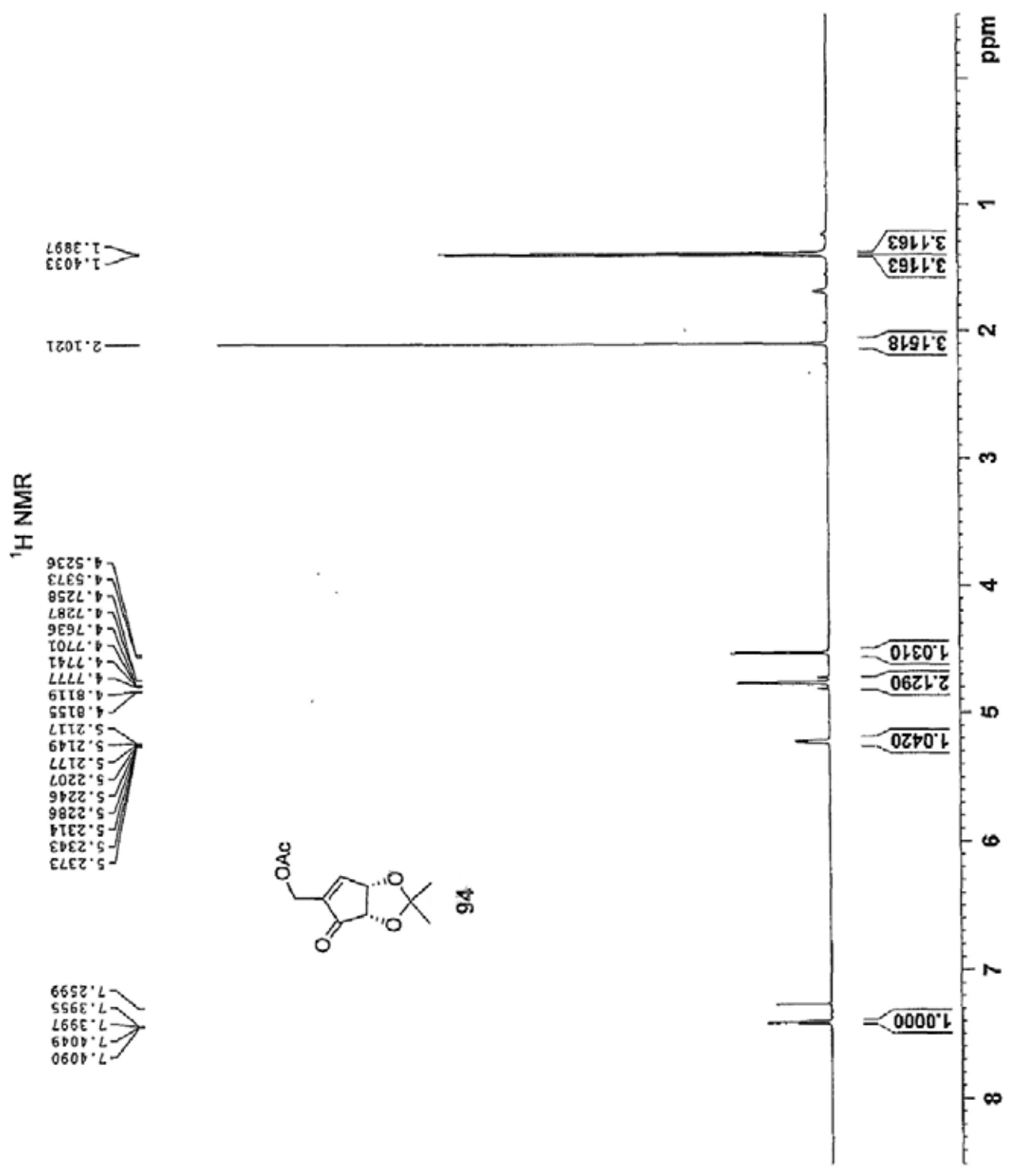

^{1}H NMR
7.4421
7.4379
7.4325
7.4283
7.2601
5.2326
5.2299
5.2272
5.2231
5.2192
5.2164
5.2136
4.5210
4.5073
4.3431
2.7207
1.3872
1.3782
NAME ah30
EXPNO 3
PROCNO 1
Date_ 20101006
Time 19 09
INSTRUM spect
PROBHD 5 mm PABBI 1H/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 4
DS 2
SWH 8223 685 Hz
FIDRES 0 125483 Hz
AQ 3 9846387 sec
RG 32
DW 60 800 usec
DE 6 50 usec
TE 294 1 K
D1 1 00000000 sec
TD0 1
CHANNEL f1
NUC1 1H
P1 7 10 usec
PL1 -2 00 dB
PL1W 13 17734718 W
SFO1 400 1324710 MHz
SI 32768
SF 400 1300051 MHz
WDW EM
SSB 0
LB 0 30 Hz
GB 0
PC 1 00
OH
O
O
O
91
1.0000
1.0227
1.0363
2.0821
0.9564
6.2072
8
7
6
5
4
3
2
1
ppm

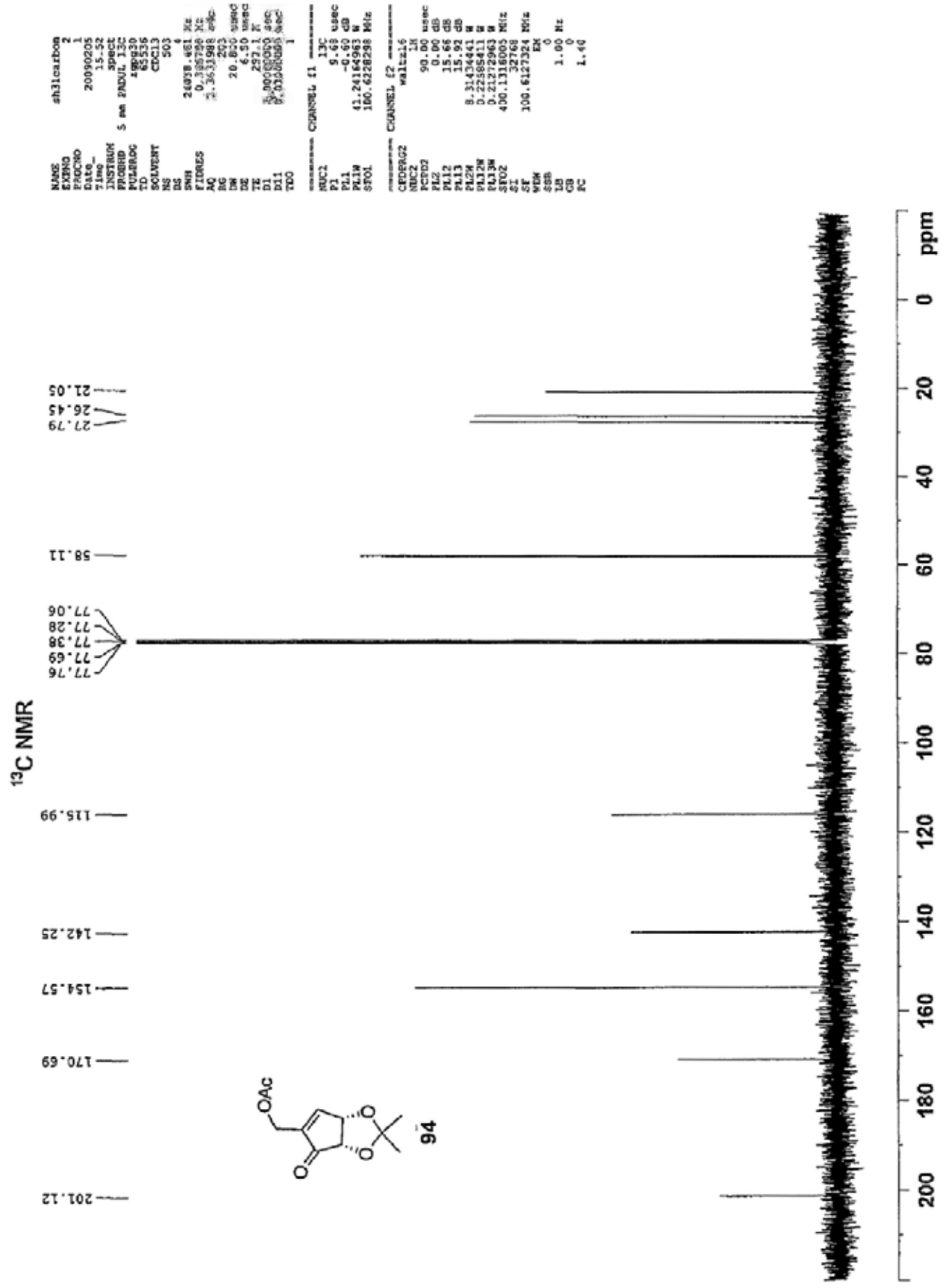
^{1}H NMR (Solvent: $CDCl_3$-D_2O)



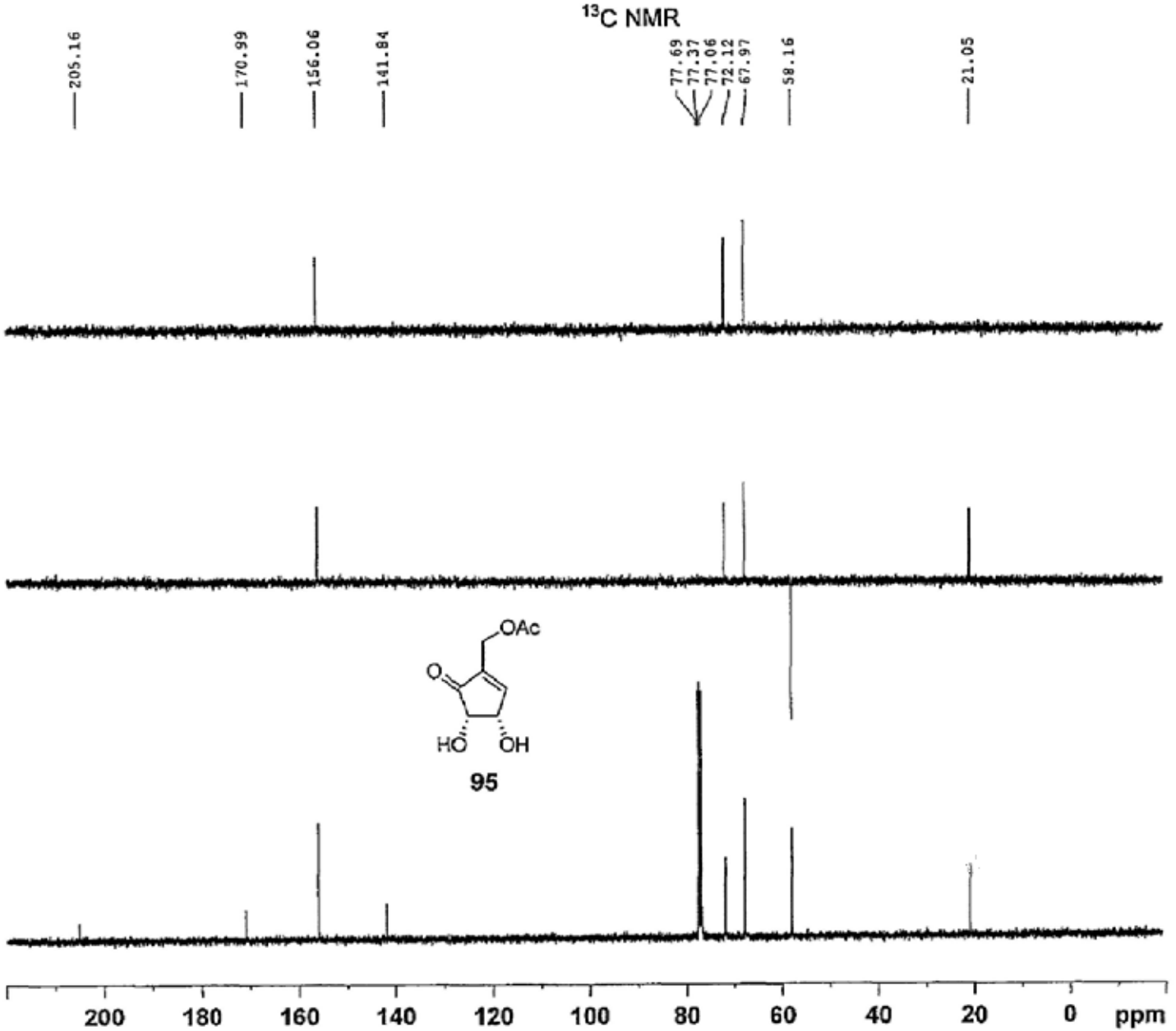


NAME	sh30carbon
EXPNO	2
PROCNO	1
Date_	20101005
Time	10.37
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	65
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	228
DW	20.800 usec
DE	6.50 usec
TE	298.5 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
========	CHANNEL f1 ========
NUC1	13C
P1	9.90 usec
PL1	-2.00 dB
PL1W	55.33689499 W
SFO1	100.6379183 MHz
========	CHANNEL f2 ========
CPDPRG2	waltz16
NUC2	1H
PCPD2	90.00 usec
PL2	-1.00 dB
PL12	15.16 dB
PL13	18.62 dB
PL2W	13.56617069 W
PL12W	0.32844096 W
PL13W	0.14806664 W
SFO2	400.1916008 MHz
SI	32768
SF	100.6278263 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

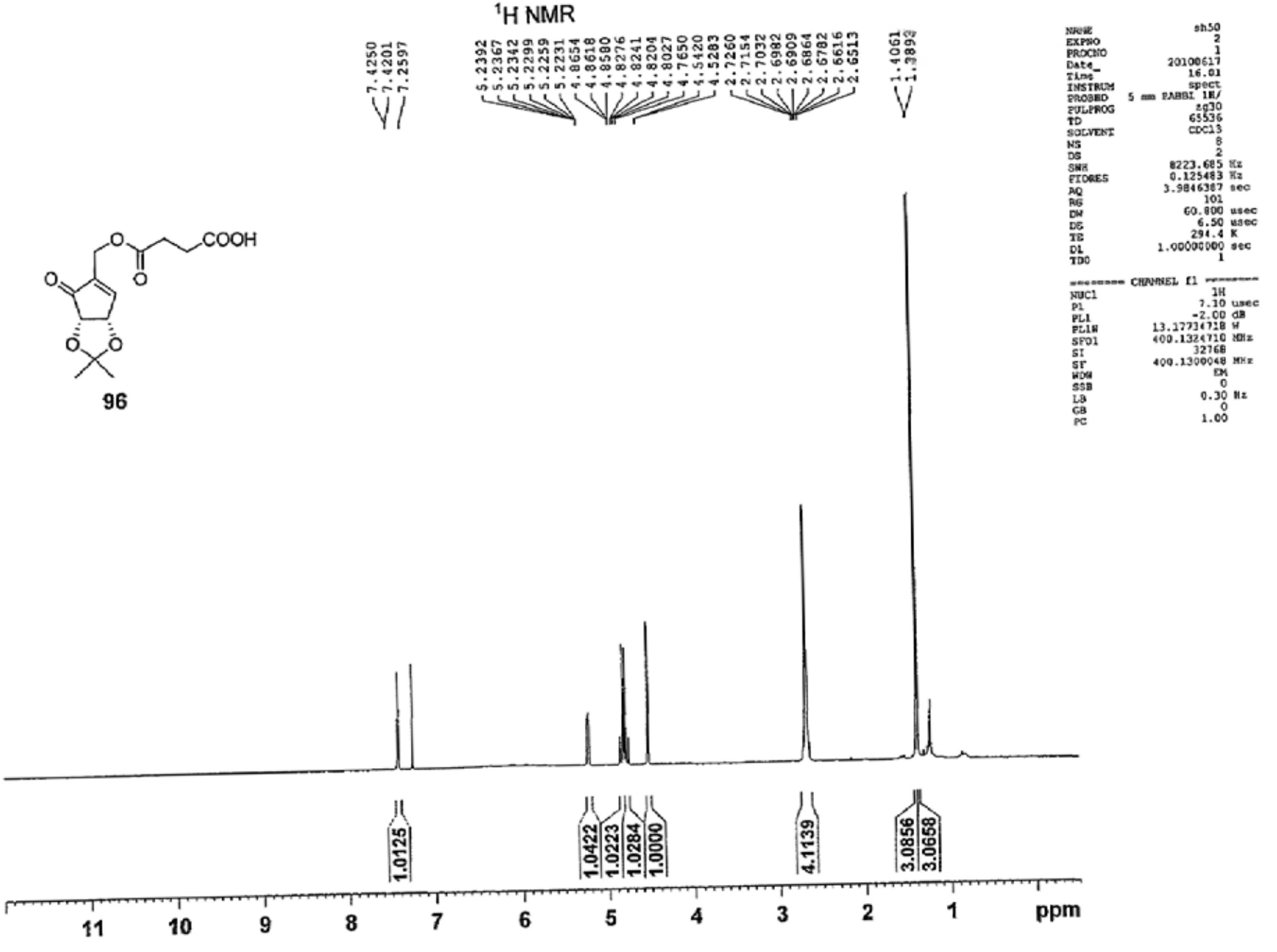

^{1}H NMR
ppm
1
2
3
4
5
6
7
8
1.0000
1.0420
2.1290
1.0310
3.1618
3.1163
3.1163
2.1021
1.4033
1.3897
7.4090
7.4049
7.3997
7.3955
7.2599
5.2373
5.2343
5.2314
5.2286
5.2246
5.2207
5.2177
5.2149
5.2117
4.8155
4.8119
4.7777
4.7741
4.7701
4.7636
4.7287
4.7258
4.5373
4.5236
OAc
O
O
O
94

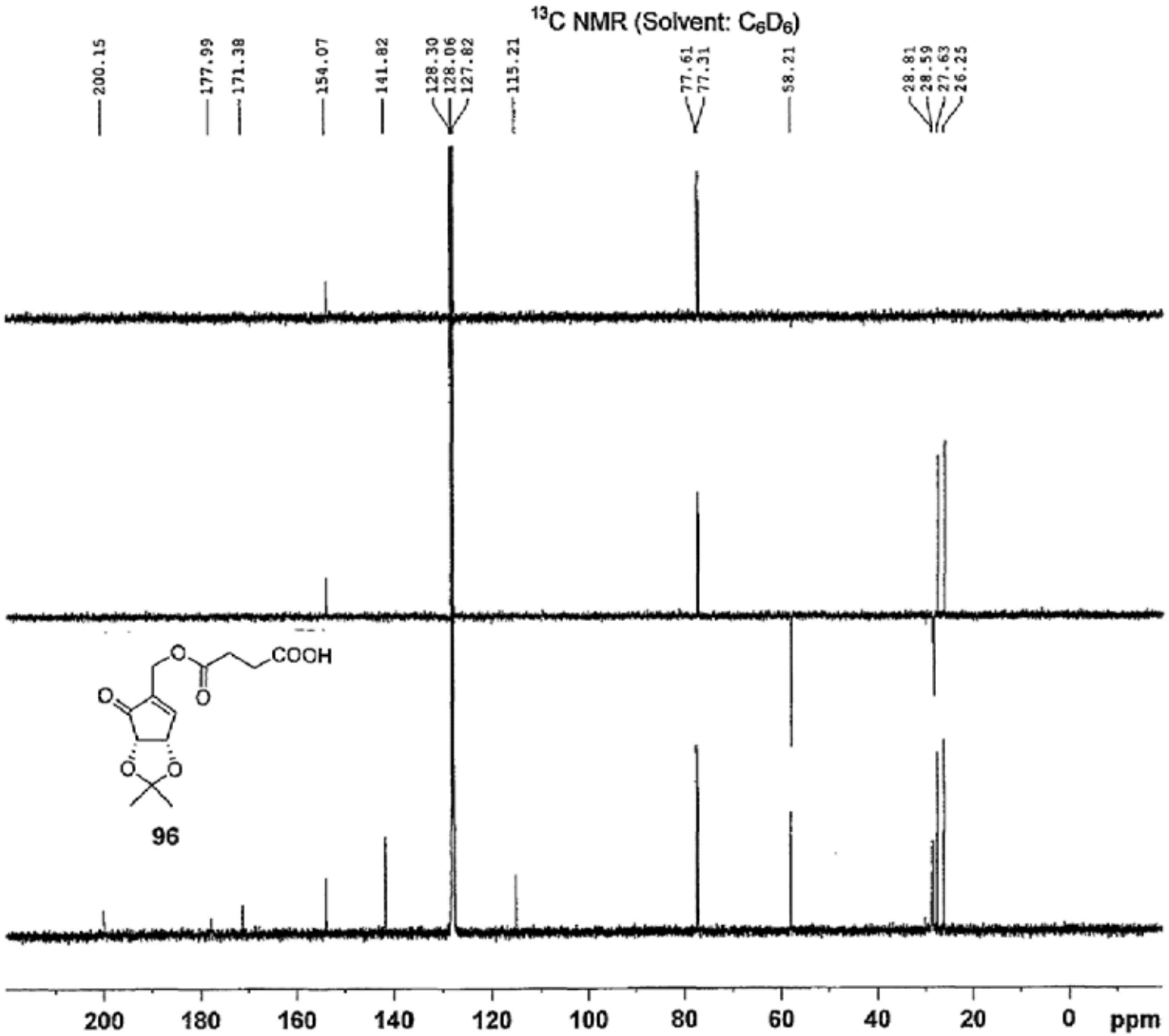

13C NMR
94
201.12
170.69
154.57
142.25
115.99
77.76
77.69
77.38
77.28
77.06
58.11
27.79
26.45
21.05
ppm


^{1}H NMR (Solvent: CD_3OD)
95
OAc
HO
OH
O
ppm



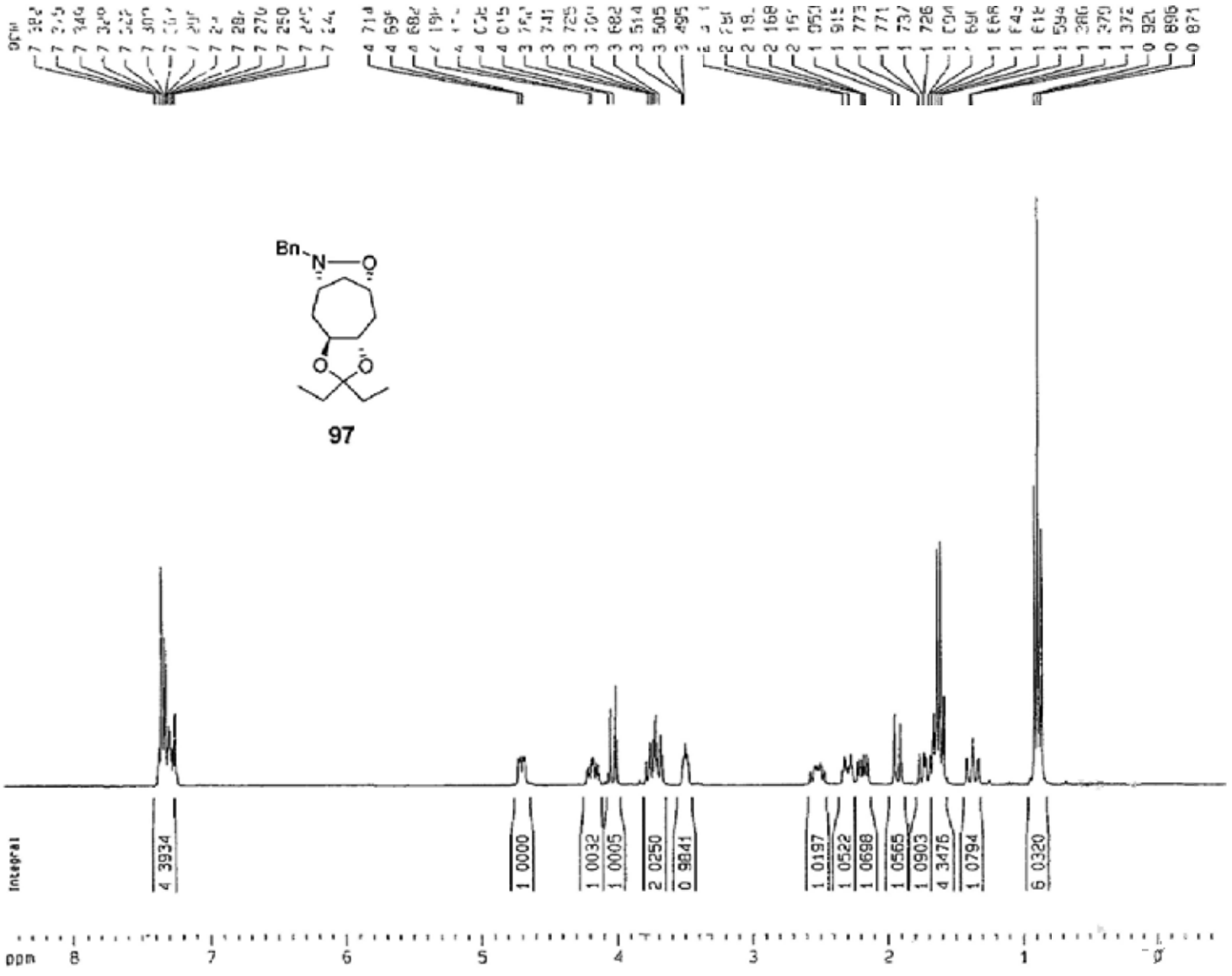
NAME	sh38carbon
EXPNO	1
PROCNO	1
Date_	20101011
Time	18.08
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	205
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	181
DW	20.800 usec
DE	6.50 usec
TE	299.6 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.90 usec
PL1	-2.00 dB
PL1W	55.33689499 W
SFO1	100.6379183 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	98.00 usec
PL2	-1.00 dB
PL12	15.16 dB
PL13	18.62 dB
PL2W	13.56617069 W
PL12W	0.32844096 W
PL13W	0.14806664 W
SFO2	400.1916008 MHz
SI	32768
SF	100.6278227 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40


^{1}H NMR
7.4250
7.4201
7.2597
5.2392
5.2367
5.2342
5.2299
5.2259
5.2231
4.8654
4.8618
4.8580
4.8276
4.8241
4.8204
4.8027
4.7650
4.5420
4.5283
2.7260
2.7154
2.7032
2.6982
2.6909
2.6864
2.6782
2.6616
2.6513
1.4061
1.3892
COOH
96
NAME sh50
EXPNO 2
PROCNO 1
Date_ 20100617
Time 16.01
INSTRUM spect
PROBHD 5 mm PABBI 1H/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 101
DW 60.800 usec
DE 6.50 usec
TE 294.4 K
D1 1.00000000 sec
TD0 1
CHANNEL f1
NUC1 1H
P1 7.10 usec
PL1 -2.00 dB
PL1W 13.17734718 W
SFO1 400.1324710 MHz
SI 32768
SF 400.1300048 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1.0125
1.0422
1.0223
1.0284
1.0000
4.1139
3.0856
3.0658
11
10
9
8
7
6
5
4
3
2
1
ppm



NAME	sh50carbon_C6D6	
EXPNO	1	
PROCNO	1	
Date_	20100716	
Time	15.35	
INSTRUM	spect	
PROBHD	5 mm PABBO BB-	
PULPROG	zgpg30	
TD	65536	
SOLVENT	C6D6	
NS	240	
DS	4	
SWH	24038.461	Hz
FIDRES	0.366798	Hz
AQ	1.3631988	sec
RG	101	
DW	20.800	usec
DE	6.50	usec
TE	298.2	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
========	CHANNEL f1	========
NUC1	13C	
P1	9.90	usec
PL1	-2.00	dB
PL1W	55.33689499	W
SFO1	100.6379183	MHz
========	CHANNEL f2	========
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	90.00	usec
PL2	-1.00	dB
PL12	15.16	dB
PL13	18.62	dB
PL2W	13.56617069	W
PL12W	0.32844096	W
PL13W	0.14806664	W
SFO2	400.1916008	MHz
SI	32768	
SF	100.6278199	MHz
WDW	EM	
SSB	0	
LB	1.00	Hz
GB	0	
PC	1.40	

^{1}H NMR



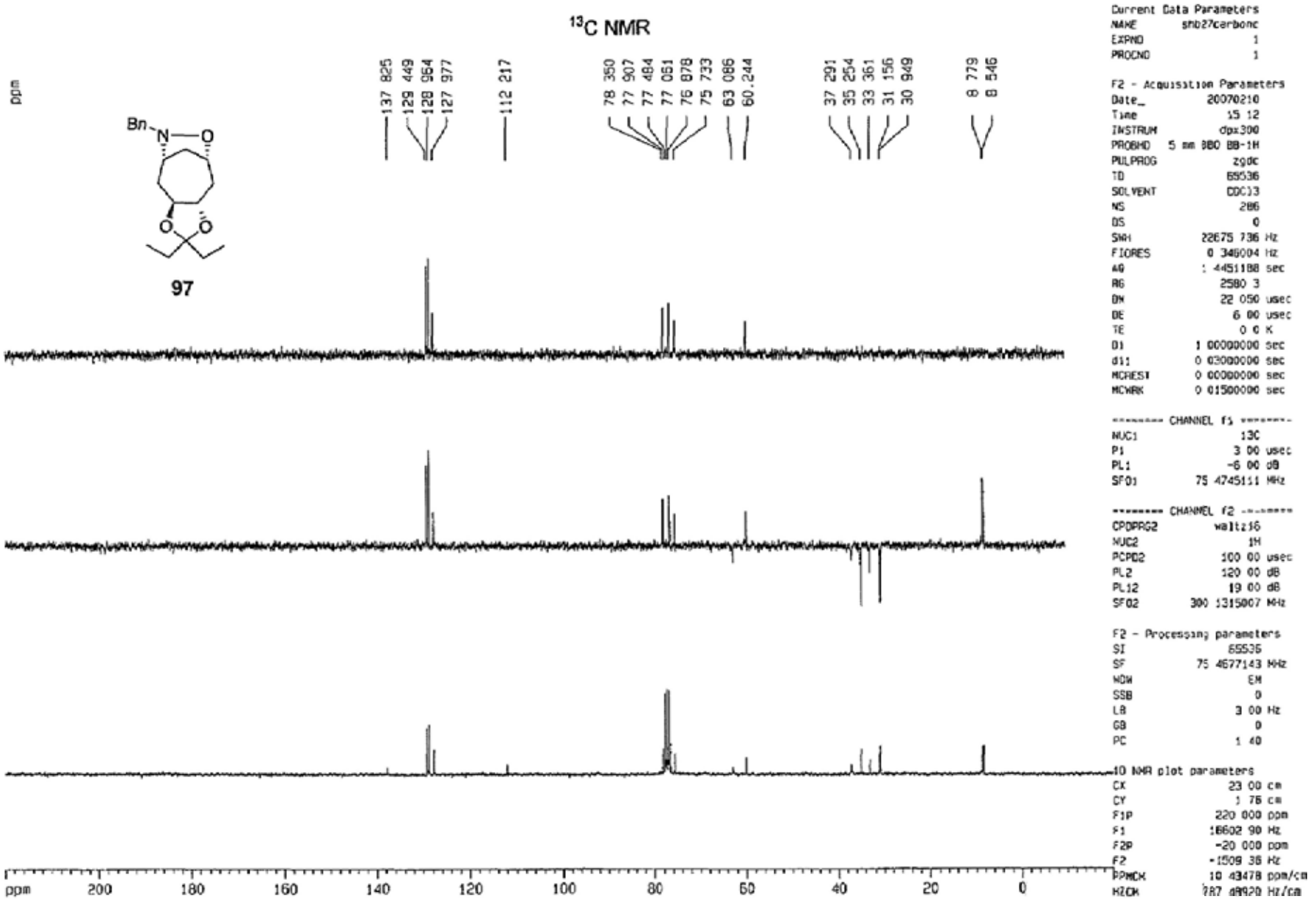
Current Data Parameters
NAME sm027
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20080425
Time 12 12
INSTRUM dpx300
PROBHD 5 mm BBO BB-1H
PULPROG zg
TD 32768
SOLVENT CDCl3
NS 8
DS 0
SWH 6992 606 Hz
FIDRES 0 274439 Hz
AQ 1 6219508 sec
RG 128
DW 55 600 usec
DE 79 43 usec
TE 295 2 K
D1 1 00000000 sec
MCREST 0 00000000 sec
MCWRK 0 01500000 sec

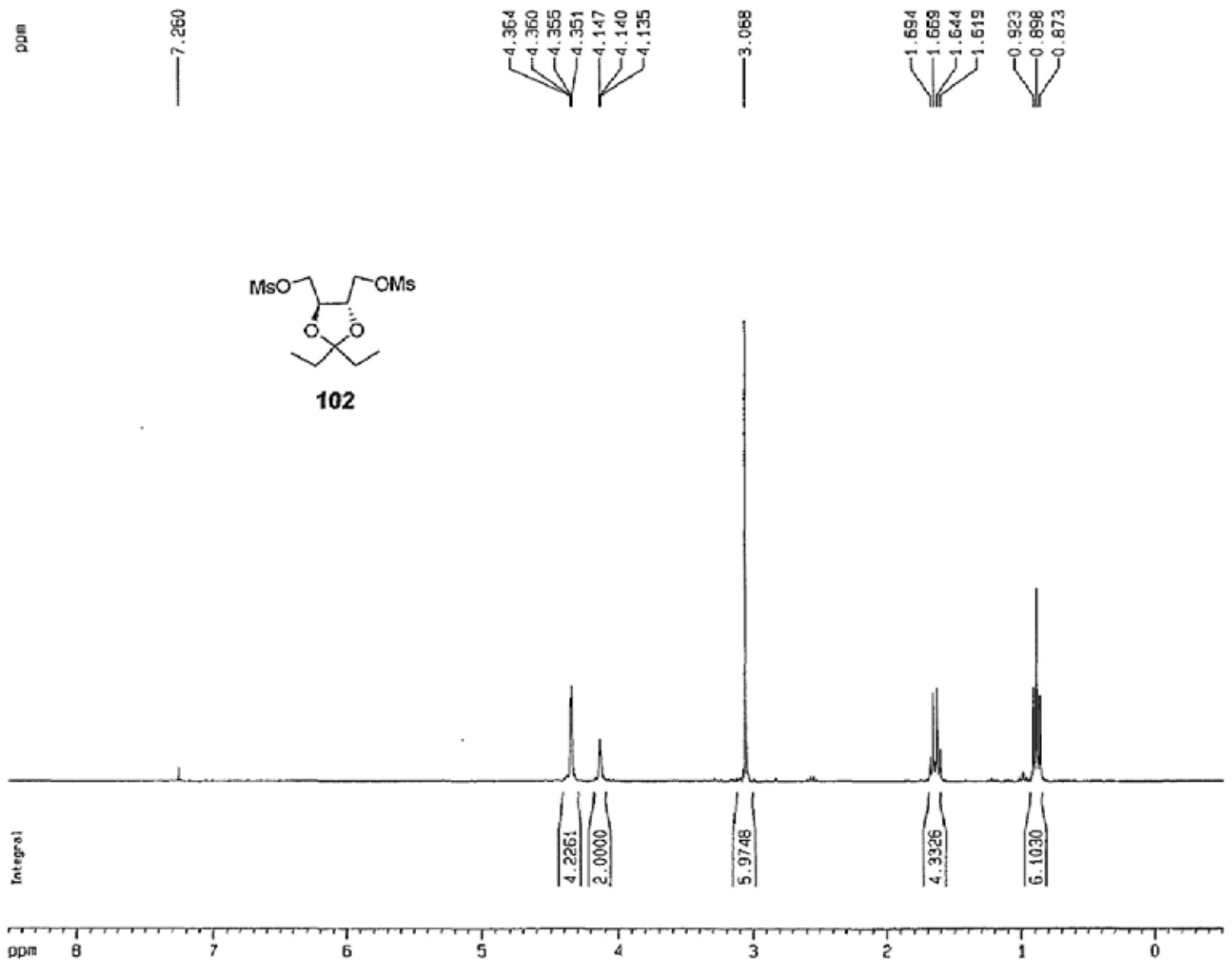
CHANNEL f1
NUC1 1H
P1 5 00 usec
PL1 -2 00 dB
SFO1 300 1312000 MHz

F2 - Processing parameters
SI 32768
SF 300 1300066 MHz
WDW EM
SSB 0
LB 0 30 Hz
GB 0
PC 1 00

1D NMR plot parameters
CX 22 00 cm
CY 10 56 cm
F1P 8 500 ppm
F1 2551 10 Hz
F2P -0 500 ppm
F2 -150 07 Hz
PPMCM 0 40909 ppm/cm
HZCM 122 78046 Hz/cm


^{13}C NMR
ppm
137.825
129.449
128.964
127.977
112.217
78.350
77.907
77.484
77.061
76.878
75.733
63.086
60.244
37.291
35.254
33.361
31.156
30.949
8.779
8.546
Bn
N
O
O
O
97
ppm
200
180
160
140
120
100
80
60
40
20
0
Current Data Parameters
NAME sn627carbonc
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20070210
Time 15 12
INSTRUM dpx300
PROBHD 5 mm BBO BB-1H
PULPROG zgdc
TD 65536
SOLVENT CDCl3
NS 286
DS 0
SWH 22675 736 Hz
FIDRES 0 346004 Hz
AQ 1 4451188 sec
RG 2580 3
DW 22 050 usec
DE 6 00 usec
TE 0 0 K
D1 1 00000000 sec
d11 0 03000000 sec
MCREST 0 00000000 sec
MCWRK 0 01500000 sec
-------- CHANNEL f1 --------
NUC1 13C
P1 3 00 usec
PL1 -6 00 dB
SFO1 75 4745111 MHz
-------- CHANNEL f2 --------
CPDPRG2 waltz16
NUC2 1H
PCPD2 100 00 usec
PL2 120 00 dB
PL12 19 00 dB
SFO2 300 1315007 MHz
F2 - Processing parameters
SI 65536
SF 75 4677143 MHz
WDW EM
SSB 0
LB 3 00 Hz
GB 0
PC 1 40
1D NMR plot parameters
CX 23 00 cm
CY 1 75 cm
F1P 220 000 ppm
F1 16602 90 Hz
F2P -20 000 ppm
F2 -1509 35 Hz
PPMCM 10 43478 ppm/cm
HZCM 787 48920 Hz/cm

^{1}H NMR



102

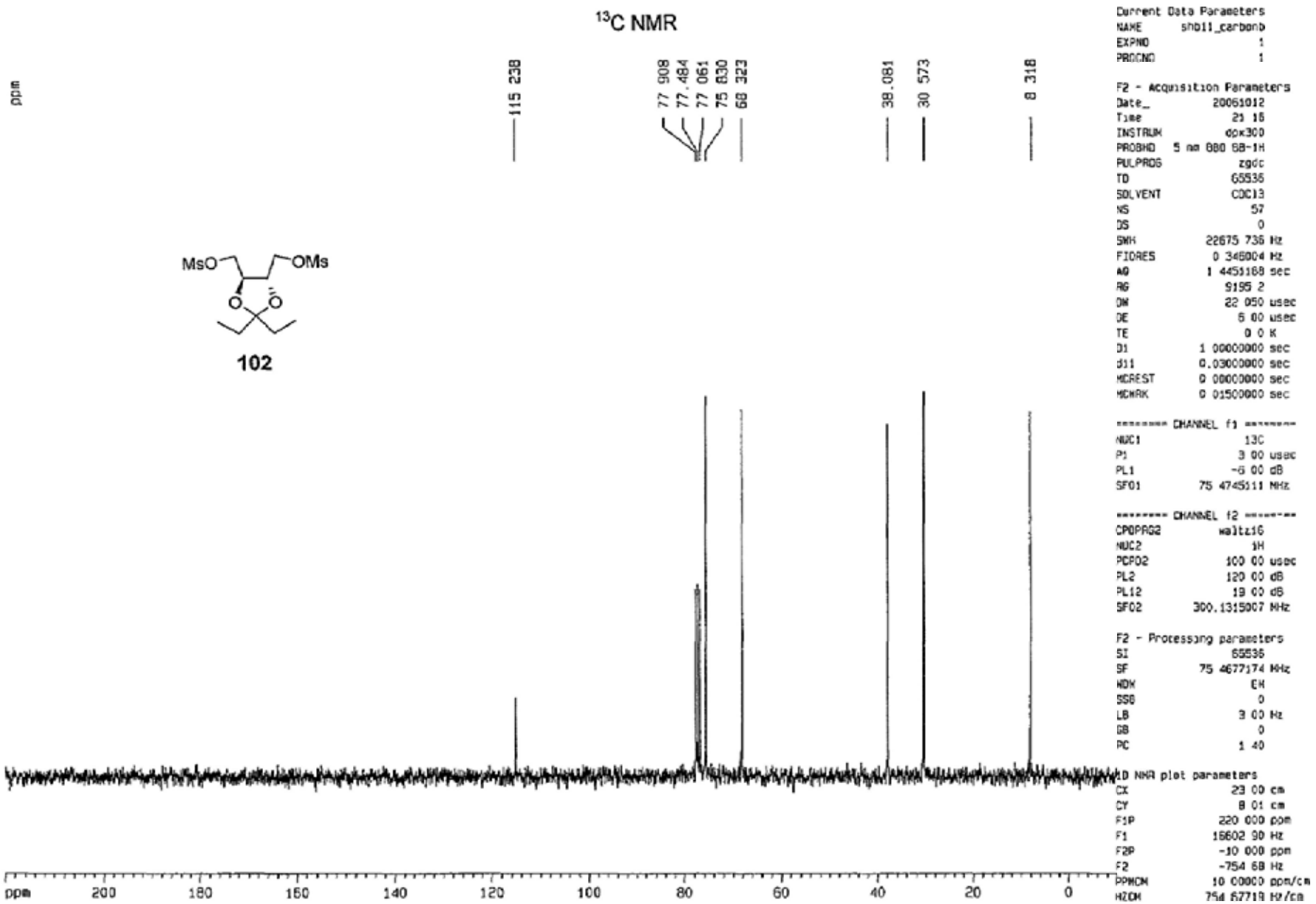
```
Current Data Parameters
NAME                  shb11b
EXPNO                      1
PROCNO                     1

F2 - Acquisition Parameters
Date_              20061012
Time                  21.12
INSTRUM               dpx300
PROBHD   5 mm BBO BB-1H
PULPROG                   zg
TD                     32768
SOLVENT                CDCl3
NS                         4
DS                         0
SWH               8992.806 Hz
FIDRES            0.274439 Hz
AQ                1.8219508 sec
RG                      71.8
DW                    55.600 usec
DE                    79.43 usec
TE                      0.0 K
D1                1.00000000 sec
MCREST            0.00000000 sec
MCWRK             0.01500000 sec

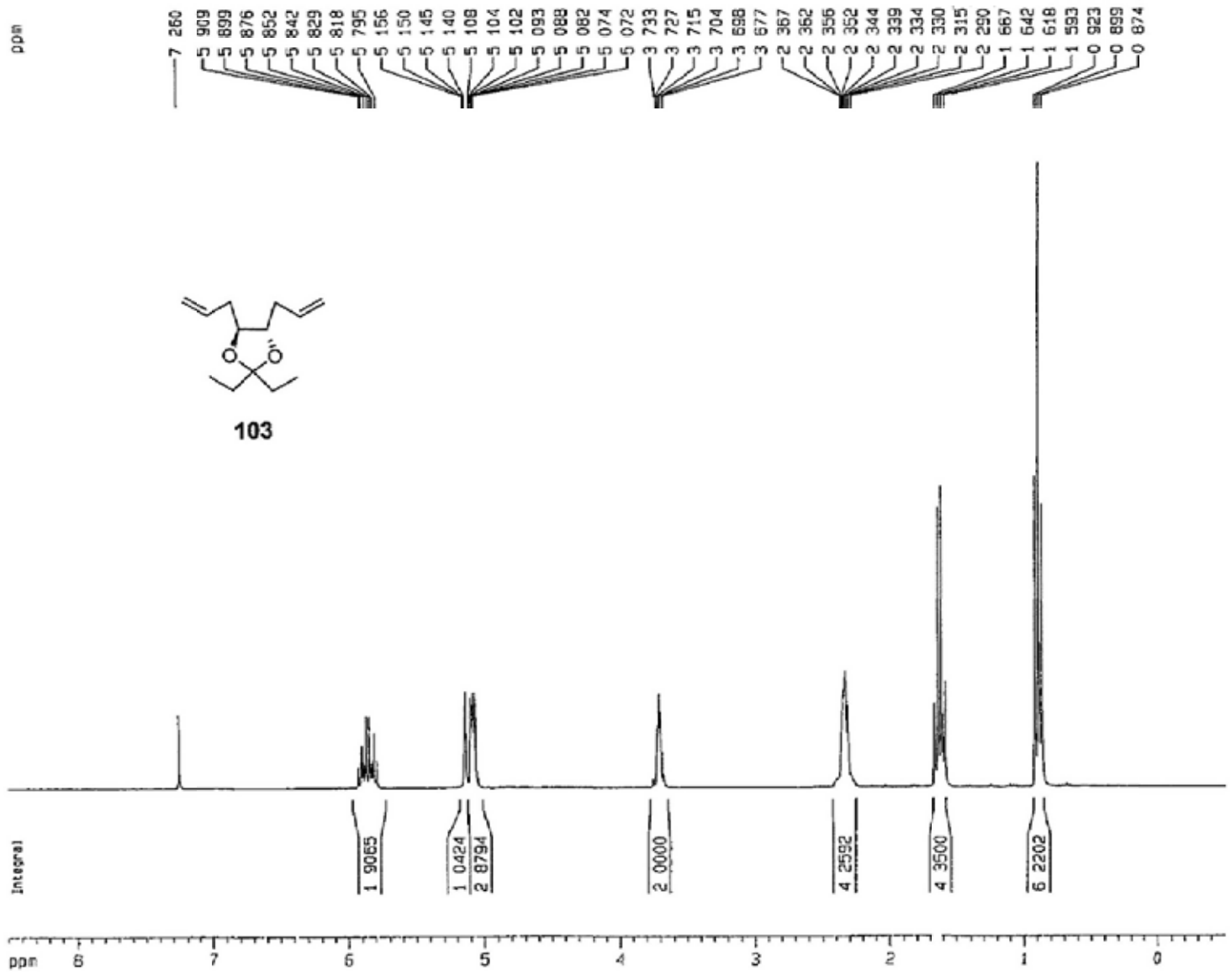
======== CHANNEL f1 ========
NUC1                      1H
P1                     5.00 usec
PL1                   -2.00 dB
SFO1             300.1312000 MHz

F2 - Processing parameters
SI                     32768
SF                300.1300063 MHz
WDW                       EM
SSB                        0
LB                      0.30 Hz
GB                         0
PC                      1.00

1D NMR plot parameters
CX                     22.00 cm
CY                      8.37 cm
F1P                    8.500 ppm
F1                  2551.10 Hz
F2P                   -0.500 ppm
F2                  -150.07 Hz
PPMCM                 0.40909 ppm/cm
HZCM                122.78046 Hz/cm
```


^{13}C NMR
ppm
115.238
77.908
77.484
77.061
75.830
68.323
38.081
30.573
8.318
MsO
OMs
102
Current Data Parameters
NAME shb11_carbonb
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20061012
Time 21 16
INSTRUM dpx300
PROBHD 5 mm BBO BB-1H
PULPROG zgdc
TD 65536
SOLVENT CDCl3
NS 57
DS 0
SWH 22675.736 Hz
FIDRES 0.346004 Hz
AQ 1.4451168 sec
RG 9195.2
DW 22.050 usec
DE 6.00 usec
TE 0.0 K
D1 1.00000000 sec
d11 0.03000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 13C
P1 3.00 usec
PL1 -6.00 dB
SFO1 75.4745111 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 120.00 dB
PL12 19.00 dB
SFO2 300.1315007 MHz
F2 - Processing parameters
SI 65536
SF 75.4677174 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
1D NMR plot parameters
CX 23.00 cm
CY 8.01 cm
F1P 220.000 ppm
F1 16602.90 Hz
F2P -10.000 ppm
F2 -754.68 Hz
PPMCM 10.00000 ppm/cm
HZCM 754.67719 Hz/cm
ppm 200 180 160 140 120 100 80 60 40 20 0

^{1}H NMR



103

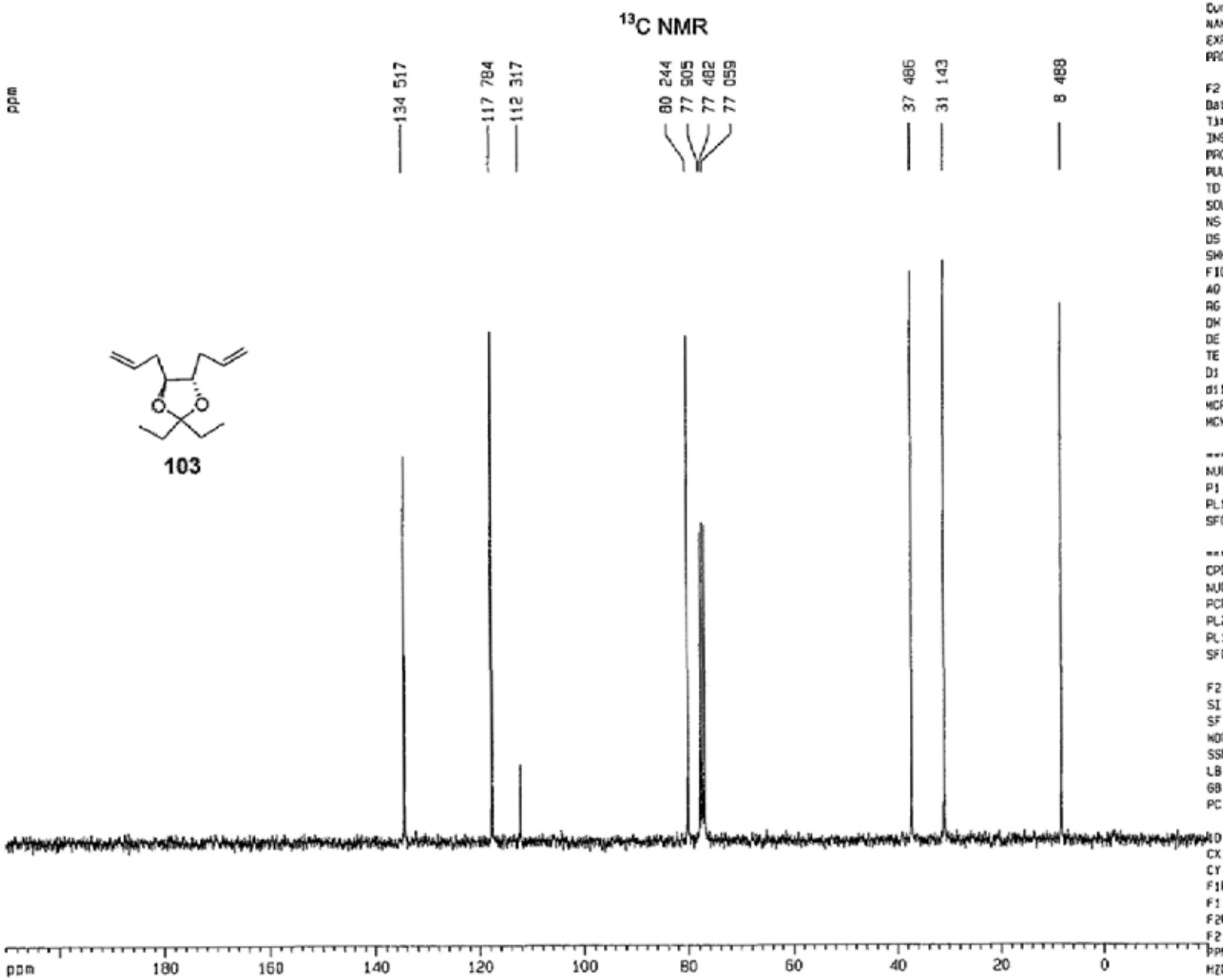
Current Data Parameters
NAME xhb12h
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20080228
Time 9 46
INSTRUM dpx300
PROBHD 5 mm BBO BB-1H
PULPROG zg
TD 32768
SOLVENT CDCl3
NS 8
DS 0
SWH [illegible]
FIDRES [illegible]
AQ [illegible]
RG [illegible] 5
DW 55 600 usec
DE 79 43 usec
TE [illegible] K
D1 [illegible]
HDREST [illegible]
HDXPR [illegible]

======== CHANNEL f1 ========
NUC1 1H
P1 5 00 usec
PL1 -2 00 dB
SFO1 300 1312000 MHz

F2 - Processing parameters
SI 32768
SF 300 1300060 MHz
WDW EM
SSB 0
LB 0 30 Hz
GB 0
PC 1 00

1D NMR plot parameters
CX 22 00 cm
CY 11 28 cm
F1P 8 500 ppm
F1 2551 11 Hz
F2P -0 500 ppm
F2 -150 07 Hz
PPMCM 0 40909 ppm/cm
HZCM 122 78047 Hz/cm



Current Data Parameters
NAME sh012carbone
EXPNO 1
PROCNO 1

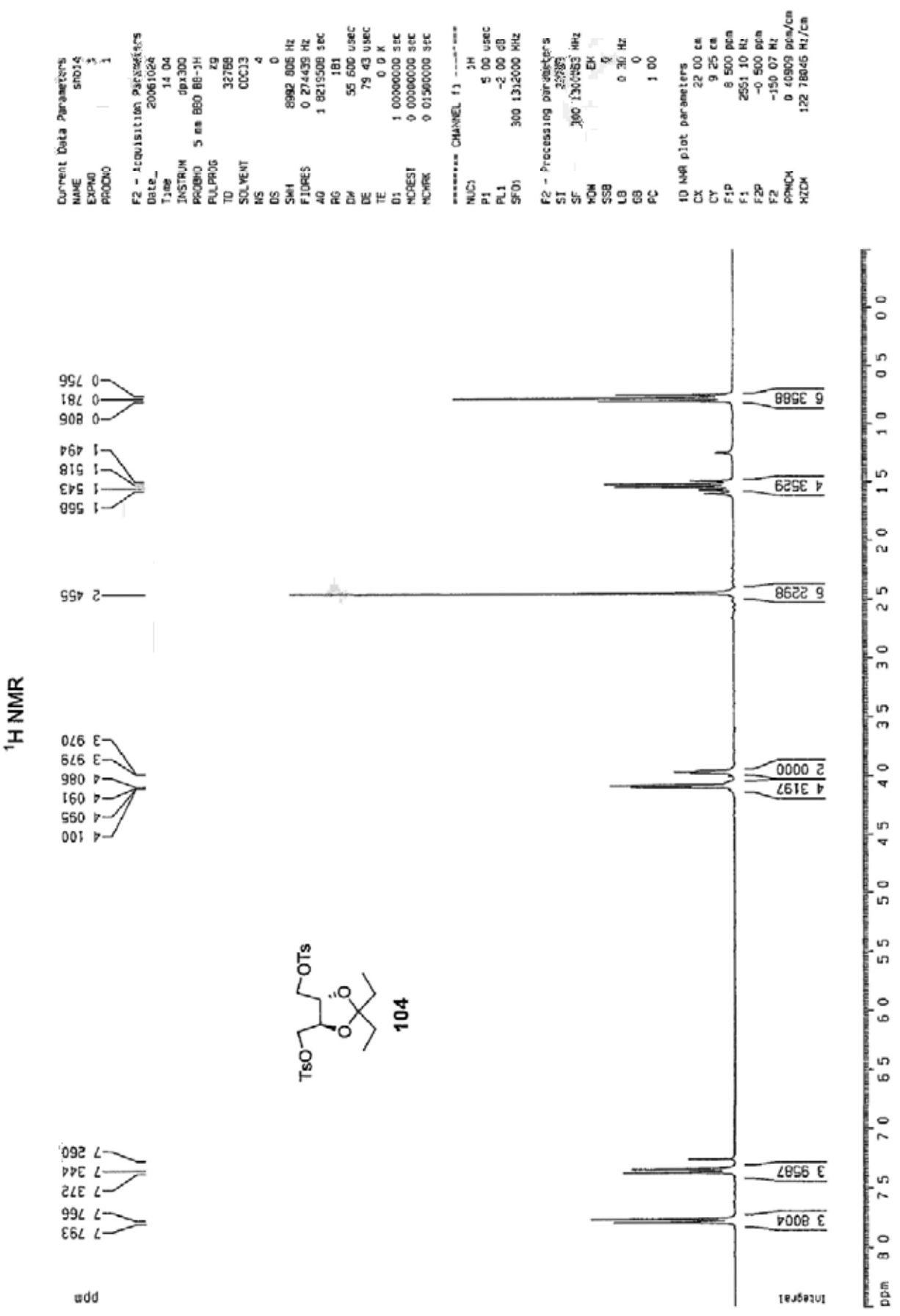
F2 - Acquisition Parameters
Date_ 20080228
Time 9 54
INSTRUM dpx300
PROBHD 5 mm BBO BB-1H
PULPROG tgdc
TD 65536
SOLVENT CDCl3
NS 270
DS 0
SWH 22675 736 Hz
FIDRES 0 346004 Hz
AQ 1 4451188 sec
RG 13004
DW 22 050 usec
DE 6 00 usec
TE 298 2 K
D1 1 00000000 sec
d11 0 03000000 sec
MCREST 0 00000000 sec
MCWRK 0 01500000 sec

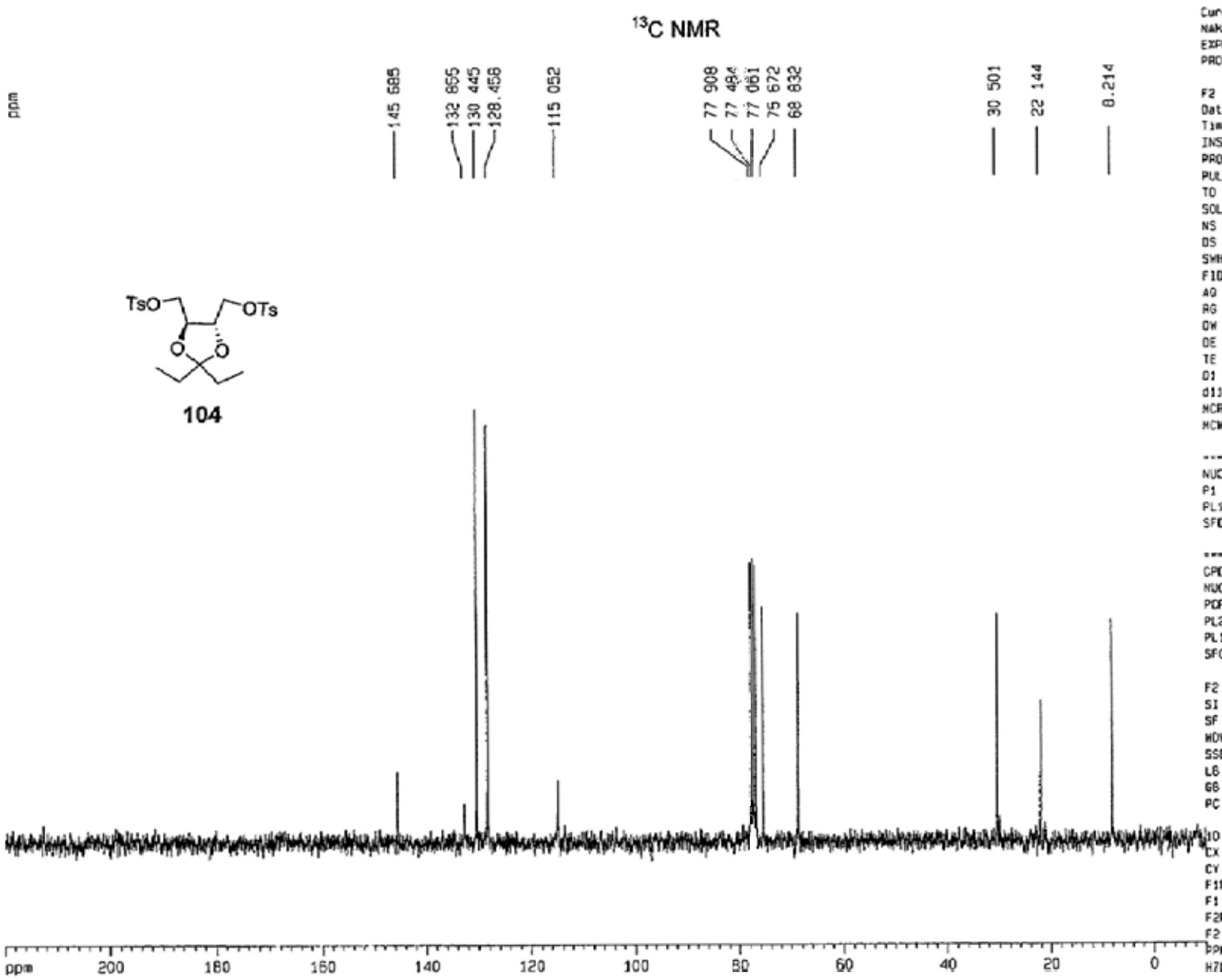
======== CHANNEL f1 ========
NUC1 13C
P1 3 00 usec
PL1 -6 00 dB
SFO1 75 4745111 MHz

======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100 00 usec
PL2 120 00 dB
PL12 19 00 dB
SFO2 300 1315007 MHz

F2 - Processing parameters
SI 65536
SF 75 4677143 MHz
WDW EM
SSB 0
LB 3 00 Hz
GB 0
PC 1 40

1D NMR plot parameters
CX 23 00 cm
CY 11 04 cm
F1P 210 000 ppm
F1 15848 22 Hz
F2P -20 000 ppm
F2 -1509 35 Hz
PPMCM 10 00000 ppm/cm
HZCM 754 67712 Hz/cm


^{1}H NMR
104
TsO
OTs
ppm
integral



Current Data Parameters
NAME shb14_carbon
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20061024
Time 14 09
INSTRUM dpx300
PROBHD 5 mm BBO BB-1H
PULPROG zgdc
TD 65536
SOLVENT CDCl3
NS 95
DS 0
SWH 22675 736 Hz
FIDRES 0.345804 Hz
AQ 1 4451188 sec
RG 10321 3
DW 22 050 usec
DE 6 00 usec
TE 0 0 K
D1 1 00000000 sec
d11 0 03000000 sec
MCREST 0 00000000 sec
MCWRK 0 01500000 sec

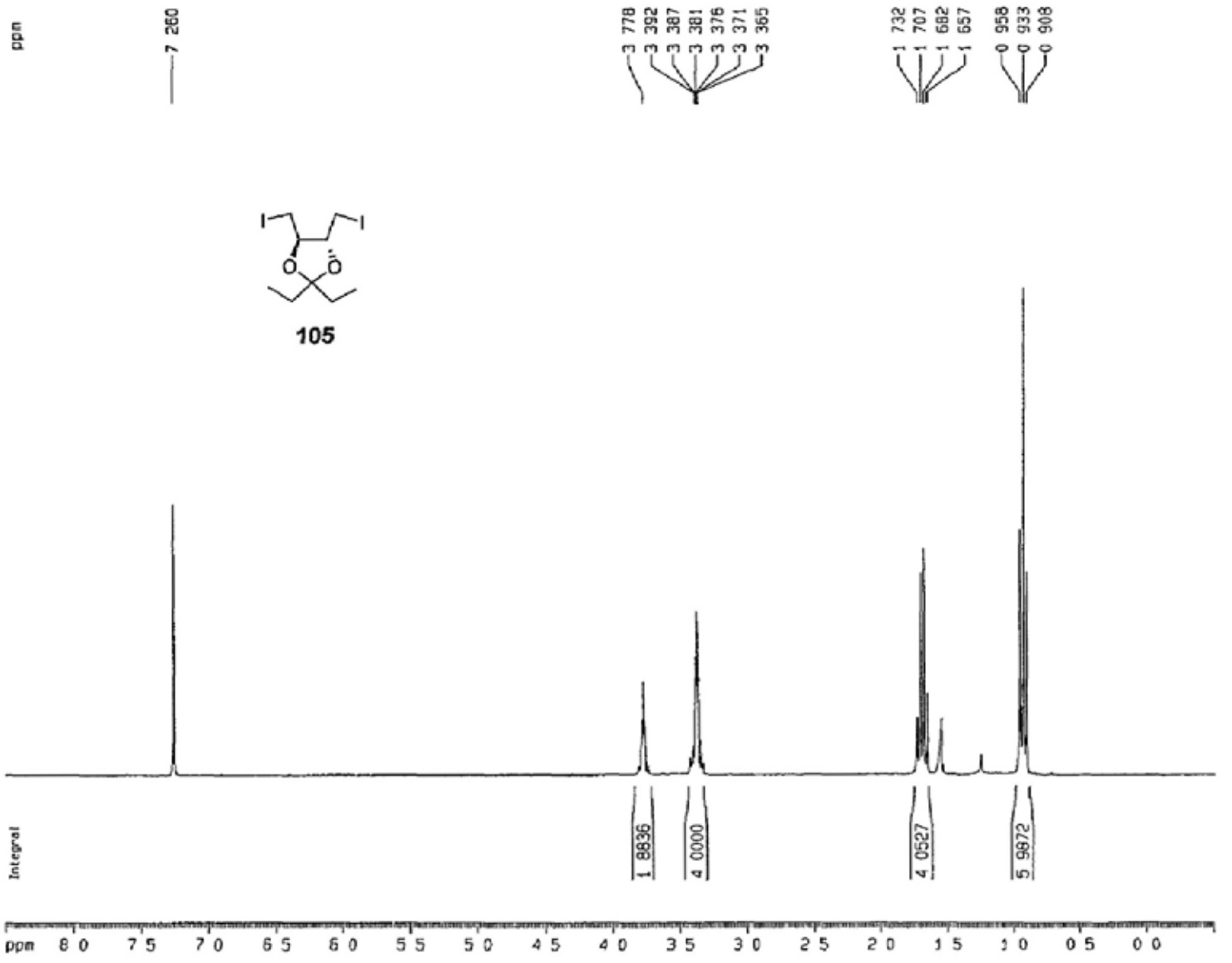
-------- CHANNEL f1 --------
NUC1 13C
P1 3 00 usec
PL1 -6 00 dB
SFO1 75 4745111 MHz

-------- CHANNEL f2 --------
CPDPRG2 waltz16
NUC2 1H
PCPD2 100 00 usec
PL2 120 00 dB
PL12 19 00 dB
SFO2 300 1315007 MHz

F2 - Processing parameters
SI 65536
SF 75 4677153 MHz
WDW EM
SSB 0
LB 3 00 Hz
GB 0
PC 1 40

1D NMR plot parameters
CX 23 00 cm
CY 8 31 cm
F1P 220 000 ppm
F1 16602 90 Hz
F2P -10 000 ppm
F2 -754 68 Hz
PPMCM 10 00000 ppm/cm
HZCM 754 67712 Hz/cm

^{1}H NMR




```
Current Data Parameters
NAME                  snb16b
EXPNO                      1
PROCNO                     1

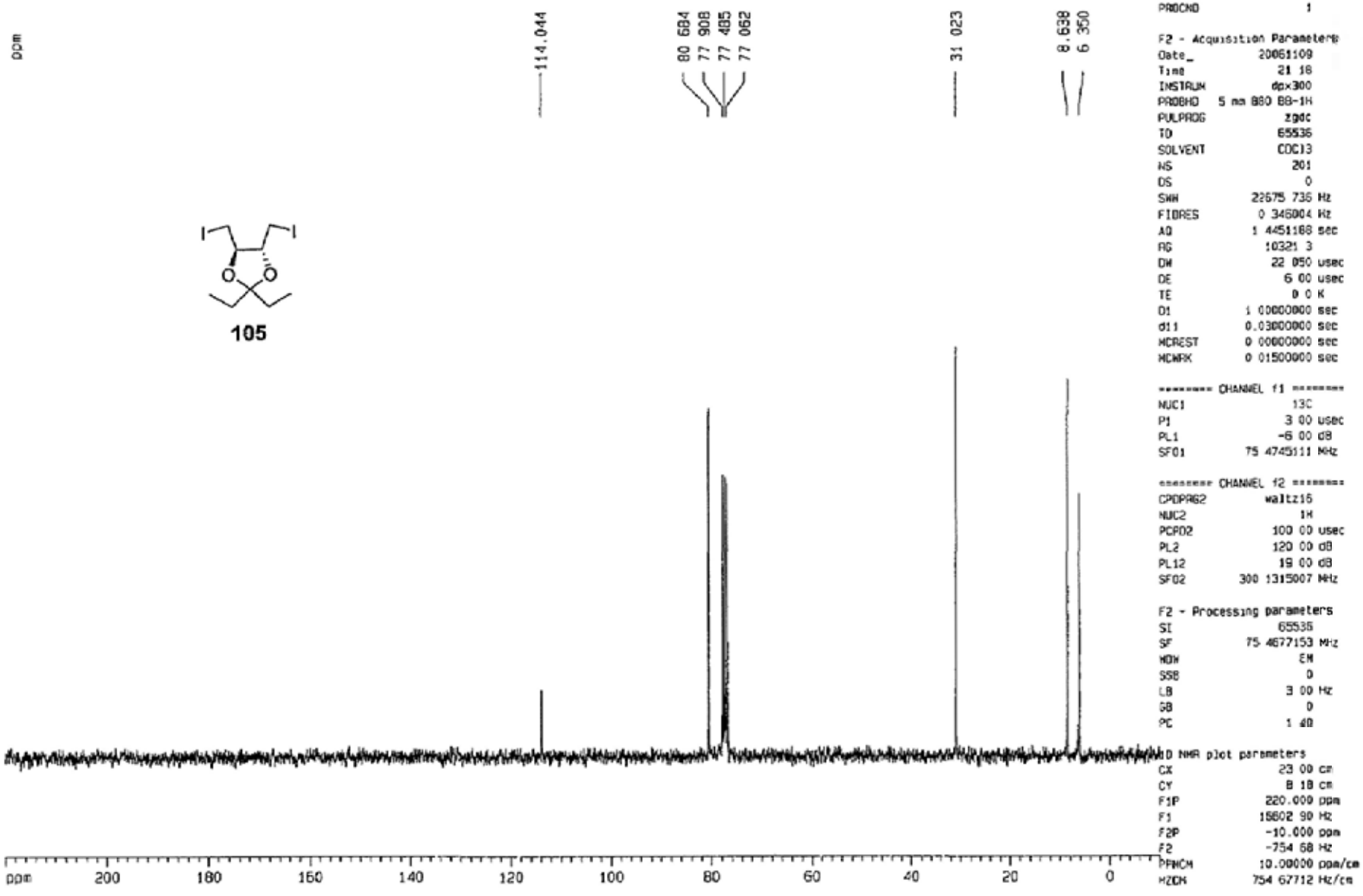
F2 - Acquisition Parameters
Date_              20051104
Time                  14 02
INSTRUM              dpx300
PROBHD   5 mm BBO BB-1H
PULPROG                   zg
TD                     32768
SOLVENT                CDCl3
NS                         8
DS                         0
SWH               8992 806 Hz
FIDRES            0 274439 Hz
AQ                1 8219508 sec
RG                    574 7
DW                   55 600 usec
DE                   79 43 usec
TE                    0 0 K
D1                1 00000000 sec
MCREST            0 00000000 sec
MCWRK             0 01500000 sec

-------- CHANNEL f1 = ------
NUC1                      1H
P1                    5 00 usec
PL1                  -2 00 dB
SFO1            300 1312000 MHz

F2 - Processing parameters
SI                     32768
SF              300 1300063 MHz
WDW                       EM
SSB                        0
LB                    0 30 Hz
GB                         0
PC                    1 00

1D NMR plot parameters
CX                   22 00 cm
CY                    8 97 cm
F1P                 8 500 ppm
F1                 2551 10 Hz
F2P                -0 500 ppm
F2                  150 07 Hz
PPMCM             0 40909 ppm/cm
HZCM             122 78045 Hz/cm
```

^{13}C NMR



105

Current Data Parameters
NAME shbi5_carbonb
EXPNO 1
PROCNO 1

F2 - Acquisition Parameters
Date_ 20061109
Time 21 18
INSTRUM dpx300
PROBHD 5 mm BBO BB-1H
PULPROG zgdc
TD 65536
SOLVENT CDCl3
NS 201
DS 0
SWH 22675 736 Hz
FIDRES 0 346004 Hz
AQ 1 4451168 sec
RG 10321 3
DW 22 050 usec
DE 6 00 usec
TE 0 0 K
D1 1 00000000 sec
d11 0.03000000 sec
MCREST 0 00000000 sec
MCWRK 0 01500000 sec

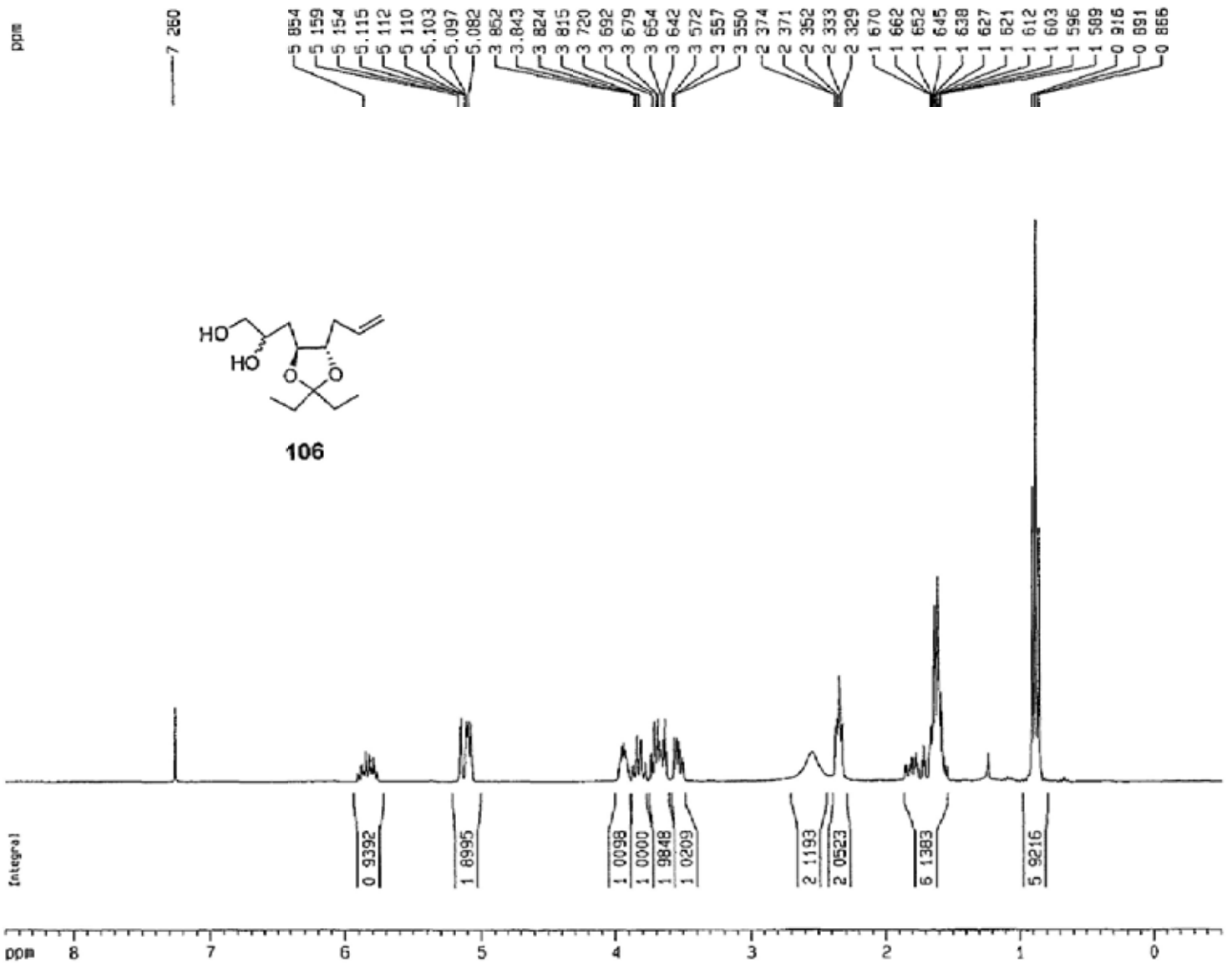
======== CHANNEL f1 ========
NUC1 13C
P1 3 00 usec
PL1 -6 00 dB
SF01 75 4745111 MHz

======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100 00 usec
PL2 120 00 dB
PL12 19 00 dB
SF02 300 1315007 MHz

F2 - Processing parameters
SI 65536
SF 75 4677153 MHz
WDW EM
SSB 0
LB 3 00 Hz
GB 0
PC 1 40

1D NMR plot parameters
CX 23 00 cm
CY 8 18 cm
F1P 220.000 ppm
F1 16602 90 Hz
F2P -10.000 ppm
F2 -754 68 Hz
PPMCM 10.00000 ppm/cm
HZCM 754 67712 Hz/cm

^{1}H NMR



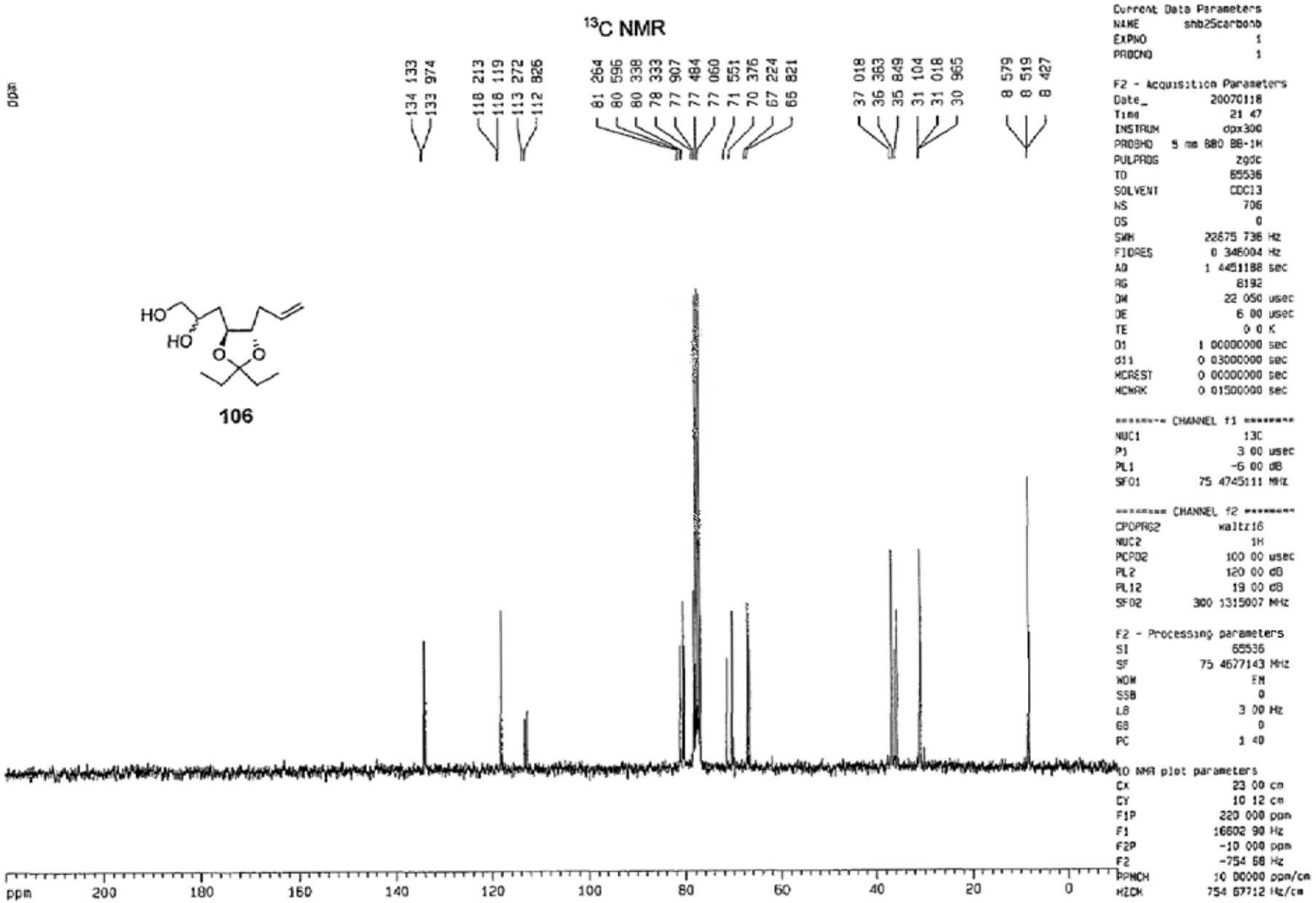

```
Current Data Parameters
NAME                  cha25d
EXPNO                      1
PROCNO                     1

F2 - Acquisition Parameters
Date_              20070118
Time                   21 37
INSTRUM                dpx300
PROBHD   5 mm BBO BB-1H
PULPROG                zg
TD                     32768
SOLVENT                CDCl3
NS                         8
DS                         0
SWH               6992 806 Hz
FIDRES            0 274439 Hz
AQ                1 8219508 sec
RG                    161 3
DW                   55 600 usec
DE                   79 43 usec
TE                     0 0 K
D1                1 00000000 sec
HCREST            0 00000000 sec
HCWRK             0 01500000 sec

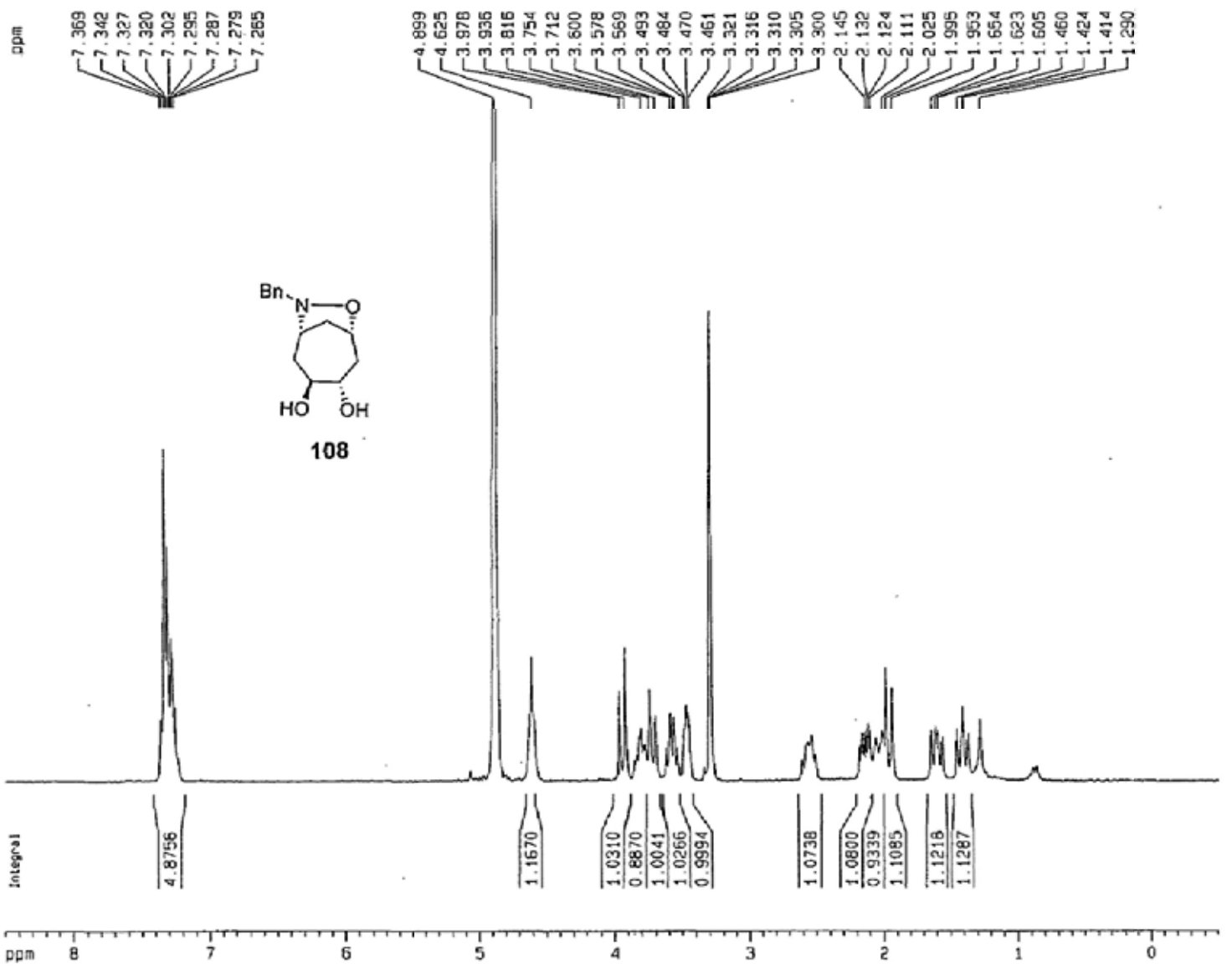
======== CHANNEL f1 ========
NUC1                      1H
P1                    5 00 usec
PL1                  -2 00 dB
SFO1             300 1312000 MHz

F2 - Processing parameters
SI                        32768
SF               300 1300053 MHz
WDW                       EM
SSB                        0
LB                    0 30 Hz
GB                         0
PC                    1 00

1D NMR plot parameters
CX                   22 00 cm
CY                   10 25 cm
F1P                  8 500 ppm
F1                 2551 10 Hz
F2P                 -0 500 ppm
F2                 -150 07 Hz
PPMCM              0 40909 ppm/cm
HZCM               122 78046 Hz/cm
```


^{13}C NMR
134.133
133.974
118.213
118.119
113.272
112.826
81.264
80.596
80.338
78.333
77.907
77.484
77.060
71.551
70.376
67.224
65.821
37.018
36.363
35.849
31.104
31.018
30.965
8.579
8.519
8.427
ppm
HO
HO
O
O
106
ppm 200 180 160 140 120 100 80 60 40 20 0
Current Data Parameters
NAME shb25carbonb
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20070118
Time 21 47
INSTRUM dpx300
PROBHD 5 mm BBO BB-1H
PULPROG zgdc
TD 65536
SOLVENT CDCl3
NS 706
DS 0
SWH 22675.736 Hz
FIDRES 0.346004 Hz
AQ 1.4451188 sec
RG 8192
DW 22.050 usec
DE 6.00 usec
TE 0.0 K
D1 1.00000000 sec
d11 0.03000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
======== CHANNEL f1 ========
NUC1 13C
P1 3.00 usec
PL1 -6.00 dB
SFO1 75.4745111 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 120.00 dB
PL12 19.00 dB
SFO2 300.1315007 MHz
F2 - Processing parameters
SI 65536
SF 75.4677143 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
1D NMR plot parameters
CX 23.00 cm
CY 10.12 cm
F1P 220.000 ppm
F1 16602.90 Hz
F2P -10.000 ppm
F2 -754.68 Hz
PPMCM 10.00000 ppm/cm
HZCM 754.67712 Hz/cm

^{1}H NMR (Solvent: CD_3OD)



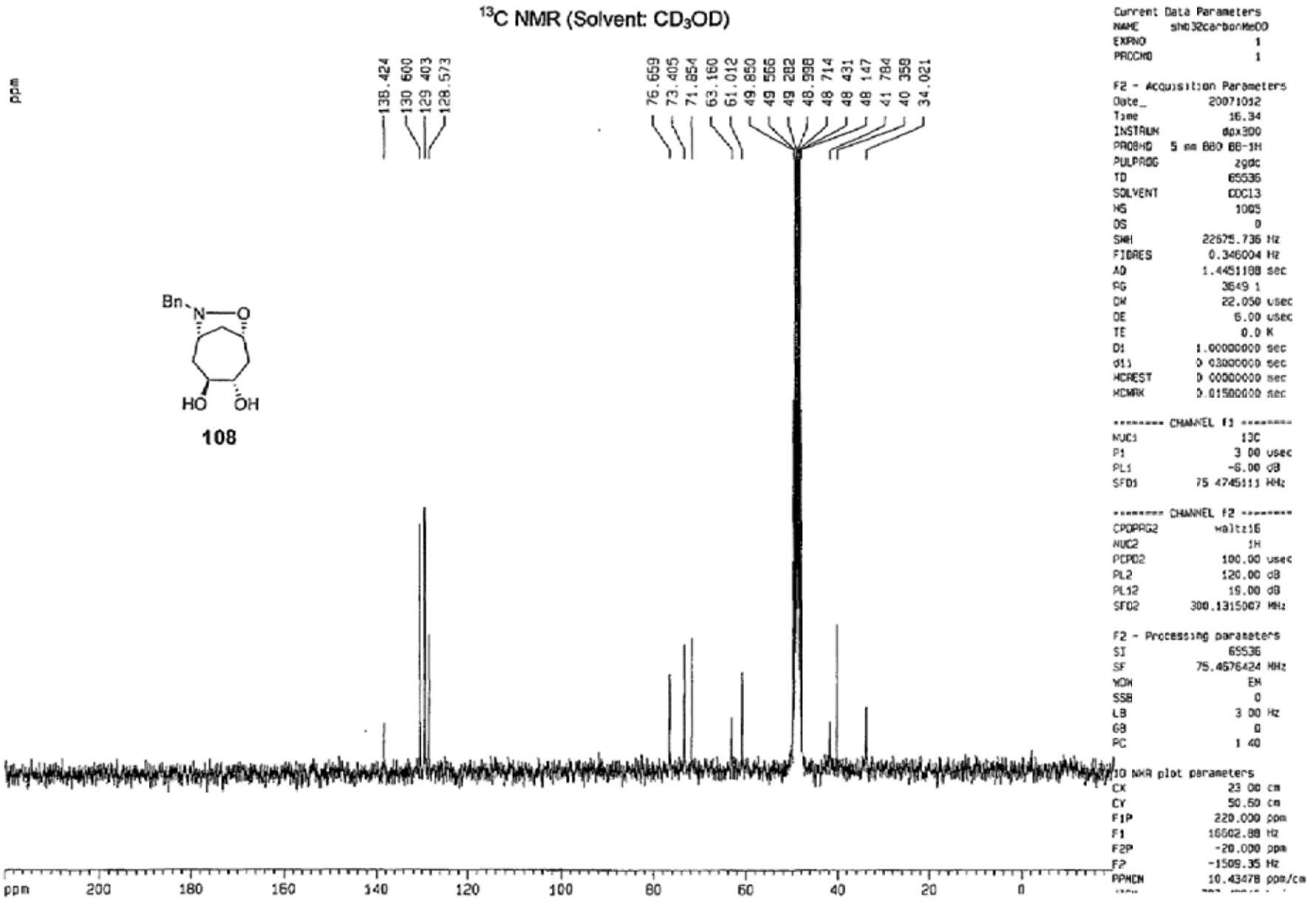

```
Current Data Parameters
NAME                  sho32e
EXPNO                      1
PROCNO                     1

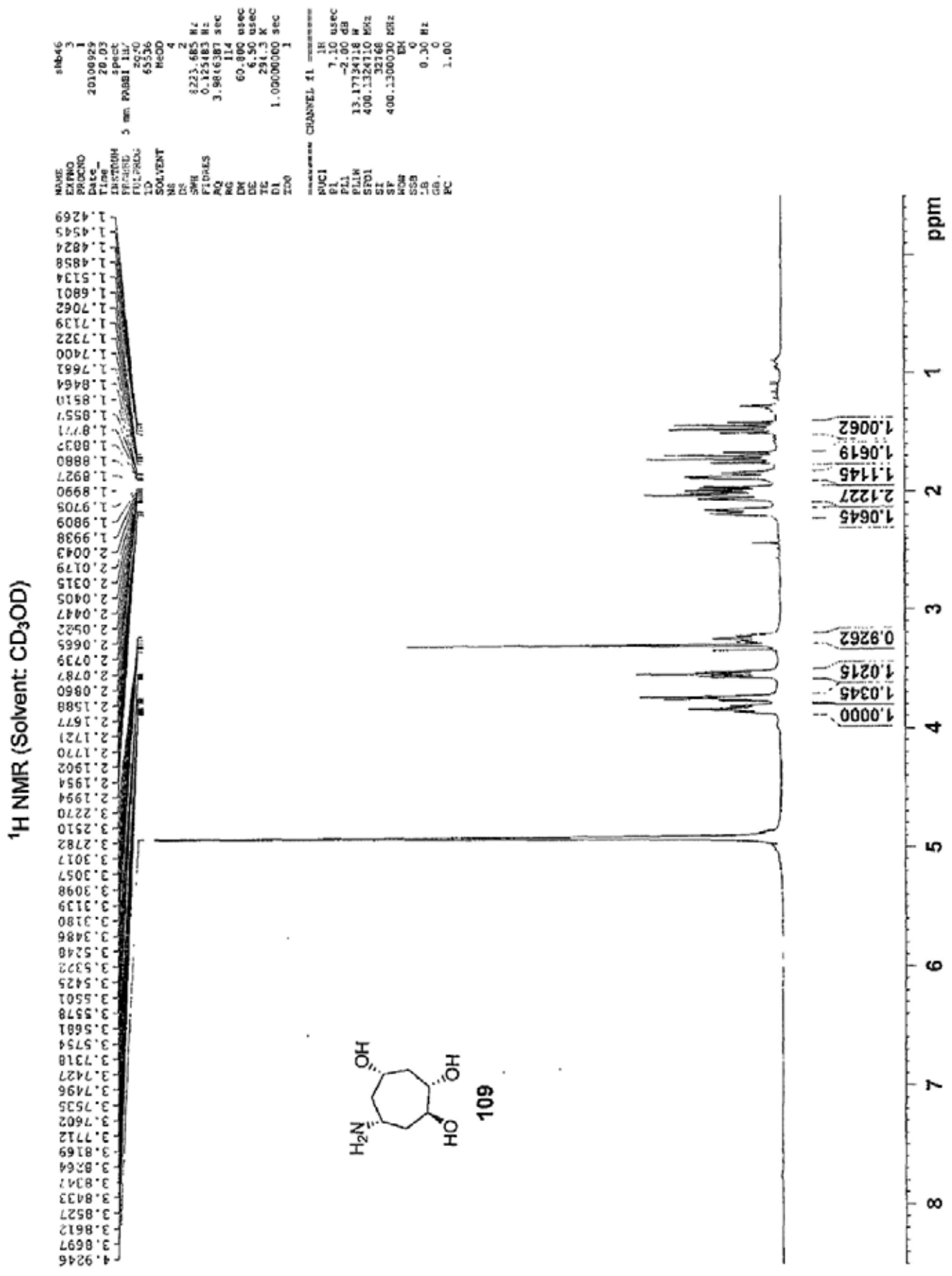
F2 - Acquisition Parameters
Date_              20071012
Time                   15.26
INSTRUM              dpx300
PROBHD   5 mm BBO BB-1H
PULPROG                zg
TD                     32768
SOLVENT                MeOD
NS                        16
DS                         0
SWH                8992.806 Hz
FIDRES             0.274439 Hz
AQ                 1.8219508 sec
RG                       362
DW                  55.600 usec
DE                  79.43 usec
TE                     0.0 K
D1                 1.00000000 sec
HDREST             0.00000000 sec
HDMRK              0.01500000 sec

======== CHANNEL f1 ========
NUC1                       1H
P1                   5.00 usec
PL1                  -2.00 dB
SFO1          300.1312000 MHz

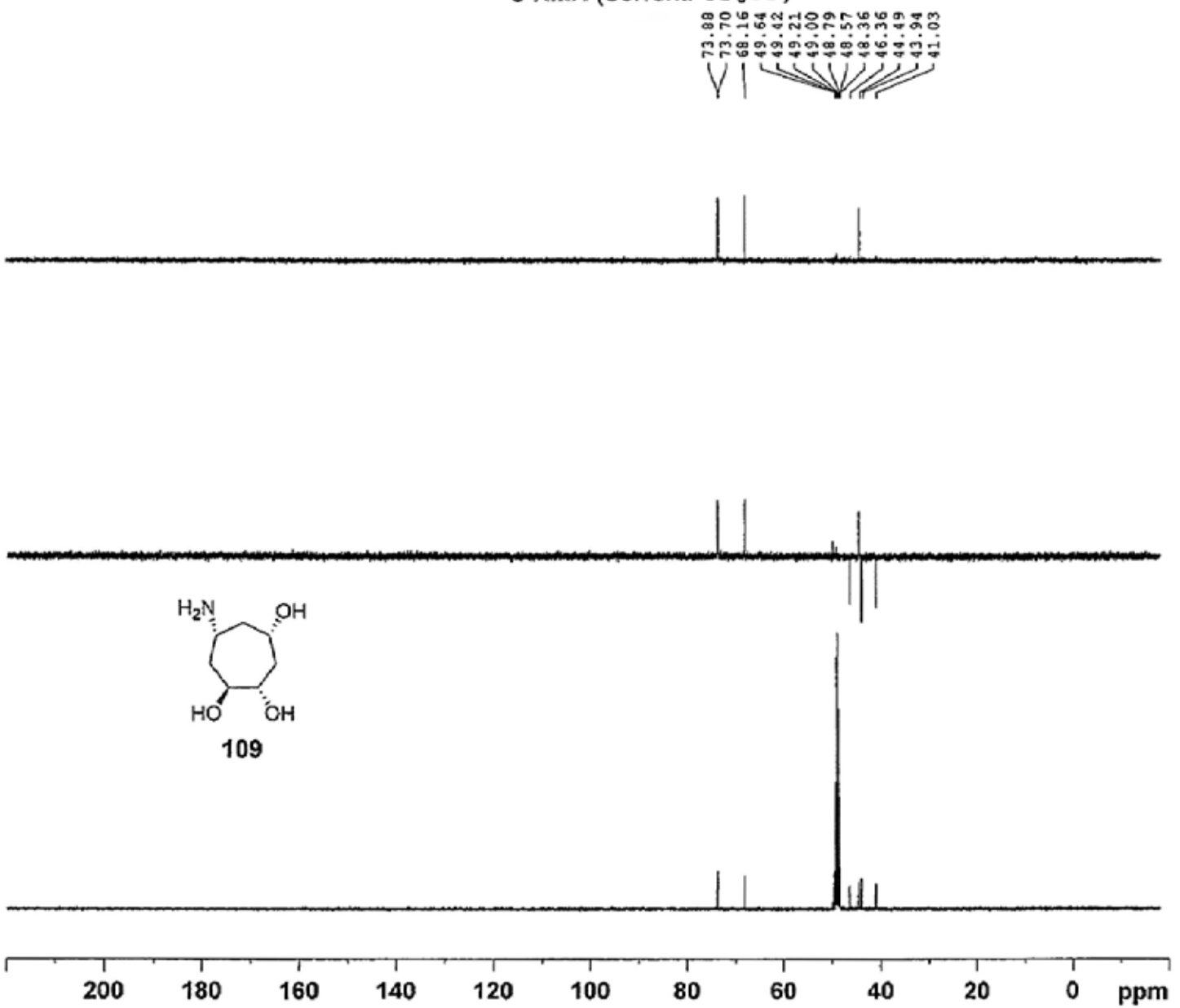
F2 - Processing parameters
SI                     32768
SF            300.1300045 MHz
WDW                       EM
SSB                        0
LB                   0.30 Hz
GB                         0
PC                    1.00

1D NMR plot parameters
CX                   22.00 cm
CY                   90.38 cm
F1P                  8.500 ppm
F1                  2551.10 Hz
F2P                 -0.500 ppm
F2                  -150.07 Hz
PPMCM             0.40909 ppm/cm
HZCM              122.78946 Hz/cm
```


^{13}C NMR (Solvent: CD_3OD)
ppm
138.424
130.600
129.403
128.573
76.659
73.405
71.654
63.160
61.012
49.850
49.566
49.282
48.998
48.714
48.431
48.147
41.784
40.358
34.021
Bn
N
O
HO
OH
108
ppm 200 180 160 140 120 100 80 60 40 20 0
Current Data Parameters
NAME sh032carbonMeOD
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20071012
Time 16.34
INSTRUM dpx300
PROBHD 5 mm BBO BB-1H
PULPROG zgdc
TD 65536
SOLVENT CDCl3
NS 1005
DS 0
SWH 22675.736 Hz
FIDRES 0.346004 Hz
AQ 1.4451188 sec
RG 3649.1
DW 22.050 usec
DE 6.00 usec
TE 0.0 K
D1 1.00000000 sec
d11 0.03000000 sec
MCREST 0.00000000 sec
MCWRK 0.01500000 sec
CHANNEL f1
NUC1 13C
P1 3.00 usec
PL1 -6.00 dB
SFO1 75.4745111 MHz
CHANNEL f2
CPDPRG2 waltz16
NUC2 1H
PCPD2 100.00 usec
PL2 120.00 dB
PL12 19.00 dB
SFO2 300.1315067 MHz
F2 - Processing parameters
SI 65536
SF 75.4576424 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.40
1D NMR plot parameters
CX 23.00 cm
CY 50.60 cm
F1P 220.000 ppm
F1 16602.88 Hz
F2P -20.000 ppm
F2 -1509.35 Hz
PPMCM 10.43478 ppm/cm

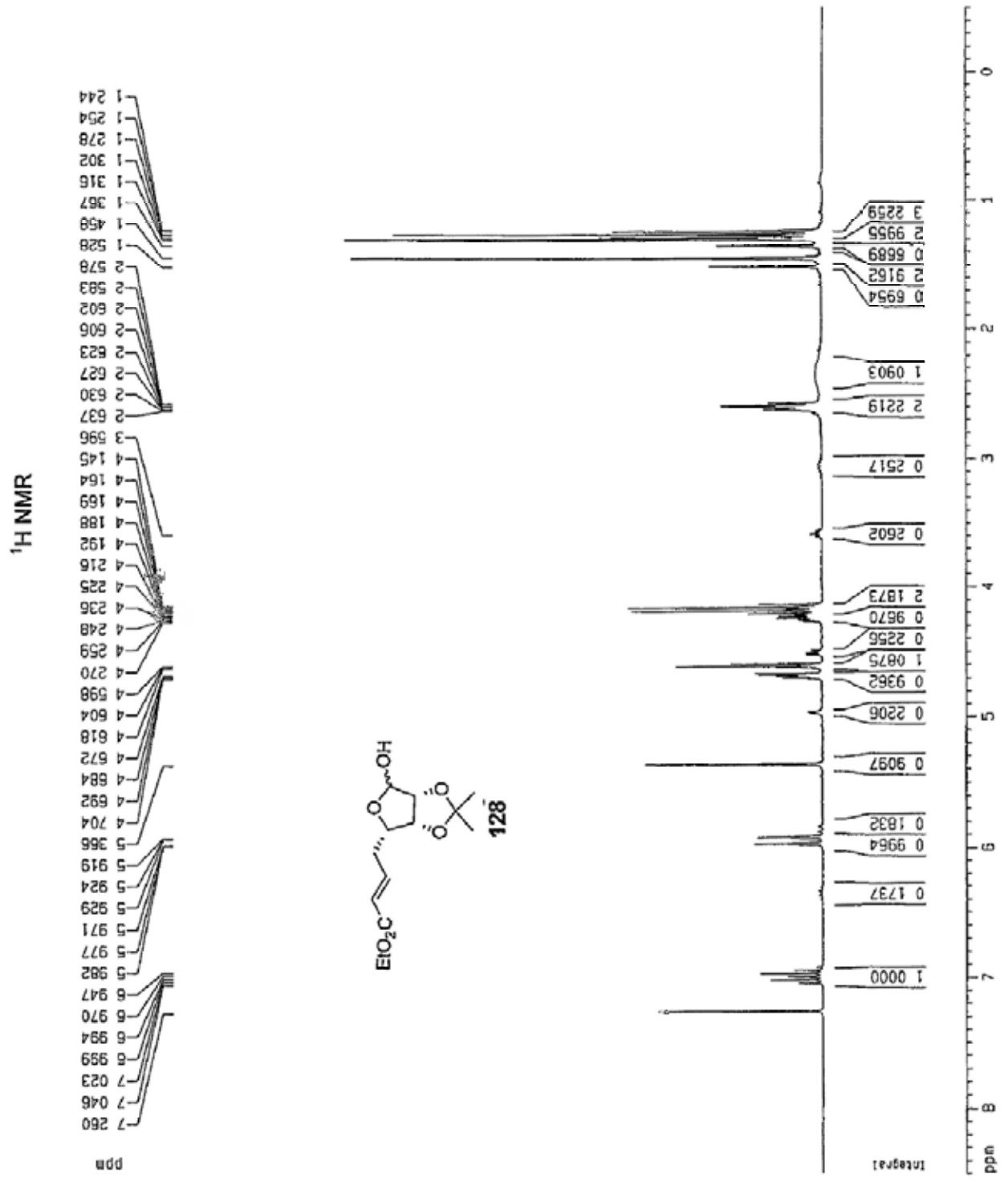

^{1}H NMR (Solvent: CD$_3$OD)
109
ppm

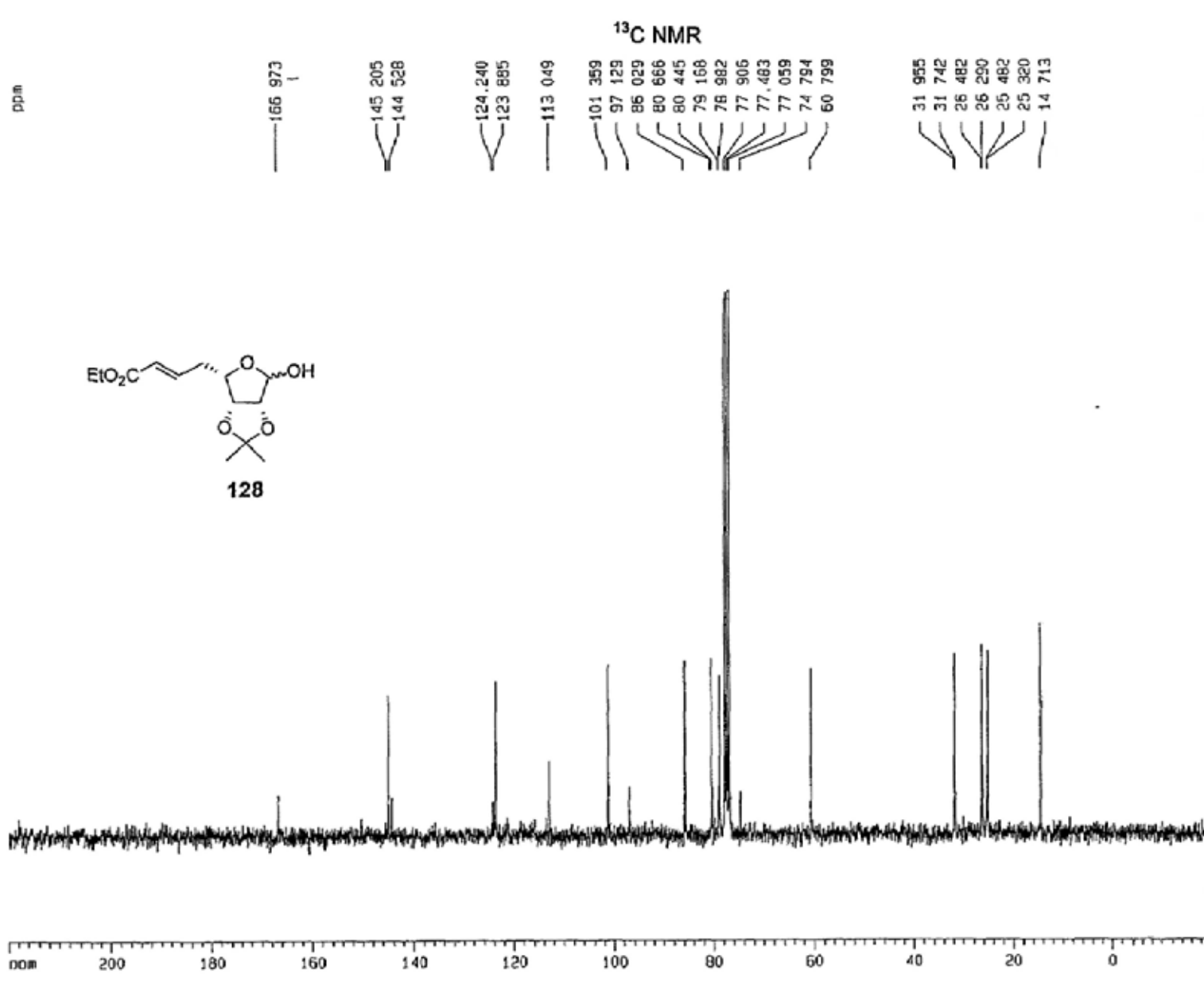
^{13}C NMR (Solvent: CD_3OD)



109

NAME	shb46carbon	
EXPNO	1	
PROCNO	1	
Date_	20100928	
Time	10.11	
INSTRUM	spect	
PROBHD	5 mm PABBO BB-	
PULPROG	zgpg30	
TD	65536	
SOLVENT	MeOD	
NS	89	
DS	4	
SWH	24038.461	Hz
FIDRES	0.366798	Hz
AQ	1.3631988	sec
RG	1620	
DW	20.800	usec
DE	6.50	usec
TE	298.5	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
========	CHANNEL f1	========
NUC1	13C	
P1	9.90	usec
PL1	-2.00	dB
PL1W	55.33699499	W
SFO1	100.6379183	MHz
========	CHANNEL f2	========
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	90.00	usec
PL2	-1.00	dB
PL12	15.16	dB
PL13	18.62	dB
PL2W	13.56617069	W
PL12W	0.32844096	W
PL13W	0.14806664	W
SFO2	400.1916008	MHz
SI	32768	
SF	100.6277170	MHz
WDW	EM	
SSB	0	
LB	1.00	Hz
GB	0	
PC	1.40	


^{1}H NMR
128
EtO2C
OH



Current Data Parameters
NAME skh51carbon
EXPNO 1
PROCNO 1

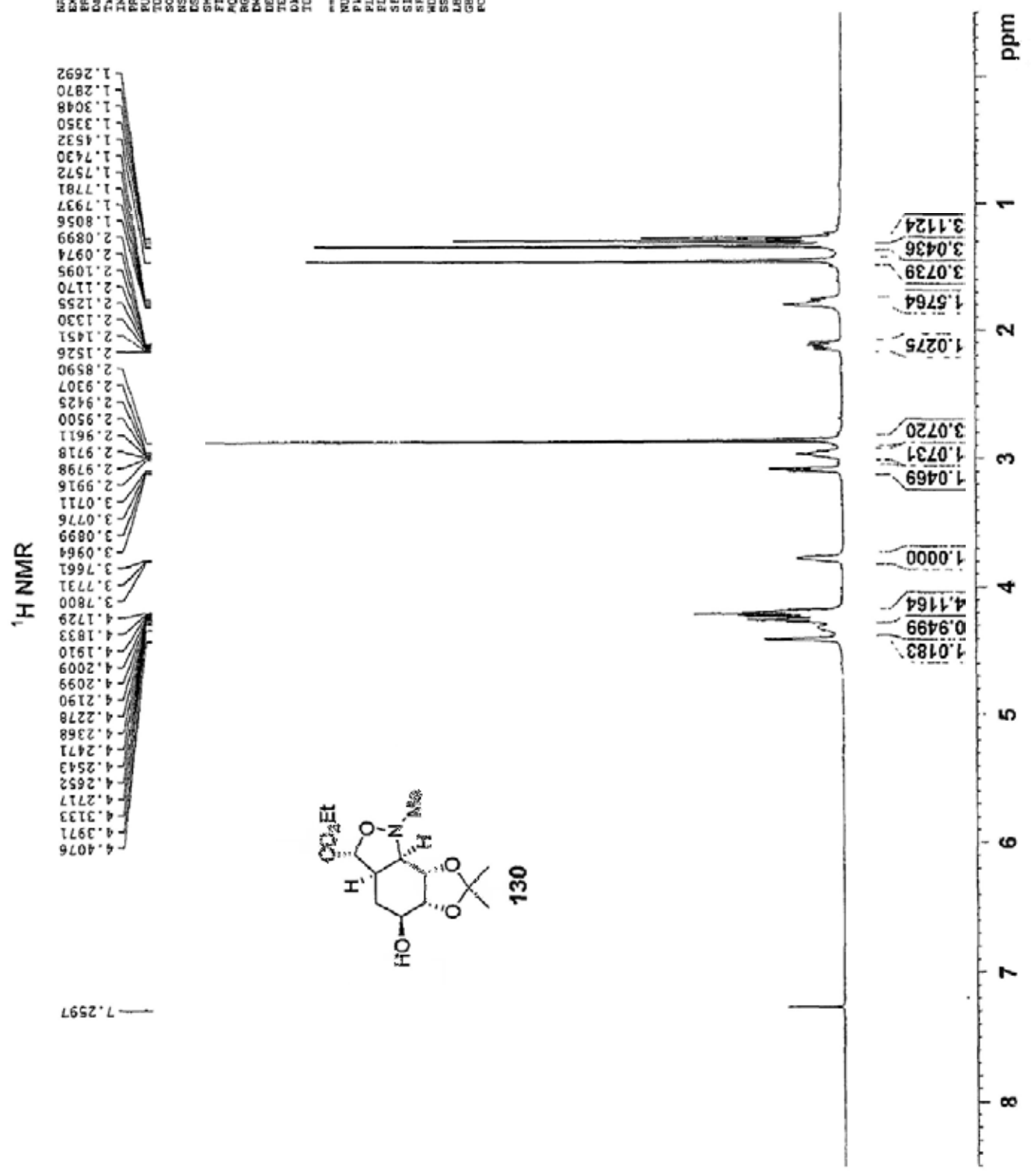
F2 - Acquisition Parameters
Date_ 20070911
Time 22 13
INSTRUM dpx300
PROBHD 5 mm BBO BB-1H
PULPROG zgdc
TD 65536
SOLVENT CDCl3
NS 380
DS 0
SWH 22675 736 Hz
FIDRES 0 346004 Hz
AQ 1 4451188 sec
RG 4597 6
DW 22 050 usec
DE 6 00 usec
TE 0 0 K
D1 1 00000000 sec
d11 0 03000000 sec
MCREST 0 00000000 sec
MCWRK 0 01500000 sec

======== CHANNEL f1 ========
NUC1 13C
P1 3 80 usec
PL1 -6 00 dB
SFO1 75 4745111 MHz

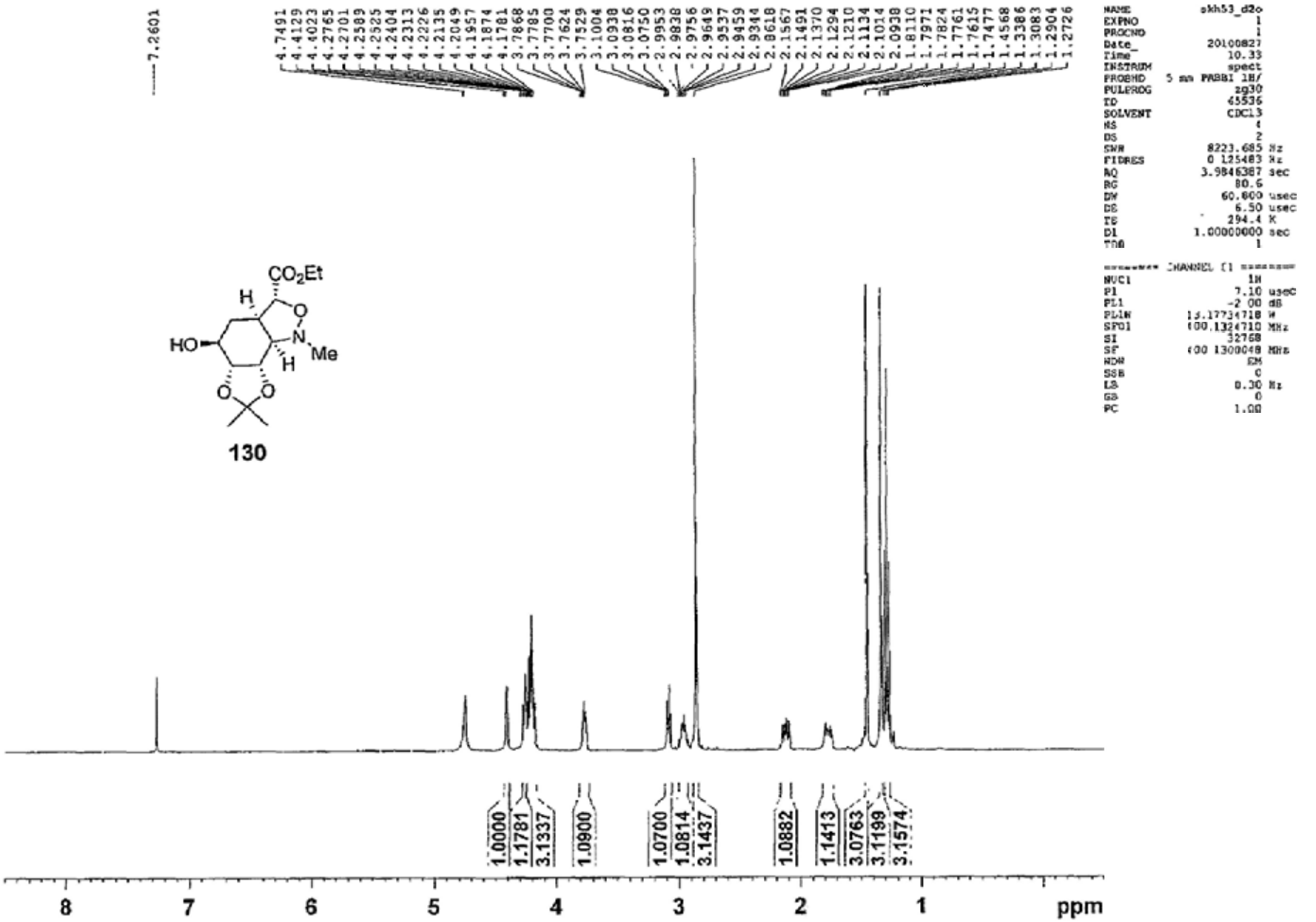
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100 00 usec
PL2 120 00 dB
PL12 19 00 dB
SFO2 300 1315007 MHz

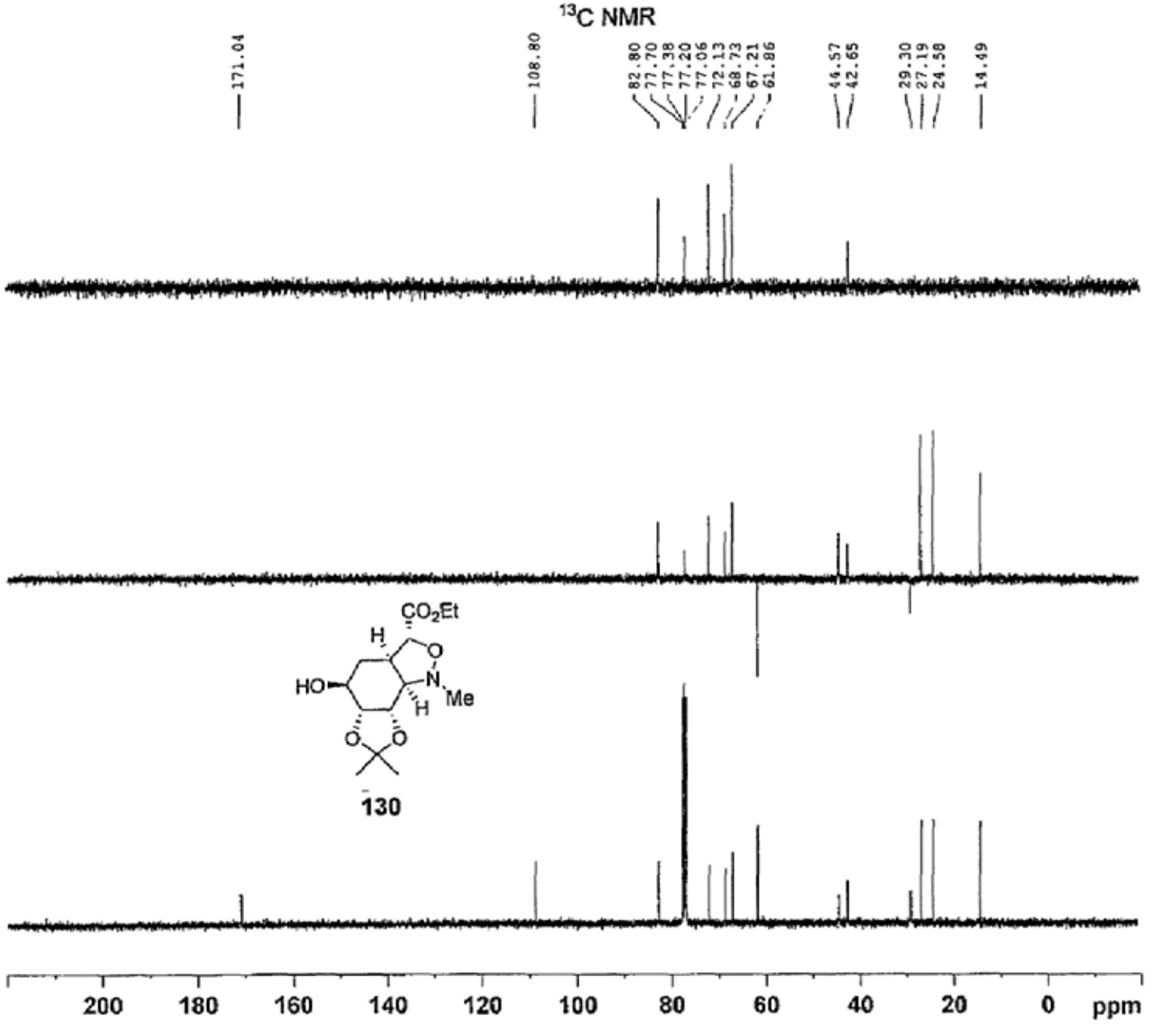
F2 - Processing parameters
SI 65536
SF 75 4677146 MHz
WDW EM
SSB 0
LB 3 00 Hz
GB 0
PC 1 40

1D NMR plot parameters
CX 23 00 cm
CY 10 44 cm
F1P 220 000 ppm
F1 16602 90 Hz
F2P -20 000 ppm
F2 -1509 35 Hz
PPMCM 10 43478 ppm/cm
HZCM 787 48914 Hz/cm


^{1}H NMR
130
ppm

^{1}H NMR (Solvent: $CDCl_3$-D_2O)

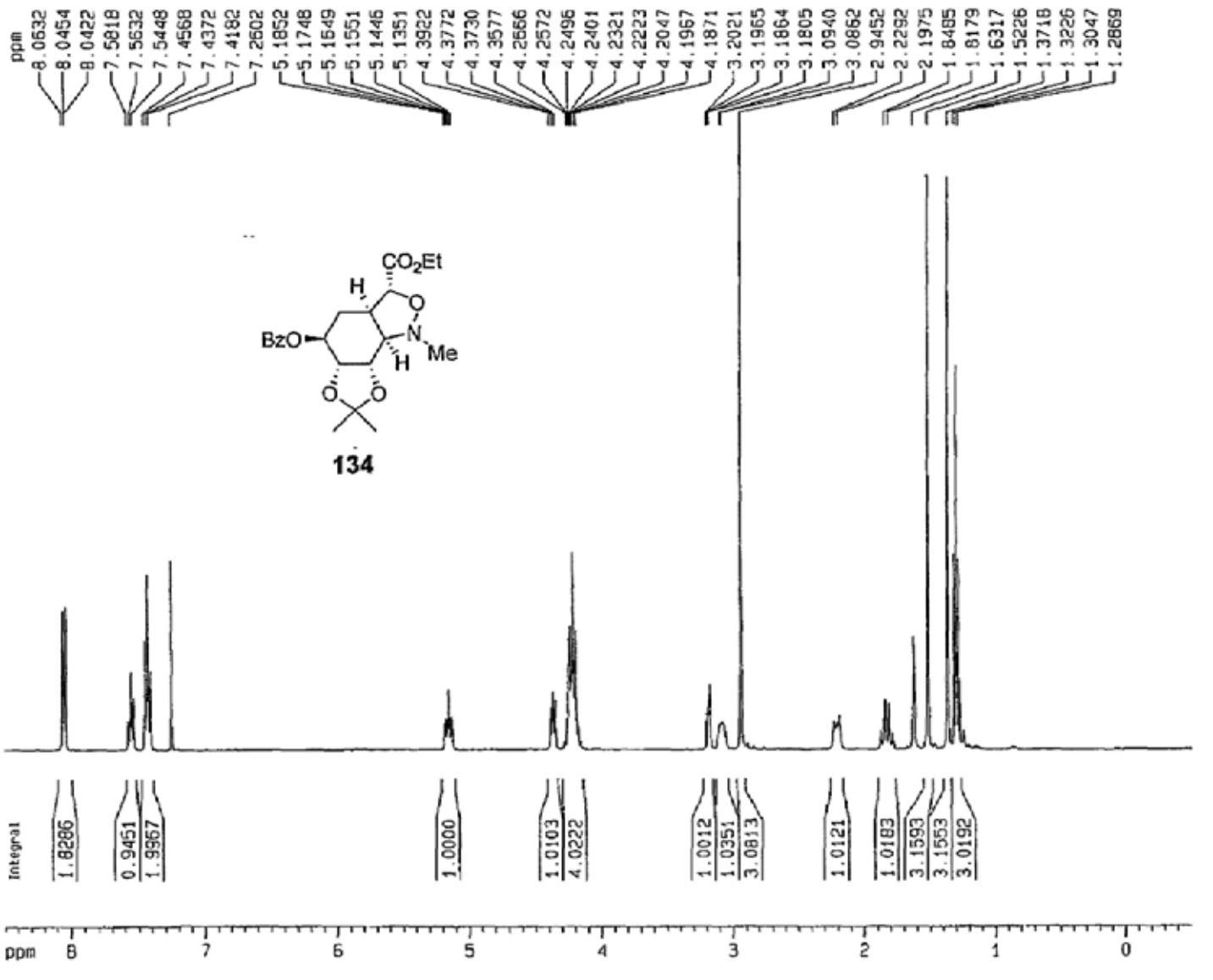




130

NAME	skh53carbon
EXPNO	1
PROCNO	1
Date_	20100826
Time	11.20
INSTRUM	spect
PROBHD	5 mm PABBI 1H/
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	270
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	673.2 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	14.50 usec
PL1	-4.00 dB
PL1W	90.22689819 W
SFO1	100.6228298 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	-2.00 dB
PL12	18.60 dB
PL13	18.80 dB
PL2W	13.17734718 W
PL12W	0.10960442 W
PL13W	0.10960442 W
SFO2	400.1316005 MHz
SI	32768
SF	100.6127346 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

^{1}H NMR



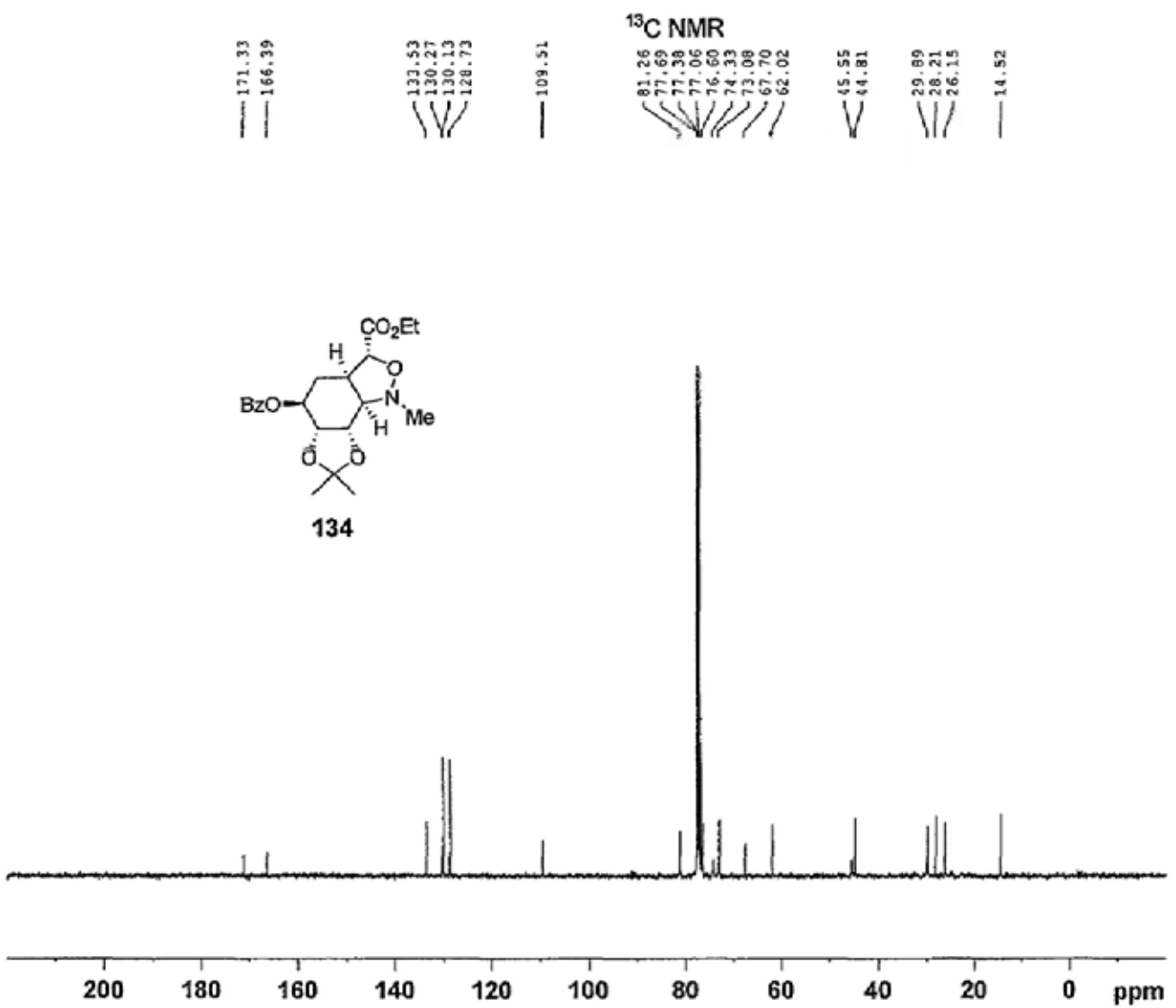

```
Current Data Parameters
NAME                  skh78b
EXPNO                      1
PROCNO                     1

F2 - Acquisition Parameters
Date_              20080214
Time                  12.22
INSTRUM               spect
PROBHD   5 mm PADUL 13C
PULPROG                zg
TD                     65536
SOLVENT                CDCl3
NS                         8
DS                         0
SWH               10000.000 Hz
FIDRES                0.152588 Hz
AQ                3.2768500 sec
RG                      71.8
DW                   50.000 usec
DE                    6.50 usec
TE                   293.4 K
D1                1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                     14.10 usec
PL1                     0.00 dB
SFO1             400.1316005 MHz

F2 - Processing parameters
SI                     65536
SF                400.1300054 MHz
WDW                       EM
SSB                        0
LB                     0.30 Hz
GB                         0
PC                      1.00

1D NMR plot parameters
CX                    20.00 cm
CY                    10.91 cm
F1P                    6.500 ppm
F1                  3401.10 Hz
F2P                   -0.500 ppm
F2                  -200.06 Hz
PPMCM                 0.45000 ppm/cm
HZCM                180.05849 Hz/cm
```



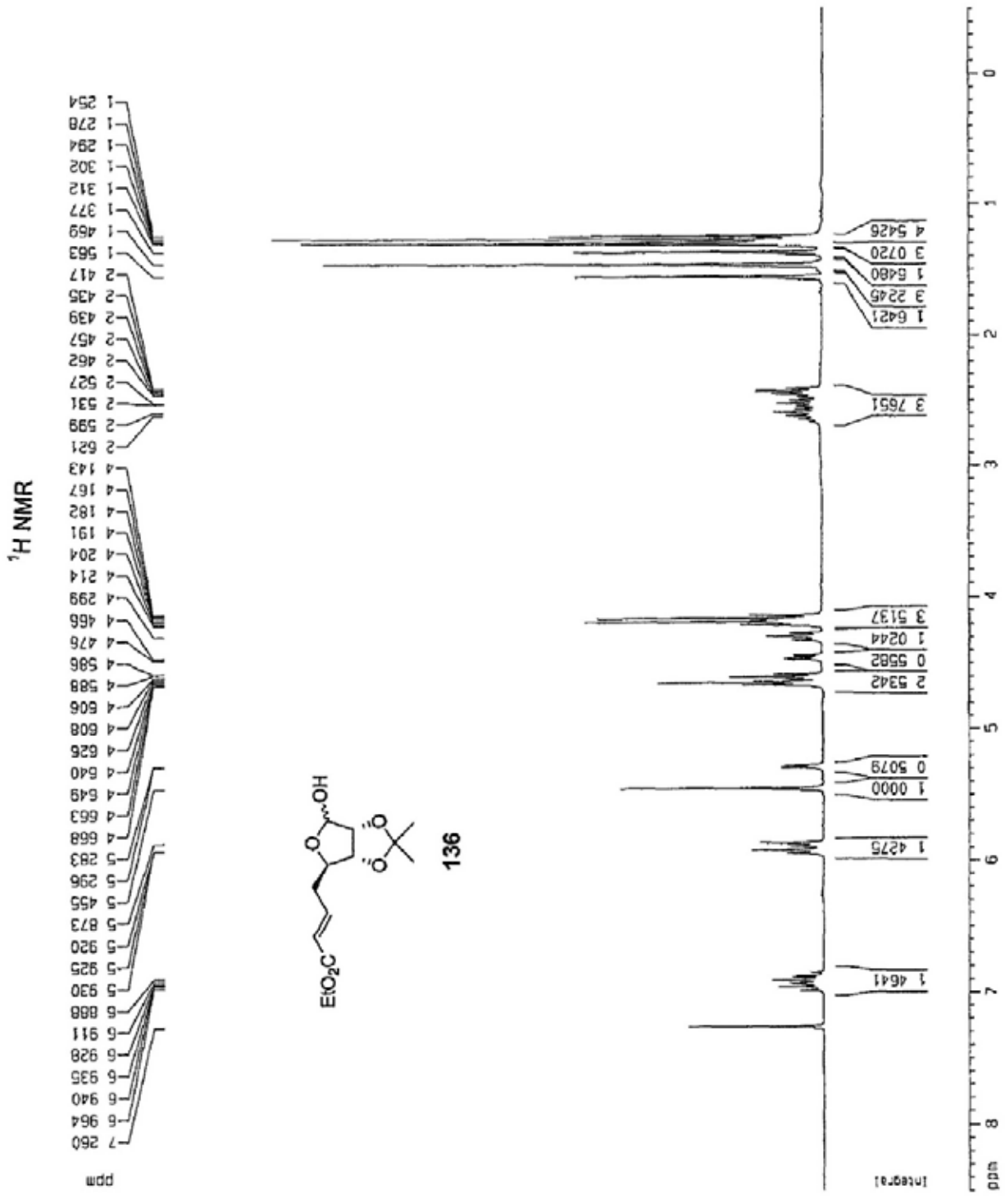

```
Current Data Parameters
NAME          skh78carbon
EXPNO                   1
PROCNO                  1

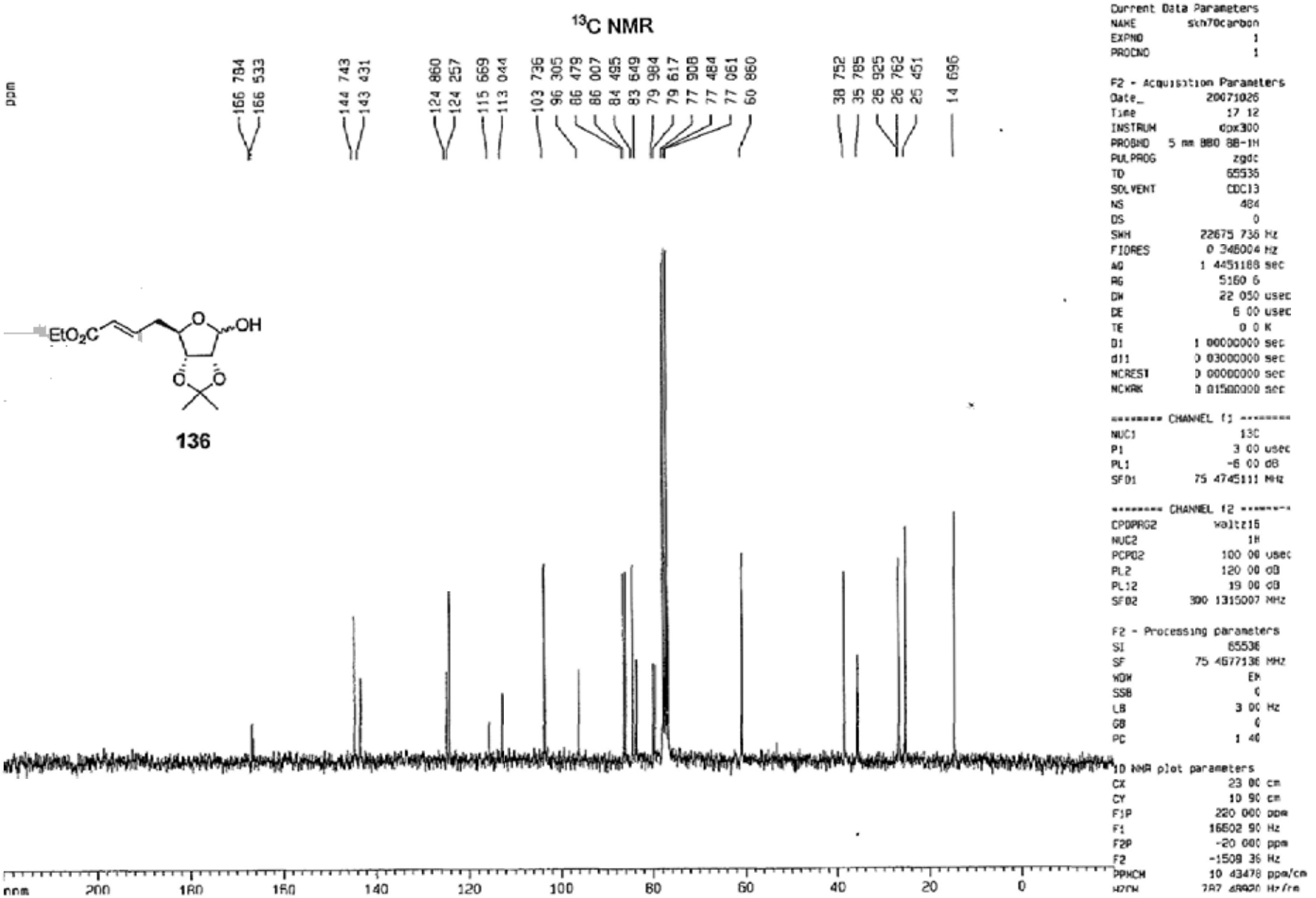
F2 - Acquisition Parameters
Date_            20080317
Time                15.33
INSTRUM             spect
PROBHD   5 mm PADUL 13C
PULPROG               zgdc
TD                  131072
SOLVENT              CDCl3
NS                     698
DS                       0
SWH             25252.525 Hz
FIDRES           0.192661 Hz
AQ               2.5952756 sec
RG                     203
DW                19.800 usec
DE                 6.50 usec
TE                 295.8 K
D1            1.00000000 sec
d11           0.03000000 sec
TD0                      1

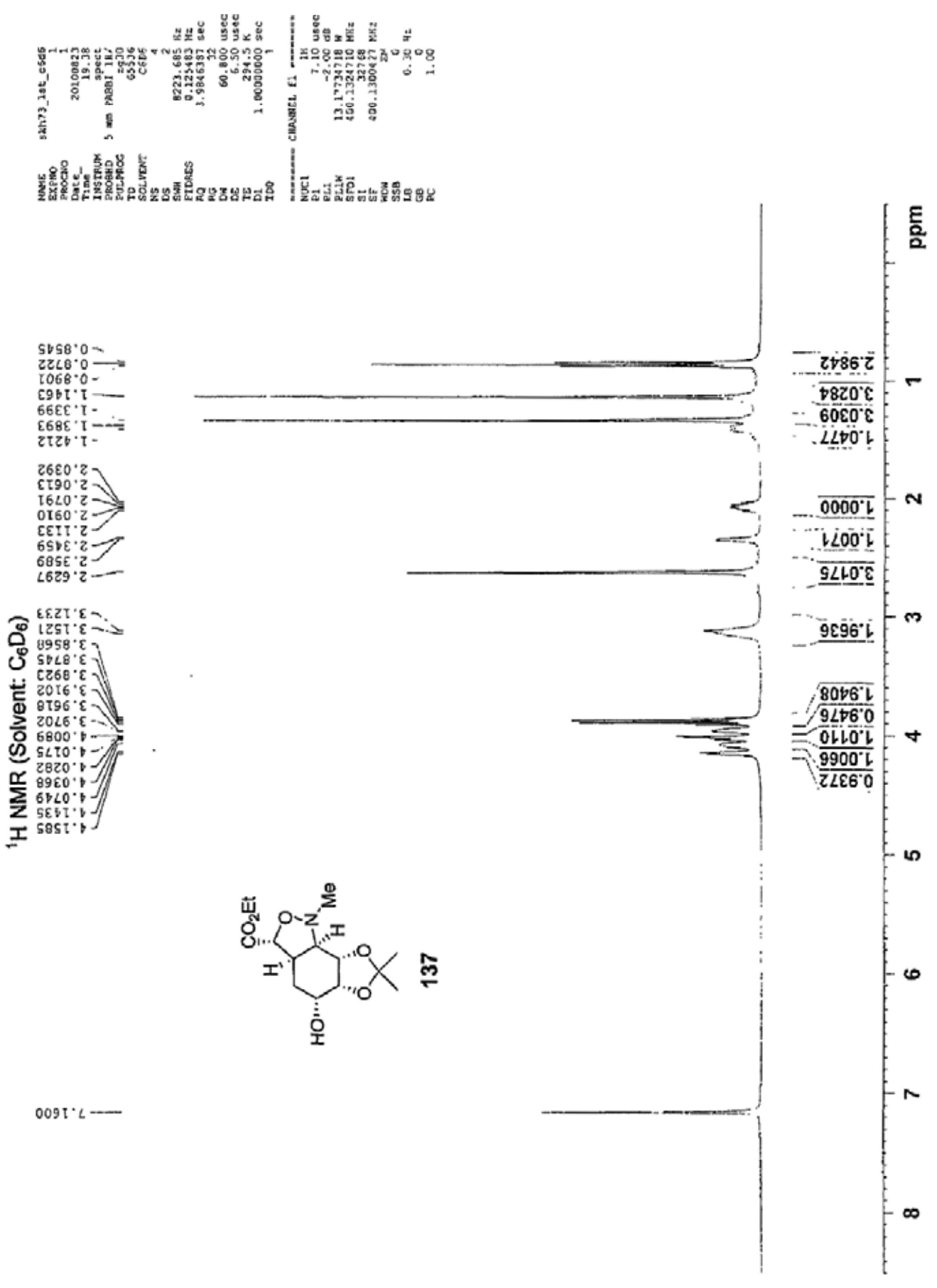
======== CHANNEL f1 ========
NUC1                   13C
P1                3.50 usec
PL1               -0.60 dB
SFO1         100.6227690 MHz

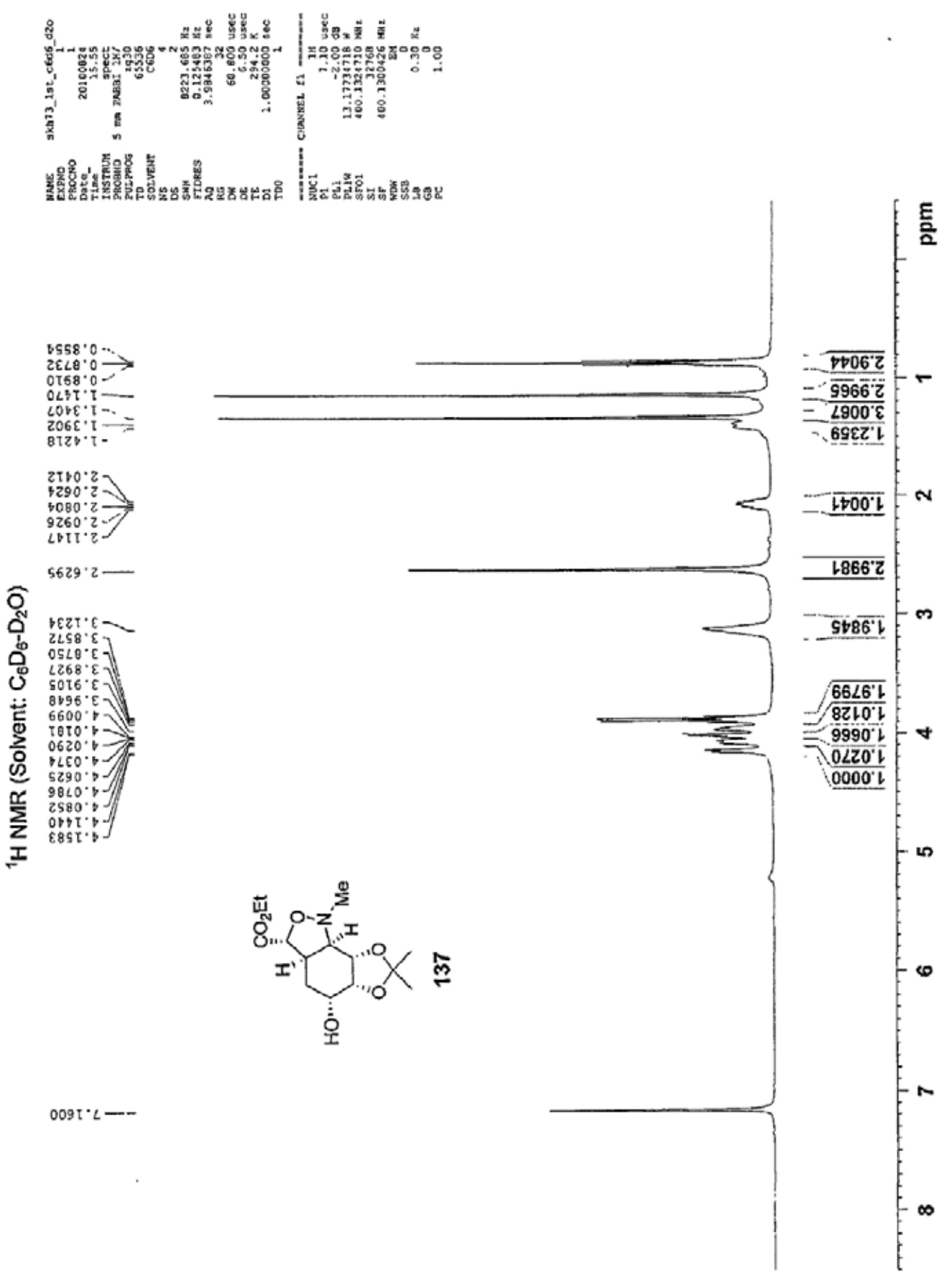
======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                   1H
PCPD2             90.00 usec
PL12              16.10 dB
PL2       0 dB
SFO2         400.1320007 MHz

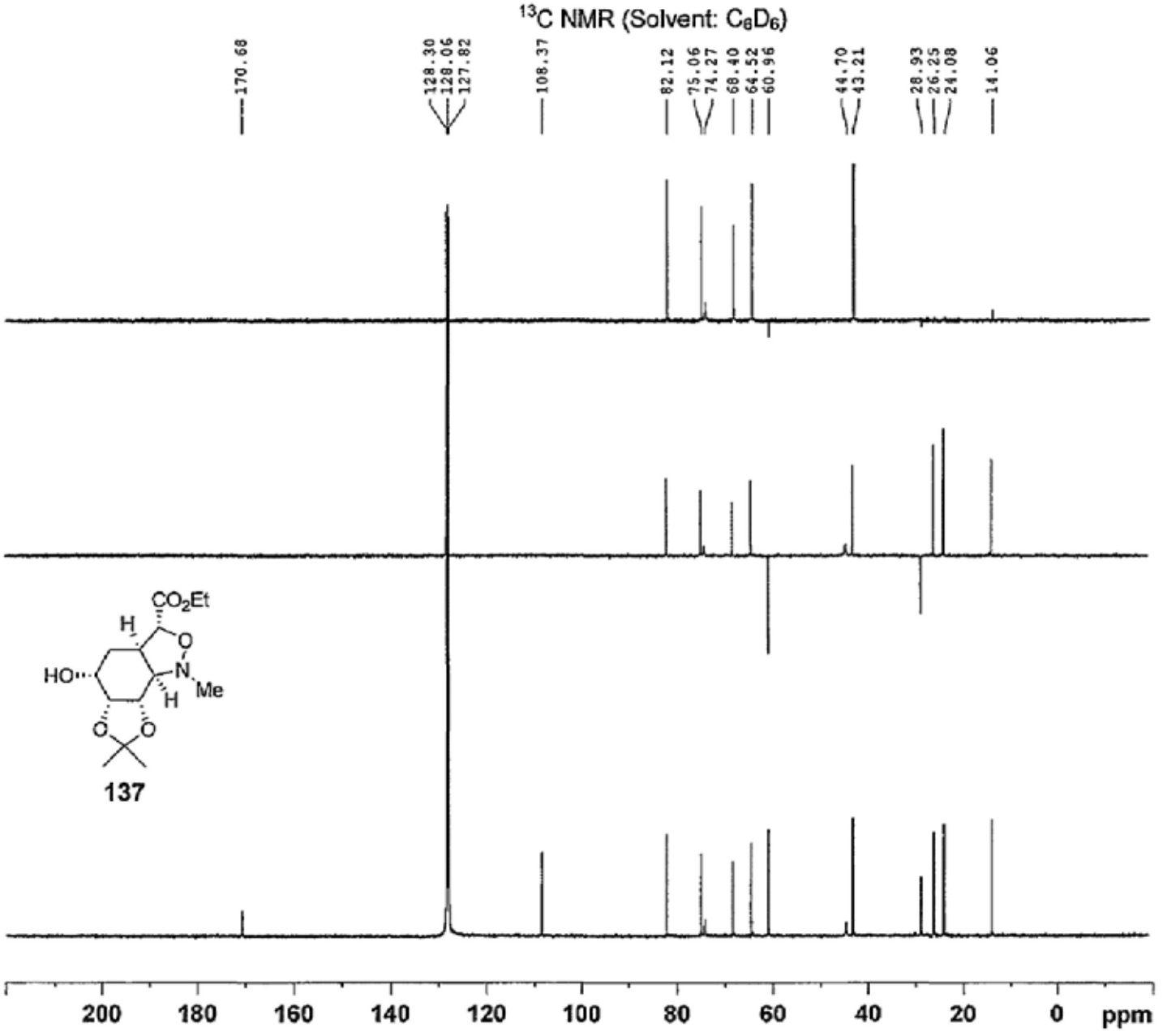
F2 - Processing parameters
SI                  131072
SF           100.6127336 MHz
WDW                    EM
SSB       0
LB                 3.00 Hz
GB        0
PC                 1.40
```


^{1}H NMR
136
EtO2C
OH
ppm
Integral


^{13}C NMR
ppm
166 784
166 533
144 743
143 431
124 860
124 257
115 669
113 044
103 736
96 305
86 479
86 007
84 495
83 649
79 984
79 617
77 908
77 484
77 061
60 860
38 752
35 785
26 925
26 762
25 451
14 696
EtO2C
OH
O
O
O
136
ppm
200
180
160
140
120
100
80
60
40
20
0
Current Data Parameters
NAME sch70carbon
EXPNO 1
PROCNO 1
F2 - Acquisition Parameters
Date_ 20071026
Time 17 12
INSTRUM dpx300
PROBHD 5 mm BBO BB-1H
PULPROG zgdc
TD 65536
SOLVENT CDCl3
NS 484
DS 0
SWH 22675 736 Hz
FIDRES 0 346004 Hz
AQ 1 4451188 sec
RG 5160 6
DW 22 050 usec
DE 6 00 usec
TE 0 0 K
D1 1 00000000 sec
d11 0 03000000 sec
MCREST 0 00000000 sec
MCWRK 0 01500000 sec
======== CHANNEL f1 ========
NUC1 13C
P1 3 00 usec
PL1 -6 00 dB
SFO1 75 4745111 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 100 00 usec
PL2 120 00 dB
PL12 19 00 dB
SFO2 300 1315007 MHz
F2 - Processing parameters
SI 65536
SF 75 4677136 MHz
WDW EM
SSB 0
LB 3 00 Hz
GB 0
PC 1 40
1D NMR plot parameters
CX 23 00 cm
CY 10 90 cm
F1P 220 000 ppm
F1 16602 90 Hz
F2P -20 000 ppm
F2 -1509 36 Hz
PPMCM 10 43478 ppm/cm
HZCM 787 48828 Hz/cm

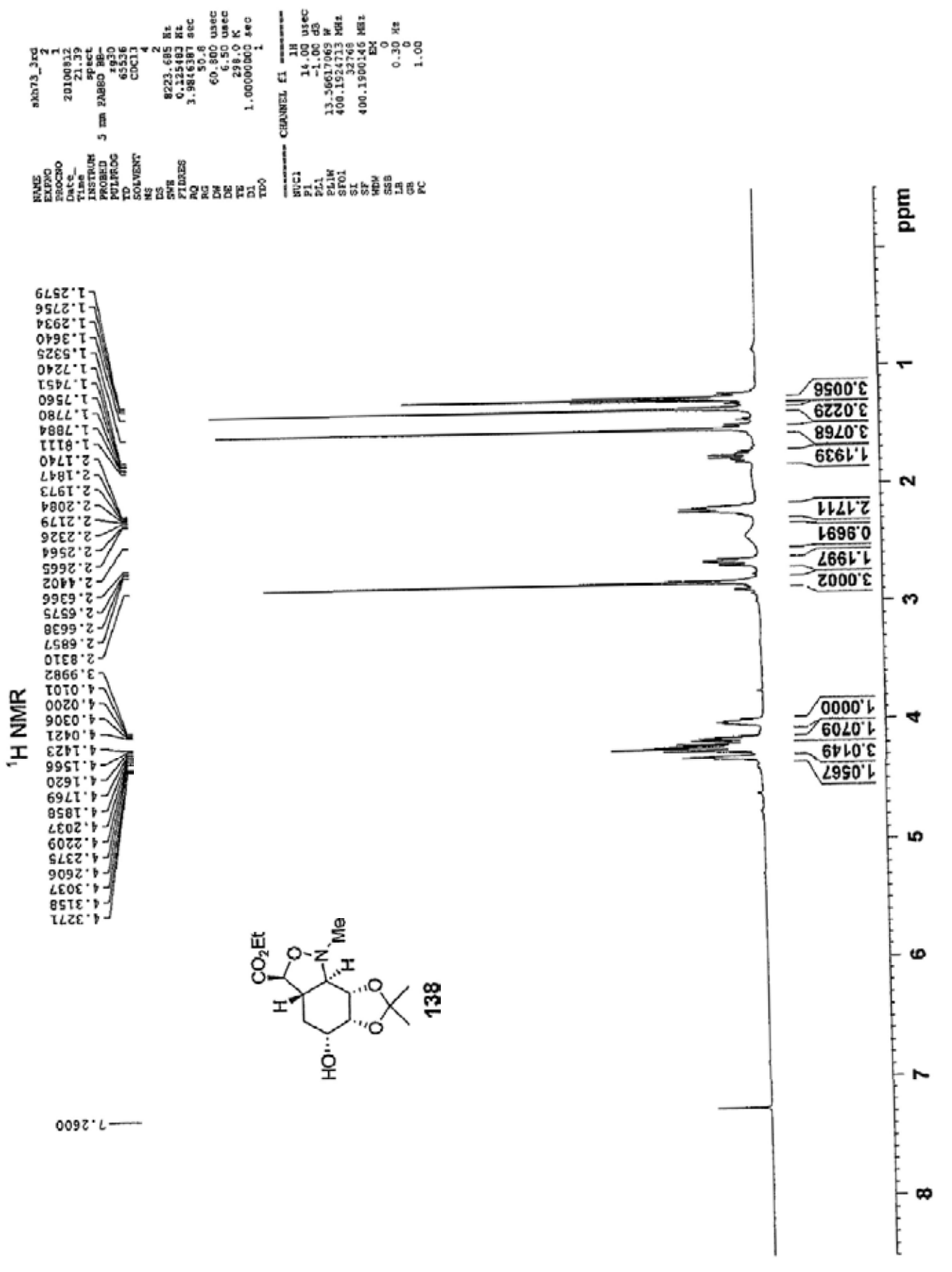

^{1}H NMR (Solvent: C_6D_6)
CO2Et
Me
H
HO
137
ppm

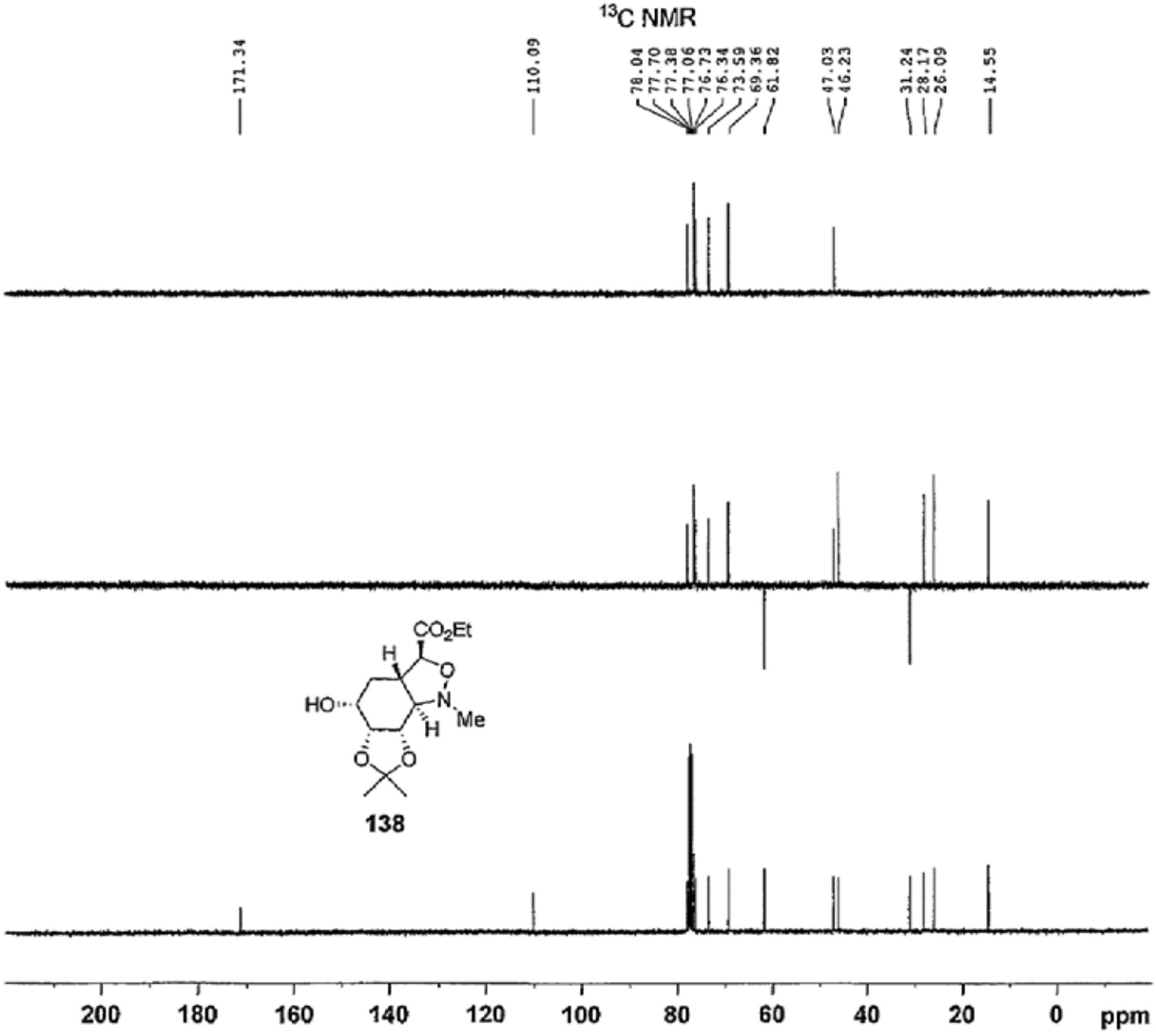

^{1}H NMR (Solvent: C_6D_6-D_2O)
137
ppm



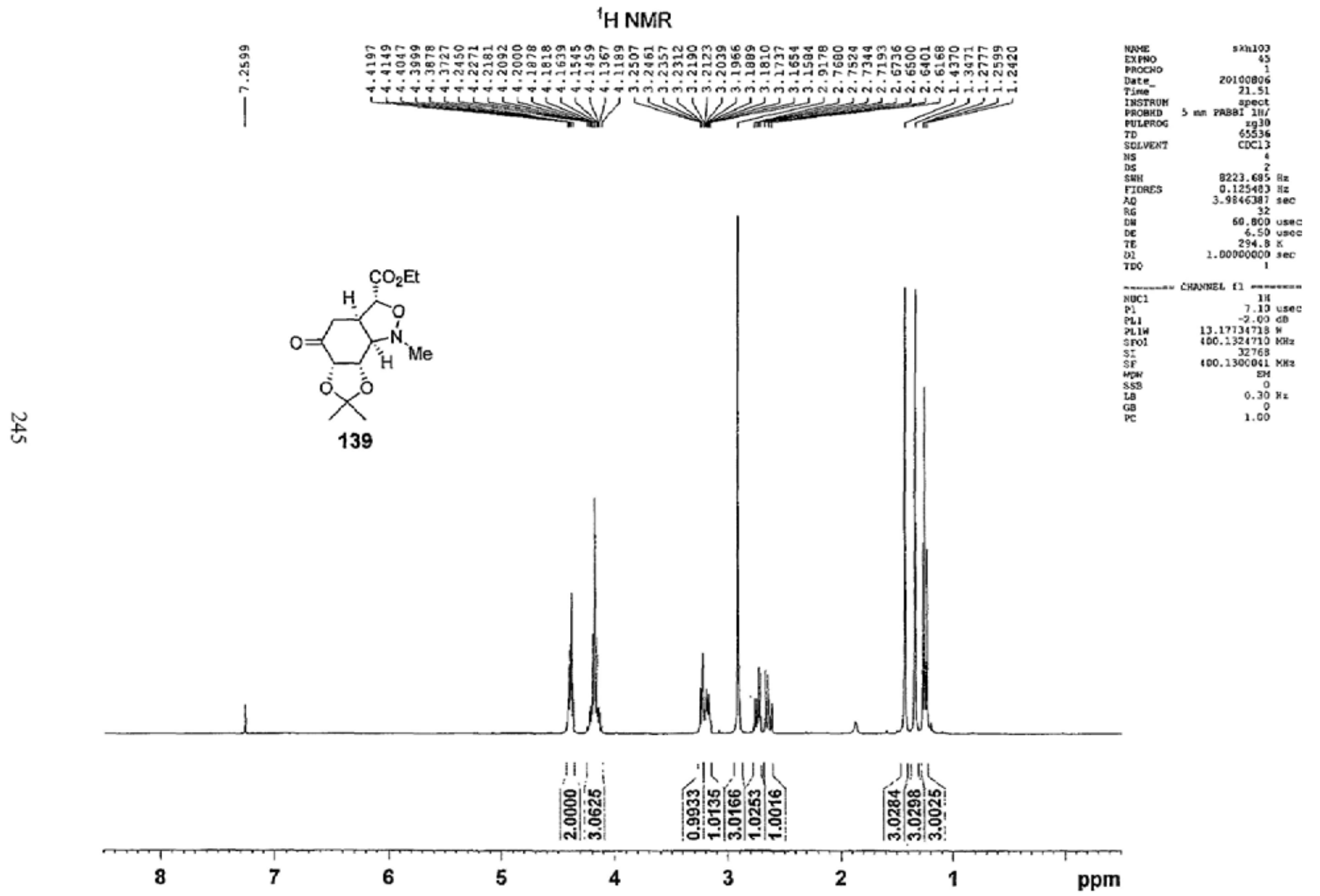
137

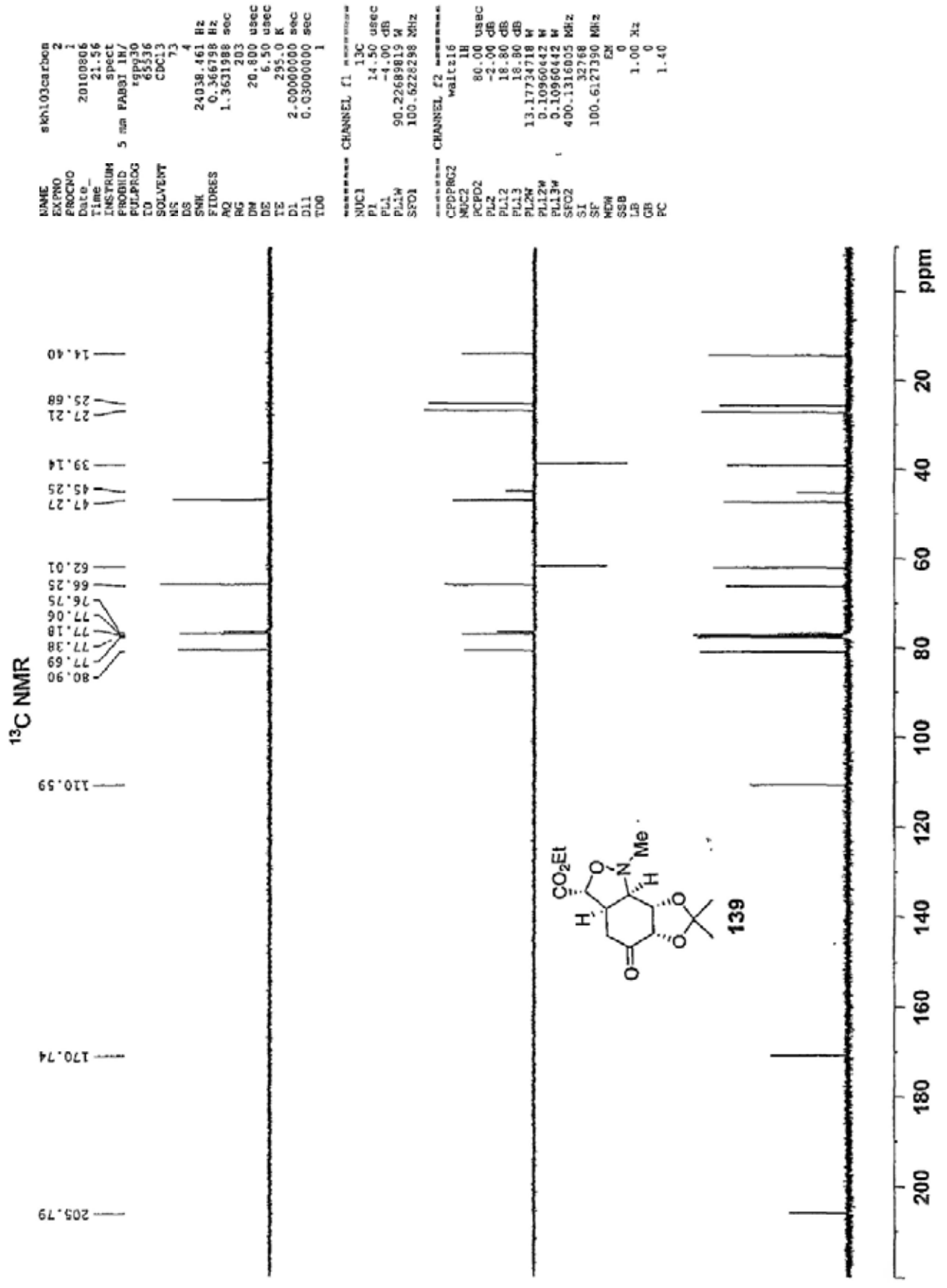
NAME	skh73_1st_carbon
EXPNO	1
PROCNO	1
Date_	20100825
Time	14.36
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	C6D6
NS	293
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	298.6 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.90 usec
PL1	-2.00 dB
PL1W	55.33689499 W
SFO1	100.6379183 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	90.00 usec
PL2	-1.00 dB
PL12	15.16 dB
PL13	18.62 dB
PL2W	13.56617069 W
PL12W	0.32844096 W
PL13W	0.14806664 W
SFO2	400.1916008 MHz
SI	32768
SF	100.6278192 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40


^{1}H NMR
ppm
CO$_2$Et
Me
HO
138

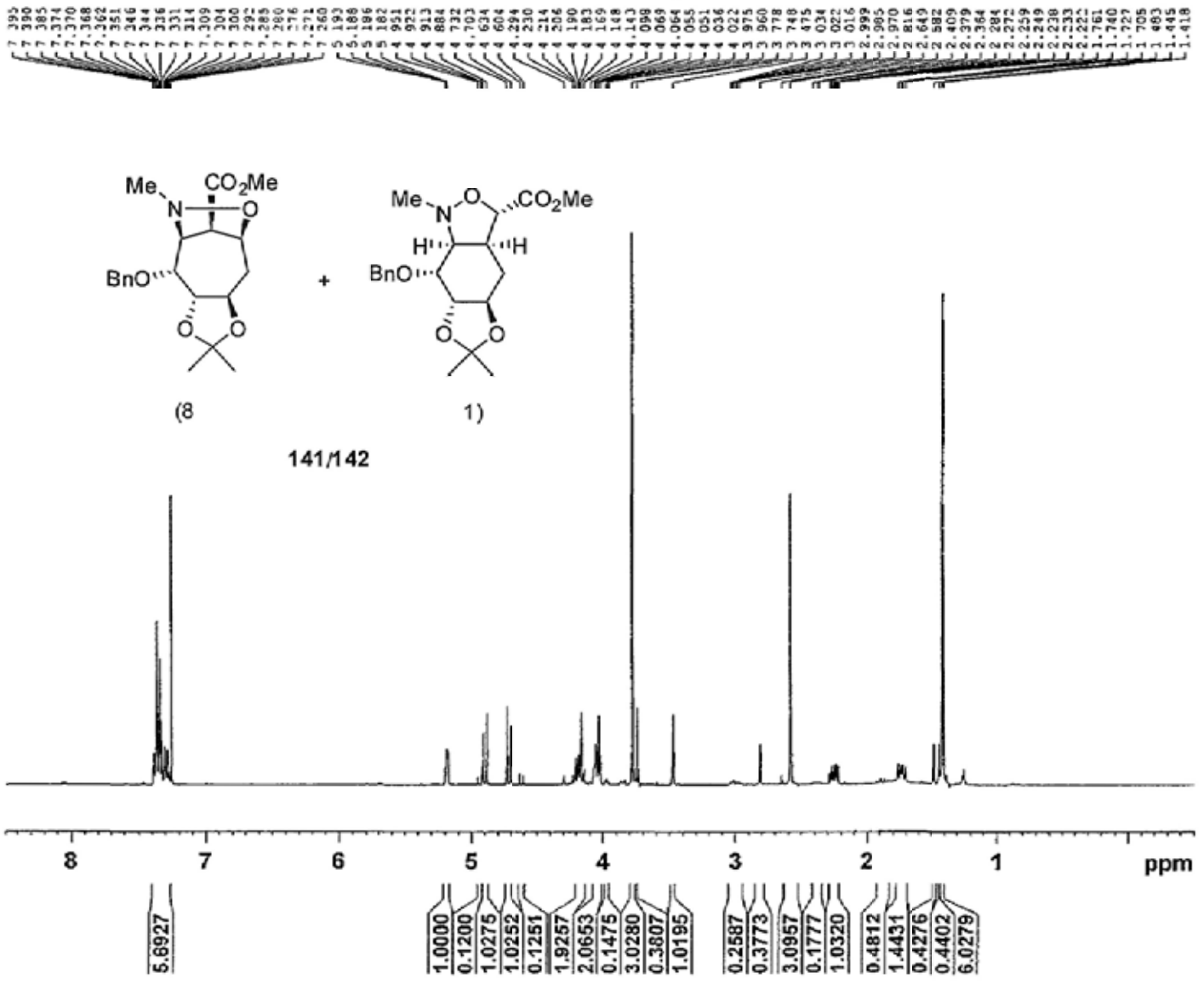


NAME	skh73_3rd_carbon
EXPNO	1
PROCNO	1
Date_	20100812
Time	21.45
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	161
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	298.6 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.90 usec
PL1	-2.00 dB
PL1W	55.33689499 W
SFO1	100.6379183 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	90.00 usec
PL2	-1.00 dB
PL12	15.16 dB
PL13	18.62 dB
PL2W	13.56617069 W
PL12W	0.32844096 W
PL13W	0.14806664 W
SFO2	400.1916008 MHz
SI	32768
SF	100.6278234 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40


^{1}H NMR
7.2599
4.4197
4.4149
4.4047
4.3999
4.3878
4.3727
4.2450
4.2271
4.2181
4.2092
4.2000
4.1878
4.1818
4.1639
4.1545
4.1459
4.1367
4.1189
3.2507
3.2461
3.2357
3.2312
3.2190
3.2123
3.2039
3.1966
3.1889
3.1810
3.1737
3.1654
3.1584
2.9178
2.7680
2.7524
2.7344
2.7193
2.6736
2.6500
2.6401
2.6168
1.4370
1.3471
1.2777
1.2599
1.2420
NAME sKh103
EXPNO 45
PROCNO 1
Date_ 20100806
Time 21.51
INSTRUM spect
PROBHD 5 mm PABBI 1H/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 4
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 32
DW 60.800 usec
DE 6.50 usec
TE 294.8 K
D1 1.00000000 sec
TD0 1
CHANNEL f1
NUC1 1H
P1 7.10 usec
PL1 -2.00 dB
PL1W 13.17734718 W
SFO1 400.1324710 MHz
SI 32768
SF 400.1300041 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
CO2Et
H
O
N
Me
H
O
O
O
O
139
2.0000
3.0625
0.9933
1.0135
3.0166
1.0253
1.0016
3.0284
3.0298
3.0025
8
7
6
5
4
3
2
1
ppm


^{13}C NMR
205.79
170.74
110.59
80.90
77.69
77.38
77.18
77.06
76.75
66.25
62.01
47.27
45.25
39.14
27.21
25.68
14.40
ppm
20
40
60
80
100
120
140
160
180
200
CO2Et
Me
139

^{1}H NMR

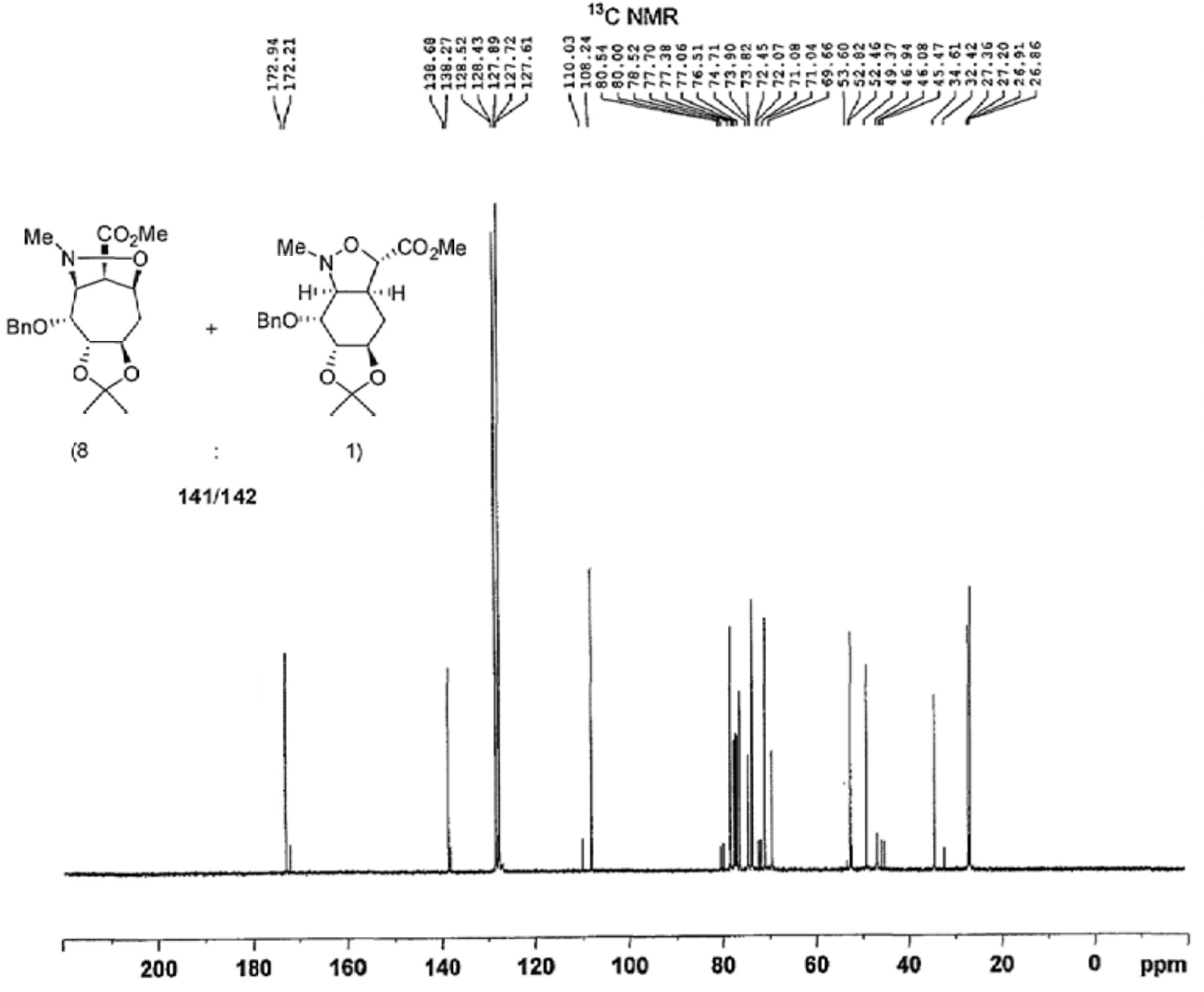



```
Current Data Parameters
NAME                  sbr09
EXPNO                     1
PROCNO                    1

F2 - Acquisition Parameters
Date_              20090514
Time                 17.39
INSTRUM              spect
PROBHD    5 mm PABBI 1H/
PULPROG               zg30
TD                   65536
SOLVENT              CDCl3
NS                       8
DS                       2
SWH               8223.685 Hz
FIDRES            0.125483 Hz
AQ                3.9846387 sec
RG                     144
DW                  60.800 usec
DE                   6.50 usec
TE                  294.3 K
D1                1.00000000 sec
TD0                      1

======== CHANNEL f1 ========
NUC1                    1H
P1                   7.10 usec
PL1                  -2.00 dB
PL1W          -1.#IND0000 W
SFO1          400.1324710 MHz

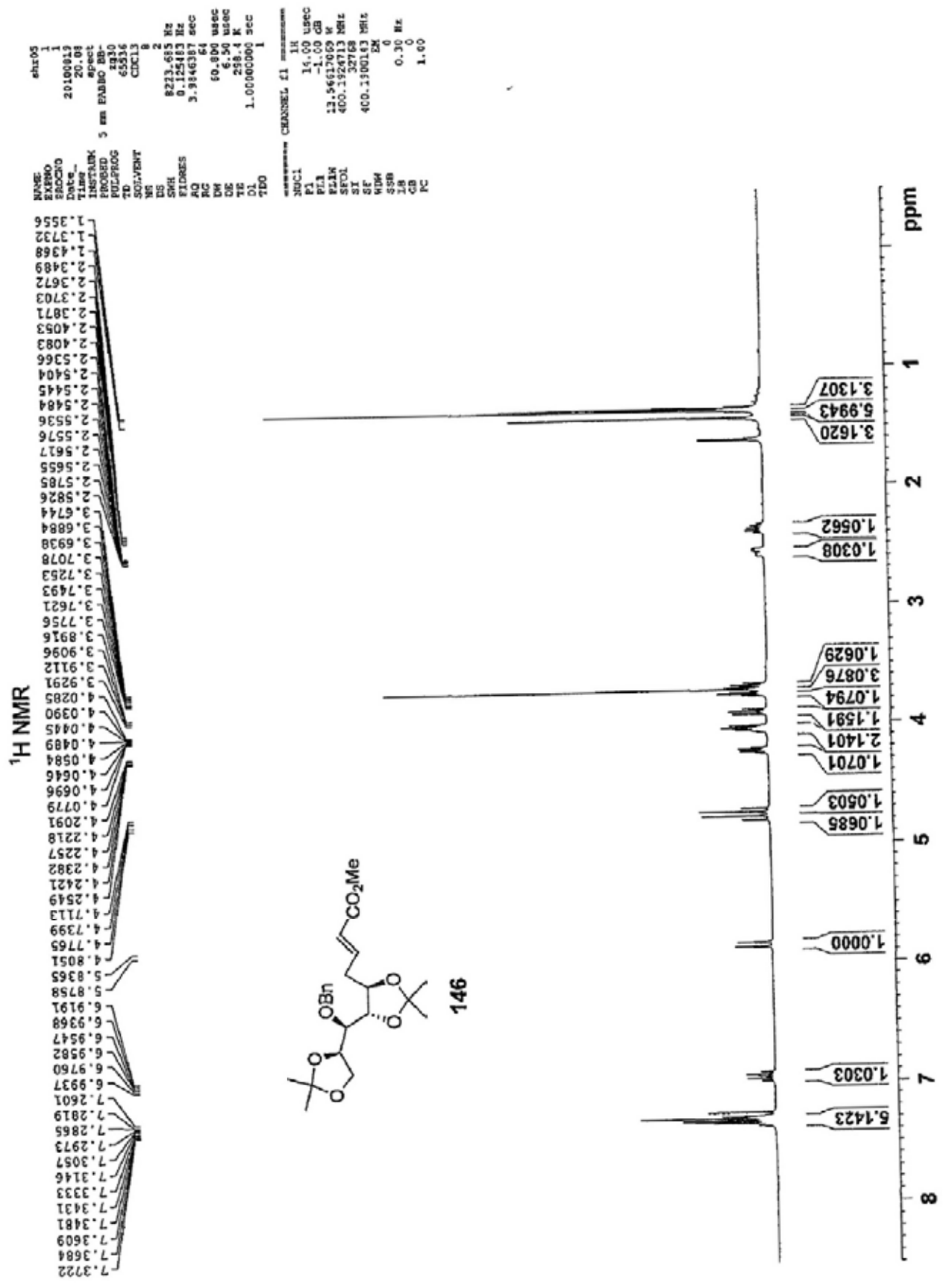
F2 - Processing parameters
SI                   32768
SF            400.1300053 MHz
WDM                     EM
SSB       0
LB                   0.30 Hz
GB        0
PC                   1.00
```

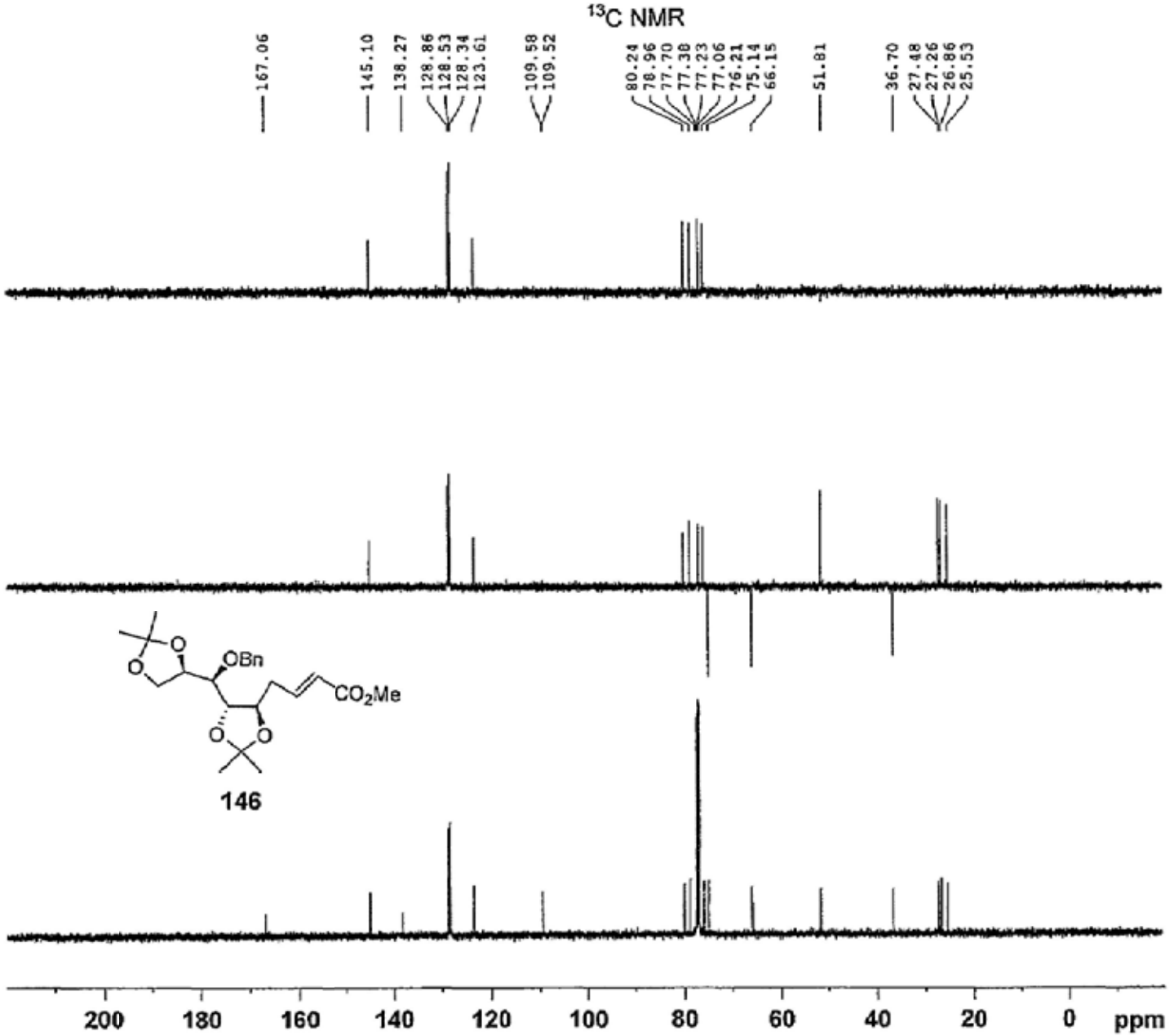



```
NAME          shx09_10carbon
EXPNO                      1
PROCNO                     1
Date_               20090610
Time                   16.00
INSTRUM                spect
PROBHD  5 mm PABBI 1H/
PULPROG                zgpg30
TD                      65536
SOLVENT                CDCl3
NS                       236
DS                         4
SWH                24038.461 Hz
FIDRES             0.366798 Hz
AQ                 1.3631988 sec
RG                       203
DW                  20.800 usec
DE                   6.50 usec
TE                   294.5 K
D1                 2.00000000 sec
D11                0.03000000 sec
TD0                        1

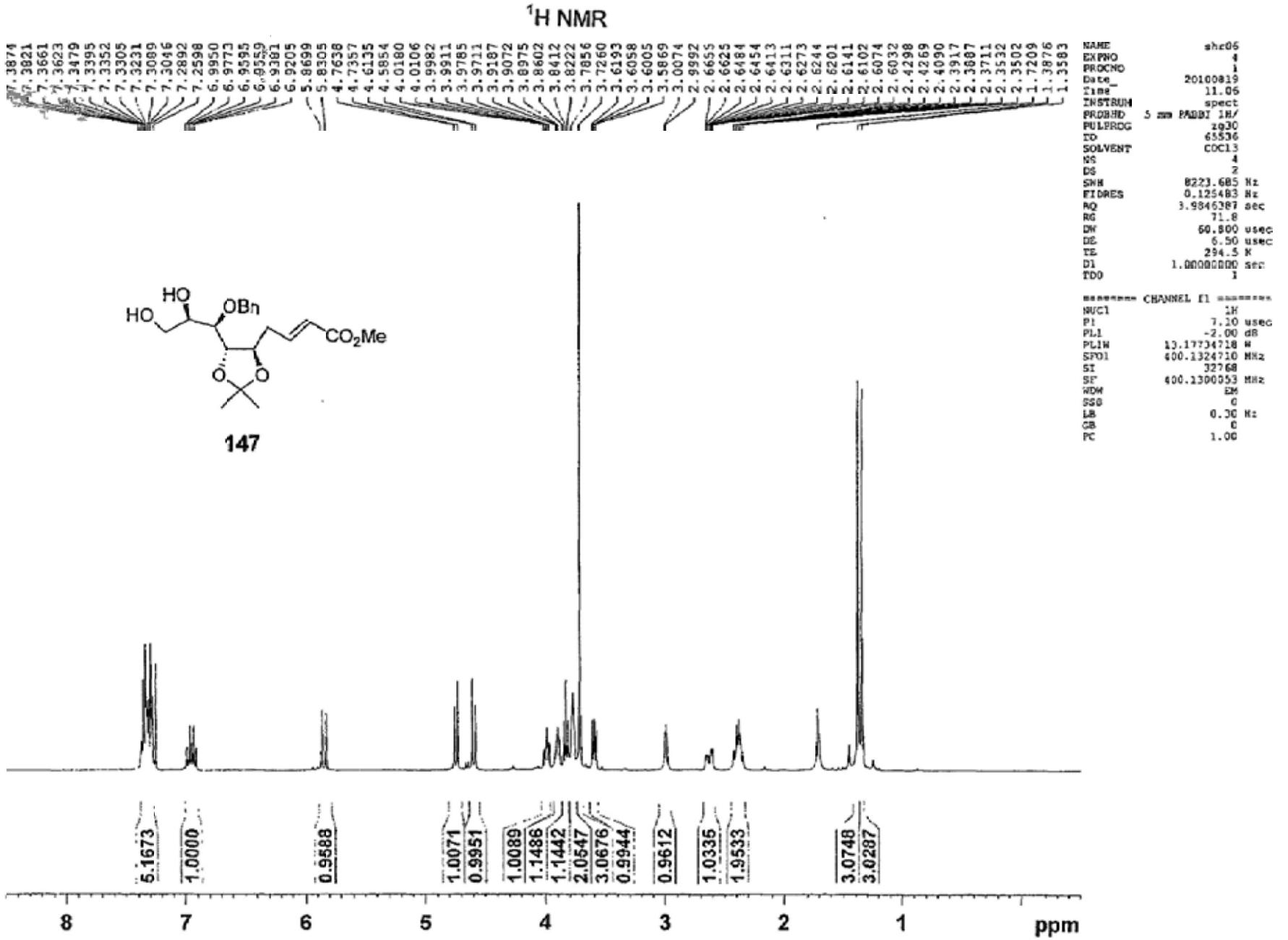
======== CHANNEL f1 ========
NUC1                     13C
P1                   14.50 usec
PL1                  -4.00 dB
PL1W            90.22689819 W
SFO1            100.6228298 MHz

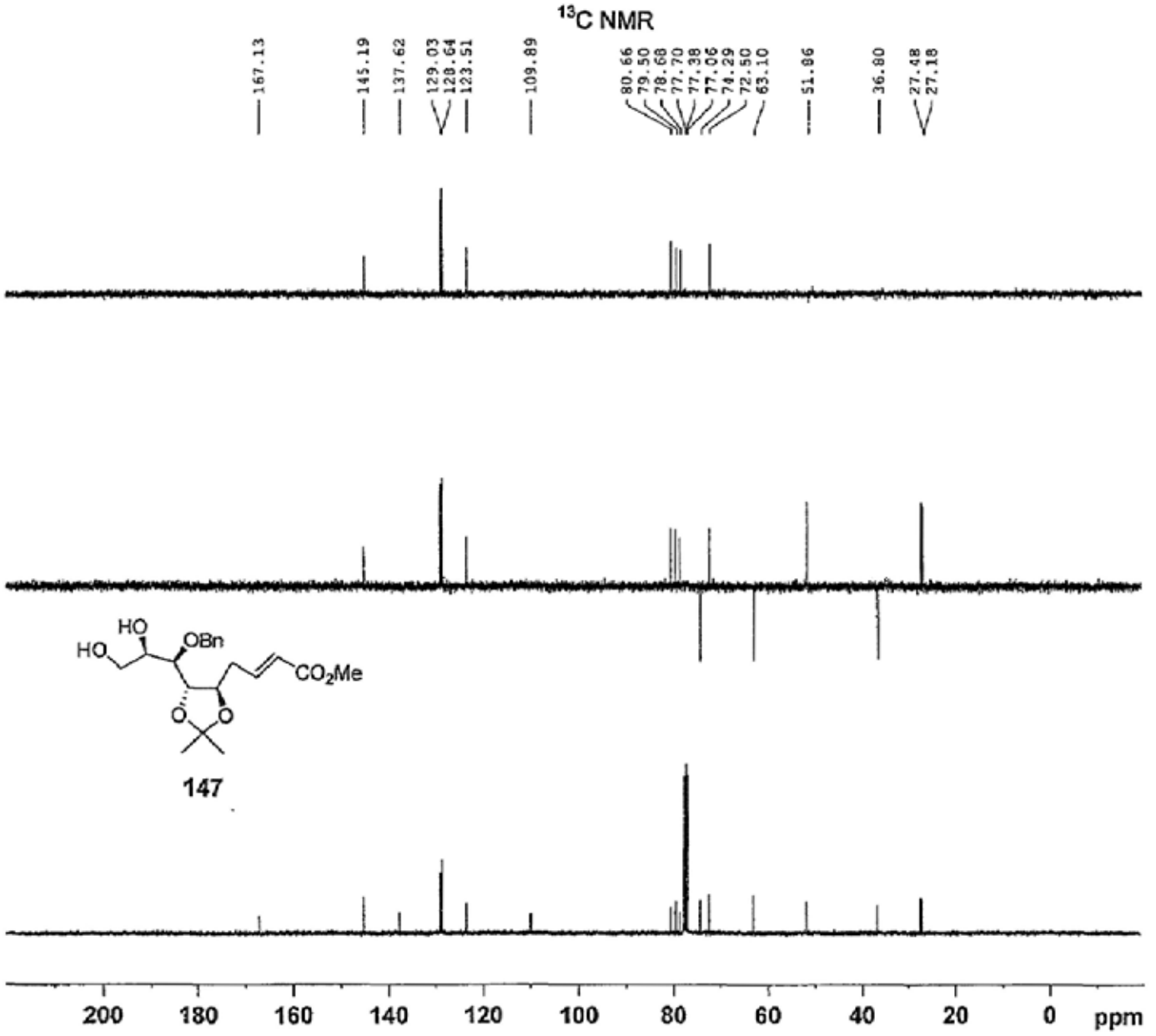
======== CHANNEL f2 ========
CPDPRG2              waltz16
NUC2                     1H
PCPD2                80.00 usec
PL2                  -2.00 dB
PL12                 18.80 dB
PL13                 18.80 dB
PL2W            13.17734718 W
PL12W            0.10960442 W
PL13W            0.10960442 W
SFO2            400.1316005 MHz
SI                     32768
SF              100.6127551 MHz
WDW                    EM
SSB                     0
LB                   1.00 Hz
GB                      0
PC                   1.40
```


1H NMR
146
OBn
CO2Me
ppm
1.0000
1.0303
5.1423
1.0685
1.0503
1.0701
2.1401
1.1591
1.0794
3.0876
1.0629
1.0308
1.0562
3.1620
5.9943
3.1307

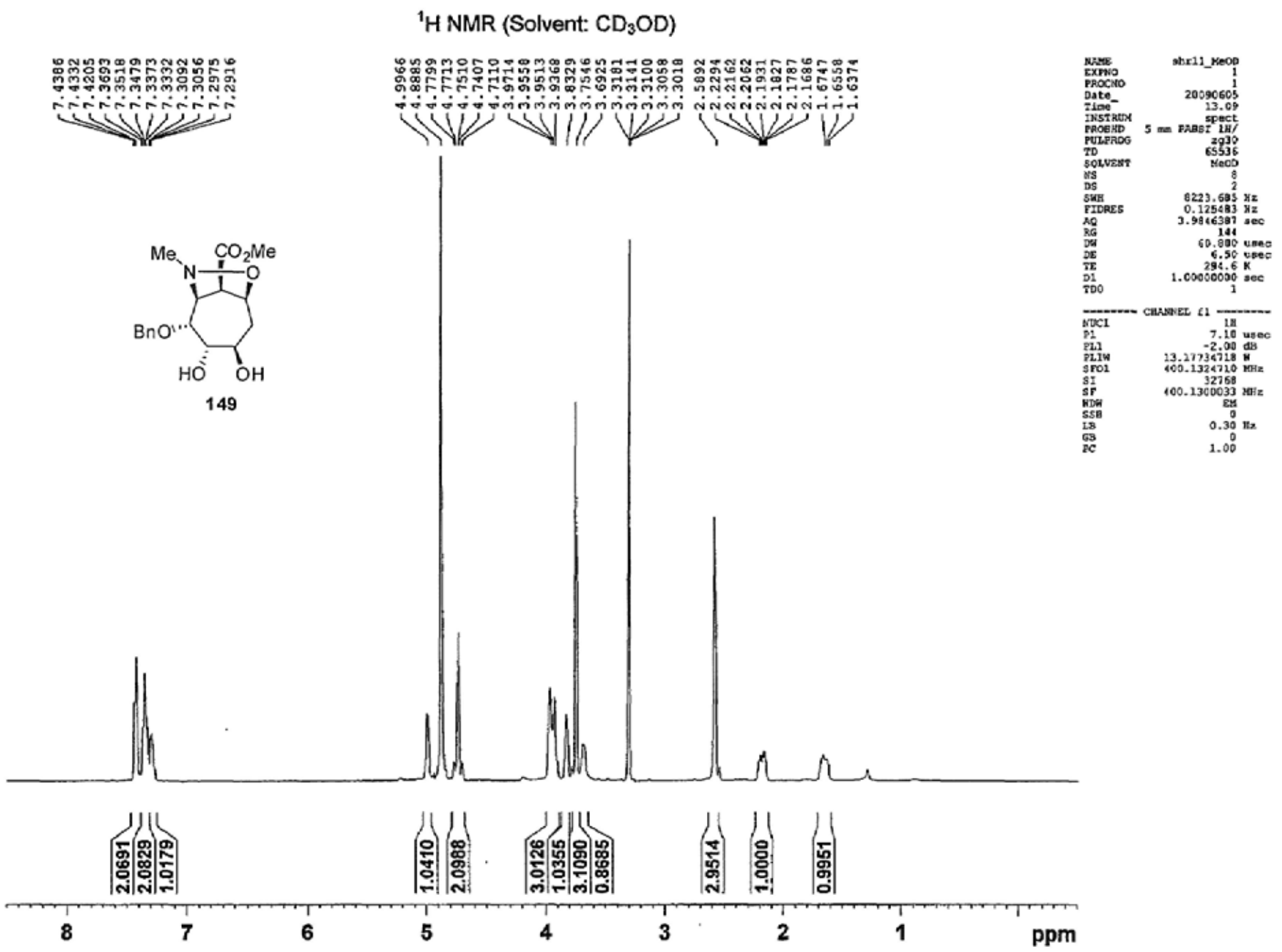


NAME	shr05carbon
EXPNO	1
PROCNO	1
Date_	20100819
Time	20.15
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	91
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	181
DW	20.800 usec
DE	6.50 usec
TE	299.2 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.90 usec
PL1	-2.00 dB
PL1W	55.33689499 W
SFO1	100.6379183 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	90.00 usec
PL2	-1.00 dB
PL12	15.16 dB
PL13	18.62 dB
PL2W	13.56617069 W
PL12W	0.32844096 W
PL13W	0.14806654 W
SFO2	400.1916008 MHz
SI	32768
SF	100.6278212 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

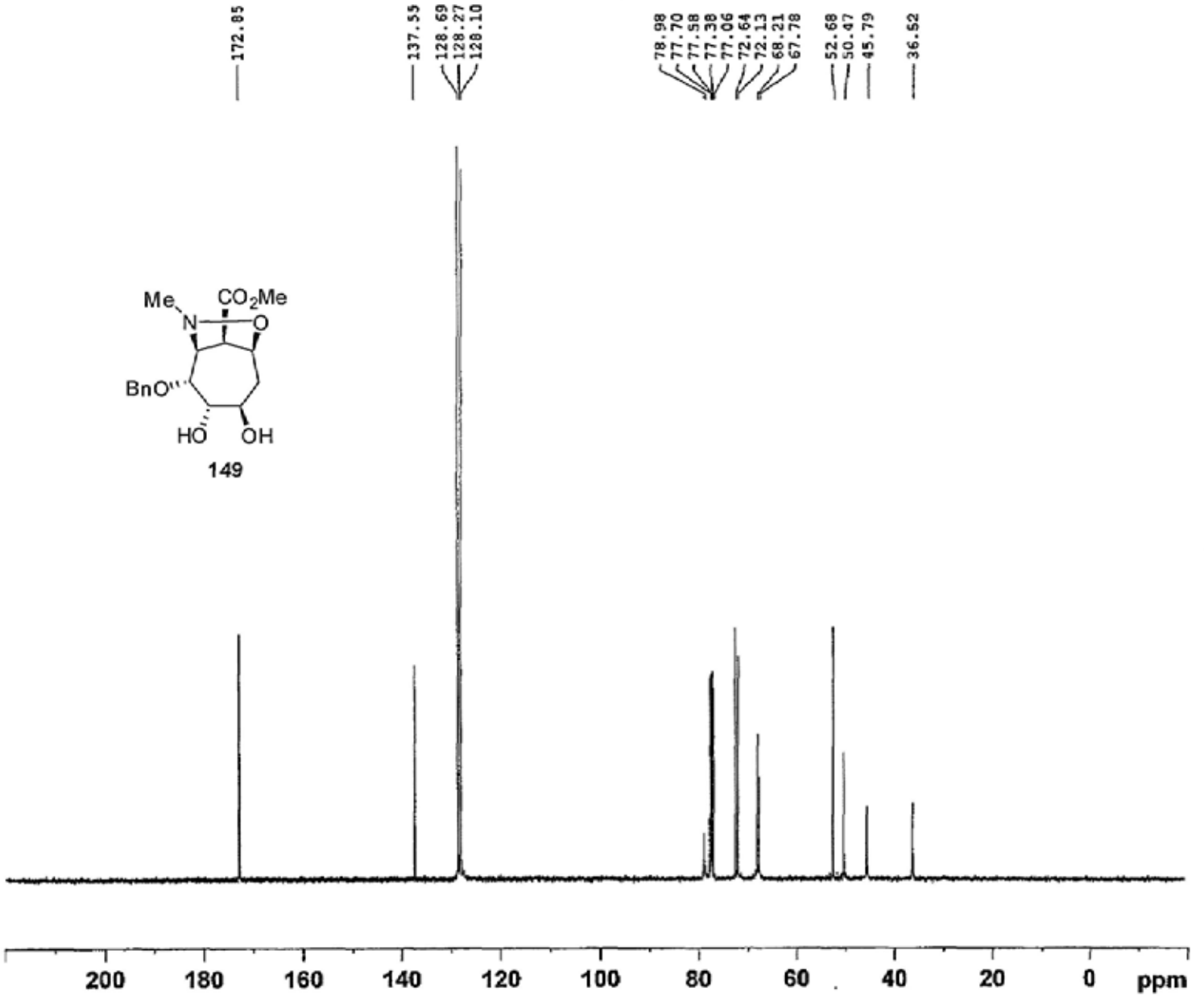

^{1}H NMR
HO
HO
OBn
CO$_2$Me
147
NAME shc05
EXPNO 4
PROCNO 1
Date_ 20100819
Time_ 11.06
INSTRUM spect
PROBHD 5 mm PABBI 1H/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 4
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 71.8
DW 60.800 usec
DE 6.50 usec
TE 294.5 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 7.10 usec
PL1 -2.00 dB
PL1W 13.17734718 W
SFO1 400.1324710 MHz
SI 32768
SF 400.1300053 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
5.1673
1.0000
0.9588
1.0071
0.9951
1.0089
1.1486
1.1442
2.0547
3.0676
0.9944
0.9612
1.0335
1.9533
3.0748
3.0287
8
7
6
5
4
3
2
1
ppm



NAME	shr06carbon
EXPNO	2
PROCNO	1
Date_	20090609
Time	13.41
INSTRUM	spect
PROBHD	5 mm PABBI 1H/
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	248
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	294.7 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
========	CHANNEL f1 ========
NUC1	13C
P1	14.50 usec
PL1	-4.00 dB
PL1W	90.22689819 W
SFO1	100.6228298 MHz
========	CHANNEL f2 ========
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	-2.00 dB
PL12	18.80 dB
PL13	18.80 dB
PL2W	13.17734718 W
PL12W	0.10960442 W
PL13W	0.10960442 W
SFO2	400.1316005 MHz
SI	32768
SF	100.6127346 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40


^{1}H NMR (Solvent: CD_3OD)
7.4386
7.4332
7.4205
7.3693
7.3518
7.3479
7.3373
7.3332
7.3092
7.3056
7.2975
7.2916
4.9966
4.8885
4.7799
4.7713
4.7510
4.7407
4.7110
3.9714
3.9558
3.9513
3.9368
3.8329
3.7546
3.6925
3.3181
3.3141
3.3100
3.3058
3.3018
2.5092
2.2294
2.2162
2.2062
2.1931
2.1827
2.1787
2.1686
1.6747
1.6558
1.6374
Me
N
CO_2Me
O
BnO
HO
OH
149
NAME shr11_MeOD
EXPNO 1
PROCNO 1
Date_ 20090605
Time 13.09
INSTRUM spect
PROBHD 5 mm PABBI 1H/
PULPRDG zg30
TD 65536
SOLVENT MeOD
NS 8
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 144
DW 60.880 usec
DE 6.50 usec
TE 294.6 K
D1 1.00000000 sec
TD0 1
CHANNEL f1
NUC1 1H
P1 7.10 usec
PL1 -2.00 dB
PLIW 13.17734718 W
SFO1 400.1324710 MHz
SI 32768
SF 400.1300033 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
2.0691
2.0829
1.0179
1.0410
2.0988
3.0126
1.0355
3.1090
0.8685
2.9514
1.0000
0.9951
8
7
6
5
4
3
2
1
ppm

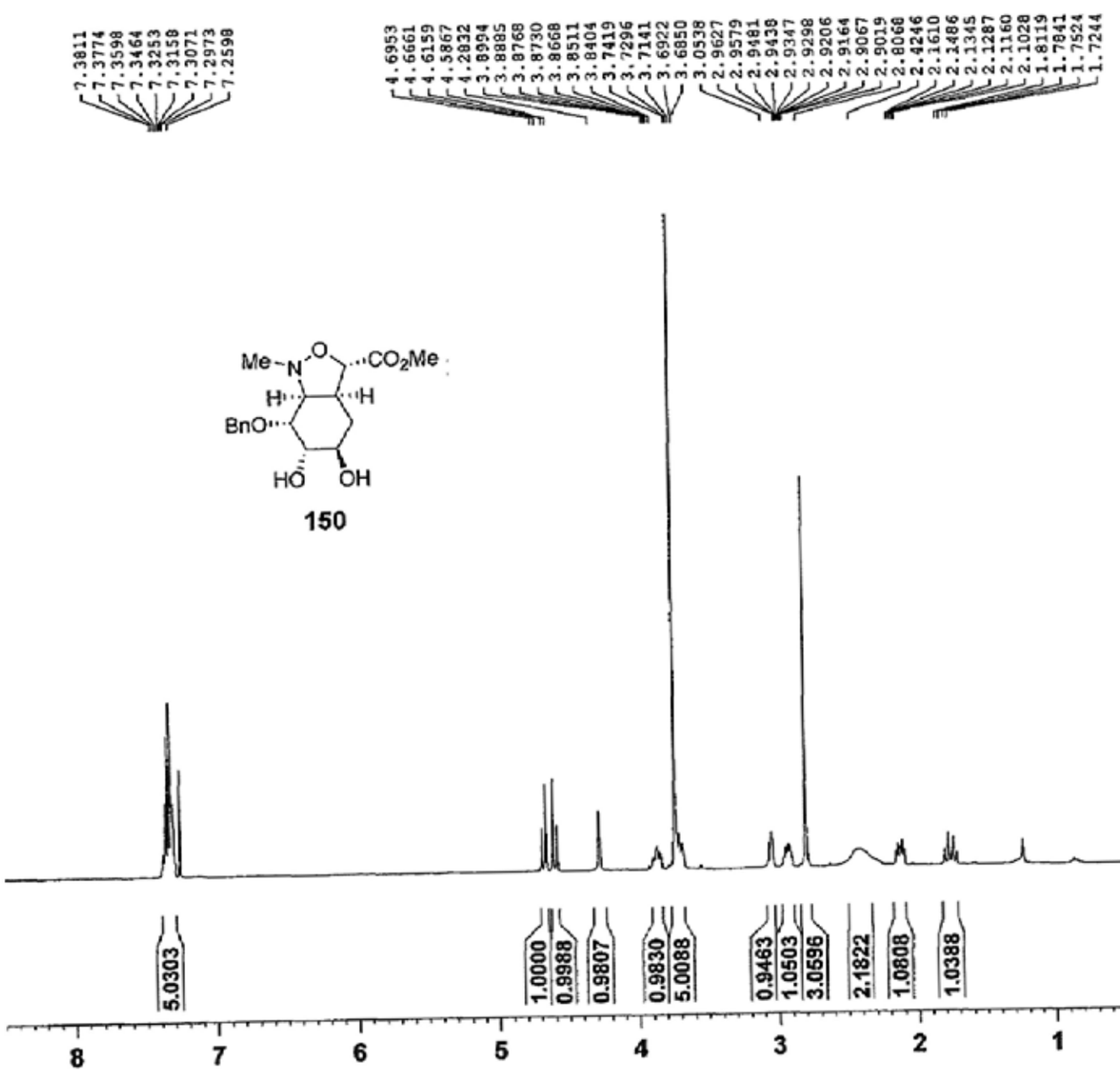
^{13}C NMR



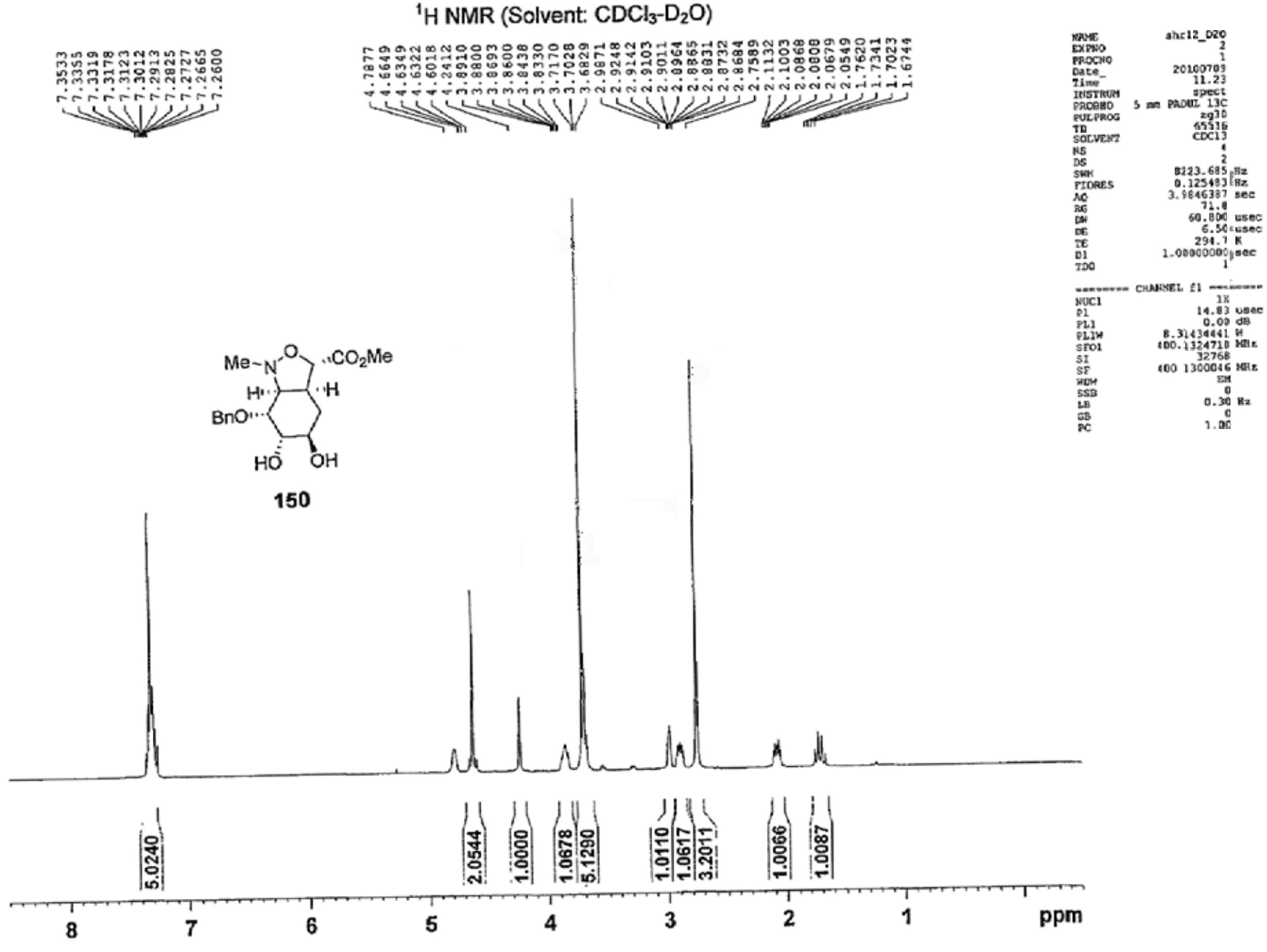
149

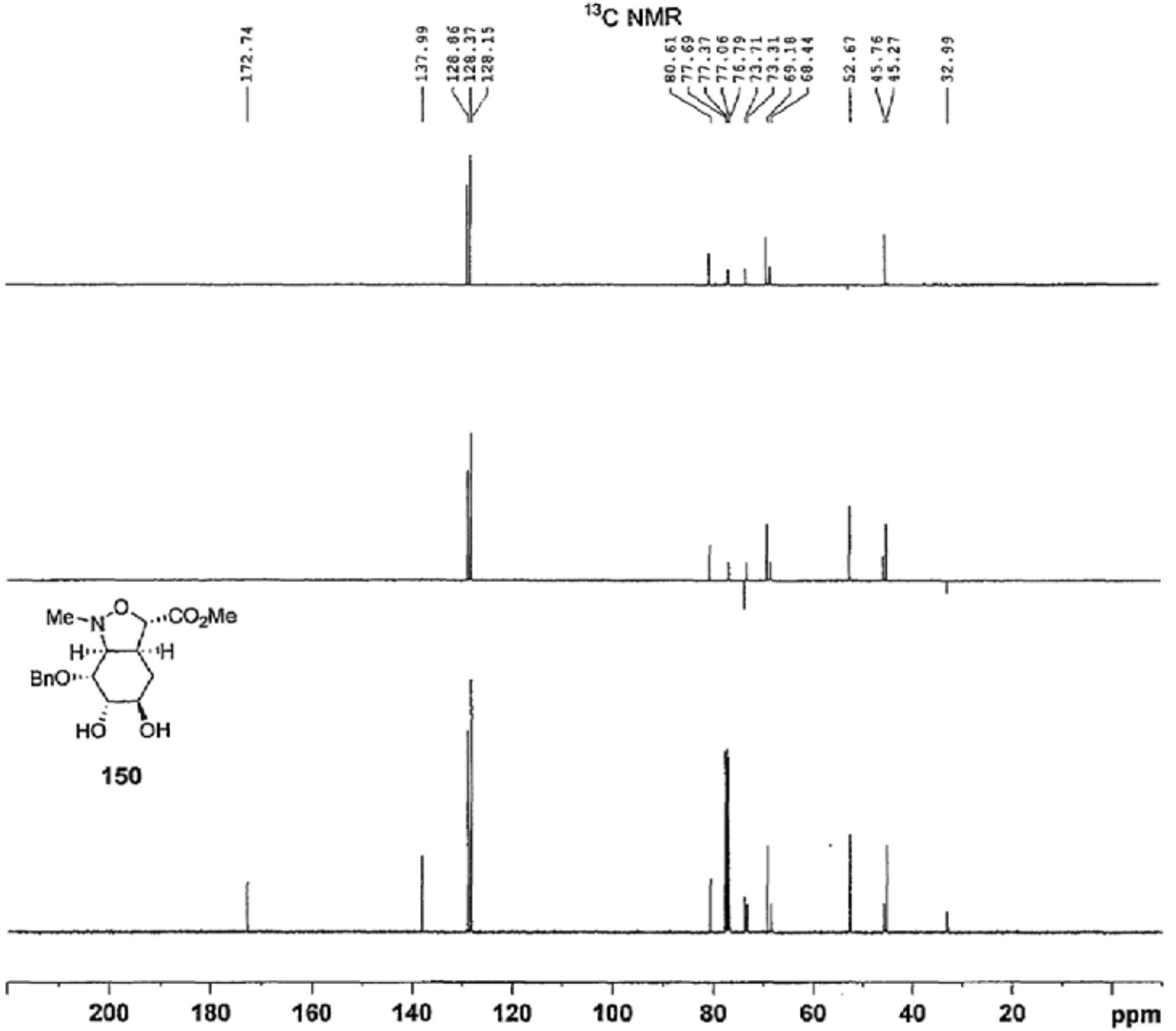
NAME	shrllcarbon
EXPNO	2
PROCNO	1
Date_	20090620
Time	10.38
INSTRUM	spect
PROBHD	5 mm PABBI 1H/
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	191
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	294.7 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	14.50 usec
PL1	-4.00 dB
PL1W	90.22689819 W
SFO1	100.6228298 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	-2.00 dB
PL12	18.80 dB
PL13	18.80 dB
PL2W	13.17734718 W
PL12W	0.10960442 W
PL13W	0.10960442 W
SFO2	400.1316005 MHz
SI	32768
SF	100.6127573 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
BC	1.40

^{1}H NMR :

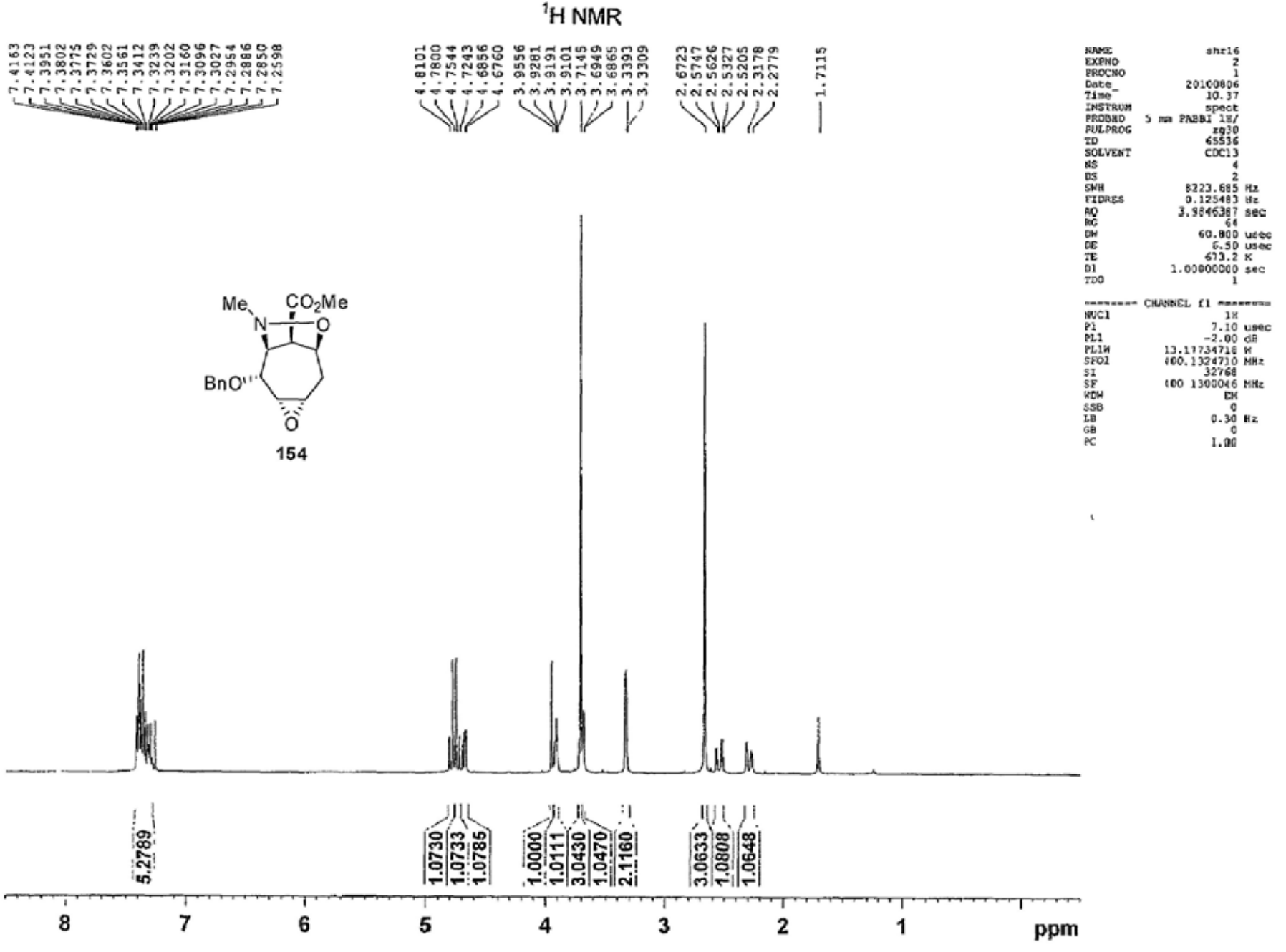


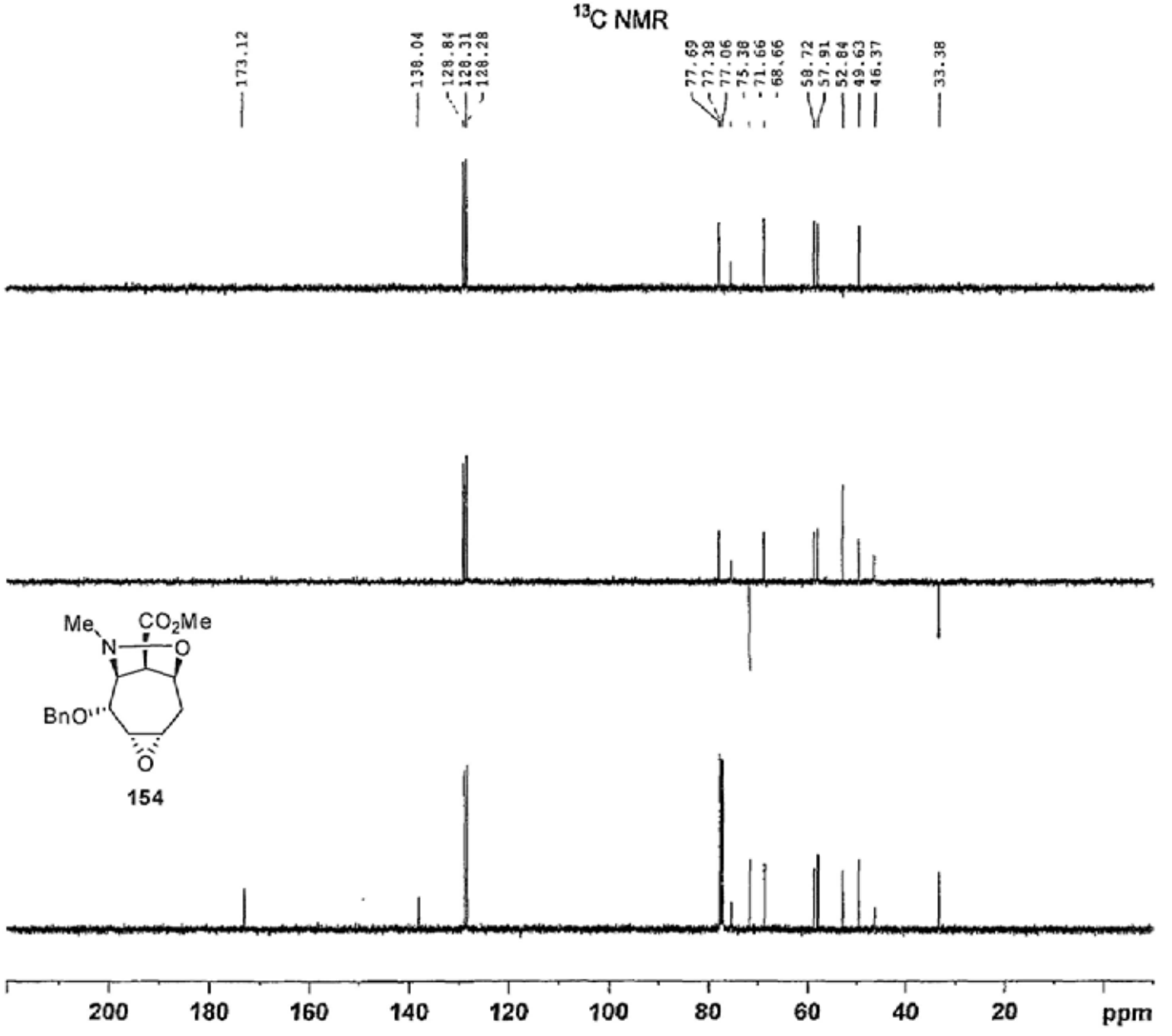
NAME	shr12
EXPNO	2
PROCNO	1
Date_	20090619
Time	13.14
INSTRUM	spect
PROBHD	5 mm PABBI 1H/
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	8
DS	2
SWH	8223.685 Hz
FIDRES	0.125483 Hz
AQ	3.9846387 sec
RG	80.6
DW	60.800 usec
DE	6.50 usec
TE	294.4 K
D1	1.00000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	1H
P1	7.10 usec
PL1	-2.00 dB
PL1W	13.17734718 W
SFO1	400.1324710 MHz
SI	32768
SF	400.1300056 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00


^{1}H NMR (Solvent: $CDCl_3$-D_2O)
7.3533
7.3355
7.3319
7.3178
7.3123
7.3012
7.2913
7.2825
7.2727
7.2665
7.2600
4.7877
4.6649
4.6349
4.6322
4.6018
4.2412
3.8910
3.8800
3.8693
3.8600
3.8438
3.8330
3.7170
3.7028
3.6829
2.9871
2.9248
2.9142
2.9103
2.9011
2.8964
2.8865
2.8831
2.8732
2.8684
2.7589
2.1132
2.1003
2.0868
2.0808
2.0679
2.0549
1.7620
1.7341
1.7023
1.6744
NAME ahc12_D2O
EXPNO 2
PROCNO 1
Date_ 20100709
Time 11.23
INSTRUM spect
PROBHD 5 mm PADUL 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 4
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 71.8
DW 60.800 usec
DE 6.50 usec
TE 294.7 K
D1 1.00000000 sec
TD0 1
CHANNEL f1
NUC1 1H
P1 14.83 usec
PL1 0.00 dB
PL1W 8.31434441 W
SFO1 400.1324710 MHz
SI 32768
SF 400.1300046 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
Me
N
O
CO2Me
H
H
BnO
HO
OH
150
5.0240
2.0544
1.0000
1.0678
5.1290
1.0110
1.0617
3.2011
1.0066
1.0087
8
7
6
5
4
3
2
1
ppm



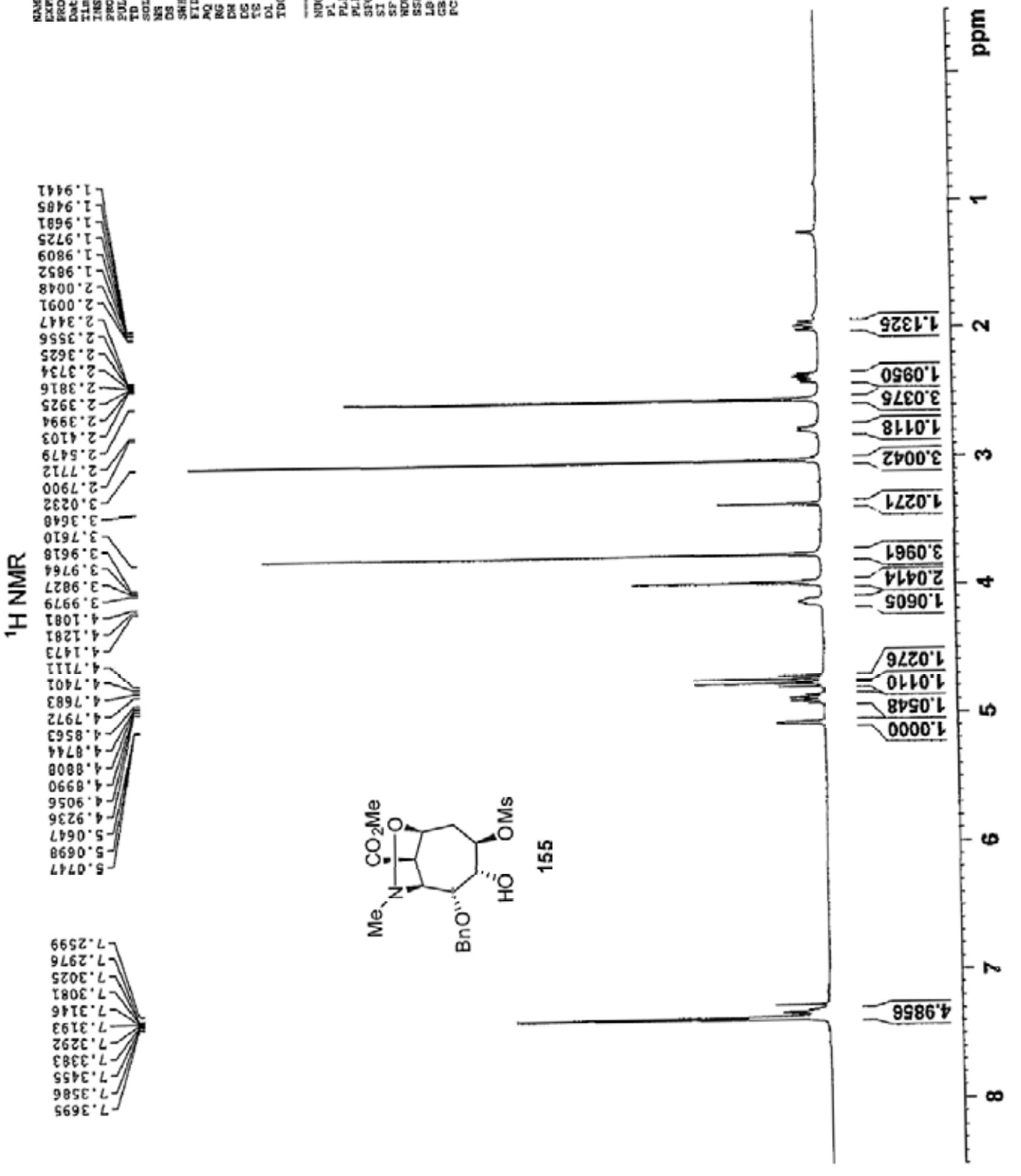
NAME	shr12carbon	
EXPNO	3	
PROCNO	1	
Date_	20100709	
Time	10.55	
INSTRUM	spect	
PROBHD	5 mm BADUL 13C	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	202	
DS	4	
SWH	24038.461	Hz
FIDRES	0.366798	Hz
AQ	1.3631988	sec
RG	203	
DW	20.800	usec
DE	6.50	usec
TE	295.4	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
========	CHANNEL f1	========
NUC1	13C	
P1	9.68	usec
PL1	-0.60	dB
PL1W	41.24164963	W
SFO1	100.6228298	MHz
========	CHANNEL f2	========
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	90.00	usec
PL2	0.00	dB
PL12	15.66	dB
PL13	15.92	dB
PL2W	8.31434411	W
PL12W	0.22585411	W
PL13W	0.21272963	W
SFO2	400.1316005	MHz
SI	32768	
SF	100.6127404	MHz
WDW	EM	
SSB	0	
LB	1.00	Hz
GB	0	
PC	1.40	

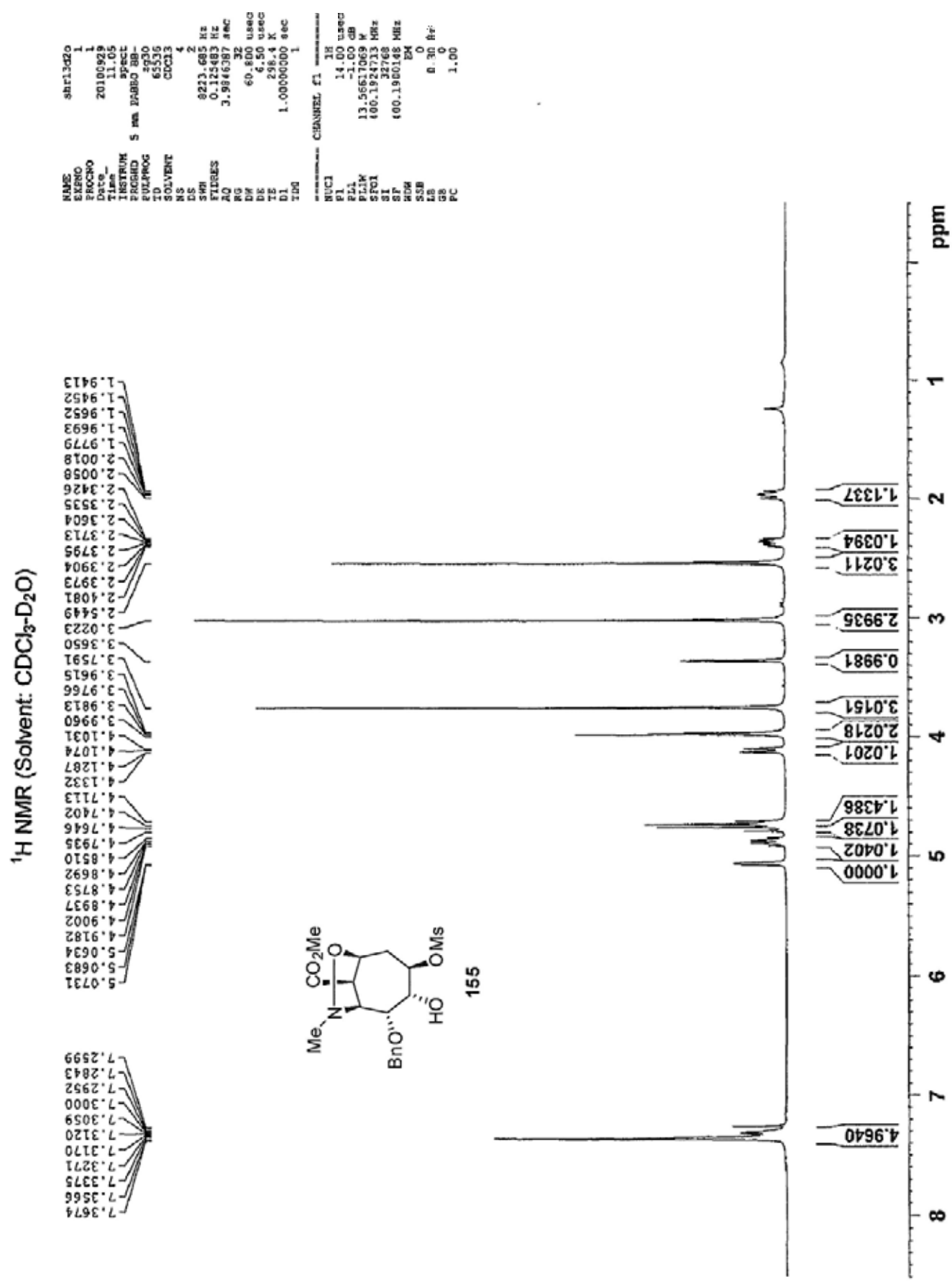

^{1}H NMR
7.4163
7.4123
7.3951
7.3802
7.3775
7.3729
7.3602
7.3561
7.3412
7.3239
7.3202
7.3160
7.3096
7.3027
7.2954
7.2886
7.2850
7.2598
4.8101
4.7800
4.7544
4.7243
4.6856
4.6760
3.9556
3.9281
3.9191
3.9101
3.7145
3.6949
3.6865
3.3393
3.3309
2.6723
2.5747
2.5626
2.5327
2.5205
2.3178
2.2779
1.7115
Me
N
CO2Me
O
BnO
O
154
NAME shz16
EXPNO 2
PROCNO 1
Date_ 20100806
Time 10.37
INSTRUM spect
PROBHD 5 mm PABBI 1H/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 4
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 64
DW 60.800 usec
DE 6.50 usec
TE 673.2 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 7.10 usec
PL1 -2.00 dB
PL1W 13.11734716 W
SFO1 400.1324710 MHz
SI 32768
SF 400.1300046 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
5.2789
1.0730
1.0733
1.0785
1.0000
1.0111
3.0430
1.0470
2.1160
3.0633
1.0808
1.0648
8
7
6
5
4
3
2
1
ppm

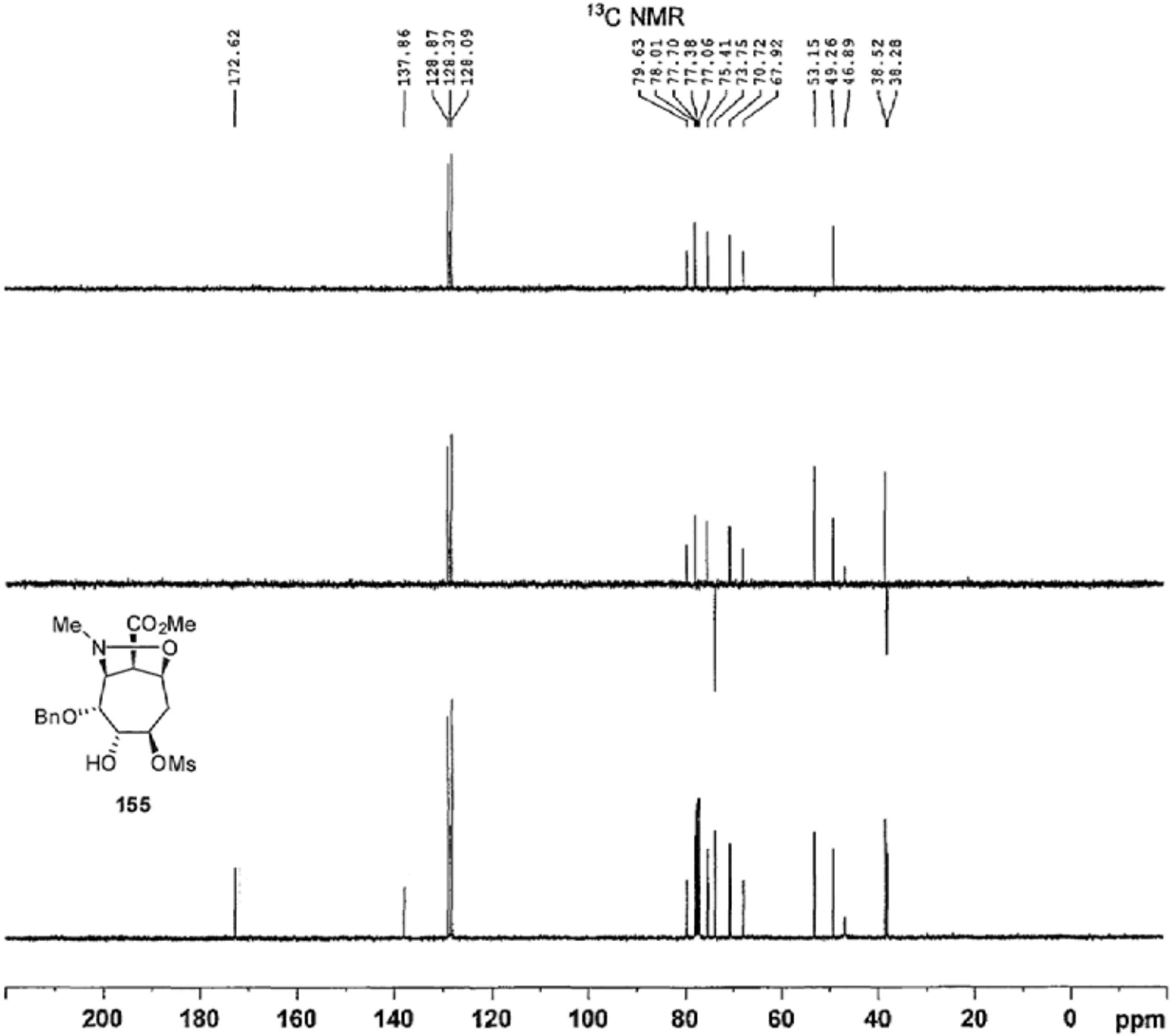


154

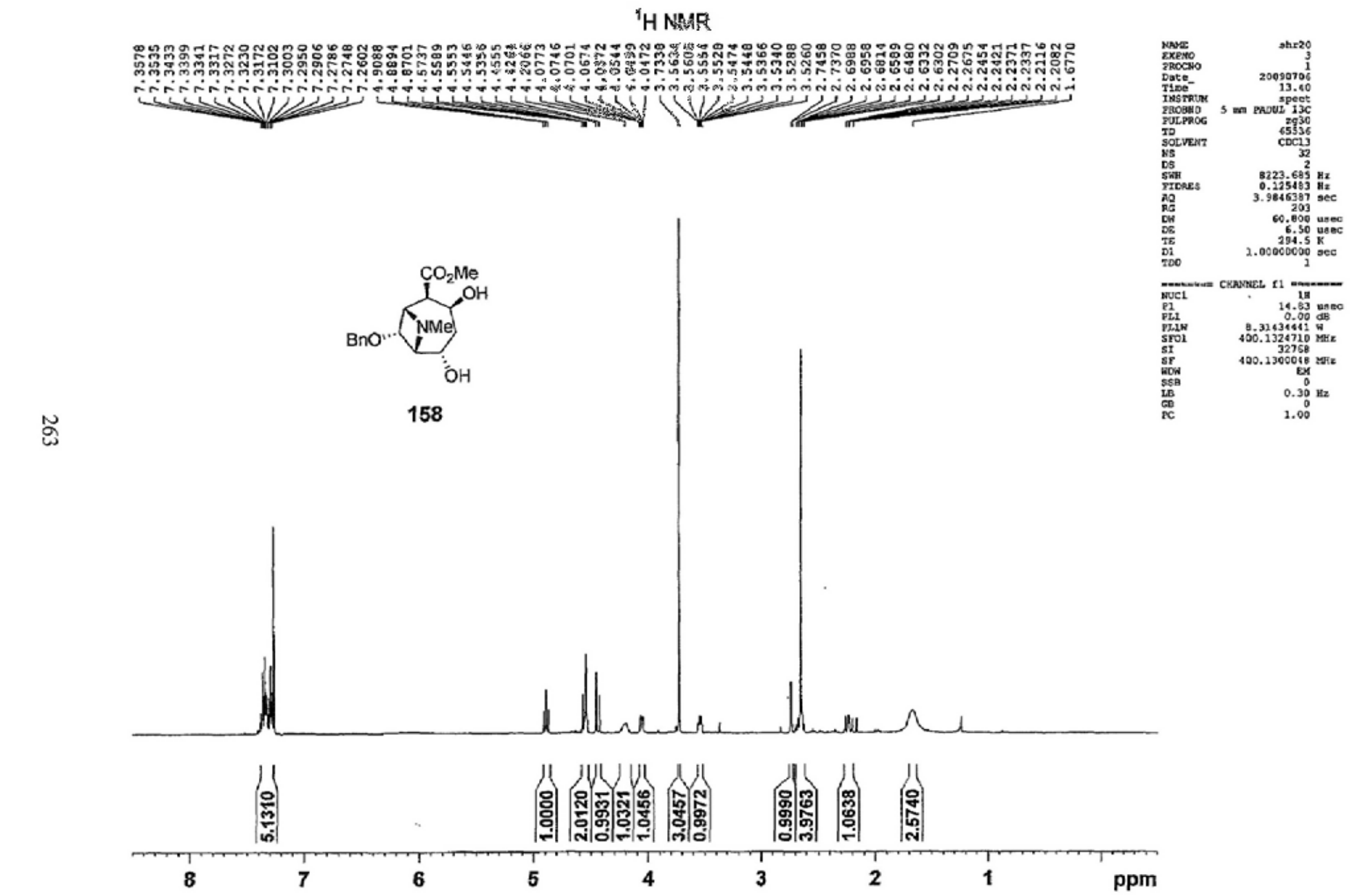
NAME	shr16carbon
EXPNO	1
PROCNO	1
Date_	20100806
Time	10.43
INSTRUM	spect
PROBHD	5 mm PABBI 1H/
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	138
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	673.2 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	14.50 usec
PL1	-4.00 dB
PL1W	90.22689819 W
SFO1	100.6228298 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	-2.00 dB
PL12	18.80 dB
PL13	18.80 dB
PL2W	13.17734718 W
PL12W	0.10960442 W
PL13W	0.10960442 W
SFO2	400.1316005 MHz
SI	32768
SF	100.6127360 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

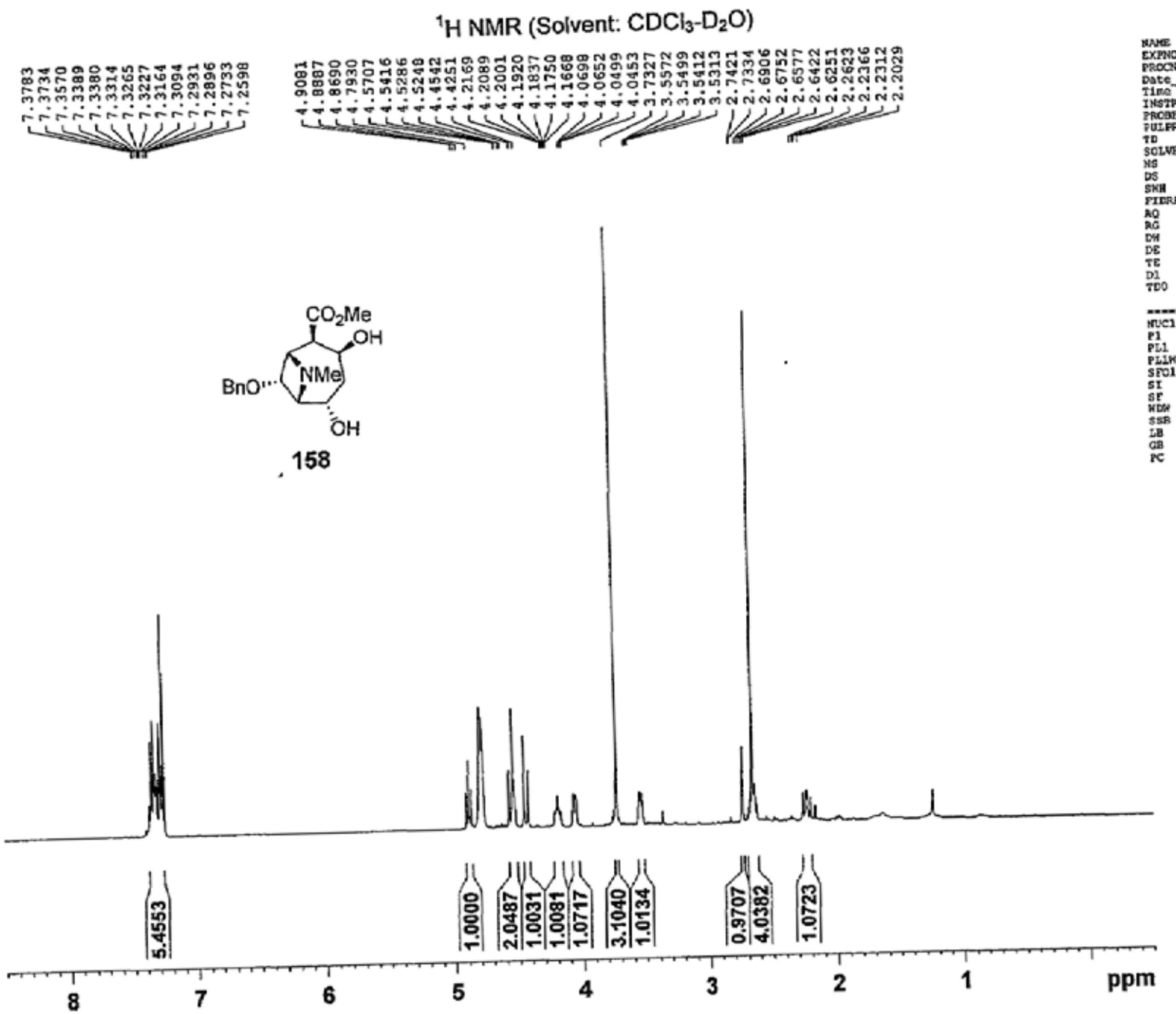

^{1}H NMR
CO2Me
OMs
HO
BnO
Me
N
155
ppm
1.1325
1.0950
3.0375
1.0118
3.0042
1.0271
3.0961
2.0414
1.0605
1.0276
1.0110
1.0548
1.0000
4.9856

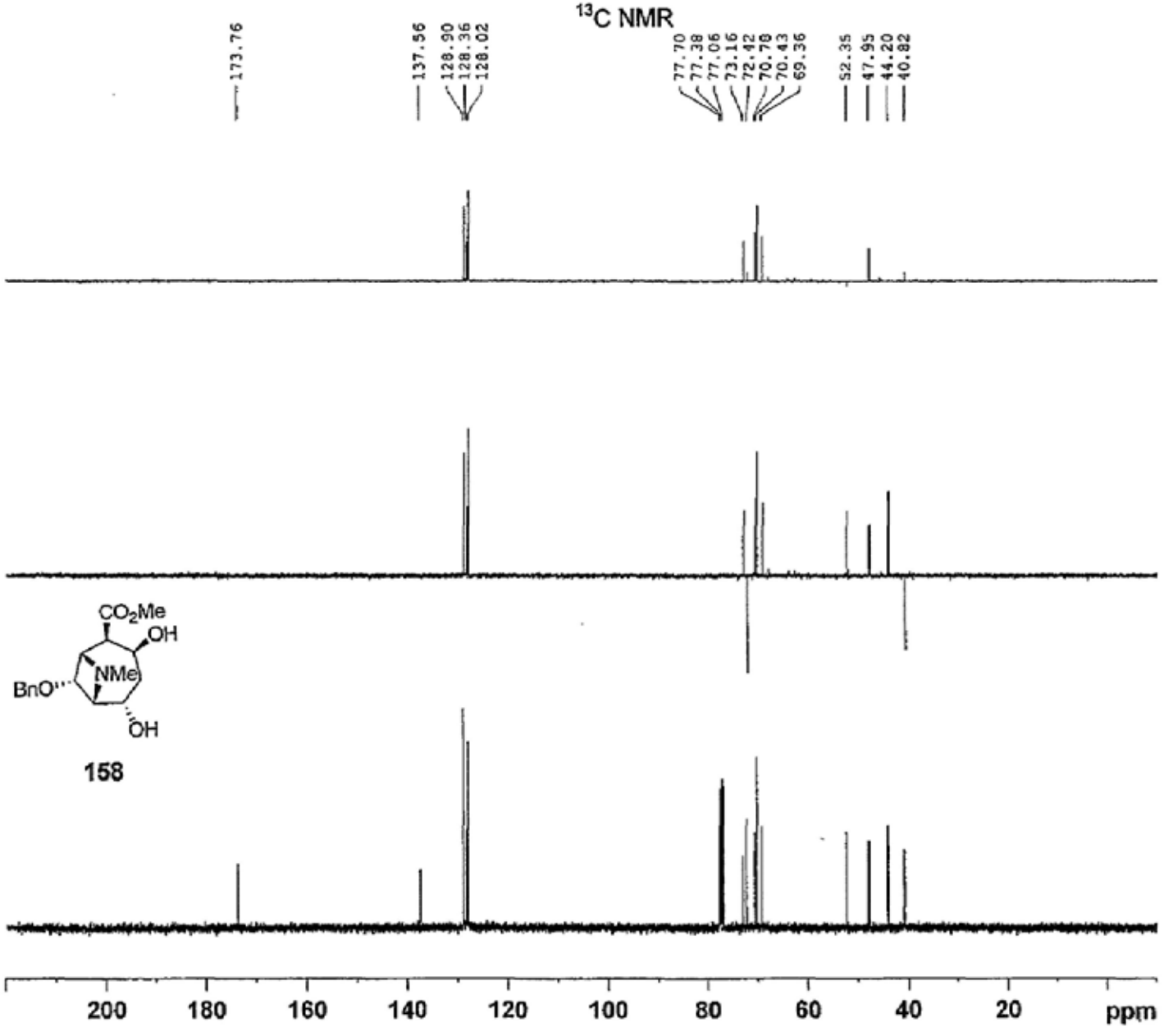

^{1}H NMR (Solvent: $CDCl_3$-D_2O)
ppm
155
Me
N
CO_2Me
O
BnO
HO
OMs
1.0000
1.0402
1.0738
1.4386
1.0201
2.0218
3.0151
0.9981
2.9935
3.0211
1.0394
1.1337
4.9640



NAME	shr13carbon
EXPNO	2
PROCNO	1
Date_	20100929
Time	10.52
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	107
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	228
DW	20.800 usec
DE	6.50 usec
TE	298.8 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.90 usec
PL1	-2.00 dB
PL1W	55.33689499 W
SFO1	100.6379183 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	90.00 usec
PL2	-1.00 dB
PL12	15.16 dB
PL13	18.62 dB
PL2W	13.56617069 W
PL12W	0.32844096 W
PL13W	0.14806664 W
SFO2	400.1916008 MHz
SI	32768
SF	100.6278285 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

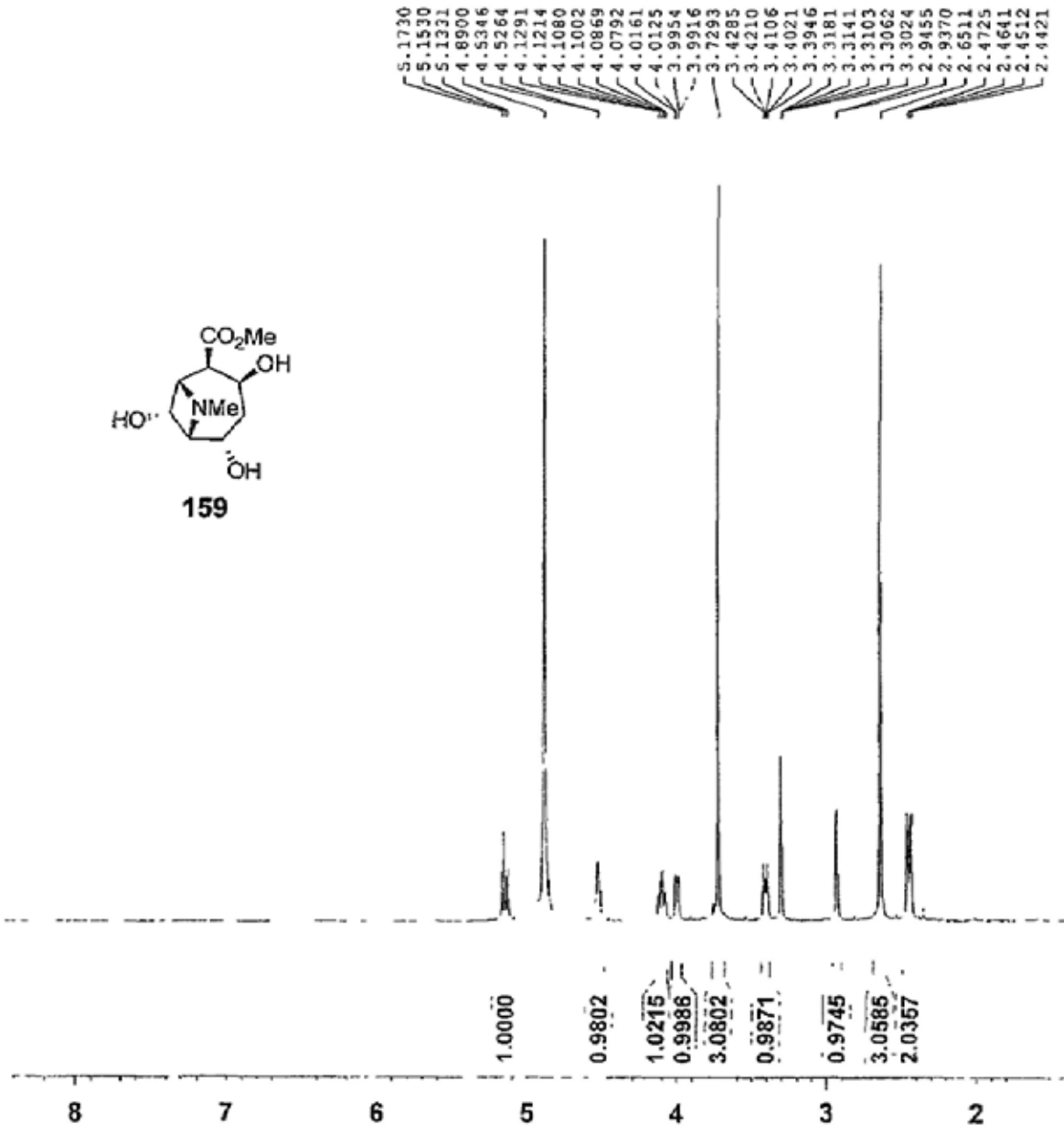

^{1}H NMR
7.3578
7.3535
7.3433
7.3399
7.3341
7.3317
7.3272
7.3230
7.3172
7.3102
7.3003
7.2950
7.2906
7.2786
7.2748
7.2602
4.9088
4.8894
4.8701
4.5737
4.5589
4.5553
4.5446
4.5358
4.5555
4.0773
4.0746
4.0701
4.0674
3.7338
3.5260
3.5288
3.5340
3.5366
3.5448
3.5474
3.5528
3.5554
3.5634
2.7458
2.7370
2.6988
2.6958
2.6814
2.6589
2.6480
2.6332
2.6302
2.2709
2.2675
2.2454
2.2421
2.2371
2.2337
2.2116
2.2082
1.6770
NAME ahz20
EXPNO 3
PROCNO 1
Date_ 20090706
Time 13.40
INSTRUM spect
PROBHD 5 mm PADUL 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 32
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 203
DW 60.800 usec
DE 6.50 usec
TE 294.5 K
D1 1.00000000 sec
TD0 1
CHANNEL f1
NUC1 1H
P1 14.83 usec
PL1 0.00 dB
PL1W 8.31434441 W
SFO1 400.1324710 MHz
SI 32768
SF 400.1300048 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
CO2Me
OH
NMe
BnO
OH
158
5.1310
1.0000
2.0120
0.9931
1.0321
1.0456
3.0457
0.9972
0.9990
3.9763
1.0638
2.5740
8
7
6
5
4
3
2
1
ppm


^{1}H NMR (Solvent: CDCl$_3$-D$_2$O)
7.3783 7.3734 7.3570 7.3389 7.3380 7.3314 7.3265 7.3227 7.3164 7.3094 7.2931 7.2896 7.2733 7.2598
4.9081 4.8887 4.8690 4.7930 4.5707 4.5416 4.5286 4.5248 4.4542 4.4251 4.2169 4.2089 4.2001 4.1920 4.1837 4.1750 4.1668 4.0698 4.0652 4.0499 4.0453 3.7327 3.5572 3.5499 3.5412 3.5313 2.7421 2.7334 2.6906 2.6752 2.6577 2.6422 2.6251 2.2623 2.2366 2.2312 2.2029
NAME shr20_D2O
EXPNO 1
PROCNO 1
Date_ 20090706
Time 14 00
INSTRUM spect
PROBHD 5 mm PABBUL 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 16
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 203
DW 60.800 usec
DE 6.50 usec
TE 294.7 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.83 usec
PL1 0.00 dB
PLIM 8.31434441 W
SFO1 400.1324710 MHz
SI 32768
SF 400.1300051 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
CO2Me
OH
NMe
BnO
OH
158
5.4553
1.0000
2.0487
1.0031
1.0081
1.0717
3.1040
1.0134
0.9707
4.0382
1.0723
8
7
6
5
4
3
2
1
ppm

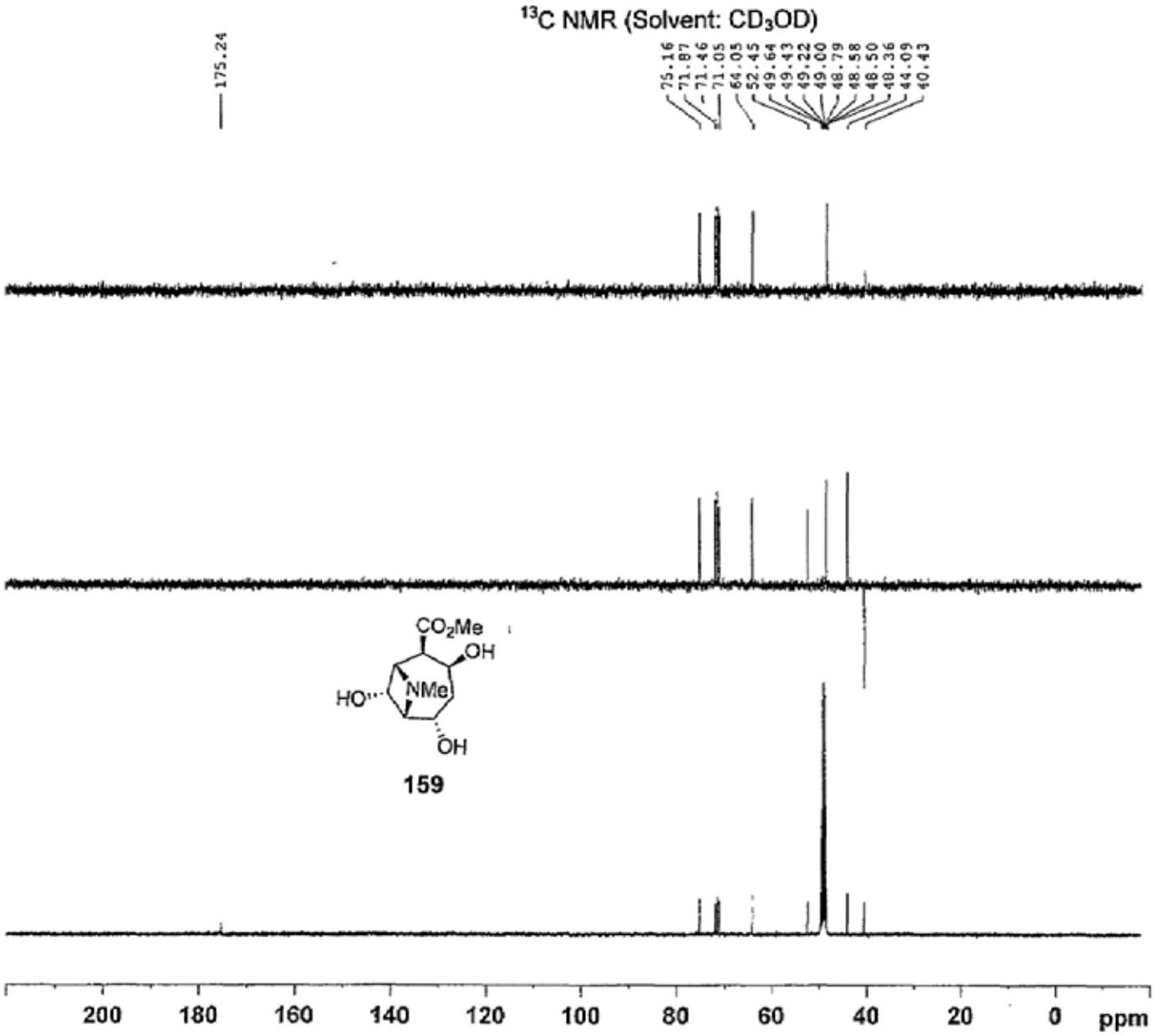


NAME	shr20carbon
EXPNO	7
PROCNO	1
Date_	20100720
Time	16.06
INSTRUM	spect
PROBHD	5 mm PABBI 1H/
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	41
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	294.5 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	14.50 usec
PL1	-4.00 dB
PL1W	90.22689819 W
SFO1	100.6228298 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	-2.00 dB
PL12	18.80 dB
PL13	18.80 dB
PL2W	13.17734718 W
PL12W	0.10960442 W
PL13W	0.10960442 W
SFO2	400.1316005 MHz
SI	32768
SF	100.6127419 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

^{1}H NMR (Solvent: CD_3OD)



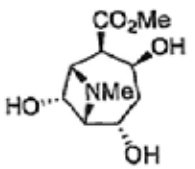
NAME	shz28MeOD
EXPNO	1
PROCNO	1
Date_	20100917
Time	11 04
INSTRUM	spect
PROBHD	5 mm PABBI 1H/
PULPROG	zg30
TD	65536
SOLVENT	MeOD
NS	8
DS	2
SWH	8223.685 Hz
FIDRES	0.125483 Hz
AQ	3.9846387 sec
RG	90.5
DW	60.800 usec
DE	6.50 usec
TE	294.3 K
D1	1.00000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	1H
P1	7.10 usec
PL1	-2.00 dB
PL1W	13.17734718 W
SFO1	400.1324710 MHz
SI	32768
SF	400.1300028 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00



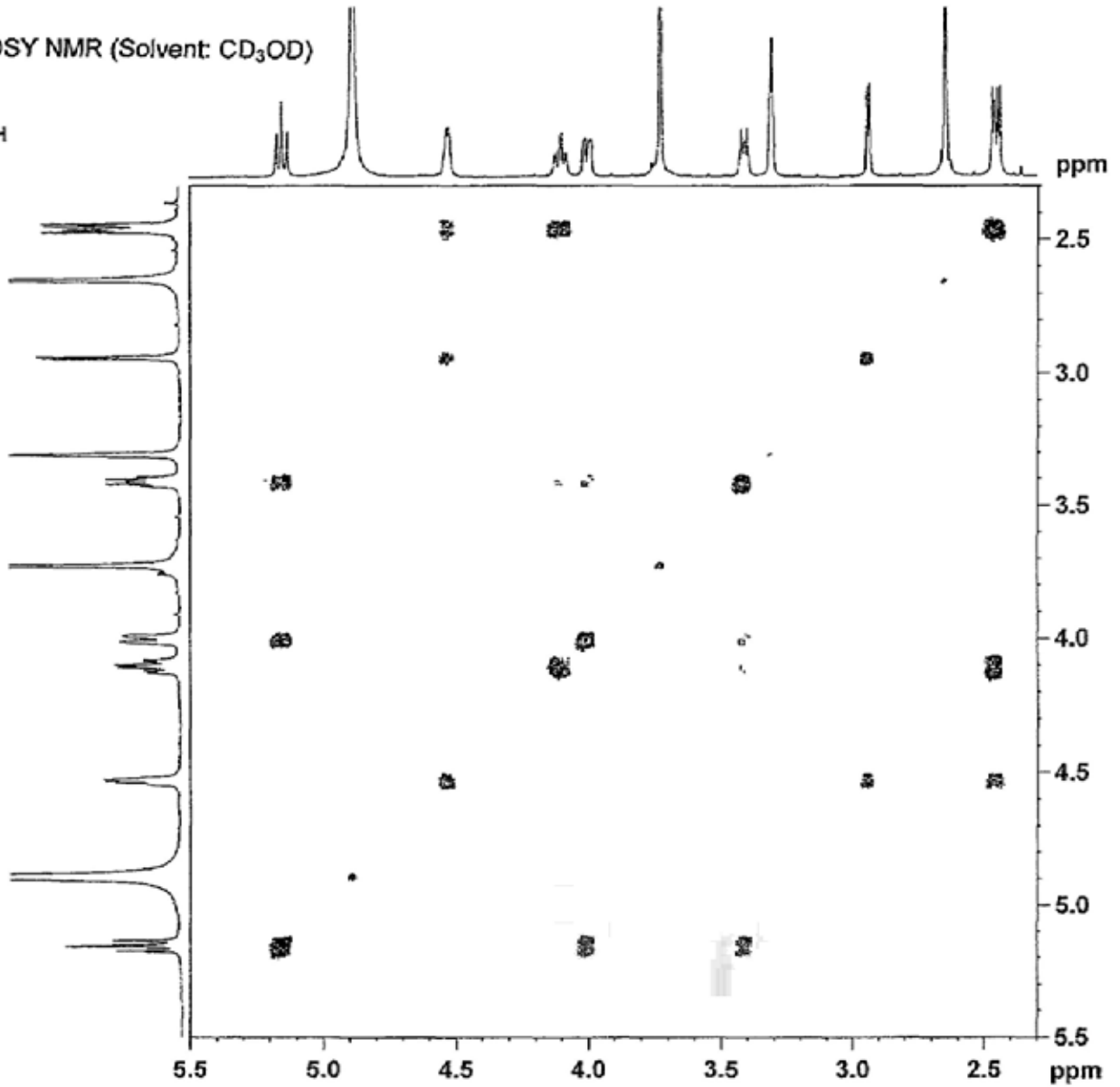
159

NAME	shr28MeODcarbon	
EXPNO	1	
PROCNO	1	
Date_	20100917	
Time	11.08	
INSTRUM	spect	
PROBHD	5 mm PABBI 1H/	
PULPROG	zgpg30	
TD	65536	
SOLVENT	MeOD	
NS	268	
DS	4	
SWH	24038.461	Hz
FIDRES	0.366798	Hz
AQ	1.3631988	sec
RG	203	
DW	20.800	usec
DE	6.50	usec
TE	294.6	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	14.50	usec
PL1	-6.00	dB
PL1W	90.22689819	W
SFO1	100.6228298	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	80.00	usec
PL2	-2.00	dB
PL12	18.80	dB
PL13	18.80	dB
PL2W	13.17734718	W
PL12W	0.10960442	W
PL13W	0.10960442	W
SFO2	400.1316005	MHz
SI	32768	
SF	100.6126271	MHz
WDW	EM	
SSB	0	
LB	1.00	Hz
GB	0	
PC	1.40	

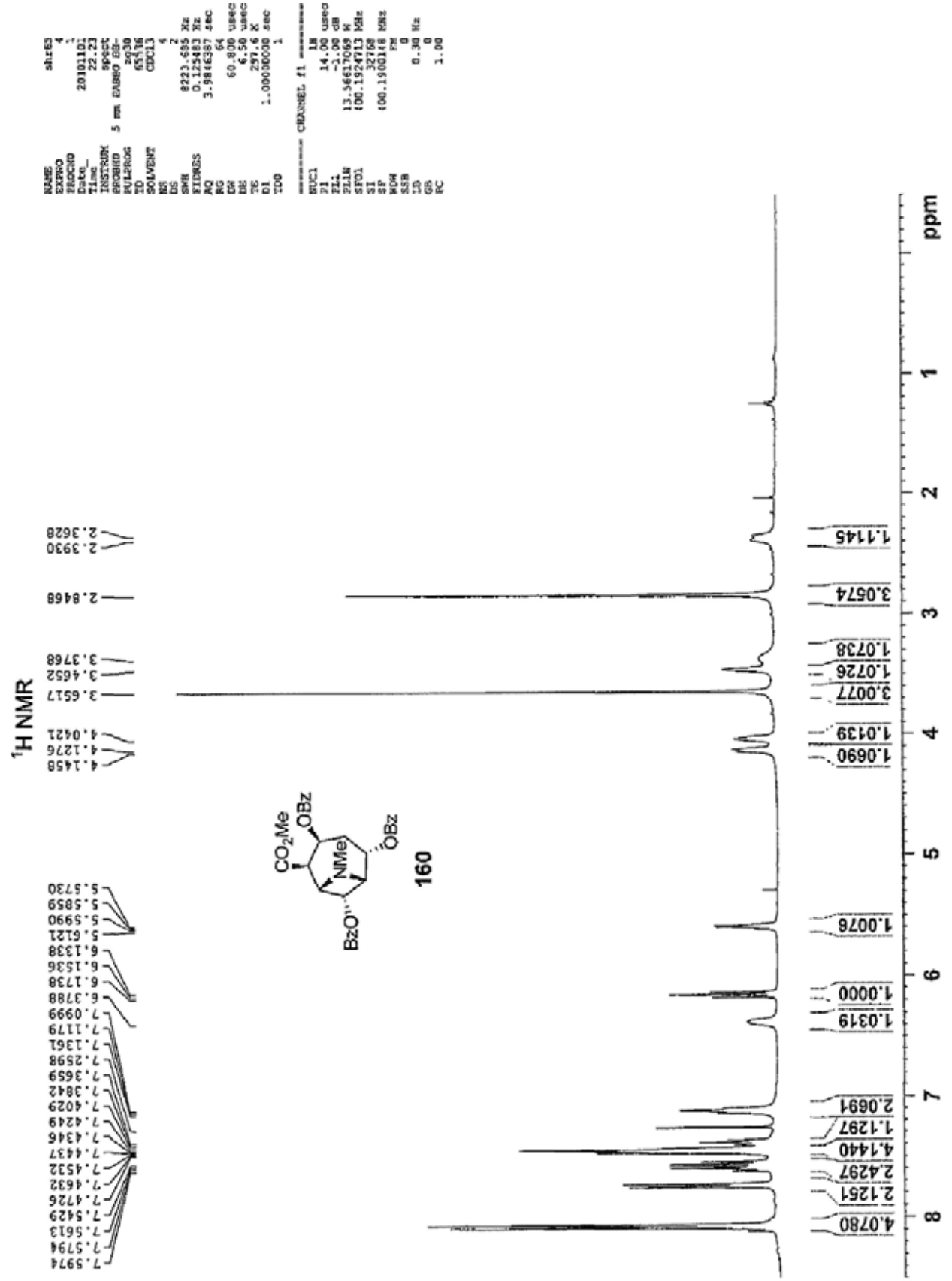
COSY NMR (Solvent: CD_3OD)

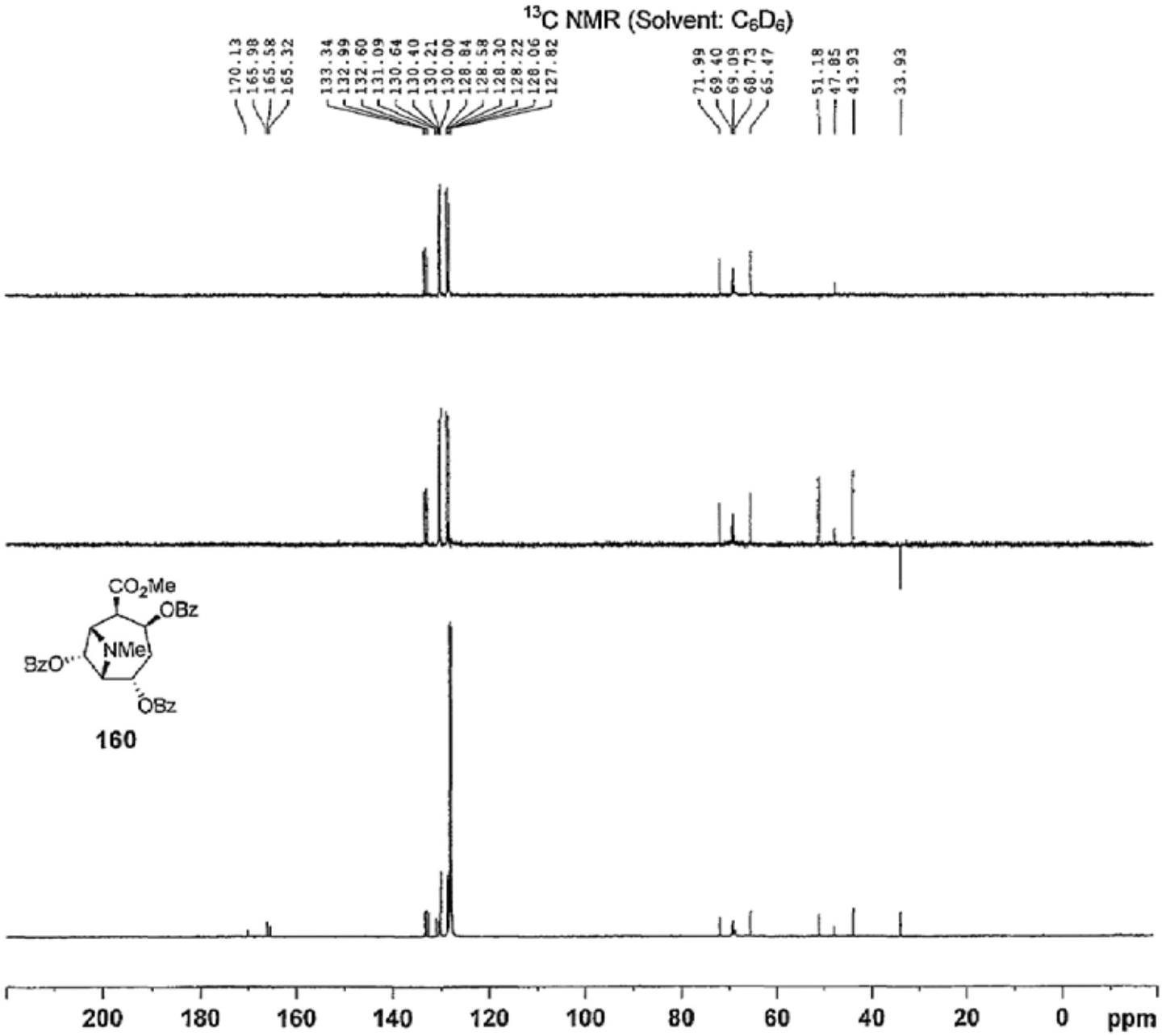


159



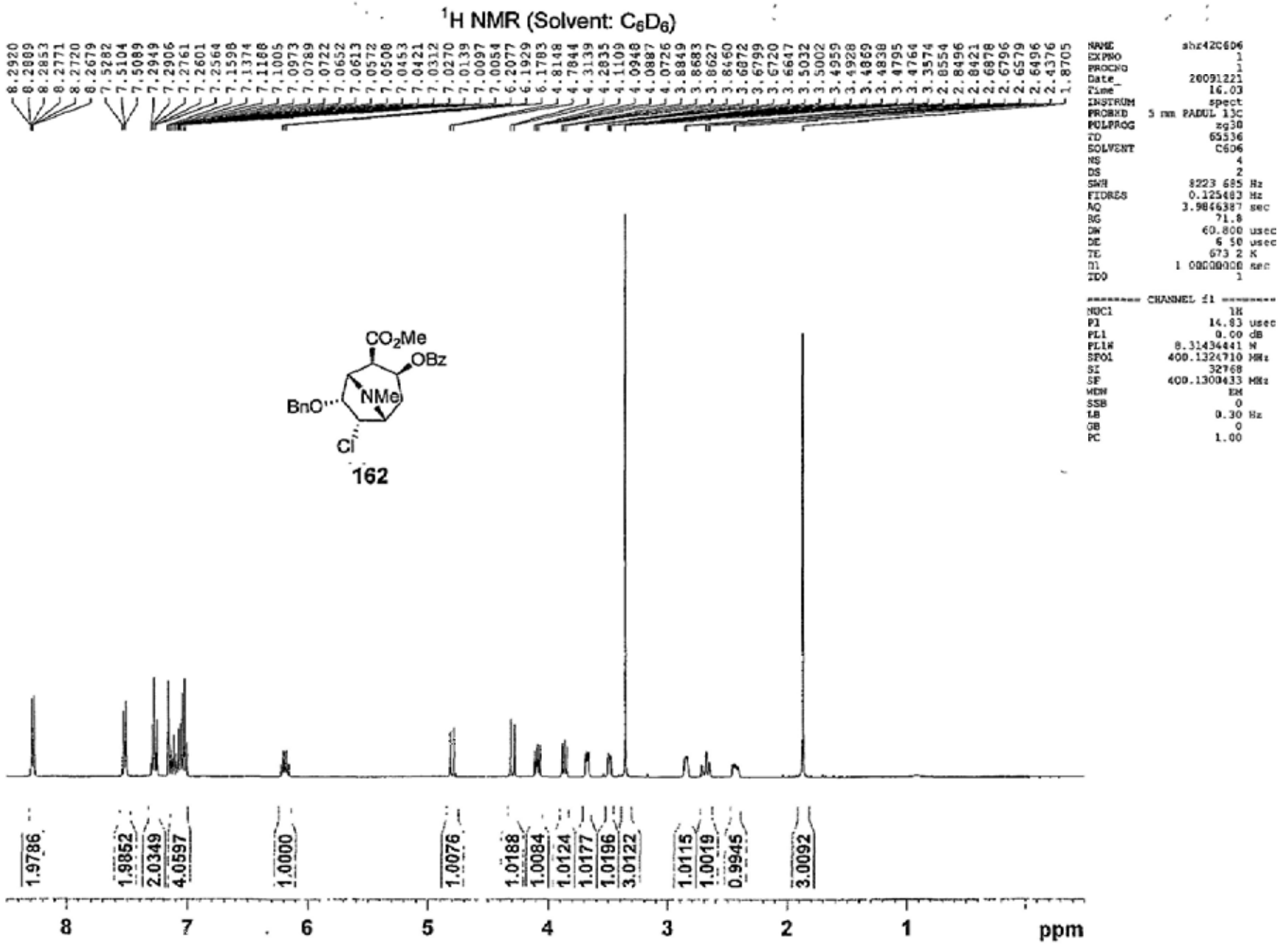
NAME	shz28MeODcosy
EXPNO	1
PROCNO	1
Date_	20100917
Time	11.40
INSTRUM	spect
PROBHD	5 mm PABBI 1H/
PULPROG	cosygpmfqf
TD	2048
SOLVENT	MeOD
NS	4
DS	8
SWH	2408.478 Hz
FIDRES	1.176015 Hz
AQ	0.4252148 sec
RG	203
DW	207.600 usec
DE	6.50 usec
TE	294.3 K
D0	0.00000300 sec
D1	2.00000000 sec
D13	0.00000400 sec
D16	0.00020000 sec
IN0	0.00041520 sec
======== CHANNEL f1 ========	
NUC1	1H
P1	7.10 usec
PL1	-2.00 dB
PL1W	13.17734718 W
SFO1	400.1318066 MHz
====== GRADIENT CHANNEL =====	
GPNAM1	SINE.100
GPNAM2	SINE.100
GPNAM3	SINE.100
GPZ1	16.00 %
GPZ2	12.00 %
GPZ3	40.00 %
P16	1000.00 usec
ND0	1
TD	128
SFO1	400.1318 MHz
FIDRES	19.816198 Hz
SW	6.019 ppm
FnMODE	QF
SI	1024
SF	400.1299985 MHz
WDW	SINE
SSB	0
LB	0.00 Hz
GB	0
PC	1.40
SI	1024
MC2	QF
SF	400.1299986 MHz
WDW	SINE
SSB	0
LB	0.00 Hz
GB	0

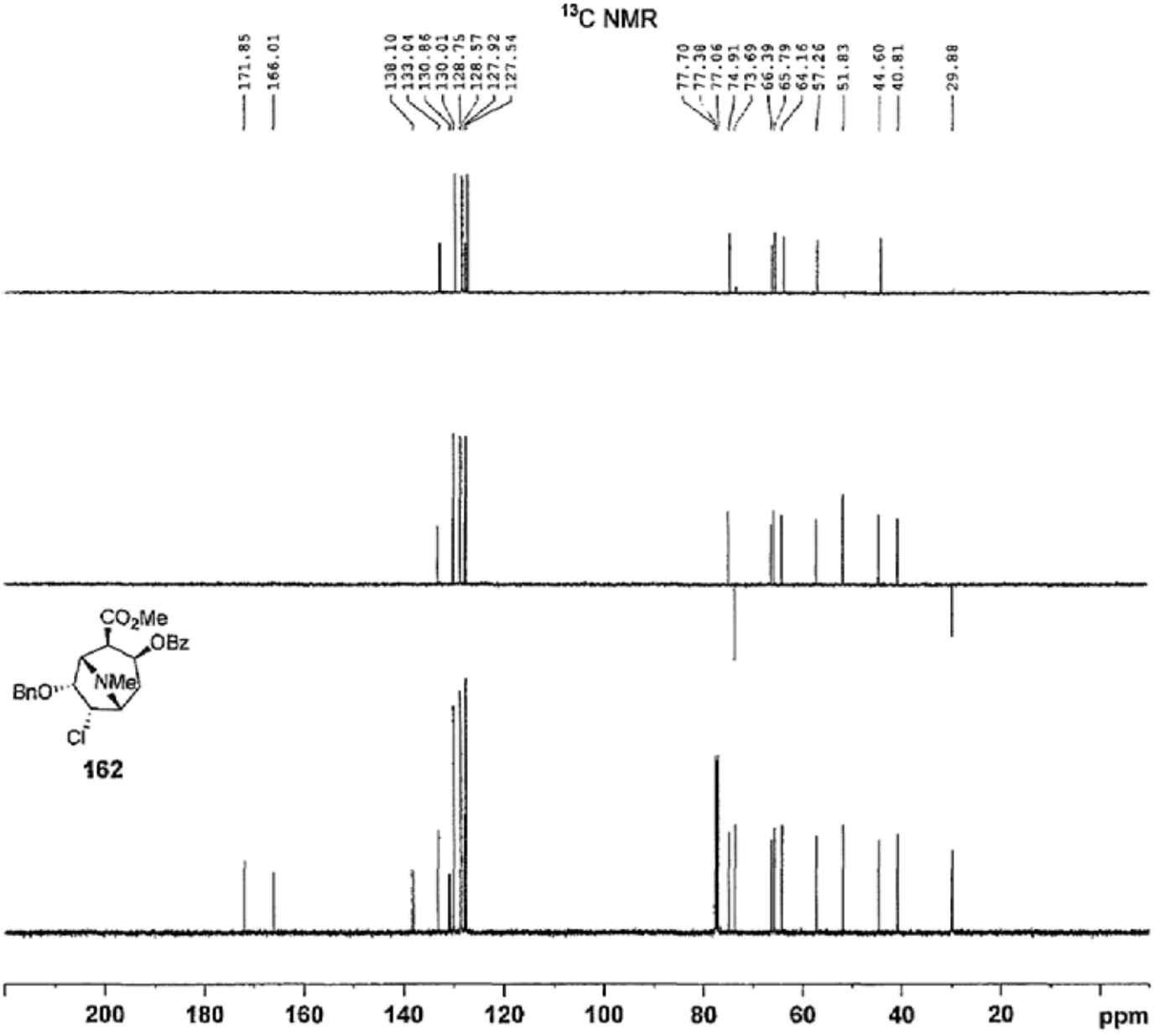

^{1}H NMR
160
ppm



160

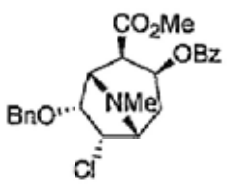
NAME	shr65c6d6carbon
EXPNO	1
PROCNO	1
Date_	20101103
Time	10.37
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	C6D6
NS	201
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	80.6
DW	20.800 usec
DE	6.50 usec
TE	298.3 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.90 usec
PL1	-2.00 dB
PL1W	55.33689499 W
SFO1	100.6379183 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	90.00 usec
PL2	-1.00 dB
PL12	15.16 dB
PL13	18.62 dB
PL2W	13.56617069 W
PL12W	0.32844096 W
PL13W	0.14806664 W
SFO2	400.1916008 MHz
SI	32768
SF	100.6278207 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40


^{1}H NMR (Solvent: C_6D_6)
8.2920 8.2869 8.2853 8.2771 8.2720 8.2679 7.5282 7.5104 7.5089 7.2949 7.2906 7.2761 7.2601 7.2564 7.1598 7.1374 7.1168 7.1005 7.0973 7.0789 7.0722 7.0652 7.0613 7.0572 7.0508 7.0453 7.0421 7.0312 7.0270 7.0139 7.0097 7.0054 6.2077 6.1929 6.1783 4.8148 4.7844 4.3139 4.2835 4.1109 4.0948 4.0887 4.0726 3.8849 3.8683 3.8627 3.8460 3.6872 3.6799 3.6720 3.6647 3.5032 3.5002 3.4959 3.4928 3.4869 3.4838 3.4795 3.4764 3.3574 2.8554 2.8496 2.8421 2.6878 2.6796 2.6579 2.6496 2.4376 1.8705
NAME shz42C606
EXPNO 1
PROCNO 1
Date_ 20091221
Time 16.03
INSTRUM spect
PROBHD 5 mm PABUL 13C
PULPROG zg30
TD 65536
SOLVENT C606
NS 4
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 71.8
DW 60.800 usec
DE 6.50 usec
TE 673.2 K
D1 1.00000000 sec
D0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.83 usec
PL1 0.00 dB
PL1W 8.31434441 W
SFO1 400.1324710 MHz
SI 32768
SF 400.1300433 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
CO_2Me
OBz
BnO
NMe
Cl
162
1.9786
1.9852
2.0349
4.0597
1.0000
1.0076
1.0188
1.0084
1.0124
1.0177
1.0196
3.0122
1.0115
1.0019
0.9945
3.0092
8
7
6
5
4
3
2
1
ppm



NAME	shr42carbon
EXPNO	4
PROCNO	1
Date_	20100719
Time	16.17
INSTRUM	spect
PROBHD	5 mm PABBI 1H/
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	161
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	294.7 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	14.50 usec
PL1	-4.00 dB
PL1W	90.22689819 W
SFO1	100.6228298 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	-2.00 dB
PL12	18.80 dB
PL13	18.80 dB
PL2W	13.17734718 W
PL12W	0.10960442 W
PL13W	0.10960442 W
SFO2	400.1316005 MHz
SI	32768
SF	100.6127404 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

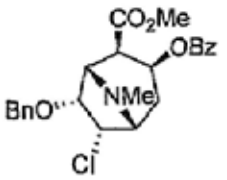
COSY NMR (Solvent: C_6D_6)



162

NAME	shr42C606cosy	
EXPNO	1	
PROCNO	1	
Date_	20091221	
Time	16.56	
INSTRUM	spect	
PROBHD	5 mm PADUL 13C	
PULPROG	cosygpmfqf	
TD	2048	
SOLVENT	C6D6	
NS	4	
DS	8	
SWH	1726.519	Hz
FIDRES	0.843027	Hz
AQ	0.5931508	sec
RG	203	
DW	289.600	usec
DE	6.50	usec
TE	673.2	K
D0	0.00000300	sec
D1	2.00000000	sec
D13	0.00000400	sec
D16	0.00020000	sec
IN0	0.00057920	sec
======== CHANNEL f1 ========		
NUC1	1H	
P1	14.83	usec
PL1	0.00	dB
PL1W	8.31434441	W
SFO1	400.1317431	MHz
====== GRADIENT CHANNEL =====		
GPNAM1	SINE.100	
GPNAM2	SINE.100	
GPNAM3	SINE.100	
GPZ1	16.00	%
GPZ2	12.00	%
GPZ3	40.00	%
P16	1000.00	usec
ND0	1	
TD	128	
SFO1	400.1317	MHz
FIDRES	13.488503	Hz
SW	4.315	ppm
FnMODE	QF	
SI	1024	
SF	400.1300422	MHz
WDW	SINE	
SSB	0	
LB	0.00	Hz
GB	0	
PC	1.40	
SI	1024	
MC2	QF	
SF	400.1300422	MHz
WDW	SINE	
SSB	0	
LB	0.00	Hz
GB	0	

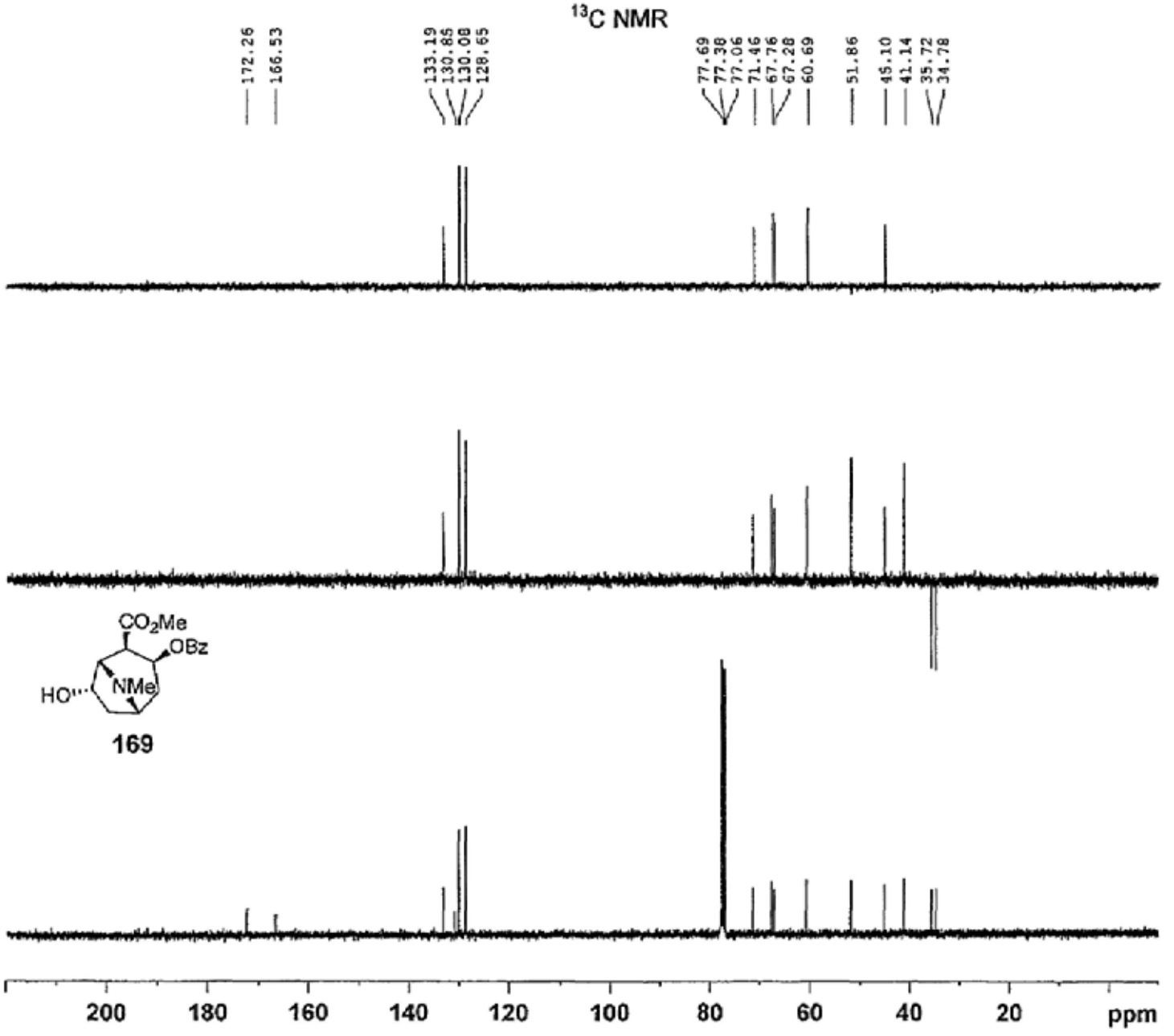
NOESY NMR (Solvent: C_6D_6)



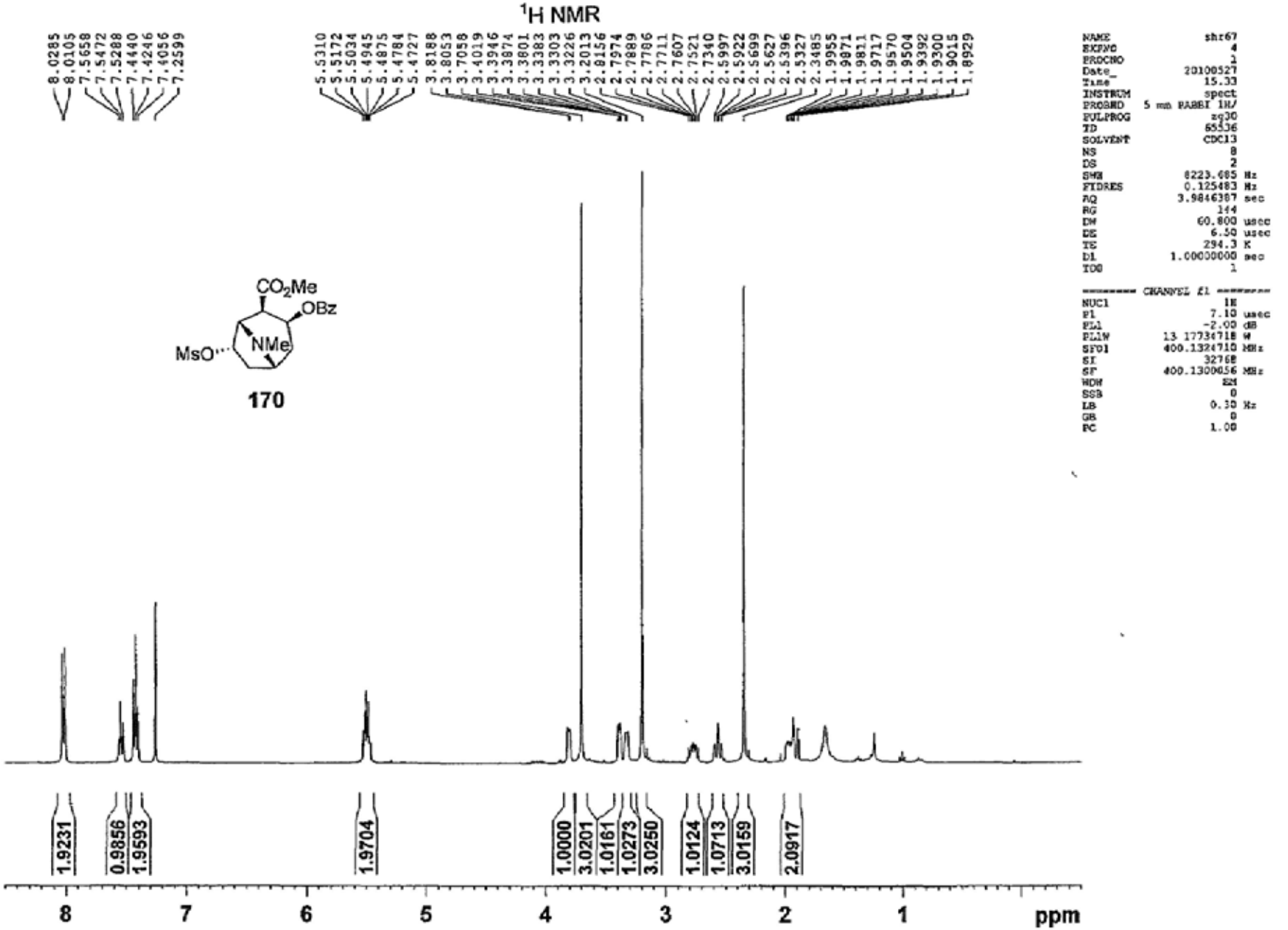
162

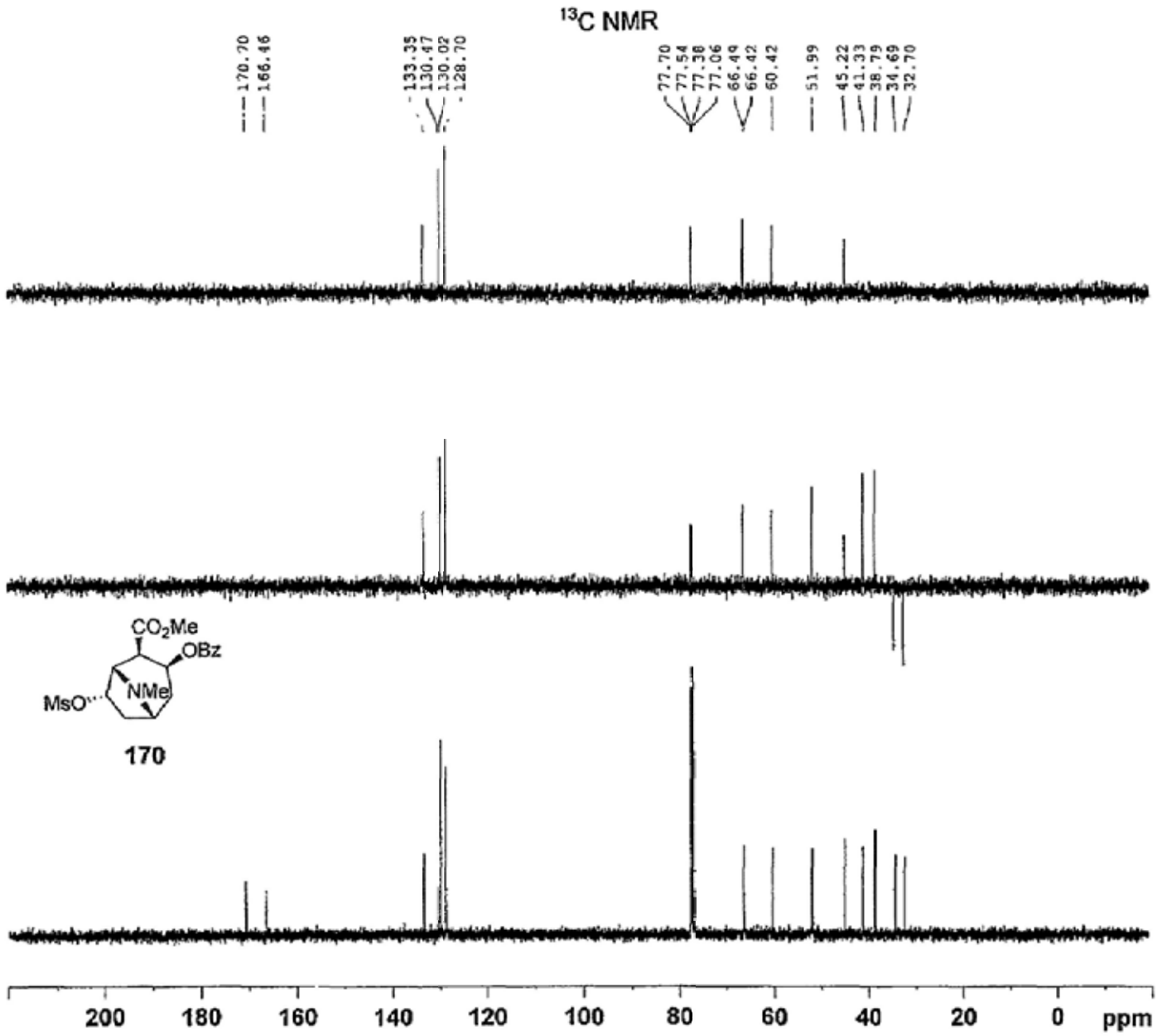
NAME	shr42C6D6noesy
EXPNO	1
PROCNO	1
Date_	20100806
Time	22.31
INSTRUM	spect
PROBHD	5 mm PABBI 1H/
PULPROG	noesyph
TD	2048
SOLVENT	C6D6
NS	32
DS	4
SWH	1822.157 Hz
FIDRES	0.889725 Hz
AQ	0.5620212 sec
RG	32
DW	274.400 usec
DE	6.50 usec
TE	294.5 K
D0	0.00026536 sec
D1	2.00000000 sec
D8	0.69999999 sec
IN0	0.00054880 sec
========	CHANNEL f1 ========
NUC1	1H
P1	7.10 usec
PL1	-2.00 dB
PL1W	13.17734718 W
SFO1	400.1317575 MHz
ND0	1
TD	256
SFO1	400.1318 MHz
FIDRES	7.117813 Hz
SW	4.554 ppm
FnMODE	States-TPPI
SI	1024
SF	400.1300418 MHz
WDW	QSINE
SSB	2
LB	0.00 Hz
GB	0
PC	1.00
SI	1024
MC2	States-TPPI
SF	400.1300421 MHz
WDW	QSINE
SSB	2
LB	0.00 Hz
GB	0

^{1}H NMR
CO$_2$Me
OBz
NMe
HO
169
ppm



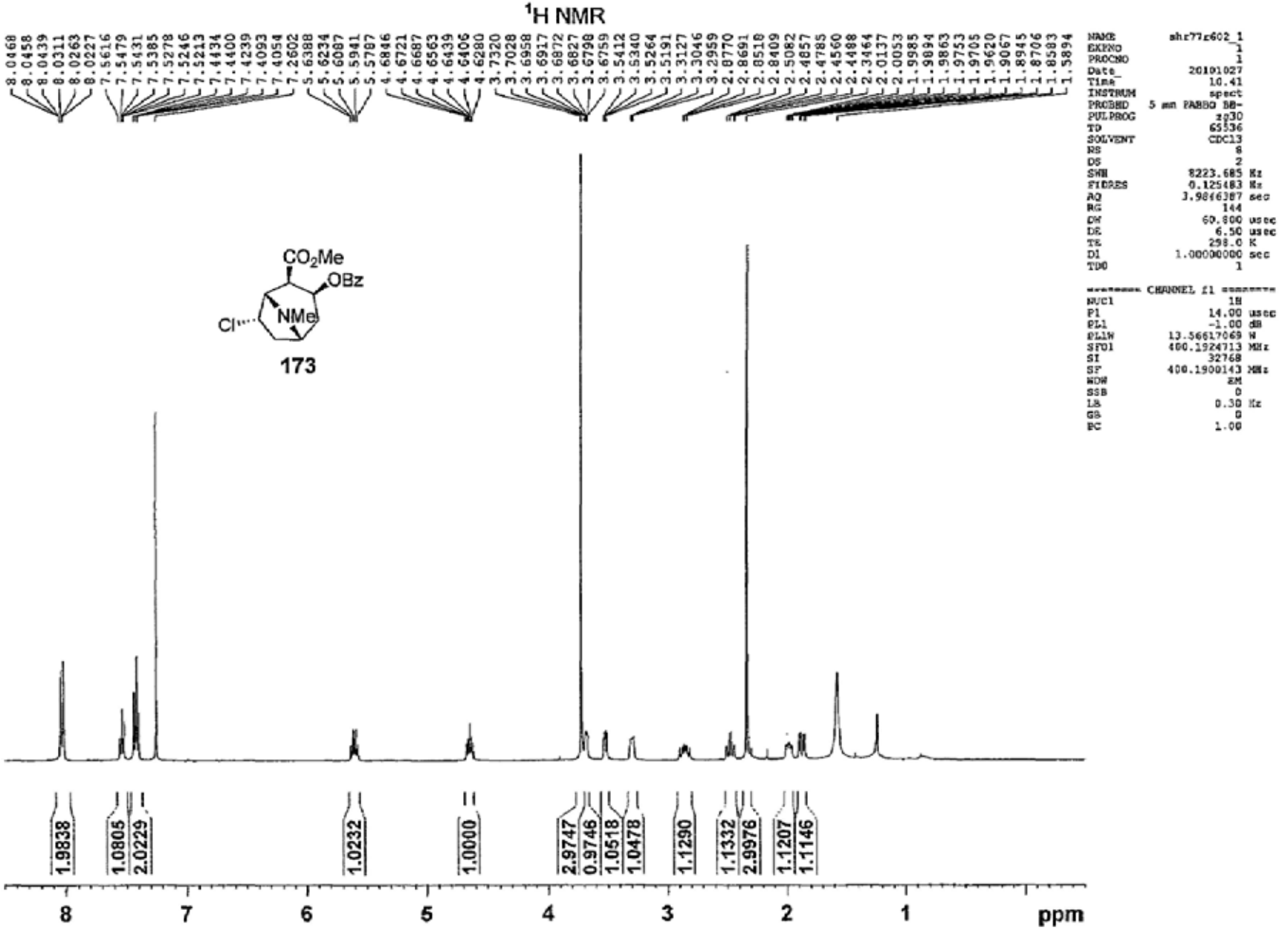
NAME	shr45carbon	
EXPNO	4	
PROCNO	1	
Date_	20100722	
Time	20.11	
INSTRUM	spect	
PROBHD	5 mm PABBO BB-	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	112	
DS	4	
SWH	24038.461	Hz
FIDRES	0.366798	Hz
AQ	1.3631988	sec
RG	181	
DW	20.800	usec
DE	6.50	usec
TE	298.5	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	9.90	usec
PL1	-2.00	dB
PL1W	55.33689499	W
SFO1	100.6379183	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	90.00	usec
PL2	-1.00	dB
PL12	15.16	dB
PL13	18.62	dB
PL2W	13.56617069	W
PL12W	0.32844096	W
PL13W	0.14806664	W
SFO2	400.1916008	MHz
SI	32768	
SF	100.6278219	MHz
WDW	EM	
SSB	0	
LB	1.00	Hz
GB	0	
PC	1.40	

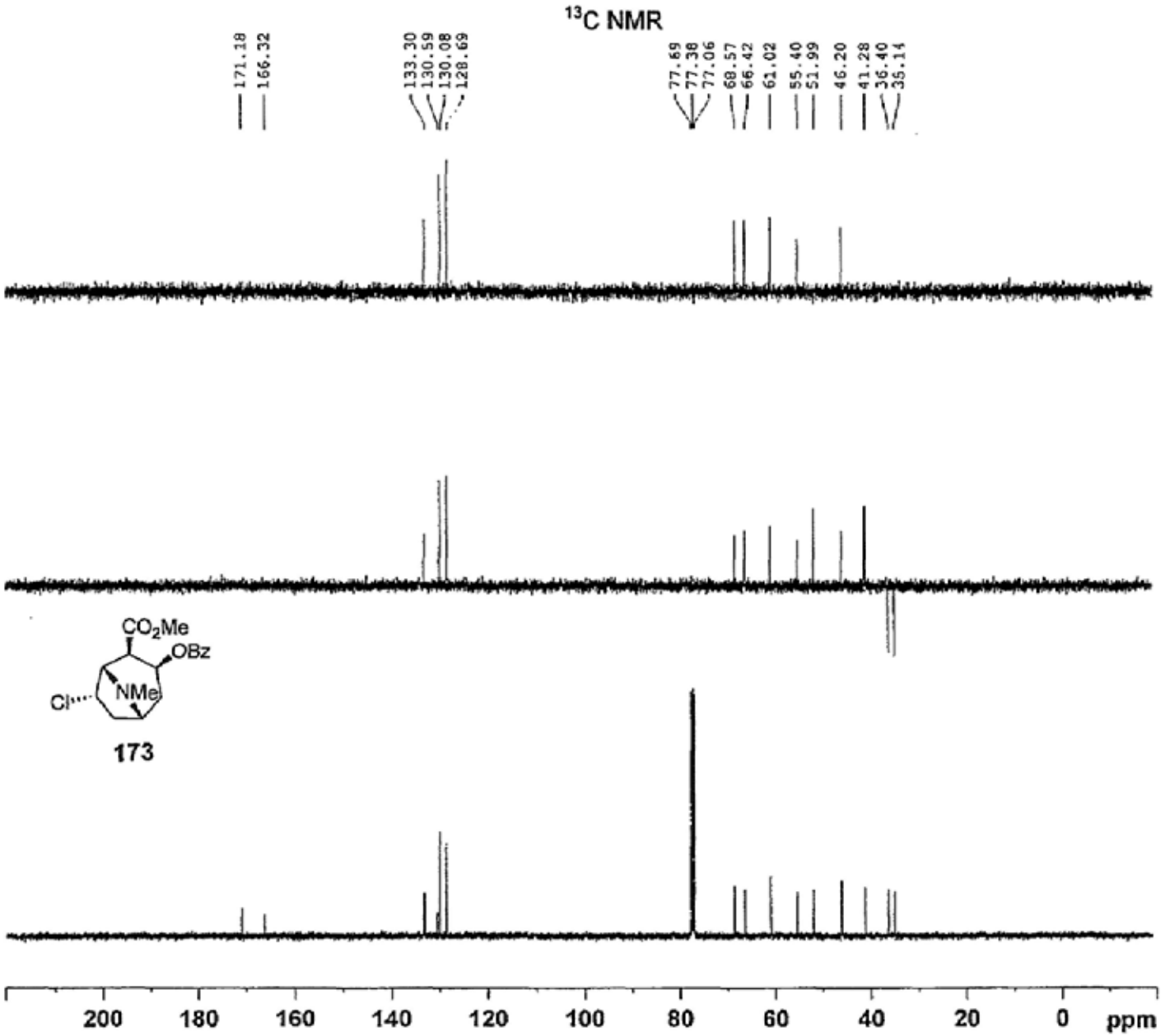

^{1}H NMR
8.0285
8.0105
7.5658
7.5472
7.5288
7.4440
7.4246
7.4056
7.2599
5.5310
5.5172
5.5034
5.4945
5.4875
5.4784
5.4727
3.8188
3.8053
3.7058
3.4019
3.3946
3.3874
3.3801
3.3383
3.3303
3.3226
3.2013
2.8156
2.7974
2.7889
2.7786
2.7711
2.7607
2.7521
2.7340
2.5997
2.5922
2.5699
2.5627
2.5396
2.5327
2.3485
1.9955
1.9871
1.9811
1.9717
1.9570
1.9504
1.9392
1.9300
1.9015
1.8929
NAME shr67
EXPNO 4
PROCNO 1
Date_ 20100527
Time 15.33
INSTRUM spect
PROBHD 5 mm PABBI 1H/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 144
DW 60.800 usec
DE 6.50 usec
TE 294.3 K
D1 1.00000000 sec
TD0 1
CHANNEL f1
NUC1 1H
P1 7.10 usec
PL1 -2.00 dB
PL1W 13.17734718 W
SFO1 400.1324710 MHz
SI 32768
SF 400.1300056 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
CO2Me
OBz
MsO
NMe
170
1.9231
0.9856
1.9593
1.9704
1.0000
3.0201
1.0161
1.0273
3.0250
1.0124
1.0713
3.0159
2.0917
8
7
6
5
4
3
2
1
ppm



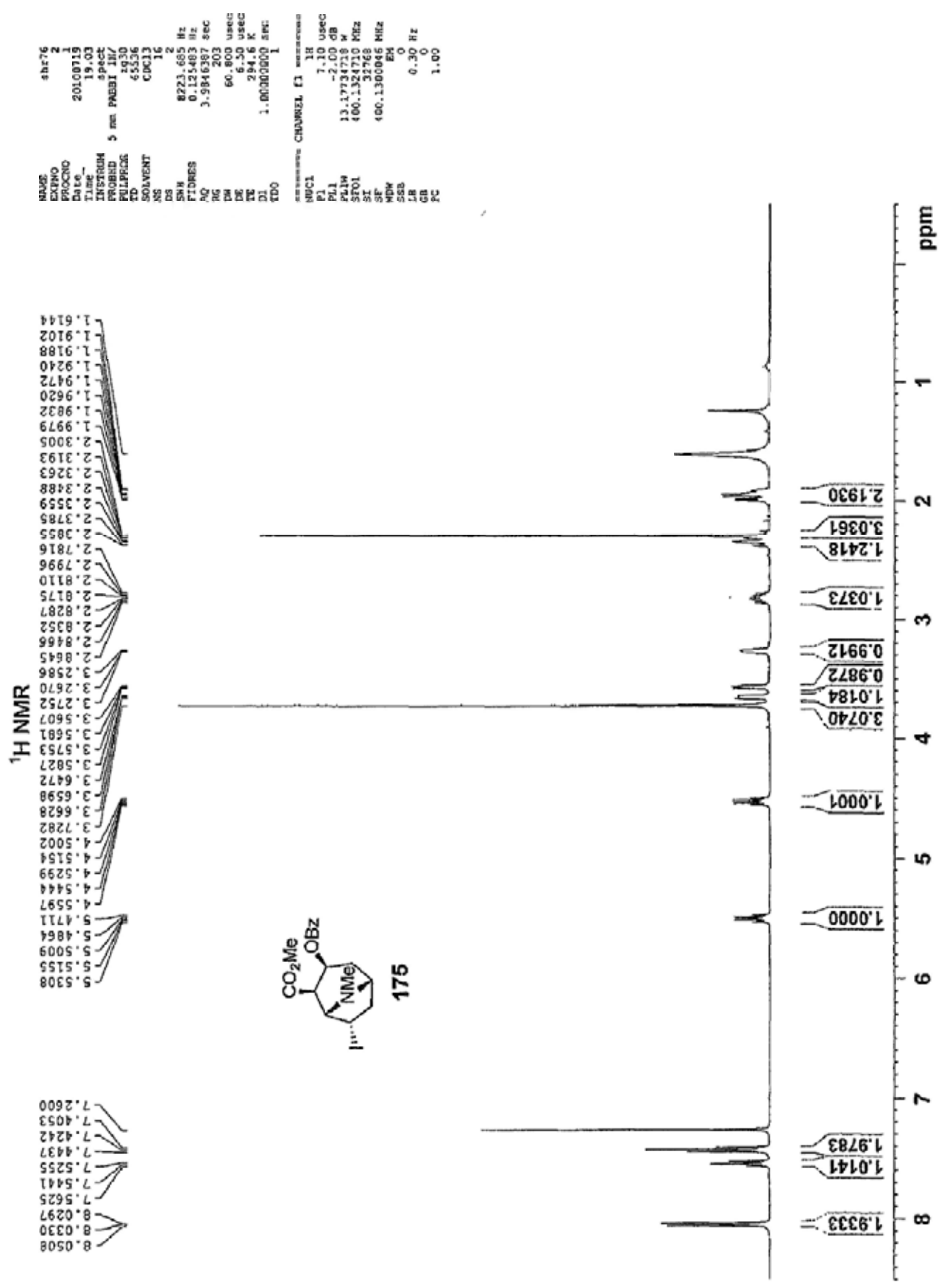
170

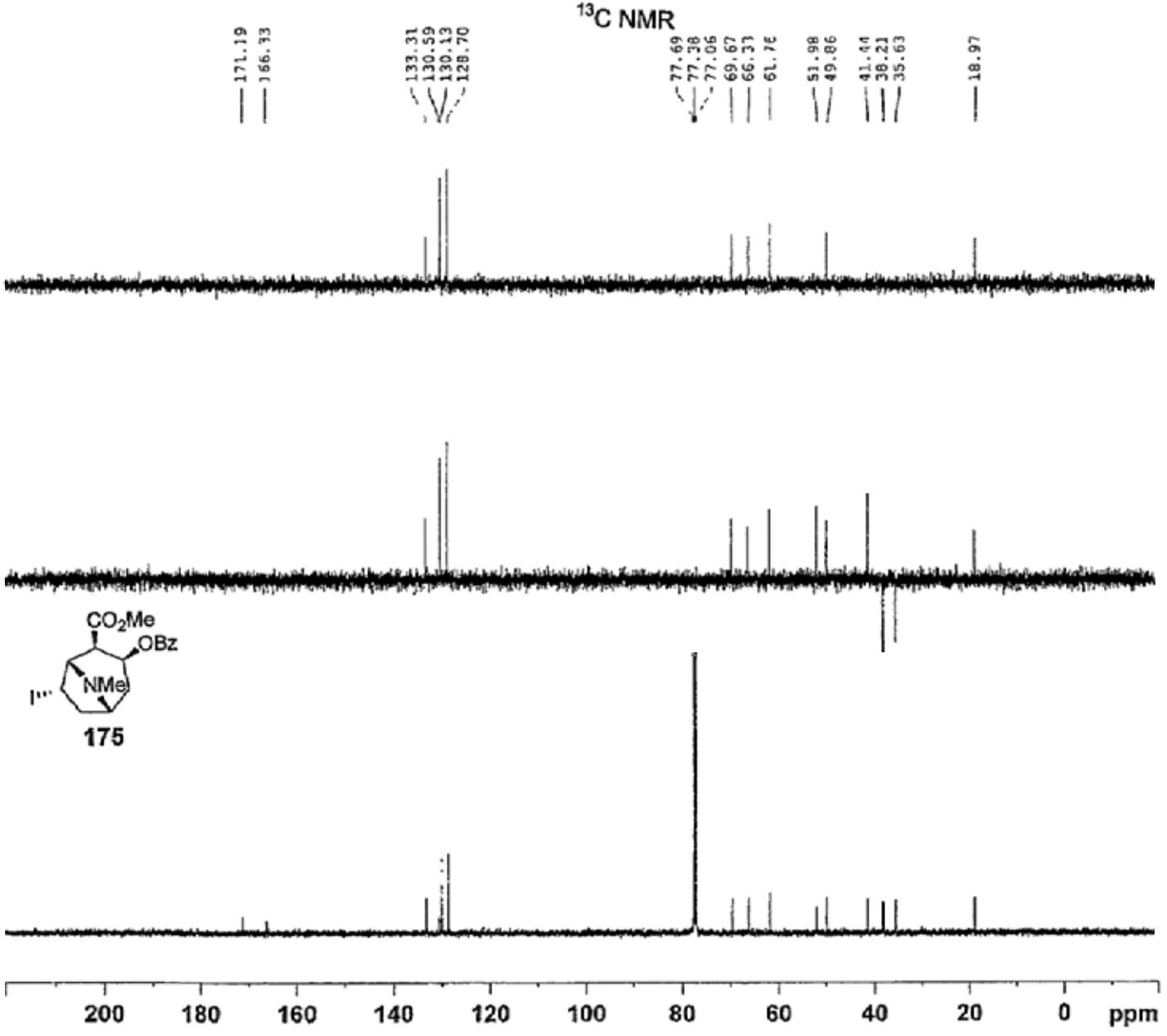
NAME	shz67carbon	
EXPNO	2	
PROCNO	1	
Date_	20100525	
Time	9.41	
INSTRUM	spect	
PROBHD	5 mm PABBI 1H/	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	74	
DS	4	
SWH	24038.461	Hz
FIDRES	0.366798	Hz
AQ	1.3631968	sec
RG	203	
DW	20.800	usec
DE	6.50	usec
TE	294.7	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
-------- CHANNEL f1 --------		
NUC1	13C	
P1	14.50	usec
PL1	-4.00	dB
PL1W	90.22689819	W
SFO1	100.6228298	MHz
-------- CHANNEL f2 --------		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	80.00	usec
PL2	-2.00	dB
PL12	18.80	dB
PL13	18.80	dB
PL2W	13.17734718	W
PL12W	0.10960442	W
PL13W	0.10960442	W
SFO2	400.1316005	MHz
SI	32768	
SF	100.6127368	MHz
WDW	EM	
SSB	0	
LB	1.00	Hz
GB	0	
PC	1.40	


^{1}H NMR
8.0468
8.0458
8.0439
8.0311
8.0263
8.0227
7.5616
7.5479
7.5431
7.5385
7.5278
7.5246
7.5213
7.4434
7.4400
7.4239
7.4093
7.4054
7.2602
5.6388
5.6234
5.6087
5.5941
5.5787
4.6846
4.6721
4.6687
4.6563
4.6439
4.6406
4.6280
3.7320
3.7028
3.6958
3.6917
3.6872
3.6827
3.6798
3.6759
3.5412
3.5340
3.5264
3.5191
3.3127
3.3046
3.2959
2.8770
2.8691
2.8518
2.8409
2.5082
2.4857
2.4785
2.4560
2.4488
2.3464
2.0137
2.0053
1.9985
1.9894
1.9863
1.9753
1.9705
1.9620
1.9067
1.8945
1.8706
1.8583
1.5894
NAME shr77z602_1
EXPNO 1
PROCNO 1
Date_ 20191027
Time 10.41
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9866387 sec
RG 144
DW 60.800 usec
DE 6.50 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1
CHANNEL f1
NUC1 1H
P1 14.00 usec
PL1 -1.00 dB
PLLW 13.56617069 W
SFO1 400.1924713 MHz
SI 32768
SF 400.1900143 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
CO2Me
OBz
NMe
Cl
173
1.9838
1.0805
2.0229
1.0232
1.0000
2.9747
0.9746
1.0518
1.0478
1.1290
1.1332
2.9976
1.1207
1.1146
8
7
6
5
4
3
2
1
ppm

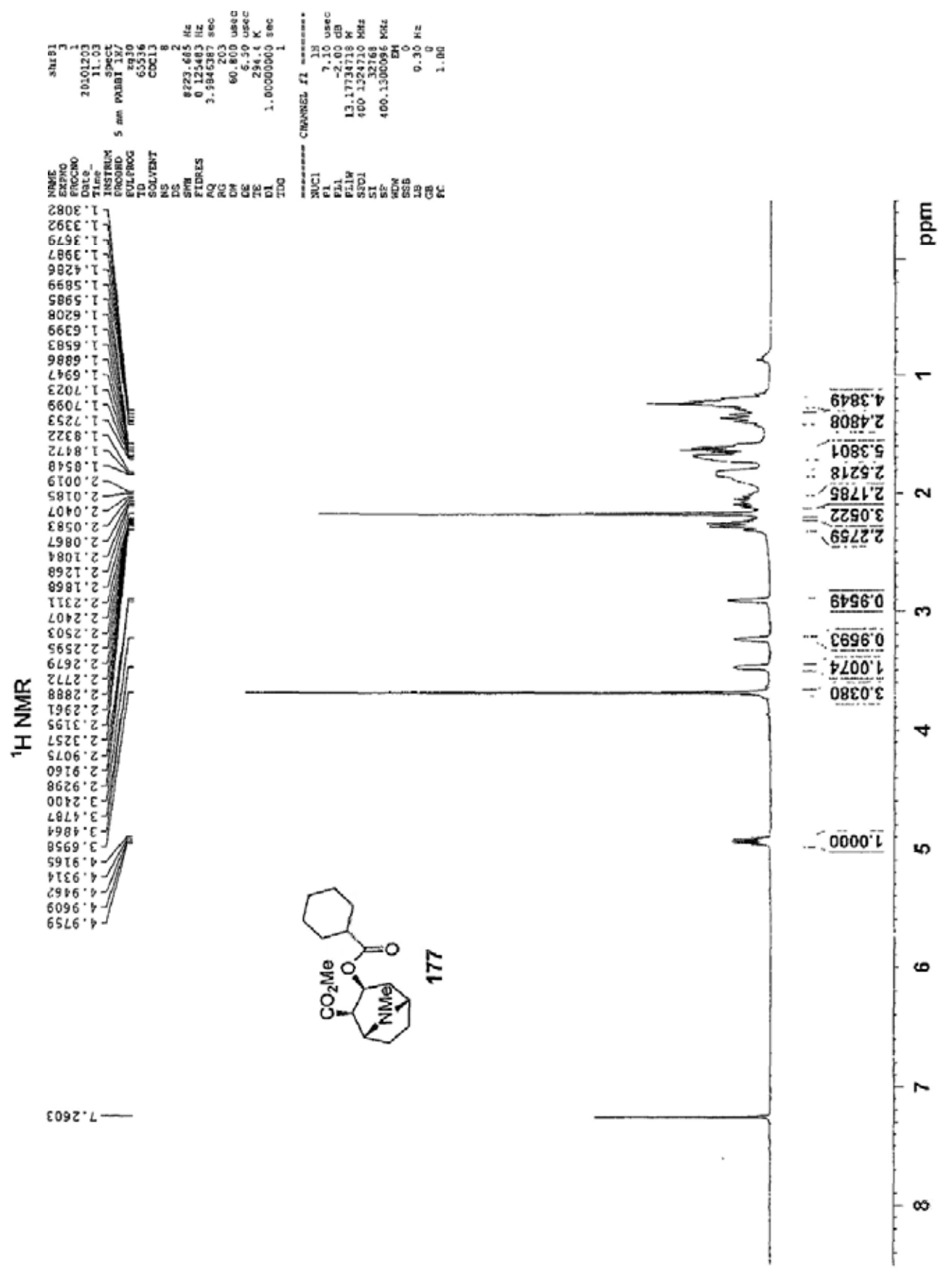


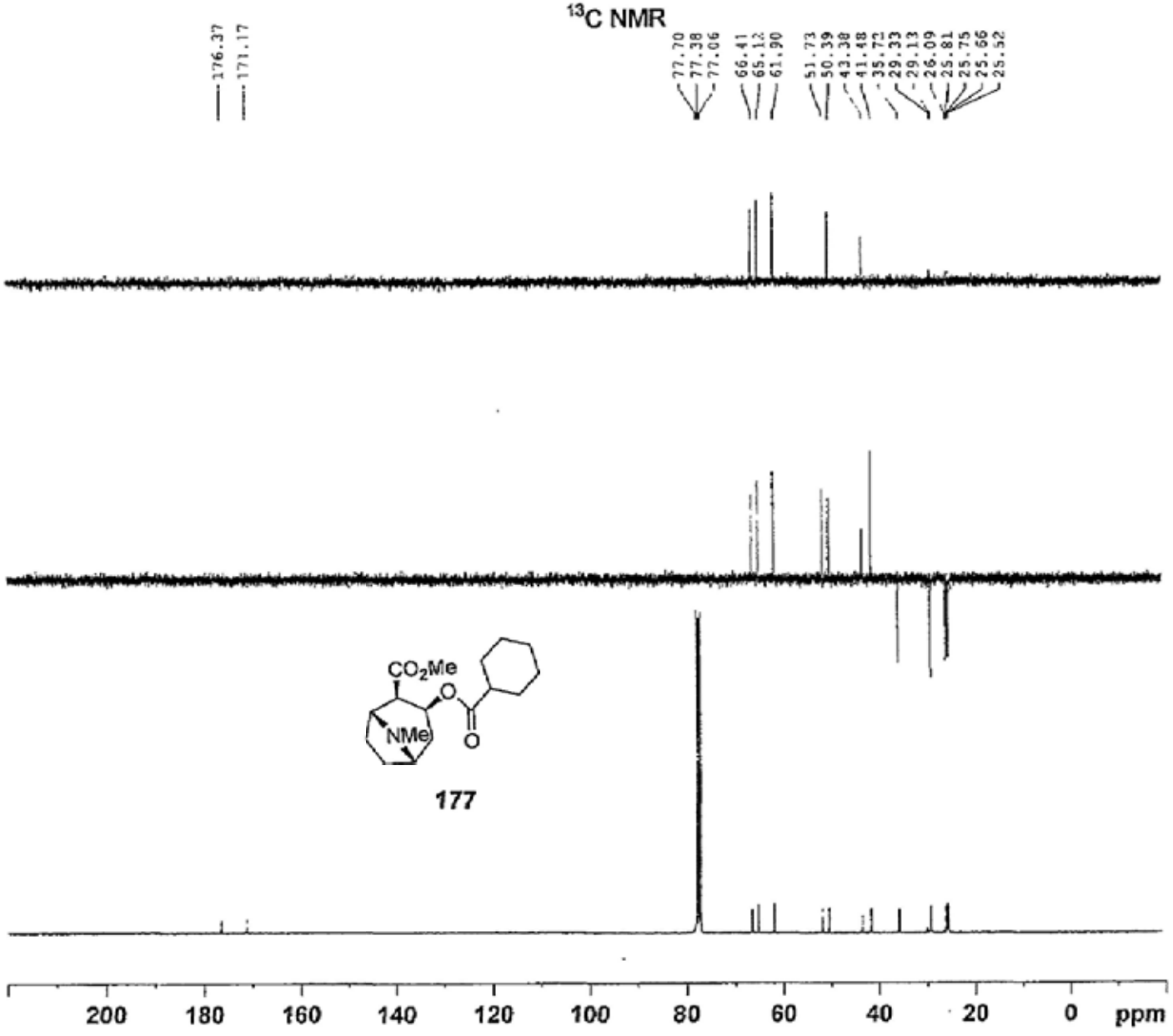
NAME	shr77carbon
EXPNO	1
PROCNO	1
Date_	20100528
Time	9.35
INSTRUM	spect
PROBHD	5 mm PABBI 1H/
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	201
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	296.9 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
========	CHANNEL f1 ========
NUC1	13C
P1	14.50 usec
PL1	-4.00 dB
PL1W	90.22689819 W
SFO1	100.6228298 MHz
========	CHANNEL f2 ========
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	-2.00 dB
PL12	18.80 dB
PL13	18.80 dB
PL2W	13.17734718 W
PL12W	0.10960442 W
PL13W	0.10960442 W
SFO2	400.1316005 MHz
SI	32768
SF	100.6127346 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40


^{1}H NMR
CO2Me
OBz
NMe
175
ppm

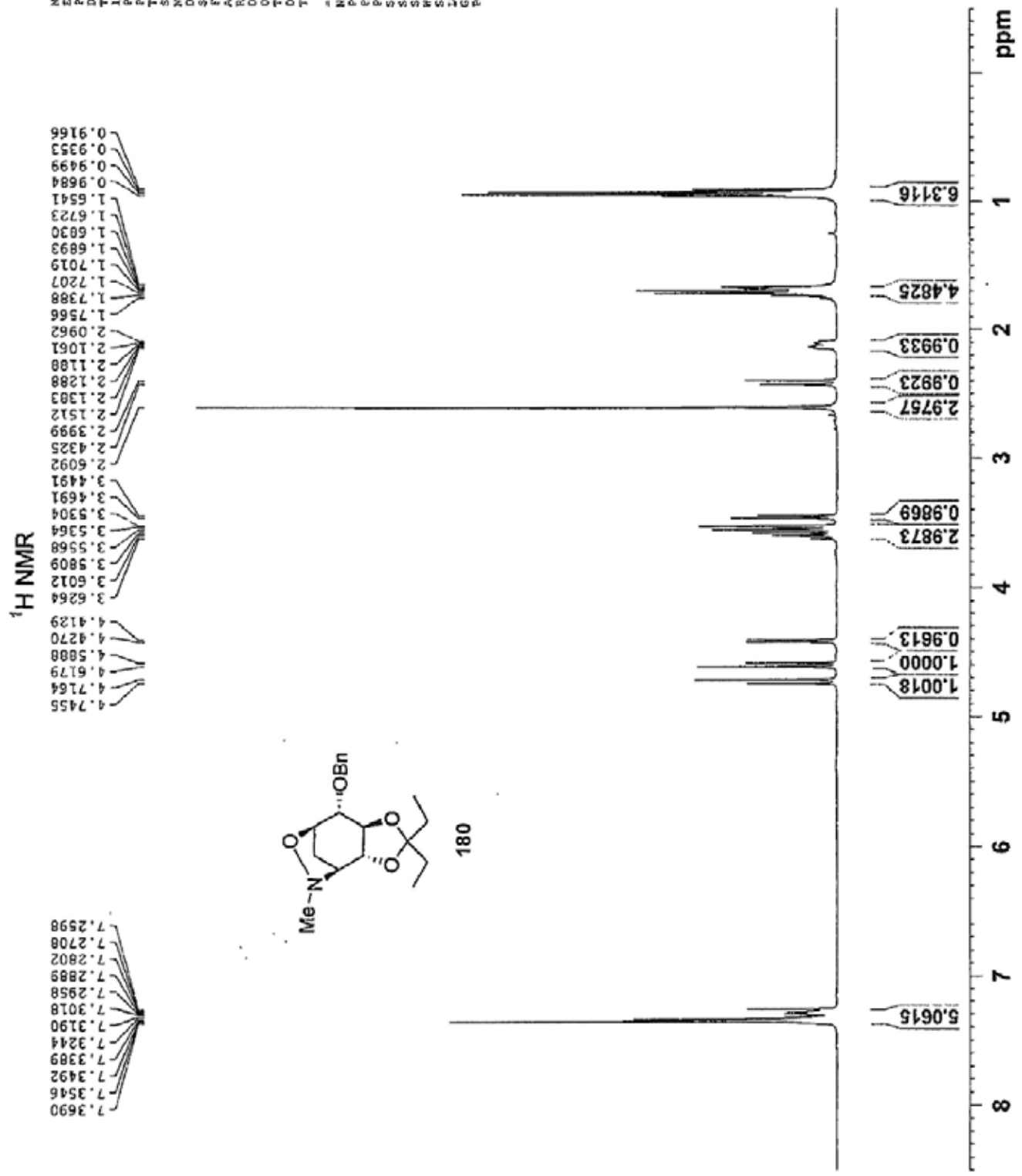


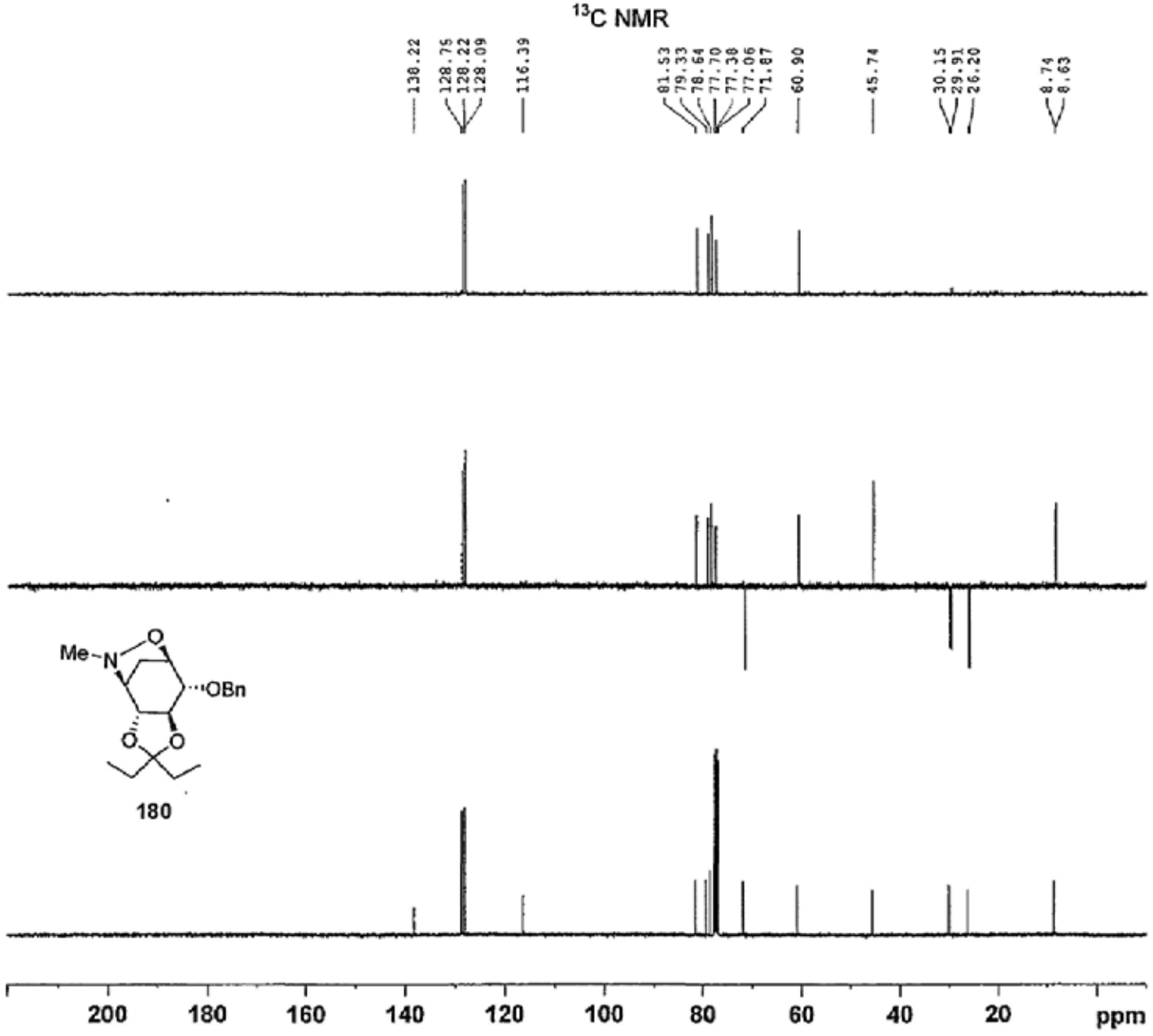
NAME	shr76carbon
EXPNO	2
PROCNO	1
Date_	20101022
Time	11.18
INSTRUM	spect
PROBHD	5 mm PADUL 13C
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	348
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	295.7 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.68 usec
PL1	-0.60 dB
PL1W	41.24164963 W
SFO1	100.6228298 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	90.00 usec
PL2	0.00 dB
PL12	15.66 dB
PL13	15.92 dB
PL2W	8.31434441 W
PL12W	0.22585411 W
PL13W	0.12272963 W
SFO2	400.1316005 MHz
SI	32768
SF	100.6127338 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40


1H NMR
CO2Me
NMe
177
ppm

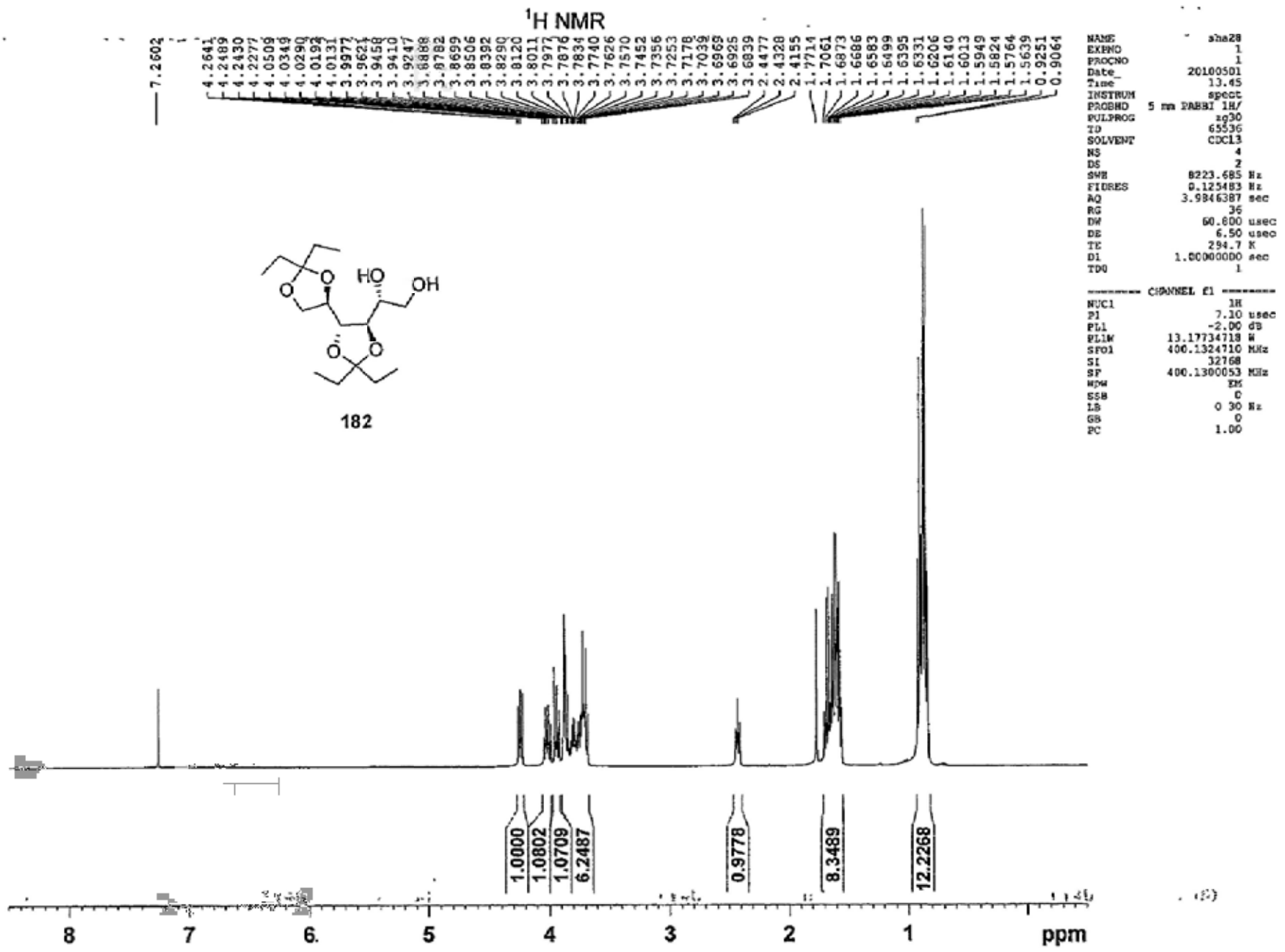


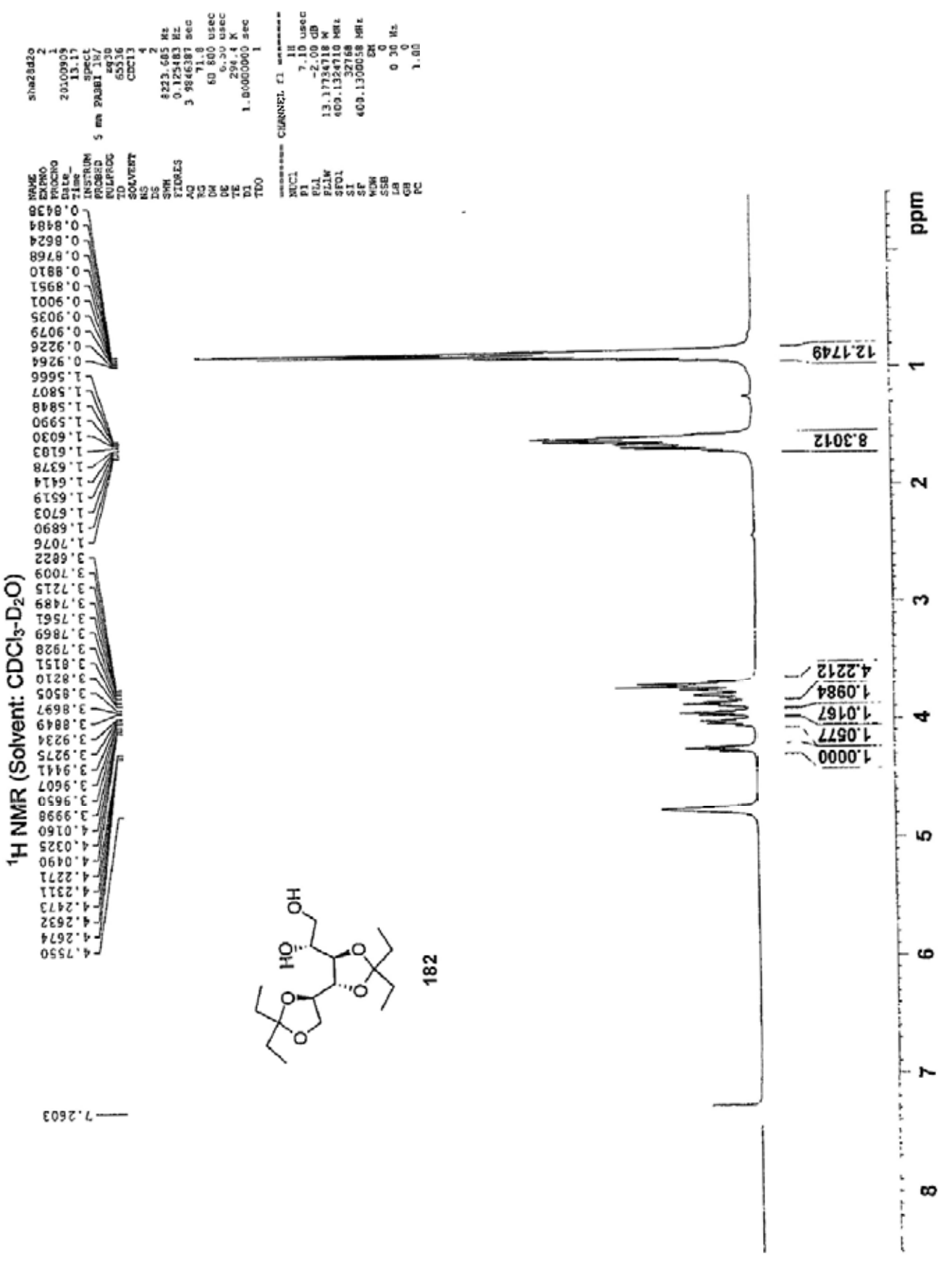
NAME	shrmicarbon
EXPNO	3
PROCNO	1
Date_	20101203
Time	22.48
INSTRUM	spect
PROBHD	5 mm PADUL 13C
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	7000
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	295.4 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
========	CHANNEL f1 ========
NUC1	13C
P1	9.68 usec
PL1	-0.60 dB
PL1W	41.24164963 W
SFO1	100.6228298 MHz
========	CHANNEL f2 ========
CPDPRG2	waltz16
NUC2	1H
PCPD2	90.00 usec
PL2	0.00 dB
PL12	15.66 dB
PL13	15.92 dB
PL2W	8.31434441 W
PL12W	0.22585411 W
PL13W	0.21272963 W
SFO2	400.1316005 MHz
SI	32768
SF	100.6127331 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40


^{1}H NMR
Me
N
OBn
180
ppm

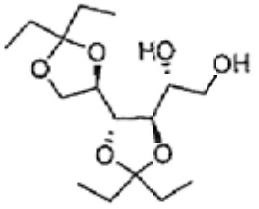


NAME	sha36carbon
EXPNO	1
PROCNO	1
Date_	20100706
Time	16.04
INSTRUM	spect
PROBHD	5 mm PADUL 13C
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	187
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	295.4 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
-------- CHANNEL f1 --------	
NUC1	13C
P1	9.68 usec
PL1	-0.60 dB
PL1W	41.24164963 W
SFO1	100.6228298 MHz
-------- CHANNEL f2 --------	
CPDPRG2	waltz16
NUC2	1H
PCPD2	90.00 usec
PL2	0.00 dB
PL12	15.66 dB
PL13	15.92 dB
PL2W	8.31434441 W
PL12W	0.22585411 W
PL13W	0.21272963 W
SFO2	400.1316005 MHz
SI	32768
SF	100.6127346 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40


^{1}H NMR
7.2602
4.2641
4.2189
4.2430
4.2277
4.0509
4.0349
4.0290
4.0192
4.0131
3.9977
3.9621
3.9458
3.9410
3.9247
3.8888
3.8782
3.8699
3.8506
3.8392
3.8290
3.8120
3.8011
3.7977
3.7876
3.7834
3.7740
3.7626
3.7570
3.7452
3.7356
3.7253
3.7178
3.7039
3.6969
3.6925
3.6839
2.4477
2.4328
2.4155
1.7714
1.7061
1.6873
1.6686
1.6583
1.6499
1.6395
1.6331
1.6206
1.6140
1.6013
1.5949
1.5824
1.5764
1.5639
0.9251
0.9064
NAME sha28
EXPNO 1
PROCNO 1
Date_ 20100501
Time 13.45
INSTRUM spect
PROBHD 5 mm DABBI 1H/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 4
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 36
DW 60.800 usec
DE 6.50 usec
TE 294.7 K
D1 1.00000000 sec
TD0 1
CHANNEL f1
NUC1 1H
P1 7.10 usec
PL1 -2.00 dB
PL1W 13.17734718 W
SFO1 400.1324710 MHz
SI 32768
SF 400.1300053 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
HO
OH
O
O
O
O
182
1.0000
1.0802
1.0709
6.2487
0.9778
8.3489
12.2268
8
7
6
5
4
3
2
1
ppm

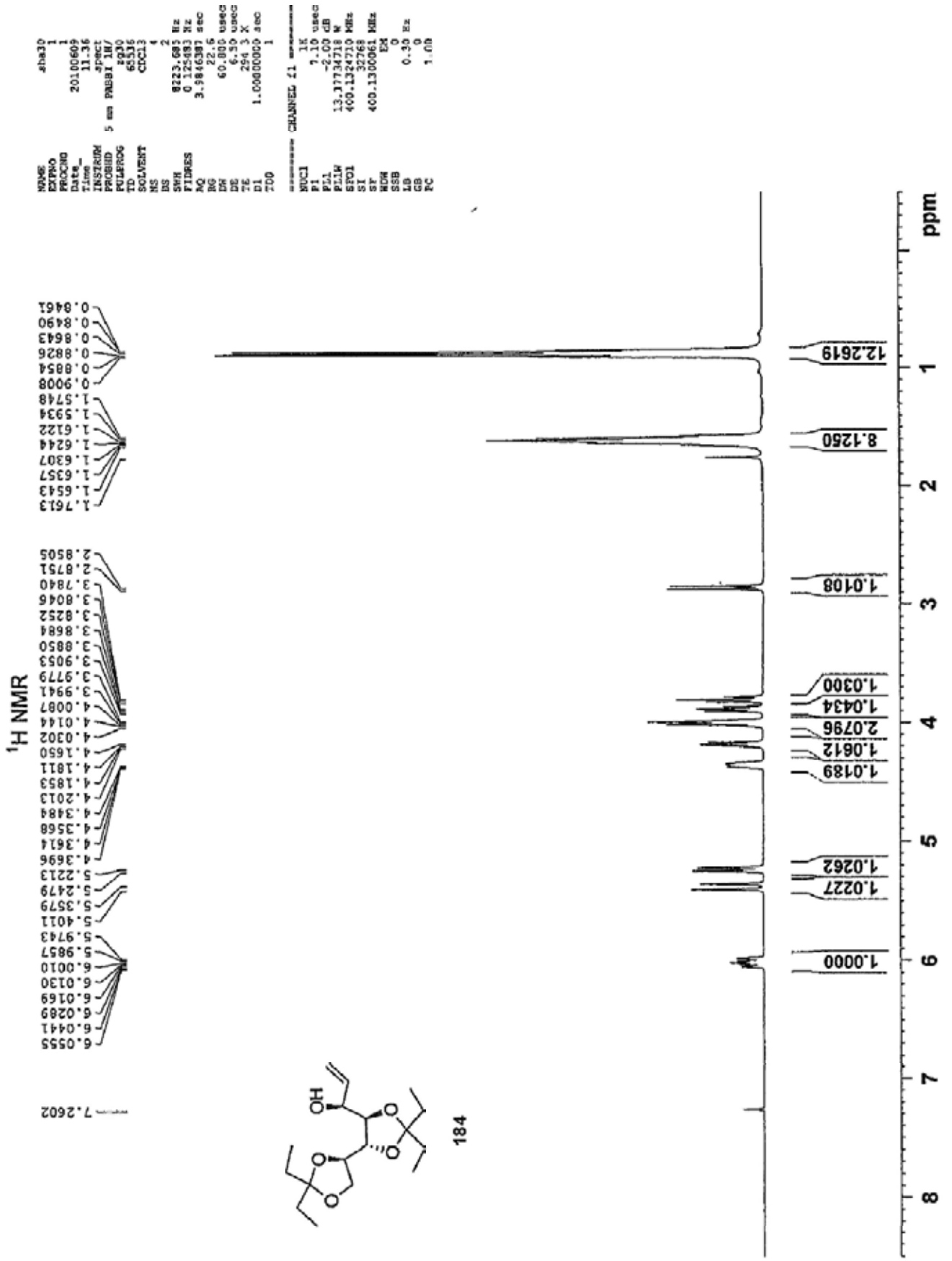

^{1}H NMR (Solvent: $CDCl_3$-D_2O)
182
12.1749
8.3012
4.2212
1.0984
1.0167
1.0577
1.0000
7.2603
ppm

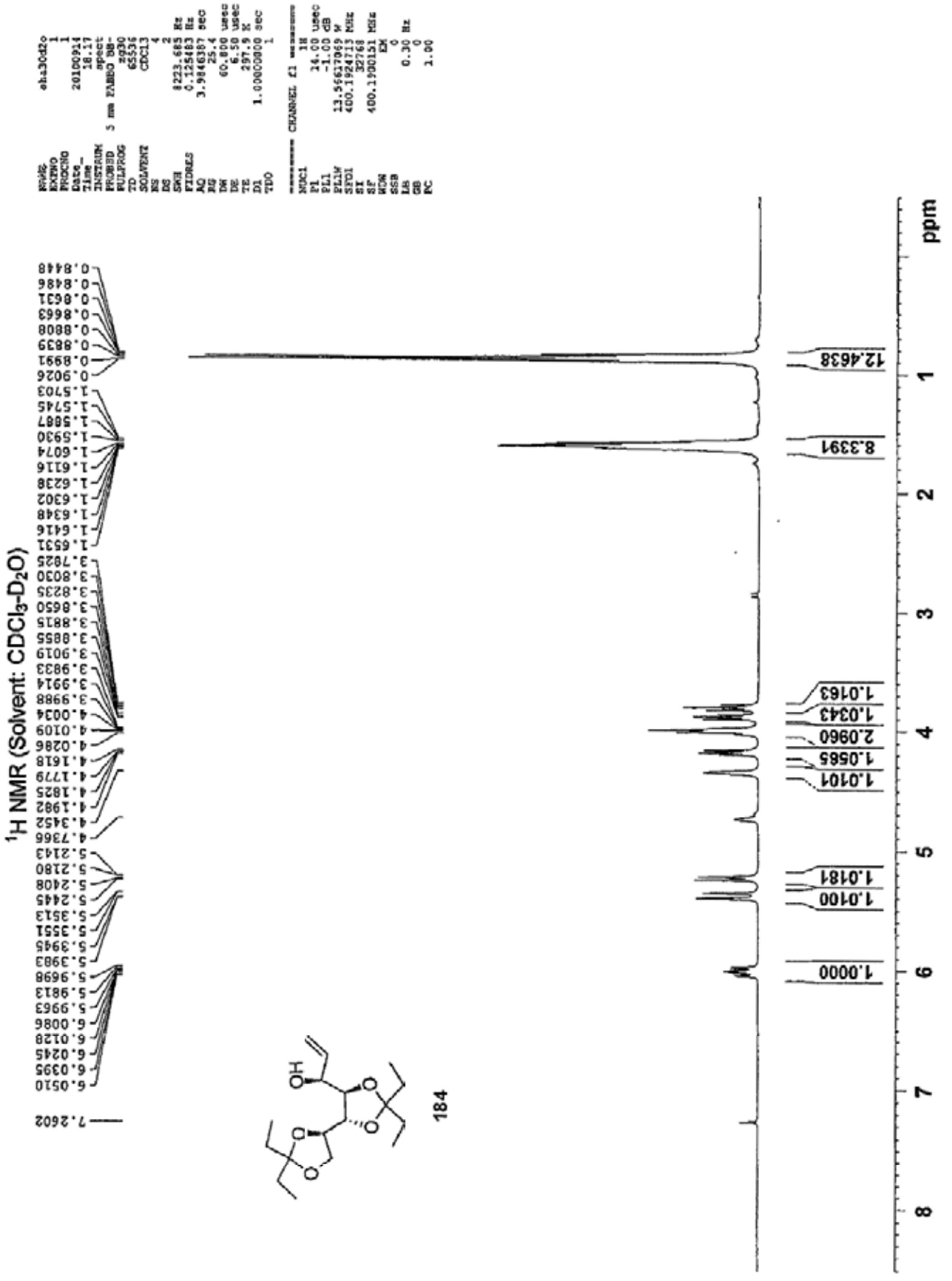
^{13}C NMR



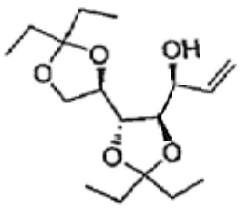
182

NAME	sha28carbon
EXPNO	1
PROCNO	1
Date_	20100301
Time	13.51
INSTRUM	spect
PROBHD	5 mm PABBI 1H/
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	178
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	295.0 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	14.50 usec
PL1	-4.00 dB
PL1W	90.22689819 W
SFO1	100.5228298 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	-2.00 dB
PL12	18.80 dB
PL13	18.80 dB
PL2W	13.17734718 W
PL12W	0.10960442 W
PL13W	0.10960442 W
SFO2	400.1316005 MHz
SI	32768
SF	100.6127338 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40


NAME sha30
EXPNO 1
PROCNO 1
Date_ 20100609
Time 11.36
INSTRUM spect
PROBHD 5 mm PABBI 1H/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 4
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 22.6
DW 60.800 usec
DE 6.50 usec
TE 294.3 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 7.10 usec
PL1 -2.00 dB
PL1W 13.17734718 W
SFO1 400.1324710 MHz
SI 32768
SF 400.1300061 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
ppm
1H NMR
12.2619
8.1250
1.0108
1.0300
1.0434
2.0796
1.0612
1.0189
1.0262
1.0227
1.0000
184


^{1}H NMR (Solvent: $CDCl_3$-D_2O)
ppm
184
12.4638
8.3391
1.0163
1.0343
2.0960
1.0585
1.0101
1.0181
1.0100
1.0000

^{13}C NMR



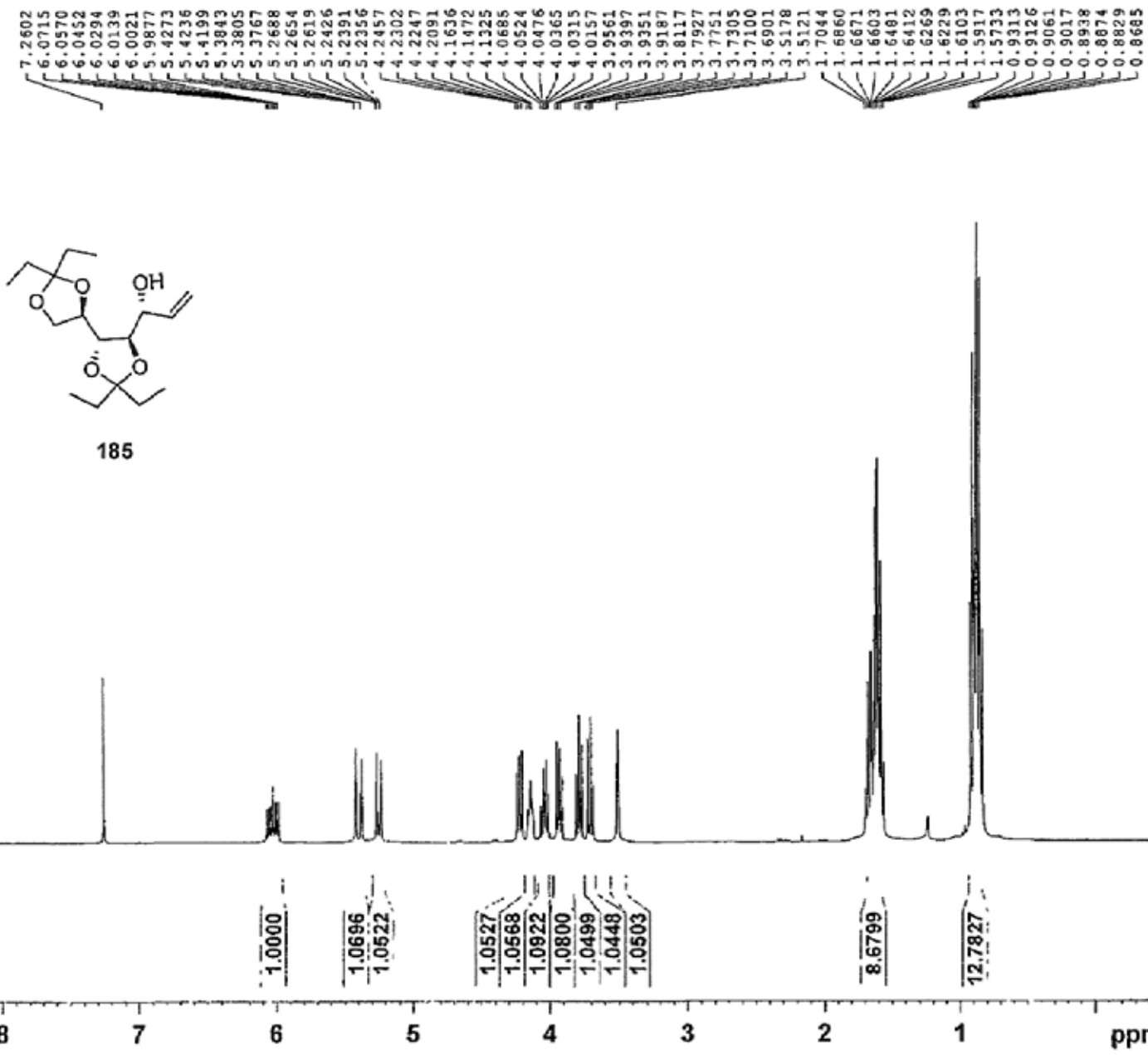
184

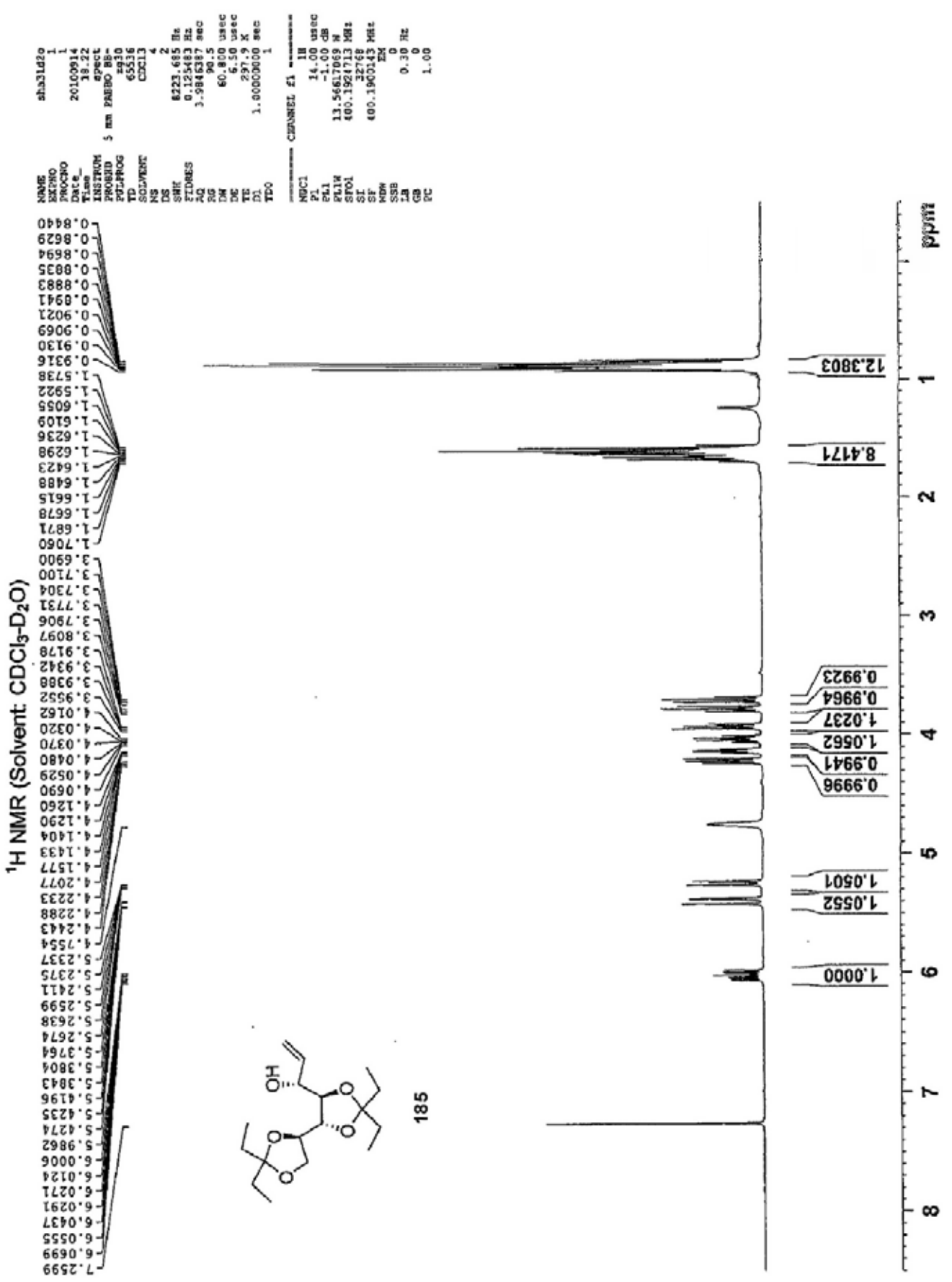
137.77
116.09
114.36
113.38
83.27
78.01
77.69
77.38
77.31
77.06
71.14
69.07
30.53
30.50
29.83
29.10
8.51
8.44
8.40
8.36

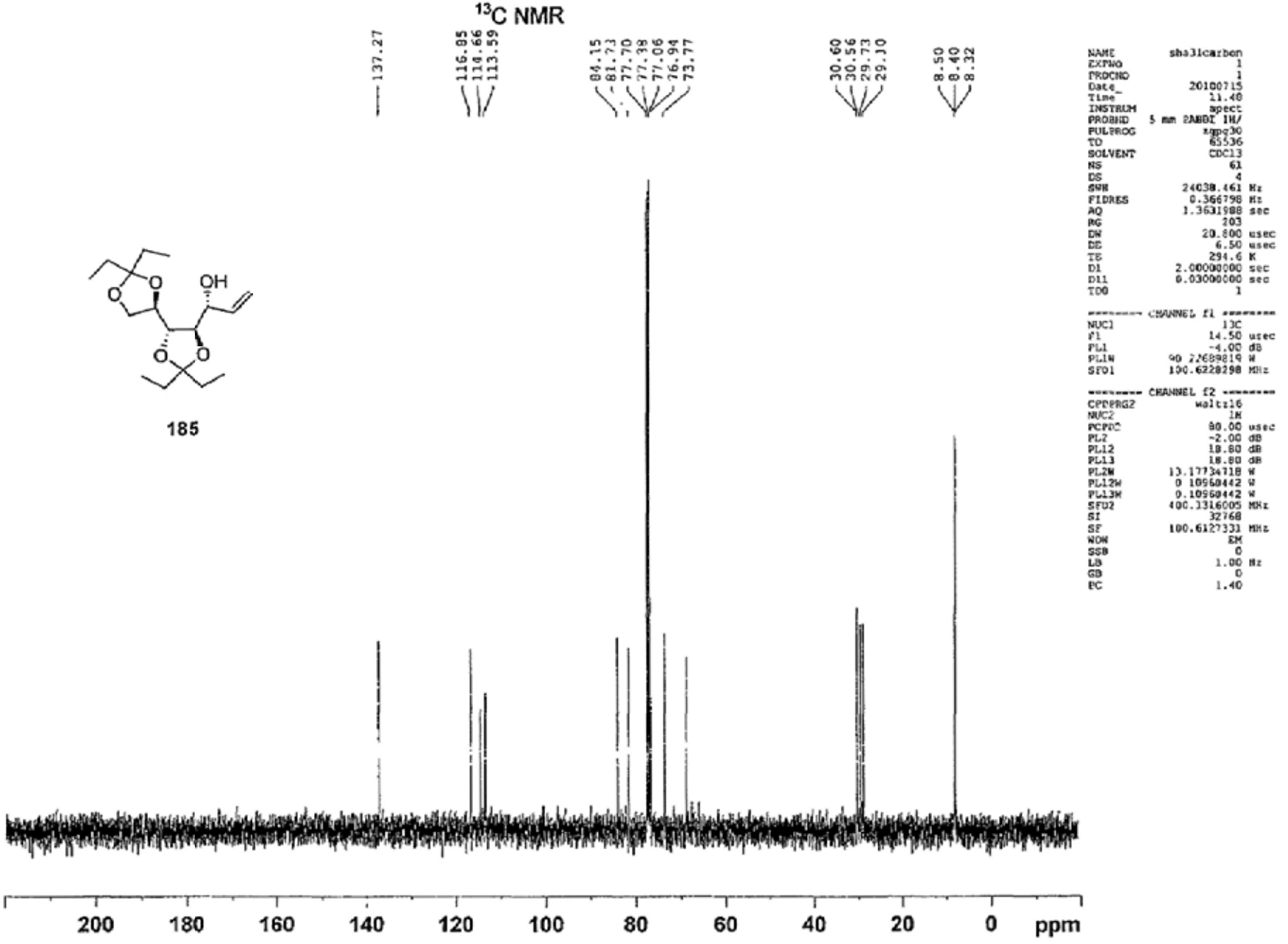
NAME	sha30cazban
EXPNO	1
PROCNO	1
Date_	20100609
Time	11.44
INSTRUM	spect
PROBHD	5 mm PABBI 1H/
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	104
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	294.6 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	14.50 usec
PL1	-4.00 dB
PL1W	90.22689819 W
SFO1	100.6228298 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	-2.00 dB
PL12	18.80 dB
PL13	18.80 dB
PL2W	13.17734718 W
PL12W	0.10960442 W
PL13W	0.10960442 W
SFO2	400.1316005 MHz
SI	32768
SF	100.6127346 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

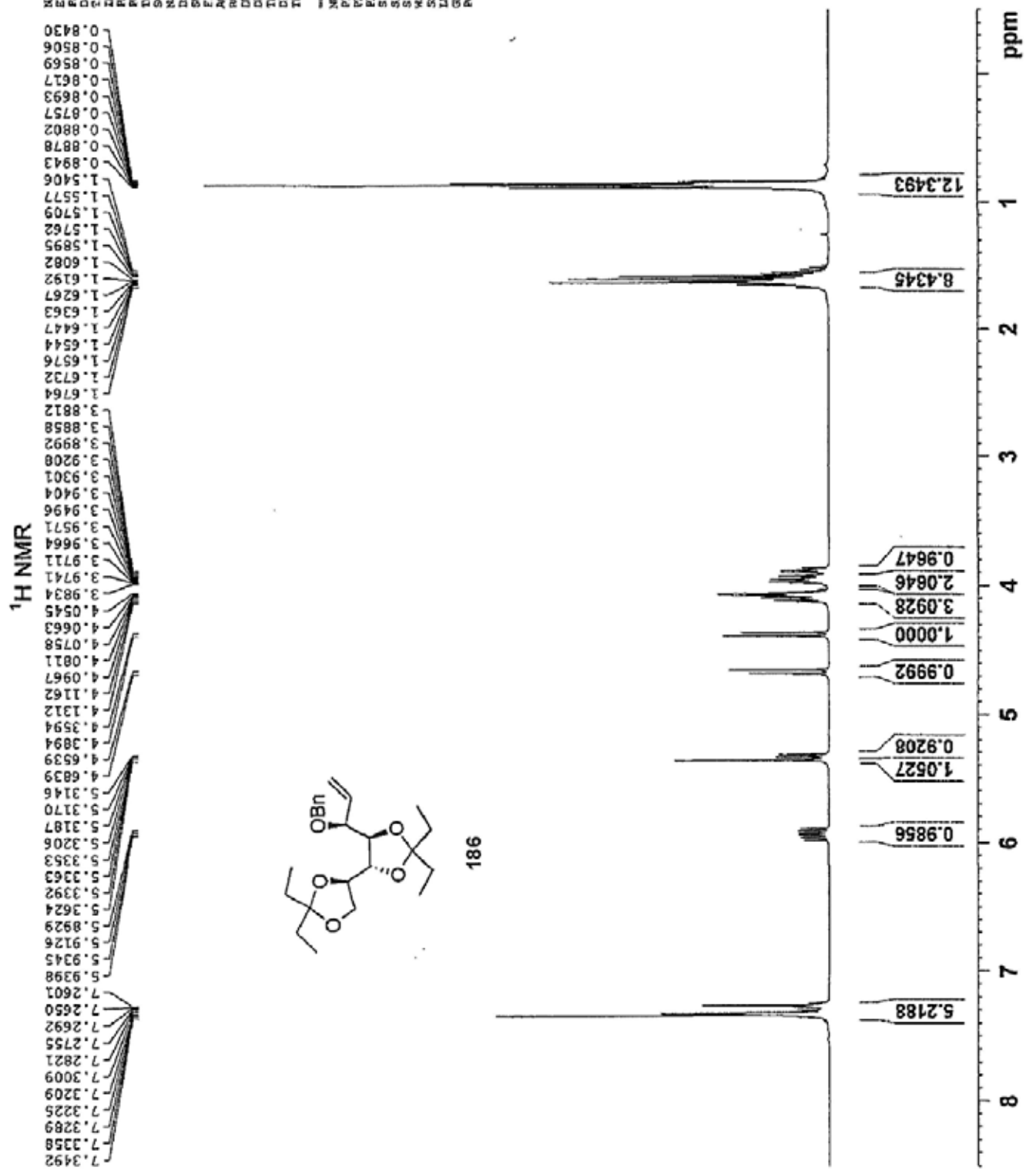
200 180 160 140 120 100 80 60 40 20 0 ppm

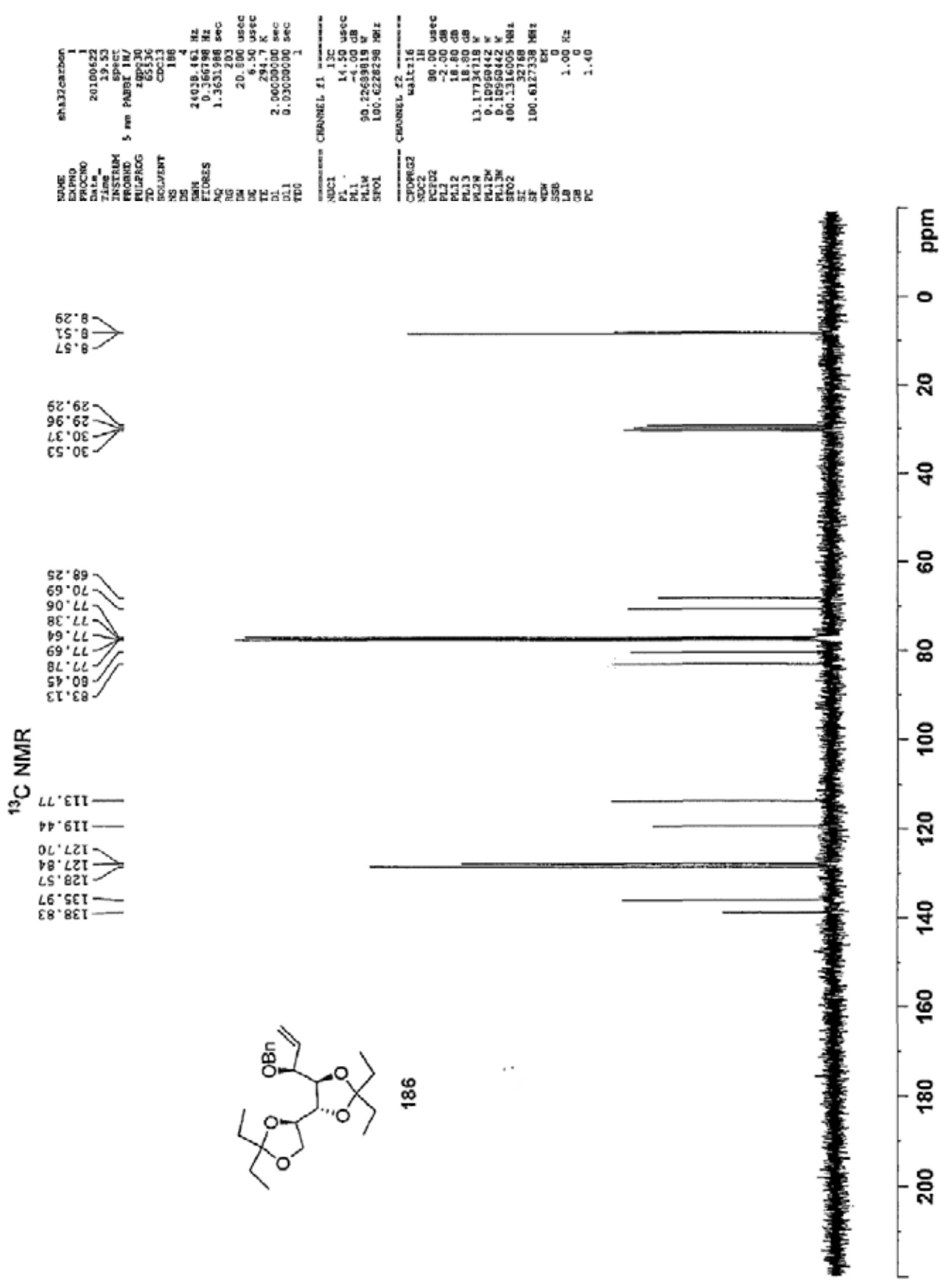
^{1}H NMR

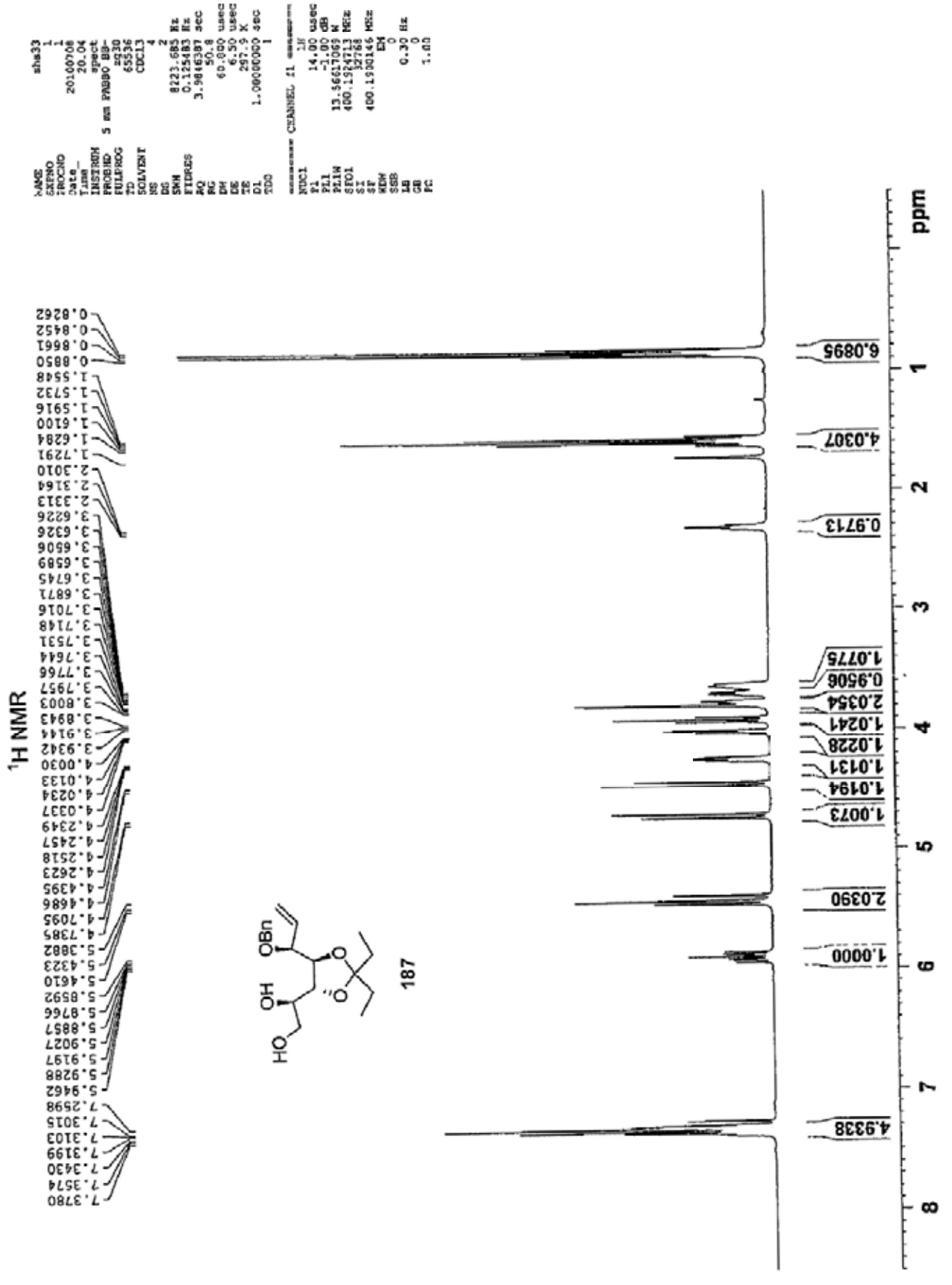

7.2602
6.0715
6.0570
6.0452
6.0294
6.0139
6.0021
5.9877
5.4273
5.4236
5.4199
5.3843
5.3805
5.3767
5.2688
5.2654
5.2619
5.2426
5.2391
5.2356
4.2457
4.2302
4.2247
4.2091
4.1636
4.1472
4.1325
4.0685
4.0524
4.0476
4.0365
4.0315
4.0157
3.9561
3.9397
3.9351
3.9187
3.8117
3.7927
3.7751
3.7305
3.7100
3.6901
3.5178
3.5121
1.7044
1.6860
1.6671
1.6603
1.6481
1.6412
1.6269
1.6229
1.6103
1.5917
1.5733
0.9313
0.9126
0.9061
0.9017
0.8938
0.8874
0.8829
0.8685
OH
O
O
O
O
185
NAME sba31
EXPNO 2
PROCNO 1
Date_ 20100812
Time 11 02
INSTRUM spect
PROBHD 5 mm PABBI 1H/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 80.6
DW 60.800 usec
DE 6.50 usec
TE 294.2 K
D1 1.00000000 sec
TD0 1
CHANNEL f1
NUC1 1H
P1 7.10 usec
PL1 -2.00 dB
PL1W 13.17734718 W
SFO1 400.1324710 MHz
SI 32768
SF 400.1300043 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
1.0000
1.0696
1.0522
1.0527
1.0568
1.0922
1.0800
1.0499
1.0448
1.0503
8.6799
12.7827
8
7
6
5
4
3
2
1
ppm

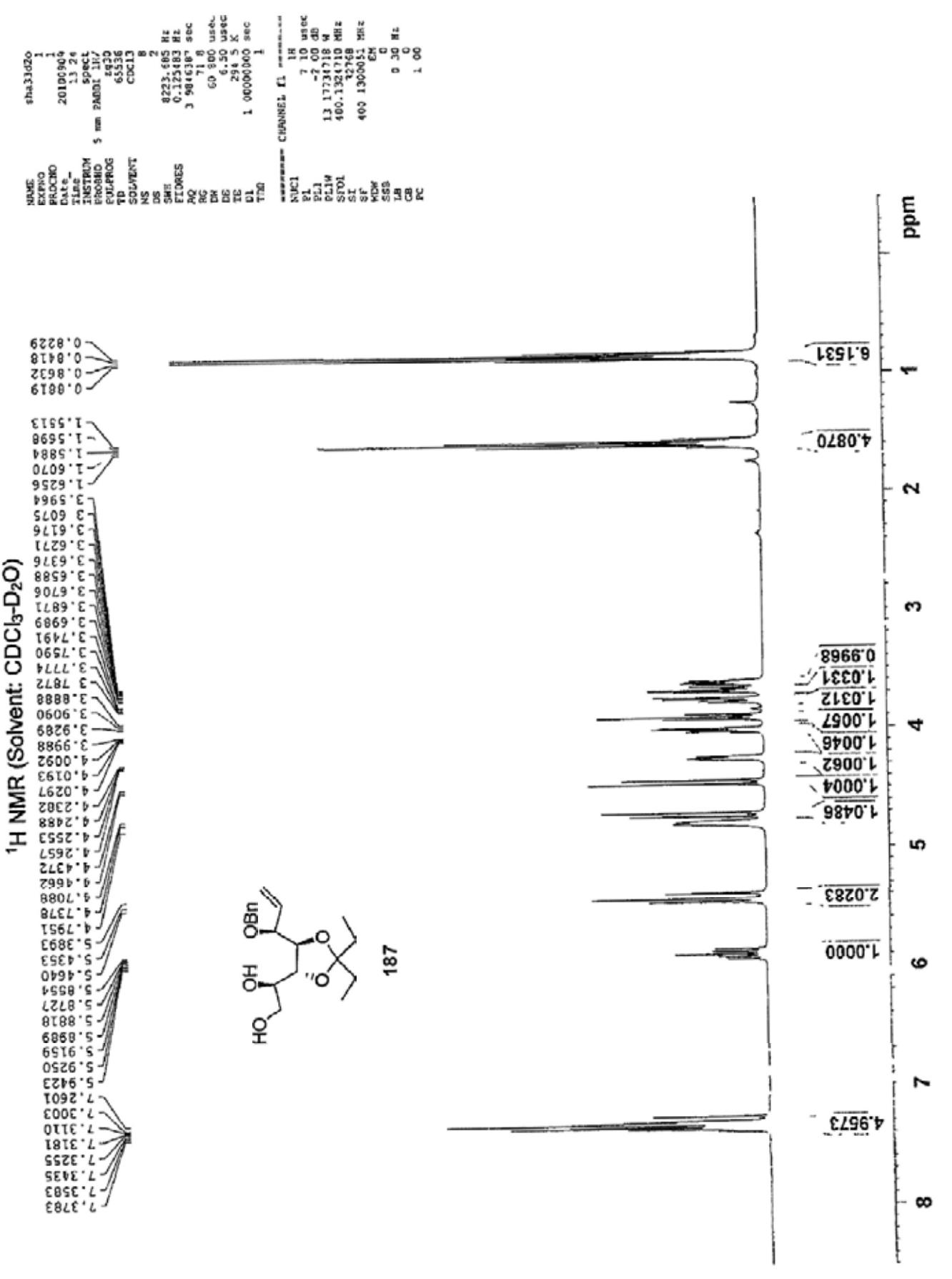

^{1}H NMR (Solvent: $CDCl_3$-D_2O)
185
12.3803
8.4171
0.9923
0.9964
1.0237
1.0562
0.9941
0.9996
1.0501
1.0552
1.0000
ppm

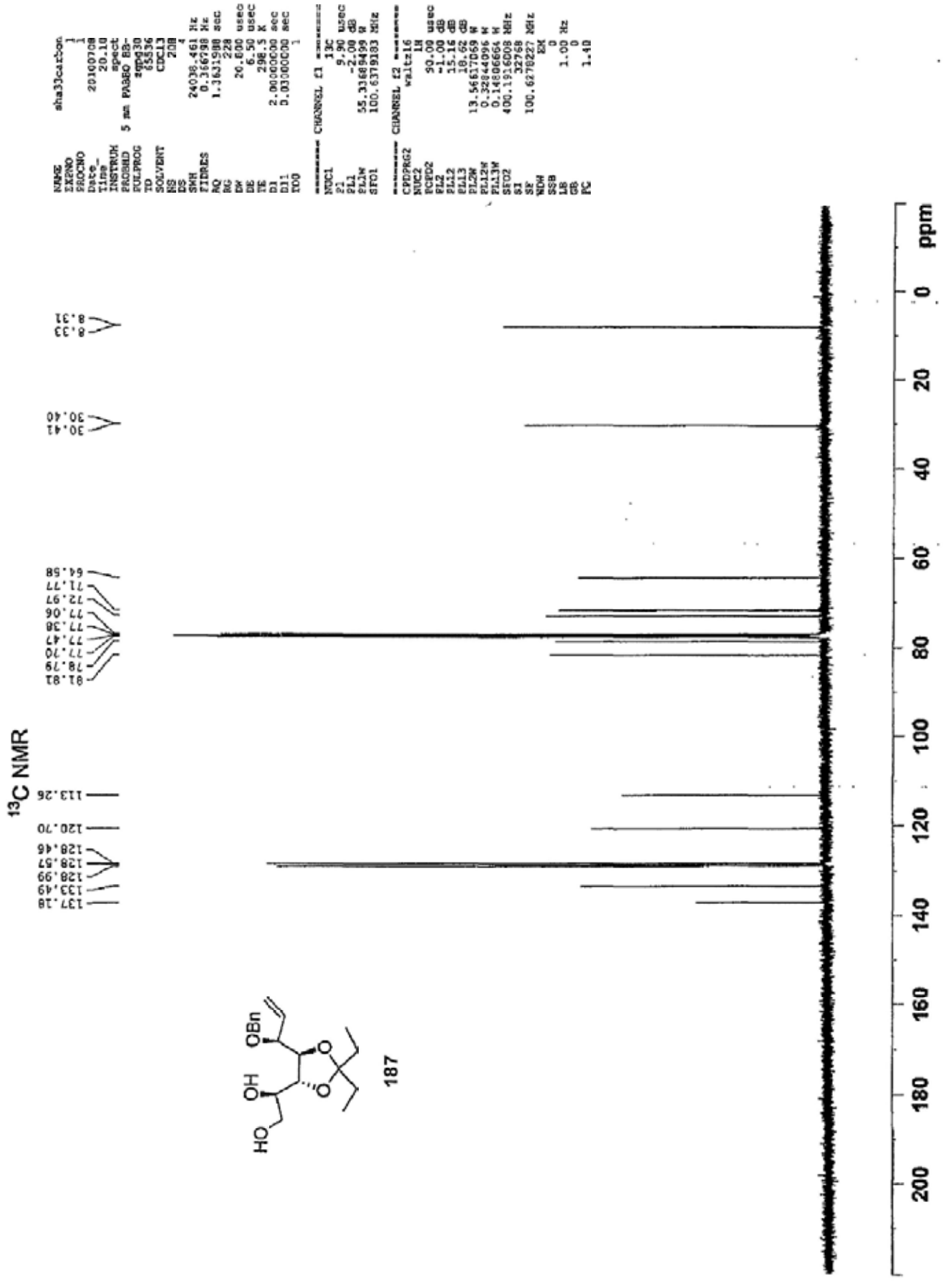

^{13}C NMR
137.27
116.85
114.66
113.59
84.15
81.73
77.70
77.38
77.06
76.94
73.77
30.60
30.56
29.73
29.10
8.50
8.40
8.32
OH
185
NAME sha3carbon
EXPNO 1
PROCNO 1
Date_ 20100715
Time 11.40
INSTRUM spect
PROBHD 5 mm PABBI 1H/
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 61
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631988 sec
RG 203
DW 20.800 usec
DE 6.50 usec
TE 294.6 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
CHANNEL f1
NUC1 13C
P1 14.50 usec
PL1 -4.00 dB
PL1W 90.27689819 W
SFO1 100.6228298 MHz
CHANNEL f2
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 usec
PL2 -2.00 dB
PL12 18.80 dB
PL13 18.80 dB
PL2W 13.17734718 W
PL12W 0.10968442 W
PL13W 0.10968442 W
SFO2 400.1316005 MHz
SI 32768
SF 100.6127331 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
200
180
160
140
120
100
80
60
40
20
0
ppm


^{1}H NMR
OBn
186
12.3493
8.4345
5.2188
0.9856
1.0527
0.9208
0.9992
1.0000
3.0928
2.0846
0.9647
ppm


^{13}C NMR
186
OBn
ppm
0
20
40
60
80
100
120
140
160
180
200
8.57
8.51
8.29
29.29
29.96
30.37
30.53
68.25
70.69
77.06
77.38
77.64
77.69
77.78
80.45
83.13
113.77
119.44
127.70
127.84
128.57
135.97
138.83


^{1}H NMR
ppm
187
OBn
OH
HO
O
O
6.0895
4.0307
0.9713
1.0775
0.9506
2.0354
1.0241
1.0228
1.0131
1.0194
1.0073
2.0390
1.0000
4.9338


^{1}H NMR (Solvent: $CDCl_3$-D_2O)
187
ppm


^{13}C NMR
187
OBn
OH
HO
ppm
0
20
40
60
80
100
120
140
160
180
200
137.18
133.49
128.99
128.57
128.46
120.70
113.26
81.81
78.79
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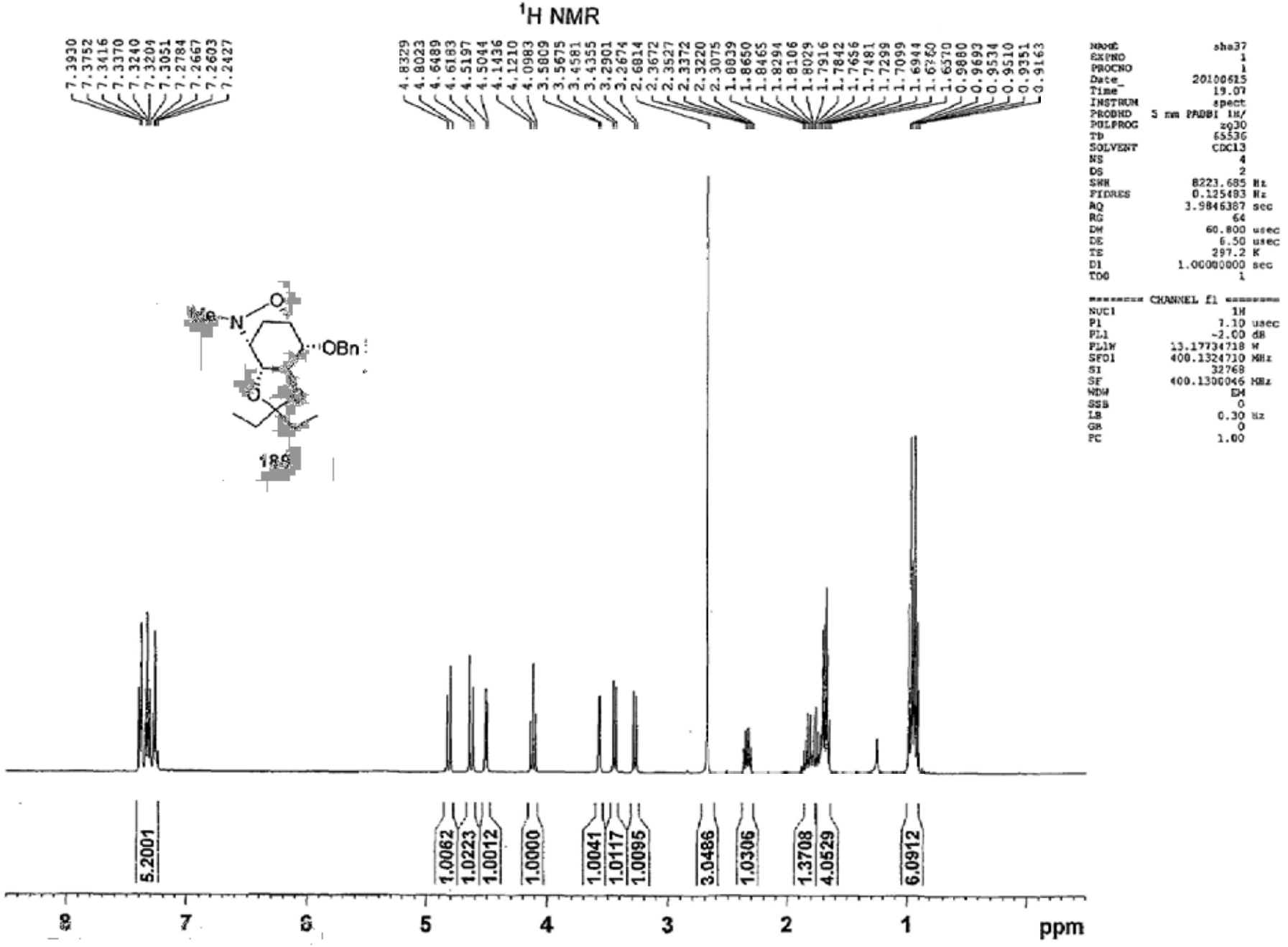
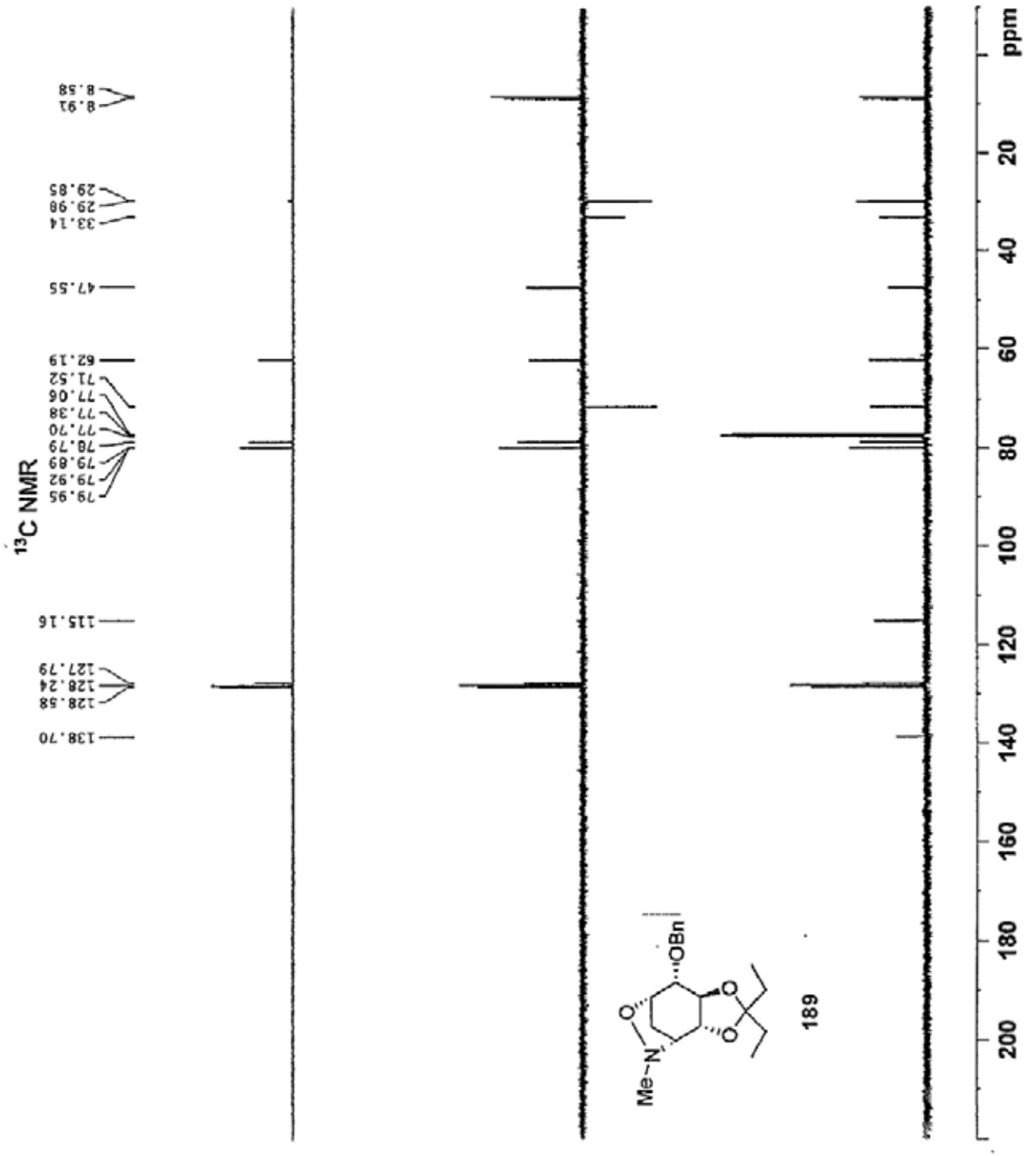
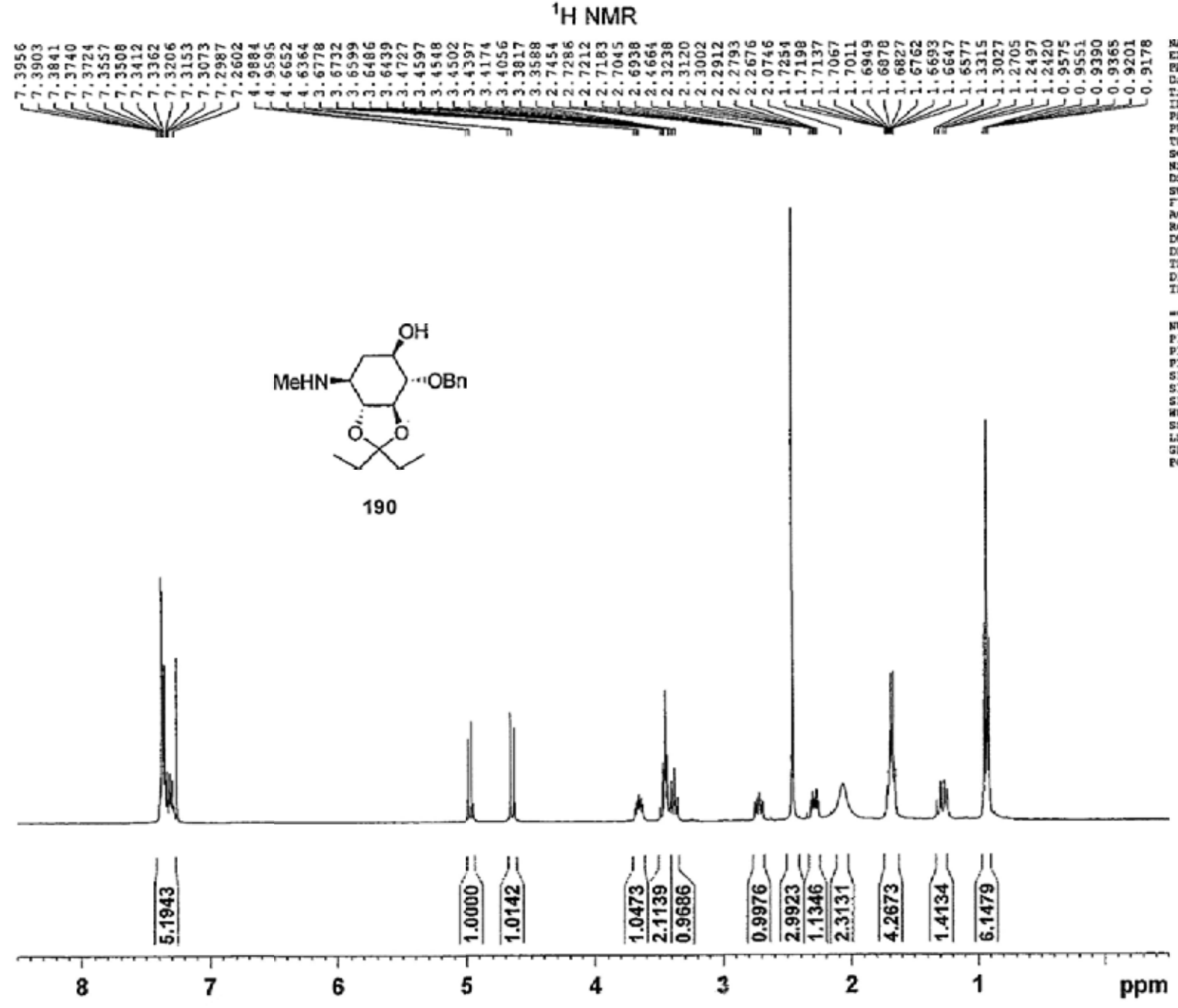
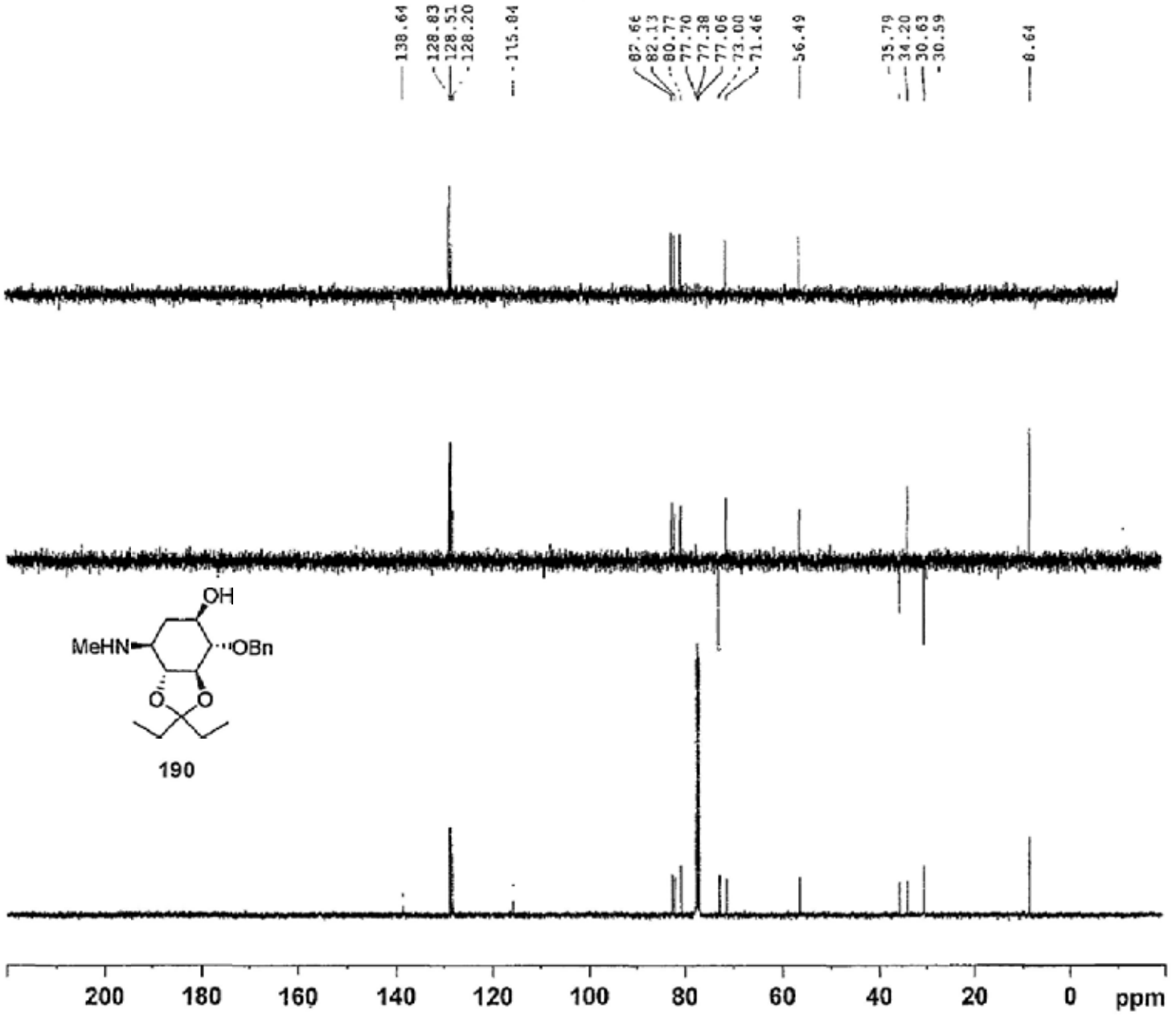
77.47
77.38
77.06
72.97
71.77
64.58
30.41
30.40
8.33
8.31


^{1}H NMR
7.3930
7.3752
7.3416
7.3370
7.3240
7.3204
7.3051
7.2784
7.2667
7.2603
7.2427
4.8329
4.8023
4.6489
4.6183
4.5197
4.5044
4.1436
4.1210
4.0983
3.5809
3.5675
3.4581
3.4355
3.2901
3.2674
2.6814
2.3672
2.3527
2.3372
2.3220
2.3075
1.8839
1.8650
1.8465
1.8294
1.8106
1.8029
1.7916
1.7842
1.7656
1.7481
1.7299
1.7099
1.6944
1.6780
1.6570
0.9880
0.9693
0.9534
0.9510
0.9351
0.9163
NAME sha37
EXPNO 1
PROCNO 1
Date_ 20100615
Time 19.07
INSTRUM spect
PROBHD 5 mm PABBI 1H/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 4
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 64
DW 60.800 usec
DE 6.50 usec
TE 297.2 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 7.10 usec
PL1 -2.00 dB
PL1W 13.17734718 W
SFO1 400.1324710 MHz
SI 32768
SF 400.1300046 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
Me
N
O
OBn
O
189
5.2001
1.0062
1.0223
1.0012
1.0000
1.0041
1.0117
1.0095
3.0486
1.0306
1.3708
4.0529
6.0912
8
7
6
5
4
3
2
1
ppm

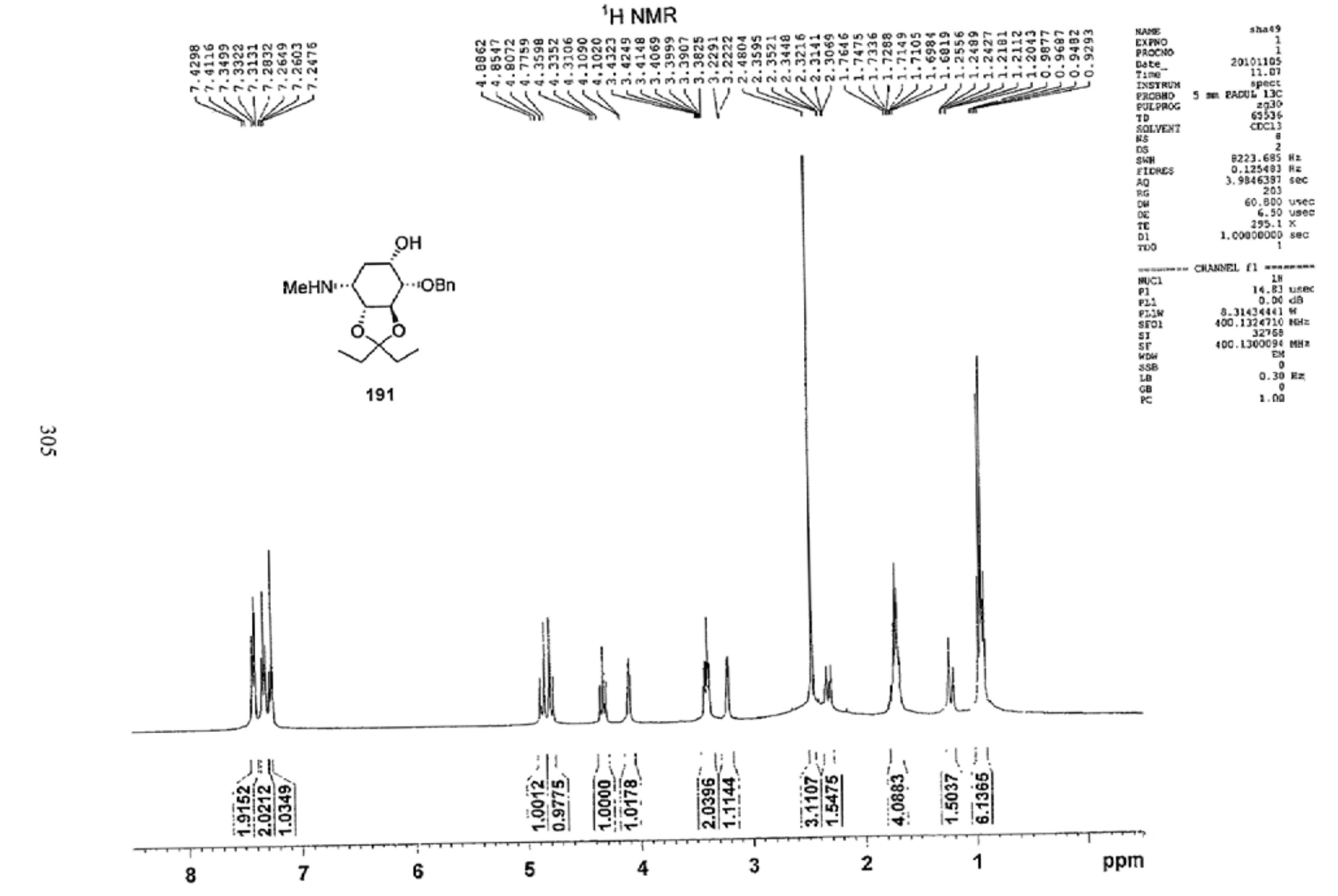

13C NMR
8.58
8.92
29.85
29.98
33.14
47.55
62.19
71.52
77.06
77.38
77.70
78.79
79.89
79.92
79.95
115.16
127.79
128.24
128.58
138.70
ppm
20
40
60
80
100
120
140
160
180
200
OBn
Me
N
O
O
O
O
189

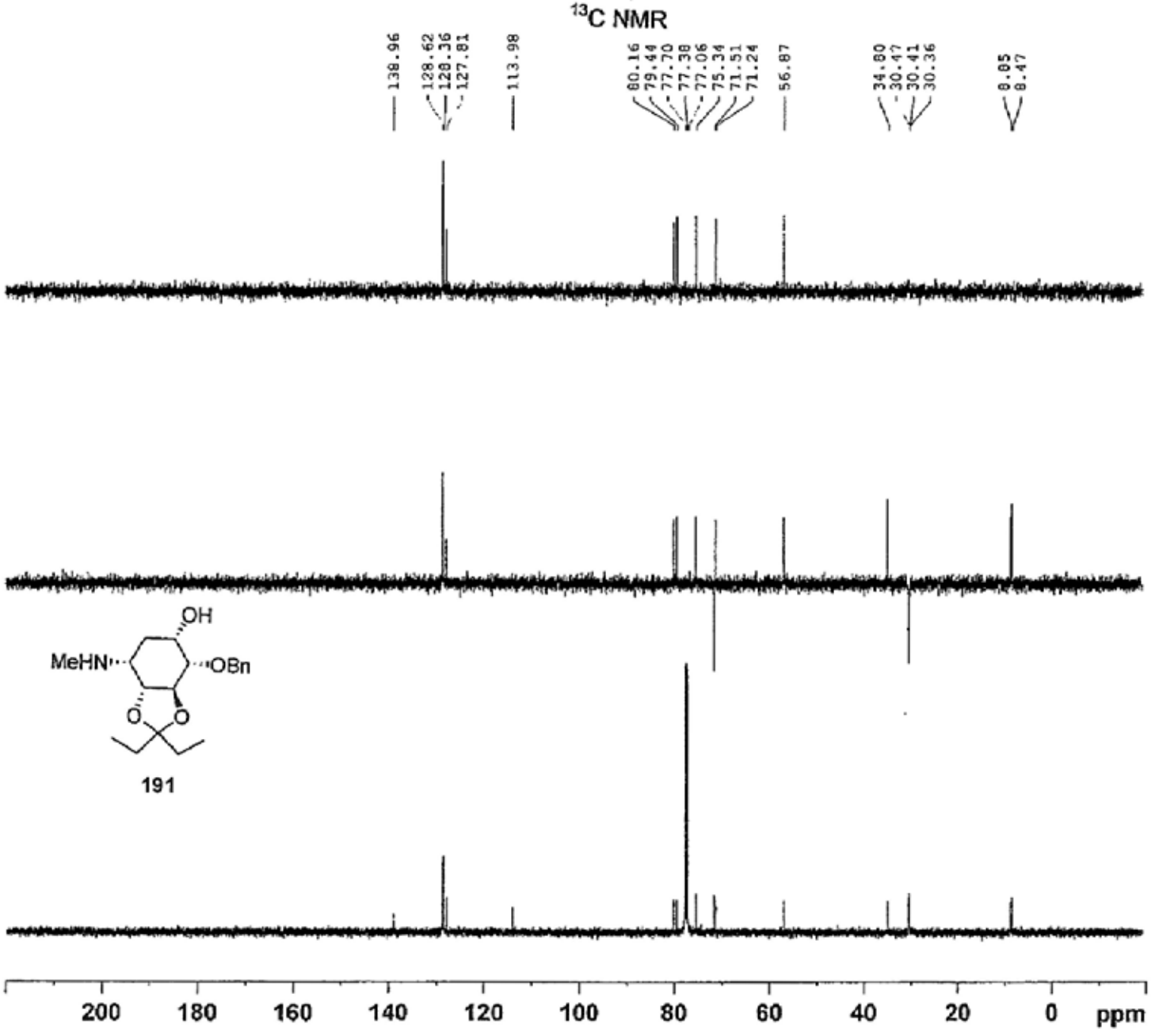

^{1}H NMR
7.3956
7.3903
7.3841
7.3740
7.3724
7.3557
7.3508
7.3412
7.3362
7.3206
7.3153
7.3073
7.2987
7.2602
4.9884
4.9595
4.6652
4.6364
3.6778
3.6732
3.6599
3.6486
3.6439
3.4727
3.4597
3.4548
3.4502
3.4397
3.4174
3.4056
3.3817
3.3588
2.7454
2.7286
2.7212
2.7183
2.7045
2.6938
2.4664
2.3238
2.3120
2.3002
2.2912
2.2793
2.2676
2.0746
1.7254
1.7198
1.7137
1.7067
1.7011
1.6949
1.6878
1.6827
1.6762
1.6693
1.6647
1.6577
1.3315
1.3027
1.2705
1.2497
1.2420
0.9575
0.9551
0.9390
0.9365
0.9201
0.9178
NAME sha5
EXPNO 2
PROCNO 1
Date_ 20101115
Time 14.23
INSTRUM spect
PROBHD 5 mm PABBL 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 203
DW 60.800 usec
DE 6.50 usec
TE 295.2 K
D1 1.00000000 sec
ID0 1
CHANNEL f1
NUC1 1H
P1 14.83 usec
PL1 0.00 dB
PL1W 8.31434441 W
SFO1 400.1324710 MHz
SI 32768
SF 400.1300094 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
OH
MeHN
OBn
O
O
190
5.1943
1.0000
1.0142
1.0473
2.1139
0.9686
0.9976
2.9923
1.1346
2.3131
4.2673
1.4134
6.1479
8
7
6
5
4
3
2
1
ppm

^{13}C NMR

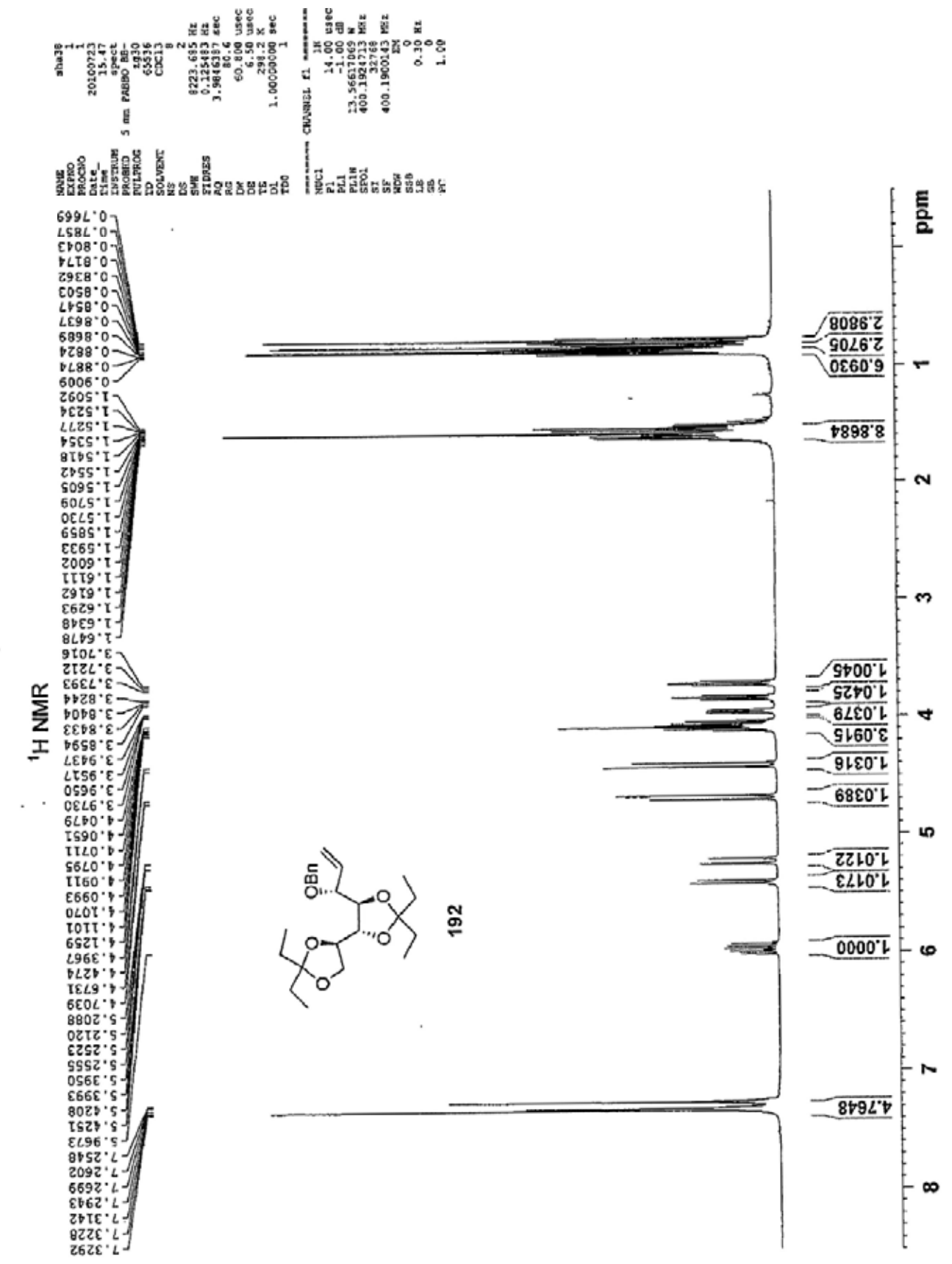


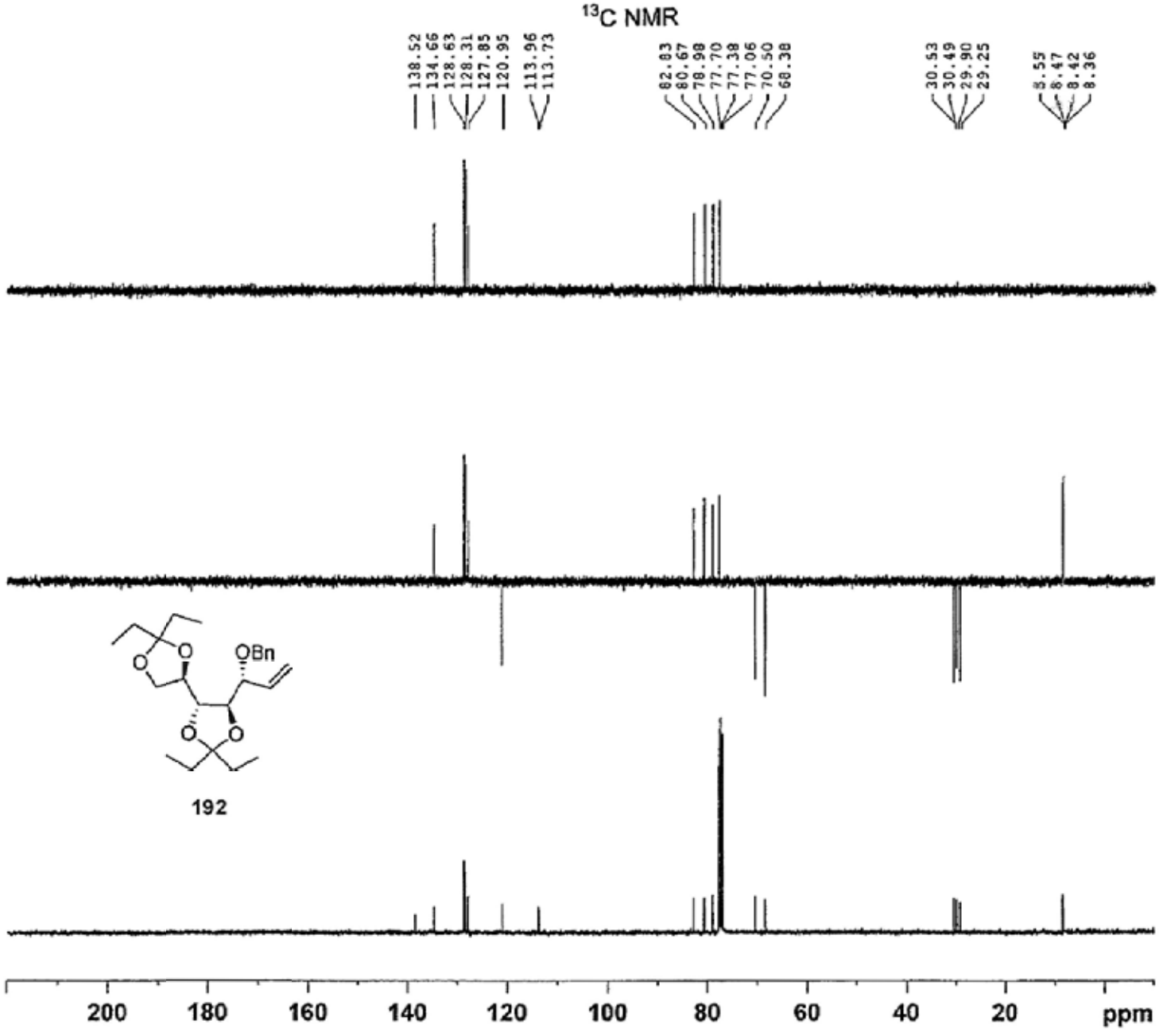
NAME	sha5icarbon
EXPNO	2
PROCNO	1
Date_	20101115
Time	14.28
INSTRUM	spect
PROBHD	5 mm PABBO BB/
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	201
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631488 sec
RG	203
DW	10.400 usec
DE	6.50 usec
TE	295.9 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.68 usec
PL1	-0.60 dB
PL1W	81.24166963 W
SFO1	100.6228298 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	90.00 usec
PL2	0.00 dB
PL12	15.66 dB
PL13	15.92 dB
PL2W	8.31434441 W
PL12W	0.22585411 W
PL13W	0.21272963 W
SFO2	400.1316005 MHz
SI	32768
SF	100.6127338 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40


^{1}H NMR
7.4298
7.4116
7.3499
7.3322
7.3131
7.2832
7.2649
7.2603
7.2476
4.8862
4.8547
4.8072
4.7759
4.3598
4.3352
4.3106
4.1090
4.1020
3.4323
3.4249
3.4148
3.4069
3.3999
3.3907
3.3825
3.2291
3.2222
2.4804
2.3595
2.3521
2.3448
2.3216
2.3141
2.3069
1.7646
1.7475
1.7336
1.7288
1.7149
1.7105
1.6984
1.6819
1.2556
1.2489
1.2427
1.2181
1.2112
1.2043
0.9877
0.9687
0.9482
0.9293
NAME sha49
EXPNO 1
PROCNO 1
Date_ 20101105
Time 11.07
INSTRUM spect
PROBHD 5 mm PADUL 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 203
DW 60.800 usec
DE 6.50 usec
TE 295.1 K
D1 1.00000000 sec
TD0 1
CHANNEL f1
NUC1 1H
P1 14.83 usec
PL1 0.00 dB
PL1W 8.31434441 W
SFO1 400.1324710 MHz
SI 32768
SF 400.1300094 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
OH
MeHN
OBn
O
O
191
1.9152
2.0212
1.0349
1.0012
0.9775
1.0000
1.0178
2.0396
1.1144
3.1107
1.5475
4.0883
1.5037
6.1365
8
7
6
5
4
3
2
1
ppm

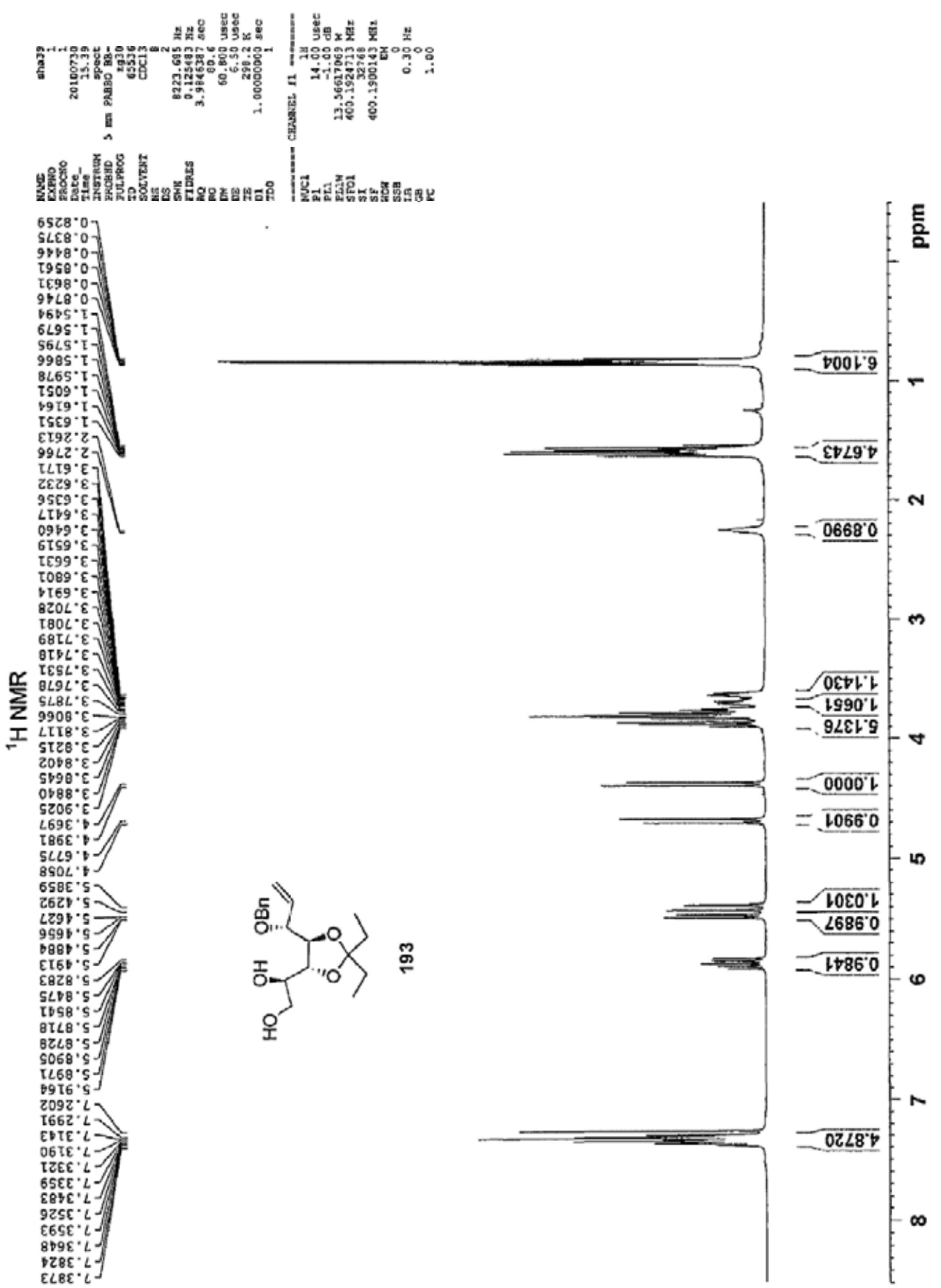


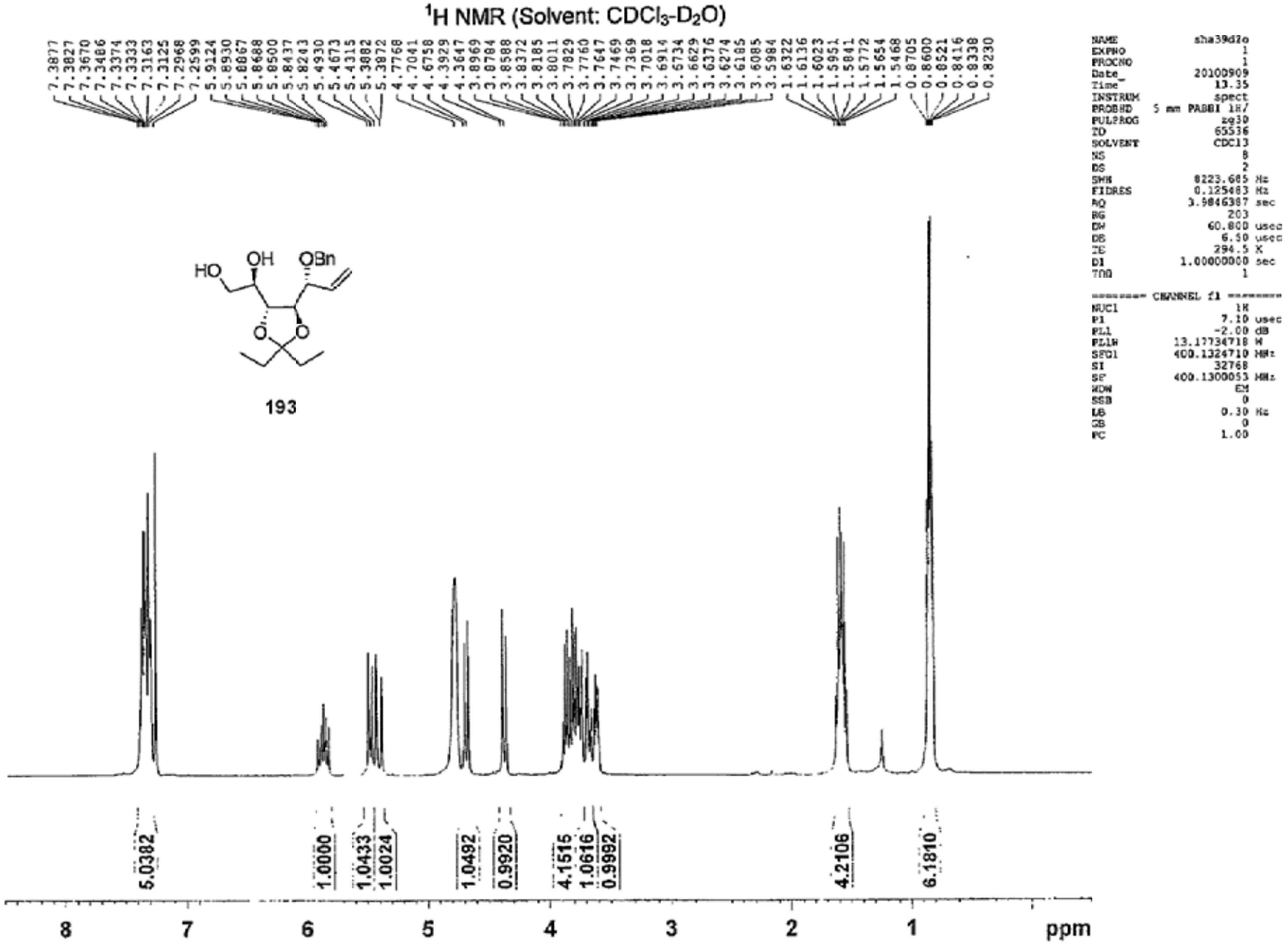
NAME	sha49carbon
EXPNO	1
PROCNO	1
Date_	20101105
Time	11.12
INSTRUM	spect
PROBHD	5 mm PABUL 13C
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	200
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	295.6 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.68 usec
PL1	-0.60 dB
PL1W	41.24164963 W
SFO1	100.6228298 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	90.00 usec
PL2	0.00 dB
PL12	15.66 dB
PL13	15.92 dB
PL2W	8.31434441 W
PL12W	0.22585413 W
PL13W	0.21272963 W
SFO2	400.1316005 MHz
SI	32768
SF	100.6127338 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

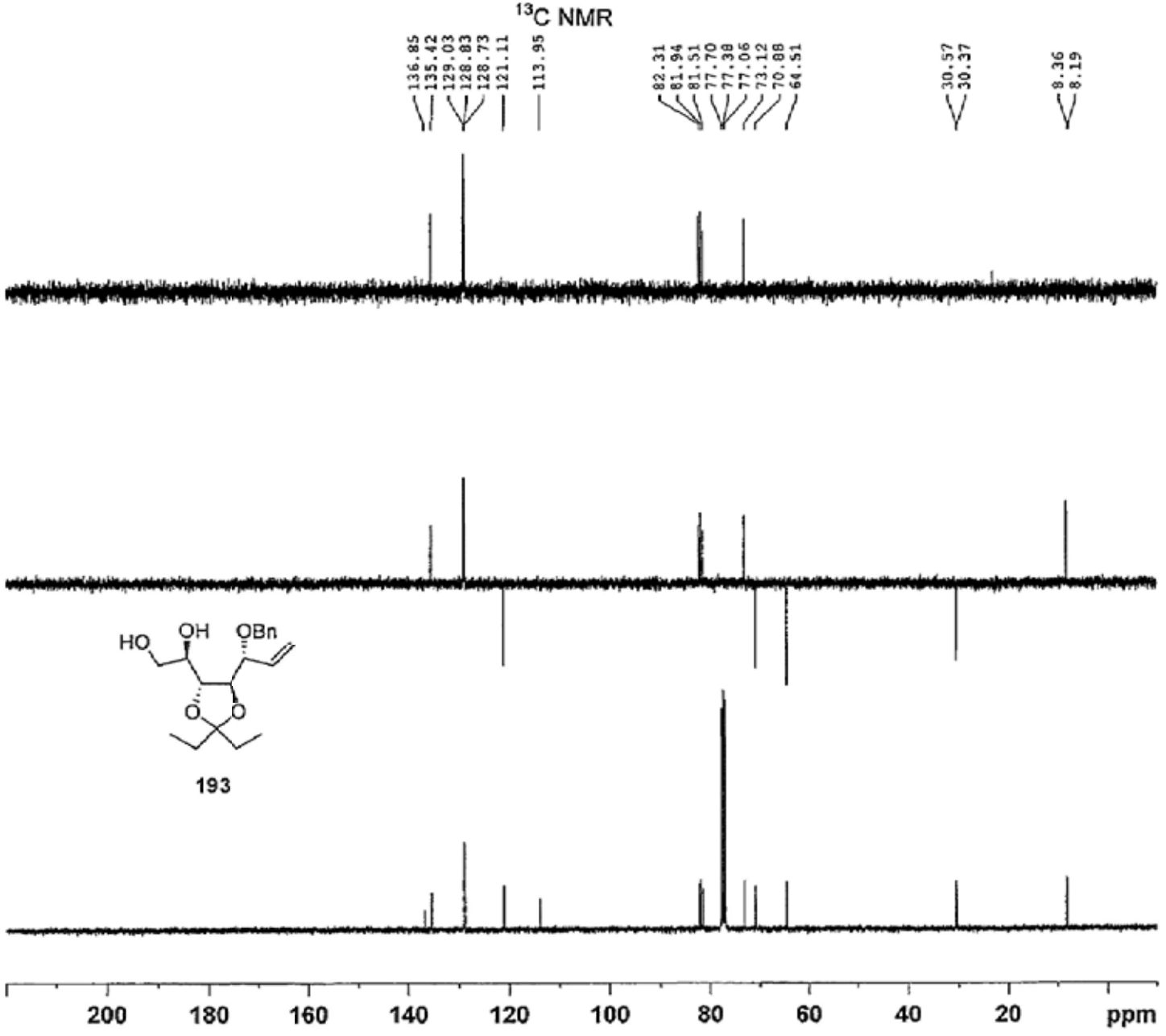

^{1}H NMR
192
OBn
ppm
1
2
3
4
5
6
7
8
6.0930
2.9705
2.9808
8.8684
1.0045
1.0425
1.0379
3.0915
1.0316
1.0389
1.0122
1.0173
1.0000
4.7648



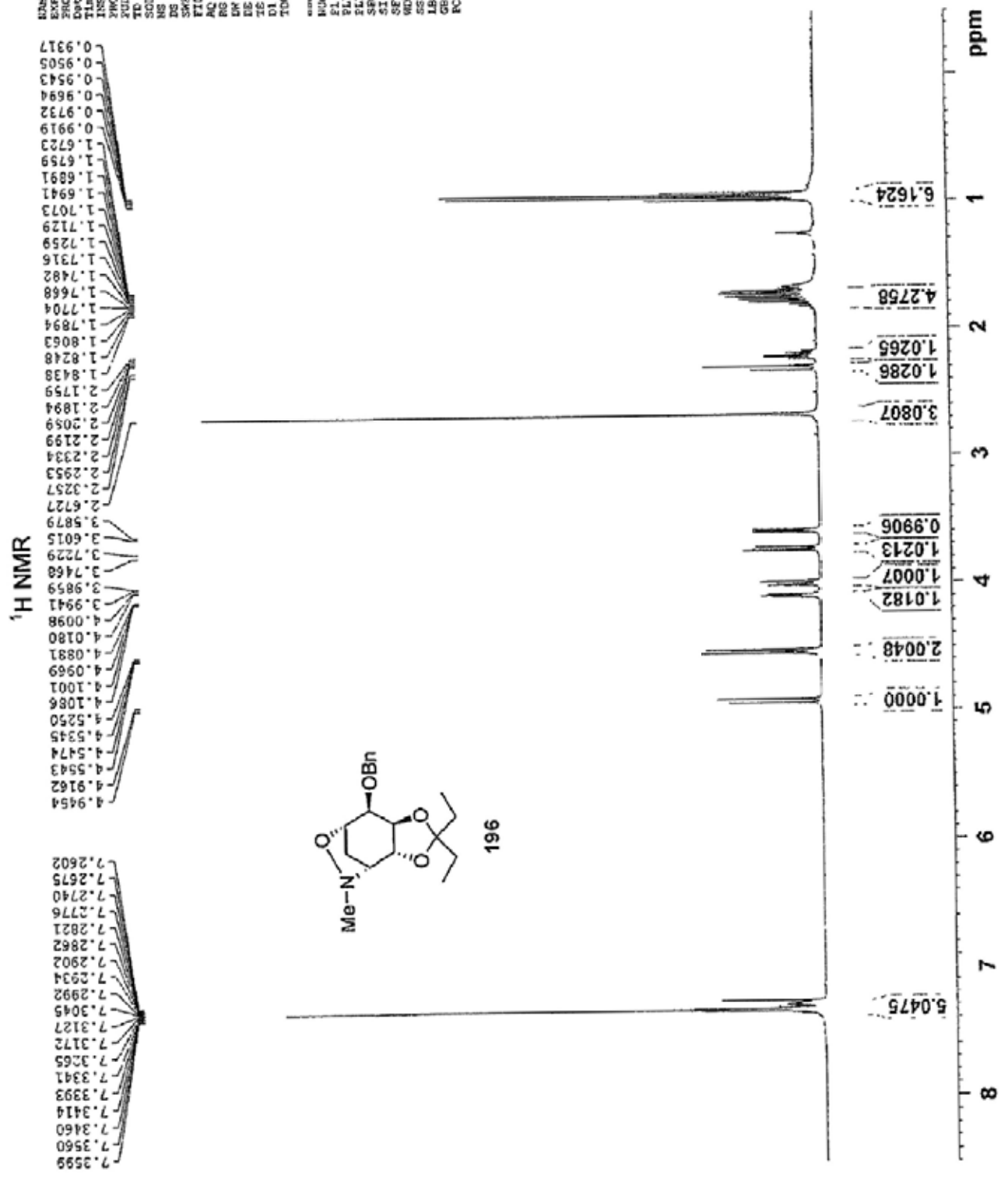
NAME	sha38carbon
EXPNO	1
PROCNO	1
Date_	20100723
Time	15.56
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	170
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631989 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	298.8 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.90 usec
PL1	-2.00 dB
PL1W	55.33689880 W
SFO1	100.6378183 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	90.00 usec
PL2	-1.00 dB
PL12	15.16 dB
PL13	18.62 dB
PL2W	13.56617069 W
PL12W	0.32844096 W
PL13W	0.14806664 W
SFO2	400.1916008 MHz
SI	32768
SF	100.6278205 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

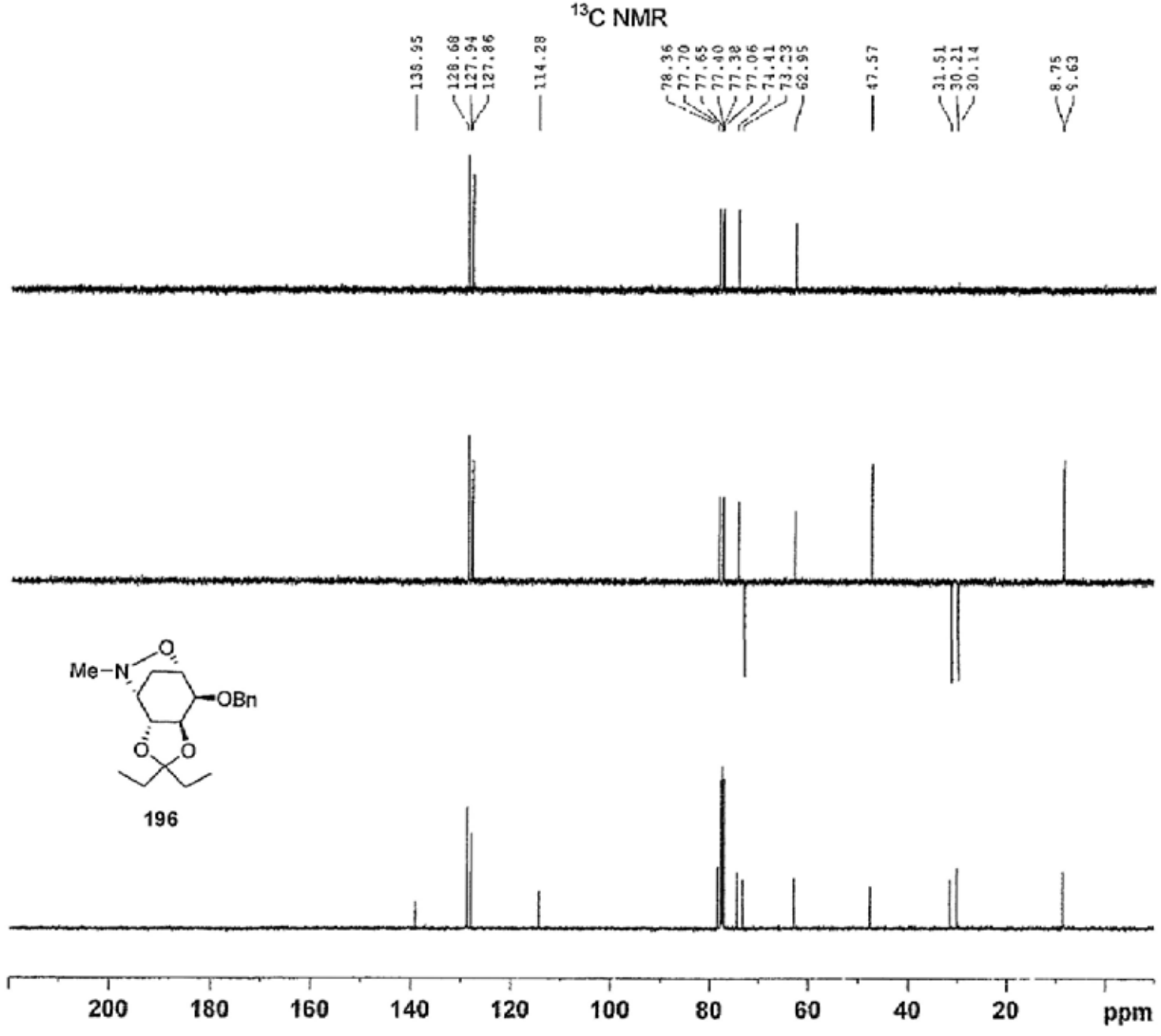

^{1}H NMR
ppm
193
OBn
OH
HO
6.1004
4.6743
0.8990
1.1430
1.0651
5.1376
1.0000
0.9901
1.0301
0.9897
0.9841
4.8720


^{1}H NMR (Solvent: $CDCl_3$-D_2O)
7.3877 7.3827 7.3670 7.3486 7.3374 7.3333 7.3163 7.3125 7.2968 7.2599 5.9124 5.8930 5.8867 5.8688 5.8500 5.8437 5.8243 5.4930 5.4673 5.4315 5.3882 5.3872 4.7768 4.7041 4.6758 4.3929 4.3647 3.8969 3.8784 3.8588 3.8372 3.8185 3.8011 3.7829 3.7760 3.7647 3.7469 3.7369 3.7018 3.6914 3.6734 3.6629 3.6376 3.6274 3.6185 3.6085 3.5984 1.6322 1.6136 1.6023 1.5951 1.5841 1.5772 1.5654 1.5468 0.8705 0.8600 0.8521 0.8416 0.8338 0.8230
HO OH OBn
O O
193
NAME sha39d2o
EXPNO 1
PROCNO 1
Date_ 20100909
Time 13.35
INSTRUM spect
PROBHD 5 mm PABBI 1H/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 203
DW 60.800 usec
DE 6.50 usec
TE 294.5 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 7.10 usec
PL1 -2.00 dB
PL1W 13.17734718 W
SFO1 400.1324710 MHz
SI 32768
SF 400.1300053 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
5.0382 1.0000 1.0433 1.0024 1.0492 0.9920 4.1515 1.0616 0.9992 4.2106 6.1810
8 7 6 5 4 3 2 1 ppm



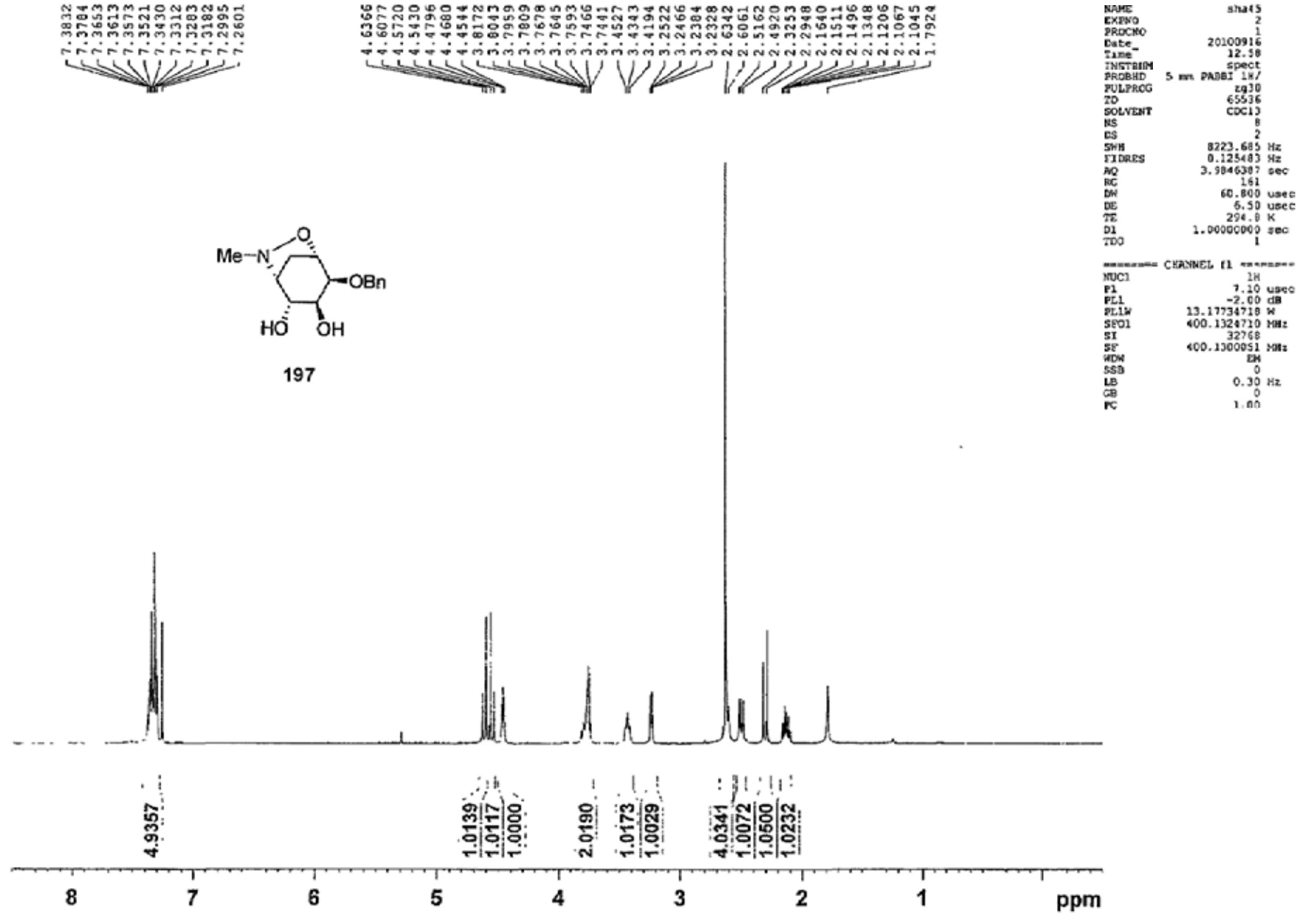
NAME	sha39carbon	
EXPNO	1	
PROCNO	1	
Date_	20100730	
Time	15.45	
INSTRUM	spect	
PROBHD	5 mm PABBO BB-	
PULPROG	zgpg30	
TD	65536	
SOLVENT	CDCl3	
NS	168	
DS	4	
SWH	24038.461	Hz
FIDRES	0.366798	Hz
AQ	1.3631988	sec
RG	161	
DW	20.800	usec
DE	6.50	usec
TE	298.4	K
D1	2.00000000	sec
D11	0.03000000	sec
TD0	1	
======== CHANNEL f1 ========		
NUC1	13C	
P1	9.90	usec
PL1	-2.00	dB
PL1W	55.33689499	W
SFO1	100.6379183	MHz
======== CHANNEL f2 ========		
CPDPRG2	waltz16	
NUC2	1H	
PCPD2	90.00	usec
PL2	-1.00	dB
PL12	15.16	dB
PL13	18.62	dB
PL2W	13.56617069	W
PL12W	0.32844096	W
PL13W	0.14806664	W
SFO2	400.1916008	MHz
SI	32768	
SF	100.6278212	MHz
WDW	EM	
SSB	0	
LB	1.00	Hz
GB	0	
PC	1.40	

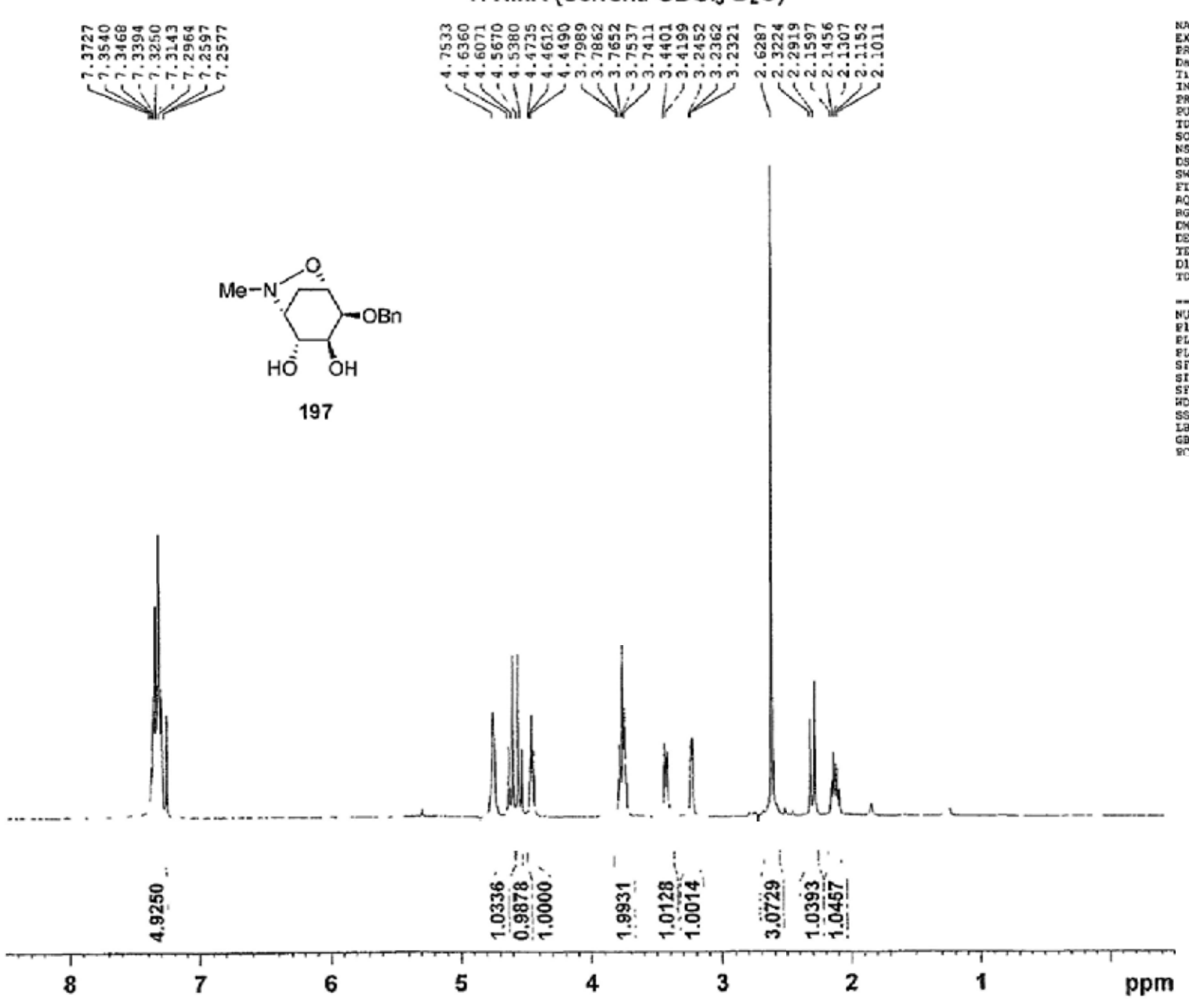

^{1}H NMR
ppm
OBn
Me—N
196

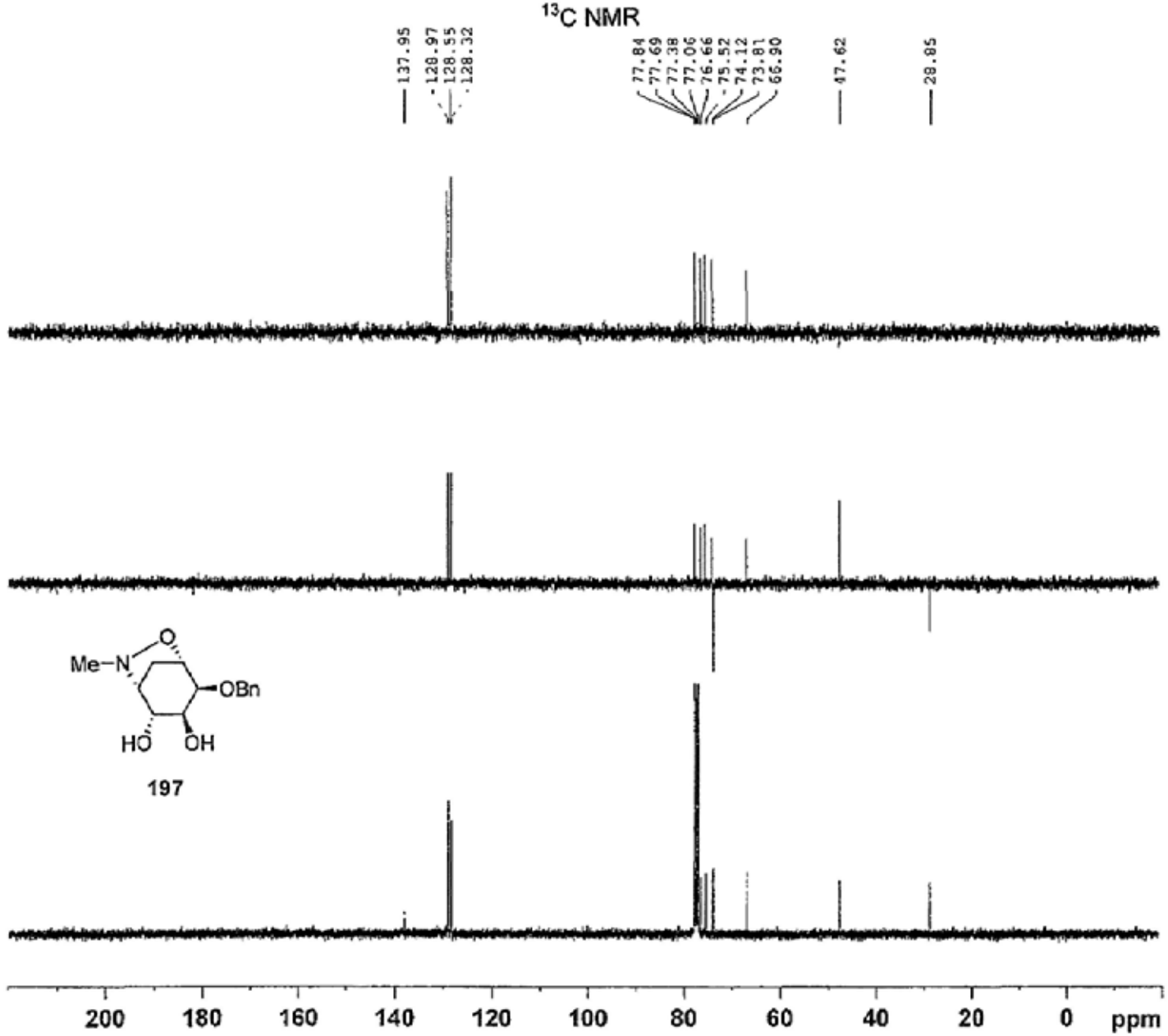


NAME	sha42carbon
EXPNO	1
PROCNO	1
Date_	20100721
Time	15.09
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	142
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3671988 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	298.6 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	9.90 usec
PL1	-1.00 dB
PL1W	55.33689499 W
SFO1	100.6379183 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	90.00 usec
PL2	-1.00 dB
PL12	15.16 dB
PL13	19.62 dB
PL2W	13.56617069 W
PL12W	0.32844096 W
PL13W	0.14806664 W
SFO2	400.1316009 MHz
SI	32768
SF	100.6279219 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

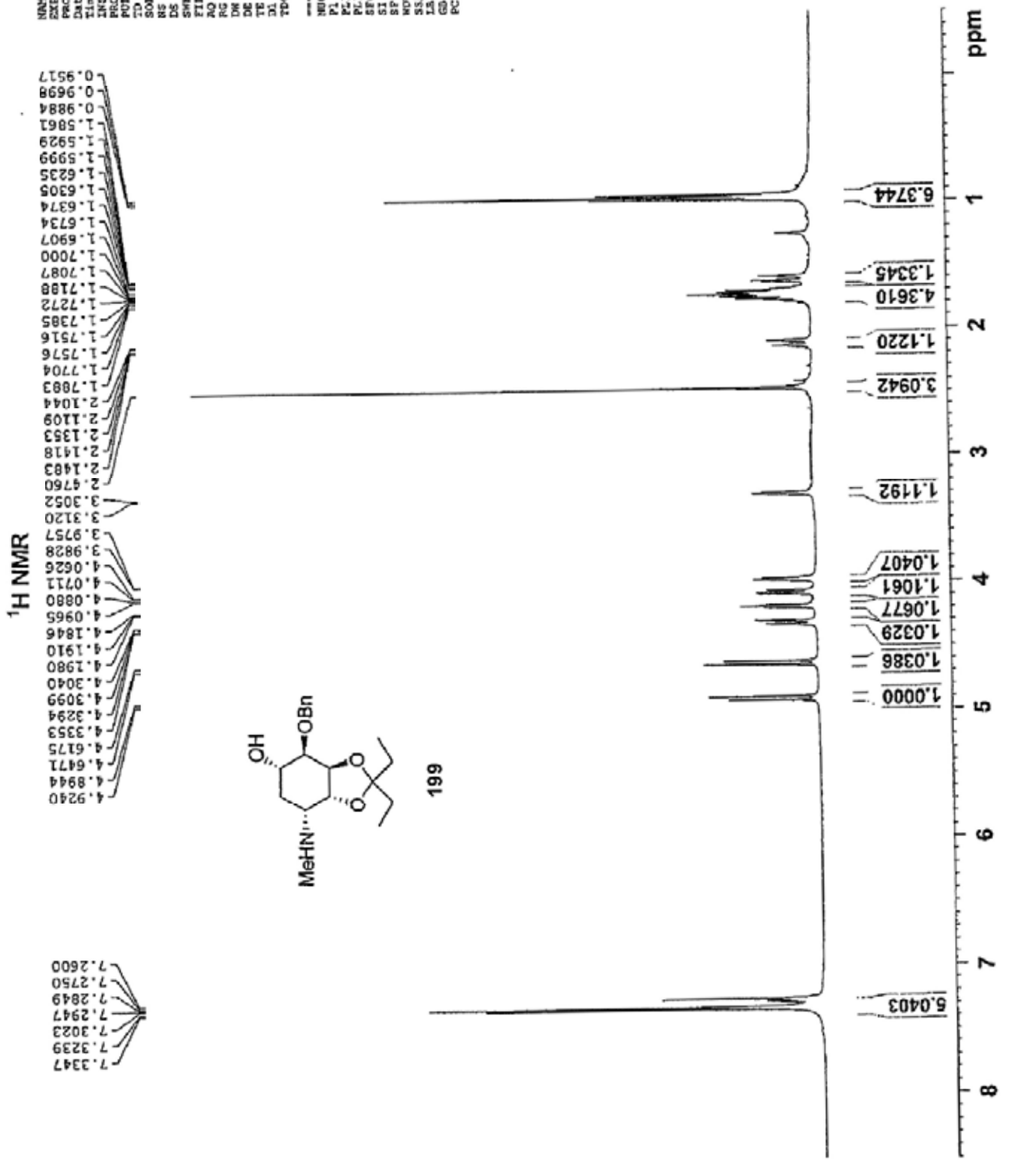
^{1}H NMR

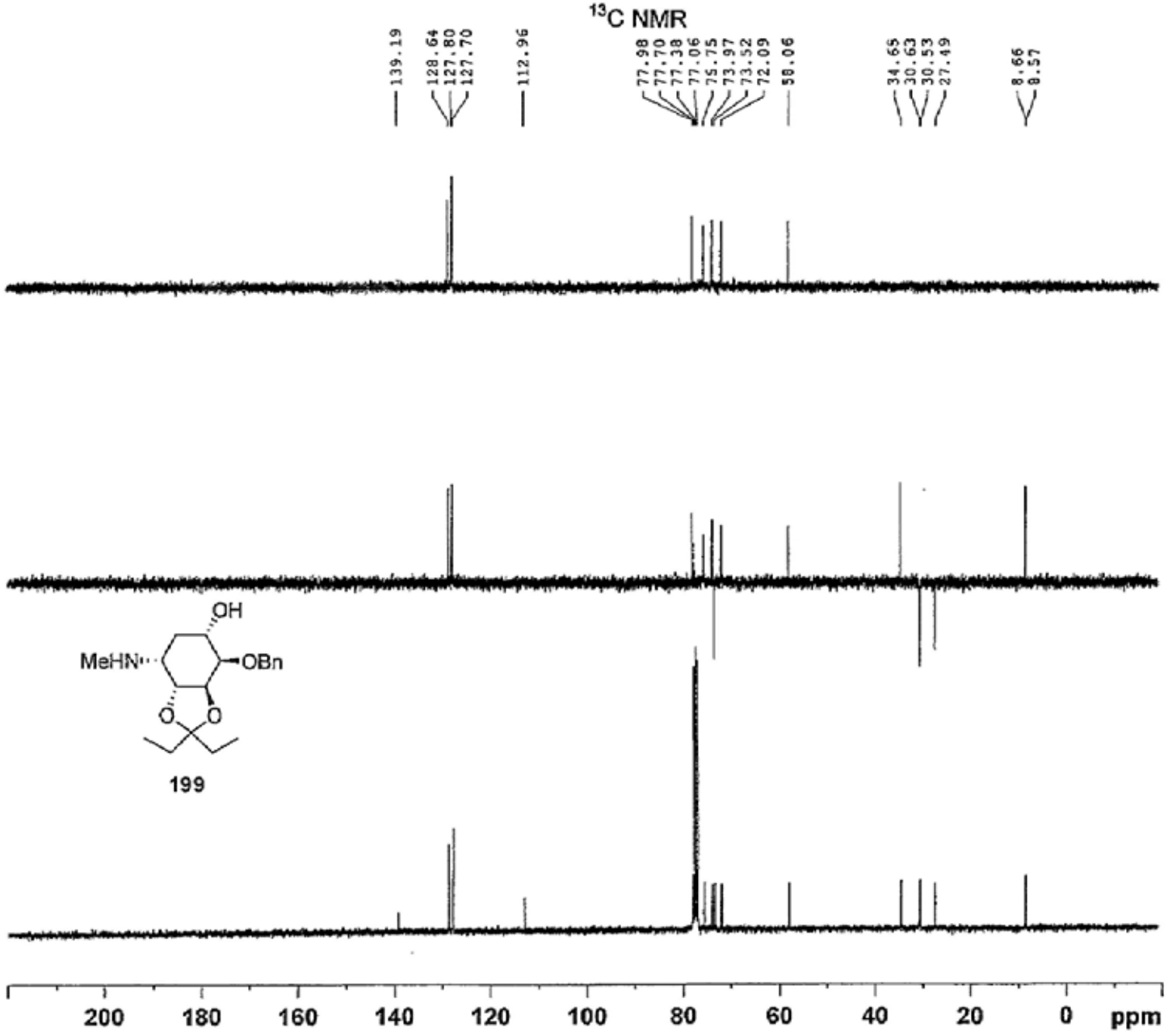

7.3832
7.3784
7.3653
7.3613
7.3573
7.3521
7.3430
7.3312
7.3283
7.3182
7.2995
7.2601
4.6366
4.6077
4.5720
4.5430
4.4796
4.4680
4.4544
3.8172
3.8043
3.7959
3.7809
3.7678
3.7645
3.7593
3.7466
3.7441
3.4527
3.4343
3.4194
3.2522
3.2466
3.2384
3.2328
2.6342
2.6061
2.5162
2.4920
2.3253
2.2948
2.1640
2.1511
2.1496
2.1348
2.1206
2.1067
2.1045
1.7924
Me–N
O
OBn
HO
OH
197
NAME sha45
EXPNO 2
PROCNO 1
Date_ 20100916
Time_ 12.58
INSTRUM spect
PROBHD 5 mm PABBI 1H/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846307 sec
RG 161
DW 60.800 usec
DE 6.50 usec
TE 294.8 K
D1 1.00000000 sec
TD0 1
CHANNEL f1
NUC1 1H
P1 7.10 usec
PL1 -2.00 dB
PL1W 13.17734718 W
SFO1 400.1324710 MHz
SI 32768
SF 400.1300051 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00
4.9357
1.0139
1.0117
1.0000
2.0190
1.0173
1.0029
4.0341
1.0072
1.0500
1.0232
8
7
6
5
4
3
2
1
ppm


^{1}H NMR (Solvent: $CDCl_3$-D_2O)
7.3727
7.3540
7.3468
7.3394
7.3250
7.3143
7.2964
7.2597
7.2577
4.7533
4.6360
4.6071
4.5670
4.5380
4.4735
4.4612
4.4490
3.7989
3.7862
3.7652
3.7537
3.7411
3.4401
3.4199
3.2452
3.2362
3.2321
2.6287
2.3224
2.2919
2.1597
2.1456
2.1307
2.1152
2.1011
Me–N
O
OBn
HO
OH
197
NAME sha45d2o
EXPNO 1
PROCNO 1
Date_ 20100916
Time 13.27
INSTRUM spect
PROBHD 5 mm PABBI 1H/
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 128
DW 60.800 usec
DE 6.50 usec
TE 294.8 K
D1 1.00000000 sec
TD0 1
CHANNEL f1
NUC1 1H
P1 7.10 usec
PL1 -2.00 dB
PL1W 13.17734718 W
SFO1 400.1324710 MHz
SI 32768
SF 400.1300058 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
4.9250
1.0336
0.9878
1.0000
1.9931
1.0128
1.0014
3.0729
1.0393
1.0457
8
7
6
5
4
3
2
1
ppm



NAME	sha45carbon
EXPNO	1
PROCNO	1
Date_	20100916
Time	13.02
INSTRUM	spect
PROBHD	5 mm PABBI 1H/
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	194
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	295.1 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	13C
P1	14.50 usec
PL1	-4.00 dB
PL1W	90.22689819 W
SFO1	100.6228298 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	-2.00 dB
PL12	18.60 dB
PL13	18.60 dB
PL2W	13.17734718 W
PL12W	0.10960442 W
PL13W	0.10960442 W
SFO2	400.1316005 MHz
SI	32768
SF	100.6127346 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40


^{1}H NMR
199
OH
OBn
MeHN
ppm
6.3744
1.3345
4.3610
1.1220
3.0942
1.1192
1.0407
1.1061
1.0677
1.0329
1.0386
1.0000
5.0403



NAME	sha46carbon
EXPNO	1
PROCNO	1
Date_	20101030
Time	12.50
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	331
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631968 sec
RG	181
DW	20.800 usec
DE	6.50 usec
TE	298.5 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
--------	CHANNEL f1 --------
NUC1	13C
P1	9.90 usec
PL1	-2.00 dB
PL1W	55.33683499 W
SFO1	100.6379183 MHz
--------	CHANNEL f2 --------
CPDPRG2	waltz16
NUC2	1H
PCPD2	90.00 usec
PL2	-1.00 dB
PL12	15.16 dB
PL13	18.62 dB
PL2W	13.56617069 W
PL12W	0.32844096 W
PL13W	0.14806664 W
SFO2	400.1916038 MHz
SI	32768
SF	100.6276212 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40