A

SYNTHESIS OF *C*-GLYCOSIDES VIA RAMBERG-BÄCKLUND REACTION

By

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

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ABSTRACT

SYNTHESIS OF *C*-GLYCOSIDES VIA RÄMBERG-BACKLUND REACTION

By

Guangli Yang

Advisor: Professor Richard W. Franck

A novel methodology has been developed in our laboratory, employing the Ramberg-Bäcklund rearrangement to synthesize *C*-glycosides. The Ramberg-Bäcklund sequence to provide *C*-glycosides includes three intermediates: thioglycoside, sulfonyl glycoside, and exo-glycal. Thio-glycosides can be easily made using different methods. Sulfone formation was routine with MMPP. The one-pot Ramberg-Bäcklund reaction of sulfone was done using $C_2Br_2F_4$, *t*-BuOH and KOH/Al_2O_3 under reflux to afford an exo-glycal intermediate. The β-*C*-glycosides can be made by hydrogenolysis of exo-glycals using H_2 and Pd/C. The α-*C*-glycosides can be made stereoselectively from exo-glycals via intramolecular ionic hydrogenation as the key step. Some of the *C*-glycerolipids that have been prepared exhibit strikingly similar in vitro antiproliferative effects to those of *O*-glycoside analogs.

This work is dedicated to

my mother and my adorable son Benjamin Huang.

ACKNOWLEGEMENTS

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Abbreviations

Ac	acetyl
RB	Ramberg-Bäcklund
DME	1,2-dimethoxyethane
THF	tetrahydrofuran
TFA	trifluoroacetic acid
DMF	N,N-Dimethylformamide
DCC	dicyclohexylcarbodiimide
MMPP	monomagnesium perphthalate
DMAP	4-N,N-dimethylaminopyridine
NBS	N-bromosuccinimide
HMPA	hexamethylphosphoramide
DTE	dithioerythritol
TBAI	tetrabutylammonium iodide
TBDMS	*tert*-butyldimethylsilyl
TMS	trimethylsilyl
p-Ts	*p*-toluenesulfonyl

1. *C*-GLYCOSIDES

1.1 Introduction

C-glycosides are 1-*C*-linked glycosyl derivatives in which the anomeric oxygen atom of a glycoside is replaced by a carbon atom (Figure 1.1). The study of *C*-glycoside analogs of bioactive natural *O*- and *N*-glycosides has received much attention during the past decade. The significance of *C*-glycosides is that they are essentially inert to degradation because the anomeric carbon has been transformed from a hydrolytically labile acetal link to an ether. The underlying assumption for use of *C*-glycoside analogs in glycobiology is that the conformational differences between the *O*- *(or* N-) linked natural material and the *C*-linked analog will be minimal. The corollary to the minimal difference hypothesis is that the recognition and binding of the *C*-analog will be similar to that of the natural material.

Figure 1.1 Definition of *C*-Glycoside

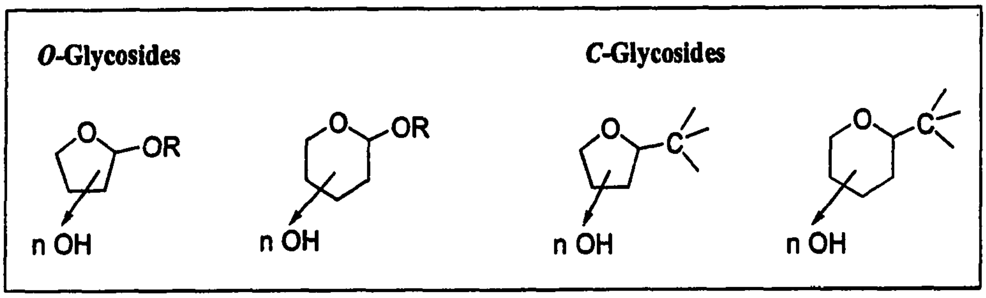


Table 1.1 illustrates the structural and chemical similarities prevalent between *C* and *O*-glycosides.[1] The bond lengths, Van der Waal radii, electronegativities and bond rotational barriers are very similar between *O* and *C*-glycosides. The largest difference between physical constants is observed for the dipole moments. Due to minor differences in conformation, both *O* and *C*-glycosides are represented by similar

antiperiplanar arrangements. These conformational similarities are illustrated in Figure 1.2. *O* and *C*-glycosides exhibit similar coupling constants in their ^{1}H NMR spectra. A summary of the respective average coupling constant is presented in Figure 1.3.

Table 1.1 Physical Properties of *O* and *C*-Glycosides

	O-Glycosides	*C*-Glycosides
Bond Length	O-C = 1.43 Å	O-C = 1.54 Å
Van der Waal	O = 1.52 Å	C = 2.0 Å
Electronegativity	O = 3.51	C = 2.35
Dipole Moment	C-O = 0.74D	C-C = 0.3D
Bond Rotational Barrier	CH_3-O-CH_3=2.7kcals/mole	CH_3- CH_3=2.88kcals/mole
H-Bonding	Two	None
Anomeric Effect	Yes	No
Exoanomeric Effect	Yes	No
Stability	Cleaved by acid and enzymes	Stable to acid and enzymes
Conformation	C_1-$C_{2'}$ antiperiplanar to O_1-C_1	$C_{1'}$-$C_{2'}$ antiperiplanar to C_1-C_2

The major difference between *C* and *O*-glycosides is the chemical reactivities (Figure 1.4). Not only are *C*-glycosides absent of anomeric effects, they are also stable to acid hydrolysis and are incapable of forming hydrogen bonds in the anomeric center. Since the *C*-glycoside linkage is not cleavable by hydrolysis, there is interest in the use of *C*-glycosides for enzymatic and metabolic studies.

Figure 1.2 Conformations of *O* and *C*-glycosides

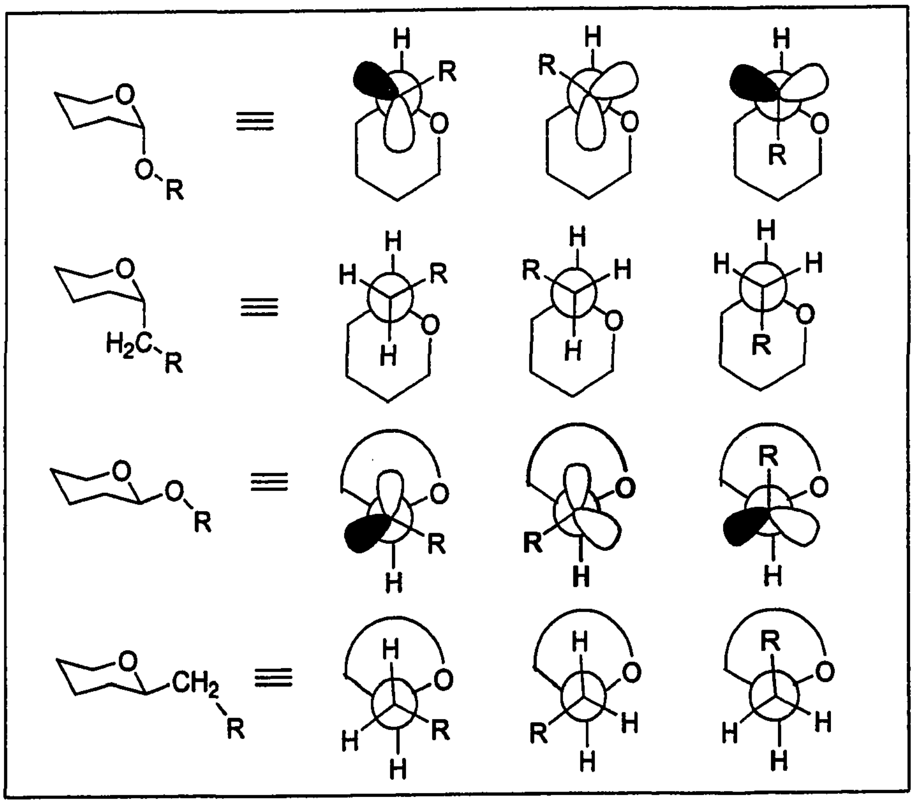


Figure 1.3 Conformations and Coupling Constants

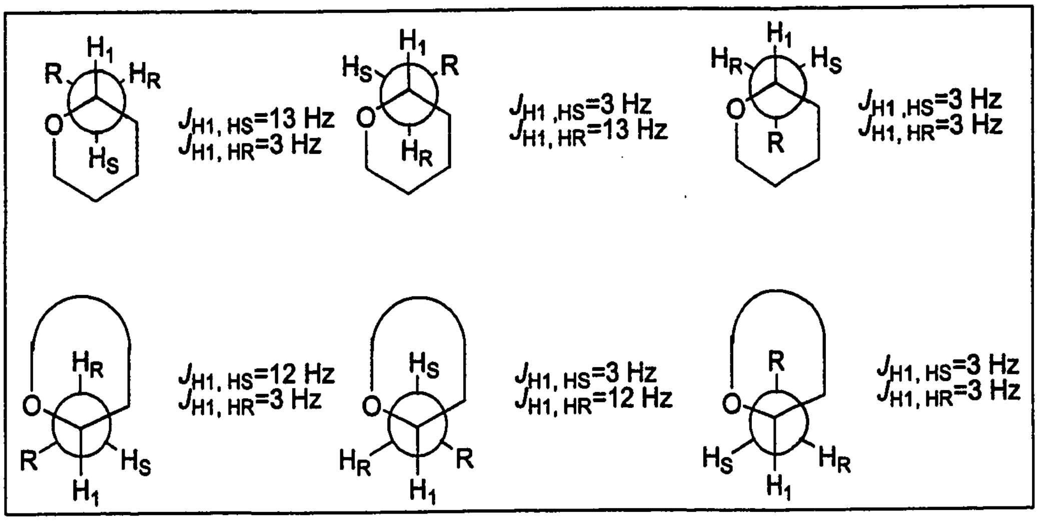
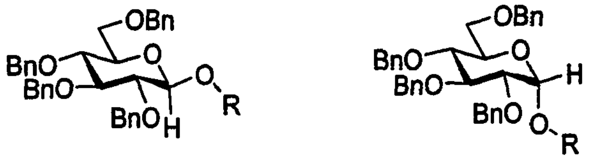


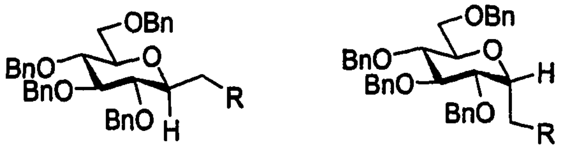
Figure 1.4 Stereoselectivities of *O* and *C*-glycosides

***O*-Glycosides**



Shape influenced by steric and electronic effects,
for example, the axial (α) isomer is *more* stable than the equatorial (β)
Unique reactivity of the anomeric carbon, an acetal which is susceptible
to both acid and enzymatic cleavage

***C*-Glycosides**

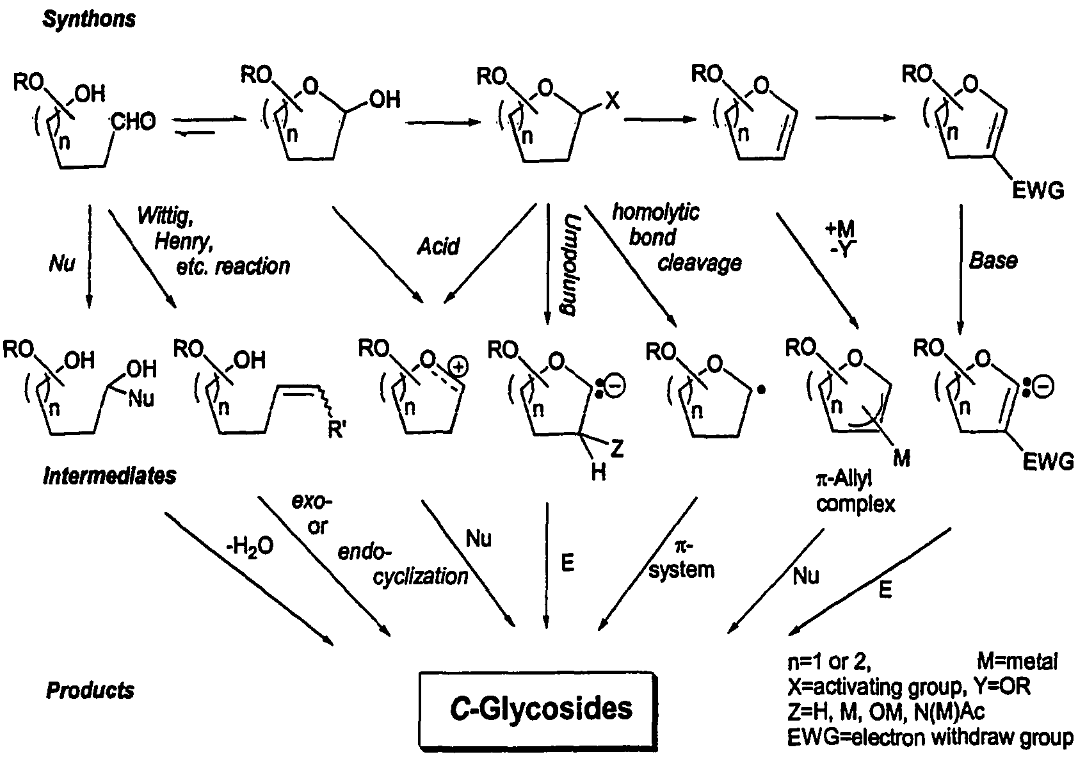


Shape influenced by steric effects,
for example, the axial (α) isomer is *less* stable than the equatorial (β)
No special reactivity of the anomeric carbon, not an acetal, thus not susceptible
to either acid or enzymatic cleavage

1.2 Synthesis of *C*-glycosides

C-glycoside synthesis has been reviewed by Levy,[1] Postema,[2] Sinay,[3] Beau,[4] Nicotra[5] and Linhardt.[6] A generalized overview of the most common synthons and intermediates in the *C*-glycosylation is shown in Scheme 1.1.[6] One can attempt to generalize about synthetic methods by listing reaction types used to form a *C-C* bond to the anomeric carbon of a sugar. Thus *C*-1 as an electrophile with initiation of electrophilicity with O, S, N, and X leaving groups is widespread as is initiation via glycals. Carbon-1 as a nucleophile is very popular with the most common anion precursor being a sulfone which is reductively cleaved to metallate *C*-1. Wittig-like approaches which open the carbohydrate ring followed by electrophilic recyclization are also popular. Free radical and organometallic approaches have received some use.

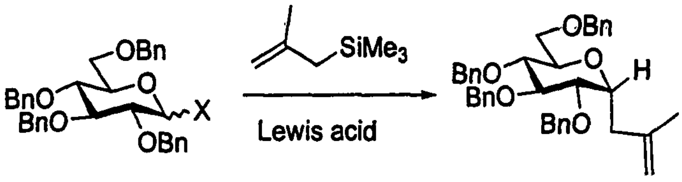
Scheme 1.1



1.2.1 Sugar Electrophiles

The most common methods for *carbon-carbon* bond formation at the anomeric carbon involves nucleophilic attack on this electrophilic center. A wide variety of electrophilic sugars have been employed, such as glycosyl halides, imidates, glycals, lactones, thioglycosides, 1,2-anhydrosugars, as well as *O*-protected glycosides such as *p*-nitrobenzoates. The carbon nucleophiles that have been used include silyl enol ethers, alkenes, allylsilanes, allylstannes, homoenolates, and organometallics such as Grignard reagents, organolithiums, cuprates, and aluminates. A Lewis acid is usually used to form an oxonium ion species which is then captured by an external carbon nucleophile, such as allylsilanes and silyl enol ethers. With D-pyranose sugars attack is often from the α-face leading to the α-*C*-glycoside. This is due to the anomeric effect of the ring oxygen which directs the incoming nucleophile to the α-face (Scheme 1.2).

Scheme 1.2



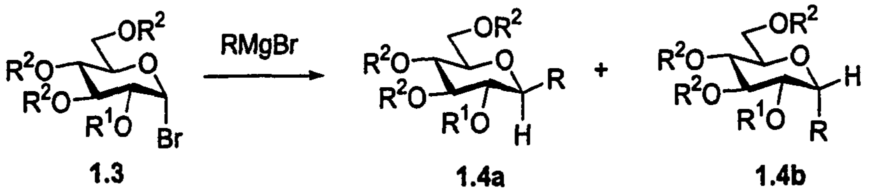
1.1

1.2

X=OH, OMe, halides, etc
Lewis acid: $BF_3.OEt_2$, TMSOTf

Organocuprate, organozinc, organolithium, organotin and Grignard reagent have also been utilized for the *C*-glycosylation of sugar halides.[1] One example demonstrates the methodology (Scheme 1.3).[7]

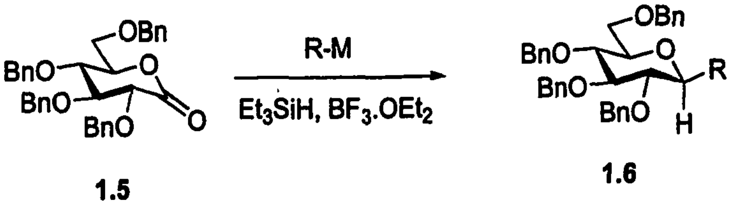
Scheme 1.3



$R^1=R^2=$Bn, Me, Silyl, α-selectivity R=allyl, vinyl, benzyl, alkynyl, α-selectivity
$R^1=$Ac, or Bz, $R^2=$Bn, Me, Silyl, β-selectivity

Kraus and Molina[8] have studied the addition of organometallic reagents to sugar lactones. The product are lactols, which then reduced by the $Et_3SiH/BF_3.Et_2O$ method to give good yields of β-*C*-glycoside (Scheme 1.4).

Scheme 1.4



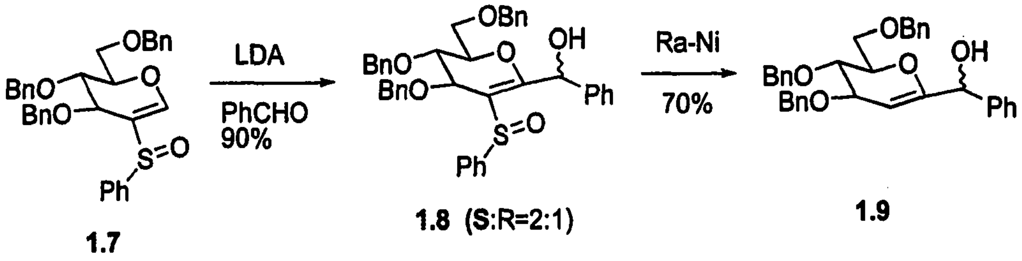
RM:	
phenyl magnesium chloride	88%
2-furyllithium	65%
2-pyridyllithium	60%
vinyl magnesium bromide	60%

1.2.2 Nucleophilic Glycosides

The character of the anomeric carbon atom can be changed from electrophilic to nucleophilic. Examples of nucleophilic sugars include *C*-1 lithiated glycals, both directed and non-directed, stannyl glycals, stannyl glycosides, copper glycosides, nitro sugars and anomeric complex derived from transition metals.

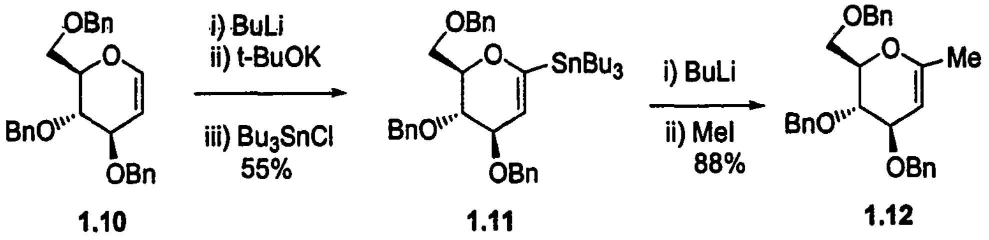
Schmidt and co-workers[9] have used *C*-2-sulfoxide-stablized *C*-1-lithiated glucal **1.7** as nucleophile. Scheme 1.5 shows an unsaturated sulfoxide which was deprotonated with LDA and subsequently treated with benzaldehyde to afford the *C*-glycoside **1.8.**

Scheme 1.5



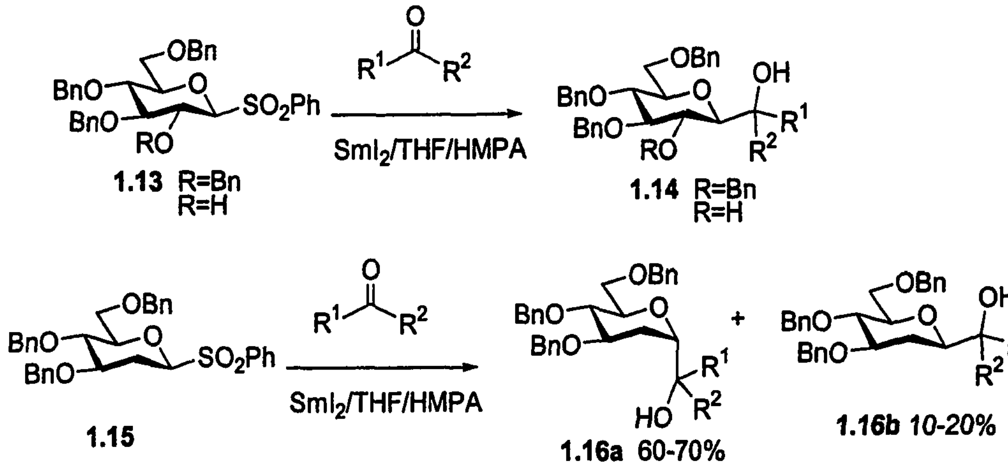
Stannyl glycals have served as *C*-glycoside precursor as shown in Scheme 1.6.[10] The protected glycal **1.10** was treated with *n*-BuLi and *t*-BuOK to yield the *C*(1)-anion which was then allowed to react with n-Bu$_3$SnCl to form the anomeric stannane **1.11.** Reaction of **1.11** with *n*-BuLi and methyl iodide then gave the *C*-glycoside **1.12.**

Scheme 1.6

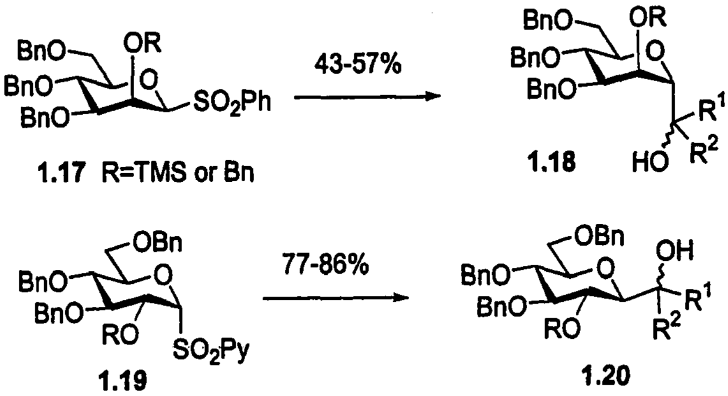


SmI$_2$ has promoted a number of important reactions in organic synthesis *via* one or two electrons transfer process since the late 1970's. Sinay[11] and Beau[12] have introduced SmI$_2$-mediated reactions for *C*-glycoside synthesis (Scheme **1.7** and **1.8** respectively). Obviously, the stereochemistry at the anomeric center is dependent on the presence of a substituent at C2 (α- product for 2-deoxy sugar, β-product for glycopyranoside).

Scheme 1.7



Scheme 1.8



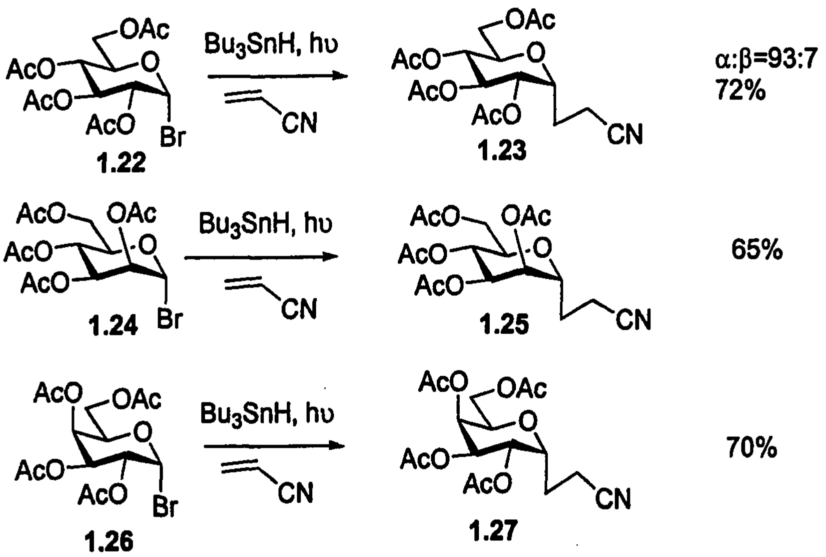
reaction condition: R^1COR^2, SmI_2, THF; If R=Ac, glucal is the major product

1.2.3 Free Radical Approaches

Free radical addition reactions are very popular and important methods for *C-C* bond formation at the anomeric center of carbohydrates. The advantages of free radical chemistry include mild reaction conditions, facile generation of anomeric radicals from available glycosyl halides, and the predictable reactivity of pyranosyl radical.[13]

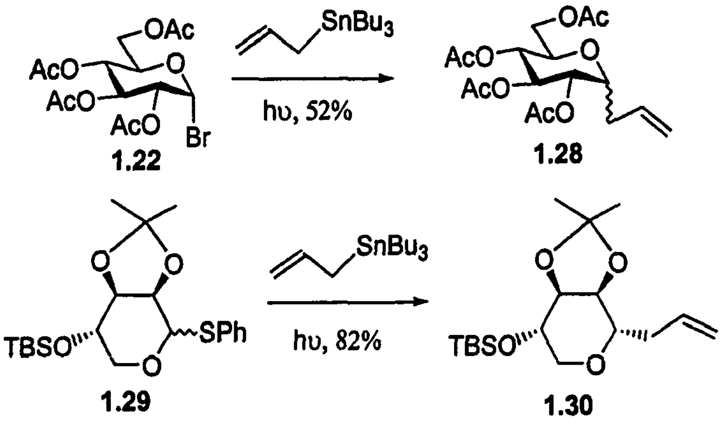
Giese has utilized the gluco, manno and galacto pyranosyl halides in the synthesis of *C*-glycosides. Reaction of the glycosyl bromide with acrylonitrile and tributyltin hydride under photolytic conditions gave the α-*C*-glycoside (Scheme 1.9).[14]

Scheme 1.9



Keck has used allylstannanes in his synthesis of *C*-glycosides (Scheme 1.10).[15] Irradiation of a mixture of glucosyl bromide and allylstannane produced the α, β isomers **1.28**. Treatment of the thioglycoside **1.29** under similar conditions produced **1.30**.

Scheme 1.10



Junker and Fessner have synthesized *C*-glycosidic phosphonates by the addition of pyranosidic and furanosidic glycosyl radicals to α-phosphoacrylates (Scheme 1.11 and Figure 1.5).[16]

Scheme 1.11

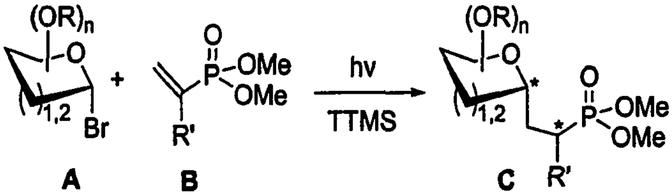
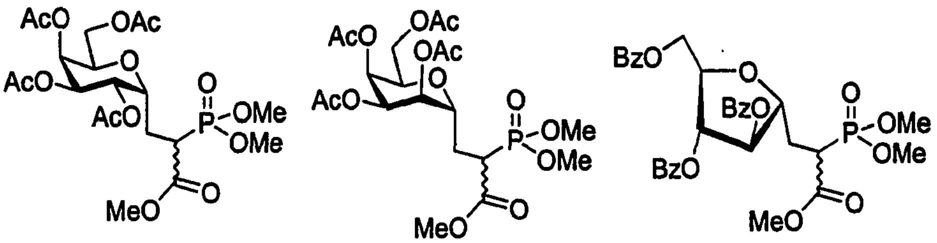


Figure 1.5 *C*-glycosidic phosphonates obtained by glycosyl radical addition to vinyl phosphonates



1.31 **1.32** **1.33**

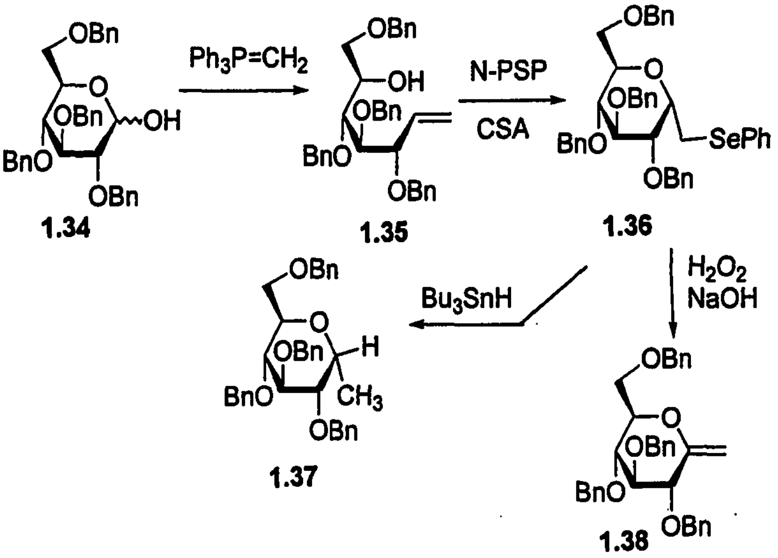
Although the free radical approach is a useful method, reduction of the radical by tributyltin hydride prior to addition or cyclization can sometimes be a problem.

1.2.4 Wittig Approaches

The Wittig reaction has also been extensively applied to *C*-glycoside synthesis. Ylides can react with lactols to yield open chain sugars which either cyclize *in situ* to produce a *C*-glycoside, or can be isolated and cyclized via other means. Both Wittig-like reactions on sugar lactones and reactions of anomeric phosphoranes with suitable carbonyl compounds have been used to construct exo-methylenic sugars.

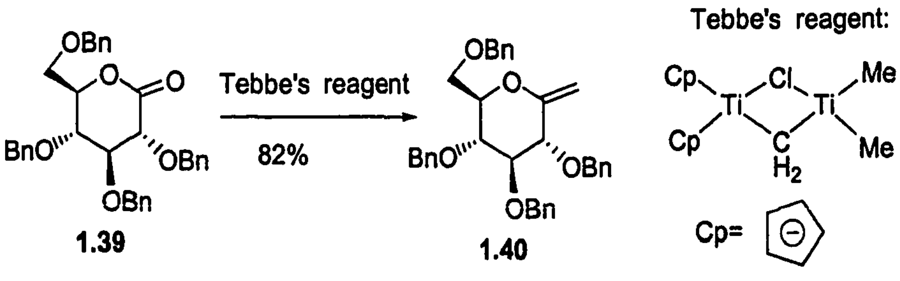
Reaction of glucose derivative **1.25** with ylide ($Ph_3P=CH_2$) gave compound **1.26** in good yield (Scheme 1.12).[15] The open chain sugar was cyclized by N-(phenylseleno)phthalimide in the presence of camphorsulfonic acid to gave the α-C-glycoside **1.36**. Treatment of **1.36** with tributyltin hydride afforded the reduced methyl glycoside **1.37**. Alternatively, the seleno group may be oxidatively eliminated with hot alkaline hydrogen peroxide to give the exo-methylene sugar.

Scheme 1.12



An alternative Wittig reaction on sugar lactone was done by Reddy.[18] When lactone **1.39** is reacted with Tebbe's reagent, the exo-methylene sugar is produced (Scheme 1.13).

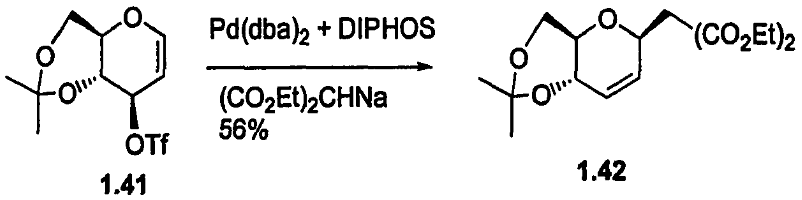
Scheme 1.13



1.2.5 Transition Metal Mediated *C*-Glycosylation

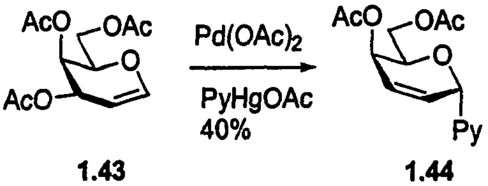
The extensive chemistry of allylic systems in the presence of Pd(0) has been applied to the preparation of *C*-glycosides.[19] Scheme 1.14 shows the reaction of glycal **1.41** in a Michael fashion with the enolate of malonic ester. The process was carried out in THF in the presence of bis(dibenzylideneacetone)-Pd(0) and bis(dipenylphosphino)ethane and gave **1.42** in 56% yield.[20]

Scheme 1.14



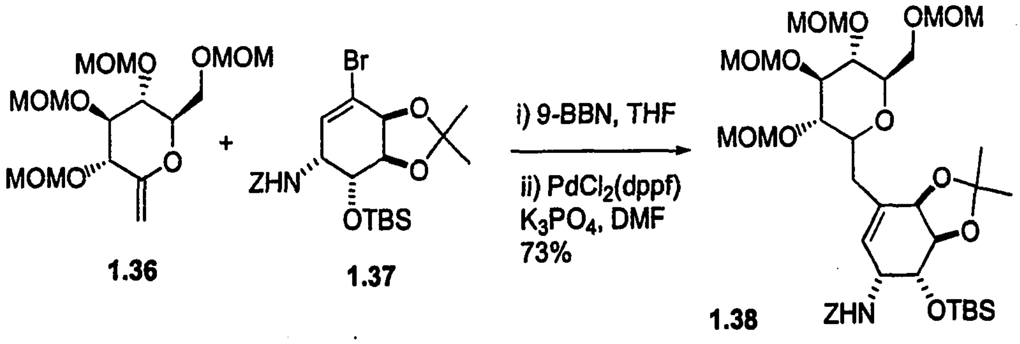
The Heck type reaction of glycal derivatives and arylpalladium complex provides *C*-glycosides under mild conditions and with high regioselectivity at the anomeric center (Scheme 1.15).[21]

Scheme 1.15



The Palladium-catalyzed Suzuki coupling has also been used in *C*-glycoside synthesis.[22] Hydroboration of exo-methylene pyranose **1.45** (9-BBN, THF, reflux), followed by Suzuki coupling of the products with vinyl bromide **1.46** ($PdCl_2$(dppf) and K_3PO_4, in aq. DMF), afforded *C*-glycoside **1.47**, as a single diastereoisomer (Scheme 1.16).[23]

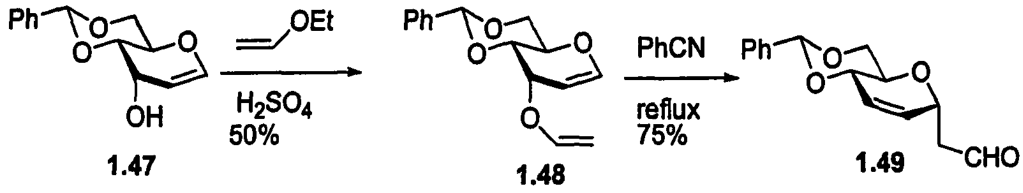
Scheme 1.16



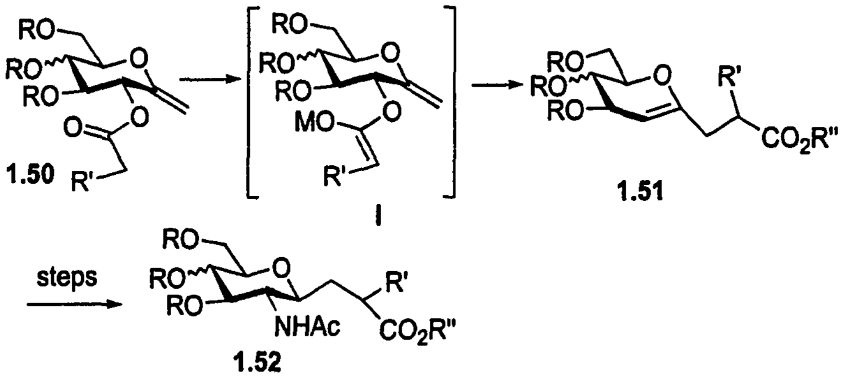
1.2.6 Concerted reactions

Concerted reaction such as [4+2] cycloadditions and sigmatropic rearrangements have also been employed to make *C*-glycosides.[24] Fraser-Reid has made functionalized *C*-glycosides using the Claisen rearrangement (Scheme 1.17).[25] Similarly, Langlois et al has a new strategy to synthesize C1-substituted glycals. The glycal was converted to β-*C*-glycoside using a Claisen-Ireland rearrangement (Scheme 1.18).[26]

Scheme 1.17



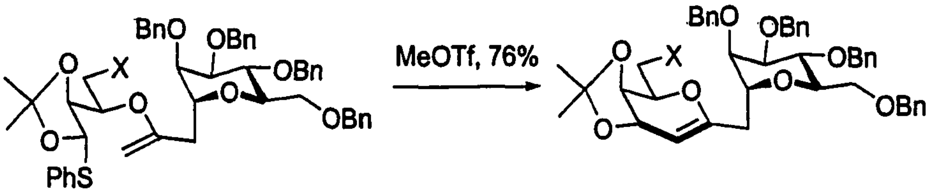
Scheme 1.18



1.2.7 *Do Novo* Approaches

There are also new methods where the carbohydrate ring is generated *via* C-C bond formation rather than the usual linking of the external group to C-1.[27-29] One of several examples is shown in Scheme 1.19.[30]

Scheme 1.19



1.53 X=OTBDPS **1.54** X=OTBDPS

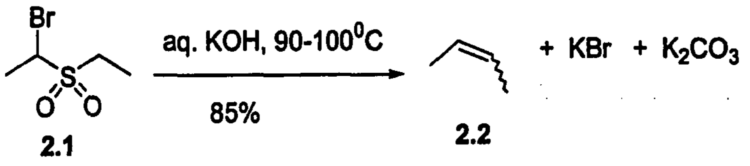
Recently, two groups, Franck's[31] and Taylor's,[32] simultaneously described a new convergent procedure for preparing *C*-glycosides *via* the Ramberg-Bäcklund (RB) rearrangement. This method is very general for *C*-glycoside synthesis. The subject of this thesis is the synthesis of *C*-glycolipids using the Ramberg-Bäcklund reaction as the key step.

2. THE RAMBERG-BÄCKLUND REARRANGEMENT

2.1 Introduction

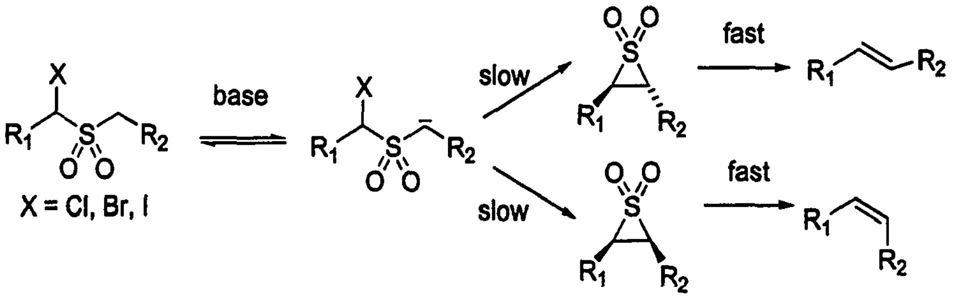
In 1940, Ramberg and Bäcklund reported a new reaction, i.e. that α-bromoethyl sulfone **2.1** was converted into 2-butene **2.2** in high yield under aqueous basic conditions (Scheme 2.1).[33] Since that time, the reaction, now known as the Ramberg-Bäcklund rearrangement, or simply as the Ramberg-Bäcklund reaction, has been used to synthesize a wide variety of alkenes,[34] such as mono-, 1,1- or 1,2-di-, tri-, tetra-substituted alkenes, cycloalkenes and conjugated alkenes, including alkenes substituted with a variety of functional groups.

Scheme 2.1



The experimental evidence[35] has long been considered to be consistent with the mechanistic scheme shown in Scheme 2.2. Step 1 involves reversible formation of the α'-anion under basic conditions. Step 2 is 1,3-elimination of halide from the sulfone α'-anion to give a thiirane 1,1-dioxide, generally as a mixture of *cis* and *trans* isomers.

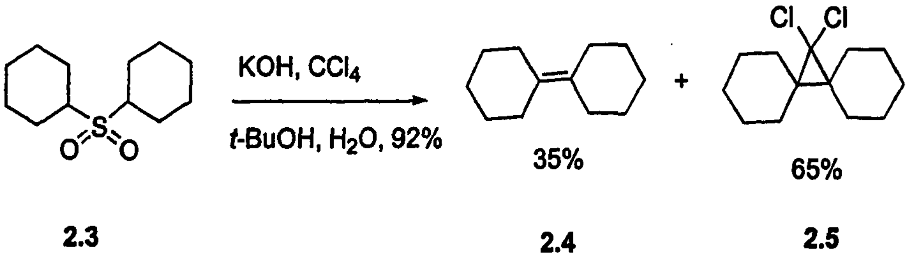
Scheme 2.2 Mechanism of the Ramberg-Bäcklund reaction



Step 2 is the rate determining step. In step 3, the thiirane dioxides lose SO_2 to give the stereoisomeric alkenes.

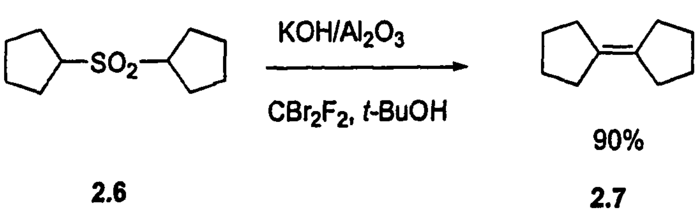
In 1969, Meyers reported an important modification of the Ramberg-Bäcklund reaction by using a suspension of powdered KOH in a mixture of CCl_4 and *t*-BuOH with the starting sulfone.[36] The shortcomings are possible multiple α-chlorination or reaction of the olefin product with dichlorocarbene to give dichlorocyclopropanes **2.5** (Scheme 2.3).[37]

Scheme 2.3



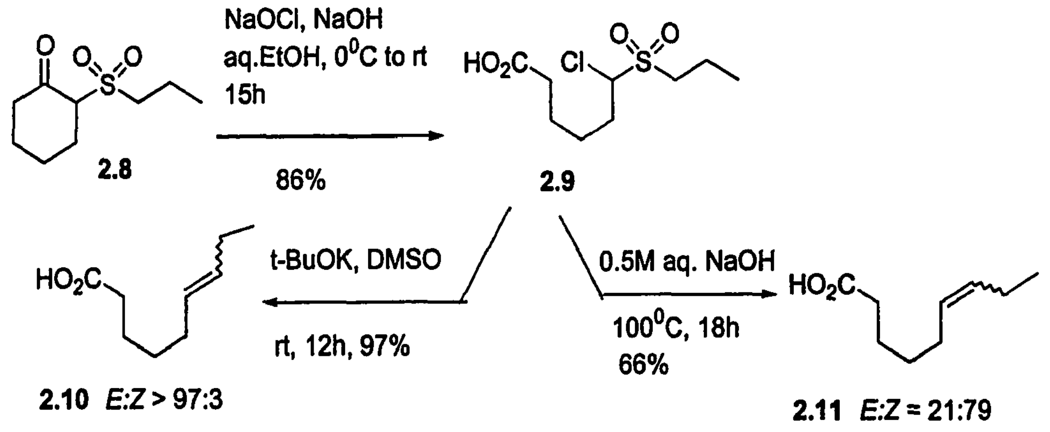
These difficulties encountered in the Meyers' procedure were completely overcome by Chan's modification i.e. that powdered KOH-CCl_4-*t*-BuOH was simply replaced by alumina supported KOH-CBr_2F_2-*t*-BuOH (Scheme 2.4).[38]

Scheme 2.4



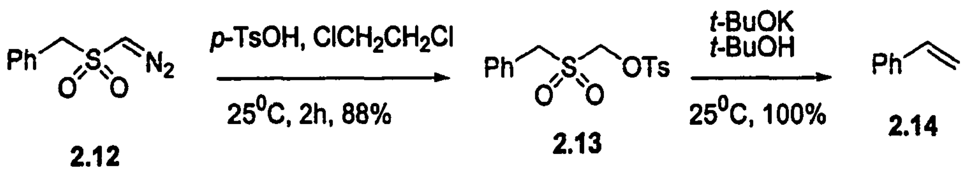
The first rearrangements of α-halo sulfone were performed using aqueous hydroxide, and these conditions are still used. However, the rearrangement takes place in a wide variety of base-solvent systems and the yield and stereochemical outcome are dependent on the conditions chosen (Scheme 2.5).[39]

Scheme 2.5



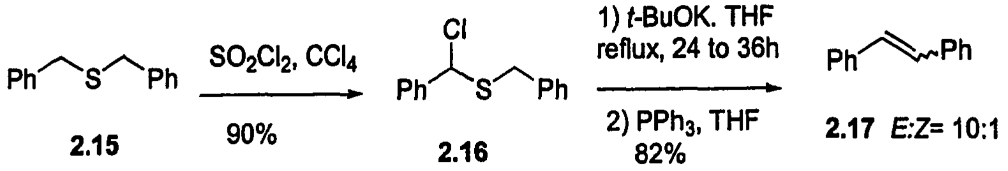
Variations of the Ramberg-Bäcklund reaction have been described in which the usual halide ion is replaced by *p*-toluenesulfonate or *p*-toluene-, alkane-, or trifluoromethane-sulfinate leaving groups. For example, Meyers has described a single transformation of the Ramberg-Bäcklund type of an α-tosyloxy sulfone (Scheme 2.6).[40] The problems are the fact that the reaction is too slow and the precursors are not easy to prepare.

Scheme 2.6



Some transformations related to the Ramberg-Bäcklund reaction have been described in which sulfide, sulfoxide, sulfonximine, phosphine oxide,[41] or phosphinate[42] groups replace the familiar sulfone group. Mitchell has reported that benzyl α-chlorobenzyl sulfides are converted into stilbenes on successive treatment with *t*-BuOK and PPh_3 (Scheme 2.7).[43] Desulfurization of an intermediate thiirane by PPh_3 is a likely pathway for this reaction.

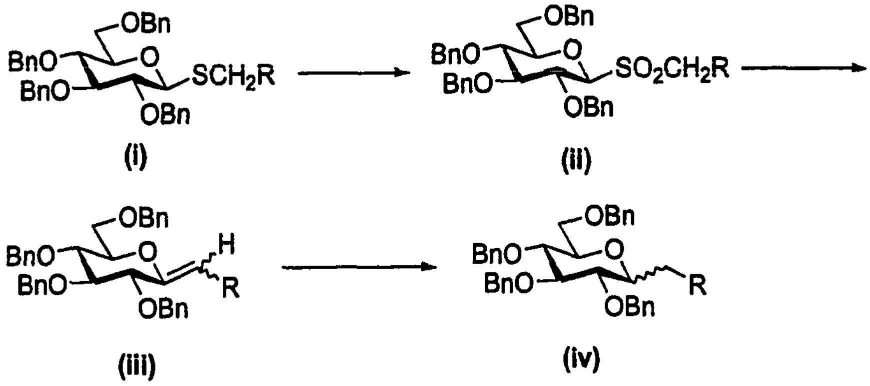
Scheme 2.7



2.2 Application of the Ramberg-Bäcklund rearrangement in *C*-glycoside synthesis

The Ramberg-Bäcklund rearrangement has been utilized for the synthesis of a number of natural products and related compounds of biological interest. In 1998, Taylor[32] used Meyers' original conditions (CCl_4, KOH) and the Chan's modified conditions (CB_2F_2, KOH-Al_2O_3) to produce exo-glycals. At the same time, Belica and Franck[31a] applied the Chan's modification of the Ramberg-Bäcklund reaction to synthesize *C*-glycosides via the exo-glycals. The Ramberg-Bäcklund sequence to

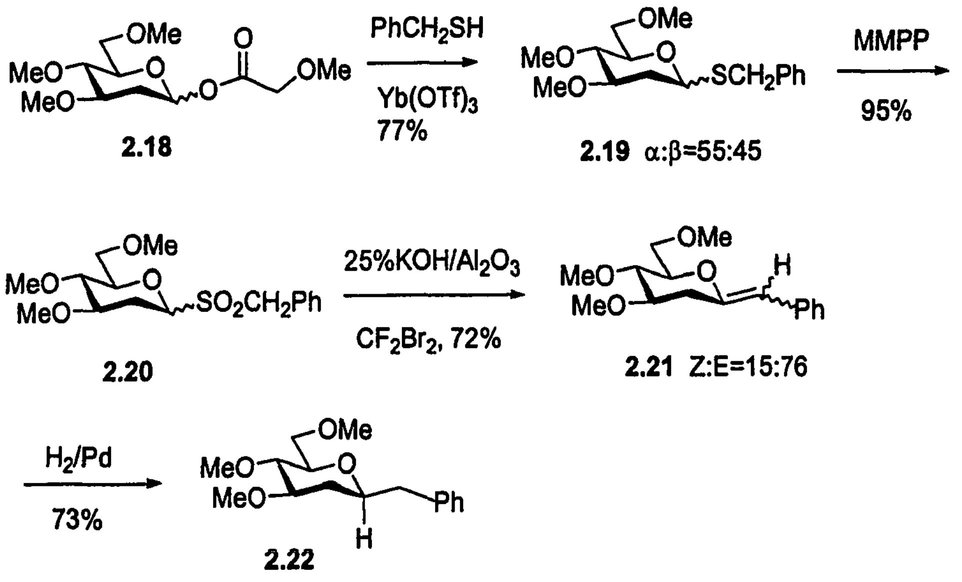
Scheme 2.8 The Ramberg-Bäcklund Route to *C*-glycosides



provide *C*-glycosides is shown in Scheme 2.8: (i) *S*-glycoside (ii) sulfonyl glycoside (iii) Ramberg-Bäcklund reaction (iv) hydrogenation.

A specific example of a benzylic *C*-glycoside is presented in detail (Scheme 2.9).[31a] *S*-glycoside **2.19** can be afforded with the Inanaga-Yb(OTf)$_3$-methoxyacetate method.[44] Sulfone formation was routine with MMPP. The Ramberg-Bäcklund conditions were those reported by Chan in which the sulfone and KOH-alunima base catalyst were mixed in a *t*-BuOH/CH_2Cl_2 mixture and then treated with an excess of CF_2Br_2 (b.p. 23 °C) at room temperature.[38] The one-flask sequence of bromination, C-C bond formation and SO_2 extrusion was quite rapid and reactions were routinely worked up in an hour or less. A simple flash chromatography gave the alkene *E*, *Z* product mixture in high yield. The product enol ethers were fairly sensitive materials so they were routinely hydrogenated with Pd catalysis to afford a mixture of *C*-glycosides with the equatorial product (β-configuration) as the major isomer. Application of this methodology to preparation of *C*-glycolipids is the goal of this thesis.

Scheme 2.9

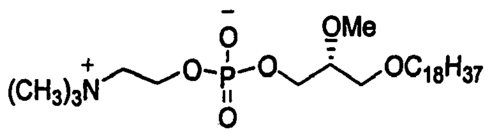


3. SYNTHESIS OF 2-DEOXY *C*-GLYCEROLIPIDS

3.1 Introduction

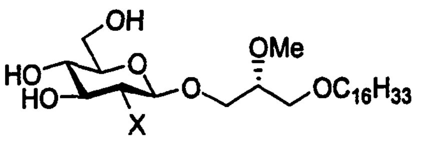
Edelfosine, 1-*O*-octadecyl-2-*O*-methyl-*sn*-glycero-3-phosphocholine (**3.1**), also known as ET-18-OCH$_3$, belongs to a family of antitumor ether lipids (AELs) that have been shown to specifically inhibit the growth of tumor cells, inhibit tumor cell invasion and metastasis, and enhance the tumoricidal capacity of macrophages (for recent reviews see refs. 45 and 46). Many AELs have been synthesized and analyzed for antitumor activity.[45, 46] ET-16-OCH$_3$-phosphonate was more active against a series of epithelial cancer cell lines *in vitro* than was the parent compound ET-18-OCH$_3$,[47] and ET-16-OCH$_3$-phosphocholine was about equipotent to ET-18-OCH$_3$ against leukemic cells *in vitro* and *in vivo*.[48, 49]

ET-18-OCH$_3$ (edelfosine)



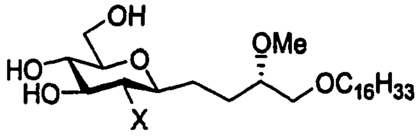
3.1

Glycosylated AELs (GAELs)



3.2 X=H
3.3 X=NH$_2$

***C*-glycosides**



3.4 X=H
3.5 X=NH$_2$

A series of glycosylated antitumor ether lipids (GAELs) has been synthesized and tested for antitumor acticity.[50-52] Among this group, Bittman has found that the 2-deoxyglucosyl- and 2-glucosamino-AELs (**3.2** and **3.3**) were particularly effective in inhibiting cancer cell growth (Table 3.1).[51, 52] Because of the advantages of *C*-glycosides, it seems reasonable to speculate that the *C*-glycosides (**3.4** and **3.5**) would have an increased lifetime and might exhibit similar antiproliferative properties to those *O*-glycosides (**3.2** and **3.3**).

Table 3.1. Growth Inhibitory Properties of edelfosine (**3.1**) and GAELs (**3.2** and **3.3**)

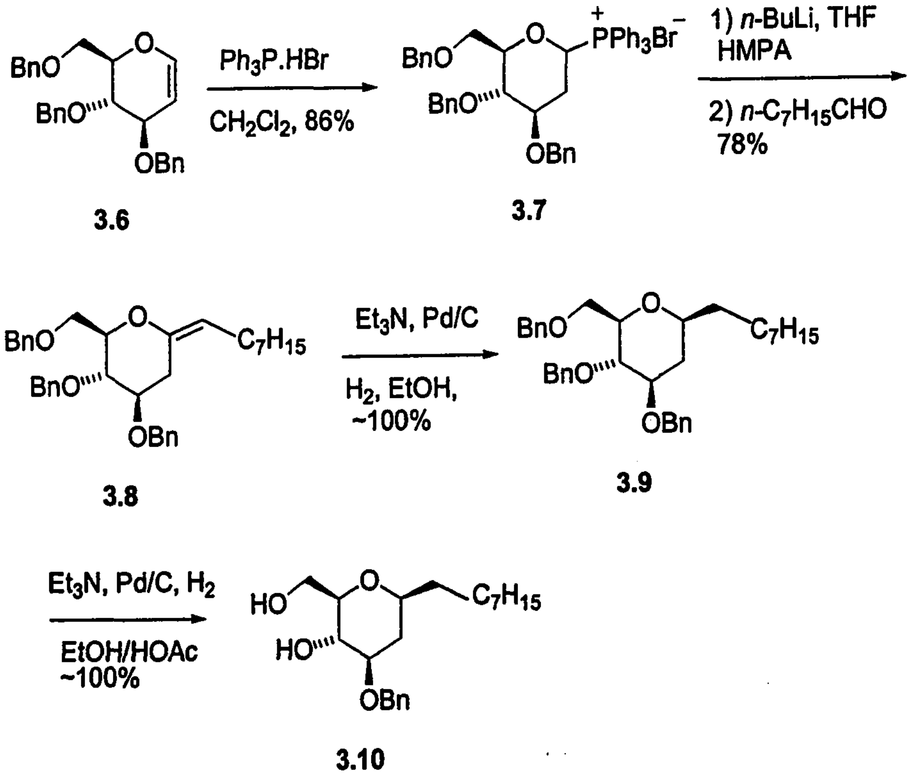
Cells	**3.1**[α]	**3.2**[α]	**3.3**[b]
A549	5.05	9.90	8.3
MCF-7	9.66	6.93	6.5
HT29	2.20	7.59	
A427			7.0

[α] Cells were treated with varying concentration of drugs for 72 h. [b] Cells were treated with varying concentration of **3.3** for 48 h.

A simple *C*-glycolipid has been prepared by Falck, Mioskowski, and co-workers.[53] They used a *C*-1 nucleophilic approach in their preparation of a 2-deoxy *C*-glycoside (Scheme 3.1). Glycal **3.6** was converted to the phosphonium bromide **3.7** by exposure to triphenylphosphine hydrobromide in dichloromethane. Ylide formation and exposure to *n*-octanal then gave the exocyclic enol ether **3.8**.

The double bond was stereoselectively hydrogenated over Pd/C in the presence of 1% triethylamine to **3.9**. Removal of the benzyl groups then provided the eight carbon *C*-glycoside **3.10**. This was a good method to synthesize a 2-deoxy *C*-glycoside; however it is probably limited to the 2-deoxy series. Our aim is to develop a general synthesis of *C*-glycosides, using the Ramberg-Bäcklund (RB) reaction as the key step (See Scheme 2.2).

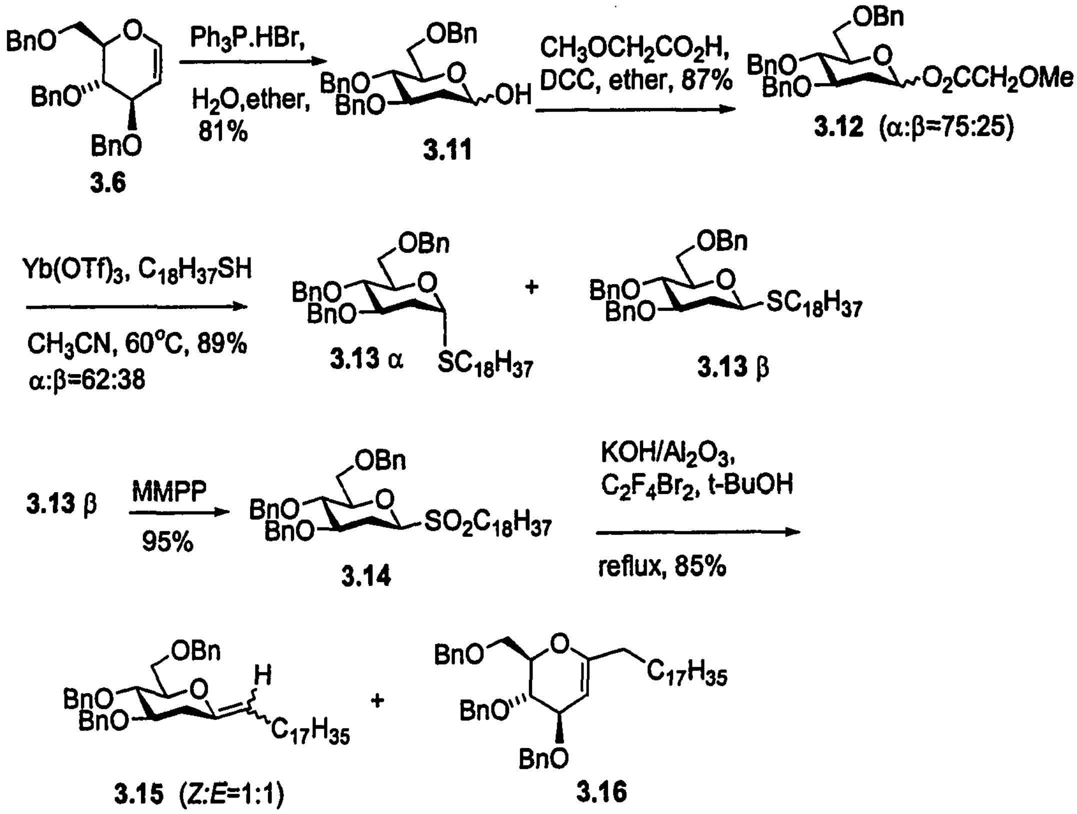
Scheme 3.1


BnO
BnO
OBn
3.6
$Ph_3P.HBr$
CH_2Cl_2, 86%
$\overset{+}{P}Ph_3Br^-$
3.7
1) n-BuLi, THF HMPA
2) n-$C_7H_{15}CHO$ 78%
C_7H_{15}
3.8
Et_3N, Pd/C
H_2, EtOH, ~100%
3.9
Et_3N, Pd/C, H_2
EtOH/HOAc ~100%
HO
HO
3.10

3.2 Synthesis of a model 2-deoxy *C*-glycoside

We first turned our attention to the use of exo-glycals for the convergent preparation of the model *C*-glycolipid **3.19** along the lines of chemistry developed by Peter Belica in our group.[31a] In our synthesis (Scheme 3.2), the benzylated thioglycoside **3.13** was made from the benzylated 2-deoxyglucose derivative **3.11** via the Inanaga-$\mathrm{Yb(OTf)_3}$ method.[44] The sulfide **3.13** was oxidized using MMPP to form sulfone **3.14** in good yield. Initial attempts with Chan's modification[38] of the one-pot RB conditions, using $\mathrm{CF_2Br_2}$ (bp 23 °C) and $\mathrm{KOH/Al_2O_3}$, and Meyers' conditions[36] ($\mathrm{CCl_4/KOH}$) failed. When $\mathrm{CF_2BrCF_2Br}$ (bp 47 °C) was used at reflux in place of $\mathrm{CF_2Br_2}$, the reaction worked quite well with β sulfone **3.14** to afford RB alkene **3.15** (*Z*:*E* = 1:1) and some endo product

Scheme 3.2



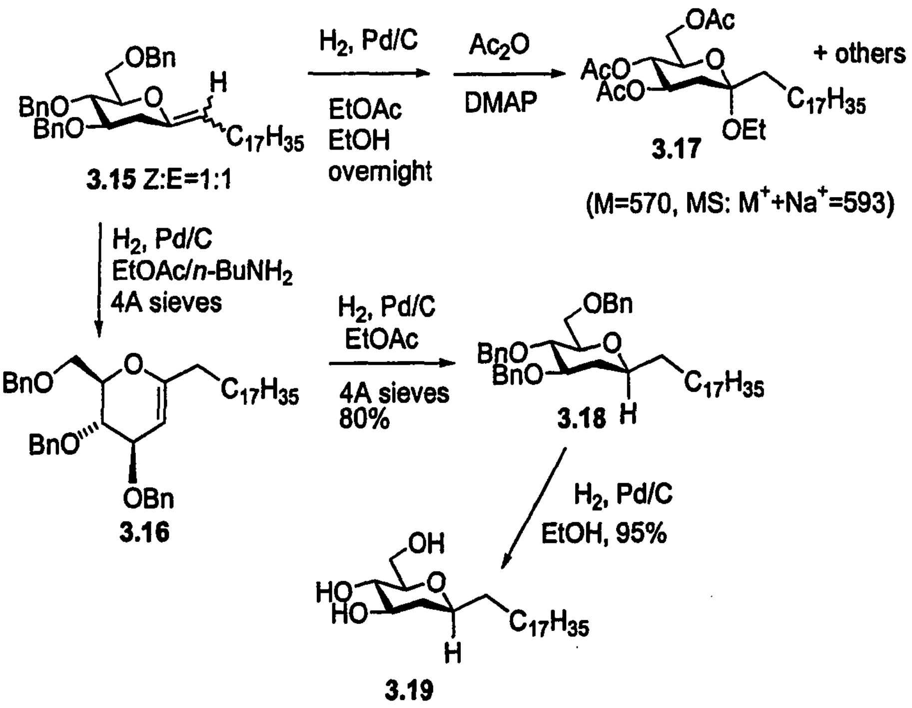
3.16 in 85% yield; some starting material was recovered as an α, β mixture. For the anomeric α sulfone **3.14**, there was very little RB reaction, with the recovered material unchanged. Table 3.2 summarizes the RB conditions we have attempted with sulfone **3.14**. If the period of storage of KOH/Alumina is over one month and an extra solvent is added, the yield of the reaction sometimes will decrease. The product enol ether **3.15** was a fairly sensitive material. Even traces of acid in $CDCl_3$ NMR solvent can isomerize some of **3.15** into **3.16**, after storage of the alkene **3.15** in an NMR tube for several days. So this ether should be made freshly before use.

Table 3.2 The RB reaction of sulfone **3.14** with $C_2Br_2F_4$ as halogen source

α:β	period of storage KOH/Al_2O_3	% KOH/Al_2O_3 (by weight)	CH_2Cl_2 (added)	reaction time	yield (%)
64:36	half year	25	yes	5h	0
64:36	1 day	25	yes	3h	26
64:36	6 days	25	no	5h	42
64:36	6 days	25	no	overnight (in a sealed tube)	50
55:45	6 days	50	no	6h	51
100:0	12 days	25	no	3h	10
0:100	6 days	25	no	5h	83
0:100	30 days	50	no	5h	94

The most unexpected problem is the reduction of the double bond in compound **3.15**. First excess Pd/C as catalyst and ethanol and ethyl acetate as solvent (Scheme 3.3) were used to make compound **3.18**. The reaction gave a mixture of several products. After acylation of the crude mixture using Ac_2O and DMAP, one side product was determined to be compound **3.17**. The presence of a quartet (2H at 3.38 ppm) and a triplet (3H at 1.20 ppm) in the ^1H NMR indicated that ethanol reacted with the double bond of **3.15** under the hydrogenation conditions, because a trace of HCl was generated from the $PdCl_2$ impurity in the Pd/C catalyst.

Scheme 3.3



An attempt was made to selectively reduce the double bond by adding a trace of *n*-butylamine.[54] However, *n*-butylamine not only inhibited the debenzylation reaction but also the reduction of the double bond. Only the endo-double bond product **3.16** was formed during the reaction (^{1}H NMR shows a triplet (2H at 1.99 ppm), corresponding to the exocylic allylic methylene proton).

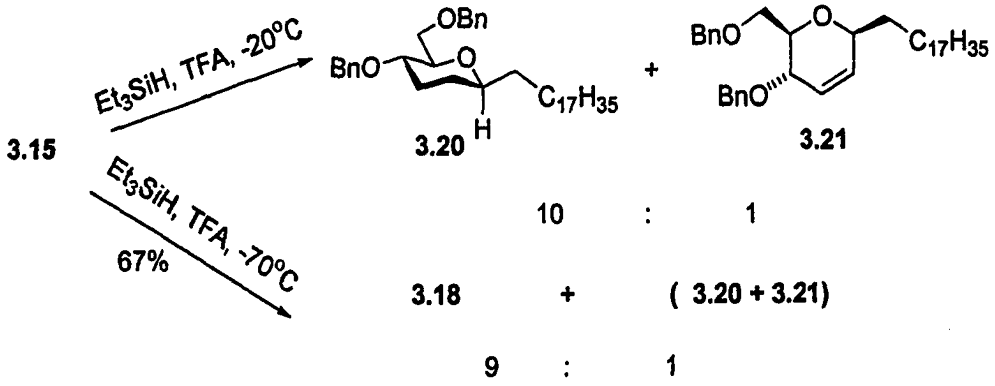
Another attempt was made to prepare compound **3.18** using less 10% Pd/C and 4Å powdered molecular sieves and ethyl acetate as solvent. The compound **3.16** was formed completely after 1 h. The product **3.18** was formed slowly in 80% overall yield after overnight reaction.

Although compound **3.18** can be made under above the conditions, the reaction was not easily controlled. Products of partial debenzylation were sometimes obtained.

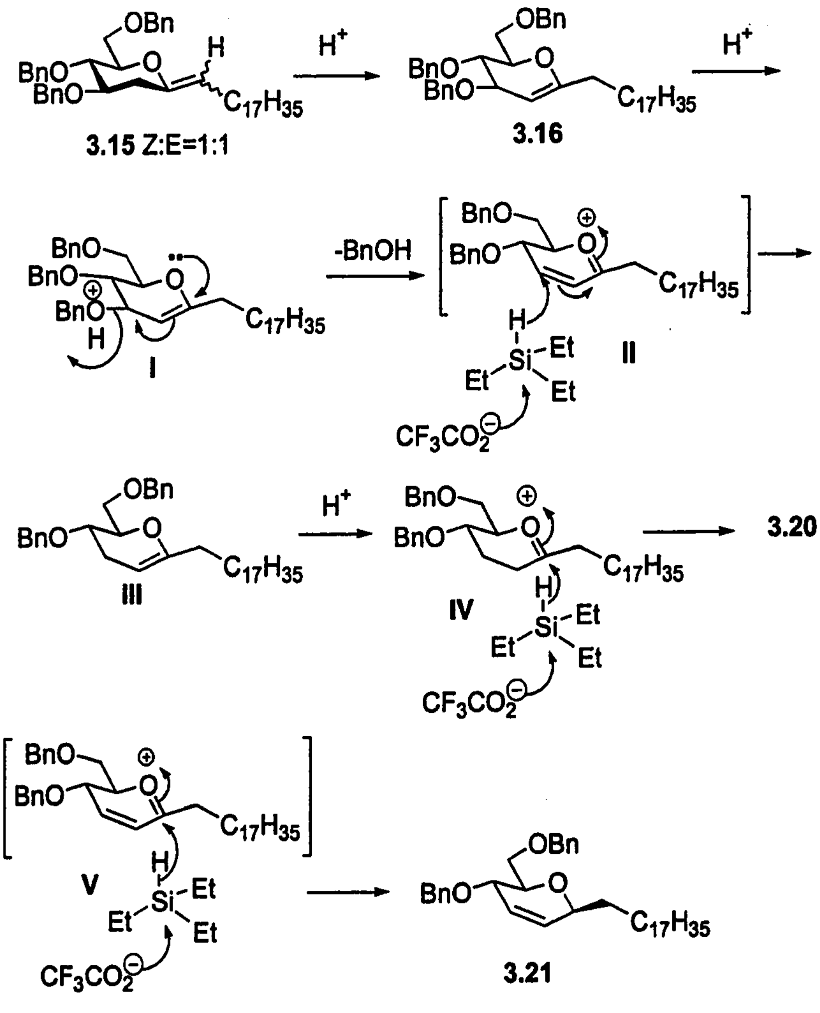
The next approach was an attempt to reduce the double bond using ionic hydrogenation.[55] Our first attempt to reduce **3.15** with Et_3SiH/TFA at –20 °C failed, giving mostly reduced Ferrier rearrangement[56] product **3.20** and unreduced Ferrier product **3.21** (Scheme 3.4). The reaction was improved to afford **3.18** in a reasonable yield by lowering the reaction temperature to –70 °C.[57] It was suggested (but not attempted) that some soft acids which would preferentially protonate the double bond rather than ether oxygens might decrease the amount of the Ferrier rearrangement reaction. A suggested mechanism for the Ferrier rearrangement of compound **3.15** is shown in Scheme 3.5.

Once *C*-glycoside **3.18** was in hand, the debenzylation step was straightforward. With 10% Pd/C as catalyst and EtOAc/ethanol as solvent, **3.19** was made in high yield (Scheme 3.3).

Scheme 3.4



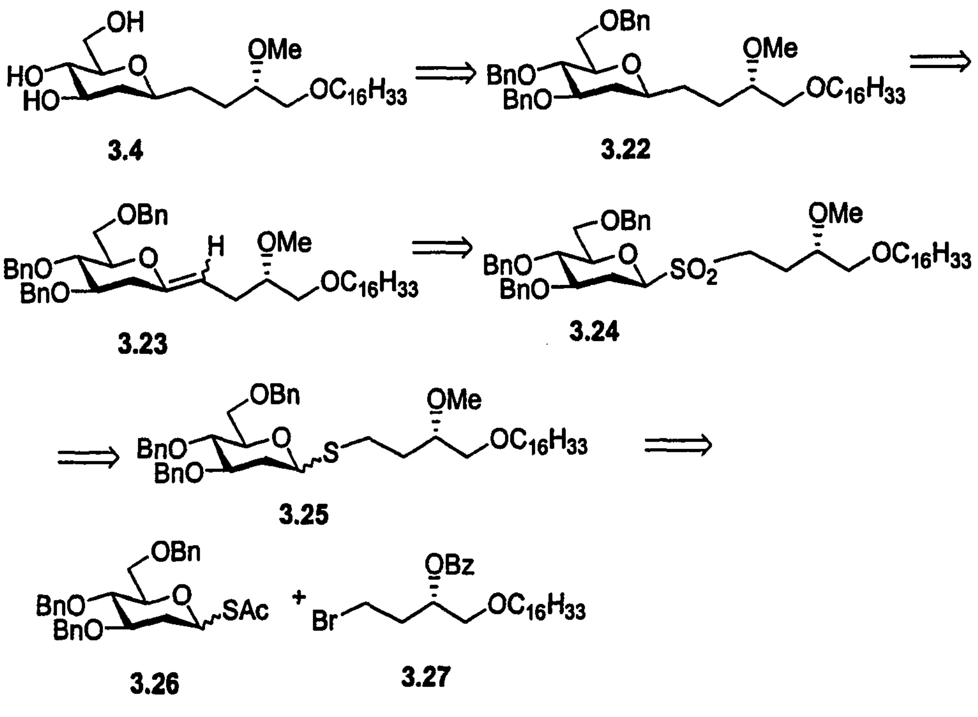
Scheme 3.5



3.3 Synthesis of 2-deoxy *C*-glyceroglycolipids

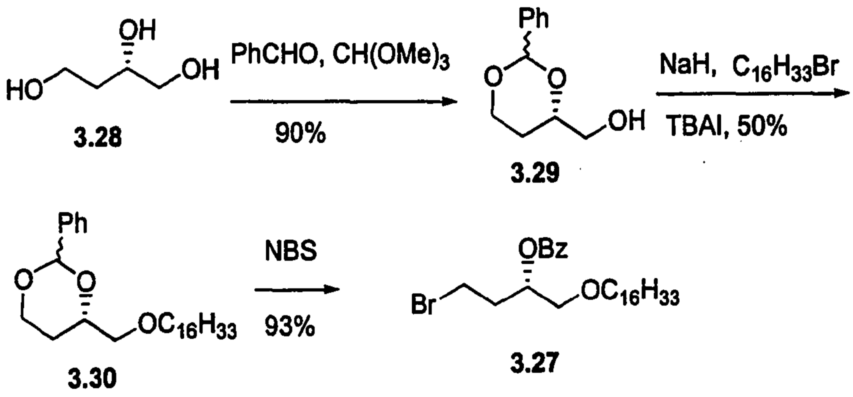
Application of this methodology to the preparation of the *C*-glycolipid of 2-deoxyglucosyl glyceride **3.4** was a goal of our work. A retrosynthesis is shown in Scheme 3.6. Tri-*O*- benzyl-*C*-glycoside **3.22** could be derived from **3.23** by selective reduction of double bond. Alkene **3.23** would come from the Ramberg-Bäcklund reaction of the glycosyl sulfone **3.24**, which in turn could be procured by oxidation of **3.25**. Ultimately, we envisioned that **3.26** and **3.27** would serve as suitable precursors to **3.25** by way of three easy steps.

Scheme 3.6



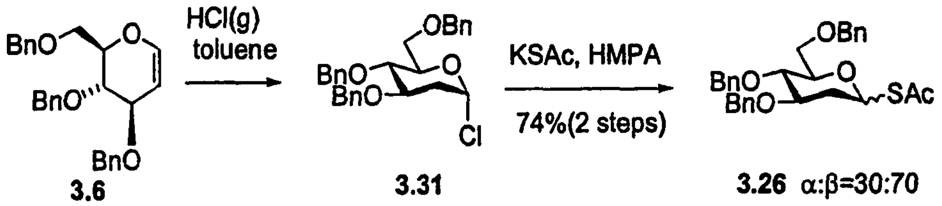
The synthesis of 1-*O*-hexadecyl-2-*O*-benzoyl-*sn*-butylbromide **3.27** has been accomplished (Scheme 3.7) starting from S-(-)-1,2,4-butanetriol **3.28**. This procedure is based on selective protection[58] of **3.28** using benzaldehyde to give 2,4-benzylidene-1,2,4-butanetriol **3.29** in 90% yield. Alkylation[58] of **3.29** with 1-bromohexadecane in the presence of TBAI afforded 1-*O*-hexadecyl-2,4-*O*-benzylidene-1,2,4-butanetriol **3.30** in 50% yield. Ether **3.30** was treated with NBS[59] to afford bromide **3.27** in 93% yield.

Scheme 3.7



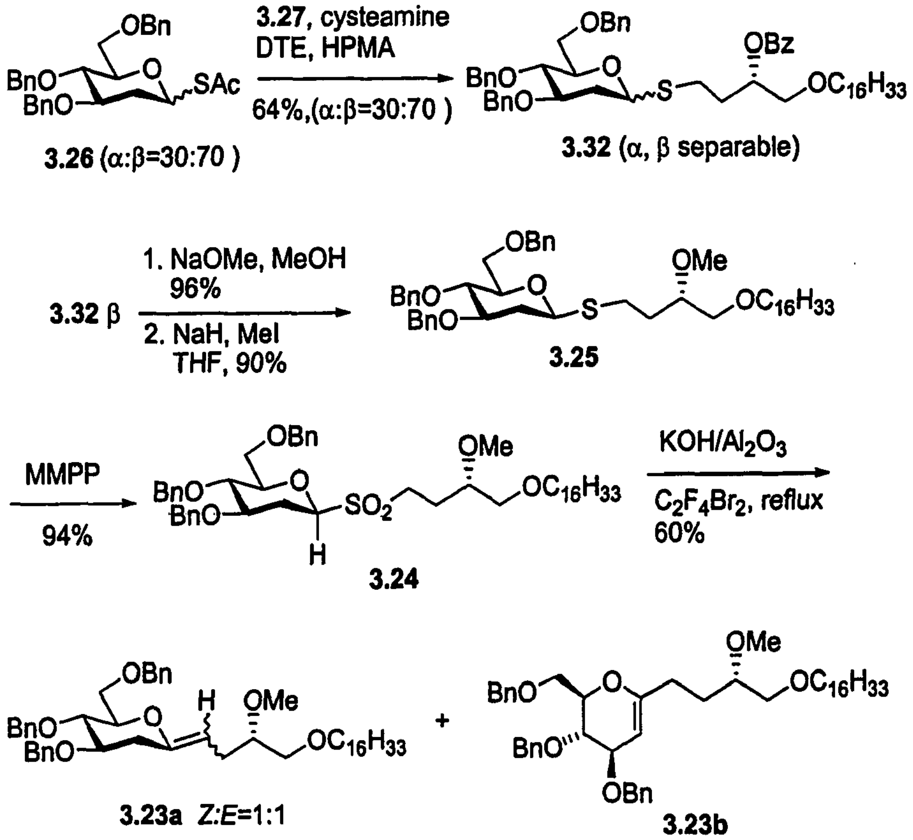
For the synthesis of 3,4,6-tri-*O*-benzyl-1-*S*-acetyl-1-thio-D-glucopyranose **3.26** (Scheme 3.8), tri-*O*-benzyl-D-glucal **3.6** was treated with HCl in toluene[60] to afford 3,4,6-tri-*O*-benzyl-2-deoxy-1-glucosylchloride **3.31**. Adduct **3.31** was treated with potassium thioacetate in HMPA[61] to afford an α/β (30:70) mixture of **3.26** in 74% overall yield.

Scheme 3.8



Thioacetate **3.26** was treated with bromide **3.27** in the presence of cysteamine and DTE[62] to afford a separable α:β (30:70) mixture of thioglycoside **3.32** in 64% yield (Scheme 3.9). Thioglycoside **3.25** was obtained by hydrolysis of **3.32** using NaOMe followed by *O*-methylation using NaH and MeI. Formation of the glycosyl sulfone **3.24** was routine with MMPP in 94% yield. The β glycosyl sulfone **3.24** was treated with 50% KOH/Al_2O_3 in CF_2BrCF_2Br and *t*-BuOH affording RB product **3.23a** and endo product **3.23b** (6:1) in 60% yield. An α and β mixture of sulfone **3.24** was recovered after chromatography. If fresh KOH/Alumina was used, the yield of the RB reaction could be higher. For the α glycosyl sulfone **3.24**, there was no RB reaction after 6 h. There was only α isomer recovered.

Scheme 3.9

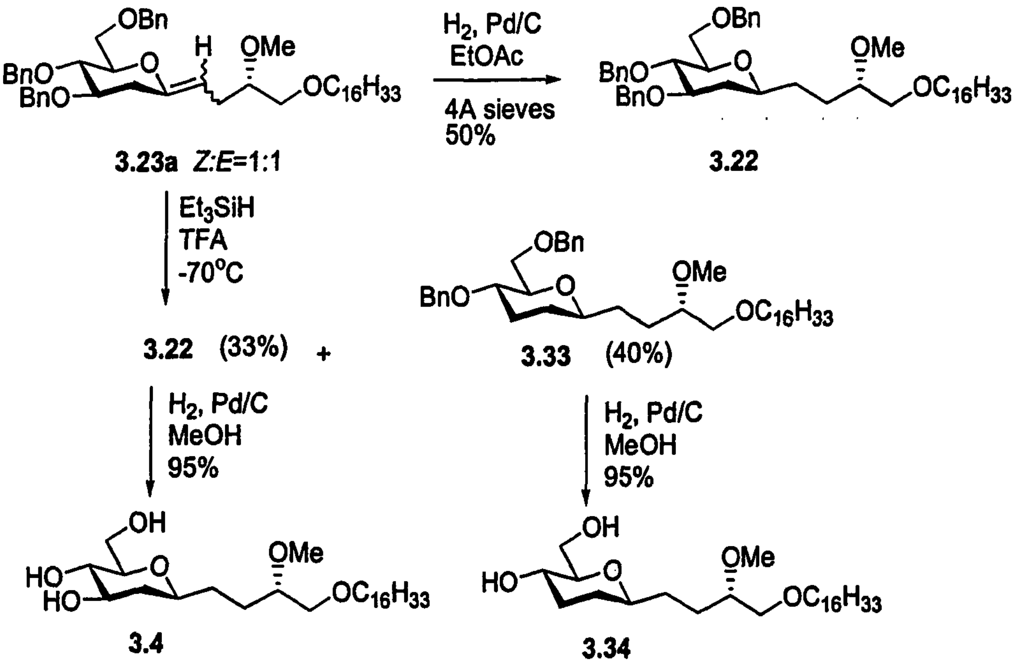


Two methods were used to synthesize *C*-glycoside **3.22** (Scheme 3.10).

1. Using Pd/C as catalyst.

Alkene **3.23a** was treated with 10% Pd/C and powdered 4Å molecular sieves in EtOAc for 10 h to afford compound **3.22** in 50% yield without debenzylation. *C*-glycoside **3.4** was afforded after **3.22** was treated with 10% Pd/C and MeOH overnight.

Scheme 3.10



2. Using Et_3SiH/TFA.

Alkene **3.23a** was treated with Et_3SiH/TFA at –70 °C in 1:7:7 ratio (**3.23a**:Et_3SiH:TFA) to afford **3.22** in 33% yield and reduced Ferrier rearrangement product **3.33** in 5:6 ratio. After hydrogenation using H_2/Pd/C, 2-deoxy *C*-glycolipid **3.4** and 2,3-dideoxy *C*-glycolipid **3.34** were afforded respectively.

2-Deoxy-C-glycolipid **3.4** was obtained in about 4.6% overall yield via 12 steps from (S)-1,2,4-butanetriol and tri-*O*-benzyl-D-glucal.

3.4 α/β glycosyl sulfone isomerization

Since the β sulfonyl glycosides **3.14** and **3.24** give a higher yield of the RB product than the α isomer in both cases, the study of isomerization of α to β becomes important. Pure α and pure β sulfonyl glycoside **3.14** were individually refluxed with *t*-BuOK in benzene and *t*-BuOH for 24 h (Table 3.3). Pure α and α:β (1:3) sulfonyl glycoside **3.14** was refluxed with 50% KOH/Al_2O_3 and 18-crown ether in THF and *t*-BuOH respectively for one week (Table 3.4). The α:β ratio of both isomers calculated from ^1H NMR is similar, so theoretically, the α:β ratio will be prone to be equal at the equilibrium stage no matter which isomer was used. In the equilibrium of α, β isomerization, the β isomer is favored.

Table 3.3 Transformation of α/β isomer of **3.14** after 24 h

Starting material **3.14**	α:β ratio from ^1H NMR
β	36:64
α	52:47

Table 3.4 Isomerization of α/β isomer of **3.14** after one week

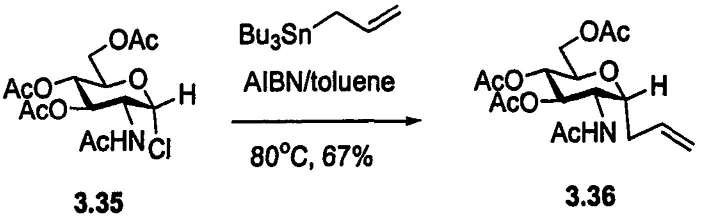
Starting material **3.14**	α:β ratio from ^1H NMR
α:β=1:3	42:58
α	44:56

An α/β (1:1) mixture of sulfone **3.14** was obtained after reflux of sulfone (α>β) with *t*-BuOK in benzene and *t*-BuOH for 10 h. This sulfone **3.14** was used as a starting material in the RB reaction to afford RB product **3.15** in 50% yield based on recovered sulfone.

3.5 Synthesis of 2-amino-2-deoxy-*C*-glycolipid

Since a rather guarded outlook for the synthesis of *C*-glycosides of 2-amino sugars was expressed in 1996,[63] several useful approaches have been reported.[64] The methods published so far for the synthesis of 2-amino-2-deoxy-*C*-glycosyl compounds mostly suffer the disadvantages of several steps, expensive starting materials, and low stereoselectivity. Horton reported the stereocontrolled α- and β-allylation of 2-amino-2-deoxy sugars at the anomeric center through a free-radical allylation reaction(Scheme 3.11).[64d] Bertozzi and co-workers published related experimental results for the synthesis of β-*C*-glycosyl derivatives of *N*-acetylglucosamine in 1996.[63]

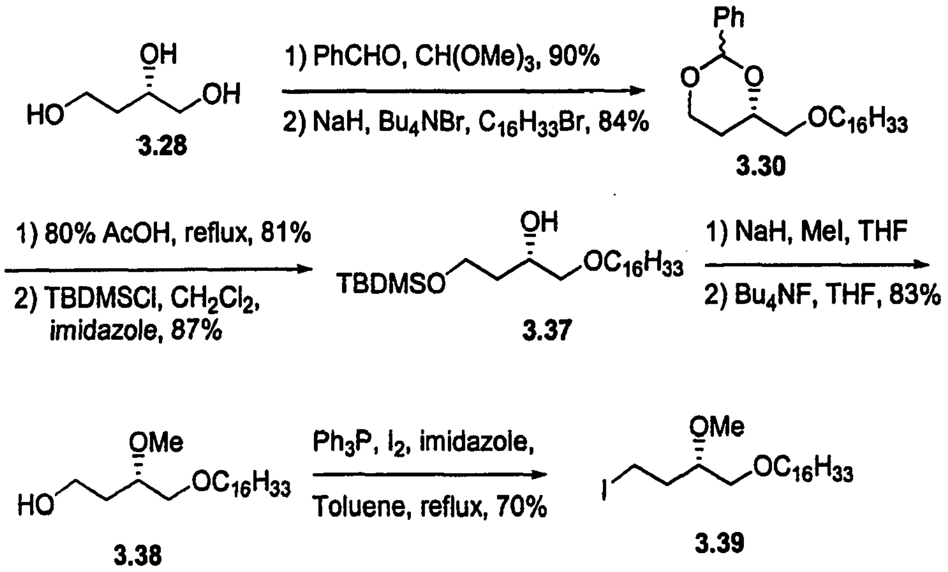
Scheme 3.11



Our plan was to compare glucosamine derivatives *O*-glycoside **3.3** and *C*-glycoside **3.5** since Bittman and coworkers had shown that the *O*-glycoside **3.3** had μmolar antiproliferative activity against several tumor cell lines.[52] This lead compound had been prepared via a zinc chloride-catalyzed version of the Koenigs Knorr reaction of 1-chloro tetra-acetylglucosamine and the appropriate modified glycerol. For the preparation of **3.5**, we chose to further test the Ramberg-Bäcklund method for the synthesis of *C*-glycosides.

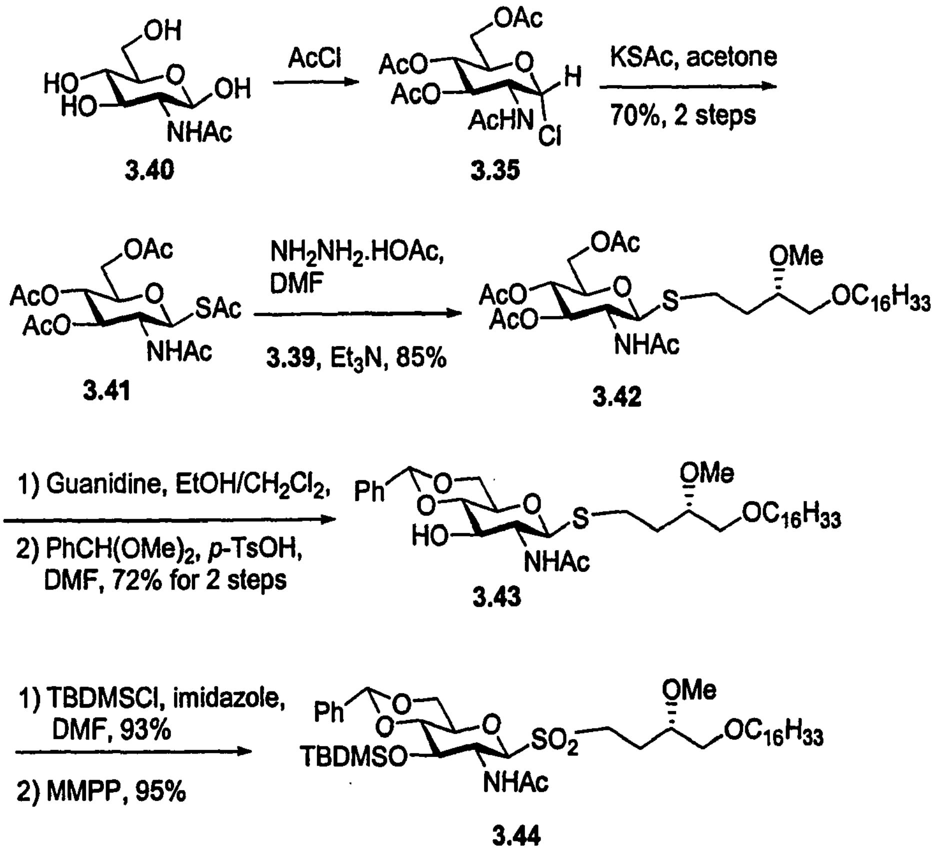
The synthetic sequence is similar to that for 2-deoxy *C*-glycoside **3.4**. In the 2-deoxy glycoside series, the methyl ether was introduced by *O*-methylation of the side chain hydroxyl in the thioglycoside precursor to the Ramberg-Bäcklund rearrangement. The corresponding methylation is not clean in the 2-acetamido glucose series because of some accompanying *N*-methylation. Therefore, we changed the sequence to synthesize the *O*-methyl side chain before making the thioglycoside. The synthesis of the lipid (*S*)-4-*O*-hexadecyl-3-*O*-methyl-1-iodobutane **3.39** was easily accomplished (Scheme 3.12) starting from (*S*)-1,2,4-butanetriol **3.28**. This procedure is based on selective protection of **3.28** followed by alkylation. Deprotection of benzylidene **3.30** using 80% acetic acid at reflux, followed by selective silylation of the primary alcohol afforded silyl ether **3.37**. *O*-Methylation followed by desilylation using Bu_4NF provided primary alcohol **3.38**. 4-*O*-Hexadecyl-3-*O*-methyl-1-iodobutane **3.39** was easily made from **3.38** and I_2/Ph_3P at reflux in toluene.[65]

Scheme 3.12



N-Acetyl-3,4,6-tri-*O*-acetyl-1-glucosamine-thioacetate **3.41** can be made from commercial *N*-acetyl-D-glucosamine **3.40** in two steps[66] (Scheme 3.13). The *S*-acetate was selectively cleaved by NH_2NH_2.HOAc in DMF. In situ alkylation with iodide **3.39**

Scheme 3.13

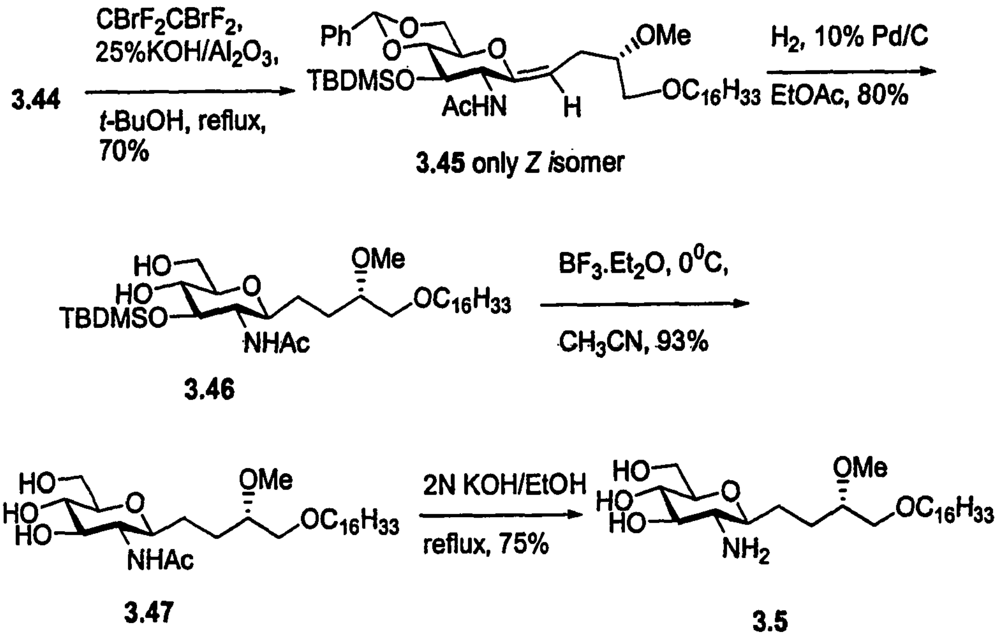


in Et_3N gave thioglycoside **3.42** in good yield.[67] Selective deprotection of the *O*-acetyl groups using guanidine[68] followed by benzylidene acetal protection of the 4,6-diol afforded thioglycoside **3.43**. Treatment of alcohol **3.43** with TBDMSCl followed by oxidation using MMPP afforded sulfone **3.44**. The Ramberg-Bäcklund (RB) rearrangement of sulfone **3.44** using 25% KOH on alumina in CF_2BrCF_2Br at reflux afforded alkene **3.45** in 78% yield. Only the *Z* isomer was obtained, which is confirmed by a NOE experiment. Figure 3.1 shows that there is a strong NOE effect between the NH and vinyl H. The yield of the reaction using freshly prepared KOH/Al_2O_3 was found to be much higher than using material that has been stored for one month in the desiccator. The RB product **3.45** is much more stable than the RB product in the 2-

deoxyglucose series. It can be stored at 0 °C for more than one month without any changes.

Deprotection and reduction of the product **3.45** using H_2 and 10% Pd/C afforded β-*C*- glycoside **3.46** in 80% yield (Scheme 3.14). Of the several methods attempted for cleavage of the silyl group with *n*-Bu_4NF, formic acid, acidic ionic exchange resin, and $BF_3.Et_2O$ conditions, only $BF_3.Et_2O$ in CH_3CN[69] gave a clean reaction. The *N*-acetyl group was cleaved using 2 N KOH/EtOH reflux at 120 °C (bath temperature) to afford the final product **3.5**.

Scheme 3.14



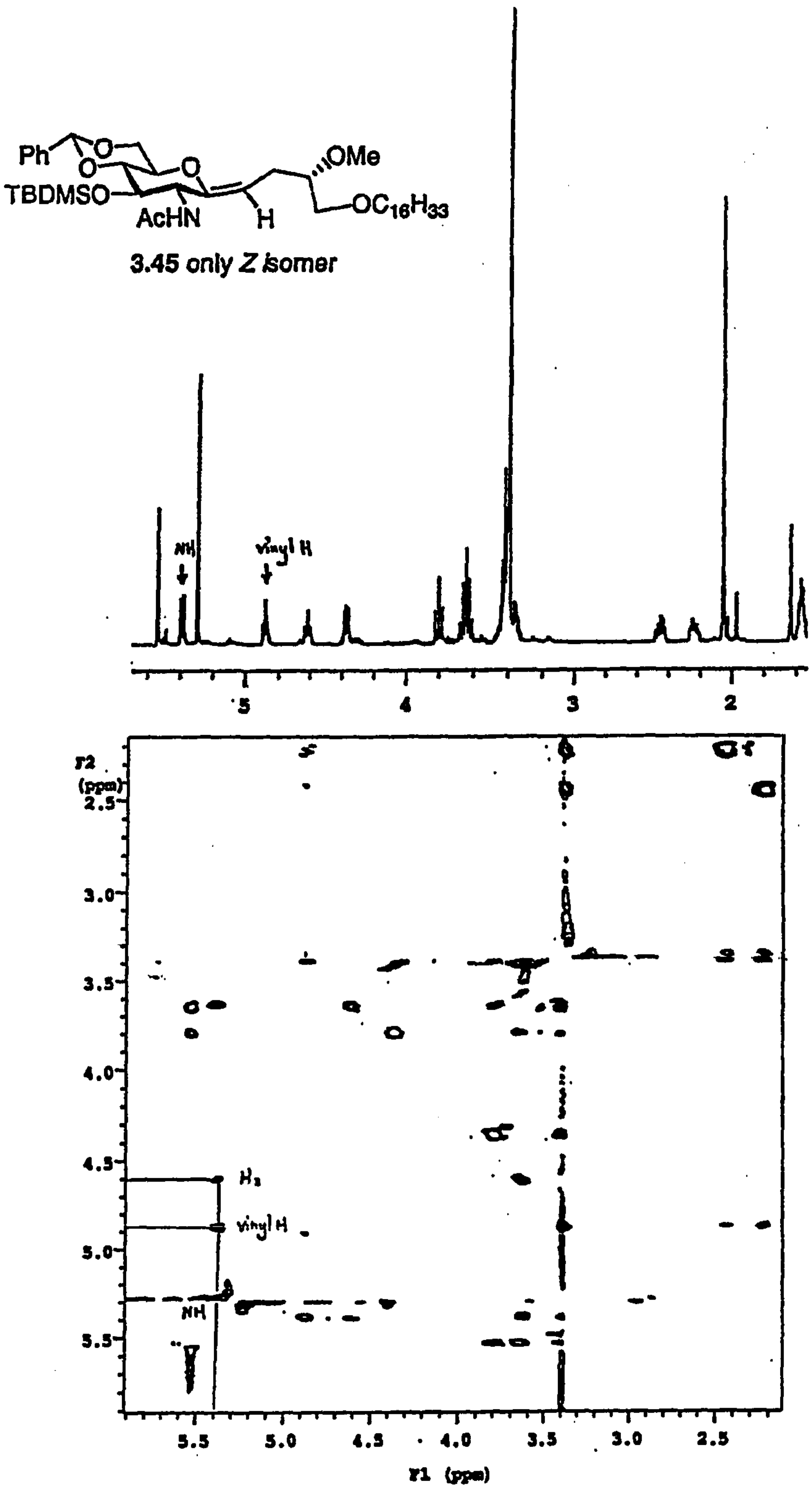
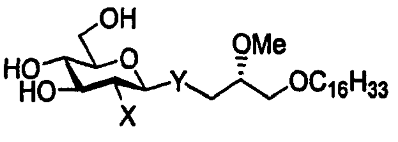


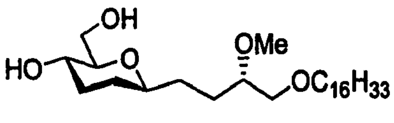
Figure 3.1 ^{1}H NMR and NOESY spectra of compound 3.45 (500MHz, in $CDCl_3$)

3.6 Biological Results and Discussion

The antiproliferative studies were done in the lab of Professor Arthur in Canada. The effects of *C*-glycoside **3.4**, and *C*-glycoside **3.34** on the proliferation of MCF-7, MDA-MB-435, MDA-MB-468, MDA-MB-231 cell lines after 48 h treatment are displayed in Figures 3.2-3.5. Table 3.5 presents the data for the *in vitro* biological evaluation of the growth inhibitory properties of *O*-glycoside **3.2**, *C*-glycoside **3.4**, and *C*-glycoside **3.34** on human tumor cells. The IC_{50} values[70] (drug concentrations required to inhibit growth by 50%) indicate that the *C*-glycoside analogs show antiproliferative properties similar to those of *O*-glycoside analog.



3.2 X=H, Y=O
3.3 X=NH$_2$, Y=O
3.4 X=H, Y=CH$_2$
3.5 X=NH$_2$, Y=CH$_2$
3.47 X=NHAc, Y=CH$_2$



3.34

Table 3.5. Growth inhibitory properties of **3.2**, **3.4** and **3.34**: IC_{50} values for inhibition of cell proliferation[a]

	IC_{50} (μM)		
breast cancer cell line	**3.2**	**3.4**	**3.34**
MCF-7	6.93[51]	25.6	21.2
MDA-MB-435		12.2	21.9
MDA-MB-468		34.4	24.2
MDA-MB-231		40.0	27.8

[a] The IC_{50} values for **3.4** and **3.34** were determined as described in ref. 66. Briefly, exponentially growing cells were incubated with the drugs (0-60 μM), and the increase in cell numbers after 48 h was determined and expressed as a percentage of the controls, which had no drug. The IC_{50} value for **3.2** was determined after a 72 h incubation period using the sulforhodamine assay described in ref. 51.

Figures 3.6-3.14 show the effect of *O*-glycoside **3.3**, *C*-glycosides (**3.5**, **3.47** and **3.4**) on the proliferation of MCF-7, MDA-MB-468, MDA-MB-231, HS578T, BT549, A498, SK-N-SH, SK-N-MC, DU145 cell lines after 48 h treatment. The IC_{50} values of **3.3** and **3.5** against those nine cells were in the range 3.1-9.1 μM (Table 3.6). SK-N-SH, SK-N-MC cells were the most sensitive to the inhibitory effects of *O*-glycoside **3.3** and *C*-glycosides **3.5**. It is worth noting that *O*-glycoside **3.3** and *C*-glycosides **3.5** have a close similarity in antiproliferative activity in all these examples. The absence of an *N*-acetyl group on the amine of **3.5** causes a marked difference in the activities of **3.5** and **3.47** compound **3.47** is not active at all. Thus the activity of **3.3** appears not to be dependent on the glycosidic oxygen in the drug.

Table 3.6 Growth inhibitory properties of **3.3** and **3.5** versus mammary tumor cell[a]

		IC_{50} (μM)			
cell line	3.3	3.5	cell line	3.3	3.5
MCF-7	8.0	8.1	MDA-MB-468	7.0	9.0
MDA-MB-231	7.1	9.1	HS578T	3.1	5.1
BT549	6.5	8.9	A498	6.9	8.5
SK-N-SH	3.8	4.1	SK-N-MC	4.1	4.1
DU145	6.5	7.9			

[a] Cells were treated with varying concentrations of **3.3** and **3.5** (0-15 μM) for 48 h. The first five are breast cancer cells, A498 is kidney cancer cells, SK-N-SH and SK-N-MC are neuronal cancer cells, DU145 is prostate cancer cells.

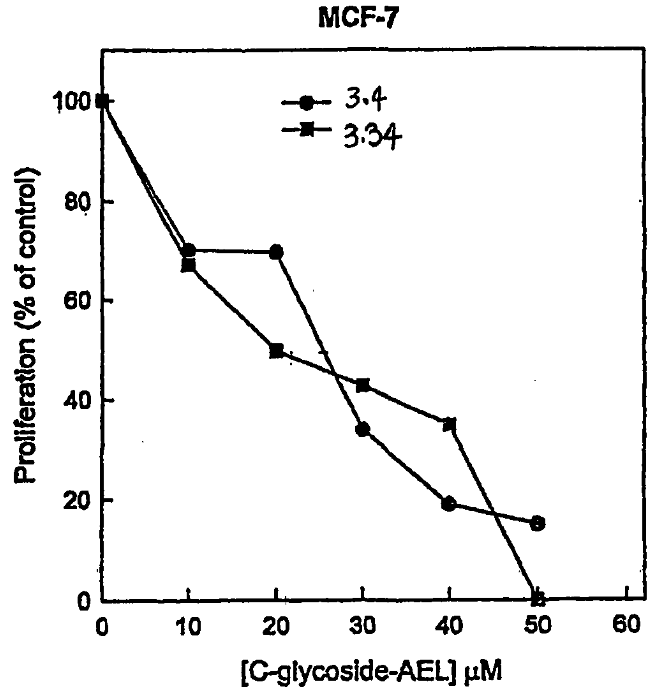


Figure 3.2 Effects of 3.4 and 3.34 on the proliferation of MCF-7 cells.

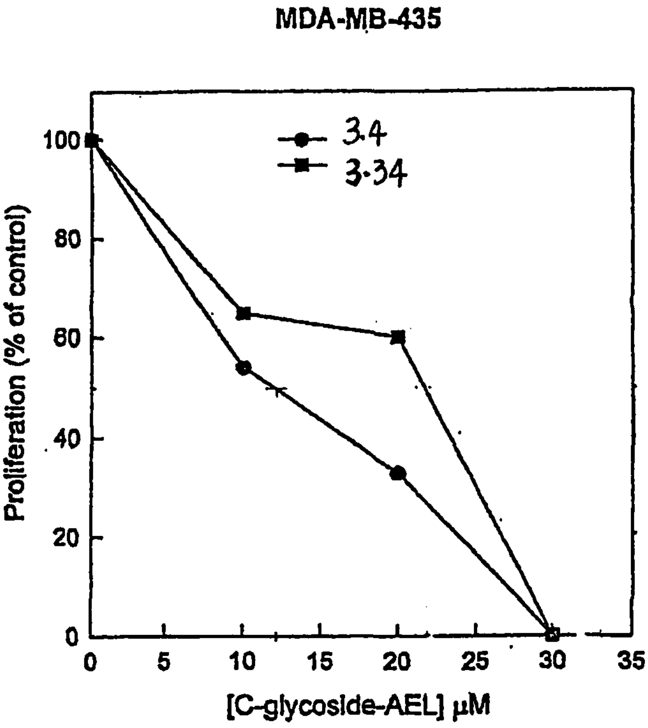


Figure 3.3 Effects of 3.4 and 3.34 on the proliferation of MDA-MB-435 cells.

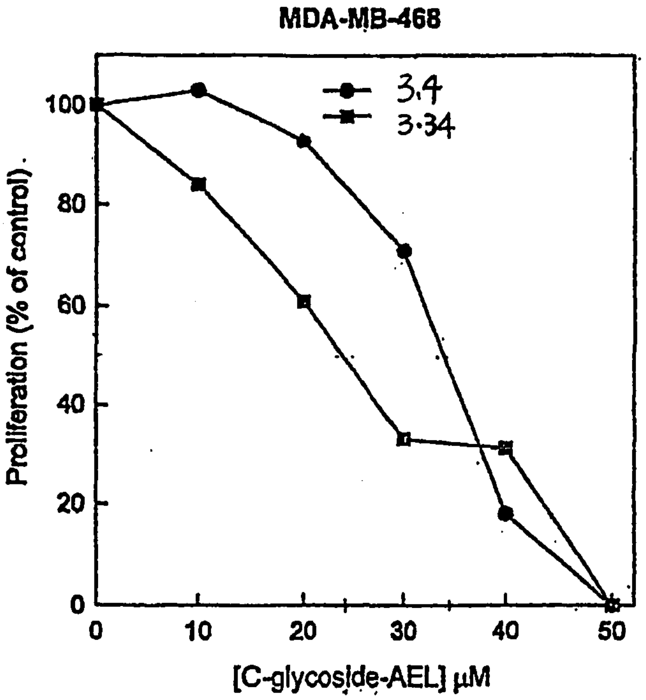


Figure 3.4 Effects of 3.4 and 3.34 on the proliferation of MDA-MB-468 cells.

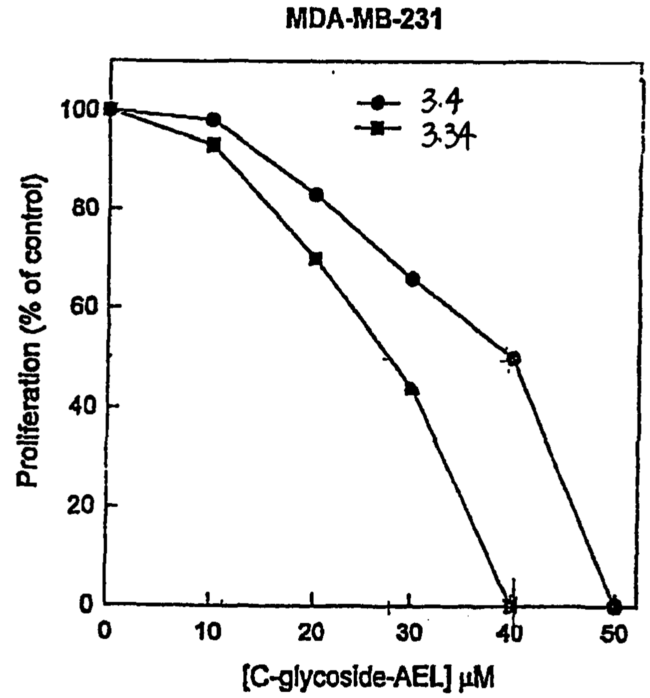

MDA-MB-231

Figure 3.5 Effects of 3.4 and 3.34 on the proliferation of MDA-MB-231 cells.

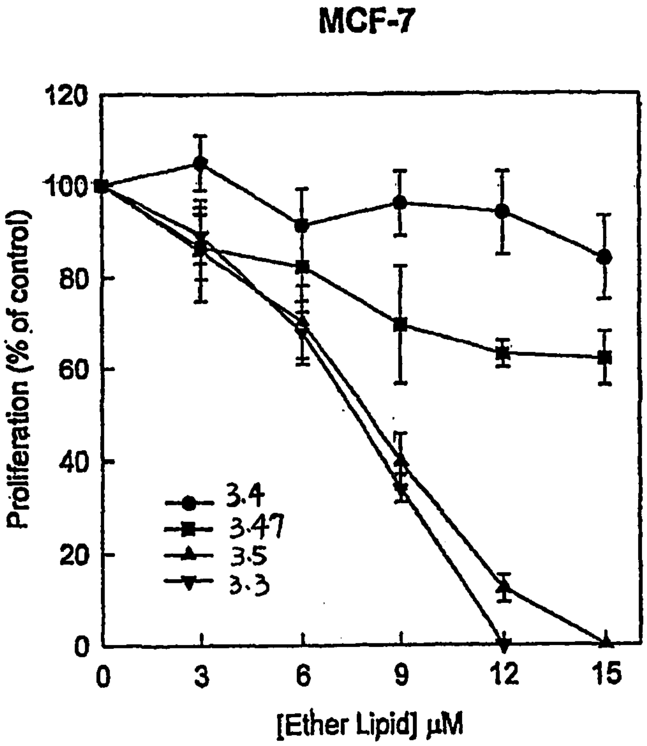

MCF-7

Figure 3.6 Effects of 3.3, 3.47, 3.4 and 3.5 on the proliferation of MCF-7 cells.

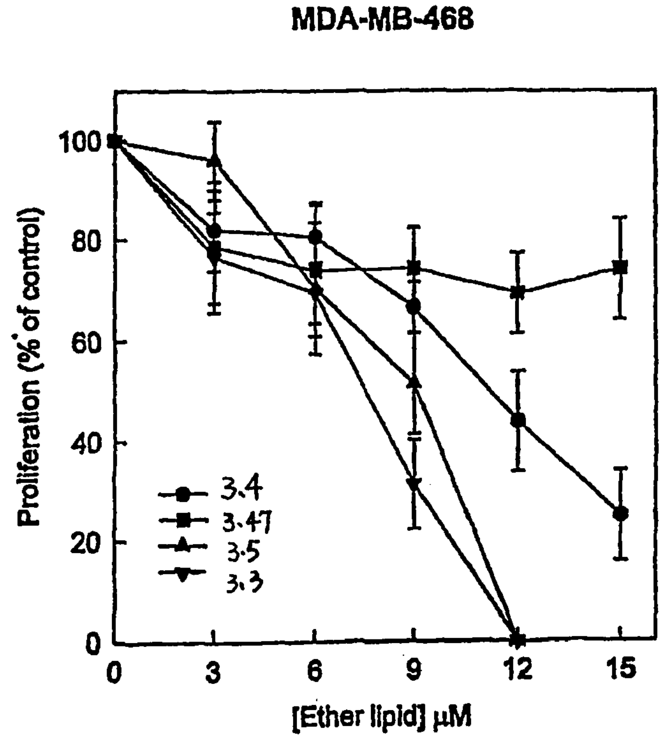


Figure 3.7 Effects of 3.3, 3.47, 3.4 and 3.5 on the proliferation of MDA-MB-468 cells.

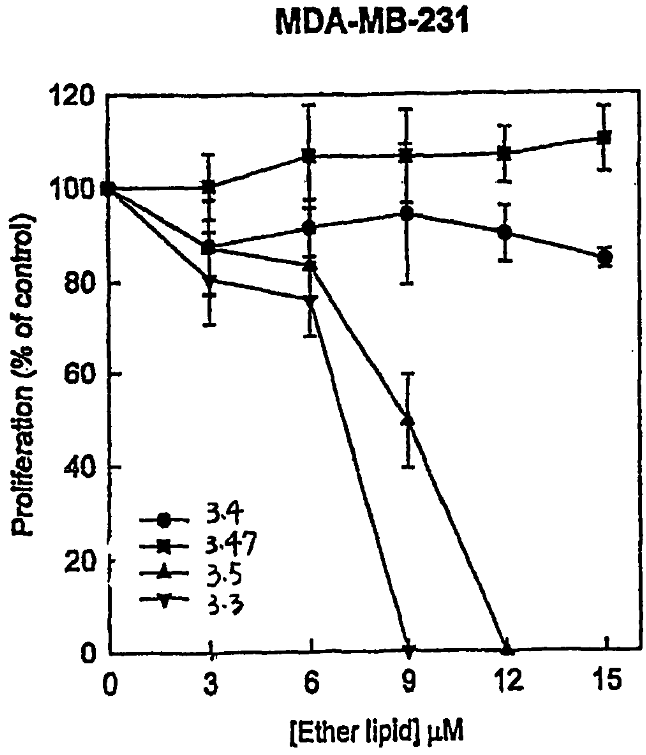


Figure 3.8 Effects of 3.3, 3.47, 3.4 and 3.5 on the proliferation of MDA-MB-231 cells.

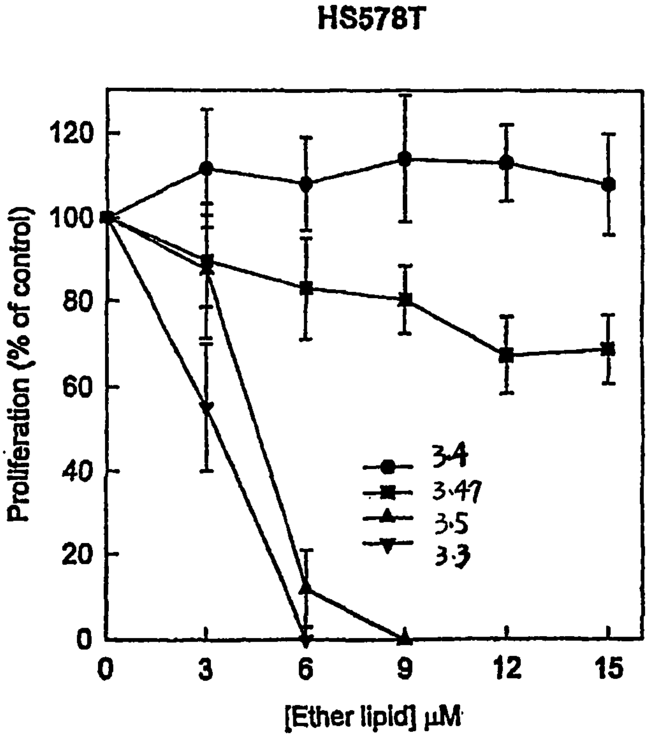


Figure 3.9 Effects of 3.3, 3.47, 3.4 and 3.5 on the proliferation of HS578T cells.

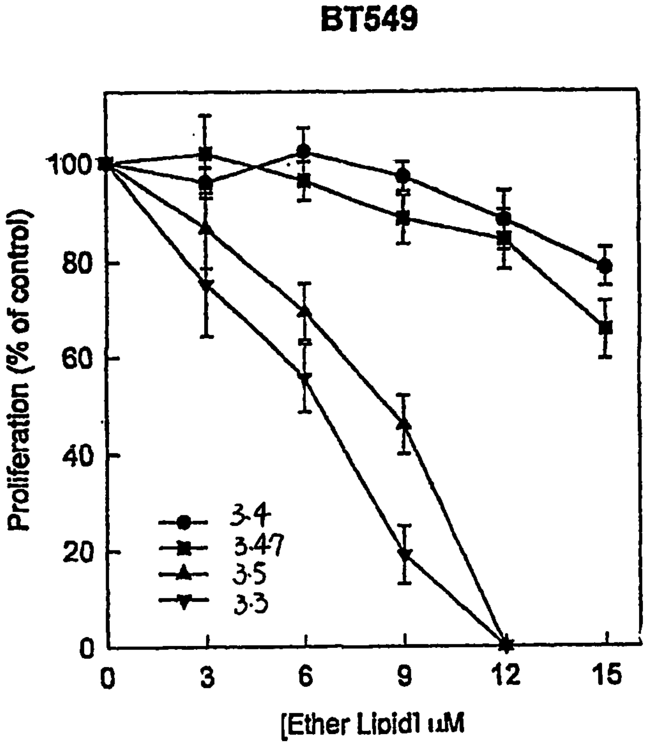


Figure 3.10 Effects of 3.3, 3.47, 3.4 and 3.5 on the proliferation of BT549 cells.

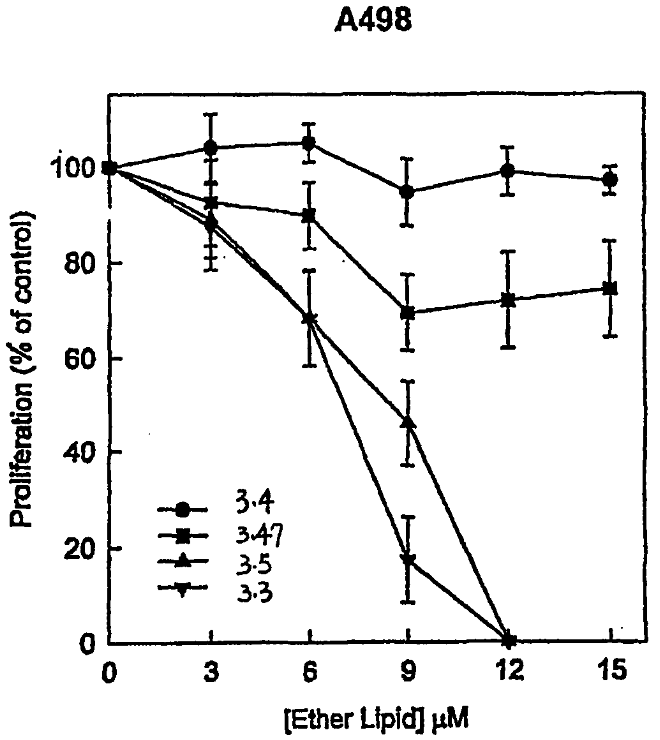


Figure 3.11 Effects of 3.3, 3.47, 3.4 and 3.5 on the proliferation of A498 cells.

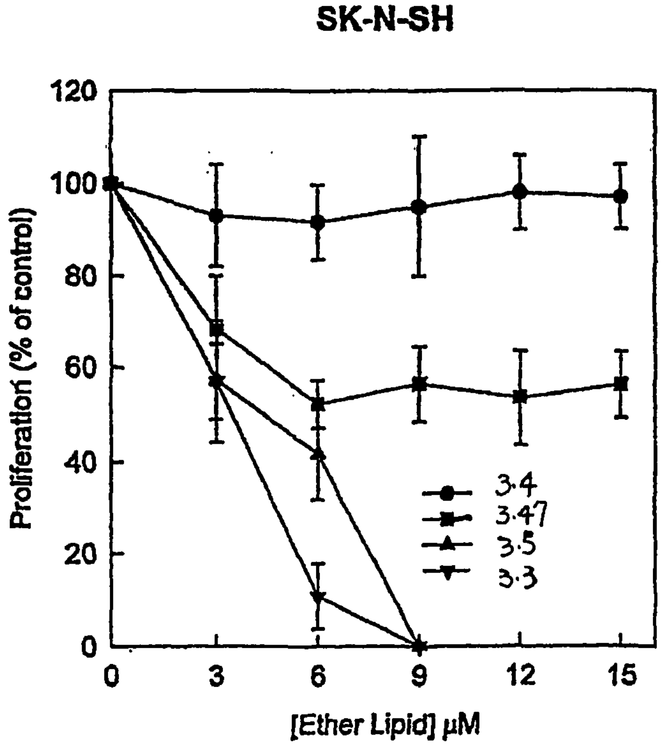


Figure 3.12 Effects of 3.3, 3.47, 3.4 and 3.5 on the proliferation of SK-N-SH cells.

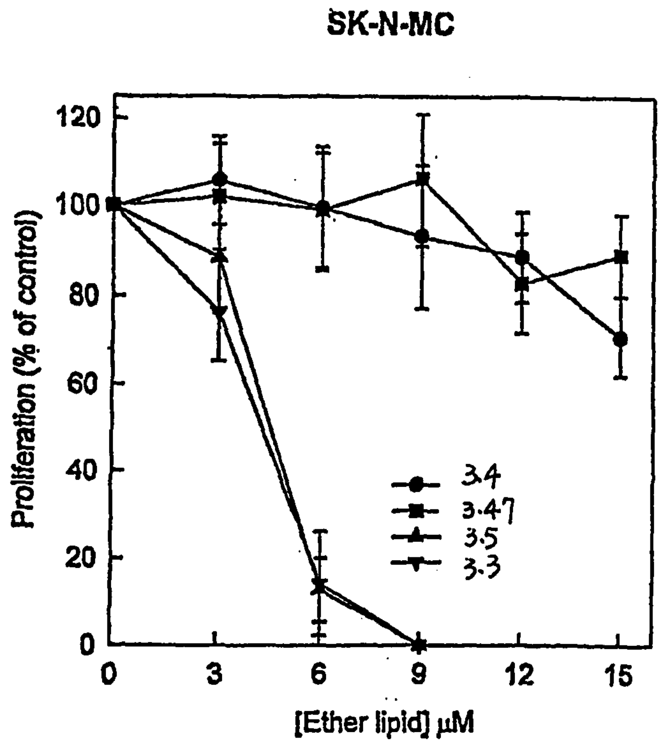


Figure 3.13 Effects of 3.3, 3.47, 3.4 and 3.5 on the proliferation of SK-N-MC cells.

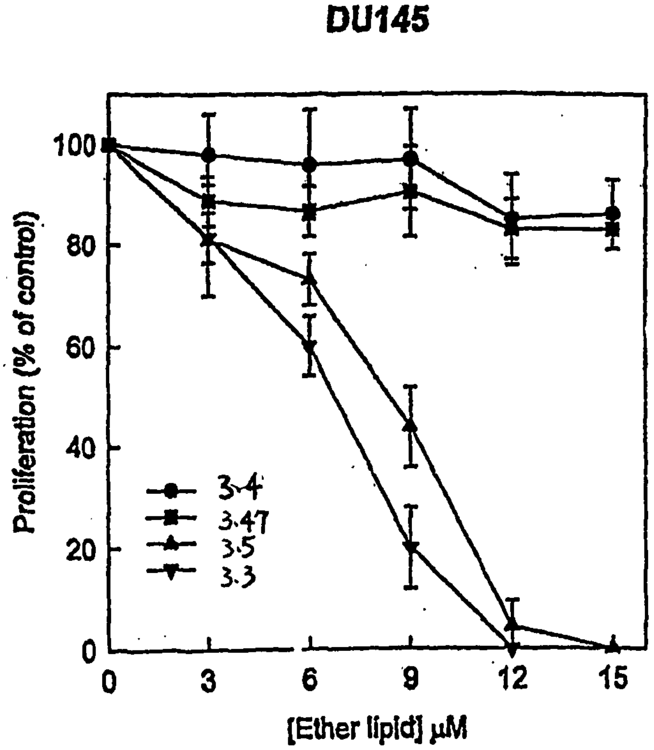
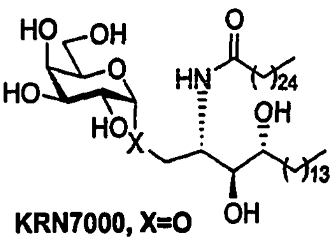


Figure 3.14 Effects of 3.3, 3.47, 3.4 and 3.5 on the proliferation of DU145 cells.

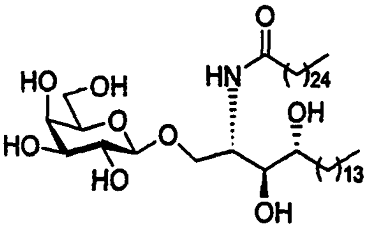
4. SYNTHESIS OF *C*-GLYCOSIDE ANALOG OF KRN 7000

4.1 Introduction

Monoglycosylated ceramides such as galactosylceramide (GalCer) are important surface molecules found in virtually all cells. Glycosphingolipids related to GalCer and their metabolites play important roles in promoting the regulation of nerve cells,[71] regulating protein kinase C activities,[72] and modulating the function of the hormone receptor.[73] The glycolipid, α-GalCer **(KRN7000)**, *is a synthetic analogue of* a natural Agelasphines family compound, which was isolated from a marine sponge in the southern part of Japan. A group led by Yosuhiko Koezuka[74, 75] discovered that **KRN 7000** showed potent tumor growth inhibitory activities in B16-bearing mice and markedly stimulated lymphocytic proliferation in allogeneic mixed leukocyte reaction. To confirm this hypothesis, they compared tumor growth inhibitory **KRN7000** and its stereoisomer **AGL-583** on mice subcutaneously inoculated with B16 cells.[76] As Figure 4.1 shows, **KRN7000** markedly suppressed the tumor growth, and its activity was stronger than that of **AGL-583**, paralleling their enhancing effects on *in vivo* NK (Natural Killer) cell activity.



KRN7000, X=O
4.1 X=CH_2



AGL-583

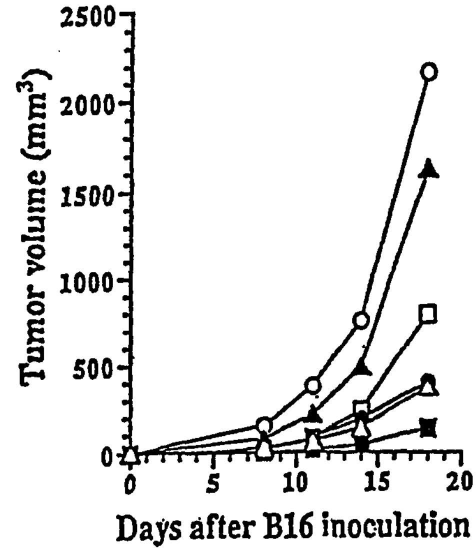
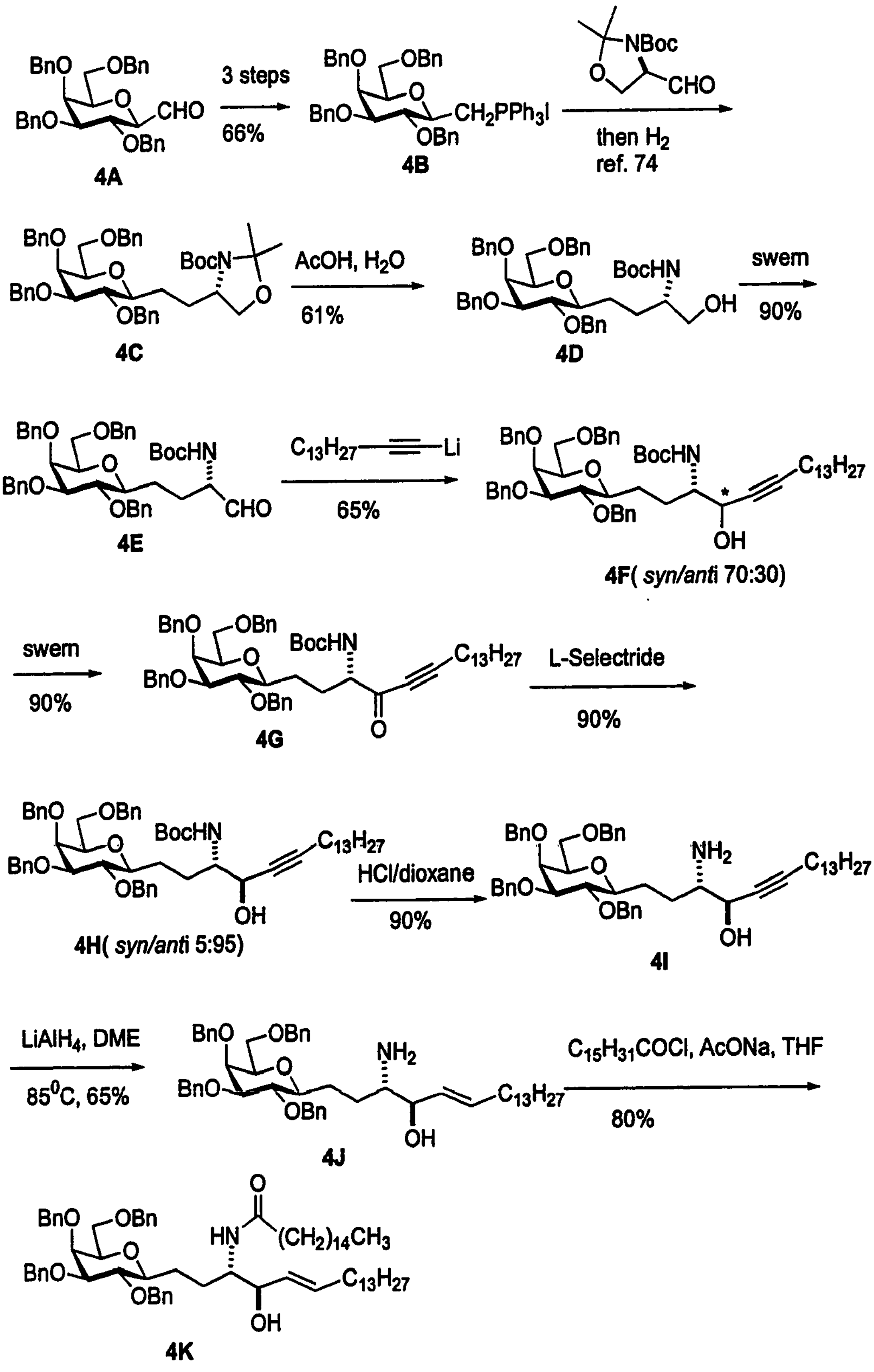


Figure 4.1 Tumor growth inhibitory effects of **KRN 7000** and **AGL-583** in combination with or without MMC on mice subcutaneously inoculated with B16 cells. B16 cells (1×10^6 cells/mouse) were subcutaneously inoculated into mice on day 0. **KRN 7000** and **AGL-583** (100 μg/kg) were intravenously administered on days 1, 5 and 9. MMC (5 mg/kg) was intravenously given on day 1. Each tumor volume per mouse was measured using callipers on days 8, 11, 14 and 18. Each point represents the mean of five mice. (○) Vehicle, (□) **KRN7000**, (▲) **AGL-583**, (●) MMC, (■) MMC+**KRN7000**, (△) MMC+**AGL-583**.
(Note: MMC is Mitomycin C)

Dondoni has synthesized the protected *C*-glycosphingolipid β-D-galactosyl *N*-palmitoyl C_{18} ceramide by a linear reaction sequence starting from a β-linked D-galactopyranosyl aldehyde (scheme 4.1).[77, 78] The bioactivity of this *C*-glycolipid was not reported. Also recently, Gurjar and Reddy reported a lengthy synthesis of α-*C*-glucosylsphingosine.[79] We applied a convergent methodology to synthesize the *C*-glycoside analog of **KRN7000** by using the Ramberg-Bäcklund reaction. There are two problems which have to be solved in this project. One is the synthesis of the homosphingosine from readily available precursors. The other is the stereoselective synthesis of the α-*C*-galactoside.

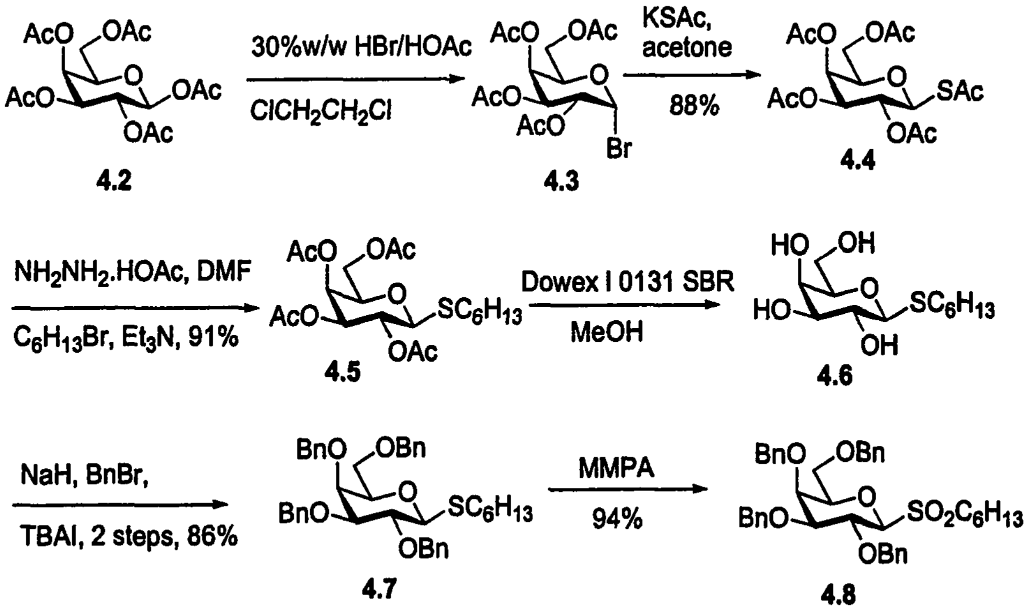
Scheme 4.1


4A
3 steps
66%
4B
CH$_2$PPh$_3$I
NBoc
CHO
then H$_2$
ref. 74
4C
AcOH, H$_2$O
61%
4D
swern
90%
4E
C$_{13}$H$_{27}$—≡—Li
65%
4F(syn/anti 70:30)
swern
90%
4G
L-Selectride
90%
4H(syn/anti 5:95)
HCl/dioxane
90%
4I
LiAlH$_4$, DME
85^{0}C, 65%
4J
C$_{15}$H$_{31}$COCl, AcONa, THF
80%
4K
BnO
OBn
BocHN
NH$_2$
OH
C$_{13}$H$_{27}$
(CH$_2$)$_{14}$CH$_3$

4.2 Synthesis of a model α-*C*-galactoside

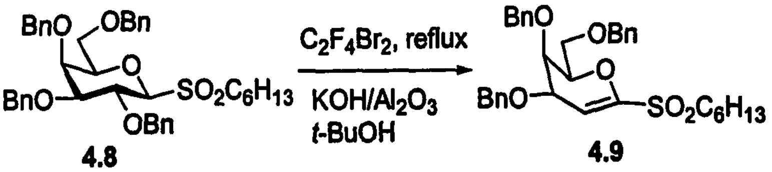
Before we began our synthesis of the target **4.1**, we planned to make a model α-*C*-galactoside to test an intramolecular hydride delivery strategy for obtaining the α-*C*-anomeric configuration. The model target chosen was the α-*C*-hexyl-galactoside.

Scheme 4.2



2,3,4,6-Tetra-*O*-acetyl-β-galactosyl thioacetate **4.4** can be obtained from β-D-galactose pentaacetate **4.2** via 2,3,4,6-tetra-O-acetyl-α-galactosyl bromide **4.3** in 88% overall yield. Treatment of thioacetate **4.4** with hydrazinium acetate in DMF under N_2 led to deprotection of the thioacetate. The freshly deprotected thio derivative was subsequently treated with $C_6H_{13}Br$ to provide thio ether **4.5** in 91% overall yield from thioacetate **4.4**. 2,3,4,6-Tetra-*O*-benzyl-β-thiogalactoside **4.7** was obtained from 2,3,4,6-tetra-*O*-acetyl-β-thio-galactoside **4.7** via two steps in 86% overall yield. The compound **4.7** was oxidized to the sulfonyl galactoside **4.8** using MMPA in good yield. Our initial attempt with one-pot Ramberg-Bäcklund conditions using 50% $KOH/Al_2O_3/C_2F_4Br_2$/*t*-

BuOH at reflux failed. Elimination of HOBn occurred to form endocyclic sulfonylglycal **4.9** instead of Ramberg-Bäcklund reaction. Apparently in this case of galactosulfone, the Ramberg-Bäcklund reaction was slower than eliminaton at the higher temperatue of 47°C. When this reaction was repeated using $C_2F_4Br_2$/*t*-BuOH at room temperature, neither RB nor elimination products were obtained. It should be noted that, in our earlier work,[31a] neither mannose- nor glucose-derived sulfones gave elimination when treated with the CF_2Br_2 (bp 23 °C) reagent. We reasoned that a distortion of the galactose ring must have occurred at the higher temperature so as to put the 2-benzyloxy group in an axial location so that it could be eliminated.[27b]

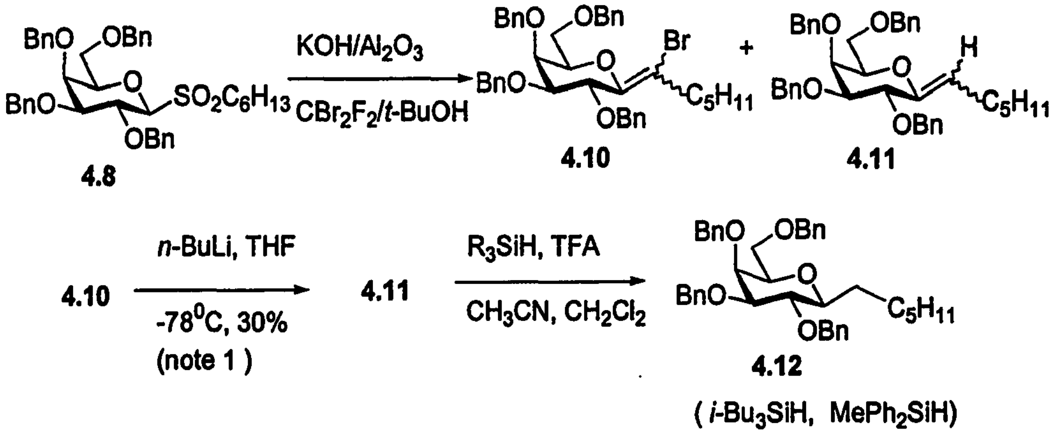


Several attempts were made to improve the Ramberg-Bäcklund reaction by using KOH/Alumina/CF_2Br_2/*t*-BuOH at room temperature (see Table 4.1). RB product **4.11** was obtained, but the over-bromination product **4.10** was formed in higher yield than **4.11** in each case. The vinyl bromide **4.10** can be dehalogenated to **4.11** using *n*-BuLi, but the yield of this conversion was too low and gave two side products as well (Scheme 4.3). The radical reaction using AIBN and Bu_3SnH didn't afford debromination.

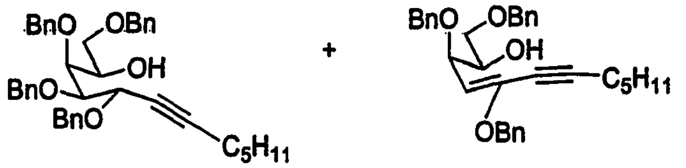
Table 4.1 RB conditions using CF_2Br_2/*t*-BuOH and 50 %KOH/Al_2O_3 at 0 °C

Entry	solvent	time (h)	4.10 (%) Z, E	4.11 (%) Z, E
1	CH_2Cl_2	24	6%, 35%	11%, 13%
2	THF	24	67%, 8%	0%, 7%
3	DME	24	80%, 11%	0%, 5%

Scheme 4.3



note 1: the other products are:

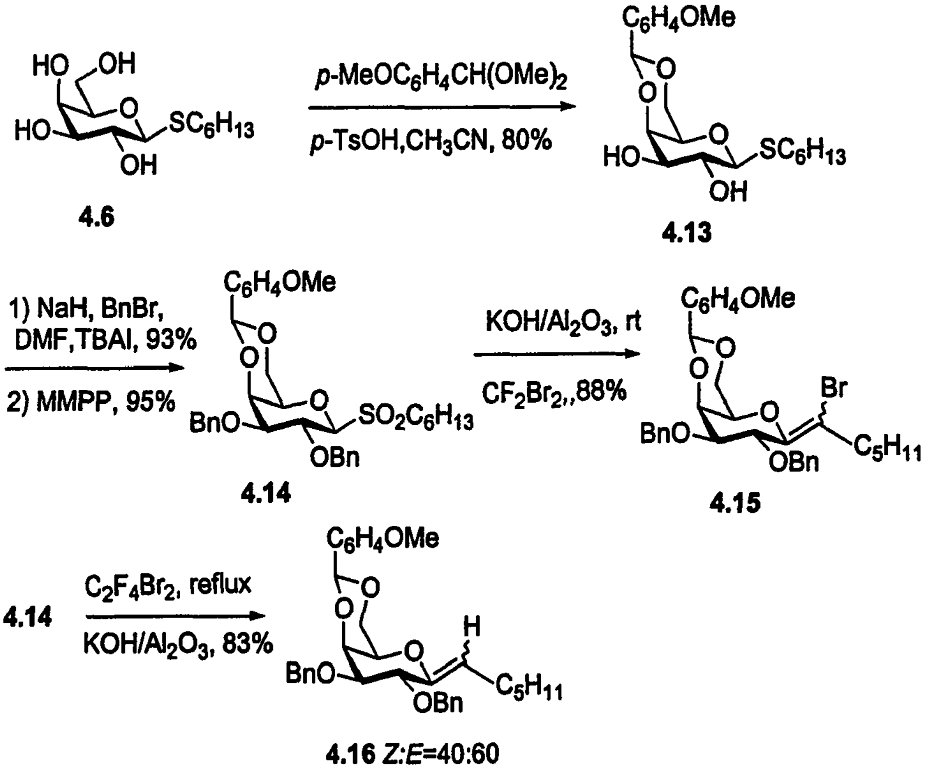


18% (M=606, MS:M^++Na^+=629) 32% (M=498, MS: M^++Na^+=521)

With the limited amount of exo-galactal **4.11**, we tried the intermolecular ionic hydrogenation using hindered silanes, but they all gave the β-*C*-glycoside **4.12**. The chemical shift of H_1 is 3.19 ppm (ddd, J=2.2, 9.0, 9.3 Hz).

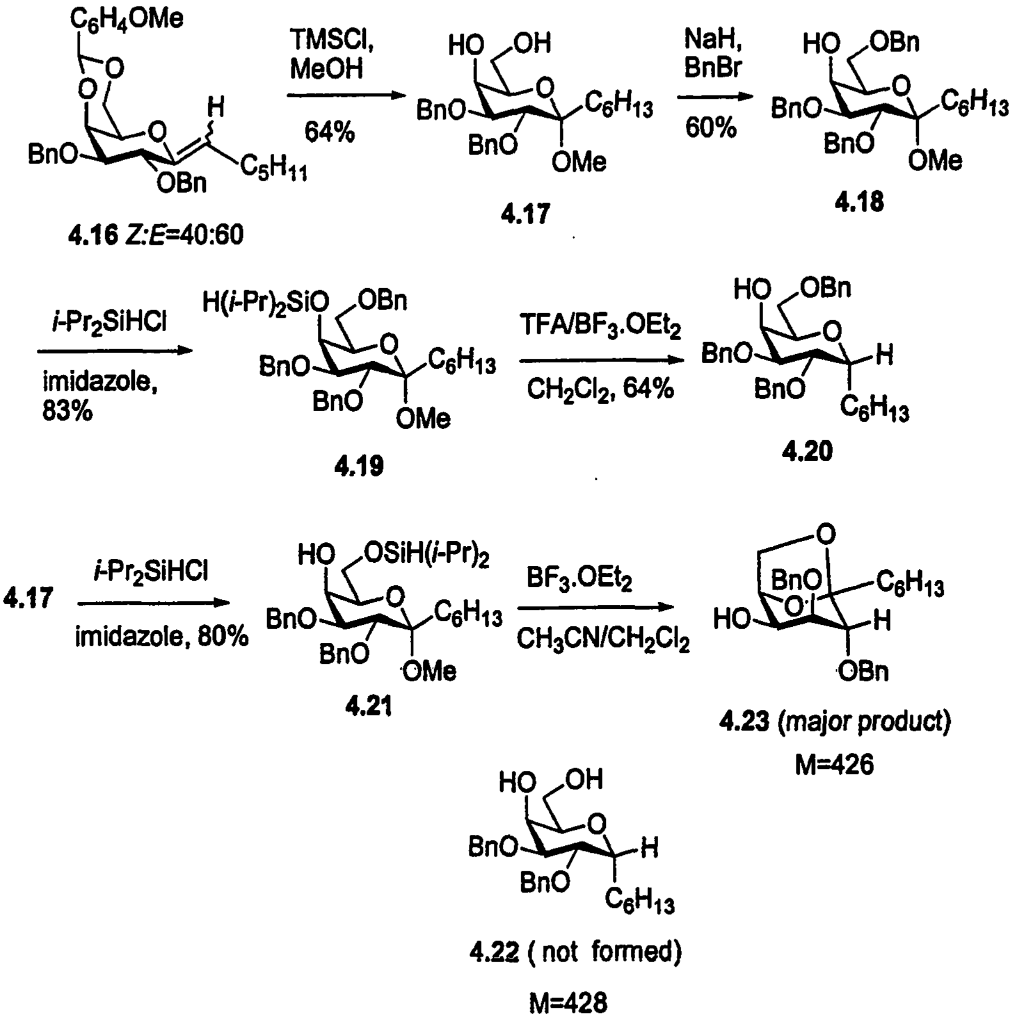
Since the sulfone **4.8** is not useful for making the RB product and α-*C*-glycoside, we prepared the bicyclic sulfone as shown in Scheme 4.4 on basis of the assumption that any twisting or flipping motion necessary to force the 2-benzyloxy group axial would be difficult.

Scheme 4.4



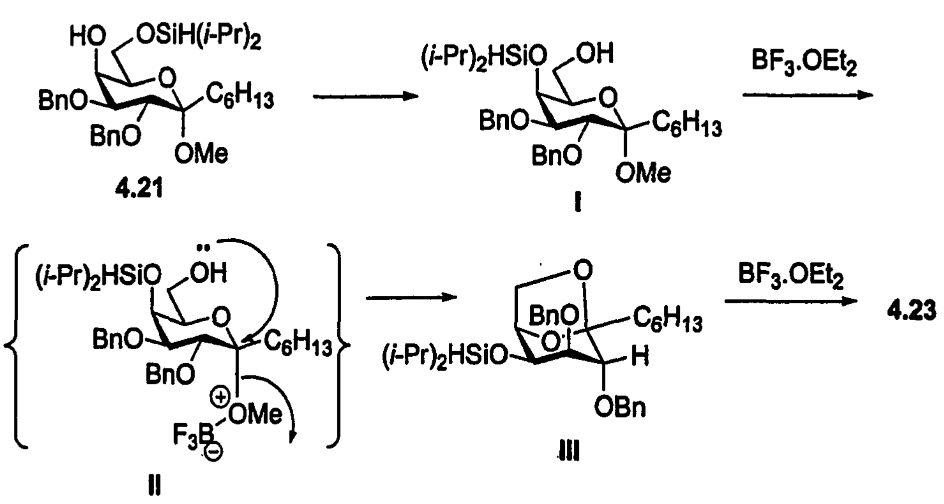
Treatment of hexyl-β-D-1-thio-galactoside **4.6** with *p*-methoxybenzaldehyde dimethyl acetal[80] and *p*-toluenesulfonic acid gave hexyl 4,6-*O*-(4-methoxybenzylidene)-β-D-1-thio-galactoside **4.13** (80%). Benzylation of **4.13** followed by oxidation of the thiogalactoside gave sulfone **4.14**. Our first attempt under standard one-pot RB conditions using KOH on alumina/CF_2Br_2/*t*-BuOH yielded the product vinyl bromide **4.15** instead of the desired alkene **4.16**. The free radical reaction using *n*-Bu_3SnH was used to debrominate, but the product was not the one we wanted. Debromination using *n*-BuLi was not valuable due to the ring cleavage. The RB reaction using $C_2F_4Br_2$/*t*-BuOH at reflux was next attempted. With this modification, the RB reaction took place in a good yield to form RB product **4.16**. The ratio of *Z*:*E* alkene isomers is 40:60. This enol ether **4.16** was very unstable and it decomposed during the ^{13}C NMR determination overnight in $CDCl_3$. Enol ether **4.16** could then be processed to form either α- or β-*C*-glycoside stereoselectively (Scheme 4.5 and 4.9).

Scheme 4.5



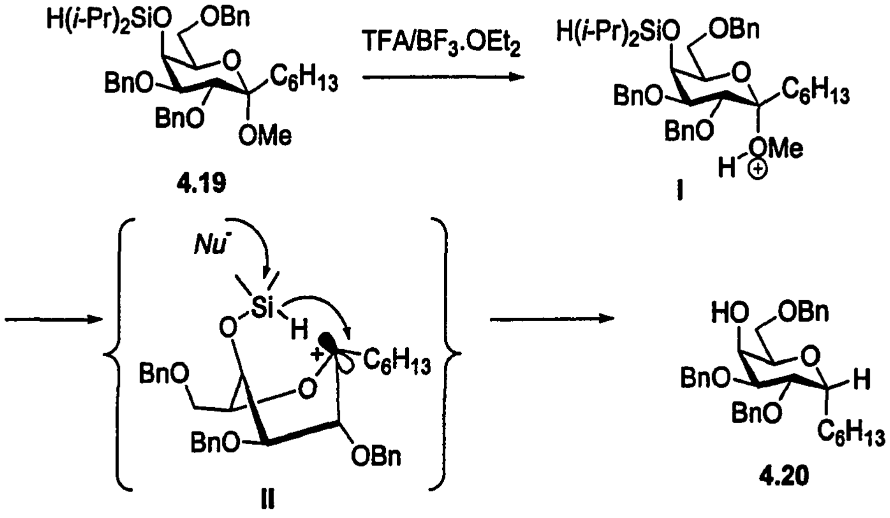
1-*O*-Methyl-2,3-dibenzyl-β-D-1-*C*-hexyl galactoside **4.17** can be made in one step by using chlorotrimethylsilane in methanol. In the first attempt, we protected the primary alcohol **4.17** to afford silyl ether **4.21** in 80% yield. But the syringe pump addition of **4.21** in CH_2Cl_2/CH_3CN (85:15) to $BF_3.Et_2O$ didn't afford the desired α-*C*-galactoside **4.22** (calcd. $C_{26}H_{36}O_5$, 428). MS shows that the molecular weight of the product is 426. We deduced the structure to be **4.23**. We assume that C6-silyl migrated C4 so that the 6-OH could trap the anomeric carbocation (Scheme 4.6).

Scheme 4.6



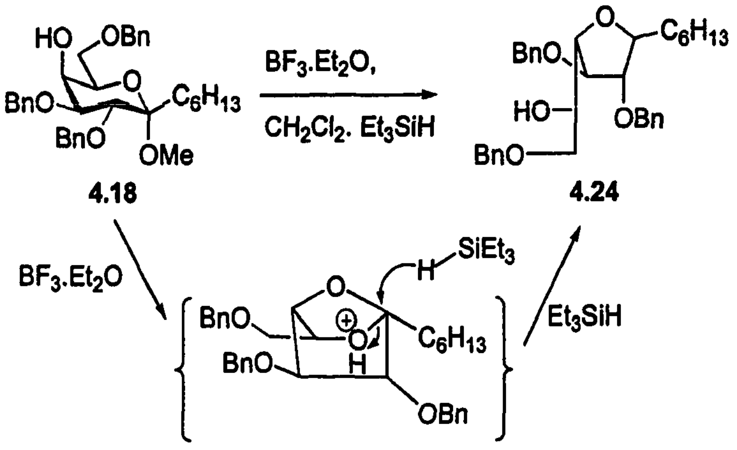
Thus we planned to protect the hydroxyl group at C4 by using *i*-Pr_2SiHCl. Selective benzylation of the primary alcohol in **4.17** afforded compound **4.18**. Silyl ether **4.19** was prepared using *i*-Pr_2SiHCl. Syringe pump addition[81] of **4.19** in CH_2Cl_2 (0.07 M) to TFA/$BF_3.OEt_2$ solution (4:1) afforded the α-*C*-galactoside **4.20** in 64% yield. The ^1H NMR shows the chemical shift of equatorial H is 4.19 ppm, J_{12}=5.8 Hz (Figure 4.2). The mechanism is shown in Scheme 4.7.

Scheme 4.7



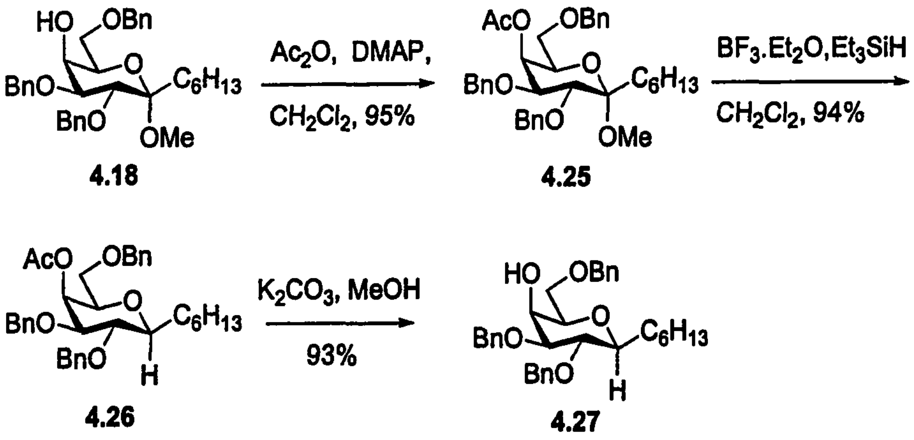
In order to confirm that compound **4.20** is the α-*C*-galactoside, we synthesized the β-*C*-galactoside. Treatment of the alcohol **4.18** with Et_3SiH and $BF_3.Et_2O$ didn't afford the desired β-*C*-galactoside. Because the C4-OH is a good nucleophile, we assumed it attacked the carbocation at C1 to form a bicyclic intermediate. This bicyclic material is then cleaved reductively to form a 5-membered ring C-glycoside **4.24** (Scheme 4.8). So the free hydroxyl group must be protected during the intermolecular reaction.

Scheme 4.8



Acylation of alcohol **4.18** afforded acetate **4.25** in 95% yield. Treatment of acetate **4.25** with Et$_3$SiH and BF$_3$.Et$_2$O afforded the β-*C*-galactoside **4.26** in 94% yield (Scheme 4.9). Deprotection of acetate **4.26** gave the β-*C*-galactoside **4.27**, the chemical shift of H$_1$ is 3.25 ppm, ddd, J=9.1, 9.1, 2.5 Hz (Figure 4.2).

Scheme 4.9



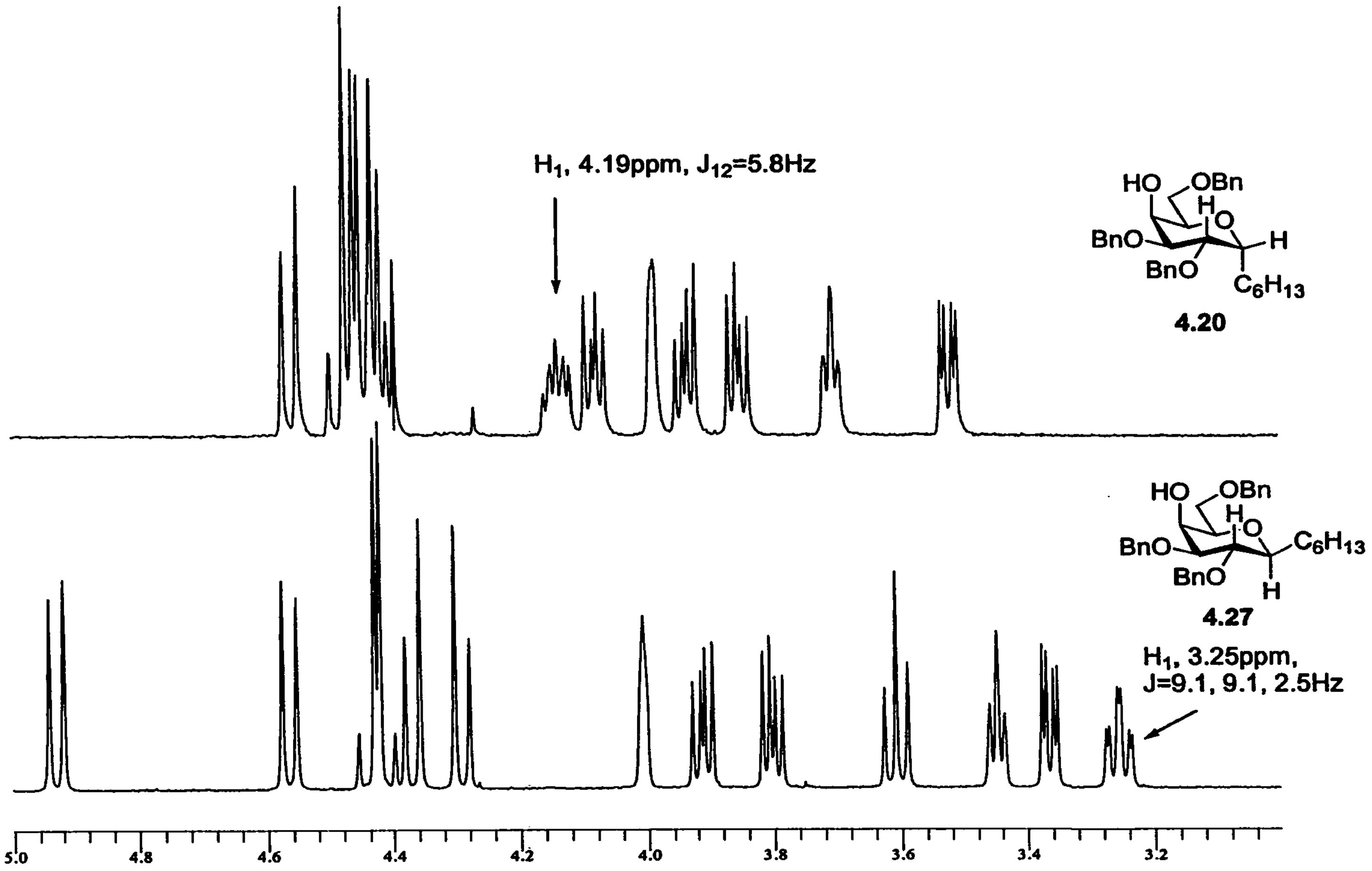


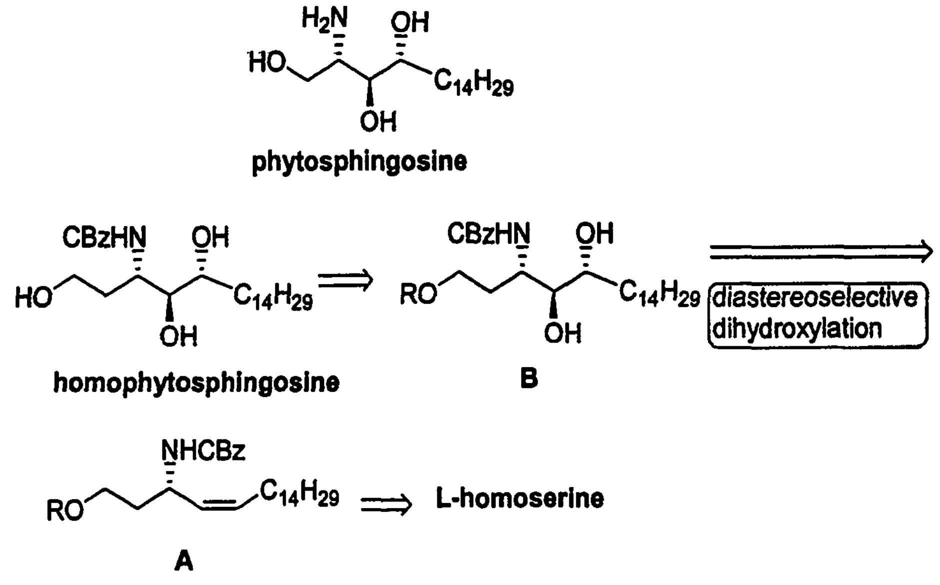
Figure 4.2 ^{1}H NMR spectra of **4.20** and **4.27** (500MHz, in C_6D_6)

4.3 Synthesis of homophytosphingosine derivative

Sphingophospholipids as well as glycerophospholipids are the main constituents of cell membrane.[82] Sphingosine functions as a protein kinase C inhibitor,[83] and ceramide and sphingosine-1-phosphate work as second messagers in the signal transduction.[84] It is also reported that phytosphingosine exists abundantly in kidney, liver and intestine of human being.[85] Because of interest in its biological activities, many synthetic methods of phytosphingosine have been reported so far,[86] but there is no synthesis of a homosphingosine such as that required for our KRN approach reported. In this project, we established a new synthetic method for the homophytosphingosine derivatives including their stereoisomers using diastereoselective dihydroxylation as a key step.

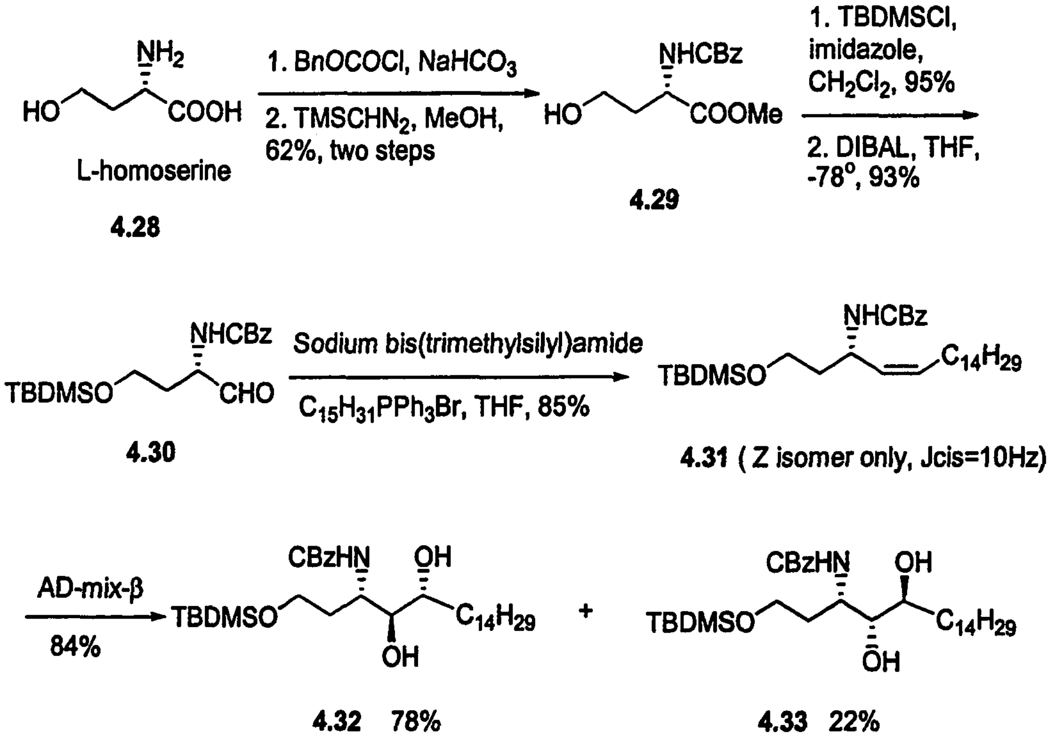
Our synthetic plan is shown in Scheme 4.10. The diastereoselective dihydroxylation of the optically active olefin A, which is readily accessible from L-homoserine, would

Scheme 4.10



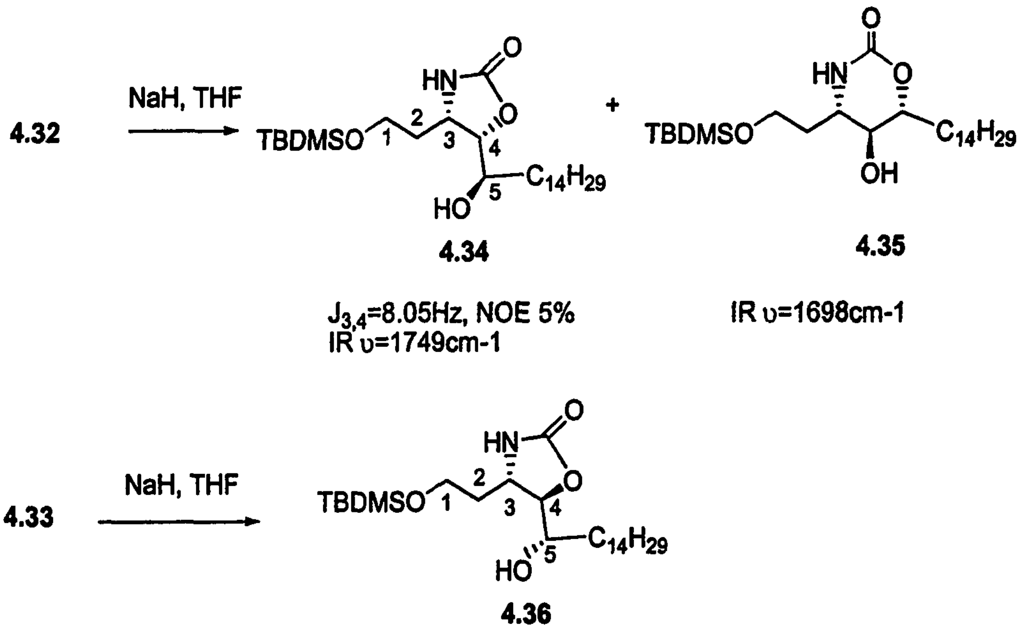
afford the protected homophytosphingosine derivative B in a stereoselective fashion. The synthetic route from commercial L-homoserine is shown in Scheme 4.11. L-homoserine **4.28** was converted into methyl ester **4.29** via two steps in 60% overall

Scheme 4.11



yield.[87, 88] After the primary alcohol was protected, the ester was reduced to an aldehyde **4.30** using diisobutylaluminum hydride (DIBAL-H) as the reducing reagent. The aldehyde was then treated with the ylide generated from pentadecylphosphonium bromide and sodium hexamethyldisilazane (NaHMDS) in THF at –75 °C, to give *Z*-olefin **4.31** as the only product.[89] Sharpless dihydroxylation[90] of the optically active *Z*-olefin using AD-mix-β gave ca. 78:22 mixture of 3S, 4S, 5R (**4.32**) and 3S, 4R, 5S (**4.33**) dihydroxylated isomers, respectively. Their relative and absolute configurations were confirmed by comparison of NMR data of their cyclic carbamate derivatives. Treatment of the 3-[N-(benzyloxycarbonyl)amino] 1,2-diols bearing an NH function (**4.32** and **4.33**) with NaH in THF[91] gave the hydroxyoxazolidinones (**4.34** and **4.36**) and six-membered hydroxy carbamate **4.35** (scheme 4.12). The relative stereochemistry at C4 and C5 was determined by measuring the coupling constants (J_{H3}-J_{H4}) and observing the NOE cross-peak between the H-3 and H-4 protons.[92]

Scheme 4.12



$J_{3,4}$=8.05Hz, NOE 5%
IR υ=1749cm-1

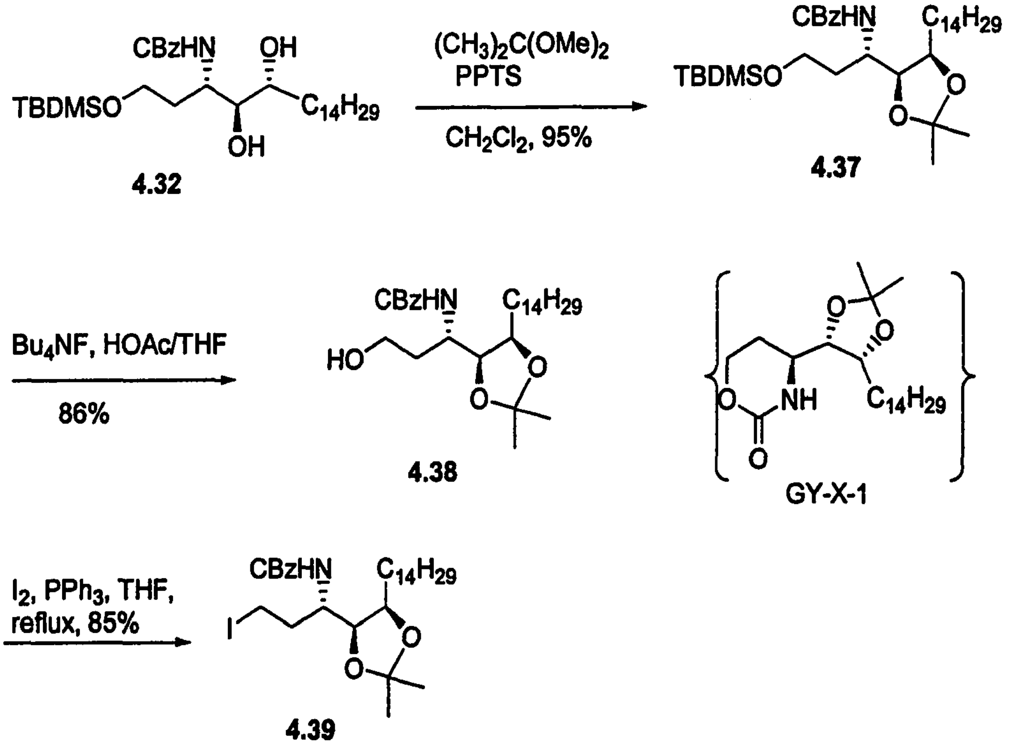
IR υ=1698cm-1

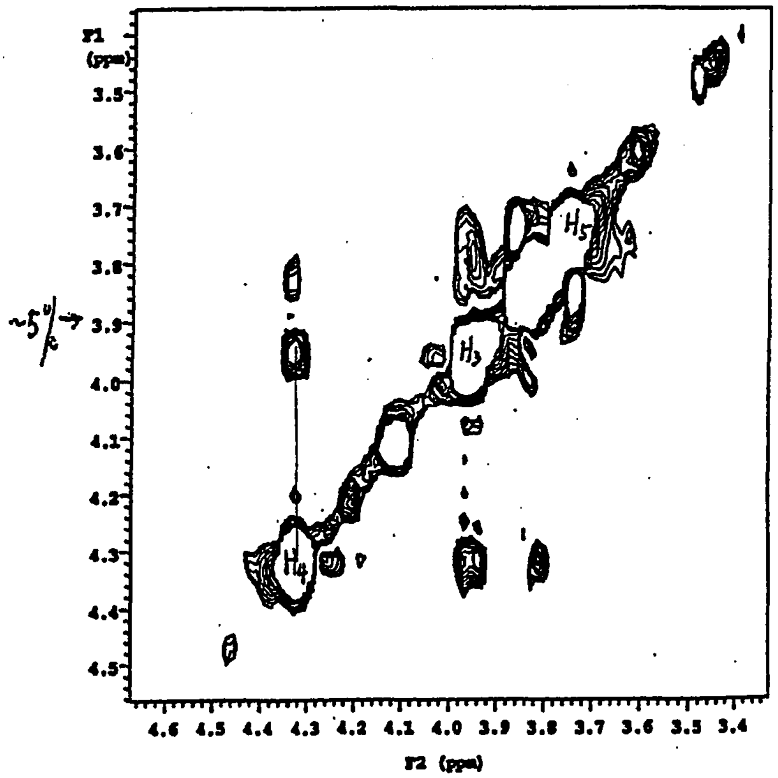
$J_{3,4}$=4.4Hz, NOE 1%
IR υ=1754cm-1

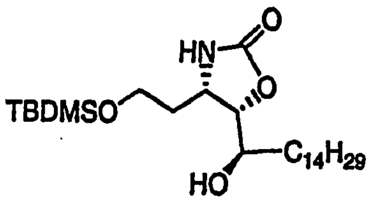
Acetonide formation was used to protect the 1,2-diols in the compound **4.32**, then **4.37** was desilylated to give the primary alcohol **4.38**. In the first attempt to cleave the silyl group using Bu_4NF in THF, compound **4.38** was formed in 50% yield and cyclic carbamate (GY-X-1) was the side product (30%), which was crystallized from ethyl acetate/hexane. The stereochemistry of **4.32** was confirmed by X-ray crystallographic analysis of GY-X-1 (Figure 4.2). In another attempt to cleave the silyl group under acidic conditions,[93] desilylation of **4.37** with 3 eq of trifluroacetic acid (TFA) in methylene chloride at 14 °C gave alcohol **4.38** in 70% yield, together with side products from cleavage of the acetonide. The best conditions were found to be *n*-

$Bu_4NF/HOAc/THF$. The iodo compound **4.39** was prepared easily by treatment of compound **4.38** with PPh_3, iodine and imidazole at reflux in THF.[65]

Scheme 4.13

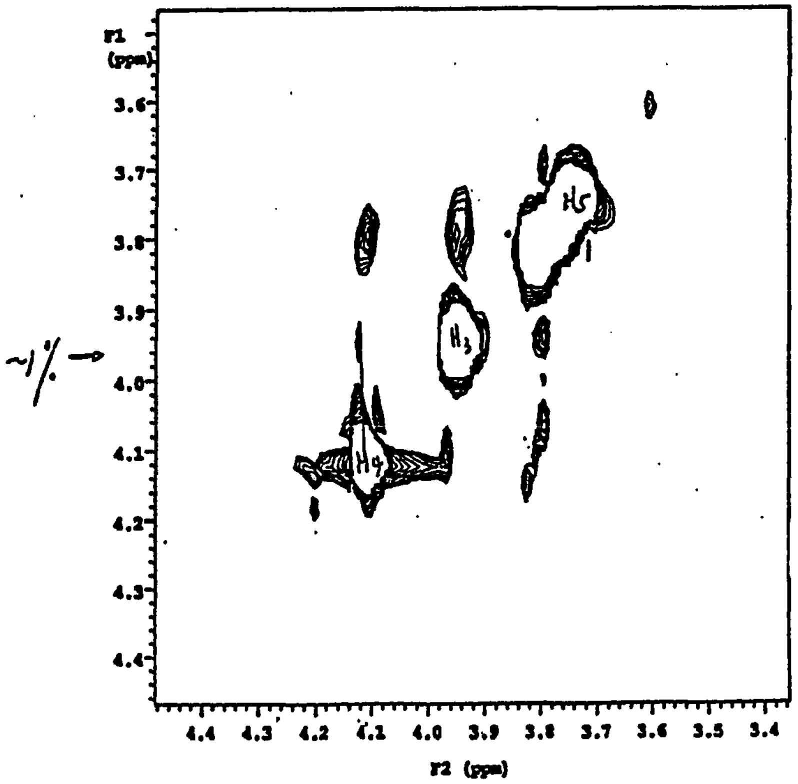


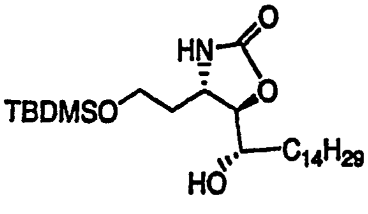




4.34

J3,4=8.05Hz, NOE 5%





4.36

J3,4=4.4Hz, NOE 1%

Figure 4.3 NOESY spectra of 4.34 and 4.36 (500MHz, in $CDCl_3$)

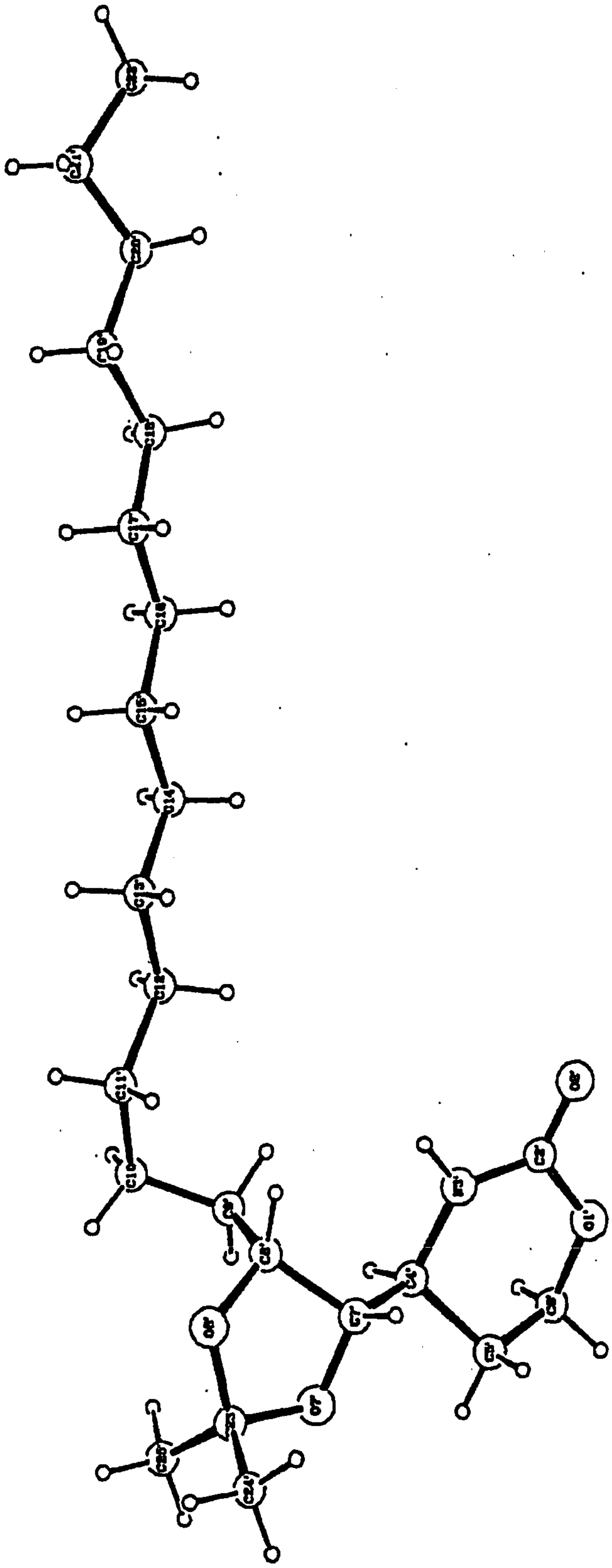
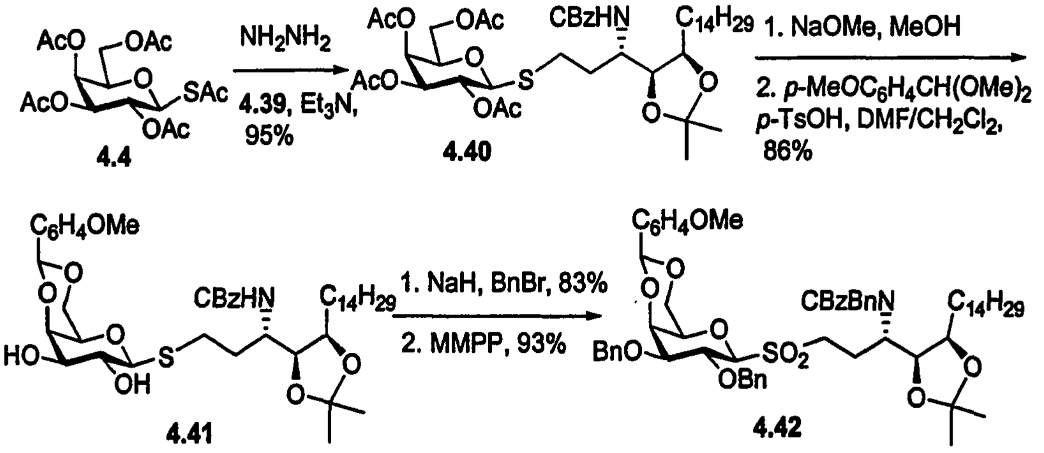


Figure 4.4 X-ray structure of the molecule of GY-X-1

4.4 Synthesis of *C*-glycoside of KRN 7000

Based on the RB approach and intramolecular ionic hydride delivery strategy to α-*C*-galactoside, the synthesis was continued by treatment of thioacetate **4.4** with hydrazinium acetate in DMF under N_2 to deprotect the thioacetate. The freshly deprotected thio derivative was subsequently treated with electrophile **4.39** to provide thiogalactoside **4.40** in 95% overall yield (Scheme 4.14). Treatment of β-D-thio-

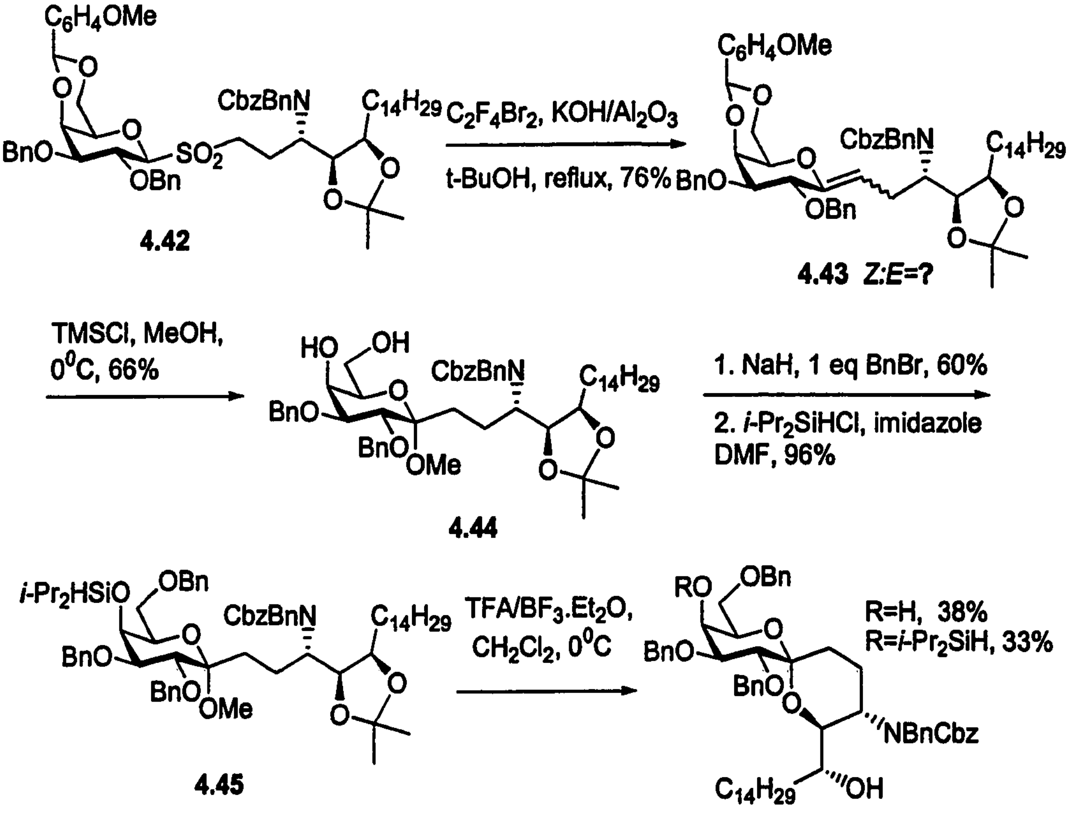
Scheme 4.14



galactoside **4.40** with NaOMe in MeOH followed by protection using *p*-methoxybenzaldehyde dimethyl acetal[80] and *p*-toluenesulfonic acid gave 4,6-*O*-(4-methoxybenzylidene)-β-D-1-thio-galactoside **4.41** in 86% yield. Benzylation of **4.41** followed by oxidation of thiogalactoside using MMPP gave sulfonyl galactoside **4.42** in good yield. It should be noted that we could not avoid N-benzlyation in this step.

The RB reaction using $C_2F_4Br_2$/*t*-BuOH at reflux afforded the product **4.43** (Scheme 4.15). The ratio of *Z*:*E* alkene isomers was not determined because of the peak broadening in the NMR. 1-*O*-Methyl-2,3-dibenzyl β-galactoside **4.44** can be made in one step by using chlorotrimethylsilane in methanol. Monobenzylation of the hydroxyl group at C6 followed by silylation of the hydroxyl group at C4 using *i*-Pr_2SiHCl afforded silyl ether **4.45**. Syringe pump addition[81] of **4.45** in CH_2Cl_2 (0.07M) to TFA/$BF_3.OEt_2$ solution (4:1) didn't afford the α-*C*-galactoside. The product was the cyclic compound **4.46**.

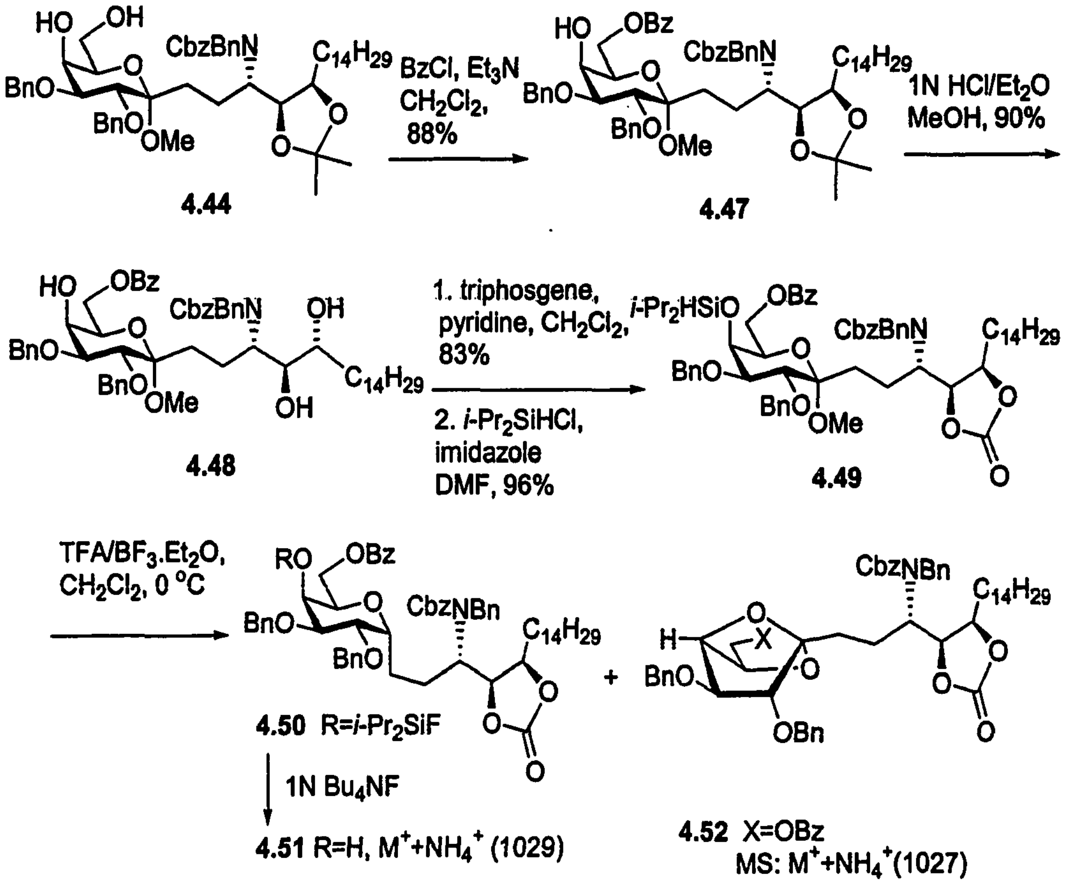
Scheme 4.15



Apparently, the isopropylidene group was cleaved under the strong acidic conditions and then the OH at C-4 trapped the carbocation at C1 to form the stable bicyclic species. Thus, it was necessary to interchange the isopropylidene protecting group for a cyclic carbonate group which we hoped would be stable to acidic conditions required for reduction of **4.44**.

Esterification of the primary hydroxyl group at C6 afforded the benzoate **4.47** in 88% yield (Scheme **4.16**). Treatment of the acetonide **4.47** with 1 N HCl/Et_2O in methanol generated the corresponding diol **4.48**. Cyclic carbonation of the diol using triphosgene[94] followed by silylation of the axial hydroxyl group at C4 afforded the silyl ether **4.49**. Pump additon[81] of of **4.49** in CH_2Cl_2 (0.01 M) to TFA/BF_3. Et_2O in CH_2Cl_2 solution (4:1, 0.05 M) afforded α-*C*-galactosides **4.50**, **4.51** (50% after desilylation of **4.50**) and the 1,4 anhydro compound **4.52** (20%). Treatment of silyl ether **4.50** with 1 N Bu_4NF in THF afforded the same product **4.51**, which was identified by ^1H NMR (anomeric H: 3.95 ppm, J_{12}=4.6 Hz) and TLC.

Scheme 4.16



In order to improve the yield of the reduction, several conditions were tried (Table 4.2). It was found out that the best condition required excess BF_3. Et_2O. It was assumed that formation of the anomeric carbocation and subsequent hydride delivery was faster than competing formation of **4.52**, which forms via desilylation prior to carbocation formation.

Table 4.2 Reduction conditions using $TFA/BF_3.Et_2O$ at 0 °C

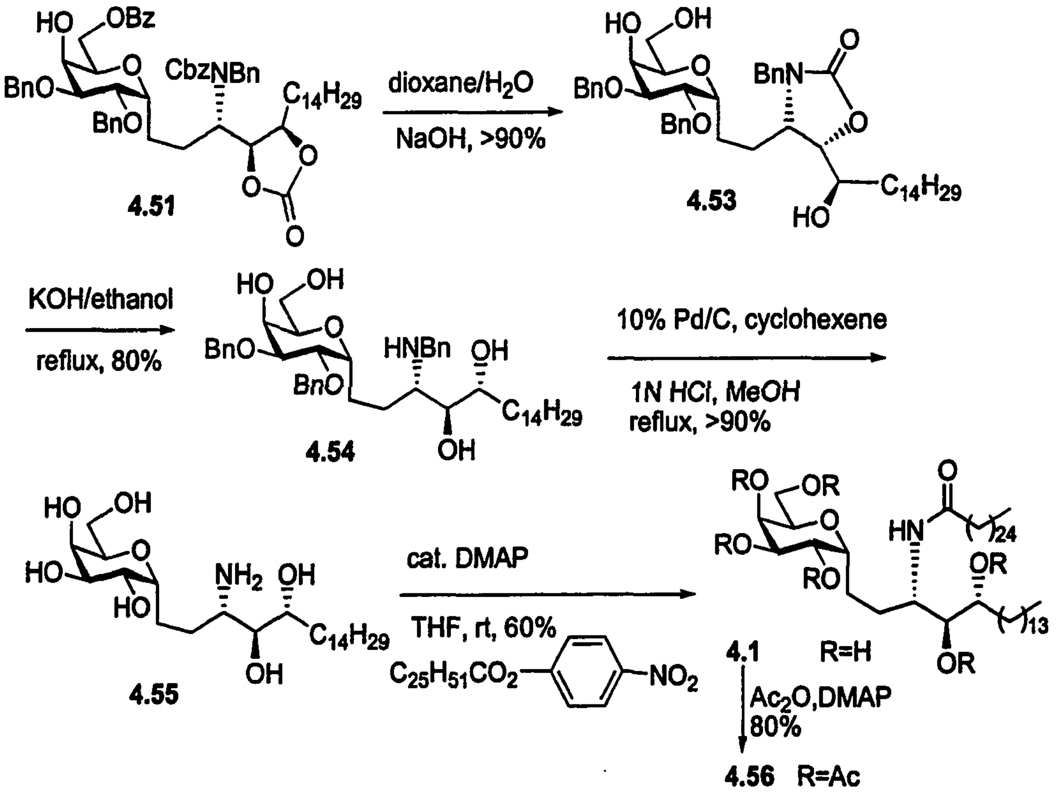
Entry	conditions (moles equivalent)	yield of **4.51**(%)^a	yield of **4.52**(%)
1	$TFA/BF_3.Et_2O$ (4:1)	50%	22%
2	TFA (5 eq)	0	50%
3	$BF_3.Et_2O$ (1 eq, -50 °C)	5%	53%
4	$BF_3.Et_2O$ (1.5 eq)	50%	15%
5	$BF_3.Et_2O$ (2 eq)	60%	20%
6	$BF_3.Et_2O$ (5 eq)	76%	15%

^{a} The yield is calculated after desilyation of compound **4.50**.

The rest of steps to obtain the final target were the most difficult tasks in the entire synthesis. The total debenzylation of compound **4.51** failed under several conditions, such as Pearlman's catalyst (H_2, 20% $Pd(OH)_2$, 30 psi) at medium pressure,[95] Birch reduction (Na/liquid NH_3),[96] 10% Pd/C and 4.4% formic acid in methanol.[97] So we decided to remove the carbonyl groups before the hydrogenation (Scheme 4.17).

Compound **4.51** was treated with NaOH and refluxed in 1:1 dioxane and H_2O to afford the oxazolidinone **4.53**, which was fully characterized. The NOE experiment shows that there is an NOE effect between H-3 and H-2', the other NOE effect between H-5 and H-2' (Figure 4.5), which confirmed that the stereochemistry of compound

Scheme 4.17



4.53 is correct (α isomer instead of β isomer). Hydrolysis of **4.53** gave the *N*-benzylamine **4.54**, which was fully debenzylated by transfer hydrogenolysis (10% Pd/C, cyclohexene)[98] to afford crude **4.55** in 80% overall yield. The fatty amide chain was then introduced using *p*-nitrophenyl hexadeconate as the acylating agent [75] to afford the target **4.1**. Final purification was done by flash chromatography on silica gel eluting

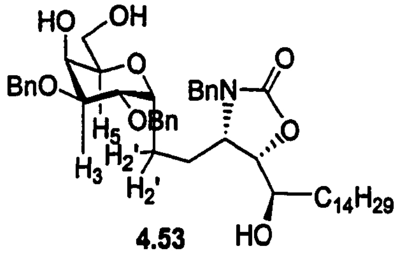
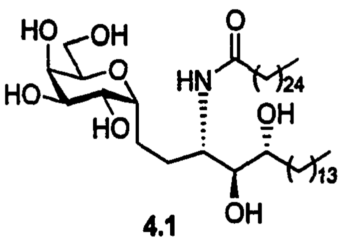


Figure 4.5 NOE effect between H_3 and H_2', H_5 and H_2'

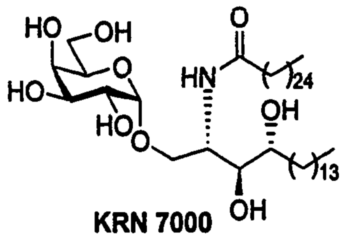
with $CHCl_3$: MeOH (4:1). The ^1H and ^{13}C NMR and optical rotation {$[\alpha]^{25}_D$ +40.8° (c 0.13, pyridine)}, mp 175-178°C, high resolution FABMS m/z 856.7601 ($C_{51}H_{101}O_8N+H^+$ requires 856.7605) obtained for a sample of **4.1**. The mass spectrum and ^1H NMR of fully acylated compound **4.56** further confirmed that **4.1** was the right compound. For **KRN 7000**: $[\alpha]^{23}_D$ +43.6° (c 1.0, pyridine), negative FABMS m/z 856 $(M-H)^-$.[75] The comparison of their NMR data was shown in Table 4.3.

Table 4.3 NMR data comparison of *C*-glycoside **4.1** and **KRN 7000** (in C_5D_5N)

entry	*C*-glycoside **4.1**	**KRN 7000**[75]
^1H NMR 500MHz	8.47 (d, J=8.8 Hz, 1H), 5.14 (m, 1H), 4.74 (dd, J=5.5, 8.8 Hz, 1H, H-2), 4.52 (m, 3H), 4.37 (dd, J=4.3, 11.0 Hz, 1H, H-6), 4.25 (m, 4H), 2.72 (m, 1H), 2.59 (m, 1H), 2.48 (m, 3H), 2.33 (m, 2H), 2.22 (m, 1H), 1.94 (m, 2H), 1.86 (m, 3H), 1.71 (m, 1H), 1.37 (s, 64H), 0.88 (t, J=6.4 Hz, 6H).	8.47 (d, J=8.5 Hz, 1H), 5.58 (d, J=3.7 Hz, 1H), 5.27 (m, 1H), 4.63-4.70 (m, 2H), 4.56 (m, 1H), 4.52 (t, J=6.1 Hz, 1H), 4.37-4.47 (m, 4H), 4.33 (m, 2H), 2.45 (t, J=7.3 Hz, 2H), 2.25-2.34 (m, 1H), 1.87-1.97 (m,1H), 1.78-1.85 (m, 2H), 1.62-1.72 (m, 1H), 1.26-1.45 (m, 66H), 0.88 (t, J=6.7 Hz, 6H).
^{13}C NMR 125MHz	173.36, 78.37, 76.90, 73.65, 72.53, 72.07, 70.46, 70.27, 62.61, 52.56, 36.86, 34.33, 32.00, 30.26, 30.07, 29.88, 29.70, 29.49, 26.42, 22.81, 14.15.	173.2, 101.5, 76.7, 73.0, 72.5, 71.6, 71.0, 70.3, 68.7, 62.7, 51.4, 36.8, 34.4, 32.1, 30.4, 30.2, 30.03, 30.00, 29.93, 29.87, 29.81, 29.76, 29.6, 26.5, 26.4, 22.9, 14.3.



4.1



KRN 7000

4.5 Summary of the Synthesis of the *C*-glycoside of KRN 7000

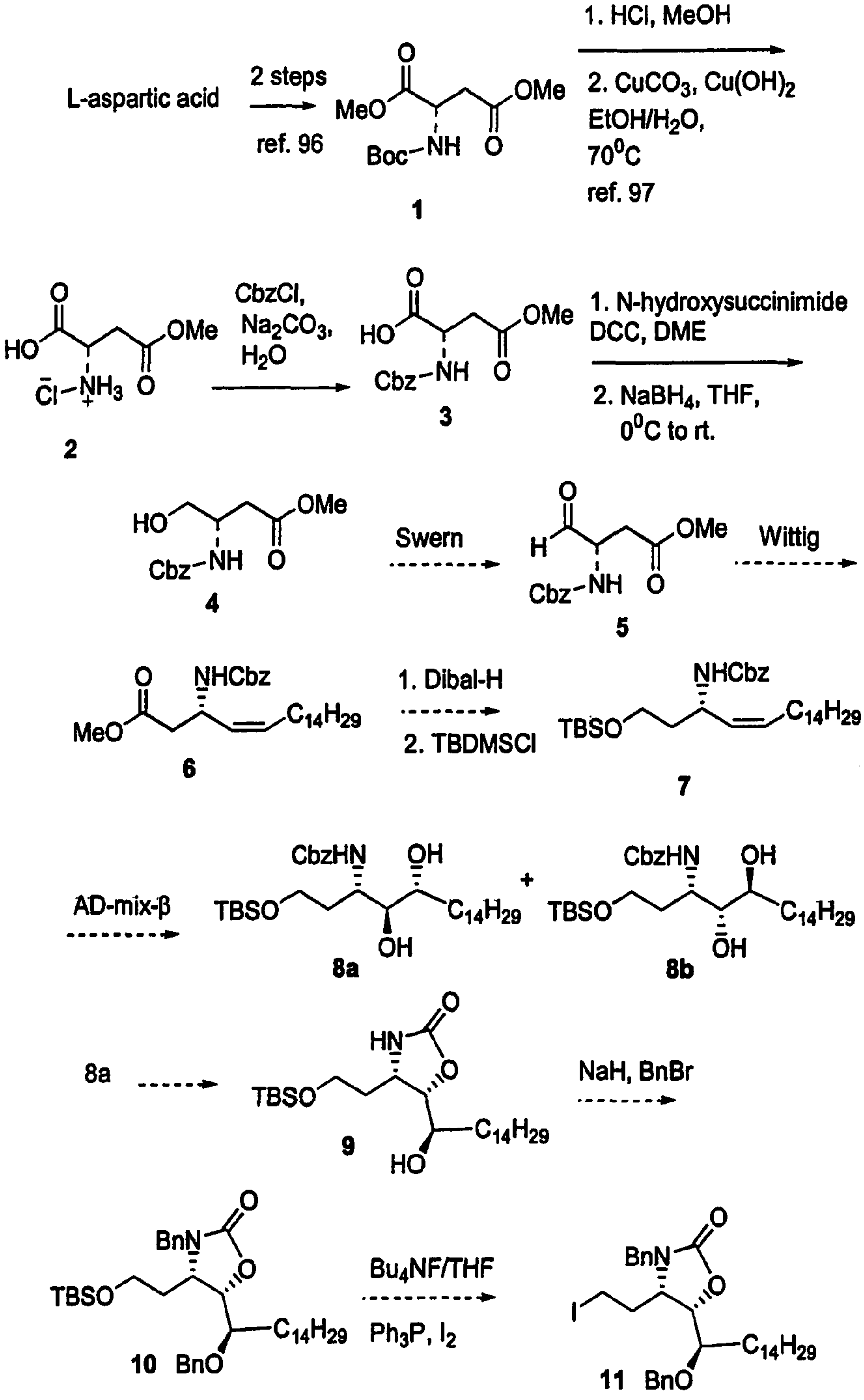
1. Homophytosphingosine derivatives can be obtained from L-homoserine via Wittig reaction and Sharpless dihydroxylation as the key steps.
2. Ramberg-Backlund reaction of sulfonyl galactosyl-ceramide proceeded smoothly using KOH/Alumina, *t*-BuOH and $C_2F_4Br_2$ at reflux.
3. α-*C*-galactoside can be made via intramolecular ionic hydrogenation. The intramolecular ionic hydrogenation requires acid stable protecting groups.
4. *C*-glycoside analogue of KRN 7000 was obtained via 28 steps in 0.97~1.0% overall yield from L-homoserine and galactose pentaacetate.

4.6 Modified synthesis of the side chain

Because L-homoserine is expensive (\$92/5 g from Novabiochem), L-aspartic acid (\$11.4 /100 g) is a more attractive precursor. The synthesis will start with fully protected (S)-aspartic acid **1** (Scheme 4.18), which can be prepared by treating aspartic acid with methanol in the presence of thionyl chloride followed by treatment with $(Boc)_2O$.[99] Treatment of **1** with methanolic hydrochloric acid solution provides the N-deprotected product, which will be then regioselectively hydrolyzed by the method reported by Gmeiner et al.[100] using $CuCO_3.Cu(OH)_2$ in an ethanol/water mixture to give **2**. The amino group in compound **2** will be protected to give **3**. The conversion of the α-carboxylate in **3** into the hydroxymethyl group to yield **4** can be accomplished by $NaBH_4$ reduction of the active ester.[101]

Oxidation of alcohol **4** will give aldehyde **5**, which can be then coupled to Wittig phosphonium salt to yield alkene **6**. Reduction of the methyl ester **6** to alcohol, followed by silylation gives olefin **7**. Sharpless dihydroxylation of olefin **7** will afford two isomers. In order to avoid the cleavage of isopropylidene and cyclization in the ionic reduction (see Scheme 4.15), we propose cyclic carbamate **9** as the protecting group. Protection of the remaining secondary alcohol, followed by deprotection of the C-1 silyl group leads to the preparation of iodide **11**.

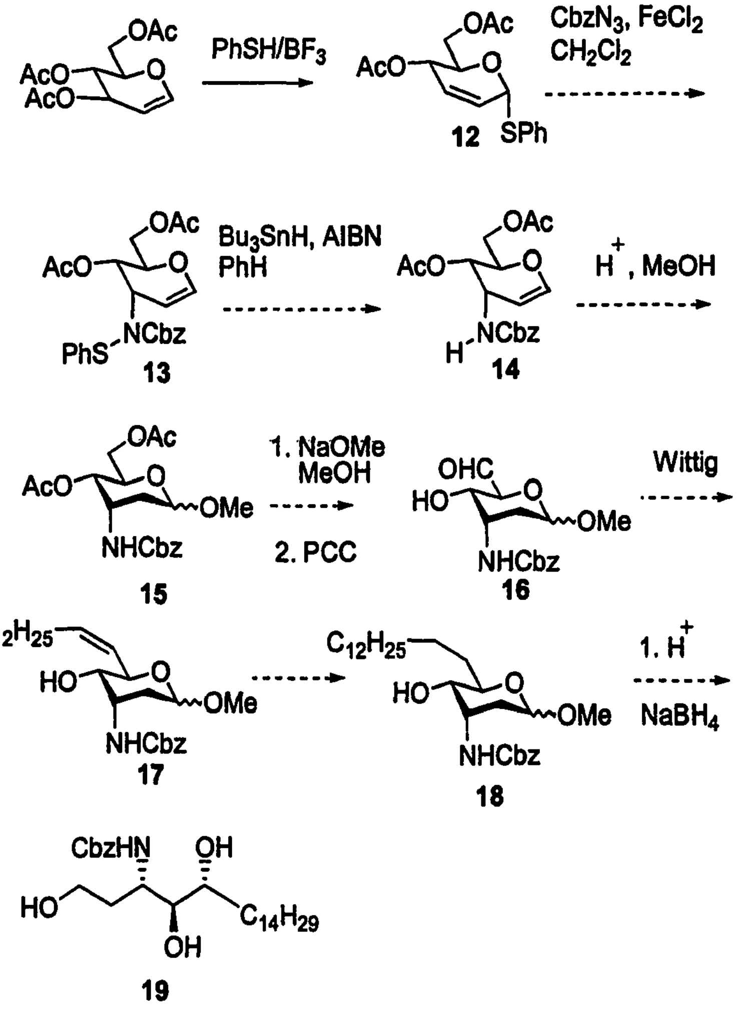
Scheme 4.18



Although this synthetic route is longer than the one we used, it will be more economical.

Since the stereoselectivity of Sharpless dihydroxylation was not high, another method was suggested by Prof. Franck. It started with tri-*O*-acetyl-D-glucal (Scheme 4.19). But in preliminary experiments, the rearrangement step (from **12** to **13**) using choramine-T was not successful. According to Bach's method[102] the addition of Fe(II) as catalyst, accelerates such a [2,3]-sigmatropic rearrangement. If this succeeds, we can make the side chain with the correct chiral centers. This synthesis will cost less and the stereoselectivity will be the best.

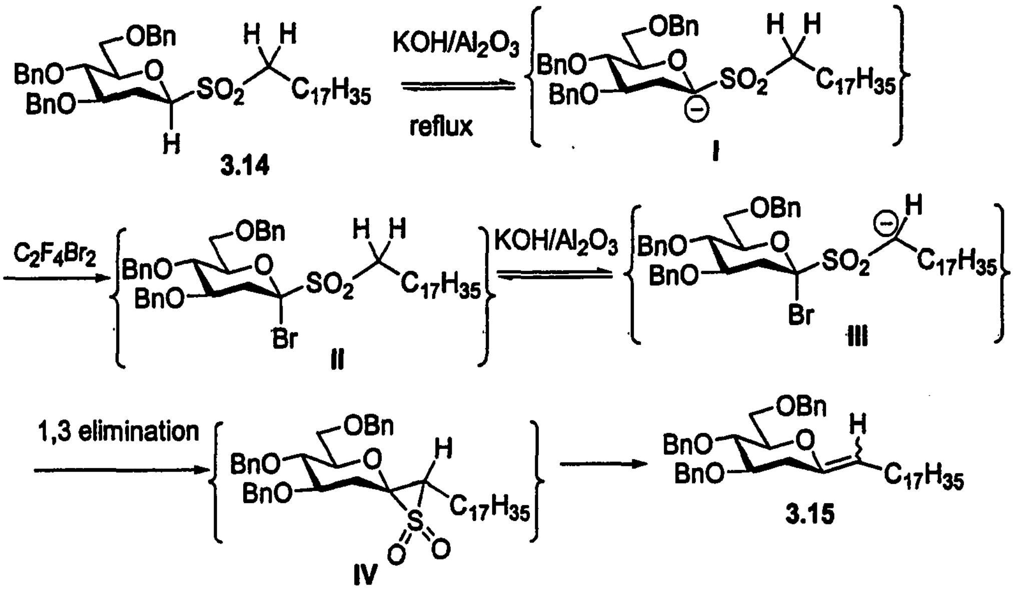
Scheme 4.19



5. DISCUSSION OF THE BROMINATION/RB-PATHWAY

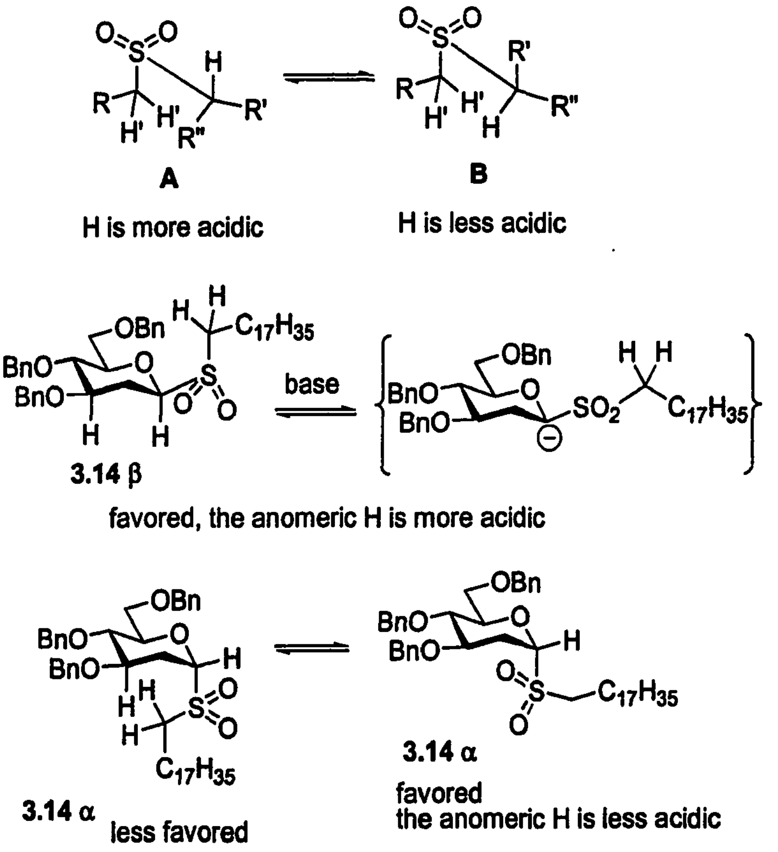
In the unsymmetrical sulfones, it is not known if the bromination of the sulfones takes place at α or α' carbon. In the 2-deoxy glucose series, we have observed that the β sulfonyl glycosides **3.14** and **3.24** gave a higher yield of the RB products than the α isomers under $KOH/Al_2O_3/CF_2BrCF_2Br$ conditions. There was no α-bromosulfone intermediate isolated, which indicated that the α-bromination took place at the anomeric center (Scheme 5.1), and the formation of the anomeric carbanion was faster in the β sulfone than that in the α sulfone.

Scheme 5.1



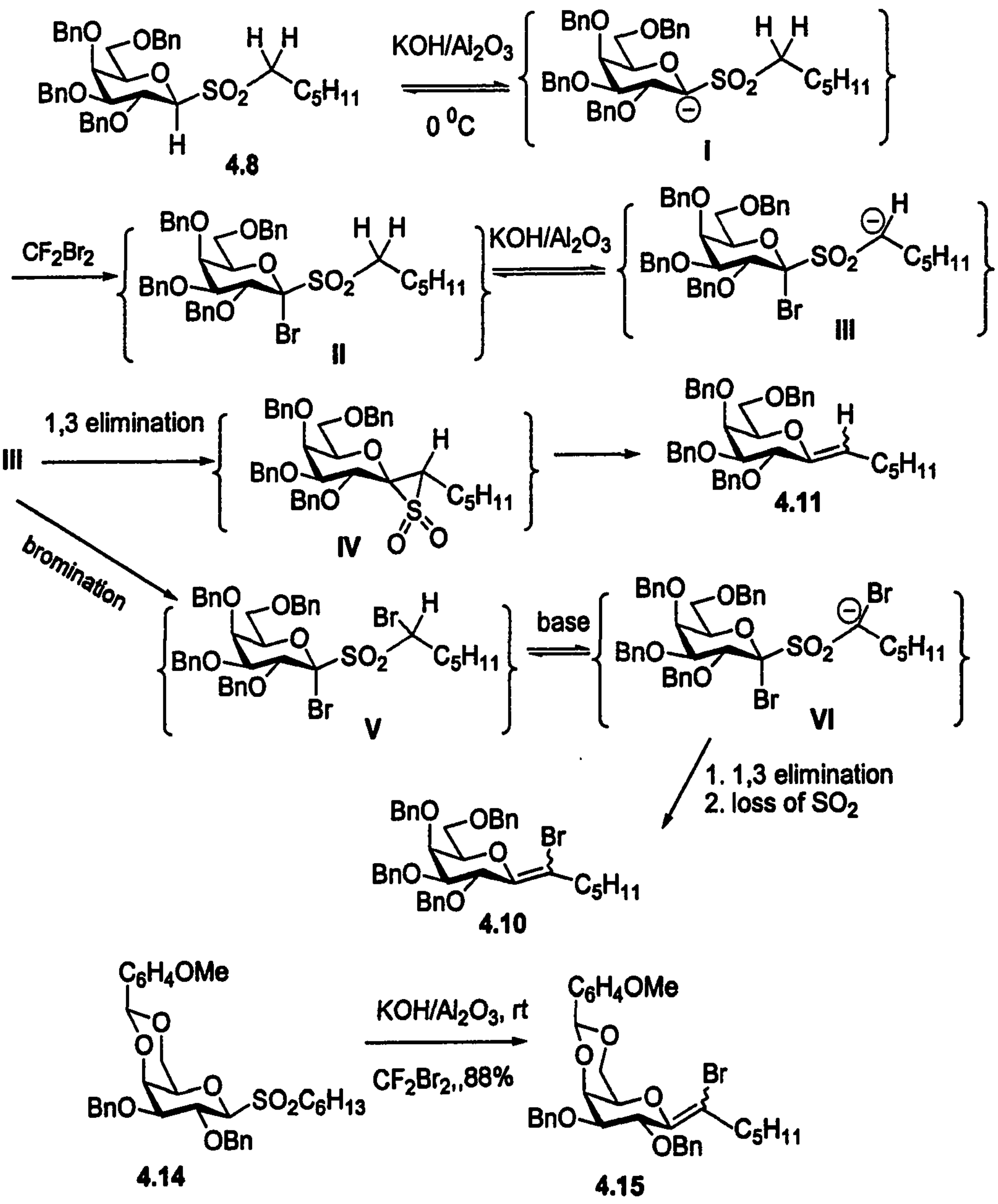
It is known that the α-H is more acidic when it has the gauche conformation A where the proton bisects the sulfone oxygens (Scheme 5.2). This explains that the anomeric proton is more acidic in the β sulfone than that in the α sulfone, because the bisected conformation in the sulfone 3.14α there would be a 1, 3 interaction between the R group and the 3, 5 axial protons of the sugar ring.

Scheme 5.2

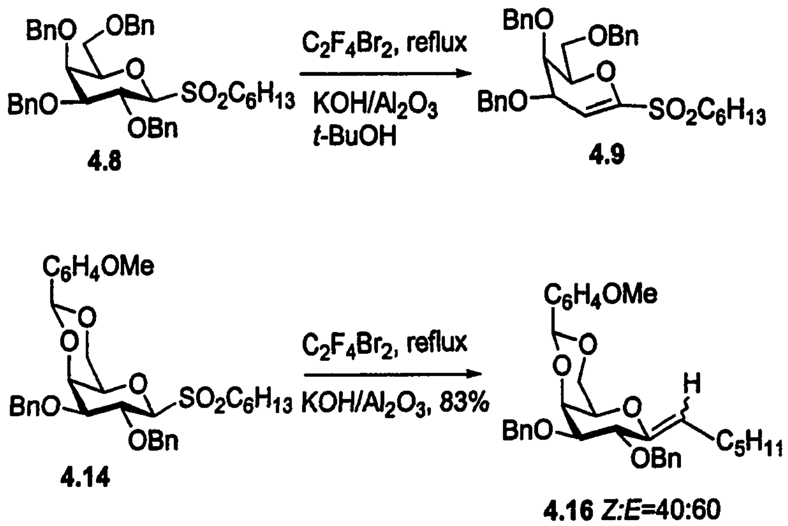


In the galactose series, the formation of anomeric carbanion can occur at low temperature (0 °C). It is assumed that CF_2Br_2 is a better brominating reagent than CF_2BrCF_2Br because the bromine transfer step is similar to SN2 reaction; therefore the Br in CF_2BrCF_2Br is more hindered and should react more slowly than CF_2Br_2. Therefore, when the galactosyl sulfones **4.8** and **4.14** were treated with CF_2Br_2 and base at 0 °C, a second bromine could be introduced faster than the RB reaction could take place. In similar experiments with CF_2BrCF_2Br, the bromination was slower, so elimination of benzyloxide from compound **4.8** and bromination/RB reaction of compound **4.14** were observed (Scheme 5.3 and 5.4).

Scheme 5.3


BnO
OBn
BnO
BnO
H H
SO2
C5H11
H
4.8
KOH/Al2O3
0 °C
I
CF2Br2
Br
II
KOH/Al2O3
III
1,3 elimination
IV
4.11
bromination
V
base
VI
1. 1,3 elimination
2. loss of SO2
4.10
C6H4OMe
SO2C6H13
KOH/Al2O3, rt
CF2Br2,,88%
4.14
4.15

Scheme 5.4


BnO
OBn
O
BnO
SO$_2$C$_6$H$_{13}$
OBn
4.8
C$_2$F$_4$Br$_2$, reflux
KOH/Al$_2$O$_3$
t-BuOH
BnO
OBn
O
BnO
SO$_2$C$_6$H$_{13}$
4.9
C$_6$H$_4$OMe
O
O
O
BnO
SO$_2$C$_6$H$_{13}$
OBn
4.14
C$_2$F$_4$Br$_2$, reflux
KOH/Al$_2$O$_3$, 83%
C$_6$H$_4$OMe
O
O
O
H
BnO
OBn
C$_5$H$_{11}$
4.16 *Z*:*E*=40:60

6. EXPERIMENTAL SECTION

General Methods. All air-moisture sensitive reactions were performed under a positive pressure of dry Ar or N_2. All solvents and reagents were distilled, dried, and /or recrystallized prior to use according to standard laboratory procedures. Analytical thin-layer chromatography (TLC) was performed on E. Merck precoated silica 60 F_{254} plates. Flash column chromatography was accomplished with E. Merck silica gel (230-400 mesh). NMR spectra were obtained on a GE QE 300 MHz spectrometer. All ^1H chemical shifts are reported in ppm relative to the internal standard tetramethylsilane (TMS, δ 0.00). ^{13}C chemical shifts are reported in ppm relative to $CDCl_3$ (center of triplet, δ 77.23). Low-resolution mass spectra were recorded at the Hunter College mass spectrometry laboratory. Optical rotations were measured at 23 °C with an Autopol III automatic polarimeter in a cell of 1-dm path length. Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected.

Tri-*O*-benzyl-2-deoxy-1-*O*-methoxyacetyl glucose (3.12) To a mixture of **3.6** (2.083 g, 5 mmol) and THF (15 mL) was added $Ph_3P.HBr$ (0.0858 g, 0.25 mmol). The solution was stirred at rt. for 10 min, and then there was added H_2O (0.135 mL, 0.017 mol). This mixture was stirred at rt. for 3 h. The mixture was treated with saturated $NaHCO_3$ (5 mL) solution and H_2O (10 mL), extracted by EtOAc (20 mL × 3). The organic phase was washed with brine, dried over Na_2SO_4, and concentrated. The residue was chromatographed on a column of silica gel (eluted with 30% EtOAc-petroleum ether) to afford 1.78 g (81%) of the glucosyl derivative **3.11** as a white solid. mp 102-104 °C; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.20-7.30 (m, 15H), 5.41 (d, J=2.3 Hz, 1H), 4.90 (dd, J=6.4, 3.0 Hz, 1H), 4.80 (m, 6H), 4.05 (m, 2H), 3.60 (m, 2H), 2.85 (s, 1H, OH), 2.32 (dd, J=4.0, 12.45 Hz, 1H), 1.70 (m, 1H).

To a mixture of the above compound **3.11** (0.194 mL, 2.53 mmol) and ether (20 mL) was added DCC (0.522 g, 2.53 mmol). The mixture was stirred at rt. for 10 min, and then methoxyacetic acid (1.10 g, 2.3 mmol) was added, followed by 4-pyrrolidinopyridine (0.034 g, 0.23 mmol). After standing overnight, the solution was filtered to remove the solid phase and then it was washed with brine (50 mL). The aqueous phase was extracted with ether (20 mL × 3), dried over Na_2SO_4 and concentrated. The residue was chromatographed on a column of silica gel (eluted with 20% EtOAc-petroleum ether) to afford 0.110 g (87%, α:β=75:25) of **3.12** as colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.20-7.30 (m, 15H), 6.30 (d, J=2.7 Hz, 3/4H), 5.77 (dd, J=10.5, 2.7 Hz, 1/4H), 4.88 (m, 1H), 4.60 (m, 6H), 3.98 (s, 2H), 3.62-3.96 (m, 4H), 3.41 (s, 3H, OMe), 2.35 (m, 1H), 1.85 (m, 1H).

Thioglycoside (3.13) A solution of **3.12** (0.358 g, 0.707 mmol) and octadecyl mercaptan (0.263 g, 0.919 mmol) in dry acetonitrile (10 mL) was warmed to 53° C (bath temp.) under nitrogen, and to this mixture was added a solution of $Yb(OTf)_3$ in acetonitrile (5 mmol/l, 0.71 mL, 0.5 mol%).[44] After stirring for 2 h, the reaction was quenched with saturated $NaHCO_3$ solution (10 mL), and extracted by CH_2Cl_2 (20 mL × 3). The organic phase was washed by H_2O, dried over Na_2SO_4 and concentrated. The residue was chromatographed on a column of 20g silica gel (eluted with 10% EtOAc-petroleum ether) to afford 0.442 g (89%, α:β=62:38, R_f of β is greater than that of α) of **3.13** as a white solid. α isomer: ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.20-7.30 (m, 15H), 4.91-4.53 (m, 6H), 4.52-4.47 (dd, J=1.5, 11.7 Hz, 1H), 3.78-3.63 (m, 3H), 3.53-3.40 (m, 2H), 2.70 (m, 2H), 2.34 (m, 1H), 1.75 (m, 1H), 1.60 (m, 2H), 1.20 (s, 30H), 0.88 (t, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 139.22, 139.15, 138.80, 129.03, 128.94, 128.50, 128.46, 128.35, 128.23, 81.34, 79.31, 78.85, 75.63, 74.17, 72.55, 71.72, 69.72, 36.75, 36.74, 31.79, 30.51, 30.36, 30.16, 30.03, 29.75, 23.51, 14.94.

β isomer: ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.35-7.21 (m, 15H), 5.45 (d, J=5.1 Hz, 1H), 4.92-4.49 (m, 6H), 4.19 (m, 1H), 3.95 (m, 1H), 3.83 (dd, J=3.67, 11.0 Hz, 1H), 3.66 (m, 2H), 2.53 (m, 2H), 2.30 (dd, J=4.76, 13.19 Hz, 1H), 2.08 (m, 1H), 1.59 (m, 2H), 1.35 (s, 30H), 0.91(t, 3H); Anal. calcd for $C_{45}H_{66}O_4S$: C, 76.87; H, 9.46; S, 4.56; found: C, 76.59; H, 9.15; S, 4.68.

Sulfone (3.14) A solution of MMPA (0.227 g, 0.45 mmol) in H_2O (2 mL) was added to a solution of **3.13** (β isomer, 0.112 g, 0.159 mmol) in EtOH (2 mL) and THF (2 mL), the mixture was kept at 55 °C for 2 h. The mixture was concentrated to dryness *in vacuo*. The residue was treated with saturated $NaHCO_3$ solution (10 mL), and extracted with EtOAc (15 mL × 3), dried over Na_2SO_4 and evaporated to dryness. The residue was purified by chromatography on silica gel eluting with 25% EtOAc/PE to afford 0.11 g (95%) of pure sulfone **3.14** (β isomer) as a white solid. When the identical reaction was carried out with the α isomer as the starting material, the α sulfone was afforded. For α isomer, mp 58-60 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.20-7.30 (m, 15H), 4.84 (dd, J=7.0, 3.3 Hz, 1H, H-1), 4.80-4.45 (m, 6H, OCH_2Ph), 4.37 (m, 1H, H-5), 4.20 (m, 1H, H-3), 3.68 (d, J=3.3 Hz, 2H, H-6), 3.58 (dd, J=7.2, 9.3 Hz, 1H, H-4), 3.06 (t, 2H), 2.82(m, 1H, H-2e), 2.06(m, 1H, H-2a), 1.30 (s, 30H), 0.90 (t, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): 138.78, 138.71, 138.53, 129.10, 129.02, 128.97, 128.44, 128.37, 128.308, 86.67, 77.53, 76.59, 75.62, 74.76, 74.06, 72.76, 69.73, 50.51, 32.73, 30.50, 30.32, 30.16, 30.08, 29.84, 29.39, 26.31, 23.50, 22.44, 14.93.

β isomer, mp 87-88 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.34-7.20 (m, 15H), 4.95-4.50 (m, 6H, OCH_2Ph), 4.30 (dd, J=11.0, 3.0 Hz, 1H, H-1), 3.76-3.51 (m, 5H), 3.60 (t, 2H), 2.65 (m, 1H, H-2e), 1.88 (m, 1H, H-a), 1.27 (s, 30H), 0.88 (t, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 137.60, 137.55, 137.32, 128.04, 127.92, 127.60, 127.38, 127.29, 127.19, 127.13, 96.90, 86.78, 79.70, 78.99, 76.78, 74.80, 72.89, 71.02, 68.60, 48.86, 31.47, 29.23, 29.06, 28.89, 28.83, 28.59, 28.15, 27.42, 22.22, 20.75, 13.64; MS: m/z 757 (M^++Na^+), (calcd for $C_{45}H_{66}O_6S$, 734).

Preparation of KOH/Alumina reagent [38] A batch of 30 g of KOH pellets was dissolved in 300 mL of MeOH and slurried with 90 g of neutral alumina (E. Merck, grade 1, 60 mesh), then the solvent was removed *in vacuo* until the alumina was again free flowing.

RB product (3.15)[31b] To a solution of compound **3.14** (β isomer, 0.100 g, 0.0136 mmol) in *t*-BuOH (1 mL) and CF_4Br_2 (3 mL), 0.25 g 50% (by weight) KOH/Al_2O_3 (prepared one week earlier) was added. This mixture was refluxed at 47 °C for 5 h. The solution was filtered through a pad of celite, which was washed with CH_2Cl_2. The residue was purified by column chromatography on silica gel eluting with 5% EtOAc-PE to afford 0.075 g (85%, Z:E=1:1) of **3.15** as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.38-7.18 (m, 15H), 5.07 (t, ½ H, vinyl H), 4.92-4.50 (m, 6.5H, including 1/2 vinyl H), 3.80-3.44 (m, 5H), 2.92 (dd, 1/2H, H_{2e}(E)), 2.67 (dd, ½H, H_{2e}(Z)), 2.30-2.00 (m, 1H, H_{2a}), 1.90 (t, 2H), 1.28 (s, 30H), 0.89 (t, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 146.38 (C-1*E*), 145.91 (C-1*Z*), 136.45, 136.36, 136.26, 126.31, 126.23, 126.00, 125.83, 125.60, 125.53, 125.37, 125.29, 109.11, 105.72, 99.41, 98.81, 95.26, 87.69, 78.16, 76.02, 75.84, 75.36, 74.93, 74.51, 72.91, 72.57, 71.99, 71.68, 71.43, 71.39, 71.28, 71.23, 71.12, 69.61, 69.35, 68.44, 68.02, 67.19, 66.30, 32.81 (C-2), 29.85, 28.03, 27.63, 27.50, 27.28, 27.15, 26.99, 24.60, 24.53, 24.21, 22.74, 22.55, 20.61, 12.03; MS: m/z 691 (M^++Na^+), (calcd for $C_{45}H_{64}O_4$, 668).

1-Octadecyl-tri-*O*-benzyl-D-glucal (3.16) A sample of **3.15** (0.10 g, 0.269 mmol) was dissolved in EtOAc (3 mL) and 95% ethanol (12 mL), and 2 drops of *n*-butyl amine[54] and 30 mg 10% Pd/C (an old sample which was bought 10 years ago) were added. The flask was purged with N_2 and evacuated. This purge/evacuate cycle was repeated with H_2. The mixture was stirred under H_2 at room temperature overnight. The mixture was filtered though celite and the catalyst plus celite were washed with EtOAc. The filtrate was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel eluting with 5% EtOAc-PE to afford 84 mg of **3.16** as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.38-7.18 (m, 15H), 4.82-4.51 (m, 6H,OCH_2Ph), 4.16 (m, 1H), 4.07 (m, 1H), 3.85-3.74 (m, 4H), 2.07 (t, 1H, allyl-H), 1.50 (m, 2H), 1.28 (s, 30H), 0.89 (t, 3H); MS: m/z 691 (M^++Na^+), (calcd for $C_{45}H_{64}O_4$, 668).

***C*-glycoside 3.18** A 50 mL 3-neck round bottom flask was charged with ethyl acetate (10 mL) and 10% Pd/C (5 mg) and some powdered 4Å molecular sieves. After the flask was purged with N_2 and evacuated several times, the procedure was repeated with H_2. The mixture was stirred under H_2 for 1/2 h, and then **3.16** (75 mg, 0.114 mmol) in EtOAc (2 mL) were injected into the flask. The mixture was stirred under H_2 at room temperature for 3 h. No debenzylation took place, but some of the starting material still remained. Additional 10% Pd/C (5 mg) was added. The mixture was stirred under hydrogen overnight. The mixture was filtered though celite and the catalyst were washed by EtOAc. The filtrate was concentrated *in vacuo*, the residue was purified on silica gel eluting with 5% EtOAc/PE to afford 60 mg (80%) of **3.18**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.37-7.19 (15H, Ar-H), 4.95-4.57 (m, 6H), 3.79-3.29 (m, 6H), 2.19-2.12 (dd, 1H, J=4.8, 11.7 Hz, H_{2e}), 1.66 (m, 1H), 1.32 (s, 34H), 0.89 (t, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 139.39, 139.28, 139.15 (C-Ph), 129.25, 129.01, 128.93, 128.76, 128.61, 128.43, 128.26, 128.17, 128.09(C-Ph), 82.06, 79.77, 79.55, 76.42, 75.66, 74.14, 72.09, 70.45 (C-1), 37.68 (C-2), 36.48, 32.73, 30.50 (CH_2), 30.16, 26.58, 23.49, 14.92 (CH_3); MS: *m/z* 693 ($M+Na^+$), (calcd for $C_{45}H_{66}O_4$, 670).

Ionic hydrogenation[55] **of 3.15** To a solution of **3.15** (0.130 g, 0.20 mmol) in CH_2Cl_2 (2 mL) and triethylsilane (0.23 mL, 1.33 mmol), TFA (0.1 mL, 1.30 mmol) was added dropwise at -70 °C for 10 min. After this reaction mixture was stirred at -70 °C for 20 min, it was brought to 0 °C for 4 h. The mixture was diluted with CH_2Cl_2 (20 mL) and extracted with saturated sodium bicarbonate solution (20 mL). The organic layer was dried over anhydrous sodium sulfate, and then concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to afford 80 mg (60%) of **3.18** as a white solid and 8 mg (7%) of **3.20** and **3.21**.

For compound **3.20**, ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.40-7.22 (m, 10H), 5.90-5.75 (m, trace of vinyl H), 4.69-4.38 (m, 4H), 3.78-3.28 (m, 5H), 2.27 (m, 2H), 1.75 (m, 2H), 1.60 (m, 2H), 1.30 (s, 32H), 0.80 (t, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 139.36, 139.22, 128.93, 128.88, 128.51, 128.37, 128.29, 128.14, 127.99, 81.42, 78.48, 74.48, 74.10, 71.81, 71.76, 71.63, 70.84, 70.73, 36.61, 32.73, 31.48, 30.50, 30.43, 30.30, 30.16, 26.66, 23.50, 14.93; MS: m/z 587 (M^++Na^+), (calcd for $C_{38}H_{60}O_3$, 564).

***C*-glycoside 3.19** To a solution of **3.18** (80 mg, 0.119 mmol) in EtOAc (1 mL) and EtOH (2 mL), 10% Pd/C (24 mg) was added. After the flask was degassed under H_2 three times, the mixture was stirred under H_2 at rt overnight. After filtration of the catalyst, and additional washing of the solid on the filter funnel with 10% MeOH/$CHCl_3$ followed by evaporation of the solvent *in vacuo*, 50 mg (95%) of **3.19** was obtained as a white solid. mp 118-120°C; ^{1}H NMR (300 MHz, $CDCl_3$ and a drop of d_4-methanol): δ 3.81 (dd, 2H, H-6), 3.55 (m, 1H, H-5), 3.30-3.18 (m, 3H), 1.98 (m, 1H, H-2e), 1.65 (m, 1H, H-2a), 1.33 (s, 34H), 1.89 (t, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$ and a few drops of d_4-methanol): δ 79.84, 76.58, 73.65, 73.51, 63.322, 39.44, 36.34, 32.67, 30.43, 30.10, 26.40, 23.43, 14.79; MS: *m/z* 423 (M^++Na^+), (cacld for $C_{24}H_{48}O_4$, 400).

(R)-2-phenyl- (S)-4-hydroxymethyl-1,3-dioxane (3.29)[58] A sample of commercially available (Aldrich) S-(-)-1,2,4-butanetriol **3.28** (2.6 g, 20.6 mmol), benzaldehyde (3.47 mL, 29 mmol) and trimethyl orthoformate (3.74 mL, 29 mmol) were dissolved in CH_2Cl_2 (80 mL) and CF_3COOH (1 mL) was added. After 24 h at rt. the reaction was quenched by the addition of NaOMe (20 mg) and diluted with 100ml ether and filtered. After the filtrate was concentrated under reduced pressure, the residue was purified by column chromatography on silica gel eluting with PE-EtOAc (5:1~1:1) to afford 3.6 g (90%) of **3.29** as colorless oil. IR (thin film) ($\nu_{O\text{-}H}$) 3422.0cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.52-7.33 (m, 5H), 5.51 (s, 1H), 4.29 (dd, J=4.1, 10.7 Hz, 1H), 3.95 (m, 2H), 3.60 (m, 2H), 2.85 (s, 1H, OH), 1.85 (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 139.10, 129.58, 128.90, 126.85, 101.96, 78.35, 67.36, 66.27, 27.69.

(R)-2-phenyl- (S)-4-hexadecyloxymethyl-1,3-dioxane (3.30)[58] To a suspension of NaH (3 g, 60% in mineral oil) in dry THF (30 mL) was added a solution of **3.29** (1.47 g, 7.6 mmol) in THF (10 mL) at 0 °C. After 1/2 h, hexadecyl bromide (3 mL, 9.88 mmol) and tetrabutyl ammonium iodide (0.28 g, 0.76 mmol) were added. The mixture was stirred overnight and the reaction was quenched by addition of MeOH (5 mL). After the solvent was removed under reduced pressure, ether and water were added. The product was extracted with ether. The organic layer was dried over Na_2SO_4 and concentrated. The product was purified by column chromatography on silica gel eluting with EtOAc-PE (5%) to afford 1.55 g (50%) of **3.30** as a white solid. mp 51-54 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.51-7.31 (m, 5H, Ph), 5.54 (s, 1H, PhCH-), 4.32-4.27 (m, 1H, -CHO), 4.10-3.94 (m, 2H, $-CH_2O-$), 3.65-3.59 (m, 4H, $-CH_2O$), 1.89-1.83 (m, 2H, $-CH_2-$), 1.62-1.54 (m, 2H), 1.25 (s, 26H), 0.88 (t, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 139.28, 129.32, 128.77, 126.79, 101.88, 77.09, 74.44, 72.61, 67.61, 32.74, 30.51, 30.30, 30.18, 29.18, 26.93, 23.51, 14.94. MS: m/z 441 (M^++Na^+), (calcd for $C_{27}H_{45}O_3$, 418).

1-*O*-hexadecyl-2-*O*-benzoyl-4-bromobutane (3.27) To a solution of **3.30** (3.0 g, 7.17 mmol) in CCl_4 (80 mL) was added NBS (1.434 g, 8.05 mmol) followed by $BaCO_3$ (0.8 g, 4.05 mmol).[59] After 4 h reflux, the reaction mixture was filtered through a pad of celite, which was washed by additional CCl_4. After concentration the residue was purified by column chromatography on silica gel eluting with ethyl ether-PE (10%) to give 3.35g (93%) of compound **3.27** as yellow oil. $[\alpha]^{23}$ -17.58° (c 0.58, $CHCl_3$); IR ($\nu_{C=O}$) 1722 cm^{-1} , ($\nu_{C\text{-}Br}$) 1271 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.06 (d, 2H), 7.55 (t, 1H), 7.44 (t, 2H), 5.41-5.36 (m, 1H, -CHO-), 3.65-3.63 (m, 2H, $-OCH_2$), 3.51-3.42 (m, 4H), 2.40-2.33 (m, 2H), 1.60 (t, 2H), 1.26 (s, 26H), 0.88 (t, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.50, 133.69, 130.73, 130.31, 128.99, 72.551, 72.46, 71.98, 35.39, 32.70, 30.47, 30.38, 30.22, 30.14, 29.46, 26.86, 23.46, 14.90; MS: *m/e* 519, 521 (M^++Na^+), (calcd for $C_{27}H_{45}O_3Br$, 496, 498).

3,4,6-Tri-*O*-benzyl-2-deoxy-1-glucosyl chloride (3.31) [60] A sample of tri-*O*-benzyl glucal **3.6** (4.45 g, 10.7 mmol) is dissolved in anhydrous toluene (20 mL). Anhydrous HCl is bubbled through this solution for 15 min at 0 °C. HCl is removed by bubbling nitrogen through the reaction mixture. After concentration for 1 h, 4.73 g of **3.31** was afforded as colorless syrup. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.35-7.17 (m, 15H), 6.30 (d, J=3.7 Hz, 1H, H-1), 4.90-4.50 (m, 6H), 4.15 (m, 1H), 4.06 (m, 1H), 3.75-3.66 (m, 3H), 5.50 (m, 1H, H-2e), 1.98 (m, 1H, H-2a).

3,4,6-Tri-*O*-benzyl-1-*S*-acetyl-1-thio-D-glucopyranose (3.26) [61] To the solution of crude **3.31** (4.73 g, 10.4 mmol) in 10 mL HMPA was added KSAc (1.94 g, 16.05 mmol). The reaction mixture was stirred at rt overnight. The reaction mixture is diluted with chloroform (100 mL), and extracted with water (100 mL × 3) to remove HMPA. The combined organic extracts are dried over sodium sulfate. After concentration *in vacuo*, yellow syrup is afforded. The residue is purified by column chromatography on silica gel eluting with EtOAc-PE (10%-15%) to afford 3.679 g (74%, α:β = 30:70) of **3.26** as yellow syrup. IR: ($\nu_{C=O}$) 1703 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.20 (d, J=5.0 Hz, 1/3.5 H, C1-He), 5.19 (dd, J=13.0, 2.0 Hz, 2.5/3.5 H, C1-Hα), 4.42-4.84 (m, 6H, 3×$PhCH_2$), 3.49-3.76 (m, 5H), 2.15-2.38 (m, 1H, C2-He), 3.35 (s, 3H, $SCOCH_3$), 1.80-1.92 (m, 1H, C2-Hα); ^{13}C NMR (75 MHz, $CDCl_3$) δ 219.07, 193.12, 138.32, 138.16, 138.12, 128.33, 128.21, 127.80, 127.59, 127.55, 97.22, 80.49, 79.62, 79.46, 78.48, 76.97, 76.54, 75.16, 74.99, 74.89, 73.40, 73.33, 71.70, 71.61, 68.78, 68.56, 36.61, 36.48, 30.57; MS: *m/e* 510(M^++NH_4^+), (calcd for $C_{29}H_{32}O_5S$, 492);

Thioglycoside 3.32 To a solution of **3.26** (1.85 g, 3.75 mmol, α:β=30:70) and **3.27** (1.24 g, 2.50 mmol) in HMPA (20 mL) were added cysteamine (0.426 g, 3.75 mmol) and DTE (0.579 g, 1.4 mmol).[62] The reaction mixture was stirred at rt. overnight. The reaction mixture was diluted with EtOAc and washed with water (3 ×) and dried over Na_2SO_4. The residue obtained after concentration was then purified by column chromatography on silica gel eluting with EtOAc-PE (15%) to afford 1.28 g (64%, α:β≈29:71) of **3.32** as yellow oil. IR ($\nu_{C=O}$) 1718 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 8.10-7.20 (m, 20H), 5.48 (d, J=4.0 Hz, 1H, trace of H-1e), 5.37 (m, 1H), 4.93-4.54 (m, 6H), 4.54-4.50 (dd, J=9.0, 4.0 Hz, 1H, H-1a), 3.73-3.40 (m, 10H), 2.89-2.76 (m, 2H), 2.40-2.35 (m, 1H), 2.18-2.11 (m, 2H), 1.80-1.75 (m, 1H), 1.56-1.47 (t, 2H), 1.29 (s, 26H), 0.91 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.66, 139.09, 138.95, 135.55, 131.52, 131.07, 131.01, 130.34, 129.47, 129.07, 128.97, 128.77, 128.62, 128.49, 128.32, 128.13, 87.41, 81.43, 80.55, 80.09, 78.60, 78.23, 75.76, 74.26, 74.13, 73.25, 72.58, 72.38, 72.31, 72.24, 70.14, 37.71, 32.74, 32.62, 30.90, 30.51, 30.44, 30.28, 30.18, 27.49, 26.91, 23.51, 14.96; MS: *m/e* 889 (M^++Na^+), (calcd for $C_{54}H_{74}O_7S$, 866; C, 74.79, H, 8.60, S, 3.70; found: C, 74.89, H, 8.53, S, 3.74%).

Thioglycoside 3.25 To a solution of β-**3.32** (0.1 g, 0.115 mmol) in 3 mL THF/MeOH (2:1) was added NaOMe (40 mg). After 6 h at rt, the mixture was extracted with water and EtOAc. The organic layer was dried over Na_2SO_4. After concentration, the residue was purified by column chromatography on silica gel eluting with EtOAc-PE (15%-50%) to afford 74 mg (85%) of product as yellow oil. IR ($\nu_{O\text{-}H}$) 3489.9 cm^{-1}; β isomer: mp 41-42 °C; $[\alpha]^{23}$ −16.9° (c 1.51, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.35-7.17 (m, 15H), 4.90-4.50 (m, 7H, 3×CH_2Ph and H_{1a}), 4.02 (m, 1H), 3.76-3.66 (m, 2H), 3.45-3.28 (m, 6H), 2.96 (m, 1H), 2.82 (m, 2H), 2.40 (dd, J=11.3, 4.7 Hz, 1H), 1.80-1.72 (m, 2H), 1.69-1.52 (t, 2H), 1.26 (s, 26H), 0.89 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.88, 138.79, 138.74, 129.07, 128.84, 128.67, 128.58, 128.50, 128.33, 128.24, 81.42, 79.86, 78.76, 75.76, 75.66, 74.12, 72.29, 72.24, 70.33, 69.96, 69.03, 37.83, 34.46, 32.73, 30.50, 30.32, 30.16, 28.58, 26.95, 23.51, 14.94; MS: *m/e* 785 (M^++Na^+), (calcd for $C_{47}H_{70}O_6S$, 762).

α isomer (oil): $[\alpha]^{23}$ +95.57° (c 0.7, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.33-7.16 (m, 15H), 5.46-5.44 (d, J=5.5 Hz, 1H), 4.90-4.47 (m, 6H, 3×CH_2Ph), 4.14 (m, 1H), 3.93 (m, 3H), 3.67 (m, 2H), 3.43 (m, 3H), 3.22 (m, 1H), 2.72 (m, 2H), 2.28 (dd, J=4.8, 13.2 Hz, 1H), 2.06 (m, 1H), 1.77 (t, 2H), 1.54 (m, 2H), 1.26 (s, 26H), 0.89 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 139.21, 139.11, 138.79, 129.05, 128.98, 128.95, 128.51, 128.36,128.27, 128.22, 81.78, 79.32, 78.76, 75.64, 75.46, 74.19, 72.55, 72,29, 71.94, 69.97, 69.82, 36.75, 34.14, 32.75, 30.51, 30.32, 30.18, 28.35, 26.97, 23.52, 14.97.

To a suspension solution of NaH (60% in mineral oil, 100 mg) in THF (3 mL) was added above compound (β, 0.184 g, 0.24 mmol). After H_2 evolution ceased, CH_3I (0.15 mL, 2.4 mmol) was added. After 1 h, the reaction was quenched by addition of MeOH (1 mL). After concentration under reduced pressure, the residue was treated with water (20 mL) and extracted with CH_2Cl_2 (20 mL × 3). The organic layer was dried over Na_2SO_4. After concentration, 0.19 g (95%) of **3.25** as a white solid was afforded after purification from chromatography on silica gel eluting with 20% EtOAc/PE. β isomer: mp 35-37 °C; $[\alpha]^{23}$ -21.05° (c 0.665, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.33-7.16 (m, 15H), 4.95-4.50 (m, 7H, 3×CH_2Ph and H_{1a}), 3.78-3.40 (m, 13H), 2.90-2.72 (m, 2H), 2.43-2.35 (m, 1H, H_{2e}), 1.88-1.72 (m, 3H), 1.60-1.52 (t, 2H), 1.26 (s, 26H), 0.89 (t, 3H);

^{13}C NMR (75 MHz, $CDCl_3$): δ 138.99, 138.97, 138.94, 129.07, 128.97, 128.63, 128.53, 128.49, 128.32, 128.15, 81.47, 80.54, 80.08, 79.38, 78.74, 75.79, 74.14, 73.20, 72.45, 72:25, 70.22, 58.48, 37.84, 32.78, 32.74, 32.50, 30.18, 27.58, 26.74, 23.51, 14.96; MS: *m/e* 799 (M^++Na^+), (Anal. calcd for $C_{48}H_{72}O_6S$, 776, C, 74.18; H, 9.34; S, 4.13. Found: C, 74.07; H, 0.09; S, 4.07).

α isomer (oil): $[\alpha]^{23}$ 76.4° (c 0.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.34-7.17 (m, 15H), 5.44 (d, J=5.5 Hz, 1H), 4.90-4.47 (m, 6H, 3×CH_2Ph), 4.14 (m, 1H), 2.92 (m, 1H), 3.83 (dd, J=3.6, 10.2 Hz, 2H), 3.63 (m, 2H), 3.40 (s, 7H), 2.65 (m, 2H), 2.29 (dd, J=4.8, 13.2 Hz, 1H), 2.06 (m, 1H), 1.80 (m, 2H), 1.58 (t, 2H), 1.26 (s, 26H), 0.89 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 139.17, 139.10, 138.75, 129.03, 128.95, 128.50, 128.33, 128.26, 81.80, 79.50, 79.23, 78.79, 75.66, 74.19, 73.20, 72.56, 72.45, 71.85, 69.65, 58.46, 36.78, 32.71, 32.62, 30.49, 30.29, 30.15, 28.21, 26.93, 23.48, 14.93.

Sulfone 3.24 To a solution of β-**3.25** (0.19 g, 0.24 mmol) in 9 mL THF/EtOH/H_2O (1:1:1) was added MMPA (0.36 g, 0.734 mmol). The mixture was stirred at 55-60 °C for 1 h. The reaction mixture was concentrated under reduced pressure; the residue was diluted with CH_2Cl_2 and washed with saturated $NaHCO_3$ solution. The organic layer was dried over Na_2SO_4. After concentration, the residue was purified by column chromatography on silica gel eluting with EtOAc-PE (40%) to afford 0.168 g (85%) of **3.24** as a white solid. IR (ν $_{S\text{-}O}$ asymmetric stretching) 1313.4 cm^{-1}, (ν $_{S\text{-}O}$ symmetric stretching) 1212.4 cm^{-1}; mp 63-65 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.33-7.17 (m, 15H), 4.96-4.54 (m, 6H, 3×CH_2Ph, 4.39-4.34 (dd, J=12.0, 1.8 Hz, 1H, H_{1a}), 3.75 (m, 3H), 3.60 (m, 2H), 3.43 (m, 5H), 3.39 (s, 3H, OCH_3), 3.25 (m, 2H, CH_2SO_2), 2.68-2.64 (m, 1H, H2e), 2.16-1.85 (m, 3H), 1.57 (t, 2H), 1.26 (s, 26H), 0.89 (t, 3H); ^{13}C NMR (75

MHz, $CDCl_3$): δ 138.67, 138.44, 138.50, 129.15, 129.05, 128.72, 128.49, 128.40, 128.33, 87.98, 80.90, 80.16, 78.58, 77.92, 76.01, 74.12, 72.55, 72.21, 69.68, 58.34, 46.41, 32.74, 30.51, 30.31, 30.18, 28.70, 26.93, 24.44, 23.52, 14.97; MS: *m/e* 831 (M^++Na^+), (calcd for $C_{48}H_{72}O_8S$, 808).

α isomer (a white solid): mp 37-39 °C; $[\alpha]^{23}$ 43.37° (c 1.6, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.32-7.18 (m, 15H), 4.90 (dd, J=2.9, 6.6 Hz, 1H), 4.85-4.50 (m, 6H, 3×CH_2Ph), 4.39 (m, 1H), 4.24 (m, 1H), 3.73 (m, 2H), 3.62 (m, 1H), 3.48-3.39 (m, 8H), 3.31-3.10 (m, 2H), 2.82 (m, 1H), 2.05 (m, 3H), 1.55 (t, 2H), 1.26 (s, 26H), 0.88 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.79, 138.73, 138.51, 129.12, 129.06, 128.99, 128.85, 128.81, 128.45, 128.41, 128.33, 87.01, 78.61, 77.48, 75.72, 74.85, 74.10, 72.784, 72.64, 72.56, 69.63, 58.36, 46.90, 32.75, 30.53, 30.32, 30.19, 26.44, 24.75, 23.54, 14.99.

Ramberg-Backlund product 3.23a [31b] A sample of sulfone **3.24** (0.135 g, 0.16 mmol, β isomer) was dissolved in CF_2BrCF_2Br (3 mL) and *t*-BuOH (1 mL). A sample of 0.25 g 50% (by weight) KOH/Al_2O_3 (which was prepared five weeks earlier) was added. The reaction mixture was refluxed at 47 °C for 6 h. The mixture was filtered through a pad of celite and the solids were washed with CH_2Cl_2. The residue was purified by column chromatography on silica gel eluting with 10% EtOAc-PE to afford 74 mg (Z:E=1:1, 60%) of **3.23a** and **3.23b**. For **3.23a**: ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.34-7.16 (m, 15H), 5.11 (t, 1/2H, vinyl H), 4.89-4.51 (m, 6.5H, 6 OCH_2Ph and 1/2 vinyl H), 3.77-3.24 (m, 10H), 3.39 (s, 3H, OCH_3), 3.0 (dd, 1/2H, J=4.6, 13.5 Hz, H_{2e}(E)), 2.28 (dd, 1/2 H, J=5.5, 14.2 Hz, H_{2e}(Z)), 2.48-2.08 (m, 3H, including H_{2a}), 1.7 (t, 2H), 1.32 (s, 26H), 0.89 (t, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 150.97, 150.27 (C-1, Z E isomer), 139.06, 139.01, 138.86, 138.81(C-Ph), 129.03, 128.97, 128.55, 128.50, 128.39, 128.28 (C-Ph), 107.21, 106.37 (vinyl C-4'), 80.91, 80.71, 80.56, 80.42, 80.14, 79.71, 78.65, 78.48, 77.94, 77.90, 75.39, 75.31, 74.23, 73.573, 72.47, 72.41, 72.32 ,72.19 , 69.94 (C-6), 58.38, 57.94 (C-OCH$_3$), 35.51 (C-2), 32.71, 30.49 (CH$_2$), 30.31, 30.23, 30.14, 29.08, 27.01, 26.94, 23.49 (CH$_2$), 14.92 (CH$_3$); MS: m/z 765 (M^++Na^+), (calcd for $C_{48}H_{70}O_6$, 742).

***C*-glycerylipid 3.22** A 50 mL 3-neck round bottom flask was charged with ethyl acetate (5 mL) and 10% Pd/C (5 mg) and some 4Å powdered molecular sieves. The flask was put through several cycles of purge/evacuate with N_2 followed by several cycles with H_2. The mixture was stirred under H_2 for 1/2 h, and then **3.23a** (40 mg, 0.054 mmol) in EtOAc (2 mL) was injected into the flask. The mixture was stirred under H_2 at room temperature for 3 h. No debenzylation took place. The mixture was filtered though celite and the catalyst were washed with EtOAc. The filtrate was concentrated *in vacuo*, the residue was purified on the silica gel eluting with 10% EtOAc/PE to afford 44 mg (99%) of endo product **3.23b**. ^{1}H NMR (300 MHz, CDCl$_3$): δ 7.34-7.22 (m, 15H), 4.79 (d, 1H), 4.71-4.50 (m, 6H), 4.17 (m, 1H), 4.08 (m, 1H), 3.87-3.73 (m, 3H), 3.64 (t, 1H), 3.43-3.30 (m, 7H), 2.18 (m, 2H), 1.70 (m, 2H), 1.56 (m, 3H), 1.27 (s, 25H), 0.88 (t, 3H); MS: *m/z* 765 (M^++Na^+), (calcd for $C_{48}H_{70}O_6$, 742).

Under the same conditions, 10% Pd/C (10 mg) was added to the solution of above endo product in EtOAc (5 mL). The mixture was stirred under H_2 at rt for overnight. The mixture was filtered though celite and the catalyst were washed by EtOAc. The filtrate was concentrated *in vacuo*, the residue was purified on the silica gel eluting with 10% EtOAc/PE to afford 23 mg (50%) of **3.22**. ^{1}H NMR (300 MHz, CDCl$_3$): δ 7.37-7.19 (15H, Ar-H), 4.93-4.54 (m, 6H, OCH$_2$Ph), 3.73-3.33 (m, 11H), 3.41 (s, 3H, OCH$_3$), 2.19-2.14 (dd, 1 H, J=4.8, 11.7 Hz, H_{2e}), 1.75-1.53 (m, 7H), 1.32 (s, 26H), 0.89 (t, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 139.32, 139.27, 139.12 (C-Ph), 129.01, 128.92, 128.58, 128.40, 128.24, 128.17, 128.09 (C-Ph), 81.95, 80.61, 79.77, 79.45, 76.21, 75.66, 74.16, 73.32, 72.43, 72.09 (C-1), 70.44, 58.18 (C-OCH_3), 37.58 (C-2), 32.71, 32.00, 30.48 (CH_2), 30.29, 30.14, 28.20, 26.94, 23.49, 14.90 (CH_3); MS: *m/z* 767 (M^++Na^+), (calcd for $C_{48}H_{72}O_6$, 744).

Ionic hydrogenation of olefin 3.23a[55] To a solution of **3.23a** (0.120 g, 0.162 mmol) in CH_2Cl_2 (2 mL) and triethylsilane (0.2 mL, 1.15 mmol), TFA (0.08 mL, 1.04 mmol) was added dropwise at –70 °C for 10 min. After this reaction mixture was stirred at –70 °C for 20 min, it was brought to 0 °C for 3 h. The mixture was diluted with CH_2Cl_2 (20 mL) and extracted with saturated sodium bicarbonate solution (20 mL). The organic layer was dried over anhydrous sodium sulfate, concentrated under reduced pressure. The residue was purified by column chromatography on silica gel to afford 40 mg (33%) of **3.22** as a white solid and 45 mg (40%) of **3.33**. For **3.33**: ^1H NMR (300 MHz, $CDCl_3$): δ 7.37-7.19 (m, 10H, Ar-H), 5.90-5.75 (m, trace of vinyl H), 4.66-4.40 (m, 4H, OCH_2Ph), 3.76-3.30 (m, 13H), 2.25 (m, 1 H), 1.75-1.53 (m, 9H), 1.32 (s, 26H), 0.89 (t, 3H, CH_3); MS of **3.33**: *m/z* 661 (M^++Na^+), (calcd for $C_{41}H_{66}O_5$, 638).

***C*-glycerylipid 3.4** To a solution of **3.22** (74 mg, 0.1 mmol) in EtOAc (1/2 mL) and MeOH (2 mL), 10% Pd/C (20 mg) was added. After the flask was degassed under H_2 three times, the mixture was stirred under H_2 at rt. for 3 h. After filtration of the catalyst which was further washed by EtOAc and evaporation of the solvent in *vacuo.* The residue was purified on the silica gel eluting with 20% MeOH/EtOAc to afford 45 mg (96%) **3.4** as a white solid. mp 62-64 °C; $[\alpha]_D$ -3.47° (c 1.5, $CHCl_3$); ^1H NMR (500

MHz, CD_2Cl_2): δ 3.80 (dd, H, J=3.2, 11.4 Hz, H_6), 3.69 (dd, 1H, J=5.1, 11.4 Hz, H_6), 3.61 (m, 1H, H_3), 3.45 (m, 1H, H_1), 3.42-3.38 (m, 4H), 3.35 (s, 3H, $-OCH_3$), 3.29 (m, 2H), 3.22 (m, 1H, H_5), 2.47 (broad peak), 2.00 (dd, 1H, J = 4.8, 12.5 Hz, H_2), 1.63-1.48 (m, 9H), 1.34-1.29 (m, 26H), 0.88 (t, 3H, J=7.0 Hz, CH_3); ^{13}C NMR (75 MHz, CD_2Cl_2): δ 80.53, 79.81, 76.29, 73.60, 73.49, 73.36 (C-1), 72.20, 63.18, 57.91, 39.84, 32.61, 31.99, 30.39, 30.20, 30.04, 28.39, 26.83, 23.38, 14.56; Anal. calcd. for $C_{27}H_{54}O_6$, C, 68.35; H, 11.39; found: C, 68.12; H, 11.12.

***C*-glycoside 3.34** To a solution of **3.33** (42 mg, 0.066 mmol) in EtOAc (1/2 mL) and MeOH (2 mL), 10% Pd/C (20 mg) was added. After the flask was degassed under H_2 three times, the mixture was stirred under H_2 at rt. for 3 h. After filtration of the catalyst and washing by EtOAc and evaporation of the solvent in *vacuo*, 30 mg (95%) of **3.34** was obtained as a white solid. mp 47-48 °C; ^1H NMR (500 MHz, C_6D_6): δ 3.77 (m, 1H), 3.70 (m, 1H), 3.42 (m., 2H), 3.34-3.30 (m, 4H), 3.27 (s, 3H, $-OCH_3$), 3.23 (m, 1H), 3.14 (m, 1H), 1.93 (broad peak), 1.73-1.54 (m, 8H), 1.41-1.05 (m, 30H), 0.87 (t, 3H, $-CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 81.99, 80.64, 77.97, 73.44, 72.42, 68.56, 64.33, 58.26, 33.43, 32.69, 32.07, 31.69, 30.40, 30.25, 30.12, 28.44, 26.90, 23.46, 14.89; Anal. calcd. for $C_{27}H_{54}O_5$, C, 70.69; H, 11.86; found: C, 70.48; H, 11.65.

Isomerization of α, β isomer 3.14

To a solution of β sulfone **3.14** (12 mg, 0.016 mmol) in benzene (1 mL) and *t*-BuOH (0.2 mL), *t*-BuOK (10 mg) was added. The reaction mixture was refluxed at 70 °C for 10h. The mixture was diluted with dichloromethane, and filtered and dried in *vacuo*. α:β ratio was determined by the H1 peak in ^1H NMR: α:β= 36:64.

α sulfone **3.14** (12 mg, 0.016 mmol) was treated under above condition for 10 h. The α:β ratio was determined by ^{1}H NMR: α:β= 52:47.

(3S)-4-*O*-Hexadecyl-1,3-butanediol Ether **3.30** (0.836 g, 2 mmol) was dissolved in 80% acetic acid (8 mL) at 90 °C. The mixture was refluxed at this temperature for 1 h. The mixture was quenched with saturated $NaHCO_3$. The mixture was then extracted with ether (3 × 30 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. The product was purified by column chromatography on silica gel, eluting with EtOAc-PE (50%) to afford 0.55 g (82%) of a white solid. mp 48 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.01 (m, 1H), 3.83 (q, 2H), 3.45 (m, 3H), 3.33 (m, 1H), 2.74 (d, J = 5.9 Hz, 1H, OH), 2.55 (t, J = 5.5 Hz, 1H, OH), 1.71 (m, 2H), 1.57 (m, 2H), 1.25 (s, 28H), 0.88 (t, J = 6.2 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 75.02, 71.86, 70.46, 61.25, 35.32, 32.22, 29.99, 29.77, 29.65, 26.42, 22.99, 14.41.

(3S)-4-*O*-Hexadecyl-1-*O*-tert-butyldimethylsilyl-3-butanol (3.37) To a solution of 4-*O*-hexadecyl-1,3-butanediol (0.5 g, 1.52 mmol) in 10 mL of CH_2Cl_2 was added TBDMSCl (0.259 g, 1.66 mmol) followed by imidazole (0.227 g, 3.33 mmol). The mixture was stirred at rt for 1 h. The mixture was filtered and the filtrate was rinsed with CH_2Cl_2. The solution was concentrated and purified by column chromatography on silica gel (eluting with EtOAc-PE 20%) to afford 0.65 g (97%) of compound **3.37**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.97 (m, 1H), 3.82 (m, 2H), 3.47-3.34 (m, 4H), 3.11 (d, J = 2.6 Hz, 1H, OH), 1.69 (m, 2H), 1.57 (m, 2H), 1.25 (s, 28H), 0.89 (m, 12H), 0.07 (m, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 75.17, 71.81, 69.69, 61.54, 35.92, 32.23, 29.99, 29.91, 29.78, 29.65, 26.43, 26.20, 22.99, 18.51, 14.41, -5.13.

4-*O*-Hexadecyl-3-*O*-methyl-1-butanol 3.38 To a suspension of NaH (60% in mineral oil, 600 mg) in THF (10 mL) was added compound **3.37** (1.185 g, 2.669 mmol). After H_2 evolution ceased, CH_3I (0.67 mL, 10.67 mmol) was added, followed by TBAI (10 mg, 0.03 mmol). After 4 h, the reaction was quenched by addition of MeOH (2 mL). After concentration under reduced pressure, the residue was treated with water (20 mL) and extracted with CH_2Cl_2 (30 mL × 3). The organic layer was dried over Na_2SO_4. After concentration, 1.22 g of colorless oil was afforded.

To a solution of the above crude product (1.22 g, 2.669 mmol) in THF (10 mL) was added 1 N *n*-Bu_4NF (5.3 mL). After the mixture was stirred at rt for 2 h, and then concentrated, the residue was treated with water and extracted with ether (3 × 30 mL). The organic layer was dried over Na_2SO_4. After concentration, 0.748 g (93% for two steps) of **3.38** was obtained as a white solid after purification by chromatography on silica gel (elution with 30% EtOAc/PE). ^1H NMR (300 MHz, $CDCl_3$); δ 3.77 (q, 2H), 3.57-3.40 (m, 8H), 2.66 (t, $J = 5.5$ Hz, 1H, OH), 1.80 (q, 2H), 1.56 (m, 2H), 1.26 (s, 28H), 0.88 (t, $J = 5.5$ Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 79.70, 72.67, 72.00, 60.56, 57.83, 34.70, 32.19, 29.87, 29.73, 29.63, 26.38, 22.96, 14.39.

4-*O*-Hexadecyl-3-*O*-methyl-1-iodobutane 3.39 To a solution of alcohol **3.38** (0.748 g, 2.174 mmol) in toluene (20 mL) was added Ph_3P (0.684 g, 2.61 mmol) and imidazole (0.325 g, 4.18 mmol) followed by iodine (0.717 g, 2.83 mmol). The mixture was heated at reflux (120 °C) for 1 h. The reaction was cooled and filtered through Celite. The filtrate was concentrated and the residue was purified by chromatography on silica gel (eluting with 5% EtOAc/PE) to afford 0.73 g (75%) of product **3.39**. mp 27-28 °C; $[\alpha]^{23}$ -16.67° (*c* 0.6, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 3.44-3.38 (m, 8H), 3.28 (m, 2H), 2.00 (q, 2H), 1.59 (m, 2H), 1.25 (s, 28H), 0.88 (t, *J* = 6.6 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 79.92, 72.08, 72.03, 58.27, 36.37, 32.21, 29.99, 29.77, 29.65, 26.43, 22.99, 14.41.

1-*S*-acetyl-2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranose 3.41[66]

After a mixture of compound **3.40** (2.0 g, 9.04 mmol) and acetyl chloride (3 mL) was stirred overnight, chloroform (30 mL) was added and the solution was poured into ice water (20 mL). The mixture was rapidly shaken, the organic layer was run into saturated sodium bicarbonate solution containing cracked ice, and the mixture was stirred at first, shaken until the acid was neutralized. The chloroform layer was separated and dried over anhydrous Na_2SO_4. The solution was concentrated *in vacuo* to afford a 2.88 g of **3.35** as a yellow solid, which was used in the next step without purification.

A mixture of the above crude product (2.0 g, 5.46 mmol), potassium thioacetate (0.624 g, 5.5 mmol), and dry acetone (20 mL) was shaken for 6 h. The solution was filtered to remove inorganic material, and the combined filtrate and chloroform washings were concentrated. The residue was purified by chromatography on silica gel (eluting with 5% EtOH/$CHCl_3$) to afford 2.04 g (92%) of product **3.41**. ^1H NMR (300 MHz, $CDCl_3$): δ 6.01 (d, *J* = 9.9 Hz, 1H, NH), 5.18-5.06 (m, 3H), 5.35 (q, 1H), 4.23 (dd, *J* = 4.4, 12.5 Hz, 1H), 4.05 (dd, *J* = 2.2, 12.4 Hz, 1H), 3.77 (m, 1H), 2.35 (s, 3H, SAc), 2.05 (s, 3H, OAc), 2.02 (s, 6H, OAc), 1.90 (s, 3H, NAc).

3(S)-(3-*O*-methyl-4-*O*-hexadecyl-1-butylthio) 2- acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranoside 3.42 To a degassed solution of thioacetate **3.41** (0.60 g, 1.476 mmol) in DMF (3 mL) was added $NH_2NH_2.HOAc$ (0.14 g, 1.48 mmol).[67] The solution was degassed at rt for 1 h. Iodide **3.39** (0.67 g, 1.47 mmol) was added, followed by triethylamine (0.24 mL, 1.47 mmol). After 5 h, ethyl acetate (40 mL) and water (20 mL) were added. The organic layer was washed with water and brine, and dried over anhydrous sodium sulfate. After evaporation of the organic solvent, the residue was purified by chromatography on silica gel (eluting with 50% EtOAc/hexane) to afford 0.874 g (87%) of β-thioglycoside **3.42** as a white solid. mp 129-131 °C; $[\alpha]^{23}$ -36.92° (*c* 0.65, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 5.77 (d, *J* = 9.5 Hz, 1H, NH), 5.12 (m, 2H), 4.58 (d, *J* = 10.6 Hz, 1H, H-1), 4.20 (dd, 1H), 4.11 (m, 2H), 3.69 (m, 1H), 3.45-3.37 (m, 8H), 2.79 (m, 2H), 2.05 (s, 3H, OAc), 2.00 (s, 3H, OAc), 1.99 (s, 3H, OAc), 1.92 (s, 3H, NAc), 1.76 (m, 2H), 1.53 (m, 2H), 1.22 (s, 26H), 0.85 (t, *J* = 6.2Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.99, 170.61, 169.99, 169.26, 84.59, 78.78, 76.09, 74.11, 72.53, 71.92, 68.73, 62.55, 57.91, 53.51, 32.12, 32.07, 29.90, 29.70, 29.56, 26.51, 26.36, 23.45, 22.90, 20.92, 20.82, 14.33; MS: *m/z* 712 (M^++Na^+), (calcd. $C_{35}H_{63}O_{10}NS$, 689).

3S-(3-*O*-methyl-4-*O*-hexadecyl-1-butylthio) 2- acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside 3.43 To a solution of acetate **3.42** (0.205 g, 0.297 mmol) in EtOH/CH_2Cl_2 (9:1, 2 mL) was added guanidine (36 mg, 0.3 mmol) as guanidine hydrochloride,[68] which was prewashed with basic ionic exchange resin. The mixture was stirred at rt for 20 min, then filtered and washed with EtOH to afford 0.13 g of a white solid.

To a solution of the above solid (0.121 g, 0.214 mmol) in 1 mL of DMF was added PhCH $(OMe)_2$ (98 μl, 0.63 mmol), followed by *p*-TsOH (4 mg). After the mixture was stirred at rt overnight, the reaction was quenched with saturated aqueous $NaHCO_3$

solution, and extracted with CH_2Cl_2. The organic layer was washed with water and brine, and dried over anhydrous sodium sulfate. After evaporation of the organic solvents, the residue was purified by chromatography on silica gel (eluting with 50% EtOAc/hexane) to afford 0.123 g (90%) of β-thioglycoside **3.43** as a white solid. $[\alpha]^{23}$ -63.68° (*c* 0.95, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.50-7.47 (m, 2H), 7.37-7.34 (m, 3H), 5.88 (d, *J* = 7.0 Hz, 1H, NH), 5.54 (s, 1H), 4.70 (d, *J* =10.2 Hz, 1H, H-1), 4.32 (dd, *J* = 5.8, 10.2 Hz, 1H, H-2), 3.97 (m, 2H), 3.75 (m, 2H), 3.61-3.35 (m, 10H), 2.82 (m, 2H), 2.04 (s, 3H, NAc), 1.82 (m, 2H), 1.57 (m, 2H), 1.25 (s, 26H), 0.88 (t, *J* = 6.6 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 171.74, 137.31, 129.26, 128.35, 126.50, 101.86, 84.61, 81.60, 78.83, 77.44, 77.41, 76.94, 73.07, 72.49, 71.96, 70.68, 68.67, 57.92, 56.46, 32.15, 30.36, 30.22, 29.92, 29.74, 29.59, 26.64, 26.38, 23.65, 22.92, 14.37.

3(S)-(3-*O*-methyl-4-*O*-hexadecyl-1-butylsulfonyl)2-acetamido-4,6-*O*-benzylidene-3-*O*-(tert-butyldimethylsilyl)-2-deoxy-β-D-glucopyranoside 3.44

To a solution of thioglycoside **3.43** (0.12 g, 0.185 mmol) in DMF (2 mL) was added TBDMSCl (0.096 g, 0.55 mmol), followed by imidazole (0.056 g, 0.83 mmol). The mixture was stirred at rt for 5 h, then filtered and rinsed with CH_2Cl_2. The solution was concentrated and purified by column chromatography on silica gel (eluting with EtOAc-PE 20%) to afford 0.65 g (93%) of thioglycoside as a colorless oil; $[\alpha]^{23}$ -42.60° (*c* 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.45-7.43 (m, 2H), 7.34-7.32 (m, 3H), 5.77 (d, *J* =8.8 Hz, 1H, NH), 5.47 (s, 1H), 4.88 (m, 1H), 4.31 (m, 1H), 4.10 (m, 1H), 3.75-3.32 (m, 12H), 2.80 (m, 2H), 1.98 (s, 3H, NAc), 1.78 (m, 2H), 1.54 (m, 2H), 1.24 (s, 26H), 1.02-0.84 (m, 12H), 0.01 (s, 3H, CH_3), -0.05 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz):

δ 169.98, 137.30, 129.09, 128.19, 126.41, 102.00, 84.44, 82.54, 78.72, 73.13, 72.60, 71.91, 70.63, 68.87, 57.92, 57.85, 32.15, 29.94, 29.74, 29.59, 26.65, 26.39, 26.13, 25.98, 23.98, 22.93, 18.37, -3.77, -4.59.

A solution of MMPA (0.166 g, 0.336 mmol) in H_2O (1 mL) was added to a solution of the above sulfide (0.128 g, 0.168 mmol) in EtOH (1 mL) and THF (1 mL). The mixture was kept at 55 °C for 1 h, then concentrated *in vacuo* to dryness. The residue was treated with 20 mL of saturated aqueous $NaHCO_3$ solution, and extracted with EtOAc (20 mL × 3), dried over Na_2SO_4, and evaporated to dryness. The residue was purified by chromatography on silica gel (eluting with 50% EtOAc/PE) to afford 1.11 g (95%) of pure sulfone **3.44** as a white solid. mp 50-53 °C; $[\alpha]^{23}$ -13.00° (*c* 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz): δ 7.46-7.43 (m, 2H), 7.34-7.33 (m, 3H), 6.33 (d, J = 7.3 Hz, 1H, NH), 5.48 (s, 1H), 5.28 (m, 1H), 4.57 (t, 1H), 4.32 (m, 1H), 3.77-3.66 (m, 2H), 3.52-3.41 (m, 8H), 3.35-3.19 (m, 2H), 1.97 (m+s, 5H), 1.55 (m, 2H), 1.25 (s, 26H), 0.89-0.82 (m, 12H), 0.01 (s, 3H), -0.05 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 171.50, 137.00, 129.22, 128.24, 126.41, 102.13, 86.43, 82.02, 78.07, 78.03, 77.37, 72.04, 70.99, 70.71, 68.43, 57.79, 53.92, 46.66, 32.18, 30.32, 30.27, 30.25, 29.94, 29.76, 29.60, 26.38, 25.99, 23.96, 23.59, 22.95, 18.42, 14.38, -3.95, -4.63.

(3S)-3-*O*-methyl-4-*O*-hexadecyl 2′-acetamido-4′,6′-*O*-benzylidene-3′-*O*-(tert-butyldimethylsilyl)-2′-deoxy-D-glucopyranosylidene butane (3.45) To a solution of sulfone **3.44** (0.12 g, 0.15 mmol) in *t*-BuOH (1.5 mL) and CF_2BrCF_2Br (2 mL) was added 0.3 g (25% by weight) of KOH/Al_2O_3 (prepared one day earlier). The mixture was heated at 47 °C overnight. The solution was filtered through a pad of Celite which was washed with CH_2Cl_2. The residue was purified by column chromatography on silica gel (eluting with 40% EtOAc-PE) to afford 0.056 g (70%, Z isomer only) of **3.45** as a colorless oil. ^{1}H NMR (500 MHz, CDCl3): δ 7.48-7.45 (m, 2H), 7.37-7.34 (m, 3H), 5.54 (s, 1H), 5.38 (d, *J* =9.3 Hz, 1H, NH), 4.88 (t, *J* = 6.8 Hz, 1H, vinyl H), 4.62 (t, *J* =8.8 Hz, 1H, H-2), 4.38 (dd, *J* =5.1, 10.5 Hz, 1H, H-6), 3.80 (t, *J* = 10.3 Hz, 1H, H-6), 3.63 (m, 2H), 3.43-3.34 (m, 9H), 2.45 (m, 1H), 2.24 (m, 1H), 2.05 (s, 3H, NAc), 1.57 (m, 2H), 1.25 (s, 26H), 0.87 (t, *J* =6.6 Hz, 3H, CH_3), 0.82 (s, 9H), 0.03 (s, 3H, CH_3), -0.04 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 169.46, 150.38, 137.15, 129.19, 128.25, 126.41, 105.65, 102.09, 82.26, 79.83, 74.59, 72.63, 71.96, 70.64, 68.95, 57.48, 54.59, 32.19,29.96, 29.79, 29.63, 26.43, 26.33, 25.91, 23.84, 22.96, 18.37, 14.39, -3.66, -4.54; MS: *m/z* 754 (M^++Na^+), (calcd. $C_{42}H_{73}O_7NSi$, 731).

(3S)-3-*O*-methyl-4-*O*-hexadecyl 2′-acetamido-4′,6′-*O*-hydroxyl-3′-*O*-(tert-butyldimethylsilyl) -2′-deoxy-β-D-glucopyranosyl butane (3.46) To a solution of compound **3.35** (30 mg, 0.041mmol) in EtOAc (5 mL) was added 10% Pd/C (20 mg). After the flask was degassed under H_2 three times, the mixture was stirred overnight under H_2 at rt. After filtration of the catalyst, washing with EtOAc, and evaporation of the solvent *in vacuo*, 23 mg (85%) of **3.46** was obtained. ^{1}H NMR (400 MHz, CDCl3): δ 5.23 (d, *J* = 8.3 Hz, 1H, NH), 3.85 (m, 1H, H-6), 3.71 (m, 1H, H-6), 3.59 (m, 2H), 3.49-3.28 (m, 11H), 2.20 (t, 1H, OH), 2.10 (d, 1H, OH), 1.97 (s, 3H, NAc), 1.68 (m, 2H), 1.55 (m, 2H), 1.24 (s, 26H), 0.88 (s, 12H), 0.11 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (CDCl3, 75 MHz): δ 169.82, 79.82, 79.00, 78.50, 77.57, 72.85, 71.95, 63.20, 57.56, 56.77, 32.19, 29.96, 29.91, 29.77, 27.79, 27.72, 26.39, 26.05, 24.06, 22.96, 18.42, 14.39, -3.55, -4.09; MS: *m/z* 668 (M^++Na^+), (calcd. $C_{35}H_{71}O_7NSi$, 645).

(3S)-3-*O*-methyl-4-*O*-hexadecyl 2′-acetamido-2′-deoxy-β-D-glucopyranosyl butane 3.47 To a solution of **3.46** (30 mg, 0.046 mmol) in 1 mL of CH_3CN was added $BF_3.Et_2O$ (20 mL) at 0 °C.[69] After 1 h, saturated aqueous $NaHCO_3$ solution was added, followed by extraction with EtOAc. The organic layer was dried over Na_2SO_4 and evaporated to dryness. The residue was purified by chromatography on silica gel (eluting with 5:1 $CHCl_3$/MeOH) to afford 23 mg (94%) of **3.47** as a white solid; mp 146-149 °C; $[\alpha]^{23}$ 11.18° (*c* 1.1, $CHCl_3$:MeOH 1:1); ^1H NMR ($CDCl_3$ and a drop of MeOH-d_4, 300 MHz): δ 7.99 (d, *J* = 8.4 Hz, 1H, NH), 3.80 (dd, *J* = 2.8, 12.1 Hz, 1H, H-6), 3.67 (dd, *J* = 4.7, 12.1 Hz, 1H, H-6), 3.55 (t, *J* = 7.7 Hz, 1H), 3.41-3.30 (m, 10H), 3.19 (m, 2H), 2.65 (broad peak, 3H), 1.97 (s, 3H, NAc), 1.63-1.49 (m, 6H), 1.21(s, 24H), 0.84(t, *J* = 6.6 Hz, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.27, 79.88, 79.31, 78.26, 77.09, 72.79, 71.97, 71.79, 62.59, 57.50, 55.98, 32.12, 30.01, 29.90, 29.69, 29.55, 27.84, 27.67, 26.29, 23.15, 22.88, 14.29; MS: *m/z* 554 (M^++Na^+), (calcd. $C_{29}H_{57}O_7N$, 531).

(3S)-3-*O*-methyl-4-*O*-hexadecyl 2′-amino-2′-deoxy-β-D-glucopyranosyl butane (3.5) *N*-Acetyl-β-*C*-glycoside **3.47** (20 mg, 0.0377 mmol) was dissolved in 2 N KOH/EtOH (2 mL). After the mixture was degassed and refluxed under N_2 at 120 °C for 6 h, the reaction was quenched with saturated NH_4Cl solution (5 mL), then extracted with $CHCl_3$ (3 x 20 mL). The organic layer was dried over Na_2SO_4 and evaporated to dryness. The residue was purified by chromatography on silica gel (eluting with 5:1

$CHCl_3$/MeOH) to afford 13 mg (74%) of **3.5** as a white solid; $[\alpha]^{23}$ -4.67° (*c* 0.6, $CHCl_3$:MeOH=2:1); ^1H NMR ($CDCl_3$ and a few drops of MeOH-d_4, 300 MHz): δ 3.73 (m, 1H), 3.66-3.17 (m, 14H), 2.52 (broad peak), 1.72-1.45 (m, 6H), 1.20 (s, 24H), 0.81 (t, *J* = 6.5 Hz, 3H); ^{13}C NMR ($CDCl_3$ and a few drops of MeOH-d_4, 75 MHz): δ 79.91, 79.66, 77.50, 77.42, 76.44, 72.75, 71.90, 71.10, 62.24, 57.69, 32.03, 29.81, 29.69, 29.47, 27.40, 26.91, 26.18, 22.81, 14.17.

β-2,3,4,6-tetra-*O*-acetyl-galactosyl thioacetate 4.4 β-D-galactose-pentaacetate **4.2** (7.807 g, 0.02 mol) in 1,2-dichloroethane (16 mL) was shaken gently with chilled 30% (w/w) HBr/HOAc (14 mL) until solution is complete. After 2 h at room temperature, methylene chloride was added, and the organic layer was washed successively with ice water and cold saturated sodium bicarbonate solution. The solution of 2,3,4,6-tetra-*O*-acetyl-α-D-galactosyl bromide **4.3** was dried with anhydrous sodium sulfate and dried *in vacuo*. A white solid (9.3 g) was obtained. ^1H NMR (300 MHz, $CDCl_3$): δ 6.69 (d, J=3.67 Hz, 1H, H-1), 5.51 (dd, J=1.1, 3.3 Hz, 1H, H-4), 5.40 (dd, J=3.3, 11.6 Hz, 1H, H-3), 5.04 (dd, J=3.66, 11.6 Hz, 1H, H-2), 4.47(t, J=6.59 Hz, 1H, H-5), 4.14(m, 2H, H-6), 2.14(s, 3H, H-OAc), 2.05(s, 3H, H-OAc), 2.00(s, 3H, H-OAc).

A mixture of 2,3,4,6-tetra-O-acetyl-α-D-galactosyl bromide **4.3** (7.0 g), potassium thioacetate (4.0 g) and dry acetone (20 mL) was shaken for 2 h, the solution was filtered and acetone washings were evaporated to a yellow solid, which was treated with choroform 100 mL. The residue was purified by chromatography on silica gel eluting with 50% EtOAc/PE to afford 5.571 g (88% overall yield from **4.2**) of **4.4** as yellow crystals. mp 113-114 °C; ^1H NMR (300 MHz, $CDCl_3$ and two drops of d_6-benzene): δ

5.38 (s, 1H, H-4), 5.33 (dd, J=4.4, 9.9 Hz, 1H, H-2), 5.23 (dd, J=4.7, 10.6 Hz, 1H, H-1), 5.06 (dd, J=3.6, 9.5 Hz, 1H, H-3), 4.02 (m, 2H, H-6), 3.83 (m, 1H, H-5), 2.13 (s, 3H, H-SAc), 1.95 (s, 3H, H-OAc), 1.89 (s, 3H, H-OAc), 1.87 (s, 6H, H-OAc); ^{13}C NMR (75 MHz, $CDCl_3$): δ 192.02 (C-SAc), 170.13, 169.86, 169.50 (C-OAc), 80.78 (C-1), 75.12, 67.43, 66.62, 61.43, 31.06 (C-SAc), 20.40, 20.79 (C-OAc).

β-2,3,4,6-tetra-O-acetyl-S-hexyl-thiogalactoside 4.5 To a degassed solution of **4.4** (1.879 g, 4.628 mmol) in DMF (5 mL), 1 M NH_2NH_2.HOAc in DMF (4.7 mL) was added. This solution was further degassed at room temperature for 1 h.[67] Hexyl bromide (0.97 mL, 6.91 mmol) was added, followed by triethyl amine (0.65 mL, 4.63 mmol). After 2 h, ethyl acetate (50 mL) and water (40 mL) were added. The organic layer was washed with water and brine, and dried over anhydrous sodium sulfate. After evaporation of the organic solvent, the residue was purified by chromatography on silica gel eluting with 50% EtOAc/Hexane to afford 1.842 g (89%) of β-thiogalactoside **4.5** as a colorless oil. ^{1}H NMR (300 M Hz, $CDCl_3$): δ 5.35 (d, J=3.3 Hz, 1H, H-4), 5.15 (t, J=10.25 Hz, 1H, H-2), 4.96 (dd, J=3.3, 9.9 Hz, 1H, H-3), 4.43 (d, J=9.9 Hz, 1H, H-1), 4.05 (m, 2H, H-6), 3.87 (t, J=6.59 Hz, 1H, H-5), 2.60 (m, 2H, H-SCH_2), 2.07 (s, 3H, H-OAc), 1.99 (s, 3H, H-OAc), 1.96 (s, 3H, H-OAc), 1.90 (s, 3H, H-OAc); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.76, 170.64,170.45, 169.97, 84.78, 75.05, 72.59, 68.01, 62.17, 32.03, 30.86, 30.38, 29.14, 23.23, 21.35, 21.27, 14.72.

2,3,4,6-tetra-*O*-benzyl-β-thiogalactoside 4.7 Into a solution of **4.5** (1.018 g, 2.27 mmol) and methanol (15 mL) was added Dowex I 0131 SBR OH^- (1.14 g). The mixture was stirred at rt. overnight. The resin was filtered off and rinsed with MeOH. The solution was concentrated until completely dry to afford 0.578 g of **4.6** as a white solid.

NaH (60% in mineral oil, 0.489 g) was added into a solution of the above product (0.568 g, 2.029 mmol) in DMF (6 mL) and THF (5 mL). The mixture was stirred at rt. for 1 h, then tetra-butylammonium iodide (0.075 g, 0.2 mmol) was added followed by benzyl bromide (1.453 mL, 12.13 mmol). After the mixture was stirred at 5 °C for 2 h, it was kept at rt. overnight. The reaction was quenched with H_2O (10 mL). The resulting solution was added to H_2O (40 mL) and extracted by CH_2Cl_2 (30 mL × 3).The organic phase was washed by H_2O several times to remove DMF, and dried over Na_2SO_4 and concentrated. The residue was chromatographed on a column of silica gel (eluted with 10% EtOAc-petroleum ether) to afford 1.183 g (90%) of **4.7** as a colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.40-7.24 (m, 20H), 4.97-4.38 (m, 9H, including H-1 at 4.38ppm), 3.95 (d, 1H, J=2.56 Hz, H-4), 3.81 (t, 1H, J=9.53, H-2), 3.61-3.54 (m, 4H), 2.71 (m, 2H, CH_2SO_2), 1.60 (m, 2H), 1.37-1.25 (m, 6H), 0.87 (t, J=6.96 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 138.94, 138.54, 138.50, 138.06, 128.53, 128.41, 128.28, 128.08, 128.00, 127.81, 127.73, 127.65, 127.56, 85.75 (C-1), 84.36, 78.73, 77.44, 75.96, 74.64, 73.94, 72.97, 69.08, 31.68, 30.95, 30.17, 28.91, 22.84, 14.33.

Sulfonyl galactoside 4.8 A solution of MMPA (2.55 g, 5.145 mmol) in H_2O (12 mL) was added to a solution of **4.7** (1.1 g, 1.719 mmol) in EtOH (12 mL) and THF (12 mL), the mixture was kept at 55 °C for 2 h. The mixture was concentrated in vacuo to dryness. The residue was treated with saturated $NaHCO_3$ solution (40 mL), and extracted with EtOAc (30 mL × 3), dried over Na_2SO_4 and evaporated to dryness. The residue was purified by chromatography on silica gel eluting with 20% EtOAc/PE to afford 1.11g (95%) of pure sulfone **4.8** as a white solid. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.32-7.12 (m, 20H), 4.88-4.23 (m, 10H, including H-1 and H-2), 3.81 (d, 1H, J=2.56

Hz, H-4), 3.59-3.42 (m, 4H), 2.95 (m, 2H, CH_2SO_2), 1.74 (m, 2H), 1.26-1.12 (m, 6H), 0.77 (t, J=6.59 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 138.40, 137.98, 137.91, 137.70, 128.79, 128.56, 128.51, 128.34, 128.03, 127.95, 127.87, 127.69, 127.60, 90.62, 83.80, 78.42, 75.69, 74.62, 74.20, 73.71, 73.14, 72.99, 68.80, 51.03, 31.37, 28.44, 22.52, 21.42, 14.16; MS: *m/z* 695 (M^++Na^+), 690 (M^++NH_4^+), (calcd. $C_{40}H_{48}O_7S$, 672).

Vinyl bromide 4.10 Dibromodifluoromethane (0.5 mL) was added to a mixture of sulfone **4.8** (0.27 g, 0.402 mmol) and 50% KOH/Al_2O_3(0.76 g) in *t*-BuOH (5 mL) and THF (10 mL) kept at 5 °C under N_2. The mixture was stirred at rt for 7 h., after which it was diluted with CH_2Cl_2 and filtered through a pad of celite. After the combined organic filtrate was concentrated, the residue was purified by silica gel chromatography (EtOAc/PE, 10%) to afford vinyl bromide **4.10** (0.14 g, E, 65%, 0.35g, Z, 15%, a trace of alkene). ^{1}H NMR (300 MHz, $CDCl_3$): E isomer: δ 7.36-7.20 (m, 20H), 4.90 (d, J=2.66 Hz, 1H), 4.66-4.41 (m, 13H), 4.24 (dd, J=2.93, 2.93 Hz, 1H), 3.96-3.88 (m, 2H), 3.77 (d, J=11.35 Hz, 1H), 2.94 (m, 1H), 2.34 (m, 1H), 1.52 (m, 2H), 1.28-1.22 (m, 4H), 0.87 (t, J=6.59 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 142.29, 138.56, 138.46, 138.41, 138.27, 134.93, 128.47, 128.38, 128.13, 128.07, 128.00, 127.98, 127.82, 127.77, 127.72, 127.63, 127.54, 121.57, 78.42, 75.96, 73.86, 73.22, 72.77, 72.66, 71.75, 70.36, 68.14, 34.12, 31.31, 28.07, 22.78, 14.33; MS: M^++Na^+, 707/709 (calcd. $C_{40}H_{45}O_5Br$, 684/686).

Alkene 4.11 To a solution of vinyl bromide **4.10** (98 mg, 0.143 mmol) in THF (2 mL), *n*-BuLi (1.6 M in hexane, 0.48 mL) was added at -78 °C. After 2 h, the reaction was quenched by adding MeOH (1 mL) and warmed up to rt, then washed with ether. The organic layer was dried over Na_2SO_4 and concentrated. The residue was chromatographed on a column of silica gel (eluted with 10% EtOAc-petroleum ether) to afford 32 mg (30%) of **4.11** as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): Z isomer: δ 7.32-7.26 (m, 20H), 5.08 (t, J=7.32 Hz, 1H, vinyl H), 4.90 (d, J=11.72 Hz, 1H), 4.79-4.44 (m, 11H), 4.27 (d, J=8.06 Hz, 1H), 4.08 (m, 1H), 3.86 (m, 1H), 3.77 (dd, J=6.59, 6.79 Hz, 1H), 3.65 (m, 2H), 2.14 (m, 2H), 1.27 (m, 6H), 0.88 (t, J=5.86 Hz, 3H).

4-Methoxybenzaldehyde dimethyl acetal[80] A solution of 4-methoxybenzaldehyde (53 mL, 0.435 mol), trimethyl orthoformate (52 mL, 0.475 mol) and *p*-toluene-sulfonic acid monohydrate (0.414 g, 2.17 mmol) was stirred at room temperature for overnight. Sodium carbonate (0.46 g) was added and the mixture was stirred for an additional 1 h. The residue was filtered and the methyl formate was distilled off at aspirator pressure without external heating. Distillation the residue gave the title compound (60 mL, 80%). (Bp 100 °C at 7 mmHg. d 1.06 g/ mL).[80] ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.37 (d, 2H), 6.9 (d, 2H), 5.3 (s, 1H), 3,82 (s, 3H), 3.33 (s, 6H).

To a mixture of hexyl-β-thiogalactoside **4.6** (0.28 g, 1 mmol), *p*-methoxybenzaldehyde dimethyl acetal (0.35 mL, 2 mmol), and dry acetonitrile (10 mL) was added *p*-toluene sulfonic acid monohydrate (12 mg) at room temperature. After 1h, the mixture was neutralized with triethyl amine (0.1 mL) and concentrated. The residue was chromatographed (SiO_2, EtOAc/PE 3:1 to 4:1) to give 0.322g (80%) of **4.13** as a white solid. mp 113-114 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.42-7.39 (d, 2H), 6.89-6.86 (d, 2H), 5.47 (s, 1H), 4.32-4.29 (d, 1H, H1, J=9.52 Hz), 4.31-4.26 (dd, 1H, H6, J=11.4, 1.46 Hz), 4.20 (d, 1H, H4, J=2.9 Hz), 3.99-3.94 (dd, 1H, H6, J=12.45, 1.83 Hz), 3.78 (s, 3H), 3.77 (t, 1H, H2, J=9.52 Hz), 3.64-3.60 (dd, 1H, H3, J=9.16, 3.66 Hz), 3.43 (d, 1H, H5, J=1.1 Hz), 2.79-2.69 (m, 3H, including OH), 1.70-1.63 (m, 3H, including

OH), 1.42-1.26 (m, 6H), 0.88 (t, 3H, J=6.6 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.39, 130.36, 127.86, 113.78, 101.51, 85.66, 75.81, 74.10, 70.33, 69.97, 69.49, 55.52, 31.62, 30.47, 29.47, 28.95, 22.82, 14.28.

Hexyl 2,3-di-*O*-benzyl-4,6-*O*-*p*-methoxybenzylidene-β-thiogalactoside β-S-galactoside **4.13** (0.3g, 0.754mmol) was dissolved in DMF (5 mL), NaH (60% in mineral oil, 0.148 g) was added, the mixture was stirred at rt. for 1/2 h, then tetra-butylammonium iodide (0.028 g) was added followed by benzyl bromide (0.36 mL, 3.02 mmol). After the mixture was stirred at room temperature for 3 h, the reaction was quenched with H_2O (10 mL). The resulting solution was added to H_2O (20 mL) and extracted by CH_2Cl_2 (30 mL × 3).The organic phase was washed with H_2O several times to remove DMF, and dried over Na_2SO_4 and concentrated. The residue was chromatographed on a column of silica gel (eluted with 30% EtOAc-petroleum ether) to afford 0.405 g product (93%) as a white solid. mp 113-115 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.48-7.26 (m, 12H), 6.92-6.88 (dd, 2H), 5.43 (s, 1H), 4.92-4.76 (m, 4H), 4.43 (d, 1H, J=9.53 Hz, H1), 4.31 (dd, 1H, J=12.45, 1.46 Hz, H6), 4.14 (d, 1H, J=3.29 Hz, H4), 3.96-3.82 (m+s, 5H, H2,H6 and OCH_3), 3.59 (dd, 1H, J=9.15, 3.29 Hz, H3), 3.34 (s, 1H, H5), 22.85-2.74 (m, 2H), 1.67 (m, 2H), 1.43-1.26 (m, 6H), 0.89 (t, 3H, J=7.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.76, 139.10, 138.97, 131.29, 128.99, 128.92, 128.49,128.40, 128.35, 114.23, 102.01, 85.23, 81.89, 77.64, 76.41, 74.66, 72.49, 70.48, 70.10, 56.06, 32.19, 30.72, 30.43, 29.55, 23.39, 14.84.

Sulfonyl galactoside 4.14 A solution of MMPA (0.636 g, 1.287 mmol) in H_2O (5 mL) was added to a solution of thiogalactoside (0.372 g, 0.644 mmol) in EtOH (5 mL) and THF (5 mL), the mixture was kept at 55 °C for 2 h. The mixture was concentrated in vacuo to dryness. The residue was treated with saturated $NaHCO_3$ solution (20 mL), and extracted with EtOAc (30 mL × 3), dried over Na_2SO_4 and evaporated to dryness. The residue was purified by chromatography on silica gel eluting with 40% EtOAc/PE to afford 0.374 g (95%) of pure sulfone **4.15** as white crystals. mp. 40-43°C; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.47-7.28 (m, 12H), 6.93-6.90 (d, 2H), 5.41 (s, 1H), 4.96-4.87 (m, 2H), 4.73 (s, 1H), 4.47-4.38 (m, 2H, H1, H2), 4.23 (dd, 1H H6, J=12.82, 1.27 Hz), 4.06 (d, 1H, H4, J=2.93 Hz), 3.90 (dd, 1H, J=12.45, 1.1 Hz, H6), 3.81 (s, 3H), 3.72 (dd, 1H, J=8.42, 3.29 Hz, H3), 3.33 (s, 1H, H5), 3.20-3.11 (m, 2H), 1.89 (m, 2H), 1.40-1.27 (m, 6H), 0.88 (t, 3H, J=6.6 Hz); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 160.36, 138.06, 130.33, 128.92, 128.57, 128.41, 128.00, 127.89, 127.80, 113.82, 101.42, 90.81, 80.99, 75.81, 73.42, 73.07, 71.94, 70.45, 69.02, 55.55, 50.72, 31.46, 28.56, 22.62, 21.38, 14.21; MS: *m/z* 633 (M^++Na^+), (calcd. $C_{34}H_{42}O_8S$, 610).

Vinyl bromide 4.15 Dibromodifluoromethane (0.5 mL) was added to a mixture of sulfone **4.14** (0.305 g, 0.5 mmol) and 25% KOH/Al_2O_3 (3 g) in *t*-BuOH (5 mL) and CH_2Cl_2(10 mL) kept at 5 °C under N_2. The mixture was stirred at rt overnight. , after which it was diluted with CH_2Cl_2 and filtered through a pad of celite. After the combined organic filtrate was concentrated, the residue was purified by silica gel chromatography (EtOAc/PE, 30%) to afford vinyl bromide **4.15** (0.268 g, 88% in conversion yield). ^1H NMR (300 MHz, $CDCl_3$): δ 7.41-7.30 (m, 12H), 6.92 (d, 2H), 5.42 (s, 1H), 5.00 (d, 1H), 4.79-4.60 (m, 4H), 4.32 (m, 2H), 4.01-3.91 (m, 3H), 3.81 (s, 3H), 3.01 (m, 1H), 2.47 (m, 1H), 1.60 (t, 2H), 1.29 (m, 6H), 0.89 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 160.85, 147.54, 139.28, 138.52, 131.09, 129.05, 128.92, 128.63, 128.55, 128.44, 128.35, 128.19, 116.32, 114.30, 114,19, 101.63, 80.59, 78.82, 72.85, 72.01, 71.72, 70.39, 56.06, 34.89, 31.89, 28.40, 23.28, 14.86; MS: M^++Na^+, 645/647 (calcd. $C_{34}H_{39}O_6Br$, 622/624).

Alkene 4.16 To a solution of **4.14** (1.09 g, 1.78 mmol) in *t*-BuOH (15 mL) and CF_4Br_2 (10 mL), 3.5 g 50% (by weight) KOH/Al_2O_3 was added. This mixture was refluxed at 47 °C overnight. The solution was filtered through a pad of celite which was washed with CH_2Cl_2. The residue was purified by chromatography on silica gel eluting with 25% EtOAc-PE to afford 0.602 g (83%, *Z*:*E*=40:60) of **4.16** as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$), **4.16*Z***: δ 7.50-7.25 (m, 12H), 6.90 (d, 2H), 5.48 (s, 1H), 5.18 (dd, 1H, J=1.8, 7.6 Hz), 4.85-4.73 (m, 4H), 4.44-4.35 (m, 2H, H2+H6), 4.21 (d, 1H, J=2.93 Hz, H4), 3.97 (dd, 1H, J=1.46, 12.45 Hz), 3.81 (s, 3H), 3.57 (dd, 1H, J=3.66, 9.89 Hz, 3H), 3.38 (s, 1H, H5), 2.11 (m, 2H), 2.11 (m, 6H), 0.88 (t, 3H, J=6.59 Hz); **4.16*E***: δ 7.43-7.26 (m, 12H), 6.88 (d, 2H), 5.44 (S, 1H), 5.38 (t, 1H, J=8.05 Hz), 4.75 (s, 2H), 4.66 (S, 1H), 4.63 (d, 1H, J=6.6 Hz, H2), 4.37 (dd, 1H, J=1.47, 12.46 Hz, H6), 4.30 (m, 1H, H4), 3.98 (dd, 1H, J=1.83, 12.45 Hz, H6), 3.84 (dd, 1H, J=3.29, 6.22 Hz, H3), 3.80 (s, 3H), 3.64 (d, 1H, J=1.83 Hz, H5), 2.17 (q, 2H), 1.37-1.24 (m, 6H), 0.87 (t, 3H, t=6.06 Hz); MS: M^++Na^+, 667 (calcd. $C_{34}H_{40}O_6$, 544).

α-1-*O*-methyl-2,3-dibenzyl- β-D-1-hexyl-*C*-galactoside 4.17 To a solution of **4.16** (*Z*+*E*, 0.242 g, 0.44 mmol) in MeOH (5 mL), TMSCl (85 μL) was added. After the mixture was stirred at rt. for 20 min and concentrated, the residue was purified by column chromatography on silica gel eluting with 35% EtOAc-PE to afford 0.13 g (64%) of product **4.17** as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$), δ 7.36-7.20 (m, 10H), 4.96 (d, 1H), 4.70 (m, 3H), 4.08 (dd, 1H, J=1.93, 3.3 Hz, H4), 4.03 (dd, 1H, J=3.3, 9.52 Hz, H3), 3.93-3.78 (m, 3H), 3.64 (m, H5), 3.23 (s, 3H), 2.61 (s, 1H), 2.15

(dd, 1H, J=4.0, 8.4 Hz), 1.71 (m, 2H), 1.18 (m, 6H), 0.86 (t, 3H, J=6.59 Hz); ^{13}C NMR (75 MHz, $CDCl_3$), δ 138.47, 138.03, 128.70, 128.60, 128.42, 128.09, 128.00, 127.85, 102.16, 80.10, 76.32, 75.52, 72.43, 70.38, 68.65, 63.25, 47.99, 32.68, 32.01, 23.94, 22.95, 14.34.

α-1-*O*-methyl-2,3,6-tri-*O*-benzyl-β-D-1-hexyl-*C*-galactoside 4.18 NaH (60%, 18mg) was added to a solution of **4.17** (0.125g, 0.273mmol) in DMF (2 mL). The mixture was stirred at rt. for 20 min, then tetra-butylammonium iodide (10 mg) was added followed by benzyl bromide (36 μL, 0.28 mmol). After the mixture was stirred 2 h, it was kept at rt. overnight. Then H_2O (1 mL) was added to quench the reaction. The resulting solution was treated with H_2O (20 mL) and extracted by CH_2Cl_2 (20 mL × 3). The organic phase was washed by brine, and dried over Na_2SO_4, and then concentrated. The residue was purified on a column of silica gel (eluted with 20% EtOAc-petroleum ether) to afford 70 mg (66%) of **4.18**. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.39-7.26 (m, 15H), 4.96 (d, 1H), 4.71 (s, 2H), 4.70 (d, 1H), 4.60 (s, 2H), 4.12 (m, 1H, H4), 3.99 (dd, 1H, J=3.3, 9.52 Hz, H3), 3.85-3.67 (m, 4H), 3.23 (s, 3H), 2.54 (s, 1H), 1.70 (t, J=8.06 Hz, 2H), 1.18 (m, 6H), 0.86 (t, J=6.96 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 138.55, 138.32, 138.19, 127.95, 127.69, 102.09, 80.29, 76.32, 75.47, 73.76, 72.21, 69.84, 69.68, 67.81, 47.97, 32.62, 31.98, 29.98, 23.91, 22.90, 14.46.

Silyl ether 4.19 To a solution of alcohol **4.18** (34 mg, 0.062 mmol) in CH_2Cl_2 (1 mL), *i*-Pr_2SiHCl (33 μL, 0.186 mmol) and imidazole (19 mg) were added. After the mixture was stirred at rt for 30 min, the solution was concentrated and purified by column chromatography on silica gel eluting with 30% EtOAc-PE to afford 32 mg (83%) of **4.19** as a colorless oil. ^{1}H NMR (300 MHz, C_6D_6), δ 7.43-7.04 (m, 15H), 5.16

(d, 1H), 4.83 (d, 1H), 4.66 (s, 1H), 4.56-4.43 (m, 4H, including Si-H), 4.28 (d, 1H,J=1.83 Hz, H4), 4.25 (d, 1H, J=9.89, H2), 4.10 (dd, 1H, J=2.56, 9.89 Hz, H3), 3.91 (t, 1H, J=6.59 Hz, H5), 3.83-3.70 (m, 2H, H6), 3.18 (s, 3H), 1.88 (m, 2H), 1.40-1.07 (m, 6H), 0.87 (t, J=6.96 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$), δ 140.08, 139.39, 139.25, 129.35, 129.14, 128.93, 128.80, 128.49, 128.19, 127.94, 103.01, 81.47, 77.50, 75.73, 74.121, 73.29, 71.73, 70.35, 48.07, 33.27, 32.73, 30.68, 24.96, 23.51, 18.53, 18.48, 18.34, 14.83, 13,83, 13.74; MS: *m/z* 685 (M^++Na^+), (calcd. $C_{40}H_{58}O_6Si$, 662).

2,3,6-tri-*O*-benzyl-α-D-1-hexyl-*C*-galactoside 4.20 Syringe pump addition [81]of a solution (32 mg **4.19** in 3 mL CH_2Cl_2) to a solution of TFA and $BF_3.Et_2O$ (4:1, 15 μL and 6 μL) in CH_2Cl_2 (3.6 mL) was carried out over a 6 h reaction time. The mixture was then treated with sat. $NaHCO_3$ (10 mL), and extracted with CH_2Cl_2 (20 mL × 3). The organic solvent was concentrated and purified by column chromatography on silica gel eluting with 20% EtOAc-PE to afford 17 mg (70%) of **4.20** as a yellow oil ^{1}H NMR (500 MHz, C_6D_6), δ 7.40-7.04 (m, 15H), 4.57-4.38 (m, 6H), 4.21-4.17 (m, 1H, J_{12}=5.79 Hz, H1), 4.15-4.12 (dd, 1H, J=5.8, 9.15 Hz, H2), 4.04 (s, 1H, H4), 4.00-3.97 (dd, 1H, J=5.8, 9.8 Hz, H6), 3.92-3.89 (dd, 1H, J=6.1, 9.7 Hz, H6), 3.76 (t, 1H, J=5.8 Hz, H5), 3.58-3.56 (dd, 1H, J=3.36, 9.16 Hz, H3), 2.40 (br, 1H), 1.67 (m, 2H), 1.31 (m, 6H), 0.88 (t, 3H); ^{13}C NMR (75 MHz, C_6D_6), δ 139.63, 139.50, 139.26, some peaks overlapped by the solvent, 78.94, 77.18, 74.53, 74.01, 73.74, 72.50, 70.82, 70.53, 68.33, 32.73, 29.99, 26.58, 25.52, 23.75, 14.75; . MS: *m/z* 541 (M^++Na^+), (cacld. $C_{33}H_{42}O_5$, 518).

Acetate 4.25 To a solution of alcohol **4.18** (60 mg, 0.109 mmol) in CH_2Cl_2 (2 mL), pyridine (88 μL, 1.09 mmol), Ac_2O (30 μL, 0.27 mmol) and DMAP (8 mg, 0.06 mmol) were added. After the mixture was stirred at rt. for 4 h, H_2O (20 mL) was added and the solution was extracted with CH_2Cl_2 (20 mL × 3). The organic solvent was concentrated and purified by column chromatography on silica gel eluting with 30% EtOAc-PE to afford 59 mg (92%) of **4.25** as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$): δ 7.35-7.14 (m, 15H), 5.64 (dd, 1H, J=1.1, 3.3 Hz, H4), 4.94 (d, 1H), 4.80 (d, 1H), 4.64-4.45 (m, 4H), 4.07 (dd, 1H, J=3.3, 9.53 Hz, H3), 3.91 (t, 1H, J=6.96 Hz, H5), 3.75 (d, 1H, J=9.89 Hz, H2), 3.48 (m, 2H, H6), 3.23 (s, 3H), 2.08 (s, 3H), 1.71 (m, 2H), 1.22 (m, 6H), 0.86 (t, J=6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.37, 138.54, 138.23, 138.03, 128.60, 128.49, 128.42, 128.30, 127.91, 127.80, 127.69, 102.17, 78.55, 76.35, 75.35, 73.75, 72.10, 68.87, 68.78, 68.40, 48.11, 32.68, 32.01, 29.92, 23.79, 22.92, 21.19, 14.35.

4-*O*-acetyl-2,3,6-tri-*O*-benzyl-1-β-hexyl-*C*-galactoside 4.26 To a solution of acetate **4.25** (59 mg, 0.1 mmol) and Et_3SiH (85 μL, 0.5 mmol) in CH_2Cl_2 (2 mL), $BF_3.Et_2O$ (25 μL, 0.2 mmol) was added. After the mixture was stirred at rt. for 1 h, cold saturated $NaHCO_3$ (10 mL) was added, and the solution was extracted with CH_2Cl_2. The organic solvent was concentrated and purified by column chromatography on silica gel eluting with 20% EtOAc-PE to afford 55mg (95%) of **4.26** as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$): δ 7.32-7.17 (m, 15H), 5.57 (d, 1H, J=3.3 Hz, H4), 4.84 (d, 1H), 4.73 (d, 1H), 4.51-4.35 (m, 4H), 3.60 (t, 1H, J=5.86 Hz, H5), 3.53 (dd, 1H, J=3.3, 9.15 Hz, H3), 3.45 (dd, 1H, J=5.86, 9.52H, H6), 3.38 (dd, 1H, J=6.96, 9.15 Hz, H6), 3.33 (t, 1H, J=9.15 Hz, H2), 3.16 (ddd, 1H, J=2.56, 8.69, 9.52 Hz, H1), 2.01 (s, 3H), 1.79 (m, 2H), 1.49-1.16 (m, 6H), 0.87 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.42, 138.55, 138.05, 137.94, 128.73, 128.50, 128.44, 128.30, 128.082, 127.85, 127.77, 82.06, 79.82, 78.87, 75.91, 75.61, 73.81, 71.75, 68.70, 67.70, 32.19, 32.07, 29.50, 25.79, 22.87, 21.25, 14.38.

2,3,6-tri-*O*-benzyl-1-β-hexyl-*C*-galactoside 4.27 To a solution of acetate **4.26** (46 mg, 0.089 mmol) in MeOH (1 mL) and THF (1 mL), K_2CO_3 (30 mg) was added. After the mixture was stirred at rt. for 5 h, the solution was filtered and concentrated. The residue was purified by column chromatography on silica gel eluting with 20% EtOAc-PE to afford 25 mg (95%, in conversion yield) of **4.27** as a colorless oil. ^1H NMR (500 MHz, C_6D_6): δ 7.35-7.05 (m, 15H), 4.92 (d, 1H), 4.56 (d, 1H), 4.44-4.37 (m, 2H), 4.36 (d, 1H), 4.28 (d, 1H), 4.00 (s, 1H, H_4), 3.91 (dd, 1H, J=6.4, 9.5 Hz, H_6), 3.79 (dd, 1H, J=5.8, 9.5 Hz, H_6), 3.60 (t, 1H, J=9.0 Hz, H_2), 3.44 (t, 1H, J=6.1 Hz, H_5), 3.35 (dd, 1H, J=3.2, 9.1 Hz, H_3), 3.25 (dd, 1H, J= 9.1, 2.5 Hz, H_1), 2.28 (s, 1H, OH), 1.96 (m, 1H), 1.75 (m, 1H), 1.61 (m, 1H), 1.52 (m, 1H), 1.24 (s, 6H), 0.83 (t, 3H, CH_3); ^{13}C NMR (75 MHz, C_6D_6): δ 139.89, 139.46, 139.090, 129.02, 128.90, 128.28, 84.39, 80.08, 79.46, 77.65, 75.81, 74.13, 71.70, 70.56, 67.43, 32.76, 30.33, 26.46, 23.55, 14.85.

L-2-[(benzyloxycarbonyl)amino]-4-hydroxybutyric acid [87] To a solution of **4.28** (4.0 g, 33.6 mmol) in 1 N $NaHCO_3$ (160 mL) was added benzyl chloroformate (6.0 mL, 37 mmol). The reaction mixture was stirred at 23 °C for 24 h and then extracted with ether (2 × 200 mL). The aqueous phase was ice cooled, carefully acidified to pH 2-3 with 3N HCl, and extracted with ethyl acetate. The extract was dried over Na_2SO_4, filtered, and evaporated to afford 6.52 g (77%) product as a white solid. ^1H NMR (Me_2CO-d_6, 300 MHz) δ 7.39-7.31 (m, 1H, C_6H_5), 6.63 (d, J=7.7 Hz, 1H, NH), 5.08 (s, 2H, CH_2Ph), 4.42 (m, 1H, CH), 3.70 (m, 2H, CH_2O), 2.05 (m, 1H), 1.91 (m, 1H).

Methyl- L-2-[(benzyloxycarbonyl)amino]-4-hydroxybutyrate 4.29 To a solution of above compound (5.7 g, 22.5 mmol) in MeOH (50 mL) was added dropwise 2 M trimethylsilyldiazomethane in hexanes (22.5 mL, 25 mmol) at 0 °C.[88] The reaction mixture was stirred at rt overnight. Basic Dowex resin was added, filtered and rinsed by methanol. After evaporation of the methanol in room temperature, the residue was purified by flash chromatography on florisil eluting with 50% PE/EtOAc to afford 4.6 g (77%) of **4.29** as a colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.35 (s, 5H, C_6H_5), 5.69 (d, J=6.6 Hz, 1H, NH), 5.12 (s, 2H, CH_2Ph), 4.55 (m, 1H), 3.76 (s, 3H, OMe), 3.70 (m, 2H), 2.81 (br, 1H, OH), 2.15 (m, 1H), 1.71 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 174.09, 153.72.136.21, 128.21, 128.61, 128.18, 67.42, 58.60, 52.77, 51.69, 35.33.

Methyl- L-2-[(benzyloxycarbonyl)amino]-4-*O*-(tert-butyldimethylsilyl)-butyrate To a solution of **4.29** (4.19 g, 15.66 mmol) in CH_2Cl_2 (20 mL) was added TBDMSCl (2.83 g, 18.8 mmol) followed by imidazole (2.55 g, 37.6 mmol). This reaction mixture was stirred at room temperature for 2h. The mixture was filtered, rinsed by CH_2Cl_2 and washed with water. The solution was concentrated and purified by chromatography on silica gel eluting with EtOAc-PE (30%) to afford 5.429 g (90%) product as a colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.34 (s, 5H, C_6H_5), 5.93 (d, J=7.7 Hz, 1H, NH), 5.10 (m, 2H, CH_2Ph), 4.45 (m, 1H), 3.73 (s, 3H, OMe), 3.68 (m, 2H), 2.00 (m, 2H), 0.87 (s, 9H), 0.04 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.72, 156.06, 136.35, 128.56, 128.12, 128.02, 66.99, 60.16, 52.88, 52.47, 34.13, 26.12, 18.46, -5.26.

L-2-[(benzyloxycarbonyl)amino]-4-*O*-(tert-butyldimethylsilyl)-butyaldehyde 4.30 To a solution of above compound (5.42 g, 15.66 mmol) in THF (20 mL) at -78 °C was added 1 M DIBAL in heptane (43 mL, 42 mmol). The reaction mixture was stirred at -78 °C for 3 h. The resulting emulsion was slowly poured into 100 mL of ice-cold 1 N HCl with stirring over 10 min, and the aqueous mixture was extracted with EtOAc (3 × 100 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel eluting with EtOAc-PE (20%) to afford 4.03 g (85%) of **4.30** as a colorless oil. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 9.59 (s, 1H, CHO), 7.35 (m, 5H, C_6H_5), 5.86 (br, 1H, NH), 5.12 (s, 2H, CH_2Ph), 4.30 (m, 1H), 3.69 (t, 2H), 2.14 (m, 2H), 0.86 (s, 9H), 0.03 (s, 3H), 0.02 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz), δ 199.01, 156.18, 136.41, 128.65, 128.29, 128.16, 67.20, 59.21, 59.13, 32.16, 26.09, 18.42, -5.21, -5.30.

Preparation of *Z*-olefin 4.31 To a suspension of pentadecylphosphonium bromide (5.52 g, 9.8 mmol; prepared from 1-bromopentadecane and triphenylphosphine, refluxed in toluene for 5 days, 98%)[89] in THF (20 mL) was added dropwise NaHMDS (0.6 M in toluene, 15 mL, 9.2 mmol) at -75 °C under nitrogen atmosphere. The solution was gradually warmed to 0 °C and stirred for 1 h. To this solution, which was cooled down to -75 °C again, aldehyde **4.30** (2.472 g, 7 mmol) in THF (8 mL) was added dropwise over 30 min. After the reaction mixture was stirred at rt for 2 h, the reaction was quenched by addition of saturated NH_4Cl (100 mL) and extracted with ether. The organic extract was washed with brine, dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel eluting with EtOAc-PE (10%) to afford 3.44g (85%) of *Z*-olefin **4.31** as a colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.34-7.31 (m, 5H, C_6H_5), 5.47 (after decoupling, d, J=10 Hz, 1H, vinyl H next to CH_2), 5.42 (m, 1H, NH), 5.27 (t, J=9.8 Hz, 1H, vinyl H next to CH), 5.09 (m, 2H, CH_2Ph), 4.58 (m, 1H), 3.67 (m, 2H), 2.11 (m, 2H), 1.73 (m, 2H), 1.25 (s, 22H), 0.89 (s, 12H), 0.05 (s, 3H), 0.04 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 155.71, 136.96, 132.39, 129.96, 128.52, 128.16, 128.02, 66.59, 60.34, 60.31, 47.24, 38.06, 32.21, 29.99, 29.85, 29.69, 29.65, 29.55, 29.50, 27.96, 26.17, 22.99, 18.43, 14.42, -5.15.

Dihydroxylation of olefin (*Z*) -4.31 using AD-mix-β

To a solution of AD-mix-β (6.294 g) and methanesulfonamide (0.427 g, 4.50 mmol) in *t*-BuOH/H_2O (1:1, 10 mL) was added *Z*-**4.31** (2.45 g, 4.49 mmol) at 0 °C under nitrogen atmosphere.[90] The mixture was stirred at rt for 48 h, quenched with $Na_2S_2O_3$ (6.7 g) and extracted with EtOAc. The organic extract was washed with 1 N KOH, H_2O, brine and dried over Na_2SO_4. After evaporation of the solvent under the reduced pressure, the diols were purified by column chromatography (EtOAc/PE=30%) to give **4.33** (3,4 syn form, 0.5 g, 19% yield) and **4.32** (3,4-anti form,1.7 g, 65% yield) as two white solids.

(3S, 4R, 5S)-1-*O*-(tert-butyldimethylsilyl)-3-[(benzyloxycarbonyl)amino-4,5-nonadecanediol 4.33 mp 39-40 °C; $[\alpha]^{25}$ 3.0° (*c* 0.9, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz): δ 6.36 (s, 5H, C_6H_5), 5.29 (d, J=8.8 Hz, 1H, NH), 5.01 (s, 2H, CH_2Ph), 4.16 (m, 1H), 3.73 (t, J=5.6 Hz, 2H), 3.59 (br, 1H), 3.34 (m, 2H), 3.04 (d, J=4.0 Hz, 1H), 1.86 (m, 2H), 1.73 (m, 1H), 1.55 (m, 1H), 1.26 (s, 24H), 0.89 (s, 12H), 0.06 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 157.64, 136.38, 128.68, 128.35, 128.22, 76.43, 71.53, 67.38, 60.08, 50.22, 49.86, 35.46, 33.52, 32.23, 30.10, 30.00, 29.96, 29.66, 26.11, 23.00, 18.43, 14.43, -5.20, -5.23.

(3S, 4S, 5R)-1-*O*-(tert-butyldimethylsilyl)-3-[(benzyloxycarbonyl)amino-4,5-nonadecanediol 4.32 mp 40-43 °C; $[\alpha]^{25}$ 16.3° (*c* 0.9, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz): δ 7.38 (s, 5H, C_6H_5), 5.61 (d, J=8.0 Hz, 1H, NH), 5.08 (s, 2H, CH_2Ph), 4.09 (m, 1H), 3.73 (m, 3H), 3.57 (m. 1H), 3.49 (m, 1H), 2.11 (br, 1H), 1.95-1.76 (m, 12H), 1.26 (s, 26H), 0.89 (s, 12H), 0.07 (s, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 156.41, 136.57, 128.58, 128.17, 128.12,76.26, 73.22, 66.95, 59.98, 51.36, 33.77, 32.19, 32.05, 29.63, 26.12, 26.04, 22.96, 18.44, -5.20, -5.27.

(3S,4S,5R)-1-*O*-(tert-butyldimethylsilyl)-3-[(benzyloxycarbonyl)amino-4,5-*O*-isopropylidene -nonadecane 4.37 To a solution of diol **4.32** (2.23 g, 3.85 mmol) in CH_2Cl_2 (30 mL) was added 2,2-dimethoxy propane (2.37 mL, 19.3 mmol) followed by PPTs (97 mg, 0.38 mmol). After the reaction mixture was stirred at rt for 1.5 h, saturated $NaHCO_3$ (50 mL) was added and extracted with CH_2Cl_2 (30 mL × 2). The organic phase was dried over Na_2SO_4. After evaporation of the solvent under the reduced pressure, the residue was purified by column chromatography (EtOAc/PE=10%) to give product 2.287 g (96%) of **4.37** as an oil. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.34 (s, 5H, C_6H_5), 5.17 (d, J=8.8 Hz, 1H, NH), 5.07 (s, 2H, CH_2Ph), 4.13 (m, 2H), 3.90 (m, 1H), 3.78-3.70 (m, 2H), 1.89 (m, 2H), 1.56 (m, 2H), 1.43 (s, 3H), 1.33 (s, 3H), 1.25 (s, 24H), 0.88 (s, 12H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 155.86, 136.77, 128.47, 128.02, 107.78, 79.39, 77.96, 66.68, 60.25, 49.19, 34.40, 32.16, 29.92, 29.59, 29.12, 27.44, 27.01, 26.13, 25.61, 22.92, 18.39, 14.35, -5.25, -5.28.

(3S, 4S, 5R)- 3-[(benzyloxycarbonyl)amino-4,5-*O*-isopropylidene -nonadecanol 4.38 To a solution of above compound (3.31 g, 5.33 mmol) in THF (25 mL) was added 1 M Bu_4NF in THF (12 mL) followed by acetic acid (0.5 mL).[93] After the reaction mixture was stirred at rt overnight, saturated $NaHCO_3$ (20 mL) was added and extracted with CH_2Cl_2 (50 mL × 2) . The organic phase was dried over Na_2SO_4. After evaporation of the solvent under the reduced pressure, the residue was purified by column chromatography (EtOAc/PE=50%) to give 2.56 g (90%) of **4.38** as a white solid. mp 58-60 °C; $[\alpha]^{25}$ −3.67° (*c* 0.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.36 (s, 5H, C_6H_5), 5.11 (s, 2H, CH_2Ph), 4.86 (br, 1H, NH), 4.12 (m, 1H), 4.03-3.92 (m, 2H), 3.72 (m, 2H), 2.82 (br, 1H, OH), 2.02 (m, 2H), 1.52 (m, 24H), 1.44 (s, 3H), 1.33 (s, 3H), 0.88 (t, J=6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 156.91, 136.38, 128.72, 128.41, 128.22, 108.28, 79.78, 78.03, 77.44, 77.39, 77.02, 67.38, 59.06, 48.70, 35.36, 32.21, 30.16, 29.99, 29.90, 29.85, 29.65, 29.25, 27.04, 25.74, 22.98, 14.42.

Compound GY-X-1 If the above reaction was done without addition of acetic acid, product GY-X-1 was obtained in 30% yield, product **4.38** was obtained in 54% yield. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.88 (s, 1H), 4.35 (m, 1H), 4.21 (m, 2H), 3.90 (dd, J=5.8, 8.4 Hz, 1H), 3.56 (m, 1H), 2.06 (m, 2H), 1.53 (m, 2H), 1.40 (s, 3H), 1.32 (s, 3H), 1.25 (s, 24H), 0.88 (t, J=6.6 Hz, 3H).

(3S,4S,5R)-1-iodo-3-[(benzyloxycarbonyl)amino-4,5-*O*-isopropylidene-nonadecane 4.39 [65] A mixture of **4.38** (2.5 g, 4.95 mmol), PPh_3 (1.63 g, 6.1 mmol), imidazole (0.87 g, 11.8 mmol) and iodine (2.03 g, 7.4 mmol) in THF(50 mL) was stirred under reflux for 2.5 h. After evaporation of the solvent, the crude product was dissolved in CH_2Cl_2 (100 mL) and solids were removed by filtration. An equal volume of saturated aqueous $NaHCO_3$ was added and the mixture was stirred for 10 min. Iodine was added in portions and when the organic phase remained iodine-colored, the mixture was stirred for an additional 10 min. Excess iodine was destroyed by the addition of saturated aqueous $Na_2S_2O_3$ solution. The organic layer was diluted with CH_2Cl_2 (50 mL), separated, washed with water (50 mL), dried over Na_2SO_4. After evaporation of the solvent under the reduced pressure, the residue was purified by column chromatography (EtOAc/PE=20%) to give 2.57 g (87%) of **4.39** as a white solid. mp 79-

81 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.33 (s, 5H, C_6H_5), 5.07 (m, 3H), 4.05 (m, 3H), 3.78 (m, 1H), 3.23 (m, 2H), 2.26 (m, 2H), 1.89 (m, 2H), 1.42 (s, 3H), 1.30 (s, 3H), 1.55-1.26 (m, 24H), 0.88 (t, J=6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 155.88, 136.35, 128.59, 128.26, 128.21, 108.11, 79.57, 77.75, 67.11, 52.56, 36.72, 32.14, 30.35, 30.26, 29.91, 29.81, 29.76, 29.58, 29.15, 27.36, 26.99, 25.51, 22.91, 14.37.

(3′S, 4′S, 5′R) 3′-[(benzyloxycarbonyl)amino-4′,5′-*O*-isopropylidene-nonadecanylthio] 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranose 4.40 To a degassed solution of β-2,3,4,6-tetra-*O*-acetyl-galactosyl thioacetate **4.4** (2.02 g, 4.98 mmol) in DMF (15 mL), NH_2NH_2.HOAc (0.47 g, 5.96 mmol) was added.[67] This solution was degassed at room temperature for 1 h. Iodide **4.39** (2.55 g, 4.14 mmol) was added, followed by triethyl amine (0.64 mL, 6.58 mmol). After 2 h, ethyl acetate (100 mL) and water (50 mL) were added. The organic layer was washed with water and brine, and dried over anhydrous sodium sulfate. After evaporation of the organic solvent, the residue was purified by chromatography on silica gel eluting with 50% EtOAc/PE to afford 3.2 g (90%) of β-thiogalactoside **4.40** as a sticky oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.32 (s, 5H), 5.42 (d, J=3.0 Hz, 1H, H-4), 5.24 (t, J=9.9 Hz, 1H, H-2), 5.10 (m, 2H), 5.03 (dd, J=3.3, 9.9 Hz, 1H, H-3), 4.83 (d, J=9.5 Hz, 1H, NH), 4.46 (d, J=9.9 Hz, 1H, H-1), 4.13 (m, 3H), 4.04 (t, J=5.8 Hz, 1H, H-5), 3.94 (t, 1H), 3.79 (m, 1H), 2.85-2.72 (m, 2H, H-SCH_2), 2.12 (s, 3H, H-OAc), 2.05 (s, 3H, H-OAc), 2.04 (s, 3H, H-OAc), 1.98 (s, 3H, H-OAc), 1.76 (m, 1H), 1.54 (m, 1H), 1.43 (s, 3H), 1.32 (s, 3H), 1.26 (s, 24H), 0.88 (t, J=6.6 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.27, 170.21,170.04 169.56, 155.77, 136.49, 128.60, 128.24, 128.12, 108.09, 84.30, 77.77, 77.45, 77.05, 76.96, 74.62, 72.05, 67.38, 67.32, 66.99, 61.43,50.97, 32.44, 32.14, 30.26, 30.18, 29.92, 29.82, 29.28, 27.55, 26.95, 26.78, 26.75, 25.64, 22.91, 21.02, 20.87, 20.84, 14.35.

(3'S, 4'S, 5'R) 3'-[(benzyloxycarbonyl)amino-4',5'-*O*-isopropylidene-nonadecanylthio]4,6-*O*-benzylidene-β-D-galactopyranose 4.41 Into the solution of thiogalacoside **4.40** (2.31g, 2.71 mmol) and Methanol (50 mL) was added NaOMe (70 mg, 1.3 mmol). The mixture was stirred at rt. until a white precipate was formed. The precipitate was dissolved in EtOAc, then acidic resin was added until the pH of the solution is neutral. The resin was filtered off and rinsed by EtOAc. The solution was concentrated until completely dry to afford 1.76 g of a white solid.

To a mixture of above solid (1.75 g, 2.57 mmol), *p*-methoxybenzaldehyde dimethyl acetal (1.1 mL, 6.42 mmol), and 50 mL dry CH_2Cl_2 and 3 mL DMF was added *p*-TsOH (29 mg) at room temperature. After 2h, the mixture was neutralized with triethyl amine (1 mL) and concentrated. The residue was chromatographed (SiO_2, EtOAc/MeOH, 100% to 95%) to give 1.72 g (86% overall yield) of **4.41** as a white solid. ^1H NMR (300 MHz, $CDCl_3$): δ 7.48 (d, J= 8.8 Hz, 2H), 7.29 (m, 5H), 6.82 (d, J=8.8 Hz, 2H), 5.43 (s, 1H), 5.06 (m, 3H), 4.17 (d, 2H), 4.16 (s, 1H), 4.05 (m, 1H), 3.90 (m, 3H), 3.75 (s, 3H), 3.61 (m, 2H), 3.39 (s, 1H), 2.89 (m, 1H), 2.68 (m, 1H), 2.05 (m, 2H), 1.80 (m, 2H), 1.60-1.20 (m, 30H), 0.88 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.14, 156.19, 136.45, 130.37, 128.56, 128.16, 128.08, 127.75, 113.61, 108.03, 101.17, 85.69, 79.64, 77.76, 75.74, 73.88, 70.19, 69.33, 68.98, 67.00, 55.38,50.59, 32.62, 32.09, 29.88, 29.79, 29.73, 29.53, 29.11, 27.50, 26.95, 25.63, 25.33, 22.87, 14.33.

(3'S, 4'S, 5'R) 3'-[(benzyloxycarbonyl)benzylamino-4',5'-*O*-isopropylidene-nonadecanylthio]4,6-*O*-benzylidene-2,3-di-O-benzyl-β-D-galactopyranose β-S-

galactoside **4.41** (1.49 g, 1.86 mmol) was dissolved in 20 mL THF and 5 mL DMF, NaH (0.6 g , 60% in mineral oil) was added, the mixture was stirred at rt. for 1/2 h, then *tetra*-butylammonium (0.068 g, 0.186 mmol) iodide was added followed by benzyl bromide (0.89 mL, 7.44 mmol). After the mixture was stirred at room temperature overnight, the reaction was quenched with 10 mL of MeOH. The resulting solution was added to H_2O (50 mL) and extracted by EtOAc (100 mL × 3). The organic phase was washed by brine, and dried over Na_2SO_4 and concentrated. The residue was chromatographed on a column of silica gel (eluted with 30% EtOAc-petroleum ether) to afford 1.62 g product (83%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.48 (d, J=8.8 Hz, 2H), 7.43-7.22 (m, 20H), 6.88 (d, J=8.8 Hz, 2H), 5.46 (s, 1H), 5.17 (m, 2H), 4.78 (m, 6H), 4.34 (m, 4H), 4.16 (d, J=3.3 Hz, 1H), 4.14 (m, 1H), 3,95 (m, 1H), 3.79 (s, 3H), 3.59 (dd, J=3.3, 9.1 Hz, 1H), 3.50 (m, 1H), 3.29 (m, 1H), 2.70 (m, 2H), 2.06 (m, 2H), 1.47-1.13 (m, 32H), 0.92 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.06, 158.66, 139.19, 138.55, 138.41, 136.43, 130.64, 128.41, 128.33, 128.09, 127.84, 127.78, 127.67, 127.50, 127.34, 127.31, 127.21, 127.08, 113.57, 107.69, 101.33, 81.23, 79.64, 79.59, 79.42, 77.88, 75.79, 73.99, 71.77, 69.99, 69.40, 55.41, 32.14, 30.99, 30.08, 29.92, 29.85, 29.63, 29.57, 27.74, 25.54, 22.91, 14.35; MS: *m/z* 1094 (M^++Na^+), (calcd. $C_{65}H_{85}O_{10}SN$, 1071).

(3′S, 4′S, 5′R) 3′-[(benzyloxycarbonyl)benzylamino-4′,5′-*O*-isopropylidene-nonadecanylsulfonyl] 4,6-*O*-benzylidene-2,3-di-*O*-benzyl-β-D-galactopyranose 4.42 A solution of MMPA (2.1 g, 4.26 mmol) in H_2O (10 mL) was added to a solution of thio-galactoside (1.52 g, 1.42 mmol) in EtOH (10 mL) and THF (10 mL), the mixture was kept at 60 °C for 3 h. The mixture was concentrated in vacuo to dryness. The residue was treated with 50 mL saturated $NaHCO_3$ solution, and extracted with EtOAc (50 mL × 3), dried over Na_2SO_4 and evaporated to dryness. The residue was purified by chromatography on silica gel eluting with 40% EtOAc/PE to afford 1.45 g (93%) of pure sulfone **4.42** as a white solid. mp 40-43 °C; ^1H NMR ($CDCl_3$, 400 MHz heated at 55 °C): δ 7.46-7.18 (m, 22H), 6.88 (d, J=8.8 Hz, 2H), 5.39 (s, 1H), 5.13 (s, 2H), 4.95 (d, 1H), 4.84 (d, 1H), 4.73 (s, 2H), 4.65 (m, 1H), 4.42 (t, J=9.6 Hz, 1H), 4.30 (m, 2H), 4.24 (s, 1H), 4.22 (d, 2H), 4.11 (d, 1H), 4.07 (m, 1H), 3.91 (dd, 1H), 3.79 (s, 3H), 3.66 (dd, 1H), 3.55 (b, 1H), 3.32 (s, 1H), 3.28 (b, 1H), 3.00 (b, 1H), 2.35 (m, 1H), 2.20 (b, 1H), 1.34 (s, 3H), 1.25 (s, 28H), 1.17 (s, 3H), 0.89 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 160.39, 156.97, 138.64, 138.07, 136.21, 130.39, 128.81, 128.68, 128.60, 128.43, 128.06, 127.90, 127.72, 127.59, 113.86, 107.98, 101.59, 80.80, 78.93, 77.93, 77.42, 76.58, 75.78, 73.27, 73.11, 72.10, 70.71, 68.92, 55.56, 32.21, 30.00, 29.96, 29.92, 29.65, 28.03, 26.36, 25.67, 22.98, 14.41; MS: *m/z* 1121 (M^++NH_4^+), (calcd. $C_{65}H_{85}O_{12}SN$, 1103).

(3′S, 4′S, 5′R) 3′-[(benzyloxycarbonyl)benzylamino-4′,5′-*O*-isopropylidene] 4,6-*O*-benzylidene-2,3-di-*O*-benzyl-β-D-galactopyranosylidene nonadecane 4.43 To a solution of **4.42** (1.45 g, 1.32 mmol) in *t*-BuOH (10 mL) and CF_2BrCF_2Br (10 mL), 4 g 25% (by weight) KOH/Al_2O_3 (prepared one day earlier) was added. This mixture was refluxed at 47 °C for 10 h. The solution was filtered through a pad of celite which was washed by CH_2Cl_2. The residue was purified by column chromatography on silica gel eluting with 25% EtOAc-PE to afford 0.6 g (60% based on recovered starting material) of **4.43** as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$), δ 7.46 (d, J=8.8 Hz, 2H), 7.39-7.10 (m, 20H), 6.87 (d, J=8.8 Hz, 2H), 5.50 (s, 1H), 5.40 (t, 1H), 5.13 (m, 2H), 4.97 (d, 1H), 4.82-4.66 (m, 5H), 4.52 (m, 1H), 4.40-4.24 (m, 3H), 4.09-3.99 (m, 2H), 3.79 (s, 3H), 3.72 (m, 1H), 3.58 (m, 1H), 3.48 (m, 1H), 2.54 (t, 2H), 1.41-1.12 (m, 32H), 0.89 (t, 3H); MS: *m/z* 1060 (M^++Na^+), (calcd. $C_{65}H_{83}O_{10}N$, 1037).

To a solution of **4.43** (*Z*+*E*, 0.6g, 0.578 mmol) in MeOH (10 mL), TMSCl (73 µL) was added at 0 °C. After the mixture was stirred at 0 °C for 30 min, saturated $NaHCO_3$ (20 mL) was added. The mixture was extracted with CH_2Cl_2 (2 × 40 mL). The organic phase was dried over Na_2SO_4, and concentrated, the residue was purified by column chromatography on silica gel eluting with 35% EtOAc-PE to afford 0.36 g (66%) of product **4.44**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.28 (m, 20H), 5.08 (m, 2H), 4.90 (d, 1H), 4.68 (s, 2H), 4.61 (d, 1H), 4.56 (d, 1H), 4.51 (d, 1H), 4.35 (d, 1H), 4.02-3.95 (m, 4H), 3.84-3.81 (m, 3H), 3.65 (m, 1H), 3.58 (m, 1H), 3.00 (s, 3H), 2.59 (broad peak, 1H), 2.23 (broad peak, 1H), 1.51 (m, 4H), 1.39 (s, 3H), 1.33 (s, 26H), 1.20 (s, 3H), 0.89 (t, 3H).

Benzoate 4.47 To a solution of **4.44** (0.36 g, 0.378 mmol) in CH_2Cl_2 (10 mL), BzCl (66 µl, 0.56 mmol) was added at 0 °C, followed by Et_3N (0.3 mL, 2.3 mmol). After the mixture was stirred at 0 °C for 2 h, 10% ammonia solution (20 mL) was added. The mixture was extracted with CH_2Cl_2 (2 × 40 mL). The organic phase was dried over Na_2SO_4, concentrated, the residue was purified by column chromatography on silica gel eluting with 25% EtOAc-PE to afford 0.365 g product **4.47** (92%).

To a solution of **4.47** (0.365 g, 0.347 mmol) in MeOH (10 mL), 1 N HCl/Et_2O (1 mL) was added at 0 °C. After the mixture was stirred at 0 °C for 2 h, saturated $NaHCO_3$ (20 mL) was added. The mixture was extracted with CH_2Cl_2 (2 × 40 mL). The organic phase was dried over Na_2SO_4, and concentrated, the residue was purified by column chromatography on silica gel eluting with 30% EtOAc-PE to afford 0.275 g (80%) of product **4.48.** ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.92 (d, J=7.3 Hz, 2H), 7.53 (t, 1H), 7.39-7.20 (s, 22H), 5.15 (d, 1H), 4.94 (m, 2H), 4.74-4.69 (m, 3H), 4.63 (br, 1H), 4.55 (m, 2H), 4.43 (br, 1H), 4.08-3.93 (m 5H), 3.55 (d, 1H), 3.42 (m, 1H), 3.11 (s, 3H), 2.17 (br, 1H), 1.76 (m, 2H), 1.47 (m, 2H), 1.25 (s, 26H), 0.89 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.35, 157.80, 138.54, 136.34, 133.09, 130.21, 129.82, 129.71, 128.66, 128.60, 128.48, 128.43, 128.22, 128.04, 127.96, 127.79, 127.60, 103.18, 79.89, 79.05, 75.91, 75.58, 73.17, 72.60, 69.34, 68.17, 67.83, 64.57, 47.81, 33.80, 33.78, 32.18, 29.96, 29.60, 27.81, 25.89, 22.93, 14.30.

Cyclic carbonate To a solution of **4.48** (0.27 g, 0.266 mmol) in CH_2Cl_2 (4 mL) and pyridine (0.13 mL), triphosgene (40 mg, 0.133 mmol) in CH_2Cl_2 (1 mL) was dropwise added at -70 °C. [94] After the addition was finished, the reaction mixture was warmed up to room temperature. After 1.5 h, the mixture was diluted with CH_2Cl_2 (30 mL), quenched with 20 mL saturated NH_4Cl, then extracted with CH_2Cl_2 (20 mL x 3). The organic phase was washed with 1 N HCl, saturated $NaHCO_3$, and brine. The organic layer was dried over Na_2SO_4, concentrated, the residue was purified by column chromatography on silica gel eluting with 20% EtOAc-PE to afford 0.265 g product (90%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.06 (d, J=7.3 Hz, 2H), 7.58 (t, 1H), 7.46 (t, 2H), 7.36-7.24 (m, 19H), 7.05 (m, 1H), 5.16 (m, 2H), 4.99 (d, 1H), 4.71-4.49 (m, 8H), 4.32 (m, 1H), 4.09 (m, 1H), 4.03 (dd, 1H), 3.90 (m, 1H), 3.82 (m, 2H), 3.14-3.05 (two singlets, 3H), 2.48 (s, 1H), 1.85 (m, 1H), 1.66 (m, 3H), 1.46 (m, 2H), 1.27 (s, 24H), 0.89 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.41, 156.85, 153.62, 138.54, 138.47, 138.34, 138.32, 138.04, 136.19, 133.13, 129.82, 128.87, 128.72, 128.56, 128.35, 128.25, 128.13, 128.08, 127.97, 127.84, 127.75, 127.61, 127.57, 127.52, 101.95, 80.64, 79.96, 79.85, 77.48, 77.42, 77.11, 77.02, 76.90, 75.41, 72.53, 69.30, 68.24, 67.69, 64.35, 55.47, 48.21, 32.28, 32.20, 29.97, 29.79, 29.73, 29.61, 29.19, 28.92, 28.47, 25.66, 22.93, 14.30.

Silyl ether 4.49 To a solution of the above material (260 mg, 0.249 mmol) in DMF (5 mL), *i*-Pr_2SiHCl (0.13 mL, 0.75 mmol) and imidazole (101 mg) were added. After the mixture was stirred at rt for 2 h, the solution was concentrated and purified by column chromatography on silica gel eluting with 30% EtOAc-PE to afford 0.228 g (87%) of **4.49** as a colorless oil. ^1H NMR (300 MHz, $CDCl_3$), δ 8.06 (d, J=7.3 Hz, 2H), 7.59 (t, 1H), 7.47 (t, 2H), 7.40-7.29 (m, 19H), 7.04 (m, 1H), 5.15 (m, 2H), 5.01 (d, 1H), 4.80 (d, 1H), 4.65 (m, 2H), 4.54-4.32 (m, 7H), 3.99 (m, 2H), 3.89 (m, 1H), 3.80 (m, 2H), 3.16-3.06 (two singlets, 3H), 1.92 (m, 1H), 1.69 (m, 1H), 1.47 (m, 2H), 1.27 (s, 26H), 1.07 (m, 14H), 0.89 (t, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.35, 156.88, 153.54, 138.68, 138.32, 133.15, 132.36, 130.36, 129.79, 128.91, 128.57, 127.47, 128.39, 128.22, 128.08, 127.90, 127.77, 127.70, 127.57, 127.51, 127.44, 127.40, 127.35, 101.95, 80.71, 80.29, 79.68, 77.43, 77.38, 77.11, 77.02, 76.98, 75.56, 73.16, 71.56, 70.55, 68.28, 64.55, 48.13, 32.21, 29.97, 29.93, 29.79, 29.71, 29.62, 29.26, 28.97, 25.57, 22.94, 17.95, 17.91, 17.84, 17.77, 14.31, 13.22, 13.16; MS: *m/z* 1173 (M^++NH_4^+), (calcd. $C_{69}H_{93}O_{12}SiN$, 1155).

α-*C*-glycoside 4.51 Syringe pump addition of a solution (92 mg, 0.079 mmol **4.49** in 6 mL CH_2Cl_2) to a solution of $BF_3.Et_2O$ (50 μL, 0.4 mmol) in 6 mL CH_2Cl_2 was carried out over a 5 h reaction time. The mixture was then treated with 20 mL sat. $NaHCO_3$, and extracted with CH_2Cl_2 (20 mL × 3). The organic solvent was concentrated to afford a mixture of **4.50** and **4.52**. MS for **4.50**: *m/z* 1161 (M^++NH_4^+), (calcd. $C_{68}H_{90}O_{11}NSiF$, 1143); ^1H NMR (500 MHz, C_6D_6) for **4.52**: δ 4.35 (dd, J=5.5, 11.0 Hz, H-6, 1H), 4.23 (dd, J=6.0, 11.0 Hz, H-6), 3.84 (t, J-5.5 Hz, H-5); MS for **4.52**: *m/z* 1027 (M^++NH_4^+), (calcd. $C_{62}H_{75}O_{11}N$, 1009).

To the above crude products in THF (5 mL) and acetic acid (30 μL), 1 N Bu_4NF (0.4 mL) was added. The reaction was stirred at rt for 1 h, the mixture was diluted with CH_2Cl_2, washed with water. The organic was dried over Na_2SO_4, concentrated, the residue was purified by column chromatography on silica gel eluting with 20% EtOAc-PE to afford 61 mg product **4.51** (76%) and 18 mg (20%) of side product **4.52**. ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.54, 156.86, 153.59, 138.48, 138.30, 138.12, 136.17, 133.10, 130.36, 129.84, 128.89, 128.71, 128.61, 128.49, 128.41, 128.27, 128.23, 128.12, 127.95, 127.85, 127.68, 80.54, 79.76, 77.76, 77.50, 77.43, 76.22, 73.67, 73.03, 72.94, 70.30, 68.32, 67.53, 63.83, 55.20, 32.18, 29.96, 29.78, 29.66, 29.60, 29.23, 28.92, 25.52, 23.06, 22.93, 14.30; MS: *m/z* 1029 (M^++NH_4^+), (calcd. $C_{62}H_{77}O_{11}N$, 1011).

Oxazolidinone 4.53 Carbonate **4.51** (66 mg, 0.065 mmol) was dissolved in 5 mL dioxane:H_2O (1:1) and treated with NaOH (0.46 g) and heated under reflux conditions at 90 °C overnight. The sample was concentrated in *vacuo* and redissolved in $CHCl_3$ and washed with saturated NH_4Cl solution. The aqueous layer was extracted with $CHCl_3$ (20 mL × 3). The organic was dried over Na_2SO_4, concentrated, the residue was dried in vacuo to afford 50 mg product **4.53** (96%). ^1H NMR (500 MHz, $CDCl_3$): δ 7.35-7.26 (m, 15H), 4.84 (d, J=15.0 Hz, 1H), 4.73 (m, 2H), 4.67 (d, J=10.0 Hz, 1H), 4.56 (d, J=11.5 Hz, 1H), 4.21 (t, J=8.5 Hz, 1H), 4.05 (d, J=15.0 Hz, 1H), 3.96-3.87 (m, 4H), 3.82 (t, J=7.5 Hz, 1H), 3.66 (d, J=10.0 Hz, 1H), 3.60 (m, 1H), 3.54 (dd, J=3.0, 8.5 Hz, 1H), 3.47 (m, 1H), 2.53 (br, 2H, OH), 2.36 (br, 1H, OH), 1.98 (m, 1H), 1.78 (m, 1H), 1.69 (m, 2H), 1.57 (m, 2H), 1.42 (m, 2H), 1.25 (m, 22H), 0.88 (t, J=6.5 Hz, 3H); ^{13}C NMR

(75 MHz, $CDCl_3$): δ 157.97, 138.50, 138.06, 128.92, 128.67, 128.58, 128.16, 127.96, 127.85, 79.49, 78.14, 76.23, 74.51, 73.81, 72.76, 71.08, 68.91, 68.41, 63.28, 57.34, 46.80, 34.99, 32.17, 29.94, 29.59, 24.94, 24.45, 22.92, 22.13, 14.30; MS: *m/z* 774 (M^++H^+), (calcd. $C_{47}H_{67}O_8N$, 773).

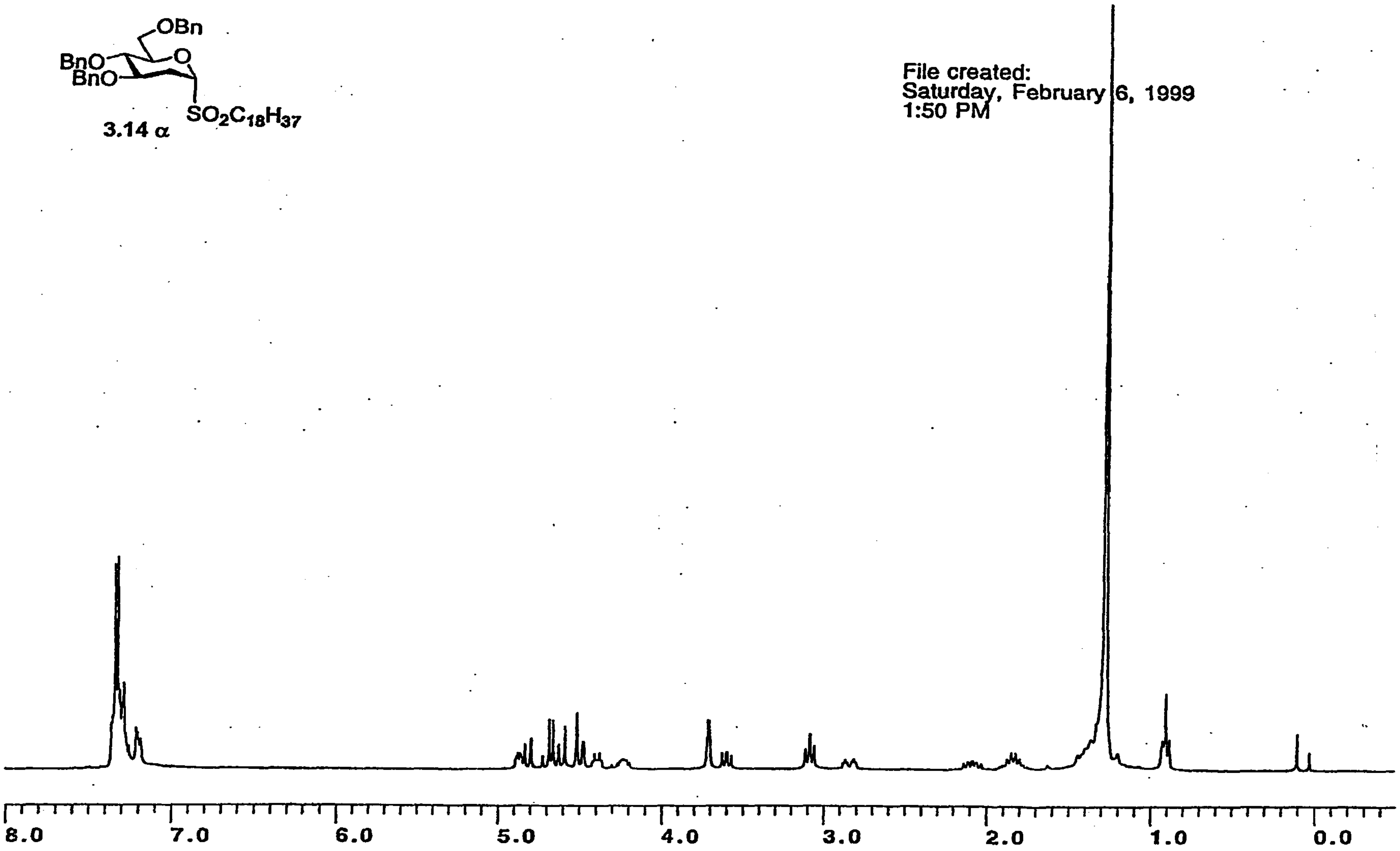
Benzylamine 4.54 The crude compound **4.53** (50 mg, 0.063 mmol) was dissolved in 5 mL EtOH and 1 mL H_2O and treated with KOH (0.5 g) at reflux overnight. The cooled solution was diluted with saturated NH_4Cl solution and extracted with EtOAc (20 mL x 3). The organic extracts were dried over Na_2SO_4, filtered, and concentrated, the residue was purified by column chromatography on silica gel eluting with $CHCl_3$:MeOH (4:1) to afford 39 mg product **4.54** (80%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.35-7.25 (m, 15H), 4.76-4.70 (m, 3H), 4.59 (d, J=11.7 Hz, 1H), 3.97-3.85 (m, 4H), 3.77 (s, 2H), 3.69 (dd, J=3.6, 12.1 Hz, 1H), 3.60 (m, 3H), 3.52 (m, 1H), 3.30 (t, J=6.6 Hz, 1H), 2.79 (br, 5H), 1.88 (m, 1H), 1.73 (m, 2H), 1.57 (m, 2H), 1.25 (s, 25H), 0.89 (t, J=6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.56, 138.19, 128.70, 128.58, 128.51, 128.17, 128.12, 127.95, 127.87, 127.43, 78.06, 76.48, 74.60, 74.42, 73.99, 73.84, 72.79, 71.34, 68.53, 68.50, 68.12, 67.70, 63.14, 60.97, 51.85, 34.66, 32.20, 30.18, 29.99, 29.63, 25.76, 25.69, 22.95, 21.91, 14.33; MS: *m/z* 478 (M^++H^+), (calcd. $C_{46}H_{69}O_7N$, 477).

3'S,4'S,5'R-3'-*N*-hexacosanoyl-4',5'-dihydroxynonadecacyl-α-*C*-D-lactopyranoside (4.1) A solution of compound **4.54** (39 mg, 0.052 mmol) in 1 mL MeOH was treated with 10% Pd/C (40 mg), 1 N HCl (52 μL, 0.052 mmol), and cylcohexene (0.2 mL).[95] The resulting slurry was heated at reflux for 4 h, then cooled to rt, filtered through a pad of celite and basic resin, and concentrated to give 23 mg of crude **4.55**.

A solution of this material in THF (1 mL) was treated with *p*-nitrophenyl hexacosanoate (75 mg, 0.144 mmol) and a crystal of DMAP.[75] The resulting solution was stirred at rt for 48 h and concentrated. The residue was purified by column chromatography on silica gel eluting with $CHCl_3$:MeOH (4:1) to afford 23 mg (60%) of product **4.1** as a white solid. mp 175-178 °C; $[\alpha]^{25}$ 40.8° (*c* 0.13, pyridine); ^1H NMR (500 MHz, C_5D_5N): δ 8.47 (d, J=8.8 Hz, 1H, NH), 6.78-6.00 (br, 6H, OH), 5.14 (m, 1H), 4.74 (dd, J=5.5, 8.8 Hz, 1H), 4.52 (m, 3H), 4.37 (dd, J=4.3, 11.0 Hz, 1H), 4.25 (m, 4H), 2.72 (m, 1H), 2.59 (m, 1H), 2.48 (m, 3H), 2.33 (m, 2H), 2.22 (m, 1H), 1.94 (m, 2H), 1.86 (m, 3H), 1.71 (m, 1H), 1.37 (s, 64H), 0.88 (t, J=6.4 Hz, 6H); ^{13}C NMR (125 MHz, C_5D_5N): δ 173.36, 78.37, 76.90, 73.65, 72.53, 72.07, 70.46, 70.27, 62.61, 52.56, 36.86, 34.33, 32.00, 30.26, 30.07, 29.88, 29.70, 29.49, 26.42, 22.81, 14.15;); FABMS (high-res.): *m/z* (calcd. $C_{51}H_{101}O_8N+H^+$, 856.7605, found 856.7601).

3′S,4′S,5′R-3′-*N*-hexacosanoyl-4′,5′-di-*O*-acetylnonadecacyl-2,3,4,6-tetra-*O*-acetyl-α-*C*-D-galactopyranoside 4.56 To a solution of **4.1** (6 mg, 5.86 μmol) in 1 mL EtOAc, Ac_2O (15 μl, 0.158 mmol) and DMAP (1 mg, 8.19 μmol) were added. The mixture was stirred at rt overnight. The residue was purified by column chromatography on silica gel eluting with EtOAc:PE (40%) to afford 5 mg product **4.56** (80%). ^1H NMR (500 MHz, C_6D_6): δ 5.56 (m, 2H), 5.42 (dd, J=3.0, 9.0 Hz, 1H), 5.27 (d, J=9.0 Hz, 2H), 5.16 (d, J=10.0 Hz, 1H), 4.46 (m, 2H), 4.33 (m, 1H), 4.10 (dd, J=5.0, 11.5 Hz, 1H), 3.74 (m, 1H), 2.01 (m, 3H), 1.83 (s, 3H), 1.81 (s, 3H), 1.78 (s, 3H), 1.73 (s, 3H), 1.70 (s, 3H), 1.62 (s, 3H), 1.45 (m, 1H), 1.35-1.31 (m, 74H), 0.90 (m, 6H); MS: *m/z* (M^++H^+), 1108, (M^++Na^+), 1130, (calcd. $C_{63}H_{113}O_{14}N$, 1107).

7. APPENDIX



3.14 α

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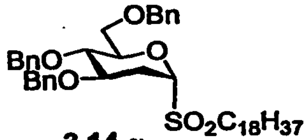
Saturday, February 6, 1999
1:50 PM



3.14 α

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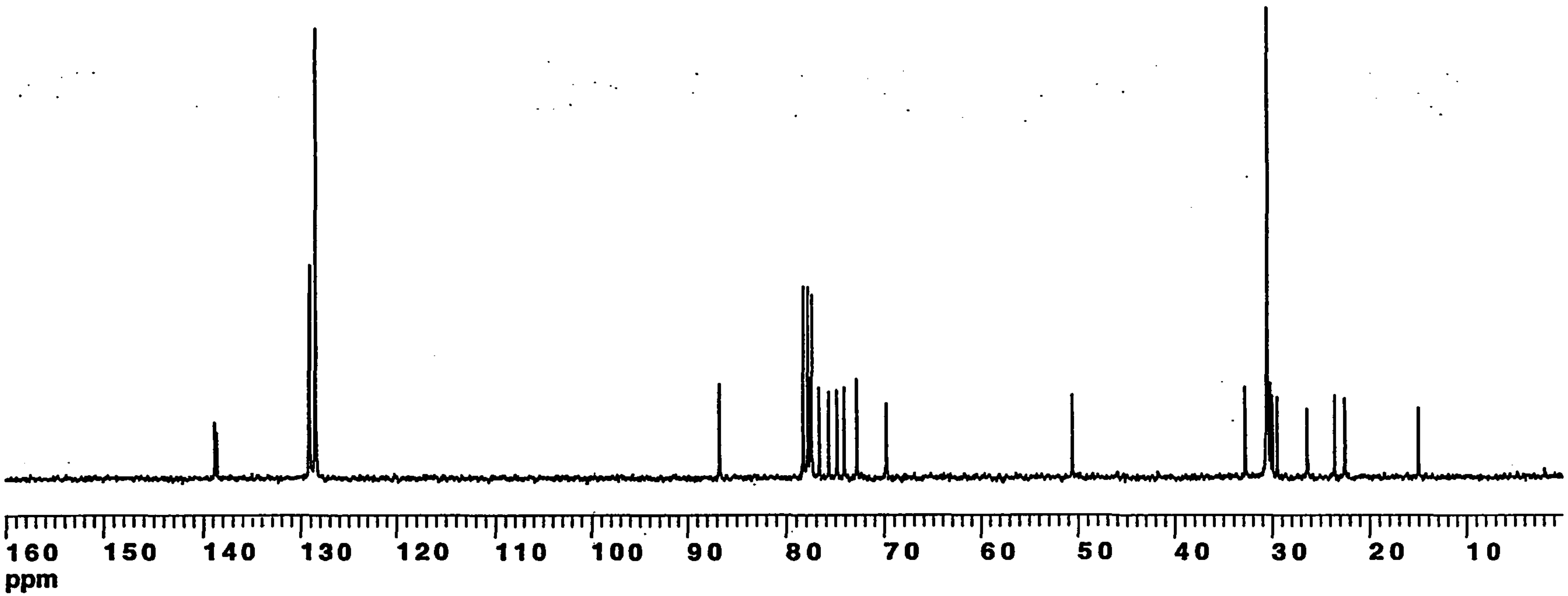
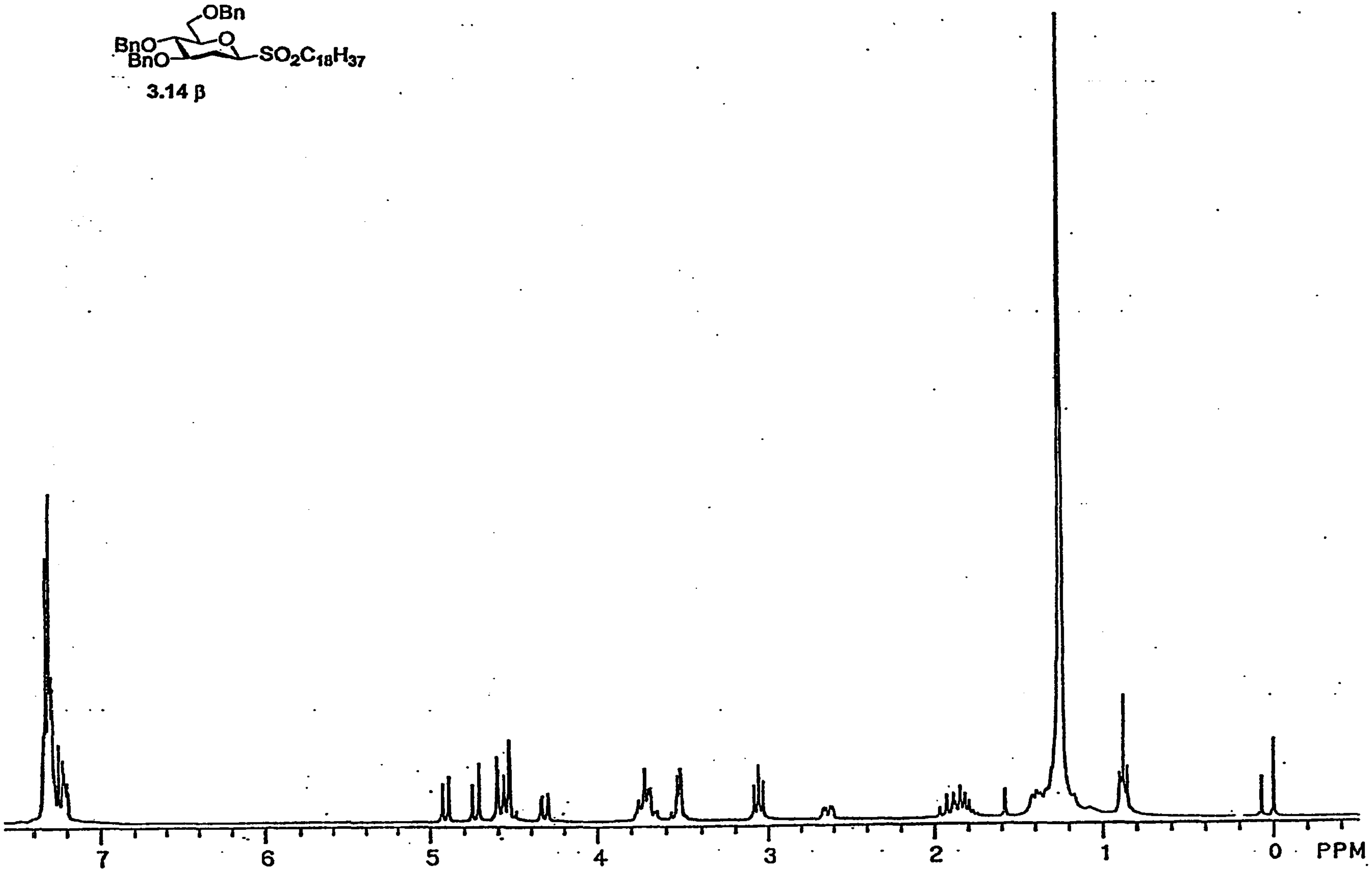
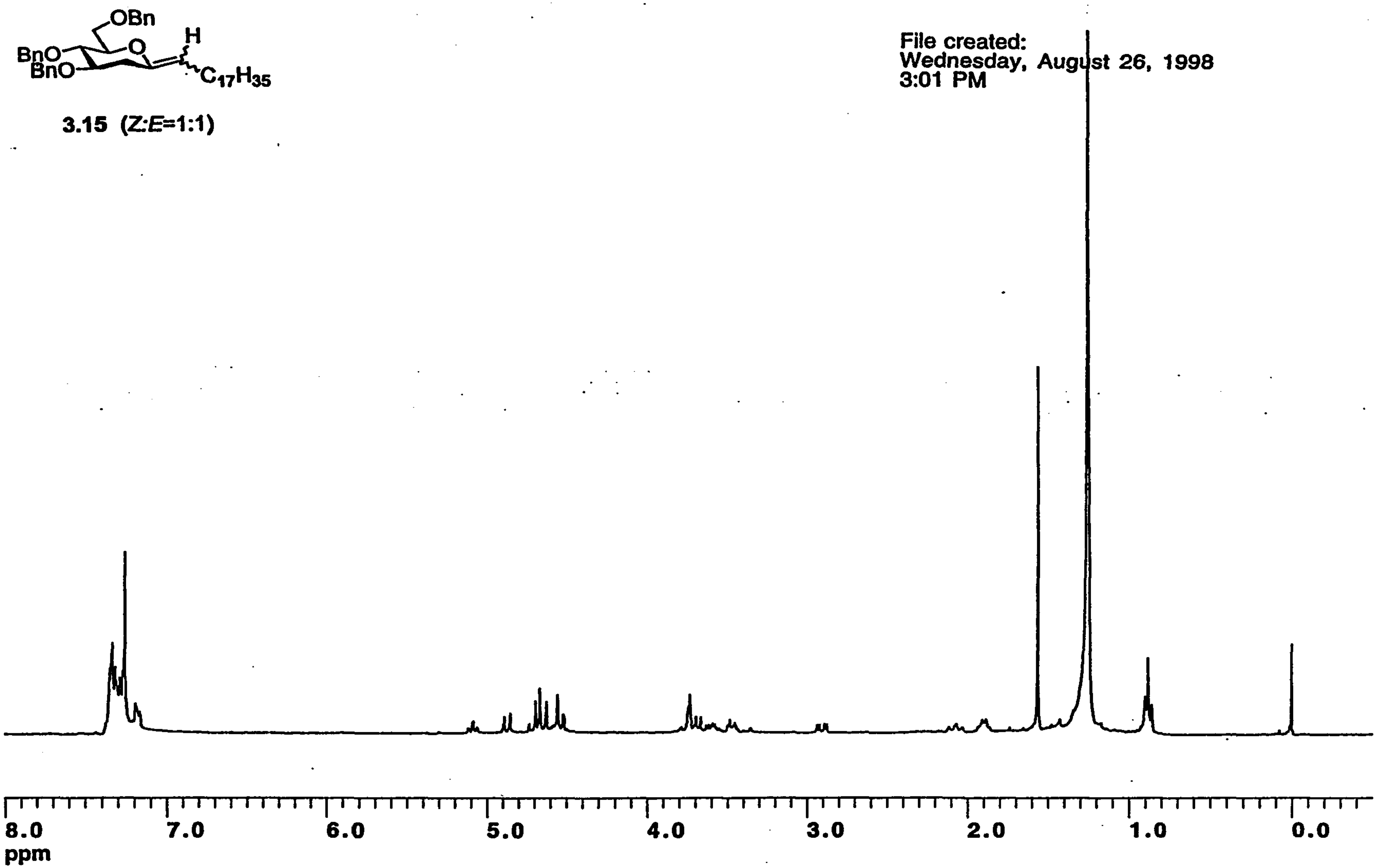




3.14 β


OBn
BnO
BnO
O
H
$C_{17}H_{35}$
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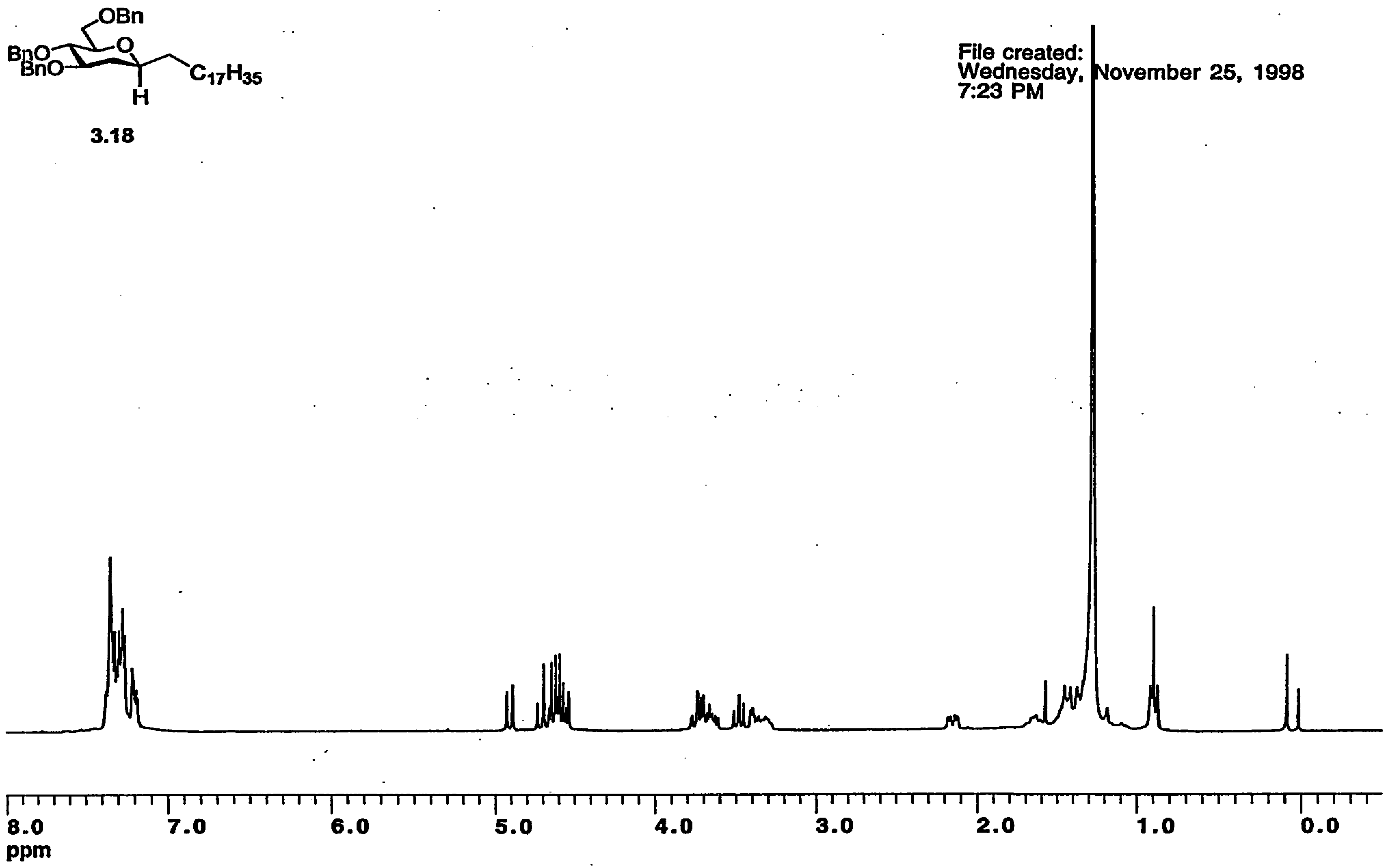
Wednesday, August 26, 1998
3:01 PM
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm

3.15 (*Z*:*E*=1:1)



3.18

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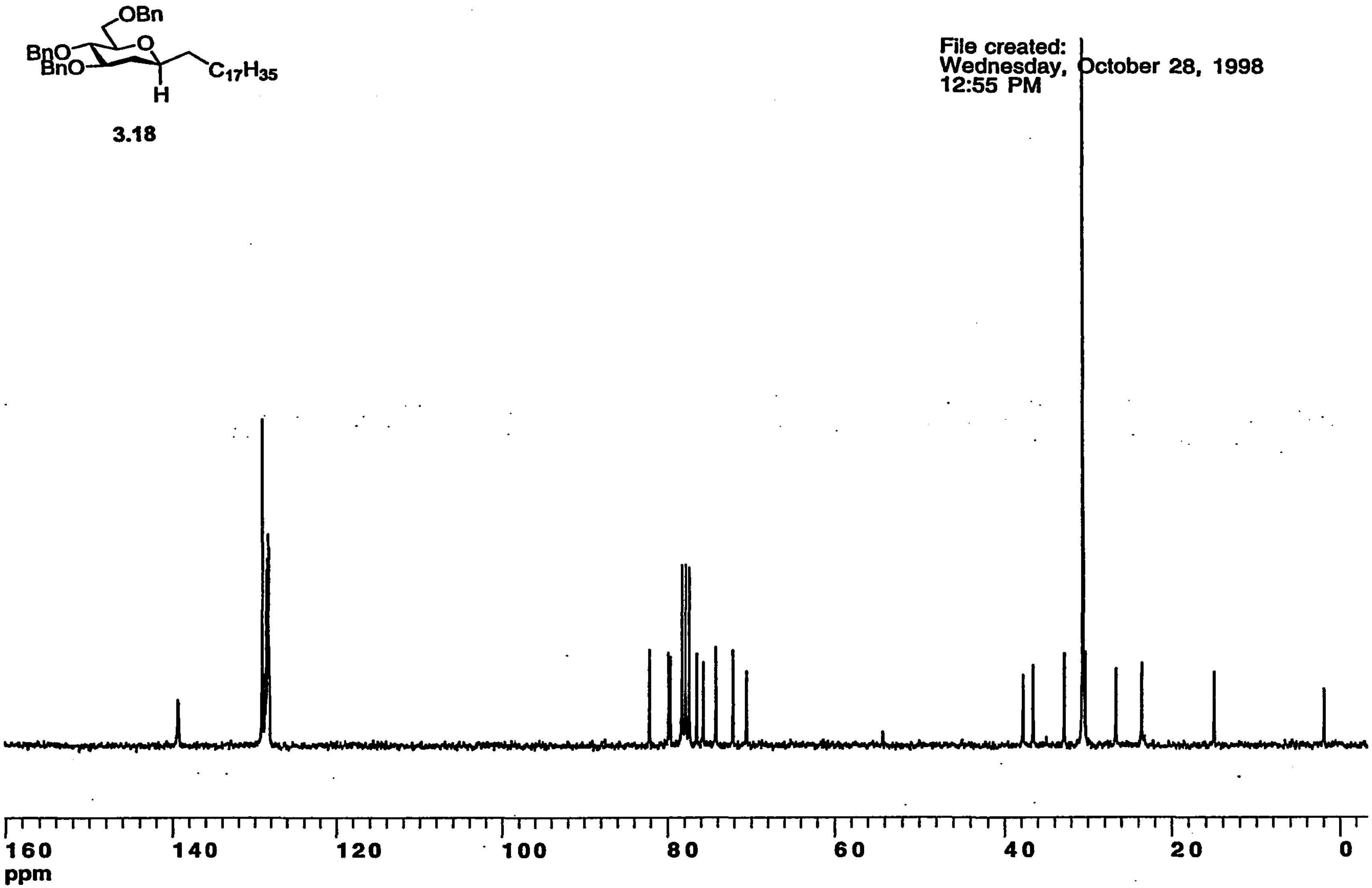
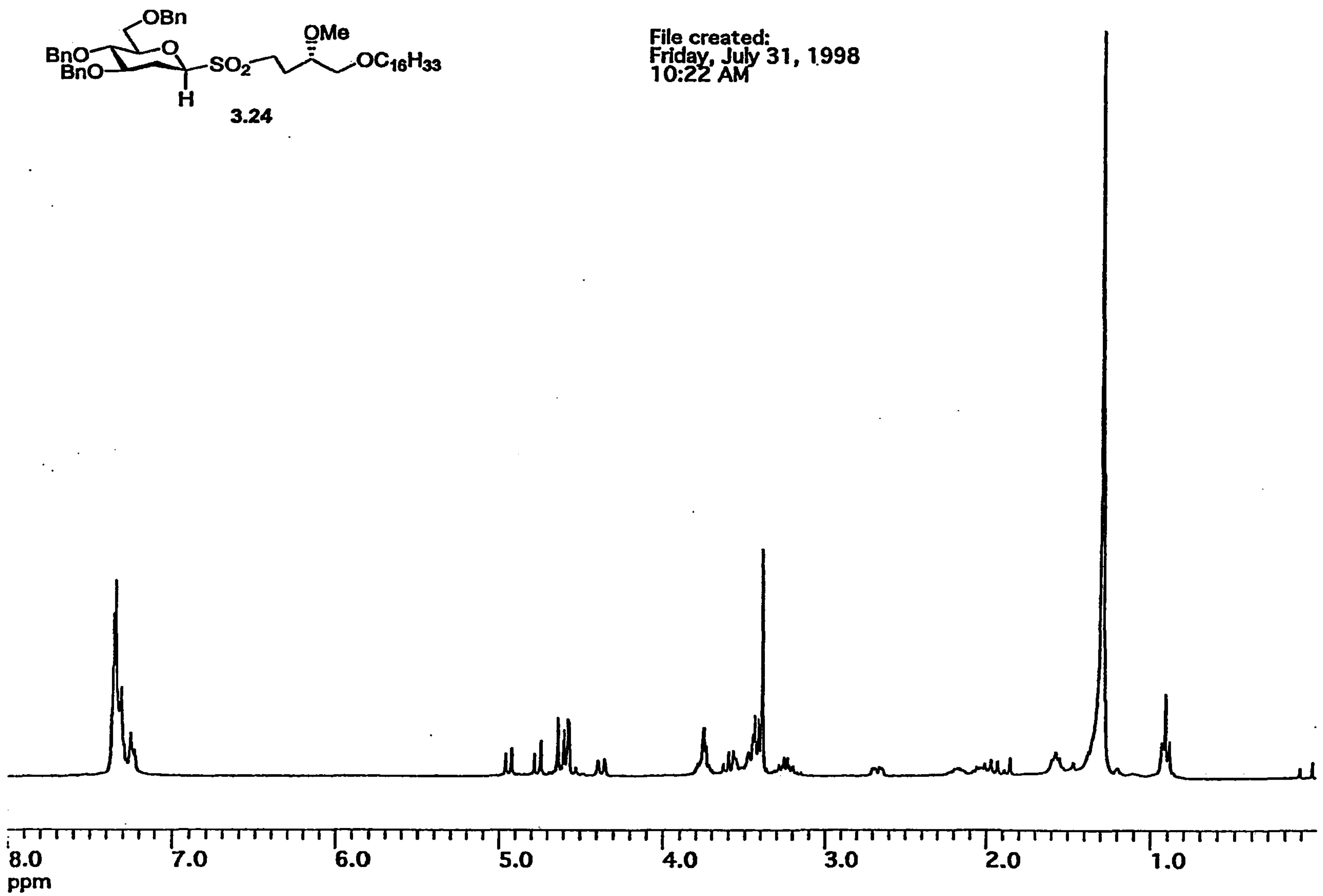

3.18

OBn
BnO
BnO
O
C17H35
H
File created:
Wednesday, October 28, 1998
12:55 PM
160
140
120
100
80
60
40
20
0
ppm



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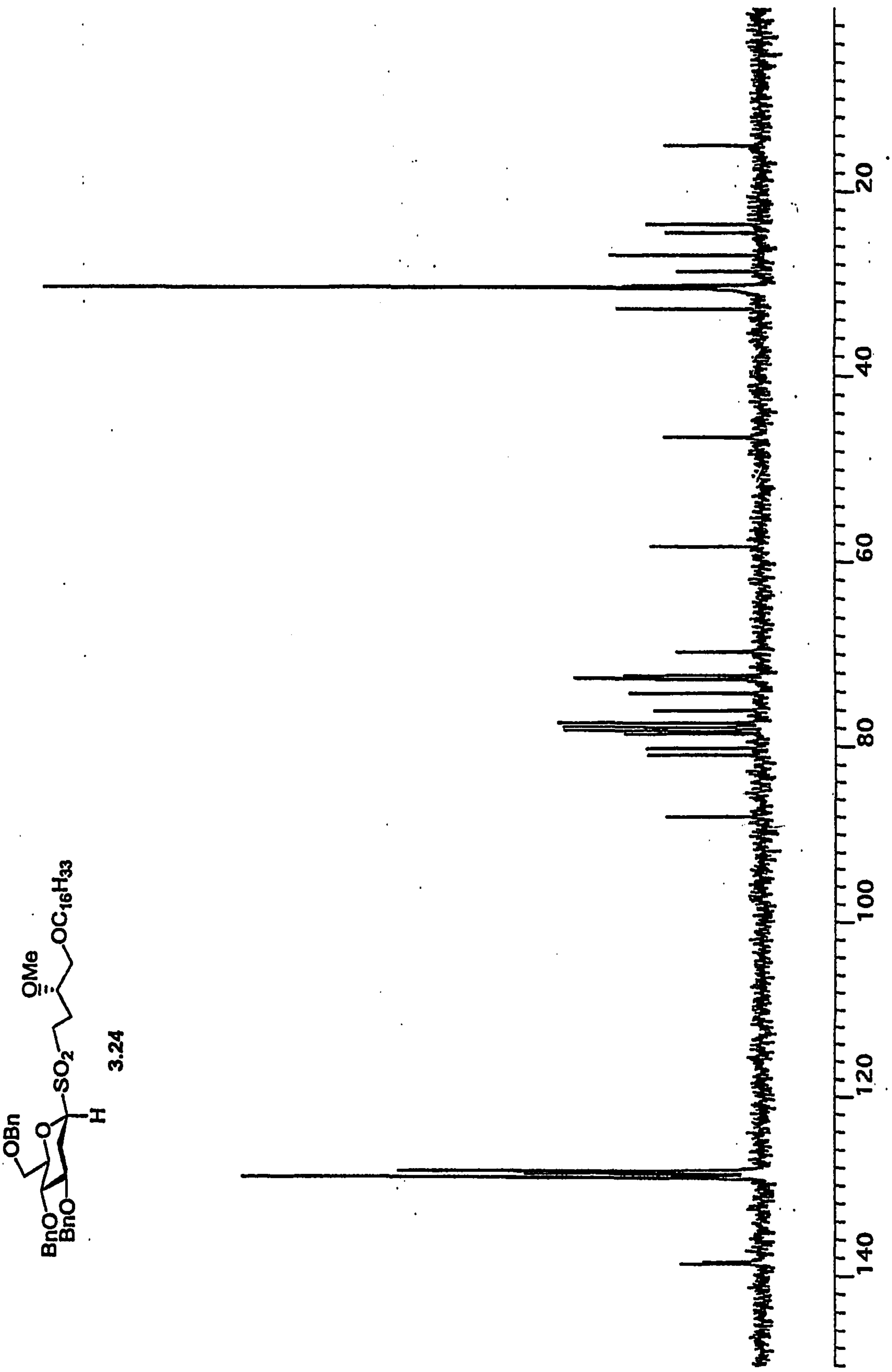
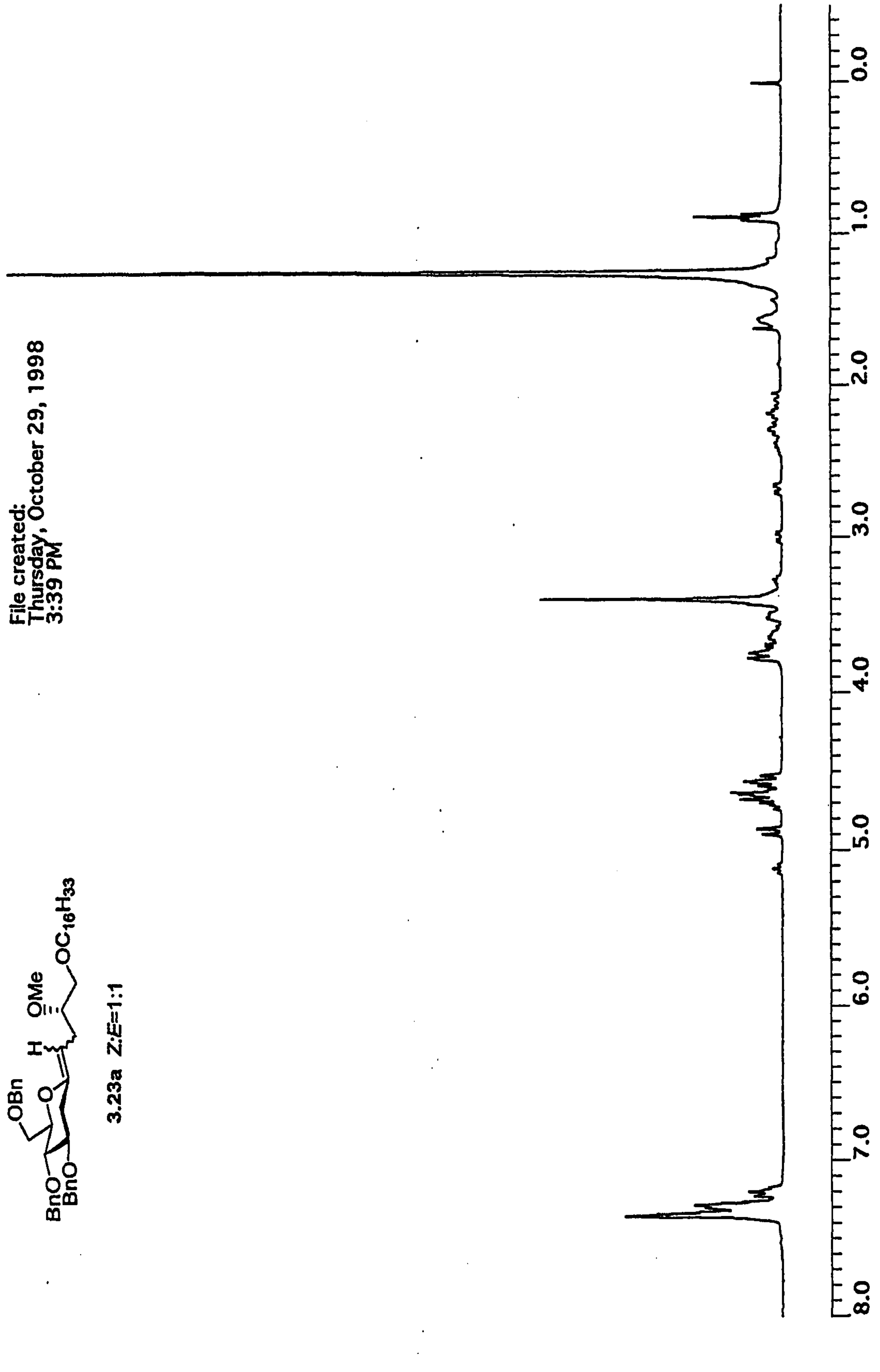


3.24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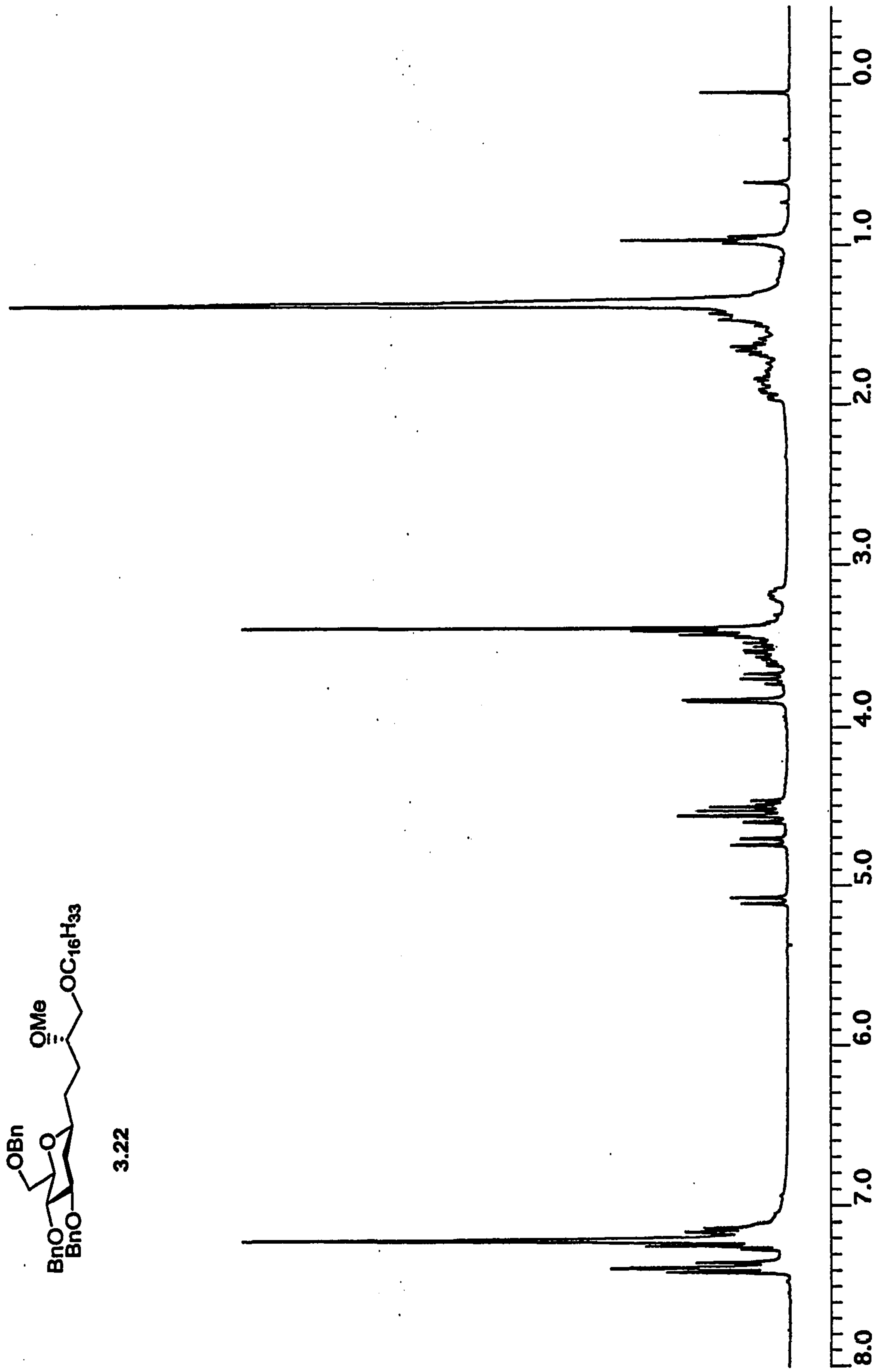
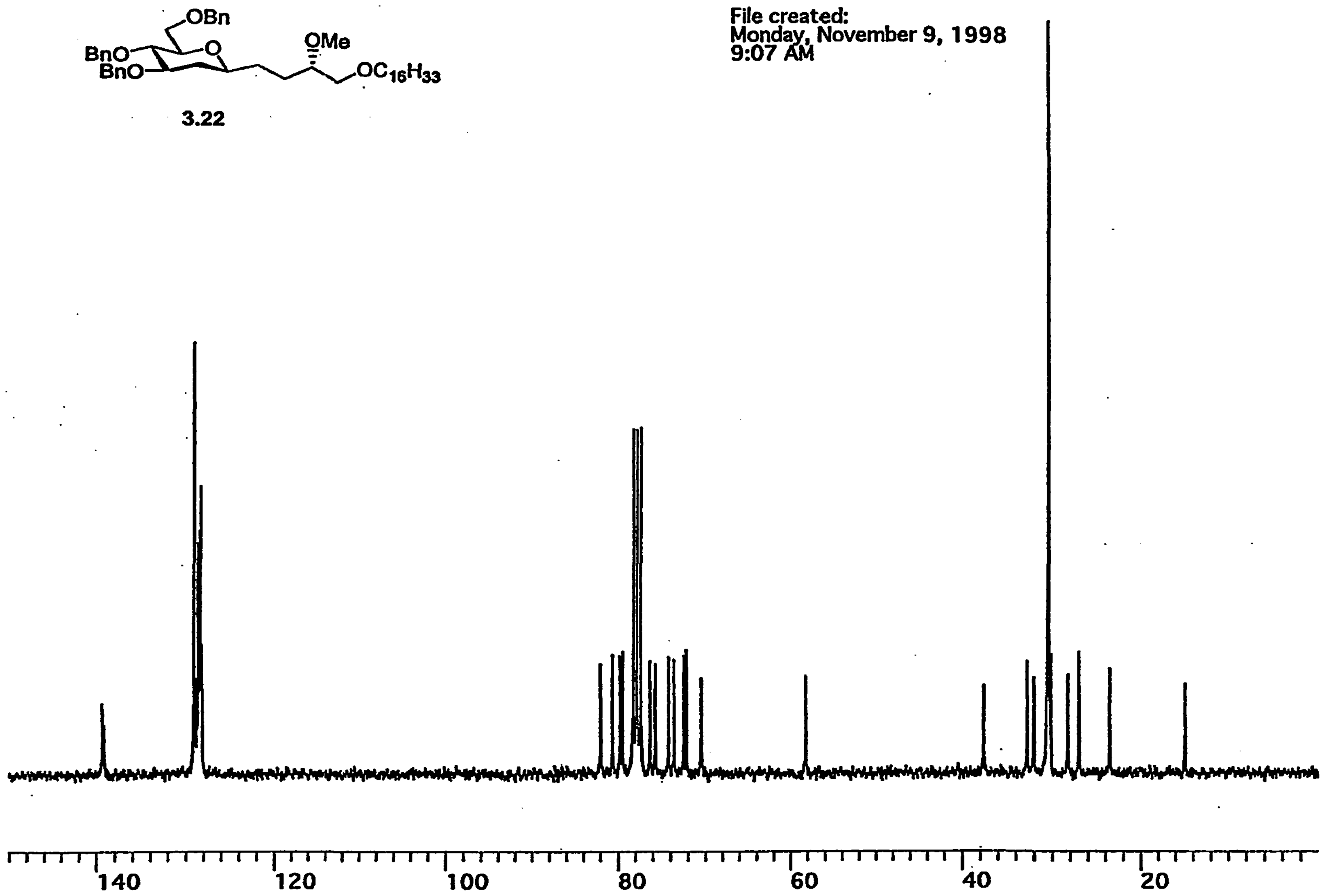
BnO
BnO
OBn
O
H
OMe
OC16H33
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0

3.23a Z:E=1:1



3.22



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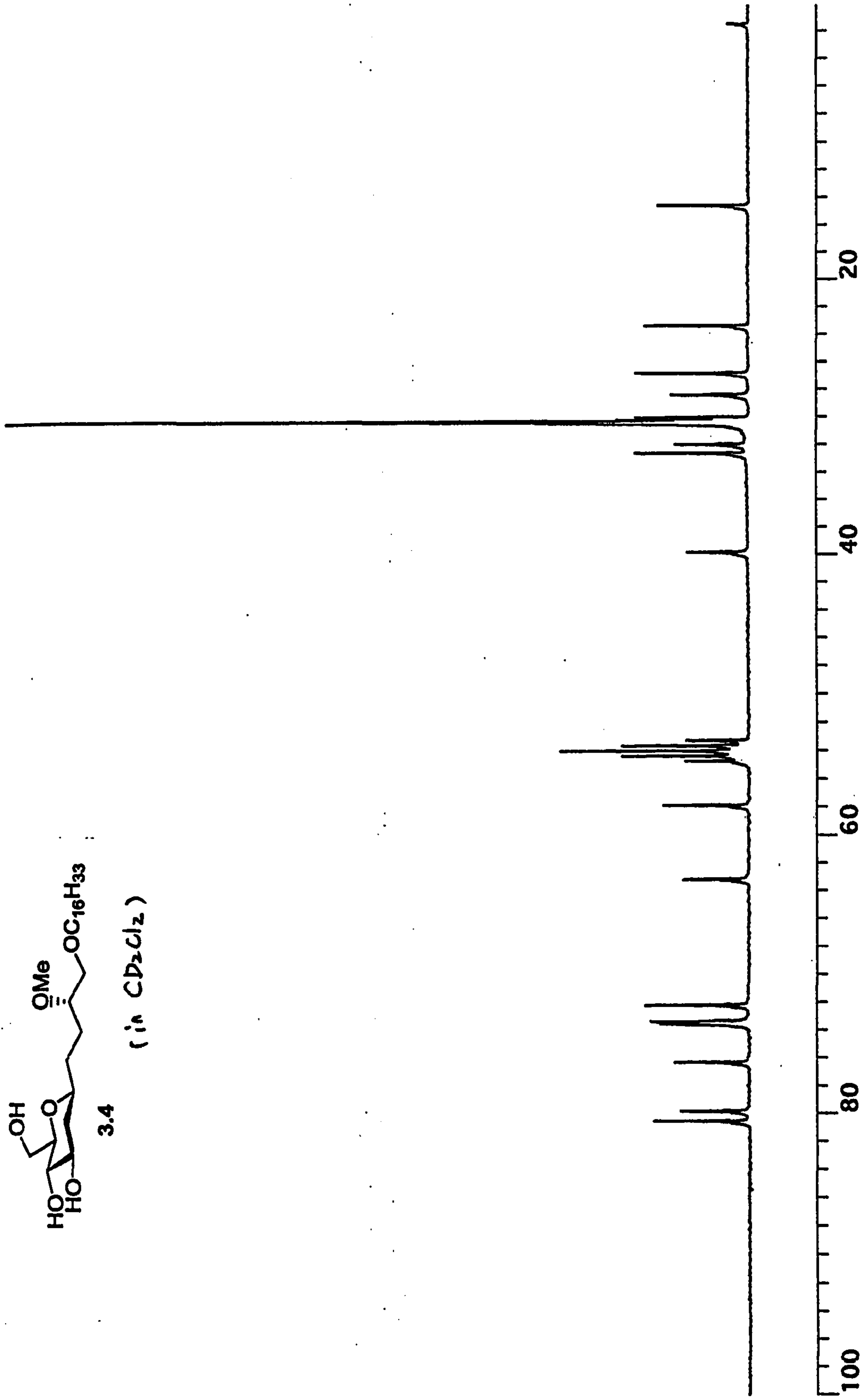
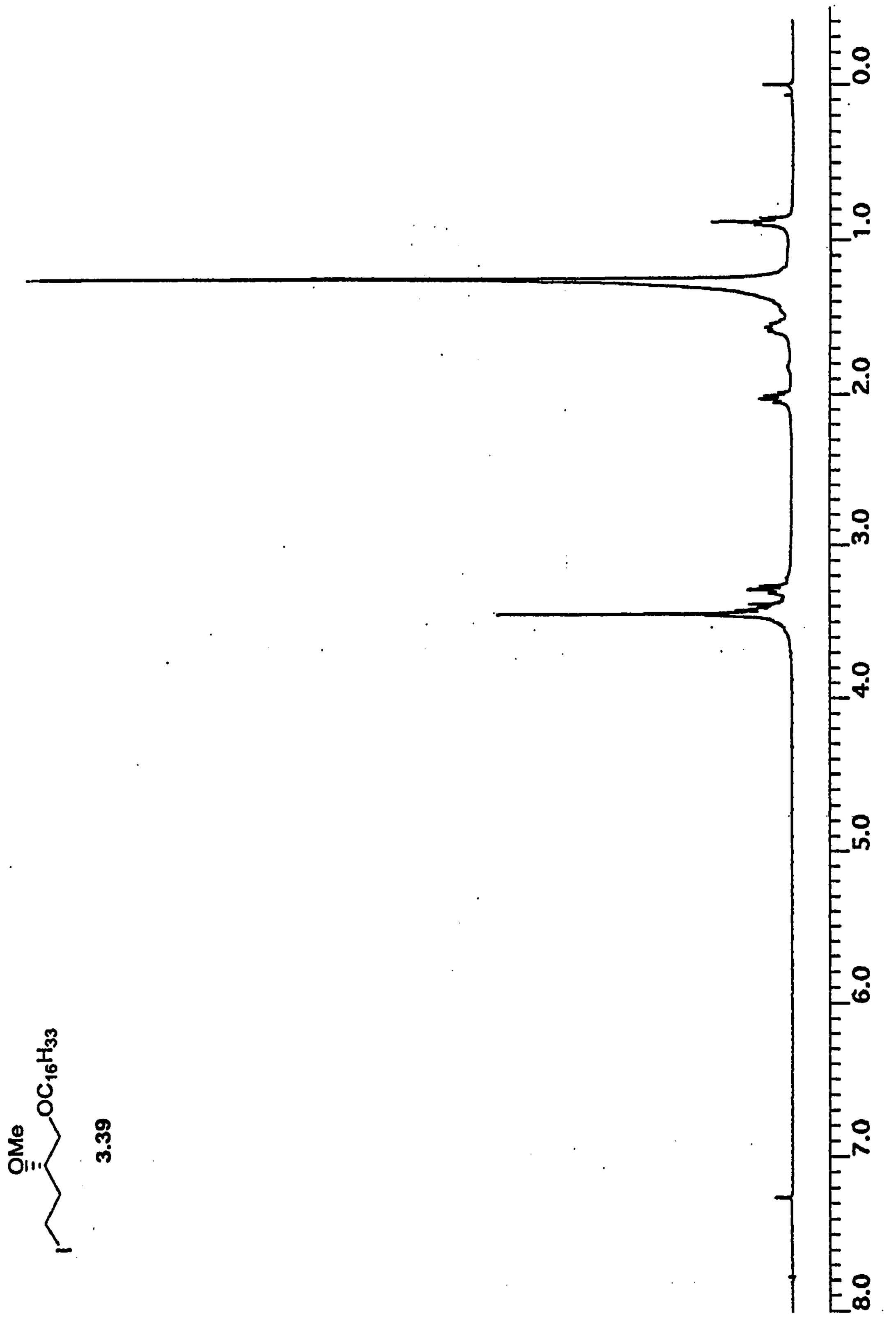
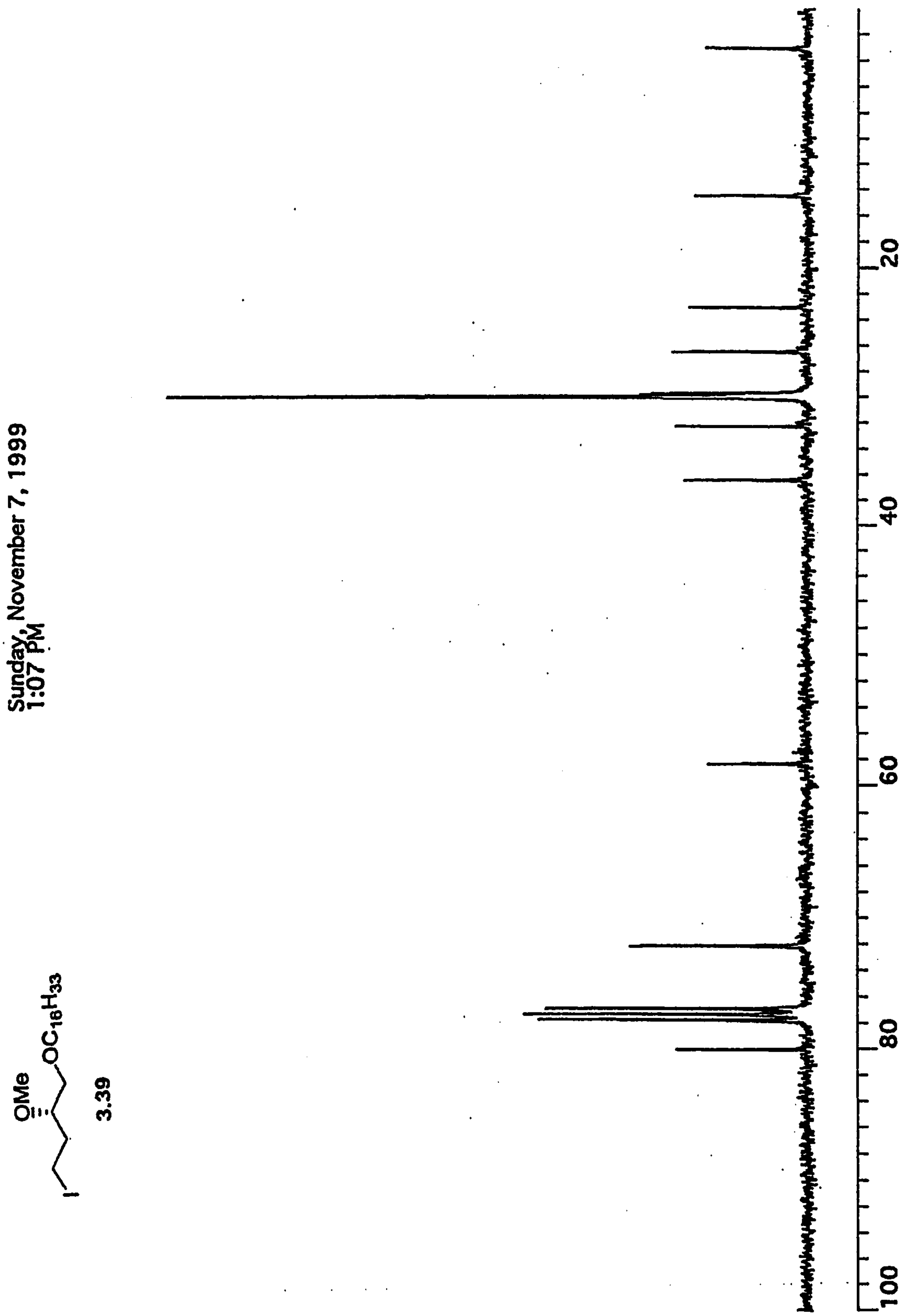


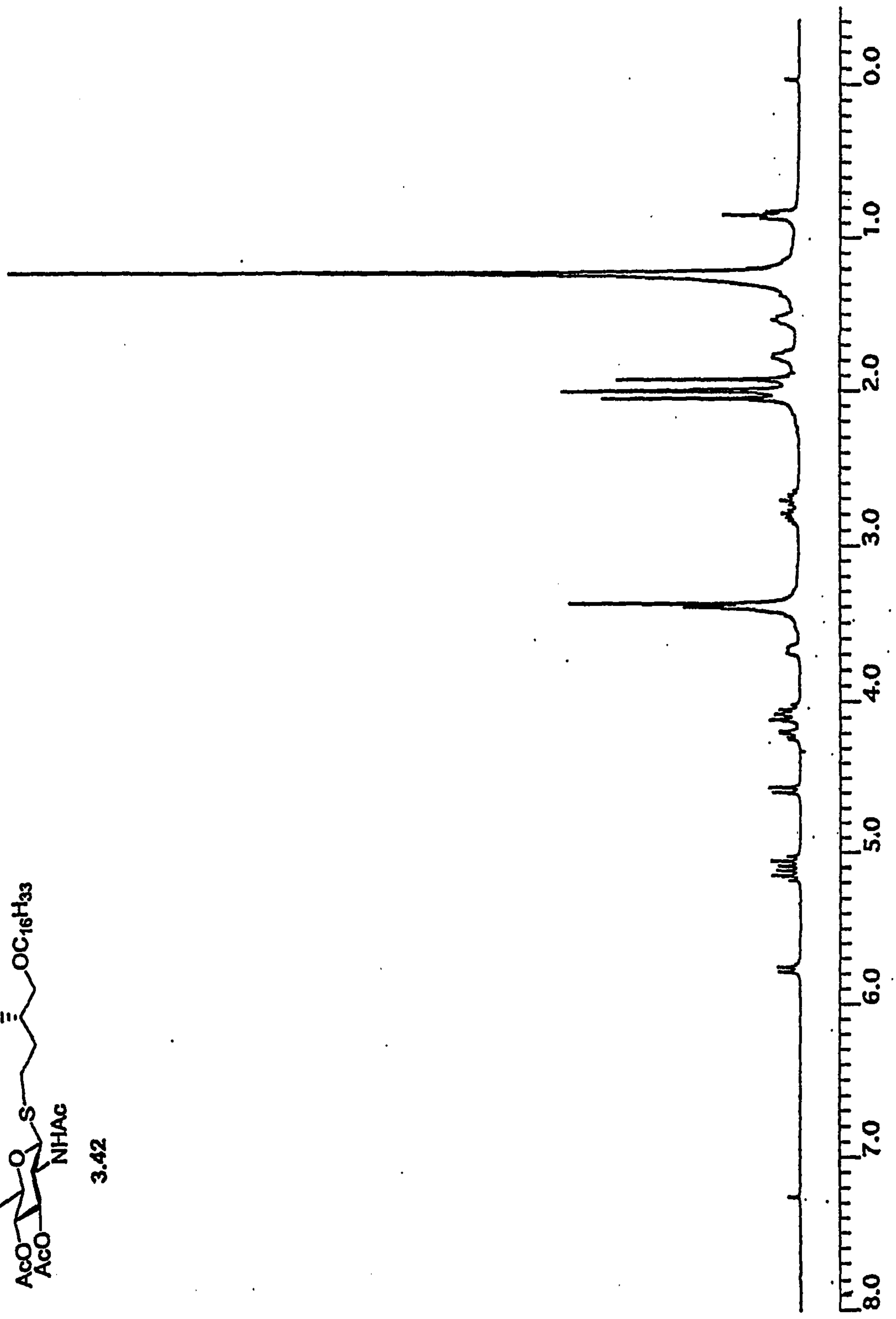
3.4

(in CD_2Cl_2)

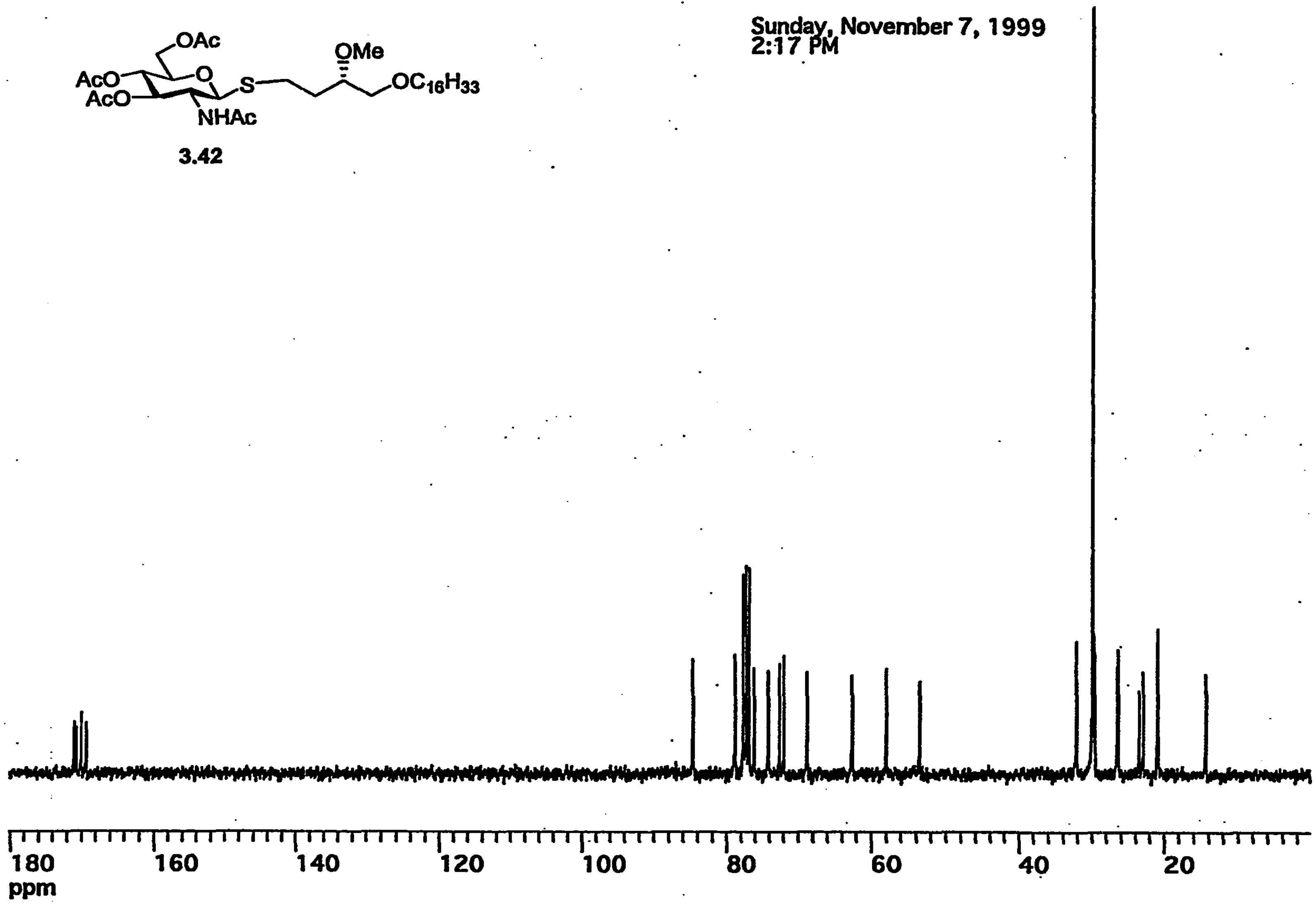


3.39


Sunday, November 7, 1999
1:07 PM
I
OMe
OC$_{16}$H$_{33}$
3.39
20
40
60
80
100

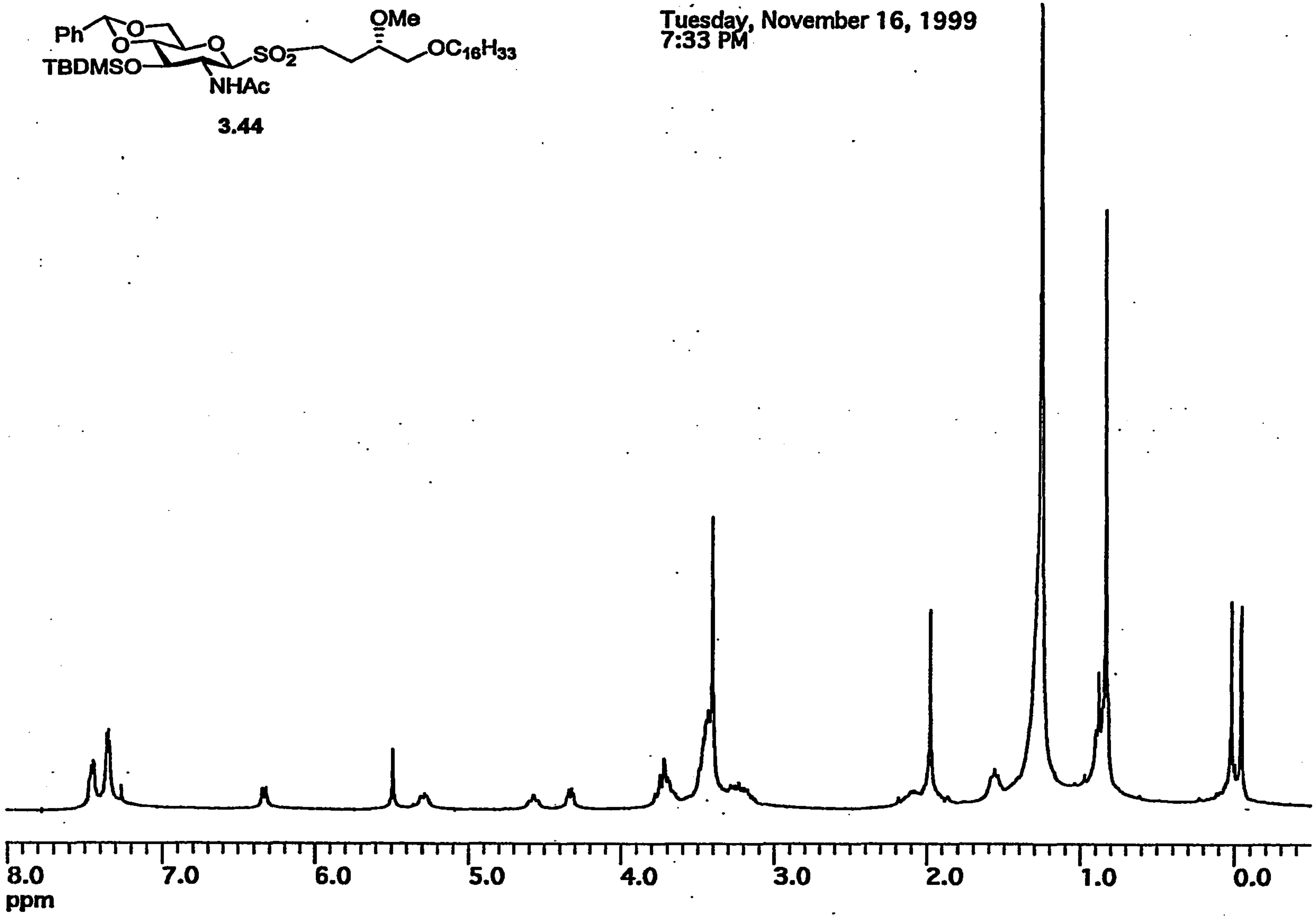


3.42



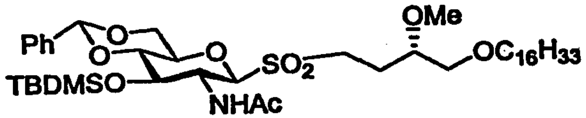
3.42

Sunday, November 7, 1999
2:17 PM



3.44

Tuesday, November 16, 1999
7:33 PM



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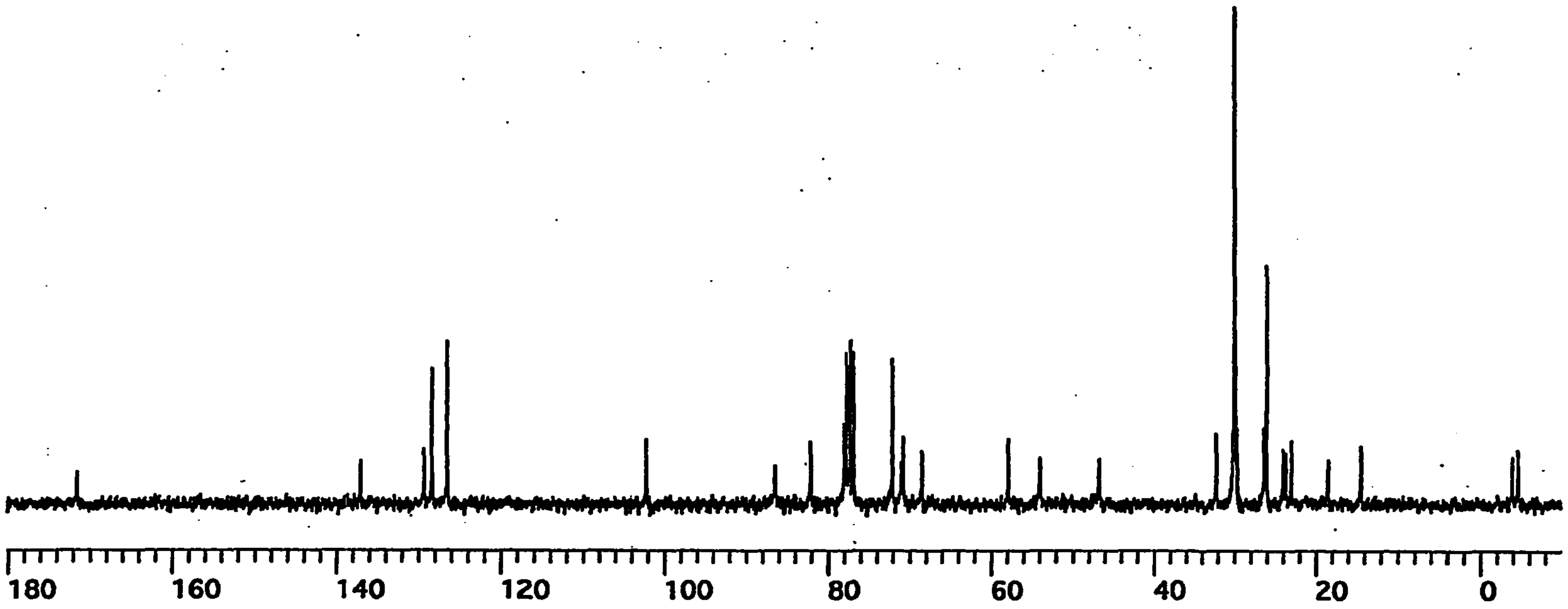
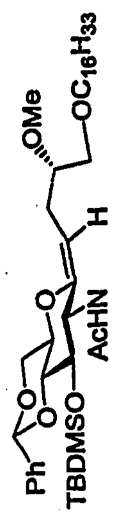
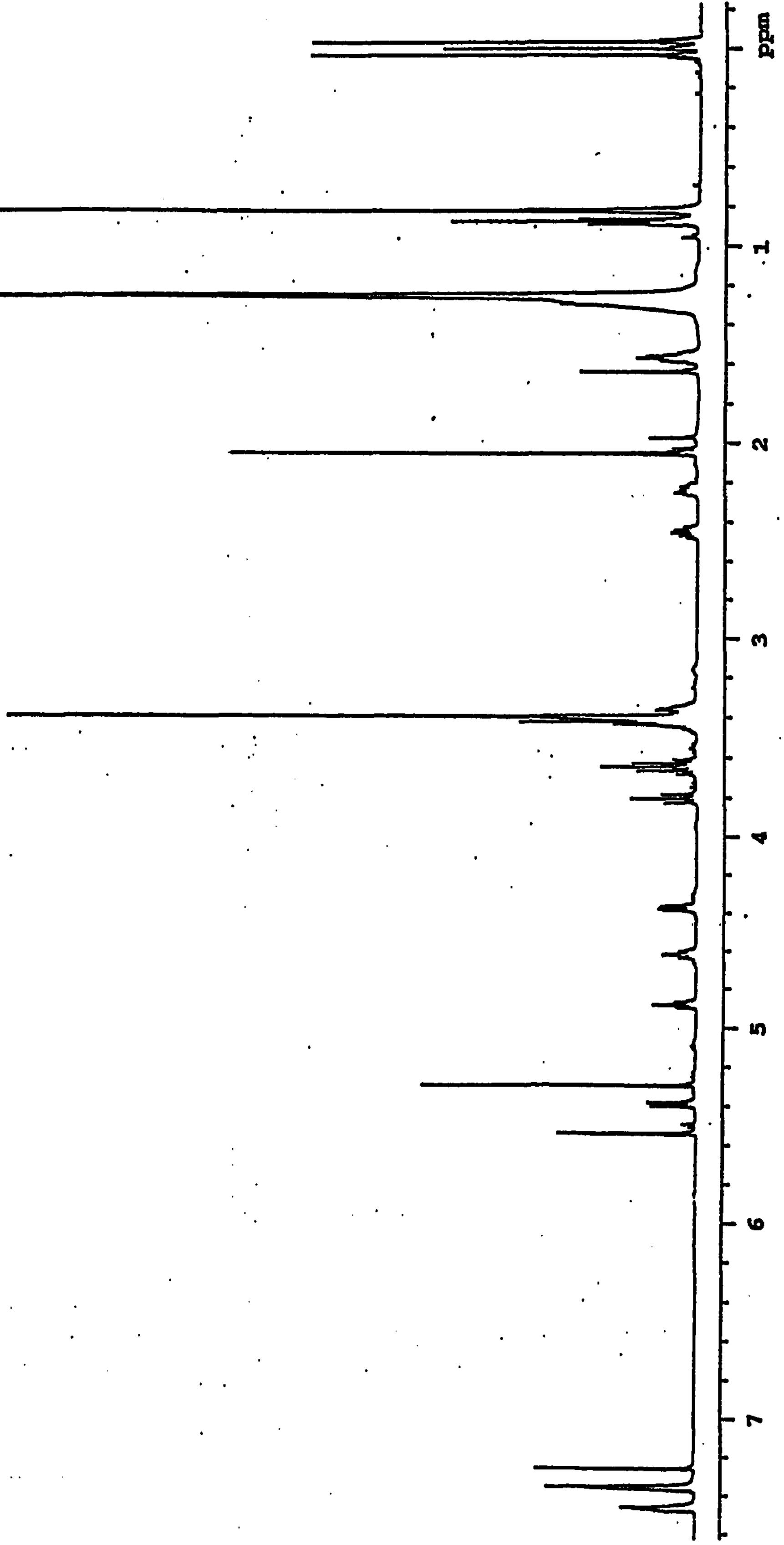
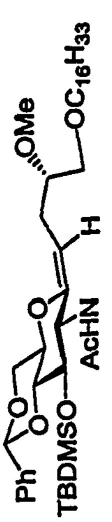


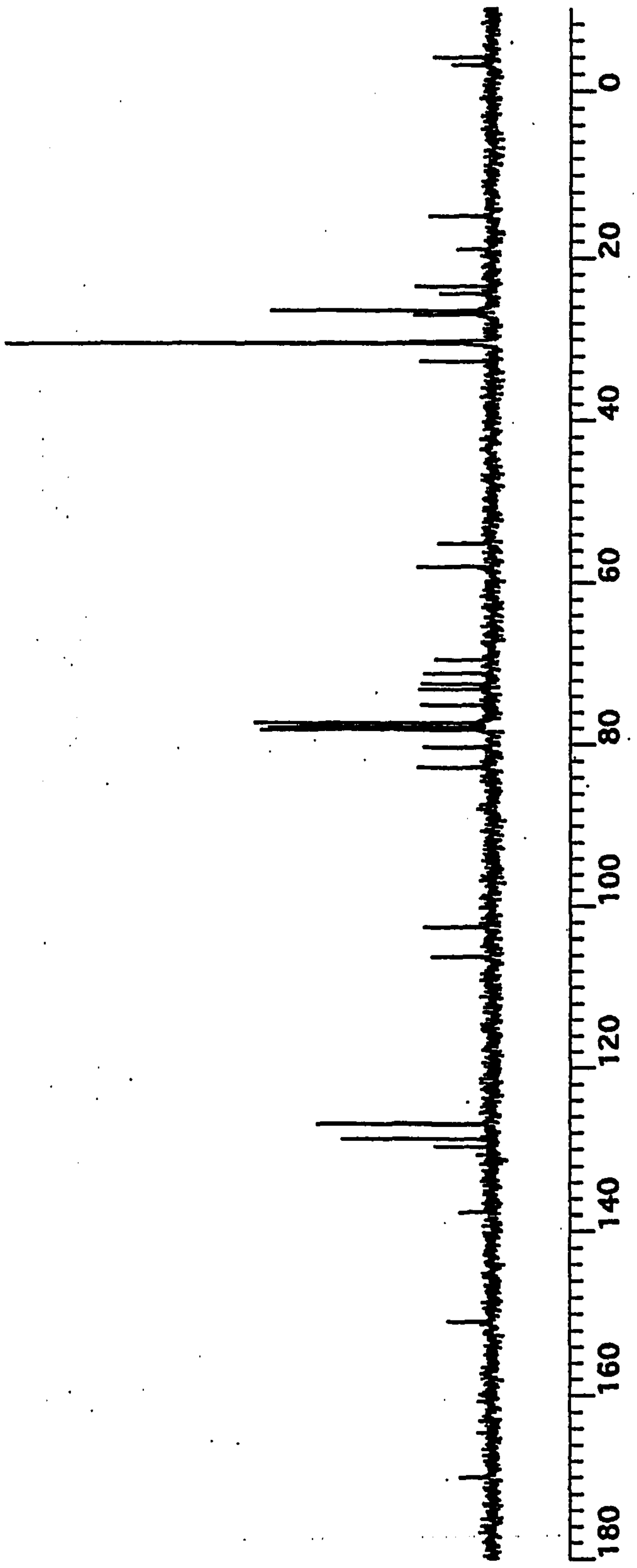


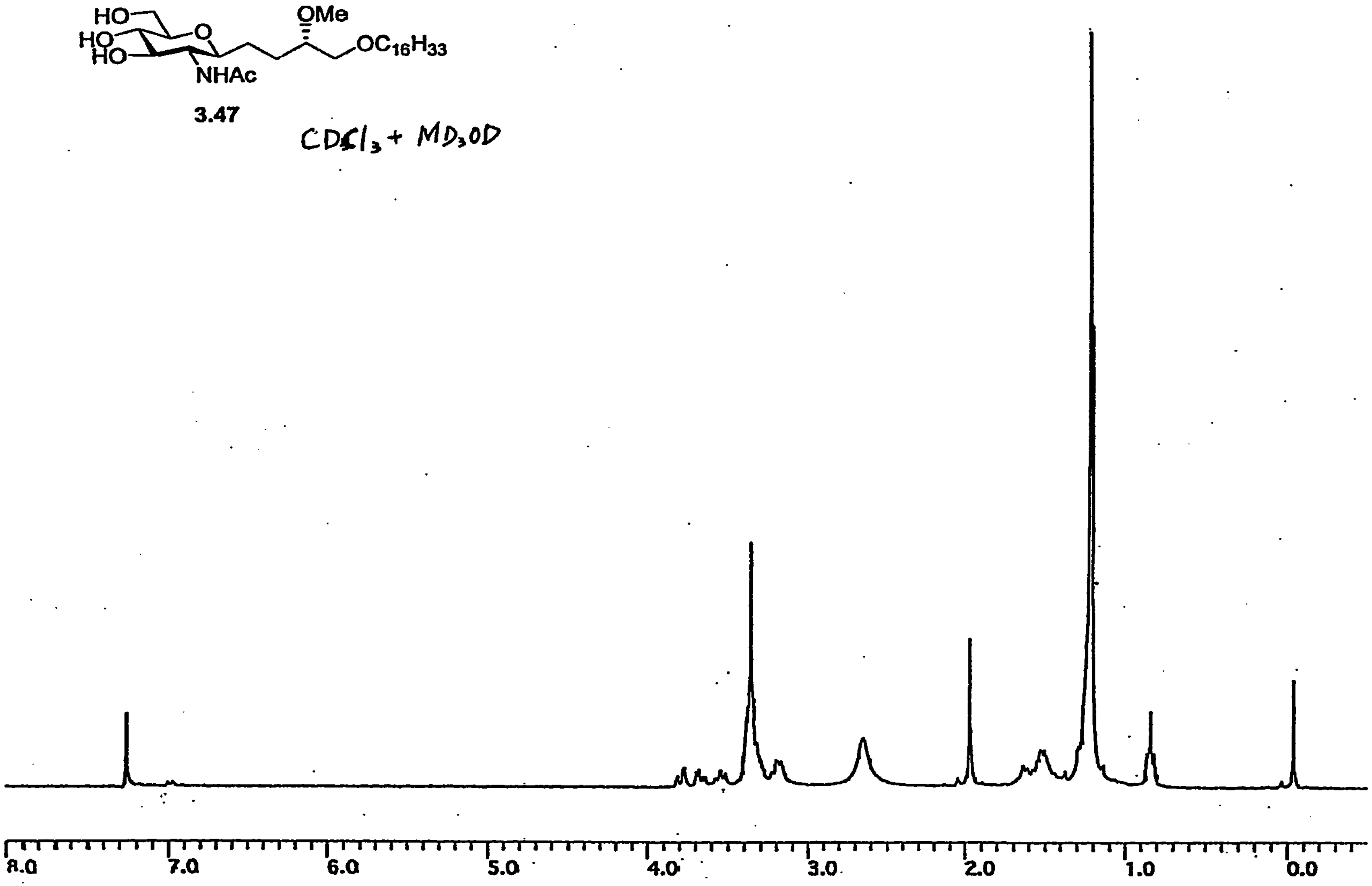
3.45 only *Z* isomer





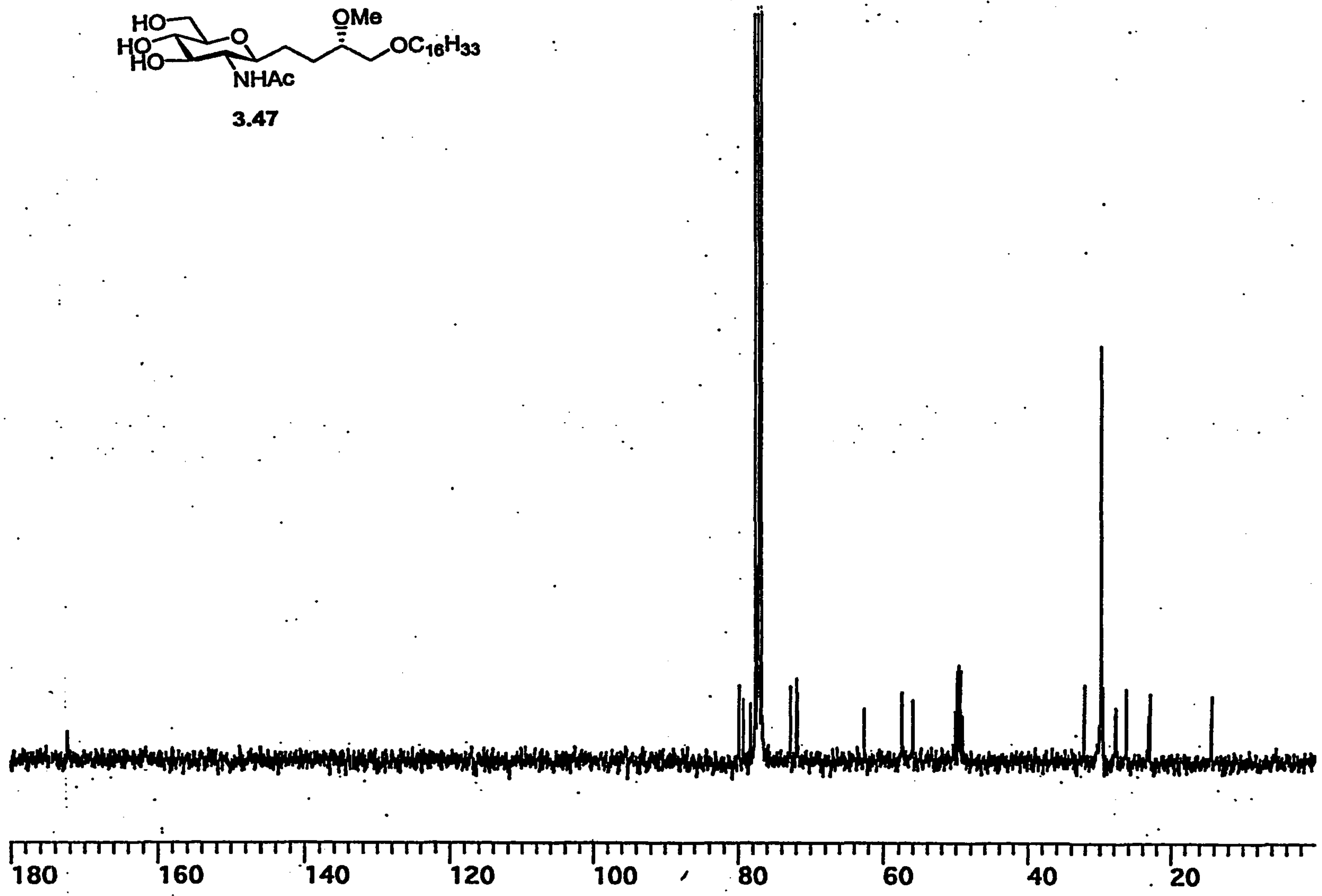
3.45 only *Z* isomer



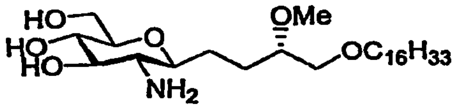


3.47

$CDCl_3 + MD_3OD$



3.47



3.5

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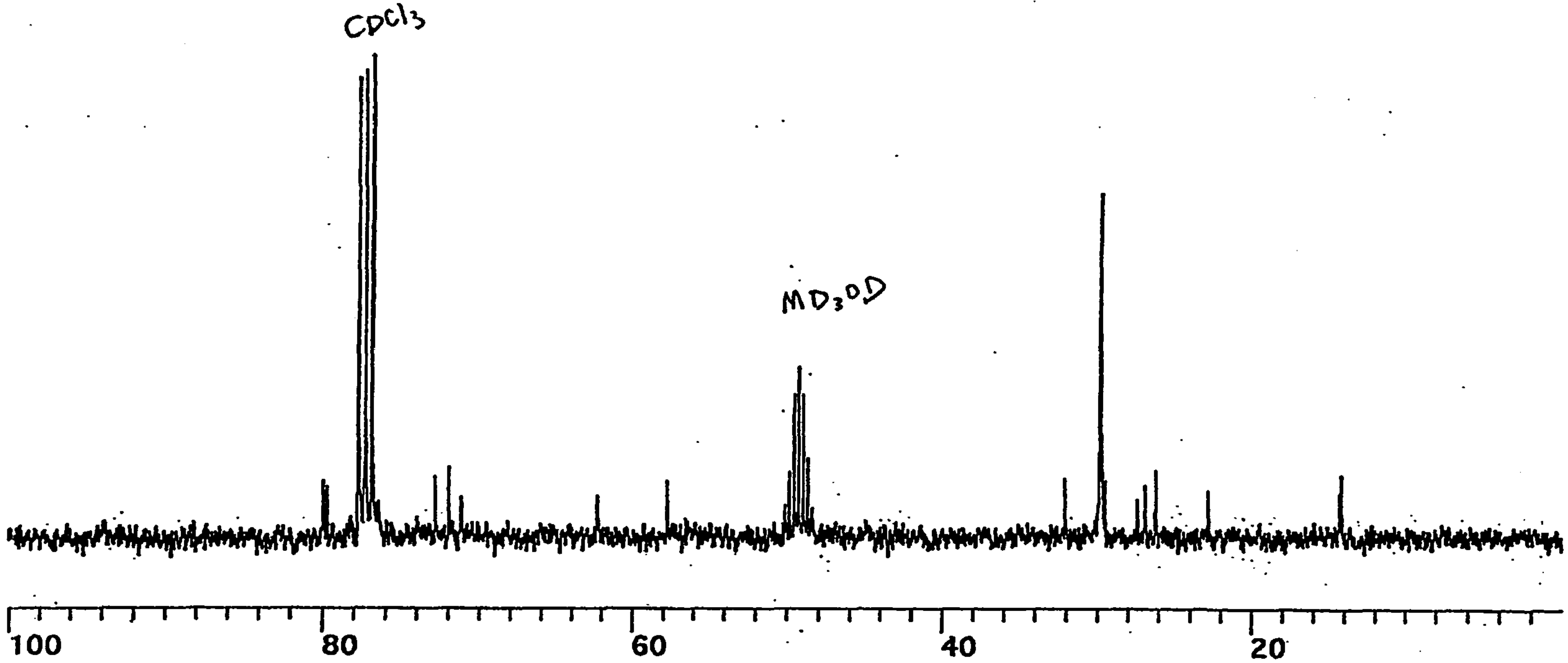

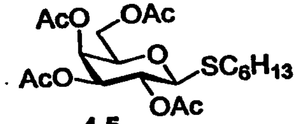

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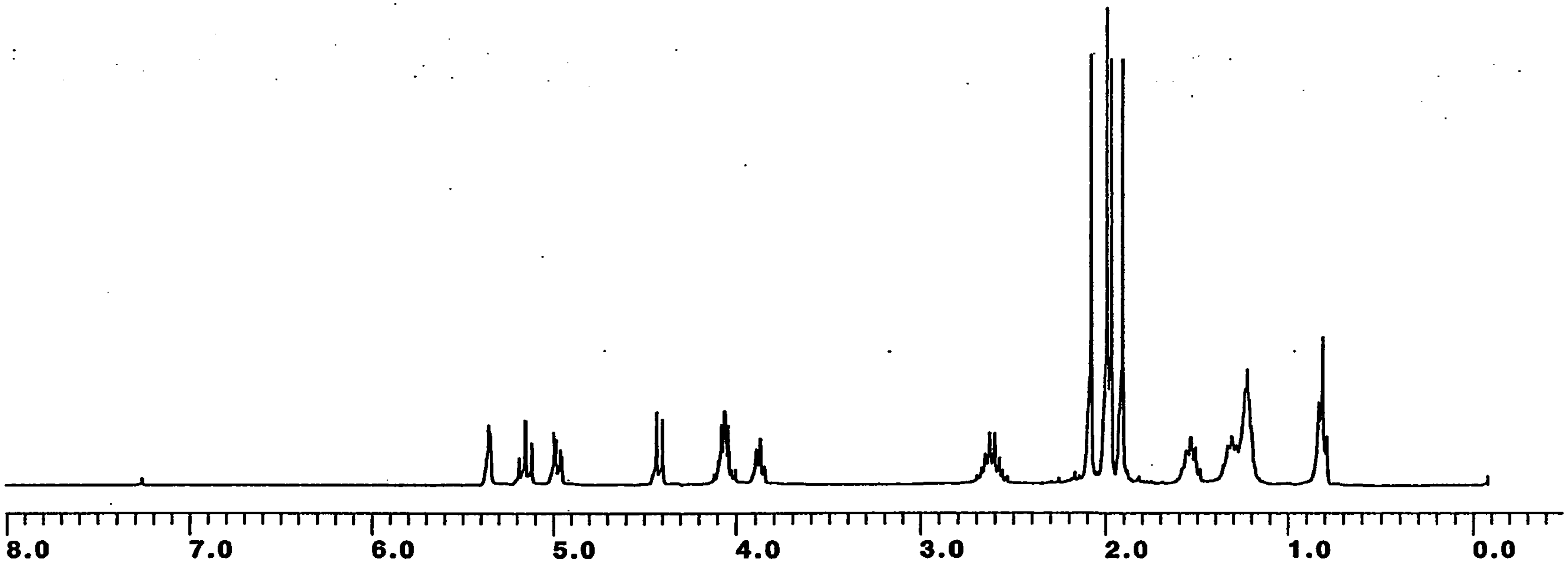

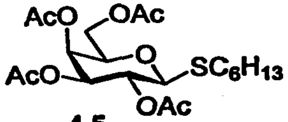

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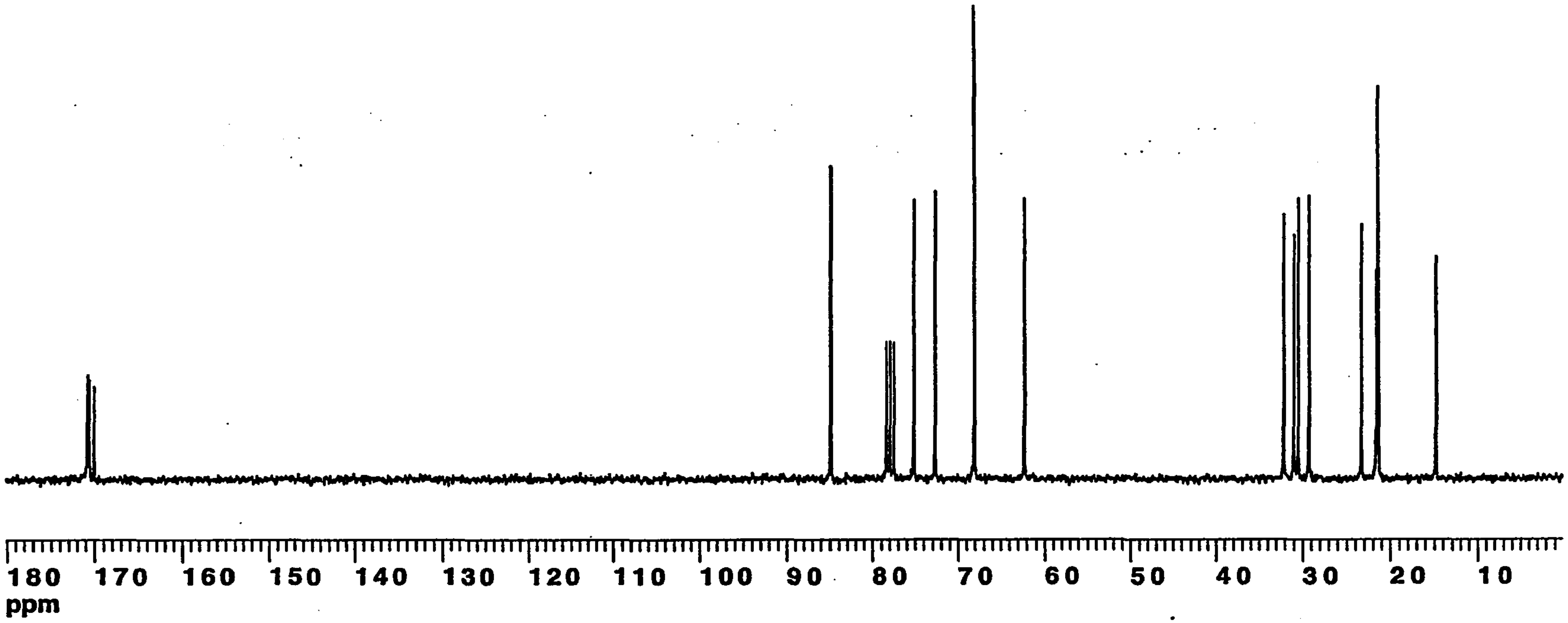

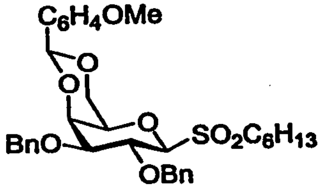

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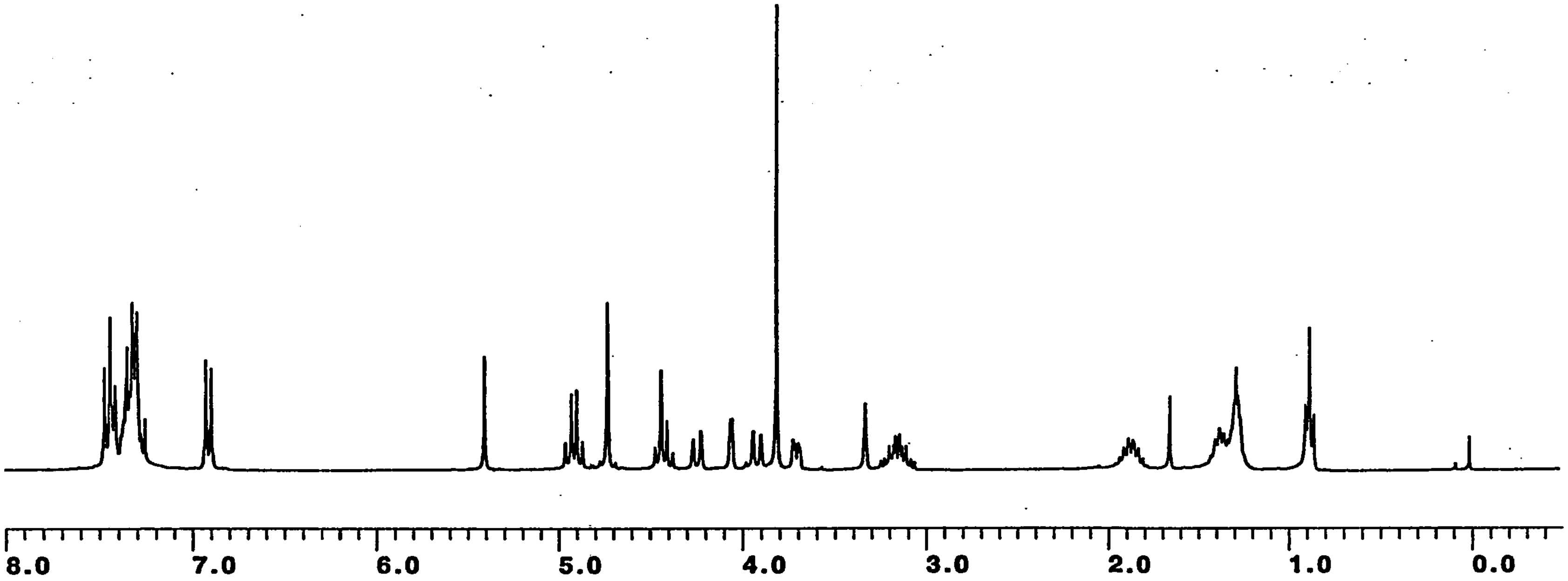

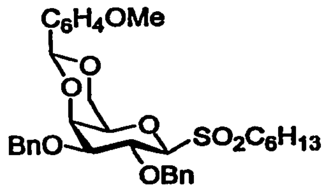

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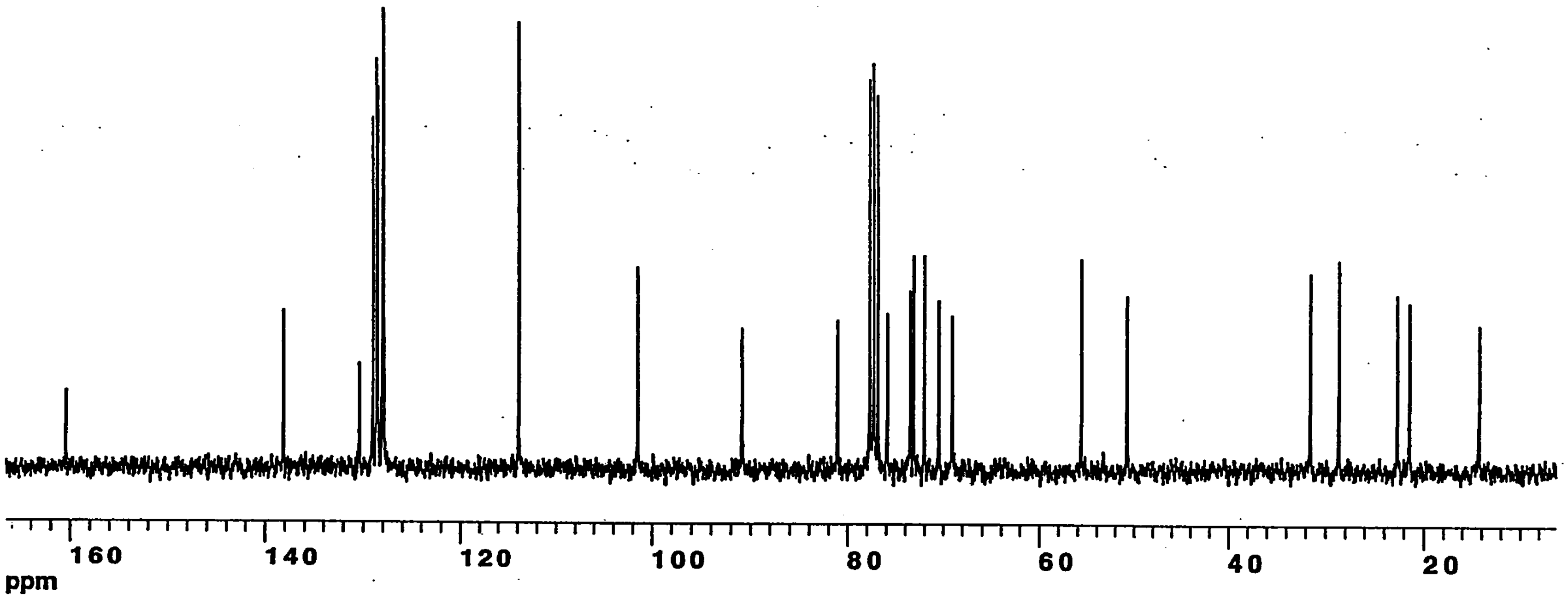

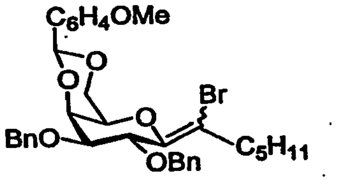

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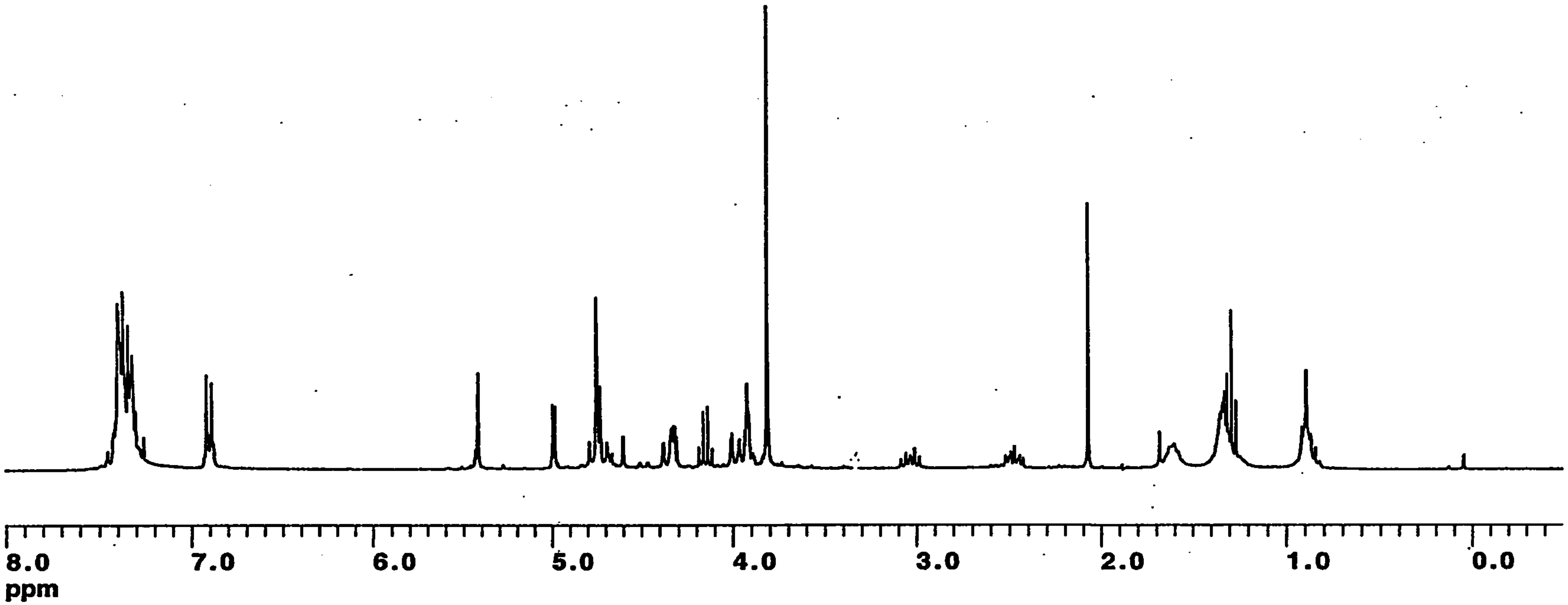

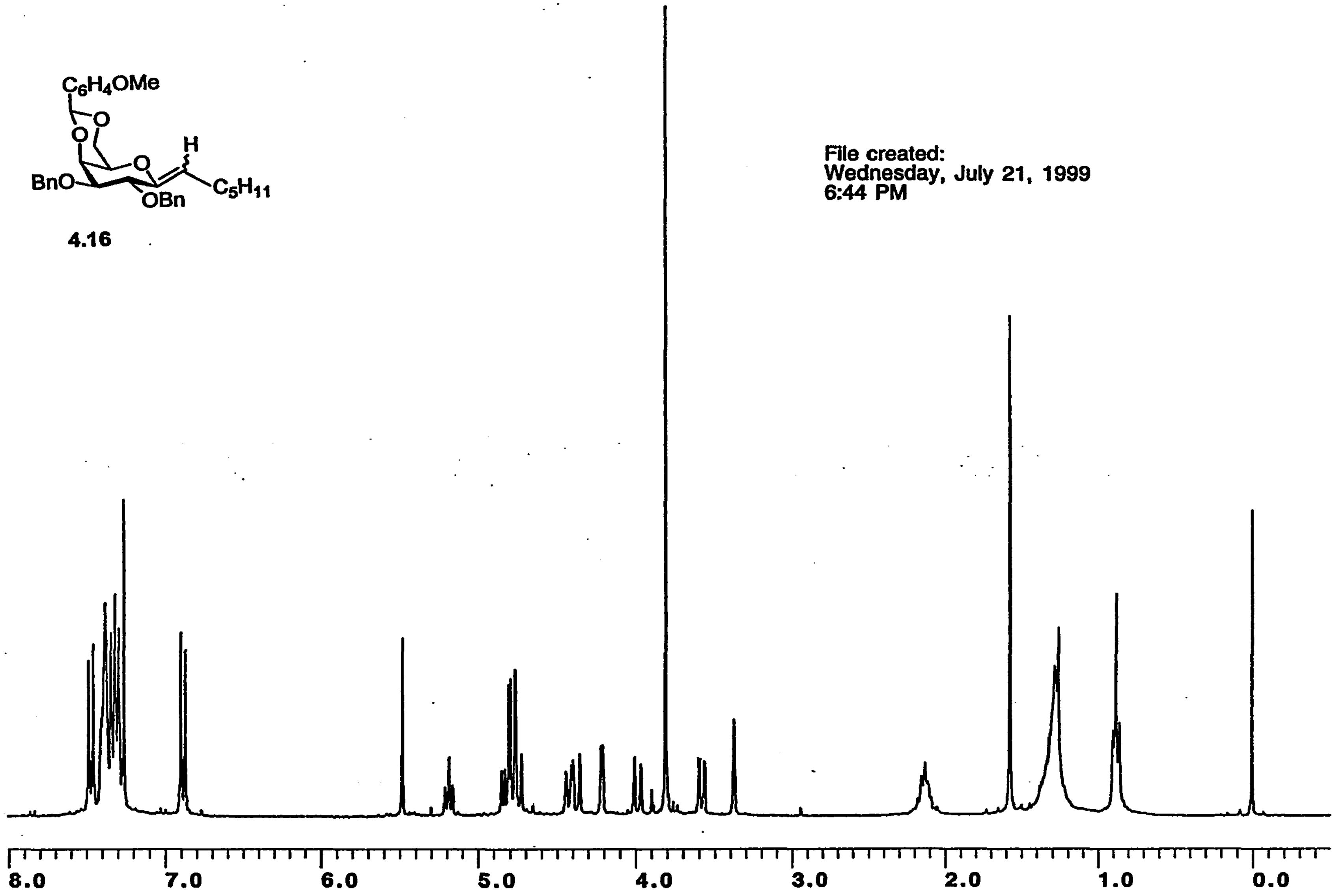

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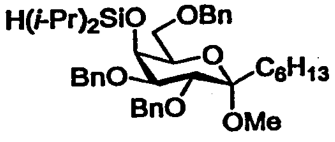

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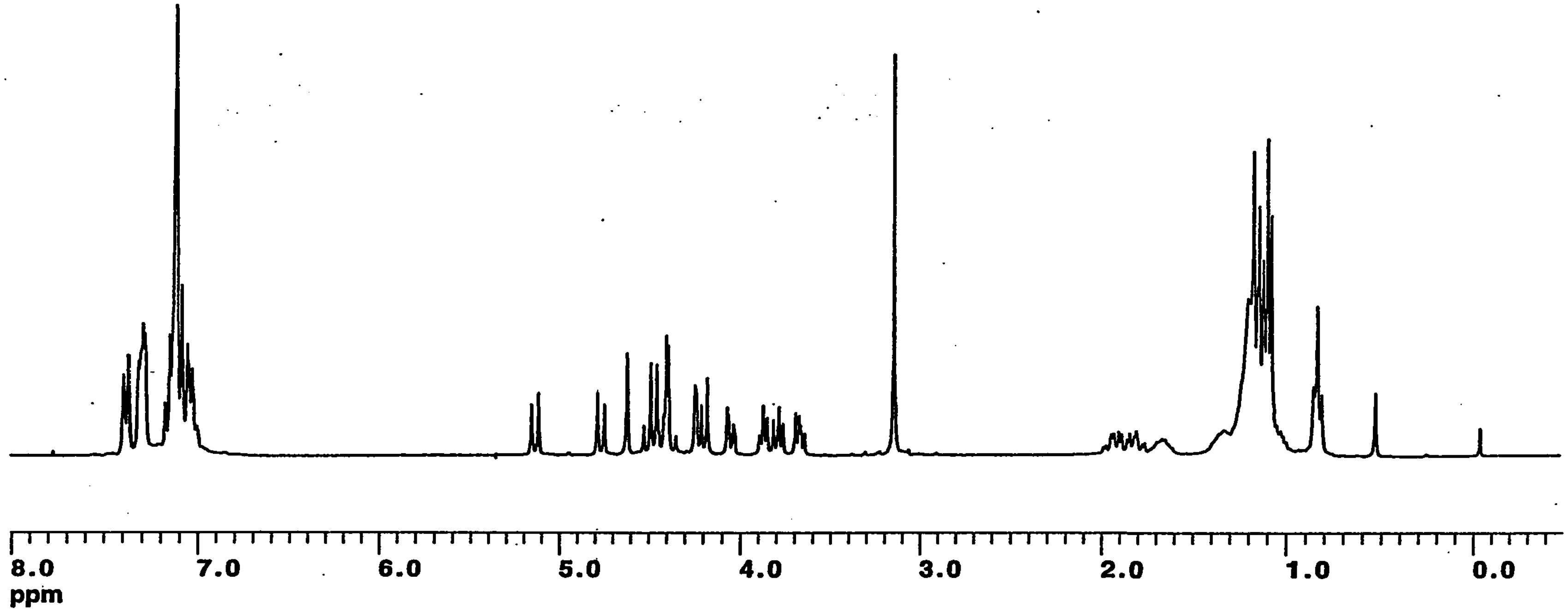

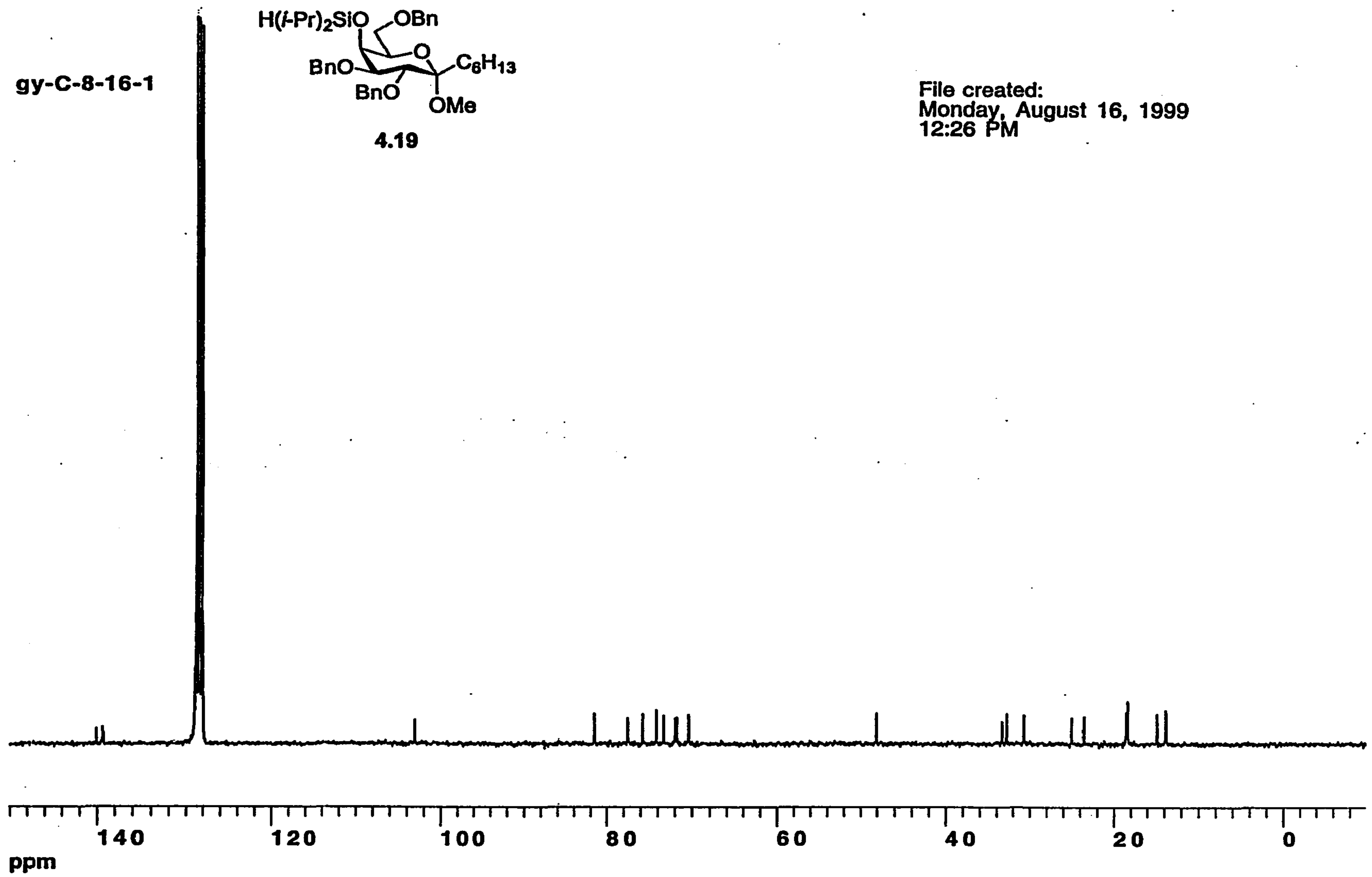

gy-C-8-16-1

4.19

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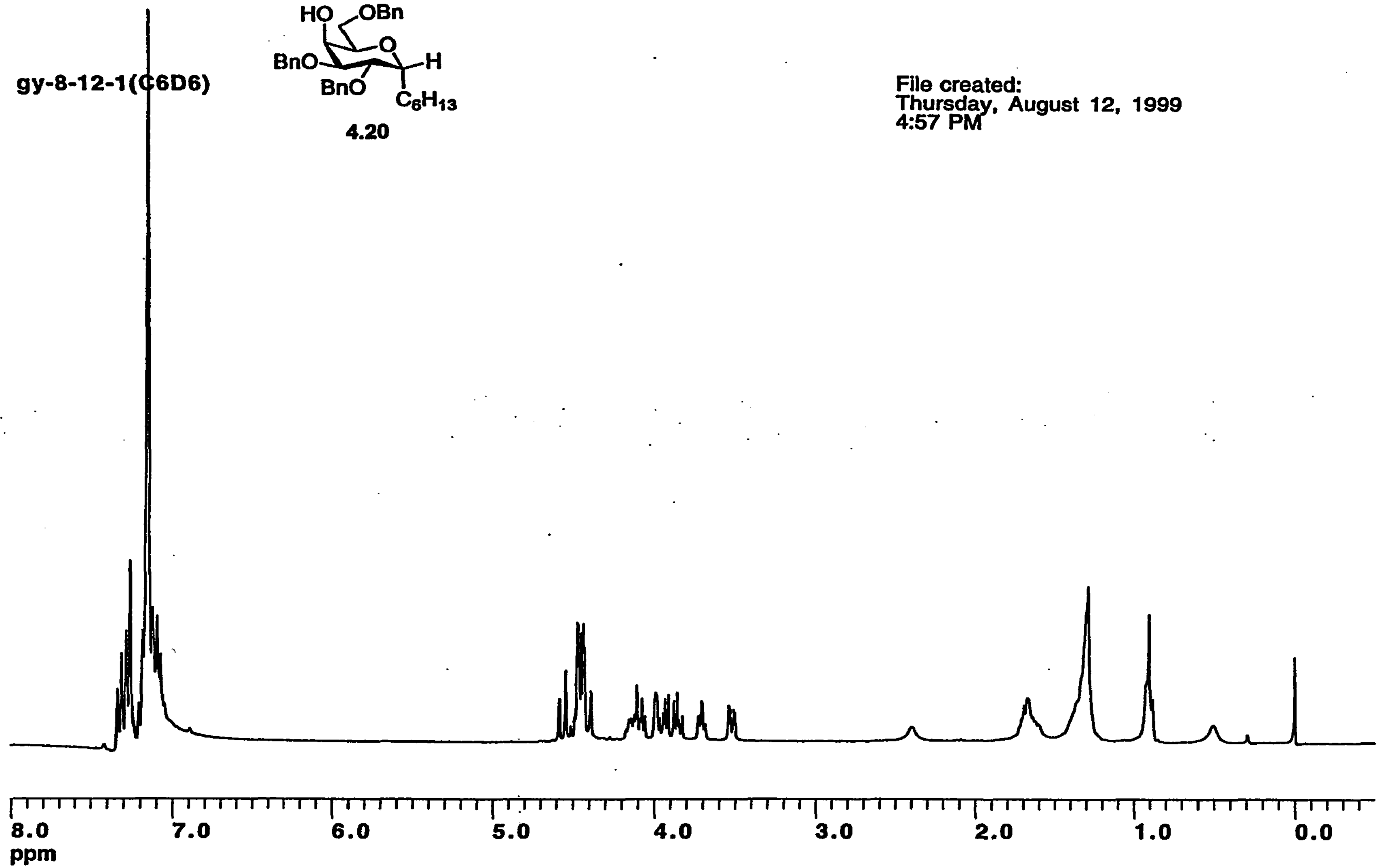
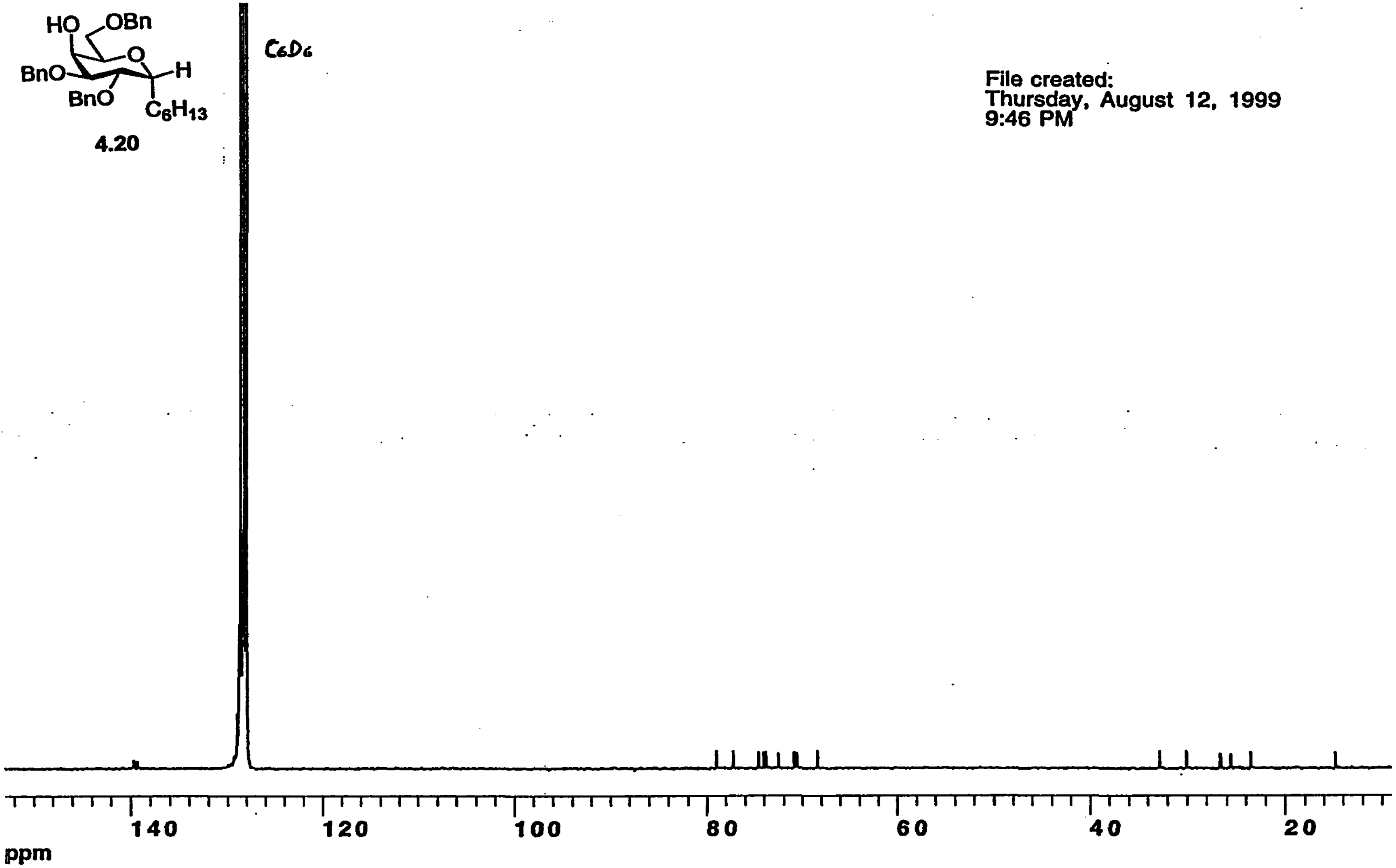

4.20
gy-8-12-1(C6D6)
HO
OBn
O
BnO
BnO
H
C6H13
File created:
Thursday, August 12, 1999
4:57 PM
8.0
ppm
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0



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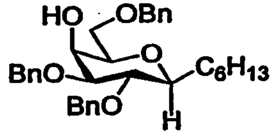

4.27

C_6D_6

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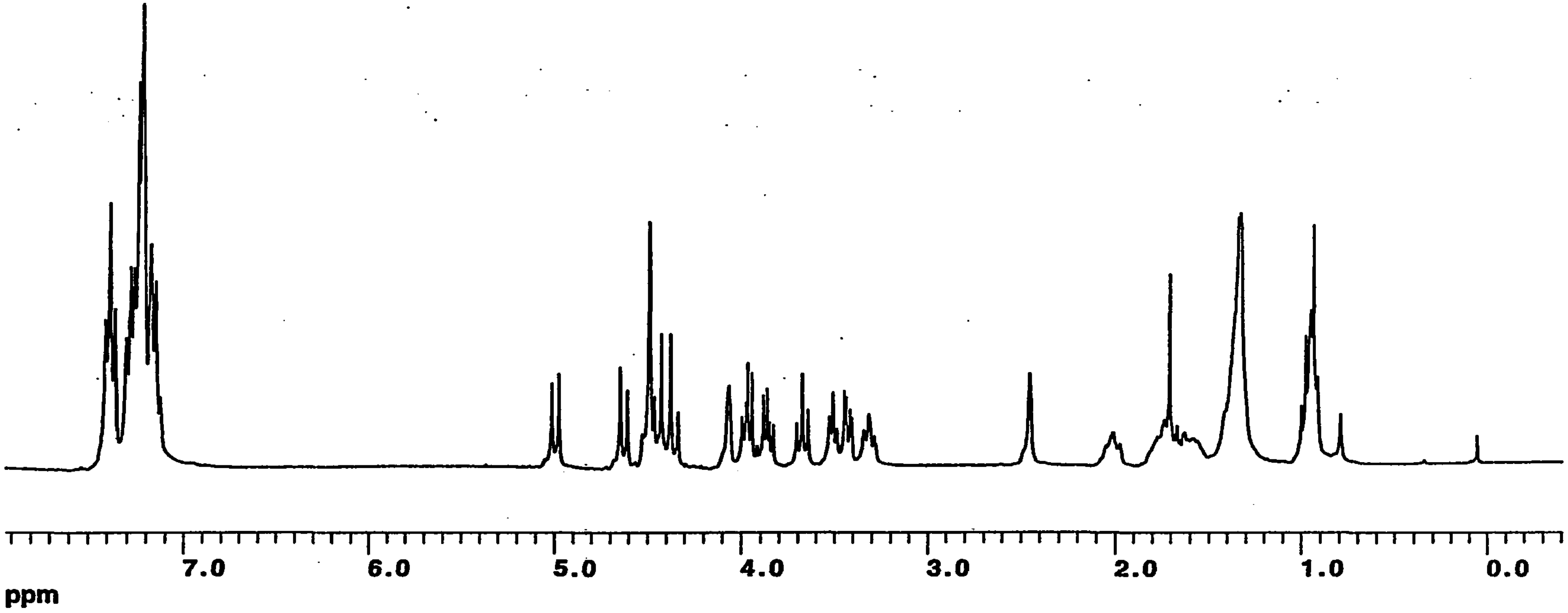

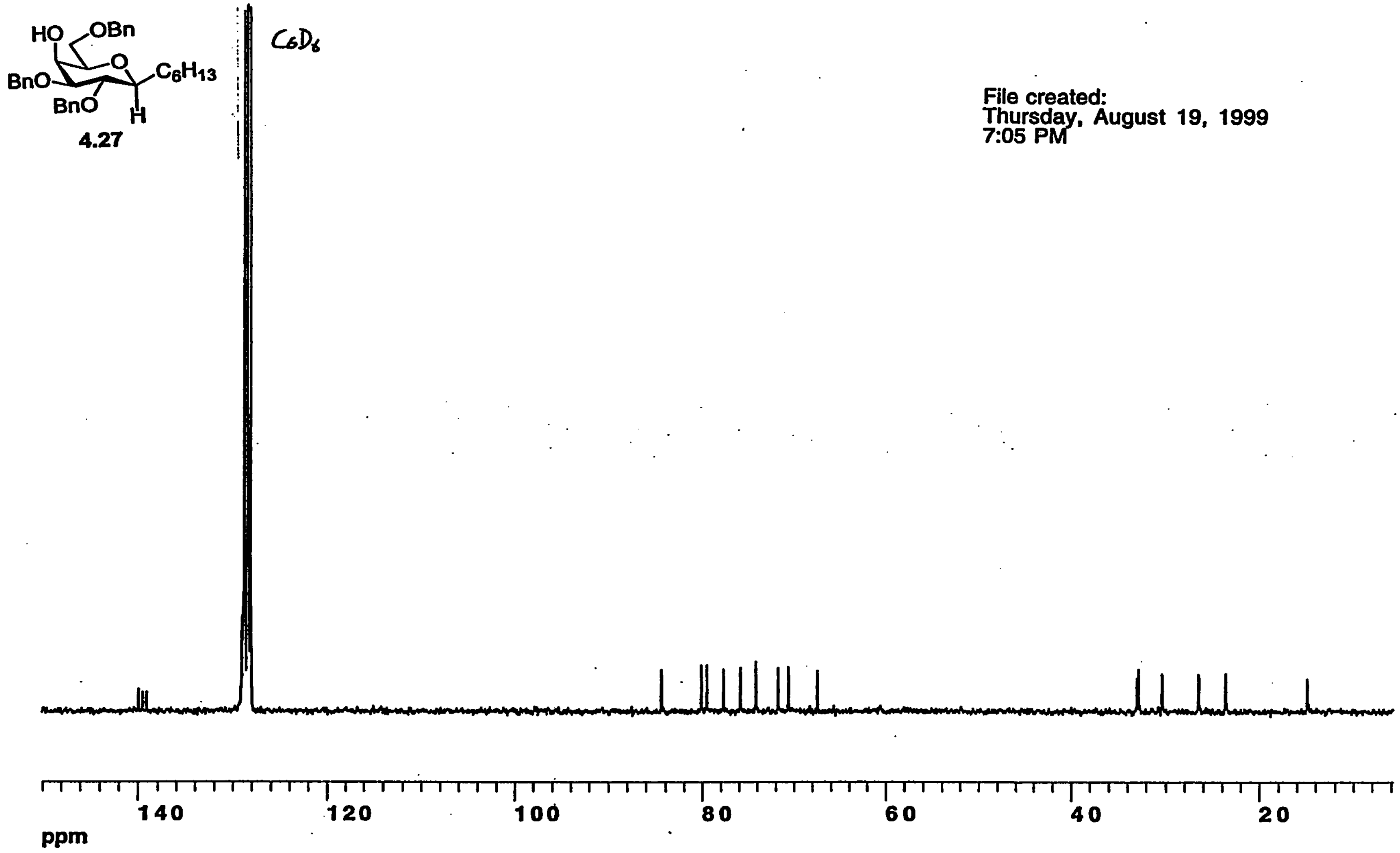

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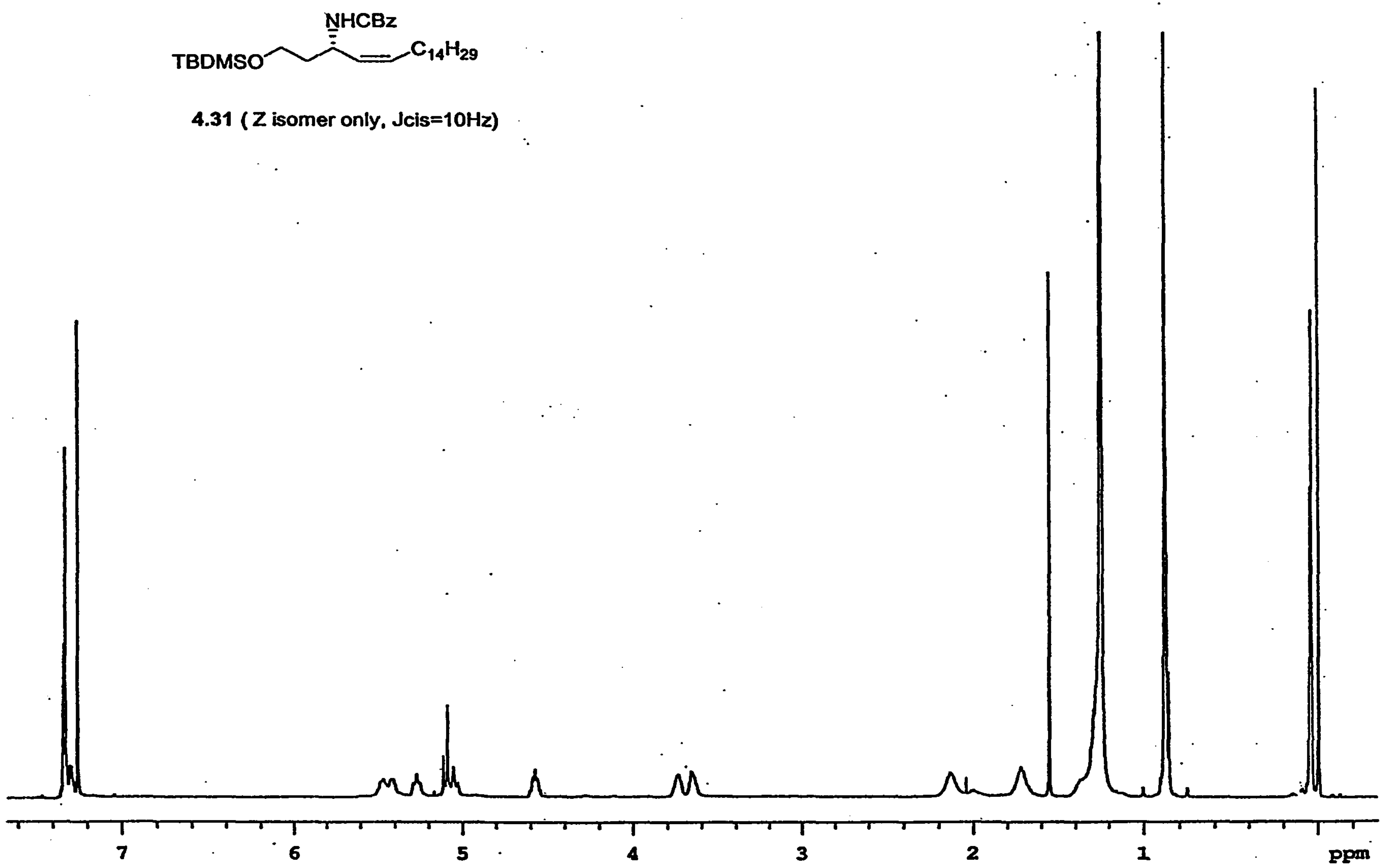

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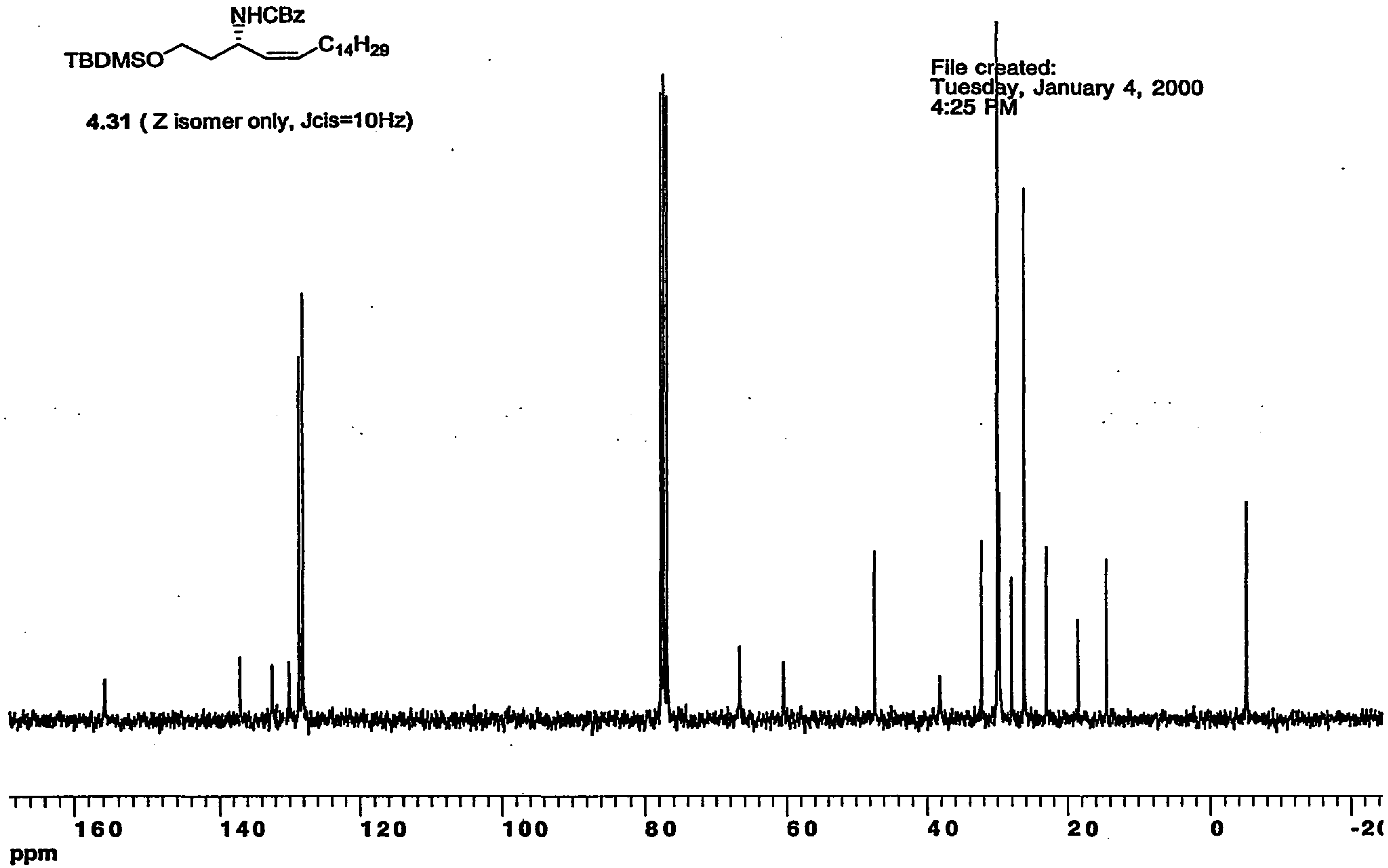
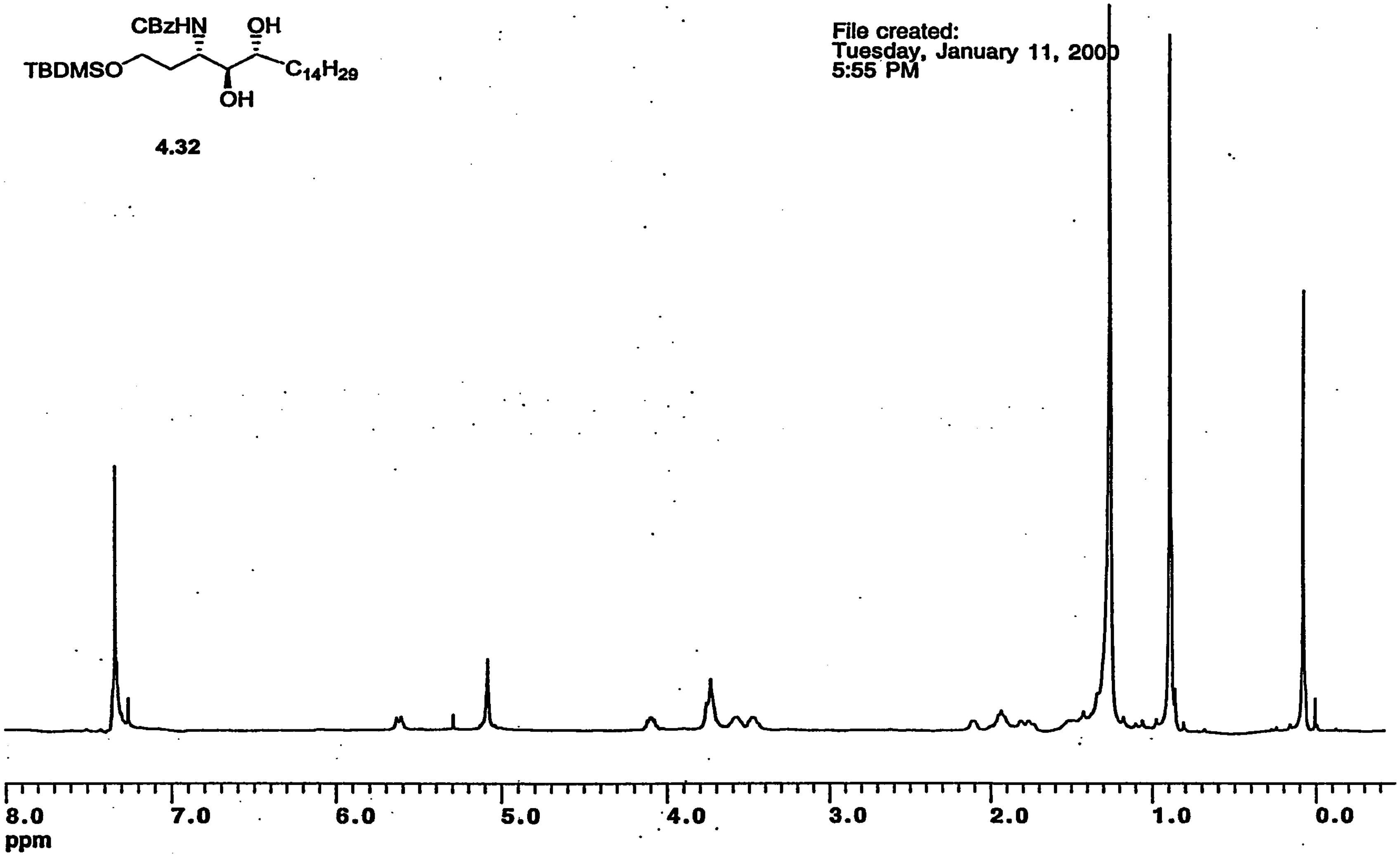


4.31 (Z isomer only, Jcis=10Hz)



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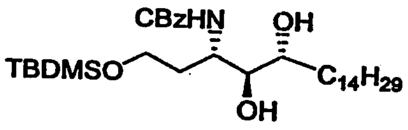

4.32

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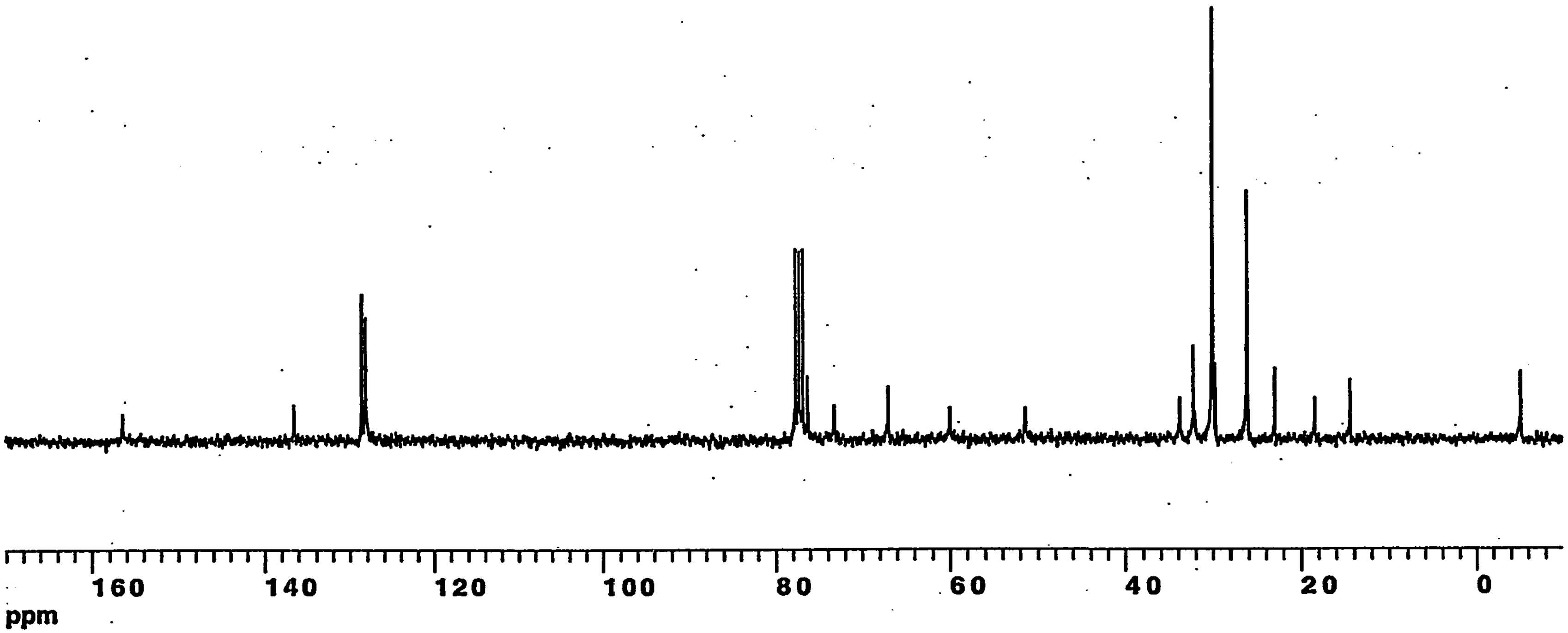

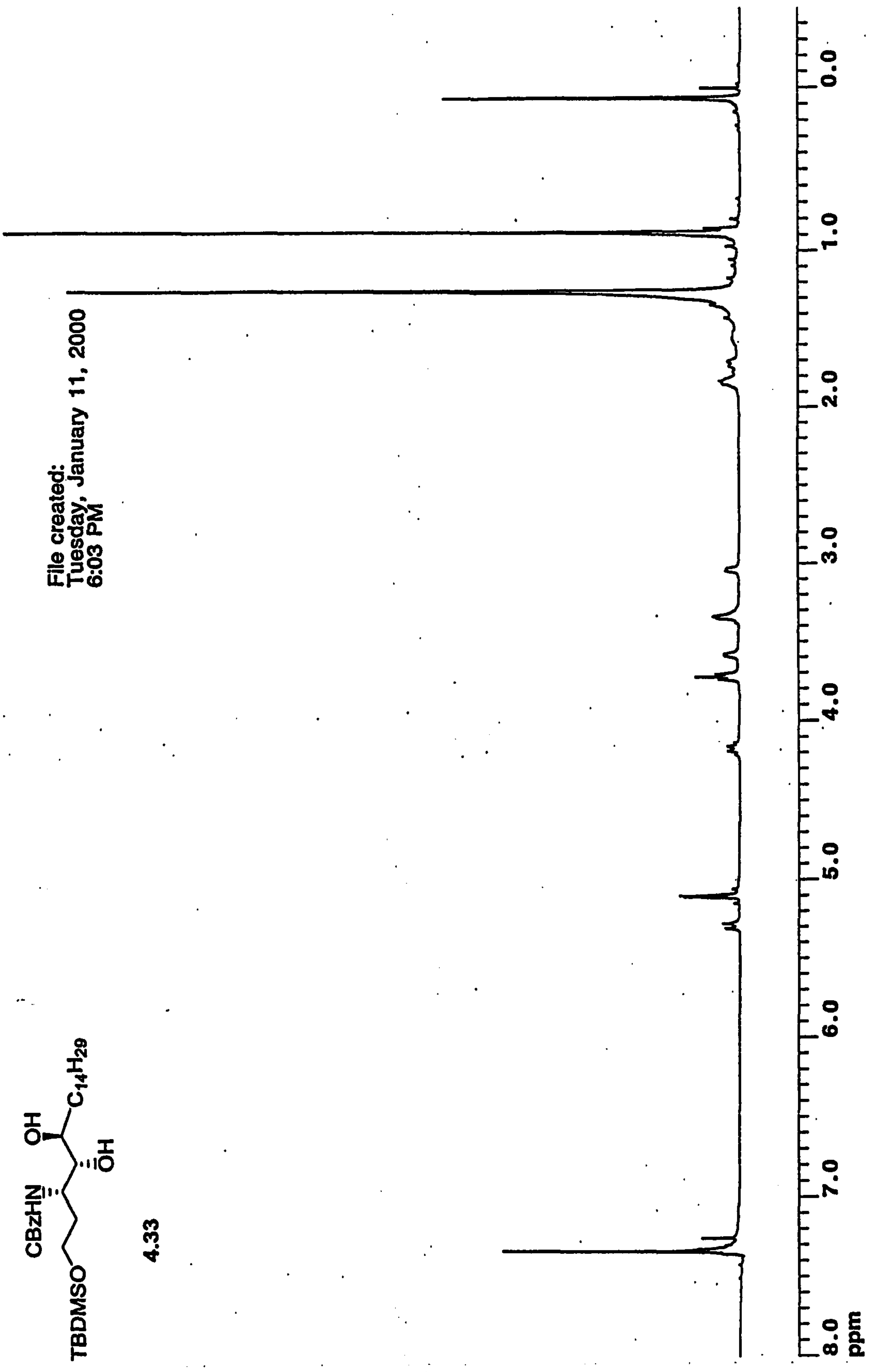
TBDMSO
CBzHN
OH
OH
$C_{14}H_{29}$
4.33
File created:
Tuesday, January 11, 2000
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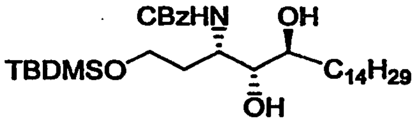
0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
ppm



4.33

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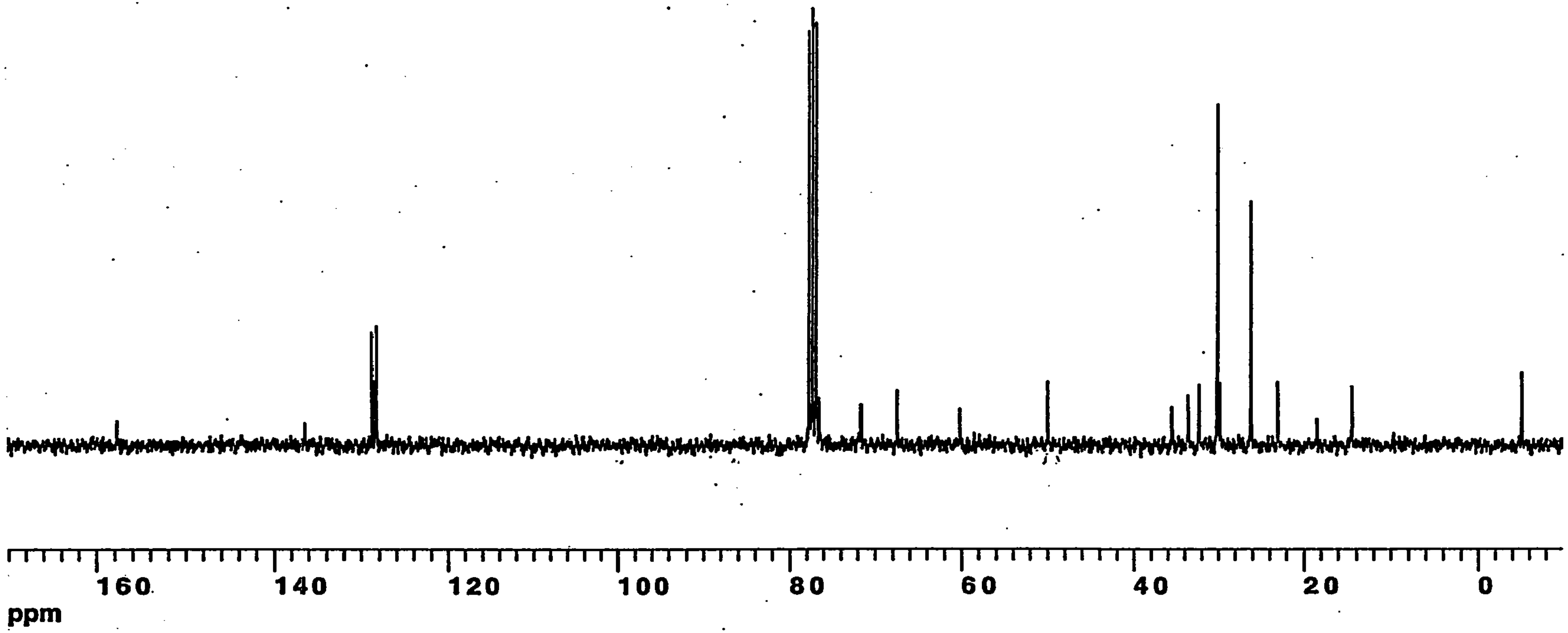

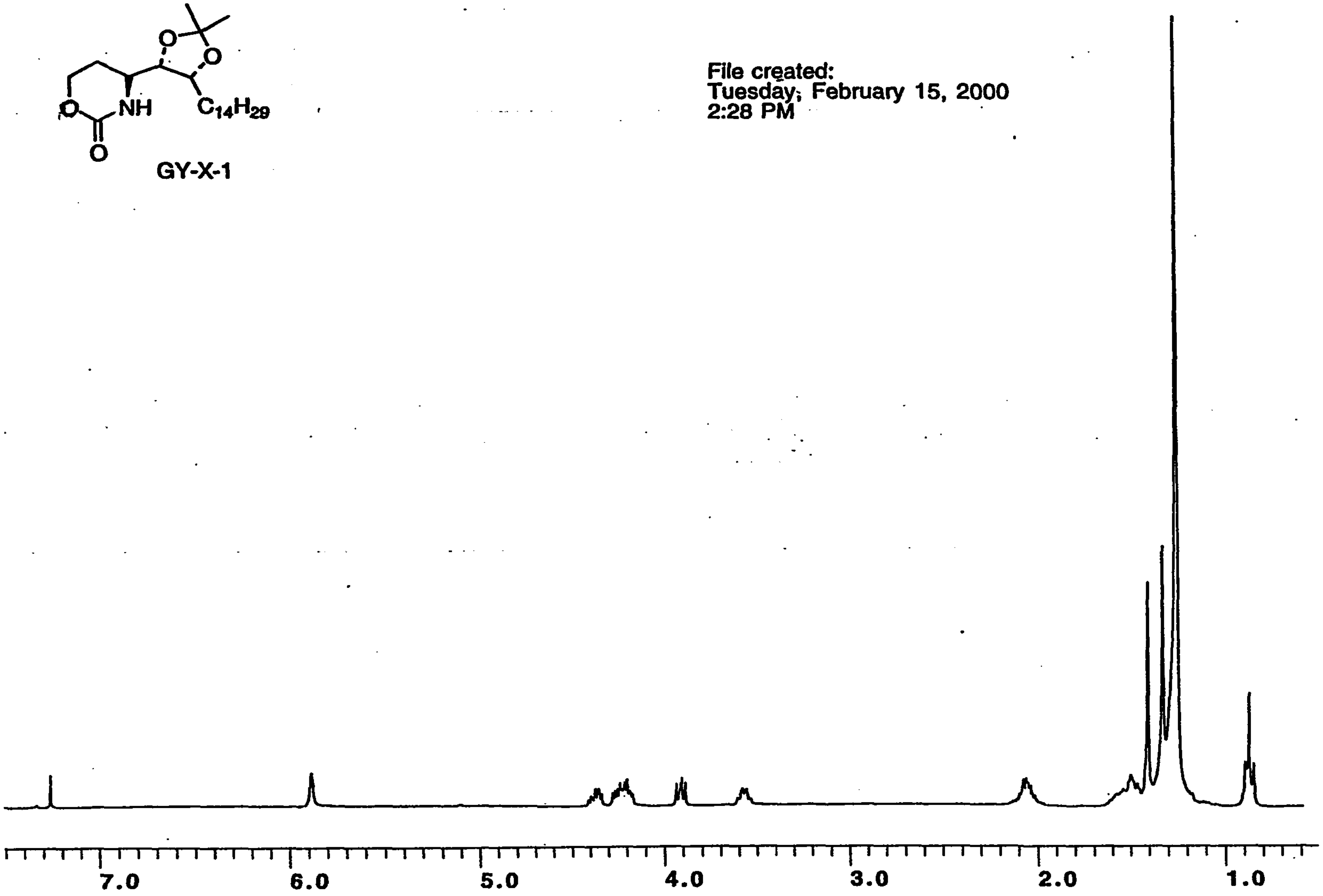

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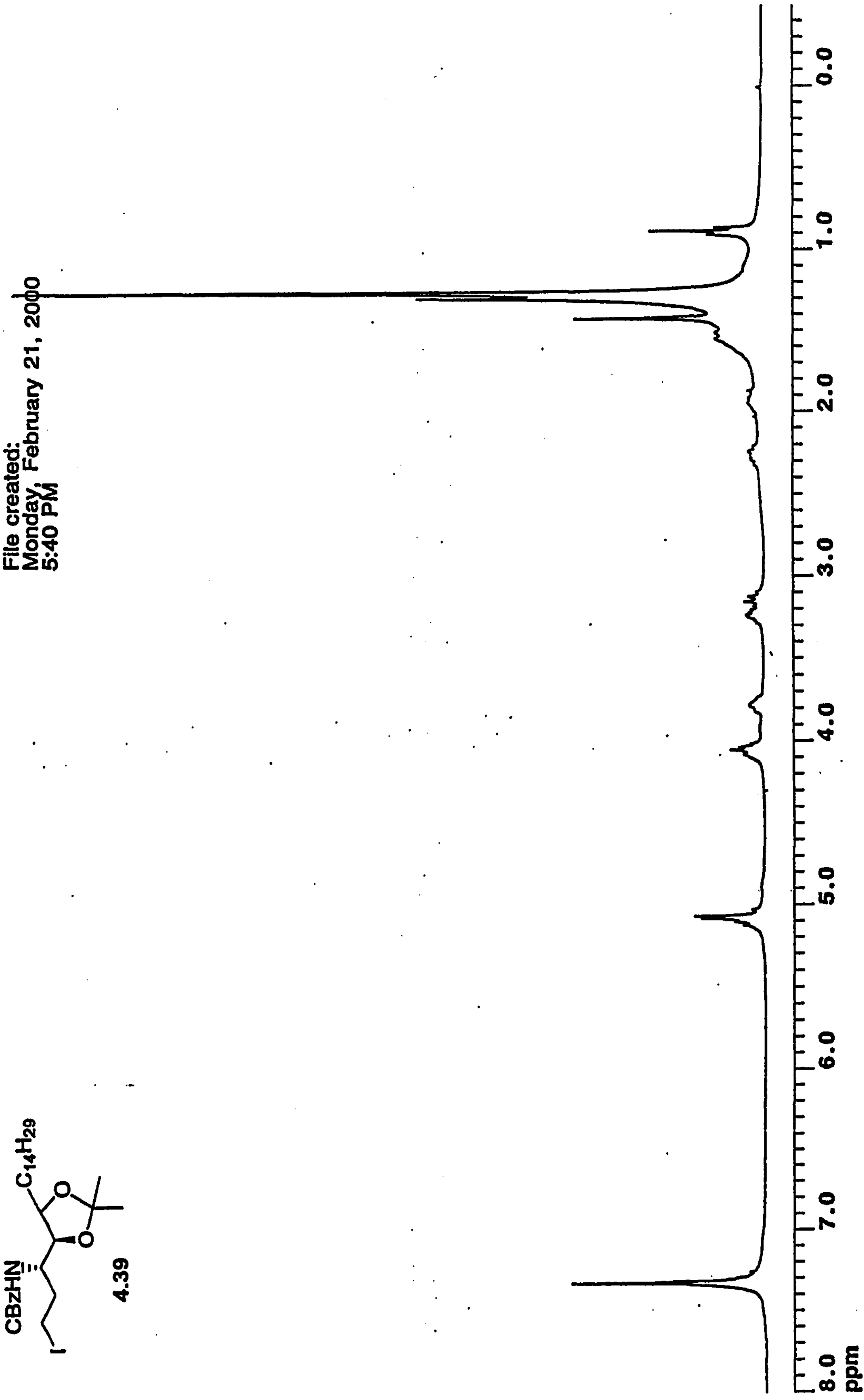
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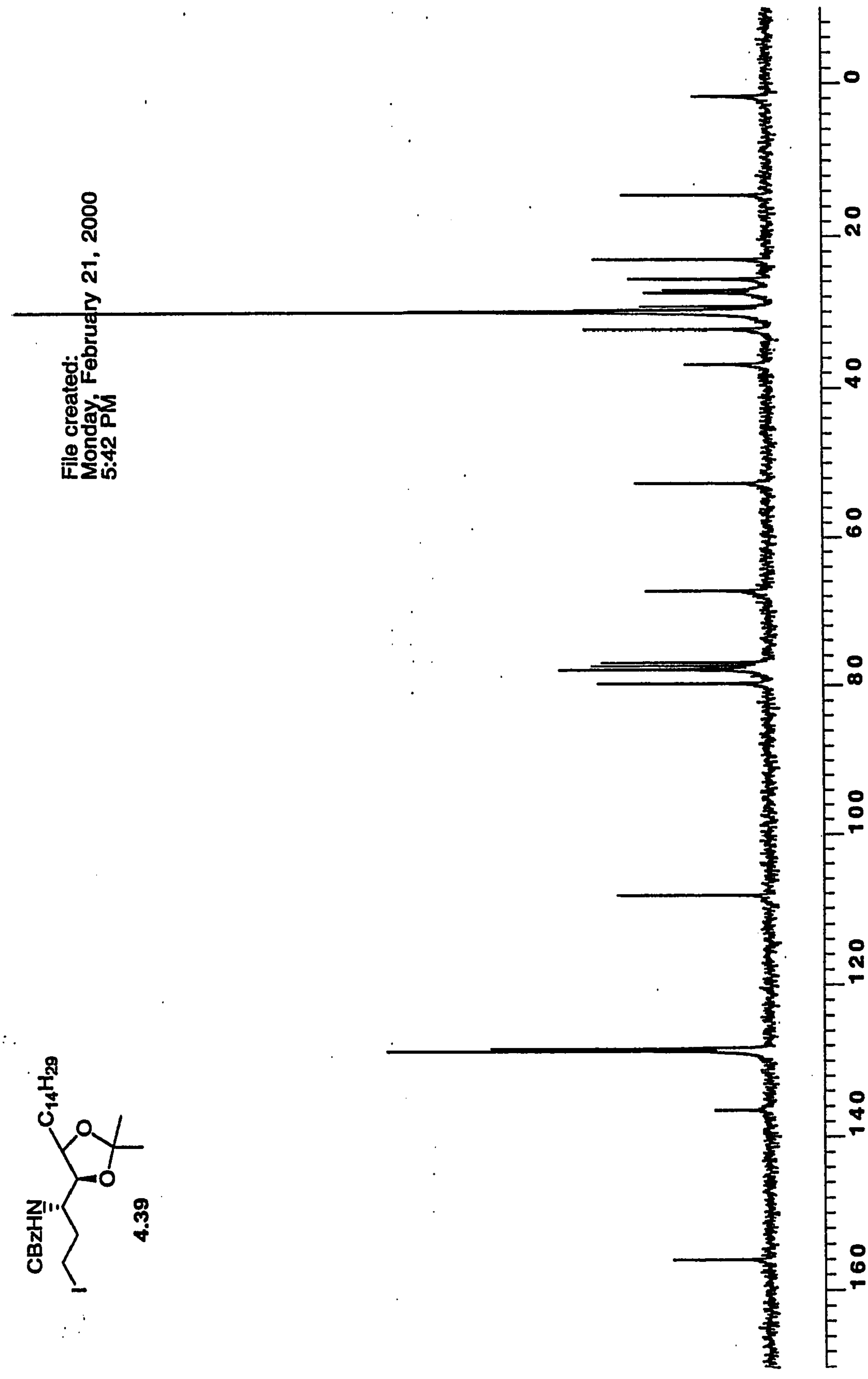
O
O
I

4.39



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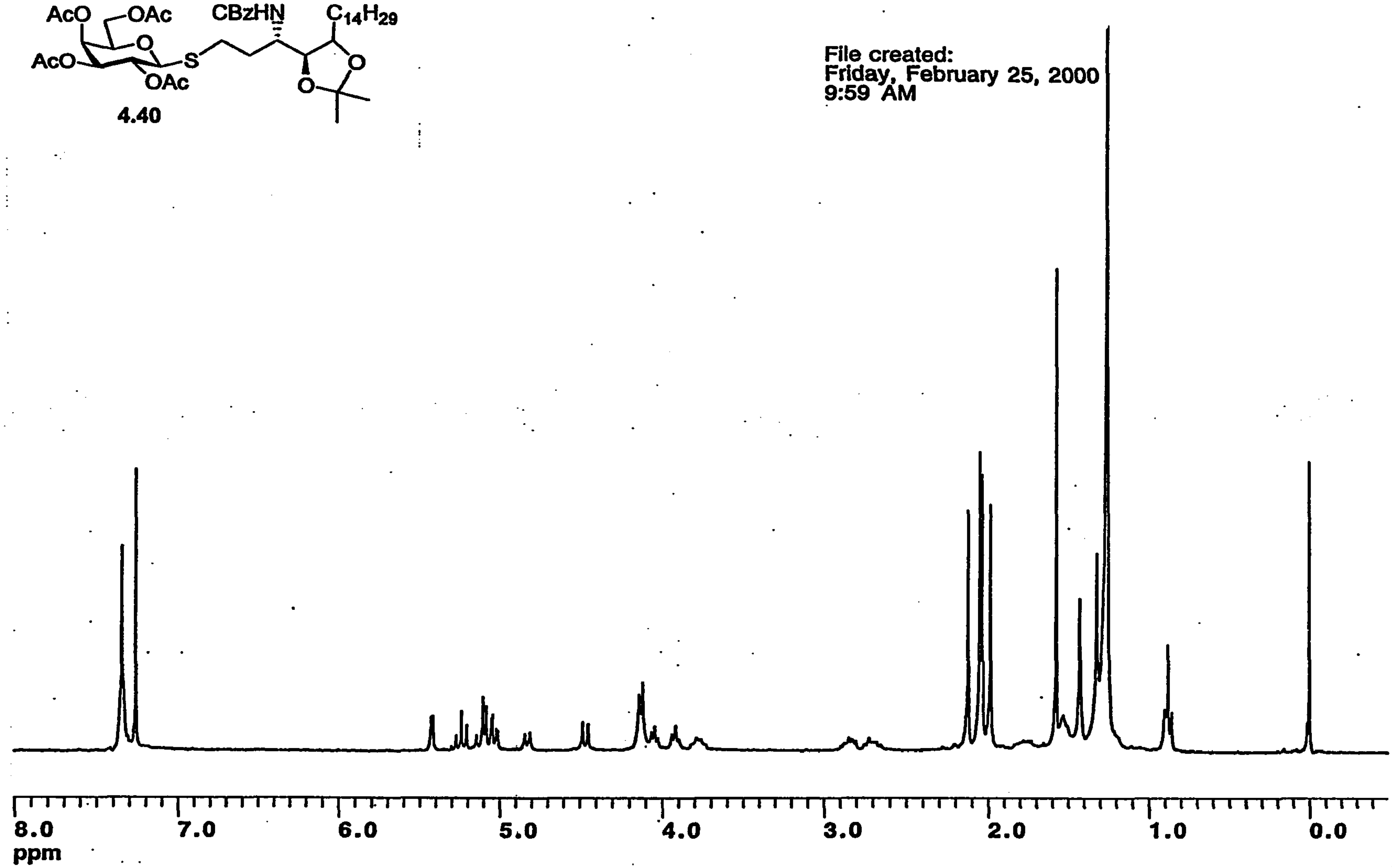
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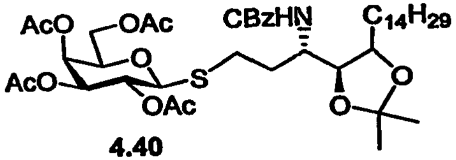

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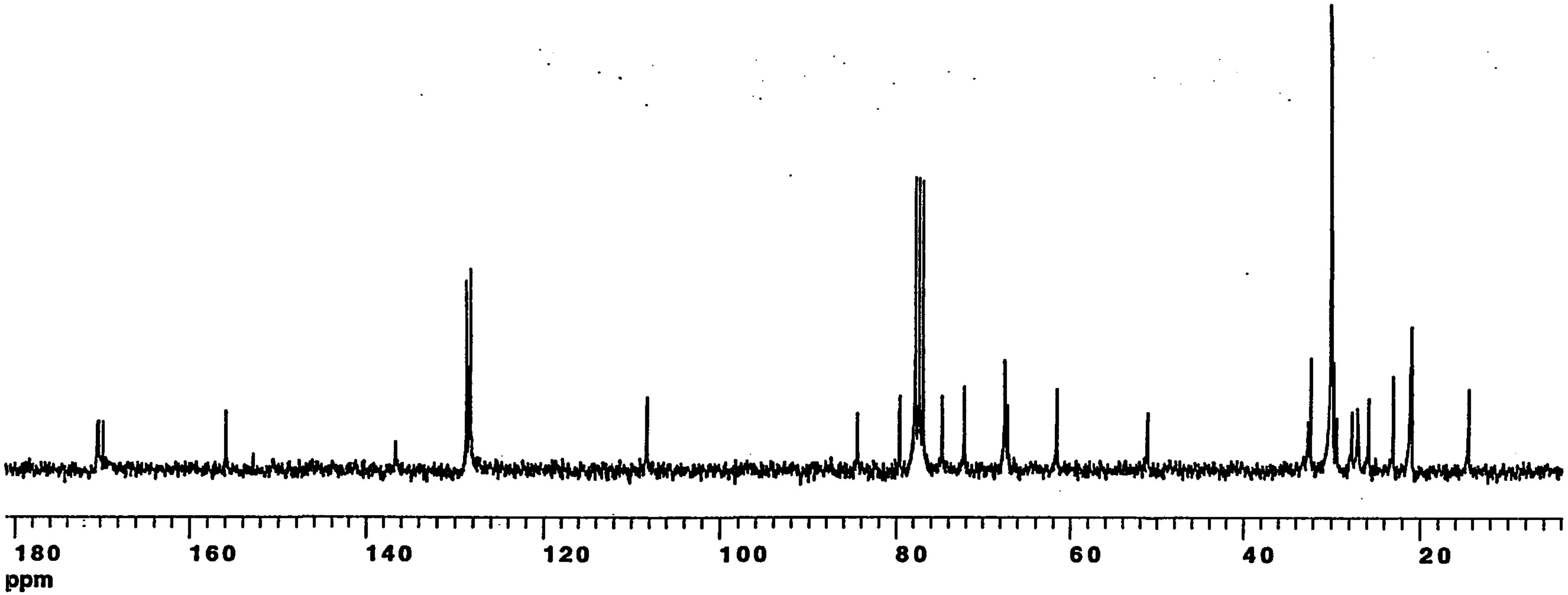

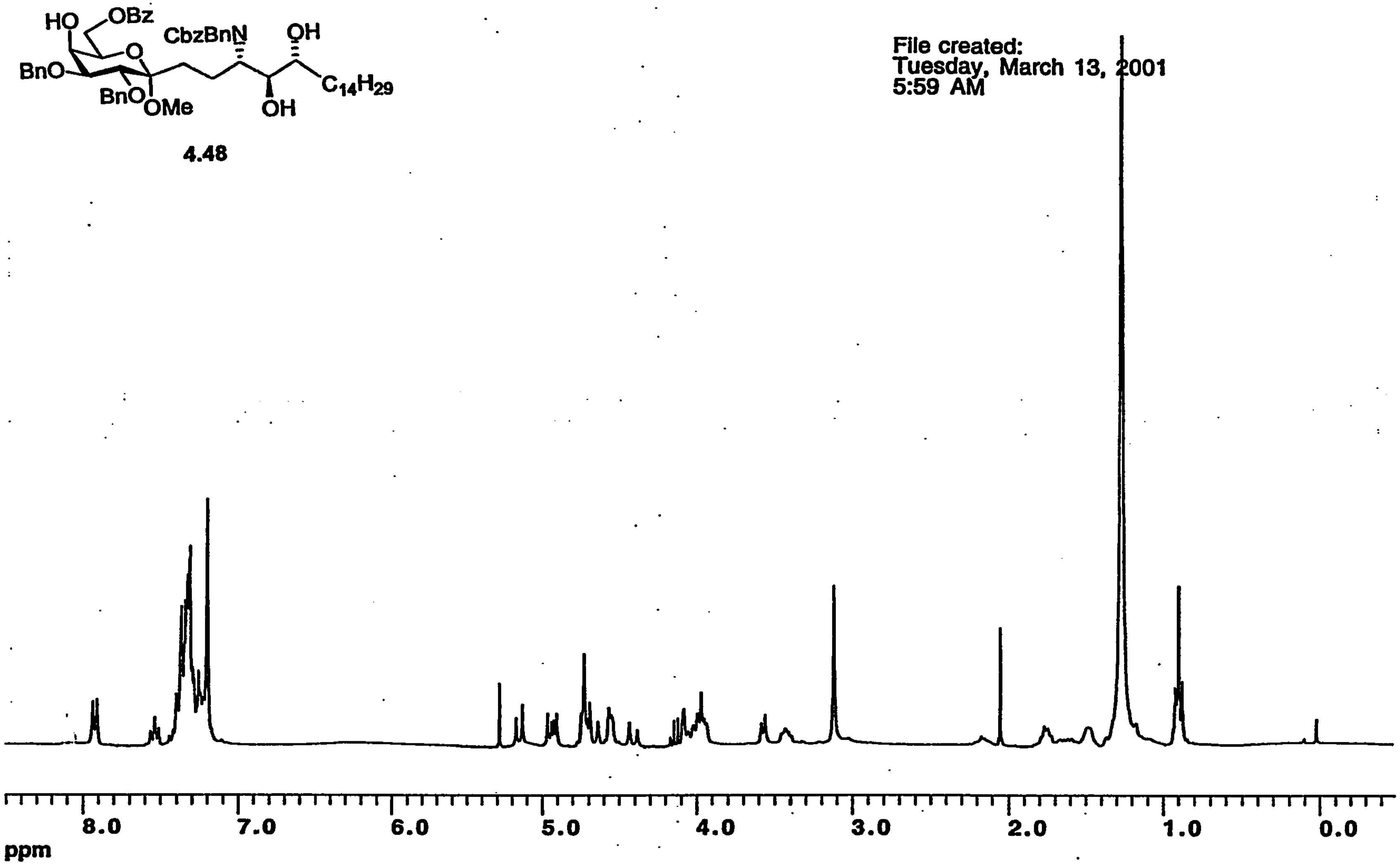

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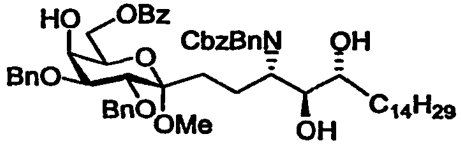

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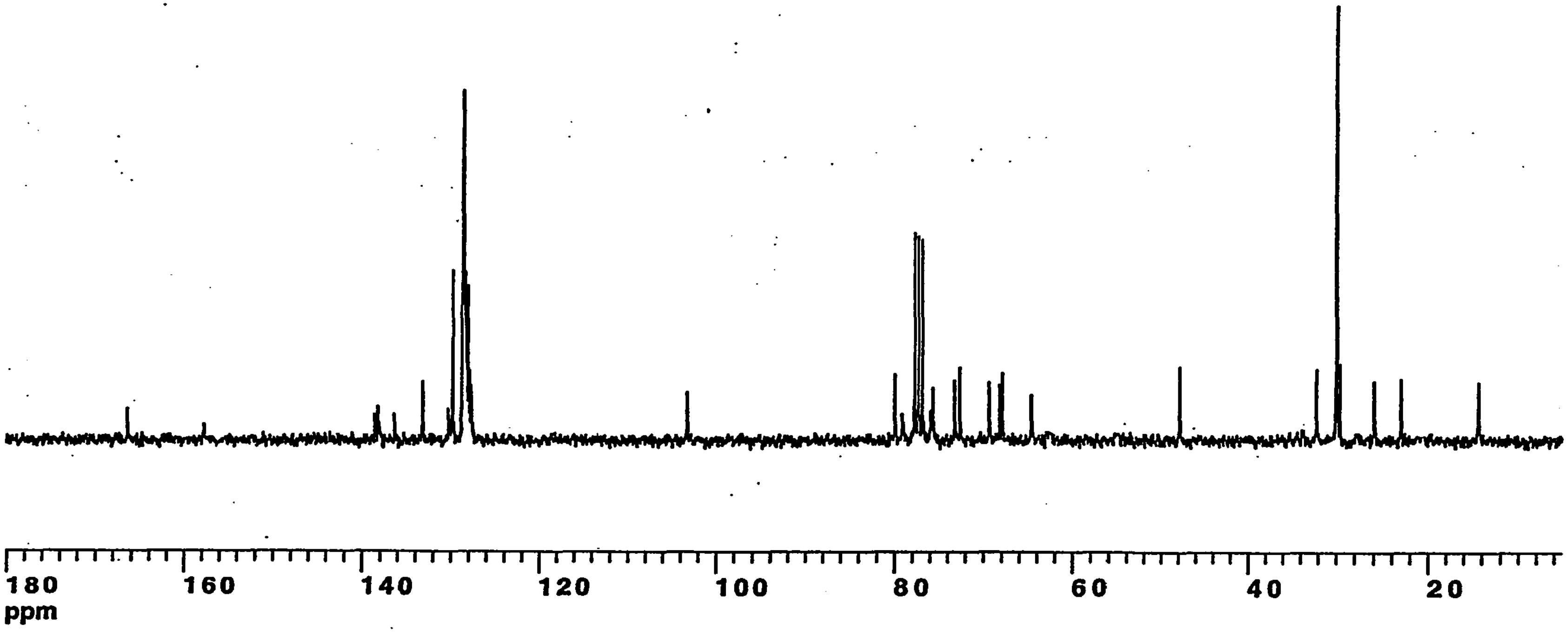

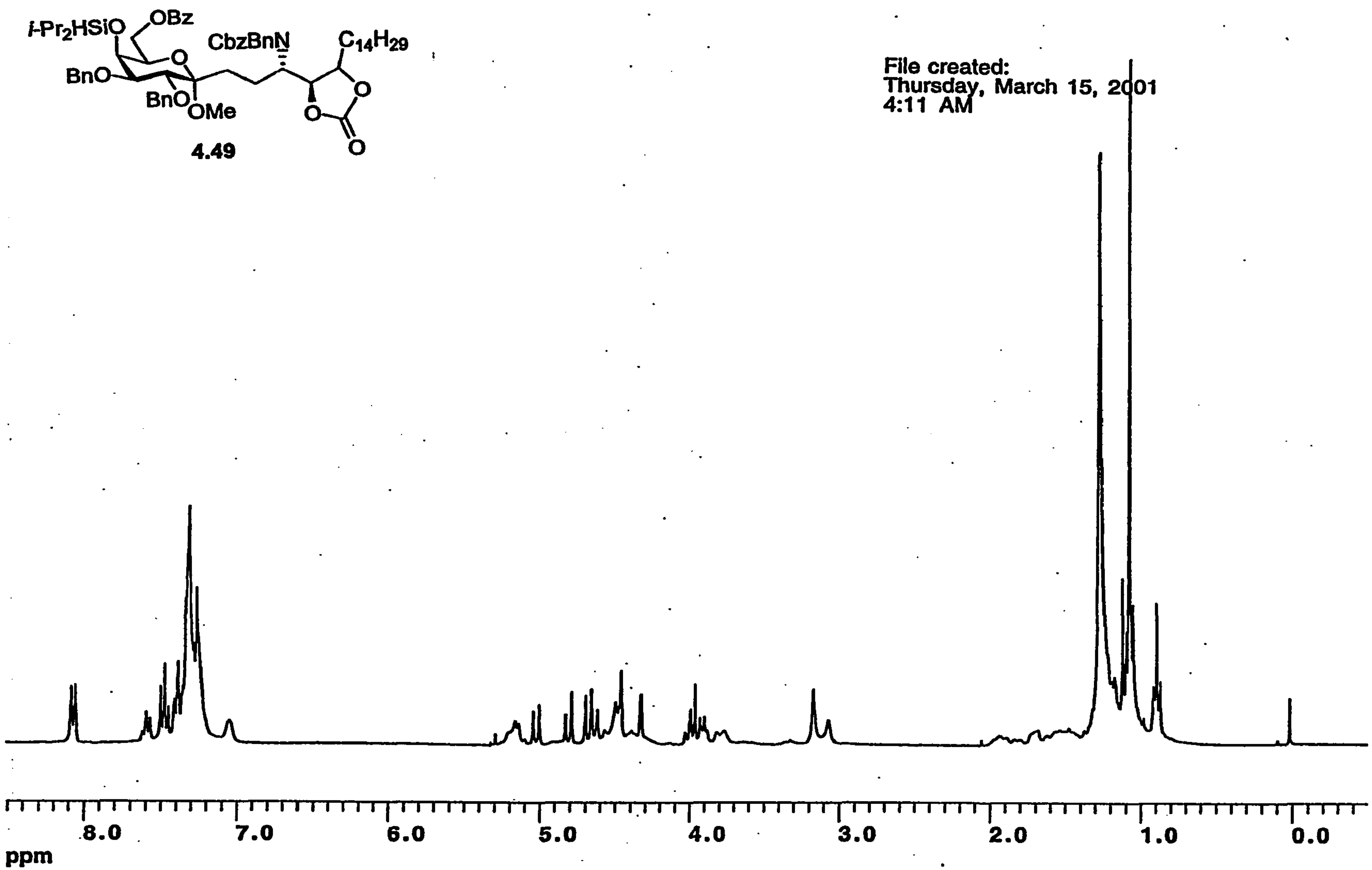

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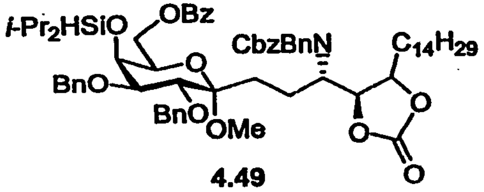

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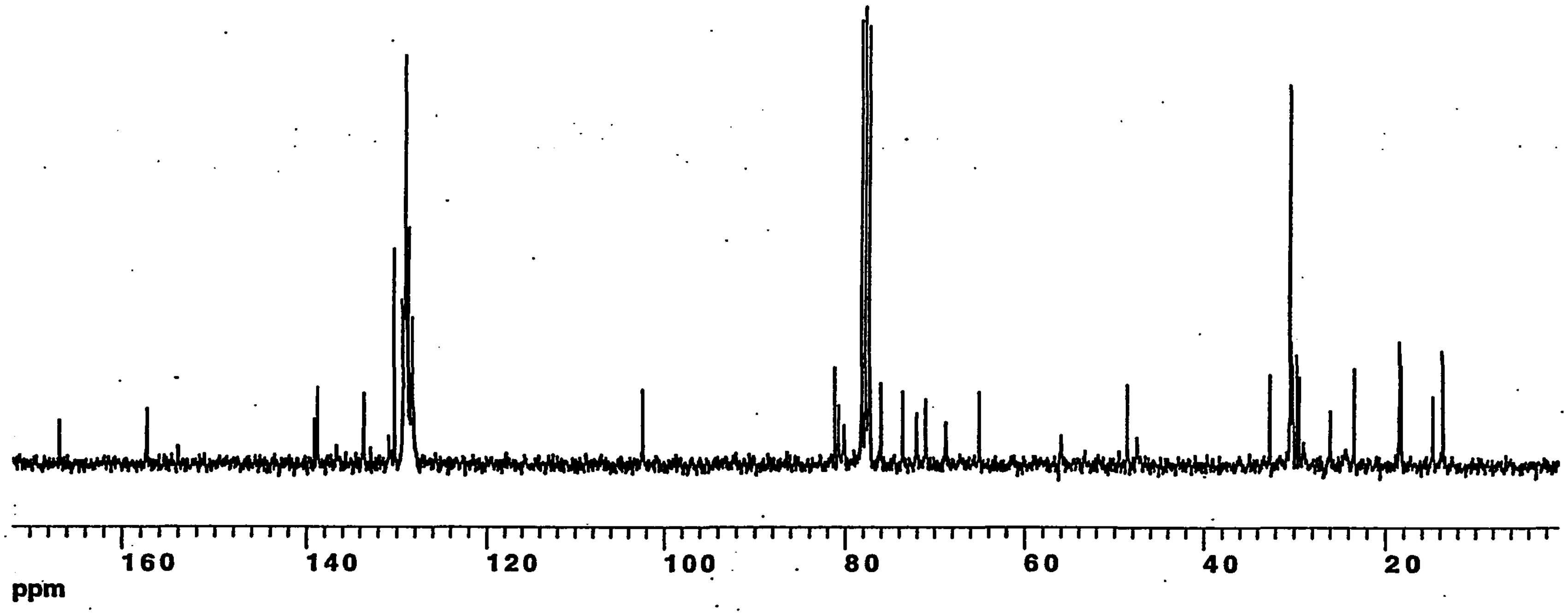

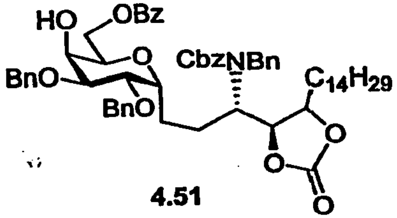

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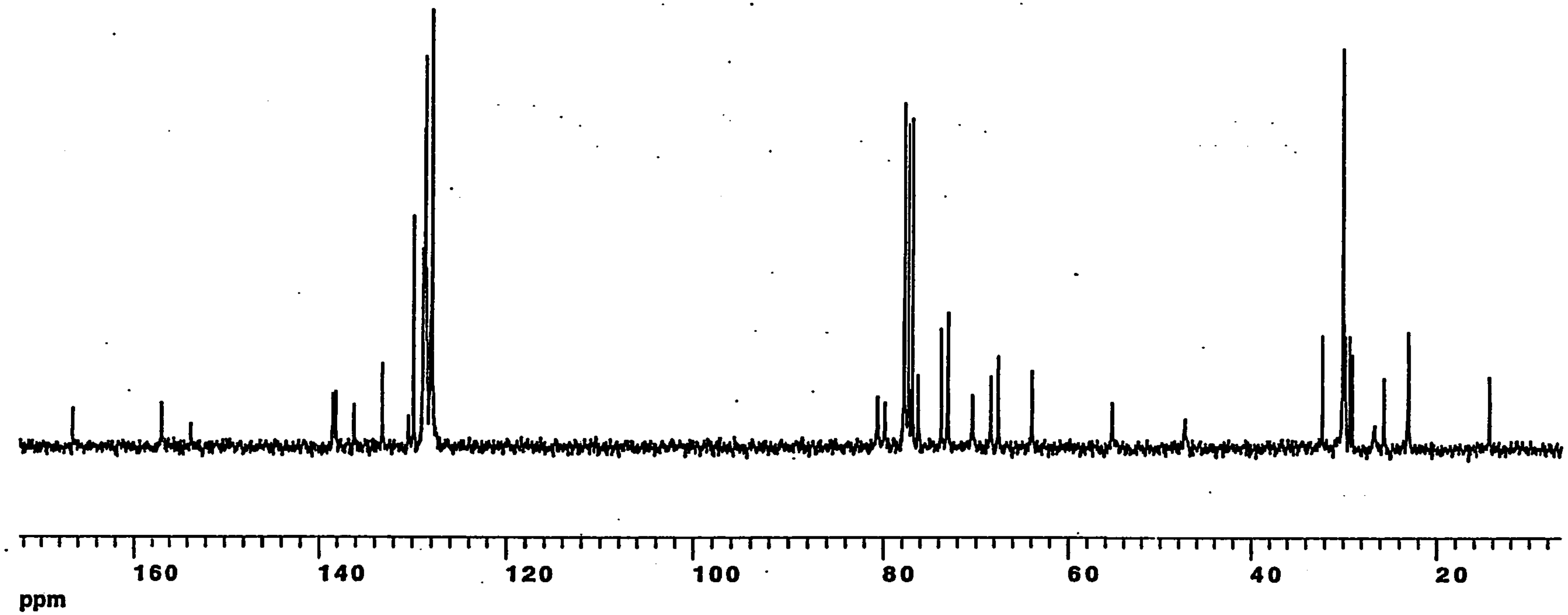

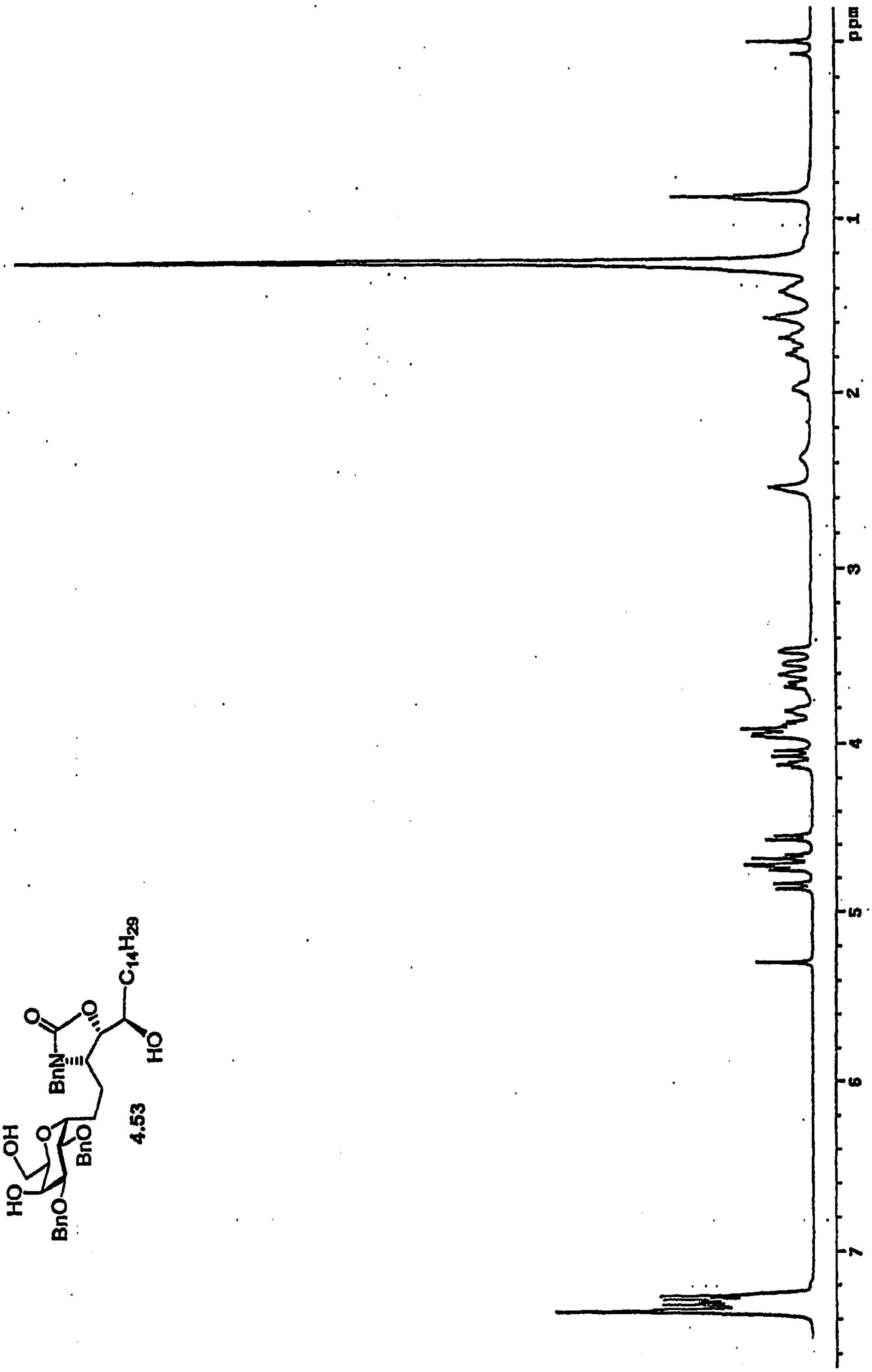
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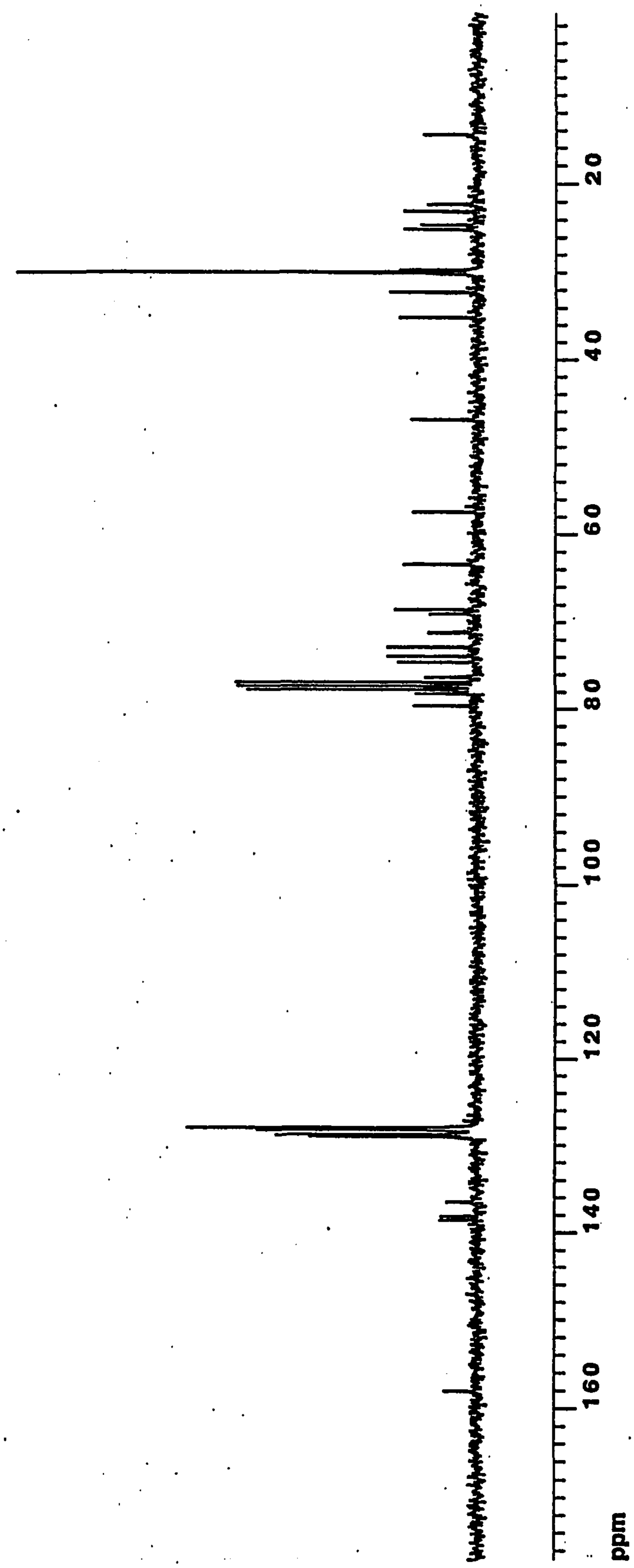

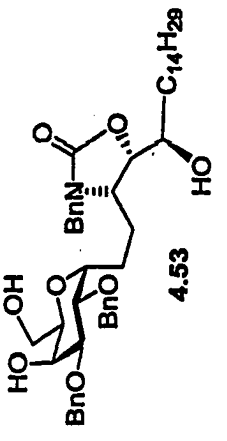

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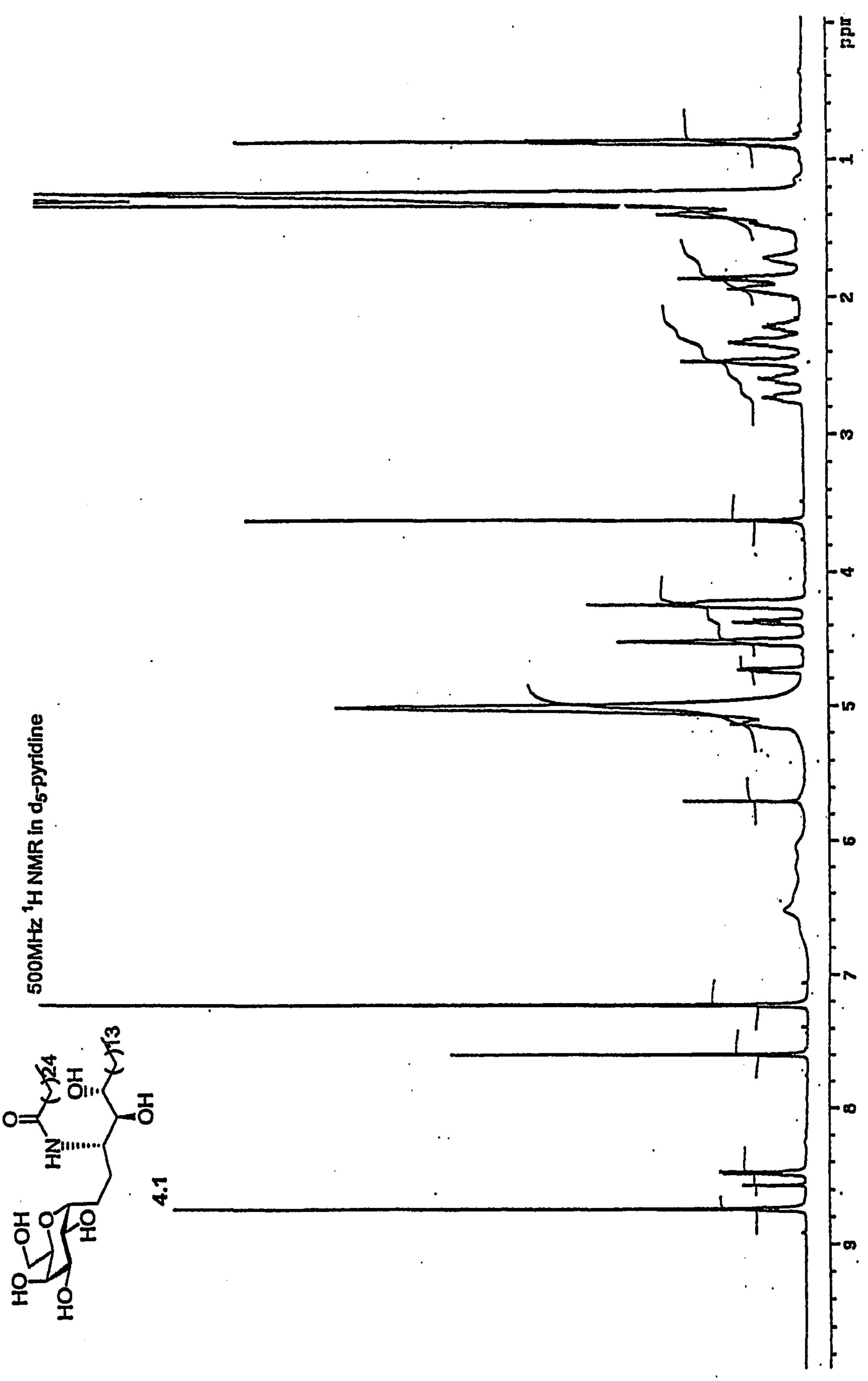
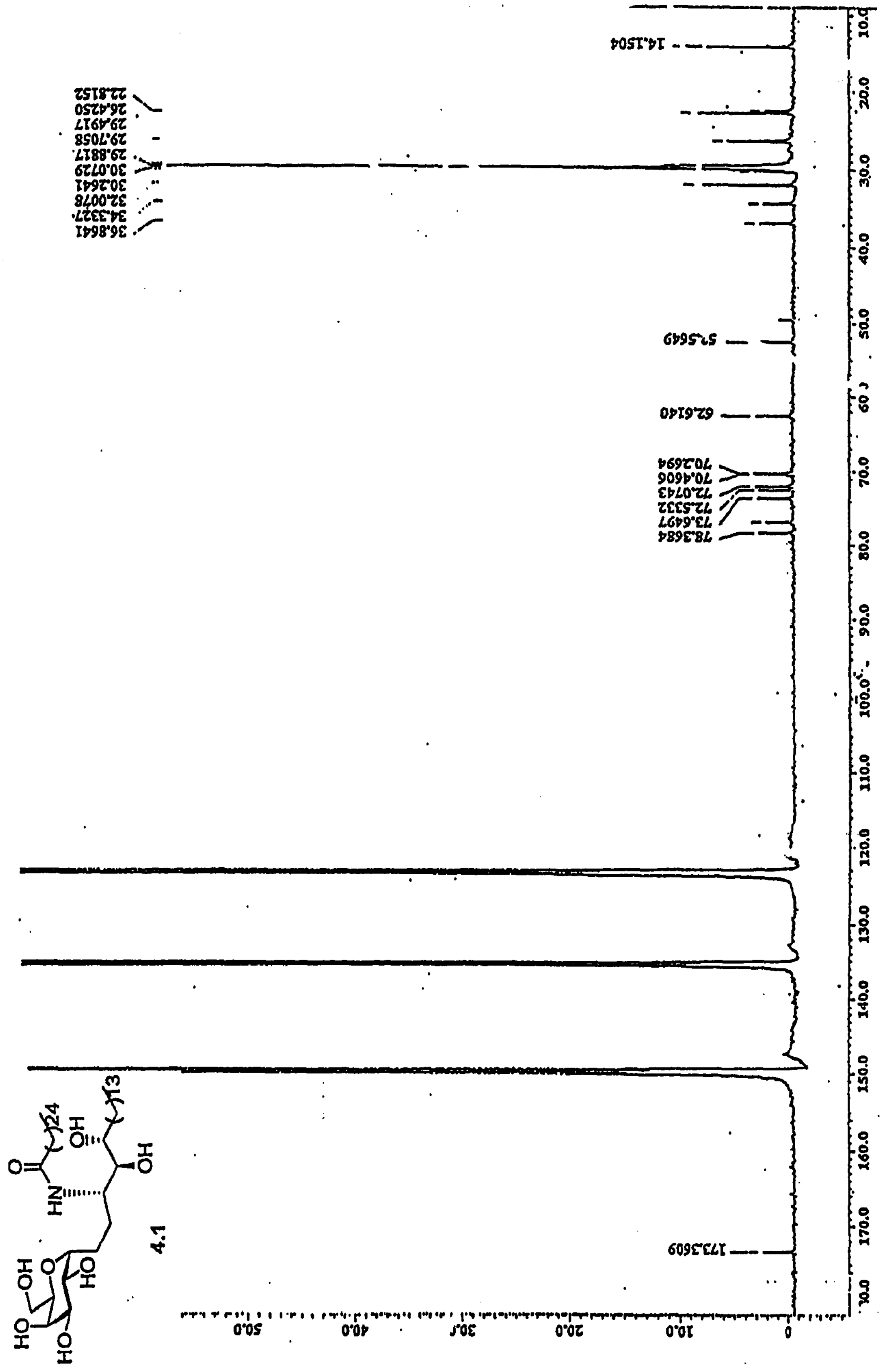


500MHz ¹H NMR in d_5-pyridine

4.1



4.1

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22.8152
26.4250
29.4917
29.7058
29.8817
30.0729
30.2641
32.0078
34.3327
36.8641
57.5649
62.6140
70.2694
70.4606
72.0743
72.5332
73.6497
78.3684
173.3609
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
90.0
100.0
110.0
120.0
130.0
140.0
150.0
160.0
170.0
0
HO
OH
O
HN
24
13

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