A

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

by

PAOLO MARIA PASETTO

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 RAMBERG-BÄCKLUND REACTION

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Paolo Maria Pasetto

Adviser: Professor Richard W. Franck

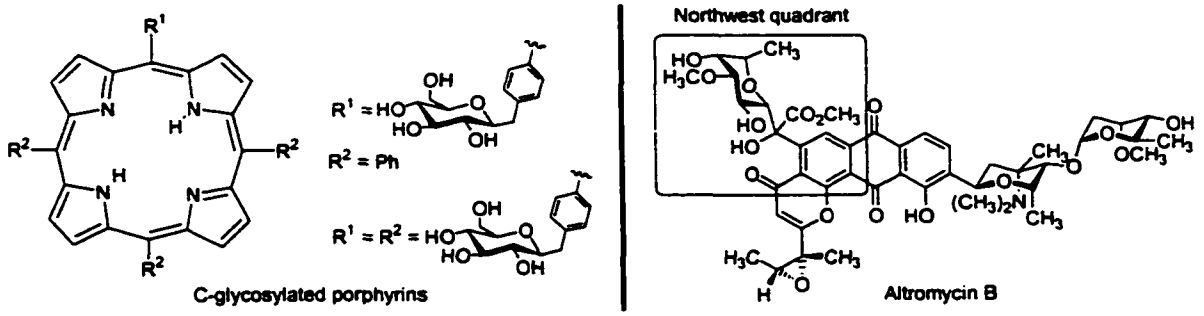
C-glycosides have attracted much attention as analogs of *O*-glycosides in which the hydrolytically labile acetal moiety of the sugar is substituted with a functionality more stable toward acids, bases and enzymes. A variety of *C*-glycosides can also be found in natural products.

The Ramberg-Bäcklund reaction is a classical method, the novel application to carbohydrate was developed in our laboratory. It has proved to be a valuable synthetic tool to the preparation of *C*-glycosides due to its high yields, the easy access of the thioglycoside starting materials and the simple reaction conditions.

We applied the Ramberg-Bäcklund reaction to two research projects, the first of which was the synthesis of *C*-glycosylated porphyrins as potential agents for photodynamic therapy, proposing an efficient synthetic strategy, which allowed us to prepare hydrolytically stable sugar porphyrins in high yields.

The second project was the synthesis of the northwest quadrant of Altromycin B, an unusual natural *C*-glycoside, which we see as an interesting and challenging problem in the employment of the Ramberg-Bäcklund reaction. The comparison of our model

compounds with the spectroscopic data of Altromycin B didn't give definitive proof of the relative stereochemistry at the quaternary center in the northwest quadrant.



Acknowledgments

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To my parents

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1. *C*-GLYCOSIDES

C-glycosides occur when the *exo*-oxygen atom is replaced by a carbon. *C*-glycosides are important because the hydrolytic lability of the glycosidic bond is eradicated by converting the acetal functionality of the *O*-glycoside to a more stable ether functional group.

The replacement of the anomeric oxygen by a methylene results in a series of structural and chemical differences between *O*- and *C*-glycosides, some of which are illustrated in Table 1.

***O*-Glycosides**	***C*-Glycosides**
Anomeric effect	No anomeric effect
Exo-anomeric effect	No *exo*-anomeric effect
Cleaved by acid and enzymes	Stable to acid and enzymes
Hydrogen bond acceptor at anomeric position	No hydrogen bond acceptor at anomeric position
Conformation governed by *exo*-anomeric effect and steric interactions	Conformation governed by steric interactions

Table 1. Comparison of some chemical and physical properties of *O*- and *C*-glycosides

Beside the differences in bond length, dipole moment, bond rotational barrier (C-O versus C-C), Van der Waals radii and electronegativity (O versus C), the most apparent difference is the absence in *C*-glycosides of the anomeric and *exo*-anomeric effect. These

are unique characteristics of saccharides and are known to play an important role in the chemical and structural behavior of *O*-glycosides. Additionally, *C*-glycosides are incapable of forming hydrogen bonds at the anomeric position because of the absence of a H-bond acceptor and this might affect the binding properties of eventual *C*-analogs of drugs containing *O*-glycosides.

Another major difference between *O*- and *C*-glycosides relates to chemical reactivity. *O*-glycosides are readily cleaved under acidic conditions and in biological systems by glycohydrolases, whereas *C*-glycosides are resistant to hydrolysis.

While the conformational behavior of the glycosidic bond in *O*-glycosides is governed by the *exo*-anomeric effect,[1] the conformation around such bond in *C*-glycosides is determined by steric interactions. The conformation of *C*-glycosides was studied in detail by Kishi who concluded that the exocyclic C-C bond assumes preferentially an antiperiplanar arrangement with respect to the C-1/C-2 endocyclic bond.[2] By coincidence in most cases this conformation is analogous to the one assumed by *O*-glycosides as illustrated in Figure 1. The conformational similarity between *C*- and *O*-glycosides has been confirmed by detailed conformational studies on the *C*-analog of lactose by Schmidt and Jimenez-Barbero[3] and by Kishi.[4]

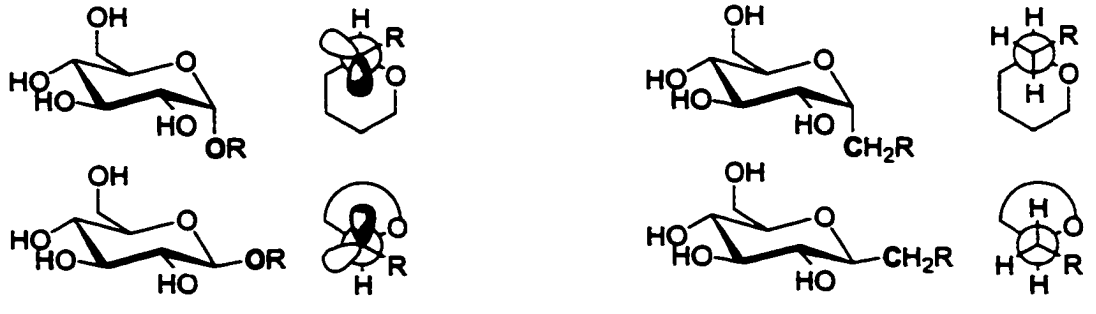
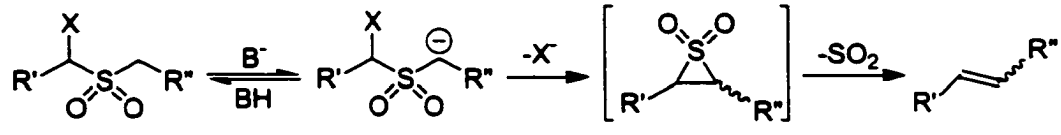


Figure 1. Preferred conformational arrangements assumed by *O*- and *C*-glycosides

The minimal conformational differences between *O*- and *C*- glycosides, along with the advantage of their chemical stability make *C*-glycosides important analogs of *O*-glycosides. Moreover in the recent years several natural occurring *C*-glycosides have been reported, some with interesting biological properties and this contributed to a large effort in the synthesis of these materials. Several synthetic approaches to *C*-glycosides have been proposed, which have been described in two books[5] and several reviews.[6]

2. THE RAMBERG-BÄCKLUND ROUTE TO *C*-GLYCOSIDES

The conversion of α-halosulfones, bearing at least one α'-hydrogen, to olefins under basic conditions (equation 1) was named after the two Swedish chemists Ramberg and Bäcklund who reported it the first time in 1940.[7] The Ramberg-Bäcklund reaction (often referred to as rearrangement) was reviewed by Paquette,[8] Clough[9] and Taylor.[10]



X = halide

Eq. 1

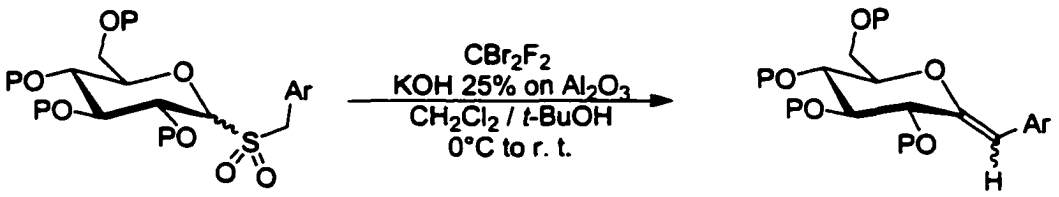
The mechanism of the Ramberg-Bäcklund reaction is believed to involve a nucleophilic displacement of halide by the sulfone α-anion, followed by extrusion of SO_2 from the resulting episulfone to yield an olefin. This proposed mechanism was discussed in great detail in the first two reviews dedicated to the Ramberg-Bäcklund reaction.[11] More recently as further support to such mechanism Taylor described the isolation of an episulfone intermediate.[12]

The original conditions proposed by Ramberg and Bäcklund involved the treatment of an α-halosulfones with 2 N aqueous KOH under reflux. Meyers in 1969 proposed an improvement of this transformation from a two-step to a one-pot reaction by converting *in situ* the sulfone to α-chlorosulfone by treatment with carbon tetrachloride

under basic condition (KOH in water/*t*-butanol).[13] A major drawback of Meyers' conditions is the formation of dichlorocyclopropane by-products arising from the Simmons-Smith addition of dichlorocarbene, generated from carbon tetrachloride under the reaction conditions, to the olefin.

More recently Chan proposed the use of dibromodifluoromethane as brominating agent along with the use of KOH supported on alumina,[14] which made the Ramberg-Bäcklund reaction a more practical and efficient way to the formation of C-C bonds.

Chan's protocol has been successfully employed in the Franck[15] and in the Taylor[16] laboratories for the synthesis of *exo*-glycals, starting from benzylic thioglycosides, which can easily be oxidized to sulfones (equation 2).

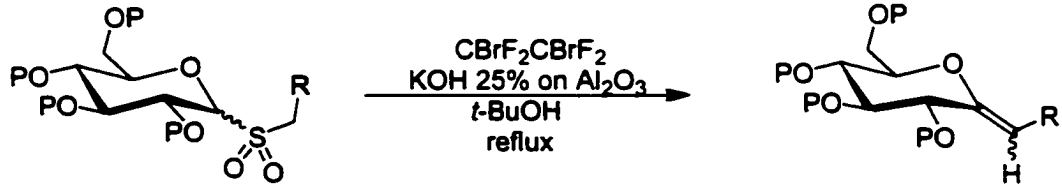


P: protecting groups stable under basic conditions

Eq. 2

However, Chan's conditions proved to be inefficient in the conversion of alkyl sulfonylglycosides to *exo*-glycals, due to the higher temperature required for the α-halogenation of the sulfone, which is not possible with the low boiling point of dibromodifluoromethane (bp 22-23 °C). This problem was solved in the Franck

laboratory by using a freon (tetrabromodifluoroethane, equation 3) with higher boiling point (bp 47 °C).[17]



R: Alkyl

Eq. 3

3. SYNTHESIS OF *C*-GLYCOSYLATED PORPHYRINS

3.1 Introduction

Porphyrins and their analogs have attracted much attention as agents employed in Photodynamic Therapy (PDT).[18] This technique utilizes porphyrins as photosensitizers for the medical treatment of some types of cancers. Porphyrin based drugs are introduced into the body and accumulate preferentially in rapidly dividing cells. Successively a carefully regulated light is shone onto the diseased tissue. When the porphyrin is hit by light at an appropriate wavelength it is converted to an excited singlet state. Then via an intersystem crossing process the excited porphyrin can be converted to a metastable triplet state. At this point the molecule can relax from the excited triplet state via a radiactive process (phosphorescence), or via spin exchange with another molecule in a triplet state. If this last process occurs with a molecule of triplet oxygen, generation of singlet oxygen occurs (Figure 2).

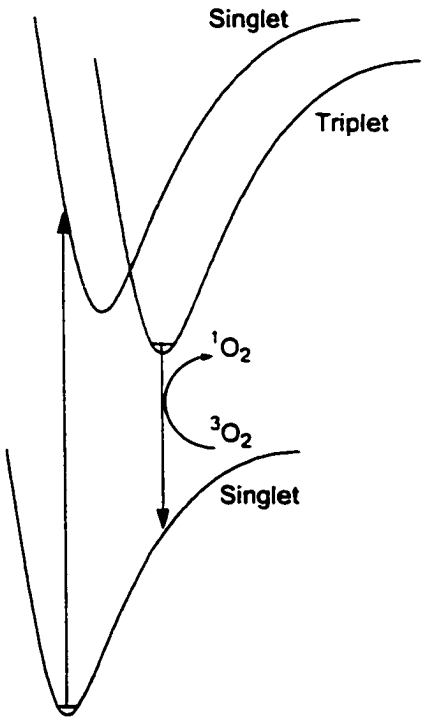


Figure 2. Singlet oxygen production

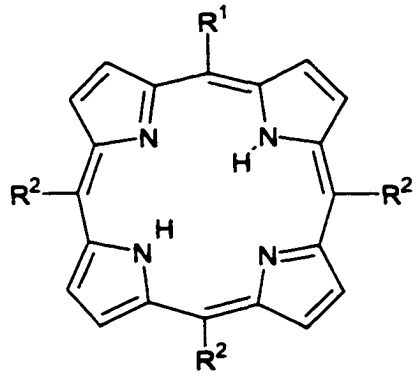
Singlet oxygen is a very reactive species with a lifetime in water of approximately 4 μs. It can undergo several reactions such as oxidations and cycloadditions, which have a disruptive effect to the biological processes. Based on this principle Photophrin,[19] a

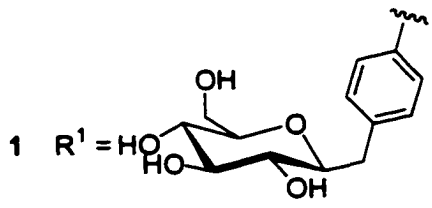
porphyrin based drug, has been developed and is currently used clinically for PDT. This drug is a mixture of hematoporphyrin oligomers and suffers from a variety of problems including solubility and dosing.[20]

In order to be utilized in the PDT porphyrins must be water-soluble. For this reason sugar conjugates of porphyrins are of great importance. Furthermore porphyrins that carry sugar moieties exhibit specific cancer cell targeting.[21] They have not only good solubility in water, but they may exhibit different membrane interactions. Sugar-specific binding to rat hepatoma cells by porphyrin glycoconjugates has been described.[22] A variety of *O*-glycosylated porphyrins have been synthesized.[23]

For most of glycoconjugate porphyrins the carbohydrates are linked to a phenolic aryl porphyrin via a glycosidic bond. An intrinsic problem for the synthesis of these *O*-glycoporphyrins is the normally very low yields obtained when the *O*-glycosyloxybenzaldehyde starting materials are subjected to the Lindsey porphyrin synthesis using BF_3 catalysis. This problem is clearly due to the instability of these materials under acidic conditions, which cause cleavage of the *O*-glycosylic bond. BF_3 catalysis may also cause a competing and yield-reducing Suzuki *O*- to *C*-rearrangement.[24] Additionally, the efficiency of *O*-glycoconjugate porphyrins can be reduced in biological systems by glycosidase enzymes that cause the hydrolysis of the glycosylic linkage. Few examples of C-glycosylated porphyrins have been reported.[25]

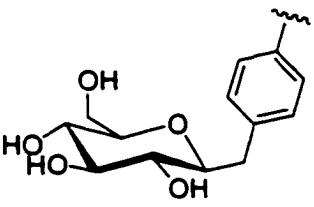
We thought that the preparation of *C*-glycosylated aryl porphyrins **1** and **2** could provide possible solutions to both the issues of poor yields and hydrolytic instability.[26]





1 R^1 = HO

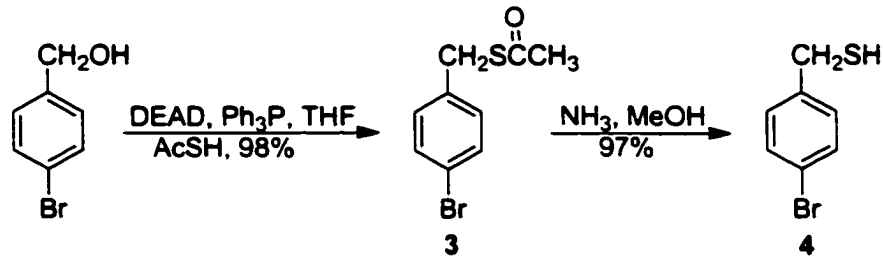
R^2 = Ph



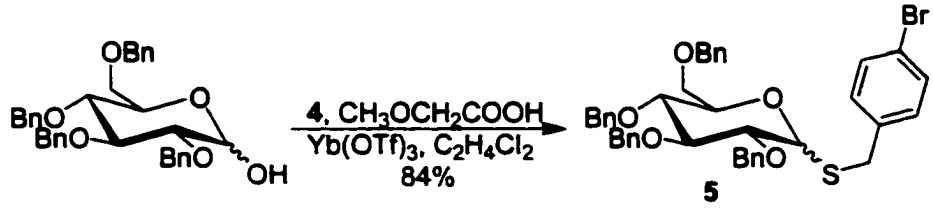
2 $R^1 = R^2$ = HO

3.2 Discussion

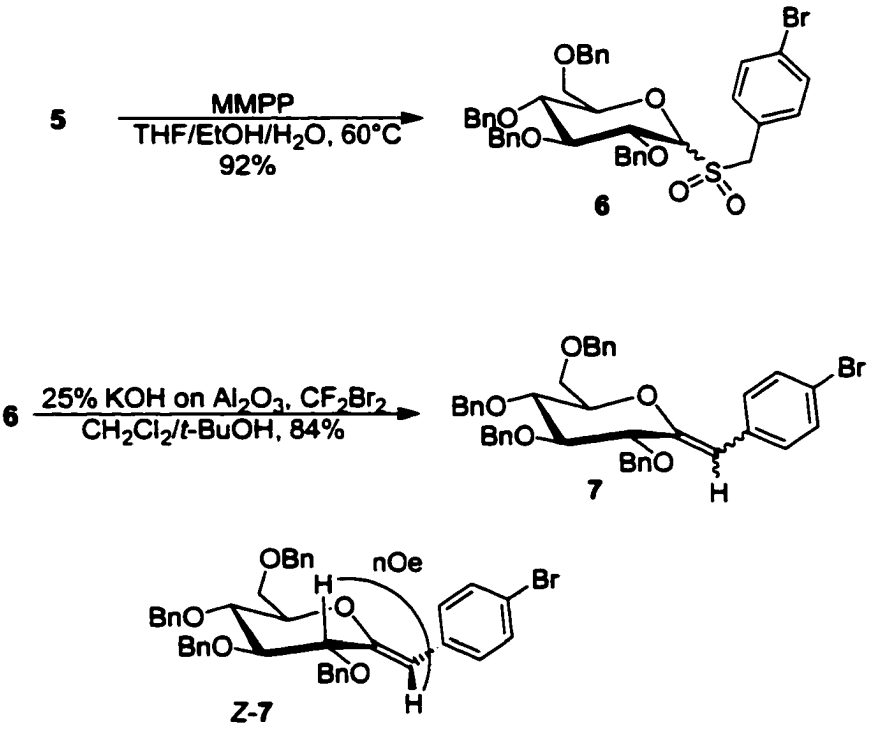
The thiolester **3** was prepared in 98% yield by the Mitsunobu reaction,[27] by treating the preformed adduct of triphenylphosphine and diethylazodicarboxylate with a mixture of 4-bromobenzyl alcohol and thiolacetic acid. The thiol **4** (97% yield) was obtained by methanolysis of **3** in a saturated solution of ammonia in methanol under nitrogen atmosphere to minimize the formation of disulfide, which was detected in traces. The product **4** was utilized in the following step without need of further purification.



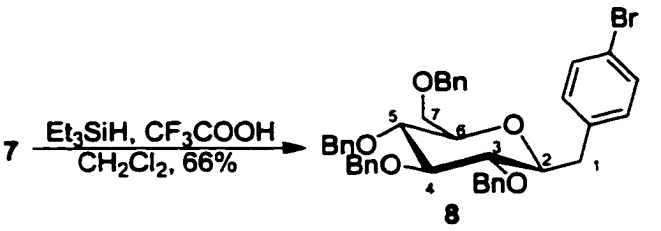
The thioglucoside **5** was prepared in 84% yield via Inanaga protocol[28] from the commercial 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose. To maximize the conversion to **5** we found it convenient to use an excess of **4** (~1.6 equiv.), that was recovered by chromatographic purification of the reaction crude.



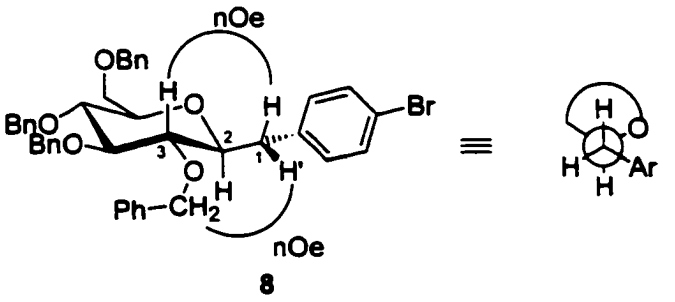
Thioglucoside **5** was then oxidized to sulfone **6** (92% yield) with magnesium monoperoxyphthalate (MMPP) followed by the Ramberg-Bäcklund reaction. The *exo*-glucal **7** was obtained in 84% yield as inseparable mixture of *E* and *Z* isomers in the ratio *Z*/*E* = 94/6. The major isomer *Z*-**7** was identified by NOESY experiment, which revealed an effect between the vinylic H-1 and H-3.



The ionic hydrogenation[29] of **7** afforded **8** (66% yield) as a single β-*C*-glucoside with no trace of the α-anomer.

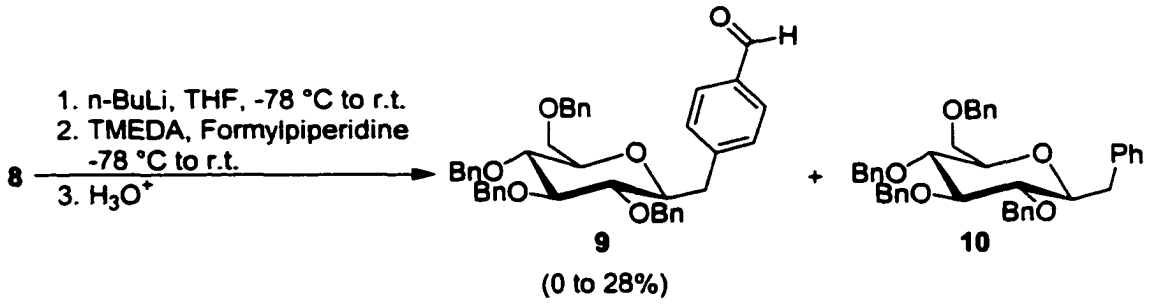


The ^{1}H-NMR spectrum of **8** shows a strong coupling constant of 9.0 Hz between one of the protons at C-1 (centered at 2.66 ppm) and the anomeric H-2 (3.43 ppm), suggesting a dihedral angle approximately between 160 and 180 , while the coupling constant between the second proton at C-1 (centered at 3.07 ppm) and H-2 is much smaller (2.2 Hz), suggesting a dihedral angle of approximately 60-80 .[2] An nOe is also observed revealing an interaction between H-1' and a benzylic CH_2 group and between H-1 and H-3. These considerations confirm the conformational arrangement described:



The formylation of **8** proved to be particularly troublesome. Treatment of the lithiated intermediate, obtained by metal – halogen exchange of **8**, with formylpiperidine[30] afforded the aldehyde **9** in yields that never exceeded 28% and usually ranged around 10%, being **10** the major product. Formylations without the employment

of TMEDA lead to the formation of the debrominated product only, with no traces of desired product.

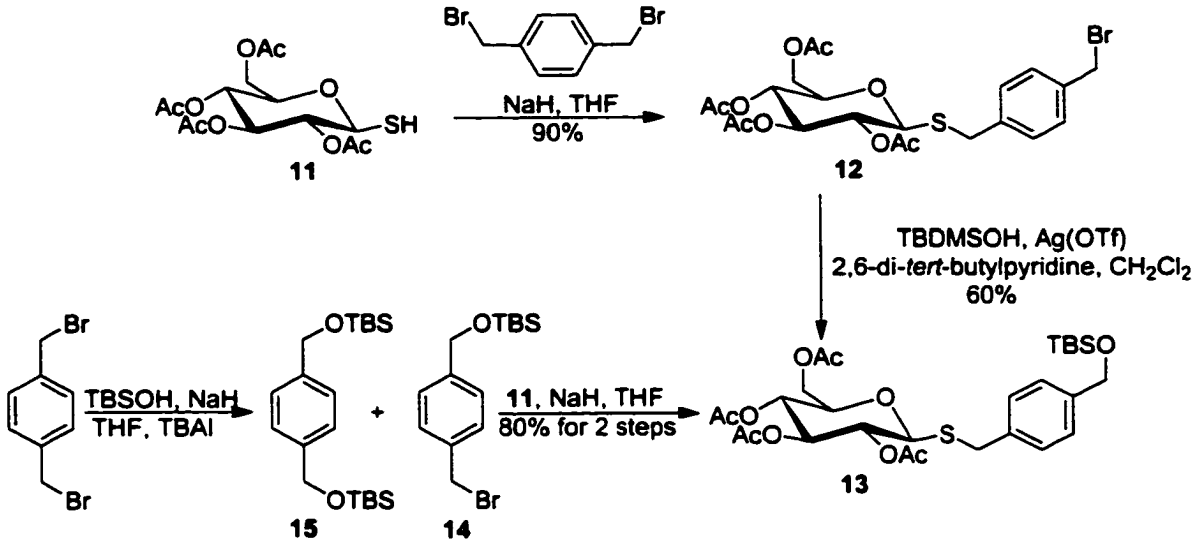


The low and not reproducible yield obtained in the formylation of **8** made us consider a different approach to **9**. Thus, we settled on the commercial α,α'-dibromo-*p*-xylene as a functional equivalent of *p*-bromomethylbenzaldehyde which would avoid the formylation step. This alternative approach required the use of 1-thio-β-D-glucose tetraacetate **11**, which was prepared from glucose tetraacetate via acetobromoglucose.[31] Since the beginning of the synthesis two possible strategies were investigated:

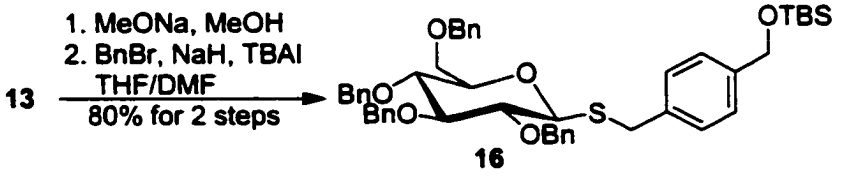
- Direct condensation of α,α'-dibromo-*p*-xylene with **11** to afford thioglucoside **12** in 90% yield. Conversion to the silylated material **13** in 60% yield was then accomplished by treatment of **12** with *tert*-butyldimethylsilanol in presence of silver triflate and 2,6-di-*tert*-butylpyridine.[32]

- The second possibility explored involved the formation of the silyl ether **14** by condensing α,α'-dibromo-*p*-xylene with sodium *tert*-butyldimethylsilanolate. Since a slight excess of silanol was used a mixture of **14** and **15** was obtained. The two products **14** and **15** were hardly separated by column chromatography, but they could be employed

as a mixture in the successive step without the necessity of further purification to obtain **13** in 80% yield.

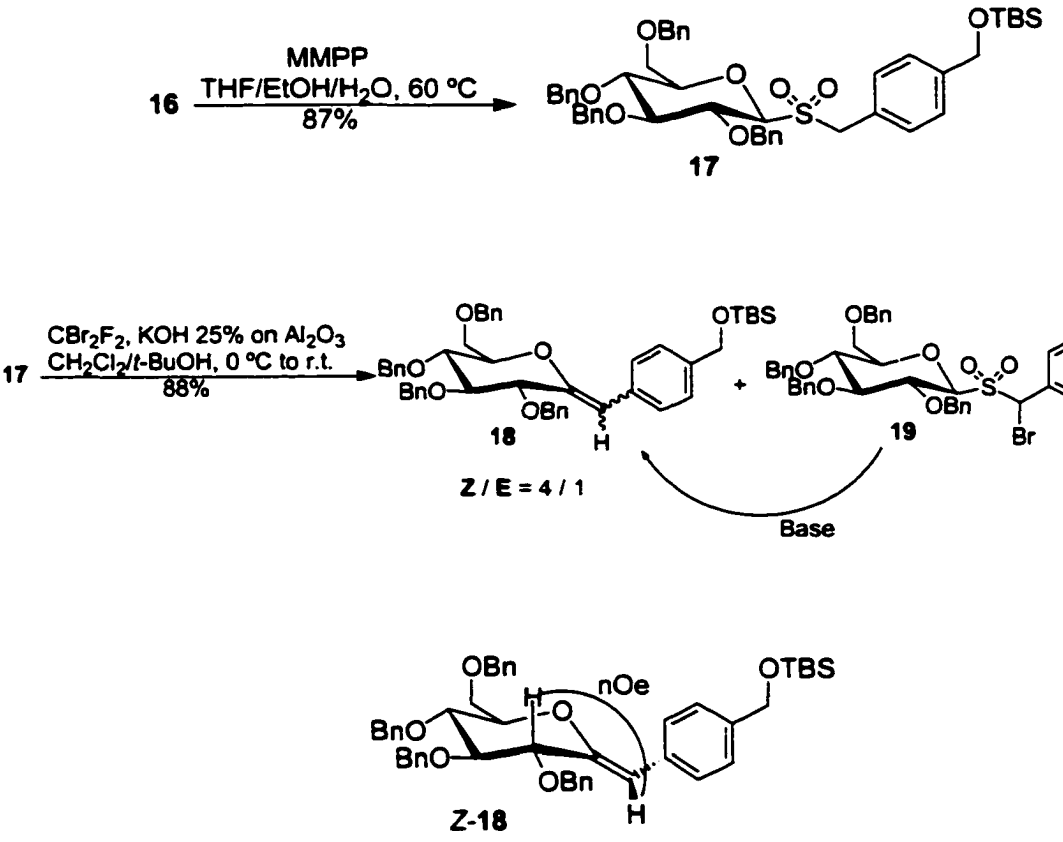


The replacement of the acetyl groups with benzyl ethers to obtain **16** was achieved by deprotection of **13** with sodium methoxide, followed by benzylation (80% yield).

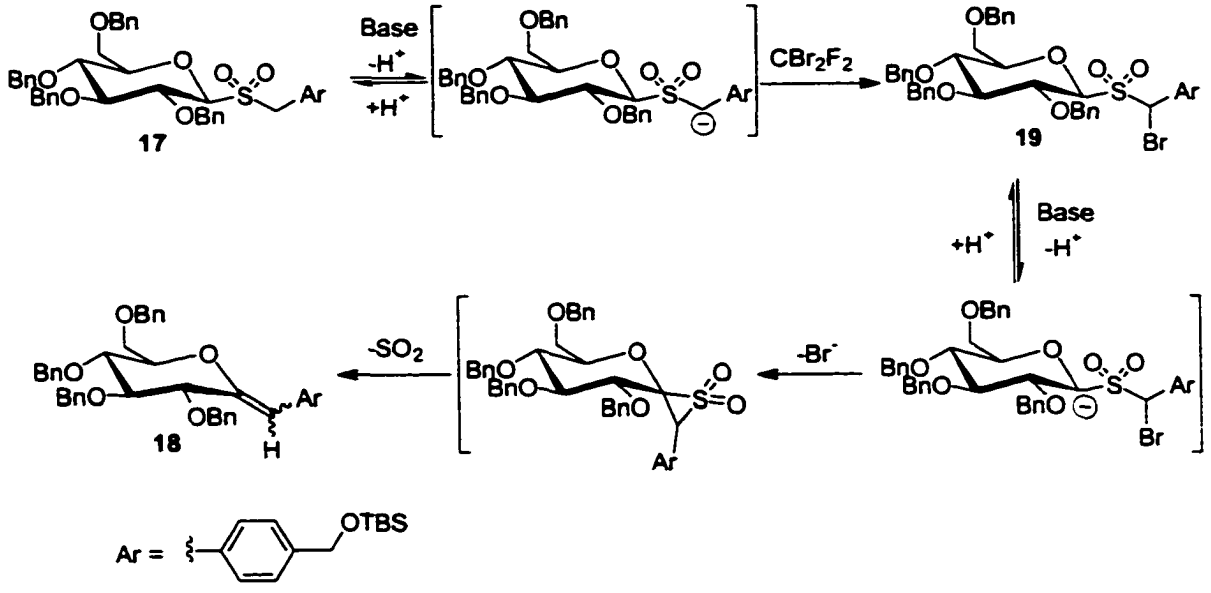


The sulfide **16** was oxidized to the sulfone **17** with MMPP in 87% yield. The resulting sulfone was employed in the Ramberg-Bäcklund synthesis of the *exo*-glucal **18**. The two isomers *Z*-**18** and *E*-**18** in the ratio 8:2 and 88% yield were identified by nOe measurements, which showed an effect between H-1 and H-3 in the case of the *Z*-isomer.

In some cases the intermediate α-bromosulfone **19** was isolated from the reaction mixture and then converted to the *exo*-glucal **18** by treatment with base.

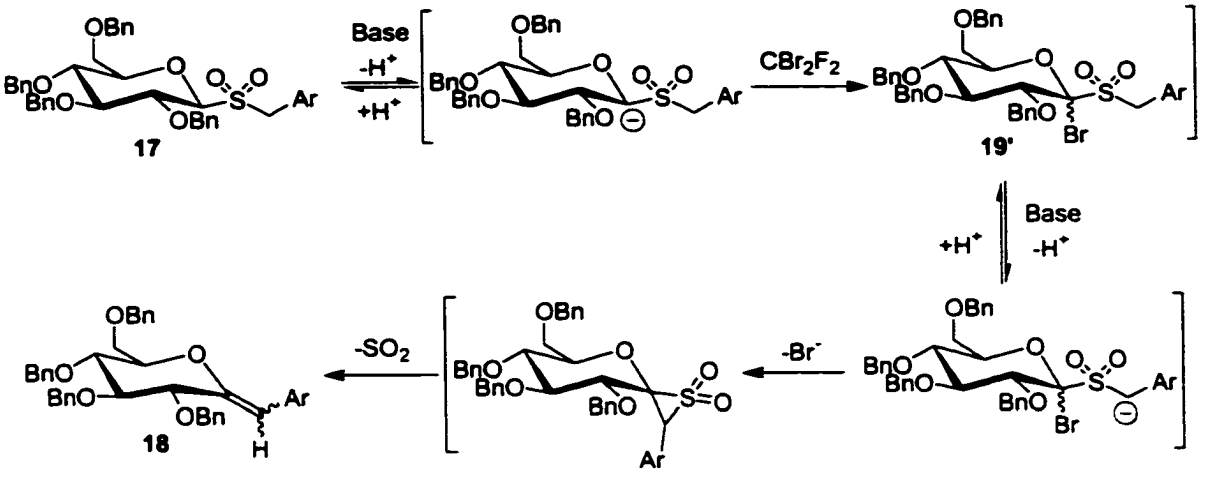


The isolation of **19** suggests a mechanism for the Ramberg-Bäcklund reaction, which involves the bromination of the benzylic carbanion, followed by internal displacement of bromide by nucleophilic attack of the anion formed at the anomeric carbon. The episulfone consequently generated is converted to the enol ether product **18** via extrusion of SO_2 (Equation 4).



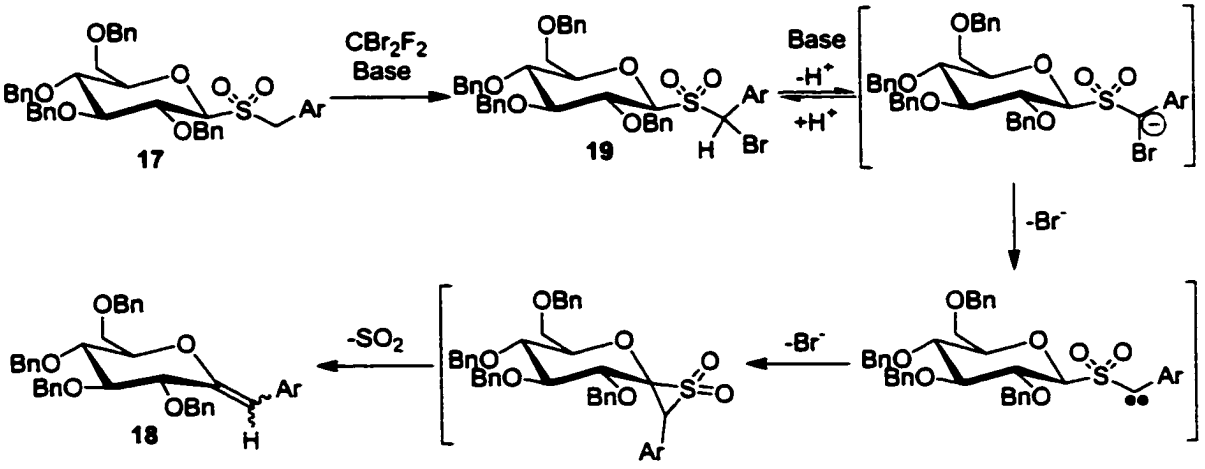
Eq. 4

The alternative possible mechanism would involve the bromination of the anomeric carbon, followed by nucleophilic substitution of the benzylic anion (Equation 5), but no trace of the anomeric bromide were detected. Even if unlikely the presence of this second mechanism can not be ruled out, since the conversion of the unstable **19'** to **18** is presumably faster than from **19** to **18** (this would explain the absence of intermediate **19'** from the reaction mixture).



Eq. 5

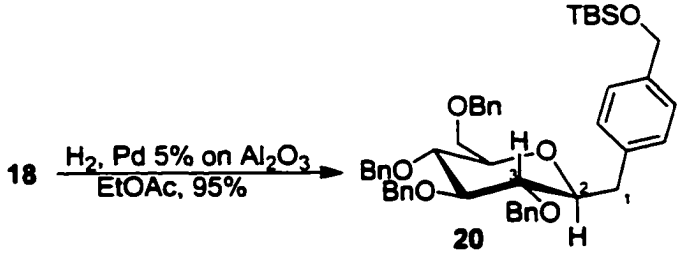
A third possible mechanism involves the deprotonation of the benzylic carbon of the α-bromosulfone **19**, followed by loss of bromide. Then the episulfone is generated by insertion of the resulting carbene into the anomeric C-H bond. Also this mechanism would be consistent with the isolation of the intermediate **19**.



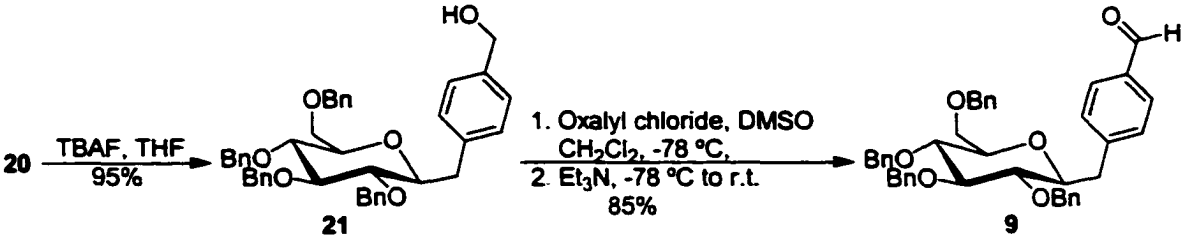
Eq. 6

Interestingly the intermediate **19** appears to be a single diastereoisomer from ^{1}H and ^{13}C-NMR spectra, but the configuration at the tertiary benzylic carbon has not been assigned.

The hydrogenation of **18** with 5% palladium on alumina afforded the *β-C*-glucoside **20** in 95% yield, identified by the coupling constant $J = 9.2$ Hz, indicating an anti-diaxial configuration of the anomeric H-2 with respect to H-3. No presence of *α*-anomer was detected. The use of palladium on alumina rather then on carbon as catalyst avoided any competitive cleavage of the benzyl ethers protecting groups.

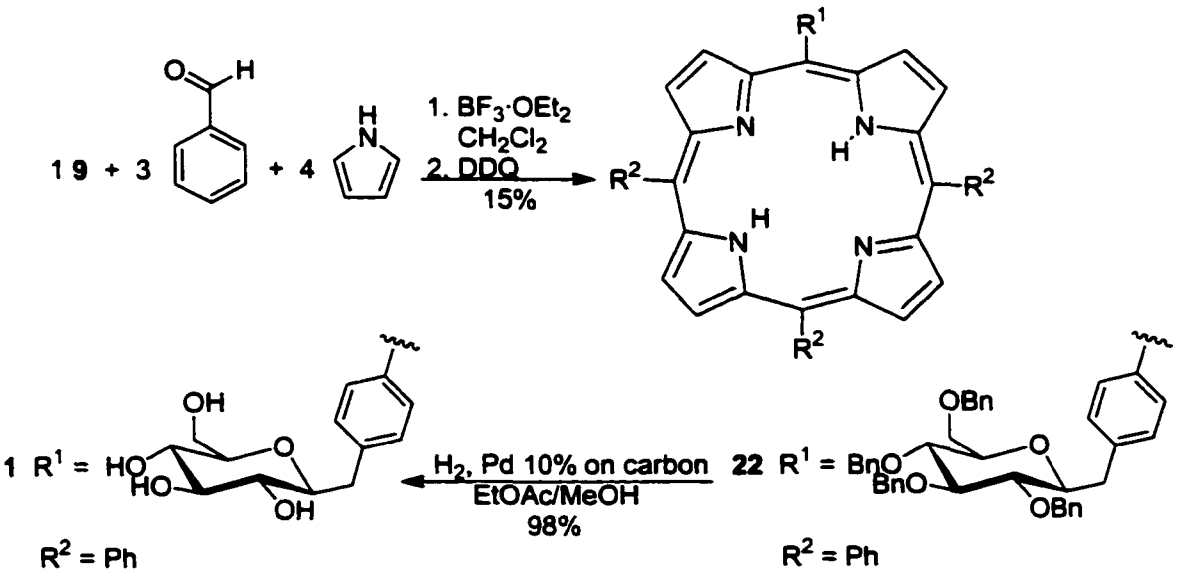


The silyl ether **20** was then cleaved with tetrabutylammonium fluoride (95% yield) and the resulting alcohol **21** was converted to aldehyde **9** by Swern oxidation[33] in 85% yield.



The aldehyde **9** was utilized in the synthesis of the porphyrins **22** and **23** under Lindsey conditions.[34] When a ratio 1/3/4 of **9**, benzaldehyde and pyrrole respectively was employed the mono-*C*-glucosylated porphyrin **22** was obtained in 15% yield, while by employing 1 equivalent each of **9** and pyrrole the tetra-*C*-glucosylated porphyrin **23** was obtained in 53% yield. The lower yield obtained for **22** than for **23** could be explained by the formation of side products as tetraphenyl porphyrin and mono-, bis-, tris- and perhaps tetra- *C*-glucosylated porphyrins. These byproducts were not characterized.

The porphyrins **22** and **23**, were fully characterized and they showed the expected spectroscopic data. The mass spectrum of the tetrasubstituted porphyrin **23** (Figure 3), was particularly useful in the characterization of this material since it showed agreement with the theoretical isotopic distribution that accounts for the 1.1% isotopic abundance of ^{13}C for a 184-carbon atom molecule.



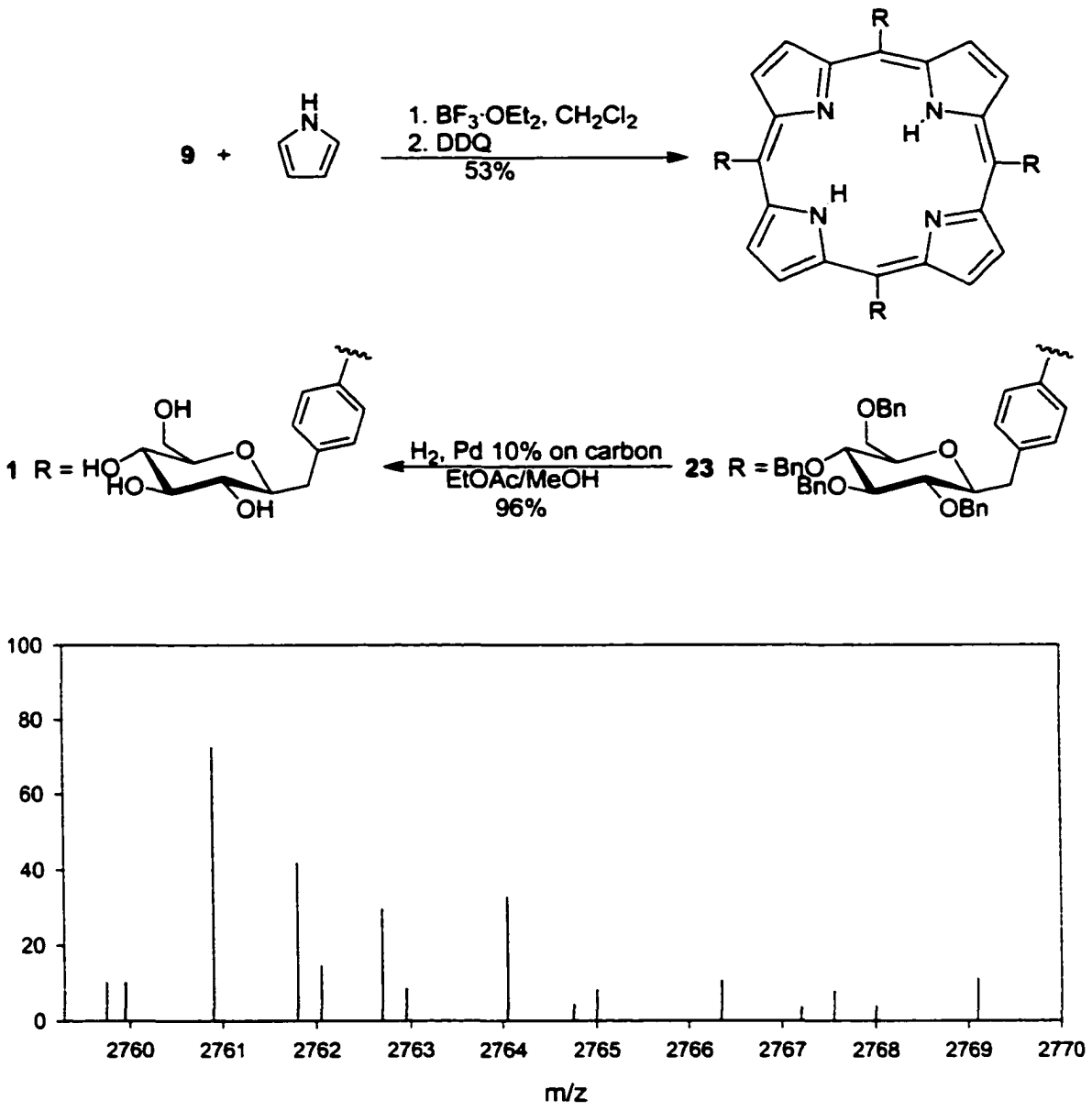
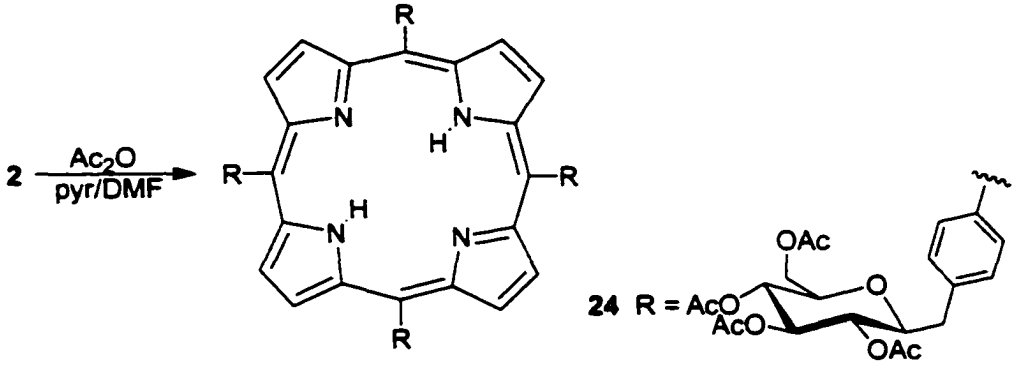


Figure 3. Mass spectrum of porphyrin **23**. The peaks correspond to the protonated porphyrin.

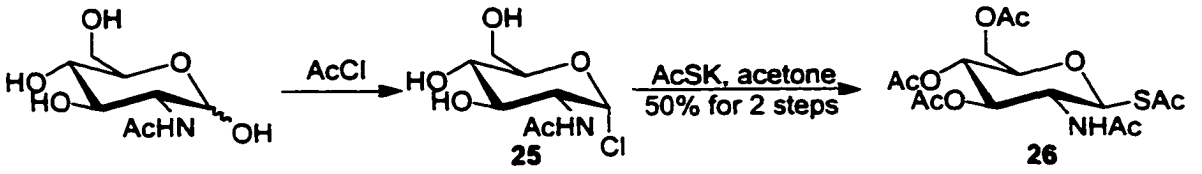
Hydrogenolysis of the benzylic protecting group yielded porphyrins **1** and **2** (95-96%). The ^{1}H- and ^{13}C-NMR signals of the tetra-*C*-glucosylated porphyrin **2** were extremely broad and an assignment of the peaks was not possible. The mass spectrum

confirmed the presence of the desired material. The broadening of the NMR resonances was probably due to aggregation of porphyrin molecules, via a mechanism that involves the pi stacking of the large hydrophobic parts of the porphyrins,[35] accentuated probably by the high polarity of the solvent (typically methanol) needed to ensure dissolution of the material. In any event it was possible to confirm the structure of **2** after acetylation of the hydroxyl groups. The acetylated product **24** could be easily purified by column chromatography and showed the expected spectroscopic data (NMR, UV and mass spectrum).

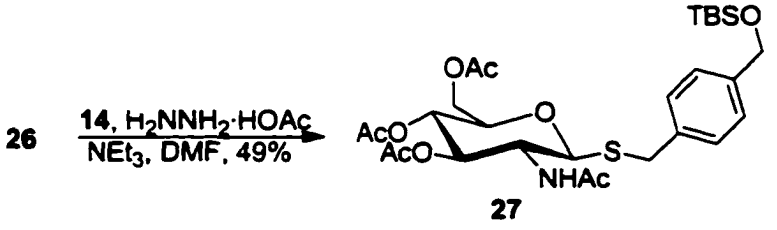


We decided then to pursue the synthesis of a porphyrin *C*-2-glucosoacetamide conjugate, in order to test the feasibility of our synthetic strategy. Moreover it has been reported that positive charges on porphyrins improve their binding ability to DNA,[1, 36] therefore making porphyrins appended with aminosugar particularly interesting materials.

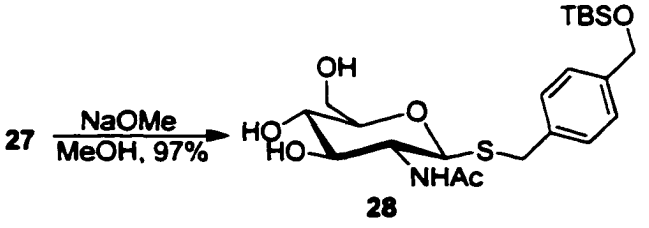
Thus the thioglucoside **26** was prepared in three steps (50% overall yield) from *N*-acetyl-D-glucosamine following a reported procedure.[37]

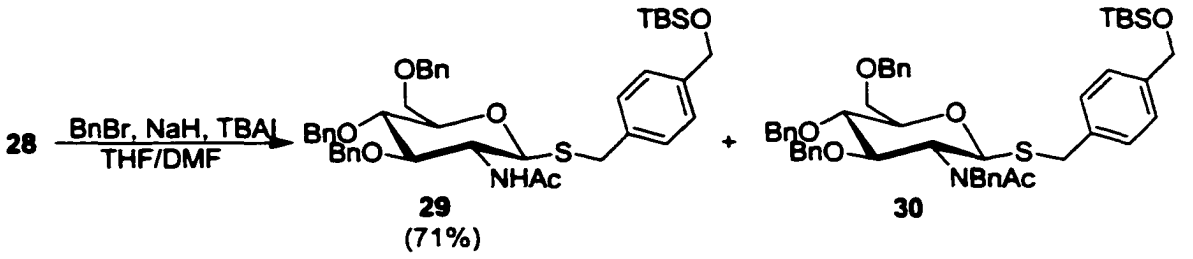


The anomeric thioacetate of **26** was cleaved selectively by treatment with hydrazine acetate and condensed in situ with the benzylic bromide **14** to obtain the thioglucoside **27** in 49% yield.[38]

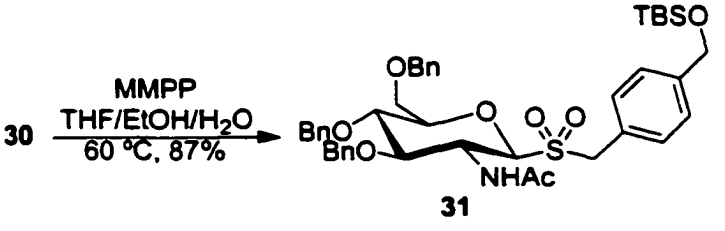


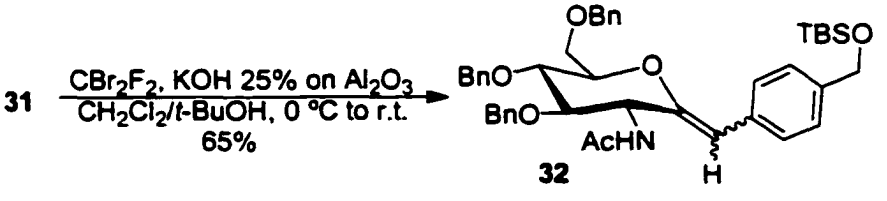
The acetyl protecting groups were cleaved with catalytic sodium methoxide (97% yield) and the hydroxyl groups in **28** were protected as benzyl ethers (**29**, 71% yield). Competitive benzylation of the acetamido group to yield ca. 20% of **30** was detected.



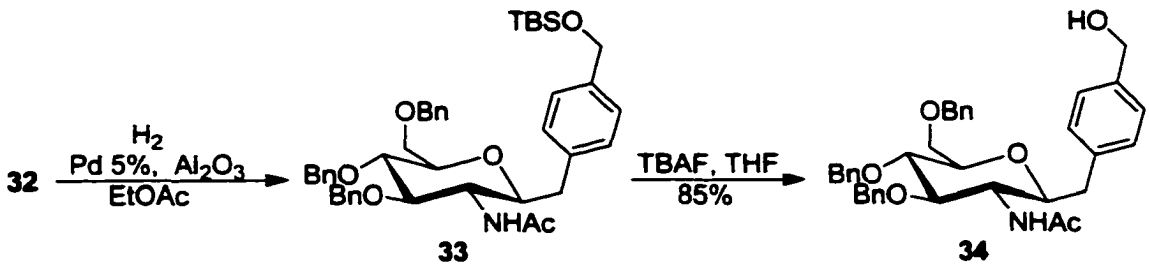


The thioglucoside **30** was oxidized to sulfone (**31**, 95% yield) and then converted to the *exo*-glycal **32** in 55% yield.

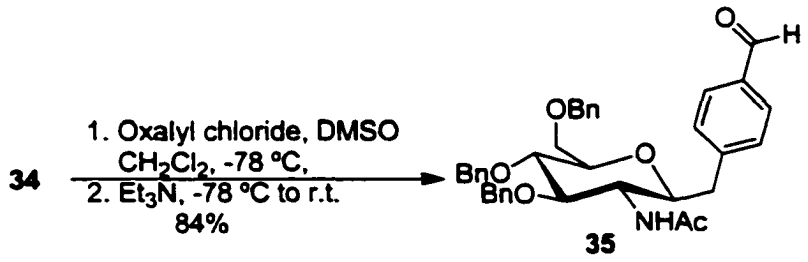


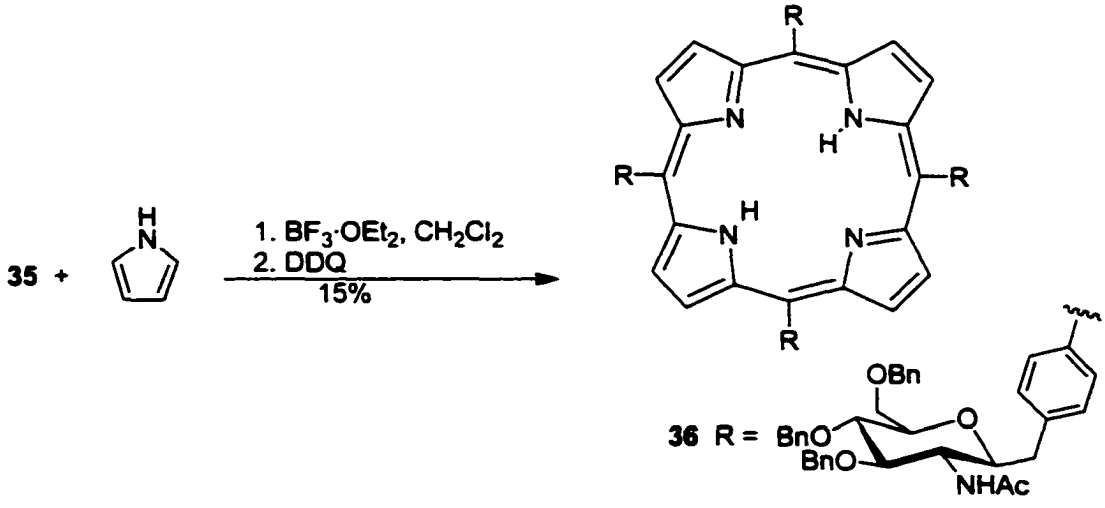


Hydrogenation of **32** catalyzed with palladium on alumina afforded the *β-C*-glucoside **33** with no formation of *α*-anomer and **33** was deprotected to obtain **34** in 85% yield over the two steps.



The alcohol **34** was converted to aldehyde **35** by Swern oxidation[33] in 84% yield and the product obtained was employed in the synthesis of the tetra-aminoglucosylated porphyrin **36** in 15% yield. The porphyrin **36** showed the expected NMR and mass spectra.





3.3 Photocleavage properties of porphyrins 1 and 2

The porphyrins **1** and **2** were tested as potential agents for photodynamic therapy by Xin Chen in Prof. Drain's laboratory. The water solubility of the porphyrins was quantified by calculation of the partition coefficient, determined by repartitioning the porphyrins in an octanol / water biphasic mixture and then by measuring the ratio of UV absorptions of the octanol layer over the water layer (Table 2). A second experiment consisted in detecting the ability of the porphyrins to bind calf thymus DNA, by examining the change in absorption of the Soret band of the porphyrin upon titration with DNA. The photocleavage properties of the porphyrins **1** and **2** were investigated by irradiating with regular lamplight a 5 μM solution of the porphyrin in presence of plasmid DNA (0.5 g/l). Small aliquots of the mixture were collected at regular 10 minute time intervals over a period of 1.5 hour and the eventual damage of DNA was checked by electrophoresis.[39]

As expected, the porphyrin **2** showed higher water solubility than **1**, but neither gave satisfactory results in the photoclevage experiment. One possible explanation of the low efficiency of these materials as photosenzitizers may be in their tendency to aggregate, consequently affecting their ability to bind the DNA.

	Partition coefficient (octanol / water)	Binding constant to calf thymus DNA (10^6 M^{-1})
1	68.3	0.05
2	29.9	0.40

Table 2. Solubility and binding properties of porphyrins **1** and **2**.

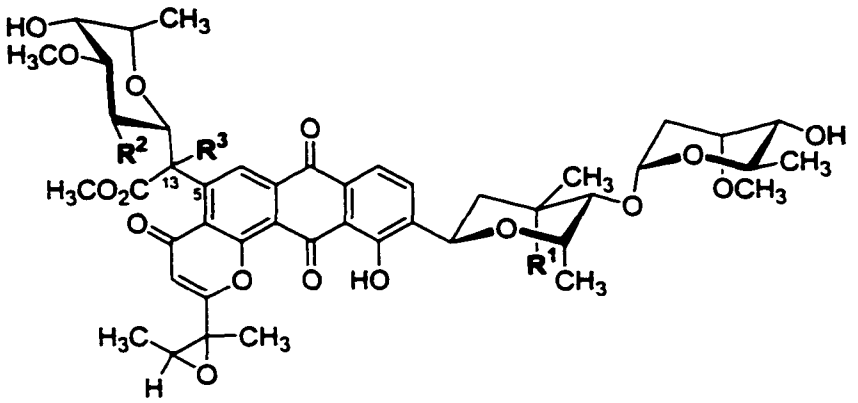
4. SYNTHESIS OF THE NORTHWEST QUADRANT OF ALTROMYCIN B

4.1 Introduction

Altromycin B is an antitumor antibiotic discovered in 1990.[40] Altromycin B is produced by an actinomycete (strain AB1246E-26) isolated from a South African bushveld soil. Along with Altromycin B eight other minor species (Altromycin A, C, D, E, F, G, H, I) have been isolated from the fermentation broth (Figure 4).[41] Altromycins are members of the family of pluramycin antibiotics. The aglycone chromophore is common for all the Altromycin A – I. Altromycin A to D and G differ from one another in the sugar regions of the molecule. Altromycin E and F are 13-deoxy. Altromycin H and I don't contain the *C*-altrose moiety in the northwest quadrant.

The structures of these molecules have been assigned on the basis of their spectroscopic data, mainly by NMR. No crystal structure is available. The stereochemistry of the carbon 13 as well as of the epoxide moiety has not been assigned. Moreover, it has not been determined whether the carbohydrate moieties are present in the D or L configuration.

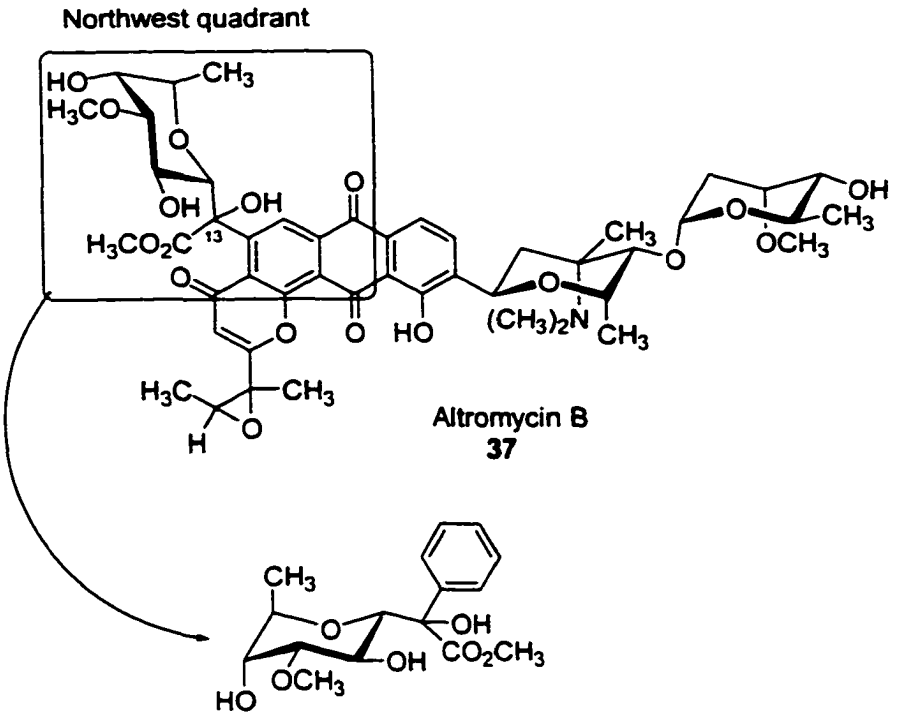
Altromycin B showed activity against several kinds of cancer. It has been demonstrated that Altromycin B forms a complex with DNA by covalently binding to the N-7 of guanine via nucleophilic attack of the guanine's nitrogen to the epoxide.[42] A biosynthetic pathway for Altromycin formation has been proposed.[43]



Altromycin	A	$R^1 = NHCH_3$	$R^2 = OH$	$R^3 = OH$
	B	$R^1 = N(CH_3)_2$	$R^2 = OH$	$R^3 = OH$
	C	$R^1 = NHCH_3$	$R^2 = H$	$R^3 = OH$
	D	$R^1 = N(CH_3)_2$	$R^2 = H$	$R^3 = OH$
	E	$R^1 = NHCH_3$	$R^2 = OH$	$R^3 = H$
	F	$R^1 = N(CH_3)_2$	$R^2 = OH$	$R^3 = H$
	G	$R^1 = NH_2$	$R^2 = OH$	$R^3 = OH$
	H	5-OH	$R^1 = NHCH_3$	
	I	5-OH	$R^1 = N(CH_3)_2$	

Figure 4. Structures of Altromycins.

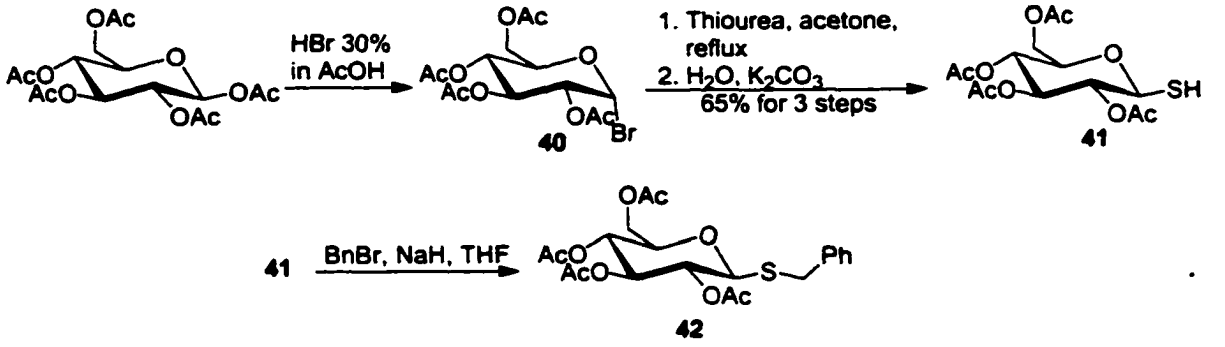
Along with a common type of *C*-glycoside linkage in the southeast, Altromycin B incorporates a rare *C*-glycoside in its northwest quadrant. The α-6-deoxy-altrose moiety is linked to the aglycone via a quaternary carbon and it assumes a flipped chair conformation.



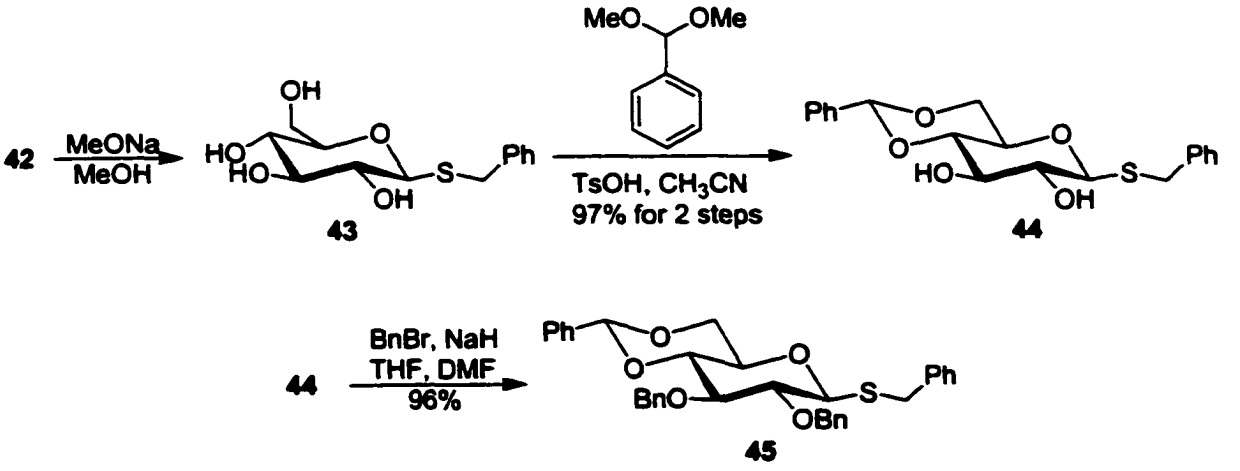
Our goal was to achieve a synthetic sequence to the northwest quadrant of Altromycin B. We studied first the feasibility of our synthetic approach by installing all the functionalities present in the target quadrant on a glucose model. We then extended our synthetic strategy to an altrose model, in order to synthesize the two epimers at C-13 (*R*-**38** and *S*-**39**). In addition to the synthesis of the northwest quadrant of Altromycin B we were interested in using our materials of known structure and stereochemistry to assign the relative stereochemistry at C-13 by comparison of the spectroscopic data of our models with that of Altromycin B.

4.2 Glucose model

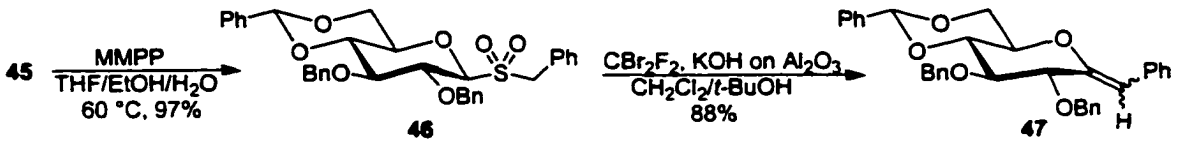
The thioglucose **41** was prepared in 3 steps from the commercially available glucose pentaacetate in 65% overall yield following published procedures.[31] By condensation of **41** with benzyl bromide the thioglucoside **42** was obtained in 70% yield.



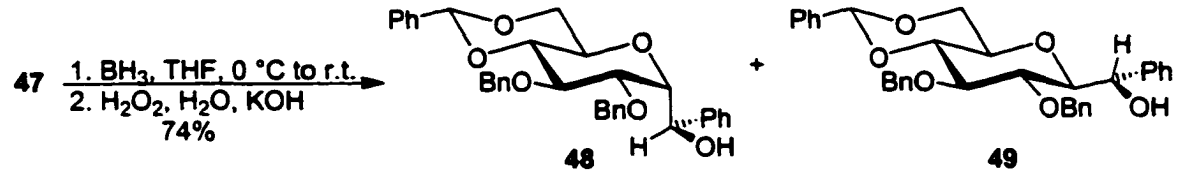
The acetyl groups were then cleaved and the thioglucoside **43** was converted to the benzyl 4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside **44** in 97% yield, followed by the protection of the position 2 and 3 with benzyl ethers (**45**, 96%).



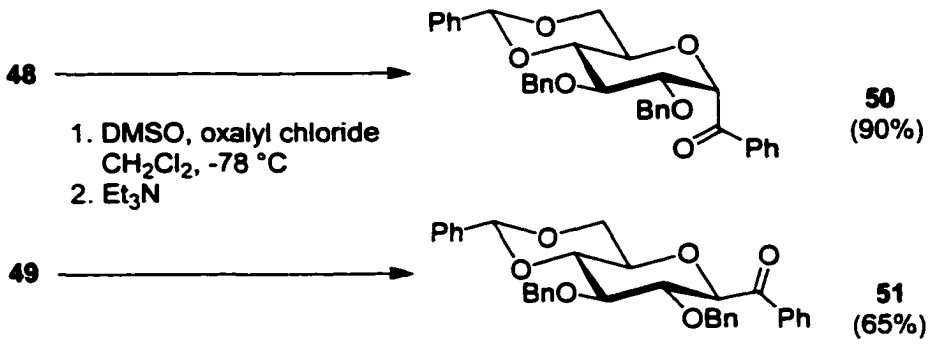
The oxidation of the sulfide **45** to sulfone **46** (97% yield) was followed by the Ramberg Bäcklund reaction. The *exo*-glucal **47** was obtained in 88% yield, in *Z/E* ratio = 6/1.



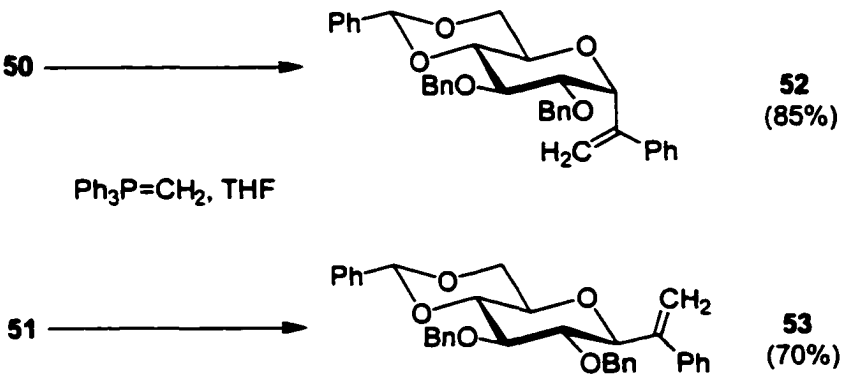
The hydroboration of the *exo*-glucal **47**, followed by in situ basic oxidation of the alkylborane intermediate afforded α-**48** and β-**49** in a ratio α/β = 6/4 and 74% overall yield.[44] The stereochemistry of the new chiral center C-1 was assigned by assuming a *syn* addition of the borane to the double bond, followed by an oxidation with retention of configuration of the organoborane intermediate.



The Swern oxidation proceeded without epimerization at the anomeric center with 90% yield for **50** and 65% for **51**.[33, 45]

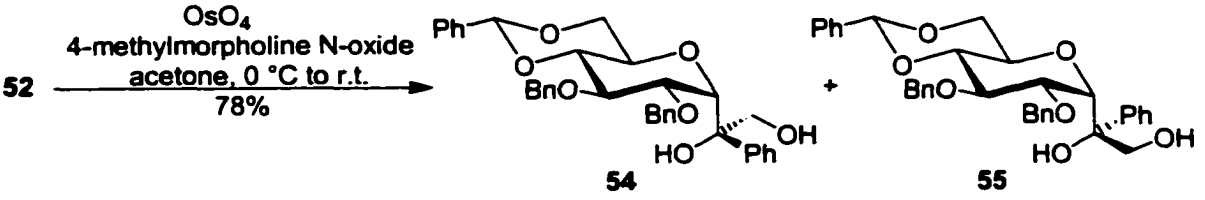


The Wittig reaction yielded respectively **52** in 85% yield and **53** in 70% (91% yield based on the 73% conversion).



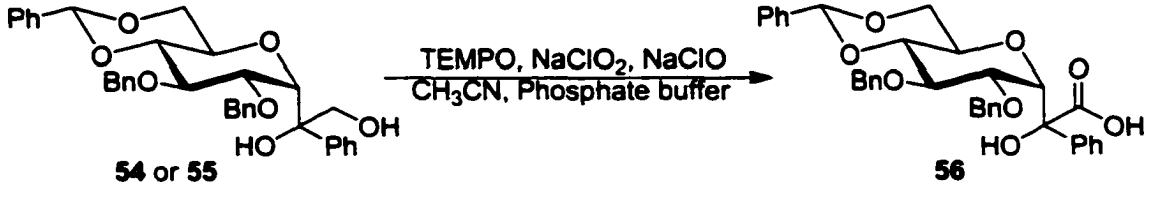
The Sharpless dihydroxylation[46] of **52** with α– and β– AD-mix didn't give any result, with recovery of the unreacted starting material, probably due to steric hindrance to oxidation.

The dihydroxylation with OsO_4 gave a mixture of two diastereomers in 3:1 ratio and 78% yield.[47] The two diastereomers were separated but it was not possible to assign the stereochemistry at the quaternary center.



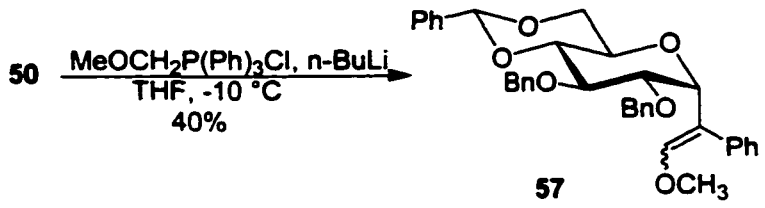
The ^{1}H-NMR of the minor product of the dihydroxylation reaction shows a pattern, which apparently is not consistent with a chair conformation. A peak centered at 3.48 ppm, assigned to the anomeric H-3, is a broad singlet with a very small coupling, detectible only from the COSY spectrum, with H-4. The small coupling constant between H-3 and H-4 could account for a distorted chair or boat conformation. Efforts to crystallize this product were unsuccessful. Also the values of the coupling constants for the major product ($J_{3,4}$ = $J_{4,5}$ = 7 Hz) suggest the presence of a distorted chair conformation.

Oxidation of **54/55** with NaClO/$NaClO_2$ catalyzed by TEMPO[48] gave a complex mixture containing the desired carboxylic acid **56**, as detected by mass spectroscopy.

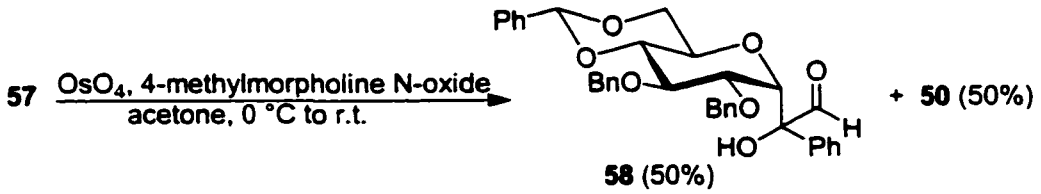


We explored another route to the product **56** by synthesizing the enol ether **57** via Wittig reaction. The yield obtained with this alternative procedure was significantly lower (40% yield, *E/Z* = 5/2). The enol ether obtained was then treated with osmium

tetraoxide to afford the aldehyde **58** in ca. 50% yield, with the formation of a large amount (50%) of the ketone **50**, resulting from the cleavage of **58**.



57



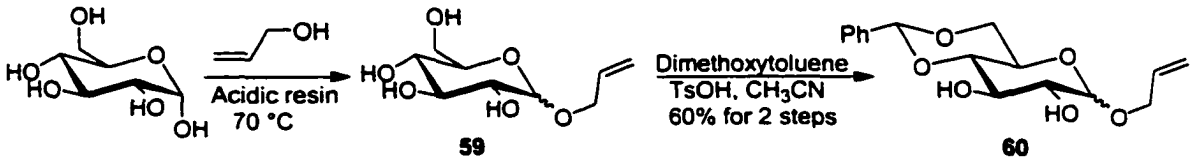
58 (50%)

The aldehyde **58** was oxidized to the carboxylic acid **56** by sodium chlorite.[49]

4.3 Altrose model

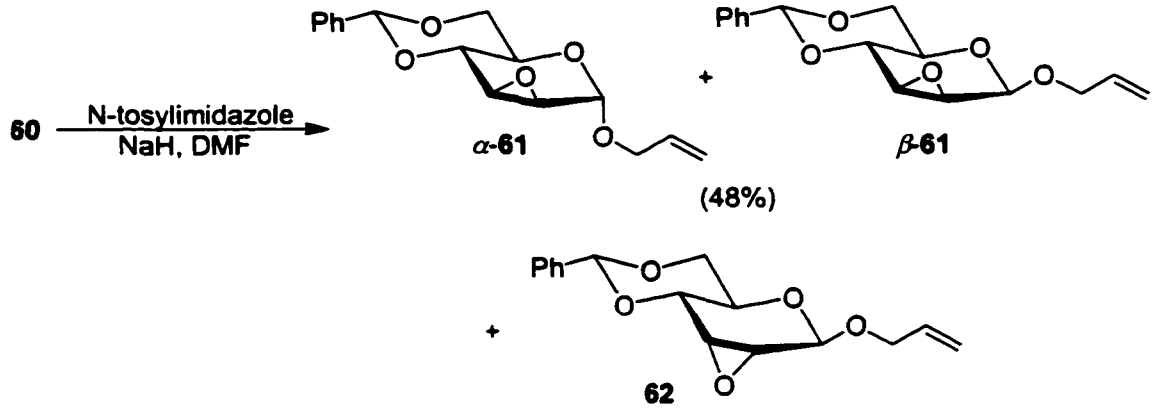
We decided to apply the synthetic sequence employed for the glucose model to an altrose model, similar to the target quadrant of Altromycin B.

Our first approach to the synthesis of the models for the northwest quadrant of Altromycin B started with the preparation of the partially protected glucose **60** by treatment of α-glucose with allyl alcohol in presence of acidic resin at reflux.[50] We obtained a 3/2 mixture of α- and β- allyl glucosides **59**, which were protected as the benzylidene to afford the allyl 4,6-*O*-benzylidene-D-glucopyranoside **60** in 60% yield over two steps.

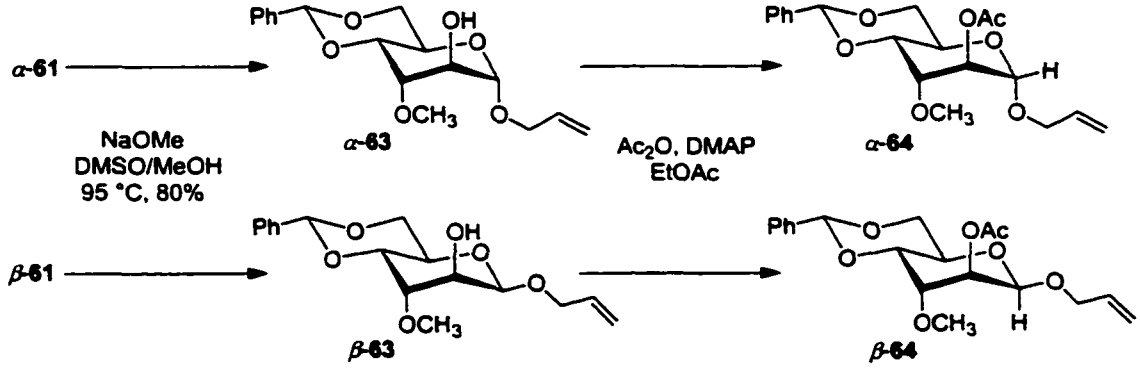


By treating **60** with *N*-tosylimidazole and 2 eq NaH a mixture of products was obtained.[51] The three main products were isolated by column chromatography. The structure of α-**61** and β-**61** was assigned after the basic opening of the epoxide with sodium methoxide and acetylation of the hydroxyl group. The ratio obtained was α-**61** : β-**61** : **62** = 2 : 1 : 1. The products α-**61** and β-**61** could be isolated as a mixture in 48% yield by crystallization from methanol and could be used as mixture for the next step. Alternatively the three products could be separated by column chromatography. The presence of the benzylidene protecting group was important in order to assure a rigid

conformation of the pyranose ring and minimize the possibility of a nucleophilic attack of the methoxide to C-2.



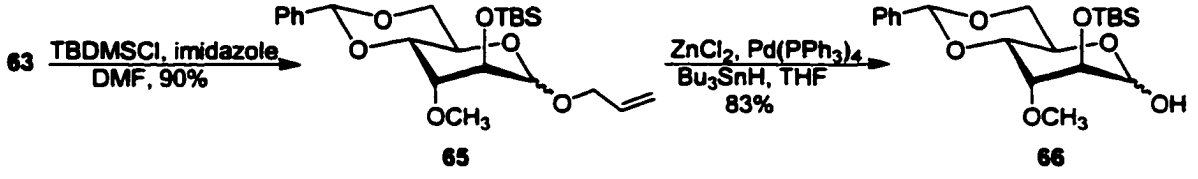
The basic opening of the epoxides α- and β-**61** by sodium methoxide in DMSO at 95 °C proceeded via nucleophilic axial attack of methoxide, producing the diaxial opening of the epoxide in 80% yield.



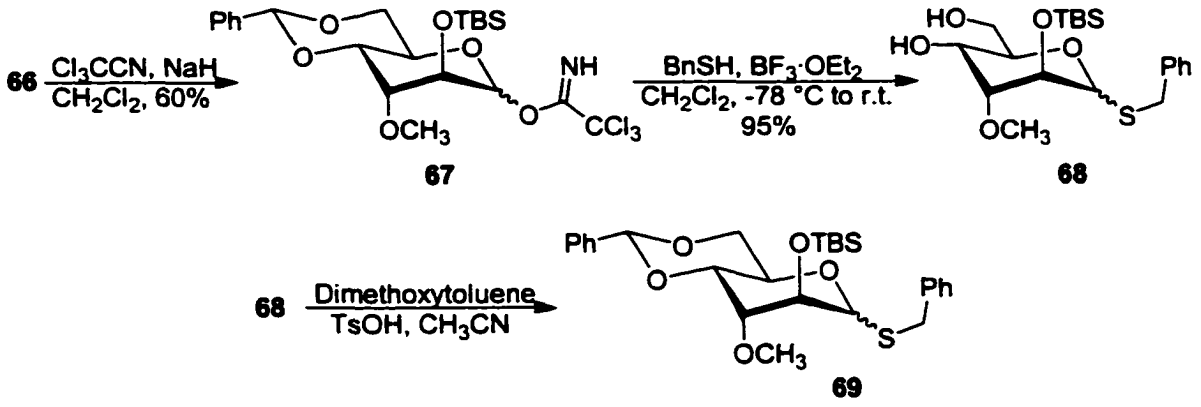
The stereochemistry at the anomeric center of α- and β-**64** was assigned by measuring the ^{13}C-^{1}H coupling constants, whose values were consistent with data reported in literature for similar models ($^{1}J^{13}C^{1}H(1)$ = ~170 for α-**64** and ~162 Hz for β-

64).[52] The stereochemistry at the anomeric center was also confirmed by the formation of traces of the allyl 3-*O*-methyl-4,6-*O*-benzylidene-β-D-glucopyranose via diequatorial opening of the epoxide *β*-**61**.

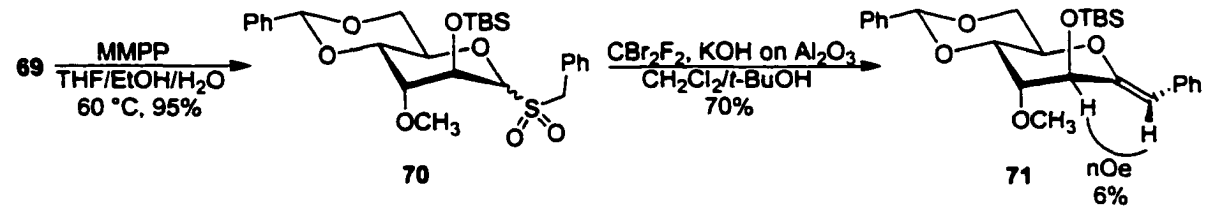
After protection of the hydroxyl group at the position 2 with silyl ether (**65**, 90% yield), the allyl ether was cleaved (**66**, 83%).[53]



The trichloroacetimidate **67** was prepared in 60% yield[54] and then employed in the synthesis of the thioglucoside **69**. Treatment of **67** with $BF_3{\cdot}OEt_2$ and benzyl mercaptan produced the thioglycoside **68** in 95% yield with the cleavage of the benzylidene, which could be reinstalled in quantitative yield. The cleavage of the benzylidene could be avoided by running the reaction at low temperature. The two step procedure (cleavage in the glycosylation step, followed by reinstallation of the benzylidene protecting group) was preferred since it allowed an easier separation of **68** from the excess benzyl mercaptan. On the contrary the similar R_f of benzyl mercaptan and **69** deriving from the temperature controlled glycosylation made the purification inefficient and consequently difficult to obtain a pure sample for **69** (besides, the contamination with even small amounts of benzyl mercaptan was very annoying, due to the strong stench of this material).

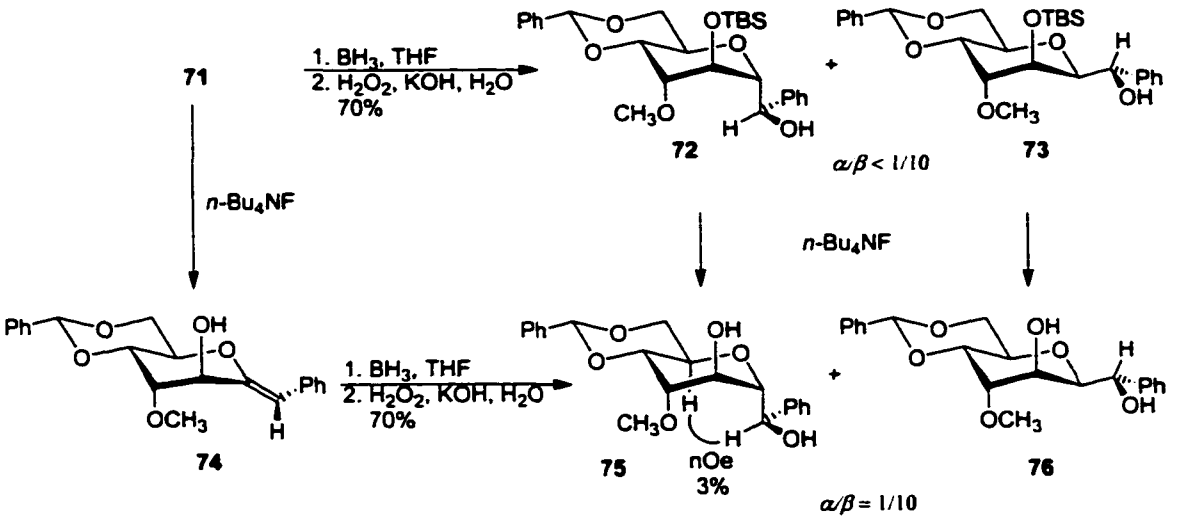


The oxidation of the sulfide **69** to sulfone (**70**, 95%), followed by the Ramberg-Bäcklund reaction afforded the *exo*-glycal **71** in 70% yield. We obtained the *Z* isomer only, identified by nOe (6%) between the vinylic proton H-1 and H-3.

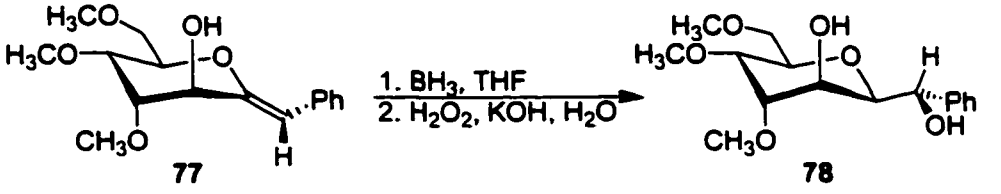


The hydroboration / oxidation sequence[44] applied to the *exo*-glycal **71** afforded the *C*-glycosides **72** and **73** in 70% yield and α/β = ~1/10. We hoped to achieve higher selectivity toward the α product by delivery of the borane from the axial hydroxyl group on C-3. The silyl ether of **71** was therefore cleaved and the hydroboration reaction on **74** was performed, unfortunately with no improvement in the α/β ratio.[55]

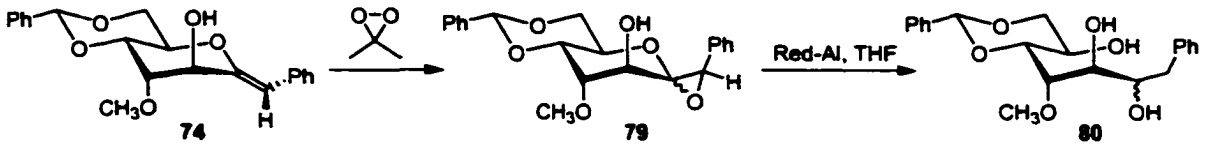
The α configuration of the minor product **75** was confirmed by nOe (3%) between H-1 and H-6. The two anomers **75** and **76** were separated by column chromatography.



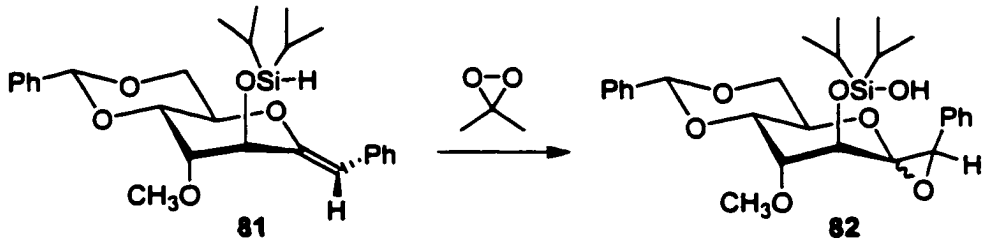
We tried to improve the α-selectivity by means of other possible approaches. With the hope that a more flexible ring could yield a better ratio the hydroboration was conducted on **77**, resulting however in the β-isomer **78** as the only product.



The hydride delivery by free hydroxyl groups that complexes an aluminum hydride to obtain a stereoelective opening of epoxides has been described.[56] So treatment of *exo*-glycal **74** with dimethyldioxirane[57] afforded the formation of the epoxide **79**,[58] which was successively treated with Red-Al with the hope that the axial hydroxyl group could coordinate aluminum hydride and β-deliver an hydride to the anomeric carbon. Unfortunately this reaction afforded the open sugar **80**, probably via hydride delivery to C-1, followed by opening of the hemiketal and reduction of the resulting ketone.

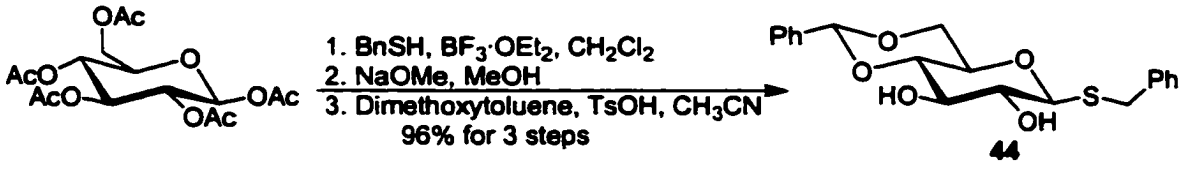


Delivery of hydride from a silyl ether was not practical since the silane was oxidized by DMDO.

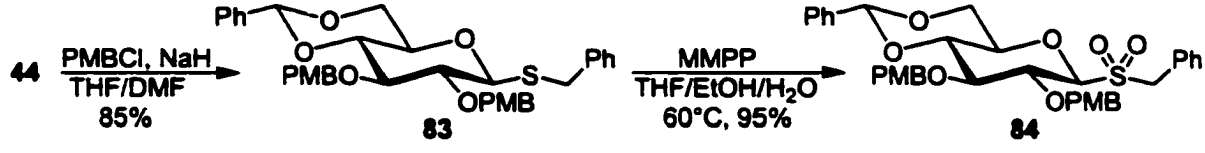


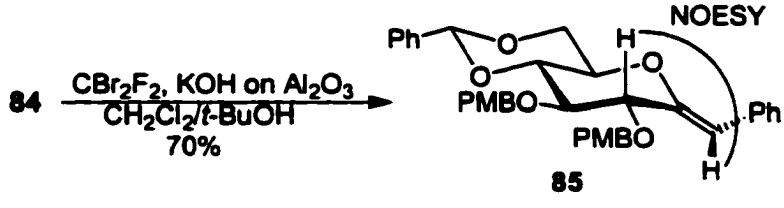
Due to the low yield obtained for the α-*C*-glycoside we decided to follow another synthetic approach. Since the hydroboration of the *exo*-glucal gave a high ratio of α/β products we decided to explore the possibility to prepare the altrose via opening of the epoxide obtained form the α-*C*-glucoside.

Thus glucose pentaacetate was treated with excess benzyl mercaptan in presence of 1 equiv $BF_3 \cdot OEt_2$.[59] Deprotection of the acetates followed by installation of a benzylidene to protect positions 4 and 6 afforded **44** in a 96% overall yield for the three steps.



Anticipating some incompatibility of benzyl ethers with our synthetic approach we opted for *p*-methoxybenzyl ethers as protecting groups for the positions 2 and 3 (**83**, 85% yield). The thioglucoside **83** was then oxidized to sulfone **84** (95% yield) and employed in the Ramberg-Bäcklund reaction to obtain the *exo*-glucal **85** in 70% yield. We obtained the *Z* isomer only as it was confirmed by a NOESY analysis, which revealed a nOe between the olefinic H-1 centered at 5.60 ppm and the axial H-3 at 3.99 ppm.



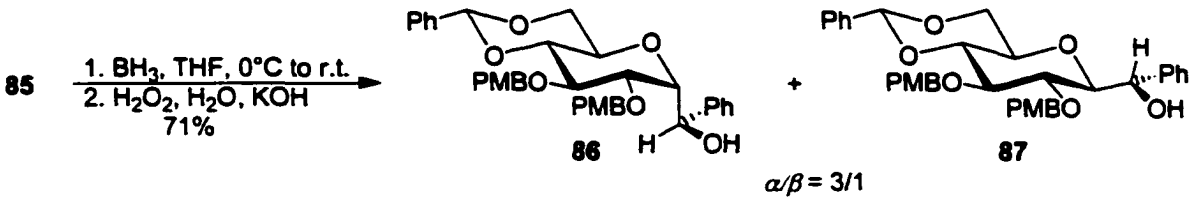


The hydroboration of the glucal **85** afforded a mixture 3/1 of the α- and β-*C*-glucosides **86** and **87** in 71% combined yield. The two products were separated by flash column chromatography on silica gel. The stereochemistry at the anomeric center of the two products can be easily identified from the coupling constants between the anomeric H-2 and the axial H-3: $J_{2,3}$ = 4.9 Hz for **86**, $J_{2,3}$ = 9.2 Hz for **87**. We also observed two

cross peaks in the NOESY of **86** which reveal an effect between H-1 (centered at 5.11 ppm) and both H-4 (at 4.07 ppm) and H-6 (multiplet with H-5 at 3.74-3.70 ppm). At this stage the stereochemistry at C-1 was assigned by assuming a *syn* addition of borane to the double bond and an oxidation with retention of configuration of the organoborane intermediate. This assumption of stereochemistry was confirmed later on in the synthesis.

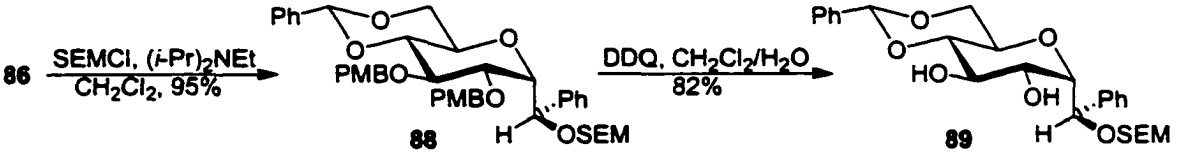
The large coupling constant (8.5 Hz) between H-1 and the anomeric H-2 indicates an *anti* relationship with a ca. 180° dihedral angle between the two protons, suggesting the favored conformation around the C-1–C-2 bond described in the equation below. The alternative *syn* relationship between H-1 and H-2, consistent with the value of the coupling constant, is not favored by steric consideration since it would involve an eclipsed conformation. Also the value observed for the coupling constant $J_{1,2}$ = 9.2 Hz in **87** suggests the conformational arrangement depicted below.[2]

The ^{1}H-NMR (25 °C, $CDCl_3$) of **86** shows a well defined triplet at 4.07 ppm for H-4 in which the coupling constant J = 7.6 Hz appears a little too small for a diaxial interaction (normally ~ 9 Hz) among H-3, H-4 and H-5, suggesting a distortion of the chair conformation due to steric congestion of the axial anomeric group.



The hydroxyl group of **86** was protected as SEM ether (**88**, 95%)[60] and the PMB ethers were cleaved with DDQ (**89**, 82%).[61]

The coupling constants $J_{2,3} = J_{3,4} = 3.1$ Hz, measured for the triplet corresponding to H-3 in **88** suggest a larger distortion of the chair to a boat conformation than in **86**, due to the presence of the more steric demanding SEM ether. The release of steric congestion in **89** after the deprotection of the PMB ethers results in a less distorted chair conformation as confirmed by the coupling constants $J_{3,4} = J_{4,5} = J_{5,6} = 9.2$ Hz, typical of an axial relationship among H-3, H-4 and H-5.



The *C*-glucoside **89** was converted to epoxide in 95% yield.[51] Two products, 2,3-anhydromannoside derivative **90** and 2,3-anhydroalloside **91**, were obtained in 4/1 ratio, and were separated by column chromatography. The anomeric proton H-2 of the major product **90** is a doublet centered at 4.22 ppm with a coupling constant $J_{2,3} = 0$ Hz, consistent with a dihedral angle close to 90° (see projection a, Figure 5) while in the epoxide **91** the anomeric proton H-2 is a doublet of doublet centered at 4.11 ppm with a coupling constant $J_{2,3} = 3.1$ Hz. Such coupling constant is probably due to a staggered relationship between H-2 and H-3 arising from a pseudo-boat conformation of the sugar ring (projection b, Figure 5). The alternative possibility for **91** is a pseudo-chair conformation, which can be ruled out since a larger coupling constant would be expected from the eclipsed relationship between H-2 and H-3 (projection c, Figure 5).

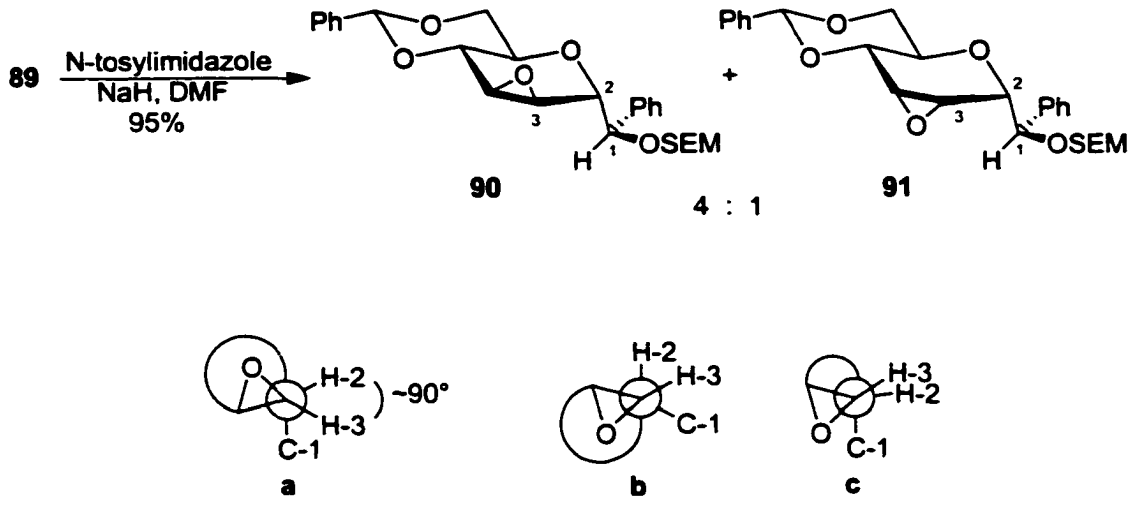
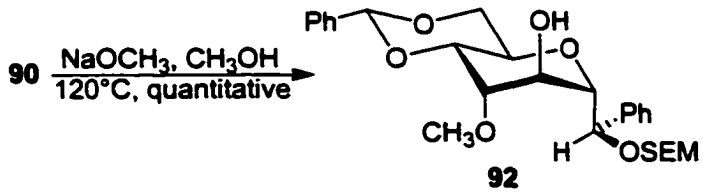


Figure 5. Projection along the C-3 – C-2 bond of **90** assuming a chair conformation of the sugar ring (**a**), **91** in a boat conformation (**b**) and in a chair conformation (**c**).

The configuration of the epoxide **90** was confirmed by basic opening with sodium methoxide (ca. 2 M in methanol) at 120 °C (pressure tube) which gave the altrose derivative **92** in quantitative yield, resulting from the diaxial opening of the epoxide with the installation of the correct functionalities at the positions 3 and 4. Lower temperatures resulted in a sluggish reaction.



Deprotection of the SEM ether in **92** with tetrabutylammonium fluoride yielded a product with identical NMR data to **75**, confirming the α-stereochemistry assigned previously.

After the cleavage of the benzylidene protecting group (85% yield) the NMR spectrum of **93** showed a coupling constant $J_{2,3} = J_{3,4} = 7.0$ Hz, which is not consistent with either one of the two possible chair conformations. The NOESY spectrum of **93** shows two diagnostic cross peaks, one revealing an effect (2% nOe) between H-1 and H-6, consistent with the conformation **93'**, and a second one revealing an effect (2% nOe) between H-3 and OH-5, which indicates the presence of the chair conformation **93"**. These NOESY signals wouldn't be compatible with boat or skew conformations, even if the presence of such conformations couldn't be ruled out from a possible dynamic equilibrium. Furthermore, low temperature ^{1}H- and ^{13}C-NMR (in THF-d_8, Figure 6) show a clear broadening and shifting of signals. These observations indicate the presence of an equilibrium between the two forms **93'** and **93"**. Unfortunately, the coalescence temperature and a separation of the signals corresponding to each conformer couldn't be reached and therefore it wasn't possible to calculate an equilibrium constant from the integration of the signals at low temperature. An approximate equilibrium constant could be extrapolated by comparing the experimental coupling constant with the expected coupling constants of the two chair-conformers (assuming that the populations of other conformers be negligible and the two chairs not distorted). So a simple mathematical equation accounting $J_{3,4} = 7$ Hz for **93** and assuming $J_{3,4} = 3$ Hz and $J_{3,4} = 9$ Hz respectively for a rigid $^{1}C_4$–type and $^{4}C_1$–type chair conformation:

$$3\,x_1 + 9\,x_2 = 7$$

$$x_1 + x_2 = 1$$

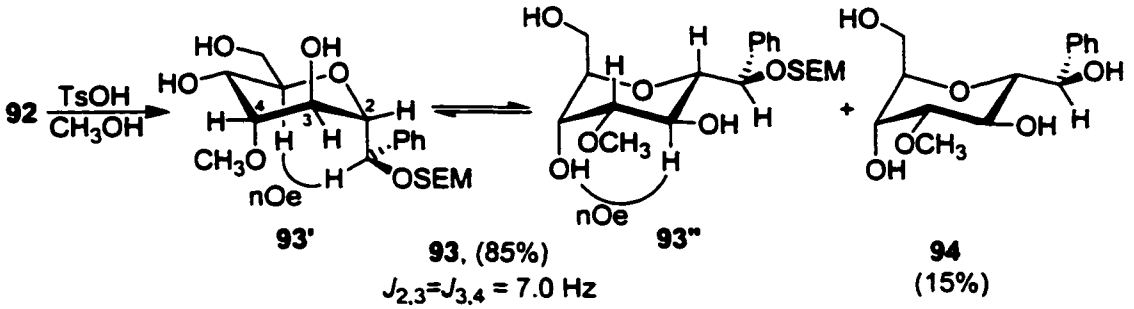
where: x_1 = molar fraction of **93'**

x_2 = molar fraction of **93"**

gives an equilibrium constant $K = x_2/x_1 = 2$ at room temperature.

Assuming $1 < J_{3,4}(^1C_4) < 3$ and $9 < J_{3,4}(^4C_1) < 10$, the equilibrium constant results in the range $1.3 < K < 3$.

A side product of the acidic cleavage of the benzylidene of **92** arose from the deprotection of the SEM ether (**94**, 15%). Such side reaction could be limited, but not avoided by carefully monitoring the reaction by TLC. In any event, product **94** could be employed in the successive steps. Longer reaction times afforded only product **94** in quantitative yield.



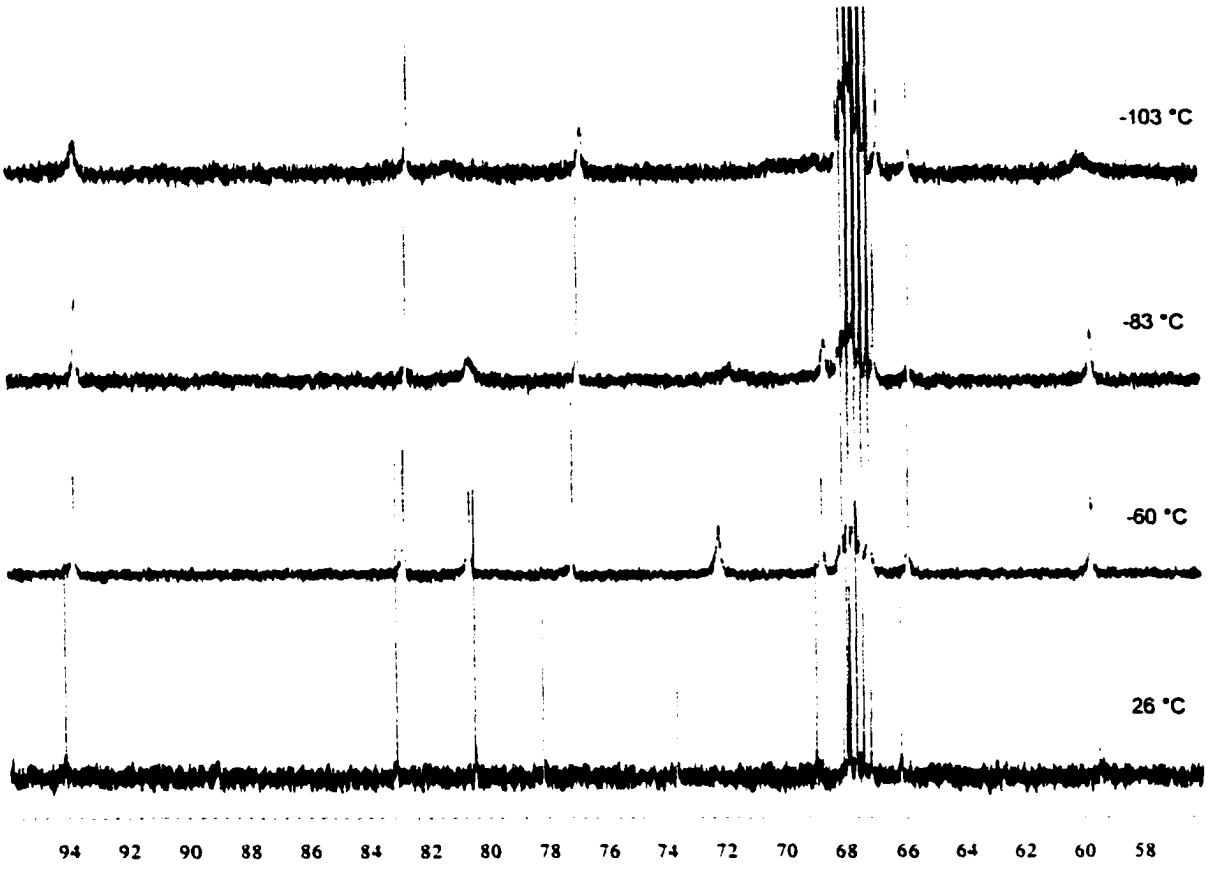
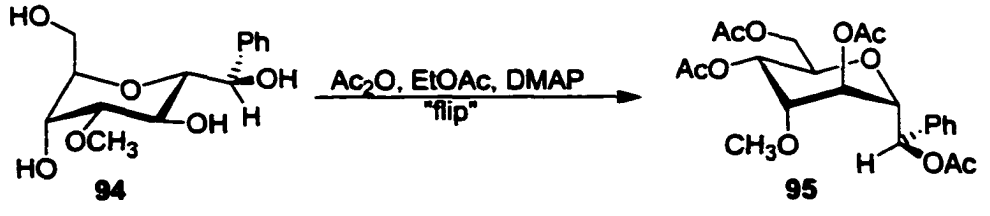


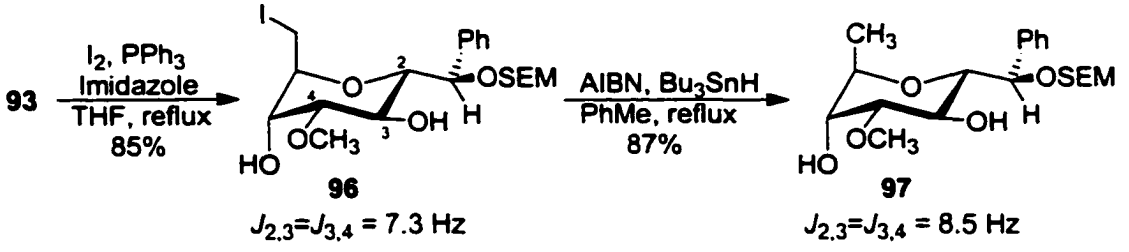
Figure 6. Carbon resonance spectrum (100 MHz, 100 Hz) of **93** as a function of temperature.

Interestingly, the acetylation of the *C*-glycoside **94**, which assumes a $^{1}C_{4}$-type preferred conformation (as evident from the coupling constants $J_{2,3} = J_{3,4} = 7.6$ Hz and $J_{4,5} = J_{5,6} = 3.2$ Hz), resulted in the flipping of the ring in **95** to a $^{4}C_{1}$-type conformation ($J_{2,3}, J_{3,4}, J_{4,5} = 2.4 - 3.6$ Hz and $J_{5,6} = 9.2$ Hz). Deprotection of the acetates with catalytic sodium methoxide in **95** afforded **94** without any trace of epimerisation at C-1.

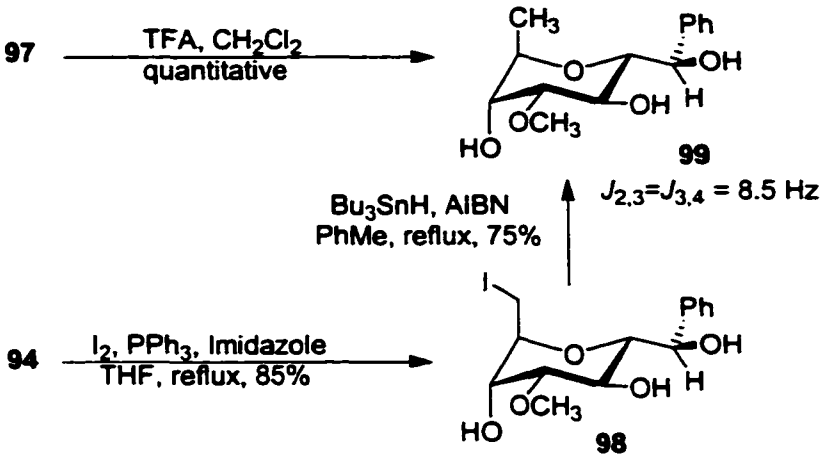


The selective iodination of the primary hydroxyl group of **93** was achieved in 85% yield.[62] Also this product probably consists of an equilibrium between the two chair conformations, as suggested by the coupling constant $J_{2,3} = J_{3,4} = 7.3$ Hz. Furthermore, also for **96** broadening and shifting of the ^{1}H-NMR signals were observed at low temperatures.

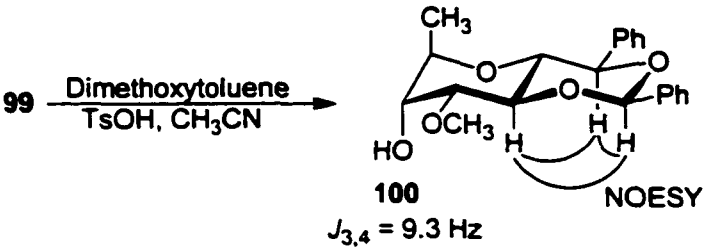
The radical deiodination afforded **97** (87% yield),[63] whose coupling constants $J_{2,3} = J_{3,4} = 8.5$ Hz suggest a flipped $^1C_4$-type conformation.



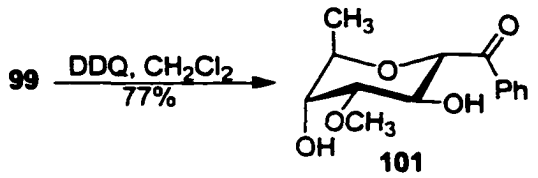
The product **99** was obtained by acidic deprotection of the SEM ether in quantitative yield[64] or as an alternative via selective iodination of the primary hydroxyl group in **94** (**98**,85% yield), followed by radical deiodination (**99**, 75%). Although this last route was shorter by one step (the deprotection of both benzylidene and SEM was achieved in a single step from **92**) and consequently preferred when we scaled up the reaction, the two-step deprotection was preferred in order to obtain analytically pure sample, since the purification of **98** from the triphenylphosphine oxide byproduct proved to be unsuccessful by conventional column chromatography. Our effort to use polymer supported triphenylphosphine in the transformation from **94** to **98** was not successful.



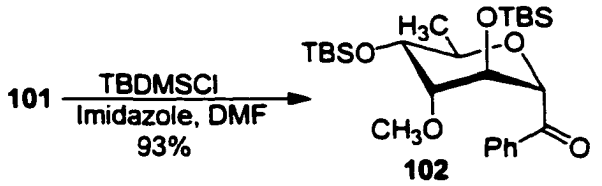
At this stage it was possible to confirm the stereochemistry at C-1 obtained in the hydroboration step from **85** to **86** by making the benzylidene derivative **100**. The NOESY spectrum indeed reveals an axial relationship among H-1, H-3 and H-8.



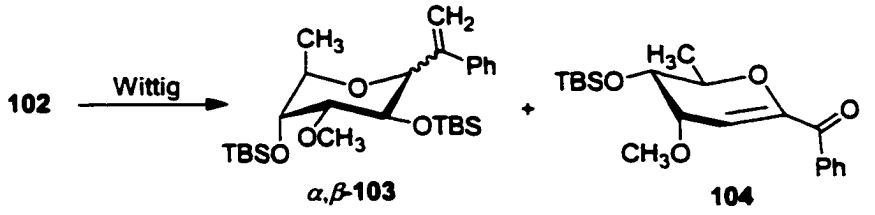
Several oxidizing reagents have been explored for the oxidation of the benzylic alcohol **98** to ketone (notably, MnO_2,[65] 4-(dimethylamino)pyridinium chlorochromate,[66] $BaMnO_4/CuSO_4/Al_2O_3$,[67] NBS), but all proved to be either not reactive or to afford a sluggish reaction. DDQ was the only oxidant that gave satisfactory results (77% yield).



The free hydroxyl groups in positions 3 and 5 were then protected as silyl ethers in 93% yield. The values of the coupling constants $J_{2,3}$ = 2.5 Hz and $J_{5,6}$ = 7.9 Hz for the product **102** suggest a preferred $^1C_4$-type conformation.

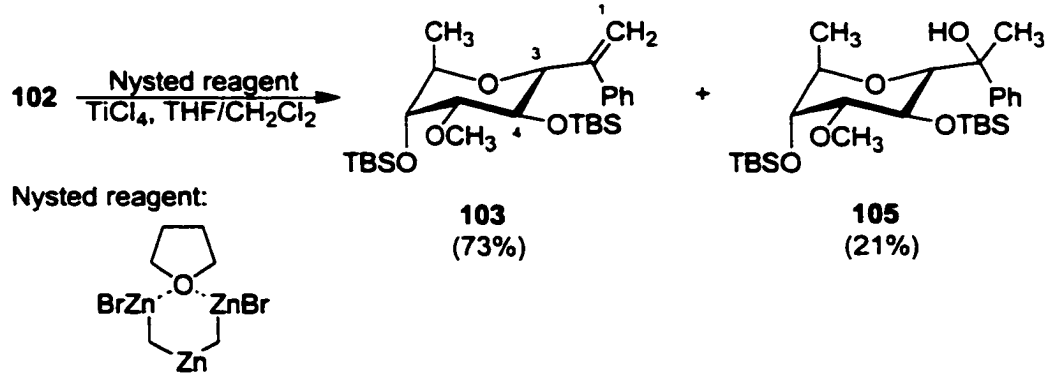


Efforts to install the methylene via Wittig procedures were unsuccessful due to epimerization at the anomeric center and competitive elimination to form the glycal **104**.

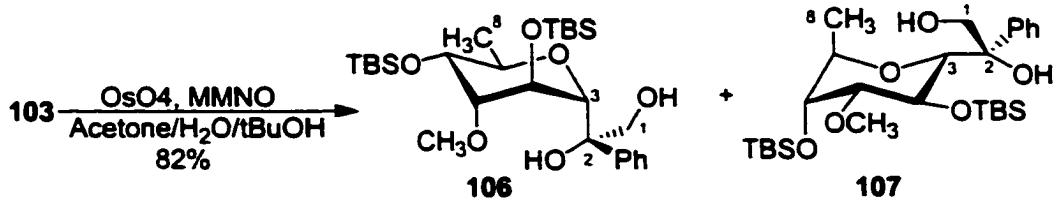


We consequently opted to employ the Nysted reagent,[68] which gave a satisfactory yield (α-**103**, 73%), with concurrent formation of the byproduct **105** (21%), derived by addition of water to the double bond catalyzed by the acidic conditions employed in the reaction. This side product can be minimized by running the reaction under rigorously

anhydrous conditions and by optimizing the reaction time. It's interesting to notice the opposite preferred conformations assumed by the pyranose ring in **102** ($^4C_1$-type, $J_{2,3}$ = 3.0 Hz, $J_{5,6}$ = 7.9 Hz) and **103** ($^1C_4$-type, $J_{3,4} = J_{4,5}$ = 7.0 Hz and $J_{5,6}$ = 3.0 Hz).

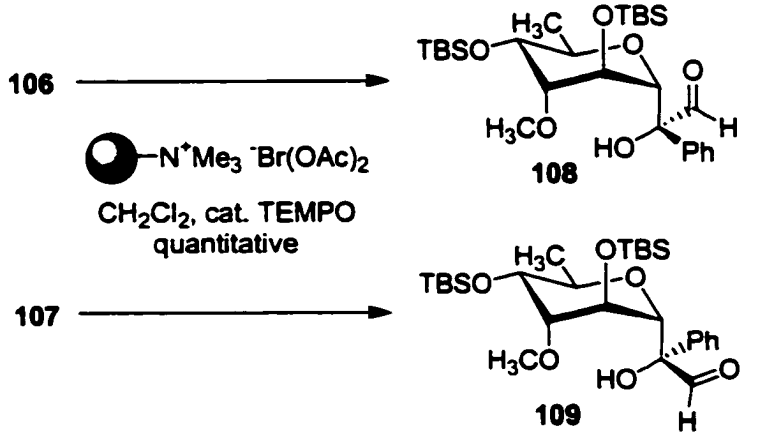


The dihydroxylation of **103** with osmium tetroxide[47] gave a separable mixture of the two epimers at C-2 **106** and **107** in 4/1 ratio and 82% combined yield. Interestingly the difference in a single stereocenter between the two C-glycosides **106** and **107** results in completely different conformational behaviors, being $^4C_1$-type the preferred conformation for the major **106** ($J_{3,4}$ = 0 Hz, $J_{4,5} = J_{5,6}$ = 3.2 Hz and $J_{6,7}$ = 9.2 Hz) and $^1C_4$-type the preferred for **107** ($J_{3,4} = J_{4,5}$ = 9.2 Hz, $J_{5,6} = J_{6,7}$ = 2.4 Hz). The configuration at the quaternary centers was assigned later in the synthesis.



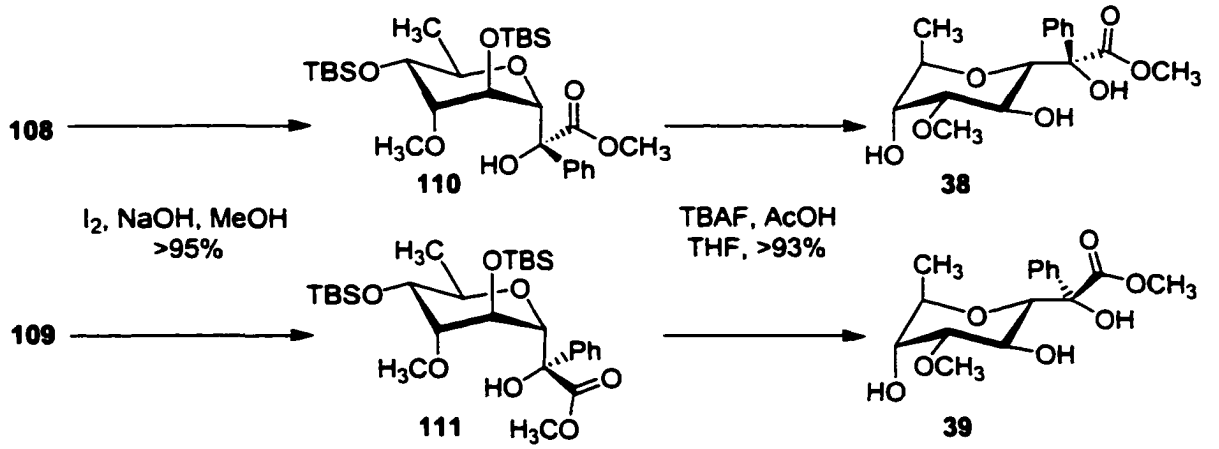
106 : **107** = **4** : 1

The oxidation of vicinal diols is reported to proceed with low yields, due to competitive cleavage of the C-C bond to form a ketone (**102** in our case). This fragmentation of the molecule is particularly accentuated when metal-containing oxidizers are employed. Methods involving IBX,[69] alkali hypochlorites[70] and more recently chlorite/hypochlorite catalyzed by TEMPO have been proposed,[48] but when we tested them on our glucose model **55** they did not give very satisfactory results in terms of yields. Therefore we were particularly glad when we observed that the oxidation of **106** and **107** employing the polymer supported bromite(I) complex recently described by Kirshning[71] gave quantitative yields. The aldehydes **108** and **109** could be isolated without further purification and directly employed in the next step. Both the products **108** and **109** assume a $^4C_1$-type conformation.

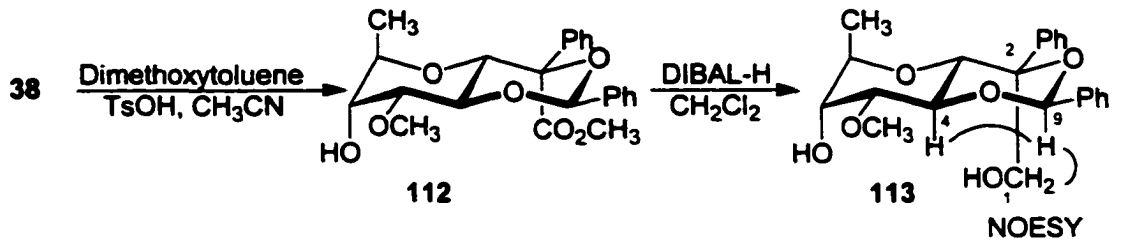


The oxidation to esters of **108** and **109** was achieved in one step and in ca. 95% yield by alkaline iodine oxidation[72] employing an inverse addition (alkaline solution added to the mixture of iodine and starting material). The TBDMS ethers were then

cleaved by action of fluoride in the presence of acetic acid to avoid the hydrolysis of the esters.



The stereochemistry at the quaternary center C-2 (corresponding to C-13 of Altromycin B) was assigned by synthesizing the benzylidene derivative **112** from **38**, followed by reduction of the ester to alcohol with DIBAL-H (**113**). The NOESY spectrum clearly shows two cross peaks, that evidence an effect between the benzylidene H-9 and respectively one proton of the methylene C-1 and H-4 (Figure 7).



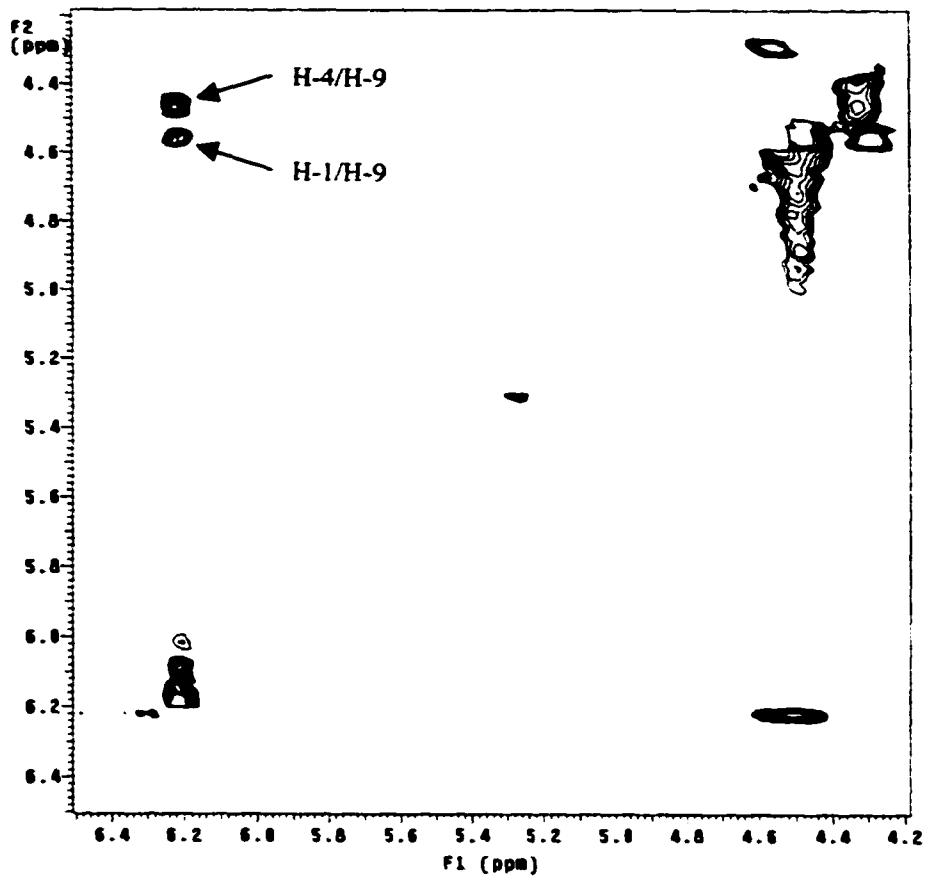
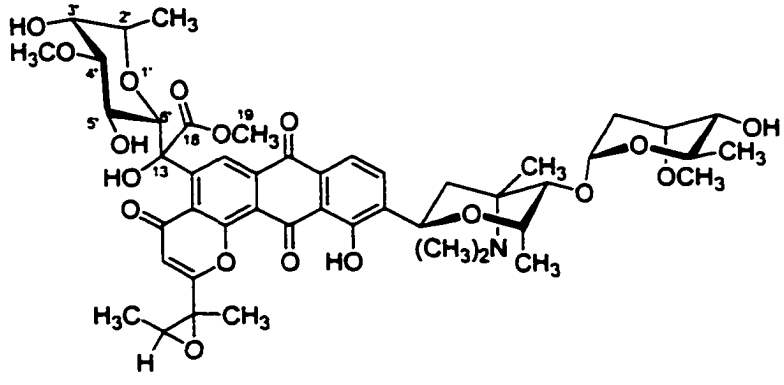


Figure 7. NOESY spectrum of **113**.

4.4 Comparison of the NMR data of the synthetic models with Altromycin B

The spectroscopic data of the two models **38** and **39** were compared with the ones of Altromycin B in order to assign the stereochemistry at the quaternary C-13 (in this section the numbering we refer to is the one adopted for Altromycin B). As expected little information about the configuration at that center was obtained from the ^{1}H-NMR spectra (Figure 8) since the differences in the chemical shifts of either one of the two models with respect to the ones of Altromycin B balance. A way to quantify the discrepancy is to calculate the average of the absolute values of the differences between the chemical shift corresponding to each proton of the two models and Altromycin B. By means of this method we obtain an average difference in chemical shift Δ = 1.72 for **38** and Δ = 1.78 for **39**.



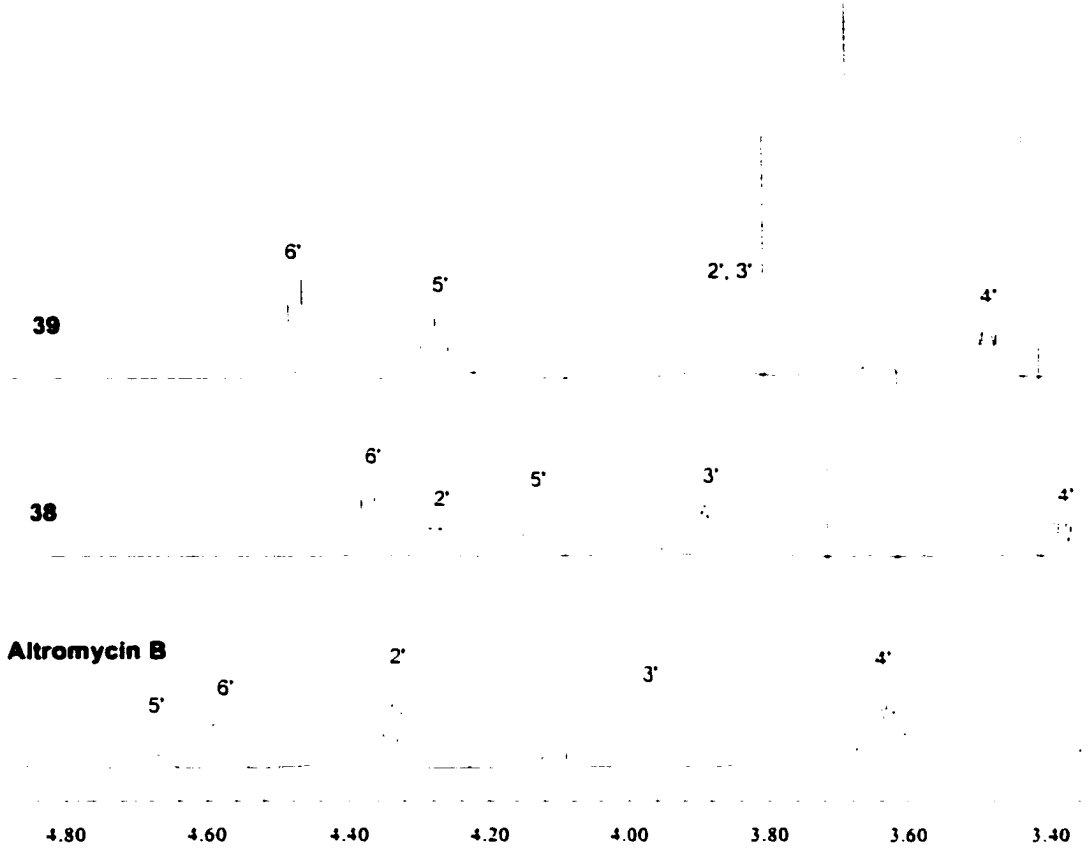


Figure 8. Comparison of ^{1}H-NMR spectra (CDCl3, 500 MHz) of Altromycin B with **38** and **39**.

Unfortunately the comparison of ^{13}C chemical shifts was not helpful either. Table 3 lists the values of chemical shifts for relevant carbons of Altromycin B and the two models. The graph 1 exemplifies the trend of the differences in chemical shifts between Altromycin B and each one of the two models.[73] The average of the absolute values of the differences in chemical shifts between Altromycin B and **38** (Δ = 0.104) and **39** (Δ = 0.119) are too close and don't allow us to assign the stereochemistry at C-13.

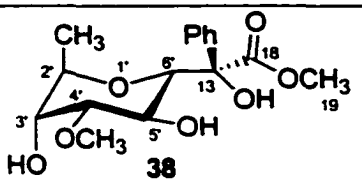
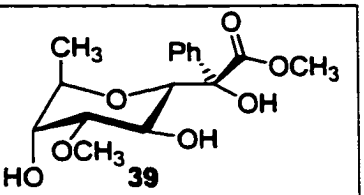
	Altromycin B	 38	 39
C-13	81.16	79.96	78.56
C-18	170.8	173.68	173.27
C-19	52.85	53.40	53.16
C-2'	74.02	73.48	73.43
C-3'	69.15	69.16	69.85
C-4'	80.43	80.84	81.61
C-5'	68.18	67.39	67.09
C-6'	73.88	77.05	75.59
CH3-2'	14.29	15.14	14.54
OCH3-4'	58.14	58.12	58.10

Table 3. Comparison of ^{13}C-NMR shift values between Altromycin B and the two models **38** and **39**.

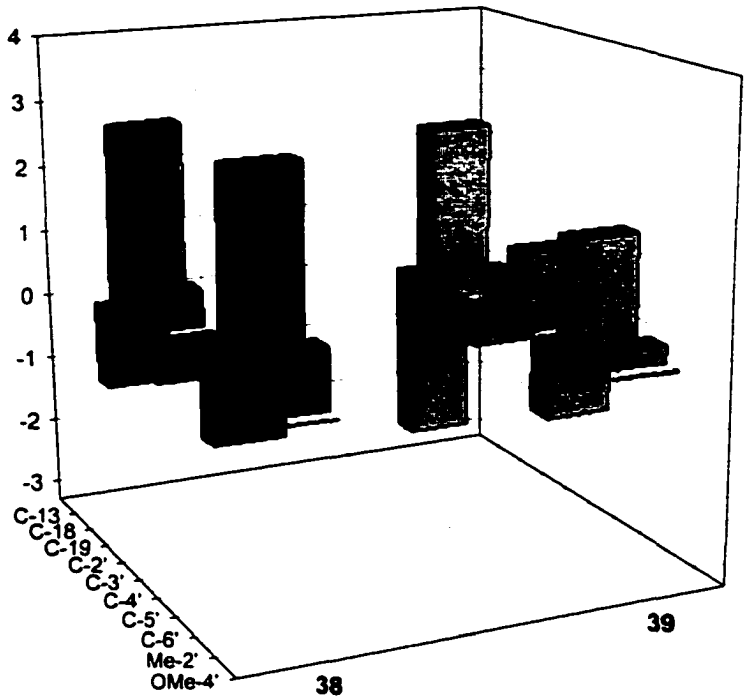
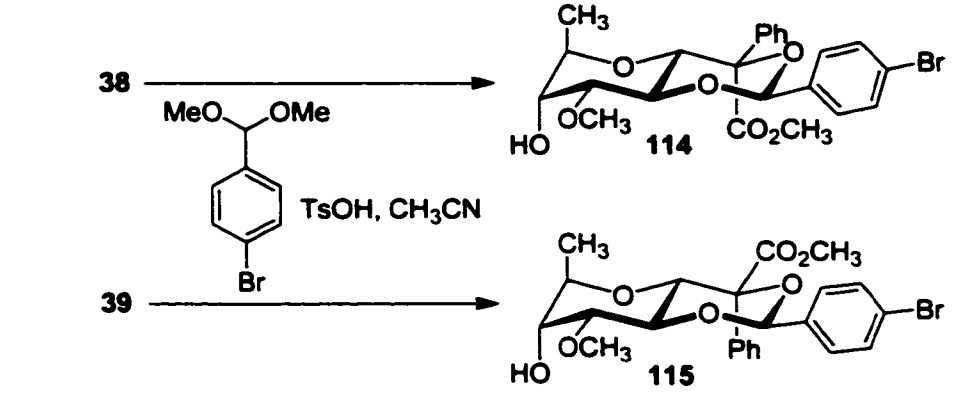
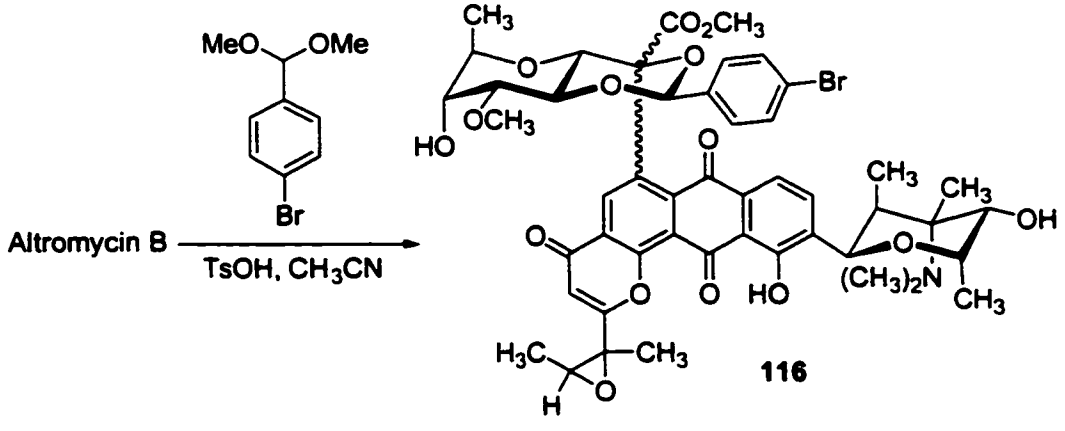


Figure 9. Graphical representation of the differences in ^{13}C-NMR shift values between Altromycin B and the two models **38** and **39**.

We then prepared the benzylidene derivative **114** and **115** of the two model compounds and the analog **116** of Altromycin B, with the hope that circular dichroism could give us some information about the stereochemistry at C-13, based on a possible Cotton effect associated with the optically active electronic transitions derived from the asymmetry induced by the presence of two chromophores in an asymmetric environment.[74] Anticipating the bathochromic effect on the UV spectrum, *para*-subsituted bromo benzylidene was chosen, also with the expectation that the presence of an heavy atom could be helpful in the resolution of eventual crystal structure of the Altromycin B derivative.





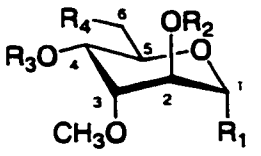
Unfortunately the circular dichroism gave ambiguous results, probably due to the presence of two different chromophores, without allowing us to assign the configuration of the C-13. Furthermore, a complete and unambiguous assignment of the structure of the derivative **116** based on ^{1}H- and ^{13}C-NMR spectra was not possible due to the complexity of the system, but the mass spectrum was in full agreement with the proposed structure. Under the acidic condition used for this reaction the 2,6-dideoxy altrose moiety in the southeast quadrant was cleaved.

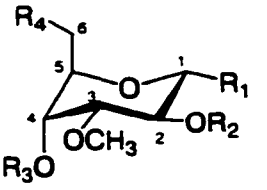
All our efforts to crystallize **116** as well as Altromycin B itself were unsuccessful.

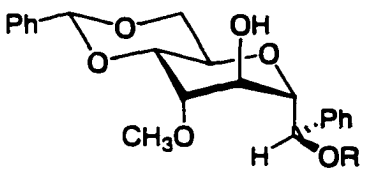
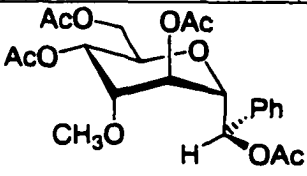
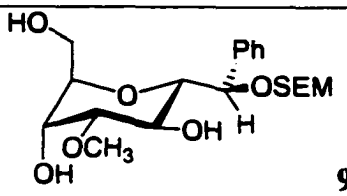
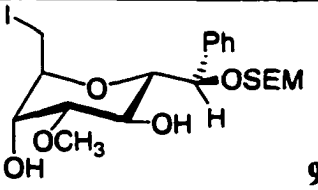
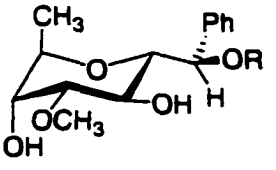
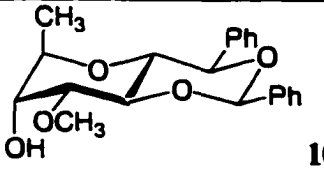
4.5 Ring conformation

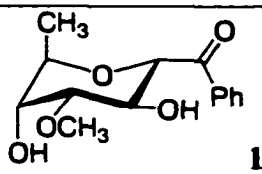
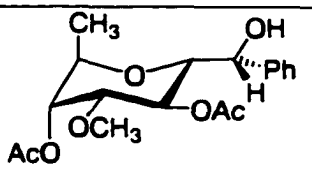
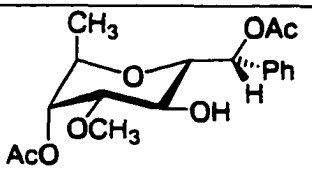
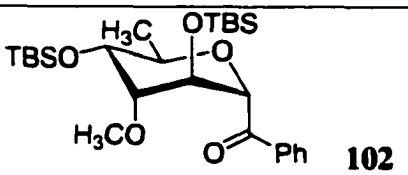
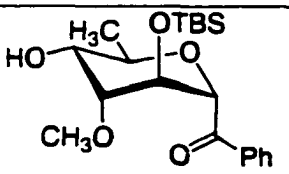
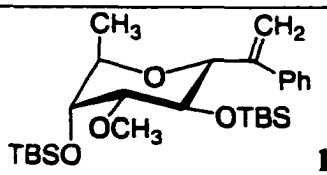
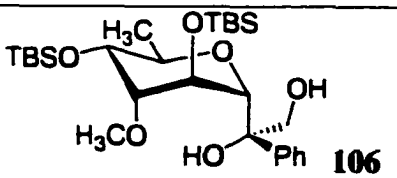
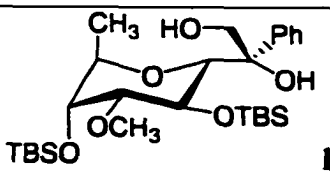
Throughout the synthesis of the northwest quadrant of Altromycin B we found it interesting to analyze the conformational features of the pyranose rings, which we tried to explain as due mostly to steric effects. We observed that even minimal differences in the structure brought about contrasting conformational behaviors, as it is evident from the two different conformations assumed by the two epimers at C-1 **106** and **107**. The conformational properties of each molecule were determined mostly by the values of the coupling constants and in some cases with the support of NOESY spectra. In Table 4 the diagnostic coupling constants of relevant compounds are reported. Each molecule is represented in the preferred conformation assumed on the basis of the values of the coupling constants. In the cases in which equilibrium between the two chair conformations could be assumed the conformation represented is the one that could be supposed to have larger population by analysis of the coupling constants.

The numbering system adopted for the structures in Table 4 can be different from the one used elsewhere in this dissertation for the same structures.





		$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$
	**75** R = H	0	3.1	2.4	9.8
	92 R = SEM			4.0	9.8
 **95**		2.4	4.0	3.4	9.2
 **93**		7.0	7.0		
 **96**		7.3	7.3	~0	4.3
	**97** R = SEM	8.5	8.5	~3.1	1.8
	99 R = H	8.5	8.5	3.1	1.8
 **100**			9.3	3.1	

 **101**	6.7	7.3	3.7	
	6.1	6.4	3.2	6.1
	9.2	9.1	3.0	2.5
 **102**	2.5	4.9	2.4	7.9
	3.1	4.3	3.1	8.5
 **103**	7.0	7.0	3.0	4.3
 **106**	0	3.7	3.1	9.2
 **107**	9.2	9.2	2.4	2.4

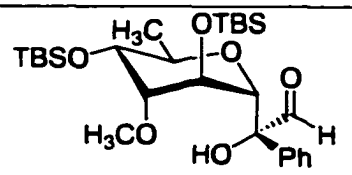
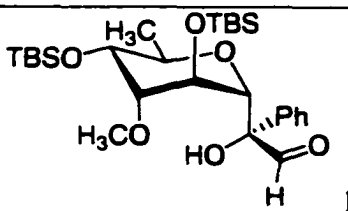
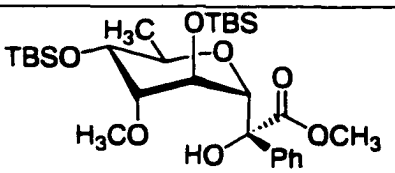
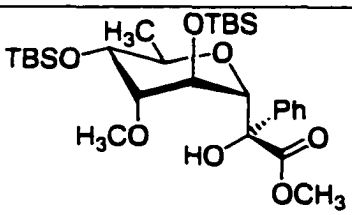
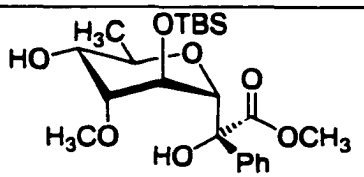
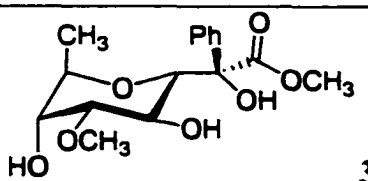
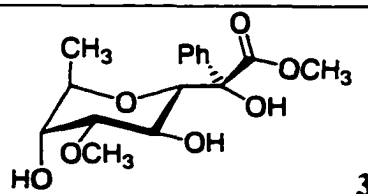
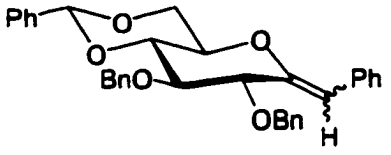
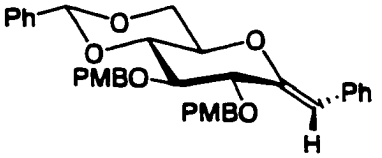
 **108**	0	3.4	3	9.6
 **109**	3	4	2.7	7
 **110**	1.3	3.2	3.2	8.9
 **111**	0	3.2	3.2	8.9
	3.2	3.4	3.8	
 **38**	9.2	9.1	3.2	1.6
 **39**	9.5	9.5	3.1	

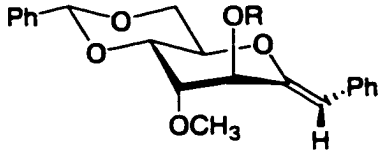
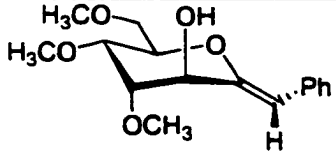
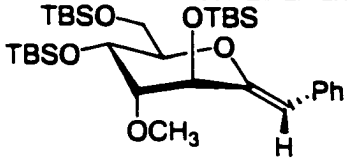
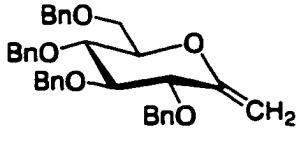
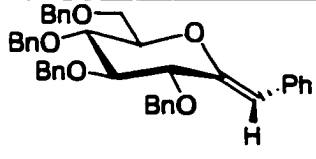
Table 4. Coupling constant values and preferred conformation in variably substituted *C*-altrosides.

4.6 Hydroboration of *exo*-glycals

In our effort to improve the selectivity toward the α-*C*-glycoside in the hydroboration step we explored different organoborane reagents, we changed the reaction conditions and solvents and, when possible, the protecting groups on the *exo*-glycals.

Table 5 summarizes our studies to optimize the hydroboration step and includes two examples previously reported.

exo-Glycal	Borane	α/β Ratio	Yield %
	THF BH_3, THF, 0°C to r.t.	3/2	74
	9-BBN, THF	NR	
	THF BH_3, THF, 0°C to r.t.	~3/1	70
	$(CH_3)S\ BH_3$, THF, 0°C to r.t.		60
	$(CH_3)S\ BH_3$, CH_2Cl_2, 0°C to r.t.		60
	$(CH_3)S\ BH_2Cl$, THF, 0°C to r.t.	NR	
	CB, THF, Wilkinson's catalyst	NR	

	R = H, TBDMS THF BH_3, THF, 0°C to r.t.	1/10	70
	THF BH_3, THF, 0°C to r.t.	<< 1/10	
	THF BH_3, THF, 0°C to r.t.	1/8	66
 (1)	9-BBN	β only	94
	THF BH_3, THF, 0°C to r.t.	1/1	79
 (2)	THF BH_3, THF, 0°C to r.t.	25/75	65

(1) RajanBabu, T. V.; Reddy, G. S. *J. Org. Chem.* **1986**, *51*, 5458.

(2) Alcaraz, M.-L.; Griffin, F. K.; Paterson, D. E.; Taylor R. J. K. *Tetrahedron Letters* **1998**, *39*, 8183.

Table 5. Examples of hydroboration of *exo*-glycal.

5. Conclusions

The Ramberg-Bäcklund reaction proved to be a valuable synthetic tool for the preparation of *C*-glycosides, its main advantages being the simple reaction conditions, easy accessibility of the thioglucoside starting materials and the inexpensive reagents employed. Many other approaches to *C*-glycosides have been described,[5, 6] and it's our opinion that each method presents advantages and disadvantages, making none of them superior to the others. Nevertheless we think that the main quality of the Ramberg-Bäcklund route to *C*-glycoside lays in its generality, since in principle it could be applied to the synthesis of virtually any *C*-glycoside in usually high yield.

The *exo*-glycal product of the Ramberg-Bäcklund reaction can be easily converted to β-*C*-glycoside by catalytic or ionic hydrogenation or further functionalized to more complexly substituted *β-C*-glycoside by addition reactions to the double bond.

Conversion of *exo*-glycals to *α-C*-glycosides has proved to be more problematic, since in our cases even the most stereoselective hydroboration yielded mixture of *α/β* products that never exceeded a 3/1 ratio. A very elegant approach to *α*-*C*-galactosides that involves an internal delivery of hydride has been achieved by Guangli Yang in Prof. Franck's laboratory,[75] but the applicability of this method to sugars other then galactose has not been demonstrated and its high selectivity toward *α-C*-glycosides is obtained at the cost of a longer synthetic path.

The synthesis of the two epimers at C-13 of the northwest quadrant of Altromycin B demonstrates that the Ramberg-Bäcklund reaction can be efficiently employed in the preparation of complex natural products containing *C*-glycosides.

Unfortunately the spectroscopic data of our synthetic models did not give definitive information regarding the relative stereochemistry of the quaternary C-13 of Altromycin B, due to the oversimplification of our models in which the polysubstituted antraquinone chromophore present in Altromycin B has been replaced by a simple phenyl group.

Another drawback of our synthesis lays in its linearity, which makes our approach not very appealing if one would eventually like to address the total synthesis of Altromycin B. We could not achieve a more convergent synthesis because this would have required a synthesis of the altrose moiety followed by its connection to the aglycone. In spite of our efforts this strategy has proved to be impractical because of the low α/β ratio obtained for the hydroboration of *exo*-glycals of altrose under various conditions.

6. EXPERIMENTAL SECTION

Instruments and Materials

NMR spectra were recorded on QE 300 MHz with a TECMAG data system, Jeol GSX 400 MHz and Varian Unity Plus 500 MHz, in deuterated solvents. The assignment of proton and carbon NMR peaks was supported by routine COSY and HSQC spectra and for some cases by NOESY spectra.

Melting points were determined on a Fisher – Johns apparatus and are uncorrected.

Elemental analyses were performed by Robertson Microlit Laboratories, Inc., Madison, NJ.

Electrospray ionization (ESI) mass spectra were performed by Dr. Clifford E. Soll at the Hunter College Mass Spectrometry Facility on an Agilent Technologies 1100 LC/MSD. Typical ESI method: solvent: 1/1 acetonitrile/water + 0.1% HOAc + 50 μl NH_4Ac, flow: 0.50 ml/min, positive ion mode, fragmentor voltage: 30-200 V, drying gas at 175 °C.

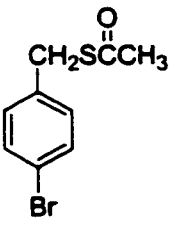
Optical rotations were measured at 25 °C on an Autopol III automatic polarimeter in a cell of 1 dm path length.

UV spectra were recorded on a Varian Cary Bio-3 UV-visible spectrophotometer, typically in double beam mode in the range 350-700 nm in 1 cm cuvette.

All air-moisture sensitive reactions were performed under a positive pressure of dry nitrogen. All solvents and reagents were purified prior to use according to standard laboratory procedures.[76] Low temperatures were recorded as bath temperatures.

Thin layer chromatography analyses were carried out on precoated aluminum sheets of silica gel 60 F 254 (Merck). Short or long wave UV light and vanillin, palladium(II) chloride, 2,4-dinitrophenylhydrazine or phosphomolybdic acid spray was used to visualize the components on the TLC plates.

Flash column chromatography[77] was carried out with silica gel 60 (230-400 mesh) purchased from EM Science, using ACS reagent grade petroleum ether, ethyl acetate, dichloromethane, chloroform and methanol as eluants.



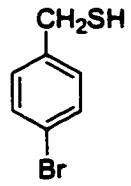
3

4-Bromobenzyl thioacetate (3).[27]

Diethylazodicarboxylate (4.65 g, 26.7 mmol) was added to a solution of triphenylphosphine (7.00 g, 26.7 mmol) in dry THF (50 mL) at 0 °C (ice bath). The mixture was stirred at 0 °C for 40 min. A white precipitate forms. A solution of 4-bromobenzyl alcohol (2.50 g, 13.4 mmol) and thiolacetic acid (2.03 g, 26.7 mmol) in THF (30 mL) was added dropwise and the mixture was stirred at 0 °C for 1.5 h, and then at room temperature for 1.5 h. The solvent was partially evaporated, brine was added and the product was extracted with dichloromethane. The organic layer was dried over sodium sulfate and then concentrated in vacuo. The product **3** (yellow oil, 3.20 g, 13.1 mmol, 98% yield) was purified by column chromatography (SiO_2, ethyl acetate 5%, petroleum ether).

^{1}H-NMR($CDCl_3$, 300 MHz): δ 7.41 (2H, d, J = 8.4 Hz), 7.16 (2H, d, J = 8.4 Hz), 4.05 (2H, s), 2.34 (3H, s).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ 194.74, 136.92, 131.82, 130.62, 121.30, 33.07, 30.56.



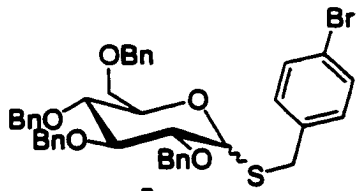
4

4-Bromobenzyl mercaptan (4).

The thiolester **3** (3.00 g, 12.2 mmol) was dissolved in methanol (30 mL). Nitrogen was bubbled in the solution. The solution was cooled at 0 °C (ice bath) and ammonia was bubbled for 30 min. Then, after stirring for 1 ½ h at room temperature the solvent was removed under reduced pressure to yield the yellow oil **4** (2.4 g, 11.8 mmol, 97% yield).

^{1}H-NMR($CDCl_3$, 300 MHz): δ 7.42 (2H, d, J = 8.4 Hz), 7.18 (2H, d, J = 8.4 Hz), 3.68 (2H, d, J = 7.7 Hz), 1.75 (1H, t, J = 7.7 Hz).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ 140.20, 131.85, 129.87, 120.98, 28.63.



5

(4-Bromobenzyl)-2,3,4,6-tetrakis-*O*-benzyl-1-thio-α,β-D-glucopyranoside (5).[28]

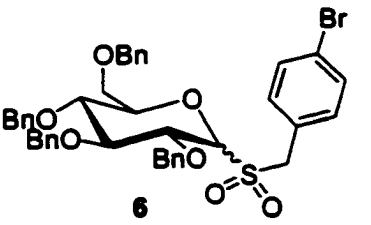
A mixture of 2,3,4,6-tetra-*O*-benzyl-D-glucopyranose (2.50 g, 4.62 mmol), **4** (1.40 g, 7.00 mmol), methoxyacetic acid (0.15 g, 1.70 mmol), ytterbium (III) triflate (0.80 g, 1.30 mmol), and activated molecular sieves (ca. 0.5 g) in dichloroethane (40 mL) was refluxed for 3 h under nitrogen. The mixture was then stirred at room temperature for 48 h. The solvent was partially evaporated, dichloromethane (ca. 10 mL) was added and the

solution was washed with water, then with a saturated solution of sodium bicarbonate. The organic layer was dried over sodium sulfate and the solvent was removed under reduced pressure. The product **5** (2.80 g, 3.90 mmol, 84% yield) was purified by flash column chromatography (SiO_2, ethyl acetate 5%, petroleum ether) and the excess of **4** was recovered.

^{1}H-NMR($CDCl_3$, 300 MHz): δ 7.40 (2H, d, J = 8.4 Hz), 7.37-7.12 (22H, m), 5.13 (1H, d, J =5.1 HZ), 4.94-4.44 and 4.22-3.43 (16H, m).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ 138.72, 138.49, 138.31, 138.20, 138.07, 137.96, 137.65, 137.30, 136.90, 131.72, 131.63, 131.54, 130.90, 128.43, 128.26, 128.06, 128.00, 127.94, 127.90, 127.78, 127.73, 127.67, 121.02, 120.87, 86.73, 83.22, 82.89, 82.20, 81.80, 79.33, 79.13, 78.15, 77.66, 75.87, 75.51, 75.19, 73.63, 72.38, 70.97, 69.35, 68.74, 33.90, 32.81.

ESI MS (calcd for $C_{41}H_{41}BrO_5S$: 724/726) *m/z* (rel. intensity): 742 ($M+NH_4^+$, 30), 743 ($M+NH_4^+$, 12), 744 ($M+NH_4^+$, 28), 745 ($M+NH_4^+$, 15), 747 ($M+ Na^+$, 92), 748 ($M+ Na^+$, 40), 749 ($M+Na^+$, 100), 750 ($M+ Na^+$, 42).



6

(4-Bromobenzyl)-2,3,4,6-tetrakis-*O*-benzyl-1-sulfonyl-α,β-D-glucopyranoside (6).

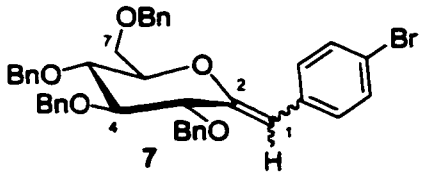
The compound **5** (2.50 g, 3.44 mmol) was dissolved in a mixture of THF (20 mL), ethanol (20 mL) and water (15 mL). Magnesium monoperphthalate (MMPP, tech., 80%, 4.2 g, 6.8 mmol) was added and the mixture was stirred for 2 h at ~60 °C. Extra MMPP

(2 g, 3.2 mmol) was added and the mixture stirred at ~60 °C for an additional 2 h. The solvent was partially evaporated. Water was added and the product was extracted with dichloromethane. The organic layer was washed with sat. $NaHCO_3$ and then dried over sodium sulfate. The solvent was removed under reduced pressure and the product **6** (white solid, 2.40 g, 3.16 mmol, 92% yield) was purified by flash column chromatography (EtOAc 10%, petroleum ether).

^{1}H-NMR($CDCl_3$, 300 MHz): δ 7.44 (2H, d, J = 8.4 Hz), 7.37-7.21, 7.19-7.16 (22H, m), 4.96-4.40 (12H, m), 4.09-4.01 (2H, m), 3.71 (1H, dd, J = 10.6, 1.8 Hz), 3.56 (1H, dd, J = 10.6, 5.9 Hz), 3.48 (1H, dd).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ 138.19, 138.05, 137.87, 137.66, 137.53, 137.32, 137.09, 132.82, 132.74, 131.98, 131.86, 128.63, 128.44, 128.41, 128.00, 127.85, 127.81, 127.63, 126.96, 126.52, 123.36, 123.13, 87.07, 86.21, 86.01, 80.43, 79.59, 78.06, 76.91, 75.92, 75.51, 75.31, 75.26, 74.54, 74.01, 73.58, 69.21, 67.72, 60.46, 57.52, 56.59.

ESI MS (calcd for $C_{41}H_{41}BrO_7S$: 756/758) *m/z* (rel. intensity): 774 ($M+NH_4^+$, 87), 775 ($M+NH_4^+$, 41), 776 ($M+NH_4^+$, 100), 777 ($M+NH_4^+$, 44), 779 ($M+ Na^+$, 68), 780 ($M+Na^+$, 30), 781 ($M+ Na^+$, 69), 782 ($M+ Na^+$, 29).



7

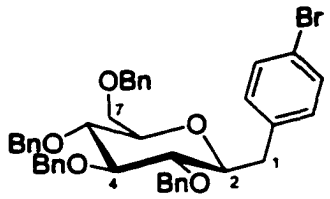
2,6-Anhydro-1-deoxy-1-(4-Bromobenzyl)-3,4,5,7-tetrakis-*O*-benzyl-D-gluco-hept-1-enitol (7).[15]

To a solution of **6** (2.00 g, 2.60 mmol) in dichloromethane (15 mL) and *t*-butanol (15 mL) at 0 °C (ice bath) under nitrogen was added KOH 25% on alumina (3 g) followed by difluorodibromomethane (2.5 mL). The mixture was stirred at low temperature for 1 h and at r.t. for 3 h. The mixture was filtered through celite and the solid was washed with dichloromethane. The combined filtrate and washings were concentrated under reduced pressure. The product **7** (1.5 g, 84% yield) was purified by flash column chromatography (SiO_2, EtOAc 5 to 10%, petroleum ether) as a mixture of *Z*-**7** and *E*-**7** isomers in the ratio *Z*/*E* = 94/6.

^{1}H-NMR($CDCl_3$, 300 MHz), mixture of *E*/*Z* isomers: δ 7.54 (2H, d, J = 8.4 Hz), 7.37-7.22, 7.22-7.17 (22H, m), 6.36 (1H, s, *E*), 5.63 (1H, s, *Z*), 4.79-4.76, 4.76-4.73 (3H, m), 4.67-4.52 (5H, m), 4.17-4.05 (1H, m), 4.00 (1H, d, J = 6.4 Hz), 3.88-3.73 (4H, m).

^{13}C-NMR ($CDCl_3$, 75 MHz), mixture of *E*/*Z* isomers: δ 149.87, 138.20, 137.91, 134.22, 131.36, 130.40, 128.64, 128.56, 128.50, 128.03, 127.99, 127.86, 120.01, 108.53, 84.57, 79.34, 78.11, 77.05, 74.19, 73.71, 73.65, 71.95, 69.43.

ESI MS (calcd for $C_{41}H_{39}BrO_5$: 690/692) *m/z* (rel. intensity): 713 ($M+Na^+$, 100), 714 ($M+Na^+$, 45), 715 ($M+Na^+$, 96), 716 ($M+Na^+$, 43).



8

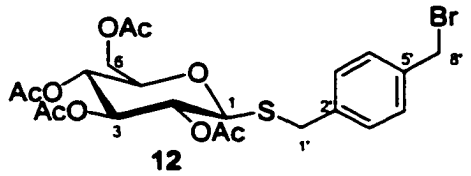
2,6-Anhydro-1-deoxy-1-(4-Bromobenzyl)-3,4,5,7-tetrakis-*O*-benzyl-β-D-gluco-heptitol (8).[29]

To a solution of **7** (500 mg, 0.72 mmol) and triethylsilane (110 mg, 0.94 mmol) in dichloromethane (3 mL) was added dropwise trifluoroacetic acid (225 mg, 1.9 mmol). After stirring under nitrogen for 4 h at room temperature brine was added and the product was extracted with dichloromethane. The organic layer was washed with a saturated solution of sodium bicarbonate and then dried over sodium sulfate. The solvent was evaporated and the product (**8**, white solid, 330 mg, 0.48 mmol, 66% yield) was purified by column chromatography (SiO_2, ethyl acetate 5%, petroleum ether).

^{1}H-NMR($CDCl_3$, 300 MHz): δ 7.35 (2H, d, J = 8.4 Hz), 7.34-7.25, 7.20-7.17 (20H, m), 7.12 (2H, d, J = 8.7 Hz), 4.95-4.79 (4H, 2 AB systems, J = 11 Hz, $PhCH_2$), 4.66-4.46 (4H, 2 AB systems, J = 11 Hz, $PhCH_2$), 3.72 (1H, d, J = 9.2 Hz), 3.68-3.65 (2H, m), 3.60 (1H, d, J = 9.2 Hz), 3.43 (1H, ddd, J = 9.2, 9.2, 2.2 Hz, H-2), 3.35-3.28 (2H, m, H-3, H-4), 3.07 (1H, dd, J = 14.3, 2.2 Hz, H-1'), 2.66 (1H, dd, J = 14.3, 8.8 Hz, H-1).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ 138.67, 138.42, 138.29, 137.88, 131.54, 131.24, 128.64, 128.57, 128.54, 128.48, 128.00, 127.88, 127.81, 127.77, 127.71, 120.20, 87.57, 81.83, 79.90, 79.17, 78.87, 75.76, 75.31, 75.19, 73.65, 69.27, 37.56.

ESI MS (calcd for $C_{41}H_{41}BrO_5$: 692/694) *m/z* (rel. intensity): 715 ($M+Na^+$, 100), 716 ($M+Na^+$, 49), 716 ($M+Na^+$, 95), 718 ($M+Na^+$, 44).



12

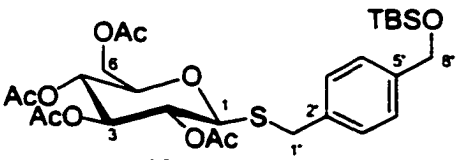
(4-Bromomethylphenylmethyl)-2,3,4,6-tetrakis-*O*-acetyl-1-thio-β-D-glucopyranoside (12).

Sodium hydride (NaH 60% in mineral oil, 220 mg, 5.5 mmol) was added to a solution of 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranose (2.0 g, 5.5 mmol) in dry THF (30 mL) in an addition funnel connected to a round bottom flask containing a solution of α,α'-dibromo-*p*-xylene (3.0 g, 11.4 mmol) in dry THF (30 mL). The mixture in the funnel was added dropwise to the flask and the resulting mixture was stirred under nitrogen at room temperature for 2 h. Then the solvent was partially evaporated, water was added and the mixture was extracted with dichloromethane. The organic phase was dried over sodium sulfate and the solvent was evaporated. The product **12** (oil, 2.41 g, 90% yield) was purified by column chromatography (SiO_2, solvent CH_2Cl_2).

^{1}H-NMR ($CDCl_3$, 500 MHz): δ 7.35 (2H, d, J = 8.6 Hz), 7.28 (2H, d, J = 8.6 Hz), 5.16 (1H, t, J = 9.8 Hz, H-3), 5.08 (2H, t, J = 9.8 Hz, H-2 and H-4), 4.49 (2H, s, H-8'), 4.31 (1H, d, J = 9.8 Hz, H-1), 4.24 (1H, dd, J = 12.2, 2.4 Hz, H-6a), 4.13 (1H, dd, J = 12.2, 2.4 Hz, H-6b), 3.93 (1H, d, J = 12.8 Hz, H-1'a), 3.82 (1H, d, J = 12.8 Hz, H-1'b), 3.61 (1H, ddd, J = 9.8, 4.9, 2.4 Hz, H-5), 2.11 (3H, s, Ac), 2.024 (3H, s, Ac), 2.020 (3H, s, Ac), 2.00 (3H, s, Ac).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ 170.61, 170.20, 169.43, 137.40, 137.13, 129.64, 129.45, 82.25, 76.14, 74.06, 70.07, 68.69, 62.48, 33.65, 33.30, 21.05, 20.94, 20.85.

ESI MS (calcd for $C_{22}H_{27}BrO_9S$: 546/548) *m/z* (rel. intensity): 564 ($M+NH_4^+$, 96), 565 ($M+NH_4^+$, 28), 566 ($M+NH_4^+$, 100), 567 ($M+NH_4^+$, 26), 569 ($M+ Na^+$, 66), 571 ($M+Na^+$, 76), 572 ($M+ Na^+$, 20).



13

(4-*O*-*tert*-Butyldimethylsilylmethylphenylmethyl)-2,3,4,6-tetrakis-*O*-acetyl-1-thio-β-D-glucopyranoside (13).[32]

Silver triflate (880 mg, 3.42 mmol) and *tert*-butyldimethylsilanol (0.54 mL, 3.43 mmol) were added to a solution of **12** (1.50 g, 2.74 mmol) and 2,6-di-*tert*-butyl-4-methylpyridine (705 mg, 3.43 mmol) in dry dichloromethane (40 mL) under N_2 at 0 °C (ice bath). The mixture was stirred for 15 min, then the cooling bath was removed and stirring was continued for 1 h. The mixture was filtered over celite and the solvent evaporated. Flash column chromatography (petroleum ether, EtOAc 20%) yielded the product **13** (1.23 g, 60%).

$[\alpha]^{25}_D$ = -78 (c = 1.36, $CHCl_3$).

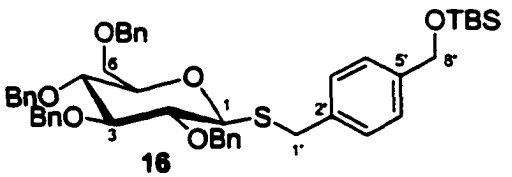
Anal. calcd for $C_{28}H_{42}O_{10}SSi$: C, 56.16; H, 7.07; S, 5.36. Found: C, 55.98; H, 6.83; S, 5.51.

^{1}H-NMR ($CDCl_3$, 500 MHz): δ 7.28 (2H, d, J = 8.5 Hz), 7.25 (2H, d, J = 8.5), 5.14 (1H, t, J = 9.2 Hz, H-3), 5.072 (1H, t, J = 9.8 Hz, H-2 or H-4), 5.070 (1H, t, J = 9.8 Hz, H-4 or H-2), 4.74 (2H, s, H-8'), 4.27 (1H, d, J = 9.8 Hz, H-1), 4.24 (1H, dd, J = 12.2, 4.9 Hz, H-

6a), 4.15(1H, dd, J = 12.2, 2.4 Hz, H-6b), 3.93 (1H, d, J = 12.8 Hz, H-1'a), 3.82 (1H, d, J = 12.8 Hz, H-1'b), 3.59 (1H, ddd, J = 9.8, 4.9, 2.4 Hz, H-5), 2.12(3H, s), 2.02 (3H, s), 2.01 (3H, s), 1.99 (3H, s), 0.95 (9H, s), 0.11 (6H, s).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ 170.62, 170.20, 169.43, 140.86, 135.42, 129.08, 126.44, 82.13, 76.10, 74.14, 70.13, 68.73, 64.93, 62.52, 33.84, 26.27, 21.16, 21.05, 20.95, 20.88, 18.75, -4.87.

ESI MS (calcd for $C_{28}H_{42}O_{10}SSi$: 598) *m/z* (rel. intensity): 616 ($M+NH_4^+$, 49), 617 ($M+NH_4^+$, 19), 621 ($M+Na^+$, 100), 622 ($M+Na^+$, 36).



16

(4-*O*-*tert*-Butyldimethylsilylmethylphenylmethyl)-2,3,4,6-tetrakis-*O*-benzyl-1-thio-β-D-glucopyranoside (16).

The thioglucoside **13** (390 mg, 0.63 mmol) was dissolved in dry methanol (10 mL) and treated with sodium methoxide (0.5 M in MeOH, 0.5 mL). The solution was stirred at room temperature for 1 h, then acidic resin (DOWEX 50X8-400. Ion-exchange resin. Strong acidic. 0.3 g) was added and the mixture filtered. The filtrate was collected and the solvent was removed in vacuo (oil pump) and then dissolved in dry THF (10 mL) and dry DMF (10 mL). Sodium hydride (60% dispersion in mineral oil, 125 mg) was added, followed by benzyl bromide (580 mg, 3.4 mmol) and tetrabutylammonium iodide (60 mg). The mixture was stirred for 8 hours at room temperature under nitrogen. The

product was extracted with dichloromethane and the organic layer was washed with a solution of ammonium chloride. The organic layer was dried over sodium sulfate and the solvent was evaporated. Flash column chromatography (petroleum ether, EtOAc 10%) yielded the oil **16** (402 mg, 80%).

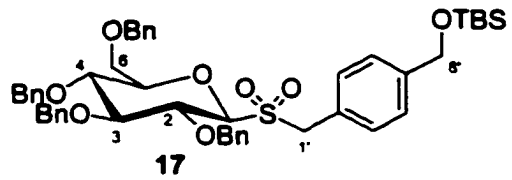
$[\alpha]^{25}_{D} = -35$ (c = 1.23, $CHCl_3$).

Anal. calcd for $C_{48}H_{58}O_6SSi$: C, 72.87; H, 7.39; S, 4.05. Found: C, 72.76; H, 7.25; S, 3.91.

^{1}H-NMR ($CDCl_3$, 500 MHz): δ 7.38-7.21 (22 H, m), 7.17-7.14 (2H, m), 4.86 (1H, d, J = 11.0 Hz), 4.83 (1H, d, J = 11.0 Hz), 4.80 (1H, d, J = 11.0 Hz), 4.79 (1H, d, J = 11.0 Hz), 4.71 (2H, s), 4.67 (1H, d, J = 10.4 Hz), 4.63 (1H, d, J = 11.0 Hz), 4.57 (1H, d, J = 11.0 Hz), 4.55 (1H, d, J = 11.0 Hz), 4.26 (1H, d, J = 9.2 Hz, H-1), 4.00 (1H, d, J = 12.8 Hz, H-1'a), 3.86 (1H, d, J = 13.4 Hz, H-1'b), 3.74 (1H, dd, J = 11.0, 1.8 Hz, H-6a), 3.69 (1H, dd, J = 11.0, 4.9 Hz, H-6b), 3.62-3.57 (2H, m, H-3 and H-4), 3.47 (1H, t, J = 9.2 Hz, H-2), 3.38 (1H, ddd, J = 9.8, 4.9, 1.8 Hz, H-5), 0.94 (9H, s), 0.10 (6H, s).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ 140.44, 138.66, 138.40, 138.24, 138.11, 136.28, 129.18, 128.51, 128.49, 128.46, 128.37, 128.03, 127.90, 127.88, 127.83, 127.73, 127.71, 126.35, 86.84, 83.37, 81.94, 79.20, 78.29, 75.90, 75.51, 75.21, 73.70, 69.42, 65.00, 34.35, 26.29, -4.86.

ESI MS (calcd for $C_{48}H_{58}O_6SSi$: 790) *m/z* (rel. intensity): 808 ($M+NH_4^+$, 100), 809 ($M+NH_4^+$, 63), 813 ($M+Na^+$, 39), 814 ($M+Na^+$, 23).



17

(4-*O*-*tert*-Butyldimethylsilylmethylphenylmethyl)-2,3,4,6-tetrakis-*O*-benzyl-1-sulfonyl-β-D-glucopyranoside (17).

The thioglucoside **16** (320 mg, 0.40 mmol) was dissolved in THF (5 mL), ethanol (5 mL) and water (5 mL). Magnesium monoperoxyphthalate hexahydrate (MMPP, 1.5 g) was added and the mixture was stirred for 2 h at ~60 °C. The solvent was partially evaporated. Water (15 mL) was added and the product was extracted with dichloromethane (3 x 10 mL). The organic layer was washed with sat. $NaHCO_3$ and then dried over sodium sulfate. The solvent was removed in vacuo and the oil **17** (280 mg, 87%) was isolated by flash column chromatography (EtOAc 10%, petroleum ether).

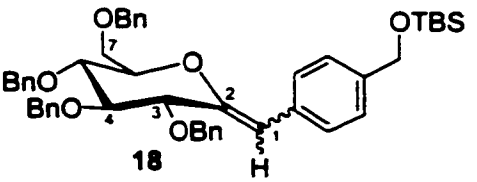
$[\alpha]^{25}_D$ = -2.9 (c = 1.05, $CHCl_3$).

Anal. calcd for $C_{48}H_{58}O_6SSi$: C, 70.04; H. 7.10. Found: C, 69.81; H, 7.05.

^{1}H-NMR ($CDCl_3$, 500 MHz): δ 7.44 (2H, d, J = 7.9 Hz), 7.38-7.23 (20H, m), 7.17-7.14 (2H, m), 4.96 (1H, d, J = 9.8 Hz), 4.90 (1H, d, J = 11.6 Hz), 4.80 (1H, d, J = 11.0 Hz), 4.80 (1H, d, J = 11.0 Hz), 4.71 (2H, s), 4.70 (1H, d, J = 12.2 Hz), 4.58 (2H, s), 4.56 (1H, d, J = 13.4 Hz), 4.53 (1H, d, J = 10.4 Hz), 4.133 (1H, d, J = 14.0 Hz), 4.129 (1H, d, J = 9.2 Hz, H-1), 4.06 (1H, d, J = 9.2 Hz, H-2), 3.75 (1H, dd, J = 11.0, 1.8 Hz, H-6a), 3.69-3.63 (2H, m, H-6b and H-3), 3.54-3.47 (2H, m, H-4 and H-5), 0.94 (9H, s), 0.10 (6H, s).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ 142.49, 138.27, 137.92, 137.75, 137.53, 131.12, 128.80. 128.57, 128.46, 128.15, 128.08, 127.95, 127.86, 127.75, 126.53, 126.04, 86.92. 86.26, 79.67, 77.40, 77.11, 76.06, 75.64, 75.37, 73.72, 69.25, 64.77, 57.24, 26.27, 18.74, -4.91.

ESI MS (calcd for $C_{48}H_{58}O_6SSi$: 822) *m/z* (rel. intensity): 840 ($M+NH_4^+$, 100), 841 ($M+NH_4^+$, 55), 845 ($M+Na^+$, 47), 846 ($M+Na^+$, 28).



18

2,6-Anhydro-1-deoxy-1-(4-*O*-*tert*-butyldimethylsilylmethylphenylmethyl)-3,4,5,7-tetrakis-*O*-benzyl-D-gluco-hept-1-enitol (18).[15]

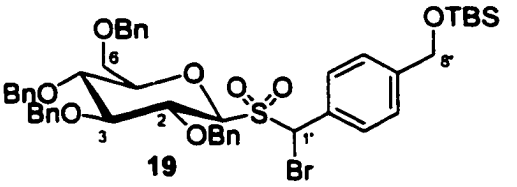
To a solution of the sulfone **17** (200 mg, 0.24 mmol) in dichloromethane (5 mL) and *t*-butanol (5 mL) at 0 °C (ice bath) under nitrogen was added KOH 25% on alumina (1.8 g), followed by difluorodibromomethane (1.0 mL). The mixture was stirred at 0 °C for 1 h and at room temperature for 3 h. The mixture was filtered through celite, the filtrate was collected and concentrated in vacuo. The crude was purified by flash column chromatography (petroleum ether, EtOAc 5%) to obtain **18** (160 mg, 88% yield). The product consists of a mixture of the two isomers *Z*-**18** and *E*-**18** in the ratio *Z*/*E* = 4/1.

In some cases the α-bromosulfone **19** was isolated from the reaction mixture.

^{1}H-NMR ($CDCl_3$, 500 MHz): δ 7.56 (2H, d, J = 8.5 Hz), 7.40-7.16 (22H, *Z*-isomer and 18H, *E*-isomer), 7.10 (2H, d, J = 7.9 Hz, *E*-isomer), 7.02-6.99 (2H, m, *E*-isomer), 6.47 (1H, s, H-1, *E*-isomer), 5.73 (1H, s, H-1, *Z*-isomer), 4.81-4.48 (10H, *Z*-isomer and 8H, *E*-isomer, series of d), 4.42 (1H, d, J = 11.6 Hz, *E*-isomer), 4.37 (1H, d, J = 11.6, *E*-isomer), 4.12 (1H, d, J = 12.2, *E*-isomer), 4.09 (1H, ddd, J = 9.8, 4.3, 1.8 Hz, H-6), 4.03 (1H, d, J = 4.3Hz, H-3, *Z*-isomer), 3.91-3.73 (5H, m), 0.97 (9H, s, *E*-isomer), 0.94 (9H, s, *Z*-

isomer), 0.13 (9H, s, *E*-isomer), 0.10 (9H, s, *Z*-isomer).

ESI MS (calcd for $C_{48}H_{56}O_6Si$: 756) *m/z* (rel. intensity): 649 (-OBn, 96), 650 (-OBn, 52), 774 ($M+NH_4^+$, 100), 775 ($M+NH_4^+$, 58), 779 ($M+Na^+$, 45), 780 ($M+Na^+$, 25).



19

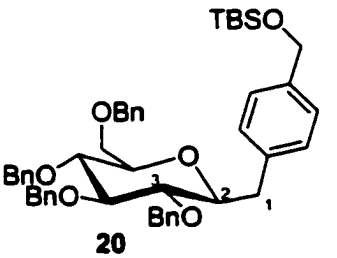
(4-*O*-*tert*-Butyldimethylsilylmethylphenylbromomethyl)-2,3,4,6-tetrakis-*O*-benzyl-1-sulfonyl-β-D-glucopyranoside (19).

The α-bromosulfone **19** was obtained as a byproduct during the preparation of the *exo*-glucal **18**. It was quantitatively converted to the desired product **18** by treatment with 25% KOH on alumina in dichloromethane/*t*-butanol.

^{1}H-NMR ($CDCCl_3$, 500 MHz): δ 7.59 (2H, d, *J* = 8.5 Hz), 7.41-7.39, 7.36-7.26 (18H, m), 7.21 (2H, d, *J* = 8.5 Hz), 7.14-7.11 (2H, m), 6.06 (1H, s, H-1'), 4.97 (1H, d, *J* = 9.2 Hz), 4.88 (1H, d, *J* = 11.0 Hz). 4.77 (2H, d, *J* = 11.0 Hz), 4.70 (1H, d, *J* = 9.2 Hz), 4.69 (2H, s), 4.61 (1H, d, *J* = 12.2 Hz), 4.54 (1H, d, *J* = 11.6 Hz), 4.51 (1H, d, *J* = 11.0 Hz), 4.09 (1H, t, *J* = 9.2 Hz, H-2), 3.94 (1H, d, *J* = 9.2 Hz, H-1), 3.67 (1H, dd, *J* = 11.0, 1.8 Hz, H-6a), 3.60 (1H, dd, *J* = 11.0, 6.1 Hz, H-6b), 3.56 (1H, t, *J* = 9.2 Hz, H-3), 3.48 (1H, t, *J* = 9.2 Hz, H-4), 3.24 (1H, ddd, *J* = 9.2, 6.1, 1.8 Hz, H-5), 0.95 (9H, s), 0.10 (6H, s).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ 144.42, 138.16, 137.79, 137.63, 137.23, 130.45, 129.82, 128.98, 128.69, 128.60 128.54, 128.16, 128.14, 127.90, 127.70, 126,30, 86.12, 85.99, 79.45, 77.41, 77.29, 76.09, 75.85, 75.42, 73.64, 68.98, 64.56, 62.16, 26.26, 18.73, -4.92.

ESI MS (calcd for $C_{48}H_{57}BrO_8SSi$: 900/902) *m/z* (rel. intensity): 918 ($M+NH_4^+$, 75), 919 ($M+NH_4^+$, 48), 920 ($M+NH_4^+$, 82), 921 ($M+NH_4^+$, 48), 923 ($M+ Na^+$, 97), 924 ($M+ Na^+$, 54), 925 ($M+Na^+$, 100), 926 ($M+ Na^+$, 55).



20

2,6-Anhydro-1-deoxy-1-(4-*O*-*tert*-butyldimethylsilylmethylphenylmethyl)-3,4,5,7-tetrakis-*O*-benzyl-β-D-gluco-heptitol (20).

The *exo*-glucal **18** (250 mg, 0.33 mmol) was dissolved in EtOAc (8 mL) in the presence of Pd 5% on alumina (20 mg). The mixture was stirred under hydrogen (balloon) for 12 hours and then it was filtered over celite. The solvent was removed in vacuo to obtain the *C*-glucoside **7** (240 mg, 95% yield).

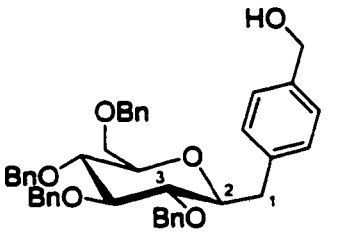
$[\alpha]^{25}_D = +2.2$ (c = 0.89, $CHCl_3$).

Anal. calcd for $C_{48}H_{58}O_6Si$: C, 75.95; H, 7.70. Found: C, 76.00, H, 7.59.

^{1}H-NMR ($CDCl_3$, 500 MHz): δ 7.36-7.22 and 7.21-7.18 (24H, m), 4.93 (2H, d, J = 11.0 Hz), 4.88 (1H, d, J = 11.0 Hz), 4.82 (1H, d, J = 11.0 Hz), 4.69 (2H, s), 4.66 (1H, d, J = 11.0 Hz), 4.60 (1H, d, J = 11.0 Hz), 4.57 (1H, d, J = 12.2 Hz), 4.50 (1H, d, J = 12.2 Hz), 3.71 (1H, t, J = 9.2 Hz, H-4 or H-5), 3.68-3.62 (3H, m, H-7a, H-7b and H-5 or H-4), 3.47 (1H, dt, J = 9.2, 1.8 Hz H-2), 3.37-3.31 (2H, m, H-3 and H-6), 3.14 (1H, dd, J = 14.0, 1.8 Hz, H-1a), 2.72 (1H, dd, J = 14.0, 9.2 Hz, H-1b), 0.94 (9H, s), 0.09 (6H, s).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ 139.32, 138.80, 138.61, 138.44, 138.41, 137.56, 129.64, 128.56, 128.52, 128.43, 128.03, 127.92, 127.82, 127.79, 127.72, 127.59, 126.03, 87.67, 82.02, 80.33, 79.27, 78.94, 75.73, 75.32, 75.16, 73.66, 69.26, 65.14, 37.90, 26.31, 18.76, -4.87.

ESI MS (calcd for $C_{48}H_{58}O_6Si$: 758) *m/z* (rel. intensity): 776 ($M+NH_4^+$, 100), 777 ($M+NH_4^+$, 55), 781 ($M+Na^+$, 25), 782 ($M+Na^+$, 23).



21

2,6-Anhydro-1-deoxy-1-(4-hydroxymethylphenylmethyl)-3,4,5,7-tetrakis-*O*-benzyl-*β*-D-gluco-heptitol (21).

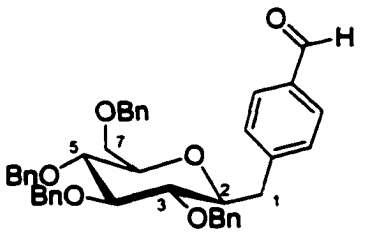
The silyl ether **20** (250 mg, 0.33 mmol) was dissolved in THF (5 mL). Tetrabutylammonium fluoride (1.0 M in THF, 350 μL) was added and the solution was stirred at room temperature for 2 hours. Brine was added and the product was extracted with dichloromethane. The organic layer was dried over Na_2SO_4 and the solvent was evaporated. The product **21** (202 mg, 95% yield) was purified by column chromatography (SiO_2, EtOAc 20%, petroleum ether).

Melting point: 75-76 °C.

^{1}H-NMR ($CDCl_3$, 500 MHz): δ 7.36 (24H, m), 4.94 (1H, d, J = 11.0 Hz), 4.93 (1H, d, J = 11.0 Hz), 4.88 (1H, d, J = 11.0 Hz), 4.82 (1H, d, J = 11.0 Hz), 4.66 (1H, d, J = 11.0 Hz),

4.62-4.58 (3H, m), 4.54 (1H, d, J = 12.2 Hz), 4.47 (1H, d, J = 12.2 Hz), 3.72 (1H, t, J = 9.2 Hz, H-4 or H-5), 3.68 (1H, dd, J = 11.0, 1.8 Hz, H-7a), 3.64 (1H, dd, J = 11.0, 4.3 Hz, H-7b), 3.62 (1H, t, J = 9.2 Hz, H-5 or H-4), 3.47 (1H, dt, J = 9.2, 2.4 Hz, H-2), 3.34 (1H, t, J = 9.2 Hz. H-3), 3.36-3.32 (1H, m, H-6), 3.14 (1H, dd, J = 14.1, 1.8 Hz, H-1a), 2.72 (1H, dd, J = 14.1, 9.2 Hz, H-1b), 1.52 (1H, t, J = 6.1 Hz, OH).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ 138.84, 138.71, 138.57, 138.42, 138.37, 138.32, 129.97, 128.60, 128.55, 128.51, 128.41, 128.02, 127.99, 127.93, 127.84, 127.81, 127.78, 127.73, 127.63, 126.98, 87.62, 82.00, 80.21, 79.31, 78.92, 75.75, 75.31, 75.15, 73.65, 69.33, 65.47, 37.91.



9

2,6-Anhydro-1-deoxy-1-(4-formylphenylmethyl)-3,4,5,7-tetrakis-*O*-benzyl-*β*-D-gluco-heptitol (9).

Method A[33]

To a solution of oxalyl chloride (80 μL, 0.9 mmol) in dry dichlorometane (3 mL) was added a solution of DMSO (120 μL, 1.6 mmol) in dry dichlorometane at –78 °C under nitrogen (0.5 mL). Stirring was continued at –78 °C for 20 min followed by dropwise addition of **21** (213 mg, 0.33 mmol) dissolved in dry dichlorometane (3 mL). The mixture was stirred at –78 °C under N_2 for 45 min, then Et_3N (0.4 mL) was added dropwise and

the mixture was stirred for 15 min. The cooling bath was removed and the mixture was stirred for 30 min. The mixture was diluted with dichlorometane (10 mL) and the organic solution was washed with aq NH_4Cl. The organic layer was dried over Na_2SO_4 and then concentrated in vacuo. Flash column chromatography (petroleum ether, EtOAc 20%) yielded **9** (180 mg, 85%).

Method B[30]

To a solution of **8** (480 mg, 0.69 mmol) in dry THF (10 mL) under nitrogen at –78 °C (CO_2/acetone bath) was added BuLi (1.6 M solution in hexane, 0.5 mL) dropwise by a syringe over 5 min. The mixture was stirred at –78 °C for 15 min, then the cooling bath was removed and the mixture was stirred for 30 min. The mixture was cooled at –78 °C and *N,N,N',N'*-tetramethylethylenediamine (0.12 mL, 0.80 mmol) was added dropwise, followed by freshly distilled formylpiperidine (0.8 mL, 7.20 mmol). The mixture was stirred for 15 min at –78 °C and then for 2.5 h at room temperature. Aqueous HCl (3N, 10 mL) was added and the product was extracted with ether. The organic layer was washed with water and with a saturated solution of sodium bicarbonate, and then dried over sodium sulfate. The product (**9**, 125 mg, best yield obtained: 29%) was purified by flash column chromatography (ethyl acetate 5 to 10%, petroleum ether).

Melting point: 92-94 °C.

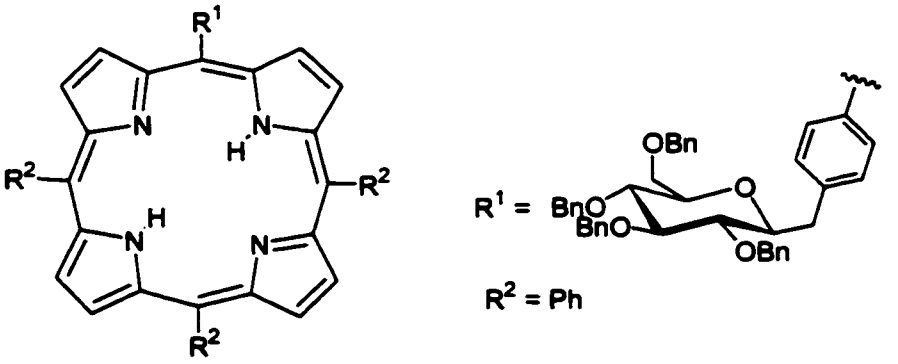
$[\alpha]^{25}_D$ = -1.9 (c = 5.4, CH_2Cl_2).

^{1}H-NMR ($CDCl_3$, 500 MHz): δ 9.94 (1H, s), 7.74 (2H, d, J = 7.7 Hz), 7.41 (2H, d, J = 7.7 Hz), 7.38-7.26 (18H, m), 7.20 (2H, m), 4.96 (1H, d, J = 10.5 Hz), 4.94 (1H, d, J = 10.5 Hz), 4.89 (1H, d, J = 11.2 Hz), 4.82 (1H, d, J = 11.2 Hz), 4.66 (1H, d, J = 11.2 Hz), 4.59 (1H, d, J = 11.2 Hz), 4.54(1H, d, J = 11.9 Hz), 4.48 (1H, d, J = 11.9 Hz), 3.72 (1H, t, J =

9.1 Hz, H-4 or H-5), 3.66-3.61 (3H, m, H-7a, H-7b and H-5 or H-4), 3.49 (1H, dt, J = 9.1, 2.1 Hz., H-2), 3.37-3.32 (2H, m, H-3 and H-6), 3.18 (1H, dd, J = 14.0, 2.1 Hz, H-1a), 2.77 (1H, dd, J = 14.0, 9.1 Hz, H-1b).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ 192.00, 146.39, 138.62, 138.37, 138.24, 134.90, 130.40, 129.71, 128.67, 128.60, 128.55, 128.48, 128.01, 127.90, 127.84, 127.81, 127.75, 87.55, 81.88, 79.73, 79.23, 78.85, 75.80, 75.37, 75.20, 73.65, 69.24, 38.41.

ESI MS (calcd for $C_{42}H_{42}O_6$: 642) *m/z* (rel. intensity): 660 ($M+NH_4^+$, 100), 661 ($M+NH_4^+$, 44), 665 ($M+Na^+$, 91), 666 ($M+Na^+$, 43).



22

5,10,15-Tris-(phenyl)-20-[(2,6-Anhydro-1-deoxy-3,4,5,7-tetrakis-*O*-benzyl-*β*-D-gluco-heptitol-1-yl)phenyl]porphyrin (22).[34]

A mixture of the aldehyde **9** (108 mg, 0.17 mmol), benzaldehyde (54 mg, 0.51 mmol), pyrrole (46 mg, 0.68 mmol) and NaCl (1 g, 20 mmol) in dichloromethane (67 mL) was purged with nitrogen under stirring. The flask was shielded from the light and BF_3·OEt_2 (9.9 μL, 0.070 mmol) was added to the mixture. The mixture was stirred under nitrogen at room temperature for 5 hours. DDQ (134 mg, 0.59 mmol) was added and the mixture

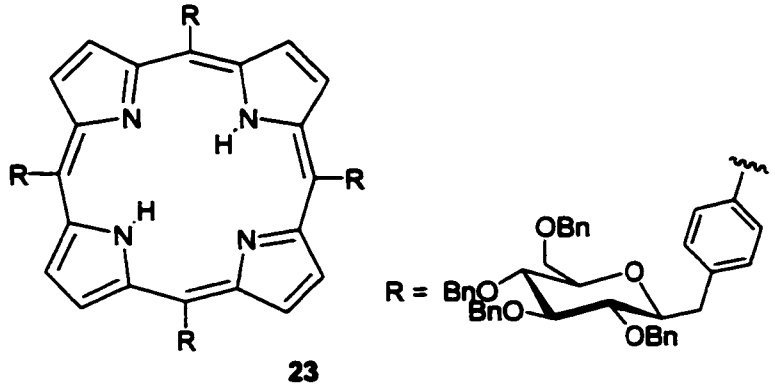
was stirred for 30 min. A saturated solution of $NaHCO_3$ (50 mL) was added, the organic layer was collected, dried over Na_2SO_4 and then the solvent was removed in vacuo. The main product **22** (30 mg, 15%) was isolated by flash column chromatography (SiO_2, CH_2Cl_2).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ 8.87-8.78 (8H, m), 8.25-8.19 (6H, m), 8.10 (2H, d, J = 8.1 Hz), 7.79-7.71 (9H, m), 7.65 (2H, d, J = 8.1 Hz), 7.47-7.15 and 7.10-7.02 (20H, m), 5.10-4.80 and 4.71-4.60 (8H, m, series of overlapping ABq, Bn), 3.90-3.73 (5H, m), 3.60-3.46 (3H, m), 3.08 (1H, dd, J = 14.6, 8.8 Hz, H-1), -2.77 (2H, s).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ 142.35, 140.05, 138.79, 138.49, 138.42, 134.68, 134.57, 131.24, 128.72, 128.63, 128.56, 128.46, 128.14, 128.06, 127.93, 127.88, 127.81, 127.76, 127.60, 126.80, 120.51, 120.22, 120.15, 87.78, 82.20, 80.35, 79.47, 79.08, 75.88, 75.51, 75.24, 73.79, 69.49, 38.16.

UV-Vis ($CHCl_3$) λ_{max}, nm: 419, 515, 551, 590, 646.

ESI MS {calcd for $C_{79}H_{66}N_4O_5$ (theoretical intensity): 1150 (100), 1152 (88), 1153 (39), 1154 (12), 1155(3)} *m/z* ($M+H^+$, rel. intensity): 1151 (100), 1152 (92), 1153 (39), 1154 (15).



23

5,10,15,20-Tetrakis-[(2,6-Anhydro-1-deoxy-3,4,5,7-tetrakis-*O*-benzyl-*β*-D-gluco-heptitol-1-yl)phenyl]porphyrin (23).[34]

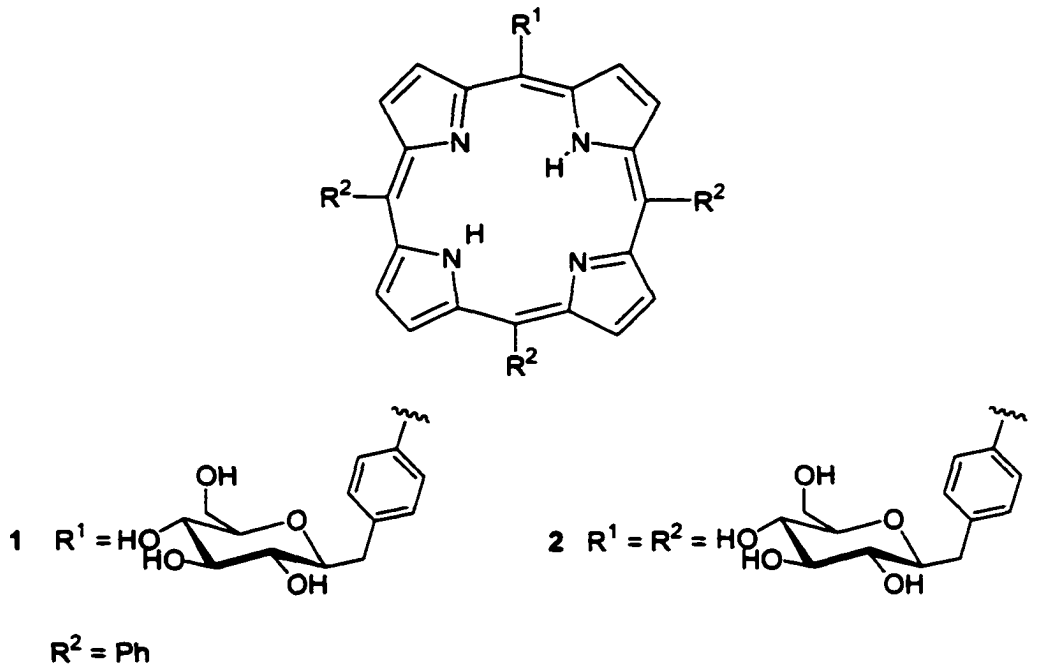
A mixture of the aldehyde **9** (173 mg, 0.27 mmol), pyrrole (18 mg, 0.27 mmol) and NaCl (350 mg, 6 mmol) in dichloromethane (27 mL) was purged with nitrogen under stirring. The flask was shielded from the light and $BF_3{\cdot}OEt_2$ (3.4 μL, 0.027 mmol) was added to the mixture. The mixture was stirred under nitrogen at room temperature for 5 hours. DDQ (57 mg, 0.25 mmol) was added and the dark mixture was stirred for 40 min. The mixture was washed with a saturated solution of $NaHCO_3$. The organic layer was dried over Na_2SO_4 and the solvent was evaporated. Flash column chromatography (eluent: CH_2Cl_2, EtOAc 10%) yielded the porphyrin **23** (100 mg, 53%).

^{1}H-NMR ($CDCl_3$, 500 MHz): δ 8.80 (8H, s), 8.10 (8H, d, J = 7.7 Hz), 7.66 (8H, d, J = 7.7 Hz), 7.47-7.23 (68H, m), 7.18 (8H, t, J = 7.7 Hz), 7.05 (8H, t, J = 7.2 Hz), 5.09 (4H, d, J = 11.0 Hz), 5.02 (4H, d, J = 11.0 Hz), 4.99 (4H, d, J = 11.0 Hz), 4.90 (4H, d, J = 11.0 Hz), 4.85 (4H, d, J = 11.0 Hz), 4.69 (4H, d, J = 11.0 Hz), 4.68 (4H, d, J = 12.4 Hz), 4.62 (4H, d, J = 12.4 Hz), 3.88 (4H, t, J = 9.0 Hz, H-4 or H-5), 3.86-3.77 (16H, m, H-7a, H-7b, H-2 and H-5 or H-4), 3.58 (4H, t, J = 9.0, H-3), 3.60-3.55 (4H, m, H-6), 3.50 (4H, d, J = 14.1, H-1a), 3.09 (4H, dd, J = 14.1, 9.0, H-1b), -2.78 (2H, s).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ 140.18, 138.80, 138.49, 138.45, 134.61, 131.28 (b), 128.72, 128.63, 128.57, 128.46, 128.15, 128.06, 127.93, 127.87, 127.78, 127.62, 120.23, 87.79, 82.26, 80.44, 79.47, 79.09, 75.88, 75.55, 75.25, 73.80, 69.48, 38.20.

UV-Vis ($CHCl_3$) λ_{max}, nm: 422, 517, 553, 592, 647.

ESI MS {calcd for $C_{184}H_{174}N_4O_{20}$ (theoretical intensity): 2759 (47), 2760 (97), 2761 (100), 2762 (79), 2763 (37), 2764 (16), 2765 (6)} *m/z* ($M+H^+$, rel. intensity): 2760 (12), 2761 (100), 2762 (80), 2763 (38), 2764 (50), 2765 (15), 2766 (18).



5,10,15-Tris-(phenyl)-20-[(2,6-Anhydro-1-deoxy-β-D-gluco-heptitol-1-yl)phenyl]porphyrin (1) and 5,10,15,20-Tetrakis-[(2,6-Anhydro-1-deoxy-β-D-gluco-heptitol-1-yl)phenyl]porphyrin (2).

The porphyrin **22** or **23** was dissolved in EtOAc (1 mL per 10 mg of porphyrin) and MeOH (1 mL per 10 mg of porphyrin). Pd 10% wt on C (1 mg per mg of porphyrin) was added. The mixture was degassed and then stirred under H_2 overnight. The mixture was filtered over celite and the solvent was removed in vacuo to yield the porphyrin **1** or **2** (95-96%).

1:

^{1}H-NMR ($CDCl_3/CD_3OD$ = 3/1, 500 MHz): δ 8.82-8.64 (8H, m), 8.13 (6H, d, J = 6.4 Hz), 8.04 (2H, d, J = 7.9 Hz), 7.71-7.66 (9H, m), 7.58 (2H, d, J = 7.9 Hz), 3.85 (1H, dd, J = 11.9, 3.1 Hz), 3.74 (1H, dd, J = 11.9, 3.1 Hz), 3.67 (1H, dd, J = 11.9, 3.1 Hz), 3.49-3.41 (2H, m), 3.35-3.27 (3H, m), 2.97 (1H, dd, J = 14.3, 8.9 Hz).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ 142.02, 139.81, 138.39, 134.42, 134.33, 127.71, 127.66, 126.58, 126.205, 120.213, 120.06, 120.02, 80.23, 79.39, 78.69, 73.88, 70.97, 62.48, 37.81.

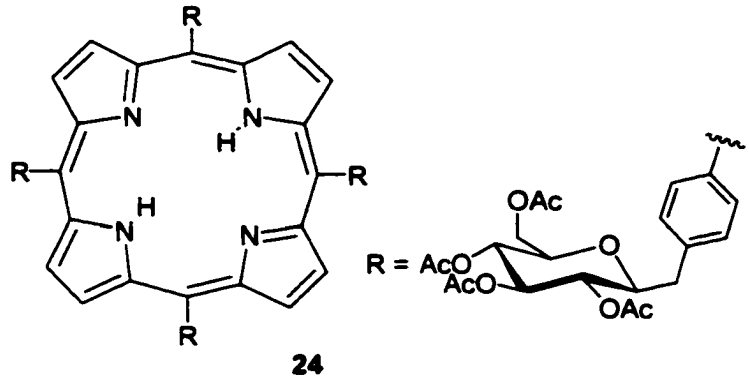
UV-Vis (CH_3OH) λ_{max}, nm: 413, 512, 547, 588, 645.

ESI MS {calcd for $C_{51}H_{42}N_4O_5$ (theoretical intensity): 790 (100), 791 (58), 792 (17), 793 (4)} *m/z* ($M+H^+$, rel. intensity): 791 (100), 792 (56), 793 (22), 794 (5).

2:

UV-Vis (CH_3OH) λ_{max}, nm: 415, 513, 547, 593, 649.

ESI MS (calcd for $C_{72}H_{78}N_4O_{20}$ (theoretical intensity): 1318 (100), 1319 (81), 1320 (37), 1321 (12), 1322 (3)} *m/z* ($M+H^+$, rel. intensity): 1319 (100), 1320 (78), 1321 (44), 1322 (14), 1323 (7).



24

5,10,15,20-Tetrakis-[(2,6-Anhydro-1-deoxy-3,4,5,7-tetrakis-*O*-acetyl-*β*-D-gluco-heptitol-1-yl)phenyl]porphyrin (24).

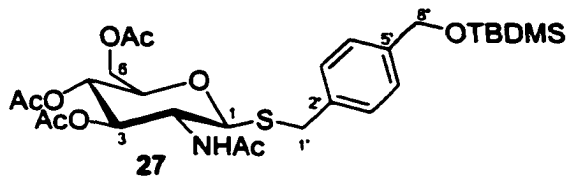
The porphyrin **2** (13 mg, 0.0098 mmol) was dissolved in DMF (0.5 mL) and pyridine (2.5 mL). Acetic anhydride (0.08 mL) was added and the mixture was stirred at r. t. overnight. Methylene chloride was (15 mL) added and the organic solution was washed with aqueous 3% HCl (3 x 10 mL). The solvent was removed in vacuo and the product **24** (16 mg, 84% yield) was purified by column chromatography (CH_2Cl_2, EtOAc 30%).

H-NMR ($CDCl_3$, 500 MHz): δ 8.85 (8H, s), 8.13 (8H, d, J = 7.7 Hz), 7.60(8H, d, J = 7.7 Hz), 5.34 (4H, t, J = 9.4 Hz, H-3), 5.23-5.14 (8H, m, H-4 and H-5), 4.35 (4H, dd, J = 12.4, 5.3 Hz, H-7a), 4.21 (4H, dd, J = 12.4, 2.1 Hz, H-7b), 4.01 (4H, m, H-2), 3.83 (4H, m, H-6), 3.20-3.15 (8H, m), 2.16 (12H, s), 2.09-2.07 (36H, m), -2.79 (2H, broad s).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ 170.73, 170.53, 169.82, 169.64, 136.90, 134.68, 127.88, 78.76, 76.08, 74.82, 74.45, 69.21, 62.77, 38.12, 21.18, 21.15, 21.02, 20.97.

UV-Vis (CH_3OH) λ_{max}, nm: 420, 517, 552, 592, 647.

ESI MS {calcd for $C_{104}H_{110}N_4O_{36}$ (theoretical intensity): 1991 (85), 1992 (100), 1993 (64), 1994 (30) 1995 (11)} *m/z* ($M+H^+$, rel. intensity): 1992 (44), 1993 (100), 1994 (38), 1995 (30).



27

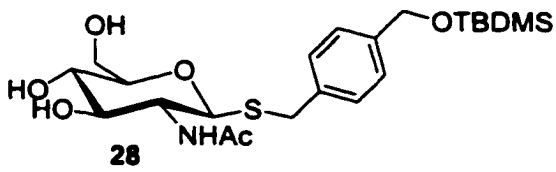
(4-*O*-*tert*-Butyldimethylsilylmethylphenylmethyl)-2-acetamido-2-deoxy-3,4,6-tris-*O*-acetyl-1-thio-β-D-glucopyranoside (27).[37]

To a solution of 1,3,4,6-tetracetyl-2-deoxy-2-acetamido-1-thioglucoside (**26**, 3.25 g, 8.0 mmol) in dry DMF (25 mL, purged with N_2) was added hydrazine acetate (740 mg, 8.0 mmol) and the mixture was stirred for 1 h at r. t. under nitrogen, followed by addition of **14** (3.1 g, 9.8 mmol) and triethylamine (1.1 mL). The mixture was stirred for 3 h and then was poured into a saturated aqueous solution of NH_4Cl (40 mL). An extraction with EtOAc (3 x 40 mL) was performed and the organic layers were collected and dried over sodium sulfate. The product **27** (2.34 g, 49%) was isolated by column chromatography (solvent: EtOAc).

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.29-7.24 (4H, m), 5.31 (1H, d, J = 9.2 Hz, NHAc), 5.09 (1H, t, J = 9.8 Hz, H-4), 4.97 (1H, t, J = 9.8 Hz, H-3), 4.74 (2H, s, H-8'), 4.26-4.15 (4H, m, H-1, H-2, H-6), 3.93 (1H, d, J = 13.4 Hz, H-1'a), 3.80 (1H, d, J = 13.4 Hz, H-1'b), 3.55 (1H, ddd, J = 9.8, 5.5, 2.4 Hz, H-5), 2.13 (3H, s, Ac), 2.02 (3H, s, Ac), 2.01 (3H, s, Ac), 1.90 (3H, s, Ac), 0.95 (9H, s, OTBDMS), 0.12 (6H, s, OTBDMS).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 171.23, 170.69, 169.99, 169.29, 140.78, 135.93, 129.12, 126.47, 83.06, 76.20 (C-5), 74.26 (C-3), 68.72 (C-4), 64.95 (C-8'), 62.72 (C-6), 53.14, 33.82 (C-1'), 26.27, 23.47, 21.06, 20.93, 20.86, 18.75, -4.88.

ESI MS (calcd for $C_{28}H_{43}NO_9SSi$: 597) *m/z* (rel. intensity): 598 ($M+H^+$, 67), 599($M+H^+$, 24), 620 ($M+Na^+$, 100), 621 ($M+Na^+$, 37).



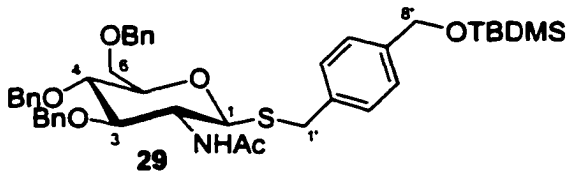
28

(4-*O*-*tert*-Butyldimethylsilylmethylphenylmethyl)-2-acetamido-2-deoxy-1-thio-β-D-glucopyranoside (28).

To the thioglucoside **27** (3.0 g, 5.02 mmol) dissolved in methanol (20 mL) was added sodium methoxide (0.1 g). The mixture was stirred at r. t. for 3 h. Acidic resin (DOWEX 50X8-400. Ion-exchange resin. Strong acidic) was added and the mixture was filtered. The solvent was removed under reduced pressure to obtain the product **28** (2.3 g, 97%), which was used for the next step without further purification.

^{1}H-NMR (300 MHz, CD_3OD): δ 7.28 (2H, d, J = 8.1 Hz), 7.23 (2H, d, J = 8.1 Hz), 4.69 (2H, s), 4.21 (1H, d, J = 10.3 Hz), 3.99 (1H, d, J = 12.8 Hz), 3.87 (1H, dd, J = 12.1, 2.2 Hz), 3.84-3.76 (2H, m), 3.67 (1H, dd, J = 12.1, 6.2 Hz), 3.30-3.27 (2H, m), 3.19 (1H, ddd, J = 9.7, 6.1, 2.2 Hz), 1.90 (3H, s), 0.93 (9H, s), 0.09 (6H, s).

^{13}C-NMR (75 MHz, CD_3OD): δ 173.44, 141.43, 138.10, 130.24, 127.46, 84.19, 82.29, 77.59, 72.29, 66.08, 63.26, 56.11, 34.28, 26.63, 23.09, 19.48, -4.85.



29

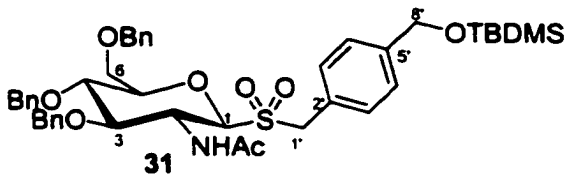
(4-*O*-*tert*-Butyldimethylsilylmethylphenylmethyl)-2-acetamido-2-deoxy-3,4,6-tris-*O*-benzyl-1-thio-β-D-glucopyranoside (29).

To a suspension of NaH (60% in mineral oil, 400 mg, 10 mmol, washed free of oil with pentane) in dry THF (20 mL) and DMF (30 mL) was added at 0 °C (ice bath) the thioglucoside **28** (1.30 g, 2.8 mmol), followed by benzyl bromide (2.1 g, 12 mmol) and tetrabutylammonium iodide (300 mg, 0.81 mmol). The mixture was stirred at r. t. overnight. Methanol (5 mL) was added and the mixture was stirred for 30 min. A saturated aqueous solution of NH_4Cl (60 mL) was added and the mixture was extracted with EtOAc (3 x 50 mL). The organic layer was dried over sodium sulfate and the product **29** (1.48 g, 71% yield) was isolated by column chromatography (petroleum ether, EtOAc 25%).

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.38-7.18 (19H, m), 5.01 (1H, d, J = 8.5 Hz, NHAc), 4.80 (1H, d, J = 11.6 Hz), 4.79 (1H, d, J = 11.0Hz), 4.70 (2H, s, H-8'), 4.65-4.56 (4H, m), 4.33 (1H, d, J = 9.8 Hz, H-1), 3.92 (1H, d, J = 13.0 Hz, H-1'a), 3.88 (1H, q, J = 9.3 Hz, H-2), 3.79 (1H, d, J = 13.0 Hz, H-1'b), 3.77-3.70 (2H, m), 3.69-3.61 (2H, m), 3.44 (1H, ddd, J = 9.2, 4.9, 2.4 Hz, H-5), 1.79 (3H, s, Ac), 0.94 (9H, s, OTBDMS), 0.10 (6H, s, OTBDMS).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 170.00, 140.35, 138.42, 138.38, 138.15, 136.53, 129.17, 128.61, 128.55, 128.50, 128.23, 128.04, 127.94, 127.82, 127.72, 126.35, 83.15, 82.60, 79.49, 78.85, 75.02, 74.84, 73.73, 69.37, 65.02, 55.05, 33.83, 26.28, 23.76, 18.75, -4.88.

ESI MS (calcd for $C_{43}H_{55}NO_6SSi$: 741) *m/z*: 759 ($M+NH_4^+$, 100), 760 ($M+NH_4^+$, 56).



(4-*O*-*tert*-Butyldimethylsilylmethylphenylmethyl)-2-acetamido-2-deoxy-3,4,6-tris-*O*-benzyl-1-sulfonyl-β-D-glucopyranoside (31).

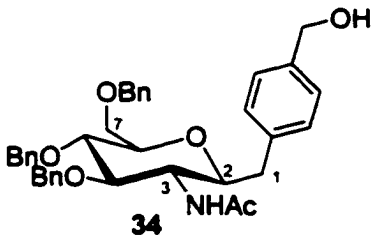
The thioglucoside **29** (1.40 g, 1.88 mmol) was dissolved in THF (20 mL), ethanol (20 mL) and water (20 mL). Magnesium monoperoxyphthalate hexahydrate (MMPP, 5 g) was added and the mixture was stirred for 3 h at 65 °C. The solvent was partially removed in vacuo, water (20 mL) was added and the product was extracted with EtOAc (60 mL). The organic layer was washed with a saturated solution of $NaHCO_3$ until no evolution of CO_2 was observed and then dried over sodium sulfate. The solvent was removed in vacuo and the crude was purified by column chromatography (solvent: petroleum ether, EtOAc 50%) to obtain the sulfone **31** (1.39 g, 95% yield).

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.43-7.23 (17H, m), 7.21-7.17 (2H, m), 5.73 (1H, d, J = 7.3 Hz, NHAc), 4.86-4.79 (3H, m, H-1), 4.71 (2H, s, H-8'), 4.66-4.54 (4H, m), 4.46 (1H, d, J = 13.4 Hz, H-1'a), 4.37 (1H, t, J = 9.2 Hz, H-3), 4.16 (1H, d, J = 14.0 Hz, H-1'b), 3.80-3.73 (2H, m, H-2, H-6a), 3.70-3.63 (2H, m, H-5, H-6b), 3.51 (1H, t, J = 9.2 Hz, H-4), 1.78 (3H, s, Ac), 0.95 (9H, s, OTBDMS), 0.10 (6H, OTBDMS).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 171.53, 142.41, 137.98, 137.93, 131.15, 128.56, 128.54, 127.95, 127.93, 127.86, 126.47, 125.27, 84.97 (C-1), 81.10 (C-3), 79.63 (C-5), 78.40 (C-

4), 75.57, 75.06, 73.57, 69.14 (C-6), 64.73, 56.24 (C-8'), 52.44 (C-2), 26.25, 23.67, 18.70, -4.95.

ESI MS (calcd for $C_{43}H_{55}NO_8SSi$: 773) *m/z* (rel. intensity): 774 ($M+H^+$, 55), 775 ($M+H^+$, 32), 791 ($M+NH_4^+$, 100), 792 ($M+NH_4^+$, 57), 796 ($M+Na^+$, 71), 797 ($M+Na^+$, 36).



34

2,6-Anhydro-1-deoxy-1-(4-hydroxymethylphenylmethyl)-3-acetamido-3-deoxy-4,5,7-tris-*O*-benzyl-β-D-gluco-heptitol (34).

The sulfone **31** (0.80 g, 1.03 mmol) was dissolved in dichloromethane (10 mL) and *t*-butanol (10 mL). The mixture was cooled in an ice bath and 30% KOH on alumina (3 g) was added, followed by difluorodibromomethane (ca. 4 mL). The mixture was stirred at 0 °C for 1 h and at room temperature for 3 h. The mixture was filtered through celite using CH_2Cl_2 as a wash. The filtrate was collected and the solvent was removed under reduced pressure. The crude was purified by flash column chromatography (petroleum ether, EtOAc 10%, Et_3N 0.3%) to obtain **32** (400 mg, 55% yield).

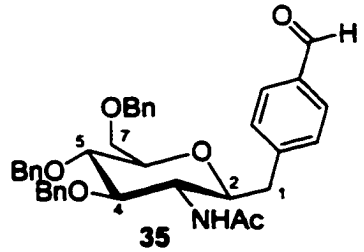
The *exo*-glucal **32** (200 mg, 0.22 mmol) was added to a slurry of Pd 5% on alumina (20 mg) in EtOAc (10 mL). The mixture was stirred under hydrogen (balloon) for 12 hours and then it was filtered over celite. The solvent was removed in vacuo and the *C*-glycoside **33** obtained was dissolved in THF (10 mL). A solution of tetrabutylammonium fluoride (1 M in THF, 0.3 mL) was added and the mixture was stirred at r. t. for 3 h.

Brine (15 mL) was added and the mixture was extracted with EtOAc (3 x 15 mL). The organic layer was dried over sodium sulfate and the solvent was removed in vacuo. The *C*-glycoside **34** (111 mg, 85% yield over the two steps) was purified by column chromatography (CH_2Cl_2, EtOAc 30%).

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.36-7.21 (19H, m), 4.98 (1H, d, J = 8.5 Hz, NHAc), 4.86 (1H, d, J = 11.6 Hz), 4.80 (1H, d, J = 11.0 Hz), 4.67-4.56 (4H, m), 4.54 (1H, d, J = 12.2 Hz), 4.48 (1H, d, J = 12.2 Hz), 3.77 (1H, q, J = 9.8 Hz, H-3), 3.71-3.58 (4H, m, H-4, H-5, H-7), 3.53 (1H, dt, J = 9.8, 3.1 Hz, H-2), 3.37 (1H, ddd, J = 9.2, 4.3, 1.8 Hz, H-6), 2.88 (1H, dd, J = 14.7, 3.1 Hz, H-1a), 2.80 (1H, dd, J =14.7, 8.5 Hz, H-1b), 1.79 (3H, s, Ac).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 170.17, 138.86, 138.61, 138.31, 129.75, 128.68, 128.55, 128.43, 128.32, 128.08, 127.97, 127.80, 127.64, 127.01, 83.26, 79.73 (C-2), 79.45 (C-6), 79.27, 74.00, 74.66, 73.70, 69.40 (C-7), 65.43, 55.72 (C-3), 38.56 (C-1), 23.81.

ESI MS (calcd for $C_{37}H_{41}NO_6$: 595) *m/z* (rel. intensity): 596 ($M+H^+$, 26), 618 ($M+Na^+$, 100), 619 ($M+Na^+$, 46).



35

2,6-Anhydro-1-deoxy-1-(4-formylphenylmethyl)-3-acetamido-3-deoxy-4,5,7-tris-*O*-benzyl-β-D-gluco-heptitol (35).[33]

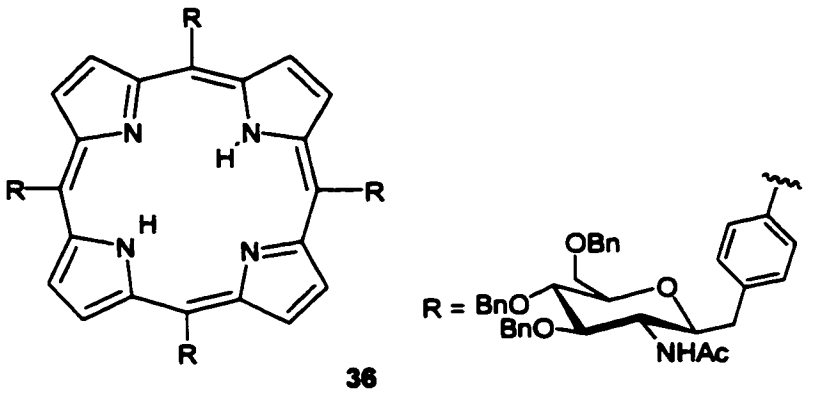
To a solution of oxalyl chloride (31 μL, 0.35 mmol) in dry dichlorometane (2 mL) was added a solution of DMSO (70 μL, 0.6 mmol) in dry dichlorometane (0.5 mL) at –78 °C

under nitrogen. Stirring was continued at –78 °C for 20 min followed by dropwise addition of **34** (76 mg, 0.13 mmol) dissolved in dry dichlorometane (2 mL). The mixture was stirred at –78 °C under N_2 for 45 min, then Et_3N (0.15 mL) was added dropwise and the mixture was stirred for 15 min. The cooling bath was removed and the mixture was stirred for 30 min. The mixture was diluted with dichlorometane (10 mL) and the organic solution was washed with sat. NH_4Cl. The organic layer was dried over Na_2SO_4 and then concentrated in vacuo. Flash column chromatography (petroleum ether, EtOAc 20%) yielded the aldehyde **35** (65 mg, 84%).

^{1}H-NMR (500 MHz, $CDCl_3$): δ 9.93 (1H, s), 7.73 (2H, d, J = 8.0 Hz), 7.40-7.22 (17H, m), 5.00 (1H, d, J = 8.7 Hz, NHAc), 4.86 (1H, d, J = 12.0 Hz), 4.81 (1H, d, J =10.7 Hz), 4.65-4.60 (2H, m), 4.54 (1H, d, J = 12.0 Hz), 4.59 (1H, d, J = 12.0 Hz), 3.78 (1H, q, J = 9.3 Hz, H-3), 3.68-3.63 and 3.62-3.53 (5H, m, H-2, H-4, H-5, H-7a, H-7b), 3.37 (1H, dt, J = 9.3, 3.3 Hz, H-6), 2.95 (1H, dd, J = 14.7, 3.3 Hz, H-1a), 2.88 (1H, dd, J = 14.7, 8.0 Hz, H-1b), 1.79 (3H, s, Ac).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 191.97, 170.30, 146.25, 138.49, 138.30, 138.10, 134.79, 130.21, 129.65, 128.65, 128.51, 128.41, 128.24, 128.03, 127.97, 127.94, 127.89, 127.67, 83.17, 79.29, 79.15, 74.98, 74.67, 73.61, 69.29 (C-7), 55.63 (C-3), 38.95 (C-1), 23.73.

ESI MS (calcd for $C_{37}H_{39}NO_6$: 593) *m/z* (rel. intensity): 594 ($M+H^+$, 100), 595 ($M+H^+$, 49), 611 ($M+NH_4^+$, 68), 612 ($M+NH_4^+$, 28), 616 ($M+Na^+$, 54), 617 ($M+Na^+$, 24).



36

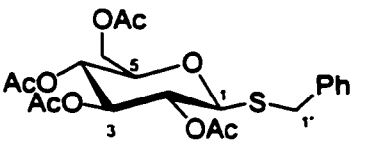
5,10,15,20-Tetrakis-[(2,6-Anhydro-1-deoxy-3-acetamido-3-deoxy-4,5,7-tris-*O*-benzyl -*β*-D-gluco-heptitol-1-yl)phenyl]porphyrin (36).[34]

A mixture of the aldehyde **35** (61 mg, 0.10 mmol), pyrrole (7 mg, 0.10 mmol) and NaCl (157 mg, 2.7 mmol) in dichloromethane (10 mL) was purged with nitrogen under stirring. The flask was shielded from the light and $BF_3{\cdot}OEt_2$ (1.25 μL, 0.01 mmol) was added to the mixture. The mixture was stirred under nitrogen at room temperature for 5 hours. DDQ (22 mg, 0.097 mmol) was added and the dark mixture was stirred for 40 min. Dichloromethane (10 mL) was added and the mixture was washed with a saturated solution of $NaHCO_3$ (10 mL). The organic layer was dried over Na_2SO_4 and the solvent was removed under reduced pressure. Flash column chromatography (SiO_2, 15 g. Solvent: CH_2Cl_2 50 mL; EtOAc 50%, CH_2Cl_2, 50 mL; MeOH 50%, EtOAc, 50 mL; then MeOH until column is clear; then CH_2Cl_2) yielded the porphyrin **36** (10 mg, 15%).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.77 (8H, s), 8.07 (8H, d, J = 8.1 Hz), 7.61 (8H, d, J = 8.1 Hz), 7.40-7.25 (48H, m), 7.19 (8H, t, J = 7.3 Hz), 7.06 (4H, t, J = 7.3 Hz), 5.17 (4H, d, J = 9.2 Hz), 4.94 (4H, d, J = 11.7 Hz), 4.88 (4H, d, J = 10.6 Hz), 4.75-4.59 (16H, m), 4.01 (4H, q, J = 9.2 Hz), 3.90-3.70 (20H, m), 3.63-3.57 (4H, m), 3.25-3.15 (8H, m), 1.92 (12H, s), -2.81 (2H, broad s).

UV-Vis ($CHCl_3$) λ_{max}, nm: 421, 517, 554, 593, 648.

ESI MS {calcd for $C_{164}H_{162}N_8O_{20}$ (theoretical intensity): 2563 (54), 2564 (100), 2565 (94), 2566 (59), 2567 (29), 2568 (11), 2569 (4)} *m/z* ($M+H^+$, rel. intensity): 2564 (28), 2565 (90), 2566 (100), 2567 (66), 2568 (20), 2569 (7).



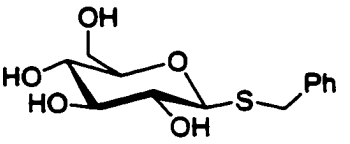
42

Benzyl-2,3,4,6-tetrakis-*O*-acetyl-1-thio-β-D-glucopyranoside (42).

A solution of 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside (7.2 g, 19.9 mmol) in dry THF (40 mL) was added to sodium hydride (NaH 60% in mineral oil, 220 mg, 5.5 mmol, washed free of oil with pentane) in dry THF (20 mL). Benzyl bromide (3.5 g, 20.0 mmol) was added dropwise and the mixture was stirred under nitrogen at room temperature for 3 h. Then the solvent was partially evaporated, brine was added and the mixture was extracted with dichloromethane. The organic layer was dried over sodium sulfate and the solvent was evaporated. The product was purified by column chromatography (solvent: petroleum ether, 20% EtOAc) to obtain the thioglucoside **42** (6.33 g, 70% yield).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.34-7.27 (5H, m), 5.18-5.03 (3H, m, H-2, H-3 and H-4), 4.29 (1H, d, J = 9.2 Hz, H-1), 4.24 (1H, dd, J = 12.5, 5.1 Hz, H-6a), 4.13 (1H, dd, J = 12.5, 2.2 Hz, H-6b), 3.94 (1H, d, J = 12.8 Hz, H-1'a), 3.83 (1H, d, J = 12.8 Hz, H-1'b), 3.59 (1H, ddd, J = 9.5, 5.1, 2.2 Hz, H-5), 2.12 (3H, s, Ac), 2.02 (6H, s, 2Ac), 2.00 (3H, s, Ac).

ESI MS (calcd for $C_{21}H_{26}O_9S$: 454) *m/z* (rel. intensity): 472 ($M+NH_4^+$, 100), 473 ($M+NH_4^+$, 25).



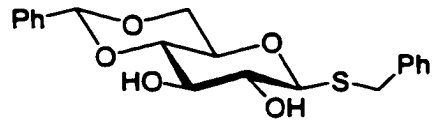
43

Benzyl-thio-β-D-glucopyranoside (43).

To the thioglucoside **42** (6.05 g, 0.013 mol) dissolved in dry methanol (60 mL) was added sodium methoxide (0.5 M in MeOH, 2 mL) and the solution was stirred at room temperature for ca. 3 h. Acidic resin (DOWEX 50X8-400. Ion-exchange resin. Strong acidic, 1 g) was added and the mixture filtered. The filtrate was collected and the solvent was removed in vacuo to obtain **43** (3.79 g, 13.0 mmol).

^{1}H-NMR (300 MHz, CD_3OD): δ 7.35 (2H, d, J = 7.3 Hz), 7.27 (2H, t, J = 7.3 Hz), 7.21 (1H, d, J = 7.3 Hz), 5.12 (1H, m), 4.99 (1H, d, J = 12.8 Hz), 4.87-4.76 (2H, m), 4.62 (1H, dd, J = 12.1, 5.9 Hz), 4.28-4.11 (4H, m).

^{13}C-NMR (75 MHz, CD_3OD): δ 139.36, 130.19, 129.34, 127.89, 85.22, 82.01, 79.72, 74.40, 71.66, 63.06, 34.45.



44

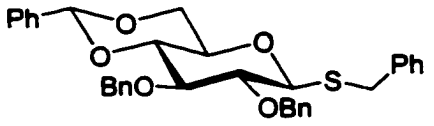
Benzyl-4,6-*O*-benzylidene-1-thio-*β*-D-glucopyranoside (44).

To a solution of thioglucoside **43** (3.79 g, 13.0 mmol) and benzaldehyde dimethyl acetal (3.8 g, 25 mmol) in dry acetonitrile (80 mL) was added *p*-toluensulfonic acid (190 mg, 1.0 mmol). The mixture was stirred for 8 h at room temperature under nitrogen. Triethylamine (2 mL) was added and the solvent was removed in vacuo. Flash column chromatography (eluent: chloroform, methanol 10%) yielded the product **44** (4.72 g, 97% yield).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.50-7.46 (2H, m), 7.39-7.30 (8H, m), 5.53 (1H, s), 4.35 (1H, d, J = 9.9 Hz), 4.32 (1H, dd, J = 9.9, 5.1 Hz), 3.96 (1H, ½ AB system, d, J = 12.8 Hz), 3.92 (1H, ½ AB system, d, J = 12.8 Hz), 3.76 (2H, t, J = 9.9 Hz), 3.56 (2H, t, J = 9.5 Hz), 3.41 (1H, dd, J = 9.9, 5.1 Hz), 2.73 (1H, bs, OH), 2.45 (1H, bd, J = 2.6 Hz, OH).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 137.31, 137.02, 129.43, 129.07, 128.89, 128.47, 127.64, 126.40, 102.15, 85.53, 80.61, 74.93, 73.50, 70.74, 68.79, 34.77.

ESI MS (calcd for $C_{20}H_{22}O_5S$: 374) *m/z* (rel. intensity): 375 ($M+H^+$, 89), 376 ($M+H^+$, 15), 392 ($M+NH_4^+$, 35), 397 ($M+Na^+$, 100), 398 ($M+Na^+$, 28), 771 ($2M+Na^+$, 64), 772 ($2M+Na^+$, 30).



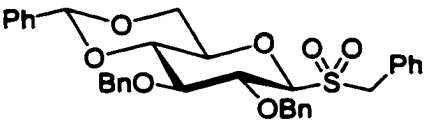
45

Benzyl-2,3-bis-*O*-benzyl-4,6-*O*-benzylidene-1-thio-*β*-D-glucopyranoside (45).

The thioglucoside **44** (4.62 g, 12.3 mmol) was treated with sodium hydride (609 mg, 25.4 mmol) in dry DMF/THF (1/1, 50 mL). Benzyl bromide (4.52 g, 26.4 mmol) and tetrabutylammonium bromide (800 mg) was added and the mixture was stirred at room temperature, under nitrogen for 8 h. Brine (50 mL) was added and the mixture was extracted with dichloromethane (3 x 20 mL). The organic layers were collected and washed with a dilute solution of NH_4Cl (4 x 20 mL). The organic layer was dried over sodium sulfate and the solvent removed in vacuo. Flash column chromatography (petroleum ether, EtOAc 30 %) yielded the product **45** (6.55 g, 96% yield).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.50-7.45 (2H, m), 7.40-7.25 (18H, m), 5.57 (1H, s), 4.91 (1H, d, J = 11.3 Hz), 4.84-4.73 (3H, m), 4.41 (1H, d, J = 9.9 Hz), 4.33 (1H, dd, J = 10.4, 4.9 Hz), 3.97 (1H, ½ AB system, d, J = 13.2 Hz), 3.89 (1H, ½ AB system, d, J = 13.2 Hz), 3.82-3.66 (3H, m), 3.52-3.45 (1H, m), 3.39-3.31 (1H, m).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 138.64, 138.19, 137.67, 137.52, 129.16, 129.07, 128.73, 128.44, 128.36, 128.14, 127.91, 127.77, 127.40, 126.18, 101.44, 84.90, 83.06, 81.93, 81.52, 76.00, 75.38, 70.47, 68.99, 35.20.



46

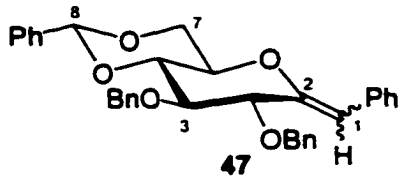
Benzyl-2,3-bis-*O*-benzyl-4,6-*O*-benzylidene-1-sulfonyl-β-D-glucopyranoside (46).

The thioglucoside **45** (4.74 g, 8.55 mmol) was dissolved in THF (60 mL), ethanol (50 mL) and water (40 mL). Magnesium monoperoxyphthalate hexahydrate (MMPP, 18 g) was added and the mixture was stirred for 3 h at ~60 °C. The solvent was partially evaporated. Water was added and the product was extracted with dichloromethane (3 x 20 mL). The organic layer was washed with a saturated solution of $NaHCO_3$ and then dried over sodium sulfate. The solvent was removed in vacuo to obtain the sulfone **46** (4.82 g, 96% yield).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.48-7.44 (2H, m), 7.41-7.26 (18H, m), 5.60 (1H, s), 4.97-4.75 (4H, m), 4.46-4.39 (2H, m), 4.31-4.12 (2H, m), 3.89 (1H, t, J = 10.3 Hz), 3.84 (1H, t, J = 9.2 Hz), 3.77 (1H, t, J= 9.5 Hz), 3.42 (1H, td, J = 9.9, 4.7 Hz).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 137.50, 136.99, 131.07, 129.27, 129.24, 129.13, 128.77, 128.54, 128.51, 128.15, 128.11, 127.95, 127.26, 126.11, 101.58, 87.99, 82.59, 80.96, 76.71, 76.05, 75.475, 70.95, 68.50, 58.19.

ESI MS (calcd for $C_{34}H_{34}O_7S$: 586) *m/z*: 609 ($M+Na^+$, 100), 610 ($M+Na^+$, 42).



47

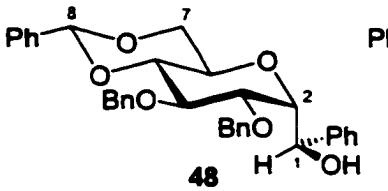
2,6-Anhydro-1-deoxy-1-phenyl-3,4-bis-*O*-benzyl-5,7-*O*-benzylidene-D-gluco-hept-1-enitol (47).[15]

The sulfone **46** (4.75 g, 8.1 mmol) was dissolved in dichloromethane (30 mL) and *t*-butanol (30 mL). The mixture was cooled in an ice bath and 30% KOH on alumina (9.5 g) was added, followed by difluorodibromomethane (3 mL). The mixture was stirred at 0 °C for 1 h and at room temperature for 3 h. The mixture was filtered through celite, the filtrate was collected and the solvent was evaporated. The crude was purified by flash column chromatography (petroleum ether, EtOAc 10%) to obtain **47** (3.72 g, 88% yield). The product consists of a mixture of the two isomers *Z*-**47** and *E*-**47** in the ratio *Z*/*E* = 5/1.

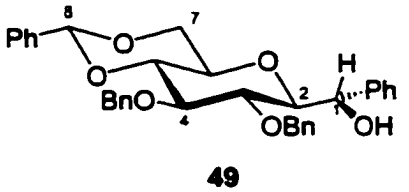
^{1}H-NMR (300 MHz, $CDCl_3$, mixture of isomers, *Z*/*E* = 5/1): δ 7.61-7.57, 7.52-7.48, 7.41-7.18 (20H, m), 6.44 (1H, s, *E*-isomer, H-1), 5.61 (1H, s, *Z*-isomer, H-1), 5.58 (1H, s, H-8), 4.74 (1H, d, J = 11.9 Hz), 4.73 (1H, d, J = 11.9 Hz), 4.68 (1H, d, J = 11.9 Hz), 4.63-4.56 (1H, m), 4.52 (1H, d, J = 11.6 Hz), 4.48 (1H, d, J = 9.8 Hz), 4.38 (1H, td, J = 10.1, 5.2 Hz), 4.04-3.85 (4H, m).

^{13}C-NMR (75 MHz, $CDCl_3$, major isomer *Z* only): δ 147.64, 138.13, 137.85, 137.35, 135.06, 129.17, 128.78, 128.59, 128.47, 128.35, 127.99, 127.90, 126.67, 126.31, 110.34, 101.59, 82.13, 81.49, 80.40, 72.69, 70.56, 69.60, 66.25.

ESI MS (calcd for $C_{34}H_{32}O_5$: 520) *m/z*: 538 ($M+NH_4^+$, 100), 539 ($M+NH_4^+$, 34).



48



49

(1-*R*)-2,6-Anhydro-1-phenyl-3,4-bis-*O*-benzyl-5,7-*O*-benzylidene-α-D-gluco-heptitol (48).[44]

(1-*S*)-2,6-Anhydro-1-phenyl-3,4-bis-*O*-benzyl-5,7-*O*-benzylidene-β-D-gluco-heptitol (49).[44]

To a solution of the *exo*-glucal **47** (910 mg, 1.74 mmol) in dry THF (30 mL) was added a solution of borane (1 M in THF, 3.5 mL) at 0 °C, under N_2. The mixture was stirred for 3 h at 0 °C to room temperature. The mixture was cooled at 0 °C, H_2O_2 (30 wt %, 12 mL) and KOH aq (5%, 12 mL) were added dropwise. The cooling bath was removed and the mixture was stirred for 40 min. The mixture was extracted with EtOAc (3 x 20 mL), the organic layer was dried over sodium sulfate and the solvent removed in vacuo. The two products **α-48** and **β-49** (α:β = 6:4) were purified by flash column chromatography (petroleum ether, 20% EtOAc, 74% yield).

48:

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.50-7.49 (2H, m), 7.41-7.28 (18H, m), 5.52 (1H, s, H-8), 5.13 (1H, dd, *J* = 8.2, 2.8 Hz, H-1), 4.94 (1H, d, *J* = 11.3 Hz, Bn), 4.86 (1H, d, *J* = 11.3 Hz, Bn), 4.81 (1H, d, *J* = 11.3 Hz, Bn), 4.65 (1H, d, *J* = 11.3 Hz, Bn), 4.12 (1H, t, *J* = 7.3 Hz, H-4), 4.07 (1H, dd, *J* = 8.2, 4.9 Hz, H-2), 4.00-3.95 (2H, m, H-3 and H-7eq), 3.85 (1H, d, *J* = 2.8 Hz, OH), 3.78-3.71 (2H, m, H-5 and H-6), 3.50-3.44 (1H, m, H-7ax).

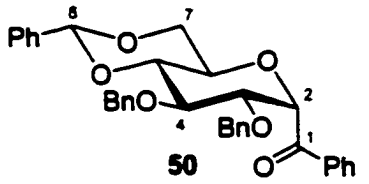
^{13}C-NMR (75 MHz, $CDCl_3$): δ 140.75, 138.36, 137.45, 137.14, 129.08, 128.82, 128.55, 128.50, 128.46, 128.41, 28.37, 128.11, 128.08, 127.93, 126.98, 126.13, 101.32 (C-8),

82.71 (C-5 or C-6), 79.98 (C-3), 79.14 (C-2), 76.74 (C-4), 74.63 (Bn), 74.35 (Bn), 73.38 (C-1), 69.56 (C-7), 65.25 (C-6 or C-5).

49:

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.49-7.46 (2H, m), 7.39-7.20 (18H, m), 5.55 (1H, s, H-8), 4.99-4.94 (3H, m, H-1 and Bn), 4.71 (1H, d, J = 11.0 Hz, Bn), 4.49 (1H, d, J = 11.3 Hz, Bn), 4.38 (1H, dd, J = 10.4, 4.9 Hz, H-7eq), 3.92 (1H, t, J = 8.9 Hz, H-4), 3.87 (1H, dd, J = 9.8, 4.0 Hz, H-2), 3.72 (1H, t, J = 10.4 Hz, H-7ax), 3.56 (1H, t, J = 9.2 Hz, H-5), 3.49 (1H, dd, J = 9.8, 4.9 Hz, H-6), 3.36 (1H, t, J = 8.9 Hz, H-3), 3.03 (1H, d, J = 6.1 Hz, OH).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 139.86, 138.33, 138.20, 137.44, 129.05, 128.55, 128.51, 128.35, 128.26, 128.24, 128.03, 127.95, 127.85, 127.66, 126.09, 101.33 (C-8), 83.78 (C-4), 82.52 (C-5), 81.95 (C-2), 79.14 (C-3), 75.15 (Bn), 74.61 (Bn), 74.47 (C-1), 70.38 (C-6), 69.00 (C-7).



50

2,6-Anhydro-1-phenyl-1-keto-3,4-bis-*O*-benzyl-5,7-*O*-benzylidene-α-D-gluco-heptitol (50).[33, 45]

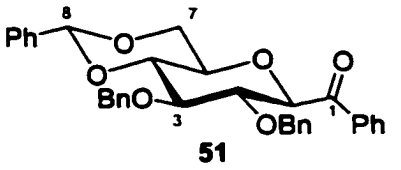
DMSO (0.23 mL, 3.3 mmol) was added dropwise to a solution of oxalyl chloride (0.14 mL, 1.6 mmol) in dry CH_2Cl_2 (3 mL) at –78 °C under N_2. The mixture was stirred at –78 °C for 20 min. Then a solution of **48** (350 mg, 0.65 mmol) in dry CH_2Cl_2 (3 mL) was

added dropwise. The mixture was stirred at –78 °C for 40 min, then Et_3N (0.7 mL, 5.2 mmol) was added dropwise and the solution was allowed to attain room temperature. CH_2Cl_2 (15 mL) was added and the organic layer was washed with aq NH_4Cl (3 x 10 mL), and then dried over sodium sulfate. Flash column chromatography (petroleum ether, 20% EtOAc) yielded **50** (315 mg, 90%).

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.89 (2H, d, J = 7.6 Hz), 7.58 (1H, t, J = 7.3 Hz), 7.50-7.43 and 7.41-7.18 (15 H, series of m), 7.13 (2H, d, J = 6.4 Hz), 5.54 (1H, s, H-8), 5.15 (1H, d, J = 6.1 Hz, H-2), 4.95 (1H, d, J = 11.3 Hz, Bn), 4.86 (1H, d, J = 11.3 Hz, Bn), 4.82 (1H, d, J = 11.9 Hz, Bn), 4.62-4.55 (2H, m, H-4 and Bn), 4.17 (1H, dd, J = 10.1, 4.9 Hz, H-7eq), 3.95-3.87 (2H, m, H-3 and H-6), 3.67 (1H, t, J = 9.5 Hz, H-5), 3.61 (1H, t, J = 10.1 Hz, H-7ax).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 196.01 (C-1), 138.89, 138.14, 137.57, 136.55, 133.49, 129.04, 128.94, 128.72, 128.51, 128.46, 128.33, 128.12, 127.98, 127.73, 126.26, 101.60 (C-8), 82.77 (C-5), 79.24 (C-4), 78.71, 75.06 (Bn), 74.66 (Bn), 73.87 (C-2), 69.48 (C-7), 66.35.

ESI MS (calcd for $C_{34}H_{32}O_6$: 536) *m/z*: 554 ($M+NH_4^+$, 100), 555 ($M+NH_4^+$, 40).



51

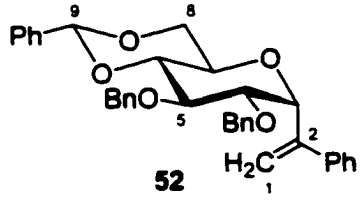
2,6-Anhydro-1-phenyl-1-keto-3,4-bis-*O*-benzyl-5,7-*O*-benzylidene-β-D-gluco-heptitol (51).[33, 45]

DMSO (78 μL, 1.1 mmol) was added dropwise to a solution of oxalyl chloride (44 μL, 0.5 mmol) in dry CH_2Cl_2 (2 mL) at –78 °C under N_2. The mixture was stirred at –78 °C for 20 min. Then a solution of **49** (170 mg, 0.32 mmol) in dry CH_2Cl_2 (2 mL) was added dropwise. The mixture was stirred at –78 °C for 40 min, then Et_3N (0.35 mL, 2.5 mmol) was added dropwise and the solution was allowed to attain room temperature. CH_2Cl_2 (8 mL) was added and the organic layer was washed with aq NH_4Cl (3 x 10 mL), and then dried over sodium sulfate. Flash column chromatography (petroleum ether, 25% EtOAc) yielded **51** (112 mg, 65%).

^{1}H-NMR (500 MHz, $CDCl_3$): δ 8.03 (2H, d, J = 7.3 Hz), 7.60 (1H, t, J = 7.3 Hz), 7.35-7.45 (4H, m), 7.42-7.35 (5H, m), 7.34-7.28 (3H, m), 7.20-7.15 (3H, m), 6.96 (2H, dd, J = 7.6, 1.8 Hz), 5.62 (1H, s, H-8), 5.02 (1H, d, J = 11.3 Hz, Bn), 4.85-4.79 (3H, m, H-2 and Bn), 4.54 (1H, d, J = 10.1 Hz, Bn), 4.36 (1H, J = 10.4, 4.9 Hz, H-7eq), 4.09 (1H, t, J = 8.9 Hz, H-3), 3.99 (1H, t, J = 8.9 Hz, H-4), 3.819 (1H, t, J = 9.2 Hz, H-5), 3.812 (1H, t, J = 10.4 Hz, H-7ax), 3.66 (1H, td, J = 9.5, 4.9 Hz, H-6).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 194.46 (C-1), 138.67, 137.96, 137.48, 136.13, 133.78, 129.29, 129.08, 128.76, 128.47, 128.37, 128.28, 128.17, 128.12, 127.79, 127.73, 126.18, 101.49 (C-8), 83.31, 82.10, 79.07, 78.71 (C-2), 75.62 (Bn), 75.29 (Bn), 71.54 (C-6), 69.00 (C-7).

ESI MS (calcd for $C_{34}H_{32}O_6$: 536) *m/z*: 554 ($M+NH_4^+$, 100), 555 ($M+NH_4^+$, 37).



52

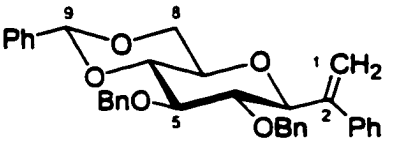
3,7-Anhydro-1,2-dideoxy-2-phenyl-4,5-bis-*O*-benzyl-6,8-*O*-benzylidene-α-D-gluco-oct-1-enitol (52).

To a mixture of methyltriphenylphosphonium bromide (715 mg, 2.0 mmol) in dry THF (20 mL) was added dropwise *n*-butyllithium (1.6 M in hexanes, 1.25 mL) at –10 °C under nitrogen. The mixture was stirred for ½ h at –10 °C, and then a solution of **50** (285 mg, 0.53 mmol) in dry THF (10 mL) was added dropwise. The mixture was stirred for 1 h at –10 °C and for 1.5 h at 0 °C to room temperature. The mixture was poured into a dilute solution of NH_4Cl (40 mL) and extracted with EtOAc (3 x 20 mL). The organic layer was dried over sodium sulfate and the solvent evaporated in vacuo. Flash column chromatography (petroleum ether, 10% EtOAc) yielded **52** (240 mg, 85%).

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.50-7.47 (2H, m), 7.40-7.27 (18H, m), 5.86 (1H, s, H-1a), 5.60 (1H, s, H-1b), 5.54 (1H, s, H-9), 5.06 (1H, d, J = 4.6 Hz, H-3), 4.83 (1H, d, J = 11.6 Hz, Bn), 4.75 (1H, d, J = 11.9 Hz, Bn), 4.70 (1H, d, J = 11.9 Hz, Bn), 4.58 (1H, d, J = 11.6 Hz, Bn), 4.14 (1H, t, J = 7.0 Hz, H-5), 4.05 (1H, dd, J = 10.4, 4.9 Hz, H-8eq), 3.89 (1H, dd, J = 6.7, 4.6 Hz, H-4), 3.81 (1H, t, J = 9.8 Hz, H-6), 3.73 (1H, td, J = 9.8, 4.9 Hz, H-7), 3.61 (1H, t, J = 10.1 Hz, H-8ax).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 144.05, 140.57, 138.59, 138.28, 137.65, 129.00, 128.48, 128.45, 128.33, 128.06, 127.90, 127.86, 127.77, 127.71, 126.91, 126.19, 118.58 (C-1), 101.29(C-9), 83.03 (C-6), 79.80 (C-4), 78.62 (C-5), 74.65 (C-3), 74.01 (Bn), 73.53 (Bn), 69.79 (C-8), 64.22 (C-7).

ESI MS (calcd for $C_{35}H_{34}O_5$: 534) *m/z* (rel. intensity): 535 ($M+H^+$, 52), 536 ($M+H^+$, 26), 552 ($M+NH_4^+$, 100), 553 ($M+NH_4^+$, 54).



53

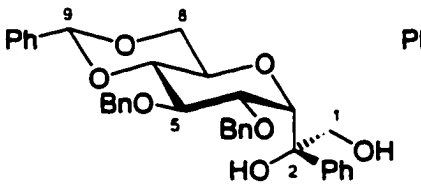
3,7-Anhydro-1,2-dideoxy-2-phenyl-4,5-bis-*O*-benzyl-6,8-*O*-benzylidene-β-D-gluco-oct-1-enitol (53).

To a mixture of methyltriphenylphosphonium bromide (75 mg, 0.21 mmol) in dry THF (5 mL) was added dropwise *n*-butyllithium (1.6 M in hexanes, 0.125 mL) at –10 °C under nitrogen. The mixture was stirred for ½ h at –10 °C, and then a solution of **51** (30 mg, 0.056 mmol) in dry THF (2.5 mL) was added dropwise. The mixture was stirred for 1 h at –10 °C and for 1.5 h at 0 °C to room temperature. The mixture was poured into a dilute solution of NH_4Cl (15 mL) and extracted with EtOAc (3 x 15 mL). The organic layer was dried over sodium sulfate and the solvent evaporated in vacuo. Flash column chromatography (petroleum ether, 10% EtOAc) yielded **53** (21 mg, 73%).

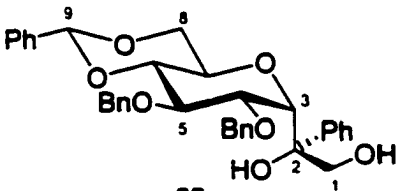
^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.55-7.50 (4H, m), 7.43-7.36 (3H, m), 7.35-7.22 (11H, m), 7.07-7.04 (2H, m), 5.64 (1H, s), 5.62 (1H, s), 5.53 (1H, s), 4.97 (1H, d, J = 11.0 Hz,

Bn), 4.76 (1H, d, J = 11.0 Hz, Bn), 4.63 (1H, d, J = 10.4 Hz, Bn), 4.44 (1H, dd, J = 10.4, 4.9 Hz, H-8eq), 4.35-4.28 (2H, 2 overlapping d, H-3 and Bn), 3.89 (1H, t, J = 9.2 Hz, H-5), 3.83 (1H, t, J = 10.4 Hz, H-8ax), 3.77 (1H, t, J = 9.2 Hz, H-6), 3.62 (1H, t, J = 9.2 Hz, H-4), 3.57 (1H, dd, J = 9.8, 4.9 Hz, H-7).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 146.68 (C-2), 139.64, 138.64, 138.27, 137.58, 129.04, 128.47, 128.38, 128.32, 128.19, 128.01, 127.91, 127.79, 127.69, 127.49, 126.16, 119.18 (C-1), 101.33 (C-9), 83.51 (C-3 or C-5), 83.37 (C-5 or C-3), 82.57 (C-6), 81.52 (C-4), 75.44 (Bn), 75.28 (Bn), 70.93 (C-7), 69.33 (C-8).



54



55

3,7-Anhydro-2-phenyl-4,5-bis-*O*-benzyl-6,8-*O*-benzylidene-α-D-gluco-octitol (54/55).[47]

Osmium tetraoxide (2.5 wt % in *t*-BuOH, 240 μL) and 4-methylmorpholine N-oxide (50 wt % in H_2O, 140 μL) was added to a solution of **52** (170 mg, 0.32 mmol) in acetone (12 mL) at 0 °C. The mixture was stirred at 0 °C for 5 h and at room temperature overnight. Sodium sulfite (20 mg) and water (10 mL) was added and the mixture was stirred for 30 min, and then extracted with EtOAc (3 x 15 mL). The organic layer was dried over sodium sulfate and the solvent removed in vacuo. The two epimers at C-2 (3:1 ratio) were isolated by flash column chromatography (petroleum ether, 20% EtOAc) with a 78% overall yield.

Major diastereoisomer:

R_f: 0.43 (petroleum ether, EtOAc 40%).

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.49-7.46 (2H,m), 7.42-7.24 (18H, m), 5.50 (1H, s, H-9), 4.84 (1H, d, J = 11.6 Hz, Bn), 4.76-4.69 (2H, m, Bn), 4.47 (1H, d, J = 11.0 Hz, Bn), 4.20 (1H, d, J = 3.4 Hz, H-3), 4.15 (1H, dd, J = 7.1, 4.8 Hz, H-4), 4.07-3.94 (5H, m, H-1a, H-6, H-7, H-8eq and OH), 3.86 (1H, t, J = 7.3 Hz, H-5), 3.63 (1H, dd, J = 11.6, 7.6 Hz, H-1b), 3.45 (1H, t, J = 9.7 Hz, H-8b), 2.70 (1H, t, J = 6.7 Hz, OH).

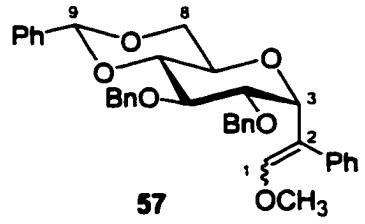
^{13}C-NMR (75 MHz, $CDCl_3$): δ 142.28, 138.15, 137.56, 136.86, 129.05, 128.82, 128.58, 128.46, 128.34, 128.29, 128.16, 128.01, 127.27, 126.19, 125.37, 101.31 (C-9), 82.65 (C-5), 79.59 (C-6), 78.85 (C-2), 77.97 (C-3), 77.91 (C-4), 73.16 (Bn), 73.12 (Bn), 70.03 (C-8), 68.24 (C-1), 64.32 (C-7).

Minor diastereoisomer:

R_f: 0.35 (petroleum ether, EtOAc 40%).

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.52-7.49, 7.47-7.44, 7.42-7.26 and 7.21-7.16 (20 H, m), 5.56 (1H, s, H-9), 4.61 (1H, d, J = 11.9 Hz, Bn), 4.50-4.41 (3H, m, H-4, H-8eq, 1H Bn), 4.34 (1H, s, OH), 4.32 (1H, d, J = 10.7 Hz, Bn), 4.10 (1H, dd, J = 10.0, 5.0 Hz), 4.03 (1H, dd, J = 11.0, 6.1 Hz), 3.97 (1H, d, J = 12.5 Hz, H-1a), 3.89 (1H, d, J = 11.0 Hz, Bn), 3.79-3.70 (3H, m, H-1b, H-8ax), 3.48 (1H, s, H-3), 2.24 (1H, OH).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 142.38, 137.57, 137.38, 136.37, 129.12, 128.72, 128.66, 128.50, 128.39, 128.32, 128.20, 128.15, 128.01, 127.60, 126.21, 125.43, 101.40, 81.87, 79.67, 78.57, 77.08, 75.35, 71.94, 71.90, 70.31, 69.20, 64.44.



57

3,7-Anhydro-2-deoxy-1-*O*-methyl-2-phenyl-4,5-bis-*O*-benzyl-6,8-*O*-benzylidene-α-D-gluco-oct-1-enitol (57).

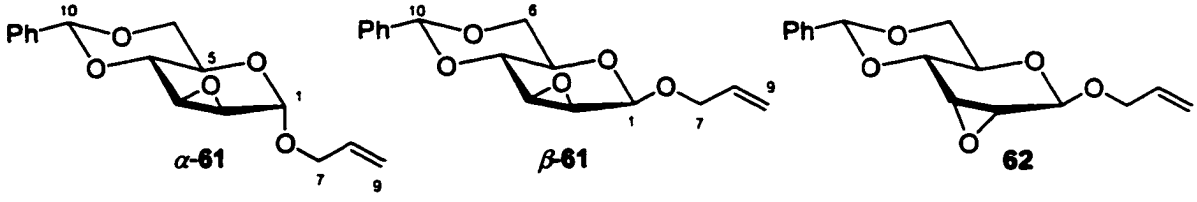
To a mixture of methoxymethyltriphenylphosphonium chloride (247 mg, 0.72 mmol) in dry THF (7 mL) was added dropwise *n*-butyllithium (1.6 M in hexanes, 0.42 mL, 0.67 mmol) at −10 °C under nitrogen. The mixture was stirred for ½ h at −10 °C, and then a solution of **50** (104 mg, 0.19 mmol) in dry THF (3 mL) was added dropwise. The mixture was stirred for 1 h at −10 °C. Water (10 mL) was added and the mixture was extracted with EtOAc (3 x 20 mL). The organic layer was dried over sodium sulfate and the solvent evaporated in vacuo. Flash column chromatography (petroleum ether, 10% EtOAc, 1% Et_3N) yielded **57** (40 mg, 38%) as a mixture of *E* and *Z* isomers (*E*:*Z* = 5:2).

^{1}H-NMR (500 MHz, C_6D_6): δ 7.66-7.52, 7.43-7.37, 7.32-7.00 (20H, m), 6.81 (1H, s, *Z*-isomer, H-1), 5.89 (1H, s, *E*-isomer, H-1), 5.58 (1H, d, J = 4.0 Hz, *E*-isomer, H-3), 5.38 (1H, s, *Z*-isomer, H-9), 5.33 (1H, s, *E*-isomer, H-9), 5.16 (1H, d, J = 4.0 Hz, *Z*-isomer, H-3), 4.90 (1H, d, J = 12.2 Hz, *Z*-isomer, Bn), 4.81 (1H, d, J = 12.4, *E*-isomer, Bn), 4.76 (1H, d, J=12.4, *E*-isomer, Bn), 4.54 (1H, d, J = 11.6, *Z*-isomer, Bn), 4.49 (1H, d, J = 11.6 Hz, *E*-isomer, Bn), 4.39 (1H, d, J = 11.6 Hz, *E*-isomer, Bn), 4.27-4.07, 3.96-3.80, 3.51-3.47 (series of m), 3.08 (3H, s, *Z*-isomer, OCH_3), 2.99 (3H, s, *E*-isomer, OCH_3).

^{13}C-NMR (75 MHz, C_6D_6, aromatic Cs not reported): δ 119.38, 101.99 (*E*-isomer), 101.94 (*Z*-isomer), 84.01 (*Z*-isomer), 83.51 (*E*-isomer), 81.21 (*E*-isomer), 80.63 (*Z*-isomer), 79.76 (*E*-isomer), 78.92 (*Z*-isomer), 75.56 (*Z*-isomer), 74.07 (*Z*-isomer), 73.81

(*Z*-isomer), 73.28 (*E*-isomer), 73.20 (*E*-isomer), 72.43 (*E*-isomer), 70.73 (*E*-isomer), 70.33 (*Z*-isomer), 65.19 (*E*-isomer), 64.40 (*Z*-isomer), 60.40 (*Z*-isomer), 59.99 (*E*-isomer).

ESI MS (calcd for $C_{36}H_{36}O_6$: 564) *m/z*: 582 ($M+NH_4^+$, 100), 583 ($M+NH_4^+$, 40).



Allyl-2,3-anhydro-4,6-*O*-benzylidene-α-D-mannopyranoside (α-61).

Allyl-2,3-anhydro-4,6-*O*-benzylidene-β-D-mannopyranoside (β-61).

Allyl-2,3-anhydro-4,6-*O*-benzylidene-β-D-allopyranoside (62).[51]

Sodium hydride (60% in mineral oil, 1.1 g, 27 mmol) was washed free of oil with pentane. Dry DMF (30 mL) was added, followed by the addition of allyl 4,6-*O*-benzylidene-D-glucopyranoside (4.16 g, 13.5 mmol) dissolved in dry DMF (30 mL). The mixture was stirred at room temperature for ½ h under N_2, then *N*-tosylimidazole (3.2 g, 14.4 mmol) was added and the mixture stirred for 4 h. The mixture was poured into iced water (500 mL) and the crystals filtered under vacuo. The product **α-61** containing variable amount of **β-61** was purified by crystallization from methanol (1.82 g, 46%). Alternatively the reaction mixture was extracted with EtOAc/sat. NH_4Cl and purified by flash column chromatography (petroleum ether, 5% EtOAc). The products **α-61**, **β-61** and **62** were isolated in the ratio 2:1:1.

α-61:

R_f: 0.44 (PE/EtOAc: 8/2).

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.52-7.48 (2H, m), 7.42-7.36 (3H, m), 5.94 (1H, ddt, J = 17.1, 10.4, 5.9 Hz, H-8), 5.57 (1H, s, H-10), 5.34 (1H, dd, J = 17.1, 1.4 Hz, H-9a), 5.25 (1H, dd, J = 10.4, 1.4 Hz, H-9b), 5.06 (1H, s, H-1), 4.30-4.23 (2H, m, H-7a and H-6eq), 4.10 (1H, dd, J = 12.8, 6.4 Hz, H-7b), 3.78 (1H, dt, J = 9.9, 4.3 Hz, H-5), 3.72 (1H, t, J = 10.1 Hz, H-6ax), 3.68 (1H, d, J = 9.2 Hz, H-4), 3.49 (1H, d, J = 3.7, H-2 or H-3), 3.21 (1H, d, J =3.7 Hz, H-3 or H-2).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 137.22, 133.77, 129.31, 128.42, 126.28, 117.90 (C-9), 102.55 (C-10), 95.26 (C-1), 75.13 (C-5), 69.57 (C-6), 69.16 (C-7), 62.03 (C-4), 54.04 (C-2 or C-3), 50.87 (C-3 or C-2).

β-61:

R_f: 0.30 (PE/EtOAc: 8/2).

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.53-7.49 (2H, m), 7.43-7.37 (3H, m), 5.97 (1H, ddt, J = 17.1, 10.6, 6.4 Hz, H-8), 5.58 (1H, s, H-10), 5.36 (1H, d, J = 17.1 Hz, H-9a), 5.26 (1H, d, J = 17.1 Hz, H-9b), 5.09 (1H, s, H-1), 4.45 (1H, dd, J = 12.8, 4.9 Hz, H-7a), 4.29 (1H, dd, J = 10.5, 4.6 Hz, H-6eq), 4.20 (1H, dd, J = 12.8, 6.4 Hz, H-7b), 3.82 (1H, t, J = 10.5 Hz, H-6ax), 3.78 (1H, d, J = 9.5 Hz, H-4), 3.53 (1H, d, J = 3.7 Hz, H-2 or H-3), 3.36 (1H, dt, J = 9.8, 4.6 Hz, H-5), 3.29 (1H, d, J = 3.7 Hz, H-3 or H-2).

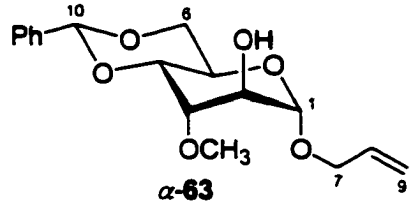
^{13}C-NMR (75 MHz, $CDCl_3$): δ 137.12, 133.71, 129.38, 128.47, 126.26, 118.17 (C-9), 102.63 (C-10), 97.93 (C-1), 74.84 (C-4), 70.51 (C-7), 69.48 (C-6), 68.76 (C-5), 55.29 (C-2 or C-3), 51.16 (C-3 or C-2).

62:

R_f: 0.38 (PE/EtOAc: 8/2).

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.52-7.49 (2H, m), 7.40-7.35 (3H, m), 5.94 (1H, ddt, J = 16.5, 11.0, 5.5 Hz, H-8), 5.58 (1H, s, H-10), 5.34 (1H, dd, J = 17.7, 1.2, Hz, H-9a), 5.25 (1H, d, J = 10.4 Hz, H-9b), 5.04 (1H, s, H-1), 4.35 (1H, dd, J = 12.4, 5.5 Hz, H-7a), 4.27-4.24 (1H, m, H-6eq), 4.14-4.09 (2H, m, H-5, H-7b), 3.75-3.71 (2H, m, H-4, H-6ax), 3.54 (1H, d, J = 4.3 Hz, H-2 or H-3), 3.38 (1H, d, J = 4.3 Hz, H-3 or H-2).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 137.26, 133.62, 129.34, 128.45, 126.41, 118.13, 102.91, 96.40, 77.83 (C-5), 70.47 (C-7), 69.28 (C-6), 61.06 (C-4), 55.70, 51.56.



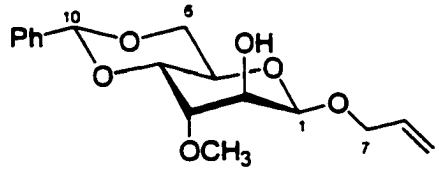
α-**63**

Allyl-3-*O*-methyl-4,6-*O*-benzylidene-α-D-altropyranoside (α-63).

Magnesium (350 mg) dissolved in dry methanol (6 mL) and sodium (450 mg) in dry methanol (6 mL) was added to a solution of α-**61** (880 mg, 3.03 mmol) in dry DMSO (20 mL). The mixture was stirred at 95 °C under N_2 for 4 h, then it was allowed to cool down at room temperature and NH_4Cl aq (30 mL) was added, followed by extraction with EtOAc (3 x 20 mL). The organic layer was dried over sodium sulfate and the solvent removed in vacuo. Flash column chromatography (petroleum ether, 30% EtOAc) yielded α-**63** (89%).

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.52-7.48 (2H, m), 7.39-7.34 (3H, m), 5.92 (1H, ddt, J = 17.4, 10.6, 4.9 Hz, H-8), 5.56 (1H, s, H-10), 5.33 (1H, dd, J = 17.4, 1.5 Hz, H-9a), 5.22 (1H, d, J = 10.6 Hz, H-9b), 4.76 (1H, s, H-1), 4.36 (1H, dt, J = 10.1, 5.2 Hz, H-5), 4.30 (1H, dd, J = 10.1, 5.2 Hz, H-6eq), 4.24 (1H, dd, J = 13.1, 4.9 Hz, H-7a), 4.10-4.04 (2H, m, H-2 and H-7b), 4.02 (1H, dd, J = 9.8, 2.8 Hz, H-4), 3.78-3.72 (2H, m, H-3 and H-6ax), 3.57 (3H, s, OCH_3), 1.93 (1H, broad s, OH).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 137.70, 133.95, 129.14, 128.35, 126.36, 117.78 (C-9), 102.56 (C-10), 99.53 (C-1), 78.15 (C-3), 77.44 (C-4), 69.81 (C-2), 69.52 (C-6), 68.51 (C-7), 60.09 (OCH_3), 59.00 (C-5).



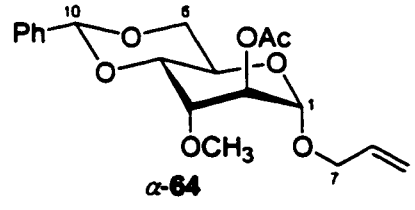
β-63

Allyl-3-*O*-methyl-4,6-*O*-benzylidene-β-D-altropyranoside (β-63).

Magnesium (300 mg) dissolved in dry methanol (5 mL) and sodium (400 mg) in dry methanol (5 mL) was added to a solution of **β-61** (820 mg, 2.82 mmol) in dry DMSO (15 mL). The mixture was stirred at 95 °C under N_2 for 4 h, then it was allowed to cool down at room temperature and NH_4Cl aq (30 mL) was added, followed by extraction with EtOAc (3 x 20 mL). The organic layer was dried over sodium sulfate and the solvent removed in vacuo. The product **β-63** was isolated in 60% yield by flash column chromatography (petroleum ether, 25% EtOAc).

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.51-7.47 (2H, m), 7.39-7.33 (3H, m), 5.92 (1H, ddt, J = 17.4,10.7, 5.8 Hz, H-8), 5.53 (1H, s, H-10), 5.31 (1H, dd, J =17.4, 1.2 Hz, H-9a), 5.23 (1H, d, J = 10.4 Hz, H-9b), 4.85 (1H, s, H-1), 4.39 (1H, dd, J = 12.5, 5.2 Hz, H-7a), 4.33 (1H, dd, J = 10.1, 4.9 Hz, H-6eq), 4.14 (1H, dd, J = 12.5, 6.4 Hz, H-7b), 4.03 (1H, dd, J = 9.8, 2.5 Hz, H-4), 3.97 (1H, dt, J =10.1, 4.9 Hz, H-5), 3.94 (1H, d, J = 2.7 Hz, H-2), 3.84 (1H, t, J = 2.7 Hz, H-3), 3.79 (1H, t, J =10.1 Hz, H-6), 3.56 (3H, s, OCH_3).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 137.71, 133.70, 129.07, 128.32, 126.27, 118.04 (C-9), 102.43 (C-8), 97.37 (C-1), 77.86 (C-3 or C-4), 77.66 (C-4 or C-3), 70.61 (C-2), 70.26 (C-7), 69.37 (C-6), 63.58 (C-5), 60.19 (OCH_3).



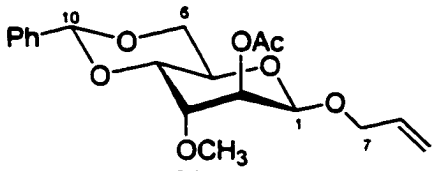
α-**64**

Allyl-2-*O*-acetyl-3-*O*-methyl-4,6-*O*-benzylidene-α-D-altropyranoside (α-64).

Acetic anhydride (30 μL, 0.32 mmol) was added to a solution of α-**63** (50 mg, 0.16 mmol) and DMAP (2 mg, 0.016 mmol) dissolved in EtOAc (6 mL). The mixture was stirred for 40 min at room temperature under N_2, then methanol (0.8 mL) was added and stirring was continued for 10 min. NH_4Cl aq (15 mL) was added, followed by extraction with EtOAc (3 x 10 mL). The organic layer was washed with NH_4Cl aq (4 x 10 mL), and then dried over sodium sulfate and the solvent was removed in vacuo to afford quantitative α-**64**.

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.52-7.48 (2H, m), 7.38-7.34 (3H, m), 5.91 (1H, dddd, J = 17.1, 10.4, 6.1, 4.7 Hz, H-8), 5.58 (1H, s, H-10), 5.33 (1H, dd, J = 17.1, 1.3 Hz, H-9a), 5.22 (1H, d, J = 10.4 Hz, H-9b), 5.14 (1H, d, J = 2.1 Hz, H-2), 4.73 (1H, s, H-1), 4.38 (1H, ddd, J = 10.1, 9.8, 5.5 Hz, H-5), 4.32 (1H, dd, J = 10.1, 5.5 Hz, H-6eq), 4.24 (1H, dd, J = 13.2, 4.7 Hz, H-7a), 4.05 (1H, dd, J = 13.2, 6.1 Hz, H-7b), 3.92 (1H, dd, J = 9.8, 2.9 Hz, H-4), 3.75 (1H, t, J = 10.1 Hz, H-6ax), 3.71 (1H, broad s, H-3), 3.58 (3H, s, OCH_3), 2.14 (3H, s, OAc).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 169.49 (OAc), 137.62, 133.74, 129.17, 128.37, 126.37, 117.72 (C-9), 102.51 (C-10), 97.06 (C-1), 77.40 (C-4), 75.68 (C-3), 70.19 (C-2), 69.46 (C-6), 68.60 (C-7), 59.77 (OCH_3), 58.66 (C-5), 21.28 (OAc).



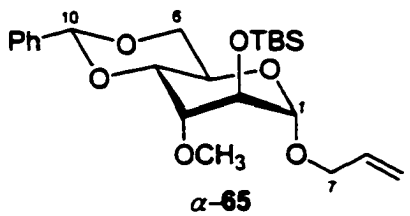
β-64

Allyl-2-*O*-acetyl-3-*O*-methyl-4,6-*O*-benzylidene-*β*-D-altropyranoside (*β*-64).

Acetic anhydride (25 μL, 0.23 mmol) was added to a solution of ***β*-63** (40 mg, 0.12 mmol) and DMAP (2 mg, 0.016 mmol) dissolved in EtOAc (6 mL). The mixture was stirred for 40 min at room temperature under N_2, then methanol (0.8 mL) was added and stirring was continued for 10 min. NH_4Cl aq (15 mL) was added, followed by extraction with EtOAc (3 x 10 mL). The organic layer was washed with NH_4Cl aq (4 x 10 mL), and then dried over sodium sulfate and the solvent was removed in vacuo to afford quantitative ***β*-64**.

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.50-7.47 (2H, m), 7.39-7.34 (3H, m), 5.89 (1H, dddd, J = 17.1, 11.0, 6.1, 5.8 Hz, H-8), 5.53 (1H, s, H-10), 5.29 (1H, dd, J = 17.1, 1.1 Hz, H-9a), 5.22-5.18 (2H, m, H-2 and H9b), 4.95 (1H, s, H-1), 4.38-4.33 (2H, m, H-7a and H-6eq), 4.11(1H, dd, J = 12.8, 6.1 Hz, H-7b), 4.01 (1H, dt, J = 9.8, 5.2 Hz, H-5), 3.89 (1H, dd, J = 9.8, 2.4 Hz, H-4), 3.83 (1H, t, J = 10.1 Hz, H-6ax), 3.76 (1H, broad t, J = 2.8 Hz, H-3), 3.74 (3H, s, OCH_3), 2.18 (3H, s, OAc).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 169.94 (Ac), 137.54, 133.62, 129.18, 128.38, 126.28, 117.74 (C-9), 102.48 (C-10), 96.58 (C-1), 77.81 (C-4), 76.59 (C-3), 70.58 (C-7), 70.19 (C-2), 69.29 (C-6), 63.83 (C-5), 60.16 (OCH_3), 21.34 (Ac).



α-**65**

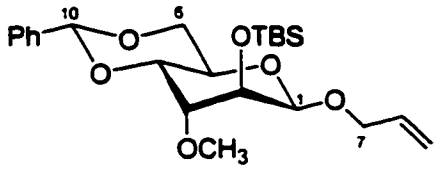
Allyl-2-*O*-*tert*-butyldimethylsilyl-3-*O*-methyl-4,6-*O*-benzylidene-α-D-altropyranoside (α-65).

A mixture of α-**63** (700 mg, 2.17 mmol), imidazole (210 mg, 3.08 mmol) and TBDMSCl (458 mg, 3.1 mmol) in dry DMF (6 mL) was stirred at r. t. under nitrogen overnight (12 h). Water (15 mL) was added and the mixture was extracted with EtOAc (3 x 15 mL). The organic layer was dried over sodium sulfate and the solvent was removed in vacuo. Column chromatography (petroleum ether, EtOAc 10%) afforded the product α-**65** (850 mg, 90% yield).

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.53-7.49 (2H, m), 7.39-7.33 (3H, m), 5.91 (1H, dddd, J = 17.1, 10.4, 6.7, 4.9 Hz, H-8), 5.57 (1H, s, H-10), 5.32 (1H, dd, J = 17.1, 1.2 Hz, H-9a), 5.21 (1H, d, J = 10.4 Hz, H-9b), 4.62 (1H, s, H-1), 4.35-4.26 (2H, m, H-5 and H-6eq), 4.22 (1H, dd, J = 13.4 Hz, 4.9 Hz, H-7a), 4.07-3.99 (3H, m, H-2, H-4 and H-7b), 3.75 (1H, t, J =9.8 Hz, H-6ax), 3.60 (1H, t, J = 2.4 Hz, H-3), 3.57 3H, s, OCH_3), 0.92 (9H, s, TBDMS), 0.11 (3H, s, TBDMS), 0.10 (3H, s, TBDMS).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 137.92, 134.18, 129.12, 128.37, 126.45, 117.61 (C-9), 102.56 (C-10), 99.80 (C-1), 79.02 (C-3), 77.61, 70.78, 69.67 (C-6), 68.28 (C-7), 60.20 (OCH_3), 58.87 (C-5), 26.09, 18.38, -3.26, -4.67.

ESI MS (calcd for $C_{23}H_{36}O_6Si$: 436) *m/z* (rel. intensity): 437 ($M+H^+$, 55), 438 ($M+H^+$, 18), 454 ($M+NH_4^+$, 100), 455 ($M+NH_4^+$, 29), 890 ($2M+NH_4^+$, 70), 891 ($2M+NH_4^+$, 40).



β-65

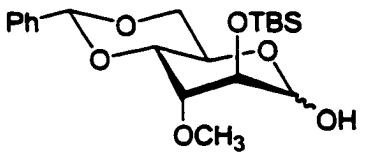
Allyl-2-*O*-*tert*-butyldimethylsilyl-3-*O*-methyl-4,6-*O*-benzylidene-β-D-altropyranoside (β-65).

A mixture of **β-63** (1.35 g, 4.20 mmol), imidazole (408 mg, 6.0 mmol) and TBDMSCl (904 mg, 6.0 mmol) in dry DMF (10 mL) was stirred at r. t. under nitrogen overnight (18 h). Water (20 mL) was added and the mixture was extracted with EtOAc (3 x 20 mL). The organic layer was dried over sodium sulfate and the solvent was removed in vacuo.

Column chromatography (petroleum ether, EtOAc 10%) afforded the product β-**65** (1.73 g, 94% yield).

^{1}H-NMR ($CDCl_3$, 500 MHz): δ 7.52-7.46 (2H, m), 7.40-7.33 (3H, m), 5.91 (1H, ddt, J = 17.1, 10.5, 5.4 Hz, H-8), 5.53 (1H, s, H-10), 5.28 (1H, d, J = 17.5 Hz, H-9a), 5.18 (1H, d, J = 10.8 Hz, H-9b), 4.74 (1H, s, H-1), 4.38 (1H, dd, J = 12.7, 5.1 Hz, H-7a), 4.31 (1H, dd, J = 10.2, 5.1 Hz, H-6eq), 4.05 (1H, dd, J = 12.7, 6.0 Hz, H-7b), 4.01 (1H, dd, J = 9.5, 2.2 Hz, H-4), 3.96-3.89 (2H, m, H-2, H-5), 3.83 (1H, t, J = 10.15 Hz, H-6ax), 3.65 (1H, t, J = 2.9 Hz, H-3), 3.55 (3H, s, OCH_3), 0.92 (9H, s), 0.12 (3H, s), 0.11 (3H, s).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ 137.96, 134.24, 129.11, 128.37, 126.41, 117.15 (C-10), 102.57 (C-10), 98.53 (C-1), 80.10 (C-3), 78.11 (C-4), 71.47, 70.53 (C-7), 69.68 (C-6), 64.03, 60.06 (OCH_3), 26.24, 18.69, -4.01, -4.93.



66

2-*O*-*tert*-Butyldimethylsilyl-3-*O*-methyl-4,6-*O*-benzylidene-α-D-altropyranose (66).[53]

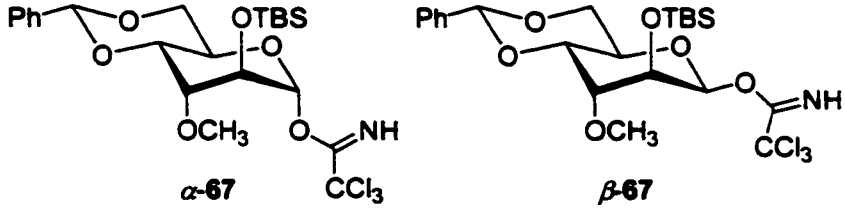
Anhydrous $ZnCl_2$ (3.70 g, 27.1 mmol) was added to the solution of α- and β-**65** (4.70 g, 10.8 mmol) in dry THF (65 mL) and the mixture was stirred at r. t. for 30 min. Tetrakis(triphenylphosphine)palladium (3.12 g, 2.70 mmol) was added and stirring was continued for 30 min. Tributyltin hydride (12.5 g, 42.9 mmol) was added dropwise to the above solution. Upon addition of Bu_3SnH the yellow mixture turned brown. After being stirred for 1.5 h, EtOAc (150 mL) was added and the organic layer was washed with 5%

HCl (3 x 30 mL) and then dried over Na_2SO_4. The solvent was removed under reduced pressure and the product **66** (3.55 g, 83% yield) was purified by column flash chromatography (petroleum ether, EtOAc 20%).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.52-7.46 and 7.40-7.33 (m), 5.56 (s), 5.51 (s), 5.04-4.95, 4.85-4.79, 4.36-4.24, 4.10-3.97, 3.91-3.82, 3.80-3.72, 3.71-3.68 (series of m), 3.63 (s), 3.56 (s), 0.96, 0.92, 0.18, 0.17, 0.13, 0.12 (series of s)

^{13}C-NMR (75 MHz, $CDCl_3$): δ 137.71, 129.19, 128.40, 126.36, 126.29, 102.69, 102.58, 96.03, 92.22, 79.84, 79.14, 71.85, 70.22, 69.86, 69.53, 63.28, 60.84, 60.23, 59.27, 26.01, 25.99, 18.34, 13.92, -4.66.

ESI MS (calcd for $C_{20}H_{32}O_6Si$: 396) *m/z* (rel. intensity): 397 ($M+H^+$, 100), 398 ($M+H^+$, 28), 414 ($M+NH_4^+$, 70), 415 ($M+NH_4^+$, 19), 815 ($2M+Na^+$, 38), 816 ($2M+Na^+$, 20).



α-67 β-67

***O*-(2-*O*-*tert*-Butyldimethylsilyl-3-*O*-methyl-4,6-*O*-benzylidene-α-D-altropyranosyl)trichloroacetimidate (α-67).**

***O*-(2-*O*-*tert*-Butyldimethylsilyl-3-*O*-methyl-4,6-*O*-benzylidene-β-D-altropyranosyl)trichloroacetimidate (β-67).**[54]

To a solution of **66** (400 mg, 1.00 mmol) and trichloroacetonitrile (1.0 mL, 10.0 mmol) in dry CH_2Cl_2 (10 mL), was added NaH (192 mg, 7.6 mmol) and the resulting mixture was stirred at r. t. for 6 h. The mixture was slowly poured in cold water (ca. 30 mL) and the

product was extracted with CH_2Cl_2 (3 x 30 mL). The organic layer was dried over Na_2SO_4 and then the solvent was removed under reduced pressure. The products α- and β- **67** (325 mg, 0.60 mmol, α/β ~ 1/4, 60% yield) were isolated by column chromatography (petroleum ether, EtOAc 10%, Et_3N 0.5%).

α-**67**:

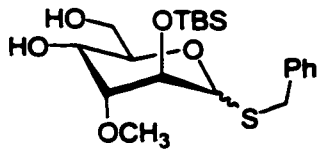
^{1}H-NMR (500 MHz, $CDCl_3$): δ 8.68 (1H, s, NH), 7.52-7.49 (2H, m), 7.39-7.34 (3H, m), 6.06 (1H, s, H-1), 5.53 (1H, s, H-8), 4.37(1H, dd, J = 10.4, 4.9 Hz, H-6eq), 4.15-4.08 (3H, m, H-2, H-4, H-5), 3.85 (1H, t, J = 9.8 Hz, H-6ax), 3.74 (1H, dd, J = 3.1, 2.4 Hz, H-3), 3.59 (3H, s, OCH_3), 0.95 (9H, s), 0.17 (3H, s), 0.15 (3H, s).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 161.37, 137.69, 129.23, 128.42, 126.41, 102.69 (C-8), 96.00 (C-1), 79.74 (C-3), 77.57, 70.34, 69.39, 64.92, 60.19 (OCH_3), 26.10, 18.40, -4.35, -4.70.

β-**67**:

^{1}H-NMR (500 MHz, $CDCl_3$): δ 8.51 (1H, s, NH), 7.53-7.50 (2H, m), 7.38-7.33 (3H, m), 5.94 (1H, s, H-1), 5.60 (1H, s, H-7), 4.50 (1H, dt, J = 10.4, 5.5 Hz, H-5), 4.34 (1H, dd, J = 10.4, 5.5 Hz, H-6eq), 4.24 (1H, d, J = 3.1 Hz, H-2), 4.10 (1H, dd, J = 9.8, 3.1 Hz, H-4), 3.77 (1H, t, J = 10.4 Hz, H-6ax), 3.68 (1H, t, J = 3.1 Hz, H-3), 3.52 (3H, s, OCH3), 0.95 (9H, s), 0.17 (3H, s), 0.16 (3H, s).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 161.20, 137.70, 129.10, 128.33, 126.47, 102.57, 98.36, 78.14, 76.74, 69.48, 67.97, 61.21, 58.86, 26.04, 18.33, -4.52, -4.698.



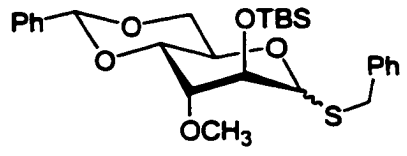
68

Benzyl-2-*O*-*tert*-butyldimethylsilyl-3-*O*-methyl-1-thio-α,β-D-altropyranoside (68).

To a solution of **67** (280 mg, 0.52 mmol) and benzyl mercaptan (106 mg, 0.85 mmol) in dry CH_2Cl_2 (106 mg, 0.85 mmol) cooled at –78 °C was added dropwise $BF_3{\cdot}OEt_2$ (6 mg, 0.04 mmol). The mixture was stirred at –78 °C for 40 min and then at r. t. for 20 min. A saturated solution of $NaHCO_3$ (15 mL) was added and the product was extracted with EtOAc (3 x 25 mL). The product **68** was isolated as a 2/1 ratio of anomers in 95% yield by column chromatography (petroleum ether, EtOAc 50%).

^{1}H-NMR ($CDCl_3$, 500 MHz): δ 7.34-7.30 (5H, m), 4.80 (1H, s), 4.04-4.02, 3.93-3.91, 3.89-3.83, 3.80-3.75, 3.74-3.68, 3.45-3.37 (series of m), 3.47 (3H, s), 3.41 (3H, s), 0.92 (9H, s), 0.81 (9H, s), 0.16 (3H, s), 0.11 (3H, s), -0.04 (3H, s), -0.10 (3H, s).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ 138.46, 138.33, 129.20, 129.05, 128.63, 127.18, 127.14, 83.99, 81.73, 81.54, 80.48, 77.31, 70.52, 69.77, 65.41, 65.33, 63.57, 63.28, 58.94. 58.61, 36.46, 35.94, 26.09, 25.92, 18.42, 18.25, -4.27, -4.41, -4.79, -4.88.



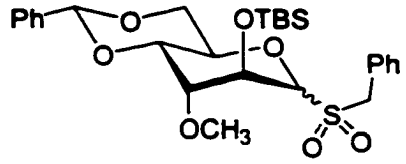
69

Benzyl-2-*O*-*tert*-butyldimethylsilyl-3-*O*-methyl-4,6-*O*-benzylidene-1-thio-α,β-D-altropyranoside (69).

A solution of **68** (1.35 g, 3.3 mmol), benzaldehyde dimethyl acetale (1.48 g) and *p*-toulensulfonic acid (60 mg), dissolved in acetonitrile (40 mL) was stirred at r. t. for 9 h. Acidic resin (DOWEX 50X8-400. Ion-exchange resin. Strong acidic. Ca. 1 g) was added and the mixture was filtered. The solvent was removed in vacuo to obtain the product **69** in 98% yield. The product consisted of a mixture of α and β anomers, but it was not possible to assign the NMR peaks corresponding to each anomer.

^{1}H-NMR ($CDCl_3$, 500 MHz, major anomer): δ 7.51-7.48(2H, m), 7.38-7.33, 7.33-7.29, 7.27-7.23 (8H, series of m), 5.52 (1H, s), 4.78 (1H, s, H-1), 4.27 (1H, dd, J = 10.4, 4.9 Hz, H-6eq), 4.00 (1H, dd, J = 9.8, 2.4 Hz, H-4), 3.92-3.86 (3H, m, H-2, H-5, H-7), 3.81 (1H, t, J = 10.4Hz, H-6ax), 3.56 (1H, t, J = 2.4 Hz, H-3), 3.48 (3H, s), 0.94 (9H, s), 0.16 (3H, s), 0.12 (3H, s).

^{13}C-NMR ($CDCl_3$, 75 MHz, major anomer): δ 138.19, 137.82, 129.14, 128.67, 128.41, 127.20, 126.40, 102.58, 82.35, 79.38, 77.71, 73.13, 69.52, 66.79, 59.89, 35.70, 26.23, 26.15, 18.49, -4.32, -4.42.



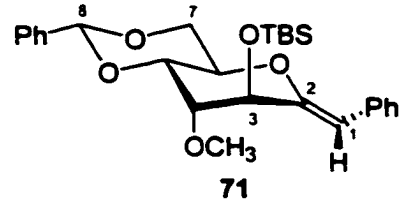
70

***O-tert*-butyldimethylsilyl-3-*O*-methyl-4,6-*O*-benzylidene-1-sulfonyl-α,β-D-altropyranoside (70).**

The thioglucoside **69** (150 mg, 0.30 mmol) was dissolved in THF (8 mL), ethanol (8 mL) and water (7 mL). Magnesium monoperoxyphthalate hexahydrate (MMPP, 500 mg) was added and the mixture was stirred for 3 h at ~65 °C. The solvent was partially evaporated. Water was added and the product was extracted with dichloromethane (3 x 15 mL). The organic layer was washed with a saturated solution of $NaHCO_3$ and then dried over sodium sulfate. The solvent was removed in vacuo to obtain the sulfone **70** (145 mg, 90% yield).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.52-7.48 and 7.42-7.34 (m), 5.552 (1H, s), 5.546 (1H, s), 4.63 (d, J = 1.1 Hz), 4.58 (1H, J = 3.3 Hz), 4.50-4.47, 4.46-4.43, 4.41-4.34, 4.23-4.20, 4.17-4.15, 4.14-4.08, 4.04-3.97, 3.69-3.65 (series of m), 3.54 (3H, s), 3.51 (3H, s), 0.97 (9H, s), 0.77 (9H, s), 0.20 (3H, s), 0.07 (3H, s), -0.05 (3H, s), -0.23 (3H, s).

ESI MS (calcd for $C_{27}H_{38}O_7SSi$: 534) *m/z* (rel. intensity): 535 ($M+H^+$, 51), 552 ($M+NH_4^+$, 100), 553 ($M+NH_4^+$, 37).



71

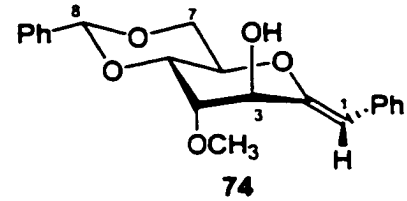
(*Z*)-2,6-Anhydro-1-deoxy-1-phenyl-3-*O*-*tert*-butyldimethylsilyl-4-*O*-methyl-5,7-*O*-benzylidene-D-altro-hept-1-enitol (71).[15]

The sulfone **70** (1.10 g, 2.06 mmol) was dissolved in dichloromethane (10 mL) and *t*-butanol (10 mL). The mixture was cooled in an ice bath and 30% KOH on alumina (3.0 g) was added, followed by difluorodibromomethane (ca. 5 mL). The mixture was stirred at 0 °C for 1 h and at room temperature for 3 h. The mixture was filtered through celite, the filtrate was collected and the solvent was removed under reduced pressure. The crude was purified by flash column chromatography (petroleum ether, EtOAc 10%, Et_3N 0.3%) to obtain **71** (1.00 g, 70% yield).

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.57 (2H, d, J = 7.3 Hz), 7.53-7.49 (2H, m), 7.40-7.35 (3H, m), 7.30 (2H, t, J = 7.3 Hz), 7.20 (1H, t, J = 7.3 Hz), 5.78 (1H, s, H-1), 5.60 (1H, s, H-8), 4.48 (1H, dd, J = 10.1, 5.2 Hz, H-7eq), 4.33-4.30 (2H, m, H-3 and H-5), 4.24 (1H, dt, J = 10.1, 5.2 Hz, H-6), 3.93 (1H, t, J = 10.1 Hz, H-7ax), 3.73 (1H, t, J = 2.7 Hz, H-4), 3.58 (3H, s, OCH_3), 0.91 (9H, s, TBDMS), 0.15 (3H, s, TBDMS), 0.09 (3H, s, TBDMS).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 151.00 (C-2), 137.66, 135.08, 129.22, 128.95, 128.42, 128.30, 126.90, 126.42, 114.43 (C-1), 102.76 (C-8), 79.49 (C-4), 77.71 (C-3 or C-5), 73.37 (C-5 or C-3), 69.63 (C-7), 67.13 (C-6), 59.65 (OCH_3), 26.08, 18.42, -4.11, -4.54.

ESI MS (calcd for $C_{27}H_{36}O_5Si$: 468) *m/z* (rel. intensity): 469 ($M+H^+$, 100), 470 ($M+H^+$, 47), 954 ($2M+NH_4^+$, 49), 955 ($2M+NH_4^+$, 29).



74

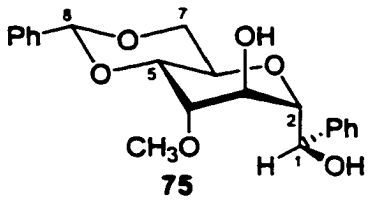
(*Z*)-2,6-Anhydro-1-deoxy-1-phenyl-4-*O*-methyl-5,7-*O*-benzylidene-D-altro-hept-1-enitol (74).

To a solution of *exo*-glycal **71** (120 mg, 0.26 mmol) dissolved in THF (6 mL) was added tetrabutylammonium fluoride (1 M in THF, 0.27 mL) and the mixture was stirred at r. t. for ca. 2 h. The solvent was removed in vacuo and the product (70 mg, 76% yield) was purified by column chromatography (petroleum ether, EtOAc 30%).

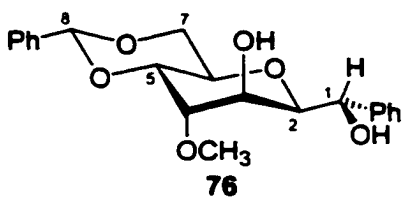
^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.58 (2H, d, J = 7.3 Hz), 7.52-7.48 (2H, m), 7.40-7.35 (3H, m), 7.30 (2H, t, J = 7.3 Hz), 7.21 (1H, d, J = 7.3 Hz), 5.76 (1H, s), 5.61 (1H, s), 4.50 (1H, dd, J = 10.4, 4.9 Hz, H-7eq), 4.37 (1H, d, J = 3.7 Hz, H-3), 4.34 (1H, dd, J = 9.8, 2.4 Hz, H-5), 4.28 (1H, dt, J = 10.0, 4.9 Hz, H-6), 3.94 (1H, t, J = 10.4 Hz, H-7ax), 3.86 (1H, t, J = 3.1 Hz, H-4), 3.58 (3H, s, OCH_3).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 151.23 (C-2), 137.81, 134.88, 129.19, 129.11, 128.39, 127.23, 126.46, 114.68 (C-1), 102.83 (C-8), 78.19 (C-4), 77.45 (C-5), 73.13 (C-3), 69.54 (C-7), 67.24 (C-6), 59.79 (OCH_3).

ESI MS (calcd for $C_{21}H_{22}O_5$: 354) *m/z* (rel. intensity): 355 ($M+H^+$, 100), 356 ($M+H^+$, 31), 377 ($M+Na^+$, 59), 378 ($M+Na^+$, 20), 731 ($2M+Na^+$, 19), 732 ($2M+Na^+$, 9).



75



76

(1-*R*)-2,6-Anhydro-1-phenyl-4-*O*-methyl-5,7-*O*-benzylidene-α-D-altro-heptitol (75).

(1-*S*)-2,6-Anhydro-1-phenyl-4-*O*-methyl-5,7-*O*-benzylidene-β-D-altro-heptitol (76).[44]

To a solution of the *exo*-glycal **74** (400 mg, 1.13 mmol) in dry THF (12 mL) was added borane (1 M in THF, 1.3 mL) at 0 °C (ice bath) under nitrogen. The mixture was stirred at low temperature for 1 h and then at r. t. for an additional 2 h. The reaction was monitored by taking a small aliquot (ca. 0.05 mL) of the reaction mixture and checking the TLC after basic oxidative work up. The reaction mixture was cooled down at 0 °C and KOH (5% in water, 2 mL) and H_2O_2 (30%, 2 mL) were added dropwise. The mixture was stirred for 30 min at r. t., water (12 mL) was added and then an extraction with EtOAc (3 x 20 mL) was performed. The organic layer was dried over sodium sulfate and the two products **75** (30 mg, 0.08 mmol, 7%) and **76** (270 mg, 0.72 mmol, 64%) were separated by column chromatography (petroleum ether, EtOAc 30%).

Alternatively, the hydroboration was conducted on the *exo*-glycal **71** (100 mg, 0.21 mmol) which was treated with borane (1 M in THF, 0.4 mL) in THF (5 mL) under the same conditions described above. After basic oxidative work up and column chromatography (petroleum ether, EtOAc 10%) an inseparable mixture of the **72** and **73** (80 mg) was obtained. An aliquot (32 mg) of this product was treated with TBAF (1 M in THF, 0.07 mL) in THF (3 mL) for 1 h at r. t. By comparison of the ^{1}H-NMR spectrum of the reaction crude with the spectra of **75** and **76**, it was possible to calculate the ratio α/β = 1/10.

75:

R_f: 0.24 (PE/EtOAc: 4/6).

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.51-7.48 (2H, m), 7.40-7.35 and 7.30-7.29 (8H, m), 5.54 (1H, s, H-8), 5.37 (1H, d, J = 8.5 Hz, H-1), 4.46 (1H, d, J = 3.1 Hz, H-3), 4.32 (1H, dt, J = 9.8, 5.5 Hz, H-6), 4.12 (1H, dd, J = 9.8, 5.5 Hz, H-7eq), 4.08 (1H, dd, J = 9.8, 2.4 Hz, H –5), 3.88 (1H, d, J = 8.5 Hz, H-2), 3.85 (1H, t, J = 3.1 Hz, H-4), 3.68 (3H, s, OCH_3), 3.59 (1H, t, J = 9.8 Hz, H-7ax).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 142.46, 137.94, 129.08, 128.64, 128.33, 128.02, 126.50, 126.36, 102.61 (C-8), 83.12 (C-2 or C-4), 78.53 (C-4 or C-2), 77.80 (C-5), 72.43 (C-1), 69.87 (C-7), 68.12 (C-3), 62.38 (C-6), 60.36 (OCH_3).

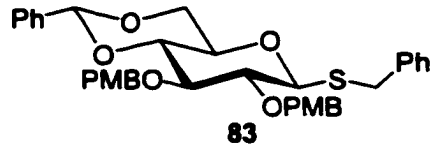
76:

R_f: 0.39 (PE/EtOAc: 4/6).

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.50-7.47 (2H, m), 7.45-7.32 (8H, m), 5.56 (1H, s, H-8), 5.20 (1H, t, J = 3.1 Hz, H-1), 4.33 (1H, dd, J = 10.4, 4.9 Hz, H-7eq), 4.15 (1H, dd, J = 9.8, 2.4 Hz, H-5), 4.05 (1H, dt, J = 9.8, 4.9 Hz, H-6), 4.00 (1H, broad s, OH), 3.88 (1H, d, J = 3.1 Hz, H-2), 3.84 (1H, broad d, J = 3.1 Hz, H-3), 3.81 (1H, t, J = 10.4 Hz, H-7ax), 3.62 (1H, t, J = 3.1 Hz, H-4), 3.42 (3H, s, OCH_3), 2.86 (1H, d, J = 3.1 Hz).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 139.15, 138.10, 129.05, 128.82, 128.34, 128.19, 126.41, 125.92, 102.64 (C-8), 78.44 (C-5), 77.62 (C-4), 77.38 (C-2), 76.15 (C-1), 69.69 (C-7), 69.27 (C-2), 67.36 (C-6), 59.83 (OCH_3).

ESI MS (calcd for $C_{21}H_{24}O_6$: 372) *m/z* (rel. intensity): 395 ($M+Na^+$, 100), 396 ($M+Na^+$, 23), 767 ($2M+Na^+$, 42), 768 ($2M+Na^+$, 22).



83

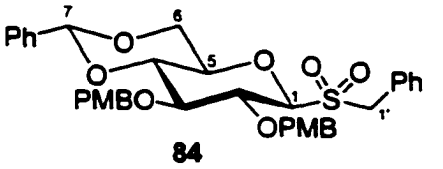
Benzyl-2,3-bis-*O*-(4-methoxybenzyl)-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (83).

The thioglucoside **44** (14.80 g, 39.5 mmol) dissolved in DMF (75 mL) and THF (40 mL) was added dropwise at 0 °C (ice bath) to a suspension of NaH (0.107 mol, 60% dispersion in mineral oil, washed free of oil with pentane) in DMF (25 mL) and THF (15 mL), followed by addition of PMBCl (0.10 mol), and tetrabutylammonium iodide (7.9 mmol). The mixture was stirred at low temperature for 30 min and then at r. t. overnight (10 h). Methanol (8 mL) was added dropwise. The mixture was stirred for 1 h and then the solvent was partially removed under reduced pressure. Saturated aqueous NH_4Cl (80 mL) was added and the product was extracted with EtOAc (3 x 40 mL). The organic layer was dried over sodium sulfate and the solvent was removed in vacuo. The crude was dissolved in EtOAc (ca. 70 mL) and such solution was poured in an Erlenmeyer flask containing petroleum ether (ca. 700 mL). The flask was stored in a freezer for 1 h and then the crystals formed were filtered and washed with cold petroleum ether (ca. 100 mL) to obtain 20.88 g (86% yield) of **83**.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.50-7.44 (2H, m), 7.38-7.21 (12H, m), 6.86-6.78 (4H, m), 5.54 (1H, s), 4.83 (1H, d, J = 11.0 Hz), 4.75-4.65 (3H, m), 4.38 (1H, d, J = 9.9 Hz), 4.30 (1H, dd, J = 10.6, 4.9 Hz), 3.95 (1H, d, J = 13.2 Hz), 3.86 (1H, d, J = 13.2 Hz), 3.76 (3H, s), 3.74 (3H, s), 3.77-3.61 (3H, m), 3.44 (1H, t, J = 9.1 Hz), 3.33 (1H, m).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 159.39, 159.27, 137.55, 137.40, 130.71, 130.27, 129.92, 129.69, 129.04, 128.95, 128.61, 128.24, 127.27, 126.06, 113.83, 101.21, 84.76, 82.57, 81.74, 81.00, 75.51, 74.93, 70.31, 68.81, 55.41, 55.38, 35.00.

ESI MS (calcd for $C_{36}H_{38}O_7S$: 614) *m/z*: 632 ($M+NH_4^+$, 100), 633 ($M+NH_4^+$, 36).



84

Benzyl-2,3-bis-*O*-(4-methoxybenzyl)-4,6-*O*-benzylidene-1-sulfonyl-β-D-glucopyranoside (84).

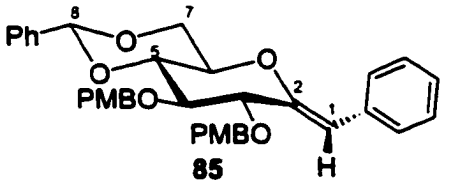
The thioglucoside **83** (11.0 g, 17.9 mmol) was dissolved in THF (50 mL), ethanol (50 mL) and water (40 mL). Magnesium monoperoxyphthalate hexahydrate (MMPP, 12 g) was added and the mixture was stirred for 3.5 h at 60 – 70 °C. The solvent was partially removed in vacuo, water (40 mL) was added and the product was extracted with EtOAc (80 mL). The organic layer was washed with a saturated solution of $NaHCO_3$ until no evolution of CO_2 was observed and then dried over sodium sulfate. The solvent was removed in vacuo and the crude was purified by column chromatography (solvent: petroleum ether, EtOAc 30%) to obtain the sulfone **84** (11.0 g, 95% yield).

^{1}H-NMR (300 MHz, $CDCl_3$): δ 7.48-7.44 (2H, m), 7.40-7.34 (8H, m), 7.30-7.23 (4H, m), 6.85-6.81 (4H, m), 5.58 (1H, s, H-7), 4.85 (1H, d, J = 11.0 Hz, PMB), 4.81 (1H, d, J = 9.8 Hz, PMB), 4.77 (1H, d, J = 9.8 Hz, PMB), 4.72 (1H, d, J = 11.0 Hz, PMB), 4.44-4.39 (2H, m, H-6eq and H-1'a), 4.27-4.21 (2H, m, H-1 and H-1'b), 4.11 (1H, t, J = 9.2

Hz, H-2), 3.87 (1H, t, J = 9.8 Hz, H-6ax), 3.82-3.71 (8H, m, H-3, H-4 and PMB), 3.39 (1H, dt, J = 9.8, 4.9 Hz, H-5).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 159.45, 159.36, 136.99, 131.00, 130.31, 129.71, 129.13, 129.06, 128.96, 128.29, 127.19, 126.04, 113.91, 113.86, 101.40, 88.00 (C-1), 82.14, 80.80, 76.41 (C-2), 75.51, 75.00, 70.80 (C-5), 68.34 (C-6), 57.99 (C-7), 55.39.

ESI MS (calcd for $C_{36}H_{38}O_9S$: 646) *m/z*: 664 ($M+NH_4^+$, 100), 665 ($M+NH_4^+$, 42).



85

(*Z*)-2,6-Anhydro-1-deoxy-1-phenyl-3,4-bis-*O*-(4-methoxybenzyl)-5,7-*O*-benzylidene-D-gluco-hept-1-enitol (85).[15]

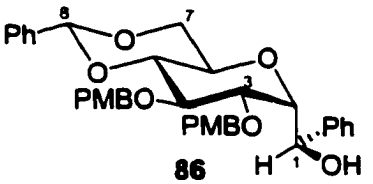
The sulfone **84** (2.70 g, 4.17 mmol) was dissolved in dichloromethane (20 mL) and *t*-butanol (20 mL). The mixture was cooled in an ice bath and 25% KOH on alumina (5.0 g) was added, followed by difluorodibromomethane (ca. 5 mL). The mixture was stirred at 0 °C for 1 h and at room temperature for 6 h. The mixture was filtered through celite, the filtrate was collected and the solvent was evaporated. The crude was purified by flash column chromatography (petroleum ether, EtOAc 10%, Et_3N 0.3%) to obtain **85** (1.69 g, 70% yield).

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.58 (2H, d, J = 7.3 Hz), 7.49 (2H, dd, J = 7.3, 1.2 Hz), 7.41-7.35 (m, 3H), 7.32 (2H, t, J = 7.3 Hz), 7.28-7.23 (4H, m), 7.20 (1H, t, J = 7.3 Hz), 6.89 (2H, d, J = 8.5 Hz), 6.85 (2H, d, J = 8.5 Hz), 5.60 (1H, s, H-1), 5.56 (1H, s, H-8),

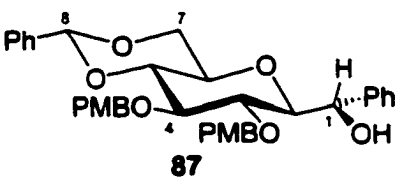
4.66 (1H, d, J = 11.6 Hz, PMB), 4.65 (1H, d, J = 11.6 Hz, PMB), 4.60 (1H, d, J = 11.6 Hz, PMB), 4.57 (1H, dd, J = 10.4, 5.5 Hz, H-7eq), 4.45 (1H, d, J = 11.6 Hz, PMB), 4.34 (1H, dt, J = 9.8, 5.5 Hz, H-6), 3.99 (1H, d, J = 2.4 Hz, H-3), 3.94 (1H, dd, J = 7.3, 2.4 Hz, H-4), 3.90-3.84 (2H, m, H-5 and H-7a), 3.82 (3H, s, PMB), 3.79 (3H, s, PMB).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 159.44, 159.37, 147.89, 137.40, 135.12, 130.28, 129.97, 129.56, 129.52, 129.09, 128.74, 128.34, 128.29, 126.58, 126.30, 114.04, 113.94, 110.16 (C-1), 101.54 (C-8), 82.14 (C-5), 81.18 (C-4), 80.17 (C-3), 72.41, 70.29, 69.56 (C-7), 66.32 (C-6), 55.45.

ESI MS (calcd for $C_{36}H_{36}O_7$: 580) m/z: 598 ($M+NH_4^+$, 100), 599 ($M+NH_4^+$, 37).



86



87

(1-*R*)-2,6-Anhydro-1-phenyl-3,4-bis-*O*-(4-methoxybenzyl)-5,7-*O*-benzylidene-*α*-D-gluco-heptitol (86).

(1-*S*)-2,6-Anhydro-1-phenyl-3,4-bis-*O*-(4-methoxybenzyl)-5,7-*O*-benzylidene-*β*-D-gluco-heptitol (87).[44]

To a solution of **85** (1.0 g, 1.7 mmol) in dry THF (20 mL) was added borane in THF (1 M, 2 mL) at 0 °C (ice bath). The mixture was stirred at low temperature for 1 h and then at r. t. for an additional 7 h and monitored by TLC after basic oxidative work up of a small aliquote (ca. 0.05 mL) of the reaction mixture. The reaction mixture was cooled down at 0 °C and KOH (5% in water, 3 mL) and H_2O_2 (30%, 3 mL) were added

dropwise. The mixture was stirred for 1.5 h at r. t., water (20 mL) was added and then an extraction with EtOAc (3 x 25 mL) was performed. The organic layer was dried over sodium sulfate and the two products **86** (533 mg, 0.89 mmol, 53%) and **87** (180 mg, 0.30 mmol, 18%) were separated by column chromatography (petroleum ether, EtOAc 10%).

86:

R_f: 0.30 (petroleum ether, EtOAc 30%)

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.51-7.47 (2H, m), 7.41-7.25 (12H, m), 6.91-9.85 (4H, m), 5.51 (1H, s, H-8), 5.11 (1H, dd, J = 8.5, 2.4 Hz, H-1), 4.86 (1H, d, J = 11.0 Hz), 4.79 (1H, d, J = 11.0 Hz), 4.74 (1H, d, J = 11.0 Hz), 4.57 (1H, d, J = 11.0 Hz), 4.07 (1H, t, J = 7.6 Hz, H-4), 4.02 (1H, dd, J = 8.5, 4.9 Hz, H-2), 3.99-3.92 (2H, m, H-3 and H-7eq), 3.90 (1H, d, J = 2.4 Hz, OH), 3.811 (3H, s, OCH_3), 3.806 (3H, s, OCH_3), 3.74-3.70 (2H, m, H-5 and H-6), 3.48-3.44 (1H, m, H-7ax).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 159.86, 159.49, 140.82, 137.52, 130.57, 130.08, 129.74, 129.31, 129.04, 128.46, 128.34, 128.02, 126.98, 126.14, 114.27, 114.02, 101.31 (C-8), 82.73 (C-5 or C-6), 79.65 (C-3), 78.79 (C-4), 76.75 (C-2), 74.21, 74.02, 73.38 (C-1), 69.56 (C-7), 65.28 (C-6 or C-5), 55.52.

ESI MS (calcd for $C_{36}H_{38}O_8$: 598) *m/z*: 616 ($M+NH_4^+$, 100), 617 ($M+NH_4^+$, 38).

87:

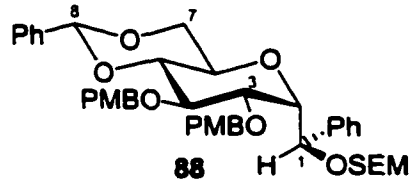
R_f: 0.18 (petroleum ether, EtOAc 30%)

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.50-7.47 (2H, m), 7.39-7.27 (8H, m), 7.22 (2H, d, J = 8.5 Hz), 7.15 (2H, d, J = 8.5 Hz), 6.87 (2H, d, J = 8.5 Hz), 6.82 (2H, d, J = 8.5 Hz), 5.54 (1H, s, H-8), 4.92-4.86 (3H, m, H-1 and PMB), 4.67 (1H, d, J = 11.0 Hz, PMB), 4.43 (1H, d, J = 10.4 Hz, PMB), 4.34 (1H, dd, J = 10.4, 4.9 Hz, H-7eq), 3.88 (1H, t, J = 9.2

Hz, H-4), 3.83-3.78 (4H, m, H-2 and OCH_3 at 3.80 ppm), 3.77 (3H, s, OCH_3), 3.69 (1H, t, J = 9.8 Hz, H-7ax), 3.54 (1H, t, J = 9.2 Hz, H-5), 3.45 (1H, td, J = 9.8, 4.9 Hz, H-6), 3.35 (1H, t, J = 9.2 Hz, H-3), 3.12 (1H, d, J = 5.5 Hz, OH).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 159.40, 159.38, 140.01, 137.50, 130.61, 130.34, 129.84, 129.39, 128.99, 128.29, 128.15, 127.94, 127.90, 126.08, 114.03, 113.98, 101.29 (C-8), 83.45 (C-4), 82.53 (C-5), 81.89 (C-2), 78.97 (C-3), 74.71, 74.54 (C-1), 74.22, 70.35 (C-6), 68.97 (C-7), 55.47, 55.42.

ESI MS (calcd for $C_{36}H_{38}O_8$: 598) *m/z*: 616 ($M+NH_4^+$, 100), 617 ($M+NH_4^+$, 37).



88

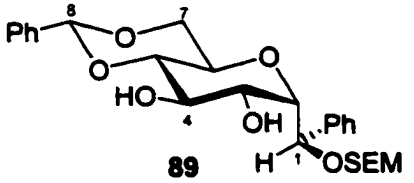
(1-*R*)-2,6-Anhydro-1-phenyl-1-*O*-[2-(trimethylsilyl)ethoxymethyl]-3,4-bis-*O*-(4-methoxybenzyl)-5,7-*O*-benzylidene-α-D-gluco-heptitol (88).[60]

The *C*-glucoside **86** (1.07 g, 1.79 mmol) was dissolved in dry methylene chloride (4 mL), in the presence of diisopropylethylamine (1.05 g, 8.1 mmol). To such solution SEMCl (0.9 g, 8.1 mmol) was added and the mixture was stirred at r. t. under nitrogen atmosphere for ca. 10 h. Methylene chloride (15 mL) was added and the organic layer was washed with sat. ammonium chloride (2 x 10 mL). The organic layer was dried over sodium sulfate and the solvent removed in vacuo. Column chromatography (solvent: EtOAc 10%, petroleum ether) afforded 1.29 g (98% yield) of the product **88**.

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.48 (2H, m), 7.39-7.26 (12H, m), 6.89-6.86 (4H, m), 5.45 (1H, s, H-8), 4.78 (1H, d, J = 8.5 Hz, H-1), 4.74 (1H, d, J = 11.6 Hz, ½ AB system, SEM), 4.72 (1H, d, J = 11.6 Hz, ½ AB system, SEM), 4.61-4.57 and 4.54-4.49 (4H, m, PMB), 4.19 (1H, dd, J = 8.5, 3.1 Hz, H-2), 4.05 (1H, t, J = 3.1 Hz, H-3), 3.97-9.92 (2H, m, H-4 and H-7), 3.83-3.79 (7H, m, H-5 and 2 OCH_3 at 3.81 ppm), 3.74 (1H, td, J = 10.3, 4.9 Hz, H-6), 3.47 (1H, ddd, J = 11.6, 9.8, 5.5 Hz, SEM), 3.39 (1H, t, J = 10.3 Hz, H-7), 3.30 (1H, ddd, J = 11.6, 9.8, 5.5 Hz, SEM), 0.73 (1H, ddd, J = 13.4, 11.6, 5.5 Hz, SEM), 0.57 (1H, ddd, J = 13.4, 11.6, 5.5 Hz, SEM), -0.11 (9H, s, SEM).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 159.30, 139.74, 137.65, 130.50, 130.22, 129.50, 129.43, 128.79, 128.25, 128.12, 127.97, 127.61, 126.09, 113.85, 100.97, 93.72, 82.19 (C-5), 78.46 (C-3), 77.81 (C-1), 77.68 (C-4), 75.82 (C-2), 72.58, 71.99, 69.84 (C-7), 65.79, 64.11 (C-6), 55.34, 18.05, -1.25.

ESI MS (calcd for $C_{42}H_{56}O_9Si$: 728) *m/z*: 746 ($M+NH_4^+$, 100), 747 ($M+NH_4^+$, 51), 751 ($M+Na^+$, 35), 752 ($M+Na^+$, 19).



89

(1-*R*)-2,6-Anhydro-1-phenyl-1-*O*-[2-(trimethylsilyl)ethoxymethyl]-5,7-*O*-benzylidene-α-D-gluco-heptitol (89).[61]

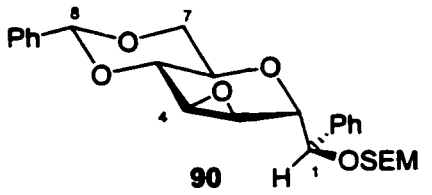
To the *C*-glucoside **88** (1.13 g, 1.55 mmol) dissolved in methylene chloride (15 mL) and water (7 mL) was added 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ, 1.0 g, 4.4

mmol). The mixture was stirred vigorously for ca. 1.5 h at r. t. A saturated solution of sodium bicarbonate in water (15 mL) was added dropwise and the product was extracted with methylene chloride (4 x 15 mL). The organic layer was dried over sodium sulfate and the solvent removed in vacuo. Column chromatography (solvent: EtOAc 15%, petroleum ether) yielded the product **89** (644 mg, 1.32 mmol, 85%).

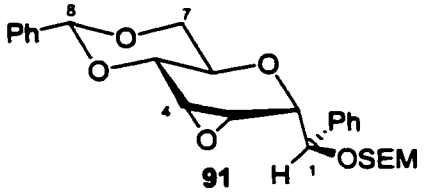
^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.52-7.48 (2H, m), 7.40-7.33 (8H, m), 5.50 (1H, s, H-8), 5.25 (1H, d, J = 8.5 Hz, H-1), 4.64 (1H, d, J = 6.7 Hz, SEM), 4.50 (1H, d, J = 6.7 Hz, SEM), 4.29 (1H, d, J = 6.1 Hz, OH), 4.26 (1H, dd, J = 8.5, 4.9 Hz, H-2), 4.11 (1H, t, J = 9.2 Hz, H-4), 3.98 (1H, ddd, J = 8.5, 6.1, 4.9 Hz, H-3), 3.94 (1H, dd, J = 10.4, 4.9 Hz, H-7), 3.78-3.71 (2H, m, H-6 and SEM), 3.58 (1H, t, J = 9.2 Hz, H-5), 3.54-3.45 (2H, m, H-7 and SEM), 2.73 (1H, bs, OH), 0.94-0.83 (2H, m, SEM), 0.01 (9H, s, SEM).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 137.64, 137.26, 129.22, 128.79, 128.37, 127.75, 126.40, 101.95 (C-8), 92.76, 82.08 (C-5), 77.54 (C-1), 76.25 (C-2), 74.18 (C-3), 72.99 (C-4), 69.41 (C-7), 66.78, 65.72 (C-6), 18.38, -1.11.

ESI MS (calcd for $C_{26}H_{40}O_7Si$: 488) *m/z* (rel. intensity): 506 ($M+NH_4^+$, 100), 507 ($M+NH_4^+$, 33), 994 ($2M+NH_4^+$, 28), 995 ($2M+NH_4^+$, 22).



90



91

(1-*R*)-2,6-Anhydro-1-phenyl-1-*O*-[2-(trimethylsilyl)ethoxymethyl]-3,4-anhydro-5,7-*O*-benzylidene-α-D-manno-heptitol (90).

(1-*R*)-2,6-Anhydro-1-phenyl-1-*O*-[2-(trimethylsilyl)ethoxymethyl]-3,4-anhydro-5,7-*O*-benzylidene-α-D-allo-heptitol (91).[51]

Sodium hydride (60% in mineral oil, 175 mg, 4.4 mmol) was washed free of oil with pentane. The *C*-glucoside **89** (990 mg, 2.03 mmol), dissolved in dry DMF (30 mL) was added dropwise at 0 °C (ice bath), under nitrogen. The mixture was stirred at 0 °C for 15 min under N_2, then a solution of *N*-tosylimidazole (511 mg, 2.3 mmol) in DMF (10 mL) was added dropwise and the mixture stirred for 15 min at 0 °C and then at r. t. for 1 h. Sat. NH_4Cl aq. (40 mL) was added and the product was extracted with EtOAc (4 x 40 mL). The organic layer was dried over sodium sulfate, the solvent removed in vacuo and the products **90** (740 mg, 1.57 mmol, 77%) and **91** (190 mg, 0.40 mmol, 20%) were isolated by column chromatography (EtOAc 5 to 10%, petroleum ether).

90:

R_f: 0.4 (PE/EtOAc: 8/2).

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.53-7.49 (2H, m), 7.42-7.31 (8H, m), 5.55 (1H, s, H-8), 5.03 (1H, d, J = 7.3 Hz, H-1), 4.69 (1H, d, J = 6.7 Hz, SEM), 4.61 (1H, d, J = 6.7 Hz, SEM), 4.22 (1H, d, J = 7.3 Hz, H-2), 4.07-4.01 (1H, m, H-7), 3.74 (1H, td, J = 9.8, 6.7 Hz, SEM), 3.63-3.49 (6H, m), 0.93-0.82 (1H, m), 0.01 (9H, s).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 138.18, 137.31, 129.25, 128.73, 128.41, 127.46, 126.25, 102.35 (C-8), 93.06, 77.92 (C-1), 76.06, 75.97, 69.79 (C-7), 66.25, 65.47, 54.68, 50.37, 18.36, -1.08.

ESI MS (calcd for $C_{26}H_{38}O_6Si$: 470) *m/z* (rel. intensity): 488 ($M+NH_4^+$, 100), 489 ($M+NH_4^+$, 34), 963 ($2M+Na^+$, 8).

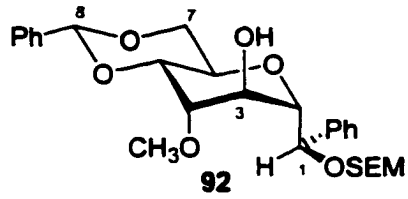
91:

R_f: 0.3 (PE/EtOAc: 8/2).

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.52-7.49 (2H, m), 7.40-7.33 and 7.32-7.28 (8H, m), 5.53 (1H, s, H-8), 4.99 (1H, d, J = 9.2 Hz, H-1), 4.72 (1H, d, J = 6.7 Hz, SEM), 4.61 (1H, d, J = 6.7 Hz, SEM), 4.11 (1H, dd, J = 9.2, 3.1 Hz, H-2), 4.01-3.93 (3H, m, H-5, H-6 and H-7eq), 3.76 (1H, ddd, J = 11.6, 9.2, 5.5 Hz, SEM), 3.74 (1H, m, H-3, partially overlapped with ddd at 3.76 ppm), 3.62 (1H, d, J = 4.9 Hz, H-4), 3.52-3.43 (2H, m, H-7ax and SEM), 0.92 (1H, ddd, J = 13.4, 11.6, 5.5 Hz), 0.78 (1H, ddd, J = 13.4, 11.6, 5.5 Hz), -0.03 (9H, s).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 139.38, 137.40, 129.25, 128.42, 128.38, 128.16, 127.73, 126.41, 102.76, 93.06, 78.35, 75.79 (C-1), 74.08 (C-2), 69.21 (C-7), 65.67, 62.40, 54.15 (C-3), 51.90 (C-4), 18.13, -1.14.

ESI MS (calcd for $C_{26}H_{38}O_6Si$: 470) *m/z* (rel. intensity): 488 ($M+NH_4^+$, 100), 489 ($M+NH_4^+$, 36), 958 ($2M+NH_4^+$, 13), 963 ($2M+Na^+$, 9).



92

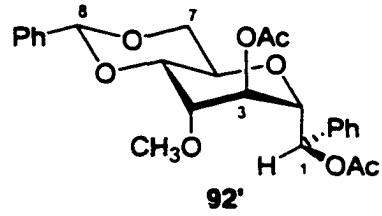
(1-*R*)-2,6-Anhydro-1-phenyl-1-*O*-[2-(trimethylsilyl)ethoxymethyl]-4-*O*-methyl-5,7-*O*-benzylidene-α-D-altro-heptitol (92).

The epoxide **90** (1.0 g, 2.1 mmol) was dissolved in a solution of sodium methoxide in methanol (ca. 2 M, 16 mL) in a pressure tube. The tube was sealed and the mixture was stirred at ca. 120 °C (oil bath) for 20 h. The solution was allowed to cool at r. t. and then acidic resin (DOWEX – 50 WX8 – 400 ion exchange resin – strongly acidic, prewashed with methanol) was added untill neutral pH (monitored by pH paper). The resin was filtered off and the solvent removed in vacuo to obtain a quantitative yield (1.0 g) of the *C*-altroside **92**.

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.50-7.46 (2H, m), 7.41-7.28 (8H, m), 5.51 (1H, s, H-8), 5.33 (1H, d, J = 10.4 Hz, H-1), 4.65 (1H, d, J = 6.1 Hz, SEM), 4.56 (1H, d, J = 6.1 Hz, SEM), 4.47 (1H, t, J = 4.0 Hz, H-3), 4.08 (1H, dt, J = 9.8, 5.5 Hz, H-6), 4.03 (1H, dd, J = 9.8, 4.0 Hz, H-7eq), 3.87-3.84 (2H, m, H-2 and H-4), 3.65 (3H, s, OCH_3), 3.56 (1H, ddd, J = 11.6, 9.2, 6.0 Hz, SEM), 3.49 (1H, t, J =10.4 Hz, H-7ax), 3.38 (1H, ddd, J = 11.6, 9.2, 6.0 Hz, SEM), 1.92 (1H, d, J = 5.5 Hz, OH), 0.80 (1H, ddd, J = 13.4, 11.6, 5.5 Hz, SEM), 0.66 (1H, ddd, J = 13.4, 11.6, 5.5 Hz, SEM), -0.04 (9H, s, SEM).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 139.98, 137.88, 129.11, 128.47, 128.38, 128.10, 127.71, 126.31, 102.47 (SEM, OCH_2O), 93.59, 81.92, 78.84, 77.88 (C-5), 75.84 (C-1), 69.61 (C-7), 68.89 (C-3), 65.81, 61.85 (C-6), 60.57, 18.16, -1.11.

ESI MS (calcd for $C_{27}H_{42}O_7Si$: 502) *m/z*: 520 ($M+NH_4^+$, 100), 521 ($M+NH_4^+$, 35).



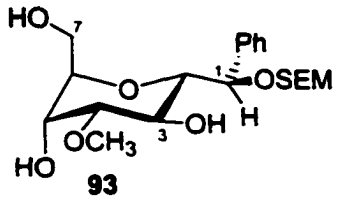
92'

(1-*R*)-2,6-Anhydro-1-phenyl-1,3-bis-*O*-acetyl-4-*O*-methyl-5,7-*O*-benzylidene-α-D-altro-heptitol (92').

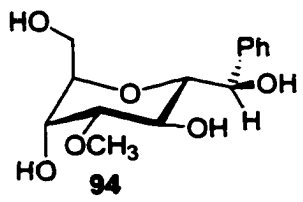
The *C*-glycoside **92** (100 mg, 0.20 mmol) was dissolved in 1 M TBAF solution in THF (5 mL). Such solution was refluxed for 2 h and then stirred overnight at r. t. A saturated aqueous solution of NH_4Cl (8 mL) was added and the mixture was extracted with EtOAc. The product **75** (30 mg) was isolated by column chromatography (petroleum ether, EtOAc 20%), and unreacted starting material (70 mg) was recovered. The product **75** was dissolved in EtOAc (5 mL) and treated with DMAP (5 mg) and Ac_2O (0.2 mL). The mixture was stirred at r. t. for 1.5 h. And then the reaction was quenched by adding saturated solution of NH_4Cl (ca. 10 mL) and the product was extracted with EtOAc. The organic layer was dried and the solvent removed under reduced pressure to obtain a pure sample of **92'**.

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.50-7.47 (2H, m), 7.41-7.30 (8H, m), 6.48 (1H, d, J = 11.0 Hz, H-1), 5.54 (1H, s, H-8), 5.40 (1H, d, J = 3.1 Hz, H-3), 4.19 (1H, dt, J = 9.8, 4.9 Hz, H-6), 4.04 (1H, d, J = 11.0 Hz, H-2), 3.96 (1H, dd, J = 10.4, 5.5 Hz, H-7eq), 3.92 (1H, dd, J = 9.8, 2.4 Hz, H-5), 3.78 (1H, t, J = 3.1 Hz, H-4), 3.59 (3H, s, OCH_3), 3.52 (1H, t, J = 10.4 Hz, H-7ax), 2.17 (3H, OAc), 2.09 (3H, OAc).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 169.75, 169.25, 138.35, 137.58, 129.18, 128.55, 128.37, 127.45, 126.31, 102.46, 77.71 (C-2), 77.44 (C-5), 75.90 (C-4), 72.49 (C-1), 69.43 (C-7), 68.85 (C-3), 61.41 (C-6), 60.02 (OCH_3), 21.41 (OAc), 21.37 (OAc).



93



94

(1-*R*)-2,6-Anhydro-1-phenyl-1-*O*-[2-(trimethylsilyl)ethoxymethyl]-4-*O*-methyl-α-D-altro-heptitol (93).

(1-*R*)-2,6-Anhydro-1-phenyl-4-*O*-methyl-α-D-altro-heptitol (94).

To the benzylidene protected *C*-glycoside **92** (1.0 g, 2.0 mmol) dissolved in methanol (50 mL) was added *p*-toluensulfonic acid monohydrate (200 mg, 1.05 mmol) and the mixture was stirred at r. t. and monitored by TLC. As the consumption of all the starting material was detected by TLC, the reaction was quenched by addition of triethylamine (3 mL). The solvent was removed under reduced pressure and the two products **93** (705 mg, 1.7 mmol, 85%) and **94** (85 mg, 0.3 mmol, 15%) were separated by column chromatography on silica gel (solvent: methanol 3%, EtOAc). Longer reaction time afforded **94** in quantitative yield.

93:

$[\alpha]^{25}_{D}$ = -57.0 (c = 2.85, CH_2Cl_2). m.p.: 64-67 °C.

Anal. calcd for $C_{20}H_{34}O_7Si$: C, 57.94; H, 8.27. Found: C, 57.93; H, 8.25.

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.40-7.29 (5H, m), 4.91 (1H, d, J = 8.5 Hz, H-1), 4.64 (1H, d, J = 6.7 Hz, SEM), 4.55 (1H, d, J = 6.7 Hz, SEM), 4.10 (1H, dt, J = 7.0, 2.4 Hz, H-3), 3.89-3.84 (2H, m, H-5 and H-6), 3.72-3.65 (2H, m, H-2 and SEM), 3.63-3.57 (1H, m, H-7a), 3.56 (3H, s, OCH_3), 3.50-3.41 (3H, m, H-4, H-7b, SEM), 3.35 (1H, d, J = 2.4 Hz, OH-3), 2.54 (1H, d, J = 4.3 Hz, OH-5), 1.32 (1H, OH-7), 0.89-0.75 (2H, m, SEM), -0.01 (9H, s, SEM).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 138.81, 128.54, 128.02, 93.08 (SEM, OCH_2O), 81.62 (C-4), 79.42 (C-1), 76.93 (C-2), 75.95 (C-5 or C-6), 69.34 (C-3), 66.27 (SEM, $O\underline{C}H_2CH_2SiMe_3$), 65.67 (C-5 or C-6), 60.64 (C-7), 58.61 (OCH_3), 18.32 (SEM, $OCH_2\underline{C}H_2SiMe_3$), -1.09 (SEM, $Si(CH_3)_3$).

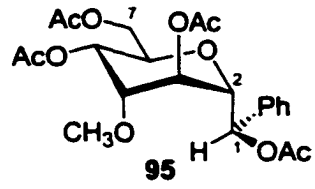
ESI MS (calcd for $C_{20}H_{38}O_7Si$: 414) *m/z* (rel. intensity): 432 ($M+NH_4^+$, 100), 433 ($M+NH_4^+$, 33), 851 ($2M+Na^+$, 16).

94:

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.44 (2H, d, J = 7.6 Hz), 7.37 (2H, t, J = 7.6 Hz), 7.32 (1H, t, J = 7.6 Hz), 4.96 (1H, d, J = 7.6 Hz, H-1), 4.14 (1H, t, J = 7.6 Hz), 3.98 (1H, ddd, J = 8.9, 4.4, 3.2 Hz, H-6), 3.94 (1H, t, J = 3.2 Hz, H-5), 3.69 (1H, dd, J = 11.4, 8.9 Hz, H-7a), 3.64 (1H, t, J = 7.6 Hz, H-2), 3.54 (3H, s, OCH_3), 3.51 (1H, dd, J = 11.4, 4.4 Hz, H-7b), 3.40 (1H, dd, J = 7.6, 3.2 Hz, H-4).

^{13}C-NMR (100 MHz, $CDCl_3$): δ 141.30, 128.77, 128.61, 127.02, 81.67 (C-4), 76.81 (C-6), 76.34 (C-2), 75.99 (C-1), 69.55 (C-3), 65.39 (C-5), 59.99 (C-7), 58.10 (OCH_3).

ESI MS (calcd for $C_{14}H_{20}O_6$: 284) *m/z* (rel. intensity): 307 ($M+Na^+$, 100), 308 ($M+Na^+$, 14), 591 ($2M+Na^+$, 6).



95

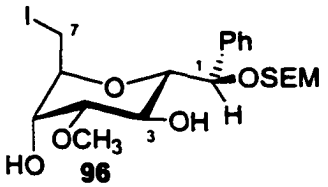
(1-*R*)-2,6-Anhydro-1-phenyl-1,3,5,7-tetrakis-*O*-acetyl-4-*O*-methyl-α-D-altro-heptitol (95).

The *C*-glycoside **94** (40 mg, 0.14 mmol), was dissolved in EtOAc (5 mL). DMAP (5 mg) and Ac_2O (0.2 mL) were added and the mixture was stirred at r. t. for 1.5 h. The reaction was quenched by adding saturated solution of NH_4Cl (ca. 10 mL) and the product was extracted with EtOAc. The organic layer was dried and the solvent removed under reduced pressure to obtain a pure sample of **95**.

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.40-7.28 (5H, m), 6.36 (1H, d, J = 9.8 Hz, H-1), 5.35 (1H, dd, J = 4.3, 2.4 Hz, H-3), 5.04 (1H, dd, J = 9.2, 3.1 Hz, H-5), 4.21 (1H, dt, J = 9.2, 2.4 Hz, H-6), 4.17-4.12 (2H, m, H-2 and H-7a), 3.89 (1H, dd, J = 11.6, 2.4 Hz, H-7b), 3.75 (1H, t, J = 3.7 Hz, H-4), 3.49 (3H, s, OCH_3), 2.11 (3H, s, OAc), 2.10 (3H, s, OAc), 2.09 (3H, s, OAc), 1.91 (3H, s, OAc).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 170.49, 169.88, 169.85, 169.31, 137.57, 128.46, 128.39, 127.71, 76.66 (C-2), 76.46 (C-4), 72.76 (C-1), 68.06 (C-6), 67.67 (C-3), 67.38 (C-5), 62.97 (C-7), 59.31 (OCH_3), 21.25, 21.06, 20.82.

ESI MS (calcd for $C_{22}H_{28}O_{10}$: 452) *m/z*: 470 ($M+NH_4^+$, 100), 471 ($M+NH_4^+$, 26).



96

(1-*R*)-2,6-Anhydro-1-phenyl-1-*O*-[2-(trimethylsilyl)ethoxymethyl]-4-*O*-methyl-7-deoxy-7-iodo-α-D-altro-heptitol (96).[62]

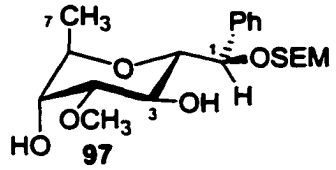
A mixture of the *C*-glycoside **93** (860 mg, 2.07 mmol), imidazole (456 mg, 6.7 mmol), triphenylphosphine (840 mg, 3.2 mmol) and iodine (863 mg, 3.4 mmol) in dry THF (35 mL) was stirred under reflux for 2 h. The solvent was removed in vacuo and the product was purified by column chromatography (EtOAc 10 to 40%, petroleum ether), to isolate the colorless oil **96** (887 mg, 1.69 mmol, 82%).

$[\alpha]^{25}_{D}$ = -52.2 (c = 1.7, $CHCl_3$).

Anal. calcd for $C_{20}H_{33}IO_6Si$: C, 45.80; H, 6.34. Found: C, 45.97; H, 6.21.

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.38 (2H, d, J = 7.3 Hz), 7.34 (2H, d, J = 7.3 Hz), 7.30 (1H, d, J = 7.3 Hz), 4.87 (1H, d, J = 7.9 Hz, H-1), 4.63 (1H, J = 6.7 Hz, SEM), 4.54 (1H, J = 6.7 Hz, SEM), 4.12 (1H, dd, J = 7.9, 4.3 Hz, H-5), 4.06 (1H, dt, J = 7.3, 2.4 Hz, H-3), 3.88 (1H, dt, J = 7.3, 4.3 Hz, H-6), 3.73-3.66 (2H, m, H-2 and SEM), 3.57 (3H, s, OCH_3), 3.48-3.41 (2H, m, H-4 and SEM), 3.39 (1H, d, J = 2.4 Hz, OH-3), 3.20 (1H, dd, J = 10.4, 6.7 Hz, H-7a), 3.07 (1H, dd, J = 10.4, 7.3 Hz, H-7b), 2.46 (1H, d, J = 4.3 Hz, OH-5), 0.90-0.77 (2H, m, SEM), -0.01 (9H, s, SEM).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 138.50, 128.41, 128.38, 128.34, 92.94 (SEM, OCH_2O), 80.69 (C-4), 79.86 (C-1), 76.60 (C-2), 75.68 (C-6), 69.55 (C-3), 67.09 (C-5), 66.22 (SEM, $O\underline{C}H_2CH_2SiMe_3$), 58.55 ($OCH_3$), 18.30 (SEM, $OCH_2\underline{C}H_2SiMe_3$), 2.92 (C-7), -1.09 (SEM, $Si(CH_3)_3$).



(1-*R*)-2,6-Anhydro-1-phenyl-1-*O*-[2-(trimethylsilyl)ethoxymethyl]-4-*O*-methyl-7-deoxy-α-D-altro-heptitol (97).[63]

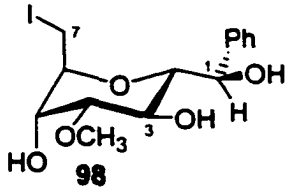
A mixture of **96** (100 mg, 0.19 mmol), tributyltin hydride (120 mg, 0.41 mmol) and AIBN (5 mg), in toluene (8 mL) was refluxed for 2 h. The solvent was removed under reduced pressure and the product **97** (60 mg, 79% yield) was isolated by column chromatography (solvent: petroleum ether, EtOAc 10 to 40%).

$[\alpha]^{25}_{D}$ = -86.0 (c = 1.5, $CHCl_3$).

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.38 (2H, d, J = 7.3 Hz), 7.32 (2H, t, J = 7.3 Hz), 7.28 (1H, t, J = 7.3Hz), 4.84 (1H, d, J = 7.3 Hz, H-1), 4.63 (1H, d, J = 6.7 Hz, SEM), 4.51 (1H, d, J = 6.7 Hz, SEM), 4.08 (1H, dq, J = 7.3, 1.8 Hz, H-6), 3.88 (1H, t, J = 8.5 Hz, H-3), 3.82 (1H, bq, J = ~3.1 Hz, H-5), 3.76-3.69 (2H, m, H-2 and SEM), 3.53 (3H, s, OCH_3), 3.48-3.42 (2H, m, H-4 and SEM), 2.43 (1H, d, J = 3.1 Hz, OH-5), 1.10 (3H, d, J = 7.3 Hz, H-7), 0.95-0.77 (2H, m, SEM), -0.01 (9H, s, SEM).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 138.92, 128.34, 128.25, 128.13, 93.01 (SEM, OCH_2O), 81.13 (C-4), 80.43 (C-1), 75.23 (C-2), 72.69 (C-6), 70.47 (C-3), 69.49 (C-5), 66.20 (SEM, $O\underline{C}H_2CH_2SiMe_3$), 58.14 ($OCH_3$), 18.42(SEM, $OCH_2\underline{C}H_2SiMe_3$), 15.48 (C-7), -1.075 (SEM, $Si(CH_3)_3$).

ESI MS (calcd for $C_{20}H_{38}O_6Si$: 398) *m/z* (rel. intensity): 416 ($M+NH_4^+$, 100), 417 ($M+NH_4^+$, 31), 819 ($2M+Na^+$, 15).



98

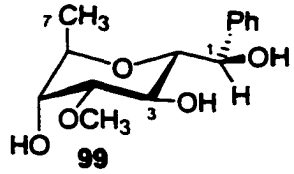
(1-*R*)-2,6-Anhydro-1-phenyl-4-*O*-methyl-7-deoxy-7-iodo-α-D-altro-heptitol (98).[62]

A mixture of the *C*-glycoside **94** (670 mg, 2.36mmol), imidazole (477 mg, 7.01 mmol), triphenylphosphine (765 mg, 2.62 mmol) and iodine (914 mg, 3.60 mmol) in dry THF (25 mL) was stirred under reflux for 2 h. The solvent was removed in vacuo and the product was purified by column chromatography (EtOAc 20 to 60%, petroleum ether), to isolate the product **98** (ca. 780 mg, 85% yield). The product resulted contaminated with triphenylphosphine oxide. Attempts to further purification were unsuccessful.

^{1}H-NMR (500 MHz, $CDCl_3$): δ Aromatic region contaminated by TPPO, 4.89 (1H, dd, J = 7.0, 3.7 Hz, H-1), 4.14 (1H, dt, J = 7.0, 3.3 Hz, H-5), 4.09-3.95 (3H, m, H-3, H-6, OH-1), 3.61 (1H, t, J = 7.7 Hz, H-2), 3.56 (1H, broad s, OH-3), 3.51 (3H, s, OCH_3), 3.38 (1H, dd, J = 7.7, 3.7 Hz, H-4), 3.23 (1H, dd, J = 10.6, 6.6 Hz, H-7a), 3.12 (1H, dd, J = 10.6, 8.1 Hz, H-7b), 2.67 (1H, d, J = 3.3 Hz, OH-5).

^{13}C-NMR (75 MHz, $CDCl_3$): δ Aromatic region contaminated by TPPO, 80.83 (C-4), 76.46 (C-6), 76.41 (C-2), 75.85 (C-1), 69.38 (C-3), 66.79 (C-5), 58.19 (OCH_3), 2.68 (C-7).

ESI MS (calcd for $C_{14}H_{19}IO_5$: 394) *m/z* (rel. intensity): 412 ($M+NH_4^+$, 100), 413 ($M+NH_4^+$, 17), 811 ($2M+Na^+$, 81), 812 ($2M+Na^+$, 25).



99

(1-*R*)-2,6-Anhydro-1-phenyl-4-*O*-methyl-7-deoxy-α-D-altro-heptitol (99).[63]

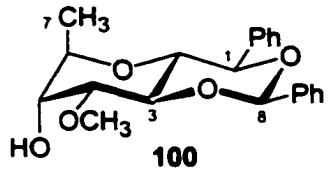
The *C*-glycoside was obtained either via radical deiodination of **98** in 75% yield (following the same procedure described for the preparation of **97**) or via deprotection of the SEM ether by treating **97** with a 2/1 solution of methylene chloride / trifluoroacetic acid (1.5 mL per 50 mg of starting material). After complete deprotection of SEM ether was detected by TLC, toluene (2 mL per mL of reaction solution) was added and the solvent was removed under reduced pressure. A second cycle of addition / evaporation of toluene afforded a pure sample of the product **99** in quantitative yield, without necessity of further purification.

$[\alpha]^{25}_{D}$ = -10.8 (c = 0.65, $CHCl_3$). m.p.: 94-96 °C.

Anal. calcd for $C_{14}H_{20}O_5$: C, 62.67; H, 7.51. Found: C, 62.71; H, 7.34.

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.42 (2H, d, J = 7.3 Hz), 7.35 (2H, t, J = 7.3 Hz), 7.29 (1H, t, J = 7.3 Hz), 4.88 (1H, d, J = 6.7 Hz, H-1), 4.15 (1H, dt, J = 7.3, 1.8 Hz, H-6), 3.94 (1H, t, J = 8.5 Hz, H-3), 3.86 (1H, dd, J = 3.1, 1.8 Hz, H-5), 3.70 (1H, dd, J = 8.5, 6.7 Hz, H-2), 3.49 (3H, s, OCH_3), 3.43 (1H, dd, J = 8.5, 3.1 Hz, H-4), 1.16 (3H, d, J = 7.3 Hz, H-7).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 141.30, 128.29, 127.86, 127.07, 81.04 (C-4), 76.26 (C-1), 74.74 (C-2), 73.02 (C-6), 70.05 (C-3), 68.94 (C-5), 57.67 (OCH_3), 15.29 (C-7).



100

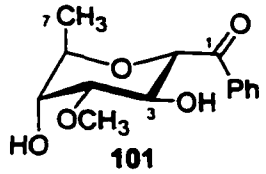
(1-*R*)-2,6-Anhydro-1-phenyl-1,3-*O*-benzylidene-4-*O*-methyl-7-deoxy-α-D-altro-heptitol (100).

A solution of *C*-glycoside **99** (14 mg, 0.05 mmol), benzaldehyde dimethyl acetale (0.08 mL) and *p*-toulensulfonic acid (1 crystal), dissolved in acetonitrile (2.5 mL) was stirred at r. t. for 2 h. Triethylamine (0.2 mL) was added and the solvent removed in vacuo. The product **100** was purified by column chromatograph (petroleum ether, EtOAc 30%).

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.57 (2H, d, J = 7.3 Hz), 7.48 (2H, d, J = 7.3 Hz), 7.39-7.28 (6H, m), 5.85 (1H, s, H-8), 4.79 (1H, d, J = 8.5 Hz, H-1), 4.26-4.21 (2H, m, H-3 and H-6), 3.96 (1H, bd, J = 3.1 Hz, H-5), 3.68 (1H, dd, J = 9.3, 3.1 Hz, H-4), 3.63-3.58 (4H, m, H-2 and OCH_3), 2.75 (1H, s, OH), 1.15 (2H, d, J = 7.3 Hz, H-7).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 138.36, 137.81, 128.99, 128.30, 127.42, 126.43, 101.62 (C-8), 81.34 (C-1), 79.38 (C-3 or C-6), 77.75 (C-4), 74.14 (C-3 or C-6), 71.36 (C-5), 70.08 (C-2), 59.04 (OCH_3), 15.41 (C-7).

ESI MS (calcd for $C_{22}H_{28}O_5$: 356) *m/z* (rel. intensity): 379 ($M+Na^+$, 100), 380 ($M+Na^+$, 21), 735 ($2M+Na^+$, 62), 726 ($2M+Na^+$, 29).



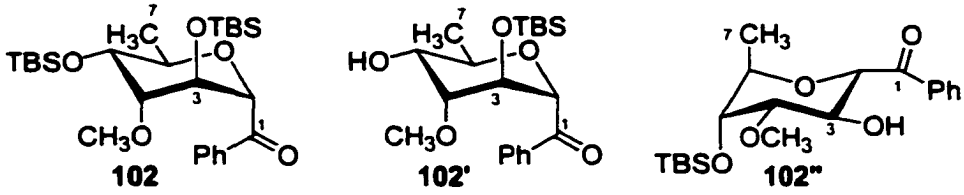
101

2,6-Anhydro-1-phenyl-1-keto-4-*O*-methyl-7-deoxy-α-D-altro-heptitol (101).

DDQ was added (250 mg, 1.1 mmol) to the *C*-glycoside **99** (250 mg, 0.93 mmol) dissolved in methylene chloride (16 mL) and the mixture was stirred for 8 h under gentle reflux. Additional DDQ (200 mg 0.88 mmol) was added and the mixture was stirred at r. t. overnight. The solvent was removed under reduced pressure and the product was purified by column chromatography on alumina (activated basic, Brokmann I, solvent: methanol 0 to 10%, EtOAc). The ketone **101** (190 mg, 0.71 mmol) was isolated in 77% yield.

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.97 (2H, d, J = 7.3 Hz), 7.57 (2H, t, J = 7.3 Hz), 7.46 (1H, t, J = 7.3 Hz), 4.71 (1H, d, J = 6.7 Hz, H-2), 4.56 (1H, bq, J = 5-7 Hz, H-3), 4.15 (1H, q, J = 6.7 Hz, H-6), 3.81 (1H, bq, J = 5.0-3.6 Hz, H-5), 3.56 (1H, dd, J = 7.3, 3.7 Hz, H-4), 3.45(3H, s, OCH_3), 2.72 (1H, d, J = 4.9 Hz, OH-3), 2.44 (1H, d, J =5.5 Hz, OH-5), 1.40 (3H, d, J = 6.7 Hz, H-7).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 197.90 (C-1), 136.04, 133.36, 129.13, 128.55, 79.96 (C-4), 77.17 (C-2), 72.68 (C-6), 69.34 (C-5), 68.03 (C-3), 58.32, 16.15 (C-7).



2,6-Anhydro-1-phenyl-1-keto-3,5-bis-*O*-*tert*-butyldimethylsilyl-4-*O*-methyl-7-deoxy-α-D-altro-heptitol (102).

2,6-Anhydro-1-phenyl-1-keto-3-*O*-*tert*-butyldimethylsilyl-4-*O*-methyl-7-deoxy-α-D-altro-heptitol (102').

2,6-Anhydro-1-phenyl-1-keto-4-*O*-methyl-5-*O*-*tert*-butyldimethylsilyl-7-deoxy-α-D-altro-heptitol (102").

A mixture of the *C*-glycoside **101** (54 mg, 0.21 mmol), imidazole (48 mg, 0.7 mmol) and TBDMSCl (105 mg, 0.7 mmol) in dry DMF (2.5 mL) was stirred at r. t. under nitrogen overnight (12 h). Water (8 mL) was added and the mixture was extracted with EtOAc (3 x 8 mL). The organic layer was dried over sodium sulfate and the solvent was removed in vacuo. Column chromatography (petroleum ether, EtOAc 5%) afforded the product **102** (oil, 97 mg, 93% yield), along with traces (ca. 6 mg) of **102'** and **102"**.

102:

$[\alpha]^{25}_{D} = 48.9$ (c = 0.9, $CHCl_3$).

Anal. calcd for $C_{26}H_{48}O_5Si_2$: C, 63.11; H, 9.37. Found: C, 63.11; H, 9.39.

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.93 (2H, d, J = 7.3 Hz), 7.51 (1H, t, J = 7.3 Hz), 7.42 (2H, t, J = 7.3 Hz), 4.74 (1H, dd, J = 4.9, 3.0 Hz, H-3), 4.61 (1H, d, J = 2.4 Hz, H-2), 3.91 (1H, quintet, J = 6.1 Hz, H-6), 3.82 (1H, dd, J = 7.9, 2.4 Hz, H-5), 3.28 (4H, s, OCH_3 and H-4), 1.17 (3H, d, J = 6.1 Hz, H-7), 0.92 (9H, s), 0.82 (9H, s), 0.11 (3H, s), 0.10 (3H, s), 0.09 (3H, s), 0.07 (3H, s).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 199.33, 137.21, 132.42, 128.67, 128.24, 82.02 (C-2), 81.88 (C-4), 71.10 (C-5), 70.10 (C-6), 69.59 (C-3), 58.29(OCH_3), 26.10, 25.96, 18.43, 18.34, 17.87, -3.22, -3.99, -4.34, -4.39, -4.50.

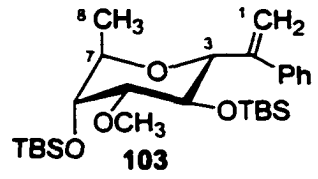
ESI MS (calcd for $C_{26}H_{46}O_5Si_2$: 494) *m/z* (rel. intensity): 495 ($M+H^+$, 20), 512 ($M+NH_4^+$, 100), 513 ($M+NH_4^+$, 40).

102':

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.94 (2H, d, J = 7.3 Hz), 7.55 (2H, t, J = 7.3 Hz), 7.44 (1H, t, J = 7.3 Hz), 4.79 (1H, dd, J = 4.3, 3.1 Hz, H-3), 4.68 (1H, d, J = 3.1 Hz, H-2), 3.68 (1H, dq, J = 8.5, 6.1 Hz, H-6), 3.64 (1H, dt, J = 8.5, 3.1 Hz, H-5), 3.39 (1H, dd, J = 4.3, 3.1 Hz, H-4), 3.31, (3H, s, OCH_3), 2.11 (1H, d, J = 9.2 Hz, OH), 1.23 (3H, d, J = 6.1 Hz, H-7), 0.90 (9H, s), 0.13 (3H, s), 0.11 (3H, s).

102":

^{1}H-NMR (500 MHz, $CDCl_3$): δ 8.03 (2H, d, J = 7.9 Hz), 7.55 (1H, t, J = 7.9 Hz), 7.44 (2H, t, J = 7.9 Hz), 4.64 (1H, d, J = 6.4 Hz, H-2), 4.56 (1H, m, H-3), 4.14 (1H, dt, J = 6.7, 4.9 Hz, H-6), 3.85 (1H, dd, 4.9, 3.0 Hz, H-5), 3.42 (1H, dd, J = 7.3, 2.4 Hz, H-4), 3.38 (3H, s, OCH_3), 2.41 (1H, d, J = 3.7 Hz, OH-3), 1.32 (3H, d, J = 6.7 Hz, H-7), 0.91 (9H, s), 0.10 (3H, s), 0.08 (3H, s).



103

3,7-Anhydro-1,2,8-trideoxy-2-phenyl-4,6-bis-*O*-*tert*-butyldimethylsilyl-5-*O*-methyl-α-D-altro-oct-1-enitol (103).[68]

To a slurry of Nysted reagent (20 wt. % suspension in THF, 320 mg, 0.7 mmol) and ketone **103** (74 mg, 0.15 mmol) in dry THF (2 mL) at –78 °C under N_2 was added dropwise a solution of $TiCl_4$ (1M in CH_2Cl_2, 0.6 mL). The mixture turned yellow and was warmed at r. t. and stirred overnight (14 h). The resulting black slurry was then cooled in a ice bath and triethylamine (0.5 mL) was added, followed by silica gel. The mixture was warmed at r. t. and was filtered through a plug of silica gel using ethyl acetate as a wash. The filtrate was concentrated in vacuo and the product **103** (oil, 54 mg, 0.11 mmol, 73%) and the side product **105** (16 mg, 0.03 mmol, 21%) were isolated by column chromatography (SiO_2, EtOAc 5%, petroleum ether).

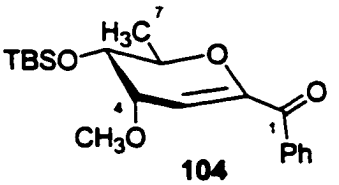
$[\alpha]^{25}_D$ = +3.6 (c = 0.83, $CHCl_3$).

Anal. calcd for $C_{27}H_{48}O_4Si_2$: C, 65.80; H, 9.82. Found: C, 65.52; H, 9.79.

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.58 (2H, d, J = 7.3 Hz), 7.29 (2H, t, J = 7.3 Hz), 7.24 (1H, t, J = 7.3 Hz), 5.48 (1H, s, H-1a), 5.37 (1H, s, H-1b), 4.40 (1H, d, J = 7.0 Hz, H-3), 4.17 (1H, dq, J = 6.7, 4.3 Hz, H-7), 4.10 (1H, t, J = 7.0 Hz, H-4), 3.92 (1H, dd, J = 4.3, 3.0 Hz, H-6), 3.25 (3H, s, OCH_3), 3.19 (1H, dd, J = 7.0, 3.0 Hz, H-5), 1.30 (3H, d, J = 6.7 Hz, H-8), 0.94 (9H, s), 0.81 (9H, s), 0.10 (3H, s), 0.09 (3H, s), -0.08 (3H, s), -0.24 (3H, s).

^{13}C-NMR (100 MHz, $CDCl_3$): δ 146.11, 139.63, 128.16, 127.61, 127.51, 116.80 (C-1), 82.68 (C-5), 79.29 (C-3), 72.40 (C-7), 70.83 (C-6), 69.84 (C-4), 57.62(OCH_3), 26.17, 26.01, 18.40, 18.36, 16.17, -4.18, -4.31, -4.63, -4.86.

ESI MS (calcd for $C_{27}H_{48}O_4Si_2$: 492) *m/z* (rel. intensity): 493 ($M+H^+$, 55), 494 ($M+H^+$, 23), 510 ($M+NH_4^+$, 100), 511 ($M+NH_4^+$, 44).



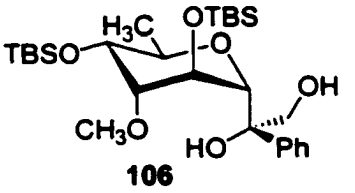
104

2,6-Anhydro-1-phenyl-1-keto-3,7-dideoxy-4-*O*-methyl-5-*O*-*tert*-butyldimethylsilyl-D-altro-hept-2-enitol (104).

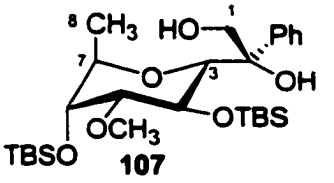
To a solution of methyltriphenylphosphonium bromide (50 mg, 0.14 mmol) in dry THF (2.5 mL) was added *n*-BuLi (1.6 M in hexanes, 0.08 mL) at –10 °C under nitrogen. The yellow mixture was stirred at –10 °C for ca. 1 h and then the *C*-glucoside **102** (20 mg, 0.41 mmol, in 2.5 mL dry THF) was added dropwise. The mixture was stirred at –10 °C for 1 h and at r. t. for 2 h. A saturated solution of NH_4Cl (8 mL) was added and an extraction with EtOAc (3 x 8 mL) was performed. The organic layer was dried and the solvent removed under reduced pressure. The product consisted of a mixture of starting material **102**, the glycal **104** and the two inseparable anomers α- and β- **103** in a ratio 1/1/1/1. The glycal **104** was isolated by column chromatography (petroleum ether, EtOAc 5%).

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.85 (2H, d, J = 7.3 Hz), 7.55 (1H, t, J = 7.3 Hz), 7.44 (2H, t, J = 7.3 Hz), 5.84 (1H, d, J = 5.5 Hz, H-3), 4.29 (1H, dq, J = 9.2, 6.7 Hz, H-6), 3.77 (1H, dd, J = 5.5, 3.7 Hz, H-4), 3.73 (1H, dd, J = 9.2, 4.3 Hz, H-5), 3.48 (3H, s, OCH_3), 1.41 (3H, d, J = 6.7 Hz, H-7), 0.95 (9H, s), 0.142 (3H, s), 0.138 (3H, s).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 204.47, 152.11, 136.68, 132.79, 129.89, 128.25, 107.79, 72.98, 72.49, 57.70, 26.14, 18.53, 18.03, -3.79, -4.37, -3.79, -4.37.



106



107

(2-*S*)-3,7-Anhydro-2-phenyl-4,6-bis-*O*-*tert*-butyldimethylsilyl-5-*O*-methyl-8-deoxy-α-D-altro-octitol (106).

(2-*R*)-3,7-Anhydro-2-phenyl-4,6-bis-*O*-*tert*-butyldimethylsilyl-5-*O*-methyl-8-deoxy-α-D-altro-octitol (107).[47]

To a solution of **103** (105 mg, 0.21 mmol) in acetone (8 mL) at 0 °C (ice bath) was added 4-methylmorpholine-*N*-oxide (50 wt. % in H_2O, 0.15 mL) and osmium tetroxide (2.5 wt. % in *t*-BuOH, 0.2 mL). The mixture was stirred at 0 °C for 6 h and then at r. t. overnight (14 h). Sodium sulfite (ca. 10 mg) was added and the mixture stirred for 1 h. Ethyl acetate was added (20 mL) and the mixture was dried over sodium sulfate. The mixture was filtered and the filtrate was concentrated under reduced pressure. The two diastereomers **106** (72 mg, 0.14mmol, 66%) and **107** (18 mg, 0.034 mmol, 16%) were isolated by column chromatography (SiO_2, EtOAc 10 %, petroleum ether).

106:

R_f: 0.24 (PE/EtOAc: 8/2).

$[\alpha]^{25}_D$ = +27.0 (c = 0.8, $CHCl_3$). m.p.: 69-71 °C.

Anal. calcd for $C_{27}H_{50}O_6Si_2$: C, 61.55; H, 9.57. Found: C, 61.30; H, 9.52.

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.46 (2H, d, J = 7.3 Hz), 7.37 (2H, t, J = 7.3 Hz), 7.26 (1H, t, J = 7.3 Hz), 5.76 (1H, s, OH-2), 4.42 (1H, dq, J = 9.2, 6.1 Hz, H-7), 4.09 (1H, dd, partially covered by s at 4.08 ppm, J = 4.3 Hz, H-1a), 4.08 (1H, s, H-3), 3.87 (1H, dd, J = 11.0, 8.5 Hz, H-1b), 3.75 (1H, dd, J = 9.2, 3.1 Hz, H-6), 3.67 (1H, d, J = 3.7 Hz, H-4), 3.56 (3H, s, OCH_3), 3.26 (1H, t, J = 3.1 Hz, H-5), 2.39 (1H, dd, J = 8.5, 4.9 Hz, OH-1), 1.23 (3H, d, J = 6.1 Hz, H-8), 0.91 (9H, s), 0.80 (9H, s), 0.10 (3H, s), 0.08 (3H, s), -0.25 (3H, s), -0.28 (3H, s).

^{13}C-NMR (100 MHz, $CDCl_3$): δ 143.67, 128.73, 127.38, 125.79, 83.69 (C-3), 81.93 (C-5), 79.02 (C-2), 71.53 (C-6), 70.13 (C-1), 68.96 (C-7), 68.54 (C-4), 60.20 (OCH_3), 25.99, 25.81, 19.10, 18.19, 17.91, -3.84, -4.57, -4.91, -5.10.

ESI MS (calcd for $C_{27}H_{50}O_6Si_2$: 526) *m/z*: 527 ($M+H^+$, 100), 528 ($M+H^+$, 42).

107:

R_f: 0.3 (PE/EtOAc: 8/2).

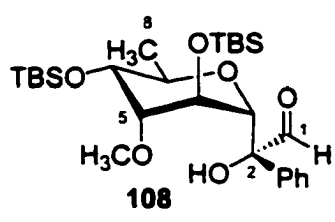
$[\alpha]^{25}_D$ = -37.9 (c = 0.8, $CHCl_3$).

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.76 (2H, d, J = 7.3 Hz), 7.28 (2H, t, J = 7.3 Hz), 7.23 (1H, t, J = 7.3 Hz), 4.68 (1H, s, OH-2), 4.17 (1H, t, J = 9.2 Hz, H-4), 4.13 (1H, dq, J = 7.3, 2.4 Hz, H-7), 3.97 (1H, d, J = 9.2 Hz, H-3), 3.94 (1H, t, J = 2.4 Hz, H-6), 3.85 (1H, broad t, J = 11 Hz, H-1a), 3.48 (1H, dd, J = 11.0, 3.7 Hz, H-1b), 3.26 (1H, dd, partially covered by s at 3.25 ppm, J = 2.4 Hz, H-5), 3.25 (3H, s, OCH_3), 2.30 (1H, dd, J = 9.8,

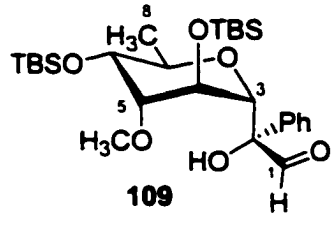
3.7 Hz, OH-1), 1.29 (3H, d, J = 7.3 Hz, H-8), 0.90 (9H, s), 0.82 (9H, s), 0.09 (3H, s), 0.04 (3H, s), –0.02 (3H, s), -0.21 (3H, s).

^{13}C-NMR (100 MHz, $CDCl_3$): δ 141.99, 127.83, 127.33, 127.28, 81.83 (C-5), 78.76 (C-2), 75.16 (C-3), 74.69 (C-7), 70.96 (C-4), 69.78 (C-6), 69.47 (C-1), 56.00 (OCH_3), 26.54, 25.86, 18.70, 18.25, 15.05, -3.38, -4.46, -4.57, -4.64.

ESI MS (calcd for $C_{27}H_{50}O_6Si_2$: 526) *m/z*: 527 ($M+H^+$, 100), 528 ($M+H^+$, 42).



108



109

(2-*R*)-3,7-Anhydro-2-phenyl-4,6-bis-*O*-*tert*-butyldimethylsilyl-5-*O*-methyl-8-deoxy-α-D-altro-octital (108).

(2-*S*)-3,7-Anhydro-2-phenyl-4,6-bis-*O*-*tert*-butyldimethylsilyl-5-*O*-methyl-8-deoxy-α-D-altro-octital (109).[71]

A mixture of the alcohol **106** or **107** (1 equiv.), freshly prepared polymer-bound bromite(I) (6 equiv.) and a catalytic amount of TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy, free radical) in dry methylene chloride (60 mL / mmol of alcohol) was stirred at r. t. until completion of the reaction (monitored by TLC, normally less then 2 h). The mixture was filtered, the resin was washed with methylene chloride and the combined filtrate and organic washings were concentrated in vacuo to yield the relative aldehydes (quantitative yield). Further purification was unnecessary and the products were directly subjected to the next step.

108:

$[\alpha]^{25}_{D}$ = +14.6 (c = 0.7, $CHCl_3$).

^{1}H-NMR (500 MHz, $CDCl_3$): δ 9.69 (1H, s, H-1), 7.54 (2H, t, J = 7.5 Hz), 7.38 (2H, t, J = 7.5 Hz), 7.29 (1H, t, J = 7.5 Hz), 6.03 (1H, s, OH), 4.50 (1H, s, H-3), 4.37 (1H, dq, J = 9.6, 6.2 Hz, H-7), 3.74 (1H, dd, J = 9.6, 2.7 Hz, H-6), 3.66 (1H, d, J = 3.4 Hz, H-4), 3.57 (3H, s, OCH_3), 3.27 (1H, t, J = 3.4 Hz, H-5), 1.19 (3H, d, J = 6.2 Hz, H-8), 0.91 (9H, s), 0.81 (9H, s), 0.09 (3H, s), 0.08 (3H, s), -0.22 (3H, s), -0.26 (3H, s).

^{13}C-NMR (100 MHz, $CDCl_3$): δ 201.29 (C-1), 138.29, 128.87, 128.10, 126.04, 84.59 (C-2), 82.62 (C-3), 81.84 (C-5), 71.52 (C-6), 69.49 (C-7), 67.93 (C-4), 60.23 (OCH_3), 25.97, 25.79, 19.00, 18.17, 17.90, -3.87, -4.61, -4.93, -5.04.

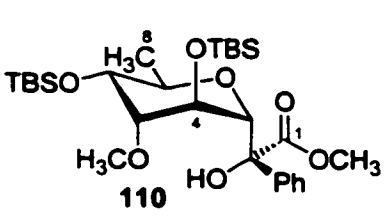
ESI MS (calcd for $C_{27}H_{48}O_6Si_2$: 524) *m/z* (rel. intensity): 525 ($M+H^+$, 92), 526 ($M+H^+$, 36), 542 ($2M+NH_4^+$, 100), 543 ($2M+NH_4^+$, 34).

109:

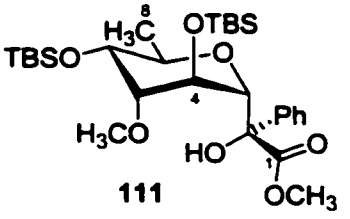
$[\alpha]^{25}_{D}$ = +37.6 (c = 0.85, $CHCl_3$).

^{1}H-NMR (500 MHz, $CDCl_3$): δ 9.53 (1H, s, H-1), 7.57 (2H, d, J = 7.5 Hz), 7.37 (2H, t, J = 7.5 Hz), 7.29 (1H, t, J = 7.5 Hz), 4.34 (1H, d, J = 2.7 Hz, H-3), 4.14 (1H, quintet, J = 6.8 Hz, H-7), 4.08 (1H, t, J = 3.8 Hz, H-4), 3.79 (1H, dd, J = 7.5, 2.7 Hz, H-6), 3.56 (3H, s, OCH_3), 3.38 (1H, dd, J = 4.8, 2.7 Hz, H-5), 1.00 (3H, d, J = 6.8 Hz, H-8), 0.91 (9H, s), 0.90 (9H, s), 0.13 (3H, s), 0.10 (3H, s), 0.09 (3H, s), 0.07 (3H, s).

^{13}C-NMR (100 MHz, $CDCl_3$): δ 201.05 (C-1), 137.07, 128.57, 127.91, 126.58, 83.92 (C-2), 82.22 (C-5), 80.99 (C-3), 71.42 (C-6), 70.31 (C-7), 70.17 (C-4), 59.50 (OCH_3), 26.09, 25.99, 18.23, 18.21, 17.69, -4.00, -4.30, -4.54, -4.60.



110



111

(2-*R*)-Methyl-3,7-anhydro-2-phenyl-4,6-bis-*O*-*tert*-butyldimethylsilyl-5-*O*-methyl-8-deoxy-α-D-altro-octitolate (110).

(2-*S*)-Methyl-3,7-anhydro-2-phenyl-4,6-bis-*O*-*tert*-butyldimethylsilyl-5-*O*-methyl-8-deoxy-α-D-altro-octitolate (111).[72]

The aldehyde **108** or **109** was dissolved in MeOH (35 mL / mmol of aldehyde) and cooled at 0 °C (ice bath). Iodine (3 equiv.) was added, followed by dropwise addition of a KOH solution in methanol (1.2 M 8 equiv.). The mixture was stirred at low temperature for 15 min and then from 0 °C to r. t. for 30 min. The reaction was quenched by addition of solid ammonium chloride and the solvent removed under reduced pressure. An extraction with EtOAc / sat. NH_4Cl yielded the product **110** or **111** in >95% purity, which can be directly employed in the next step. Otherwise analytically pure sample could be obtained via column chromatography (EtOAc 5%, petroleum ether).

110:

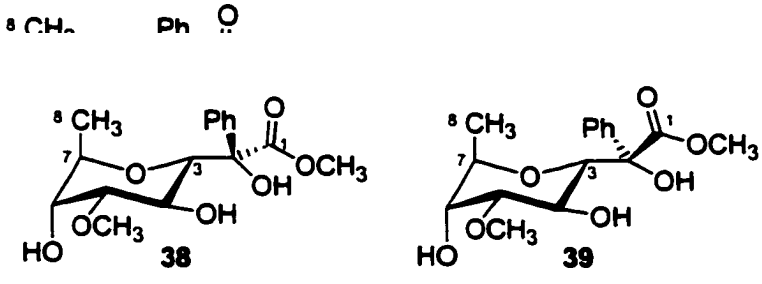
^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.71 (2H, d, J = 7.6 Hz), 7.36 (2H, t, J = 7.6 Hz), 7.29 (1H, t, J = 7.6 Hz), 5.80 (1H, s, OH), 4.60 (1H, broad s, H-3), 4.37 (1H, dq, J = 8.9, 6.3 Hz, H-7), 3.77 (3H, s, CO_2CH_3), 3.76 (1H, dd, partially covered by s at 3.77 ppm, J = 2.6 Hz, H-6), 3.69 (1H, dd, J = 3.2, 1.3 Hz, H-4), 3.55 (3H, s, OCH_3), 3.26 (1H, t, J = 3.2 Hz, H-5), 1.21 (3H, d, J = 6.3 Hz, H-8), 0.90 (9H, s), 0.80 (9H, s), 0.09 (3H, s), 0.07 (3H, s), -0.22 (3H, s), -0.34 (3H, s).

^{13}C-NMR (100 MHz, $CDCl_3$): δ 173.09 (C-1), 139.83, 128.62, 128.12, 126.26, 83.21 (C-3), 82.55 (C-2), 82.09 (C-5), 71.85 (C-6), 69.82 (C-7), 67.93 (C-4), 60.20 (OCH_3), 53.02 (CO_2CH_3), 25.97, 25.86, 18.84, 18.16, 17.91, -3.81, -4.64, -4.89, -5.07.

ESI MS (calcd for $C_{28}H_{50}O_7Si_2$: 554) *m/z*: 555 ($M+H^+$, 100), 556 ($M+H^+$, 43).

111:

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.68 (2H, d, J = 7.6 Hz), 7.34 (2H, t, J = 7.6 Hz), 7.26 (1H, covered by $CHCl_3$ at 7.26 ppm), 6.05 (1H, broad s, OH), 4.49 (1H, s, H-3), 4.32 (1H, dq, J = 8.9, 6.3 Hz, H-7), 4.07 (1H, d, J = 3.2 Hz, H-4), 3.76 (1H, dd, J = 8.9, 3.2 Hz, H-6), 3.73 (3H, s, CO_2CH_3), 3.62 (3H, s, OCH_3), 3.41 (1H, t, J = 3.2 Hz, H-5), 0.99, (3H, d, J = 6.3 Hz, H-8), 0.92 (9H, s), 0.91 (9H, s), 0.16 (3H, s), 0.12 (3H, s), 0.09 (3H, s), 0.07 (3H, s).



(2-*R*)-Methyl-3,7-anhydro-2-phenyl-5-*O*-methyl-8-deoxy-α-D-altro-octitolate (38).

(2-*S*)-Methyl-3,7-anhydro-2-phenyl-5-*O*-methyl-8-deoxy-α-D-altro-octitolate (39).

To a solution of *C*-glycoside **110** or **111** dissolved in THF (1 mL per 0.01 mmol of starting material) in the presence of AcOH (0.5 equiv) was added tetrabutylammonium fluoride (1 M in THF, ca. 3 equiv) and the mixture was stirred at r. t. for ca. 6 h. The solvent was removed in vacuo and the product **38** or **39** was purified by column

chromatography (petroleum ether, EtOAc 50%). The yield was typically > 93%. In one occasion traces of the partially deprotected **110'** were isolated.

38:

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.81 (2H, d, J = 7.0 Hz), 7.39 (2H, t, J = 7.0 Hz), 7.32 (1H, t, J = 7.0 Hz), 4.37 (1H, d, J = 9.2 Hz, H-3), 4.27 (1H, dq, J = 7.0, 1.3 Hz, H-7), 4.13 (1H, t, J = 9.1 Hz, H-4), 3.89 (1H, dd, J = 3.2, 1.9 Hz, H-6), 3.80 (3H, s, CO_2CH_3), 3.44 (3H, OCH_3), 3.38 (1H, dd, J = 8.9, 3.2 Hz, H-5), 1.32 (3H, d, J = 7.0 Hz, H-8).

^{13}C-NMR (100 MHz, $CDCl_3$): δ 173.68 (C-1), 137.51, 128.71, 128.62, 126.11, 80.84 (C-5), 79.96 (C-2), 77.05 (C-3), 73.48 (C-7), 69.16 (C-6), 67.39 (C-4), 58.12 (OCH_3), 53.40 (CO_2CH_3), 15.14 (C-8).

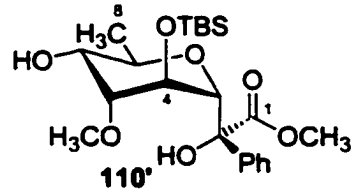
ESI MS (calcd for $C_{16}H_{22}O_7$: 326) *m/z* (rel. intensity): 349 ($M+Na^+$, 100), 350 ($M+Na^+$, 19), 675 ($2M+Na^+$, 38), 676 ($2M+Na^+$, 15).

39:

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.61 (2H, d, J = 7.6 Hz), 7.31 (2H, t, J = 7.6 Hz), 7.24 (1H, t, J = 7.6 Hz), 4.47 (1H, d, J = 9.5 Hz, H-3), 4.27 (1H, t, J = 9.5 Hz, H-4), 3.85 (2H, broad s, H-6 and H-7), 3.69 (3H, s, CO_2CH_3), 3.59 (3H, s, OCH_3), 3.48 (1H, dd, J = 9.5, 3.1 Hz, H-5), 1.12 (3H, d, J = 5.7 Hz, H-8).

^{13}C-NMR (100 MHz, $CDCl_3$): δ 173.27 (C-1), 140.68, 128.04, 127.61, 126.35, 81.61 (C-5), 78.56 (C-2), 75.59 (C-3), 73.43 (C-7), 69.85 (C-6), 67.09 (C-4), 58.10 (OCH_3), 53.16 (CO_2CH_3), 14.54 (C-8).

ESI MS (calcd for $C_{16}H_{22}O_7$: 326) *m/z* (rel. intensity): 349 ($M+Na^+$, 100), 350 ($M+Na^+$, 19), 675 ($2M+Na^+$, 38), 676 ($2M+Na^+$, 14).



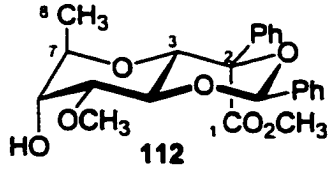
110'

(2-*R*)-Methyl-3,7-anhydro-2-phenyl-4-*O*-*tert*-butyldimethylsilyl-5-*O*-methyl-8-deoxy-*α*-D-altro-octitolate (110').

The C-glycoside **110'** was isolated in traces as partially deprotected byproduct of the desilylation of **110**.

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.70 (2H, d, J = 7.0 Hz), 7.36 (2H, t, J = 7.0 Hz), 7.30 (1H, t, J = 7.0 Hz), 5.08 (1H, s, OH-2), 4.61 (1H, d, J = 3.2 Hz, H-3), 4.24 (1H, quintet, J = 6.4 Hz, H-7), 3.87 (1H, t, J = 3.8 Hz, H-4), 3.76 (3H, s, CO_2CH_3), 3.66 (1H, broad s, H-6), 3.47 (3H, s, OCH_3), 3.36 (1H, t, J = 3.8 Hz, H-5), 2.15 (1H, broad s, OH-6), 1.30 (3H, d, J = 6.4 Hz, H-8), 0.76 (9H, s), -0.20 (3H, s), -0.36 (3H, s).

^{13}C-NMR (100 MHz, $CDCl_3$): δ 173.33 (C-1), 139.38, 128.59, 128.22, 126.37, 82.11 (C-2), 81.78 (C-5), 81.41 (C-3), 71.16 (C-7), 69.55 (C-6), 66.21 (C-4), 58.64 (OCH_3), 53.20 (CO_2CH_3), 46.99, 25.95, 18.06, 17.99, -4.74, -4.75.



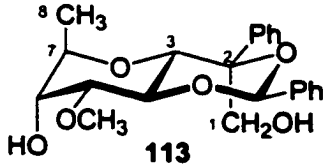
112

(2-*R*)-Methyl-3,7-anhydro-2-phenyl-2,4-*O*-benzylidene-5-*O*-methyl-8-deoxy-*α*-D-altro-octitolate (112).

A solution of *C*-glycoside **38** (5 mg, 0.015 mmol), benzaldehyde dimethyl acetale (0.07 mL) and *p*-toulensulfonic acid (1 crystal), dissolved in acetonitrile (1.5 mL) was stirred at r. t. for 3 h. Acidic resin (DOWEX 50X8-400. Ion-exchange resin. Strong acidic. Ca. 10 mg) was added and the mixture was filtered. The solvent was removed in vacuo.

^{1}H-NMR (500 MHz, C_6D_6): δ 8.02 (2H, d, J = 7.6 Hz), 7.77 (2H, d, J = 7.6 Hz), 7.24-7.09 (6H, m), 6.54 (1H, s, H-9), 4.81 (1H, t, J = 9.5 Hz, H-4), 4.30 (1H, dq, J = 7, 1.3 Hz, H-7), 3.85 (1H, d, J = 10.2 Hz, H-3), 3.54 (1H, dd, J = 3.2, 1.3 Hz, H-6), 3.28-3.25 (7H, m, H-5, OCH_3 and CO_2CH_3), 0.68 (3H, d, J = 7.0 Hz, H-8).

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.66 (2H, d, J = 8.3 Hz), 7.60 (2H, d, J = 8.3 Hz), 7.43-7.29 (6H, m), 6.13 (1H, s, H-9), 4.57 (1H, t, J = 9.5 Hz, H-4), 4.39 (1H, q, J = 8.3 Hz, H-7), 3.94 (1H, broad s, H-6), 3.78-3.75 (4H, m, H-3 and CO_2CH_3), 3.58-3.55 (4H, m, H-5 and OCH_3), 1.17 (3H, d, J = 7 Hz, H-8).



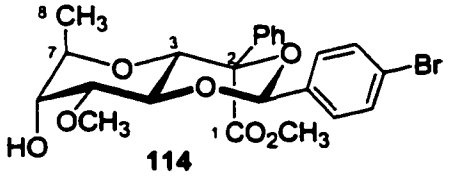
113

(2-*S*)-Methyl-3,7-anhydro-2-phenyl-2,4-*O*-benzylidene-5-*O*-methyl-8-deoxy-α-D-altro-octitol (113).

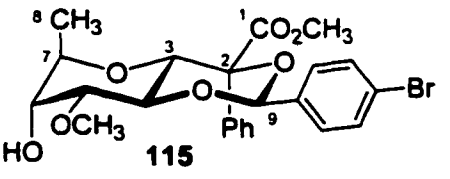
To a solution of **112** (5 mg, 0.012 mmol), in CH_2Cl_2 (1.5 mL) was added DIBAL-H (1 M in hexanes, 28 μL) at –78 °C under nitrogen. The mixture was stirred at –78 °C for 1.5 h and then at r. t. for 1.5 h. EtOAc (0.2 mL) was added and the mixture was stirred for 30

min. The solvent was removed under reduced pressure and the product was purified by column chromatography (petroleum ether, EtOAc 50%).

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.74 (2H, d, J = 7.6 Hz), 7.62 (2H, d, J = 7 Hz), 7.44-7.34 (5H, m), 7.29 (1H, t, J = 7 Hz), 6.22 (1H, s, H-9), 4.56 (1H, dd, J = 12.7, 5.7 Hz, H-1a), 4.48 (1H, t, J = 10 Hz, H-4), 4.35 (1H, t, J = 7.6 Hz, H-7), 4.31 (1H, dd, J = 12.7, 7.0 Hz, H-1b), 3.93 (1H, d, J = 3.2 Hz, H-6), 3.76 (1H, d, J = 10 Hz, H-3), 3.56 (1H, s, OCH_3), 3.52 (1H, dd, J = 9.5, 3.2 Hz, H-5), 1.69 (1H, t, J = 7 Hz, OH-1), 1.16 (3H, d, J = 7.6 Hz, H-8).



114



115

(2-*R*)-Methyl-3,7-anhydro-2-phenyl-2,4-*O*-(4-bromobenzylidene)-5-*O*-methyl-8-deoxy-*α*-D-altro-octitolate (114).

(2-*S*)-Methyl-3,7-anhydro-2-phenyl-2,4-*O*-(4-bromobenzylidene)-5-*O*-methyl-8-deoxy-*α*-D-altro-octitolate (115).

A solution of *C*-glycoside **38** or **39** (5 mg, 0.015 mmol), *p*-bromobenzaldehyde dimethyl acetale (8 μL) and *p*-toulensulfonic acid (1 crystal), dissolved in acetonitrile (1.5 mL) was stirred at r. t. for 2 h. Triethylamine (0.2 mL) was added and the solvent removed in vacuo. The product **114** or **115** (quantitative yield) was purified by column chromatography (petroleum ether, EtOAc 40%).

114:

^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.63 (2H, dd, J = 8.3, 1.9Hz), 7.53 (2H, d, J = 8.3 Hz), 7.47 (2H, d, J = 8.3 Hz), 7.37-7.31 (3H, m), 6.12 (1H, s, H-9), 4.53 (1H, t, J = 9.5 Hz, H-4), 4.40 (1H, q, J = 7.0 Hz, H-7), 3.94 (1H, broad s, H-6), 3.78 (3H, s, CO_2CH_3), 3.77 (1H, d, H-3, partially overlapped with s at 3.78 ppm), 3.56 (3H, s, OCH_3), 3.55 (1H, dd, J = 3.2 Hz, H-5, partially overlapped with s at 3.56 ppm), 2.62 (1H, d, J = 2.5 Hz, OH), 1.19 (3H, d, J = 7.0 Hz, H-8).

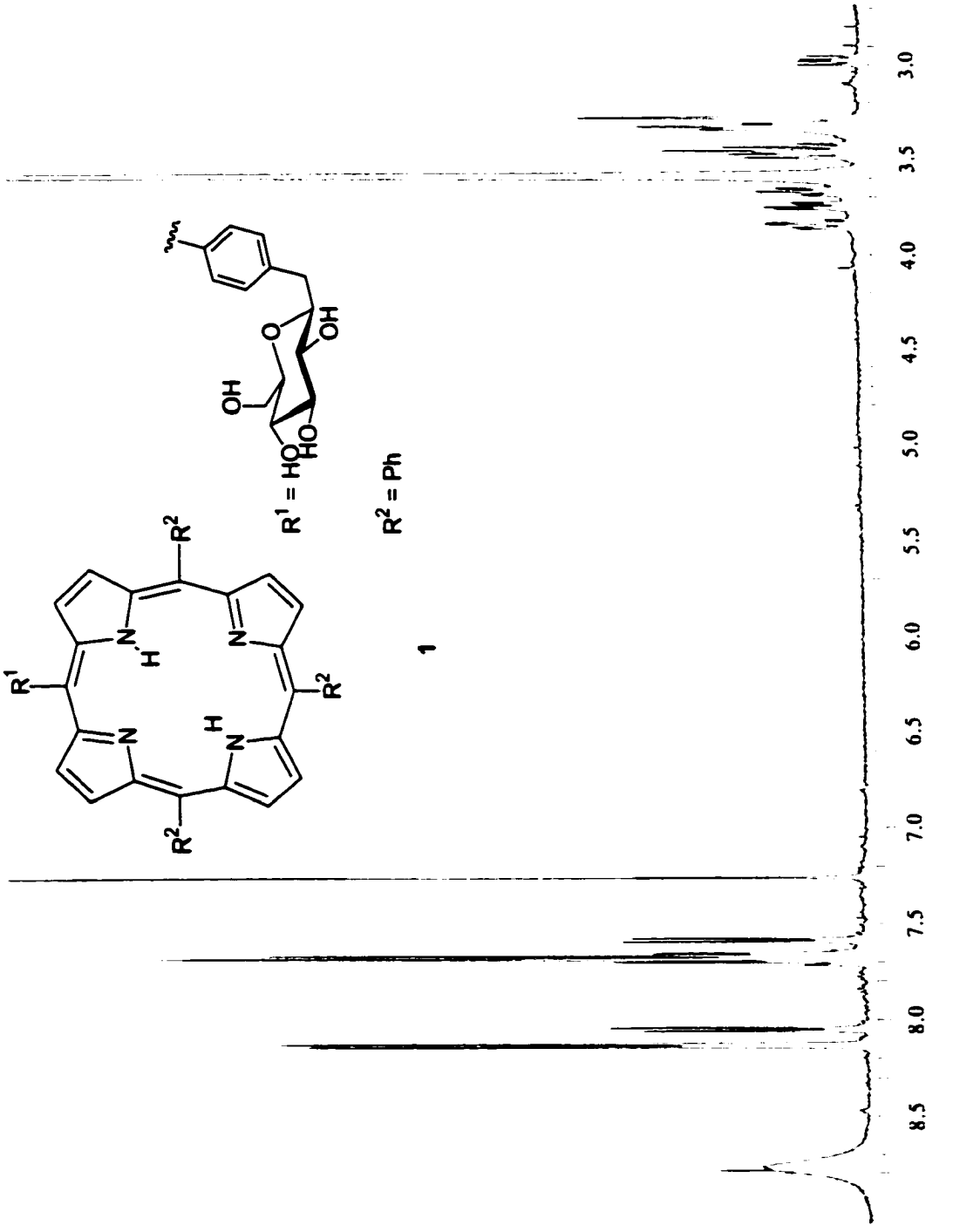
^{13}C-NMR (100 MHz, $CDCl_3$): δ 170.28 (C-1), 139.19, 136.72, 131.63, 128.46, 128.34, 128.22, 125.95, 97.86 (C-9), 81.38 (C-2), 78.12 (C-5), 75.55 (C-4), 74.43 (C-7), 72.17 (C-3), 70.76 (C-6), 58.79 (OCH_3), 52.84 (CO_2CH_3), 14.74 (C-8).

115:

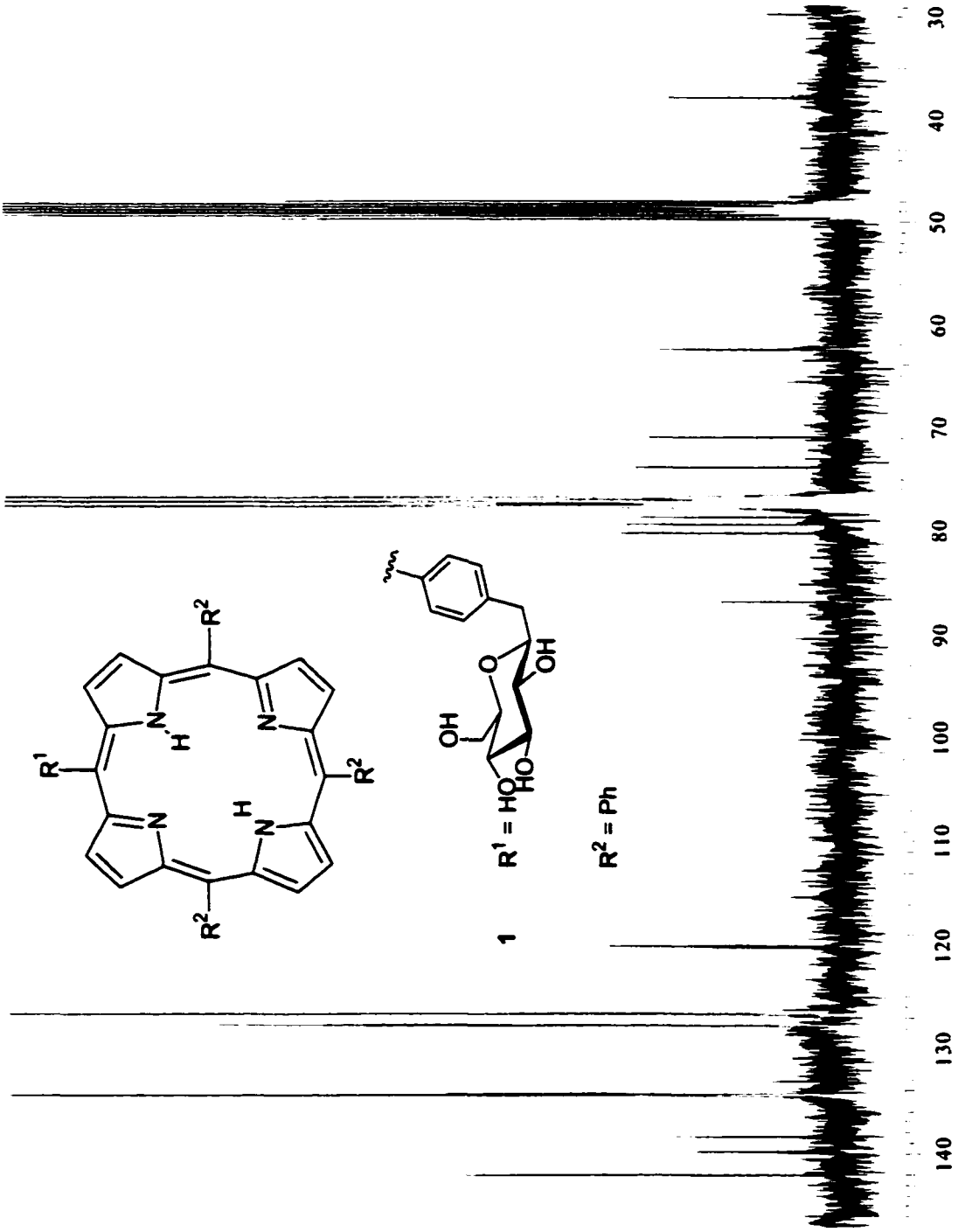
^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.96 (2H, d, J = 8.9 Hz), 7.49 (2H, d, J = 8.3 Hz), 7.43-7.33 (5H, m), 5.57 (1H, s, H-9), 4.47 (1H, q, J = 7.0 Hz, H-7), 4.44-4.38 (2H, m, H-3 and H-4), 3.99 (1H, d, J = 1.9 Hz, H-6), 3.72 (3H, s, CO_2CH_3), 3.62 (1H, dd, J = 8.3, 3.2 Hz, H-5), 3.53 (3H, s, OCH_3), 2.60 (1H, s, OH), 1.38 (3H, d, J = 7.0 Hz, H-8).

^{13}C-NMR (100 MHz, $CDCl_3$): δ 170.53 (C-1), 136.41, 135.67, 131.62, 129.11, 128.87, 128.78, 128.27, 123.35, 95.86 (C-9), 81.89 (C-2), 78.21 (C-5), 74.26 (C-3 or C-7), 74.06 (C-3 or C-7), 71.36 (C-4), 70.72 (C-6), 58.90 (OCH_3), 53.26 (CO_2CH_3), 14.56 (C-8).

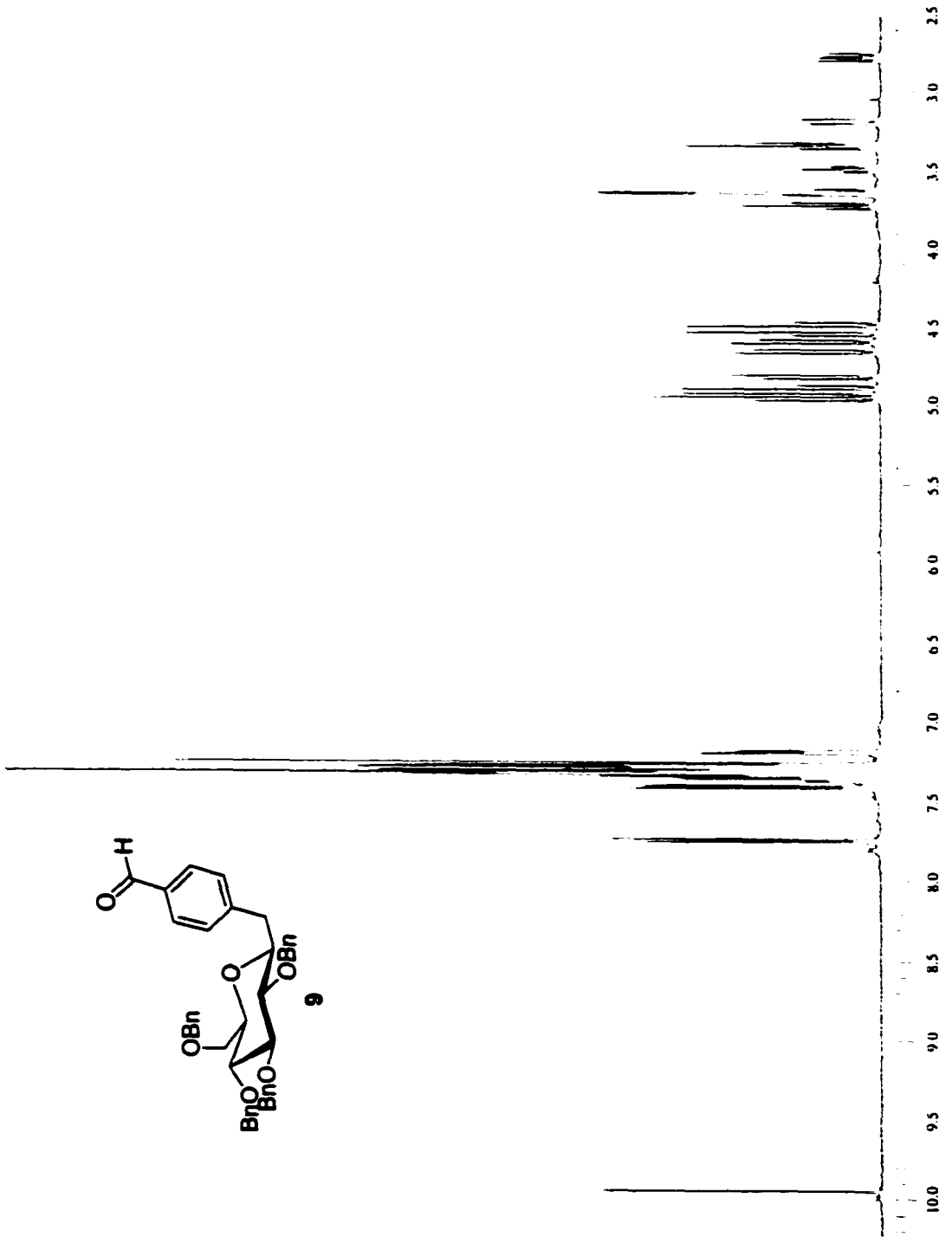
7. Appendix



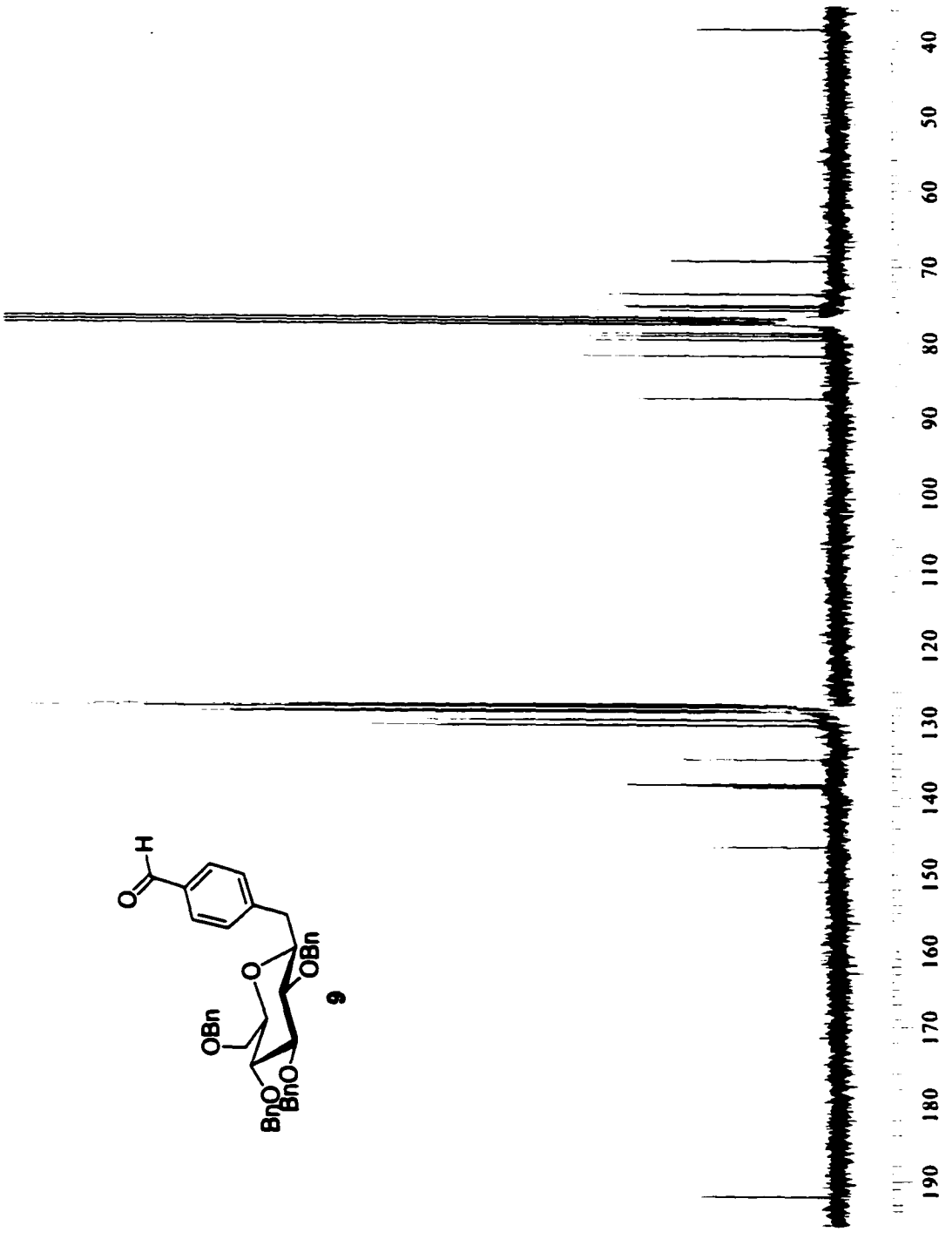
^{1}H-NMR spectrum (500 MHz, $CDCl_3/CD_3O_3$ = 3/1) of **1**



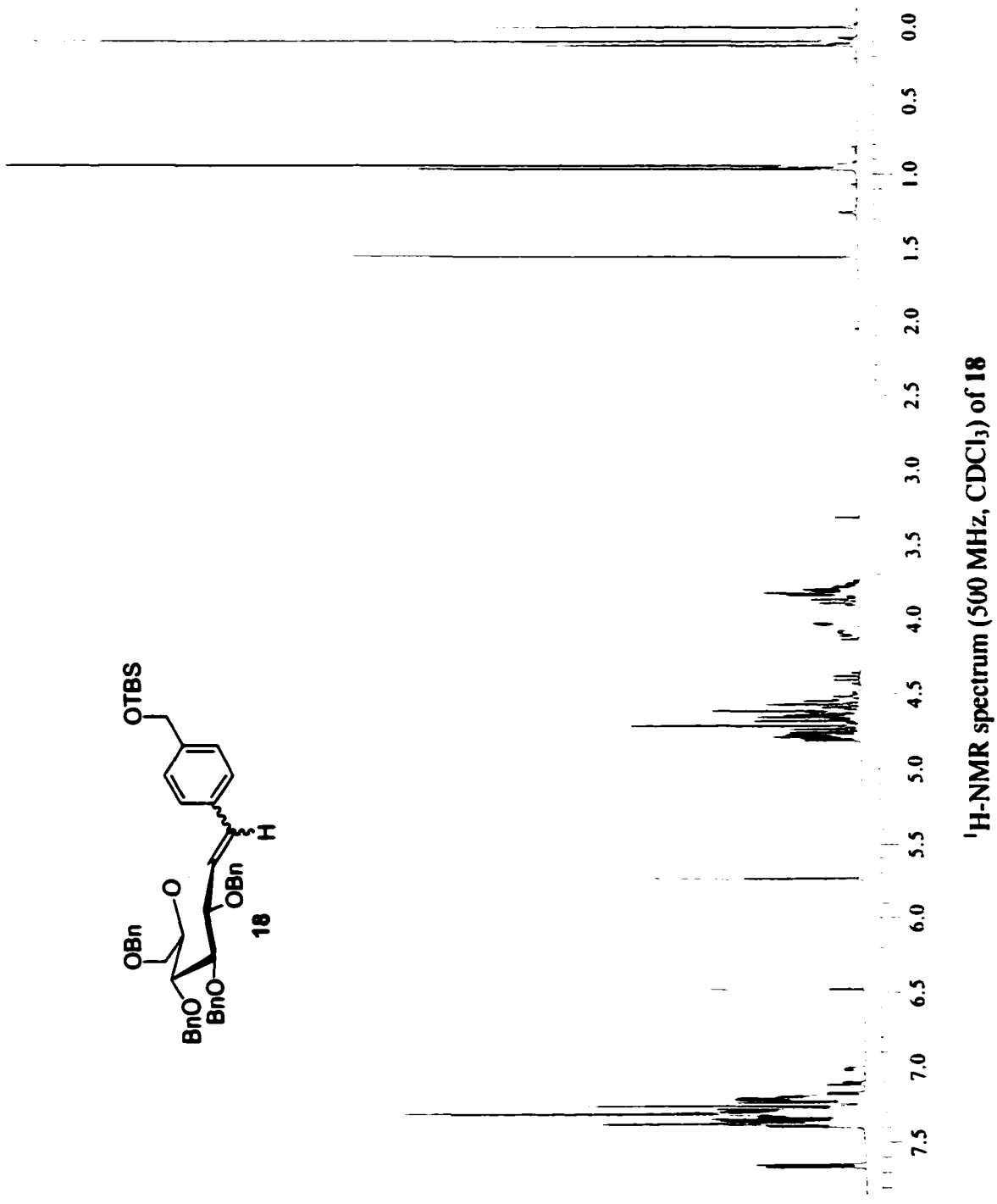
^{13}C-NMR spectrum (75 MHz, $CDCl_3/CD_3O_3$ = 3/1) of **1**



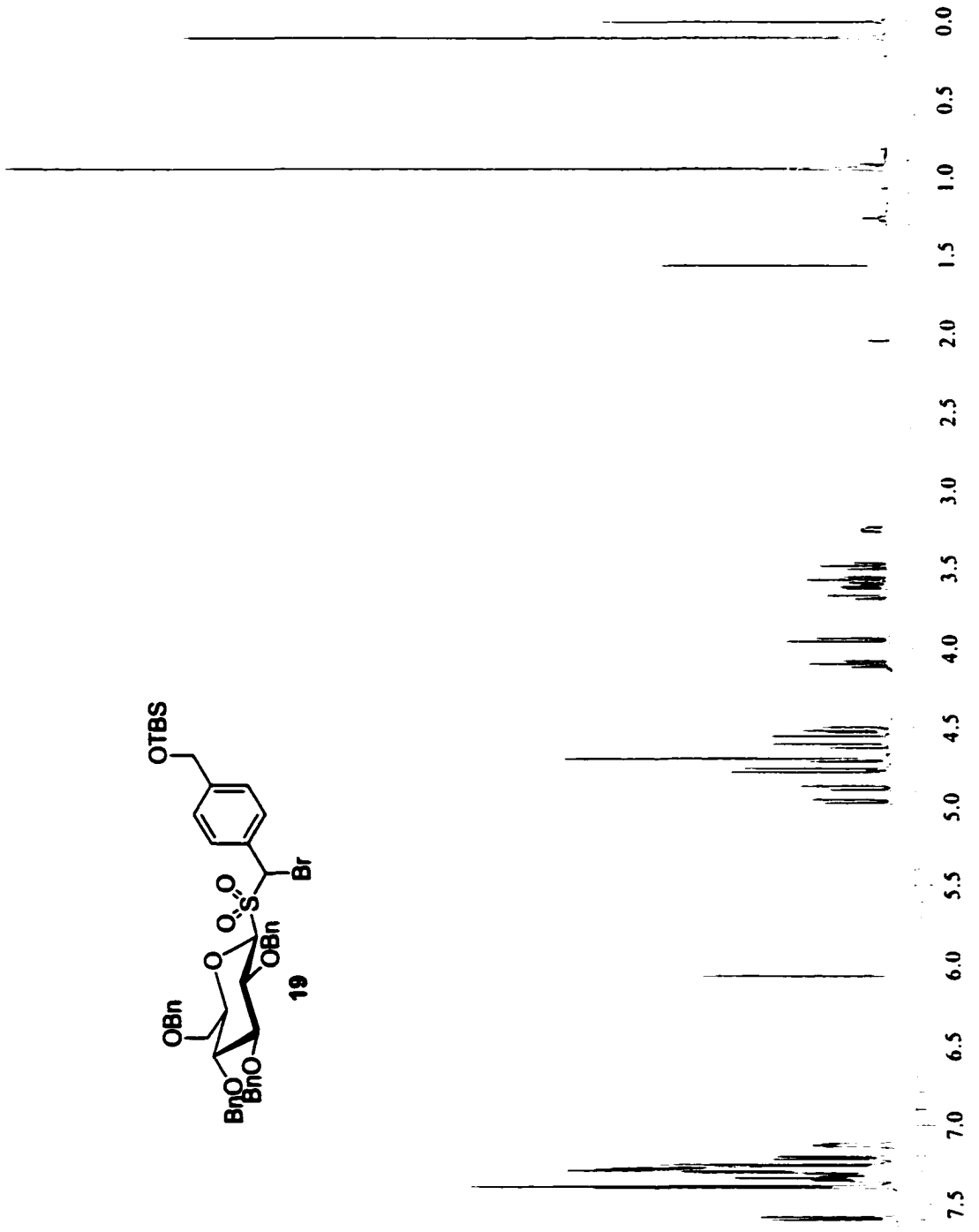
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **9**



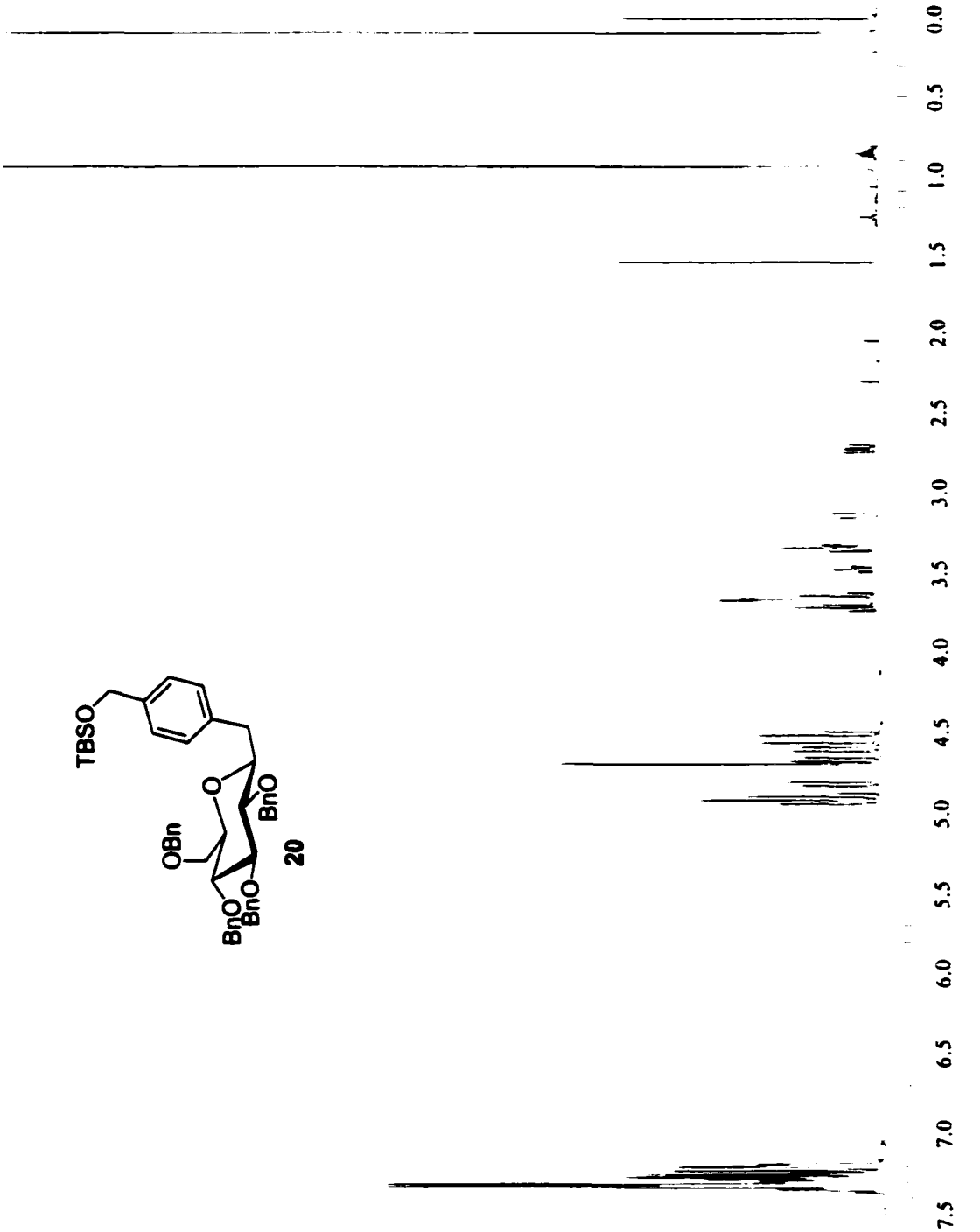
^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **9**



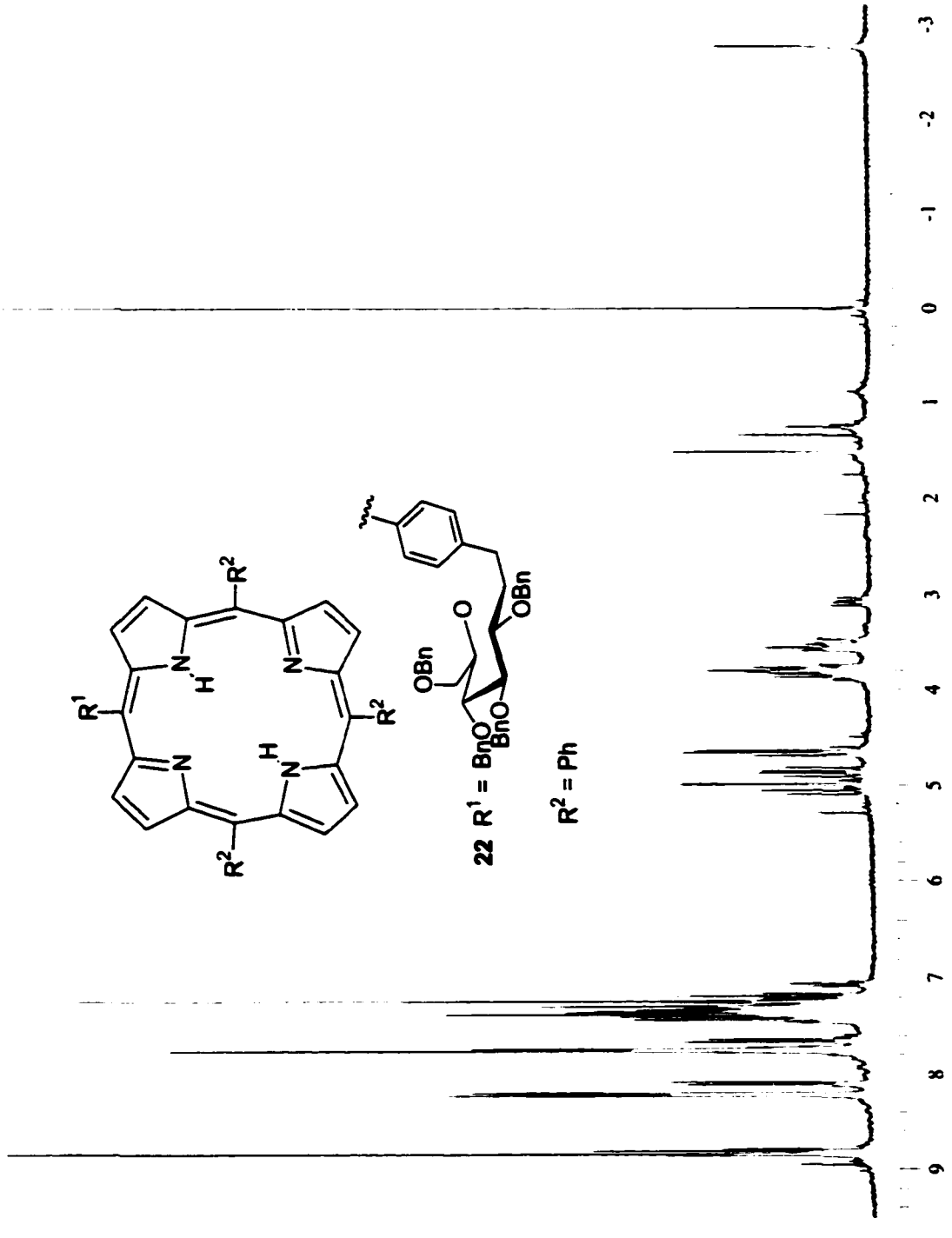
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **18**



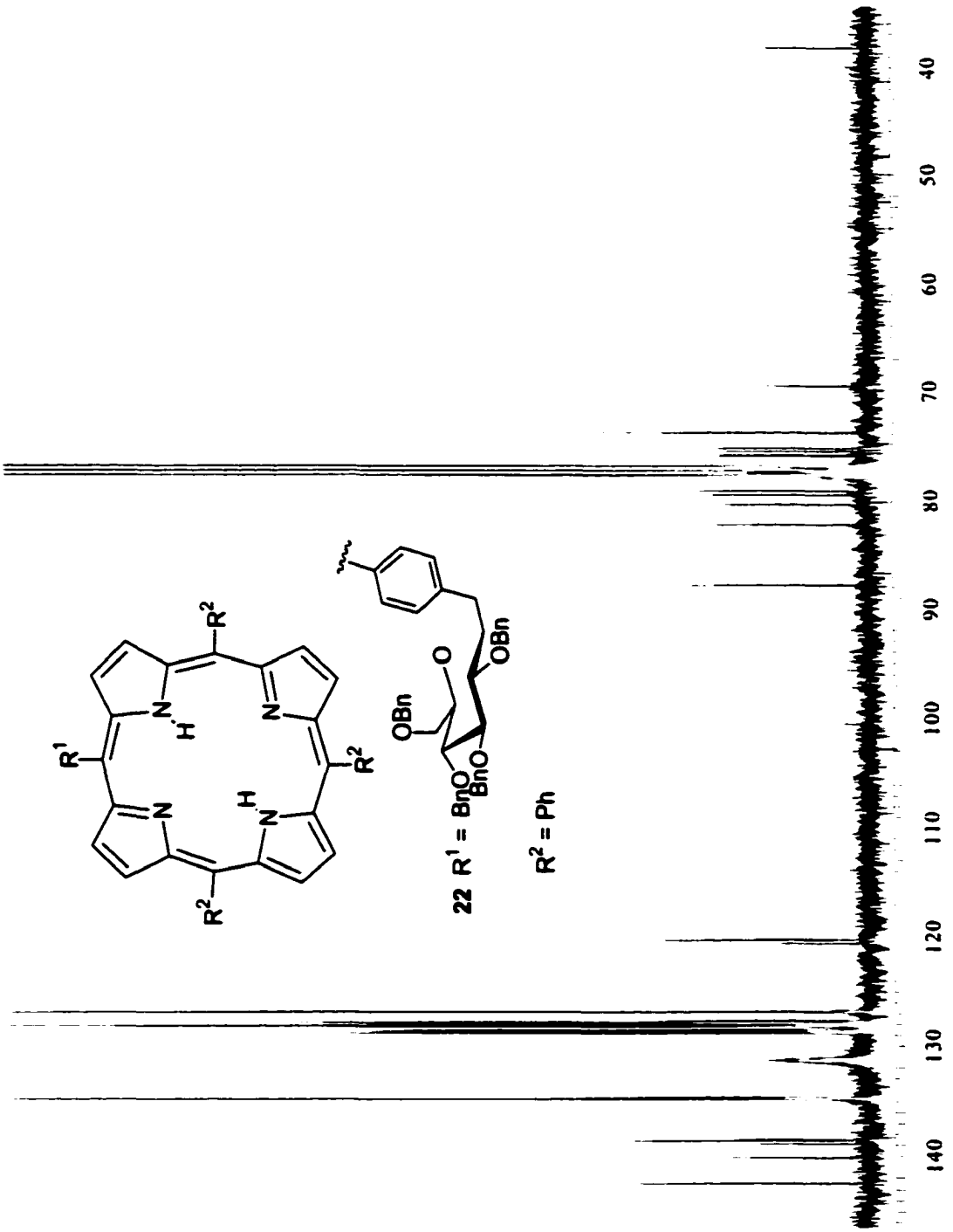
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **19**



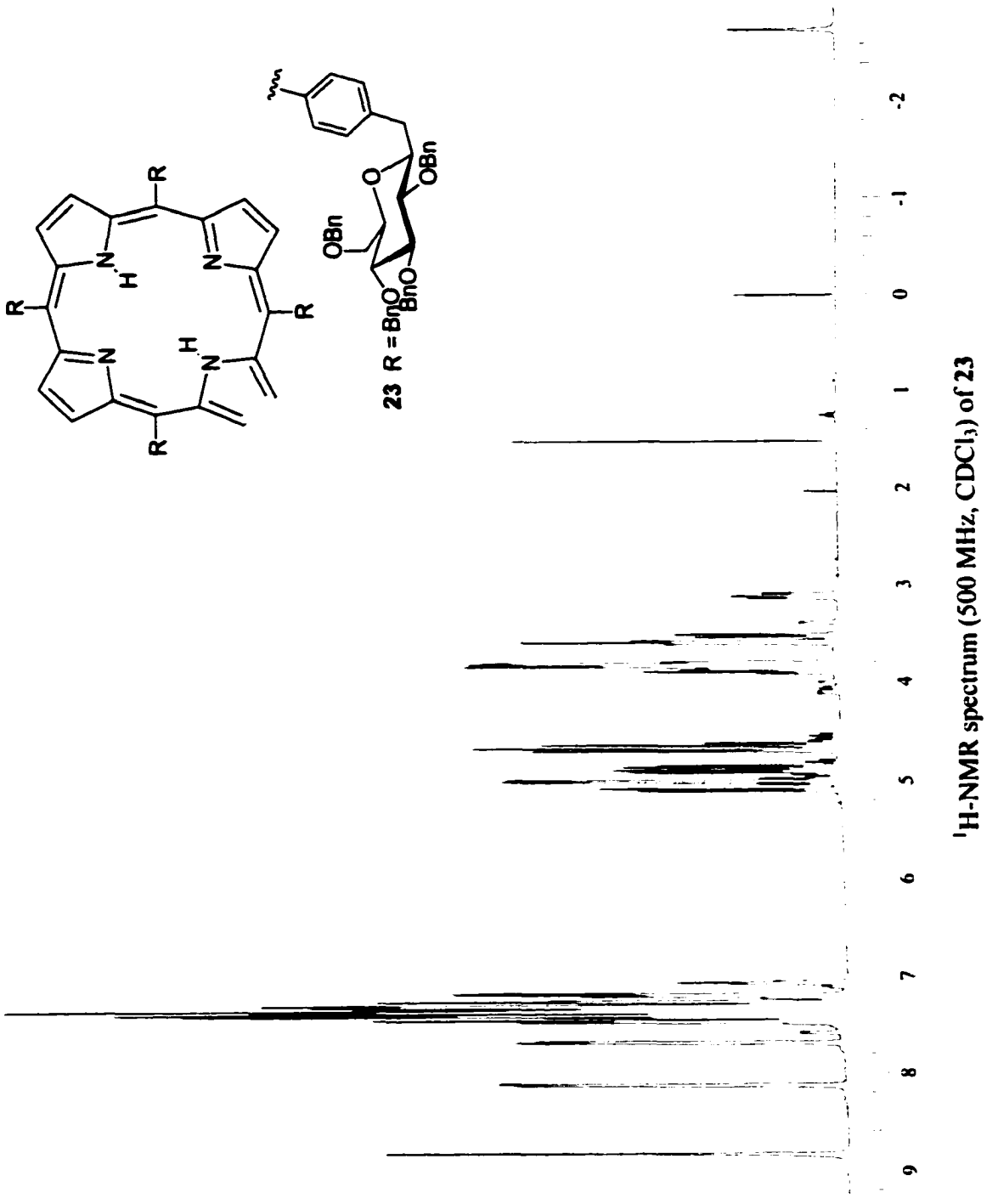
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **20**



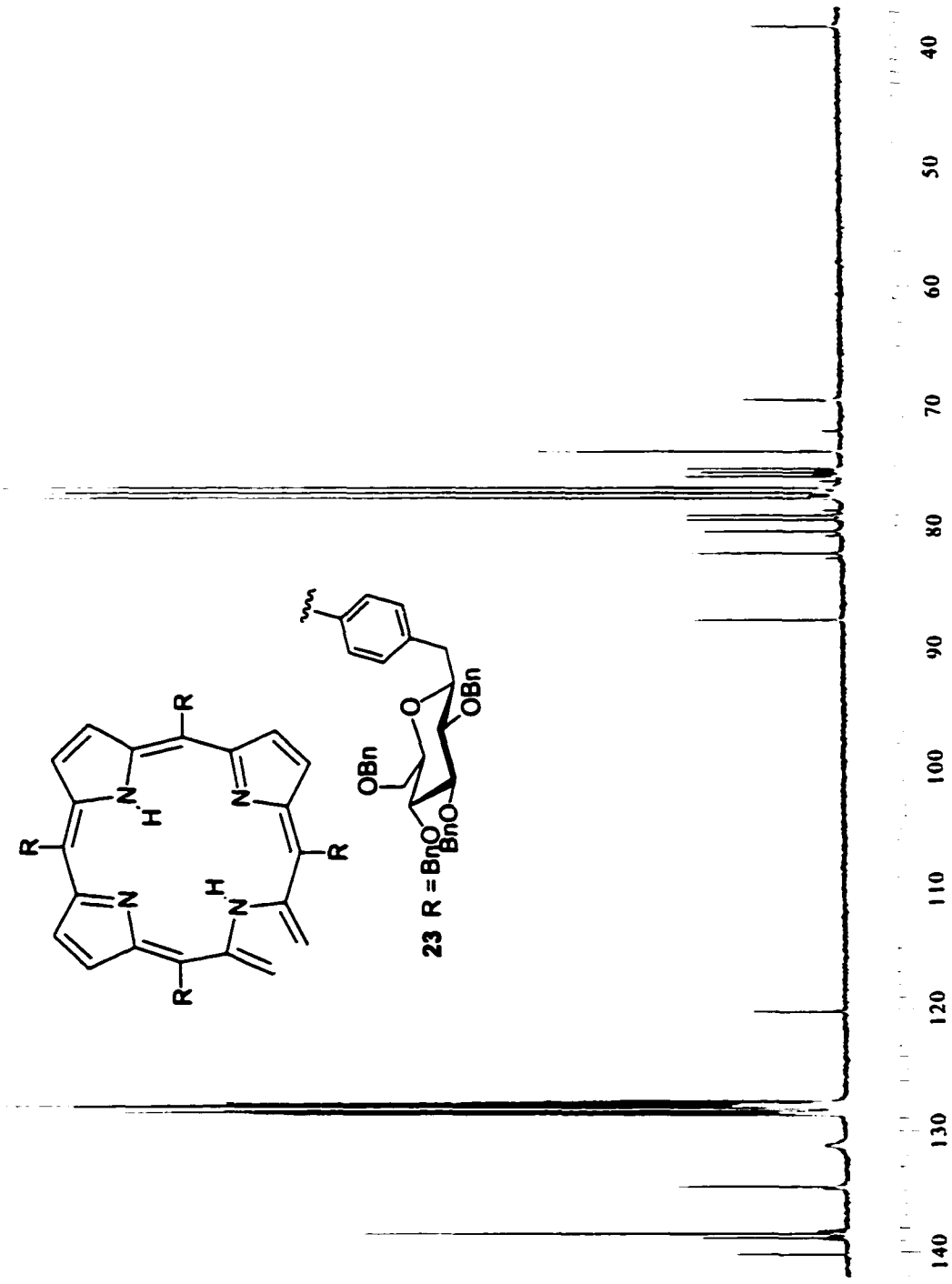
^{1}H-NMR spectrum (300 MHz, $CDCl_3$) of **22**



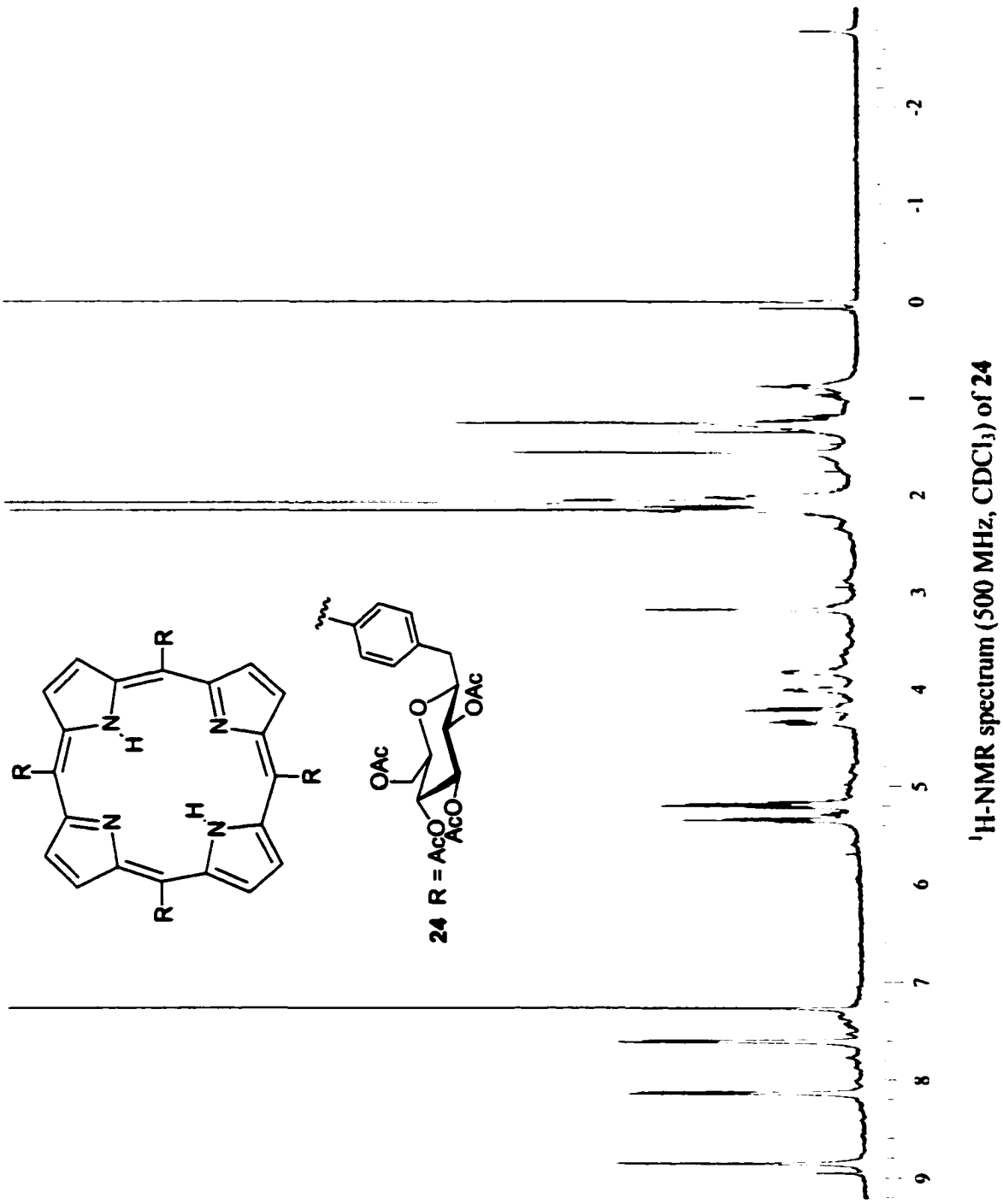
^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **22**



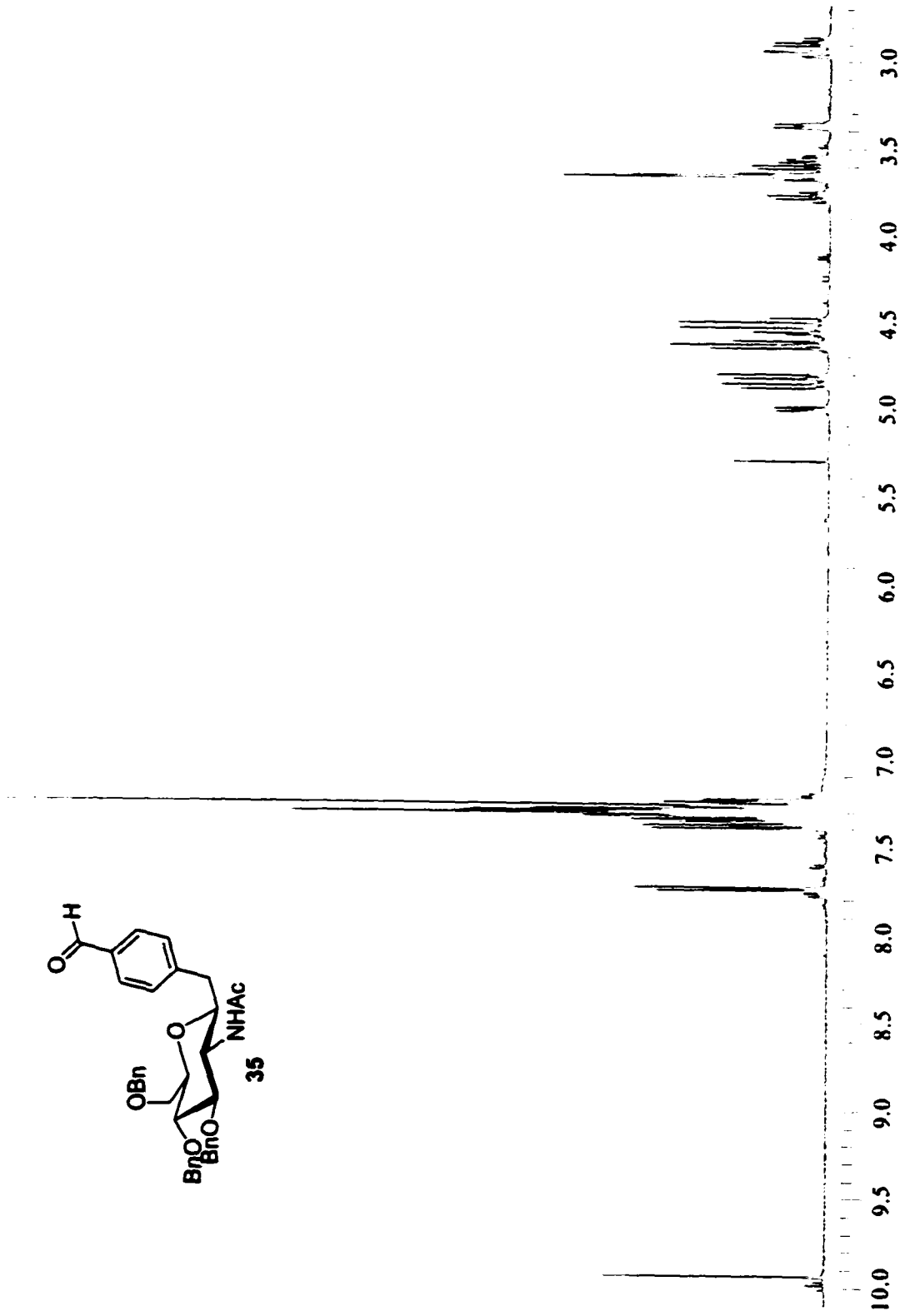
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **23**



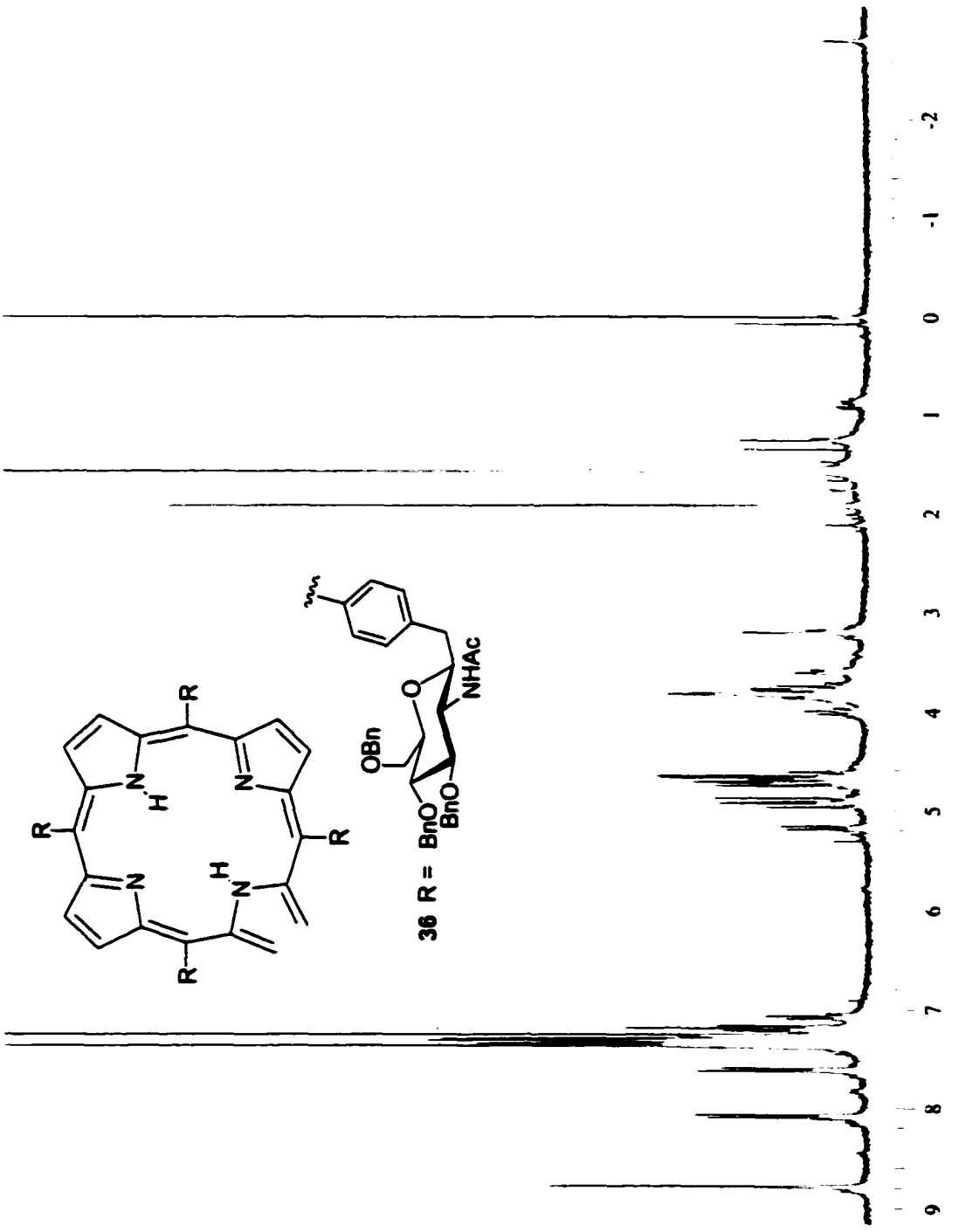
^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **23**



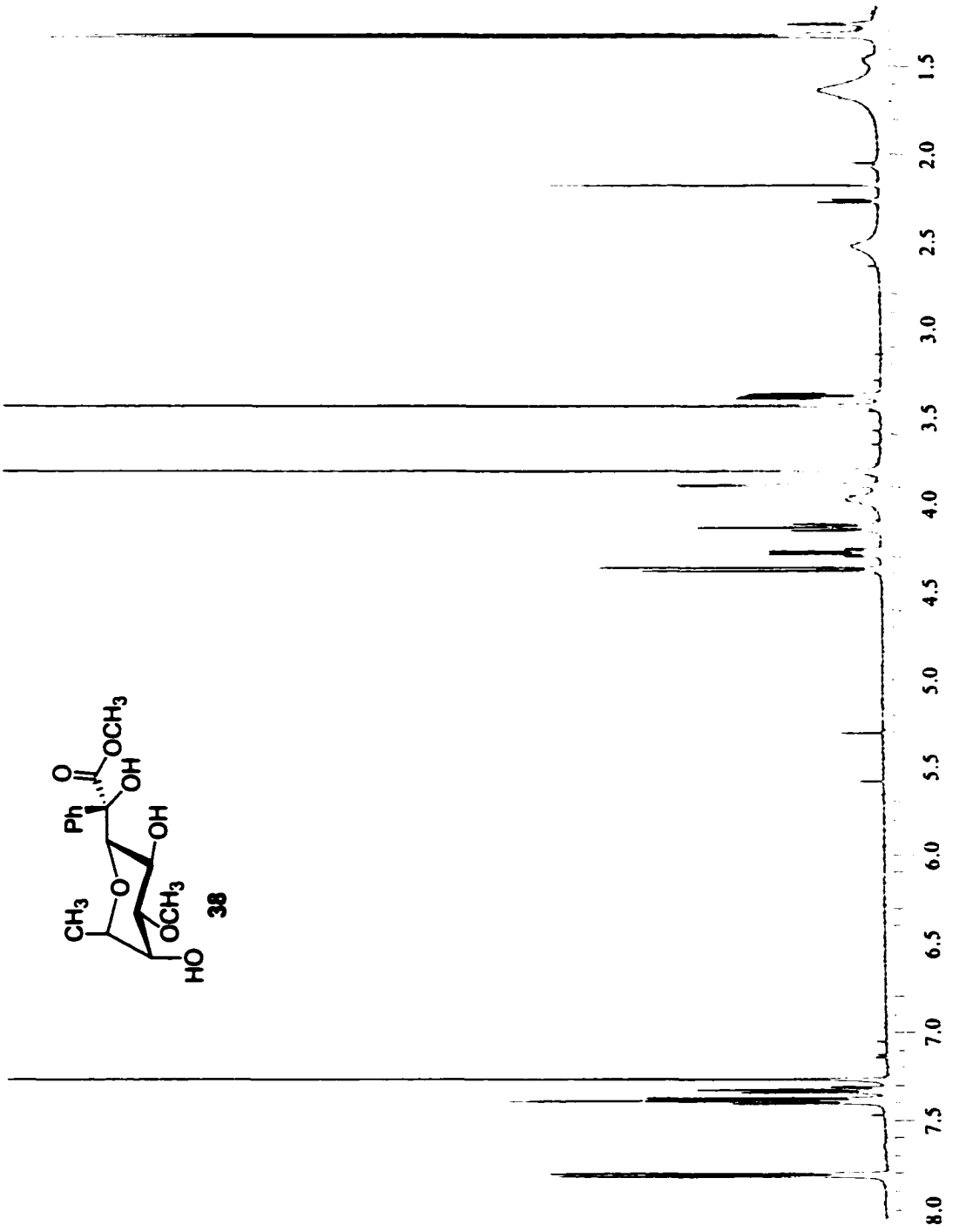
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **24**



^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **35**

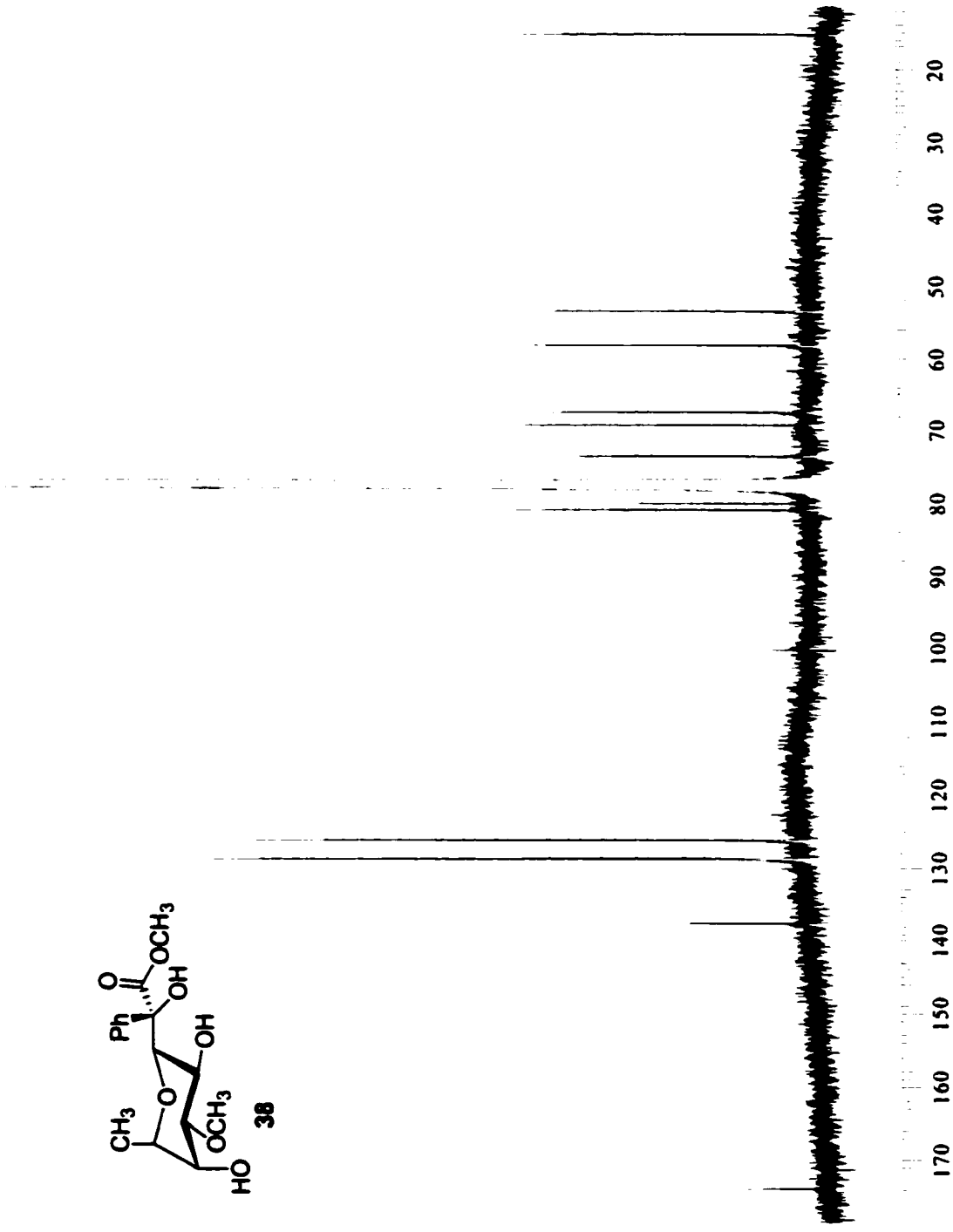


^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **36**

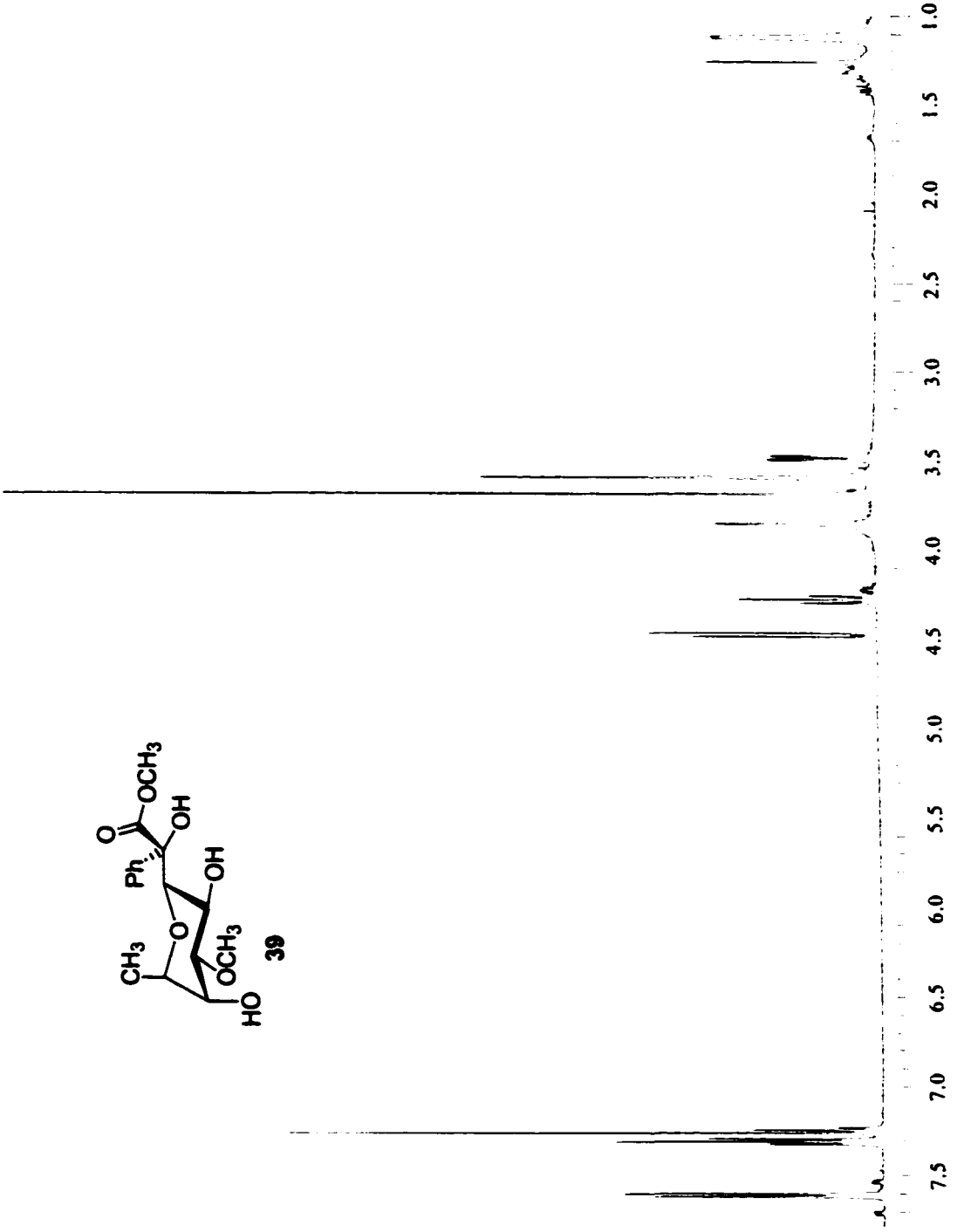


38

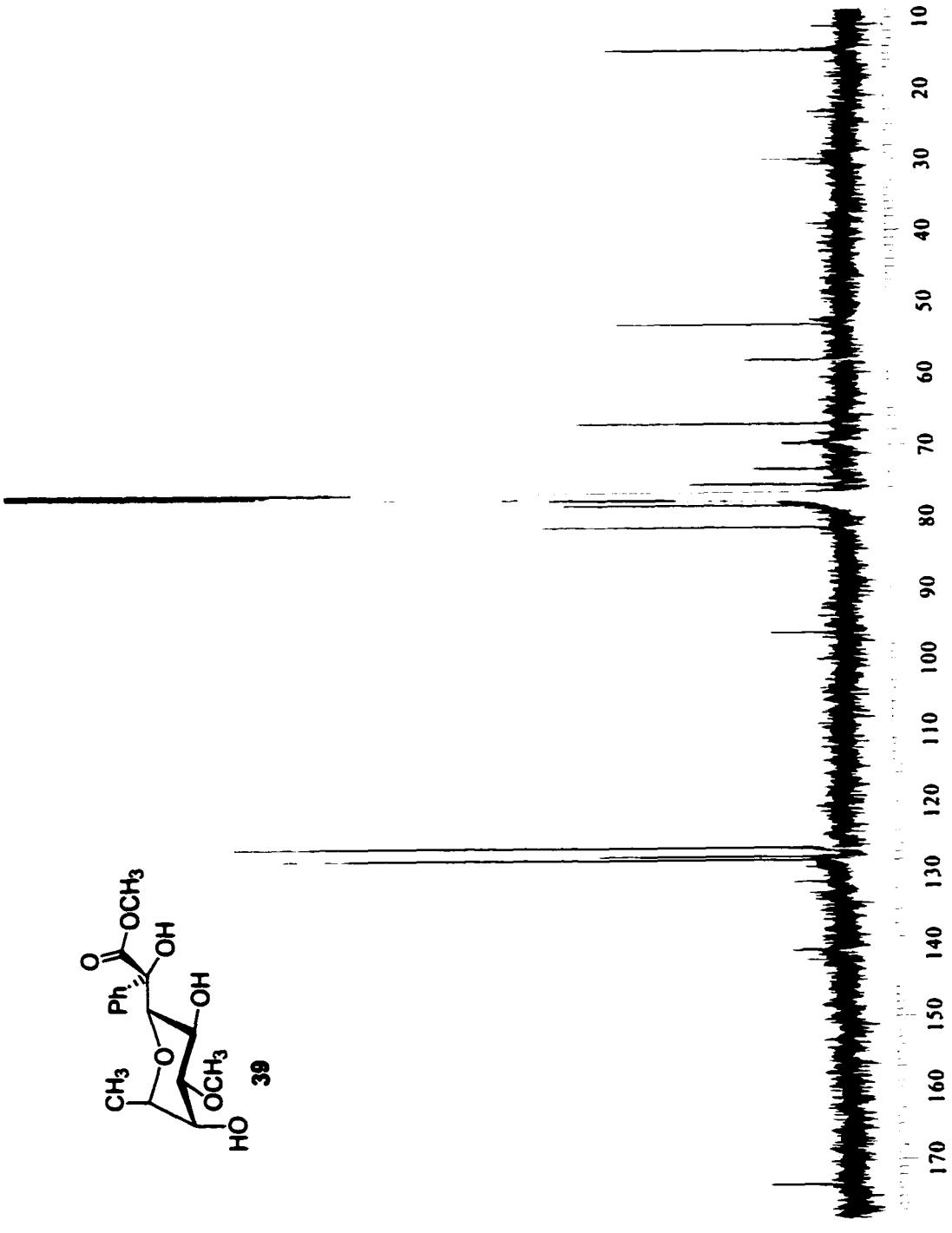
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **38**



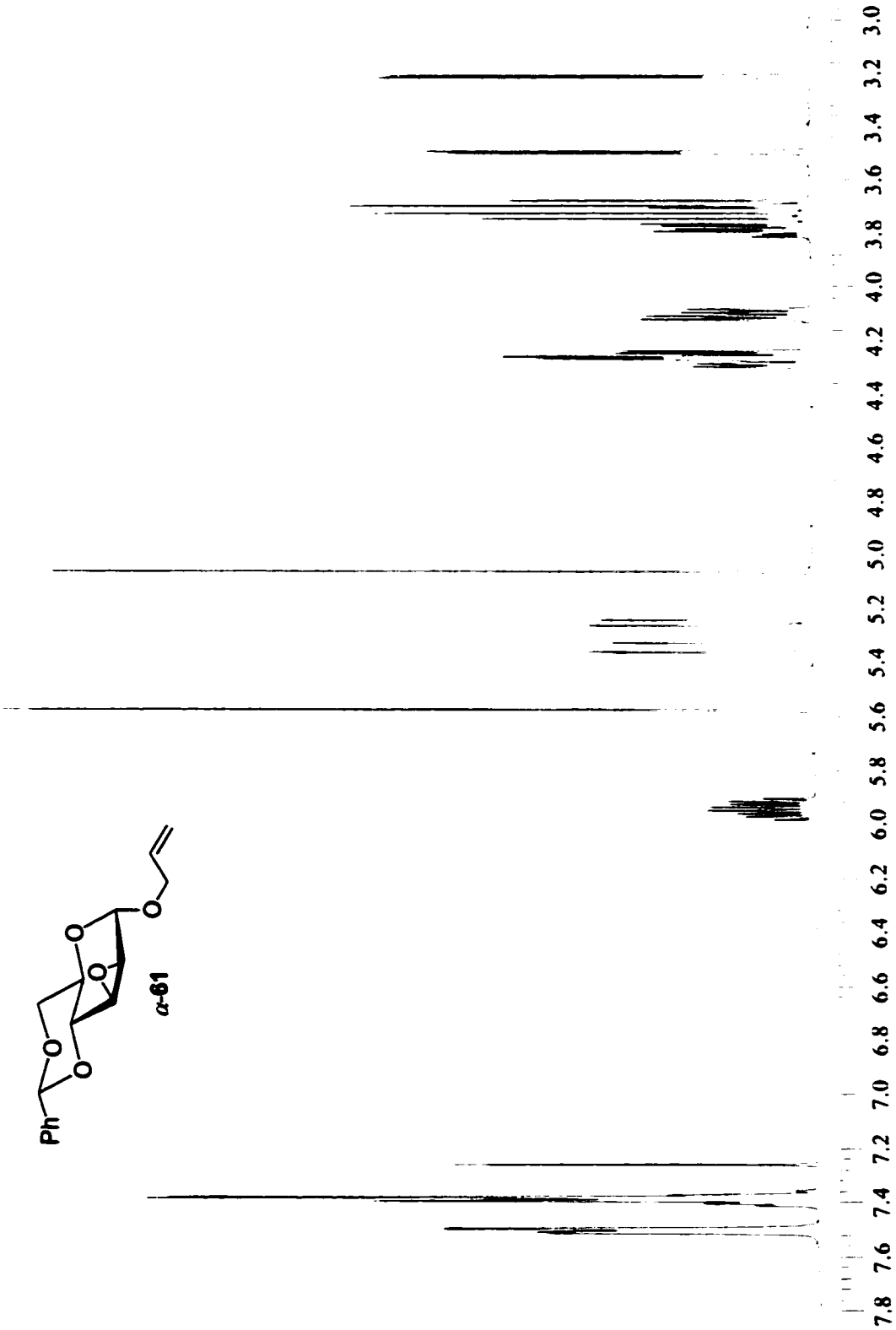
^{13}C-NMR spectrum (100 MHz, $CDCl_3$) of **38**



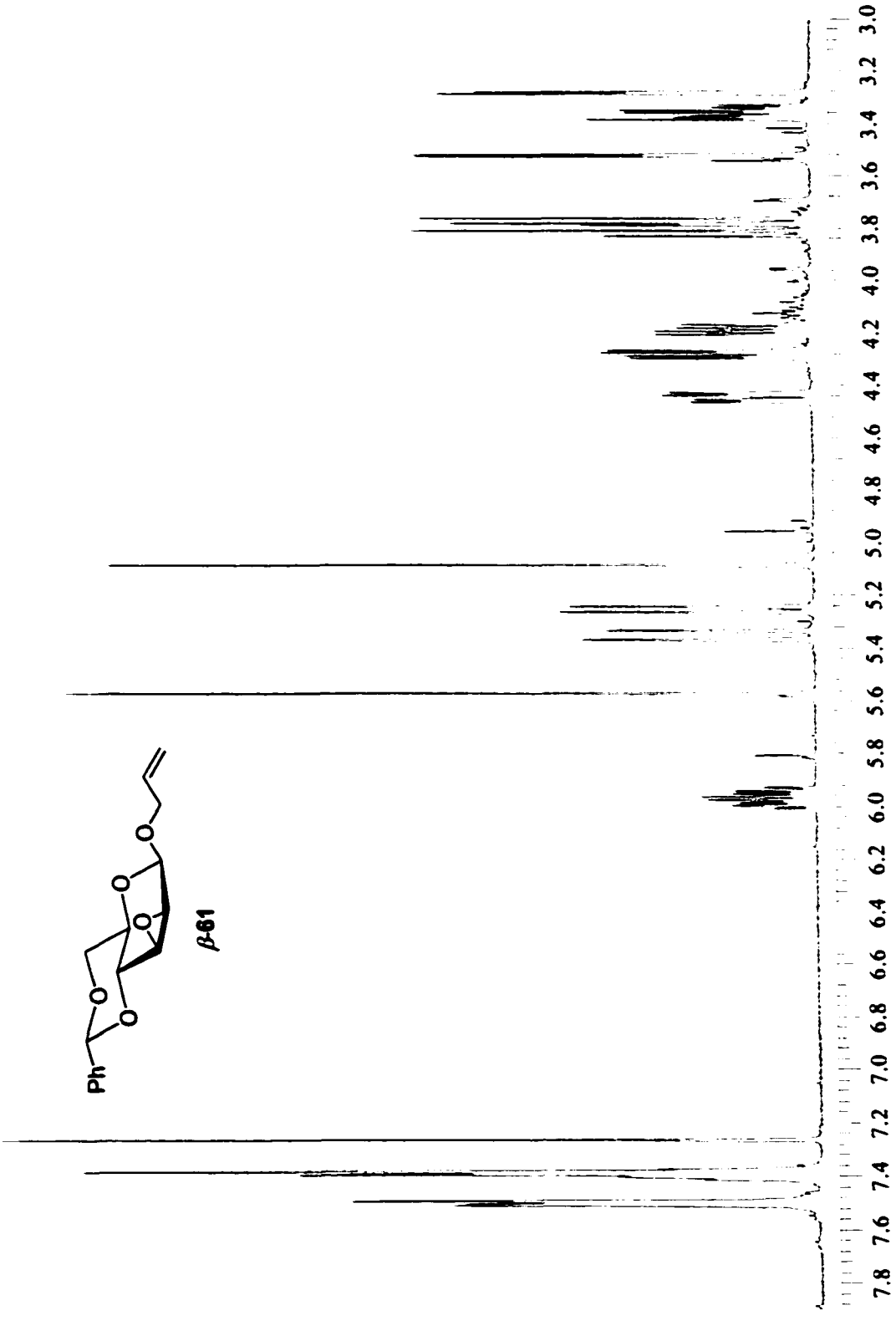
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **39**



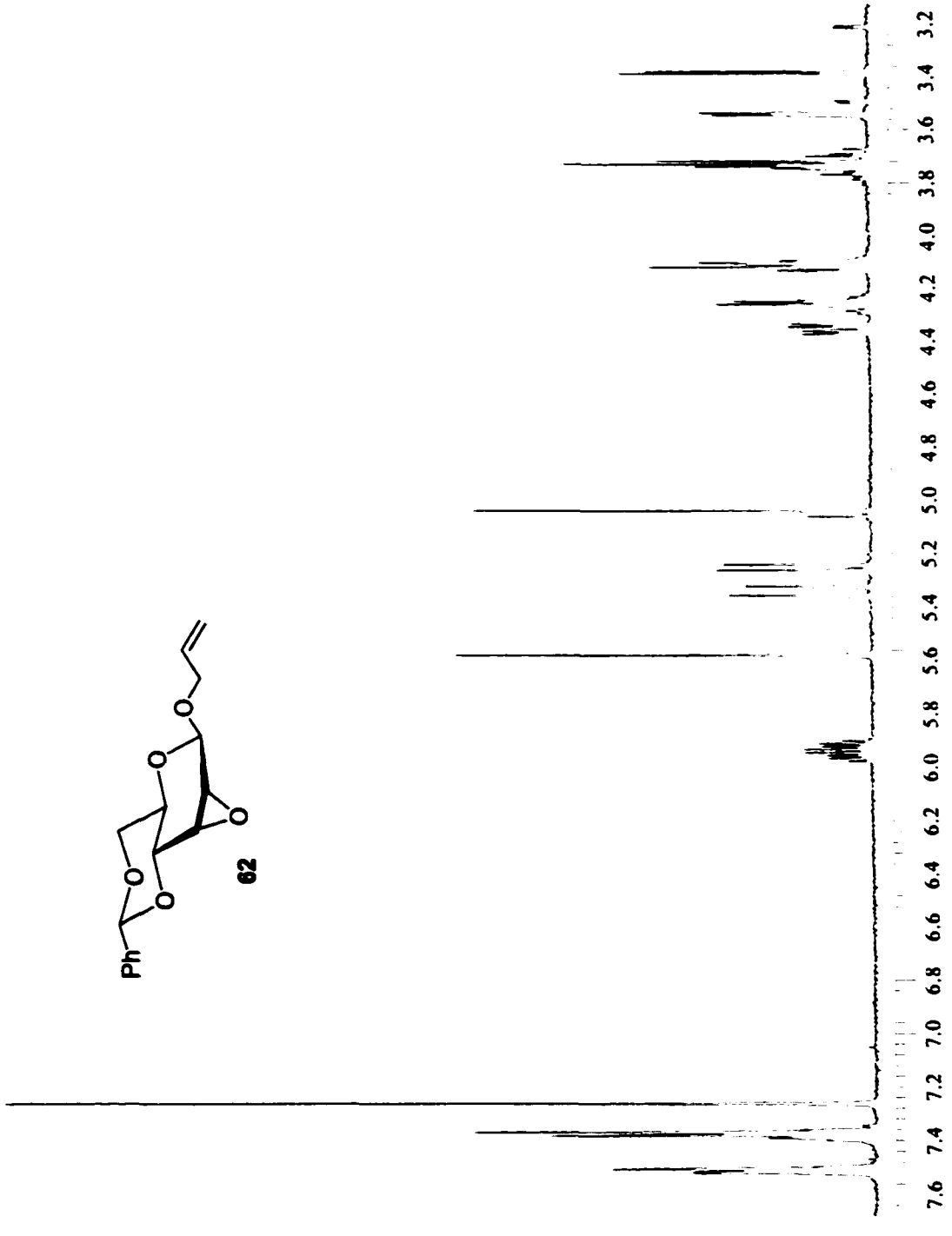
^{13}C-NMR spectrum (100 MHz, $CDCl_3$) of **39**



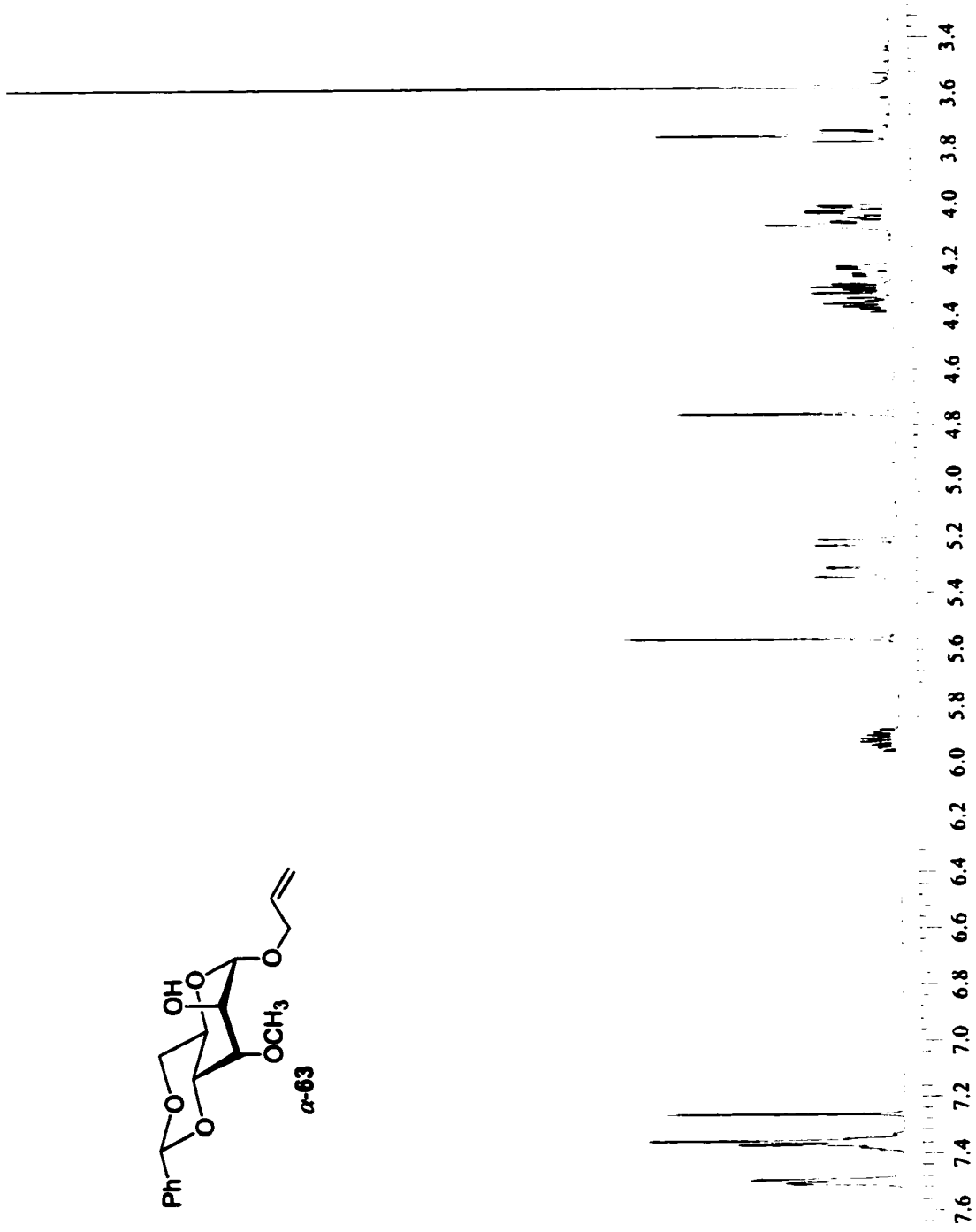
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **α-61**



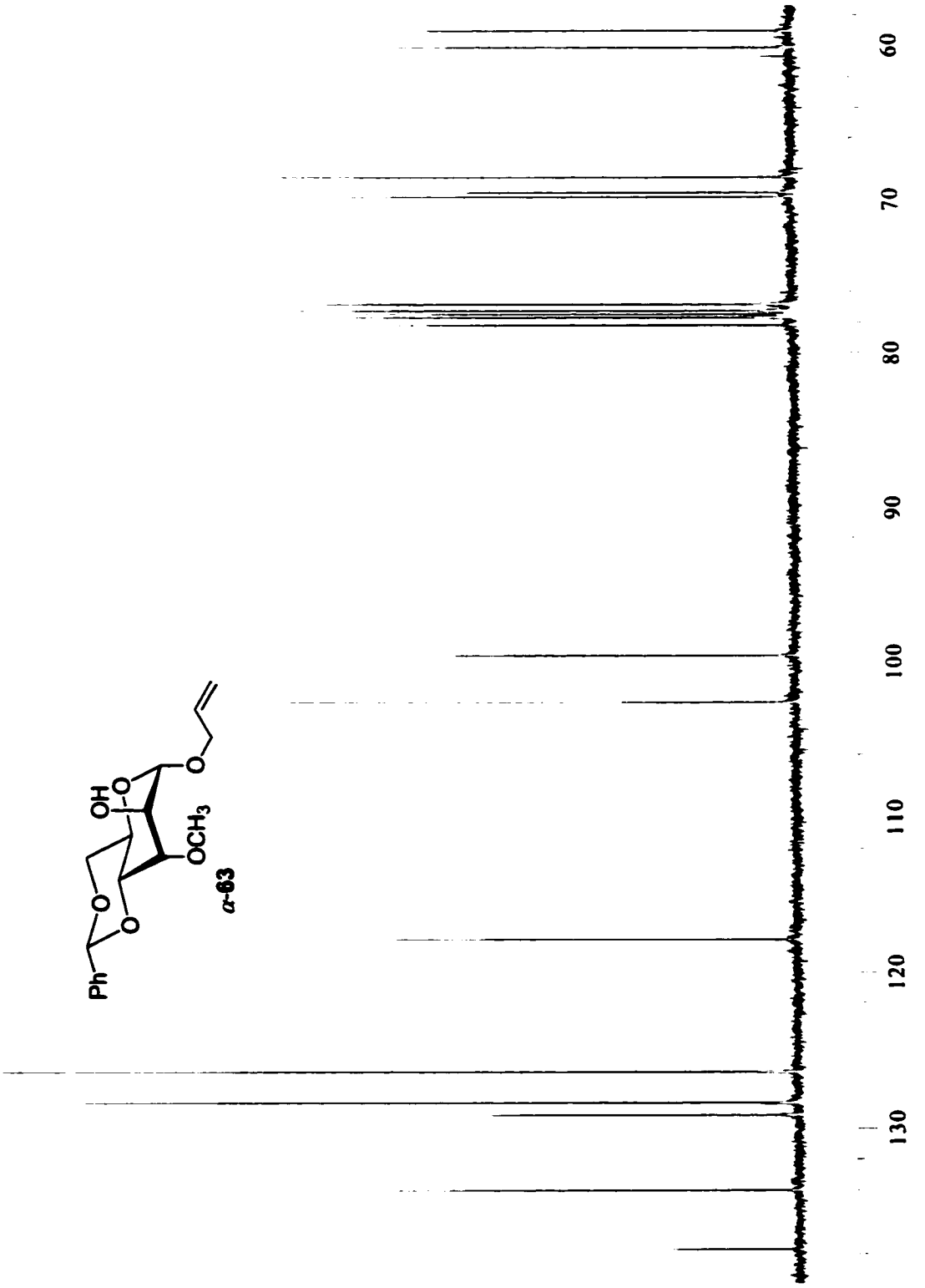
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **β-61**



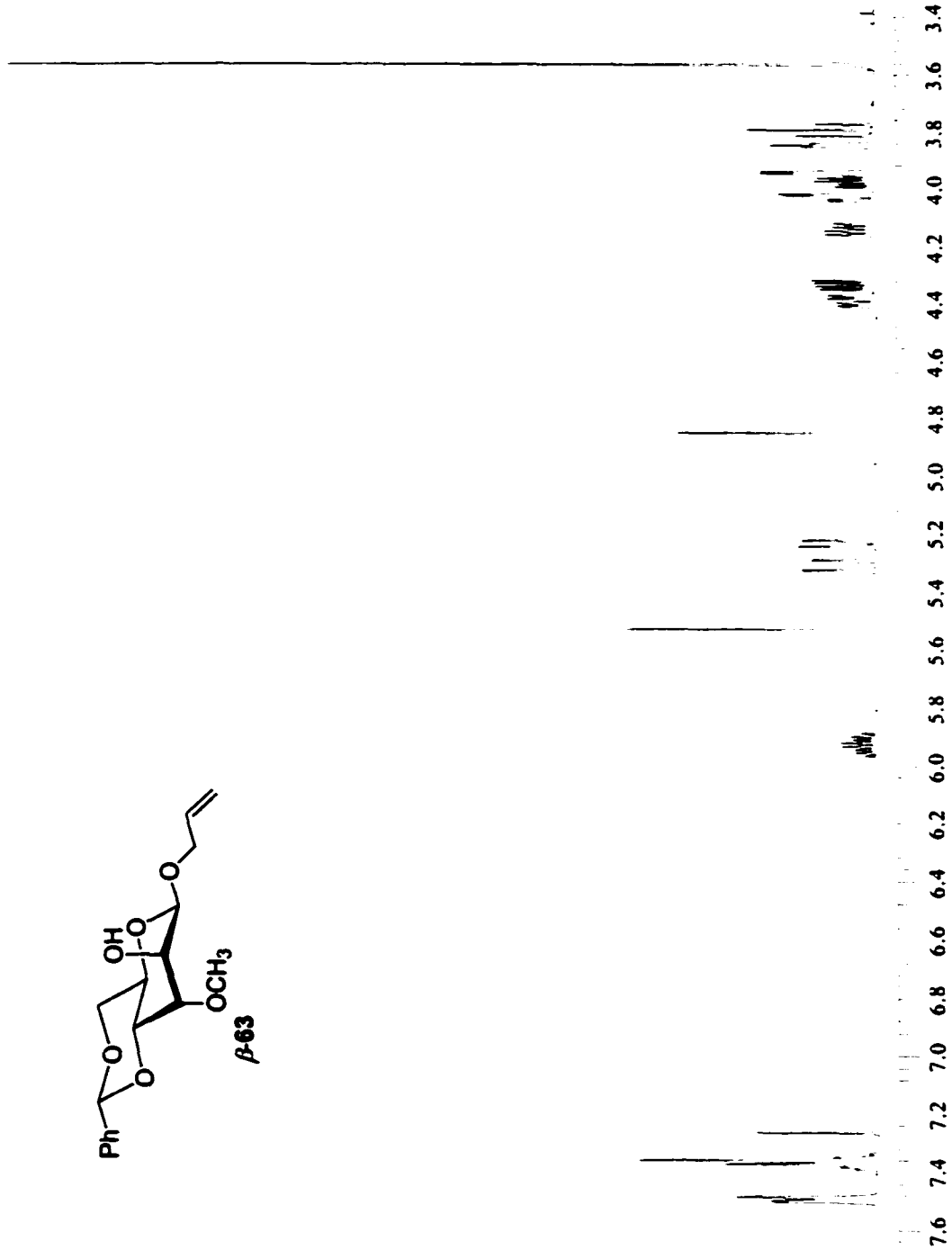
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **62**



^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **α-63**

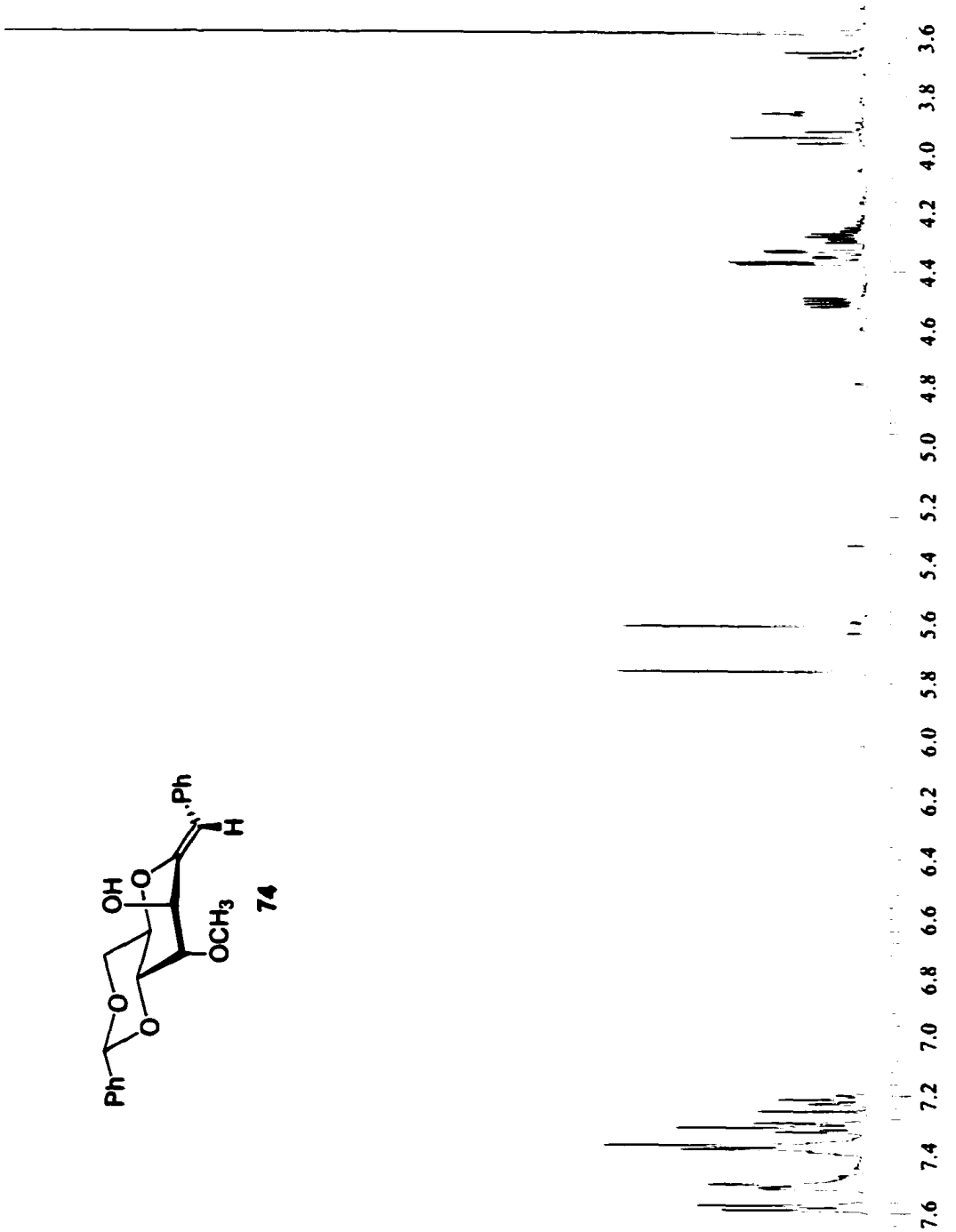


^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of *α*-63

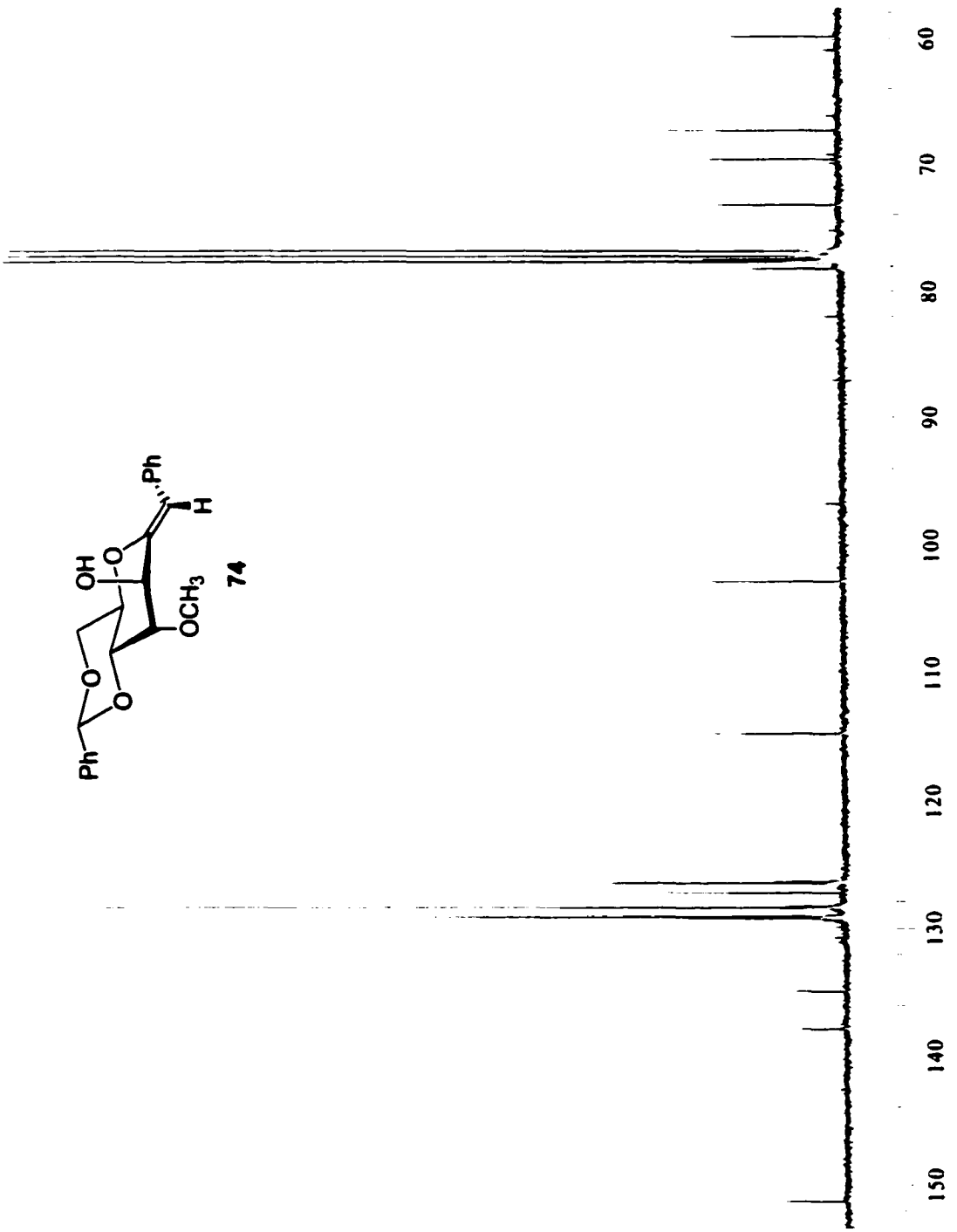


^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **β-63**

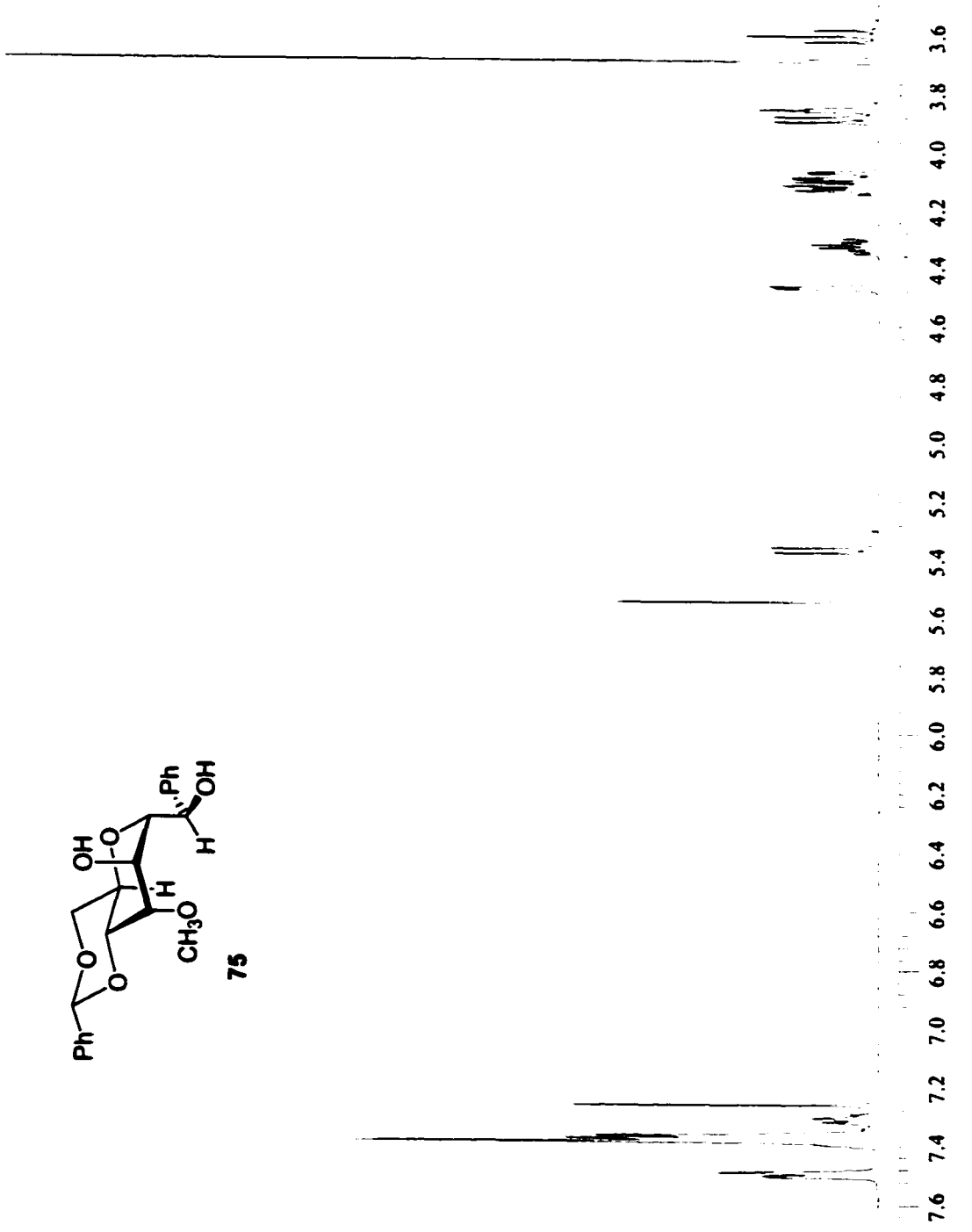
^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **β-63**



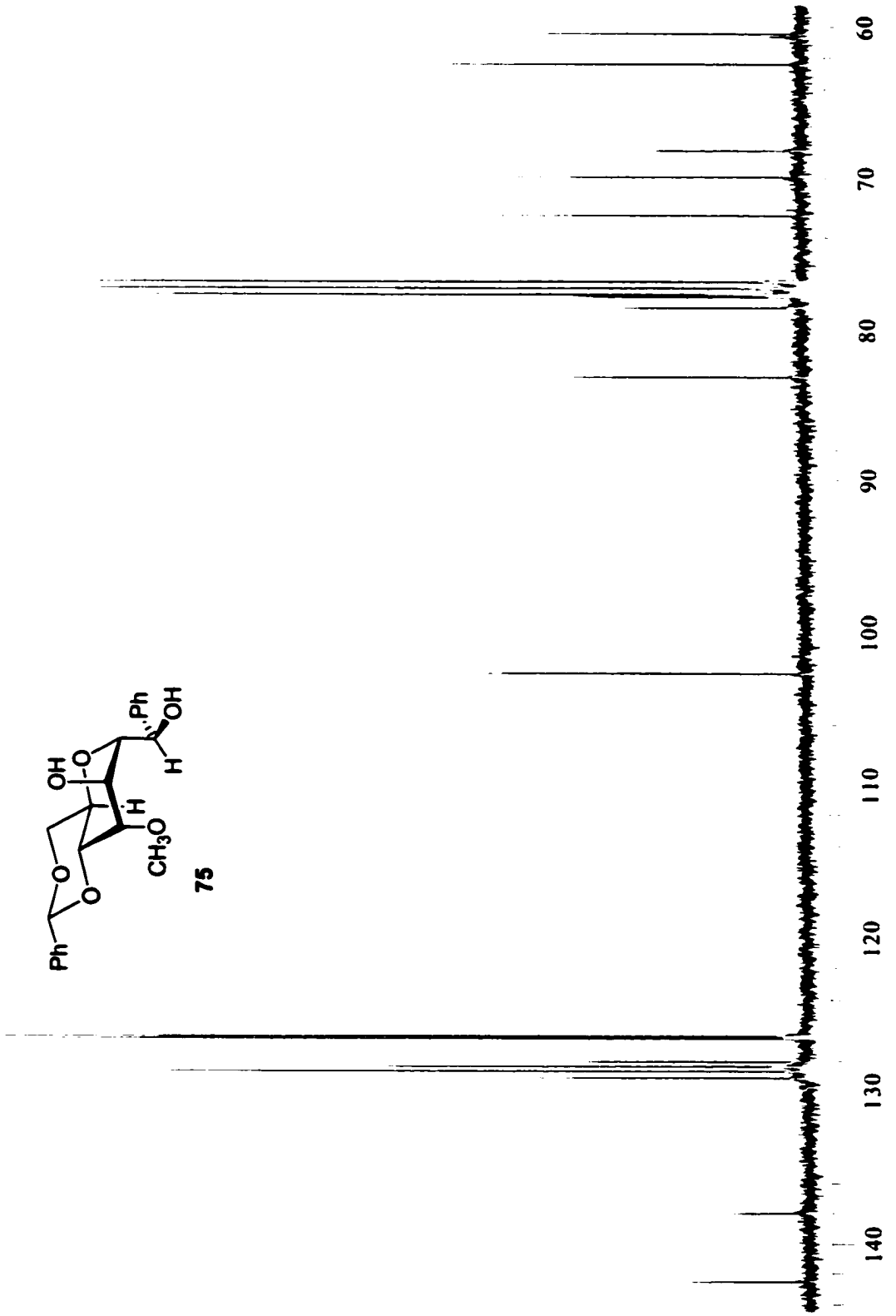
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **74**



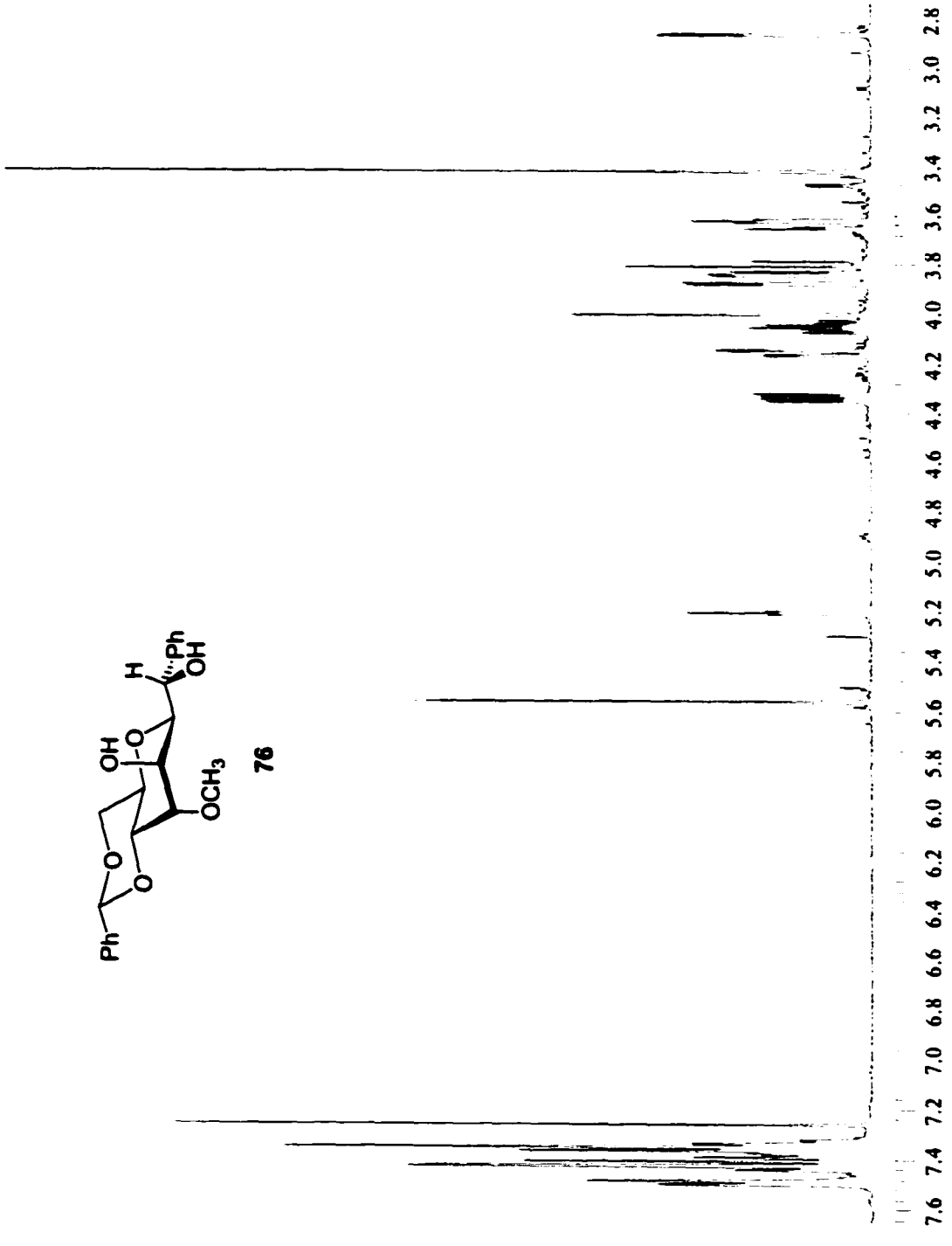
^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **74**



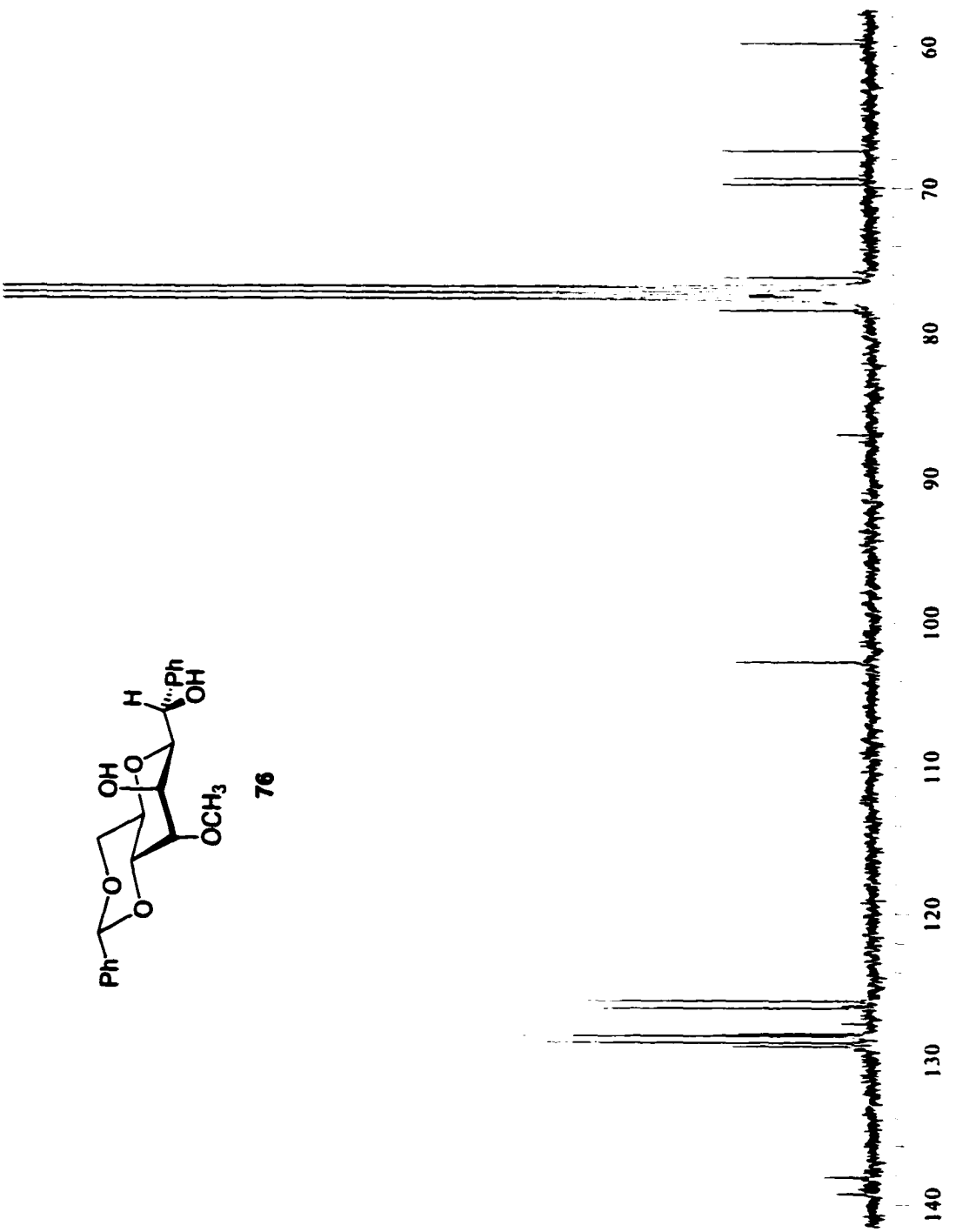
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **75**



^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **75**

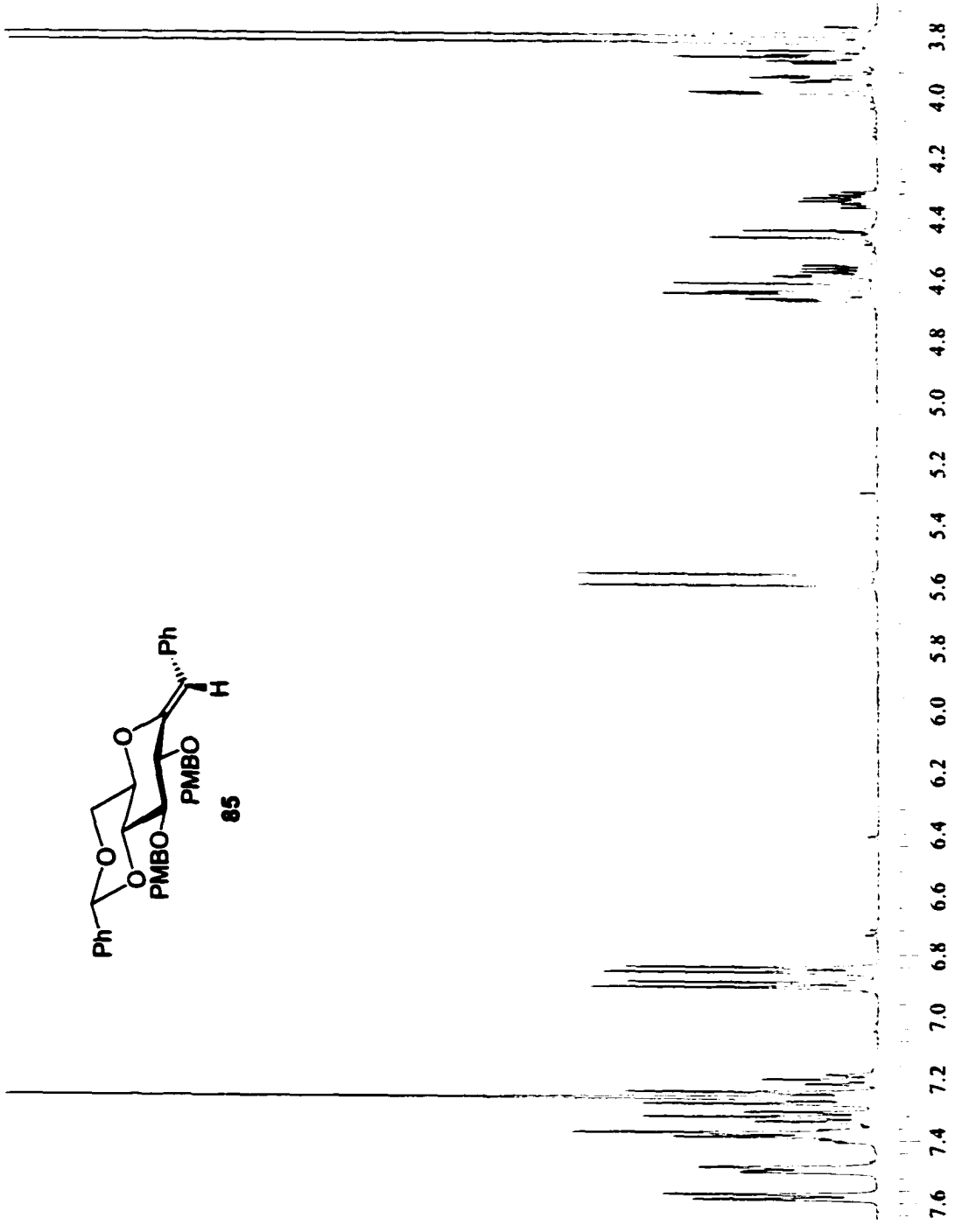


^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **76**

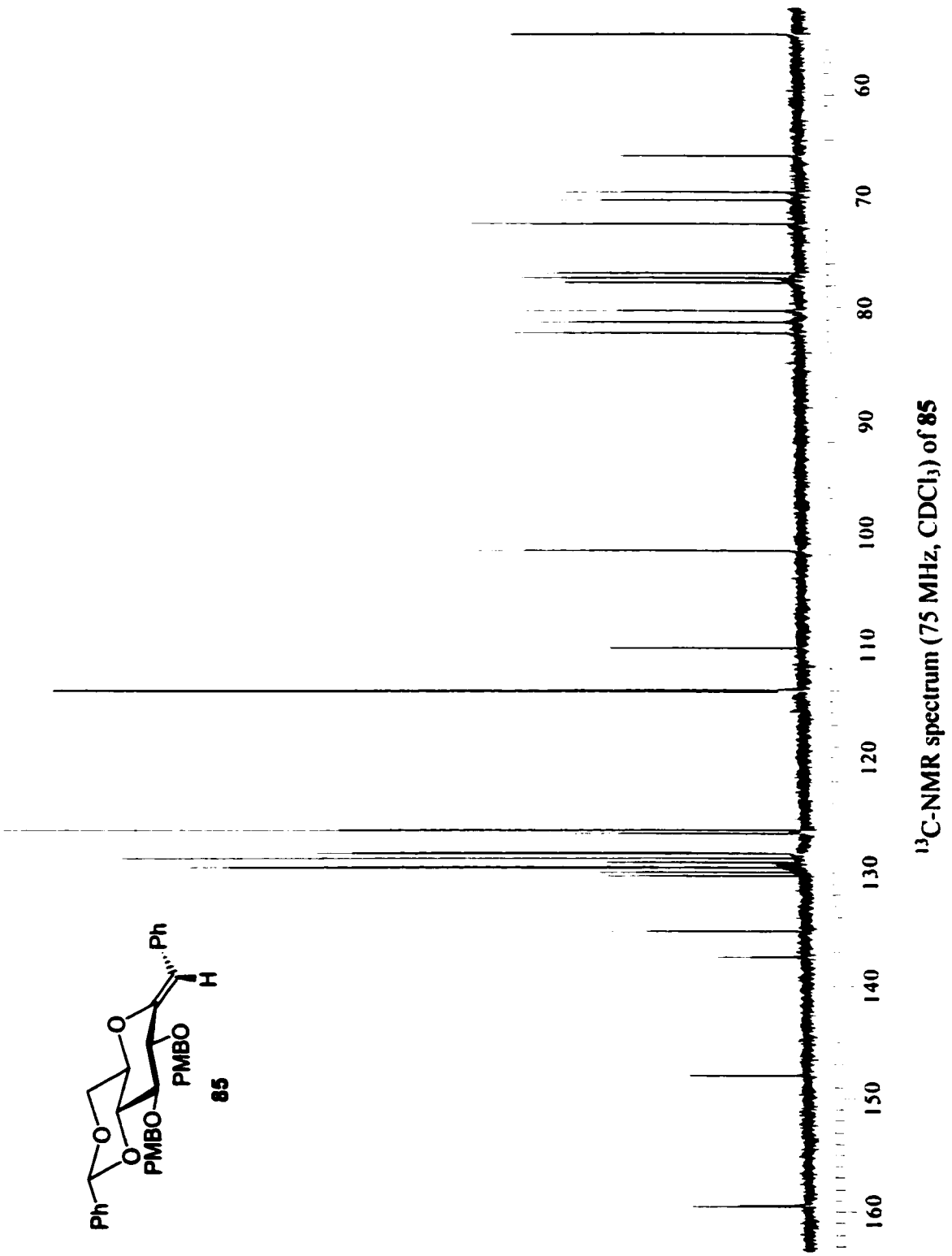


^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **76**

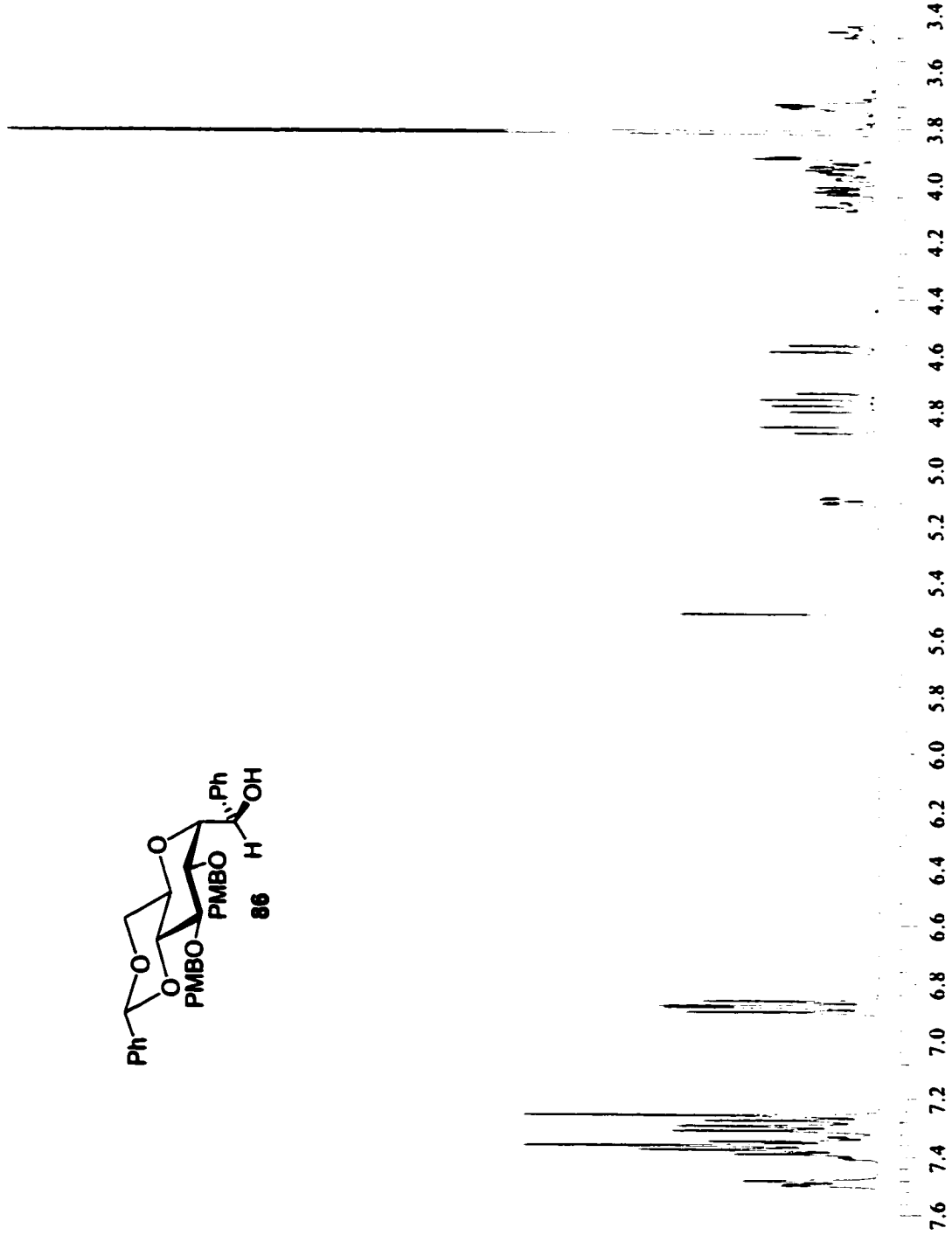
76



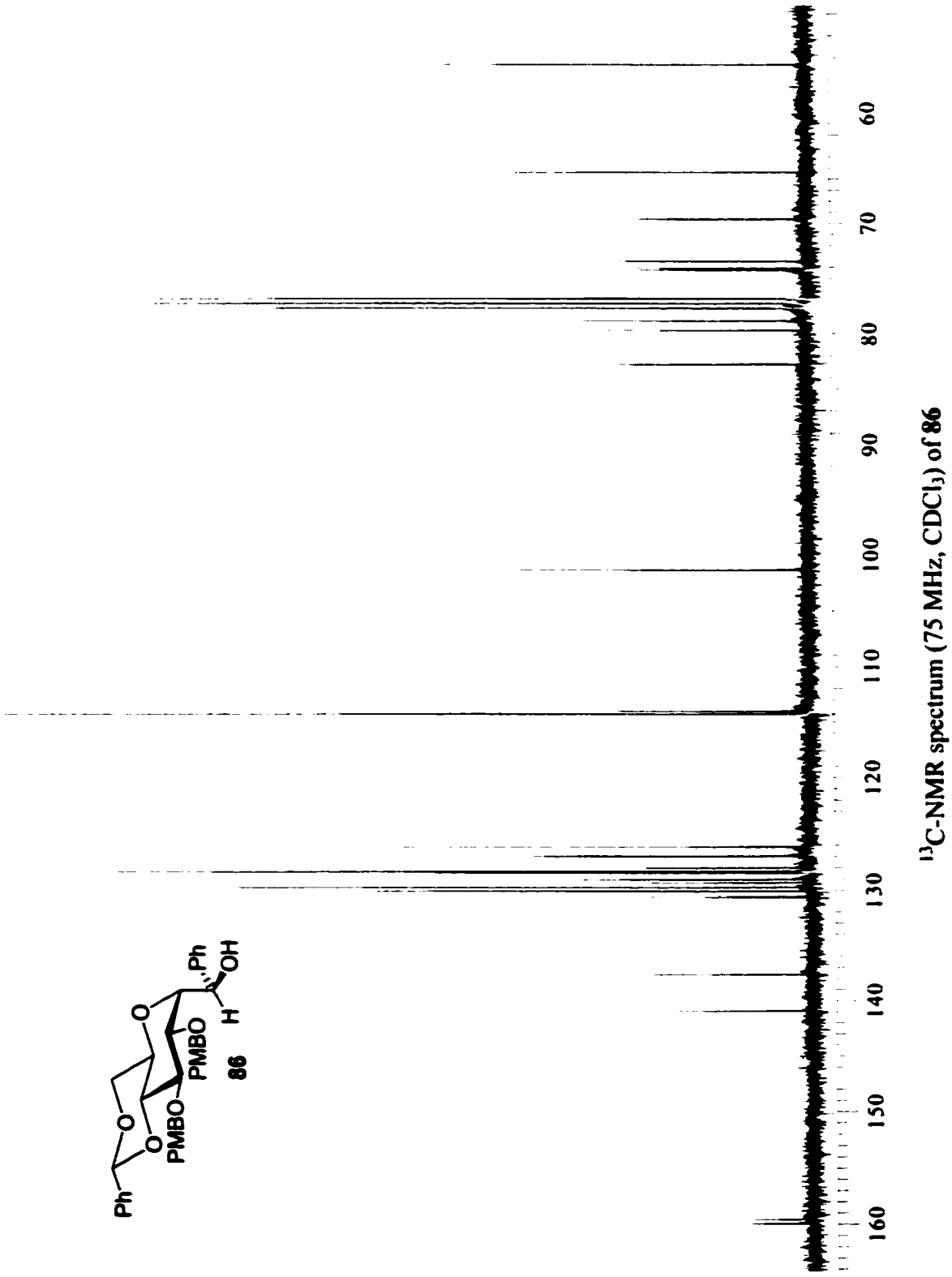
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **85**



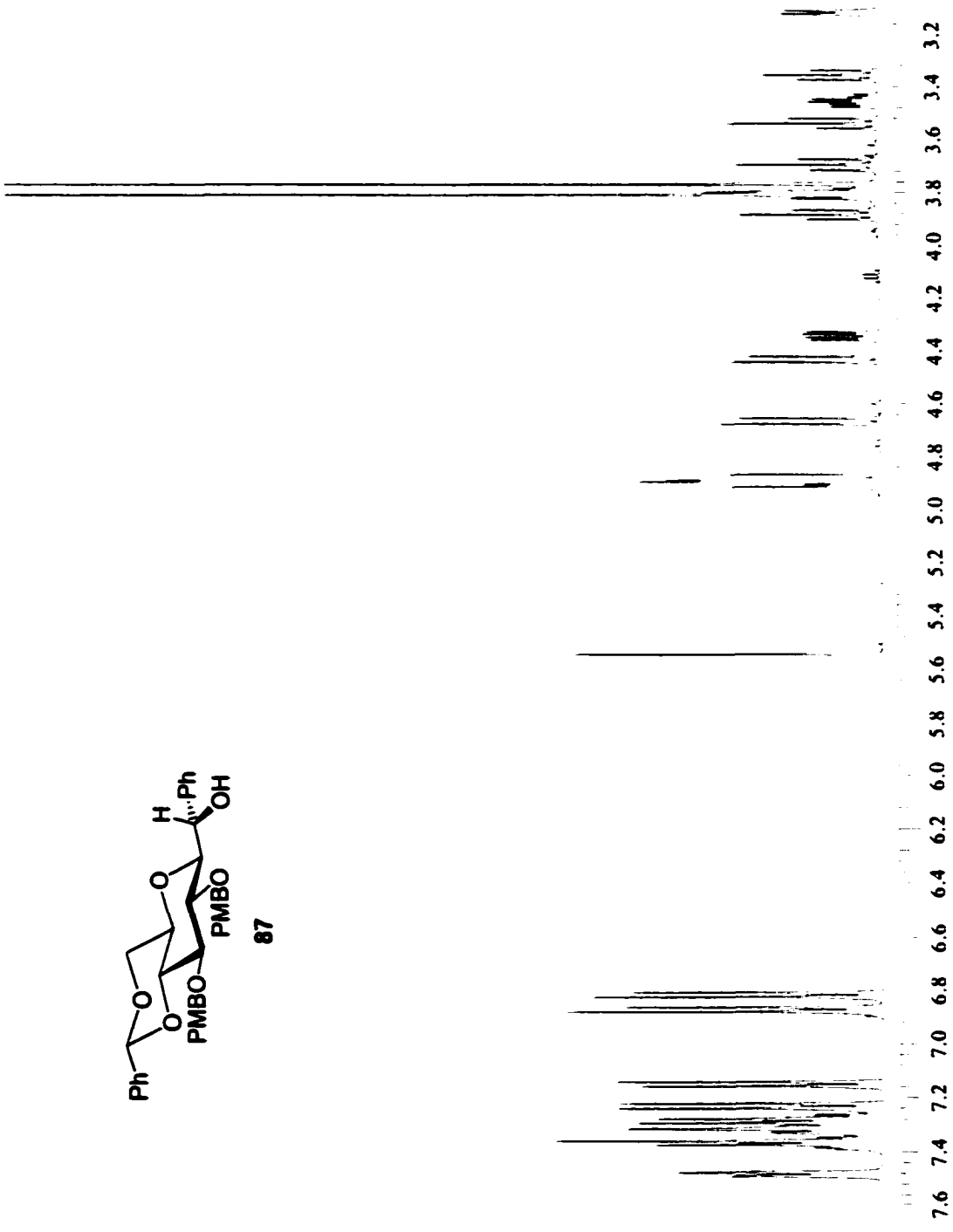
^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **85**



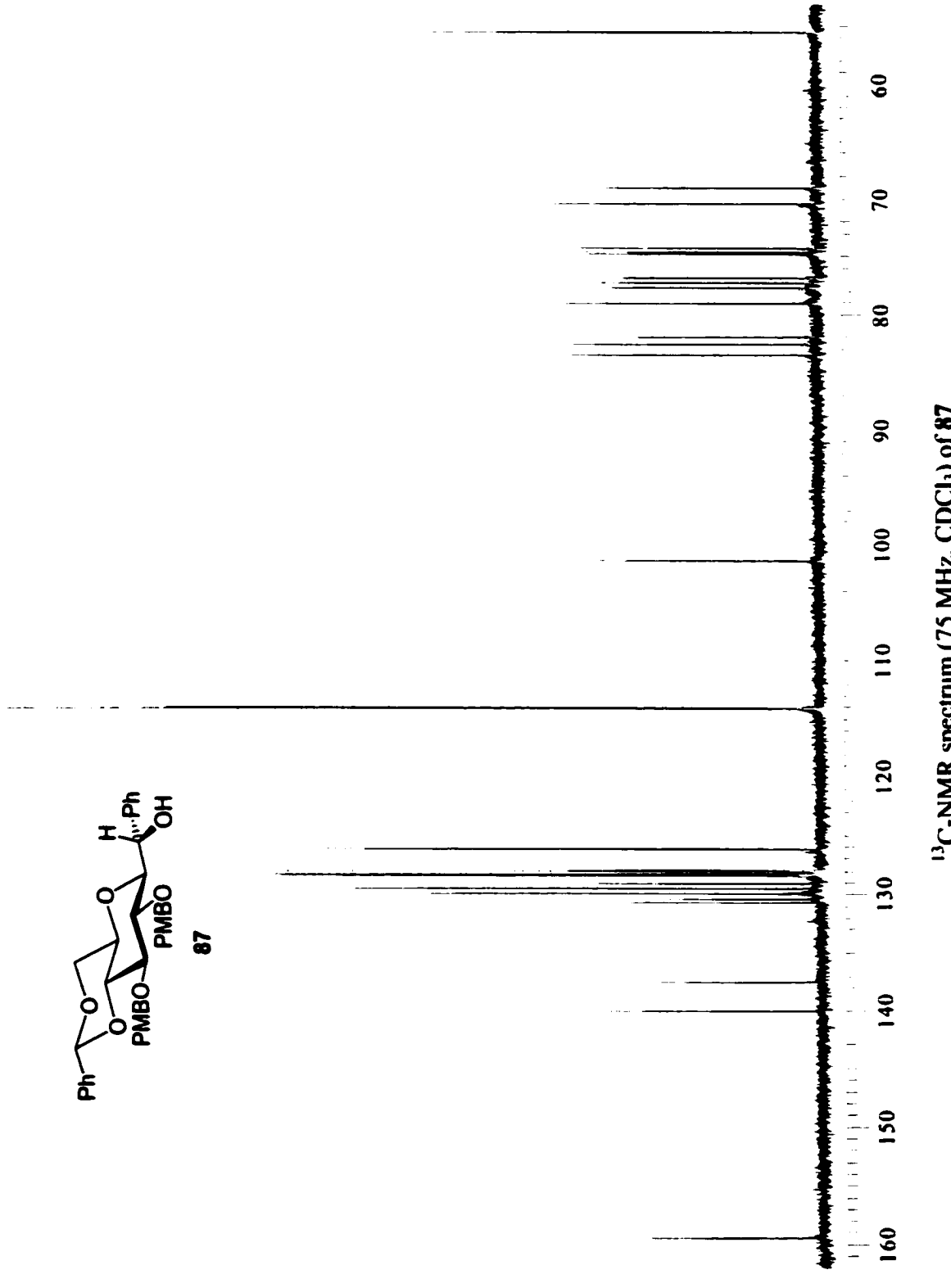
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **86**



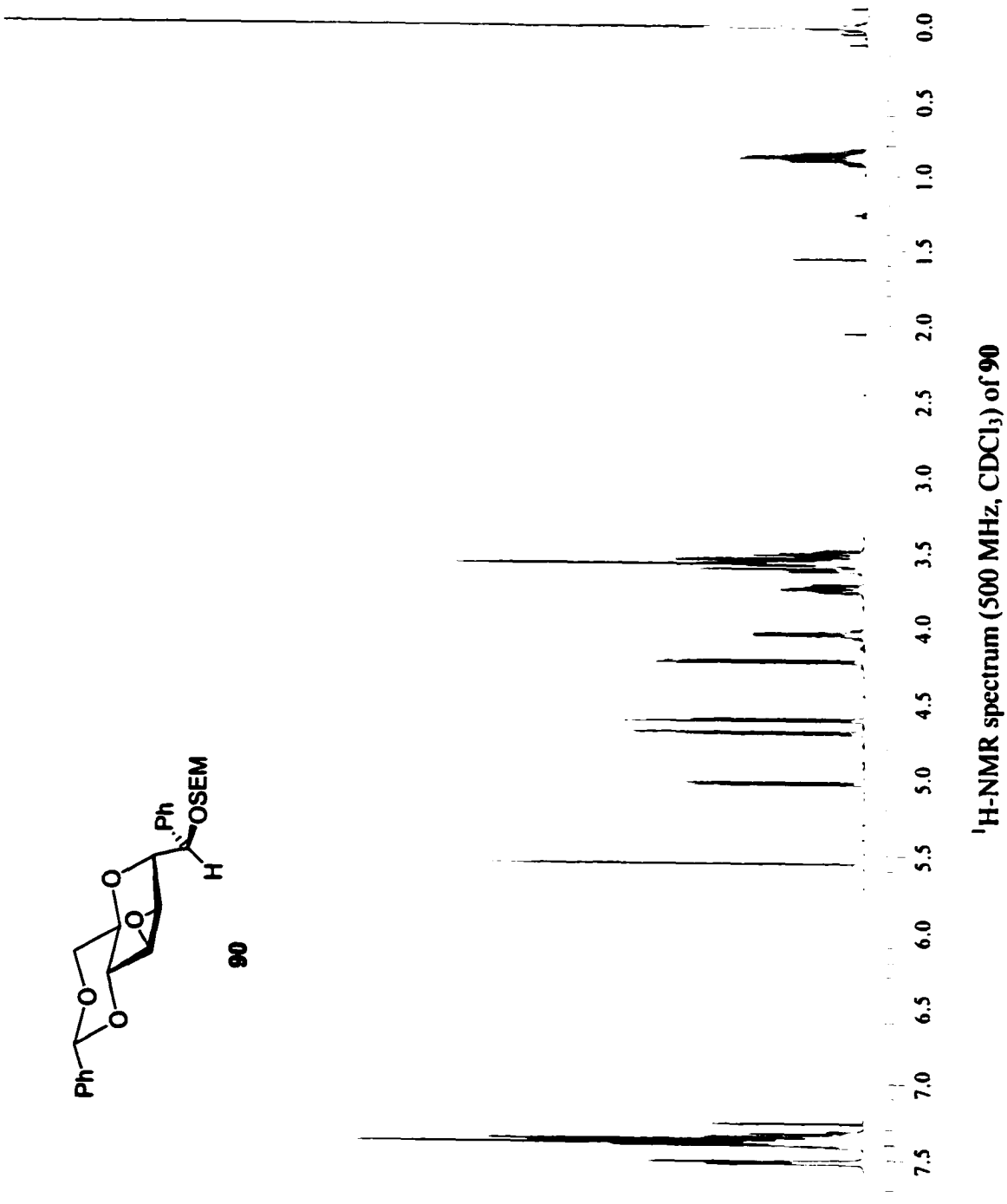
^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **86**



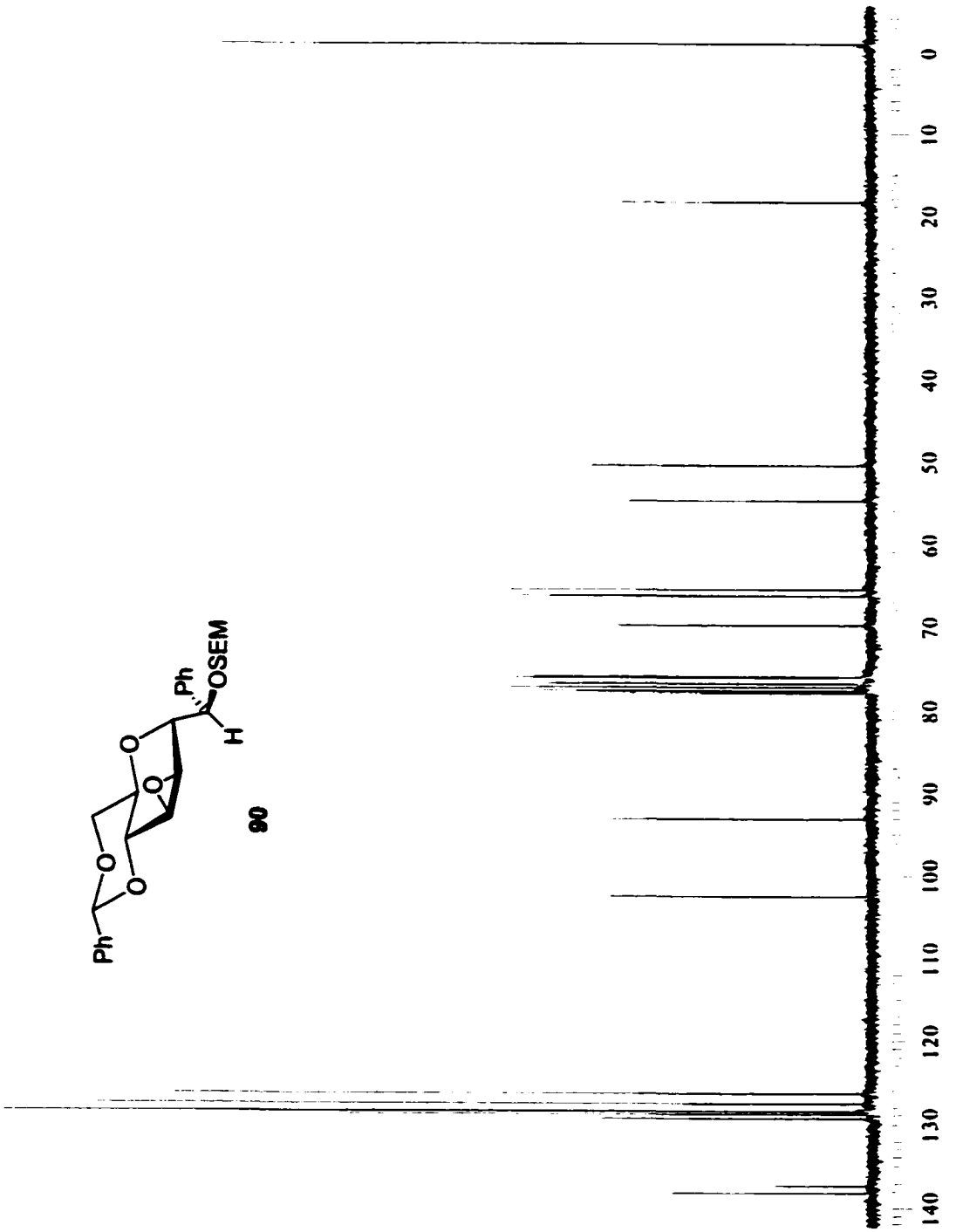
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **87**



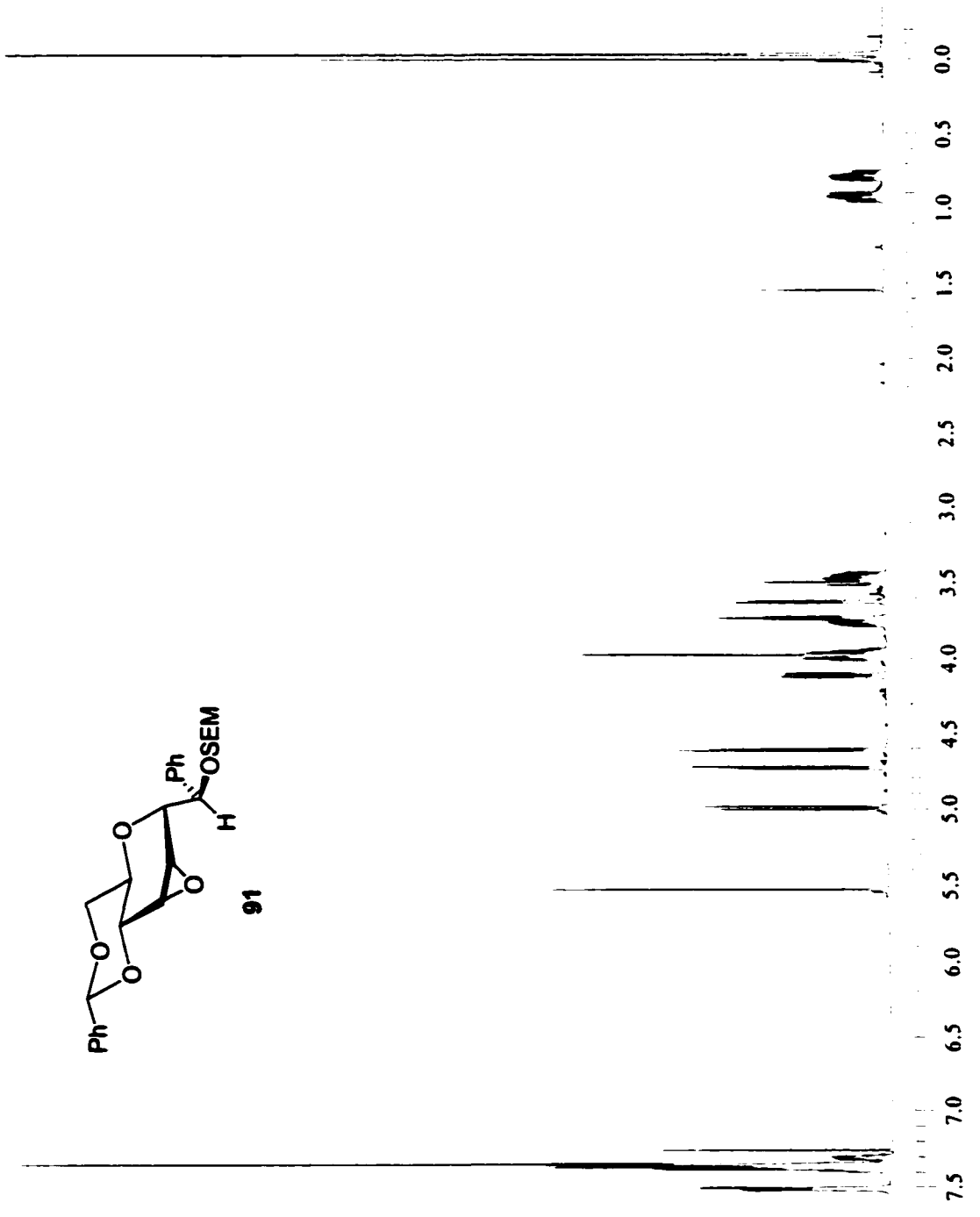
^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **87**



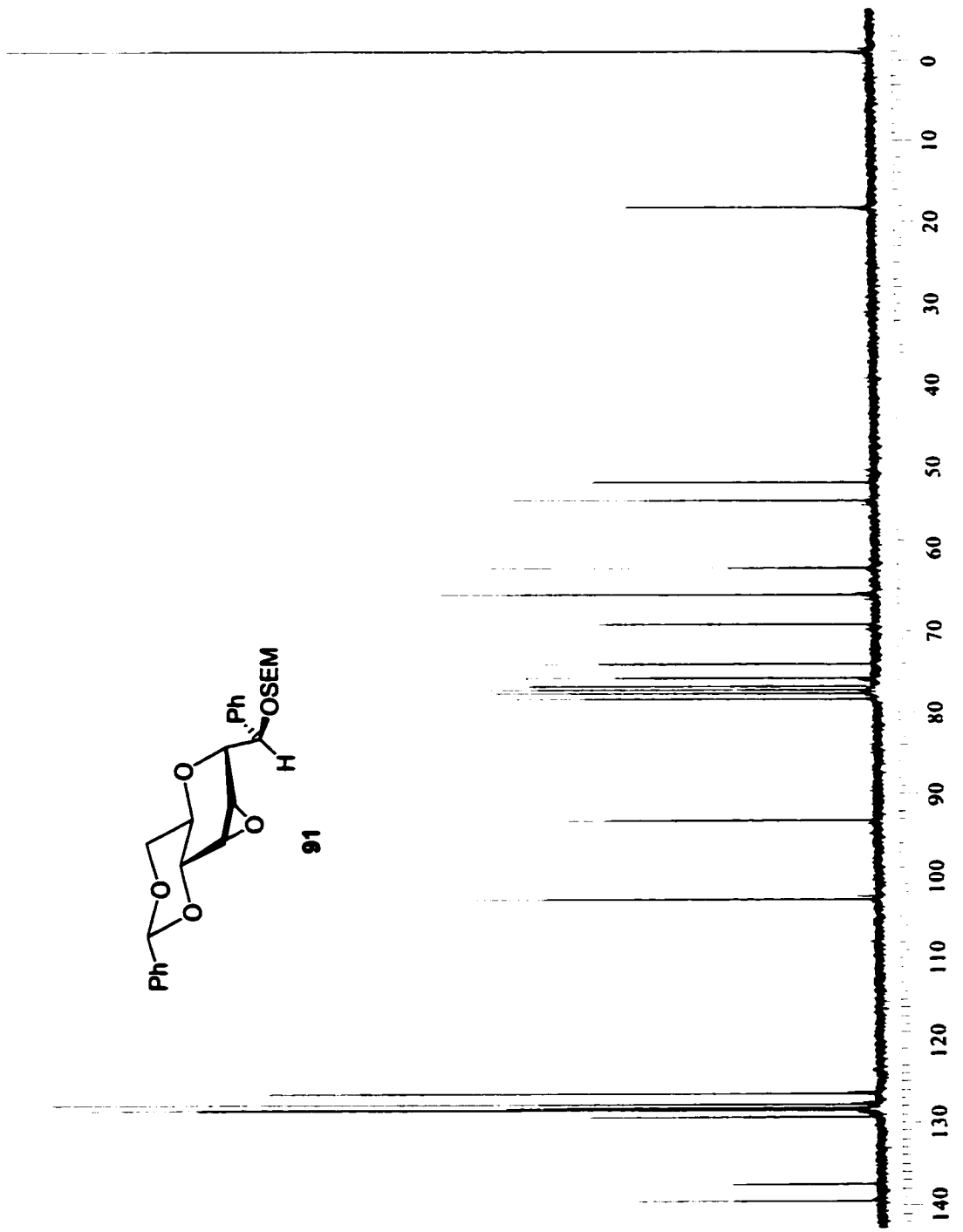
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **90**



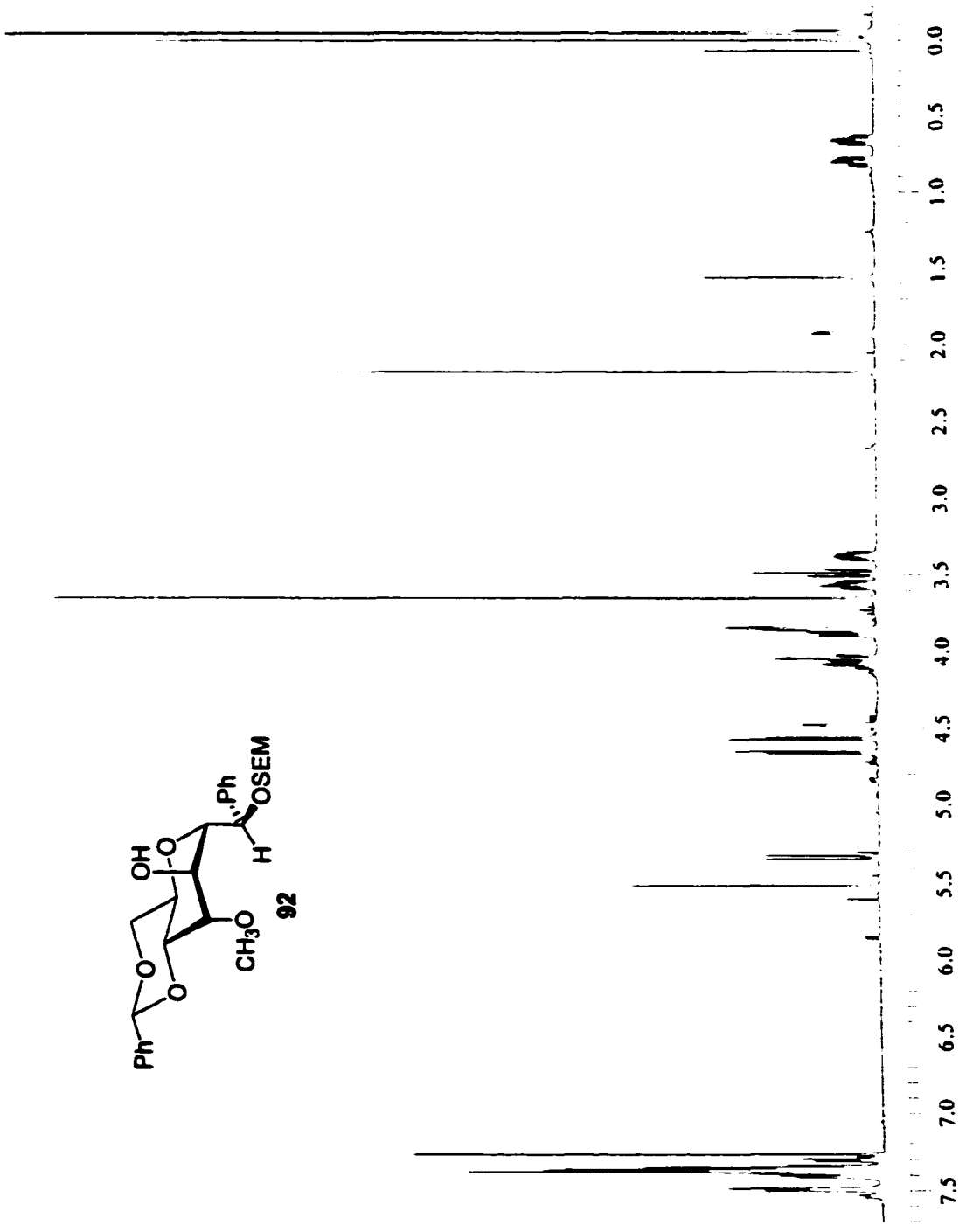
^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **90**



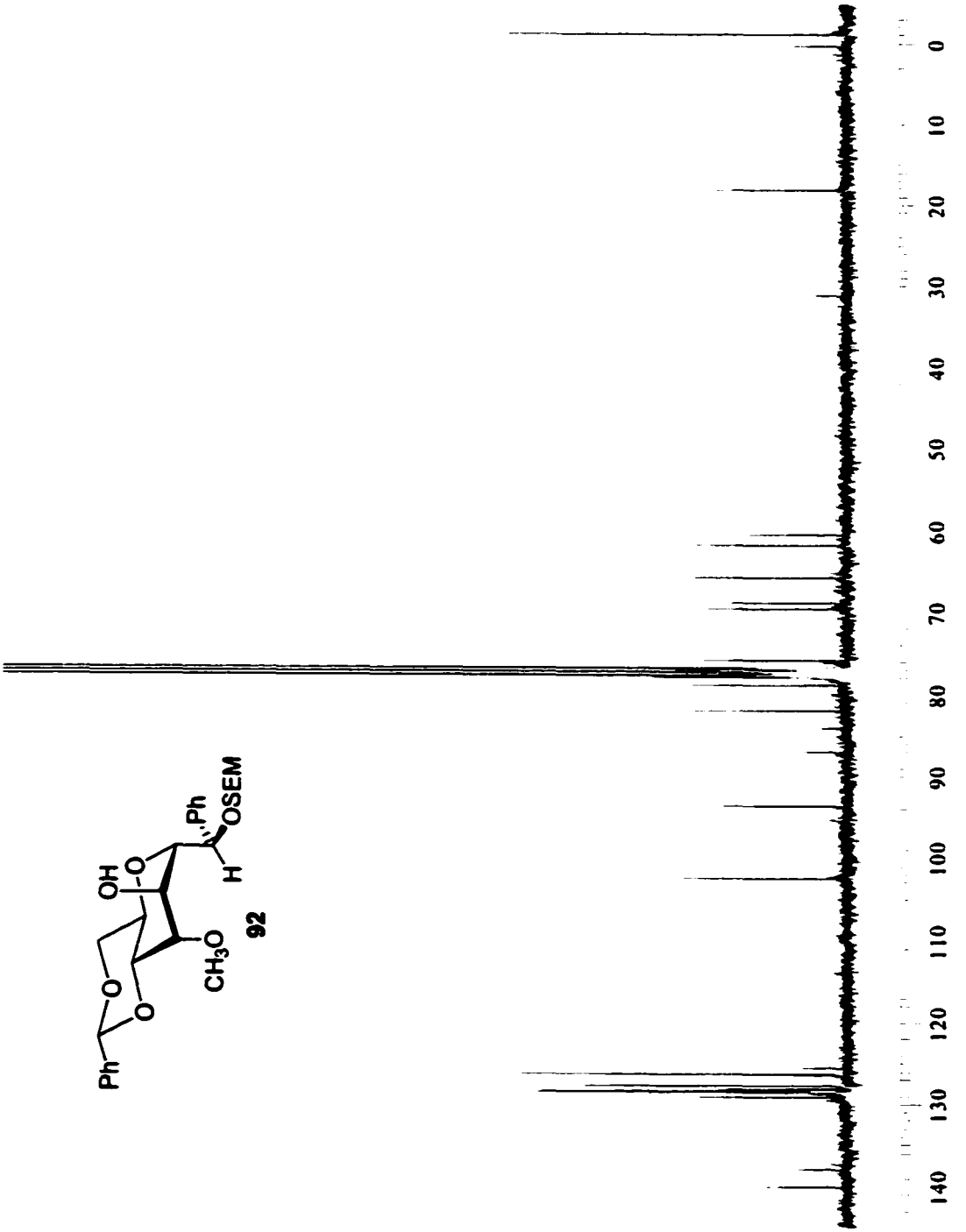
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **91**



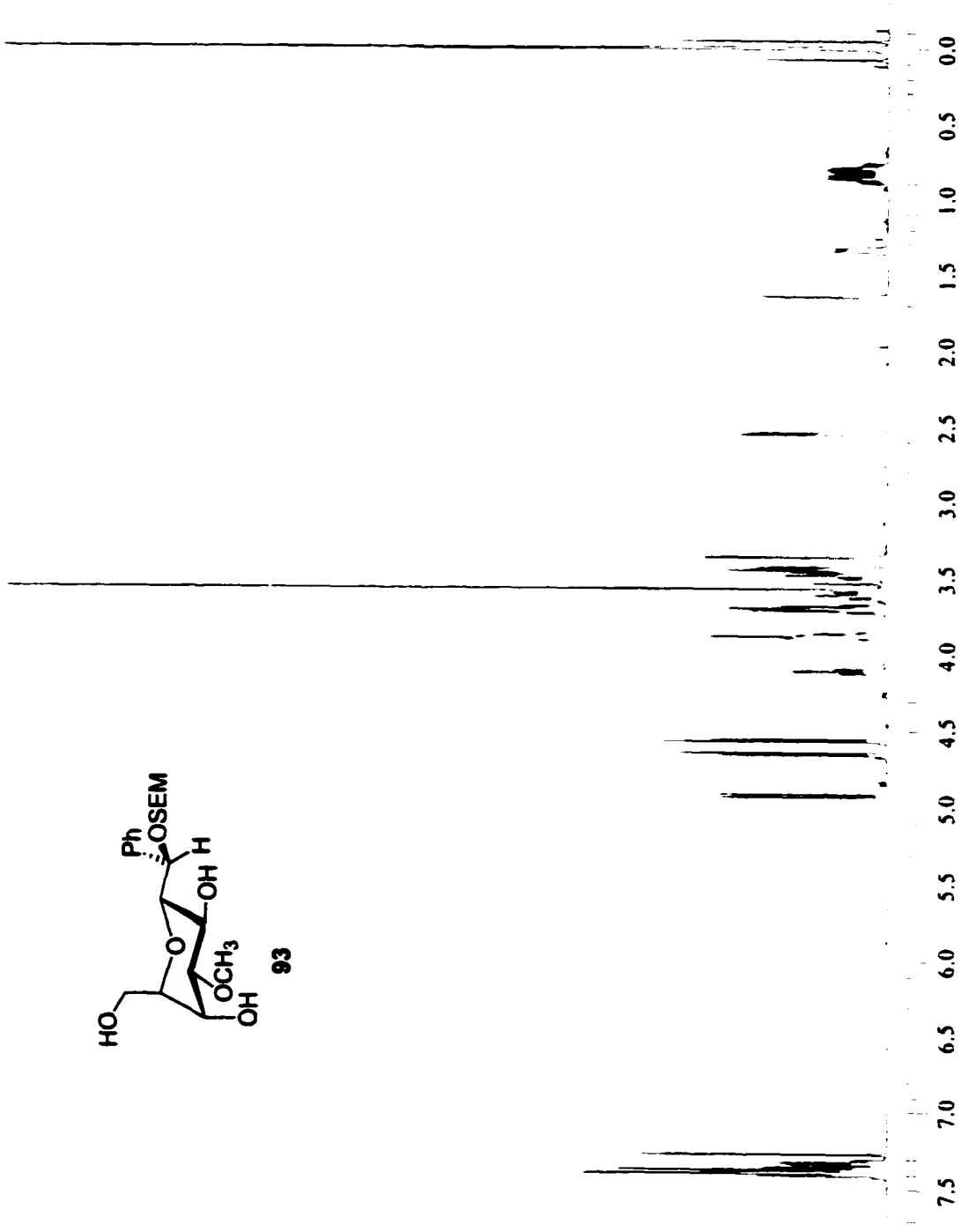
^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **91**



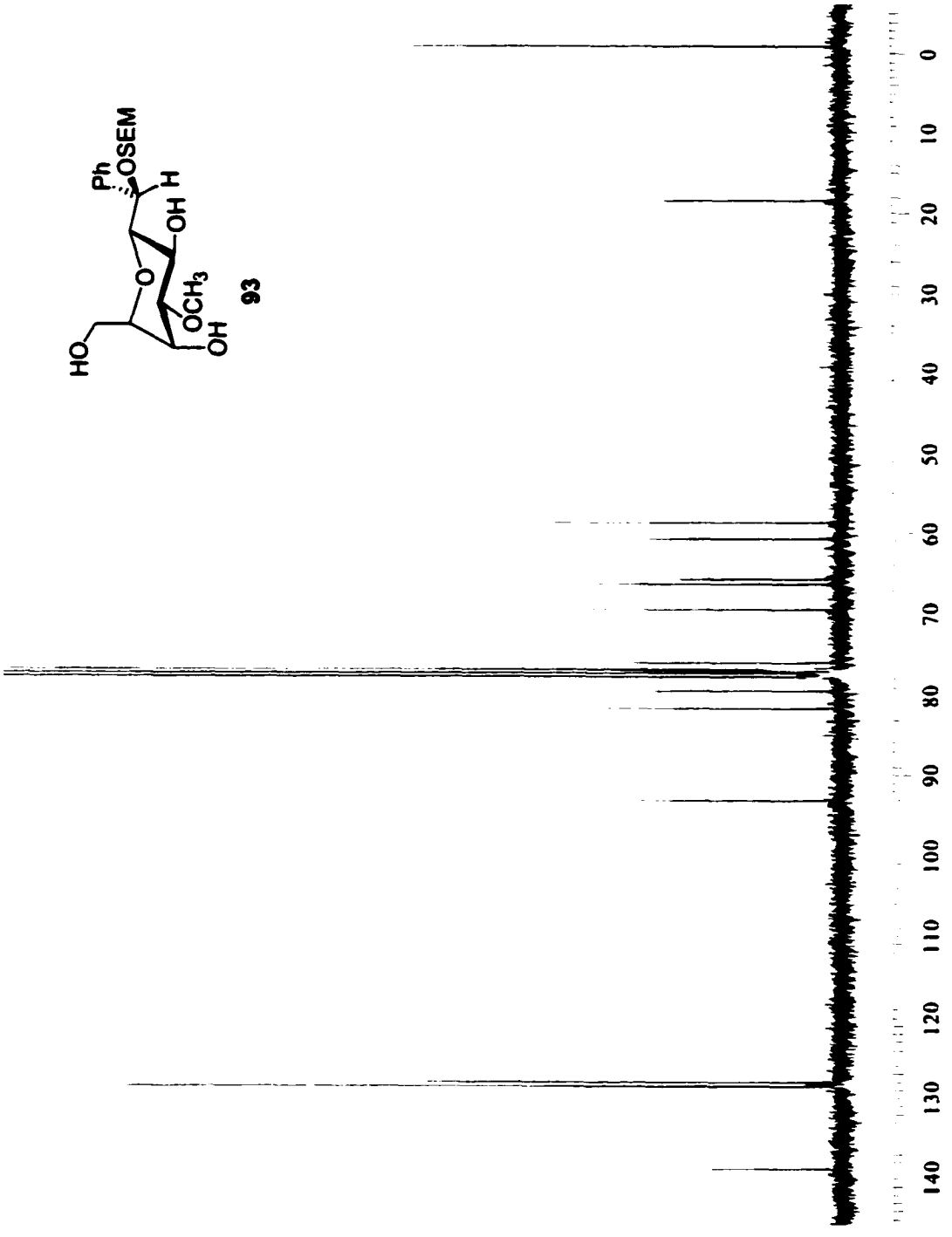
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **92**



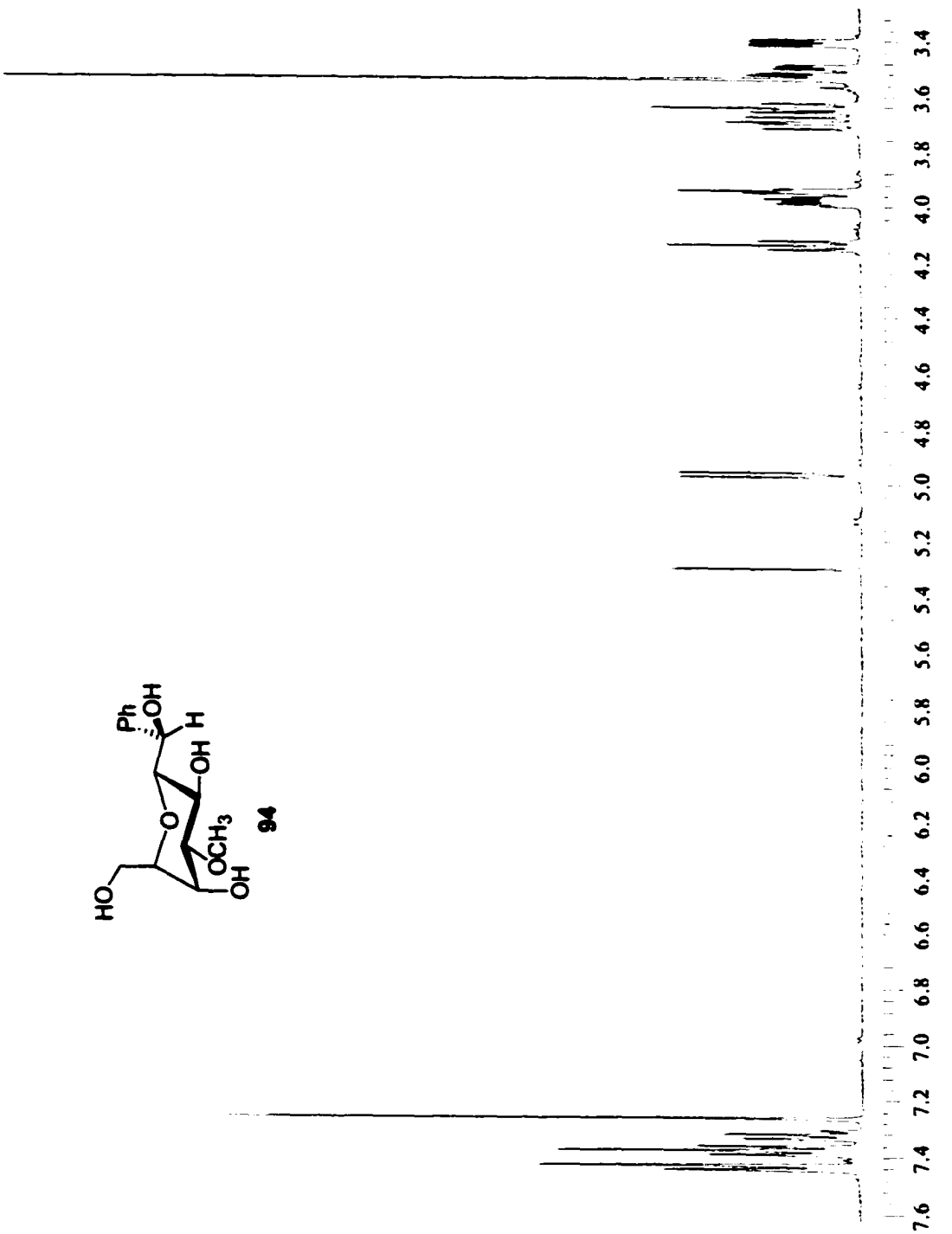
^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **92**



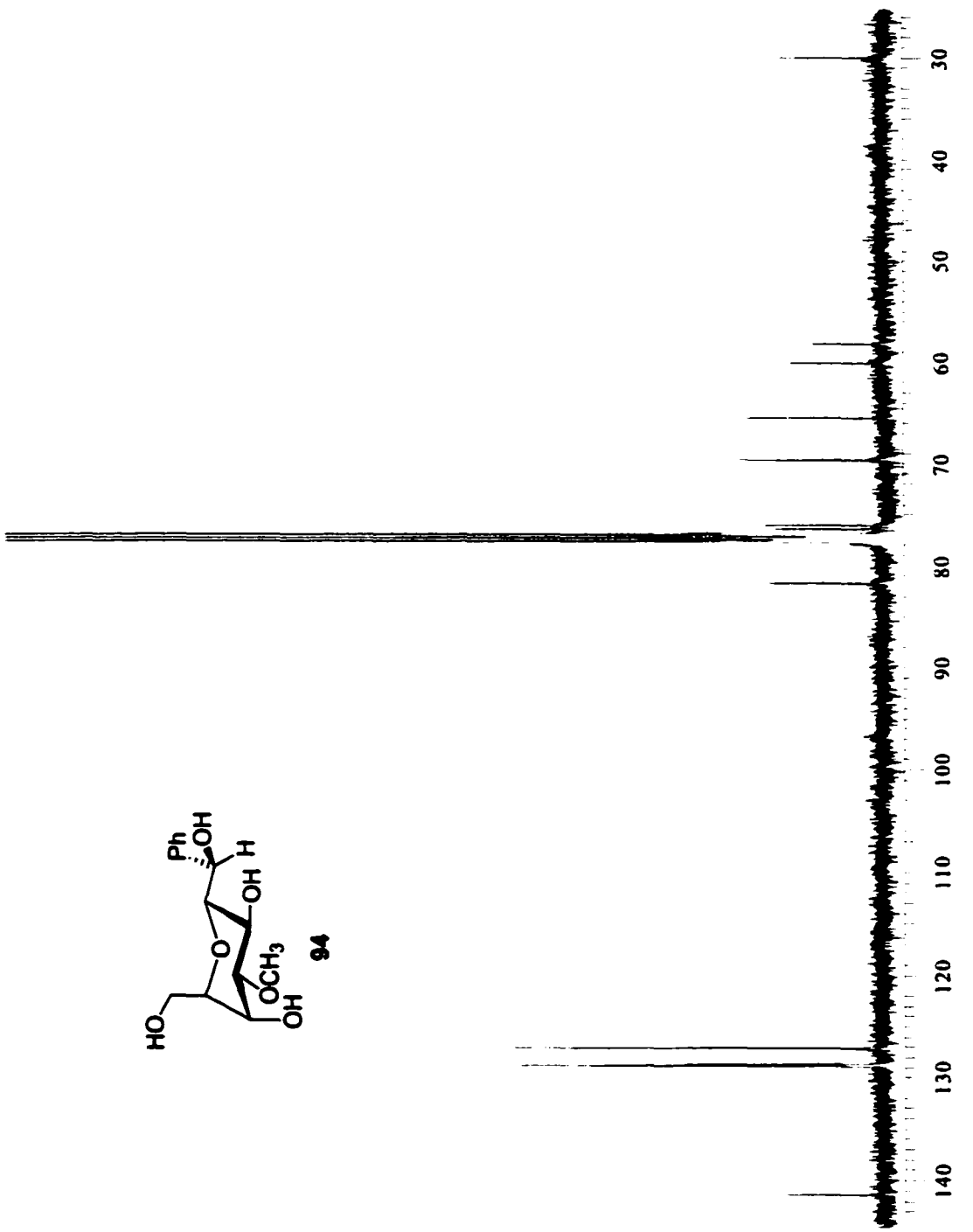
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **93**



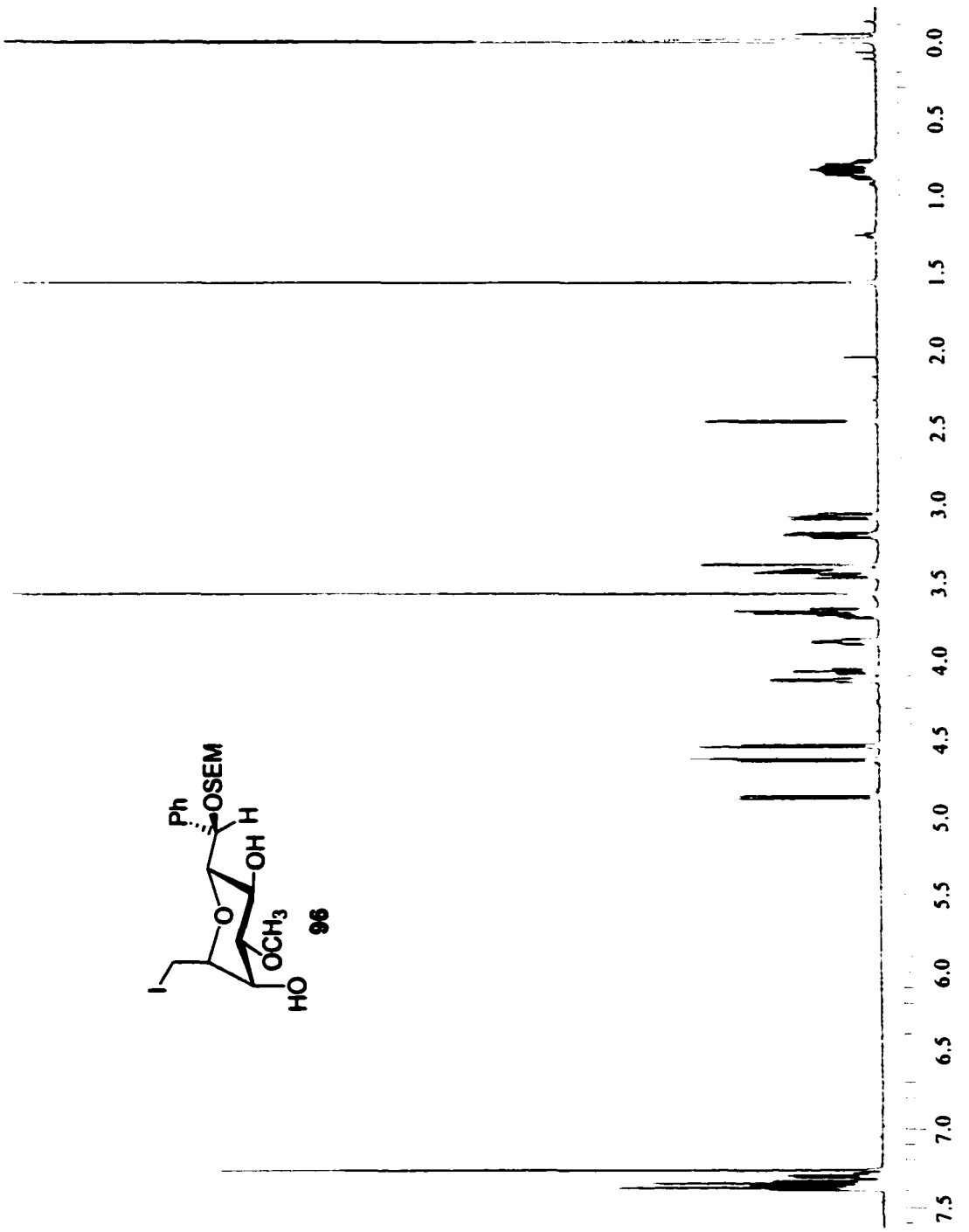
^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **93**



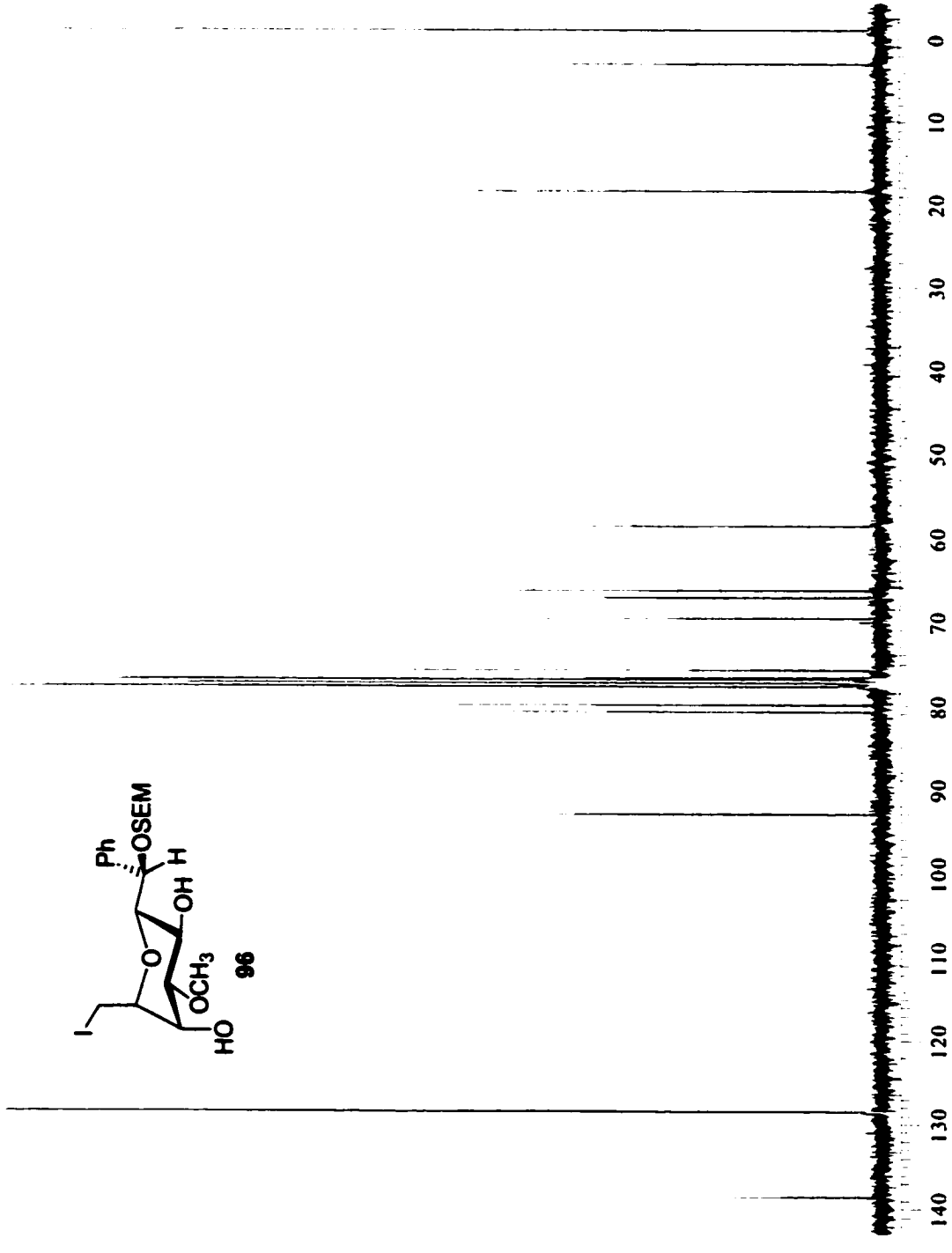
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **94**



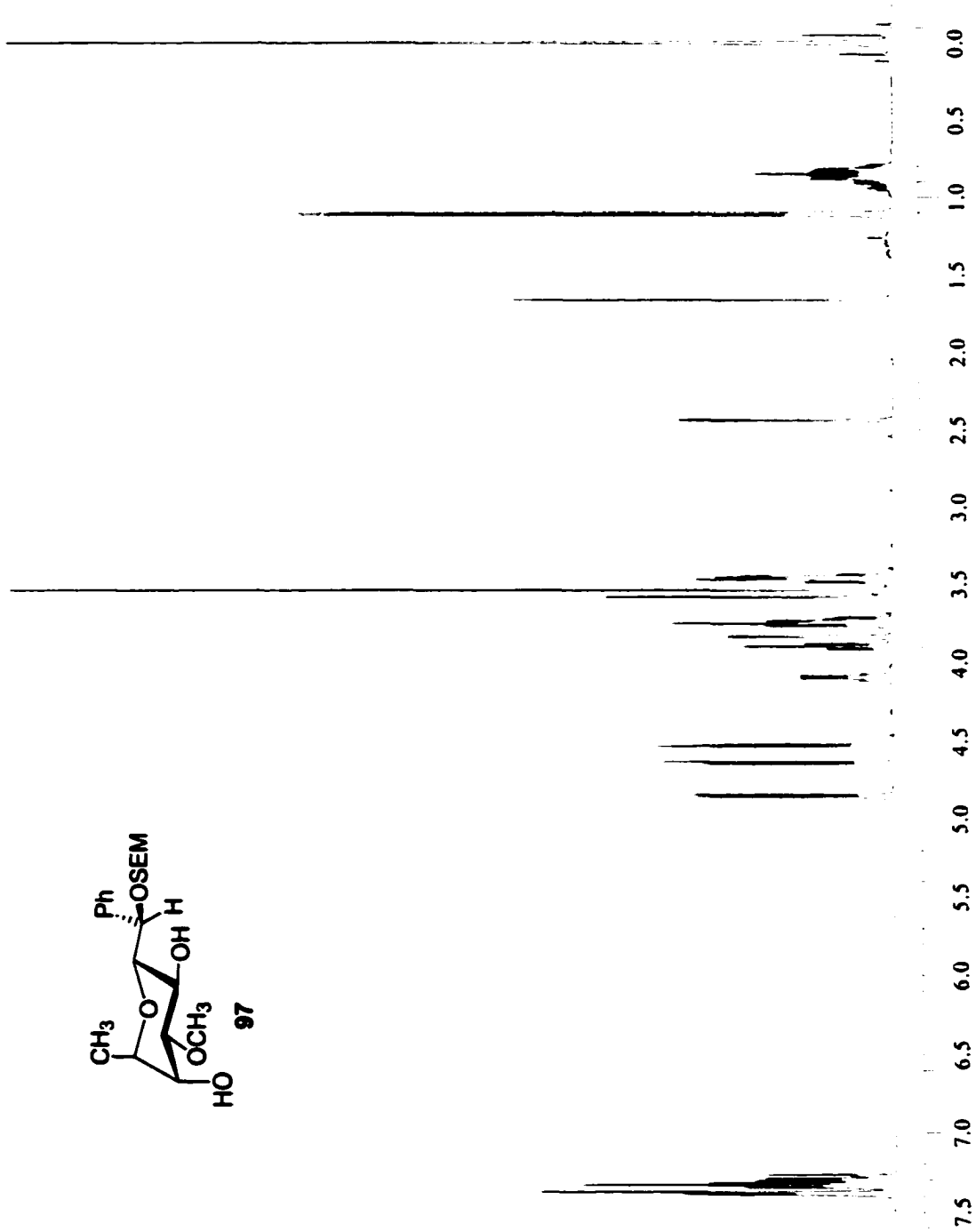
^{13}C-NMR spectrum (100 MHz, $CDCl_3$) of **94**



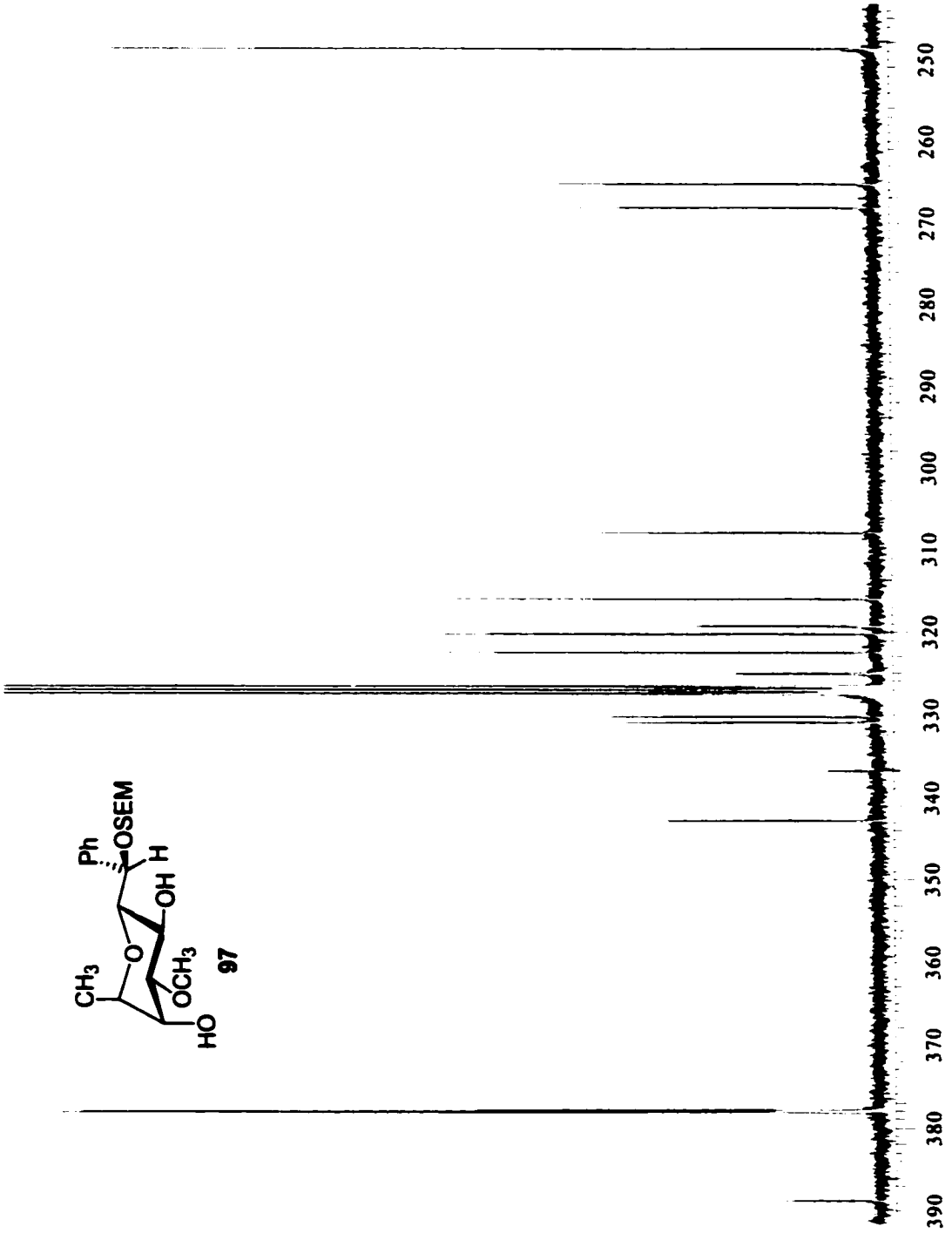
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **96**



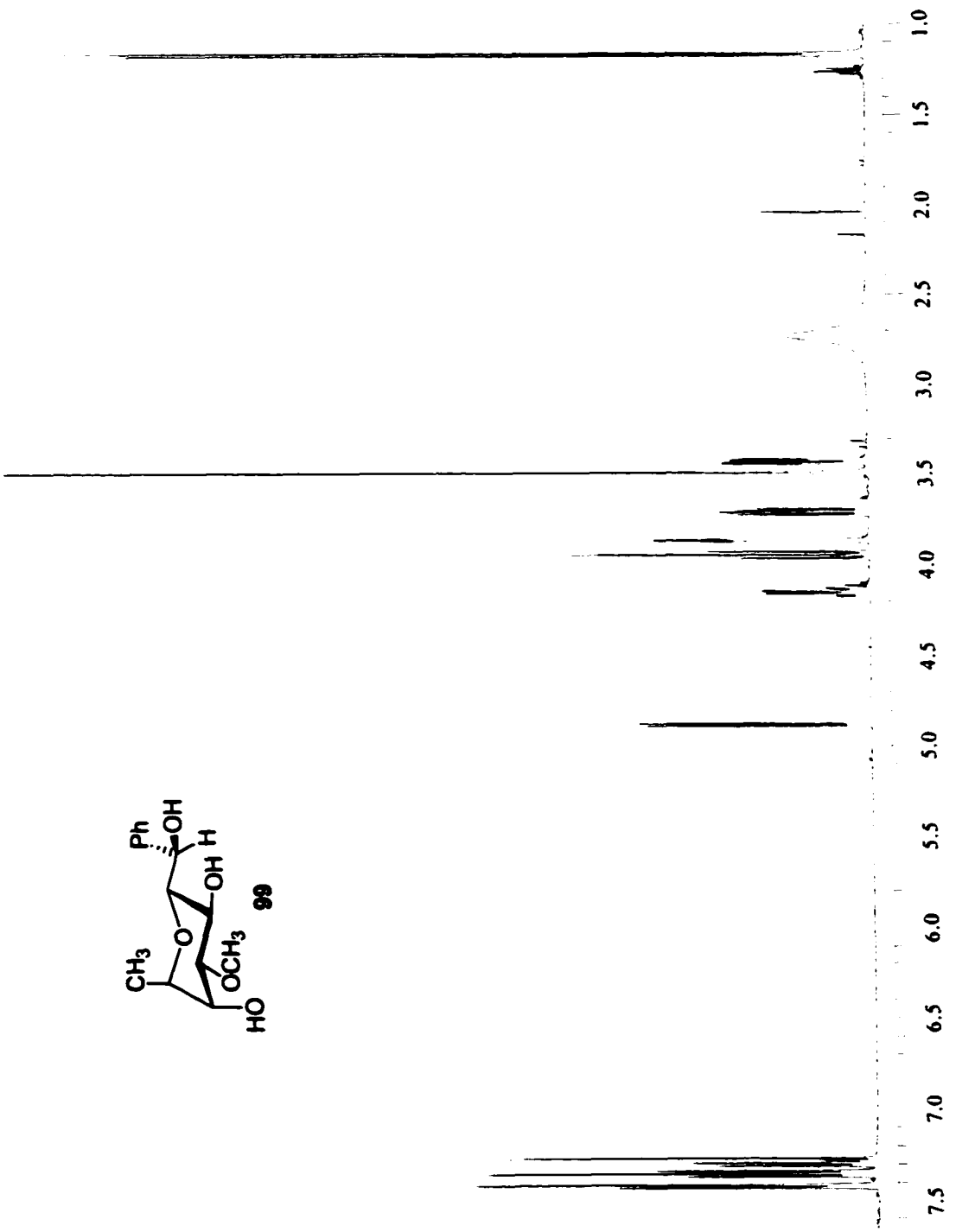
^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **96**



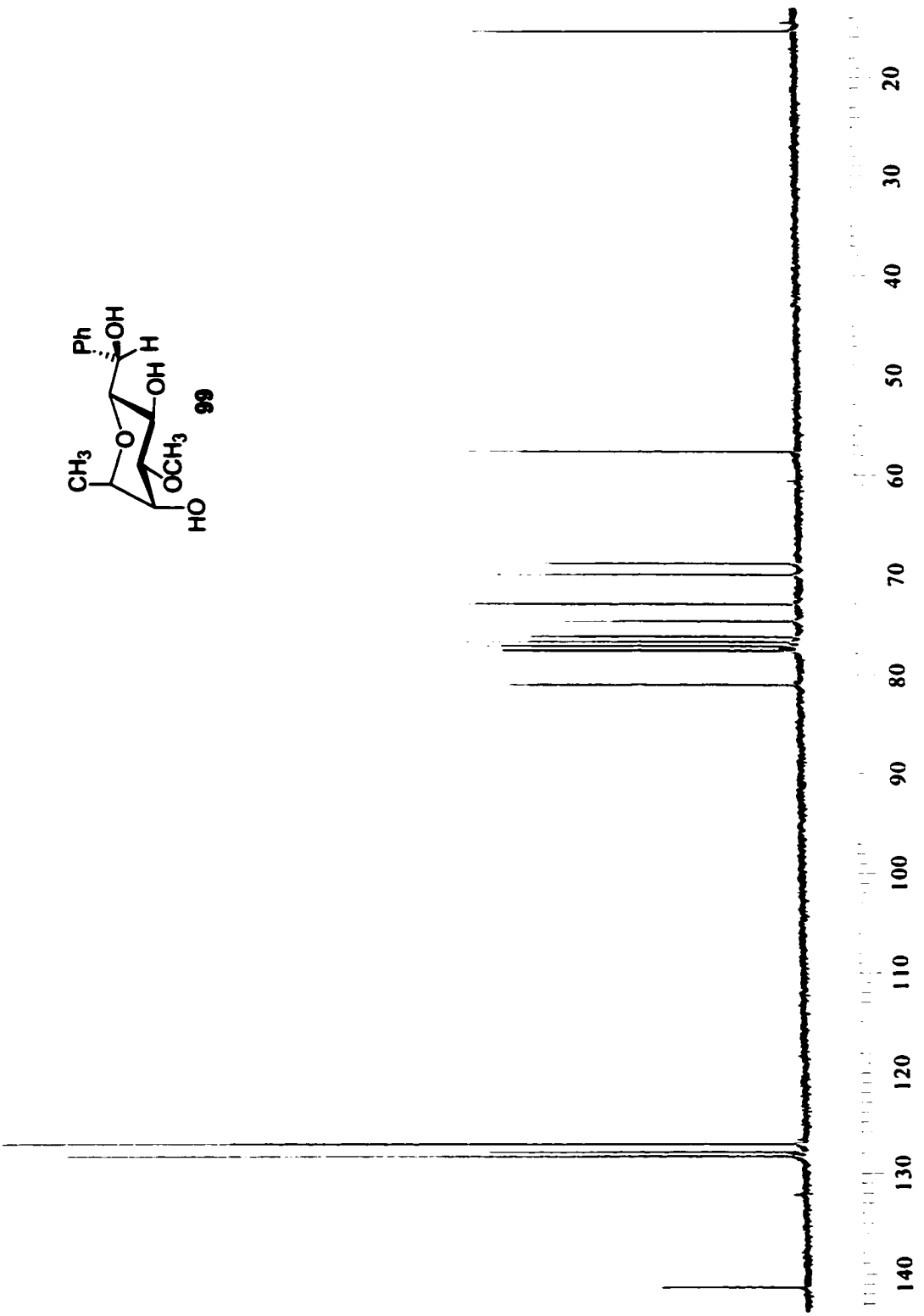
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **97**



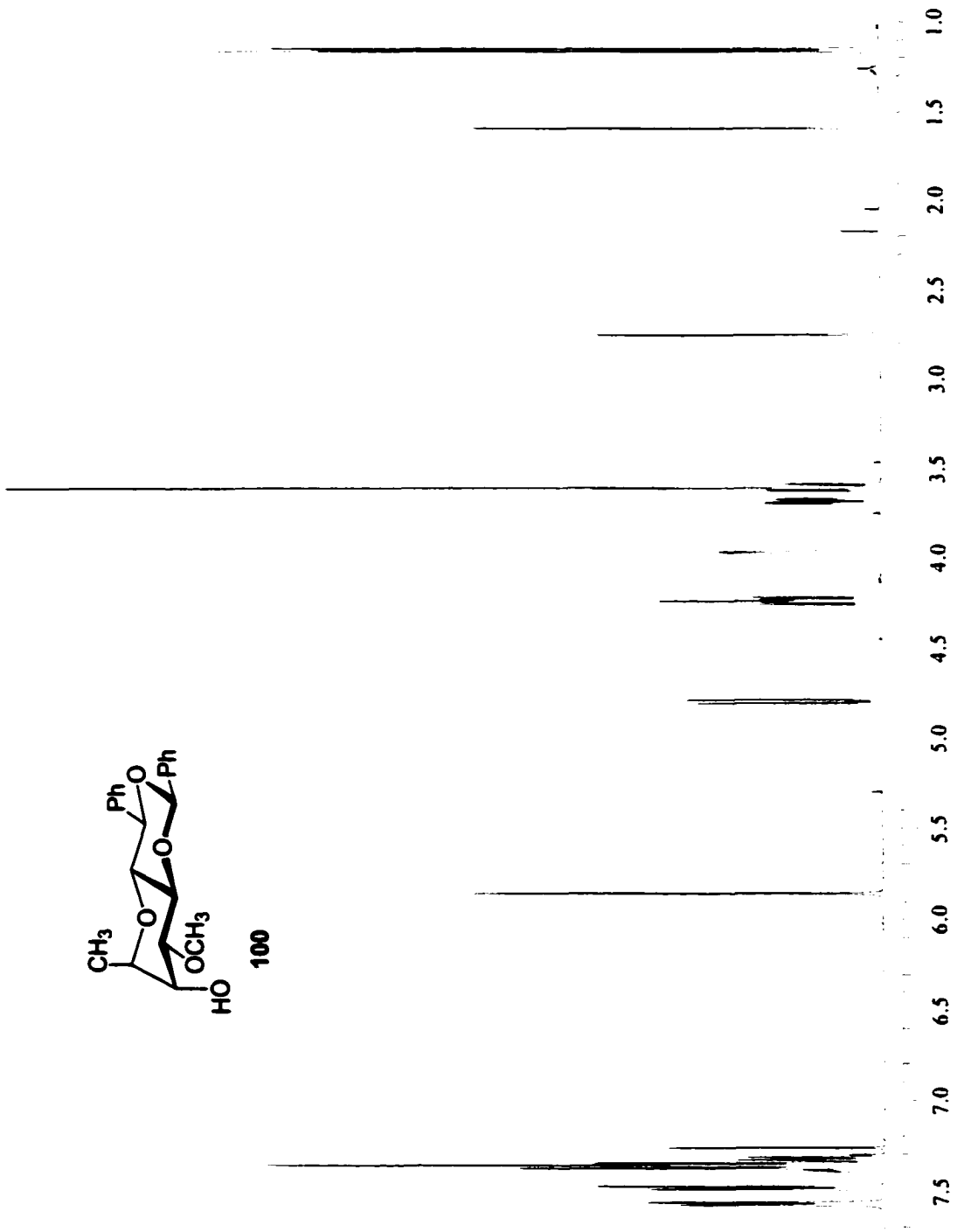
^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **97**



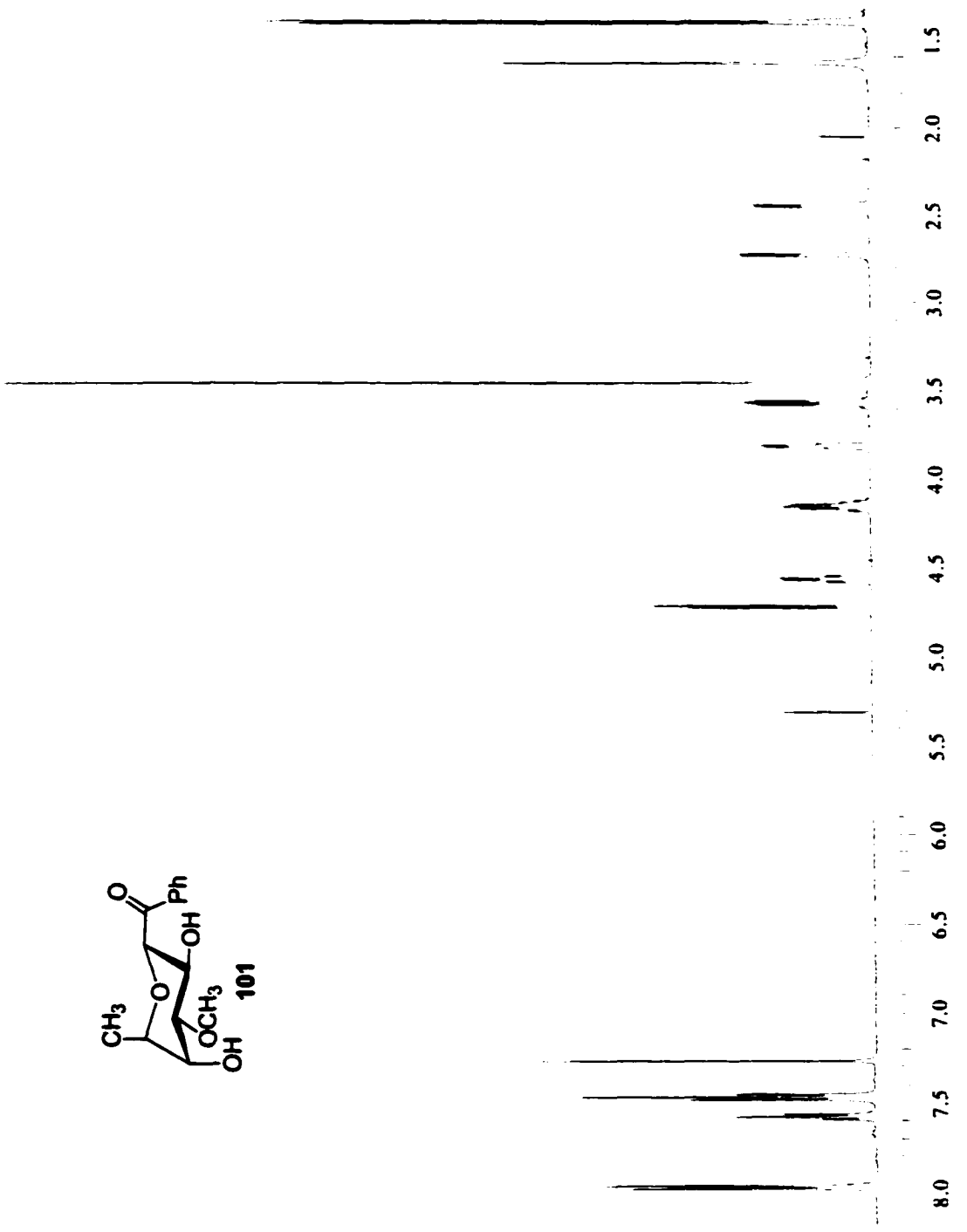
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **99**



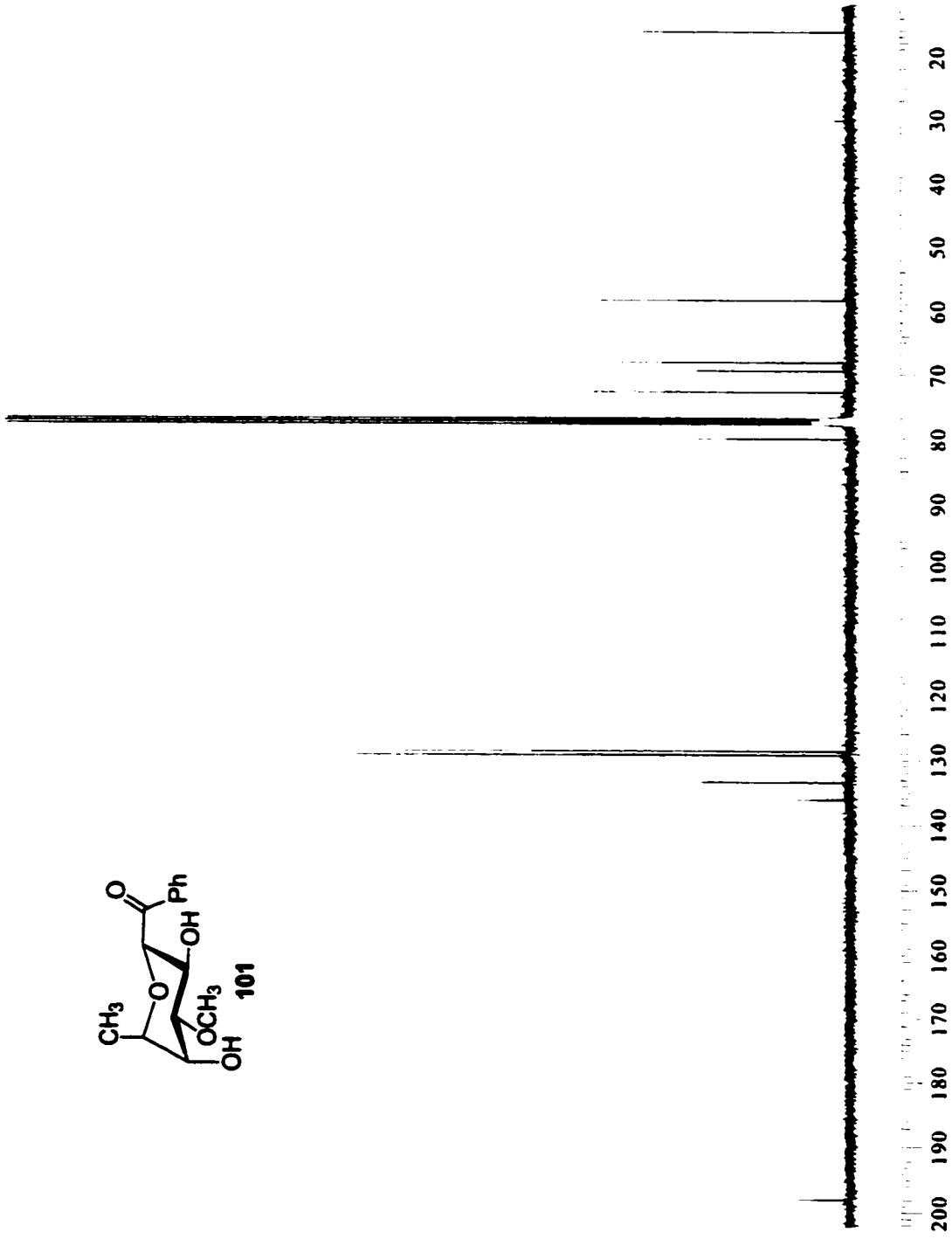
^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **99**



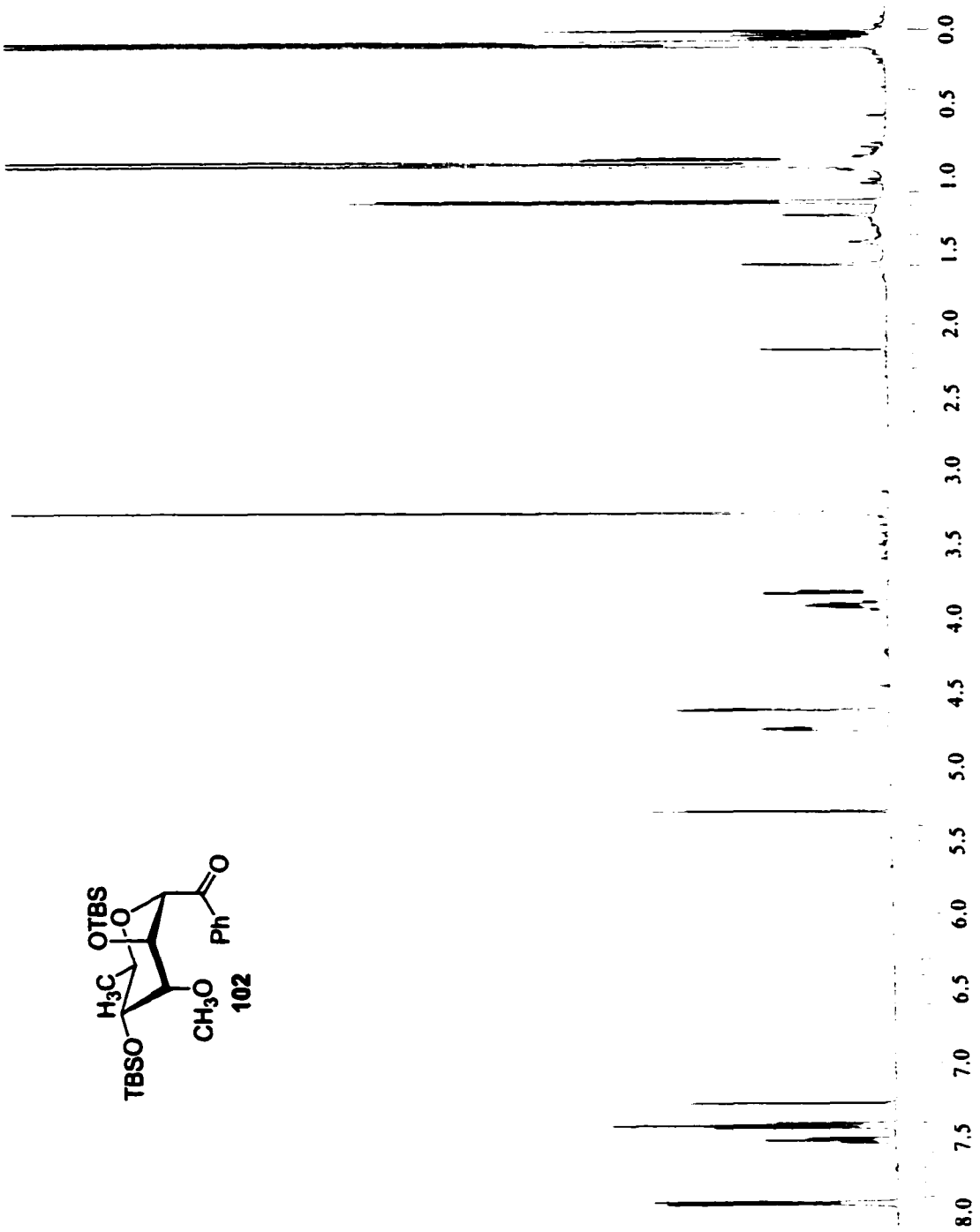
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **100**



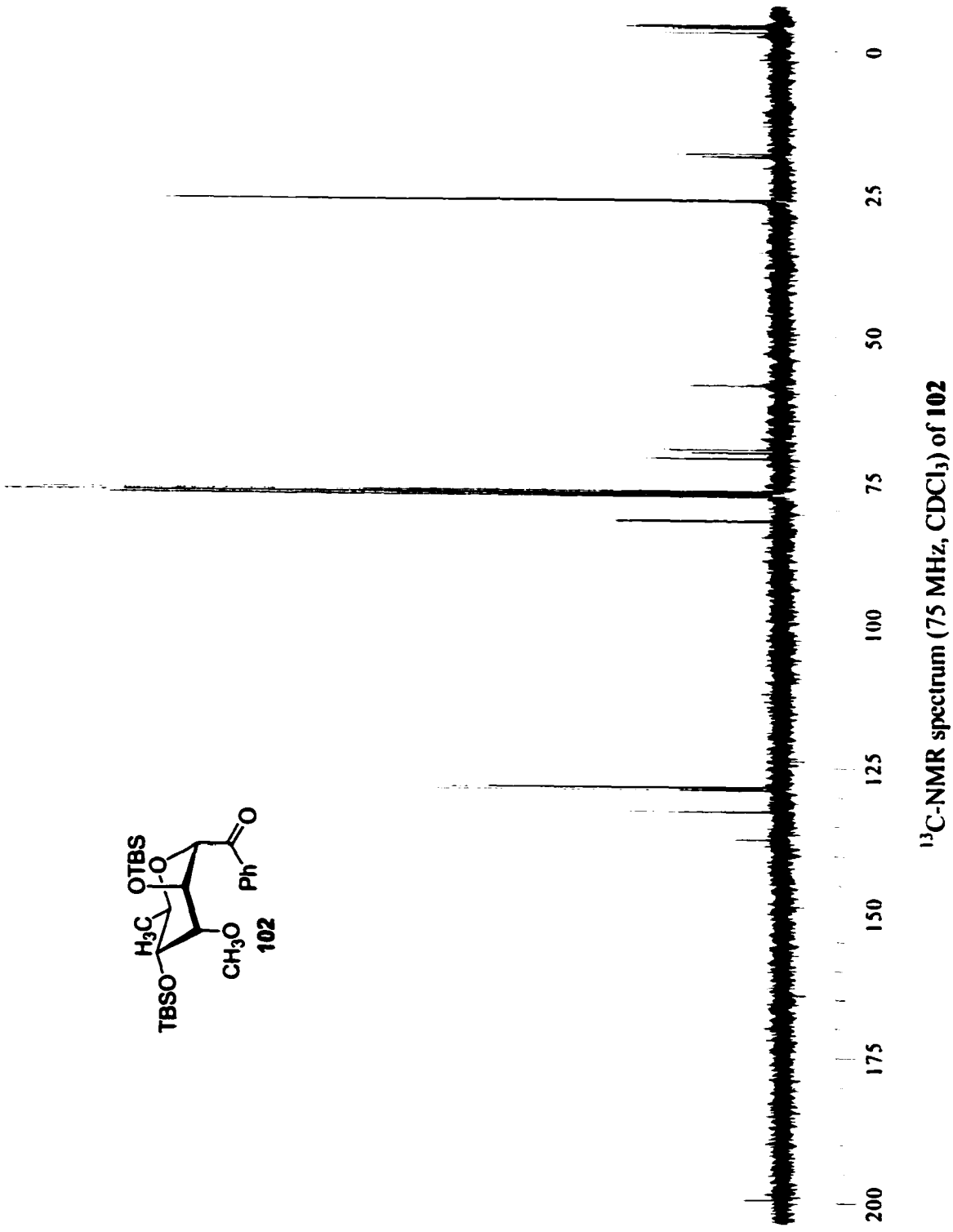
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **101**



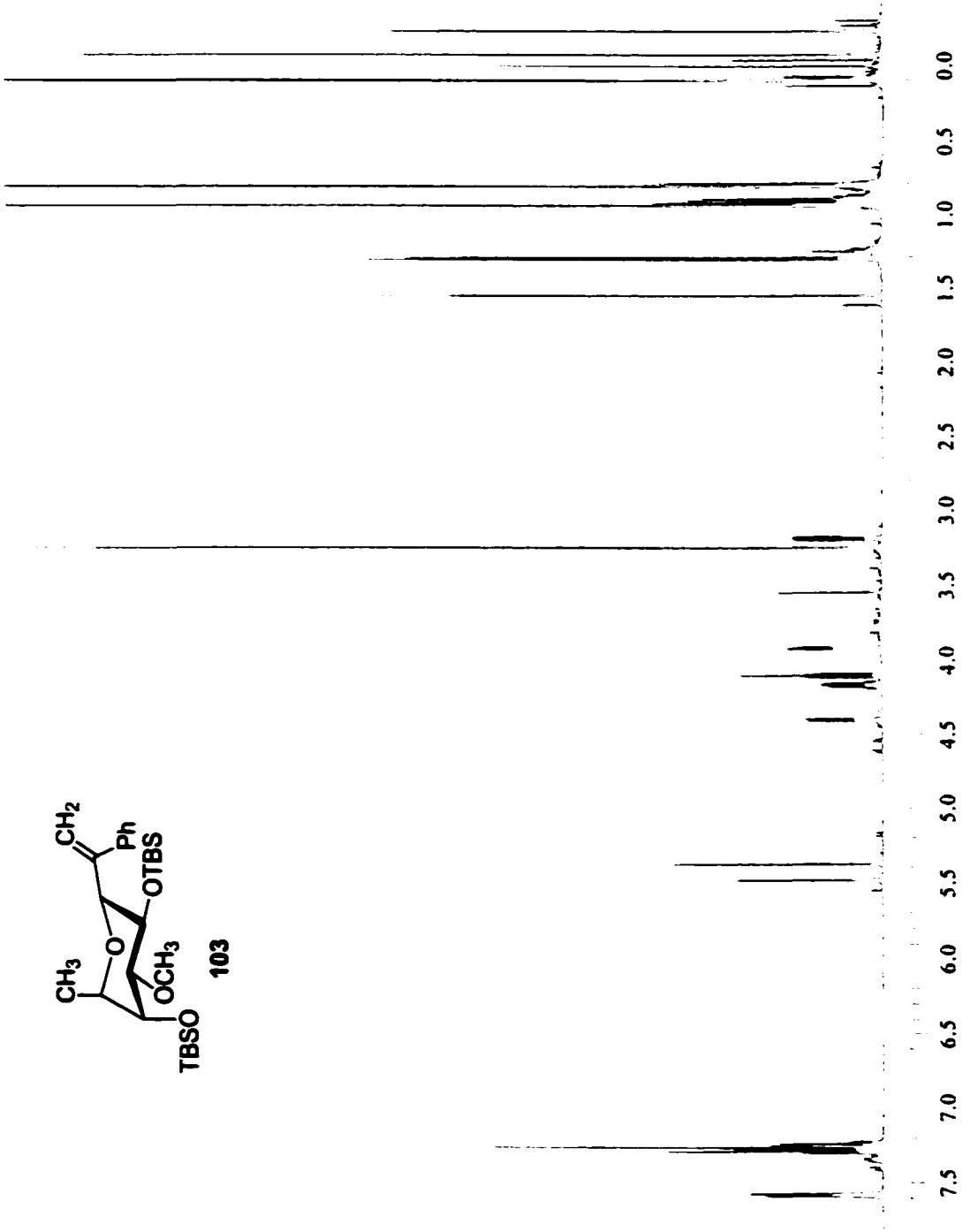
^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **101**



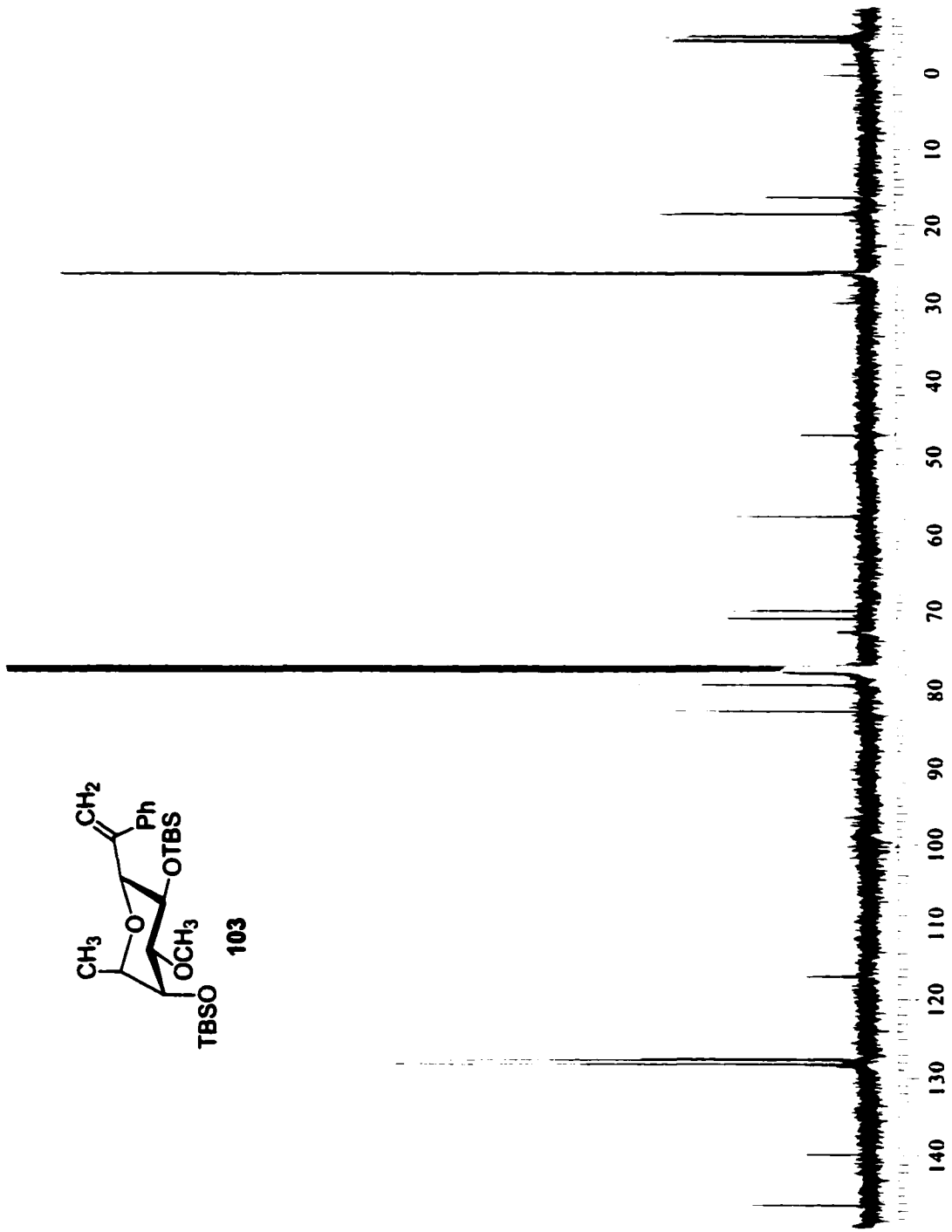
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **102**



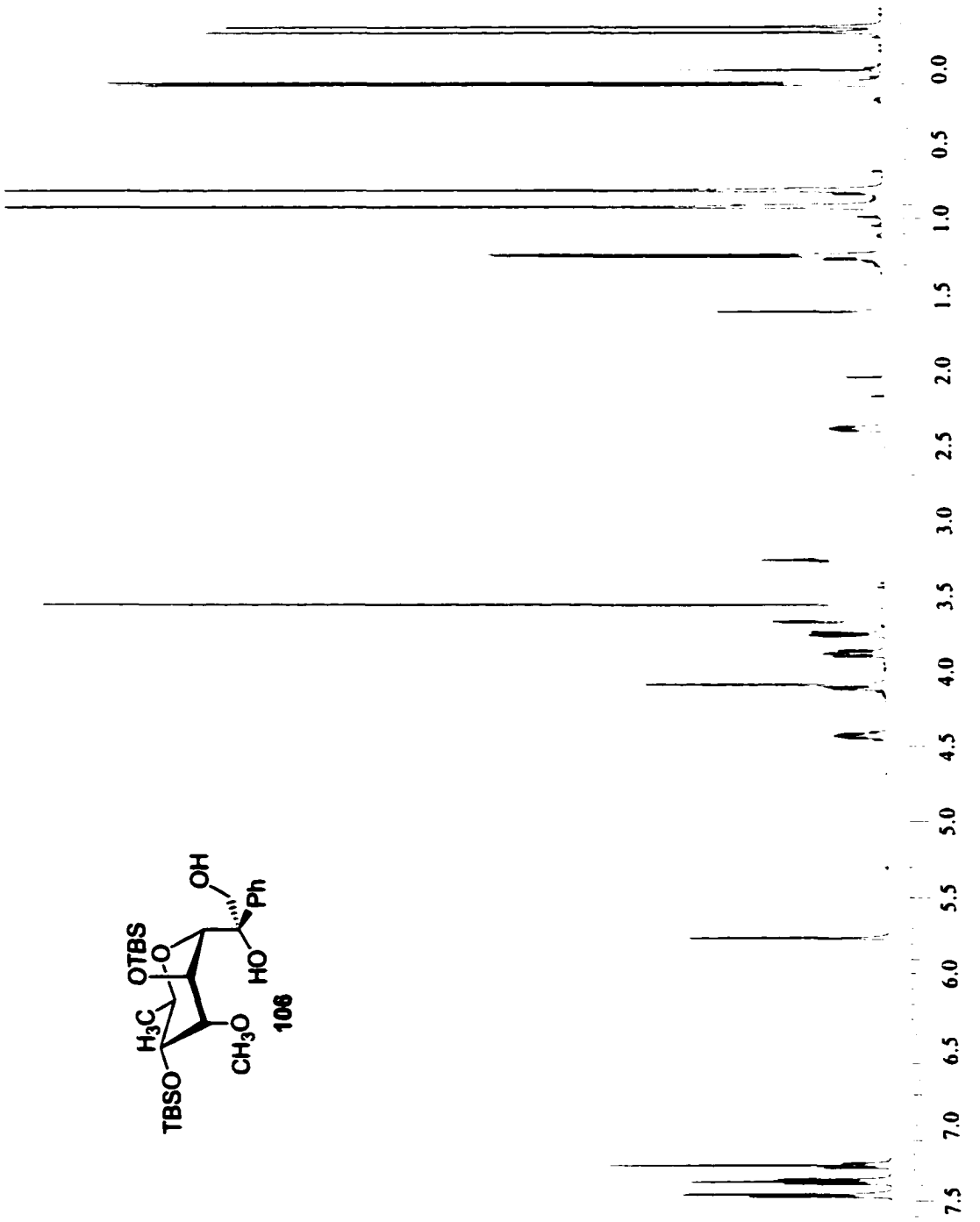
^{13}C-NMR spectrum (75 MHz, $CDCl_3$) of **102**



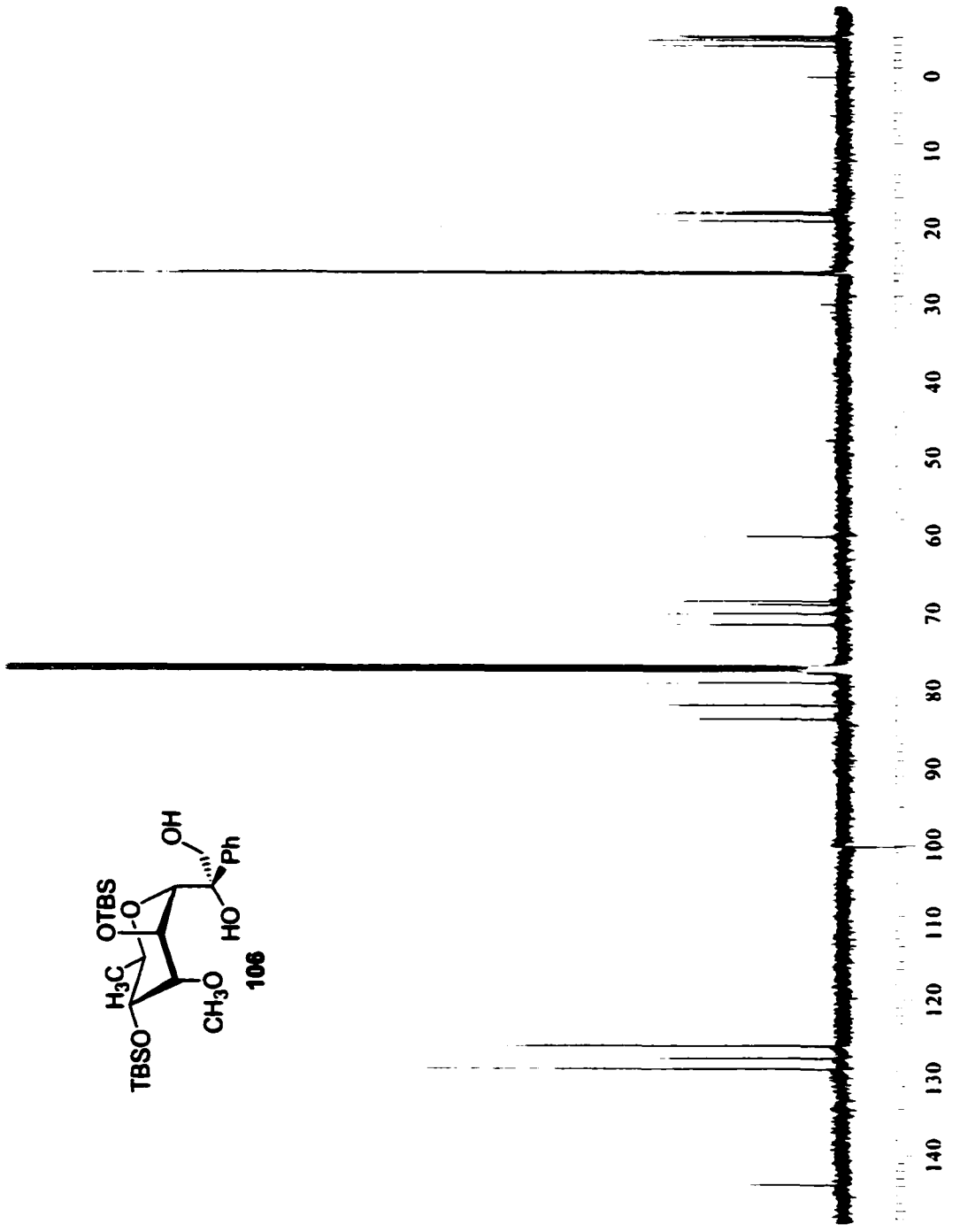
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **103**



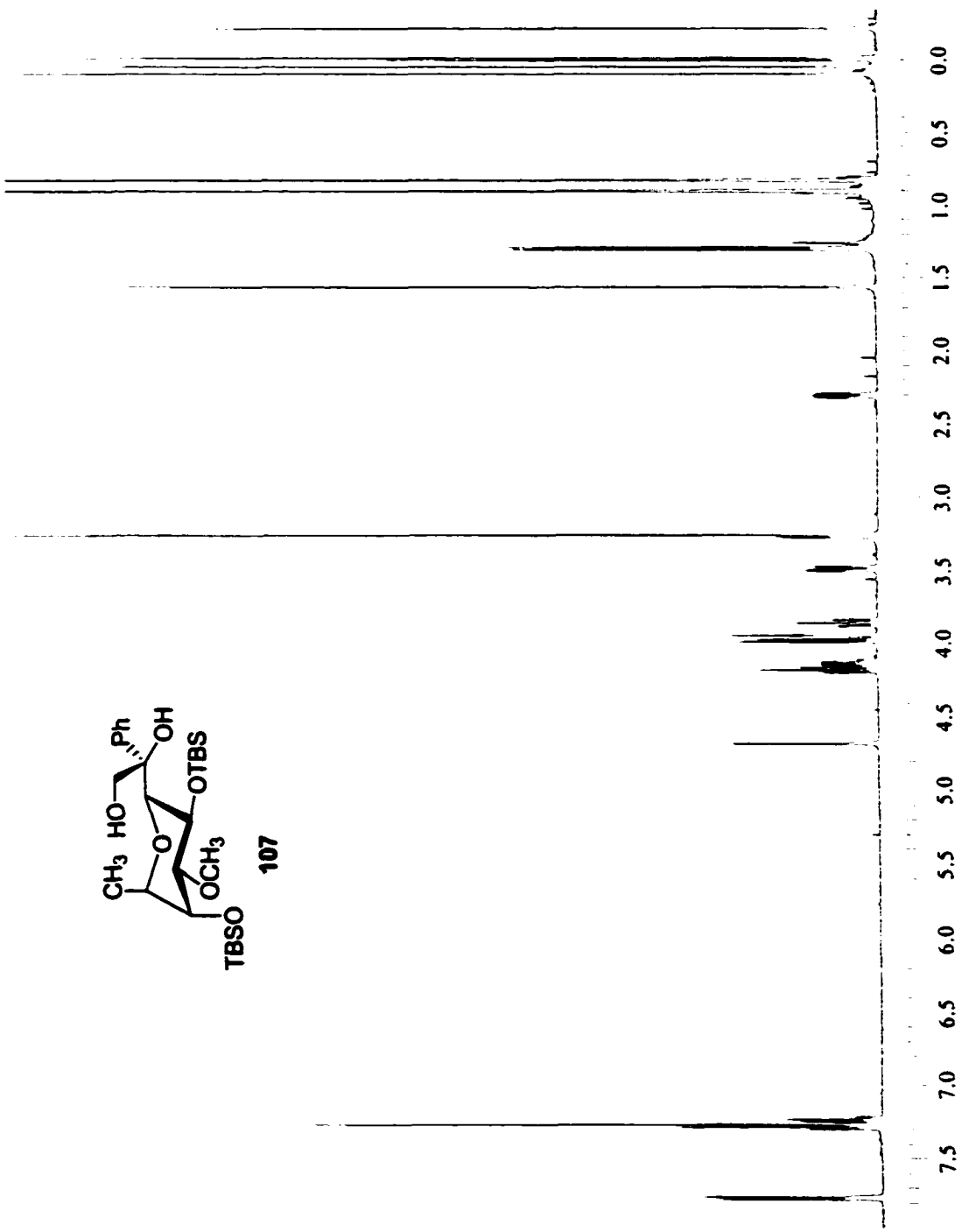
^{13}C-NMR spectrum (100 MHz, $CDCl_3$) of **103**



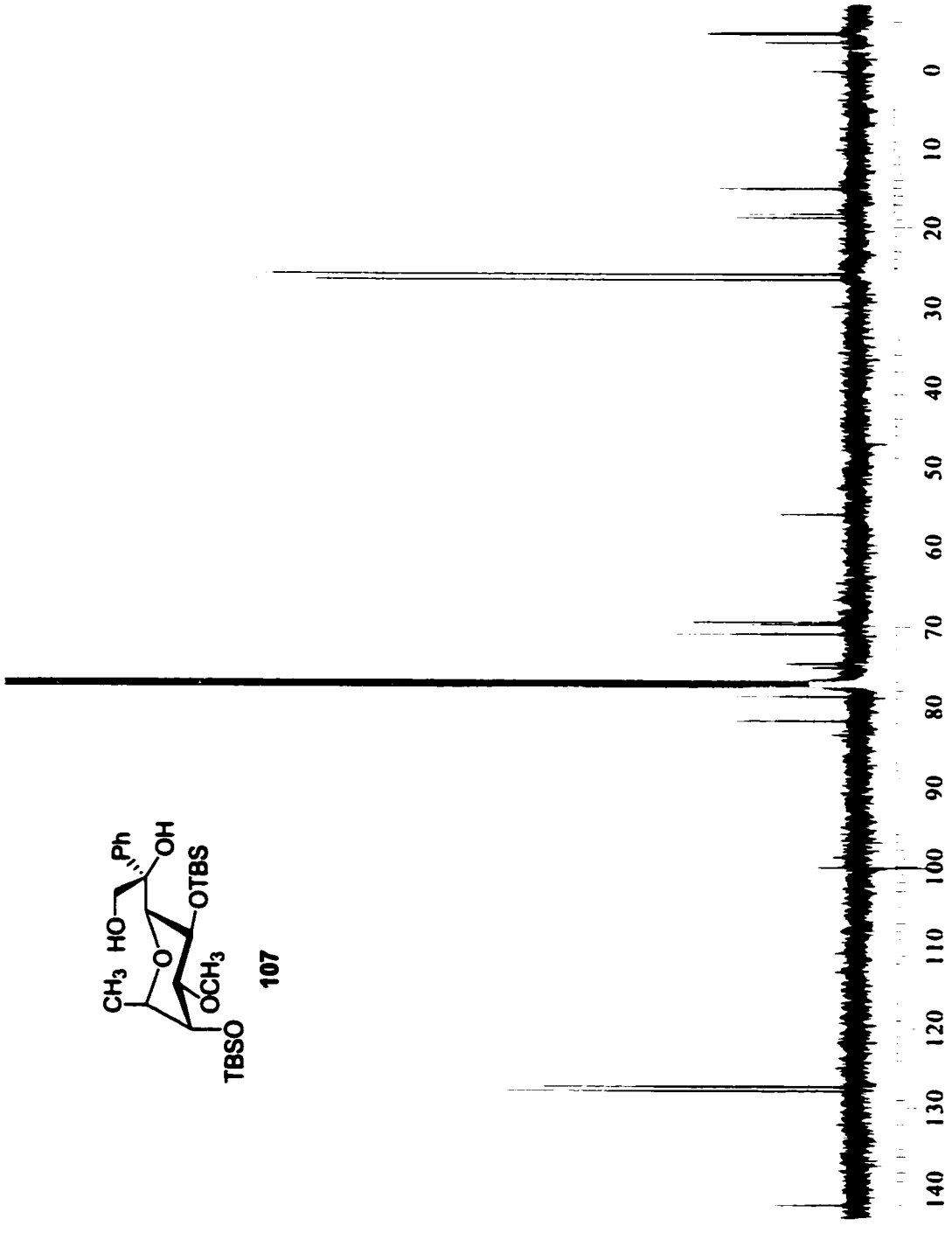
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **106**



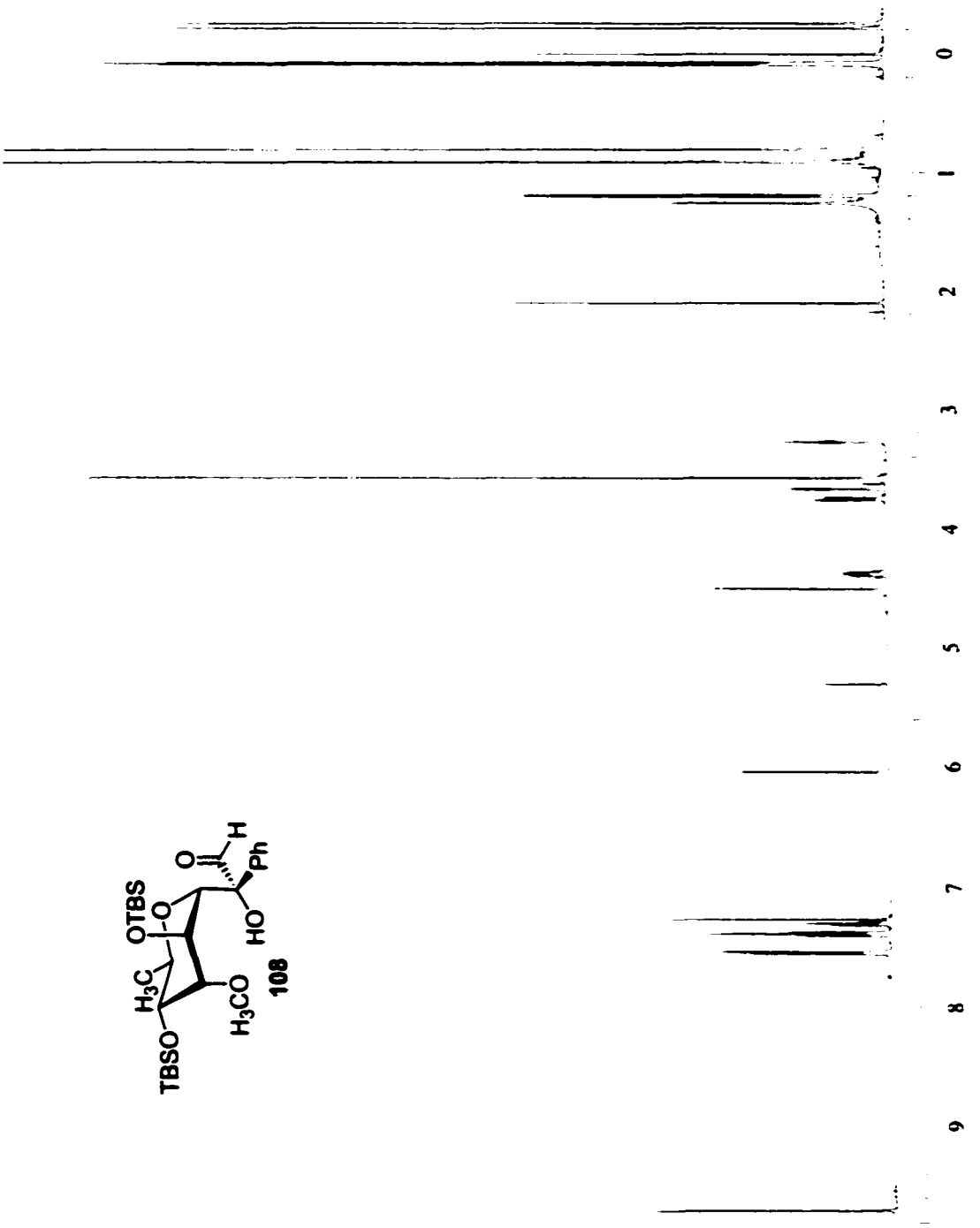
^{13}C-NMR spectrum (100 MHz, $CDCl_3$) of **106**



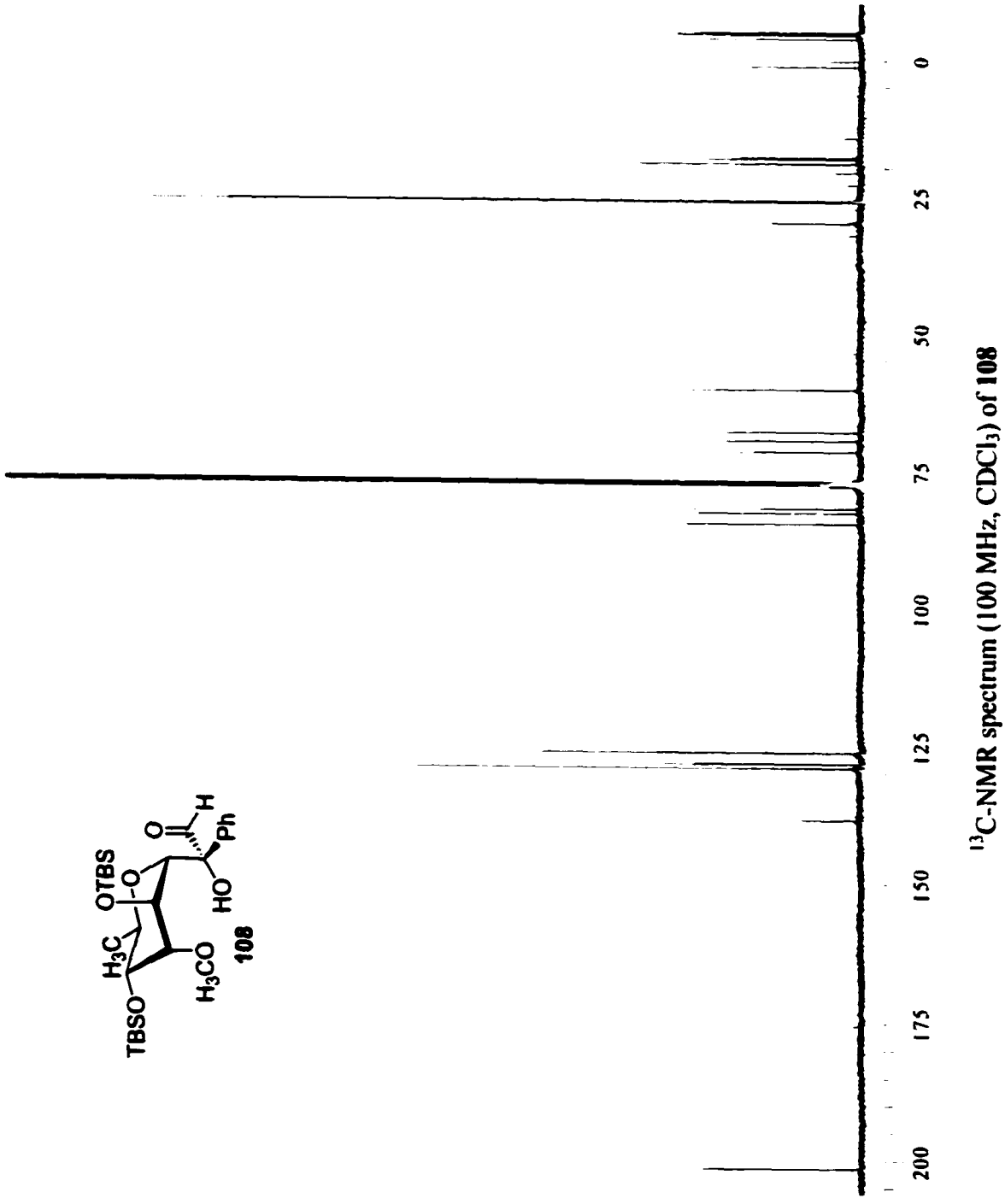
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **107**



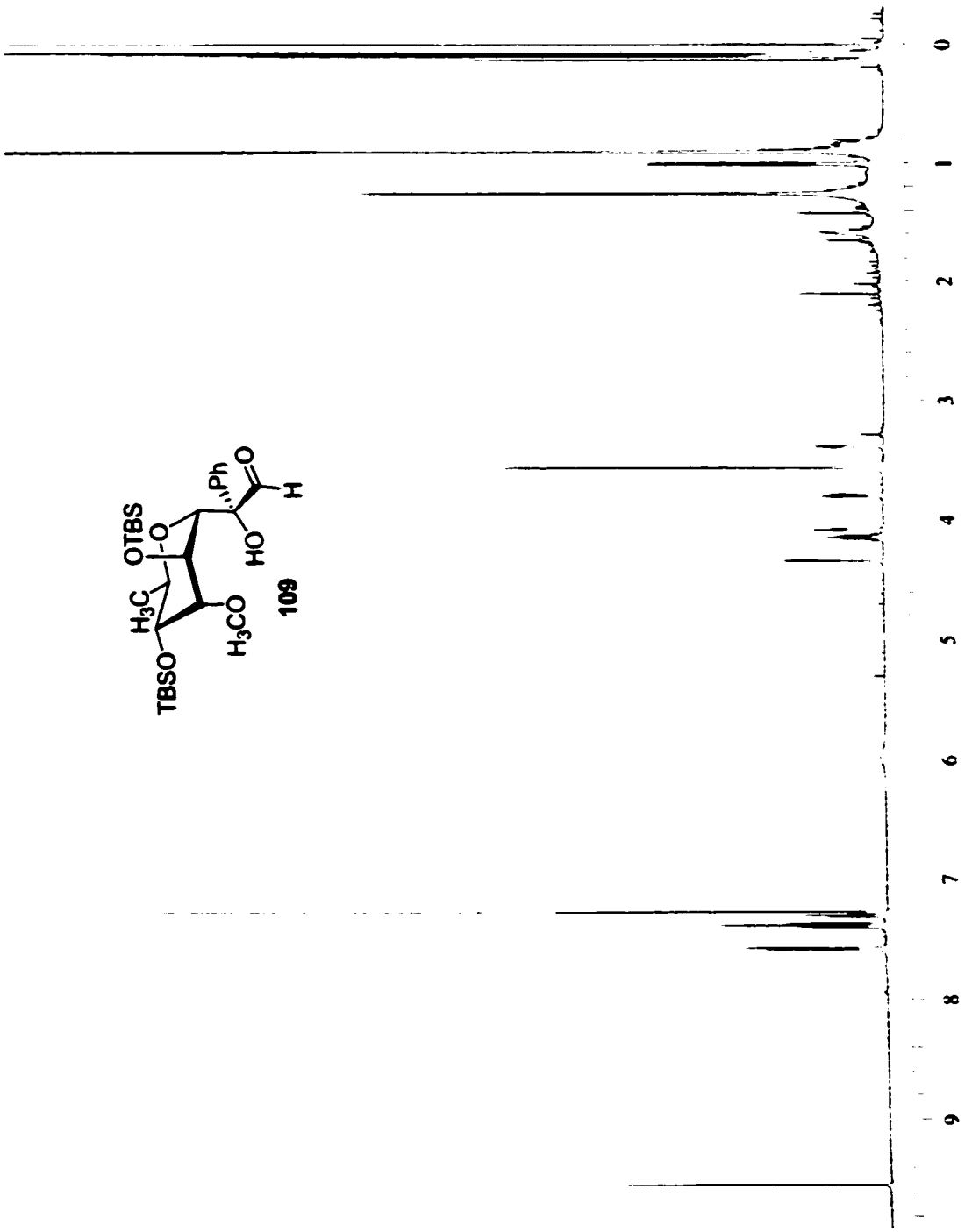
^{13}C-NMR spectrum (100 MHz, $CDCl_3$) of **107**



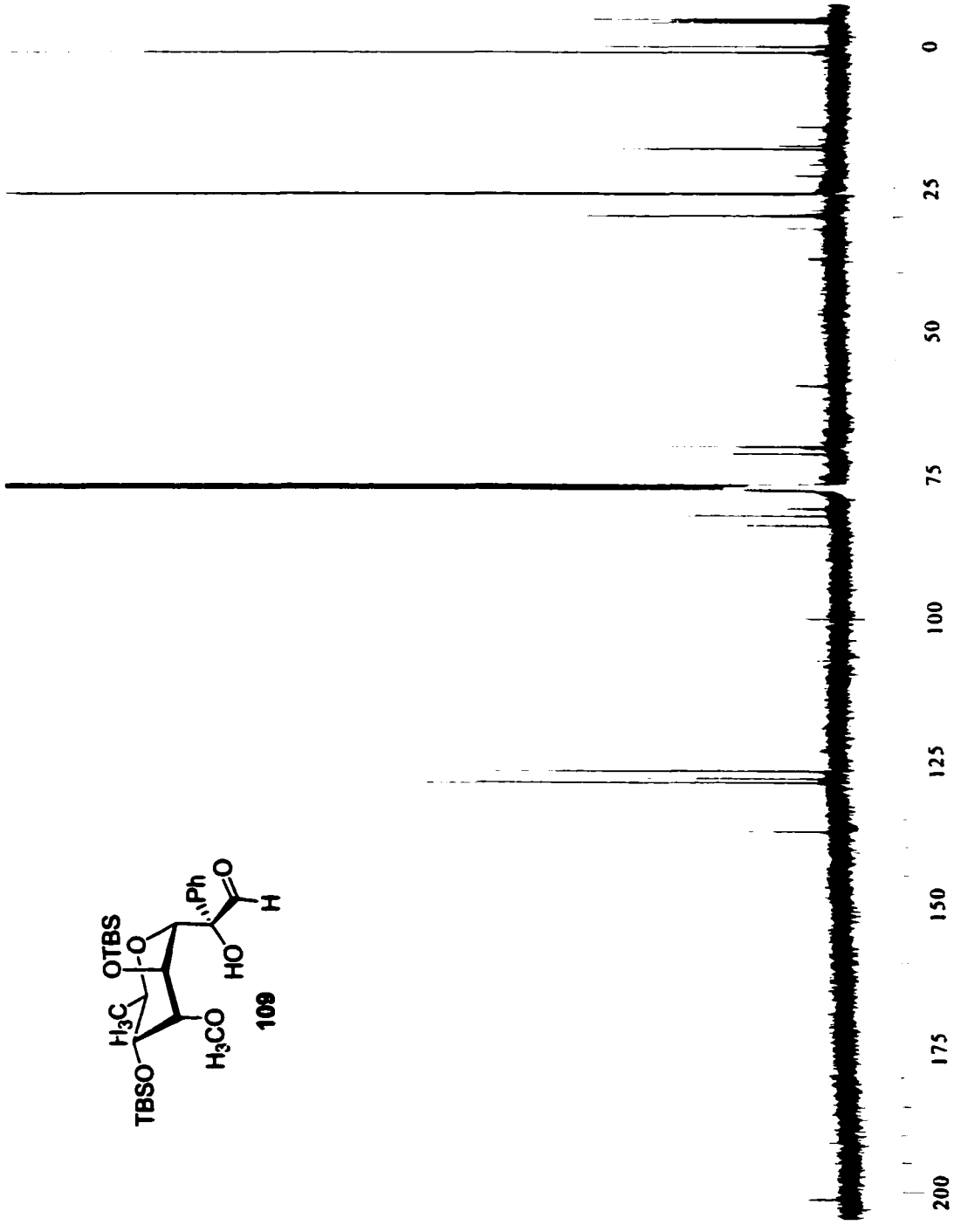
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **108**



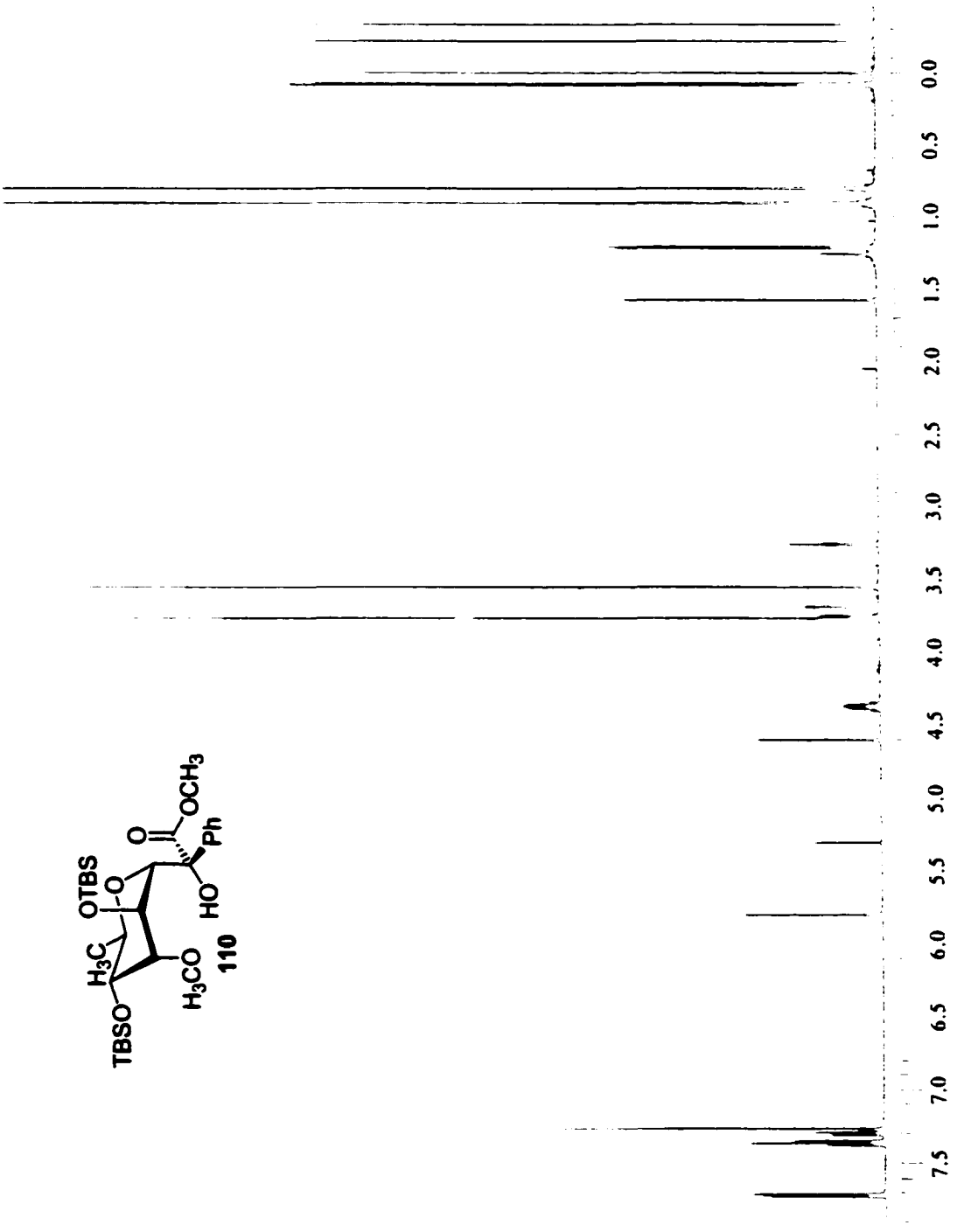
^{13}C-NMR spectrum (100 MHz, $CDCl_3$) of **108**



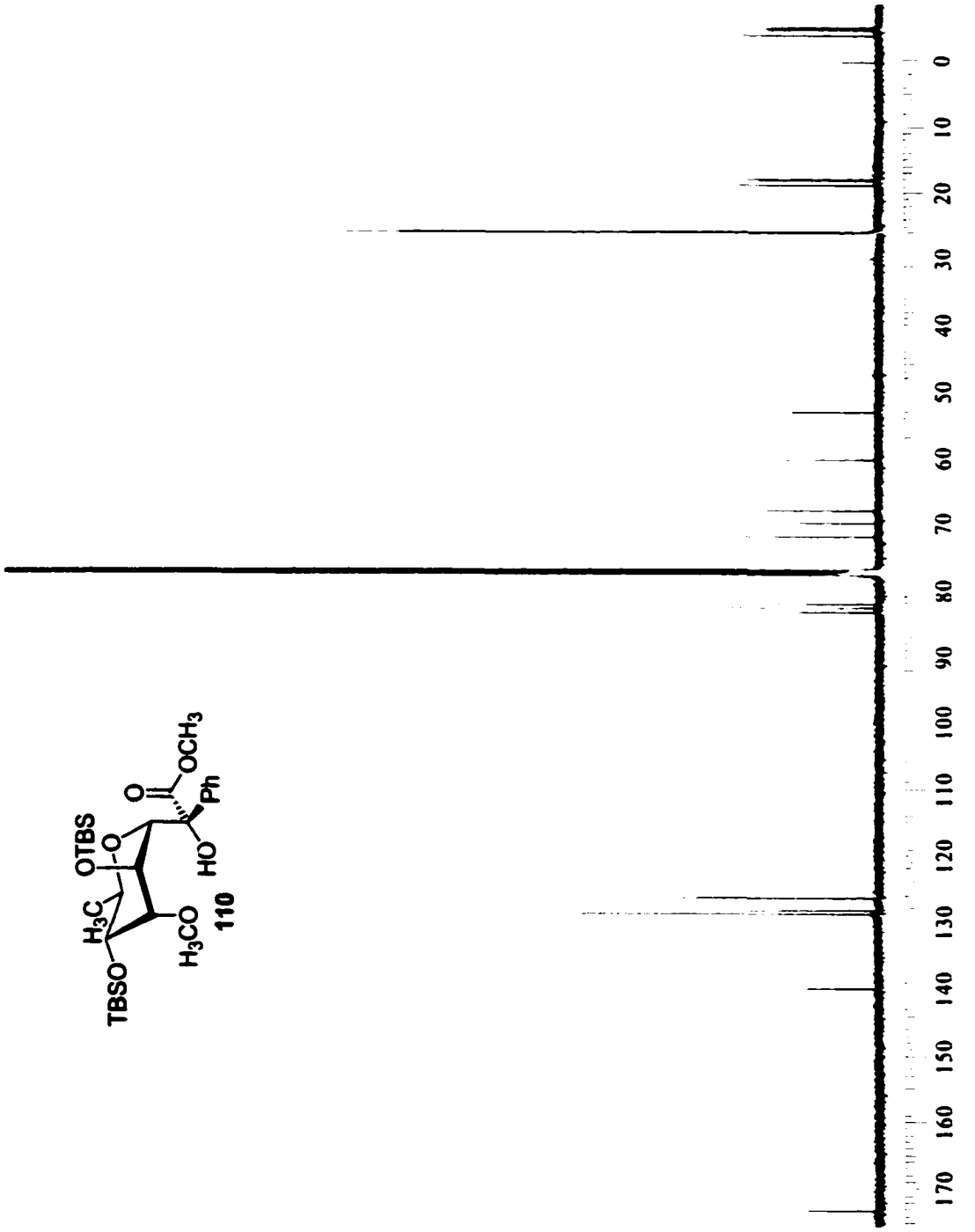
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **109**



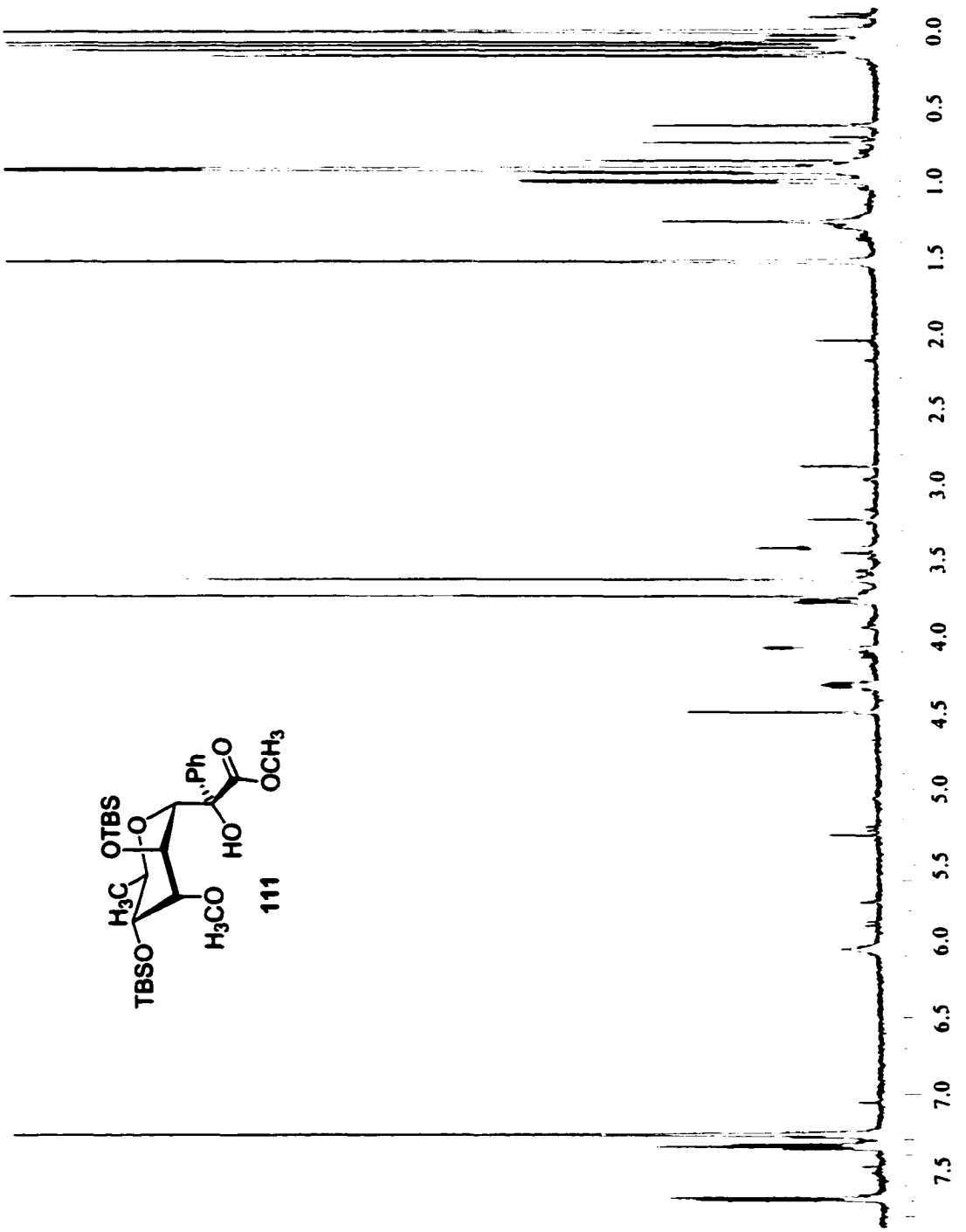
^{13}C-NMR spectrum (100 MHz, $CDCl_3$) of **109**



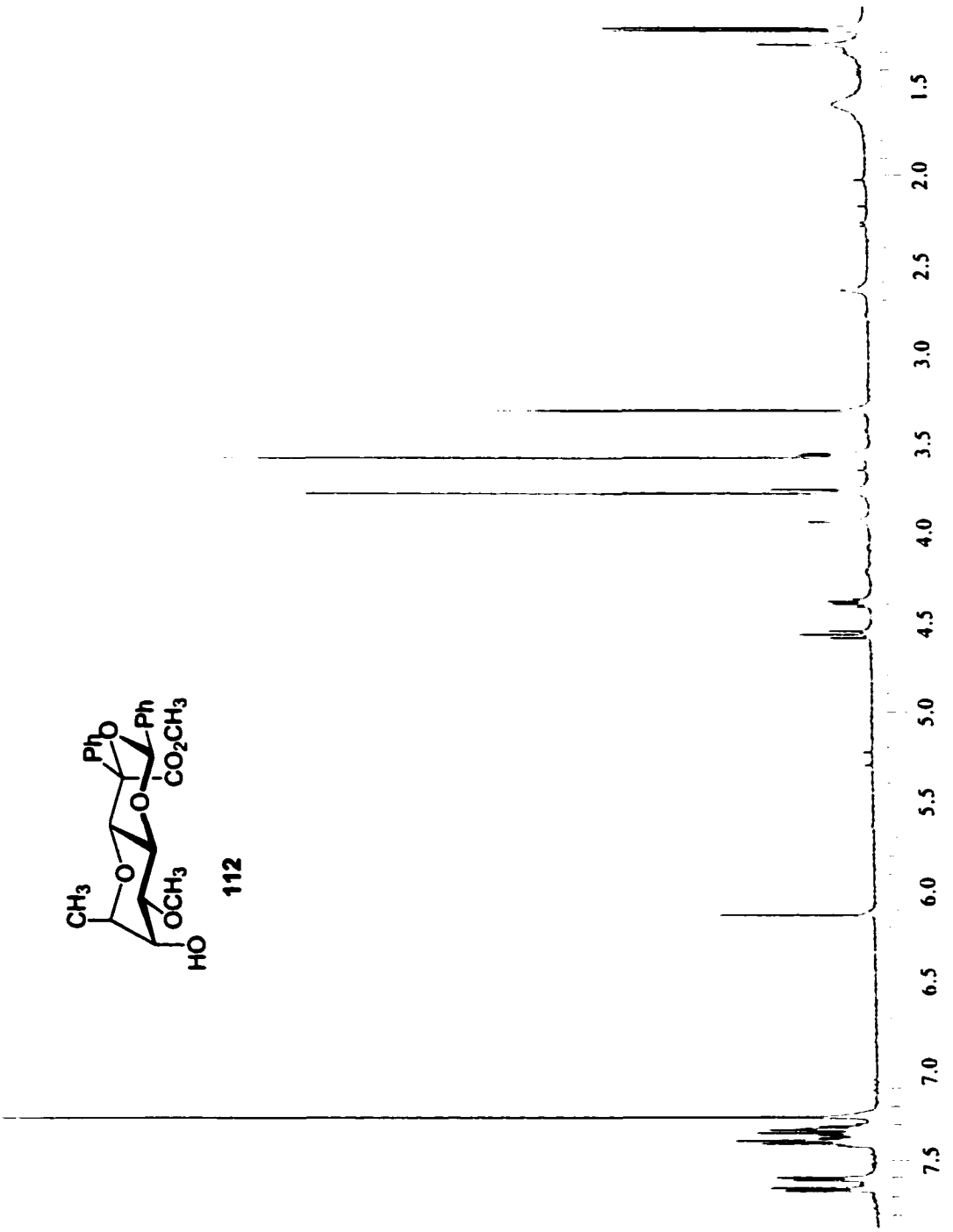
^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **110**



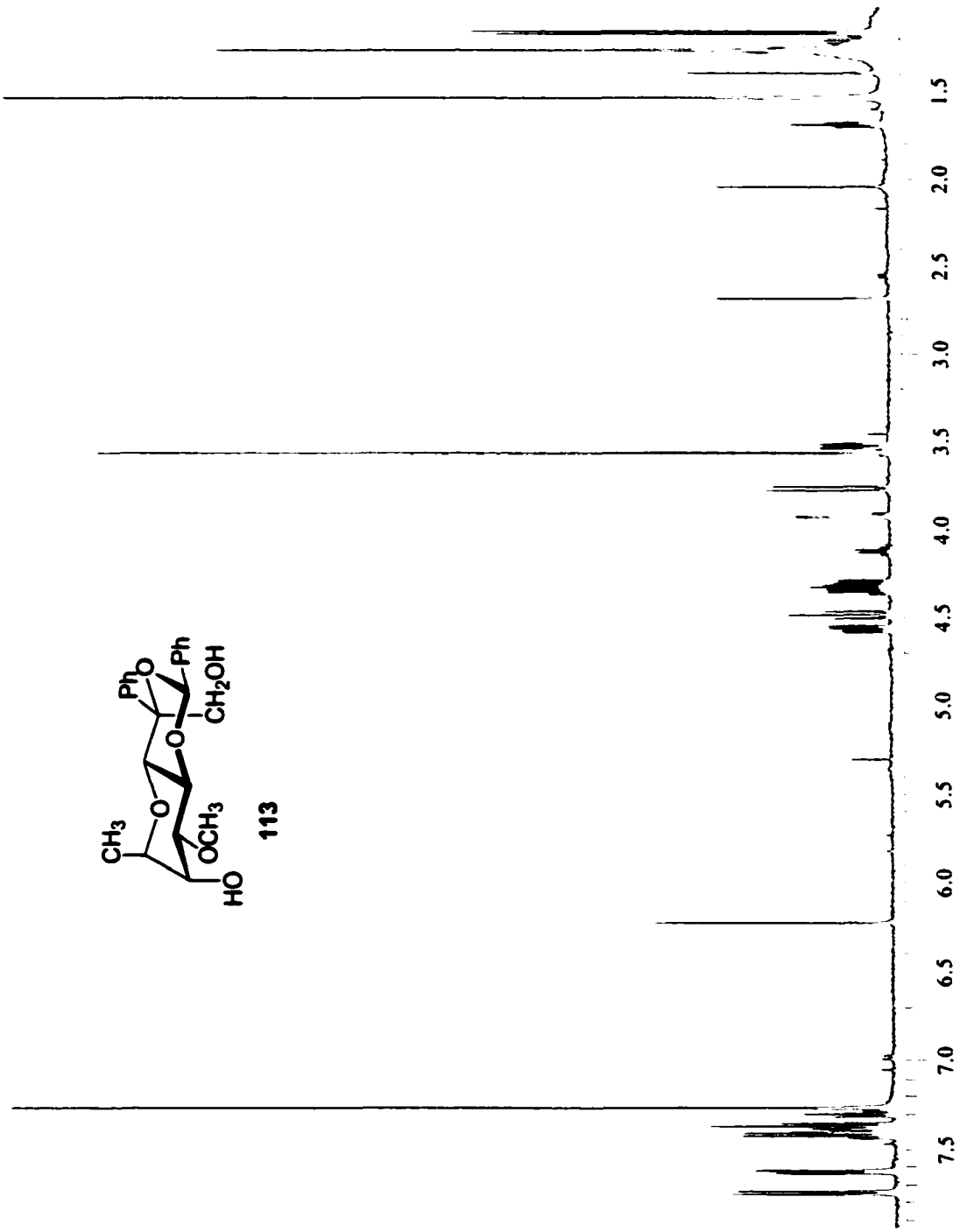
^{13}C-NMR spectrum (100 MHz, $CDCl_3$) of **110**



^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **111**



^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **112**



^{1}H-NMR spectrum (500 MHz, $CDCl_3$) of **113**

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