Pergamon

*Tetrahedron* Vol. 51, No. 33, pp. 9063-9078, 1995

0040-4020/95 $9.50+0.00

0040-4020(95)00505-6

# Synthesis of the First Pseudosugar-C-disaccharide. A Potential Antigen for Eliciting Glycoside-bond Forming Antibodies with Catalytic Groups.

Christel Barbaud, Mikael Bols*, Inge Lundt

*Department of Organic Chemistry, The Technical University of Denmark, Building 201, DK-2800 Lyngby, Denmark*

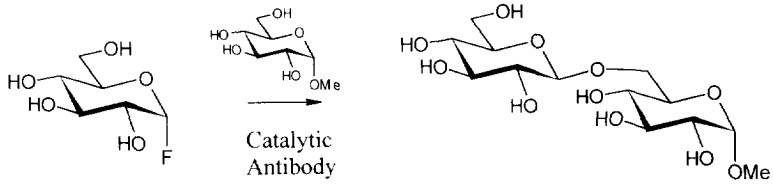
Michael R. Sierks

*Department of Chemical and Biochemical Engineering, University of Maryland, Baltimore County, Baltimore MD 21228-5998, USA*

**Abstract:** A number of synthetic routes to the first pseudo-C-disaccharide ever prepared has been studied. The compound, methyl 7-((*1S,3R,4R,5S,6S*)-1-amino-3-hydroxymethyl-4,5,6-trihydroxycyclohexyl)-6,7-dideoxy-α-D-*gluco*-heptopyranoside (**1**), is structurally related to cellobiose, but includes a crucial amino-functionality at the pseudoanomeric centre. It was prepared by 1,2-addition of the anion of methyl 6,7-dideoxy-2,3,4-tri-*O*-benzyl-α-D-*gluco*-hept-6-ynopyranoside to (*4R,5S,6R*)-3-benzyloxymethyl-4,5,6-tribenzyloxy-2-cyclohexenone followed by stereoselective conversion of the tertiary alcohol to azide and finally reduction.

## INTRODUCTION

Development of methods that will provide more ready access to complex oligosaccharides is an area of considerable interest to the scientific community. Both chemical[1] and enzymatic[2] methods of oligosaccharide synthesis are available but both have limitations. Chemical methods are very time consuming and require many steps, while enzymatic methods are very limited in which types of linkages can be made. As the oligosaccharide is an important biopolymer with many interesting, potential applications[3] easier synthesis would also be of economic importance. Catalytic antibodies could provide the much sought wonder method for glycoside synthesis, particularly with the advent of phage display library methods for much easier access to antibodies[4].




Scheme 1

Consequently we have been involved in a project with the aim of obtaining glycoside-bond

forming antibodies. The major problem in such work is designing the structure of the antigen. Traditionally this involves preparing a transition state analogue for the reaction. This approach has the drawback that the antibodies that bind to such a compound not necessarily have any catalytic groups and thus are potentially less efficient than an enzyme. We have therefore decided to pursue a different approach by preparing an antigen that should bind to antibodies with properly positioned catalytic groups. Our initial aim was to screen for antibodies that could catalyse the condensation of glucosyl fluoride with another molecule of

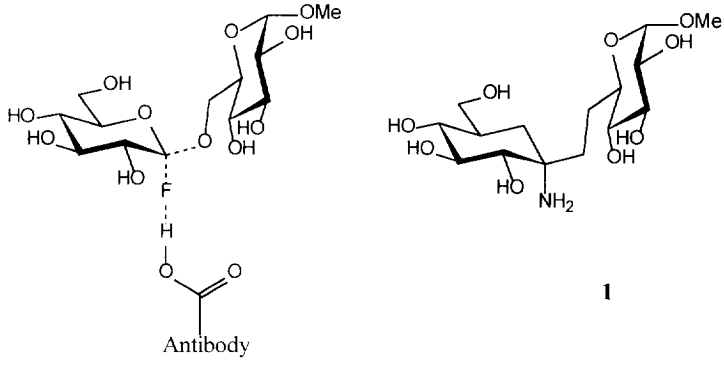



Fig 1

glucose in a regio- and stereospecific manner as shown in Scheme 1. To catalyse such a process the antibody would be expected to have an acidic group positioned in a way so that it would protonate the fluorine-atom, thus increasing its leavinggroup ability (Fig 1). Compound **1**, which contains an aminogroup at the pseudoanomeric centre, would be expected to bind well to such an antibody, and thus be a good antigen for obtaining the desired antibodies. This paper describes the successful synthesis of **1**, the first pseudo-C-disaccharide ever prepared.

## RESULTS AND DISCUSSION

It was initially decided that both **1** or its deoxy-analogue **1a** would be suitable for our purpose. Thus a number of retrosynthetic routes to the targets **1** or **1a** were planned (Fig 2). First we considered route 1 where **1** or **1a** was obtained by hydrolysis and Hoffman rearrangement of the corresponding nitrile **2**. The nitrile **2** might be obtained from either dialkylation of nitrile **3** with ditosylate **4** forming a cyclohexanering (route 1A), or, alternatively, by α-alkylation of the nitrile **5** by tosylate **6** (route 1B). Nitrile **5** was to be derived from ditosylate **4** by reaction with cyanomalonic ester followed by decarboxylation. Compounds **3** and **6** should be available by chain-extension of D-glucose, while **4** had a similar structure to a synthon recently employed by us in the synthesis of isofagomine[5]. As an alternative we considered route 2 where **1** was to be obtained by addition to imine **7** of the alkyne anion **8** followed by hydrogenation. The imine **7** should be derived from the corresponding ketone, which is known[6]. The alkyne **8** could be obtained from D-glucose by known chain extension processes.

Exploring route 1A the synthesis of nitrile **3** was studied (scheme 2). Radical chain extension of known iodide **9**[7] with acrylonitrile and tributyltin hydride did however not lead to the expected product **3** (R = Bn), but gave a unclean mixture of compounds in which **3** did not seem to be a major component. Under optimum conditions a 69% yield of the compound **10** was obtained.

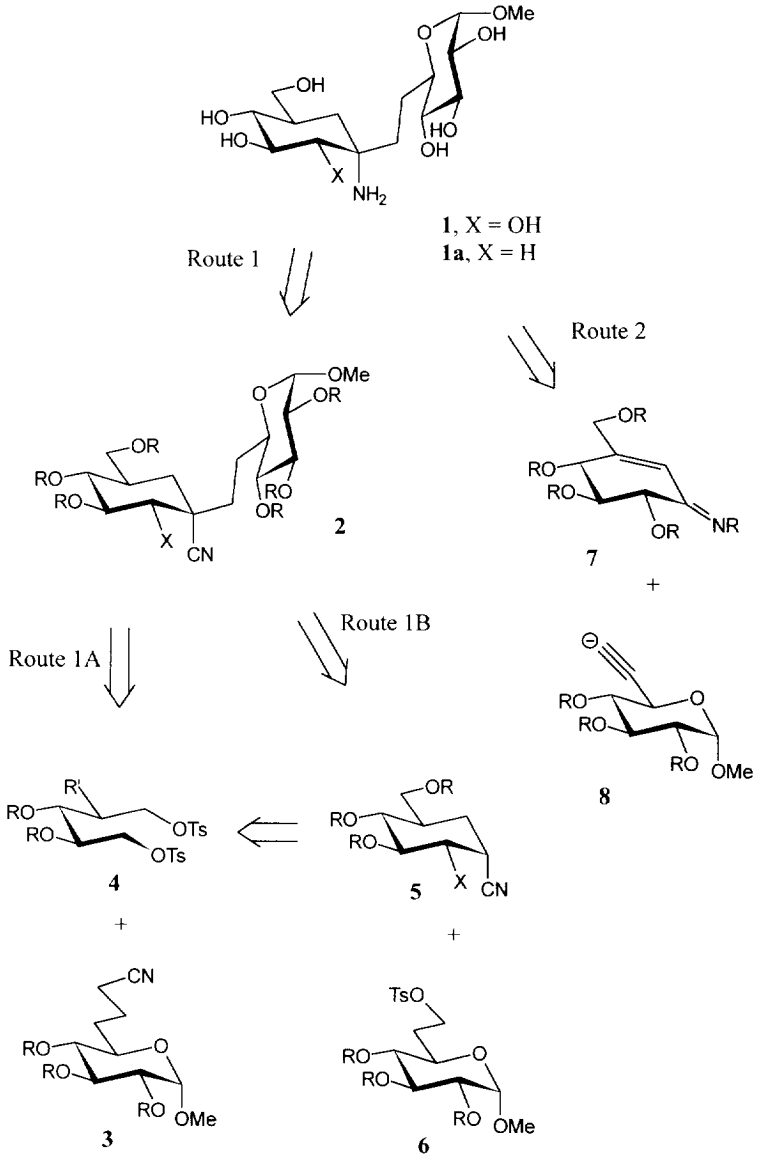
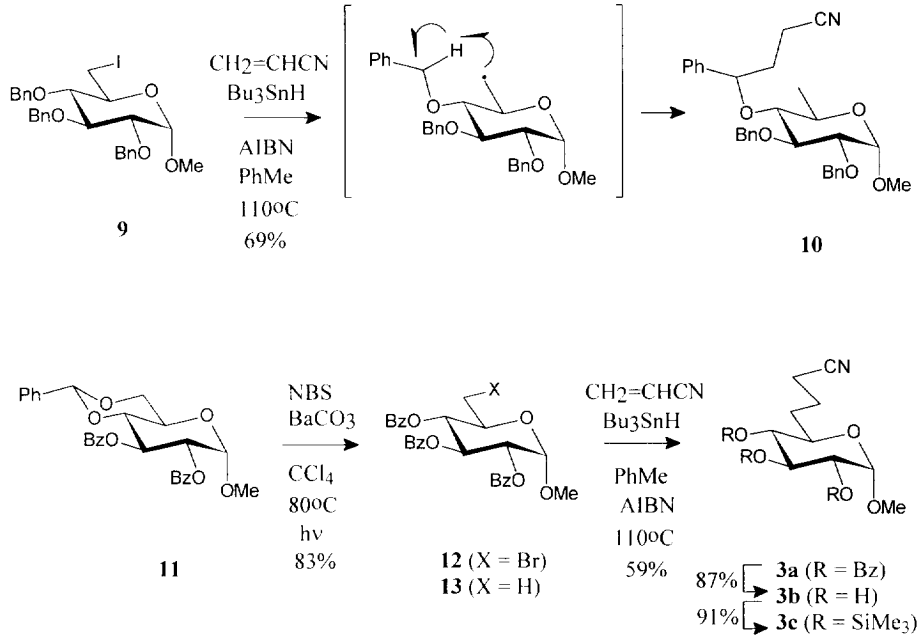



Fig 2

This product was formed by H-abstraction of the neighbouring benzylic proton by the initially formed C-6 radical. This forms a more stable radical (scheme 2), which subsequently reacts with acrylonitrile. We therefore realised that the benzylgroup was unsuitable as protection group in this case and that the benzoylgroup would be more desirable. This would, however, require a later interconversion of protection groups, because the benzoylgroup would not be stable during the alkylation of the nitrile. Thus the known benzylidene derivative **11**[8] was subjected to the Hanessian reaction[9] to give the bromide **12** in 83 % yield.

This bromide was converted to the desired nitrile **3a** by a radical reaction with acrylonitrile and tributyltin hydride in 59 % yield. As biproduct the reduced compound **13**[10] was isolated in 11 % yield. **3a** was debenzoylated to the hydroxycompound **3b** in 87 % yield, and silylated to give the trisilyl ether **3c** in 91 % yield.



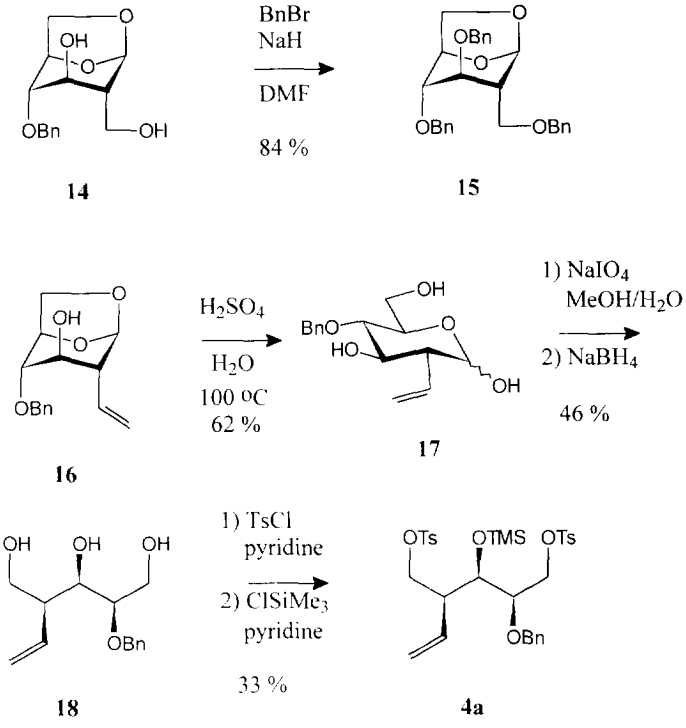

Scheme 2

The other half of the target molecule was synthon **4**. Compound **4** (R' = $CH_2OR$) we anticipated was available from compound **14**, a compound we had prepared previously[5], by benzylation, hydrolysis of the 1,6-anhydro-bond, periodate cleavage between C-5 and C-6, reduction and tosylation. Thus benzylation of **14** with benzyl bromide and sodium hydride in DMF gave the benzylated compound **15** in 84 % yield (scheme 3). However, hydrolysis of **15** with dilute sulphuric acid did not, as anticipated, lead to smooth cleavage of the internal acetal, but gave a complex mixture. A closer study of the reaction seemed to reveal that one or more benzyloxygroups were being eliminated during the hydrolysis.

As the successful hydrolysis of **14** was known[5], it was concluded that hydrolysis of its precursor **16** probably also could be done, and the product could then be converted to **4** (R' = $CH{=}CH_2$) by a similar sequence of reactions as those originally planned. So accordingly vinyl compound **16**[5] was hydrolysed briefly in hot 1 M sulphuric acid to give **17** in 62 % yield. Treatment of **17** with excess sodium periodate in methanol/water at 45 °C for 6 h gave a dialdehyde that was reduced *in situ* with $NaBH_4$ to give the triol **18** in 46% yield for the two steps. Selective tosylation of the two primary alcohols in **18** using 2.2 equivalent of tosyl chloride in pyridine at 0 °C, followed by silylation with TMSCl and DMAP gave the ditosylate **4a** in 33 % yield from **18**.

We were now ready for the crucial coupling of **3c** and **4a** to form a cyclohexane ring. As a model experiment, **3c** was first reacted with 1 mole of dibromopentane and 2 moles of LDA at -78 °C (scheme 4). The result was a 70% yield of the expected cyclohexane derivative **19**. When only 1 equivalent of LDA was employed the monoalkylated product **20** was isolated. When **4a** was substituted for dibromopentane in the reaction neither the desired dialkylation product nor any monoalkylation products were obtained, but rather

the nitrile **3c** remained unchanged. The lack of reactivity of **4a** was puzzling and was further investigated with model experiments.

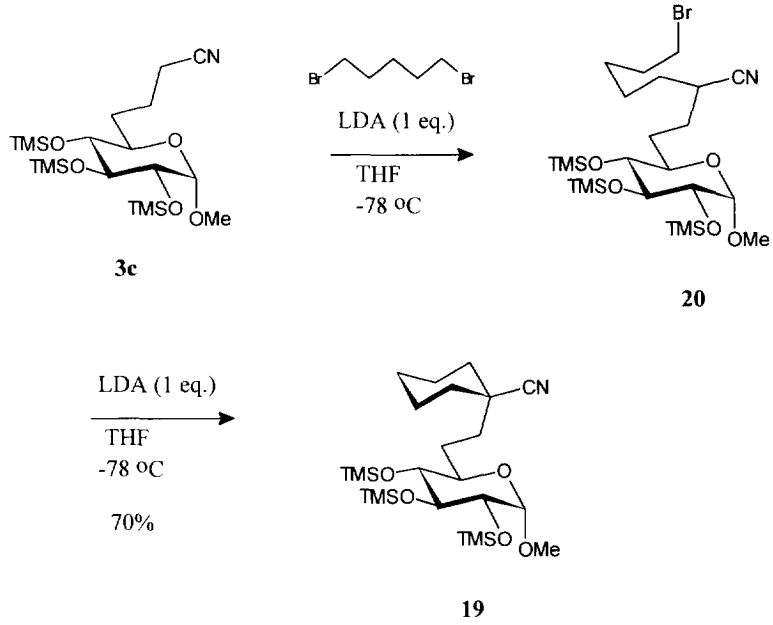



Scheme 3

A selection of pentitol tribenzyl ethers were prepared for this purpose. Thus known 2,3,4-tri-*O*-benzyl-D-arabinitol[11] (**21**) was converted to the ditosylate **22**, dibromide **23** or ditriflate **24** (scheme 5), while 2,3,4-tri-*O*-benzylxylitol[12] (**25**) was converted to the dimesylate **26** and the ditriflate **27**. However, neither **22**, **23** and **26** nor the triflates **24** and **27** did react with **3c** under the conditions successful for its condensation with 1,5-dibromopentane. In all cases the nitrile **3c** seemed not to react, while the electrophile seemed to degrade to a complex mixture. We then decided to attempt to carry out the dialkylation of the simpler, more stable, carbanion of 2- cyanoacetic acid methylester with **26** and **27**, having the expectation that such a reaction after hydrolysis and decarboxylation would lead to a cyanocyclohexane analogous to **5**. This could then be used in the synthesis route 1B (fig 2). A cyclisation of this type had also previously been reported[13]. Reaction of **26** with methyl 2-cyanoacetate and NaH in DMSO gave mainly one product, the racemic tetrahydrofuran **28**, which was isolated in 54 % yield. Similarly the more reactive triflate **27** led to the monoalkylated tetrahydrofuran **29**. In both cases the initial reaction is nucleophilic substitution of a leavinggroup by a benzylic oxygen, followed by loss of a benzylgroup. In the latter case, due to the high reactivity of the triflate, the remaining leavinggroup was substituted with cyanoacetate. Later it was discovered, that the precursor **26** actually under prolonged storage spontaneously cyclised into **28**.

After viewing these results it was reasonable to conclude that similar selfcondensation reactions were occurring to **4a**, **22**,**23**,**24**,**26** and **27** in the reaction with **3c** and LDA. The extreme ease that these δ-benzyloxyalkyl sulfonates undergo cyclisation seemed surprising, but there is

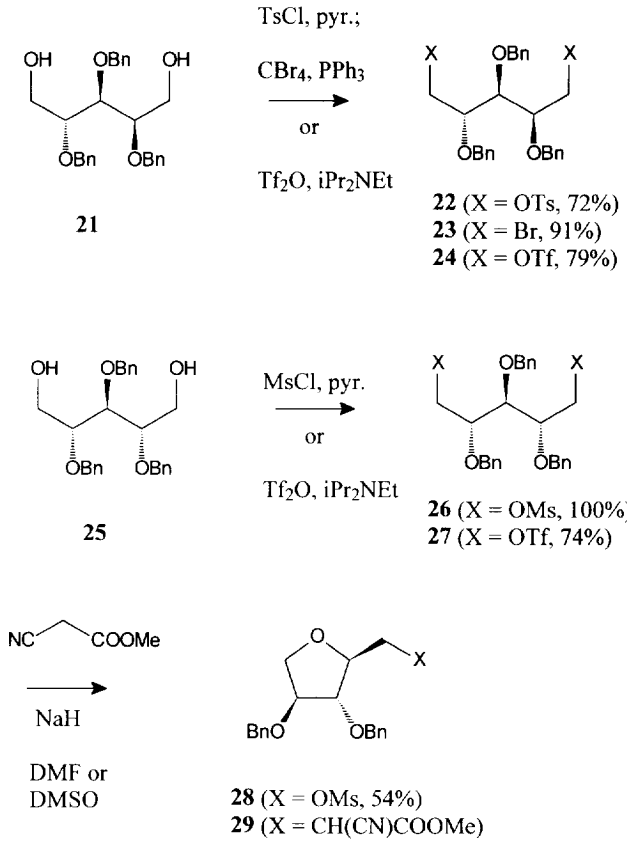
actually a literature precedent for this type of reaction[11]. Though the problem probably could be circumvented by employing other protection groups than benzyl in the electrophile, it was concluded that it would require much work to make such electrophiles, particularly one analogous to **4**. We therefore turned our attention to route 2.




**3c** **20** **19**

Scheme 4

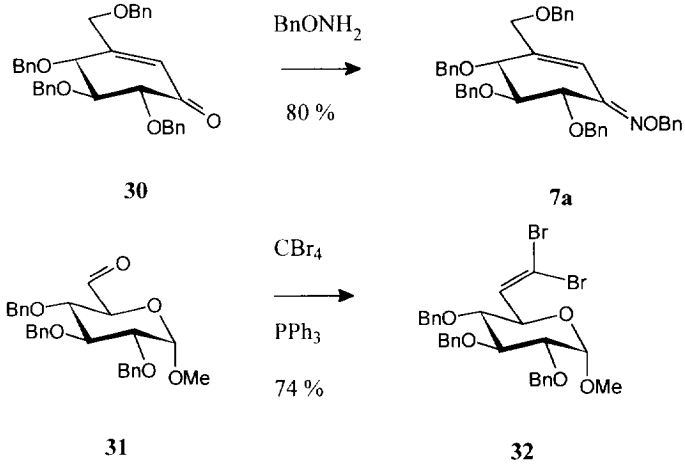
The key step in route 2 (fig 2) was nucleophilic addition of the lithium salt of the alkyne anion **8** to the imine of a cyclohexenone. Compound **8** has previously been added to a lactone in order to prepare C-glycosides[14], and it was therefore reasonable to assume that **8** could be added to a ketone or an imine. Unsaturated ketone **30** was an attractive synthon and could be prepared easily in 5 steps from 2,3,4,6-tetra-*O*-benzyl-D-glucose[6]. Initial investigation showed that saturation of the double bond in **30** by hydrogenation was not stereoselective, but gave a 1:1 mixture of diastereoisomers. Therefore it was decided to carry out the coupling reactions with the double bond present and do the saturation of the double bond in the C-disaccharide formed where more steric bias could be expected. To introduce the amino group at the crucial tertiary centre it seemed essential to convert ketone **30** to an imine. Reports in the literature indicated that organometalic reagents could be added to imines[15] or oximes[16], with the former case being more successful. Attempts of making an imine of **30** with benzylamine failed however, due to inertness of the ketone. On the other hand **30** could successfully be converted to the oxime **7a** in 80 % yield by reaction with *O*-benzylhydroxylamine (scheme 6). To obtain synthon **8**, the aldehyde **31**, obtained by oxidation of a known precursor, was converted into the bromoolefin **32** in 74 % yield using carbontetrabromide and triphenylphosphine. Oxime **7a** proved however totally resistant to the alkynyl lithium **8** obtained from reaction of bromoolefin **32** with butyl lithium according to the general procedure by Kishi[17]. On the other hand it was however possible to react **8**, as obtained from **32**, with the ketone **30**, to give the two stereoisomeric alcohols **33** and **34** in 87 % yield in ratio 1:2 (scheme 7). The two isomers could be separated, however we were not able to determine the configuration of the new chiral center of **33** and **34** due to the lack of useful protons in these compounds for NOE experiments. Initially it was not anticipated that the tertiary alcohols in **33** and **34** could be substituted with a nitrogen functionality, but with the failure of the imine/oxime addition strategy this was reconsidered. Though it was found that SN2 substitution




Scheme 5

of even the triflates of **33** or **34** was impossible, it proved possible to substitute the OH by a SN1 reaction by employing $BF_3$ and $Me_3SiN_3$[18]. With these two reagents in toluene the mixture of **33** and **34** led to a 37 % yield of a separable mixture of azides **35** and **36** (scheme 7). Though the yield was low this reaction was quite attractive, because of the relatively ready availability of the starting materials. If either of the pure alcohols **33** or **34** was used a mixture of azides were still obtained under these conditions. However, it was found that if the pure alcohol **33** was treated with $BF_3$ in neat $Me_3SiN_3$ only the azide **36** was obtained. Furthermore from the pure alcohol **34** the other azide **35** was received under these conditions.

Finally, the two diastereomeric azides were hydrogenated with palladium on carbon as a catalyst. Earlier experiments had shown that saturation of the double bond of **30** by hydrogenation gave a mixture of epimers at C-5. It was, however, anticipated that the C-glycoside substituent of **35** and **36** would be bulky enough to direct hydrogenation of the double bond from the less hindered side. This turned out to be the case. The azide **35** gave the totally reduced L-*ido* compound **37** in 66 % yield as a single product (scheme 8). The *ido*-configuration of the cyclohexane-ring was deduced from the proton NMR-spectrum. $J_{2'-3'}$ and $J_{3'-4'}$ were small, 3.5-4 Hz, consistent with the $^1C_4$ conformation havin both the hydroxymethyl and the C-glycoside in equatorial position. Similarly, **36** was converted to the target molecule **1** in a quantitative yield. The *gluco*-configuration of the cyclohexane-ring was deduced from the proton NMR-spectrum. $J_{2'-3'}$ and $J_{5'-6ax'}$ were both large consistent with the normal $^4C_1$ conformation of compounds with *gluco*-configuration.




Scheme 6

The configuration at C-1' was determined from a NOESY-spectrum with zero quantum contributions surpressed.[19] Correlation's were found from the two H-7 to the two axial protons H-2' and H-6ax' showing proximity between them. The configuration of **1** was thus determined to be pseudo β-D-*gluco*. Since **36** must have the same configuration at C-1', the configuration of **36** had now also been determined. Because **36** had the opposite configuration of **35** at C-1', the entire configuration of **35** and **37** were now also known.

Thus we have synthesised the first two pseudo-sugar-C-glycosides as potential antigens for glycoside-forming antibodies. Further studies will aim at developing such antibodies.

## ACKNOWLEDGMENTS

We thank the Danish Natural and Technical Research councils for a postdoctoral grant for C. B., and NATO for supporting us with Collaborative Research Grant 930718. We also thank Bent Ole Pedersen, Carlsberg Laboratory for assistance with the NOE experiments.

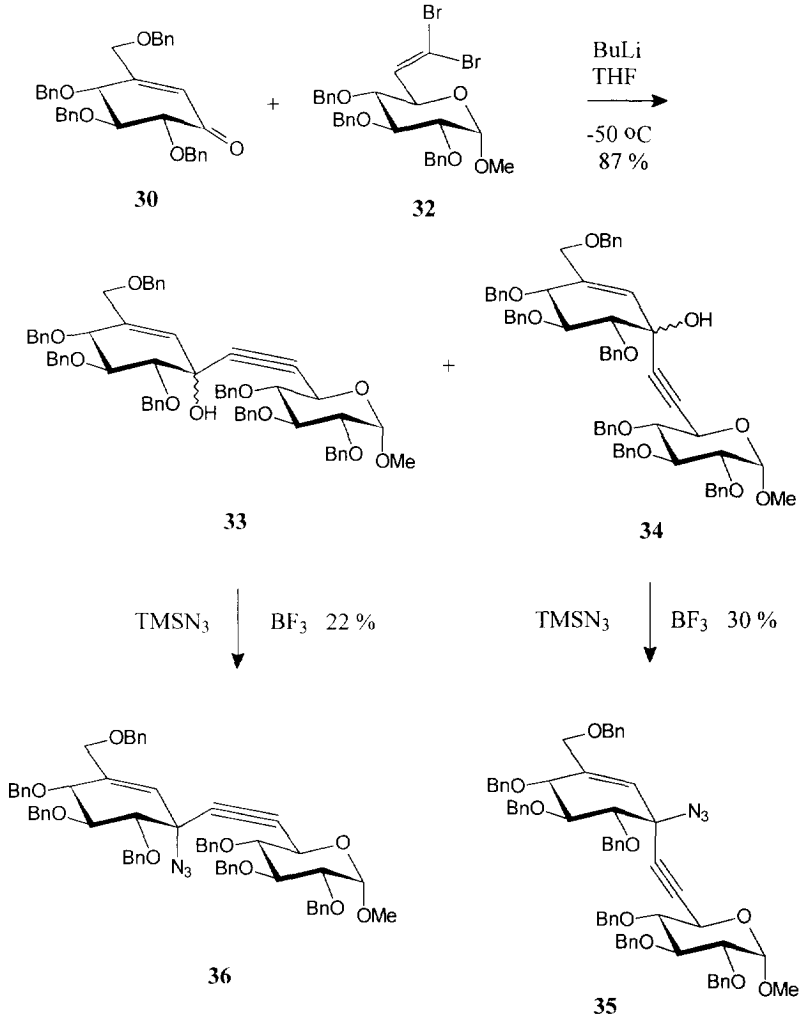
## EXPERIMENTAL SECTION

$^{13}$C-NMR and $^{1}$H-NMR spectra were recorded on Bruker instruments AC 200, AC 250 and AM 500. $D_2O$ was used as solvent with DHO ($^{1}$H-NMR: δ 4.7 ppm) and acetone ($^{1}$H-NMR: δ 2.05 ppm; $^{13}$C-NMR: δ 29.8 ppm) as reference. With $CHCl_3$ as solvent TMS and $CHCl_3$ ($^{13}$C-NMR: δ 76.93 ppm) were used as references. Mass spectra were obtained on a VG TRIO-2 instrument. Melting points are uncorrected. Optical rotations were measured on a Perkin Elmer 141 polarimeter. Microanalyses were carried out by Leo Microanalytical Laboratory. Concentrations were performed on a rotary evaporator at a temperature below 40 °C. Dry tetrahydrofuran and diethyl ether were prepared by distillation from sodium and benzophenone. Borontrifluoroetherate was distilled (Bp 124-125 °C) and stored under argon at 5 °C and used within a week.

*Methyl 2,3-di-O-benzyl-6-deoxy-4-O-(1-phenyl-3-cyanopropyl)-α-D-glucopyranoside* (**10**).

A solution of **9** (155 mg, 0.27 mmol) in dry toluene (13.5 ml) with acrylonitrile (177 µl, 10 equiv.) was treated at reflux, under argon, with a solution of tributyltin hydride (145 µl, 2 equiv.) and AIBN (9 mg, 0.2 equiv.) in toluene (3 ml). After 8 h, the solution was concentrated in *vacuo*. Flash chromatography (pentane-ethyl acetate 5:1, v/v) yielded the compound **10** as a syrup (93 mg, 69%). $^{1}$H-NMR: δ 1.38 (d, 3H,

$J_{5,6}$ 6.2 Hz, H-6); 3.19 (dd, 1H, $J_{3,4}$ 9, $J_{4,5}$ 9 Hz, H-4); 3.39 (s, 3H, OMe); 3.46 (dd, 1H, $J_{1,2}$ 3.5, $J_{2,3}$ 10 Hz, H-2); 3.8 (m, 2H, H-3, H-5); 4.5 (d, 1H, $J_{1,2}$ 3,5 Hz, H-1); 4.25-4.9 (m, 5H, H-7, 2 $CH_2$Ph). $^{13}$C-NMR: δ 12.5 (C-9), 13.5 (C-7), 18.7 (C-6), 32.5 (C-8), 55.0 (OMe), 66.1 (C-5), 73.0, 74.9 (2 $CH_2$Ph), 79.6, 80.2, 81.1 (C-2, 3, 4), 97.6 (C-1), 119.0 (C≡N). MS (CI, $NH_3$): m/z 519 (M + 18).




Scheme 7

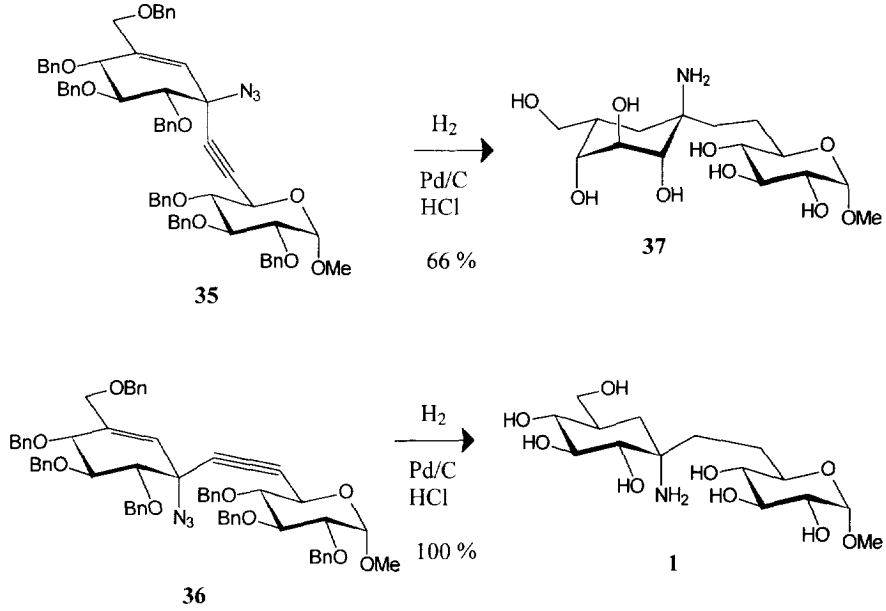
*Methyl 2,3,4-tri-O-benzoyl-6-bromo-6-deoxy-α-D-glucopyranoside* (**12**).

A solution of methyl 2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-α-D-glucopyranoside (**11**, 5 g, 10 mmol) in carbon tetrachloride (100 ml) was treated at 80 °C with *N*-bromosuccinimide (2.36 g, 1.3 equiv.) and barium carbonate (10.06 g, 5 equiv.). The reaction was initialised by irradiation with a light bulb (150 watts). After stirring for 1 h, the solution was filtered through celite and concentrated in *vacuo*. Crystallisation from methanol yielded the compound **12** as a colorless solid (4.80 g, 83%), Mp 128-130 °C. $[\alpha]_D^{22}$ + 46.4° (*c*

1.06, $CHCl_3$). $^1$H-NMR ($CDCl_3$): δ 3.54 (s, 3H, OMe); 3.58 (m, 2H, H-6ax, H-6eq); 4.3 (ddd, 1H, $J_{4,5}$ 10, $J_{5,6ax}$ 7.5, $J_{5,6eq}$ 2.5 Hz, H-5); 5.29 (d, 1H, $J_{1,2}$ 2.5 Hz, H-1), 5.3 (d, 1H, $J_{1,2}$ 2.5, $J_{2,3}$ 9 Hz, H-2); 5.49 (dd, 1H, $J_{3,4}$ 9, $J_{4,5}$ 10 Hz, H-4), 6.18 (dd, 1H, $J_{2,3}$ 9, $J_{3,4}$ 9 Hz, H-3); 7.4-8.3 (m, 15H, 3 Ph). $^{13}$C-NMR ($CDCl_3$): δ 31.2 (C-6), 55.6 ($OCH_3$), 69, 70, 71.3, 71.8 (C-2, 3, 4, 5), 96.8 (C-1). MS (CI, $NH_3$): m/z 105 ($PhCO^+$), 587 (M + 18). Anal. Calc. for $C_{28}H_{25}BrO_8$ (M = 569.409), C, 59.06; H, 4.42. Found: C, 58.87; H, 4.43.

*Methyl 2,3,4-tri-*O*-benzoyl-8-*C*-cyano-6,7,8-trideoxy-*α*-*D*-*gluco*-octopyranoside* (**3a**).

A solution of **12** (3 g, 5.26 mmol) in dry toluene (10 ml) with acrylonitrile (3.47 ml, 10 equiv.) was treated at reflux, under argon, with a solution of tributyltin hydride (2.55 ml, 1.8 equiv.) and AIBN (173 mg, 0.2 equiv.) in toluene (20 ml). After 1 h, the solution was concentrated in *vacuo*. Flash chromatography (pentane-ethyl acetate 5:1 and 3:1, v/v) yielded the compounds **3a** (syrup, 1.69 g, 59%) and **13**[10] (syrup, 294 mg, 11%). Compound **3a**: $[\alpha]_D^{22}$ + 51.6° (*c* 1.11; $CHCl_3$). $^1$H-NMR ($CDCl_3$): δ 1.2-2.5 (m, 6H, H-6, H-7, H-8); 3.47 (s, 3H, OMe), 4.09 (ddd, 1H, $J_{4,5}$ 10, $J_{5,6}$ 7.5, $J_{5,6'}$ 3 Hz, H-5); 5.19 (d, 1H, $J_{1,2}$ 3 Hz, H-1); 5.23 (dd, 1H, $J_{1,2}$ 3, $J_{2,3}$ 10 Hz, H-2); 5.39 (dd, 1H, $J_{3,4}$ 10, $J_{4,5}$ 10 Hz, H-4); 6.12 (dd, 1H, $J_{2,3}$ 10, $J_{3,4}$ 10 Hz, H-3); 7.4-8 (m, 15H, 3Ph). $^{13}$C-NMR ($CDCl_3$): δ 17.1 (C-8), 21.2 (C-7), 29.9 (C-6), 55.5 ($OCH_3$), 68.3 (C-5), 70.2 (C-4), 72.0 (2C, C-2, 3), 96.8 (C-1), 119 (C≡N). MS (CI, $NH_3$): m/z 561 (M + 18).
Compound **13**: $^1$H-NMR ($CDCl_3$): δ 1.35 (d, 3H, $J_{5,6}$ 6.5 Hz, H-6); 3.47 (s, 3H, OMe); 4.19 (td, 1H, $J_{4,5}$ 9, $J_{5,6}$ 6.5 Hz, H-5); 5.18 (d, 1H, $J_{1,2}$ 3.5 Hz, H-1); 5.26 (dd, 1H, $J_{1,2}$ 3.5, $J_{2,3}$ 10 Hz, H-2); 5.35 (dd, 1H, $J_{3,4}$ 10, $J_{4,5}$ 9 Hz, H-4); 6.12 (dd, 1H, $J_{2,3}$ 10, $J_{3,4}$ 10 Hz, H-3); 7.24-8.02 (m, 15H, 3 Ph). $^{13}$ C-NMR ($CDCl_3$): δ 96.8 (C-1), 73.9 (C-2), 72.3 (C-3), 70.2 (C-4), 65.4 (C-5), 55.4 (OMe), 17.3 (Me).




Scheme 8

*Methyl 8-*C*-cyano-6,7,8-trideoxy-*α*-*D*-*gluco*-octopyranoside* (**3b**).

A solution of **3a** (600 mg, 1.10 mmol) in methanol (4 ml) was treated with sodium methanolate (1N, 0.4 ml). After stirring 1 h at room temperature, the solution was neutralised with ion exchange resin (IR 120, $H^+$). The solution was filtered, concentrated under pressure and coevaporated with water (to remove the methyl benzoate) and toluene. Flash chromatography (dichloromethane-methanol 9:1; v/v) yielded the

compound **3b** as a foam (221 mg, 87%). $[\alpha]_D^{22}$ + 138° (*c* 1.00; $CHCl_3$). $^1$H-NMR ($CDCl_3$): δ 1.5-2.5 (m, 6H, H-6, H-7, H-8); 3.17 (dd, 1H, $J_{3,4}$ 8.5, $J_{4,5}$ 10 Hz, H-4); 3.4 (s, 3H, OMe); 3.43 - 3.54 (m, 2H, H-2, H-5); 3.66 (dd, 1H, $J_{2,3}$ 10, $J_{3,4}$ 8.5 Hz, H-3); 4.68 (d, 1H, $J_{1,2}$ 3.5 Hz, H-1). $^{13}$C-NMR ($CDCl_3$): δ 17.0 (C-8), 21.4 (C-7), 30.1 (C-6), 55 ($OCH_3$), 70.2, 71.9, 73.5, 73.9 (C-2, 3, 4, 5), 99.2 (C-1), 119.6 (C≡N). MS (CI, $NH_3$) m/z: 249 (M + 18). Anal. Calc. for $C_{10}H_{17}NO_5$ (M = 231.248); C, 51.94; H, 7.41. Found: C, 51.55; H, 7.86.

*Methyl 8-*C*-cyano-6,7,8-trideoxy-2,3,4-tri-*O*-trimethylsilyl-α-D-*gluco*-octopyranoside* (**3c**).

A solution of **3b** (200 mg, 0.86 mmol) in dry pyridine (6 ml) was treated at 0 °C, under argon, with trimethylsilyl chloride (658 µl, 6 equiv.). After 1 h, the solution was diluted with dichloromethane, washed with water, dried ($Na_2SO_4$), filtered, concentrated in *vacuo* and coevaporated with toluene. Flash chromatography (pentane-ethyl acetate 12:1, v/v) yielded the compound **3c** as an oil (352 mg, 91%). $[\alpha]_D^{22}$ + 84° (*c* 1.19; $CHCl_3$). $^1$H-NMR ($CDCl_3$): δ 0.13 (3s, 27 H, 3 $SiMe_3$); 1.33 - 2.43 (m, 6H, H-6, H-7, H-8); 3.18 (dd, 1H, $J_{3,4}$ 8, $J_{4,5}$ 9 Hz, H-4); 3.2 (s, 3H, OMe); 3.47 (dd, 1H, $J_{1,2}$ 3.8, $J_{2,3}$ 9.5 Hz, H-2); 3.5 (m, 1H, H-5); 3.72 (dd, 1H, $J_{2,3}$ 9.5, $J_{3,4}$ 8 Hz, H-3), 4.56 (d, 1H, $J_{1,2}$ 3.8 Hz, H-1). $^{13}$C-NMR ($CDCl_3$): δ 0.4, 1.1 ($SiMe_3$), 17.1 (C-8), 22 (C-7), 31 (C-6), 54.7 ($OCH_3$), 70.4, 73.8, 74.8, 76.2 (C-2, 3, 4, 5), 99.7 (C-1), 119 (C≡N). MS (CI, $NH_3$): m/z 465 (M + 18). Anal. Calc. for $C_{19}H_{41}NO_5Si_3$ (M = 447.7955); C, 50.96; H, 9.23. Found: C, 50.89; H, 9.11.

*1,6-Anhydro-tri-*O*-benzyl-2-deoxy-2-*C*-hydroxymethyl-β-D-glucopyranose* (**15**).

A solution of **14** (2.4 g, 9 mmol) in DMF (50 ml) was treated at 0 °C with NaH (1.80 g, 5 equiv.). After stirring 15 min at this temperature, benzylbromide was added slowly (2.8 ml, 2.6 equiv.). The solution was allowed to come to room temperature and stirred for 1 h. Afterwards, the mixture was neutralised with methanol and concentrated in *vacuo*. The residue was extracted with $CH_2Cl_2$ and washed with saturated $NH_4Cl$ and water. The organic phase was dried ($Na_2SO_4$), filtered and concentrated in *vacuo*. Flash chromatography (pentane-ethyl acetate 4:1, v/v) yielded the compound **15** as an oil (3.36 g, 84%). $[\alpha]_D^{22}$ - 15.7° (*c* 1.27, chloroform). $^{13}$C-NMR ($CDCl_3$): δ 43.8 (C-2); 64.9 (C-6); 69.3 (C-5); 71.0, 71.4, 73.3, 73.5, 74.5, 77.0 (3 $CH_2$Ph, C-3, C-4, C-7); 101.2 (C-1). MS (CI, $NH_3$): m/z 464 (M + 18).

*4-*O*-Benzyl-2-deoxy-2-*C*-vinyl-D-glucopyranose* (**17**).

A solution of **16** (478 mg, 1.82 mmol) in $H_2SO_4$ 1M (5 ml) was heated at reflux for 5-10 min. When all the compound was dissolved, the solution was neutralised with $Na_2CO_3$. Afterwards, the mixture was extracted with ethyl acetate, washed with water, dried ($Na_2SO_4$), filtered and concentrated in *vacuo*. Flash chromatography (pentane-ethyl acetate 1:2, v/v) yielded the compound **17** (316 mg, 62%). $[\alpha]_D^{22}$ +63.8° (*c* 0.1, EtOH), $^{13}$C-NMR ($CDCl_3$): δ 52.8 (C-2, α); 54.9 (C-2, β); 61.7 (C-5, α); 62.2 (C-5, β); 70.9, 71.0 (C-6, α,β); 74.0, 74.6, 75.2 ($CH_2$Ph, C-3); 77.9 (C-4, α); 79.0 (C-4, β); 93.9 (C-1, α); 96.0 (C-1, β); 119.8, 120.3 (C-8, α,β); 133.5, 134.6 (C-7, α,β). MS (CI, $NH_3$): m/z 298 (M + 18).

*4-*O*-benzyl-2-deoxy-2-*C*-vinyl-D-xylitol* (**18**).

A solution of **17** (316 mg, 1.12 mmol) in methanol (4 ml) was treated with an aqeous solution of $NaIO_4$ (1.2 g, 5 equiv., 12 ml). Methanol (6 ml) was added and the mixture was heated at 45 °C for 6 h. After filtration of the $NaIO_3$ precipitate and concentration in *vacuo*, the residue was dissolved in ethanol-water (1:1, v/v, 8 ml) and a solution of $NaBH_4$ (298 mg, 7 equiv.) in ethanol-water (1:1, v/v, 12 ml) was slowly added, keeping the temperature of the mixture between 0 °C and 10 °C. Afterwards, the solution was neutralised with ion exchange resin (IR 120, $H^+$), filtered, washed with methanol and concentrated in *vacuo* and finally coevaporated with methanol. Flash chromatography using ethyl acetate as the eluent yielded the compound **18** (130 mg, 46%). $[\alpha]_D^{22}$ -10° (*c* 0.04, EtOH). $^1$H-NMR ($CDCl_3$): δ 3.3-4.1 (m, 7H); 4.5-4.7 (m, 2H, $CH_2$Ph); 5.12 (dd, 1H, $J_{a,c}$ 17.5, $J_{b,c}$ 1.5 Hz, H-c); 5.17 (dd, 1H, $J_{a,c}$ 11 Hz, H-b); 5.84 (ddd, 1H, $J_{a,2}$ 9.5

Hz, H-a); 7.25-7.4 (m, 5H, Ph). $^{13}$C-NMR ($CDCl_3$): δ 48.2 (C-2); 60.1 (C-5); 63.6 (C-1); 70.1 (C-3); 72.5 (*C*$H_2$Ph); 80.9 (C-4); 118.5 (CH=*C*$H_2$); 134.4 (*C*H=$CH_2$). MS (CI, $NH_3$): m/z 270 (M + 18).

*4-O-Benzyl-2-deoxy-1,5-di-O-tosyl-2-C-vinyl-3-O-trimethylsilyl-D-xylitol* (**4a**).

A solution of **18** (50 mg, 0.19 mmol) in pyridine (1 ml) was treated at 0 °C, under argon, with TsCl (83 mg, 2.2 equiv.) and DMAP. After stirring for 1 day at room temperature, the mixture was extracted with $CH_2Cl_2$, washed with $KHSO_4$ (10% aqueous) and water, dried ($Na_2SO_4$), filtered and concentrated in *vacuo*. The residue in a solution of pyridine (1 ml) was treated directly at 0 °C with TMSCl (35 µl, 2 equiv.) and DMAP. The solution was kept at room temperature for 3 h, followed by extracted with $CH_2Cl_2$, washed with water, dried ($Na_2SO_4$), filtered, concentrated in *vacuo*, and finally coevaporated with toluene. Flash chromatography (pentane-ethyl acetate 5:1, v/v) yielded the compound **4a** as an oil (42 mg, 33%) for 2 steps. $^1$H-NMR ($CDCl_3$): δ 0.1 (s, 9H, $Si(Me)_3$); 2.44 (s, 6H, 2 Me); 2.59 (dddd, 1H, $J_{1,2}$ 3, $J_{1',2}$ 9.5, $J_{2,3}$ 8, $J_{2,Ha}$ 9.5 Hz, H-2); 3.54 (ddd, 1H, $J_{3,4}$ 9, $J_{4,5}$ 3, $J_{4,5'}$ 6.5 Hz, H-4); 3.84 (dd, 1H, $J_{1',2}$ 9.5, $J_{1,1'}$ 6 Hz, H-1'); 3.88 (dd, 1H, $J_{1,2}$ 3, $J_{1,1'}$ 6 Hz, H-1); 3.97 (dd, 1H, $J_{2,3}$ 8, $J_{3,4}$ 9 Hz, H-3); 4.03 (dd, 1H, $J_{4,5'}$ 6.5, $J_{5,5'}$ 11 Hz, H-5'); 4.15 (dd, 1H, $J_{4,5}$ 3, $J_{5,5'}$ 11 Hz, H-5), 4.4-4.57 (m, 2H, *C*$H_2$Ph); 5.04 (dd, 1H, $J_{a,c}$ 17.5, $J_{b,c}$ 1.5 Hz, H-c); 5.11 (dd, 1H, $J_{a,Hb}$ 11, H-b); 5.6 (ddd, 1H, $J_{a,2}$ 9, H-a); 7.2-7.7 (m, 9H, 3 Ph). $^{13}$C-NMR ($CDCl_3$): δ -0.05 ($SiMe_3$); 21.5 (2 Me); 46 (C-2); 69.2, 70, 70.5 (C-1, C-3, C-5); 72.7 (*C*$H_2$Ph); 79 (C-4); 120.5 (CH=*C*$H_2$); 133.5 (*C*H=$CH_2$).

*Methyl 7-C-(1-cyanocyclohexyl)-6,7-dideoxy-2,3,4-tri-O-trimethylsilyl-α-D-gluco-heptopyranoside* (**19**).

A solution of **3c** (50 mg, 0.1 mmol) and 1,5-dibromopentane (16 µl, 1.1 equiv.) in dry tetrahydrofuran (0.2 ml) was treated at -78 °C, under argon, with LDA (2 equiv.). The mixture was stirred for 30 min at this temperature. The reaction was quenched at 0 °C with saturated $NH_4Cl$ and diluted with ethyl acetate and washed with water. The solution was dried ($Na_2SO_4$), filtered and concentrated in *vacuo*. Flash chromatography (pentane-ethyl acetate 15:1, v/v) yielded the compound **19** as an oil (40 mg, 70%). $[\alpha]_D^{22}$ + 74.8° (*c* 0.72; $CHCl_3$). $^1$H-NMR ($CDCl_3$): δ 0.15, 0.20, 0.25 (3s, 27 H, 3 $SiMe_3$); 1.1-2.1 (m, 14 H, H-6, H-7, cyclohexyl); 3.19 (dd, 1H, $J_{3,4}$ 8.2, $J_{4,5}$ 9.5 Hz, H-4); 3.31 (s, 3H, OMe); 3.4 (m, 1H, H-5); 3.48 (dd, 1H, $J_{1,2}$ 3.8, $J_{2,3}$ 9.2 Hz, H-2); 3.72 (dd, 1H, $J_{2,3}$ 9.2, $J_{3,4}$ 8.2 Hz, H-3); 4.57 (d, 1H, $J_{1,2}$ 3.8 Hz, H-1). $^{13}$C-NMR ($CDCl_3$): δ 0.3, 1.1 ($SiMe_3$), 22.9, 25.3, 27.1 (3 $CH_2$), 35.5, 35.7, 36.8, 38.6 (C-6, C-7, 2 $CH_2$), 54.6 ($OCH_3$), 70.7, 73.8, 74.6, 76.3 (C-2, 3, 4, 5), 99.5 (C-1), 123.2 (C≡N). MS (CI, $NH_3$) m/z 533 (M + 18). Anal. Calc. for $C_{24}H_{49}NO_5Si_3$ (M = 515.9145): C, 55.87; H, 9,57; N, 2.71. Found: C, 55.84; H, 9.59; N, 2.73.

If the reaction was carried out with 1 equiv. of LDA, the compound **20** could be isolated by flash chromatography in pentane-ethyl acetate 15:1, v/v. $^1$H-NMR ($CDCl_3$): δ 0.14, 0.16, 0.19 (3s, 27H, 3 $SiMe_3$); 1.4-1.7 (m, 8H, H-6, H-7, H-9, H-10); 1.8-1.95 (m, 4H, H-11, H-12); 2.5-2.62 (m, 3H, H-8, H-13); 3.18 (dd, 1H, $J_{3,4}$ 8, $J_{4,5}$ 9 Hz, H-4); 3.31 (s, 3H, OMe); 3.41 (m, 1H, H-5); 3.47 (dd, 1H, $J_{1,2}$ 3.8, $J_{2,3}$ 9.2 Hz, H-2); 3.72 (dd, 1H, $J_{2,3}$ 9.2, $J_{3,4}$ 8 Hz, H-3); 4.57 (d, 1H, $J_{1,2}$ 3.8 Hz, H-1).

*2,3,4-Tri-O-benzyl-1,5-di-O-tosyl-D-arabinitol* (**22**).

A solution of **21**[11] (250 mg, 0.59 mmol) in pyridine (5 ml) was treated, under argon, at 0 °C with tosylchloride (338 mg, 3 equiv.) and DMAP. The mixture was stirred at room temperature for 24 h. The reaction was extracted with $CH_2Cl_2$ and washed with 10% $KHSO_4$ aqueous and saturated $NaHCO_3$, and dried ($Na_2SO_4$), filtered, concentrated and coevaporated with toluene. Flash chromatography (pentane-ethyl acetate 3:1 v/v) yielded the compound **22** as a solid (311 mg, 72%). Mp 105-107 °C, $[\alpha]_D^{22}$ - 0.8 ° (*c* 0.9, chloroform). (Lit.[11]: Mp 97-99 °C, $[\alpha]_D^{22}$ ~ 0 ° (*c* 2.1, DMSO). $^{13}$C-NMR ($CDCl_3$): δ 21.5 (Me), 68.7, 69.2 (C-1, 5), 72.2, 73.2, 74.0 (3 *C*$H_2$Ph), 76.4, 76.7, 77.4 (C-2, 3, 4).

*2,3,4-Tri-O-benzyl-1,5-di-O-bromo-1,5-dideoxy-D-arabinitol* (**23**).

A solution of **21**[11] (500 mg, 1.18 mmol) in dry pyridine (30 ml) was treated, under argon, at 0 °C with triphenylphosphine (1.24 g, 4 equiv.) and carbon tetrabromide (1.17 g, 3 equiv.). The mixture was stirred at room temperature until TLC showed no starting material left. Addition of methanol followed by concentration in *vacuo* gave a residue, which by flash chromatography (pentane-ethyl acetate 12:1, v/v) yielded the compound **23** as an oil (592 mg, 91%). $^{13}$C-NMR ($CDCl_3$): δ 30.3, 33.3 (C-1, 5), 71.6, 73.0, 75.1 (3 $CH_2$Ph), 77.7, 78.2, 79.1 (C-2, 3, 4). MS (CI, $NH_3$) m/z 564 ($^{79}$Br, M + 18), 568 ($^{81}$Br, M + 18).

*2,3,4-Tri-O-benzyl-1,5-di-O-trifluoromethanesulphonyl-D-arabinitol* (**24**).

A solution of **21**[11] (50 mg, 0.12 mmol) in dry $CH_2Cl_2$ (2 ml) was treated, under argon, at -78 °C with diisopropylethylamine (82 µl, 4 equiv.) and $Tf_2O$ (119 µl, 6 equiv.) in $CH_2Cl_2$ (1 ml). The mixture was stirred at this temperature for 2 h. The reaction was quenched at 0 °C with saturated $NaHCO_3$. The solution was extracted with ethyl acetate and washed with brine, dried ($Na_2SO_4$), filtered and concentrated in *vacuo*. Flash chromatography (pentane-ethyl acetate 6:1, v/v) yielded the compound **24** as an oil (64 mg, 79%). $^{13}$C-NMR ($CDCl_3$): δ 71.4 (C-1), 71.9 (2 $CH_2$Ph, C-5), 74.8 ($CH_2$Ph), 80.3, 82.0, 83.1 (C-2, 3, 4).

*2,3,4-Tri-O-benzyl-1,5-di-O-methanesulphonyl-xylitol* (**26**).

A solution of **25**[12] (800 mg, 1.89 mmol) in dry pyridine (20 ml) was treated, under argon, at 0 °C with mesyl chloride (880 µl, 6 equiv.). The mixture was stirred at room temperature for 1 h. The reaction was extracted with $CH_2Cl_2$ and washed with $KHSO_4$ (10% aqueous) and saturated $NaHCO_3$. Then the solution was dried ($Na_2SO_4$), filtered, concentrated in *vacuo* and coevaporated with toluene. Flash chromatography (toluene-ethyl acetate 4:1, v/v) yielded quantitatively the compound **26** as an oil (1.09 g, 100%). $^1$H-NMR ($CDCl_3$): δ 2.85 (s, 6H, 2 Me); 3.67 (dd, 1H, $J_{2,3}$ 5, $J_{3,4}$ 5 Hz, H-3); 3.95 (ddd, 2H, H-2, H-4), 4.21 (dd, 2H, $H_1$, $H_5$); 4.36 (dd, 2H, $H_1$, $H_5$); 4.53-4.72 (2s, m, 6H, 3 $CH_2$Ph). $^{13}$C-NMR ($CDCl_3$): δ 36.9 (2 Me), 69.0 (2C, C-1, 5), 73.2 ($CH_2$Ph), 73.9 ($CH_2$Ph), 75.8 (2C, C-2, 4), 76.2 (C-3).

*2,3,4-tri-O-benzyl-1,5-di-O-trifluoromethanesulfonyl-xylitol* (**27**).

A solution of **25**[12] (300 mg, 0.71 mmol) in dry $CH_2Cl_2$ (15 ml) was treated, under argon, at -78 °C with a solution of $Tf_2O$ (716 µl, 6 equiv.) in $CH_2Cl_2$ (5 ml) and i-$Pr_2$NEt (495 µl, 4 equiv.). After 30 min, the reaction was quenched at 0 °C with saturated $NaHCO_3$. The mixture was extracted with $CH_2Cl_2$, washed with brine, dried ($Na_2SO_4$), filtered and concentrated in *vacuo*. Flash chromatography (toluene-ethyl acetate: 6:1, v/v) yielded the compound **27** as an oil (359 mg, 74%). $^{13}$C-NMR ($CDCl_3$): δ 71.3, 71.4 (C-1, 5); 71.9, 72.0, 74.5 (3 $CH_2$Ph); 77.2 (C-3); 81.1, 81.5 (C-2, 4).

*1,4-Anhydro-2,3-di-O-benzyl-5-O-methanesulphonyl-D/L-xylitol* (**28**).

A solution of **26** (300 mg, 0.5 mmol) in DMSO (5 ml) and NaI (8 mg, 10%) were added to the solution of methylcyanoacetate (114 µl, 2.5 equiv.) and NaH (52 mg, 2.5 equiv.) in DMSO (2 ml). The mixture was stirred at 90 °C for 5 h. After adding MeOH and concentration, the residue was extracted with $CH_2Cl_2$, washed with saturated $NH_4Cl$ and water, dried ($Na_2SO_4$), filtered and concentrated in *vacuo*. Flash chromatography (toluene-ethyl acetate 10:1, v/v) yielded the compound **28** as an oil (110 mg, 54%).$^{13}$C NMR ($CDCl_3$): δ 37.3 (Me), 68.4 (C-5), 71.3, 71.5 (2 $CH_2$Ph), 72.0 (C-1), 77.9 (C-2), 81.2, 81.7 (C-3, 4). MS (CI, $NH_3$): m/z 410 (M + 18).

*1,4-Anhydro-2,3-di-O-benzyl-5-deoxy-5-(methylcyanoacetyl)-D/L-xylitol* (**29**).

A solution of **27** (359 mg, 0.52 mmol) in DMSO (5 ml) was added to a solution of methylcyanoacetate (115 µl, 2.5 equiv.) and NaH (52 mg, 2.5 equiv.) in DMSO (2 ml) at room temperature. After 15 min, methanol was added and the solution concentrated in *vacuo*. The residue was extracted with $CH_2Cl_2$, washed with saturated $NH_4Cl$ and water, dried ($Na_2SO_4$), filtered and concentrated. Flash chromatography (toluene-ethyl acetate: 8:1 v/v) yielded an oil of **29** (240 mg, quant.) as a mixture of

diastereoisomers. $^{13}$C-NMR ($CDCl_3$): δ 29.2, 29.5 (2 C-5); 33.9, 34.8 (2 C-6); 53.4 (2 Me); 71.2, 71.5 (4 $CH_2$Ph); 71.8 (2 C-1); 76.9 (2 C-4); 81.8, 81.9, 82.1, 82,3 (2 C-2, 2 C-3). MS (CI, $NH_3$): m/z 396 (M+1); 413 (M + 18).

*Oxime* **7a**.

A solution of the ketone **30**[6] (100 mg, 0.18 mmol) in methanol (4 ml) was treated with $BnONH_2$ (230 mg, 10 equiv.) in methanol (6 ml) at reflux. After stirring 30 min at 65 °C, the mixture was concentrated in *vacuo*. The residue was extracted with chloroform and the combined extracts were concentrated. Flash chromatography (toluene-ethyl acetate 10:1, v/v) yielded the oxime **7a** as an oil (95 mg, 80%). $[\alpha]_D^{22}$ -33.4 ° (*c* 0.9, chloroform). $^1$H-NMR ($CDCl_3$): δ 4.05 (dd, 1H, $J_{2\text{-}3}$ 6.5, $J_{3\text{-}4}$ 4.5 Hz, H-); 4.14 (d, 1H, $J_{7a\text{-}7b}$ 13.5 Hz, H-7); 4.24 (d, 1H, $J_{3\text{-}4}$ 4.5 Hz, H-4); 4.27 (d, 1H, $J_{2\text{-}3}$ 6.5 Hz, H-2); 4.34 (d, 1H, $J_{7a\text{-}7b}$ 13.5 Hz, H-7); 4.43-4.9 (5 m, 10H, S $CH_2$Ph); 6.6 (s, 1H, H-6); 7.2-7.5 (m, 25H, 5 Ph). $^{13}$C-NMR ($CDCl_3$): δ 70.2, 71.9, 72.2, 73.3, 73.6, 75.5, 76.0, 76.1, 78.6 (5 $CH_2$Ph, C-2, C-3, C-4, C-7); 114.3 (C-6); 144.2 (C-5); 150.2 (C-1). MS (CI, $NH_3$): m/z 640 (M+1); 657 (M + 18).

*Methyl 7,7-dibromo-6,7-dideoxy-2,3,4-tri-*O*-benzyl-α-*D*-*gluco*-hept-6-enopyranoside* (**32**).

Methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside[20] (1.0 g, 2.15 mmol) was oxidised according to the usual Swern procedure: To a solution of oxalyl chloride (283 µl, 3.25 mmol) in dichloromethane (4 ml) at -65 °C was added a solution of DMSO (533 µl, 7.52 mmol) in dichloromethane (2 ml). After stirring for 5 min at -65 °C the glucoside (1.0 g, 2.15 mmol) in dichloromethane (2 ml) was added during 5 min. The mixture was then stirred for further 5 min, and then heated to -50 °C. Triethylamine (1.95 ml, 14 mmol) was added, and the reaction was allowed to reach at room temperature over the course of ½ h. Dichloromethane was added, and the organic phase was washed with water (2 x), NaCl-solution (sat.), dried ($Na_2SO_4$), and concentrated. Evaporation 3 times with toluene left the crude aldehyde **31** which was used directly as described below. The crude aldehyde **31** was coevaporated with toluene and used without further purification. A vigorously stirred solution of carbontetrabromide (1.52 g, 2.13 equiv.) in $CH_2Cl_2$ (3 ml) at 0 °C under argon was treated with triphenylphosphine (2.44 g, 4.3 equiv.) and stirred at room temperature for 20 min. The resulting bright orange slurry was cooled at 0 °C, and the solution of the aldehyde (2.15 mmol) in $CH_2Cl_2$ (2 ml) was added dropwise. The mixture was stirred for 5 min at 0 °C and 30 min at room temperature. Silica gel chromatography (flash silica, toluene-ether-pentane 7:1:2, v/v/v) yielded the dibromoolefin **32** as a solid (982 mg, 74%). Mp 88-90 ° C, $[\alpha]_D^{22}$ +5.9 ° (*c* 1.32, chloroform). $^1$H-NMR (300 MHz, $CDCl_3$): δ 3.35 (dd, 1H, $J_{3\text{-}4}$ 8.5, $J_{4\text{-}5}$ 9.5 Hz, H-4); 3.42 (s, 3H, OMe); 3.5 (dd, 1H, $J_{1\text{-}2}$ 3.7, $J_{2\text{-}3}$ 9.5 Hz, H-2); 4.02 (dd, 1H, $J_{2\text{-}3}$ 9.5, $J_{3\text{-}4}$ 8.5 Hz, H-3); 4.41 (dd, 1H, $J_{4\text{-}5}$ 9.5, $J_{5\text{-}6}$ 9 Hz, H-5); 4.54 (d, 1H, $J_{1\text{-}2}$ 3.7 Hz, H-1); 4.73, 4.92 (3 m, 6H, 3 $CH_2$Ph); 6.25 (d, 1H, $J_{5\text{-}6}$ 9 Hz, H-6); 7.3-7.4 (m, 15H, 3 Ph). $^{13}$C-NMR (300 MHz, $CDCl_3$): δ 135 (C-6); 132 ($CBr_2$); 98 (C-1); 81 (C-4); 80 (C-3); 79 (C-2); 75.8, 75, 73 (3 $CH_2$Ph); 70 (C-5), 55 (OMe). Anal. Calc. for $C_{29}H_{30}Br_2O_5$ (M = 618,372): C, 56.33; H, 4.89; Br, 25.84. Found: C, 56.26; H, 4.91; Br, 25.63.

*Alcohols* **33** *and* **34**.

A solution of the dibromoolefin **32** (210 mg, 0.34 mmol) in dry THF (2 ml) was treated, under argon, at -50 °C with BuLi 1.6 M (850 µl, 4 equiv.). A solution of ketone **30** (200 mg, 0.37 mmol) in dry THF (2 ml) was added at this temperature. After stirring for 1 h, the reaction was warmed to room temperature and quenched with saturated $NH_4Cl$. The reaction was extracted with ethyl acetate, washed with water, dried ($Na_2SO_4$), filtered and concentrated in *vacuo*. Flash chromatography (pentane-ethyl acetate 5:1, v/v) yielded **33** (96 mg, 28%) as the fastest moving compound, followed by **34** (199 mg, 59%). Total yield of **33** and **34**: 295 mg (87%).

**33**: Mp 100-102 °C, $[\alpha]_D^{22}$ - 32.2 ° (*c* 0.98, chloroform). $^1$H-NMR ($CDCl_3$): δ 3.25 (m, 1H, OH); 3.4 (s, 3H, OMe); 3.53 (dd, 1H, $J_{3\text{-}4}$ 10, $J_{4\text{-}5}$ 10 Hz, H-4); 3.54 (dd, 1H, $J_{1\text{-}2}$ 3.7, $J_{2\text{-}3}$ 9 Hz, H-2); 3.91 (dd, 1H, $J_{2\text{-}3}$ 9, $J_{3\text{-}4}$

10 Hz, H-3); 4.57 (d, 1H, $J_{1-2}$ 3.7 Hz, H-1); 4.45-5 (7 m, 14H, 7 $CH_2$Ph); 5.89 (d, 1H, C=C*H*); 7.2-7.4 (m, 35 H, 7 Ph). $^{13}$C-NMR ($CDCl_3$): δ 55.5 (OMe); 61.6 (C-5); 67.4 (C-5'); 69.7 (C-1'); 72.6, 73.5, 74.2, 75.2, 75.4, 75.8, 76.1 (7 $CH_2$Ph); 79.1, 79.4, 80.8, 81.2, 82.0, 83.3 (C-2, C-3, C-4, C-2', C-3', C-4'); 98.3 (C-1); 124.8 (C=*CH*); 139.7 (*C*=CH). Anal. Calc. for $C_{64}H_{64}O_{10}$ + 1 $H_2O$ (M = 993.206); C, 76.02; H, 6.38; Found: C, 76.16; H, 6.52.

**34:** $[\alpha]_D^{22}$ + 30.7° (*c* 1.0; chloroform). $^1$H-NMR ($CDCl_3$): δ 2.55 (m, 1H, OH); 3.4 (s, 3H, OMe); 3.5 (dd, 1H, $J_{1-2}$ 3.7, $J_{2-3}$ 10 Hz, H-2); 3.52 (dd, 1H, $J_{3-4}$ 9, $J_{4-5}$ 10 Hz, H-4); ); 3.6 (d, 1H, $J_{2'-3'}$ 10 Hz, H-2'); 3.8 (d, 1H, $J_{5a''-5b''}$ 12 Hz, H-5a"); 3.87 (dd, 1H, $J_{2-3}$ 10, $J_{3-4}$ 9 Hz, H-3); 4.05 (dd, 1H, $J_{3'-4'}$ 7 Hz, H-3'); 4.1 (d, 1H, $CH_2$Ph); ); 4.12 (d, 1H, H-5b"); 4.25 (d, 1H, H-4'); 4.35-4.45 (2d, 2H, $CH_2$Ph); 4.45 (d, 1H, H-5); 4.55 (d, 1H, H-1); 4.6-4.95 (10d, 10H, $CH_2$Ph); 5.05 (d, 1H, $CH_2$Ph); 5.72 (d, 1H, H-6'); 7.1-7.4 (m, 35H, 7 Ph). $^{13}$C-NMR ($CDCl_3$): δ 55.6 (OMe); 61.7 (C-5); 69.5 (C-5''); 70.7 (C-1'); 72.2, 73.3, 74.2, 74.7, 75.0, 75.7 (7 $CH_2$Ph), 78.7, 79.6, 80.6, 82.1, 82.9, 84.2 (C-2, C-3, C-4, C-2', C-3', C-4'), 98.2 (C-1), 138.1 (C=*CH*).

*Azide* **35**.

To a solution of the alcohol **34** (260 mg, 0.26 mmol) in $TMSN_3$ (3 ml) was added $BF_3$-$Et_2O$ (38 µl, 1.2 equiv.). After stirring for 2 h at room temperature, the mixture was poured in water and extracted with $CH_2Cl_2$. The organic phase was washed with saturated $NaHCO_3$, water, dried ($Na_2SO_4$), filtered and concentrated in *vacuo*. Flash chromatography (pentane-ethyl acetate 6:1, v/v) yielded the azide **35** as an oil (80 mg, 30%). $[\alpha]_D^{22}$ + 48.4° (*c* 1.05; chloroform). $^1$H-NMR ($CDCl_3$): δ 3.38 (s, 3H, OMe); 3.45-3.54 (m, 2H, H-2, H-4); 3.67-4.22 (m, 7H); 4.4-4.94 (7 m, 14H, 7 $CH_2$Ph); 4.63 (d, 1H, $J_{1-2}$ 3.7 Hz, H-1); 6.11 (d, 1H, H-6'); 7.17-7.4 (m, 35H, 7 Ph). $^{13}$C-NMR ($CDCl_3$): δ 55.5 (OMe); 61.0 (C-1'); 62.0 (C-5); 67.8 (C-5''); 72.4, 73.5, 73.6, 73.8, 75.2, 75.4, 75.7 (7 $CH_2$Ph); 79.0, 80.4, 80.8, 81.0, 82.0, 82.2 (C-2, C-3, C-4, C-2', C-3', C-4'); 89.0 (C≡C); 98.3 (C-1); 124.7 (C = *CH*); 134.0 (*C* = CH). IR 2120 $cm^{-1}$ (C-$N_3$ bond).

*Azide* **36**.

The synthesis of the azide **36** was carried out from the alcohol **33** (156 mg, 0.157 mmol) according to the same procedure. Flash chromatography (pentane-ethyl acetate 5:1, v/v) yielded the azide **36** (35 mg, 22%) and 60 mg of a mixture of different compounds. $[\alpha]_D^{22}$ + 15.2° (*c* 1.13; chloroform). $^1$H-NMR ($D_2O$): δ 3.37 (s, 3H, OMe); 3.38-3.54 (m, 3H); 3.66 (d, 1H, *J* 9.5 Hz); 3.88 (dd, 1H, *J* 9, 9.5 Hz); 4.1 (m, 1H); 4.35-3.96 (7 m, 17H); 4.68 (d, 1H, $J_{1-2}$ 3.7 Hz, H-1); 6.09 (d, 1H, H-6'); 7.16-7.4 (m, 35H, 7 Ph). $^{13}$C-NMR ($CDCl_3$): δ 55.5 (OMe); 61.9 (C-5); 65.1 (C-5''); 65.4 (C-1'); 71.2, 73.3, 73.4, 73.7, 75.4, 75.4, 75.7 (7 $CH_2$Ph); 78.0, 79.0, 80.8, 81.0, 81.0, 82.0 (C-2, C-3, C-4, C-2', C-3', C-4'), 88.8 (C≡C); 98.3 (C-1); 126.8 (C = *CH*); 133.1 (*C* = CH). IR 2120 $cm^{-1}$ (C-$N_3$ bond).

*Amine* **37**.

A solution of the azide **35** (80 mg, 78.5 µmol) in EtOH (20 ml) and HCl 0.5 M (2 ml) was hydrogenated at 101 kPa in presence of Pd/C for 24 h at room temperature. The mixture was then filtered on celite and washed with EtOH to give the β-L-*ido* compound **37** (21 mg, 66%). $[\alpha]_D^{22}$ + 29.0° (*c* 1.0; $H_2O$). $^1$H-NMR ($D_2O$): δ 1.44-2.02 (m, 7H, H-6, H-7, H-5', H-6'); 3.2 (dd, 1H, *J* 9, *J* 9 Hz, H-4); 3.4 (s, 3H, OMe); 3.43-3.55 (m, 4H); ); 3.85 (bs, 1H, H-4'); 3.9 (d, 1H, *J* 12 Hz, H-3); 3.95 (bs, 1H, H-2'); 4.1 (dd, 1H, *J* 3.5, *J* 4 Hz, H-3'); 4.75 (d, 1H, $J_{1-2}$ 3.8 Hz, H-1). $^{13}$C-NMR ($D_2O$): δ 26.9, 27.1, 28.6 (C-6, C-7, C-6'); 31.4 (C-5'); 55.8 (OMe); 60.2 (C-1'); 64.4 (C-5''); 69.2, 71.2, 71.2, 71.8, 72.1, 73.9, 74.1 (C-2, C-3, C-4, C-5, C-2', C-3', C-4'); 99.8 (C-1).

*Amine* **1**.

The synthesis of the β-D-*gluco* compound **1** (14 mg, 100%) was carried out from the azide **36** (35 mg, 34.3 µmol) according to the procedure described above. $[\alpha]_D^{22}$ + 46.4° (*c* 0.28; $H_2O$).$^1$H-NMR ($D_2O$). δ 1.25

(m, 1H, H-6a); 1.38 (m, 1H, H-6b); 1.45 (dd, 1H, $J_{6ax'\text{-}6eq'}$ 15 Hz, H-6ax'); 1.58 (m, 1H, H-5'); 1.95 (m, 1H, H-7a); 2.05 (m, 1H, H-7b); 2.15 (dd, 1H, $J_{5'\text{-}6eq'}$ 3.5 Hz, H-6eq'); 3.2-3.65 (m, 11H); 3.85 (d, 1H, $J_{2'\text{-}3'}$ 11 Hz, H-2'); 4.8 (d, 1H, $J_{1\text{-}2}$ 3.5 Hz, H-1). $^{13}$C-NMR ($D_2O$): δ 27.2, 27.9, 32.4 (C-6, C-7, C-6'); 36.9 (C-5'); 55.8 (OMe); 61.0 (C-1'); 65.4 (C-5''); 71.9, 72.2, 72.2, 73.9, 74.1, 75.5, 75.7 (C-2, C-3, C-4, C-5, C-2', C-3', C-4'); 99.8 (C-1).

## REFERENCES


1. Toshima, K.; Tatsuta, K. *Chem. Rev.* **1993** *93* 1503-1531. Banoub, J.; Boullanger, P.; Lafont, D. *Chem. Rev.* **1992** *92* 1167-1195. Sinaÿ, P. *Carbohydr.Res.* **1991** *63* 519-528. Schmidt, R. R. *Angew.Chem.* **1986** *98* 213-236. Paulsen, H. *Angew.Chem. Int. Ed. Engl.* **1982** *21* 155-224.
2. Oehrlein, R.; Hindsgaul, O.; Palcic, M. M. *Carbohydr.Res.* **1993** *244* 149-159. Look, G. C.; Wong, C.-H. *Tetrahedron Lett.* **1992** *33* 4253-4256. Gygax, D.; Spies, P.; Winkler, T.; Pfaar, U. *Tetrahedron* **1991** *47* 5119-5122. Turner, N. J.; Webberley, M. C. *J. Chem. Soc. Chem. Commun.* **1991** 1349-1350. Turner, N. J. *Natural Product Reports* **1989** *6* 625-644. Nilsson, K. G. I. *Carbohydr.Res.* **1988** *180* 53-59.
3. Borman, S. *Chemical & Engineering News* **1993** *june 28* 27-34.
4. Burton, D. R. *Acc.Chem.Res.* **1993** *26* 405-411.
5. Jespersen, T. M.; Bols, M.; Skrydstrup, T.; Sierks, M. *Tetrahedron* **1994** *50* 13449-13460.
6. Horii, S.; Fukase, H. *European patent* EP 0 240 175 B1 **1987**.
7. Sakairi, N.; Kuzuhara, H. *Tetrahedron Lett.* **1982** *23* 5327-5330.
8. Jansson, P. E.; Lindberg, J.; Widmalm, G. *Acta Chem. Scand.* **1993** *47* 711-715.
9. Hanessian, S. *Methods Carbohydr. Chem.* **1972** *6* 183-189.
10. Jeppesen, L. M.; Lundt, I.; Pedersen, C. *Acta Chem. Scand.* **1973** *27* 3579-3585.
11. Gray, G. R.; Hartmann, F. C.; Barker, R. *J.Org.Chem.* **1965** *30* 2020-2024.
12. Burgess, K.; Henderson, I. *Tetrahedron Lett.* **1991** *32* 5701-5704.
13. Stork, G.; Saccomano, N. A. *Tetrahedron Lett.* **1987** *28* 2087-2090.
14. Rouzaud, D.; Sinay, P. *J.Chem.Soc.Chem.Commun.* **1983** 1353-1354.
15. Richey, Jr. H. G.; McLane, R. C.; Phillips, C. J. *Tetrahedron Lett.* **1976** 233-234.
16. Huet, J. *Bull.Soc.Chim.Fr.* **1964** *30* 952-978.
17. Goekjian, P. G.; Wu, T. C.; Kang, H. Y.; Kishi, Y. *J.Org.Chem.* **1991** *56* 6422-6434.
18. Kojiara, A.; Zwirzak, A. *Tetrahedron Lett.* **1987** *28* 6513-6516.
19. Otting, G. *J. Magn. Reson.* **1990** *86* 496-508.
20. Liptak, A.; Jodal, I.; Nanasi, P. *Carbohydr. Res* **1975** *44* 1-11.


(*Received in UK* 15 *May* 1995; *revised* 16 *June* 1995; *accepted* 23 *June* 1995)