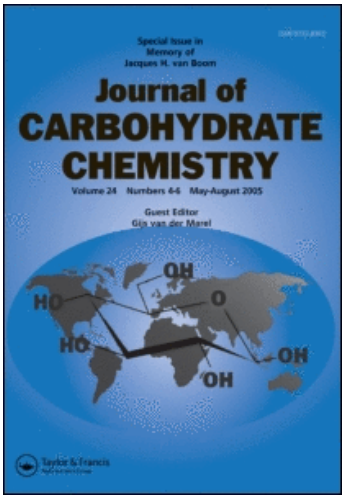

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EFFECT OF PROTECTING GROUPS AND SOLVENTS IN ANOMERIC *O*-ALKYLATION OF MANNOPYRANOSE[1]

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ABSTRACT

Anomeric *O*-alkylation of mannopyranoses with various protecting groups was investigated using mannose derivatives and 2,3-*O*-isopropylidene-1-*O*-trifluoromethanesulfonyl-D-glycerol (**1**) as alkylating agent. Generally, in polar solvents higher α/β ratios were obtained than in nonpolar solvents. Sterically demanding protecting groups at the 6-*O*-position and polar solvents led to higher yields. Reactivity differences were explained by different complex formation. Based on these results mannopyranosyl-α(1-4) glucopyranosides **26** and **27** were synthesized using mannose derivatives **5** and **6** having a 6-*O*-(*p*-methoxyphenyl)diphenylmethyl group and galactosyl trifluoromethanesulfonate **24** or nonafluorobutanesulfonate (nonaflate) **25**, respectively, as alkylating agents.

INTRODUCTION

The anomeric *O*-alkylation method has been developed in our group[1-3] and it has become a very convenient method for glycoside bond formation. In further investigations this reaction was studied using partially protected sugars[4] or even those without protecting groups.[5] Though the relationship between protecting groups and solvents is very important in anomeric *O*-alkylation, this influence has not been examined thoroughly.

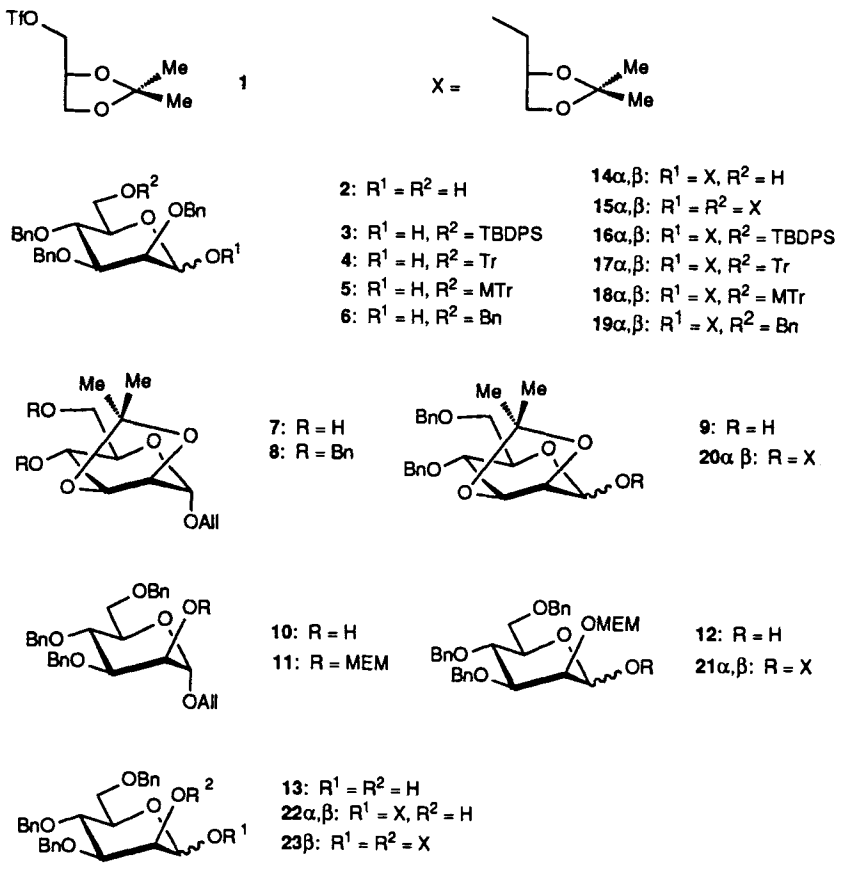
Stereoselectivity in mannopyranoside synthesis using the anomeric *O*-alkylation method is determined by the equilibrium between the two possible 1-oxides (α and β), their rate of equilibration, and their relative reactivities; i.e., α- and β-glycosides are produced directly from the corresponding 1-*O*-anions. In nonpolar solvents, due to the anomeric effect, the α-oxide is thermodynamically favored, but the β-oxide reacts faster owing to its higher reactivity based on the kinetic anomeric effect.[6] Therefore, generally greater amounts of the β–glycoside are obtained, though this depends on the temperature[7] and the kind of protecting groups[7] used. On the other hand, polar solvents, such as solvent-mixtures of hexamethylphosphoric triamide (HMPT) and dimethylformamide (DMF), lead to α-linked disaccharides.[3] These results are now supported by more systematic investigations.

RESULTS AND DISCUSSION

Synthesis of 2,3-*O*-isopropylidene-1-*O*-D-mannopyranosyl-D-glycerol

We have investigated the influence of protecting groups and solvents using glycerol triflate **1** as alkylating agent and the mannose derivatives **2-6**,**9**,**12**, and **13** as 1-*O*-unprotected sugars, respectively (Scheme 1). Sodium hydride was chosen as the base and the solvents used were dichloromethane, tetrahydrofuran, acetonitrile, and HMPT/DMF (mixture).

The 1-*O*-unprotected sugars **3** and **4** were synthesized from 2,3,4-tri-*O*-benzyl-D-mannopyranose **2**[7] in a similar manner using *tert*-butylchlorodiphenylsilane and chlorotriphenylmethane in pyridine to yield **3** (53%) and **4** (56%), respectively. Compounds **5** and **6** are known.[7] Compound **9** was synthesized as follows: regioselective isopropylidenation of allyl α-D-mannopyranoside[8] in acetone with 2,2-dimethoxypropane in the presence of *p*-toluenesulfonic acid gave the 2,3-*O*-isopropylidene derivative **7** as intermediate; the hydroxy groups at positions 4 and 6 were benzylated using sodium hydride and benzyl bromide in DMF to yield **8** (30%, 2 steps). The allyl ether of **8** was rearranged to the 1-propenyl ether by potassium *tert*-butoxide in dimethylsulfoxide (DMSO) at 100 °C; hydrolysis with mercury (II) chloride/mercury (II) oxide in acetone-water afforded **9** (82%). Compound **12** was synthesized by introduction of a 2-methoxyethoxymethyl (MEM) group at *O*-2 of allyl 3,4,6-tri-*O*-benzyl-α-D-mannopyranoside **10**[9] using MEM chloride and *N*-ethyldiisopropylamine in dichloromethane furnishing **11** as intermediate; ensuing deallylation as described above gave **12** in 85% yield. Compound **13** is known.[7] **1** was reacted with each mannose derivative mentioned above to yield the glycosides **14**α,β-**23**β. The results are summarized in Table 1.



Scheme 1

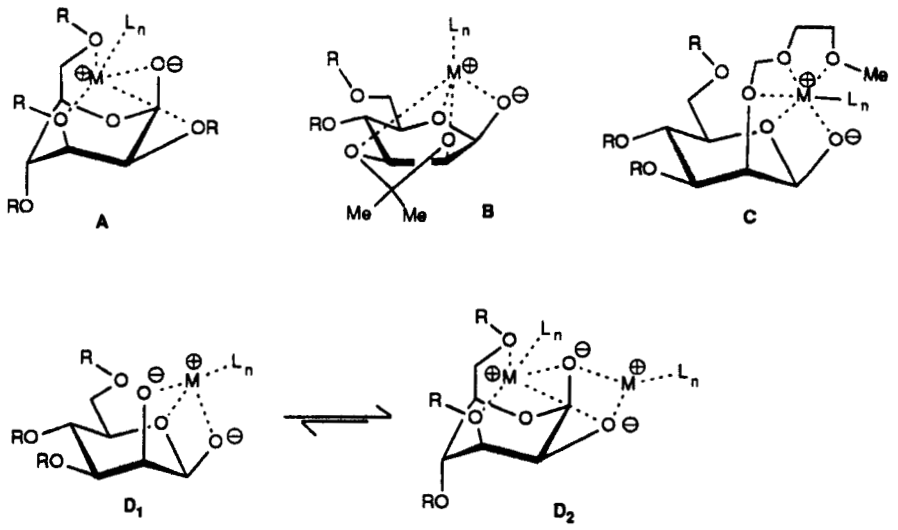
As a general tendency, the more polar the solvent became the more glycoside, particulary α-isomer, was obtained. On account of the kinetic anomeric effect the β-oxide reacts preferentially; therefore, in nonpolar solvents in which the kinetic anomeric effect is stronger, β-glycosides were mainly obtained. When highly polar acetonitrile was used, α-glycosides were preferentially obtained.

Protecting groups also have a great effect on the yields, especially the sterically hindered *tert*-butyldiphenylsilyl (TBDPS), triphenylmethyl (Tr) and (*p*-methoxyphenyl)-diphenylmethyl (MTr) groups of compounds **3-5** led to better yields. On the other hand, **6**[10] and **12**, having a benzyl group at *O*-6 instead of a big protective group and a MEM group at *O*-2, gave lower yields. The use of compounds **2** and **9** in THF and in dichloromethane as solvents also resulted in lower yields. These results cannot be explained by the different inductive effects of the protecting groups.

Table 1. Reaction of **1** with **2-6, 9, 12, 13**[a]

Compound	Reaction Time [h], Products (Yield [%])							
	in CH_2Cl_2		in THF		in CH_3CN		in HMPT/DMF	
2	50	**14α** (3) **14β** (54)	24	**14α** (6) **14β** (21)	3	**14α** (14), **15α** (11) **14β** (25), **15β** (20)	-	
3	1	**16α** (13) **16β** (41)	3	**16α** (14) **16β** (73)	0.15	**16α** (56) **16β** (30)	-	
4	5	**17α** (12) **17β** (48)	3	**17α** (3) **17β** (62)	0.16	**17α** (54) **17β** (38)	-	
5	51	**18α** (9) **18β** (62)	3	**18α** (15) **18β** (74)	1	**18α** (58) **18β** (37)	4.5	**18α** (21)
6	17	**19α** (3) **19β** (31)	22	**19α** (7) **19β** (34)	0.8	**19α** (34) **19β** (33)	-	
	10[b]	**19α** (2) **19β** (2)		-		-	-	
9	50	**20α** (trace) **20β** (27)	24	**20α** (9) **20β** (61)	0.8	**20α** (18) **20β** (58)	-	
12	2	**21α** (8) **21β** (26)		no reaction	0.8	**21α** (23) **21β** (48)	-	
13	3	**22β** (42) **23β** (16)	24	**22β** (62)	11	**22α** (2) **22β** (53), **23β** (27)	19	**22α** **22β,23β** (traces)
	14[c]	**22β** (28)	24[c]	**22β** (29)		-	-	
	24[d]	**22β** (48) **23β** (14)		-		-	-	

a. For experimental details, see general procedure
b. At -10 °C
c. Addition of 1 equivalent of NaH
d. Addition of 2 equivalents of NaH



Scheme 2

Although sterically bulky groups usually exert a negative effect on yields, large substituents gave better yields in our case, as mentioned above. Therefore, possible complex formation may play a major effect as discussed below. Thus, when a stable complex **A** (Scheme 2) can be formed during the reaction, the rate of the glycosylation reaction seems to be reduced; bulky groups at *O*-6 obviously destabilize $^1C_4$ conformations, thus inhibiting stable $^1C_4$ complex formation between the 1-*O*-oxide and *O*-6 as shown in **A** (Scheme 2).

Complex **A** formation should be favored at low temperatures, thus lowering the yields. Compound **9**, which prefers a skew boat conformation, could generate a complex **B** with *O*-2, *O*-5, and 1-β-oxide and possibly *O*-3 as ligands. But when complex formation is suppressed by THF as a ligand, then the yields became higher. This explanation is in accord with the results from **2**, which could form a complex between 1-*O*-oxide, *O*-2, *O*-3, and *O*-6 (Scheme 2, **A**). Especially, the lack of a protective group at *O*-6 seems to support complex formation. The use of an excess amount of sodium hydride for **13** led to a vicinal dianion at *O*-1 and *O*-2 and possibly reaction via complex $\mathbf{D_1}$ or $\mathbf{D_2}$ (Scheme 2); thus relatively better yields and, expectedly, only the β-anomer was then obtained. Obviously, when 1 equivalent of sodium hydride was used yields became lower. Compound **12** possesses a bidentate ligand like a crown ether (the MEM group), thus presumably forming strong complexes (**C** in Scheme 2). In THF compounds **21**α,β were

Table 2. Reaction of **5** and **6** with **24** and **25**[a]

Starting Materials	Solvent	Temp. [°C]	Time [h]	Products	Yield [%]
5 + **24**	A[b]	- 10	2	**26**	61
	A[b]	r.t.	24	decomp.	
	DMF	r.t.	24	decomp.	
	THF	- 10	72	decomp.	
	CH_2Cl_2	r.t.	24	no reaction	
	Toluene[c]	- 10	24	**26**	5
	Toluene[c]	r.t.	22	**26**	8
				29α	14
				29β	19
5 + **25**	A[b]	- 10	3	**26**	83
6 + **24**	A[b]	- 10	2	**27**	44

a. For details, see Experimental

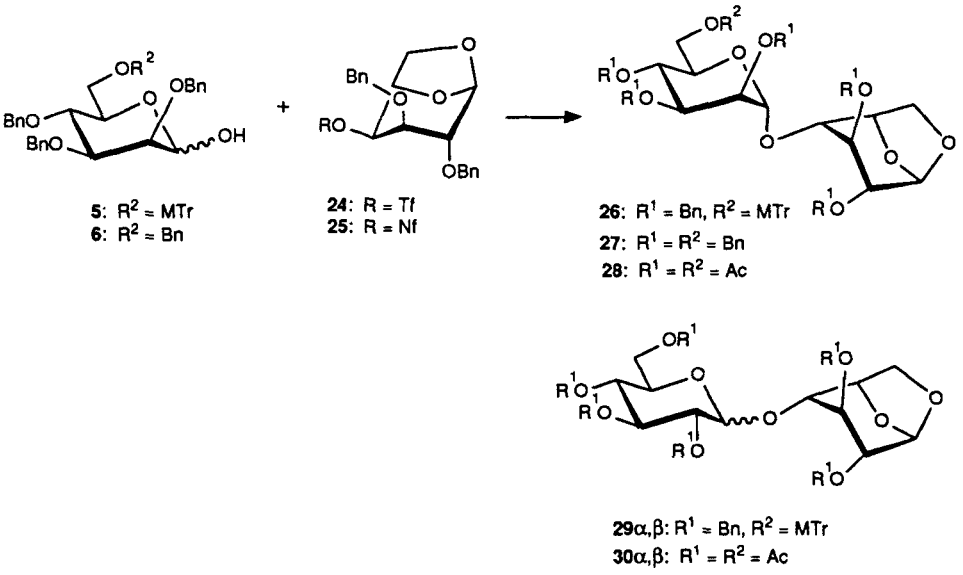
b. A: HMPT/DMF = 2:1

c. Addition of 1.5 equivalents of 15-crown-5

obtained in low yields only; by-products were not formed and excess sodium hydride was still present after the reaction. Acetonitrile has a higher polarity than dichloromethane and THF; therefore, it will interfere with complex formation to furnish glycosides in better yields.

Syntheses of 1,6-anhydro-4-*O*-α-D-mannopyranosyl-β-D-glucose derivatives

Secondary triflates generally exhibit lower reactivities than primary triflates. In a previous paper[3] we have reported as a better solvent combination HMPT-DMF (2:1) which leads to activation of the 1-*O*-oxide to yield higher α-glycoside ratios. These solvents proved to be effective only for secondary triflates (see Table 1). As shown in Table 2, we have investigated in this solvent mixture the glycosylation of **5**, which is thought to be a suitable 1-*O*-unprotected sugar having a large protecting group at *O*-6, with 1,6-anhydro-2,3-di-*O*-benzyl-4-*O*-trifluoromethanesulfonyl-β-D-galactopyranose **24**[12] as alkylating agent at -10 °C. The reaction was finished within 2.5 hours to give α-disaccharide **26** in 61% yield. Compound **5** was proven to be a more reactive glycosyloxide donor than **6**, because in the same reaction **6** and **24** gave **27** only in 44% yield.[3]



Scheme 3

Higher temperatures employed for these reactions resulted in decomposition of the substrates and use of other solvents having lower polarities, such as THF or dichloromethane, gave no better yields. A crown ether was previously utilized in our group[4] to activate the anomeric oxide. With crown ether in toluene at low temperatures no good results were obtained and at room temperature the donor epimerised to give α- and β-glucosyl glucose (**29**α,β) in 14% and 19% yields, respectively; **26** was obtained in only 8% yield. These results indicated that further activation of mannose is limited. For structural assignments compounds **27** and **29**α,β were converted into the *O*-acetyl protected derivatives **28** and **30**α,β, respectively.

In another experiment the alkylating agent was activated using a stronger leaving group; nonafluorobutanesulfonate is more effective than triflate. Compounds **5** and **25** reacted under the same conditions as the triflate **24**, thus giving **26** in 83% yield.

As a conclusion, mannopyranosyl glycerols can be obtained via anomeric *O*-alkylation in high yields using either large protecting groups at *O*-6 of the 1-*O*-unprotected mannose residue or acetonitrile as solvent independent of the protecting groups so as to break stable complex formation. In HMPT-DMF α-mannopyranosyl-(1-4)-glucopyranoses can be obtained in high yields, when large protecting groups at *O*-6 are employed; the use of nonaflate as leaving group proved to be particularly efficient.

EXPERIMENTAL

Solvents were purified in the usual way; the petroleum ether used had a boiling range of 30-60 °C. Melting points are uncorrected. ^{1}H NMR spectra (internal standard tetramethylsilane) were recorded by Bruker AC 250 Cryospec. Flash chromatography was carried out on silica gel (Baker; 0.03-0.060 mm). Foil plates silica gel 60 F_{254} (Merck, layer thickness 0.2 mm) were used for thin layer chromatography (TLC). Silica gel 60 F_{254} PLC plates on glass, layer thickness 1 mm, were used for preparative TLC. Elemental analysis was carried out using Heraeus CHN-O-Rapid. Optical rotations were measured by Perkin-Elmer polarimeter 241/MS, 1-dm cell at 20 °C. Mass spectra were measured by Varian Mass spectrometer MAT 312 EI-MS (70 eV) and MAT 312/AMD 5000 FAB-MS (70 eV).

2,3,4-Tri-*O*-benzyl-6-*O*-(*tert*-butyldiphenylsilyl)-D-mannopyranose (3). *Tert*-butyldiphenylchlorosilane (1.8 mL, 6.9 mmol) was added to a solution of 2,3,4-tri-*O*-benzyl-D-mannopyranose (**2**)[7] (1.66 g, 3.66 mmol) in pyridine (60 mL) at -20 °C with stirring and the mixture was allowed to warm to room temperature. After 4 days the solution was poured into ice-water, extracted with ethyl acetate, the extract washed with aqueous sodium hydrogencarbonate and brine, dried over magnesium sulfate, and concentrated. The residue was purified by silica gel column chromatography (8:1 petroleum ether/ethyl acetate) to give **3** (1.34 g, 53%) as a syrup: R_f 0.44 (3:1 petroleum ether/ethyl acetate); ^{1}H NMR ($CDCl_3$) δ 1.05 (s, 9H, *tert*-Butyl), 3.33 (d, 1H, $J_{1,OH}$ = 3.6 Hz, OH-1), 3.74-4.16 (m, 6H, H-2,3,4,5,6,6'), 4.56-4.93 (m, 6H, $3CH_2$), 5.20 (m, 1H, H-1), 7.08-7.44 (m, 21H, $4.2C_6H_5$), 7.64-7.80 (m, 4H, $0.8C_6H_5$).

Anal. Calcd for $C_{43}H_{48}SiO_6$: C, 74.95; H, 7.04. Found: C, 74.82; H, 7.02.

2,3,4-Tri-*O*-benzyl-6-*O*-triphenylmethyl-D-mannopyranose (4). Triphenylchloromethane (2.71 g, 9.72 mmol) was added to the solution of **2** (2.92 g, 6.48 mmol) in pyridine (20 mL) at 60 °C with stirring. After 7 h the reaction was quenched and purification was performed as described for **3** to yield **4** (2.48 g, 56%) as a syrup: MS (EI): *m/z* = 399 $(M-H)^+$, 309 $(M-Bn)^+$; ^{1}H NMR ($CDCl_3$) δ 3.26 (dd, 1H, $J_{5,6}$ = 4.4 Hz, $J_{6,6'}$ = 10.0 Hz, H-6), 3.51 (dd, 1H, $J_{2,3}$ = 1.6 Hz, $J_{3,4}$ = 10.0 Hz, H-3), 3.84 (dd, 1H, $J_{1,2}$ = 1.5 Hz, H-2), 3.95 (dd, 1H, $J_{4,5}$ = 9.3 Hz, H-5), 4.14 (dd, 1H, H-4), 4.29 (d, 1H, H-6'), 4.62-4.77 (m, 5H, $2.5CH_2$), 5.32 (d, 1H, J = 12.5 Hz, $0.5CH_2$), 5.32 (d, 1H, H-1), 6.88-6.92 (m, 2H, $0.4C_6H_5$), 7.17-7.61 (m, 28H, $5.6C_6H_5$).

Allyl 4,6-Di-*O*-benzyl-2,3-*O*-isopropylidene-α-D-mannopyranoside (8). Mannose (60 g) was added to allyl alcohol (120 mL) which contained 3 g of hydrogen chloride and the reaction mixture was stirred at 70 °C for 5 h.[8] To the solution was

added an excess amount of aqueous ammonia and the resulting solution was then concentrated to dryness. The residue was dissolved in dry acetone (900 mL) and 2,2-dimethoxypropane (270 mL) and *p*-toluenesulfonic acid (120 mg) was added with stirring. After 15 h triethylamine (2 mL) was added and the solution was concentrated. To a solution of the residue in acetone (900 mL) and water (900 mL) *p*-toluenesulfonic acid (9 g) was added with stirring. After 4 h sodium hydrogencarbonate (15 g) was added to the solution and the mixture was concentrated. The residue was diluted with water and extracted with petroleum ether to yield allyl 2,3,4,6-di-*O*-isopropylidene-α-D-mannopyranoside (5.4 g, 5.5% from mannose). The water layer was extracted with chloroform to give allyl 2,3-*O*-isopropylidene-α-D-mannopyranoside (**7**) (42.2 g, 49% from mannose). Without further purification **7** (1.67 g, 6.42 mmol) was dried and diluted with DMF (5 mL). This solution was added dropwise with stirring to a suspension of sodium hydride (0.40 g, 17 mmol) in DMF. After 3 h benzyl bromide (2.0 mL, 17 mmol) was added to the solution and stirred for 13 h, poured into ice and aqueous ammonium chloride, extracted with ether, the extract washed with aqueous sodium hydrogencarbonate and brine, dried over magnesium sulfate and concentrated. The residue was purified by silica gel column chromatography (7:1 petroleum ether/ethyl acetate) to yield **8** (1.75 g, 62%) as a syrup: $[\alpha]_D$ + 37.0° (*c* 1.16, chloroform); MS (EI): *m/z* = 440 $(M)^+$, 425 $(M\text{-}Me)^+$, 349 $(M\text{-}Bn)^+$; ^1H NMR ($CDCl_3$) δ 1.37, 1.51 (2s, 6H, $2CH_3$), 3.57 (dd, 1H, $J_{5,6}$ = 6.9 Hz, $J_{6,6'}$ = 10.1 Hz, H-6), 3.65-3.83 (m, 3H, H-4,5,6'), 4.01 (ddq, 1H, $0.5OCH_2$), 4.17 (dd, 1H, $J_{1,2}$ < 0.5 Hz, $J_{2,3}$ = 5.8 Hz, H-2), 4.22 (ddq, 1H, $0.5OCH_2$), 4.33 (t, 1H, H-3), 4.54, 4.63 (2d, 2H, J = 12.2 Hz, CH_2), 5.11 (d, 1H, H-1), 5.16-5.32 (m, 2H, $=CH_2$), 5.82-5.92 (m, 1H, =CH), 7.25-7.35 (m, 10H, $2C_6H_5$).

2,3-*O*-Isopropylidene-4,6-di-*O*-benzyl-D-mannopyranose (9). A solution of **8** (5.65 g, 12.8 mmol) and potassium *tert*-butoxide (0.72 g, 6.4 mmol) in DMSO (20 mL) was stirred at 100 °C for 30 min. The solution was cooled, diluted with water (20 mL), extracted with ether and the extract concentrated. The residue was dissolved in acetone (140 mL) and water (14 mL), and mercury (II) oxide (3.28 g), then mercury (II) chloride (3.28 g, 11.9 mmol) in acetone (10 mL) and water (5 mL) were added dropwise with stirring. After 10 min sodium hydrogencarbonate (3 g) was added to the solution, the solution was filtered through Celite and washed with acetone. This filtrate was concentrated and the residue was diluted with ether, washed with aqueous sodium iodide and the ether layer was dried over magnesium sulfate. Crude products were purified by silica gel column chromatography (6:1 petroleum ether/ethyl acetate) to yield **9** (4.23 g, 82%) as a syrup: R_f 0.41 (2:1 petroleum ether/ethyl acetate); MS (EI): *m/z* = 399 $(M\text{-}H)^+$, 309 $(M\text{-}Bn)^+$; ^1H NMR ($CDCl_3$) δ 1.37, 1.50 (2s, 6H, $2CH_3$), 3.27 (d, 1H, $J_{1,OH}$ =

4.4 Hz, OH-1), 3.54 (dd, 1H, $J_{3,4}$ = 6.7 Hz, $J_{4,5}$ = 9.1 Hz, H-4), 3.61 (dd, 1H, $J_{5,6}$ = 6.0 Hz, $J_{6,6'}$ = 10.4 Hz, H-6), 3.73 (dd, 1H, $J_{5,6'}$ = 2.9 Hz, H-6'), 4.05 (ddd, 1H, H-5), 4.17 (d, 1H, $J_{2,3}$ = 6.0 Hz, H-2), 4.37 (t, 1H, H-3), 4.53, 4.82 (2d, 2H, J = 11.5 Hz, CH_2), 4.55, 4.59 (2d, 2H, J = 10.5 Hz, CH_2), 5.39 (d, 1H, H-1), 7.22-7.33 (m, 10H, $2C_6H_5$).

3,4,6-Tri-*O*-benzyl-2-*O*-(2-methoxyethoxymethyl)-α-D-mannopyranose (12). 2-Methoxyethoxymethyl chloride (0.11 mL, 0.96 mmol) was added to a solution of allyl 3,4,6-tri-*O*-benzyl-α-D-mannopyranoside (**10**)[9] (154 mg, 0.31 mmol) and *N*-ethyldiisopropylamine (0.16 mL, 0.92 mmol) in dichloromethane (2 mL) with stirring. After 3 d the solution was diluted with dichloromethane and washed with aqueous sodium hydrogencarbonate. The organic layer was dried over magnesium sulfate and concentrated. The residue was purified by silica gel column chromatography, (7:1 petroleum ether/ethyl acetate) to yield **11** (156 mg, 86%) as a syrup, R_F 0.45 (2:1 petroleum ether/ethyl acetate). A solution of **11** (1.26 g, 2.18 mmol) and potassium *tert*-butoxide (0.36 g, 3.2 mmol) in dichloromethane (5 mL) was stirred at 100 °C for 13 h. Ice and aqueous ammonium chloride were added to the reaction mixture which was then extracted with ether and the extract washed with aqueous sodium hydrogencarbonate and brine. The organic layer was dried over magnesium sulfate and concentrated. The residue was dissolved in acetone (40 mL), water (5 mL) and mercury (II) oxide (0.6 g) and then mercury (II) chloride (0.6 g) in acetone (2 mL) and water (1 mL) were added dropwise with stirring. After 40 min excess amount of sodium carbonate was added to the solution, the mixture was filtered through Celite and washed with acetone. The filtrate was concentrated and the residue was diluted with ether, washed with aqueous sodium iodide and the ether layer was dried over magnesium sulfate. Crude products were purified by silica gel column chromatography (4:1 petroleum ether/ethyl acetate) to yield **12** (1.00 g, 85%) as a syrup: R_f 0.07 (2:1 petroleum ether/ethyl acetate) MS (EI): *m/z* = 537 $(M-H)^+$, 420 $(M-H_2O)^+$, 449 $(M-MEM)^+$, 431 $(M-MEM-H_2O)^+$, 371 $(M-MEM-Bn-H)^+$; ^1H NMR ($CDCl_3$) δ 2.97 (d, 1H, $J_{1,OH}$ = 3.5 Hz, OH-1), 3.36 (s, 3H, CH_3), 3.47 (t, 2H, J = 4.5 Hz, OCH_2), 3.67-4.03 (m, 8H, H-2,3,4,5,6,6',OCH_2), 4.46-4.90 (m, 8H, $3CH_2$, OCH_2O), 5.30 (m, 1H, H-1), 7.14-7.33 (m, 15H, $3C_6H_5$).

General synthetic methods for the reactions with 1. To a 4 mL solution of the mannose derivative (0.5 mmol) was added sodium hydride (95%, 18 mg, 0.72 mmol) with stirring. After 15 min **1**, dissolved in the same solvent (1 mL), was added dropwise to the above solution at room temperature. In the case of reaction at -10 °C, the solution was stirred for 15 min after sodium hydride was added, the reaction mixture cooled to -10 °C and stirred for 10 min and then the triflate solution was added. When the mannose derivatives had disappeared on TLC or the reaction did not proceed any more,

ice was added to the reaction mixture which was then extracted with dichloromethane; in the case of HMPA-DMF as solvents the reaction mixture was extracted with ethyl acetate. The organic layer was washed with aqueous sodium hydrogencarbonate and brine, dried over magnesium sulfate and concentrated. The residue was separated by silica gel column chromatography. The results are shown in Table 1.

2,3-*O*-Isopropylidene-1-*O*-(2,3,4-tri-*O*-benzyl-α- and β-D-mannopyranosyl)-D-glycerol (14α and 14β). Both ^{1}H NMR spectra were in agreement with those reported.[7]

2,3-*O*-Isopropylidene-1-*O*-[2,3,4-tri-*O*-benzyl-6-*O*-(2,2-dimethyl-1,3-dioxolan-4*R*-yl)-α- and β-D-mannopyranosyl]-D-glycerol (15α and 15β). 15α: $[\alpha]_D$ = + 33.8° (*c* 1.07, chloroform); MS (EI): *m/z* = 663 (M-Me)$^+$, 587 (M-Bn)$^+$; ^{1}H NMR ($CDCl_3$) δ 1.33, 1.35, 1.38, 1.39 (4s, 12H, $4CH_3$), 3.44 (dd, 1H, $J_{5',6'a}$ = 6.3 Hz, $J_{6'a,6'b}$ = 10.4 Hz, H-6'a), 3.51-4.04 (m, 13H, H-1a,1b,3a,3b,2',3',4',5',6'b,1"a,1"b,3"a,3"b), 4.19-4.28 (m, 2H, H-2,2"), 4.62 (s, 2H, CH_2), 4.63, 4.92 (2d, 2H, J = 10.8 Hz, CH_2), 4.69, 4.75 (2d, 2H, J = 12.4 Hz, CH_2), 4.87 (dd, 1H, $J_{1',2'}$ = 1.5 Hz, H-1'), 7.25-7.38 (m, 15H, $3C_6H_5$). **15β:** $[\alpha]_D$ = -30.3° (*c* 1.09, chloroform); ^{1}H NMR ($CDCl_3$) δ 1.33, 1.36, 1.38, 1.40 (4s, 12H, $4CH_3$), 3.36-4.06 (m, 14H, H-1a,1b,3a,3b,2',3',4',5',6'a,6'b,1"a,1"b,3"a,3"b), 4.20-4.31 (m, 2H, H-2,2"), 4.41 (s, 1H, H-1'), 4.46, 4.52 (2d, 2H, J = 11.9 Hz, CH_2), 4.63, 4.93 (2d, 2H, J = 10.9 Hz, CH_2), 4.82, 4.93 (2d, 2H, J = 12.4 Hz, CH_2), 7.24-7.46 (m, 15H, $3C_6H_5$).

Anal. Calcd for $C_{39}H_{50}O_{10}$: C, 68.99; H, 7.44. Found: C, 68.86; H, 7.41.

2,3-*O*-Isopropylidene-1-*O*-[2,3,4-tri-*O*-benzyl-6-*O*-(*tert*-butyldiphenylsilyl)-α- and β-D-mannopyranosyl]-D-glycerol (16α and 16β). 16α: R_f 0.65 (3:1 petroleum ether/ethyl acetate); $[\alpha]_D$ = + 20.2° (*c* 0.63, chloroform); MS (EI): *m/z* = 787 (M-Me)$^+$, 711 (M-Bn)$^+$; ^{1}H NMR ($CDCl_3$) δ 1.06 (s, 9H, *tert*-Butyl), 1.34, 1.38 (2s, 6H, $2CH_3$), 3.44 (dd, 1H, $J_{1a,1b}$ = 10.4 Hz, $J_{1a,2}$ = 6.6 Hz, H-1a), 3.57 (dd, 1H, $J_{2,3a}$ = 6.9 Hz, $J_{3a,3b}$ = 8.1 Hz, H-3a), 3.65-4.10 (m, 8H, H-1b,3b,2',3',4',5',6'a,6'b), 4.22 (m, 1H, H-2), 4.56, 4.99 (2d, 2H, J = 10.7 Hz, CH_2), 4.66 (s, 2H, CH_2), 4.70, 4.81 (2d, 2H, J = 12.5 Hz, CH_2), 5.00 (broad s, 1H, H-1'), 7.11-7.46 (m, 21H, $21/5C_6H_5$), 7.62-7.81 (m, 4H, $4/5C_6H_5$). **16β:** R_F 0.60 (3:1 petroleum ether/ethyl acetate); $[\alpha]_D$ = -30.3° (*c* 1.04, chloroform); MS (EI): *m/z* = 787 (M-Me)$^+$, 745 (M-Bu)$^+$; ^{1}H NMR ($CDCl_3$) δ 1.04 (s, 9H, *tert*-Butyl), 1.36, 1.41 (2s, 6H, $2CH_3$), 3.32-4.35 (m, 11H, H-1a,1b,2,3a,3b,2',3',4',5',6'a,6'b), 4.45 (s, 1H, H-1'), 4.52, 4.58 (2d, 2H, J = 12.0 Hz, CH_2), 4.59, 4.93 (2d, 2H, J = 10.6 Hz, CH_2), 4.86, 4.96 (2d, 2H, J = 12.4 Hz, CH_2), 7.12-7.51 (m, 21H, $4.2C_6H_5$), 7.66-7.80 (m, 4H, $0.8C_6H_5$).

2,3-*O*-Isopropylidene-1-*O*-(2,3,4-tri-*O*-benzyl-6-*O*-triphenylmethyl-α- and β-D-mannopyranosyl)-D-glycerol (17α and 17β). 17α: R_f 0.62 (3:1 petroleum ether/ethyl

acetate); $[\alpha]_D$ = +23.2° (*c* 1.21, chloroform); MS (EI): *m/z* = 791 (M-Me)$^+$, 715 (M-Bn)$^+$, 623 (M-2Bn)$^+$, 563 (M-Tr)$^+$; ^{1}H NMR ($CDCl_3$) δ 1.35, 1.40 (2s, 6H, $2CH_3$), 3.28 (dd, 1H, $J_{5',6'a}$ = 5.4 Hz, $J_{6'a,6'b}$ = 9.8 Hz, H-6'a), 3.49-4.06 (m, 8H, H-1a,1b,3a,3b,3',4',5',6'b), 3.91 (s, 1H, H-2'), 4.25-4.29 (m, 2H, H-2, $0.5CH_2$), 4.65-4.88 (m, 5H, $2.5CH_2$), 4.98 (s, 1H, H-1'), 6.83-6.93 (m, $0.4C_6H_5$), 7.12-7.58 (m, 28H, $5.6C_6H_5$). **17β**: R_f 0.62 (3:1 petroleum ether/ethyl acetate); $[\alpha]_D$ = -25.9° (*c* 1.04, chloroform); MS (EI): *m/z* = 791 (M-Me)$^+$, 563 (M-Tr)$^+$; ^{1}H NMR ($CDCl_3$) δ 1.35, 1.41 (2s, 6H, $2CH_3$), 3.29 (dd, 1H, $J_{5',6'a}$ = 5.4 Hz, $J_{6'a,6'b}$ = 9.8 Hz, H-6'a), 3.37-4.17 (m, 9H, H-1a,1b,3a,3b,2',3',4',5',6'b), 4.30, 4.75 (2d, 2H, J = 10.2 Hz, CH_2), 4.35 (m, 1H, H-2), 4.48 (s, 1H, H-1'), 4.55, 4.60 (2d, 2H, J = 12.2 Hz, CH_2), 4.88, 5.00 (2d, 2H, J = 13.2 Hz, CH_2), 6.38-6.95 (m, 4H, $0.8C_6H_5$), 7.10-7.39 (m, 18 H, $3.6C_6H_5$), 7.39-7.60 (m, 8H, $1.6C_6H_5$).

2,3-*O*-Isopropylidene-1-*O*-[2,3,4-tri-*O*-benzyl-6-*O*-(*p*-methoxyphenyl)diphenylmethyl-α- and β-D-mannopyranosyl]-D-glycerol (18α and 18β).[7] **18α**: R_f 0.67 (3:1 petroleum ether/ethyl acetate); $[\alpha]_D$ = + 19.8° (*c* 1.12, chloroform); MS (EI): *m/z* = 836 (M)$^+$, 821 (M-Me)$^+$, 759 (M-Ph)$^+$, 704 (M-aglycon)$^+$, 563 (M-MTr)$^+$; ^{1}H NMR ($CDCl_3$) δ 1.35, 1.40 (2s, 6H, $2CH_3$), 3.27 (dd, 1H, $J_{5',6'a}$ = 5.3 Hz, $J_{6'a,6'b}$ = 9.8 Hz, H-6'a), 3.50 (d, 1H, $J_{3',4'}$ = 9.4 Hz, H-3'), 3.52 (dd, 1H, $J_{1a,2}$ = 6.6 Hz, $J_{1a,1b}$ = 10.4 Hz, H-1a), 3.64 (dd, 1H, $J_{2,3a}$ = 6.6 Hz, $J_{3a,3b}$ = 8.2 Hz, H-3a), 3.75 (s, 3H, OCH_3), 3.73-3.79 (m, 2H, H-1b,5'), 3.88 (m, 1H, H-6'b), 3.90 (s, 1H, H-2'), 4.03 (t, 1H, $J_{4',5'}$ = 9.4 Hz, H-4'), 4.03 (dd, 1H, $J_{2,3b}$ = 6.5 Hz, H-3b), 4.27 (m, 1H, H-2), 4.27, 4.74 (2d, 2H, J = 10.6 Hz, CH_2), 4.65 (s, 2H, CH_2), 4.75, 4.85 (2d, 2H, J = 12.5 Hz, CH_2), 4.97 (s, 1H, H-1'), 6.76-6.90 (m, 4H, $0.8C_6H_5$), 7.15-7.58 (m, 25H, $5C_6H_5$). **18β**: R_F 0.64 (3:1 petroleum ether/ethyl acetate); $[\alpha]_D$ = -24.6° (*c* 1.07, chloroform); MS (EI): *m/z* = 836 (M)$^+$, 821 (M-Me)$^+$, 563 (M-MTr)$^+$; ^{1}H NMR ($CDCl_3$) δ 1.35, 1.41 (2s, 6H, $2CH_3$), 3.30 (dd, 1H, $J_{5',6'a}$ = 4.6 Hz, $J_{6'a,6'b}$ = 9.7 Hz, H-6'a), 3.38-3.69 (m, 3H, H-1a,1b,3a), 3.55 (d, 1H, $J_{2',3'}$ = 1.3 Hz, $J_{3',4'}$ = 9.7 Hz, H-3'), 3.73 (s, 3H, OCH_3), 3.85-4.12 (m, 4H, H-3b,4',5',6b), 3.95 (d, 1H, H-2'), 4.28-4.37 (m, 1H, H-2), 4.30, 4.76 (2d, 2H, J = 10.3 Hz, CH_2), 4.48 (s, 1H, H-1'), 4.58 (d, 2H, J = 1.9 Hz, CH_2), 4.88, 5.01 (2d, 2H, J = 12.4 Hz, CH_2), 6.75-6.92 (m, 4H, $0.8C_6H_5$), 7.16-7.56 (m, 25H, $5C_6H_5$).

2,3-*O*-Isopropylidene-1-*O*-(2,3,4,6-tetra-*O*-benzyl-α- and β-D-mannopyranosyl)-D-glycerol (19α and 19β). 19α: R_f 0.56 (2:1 petroleum ether/ethyl acetate); $[\alpha]_D$ = + 34.3° (*c* 0.86, chloroform); MS (EI): *m/z* = 639 (M-Me)$^+$, 563 (M-Bn)$^+$, 431 (M-Bn-aglycon)$^+$; ^{1}H NMR ($CDCl_3$) δ 1.34, 1.38 (2s, 6H, $2CH_3$), 3.46 (dd, 1H, $J_{5',6'a}$ = 6.4 Hz, $J_{6'a,6'b}$ = 10.4 Hz, H-6'a), 3.60 (dd, 1H, $J_{1a,1b}$ = 8.3 Hz, $J_{1a,2}$ = 6.7 Hz, H-1a), 3.67 (dd, 1H, $J_{2,3a}$ = 4.8 Hz, $J_{3a,3b}$ = 10.4 Hz, H-3a), 3.72-3.79 (m, 3H, H-1b,3',5'), 3.86 (m, 1H,

H-2'), 3.88 (dd, 1H, $J_{2,3b}$ = 2.0 Hz, H-3b), 3.97 (m, 1H, H-6'b), 3.99 (dd, 1H, J = 6.4 and 8.2 Hz, H-4'), 4.22 (m, 1H, H-2), 4.51, 4.87 (2d, 2H, J = 10.8 Hz, CH_2), 4.53, 4.64 (2d, 2H, J = 12.1 Hz, CH_2), 4.62 (s, 2H, CH_2), 4.70, 4.76 (2d, 2H, J = 12.5 Hz, CH_2), 4.91 (d, 1H, $J_{1,2}$ = 1.5 Hz, H-1'), 7.14-7.39 (m, 20H, $4C_6H_5$). **19β**: R_f 0.47 (2:1 petroleum ether/ethyl acetate); $[\alpha]_D$ = -36.5° (*c*0.90, chloroform); MS (EI): *m/z* = 639 $(M\text{-}Me)^+$, 563 $(M\text{-}Bn)^+$, 431 $(M\text{-}Bn\text{-}aglycon)^+$; ^1H NMR ($CDCl_3$) δ 1.36, 1.40 (2s, 6H, $2CH_3$), 3.41-4.06 (m, 10H, H-1a,1b,3a,3b,2',3',4',5',6'a,6'b), 4.30 (m, 1H, H-2), 4.43 (s, 1H, H-1'), 4.45, 4.52 (2d, 2H, J = 12.4 Hz, CH_2), 4.53, 4.89 (2d, 2H, J = 10.6 Hz, CH_2), 4.55, 4.62 (2d, 2H, J = 12.1 Hz, CH_2), 4.83, 4.95 (2d, 2H, J = 12.4 Hz, CH_2), 7.16-7.47 (m, 20H, $4C_6H_5$).

2,3-*O*-Isopropylidene-1-*O*-(4,6-di-*O*-benzyl-2,3-*O*-isopropylidene-α- and β-D-mannopyranosyl)-D-glycerol (20α and 20β). 20α: R_f 0.87 (7:3 toluene/acetone); mp 68-70 °C (recrystallized from heptane); $[\alpha]_D$ = + 34.7° (*c* 1.02, chloroform); ^1H NMR ($CDCl_3$) δ 1.35, 1.36, 1.40, 1.51 (4s, 12H, $4CH_3$), 3.50 (dd, 1H, $J_{1a,1b}$ = 10.2 Hz, $J_{1a,2}$ = 6.9 Hz, H-1a), 3.57 (t, 1H, $J_{3',4'} = J_{4',5'}$ = 6.6 Hz, H-4'), 3.60 (dd, $J_{2,3a}$ = 6.5 Hz, $J_{3a,3b}$ = 8.3 Hz, H-3a), 3.65 (dd, 1H, $J_{5',6'a}$ = 5.9 Hz, $J_{6'a,6'b}$ = 10.7 Hz, H-6'a), 3.73-3.80 (m, 3H, H-1b,5',6'b), 3.99 (dd, 1H, $J_{2,3b}$ = 6.6 Hz, H-3b), 4.22 (d, 1H, $J_{1',2'}$ = 5.8 Hz, H-2'), 4.28 (m, 1H, H-2), 4.31 (dd, 1H, H-3'), 4.53, 4.61 (2d, 2H, J = 12.1 Hz, CH_2), 4.53, 4.86 (2d, 2H, J = 10.5 Hz, CH_2), 5.09 (s, 1H, H-1'), 7.26-7.33 (m, 10H, $2C_6H_5$).

Anal. Calcd for $C_{29}H_{38}O_8$: C, 67.67; H, 7.46. Found: C, 67.55; H, 7.53.

20β: R_f 0.74 (7:3 toluene/acetone); $[\alpha]_D$ = -3.68° (*c* 1.14, chloroform); ^1H NMR ($CDCl_3$) δ 1.33, 1.38, 1.40, 1.52 (4s, 12H, $4CH_3$), 3.41-4.09 (m, 7H, H-1a,1b,3a,3b,4',6'a,6'b), 3.99 (m, 1H, H-5'), 4.25 (dd, 1H, $J_{1',2'}$ = 2.3 Hz, $J_{2',3'}$ = 6.4 Hz, H-2'), 4.28 (m, 1H, H-2), 4.31 (t, 1H, H-3'), 4.54, 4.81 (2d, 2H, J = 12.2 Hz, CH_2), 4.57 (s, 2H, CH_2), 4.83 (d, 1H, H-1'), 7.23-7.35 (m, 10H, $2C_6H_5$).

Anal. Calcd for $C_{29}H_{38}O_8$: C, 67.67; H, 7.46. Found: C, 67.40; H, 7.30.

2,3-*O*-Isopropylidene-1-*O*-[3,4,6-tri-*O*-benzyl-2-*O*-(2-methoxyethoxymethyl)-α- and β-D-mannopyranosyl]-D-glycerol (21α and 21β). 21α: R_f 0.67 (1:1 petroleum ether/ethyl acetate): $[\alpha]_D$ = +42.8° (*c* 1.27, chloroform); ^1H NMR ($CDCl_3$) δ 1.35, 1.39 (2s, 6H, $2CH_3$), 3.36 (s, 3H, OCH_3), 3.46 (t, 2H, J = 4.6 Hz, OCH_2), 3.50 (dd, 1H, $J_{1a,1b}$ = 10.4 Hz, $J_{1a,2}$ = 6.0 Hz, H-1a), 3.65 (dd, 1H, $J_{2,3a}$ = 6.5 Hz, $J_{3a,3b}$ = 8.3 Hz, H-3a), 3.67 (dd, 1H, $J_{1b,2}$ = 5.0 Hz, H-1b), 3.73 (t, 2H, OCH_2), 3.71-3.92 (m, 5H, H-3',4',5',6'a,6'b), 4.02 (dd, 1H, $J_{2,3b}$ = 6.5 Hz, H-3b), 4.08 (m, 1H, H-2'), 4.25 (m, 1H, H-2), 4.50, 4.87 (2d, 2H, J = 10.9 Hz, CH_2), 4.53, 4.63 (2d, 2H, J = 12.2 Hz, CH_2), 4.66, 4.72 (2d, 2H, J = 11.7 Hz, CH_2), 4.85 (s, 2H, OCH_2O), 4.96 (d, 1H, $J_{1',2'}$ = 1.8 Hz, H-1'), 7.14-7.36 (m, 15H, $3C_6H_5$).

Anal. Calcd for $C_{37}H_{48}O_{10}$: C, 68.07; H, 7.43. Found: C, 67.80; H, 7.45.

21β: R_f 0.50 (1:1 petroleum ether/ethyl acetate); $[\alpha]_D$ = -27.5° (*c* 1.15, chloroform); ^1H NMR ($CDCl_3$) δ 1.34, 1.40 (2s, 6H, $2CH_3$), 3.34 (s, 3H, OCH_3), 3.42 (t, 2H, J = 4.6 Hz, OCH_2), 3.42-4.05 (m, 11H, H-1a,1b,3a,3b,3',4',5',6'a,6'b,OCH_2), 4.22-4.32 (m, 2H, H-2,2'), 4.45 (s, 1H, H-1'), 4.52, 4.88 (2d, 2H, J = 10.8 Hz, CH_2), 4.54, 4.80 (2d, 2H, J = 12.1 Hz, CH_2), 4.63, 4.80 (2d, 2H, J = 11.8 Hz, CH_2), 4.97 (s, 2H, OCH_2O), 7.15-7.40 (m, 15H, $3C_6H_5$).

Anal. Calcd for $C_{37}H_{48}O_{10}$: C, 68.07; H, 7.43. Found: C, 68.90; H, 7.43.

2,3-*O*-Isopropylidene-1-*O*-(3,4,6-tri-*O*-benzyl-α- and β-D-mannopyranosyl)-D-glycerol (22α and 22β). Both ^1H NMR spectra were in agreement with those reported.[13]

2,3-*O*-Isopropylidene-1-*O*-[3,4,6-tri-*O*-benzyl-2-*O*-(2,2-dimethyl-1,3-dioxolan-4*R*-yl)-β-D-mannopyranosyl]-D-glycerol (23). R_f 0.62 (1:1 petroleum ether/ethyl acetate); $[\alpha]_D$ = -10.9° (*c* 1.17, chloroform); ^1H NMR ($CDCl_3$) δ 1.35, 1.39 (each s, 12H, 4 CH_3), 3.37-4.09 (m, 14H, H-1a,1b,3a,3b,2',3',4',5',6'a,6'b,1"a,1"b,3"a,3"b), 4.23-4.35 (m, 2H, H-2,2"), 4.40 (s, 1H, H-1'), 4.50, 4.85 (2d, 2H, J = 10.8 Hz, CH_2), 4.52, 4.60 (2d, 2H, J = 12.1 Hz, CH_2), 4.65, 4.72 (2d, 2H, J = 11.7 Hz, CH_2), 7.15-7.38 (m, 15H, $3C_6H_5$).

Anal. Calcd for $C_{39}H_{50}O_{10}$: C, 68.99; H, 7.44. Found: C, 68.84; H, 7.28.

1,6-Anhydro-2,3-di-*O*-benzyl-4-*O*-nonafluorobutanesulfonyl-β-D-galactopyranose (25). Nonafluorobutanesulfonic acid anhydride[14] (0.48 mL, 1.39 mmol) was added dropwise to a solution of 1,6-anhydro-2,3-di-*O*-benzyl-β-D-galactopyranose [15] (0.35 g, 1.03 mmol) in pyridine (0.56 mL) at 0 °C with stirring. The reaction mixture was raised to room temperature and, after 15 h, was diluted with dichloromethane, washed with ice-cold water and aqueous sodium hydrogencarbonate, dried over magnesium sulfate and concentrated. The residue was purified by silica gel column chromatography (20:1 petroleum ether/ethyl acetate) which contained sodium sulfate to yield **25** (0.47 g, 72%): R_f 0.77 (3:1 petroleum ether/ethyl acetate); $[\alpha]_D$ = -23.7° (*c* 1.18, chloroform); MS (EI): *m/z* = 624 $(M)^+$, 533 $(M\text{-}Bn)^+$, MS (FAB, negative ion): *m/z* = 599 $[(C_4F_9SO_3)_2H]^-$, 533 $(M\text{-}Bn)^-$, 405 $(M\text{-}C_4F_9)^-$, 299 $(C_4F_9SO_3)^-$; ^1H NMR ($CDCl_3$), δ 3.57 (t, 1H, $J_{1,2} = J_{2,3}$ = 1.5 Hz, H-2), 3.71 (dd, 1H, $J_{5,6}$ = 7.2 Hz, $J_{6,6'}$ = 4.9 Hz, H-6), 3.94 (dd, 1H, $J_{3,4}$ = 5.3 Hz, H-3), 4.38, 4.43, 4.46, 4.55 (4d, 4H, J = 12.3 Hz, $2CH_2$), 4.49 (d, 1H, H-6'), 4.57 (dd, 1H, $J_{4,5}$ = 4.5 Hz, H-5), 5.21 (dd, 1H, H-4), 5.37 (d, 1H, H-1), 7.22-7.39 (m, 10H, $2C_6H_5$).

1,6-Anhydro-2,3-di-*O*-benzyl-4-*O*-[2,3,4-tri-*O*-benzyl-6-*O*-(*p*-methoxyphenyl)-diphenylmethyl-α-D-mannopyranosyl]-β-D-glucopyranose (26). i) By coupling of **5** with **24**.[12] **5** (428.6 mg, 0.59 mmol) was dissolved in HMPT (4 mL) and DMF (2 mL),

and sodium hydride (23 mg, 0.96 mmol) was added with stirring at -10 °C for 15 min. Then to this solution **24** (423.2 mg, 0.89 mmol) in HMPT (1 mL) and DMF (0.5 mL) was added dropwise. After 2.5 h the reaction did not proceed any more. Ice was then added to the reaction mixture which was then extracted with ethyl acetate, washed with aqueous sodium hydrogencarbonate and brine, dried over magnesium sulfate and concentrated. The crude products were purified by silica gel column chromatography (7:1 → 2:1 petroleum ether/ethyl acetate) to yield **26** (376.0 mg, 61%) as a syrup.

ii) By coupling of **5** with **25**. **5** (450.9 mg, 0.62 mmol) in HMPT (4 mL) and DMF (2 mL), sodium hydride (23 mg, 0.96 mmol) and **25** (526.8 mg, 0.83 mmol) in HMPT (1 mL) and DMF (0.5 mL) were reacted as described above. The reaction was finished within 3 h and **26** (537.1 mg, 82%) was obtained: R_f 0.53 (3:1 petroleum ether/ethyl acetate); $[\alpha]_D$ = +2.9° (*c* 1.19, chloroform); MS (EI): *m/z* = 773 $(M\text{-}MTr)^+$; ^1H NMR ($CDCl_3$) δ 3.31 (m, 1H, H-2), 3.34 (dd, 1H, $J_{5',6'a}$ = 5.5 Hz, $J_{6'a,6'b}$ = 9.3 Hz, H-6'a), 3.46 (m, 1H, H-3), 3.53 (d, 1H, H-6'b), 3.71 (m, 1H, H-6a), 3.74 (s, 3H, OCH_3), 3.76-3.96 (m, 5H, H-4,2',3',4',5'), 4.06 (dd, 1H, $J_{6a,6b}$ = 7.2 Hz, H-6b), 4.24, 4.35 (2d, 2H, J = 12.5 Hz, CH_2), 4.27, 4.73 (2d, 2H, J = 10.2 Hz, CH_2), 4.56 (d, 2H, J < 1 Hz, CH_2), 4.60, 4.74 (2d, 2H, J = 12.4 Hz, CH_2), 4.64 (s, 2H, CH_2), 5.00 (d, 1H, $J_{1',2'}$ < 1 Hz, H-1'), 5.43 (m, 1H, H-1), 6.76-6.91 (m, 4H, $0.8C_6H_5$), 7.18-7.52 (m, 35H, $7C_6H_5$): ^{13}C NMR ($CDCl_3$) δ 54.9 (OCH_3), 96.2 (C-1), 100.2 (C-1').

Anal. Calcd for $C_{67}H_{66}O_{11}$: C, 76.73; H, 6.36. Found: C, 76.58; H, 6.22.

1,6-Anhydro- 2,3-di-*O*-benzyl -4-*O*-(2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl)-β-D-glucopyranose (27). **6** (303.6 mg, 0.56 mmol) was dissolved in HMPT (6 mL) and DMF (3 mL) and sodium hydride (53 mg, 2.2 mmol) was added with stirring at -10 °C for 15 min; then to this solution **24** (400.0 mg, 0.84 mmol) in HMPT (3 mL) and DMF (1.5 mL) was added dropwise. After 14 h both starting materials had disappeared on TLC. To the reaction mixture was added ice, and it was treated in the same manner as described for **26**; **27** was obtained (212.0 mg, 44%) as a syrup. ^1H NMR data were in agreement with those reported.[16]

2,3-Di-*O*-acetyl-1,6-anhydro-4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)-β-D-glucopyranose (28). **26** (80.6 mg, 77.1 μmol) was dissolved in ethanol (5 mL) and a catalytic amount of palladium on charcoal and 2 drops of acetic acid were added. The reaction mixture was stirred under hydrogen atmosphere for 3 h, filtered and the filtrate was concentrated under reduced pressure. The residue was acetylated with acetic anhydride and pyridine to give **28** (37.5 mg, 84%): The ^1H NMR data were in agreement with those reported.[2]

2,3-Di-*O*-acetyl-1,6-anhydro-4-*O*-(2,3,4,6-tetra-*O*-acetyl-α- and β-D-glucopyranosyl)-β-D-glucopyranose (30α and 30β). **5** (300.7 mg, 0.42 mmol) and 15-crown-5

(0.13 mL, 0.65 mmol) were dissolved in toluene (4 mL) and sodium hydride (17 mg, 0.71 mmol was added with stirring. After 15 min **24** (317.0 mg, 0.67 mmol) in toluene (1 mL) was added dropwise to this solution with stirring. After 22 h ice was added to the reaction mixture which was then extracted with ethyl acetate, washed with aqueous sodium hydrogencarbonate and brine, the extract dried over magnesium sulfate and concentrated. The crude products were purified by silica gel column chromatography (7:1 petroleum ether/ethyl acetate) to yield 197 mg of a mixture of products which contained **26** (35 mg, 8%), **29α** (59 mg, 14%), **29β** (85 mg, 19%) and **5** (17 mg, 6%). This mixture was separated by preparative TLC (3:1 petroleum ether/ethyl acetate) to give pure products. **29α** and **29β** were debenzylated and acetylated to give **30α** and **30β**, respectively.

30α:[17] **29α** (6.8 mg, 6.5 μmol) was diluted in ethanol (1 mL) and debenzylated and acetylated as described for **28**, to give **30α** quantitatively. R_f 0.27 (1:1 petroleum ether/ethyl acetate); ^{1}H NMR ($CDCl_3$) δ 2.02, 2.04, 2.05, 2.08, 2.09, 2.11, 2.21 (6s, 18H, $6CH_3$), 3.46 (broad s, 1H, H-4), 3.79 (dd, 1H, $J_{5,6a}$ = 5.8 Hz, $J_{6a,6b}$ = 7.6 Hz, H-6a), 3.89 (d, 1H, H-6b), 4.19 (m, 2H, H-6'a,6'b), 4.42 (dt, 1H, $J_{4',5'}$ = 10.3 Hz, $J_{5',6'a}$ = $J_{5',6'b}$ = 3.5 Hz, H-5'), 4.59 (broad s, 1H, H-2), 4.75 (broad d, 1H, H-5), 4.82 (m, 1H, H-3), 4.84 (dd, 1H, $J_{1',2'}$ = 3.7 Hz, $H_{2',3'}$ = 10.4 Hz, H-2'), 5.07 (t, 1H, H-4'), 5.29 (d, 1H, H-1'), 5.48 (broad s, 1H, H-1), 5.54 (t, 1H, H-3').

30β:[18] **29β** (20.3 mg, 19.4 μmol) was diluted in ethanol (2 mL) and debenzylated and acetylated as described for **28**, to give **30β** quantitatively. R_f 0.14 (1:1 petroleum ether/ethyl acetate); ^{1}H NMR ($CDCl_3$) δ 2.00, 2.04, 2.05, 2.08, 2.11, 2.12 (6s, 18H, $6CH_3$), 3.54 (broad s, 1H, H-4), 3.77-3.84 (m, 2H, H-6a,5'), 3.98 (d, 1H, $J_{6a,6b}$ = 7.8 Hz, H-6b), 4.09 (dd, 1H, $J_{5',6'a}$ = 2.1 Hz, $J_{6'a,6'b}$ = 12.3 Hz, H-6'a), 4.24 (dd, 1H, $J_{5',6'b}$ = 5.0 Hz, H-6'b), 4.55 (broad s, 1H, H-2), 4.59 (broad d, 1H, $J_{5,6a}$ = 5.3 Hz, H-5), 4.88 (d, 1H, $J_{1',2'}$ = 8.1 Hz, H-1'), 5.04 (t, 1H, H-2'), 5.06 (t, 1H, $J_{3',4'}$ = $J_{4',5'}$ = 9.4 Hz, H-4'), 5.20 (broad s, 1H, H-3), 5.22 (t, 1H, H-3'), 5.46 (broad s, 1H, H-1).

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