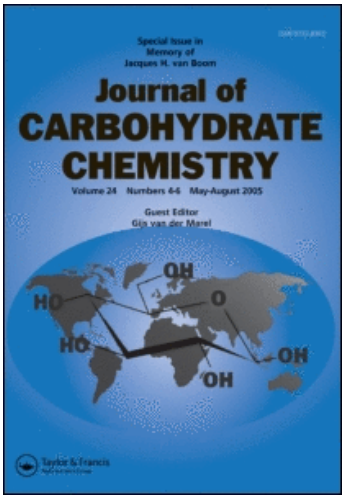

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1-O-Alkylation of D-Glucopyranose

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1-O-ALKYLATION OF D-GLUCOPYRANOSE [1]

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ABSTRACT

Direct 1-O-methylation of 1-O-metalated 2,3,4,6-tetra-O-benzyl-D-glucose (1) with methyl trifluoromethanesulfonate (3a) as a strong alkylating agent led to the methyl glucopyranosides 4a with the α/β anomer ratios varying from 4:1 to 1:11 depending on solvent and temperature. With the less electrophilic trifluoromethanesulfonates of D-glucose 3b and 3c, of D-ribose 3d, and D-glycerol (3e) as alkylating agents, 1 gave the β-disaccharides and β-glycosides 4b-β - 4e-β, exclusively. Product formation is discussed in terms of the various nucleophilicities of the starting materials and in terms of different internal complexation. Introduction of the sterically demanding (p-methoxyphenyl)diphenylmethyl protecting group in 6-O-position of 2,3,4-tri-O-benzyl-D-glucose to form 8 and subsequent 1-O-metalation and reaction with trifluoromethanesulfonate 3c gave the α-connected isomaltoside 9c-α. However, from 1-O-metalated 8 and the trifluoromethanesulfonates of glycerol 3e and 3f under identical reaction conditions, only the β-connected glycosides 9e-β and 9f-β, respectively, were obtained. Structures were assigned by ^{1}H NMR and by deprotection to known compounds.

INTRODUCTION

Stereoselective formation of the glycosidic bond in disaccharide syntheses is generally achieved by nucleophilic displacement of a readily cleaved group at the anomeric center of the sugar.[2] The direct 1-O-alkylation of furanoses

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and pyranoses or corresponding metalated derivatives, well known with methyl iodide and dimethyl sulfate,[3,4] was recently accomplished by us in the chemically and stereochemically highly selective syntheses of α- or β-disaccharides of D-ribofuranose,[5] D-mannofuranose,[6,7] D-mannopyranose,[7] D-galactopyranose, and D-glucopyranose.[8] This directed synthesis was especially successful with partially protected carbohydrate derivatives.[5,7,8] From 2,3,4-tri-O-benzyl-D-glucose, β-D-glucopyranosides were obtained almost exclusively.[8] We report here upon the influence of 6-O-substituents on the α/β ratio during 1-O-alkylation of 2,3,4-tri-O-benzyl protected D-glucose. Interest in these investigations was due to the observed high α-selectivities in glycoside formation when sterically demanding 6-O-substituents were present.[5,8]

RESULTS AND DISCUSSION

Pfeffer and coworkers[9] demonstrated by ^{13}C NMR investigations that 2,3,4,6-tetra-O-benzyl-D-glucopyranose (1) exists at room temperature in benzene or tetrahydrofuran in an anomer ratio of $\alpha:\beta \approx 2:3$. This ratio was only slightly changed to $\alpha:\beta \approx 1:1$ upon 1-O-lithiation (FIG.1). However, acylation of these lithiated species with decanoyl chloride to produce the anomeric mixture 2 gave a completely different result.[9] The anomer ratio was highly dependent on the solvent and the temperature used (FIG.1). The result was explained in terms of intramolecular complexation in the transition state in forming the β-product and in terms of the strong temperature dependence of the activation entropy term.[9]

With the 1-O-sodium salt of 1 and methyl trifluoromethanesulfonate (3a) as the methylating agent, we now have investigated the dependance of the α/β selectivity of methyl glucopyranoside 4a formation on solvent and temperature (FIG.1). A result similar to that obtained for 2 was observed; however, product formation clearly favored the β-anomer 4a-β at higher temperatures. In tetrahydrofuran the α/β ratio of 4:1

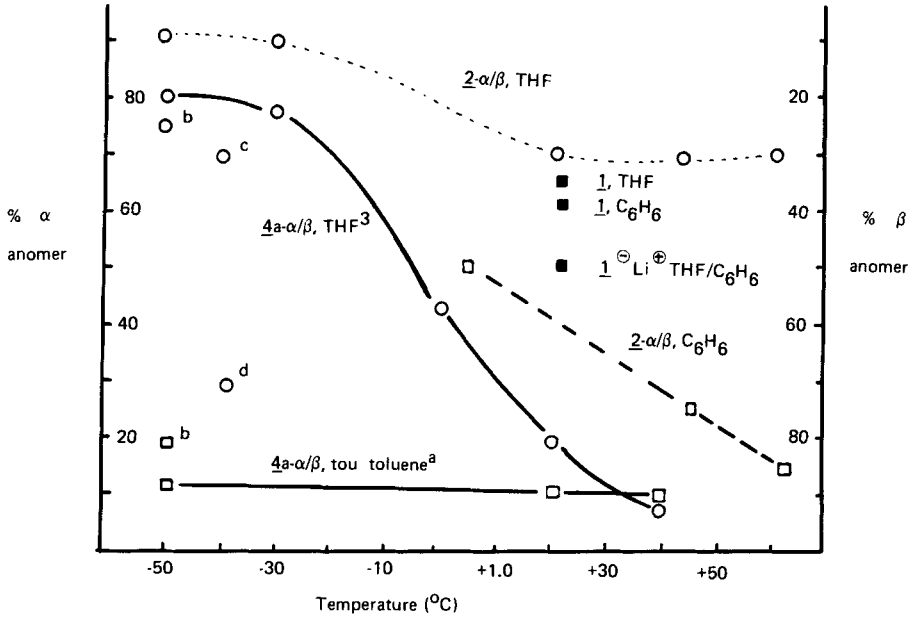
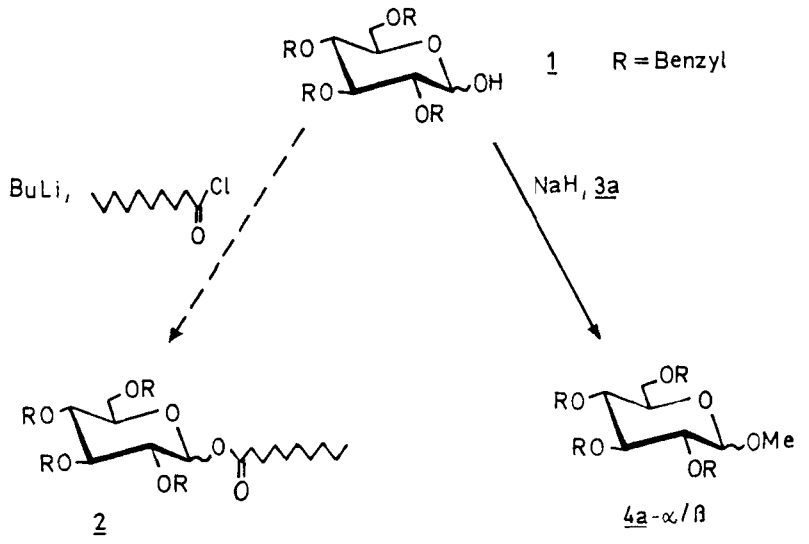


FIG. 1:

Anomer ratio of 1, its lithium salt ($1^{\ominus}Li^{\oplus}$), and its reaction products (2) with decanoylchloride (ref. 9), and products 4a with 3a (Scheme 1). For further details (a) see experimental section (THF = tetrahydrofuran); (b) addition of equimolar amounts of crown ether in THF (O) and in toluene (□) at -50 °C; (c) 1 dissolved in THF at 40 °C, then cooled to -40 °C, NaH added after 6 h, and 3a added after 15 min; (d) 1 dissolved in THF at 40 °C, NaH added, cooled to -40 °C after 15 min, and 3a added after 15 min.

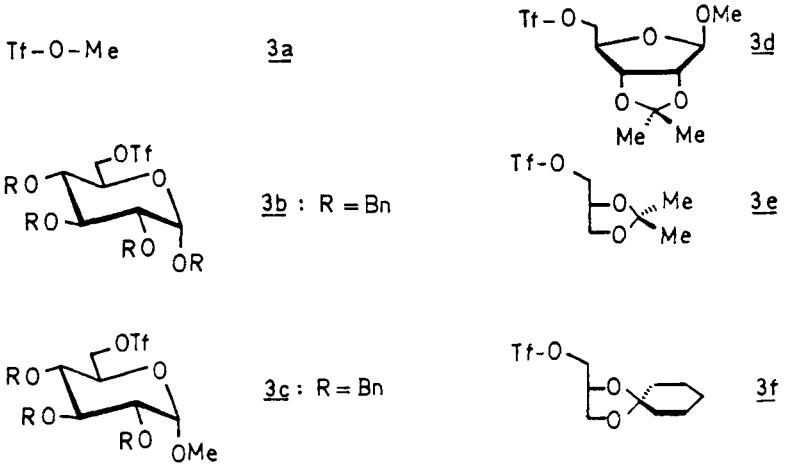
at -50 °C was changed to 1:11 at +40 °C. In toluene the anomer ratio at -50 °C, which was already 1:8, was shifted to 1:10 at +40 °C. Because the electrophilicity of 3a is lower than that of an acid chloride, the tendency for increased β-anomer (4a-β) formation is attributed to the higher nucleophilicity of the β-1-alkoxide of 1 when compared to the corresponding α-1-alkoxide due to the anomeric effect.[10] This explanation is supported by crown ether addition to the reaction mixtures (FIG.1: b). Neither in tetrahydrofuran nor in toluene at



Scheme 1

-50 °C was a significant change of the anomer ratio observed upon addition of a crown ether. Therefore, in contrast to the D-mannofuranose system,[6,7] intramolecular complexation does not play a dominant role here. However, the rate of anomerization influences the anomer ratio of the product, because 1 dissolved in tetrahydrofuran at +40 °C gives a strikingly different result depending upon the order in which the operations of cooling to -40 °C and of addition of sodium hydride were performed (FIG.1: c,d)

If the different nucleophilicity of the α- and β-1-alkoxides of 1 is a major controlling factor in anomer formation, then the less electrophilic trifluoromethanesulfonates 3b - 3e [11] (Scheme 2) should react to give even more selective formation of the β-anomers. This was indeed observed, only the β-anomers 4b-β - 4e-β were obtained (Scheme 3). The structures of the gentiobiose derivatives 4b-β and 4c-β were proven by hydrogenolytic debenzylation which gave gentiobiose 5b-β and methylgentiobioside 5c-β, respectively. Compound 4d-β afforded after

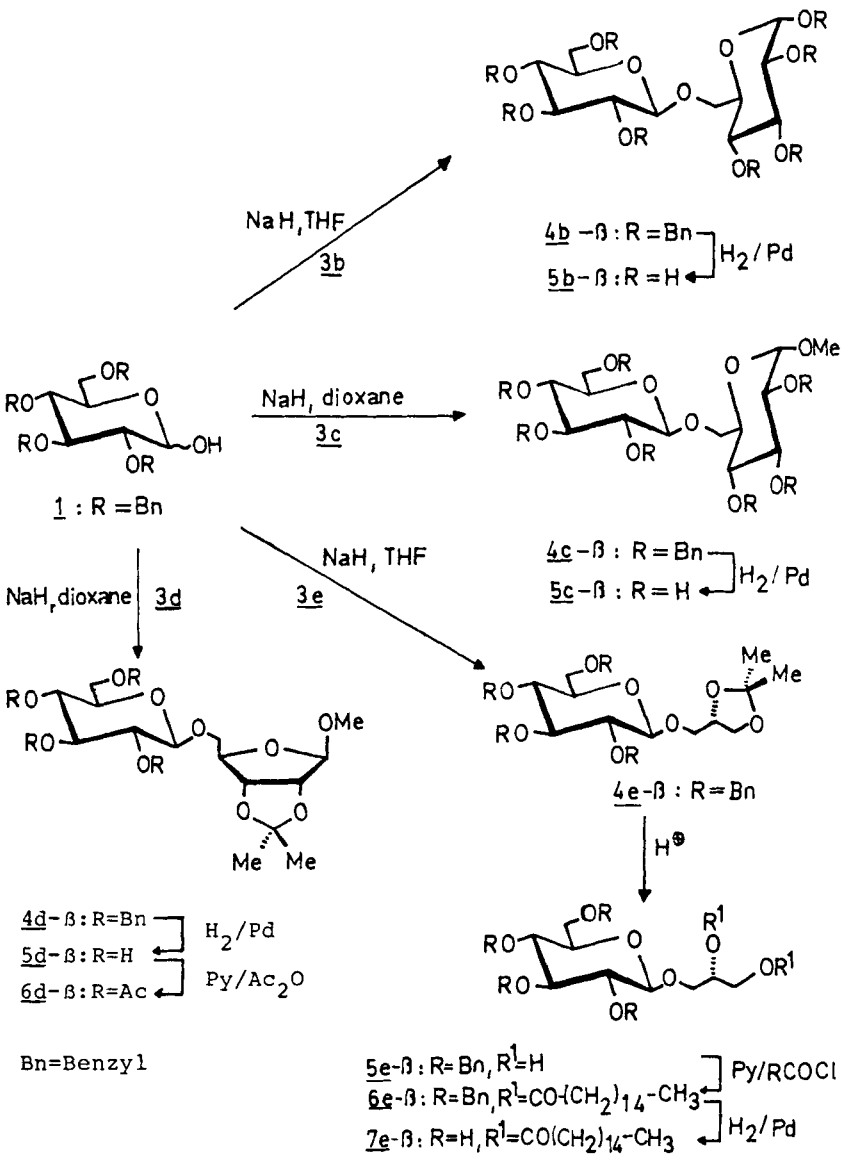


Bn = Benzyl
Tf = Trifluoromethylsulfonyl

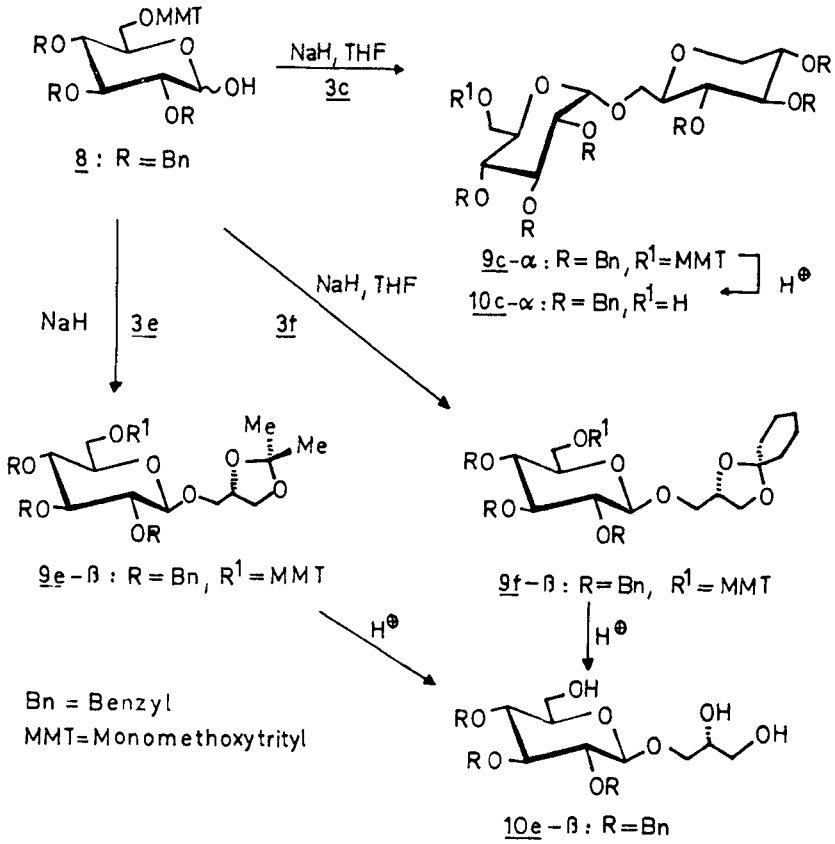
Scheme 2

debenzylation 5d-β, subsequent acylation gave compound 6d-β, whose structure was assigned by the ^{1}H NMR data. Deisopropylidenation of 4e-β gave 5e-β, which was acylated with palmitoyl chloride to compound 6e-β. After hydrogenolytic debenzylation,the glycolipid analogue 7e-β was obtained.

The exclusive formation of β-anomers from 1 with a 6-O-benzyl protecting group and 3b-3e as electrophiles, led us to investigate the 1-O-alkylation of a glucose derivative with a sterically more demanding protecting group at the 6-position. It was thought that steric constraints might favor α-anomer formation. Therefore, 2,3,4-tri-O-benzyl-D-glucose was treated with monomethoxytrityl chloride in pyridine and the 6-O-monomethoxytritylated glucose derivative 8 was obtained in good yield (Scheme 4). 1-O-Sodium alkoxide formation with sodium hydride in tetrahydrofuran and alkylation with 3c yielded the α-linked isomaltoside derivative 9c-α. Subsequent acid catalyzed cleavage of the mono-



Scheme 3



Scheme 4

methoxtrityl group gave compound 10c-α. However, the trifluoromethanesulfonates 3e and 3f, which are presumably less electrophilic than 3c,[11] gave on alkylation of the 1-alkoxide of 8 exclusively the β - anomers 9e-β and 9f-β, respectively. Neither solvent change nor lowering the reaction temperature to -30 °C in tetrahydrofuran changed this result.[12] Acid treatment of 9e-β and 9f-β led to partial deprotection resulting in the identical glucopyranosylglycerol 10e-β.

Thus, according to these investigations 1-O-alkylation of 1-O- deprotonated 2,3,4-tri-O-benzyl-D-glucose is more dependent on the difference in nucleophilicity of the α- than β-1-alkoxide and the electrophilicity of the trifluoromethanesulfonates than on intramolecular complexation effects.

EXPERIMENTAL

General Procedures. Melting points are uncorrected. ^{1}H NMR spectra were recorded in the solvents noted (Me_4Si, 0.00ppm) with a Bruker CW-80 spectrometer. R_F values refer to TLC performed on silica gel (Merck) with the solvent systems noted. Column chromatography was performed with silica gel (Merck, 70-325 mesh) with the solvent systems noted. Preparative thin-layer chromatography was done using glass plates (20 cm x 20 cm) coated with silica gel (PF-254, Merck) with the solvent systems noted. Optical rotation was determined with a Perkin-Elmer 241 MC.

Benzyl 2,3,4-Tri-O-benzyl-6-O-trifluoromethylsulfonyl-α-D-glucopyranoside (3b). Benzyl 2,3,4-tri-O-benzyl-α-D-glucopyranoside[13] (0.70 g, 1.29 mmol) and triethylamine (0.2 ml, 1.43 mmol) were dissolved in 50 ml of benzene, the solution was cooled until the solvent started to freeze,and then trifluoromethanesulfonic anhydride (0.24 ml, 1.43 mmol) was added. The reaction mixture was then concentrated and the crude product filtered with petroleum ether/ethyl acetate (85:15) through silica gel (5g). After evaporation of the solvent, 3b was obtained as an almost colorless oil (580 mg, 67 %), which decomposed readily on standing; therefore, it was used without further purification: TLC R_F= 0.40 (petroleum ether/ethyl acetate = 85:15).

Methyl 2,3,4-Tri-O-benzyl-6-O-trifluoromethylsulfonyl-α-D-glucopyranoside (3c). Methyl 2,3,4-tri-O-benzyl-α-D-glucopyranoside[14] (464 mg, 1 mmol) and triethylamine (0.14 ml, 1 mmol) were dissolved in 10 ml of benzene, the solution

was cooled until the solvent started to freeze, and then trifluoromethanesulfonic anhydride (0.166 ml, 1 mmol) was added. Thereafter, the reaction mixture was concentrated and the crude product filtered with petroleum ether/ethyl acetate (85:15) through silica gel (4 g). After evaporation of the solvent, 3c was obtained as an almost colorless oil (540 mg, 91 %): TLC R_F= 0.67 (toluene/ethyl acetate = 9:1); ^{1}H NMR ($CDCl_3$) δ 7.4-7.1 (m,15H), 5.10-4.45 (m,6H), 4.13-3.75 (m,2H), 3.60-3.34 (m,5H), 3.34 (s,3H,OCH_3).

Anal. Calcd for $C_{29}H_{31}F_3O_8S$ (596.62): C, 58.38; H, 5.23; S, 5.37. Found: C, 58.15; H, 5.25; S, 5.58.

Methyl 2,3-O-Isopropylidene-5-O-trifluoromethylsulfonyl-β-D-ribofuranoside (3d).[15] Methyl 2,3-O-isopropylidene-β-D-ribofuranoside[16] (408 mg, 2 mmol) and triethylamine (0.28 ml, 2 mmol) were dissolved in 5 ml of benzene, the solution was cooled until the solvent started to freeze, and then trifluoromethanesulfonic anhydride (0.332 ml, 2 mmol) was added. Thereafter, the reaction mixture was concentrated and the crude product was filtered with benzene through silica gel (5g). After evaporation of the solvent, 3d was obtained as a colorless oil (614 mg, 90 %), which gave a clean ^{1}H NMR spectrum, but which decomposed readily on standing: TLC R_F= 0.70 (benzene/acetone = 40:1); ^{1}H NMR δ 4.95 (s,1H,H-1), 4.59 (s,2H,H-2,H-3), 4.43 (s,3H,H-4,H-5, H-5'), 3.32 (s,3H,OCH_3), 1.48, 1.31 (2s,6H,$2CH_3$).

2,3-O-Isopropylidene-1-O-trifluoromethylsulfonyl-D-glycerol (3e).[17] 2,3-O-Isopropylidene-D-glycerol[17] (400 mg, 3 mmol) and triethylamine (0.5 ml, 3.6 mmol) were dissolved in 30 ml of benzene, the solution was cooled until the solvent started to freeze, and then trifluoromethanesulfonic anhydride (0.5 ml, 3 mmol) was added. Thereafter, the reaction mixture was concentrated and the crude product was filtered with benzene through silica gel (5 g). After evaporation of the solvent, 3e was obtained as an almost colorless oil (722 mg, 91%), which gave a clean ^{1}H NMR spectrum, but which decomposed readily on standing: TLC R_F= 0.78 (toluene/ethyl acetate = 9:1); ^{1}H NMR ($CDCl_3$) δ 4.50-4.42 (m,2H,

H-1,H-1'), 4.35-3.75 (m,3H,H-2,H-3,H-3'), 1.45, 1.37 (2s,6H, $2CH_3$).

2,3-O-Cyclohexylidene-1-O-trifluoromethylsulfonyl-D-glycerol (3f). 2,3-O-Cyclohexylidene-D-glycerol[18] (258 mg, 1.5 mmol) was reacted with trifluoromethanesulfonic anhydride (0.26 ml, 1.5 mmol) as described above. Compound 3f was obtained as a colorless oil (420 mg, 92%), which decomposed readily on standing; therefore, it was used without further purification: R_F = 0.80 (toluene/ethyl acetate = 9:1); ^1H NMR ($CDCl_3$) δ 4.41 (br.s,2H,H-1,H-1'), 4.38-3.70 (m,3H,H-2,H-3,H-3'), 1.58 (mc,11H,C_6H_{11}).

Methyl 2,3,4,6-Tetra-O-benzyl-α- and -β-D-glucopyranoside (4a-α and 4a-β). 2,3,4,6-Tetra-O-benzyl-D-glucopyranose (1, 540 mg, 1 mmol) was dissolved in 10 ml of dry tetrahydrofuran at -50 °C. Sodium hydride (ca. 100 mg) was added and after 10 min 3a (0.11 ml, 1 mmol) was added to the solution. After 2 h the solution was decanted from the solid material. The solution was concentrated and the anomers separated by preparative thin-layer chromatography (petroleum ether/ethyl acetate = 4:1): yield 65 mg (12 %) of 4a-α; $[\alpha]_{578}^{24}$ = +20.9 ° (c=1.17,$CHCl_3$); TLC R_F= 0.50 (petroleum ether/ethyl acetate = 4:1); yield 320 mg (58 %) of 4a-β; $[\alpha]_{578}^{20}$ = +13.1 ° (c=1,$CHCl_3$); TLC R_F= 0.50 (petroleum ether/ethyl acetate = 4:1); mp 68 °C (lit.[19] mp 68-69 °C, 74-75 °C). Compounds 4a-α and 4a-β had identical ^1H NMR spectral data and optical rotation with authentic material.[19,20]

The results shown in FIG.1 were obtained by application of the same procedure. Reaction time and temperatures for the methylation: -50 °C, -0 °C: 15 h; 40 °C: 2 h. Yields were 60-70 %. For further details see FIG.1.

Benzyl 6-O-(2,3,4,6-Tetra-O-benzyl-β-D-glucopyranosyl)-2,3,4-tri-O-benzyl-α-D-glucopyranoside (4b-β). Compound 1 (1.08 g, 2 mmol) was dissolved in 50 ml of dry tetrahydrofuran at room temperature. Sodium hydride (ca. 200 mg) and, after 15 min, 3b (1.345 g, 2 mmol) was added to the solution. After 5 h the solution was decanted from the solid material and the solution was concentrated and filtered through sili-

ca gel with benzene/acetone (40:1). The product crystallized from petroleum ether (bp 100-140 °C): yield 1.51 g (71%); mp 128 °C: $[\alpha]_{578}^{20}$ = +32.6° (c=1,$CHCl_3$); TLC R_F= 0.20 (benzene/acetone = 40:1); ^1H NMR ($CDCl_3$): δ 7.5-7.0 (m,40H), 5.1-3.3 (m,30H).

Anal. Calcd for $C_{68}H_{70}O_{11}$ (1063.3): C, 76.81; H 6.63. Found: C, 76.46; H, 6.53.

Methyl 6-O-(2,3,4,6-Tetra-O-benzyl-β-D-glucopyranosyl)-2,3,4-tri-O-benzyl-α-D-glucopyranoside (4c-β). Compound 1 (540 mg, 1 mmol) was treated with sodium hydride (ca. 100 mg) and 3c (597 mg, 1 mmol) in 30 ml of dry dioxane as described for 4b-β. After 8 h the solution was decanted from the solid material and the solution concentrated and filtered through silica gel with petroleum ether/ethyl acetate (9:1). The product was crystallized from petroleum ether (bp 100-140 °C): yield 0.60 g (61%); mp 133-134 °C (lit.[20] 131-133 °C); $[\alpha]_{578}^{20}$ = +17.1 ° (c=1,$CHCl_3$) (lit.[20] +17.9 °(c=1 $CHCl_3$); TLC R_F= 0.20 (petroleum ether/ethyl acetate = 4:1); ^1H NMR ($CDCl_3$) δ 7.5-7.0 (m,35H), 5.1-3.3 (m,28H), 3.28 (s,3H,OCH_3).

Anal. Calcd for $C_{62}H_{66}O_{11}$ (987.19): C, 75.43; H,6.75. Found: C, 75.57: H, 6.64.

Methyl 5-O-(2,3,4,6-Tetra-O-benzyl-β-D-glucopyranosyl)-2,3-O-isopropylidene-β-D-ribofuranoside (4d-β). Compound 1 (3.024 g, 5.60 mmol) was treated with sodium hydride (ca. 300 mg) and 3d (1.82 g, 5.60 mmol) in 30 ml of dry dioxane as described for 4b-β. After 12 h the reaction mixture was filtered, the solution concentrated, and the residue chromatographed on silica gel (petroleum ether/ethyl acetate = 4:1). The product crystallized from petroleum ether (bp 80-120 °C): yield 2.85 g (70%); mp 56 °C; $[\alpha]_{578}^{20}$ = +15.6 °(c=1, $CHCl_3$); TLC R_F= 0.47 (petroleum ether/ethyl acetate = 4:1); ^1H NMR ($CDCl_3$) δ 7.4-7.0 (m,20H), 5.02-4.27 (m,13H), 4.0-3.25 (m,8H), 3.25 (s,3H,OCH_3), 1.48, 1.29 (2s, 6H,$C(CH_3)_2$).

Anal. Calcd for $C_{43}H_{50}O_{10}$ (726.86): C, 71.05; H, 6.93. Found: C, 71.12; H, 6.90.

1-O-(2,3,4,6-Tetra-O-benzyl-β-D-glucopyranosyl)-2,3-O-isopropylidene-D-glycerol (4e-β). Compound 1 (540 mg, 1 mmol) was treated at -10 °C with sodium hydride (ca. 100 mg) and 3e (264 mg, 1 mmol) in 30 ml of dry tetrahydrofuran as described for 4b-β. After 3 h excess sodium hydride was destroyed with methanol, the reaction mixture concentrated, and the residue extracted with chloroform. The chloroform extract was concentrated and the residue crystallized from ether: yield 580 mg (89%) colorless crystals; mp 83-84 °C; $[\alpha]_{578}^{20}$ = +15,4 °(c=0.875,$CHCl_3$); TLC R_F= 0.30 (toluene/ethyl acetate = 9:1); ^{1}H NMR ($CDCl_3$) δ 7.38 (br.s,2OH,4C_6H_5), 5.1-3.4 (m,2OH), 1.43,1.38 (2s,6H,C(CH_3)$_2$).

Anal. Calcd for $C_{4O}H_{46}O_8$ (654.8): C, 73.37; N, 7.08. Found: C, 73.21; H, 7.14.

6-O-(β-D-Glucopyranosyl)-D-glucose (5b-β,Gentiobiose). Compound 4b-β (0.20 g, 0.188 mmol) was hydrogenated at room temperature in the presence of Pd-black in 20 ml of acetic acid. The catalyst was removed after complete debenzylation by filtration and the solution was concentrated. The residue was dissolved in 1 ml of water and methanol was added until the solution became turbid. At -5 °C crystallization occurred. The solvent was decanted and the water solution from the crystals was freeze dried: yield 45 mg (70 %); $[\alpha]_{578}^{20}$ = +14.0° (c=1, H_2O, 4h); The compound was identical in melting point and optical rotation with authentic material.

Anal. Calcd for $C_{12}H_{22}O_{11}\cdot 1.5H_2O$ (369.2): C, 39.03; H, 6.82. Found: C, 39.20; H, 6.68.

Methyl 6-O-(β-D-Glucopyranosyl)-α-D-glucopyranoside (5c-β). Compound 4c-β (197 mg, 0.2 mmol) was hydrogenated as described for 5b-β: yield 285 mg (80 %); $[\alpha]_{589}^{20}$ = +62° (c=1,H_2O) (lit.[21] $[\alpha]_{589}^{24}$ = +64° (c=1,H_2O)).

Methyl 5-O-(β-D-Glucopyranosyl)-2,3-O-isopropylidene-β-D-ribofuranoside (5d-β). Compound 4d-β (1.30 g, 1.8 mmol) was hydrogenated at room temperature in the presence of Pd-black in 30 ml of ethyl acetate. The catalyst was removed after complete debenzylation. After concentration of the solution under reduced pressure, a viscous, hydroscopic

oil was obtained: yield 632 mg (96 %); $[\alpha]_{578}^{20}$ = -44.4° (c=1, $CHCl_3$); TLC R_F= 0.50 (chloroform/methanol = 85:15); ^{1}H NMR (CD_3OD) δ 4.91 (s,1H,H-1), 4.56 (d,1H,H-2), 4.50 (d,1H,H-3), 4.45-3.40 (m), 3.30 (s,3H,OCH_3), 1.48,1.31 (2s,6H,$C(CH_3)_2$).

Anal. Calcd for $C_{15}H_{26}O_{10}\cdot 1H_2O$ (384.35): C, 46.87; H, 7.34. Found: C, 46.85; H, 7.33.

1-O-(2,3,4,6-Tetra-O-benzyl-β-D-glucopyranosyl)-D-glycerol (5e-β). Compound 4e-β (2.0 g, 3 mmol) was treated with 100 ml of 10 % aqueous acetic acid at 100 °C for 15 h. After neutralization with sodium bicarbonate, the mixture was extracted with chloroform. The extract was concentrated and the crude material chromatographed on silica gel with toluene/ethyl acetate (1:1): yield 1.0 g (54%) colorless crystals, mp 76-78 °C; $[\alpha]_{578}^{20}$ = +16.9 ° (c=0.758,$CHCl_3$); TLC R_F= 0.09 (toluene/ethyl acetate = 1:1); ^{1}H NMR ($CDCl_3$) δ 7.43 (br.s,2OH,$4C_6H_5$), 5.0-3.5 (m,2OH), 2.73 (s,2H,2OH).

Anal. Calcd for $C_{37}H_{42}O_8$ (614.73): C, 72.29; H, 6.88. Found: C, 72.15; H, 6.93.

Methyl 5-O-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-2,3-O-isopropylidene-β-D-ribofuranoside (6d-β). Compound 5d-β (610 mg, 1.65 mmol) was treated with 10 ml of acetic anhydride and 15 ml of pyridine at room temperature. After 4 h the reaction mixture was dissolved in 150 ml of chloroform, the mixture was washed two times with dilute hydrochloric acid and then with water. The organic layer was dried with calcium chloride, filtered, and concentrated. The remaining oil was dissolved in dichloromethane. Addition of petroleum ether (bp 100-140 °C) led after standing to the precipitation of colorless crystals: yield 0.75 g (85%); mp 108 °C; $[\alpha]_{578}^{20}$ = -57.9 ° (c=1,$CHCl_3$); TLC R_F = 0.54 (benzene/ acetone = 4:1); ^{1}H NMR ($CDCl_3$) δ 5.27-3.45 (m,13H), 4.88 (s,1H,H-1), 4.70 (d,1H, H-1';$J_{1',2'}$= 9 Hz), 4.56 (d,1H,H-2), 4.50 (d,1H,H-3), 2.06, 2.03, 2.00, 1.98 (4s,12H,4CO-CH_3), 1.45, 1.28 (2s,6H,$C(CH_3)_2$).

Anal. Calcd for $C_{23}H_{34}O_{14}$ (534.4): C, 51.69; H, 6.41. Found: C, 51.85; H, 6.38.

2,3-Di-O-palmitoyl-1-O-(2,3,4,6-tetra-O-benzyl-β-D-glucopyranosyl)-D-glycerol (6e-β). Compound 5e-β (0.50 g, 0.81 mmol) was dissolved in 30 ml of toluene and 3 ml of pyridine at 0 °C and treated with palmitoyl chloride (0.68 g, 2.5 mmol). The mixture was refluxed for 7 h, the precipitate was filtered, and the solution concentrated. The solid material was purified by chromatography on silica gel with toluene/ethyl acetate (7:3): yield 640 mg (73%); $[\alpha]_{578}^{20}$ = +9.9 ° (c=0.78,$CHCl_3$); TLC R_F= 0.53 (toluene/ethyl acetate = 9:1); ^{1}H NMR ($CDCl_3$) δ 7.45-7.20 (m,20H,4C_6H_5), 5.0-3.4 (m,20H), 2.56 (br.t,4H,2CO-CH_2-), 1.27 (br.s,52H), 0.90 (br.t,6H,2CH_2-CH_3).

Anal. Calcd for $C_{69}H_{102}O_{10}$ (1091.54): C, 75.90; H, 9.44. Found: C, 75.66; H, 9.12.

2,3-O-Dipalmitoyl-1-O-(β-D-glucopyranosyl)-D-glycerol (7e-β). Compound 6e-β (220 mg, 0.2 mmol) was hydrogenated as described for 4b-β: yield 104 mg (71%), which is identical in melting point and optical rotation with autentic material.[22]

2,3,4-Tri-O-benzyl-6-O-((p-methoxyphenyl)diphenylmethyl)-D-glucose (8). 2,3,4-Tri-O-benzyl-D-glucose [23] (1.802 g, 4 mmol) was dissolved in 30 ml of pyridine and (p-methoxyphenyl)diphenylmethyl chloride [24] (1.175 g, 4 mmol) added. The reaction mixture was heated to 80 °C for 1 d, cooled and treated with dilute hydrochloric acid and chloroform. The chloroform layer was washed with water to neutrality, dried with potassium carbonate, filtered, and the solvent evaporated. The residue was purified by silica gel chromatography with benzene/acetone (19:1): yield 2.21 g (78%) of slightly yellow product; TLC R_F = 0.38, 0.48 for the α- and β-anomers, respectively (benzene/acetone = 17:3); ^{1}H NMR ($CDCl_3$) δ 7.5-7.0 (m,29H),5.35 (d,0.5H,α-H-1), 5.01-3.10 (m,13.5H), 3.71 (s,3H,OCH_3);

Anal. Calcd for $C_{47}H_{46}O_6$ (705.88): C, 79.86; H, 6.56. Found: C, 79.67; H, 6.44.

Methyl 2,3,4-Tri-O-benzyl-6-O-[6-O-(p-methoxyphenyl)diphenylmethyl-2,3,4-tri-O-benzyl-α-D-glucopyranosyl]-α-

D-glucopyranoside (9c-α) and Methyl 2,3,4-Tri-O-benzyl-6-O-(2,3,4-tri-O-benzyl-α-D-glucopyranosyl)-α-D-glucopyranoside (10c-α). Compound 8 (707 mg, 1 mmol) was treated with sodium hydride (ca. 100 mg) and 3c (597 mg, 1 mmol) in 30 ml of dry tetrahydrofuran at -10 °C as described for 4b-β. After 14 h the formation of 9c-α was complete (TLC R_F= 0.62 in benzene/acetone = 4:1). The solution was decanted from the solid material (mainly excess sodium hydride), concentrated, and dissolved in 40 ml of dioxane and 20 ml of acetic acid. Water was added until the reaction mixture became turbid and then the mixture was heated to 70 °C for 16 h. The solvents were evaporated and the residue was filtered through silica gel at first with benzene/acetone = 19:1 and then the product was eluted with benzene/acetone = 9:1. The solid product crystallized from petroleum ether (bp 100-140 °C): overall yield 61 mg (67%); mp 102 °C (lit.[25] 104 °C); $[\alpha]^{20}_{578}$ = +59 °(c=1,$CHCl_3$) (lit.[26] $[\alpha]^{25}_{D}$ = + 62.9 °(c=1,$CHCl_3$)); TLC R_F= 0.47 (benzene/acetone = 9:1); ^{1}H NMR ($CDCl_3$) δ 7.5 - 7.1 (m,30,6C_6H_5), 5.05-3.35 (m,26H), 3.35 (s,3H,OCH_3), 2.75 (br.s, 1H,OH).

Anal. Calcd for $C_{55}H_{60}O_{11}$ (897.08): C, 73.64; H, 6.74. Found: C, 73.80; H, 7.00.

2,3-O-Isopropylidene-1-O-[2,3,4-tri-O-benzyl-6-O-(p-methoxphenyl)diphenylmethyl-β-D-glucopyranosyl]-D-glycerol (9e-β) and 1-O-(2,3,4-Tri-O-benzyl-β-D-glucopyranosyl)-D-glycerol (10e-β). Compound 8 (7.7 mg, 1 mmol) was treated at -10 °C with sodium hydride (ca. 100mg) and 3e (264 mg, 1 mmol) in 30 ml of dry tetrahydrofuran as described for 4b- β. After 1 d formation of 9e-β was complete (TLC R_F= 0.78 with benzene/acetone = 19:1). Excess sodium hydride was destroyed with methanol and the yellow mixture concentrated. The residue was dissolved in 40 ml of dioxane and 20 ml of acetic acid. Water was added until the reaction mixture became turbid and then the mixture was heated to 70 °C for 18 h. The solvents were evaporated and the residue purified by silica gel chromatography with

toluene/acetone (1:1). The product crystallized on standing: yield 120 mg (74%); mp 78-80 °C; TLC R_F= 0.35 (toluene/acetone = 1:1); $[\alpha]_{578}^{20}$ = +8.3 °(c=0.71,$CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 7.35, 7.32 (2br.s,15H,3C_6H_5), 5.00-3.40 (m,18H), 3.08 (br.s,3H,3OH).[26]

Anal. Calcd for $C_{30}H_{36}O_8$ (523.61): C, 68.68; H, 6.92. Found: C, 68.70; H, 6.99.

2,3-O-Cyclohexylidene-1-O-[2,3,4-tri-O-benzyl-6-O-(p-methoxphenyl)diphenylmethyl-β-D-glucopyranosyl]-D-glycerol (9f-β) and 10e-β. Compound 8 and 3f were transformed into 9f-β (TLC R_F= 0.30 with toluene/ethyl acetate = 9:1) as described for 9e-β. Subsequent acid treatment as described for 9e-β led to a product identical with 10e-β in 79% yield.

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REFERENCES AND FOOTNOTES

1. O-Alkylation at the anomeric center, part 5. For part 4, see ref. 7.

2. G. Wulff and G. Röhle, Angew. Chem. 86, 173 (1974); Angew. Chem. Int. Ed. Engl. 13, 157 (1974); C. Schuerch, Acc. Chem. Res. 6, 184 (1973); A.F. Bochkov and G.E. Zaikov, Chemistry of the O-Glycosidic Bond, Formation and Cleavage, Pergamon Press, Oxford 1979; H. Paulsen, Angew. Chem. 94, 184 (1982); Angew. Chem. Int. Ed. Engl. 21, 155 (1982), and references cited therein.

3. T. Purdie and J.C. Irvine, J. Chem. Soc. 83, 1021 (1903); W.N. Haworth, ibid.107, 8 (1919); H. Bredereck, G. Hagelloch, and E. Hambsch, Chem. Ber. 87, 35 (1954); R. Kuhn, H. Trischmann, and J. Löw, Angew. Chem. 67, 32 (1955); D. Roth and W. Pigman, J. Am. Chem. Soc. 82, 4608 (1960); D.M. Hall and O.A.Stanem, Carbohydr. Res. 12, 421 (1970); A.H. Haines and K.C. Symes, J. Chem. Soc. C, 1971, 2331; A.H. Haines, Adv. Carbohydr. Chem. Biochem. 33, 55(1976); A.Zamojski and H. Bazymska, Rocz. Chem. 49, 2113 (1975), and references cited therein.

4. Trehaloses were obtained on this basis: H. Bredereck and E. Hambsch, Chem. Ber. 87, 38 (1954).

5. R.R. Schmidt and M. Reichrath, Angew. Chem. 91, 497 (1979); Angew. Chem. Int. Ed. Engl. 18, 466 (1979).

6. R.R. Schmidt, M. Reichrath, and U. Moering, Tetrahedron Lett. 21, 3561 (1980).

7. R.R. Schmidt, U. Moering, and M. Reichrath, Chem. Ber. 115, 39 (1982).

8. R.R. Schmidt, U. Moering, and M. Reichrath, Tetrahedron Lett. 21, 3565 (1980).

9. P.E. Pfeffer, G.G. Moore, P.D. Hoagland, and E.S. Rothman in; "Synthetic Methods for Carbohydrates", Vol. 39; H.S.El Khadem, Ed; American Chemical Society, Symposium Series, 1976, p. 155.

10. Reactions of other electrophiles with the anomeric oxygen atom were explained recently on the same basis. V.G.S. Box, Heterocycles 19, 1939 (1982).

11. According to earlier findings (see ref. 7) the electrophilic order of the trifluoromethanesulfonates seems to be 3a > 3b, 3c, 3d > 3e, 3g.

12. U. Moering, Diplomarbeit, Univ. Konstanz, 1980.

13. P.R. Adams, R. Harrison, T.D. Inch, and P. Rich, Biochem. J. 155, 1 (1976).

14. A. Lipták, I. Jodál, and P. Nánasi, Carbohydr. Res. 44, 1 (1975).

15. Compound 3d was generated by a different procedure, R.W. Binkley, M.G. Ambrose, and D.G, Hehemann, J. Org. Chem. 45, 4387 (1980).

16. N.J. Leonard and K.L. Carraway, J. Heterocycl. Chem. 3, 485 (1966).

17. Compound 3e was recently generated by a different procedure and applied in glycolipid synthesis: J.J. Oltvoort, C.A.A. van Boeckel, J.H. de Koning, and J.H. van Boom, Rec. J. Royal Neth. Chem. Soc. 101, 87 (1982) - For the synthesis of 2,3-O-isopropylidene-D-glycerol see: E. Baer and H.O.L. Fischer, J. Biol. Chem. 128, 463 (1939).

18. M. Stumpp, Dissertation, Univ. Konstanz, in preparation.

19. M.E. Tate and C.J. Bishop, Can. J. Chem. 41, 1801 (1963); O.T. Schmidt, T. Auer, and H. Schmadel, Chem. Ber. 93,

556 (1960); P.W. Austin, F.E. Hardy, J.G. Buchanan, and J. Baddiley, J. Chem. Soc. 1964, 2128; F.J. Kranzer and C. Schuerch, Carbohydr. Res. 34, 71 (1974); S. Koto, N. Morishina, and S. Zen, Bull. Chem. Soc. Jpn. 52, 784 (1979).

20. J. Michel, Dissertation, Univ. Konstanz, 1983

21. C.S. Hudson, J. Am. Chem. Soc. 47, 872 (1925).

22. V.I. Sherets, A.I. Bashkatova, and R.P. Eustigneeva, Chem. Phys. Lipids. 10, 267 (1973).

23. G. Zemplen and Z. Csürös, Chem. Ber. 70, 1848 (1937).

24. Y. Lapidot, N. de Groot, S. Rappoport, and D. Hamburger, Biochem. Biophys. Acta 149, 532 (1967).

25. R. Eby and C. Schuerch, Carbohydr. Res. 50, 203 (1976).

26. The β-configuration of compound 10e-β was assigned by comparison with previous investigations: [8,12] 2,3,4-Tri-O-benzylglucose and 3e afforded a product A whose β-configuration was assigned by debenzylation and subsequent acetylation yielding the known 1-O-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-2,3-O-isopropylidene-D-glycerol: T. Ogawa, K. Katano, and M. Matsui; Carbohydr. Res. 70, 37 (1979). Mild acidic deisopropylidenation of A afforded a compound identical in melting point, optical rotation and ^{1}H NMR spectral data with 10e-β.