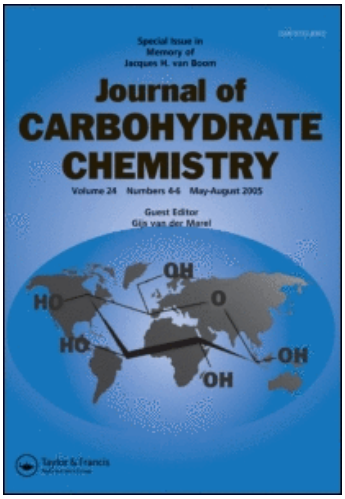


Journal of Carbohydrate Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713617200

α-Glucosylation Reactions with 2,3,4,6-Tetra-O-Benzyl-β-D-Glucopyranosyl Fluoride and Triflic Anhydride as Promoter

Hans Peter Wessel; Nicolas Ruiz

To cite this Article Wessel, Hans Peter and Ruiz, Nicolas(1991) 'α-Glucosylation Reactions with 2,3,4,6-Tetra-O-Benzyl-β-D-Glucopyranosyl Fluoride and Triflic Anhydride as Promoter', Journal of Carbohydrate Chemistry, 10: 5, 901 — 910
To link to this Article: DOI: 10.1080/07328309108543958
URL: http://dx.doi.org/10.1080/07328309108543958

J. CARBOHYDRATE CHEMISTRY, 10(5), 901-910 (1991)

α-GLUCOSYLATION REACTIONS WITH 2,3,4,6-TETRA-O-BENZYL-β-D-GLUCOPYRANOSYL FLUORIDE AND TRIFLIC ANHYDRIDE AS PROMOTER

Hans Peter Wessel* and Nicolas Ruiz

Pharmaceutical Research Department
F. Hoffmann-La Roche Ltd.
CH 4002 Basel, Switzerland

Received February 28, 1991 - Final Form July 19, 1991

ABSTRACT

Triflic anhydride is a suitable promoter for the glucosylation of glycosyl aceptors of medium or low reactivity using 2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosyl fluoride as donor. In the glucosylation of reactive hydroxyl groups competing triflate formation was observed. The use of molecular sieves as acid scavenger allows the formation of triflates of reactive alcohols under non-basic conditions.

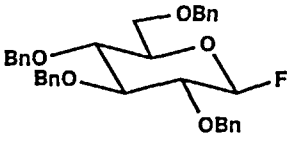
INTRODUCTION

One of the glycosylation methods showing good promise for difficult *cis*-glycosylation reactions is based on the use of glycosyl fluorides.[1] This methodology avoids heavy metal catalysts used in the classical Königs-Knorr reactions and employs Lewis acids as promoters instead. Promoters first used by Mukaiyama et al. were mixtures of stannous chloride and silver perchlorate[1] or trityl perchlorate,[2] now more often used is the stannous chloride/silver triflate variant.[3] Tetrafluorosilane or trimethylsilyl triflate were proposed as promoters for glycosylations of free or silylated hydroxyl compounds.[4] Boron trifluoride etherate was employed by Nicolaou et al.[5] and Kunz et al.;[6] Thiem and Kreuzer[7] have successfully investigated tin tetrafluoride and especially titanium tetrafluoride as catalysts. More recently, biscyclopentadienylzirconium dichloride/silver perchlorate, originally applied for *trans*-glycosylations,[8] was effective in promoting demanding

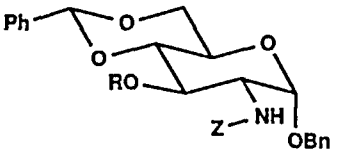
cis-glycosylation reactions.[9] Ogawa et al. also utilized tin(II) triflate or tributyltin triflate as promoters[10] in α-glycosylations.[11] We have compared the reactivity of some of the promoters mentioned and found triflic anhydride to be very strong in the glucosylation of an unreactive disaccharide acceptor using 2,3,4,6-tetra-*O*-benzyl glucopyranosyl fluoride (**1**)[1] as donor.[12] This report deals with the glucosylation of various glycosyl acceptors using fluoride **1** and triflic anhydride as promoter.

RESULTS AND DISCUSSION

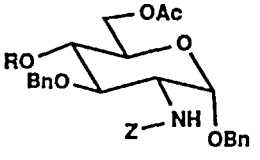
In all glucosylation reactions diethyl ether was the preferred solvent, which favours the formation of *cis*-glycosides.[4,7] Thus, reaction of hydroxyl component **2**[13] with fluoride **1** afforded exclusively the α-linked disaccharide **3** in good yield (71%). An analogous glucosamine glycosyl acceptor **4**[14] with free hydroxyl group in the 4-position gave, however, the α-linked disaccharide **5** in 58% yield along with the corresponding β-linked disaccharide **6** (26%). Both compounds, easily separable by column chromatography, were unequivocally identified by ^{1}H NMR spectroscopy. This relatively low selectivity on a 4-hydroxyl group is surprising because a 4-hydroxyl group is usually less reactive than a 3-hydroxyl group[15] (as in **2**) and a higher α/β-selectivity would be expected.[16] It should be noted, however, that both reactions were started in suspension due to the low solubility of the hydroxyl components. Glucosylation of the 4′-hydroxyl group of disaccharide **7**[14] furnished trisaccharide **8** with a 4:1 α/β-selectivity (82% α, 18% β by integration of ^{1}H NMR O-methyl signals) in 50% yield along with recovered starting material **7** (47%). Ring protons of the main component with α-linked glucose could be assigned completely using the 1D TOCSY technique, which also proved the presence of the β-linked component by excitement of the isolated H-1″ at δ = 4.29 ppm (see experimental part). This is another[17] example of the advantageous application of 1D TOCSY in carbohydrate chemistry. Glucosylation of glucosan derivative **9**[18] with fluoride **1** and triflic anhydride gave a good yield (70%) of α-linked disaccharide **10**, the structure of which was confirmed by ^{1}H NMR spectroscopy using COSY and selective irradiations. A small amount of a second disaccharide



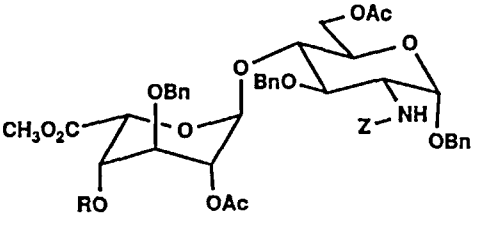
1



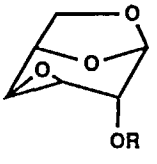
2 R = H
3 R = α-TBG



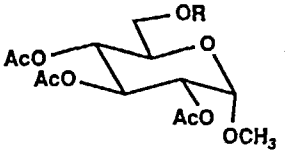
4 R = H
5 R = α-TBG
6 R = β-TBG



7 R = H
8 R = TBG



9 R = H
10 R = α-TBG



11 R = H
12 R = α-TBG
13 R = Tf

Bn = Benzyl

Ph = Phenyl

Z = Benzyloxycarbonyl

TBG = 2,3,4,6-Tetra-O-benzyl-D-glucopyranosyl

Tf = Trifluoromethylsulfonyl

Scheme 1

compound was isolated which was not a β-linked analogue according to the ^{1}H NMR spectrum, but the exact structure could not be elucidated.

Triflic anhydride promoted reaction of fluoride **1** with the primary hydroxyl group of glucose derivative **11** led to the isolation of α-linked disaccharide **12** which contained a small amount (ca. 3%) of a by-product with δ_{OCH3} = 3.37 ppm, presumably the β-linked disaccharide. The yield of **12** was 54% when the reaction was carried out at -40 °C. If the reaction was started at -20 °C and the mixture was warmed up to 0 °C within one hour the yield of glycosylation product was reduced drastically to 11% with concomitant decrease of α/β-selectivity(α/β = 2:1). The explanation for this behaviour is a side reaction in which the primary triflate **13** is formed. A similar reaction pattern was observed with other reactive alcohols. That the triflate formation can take place without a base demonstrates that 4 Å molecular sieves are a potent scavenger of triflic acid. As a matter of fact, the primary alcohol could be converted into its triflate with triflic anhydride in the presence of molecular sieves practically quantitatively (by TLC), chromatography and crystallization gave 58% of pure triflate **13**. Thus, a method for the formation of triflates under non-basic conditions is provided.

In summary, the results show that triflic anhydride is a suitable promoter for the glucosylation of glycosyl acceptors of medium or low reactivity. In the glucosylation of reactive hydroxyl groups competing triflate formation has to be taken into account.

EXPERIMENTAL

General Procedures. See lit. 19. MS: MS 902 (AEI) with data system DS 2050 (VG) for FAB. ^{1}H NMR: Bruker AC 250 (250 MHz) and AM 400 (400 MHz) with Aspect 3000.

Benzyl 3-O-(2,3,4,6-Tetra-O-benzyl-α-D-glucopyranosyl)-4,6-O-benzylidene-2-[1-(benzyloxy)formamido]-2-deoxy-α-D-glucopyranoside (3). To a suspension of fluoride **1**[1] (500 mg, 0.92 mmol), hydroxyl component **213** (226 mg, 0.46 mmol) and 4 Å molecular sieves (ca. 1 g) in dry ether (40 mL) was added dropwise a solution of triflic anhydride (75 µL, 0.46 mmol) in dry ether (10 mL) at -20 °C. The reaction mixture was allowed to slowly warm up to room

temperature. After stirring for 20 h the mixture was filtered over *Speedex* and washed with cold aqueous bicarbonate solution and water. The organic phase was dried over sodium sulfate and concentrated. Chromatography (ethyl acetate/hexane 1:4) of the crude product furnished pure **3** (330 mg, 71%). Impure fractions were rechromatographed using the same solvent system to yield another 50 mg of **3** (11%) as a colourless syrup; $[\alpha]_D^{20}$ +88.5° (c 0.4, dioxane); MS (FAB) 1036 (15%, $M+Na^+$); ^1H NMR ($CDCl_3$) δ 7.28-7.01 (m, 33H, aromatic), 6.82-6.80 (m ~d, 2H, aromatic), 5.48 (d, $J_{1',2'}$ = 3.8 Hz, H-1'), 5.41 (s, 1H, benzylidene), 5.40 (d, J ≈ 8 Hz, NH-2), 4.94 (d, $J_{1,2}$ = 3.4 Hz, H-1), 5.08, 4.98, 4.80, 4.79, 4.77, 4.68, 4.51, 4.50, 4.44, 4.37, 4.30, 4.24 (12d, 12H, $PhCH_2$), 4.18 (dd ~t, H-3), 4.16 (dd, H_{equ}-6),, 4.15 (m, H-2), 4.03 (ddd, H-5'), 3.92 (m, H-5), 3.91 (dd ~t, $J_{3',4'}$ ≈ 9.4 Hz, H-3'), 3.86 (dd ~t, $J_{4,5}$ = 10.2 Hz, H-4), 3.73 (dd ~t, $J_{4',5'}$ = 10.2 Hz, H-4'), 3.59 (dd, $J_{5'6a'}$ = 1.6 Hz, $J_{6a'6b'}$ = 10.0 Hz, H_a-6), 3.45 (dd, $J_{5'6b'}$ = 5.6 Hz, H_b-6), 3.42 (dd, $J_{2',3'}$ = 9.6 Hz, H-2'), 3.38 (dd ~t, H_{ax}-6').

Anal. Calcd for $C_{62}H_{63}NO_{12}$: C, 73.43; H, 6.26; N, 1.38. Found: C, 73.37; H, 6.51; N, 1.23.

Benzyl 6-O-Acetyl-3-O-benzyl-4-O-(2,3,4,6-tetra-O-benzyl-α-D-glucopyranosyl)-2-[1-(benzyloxy)formamido]-2-deoxy-α-D-glucopyranoside (5) and Benzyl 6-O-Acetyl-3-O-benzyl-4-O-(2,3,4,6-tetra-O-benzyl-β-D-glucopyranosyl)-2-[1-(benzyloxy)formamido]-2-deoxy-α-D-glucopyranoside (6). To a suspension of fluoride **1** (500 mg, 0.92 mmol), hydroxyl component **4**[14] (247 mg, 0.46 mmol), and activated 4 Å molecular sieves (ca. 1 g) in dry ether (55 mL) was added dropwise a solution of triflic anhydride (75 μL, 0.46 mmol) in dry ether (10 mL) at 0 °C. After stirring for 20 h at 0°C the reaction mixture was worked up as described for **3**. Chromatography of the crude product (ethyl acetate/hexane 1:3) gave crystalline **5** (282 mg, 58%) followed by **6** (126 mg, 26%).

5: Colourless crystals from ether/hexane, mp 92.5-92.7 °C; $[\alpha]_D^{20}$ +94.5° (*c* 0.4, dioxane); IR (KBr) 3356 (NH), 1724 (C=O), 1598, 1498 (aromat), 1531 (amid II), 1251 (ester), 1138, 1068, 1032 (ether), 736, 698 (monosubstituted phenyl); MS (FAB) 1080 (55%, $M+Na^+$), 1096 (30%, $M+K^+$); ^1H NMR ($CDCl_3$) δ 7.37-7.13 (m, 35H, aromatic), 5.36 (m, $J_{1',2'}$ =

3.5 Hz, H-1'), 4.99 (s, 2H, $PhCH_2$), 4.89 (d, NH), 4.89, 4.88, 4.87, 4.80, 4.79, 4.66, 4.61, 4.58, 4.54, 4.48, 4.47, 4.45 (12d, 12H, $PhCH_2$), 4.70 (d, H-1), 4.46 (dd, H_a-6), 4.27 (dd, $J_{5,6b}$ = 3.6 Hz, $J_{6a,6b}$ = 12.0 Hz, H_b-6), 4.10 (ddd, $J_{1,2}$ = 3.6 Hz, $J_{2,3} \approx J_{2,NH} \approx$ 10 Hz, H-2), 3.96 (dd ~ t, $J_{4,5}$ = 9.5 Hz, H-4), 3.93 (dd ~ t, $J_{3',4'}$ = 10.5 Hz, H-3'), 3.90 (ddd, H-5), 3.83 (dd, $J_{2,3}$ = 10.0 Hz, $J_{3,4}$ = 8.5 Hz, H-3), 3.75 (ddd ~ br.d, H-5'), 3.69 (dd, $J_{5',6a'}$ = 3.3 Hz, $J_{6a',6b'}$ = 10.3 Hz, H_b-6'), 3.65 (dd ~ t, $J_{4',5'} \approx$ 10 Hz, H-4'), 3.58 (dd, $J_{5',6'b}$ = 1.2 Hz, H_b-6'), 3.49 (dd, $J_{2',3'}$ = 10.0 Hz, H-2'), 2.02 (s, OAc).

Anal. Calcd for $C_{64}H_{67}NO_{13}$: C, 72.64; H, 6.38; N, 1.32. Found: C, 72.54; H 6.28; N, 1.35.

6: Colourless crystals from ether/hexane, mp 102.5-103.8 °C; $[\alpha]_D^{20}$ +53.6° (c 0.8, dioxane); IR (KBr) 3344 (NH), 1738 (C=O), 1605, 1500 (aromat), 1512 (amid II), 1238, 1210 (ester), 1069, 1029 (ether), 736, 698 (monosubstituted phenyl); MS (FAB) 1080 (58%, $M+Na^+$), 1096 (35%, $M+K^+$); ^1H NMR ($CDCl_3$) δ 7.24-7.06 (m, 35H, aromatic), 4.99, 4.96, 4.95, 4.82, 4.74, 4.73, 4.71, 4.57, 4.52, 4.46, 4.38 (12d, 12H, $PhCH_2$), 4.83 (d, H-1), 4.71 (d, NH), 4.33 (d, $J_{1',2'}$ = 7.8 Hz, H-1'), 4.28 (dd, $J_{5,6a}$ = 1.6 Hz, H_a-6), 4.275 (s, 2H, $PhCH_2$), 4.19 (dd, $J_{5,6b}$ = 4.5 Hz, $J_{6a,6b}$ = 12.1 Hz, H_b-6), 3.91 (ddd ~ dt, $J_{1,2}$ = 3.6 Hz, $J_{2,3} \approx J_{2,NH} \approx$ 10 Hz, H-2), 3.82 (dd ~ t, $J_{3,4}$= 8.8 Hz, H-4), 3.68 (ddd, $J_{4,5}$ = 10.0 = Hz, H-5), 3.61 (dd, $J_{5',6a'}$ = 1.2 Hz, H_a-6'), 3.58 (m, H-3'), 3.57 (m, H-4'), 3.53 (dd ~ t, H-3), 3.50 (dd, $J_{5',6b'} \approx$ 4.3 Hz, $J_{6a',6b'}$ = 10.6 Hz, H_b-6'), 3.37 (m_c, H-2'), 3.31 (m_c, H-5'), 1.95 (s, OAc).

Anal. Calcd for $C_{64}H_{67}NO_{13}$: C, 72.64; H, 6.38; N, 1.32. Found: C, 72.45; H, 6.45; N, 1.30.

Benzyl 6-O-Acetyl-3-O-benzyl-2-[1-(benzyloxy)formamido]-2-deoxy-4-O-[methyl 2-O-acetyl-3-O-benzyl-4-O-(2,3,4,6-tetra-O-benzyl-D-glucopyranosyl)-α-L-idopyranosyluronate]-α-D-glucopyranoside (8). To a solution of fluoride 1 (500 mg, 0.92 mmol) and hydroxyl compound 7[14] (395 mg, 0.46 mmol) in dry ether (50 mL) and tetrahydrofuran (20 mL) was added dropwise a solution of triflic anhydride (75 µL, 0.46 mmol) in dry ether (10 mL) at -20 °C in the presence of 4 Å molecular sieves (ca. 1 g). After 2d at 0 °C and 2d at room temperature the reaction was not completed, and the same amount of ethereal triflic anhydride solution was added. This addition did not

change the composition of the reaction mixture as judged by TLC. After a total of 7d the reaction mixture was worked up as described for **3** and submitted to chromatography (ethyl acetate/hexane 1:2) to give **8** (306 mg, 50%). In a further fraction unreacted starting material **7** was recovered (185 mg).

8: Colourless syrup; IR (film) 3355 (NH), 1738 (C=O), 1606, 1500 (aromat), 1508 (amid II), 1238 (ester), 1109, 1079, 1029 (ether), 738, 698 (monosubstituted phenyl); MS (FAB) 1402 (53%, $M+Na^+$), 1418 (30%, $M+K^+$); ^1H NMR ($CDCl_3$) δ 7.33-7.11 (m, 40H, aromatic), α-linked main product: 5.14 (d, $J_{1',2'}$ = 2.1 Hz, H-1'), 4.96 (s, 2H, CH_2Ph), 4.88 (br.s, 2H, H-1, H-2'), 4.82 (d, H-1''), 4.78 (d, H-5'), 4.37 (dd ~ br.d, H-6a), 4.19 (dd, $J_{5,6b}$ = 3.8 Hz, $J_{6a,6b}$ = 11.8 Hz, H-6b), 4.04 (ddd ~ dt, $J_{1,2}$ = 3.5 Hz, $J_{2,NH}$ ≈ 10 Hz, $J_{2,3}$ ≈ 10 Hz, H-2), 3.95 (dd ~ t, $J_{2',3'}$ ≈ 3 Hz, $J_{3'4'}$ ≈ 4.6 Hz, H-3'), 3.92 (dd ~ t, $J_{4',5'}$ ≈ 3.4 Hz, H-4'), 3.91 (dd ~ t, H-4), 3.85 (dd ~ t, $J_{3'',4''}$ = 9.4 Hz, H-3''), 3.81 (ddd ~ br.d, H - 5), 3.79 (ddd ~ br.d, $J_{4'',5''}$ = 9.6 Hz, H-5''), 3.67 (dd, $J_{5'',6a''}$ = 2 Hz, $J_{6a'',6b''}$ = 10.8 Hz, H-6a''), 3.66 (dd ~ t, H-4''), 3.59 (dd ~ t, H-3), 3.55 (dd, $J_{5'',6b''}$ = 1.6 Hz, H-6b''), 3.44 (dd, $J_{1'',2''}$ = 3.4 Hz, $J_{2'',3''}$ = 9.6 Hz, H-2''), 3.42 (s, OCH_3), 2.125 (s, OAc), 1.92 (s, OAc), β-linked by-product: 5.14 (d, H-1'), 4.91 (d, $J_{4',5'}$ = 2.1 Hz, H-5'), 4.86 (br.s, H-2'), 4.29 (d, $J_{1'',2''}$ = 7.8 Hz, H-1''), 4.19 (br.s, H-3'), 3.57-3.52 (m, 2H, H-3'', H-4''), 3.38 (dd, $J_{5'',6b''}$ = 1 Hz, $J_{6a'',6b''}$ = 11 Hz, H-6b''), 3.29 (m, H-5), 3.27 (dd ~ t, $J_{2'',3''}$ = 9 Hz, H-2''), 3.23 (s, OCH_3), 2.12 (s, OAc), 1.93 (s, OAc).

Anal. Calcd for $C_{80}H_{85}NO_{20}$: C, 69.60; H, 6.21; N, 1.01. Found: C, 68.97; H, 5.98; N, 0.97.

1,6;3,4-Dianhydro-2-O-(2,3,4,6-tetra-O-benzyl-α-D-glucopyranosyl)-β-D-galactopyranose (10). To a solution of fluoride **1** (500 mg, 0.92 mmol) and hydroxyl component **9**[18] (66 mg, 0.46 mmol) in abs. ether (10 mL) was added dropwise triflic anhydride (75 µL, 0.46 mmol) in ether (10 mL) at -20 °C in the presence of 4 Å molecular sieves (ca. 1 g). After stirring for 27 h the reaction was worked up as described for **3**. Chromatography (ethyl acetate/hexane 1:3) gave **10** (216 mg, 70%) as colourless syrup; $[\alpha]_D^{20}$ +46.5° (*c* 0.2, dioxane); IR (film) 1605, 1496 (aromat), 1070, 1000 (ether), 739, 698

(monosubstituted phenyl); MS (CI) 684 (68%, $M+NH_4^+$); ^1H NMR ($CDCl_3$) δ 7.34-7.26 (m, 17H, aromatic), 7.14-7.12 (m, 3H, aromatic), 5.23 (br.s, H-1), 4.98, 4.81 (2d, J = 10.8 Hz, $PhCH_2$), 4.86 (d, H-1'), 4.85 (m, H-5), 4.83, 4.47 (2d, J = 10.2 Hz, $PhCH_2$), 4.82, 4.61 (2d, J = 12.0 Hz, $PhCH_2$), 4.59, 4.46 (2d, J = 10.8 Hz, $PhCH_2$), 4.01 (dd ~ t, $J_{3',4'}$ = 8.8 Hz, H-3'), 3.97 (d, $J_{5,6a}$ < 0.5 Hz, $J_{6a,6b}$ = 6.5 Hz, H_a-6), 3.86 (ddd, $J_{4',5'}$ = 10.0 Hz, H-5'), 3.72 (dd, $J_{5',6a'}$ = 3.7 Hz, $J_{6a',6b'}$ = 10.0 Hz, H_a-6'), 3.68 (s, H-2), 3.65 (dd ~ t, H-4'), 3.63 (dd, $J_{5',6b'}$ = 2.0 Hz, H_b- 6'), 3.57 (dd, $J_{1',2'}$ = 4.0 Hz, $J_{2',3'}$ = 9.4 Hz, H-2'), 3.54 (dd ~t, $J_{4,5}$ = 4.9 Hz, H-4), 3.53 (dd, $J_{5,6b}$ = 4.9 Hz, H_b-6), 3.22 (dd, $J_{1,3}$ = 1.5 Hz, $J_{3,4}$ = 3.9 Hz, H-3).

Methyl 2,3,4-Tri-O-acetyl-6-O-(2,3,4,6-tetra-O-benzyl-α-D-glucopyranosyl)-α-D-glucopyranoside (12). To a solution of fluoride **1** (500 mg, 0.92 mmol) and triflic anhydride (75 μL, 0.46 mmol) in abs. ether (20 mL) was added the hydroxyl component **11** (150 mg, .0.47 mmol) at -40 °C in presence of 4 Å molecular sieves. After 48 h the reaction mixture was poured onto cold aqueous sodium bicarbonate solution. Extraction with ether, drying over sodium sulfate, and chromatography (ethyl acetate/hexane 1:2) gave **12** (208 mg, 54%), containing a small amount (ca. 3%, judged by ^1H NMR, integral of OCH_3 signal at 3.36 and 3.37 ppm) of another substance which could not be removed by chromatography. Colourless syrup, $[\alpha]_D^{20}$ +106° (c 0.2, dioxane); IR (film) 1752 (C=O), 1223 (ester), 1161, 1040 (ether), 740, 698 monosubstituted phenyl; MS (FAB) 843 (22%, $M+H^+$), 865 (32%, $M+Na^+$), 881 (15%, $M+K^+$); ^1H NMR ($CDCl_3$) δ 7.38-7.23 (m, 18H, aromatic), 7.16-7.11 (m, 2H, aromatic), 5.47 (dd ~ t, $J_{3,4}$ = 9.7 Hz, H-3), 5.00 (dd ~ t, $J_{4,5}$ = 10.0 Hz, H-4), 4.94, 4.80 (2d, J = 11.0 Hz, $PhCH_2$), 4.90 (d, $J_{1,2}$ = 3.4 Hz, H-1), 4.82, 4.46 (2d, J = 11.0 Hz, $PhCH_2$), 4,82 (dd, $J_{2,3}$ = 10.1 Hz, H-2), 4.77 (d, $J_{1',2'}$ = 3.5 Hz, H-1'), 4.77, 4.66 (2d, J = 12.2 Hz, $PhCH_2$), 4.59, 4.45 (2d, J = 12.0 Hz, $PhCH_2$), 4.01 (ddd, $J_{5,6b}$ = 2.5 Hz, H-5), 3.95 (dd ~ t, $J_{3',4'}$ = 9.3 Hz, H-3'), 3.83 (ddd ~ dt, H-5'), 3.71 (dd, $J_{5,6a}$ = 6.3 Hz, $J_{6a,6b}$ = 11.0 Hz, H_a-6), 3.69 (dd, $J_{5'6a'}$ = 3.6 Hz, $J_{6a',6b'}$ = 10.5 Hz, H_a-6'), 3.63 (dd ~ t, $J_{4',5'}$ = 9.8 Hz, H-4'), 3.59 (dd, $J_{5',6b'}$ = 2.0 Hz, H_b- 6'), 3.55 (dd, $J_{2',3'}$ = 9.7 Hz, H-2'), 3.50 (dd, $J_{6a,6b}$ = 11.0 Hz, H_b-6), 3.56 (s, 3H, OCH_3), 2.07, 2.01, 2.00 (3s, 9H, OAc).

Anal. Calcd for $C_{47}H_{54}O_{14}$: C, 66.97; H, 6.46. Found: C, 66.88; H, 6.44.

Methyl 2,3,4-Tri-O-acetyl-6-O-trifluoromethylsulfonyl-α-D-glucopyranoside (13). To a solution of alcohol **11** (150 mg, 0.47 mmol) in abs. ether (10 mL) was added dropwise a solution of triflic anhydride (85 mL, 0.51 mmol) in abs. ether (10 mL) at 0 °C in the presence of 4 Å molecular sieves. After 4.5 h the reaction mixture was filtered, concentrated, and chromatographed (ethyl acetate/hexane 1:2) to give **13** (189 mg), crystallization from ethyl acetate furnished colourless crystals (123 mg, 58%) of pure **13**, mp 76-77 °C; $[\alpha]_D^{20}$ 104.7° (*c* 1.0, dioxane); IR (KBr) 1752 (C=O), 1604, 1498 (aromat), 1221 (ester), 1146, 1038 (SO_2, ether), 750, 700 (monosubstituted phenyl); MS (FAB) 475 (30%, $M+Na^+$), 491 (20%, $M+K^+$); ^1H NMR ($CDCl_3$) δ 5.51 (dd, $J_{3,4}$ = 9.2 Hz, H-3), 4.99 (d, $J_{1,2}$ = 3.6 Hz, H-1), 4.97 (dd ~ t, H-4), 4.87 (dd, $J_{2,3}$ = 10.3 Hz, H-2), 4.55 (dd, $J_{5,6a}$ = 5.9 Hz, $J_{6a,6b}$ = 11.0 Hz, H_a-6), 4.48 (dd, $J_{5,6b}$ = 2.4 Hz, H_b-6), 4.10 (ddd, $J_{4,5}$ = 10.0 Hz, H-5), 3.43 (s, 3H, OCH_3), 2.08, 2.06, 2.02 (3s, 9H, OAc).
Anal. Calcd for $C_{14}H_{19}F_3O_{11}S$: C, 37.17; H, 4.23; S, 7.09. Found: C, 37.14; H, 4,38; S, 6.93.

ACKNOWLEDGEMENTS

The skillful technical assistance of Mr. R. Keller is gratefully acknowledged. We wish to thank our colleagues from the Central Research Department for the determination of physical data: Dr. W. Arnold (NMR), Dr. G. Englert (NMR), Mr. W. Meister (MS), Dr. S. Müller (MA), and Dr. W. Vetter (MS), and Mrs. S. Lardelli for typing the manuscript.

REFERENCES AND FOOTNOTES

1. T. Mukaiyama, Y. Murai, and S. Shoda, *Chem. Letters*, 431 (1981).
2. T. Mukaiyama, Y. Hashimoto, and S. Shoda, *Chem. Letters*, 935 (1983).
3. Y. Takahashi and T. Ogawa, *Carbohydr. Res.*, **164**, 277 (1987).
4. S. Hashimoto, M. Hayashi, and R. Noyori, *Tetrahedron Lett.*, 25 1379 (1984).
5. K.C. Nicolaou, A. Chucholowski, R.E. Dolle, and J.L. Randall, *J. Chem. Soc., Chem. Commun.*, 1155 (1984).

6. a) H. Kunz and H. Waldmann, *J. Chem. Soc., Chem. Commun.*, 638 (1985);
b) H. Kunz and W. Sager, *Helv. Chim. Acta*, **68**, 283 (1985).

7. M. Kreuzer and J. Thiem, *Carbohydr. Res.*, **149**, 347 (1986).

8. T. Matsumoto, H. Maeta, K. Suzuki, and G. Tsuchihashi, *Tetrahedron Lett.*, **29**, 3567 (1988).

9. C. Murakata and T. Ogawa, *Tetrahedron Lett.*, **31**, 2439 (1990).

10. Y. Ito and T. Ogawa, *Tetrahedron Lett.*, **28**, 6221 (1987).

11. Y. Nakahara and T. Ogawa, *Carbohydr. Res.*, **200**, 363 (1990).

12. H.P. Wessel, *Tetrahedron Lett.*, **31**, 6863 (1990).

13. P.C. Wyss and J. Kiss, *Helv. Chim. Acta*, **58**, 1833 (1975).

14. a) J.-C. Jacquinet, M. Petitou, Ph. Duchossoy, J. Lederman, J. Choay, G. Torri, and P. Sinaÿ, *Carbohydr. Res.*, **130**, 221 (1984);
b) H.P. Wessel, L. Labler, and T.B. Tschopp, *Helv. Chim. Acta*, **72**, 1268 (1989).

15. H. Paulsen and Č. Kolař, *Chem. Ber.*, **114**, 306 (1981).

16. See for example: G.H. Veeneman and J.H. van Boom, *Tetrahedron Lett.*, **31**, 275 (1990).

17. H.P. Wessel, G. Englert, and P. Stangier , *Helv. Chim. Acta*, **74**, 682 (1991).

18. J. Staněk, jr. and M. Černý, *Synthesis*, 698 (1982).

19. H.P. Wessel, J. *Carbohydr. Chem.*, **8**, 443 (1989).