2-(Trimethylsilyl)ethyl Glycosides. Transformation into Glycopyranosyl Chlorides

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2-(Trimethylsilyl)ethyl (TMSET) glycosides were transformed in high yields into the corresponding 1-chloro sugars by treatment with 1,1-dichloromethyl methyl ether/zinc chloride. With acetyl, benzoyl, and benzyl protection of the 2-position, the α-glycopyranosyl chloride was the major product, whereas with the 2-phthalimido sugar **13**, the β-chloride **21** was obtained. The fully benzylated TMSET glucopyranoside **1** gave the α-chloro sugar **22** carrying a 6-*O*-formyl group whereas the partially benzylated sugars **16** and **17** gave the chloro sugars with all protecting groups intact.

The choice of the anomeric protecting group in the synthesis of oligosaccharides is important for several reasons. It should be compatible with a series of different reaction conditions that are to be utilized in the synthesis, it should be removable without affecting the remaining glycosidic bonds of the oligosaccharide, and preferentially, it should be transformable into activated derivatives for further glycoside synthesis. We have reported that 2-(trimethylsilyl)ethyl (TMSET) glycosides fulfill these criteria by being stable under the majority of reaction conditions used in oligosaccharide synthesis.[1] Furthermore, TMSET glycosides can be transformed into the corresponding hemiacetals and 1-*O*-acyl sugars in high yields,[1] the latter being obtained with conserved anomeric configuration. Recently we reported the transformation of TMSET glycosides into trimethylsilyl and methoxymethyl glycosides.[2] Hemiacetal and 1-*O*-acyl sugars are well-known intermediates for the preparation of activated derivatives such as trichloroacetimidates and halo sugars. We now report the direct transformation of TMSET glycosides into the corresponding 1-chloro sugars.

The anomeric oxygen atom of TMSET glycosides is more basic than that of normal glycosides because of the silicon β effect.[3] TMSET glycosides therefore react rapidly (cf. Table I in ref 1) with many electrophilic reagents.[1] The silicon atom will thereby be sensitive to attack by nucleophiles and the TMSET group will fragment into a silicon derivative and ethylene, thus leaving the sugar with its anomeric oxygen atom coupled to the electrophilic part of the reagent.[1,2]

The increased reactivity of TMSET glycosides versus other alkyl glycosides is also indicated by the rapid hydrolysis of 2-(trimethylsilyl)ethyl 2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranoside[1] (**1**, Chart I) as compared to the corresponding methyl and isopropyl 2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranosides (**2** and **3**) (Table I). The comparably low yield of 2,3,4,6-tetra-*O*-benzyl-β/α-D-glucopyranose (**4**) from the latter two glucosides is probably due to the longer reaction time (causing some adverse reactions).

Glycopyranosyl halides are traditionally prepared from the corresponding 1-*O*-acetyl or hemiacetal derivative. It has been reported that sugar 1-*O*-acetates and methyl glycosides can be transformed into the corresponding 1-chloro sugars by treatment with 1,1-dichloromethyl methyl ether/zinc chloride.[4,5] We investigated this and similar reagents for the direct synthesis of 1-chloro sugars from TMSET glycosides. In a preliminary study with 2-(trimethylsilyl)ethyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside[1] (**5**) we found that 1,1-dichloromethyl methyl ether/boron trifluoride etherate failed to produce the desired 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl chloride in high yield because the boron trifluoride etherate reacted faster with the TMSET group of **5** than with 1,1-dichloromethyl methyl ether. Instead, the hemiacetal 2,3,4,6-tetra-*O*-acetyl-β/α-D-glucopyranose was detected by TLC, and was probably formed by hydrolysis of an intermediate Glc-OBF_2 derivative[1] on the TLC plate. With 1,1-dichloromethyl methyl ether/tin tetrachloride, 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl chloride (**9**) was formed rapidly and in high yield. However, since tin tetrachloride causes anomerization of glycosides[6] and since

Table I. Reaction Time and Yield of 2,3,4,6-Tetra-*O*-benzyl-β/α-D-glucopyranose (4) in the Hydrolysis of 2-(Trimethylsilyl)ethyl (1), Methyl (2), and Isopropyl 2,3,4,6-Tetra-*O*-benzyl-β-D-glucopyranoside (3)

starting mtrl	reactn time,[a] min	yield of 4,[b] %
1	30	92
2	240	82
3	180	80

[a] Time required for complete conversion of starting material. [b] Yield of chromatographed product (see Experimental Section).

Table II. Yield and β/α-Composition of 2,3,4,6-Tetra-*O*-acetyl-D-glucopyranosyl Chloride (9) from Treatment of 5–8 (see Chart I) with 1,1-Dichloromethyl Methyl Ether/Zinc Chloride in Chloroform at Room Temperature

starting mtrl	reactn time, h	β/α ratio of remaining start. mtrl[a]	convn to 9, % (β/α ratio[a])
5	2	–	100 (21/79)
5	24	–	100 (0/100)
6	2	91:9	7 (50/50)
6	24	67:33	53 (5/95)
7	24	7:93	19 (5/95)[b]
8	2	not dtmnd	90[b] (50/50)[b]

[a] Determined by ^1H NMR analysis of the crude product. [b] Determined by TLC.[7]

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(1) Jansson, K.; Ahlfors, S.; Frejd, T.; Kihlberg, J.; Magnusson, G.; Dahmen, J.; Noori, G.; Stenvall, K. *J. Org. Chem.* **1988**, *53*, 5629–5647.
(2) Jansson, K.; Magnusson, G. *Tetrahedron* **1990**, *46*, 59–64.
(3) Jarvie, A. W. P. *Organomet. Chem. Rev. A* **1970**, *6*, 153–207. Wierschke, S. G.; Chandrasekhar, J.; Jorgensen, W. L. *J. Am. Chem. Soc.* **1985**, *107*, 1496–1500. Lambert, J. B.; Wang, G.; Finzel, R. B.; Teramura, D. H. *J. Am. Chem. Soc.* **1987**, *109*, 7838–7845. Ryu, I.; Hirai, A.; Suzuki, H.; Sonoda, N.; Murai, S. *J. Org. Chem.* **1990**, *55*, 1409–1410.
(4) Gross, H.; Farkas, I.; Bognár, R. *Z. Chem.* **1978**, *18*, 201–210 and references therein.
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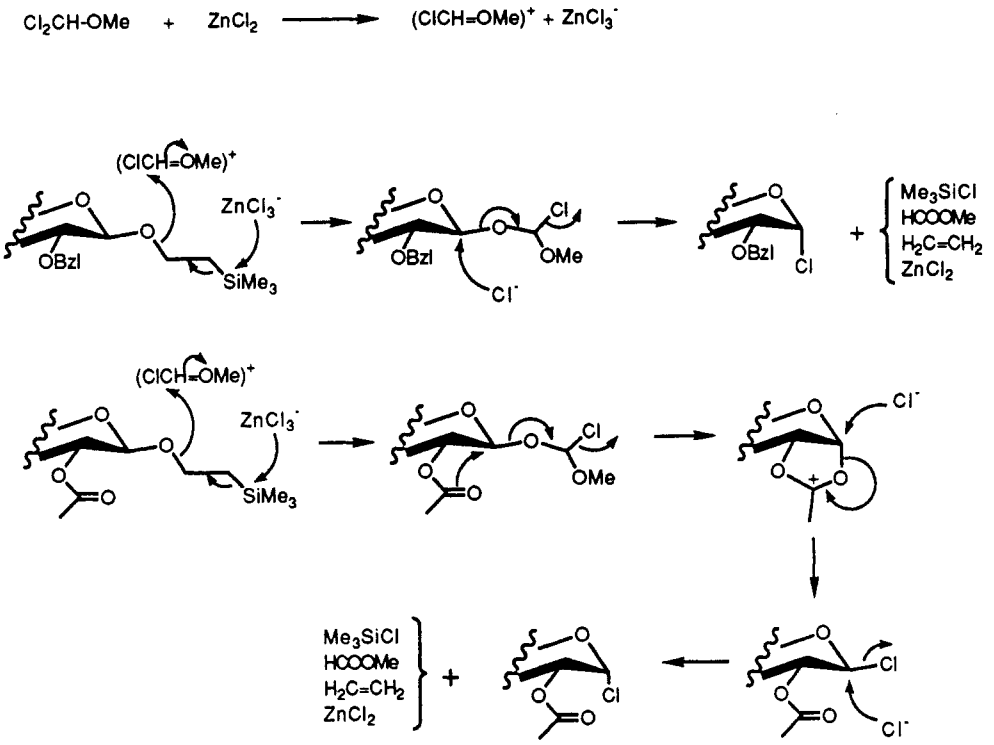
0022-3263/90/1955-3181$02.50/0

Scheme I



it is known that benzyl groups may be cleaved by strong Lewis acids,[6] we turned our attention to zinc chloride, which is a weaker Lewis acid.

In a comparative study of **5**, methyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (**6**), isopropyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (**7**), and 1,2,3,4,6-penta-*O*-acetyl-β-D-glucopyranose (**8**), it was found that 1,1-dichloromethyl methyl ether/zinc chloride effected the formation of **9** more rapidly and in higher yield with **5** than with **6**–**8** (Table II). A β/α-mixture of **9** was formed initially, which slowly anomerized into the pure α-anomer **9**. The TMSET glucoside **5** reacted more rapidly than the methyl and isopropyl glucosides **6** and **7**, partly because the latter two compounds underwent anomerization to the less reactive α-glycosides during the reaction. Compound **5** reacted at least as fast as glucose pentaacetate (**8**). The results are summarized in Table II.

The probable reaction path for direct conversion of TMSET glycosides into the corresponding 1-chloro sugars is depicted in Scheme I. Except for zinc chloride, which is used in catalytic (ca. 10%) amount, all the reaction byproducts are volatile and thereby easily removed. The formation of ethylene from fragmentation of the TMSET group effectively drives the reaction to completion and also helps in avoiding anomerization of the starting material, which in the case of the methyl and isopropyl glycosides **6** and **7** retarded the formation of the desired 1-chloro sugar.

The nonanomeric protecting groups were important for the outcome of the reaction (Table III). The O-acylated and N-phthaloylated compounds **5**, 2-(trimethylsilyl)ethyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (**10**), 2-(trimethylsilyl)ethyl 3,4,6-tri-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-β-D-glucopyranoside (**11**), 2-(trimethylsilyl)ethyl 2,3,6-tri-*O*-benzoyl-4-*O*-[6-*O*-acetyl-2,3-di-*O*-benzoyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl)-β-D-galactopyranosyl]-β-D-glucopyranoside (**12**), and 2-(trimethylsilyl)ethyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranoside[1] (**13**) were fully compatible with the conditions and gave the products in high yields (**9**, **18**–**21**). It should be noted that compound **21** was obtained as a β/α-mixture with β dominating and that the pure β-anomer was obtained by crystallization. The reason might be found in steric hindrance of the phthalimido group against chloride ion attack from the α-side of the pyranosidic ring (cf. Scheme I). 2-(Trimethylsilyl)ethyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-galactopyranoside (**14**) was the only investigated compound that failed to give a well-defined product; several unidentified polar products were formed.

The primary benzyloxy group of **1** seems to be sufficiently nucleophilic to compete with the TMSET group for the electrophilic species $(ClCH{=}OMe)^+$, since the major product (**22**) contained a 6-*O*-formyl group. Compound **22** may be of value in the synthesis of 1–6 oligoglucosides. The formation of benzyl chloride during the reaction (determined by GLC and by the characteristic

Table III. Yield, Reaction Time, and β/α Ratio of the 1-Chloro Sugars 9, 18–24 Formed by Treatment of TMSET Glycosides with 1,1-Dichloromethyl Methyl Ether/Zinc Chloride (See Experimental Section)

TMSET glycoside	reaction time, h	product	yield, % chrom[a]	yield, % cryst[a]
5	19	9	98	91
10	22	18	99	87
11	18	19	98	93
12	19	20	96	
13	21	21	99[b]	69[c]
1	5	22	52	
14	25	*d*		
16	3	23	98[e]	
17	1.5	24	83	62

[a] Isolated yield by chromatography or crystallization of the chromatographed material; only the α-anomer was detected by ^1H NMR spectroscopy unless otherwise stated. [b] β/α, 88:12. [c] Pure β anomer. [d] Complex reaction mixture. [e] β/α, 8:92.

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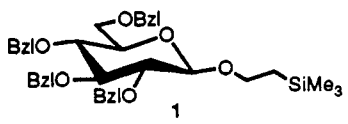
Chart I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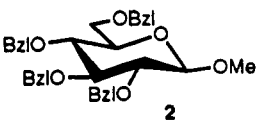
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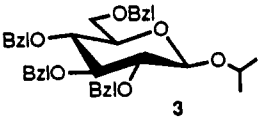
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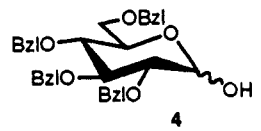
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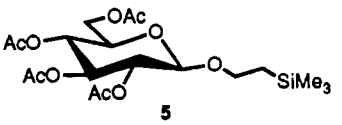
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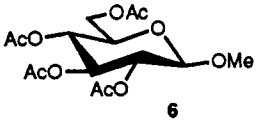
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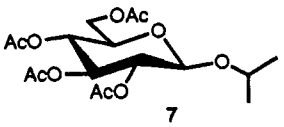
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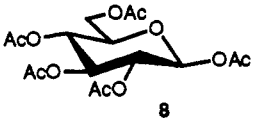
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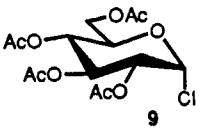
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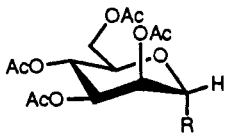
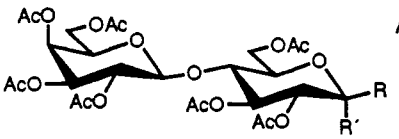
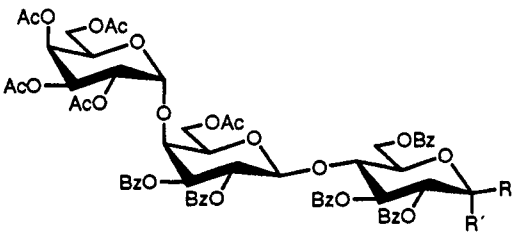
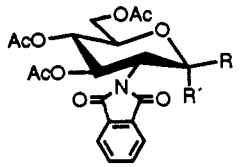
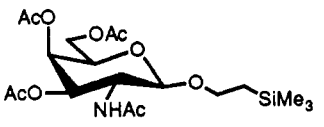

10: R = $OCH_2CH_2SiMe_3$
18: R = Cl


11: R = $OCH_2CH_2SiMe_3$; R′ = H
19: R = H; R′ = Cl


12: R = $OCH_2CH_2SiMe_3$; R′ = H
20: R = H; R′ = Cl


13: R = $OCH_2CH_2SiMe_3$; R′ = H
21: R = Cl; R′ = H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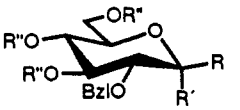
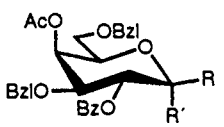
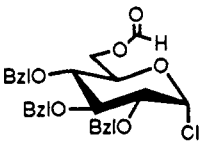

15: R = $OCH_2CH_2SiMe_3$; R′ = R″ = H
16: R = $OCH_2CH_2SiMe_3$; R′ = H; R″ = Ac
23: R = H; R′ = Cl; R″ = Ac


17: R = $OCH_2CH_2SiMe_3$; R′ = H
24: R = H; R′ = Cl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odor of benzyl chloride in the crude product) corroborates the suggested reaction path shown in Scheme II. The cleavage of both primary and secondary benzyloxy groups in sugars using various Lewis acids have been reported.[5,6] In contrast, the secondary benzyloxy group of 2-(trimethylsilyl)ethyl 3,4,6-tri-*O*-acetyl-2-*O*-benzyl-β-D-glucopyranoside (**16**) was fully compatible with the reaction conditions, and the primary benzyloxy group of 2-(trimethylsilyl)ethyl 4-*O*-acetyl-2-*O*-benzoyl-3,6-di-*O*-benzyl-β-D-galactopyranoside[1] (**17**) was stable enough to permit the preparation of the chloro sugar **24** as the major product. This indicates that electron-withdrawing groups in the sugar ring can stabilize benzyloxy groups against electrophilic cleavage.

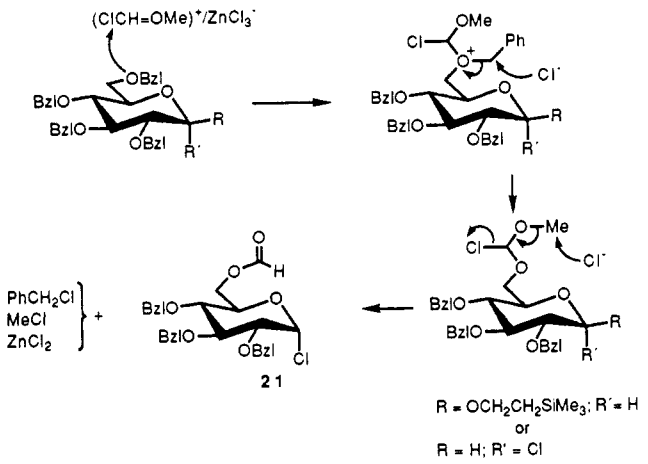
In summary, TMSET glycosides can be transformed into the corresponding 1-chloro sugars under mild conditions and in high yields. The byproducts of the reaction (except zinc chloride) are volatile and can be easily removed, thereby leaving a crude product that is easily purified for further use as glycosylation reagent. The procedure is especially important for the synthesis of oligosaccharidic glycoconjugates where it is crucial to have access to reliable methods for activation of the anomeric position toward the end of a long synthetic sequence.

Experimental Section

Thin-layer chromatography (TLC) was performed on Kieselgel 60 F_{254} (Merck). Chloro sugars were selectively detected as brown spots on the TLC plate by heating to ca. 200 °C for ca. 5 min.[7] Charring with 30% aqueous sulfuric acid gave the fully developed plate. Products were chromatographed on Kieselgel 60 (Merck,

(7) Magnusson, G.; Noori, G.; Dahmén, J.; Frejd, T.; Lave, T. *Acta Chem Scand. B* **1981**, *35*, 213–216.

Scheme II



230–400 mesh). Melting points are uncorrected. NMR spectra were recorded in $CDCl_3$ with $CHCl_3$ as internal standard (δ 7.26 ppm) using a Varian XL 300 instrument. The chloro sugars were obtained as α-anomers unless stated otherwise. Anomeric ratios were determined by ^1H NMR analysis. Optical rotations were measured with a Perkin-Elmer 141 polarimeter.

TMSET glycosides[1] **1**, **5**, **10–13**, and **17**, methyl glucosides[8,9] **2** and **6**, and the isopropyl glucoside **7**[10] have been reported.

Isopropyl 2,3,4,6-Tetra-*O*-benzyl-β-D-glucopyranoside (3). Compound **7**[10] was deacetylated with methanolic sodium methoxide, and the product was benzylated with benzyl bromide/sodium hydride in *N,N*-dimethylformamide in the usual way[1] to give **3** (74%): mp 107–108 °C (MeOH); $[\alpha]^{25}_D$ +11° (*c* 1, $CDCl_3$); ^1H NMR δ 4.53–5.00 (8 H, $PhCH_2$), 4.47 (d, 1 H, *J* = 7.8 Hz, H-1), 4.03 (heptet, 1 H, *J* = 6.2 Hz, $CHMe_2$), 3.74, 3.66 (dd, 1 H each, *J* = 10.8, 4.9, 2.0 Hz, H-6), 3.64, 3.55 (t, 1 H each, H-3,4), 3.46 (m, 1 H, H-5), 3.44 (dd, 1 H, *J* = 9.0, 7.8 Hz, H-2), 1.32, 1.25 (d, 3 H each, *J* = 6.2 Hz, $CHMe_2$).

2-(Trimethylsilyl)ethyl 2-*O*-Benzyl-β-D-glucopyranoside (15). 2-(Trimethylsilyl)ethyl 2-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranoside[1] (1170 mg, 2.55 mmol) was dissolved in methanol (25 mL), iodine[12] (250 mg) was added, and the mixture was heated at reflux for 2 h. Excess solid sodium thiosulfate was added, and the solvent was removed. The residue was chromatographed (SiO_2, EtOAc/MeOH, 40:1) to give **15** (615 mg, 65%): mp 133–134 °C (EtOAc/heptane); $[\alpha]^{20}_D$ −3° (*c* 1, $CHCl_3$); ^1H NMR δ 7.29–7.38 (5 H, Ph-H), 4.98, 4.66 (AB q, 1 H each, *J* = 11.5 Hz, $PhCH_2$), 4.46 (d, 1 H, *J* = 7.8 Hz, H-1), 1.03 (m, 2 H, CH_2Si), 0.04 (s, 9 H, $SiMe_3$). Anal. Calcd for $C_{18}H_{30}O_6Si$: C, 58.4; H, 8.2. Found: C, 58.5; H, 7.8.

2-(Trimethylsilyl)ethyl 3,4,6-Tri-*O*-acetyl-2-*O*-benzyl-β-D-glucopyranoside (16). Compound **15** (448 mg, 1.21 mmol) was dissolved in pyridine (10 mL) and acetic anhydride (7 mL) was added. When the acetylation was complete (TLC), the solvent was removed and the residue was chromatographed (SiO_2, EtOAc/heptane, 2:3) to give **16** (574 mg, 95%) as a syrup: $[\alpha]^{20}_D$ +30° (*c* 1, $CHCl_3$); ^1H NMR δ 5.14 (t, 1 H, *J* = 9.5 Hz, H-3), 4.98 (t, 1 H, *J* = 9.7 Hz, H-4), 4.84, 4.63 (AB q, 1 H each, *J* = 11.9 Hz, $PhCH_2$), 4.48 (d, 1 H, *J* = 7.8 Hz, H-1), 4.26, 4.10 (dd, 1 H each, *J* = 12.2, 4.8, 2.4 Hz, H-6), 3.40 (dd, 1 H, *J* = 9.5, 7.8 Hz, H-2), 1.90–2.07 (3 s, 3 H each, OAc), 1.04 (m, 2 H, CH_2Si), 0.04 (s, 9 H, $SiMe_3$). Anal. Calcd for $C_{24}H_{36}O_9Si$: C, 58.0; H, 7.3. Found: C, 57.9; H, 7.2.

2,3,4,6-Tetra-*O*-benzyl-β/α-D-glucopyranose (4): Comparative Investigation of the Glycosides 1–3. The glucoside (1–3, 0.2 mmol) was dissolved in acetic acid (2 mL), and the mixture was heated to 80 °C. Aqueous trifluoromethanesulfonic acid (2 M, 0.4 mL) was added, and the mixture was stirred at 80 °C for the required time (see Table I), cooled, and diluted with dichloromethane. The mixture was washed with saturated aqueous sodium hydrogencarbonate and water, dried (Na_2SO_4), and concentrated, and the residue (which contained ca. 5% of the corresponding 1-*O*-acetate as a byproduct; β/α ca. 1:4 according to ^1H NMR) was chromatographed (SiO_2, CH_2Cl_2/EtOAc, 10:1) to give **4** in the yields shown in Table I: β/α, ca. 1:4. Crystallization from ethyl acetate gave **4** as the α-anomer:[13,1] mp 150–152 °C.

2,3,4,6-Tetra-*O*-acetyl-β/α-D-glucopyranosyl Chloride (9): Comparative Investigation of the Starting Materials 5–8. The compound, **5**–**8** (0.2 mmol), was treated essentially as in the preparation of **9** below and for the time indicated in Table II. The reaction mixture (without evaporation of solvent) was added to a column of silica and eluted with ethyl acetate/heptane (1:1) to remove the zinc chloride. The eluate was concentrated, and the residue was analyzed by ^1H NMR spectroscopy. The results are shown in Table II. 2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl chloride[11] had the following ^1H NMR data: δ 5.30 (m, 1 H, H-1), 5.18 (3 H, H-2,3,4), 4.26, 4.17 (dd, 1 H each, *J* = 12.6, 4.8, 2.4 Hz, H-6), 3.81 (m, 1 H, H-5), 2.01–2.11 (4 s, 3 H each, OAc).

2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl Chloride (9). 2-(Trimethylsilyl)ethyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside[1] (**5**; 449 mg, 1.0 mmol) was added to a cylindrical flask containing a magnetic stirring bar. The flask was evacuated and filled with nitrogen, and chloroform (7 mL, purified by passage through alumina, activity 1) was added. The solution was stirred, and zinc chloride (ca. 0.1 mmol; fused, crushed, and protected from moisture) was added, followed by 1,1-dichloromethyl methyl ether (467 μL, 5.0 mmol). The reaction was monitored by TLC (SiO_2, EtOAc/heptane, 1:1). The starting material was consumed within 2 h, and a β/α mixture of **9** was formed. The mixture was left for 17 h in order to form the more stable α-anomer, and the volatiles were carefully removed. The residue was chromatographed (SiO_2, EtOAc/heptane, 1:1) to give crystalline **9** (359 mg, 98%). Recrystallization from ether/hexane gave **9** (334 mg, 91%) as the α-anomer: mp 72–73 °C; $[\alpha]^{20}_D$ +163° (*c* 1, $CHCl_3$) (lit.[14] mp 73 °C; $[\alpha]^{20}_D$ +167.85°); ^1H NMR δ 6.29 (d, 1 H, *J* = 3.9 Hz, H-1), 5.55 (t, 1 H, *J* = 10.0 Hz, H-3), 5.13 (t, 1 H, *J* = 9.7 Hz, H-4), 5.01 (dd, 1 H, *J* = 10.1, 4.0 Hz, H-2), 4.30 (2 H, H-5,6), 4.12 (m, 1 H, H-6).

2-(Trimethylsilyl)ethyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-galactopyranoside (14) was synthesized essentially as described for the corresponding gluco compound.[1] Compound **14**: mp 125–126 °C (ether/hexane); $[\alpha]^{20}_D$ −22° (*c* 1, $CHCl_3$); ^1H NMR δ 5.38 (3 H, H-3,4 and NH), 4.77 (d, 1 H, *J* = 8.3 Hz, H-1), 4.15 (m, 2 H, H-6), 3.90 (3 H, H-2,5 and OCH_2CH_2), 1.94–2.14 (4 s, 3 H each, OAc), 0.96 (m, 2 H, CH_2Si), 0.01 (s, 9 H, $SiMe_3$).

2,3,4,6-Tetra-*O*-acetyl-α-D-mannopyranosyl Chloride (18). 2-(Trimethylsilyl)ethyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside[1] (**10**; 44.9 mg, 0.1 mmol) was treated as described in the preparation of **9**. After 22 h, the volatiles were removed and the residue was chromatographed (SiO_2, EtOAc/heptane, 1:1) to give **18** (36 mg, 99%). Recrystallization from ether/hexane gave **18** (32 mg, 87%) as the α-anomer: mp 78–79 °C; $[\alpha]^{20}_D$ +89° (*c* 1, $CHCl_3$) (lit.[14] mp 81 °C; $[\alpha]^{20}_D$ +90.58°); ^1H NMR δ 5.99 (d, 1 H, *J* = 1.6 Hz, H-1), 5.61 (dd, 1 H, *J* = 10.1, 3.4 Hz, H-3), 5.39 (dd, 1 H, *J* = 3.4, 1.6 Hz, H-2), 5.35 (t, 1 H, *J* = 10.1 Hz, H-4).

2,3,6-Tri-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-α-D-glucopyranosyl Chloride (19). 2-(Trimethylsilyl)ethyl 2,3,6-tri-*O*-acetyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-β-D-glucopyranoside[1] (**11**; 737 mg, 1.0 mmol) was treated as described in the preparation of **9**. After 18 h, the volatiles were removed and the residue was chromatographed (SiO_2, EtOAc/heptane, 2:1) to give crystalline **19** (641 mg, 98%). Recrystallization from ethyl acetate/hexane gave **19** (609 mg, 93%) as the α-anomer: mp 122–124 °C; $[\alpha]^{20}_D$ +81° (*c* 2, $CHCl_3$) (lit.[14] mp 122 °C; $[\alpha]^{20}_D$ +83.97°); ^1H NMR δ 6.20 (d,

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1 H, J = 4.0 Hz, H-1), 5.56 (br t, 1 H, J = 9.7 Hz, H-3), 5.36 (dd, 1 H, J = 3.5, 1.1 Hz, H-4'), 5.13 (dd, 1 H, J = 10.4, 7.8 Hz, H-2'), 4.96 (dd, 1 H, J = 10.4, 3.5 Hz, H-3'), 4.93 (dd, 1 H, J = 10.0, 4.0 Hz, H-2), 4.50 (d, 1 H, J = 7.8 Hz, H-1'), 4.24 (m, 1 H, H-5), 3.88 (br dt, 1 H, J = 7.0, 1.1 Hz, H-5'), 3.84 (t, 1 H, J = 9.7 Hz, H-4).

2,3,6-Tri-*O*-benzoyl-4-*O*-[6-*O*-acetyl-2,3-di-*O*-benzoyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl)-β-D-galactopyranosyl]-α-D-glucopyranosyl Chloride (20). 2-(Trimethylsilyl)ethyl 2,3,6-tri-*O*-benzoyl-4-*O*-[6-*O*-acetyl-2,3-di-*O*-benzoyl-4-*O*-(2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl)-β-D-galactopyranosyl]-β-D-glucopyranoside[1] (**12**; 33.4 mg, 0.025 mmol) was treated as described in the preparation of **9**. After 19 h, the mixture (without evaporation of volatiles) was chromatographed (SiO_2, EtOAc/heptane, 3:2) to give **20** (30 mg, 96%): $[\alpha]^{20}_D$ +148° (c 3, $CDCl_3$); ^1H NMR δ 6.39 (d, 1 H, J = 4.0 Hz, H-1), 6.16 (t, 1 H, J = 9.6 Hz, H-3), 5.68 (dd, 1 H, J = 10.8, 7.8 Hz, H-2'), 5.48 (d, 1 H, J = 2.1 Hz, H-4''), 4.97 (d, 1 H, J = 3.7 Hz, H-1''), 4.91 (d, 1 H, J = 7.8 Hz, H-1'). Anal. Calcd for $C_{63}H_{61}ClO_{25}$: C, 60.4; H, 4.9. Found: C, 60.0; H, 4.7.

3,4,6-Tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl Chloride (21). 2-(Trimethylsilyl)ethyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranoside[1] (**13**; 107 mg, 0.2 mmol) was treated as described in the preparation of **9**. After 21 h, the volatiles were removed and the residue was chromatographed (SiO_2, EtOAc/heptane, 3:2) to give a β/α-mixture of **21** (90 mg, 99%; β/α, 88:12). Crystallization from ether/hexane gave **21** (63 mg, 69%) as the β-anomer: mp 148–151 °C; $[\alpha]^{20}_D$ +62° (c 1, $CDCl_3$) [lit.[15] mp 154 °C; $[\alpha]^{19}_D$ +27.5° (c 3.2, C_6H_6)]; ^1H NMR δ 7.70–7.90 (4 H, Ph-H), 6.19 (d, 1 H, J = 9.3 Hz, H-1), 5.79 (dd, 1 H, J = 10.4, 9.2 Hz, H-3), 5.25 (dd, 1 H, J = 10.2, 9.2 Hz, H-4), 4.52 (dd, 1 H, J = 10.4, 9.3 Hz, H-2), 4.33, 4.20 (dd, 1 H each, J = 12.5, 4.7, 2.1 Hz, H-6), 3.98 (ddd, 1 H, J = 10.2, 4.7, 2.1 Hz, H-5). Anal. Calcd for $C_{20}H_{20}ClNO_9$: C, 52.9; H, 4.4. Found: C, 53.1; H, 4.3.

2,3,4-Tri-*O*-benzyl-6-*O*-formyl-α-D-glucopyranosyl Chloride (22). 2-(Trimethylsilyl)ethyl 2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranoside[1] (1; 128 mg, 0.2 mmol) was treated as described in the preparation of **9**. After 5 h, the mixture (without evaporation of volatiles) was chromatographed (SiO_2, EtOAc/heptane, 1:2) to give **22** (52 mg, 52%): $[\alpha]^{20}_D$ +81° (c 3, $CDCl_3$); ^1H NMR δ 7.97 (d, 1 H, J = 0.8 Hz, CHO), 7.20–7.40 (15 H, Ph-H), 6.01 (d, 1 H, J = 3.7 Hz, H-1), 4.58–5.04 (6 H, $PhCH_2$), 4.36 (m, 2 H, H-6), 4.18 (m, 1 H, H-5), 4.08 (t, 1 H, J = 9.3 Hz, H-3), 3.71 (dd, 1 H, J = 9.3, 3.7 Hz, H-2), 3.56 (dd, 1 H, J = 10.2, 9.0 Hz, H-4); ^{13}C NMR δ 160.3 (1 C, CHO), 92.7 (1 C, C-1). Anal. Calcd for $C_{28}H_{29}ClO_6$: C, 67.7; H, 5.9. Found: C, 67.2; H, 5.8.

3,4,6-Tri-*O*-acetyl-2-*O*-benzyl-α-D-glucopyranosyl Chloride (23). 2-(Trimethylsilyl)ethyl 3,4,6-tri-*O*-acetyl-2-*O*-benzyl-β-D-glucopyranoside (**16**; 149 mg, 0.3 mmol) was treated as described in the preparation of **9**. After 3 h, the volatiles were removed and the residue was chromatographed (SiO_2, EtOAc/heptane, 2:3) to give a β/α-mixture of **23** (122 mg, 98%, β/α 8:92): $[\alpha]^{20}_D$ +103° (c 1, $CHCl_3$); ^1H NMR δ 7.30–7.40 (5 H, Ph-H), 6.01 (d, 1 H, J = 3.9 Hz, H-1), 5.48 (t, 1 H, J = 9.7 Hz, H-3), 5.03 (t, 1 H, J = 9.7 Hz, H-4), 4.62, 4.66 (AB q, 1 H each, J = 12.1 Hz, $PhCH_2$), 4.05–4.35 (3 H, H-5,6), 3.75 (dd, 1 H, J = 9.7, 3.9 Hz, H-2). Anal. Calcd for $C_{19}H_{23}ClO_8$: C, 55.0; H, 5.6. Found: C, 55.3; H, 5.6.

4-*O*-Acetyl-2-*O*-benzoyl-3,6-di-*O*-benzyl-α-D-galactopyranosyl Chloride (24). 2-(Trimethylsilyl)ethyl 4-*O*-acetyl-2-*O*-benzoyl-3,6-di-*O*-benzyl-β-D-galactopyranoside (**17**;[1] 182 mg, 0.3 mmol) was treated as described in the preparation of **9**. After 1.5 h, the volatiles were removed, and the residue was chromatographed (SiO_2, EtOAc/heptane, 2:7) to give **24** [136 mg, 83%; $[\alpha]^{20}_D$ +172° (c 1, $CDCl_3$)]. Crystallization from ether/hexane gave **24** (101 mg, 62%) as the α-anomer: mp 112–113 °C; $[\alpha]^{20}_D$ +173° (c 2, $CDCl_3$); ^1H NMR δ 6.45 (d, 1 H, J = 3.9 Hz, H-1), 5.76 (dd, 1 H, J = 3.3, 1.0 Hz, H-4), 5.45 (dd, 1 H, J = 10.2, 3.9 Hz, H-2), 4.45 (br t, 1 H, J = 6.3 Hz, H-5), 4.13 (dd, 1 H, J = 10.2, 3.3 Hz, H-3), 3.56 (m, 2 H, H-6). Anal. Calcd for $C_{29}H_{29}ClO_7$: C, 66.3; H, 5.6. Found: C, 66.4; H, 5.8.

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Registry No. **1**, 115969-49-8; **2**, 19488-61-0; **3**, 114967-51-0; α-**4**, 6564-72-3; β-**4**, 59531-24-7; **5**, 81342-44-1; **6**, 4860-85-9; **7**, 6586-70-5; **8**, 604-69-3; α-**9**, 4451-35-8; β-**9**, 4451-36-9; **10**, 117252-67-2; **11**, 103082-77-5; **12**, 117252-78-5; **13**, 117252-69-4; **14**, 125034-28-8; **15**, 126257-35-0; **16**, 126257-36-1; **17**, 117252-73-0; **18**, 14257-40-0; **19**, 14227-58-8; **20**, 126257-37-2; α-**21**, 63000-68-0; β-**21**, 7772-87-4; **22**, 126257-38-3; α-**23**, 55287-60-0; β-**23**, 55287-65-5; **24**, 93496-15-2; 2-(trimethylsilyl)ethyl 2-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranoside, 117253-11-9.

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