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Note

A novel method for the preparation of β-D-glycopyranosyl chlorides

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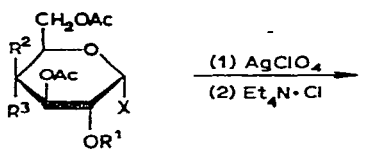
In a previous paper[1], it was reported that 3,4,6-tri-*O*-acetyl-2-chloro-2-deoxy-β-D-glucopyranosyl chloride and 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl chloride were obtained in good yields when the corresponding α-D-glucosyl chlorides were treated with silver perchlorate in anhydrous ether, followed by tetraethylammonium chloride in acetonitrile.

In order to establish that this procedure is generally applicable, the synthesis of several β-D-glycopyranosyl chlorides was carried out. The reactions **1**→**2** proceeded smoothly in all cases, usually reaching completion in ~30 min, and the β-D-glycosyl chlorides were obtained in high yields (70–95%).



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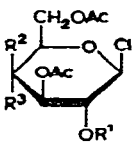

2

1a	R^1 = Ts, R^2 = H, R^3 = OAc, X = Br	2a R^1 = Ts, R^2 = H, R^3 = OAc	(93%)
1b	R^1 = SO_2CH_2COPh, R^2 = H, R^3 = OAc, X = Br	2b R^1 = SO_2CH_2COPh, R^2 = H, R^3 = OAc	(95%)
1c	R^1 = CH_2Ph, R^2 = H, R^3 = OAc, X = Cl	2c R^1 = CH_2Ph, R^2 = H, R^3 = OAc	(70%)
1d	R^1 = CH_2Ph, R^2 = OAc, R^3 = H, X = Cl	2d R^1 = CH_2Ph, R^2 = OAc, R^3 = H	(80%)

2-*O*-(ω-Acetophenonesulphonyl)-3,4,6-tri-*O*-acetyl-α-D-glucopyranosyl bromide (**1b**) was prepared by treatment of 1,3,4,6-tetra-*O*-acetyl-α-D-glucopyranose[2] with

ω-acetophenonesulphonyl chloride[3], followed by hydrogen bromide. 3,4,6-Tri-*O*-acetyl-2-*O*-benzyl-α-D-galactopyranosyl chloride (**1d**) was prepared from 1,6-anhydro-3,4-*O*-isopropylidene-β-D-galactopyranose[4] by benzylation, hydrolysis of the isopropylidene group, reacetylation, and opening of the 1,6-anhydro ring by treatment with titanium tetrachloride and acetyl chloride, successively.

EXPERIMENTAL

2-O-(ω-Acetophenonesulphonyl)-1,3,4,6-tetra-O-acetyl-α-D-glucopyranose (**3**). — To a solution of 1,3,4,6-tetra-*O*-acetyl-α-D-glucopyranose[2] (3.3 g) and pyridine (1.5 g) in dichloromethane (20 ml) was added ω-acetophenonesulphonyl chloride[3] (4.13 g). The mixture was kept at room temperature for 6 h and then poured on to ice. The mixture was extracted with dichloromethane, and the extract was washed successively with water, aqueous sodium hydrogen carbonate, water, dilute hydrochloric acid, and water, dried over sodium sulphate, and evaporated to dryness. The residue was recrystallized from methanol to give 4.91 g (97.2%) of **3**, m.p. 130–131°, $[\alpha]_D^{24}$ +86.2 ±1.3° (*c* 0.98, chloroform).

Anal. Calc. for $C_{22}H_{26}O_{13}S$: C, 49.81; H, 4.94; S, 6.04. Found: C, 49.94; H, 5.00; S, 6.30.

2-O-(ω-Acetophenonesulphonyl)-3,4,6-tri-O-acetyl-α-D-glucopyranosyl bromide (**1b**). — A solution of **3** (5.14 g) in 40% hydrogen bromide in glacial acetic acid (50 ml) was kept at room temperature for 19 h and then poured on to ice. The mixture was extracted with dichloromethane, and the extract was washed with water, aqueous sodium hydrogen carbonate, and water, dried over sodium sulphate, and evaporated to dryness. The residue was crystallized from ether to give 4.68 g (88%) of **1b**, m.p. 115–116°, $[\alpha]_D^{24}$ +142.5 ±1.8° (*c* 1.0, chloroform). N.m.r. (60 MHz, $CDCl_3$, internal tetramethylsilane) data: τ 3.32 (1-proton doublet, $J_{1,2}$ 4.0 Hz, H-1).

Anal. Calc. for $C_{20}H_{23}BrO_{11}S$: C, 43.57; H, 4.20; Br, 14.49; S, 5.82. Found: C, 43.37; H, 4.15; Br, 14.61; S, 6.00.

3,4,6-Tri-O-acetyl-2-O-benzyl-α-D-glucopyranosyl chloride (**1c**). — To a solution of 1,3,4,6-tetra-*O*-acetyl-2-*O*-benzyl-β-D-glucopyranose[5] (3 g) in chloroform (40 ml) was added titanium tetrachloride (1.55 g), and the mixture was refluxed for 30 min and then poured on to ice. The organic layer was separated, washed with water, dried over sodium sulphate, and evaporated to dryness. The residue was crystallized from ether–light petroleum, with seeding, to give 1.43 g of **1c**, m.p. 88.5–89.5°, $[\alpha]_D^{22}$ +125.3 ±1.7° (*c* 0.998, chloroform). N.m.r. data: τ 3.97 (1-proton doublet, $J_{1,2}$ 4.0 Hz, H-1).

Anal. Calc. for $C_{19}H_{23}ClO_8$: C, 55.02; H, 5.59; Cl, 8.54. Found: C, 54.80; H, 5.60; Cl, 8.61.

1,6-Anhydro-2-O-benzyl-3,4-O-isopropylidene-β-D-galactopyranose (**4**). — A mixture of 1,6-anhydro-3,4-*O*-isopropylidene-β-D-galactopyranose[4] (5.82 g), silver oxide (22 g), benzyl bromide (26.4 g), and *N*,*N*-dimethylformamide (25 ml) was stirred at room temperature overnight and then filtered to remove the inorganic salts. The filtrate was evaporated under diminished pressure and the residue was chromato-

graphed on neutral alumina (280 g). Portions eluted with light petroleum were discarded. Portions eluted with benzene–light petroleum were collected, and the product therein was recrystallized from light petroleum to give 7.002 g of **4**, m.p. 84–85.5°, $[\alpha]_D^{22}$ −81.9 ±1.4° (*c* 0.872, chloroform).

Anal. Calc. for $C_{16}H_{20}O_5$: C, 66.02; H, 6.95. Found: C, 65.74; H, 6.89.

1,6-Anhydro-2-O-benzyl-β-D-galactopyranose (**5**). — A solution of **4** (1 g) in 80% acetic acid (20 ml) was refluxed for 1 h on an oil bath and then poured on to ice. The mixture was extracted with dichloromethane, as described for **1b**, to give 609 mg of **5**, m.p. 104–105° (from ether–dichloromethane), $[\alpha]_D^{22}$ −76.2 ±2.2° (*c* 0.533, chloroform).

Anal. Calc. for $C_{13}H_{16}O_5$: C, 61.89; H, 6.39. Found: C, 62.02; H, 6.52.

3,4,6-Tri-O-acetyl-2-O-benzyl-α-D-galactopyranosyl chloride (**1d**). — **5** (1.417 g) was acetylated with acetic anhydride (10 ml) and pyridine (15 ml). To a solution of the syrupy product (1.90 g) in acetyl chloride (40 ml) was added titanium tetrachloride (400 mg) at 0°. After 40 min, the mixture was poured on to ice and extracted with dichloromethane, as described for **1b**. The resulting residue was purified by preparative t.l.c. on silica gel, using 5:1 benzene–ethyl acetate as the developer, and a zone at R_F 0.42 was collected and extracted with ether. The solvent was evaporated to give syrupy **1d** (1.05 g), $[\alpha]_D^{23}$ +110.4 ±2.3° (*c* 0.658, chloroform). N.m.r. data: τ 3.87 (1-proton doublet, $J_{1,2}$ 4 Hz, H-1).

General procedure for preparation of β-D-glycopyranosyl chlorides **2a–d**. — Preparations of the β-D-glycosyl chlorides **2a–d** were carried out in the same manner as here described for 3,4,6-tri-*O*-acetyl-2-*O*-*p*-tolylsulphonyl-β-D-glucopyranosyl chloride (**2a**). The reaction mixture obtained from 80mM ethereal silver perchlorate (7.17 ml) and **1a** (300 mg) was stirred at 0° for 10 min and cooled to −20°. 0.45M Tetraethylammonium chloride in acetonitrile (2 ml) was added to the mixture and stirring was continued for a further 20 min. The insoluble salt was filtered off and washed with ether. The combined filtrate and washings were washed with water, dried over sodium sulphate, and evaporated to dryness. The residue was crystallized from ether–light petroleum to give 257 mg of **2a**, m.p. 147–149°, $[\alpha]_D^{22}$ +22.0 ±0.6° (*c* 1.045, chloroform); lit.[6] m.p. 144–146°, $[\alpha]_D^{19}$ +18° (chloroform).

Anal. Calc. for $C_{18}H_{23}ClO_{10}S$: C, 47.65; H, 4.84; Cl, 7.40; S, 6.70. Found: C, 47.84; H, 4.99; Cl, 7.62; S, 6.76.

In this manner, the following compounds were obtained:

2b, m.p. 64–66° (recrystallized from carbon tetrachloride), $[\alpha]_D^{24}$ +11.5 ±0.5° (*c* 0.966, chloroform).

Anal. Calc. for $C_{20}H_{23}ClO_{11}S \cdot 1.5\ CCl_4$: C, 35.00; H, 3.14; Cl, 33.65; S, 4.35. Found: C, 34.77; H, 3.04; Cl, 33.87; S, 4.63.

2c, m.p. 127.5–128.5° (recrystallized from ether–light petroleum), $[\alpha]_D^{22}$ +51.4 ±0.9° (*c* 1.015, chloroform). N.m.r. data: τ 4.73 (1-proton doublet, $J_{1,2}$ 8.3 Hz, H-1).

Anal. Calc. for $C_{19}H_{23}ClO_8$: C, 55.02; H, 5.59; Cl, 8.54. Found: C, 55.32; H, 5.69; Cl, 8.26.

2d, syrup, $[\alpha]_D^{24}$ +45.8 ±1.5° (*c* 0.563, chloroform). N.m.r. data: τ 4.77 (1-proton doublet, $J_{1,2}$ 8.5 Hz, H-1).

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