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Note

Regioselective *p*-toluenesulfonylation of benzyl 4′,6′-*O*-benzylidene-β-maltoside

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Dutton and Slessor[1] stated that attempted regioselective *p*-toluenesulfonylation of benzyl 4′,6′-*O*-benzylidene-β-maltoside[2,3] (**1**), with a view to obtaining benzyl 4′,6′-*O*-benzylidene-6-*O*-*p*-tolylsulfonyl-β-maltoside (**2**) as an intermediate suitable for chemical modification of the 6-position in maltose, was unsuccessful because of the formation of two mono- and one di-*O*-*p*-tolylsulfonyl derivatives. However, we have recently shown that selective *p*-toluenesulfonylation of methyl 4′,6′-*O*-benzylidene-β-maltoside (**3**) with 2 mol. equiv. of reagent in pyridine, followed by acetylation, gives a mixture from which methyl 2,3,2′,3′-tetra-*O*-acetyl-4′,6′-*O*-benzylidene-6-*O*-*p*-tolylsulfonyl-β-maltoside (**4**) may be directly isolated crystalline in 66% yield[4]. We report here a re-investigation of the regioselective *p*-toluenesulfonylation of **1**.

Treatment of **1** with 1.7 mol. equiv. of *p*-toluenesulfonyl chloride in pyridine at −20° gave a mixture of one major and two minor products, together with a trace of unreacted **1** (t.l.c.), which could not be separated either by column chromatography or by fractional crystallization. The mixture was acetylated to afford a mixture shown by t.l.c. to contain one major product as well as one faster-migrating and two slower-moving, minor products. The major product was isolated crystalline from the mixture in 72% yield by chromatography on a dry-packed[5] column of silica gel and it was assigned the structure benzyl 2,3,2′,3′-tetra-*O*-acetyl-4′,6′-*O*-benzylidene-6-*O*-*p*-tolylsulfonyl-β-maltoside (**5**) on the basis of the following observations. The n.m.r. spectrum of **5** for a solution in chloroform-*d* showed a 14-proton multiplet at δ 7.91–7.04 for aromatic protons, a 1-proton singlet at δ 5.52 for a benzylidene methine group, a 3-proton singlet at δ 2.28 for an aryl-methyl group, and four 3-proton singlets at δ 2.03, 2.02, 1.98, and 1.96 for acetyl groups, which, combined with the results of the elemental analysis, suggested a tetra-*O*-acetyl-mono-*O*-benzylidene-mono-*O*-*p*-tolylsulfonyl derivative. Treatment of **5** with sodium iodide in *N*,*N*-dimethylformamide readily displaced the tosyloxy group by iodine to give crystalline benzyl 2,3,2′,3′-tetra-*O*-acetyl-4′,6′-*O*-benzylidene-6-deoxy-6-iodo-β-maltoside (**6**), proving that the sulfonyloxy group of **5** was located at C-6. Removal of the benzylidene

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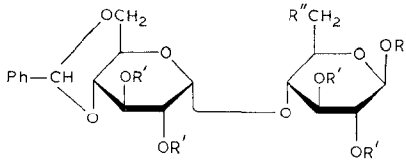
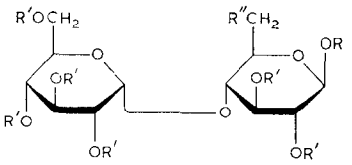


1 R = Bzl, R′ = H, R″ = OH
2 R = Bzl, R′ = H, R″ = OTs
3 R = Me, R′ = H, R″ = OH
4 R = Me, R′ = Ac, R″ = OTs
5 R = Bzl, R′ = Ac, R″ = OTs
6 R = Bzl, R′ = Ac, R″ = I



7 R = Bzl, R′ = Ac, R″ = I
8 R = Bzl, R′ = Ac, R″ = H
9 R = R′ = Ac, R″ = H

group from **6** by aqueous acetic acid, followed by acetylation, afforded crystalline benzyl 6-deoxy-6-iodo-β-maltoside hexaacetate (**7**), which was reductively dehalogenated with Raney nickel in the presence of hydrazine hydrate[4] to give, without hydrogenolysis of the aglycon, crystalline benzyl 6-deoxy-β-maltoside hexaacetate (**8**). The n.m.r. spectrum of **8** in chloroform-*d* showed a 3-proton doublet (*J* 6.0 Hz) and δ 1.43 for the methyl group at C-5. Catalytic hydrogenation of **8** over palladium-on-charcoal and subsequent acetylation furnished the known[6,7] 1,2,3,2′,3′,4′,6′-hepta-*O*-acetyl-6-deoxy-β-maltose (**9**), confirming the structure of **5**.

Thus, in contrast to the result obtained earlier by Dutton and Slessor[1], it is shown that HO-6 of **1** is preferentially esterified by *p*-toluenesulfonyl chloride under conditions comparable to those reported[4] for **3**.

EXPERIMENTAL

General methods. — Unless otherwise stated, the general experimental conditions were the same as those described previously[4]. T.l.c. was performed on Silica gel No 7731 (Merck), detection being effected by spraying the plates with 5% sulfuric acid in ethanol followed by heating. Dry-column chromatography was performed on Silica gel No 7734 (Merck) according to the procedure described earlier[5].

*Benzyl 2,3-di-*O*-acetyl-4-*O*-(2,3-di-*O*-acetyl-4,6-*O*-benzylidene-α-*D*-glucopyranosyl)-6-*O*-p-tolylsulfonyl-β-*D*-glucopyranoside* (**5**). — Compound **1** (2.85 g) was treated with *p*-toluenesulfonyl chloride (1.77 g, 1.7 mol. equiv.) in anhydrous pyridine (30 mL) as described earlier[4]. The mixture was stored for 16 h at 0°, whereupon t.l.c. (4:1, v/v, benzene–ethanol) showed the presence of a major component (R_F 0.45), together with two minor ones (R_F 0.53 and 0.51) and a trace of **1** (R_F 0.36). The mixture was treated with acetic anhydride (20 mL) and processed as described earlier[4]. T.l.c. (4:1, v/v, benzene–ethyl acetate) then indicated the presence of **5** (R_F 0.45) as the major product, in addition to three minor products (R_F 0.54, 0.35, and 0.25). The mixture was fractionated on a dry-packed column (40 × 520 mm) of silica gel with 4:1 (v/v) benzene–ethyl acetate. The appropriate fractions containing the major product were evaporated and the residue was recrystallized from ethanol–

chloroform to give **5** (3.32 g, 72%), m.p. 162–163°, $[\alpha]_D^{20}$ +3.9° (*c* 3.1, chloroform).

Anal. Calc. for $C_{41}H_{46}O_{17}S$: C, 58.43; H, 5.50; S, 3.80. Found: C, 58.58; H, 5.56; S, 3.71.

None of the minor products were isolated or identified.

Benzyl 2,3-di-O-acetyl-6-deoxy-4-O-(2,3-di-O-acetyl-4,6-O-benzylidene-α-D-glucopyranosyl)-6-iodo-β-D-glucopyranoside (**6**). — A solution of **5** (2.52 g) in dry *N,N*-dimethylformamide (30 mL) was stirred with sodium iodide (5 g) for 2 h at 100°. The mixture was processed as described earlier[4] to give **6** (2.01 g, 84%), m.p. 221–222° (ethanol–chloroform), $[\alpha]_D^{20}$ +4.5° (*c* 3.1, chloroform); n.m.r. data: δ 7.42–7.32 (m, 10 H, 2 Ph), 5.52 (s, 1 H, benzylic-H), 2.03 (s, 6 H, 2 OAc), 1.98 (s, 3 H, OAc), and 1.97 (s, 3 H, OAc).

Anal. Calc. for $C_{34}H_{39}IO_{14}$: C, 51.14; H, 4.92; I, 15.89. Found: C, 51.27; H, 5.03; I, 15.76.

Benzyl 2,3-di-O-acetyl-6-deoxy-6-iodo-4-O-(2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl)-β-D-glucopyranoside (**7**). — Treatment of **6** (1.80 g) in acetic acid (20 mL) and water (13 mL) at 100°, followed by acetylation with 1:1 (v/v) acetic anhydride–pyridine (16 mL), and conventional isolation as described earlier[4], gave **7** (1.61 g, 90%), m.p. 161–162° (ethanol), $[\alpha]_D^{20}$ +17.9° (*c* 3.1, chloroform); n.m.r. data: δ 7.33 (s, 5 H, Ph) and 2.17–1.98 (overlapping singlets, 18 H, 6 OAc).

Anal. Calc. for $C_{31}H_{39}IO_{16}$: C, 46.86; H, 4.95; I, 15.97. Found: C, 46.73; H, 5.07; I, 16.06.

Benzyl 2,3-di-O-acetyl-6-deoxy-4-O-(2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl)-β-D-glucopyranoside (**8**). — Treatment of **7** (1.36 g) in methanol (60 mL) with Raney nickel (~2 g), barium carbonate (6 g), and hydrazine hydrate (3 mL), as described earlier[4], gave **8** (0.98 g, 85%), m.p. 125–126° (ethanol), $[\alpha]_D^{20}$ +26.7° (*c* 1.1, chloroform).

Anal. Calc. for $C_{31}H_{40}O_{16}$: C, 55.69; H, 6.03. Found: C, 55.77; H, 6.10.

1,2,3-Tri-O-acetyl-6-deoxy-4-O-(2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl)-β-D-glucopyranose (**9**). — A solution of **8** (0.56 g) in acetic acid (15 mL) was hydrogenated in the presence of 10% palladium-on-carbon (0.6 g) at normal pressure for 2 days at room temperature. The mixture was filtered, and the filtrate was evaporated to give a powder that was boiled with acetic anhydride (6 mL) and sodium acetate (0.5 g) under reflux for 15 min. Conventional isolation by pouring into ice–water gave **9** (0.41 g, 79%), m.p. 165–166° (ethanol), $[\alpha]_D^{20}$ +64.5° (*c* 2.5, chloroform); lit. m.p. 160–161°, $[\alpha]_D^{24}$ +70.5° (*c* 1.10, chloroform)[6]; m.p. 165–166° (ethanol), $[\alpha]_D^{22}$ +64.3° (*c* 0.8, chloroform)[7].

REFERENCES

1 G. G. S. Dutton and K. N. Slessor, *Can. J. Chem.*, 44 (1966) 1069–1074.
2 K. Hess, H. v. Hammerstein, and W. Gramberg, *Ber.*, 70 (1937) 1134–1138.
3 A. Klemer, *Chem. Ber.*, 92 (1959) 218–226.
4 K. Takeo, *Carbohydr. Res.*, 69 (1979) 272–276.
5 L. Hough, A. K. Palmer, and A. C. Richardson, *J. Chem. Soc., Perkin Trans. 1*, (1972) 2513–2517.
6 J. Guerrera and C. E. Wells, *Carbohydr. Res.*, 27 (1973) 471–474.
7 M. Mori, M. Haga, and S. Tejima, *Chem. Pharm. Bull.*, 22 (1974) 1331–1338.