Note

Alternative syntheses of methylated sugars
Part III. Methyl furanosides of 3-*O*-methyl- and 2,3-di-*O*-methyl-D-xylose[1]

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The starting material for the synthesis of the title compounds was 1,2-*O*-isopropylidene-3-*O*-methyl-α-D-xylofuranose which was first benzylated and then methanolysed to give methyl 5-*O*-benzyl-3-*O*-methyl-α,β-D-xylofuranoside. The anomers were separated by chromatography on silica gel and, in constrast to the methyl 2-*O*-methyl-D-xylofuranosides[2], the faster-moving component was the α-D anomer. Debenzylation of the pure anomers gave methyl 3-*O*-methyl-α- and -β-D-xylofuranoside of which the latter was crystalline.

Methylation of methyl 5-*O*-benzyl-3-*O*-methyl-α,β-D-xylofuranoside, followed by chromatography on silica gel, gave methyl 5-*O*-benzyl-2,3-di-*O*-methyl-α- and -β-D-xylofuranoside; the α-anomer had the lower mobility. Debenzylation of the foregoing glycosides gave crystalline methyl 2,3-di-*O*-methyl-α- and -β-D-xylofuranoside.

EXPERIMENTAL

Melting points were determined on a Kofler hot-stage. Optical rotations were determined with a Bendix–Ericson automatic polarimeter. Thin-layer chromatography (t.l.c.) was carried out on Silica gel G with *A* hexane–ethyl acetate, 6:1; *B* benzene–ethyl acetate, 4:1; *C* chloroform–acetone, 9:4; *D* benzene–ethyl acetate, 8:1; and *E* carbon tetrachloride–acetone, 3:1. Detection was effected with 5% ethanolic sulphuric acid and heating. Column chromatography was carried out on silica gel (0.15–0.25 mm) with solvent mixtures *F* benzene–ethyl acetate, 6:1, and *G* hexane–ethyl acetate, 6:1. Solvents were removed under diminished pressure on a rotary evaporator at <40°.

5-O-Benzyl-1,2-O-isopropylidene-3-O-methyl-α-D-xylofuranose (**1**). —Chromatographically homogeneous 1,2-*O*-isopropylidene-3-*O*-methyl-α-D-xylofuranose[3] {38 g, b.p. 92–94°/0.01 mmHg, $[\alpha]_D^{24}$ $-57.6°$ (*c* 1.43, ethanol)} was dissolved in benzyl chloride (38 ml), and powdered potassium hydroxide (48 g) was added. The reaction mixture was vigorously stirred at 110–115° for ~1 h; the reaction was then complete (t.l.c., solvent *A*). The product (54 g, 99.4%, R_F 0.61), isolated in the usual manner, had b.p. 139–140°/0.01 mmHg, $[\alpha]_D^{24}$ −45.4° (c 1.31, ethanol), and was chromatographically homogeneous (Found: C, 64.80; H, 7.82; OMe, 10.70. $C_{16}H_{22}O_5$ calc.: C, 65.28; H, 7.53; OMe, 10.54%).

Methyl 5-O-benzyl-3-O-methyl-α- and β-D-xylofuranoside. — Compound **1** (54 g) was treated with boiling 0.7% methanolic hydrogen chloride (680 ml) for 1 h. T.l.c. (solvent *B*) then showed no starting material (R_F 0.78) to be present, but two products (R_F 0.39 and 0.25) were detected. The mixture was neutralised with lead carbonate, filtered, and concentrated to give a syrup (47.2 g, 95.7%), a portion (30 g) of which was eluted from a column (130 × 3 cm) of silica gel with solvent *F*.

Eluted first was methyl 5-*O*-benzyl-3-*O*-methyl-α-D-xylofuranoside (9.4 g, 31%), b.p. 129°/0.01 mmHg, $[\alpha]_D^{25}$ +96.5° (c 1.44, ethanol) (Found: C, 62.56; H, 7.48; OMe, 23.47. $C_{14}H_{20}O_5$ calc.: C, 62.67; H, 7.51; OMe, 23.13%).

Subsequently eluted was methyl 5-*O*-benzyl-3-*O*-methyl-β-D-xylofuranoside (8 g, 26%), b.p. 154–155°/0.01 mmHg, m.p. 63.5–64.5° (from ether), $[\alpha]_D^{25}$ −73.5° (ethanol) (Found: C, 62.37; H, 7.50; OMe, 23.27%).

Methyl 3-O-methyl-α-D-xylofuranoside. — Methyl 5-*O*-benzyl-3-*O*-methyl-α-D-xylofuranoside (9.4 g) was debenzylated with sodium (1.8 g) in liquid ammonia (300 ml), and the reaction mixture was worked up, as described earlier[2], to give chromatographically homogeneous (R_F 0.23, solvent *C*; *cf.* starting material R_F 0.80) title product (6 g, 96%), $[\alpha]_D^{25}$ +143.9° (c 1.59, ethanol) (Found: C, 46.3; H, 7.94; OMe, 34.97. $C_7H_{14}O_5$ calc.: C, 47.18; H, 7.91; OMe, 34.83%).

The 2,5-di-*p*-nitrobenzoate had m.p. 138–139° (from ethanol), $[\alpha]_D^{25}$ +94.5° (c 1.09, acetone) (Found C, 52.79; H, 4.22; N, 5.99. $C_{21}H_{20}N_2O_{11}$ calc.: C, 52.94; H, 4.23; N, 5.88).

Methyl 3-O-methyl-β-D-xylofuranoside. — Methyl 5-*O*-benzyl-3-*O*-methyl-β-D-xylofuranoside (8 g) was debenzylated, as described above, to give the title compound (5 g, 94%), m.p. 73–75° (from acetone), $[\alpha]_D^{25}$ −131.8° (c 0.96, ethanol) (Found: C, 46.89; H, 7.97; OMe, 34.41%).

Methyl 5-O-benzyl-2,3-di-O-methyl-α- and *-β-D-xylofuranoside.* — Methyl 5-*O*-benzyl-3-*O*-methyl-α,β-D-xylofuranoside (30 g, described above) was dissolved in tetrahydrofuran (120 ml), and powdered sodium hydroxide (18 g) was added. Methyl sulphate (22 ml) was added dropwise with stirring and the temperature was kept at 50° for 1 h. T.l.c. (solvent *D*) then showed that the reaction was complete and that two products (R_F 0.20 and 0.35, *cf.* 0.04 and 0.27 for the starting material) were formed.

The product mixture (30 g, 95%), isolated in the usual manner, was eluted from a column (130 × 3 cm) of silica gel (solvent *G*) to give methyl 5-*O*-benzyl-2,3-di-*O*-methyl-β-D-xylofuranoside (14.5 g, 46%), b.p. 119–121°/0.01 mmHg, $[\alpha]_D^{24}$ −56.8° (c 1.01, ethanol) (Found: C, 63.53; H, 7.80. $C_{15}H_{22}O_5$ calc.: C, 63.80; H, 7.85%).

Subsequently eluted was methyl 5-*O*-benzyl-2,3-di-*O*-methyl-α-D-xylofuranoside (8.8 g, 28%), b.p. 129–131°/0.01 mmHg, $[\alpha]_D^{24}$ +11.4° (c 1.16, ethanol) (Found: C, 63.52; H, 7.75%).

An intermediate, mixed fraction was also obtained.

*Methyl 2,3-di-*O*-methyl-β-*D*-xylofuranoside.* — Methyl 5-*O*-benzyl-2,3-di-O-methyl-β-D-xylofuranoside (14.5 g) was debenzylated[2] with sodium (2.5 g) in liquid ammonia (300 ml) to give the chromatographically homogeneous (R_F 0.35, solvent *E*; *cf.* 0.78 for the starting material) title product (8.4 g, 89%), b.p. 75°/0.01 mmHg, m.p. 26–28° (after trituration with cyclohexane), $[\alpha]_D^{24}$ $-101.8°$ (*c* 1.01. ethanol) (Found: C, 49.62; H, 8.41; OMe, 47.70. $C_8H_{16}O_5$ calc.: C, 49.98; H, 8.39; OMe, 48.43%).

*Methyl 2,3-di-*O*-methyl-α-*D*-xylofuranoside.* — Methyl 5-*O*-benzyl-2,3-di-*O*-methyl-α-D-xylofuranoside (8.8 g) was debenzylated, as described above, to give the title compound (4.4 g, 73%), m.p. 82–83° (from ether), $[\alpha]_D^{24}$ $+17.42°$ (*c* 1.99, ethanol) (Found: C, 49.49; H, 8.49; OMe, 48.52%).

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