Note

Alternative syntheses of methylated sugars
Part VII[1]. 4-*O*-Methyl-β-L-arabinopyranose

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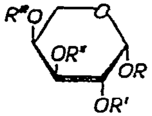
The fact that monosaccharides bearing base-labile substituents can be methylated[2] with diazomethane in the presence of a catalytic amount of boron trifluoride etherate, without migration of the labile substituents, permits a synthesis of 4-*O*-methyl-L-arabinose which is more convenient than that reported[3].

Starting with methyl 2,3-di-*O*-benzoyl-β-L-arabinopyranoside (**2**), the yield of which could be substantially improved by conducting the partial benzoylation of methyl β-L-arabinopyranoside (**1**) in a more dilute solution and at a lower temperature than originally suggested[4], methylation with diazomethane–boron trifluoride etherate afforded 86.5% of methyl 2,3-di-*O*-benzoyl-4-*O*-methyl-β-L-arabinopyranoside (**3**). Debenzoylation of **3** with methanolic sodium methoxide gave known methyl 4-*O*-methyl-β-L-arabinopyranoside[3] (**4**). 4-*O*-Methyl-L-arabinopyranose (**5**), formed on acid hydrolysis of **4**, was obtained crystalline for the first time, and the β-L configuration was assigned on the basis of n.m.r. data (see Experimental).



1 $R = Me$, $R' = R'' = R''' = H$
2 $R = Me$, $R' = R'' = Bz$, $R''' = H$
3 $R = R''' = Me$, $R' = R'' = Bz$
4 $R = R''' = Me$, $R' = R'' = H$
5 $R = R' = R'' = H$, $R''' = Me$

EXPERIMENTAL

Melting points were determined on a Kofler hot-stage. Optical rotations were measured on a Bendix–Ericsson automatic polarimeter. Thin-layer chromatography (t.l.c.) was performed on Silica gel G using *A* benzene–ethyl acetate (6:1), *B* benzene–

ethyl acetate (8:1), and *C* chloroform–methanol (6:1), and detection by charring with 5% sulphuric acid in ethanol. Solvents were removed under diminished pressure at <40°. N.m.r. spectra were measured with an 80-MHz Tesla BS 487 B spectrometer.

Methyl 2,3-di-O-benzoyl-β-L-arabinopyranoside (**2**). — Benzoyl chloride (31.1 ml) was added dropwise and with the exclusion of moisture to a stirred solution of **1**[5] (19 g) in dry pyridine (500 ml) at −20°. Stirring was then continued for 20 min, at which time t.l.c. (solvent *A*) showed the presence of one major product (R_F 0.4), indistinguishable from authentic[4] **2**. Isolation in the usual manner gave **2** (28.7 g in two crops, 66.5%), m.p. 141–142°, $[\alpha]_D^{24}$ +207.5° (*c* 1.1, chloroform); lit.[4] yield 44%, m.p. 141.5–142.5°, $[\alpha]_D^{20}$ +210°.

Methyl 2,3-di-O-benzoyl-4-O-methyl-β-L-arabinopyranoside (**3**). — Compound **2** (18 g) dissolved in dichloromethane (90 ml) at −20° was treated, with stirring, with freshly distilled boron trifluoride etherate (0.05 ml) and 1% diazomethane in dichloromethane (20 ml). The temperature of the reaction mixture was kept below −15°, and further portions (~20) of the reagents were added until t.l.c. (solvent *B*) showed complete disappearance of the starting material. One product (R_F 0.5, *cf.* 0.2 for the starting material) was detected. Polymethylene, the reaction by-product, was removed, and the filtrate was washed successively with saturated, aqueous sodium hydrogen carbonate and water. The dried (Na_2SO_4) chloroform solution was concentrated, and the residue was recrystallised twice from ethanol to afford **3** (16.2 g, 86.5%), m.p. 119–121°, $[\alpha]_D^{24}$ +201° (*c* 0.99, chloroform) (Found: C, 65.20; H, 5.75; OMe, 16.26. $C_{21}H_{22}O_7$ calc.: C, 65.27; H, 5.74; OMe, 16.06%).

4-O-Methyl-β-L-arabinopyranose (**5**). — Compound **3** (15 g) was debenzoylated with methanol containing a catalytic amount of sodium methoxide, and the product was isolated in the usual manner. Recrystallisation from dry ethyl acetate gave **4** (6.1 g, 85%), m.p. 113–114°, $[\alpha]_D^{24}$ +239° (*c* 0.93, methanol); lit.[3] m.p. 112–114° and $[\alpha]_D^{28}$ +213°.

The glycoside **4** (3.5 g) was treated with 5% hydrochloric acid (70 ml) at 95° for 15 min, at which time t.l.c. (solvent *C*) showed that hydrolysis was complete. The mixture was neutralised with lead carbonate and concentrated to dryness, and the residue was extracted with hot acetone. The extract was evaporated, and the residue was eluted from a small column of silica gel with solvent *C* to give chromatographically homogeneous **5** (2.7 g, 83%), $[\alpha]_D^{24}$ +128° (*c* 1.33, water). The syrup spontaneously crystallised on standing at room temperature for a week. Several recrystallisations from dry acetone gave the β-L form of the sugar, m.p. 107–110°, $[\alpha]_D^{26}$ +200° (initial, extrapolated), $+182.8$ (2 min)$\rightarrow +134.6°$ (60 min, equil., *c* 1.34, water); lit. for amorphous 4-*O*-methyl-L-arabinopyranose[3], $[\alpha]_D^{27}$ $+132 \pm 2°$, for the D enantiomorph[6], m.p. 109–110°, $[\alpha]_D^{20}$ -201 (initial, extrapolated)$\rightarrow -135°$ (equil.) (Found: C, 43.90; H, 7,34; OMe 18.90. $C_6H_{12}O_5$ calc.: C, 43.90; H, 7.37; OMe 18.91%).

The n.m.r. spectrum of crystalline **5** in deuteriomethyl sulphoxide[7] showed, *inter alia*, signals for HO-1 at τ 3.9 (doublet, *J* 5.5 Hz) and for H-1 at 5.12 (quartet, $J_{1,2}$ 2.9 Hz) indicative of the β-L configuration. The n.m.r. spectrum in D_2O taken

20 min after dissolution showed two doublets for H-1 at τ 4.83 ($J_{1,2}$ 3.5 Hz) and 5.5 ($J_{1,2}$ 7.6 Hz) for the β-L and α-L forms, respectively.

A sample of 4-*O*-methyl-β-L-arabinopyranose was converted into the phenylosazone, m.p. 175–177°, lit.[3] m.p. 176–177.5°.

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