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Note

Partial acetylation of β-L(and D)-arabinose and methyl β-L(and D)-arabinopyranoside, and related ^{13}C-n.m.r. studies

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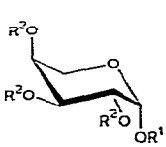
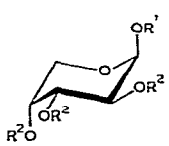
Partial acetylation of some pyranoses and pyranosides can be accomplished[1] with a good degree of selectivity, to give synthetically useful intermediates. We now report on the partial acetylation of L(and D)-arabinose and, also, the corresponding methyl β-L(and D)-glycopyranosides using acetic anhydride–sodium acetate and glacial acetic acid.

Treatment of β-L-arabinose (**1**) with 3 mol of acetic anhydride for 4 days at room temperature gave a product mixture from which 1,2,3,4-tetra-*O*-acetyl-α-L-arabinopyranose (**5**, 21%) and 1,2,4-tri-*O*-acetyl-α-L-arabinopyranose (**6**, 10.5%) were isolated crystalline after chromatography. The large $J_{1,2}$ value (7.5 Hz) in the p.m.r. spectrum of **6** indicated that H-1 was axial and was consistent with the $^4C_1$ conformation. Complete assignment was made by spin decoupling. Irradiation of the HO signal at δ 2.83 resolved the multiplet at δ 3.9 as a doublet of doublets (*J* 8, 3.5 Hz), a pattern which suggested that this signal was due to H-3 coupled with H-2 (ax) and H-4 (eq). This conclusion was confirmed by irradiation of the 2-proton multiplet (δ 5.24–5.02) which resolved the H-1 signal (δ 5.64) as a singlet, both H-5 signals as doublets (*J* 13 Hz), and the multiplet at δ 3.9 as a doublet ($J_{H,OH}$ 8 Hz). Thus, the low-field signals at δ 5.24–5.02 were assigned to H-2,4 and the structure of **6** was confirmed. Methylation of **6** with diazomethane–boron trifluoride etherate yielded chromatographically homogeneous 1,2,4-tri-*O*-acetyl-3-*O*-methyl-α-L-arabinopyranose (**7**), which was identified by its p.m.r. spectrum.

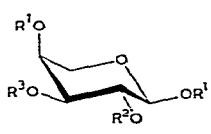
Similar esterification of β-D-arabinose (**2**) yielded crystalline α-D-arabino-



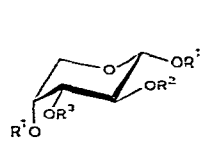
1 $R^1 = R^2 = H$
3 $R^1 = Me, R^2 = H$
10 $R^1 = Me, R^2 = Ac$



2 $R^1 = R^2 = H$
4 $R^1 = Me, R^2 = H$
11 $R^1 = Me, R^2 = Ac$



5 $R^1 = R^2 = R^3 = Ac$
6 $R^1 = R^2 = Ac, R^3 = H$
7 $R^1 = R^3 = Ac, R^2 = H$



8 $R^1 = R^2 = Ac, R^3 =$
9 $R^1 = R^2 = R^3 = Ac$

pyranose 1,2,4-triacetate (**8**, 7%), and chromatography of the mother liquor yielded tetra-*O*-acetyl-α-D-arabinopyranose (**9**, 23.5%) and more **8** (6.6%).

The reactivities of the secondary hydroxyl groups of carbohydrates towards acetylating agents are varied[2], and the selective benzoylation of some aldoses and aldosides has provided synthetically useful derivatives. Tetramolar benzoylation[3] of β-L-arabinopyranose afforded the syrupy 1,2,3-tri-*O*-benzoyl-β-L-arabinopyranose and a small proportion of the crystalline β-1,2,4-tribenzoate, and selective benzoylation of benzyl[4] and methyl β-L-arabinopyranoside[5] yielded the 2,3-dibenzoates. Sulphonation of methyl 2-*O*-benzoyl-β-L-arabinopyranoside gave the 3-tosylate[6]. The trimolar acetylation of D-arabinose described above provides a useful, alternative preparation of the triacetate **8**[7] with HO-3 unsubstituted. In partial acetylation of benzyl α-D-mannopyranoside[8] and D-mannose[1], HO-2 (axial) was, also, selectively esterified.

The signal for C-1 in the ^{13}C-n.m.r. spectra (Table I) of **5** and **6** occurred at lowest field (~92 p.p.m.). The high-field signal (~63 p.p.m.) was due to C-5, since the decoupled off-resonance spectrum showed this signal as a triplet, reflecting coupling to two protons. The signals of the other ring-carbon atoms were assigned by heteronuclear spin-decoupling experiments. The downfield shift in the signals of C-2 and C-4 of **6** relative to those of C-2 and C-4 of **5** is accompanied by only a slightly affected signal for C-3. This is unusual, in that the signal for a C-OAc carbon normally occurs at higher field than that of the corresponding hydroxyl-bearing carbon[9]. As expected, the ^{13}C-spectra of **9** and **8** were identical with those of the L enantiomers **5** and **6**, respectively.

Treatment of methyl β-L- (**3**) and β-D-arabinopyranoside (**4**) with 3 equiv. of acetic anhydride indicated low selectivity. Tetramolar acetylation of **3** gave, after chromatography, the 2,3,4-triacetate **10** (14.7%) and a syrupy diacetate fraction (27%). The p.m.r. spectrum of **10** contained a doublet for H-1 at δ 4.96 ($J_{1,2}$ 3.5 Hz) as expected, and ^{13}C-n.m.r. data (Table I) showed that MeO-1ax caused the expected upfield shift in the signal for C-5 relative to that in the spectrum of the α-L-tetraacetate **5**, but had little or no effect on the signals for C-2 and C-3 which are normally shifted upfield by an axial anomeric substituent. T.l.c. indicated that the syrupy diacetate fraction contained one component. However, the relative intensities of the

TABLE I

^{13}C-N.M.R. DATA FOR ARABINOSE DERIVATIVES[a]

Compound	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*CH_3O*	*CH_3CO*	*CH_3CO*
5(9)	92.1	68.2	69.9	67.1	63.8	—	20.6	168.9–170.0
6(8)	92.1	71.4	70.2	70.2	63.7	—	20.8	169.1–170.5
10(11)	97.6	68.4	69.2	67.2	60.3	55.5	20.8	169.8–170.3

[a]Measured in $CDCl_3$ solution. Chemical shifts in p.p.m. downfield from that of Me_4Si.

two methoxyl signals (at δ 3.38 and 3.32) in the p.m.r. spectrum of the fraction indicated a mixture of diacetates in a ratio of 2:1, and this was supported by examination of the signals for acetoxyl protons of which there were two pairs in a 2:1 ratio. The methoxyl signal of the minor diacetate and methyl 2,3,4-tri-*O*-acetyl-β-L-arabinopyranoside (**10**) had identical chemical shifts (δ 3.38), suggesting that this diacetate was substituted at C-2. The major methoxyl signal occurred at slightly higher field (δ 3.32), a shift which is consistent with a free hydroxyl group at C-2. It was also possible to identify a 1-proton doublet (J 4 Hz) at δ 4.76 and a 1-proton doublet of doublets (J 8, 4 Hz) at δ 4.1 which were assigned to H-1 and H-2, respectively, of the major diacetate. These chemical shifts were also consistent with a free hydroxyl group at C-2. On the basis of the n.m.r. data, it was concluded that the mixture contained mainly methyl 3,4-di-*O*-acetyl-β-L-arabinopyranoside together with, probably, the 2,4-diacetate by analogy with the products of selective acetylation of D- and L-arabinose. This observation is quite striking, because the electron-withdrawing effect of the anomeric centre makes HO-2 more acidic and should favour substitution at this site. For example, on partial acetylation of benzyl 4-*O*-methyl-β-D-xylopyranoside with acetic anhydride and sodium acetate[10], HO-2 is the more reactive. Tetramolar acetylation of methyl β-D-arabinopyranoside gave the crystalline 2,3,4-triacetate **11** (15%) and 24.4% of a 2:1 mixture of the 3,4- and, probably, the 2,4-diacetate, with the same p.m.r. characteristics as those of **3**.

EXPERIMENTAL

Unless otherwise stated, the general experimental conditions were the same as those described previously[1]. Column chromatography was performed on silica gel which had been pre-heated at 500° for 24 h.

Acetylation procedure. — (*a*) To a mixture of the sugar (2 g, 13.3 mmol), acetic anhydride (3.8 ml, 40 mmol), and sodium acetate (1 g) was added acetic acid (5 ml) for mobility, and the slurry was stirred at room temperature for 4 days. Water (~20 ml) was added and the mixture was extracted with chloroform (3 × 50 ml). The combined extracts were washed with saturated, aqueous sodium hydrogencarbonate and water, dried ($MgSO_4$), and concentrated, with removal of excess of acetic anhydride in an azeotrope with methanol, to give a syrupy product.

(*b*) A mixture of the glycoside (1 g, 6.1 mmol), acetic anhydride (2.3 ml, 24.4 mmol), anhydrous sodium acetate (500 mg), and acetic acid (5 ml) was stirred at room temperature for 4 days, and then worked-up as described in (*a*).

Acetylation of β-L- (**1**) *and* D-*arabinose* (**2**). — T.l.c. of the syrupy reaction product (2.15 g) revealed two major components which were separated on a column (36 × 2.5 cm) of silica gel (200-ml fractions).

Elution of the product from **1** with ether–benzene (2:98) (fractions 1–6) gave the tetra-acetate **5** (900 mg), m.p. 89–94° (from ethanol), $[\alpha]_D$ +42° (c 0.5, chloroform); lit.[11] m.p. 88–92°, $[\alpha]_D$ +43° (chloroform).

Continued elution with ether–benzene (2:98) gave fractions 7–11 (triacetate **6** contaminated with a trace of **5**).

Elution with ether–benzene (5:95) gave chromatographically homogeneous α-1,2,4-triacetate **6** (400 mg), m.p. 156–159° (from chloroform–light petroleum), $[\alpha]_D$ +89° (*c* 0.6, chloroform). P.m.r. data ($CDCl_3$): δ 5.64 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 5.24–5.02 (m, 2 H, H-2,4), 4.10 (dd, 1 H, $J_{5,5'}$ 13, $J_{5,4}$ 3.5 Hz, H-5), 3.9 (m, 1 H, H-3), 3.72 (dd, 1 H, $J_{5',5}$ 13, $J_{5',4}$ 2 Hz, H-5'), 2.83 (dd, 1 H, *J* 8 Hz, HO-3), and 2.37–2.04 (3 s, 9 H, 3 AcO).

Anal. Calc. for $C_{11}H_{16}O_8$: C, 47.82; H, 5.79. Found: C, 48.37; H, 5.54.

Fractional crystallisation from benzene of the chloroform-soluble reaction product (1.9 g) from β-D-arabinose gave the 1,2,4-triacetate **8** (270 mg), m.p. 156–158°, $[\alpha]_D$ −88° (*c* 0.6, chloroform); lit.[7] m.p. 167–169°, $[\alpha]_D$ −70°. Chromatography of the mother liquor, as described above, gave the tetra-acetate **9** (1 g), m.p. 89–90° (from ethanol). $[\alpha]_D$ −45° (*c* 0.5, chloroform) {lit.[7] m.p. 94–95°, $[\alpha]_D$ −40° (chloroform)}; and the triacetate **8** (6.6%), m.p. 154–156° (from light petroleum–chloroform).

*Acetylation of methyl β-*L*- (**3**) and -*D*-arabinopyranoside* (**4**). — T.l.c. of the chloroform-soluble material (880 mg) from **3** revealed a complex mixture which was fractionated on a column (12 × 2.5 cm) of silica gel (200-ml fractions).

Elution with ether–benzene (1:99) (fractions 1–9) gave the methyl 2,3,4-triacetate **10** (250 mg), m.p. 78° (from chloroform–light petroleum), $[\alpha]_D$ +208° (*c* 0.9, chloroform); lit.[12] m.p. 85°, $[\alpha]_D$ +182° (chloroform).

Continued elution gave fractions 10–13 (traces of triacetate and diacetates).

Fractions 14–39, eluted with ether–benzene (2:89), gave a syrup (410 mg) which contained two diacetates in the ratio of 2:1. The p.m.r. spectrum showed that the major component was the 3,4-diacetate, and indicated (but did not prove) that the minor component was the 2,4-diacetate.

The chloroform-soluble reaction product (800 mg) from **4** was fractionated, essentially as described above, to give the triacetate **11** (270 mg), m.p. 77° (from ethanol), $[\alpha]_D$ −215° (*c* 0.9, chloroform), and a 2:1 mixture (370 mg) of 3,4- and 2,4-diacetates.

*1,2,4-Tri-*O*-acetyl-3-*O*-methyl-α-*L*-arabinopyranose* (**7**). — To a solution of **6** (70 mg) in dichloromethane (5 ml) at −5° was added boron trifluoride etherate (0.01 ml), and the solution was kept at −5° during the addition of excess of diazomethane in dichloromethane. The mixture was kept for 1 h, to allow all colour to discharge. T.l.c. then showed 90% conversion into a faster-moving product. Polymethylene was removed and the filtrate was concentrated, to give **7** (65 mg), $[\alpha]_D$ +58° (*c* 0.59, chloroform). N.m.r. data ($CDCl_3$): δ 4.44 (d, 1 H, $J_{1,2}$ 6.5 Hz, H-1), 4.74 (m, 1 H, H-4), 4.88 (dd, 1 H, $J_{2,3}$ 8, $J_{2,1}$ 6.5 Hz, H-2), 5.98 (dd, 1 H, $J_{5,5'}$ 13, $J_{5,4}$ 4 Hz, H-5), 6.36 (dd, 1 H, $J_{5',5}$ 13, $J_{5',4}$ 2 Hz, H-5'), 6.5 (dd, 1 H, $J_{3,2}$ 8, $J_{3,4}$ 3.5 Hz, H-3), 6.64 (s, 3 H, OMe), and 7.88–7.96 (9 H, 3 AcO).

Anal. Calc. for $C_{12}H_{18}O_8$: C, 49.65; H, 6.20. Found: C, 49.91; H, 5.93.

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