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Note

Acetonation of L-fucose, L-rhamnose, and 2-deoxy-D-*erythro*-pentose under kinetically controlled conditions

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The procedure[1] for kinetically controlled acetonation of sugars by the action of 2-methoxypropene is here applied with the title deoxy sugars to afford, in good yield, the crystalline 3,4-isopropylidene acetal (**2**) of L-fucopyranose (**1**); in 80% yield, the crystalline 2,3-isopropylidene acetal (**5**) of L-rhamnofuranose; and, in 85% yield, the hitherto-unreported 2-deoxy-3,4-*O*-isopropylidene-D-*erythro*-pentopyranose (**8**).

The observed course of the reactions conforms with the general principles already advanced[1] for this kinetically controlled, acetonation reaction, and further documents the generality of these principles. Acetonation takes place more rapidly than tautomerization and, as these three sugars do not have a primary hydroxyl group in the tautomer favored at the outset, they react preferentially at vicinal *cis*-diol groups not involving the anomeric hydroxyl group, to give dioxolane derivatives.

The behavior of the 6-deoxyaldohexoses parallels that of the homomorphic aldopentoses, which are the respective 5-demethyl analogs. Thus, acetonation of L-fucose (**1**) with an excess of 2-methoxypropene gives the crystalline 3,4-*O*-isopropylidene-α-L-fucopyranose (**2**, α anomer), a product showing a small downward mutarotation in water. The identity of **2** was indicated by m.p. and $[\alpha]_D$ comparisons with the D enantiomer, which has been prepared[2] in 40% yield from D-fucose by thermodynamically controlled acetonation. The ^{1}H-n.m.r. spectrum of **2** in dimethyl sulfoxide-d_6 showed the presence of <10% of the β anomer. Acetylation of **2** gave the syrupy 1,2-diacetate **3**, which was mainly the α-L anomer. The n.m.r. spectrum of **3** clearly established 3,4-acetal substitution on the pyranoid ring-form of the 6-deoxyhexose; the H-1 and H-2 signals are observed at characteristic low field, as expected from acetylation of O-1 and O-2.

The starting aldose **1**, the crystalline acetal **2**, and the syrupy diacetate **3** were all principally the α-L anomers; the small proportion of β anomer present in **3**, and observed in **2** by n.m.r. spectroscopy, may have arisen from anomerization of the product during and after acetonation.

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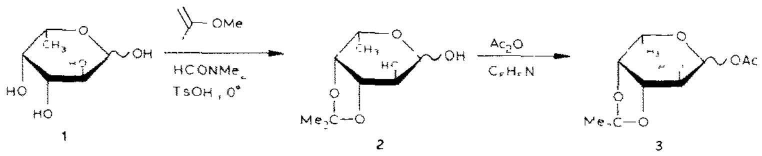

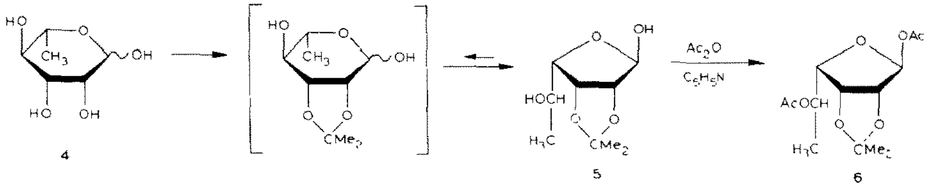

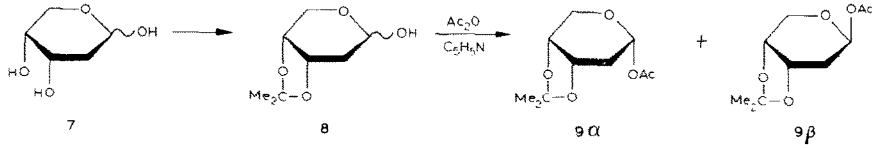

The behavior of **1** thus closely parallels that of its 5-demethyl analog, D-arabinose, which undergoes[3] comparable acetonation to give 60–70% of the 3,4-isopropylidene acetal of β-D-arabinopyranose.

Acetonation of L-rhamnose (**4**) gave an excellent yield (85%) of a crystalline monoacetal identical with the known[4–6] 2,3-*O*-isopropylidene-α-L-rhamnofuranose (**5**), further characterized as its known[6], crystalline 1,5-diacetate (**6**). It may be supposed that this reaction proceeds by a course quite comparable to that exhibited[1,7] by lyxose, its 5-demethyl homomorph; acetonation of the aldopyranose **4** at the *cis*-diol grouping (O-2, O-3) would give initially 2,3-*O*-isopropylidene-L-rhamnopyranose, which would be expected to gain stability by subsequently tautomerizing from this bicyclo[4.3.0] system to the furanose form **5**, which has the (more-stable) bicyclo[3.3.0] ring-system. The essentially exclusive formation of the α-L anomer was to be expected, as the β anomer would have the all-*cis* arrangement of substituents on the furanose ring.

The fact that O-4 of L-fucose is engaged in the acetal ring in its acetonation product **2** prevents this bicyclo[4.3.0] fused-ring system from undergoing the stabilization through tautomerization observed with the L-rhamnose derivative.

2-Deoxy-D-*erythro*-pentose exists[8] at 0° mainly as pyranose forms (**7**) although the proportion of furanose forms in water increases substantially at higher temperatures[8]. Acetonation with 2-methoxypropene gives an 85–90% yield of the pyranoid 3,4-monoacetal **8** as a syrup containing ~80% of the β and ~20% of the α anomer. The syrupy 1-acetates of these anomers (**9α** and **9β**) could be separated pure by chromatography, and be differentiated unequivocally by their specific rotations. Anomeric attribution from n.m.r. data alone would have been somewhat ambiguous. The chemical-shift and coupling data from the ^{1}H-n.m.r. spectra of **8** and **9α** and **9β** left no doubt that the compounds are 3,4-substituted pyranoses; the spectrum of **9β** was particularly well resolved.

No significant side-product was detected in the acetonation of **7** with 2-methoxypropene. In the acetonation of D-ribose, minor proportions of the 2,3-monoacetal and the 1,5:2,3-diacetal of β-D-ribofuranose were detected[5], but formation of these products may be attributed to formation of the pyranoid 2,3-acetal, tautomerization to the furanose form, and subsequent formation of the 1,5-acetal bridge. This course is not open for **7**, as there is no hydroxyl group present at C-2. The observed difference in behavior between D-ribose and **7** reinforces the hypothesis that D-ribose reacts mainly in the pyranose form, and tautomerizes after acetonation.

The foregoing products of kinetically controlled acetonation are preparatively useful. The L-fucose derivative **2** provides access to L-fucopyranosyl derivatives, especially to important glycosides and oligosaccharides linked through O-2. The classic, thermodynamically controlled acetonation product of L-fucose is 1,2:3,4-di-*O*-isopropylidene-α-L-fucopyranose (the same mode of substitution as for galactose and arabinose)[9], from which derivative no direct glycosyl coupling-reaction is available. The other two acetal products likewise afford simple access to reactants for glycosidic coupling, and C-1 chain-extension.

EXPERIMENTAL

General methods. — For these, see previous papers in this series[1,3].

*3,4-O-Isopropylidene-*L*-fucopyranose* (**2**). — A solution of L-fucose (**1**; 4.92 g, 30 mmol) in anhydrous *N*,*N*-dimethylformamide (50 mL) was stirred with a desiccant (Drierite or Sikkon, 1 g) at 0° (ice bath), and 2-methoxypropene (2.16 g, 30 mmol) was added, followed by *p*-toluenesulfonic acid (~20 mg). After 1 h at 0°, an additional stoichiometric amount of reagent (2.16 g) was added, and stirring was continued for 2 h at 0°. Sodium carbonate (~5 g) was added, and the mixture was stirred for a further 1 h at room temperature. The solids were filtered off, and the filtrate was evaporated under diminished pressure at 40° to a syrup that contained (t.l.c., ethyl acetate) one major product plus minor, fast-migrating components. Rapid chromatography of the product on a column of silica gel gave pure, crystalline **2**; yield 3.7 g (~60%); m.p. 110–111°, $[\alpha]_D^{21}$ −90 → −68° (24 h, equil.; *c* 0.2, water) (lit.[2] for the D enantiomer, m.p. 110–111°, $[\alpha]_D$ +86 → +71°); n.m.r. (Me_2SO-d_6): δ 6.16 ($J_{1,OH}$ 5.0 Hz, HO-1; a second doublet of intensity <10% of this one was observed at δ 6.45 ($J_{1,OH}$ 6.8 Hz), 4.83 (dd, $J_{1,2}$ 3.6 Hz, H-1), 4.74 (d, $J_{2,OH}$ 6.8 Hz, HO-2; all HO signals disappeared following addition of D_2O), 3.2–4.4 (m, H-2,3,4,5), 1.41 (s) and 1.30 (s, CMe_2), and 1.23 (d, $J_{5,6}$ 6.8 Hz, H-6).

The reaction requires scrupulously anhydrous conditions; failure to maintain these led to decreased yields (30–40%) of product, accompanied by unreacted starting material and additional side-products.

*1,2-Di-*O*-acetyl-3,4-*O*-isopropylidene-*L*-fucopyranose* (**3**). — The preceding product (**2**; 1 g, 5 mmol) was conventionally acetylated at 0° with acetic anhydride (2 g, 20 mmol) in pyridine (10 mL), to give a syrup showing (t.l.c.) two closely migrating spots corresponding (n.m.r.) to the anomers of **3**. Rapid column-chromatography (1:2 ethyl acetate–petroleum ether) gave an analytical sample of **3**; $[\alpha]_D^{21}$ $-103°$ (c 0.1, chloroform); n.m.r. ($CDCl_3$): δ 6.16 (d, $J_{1,2}$ 3.6 Hz, H-1α), 5.55 (d, $J_{1,2}$ 8.5 Hz, H-1β), 5.06 (dd, $J_{2,3}$ 7.2 Hz, H-2α), 5.09 (dd, $J_{2,3}$ 7.4 Hz, H-2β), 3.8–4.4 (m, H-3,4,5), 2.0–2.2 (m, OAc), and 1.1–1.5 (m, CMe_2, H-6).

*2,3-*O*-Isopropylidene-α-*L*-rhamnofuranose* (**5**). — The procedure used for L-fucose was applied with L-rhamnose (**4**; 4.22 g, 30 mmol), except that twice the stoichiometric amount of 2-methoxypropene (4.32 g, 60 mmol) was added directly at the beginning of the reaction. T.l.c. of the crude, amorphous residue (that remained after removal of the solvent) showed essentially only one spot (purity >95% by n.m.r.) corresponding to compound **5**; yield 5.2 g (~85%). Purification by rapid column-chromatography (1:1 ethyl acetate–petroleum ether) gave pure, syrupy **5** (4.9 g, 80%) that eventually crystallized by slow evaporation from the chromatography solvent; m.p. 90–91°, $[\alpha]_D^{21}$ $+10°$ (equil., 24 h; c 0.1, water) (lit.[4] m.p. 87–89°, $[\alpha]_{546}$ $+17.8°$; m.p. 90–91°, $[\alpha]_D$ $+17.5°$ (ref. 5); and[6] m.p. 92–93°); n.m.r. (Me_2SO-d_6) data in close agreement with reported[6] values, except for an additional, low-field doublet (δ 6.42, $J_{1,OH}$ 4.6 Hz) having 10–15% of the intensity of the HO-1α doublet ($J_{1,OH}$ 4.4 Hz), attributable to an additional tautomer of **5**.

*1,5-Di-*O*-acetyl-α-*L*-rhamnofuranose* (**6**). — Acetylation of **5** with acetic anhydride–pyridine as described for **2** gave compound **6**; yield 85%, m.p. 53–55°, $[\alpha]_D^{21}$ $-41°$ (c 0.2, chloroform) (lit.[6] m.p. 54–55°, $[\alpha]_D$ $-43°$); the n.m.r. data were in close accord with data previously reported[6].

*2-Deoxy-3,4-*O*-isopropylidene-*D-erythro*-pentopyranose* (**8**). — Acetonation as described for L-rhamnose was performed with 2-deoxy-D-*erythro*-pentose (**7**; 4.0 g, 30 mmol), to give a syrupy, chromatographically homogeneous product (yield 4.7 g, 90%); further purification by column chromatography (1:1 ethyl acetate–petroleum ether) afforded pure **8** (4.4 g, 85%); $[\alpha]_D^{21}$ $-46°$ (c 0.1, water); n.m.r. (Me_2SO-d_6): δ 6.41 (d) and 6.28 (d) ($J_{1,OH}$ 6.0 and 5.0 Hz, respectively, HO-1 of anomers in 4:1 ratio), 5.03 m (becoming dd after D_2O exchange, with disappearance of HO-1 signals, $J_{1,2}$ 4.4 and $J_{1,2'}$ 6.8 Hz, H-1), 4.6–3.8 (m, H-3,4), 3.70 (m, H-5,5′) 2.2–1.6 (m, H-2,2′), and 1.42 (s) and 1.30 (s) (CMe_2).

Anal. Calc. for $C_8H_{14}O_4$: C, 55.17; H, 8.05; O, 36.78. Found: C, 55.09; H, 7.98; O, 36.84.

*1-*O*-Acetyl-2-deoxy-3,4-*O*-isopropylidene-α- (**9α**) and -β- (**9β**)-*D-erythro*-pentopyranose.* — Acetylation of **8** (5.2 g, 30 mmol), as for **2**, in pyridine gave **9α,β** as a syrup, yield 5.6 g (87%), that showed (t.l.c.) two closely migrating spots. Separation of a 2-g aliquot was achieved on a column (Lobar, Merck, type A) with 1:2 ethyl acetate–petroleum ether, to give, in order of elution, pure **9α** (0.35 g), a mixture of **9α** and **9β** (0.30 g), and pure **9β** (1.1 g).

Compound **9α** was a syrup; $[\alpha]_D^{21}$ $+52°$ (c 0.1, chloroform); n.m.r. (Me_2CO-

d_6): δ 5.96 (dd, $J_{1,2}$ 4.5, $J_{1,2'}$ 6.4 Hz, H-1), 4.40 (m, H-3), 3.7–4.2 (H-4,5,5′), 1.6–2.4 (m, H-2,2′), 2.07 (s, OAc), and 1.52 (s) and 1.34 (s) (CMe_2). Compound **9β** was also a syrup; $[\alpha]_D^{21}$ −89° (*c* 0.1, chloroform); n.m.r. (Me_2CO-d_6): δ 6.20 (dd, $J_{1,2}$ 5.4, $J_{1,2'}$ 7.2 Hz, H-1), 4.63 (sx, $J_{2,3} \approx J_{2',3} = 3.6$, $J_{3,4}$ 7.2 Hz, H-3), 4.31 (dt, $J_{4,5}$ 2.0, H-4), 3.97 (q, $J_{5,5'}$ 12.8 Hz, H-5), and 3.68 (q, $J_{4,5'}$ 2.2 Hz, H-5′).

Anal. Calc. for $C_{10}H_{16}O_5$ (mixture of **9α** and **9β**): C, 55.56; H, 7.41, O, 37.04. Found: C, 55.49; H, 7.38; O, 37.12.

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