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Note

New syntheses of isopropylidene derivatives of D-gluco-, D-xylo-, and D-ribo-furanose by hydrolysis of related glycofuranosylamines

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Protection of vicinal and related glycols by the formation of isopropylidene derivatives is a well-established procedure of proven value, especially in carbohydrate chemistry. However, certain derivatives are difficult to prepare in reasonable yields. Thus, 1,2-mono-*O*- and 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose are readily prepared in excellent yield from D-glucose, acetone, and an acid catalyst[1], but the 5,6-mono-*O*-isopropylidene derivative (**1a**) is much less accessible. It is a minor component (3.1%) in the mixture of products obtained from the acid-catalysed acetonation of D-glucose with 2,2-dimethoxypropane in *N*,*N*-dimethylformamide[2]. Similarly, acetonation of D-xylose with 2,2-dimethoxypropane gives a mixture of four products[3] from which the 3,5-*O*-isopropylidene derivative (**2a**) is obtained (32%) only after extensive chromatographic purification.

In contrast to the reactions described above, acetonation of appropriate glycosylamines with acetone, 2,2-dimethoxypropane, and an excess of toluene-*p*-sulphonic acid produces a single crystalline derivative[4,5]. Thus, the crystalline compounds D-glucosylamine, D-xylosylamine, and D-ribosylamine are converted into the corresponding toluene-*p*-sulphonate salts of the isopropylidene derivatives (**1b**, **2b**, and **3b**). The availability of these compounds offers a potentially valuable route to the corresponding isopropylideneglycofuranoses **1a**, **2a**, and **3a**, and we now report the preparation in good yield of such compounds, free from isomeric or related derivatives.

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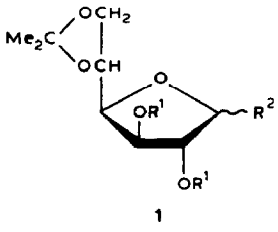

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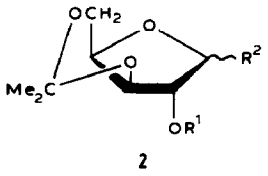

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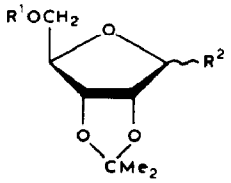

3

	R^1	R^2
a	H	OH
b	H	$NH_3^+MeC_6H_4SO_3^-$
c	H	NH_2
d	Ac	OAc

5,6-*O*-Isopropylidene-α,β-D-glucofuranosylamine (**1c**) was obtained from **1b** by treatment with sodium methoxide, and then hydrolysed at room temperature and pH 5 to afford **1a** (47%) as the major product, α,β-ratio 1:1. Similarly, hydrolysis of 3,5-*O*-isopropylidene-α,β-D-xylofuranosylamine (**2c**) produced **2a** (70%). The anomeric ratio for **2a** was 1.2:1, which must be different from the unspecified value for **2a** obtained by the method of Kiso and Hasegawa[3], as judged by the $[\alpha]_D$ values. This ratio becomes ~4:1 in the acetyl derivative (**2d**), whereas, previously, only the α anomer was obtained[3]. Hydrolysis of 2,3-*O*-isopropylidene-α,β-D-ribofuranosylamine (**3c**) gave **3a** (62%) with an α,β-ratio of 1:9, similar to that obtained by other methods[3].

The structure of the hydrolysis products was confirmed by comparison (t.l.c.) with authentic material made by the alternative, less efficient literature[2,3] methods, involving the direct acetonation of the respective sugars. The published ^{1}H-n.m.r. data for **1a**–**3a** and their acetyl derivatives were obtained at low field, and new n.m.r. data for these compounds are now reported.

EXPERIMENTAL

General methods. — Melting points are uncorrected. Mass spectra were recorded with an AEI M5902 spectrometer, and n.m.r. spectra were recorded at 270 MHz with a JEOL GX270 spectrometer for solutions in $CDCl_3$, unless otherwise stated.

5,6-O-Isopropylidene-α,β-D-glucofuranose (**1a**). — Sodium methoxide (0.28 g, 5.14 mmol) was added to a solution of 5,6-*O*-isopropylidene-D-glucofuranosylamine toluene-*p*-sulphonate (**1b**; 2.00 g, 5.16 mmol) in water (10 mL). After stirring for 10 min, the pH of the solution was adjusted to 5 with acetic acid. After 30 min, the reaction was complete (t.l.c.) and the solution was concentrated to dryness *in vacuo* (35°). The resulting foam was applied to a column (25 × 2.5 cm) of silica gel and eluted with chloroform–methanol (97:3) to yield **1a** (530 mg, 47%), as needles (from EtOAc), m.p. 117–118°, $[\alpha]_D^{22}$ +1° (*c* 4.5, methanol) {lit.[2] m.p. 117.5–118.5°, $[\alpha]_D$ +7° (water)}, α,β-ratio 1:1 in $CDCl_3$ and 3:1 in Me_2SO. ^{1}H-N.m.r. data (Me_2SO): α anomer, δ 1.25,

1.30 (2 s, 6 H, Me_2C), 3.68 (m, 1 H, H–3), 3.76 (m, 1 H, H-6a), 3.93 (m, 1 H, H-6b), 3.95 (m, 1 H, H-4), 4.0 (m, 1 H, H-2), 4.15 (m, 1 H, H-5), 5.04 (s, 1 H, HO-2), 5.14 (d, 1 H, HO-3), 5.21 (dd, 1 H, $J_{1,OH}$ 8.4, $J_{1,2}$ 3.5 Hz, H-1), 5.91 (s, 1 H, HO-1); β anomer, δ 1.25, 1.30 (2 s, 6 H, Me_2C), 3.8–4.0 (m, 5 H, H-2,3,4,6a,6b), 4.28 (m, 1 H, H-5), 4.93 (s, 1 H, $J_{1,2}$ < 1 Hz, H-1), 4.90 (s, 1 H, HO-3), 5.23 (s, 1 H, HO-2), 5.85 (s, 1 H, HO-1). Mass spectrum: *m/z* 205 (9.2%, M^+ – Me), 187 (31, M^+ – Me – H_2O), 145 (4.2, M^+ – Me – AcOH), 131 (4.6), 127 (7.4), 115 (4.5), 103 (6.3), 102 (5.3), 101 (78), 85 (11.7), 73 (18), 72 (9), 69 (7.6), 61 (17.5), 59 (60, Me_2C^+OH), 57 (17), 43 (100, Me_2C^+CO).

Compound **1a** was identical on the basis of t.l.c. evidence [R_F 0.69 in 1-butanol–acetic acid–water (6:2:2), 0.27 in chloroform–methanol (9:1), and 0.71 in ethyl acetate] to the compound synthesised by the method of Kiso and Hasegawa[2]. The triacetate **1d** was prepared[2] with an α,β-ratio of 5:1, $[\alpha]_D^{25}$ +33° (*c* 1.7, chloroform). N.m.r. data ($CDCl_3$): ^{1}H, α anomer, δ 1.3, 1.35 (2 s, 6 H, Me_2C), 2.08, 2.095, 2.10 (3 s, each 3 H, 3 Ac), 3.95 (m, 1 H, H-6a), 4.15 (m, 1 H, H-5), 4.3 (m, 1 H, H-4), 4.46 (m, 1 H, H-6b), 5.22 (dd, 1 H, $J_{1,2}$ 4.5, $J_{2,3}$ 5.1 Hz, H-2), 5.59 (dd, 1 H, $J_{3,4}$ 6.1 Hz, H-3), 6.38 (d, 1 H, H-1); β anomer, δ 1.25 (s, 6 H, Me_2C), 2.05, 2.12, 2.125 (3 s, each 3 H, 3 Ac), 5.16 (d, 1 H, $J_{2,3}$ 1.0 Hz, H-2), 5.37 (dd, 1 H, $J_{3,4}$ 4.7 Hz, H-3), 6.08 (s, 1 H, $J_{1,2}$ < 1 Hz, H-1); ^{13}C, α anomer, δ 20.8, 20.9 (2 Me), 25.4, 26.7, 29.7 (3 CH_3CO), 66.9 (C-6), 73.3, 73.7, 75.7, 78.1 (C-2,3,4,5), 93.1 (C-1), 169.4, 169.7, 170.1 (3 CO); β anomer, δ 67.2 (C-6), 99.1 (C-1). Mass spectrum: *m/z* 331 (11.7%, M^+ – Me), 169 (11.2), 127 (15), 101 (70.5), 43 (100).

3,5-O-Isopropylidene-α,β-D-xylofuranose (**2a**). — Sodium methoxide (0.3 g, 5.54 mmol) was added to a solution of 3,5-*O*-isopropylidene-D-xylofuranosylamine toluene-*p*-sulphonate (**2b**; 2.0 g, 5.54 mmol) in dichloromethane (40 mL), and the suspension was agitated for 30 min. Sodium toluene-*p*-sulphonate was removed by centrifugation and the supernatant solution was concentrated to dryness *in vacuo* (35°). The resulting foam was dissolved in water (10 mL), and the pH of the solution adjusted to 5 with acetic acid. Hydrolysis was complete in ~30 min (t.l.c.) and the solution was concentrated to dryness *in vacuo* (35°). The syrupy residue was applied to a column (25 × 2.5 cm) of silica gel and eluted with chloroform–methanol (97:3) to yield **2a** (740 mg, 70%), isolated as a syrup, $[\alpha]_D^{22}$ −5° (*c* 2.9, methanol) {lit.[3] $[\alpha]_D$ +19° (methanol)}, α,β-ratio 1.2:1 in $CDCl_3$. ^{1}H-N.m.r. data ($CDCl_3$): α anomer, δ 1.38, 1.44 (2 s, 6 H, Me_2C), 4.0–4.2 (m, 4 H, H-2,3,5a,5b), 4.28 (m, 1 H, H-4), 5.68 (d, 1 H, $J_{1,2}$ 4 Hz, H-1); β anomer, δ 1.42, 1.47 (2 s, 6 H, Me_2C), 4.0–4.2 (m, 5 H, H-2,3,4,5a,5b), 5.18 (bs, 1 H, H-1). Mass spectrum: *m/z* 175 (12.6%, M^+ – Me), 131 (10), 73 (100), 59 (86, Me_2C^+OH), 57 (22.5), 43 (98).

Compound **2a** was identical on the basis of t.l.c. evidence [R_F 0.54 in 1-butanol–acetic acid–water (6:2:2), 0.76 in chloroform–methanol (9:1), and 0.57 in ethyl acetate] to the compound synthesised by the method of Kiso and Hasegawa[3]. The diacetate **2d** was prepared[3] with an α,β-ratio of 4:1, $[\alpha]_D^{25}$ +42° (*c* 5.0, chloroform) {lit.[3] $[\alpha]_D$ +77° (chloroform)}. N.m.r. data ($CDCl_3$): ^{1}H, α anomer, δ 1.39, 1.42 (2 s, 6 H, Me_2C), 2.08, 2.10 (2 s, 6 H, 2 Ac), 3.92 (dd, 1 H, $J_{4,5a}$ 4.1, $J_{5a,5b}$ 12.9 Hz, H-5a), 4.03 (dd, 1 H, $J_{4,5b}$ 4.0 Hz, H-5b), 4.21 (m, 1 H, H-4), 4.38 (dd, 1 H, $J_{2,3}$ 1.8, $J_{3,4}$ 3.8 Hz, H-3), 5.22 (dd, 1 H, $J_{1,2}$ 4.5 Hz, H-2), 6.50 (d, 1 H, H-1); β anomer, δ 1.39, 1.42 (2 s, 6 H, Me_2C), 2.08, 2.10 (2 s, 6

H, 2 Ac), 3.9–4.4 (m, 4 H, H-3,4,5a,5b), 5.7 (d, 1 H, $J_{2,3}$ 6.9 Hz, H-2), 6.15 (s, 1 H, $J_{1,2} < 1$ Hz, H-1); ^{13}C, α anomer, δ 18.8, 19.2 (2 Me), 28.8, 29.0 (2 CH_3CO), 60.7 (C-5), 71.3 (C-3), 75.3 (C-2), 79.8 (C-4), 97.4 (C-1); β anomer, δ 18.1 (Me), 29.3 (CH_3CO), 61.2 (C-5), 73.3 (C-2), 74.2 (C-3), 76.2 (C-4), 103.9 (C-1). Mass spectrum: *m/z* 259 (11%, M^+ − Me), 173 (12), 157 (12), 139 (12.4), 128 (11), 115 (20), 97 (15), 69 (10.7), 59 (16), 43 (100).

2,3-O-Isopropylidene-α,β-D-ribofuranose[8] (**3a**). — Using the procedure described for the preparation of **2a**, 2,3-*O*-isopropylidene-D-ribofuranosylamine toluene-*p*-sulphonate (**3b**; 5.0 g, 13.85 mmol) gave **3a** (1.63 g, 62%), $[\alpha]_D^{25}$ −34° (*c* 1.5, methanol) {lit.[3] $[\alpha]_D$ −37° (acetone)}, α,β-ratio 1:9 in Me_2SO. ^{1}H-N.m.r. data ($CDCl_3$): α anomer, δ 1.41, 1.58 (2 s, 6 H, CMe_2), 3.65 (dd, 1 H, $J_{4,5a}$ 4.0, $J_{5a,5b}$ 11.7 Hz, H-5a), 3.69 (dd, 1 H, $J_{4,5b}$ 3.2 Hz, H-5b), 4.19 (m, 1 H, H-4), 4.66 (dd, 1 H, $J_{1,2}$ 4.3, $J_{2,3}$ 6.6 Hz, H-2), 4.74 (dd, 1 H, $J_{3,4}$ 2.5 Hz, H-3), 5.44 (dd, 1 H, H-1); β anomer, δ 1.33, 1.49 (2 s, 6 H, CMe_2), 3.71 (dd, 1 H, $J_{4,5a}$ 3.0, $J_{5a,5b}$ 12.0 Hz, H-5a), 3.76 (dd, 1 H, $J_{4,5b}$ 2.5 Hz, H-5b), 4.4 (m, 1 H, H-4), 4.59 (d, 1 H, $J_{2,3}$ 6.0 Hz, H-2), 4.84 (d, 1 H, H-3), 5.41 (s, 1 H, $J_{1,2} < 1$ Hz, H-1). Mass spectrum: *m/z* 175 (21%, M^+ − Me), 159 (10, M^+ − CH_2OH), 86 (13), 85 (12), 73 (19), 69 (12), 68 (28), 59 (100, Me_2C^+OH), 57 (27), 43 (83).

Compound **3a** was identical on the basis of t.l.c. evidence (R_f 0.66 in 1-butanol–acetic acid–water (6:2:2), 0.35 in chloroform–methanol (9:1), and 0.43 in ethyl acetate) to the compound synthesised by the method of Kiso and Hasegawa[3]. The diacetate **3d** was prepared[3] with an α,β-ratio of 1:4; $[\alpha]_D^{22}$ −30° (*c* 1.9, chloroform). N.m.r. data ($CDCl_3$): ^{1}H, α anomer, δ 1.38, 1.56 (2 s, 6 H, Me_2C), 2.06 (s, 6 H, 2 Ac), 4.15 (m, 1 H, H-4), 4.19 (dd, 1 H, $J_{4,5}$, $J_{5a,5b}$ 12.0 Hz, H-5a), 4.28 (dd, 1 H, $J_{4,5b}$ 3.7 Hz, H-5b), 4.63 (dd, 1 H, $J_{1,2}$ 4.5, $J_{2,3}$ 7.0 Hz, H-2), 4.64 (dd, 1 H, $J_{3,4}$ 2.8 Hz, H-3), 6.19 (d, 1 H, $J_{1,2}$ 4.5 Hz, H-1); β anomer, δ 1.34, 1.50 (2 s, 6 H, Me_2C), 2.10 (s, 6 H, 2 Ac), 4.11 (m, 1 H, H-5a), 4.15 (m, 1 H, H-5b), 4.47 (m, 1 H, H-4), 4.73 (m, 2 H, H-2,3), 6.24 (s, 1 H, H-1); ^{13}C, α anomer, δ 21.2, 21.2 (2 Me), 25.5, 26.0 (2 CH_3CO), 64.0 (C-5), 80.3 (C-2), 80.4 (C-3), 8.09 (C-4), 96.5 (C-1), 113.2 (CMe_2), 169.3, 170.5 (2 CO); β anomer, δ 20.8 (Me), 25.1, 26.4 (2 CH_3CO), 64.1 (C-5), 81.6 (C-3), 85.1, 85.4 (C-2,4), 113.3 (CMe_2), 169.5 (CO). Mass spectrum: *m/z* 259 (16%, M^+ − Me), 215 (8, M^+ − Ac), 173 (9.7), 139 (18.2), 97 (16.2), 85 (13.7), 69 (10.9), 59 (14.7), 43 (100).

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REFERENCES

1 M. R. Islam and M. Mosihuzzaman, *Dacca University Studies*, 24 (1976) 15–20.
2 M. Kiso and A. Hasegawa, *Carbohydr. Res.*, 52 (1976) 87–94.
3 M. Kiso and A. Hasegawa, *Carbohydr. Res.*, 52 (1976) 95–101.
4 N. J. Cusack, B. J. Hildick, D. H. Robinson, P. W. Rugg, and G. Shaw, *J. Chem. Soc., Perkin Trans. 1*, (1973) 1720–1731.
5 N. J. Cusack, D. H. Robinson, P. W. Rugg, G. Shaw, and R. Lofthouse, *J. Chem. Soc., Perkin Trans. 1*, (1974) 73–81.