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Preliminary communication

Synthesis of 2,3,6-trideoxy-3-*C*-methyl-4-*O*-methyl-3-nitro-L-*xylo*-hexopyranose (L-rubranitrose)

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For rubranitrose, a component of the antibiotic rubradirin[1], the structure was reported to be 2,3,6-trideoxy-3-*C*-methyl-4-*O*-methyl-3-nitro-L-*xylo*-hexopyranose (**1**) from X-ray analysis, and the c.d. spectrum[2], in which a positive Cotton effect was observed, opposite in sign to that of L-evernitrose[3] (**2**). Recently, from comparison of the c.d. spectrum and rotational value with those of D-kijanose (**3**), whose configuration was assigned by Hudson's Rules of Isorotation, Mallams *et al.*[4] pointed out that **1** should have the D configuration. This communication describes the synthesis of **1**, and proof of the correctness of the deduction of Mallams and co-workers[4].

In a similar way to the synthesis[5] of **2**, compound **1** was synthesized *via* the cyanomesylation of the corresponding hexopyranosid-3-ulose (**10**). For the preparation of **10**, methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*ribo*-hexopyranoside[6] was treated with *N*-bromosuccinimide and barium carbonate in carbon tetrachloride, to give methyl 4-*O*-benzoyl-6-bromo-2,6-dideoxy-α-D-*ribo*-hexopyranoside {**4**; a syrup, $[\alpha]_D^{22}$ +93° (*c* 1.0)} in 95% yield. Concurrent migration of the benzoyl group of **4** and 4-*O*-methylation were accomplished by treatment with silver oxide and methyl iodide in *N*,*N*-dimethylformamide, to yield **5** {a syrup. $[\alpha]_D^{22}$ +70° (*c* 1.9); n.m.r. data ($CDCl_3$): δ 8.16–7.90 and 7.60–7.32 (m, 5 H, OBz), 5.67 (q, 1 H, $J_{3,4}$ 4.5 Hz, H-3), 4.78 (bd, 1 H, $J_{1,2a}$ 4.5 Hz, H-1), 4.44 (dd, 1 H, $J_{4,5}$ 9.0 Hz, H-4), 4.27 (oct, 1 H, $J_{5,6}$ 4.5, $J_{5,6'}$ 1.5 Hz, H-5), 3.76–3.60 (m, 2 H, H-6,6'), 3.43 (s, 3 H, OMe-1), 3.39 (s, 3 H, OMe-4), 2.26 (dd, 1 H, $J_{2e,3}$ 4.5 Hz, H-2*e*), and 1.98 (dt, 1 H, $J_{2a,2e}$ 15.5, $J_{2a,3}$ 4.5 Hz, H-2*a*)} in 91% yield.

Treatment of **5** in pyridine with silver fluoride in the dark gave a 3:2 mixture of the desired methyl 3-*O*-benzoyl-2,6-dideoxy-4-*O*-methyl-α-D-*erythro*-hex-5-enopyranoside (**7**) and the 6-fluoro derivative (**6**). Because this mixture could not be separated, **7** was isolated after conversion into methyl 2,6-dideoxy-4-*O*-methyl-β-L-*ribo*-hexopyranoside (**9**) {49% from **5**; m.p. 143–144°, $[\alpha]_D^{22}$ +34° (*c* 1.0); n.m.r.: δ 4.28 (dd, 1 H, $J_{1,2e}$ 2.5, $J_{1,2a}$ 9.6 Hz, H-1), 3.9–3.2 (m, 2 H, H-3,5), 3.64 (s, 3 H, OMe-4), 3.51 (s, 3 H, OMe-1) 3.16 (bd, 1 H, $J_{3,4}$ 4.0 Hz, H-4), 2.22 (bs, 1 H, OH), 1.98 (oct, 1 H, $J_{2e,3}$ 5.2 Hz, H-2*e*), 1.60 (dt, $J_{2a,2e} = J_{2a,3}$ = 12 Hz, H-2*a*), and 1.28 (d, 3 H, $J_{5,6}$

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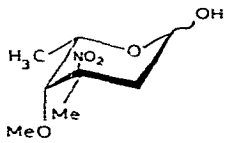

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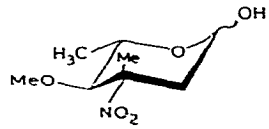

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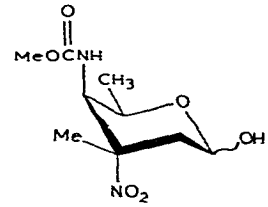

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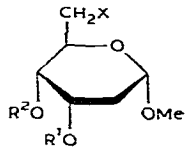
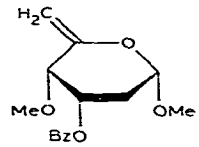
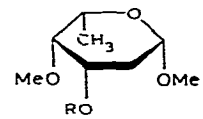


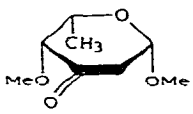
4 R^1 = H, R^2 = Bz, X = Br
5 R^1 = Bz, R^2 = Me, X = Br
6 R^1 = Bz, R^2 = Me, X = F
Bz = PhCO



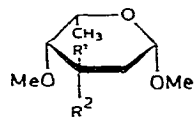
7



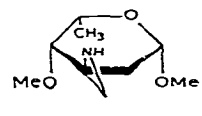
8 R = Bz
9 R = H



10



11 R^1 = CN, R^2 = OMs
12 R^1 = NH_2, R^2 = Me
13 R^1 = NO_2, R^2 = Me
Ms = SO_2Me



14

6.5 Hz, H-6)} by successive catalytic hydrogenation and *O*-debenzoylation. Oxidation of **9** in dichloromethane with pyridinium chlorochromate gave the corresponding hexopyranosid-3-ulose (**10**) {m.p. 39–40°, $[\alpha]_D^{22}$ +92° (*c* 1.05); n.m.r.: δ 4.55 (dd, 1 H, $J_{1,2a}$ 8.5, $J_{1,2e}$ 3.0 Hz, H-1), 3.74 (dq, 1 H, $J_{4,5}$ 3.0, $J_{5,6}$ 6.5 Hz, H-5), 3.56 (s, 3 H, OMe-4), 3.41 (s, 3 H, OMe-1), 3.37 (d, 1 H, H-4), 2.83 (dd, 1 H, $J_{2a,2e}$ 13.0 Hz, H-2*a*), 2.57 (dd, 1 H, H-2*e*), and 1.40 (d, 3 H, H-6)} in 76% yield.

One-flask cyanomesylation of **10** by treatment overnight with hydrogen cyanide in pyridine, and then with methanesulfonyl chloride for two days at room temperature, gave exclusively 3-*C*-cyano-2,6-dideoxy-4-*O*-methyl-3-*O*-(methylsulfonyl)-β-L-*ribo*-hexopyranoside (**11**) {m.p. 94.5°; $[\alpha]_D^{22}$ –2.3° (*c* 1.0); n.m.r.: δ 4.62 (dd, 1 H, $J_{1,2a}$ 8.5, $J_{1,2e}$ 3.0 Hz, H-1), 3.91 (bq, 1 H, $J_{5,6}$ 6.3 Hz, H-5), 3.75 (s, 3 H, $MeSO_2$), ~3.77 (bs, 1 H, H-4), 3.59 (s, 3 H, OMe-4), 3.32 (s, 3 H, OMe-1), 2.45 (dd, 1 H, J_{gem} 13.0 Hz, H-2*e*), 2.33 (dd, 1 H, H-2*a*), and 1.40 (d, 3 H, H-6)} in 65% yield. Treatment of **11** in

ether with lithium aluminum hydride gave the corresponding spiro aziridine (**14**) {a syrup; n.m.r.: δ 4.60 (dd, 1 H, $J_{1,2a}$ 9.5, $J_{1,2e}$ 2.5 Hz, H-1), 3.89 (dq, $J_{4,5}$ 2.0, $J_{5,6}$ 6.5 Hz, H-5), 3.54 (d, 1 H. H-4), 3.52 (s, 3 H, OMe-4), 3.46 (s, 3 H, OMe-1), 2.45–2.15 (m, 2 H, J_{gem} 11.0 Hz, H-2*a*,2*e*), 1.86 (d, 2 H, $J_{CH_2,NH}$ 8.0 Hz, NCH_2), 1.60 (bs, 1 H, NH), and 1.31 (d, 3 H, H-6)} in 65% yield, which showed no significant, optical rotational value.

Hydrogenolysis of **14** in the presence of Raney nickel gave, quantitatively, the corresponding branched amino sugar (**12**) as a syrup; this was oxidized with *m*-chloroperoxybenzoic acid, to give methyl 2,3,6-trideoxy-3-*C*-methyl-4-*O*-methyl-3-nitro-β-L-*xylo*-hexopyranoside (**13**) {a syrup, $[\alpha]_D^{22}$ −16° (*c* 0.83); n.m.r.: δ 4.46 (dd, 1 H, $J_{1,2a}$ 9.5, $J_{1,2e}$ 2.2 Hz, H-1), 3.8–3.5 (m, 2 H, H-4,5), 3.68 (s, 3 H, OMe-4), 3.54 (s, 3 H, OMe-1), 2.0–1.6 (m, 2 H, H-2*a*,2*e*), 1.68 (s, 3 H, CMe), and 1.36 (d, 3 H, H-6)} in 56% yield from **10**. Hydrolysis of **13** with 0.05M sulfuric acid in aqueous 1,4-dioxane gave a mixture of the anomers of **1** {m.p. 147–148°, $[\alpha]_D^{22}$ −76° (*c* 0.48, ethanol); lit.[2] β-**1**, m.p. 150–153°, $[\alpha]_D$ +86° (*c* 1, ethanol)} in 98% yield. The ^{1}H-n.m.r. spectrum of the synthetic **1** showed the presence of the anomers, with patterns closely similar to those reported, and the ^{13}C-n.m.r. spectrum indicated the presence of equatorially oriented *C*-methyl groups (25.1 and 25.9 ppm). Both the opposite sign of the optical rotational value and of the Cotton effect (the molar ellipticity at 285 nm of **1** in methanol was −1580; lit.[2] for the β-acetate of the natural compound, +2500) between synthetic **1** and the natural product proved that the latter has the D configuration, as was deduced by Mallams *et al.*[4].

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