Note

A convenient synthesis of 2,6-diamino-2,6-dideoxy-D-gulose

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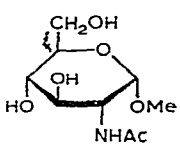
(Received May 22nd, 1972; accepted for publication, June 1st, 1972)

The synthesis of 2,6-diamino-2,6-dideoxyhexoses has assumed importance since the discovery of 2,6-diamino-2,6-dideoxy-D-glucose[1] and 2,6-diamino-2,6-dideoxy-L-idose[1,2] as components of the neomycin antibiotics[3]. Representatives of this series having the D-*allo*[4], D-*altro*[5], D-*galacto*[6], D-*gluco*[7], D-*gulo*[8], L-*ido*[9], and D-*manno* configurations[10] have been reported to date.

The synthesis of 2,6-diamino-2,6-dideoxy-D-gulose (**6**) presently described originated from an attempt to prepare derivatives of the antibiotic sugar purpurosamine C (2,6-diamino-2,3,4,6-tetradeoxy-D-*erythro*-hexose)[11] by way of the unsaturated sugar **7**, which we hoped to obtain from methyl 2,6-diacetamido-2,6-dideoxy-3,4-di-*O*-methanesulphonyl-α-D-glucopyranoside (**4**) by using the Tipson–Cohen procedure[12]. The latter compound was readily obtained by conversion of methyl 2-acetamido-2-deoxy-α-D-glucopyranoside[13] (**1**) into the trimethanesulphonate **2**, which was further transformed into the 6-azide **3** by selective replacement of the primary sulphonyloxy group with sodium azide in methyl sulphoxide. Catalytic hydrogenation of the azide **3** in methanol in the presence of acetic anhydride afforded methyl 2,6-diacetamido-2,6-dideoxy-3,4-di-*O*-methanesulphonyl-α-D-glucopyranoside (**4**). We have found this route to compound **4** to be preferable to one involving an azide-exchange on methyl 2-acetamido-2-deoxy-6-*O*-toluene-*p*-sulphonyl-α-D-gluco-



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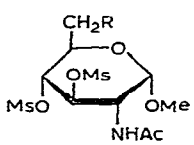
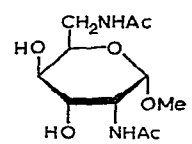


2 R = OMs
3 R = N3
4 R = NHAc



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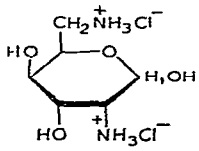

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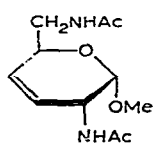

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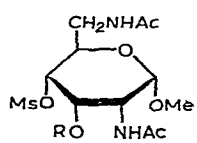

8 R=H
9 R=Ms

pyranoside[7a], since the latter procedure necessitated chromatographic purification of the sulphonate.

Attempts to convert the dimethanesulphonate **4** into the unsaturated sugar **7** by the Tipson–Cohen procedure[12] (sodium iodide–*N*,*N*-dimethylformamide–zinc dust) were unsuccessful and no characterisable products could be obtained. Efforts were then directed towards the synthesis of methyl 2,6-diacetamido-2,6-dideoxy-3,4-di-*O*-methanesulphonyl-α-D-allopyranoside (**9**), which it was hoped might be more readily converted into **7**. It seemed that this objective might be achieved from **4** by preferential solvolysis of the 3-methanesulphonyloxy group involving participation by the neighbouring 2-acetamido group. The resulting alcohol **8** could then be sulphonylated to give **9**. However, solvolysis of the dimethanesulphonate **4** in boiling 95% 2-methoxyethanol gave almost exclusively a product that was devoid of sulphonate groups. The product was assigned the structure methyl 2,6-diacetamido-2,6-dideoxy-α-D-gulopyranoside (**5**) on the assumption that the acetamido groups at C-2 and C-6 had participated in the solvolysis of the sulphonate groups at C-3 and C-4, respectively. Such participations would, of course, lead to inversion of configuration at the relevant centres[14]. This assignment was substantiated when hydrolysis of **5** with dilute hydrochloric acid afforded 2,6-diamino-2,6-dideoxy-D-gulose (**6**) (isolated as the crystalline dihydrochloride), whose mutarotation in water closely resembled that previously reported[8] for this compound. The above route to the diamino sugar **6** is much more direct than that hitherto described[8].

Finally, it is noteworthy that successful syntheses of purpurosamine C[15] and its C-2 epimer (*epi*-purpurosamine C)[16] have been reported recently; in the former synthesis, the Tipson–Cohen procedure was applied successfully to a 2,6-di(methoxycarbonylamino) analogue of the dimethanesulphonate **4**.

EXPERIMENTAL

Thin-layer chromatography (t.l.c.) was performed on Kieselgel G, and detection was effected with vanillin–sulphuric acid[17]. N.m.r. spectra were routinely measured with a Perkin–Elmer R-10 spectrometer and were compatible with the assigned structures; infrared spectra were recorded for Nujol mulls with a Perkin–Elmer Infracord spectrometer. Light petroleum refers to the fraction having b.p. 40–60°.

*Methyl 2-acetamido-2-deoxy-3,4,6-tri-*O*-methanesulphonyl-α-*D*-glucopyranoside* (**2**). — A cooled (0°) solution of methyl 2-acetamido-2-deoxy-α-D-glucopyranoside[13] (5 g) in pyridine (20 ml) was treated with a cold solution of methanesulphonyl chloride (*ca.* 5 mol.) in pyridine (20 ml) for 1 h at 0° and afterwards for 3 h at room temperature; t.l.c. (acetone–light petroleum, 2:1) then indicated that the starting material had reacted completely. Work up in the usual manner gave the trimethanesulphonate **2** (5.12 g), m.p. 175–176° (from ethanol), $[\alpha]_D$ +77° (*c* 1, methyl sulphoxide) (Found: C, 30.7; H, 5.0; N, 3.2; S, 20.8. $C_{12}H_{23}NO_{12}S_3$ calc.: C, 30.7; H, 4.9; N, 3.0; S, 20.5%).

*Methyl 2-acetamido-6-azido-2,6-dideoxy-3,4-di-*O*-methanesulphonyl-α-*D*-gluco-*

pyranoside (**3**). — A solution of the trimethanesulphonate **2** (3.5 g) in methyl sulphoxide (30 ml) containing sodium azide (0.7 g) was heated at 100° for 90 min; t.l.c. (acetone–light petroleum, 2:1) then showed the formation of principally one product. The cooled reaction mixture was partitioned between chloroform and water, and the dried ($MgSO_4$) organic layer was concentrated under reduced pressure. The residual syrup was crystallised from chloroform–light petroleum to give the monoazide **3** (2.35 g), m.p. 159–160°, $[\alpha]_D$ +89° (*c* 0.95, chloroform), ν_{max} 2100 cm^{-1} (N_3) (Found: C, 32.0; H, 4.9; N, 13.8; S, 15.4. $C_{11}H_{20}N_4O_9S_2$ calc.: C, 31.7; H, 4.8; N, 13.5; S, 15.4%).

*Methyl 2,6-diacetamido-2,6-dideoxy-3,4-di-*O*-methanesulphonyl-α-*D*-glucopyranoside* (**4**). — A solution of the azide **3** (2 g) in dry methanol (30 ml) containing acetic anhydride (0.5 ml) and 5% palladised carbon (0.2 g) was shaken with a slight overpressure of hydrogen for 3 h at room temperature; t.l.c. (acetone–light petroleum, 1:1) then showed that the reaction was completed. The catalyst was filtered off, the solvents were removed, and the resulting solid was recrystallised from ethanol to give the diamide **4** (1.9 g), m.p. 179–180°, $[\alpha]_D$ +97° (*c* 0.6, methanol), ν_{max} 1650 and 1540 cm^{-1} (NHAc) (Found: C, 36.2; H, 5.5; S, 14.55. $C_{13}H_{24}N_2O_{10}S_2$ calc.: C, 35.8; H, 5.5; S, 14.7%).

The diamide **4** had mixed m.p. 178.5–180° with the product obtained by methanesulphonylation of methyl 2,6-diacetamido-2,6-dideoxy-α-D-glucopyranoside, prepared less conveniently by way of an azide-exchange on methyl 2-acetamido-2-deoxy-6-*O*-toluene-*p*-sulphonyl-α-D-glucopyranoside[7a].

Methyl 2,6-diacetamido-2,6-dideoxy-α-D-gulopyranoside (**5**). — A solution of the diacetamido derivative **4** (1 g) in 95% 2-methoxyethanol (10 ml) containing sodium acetate (0.8 g) was gently boiled under reflux for 24 h, whereupon t.l.c. (acetone–light petroleum–methanol, 2:2:1) revealed that the starting material had reacted completely. Solids were filtered off, the filtrate was concentrated, and the residue was extracted with chloroform (5 × 25 ml). Chromatography of the concentrated extract on silica gel (elution with acetone–light petroleum–methanol, 2:2:1) afforded compound **5** (0.48 g), m.p. 197–198° (from ethanol), $[\alpha]_D$ +116° (*c* 1, pyridine), ν_{max} 3400 (OH), and 1650 and 1530 cm^{-1} (NHAc) (Found: C, 47.5; H, 7.2; N, 10.0. $C_{11}H_{20}N_2O_6$ calc.: C, 47.8; H, 7.2; N, 10.1%).

*2,6-Diamino-2,6-dideoxy-*D*-gulose dihydrochloride* (**6**). — A solution of the glycoside **5** (0.1 g) in 2M hydrochloric acid (5 ml) was heated on a boiling water-bath for 2 h, whereafter the hydrolysate was treated with a little charcoal and cooled to room temperature. Solids were filtered off and the filtrate was concentrated under reduced pressure with repeated additions of water. The resulting syrup was dissolved in a little hot methanol, and the solution was filtered and cooled to give the dihydrochloride **6** (42 mg), m.p. 160–162° (dec.), $[\alpha]_D$ +33° (5 min)→−4° (equil., *c* 0.75, water) (Found: C, 28.9; H, 6.2; N, 10.9. $C_6H_{14}N_2O_4 \cdot 2HCl$ calc.: C, 28.7; H, 6.4; N, 11.2%). Gross *et al.*[8] recorded $[\alpha]_D$ +35° (10 min)→−10° (36 h, *c* 2.7, water) for their preparation, but no melting point was given.

ACKNOWLEDGMENT

One of us (I.D.) is indebted to the University of Aleppo for financial support through a grant administered by the Ford Foundation.

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