Preliminary communication

Synthesis of 2-deoxy-2-methylamino-D-gulose, a component of streptothricin-like antibiotics

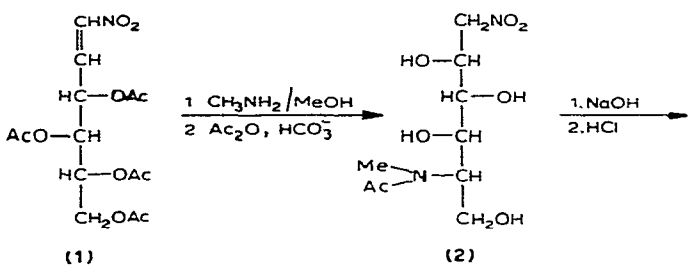
The present communication describes the synthesis of 2-deoxy-2-methylamino-D-gulose, reported to be a component of the streptothricin-like antibiotic, LL-AC 541[1], and possibly of the similar antibiotic BD-12 isolated in our laboratory[2].

Addition of methylamine to tetra-*O*-acetyl-1-nitro-1-hexene-D-*xylo*-3,4,5,6-tetrol (1) synthesized by the method of Sowden and Fischer[3] from D-xylose and nitromethane gave a syrupy mixture presumably consisting of 5,6-dideoxy-5-methylacetamido-6-nitro-L-glucitol (2) in preponderant proportion and of the corresponding D-iditol derivative[4]. On treatment with conc. hydrochloric acid (Nef reaction)[5], the sodium salt of the above mixture gave a crude 2-deoxy-2-methylaminohexose, which was chromatographed on Dowex-50 (H^+) with 0.2M hydrochloric acid as developing agent. The main fractions showing a positive Elson–Morgan test and containing a single component, as shown by paper chromatography, were evaporated to give a 2-deoxy-2-methylaminohexose hydrochloride (yield 25%). This was repeatedly recrystallized from methanol–ethanol to give pure 2-deoxy-2-methylamino-D-gulose hydrochloride (3) as white needles, m.p. 181° (dec.); $[\alpha]_D^{26}$ +38.5° (after 5 min) → -28° (after 20 h) (*c* 1, water); R_F 0.72 on Whatman No. 1 paper in ethyl acetate–acetic acid–pyridine–water (5:5:1:3)[6].

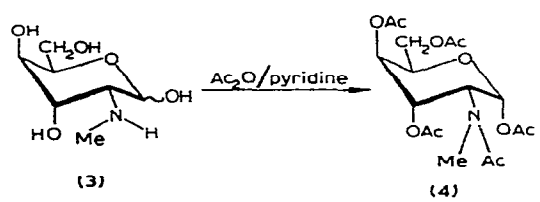
Anal. Calc. for $C_7H_{15}NO_5 \cdot HCl$: C, 36.61; H, 7.02; N, 6.10. Found: C, 36.72; H, 7.13; N, 6.49.

The pentaacetate (4) was obtained from 3 with pyridine–acetic anhydride; m.p. 175–176°, $[\alpha]_D^{21}$ +72° (*c* 1, chloroform).

Anal. Calc. for $C_{17}H_{25}NO_{10}$: C, 50.62; H, 6.25; N, 3.47. Found: C, 50.64; H, 6.41; N, 3.15.



(1) (2)



(3) (4)

The structure of 3 was established by positive Tollens and Elson–Morgan tests and by a negative ninhydrin test indicating the *N*-substitution of the 2-amino-2-deoxy-aldose.

The n.m.r. spectra were recorded with a JEOL-JNM-C-60 spectrometer at 60 MHz and are expressed as p.p.m. from an external tetramethylsilane reference (δ-scale) for deuterium oxide solution or from an internal tetramethylsilane reference for deuterated chloroform solution. The n.m.r. signal of 3 at δ 2.98 (3 H, singlet) in deuterium oxide solution confirmed the presence of the *N*-methyl group. The configuration of C-3, C-4 and C-5 is unequivocal, because 3 was derived from D-xylose. In a freshly prepared deuterium oxide solution of 3 at 26°, a pair of doublets corresponding to a total of one proton (intensity ratio, 3:2) at δ 5.58 (J 3.0 Hz) and δ 5.22 (J 8.0 Hz) and a triplet and a quartet corresponding to a total of one proton (intensity ratio 3.3:2) at δ 3.63 (J 3.0 and 3.0 Hz) and δ 3.30 (J 3.0 and 8.0 Hz) were observed. After 4 h, both intensity ratios had changed to 1:3 owing to mutarotation.

On the basis of Lemieux[1] and Stevens' work[7], the n.m.r. signals of 3 were assigned as follows: doublet at δ 5.58 to H-1-α with $J^{\alpha}_{1,2}$ 3.0 Hz; doublet at δ 5.22 to H-1-β with $J^{\beta}_{1,2}$ 8.0 Hz; triplet at δ 3.63 to H-2-α with $J^{\alpha}_{1,2} = J^{\alpha}_{2,3}$ 3.0 Hz; quartet at δ 3.30 to H-2-β with $J^{\beta}_{1,2}$ 8.0 and $J^{\beta}_{2,3}$ 3.0 Hz. These assignments were confirmed by spin-decoupling experiments.

The n.m.r. signal at δ 6.13 (doublet, H-1, J 3.0 Hz) of 4 indicated that it was the α-pentaacetate. Signals at δ 5.50 (1 H, triplet, J 3.0 and 3.0 Hz) and 5.25 (1 H, triplet, J 3.0 and 3.0 Hz) were attributed to H-2 and H-3 respectively. The large coupling constant between H-1-β and H-2-β ($J_{1,2}$ 8 Hz) indicated an axial orientation of H-2. Therefore, the small coupling constant between H-2 and H-3 ($J_{2,3}$ 3 Hz) suggested an equatorial orientation of H-3. thus indicating a *cis* relationship between C-2 and C-3, in agreement with the *gulo* configuration.

2-Deoxy-2-methylamino-D-gulose was a major product of the present reaction. No other Elson–Morgan positive substances, except 3 could be isolated from the crude reaction product, although some could be detected on paper chromatogram.

The R_F value and g.l.c. pattern of the per(trimethylsilyl)derivative of 3 were identical with those of the 2-deoxy-2-methylaminohexose isolated from the antibiotic BD-12.

The procedure described in this communication is different from that briefly reported by Noorzad *et al.*[8]. Direct comparison of the 2-deoxy-2-methylamino-D-gulose reported in this communication with that synthesized by Noorzad *et al.*[8] showed both compounds to be identical.

The authors thank Dr. T. Okuda, manager of this laboratory, for his encouragement, Dr. K. Kotera and his collaborators of the Analytical Center of this Company for the instrumental and elementary analyses and Dr. H. K. Zimmerman for a sample of synthetic 2-deoxy-2-methylamino-D-gulose.

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REFERENCES

1 D. B. Borders, W. K. Hausman, E. R. Wetzel, and E. L. Patterson, *Tetrahedron Lett.*, (1967) 4187.
2 Y. Ito, Y. Ohashi, Y. Sakurai, M. Sakurazawa, S. Awataguchi and T. Okuda, *J. Antibiotics*, 21 (1968) 307.
3 J. C. Sowden and H. O. L. Fischer, *J. Amer. Chem. Soc.*, 69 (1947) 1048.
4 *cf.* J. C. Sowden and M. L. Oftedahl, *J. Org. Chem.*, 26 (1961) 2153.
5 J. C. Sowden and H. O. L. Fischer, *J. Amer. Chem. Soc.*, 66 (1944) 1312.
6 F. G. Fischer and H. J. Nebel, *Z. Physiol. Chem.*, 302 (1955) 10.
7 R. U. Lemieux and J. D. Stevens, *Canad. J. Chem.*, 44 (1966) 249.
8 H. Noorzad, H. K. Zimmerman, and P. H. Gross, *Abstr. Papers Amer. Chem. Soc. Meeting*, 155 (1968) 18C.

(Received September 30th, 1968; in revised form, November 18th, 1968)

Carbohyd. Res., 9 (1969) 125–127

Announcement

The *Carbohydrate Discussion Group* (A Chemical Society Subject Group) is holding a meeting at the University College of North Wales at Bangor from March 31st to April 2nd, 1969. The meeting will include a small symposium on polysaccharide chemistry.

For further details of this meeting, please write to Dr. N. A. Hughes, Department of Organic Chemistry, The University, Newcastle upon Tyne NE1 7RU.