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Note

2-Amino-2-deoxy-D-*glycero*-α-L-*gluco*-heptose hydrochloride: structural study by ^{1}H-n.m.r. spectroscopy

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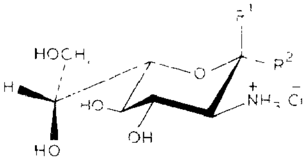
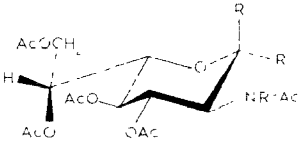
The aminonitrile synthesis of 2-amino-2-deoxyaldoses constitutes a general method for preparing aminoaldoses from aldoses, and it has been widely applied to the preparation of pentosamines and hexosamines by Kuhn and Kirschenlohr[1]. The application of this method to D-galactose yielded a heptosamine which was named "D-galaheptosamin", without specification of the configuration of C-2

We have now repeated this synthesis, and have assigned the configuration of 2-amino-2-deoxy-D-*glycero*-α-L-*gluco*-heptose hydrochloride (**1**) to the crystalline solid that was obtained. This assignment was supported by the ^{1}H-n.m.r. spectra recorded for compound **1** and some of its derivatives. As is shown in Fig. 1, the ^{1}H-n.m.r. spectrum of **1** recorded immediately after it had dissolved showed only an anomeric-proton signal corresponding to the equatorial proton of the α anomer ($J_{1,2}$ 3.3 Hz). In the spectrum recorded when mutarotational equilibrium had been reached, the signal corresponding to both anomers could be detected ($J_{1,2}$ for the β anomer, 8.3 Hz). From the integral of this spectrum, the anomeric proportions were determined to be 66% of the α and 34% of the β anomer.

The ^{1}H-n.m.r. spectra recorded for the acyl derivatives **2** and **3** (see Table I) showed high values (~10 Hz) for the coupling constants $J_{2,3}$, $J_{3,4}$, and $J_{4,5}$, in agreement with the *trans*-diaxial dispositions for these protons in the proposed configuration D-*glycero*-L-*gluco*. The small value (~2 Hz) of $J_{5,6}$ showed a *gauche* disposition for these protons.



1α R^1 = OH, R^2 = H
2β R^1 = H, R^2 = OH



2α R^1 = OAc, R^2 = R^3 = H
2β R^1 = R^3 = H, R^2 = OAc
3α R^1 = OAc, R^2 = H, R^3 = Bz
3β R^1 = H, R^2 = OAc, R^3 = Bz

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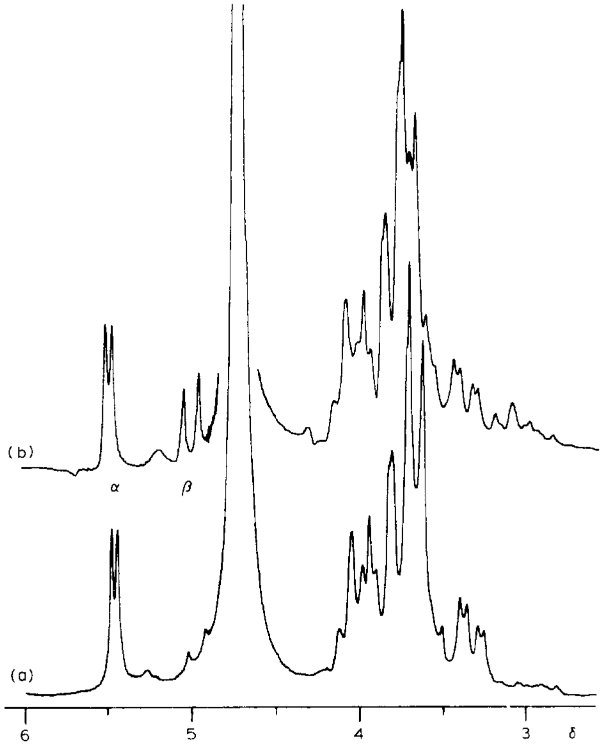

Fig. 1. ^{1}H-N.m.r. spectrum of 2-amino-2-deoxy-D-*glycero*-L-*gluco*-heptose in D_2O: (a) immediately after it was dissolved; (b) when the mutarotational equilibrium was reached.

EXPERIMENTAL

General methods. — Solutions were evaporated *in vacuo* at temperatures below 40°. Melting points were determined with a Gallenkamp apparatus, and are uncorrected. Optical rotations were measured with a Perkin–Elmer 141 polarimeter (10-cm cell). Paper chromatography was performed on Whatman No. 1 paper, by the ascending tehnique, with 1:1:1 1-butanol–pyridine–water as the eluant and silver nitrate–sodium hydroxide as the indicator. T.l.c. was conducted on plates coated with 0.25-mm, and p.l.c. on plates coated with 1-mm, layers of silica gel, Merck GF-254 and Merck 60 PF-254, respectively, with 3:2 benzene–ether as the eluant; the components were located by exposure to either u.v. light or iodine vapor. Column chromatography was performed on silica gel (Merck No. 60, 0.05–0.2 mm) with a benzene–ether gradient. I.r. spectra (KBr discs) were recorded with Beckman IR-33 and Perkin–Elmer 399 spectrometers. ^{1}H-N.m.r. spectra (90 MHz) were recorded with a Perkin–Elmer spectrometer, and coupling constants were measured directly from spectra recorded at 300-Hz sweep-width. Assignments were confirmed by double-resonance experiments.

TABLE I

CHEMICAL SHIFTS (δ) AND COUPLING CONSTANTS (J, Hz) FOR COMPOUNDS 2 AND 3 AT 90 MHz^{a,b}

Compound no	*H-1*	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*H-7*	*H-7'*	*N-H*	*Ph*	*Ac*
2α^c	6.17 d $J_{1,2}$ 3.6	4.50 td	5.00–5.45 m	5.00–5.45 m	3.95–4.20 m	5.00–5.45 m	← 3.95–4.20 m →		6.65 d J_{NH} 9.0	—	2.20 s (3H) 2.11 s (3H) 2.04 s (6H) 2.01 s (3H) 1.94 s (3H)
2α^d	6.40 d $J_{1,2}$ 3.6	4.86 td $J_{2,3}$ 9.6	5.64 t $J_{3,4}$ 9.7	5.36 t $J_{4,5}$ 9.3	4.20–4.47 m	5.44 m	← 4.20–4.47 m →		8.84 d J_{NH} 9.2	—	2.07 s (3H) 2.00 s (6H) 1.98 s (3H) 1.96 s (6H)
2β	5.78 d $J_{1,2}$ 9.0	4.08–4.50 m $J_{2,3}$ 9.0	5.32 t $J_{3,4}$ 9.3	5.10 t $J_{4,5}$ 9.7	3.97 dd $J_{5,6}$ 1.7	5.31 m	← 4.08–4.50 m →		6.55 d J_{NH} 9.0	—	2.12 s (6H) 2.04 s (6H) 2.01 s (3H) 1.94 s (3H)
2β^d	6.00 d $J_{1,2}$ 9.0	4.45–4.85 m $J_{2,3}$ 10.0	5.84 t $J_{3,4}$ 10.0	5.49 t $J_{4,5}$ 10.0	4.31 dd $J_{5,6}$ 2.5	5.59 m	← 4.45–4.85 m →		9.23 d J_{NH} 9.0	—	2.10 s (3H) 2.05 s (6H) 2.00 s (3H) 1.98 s (3H) 1.94 s (3H)

3α[c]	6.38 d $J_{1,2}$ 3.3	5.18 dd $J_{2,3}$ 11.3	5.98 dd $J_{3,4}$ 9.0	5.09 dd $J_{4,5}$ 10.3	4.15–4.37 m $J_{5,6}$ 2.3	5.32 m[e]	←4.15–4.37 m→		—	7.31–7.85 m	2.14 s (3H) 2.04 s (3H) 2.01 s (3H) 1.88 s (3H) 1.85 s (3H) 1.78 s (3H)
3α[d]	6.78 d $J_{1,2}$ 3.0	5.51 dd $J_{2,3}$ 11.3	6.37 dd $J_{3,4}$ 9.0	5.45 dd $J_{4,5}$ 10.3	4.33–5.70 m $J_{5,6}$ 2.3	5.49 m[e]	←4.35–5.70 m→		—	7.15–8.00 m	2.06 s (3H) 2.01 s (3H) 1.97 s (3H) 1.92 s (3H) 1.86 s (3H) 1.81 s (3H)
3β[c]	6.52 d $J_{1,2}$ 8.0	4.30 m[f] $J_{2,3}$ 10.3	5.95 dd $J_{3,4}$ 9.0	5.12 dd $J_{4,5}$ 10.2	4.04 dd $J_{5,6}$ 2.3	5.33 m[e] $J_{6,7}$ 5.6 $J_{6,7'}$ 7.0	4.31 dd $J_{7,7'}$ −11.3	4.12 dd	—	7.40–8.25 m	2.09 s (6H) 2.05 s (6H) 2.00 s (3H) 1.99 s (3H)
3β[d]	7.00 d $J_{1,2}$ 9.0	4.30–4.75 m $J_{2,3}$ 9.0	6.38 dd $J_{3,4}$ 10.5	5.53 t $J_{4,5}$ 10.5	4.30–4.75 m	5.60 m	←4.30–4.75 m→		—	7.18–7.95 m	2.09 s (6H) 2.05 s (3H) 2.03 s (3H) 2.00 s (6H)

[a]The spectrometer was locked on the signal of internal Me_4Si [b]The spectra were recorded at 35.5°. Signal multiplicities: d, doublet; dd, double doublet, m, multiplet, s, singlet, t, triplet; td, triple doublet. [c]In $CDCl_3$ [d]In pyridine-d_5 [e]Two double doublets superimposed [f]Covered by signals of H-7 and H-7′.

*2-Amino-2-deoxy-*D-glycero-α-L-gluco-*heptose hydrochloride* (**1α**). — The method of Kuhn and Kirschenlohr[1] was used. After recrystallization from water by addition of methanol, the pure product (70%) was obtained; m.p. 157–159° (dec.), $[\alpha]_D^{24}$ −85 → −69° (24 h; *c* 1.3, water) [lit.[1] m.p. 160°, $[\alpha]_D^{24}$ −77.5° → −66.5° (*c* 1.3, water)].

Anal. Calc. for $C_7H_{16}ClNO_6$: C, 34.21; H, 6.56; Cl, 14.44; N, 5.69. Found: C, 33.95; H, 6.52; Cl, 13.96; N, 5.69.

*2-Acetamido-1,3,4,6,7-penta-O-acetyl-2-deoxy-*D-glycero-*α-(and β)-*L-gluco-*heptopyranose* (**2α** *and* **2β**). — A suspension of **1** (3.0 g, 12.2 mmol) in pyridine (35 mL) was treated with acetic anhydride (25 mL, 245.0 mmol). The mixture was stirred while being heated for 1 h at 60°, and was then kept for 5 days at room temperature. The solution was poured into ice–water (150 mL), and extracted with chloroform (3 × 50 mL). The extracts were combined, washed successively with M hydrochloric acid (3 × 50 mL), a saturated solution of sodium hydrogencarbonate (3 × 50 mL), and water, dried (Na_2SO_4), and evaporated under diminished pressure; the syrupy residue crystallized from methanol to give **2β** (0.6 g, 9%). Recrystallized from methanol, m.p 221–223°, $[\alpha]_D^{24}$ +32.5° (*c* 0.5, chloroform); ν_{max} 3370 (NH), 1745 (C=O ester), 1660 (Amide I), and 1515 cm^{-1} (Amide II); ^{1}H-n.m.r. data are given in Table I.

Anal. Calc. for $C_{19}H_{27}NO_{12}$: C, 49.45; H, 5.89; N, 3.03. Found: C, 49.22; H, 5.84; N, 3.16.

Concentration of the methanolic mother-liquors gave **2α** (3.4 g, 55%); recrystallized from water, m.p. 82–84°, $[\alpha]_D^{24}$ −45.3° (*c* 0.5, chloroform); ν_{max} 3350 (NH), 1750 (C=O ester), 1655 (Amide I), and 1530 cm^{-1} (Amide II); ^{1}H-n.m.r. data are given in Table I.

Anal. Calc. for $C_{19}H_{27}NO_{12}$: C, 49.45; H, 5.89; N, 3.03. Found: C, 49.05; H, 5.87; N, 3.25.

*1,3,4,6,7-Penta-O-acetyl-2-(N-acetylbenzamido)-2-deoxy-*D-glycero-α-L-gluco-*heptopyranose* (**3α**). — A solution of **2α** (2.0 g, 4.3 mmol) in dry pyridine (7.0 mL) was treated with benzoyl chloride (1.3 mL, 12.2 mmol). After being heated under reflux for 5 h, the solution was cooled to room temperature, poured into ice–water, and extracted with chloroform (3 × 20 mL). The extracts were combined, successively washed with a saturated solution of $CuSO_4$ (3 × 20 mL), and water, dried ($MgSO_4$), concentrated, and decolorized with charcoal. The product (**3α**) was obtained by preparative t.l.c., and crystallization from methanol–water; yield 0.9 g (37%); m.p. 79–81°, $[\alpha]_D^{24}$ −32° (*c* 0.5, chloroform); ν_{max} 1745 (C=O ester), 1655 (C=O amide), 1590 and 1440 cm^{-1} (C=C aromatic); ^{1}H-n.m.r. data are given in Table I.

Anal. Calc. for $C_{26}H_{31}NO_{13}$: C, 55.22; H, 5.52; N, 2.47. Found: C, 54.94; H, 5.55; N, 2.50.

*1,3,4,6,7-Penta-O-acetyl-2-(N-acetylbenzamido)-2-deoxy-*D-glycero-β-L-gluco-*heptopyranose* (**3β**). — A solution of **2β** (3.0 g, 6.5 mmol) in dry pyridine (15 mL) was treated with benzoyl chloride (1.5 mL, 13.0 mmol). After being stirred for

24 h at room temperature, the solution was poured into ice–water, and extracted with dichloromethane (3 × 30 mL). The extracts were combined, washed successively with M hydrochloric acid, a saturated solution of sodium hydrogencarbonate, and water, dried ($MgSO_4$), evaporated, and the residue purified by column chromatography (gradient benzene → ether), to give amorphous **3β** (1.1 g, 30%); m.p. 59–61°, $[\alpha]_D^{24}$ +35.3° (*c* 0.5, chloroform); ν_{max} 1740 (C=O ester), 1660 (C=O amide), 1590 and 1440 cm^{-1} (C=C aromatic); ^{1}H-n.m.r. data are given in Table I.

Anal. Calc. for $C_{26}H_{31}NO_{13}$: C, 55.22; H, 5.52; N, 2.47. Found: C, 54.92; H, 5.52; N, 2.60.

REFERENCE

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