

Preparation and X-Ray Crystal Structures of Two 1-Amino-2,6-anhydro-1,3,4-trideoxy-D-erythro- and L-glycero-heptitol Derivatives

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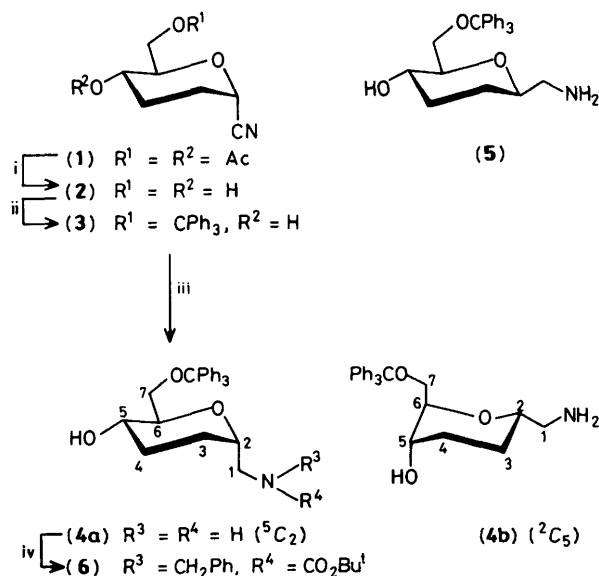
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The structures of the 1-amino-2,6-anhydro-heptitol derivatives (4) and (6), prepared from nitrile (3), were determined by X-ray crystallography.

In connection with a programme directed towards the synthesis of novel optically active building blocks, it was necessary to synthesise the amino alcohol (4). To this end, the nitrile (1), easily accessible from 3,4,6-tri-O-acetyl-D-glucal,¹ was converted to the alcohol (3),[†] by hydrolysis giving (2)[†] and tritylation as indicated in Scheme 1. Reduction of (3) with LiAlH₄ of lower quality gave a mixture of diastereoisomers, presumably (4) and (5), owing to epimerization at C(2), while the use of fresh reagent led reproducibly to a single isomer. Inspection of the ¹H n.m.r. (400 MHz) spectrum of the diastereoisomerically pure reduction product revealed a value of 10.5 Hz for the sum of coupling constants HC(2)–H₂C(3) in addition to a rather small coupling constant of 6 Hz for HC(6)–HC(5), which was inconsistent with conformation (4a). These observations prompted us to establish the stereochemistry of the reduction product by X-ray crystallographic analysis.



[†] All new compounds synthesised showed satisfactory analytical data. Selected spectroscopic data for (4): [α]_D²⁰ –9.5° (c 1.0, CHCl₃); ¹H n.m.r. (CDCl₃) δ 1.50–1.75 (m, 4 H), 1.96 (br. s, 3 H), 2.57 (dd, *J* 4.5 and 13.5 Hz, 1 H), 2.93 (dd, *J* 9 and 13.5 Hz, 1 H), 3.26 (dd, *J* 7 and 9.5 Hz, 1 H), 3.44 (dd, *J* 5.5 and 9.5 Hz, 1 H), 3.51 (m, Σ *J* 24 Hz, 1 H, affected by irradiation at δ 2.57), 3.64 (m, 1 H), 3.70 (m, Σ *J* 18.5 Hz, 1 H, affected by irradiation at δ 3.26); ¹³C n.m.r. (CDCl₃, 62.9 MHz) δ 23.8 (t), 26.5 (t), 43.7 (t), 64.2 (t), 67.5 (d), 72.8 (d), 74.7 (d), 87.2 (s), 127.2 (d), 127.9 (d), 128.6 (d), 143.6 (s).

Scheme 1. Reagents and conditions: i, MeOH, cat. Na (s), 0–5 °C (84%); ii, Ph₃CCl, NEt₃, CH₂Cl₂, cat. 4-dimethylaminopyridine (quant.); iii, LiAlH₄, tetrahydrofuran (THF), 0–5 °C (92%); iv, benzaldehyde, NaBH₄, MeOH followed by di-t-butylidicarbonate, THF, pyridine, room temperature (60% overall).

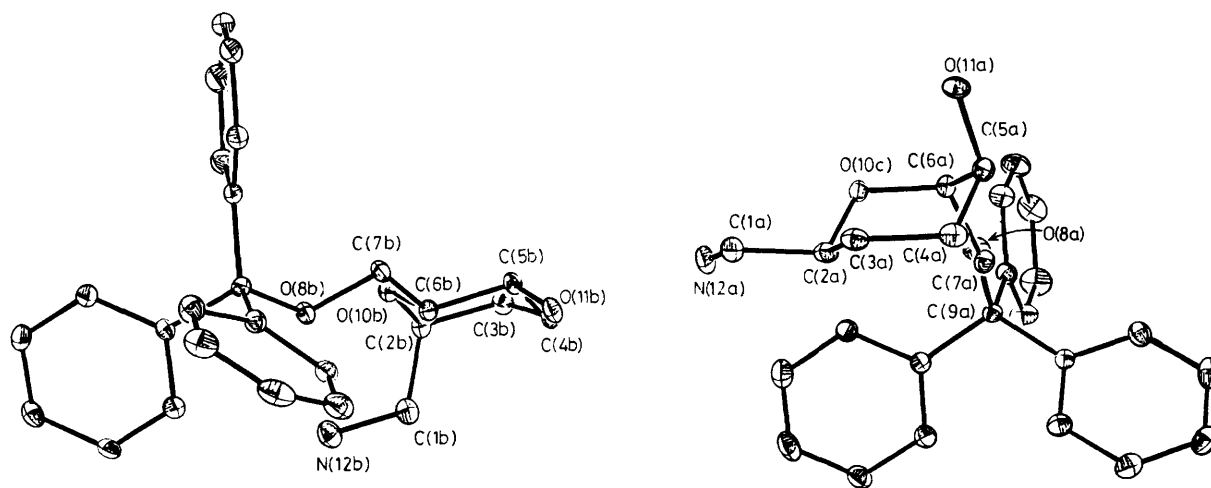


Figure 1. An ORTEP plot showing the two conformers (4a) and (4b) in the asymmetric unit; hydrogen atoms have been omitted for clarity.

Recrystallisation of (4) from ethyl acetate provided crystals, m.p. 160–161 °C, suitable for X-ray diffraction \ddagger . As shown in Figure 1, there are two symmetrically independent molecules in the asymmetric unit. To the best of our knowledge, this is the first example of a pyranosidic monosaccharide containing the two possible chair conformations, 5C_2 (4a) and 2C_5 (4b), side by side in the unit cell. \S The two conformers are stabilised by the network of hydrogen bond systems N(12a) \cdots O(11b) (2.693 Å), O(11a) \cdots O(11b) (2.786 Å), and N(12b) \cdots O(10b) (2.897 Å). In contrast, the protected derivative (6), obtained by the two step protocol given in Scheme 1, forms a

\ddagger Crystal data for (4): $C_{26}H_{29}NO_3$, $M = 403.52$, orthorhombic, space group $P2_12_12_1$, $a = 9.176(17)$, $b = 16.056(28)$, $c = 29.389(30)$ Å, $U = 4330(12)$ Å 3 , $D_c = 1.24$ g cm $^{-3}$, $Z = 8$, $\mu = 0.07$ mm $^{-1}$, $F(000) = 1712$, scan speed 0.95–10° min $^{-1}$, scan width 0.6°. (6): $C_{38}H_{43}NO_5$, $M = 561.77$, m.p. 119–121 °C (from MeOH), monoclinic, space group $P2_1$, $a = 8.861(2)$, $b = 18.089(3)$, $c = 11.007(2)$ Å, $\beta = 110.90(2)^\circ$, $U = 1648.2$ Å 3 , $D_c = 1.13$ g cm $^{-3}$, $Z = 2$, $\mu = 0.07$ mm $^{-1}$, $F(000) = 604$, scan speed 1.05–10° min $^{-1}$, scan width 0.8°. $\theta_{max} = 28^\circ$ for both compounds. All crystallographic measurements were made on a Nicolet R3m four-circle diffractometer fitted with a graphite monochromator ($\lambda = 0.71069$ Å) operating in the ω scan mode at 174 K. The structures were solved by direct methods using SHELXS-86. 4 Final refinement was done with blocked matrix least squares of SHELXTL. 4 All non-hydrogen atoms were refined anisotropically. The positions of the hydrogen atoms of the OH- and NH $_2$ -groups were found from a Fourier difference map. The remaining hydrogen atom co-ordinates were calculated using known geometries. For (4), the weighting scheme $w = [\sigma^2(F_o) + 0.007(F_o)^2]^{-1}$ was used resulting in final R and R_w values of 0.05 and 0.05 respectively (773 parameters, 4090 observed data). For (6), the weighting scheme $w = [\sigma^2(F_o) + 0.001(F_o)^2]^{-1}$ led to final R and R_w values of 0.046 and 0.050 (398 parameters, 2892 observed data). Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge crystallographic Data Centre. See Notice to Authors, Issue No. 1.

\S Although several crystal structures of polysubstituted tetrahydropyrans exhibiting two or more independent molecules in the asymmetric unit do exist, these conformers are most often very similar to each other. An interesting case of a disaccharide with two quite different conformers in the unit cell has been reported. 2

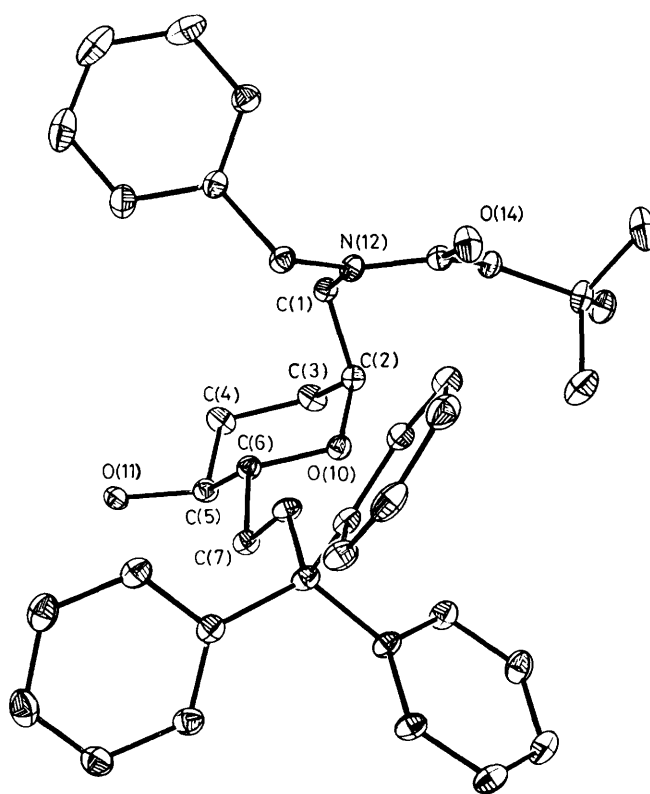


Figure 2. An ORTEP plot of the protected amino alcohol (6); hydrogen atoms not shown.

single conformer in the asymmetric unit (Figure 2) with an intermolecular hydrogen bond O(11) \cdots O(14) (2.682 Å).

Force field calculations (MM2) 3 led to the conclusion that the energy difference between (4a) and (4b) is less than 1 kcal/mol (1 cal = 4.184 J). The observed coupling constants mentioned above might be expected to reflect the fast

equilibration, (4a) \rightleftharpoons (4b), in solution. Unfortunately ^1H n.m.r. spectroscopic studies at temperatures below that of rapid conformational interconversion failed, owing to insurmountable solubility problems.

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