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Note

First crystallographic evidence for the formation of β-D-ribopyranosylamine from the reaction of ammonia with of D-ribose

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Abstract

β-D-Ribopyranosylamine was synthesized and characterized using analytical, spectral and single-crystal X-ray diffraction methods. The molecule exists in the chair form with the $^4C_1$ conformation. The β anomeric form of C-1 is supported by the dihedral angles. The molecule exhibits both intra- and intermolecular hydrogen-bond interactions of the type O–H···O, N–H···O and C–H···O, and these are interconnected to each other to form chains. © 2003 Elsevier Science Ltd. All rights reserved.

Keywords: D-Ribopyranosylamine; Single-crystal X-ray diffraction; Glycosyl amines

The role of glycoconjugates in molecular recognition is an important subject of current interest.[1] Synthetic glycoconjugates including neoglycoproteins, neoglycolipids and glycosylated materials are used to characterize and study the properties of endogeneous lectins as well as to target drugs, oligonucleotides and genes.[2] The accurate determination of structures of these compounds, along with establishing the weak intermolecular interactions present in their crystal lattices, will ultimately be responsible for understanding their function and properties. Moreover, the D-ribosylamine is a valuable intermediate in the synthesis of various nitrogen-containing D-ribosyl derivatives.

In 1915, efforts of Levene's group resulted in the synthesis of a mixture of mono- and di-D-ribosylamine,[3] and their continued efforts later resulted in making the product in high yields when the reagents used were dry.[4] With a marginally modified procedure, Tipson[5] demonstrated the synthesis of pure D-ribosylamine and di-D-ribosylamine in 1961. Later on, Shaw and co-workers,[6] whose interest lay in making heterocyclic compounds, once again reported the synthesis of D-ribosylamine with some simplified procedures. These workers provided a chemical proof for the presence of the pyranose structure by condensing this product with ethyl *N*-(α-cyano-β-ethoxy acryloyl)carbamate to afford ribopyranosyl uracil, which was shown to absorb two molar equivalents of periodate to result in one molar equivalent of formic acid. However, until now no crystal structure has been reported supporting the pyranose form of this compound.

Therefore, we have developed a method wherein we obtain not only pure product of D-ribosylamine, but we are also able to get single crystals of X-ray diffraction quality as reported in this Note. Thus, in this Note we provide the first crystal structure evidence that establishes the pyranose form as that of the product by X-ray diffraction. In continuation with our ongoing work in the field of glycosylamines and their derivatives, herein we report detailed characterization using elemental analysis, FTIR, ^{1}H NMR, optical rotation as given in Section 1, as well as the crystal structure of β-D-ribopyranosylamine. OH proton resonances were further crosschecked by measuring the spectra after D_2O addition, followed by exchange. The ^{1}H NMR spectrum is consistent with the structure, and the corresponding assignment is given in Section 1.

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Table 1
Summary of crystallographic data for **1**

	1
Molecular formula	$C_5H_{11}NO_4$
Formula weight	149.15
T (K)	293(2)
Crystal system	monoclinic
Space group	$P2_1$
Unit cell dimensions	
a (Å)	6.652(2)
b (Å)	5.350(1)
c (Å)	9.319(1)
β (°)	93.97
V (Å^3)	330.81(12)
Z	2
D_{calc} (Mg m^{-3})	1.497
Reflections collected	4270
Independent reflections	2421 [$R_{int} = 0.0288$]
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0331$, $wR_2 = 0.0822$
R indices (all data)	$R_1 = 0.0389$, $wR_2 = 0.0864$

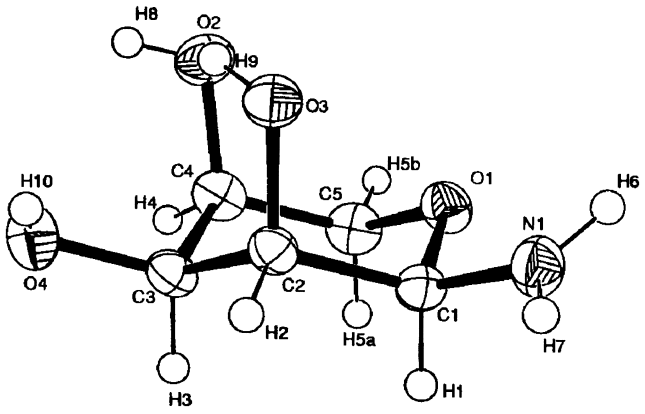

Fig. 1. Molecular structure of **1**.

The compound crystallizes in a $P2_1$ space group in the monoclinic system. Details of data collection and structure refinement are given in Table 1. In the molecular structure, β-D-ribopyranosylamine (**1**) adapts a pyranose form where C-1 is derivatized with an –NH_2 group by replacing the –OH group, and the O-5 is involved in ring formation. As a result of this, β-D-ribopyranosylamine, exhibits only three –OH groups attached to C-2, C-3 and C-4 centers in the molecule. The molecular structure of **1** is provided in Fig. 1 as an ORTEP drawing.[7] Cremer–Pople puckering parameters and asymmetry parameters[8–10] obtained using the program PLATON-99, are as follows: $Q = (0.578$ Å), $\theta = (1.8°)$, $\phi = (91.90°)$; $\Delta Cs(O\text{-}1,\ C\text{-}3) = 0°$, $\Delta Cs(C\text{-}1,\ C\text{-}4) = 0°$, $\Delta Cs(C\text{-}2,\ C\text{-}5) = 0°$. This data further supports the chair form of the six-membered ring. Further, the metric data (Table 2) was found to be quite normal and agrees well with the reported values for similar bonds. The conformation of the pyranose ring is a $^4C_1$ chair type, and the saccharide moiety is present in the β anomeric form. All these conformational features can be clearly viewed from the stereoview given in Fig. 2. Selected torsion angles are provided in Table 2 to represent the conformation of the molecule. The torsion angles, C(5)–O(1)–C(1)–N(1) and C(3)–C(2)–C(1)–N(1) imply that C(5)–O(1) and C(3)–C(2) are *anti* to C(1)–N(1), and this also supports the β anomeric form at C-1. Further the torsional angles O(3)–C(2)–C(1)–N(1), O(4)–C(3)–C(2)–O(3) and O(4)–C(3)–C(4)–O(2) show *gauche* interactions, and the fact that C(1)–N(1) and C(3)–O(4) are in equatorial positions and C(2)–O(3) and C(4)–O(2) are in the axial position.

In the crystal structure, β-D-ribopyranosylamine exhibits four intramolecular hydrogen bonds of O–H···O type in which, two interactions are from HO-2, one from HO-3 and the fourth from HO-4. Further, each molecule in the lattice is interacting with its symmetry-related four neighbor molecules via four intermolecular hydrogen bonds, in which one is O–H···O, two are C–H···O and the fourth one of N–H···O type of interactions. The data corresponding to the intra- and intermolecular hydrogen-bond interactions present in the crystal are given in Table 3. These intermolecular interactions are manifested to result in the formation of chains of molecules and further the adjacent chains interact as shown in the lattice structure (Fig. 3).

Thus the crystal structure of β-D-ribopyranosylamine is clearly indicative of the presence of pyranose structure as shown for the first time by X-ray diffraction studies. This molecule also exists in the β anomeric form. As we go from D-ribose, which is a mixture of α and β anomers, to β-D-ribopyranosylamine, the solution optical rotation changes from -17 ± 1 to $-34 \pm 1°$, which is in conformity with the formation of the β anomeric form. However, when a saccharide was modified at C-1 through glycosylation to result in C-1-N-glycosides, the C-1 anomeric nature was switched over from α to β owing to the stability of the resultant C-1-N-glycosylated product, as identified in case of D-glucose-derived products[11] reported by us, and D-mannose- and D-galactose-derived[12,13] products reported in the literature. Such anomeric conversion is generally identified primarily based on ^{1}H NMR spectra at least in case of the D-glucose-based derivatives.

1. Experimental

All analytical and spectral measurements were carried out using the experimental details given in our earlier paper.[11a] β-D-Ribopyranosylamine (**1**) was synthesized as per the reported procedure[6] with some modifications

Table 2
Selected bond lengths (Å), bond angles (°) and torsion angles (°) for **1**

Bond lengths			
C(1)–N(1)	1.438(2)	C(3)–C(4)	1.527(2)
C(1)–O(1)	1.440(2)	C(4)–O(2)	1.438(2)
C(1)–C(2)	1.529(2)	C(4)–C(5)	1.515(2)
C(2)–O(3)	1.434(2)	C(5)–O(1)	1.439(2)
C(2)–C(3)	1.528(2)	C(3)–O(4)	1.419(2)
Bond angles			
N(1)–C(1)–O(1)	109.5(1)	O(4)–C(3)–C(2)	108.9(1)
N(1)–C(1)–C(2)	110.9(1)	C(4)–C(3)–C(2)	110.1(1)
O(1)–C(1)–C(2)	110.0(2)	O(2)–C(4)–C(5)	110.8(1)
O(3)–C(2)–C(3)	111.3(1)	O(2)–C(4)–C(3)	110.6(1)
O(3)–C(2)–C(1)	108.4(1)	C(5)–C(4)–C(3)	109.5(1)
C(3)–C(2)–C(1)	109.3(1)	O(1)–C(5)–C(4)	111.7(1)
O(4)–C(3)–C(4)	111.8(1)	C(5)–O(1)–C(1)	112.4(1)
Torsion angles			
N(1)–C(1)–C(2)–O(3)	57.8(2)	C(2)–C(3)–C(4)–O(2)	−68.0(1)
O(1)–C(1)–C(2)–O(3)	−63.5(1)	O(4)–C(3)–C(4)–C(5)	175.7(1)
N(1)–C(1)–C(2)–C(3)	179.3(1)	C(2)–C(3)–C(4)–C(5)	54.4(2)
O(1)–C(1)–C(2)–C(3)	58.0(2)	O(2)–C(4)–C(5)–O(1)	66.5(2)
O(3)–C(2)–C(3)–O(4)	−59.0(2)	C(3)–C(4)–C(5)–O(1)	−55.8(2)
C(1)–C(2)–C(3)–O(4)	−178.7(1)	C(4)–C(5)–O(1)–C(1)	59.8(2)
O(3)–C(2)–C(3)–C(4)	63.9(2)	N(1)–C(1)–O(1)–C(5)	177.5(1)
C(1)–C(2)–C(3)–C(4)	−55.9(2)	C(2)–C(1)–O(1)–C(5)	−60.4(2)
O(4)–C(3)–C(4)–O(2)	53.2(2)		

in order to obtain single crystals. A suspension containing anhydrous D-ribose (5 g, 0.033 mol) in 5 mL of dry MeOH was purged with ammonia at 0–5 °C until all the ribose dissolved. The ammonia purging was continued for another 10–15 min. Later the reaction mixture was maintained under an atmosphere of ammonia at 0–5 °C overnight. The flask containing the reaction mixture was immediately closed with a stopper and stored at 0–5 °C in a refrigerator. After 2–3 days, colorless crystals started appearing, and soon a hard rosette of material was stuck to the surface of flask. The pure crystals were isolated and washed with MeOH. The improper drying of D-ribose results in the formation of bis-glycosylamine along with the β-D-ribopyranosylamine, thereby reducing the yield of mono glycosylamine product. Although the yield was low, we obtained the product as single crystals suitable for X-ray diffraction studies. Yield: 1.11 g, 23%, mp: 127–129 °C; FTIR (KBr): ν 3356, 3291, 2928, 1584, 1479, 1451, 1357, 1071, 730 cm^{-1}; ^1H NMR (Me_2SO-d_6): δ 2.349 (b, 2 H, NH_2), 3.902 (s, 1 H, H-1), 3.307–3.670 (m, 5 H, H-2, H-3, H-4 and two of H-5), 4.501 (d, 1 H, one OH), 4.793–4.855 (m, 2 H, two OH's). Anal. Calcd for $C_5H_{11}NO_4$: C, 40.26; H, 7.43; N, 9.39. Found: C, 40.29; H, 6.95; N, 9.31. $[\alpha]_D^{25}$ $-34.0° \pm (1°)$ (c 1, water).

1.1. Crystal structure determination

The procedures used for the data collection, solving and refining the structure, and the figure production were same as that reported in our earlier paper.[11a]

2. Supplementary material

Full crystallographic details, excluding structure factors, have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. 199565 for structure **1**. This data may be obtained, on request, from The Director, CCDC, 12 Union Road, Cambridge, CBZ 1EZ, UK (Tel.: +44-1223-336-408; fax: +44-1223-336-033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

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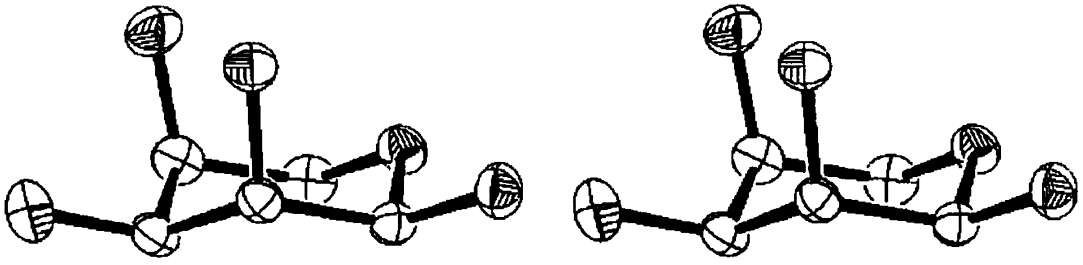

Fig. 2. Stereoview of **1** showing 50% probability thermal ellipsoids using ORTEP.

Table 3
Hydrogen bond data for **1**

D–H···A	d(D···H) (Å)	d(H···A) (Å)	d(D···A) (Å)	<(DHA) (°)	Symmetry
N(1)–H(7)···O(3)	0.860	2.014	2.818	155.1	$1-x, -1/2+y, -z$
O(2)–H(8)···O(4)	0.820	2.497	2.822	105.0	
O(2)–H(8)···O(4)	0.820	2.045	2.811	155.2	$1-x, 1/2+y, 1-z$
O(3)–H(9)···O(2)	0.820	2.125	2.726	130.0	
O(3)–H(9)···O(4)	0.820	2.506	2.836	105.4	
O(4)–H(10)···O(3)	0.820	2.482	2.836	107.3	
C(1)–H(1)···O(3)	0.980	2.588	3.517	158.3	$x, -1+y, z$
C(5)–H(5B)···O4	0.970	2.412	3.374	171.0	$-1+x, y, z$

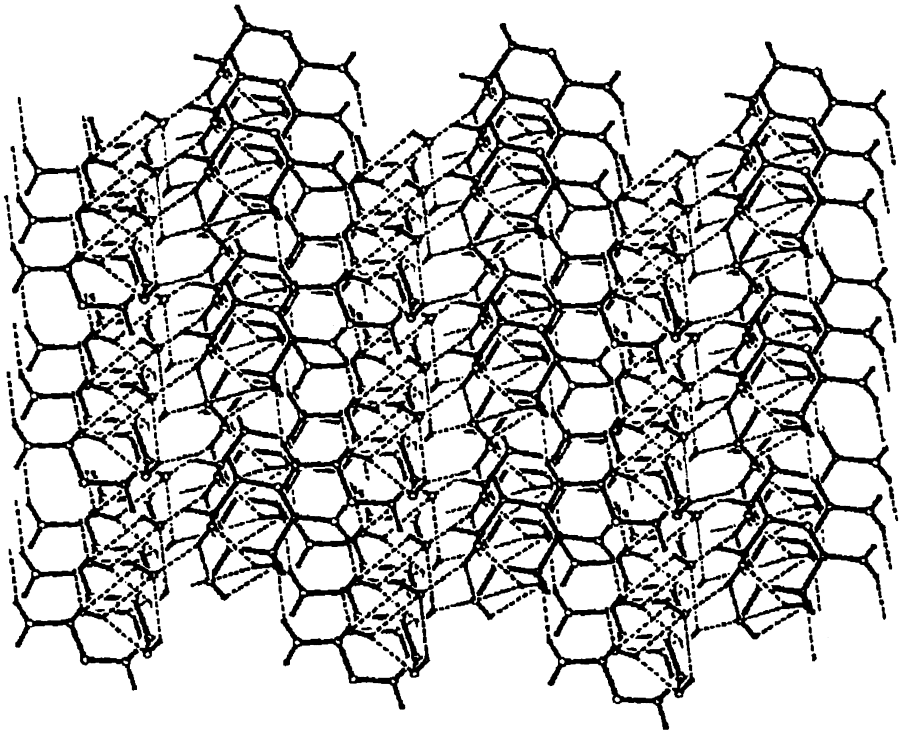

Fig. 3. Lattice structure of **1**.

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