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Structure of α-D-Galactosamine-1-phosphate Monohydrate*

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Abstracts

Crystals of α-D-galactosamine phosphate monohydrate, $C_6H_{14}NO_8P.H_2O$, belong to the orthorhombic space group $P2_12_12_1$, with unit-cell constants $a = 13\cdot389$ (1), $b = 9\cdot117$ (1), $c = 8\cdot686$ (1) Å; $Z = 4$. The structure was solved by the Patterson and tangent-refinement techniques. Atomic parameters were refined by the full-matrix least-squares method. The final R factor is 0·043 for 1045 intensities. The differences in the endocyclic C–O bond distances involving the anomeric center, the C(5)–O(5)–C(1)–O(1)–P bond sequence [C(5)–O(5) 1·464 (5), O(5)–C(1) 1·404 (5), C(1)–O(1) 1·435 (5) Å], appear to be accentuated when compared to those observed in α-methyl glycopyranosides due to the extended 'conjugation' resulting from the possible interaction of the lone-pair orbitals of the anomeric O(1) atom with the P *d* orbitals. The other bond distances and angles for the saccharide and phosphate moieties are in agreement with previously observed values for similar systems. The pyranoid ring is in the $^4C_1$ conformation with the endocyclic torsional angles ranging from 54·3 to 59·4° (mean 57·0°). The exocyclic C(5)–C(6) bond torsion angle of the galactose is in the preferred *trans* conformation. The crystal lattice is stabilized by an intricate three-dimensional network of hydrogen bonds. The equatorial C(2) ammonium group and the axial C(4) hydroxyl group are involved in three hydrogen bonds each, while the equatorial C(3) and C(6) hydroxyls are involved in only two hydrogen bonds. The phosphate group is involved in five hydrogen bonds.

Introduction

As part of a general program of research in these laboratories on the molecular structures of sugar phosphates we have determined the crystal structure of α-D-galactosamine-1-phosphate monohydrate, an activated amino sugar. The 1-phosphate sugar esters possess 'intermediate' energy phosphate bonds, *i.e.* the free energy of hydrolysis of these bonds is about 17–21 kJ mol^{-1} as compared to 29–38 kJ mol^{-1} for adenosine triphosphate, and are required as substrates by the phosphorylases and the transferases for the formation of glycosidic bonds. Although free galactosamine does not occur extensively in higher organisms, it does constitute a significant portion of the cell-wall polysaccharides of bacteria and fungi, while *N*-acetyl substituted galactosamine is an important component of the mucopolysaccharides, glycosphingolipids, and glycoproteins of higher organisms.

Experimental

Crystalline α-D-galactosamine-1-phosphate was prepared enzymatically in relatively large quantities and crystals from such a preparation were kindly supplied by Dr D. M. Carlson for this study. The crystals, which had an amber tinge, were multi-faceted prisms that measured as long as 1·0 mm on a side. A section measuring approximately 0·20 × 0·35 × 0·47 mm was trimmed from one of the larger crystals and mounted along the c axis. Accurate unit-cell dimensions were obtained from a least-squares fit of the diffractometer angles χ, φ, and 2θ for 36 reflections with $2\theta \geq 40°$ measured using Ni-filtered Cu $K\alpha$ radiation. These and other pertinent crystal data are given in Table 1. It was found that the structure is a monohydrate.

Table 1. *Crystal data for* α-D-*galactosamine*-1-*phosphate monohydrate*

Empirical formula	$C_6H_{14}NO_8P.H_2O$
Unit-cell dimensions	
a	$13\cdot389 \pm 0\cdot001$ Å
b	$9\cdot117 \pm 0\cdot001$
c	$8\cdot686 \pm 0\cdot001$
Space group	$P2_12_12_1$
V	1060 Å^3
Z	4
D_x	1·737 Mg m^{-3}
D_m	1·736
μ	2·752 mm^{-1}
Dimensions of crystal	0·20 × 0·35 × 0·47 mm

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* The structure was solved while the authors were at Case Western Reserve University, Cleveland, Ohio 44106, USA.

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1068 independent reflections were measured using the θ–2θ scan technique with Ni-filtered Cu $K\alpha$ radiation out to the instrumental limit of 133·7 (2)°. The reflections were scanned at the rate of 2° (2θ) $\min^{-1}$ and background counts were measured at either extremity of the peaks for 30s. The data were corrected for the variation in the standard reflection, which was only 2%, and the usual Lorentz and polarization factors.

Structure determination and refinement

The P atom was located in the Harker sections of a Patterson synthesis calculated using $E^2 - 1$ as coefficients. The P phases were refined by the tangent formula (Karle & Hauptman, 1956) using the programs written by Hall (1968). The resulting E map revealed the positions of the entire structure with the exception of the water molecule which was located in a subsequent difference Fourier map. The atomic parameters were refined by the full-matrix least-squares method (Busing, Martin & Levy, 1962), first with isotropic (R = 0·084) and then with anisotropic temperature factors (R = 0·064). A difference Fourier map revealed all the H atom positions. Inclusion of these in the final refinement cycles with their thermal parameters held fixed at B = 3·5 Å^2 gave an R index of 0·043. The shift/error ratios for all the parameters were less than 0·10. There were no peaks higher than 0·10 e Å^{-3} in the final difference electron density map.

The weighting function used during the refinement was based on counting statistics (Stout & Jensen, 1968). The atomic scattering factors for non-hydrogen atoms were from Cromer & Waber (1965), while those of H atoms were from Stewart, Davidson & Simpson (1965).*

Results and discussion

The positional and thermal parameters (B_{eq}) for the non-hydrogen atoms and the H atoms are given in Table 2. Fig. 1 is an *ORTEP* (Johnson, 1965) drawing of the molecule. The bond lengths, bond angles and torsion angles involving non-hydrogen atoms are shown in Fig. 2. The average C—C and C—O bond lengths of 1·522 (6) and 1·426 (5) Å, respectively, are similar to values reported previously (Fries, Rao & Sundaralingam, 1970; Arnott & Scott, 1972; Jeffrey, McMullan & Takagi, 1977). The C—N$^+$ bond distance of 1·496 (5) Å is also within the expected range, as are the bond distances and angles involving the monoanionic phosphate ester (Sundaralingam & Putkey, 1970).

Table 2. *Fractional positional parameters and equivalent isotropic temperature factors (B_{eq}) of galactosamine-*1*-phosphate*

B_{eq} is defined as $B_{eq} = \frac{4}{3}\sum_i \sum_j \mathbf{a}_i.\mathbf{a}_j\beta_{ij}$ where $\mathbf{a}_i$'s are cell constants in direct space.

	x	y	z	B_{eq} (Å^2)
P(1)	0·2175 (1)	0·8935 (1)	0·0523 (1)	1·00
O(1)	0·1820 (2)	0·7285 (3)	0·0865 (3)	1·49
O(3)	−0·0243 (2)	0·3834 (3)	0·1917 (3)	1·92
O(4)	0·1042 (2)	0·2614 (3)	−0·0189 (4)	1·90
O(5)	0·2186 (2)	0·5270 (3)	−0·0673 (3)	1·57
O(6)	0·4138 (2)	0·3875 (1)	0·0181 (5)	2·89
O(7)	0·2952 (2)	0·9178 (2)	0·1827 (4)	2·27
O(8)	0·1286 (2)	0·9911 (3)	0·0743 (4)	1·87
O(9)	0·2692 (2)	0·8992 (3)	−0·1020 (4)	1·90
O(10)	0·4625 (3)	0·6425 (4)	0·1836 (4)	3·20
N(2)	−0·0251 (2)	0·6786 (4)	0·0628 (4)	1·53
C(1)	0·1461 (1)	0·6333 (4)	−0·0328 (5)	1·30
C(2)	0·0481 (3)	0·5615 (4)	0·0201 (5)	1·33
C(3)	0·0661 (3)	0·4581 (4)	0·1527 (5)	1·32
C(4)	0·1432 (3)	0·3441 (5)	0·1036 (5)	1·63
C(5)	0·2382 (3)	0·4247 (4)	0·0590 (5)	1·28
C(6)	0·3189 (3)	0·3190 (4)	0·0048 (6)	1·84
H(C1)	0·128 (3)	0·706 (5)	−0·133 (6)	
H(C2)	0·017 (3)	0·494 (4)	−0·071 (6)	
H(C3)	0·092 (3)	0·467 (5)	0·229 (6)	
H(C4)	0·159 (3)	0·274 (5)	0·187 (6)	
H(C5)	0·270 (3)	0·496 (5)	0·142 (6)	
H1(C6)	0·304 (3)	0·277 (5)	−0·092 (6)	
H'(C6)	0·316 (3)	0·211 (4)	0·052 (6)	
H(N2)	−0·038 (4)	0·743 (4)	−0·024 (6)	
H'(N2)	−0·084 (3)	0·633 (5)	0·084 (6)	
H''(N2)	0·001 (3)	0·748 (5)	0·162 (6)	
H(O3)	−0·083 (3)	0·426 (5)	0·256 (6)	
H(O4)	0·117 (3)	0·146 (5)	−0·021 (6)	
H(O6)	0·462 (4)	0·301 (4)	0·022 (6)	
H(O7)	0·271 (3)	0·996 (5)	0·242 (6)	
H(O10)	0·425 (3)	0·571 (6)	0·146 (7)	
H'(O10)	0·427 (4)	0·672 (6)	0·236 (7)	

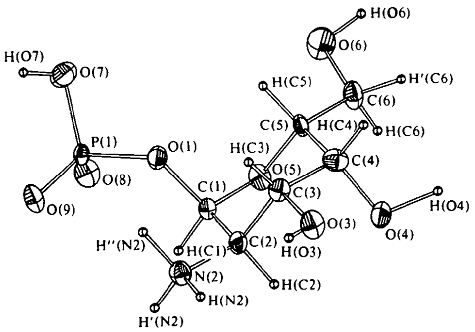
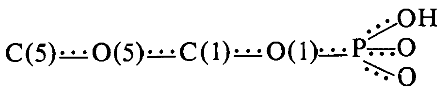


Fig. 1. An *ORTEP* drawing of α-D-galactosamine-1-phosphate showing the molecular conformation and atom numbering.

The consequence of the anomeric effect on the C—O bond distances of the



$$C(5)\cdots O(5)\cdots C(1)\cdots O(1)\cdots P\begin{matrix}\cdot\cdot OH\\ \cdot\cdot O\\ \cdot\cdot O\end{matrix}$$

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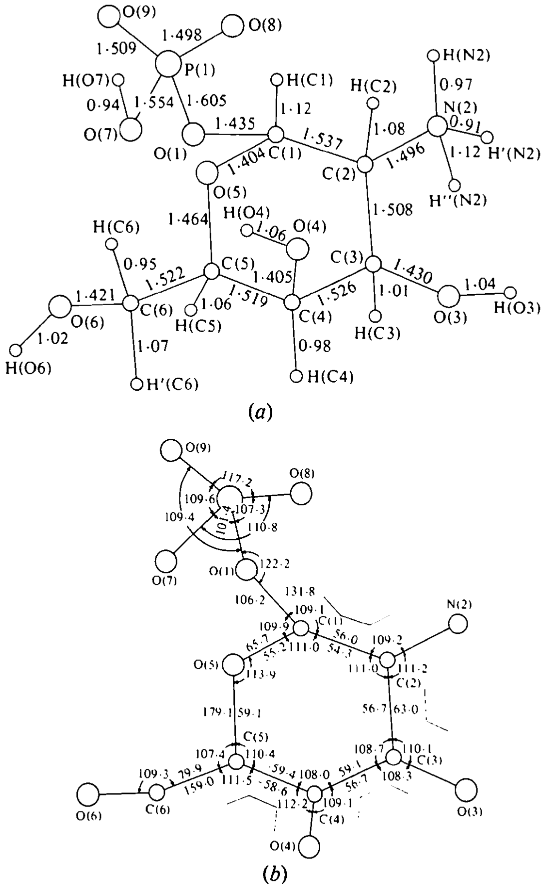
* Lists of structure factors and anisotropic thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 35381 (6 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.



(*a*)

(*b*)

Fig. 2. Schematic drawings showing (*a*) bond distances (Å) in α-D-galactosamine-1-phosphate and (*b*) bond angles (°), endocyclic and exocyclic torsion angles (°) involving the substituents in α-D-galactosamine-1-phosphate. Mean e.s.d.'s in the bond lengths are 0·006 for C—C, 0·005 for C—O, 0·005 for C—N, and 0·003 Å for P—O bonds, and in the bond angles 0·35° for those involving C, O and N atoms, and 0·21° for those involving P and O atoms. The mean standard deviation in the torsion angles is 0·4°.

[C(5)—O(5) 1·464, O(5)—C(1) 1·404, C(1)—O(1) 1·435, O(1)—P 1·605 Å] fragment of the sugar phosphate is similar to that found in the axial methyl glycopyranosides (Jeffrey, Pople, Binkley & Vishveshwara, 1978). The enhanced difference (12σ) in the endocyclic C—O bond lengths appears to be a consequence of the possible interaction of the lone-pair orbitals of the anomeric O(1) atom with the P *d* orbitals.

The axial C(4)—O(4) hydroxyl bond, 1·405 (5) Å, is significantly shorter than the equatorial C(3)—O(3) hydroxyl bond, 1·430 (5) Å.

The endocyclic bond angles at C(3) and C(4) are significantly smaller than that at C(2). This probably results from the nature and orientation of the substituents. The glycosidic bridge angle C(1)—O(1)—P(1) is 122·2 (3)°, which is about 7° larger than the corresponding C—O—C angle in the methyl glycosides (Jeffrey, McMullan & Takagi, 1977; Sundaralingam, 1968). The increase in the angle probably relieves steric interaction between the bulky phosphate group and the sugar. The axially substituted hexose-1-phosphate esters exhibit standard free energies of hydrolysis which are about 9·2 to 14·2 kJ mol^{-1} (Atkinson & Morton, 1960) more negative than the related hexose-6-phosphate. Since the geometry of the phosphate moiety in the present structure is similar to other known monoanionic phosphate esters (Sundaralingam & Putkey, 1970), the origin of these energy differences appears to be independent of the geometry of the phosphate ester group.

Molecular conformation

The galactose ring exhibits the $^4C_1$ pucker. The Cremer & Pople (1975) puckering parameters Q, θ and φ are 0·58 (1), 5·9 (5) and 225·3 (4·8)° respectively. The phosphate P—O bonds are partially staggered with respect to the glycosidic bond C(1)—O(1). The NH_3^+ group at C(2) is also staggered with respect to the sugar ring bonds. The conformation about the exocyclic C(5)—C(6) bond is *trans* [C(4)—C(5)—C(6)—O(6) = −159·0 (6)°] which is the most favored conformation for a galactose sugar.

Molecular packing and hydrogen bonding

The molecular packing and the hydrogen bonding are shown in Fig. 3 and the hydrogen-bond distances and angles are listed in Table 3. There are 15 hydrogen bonds to a molecule of which 9 are independent. The

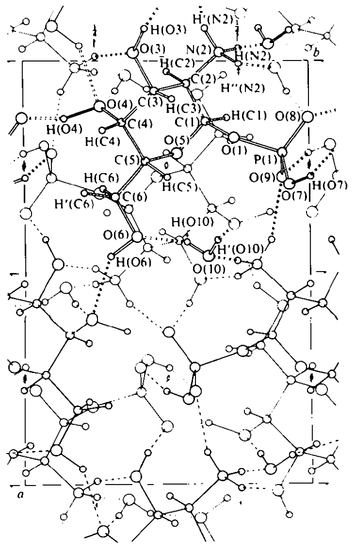


Fig. 3. A *c*-axis view of the crystal packing and hydrogen-bonding scheme in α-D-galactosamine-1-phosphate monohydrate. Note the 15 hydrogen-bonding interactions to each molecule.

Table 3. *Hydrogen bonding in* α-D-*galactosamine*-1-*phosphate monohydrate*

D–H$\cdots A$	Symmetry code	D–H (Å)	$D\cdots A$ (Å)	H$\cdots A$ (Å)	D–H$\cdots A$ (°)
O(10)–H(O10)···O(6)	*a*	0·89 (5)	2·754 (5)	2·01 (6)	169 (6)
O(10)–H′(O10)···O(4)	*e*	0·71 (6)	2·871 (5)	2·25 (6)	147 (7)
O(4)–H(O4)···O(8)	*b*	1·07 (5)	2·614 (4)	1·65 (5)	149 (4)
O(6)–H(O6)···O(4)	*c*	1·02 (4)	2·889 (4)	1·99 (5)	146 (4)
N(2)–H(N2)···O(10)	*d*	0·97 (5)	2·696 (5)	1·73 (5)	170 (4)
N(2)–H′(N2)···O(9)	*d*	0·92 (4)	2·863 (4)	1·99 (4)	160 (4)
N(2)–H″(N2)···O(3)	*f*	1·12 (5)	2·911 (4)	1·80 (5)	169 (4)
O(3)–H(O3)···O(8)	*g*	1·04 (5)	2·653 (4)	1·71 (5)	150 (4)
O(7)–H(O7)···O(9)	*h*	0·94 (5)	2·652 (4)	1·74 (5)	149 (5)

Symmetry code

(*a*) x,y,z

(*b*) $x, 1-y, z$

(*c*) $\frac{1}{2}+x, \frac{1}{2}-y, -z$

(*d*) $\frac{1}{2}+x, \frac{3}{2}-y, -z$

(*e*) $\frac{1}{2}-x, 1-y, z-\frac{1}{2}$

(*f*) $-x, y-\frac{1}{2}, \frac{1}{2}-z$

(*g*) $-x, \frac{1}{2}+y, \frac{1}{2}-z$

(*h*) $\frac{1}{2}-x, 2-y, \frac{1}{2}+z$

phosphate group is engaged in only five hydrogen bonds. The presence of metal ions usually increases the number of hydrogen bonds (~9) to the phosphate by virtue of increasing the amount of water of hydration (Swaminathan & Sundaralingam, 1979). The O(9) atom of the phosphate group is hydrogen bonded to the NH_3^+ group and O(7)—H of a neighboring molecule to form an infinite spiral about the twofold screw axis parallel to the crystallographic *c* axis. The O(7)—H of the phosphate also accepts a hydrogen bond from the ammonium group. The water molecule is not hydrogen bonded to the phosphate group but bridges the O(6) and O(4) atoms of 2_1-related molecules and accepts a hydrogen bond from the ammonium group of a third molecule. The ring O(5) atom and the phosphate ester O(1) atom are not engaged in hydrogen bonding.

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The Structure of Methoin: an Anticonvulsant Drug

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Abstract

$C_{12}H_{14}N_2O_2$, orthorhombic, *Pbca*, $a = 27{\cdot}336\ (24)$, $b = 10{\cdot}002\ (9)$, $c = 8{\cdot}477\ (8)$ Å, $Z = 8$, $D_c = 1{\cdot}249$ Mg m^{-3}, μ(Cu $K\alpha$) = 0·622 mm^{-1}. The crystal used for X-ray analysis was prepared from material purchased from Aldrich Chemical Co., Inc. $R_o = 0{\cdot}078$ for 1310 observed reflections and $R = 0{\cdot}098$ for 1673 measured